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A Targeted-Modification Study of Choline and Geranate (CAGE) Analogues

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Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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Abstract

The use of ionic liquids in pharmaceutical applications, such as in the formulation and delivery of drugs, has garnered significant interest in recent years. One ionic liquid that has shown promise as a drug delivery agent is 1:2 choline and geranate (CAGE), which can improve the transdermal penetration of model drugs and can help stabilise proteins for oral delivery. An important first step in understanding the behaviour of 1:2 CAGE is identifying the underlying structure-property relationships, by studying systems with similar structures. This work presents a targeted-modification study in which three structural features that exist in 1:2 CAGE have been varied in order to understand their effect on the ionic liquid properties. Two cation species and four carboxylic acid species were employed and a total of six 1:2 ionic liquids were synthesised, including 1:2 CAGE. The thermal behaviour of these systems was analysed using differential scanning calorimetry and dynamic mechanical analysis, while their structuring was investigated using several different techniques, the most relevant being X-ray scattering. Almost all of the ionic liquids exhibited lamellar liquid crystalline mesophases, which collapse to an isotropic liquid structure when heated. The stability of these mesophases is heavily influenced by the nature of the species present in the system. Generally, linear, saturated anions led to a more stable liquid crystalline mesophase, while the presence of a hydroxyl group on the cation was found to further stabilise this structure. However, these observations do not hold true for all systems. Some of the ionic liquids in this work show the coexistence of multiple liquid crystalline mesophases within their structure. Often, but not always, these additional mesophases have a lamellar bilayer structure; in some cases, however, their geometry remains undetermined.

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Publications

Below is a list of publications that came as a result of the research presented in this thesis.

- A. Dobre, S. Koutsoukos, F. Philippi, D. Rauber, C. W. M. Kay, O. Palumbo, M. M. Roessler and T. Welton, *Phys. Chem. Chem. Phys.*, 2024, **26**, 8858–8872.
- G. M. Neville, A. Dobre, G. J. Smith, S. Micciulla, N. J. Brooks, T. Arnold, T. Welton and K. J. Edler, *Adv. Funct. Mater.*, 2024, **34**, 2306644.
- S. Koutsoukos, J. Becker, A. Dobre, Z. Fan, F. Othman, F. Philippi, G. J. Smith and T. Welton, *Nat. Rev. Methods Primer*, 2022, **2**, 49.

Contents

1	Introduction	1
1.1	1:2 Choline and Geranate (1:2 CAGE)	3
1.1.1	Structure and classification	3
1.1.2	Pharmaceutical relevance and mechanisms of action	6
1.2	Structure-property relationships in CAGE-like ionic liquids	9
1.2.1	Aims and Objectives	14
1.3	1:2 CAGE: ionic liquid or deep eutectic solvent?	15
1.3.1	Deep Eutectic Solvents (DESs)	16
1.3.2	1:2 CAGE and related systems	19
1.4	X-ray scattering	22
1.5	Liquid Crystals	26
2	1:2 ButylTrimethylAmmonium And OCtanoate (BTMAAOC)	32
2.1	Thermal behaviour	33
2.1.1	Dynamic Mechanical Analysis	36
2.2	Viscosity	43

2.2.1	Dynamic viscosity	43
2.2.2	Oscillating viscosity	45
2.3	Structuring	48
2.3.1	NMR	48
2.3.2	X-ray scattering	50
2.4	Chapter summary	61
3	Choline And OCtanoate (1:2 CAOC)	64
3.1	Thermal behaviour	65
3.1.1	Dynamic Mechanical Analysis	68
3.2	Viscosity	72
3.2.1	Dynamic viscosity	72
3.2.2	Oscillating viscosity	74
3.3	Structuring	77
3.3.1	NMR	77
3.3.2	X-ray scattering	81
3.4	Chapter summary	86
4	1:2 ButylTriMethylAmmonium And GERanate (BTMAAGE)	89
4.1	Thermal behaviour	90
4.1.1	Dynamic Mechanical Analysis	94
4.2	Viscosity	97

4.3	Structuring	101
4.3.1	NMR	101
4.3.2	X-ray scattering	103
4.4	Chapter summary	112
5	1:2 Choline And 2-OCtenoate (CA2OE)	115
5.1	Thermal behaviour	116
5.1.1	Dynamic Mechanical Analysis	120
5.2	Structuring	123
5.2.1	NMR	124
5.2.2	X-ray scattering	125
5.3	Chapter summary	136
6	1:2 Choline And CItronellate (CACI)	139
6.1	Thermal Behaviour	140
6.1.1	Dynamic Mechanical Analysis	142
6.2	Viscosity	146
6.3	Structuring	149
6.3.1	NMR	149
6.3.2	X-ray scattering	150
6.4	Chapter summary	154
7	1:2 Choline And GERanate (1:2 CAGE)	156

7.1	Thermal Behaviour	157
7.1.1	Dynamic Mechanical Analysis	160
7.2	Viscosity	164
7.3	Structuring	167
7.3.1	NMR	167
7.3.2	X-ray scattering	168
7.4	Thermal Decomposition	173
8	Summary and outlook	179
8.1	Future work	185
9	Synthesis and Methods	189
9.1	Purification of Starting Materials	191
9.2	Synthesis of cholinium-based ILs	193
9.3	Synthesis of butyltrimethylammonium-based systems	198
9.4	General experimental procedures	200
9.4.1	General considerations	200
9.4.2	General procedure A: synthesis of cholinium ILs	201
9.4.3	General procedure B: synthesis of 1:1 BTMA ILs	201
9.4.4	General Procedure C: synthesis of 1:2 BTMA ILs	202
9.4.5	Experimental Details	202
9.5	Physicochemical Measurements	211

9.5.1	X-ray Scattering Measurements	211
9.5.2	Polarising Microscopy (PLM)	212
9.5.3	Differential Scanning Calorimetry (DSC)	212
9.5.4	Dynamic Mechanical Analysis (DMA)	212
9.5.5	Thermogravimetric Analysis (TGA)	213
9.5.6	Rheology Measurements	213
9.5.7	Solid-state NMR measurements	214
Bibliography		214
Appendix		226
A Differential scanning calorimetry (DSC) data for 1:2 ILs		227
B DSC data for 1:1 ILs and neat acids		229
C Dynamic viscosity measurements		235
D Isoconversional kinetic analysis of 1:2 BTMAAOC		237

List of Abbreviations

API	Active Pharmaceutical Ingredient
BTMAAGE	Butyltrimethylammonium and Geranate
BTMAAOC	Butyltrimethylammonium and Octanoate
CA2OE	Choline and 2-Octenoate
CACI	Choline and Citronellate
CAGE	Choline and Geranate
CAOC	Choline and Octanoate
DES	Deep Eutectic Solvent
DMA	Dynamic Mechanical Analysis
DSC	Differential Scanning Calorimetry
HBA	Hydrogen Bond Acceptor
HBD	Hydrogen Bond Donor
HPLC	High-Performance Liquid Chromatography
IL	Ionic Liquid
L_α	Fluid lamellar phase
L_β	Lamellar gel phase
LC	Liquid crystal
MAS	Magic angle spinning
MD	Molecular dynamics
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser Effect Spectroscopy
PLM	Polarised-light microscopy
RTIL	Room-temperature ionic liquid
SAXS	Small-angle X-ray scattering

SLE	Solid-liquid equilibrium
SS	Solid-state
TGA	Thermogravimetric analysis
WAXS	Wide-angle X-ray scattering

List of Tables

1.1	Melting point temperatures of the 1:2 ILs in this work and of the corresponding 1:1 salts and carboxylic acids	21
2.1	Best-fit parameters τ_0 , B, T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation	43
2.2	Best-fit parameters η_0 , B and T_0 used to fit viscosity data according to the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD)	44
2.3	Estimated length and area values for the 1:2 BTMAAOC unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.	55
2.4	Temperatures of the liquid crystal to isotropic liquid transitions	61
3.1	Best-fit parameters τ_0 , B, T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 CAOC (top row). For comparison, data is also shown for 1:2 BTMAAOC. .	71
3.2	Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD)	73

3.3	Estimated length and area values for the 1:2 CAOC unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.	85
3.4	Temperatures of the liquid crystal to isotropic liquid transitions	87
4.1	Best-fit parameters τ_0 , B, T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 BTMAAGE (top row). For comparison, data is also shown for the other 1:2 ILs discussed so far.	97
4.2	Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD, Equation 2.8). Highlighted data corresponds to 1:2 BTMAAGE.	100
4.3	Estimated length and area values for the 1:2 BTMAAGE unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.	109
4.4	Temperatures of the liquid crystal to isotropic liquid transitions	112
5.1	Estimated length and area values for the 1:2 CA2OE unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.	132
5.2	Temperatures of the liquid crystal to isotropic liquid transitions	137
6.1	Best-fit parameters τ_0 , B, T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 CACI (top row). For comparison, data is also shown for the other 1:2 ILs discussed so far.	146
6.2	Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD, Equation 2.8)	148

6.3	Temperatures of the liquid crystal to isotropic liquid transitions for 1:2 CACI and previously discussed ILs	154
7.1	Best-fit parameters τ_0 , B, T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 CAGE (top row). For comparison, data is also shown for the other 1:2 ILs discussed so far.	163
7.2	Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD, Equation 2.8)	165
7.3	Estimated length and area values for the 1:2 CAGE unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.	172
7.4	Temperatures of the liquid crystal to isotropic liquid transitions for all ILs in this work	173
7.5	TGA data for the studied 1:2 ILs	174
8.1	Temperatures of the liquid crystal to isotropic liquid transitions for all 1:2 ILs in this work. Above these transition temperatures, the ILs are in the isotropic liquid phase, which is comprised of distinct polar and nonpolar nanodomains. .	182
A.1	DSC data for the 1:2 ILs. T_g is the temperature of the glass transition, T_{cc} is the temperature of the cold crystallisation, T_m is the temperature of the endothermic melting transition and T_{L-L} is the temperature of the liquid crystal to isotropic transition. All temperatures are measured during the heating cycle. The enthalpy values are calculated as the area under the curve. The entropy values are calculated by dividing the enthalpy by the transition temperature (in Kelvin).	228
C.1	Experimental viscosities of the 1:2 ILs. δ is calculated according to Equation C.1	236

D.1	Activation energies E_a calculated using the KAS method for 1:2 BTMAAOC . .	241
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List of Figures

1.1	<i>Top:</i> Scheme showing the general synthesis of a CAGE system. X and Y represent the equivalents of cholinium salt and geranic acid used in the synthesis. The final system is referred to as 'X:Y CAGE'. <i>Bottom:</i> Some of the most common CAGE systems reported in the literature. These structures only showcase the species present in each system, without depicting the actual molecular arrangement or intermolecular interactions.	3
1.2	Structure of 1:2 CAGE showing the complex $[(\text{geranate})_2\text{H}]^-$ anion formed in situ. The cholinium cation is oriented in a way that allows for rapid proton exchange via hydrogen bonding.	4
1.3	Ions commonly used in the synthesis of room-temperature ionic liquids	5
1.4	The three structural features of 1:2 CAGE selected for the targeted-modification study	10
1.5	Structures of the cation and carboxylic acid species used in the synthesis of CAGE-like systems in this work	11
1.6	The 1:2 ILs discussed in this work, in increasing order of structural complexity .	13
1.7	Solid-Liquid Equilibrium (SLE) phase diagram of a theoretical binary mixture. The black line shows the behaviour of an ideal mixture. The red line shows a negative deviation from ideality, characteristic of a deep eutectic. The green and blue lines show positive and asymmetric deviations from ideality, respectively. Reprinted with permission from Reference [57], published by Annual Reviews. .	17

1.8	Two different depictions of the 1:2 CAGE system. <i>Left:</i> as single ionic compound. <i>Right:</i> as a mixture with two components.	20
1.9	Diagram showing the scattering of X-rays by an ordered crystal lattice. Adapted from Reference [77], published by Wiley.	23
1.10	Diagram of a general transmission SAXS setup. A bright ring is obtained on the detector at $q = 4\pi\sin\theta$	24
1.11	Layout of the I22 X-ray scattering beamline at the Diamond Light Source synchrotron facility. Adapted from Reference [78], published by IUCr Journals. . . .	25
1.12	Top: phases present in a thermotropic liquid crystal. Bottom: structures of smectic (Sm) and nematic LC phases. Reproduced from reference [89], published by Elsevier.	27
1.13	The different configurations of a polarised-light microscope and the effect of an anisotropic sample on the polarised light. Reproduced from reference [99], published by Springer International.	29
2.1	1:2 BTMAAOC	33
2.2	DSC traces of 1:2 BTMAAOC with annotated transition temperatures. The heating and cooling rates are $5\text{ }^{\circ}\text{C min}^{-1}$	34
2.3	1:2 BTMAAOC before and after the liquid-crystal-to-isotropic phase transition .	35
2.4	Polarised-light microscope images of 1:2 BTMAAOC taken with $4\times$ magnification. <i>Top:</i> images at $5\text{--}10\text{ }^{\circ}\text{C}$, taken on cooling. When pressing the glass cover slip, the birefringent texture (bright areas) shows liquid-like fluid behaviour, indicating it is associated with a liquid crystalline phase. <i>Bottom:</i> images at $25\text{ }^{\circ}\text{C}$, taken on heating from $5\text{ }^{\circ}\text{C}$. At and above this temperature, the sample is isotropic and shows no birefringence, rendering the images (almost) entirely black.	36

2.5	DMA data for 1:2 BTMAAOC, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.	39
2.6	$\tan \delta$ measured for 1:2 BTMAAOC on cooling. Lines are guides for the eye. . .	39
2.7	$\tan \delta$ measured for 1:2 BTMAAOC on cooling at $f = 1$ and 5 Hz. Only the data corresponding to the thermally activated relaxation is shown. The solid lines are the result of a simultaneous fit for the two frequencies. Before fitting, a linear background subtraction was performed. The data recorded at $f = 10$ Hz could not be included in the fit due to overlap with the LC-isotropic phase transition peak.	42
2.8	Dynamic viscosity data (symbols) for 1:2 BTMAAOC in the isotropic liquid phase. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation (line) with fit parameters shown in Table 2.2.	45
2.9	Complex viscosity of 1:2 BTMAAOC. The liquid crystal phase (blue) shows shear-thinning behaviour, while the isotropic liquid phase (red) shows Newtonian flow behaviour.	47
2.10	Log-log plot of the complex viscosity of liquid crystalline 1:2 BTMAAOC against shear rate. The complex viscosity decreases linearly with increasing shear rate (shear-thinning behaviour).	47
2.11	Oscillating rheometry data for 1:2 BTMAAOC in the liquid crystalline phase . .	48
2.12	^1H - ^1H SS-MAS NOESY NMR of 1:2 BTMAAOC recorded at 20 °C (liquid crystalline phase). Crosspeaks resulting from intramolecular interactions are circled (black dotted lines). The corresponding interactions are indicated using blue highlights and blue dotted lines.	49
2.13	^1H - ^1H SS-MAS NOESY NMR of 1:2 BTMAAOC recorded at 60 °C (isotropic liquid phase)	49
2.14	X-ray scattering data of 1:2 BTMAAOC at various temperatures	52

2.15	Possible structure of liquid crystalline 1:2 BTMAAOC. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 20.3 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner (associated with a complex $[(\text{octanoate})_2\text{H}]^-$ anion), the real system is a dynamic one, in which hydrogen bonds are always breaking and forming.	53
2.16	WAXS pattern of 1:2 BTMAAOC at 15 °C. Inset is a close-up of the region indicated by the red box, covering a q -range of 0.2–1.0 Å ⁻¹	57
2.17	Bulk structure and scattering profile of a general ionic liquid. The scattering profile shows three peaks characteristic of IL structuring. The coloured arrows indicate the interactions / distances associated with each peak. Figure adapted from Reference [84], published by the Royal Society of Chemistry.	59
3.1	1:2 CAOC	64
3.2	DSC traces of 1:2 CAOC with annotated transition temperatures. The heating and cooling rates are 5 °C min ⁻¹	66
3.3	Polarised-light microscope images of 1:2 CAOC, taken on heating. <i>Top</i> : images of the liquid crystalline phase, taken at 15 °C with 4×(left) and 10×(right) magnification. The light areas are indicative of birefringence, a characteristic of liquid crystalline materials. Additionally, when pressed, the birefringent texture shows liquid-like fluid behaviour, indicating it is associated with a liquid crystalline phase. <i>Bottom</i> : images of the isotropic phase, taken at 58 °C (left) and 60 °C (right).	67
3.4	1:2 CAOC before and after the LC-isotropic phase transition	68
3.5	DMA data for 1:2 CAOC, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols)	70

3.6	$\tan \delta$ measured for 1:2 CAOC on cooling	70
3.7	$\tan \delta$ measured for 1:2 CAOC on cooling at $f = 1, 5$, and 10 Hz. Only the data corresponding to the thermally-activated relaxation is shown. The solid lines are the result of a simultaneous fit across the three frequencies. Before fitting, a linear background subtraction was performed.	71
3.8	Dynamic viscosity data (symbols) for 1:2 CAOC in the isotropic phase (shown in orange). The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation (line), with the fit parameters shown in Table 3.2.	73
3.9	Complex viscosity of 1:2 CAOC. The liquid crystal phase (blue) shows shear-thinning behaviour, while the isotropic liquid phase (red) shows Newtonian flow behaviour.	75
3.10	Log-log plot of the complex viscosity of liquid crystalline 1:2 CAOC against shear rate. The complex viscosity decreases linearly with increasing shear rate (shear-thinning behaviour).	75
3.11	Oscillating rheometry data for 1:2 CAOC in the liquid crystalline phase, shown as filled, opaque symbols. For comparison, oscillating rheometry data for the liquid crystalline 1:2 BTMAAOC is also shown as filled symbols with a faded appearance.	76
3.12	Log-log plot of the complex viscosity η^* of liquid crystalline 1:2 CAOC (blue) and 1:2 BTMAAOC (orange) against shear rate. The filled symbols are used to emphasise that the lowest viscosities recorded for 1:2 CAOC (at 50°C , filled blue diamonds) are greater than the highest viscosities recorded for 1:2 BTMAAOC (at 25°C , filled orange triangles) across all measured shear rates.	77
3.13	^1H - ^1H NOESY of neat 1:2 CAOC at 20°C (liquid crystalline phase). Reproduced from reference [15].	78
3.14	^1H - ^1H NOESY of neat 1:2 CAOC at 60°C (isotropic liquid phase). Data collected and analysed by Dr. Mohit Devgan.	78

3.15	Solid state MAS ^1H NMR of 1:2 CAOC at 20 and 60 $^\circ\text{C}$	80
3.16	X-ray scattering data of 1:2 CAOC at various temperatures.	82
3.17	Possible structure of liquid crystalline 1:2 CAOC. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 22.4 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner (associated with a complex $[(\text{octanoate})_2\text{H}]^-$ anion), the real system is a dynamic one, in which hydrogen bonds are always breaking and forming. . . .	83
4.1	1:2 BTMAAGE	90
4.2	DSC traces of 1:2 BTMAAGE with annotated transition temperatures. The heating and cooling rates are 5 $^\circ\text{C min}^{-1}$	90
4.3	Polarised-light microscope images of 1:2 BTMAAGE taken with 4 $\times$ magnification. <i>Top</i> : on cooling to 10 $^\circ\text{C}$ (left) the sample showed large areas of birefringence with a liquid-like behaviour, indicative of a liquid-crystalline phase. On heating to 20 $^\circ\text{C}$ (right) a Maltese cross pattern, associated with a lamellar mesophase, was observed. <i>Bottom</i> : the IL was heated above the temperature of the LC-isotropic phase transition. At 27 $^\circ\text{C}$ the sample is in an isotropic liquid state and shows no birefringence (the image is entirely dark).	92
4.4	1:2 BTMAAGE before and after the liquid-crystal-to-isotropic phase transition .	93
4.5	DMA data for 1:2 BTMAAGE, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye. . . .	95
4.6	$\tan \delta$ measured for 1:2 BTMAAGE on cooling. Lines are guides for the eye. . .	95

4.7	$\tan \delta$ measured for 1:2 BTMAAGE on cooling at $f = 1, 5$ and 10 Hz. Only data corresponding to the thermally activated relaxation is shown. Solid lines are the result of a simultaneous fit for the three frequencies. Before fitting, a linear background subtraction was performed.	96
4.8	Dynamic viscosity data for the studied 1:2 ILs. 1:2 BTMAAGE (shown in green) is an isotropic liquid over the entire studied temperature range. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation, with fit parameters shown in Table 4.2.	98
4.9	Solid state MAS ^1H NMR of 1:2 BTMAAGE at 5 and 50 $^{\circ}\text{C}$	102
4.10	^1H - ^1H NOESY of neat 1:2 BTMAAGE at 5 $^{\circ}\text{C}$ (liquid crystalline phase)	104
4.11	^1H - ^1H NOESY of neat 1:2 BTMAAGE at 50 $^{\circ}\text{C}$ (isotropic liquid phase)	104
4.12	X-ray scattering data of 1:2 BTMAAGE at various temperatures. <i>Note:</i> two different y-scales are used for the SAXS graphs. One scale is used for the 5 – 25 $^{\circ}\text{C}$ graphs (determined by the height of the peak at $0.32 \text{ \AA}^{-1}$) and another is used for the 35 – 55 $^{\circ}\text{C}$ graphs (determined by the feature at $0.10 \text{ \AA}^{-1}$).	106
4.13	Possible structure of liquid crystalline 1:2 BTMAAGE. The molecules are arranged in lamellar bilayers with an approximate d -spacing of $19.6 \text{ \AA}$. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner (associated with a complex $[(\text{geranate})_2\text{H}]^-$ anion), the real system is a dynamic one, in which hydrogen bonds are always breaking and forming.	107
4.14	Selected WAXS data showing the variation of Peak A with temperature	110
4.15	Selected SAXS data showing the variation of Peak B with temperature	110
5.1	1:2 CA2OE	115

5.2	DSC traces of 1:2 CA2OE with annotated transition temperatures. The heating and cooling rates are 5 °C min ⁻¹	116
5.3	Polarised-light microscope images of 1:2 CA2OE taken with 4× magnification. The sample was heated from 16 °C (top left) to 25 °C (top right), then cooled back down to 16 °C (bottom right). The same sample was then further cooled to 5 °C (bottom left).	118
5.4	Samples of 1:2 CA2OE at temperatures above and below the crystallisation transition temperature	119
5.5	DMA data for 1:2 CA2OE, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols).	122
5.6	tan δ measured for 1:2 CA2OE on cooling.	122
5.7	Solid state MAS ¹ H NMR of 1:2 CA2OE at 5 and 50 °C	125
5.8	¹ H- ¹ H NOESY of neat 1:2 CA2OE at 5 °C (liquid crystalline phase). Crosspeaks resulting from intramolecular interactions are circles (black dotted lines). The corresponding interactions are indicated using blue highlights and blue dotted lines.	126
5.9	¹ H- ¹ H NOESY of neat 1:2 CA2OE at 50 °C (isotropic liquid phase)	126
5.10	X-ray scattering data of 1:2 CA2OE at various temperatures.	127
5.11	X-ray scattering profiles of 1:2 CA2OE at 5 °C	128

5.12	Possible structure of the main LC phase of 1:2 CA2OE. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 20.9 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner, in reality the system is a dynamic one, in which hydrogen bonds are always breaking and forming and protons are exchanged between different species.	131
5.13	Selected SAXS data showing the variation of Peaks A and B with temperature .	134
5.14	Selected WAXS data showing the variation of Peaks C and D with temperature	134
6.1	1:2 CACI	139
6.2	DSC traces of 1:2 CACI with annotated transition temperatures. The heating and cooling rates are 5 °C min ⁻¹	140
6.3	Samples of 1:2 CACI at temperatures above and below the crystallisation transition temperature	141
6.4	Microscope images of 1:2 CACI at room temperature. The sample is not birefringent — the image taken using polarised light is entirely dark.	142
6.5	DMA data for 1:2 CACI, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.	144
6.6	$\tan \delta$ measured for 1:2 CACI on cooling. Lines are guides for the eye.	144
6.7	$\tan \delta$ measured for 1:2 CACI on cooling at $f = 1, 5$ and 10 Hz. Only the data corresponding to the thermally activated relaxation is shown. The solid lines are the result of a simultaneous fit for the three frequencies. Before fitting, a linear background subtraction was performed.	145

6.8	Dynamic viscosity data for the studied 1:2 ILs. 1:2 CACI (shown in red) is an isotropic liquid over the entire studied temperature range. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation, with fit parameters shown in Table 6.2.	147
6.9	Solid state MAS ^1H NMR of 1:2 CACI at 5 and 50 $^\circ\text{C}$	149
6.10	^1H - ^1H NOESY of neat 1:2 CACI at 5 $^\circ\text{C}$	151
6.11	^1H - ^1H NOESY of neat 1:2 CACI at 50 $^\circ\text{C}$	151
6.12	X-ray scattering data of 1:2 CACI at various temperatures.	152
7.1	1:2 CAGE	157
7.2	DSC traces of 1:2 CAGE with annotated transition temperatures. The heating and cooling rates are 5 $^\circ\text{C min}^{-1}$	157
7.3	Samples of 1:2 CAGE at temperatures above and below the crystallisation transition temperature	158
7.4	Microscope images of 1:2 CAGE at room temperature using $4\times$ magnification. The sample is not birefringent — the image taken using polarised light is entirely dark.	159
7.5	DMA data for 1:2 CAGE, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.	161
7.6	$\tan \delta$ measured for 1:2 CAGE on cooling. Lines are guides for the eye.	161
7.7	$\tan \delta$ measured for 1:2 CAGE on cooling at $f = 1, 5$ and 10 Hz. Only the data corresponding to the thermally activated relaxation is shown. The solid lines are the result of a simultaneous fit for the three frequencies. Before fitting, a linear background subtraction was performed.	163

7.8	Dynamic viscosity data for the studied 1:2 ILs. 1:2 CAGE (shown in grey) is an isotropic liquid over the entire studied temperature range. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation, with fit parameters shown in Table 7.2.	165
7.9	^1H - ^1H NOESY of neat 1:2 CAGE at 20 °C. Reproduced from reference [15]. . . .	167
7.10	Solid state MAS ^1H NMR of 1:2 CAGE at 20 °C. Reproduced from reference [15].	168
7.11	X-ray scattering data of 1:2 CAGE at various temperatures.	169
7.12	Possible structure of the main LC phase of 1:2 CAGE. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 22.4 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner, in reality the system is a dynamic one, in which hydrogen bonds are always breaking and forming and protons are exchanged between different species.	171
7.13	TGA curves for all six 1:2 systems discussed in this work. Data was collected using a heating rate of 5 °C min ⁻¹	174
7.14	Isothermal TGA data for 1:2 BTMAAOC	176
7.15	Analysis of $t_{0.99}$ for the isothermal decomposition of 1:2 BTMAAOC	177
7.16	Isothermal TGA data for 1:2 CAOC	177
8.1	Structures of the 1:2 ILs discussed in this work	180
8.2	The 1:2 ILs discussed in this work, the structural features (SFs) they contain and an overview of their liquid crystalline mesophases	181
8.3	Carboxylic acid species that could be used in future for the synthesis of 1:2 CAGE-like ILs	186

9.1	Geranic acid at room temperature.	192
9.2	Crystal structure of geranic acid, recrystallised from hexane, obtained by single-crystal X-ray crystallography. Two molecules are shown. Because a different purification method was used compared to the literature (recrystallisation from hexane, rather than acetone) the crystal structure was recorded in order to confirm that this afforded the E-isomer of 3,7-dimethylocta-2,6-dienoic acid (i.e. geranic acid).	193
9.3	1:2 CAGE dried under vacuum at 40 °C.	197
9.4	1:2 CAGE prepared without heating.	197
B.1	DSC traces of geranic acid, collected using a heating and cooling rate of 5 °C/min	229
B.2	DSC traces of citronellic acid, collected using a heating and cooling rate of 5 °C/min	230
B.3	DSC traces of octanoic acid, collected using a heating and cooling rate of 5 °C/min	230
B.4	DSC traces of 2-octenoic acid, collected using a heating and cooling rate of 5 °C/min	231
B.5	DSC traces of 1:1 choline and octanoate (CAOC), collected using a heating and cooling rate of 5 °C/min	231
B.6	DSC traces of 1:1 choline and 2-octenoate (CA2OE), collected using a heating and cooling rate of 5 °C/min	232
B.7	DSC traces of 1:1 butyltrimethylammonium and octenoate (BTMAAOC), collected using a heating and cooling rate of 5 °C/min	232
B.8	DSC traces of 1:1 butyltrimethylammonium and geranate (BTMAAGE), collected using a heating and cooling rate of 5 °C/min	233
B.9	DSC traces of 1:1 choline and citronellate (CACI), collected using a heating and cooling rate of 5 °C/min	233

B.10 DSC traces of 1:1 choline and geranate (CAGE), collected using a heating and cooling rate of 5 °C/min	234
D.1 Kissinger-Akahira-Sunose plot for 1:2 BTMAAOC. Conversion values are between 0.05 and 0.95, with a step of 0.05. The heating rates are 2.5, 5, 10, and 15 °C min ⁻¹	240
D.2 Variation of the activation energy E_α (KAS method) with the extent of conversion α for 1:2 BTMAAOC	241

Chapter 1

Introduction

The pharmaceutical industry is one of the largest in the world, having an estimated value of 1.6 trillion USD in 2023.¹

One of the main research topics in this field is drug formulation and delivery, which aims to improve the way drugs are administered and enhance their bioavailability and stability.²⁻⁴ Bioavailability refers to how much of the administered active pharmaceutical ingredient (API) is absorbed by the body;⁵ this depends on the structure and properties of the API, as well as the route of administration. Currently, common drug delivery methods include oral, topical, and intravenous delivery, each having its own advantages and disadvantages. While intravenous delivery is considered to be the most efficient, with a bioavailability of 100%,⁶ this method is often painful and uncomfortable as it relies on the use of needles. Moreover, it usually requires the help of a specialist medical professional or a carer, as self-administering an intravenous injection is difficult and not an option for many. These issues are all amplified in situations where drugs need to be administered regularly in this manner, such as in the case of type 1 diabetics. Solutions include the use of devices such as insulin pumps, but the level of comfort they provide is still far inferior to that of a possible oral or topical alternative.

Oral delivery involves formulating the API into a tablet, capsule or syrup, meant to be ingested. Topical delivery relies on creams, gels or patches containing the API, which are applied on and absorbed through the skin. These methods are more convenient and easy to administer and the formulations do not usually require specialised storage conditions (although there are some

exceptions, particularly for topical treatments which may require refrigeration). The main issue with both topical and oral formulations is the fact that the API has to overcome a biological barrier in order to be absorbed into the bloodstream. For oral drug delivery, the barrier can be the buccal or intestinal mucosa, while for transdermal delivery the barrier is the skin, particularly the top layer of skin, the stratum corneum.^{7,8} Recently, a system referred to as choline and geranate (CAGE) was found to aid in the transdermal and oral delivery of pharmaceutically relevant molecules.^{9–11} Before discussing the potential use of CAGE compounds as drug delivery agents (Section 1.1.2) it is important to first understand the exactly what the terms 'choline and geranate' refer to.

Choline And GERanate (CAGE) is the name given to a family of systems comprised of cholinium cations, geranate anions and/or geranic acid molecules, in varying ratios. Usually, these systems are synthesised by mixing together a cholinium salt (usually bicarbonate) and geranic acid in various proportions.^{9,12} Depending on the ratio of these two starting materials, different varieties of the CAGE system can be obtained. The naming convention that is most common in the literature is to specify the ratio of cholinium salt to geranic acid that was employed in the synthesis of such a system, either before or after the abbreviation 'CAGE'. For example, a system that was synthesised by reacting 1 equivalent of cholinium bicarbonate with 2 equivalents of geranic acid can be referred to as '1:2 CAGE' or 'CAGE 1:2'. Both versions can be seen in the literature; in this work, the former convention (ratio, followed by abbreviation) will be used for all CAGE and CAGE-like systems. The term 'CAGE' will be used to refer to choline-and-geranate systems in a general sense, when specifying a ratio is not necessary. A general reaction scheme showcasing the synthesis of CAGE systems is shown in Figure 1.1. X and Y represent the equivalents of cholinium bicarbonate and geranic acid used in the synthesis, with the final system denoted as 'X:Y CAGE'. No structure is shown for this generic CAGE system because the species present in the system at the end of the synthesis depend on the ratio of the starting materials. Broadly, a neutralisation reaction is expected to occur between the anion of the cholinium salt (a base) and the geranic acid, until the limiting reagent is used up; this results in the formation of geranate anions (and residual water and carbon dioxide). Excess cholinium bicarbonate or excess geranic acid can remain in the system if the ratio is not 1:1. However, these do not necessarily exist as standalone, neutral species; as will be shown throughout this work, CAGE and CAGE-like systems can exhibit complex hydrogen-bonding networks. Several different CAGE systems have been reported in the literature; some common examples are given

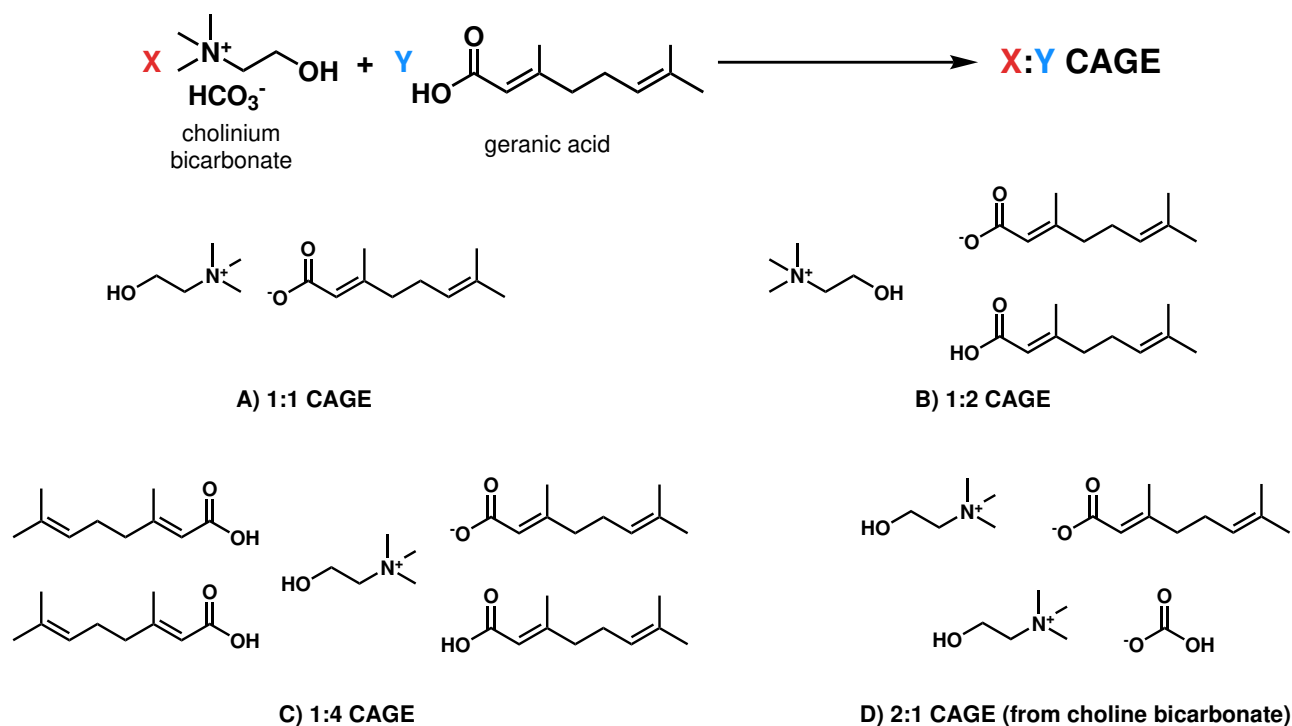


Figure 1.1. *Top:* Scheme showing the general synthesis of a CAGE system. X and Y represent the equivalents of cholinium salt and geranic acid used in the synthesis. The final system is referred to as 'X:Y CAGE'. *Bottom:* Some of the most common CAGE systems reported in the literature. These structures only showcase the species present in each system, without depicting the actual molecular arrangement or intermolecular interactions.

in Figure 1.1.^{9,12} These are only meant to show the species present in each system, without necessarily describing the intermolecular interactions that occur between them.

1.1 1:2 Choline and Geranate (1:2 CAGE)

1.1.1 Structure and classification

The most widely studied CAGE system, and the one that forms the basis of the present work, is 1:2 CAGE, which is usually synthesised using a 1:2 ratio of cholinium bicarbonate to geranic acid (discussed in more detail in Chapter 9) and is nominally comprised of a cholinium cation, a geranate anion, and a geranic acid molecule. In reality, however, the acidic proton is thought to be shared between two geranate moieties via hydrogen-bonding, with the negative charge delocalised across the entire headgroup, as shown in Figure 1.2.

This is based on the work of Mann *et al.*, who have previously used solid-state ^1H NMR and mass

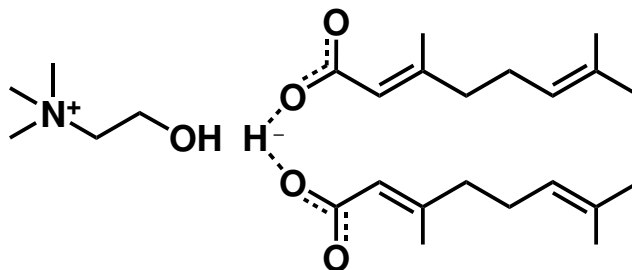


Figure 1.2. Structure of 1:2 CAGE showing the complex $[(\text{geranate})_2\text{H}]^-$ anion formed in situ.

The cholinium cation is oriented in a way that allows for rapid proton exchange via hydrogen bonding.

spectrometry to investigate the nature of the species present in CAGE-Oct, an analogue of 1:2 CAGE (an IL with a similar structure and composition). CAGE-Oct was synthesised by mixing octanoic acid with 1:1 CAGE in equimolar proportions. NMR and mass spectrometry studies showed no evidence for the existence of free acid in the system. Instead, a statistical distribution of anions was observed, with $[(\text{geranate})\text{H}(\text{octanoate})]^-$, $[(\text{geranate})_2\text{H}]^-$, and $[(\text{octanoate})_2\text{H}]^-$ anions existing in a roughly 2:1:1 ratio. Despite this, the geranate, octanoate and cholinium molecules each showed a single set of proton NMR resonances, indicating that rapid anion metathesis leads to an averaging of the proton NMR chemical shifts.¹³

An additional finding by Mann *et al.* concerns the interaction of the complex anions with the cholinium cation. The ^1H NMR of CAGE-Oct showed a single peak corresponding to the -COOH and -OH protons, at 9.5 ppm (the average of the expected values for the individual -COOH and -OH resonances). This indicates that the anions form hydrogen bonded clusters with the cholinium cation, in which rapid proton exchange (on the NMR timescale) occurs between the hydroxyl group of the cholinium cation and the acidic proton of the anion species.¹³ This feature (a single average resonance for the -COOH/-OH protons) has also been seen in the ^1H NMR spectra of 1:2 CAGE and other structurally similar systems, indicating that hydrogen-bonding interactions and rapid proton exchange are present.^{14,15}

Applying these findings to the 1:2 CAGE system, the structure shown in Figure 1.2 emerges as a real-life depiction of the molecular arrangement and interactions present in 1:2 CAGE. The geranic acid molecule does not exist as free acid, but instead becomes part of a complex $[(\text{geranate})_2\text{H}]^-$ anion, in which one proton is shared between two geranate moieties and the negative charge is delocalised across the entire headgroup. The cholinium cation is oriented with the hydroxyl group proximal to the anion, which allows the hydrogen-bonding interactions

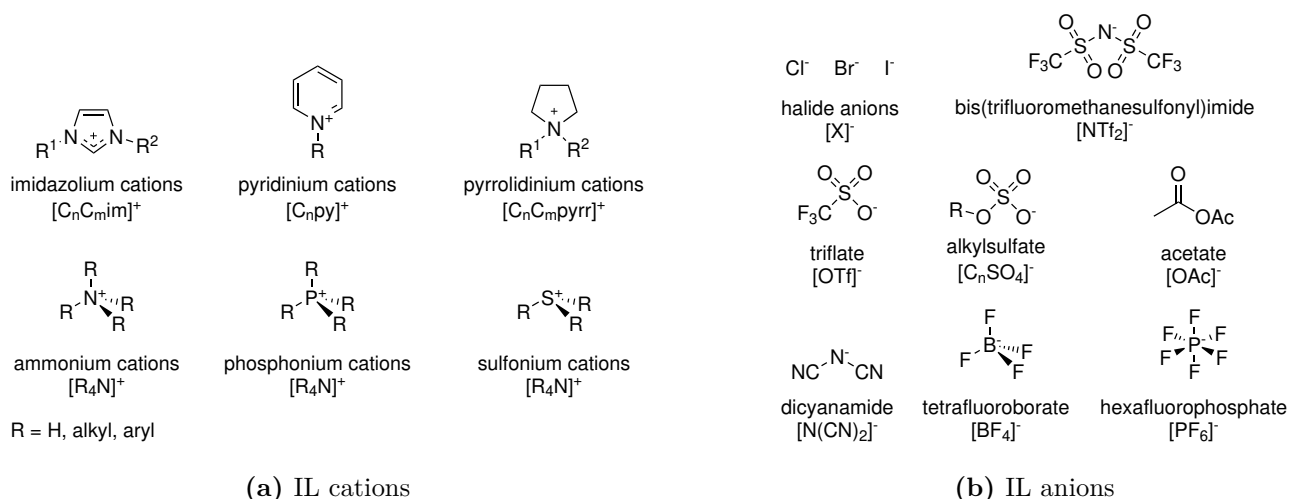


Figure 1.3. Ions commonly used in the synthesis of room-temperature ionic liquids

and rapid proton exchange to occur.

Based on the literature findings discussed so far, 1:2 CAGE is thought to consist only of ionic species, as depicted in Figure 1.2 (showing no free acid), meaning that it can be classified as an ionic liquid. The simplest definition of ionic liquids (ILs) is that they are liquids composed entirely of ions.^{16,17} Because of the wide variety of systems that can be described this way, there have been numerous discussions within the field that have attempted to redefine ILs in a stricter way, such as the often-cited constraint that ILs must have melting points around of below 100 °C. This is intended to differentiate ILs from molten salts, but the choice of temperature is arbitrary and has no real scientific basis; at their core, both ILs and molten salts are simply salts in their liquid state.^{17,18} Still, this convention arose out of practicality, as salts with low melting points are easier to synthesise and handle and are more likely to have a wider range of applications. Nowadays, most of the research on ILs deals with a sub-class of ILs which melt at or around room temperature and which are aptly referred to as room temperature ionic liquids (RTILs).^{16,19} The low melting points of these systems are achieved by the use of large, asymmetric ions — some commonly used ions are shown in Figure 1.3.

Considering the 1:2 CAGE system, its constituent ions are an ammonium cation, which has been used in RTILs,²⁰ and a large [(geranate)₂H]⁻ anion, with a diffuse negative charge. As 1:2 CAGE is entirely composed of ions and is liquid at room temperature, it can be classified as a room temperature ionic liquid and will be referred to as an IL throughout this work. Many publications have also referred to 1:2 CAGE as an ionic liquid, although there is some debate in

the literature as to whether 1:2 CAGE should be classified as a deep eutectic solvent (DES).²¹ This is discussed in more detail in Section 1.3, which attempts to define deep eutectic solvents, identify the differences between ILs and DESs, and categorise each of the CAGE-like systems that will be presented in this work as an IL, a DES, or both.

1.1.2 Pharmaceutical relevance and mechanisms of action

1:2 CAGE was first reported on by Zakrewsky *et al.* in 2014, in a publication investigating the potential use of ILs and DESs for the treatment of skin infections.⁹ Out of the 12 different systems studied by Zakrewsky *et al.*, 1:2 CAGE emerged as the most promising one, with good antimicrobial activity, low cytotoxicity, and the ability to disrupt bacterial biofilms and enhance the skin permeation of a model antibiotic. It also showed a reduced potential for causing skin irritation compared to the individual starting materials, suggesting that the behaviour of the 1:2 system is more complex than that of a simple mixture. These findings sparked an interest in the 1:2 CAGE system with numerous studies on its potential use as a drug delivery agent being published since 2014. In vitro studies showed that 1:2 CAGE can be used to increase the transdermal transport of macromolecules, such as large proteins and polysaccharides.^{10,22} In vivo, 1:2 CAGE was used to aid in the oral and transdermal delivery of pharmaceutically relevant molecules and was shown to improve the stability of insulin when administered as part of a CAGE-insulin formulation.^{10,11,23}

The mechanism by which 1:2 CAGE improves the transdermal permeation of drugs has not been fully described, but a leading theory is that 1:2 CAGE causes lipid extraction and lipid fluidization, both of which are behaviours commonly observed for chemical permeation enhancers.^{22,24,25} The main barrier in the transdermal delivery of drugs is the top layer of skin, the stratum corneum, which is made up of keratin-based cells dispersed amongst a lipid matrix.²⁶ The efficacy of transdermal delivery is often dependent on the rate of diffusion across the stratum corneum. Mitragotri *et al.* used Fourier Transform Infrared (FTIR) spectroscopy to show that 1:2 CAGE leads to a decrease in the amount of lipid matter present in the stratum corneum of a porcine skin sample. The removed lipids were replaced with a CAGE-water mixture, disrupting the skin barrier and leading to a faster diffusion of the model solute across this membrane.^{22,27} FTIR spectroscopy also showed a lipid fluidization effect, in which 1:2 CAGE is thought to permeate the lipid bilayer and decrease the strength of the intermolecular interac-

tions.^{25,27} Additionally, a study looking at several CAGE-like ILs and DESs showed that these systems have a lower irritation potential than conventional permeation enhancers.²⁵

1:2 CAGE has also been used as part of more complex formulations: Vadiya *et al.* and Peng *et al.* used mucoadhesive gel patches (formulated using inactive ingredients, such as chitosan) in the oral delivery of CAGE-insulin mixtures, with 1:2 CAGE acting as a permeation enhancer.^{28,29} Additionally, because 1:2 CAGE has some intrinsic antiseptic and antibacterial properties,^{12,30,31} it has also been employed as an active ingredient. Ko *et al.* have reported the formulation of a CAGE-based gel used in a clinical setting for the treatment of rosacea (a skin condition),³² while Shevachman *et al.* have formulated a 'skin protectant' (akin to a hand sanitizer) in which the active ingredient is thought to be a choline and geranate mixture (of unspecified ratio).³³

To better understand the root of its antibacterial properties, Greene *et al.* used molecular modelling to investigate the interactions between 1:2 CAGE and a model lipid membrane.³¹ The simulations showed that the geranate/geranic acid species insert into the membrane, while the cholinium cation remained outside of the bilayer, in the adjacent water layer. The geranate anions were found to insert into the membrane in a fixed position, parallel to the existing lipids; geranic acid, on the other hand, was able to move between the two leaves that make up the bilayer and, over time, permeate the entire membrane. Greene *et al.* suggest that this insertion mechanism leads to membrane thinning and, subsequently, cell death.³¹

These findings are similar to those of Neville *et al.*, who used neutron reflectivity to investigate the interactions between a lipid bilayer and two different ionic liquids: 1:2 CAGE and 1:2 choline and octanoate (synthesised using two equivalents of octanoic acid).³⁴ They found that the constituents of 1:2 CAGE inserted into the bilayer in a 1:1 ratio (cholinium cation to geranate anion), occupying the space between the existing lipids. The presence of geranate anions in the hydrophobic region caused a disruption in the packing of the alkyl tails, but did not have a negative impact on the integrity of the bilayer. 1:2 Choline and octanoate also inserted into the bilayer with a 1:1 cation to anion ratio, but did so via an extraction mechanism, with its constituents *replacing* existing lipid molecules.³⁴ A separate study showed that 1:2 choline and octanoate can improve the transdermal penetration of drugs almost as much as 1:2 CAGE, particularly for hydrophobic molecules.³⁵ These findings indicate that while CAGE-like systems may show similar results when used as permeation enhancers, the underlying mechanisms, and

therefore the possible side-effects, may vary significantly with structure.

Systems with similar compositions and/or structures as 1:2 CAGE have also been reported in the literature. Generally, these are also formally comprised of an ammonium cation, a carboxylate anion and a carboxylic acid molecule (usually, but not always, with the same structure as the anion). In the article that introduces 1:2 CAGE, Zakrewsky *et al.* discuss some structurally similar compounds, including choline hexanoate, choline oleate and choline malonate, the latter using a single equivalent of a dicarboxylic acid, which is partially deprotonated.⁹ The transdermal delivery potential of these systems varied greatly, with choline hexanoate in particular having a negative effect (reduced permeation). Choline oleate showed a somewhat targeted effect, increasing the absorption of the drug primarily into the deep layers of skin.⁹

In another study, Tanner *et al.* investigated the transdermal transport ability of several CAGE-like systems, in which the cation and anion were varied independently from each other (i.e. cation derivatives were always paired with geranic acid, while anion derivatives were always paired with cholinium).³⁵ The cation variations involved lengthening the alkyl chains, while the carboxylic acids used in the synthesis varied from ones that are structurally similar to geranic acid, such as citronellic acid and decanoic acid, to ones that are significantly different, such as salicylic acid — an aromatic acid — and glycolic acid — an alpha-hydroxy acid. Again, the delivery potential of the different systems varied with structure, with larger, bulkier ions leading to an improved performance. Increased cation-anion interactions (measured as number of crosspeaks in NOESY NMR spectra) were found to correlate with a weaker ability to deliver the model drug across the skin membrane. The exact mechanism behind this effect is unknown, but is thought to rely on the interaction of the geranate anion with the membrane. Tanner *et al.* have put forward the hypothesis that strong anion-cation interactions may 'trap' the anion and therefore reduce the extent to which it interacts with the skin barrier.³⁵ When it comes to the antibacterial properties of CAGE-like systems, Chism *et al.* showed that the length of the anion/acid chain has a significant effect on this property. Longer chains (8–12 carbons) had the strongest antibacterial effect, as did systems with a 1:2 ratio (compared to the equivalent equimolar system).³⁶ The effect of using different cholinium to geranic acid ratios on the transdermal delivery ability of CAGE systems has also been reported on in the literature. Tanner *et al.* have investigated how CAGE systems with different ratios perform

in delivering insulin into skin. Compared to a saline solution, only systems with an excess of geranic acid (1:2 CAGE and 1:4 CAGE) showed an increase in the amount of insulin deposited into the skin; the other two systems (1:1 CAGE and 2:1 CAGE) did not show any significant permeation enhancement.²⁷ More recently, Albadawi *et al.* have focused on the 1:1 CAGE ionic liquid, which is comprised of a cholinium cation and a geranate anion (essentially a cholinium geranate salt). They have shown that 1:1 CAGE has potential uses in the oncological field, either directly as an anticancer active ingredient or as a delivery aid for other therapeutics.³⁷

1.2 Structure-property relationships in CAGE-like ionic liquids

All of the publications discussed so far make a compelling case for the study of 1:2 CAGE, as this system appears to be an extremely promising candidate for use in a variety of pharmaceutical applications. The majority of available publications have focused on the pharmaceutically relevant effects of 1:2 CAGE, such as its transdermal transport and antibacterial properties, and on the possible underlying mechanisms. Far fewer have attempted to investigate the physicochemical properties of 1:2 CAGE or the link between these properties and the structure of the species present in the system.^{13,14,35}

As mentioned previously, 1:2 CAGE is an ionic liquid, whose properties are highly dependent on the structure of its constituent species. This is an important feature of all ionic liquid systems and has earned them the title of 'designer solvents', which refers to the fact that it is possible to 'design' an ionic liquid with specific properties simply by choosing appropriate cation and anion species.³⁸ As a result, understanding the structure-property relationships (SPR) of ionic liquids is crucial for the development of new systems, with quantitative structure-property relationship studies becoming increasingly common.^{39,40} In order to facilitate the use of 1:2 CAGE and CAGE-like systems in an industrial setting, it is necessary to first understand how their behaviour changes with structure and how the structure-property relationships can be exploited to design CAGE-like systems with properties tailored for specific applications.

This work aims to provide an understanding of the structure-property relationships that govern the behaviour of 1:2 CAGE and of other structurally related systems. Six different ionic liquids, including 1:2 CAGE, were synthesised and their physicochemical and structural properties

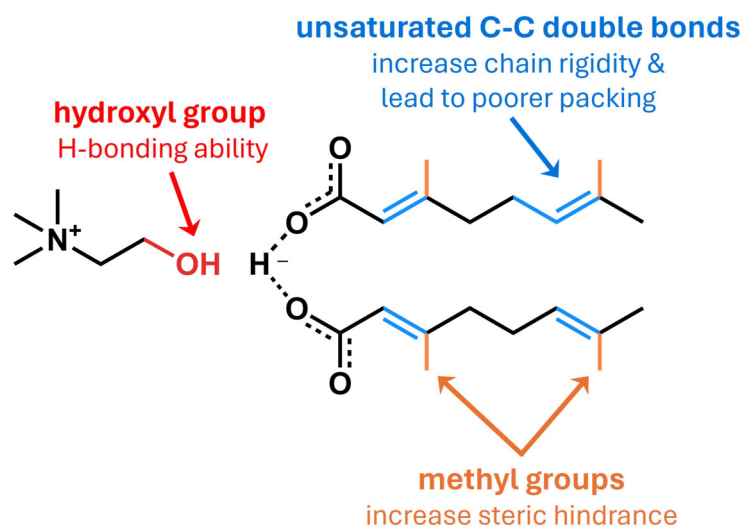


Figure 1.4. The three structural features of 1:2 CAGE selected for the targeted-modification study were analysed and compared. The structures of these CAGE-like systems (also referred to as CAGE analogues throughout this work) were chosen using a systematic targeted modification approach. First, three main structural features of 1:2 CAGE were identified, as indicated in Figure 1.4.

The first feature is the hydroxyl group of the cholinium cation, highlighted in red in Figure 1.4. This confers hydrogen-bonding ability to the cation and allows it to interact with the anion species not just through electrostatic interactions, but also through the formation of a hydrogen bond between the hydroxyl group and the headgroup of the complex anion. Hydrogen bonding in ionic liquids is a complex phenomenon that has been extensively studied.^{41–43} Hydrogen bonds can significantly influence the properties and behaviours of ionic liquids, including their ability to solvate hydrogen-bonding molecules and their interactions with water.^{44–47} Additionally, hydrogen bonds are often a key factor in self-assembly and aggregation processes, resulting in the formation of structures with large-scale ordering, such as liquid crystals.^{48–51}

The second feature, shown in orange in Figure 1.4, is the presence of branching methyl groups in the alkyl chain of the geranate anions. These are thought to increase the steric hindrance, causing poorer packing of the alkyl tails and a greater level of disorder. The third and final feature is the presence of unsaturated carbon-carbon double bonds in the anion alkyl chains, highlighted in blue in Figure 1.4. Double bonds increase chain rigidity and further contribute to the poor packing of the alkyl tails. Drawing a parallel between the structure of 1:2 CAGE and that of the lipids found in the skin barrier, the cation and negatively charged moiety of the

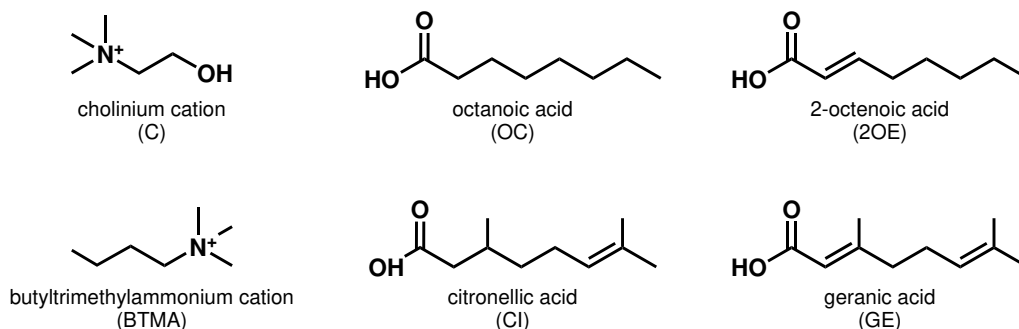


Figure 1.5. Structures of the cation and carboxylic acid species used in the synthesis of CAGE-like systems in this work

anion are equivalent to a polar headgroup, while the geranate chains are equivalent to the long alkyl chains of the lipids. For lipids, the presence of branching groups and C-C double bonds has been shown to lead to poorer packing of the lipid tails and thus lead to a more disordered, less structured system.^{52,53} Based on this, it is expected that removing the branching methyl groups and/or the double bonds will lead to more ordered systems. This idea is supported by the work of Mann *et al.*, who reported the synthesis of a CAGE-like ionic liquid using one equivalent of geranic acid and one equivalent of octanoic acid.¹³ Octanoic acid is a linear, saturated carboxylic acid, with an alkyl chain that is the same length as that of geranic acid (eight carbon atoms). Mann *et al.* showed that replacing just one equivalent of geranic acid with octanoic acid causes the resulting IL to have a liquid crystalline structure, in which the carboxylic acid tails pack into lamellar bilayers,¹³ similar to the structure of the lipid matrix found in the stratum corneum of skin.²⁶

To investigate the effect that the cholinium hydroxyl group (and the resulting hydrogen-bonding interactions) has on the properties of 1:2 CAGE, analogues of 1:2 CAGE were synthesised where the cholinium cation was replaced by a butyltrimethylammonium (BTMA) cation. BTMA is an ammonium cation with the same shape as cholinium (both cations are shown in Figure 1.5) with the only significant difference between the two being that the hydroxyl group is not present in BTMA, where it has been replaced with an alkyl chain.

To investigate how the branching methyl groups and double bonds present in the alkyl chain of the anion species affect the IL properties, analogues of 1:2 CAGE were synthesised using different carboxylic acids. In addition to geranic acid, three other acids were chosen, all of which contain eight carbon atoms in their alkyl chain backbone (the same as geranic acid). The structures of all cation and acid species used in this work are shown in Figure 1.5. The

simplest acid is octanoic acid, which is linear and unsaturated, and is expected to result in ionic liquids with the highest degree of ordering. Taking this as a baseline, the structures of the other acids were chosen such that the two structural features are gradually introduced into the ionic liquid systems. The next acid in terms of structural complexity is 2-octenoic acid, which contains a double bond in the C2-C3 position of the alkyl chain, but no branching methyl groups. The branching feature is then introduced in citronellic acid, which contains two branching methyl groups, on carbon atoms C3 and C7 (the same as for geranic acid). The alkyl chain of citronellic acid also contains a double bond (C6-C7). Finally, geranic acid is the most structurally complex, containing an additional double bond (compared to citronellic acid) in the C6-C7 position.

The two cations (cholinium and BTMA) and the four acid species described above were used to synthesise six different CAGE-like systems, all using a 1:2 ratio of cation salt to carboxylic acid. The structures of these systems, in increasing order of complexity, are given in Figure 1.6. The short name of each system was constructed following the example of 'CAGE', which was first introduced by Zakrewsky *et al.* in 2016.³⁰ 'CAGE' stands for 'Choline And GERanate' and is made up of the first letters of each word, except for the anion species, where it takes the first two letters.³⁰ For the systems described in this work, the same format was used, with two modifications: the butyltrimethylammonium cation was shortened as 'BTMA' and the 2-octenoate anion was abbreviated as '2OE' to avoid confusion with the octanoate anion (abbreviated as 'OC'). Figure 1.6 includes both the full name and the abbreviation for each CAGE-like system; the individual abbreviations for each cation and acid species are also shown in Figure 1.5.

In all of the 1:2 systems in this work the anion and acid species are thought to form a complex anion with the structure $[(\text{carboxylate})_2\text{H}]^-$, as shown in Figure 1.6. rather than individual carboxylic acid and carboxylate species. This is based on the work of Mann *et al.*, which was discussed near the beginning of this chapter,¹³ and is supported by solid-state NMR spectra, which will be shown in subsequent chapters. Briefly, for the 1:2 systems discussed in this work, the NMR spectra show a single peak corresponding to the acidic proton, with a chemical shift that is higher than would be expected for the free acid. This downfield shift is thought to be due to the fact that the proton is more deshielded than it would be in the neat acid, as a consequence of being shared between two carboxylate moieties. Based on this, 1:2 CAGE

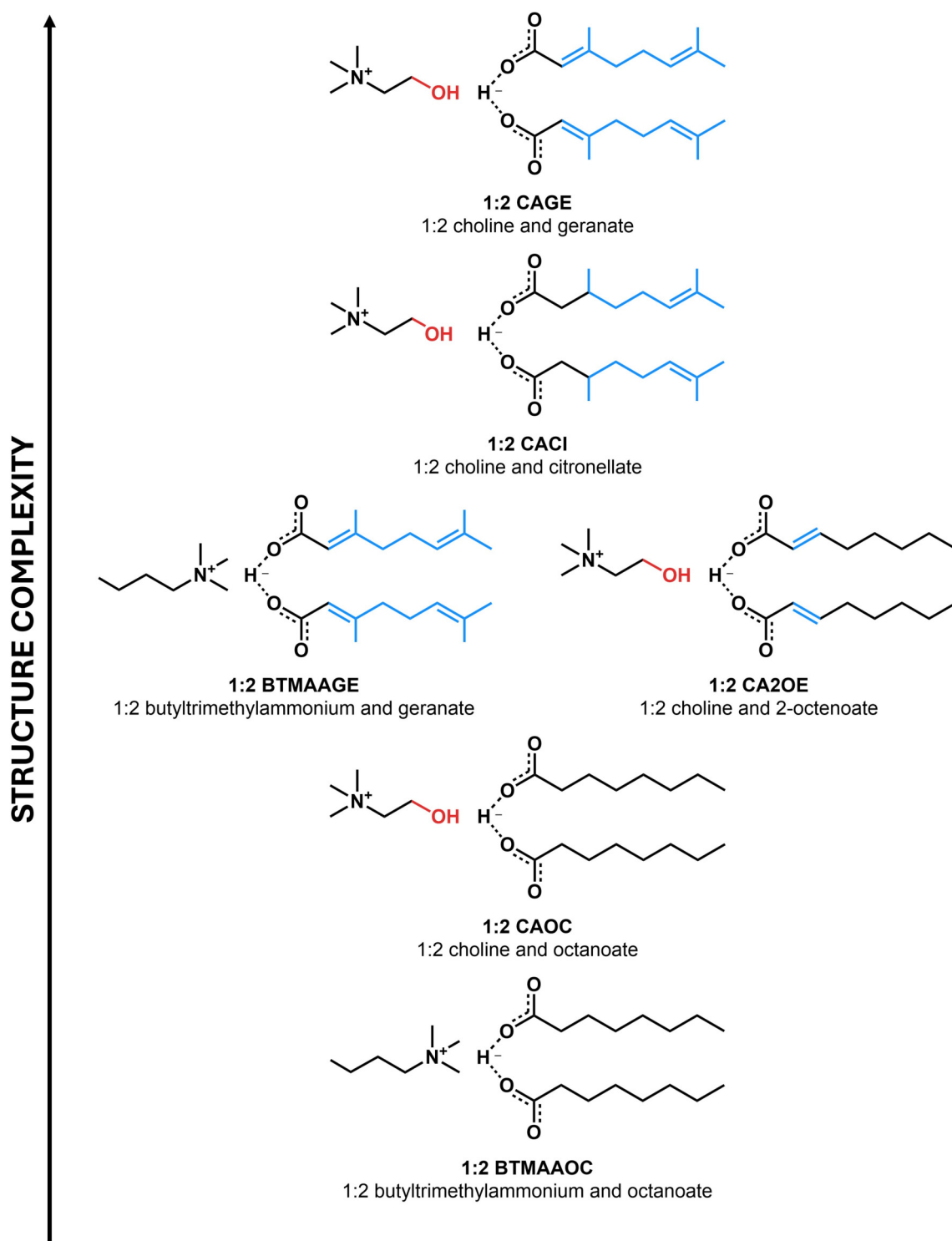


Figure 1.6. The 1:2 ILs discussed in this work, in increasing order of structural complexity

and the five 1:2 CAGE-like systems in this work are assumed to contain only ionic species: a cholinium or BTMA cation, and a complex $[(\text{carboxylate})_2\text{H}]^-$. It should be noted, however, that the complex anion is simply a static depiction of a dynamic system; the hydrogen bonds between the acid and anion species, as well as between the acidic proton and the hydroxyl group (in cholinium-based ILs) are not fixed, but rather are constantly breaking and reforming, with the protons being exchanged between different anion, acid and cation molecules. One final thing to note is that all of the 1:2 systems in this work show a transition to a liquid phase at or around room temperature and so are considered to be ionic liquids. Some of these systems can also be classified as deep eutectic solvents (DESs), although this requires a more nuanced approach. DESs and the classification of the systems in this work is discussed in more detail in Section 1.3.

As shown in Figure 1.6 the simplest of these systems is 1:2 butyltrimethylammonium and octanoate (BTMAAOC), which will be discussed first. Each subsequent chapter will deal with the next IL in this hierarchy, building up the structural complexity of the ILs, with 1:2 choline and geranate (CAGE) being the last system to be discussed. The structural differences between each complex IL and 1:2 BTMAAOC are indicated in Figure 1.6: the presence of a hydroxyl group on the cation is highlighted in red, while any double bonds and branching groups on the anion alkyl chains are shown in blue. In each chapter, one of the six ILs will be investigated and its properties compared with those of previously discussed systems, in order to understand the effect of the different structural features. The thermal behaviour of the ILs was investigated using differential scanning calorimetry (DSC) and dynamic mechanical analysis (DMA), among other techniques, while X-ray scattering measurements were used to gain an understanding of the molecular arrangements and structuring present in each system.

1.2.1 Aims and Objectives

This is a brief overview of the main aims & objectives of this work.

- Devise a targeted-modification approach to selecting several CAGE-like ILs in order to understand the structure-property relationships that govern these systems
- Cation species: two cation species (cholinium and butyltrimethylammonium) will be used in order to vary the ability of the cation to participate in hydrogen-bonding

- Anion / acid species: four carboxylic acid species will be used as starting materials in order to vary the degree of branching and unsaturation present in the acid/anion species in the IL
- Synthesise six different ILs, including 1:2 CAGE (the most structurally complex) and 1:2 BTMAAOC (the simplest IL)
- Improve the purification process for geranic acid (crystallisation from a solvent) by using hexane instead of acetone
- Improve the purity of the synthesised ILs by using lower temperatures during synthesis, handling and storage. The purity is primarily assessed visually, as exposure to high temperatures causes the ILs to take on a yellow or orange colour
- Investigate the thermal behaviour of the synthesised ILs. Techniques include DSC, DMA, and variable-temperature viscosity measurements.
- Investigate the structure and molecular arrangement of the synthesised ILs. Techniques include NOESY NMR spectroscopy and X-ray scattering.
- Compare the data gathered on the different ILs in order to understand the effect of the structural features on thermal transitions and molecular packing
- Investigate and compare the thermal decomposition process for the different ILs using thermogravimetric analysis (TGA)

1.3 1:2 CAGE: ionic liquid or deep eutectic solvent?

As mentioned previously, 1:2 CAGE has been referred to as both an ionic liquid and a deep eutectic solvent in the literature, and some debate still exists regarding its classification.²¹ In the present work, 1:2 CAGE, along with all other 1:2 systems discussed here, are considered ionic liquids, as there is no evidence for the existence of the free carboxylic acid species. Instead, the 1:2 systems are comprised entirely of ions, namely an ammonium cation and a complex $[(\text{carboxylate})_2\text{H}]^-$ anion. The classification of 1:2 CAGE and of other related systems as deep eutectic solvents (DESs) is more difficult and first requires that the concept of a DES is clearly defined.

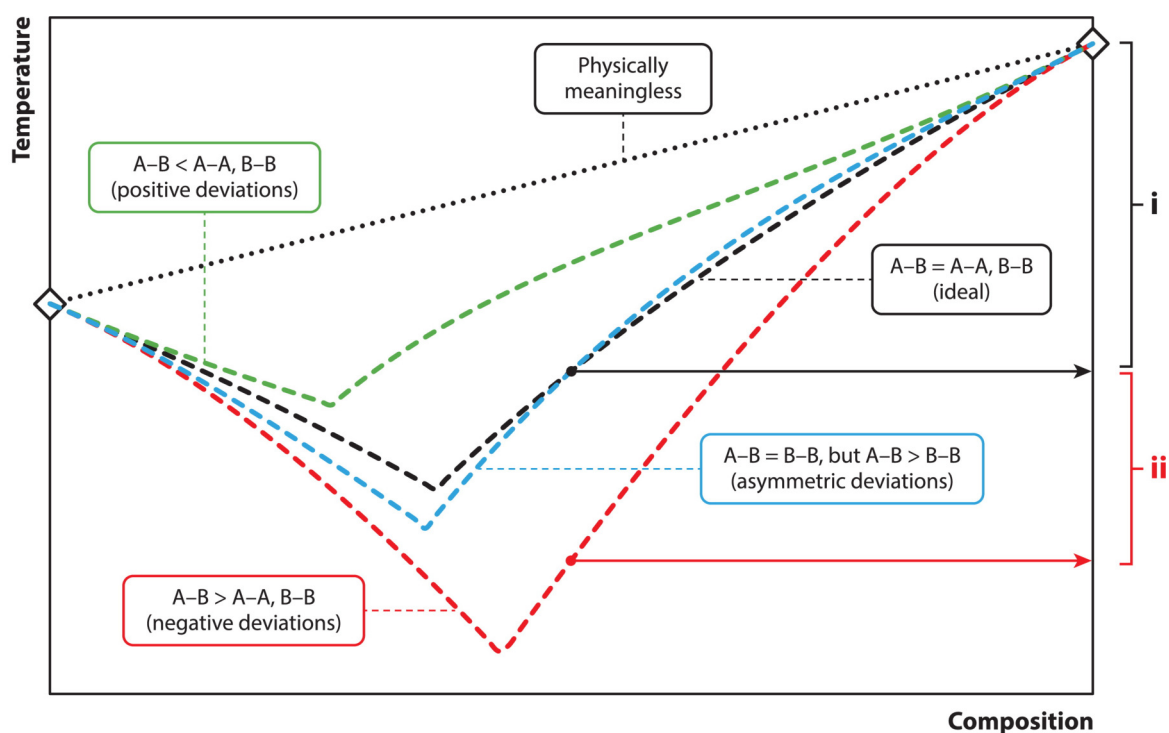
1.3.1 Deep Eutectic Solvents (DESs)

Because their properties are often similar to those of ILs, DESs were originally viewed as a subclass of the ionic liquid family.^{17,54} However, several arguments opposing this have been brought forward by those who believe DESs should be regarded as a separate class of compounds,^{55–57} with this discussion being fuelled primarily by the fact that the definition of a DES is not entirely clear.

The term 'deep eutectic solvent' was first introduced by Abbott *et al.* in 2003, to describe a eutectic mixture of choline chloride and urea, where the melting point of the mixture was significantly lower than the melting point of either individual component.⁵⁴ The qualifier 'deep' was used to emphasise that the melting point of the mixture was *significantly* lower than the melting points of the starting materials; they attributed this effect to the formation of a hydrogen-bonding complex between the species present in the system.⁵⁴ In 2014, Abbott *et al.* provided a more general definition of DESs, stating that they are mixtures of Lewis or Bronsted acids and bases, in which the observed decrease in melting point is due to charge delocalisation through hydrogen bonding between the different species.⁵⁸ Regarding the debate on whether DESs are an IL subclass, it should be noted that Abbott *et al.* clearly state in their 2014 review that ILs and DESs are distinct compound classes.⁵⁸ Despite this, many publications exist that use the term DES to describe systems that do not fit the definition of Abbott *et al.*,^{59,60} or which offer definitions of a DES that are similar, but not the same, as the one given by Abbott *et al.*^{61–63} In light of these inconsistencies, Coutinho *et al.* have expressed their views on this issue in several publications.^{57,64,65} The most recent of these presents a thorough discussion of what should and should not constitute a DES and offers the following definition:⁵⁷

'A eutectic solvent is a eutectic-type system that is a liquid at a given desired temperature where at least one of its components would, otherwise, be a solid unfit to be applied as a solvent. A deep eutectic solvent is a eutectic solvent whose components present enthalpic-driven negative deviations from thermodynamic ideality.'

This complex definition combines several different concepts in a 'nesting' fashion: DESs are defined as a subclass of *eutectic solvents*, which in turn are defined as a subclass of *eutectic systems*. In order to be able to assess whether the systems in this work can be considered DESs,



AR Abranches DO, Coutinho JAP. 2023
Annu. Rev. Chem. Biomol. Eng. 14:141–63

Figure 1.7. Solid-Liquid Equilibrium (SLE) phase diagram of a theoretical binary mixture. The black line shows the behaviour of an ideal mixture. The red line shows a negative deviation from ideality, characteristic of a deep eutectic. The green and blue lines show positive and asymmetric deviations from ideality, respectively. Reprinted with permission from Reference [57], published by Annual Reviews.

it is necessary to first understand each of these concepts and how Coutinho *et al.* combine them in their definition.

The concept of a 'eutectic system' will be discussed first. The term 'eutectic' means 'well melting' and was coined by Frederick Guthrie in 1884 to describe the behaviour of a mixture (containing at least two components) which melts at a single temperature that is lower than the melting point of any of its individual component parts.⁶⁶ The behaviour of such a mixture is often described using a solid-liquid equilibrium (SLE) phase diagram, in which the x-axis represents the composition of the mixture and the y-axis the temperature. On the SLE phase diagram of a theoretical binary mixture (Figure 1.7, reproduced from Reference [57]), the eutectic point is the point whose coordinates correspond to the lowest melting temperature of the mixture and to the composition of the mixture at this temperature (also known as the eutectic composition).^{58,65,66}

A depression of the melting point (giving rise to the characteristic 'V'-shape of the SLE phase diagram) is present in most mixtures, as a result of the fact that none of the components exist in their pure state; the simple presence of other components leads to a decrease in melting point, even without the presence of favourable interactions between the different species.^{57,65} Taking this definition of a eutectic, Coutinho *et al.* apply a further restriction and define a eutectic *solvent* as a eutectic system which is liquid at the desired temperature and for which at least one of the constituent parts would otherwise be solid at this temperature (being rendered a liquid as a result of the eutectic effect).^{57,65}

Having successfully defined a eutectic solvent, the final 'building block' towards the definition of a DES is the qualifier *deep*, whose purpose is to differentiate DES systems from simple eutectic solvents. As was discussed earlier, all eutectic mixtures, and thus all eutectic solvents, have a lower melting point than their individual components. What matters when determining whether a eutectic solvent is 'deep' are the magnitude of the melting point depression and the reason this depression is occurring. The first constraint requires that the melting point of a DES must be lower than would be expected for an ideal mixture with the same composition. Figure 1.7 shows the SLE diagrams of an ideal mixture and a deep eutectic using black and red dashed lines, respectively. The 'deep' adjective in 'deep eutectic solvent' refers to the additional decrease in melting point observed for the deep eutectic mixture compared to the ideal mixture. In Figure 1.7, this difference is indicated for the point corresponding to an equimolar mixture; *i* marks the melting point depression of an ideal eutectic mixture, while *ii* is used to mark the additional decrease shown by a deep eutectic mixture. The second constraint is that this additional decrease in melting point must be enthalpically driven, i.e. driven by favourable interactions between the different constituents, such as the formation of hydrogen or halogen bonds. Coutinho *et al.* make sure to differentiate DESs both from systems where a decrease in melting point is caused primarily by entropic reasons⁶⁷ and from systems where, instead of a proton being shared via hydrogen bonding, the acidity difference between the components is significant enough that proton transfer occurs instead (leading to the formation of a protic IL instead of a DES).⁴⁸

It should be noted here that the definitions provided by both Coutinho and Abbott highlight two clear differences between ILs and DESs. First, ILs are pure compounds, while DESs are mixtures; second, ILs only contain ionic species, while for DESs such a restriction does not exist

- they can, and often do, contain both ionic and neutral species. Despite this, it is possible for a system to be considered both an ionic liquid and a deep eutectic solvent, depending on the nature of its constituent species of the interactions present in the system.

1.3.2 1:2 CAGE and related systems

Having successfully established the rules that define a DES, it is now possible to decide whether the systems in this work fall under this umbrella or not. It must be noted here that while this classification is not strictly necessary, it is thought to be helpful. Being able to classify a new system as part of the IL or DES family, or any other class of compounds helps communicate some of the key traits of that system in a succinct and efficient manner.

Based on the definition of Coutinho *et al.*, a DES must fulfill three criteria: it must be eutectic system, it must be liquid and contain a component that would otherwise be a solid, and its low melting point must be in part due to the presence of thermodynamically favourable intermolecular interactions.⁵⁷ In order to determine whether these systems are eutectics, 1:2 CAGE will be considered as an example. This IL can be looked at in two different ways, described in Figure 1.8. One way considers 1:2 CAGE to be comprised of a cholinium cation and a $[(\text{geranate})_2\text{H}]^-$ anion. However, since these are individual ions, their melting point cannot be determined and therefore cannot be compared with the melting point of 1:2 CAGE, in order to decide whether this fulfills the condition of a eutectic system. A different way to approach this problem is to look at 1:2 CAGE as a mixture of a 1:1 cholinium geranate salt and geranic acid. Each of these components is a standalone chemical compound, with a measurable melting point. For the ILs in this work, four of the 1:1 ammonium carboxylate salts are room-temperature solids with relatively high melting points; these were measured using a melting point apparatus, with a heating rate of $5\text{ }^\circ\text{C min}^{-1}$. The other two 1:1 salts, namely 1:1 CAOC and 1:1 CA2OE, are viscous, gel-like materials at room temperature. The melting point of these salts was taken as the temperature of the endothermic peak observed in the differential scanning calorimetry (DSC) traces. The melting points of the neat carboxylic acids are reported as the temperature of the endothermic melting peak observed by DSC. Citronellic acid does not show any crystallisation or melting transitions; the temperature of the glass transition measured on heating is given in parentheses. The acid is thought to be in a liquid state above this temperature, but it should be noted that this is not a true melting point.

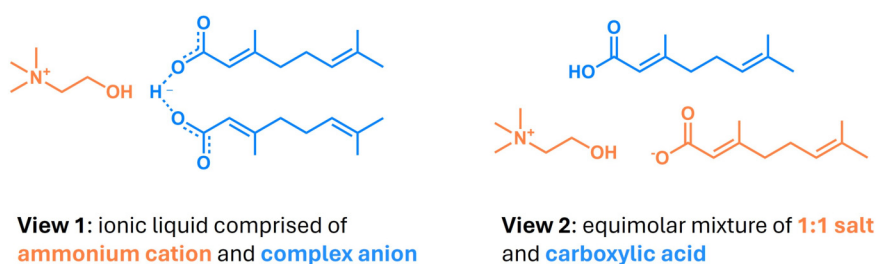


Figure 1.8. Two different depictions of the 1:2 CAGE system. *Left:* as single ionic compound. *Right:* as a mixture with two components.

All DSC measurements of 1:1 salts and neat acids were performed by myself and Dr. Oriele Palumbo at the Sapienza University of Rome. Graphs are shown in Appendix B.

For the 1:2 ILs, the determination of a 'melting point' is not as simple, as these systems have more complex thermal behaviours. The phase changes exhibited by the 1:2 systems have been investigated using DSC measurements and are discussed in more detail in the subsequent chapters. All of the 1:2 ILs discussed in this work exhibit (or are thought to exhibit) a liquid crystalline (LC) mesophase (meaning 'intermediate phase'), in addition to a more conventional isotropic liquid phase. For each system, two different 'melting point' temperatures are given in Table 1.1.

The first is the temperature at which the IL changes from a solid (or partially solid) phase to the liquid crystalline mesophase. For ILs that show a cold crystallisation transition (where the sample crystallises on heating the supercooled IL, rather than on cooling), the melting point is given as the temperature of the endothermic peak associated with the melting of this (partially) crystalline phase. For ILs that only show a reversible glass transition, with no additional crystallisation or melting peaks visible in the DSC, the melting point is given as the glass transition temperature measured on heating. It should be noted that the glass transition is not the same as a melting transition and that this temperature is not a true melting point. The second melting temperature given in Table 1.1 is the temperature at which the IL transitions from the liquid crystalline mesophase to an isotropic liquid phase. This is given as the temperature of the endothermic peak observed in the DSC upon heating. None of these temperatures is a 'true' melting point (which implies a solid to liquid transition), as the liquid crystalline state is distinct from both a solid and a liquid phase.

For the purposes of determining whether the 1:2 ILs in this work fall under the DES umbrella,

the 'melting point' temperature is taken as the temperature of the liquid crystal to isotropic liquid transition ($T_{\text{LC-liquid}}$) shown in Table 1.1. This transition will be discussed in more detail for each IL in the subsequent chapters of this thesis. For each IL, if the $T_{\text{LC-liquid}}$ temperature is lower than the melting points of the corresponding 1:1 salt and carboxylic acid, then the IL is considered to be a eutectic system. This condition is true only for the first three ILs in Table 1.1: 1:2 BTMAAOC, 1:2 BTMAAGE and 1:2 CAGE. At this temperature, the systems are liquid and are contain a component that would otherwise be a solid (the 1:1 salts, which have significantly higher melting points). The last condition imposed by Coutinho *et al.* — that the decrease in melting point depression is greater than ideality, due to enthalpically favourable interactions — cannot be determined simply by considering the melting points and would require both theoretically and experimentally derived SLE diagrams for each system. However, it is possible to state that strong hydrogen-bonding interactions occur between the acid and anion species in all 1:2 systems (as discussed previously) and, in the case of cholinium-based ILs, such as 1:2 CAGE, between all three constituent species. While the BTMA cation does not contain a hydroxyl group, it is possible that it can participate in hydrogen-bonding interactions through the methyl groups on the nitrogen atom; CH_3 groups in a tetramethylammonium cation have been shown to form hydrogen bonds with water molecules in their hydration shell.⁶⁸ Strong hydrogen bonding between the components of a mixture has been shown to cause negative deviations from ideality (i.e. the experimental eutectic point being lower than the theoretically calculated one).⁶⁹ Based on this, three of the 1:2 systems — 1:2 BTMAAOC, 1:2 BTMAAGE and 1:2 CAGE — are considered to be both ILs and DESs, while three — 1:2 CACI, 1:2 CAOC and 1:2 CA2OE — are ILs, but not DESs.

IL	$T_{\text{solid-LC}}$	$T_{\text{LC-liquid}}$	m.p. of 1:1 salt	m.p. of acid	DES?
1:2 BTMAAOC	−20 °C	17 °C	162–168 °C	18 °C DSC	Yes
1:2 BTMAAGE	−78 °C	24 °C	149–152 °C	21 °C	Yes
1:2 CAGE	−83 °C	−10 °C	110–170 °C	23 °C	Yes
1:2 CACI	−80 °C	−10 °C	102–112 °C	N/A (−86)	No
1:2 CAOC	−28 °C	52 °C	15 °C	18 °C	No
1:2 CA2OE	−3–4 °C	12 °C	6 °C	9 °C	No

Table 1.1. Melting point temperatures of the 1:2 ILs in this work and of the corresponding 1:1 salts and carboxylic acids

1.4 X-ray scattering

Small-angle X-ray scattering (SAXS) is a technique commonly used to investigate the structure of weakly- or partially-ordered materials. By irradiating a sample with X-rays and recording the resulting scattering pattern, information such as the shape, size and size distribution of the scattering units can be obtained.⁷⁰ SAXS measurements are used in a plethora of fields, such as medicine, materials and biological sciences, and the food industry.^{71–76}

Since their discovery by Wilhelm Röntgen in 1895, X-rays have been at the forefront of scientific progress. They are extensively used in the medical field as imaging tools and they were a key factor in understanding atomic structure (Henry Moseley, 1913) and in discovering the structure of DNA (Rosalind Franklin, 1952).⁷⁷ The latter is a prime example of how X-rays can be used to determine the atomic and molecular structure of materials. This is possible because the range of X-ray wavelengths includes wavelengths of a similar magnitude to the interatomic distances typically found in solid materials (10^{-9} – 10^{-10} m).⁷⁷

Generally, for an X-ray scattering experiment, the sample is placed between the source of an X-ray beam and a detector, which records the intensity of the scattered waves. While the X-ray photons can interact with the irradiated material in different ways, for structural determination purposes the most important of these is elastic scattering. This means that the scattering occurs without energy loss, such that the frequency of the scattered waves is the same as that of the incident wave.⁷⁷ The scattered waves interfere with each other, either constructively, amplifying the intensity of the signal and resulting in a bright area on the detector, or destructively, reducing or destroying the signal and resulting in a dark area. In an ordered structure, such as a crystal lattice, the scattering units (atoms and/or molecules) form a repeating pattern, with a characteristic interplanar distance d , as depicted in Figure 1.9 (reproduced from Reference [77]). For constructive interference to occur, the scattered waves must be in-phase, which happens when Bragg’s Law

$$n\lambda = 2d\sin\theta \tag{1.1}$$

is obeyed.^{70,77} Here, n is an integer, λ is the wavelength of the incident beam and d is the distance between adjacent atomic planes. The scattering angle θ is defined as the angle between the incident beam and the plane of the scattering unit; the scattered beams that obey Bragg’s law (that are in-phase with each other and will result in constructive interference) are the

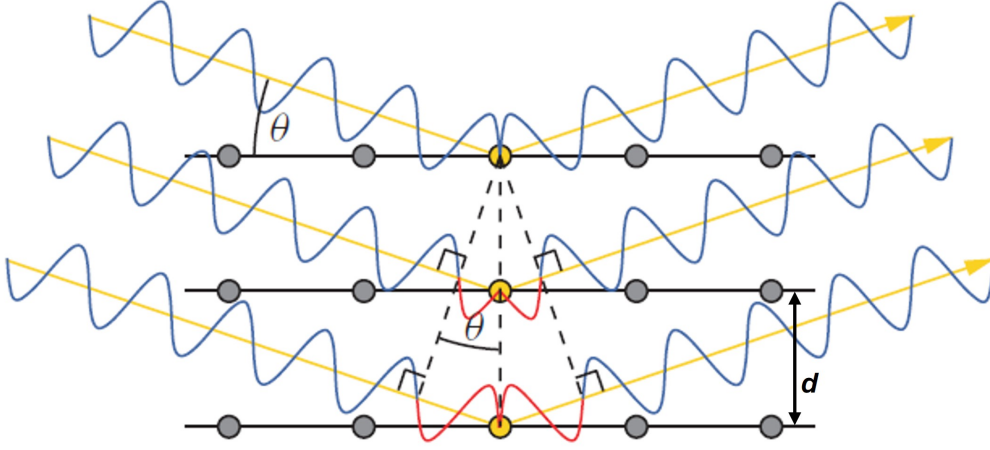


Figure 1.9. Diagram showing the scattering of X-rays by an ordered crystal lattice. Adapted from Reference [77], published by Wiley.

ones scattered at the same angle θ (measured between the scattered beam and the plane of the scattering unit). This can also be rephrased to state that when Bragg's law is obeyed, the angle between the incident beam and the scattered beam is equal to 2θ . While the X-ray photons are scattered in multiple directions, Figure 1.9 only shows the X-ray beams scattered at angle θ .⁷⁷

The setup of a typical SAXS measurement is shown in Figure 1.10. The sample is irradiated with an X-ray beam and the intensity of the scattered signal is recorded using a 2D detector. The scattering intensity is related to the amplitude of the scattered waves, and so is affected by wave interference. The constructive and destructive interference of the scattered X-rays gives rise to a pattern of light and dark areas, known as a scattering pattern. On a 2D detector, this appears as bright concentric circles, with the position of each ring being associated with a specific scattering angle θ . Bragg's law establishes a relationship between the scattering angle θ and the interplanar distance d :

$$d = \frac{n\lambda}{2\sin\theta} \quad (1.2)$$

Usually, samples scatter isotropically, meaning that the 2D pattern can be integrated to give a 1D pattern of peaks. The intensity of these peaks corresponds to the intensity of the signal recorded by the detector, and depends on several factors, such as the number, position and size of the scattering units, and on their scattering ability (related to the electronic structure of the particles).⁷⁰

The position of the peaks (the X-axis) can be given as the scattering angle (usually as 2θ), but

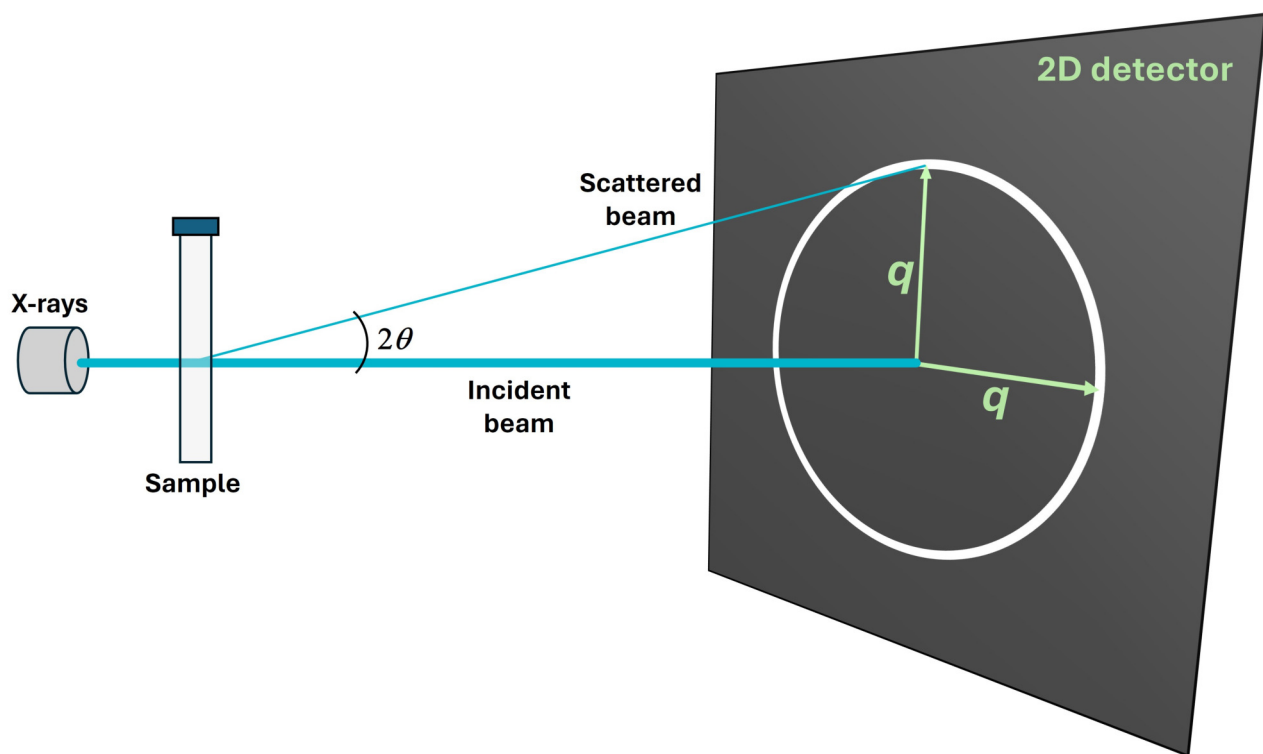


Figure 1.10. Diagram of a general transmission SAXS setup. A bright ring is obtained on the detector at $q = 4\pi\sin\theta$.

most often it is expressed in terms of q , which is known as the 'magnitude of the momentum transfer vector' or 'the length of the scattering vector'.⁷⁰ q is a function of the scattering angle θ and is defined as

$$q = \frac{4\pi\sin\theta}{\lambda} \quad (1.3)$$

q represents a reciprocal space, usually given in units of inverse nanometres (nm^{-1}) or inverse Ångstrom ($\text{\AA}^{-1}$). The relationship between q and the real-life distance d is

$$\begin{aligned} q &= 2\pi/d \\ d &= 2\pi/q \end{aligned} \quad (1.4)$$

While some SAXS measurements can be performed on standard benchtop instruments, a synchrotron is often necessary for experiments that require improved resolutions, short timescales and fast sample throughput. The experiments in this work were performed on the I22 beamline at the Diamond Light Source synchrotron facility, in the UK.⁷⁸ To illustrate the workings of a synchrotron beamline, Figure 1.11 shows the layout of the I22 beamline.⁷⁸ Synchrotrons produce high-intensity beams by accelerating electrons using a system of magnets known as an undulator. The light emitted by the electrons covers multiple wavelengths, so it is filtered to the

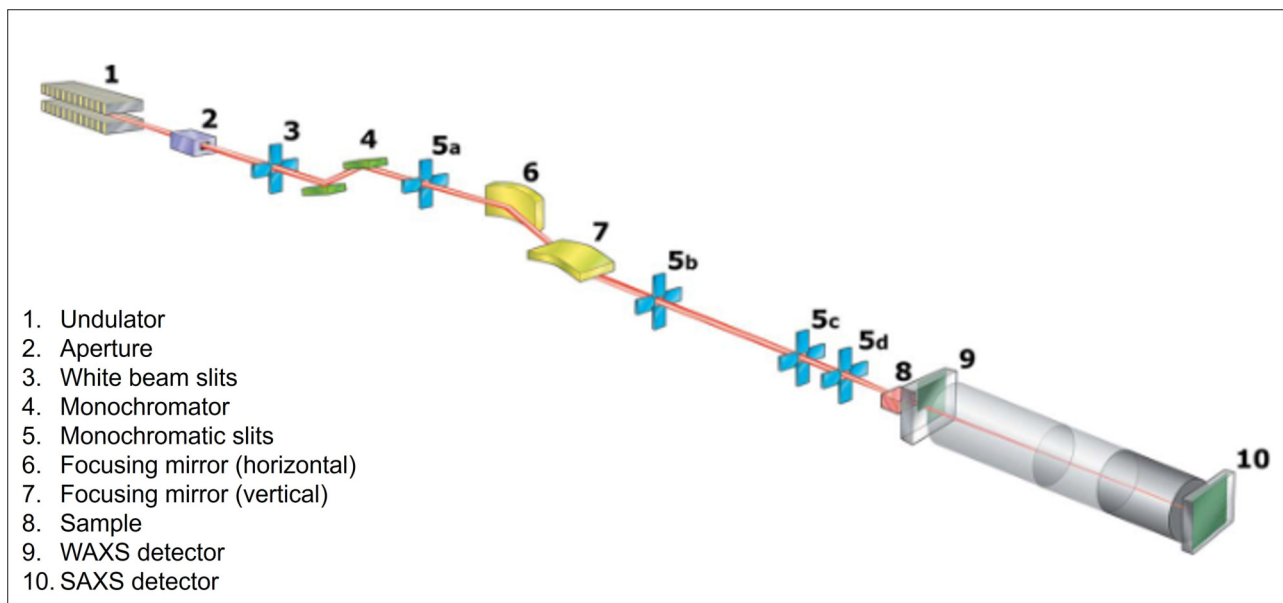


Figure 1.11. Layout of the I22 X-ray scattering beamline at the Diamond Light Source synchrotron facility. Adapted from Reference [78], published by IUCr Journals.

required wavelength using a monochromator. It is then further focused using a system of slits and mirrors to achieve a high-resolution X-ray beam with which the sample is irradiated. A variety of sample environments, for both solid and liquid samples, can be used at a synchrotron facility, allowing for the design of unique experiments. The detector setup usually involves one or two detectors, whose position relative to the sample can be changed to give access to different q -ranges. Given the relationships between q , the scattering angle θ and the distance d (also known as d -spacing), small scattering angles correspond to small q -values and relatively large real-life distances. Wide-angle X-ray scattering (WAXS) is a complementary technique to SAXS, which deals with greater scattering angles and q -values and can therefore detect ordering on very small scales. The I22 beamline uses two different detectors, placed at different distances away from the sample (with the WAXS detector being closer), in order to cover a large q -range. In this work, the q -range covered by the SAXS and WAXS measurements was approximately $q = 0.02\text{--}6 \text{ \AA}^{-1}$, corresponding to real-life distances of $d = 1\text{--}300 \text{ \AA}$. It should be noted that the distinction between SAXS and WAXS is somewhat arbitrary and is primarily employed out of practicality. The two represent the same technique (X-ray scattering), as evidenced by the fact that 'intermediate' q -values can be recorded using either setup and will fall under either category, depending on the magnitude of the q -range covered by an experiment.

X-ray scattering is one of the most important techniques used to understand the structural

correlations in liquid and liquid crystalline materials, including ionic liquids,^{79–86} and has been a key tool in the study of the liquid crystalline phases exhibited by the systems in this work.

1.5 Liquid Crystals

Pure substances usually exhibit three well-known phases (solid, liquid, and gas), changing from one phase to another via a first-order phase transition. However, some materials or mixtures also exhibit one or more mesophases (from Greek *meso*- meaning ‘middle’), which are intermediate phases with properties that lie between those of a crystalline solid and a liquid. These phases are aptly referred to as liquid crystalline phases and the materials are referred to as liquid crystals (LCs). The structuring of LCs usually shows a degree of ordering, but to a lesser extent than a crystalline solid, while still retaining some mobility. Similarly, Tschierske defines LCs as materials which show long-range order (similar to solids), but no fixed position of individual molecules (similar to liquids).⁸⁷

Liquid crystalline behaviour has been observed for many materials, including polymers, surfactants and biological molecules such as membrane lipids and cholesteryl esters.⁸⁸ Generally, mixtures (such as aqueous surfactant solutions) exhibit *lyotropic* behaviour, in which the formation of LCs is dependent on the surfactant concentration. Pure substances, such as ionic liquids, usually exhibit *thermotropic* behaviour, where the LC mesophase only exists at specific temperatures. The LC phase is obtained by heating the solid sample past its melting point; further heating leads to a transition of the LC phase into an isotropic liquid phase (Figure 1.12).^{89,90} It should be noted that before the isotropic phase is reached a material can show thermal transitions between multiple different LC phases; in this case, it is referred to as a polymorphic sample.⁹⁰

There are several different types of liquid crystals whose formation depends on the nature and shape of the molecules present in the mesomorphic system. The simplest type are nematic LCs, which show only orientational order; this means that the molecules (or groups of molecules) are oriented in the same direction, parallel to each other. More complex LC phases (also) show positional order, which gives rise to repeating structures, such as stacks of parallel layers (smectic LCs), cubic structures (cubic LCs) or columns (columnar LCs).^{87,91} The molecular arrangements of nematic and smectic LC phases are shown in Figure 1.12. It is important to

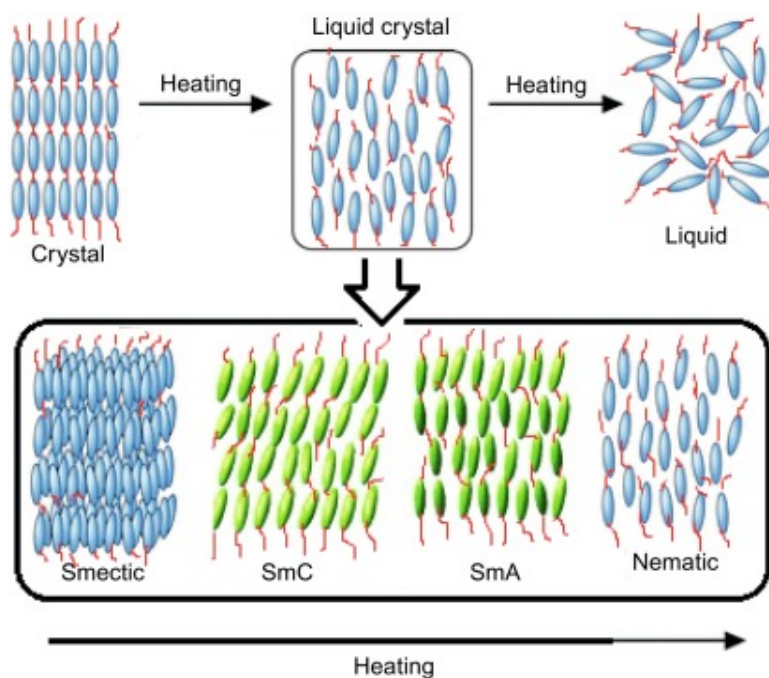


Figure 1.12. Top: phases present in a thermotropic liquid crystal. Bottom: structures of smectic (Sm) and nematic LC phases. Reproduced from reference [89], published by Elsevier.

note here that each of these terms encompasses several subclasses, depending on the nature of the molecules and the ordering of the LC system. In thermotropic (neat) systems different smectic phases are denoted by letters (SmA, SmB, SmC) while in lyotropic systems (often surfactant-water mixtures) they are differentiated using a Greek letter subscript (e.g. lamellar (L_α) and gel (L_β) mesophases).^{92,93} It should be noted here that not all surfactant mesophases are lyotropic. Some surfactants have been shown to form liquid crystalline phases in the absence of water (or at very low hydration); in this case, no solvent is present and the LCs are therefore classed as thermotropic.^{91,94,95} The exact hydration at which a surfactant-water system is considered lyotropic rather than thermotropic depends on the nature of the surfactant and the structure of the mesophase, but generally a LC system is considered lyotropic if it contains a significant proportion (>10 wt%) of water.⁹⁴

The ILs studied in this work have amphiphilic structures which closely resemble surfactants and possess a significant degree of hygroscopicity. These ILs form liquid crystalline phases with layered structures, consisting of a one-dimensional lattice of parallel layers in which the molecules are perpendicular to the plane of the layer.^{79,96} The LC phases observed for the neat ILs in this work show a temperature dependence (collapsing to an isotropic phase on heating) and so can be classed as thermotropic if the hydration of the IL is deemed negligible.

Usually, in the literature, such phases are referred to as 'smectic'. However, all ILs discussed in this work contain a small amount of moisture, with the water contents of the dried ILs varying between 0.1 and 0.6 wt% (1000–6000 ppm, or 2–13 mol%); in contrast, ILs containing the hydrophobic $[\text{NTf}_2]^-$ anion have been reported to contain less than 100 ppm water.^{86,97} Additionally, the observed mesophases also show a concentration dependence, with similar LC phases reported in the literature for a range of IL-water mixtures.^{14,98} Because of this, the layered liquid crystalline phases exhibited by the ILs in this work will be referred to as lamellar phases (nomenclature that is generally used for lyotropic systems in the literature).

In the study of mesomorphic systems, two main techniques can be used to identify and classify LC phases: polarised-light microscopy and X-ray scattering. Polarised-light microscopy (PLM) is used to visualise and photograph samples that are optically anisotropic (birefringent). A typical PLM setup involves a microscope containing two polarising filters. The first, referred to as a polariser, is fixed and is placed between the light source and the sample; this filter has the purpose of polarising the incident light before it reaches the sample. The second is called the analyser, and it is placed between the sample and the eyepiece. The orientation of the analyser can be changed manually or, if needed, this filter can be removed temporarily.⁹⁹ Figure 1.13 shows the two possible filter configurations. When the polariser and analyser are parallel (or when the analyser is removed), the incident light can pass through and reach the eye of the user. This is often called the brightfield mode and results in a standard image. If instead the two filters are perpendicular to each other, then the polarised light cannot pass through the analyser filter. In the absence of a sample, this polarised mode results in an image that is completely dark; the same is true for an optically isotropic sample, for which the refractive index is the same in all directions. An optically anisotropic sample, on the other hand, has multiple refractive indices and splits the polarised light into two components (the sample is birefringent). These rays travel through the material with different velocities, becoming out of phase with each other; the emergent light (formed from the interference of the two components) is no longer perfectly aligned with the incident beam, and so it can (partially) pass through the analyser filter. In the resulting image, the optically anisotropic sample appears bright on an otherwise dark background.⁹⁹

Liquid crystalline phases are birefringent and different mesophases have characteristic textures when observed under a polarised-light microscope, making it possible to differentiate between

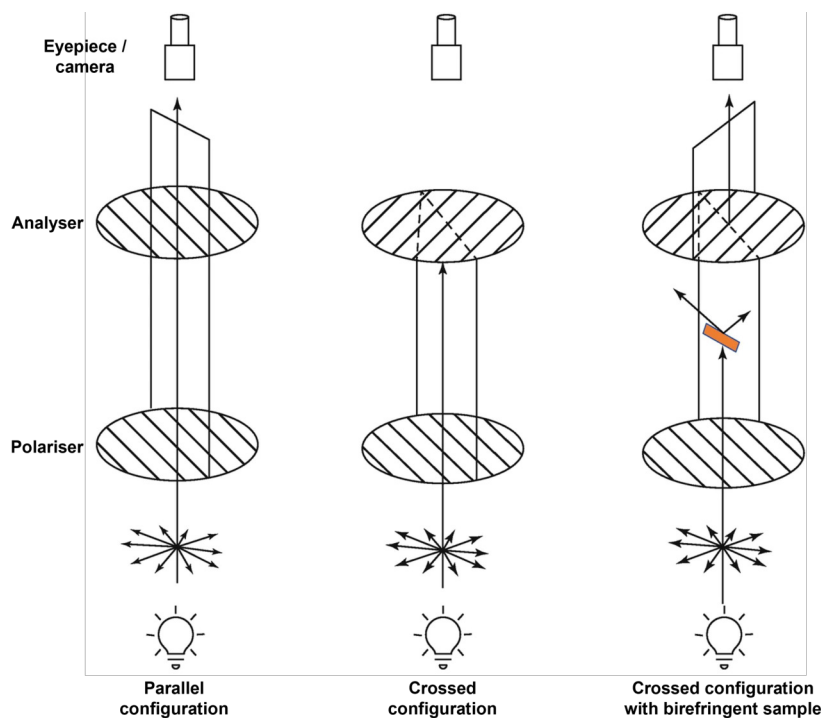


Figure 1.13. The different configurations of a polarised-light microscope and the effect of an anisotropic sample on the polarised light. Reproduced from reference [99], published by Springer International.

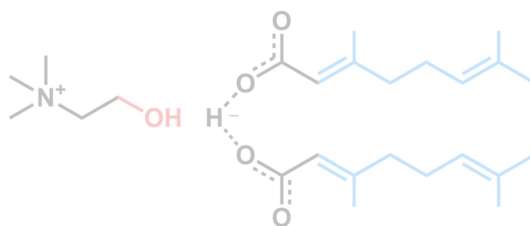
them. Generally, nematic phases have a schlieren or thread-like texture,⁹³ while smectic phases can show a wide variety of optical textures, depending on the nature of the molecules forming the mesophase. Possible smectic textures include focal conic textures (for smectic A phases) and striated, broken-fan, or schlieren textures (for smectic C phases).⁹³ Lamellar phases usually exhibit an oily streak texture or a Maltese cross pattern.^{92,100} The only mesophase that does not show birefringence is the cubic mesophase, which has a high degree of symmetry and is optically isotropic.⁹²

Small-angle X-ray scattering (SAXS) and wide-angle X-ray scattering (WAXS) measurements can be used to gain information about the long- and short-range ordering of the system respectively. These techniques can help identify specific mesophases and determine the size of the repeating units. The position of a peak in q -space corresponds to a real-life distance d , calculated according to $q = 2\pi/d$; this is referred to as the ' d -spacing' and corresponds to the size of the repeating units that make up the mesophase. The shape of the peak can provide information about the size distribution of the repeating units: a narrow, sharp peak suggests that the repeating units are uniform in size, while a broader, more diffuse peak, suggests that

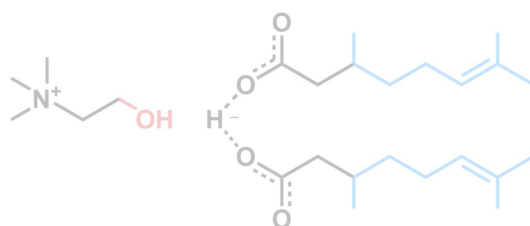
the mesophase contains a distribution of differently-sized units.

Different mesophases give rise to distinct scattering patterns in the SAXS region. Most relevant here is the smectic / lamellar pattern, which involves sharp peaks at position d , $2d$, $3d$, etc (i.e. their q -values are in a 1:2:3 ratio).⁷⁹ In the WAXS domain, lamellar L_α phases also show a diffuse peak around $q = 1.4 \text{ \AA}^{-1}$ ($d = 4.5 \text{ \AA}$), which corresponds to the distance between the fluid nonpolar alkyl chains. In gel L_β phases the alkyl chains are more rigid and usually fully extended, giving rise to a broad WAXS peak around $q = 1.5 \text{ \AA}^{-1}$ ($d = 4.1\text{--}4.2 \text{ \AA}$).⁹²

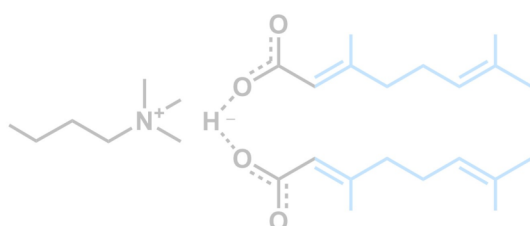
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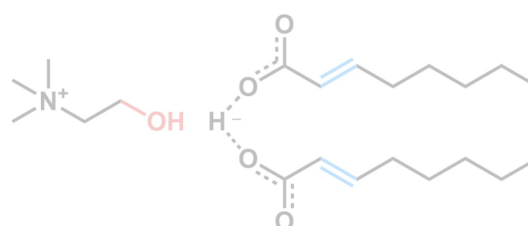
1:2 CAGE



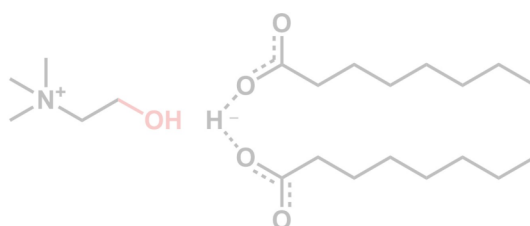
1:2 CACI



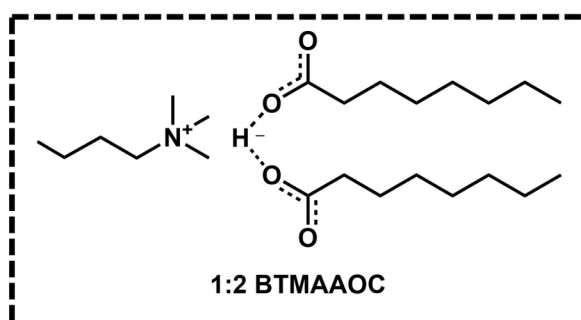
1:2 BTMAAGE



1:2 CA2OE



1:2 CAOC



1:2 BTMAAOC

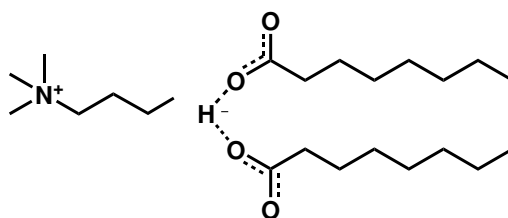
Chapter 2

1:2 ButylTrimethylAmmonium And OCtanoate (BTMAAOC)

The results presented in this chapter have been partially published in Reference [101].

Each of the six 1:2 ionic liquids (ILs) in this work has a chapter dedicated to it, where its behaviour and properties are discussed and compared with those of the ILs that had been covered previously. This chapter structure was chosen in order to give a complete picture of each system (rather than discussing individual techniques). The order of the ILs is that shown in Figure 1.6, starting with the IL with the simplest structure and gradually building up the structural complexity. This allows for an easier comparison between the systems and helps identify the effect of the different structural features on the IL properties. This figure is also reproduced before the start of each chapter, with the IL to be discussed in that chapter marked by a dashed border. ILs that are yet to be discussed are shown as 'greyed out', while ILs that have already been discussed are shown at full opacity.

For each system, the thermal behaviour of the IL was investigated using differential scanning calorimetry (DSC) and dynamic mechanical analysis (DMA), in order to understand the nature of the thermal transitions exhibited by each system. The viscosity of the ILs was measured using dynamic and/or oscillating rheometry. The structuring and molecular packing present in each IL was investigated using several techniques, including solid-state magic-angle spinning (SS-MAS) NMR, variable-temperature X-ray scattering and polarised-light microscopy. Finally,

**Figure 2.1.** 1:2 BTMAAOC

the thermal decomposition of the ILs was studied using thermogravimetric analysis (TGA). The TGA data is not presented in each chapter, but instead it is reported and discussed in full at the end of Chapter 7, the last of the IL chapters.

The present chapter is the first to deal with an ionic liquid, in this case 1:2 butyltrimethylammonium and octanoate (BTMAAOC), the IL with the simplest structure. This is shown in Figure 2.1. 1:2 BTMAAOC does not contain any of the three structural features that were identified in 1:2 CAGE and which have been varied upon throughout this work. The cation of 1:2 BTMAAOC is a butyltrimethylammonium (BTMA) cation, which does not form significant hydrogen-bonding interactions with the anion headgroups. This is thought to lead to weaker intermolecular interactions and therefore to a system with a less ordered structure. The carboxylic acid used in the synthesis of 1:2 BTMAAOC is octanoic acid, which is the only linear, saturated acid used in this work. Octanoic acid is expected to lead to a more ordered system, as the alkyl tails are expected to pack efficiently, resulting in strong Van der Waals interactions. All of the techniques mentioned above will be discussed throughout this chapter in order to build a picture of the structuring and interactions that occur in 1:2 BTMAAOC and that lead to the observed behaviours.

2.1 Thermal behaviour

The thermal behaviour of 1:2 BTMAAOC was investigated using differential scanning calorimetry (DSC) and dynamic mechanical analysis (DMA). The DSC measurements were performed by Dr. Daniel Rauber at the University of Saarland, Germany, and analysed by me using OriginPro (2020). DSC traces for 1:2 BTMAAOC, collected with a scan rate of 5 °C/min, are shown in Figure 2.2. Three consecutive heating-cooling cycles were run in order to show reproducibility.

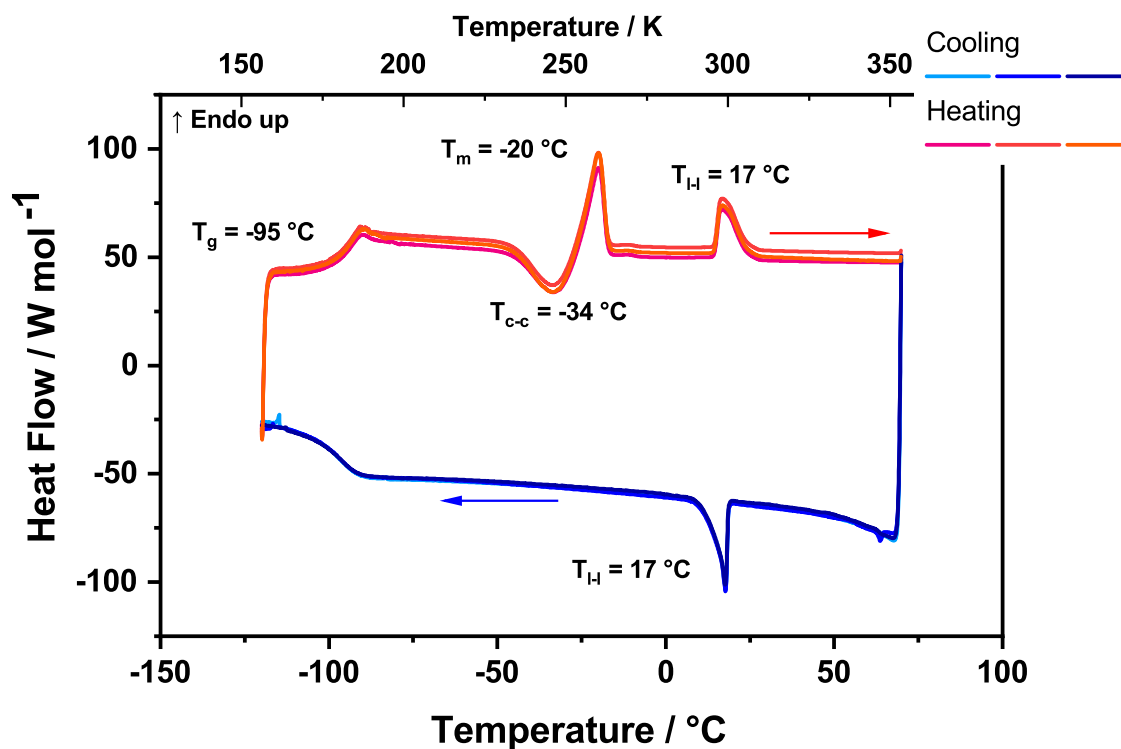
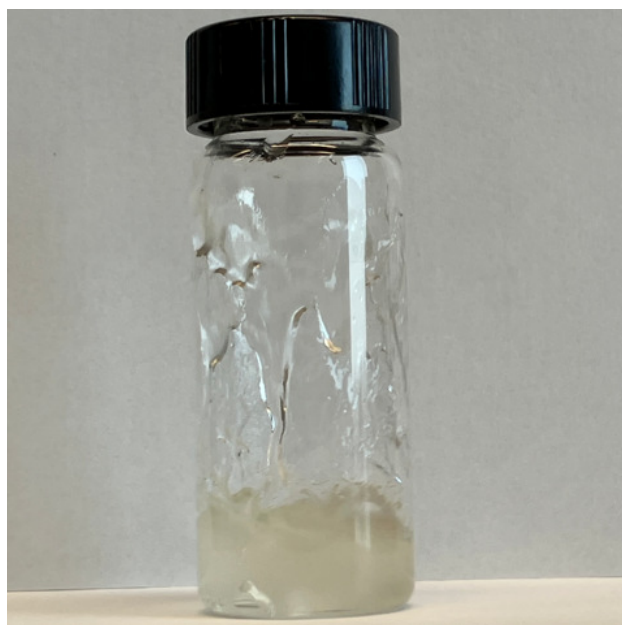


Figure 2.2. DSC traces of 1:2 BTMAAOC with annotated transition temperatures. The heating and cooling rates are 5 °C min^{-1} .

The thermal behaviour of 1:2 BTMAAOC shows a reversible glass transition at $T_g = -95\text{ °C}$ and, on heating from the glass phase, a cold crystallisation transition at $T_{c-c} = -34\text{ °C}$. Cold crystallisations have been observed for other IL systems,^{102,103} and involve crystallisation of the IL not on cooling, but rather on heating of the supercooled sample. This is followed rapidly by a melting transition at $T_m = -20\text{ °C}$ to a liquid crystalline phase. The nature of this phase was determined based on polarising microscopy images (Figure 2.4, top) and X-ray scattering data (discussed in the next section). Microscope images (taken using polarised light) of the liquid crystal and isotropic phases of 1:2 BTMAAOC are shown in Figure 2.4. The sample was observed in air. At $5\text{--}10\text{ °C}$ 1:2 BTMAAOC shows large areas of brightness and, in places, shows a streaky, marble-like texture indicative of a lamellar liquid crystal phase.⁹²

The last DSC peaks observed for 1:2 BTMAAOC correspond to a reversible transition at $T_{l-i} = 17\text{ °C}$. This is a transition from the liquid crystalline mesophase to an isotropic liquid phase (LC-isotropic transition). Visually, the IL appears as an opaque gel when in the liquid crystalline state and changes to a viscous but free-flowing liquid in the isotropic liquid phase (Figure 2.3). PLM images (2.4, bottom) show that the brightness of the LC phase disappears as the sample is heated, in agreement with the LC-isotropic transition observed by DSC. The



(a) Liquid crystalline phase



(b) Isotropic liquid phase

Figure 2.3. 1:2 BTMAAOC before and after the liquid-crystal-to-isotropic phase transition

temperature of the PLM setup was set using a heated sample stage and a liquid nitrogen cooling system, with a heating rate of $5\text{ }^{\circ}\text{C min}^{-1}$. At $25\text{ }^{\circ}\text{C}$ the image is entirely dark, showing no signs of birefringence and confirming that this phase is optically isotropic. More detail about the structuring of the two phases is given in Section 2.3, where X-ray scattering and NMR measurements are discussed.

So far, DSC and polarised-light microscopy have been used to describe the thermal behaviour of 1:2 BTMAAOC. While DSC is useful in identifying the thermal transitions of a system, it provides little information about the nature of the changes that occur in the sample. Meanwhile, polarised-light microscopy can help differentiate between the liquid crystalline and isotropic phases, but the heating rate is not as precise and the sample is exposed to air throughout the observation. To complement the data obtained so far, dynamic mechanical analysis (DMA) has been used to investigate the mechanical properties of 1:2 BTMAAOC at three different frequencies ($f = 1, 5$ and 10 Hz) and across a wide temperature range -110 – $60\text{ }^{\circ}\text{C}$. This technique provides accurate temperature control and requires only a brief exposure to air, during sample loading.

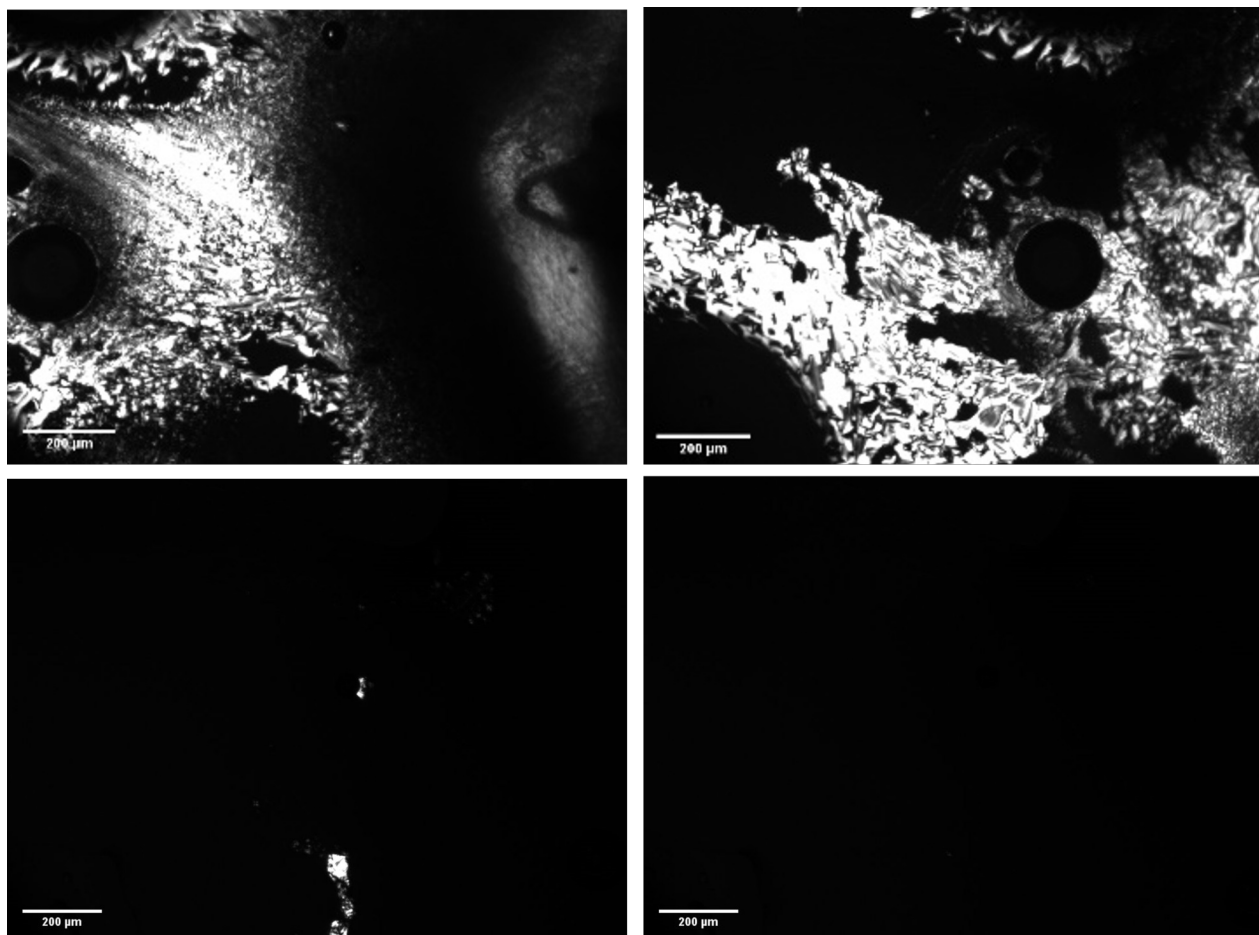


Figure 2.4. Polarised-light microscope images of 1:2 BTMAAOC taken with $4\times$ magnification. *Top:* images at 5–10 °C, taken on cooling. When pressing the glass cover slip, the birefringent texture (bright areas) shows liquid-like fluid behaviour, indicating it is associated with a liquid crystalline phase. *Bottom:* images at 25 °C, taken on heating from 5 °C. At and above this temperature, the sample is isotropic and shows no birefringence, rendering the images (almost) entirely black.

2.1.1 Dynamic Mechanical Analysis

Dynamic mechanical analysis (DMA) is a technique used to investigate how the mechanical properties of a sample change upon heating and cooling; it can be thought of as a combination of rheometry (measuring sample deformation) and DSC (the measurement is a function of temperature). In DMA, an oscillating force (stress) is applied to the sample and the resulting oscillating deformation (strain) is measured as a function of temperature, time, and/or frequency. Since both stress and strain are oscillating, there is often a phase difference (δ) between the two, depending on the measured system.¹⁰⁴

As long as the structure of the sample is not destroyed (by exceeding the stress limit of the linear viscoelastic region) then the sample behaves viscoelastically, meaning that the stress and strain are proportional (Hooke's Law); the ratio of stress to strain is known as the modulus (E). If the sample is perfectly elastic, $\delta = 0^\circ$, meaning that the stress and strain are perfectly in-phase. If the sample is entirely viscous then $\delta = 90^\circ$. Most materials, however, have both viscous and elastic contributions to their behaviour ($0^\circ < \delta < 90^\circ$) which can be disentangled. The elastic (solid) contribution is represented by the storage modulus (E'), while the viscous (fluid) contribution is represented by the loss modulus (E''); the ratio of the two moduli is the loss tangent ($\tan \delta$), defined in Equation 2.1.¹⁰⁵

$$\tan \delta = E''/E' \quad (2.1)$$

DMA is commonly used to study the behaviour of polymers and adhesives and, more recently, it has been used to study ILs.^{106–109} This technique can be used to measure $\tan \delta$, E' and E'' of a sample on heating and cooling, so is particularly useful for systems that present phase transitions and/or dynamic relaxations. Additionally, depending on the geometry used, different kinds of stress can be applied to the sample, including shear, compression, tension, or a combination thereof. In this work, the storage modulus and the $\tan \delta$ of ILs were measured on both heating and cooling. Data were collected and analysed by myself and Dr. Oriele Palumbo at the Sapienza University of Rome, Italy. The samples were loaded into a stainless steel material pocket and measured using a three point bending configuration. Due to the spatial isotropy of liquids, the mechanical modulus measured here (denoted by the symbol M') is a combination of both the shear and the bulk modulus (contains both bulk and shear components).^{102,106–108}

Figure 2.5 shows the $\tan \delta$ and storage modulus (M') data measured for 1:2 BTMAAOC at a frequency of 1 Hz. The storage modulus M' contains contributions from both the sample and the metal pocket used to hold the sample (considered a background signal). Because the two contributions cannot be disentangled, the modulus is reported not as an absolute value, but as a relative variation with respect to the value at 298 K (approximately 25 °C).^{106,107}

The thermal transitions seen in the DMA data are in agreement with the previously discussed DSC measurements. At low temperatures, there is an intense narrow peak in the $\tan \delta$ data, whose position shifts only marginally with frequency, and a significant increase (on cooling)

and decrease (on heating) of the relative change in modulus. These features correspond to the glass transition observed by DSC at $-95\text{ }^{\circ}\text{C}$. Based on DMA data, the glass transition temperature can be defined in several ways; the two most common ones are as the maximum of the $\tan \delta$ peak and as the onset temperature of the decrease in M' (on heating). Here, these temperatures are $-77\text{ }^{\circ}\text{C}$ (196 K) and $-98\text{ }^{\circ}\text{C}$ (175 K) respectively. The T_g derived from the M' data is in good agreement with the T_g measured by DSC (while the T_g derived from the $\tan \delta$ peak is higher). This is a common occurrence when comparing the two techniques,^{110–112} and it arises because the glass transition does not occur at a single temperature, but rather over a temperature range. The temperature derived from M' data corresponds to the start of the transition, while the $\tan \delta$ temperature occurs at or near the end of the transition and corresponds to the point in the glass transition region where the viscous contribution is highest. Additionally, the glass transition involves multiple modes of molecular motion, with different techniques responding to different degrees and types of motion.^{110,112} A study by Zhao *et al.* on polymers proposes that the T_g determined from $\tan \delta$ data is influenced primarily by entropic motions, while the T_g determined from M' and DSC data are representative of enthalpic molecular motions (and are therefore similar in value).^{112,113} Two other features — a broad peak in the $\tan \delta$ and a variation in the M' — are present around $-28\text{ }^{\circ}\text{C}$ (245 K). These only appear in the data measured on heating and are associated with the cold crystallisation transition, as the temperatures at which they occur are the same regardless of measurement frequency.

Finally, considering the data measured on heating, the LC-isotropic phase transition gives rise to a small decrease at $29\text{ }^{\circ}\text{C}$ (302 K) in the M' modulus and to an abrupt decrease in the $\tan \delta$ at $37\text{ }^{\circ}\text{C}$ (310 K). In the $\tan \delta$ data measured on cooling, this transition gives rise to a small step on the high-temperature side of the broad peak centred around $7\text{ }^{\circ}\text{C}$ (280 K); due to significant overlap between these two features, the T_{1-1} cannot be accurately stated. The T_{1-1} measured by DSC is approximately $20\text{ }^{\circ}\text{C}$ lower than that determined from the $\tan \delta$ data (measured on heating). This is most likely due to the samples containing different amounts of moisture, resulting from the way the samples were handled — the DSC sample was loaded and sealed under a nitrogen atmosphere, while the DMA sample was handled in air.

The last feature in Figure 2.5 is the broad peak observed at 287 K in the $\tan \delta$ measured on cooling. While the previously discussed features appear at roughly the same temperature

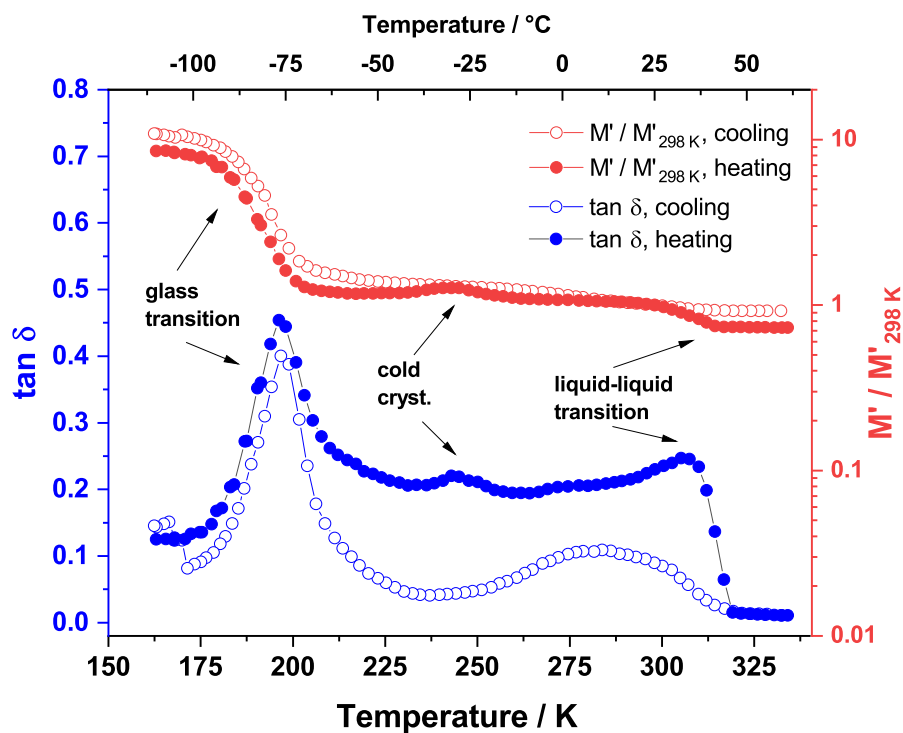


Figure 2.5. DMA data for 1:2 BTMAAOC, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.

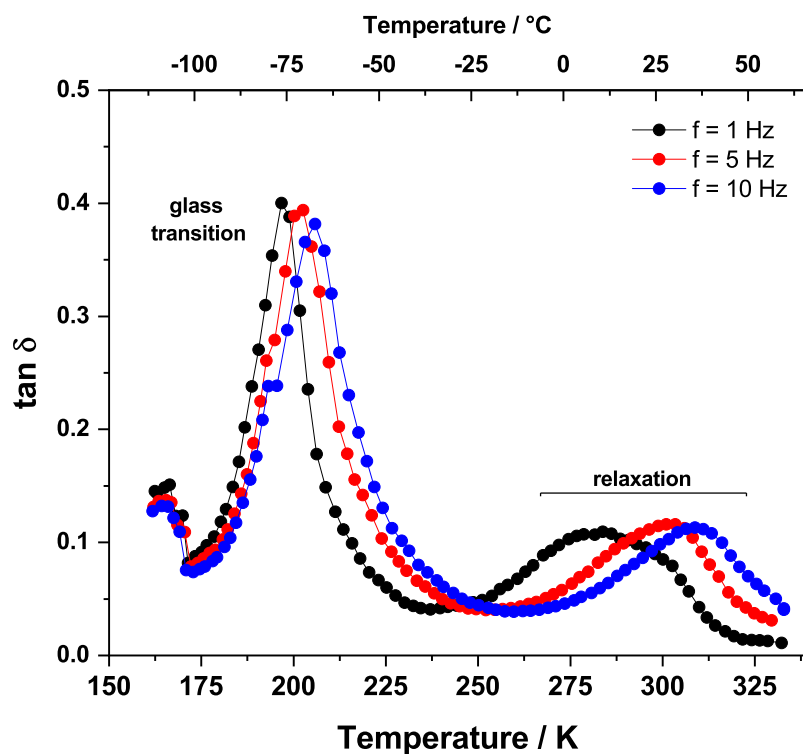


Figure 2.6. $\tan \delta$ measured for 1:2 BTMAAOC on cooling. Lines are guides for the eye.

regardless of frequency, this $\tan \delta$ peak shifts to higher temperatures as the measurement frequency increases (Figure 2.6). This is indicative of a thermally-activated relaxation process related to viscous flow (not of a phase transition) and has been reported in the literature for ionic liquids.^{102,106,108}

This process can be described using a two-state model, in which the relaxing units can transition between two different states; these can be individual minimum-energy configurations, or groups of several such configurations which are only separated by small energy barriers. The energy difference between the two states is denoted as ΔE .

The rate of the transition between two states is τ^{-1} , the inverse of the relaxation time τ . For a standard anelastic solid, the energy dissipation reaches a maximum when the expression $\omega\tau = 1$, known as the Debye relaxation condition, is true. For a single relaxation time, the loss tangent $\tan \delta$ is given by:

$$\tan \delta = \frac{\Delta(T)}{(\omega\tau)^\alpha + (\omega\tau)^{-\alpha}} \quad (2.2)$$

where ω is the angular vibration frequency, τ is the relaxation time, and α is the Fuoss-Kirkwood width parameter. For a single-time Debye relaxation $\alpha = 1$, while $\alpha < 1$ results in peaks that are broader than Debye ones.¹¹⁴ $\Delta(T)$ is the relaxation intensity and it is proportional to the elastic modulus, to the concentration of the relaxing species and to the change in the local distortion caused by the transition.¹¹⁵

The relaxation time associated with this process is temperature-dependent and can usually be described by the Arrhenius equation:

$$\tau = \tau_0 e^{W/kT} \quad (2.3)$$

However, the dynamic properties of ionic liquids, such as viscosity and diffusion coefficients, have been shown to deviate significantly from Arrhenius behaviour at and below room temperature.^{116,117} Instead, the behaviour of ILs is most commonly described using the Vogel-Fulcher-Tammann (VFT) equation; the temperature-dependence of τ is expressed as:

$$\tau = \tau_0 e^{\frac{B}{k(T-T_0)}} \quad (2.4)$$

where τ_0 , B and T_0 are empirical fit parameters. B represents an apparent activation energy (when expressed in kJ mol^{-1}) or the equivalent temperature of this activation energy (when expressed in Kelvin).

For two non-equivalent sites with an energy difference ΔE the relaxation intensity $\Delta(T)$ is proportional to the populations of the two configurations (c_1, c_2) according to equation^{106,107,115}

$$\Delta(T) \propto \frac{1}{T} \frac{c_1 c_2}{c} \propto \frac{c}{T} \text{sech}^2\left(\frac{\Delta E}{2kT}\right) \quad (2.5)$$

Combining equations 2.2 and 2.5 and the trigonometrical identity $\text{sech}(x) = \frac{1}{\cosh(x)}$, a general expression for $\tan \delta$ can be given as^{106,107}

$$\tan \delta = \frac{c}{T \cosh^2\left(\frac{\Delta E}{2kT}\right)} \frac{1}{(\omega\tau)^\alpha + (\omega\tau)^{-\alpha}} \quad (2.6)$$

where c is a collective fit parameter.

Based on the equations discussed so far, the relaxation peaks can be distinguished from peaks corresponding to thermal phase transitions by the fact that the position of a relaxation peak is frequency-dependent: as $\omega = 2\pi f$ increases, the peak maximum shifts to a higher temperature. Peaks related to the occurrence of phase transitions, on the other hand, do not shift with frequency. For a relaxation process occurring between two states, the relative intensity of the peaks can be related to their energy difference. If the two states are non-equivalent ($\Delta E \neq 0$), the intensity of the peaks increases with increasing frequency / temperature. If, on the other hand, the sites have equivalent energies ($\Delta E = 0$), the relaxation intensity follows the opposite trend and decreases with increasing frequency.

The $\tan \delta$ peaks (measured at $f = 1$ and 5 Hz on cooling) associated with the thermally-activated relaxation are shown in Figure 2.7. The data was fitted according to equations 2.4 and 2.6. Only the data associated with the relaxation was used and a linear background subtraction was performed before fitting. The $\tan \delta$ data recorded at $f = 10$ Hz could not be included in the fit due to extensive overlap between the high-temperature side of the relaxation peak and the peak corresponding to the eLC-isotropic phase transition. A less significant effect of this overlap can be seen on the high-temperature side of the $\tan \delta$ peak at $f = 5$ Hz in Figure 2.7, where the fit line begins to deviate away from the measured data. Best-fit parameters τ_0 , B , T_0 , and α are given in Table 2.1.

The peak intensities are nearly identical at all three frequencies and the optimal fit was obtained when the energy difference ΔE was set to zero. Along with the fact that the activation energy is relatively small (9.0 kJ mol^{-1}), this indicates that the relaxation is of an intermolecular nature. Considering that the calculated τ_0 is on the order of 10^{-7} s it can be concluded that

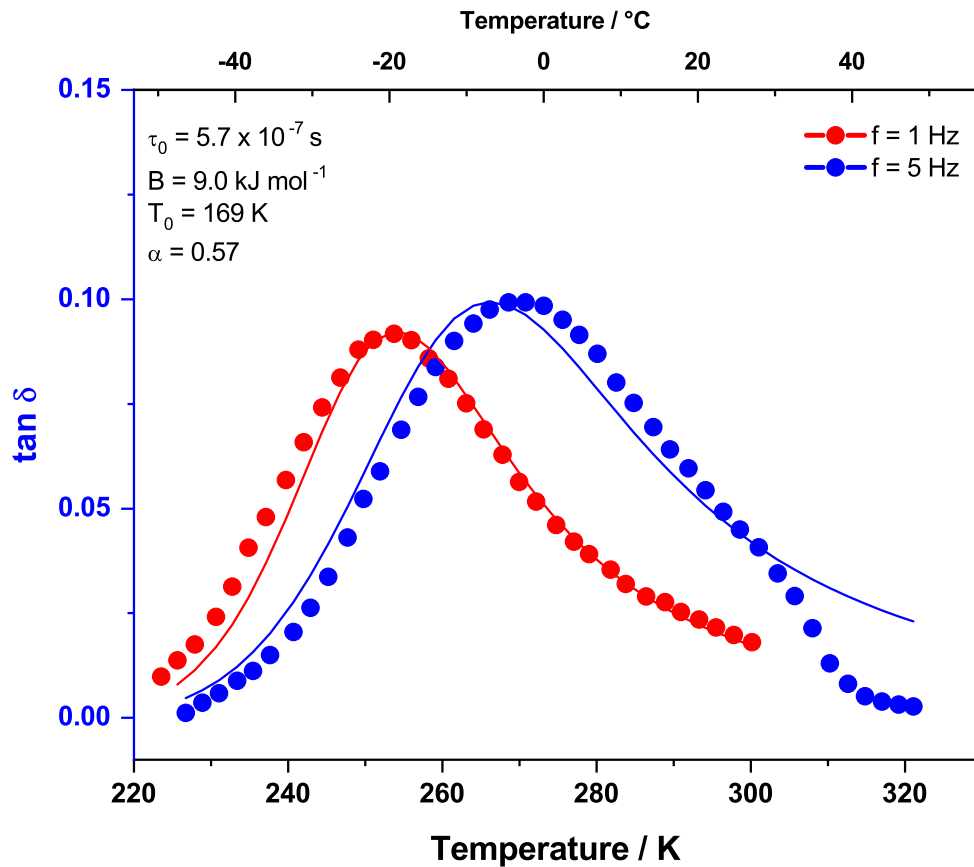


Figure 2.7. $\tan \delta$ measured for 1:2 BTMAAOC on cooling at $f = 1$ and 5 Hz. Only the data corresponding to the thermally activated relaxation is shown. The solid lines are the result of a simultaneous fit for the two frequencies. Before fitting, a linear background subtraction was performed. The data recorded at $f = 10$ Hz could not be included in the fit due to overlap with the LC-isotropic phase transition peak.

Table 2.1. Best-fit parameters τ_0 , B , T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation

Sample	$\tau_0 / 10^{-7} \text{ s}$	B / K	$B / \text{kJ mol}^{-1}$	T_0 / K	α
1:2 BTMAAOC	5.7 ± 2.0	1076 ± 26	9.0 ± 0.1	169 ± 2	0.57 ± 0.09

the thermally-activated relaxation observed for 1:2 BTMAAOC is an intermolecular diffusive process. A similar process has been previously reported for the $[\text{C}_4\text{C}_{1\text{im}}][\text{B}(\text{CN})_4]$ ionic liquid.¹⁰² It should be noted, however, that this is somewhat unusual as ionic liquids (and other viscous liquids approaching the glass transition) generally have τ_0 values of 10^{-13} – 10^{-14} s. These values are indicative of intramolecular processes dominated by conformational changes and ion flexibility.^{102,109,118} Finally, the value of α being less than one indicates that there is interaction between the relaxing units.

2.2 Viscosity

Viscosity measurements were performed by Dr. Daniel Rauber at the University of Saarland, Germany. All data analysis was performed by myself. Dynamic viscosity was used to characterise the behaviour of the IL in the isotropic phase, while oscillating viscosity measurements were performed on the liquid-crystalline sample.

2.2.1 Dynamic viscosity

Dynamic steady-shear viscosity (η) was measured over a temperature range of 25–105 °C (298.15–378.15 K). At temperatures 25–40 °C, the viscosity showed a significant dependence on the shear rate, decreasing by almost half when the shear rate was increased from 50 s^{-1} to 150 s^{-1} . At these temperatures, 1:2 BTMAAOC is in the liquid crystalline state: the IL has a gel-like consistency and a complex, viscoelastic behaviour, which cannot be accurately characterised using dynamic viscosity. This data will not be discussed; instead, the rheology of the liquid crystalline phase was investigated using oscillating viscosity measurements, which are discussed in the following subsection.

At temperatures ≥ 45 °C, 1:2 BTMAAGE showed Newtonian flow behaviour (near-constant viscosity at all shear rates), which has previously been reported for neat 1:2 CAGE at room

Table 2.2. Best-fit parameters η_0 , B and T_0 used to fit viscosity data according to the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD)

Sample	η_0 / mPa s	B / K	B / kJ mol ⁻¹	T_0 / K	AAD / %
1:2 BTMAAOC	0.0601	1135.71	9.44	172.99	0.006

temperature.¹⁴ The viscosity values for each temperature were averaged across the range of shear rates. The average viscosity values at each temperature are given in Appendix C. The temperature-dependence of the average viscosities can be described using the Vogel-Fulcher-Tammann (VFT) equation:

$$\eta = \eta_0 \cdot e^{\frac{B}{T-T_0}} \quad (2.7)$$

where η_0 , B and T_0 are empirical fit parameters. T_0 represents the temperature at which viscosity becomes infinite.¹¹⁶ This is common for ILs, whose properties tend to deviate from Arrhenius behaviour at low temperatures.^{116,117}

The average viscosities of 1:2 BTMAAOC and the lines of best fit (according to equation 2.7) are shown in Figure 2.8. Best-fit parameters and the absolute average deviation (AAD) are given in Table 2.2. The AAD was calculated according to Equation 2.8.

$$AAD = \frac{100}{N} \sum_{i=1}^N \left(\frac{\eta_{exp_i} - \eta_{calc_i}}{\eta_{exp_i}} \right) \quad (2.8)$$

where η_{exp} refers to experimental viscosity values and η_{calc} to viscosities obtained from the VFT fit (Equation 2.7).

The calculated B and T_0 parameters are comparable to those obtained from the fitting of the thermally-activated relaxation peak observed by DMA (Table 2.1). However, it must be noted that the two techniques are not performed on the same phase of the IL: the relaxation peaks observed by DMA occur at temperatures corresponding to the liquid crystalline phase, while the dynamic viscosity reflects the isotropic liquid phase of the sample. This showcases the fact that the different techniques provide consistent results about the viscous flow process and that the parameters of the observed dynamics are consistent between the liquid crystal and isotropic phases.

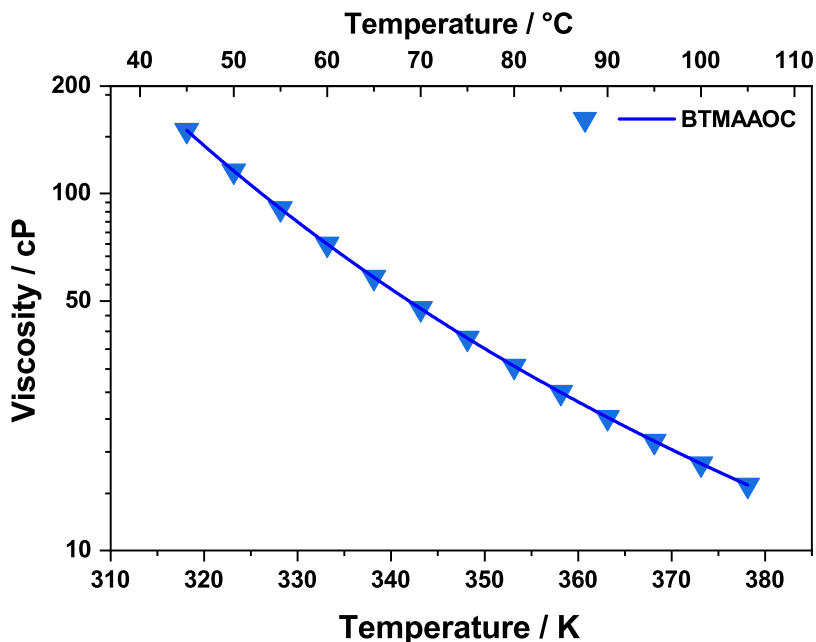


Figure 2.8. Dynamic viscosity data (symbols) for 1:2 BTMAAOC in the isotropic liquid phase. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation (line) with fit parameters shown in Table 2.2.

2.2.2 Oscillating viscosity

Apart from the isotropic phase, whose viscosity could be measured using dynamic rheometry, 1:2 BTMAAOC also exhibits a more structured liquid-crystalline state. This shows viscoelastic behaviour, which cannot be characterised using dynamic viscosity. Instead, oscillating viscosity measurements were performed over a temperature range of 25–50 °C (298.15–323.15 K). This technique measures the complex viscosity, denoted by the symbol η^* , which is comparable, but not identical, to the dynamic viscosity (η). Briefly, the dynamic viscosity is measured under a steady-shear regime and is defined as the ratio of shear stress to shear strain. The complex viscosity is measured using an oscillating stress, which elicits an oscillating response; η^* is defined as the complex modulus E^* divided by the frequency ω .

Figure 2.9 shows the complex viscosity measured for 1:2 BTMAAOC between 25 and 50 °C, which follows two distinct trends: at temperatures ≤ 35 °C (blue data) the viscosity is high at low shear rates (around 3×10^5 Pa s) and decreases with increasing shear rate. At temperatures ≥ 40 °C (red data) the viscosity is low and it is near-constant at all shear rates. The change from shear-thinning to Newtonian flow behaviour is the result of 1:2 BTMAAOC undergoing a phase transition, from a highly ordered liquid crystal to a free-flowing isotropic liquid. The

temperature that this change occurs at is higher than the transition temperature measured by DSC ($T_{11} = 17\text{ }^{\circ}\text{C}$), but is in good agreement with the transition temperature determined from the DMA data ($T_{11} \approx 30\text{--}37\text{ }^{\circ}\text{C}$). Some discrepancy between the different techniques is normal, as the exact value of the transition temperature depends on several factors, such as the thermal history and moisture content of the samples. Based on these observations, the rheology data measured at $25\text{--}35\text{ }^{\circ}\text{C}$ is attributed to the liquid crystalline phase, while data measured at higher temperatures corresponds to the isotropic liquid phase. Figure 2.10 shows how, on a log-log plot, the complex viscosity of the liquid crystalline phase decreases linearly with increasing shear rate. This indicates that the liquid crystalline sample exhibits a non-Newtonian, shear-thinning behaviour at all measured shear rates.

While non-Newtonian behaviour is often observed for viscoelastic materials, further measurements are required in order to fully characterise the behaviour of the liquid crystalline and isotropic phases of 1:2 BTMAAOC. The storage modulus (E'), loss modulus (E'') and loss tangent ($\tan \delta$) were measured using oscillating rheometry over an angular frequency range of $\omega = 0.01\text{--}100\text{ rad s}^{-1}$ and a temperature range of $25\text{--}35\text{ }^{\circ}\text{C}$ (Figure 2.11). E' and E'' are the elastic and viscous components of the complex modulus (which is measured as a ratio of stress and strain) and provide a way to disentangle viscoelastic behaviour.

The letter E is used here to denote the storage modulus, while in the previous section the storage modulus measured by DMA was denoted by the letter M . Even though they represent the same physical characteristic of the sample, the exact values of M' (measured by DMA) and E' (measured by oscillating rheometry) are not directly comparable. As mentioned in the DMA section, M' contains both bulk and shear components and, additionally, contains a background contribution from the stainless steel material pocket used in the measurement. Despite these differences, DMA and oscillating rheometry provide valuable information about how the behaviour of the sample is affected by changes in temperature and shear rate, respectively.

In the liquid crystalline phase, 1:2 BTMAAOC is a viscoelastic solid, with $E' > E''$ and $\tan \delta < 0.4$ (in agreement with DMA data) at all temperatures and shear rates. E' appears almost constant across all shear rates, while E'' undergoes a slight decrease, followed by a significant increase as the shear rate increases. This is typical of viscoelastic solid behaviour, associated with the rubbery plateau region of oscillatory stress response.¹⁰⁵ The existence of a significant storage modulus also supports the idea that the sample is in the liquid crystalline state at all

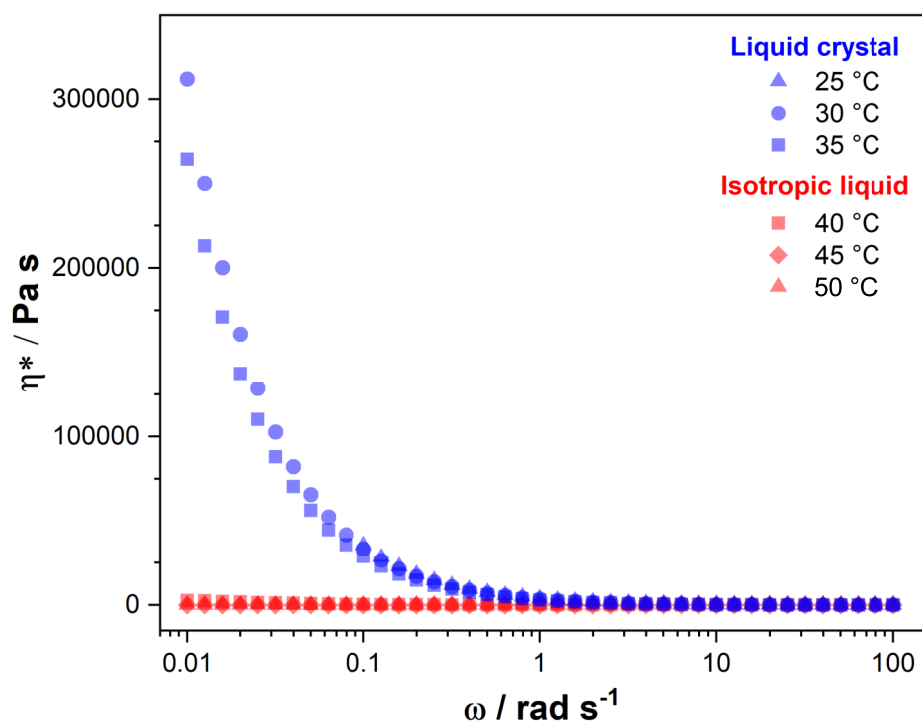


Figure 2.9. Complex viscosity of 1:2 BTMAAOC. The liquid crystal phase (blue) shows shear-thinning behaviour, while the isotropic liquid phase (red) shows Newtonian flow behaviour.

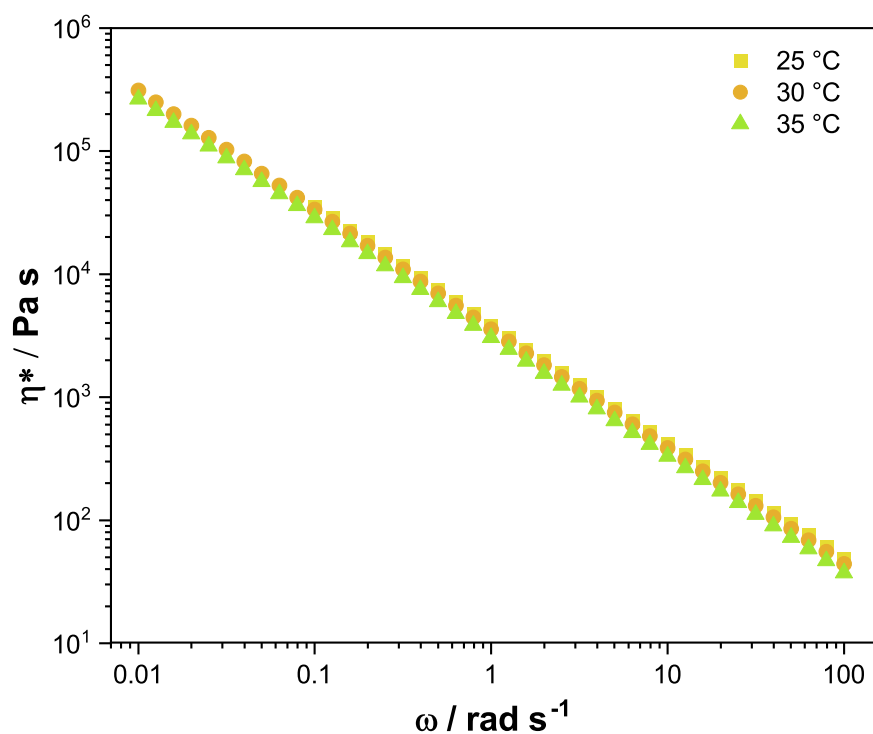


Figure 2.10. Log-log plot of the complex viscosity of liquid crystalline 1:2 BTMAAOC against shear rate. The complex viscosity decreases linearly with increasing shear rate (shear-thinning behaviour).

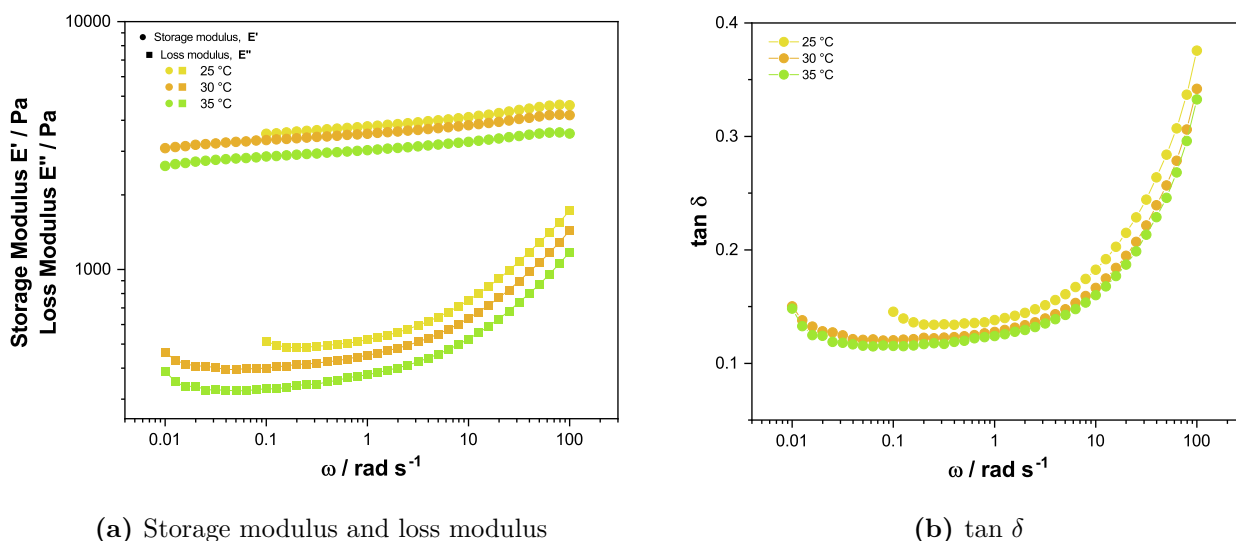


Figure 2.11. Oscillating rheometry data for 1:2 BTMAAOC in the liquid crystalline phase

temperatures shown; a liquid sample would have a negligible (near zero) storage modulus. This suggests that the liquid crystalline phase possesses some degree of ordering, in agreement with the polarised-light microscope images in Figure 2.4. The following section aims to provide more information on the type of structuring present in 1:2 BTMAAOC.

2.3 Structuring

2.3.1 NMR

The solid-state magic-angle spinning (MAS) ¹H–¹H NOESY NMR of 1:2 BTMAAOC was recorded at 20 °C and 60 °C by Dr. Mohit Devgan at Imperial College London. In both cases, the sample was heated to these temperatures from ambient temperature (approximately 15 °C).

The NOESY spectrum recorded at 20 °C is shown in Figure 2.12. According to the DSC data, the IL is in the liquid crystalline state at this temperature. The structure shown on the left side of Figure 2.12 is not meant to represent the real arrangement of molecules in 1:2 BTMAAOC and is used only to illustrate the different intermolecular interactions that give rise to crosspeaks (blue highlights and dotted lines). The charged headgroup of the BTMA cation (protons A, B) shows crosspeaks with the octyl chains of the anions (protons F, G, H, I). Additionally, the C2 proton of the octanoate anions (labeled I) shows weak crosspeaks with the butyl chain of the BTMA cation (protons C and D). The 1D ¹H SS-MAS NMR spectrum

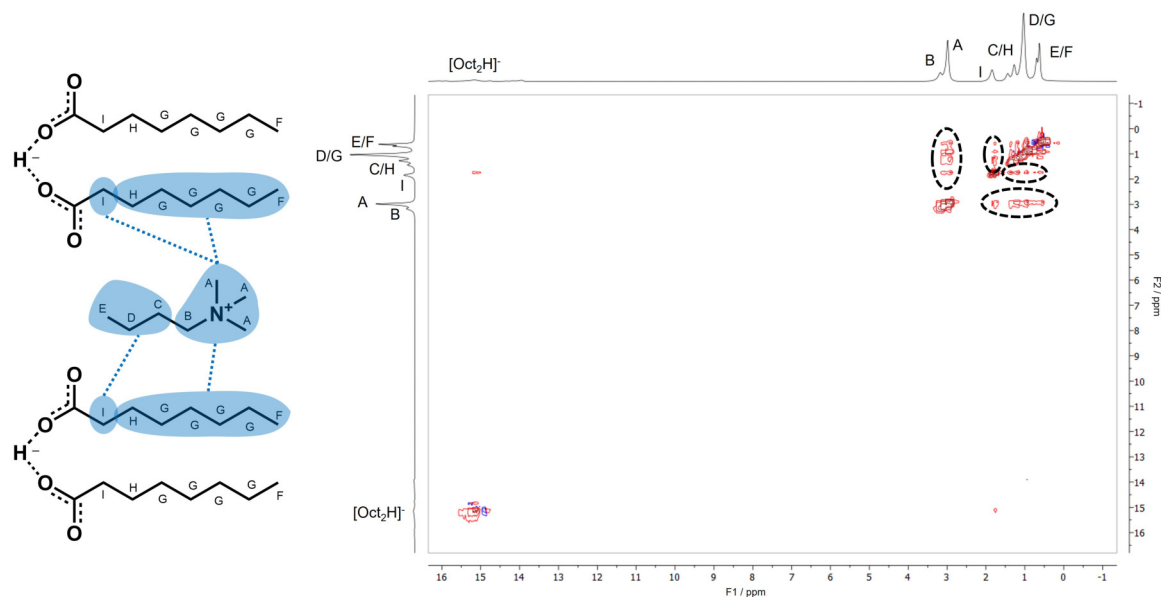


Figure 2.12. ^1H - ^1H SS-MAS NOESY NMR of 1:2 BTMAAOC recorded at 20 °C (liquid crystalline phase). Crosspeaks resulting from intramolecular interactions are circled (black dotted lines). The corresponding interactions are indicated using blue highlights and blue dotted lines.

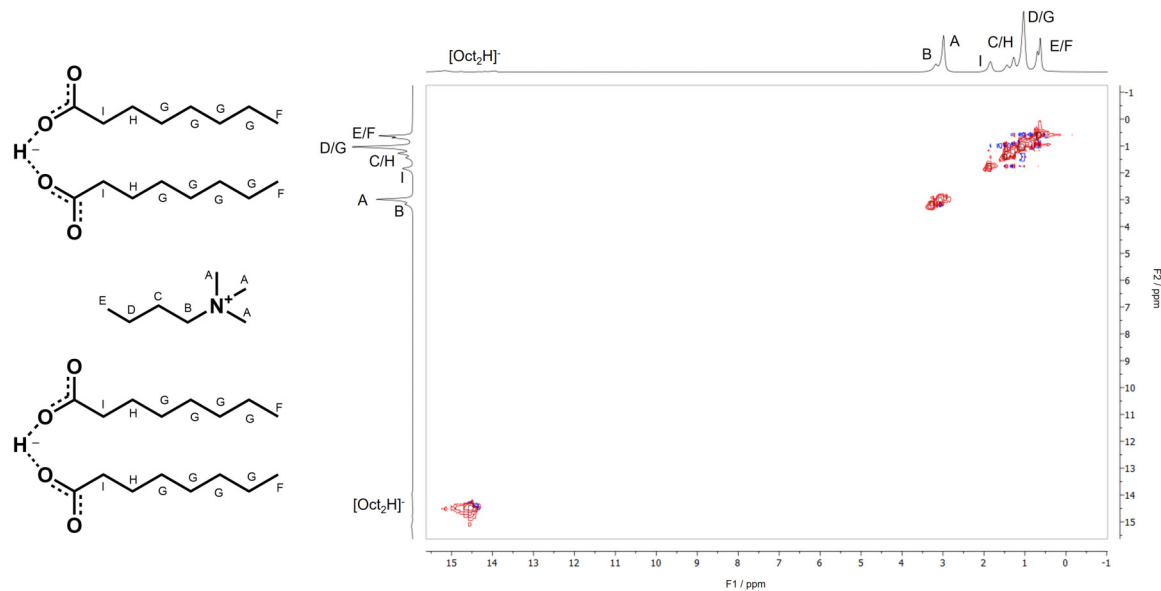


Figure 2.13. ^1H - ^1H SS-MAS NOESY NMR of 1:2 BTMAAOC recorded at 60 °C (isotropic liquid phase)

shows a signal at approximately 15 ppm, which is attributed to the proton associated with the anion complex. The idea that this proton is shared between the two geranate moieties is based on findings by Mann *et al.* on the CAGE-Oct system (discussed in more detail in Chapter 1). CAGE-Oct is synthesised using one equivalent of geranic acid and one equivalent of octanoic acid, and contains $[(\text{geranate})\text{H}(\text{octanoate})]^-$, $[(\text{geranate})_2\text{H}]^-$, and $[(\text{octanoate})_2\text{H}]^-$ clusters, with the acidic proton always being shared between two carboxylate moieties.¹³ Here, 1:2 BTMAAOC is synthesised using two equivalents of octanoic acid, so it is assumed that a complex $[(\text{octanoate})_2\text{H}]^-$ anion is formed in situ, with two octanoate moieties sharing one proton. The NMR signal of this proton appears at 15 ppm, a slightly higher value than would be expected for a carboxylic acid; this is due to the proton being shared between two anions, which causes it to be more deshielded than it would be in the acid species. Unlike in the case of CAGE-Oct, it is expected that in 1:2 BTMAAOC the main cation-anion interaction is electrostatic in nature, as the BTMA cation cannot engage in hydrogen bonding due to the lack of a hydroxyl group. While in CAGE-Oct the acidic proton exchanges with the cholinium hydroxyl proton,¹³ leading to the signal appearing at a lower, average chemical shift, no such interaction is present in 1:2 BTMAAOC. The NOESY spectrum recorded at 60 °C is shown in Figure 2.13. This temperature is significantly higher than any of the LC-isotropic phase transition temperatures measured by other techniques, and so it can be stated with certainty that the sample is in the isotropic liquid state. No crosspeaks are visible in the spectrum; while this suggests the lack of any significant intermolecular interactions, it could be an effect of the high temperature of the measurement. Using lower temperatures (or longer relaxation times) for NOESY spectra of isotropic BTMAAOC may prove more useful in future experiments.

While the information provided by the NOESY experiment is useful in trying to decipher the structure of 1:2 BTMAAOC, it is not sufficient, and must be considered alongside other techniques, such as polarised-light microscopy and X-ray scattering, in order to provide a more complete picture.

2.3.2 X-ray scattering

As discussed previously, polarised-light microscope images (Figure 2.4) show that neat 1:2 BTMAAOC is birefringent at low temperatures, suggesting that it has an ordered, liquid crystalline structure. This birefringence disappears when the sample is heated to 25 °C, slightly

above the temperature of the LC-isotropic phase transition observed by DSC. In order to better understand how the IL is structured — and how this structuring is affected by temperature — small-angle X-ray scattering (SAXS) and wide-angle X-ray scattering (WAXS) measurements were performed on neat 1:2 BTMAAOC over a temperature range of 5–60 °C (Figure 2.14a). Data was collected by Dr. Chi L. Chan and Dr. Mohit Devgan on the I22 beamline at Diamond Light Source, Didcot, Oxfordshire and analysed by myself.

SAXS data can provide information about relatively large structures (on the nanometer scale), while WAXS is used to probe much smaller distances (on the Angstrom scale), similar to techniques such as powder diffraction and single-crystal X-ray crystallography. The data discussed in this work is shown in reciprocal q -space, with $q = 2\pi/d$, where d represents a real-life distance. Here, SAXS was recorded over a q -range of 0.02–0.48 Å⁻¹, corresponding to real-life distances of approximately 13–300 Å. WAXS was recorded over a q -range of 0.16–6 Å⁻¹, corresponding to real-life distances of 1–40 Å. The q -range between 0.16–0.48 Å⁻¹ represents an overlap between the SAXS and WAXS ranges and is best captured using the SAXS detector. Thus, this data was only included in the SAXS profiles, with the WAXS data shown here starting at $q = 0.48$ Å⁻¹. The data are shown in Figure 2.14.

Figure 2.14a shows the SAXS data for 1:2 BTMAAOC at all temperatures. At 5–25 °C the profiles show a sharp peak that suggests the IL has a highly ordered, lamellar liquid crystalline structure at these temperatures, in agreement with the DSC and DMA data. The position q of the peak can be used to calculate the size of the repeating unit (the d -spacing) according to the equation $d = 2\pi/q$. At 5 °C, the sharp peak appears at $q = 0.31$ Å⁻¹, resulting in a d -spacing of approximately 20.3 Å. As the temperature of the measurement increases, the position of the sharp peak shifts to slightly higher q values, corresponding to a slight decrease in the d -spacing. At the same temperatures (5–25 °C) the WAXS data (Figure 2.14b) shows a broad peak which is slightly asymmetric on the high- q side. This is centred around $q = 1.43$ Å⁻¹ at 5 °C (corresponding to a real-life distance of 4.3 Å) and shifts to a slightly lower q value as the temperature of the measurement increases. In the case of surfactant lamellar liquid crystals (which, as mentioned, are structurally similar to the systems discussed in this work) this peak corresponds to the distance between adjacent alkyl chains in the nonpolar region. The position and shape of the peak observed for 1:2 BTMAAOC indicate that the IL exhibits a disordered lamellar phase L_α liquid crystalline phase, in which the alkyl chains are somewhat

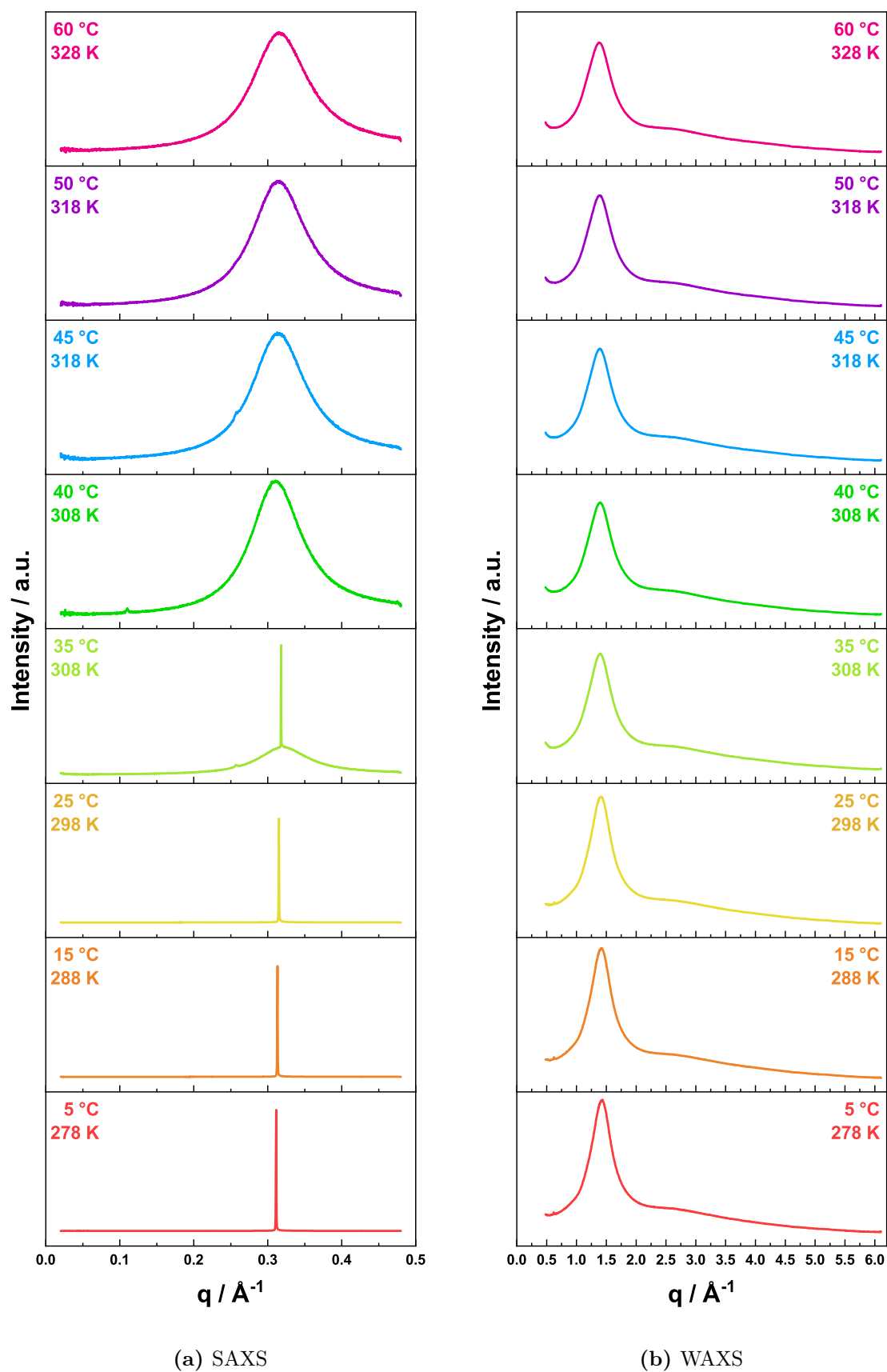


Figure 2.14. X-ray scattering data of 1:2 BTMAAOC at various temperatures

fluid and may be curled or bent.^{119,120}

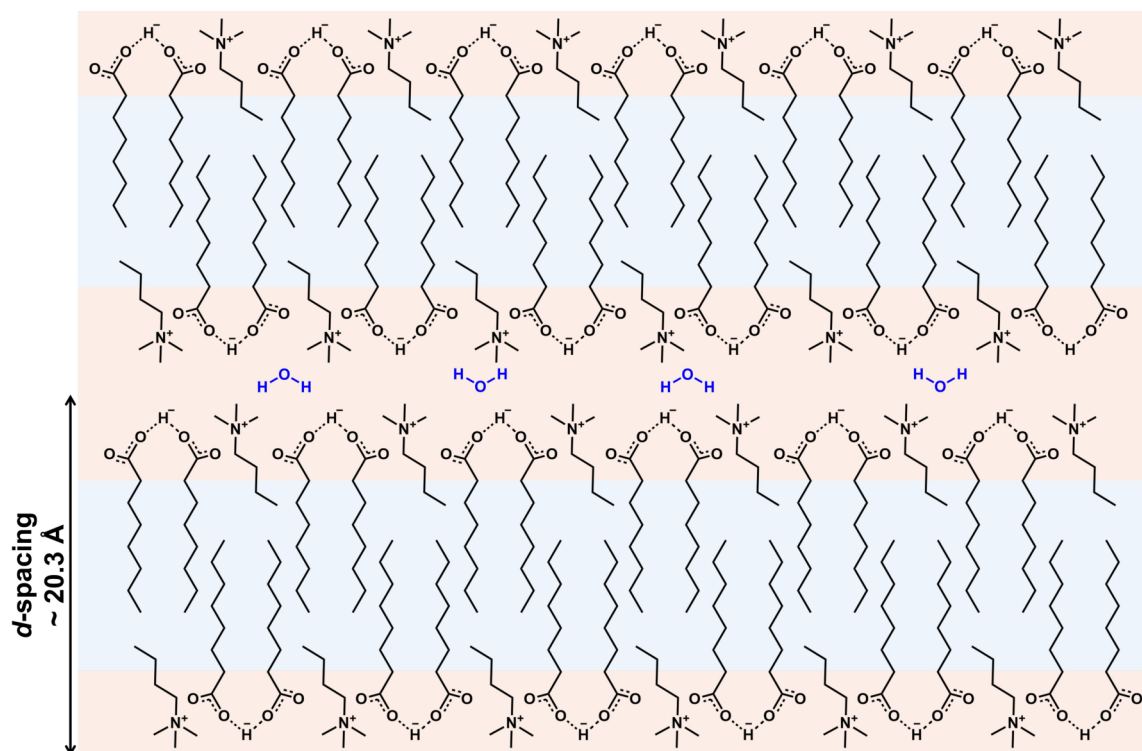


Figure 2.15. Possible structure of liquid crystalline 1:2 BTMAAOC. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 20.3 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner (associated with a complex $[(\text{octanoate})_2\text{H}]^-$ anion), the real system is a dynamic one, in which hydrogen bonds are always breaking and forming.

Figure 2.15 shows a representation of the bilayer structure that is thought to exist in the liquid crystalline phase of 1:2 BTMAAOC (i.e. between 5 and 25 °C). The bulk of the bilayer is comprised of anion species, which arrange parallel to each other, with the alkyl chains forming a nonpolar region and the charged headgroups being part of the polar region. It should be noted here that the way the $[(\text{octanoate})_2\text{H}]^-$ anion is depicted in the structure of 1:2 BTMAAOC, with a proton shared between two octanoate moieties, is a static representation of the IL structure. In reality, the system is dynamic and hydrogen bonds are constantly breaking and forming. An acidic proton is therefore not always associated with the same $[(\text{octanoate})_2\text{H}]^-$ anion but instead is mobile and is constantly exchanged between different octanoate moieties.

While the position of the BTMA cations within this bilayer cannot be determined directly from

the SAXS data, an assumption can be made by taking into account several factors, such as the hydrophobic and electrostatic interactions present in the system. As the BTMA cation is positively charged, it is most likely to reside in the polar region of the bilayer, in the vicinity of the negatively charged anion headgroups. This ensures charge neutrality through favourable cation-anion interactions and also minimises energetically demanding anion-anion interactions. Additionally, this placement allows for hydrophobic interactions between the anion alkyl chains; the alternative placement — with the cation residing in the nonpolar region — would disrupt these hydrophobic interactions and would be energetically unfavourable. The NOESY data recorded at 20 °C (Figure 2.12) also suggests a similar placement — with the BTMA cation proximal to the carboxylate end of the anion — as it shows crosspeaks between the C2 protons of anion and the butyl protons of the cation, as well as crosspeaks between the anion C2 protons and the cation NMe₃ protons. It should be noted here that the NOESY spectrum also shows crosspeaks between the NMe₃ methyl protons on the cation and the C3–C8 protons of the anion alkyl chains. The presence of these crosspeaks suggests that the protons are spatially close to each other, which in this case would require the positively charged cation to sit within the nonpolar domain. As mentioned, this would be energetically unfavourable, and the cation is thought to reside in the polar region, as shown in Figure 2.15. As this arrangement would not allow through-space interactions between the cation headgroup and the anion alkyl chains, a different explanation must be provided for the observed NOESY crosspeaks. In the literature, a similar effect is reported by Chen and Stark in a 1996 publication.¹²¹ Studying phospholipid samples with a bilayer structure, they observed NOESY crosspeaks between the methyl protons of the choline headgroup and the terminal methyl groups of the alkyl chains. Chen and Stark suggest that these crosspeaks are not due to the spatial proximity of the involved protons, but rather due to spin diffusion through the alkyl chain, facilitated by the increased level of ordering present in phospholipid bilayers.¹²¹ A similar effect could be occurring in liquid crystalline 1:2 BTMAAOC, where the cation is only proximal to the anion headgroup and to the C2 protons (labelled I in Figure 2.12), but shows crosspeaks with the other alkyl chain protons (labelled F, G, H) due to spin diffusion through the long alkyl chain. Similar spin-diffusion effects have been observed for macromolecules such as proteins.^{121,122}

Figure 2.15 also shows the presence of water, which is thought to reside in the polar domain, between adjacent IL bilayers. The water content of 1:2 BTMAAOC (after drying under high vacuum for 24 h) was measured using Karl-Fischer titration and was found to be approximately

Table 2.3. Estimated length and area values for the 1:2 BTMAAOC unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.

Chain position	d -spacing (20.3 Å)	Unit length	Unit area
No interdigitation	$d = 2 \times l_{\text{unit}}$	$l_{\text{min}} = 10.15 \text{ Å}$	$A_{\text{max}} = 66.0 \text{ Å}^2$
Partly interdigitated	$d = 1.5 \times l_{\text{unit}}$	$l_{\text{int}} = 13.53 \text{ Å}$	$A_{\text{int}} = 49.5 \text{ Å}^2$
Fully interdigitated	$d = l_{\text{unit}}$	$l_{\text{max}} = 20.3 \text{ Å}$	$A_{\text{min}} = 29.0 \text{ Å}^2$

0.4 wt% (8.3 mol%), corresponding to a ratio of 11:1 IL molecules to water molecules. Taking into account the hydrophobic effect, the water molecules are thought to reside in the polar domain, near the anion headgroups and positively charged BTMA ions. As discussed previously, the work of Mann *et al.* showed that in CAGE-Oct, a 1:2 CAGE analogue, the main cation-anion interaction is through hydrogen bonding between the hydroxyl groups of the cholinium cation and the headgroup of the anion complex. Because the BTMA cation does not contain a hydroxyl group, the residual water molecules are thought to serve an important role in the structuring of 1:2 BTMAAOC, engaging in hydrogen-bonding with the anion headgroups and helping to stabilise the bilayer structure. This is possibly the reason for the pronounced hygroscopic character of 1:2 BTMAAOC; this IL rapidly takes up moisture when exposed to air and is significantly more difficult to dry than 1:2 CAOC, its cholinium-containing counterpart (after drying, the water content of 1:2 CAOC was measured as 0.07 wt%).

In order to assess how reasonable this bilayer model is, the cross-sectional area per 1:2 BTMAAOC unit was estimated using the bilayer size (d -spacing) and the density of the IL. A 1:2 BTMAAOC is considered to comprise a BTMA cation, an octanoic acid molecule and an octanoate anion (where the latter two species may or may not form a complex anion in which the acidic proton is shared and the negative charge is delocalised across the entire headgroup).

For 1:2 BTMAAOC, the area per unit can be estimated by dividing the volume of the BTMAAOC unit by its length. The volume of one 1:2 BTMAAOC unit was calculated using the density of the IL; as this could not be obtained experimentally and has not been reported in the literature, the density of 1:2 BTMAAOC is assumed to be the same as the density of 1:2 CAGE, which was reported by Zakrewsky *et al.* to be 0.99 g mL^{-1} .⁹ Based on this, the volume of a 1:2 BTMAAOC unit is approximately 670 Å^3 . The length of the 1:2 BTMAAOC unit can be

calculated from the size of the bilayer (the d -spacing, equal to 20.3 Å) and depends on the amount of interdigitation between the alkyl chains. For fully interdigitated alkyl chains, the d -spacing is roughly equal to the unit length, giving the maximum unit length as $l_{\max} = 20.3$ Å. If there is no interdigitation, then the d -spacing would be equal to roughly twice the length of the BTMAAOC unit, giving the minimum unit length as $l_{\min} = 10.15$ Å. In reality, some amount of interdigitation is expected, and so the unit length is thought to be somewhere between these two values. As an example, an intermediate l_{int} value, corresponding to the d -spacing being equal to 1.5 times the unit length, was calculated as $l_{\text{intermediate}} = 13.53$ Å. These unit length values, as well as the corresponding cross-sectional areas, are given in Table 2.3. Comparing these values with the cross-sectional areas of other lipids (as reported in the literature) can give an indication of the validity of this bilayer model and on the degree of interdigitation present in the system. For dioleoylphosphatidylcholine (DOPC) and dipalmitoylphosphatidylcholine (DPPC) the cross-sectional area was reported to be between 40 and 70 Å²,¹²³ while for other phosphatidylcholine (PC) lipids the headgroup area was reported to be approximately 70 Å².¹²⁴ As can be seen from Table 2.3, these values are similar to the values estimated for LC 1:2 BTMAAOC, in particular to the values obtained when the chains are partially or not at all interdigitated ($d = 1.5\text{--}2 \times l_{\text{unit}}$). This suggests that the bilayer structure depicted in Figure 2.15 is a reasonable depiction of the structure of liquid crystalline 1:2 BTMAAOC.

One final aspect that must be discussed when considering the low-temperature SAXS-WAXS data is that at 5–15 °C the scattering patterns of 1:2 BTMAAOC show two distinct sets of peaks. To showcase this, the WAXS pattern recorded at 15 °C is shown in more detail in Figure 2.16. The data shown here covers a q -range of 0.15–2.0 Å^{−1} and includes the region of overlap between the WAXS and SAXS detectors.

In the full-scale graph, the most prominent feature is the narrow, intense peak at $q = 0.31$ Å^{−1}. The inset shows a zoomed-in section of the graph, between 0.2 and 1.0 Å^{−1}. Here, several peaks are visible, at q -values of $q_{A_1} = 0.26$ Å^{−1}, $q_{B_1} = 0.31$ Å^{−1}, $q_{A_2} = 0.52$ Å^{−1}, and $q_{B_2} = 0.62$ Å^{−1}. The feature at q_{B_1} which cannot be seen in its entirety is the intense peak seen in the full-scale graph; the other three peaks are extremely low in intensity and required zooming-in in this way in order to be seen properly. Despite this, they are recognizable as distinct features and not noise or artefacts, with the exception of the peak at $q_{A_2} = 0.52$ Å^{−1} which is extremely small and almost indistinguishable from noise. Still, the q -value of its position is double that

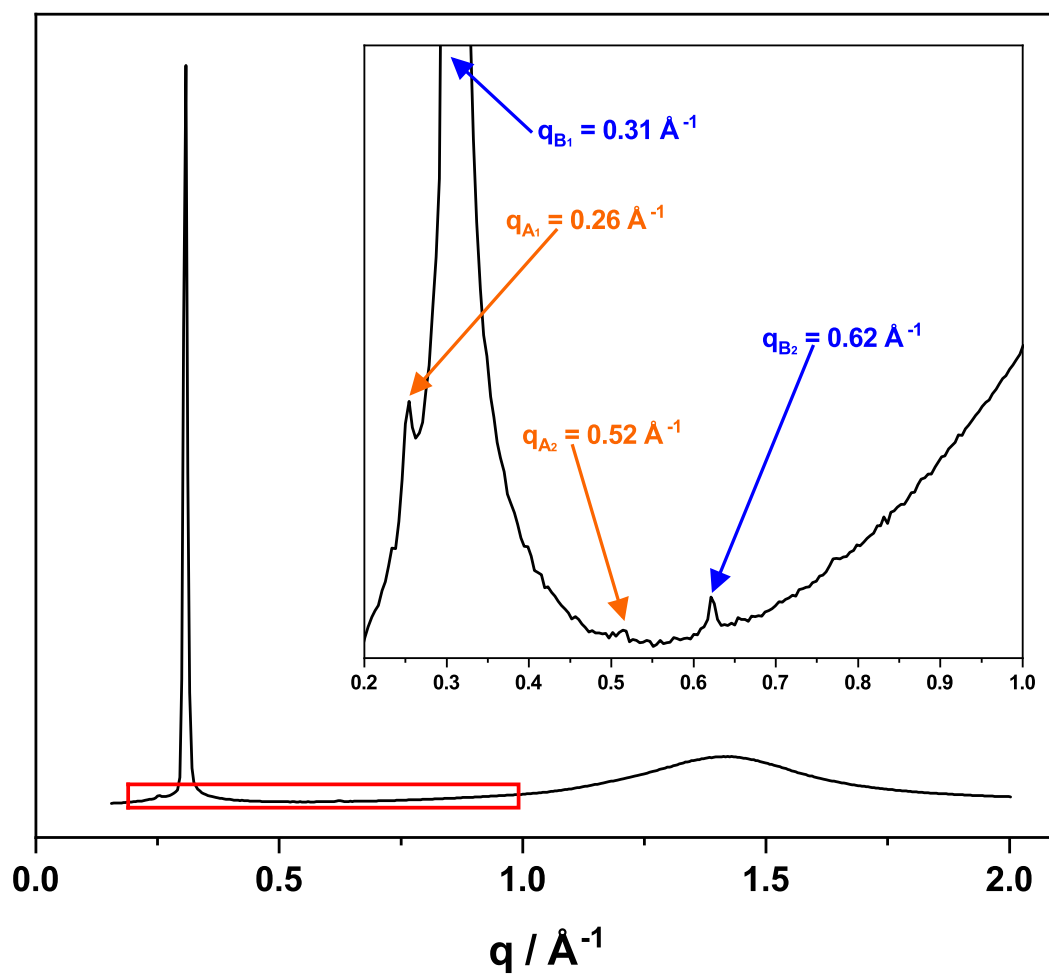


Figure 2.16. WAXS pattern of 1:2 BTMAAOC at 15 °C. Inset is a close-up of the region indicated by the red box, covering a q -range of 0.2–1.0 $\text{\AA}^{-1}$

of the peak at $0.26 \text{ \AA}^{-1}$, which corresponds to a pattern characteristic of smectic / lamellar liquid crystals with a layered structure; this supports the theory that this peak is not a random artefact but rather a meaningful piece of data.

These four peaks (indicated by arrows) can be grouped into two sets of two, coloured here in orange (set A) and blue (set B). For each set, the ratio of the two q -values is 1:2, meaning that the position of the peak at higher q is roughly double that of the peak at lower q (within the set). This, along with the fact that the peaks are sharp, rather than broad, suggests that each set of peaks corresponds to a distinct lamellar liquid crystalline phase.⁷⁹ The main structure in 1:2 BTMAAOC is the lamellar LC phase with a d -spacing of $20.3 \text{ \AA}$ associated with the peaks in set B, i.e. the very intense, narrow peak at $q_{B_1} = 0.31 \text{ \AA}^{-1}$ and the small, sharp peak at $q_{B_2} = 0.62 \text{ \AA}^{-1}$. The other set of peaks (set A) is associated with a second LC phase, with a slightly higher d -spacing of approximately $24.2 \text{ \AA}$. These scattering peaks are very low in intensity compared to the peaks in set B, with the height of peak A_1 being less than 2% of the height of peak B_1 . Taking this into account, it is thought that this second LC phase represents only a small proportion of the IL sample and it is not expected to have a significant effect on the observed properties of 1:2 BTMAAOC. The reason for the existence of this second LC phase is unknown.

As the temperature of the measurements increases, the shape of the scattering peaks changes. At $35 \text{ }^\circ\text{C}$ there is a significant change in the SAXS data (Figure 2.14). The feature at $q = 0.32 \text{ \AA}^{-1}$ appears to be an overlap of two peaks: an intense, sharp peak, similar to those observed at lower temperatures and indicative of an ordered, lamellar structure, and a broad, lower-intensity peak, which suggests a more disordered structure, with multiple preferred repeat spacings. Previous measurements have shown that 1:2 BTMAAOC undergoes a liquid-crystal-to-isotropic phase transition (from a liquid crystalline state to an isotropic liquid one). On DSC curves, this transition gave rise to an endothermic peak at $17 \text{ }^\circ\text{C}$, while in PLM photographs the birefringence associated with the LC phase was lost around $25 \text{ }^\circ\text{C}$. The change in the shape of SAXS peaks from sharp to broad is attributed to the same LC-isotropic transition. The temperature at which the onset of this transition is observed in the SAXS is higher than both the DSC and PLM transition temperatures, but is in good agreement with the transition temperatures determined from DMA and viscosity data ($35\text{--}40 \text{ }^\circ\text{C}$). The discrepancy between the transition temperatures measured by different techniques could be due to a number of

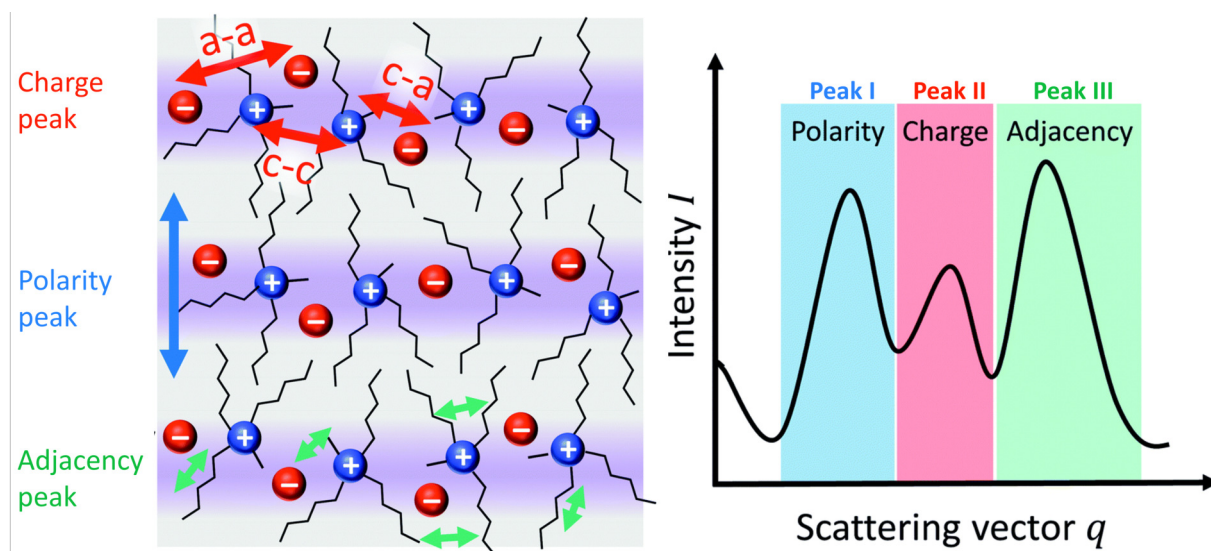


Figure 2.17. Bulk structure and scattering profile of a general ionic liquid. The scattering profile shows three peaks characteristic of IL structuring. The coloured arrows indicate the interactions / distances associated with each peak. Figure adapted from Reference [84], published by the Royal Society of Chemistry.

reasons, such as the samples containing different amounts of moisture.

As the temperature reaches 40 °C, it can be seen that the sharp peak disappears completely and the only feature present is a broad peak at $q = 0.31 \text{ \AA}^{-1}$. This is indicative of an isotropic liquid phase which possesses some degree of intrinsic ordering (a liquid with little to no ordering, e.g. ethanol, would not give rise to a peak in this q -region). The origins of this peak can be explained by considering the fact that 1:2 BTMAAOC is an ionic liquid, and examining the interactions and nanostructuring that characterise these kinds of systems. SAXS and WAXS have been extensively used in the study of ionic liquids, in order to understand the ion interactions, molecular arrangement and nanostructuring present in a variety of systems.^{80,83,84} For a general ionic liquid in the isotropic liquid phase the SAXS-WAXS data shows three distinct peaks (Figure 2.17).

Peak I (usually the lowest q value, the 'prepeak' or 'polarity' peak) is indicative of long-range structuring and is strongly correlated with the presence of nanoheterogeneity (polar and nonpolar nanodomains) in the IL. A 2006 paper by Canongia-Lopez and Padua used computer simulations to investigate the structuring of 1-alkyl-3-methylimidazolium ($[C_nC_1\text{im}]$) ILs ($2 \leq n \leq 12$).¹²⁵ In all cases, the polar moieties formed a continuous network, while the structure of the nonpolar domain was found to depend strongly on the length n of the

imidazolium alkyl chain. Small alkyl chains resulted in the formation of multiple discrete nonpolar domains, dispersed within the polar network. As the length of the alkyl chain was increased, the microdisperse nonpolar domains aggregated, forming larger and more cohesive regions. ILs with $n \geq 6$ showed the presence of one continuous nonpolar region, coexisting with the polar domain.¹²⁵ A subsequent study by Triolo *et al.* showed that the $[C_nC_1im]$ ILs which possess distinct nanodomains (i.e. $n \geq 6$) give rise to a clear peak in the low- q region ($0.2\text{--}0.5 \text{ \AA}^{-1}$).⁸⁰ As the length of the alkyl chain is increased this peak becomes sharper and shifts to lower q values, with the size of the repeating units (d -spacing) increasing linearly with n .⁸⁰ This prepeak is not observed for imidazolium ILs with very short chains (e.g. $[C_1C_1im]$, $[C_2C_1im]$) or for molecular solvents; its absence is indicative of a lack of polar-apolar alternation.¹⁹

For 1:2 BTMAAOC, the prepeak appears at approximately $0.32 \text{ \AA}^{-1}$ at temperatures between 40 and 60 °C (as well as at 35 °C, overlapping with the sharp peak). The position and shape of this peak, which appears very similar to the prepeaks observed for more conventional ILs, suggests that the isotropic phase of 1:2 BTMAAOC possesses some degree of nanostructuring, consisting of distinct polar and nonpolar nanodomains. In imidazolium ILs, the formation of such nanodomains is driven by the presence of long alkyl chains on the cation, which are able to form a contiguous nonpolar domain; the anions and charged moiety of the cation form the polar domain. An analogous structuring is likely present in 1:2 BTMAAOC, in which the long alkyl chains of the anions form a nonpolar domain, while the polar domain consists of the charged anion headgroups and cations.

Peak II (the 'charge' peak) shown in Figure 2.17 appears because of the charge alternation present in ILs and corresponds to the distance between polar groups with the same charge. The intensity of peak II comes from an interference of positive peaks associated with same-charge (cation-cation and anion-anion) interactions, and negative peaks (antipeaks), associated with opposite-charge (cation-anion) interactions. Because of this, peak II can sometimes be very weak, appearing as a shoulder, or can be completely absent in cases when the positive and negative peaks cancel each other out.¹⁹ This appears to be the case in 1:2 BTMAAOC, where the region corresponding to peak II does not show any significant features. In future, computational methods like those used by Margulis *et al.* could be useful in elucidating the contributions to the charge peak in 1:2 BTMAAOC and similar ILs.^{19,126}

Finally, peak III (the 'adjacency' peak) is observed for both ILs and molecular solvents and

its position depends on the distance between neighbouring groups.^{127,128} For ILs, it is generally associated with the distance between adjacent groups with opposite charge (cation-anion interactions), as well as with the distance between adjacent alkyl chains (chain-chain correlation length). In ILs with hydrocarbon alkyl chains, the chain-chain and cation-anion distances in these systems are similar to each other and therefore give rise to a single broad peak in the WAXS region.¹²⁸ In the case of isotropic 1:2 BTMAAOC, peak III appears in the WAXS data at all temperatures (40–60 °C) as a broad, intense feature centred around $q = 1.4 \text{ \AA}^{-1}$. Similar adjacency peaks have been reported in the literature for ILs containing alkyylimidazolium cations; for example, Elstone *et al.* report that for $[\text{C}_2\text{C}_1\text{im}][\text{NTf}_2]$ peak III is a broad feature around $q = 1.4 \text{ \AA}^{-1}$.

2.4 Chapter summary

The thermal behaviour of 1:2 BTMAAOC is complex, but not unusual for an ionic liquid. It exhibits a reversible glass transition and a cold crystallisation (followed by melting), as well as a reversible transition between a liquid crystalline mesophase and an isotropic liquid phase. The temperature of this liquid crystal to isotropic transition is approximately 17 °C when measured by DSC, but appears higher (around 35 °C) when different techniques are used. For comparison, Table 2.4 shows the temperatures of this transition measured by DSC, PLM, DMA, rheometry and X-ray scattering.

Table 2.4. Temperatures of the liquid crystal to isotropic liquid transitions

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 BTMAAOC	17	25	37*	35–40	35

^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling

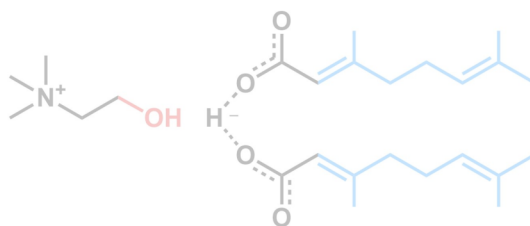
^d Temp. above which IL shows Newtonian flow behaviour

^e Temp. at which sharp LC peak disappears * Tan δ peak on heating

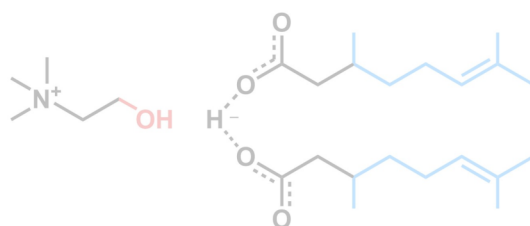
In the liquid crystalline temperature window, the predominant phase in 1:2 BTMAAOC is a lamellar liquid crystalline mesophase, with a repeating unit size of approximately 20.3 Å. The IL molecules are arranged in repeating bilayers, with the polar region of the bilayers consisting of anion headgroups, while the nonpolar region is primarily made up of the anion alkyl tails.

The BTMA cations are thought to reside within the polar region of the bilayer, near the anion headgroups, with the butyl tails possibly 'poking' into the nonpolar domain. The X-ray scattering profiles of 1:2 BTMAAGE also showed the existence of a second lamellar LC phase, with a slightly larger d -spacing of 24.2 Å. This phase is thought to comprise only a small portion of the IL sample and the reason for its presence in 1:2 BTMAAGE is unknown at the moment.

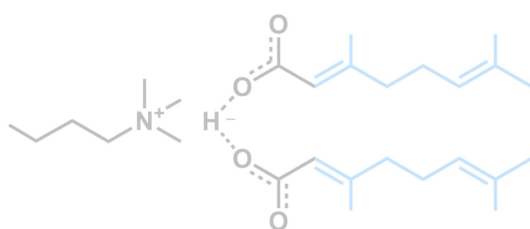
STRUCTURE COMPLEXITY



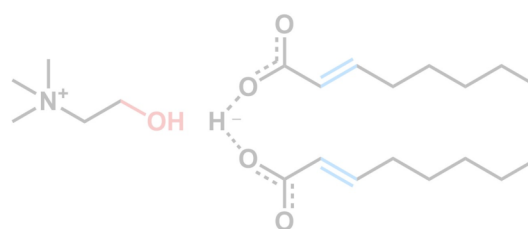
1:2 CAGE



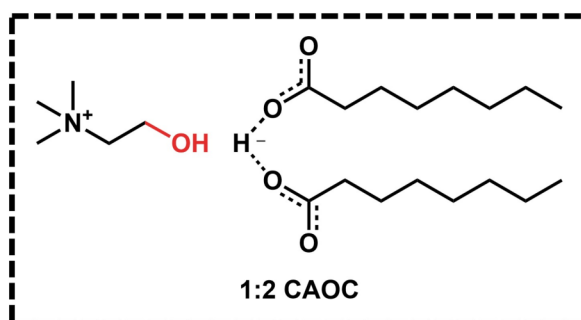
1:2 CACI



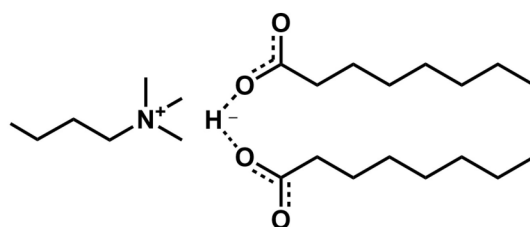
1:2 BTMAAGE



1:2 CA2OE



1:2 CAOC



1:2 BTMAAOC

Chapter 3

Choline And OCtanoate (1:2 CAOC)

The results presented in this chapter have been partially published in Reference [101].

The next ionic liquid to be discussed is 1:2 choline and octanoate (CAOC), shown in Figure 3.1. This IL is synthesised using cholinium bicarbonate and octanoic acid in a 1:2 ratio. The cholinium cation contains a hydroxyl group (highlighted in red in Figure 3.1), which can participate in hydrogen bonding with the complex anion, forming a cation-anion cluster in which the hydroxyl proton and the acidic proton undergo rapid exchange. As will be discussed in Section 3.3, the two protons experience an average environment and thus give rise to a single peak in the NMR (see Section 3.3). However, it should be noted that the complex anions are a static depiction of a dynamic system — in reality, the hydrogen bonds in 1:2 CAOC are constantly breaking and reforming and the protons are mobile and exchange between different cation/anion molecules.

This IL was chosen in order to assess the effect of the cholinium hydroxyl group on the properties of the system. Comparing 1:2 CAOC to the previously discussed IL, 1:2 butyltrimethyl-

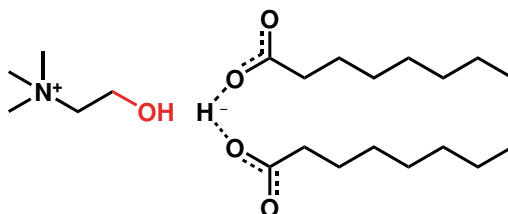


Figure 3.1. 1:2 CAOC

ammonium and octanoate (BTMAAOC), the two systems contain the same anion species ($[\text{octanoate}_2\text{H}]^-$), but different cations (cholinium and butyltrimethylammonium, respectively). This means that any differences in the properties of the two ILs are expected to be caused by the difference in cation structure, namely the presence or lack of a hydroxyl group. The data presented in this chapter aims to showcase the thermal behaviour of 1:2 CAOC and the structuring of the different phases exhibited by the IL. The discussed techniques include differential scanning calorimetry (DSC), dynamic mechanical analysis (DMA), polarised-light microscopy (PLM), small-angle and wide-angle X-ray scattering (SAXS and WAXS) and solid-state magic angle-spinning (SS-MAS) NMR.

3.1 Thermal behaviour

The thermal behaviour of 1:2 choline and octanoate (CAOC) was investigated using differential scanning calorimetry (DSC) and dynamic mechanical analysis (DMA).

DSC measurements were run by Dr. Daniel Rauber at the University of Saarland, Germany, and analysed by myself. Data was collected using a scan rate of $5\text{ }^\circ\text{C min}^{-1}$. Three consecutive heating-cooling cycles were run in order to show reproducibility (Figure 3.2).

1:2 CAOC shows a reversible glass transition at $T_g = -95\text{ }^\circ\text{C}$ (as a step in the baseline), a cold crystallisation transition, on heating, at $T_{c-c} = -35\text{ }^\circ\text{C}$ (may only be a partial crystallisation, as the exothermic peak is small and broad), and a subsequent melting transition at $T_m = -28\text{ }^\circ\text{C}$. Above this temperature, 1:2 CAOC exists in a liquid crystalline state, as evidenced by the polarised-light microscopy (PLM) images shown in Figure 3.3 (top). At $4\times$ magnification, the sample shows large areas of brightness, with a streaky, marble-like texture. When the magnification is increased to $10\times$, a clear pattern of Maltese crosses can be seen in addition to some bright streaks. Both of these textures are characteristic of a lamellar liquid crystalline phase.⁷⁹

The last set of DSC peaks observed for 1:2 CAOC consists of an exothermic peak at $50\text{ }^\circ\text{C}$, on cooling, and a corresponding endothermic peak at $52\text{ }^\circ\text{C}$ on heating. These are associated with a reversible liquid-crystal-to-isotropic phase transition, in which the sample changes from a liquid crystal (LC) to an isotropic liquid on heating (and vice versa on cooling). Visually, the IL appears very similar to 1:2 butyltrimethylammonium and octanoate (BTMAAOC): a

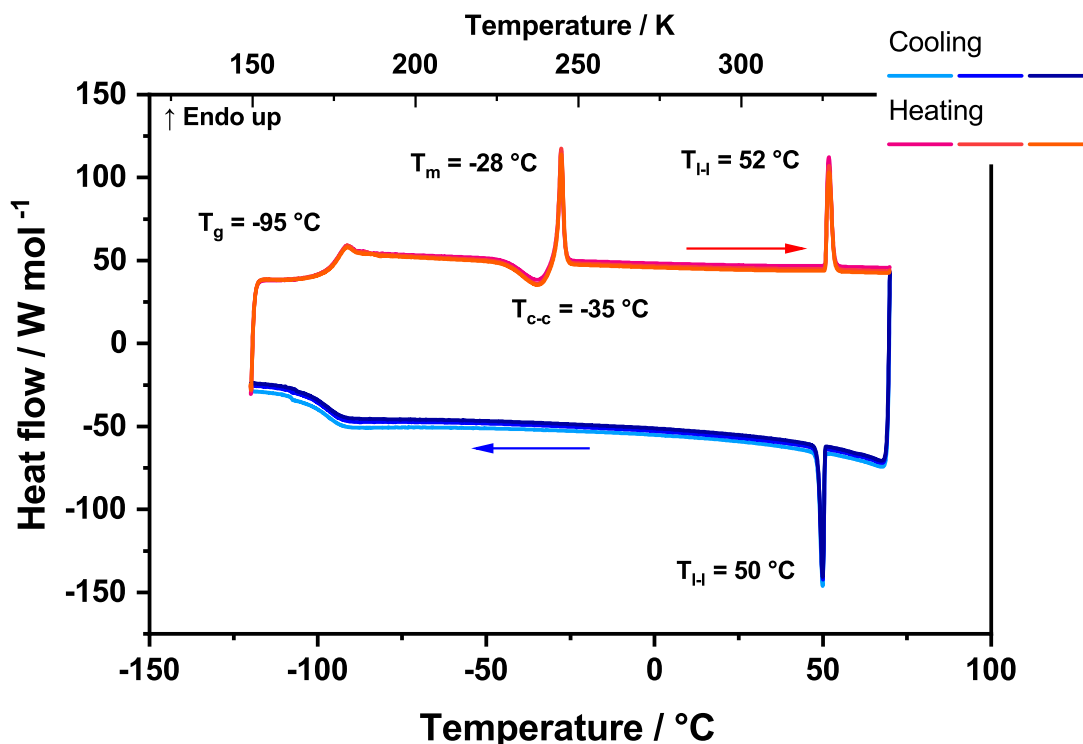


Figure 3.2. DSC traces of 1:2 CAOC with annotated transition temperatures. The heating and cooling rates are 5 °C min^{-1} .

thick, opaque gel in the LC phase and a viscous liquid in the isotropic liquid phase (Figure 3.4). PLM pictures (Figure 3.3, bottom) show that the birefringence of 1:2 CAOC begins to disappear when the sample is heated above the LC-isotropic transition temperature. At 58 °C some areas of birefringence (including Maltese crosses) can still be seen, but by 60 °C the image is completely dark, suggesting that the sample is an isotropic liquid at this temperature. The heating rate of the PLM stage was approximately 5 °C min^{-1} . The nature of each phase (liquid crystal and isotropic) is also supported by X-ray scattering data, which is discussed in Section 3.3.

The thermal behaviour of 1:2 CAOC is very similar to that observed for 1:2 BTMAAOC, showing the same types of transitions and, in some cases (T_g and T_{c-c}) nearly identical transition temperatures. There is a small difference in T_m between the two systems, with the transition to liquid crystal occurring at a lower temperature for 1:2 CAOC ($T_m = -28\text{ °C}$ for 1:2 CAOC, compared to $T_m = -20\text{ °C}$ for 1:2 BTMAAOC). There is also a significant difference between the temperatures of the liquid crystal to isotropic transitions (T_{LI}). In the case of 1:2 BTMAAOC, the LC to isotropic transition is observed by DSC at 17 °C , while for 1:2 CAOC this transition occurs at 52 °C , 35 °C higher. This means that the LC phase of 1:2 CAOC is

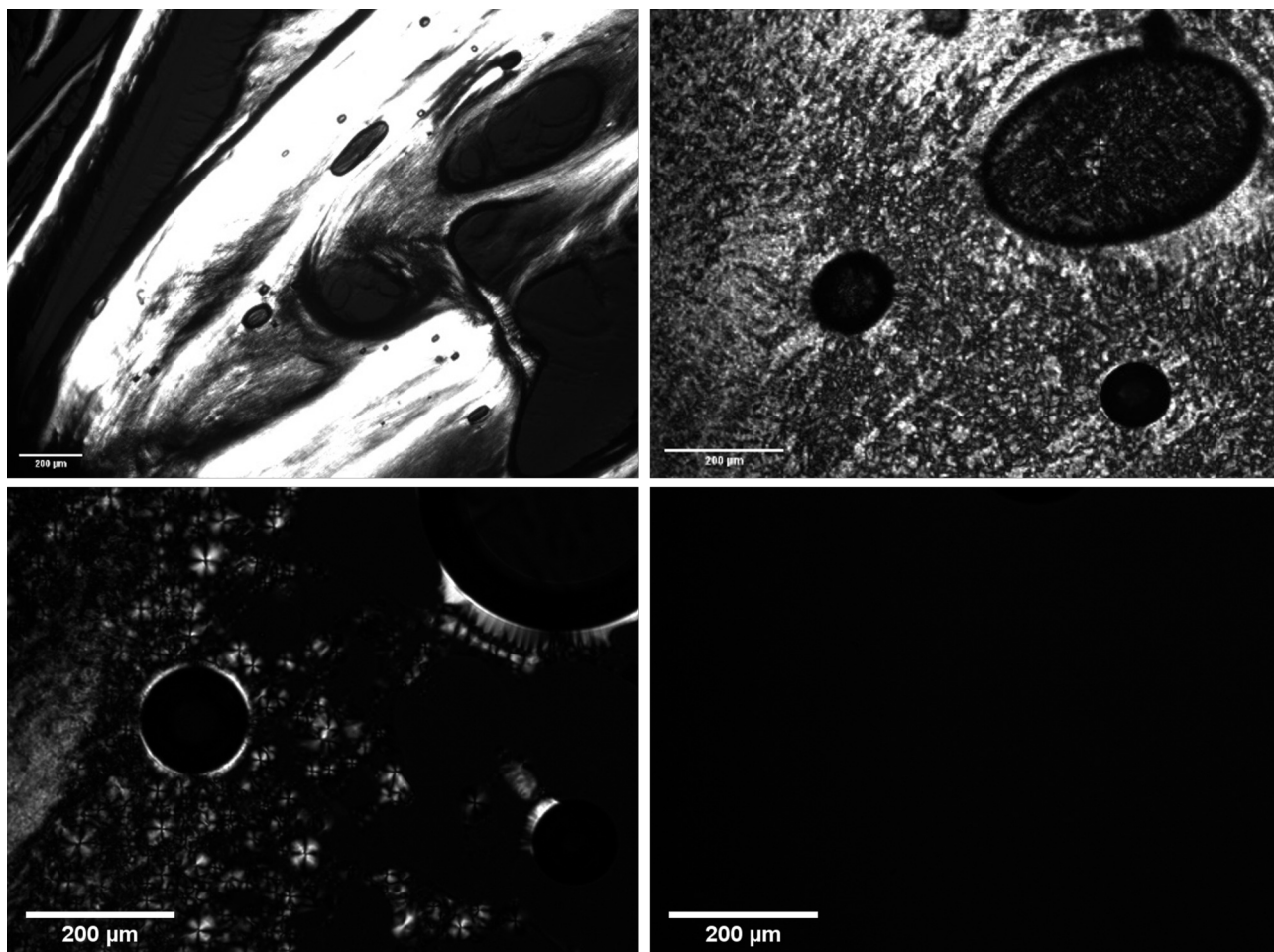
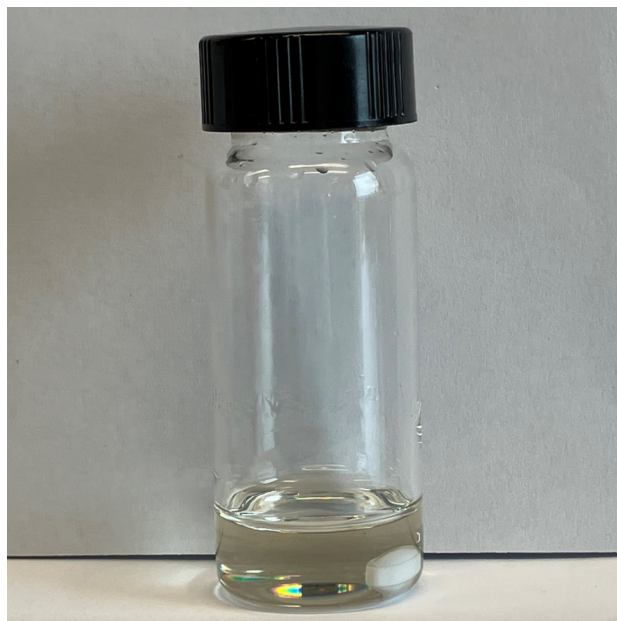


Figure 3.3. Polarised-light microscope images of 1:2 CAOC, taken on heating. *Top:* images of the liquid crystalline phase, taken at 15 °C with 4×(left) and 10×(right) magnification. The light areas are indicative of birefringence, a characteristic of liquid crystalline materials. Additionally, when pressed, the birefringent texture shows liquid-like fluid behaviour, indicating it is associated with a liquid crystalline phase. *Bottom:* images of the isotropic phase, taken at 58 °C (left) and 60 °C (right).



(a) Liquid crystalline phase



(b) Isotropic liquid phase

Figure 3.4. 1:2 CAOC before and after the LC-isotropic phase transition

stable over a larger temperature window (-28 – 52 °C) than the LC phase of 1:2 BTMAAOC (-20 – 17 °C).

The main structural difference between these ILs is the nature of the cationic species, which is a butyltrimethylammonium (BTMA) cation in 1:2 BTMAAOC and a cholinium cation in 1:2 CAOC. The latter contains a hydroxyl group, which allows it to interact with the anion species not only through Coulombic interactions (as is the case for the BTMA cation), but also through hydrogen bonds. These additional interactions lead to a more structured system in 1:2 CAOC and thus to the increased stability observed for the LC phase. The structuring of the 1:2 CAOC system will be discussed in greater detail in Section 3.3.

3.1.1 Dynamic Mechanical Analysis

In addition to the DSC and PLM data, dynamic mechanical analysis (DMA) measurements were performed in order to understand the effect of the thermal transitions on the IL rheology. Measurements were run by myself and Dr. Oriele Palumbo at the Sapienza University of Rome and analysed by myself. Data was collected over a temperature range of -140 – 70 °C, at three different frequencies ($f = 1, 5$ and 10 Hz). Figure 3.5 shows the DMA data (storage modulus M' and loss tangent $\tan \delta$) collected for 1:2 CAOC at $f = 1$ Hz on cooling and subsequent

heating. As before, the modulus is reported as a relative variation with respect to the value at 298 K (25 °C) — this is denoted as M'_{298K} .

The transitions observed by DSC are also present in the DMA data. The signature of the glass transition is the intense, narrow peak in $\tan \delta$ that is observed on both heating and cooling at approximately 187 K (−86 °C). This is accompanied by a corresponding change in the storage modulus: a sharp increase on cooling and decrease on heating. The onset temperature of the decrease in M' on heating is approximately 174 K (−99 °C). As was the case for 1:2 BTMAAOC, the glass transition temperature T_g obtained from the M' data agrees with the T_g obtained from the DSC measurements, while the T_g that corresponds to the $\tan \delta$ peak is slightly higher (by approximately 10 °C).

The data obtained on heating also shows some features that do not occur on cooling: a peak in the $\tan \delta$ around 230 K (−45 °C) and an increase, rapidly followed by a decrease, in the storage modulus M' . These are associated with the cold crystallisation and melting transitions. Finally, the $\tan \delta$ data measured on cooling shows a broad peak centred around 255 K (−18 °C) which has a small shoulder feature at 325 K (52 °C). As can be seen from Figure 3.6, which shows the $\tan \delta$ data measured on cooling at $f = 1, 5$ and 10 Hz, the position of the shoulder peak is frequency-independent, indicating that it is associated with a thermal transition — specifically, the liquid crystal to isotropic transition. Here, the temperature of this transition (52 °C) agrees well with the temperature obtained from DSC data ($T_{1-1} = 50$ °C on cooling).

Unlike the other features, the broad peak seen at 255 K (−18 °C) in Figure 3.5 shifts to higher temperatures as the frequency of the measurement increases (this feature is marked 'relaxation' in Figure 3.6). These peaks do not correspond to a thermal phase transition, but rather to a thermally activated relaxation. The relevant theory and equations are discussed in more detail in Section 2.1.1. The data associated with the relaxation process was fitted according to equations 2.4 and 2.6 (a linear background subtraction was performed before fitting). Measurements performed at all three frequencies ($f = 1, 5$, and 10 Hz) were successfully included in the fit (unlike in the case of 1:2 BTMAAOC, where the $f = 10$ Hz data could not be used). However, due to overlap between the thermally activated relaxation peak and the peak corresponding to the LC-isotropic phase transition, the fit on the high-temperature side shows a slight deviation from the experimental data. Experimental and fitted data are shown in Figure 3.7, with the best-fit parameters given in Table 3.1.

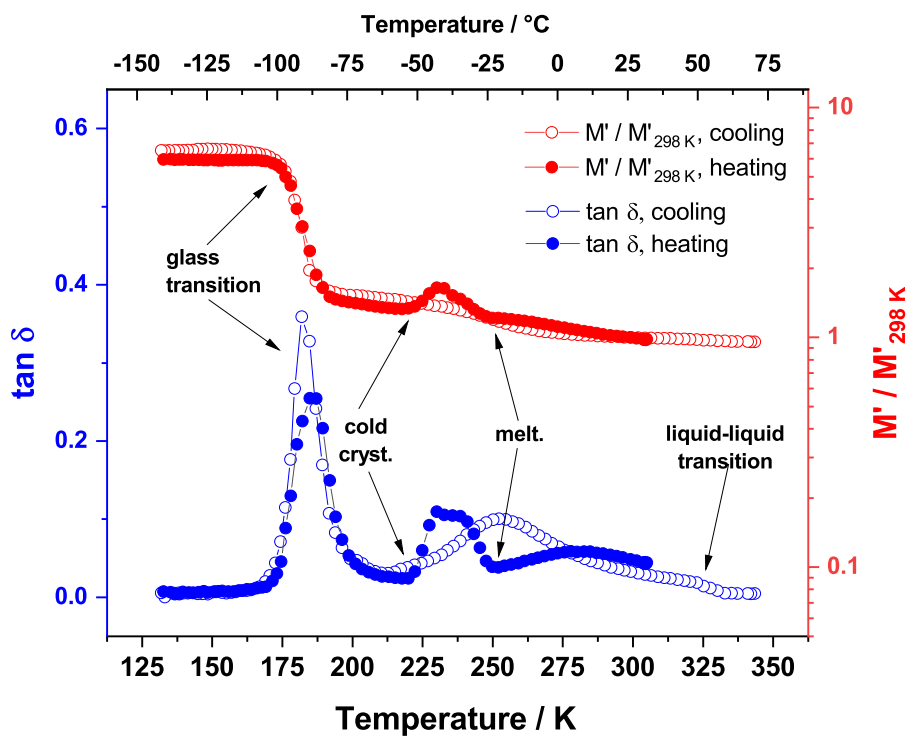


Figure 3.5. DMA data for 1:2 CAOC, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols)

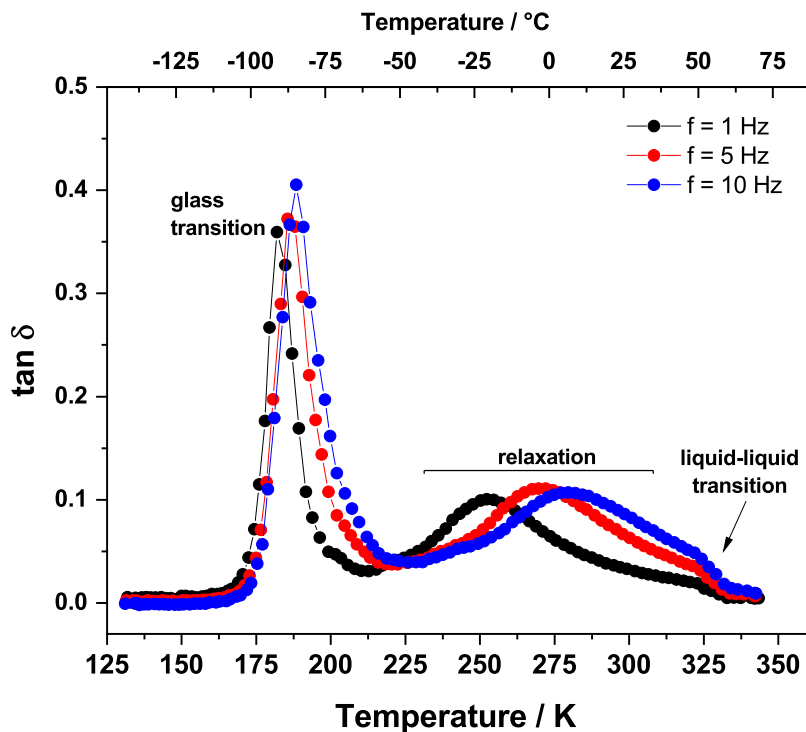


Figure 3.6. $\tan \delta$ measured for 1:2 CAOC on cooling

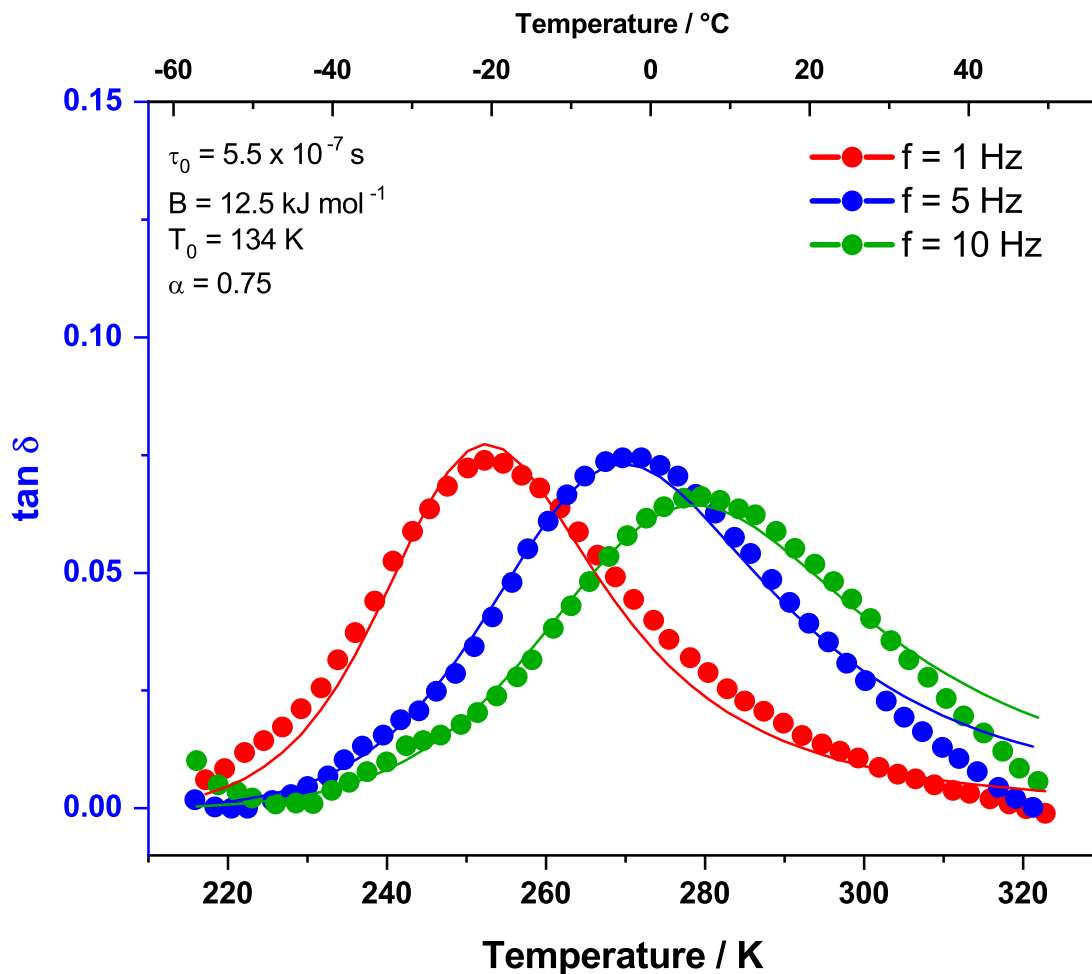


Figure 3.7. $\tan \delta$ measured for 1:2 CAOC on cooling at $f = 1, 5$, and 10 Hz. Only the data corresponding to the thermally-activated relaxation is shown. The solid lines are the result of a simultaneous fit across the three frequencies. Before fitting, a linear background subtraction was performed.

Table 3.1. Best-fit parameters τ_0 , B , T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 CAOC (top row). For comparison, data is also shown for 1:2 BTMAAOC.

Sample	$\tau_0 / 10^{-7} \text{ s}$	B / K	$B / \text{kJ mol}^{-1}$	T_0 / K	α
1:2 CAOC	5.5 ± 0.1	1503 ± 19	12.5 ± 0.2	134 ± 2	0.75 ± 0.01
1:2 BTMAAOC	5.7 ± 2.0	1076 ± 26	9.0 ± 0.1	169 ± 2	0.57 ± 0.09

The peak intensities do not increase with frequency, indicating that the relaxation process occurs between two configurations with equivalent energies. Accordingly, the best fit was obtained when the energy difference $\Delta E = 0$. The calculated activation energy B was slightly higher than for 1:2 BTMAAOC. This suggests that the interactions present in 1:2 CAOC are stronger than those in 1:2 BTMAAOC, which agrees with the trend observed for the temperatures of the LC-isotropic transitions and with the hypothesis that the presence of the hydroxyl group leads to increased hydrogen bonding and stronger interactions. Still, the activation energy remains relatively small ($B = 12.5 \text{ kJ mol}^{-1}$), and the relaxation time τ_0 is nearly identical to that calculated for 1:2 BTMAAOC (on the order of 10^{-7} s). Together, these parameters suggest that the thermally activated relaxation in 1:2 CAOC is an intermolecular diffusive process, similar to that observed for 1:2 BTMAAOC. Finally, the best-fit value of α is below one and suggests that there is interaction between the relaxing units.

3.2 Viscosity

Viscosity measurements were performed by Dr. Daniel Rauber at the University of Saarland, Germany. All data analysis was performed by myself. Dynamic viscosity measurements were used for the IL in the isotropic phase, while the liquid crystal phase was investigated using oscillating viscosity measurements.

3.2.1 Dynamic viscosity

Dynamic viscosity measurements were performed over the temperature range 55–105 °C (328.15–378.15 K). 1:2 CAOC is in the isotropic phase at these temperatures and shows Newtonian flow behaviour, where its viscosity does not vary significantly with shear rate. Thus, for each temperature, the viscosity values were averaged across the entire range of shear rates (50–150 s^{-1}). These values are shown in Figure 3.8 in orange (filled symbols); viscosity data for 1:2 BTMAAOC is also shown here in blue to aid comparison. As was the case for isotropic 1:2 BTMAAOC, the viscosity of isotropic 1:2 CAOC varies with temperature according to the Vogel-Fulcher-Tammann (VFT) equation. The line of best fit is shown in Figure 3.8, also in orange; best-fit parameters and the absolute average deviation (AAD, Equation 2.8) are given in Table 3.2.

Table 3.2. Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD)

Sample	η_0 / mPa s	B / K	B / kJ mol ⁻¹	T_0 / K	AAD / %
1:2 CAOC	0.0412	1517.05	12.61	146.90	0.02
1:2 BTMAAOC	0.0601	1135.71	9.44	172.99	0.006

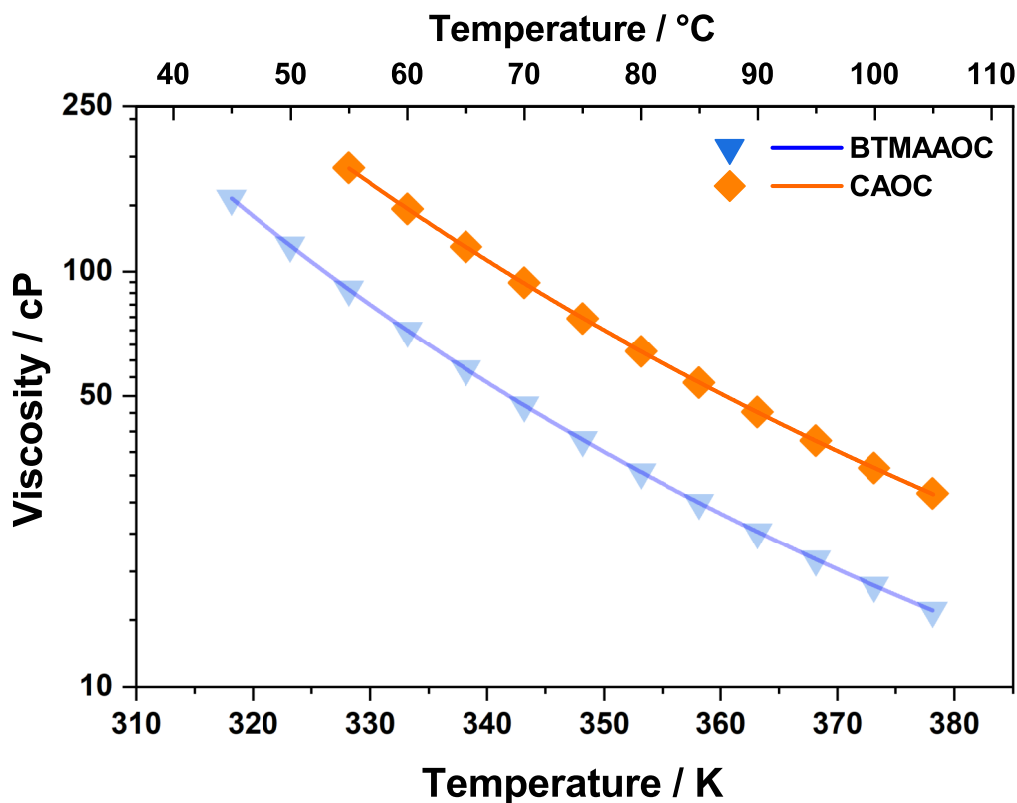


Figure 3.8. Dynamic viscosity data (symbols) for 1:2 CAOC in the isotropic phase (shown in orange). The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation (line), with the fit parameters shown in Table 3.2.

Parameters B and T_0 are comparable to those calculated from DMA data associated with the thermally activated relaxation. As mentioned before, the DMA data pertains to the liquid crystalline phase of the IL, while the dynamic viscosity measurements are performed on the isotropic phase. Nonetheless, the parameters derived from these two techniques agree for both 1:2 CAOC and, as previously seen, for 1:2 BTMAAOC. This indicates that the dynamics of viscous flow are similar across the two phases (LC and isotropic). Comparing 1:2 CAOC and 1:2 BTMAAOC, Figure 3.8 shows that isotropic 1:2 CAOC has a greater viscosity than isotropic 1:2

BTMAAOC at all studied temperatures. Once again, this suggests the existence of stronger intramolecular interactions in 1:2 CAOC as a result of the cation's ability to participate in hydrogen bonding.

3.2.2 Oscillating viscosity

The liquid crystalline phase of 1:2 CAOC shows viscoelastic behaviour, which was characterised using oscillating rheometry over a temperature range of 30–70 °C (303.15–343.15 K). It should be noted here that this technique measures the complex viscosity η^* , which is not identical to the viscosity η measured by the dynamic method. Figure 3.9 shows the dependence of complex viscosity on the shear rate ω (measured in rad s^{-1}). The data shown in blue is recorded at temperatures ≤ 50 °C and corresponds to the liquid crystalline phase of 1:2 CAOC. At these temperatures, the IL has a high viscosity at low shear rates (approximately 7×10^5 Pa s at its highest). As the shear rate is increased, the complex viscosity decreases; on a log-log plot this decrease is linear (Figure 3.10). Similar shear-thinning behaviour was also observed for liquid crystalline 1:2 BTMAAOC and has been reported in the literature for some more common ILs (even though these do not exhibit a LC phase).^{129,130} Once temperatures above 50 °C are reached, the complex viscosity is greatly reduced and does not vary significantly with shear rate. This data, shown in red, is associated with the isotropic liquid phase of 1:2 CAOC, whose rheological properties have been investigated by dynamic rheometry and discussed in the previous section. The temperature at which this change in behaviour occurs (somewhere between 50 and 55 °C) is in agreement with the temperature of the LC-isotropic transition measured by DSC and DMA.

Oscillating rheometry was also used to measure the storage and loss moduli E' and E'' , as well as the loss tangent $\tan \delta$ of 1:2 CAOC at temperatures between 30–50 °C (303.15–343.15 K). The loss tangent $\tan \delta$ (Figure 3.11b) is small (<0.2 at all temperatures and shear rates) which agrees with the $\tan \delta$ measured by DMA. The storage modulus E' does not vary significantly with shear rate, while the loss modulus E'' undergoes a decrease at low shear rates and an increase at high shear rates. This behaviour was also observed for 1:2 BTMAAOC and is typical of viscoelastic solids. E' is higher than E'' at all temperatures and shear rates (Figure 3.11a), indicating that the LC phase of 1:2 CAOC has primarily elastic solid behaviour. The fact that a significant storage modulus was measured by both oscillating rheometry and DMA

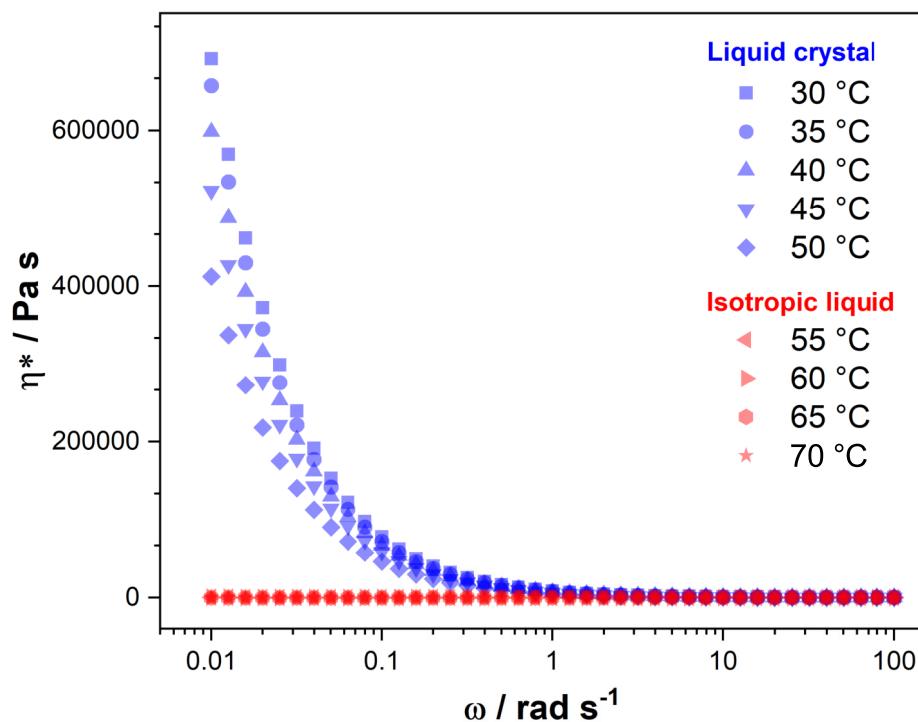


Figure 3.9. Complex viscosity of 1:2 CAOC. The liquid crystal phase (blue) shows shear-thinning behaviour, while the isotropic liquid phase (red) shows Newtonian flow behaviour.

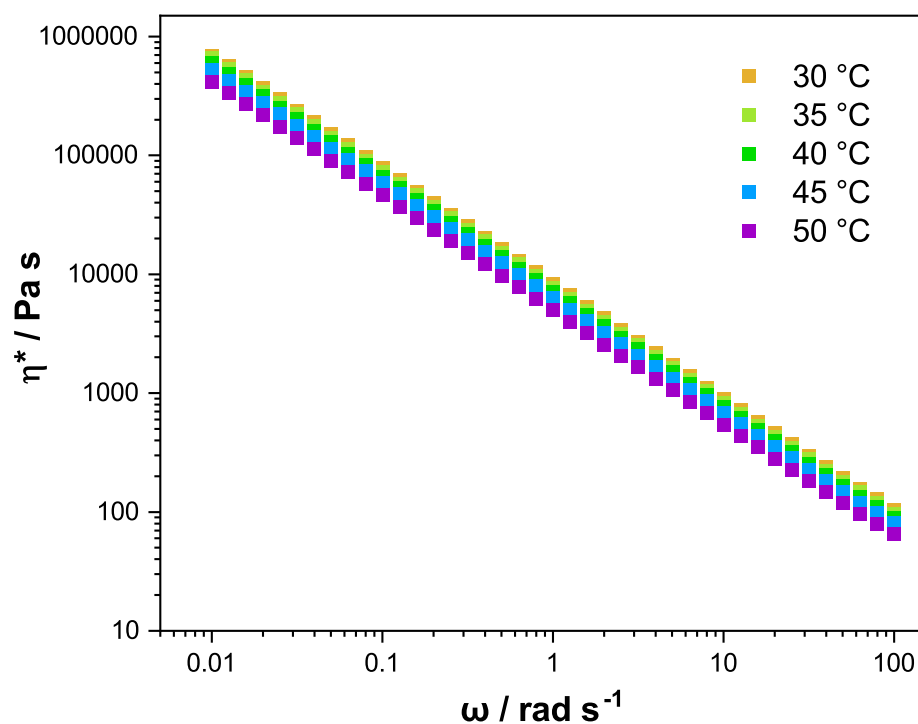


Figure 3.10. Log-log plot of the complex viscosity of liquid crystalline 1:2 CAOC against shear rate. The complex viscosity decreases linearly with increasing shear rate (shear-thinning behaviour).

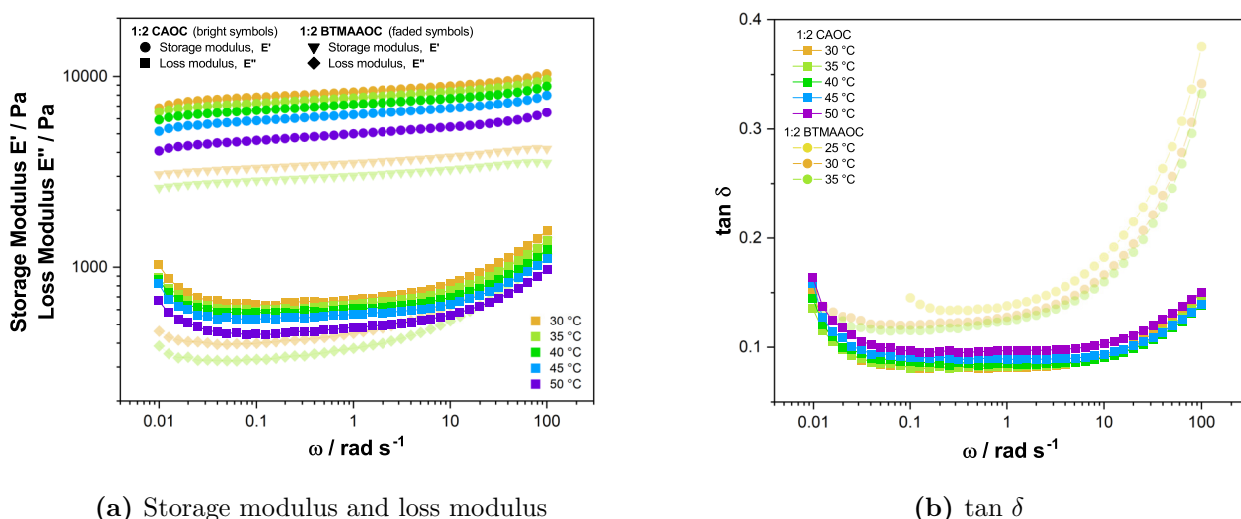


Figure 3.11. Oscillating rheometry data for 1:2 CAOC in the liquid crystalline phase, shown as filled, opaque symbols. For comparison, oscillating rheometry data for the liquid crystalline 1:2 BTMAAOC is also shown as filled symbols with a faded appearance.

supports the fact that this phase is a liquid crystalline one (as for a typical isotropic liquid E' would be near zero).

Comparing the rheology of 1:2 CAOC and 1:2 BTMAAOC (in their LC phases), the behaviour of 1:2 CAOC has a stronger elastic contribution, with higher E' and lower $\tan \delta$ values than 1:2 BTMAAOC. Additionally, 1:2 CAOC has a higher viscosity than 1:2 BTMAAOC. The complex viscosities of the two liquid crystalline ILs are shown in Figure 3.12 as a log-log plot against shear rate. At equal shear rates, the complex viscosity of 1:2 CAOC is greater than the viscosity of 1:2 BTMAAOC, regardless of the sample temperature. For example, at $\omega = 1 \text{ rad s}^{-1}$, the lowest viscosity measured for 1:2 CAOC (at 50 °C) is still slightly higher than the highest viscosity measured for 1:2 BTMAAOC (at 25 °C): $\eta^*_{1:2 \text{ CAOC}, 50 \text{ °C}} > \eta^*_{1:2 \text{ BTMAAOC}, 25 \text{ °C}}$. All of this supports the fact that the presence of a hydroxyl group in 1:2 CAOC leads to stronger interactions and a higher degree of ordering in the IL structure. Oscillating rheometry measurements were also run at higher temperatures, above the temperature of the LC-isotropic phase transition for both 1:2 CAOC and 1:2 BTMAAOC, but the data could not be accurately recorded. At these temperatures, E' tends to zero, driving $\tan \delta$ to infinity, further supporting the fact that the phase exhibited by the two ILs at high temperatures ($T > T_{\text{LI}}$) is an isotropic liquid phase.

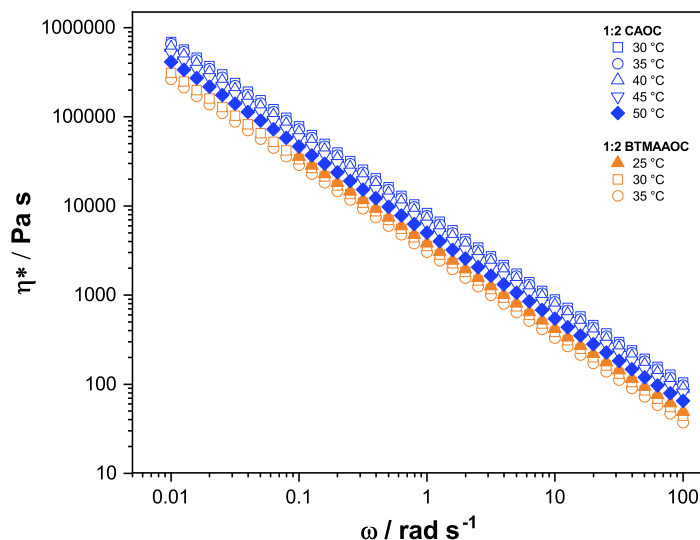


Figure 3.12. Log-log plot of the complex viscosity η^* of liquid crystalline 1:2 CAOC (blue) and 1:2 BTMAAOC (orange) against shear rate. The filled symbols are used to emphasise that the lowest viscosities recorded for 1:2 CAOC (at 50 °C, filled blue diamonds) are greater than the highest viscosities recorded for 1:2 BTMAAOC (at 25 °C, filled orange triangles) across all measured shear rates.

3.3 Structuring

3.3.1 NMR

Solid-state MAS ^1H - ^1H NOESY and 1D ^1H NMR spectra of 1:2 CAOC were recorded and analysed by Dr. Mohit Devgan at Imperial College London. Two temperatures were chosen based on DSC and PLM data such that both the liquid crystalline (at 20 °C) and isotropic liquid (60 °C) phases are studied. In both cases, the sample was heated to these temperatures from ambient temperature (approximately 15 °C). The ^1H - ^1H NOESY spectra are shown in Figures 3.13 and 3.14 respectively.

It must be noted here that the 1D and the 60 °C NOESY spectra were recorded using the same sample. This was synthesised and prepared for the measurement by myself, with the NMR sample being handled and prepared under dry conditions. The NOESY recorded at 20 °C is taken from the published thesis of Dr. Mohit Devgan.¹⁵ The sample for this measurement was prepared separately by Dr. Mohit Devgan and was handled in air, leading to a higher moisture content. In the NMR data, the main effect of the sample hydration is on the downfield signal appearing around 8 ppm in the 20 °C NOESY and around 10.7 ppm in the 60 °C NOESY and

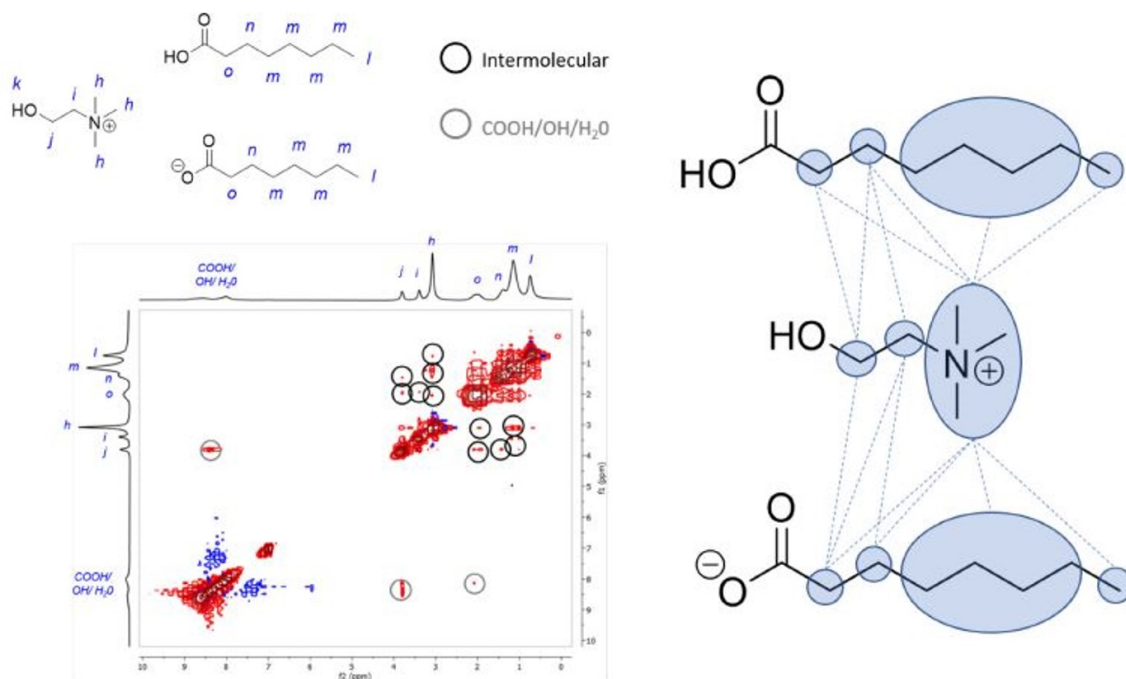


Figure 3.13. ^1H - ^1H NOESY of neat 1:2 CAOC at 20 °C (liquid crystalline phase). Reproduced from reference [15].

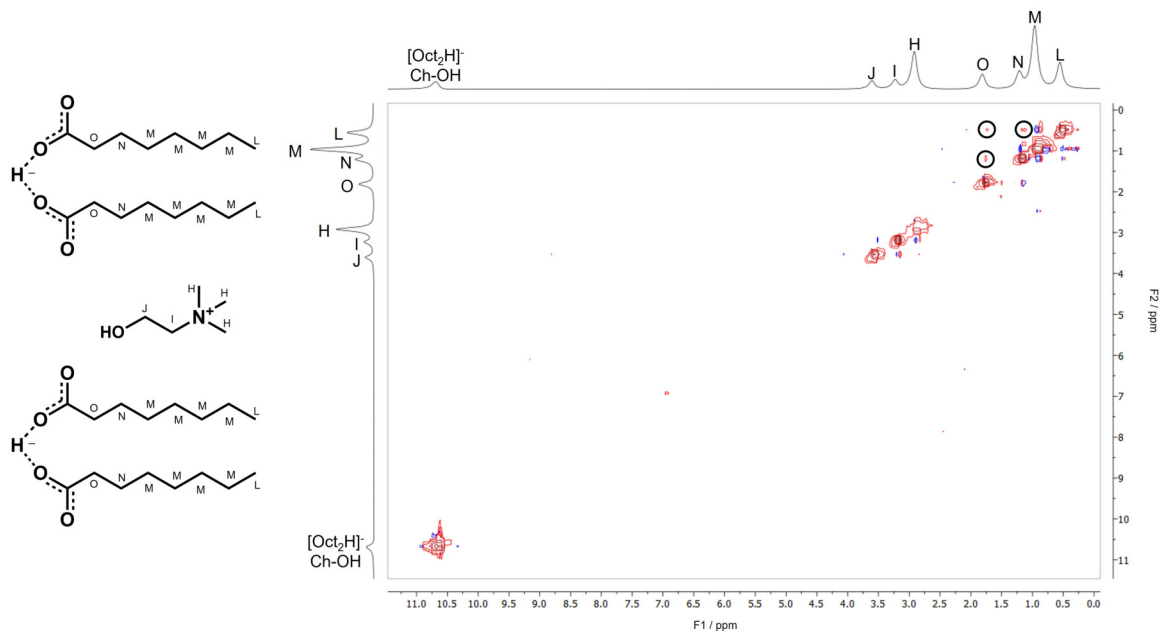


Figure 3.14. ^1H - ^1H NOESY of neat 1:2 CAOC at 60 °C (isotropic liquid phase). Data collected and analysed by Dr. Mohit Devgan.

1D spectra. The protons that give rise to these peaks are the proton of the cholinium hydroxyl group (Ch-OH) and the acidic proton associated with the complex anion ($[\text{Oct}_2\text{H}]^-$). In the sample with a lower water content, this results in a single NMR signal for both protons, labelled as ' $[\text{Oct}_2\text{H}]^-/\text{Ch-OH}$ ' in Figure 3.14. The chemical shift of this signal is 10.7 ppm, which is around the average of the expected chemical shifts for the individual protons¹³ (approximately 5-6 ppm for the hydroxyl proton and 15 ppm for the acidic proton — this value is higher than would be expected for a carboxylic acid proton, as the $[\text{Oct}_2\text{H}]^-$ is more deshielded due to being shared between two carboxylate anions). This is in agreement with previous findings by Mann *et al.* on the CAGE-Oct system where the same rapid proton exchange was observed by NMR.¹³ This indicates that in 1:2 CAOC the two protons interact via hydrogen bonding and undergo rapid proton exchange, thus experiencing a single, averaged, NMR environment.

Additionally, both the cholinium hydroxyl group and the anion headgroup can interact with water present in the system via hydrogen bonding and undergo proton exchange not only with each other, but with the water protons as well. This means that an increased water content can affect the position and appearance of the downfield peak associated with these protons, which can be seen in the 20 °C NOESY (Figure 3.13). As mentioned, the sample used for this measurement is expected to have a higher water content; accordingly, the NMR signal of the hydroxyl and acidic anion protons appears shifted to lower ppm (approximately 8–9 ppm) compared to the signal seen in the 60 °C NOESY. The signal also appears split, showing two distinct peaks; this suggests that the protons experience two different environments, which will depend on the way that they are solvated by the water molecules.

Figure 3.15 shows the solid-state 1D ^1H NMR spectra of 1:2 CAOC at 20 °C and 60 °C. The spectra show the same set of peaks, with two main differences. First, the signals recorded at 20 °C appear slightly broadened. This is due to the sample having a higher viscosity at 20 °C (in the LC phase), which has been shown to cause lower relaxation times and broader spectral features.^{131,132} Second, at the higher temperature the peaks are shifted slightly upfield (lower chemical shifts). While this effect is relatively small for the alkyl protons, it is much more evident when it comes to the peak labelled ' $[\text{Oct}_2\text{H}]^-/\text{Ch-OH}$ ', which is associated with the $[\text{Oct}_2\text{H}]^-$ anion and the cholinium hydroxyl group. This is because the protons that give rise to this signal engage in hydrogen bonding, both with each other (leading to rapid proton exchange, as mentioned) and, in the case of the acidic proton, with two octanoate moieties.

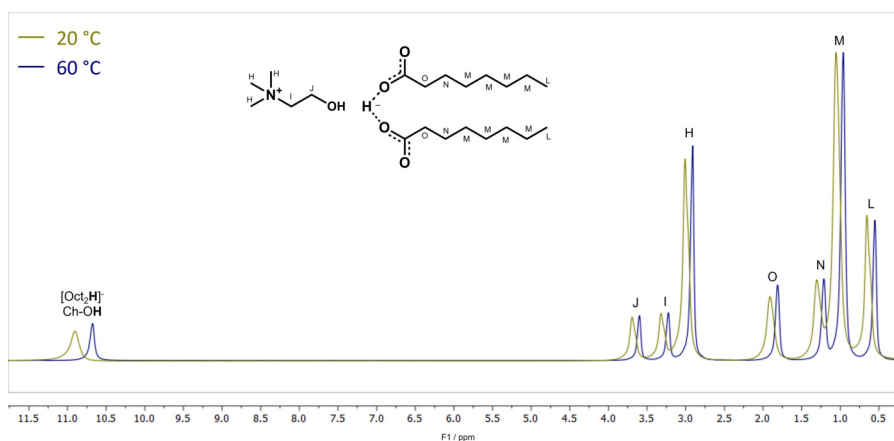


Figure 3.15. Solid state MAS ^1H NMR of 1:2 CAOC at 20 and 60 °C

As the [Oct₂H]⁺ proton is 'shared' between two carboxylate anions it is more deshielded, and thus has a higher chemical shift, than would be expected for a typical carboxylic acid proton. As the temperature of the measurement is increased, the hydrogen-bonding interactions in the system become weaker; this leads to the [Oct₂H]⁺ proton becoming less deshielded and therefore causing the [Oct₂H]⁺ / Ch-OH NMR signal to have a slightly higher chemical shift at 60 °C than at 20 °C. The alkyl protons, on the other hand, are not believed to experience significant hydrogen bonding, and thus the extent to which their signals shift is much smaller.

The NOESY spectrum recorded at 20 °C provides information on the molecular arrangement present in the liquid crystalline phase of 1:2 CAOC. The spectrum is shown in Figure 3.13, along with a schematic of the 1:2 CAOC structure showcasing the observed intermolecular interactions (blue highlights). The trimethylammonium moiety of the cholinium cations (protons labelled H) shows strong crosspeaks with the protons in the middle of the octyl chains (M and N), as well as weaker interactions with the octyl protons on either side of these (L and O). Protons I and J on the hydroxyethyl chain of the cation show crosspeaks with the octyl chain protons that are proximal to the carboxylate headgroup (protons O and N). Additionally, proton J (adjacent to the hydroxyl group) shows a crosspeak with the signals at approximately 8.0 ppm, which corresponds to the protons of the hydroxyl and carboxylic acid groups (as well as any water present in the system). When the sample is heated to 60 °C, almost all of the interactions observed at 20 °C disappear, confirming that the sample is no longer in the liquid crystalline state. Instead, it is in an isotropic liquid state, where the only notable crosspeaks observed in the NOESY are between protons on the alkyl chains of the [Oct₂H]⁺ anion (namely proton O interacting with protons L and M, as well as proton N interacting with proton L). Although

these crosspeaks are weak, they suggest the presence of intermolecular interactions between adjacent octyl chains. This is likely explained by the presence of segregated polar and nonpolar domains in the IL (as was observed from SAXS data for the isotropic 1:2 BTMAAOC), with the former consisting primarily of the anion octyl chains.

3.3.2 X-ray scattering

The thermal behaviour of 1:2 CAOC showed a reversible phase transition around 50 °C, which was defined as a liquid-crystal-to-isotropic (LC-isotropic) phase transition. The PLM photographs confirmed that the lower-temperature phase was liquid crystalline (showing birefringent areas with textures indicative of a layered structure), while the NOESY NMR data suggested that the cholinium cation sits alongside the anion chains. Neither of these techniques can provide specific information about the structuring of the LC phase (such as the size of the repeating unit). To improve upon this, X-ray scattering (SAXS and WAXS) measurements were performed for neat 1:2 CAOC over a wide temperature range (5–60 °C). The samples were synthesised and prepared by myself. Scattering profiles were recorded by Dr. Chi L. Chan and Dr. Mohit Devgan on the I22 beamline at Diamond Light Source, Oxford, and analysed by myself. Data is shown in Figure 3.16.

The X-ray scattering profiles collected for 1:2 CAOC (Figure 3.16) are similar to those observed for 1:2 BTMAAOC (Figure 2.14). At temperatures between 5–50 °C the SAXS data shows a sharp peak, indicative of a lamellar liquid crystalline structure, in agreement with the PLM data. Unlike 1:2 BTMAAOC, which showed two distinct sets of sharp peaks in its SAXS/WAXS profile, liquid crystalline 1:2 CAOC only shows one set of peaks at all temperatures between 5 and 50 °C.

At 5 °C, the sharp peak appears in the SAXS profile at $q = 0.28 \text{ \AA}^{-1}$, corresponding to a lamellar d -spacing of approximately 22.4 Å. Generally, ordered lamellar mesophases give rise to pseudo-Bragg peaks whose positions in the q -space are in a 1:2:3:4 ratio. The peak seen in the SAXS data at $q = 0.28 \text{ \AA}^{-1}$ is the first of these pseudo-Bragg peaks and corresponds to a d -spacing of 22.4 Å. The second peak would be expected at $q = 0.56 \text{ \AA}^{-1}$, which is outside of the SAXS measurement range. Looking at the WAXS data, a sharp, low-intensity peak can be seen at this q value, confirming the ordered lamellar structure of the sample. Additionally, the

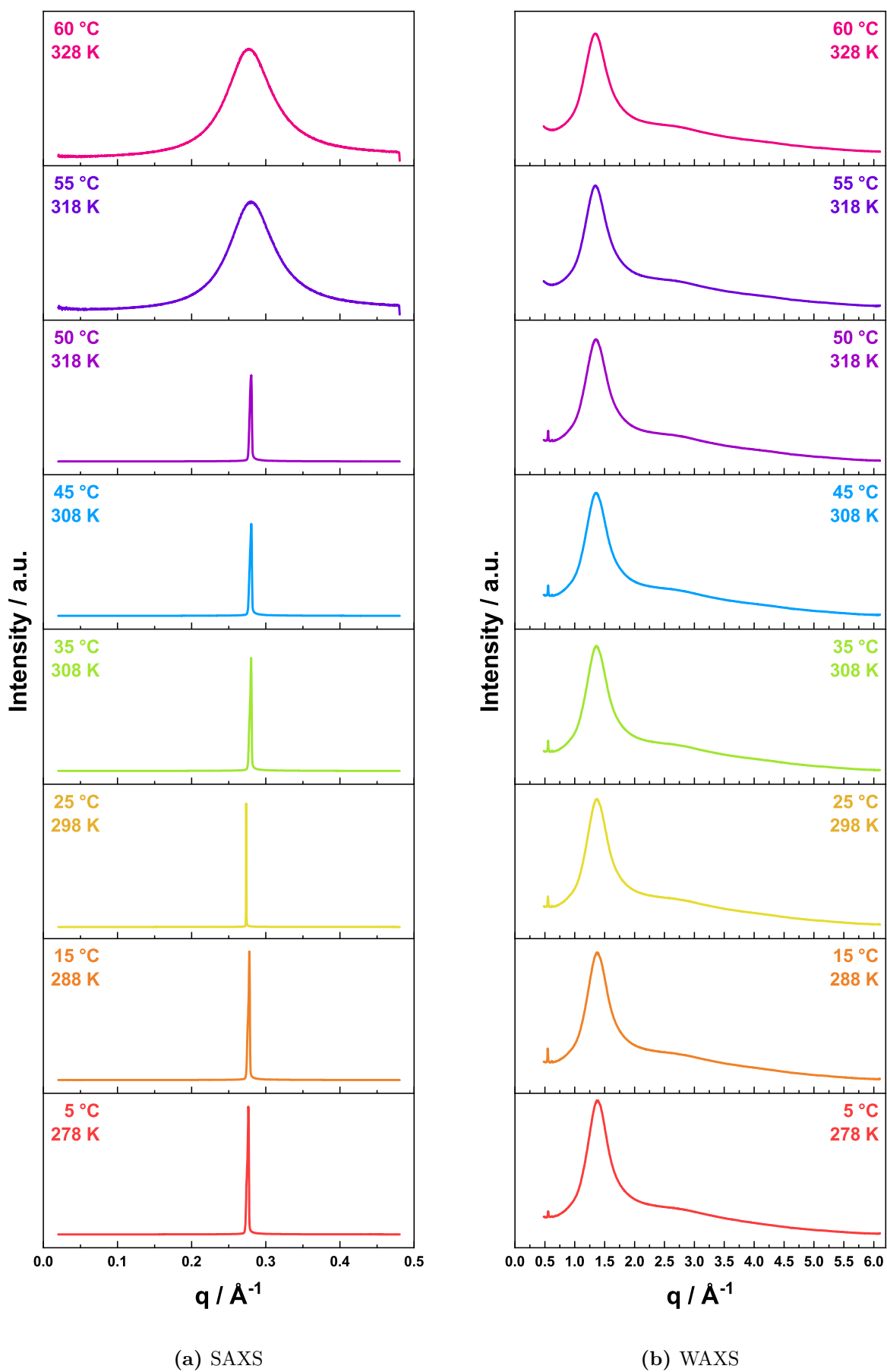


Figure 3.16. X-ray scattering data of 1:2 CAOC at various temperatures.

WAXS data also shows a broad peak at $q = 1.38 \text{ \AA}^{-1}$ (corresponding to a real-life distance of $4.6 \text{ \AA}$). The shape and position of this peak suggest that the mesophase is a fluid lamellar L_α phase, in which the alkyl chains are disordered and have a liquid-like behaviour.^{119,120}

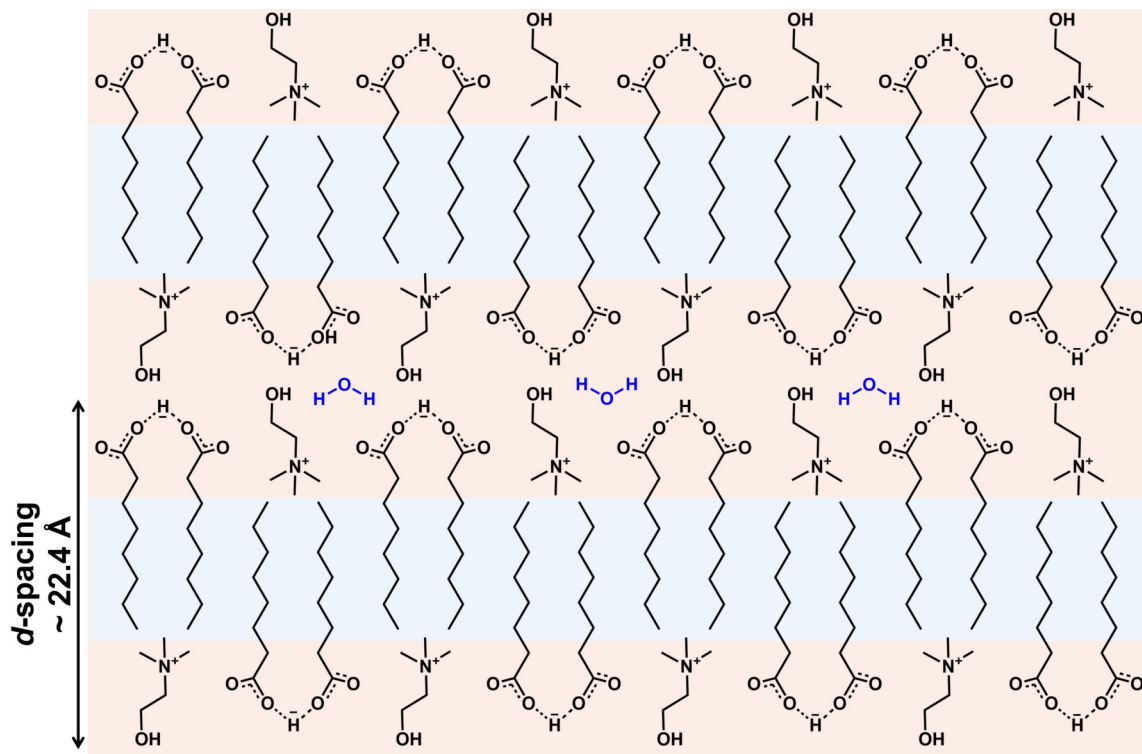


Figure 3.17. Possible structure of liquid crystalline 1:2 CAOC. The molecules are arranged in lamellar bilayers with an approximate d -spacing of $22.4 \text{ \AA}$. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner (associated with a complex $[(\text{octanoate})_2\text{H}]^-$ anion), the real system is a dynamic one, in which hydrogen bonds are always breaking and forming.

A possible lamellar bilayer structure for 1:2 CAOC is shown in Figure 3.17, with the width of a single bilayer ($d\text{-spacing} = 22.4 \text{ \AA}$) indicated on the left-hand side. The bilayer consists of polar regions, comprised of the cation species and the anion headgroups, and nonpolar regions, comprised of the anion alkyl tails. A fully extended octanoic acid molecule measures approximately $10.5 \text{ \AA}$ (COOH-CH_3). This would result in a theoretical bilayer thickness of $21.0 \text{ \AA}$ ($2 \times 10.5 \text{ \AA}$), which is very close to the d -spacing indicated by the SAXS peak ($22.4 \text{ \AA}$). Like in the case of 1:2 BTMAAOC, it is thought that the alkyl tails of the anions in 1:2 CAOC are interdigitated to some extent, in order to accommodate the cations and large anion headgroups. Additionally, while the chains are shown as fully extended, in reality they have a

fluid quality and are likely to be curled or bent to some extent (fluid lamellar L_α phase).

The SAXS data does not provide information on the position of the cation within the lamellar bilayer. The NOESY data in Figure 3.13 indicates that the cholinium hydroxyl group should be proximal to the $[(\text{octanoate})_2\text{H}]^-$ anion headgroup, in order to allow the observed proton exchange to occur (the acidic and hydroxyl protons only show one averaged NMR signal). Based on this, and on the need for charge neutrality (cation-anion alternation), the cholinium cation is thought to reside in the polar region of the bilayer, near the anion headgroups. This is similar to the position of the cation in the lamellar bilayer structure proposed for 1:2 BTMAAOC. This placement allows for the formation of hydrogen bonds between the hydroxyl group of the cation and the anion headgroup, allowing the hydroxyl and acidic protons to be exchanged. It should be noted, however, that the NOESY spectrum also shows crosspeaks between the cation NMe_3 protons and the protons of the anion alkyl chain. While this may seem to suggest that the cation is spatially proximal to the alkyl tails, this is extremely unlikely, as the presence of the cholinium cation in the nonpolar region would disrupt the hydrophobic interactions between the alkyl tails and therefore be energetically unfavourable. A more reasonable explanation for the observed crosspeaks is that these occur due to spin diffusion throughout the anion alkyl chain. This means that the cation resides near the anion headgroup and the adjacent alkyl chain proton (labelled O), but shows crosspeaks with protons further down the chain due to the spin diffusion effect as reported by Stark et al.¹²¹ A similar effect was observed for 1:2 BTMAAOC in the previous chapter.

As was the case for 1:2 BTMAAOC, one way to verify how reasonable the proposed bilayer model is is to estimate the cross-sectional area per unit (consisting of a cholinium cation, an octanoate anion and an octanoic acid molecule) and compare this to literature values reported for phospholipid bilayers. The area per unit can be estimated by dividing the unit volume by the unit length. The volume of one 1:2 CAOC unit was calculated to be approximately $650 \text{ \AA}^3$; as the density of 1:2 CAOC could not be obtained experimentally, it was approximated by the density of 1:2 CAGE (0.99 g mL^{-1}).⁹ The length of a 1:2 CAOC unit can be calculated from the d -spacing of the bilayer and depends on the amount of interdigitation between the anion alkyl tails. The estimated unit length and cross-sectional areas are given in Table 3.3. These values (particularly those where partial interdigitation is assumed) are similar to the area values reported in the literature for phospholipids such as phosphatidylcholine ($70 \text{ \AA}^2$)¹²⁴ and

Table 3.3. Estimated length and area values for the 1:2 CAOC unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.

Chain position	d -spacing (20.3 Å)	Unit length	Unit area
No interdigitation	$d = 2 \times l_{\text{unit}}$	$l_{\text{min}} = 11.2 \text{ Å}$	$A_{\text{max}} = 58.0 \text{ Å}^2$
Partly interdigitated	$d = 1.5 \times l_{\text{unit}}$	$l_{\text{int}} = 14.9 \text{ Å}$	$A_{\text{int}} = 43.5 \text{ Å}^2$
Fully interdigitated	$d = l_{\text{unit}}$	$l_{\text{max}} = 22.4 \text{ Å}$	$A_{\text{min}} = 29.0 \text{ Å}^2$

DOPC and DPPC ($40\text{--}70 \text{ Å}^2$).¹²³ This suggests that the proposed bilayer model is a reasonable structure for the LC phase of 1:2 CAOC.

It should be mentioned here that Figure 3.17 also shows the presence of some residual water molecules within the bilayer. Generally, for a lamellar mesophase, the d -spacing corresponds to the thickness of the bilayer and of the water layer separating two adjacent bilayers. Here, the 1:2 CAOC sample was dried on a high vacuum line for 24 h before use and the X-ray capillary was loaded and sealed under a nitrogen atmosphere. The water content of the dried IL was measured to be 0.07 wt% (1.5 mol%) using Karl-Fisher titration; based on this, it is assumed that the thickness of the water layer is negligible. Instead, residual water is thought to reside in the polar region of the bilayer and participate in hydrogen bonding with the hydroxyl group of the cation and with the anion headgroup.

As mentioned, the SAXS and WAXS profiles of 1:2 CAOC were recorded at temperatures between 5 and 60 °C (Figure 3.16). Between 5 and 50 °C there is very little change in the data, with the sharp peak being maintained. This peak appears at around $q = 0.27\text{--}0.28 \text{ Å}^{-1}$, while a second low-intensity peak is visible in the WAXS at $2q$. This indicates that the LC phase of 1:2 CAOC is maintained up to a temperature of 50 °C, which is in agreement with the PLM and DSC data. As the temperature increases, the position of the sharp peak observed in the SAXS shifts slightly to higher q , which corresponds to a slight decrease in the d -spacing. This is expected and is due to increased fluidity of the anion alkyl chains at higher temperatures. The WAXS data also shows a broader peak whose position ranges between $q = 1.35\text{--}1.38 \text{ Å}^{-1}$ (decreasing as the temperature increases). As mentioned previously, this peak is indicative of a fluid lamellar L_α system; a similar mesophase, the liquid-ordered L_o phase, is usually characterised by a similar WAXS feature to the L_α phase, but shows a higher temperature

dependence, which is not observed here.¹¹⁹

When the temperature is increased to 55 °C and above, the SAXS profile changes dramatically: the sharp peak is replaced by a broad feature centred around $q = 0.28 \text{ \AA}^{-1}$, corresponding to a real-life distance of approximately 22.4 Å. This change was also observed for 1:2 BTMAAOC and is associated with a transition from the lamellar liquid crystalline mesophase to an isotropic liquid phase. The temperature at which this transition is observed in the SAXS is in agreement with the $T_{\text{L-I}}$ temperature measured by DSC (all LC to isotropic transition temperatures for 1:2 CAOC and 1:2 BTMAAOC are given in Table 3.4). A broad feature in the X-ray scattering pattern is commonly observed for ILs and is caused by the presence of discrete polar and nonpolar domains in the IL structure.¹²⁷ This is discussed in more detail in Chapter 2. In the WAXS profile, the low-intensity sharp peak associated with the LC phase also disappears at these temperatures. The broad WAXS peak is still present and does not show any significant changes in shape or position with changing temperatures. In ionic liquids, this peak is referred to as the 'adjacency' peak and is indicative of the average anion-cation distance, as well as the chain-chain correlation distance. For 1:2 CAOC, this peak appears at approximately $1.4 \text{ \AA}^{-1}$, similar to the peak observed for isotropic 1:2 BTMAAOC and to adjacency peaks reported in the literature for other, more conventional ILs.^{84,128}

3.4 Chapter summary

The thermal behaviour of 1:2 CAOC is very similar to that of 1:2 BTMAAOC, with the main difference being that the temperature of the transition from a liquid crystal phase to an isotropic phase is higher for 1:2 CAOC. This increased stability of the LC phase is attributed to the increased hydrogen bonding resulting from the presence of a hydroxyl group on the cation. The liquid crystalline mesophase exhibited by 1:2 CAOC is also different from that of 1:2 BTMAAOC, in that only one set of scattering peaks is observed for 1:2 CAOC.

It should also be noted that 1:2 CAOC contained a much smaller amount of water after drying compared to 1:2 BTMAAOC. Once again, this is thought to be due to the cation hydroxyl group and its hydrogen-bonding ability. Hydrogen bonds are thought to stabilise the LC bilayer. In 1:2 CAOC, H-bonding interactions can occur between the anion headgroups and the cation hydroxyl groups. In 1:2 BTMAAOC, however, it is possible that water molecules fulfill this

Table 3.4. Temperatures of the liquid crystal to isotropic liquid transitions

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 CAOC	52	60	57	50–55	50–55
1:2 BTMAAOC	17	25	37 [*]	35–40	35

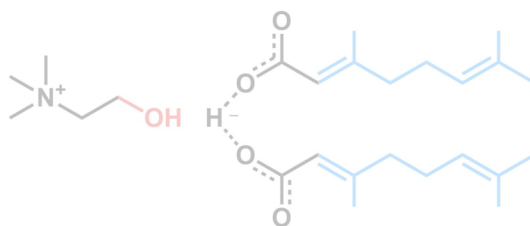
^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling

^d Temp. above which IL shows Newtonian flow behaviour

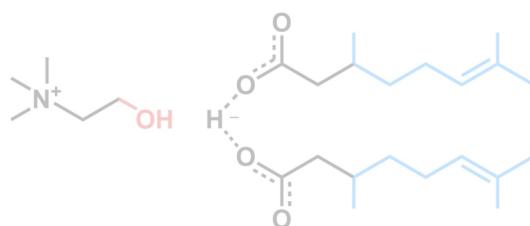
^e Temp. at which sharp LC peak disappears ^{*} Tan δ peak on heating

role instead, and help contribute to the structure and stability of the LC bilayers. This is perhaps the reason why water is more difficult to remove in 1:2 BTMAAOC and why this IL has a pronounced hygroscopic nature.

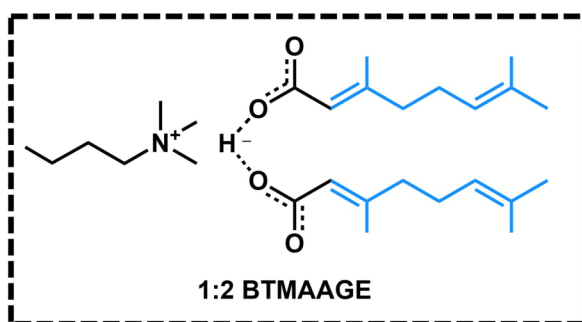
STRUCTURE COMPLEXITY



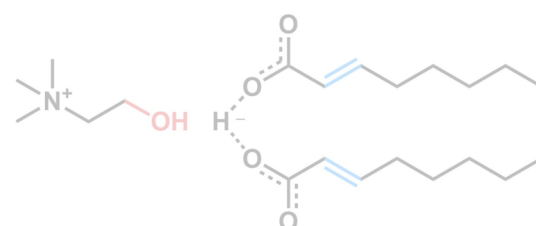
1:2 CAGE



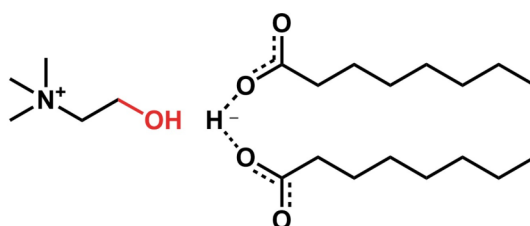
1:2 CACI



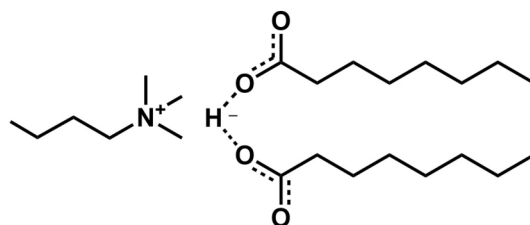
1:2 BTMAAGE



1:2 CA2OE



1:2 CAOC



1:2 BTMAAOC

Chapter 4

1:2 ButylTriMethylAmmonium And GERanate (BTMAAGE)

This chapter looks at the properties and behaviour of 1:2 butyltrimethylammonium and geranate (BTMAAGE), shown in Figure 4.1. Like 1:2 BTMAAOC, this IL contains a butyltrimethylammonium (BTMA) cation, which lacks the ability to form hydrogen bonds with the anion; the main cation-anion interaction is of an electrostatic nature. The carboxylic acid, however, is more complex than in the case of both 1:2 BTMAAOC and 1:2 CAOC. 1:2 BTMAAGE is synthesised using geranic acid, which has a branched, unsaturated alkyl chain. This is more sterically hindered and more conformationally restricted than any other acid used in this work, so it is expected to result in more disordered systems. Because 1:2 BTMAAGE also lacks the cation-anion hydrogen-bonding interactions, this IL was expected to have the least efficient molecular packing and the most disordered structure of all six 1:2 ILs in this work. The thermal behaviour of 1:2 BTMAAGE was investigated using differential scanning calorimetry (DSC) and dynamic mechanical analysis (DMA) and the structuring of the system was assessed using polarised-light microscopy, solid-state magic-angle spinning (SS-MAS) NMR, and small- and wide-angle X-ray scattering (SAXS and WAXS).

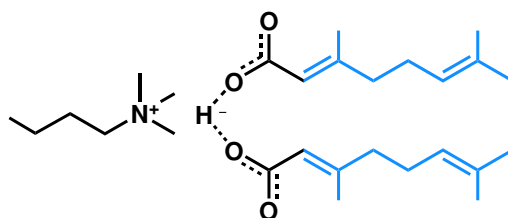


Figure 4.1. 1:2 BTMAAGE

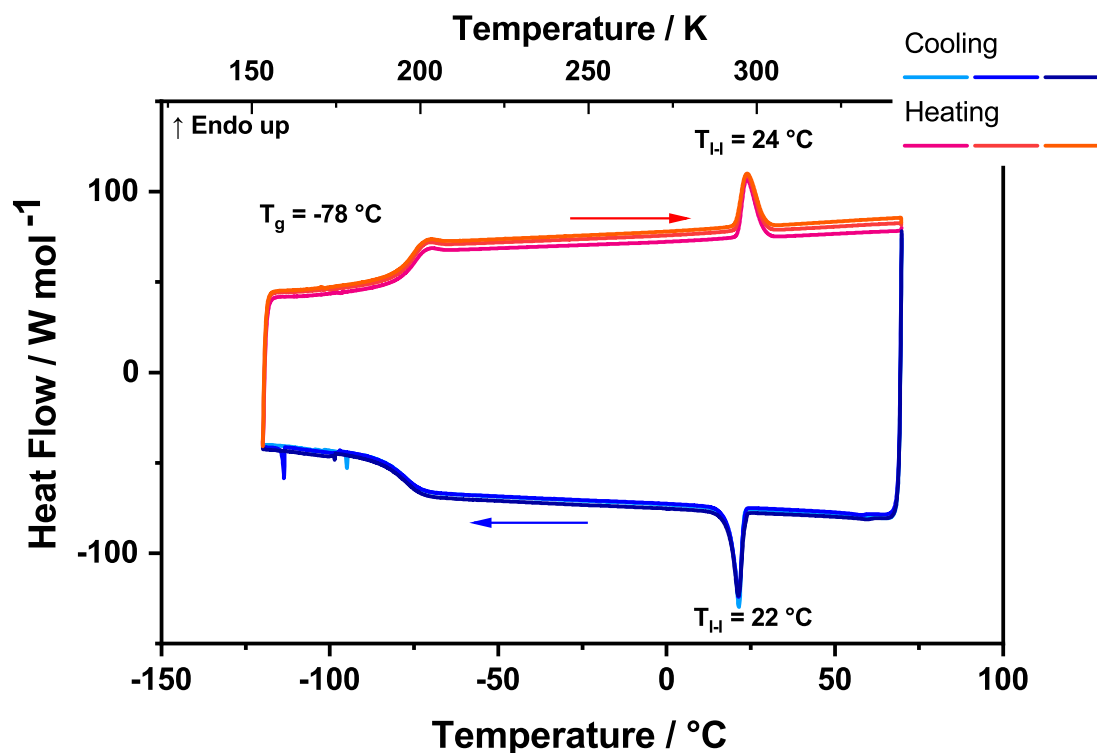


Figure 4.2. DSC traces of 1:2 BTMAAGE with annotated transition temperatures. The heating and cooling rates are $5\text{ }^{\circ}\text{C min}^{-1}$.

4.1 Thermal behaviour

DSC measurements of 1:2 BTMAAGE were run by Dr. Daniel Rauber at the University of Saarland, Germany, and analysed by myself. Three consecutive heating-cooling cycles were run in order to show reproducibility. Data was collected using a scan rate of $5\text{ }^{\circ}\text{C min}^{-1}$ (Figure 4.2).

1:2 BTMAAGE has a similar thermal behaviour to 1:2 BTMAAOC and 1:2 CAOC, with a few key differences. First, 1:2 BTMAAGE only shows two thermal transitions over the entire temperature range: a reversible glass transition and a reversible liquid-crystal-to-isotropic phase transition. The glass transition temperature extracted from the DSC data is $T_g = -78\text{ }^{\circ}\text{C}$,

which is approximately 20 °C higher than the glass transition temperatures of 1:2 BTMAAOC and 1:2 CAOC (approximately −95 °C for both). 1:2 BTMAAGE contains geranate anions, which have a branched, unsaturated alkyl chain. This is expected to lead to poorer packing and weaker intermolecular interactions, which would, in theory, result in 1:2 BTMAAGE having a *lower* T_g than ILs containing the linear, saturated octanoate anion — however, this is not true for the T_g values measured in this work. As glass transitions are complex processes, T_g can be influenced by numerous factors, including the amount of moisture present in the different IL samples.

At temperatures above T_g 1:2 BTMAAGE is in a liquid crystalline (LC) state, which was characterised using polarised-light microscopy (PLM), shown in Figure 4.3 (top). At 10 and 20 °C the photographs show large areas of birefringence, with some brighter, streaky areas as well as small areas of a Maltese cross pattern; both of these textures are associated with a layered liquid crystalline phase (lamellar or smectic). Additionally, some regions show a pattern resembling the focal conic fan texture generally observed for smectic A phases,¹³³ further supporting the idea of a layered liquid crystalline structure for 1:2 BTMAAGE. In the LC phase, the IL is an opaque, highly viscous gel (Figure 4.4a), similar in appearance to liquid crystalline 1:2 BTMAAOC and 1:2 CAOC.

As the IL is heated further, variable-temperature PLM showed that at 24 °C the birefringence begins to disappear gradually; at 27 °C the image is entirely dark (Figure 4.3, bottom). At this temperature, the appearance of 1:2 BTMAAGE also changes (Figure 4.4b); the IL is now a clear, viscous but flowing liquid, similar to 1:2 BTMAAOC and 1:2 CAOC in the isotropic liquid phase. These changes are associated with the second set of peaks observed in the DSC: an endothermic peak at 24 °C on heating and an exothermic peak at 22 °C on cooling. The loss of birefringence and the visual appearance of the 1:2 BTMAAGE sample indicate that during this transition the IL changes from a liquid crystalline state to an isotropic liquid phase. The nature of the two phases was examined in more detail using X-ray scattering (SAXS and WAXS) and NMR measurements, which are discussed in Section 4.3.

Similar liquid-crystal-to-isotropic (LC-isotropic) transitions were observed for 1:2 BTMAAOC (at 17 °C) and 1:2 CAOC (at 52 °C). The temperatures at which this transition occurs vary in the order 1:2 CAOC > 1:2 BTMAAGE > 1:2 BTMAAOC. The fact that 1:2 CAOC shows the highest stability of the LC phase is primarily attributed to the cholinium cation, which

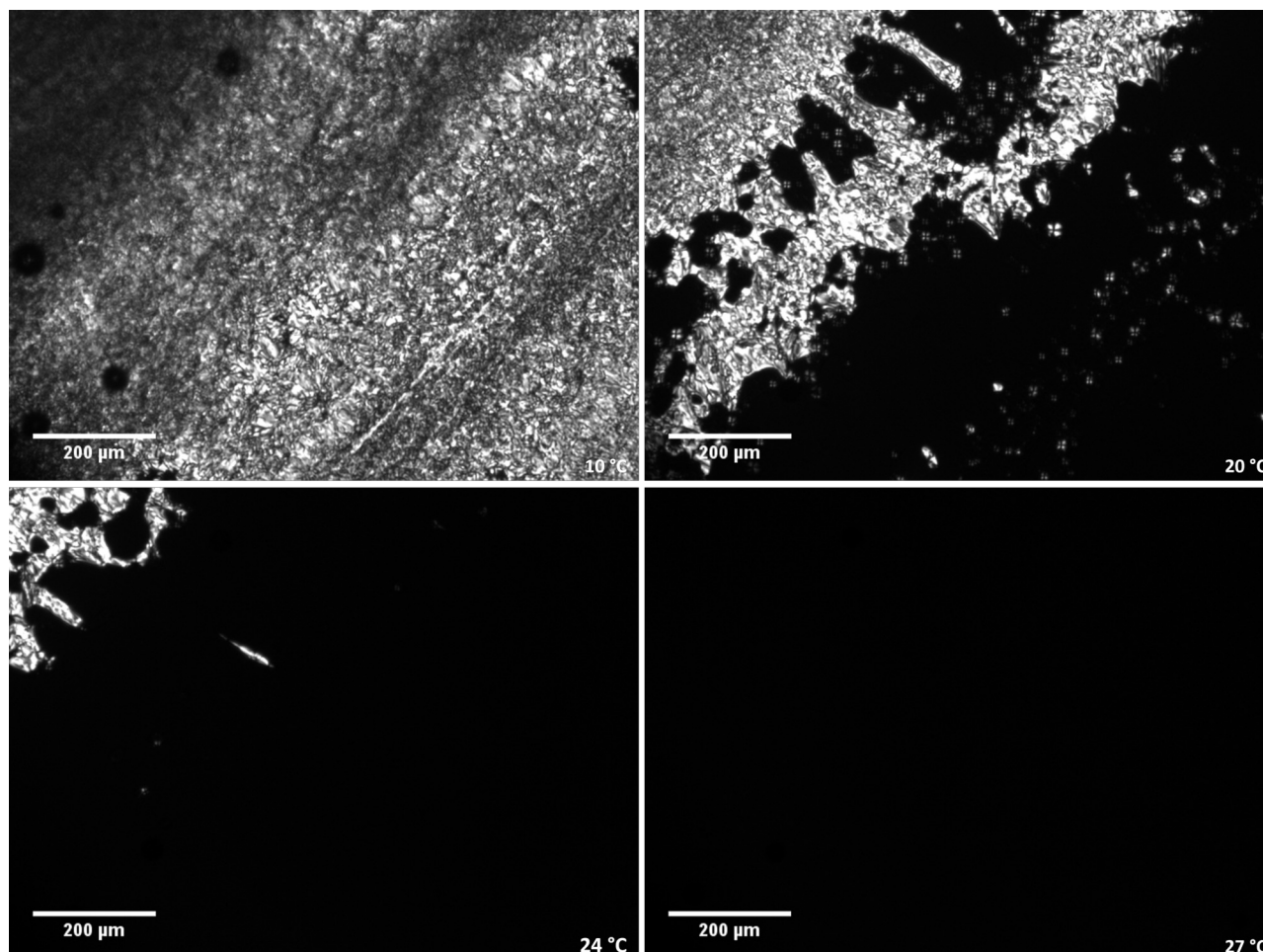


Figure 4.3. Polarised-light microscope images of 1:2 BTMAAGE taken with $4\times$ magnification.

Top: on cooling to 10 °C (left) the sample showed large areas of birefringence with a liquid-like behaviour, indicative of a liquid-crystalline phase. On heating to 20 °C (right) a Maltese cross pattern, associated with a lamellar mesophase, was observed. *Bottom:* the IL was heated above the temperature of the LC-isotropic phase transition. At 27 °C the sample is in an isotropic liquid state and shows no birefringence (the image is entirely dark).



(a) Liquid crystalline phase



(b) Isotropic liquid phase

Figure 4.4. 1:2 BTMAAGE before and after the liquid-crystal-to-isotropic phase transition

helps stabilise the LC phase through hydrogen bonding. Additionally, the octanoate anions with linear, unsaturated chains contribute to efficient packing and are thought to increase the stability of the LC phase compared to 1:2 BTMAAGE, which contains the more sterically demanding geranate anions. However, the effect of the anion structure on the stability of the LC phase appears to be more complex than this, as the T_{1-1} (measured by DSC) of 1:2 BTMAAGE is higher than that of 1:2 BTMAAOC. The only structural difference between the two ILs is the nature of the anion species: 1:2 BTMAAOC contains octanoate anions, which are linear and saturated, while 1:2 BTMAAGE contains geranate anions, with branching methyl groups and carbon-carbon double bonds. Since the two ILs contain the same cation, it is expected that this difference in anions will be driving force behind any dissimilarities. The increased steric hindrance of geranate anions was expected to lead to weaker intermolecular interactions in the LC phase and therefore to a lower T_{1-1} for 1:2 BTMAAGE. While this does not hold true when comparing the T_{1-1} values obtained from DSC measurements (with the transition temperature of 1:2 BTMAAGE being slightly higher than that of 1:2 BTMAAOC), it is important to note here that different techniques show the opposite trend. The SAXS/WAXS profiles collected for 1:2 BTMAAOC show the LC phase persisting up to a temperature of 35 °C, while the DMA data shows a decrease in storage modulus at 37 °C associated with this transition. These techniques suggest that the LC phase is more stable in 1:2 BTMAAOC, but not to a significant

extent (SAXS shows that the LC phase of 1:2 BTMAAGE collapses between 25 and 35 °C). The discrepancy between the T_{LI} of 1:2 BTMAAOC measured by different techniques is most likely due to the samples containing different amounts of moisture.

4.1.1 Dynamic Mechanical Analysis

The thermal behaviour and mechanical properties of 1:2 BTMAAGE were further investigated using dynamic mechanical analysis (DMA). Measurements were performed at three different frequencies ($f = 1, 5$ and 10 Hz), over a temperature range of -120 – 70 °C (150 – 345 K). Data collected at $f = 1$ Hz on cooling and subsequent heating is shown in Figure 4.5. The storage modulus M' is reported as a relative variation with respect to the value at 298 K (25 °C).

The smaller peak at 194 K (-79 °C) and the change in M' — a decrease on heating starting at 184 K (-89 °C) — are associated with the glass transition observed by DSC at 195 K (-78 °C). The T_g temperature of the tan delta peak agrees with the T_g observed in the DSC data, while the T_g calculated as the onset temperature of the decrease in M' is slightly lower. As discussed previously, this discrepancy is expected as the glass transition occurs over a range of temperatures, with the different ways of calculating T_g corresponding to different points in the transition.¹¹⁰

The LC-isotropic phase transition observed by DSC at 297 K (24 °C) does not result in any significant changes in M' , suggesting that the LC phase and the isotropic liquid phase have similar storage modulus values. In the tan δ data measured on cooling, a very low intensity peak associated with this transition can be seen in Figure 4.6 at approximately 288 K (15 °C).

The remaining features observed in the DMA data are a change in the relative modulus M' (as an increase on cooling and a decrease on heating) and a peak in tan δ appearing at approximately 230 K (-45 °C) at $f = 1$ Hz, both of which are associated with the same process. Because the position of the tan δ peak shifts towards higher temperatures as the frequency of the measurement increases (Figure 4.6), it can be concluded that this process is not a phase transition (for which the peak position would be constant), but rather a thermally activated relaxation related to viscous flow. Similar processes were also observed for 1:2 BTMAAOC and 1:2 CAOC.

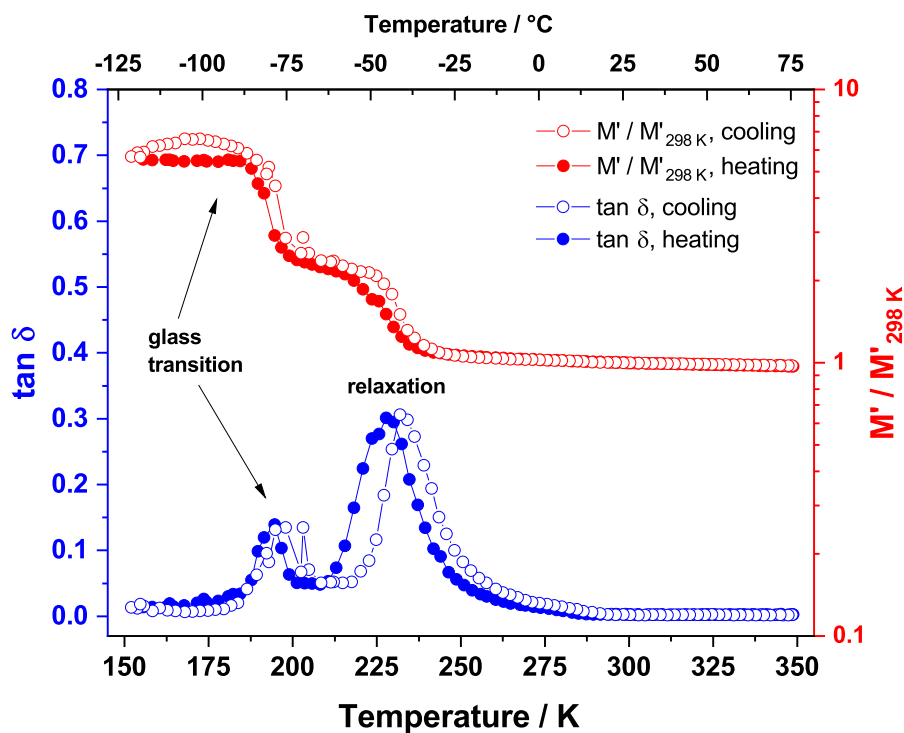


Figure 4.5. DMA data for 1:2 BTMAAGE, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.

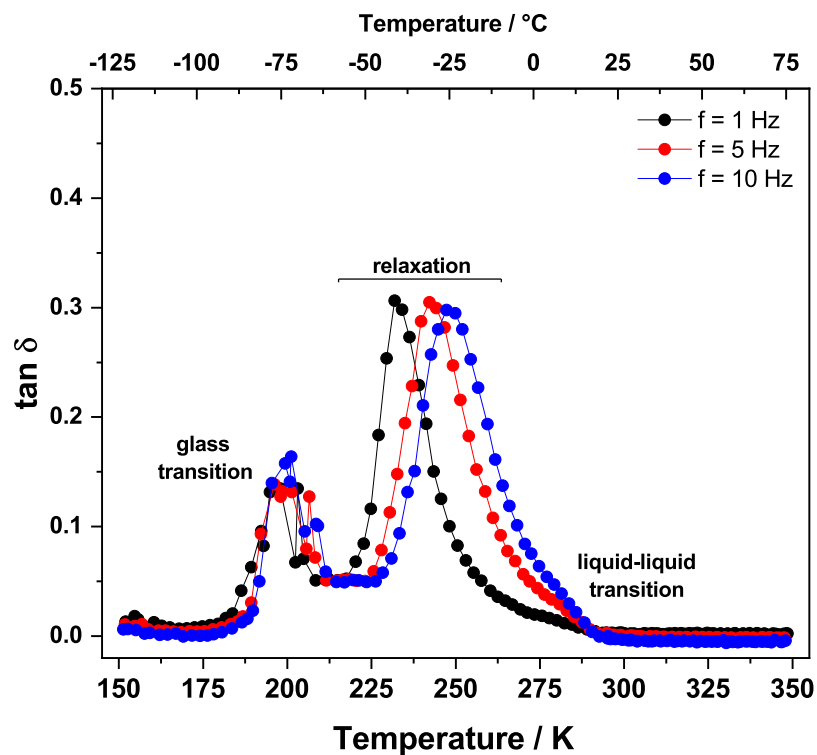


Figure 4.6. $\tan \delta$ measured for 1:2 BTMAAGE on cooling. Lines are guides for the eye.

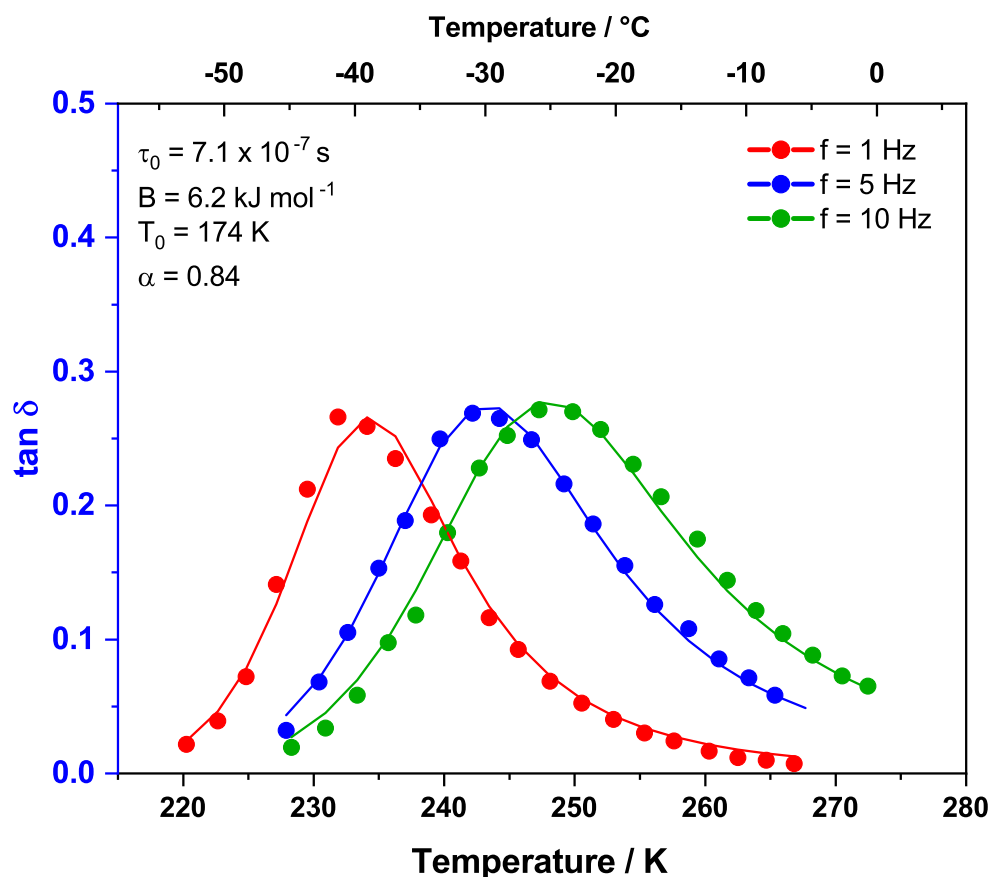


Figure 4.7. $\tan \delta$ measured for 1:2 BTMAAGE on cooling at $f = 1, 5$ and 10 Hz. Only data corresponding to the thermally activated relaxation is shown. Solid lines are the result of a simultaneous fit for the three frequencies. Before fitting, a linear background subtraction was performed.

The $\tan \delta$ data corresponding to the relaxation peak was fitted according to equations 2.4 and 2.6 after performing a linear background subtraction (Figure 4.7). The best-fit parameters are given in Table 4.1, alongside the parameters calculated for the relaxation processes observed in 1:2 BTMAAOC and 1:2 CAOC. These equations approximate the relaxation process as a transition between two states separated by an energy barrier ΔE . Here, the peak heights decrease slightly as the frequency of the measurement increases, indicating that the two states have equivalent energies (i.e. $\Delta E = 0$). The relaxation time τ_0 is on the order of 10^{-7} s and the activation energy was calculated to be $B = 6.2 \text{ kJ mol}^{-1}$, suggesting that the relaxation occurring in 1:2 BTMAAGE is an intermolecular diffusive process, similar to what was observed for the previously discussed ILs. The Fuoss-Kirkwood width parameter α is less than one, meaning that the relaxing units interact with each other. Additionally, the activation energy parameter B is comparable to the energies obtained for 1:2 BTMAAOC and 1:2 CAOC and is the smallest of the three values ($B_{\text{CAOC}} > B_{\text{BTMAAOC}} > B_{\text{BTMAAGE}}$). This suggests that

Table 4.1. Best-fit parameters τ_0 , B , T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 BTMAAGE (top row). For comparison, data is also shown for the other 1:2 ILs discussed so far.

Sample	$\tau_0 / 10^{-7} \text{ s}$	B / K	$B / \text{kJ mol}^{-1}$	T_0 / K	α
1:2 BTMAAGE	7.1 ± 0.1	750 ± 8	6.2 ± 0.1	174.0 ± 0.1	0.84 ± 0.01
1:2 CAOC	5.5 ± 0.1	1503 ± 19	12.5 ± 0.2	134 ± 2	0.75 ± 0.01
1:2 BTMAAOC	5.7 ± 2.0	1076 ± 26	9.0 ± 0.1	169 ± 2	0.57 ± 0.09

the strengths of intermolecular interactions decrease in the order 1:2 CAOC > 1:2 BTMAAOC > 1:2 BTMAAGE, which can be attributed to the differences in structure between the constituent species of these ILs. Comparing 1:2 CAOC and 1:2 BTMAAOC, the lack of a hydroxyl group in the cation structure leads to weaker interactions; comparing 1:2 BTMAAOC and 1:2 BTMAAGE, the increased steric hindrance provided by the methyl groups and the presence of carbon-carbon double bonds on the anion chain serves to further decrease the strength of the interactions.

4.2 Viscosity

Viscosity measurements were performed by Dr. Daniel Rauber at the University of Saarland, Germany. Data analysis was performed by myself. Dynamic viscosity measurements were performed over a temperature range of 25–105 °C (298.15–378.15 K). At these temperatures, the IL is in the isotropic liquid phase and shows Newtonian flow behaviour (viscosity is independent of shear rate). For each temperature, the viscosity data was averaged across all shear rates and the temperature-dependence of viscosity was fitted according to the VFT equation. The experimental data and the fitted data are shown in green in Figure 4.8. This figure also includes dynamic viscosity data for the isotropic phase of the previously discussed ILs, 1:2 BTMAAOC and 1:2 CAOC. The best-fit parameters of the VFT equation are shown in Table 4.2, alongside the parameters calculated for 1:2 BTMAAOC and 1:2 CAOC. It should be noted that the liquid crystalline phase of 1:2 BTMAAGE was not investigated here, as no viscosity measurements were performed below room temperature. The data shows that at the same temperature, the viscosities of the three ILs studied so far vary in the order 1:2 CAOC > 1:2 BTMAAGE > 1:2 BTMAAOC. The same trend is followed by the activation energy parameters B calculated

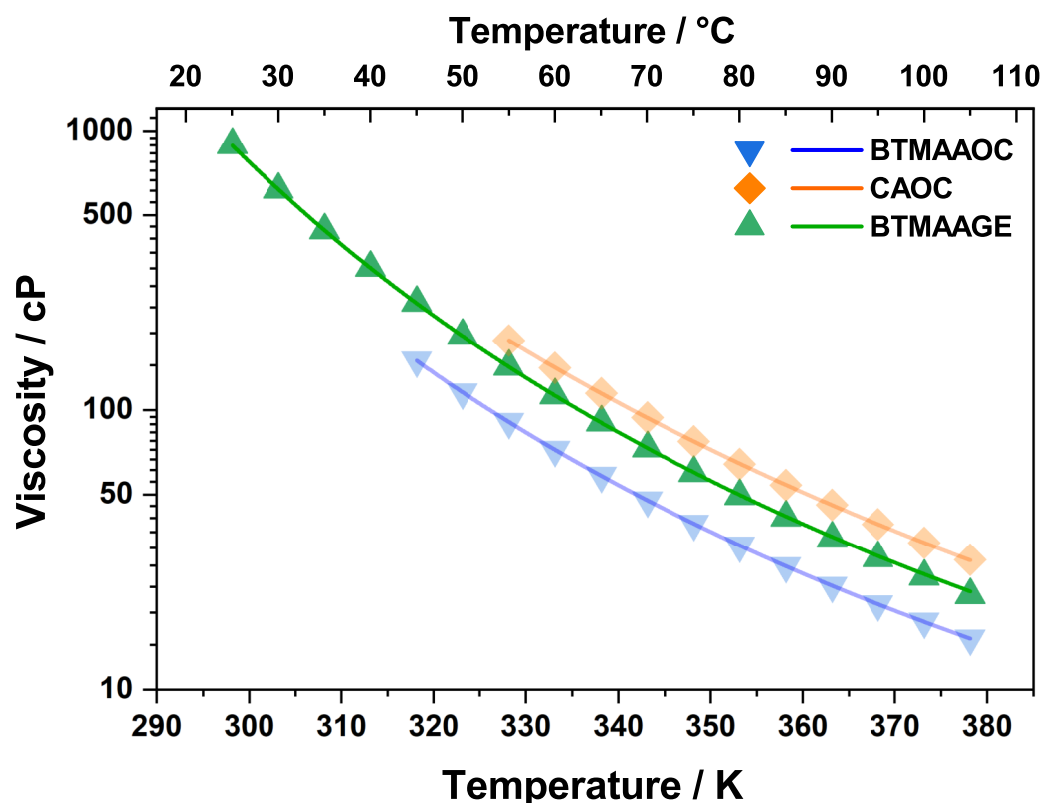


Figure 4.8. Dynamic viscosity data for the studied 1:2 ILs. 1:2 BTMAAGE (shown in green) is an isotropic liquid over the entire studied temperature range. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation, with fit parameters shown in Table 4.2.

from the VFT fit of the viscosities.

The viscosity of an IL is influenced primarily by the strength and nature of the intermolecular interactions (Coulombic, Van der Waals, hydrogen-bonding) present in the system.³⁹ As the contribution of each individual factor affecting viscosity cannot be easily disentangled, the study of structure-property relationships (SPR) is an essential tool for understanding the behaviour of ILs. To identify these relationships, a systematic comparison of different systems and their properties is often undertaken in order to isolate the effects of specific structural moieties, with such studies showing that IL viscosity is affected by the size, nature, shape and geometry of the constituent anion and cation species.^{134–136} However, most of the literature findings on this topic deal with 'conventional' ILs, i.e. ones containing large, asymmetric, alkyl-substituted cations (such as imidazolium or pyrrolidinium). In these systems, the formation of distinct polar and nonpolar nanodomains is driven by the length of the cationic alkyl chain. When these chains are sufficiently long, they aggregate into a discrete nonpolar domain, while the charged part of the cation forms a polar domain alongside the anions. While the 1:2 ILs discussed in this

work do show a similar nanostructuring consisting of discrete domains, the 'roles' played by the cations and anions are, in a way, reversed. Here, the polar domain consists primarily of cations (alongside the anion headgroups), while the formation of the nonpolar domain is driven by the presence of long alkyl tails on the carboxylate anions. Thus, when discussing the 1:2 ILs in this work — particularly when comparing their properties and structures to more conventional ILs — it is important to acknowledge that the role played by the anions in these ILs is analogous to the role played by cations in e.g. imidazolium-based ILs. Based on this, it is possible to consider some of the structure-property effects on IL viscosity that have been reported in the literature and apply these to the 1:2 CAOC, 1:2 BTMAAGE and 1:2 BTMAAOC systems.

The fact that 1:2 CAOC has the highest viscosity and activation energy can be explained by the presence of the hydroxyl group on the cholinium cation. This facilitates the formation of hydrogen-bonding interactions between the cation and anion species, resulting in stronger intermolecular forces. The other ILs contain a BTMA cation, in which the hydroxyl group has been replaced with an alkyl moiety; this reduces the strength of the cation-anion interactions (hydrogen-bonding interactions are not possible), leading to lower viscosities and activation energies. This is in agreement with findings by Koi *et al.*, who reported that ILs containing spherical anions have greater viscosities than ILs with more asymmetrical or more weakly-coordinating anions. They have also stated that, in imidazolium-based ILs, changing the structure of the anion often has a more significant impact on the IL viscosity compared to a change in the length of the cation alkyl chain.¹³⁷ Considering the fact that anions in 'conventional' ILs are analogous to the cations in the ILs discussed in this work, this suggests that the cholinium-to-BTMA change may have a stronger effect on the IL viscosity than a change in the carboxylate anion structure.

Comparing 1:2 BTMAAGE and 1:2 BTMAAOC, the former IL has a higher viscosity. The main structural difference between these systems is the nature of the carboxylate anions. In 1:2 BTMAAOC, the octanoate anion contains a linear, saturated alkyl chain, while in 1:2 BTMAAGE the geranate anion contains a branched, unsaturated chain, with two carbon-carbon double bonds and two branching methyl groups. One possible explanation for the observed viscosity trend is that the branching methyl groups present on the geranate anions lead to an increase in Van der Waals forces in the 1:2 BTMAAGE system, and thus to a greater viscosity. This agrees with findings by Koutsoukos *et al.*, who studied the viscosities of

Table 4.2. Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD, Equation 2.8). Highlighted data corresponds to 1:2 BTMAAGE.

Sample	η_0 / mPa s	B / K	B / kJ mol ⁻¹	T_0 / K	AAD / %
1:2 BTMAAGE	0.0780	1151.20	9.57	174.94	0.5
1:2 CAOC	0.0412	1517.05	12.61	146.90	0.02
1:2 BTMAAOC	0.0601	1135.71	9.44	172.99	0.006

several long-chain imidazolium-based ILs and found that branched substituents lead to higher viscosities than linear ones.⁸⁶ Watanabe *et al.* have also reported that an increase in Van der Waals forces (associated with an increase in alkyl chain length in $[C_nC_{1im}][NTf_2]$ ILs) leads to greater IL viscosities.¹³⁵ Another factor could be the fact that 1:2 BTMAAGE has a greater molecular weight than 1:2 BTMAAOC, with a positive linear correlation between viscosity and molecular weight being reported by Barthen *et al.*¹³⁸

Finally, another factor leading to the higher viscosity of 1:2 BTMAAGE could be the fact that carbon-carbon double bonds are present in the structure of the anions in 1:2 BTMAAGE. The double bonds increase the rigidity of the geranate anion and restrict its flexibility compared to the octanoate anion present in 1:2 BTMAAOC. Philippi *et al.* have stated that the viscosity of an IL is significantly higher than that of an equivalent molecular solvent due to two main factors.¹³⁹ The first is Coulombic compaction resulting from the higher IL density, while the second is the formation of an extended charge network due to the ionic nature of the constituent species. They report that one way to mitigate the effect of Coulombic compaction is to increase the conformational flexibility of the species that make up the IL. This leads to improved dynamics (viscous flow and ion diffusion) in the system and thus to a lower viscosity. For 1:2 BTMAAGE and 1:2 BTMAAOC, this idea is also supported by the activation energies B , calculated from fitting the temperature-dependent viscosity data to the VFT equation. This parameter follows the same trend as the viscosity, with $B_{BTMAAGE} > B_{BTMAAOC}$, suggesting that the viscous flow process in 1:2 BTMAAGE is slightly more restricted than in 1:2 BTMAAOC. This difference in activation energies is, however, very small, and is most likely not indicative of significant differences between the two systems.

Two of the best-fit parameters in Table 4.2 can be compared with parameters obtained from

fitting the DMA $\tan \delta$ data corresponding to the thermally activated relaxation (Table 4.1). T_0 has roughly the same value in both cases, while the activation energy obtained from the viscosity data ($B_{\text{visc}} = 9.57 \text{ kJ mol}^{-1}$) is higher than the activation energy given by the fit of DMA data ($B_{\text{relax}} = 6.2 \text{ kJ mol}^{-1}$). This difference is most likely explained by the fact that the two techniques (and the respective activation energies) describe different phases of the IL. The thermally activated relaxation observed by DMA occurs over a temperature range of -53 – $0 \text{ }^\circ\text{C}$ (220 – 272 K), which is entirely within the liquid crystalline window of 1:2 BTMAAGE. The viscosity measurements, on the other hand, were performed on the isotropic liquid phase. The difference between the two activation energy values is relatively small, suggesting that the dynamics controlling viscous flow in the two phases of the IL do not differ significantly. This discrepancy could also come from the fact that the way the fit is performed for the two techniques is different: the viscosity fit uses individual points (viscosities) and aims to find their temperature dependence; the DMA fit, on the other hand, uses the shape of the relaxation peak, which introduces additional parameters (the width parameter α , as well as some intensity parameters) into the fitting process. Thus, a parameter describing viscous flow (such as the activation energy) can be expected to show variation when derived from different techniques. It should be noted here that a discrepancy is also observed in the trends followed by the activation energies of the three ILs (1:2 BTMAAOC, 1:2 CAOC and 1:2 BTMAAGE) when comparing DMA and viscosity data. The energies calculated from the thermally activated relaxation data vary in the order $1:2 \text{ BTMAAGE} < 1:2 \text{ BTMAAOC}$, while the viscosity-derived values are nearly identical (with the activation energy of 1:2 BTMAAGE being marginally higher). Again, this could be explained by the fact that each technique probes a different phase of the IL; additionally, while the two activation energies are both related to dynamic processes within the IL bulk, it is likely that the dynamics describing the thermally activated relaxation and the viscous shear flow are not identical.

4.3 Structuring

4.3.1 NMR

Solid-state magic-angle spinning (MAS) NMR spectra of 1:2 BTMAAGE were recorded by myself and Dr. Anjali Menakath at the University of Warwick, UK and analysed by myself.

Spectra were recorded at 5 and 50 °C as, according to DSC and PLM data, these temperatures correspond to the liquid crystalline and isotropic liquid phases, respectively. Both ^1H - ^1H NOESY and 1D ^1H NMR spectra were recorded.

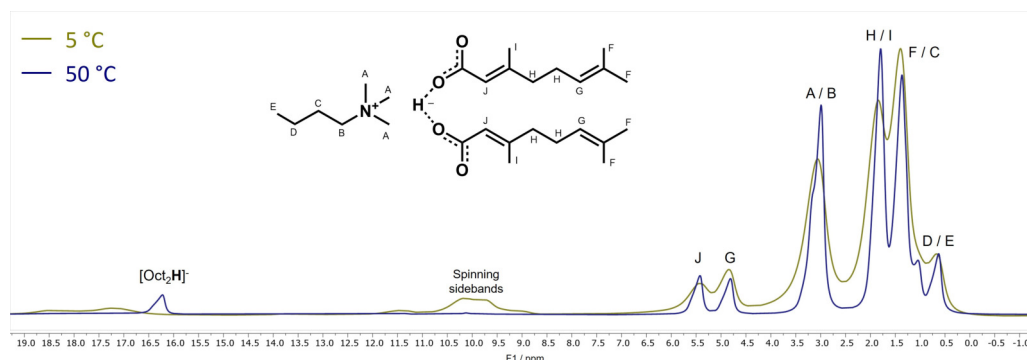


Figure 4.9. Solid state MAS ^1H NMR of 1:2 BTMAAGE at 5 and 50 °C

1D spectra are shown in Figure 4.9. The same set of resonances can be seen in both spectra, with the main difference being that the peaks are broader and less well-defined at 5 °C. This is expected, as the sample is in a liquid crystalline state, which is not isotropic but instead is characterised by positional and / or orientational order.^{87,91} The broad feature centred around 10 ppm is a spinning sideband resulting from this anisotropy. Additionally, while the viscosity of the LC sample has not been measured, this is believed to be significantly higher than the viscosity of the isotropic phase (as was observed for 1:2 BTMAAOC and 1:2 CAOC); higher viscosity correlates with broader spectral features.¹³¹ The appearance of sidebands and the spectral resolution can be improved in future measurements by increasing the spinning rate.

The position of the peaks does not change significantly between the two spectra, with the exception of the downfield peak corresponding to the acidic $[\text{Oct}_2\text{H}]^+$ proton. At 50 °C this peak appears sharper and is shifted to a lower chemical shift than in the spectrum recorded at 5 °C. This effect was also observed in 1:2 CAOC and can be attributed to the weakening of hydrogen bonding in the higher-temperature sample. In all of the 1:2 systems, including 1:2 BTMAAGE, the acidic proton is shared between two carboxylate anions through hydrogen bonding. This forms a complex anion where the negative charge is delocalised across the entire headgroup and causes this proton to be more deshielded than it would be in the neat acid. Generally, carboxylic acid protons have a chemical shift of 11–12 ppm; the acidic proton in 1:2 BTMAAGE has a chemical shift of 16.3 ppm. As the temperature of the measurement increases, the hydrogen bonding in the complex anion weakens, leading to the proton becoming

less deshielded and the signal shifting to slightly lower ppm.

The ^1H - ^1H NOESY spectra recorded at 5 °C and 50 °C are shown in Figures 4.10 and 4.11 respectively. The structure of 1:2 BTMAAGE shown on the left-hand side of these figures is not meant to represent a real arrangement of molecules; it is only used to illustrate the intermolecular interactions associated with the observed crosspeaks. These crosspeaks are indicated by black, dotted line circles, while the interactions are marked on the 1:2 BTMAAGE structure using blue highlights and dotted lines.

At 5 °C, 1:2 BTMAAGE is in the liquid crystalline phase and shows several crosspeaks in the NOESY spectrum. The positively-charged headgroup of the BTMA cation (protons A and B) interacts with the alkyl chain of the geranate anion, showing crosspeaks both with the terminal methyl groups (protons labeled F) and with protons located further towards the anion headgroup (protons H and I). The butyl chain of the BTMA cation (protons C, D and E) also shows crosspeaks with the geranate chain (protons F, G, H, I). At 50 °C 1:2 BTMAAGE is in the isotropic liquid state. The NOESY spectrum shows some low-intensity crosspeaks between the BTMA protons (A, B, D, E) and the anion alkyl chain protons (H, I). These are thought to be due to interactions occurring at the boundary between the polar and nonpolar domains. No other significant intermolecular interactions can be identified in the isotropic liquid phase.

4.3.2 X-ray scattering

So far, DSC, DMA, PLM and NMR data have been used to establish that 1:2 BTMAAGE behaves in a similar way to 1:2 BTMAAOC AND 1:2 CAOC, showing a liquid crystalline mesophase at low temperatures and an isotropic liquid phase at temperatures above 25 °C. The structuring of these phases was investigated using X-ray scattering measurements, performed on beamline I22 at Diamond Light Source, Oxford. Data were collected by Dr. Chi L. Chan and Dr. Mohit Devgan and analysed by myself. Measurements were performed every 10 °C over a temperature range of 5–55 °C. The SAXS and WAXS plots are shown in Figure 4.12. It should be noted that WAXS data was recorded over a q range of 0.18–6.6 $\text{\AA}^{-1}$, with the region between 0.18 and 0.33 $\text{\AA}^{-1}$ representing an overlap between the SAXS and WAXS detectors. Low- q data is best captured using the SAXS detector and so the data points in this range were only included in the SAXS profiles. For the sake of clarity, data points associated with the

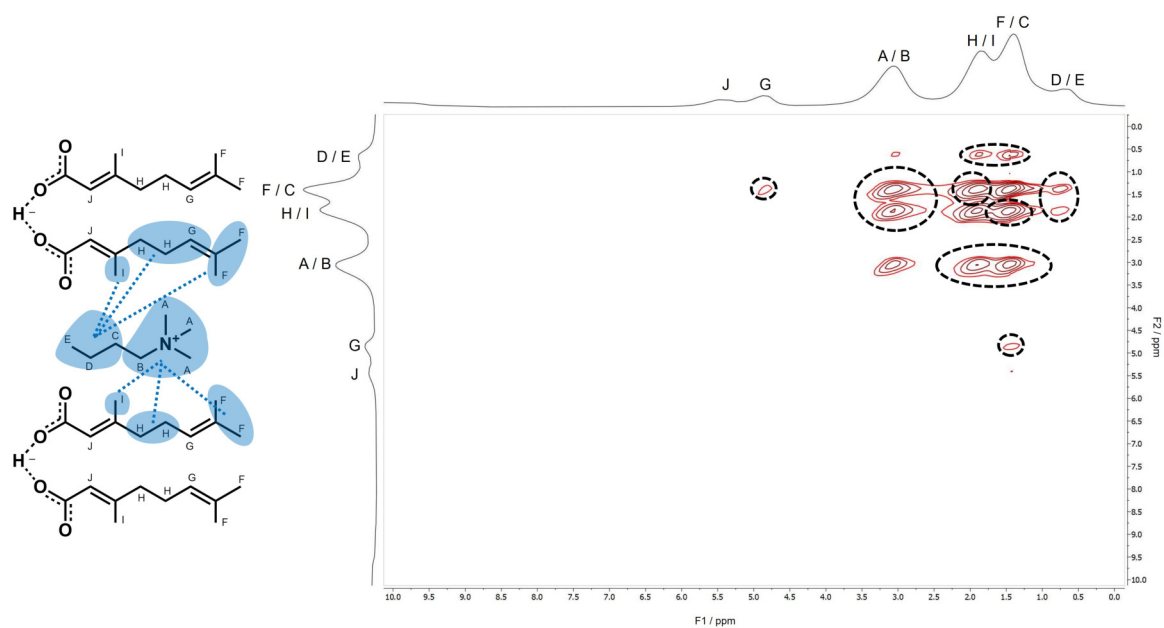


Figure 4.10. ^1H - ^1H NOESY of neat 1:2 BTMAAGE at 5 °C (liquid crystalline phase)

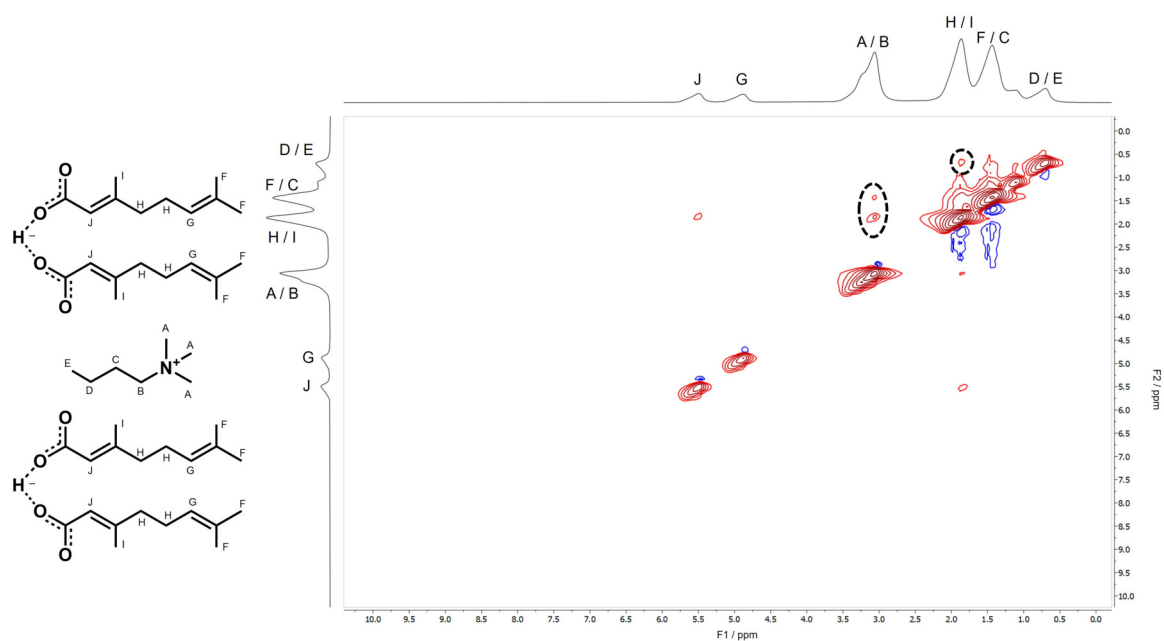


Figure 4.11. ^1H - ^1H NOESY of neat 1:2 BTMAAGE at 50 °C (isotropic liquid phase)

sharp peak at approximately $0.32 \text{ \AA}^{-1}$ were excluded from the WAXS profiles, with the data shown here starting at $q = 0.45 \text{ \AA}^{-1}$.

Several features can be seen in the SAXS/WAXS profiles. First, the data recorded at $5 \text{ }^{\circ}\text{C}$ will be discussed, in order to establish the structuring of the IL at the lowest probed temperature (where it is expected to show the highest degree of ordering). Then, the variable-temperature data will be presented and any changes in the SAXS/WAXS profiles with increasing temperature identified.

In the SAXS data recorded at $5 \text{ }^{\circ}\text{C}$ two main features can be observed. The highest intensity feature is the sharp peak at approximately $0.32 \text{ \AA}^{-1}$, labelled as Peak A. This peak indicates that the dominant structure is liquid crystalline in nature, with a repeating distance of approximately $19.6 \text{ \AA}$. The second feature is the sharp peak at $q = 0.10 \text{ \AA}^{-1}$, labelled as Peak B. Generally, LC phases with a layered structure (lamellar or smectic) show multiple sharp peaks with q values in a 1:2:3:4 etc. ratio — other LC arrangements give rise to different patterns. Here, however, no such relationship exists between the positions of these two peaks. Additionally, the two features behave differently with increasing temperature: above $25 \text{ }^{\circ}\text{C}$ the peak at $q = 0.32 \text{ \AA}^{-1}$ is broader and has a significantly lower intensity, while the peak at $0.10 \text{ \AA}^{-1}$ remains relatively sharp and shows only a small decrease intensity. All of this suggests that the two features are not associated with the same mesophase and that a second liquid crystalline arrangement exists within the IL. This is associated with peak B, at $q = 0.10 \text{ \AA}^{-1}$, corresponding to a repeating distance of approximately $61.6 \text{ \AA}$. This peak has a significantly lower intensity (and area) than the feature at $q = 0.32 \text{ \AA}^{-1}$; as the relative area of a scattering peak is usually proportional to the amount of sample in the corresponding configuration, this suggests that this secondary phase represents only a small part of the IL sample (although it is acknowledged that peak intensity / area is also affected by several other factors). These findings are similar to the structural observations made for 1:2 BTMAAOC, where two sets of scattering peaks corresponding to two different structural arrangements can be seen in the SAXS-WAXS data. For both 1:2 BTMAAOC and 1:2 BTMAAGE, the reason for the existence of this second set of peaks is unknown. It is possible that this is the effect of a small amount of sample crystallising, but there is no experimental evidence to support this.

The predominant phase of 1:2 BTMAAGE is associated with scattering peak A at $q = 0.32 \text{ \AA}^{-1}$, which corresponds to a repeating unit distance of $19.6 \text{ \AA}$. This is equal to twice the length of

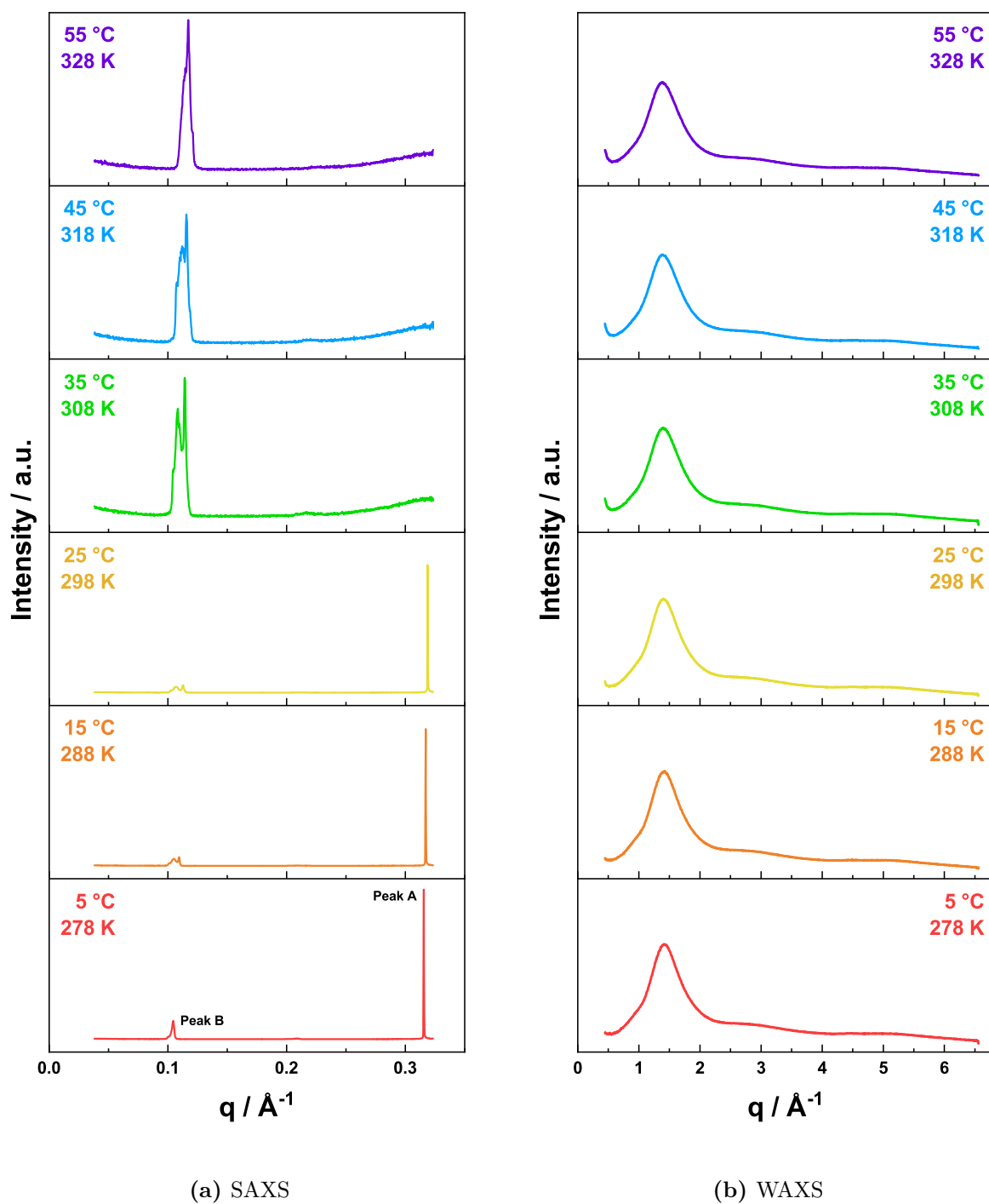


Figure 4.12. X-ray scattering data of 1:2 BTMAAGE at various temperatures. *Note:* two different y-scales are used for the SAXS graphs. One scale is used for the 5–25 °C graphs (determined by the height of the peak at $0.32 \text{\AA}^{-1}$) and another is used for the 35–55 °C graphs (determined by the feature at $0.10 \text{\AA}^{-1}$).

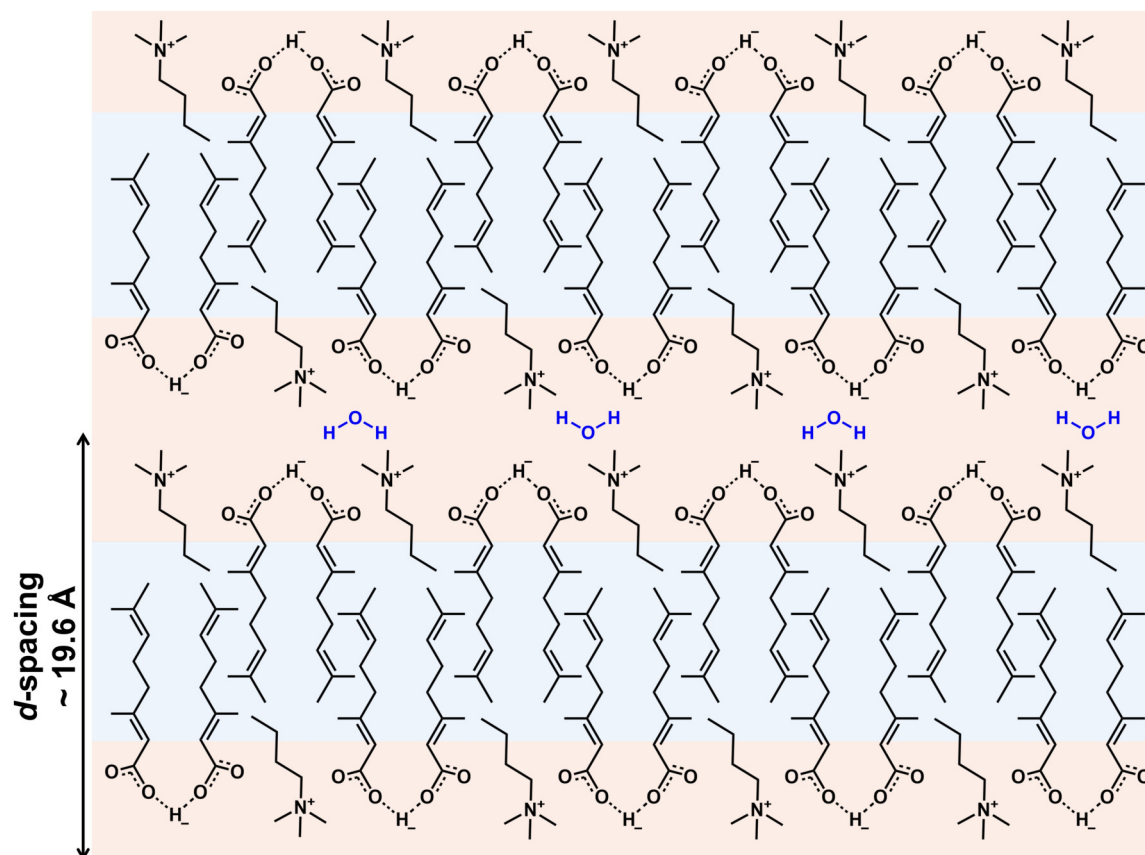


Figure 4.13. Possible structure of liquid crystalline 1:2 BTMAAGE. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 19.6 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner (associated with a complex $[(\text{geranate})_2H]^-$ anion), the real system is a dynamic one, in which hydrogen bonds are always breaking and forming.

the fully extended $[(\text{geranate})_2\text{H}]^-$ anion (approx. $9.71 \text{ \AA}$), which is consistent with a lamellar bilayer structure. Higher order peaks associated with this phase are not present, indicating that the packing of the lamellar layers does not possess long-range ordering. A possible structure for the lamellar bilayers present in 1:2 BTMAAGE is shown in Figure 4.13. The nonpolar region of the bilayer is comprised on the anion alkyl tails, while the polar region is comprised of the anion headgroups and the BTMA cation (although the butyl tail of the cation may partially reside in the nonpolar domain). The WAXS data (Figure 4.12b) shows a broad, somewhat asymmetric peak at $q = 1.47 \text{ \AA}^{-1}$, corresponding to a real-life distance of $4.42 \text{ \AA}$. While the alkyl tails of the geranate anions are shown here as fully extended, the WAXS data indicates that in reality these tails are disordered, with some degree of rotational and translational freedom, making the observed mesophase a fluid lamellar L_α phase.^{79,92}

The BTMA cation is thought to reside in the polar region, near the anion headgroups, as this ensures charge neutrality. As the SAXS data cannot provide information on the position of the cation, the only experimental data regarding this is in the NOESY spectrum shown in Figure 4.10. This shows crosspeaks between the BTMA methyl protons and most of the protons on the anion alkyl chain. Based on this data, An alternative placement — with the cation residing in the nonpolar region — was considered briefly. However, placing the cation amongst the anion alkyl tails would be energetically unfavourable, as it would result in anion-anion interactions in the polar domain and would disrupt the hydrophobic interactions occurring between the alkyl tails in the nonpolar region of the bilayer. In the proposed bilayer structure, the cation methyl groups are proximal to the terminal methyl groups of the anion tails (giving rise to the crosspeaks between protons A/B and protons F/G). The crosspeaks between the cation methyl protons (A/B) and the other anion alkyl chain protons are thought to occur due to spin diffusion through the alkyl chain, which is facilitated by the highly ordered bilayer structure. This effect has been reported in the literature by Stark et al.¹²¹ for phospholipid bilayer and it is also to occur in the other ILs in this work.

Table 4.3 shows estimated unit length and unit area values calculated for the proposed 1:2 BTMAAGE bilayer structure. These calculations are similar to those performed for the other ILs and are explained in more detail in Chapter 2. Here, the 'unit' is a cluster consisting of a BTMA cation, a geranate anion and a geranic acid molecule (i.e. a 1:2 BTMAAGE unit). As was the case with the previously discussed ILs, the density of 1:2 BTMAAGE could not

Table 4.3. Estimated length and area values for the 1:2 BTMAAGE unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.

Chain position	d -spacing (19.6 Å)	Unit length	Unit area
No interdigitation	$d = 2 \times l_{\text{unit}}$	$l_{\text{min}} = 9.8 \text{ Å}$	$A_{\text{max}} = 76.5 \text{ Å}^2$
Partly interdigitated	$d = 1.5 \times l_{\text{unit}}$	$l_{\text{int}} = 13.07 \text{ Å}$	$A_{\text{int}} = 57.4 \text{ Å}^2$
Fully interdigitated	$d = l_{\text{unit}}$	$l_{\text{max}} = 19.6 \text{ Å}$	$A_{\text{min}} = 38.3 \text{ Å}^2$

be determined experimentally; the density of 1:2 CAGE (0.99 g mL^{-1}) was used instead.⁹ The proposed bilayer structure is similar to phospholipid bilayers, such as those formed by DOPC and DPPC and the estimated area values (particularly for partially interdigitated chains) are similar to the literature values reported for other phospholipid bilayers ($40\text{--}70 \text{ Å}^2$).^{123,124}

In order to understand how the structuring of 1:2 BTMAAGE changes with temperature, SAXS and WAXS profiles were recorded at several temperatures within the $5\text{--}55 \text{ °C}$ range. These are shown in Figure 4.12. A note must be made here regarding the scale of the Y-axis (representing intensity, in arbitrary units) of the plots shown here. Because the intensity of the WAXS peak does not change significantly with temperature, all WAXS plots have the same Y-scale and thus the data is easy to compare. The SAXS plots, however, have different Y-scales depending on the intensity of the most prominent peak / feature. The $5\text{--}25 \text{ °C}$ graphs all have the same y-scale, determined by the height of the peak at 0.32 Å^{-1} . For the $35\text{--}55 \text{ °C}$ graphs, the scale is determined by the feature at approximately 0.10 Å^{-1} and is, once again, consistent between the three plots. Because the graphs have two different Y-scales, it is difficult to assess how the intensity of a peak changes with temperature. Thus, in order to facilitate comparison, close-up graphs of peaks A and B at all measured temperatures are provided. Figure 4.14 shows WAXS data associated with peak A. Because the position of peak A is close to the boundary of the SAXS detector, this feature cannot be seen in its entirety in the SAXS data, particularly at temperatures above 25 °C , where it is significantly broader. For this reason, data recorded on the WAXS detector is used to show the behaviour of peak A with temperature. Peak B is entirely within the range of the SAXS detector, and so selected SAXS data associated with this feature are shown in Figure 4.15.

The first feature to be discussed is peak A. As mentioned, at 5 °C this appears as a sharp,

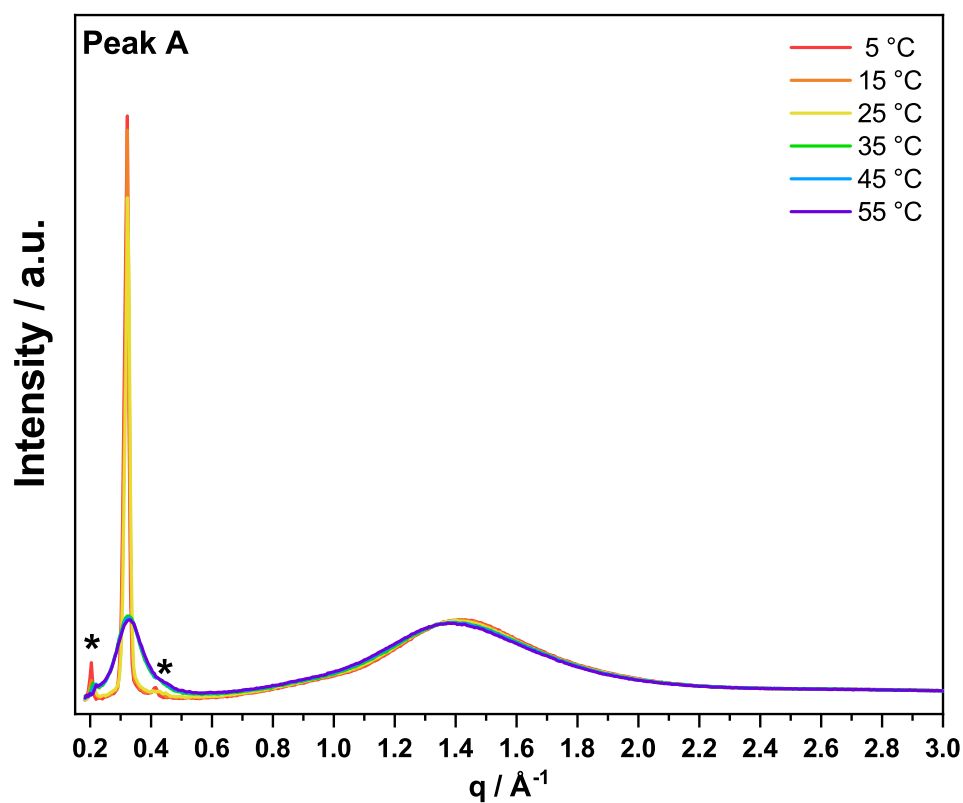


Figure 4.14. Selected WAXS data showing the variation of Peak A with temperature

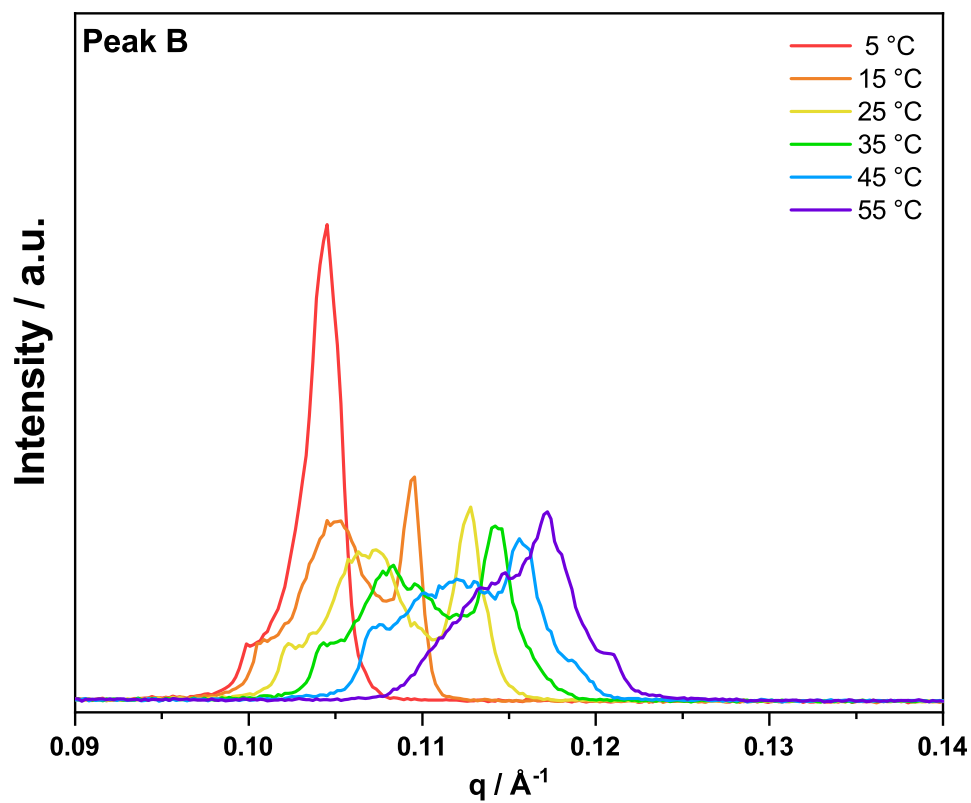


Figure 4.15. Selected SAXS data showing the variation of Peak B with temperature

intense peak at $q = 0.32 \text{ \AA}^{-1}$. As the temperature increases, the peak remains unchanged at 15 and 25 °C, showing that the liquid crystalline bilayer is maintained. At 35 °C the peak becomes broad and decreases in intensity, appearing very similar to the features observed for 1:2 BTMAOC and 1:2 CAOC in the isotropic phase. The change from a sharp peak to a broad feature occurs at a temperature between 25 and 35 °C, in agreement with the temperature of the LC-to-isotropic transition of 1:2 BTMAAGE as measured by DSC and PLM. The shape of peak A (broad, rather than sharp) at 35 °C and above indicates that while the IL is no longer in a liquid crystalline state, it still retains some degree of intrinsic ordering. For ILs, the presence of a peak in this region is associated with long-range structuring, in the form of segregated polar and nonpolar nanodomains.

Peak B is thought to be associated with a second phase present in the 1:2 BTMAAGE sample. As mentioned previously, this is thought to comprise only a small part of the sample and it is not believed to have a significant effect on the measured properties of the IL. The behaviour of Peak B with increasing temperature is shown in Figure 4.15. At 5 °C this feature appears as a sharp peak at $q = 0.10 \text{ \AA}^{-1}$, with a shoulder on the low- q side. This corresponds to a d -spacing of 61.6 Å. This is equal to approximately six times the length of the $[\text{geranate}_2\text{H}]^-$ anion, or three times the length of a bilayer. The relatively sharp shape of the peak suggests that the phase it is associated with has a high degree of ordering (a single preferred repeat spacing); this might be crystalline or liquid crystalline in nature. If Peak B is considered the first-order reflection arising from this LC phase, two higher-order reflections can be seen in the WAXS data in Figure 4.14, marked with asterisks. These low-intensity peaks appear at $q = 0.20 \text{ \AA}^{-1}$ and $q = 0.41 \text{ \AA}^{-1}$, which are in a ratio of 2:1 and 4:1 to the q -value of peak B respectively. This is in agreement with the $q, 2q, 3q, 4q$ etc. pattern usually associated with lamellar LC structures. The third-order reflection, which would be expected at $q = 0.3 \text{ \AA}^{-1}$ (3:1 ratio w.r.t. peak B) is not visible; given the low intensity of the higher-order peaks, this is most likely obscured by peak A ($q = 0.32 \text{ \AA}^{-1}$).

At 15 °C, peak B splits, giving rise to a broad peak at $q = 0.105 \text{ \AA}^{-1}$ and a sharp peak at $q = 0.109 \text{ \AA}^{-1}$. As the temperature increases further, both of these features shift to higher q -values, corresponding to a decrease in d -spacing. The peaks also decrease in intensity and the peak shapes become broader, suggesting that the structure of the water-rich phase is becoming more disordered. The shape of the lower- q peak is very broad and asymmetric, suggesting

a structure with a high degree of disorder and several preferred repeat spacings. At 55 °C the peak at lower q is no longer well-defined and only appears as a shoulder. The peak at higher q remains relatively sharp up to 25 °C, and becomes broader and more asymmetric at higher temperatures. The small peaks observed in the WAXS profile (Figure 4.14), marked with asterisks, are thought to be higher-order peaks associated with this second phase; these small peaks also change in shape and intensity as the temperature increases. The second-order peak (the asterisk peak at lower q) becomes broader and shifts to higher q values. The fourth-order peak (the asterisk peak at higher q) is only present at 5 °C and disappears at higher temperatures. The broadening of the peaks and the disappearance of this higher-order peak indicate that as the temperature increases this second phase becomes increasingly more disordered and loses its long-range ordering. Further experiments are necessary in order to determine the exact nature of this phase and the reason for its presence in the 1:2 BTMAAGE sample.

4.4 Chapter summary

Table 4.4. Temperatures of the liquid crystal to isotropic liquid transitions

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 BTMAAGE	24	27	15	< 25	25–35
1:2 CAOC	52	60	57	50–55	50–55
1:2 BTMAAOC	17	25	37*	35–40	35

^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling

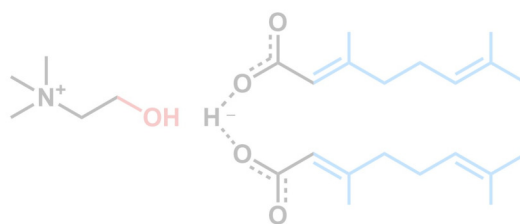
^d Temp. above which IL shows Newtonian flow behaviour

^e Temp. at which sharp LC peak disappears * Tan δ peak on heating

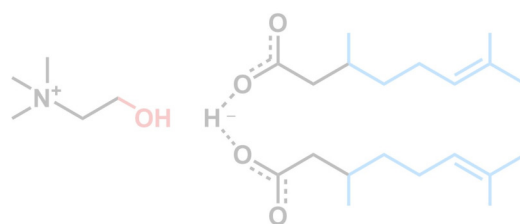
The thermal behaviour of 1:2 BTMAAGE is simpler than that of 1:2 BTMAAOC and 1:2 CAOC, with no cold crystallisation (or crystallisation) transition. 1:2 BTMAAGE undergoes only two transitions: a reversible glass transition at low temperatures and a reversible transition between a LC phase and an isotropic liquid phase. The structuring of 1:2 BTMAAGE appears similar to that of 1:2 BTMAAOC and 1:2 CAOC, showing primarily a lamellar bilayer liquid crystalline structure at temperatures 5–25 °C and an isotropic liquid structure at 35 °C and

above. The temperatures of the LC to isotropic transition observed for 1:2 BTMAAGE and for the previously discussed ILs are given in Table 4.4, to show how this temperature varies with IL and with technique. The presence of a second set of peaks in the SAXS/WAXS scattering profiles suggests that a second, distinct phase is also present in the studied sample of 1:2 BTMAAGE. The shape and pattern of these peaks suggests that this phase may be crystalline or liquid crystalline in nature, possibly with a lamellar bilayer structure (based on the pattern formed by the peak positions in q -space). More work is needed to confirm the nature and structure of this second LC phase, as well as to elucidate the reason for its formation.

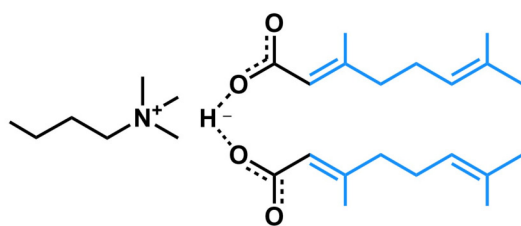
STRUCTURE COMPLEXITY



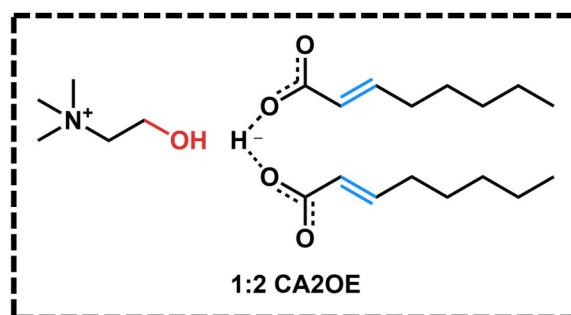
1:2 CAGE



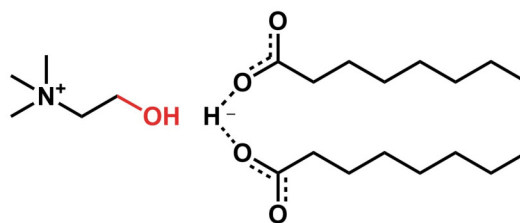
1:2 CACI



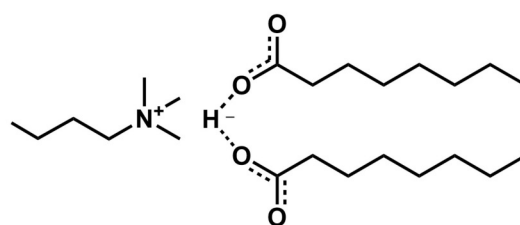
1:2 BTMAAGE



1:2 CA2OE



1:2 CAOC



1:2 BTMAAOC

Chapter 5

1:2 Choline And 2-OCtenoate (CA2OE)

This chapter looks at the 1:2 choline and 2-octenoate (CA2OE) ionic liquid. The structure of the IL is shown in Figure 5.1. 1:2 CA2OE is synthesised using one equivalent of cholinium bicarbonate and two equivalents of 2-octenoic acid. Like in the case of the other 1:2 ILs, a complex anion is formed, in which two 2-octenoate moieties share one proton, with the negative charge being delocalised across the headgroup (as shown in Figure 5.1).

2-Octenoic acid was chosen in order to isolate the effect of the double bonds in the alkyl chain on the properties of the IL. This acid has a very similar structure to octanoic acid (which is the simplest acid used), with the only difference being that 2-octenoic acid contains a carbon-carbon double bond in the C2–C3 position of the acid. Nonetheless, the structure of 2-octenoic acid is still simpler than that of geranic acid (with no branching groups and no double bond in the C6–C7 position). Like 1:2 CAGE, 1:2 CA2OE contains a cholinium cation, so any differences in properties and behaviour between the two ILs are expected to be driven by differences in

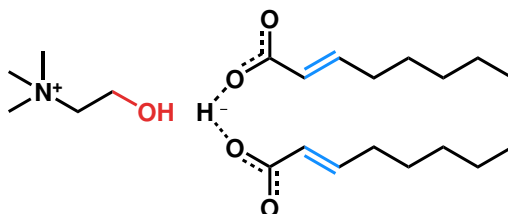


Figure 5.1. 1:2 CA2OE

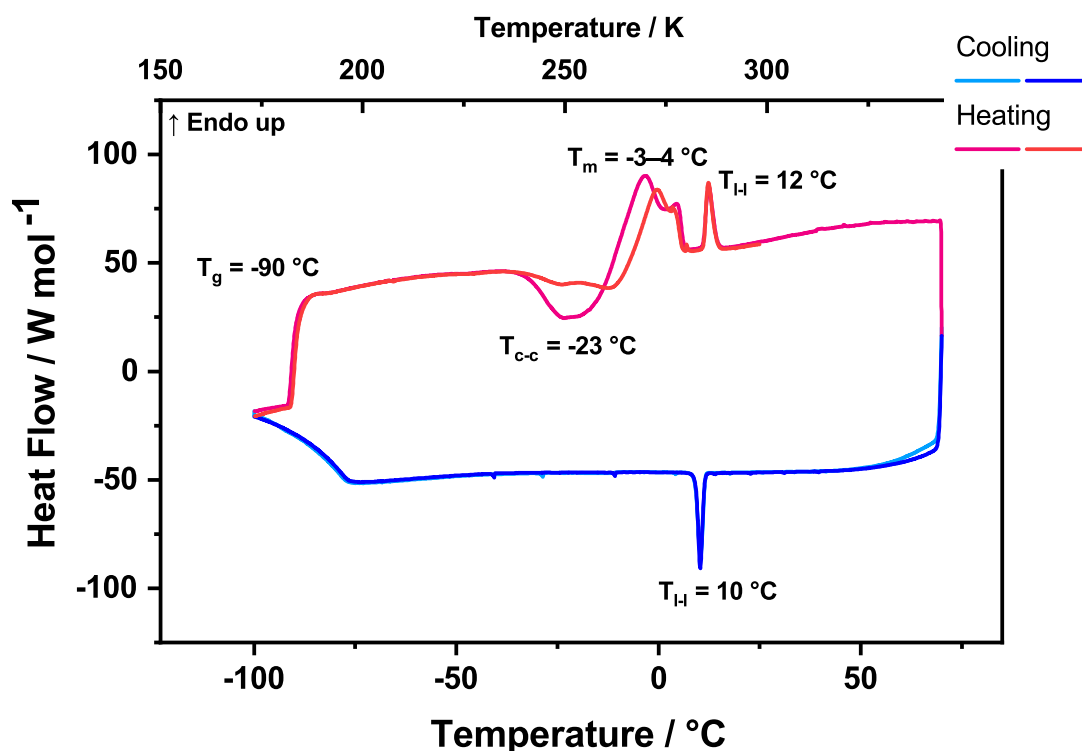


Figure 5.2. DSC traces of 1:2 CA2OE with annotated transition temperatures. The heating and cooling rates are 5 °C min^{-1} .

the acid / anion structure.

The first part of this chapter discusses the thermal behaviour of 1:2 CA2OE. This includes techniques such as differential scanning calorimetry (DSC), dynamic mechanical analysis (DMA) and polarised-light microscopy (PLM). The second part deals with the nanoscale structuring of the ionic liquid, investigated using small- and wide-angle X-ray scattering (SAXS and WAXS) and solid-state magic angle-spinning (SS-MAS) NMR.

5.1 Thermal behaviour

DSC measurements of 1:2 CA2OE were performed and analysed by myself at the Sapienza University of Rome, Italy. Heating and cooling rates were 5 °C min^{-1} . Two consecutive heating/cooling cycles were run. The IL showed a glass transition at $T_g = -90\text{ °C}$. As mentioned in Chapter 4, it is believed that the structure of the anion (and thus of the acid used in the synthesis) has a significant influence on the temperature of the glass transition. The T_g of 1:2 CA2OE is similar to the glass transition temperatures observed for 1:2 BTMAAOC and 1:2 CAOC; this is expected, as the structures of 2-octenoic acid and octanoic acid are very similar,

with the only difference being that the former contains a C2-C3 carbon-carbon double bond.

On heating, 1:2 CA2OE showed a cold crystallisation transition at approximately $T_{c-c} = -23\text{ }^{\circ}\text{C}$, meaning that the IL crystallised on heating from the glass phase, rather than on cooling from a liquid phase. Cold crystallisation transitions have been observed for other ILs, including 1:2 BTMAAOC and 1:2 CAOC. The thermal history of the 1:2 CA2OE sample seemed to affect this transition, as the exothermic peak was significantly larger in the first heating trace compared to the second. The cold crystallisation was rapidly followed by a two-step melting transition indicated by the two endothermic peaks in the region $T_m = -3\text{--}4\text{ }^{\circ}\text{C}$. Once again, this transition is affected slightly by the thermal history of the sample, with the lower-temperature endothermic peak being more intense in the first heating run. The higher-temperature peak is consistent between the two runs, both in intensity and position. At temperatures above T_m , 1:2 CA2OE is in a liquid crystalline phase, as evidenced by the polarised-light microscope (PLM) photographs in Figure 5.3. The last set of peaks observed in the DSC consists of an endothermic peak at $12\text{ }^{\circ}\text{C}$ and an exothermic peak at $10\text{ }^{\circ}\text{C}$. These features are associated with a phase transition between a liquid crystalline mesophase and an isotropic liquid phase (LC-isotropic transition) and are very similar to those observed for 1:2 BTMAAOC (at $17\text{ }^{\circ}\text{C}$), 1:2 CAOC (at $52\text{ }^{\circ}\text{C}$) and 1:2 BTMAAGE (at $24\text{ }^{\circ}\text{C}$). To confirm the nature of this transition, the optical properties of the IL were investigated using polarised-light microscopy (PLM).

The top-left image of Figure 5.3 shows a sample of 1:2 CA2OE at $16\text{ }^{\circ}\text{C}$ viewed through crossed polarisers. The IL is birefringent and gives rise to a pattern of Maltese crosses indicative of a lamellar liquid crystal phase. Comparing this image to PLM images of previously discussed ILs, the main difference is that for 1:2 CA2OE the bright (birefringent) area constitutes only a small portion of the entire image. In the case of 1:2 CAOC, for example, the entire image is covered with a bright, streaky, marble-like texture (Figure 3.3). Here, the birefringent areas observed for 1:2 CA2OE only cover a small proportion of the image and appear as individual, discrete Maltese crosses. This is most likely because only a small portion of the sample is in a liquid crystalline state; the temperature at which the photograph was taken is above the temperature of the liquid crystal to isotropic phase transition observed by DSC. Alternatively, it could be a result of the lamellar phase being aligned homeotropically, i.e. with the long axes of the molecules perpendicular to the substrate plane. This causes the sample to appear dark when viewed through the PLM, despite having a lamellar liquid crystalline structure.⁹³ The

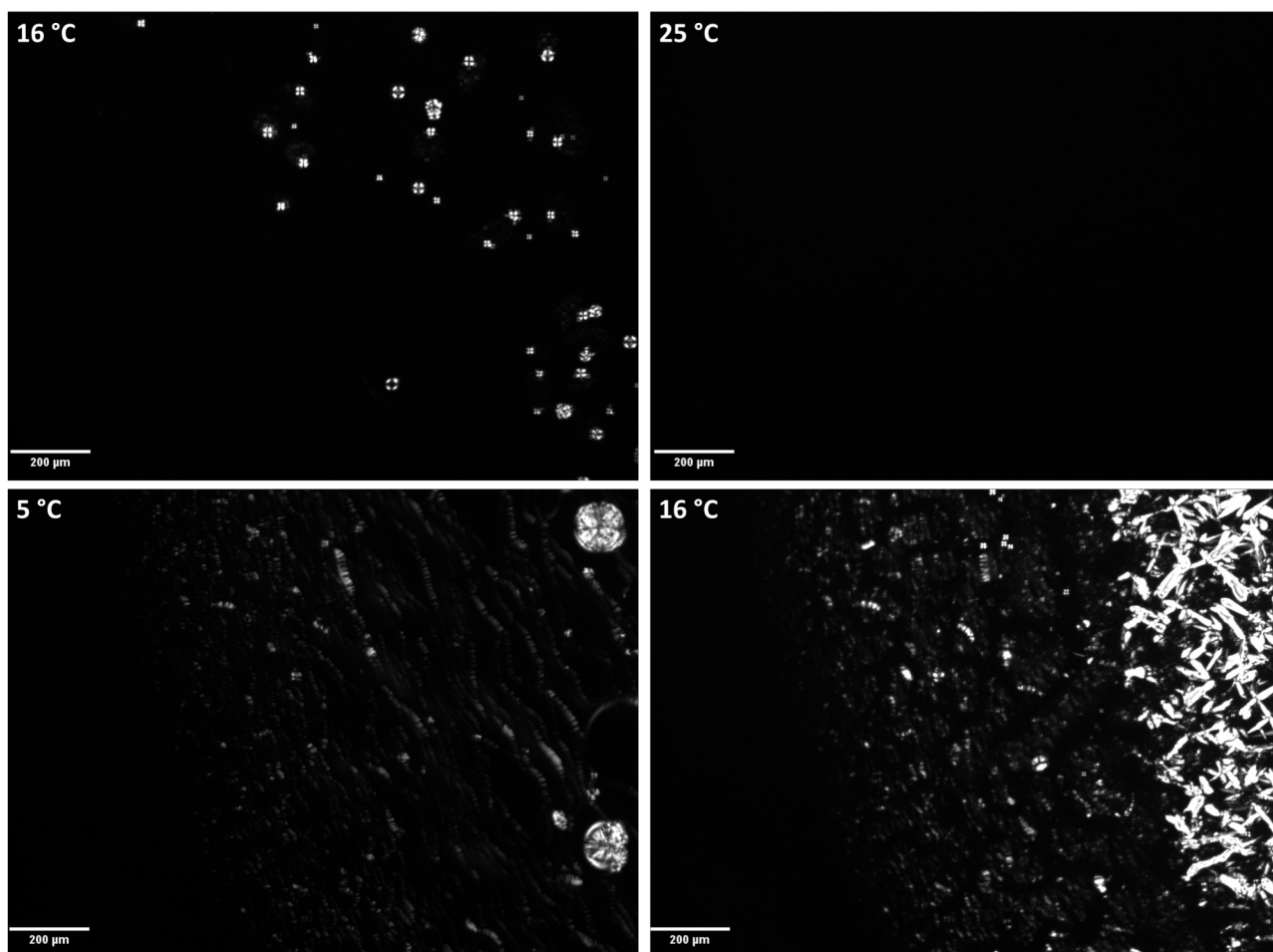


Figure 5.3. Polarised-light microscope images of 1:2 CA2OE taken with $4\times$ magnification. The sample was heated from 16 °C (top left) to 25 °C (top right), then cooled back down to 16 °C (bottom right). The same sample was then further cooled to 5 °C (bottom left).

same 1:2 CA2OE sample was then heated to 25 °C, with the PLM photograph shown in the top-right of Figure 5.3. The birefringent areas have disappeared and the image is completely dark, suggesting that the sample is now in the isotropic phase.

Based on the PLM photographs, the temperature at which the birefringence disappears on heating is 25 °C, while the temperature at which it reappears on cooling is approximately 19 °C (image not shown here). These temperatures are higher than the temperature of the LC-isotropic transition as measured by DSC ($T_{I-1} = 12$ °C). The same trend was observed for 1:2 BTMAAOC, where sample birefringence was found to disappear at 25 °C, while T_{I-1} was measured to be 17 °C by DSC. This is caused by some key differences between the DSC and the PLM techniques. First, the PLM setup reports the temperature of the sample stage, which is likely to differ from the temperature of the sample. Additionally, the DSC measurement is



(a) 1:2 CA2OE at room temperature



(b) 1:2 CA2OE cooled to 4 °C

Figure 5.4. Samples of 1:2 CA2OE at temperatures above and below the crystallisation transition temperature

performed under air-free, dry conditions, while the PLM photographs are taken while the IL is exposed to air and environmental moisture. Efforts were made to keep the PLM sample as dry as possible by quickly loading it onto a microscope slide which was then placed inside a covered sample stage. Still, this was not hermetically sealed or purged with nitrogen and given the hygroscopic nature of the IL it is likely that a small amount of moisture was taken up by the sample.

Visual inspection of a 1:2 CA2OE sample at 4 °C and 20 °C (Figure 5.4) demonstrated a similar behaviour to previously discussed ILs: 1:2 CA2OE showed a decrease in both opacity and viscosity upon heating past the temperature of the LC-isotropic phase transition. At 4 °C 1:2 CA2OE is in the liquid crystalline state and appears as an opaque, very viscous, gel-like material, with a light yellow colour. The colour is believed to be caused by heat, as the IL is handled at room temperature (15–20 °C) during the synthesis and drying process. The intensity of the colour was found to be further exacerbated by prolonged (> 1 week) exposure to heat (as low as room temperature). At 20 °C, isotropic 1:2 CA2OE (Figure 5.4a) is a clear, viscous, flowing liquid with a very pale yellow colour. The yellow colour appears less prominent than for the liquid crystalline IL due to the change in sample opacity.

The last two PLM images in Figure 5.3 (bottom, left and right) are taken during a cooling process, in which the sample that was initially heated to 25 °C is cooled back down to 16 °C and then further to 5 °C. A sample stage equipped with liquid nitrogen cooling was used, with a cooling rate of 5 °C min⁻¹. At 16 °C (bottom-right) the image shows birefringence covering a significantly larger area than in the original image taken at the same temperature (top-left). The right-hand side of the image shows a needle-like (batonet) pattern, which appears similar to textures that have been reported for smectic mesophases.^{140–142} Maltese crosses, which are also indicative of a layered liquid crystalline structure, can be seen throughout the image as well. As the sample is cooled to 5 °C, the birefringent area becomes less bright, with a layered rope-like pattern. Some large, bright Maltese crosses are also visible, as well as a small area showing intense brightness but a less well-defined pattern. The presence of several different textures suggests that more than one LC phase could be present in the 1:2 CA2OE sample. The Maltese cross and batonet patterns suggest that the mesophase(s) are smectic / lamellar in nature, meaning that the molecules arrange in ordered layers, similar to the behaviour observed for the ILs discussed previously. One reason for the presence of multiple mesophases could be the water content of the sample. Prior to any measurements, 1:2 CA2OE was dried on a high-vacuum Schlenk line to a water content of 0.4 wt% (8 mol%), measured using Karl-Fischer titration. Other ILs, such as 1:2 BTMAAOC (8 mol% water) and 1:2 BTMAAGE (13 mol% water), were each shown to contain two different lamellar mesophases. For these ILs, the small amount of water is thought to lead to the formation of a water-poor (neat IL) phase and a water-rich phase. X-ray scattering measurements of 1:2 CA2OE (section 5.2) also show multiple sets of peaks, indicating the presence of more than one mesophase in the IL structure. The PLM sample is likely to have a higher moisture content than the dried IL used in X-ray scattering measurements, as the hygroscopic IL was exposed to air during the measurements. It is also possible that uneven absorption of atmospheric moisture across the sample surface during the PLM measurement could lead to the formation of multiple LC structures with different hydration levels, resulting in the presence of different textures in PLM images.

5.1.1 Dynamic Mechanical Analysis

The thermal behaviour of 1:2 CA2OE was also investigated using dynamic mechanical analysis (DMA). Data was collected over a temperature range of -112–45 °C (160–318 K) and at three different frequencies ($f = 1, 5$ and 10 Hz). Figure 5.5 shows the $\tan \delta$ data and the relative

change in storage modulus $M'/M'_{298\text{ K}}$ (w.r.t. the value at 298 K or 25 °C) measured at $f = 1$ Hz on cooling and subsequent heating.

The glass transition observed by DSC at -90 °C is clearly visible in the data collected at $f = 1$ Hz and appears more complex than in the case of the other ILs discussed so far. In the $\tan \delta$ data collected on heating, the glass transition gives rise to a feature with multiple peak maxima, while the relative change in modulus shows a multi-step decrease on heating. The DSC data (Figure 5.2) shows that the sample only undergoes a single glass transition; based on the shapes of the DMA features, it is possible that this occurs as a multi-step process. Margulis *et al.* studied the behaviour of $[P_{666,14}][NTf_2]$ on cooling, at temperatures near to the glass transition temperature T_g and found that the vitrification process occurs separately for the polar and nonpolar domains of the IL.¹⁴³ On cooling, the polar domain shows solid-like behaviour first (at a higher temperature), with the nonpolar domain then undergoing vitrification as the temperature is decreased further. While this phenomenon was only investigated for one system, Margulis *et al.* have postulated that it could be generally applicable for ILs with significant nonpolar character (such as the systems discussed in this work).¹⁴³ It is possible that the appearance of the DMA data collected on heating is a reflection of this two-step vitrification process; however, since the DSC data only shows one transition it is more likely that this is caused by the presence of noise and could be improved if the measurement was repeated. The fact that the data collected on cooling does not have the same 'multi-step' appearance seems to support the idea that this is simply noise.

Apart from the feature associated with the glass transition, the $\tan \delta$ data also shows small fluctuations (broad peaks) at -55 °C (218 K), -34 °C (239 K) and -6 °C (267 K). The last two peaks are not present in the $\tan \delta$ data collected on cooling and are associated with the cold crystallisation transition and subsequent melting observed by DSC. The broad peak at -55 °C however, is present in the data measured on cooling at all three frequencies (Figure 5.6). The fact that this feature appears at the same temperature regardless of the measurement frequency is indicative of a phase transition (a thermally-activated relaxation peak would shift with frequency). M' shows a small increase at the corresponding temperature, indicating that this process causes a stiffening of the IL sample. Because both the M' increase and the intensity of the $\tan \delta$ peak are small and the DSC data does not show any peaks at this temperature, it is possible that this is simply an effect of the thermal history of the sample. The last feature

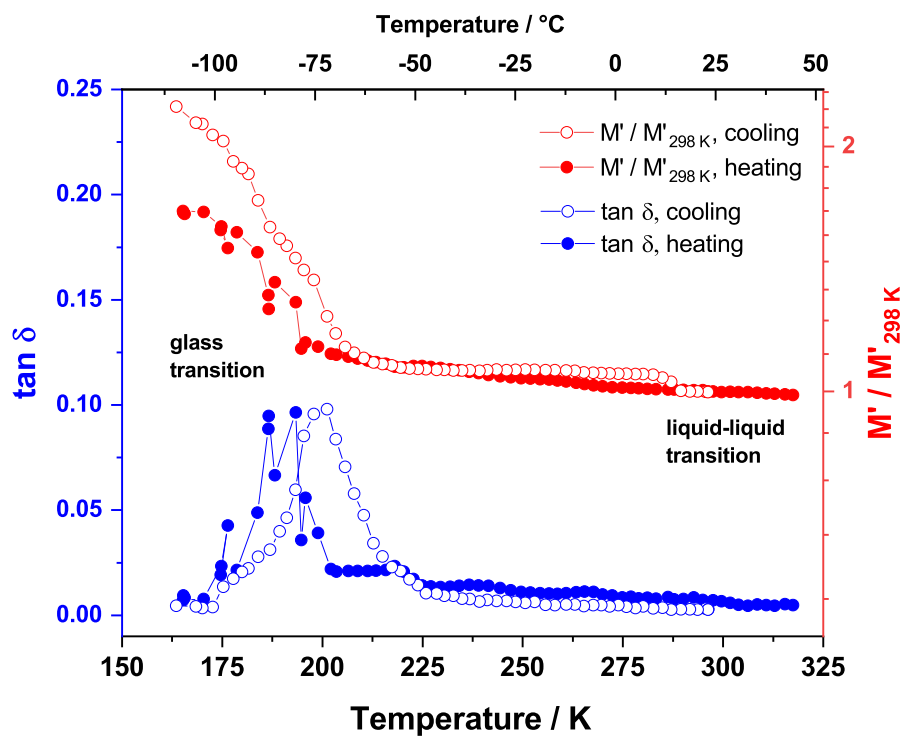


Figure 5.5. DMA data for 1:2 CA2OE, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols).

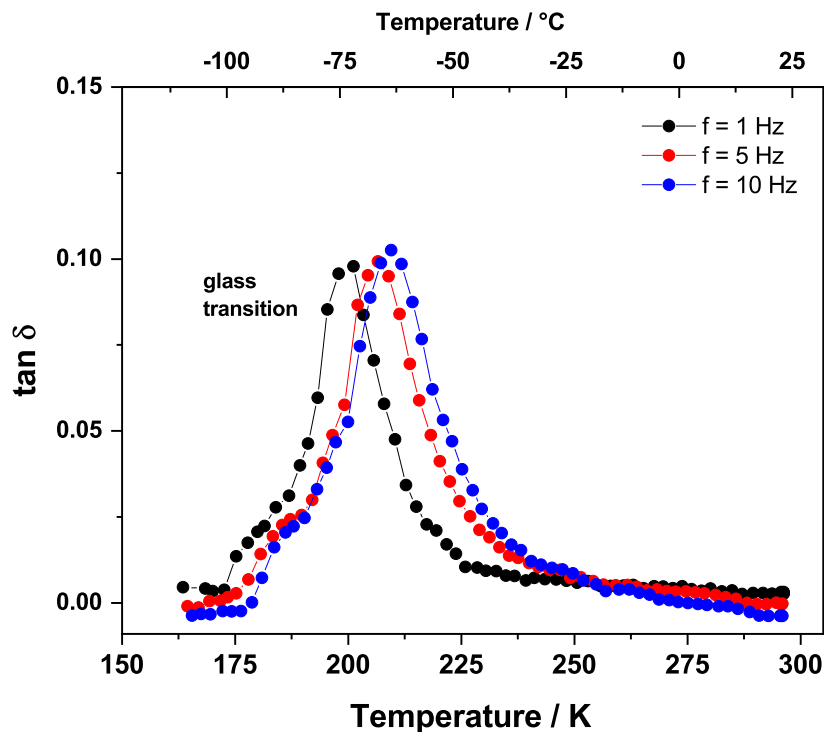


Figure 5.6. $\tan \delta$ measured for 1:2 CA2OE on cooling.

observed in the DMA data is a small increase in the modulus recorded on cooling, associated with the transition from the isotropic liquid phase to the liquid crystalline one. A corresponding feature is not observed upon heating, which could once again be due to the thermal history of the sample.

The $\tan \delta$ data collected at different frequencies is shown in Figure 5.6. Unlike in the case of the other ILs, no features associated with a thermally activated relaxation can be observed here. One reason for this could be that 1:2 CA2OE does not undergo such a relaxation, making it unique compared to the other five ILs discussed in this work. Another possibility is that the IL does undergo a relaxation but that the $\tan \delta$ features resulting from this process are overlapping with the glass transition peaks. A small variation on the high-temperature side of the glass transition peaks suggests that this might be the case. If a relaxation does occur, it appears to have a lower activation energy than in the case of the other ILs; lower activation energies mean the peaks will be observed at lower temperatures, which in this case would make them difficult to detect. As the position of the relaxation peaks is dependent on the measurement frequency, future measurements could use a wider temperature range (lower temperatures) and/or different measurement frequencies in order to detect these features. The fact that the relaxation peaks are not present (or simply not visible) in these graphs, along with the fact that the viscosity of 1:2 CA2OE could not be measured, due to instrument issues, means that no data relating to the dynamics of viscous flow in 1:2 CA2OE was obtained; a comparison with the other 1:2 IL systems discussed in this work is not possible. Future work involving the 1:2 CA2OE IL should include repeating the DMA measurements. Several heating-cooling cycles should be run in order to eliminate the thermal history of the sample and different heating rates and frequencies should be tested if possible.

5.2 Structuring

1:2 CA2OE undergoes a transition from a liquid crystalline phase to an isotropic liquid phase on heating. Photographs taken using crossed polarisers showed textures indicative of a layered, lamellar structure in the LC phase. However, based on the observed birefringence patterns, it is difficult to determine whether more than one mesophase is present. PLM also cannot provide specific information on the arrangement of the molecules within the LC structure. Solid-state magic-angle spinning (MAS) NMR and small- and wide-angle X-ray scattering (SAXS and

WAXS) measurements are shown and discussed in the present section; this aims to provide a better understanding of the structuring present in 1:2 CA2OE, in both the LC and isotropic phases.

5.2.1 NMR

Solid-state magic angle spinning (MAS) NMR spectra of 1:2 CA2OE were recorded by Dr Anjali Menakath at the University of Warwick, UK and analysed by myself. Data recorded at 5 °C is indicative of the liquid crystalline phase, while data recorded at 50 °C corresponds to the isotropic liquid phase. Figure 5.7 shows the 1D ^1H NMR of 1:2 CA2OE at these temperatures. Both spectra show the same set of peaks, which appear slightly broader at 5 °C; this effect is expected and was also observed for the other ILs. The peak position also shows a behaviour that was encountered for the other ILs: while the alkyl peaks appear at roughly the same chemical shift regardless of temperature, the downfield peak in the region of 10–12 ppm shows a shift to lower ppm as the temperature is increased. This peak appears at 10.8 ppm at 5 °C and at 10.4 ppm at 50 °C. Its position represents an average of two different proton environments: the hydroxyl proton of the cholinium cation (Ch-OH) and the acidic proton of the complex $[(2\text{-octenoate})_2\text{H}]^-$ anion, which undergo rapid exchange via hydrogen bonding.¹³ Individually, the Ch-OH proton would be expected at approximately 5–6 ppm, while the $[(2\text{-octenoate})_2\text{H}]^-$ proton would be expected to show a signal in the 14–16 ppm range. Similar chemical shifts were observed for the acidic protons in 1:2 BTMAAOC (15.0 ppm) and 1:2 BTMAAGE (16.3 ppm). The position of the peak that appears in the 1D ^1H spectrum is expected to be an average of these signals. The upfield shift with increasing temperature is likely to be a result of two different effects: a decrease in the hydrogen-bonding strength between this proton and the carboxylate anions (making it less deshielded) and a faster exchange rate between this acidic proton and the hydroxyl proton.

The nature of the interactions in the liquid crystalline and isotropic phases were investigated using ^1H - ^1H NOESY NMR at 5 °C (Figure 5.8) and 50 °C (Figure 5.9). As was the case with the other ILs, the structure shown here consists of 1.5 equivalents of 1:2 CA2OE, showing one cation and two complex anions; this is only used to illustrate the intermolecular interactions and is not a representation of the real molecular arrangement.

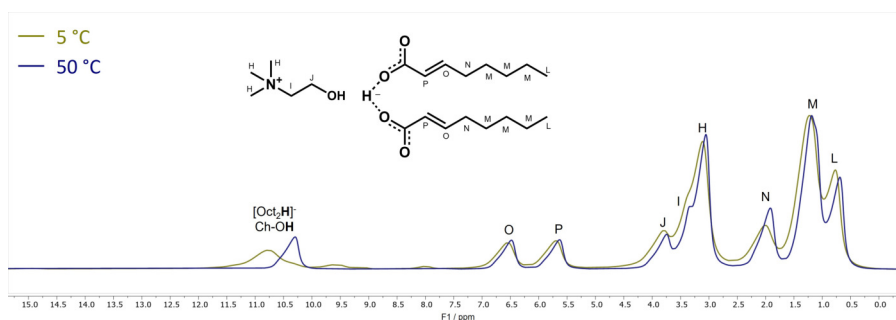


Figure 5.7. Solid state MAS ^1H NMR of 1:2 CA2OE at 5 and 50 $^{\circ}\text{C}$

At 5 $^{\circ}\text{C}$ the IL is thought to be in the liquid crystalline phase. The NOESY spectrum shows crosspeaks indicative of intermolecular interactions between the methyl protons of the cation (H) and the protons of the anion alkyl chains (M, N, O, P). The C(1) and C(2) protons of the cation (labelled I and J respectively) also show crosspeaks with the anion alkyl chain protons (L and M). Finally, the peak at approximately 10.5 ppm, corresponding to the Ch-OH and $[\text{2-Oct}_2\text{H}]^-$ protons, shows crosspeaks with anion protons L and M, as well as with protons of the cation headgroup (H and I). The intermolecular interactions of 1:2 CA2OE are very similar to those observed for 1:2 CAOC. This is expected, as the constituent species of 1:2 CAOC are structurally very similar to those of 1:2 CA2OE. In the NOESY spectrum recorded at 50 $^{\circ}\text{C}$, where the IL is in the isotropic liquid state, no significant crosspeaks can be observed.

5.2.2 X-ray scattering

To obtain more detailed information about the structuring present in 1:2 CA2OE, small-angle and wide-angle X-ray scattering measurements (SAXS and WAXS) were performed for the neat IL over a temperature range of 5–55 $^{\circ}\text{C}$ (every 10 $^{\circ}\text{C}$). Scattering profiles were recorded by Dr. Chi L. Chan and Dr. Mohit Devgan on the I22 beamline at Diamond Light Source, Oxford, and analysed by myself. The SAXS and WAXS profiles recorded at all temperatures are shown in Figure 5.10. It should be noted that the Y-axis scales are not the same for all plots, as they have been set in a way that optimises data visualisation. For plots showing the data using a single Y-axis scale see Figures 5.13 and 5.14 for SAXS and WAXS profiles respectively.

At 5 $^{\circ}\text{C}$, the SAXS data shows several features, labelled using the letters A–C. Peak A is a sharp feature at $q = 0.095 \text{ \AA}^{-1}$. This is the first (lowest q) of a series of three peaks between 0.09–0.11 $\text{\AA}^{-1}$ which become broader and less intense as q increases. Peak B is a low intensity feature at $q_B = 0.19 \text{ \AA}^{-1}$, while peak C is an intense, sharp peak at $q_C = 0.30 \text{ \AA}^{-1}$. To improve

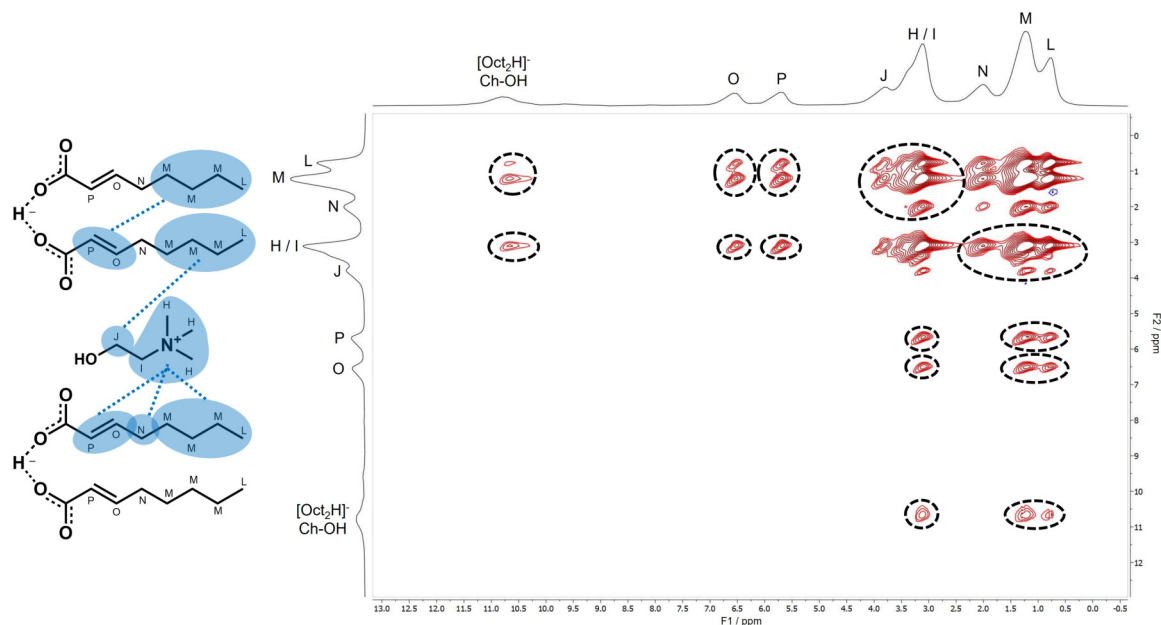


Figure 5.8. ^1H - ^1H NOESY of neat 1:2 CA2OE at 5 °C (liquid crystalline phase). Crosspeaks resulting from intramolecular interactions are circles (black dotted lines). The corresponding interactions are indicated using blue highlights and blue dotted lines.

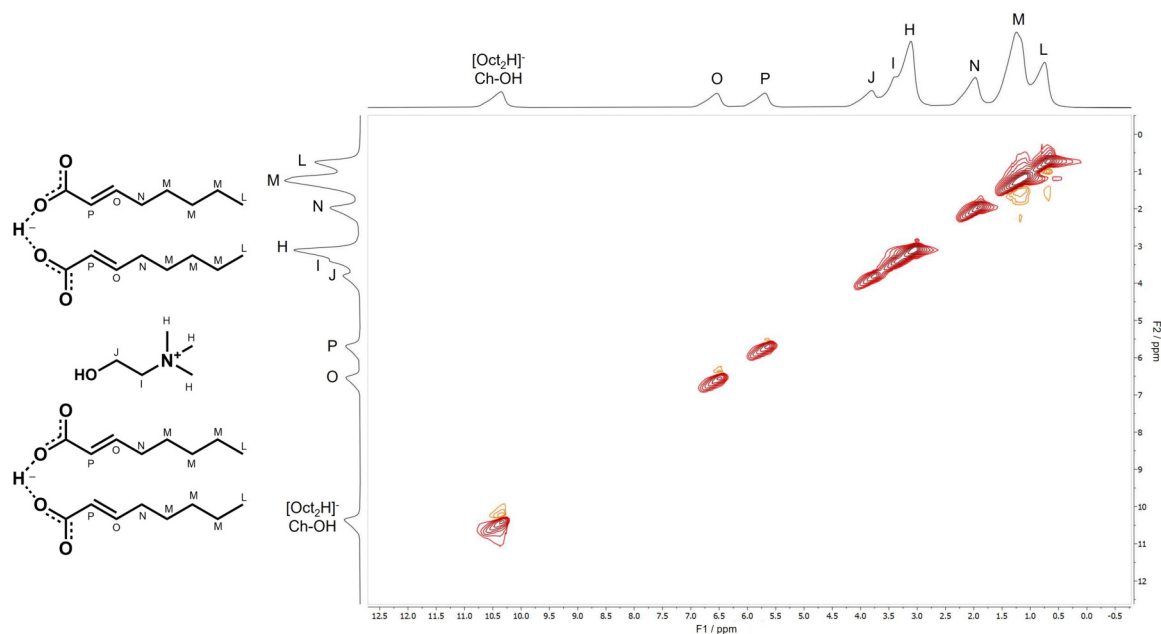


Figure 5.9. ^1H - ^1H NOESY of neat 1:2 CA2OE at 50 °C (isotropic liquid phase)

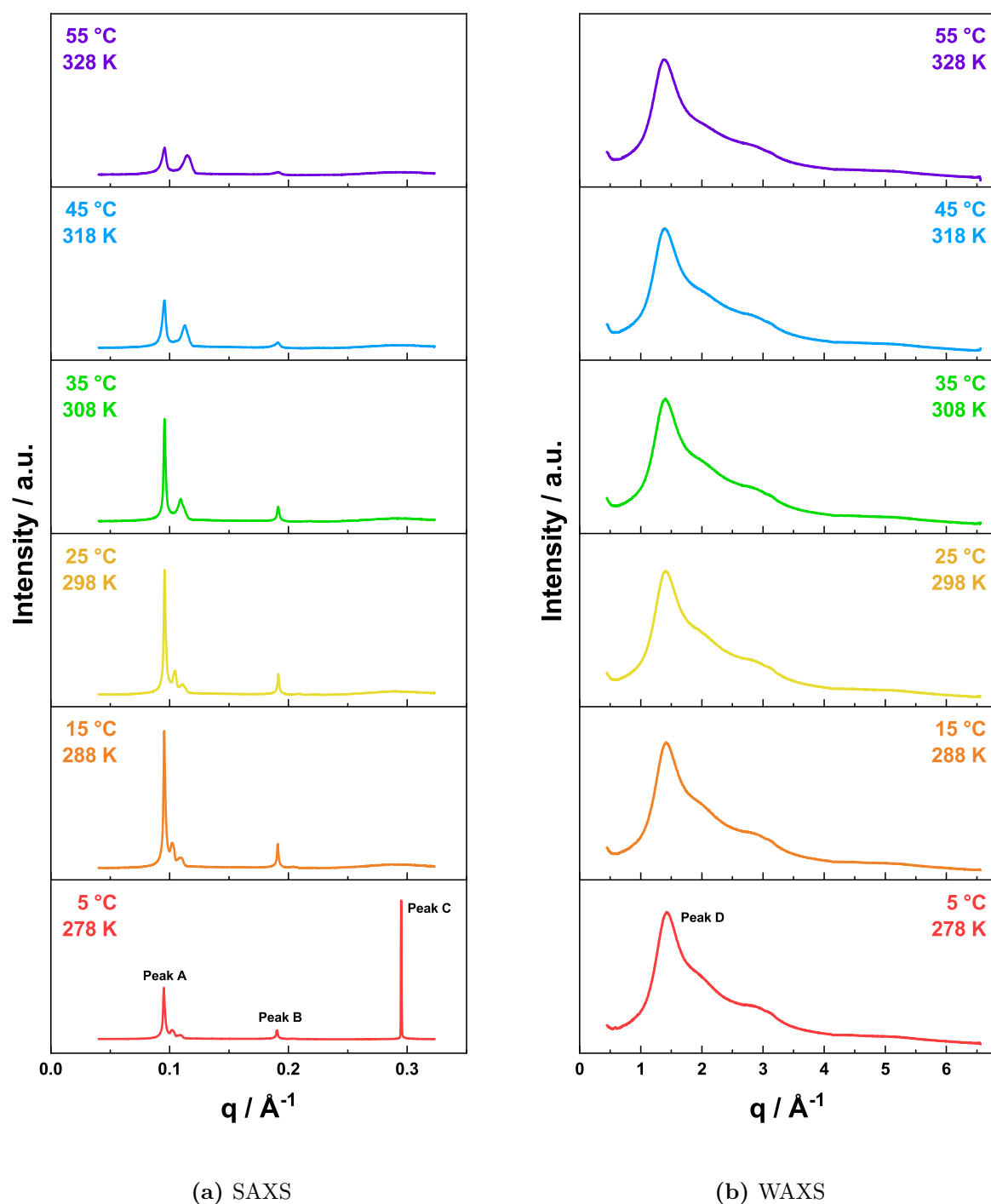


Figure 5.10. X-ray scattering data of 1:2 CA2OE at various temperatures.

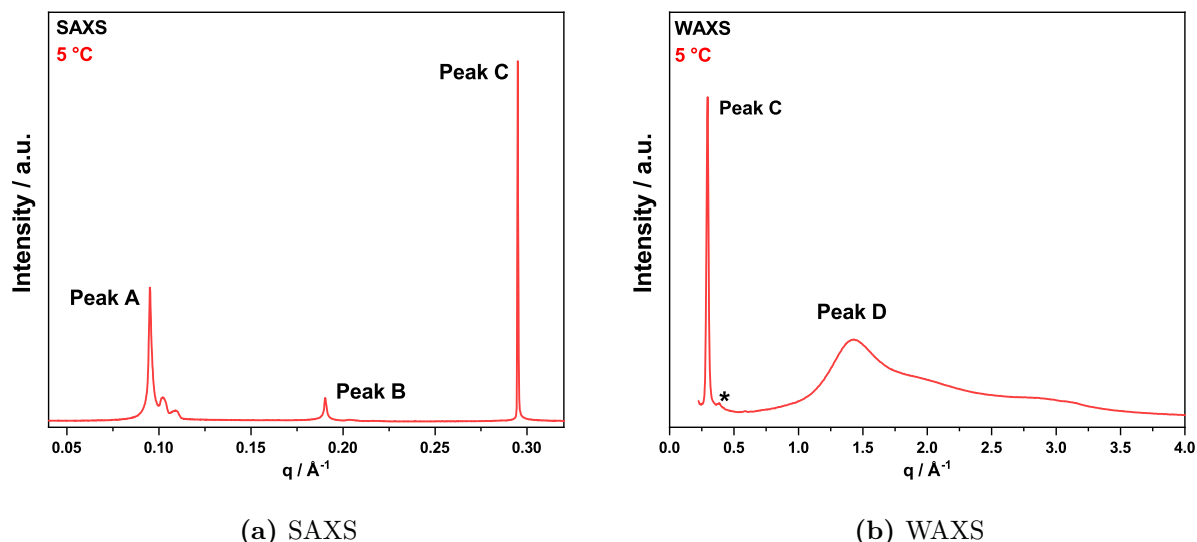


Figure 5.11. X-ray scattering profiles of 1:2 CA2OE at 5 °C

the visibility of all of these features, Figure 5.11a shows only the SAXS profile of 1:2 CA2OE at 5 °C (this is the same data as that used in the bottom plot of Figure 5.10a).

As mentioned previously, liquid crystalline mesophases with a layered structure (smectic or lamellar) usually give rise to a pattern of sharp pseudo-Bragg peaks, whose positions are in a 1:2:3:4 ratio (i.e. a second-order peak appears at double the q -value of the first-order peak).⁷⁹ In the case of 1:2 CA2OE, peaks A and B form such a pattern, with peak B being the second-order reflection at $q_B = 2 q_A$. The third-order reflection of peak A is expected to be a low intensity feature, but this is not visible in the SAXS profile due to the presence of peak C at a very similar q value. Finally, the fourth-order reflection is observed in the WAXS profile. WAXS data collected between 0.18–4.0 $\text{\AA}^{-1}$ at 5 °C is shown in Figure 5.11b. The small shoulder marked with an asterisk appears at $q^* = 0.38 \text{ \AA}^{-1}$, which is equal to $4q_A$.

It should be noted here that while peak C might appear to be the third-order reflection associated with peak A (as $q_C \approx 3 q_A$), this is not the case. Generally, the intensity of the pseudo-Bragg peaks decreases with increasing order, with the first-order peak being the strongest. Because peak C is much higher in intensity than peak A, this suggests that the two features are associated with different mesophases. This is also supported by the behaviour of the two features, peak A and peak C, with increasing temperature (Figure 5.13). When the temperature of the IL is increased to 15 °C, peak A remains sharp and relatively intense (as does peak B), suggesting that the associated mesophase is still present. Peak C, however, shows a

drastic change in both intensity and shape, becoming a very broad, low-intensity feature. This change is associated with the transition from a liquid crystalline phase to an isotropic liquid one; for 1:2 CA2OE, such a transition was observed by DSC and PLM at approximately 12 and 16 °C respectively. Once again, this suggests that two different mesophases are present in 1:2 CA2OE: one associated with peaks A and B, which is maintained at higher temperatures, and one associated with peak C, which collapses at a temperature between 5 and 15 °C ($T_{L-I} = 12$ °C measured by DSC on heating). Based on relative peak intensity, the predominant phase is thought to be the one associated with peak C, while the secondary mesophase(s) (giving rise to peaks A and B) appears to comprise only a small part of the IL sample.

The low- q region ($q = 0.18\text{--}4.0 \text{ \AA}^{-1}$) of the WAXS profile of 1:2 CA2OE recorded at 5 °C is shown in Figure 5.11b. This includes peak C and the small shoulder (marked with an asterisk) that is the fourth-order reflection associated with the mesophase of peak A. Peak C appears at $q_C = 0.30 \text{ \AA}^{-1}$, which corresponds to a repeating unit size of 20.9 Å. The size of a 2-octenoate anion was calculated using Chem3D to be approximately 10.8 Å, which would result in a theoretical bilayer size of 21.6 Å. As the d -spacing derived from the position of peak C is very close to this theoretical value, this suggests that the water-poor phase of 1:2 CA2OE has a lamellar bilayer structure. No higher-order peaks can be observed: a second-order peak would be expected at $q = 0.60 \text{ \AA}^{-1}$, but this is not present in the WAXS.

The other feature observed in the WAXS data recorded at 5 °C is a broad, asymmetric peak (labelled D). A peak in this region is commonly observed for both ILs (associated with inter-molecular interactions between neighbouring groups) and for lamellar liquid crystal phases of amphiphilic molecules (associated with the distance between neighbouring alkyl chains). In the WAXS profile of 1:2 CA2OE, peak D appears at $q_D = 1.43 \text{ \AA}^{-1}$, corresponding to a real-life distance of approximately 4.39 Å. Usually, a gel L_β phase gives rise to a sharp peak in the WAXS region, at $q = 1.5 \text{ \AA}^{-1}$ ($d = 4.2 \text{ \AA}$), while a fluid lamellar L_α phase gives rise to a broad peak at $q = 1.4 \text{ \AA}^{-1}$ ($d = 4.5 \text{ \AA}$).^{144,145} Peak D appears at a q -value that is in-between the values expected for L_α and L_β , and is accompanied by some low-intensity, broad, shoulder-like features at higher q (at approximately 2.0 and 3.0 $\text{\AA}^{-1}$). Based on the position and appearance of peaks C and D, the predominant mesophase present in 1:2 CA2OE is thought to be a highly disordered L_β phase.^{79,146} The shape of peak D also shows asymmetry on the high- q side. This suggests the presence of multiple preferred repeat spacings and seems to support the conclusion

drawn from the SAXS data, which is that 1:2 CA2OE shows multiple coexistent mesophases.

A proposed lamellar bilayer structure for the LC phase of 1:2 CA2OE is shown in Figure 5.12. Nonpolar regions consist of the alkyl tails of the 2-octenoate / 2-octenoic acid species, which are thought to be interdigitated to some degree. Additionally, based on the shape and position of peak D in the WAXS profile, the LC phase present in 1:2 CA2OE is thought to be a fluid lamellar a highly disordered L_β phase, meaning that the alkyl tails have a fluid nature and are curled and/or bent to some extent. The polar regions contain the cholinium cations and the negatively charged anion headgroups. Because the placement of the cation cannot be deduced directly from SAXS data, this is instead determined by taking into account the energetic costs associated with different cation placements, as well as by considering the intermolecular interactions observed in the NOESY NMR spectrum. First, placing the cation in the nonpolar region would be extremely energetically costly, as it would disrupt hydrophobic interactions between the alkyl tails and would lead to unfavourable anion-anion interactions in the polar domain. Instead, if the cation resides in the polar domain, favourable interactions, such as cation-anion electrostatic interactions and hydrophobic interactions between adjacent alkyl tails, are possible. Additionally, this cation placement allows for the formation of hydrogen bonds between the cholinium hydroxyl group and the anion headgroup.

The solid-state NMR spectra of 1:2 CA2OE show a single peak for these protons, indicating that rapid proton exchange occurs between the two species. This exchange can occur more easily to occur if the cation resides in the polar region of the bilayer, rather than the nonpolar one. The NOESY data shown in Figure 5.8 shows crosspeaks between the methyl protons of the anion and all of the anion alkyl chain protons. This is similar to interactions observed for the other ILs discussed in this work. These crosspeaks seem to suggest that the positively charged cation headgroup is found in the vicinity of the alkyl tails (i.e. in the nonpolar domain); however, since it has been established that this would be energetically unfavourable, a different explanation is required. As was mentioned for the previously discussed ILs, the methyl groups of the cation are thought to be proximal to the terminal methyl protons of the anion alkyl tails. Because the bilayer structure of the IL is highly ordered, this is thought to facilitate spin diffusion throughout the anion alkyl chain.¹²¹ This leads to the NOESY spectrum showing crosspeaks between the cation protons and protons that are further down the anion alkyl chain, without these being close to each other in space. Similar effects were observed for the other

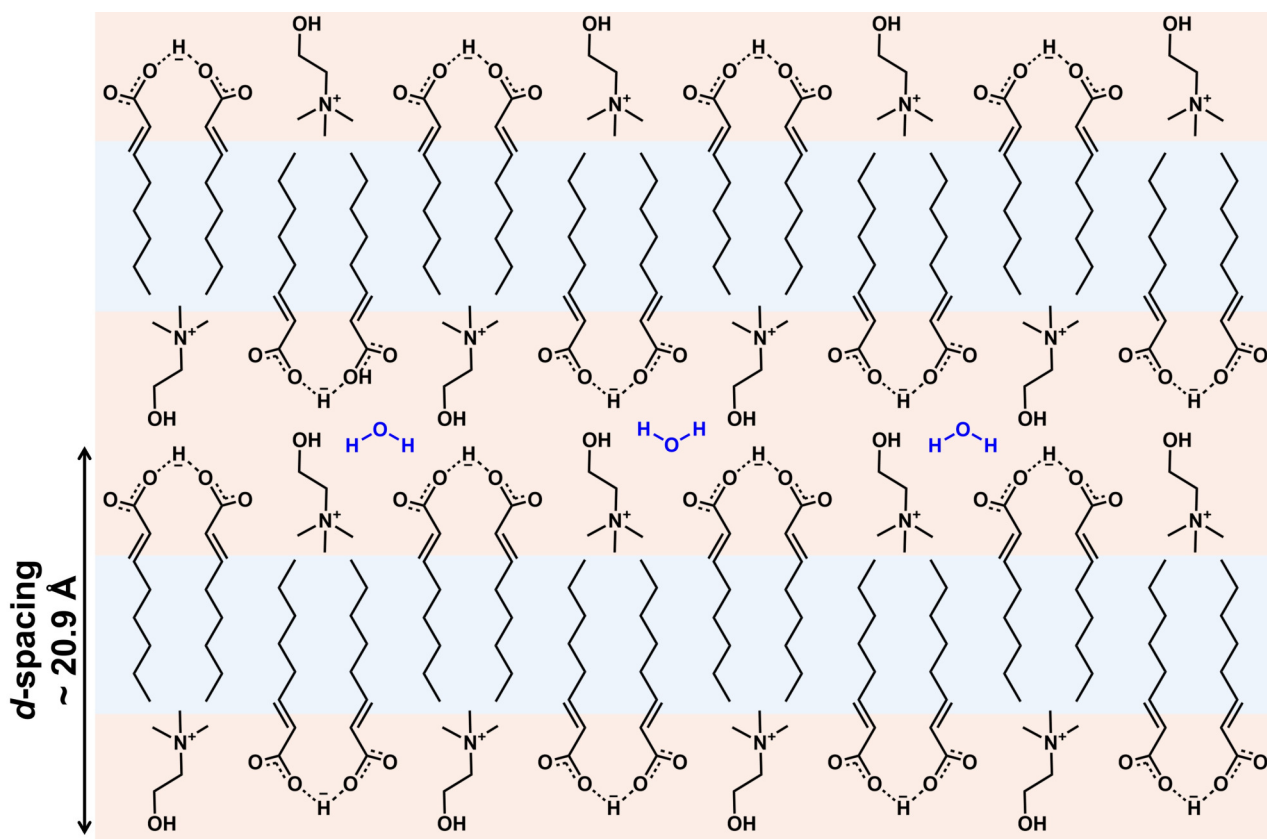


Figure 5.12. Possible structure of the main LC phase of 1:2 CA2OE. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 20.9 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner, in reality the system is a dynamic one, in which hydrogen bonds are always breaking and forming and protons are exchanged between different species.

ILs with lamellar bilayer structures in this work.

In order to verify how reasonable the proposed bilayer model is, the cross-sectional area per unit was estimated and compared to literature values for similar lipid bilayers. A 'unit' of 1:2 CA2OE is considered to be comprised of a cholinium cation, a 2-octenoate anion and a 2-octenoic acid molecule. The area per unit can be estimated by dividing the unit volume by the unit length, while the unit volume can be calculated using the density of the IL. As the density of 1:2 CA2OE could not be obtained experimentally, it was approximated by the density of 1:2 CAGE (0.99 g mL^{-1}).⁹ The volume of one 1:2 CA2OE unit was calculated to be approximately 644 Å^3 . The length of a single unit can be approximated by considering the size of the bilayer (the d -spacing) and the degree of interdigitation between the alkyl tails on the

Table 5.1. Estimated length and area values for the 1:2 CA2OE unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.

Chain position	d -spacing (20.9 Å)	Unit length	Unit area
No interdigitation	$d = 2 \times l_{\text{unit}}$	$l_{\text{min}} = 10.5 \text{ Å}$	$A_{\text{max}} = 61.3 \text{ Å}^2$
Partly interdigitated	$d = 1.5 \times l_{\text{unit}}$	$l_{\text{int}} = 13.9 \text{ Å}$	$A_{\text{int}} = 46.2 \text{ Å}^2$
Fully interdigitated	$d = l_{\text{unit}}$	$l_{\text{max}} = 20.9 \text{ Å}$	$A_{\text{min}} = 31.6 \text{ Å}^2$

two sides of the bilayer. The estimated unit length and cross-sectional areas are given in Table 5.1. These values (particularly those where partial interdigitation is assumed) are similar to the area values calculated for the other IL bilayers in this work and are also similar to literature literature for phospholipids with similar bilayer structures (40–70 Å²).^{123,124} All of this suggests that the proposed bilayer model is a reasonable structure for the LC phase of 1:2 CA2OE.

The appearance of the X-ray scattering data collected for 1:2 CA2OE at 5 °C is very similar to that of scattering data collected for 1:2 BTMAAGE in the liquid crystalline phase (Figures 4.15 and 4.14). The SAXS profile of 1:2 BTMAAGE also shows two different sets of peaks, which were attributed to two different mesophases. The predominant phase in 1:2 BTMAAGE is a neat IL phase with a fluid lamellar L_α structuring, with a repeating unit size of 19.6 Å⁻¹. On heating, this structure collapses to an isotropic liquid phase, in agreement with the LC to isotropic transition observed in the DSC and PLM data. The other mesophase observed in 1:2 BTMAAGE is also lamellar in nature, with a significantly larger repeating unit (61.6 Å⁻¹).

The remaining features in the SAXS profile are peaks A and B, which are thought to be associated with a secondary LC phase. The feature labelled as 'Peak A' includes three different peaks: $q_{A1} = 0.095 \text{ Å}^{-1}$, $q_{A2} = 0.102 \text{ Å}^{-1}$ and $q_{A3} = 0.109 \text{ Å}^{-1}$. Attempts to positions of these peaks to common LC patterns were unsuccessful. The tested patterns include lamellar (a ratio of 1:2:3), hexagonal (a ratio of 1: $\sqrt{3}$: $\sqrt{4}$), or Pn3m cubic (a ratio of $\sqrt{2}$: $\sqrt{3}$: $\sqrt{4}$) and Ia3d gyroid (a ratio of $\sqrt{6}$: $\sqrt{8}$: $\sqrt{14}$). Additionally, the behaviour of each of the three peaks with increasing temperature (Figure 5.13) is different; most notably, the position of peak A1 remains constant, while peaks A2 and A3 shift to higher q . This suggests that the peaks are caused by the presence of different structures within this secondary phase, with multiple preferred repeat spacings and a high degree of disorder.

Peak A1 is the most intense and its shape (narrow, sharp peak) suggests that at 5 °C the predominant structure in this LC phase is a liquid crystalline one. Peak B appears at $q_B = 0.19 \text{ \AA}^{-1}$, which is double the q -value of peak A1. The WAXS data also shows a low-intensity peak, marked with an asterisk, at $q^* = 0.38 \text{ \AA}^{-1}$, which is four times the q -value of peak A1. This pattern is characteristic of a lamellar phase, with peaks A1, B and * being the first, second and fourth-order pseudo-Bragg peaks, respectively. The size of the repeating unit can be calculated from q_A to be approximately 66.0 Å. The theoretical size of a single bilayer is $2 \times l_{\text{anion}} = 21.6 \text{ \AA}$, meaning that the size of the repeating unit in this mesophase is approximately three times the size of a single bilayer. A very similar mesophase, with a repeat unit distance of approximately three times the length of a bilayer, was observed for 1:2 BTMAAGE.

The other peaks observed at low q (A2 and A3) do not seem to fit any known pattern associated with a LC phase. It is likely that these peaks are associated with a different LC mesophase than either peak C or peaks A1/B/*, the nature of which cannot be determined at present. The d -spacings resulting from these peaks are slightly smaller compared to peak A1 (62 Å for peak A2 and 58 Å for peak A3). This is most likely due to an increase in the disorder of the nonpolar region. It should be noted here that peaks A1, A2 and A3 become broader with increasing q (A1 being the sharpest peak and A3 the broadest), suggesting that the long-range order of the mesophases also decreases with increasing q . The higher-order reflections (or lack thereof) also seems to agree with this. The mesophase associated with peak A2 only shows a broad, very low intensity second-order reflection at $0.20 \text{ \AA}^{-1}$ ($2q_{A2}$); no higher-order reflections are observed for the mesophase associated with peak A3. While it was initially thought that these peaks might be due to the partial crystallisation of the sample, no evidence was found in the X-ray data that supports this hypothesis. At the moment, the reason for the presence of secondary LC phases in 1:2 BTMAAGE and 1:2 CA2OE is unknown and requires further study.

In order to understand how the structuring of the IL changes with temperature, SAXS and WAXS data were collected over a temperature range of 5–55 °C. The SAXS profiles are shown in Figure 5.13. As the temperature increases, the position of peak A1 remains unchanged. The peak shape becomes broader and less intense, but remains relatively sharp compared to the other features in the SAXS profile (most notably peak C, which broadens significantly). This, along with the fact that peak B (the second-order reflection) is still present even at

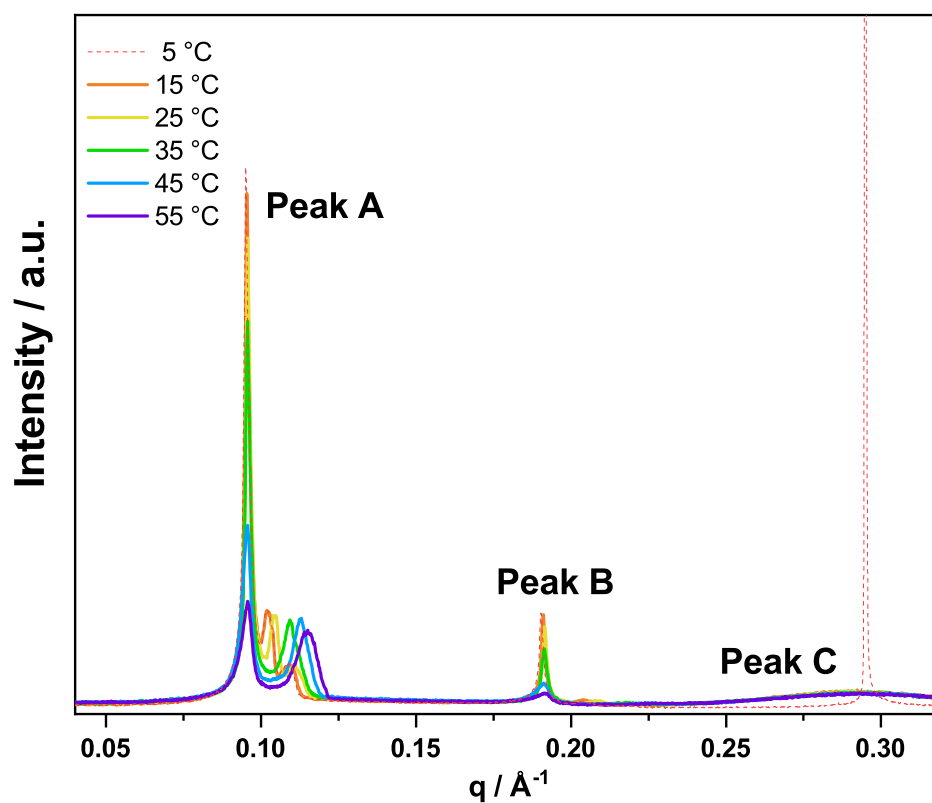


Figure 5.13. Selected SAXS data showing the variation of Peaks A and B with temperature

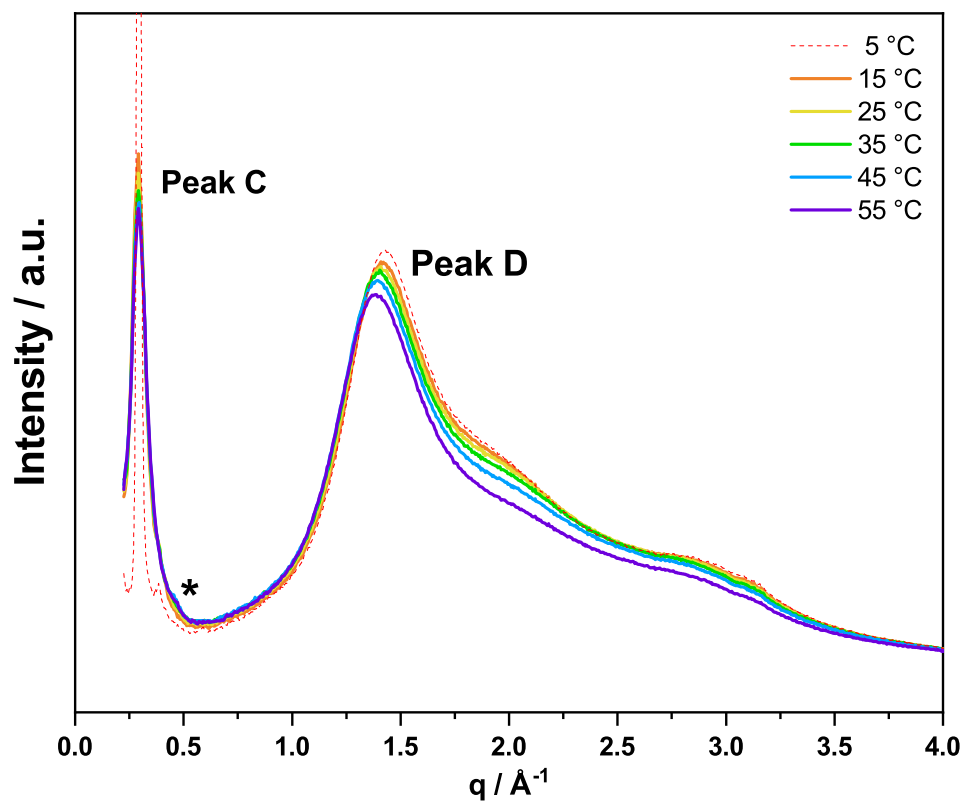


Figure 5.14. Selected WAXS data showing the variation of Peaks C and D with temperature

55 °C (although very broad and low in intensity), suggests that the secondary LC phase of 1:2 CA2OE maintains its structure at relatively high temperatures. The fourth-order reflection peak (marked with an asterisk in Figure 5.14) does become broader and almost disappears with increasing temperature, suggesting that the long-range structuring of this mesophase is disrupted at high temperatures.

The behaviour of peaks A2 and A3 is more difficult to analyse, as the two shift to lower q with increasing temperature and overlap almost entirely at high temperatures. Both peaks become broader and no higher-order reflections can be seen above 25 °C, suggesting that these mesophases become more disordered with increasing temperature. The shape of peak A2 at 45 and 55 °C is very broad, suggesting that the lamellar structuring that gives rise to this feature may collapse to an isotropic liquid phase at these temperatures.

Finally, peak C, which is an intense, sharp feature at 5 °C, becomes significantly broader and lower in intensity at 15 °C. Due to the scale of the other features in the SAXS profile, peak C is very difficult to view in Figure 5.13. As its position is within the overlap range of the SAXS and WAXS detectors, peak C can also be included in the WAXS data. This is shown in Figure 5.14, spanning a q -range of 0.18–4.0 Å⁻¹. Because at 15 °C and above, peak C is significantly lower in intensity than at 5 °C, Figure 5.14 (which shows the WAXS profiles at all temperatures) uses a smaller Y-axis scale than Figure 5.11b (which only shows the data collected at 5 °C). This serves to better showcase any changes in the shape and intensity of peaks C and D, particularly at temperatures above 5 °C. For reference, the WAXS profile recorded at 5 °C is included in Figure 5.14 (dotted red line) even though the high-intensity data points are not visible due to the scale.

As mentioned, peak C becomes very broad upon heating to 15 °C. This dramatic change is associated with the liquid crystal to isotropic liquid transition observed by DSC ($T_{1-1} = 12$ °C on heating) and PLM (total loss of birefringence around 25 °C) for 1:2 CA2OE. Similar changes in peak shape have been observed for other ILs discussed in this work (1:2 BTMAAOC, 1:2 CAOC and 1:2 BTMAAGE), at temperatures similar to their LC-to-isotropic transition temperatures (all LC to isotropic transition temperatures are shown in Table 5.2). The fact that a broad peak is retained suggests that the isotropic IL shows nanodomain structuring (discrete polar and nonpolar domains) similar to long-chain imidazolium ILs.^{80,86,125} For 1:2 CA2OE, the polar domain is thought to consist primarily of anion headgroups and cholinium

cations, with the nonpolar region comprised of the anion alkyl chains. Of course, extensive computational simulations would be required to clearly determine the structure of the ILs discussed in this work.

The last feature observed in the WAXS (Figure 5.14) is peak D, associated with the distance between adjacent alkyl chains. Peak D appears at $q_D = 1.43 \text{ \AA}^{-1}$ at 5 °C and shifts to lower q and becomes broader as the temperature increases ($q_D = 1.39 \text{ \AA}^{-1}$ at 55 °C). This suggests that the anion alkyl chains become more disordered with increasing temperature; this is expected, as higher temperatures lead to an increase in the rotational freedom of the alkyl chains. At and above 15 °C 1:2 CA2OE is in an isotropic liquid state, for which peak D is indicative of the distance between neighbouring groups, including the chain-chain spacing and the average cation-anion distance. These two distances are very similar and so give rise to a single broad feature in the WAXS profile. The position of peak D is similar to adjacency peaks observed for other ILs, both in this work and in the literature.⁸⁴

5.3 Chapter summary

While 1:2 CA2OE shows similar thermal transitions to 1:2 BTMAAOC and 1:2 CAOC, the temperature of the liquid crystal to isotropic transition is lower than for any of the ILs that were discussed previously (Table 5.2). Compared to 1:2 CAOC and 1:2 BTMAAOC, this is expected and is attributed to the presence of a double bond in the anion alkyl chain that leads to poorer alkyl tail packing. Compared to 1:2 BTMAAGE, however, 1:2 CA2OE was initially expected to have a more stable LC phase, given the presence of a hydroxyl group on the cation. This does not seem to be the case, however, with the structuring of 1:2 CA2OE being more complex than initially expected. Like 1:2 BTMAAGE, 1:2 CA2OE also shows multiple sets of scattering peaks. The predominant phase present in LC 1:2 CA2OE is a disordered L_β lamellar gel phase. This gives rise to an intense, sharp peak in the SAXS profile, corresponding to a d -spacing of 20.9 Å. Other low-intensity scattering peaks can be seen in the SAXS profile of 1:2 CA2OE, which are thought to be associated with additional LC mesophases present in the IL. Based on the way the peaks change with increasing temperature, it seems that there are at least two different mesophases giving rise to these low- q peaks, with d -spacings of 58–66 Å (roughly three times the size of a single bilayer). The peaks do not fit any known LC phase pattern (e.g. lamellar, cubic, gyroid, etc) so the geometry of these phases is undetermined at

Table 5.2. Temperatures of the liquid crystal to isotropic liquid transitions

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 CA2OE	12	25	n/a [*]	n/a	5–15
1:2 BTMAAGE	24	27	15	< 25	25–35
1:2 CAOC	52	60	57	50–55	50–55
1:2 BTMAAOC	17	25	37 ^{**}	35–40	35

^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling

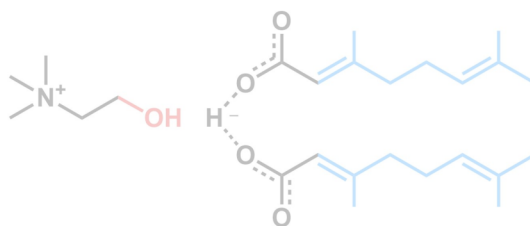
^d Temp. above which IL shows Newtonian flow behaviour

^e Temp. at which sharp LC peak disappears

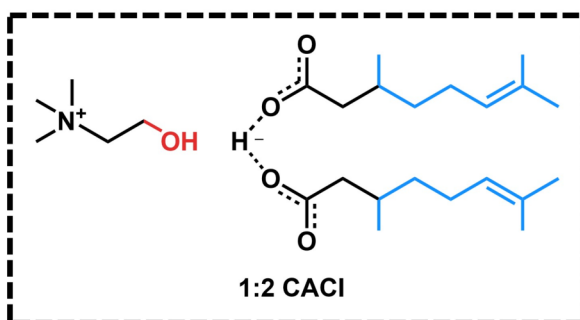
^{*} Not observed ^{**} Tan δ peak on heating

the moment. The reason for the presence of this secondary phase is unknown at the moment. Considering the data on 1:2 CA2OE and 1:2 BTMAAGE, it appears that the two ILs with intermediate degrees of structural complexity seem to have liquid crystalline structures that are not easy to understand using simple scattering measurements. Additional work, perhaps molecular dynamics simulations could help provide a better understanding of these systems.

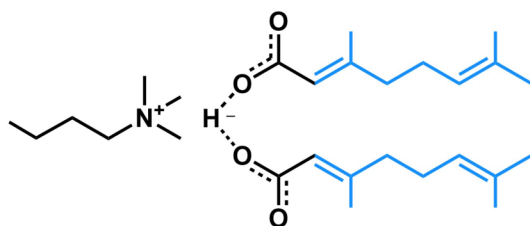
STRUCTURE COMPLEXITY



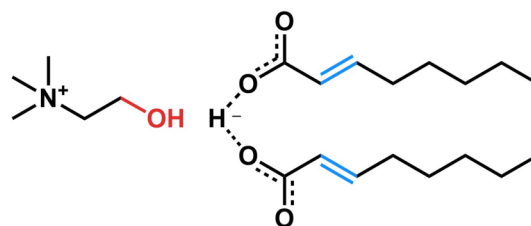
1:2 CAGE



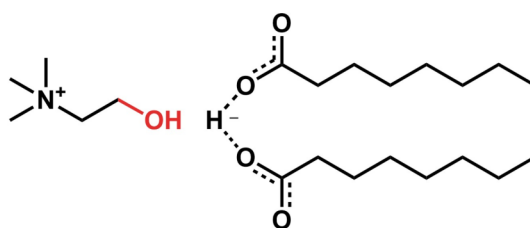
1:2 CACI



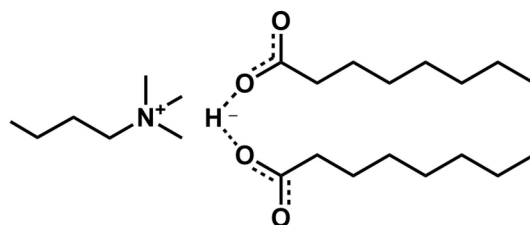
1:2 BTMAAGE



1:2 CA2OE



1:2 CAOC



1:2 BTMAAOC

Chapter 6

1:2 Choline And Citronellate (CACI)

This chapter presents data on the ionic liquid 1:2 choline and citronellate (CACI), whose thermal behaviour, rheology and structuring were investigated using differential scanning calorimetry (DSC), dynamic mechanical analysis (DMA), polarised-light microscopy (PLM), dynamic viscosity and X-ray scattering. 1:2 CACI is comprised of a cholinium cation and a complex $[(\text{citronellate})_2\text{H}]^-$ anion, as shown in Figure 6.1. Of all 1:2 ILs discussed in this work, 1:2 CACI is the most structurally similar to 1:2 CAGE, with the only difference being the C2–C3 bond, which is a single bond in citronellic acid but a double bond in geranic acid. This IL is expected to behave similarly to 1:2 CAGE, while having some advantages over it, including an easier synthesis (the acid is purified through distillation rather than crystallisation) and an apparent increase in thermal stability. This latter property refers to the fact that 1:2 CACI remains colourless even if heated slightly; however, this observation does not guarantee that 1:2 CACI does not decompose, as it is possible that the decomposition products are simply colourless. However, no unexplained NMR peaks were observed for stored samples of 1:2 CACI, while the NMR spectrum of discoloured (yellow) 1:2 CAGE does show some small peaks in the alkyl region.

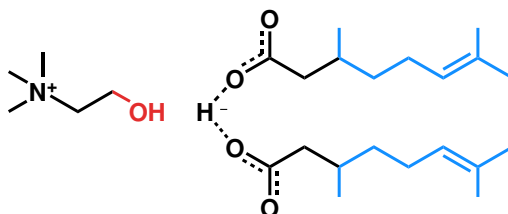


Figure 6.1. 1:2 CACI

6.1 Thermal Behaviour

DSC measurements were performed by Dr. Daniel Rauber at the University of Saarland, Germany, and analysed by myself. Data was collected using a scan rate of $5\text{ }^{\circ}\text{C min}^{-1}$. Three consecutive heating-cooling cycles were run in order to show reproducibility (Figure 6.2). 1:2 CACI shows a glass transition at $T_g = -80\text{ }^{\circ}\text{C}$, a crystallisation at $T_c = -15\text{ }^{\circ}\text{C}$ and a corresponding melting at $T_m = -10\text{ }^{\circ}\text{C}$. Unlike the other cholinium-based ILs discussed so far, 1:2 CACI does not undergo a cold crystallisation.

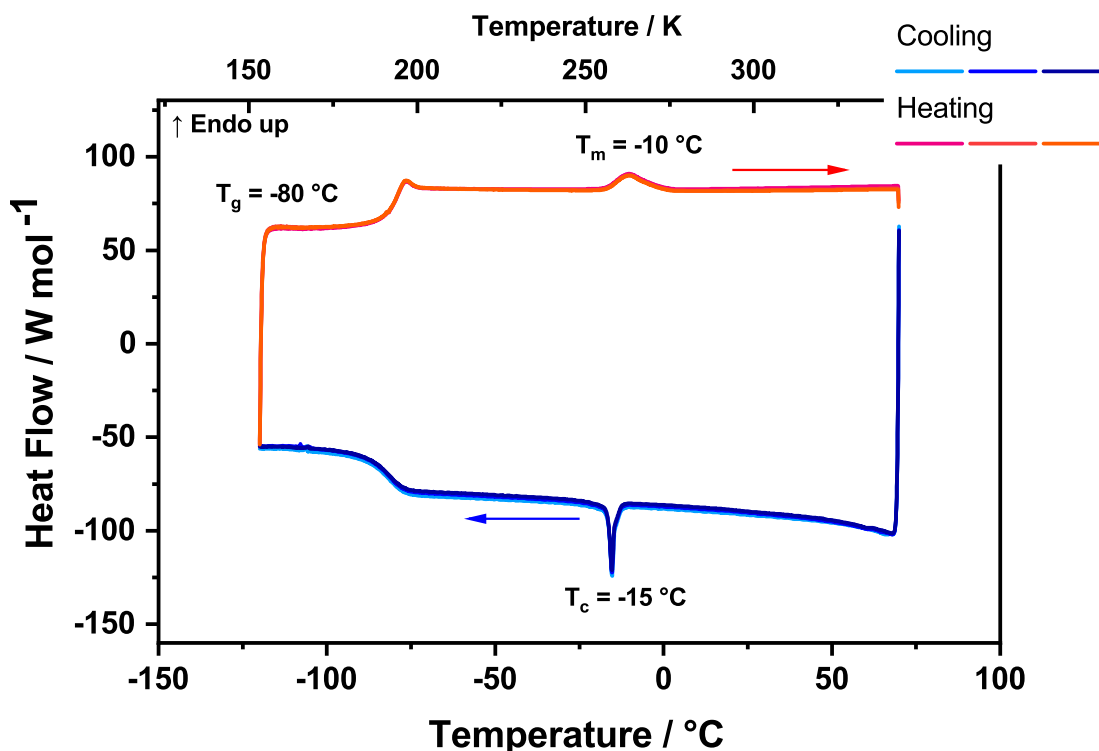


Figure 6.2. DSC traces of 1:2 CACI with annotated transition temperatures. The heating and cooling rates are $5\text{ }^{\circ}\text{C min}^{-1}$.

At room temperature, 1:2 CACI is an isotropic liquid, as shown by the polarised-light microscopy (PLM) photograph in Figure 6.4. The image is entirely dark, with no areas of birefringence. The SAXS profile of 1:2 CACI (Figure 6.12a) shows a single broad peak at $25\text{ }^{\circ}\text{C}$, confirming that 1:2 CACI is an isotropic liquid. On cooling from room temperature, the first transition observed is a crystallisation transition, giving rise to a sharp exothermic peak at $T_c = -15\text{ }^{\circ}\text{C}$. Visually, when 1:2 CACI is cooled below T_c (Figure 6.3b) it does not become solid, but instead changes to a very viscous, opaque, gel-like consistency, and is similar in appearance to the liquid crystalline phases of previously discussed ILs (see Figures 2.3a, 3.4a, 4.4a). All



(a) 1:2 CACI at room temperature

(b) 1:2 CACI cooled to $-20\text{ }^{\circ}\text{C}$

Figure 6.3. Samples of 1:2 CACI at temperatures above and below the crystallisation transition temperature

other ILs in this work exhibit a liquid crystalline phase, with a reversible LC to isotropic transition seen in the DSC. This includes 1:2 BTMAAGE and 1:2 CAGE, which are structurally very similar to 1:2 CACI; the only differences are the nature of the cation (for 1:2 BTMAAGE) and the presence of an additional double bond in the anion alkyl chain (for 1:2 CAGE). Data on 1:2 BTMAAGE is given in Chapter 4, while 1:2 CAGE will be discussed in Chapter 7. Notably, the DSC trace of 1:2 CAGE shows the same exothermic transition at $-15\text{ }^{\circ}\text{C}$ as is observed for 1:2 CACI and the two ILs are not only very similar in structure, but also in appearance — both at room temperature (flowing, viscous liquids) and at $-20\text{ }^{\circ}\text{C}$ (opaque and gel-like). Based on this, it is possible that the two peaks observed in the DSC trace of 1:2 CACI at $T_c = 15\text{ }^{\circ}\text{C}$ and $T_m = -10\text{ }^{\circ}\text{C}$ correspond to a reversible LC to isotropic transition and that below T_c 1:2 CACI is in a liquid crystalline state. Unfortunately, PLM and X-ray scattering measurements could not be performed at temperatures below $5\text{ }^{\circ}\text{C}$, and so the nature of this phase cannot be confirmed. PLM measurements were run in air, and so temperatures near and below $0\text{ }^{\circ}\text{C}$ lead to condensation. If the IL was not covered with a glass slip or with the cover of the microscope stage, moisture droplets were in direct contact with the sample, leading to erroneous results; if the slide was covered, moisture condensed onto the glass cover and the sample could not be photographed. X-ray scattering measurements use a water bath to set the temperature of the samples, and this cannot be cooled below $5\text{ }^{\circ}\text{C}$. Because the nature of this

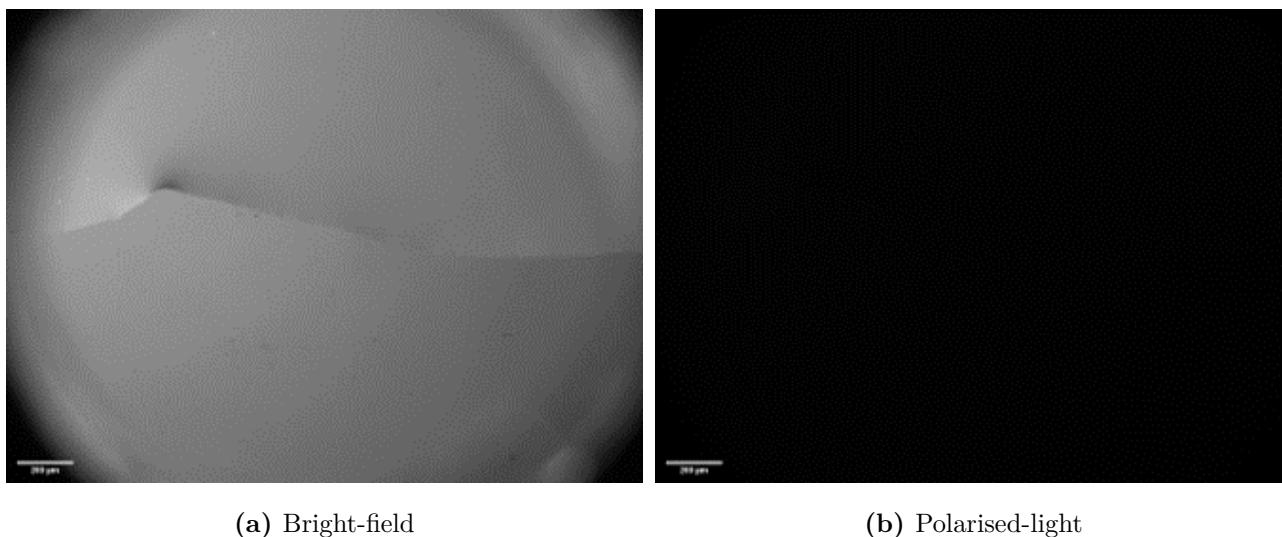


Figure 6.4. Microscope images of 1:2 CACI at room temperature. The sample is not birefringent — the image taken using polarised light is entirely dark.

phase transition cannot be confirmed, the two DSC peaks are referred to as 'crystallisation' and 'melting' transitions.

At very low temperatures, a glass transition is observed at $T_g = -80\text{ }^{\circ}\text{C}$ (measured on heating). The glass transition temperature of 1:2 CACI is similar to that of 1:2 BTMAAGE ($-78\text{ }^{\circ}\text{C}$); as the citronellate and geranate anions are structurally similar, this suggests that the nature of the anions has the most significant effect on the T_g . The two ILs containing octanoate anions (1:2 BTMAAOC and 1:2 CAOC) have identical glass transition temperatures ($-95\text{ }^{\circ}\text{C}$ for both ILs), which seems to agree with the idea that the T_g is primarily influenced by the anion structure.

6.1.1 Dynamic Mechanical Analysis

In addition to DSC measurements, the thermal behaviour and mechanical properties of 1:2 CACI were also investigated using dynamic mechanical analysis (DMA). The measurements were performed by myself and Dr. Oriele Palumbo at the Sapienza University of Rome, Italy and data was analysed by myself using OriginPro (2020). The storage modulus M' and the loss tangent $\tan \delta$ were measured over a temperature range of -100 – $30\text{ }^{\circ}\text{C}$ (173 – 303 K) at three different frequencies ($f = 1, 5$ and 10 Hz). It should be noted that the storage modulus contains both bulk and shear components due to the use of a three-point bending geometry. Additionally, because the modulus also contains contributions from the metal pocket used to

hold the sample, it is not reported as an absolute value, but rather as the relative change with respect to the value at 25 °C (298 K). This is denoted as $M' / M'_{298\text{ K}}$.

Figure 6.5 shows the DMA data ($M' / M'_{298\text{ K}}$ and $\tan \delta$) collected at $f = 1$ Hz on cooling and subsequent heating. The glass transition observed by DSC at $T_g = -80$ °C is also observed here, giving rise to a peak in the $\tan \delta$ at -84 °C and a step in the relative storage modulus (an increase on cooling and a decrease on heating). The onset temperature of the decrease in M' on heating is approximately -90 °C. It should be noted that both the $\tan \delta$ feature (showing multiple peaks) and the step in M' (appearing somewhat jagged). This is similar to the behaviour observed for 1:2 choline and 2-octanoate (CA2OE), and is most likely due to the presence of noise in the recorded data. It could also indicate that the glass transition occurs as a two-step process, but the 'steps' in the data are not distinct enough to support this.

Two other features can be observed in Figure 6.5. The first is the broad peak in $\tan \delta$ at -32 °C (241 K), accompanied by a slight step in the storage modulus. The second is the small shoulder on the high-temperature side of this broad peak, at approximately -5 °C (268 K). This latter feature appears at the same temperature regardless of the measurement frequency (Figure 6.6), although at $f = 10$ Hz the overlap with the more intense, broad peak makes it difficult to identify. The fact that it is frequency-independent means that this feature is associated with a phase transition, namely the reversible crystallisation/melting process observed by DSC at $T_c = -15$ °C and $T_m = -10$ °C respectively. This phase transition also gives rise to a small increase in the storage modulus on cooling (Figure 6.5). The magnitude of the relative change in M' is very small, suggesting that this transition does not have a significant impact on the viscoelastic properties of the IL. It is possible that this transition is not a true crystallisation, but rather a change from an isotropic liquid to a liquid crystalline phase on cooling (and vice versa on heating), although, as mentioned previously, the nature of the lower-temperature phase could not be determined experimentally.

Unlike the small shoulder feature, the broad $\tan \delta$ peak observed at -32 °C (241 K) in Figure 6.5 is affected by the frequency of the measurement. Figure 6.6 shows the $\tan \delta$ data recorded on cooling at $f = 1, 5$ and 10 Hz. As the frequency of the measurement increases, the position of the broad $\tan \delta$ peak shifts to higher temperatures. Based on this, the peak can be attributed not to a phase transition, but to a thermally-activated relaxation related to viscous flow. Similar processes were observed for all of the previously-discussed ILs, with the exception of 1:2 CA2OE.

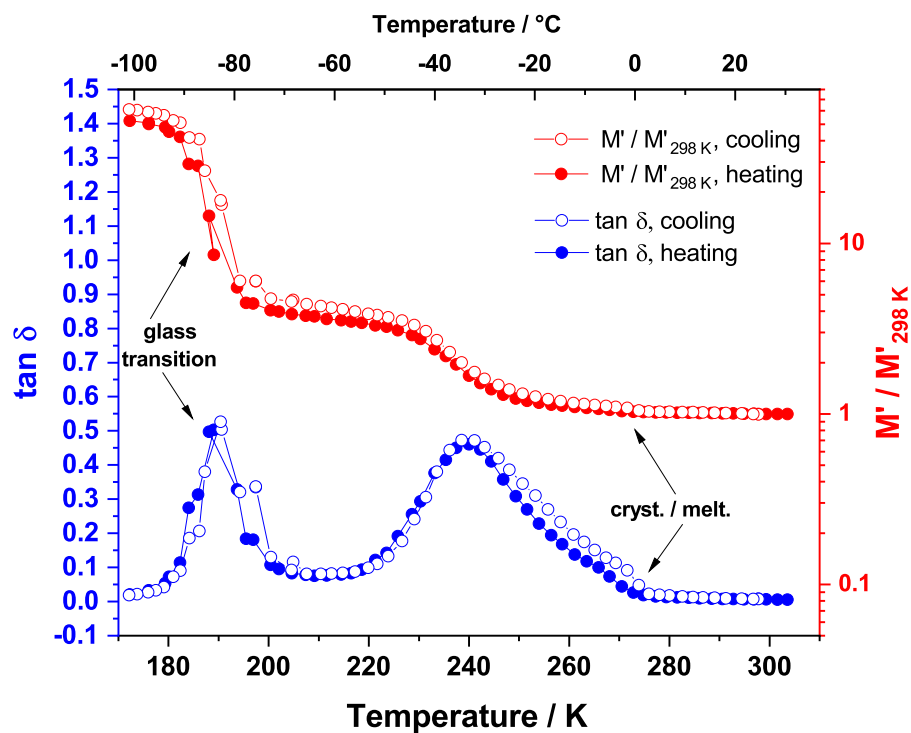


Figure 6.5. DMA data for 1:2 CACI, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.

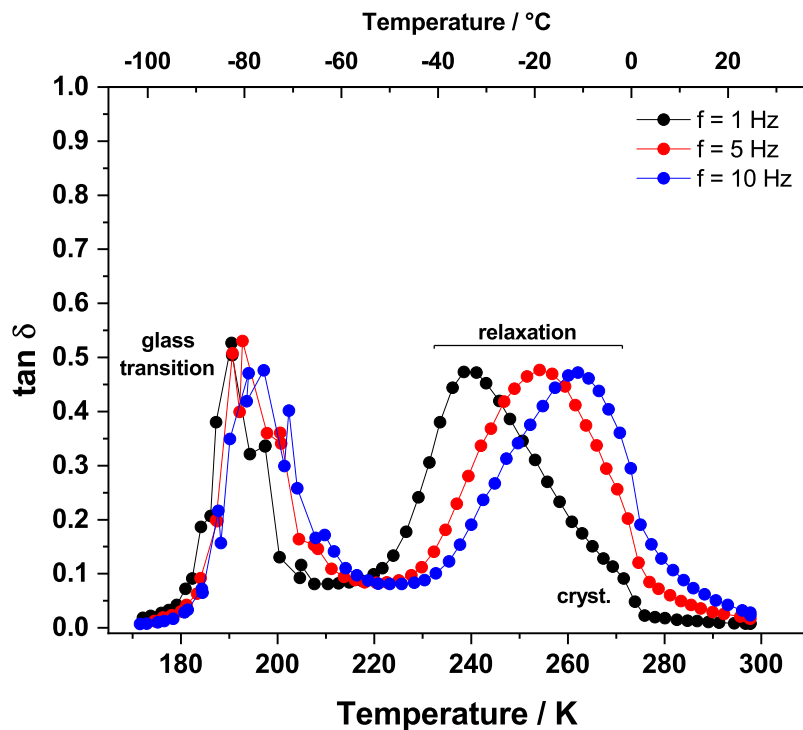


Figure 6.6. $\tan \delta$ measured for 1:2 CACI on cooling. Lines are guides for the eye.

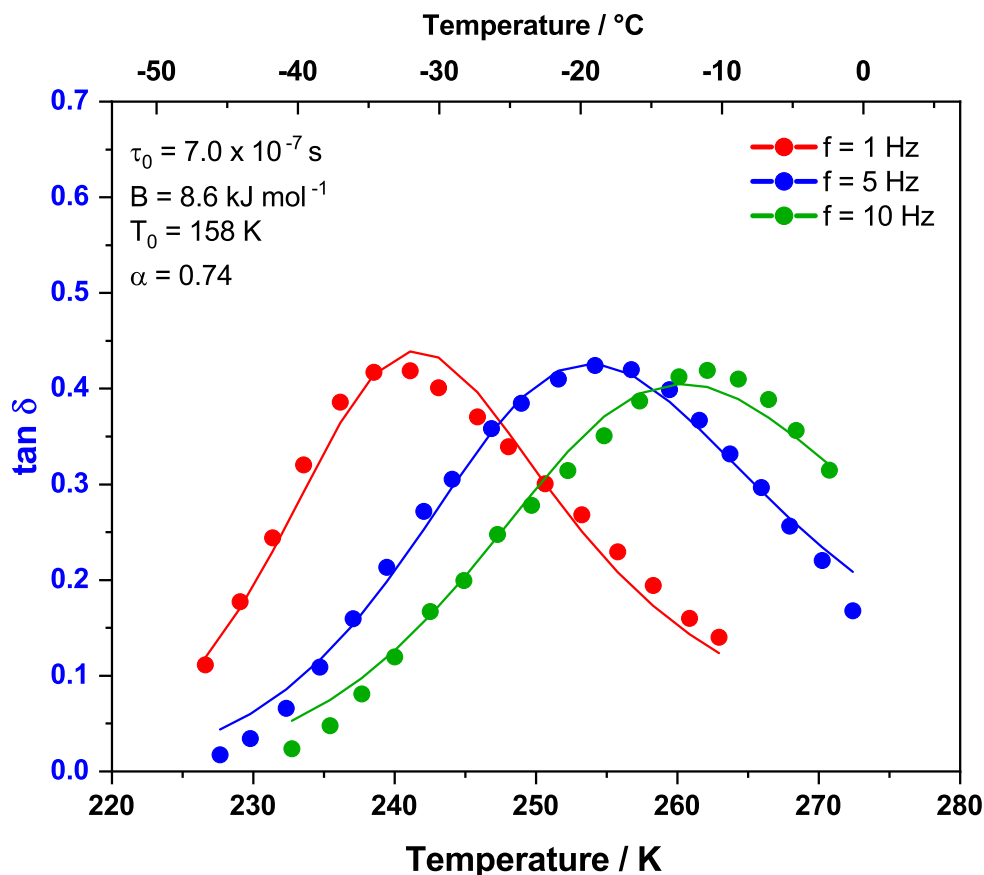


Figure 6.7. $\tan \delta$ measured for 1:2 CACI on cooling at $f = 1, 5$ and 10 Hz. Only the data corresponding to the thermally activated relaxation is shown. The solid lines are the result of a simultaneous fit for the three frequencies. Before fitting, a linear background subtraction was performed.

The relaxation process can be described using a two-state model, in which the system is assumed to transition between two different minimum-energy configurations, separated by an energy barrier ΔE . The relevant theory and equations are given in Section 2.1.1. For 1:2 CACI, the data was fitted according to equations 2.4 and 2.6. Only the $\tan \delta$ data corresponding to the broad relaxation peaks was included in the fit and a linear background subtraction was performed before fitting. The raw and fitted data are shown in Figure 6.7 and the best-fit parameters are given in Table 6.1 (along with the parameters obtained for previously discussed ILs).

The intensity of the peaks in Figure 6.7 does not increase with frequency, indicating that the two states have equivalent energies; the best fit was indeed obtained for $\Delta E = 0$. Parameter τ_0 was found to be on the order of 10^{-7} s and the calculated activation energy B was relatively small (8.6 kJ mol^{-1}). This suggests that the thermally-activated relaxation in 1:2 CACI proceeds

Table 6.1. Best-fit parameters τ_0 , B , T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 CACI (top row). For comparison, data is also shown for the other 1:2 ILs discussed so far.

Sample	$\tau_0 / 10^{-7} \text{ s}$	B / K	$B / \text{kJ mol}^{-1}$	T_0 / K	α
1:2 CACI	7.0 ± 0.2	1030 ± 19	8.6 ± 0.2	158.0 ± 0.2	0.74 ± 0.40
1:2 BTMAAGE	7.1 ± 0.1	750 ± 8	6.2 ± 0.1	174.0 ± 0.1	0.84 ± 0.01
1:2 CAOC	5.5 ± 0.1	1503 ± 19	12.5 ± 0.2	134 ± 2	0.75 ± 0.01
1:2 BTMAAOC	5.7 ± 2.0	1076 ± 26	9.0 ± 0.1	169 ± 2	0.57 ± 0.09

through an intermolecular diffusive process (as is the case for the other 1:2 ILs discussed in this work). The Fuoss-Kirkwood width parameter α is related to the breadth of the peak; for an ideal, single-time relaxation process $\alpha = 1$. Here, $\alpha < 1$ indicates that the relaxing units interact with each other.¹⁰⁸ The best-fit parameters obtained for 1:2 CACI are very similar to those found for the other ILs. The relaxation time τ_0 of 1:2 CACI is very similar to that of 1:2 BTMAAGE (approximately 0.7 μs), both of which are slightly higher than the relaxation times of the two octanoate-based ILs (0.55–0.57 μs). This suggests that the structure of the anion affects the relaxation rate, with the more complex geranate and citronellate leading to slower relaxation rates (higher relaxation times). The activation energy B of 1:2 CACI is similar to that of 1:2 BTMAAOC, with the overall trend being $B_{\text{CAOC}} > B_{\text{BTMAAOC}} \approx B_{\text{CACI}} > B_{\text{BTMAAGE}}$. It should be noted that in all cases the thermally activated relaxation occurs at temperatures corresponding to the liquid crystalline phase of the ILs (in the case of 1:2 CACI, the relaxation occurs below the crystallisation temperature T_c). The observed trend suggests that the interactions present in these systems are weaker in ILs containing geranate and citronellate anions; this seems to support the hypothesis that the more structurally complex acids lead to ILs with poorer molecular packing and a lower degree of ordering in their structures.

6.2 Viscosity

The rheology of the 1:2 CACI IL was also investigated using dynamic viscosity measurements. These were performed by Dr. Daniel Rauber at the University of Saarland, Germany. Data analysis was performed by myself. The IL is in the isotropic liquid phase at all temperatures

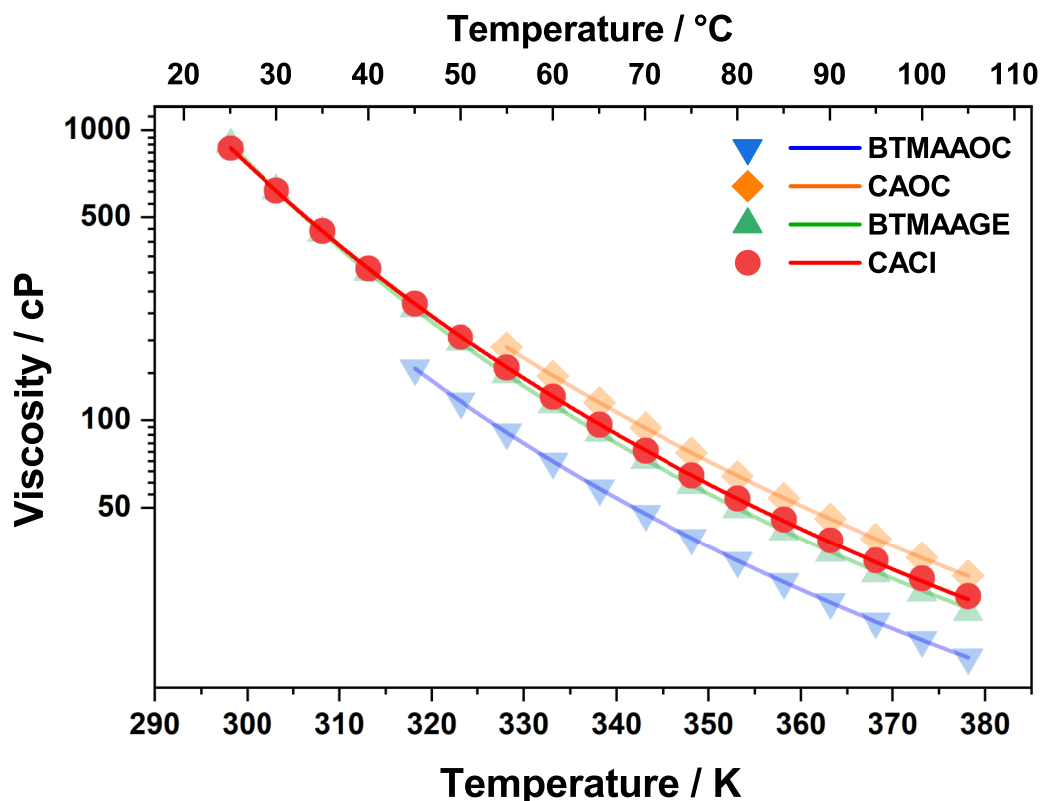


Figure 6.8. Dynamic viscosity data for the studied 1:2 ILs. 1:2 CACI (shown in red) is an isotropic liquid over the entire studied temperature range. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation, with fit parameters shown in Table 6.2.

between 25–105 °C (298–378 K) and shows Newtonian flow behaviour (viscosity is independent of shear rate). The viscosity values collected at each temperature were averaged across the range of shear rates (50–150 s⁻¹) and then fitted to the Vogel-Fulcher-Tammann (VFT) equation (Equation 2.7); experimental and fitted data are shown in Figure 6.8 in red. Dynamic viscosity data for the previously discussed ILs is also included in Figure 6.8; for 1:2 BTMAAOC and 1:2 CAOC only data corresponding to the isotropic liquid phase is shown. The best-fit parameters obtained from the VFT fit are given in Table 6.2.

The viscosity of 1:2 CACI is very similar to that of isotropic 1:2 BTMAAGE, with the viscosities of the four ILs varying in the order 1:2 CAOC > 1:2 CACI $\approx$ 1:2 BTMAAGE > 1:2 BTMAAOC; the activation energy parameter B , derived from the VFT fit of the temperature-dependent viscosities, also follows this same trend. The viscosities of 1:2 CAOC, 1:2 BTMAAGE and 1:2 BTMAAOC have already been compared in Chapter 4, where several factors that may contribute to an increased viscosity were identified. Briefly, these include higher molecular weights,¹³⁸ branching groups on the anion alkyl chains,^{86,135} and a more restricted conforma-

Table 6.2. Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD, Equation 2.8)

Sample	η_0 / mPa s	B / K	B / kJ mol ⁻¹	T_0 / K	AAD / %
1:2 CACI	0.0490	1354.47	11.26	159.66	0.4
1:2 BTMAAGE	0.0780	1151.20	9.57	174.94	0.5
1:2 CAOC	0.0412	1517.05	12.61	146.90	0.02
1:2 BTMAAOC	0.0601	1135.71	9.44	172.99	0.006

tional flexibility of the species comprising the IL.¹³⁹ 1:2 CACI has the second highest molecular weight (only slightly lower than that of 1:2 BTMAAGE) and contains a structurally complex [(citronellate)₂H]⁻ anion; this is similar to the [(geranate)₂H]⁻ anion in terms of branching groups, but has a slightly higher conformational flexibility, as it lacks the C2-C3 double bond that is present in the geranate anion (this is only a single bond in citronellate). The activation energy calculated for 1:2 CACI is higher than that of 1:2 BTMAAGE (11.3 kJ mol⁻¹ and 9.6 kJ mol⁻¹), suggesting that the dynamics of viscous flow are more restricted; however, it should be noted that this is a property of the bulk IL, and so is affected not only by the structure of the anion, but also by that of the cation and by the interaction between the two species. 1:2 CACI contains a cholinium cation, which allows for the formation of hydrogen bonds between the cation hydroxyl group and the anion headgroup; the increased interactions strength resulting from this is likely to lead to a higher activation energy. Additionally, stronger anion-cation interactions were also found to increase the viscosity of a system;¹³⁷ the increased hydrogen bonding is likely to be one of the reasons why the cholinium-containing ILs have greater viscosities than those containing a BTMA cation.

Some of the best-fit parameters derived from the VFT fit of viscosity can be directly compared to parameters extracted from the fitting of DMA $\tan \delta$ data corresponding to the thermally-activated relaxation (given in Table 6.1). The T_0 values are in good agreement between the two techniques, while the activation energies differ slightly. The B value obtained from viscosity data is higher than that obtained from relaxation data: $B_{\text{visc}} = 11.3$ kJ mol⁻¹ and $B_{\text{relax}} = 8.6$ kJ mol⁻¹ (a difference of approximately 3 kJ mol⁻¹). This is very similar to what was observed for 1:2 BTMAAGE, where B_{visc} was found to be greater than B_{relax} , also by roughly 3 kJ mol⁻¹. This difference is thought to be due to the fact that the two values are associated

with different phases: dynamic viscosity measurements are performed on the isotropic liquid phase, while the relaxation occurs at temperatures where 1:2 CACI is thought to be in a (partially) crystalline state. Nonetheless, the difference between B_{visc} and B_{relax} is not large (small discrepancies are common when comparing different techniques) and it suggests that the dynamics of viscous flow are similar (but not necessarily the same) in the two phases of the IL.

6.3 Structuring

6.3.1 NMR

Solid-state magic-angle spinning (MAS) NMR spectra of 1:2 CACI were recorded by myself and Dr. Anjali Menakath at the University of Warwick, UK and analysed by myself. 1D ^1H and ^1H - ^1H NOESY NMR spectra were recorded at 5 °C and 50 °C; 1:2 CACI is in the isotropic liquid phase at both of these temperatures.

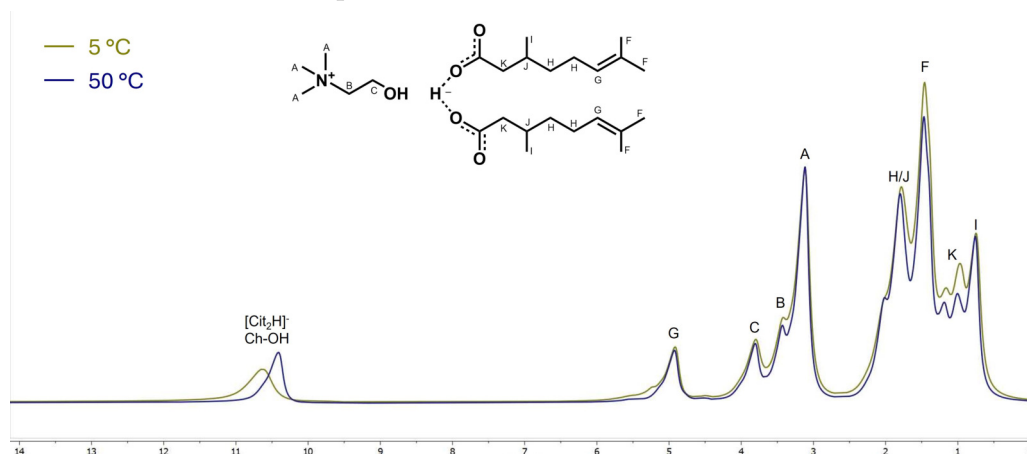


Figure 6.9. Solid state MAS ^1H NMR of 1:2 CACI at 5 and 50 °C

1D ^1H spectra are shown in Figure 6.9. As was the case with previously discussed ILs, the spectra collected at 5 °C and 50 °C show the same resonances. The peaks are broader at the lower temperature, likely due to the IL having a greater viscosity.¹³¹ Between 0 and 6 ppm, the peaks correspond to alkyl and alkene protons, and do not shift position with temperature. The downfield peak corresponds to two protons: that of the cholinium hydroxyl group and that of the complex $[(\text{citronellate})_2\text{H}]^-$ anion. The position of this peak is an average of the expected chemical shifts for the two peaks: approximately 5-6 ppm for the hydroxyl proton and approximately 15-16 ppm for the acidic proton. The latter is a higher chemical shift than would normally be expected for a carboxylic acid due to the fact that the proton is shared between

two citronellate moieties, and thus is more deshielded. The peak observed in the NMR appears at 10.6 ppm at 5 °C and at 10.3 ppm at 50 °C. The slight upfield shift is most likely due to the strength of the hydrogen bonding decreasing slightly as the temperature is increased, leading to the proton becoming less deshielded and the average chemical shift of the two environments increasing.

The SS-MAS ^1H - ^1H NOESY spectra recorded at 5 °C and 50 °C are shown in Figures 6.10 and 6.11 respectively. At both temperatures, 1:2 CACI is in an isotropic liquid phase, but the number of crosspeaks observed in the NOESY decreases when the temperature is increased. This is most likely not due to a significant change in structuring, but to an increase in disorder and molecular motion associated with the higher temperature. At 5 °C, crosspeaks are observed between the cation headgroup (protons A and B) and the anion alkyl chain, as well as the acidic proton of the complex anion. This proton also shows a weak crosspeak with the terminal methyl groups of the citronellate anion (protons labelled F). Crosspeaks are also observed between different protons on the anion alkyl chain, which may correspond to both intermolecular and intramolecular interactions. The fact that the hydroxyl group proton and the acidic proton give rise to a single peak indicates that the cation and anion form a hydrogen bonded cluster in which the two protons can rapidly exchange.

6.3.2 X-ray scattering

PLM and NOESY data has shown that room temperature 1:2 CACI has an isotropic liquid structure in which preferred intermolecular interactions give rise to NOESY crosspeaks between the cation and the anion alkyl chain. To further investigate the structuring of the IL, small-angle and wide-angle X-ray scattering measurements (SAXS and WAXS) were performed over a temperature range of 5–55 °C. The scattering profiles were collected by Dr. Chi L. Chan and Dr. Mohit Devgan on beamline I22 at Diamond Light Source, Didcot, Oxfordshire. Data analysis was performed by myself. The SAXS and WAXS profiles collected at different temperatures are shown in Figure 6.12.

The SAXS data covers a q -range of 0.05–0.32 $\text{\AA}^{-1}$. The only feature visible in the SAXS profile of 1:2 CACI is a broad peak centred around $q = 0.30 \text{ \AA}^{-1}$. Because of the q -range covered by the detector, this peak is cut off in the SAXS data, but is present in its entirety in the

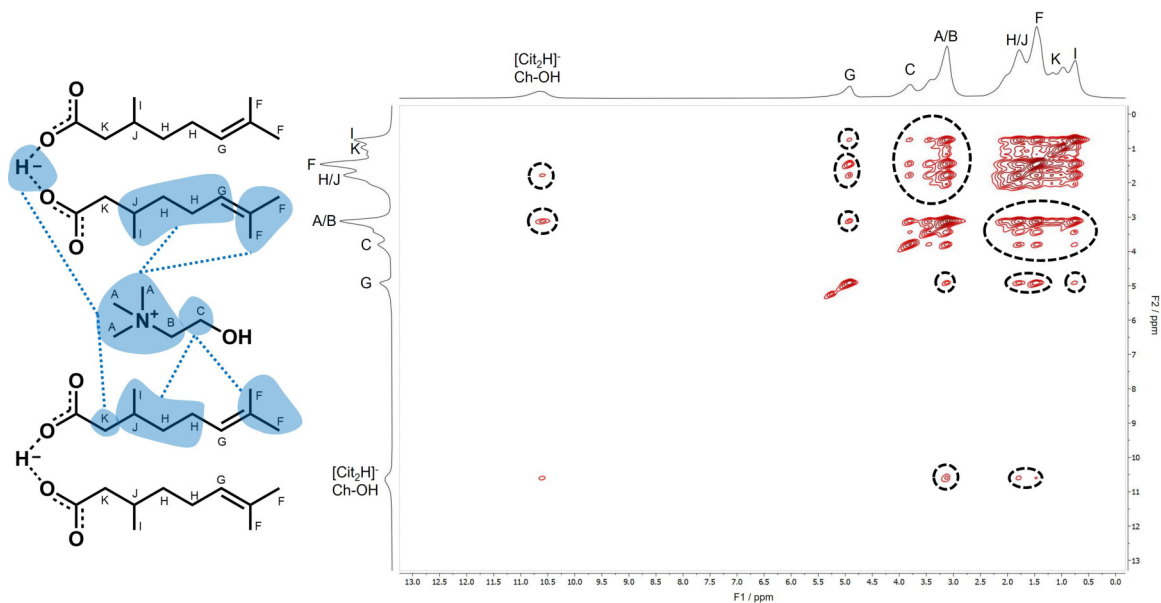


Figure 6.10. ^1H - ^1H NOESY of neat 1:2 CACI at 5 °C

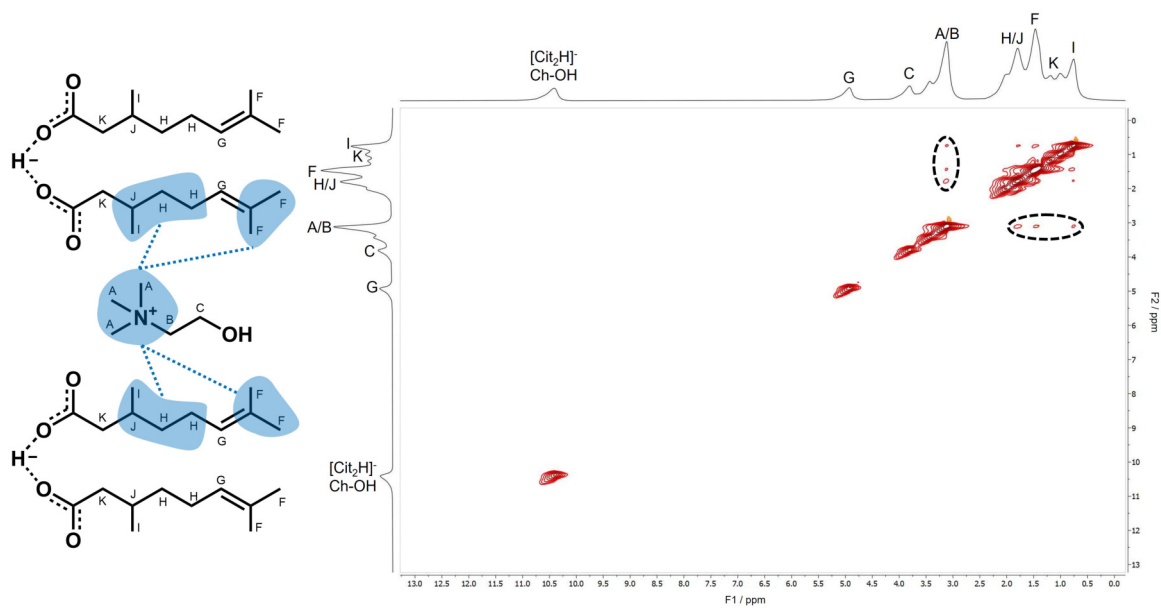


Figure 6.11. ^1H - ^1H NOESY of neat 1:2 CACI at 50 °C

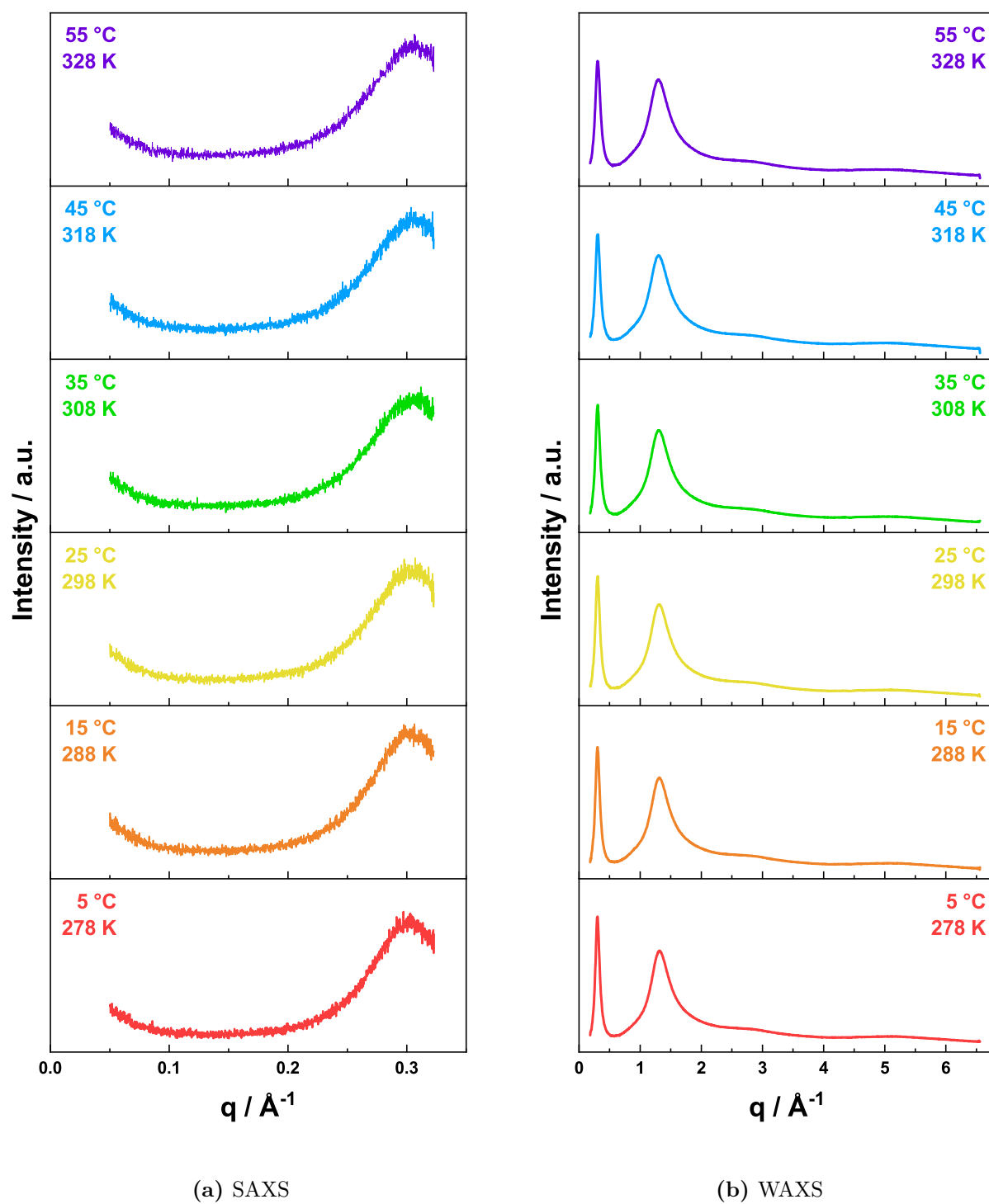


Figure 6.12. X-ray scattering data of 1:2 CACI at various temperatures.

WAXS data (covering a range of $0.18\text{--}6.55\text{ \AA}^{-1}$). The position of the peak is consistent at all temperatures. The broad shape of this peak indicates that the IL does not possess a liquid crystalline structure and is instead an isotropic liquid at all measured temperatures. Generally, the X-ray scattering profile of an ionic liquid shows three main features (this is discussed in more detail in Section 4.3.2). The first is the 'prepeak', usually at the lowest q , which for 1:2 CACI is the broad peak at $q = 0.30\text{ \AA}^{-1}$. The presence of this peak in the scattering profile indicates that the structure of the IL shows nanoheterogeneity, meaning that the polar and nonpolar moieties of the IL form distinct, segregated nanodomains. In order to minimise energetically unfavourable interactions, it is thought that the polar domain is comprised of the cholinium cation and the negatively-charged anion headgroup, while the nonpolar domain is comprised of the anion alkyl tails. The NOESY data shown in Figure 6.10 indicates that the cation hydroxyl group and the anion headgroup interact via hydrogen bonding, while the the $[\text{NMe}_3]^+$ group shows crosspeaks the acidic proton of the $[(\text{citronellate})_2\text{H}]^-$ anion. These interactions which are in agreement with the proposed structure of 1:2 CACI. Additional crosspeaks are seen in the NOESY between the cation NMe_3 methyl protons and the protons of the anion alkyl chain. The exact reason for the presence of these crosspeaks is unknown, but is thought to be due to the dynamic nature of the IL and not because the cation resides in the nonpolar domain. Additionally, the observed crosspeaks could occur because of through-space interactions at the boundary between polar and nonpolar domains, as well as because of possible spin-diffusion effects as observed in the liquid crystalline phases of the other ILs in this work.¹²¹

The next peak usually observed for ILs is referred to as the 'charge' peak and is associated with the distance between polar groups with the same charge. However, this peak is not visible for any of the ILs in this work, which could be due to the absence of charge alternation (e.g. if the cation is entirely 'encased' within the nonpolar domain) or due to the positive and negative contributions to this peak cancelling out.¹⁹ The final peak is usually observed above $q = 1\text{ \AA}^{-1}$; for 1:2 CACI this is the broad peak seen in the WAXS profile at $q = 1.31\text{ \AA}^{-1}$. This is observed for all ILs (as well as for molecular solvents) and is indicative of the average anion-cation distance and, in ILs with long hydrocarbon chains — such as the systems discussed in this work — of the average chain-chain separation.

6.4 Chapter summary

Table 6.3. Temperatures of the liquid crystal to isotropic liquid transitions for 1:2 CACI and previously discussed ILs

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 CACI	−10	n/a	−2	n/a	< 5
1:2 CA2OE	12	25	n/a [*]	n/a	5–15
1:2 BTMAAGE	24	27	15	< 25	25–35
1:2 CAOC	52	60	57	50–55	50–55
1:2 BTMAAOC	17	25	37 ^{**}	35–40	35

^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling at $f = 1$ Hz

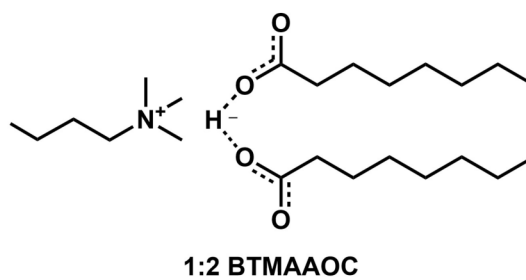
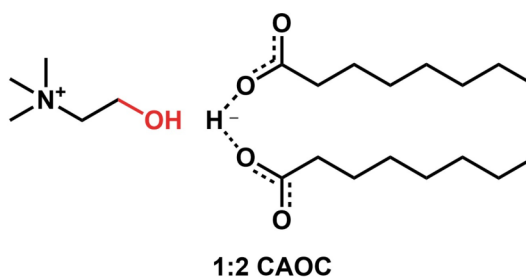
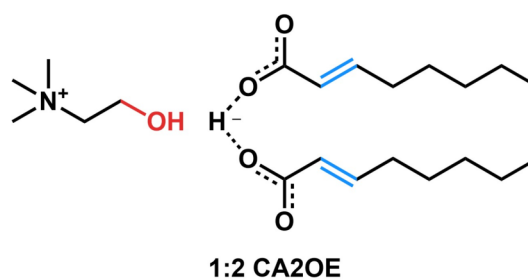
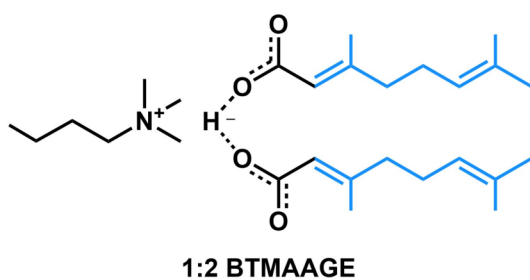
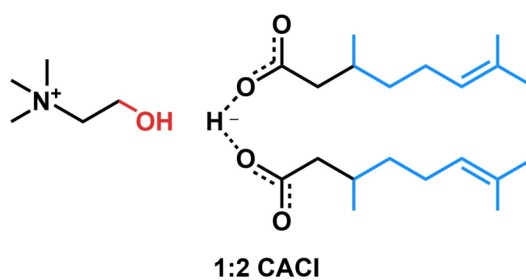
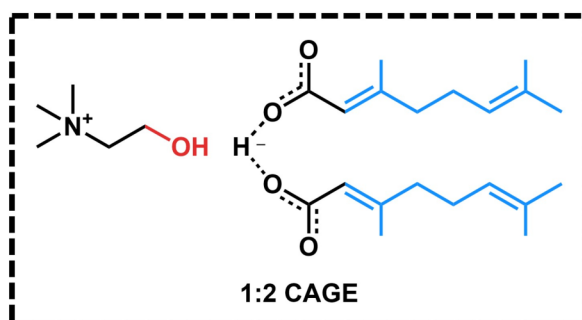
^d Temp. above which IL shows Newtonian flow behaviour

^e Temp. at which sharp LC peak disappears

^{*} Not observed ^{**} Tan δ peak on heating

1:2 CACI is, along with 1:2 CAGE, the most structurally complex IL. While its DSC profile is very similar to that of 1:2 BTMAAGE (no cold crystallisation or crystallisation transition), 1:2 CACI stands out in that the temperature of its liquid crystal to isotropic liquid transition is extremely low. Because scattering or PLM measurements could not be performed at temperatures below 0 °C, the nature of the LC phase could not be confirmed. However, by comparison with the other ILs, particularly 1:2 CAGE (Chapter 7) it is possible that 1:2 CACI may exhibit a liquid crystalline mesophase, similar to the one observed for 1:2 CAGE at low temperatures. Still, this is simply speculation based on the behaviour of similarly-structured ILs. The use of a PLM setup in a moisture-free environment (e.g. a glove box) could be useful in identifying the nature of this phase, as the predominant issue when using a PLM instrument in air is moisture absorption by the sample and the condensation of water droplets on the sample and sample slide.

STRUCTURE COMPLEXITY



Chapter 7

1:2 Choline And GERanate (1:2 CAGE)

The results presented in this chapter have been partially published in Reference [101].

This final chapter on 1:2 ionic liquids looks at the properties and behaviour of 1:2 choline and geranate (CAGE). This is the most structurally complex of all ILs discussed in this work, containing a cholinium cation, which can engage in hydrogen bonding via a hydroxyl group, and a [(geranate)₂H][−] anion, the alkyl tails of which possess both unsaturation and branching methyl groups. The structure of 1:2 CAGE is shown in Figure 7.1. 1:2 CAGE was first reported in the literature in 2014 by Zakrewsky *et al.*⁹ and has since been studied extensively, mostly for its transdermal penetration and antibacterial properties.^{10,12,30} Despite this, some of the data reported in the literature is not always optimal, as the samples of 1:2 CAGE used in these studies often contain significant amounts of moisture or have been dried at elevated temperatures, which promote thermal decomposition and the formation of coloured impurities. The data present in the current chapter was collected using samples of 1:2 CAGE synthesised in our lab, which were never exposed to temperatures above 15–20 °C (ambient temperature in our lab), were stored at −20 °C when not in use and were dried for at least 24 h at ambient temperature using a high-vacuum line. Measurement samples were prepared under dry, air-free conditions whenever possible. The purpose of this chapter is to present data regarding the thermal behaviour, rheology, and structuring of 1:2 CAGE; techniques include differential scanning calorimetry (DSC), dynamic mechanical analysis (DMA), dynamic viscosity, X-ray scattering. These findings are also compared with those obtained for the other 1:2 ILs discussed in this work, with the aim of providing a better understanding of the structure-property relationships

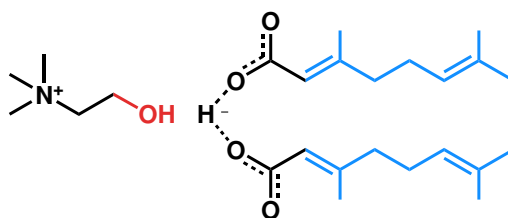


Figure 7.1. 1:2 CAGE

that govern 1:2 CAGE and other structurally similar systems.

7.1 Thermal Behaviour

DSC measurements were run by Dr. Daniel Rauber at the University of Saarland, Germany, and analysed by myself. Three consecutive heating-cooling cycles were run, with a scan rate of $5\text{ }^{\circ}\text{C min}^{-1}$. The DSC traces are shown in Figure 7.2.

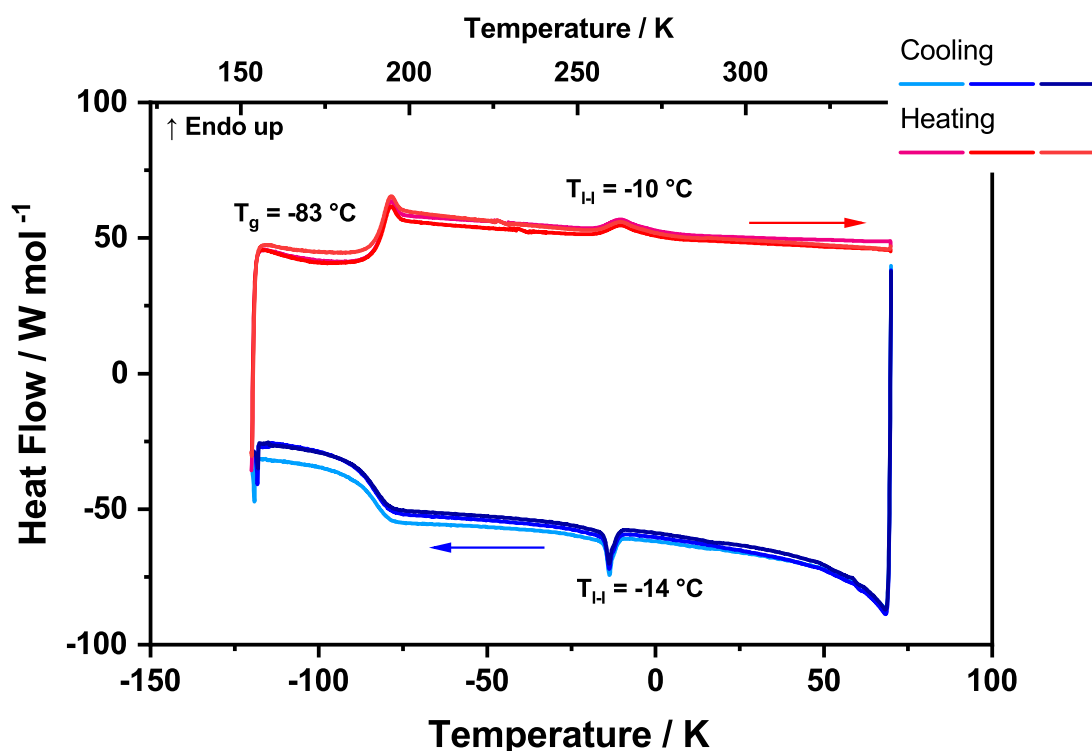


Figure 7.2. DSC traces of 1:2 CAGE with annotated transition temperatures. The heating and cooling rates are $5\text{ }^{\circ}\text{C min}^{-1}$.

The thermal behaviour of 1:2 CAGE is relatively simple, and very similar to that of 1:2 CACl. The DSC traces show an exothermic peak at $T_{L1} = -14\text{ }^{\circ}\text{C}$ on cooling and a corresponding endothermic peak at $T_{L1} = -10\text{ }^{\circ}\text{C}$ on heating. These features are small and, in the case of



(a) 1:2 CAGE at room temperature.



(b) 1:2 CAGE cooled to $-20\text{ }^{\circ}\text{C}$.

Figure 7.3. Samples of 1:2 CAGE at temperatures above and below the crystallisation transition temperature

the endothermic peak, rather broad, which suggests that this is not a solid-to-liquid transition (and vice versa). This is similar to the behaviour observed for 1:2 CACI, for which the DSC peaks (at very similar temperatures to those seen here for 1:2 CAGE) are assumed to be due to a phase transition between a liquid crystal phase and an isotropic liquid phase (LC-isotropic transition, as observed for other ILs in this work). However, due to the low temperatures required, the existence of the liquid crystalline phase could not be confirmed for 1:2 CACI.

Figure 7.3 shows a visual comparison of room-temperature 1:2 CAGE and 'frozen' 1:2 CAGE, which was stored in a $-20\text{ }^{\circ}\text{C}$ freezer overnight (the photograph is taken at room temperature, immediately after removing the sample from the freezer). On cooling to $-20\text{ }^{\circ}\text{C}$ (below the T_c measured by DSC) 1:2 CAGE turns from a clear liquid, which is viscous but flowing, to a gel with a much higher viscosity and an opaque appearance (Figure 7.3b). This shows that 1:2 CAGE does not crystallise to a solid upon cooling; however, it should be noted that with this method the rate of cooling is faster than for the DSC measurement. An attempt at recording a crystal structure of 1:2 CAGE was also made, by loading a small amount of sample onto a CryoLoop and slowly cooling it in situ, using a cryogenic gas stream, but the scattering of the sample was too weak to be measured.

1:2 CAGE at $-20\text{ }^{\circ}\text{C}$ (Figure 7.3b) is similar in appearance to 1:2 CACI at this temperature

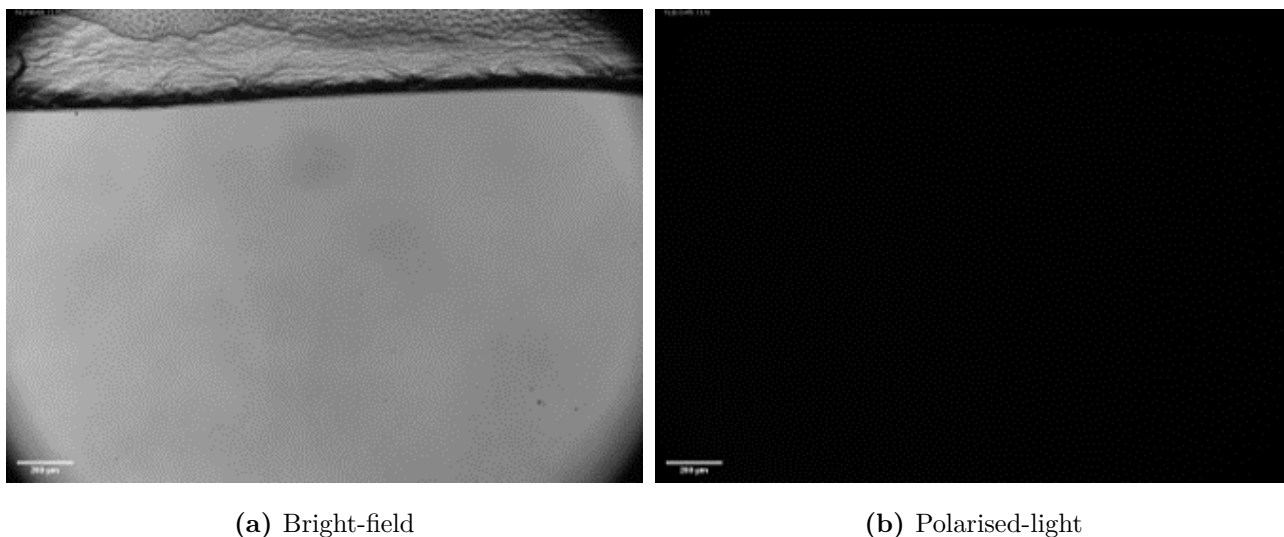


Figure 7.4. Microscope images of 1:2 CAGE at room temperature using $4\times$ magnification. The sample is not birefringent — the image taken using polarised light is entirely dark.

(6.3b, thought to be in a LC phase), as well as to the liquid crystalline phases of other ILs in this work, such as 1:2 BTMAAOC (Figure 2.3a), 1:2 CAOC (Figure 3.4a) and 1:2 BTMAAGE (Figure 4.4a). Based on this, it seems likely that at temperatures below $T_{1-1} = -14\text{ }^{\circ}\text{C}$ 1:2 CAGE is also in a liquid crystalline phase. As mentioned when discussing 1:2 CACI, polarised-light microscopy and X-ray scattering could not be performed at temperatures below $0\text{ }^{\circ}\text{C}$ in order to investigate this phase. However, the SAXS profile of 1:2 CAGE recorded at $5\text{ }^{\circ}\text{C}$ (Figure 7.11a) shows a single sharp peak, which indicates that the IL is in a liquid crystalline phase. The nature of this phase was also confirmed using PLM: Figure 7.4 shows that a sample of 1:2 CAGE at room temperature (approximately $15\text{ }^{\circ}\text{C}$) is optically isotropic (not birefringent). The remaining SAXS profiles of 1:2 CAGE, recorded between $15\text{--}55\text{ }^{\circ}\text{C}$, show a broad peak, indicative of an isotropic liquid phase; this data is discussed in more detail in Section 7.3. It is acknowledged that even at $5\text{ }^{\circ}\text{C}$ the sample is at a higher temperature than the transition temperature $T_{1-1} = -10\text{ }^{\circ}\text{C}$ observed by DSC, and would be expected to be an isotropic liquid. However, discrepancies between transition temperatures measured by different techniques are not unusual, with SAXS often showing a higher transition temperature than DSC. Table 7.4 (also included at the end of each chapter) shows how the LC-isotropic transition temperature of the different 1:2 ILs varies with technique. The largest such difference was observed for 1:2 BTMAAGE, between the temperatures derived from DSC and SAXS measurements (Chapter 4), with the SAXS temperature being almost $20\text{ }^{\circ}\text{C}$ higher.

The last transition observed in the DSC traces of 1:2 CAGE (Figure 7.2) is a reversible glass

transition at $T_g = -83$ °C. In the literature, Tanner *et al.* found that 1:2 CAGE shows a glass transition at -78 °C,²⁷ which is similar to (although slightly higher than) the temperature reported in the present work. Ko *et al.* also reported a glass transition temperature of -68 °C,³² which is 15 °C higher than the one measured for our sample. Neither publication reports a liquid crystal to isotropic liquid transition, but Tanner *et al.* report a cold crystallisation event at -42 °C, while Ko *et al.* report a small exothermic peak around -80 °C, which they believe may be due to cold crystallisation.^{27,32}

There are several possible explanations for these discrepancies, resulting from the way the two samples of 1:2 CAGE were handled after synthesis. It is likely that the samples contain different amounts of moisture and/or decomposition products, which may affect the observed transitions. Both publications report that the IL was dried at 60 °C; this would result in a low moisture content but would promote thermal decomposition. Our method aimed to minimise both of these contaminants: 1:2 CAGE was dried at room temperature, on a high-vacuum Schlenk line at room temperature (approximately 15 °C), and was kept cold (-20 °C) whenever possible to discourage decomposition. The DSC sample was loaded and sealed under dry conditions. The water content of dried 1:2 CAGE was measured to be 0.3 wt% (approximately 7 mol%).

7.1.1 Dynamic Mechanical Analysis

In order to gain a better understanding of the thermal behaviour of 1:2 CAGE, dynamic mechanical analysis (DMA) was used to investigate the rheological properties of 1:2 CAGE with changing temperature. Data was collected by myself and Dr. Oriele Palumbo at the Sapienza University of Rome, Italy, and analysed by myself. The storage modulus M' and the loss tangent $\tan \delta$ were measured at three different frequencies ($f = 1, 5$ and 10 Hz) over a temperature range of -100 – 30 °C (173 – 302 K). The storage modulus is reported here as the relative change with respect to the value at 25 °C (298 K), $M' / M'_{298\text{ K}}$ to remove the contribution of the metal pocket used to hold the sample. Figure 7.5 shows the relative change in storage modulus and the $\tan \delta$ measured at $f = 1$ Hz on both heating and cooling.

The thermal transitions observed by DMA were in agreement with the DSC data. The glass transition observed at -83 °C (190 K) by DSC gives rise to an intense peak in the $\tan \delta$ at -80 °C on both heating and cooling. Around the same temperature, the relative change in

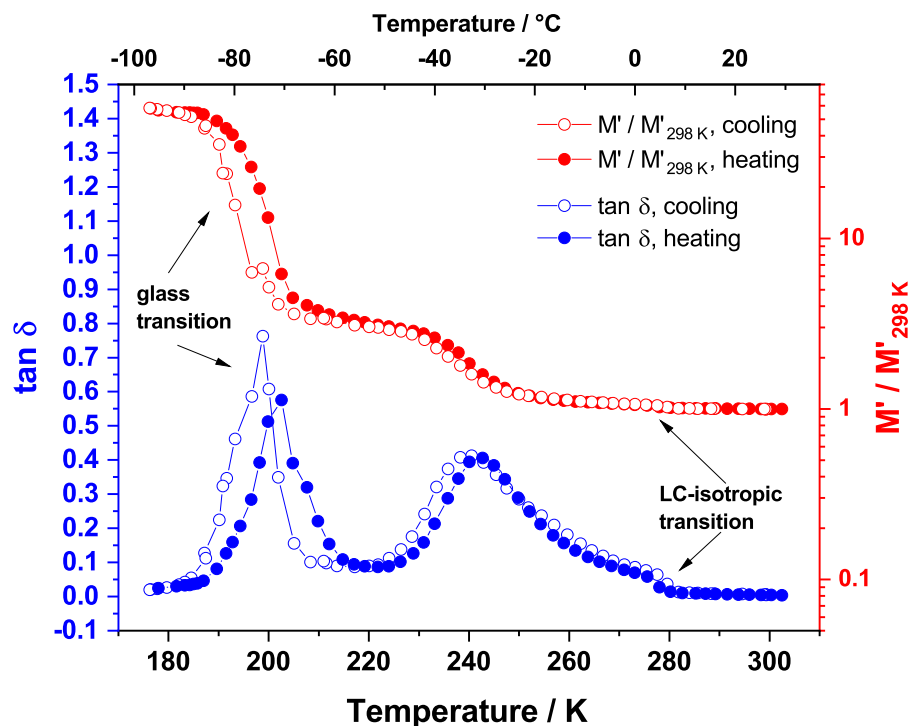


Figure 7.5. DMA data for 1:2 CAGE, measured at a frequency of 1 Hz on heating (filled symbols) and cooling (open symbols). Lines are guides for the eye.

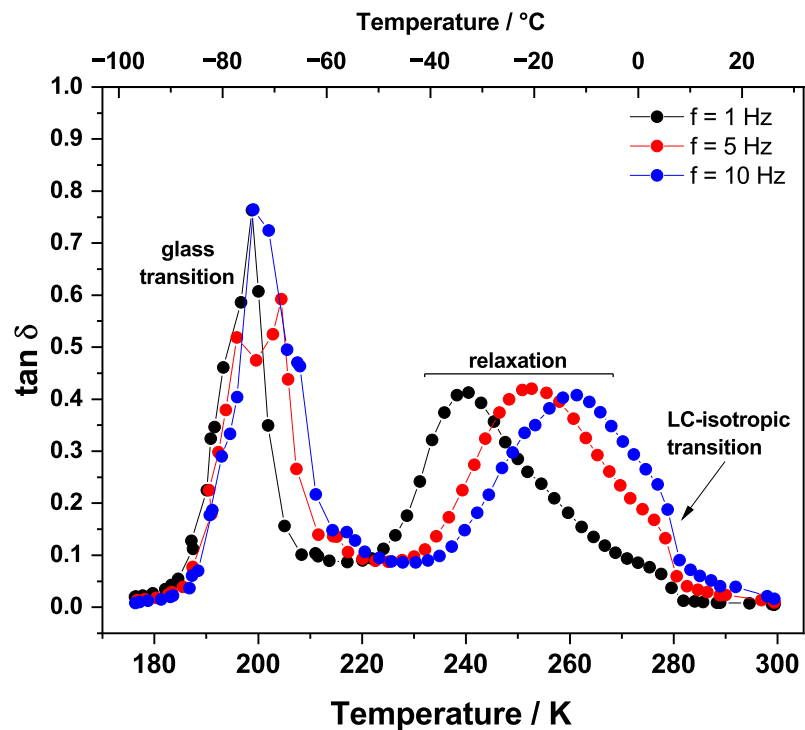


Figure 7.6. $\tan \delta$ measured for 1:2 CAGE on cooling. Lines are guides for the eye.

modulus shows a significant increase on cooling (and a corresponding decrease on heating), indicative of a glass transition.

The $\tan \delta$ data shows a small feature at 0 °C (273 K), while the modulus shows a small variation at the same temperature. These features are likely to correspond to the transition between the liquid crystalline phase and the isotropic liquid phase observed by DSC and SAXS. The fact that the change in modulus is small indicates that the stiffness (solid-like behaviour) of the IL is not significantly different between the two phases; this agrees with the observation that the IL does not fully crystallise to a solid (which would result in a larger increase in modulus on cooling).

The last feature observed in the DMA is the broad $\tan \delta$ peak observed at approximately -28 °C (245 K) in Figure 7.5. Figure 7.6 shows the $\tan \delta$ data for 1:2 CAGE collected at all three frequencies on cooling. The position of this peak (labelled 'relaxation') shifts to higher temperatures as the frequency of the measurement increases, which is characteristic of a peak corresponding to a thermally activated relaxation (rather than a phase transition). The relaxation can be described as a transition between two minimum energy states (configurations) with an energy difference ΔE . Here, the intensity of the peaks is constant regardless of frequency, meaning that the two states have equivalent energies ($\Delta E = 0$). Figure 7.7 shows the $\tan \delta$ peak of the thermally activated relaxation, as well as the lines of best fit corresponding to the two-state model approximation (relevant theory is given in Section 2.1.1). The data was simultaneously fitted according to equations 2.4 and 2.6 after performing a linear background subtraction. The best-fit parameters (obtained when $\Delta E = 0$) are given in Table 7.1; parameters obtained for other ILs in this work (that show a thermally activated relaxation peak in the $\tan \delta$) are also included in this table. The calculated best-fit parameters for 1:2 CAGE (τ_0 on the order of 10^{-7} s and a small activation energy $B = 8.5$ kJ mol $^{-1}$) indicate that the thermally activated relaxation is an intermolecular, diffusive process, similar to what was observed for all other ILs in this work (except 1:2 CA2OE, which did not show a relaxation peak). The width parameter α is less than one, which suggests interactions between the relaxing units.

The best-fit parameters calculated for 1:2 CAGE are comparable to those obtained for 1:2 CACI; this is expected, as the two ILs have extremely similar structures and are expected to behave in similar ways. Generally, the relaxation times obtained for octanoate-based ILs (1:2 CAOC and 1:2 BTMAAOC, $\tau_0 \approx 5.5 \times 10^{-7}$ s) are slightly smaller than the relaxation

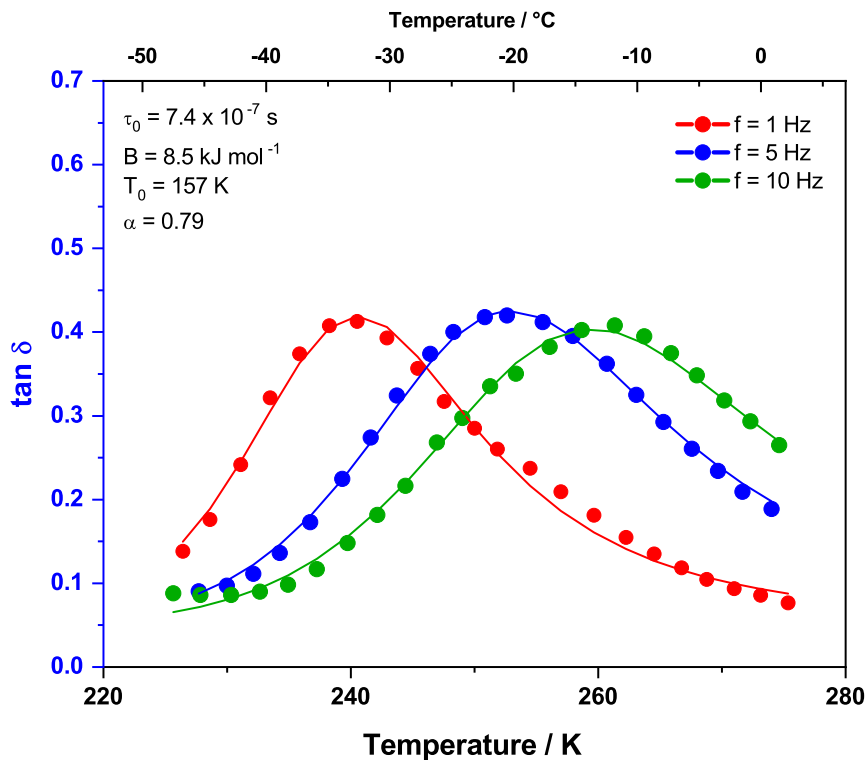


Figure 7.7. $\tan \delta$ measured for 1:2 CAGE on cooling at $f = 1, 5$ and 10 Hz. Only the data corresponding to the thermally activated relaxation is shown. The solid lines are the result of a simultaneous fit for the three frequencies. Before fitting, a linear background subtraction was performed.

Table 7.1. Best-fit parameters τ_0 , B , T_0 and α obtained from the simultaneous fitting of DMA $\tan \delta$ data associated with the thermally activated relaxation observed for 1:2 CAGE (top row). For comparison, data is also shown for the other 1:2 ILs discussed so far.

Sample	$\tau_0 / 10^{-7} \text{ s}$	B / K	$B / \text{kJ mol}^{-1}$	T_0 / K	α
1:2 CAGE	7.4 ± 0.2	1023 ± 14	8.5 ± 0.1	157 ± 3	0.79 ± 0.02
1:2 CACI	7.0 ± 0.2	1030 ± 19	8.6 ± 0.2	158.0 ± 0.2	0.74 ± 0.40
1:2 BTMAAGE	7.1 ± 0.1	750 ± 8	6.2 ± 0.1	174.0 ± 0.1	0.84 ± 0.01
1:2 CAOC	5.5 ± 0.1	1503 ± 19	12.5 ± 0.2	134 ± 2	0.75 ± 0.01
1:2 BTMAAOC	5.7 ± 2.0	1076 ± 26	9.0 ± 0.1	169 ± 2	0.57 ± 0.09

times obtained for ILs with more structurally complex anions (1:2 CACI, 1:2 BTMAAGE and 1:2 CACI, $\tau_0 = 7.0\text{--}7.4 \times 10^{-7}$ s). This suggests that the relaxation time (and therefore the relaxation rate) is influenced primarily by the structure of the anion species. Anions that are more sterically hindered and/or that have a lower degree of conformational flexibility (due to e.g. the presence of double bonds, as is the case for geranate and citronellate anions) seem to lead to slower relaxations (higher τ_0). The activation energy B varies according to the trend $B_{\text{CAOC}} > B_{\text{BTMAAOC}} \approx B_{\text{CACI}} \approx B_{\text{CAGE}} > B_{\text{BTMAAGE}}$. The greatest activation energy was obtained for 1:2 CAOC; this agrees with the initial hypothesis that 1:2 CAOC has the strongest intermolecular interactions, due to the ability of the cation to engage in hydrogen bonding and the lack of double bonds and branching groups disrupting the packing of the anion tails. The lowest B value corresponds to 1:2 BTMAAGE, which is structurally the most dissimilar to 1:2 CAOC; this seems to support the initial hypothesis that the branched, unsaturated geranate anion and the cation's lack of a hydroxyl group would lead to weaker intermolecular interactions. The remaining ILs have intermediate B values. While these are relatively close, it should be noted that B_{BTMAAOC} is slightly higher than the energies of 1:2 CACI and 1:2 CAGE. This trend seems to support our initial hypotheses regarding the strength of intermolecular interactions in the different ILs; it also suggests that, as in the case of the relaxation times, the activation energy of the thermally activated relaxation process is most strongly influenced by the nature of the anion species.

7.2 Viscosity

The rheology of 1:2 CAGE was also investigated using dynamic viscosity measurements, performed by Dr. Daniel Rauber at the University of Saarland, Germany and analysed by myself. A temperature range of 25–105 °C and a range of shear rates of 50–150 s⁻¹ were used. 1:2 CAGE is in the isotropic liquid phase at all temperatures and its viscosity changes very little with increasing shear rate (Newtonian flow behaviour). For each temperature point, the viscosities were averaged across the entire range of shear rates; the average values were fitted according to the Vogel-Fulcher-Tammann (VFT) equation (Equation 2.7). Experimental and fitted data are shown in Figure 7.8 in black. Best-fit parameters are given in Table 7.2. It should be noted that for all ILs, dynamic viscosity data was only collected for the isotropic liquid phase.

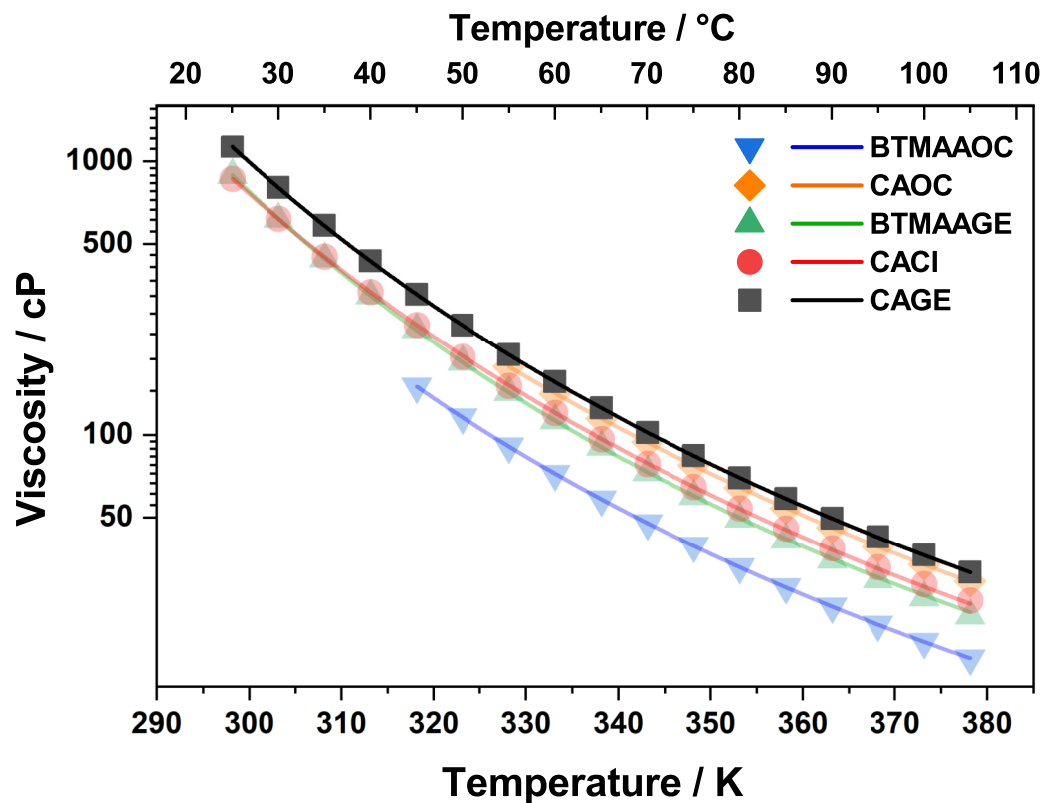


Figure 7.8. Dynamic viscosity data for the studied 1:2 ILs. 1:2 CAGE (shown in grey) is an isotropic liquid over the entire studied temperature range. The data was fitted to the Vogel-Fulcher-Tammann (VFT) equation, with fit parameters shown in Table 7.2.

Table 7.2. Best-fit parameters η_0 , B and T_0 from the fitting of viscosity data using the Vogel-Fulcher-Tammann (VFT) equation and the absolute average deviation (AAD, Equation 2.8)

Sample	η_0 / mPa s	B / K	B / kJ mol ⁻¹	T_0 / K	AAD / %
1:2 CAGE	0.0766	1290.87	10.73	163.72	0.004
1:2 CACI	0.0490	1354.47	11.26	159.66	0.4
1:2 BTMAAGE	0.0780	1151.20	9.57	174.94	0.5
1:2 CAOC	0.0412	1517.05	12.61	146.90	0.02
1:2 BTMAAOC	0.0601	1135.71	9.44	172.99	0.006

The viscosity of 1:2 CAGE is similar to that of 1:2 CAOC, with these two ILs having the highest viscosities of all investigated systems. For 1:2 CAGE, the high viscosity can be attributed to the high molecular weight of the IL and to the decrease in conformational flexibility caused by the presence of two double bonds in the geranate alkyl chain.^{138,139}

The activation energy parameters obtained from the viscosity fits varies in the order $B_{\text{CAOC}} > B_{\text{CACI}} > B_{\text{CAGE}} > B_{\text{BTMAAGE}} > B_{\text{BTMAAOC}}$. The dynamics of viscous flow are the least restricted (smallest B) in the two ILs containing BTMA cations, which also show the lowest viscosities. This is expected, as the strength of cation-anion interactions was shown to affect viscosity, with weaker interactions leading to lower viscosities. The cholinium-based ILs are thought to have stronger cation-anion interactions, as cholinium has the ability to form hydrogen bonds; this results in higher viscosities and larger activation energy values. It should be noted that the viscosity and activation energy of 1:2 CAOC are high despite the lack of features in the anion structure that would cause an increase in viscosity (such as branching groups and double bonds). While the nature of the cation has a strong influence on the viscosity of 1:2 CAOC, it is likely that another factor contributing to the high viscosity of 1:2 CAOC is the low water content of the sample (approximately 0.07 wt% or 1.5 mol%).

The B value obtained for 1:2 CAGE (10.7 kJ mol^{-1}) is in-between the values calculated for 1:2 CACI (11.3 kJ mol^{-1}) and 1:2 BTMAAGE (9.6 kJ mol^{-1}). As with the viscosity, there are several factors affecting this parameter. The additional double bond in the geranate chain (compared to citronellate) leads to a more restricted system, as does the presence of the hydroxyl group in the cholinium cation (compared to BTMA). 1:2 BTMAAGE contains a geranate anion, but no hydroxyl group; 1:2 CACI contains a hydroxyl group in the cation structure, but one fewer double bonds in the citronellate anion. 1:2 CAGE contains both a hydroxyl group and a geranate anion, but has a smaller activation energy than 1:2 CACI. This could be once again attributed to the level of dryness that was achieved for these particular samples. 1:2 CACI was measured to have a low water content, of approximately 2 mol%, while 1:2 CAGE was found to contain more than three times as much water (approximately 7 mol%).

Finally, some of the parameters obtained from the VFT fit of the viscosities can be compared with parameters obtained from fitting the $\tan \delta$ data associated with the thermally activated relaxation. The T_0 and B values are similar between the two techniques, but the activation energy obtained from viscosity data $B_{\text{visc}} = 10.7 \text{ kJ mol}^{-1}$ is slightly higher than the activation

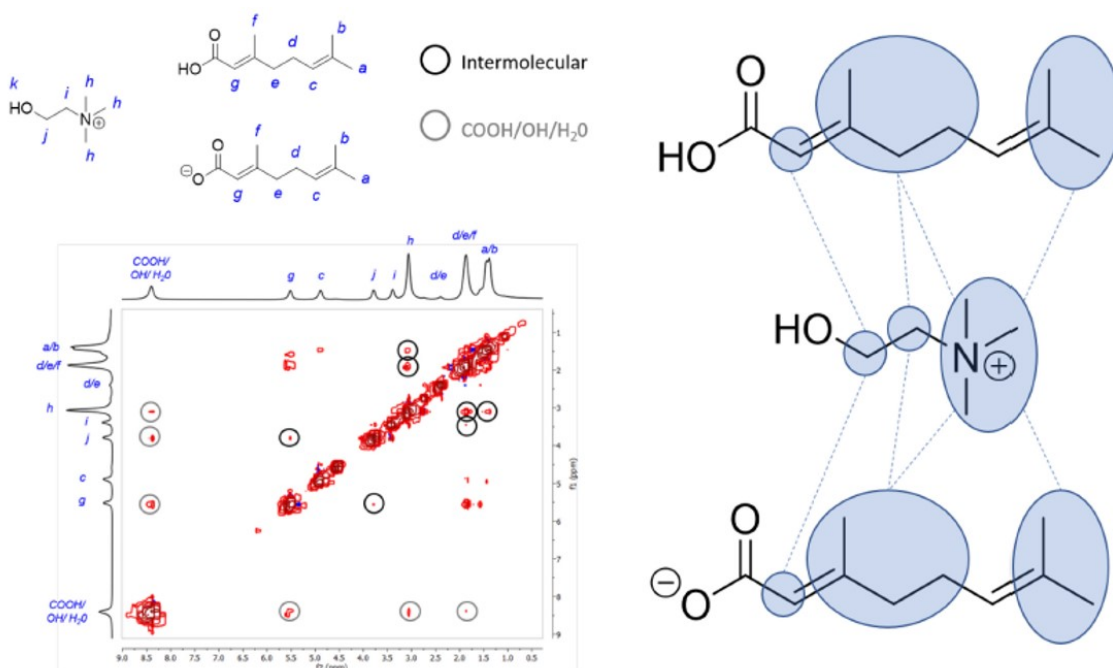


Figure 7.9. ^1H - ^1H NOESY of neat 1:2 CAGE at 20 °C. Reproduced from reference [15].

energy calculated from DMA data $B_{\text{relax}} = 8.5 \text{ kJ mol}^{-1}$. A similar observation was made for 1:2 CACI and 1:2 BTMAAGE and the difference between the two values was attributed to the fact that the two techniques describe different phases: the viscosity data is associated with the isotropic phase of the ILs, while the relaxation process occurs at low temperatures, where the ILs are in a liquid crystalline phase.

7.3 Structuring

7.3.1 NMR

Solid-state MAS ^1H - ^1H NOESY and 1D ^1H NMR spectra of 1:2 CAGE were recorded and analysed by Dr. Mohit Devgan at Imperial College London. The spectra shown in this section are reproduced from the thesis of Dr. Devgan (Reference [15]). Figure 7.9 shows the solid-state MAS ^1H - ^1H NOESY spectrum of 1:2 CAGE recorded at 20 °C. It should be noted that the structure of 1:2 CAGE shown in this figure is not necessarily meant to represent a real-life molecular arrangement; it is simply used to illustrate the observed interactions.

The cation headgroup NMe_3 shows crosspeaks with the terminal methyl groups of the geranate anion, as well as with the middle protons of the alkyl chain (labelled here as d and e). It

also shows crosspeaks with the acidic proton of the $[(\text{geranate})_2\text{H}]^-$ anion. The other cholinium protons (labelled i and j) show crosspeaks with the alkyl chain of the anion; the j protons in particular show an interaction with proton g , which is adjacent to the carboxylate group. The 1D ^1H NMR (Figure 7.10) shows a single peak for the hydroxyl proton and the acidic $[(\text{geranate})_2\text{H}]^-$ proton (with a chemical shift that is the average of the expected individual shifts), which indicates that the two protons undergo rapid exchange via hydrogen bonding. This was also observed for other cholinium-based ILs, both in this work and in the literature.¹³

At 20 °C 1:2 CAGE is in the isotropic liquid phase; X-ray scattering measurements (Section 7.3.2) showed that the structure of isotropic 1:2 CAGE consists of segregated polar and nonpolar regions. The NOESY data shows crosspeaks between the NMe_3 protons of the cation and the protons of the anion alkyl tail, suggesting that these are in close proximity within the isotropic phase of the IL. While the cation is thought to reside primarily within the polar domain, it is possible that it 'pokes into' the nonpolar region or that some through-space NOESY interactions occur at the boundary between the polar and nonpolar domains.

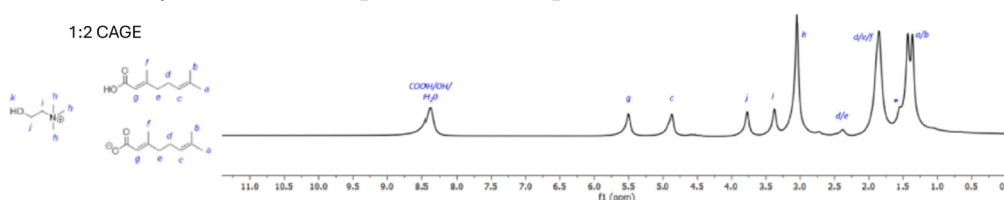


Figure 7.10. Solid state MAS ^1H NMR of 1:2 CAGE at 20 °C. Reproduced from reference [15].

7.3.2 X-ray scattering

In order to better understand the structuring of 1:2 CAGE, small- and wide-angle X-ray scattering (SAXS and WAXS) measurements were performed. Data was collected by Dr. Chi L. Chan and Dr. Mohit Devgan on beamline I22 at Diamond Light Source, Oxfordshire, and analysed by myself. Scattering profiles recorded over a temperature range of 5–55 °C are shown in Figure 7.11. The WAXS profiles were collected over a q -range of 0.18–6.5 $\text{\AA}^{-1}$, but the data shown here begins at $q = 0.44 \text{ \AA}^{-1}$. This was done in order to exclude the peak that is also observed in the SAXS profiles and allow for a more optimal visualisation of the remaining WAXS data.

At 5 °C, the SAXS profile of 1:2 CAGE shows a sharp, intense peak, indicative of a liquid crystalline phase. This peak appears at $q = 0.28 \text{ \AA}^{-1}$, corresponding to a real life d -spacing

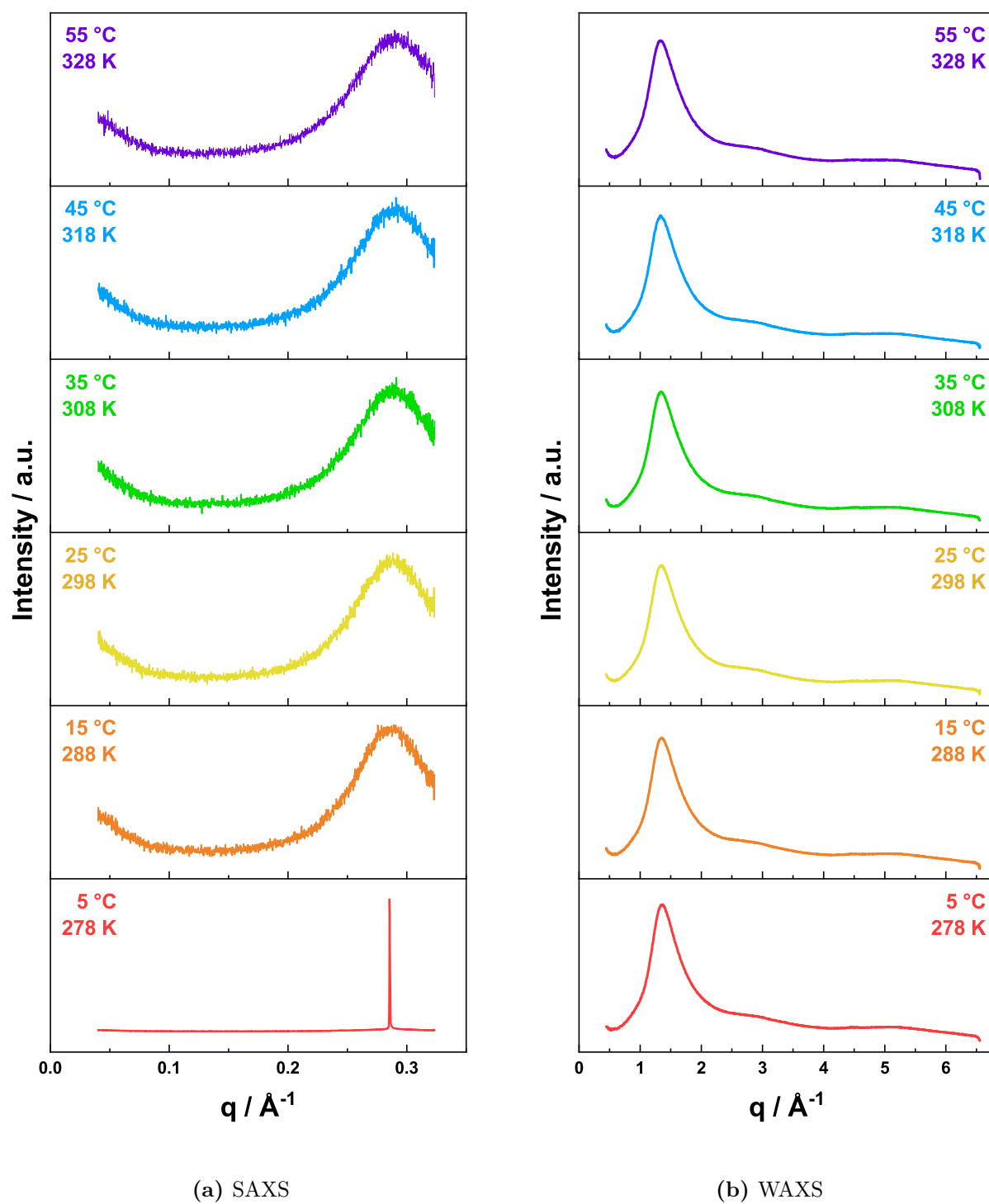


Figure 7.11. X-ray scattering data of 1:2 CAGE at various temperatures.

of 22.4 Å. The length of a geranate anion is approximately $l_{\text{anion}} = 10.0$ Å (measured using Chem3D). Even though no higher-order peaks can be observed in the scattering data, the peak shape and the fact that the size of the repeating unit is approximately twice the length of the anion suggest that liquid crystalline 1:2 CAGE has a lamellar bilayer structure.

A proposed lamellar bilayer structure for the LC phase of 1:2 CAGE is shown in Figure 7.12. This is very similar to the lamellar bilayer arrangements proposed for the other ILs in this work, with the anion alkyl tails being interdigitated and fluid to some extent. These forming the nonpolar regions of the bilayers, while the polar regions are thought to consist of the negatively charged anion headgroups and the cholinium cations. The position of the cation within the bilayer is not directly indicated by the SAXS data. However, the cholinium species is thought to reside within the polar region of the lamellar bilayer based on two main energetic considerations. First, the need for charge neutrality (cation-anion alternation) requires the positively charged ammonium group to exist in the vicinity of the negatively charged anion headgroup. Second, placing the cation in the nonpolar region (instead of the polar region) would be associated with a high energetic cost as it would prevent favourable hydrophobic interactions between neighbouring alkyl chains. Additionally, placing the cation in the polar region means that a hydrogen-bond network can form between the cholinium hydroxyl groups and the acidic proton of the anions; the proton exchange reported by Mann *et al.* is therefore possible in this configuration.¹³ It should be noted here that NOESY NMR data was not collected for 1:2 CAGE in the liquid crystalline phase (the lowest-temperature NOESY was recorded at 20 °C by Dr. Mohit Devgan).¹⁵ Future work on this system should involve collecting solid-state NMR spectra at low temperatures (below 5 °C, based on SAXS data).

As was the case with the previously discussed ILs, the cross-sectional area per unit of 1:2 CAGE in this bilayer structure was estimated and compared to literature values for similar lipid bilayers. A 'unit' of 1:2 CAGE consists of a cholinium cation, a geranate anion and a geranic acid molecule. The area per unit can be estimated by dividing the unit volume by the unit length. The volume of one 1:2 CAGE unit was calculated to be approximately 730 Å³. The density of 1:2 CAGE (0.99 g mL⁻¹) was taken from the work of Zakrewsky *et al.*⁹ The estimated unit length (for three different degrees of chain interdigitation) and the corresponding cross-sectional areas are given in Table 7.3. The area values are very similar to reported literature values for phospholipid lamellar bilayers (40–70 Å²)^{123,124} indicating that the proposed lamellar

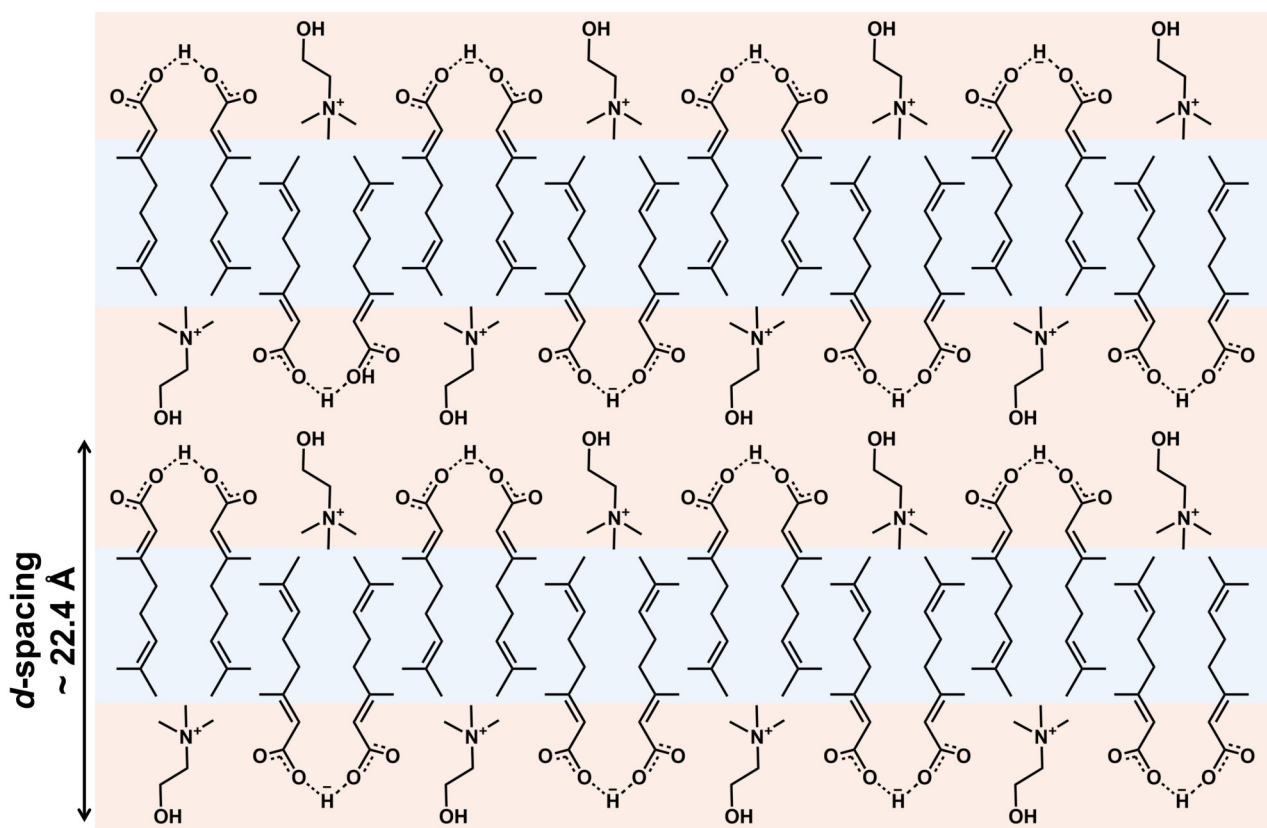


Figure 7.12. Possible structure of the main LC phase of 1:2 CAGE. The molecules are arranged in lamellar bilayers with an approximate d -spacing of 22.4 Å. Two adjacent bilayers are shown, with polar regions highlighted in orange and nonpolar regions highlighted in blue. It must be noted that while the alkyl chains are depicted as 'straight' in this figure, in reality they are somewhat fluid and may be curled or bent to some extent. Similarly, while the acidic protons are shown in a 'static' manner, in reality the system is a dynamic one, in which hydrogen bonds are always breaking and forming and protons are exchanged between different species.

bilayer structure is a reasonable model for the LC phase of 1:2 CAGE.

Figure 5.12 also shows some water molecules, representing any residual moisture that may be present in the system. This is because 1:2 CAGE, like the other ILs in this work, is hygroscopic and difficult to dry. In our lab, 1:2 CAGE was dried for 24 h on a high vacuum line and the X-ray scattering samples were then loaded and sealed in a glovebox, in order to minimise moisture intake. The water content of the 1:2 CAGE dried in this way was measured to be 0.3 wt% (6.8 mol%), which corresponds to a ratio of 14 IL molecules for every one water molecule. This is a very small amount of moisture and would result in a water layer with a negligible thickness. It is also possible that, due to the ability of the cation and anion to form hydrogen bonds, the water does not coalesce into a clear layer and instead is dispersed within the polar regions of

Table 7.3. Estimated length and area values for the 1:2 CAGE unit in a LC bilayer structure. Three different values are reported, depending on the degree of interdigitation between the alkyl chains forming a single bilayer.

Chain position	d -spacing (22.4 Å)	Unit length	Unit area
No interdigitation	$d = 2 \times l_{\text{unit}}$	$l_{\text{min}} = 11.2 \text{ Å}$	$A_{\text{max}} = 65.2 \text{ Å}^2$
Partly interdigitated	$d = 1.5 \times l_{\text{unit}}$	$l_{\text{int}} = 14.9 \text{ Å}$	$A_{\text{int}} = 48.9 \text{ Å}^2$
Fully interdigitated	$d = l_{\text{unit}}$	$l_{\text{max}} = 22.4 \text{ Å}$	$A_{\text{min}} = 32.6 \text{ Å}^2$

the bilayers, as suggested in Figure 5.12.

At higher temperatures (15–55 °C) the SAXS data shows a single broad peak centred around $q = 0.28 \text{ Å}^{-1}$, while the WAXS data shows a peak at $q = 1.35 \text{ Å}^{-1}$. The change from a sharp to a broad peak shape is associated with the transition between a liquid crystalline phase and an isotropic liquid phase. This was observed by DSC at –15 °C for 1:2 CAGE and similar phase transitions were also reported for other ILs in this work. At 15–55 °C, 1:2 CAGE is in an isotropic liquid phase and behaves in a similar way to more conventional ILs, specifically ones containing long-chain imidazolium cations. Such systems are not isotropic in the truest sense of the word, as they show a degree of nanostructuring, characterised by the formation of distinct polar and nonpolar domains. In long-chain imidazolium ILs, the polar domain consists of charged moieties, while the nonpolar domain is formed by the aggregation of the long alkyl tails on the cation. The X-ray scattering profile of such an IL usually shows three different features. The first is a low- q peak (the ‘prepeak’ or polarity peak) that arises from the alternation of polar and nonpolar regions; this peak indicates that the IL shows this long-range nanodomain structuring.^{80,125} For 1:2 CAGE, the prepeak is the broad feature centred around $q = 0.28 \text{ Å}^{-1}$. This suggests that the isotropic liquid phase of 1:2 CAGE is structurally nanoheterogeneous and is comprised of distinct polar and nonpolar nanodomains; the former is thought to consist of the cholinium cation and of the negatively charged anion headgroups (as well as any water molecules present in the system), while the latter is primarily made up of the geranate alkyl tails. The second peak that is usually observed for conventional ILs is the ‘charge’ peak, which arises from the presence of charge alternation within the IL structure. Positive contributions to the intensity of this peak come from cation-cation and anion-anion interactions, while negative contributions come from cation-anion interactions. This peak is not observed for 1:2 CAGE, most likely because the different types of contributions cancel

each other out.¹⁹ The third and final peak is the 'adjacency' peak, observed at higher q , which arises from a variety of interactions between adjacent atoms. For ILs with long hydrocarbon alkyl chains, this peak is usually indicative of two similar distances: the chain-chain correlation length and the average cation-anion spacing. For 1:2 CAGE, this peak appears in the WAXS profile at $q = 1.34 \text{ \AA}^{-1}$.

Table 7.4. Temperatures of the liquid crystal to isotropic liquid transitions for all ILs in this work

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 CAGE	−10	n/a	2	n/a	5–15
1:2 CACl	−10	n/a	−2	n/a	< 5
1:2 CA2OE	12	25	n/a [*]	n/a	5–15
1:2 BTMAAGE	24	27	15	< 25	25–35
1:2 CAOC	52	60	57	50–55	50–55
1:2 BTMAAOC	17	25	37 ^{**}	35–40	35

^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling at $f = 1 \text{ Hz}$

^d Temp. above which IL shows Newtonian flow behaviour

^e Temp. at which sharp LC peak disappears

^{*} Not observed ^{**} Tan δ peak on heating

7.4 Thermal Decomposition

In addition to the data presented for each system in the previous chapters, the thermal decomposition of the ILs was investigated using thermogravimetric analysis (TGA). This is presented here, rather than in each individual chapter as it is best discussed by comparing the behaviour of the different systems.

The short-term thermal stability of the ILs was studied using a heating rate of 5 °C min^{-1} , up to a temperature of 300 °C . The decomposition curves for all ILs are shown in Figure 7.13). Each TGA curve is characterised by four parameters: T_{onset} — the temperature corresponding to a mass loss of 10%, T_{half} — the temperature corresponding to a mass loss of 50%, T_{max} — the temperature at which the fastest rate of decomposition was observed (calculated from the

Table 7.5. TGA data for the studied 1:2 ILs

Sample	$T_{\text{onset}} / ^\circ\text{C}$	$T_{\text{half}} / ^\circ\text{C}$	$T_{\text{max}} / ^\circ\text{C}$	C. residue / %
1:2 CAGE	181	210	217	0.80
1:2 CACl	169	201	207	0.81
1:2 CA2OE	174	209	217	1.6
1:2 BTMAAGE	182	207	214	0.48
1:2 CAOC	147	190	201	1.7
1:2 BTMAAOC	175	201	210	0.23

peak of the first derivative), and M_{carb} — the mass of the carbonaceous residue left at the end of the measurement (normalised with respect to the initial sample weight). These values are given in Table 7.5.

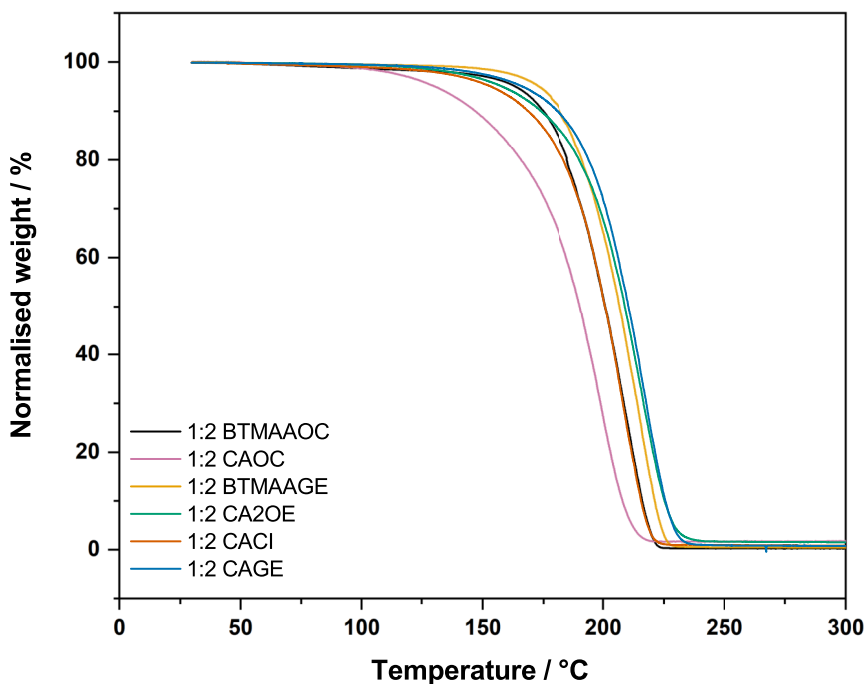


Figure 7.13. TGA curves for all six 1:2 systems discussed in this work. Data was collected using a heating rate of $5\text{ }^\circ\text{C min}^{-1}$.

While all 1:2 ILs undergo a one-step decomposition, the parameters describing the decomposition vary between the different systems. 1:2 CAOC shows the lowest temperatures for all three temperature parameters (T_{onset} , T_{half} and T_{max}). Ignoring the values corresponding to 1:2 CAOC, the T_{half} and T_{max} values only show a small variation, covering a temperature range

of 201–210 °C and 207–217 °C. The relative mass of the carbonaceous residue left over at the end of the measurement is small for all of the ILs, but it should be noted that it is highest (approximately 1.7%) for 1:2 CAOC and 1:2 CA2OE.

The temperature of decomposition onset T_{onset} shows the greatest variation and is perhaps the most significant parameter, as it signals the temperature above which the ILs are no longer fit for use in a practical application (the IL decomposition is significant above T_{onset}). For the 1:2 ILs in this work, the T_{onset} varies in the order CAOC < CACI < CA2OE $\approx$ BTMAAOC < CAGE $\approx$ BTMAAGE. This does not seem to follow any clear trend with respect to structuring, but some aspects of interest can be identified. The decomposition temperatures of 1:2 CA2OE and 1:2 CAGE are higher than those of 1:2 CAOC and 1:2 CACI respectively, with the only structural difference between these pairs of ILs being the presence of the C2-C3 double bond in the anion alkyl chains of 1:2 CA2OE and 1:2 CAGE (this is a single bond in 1:2 CAOC and 1:2 CACI). This seems to suggest that the presence of double bonds in the anion alkyl chain leads to a small increase in the thermal stability of the IL.

1:2 CAOC decomposes most readily, with $T_{\text{onset, CAOC}} = 147$ °C being significantly lower than for the other ILs (the next lowest temperature is $T_{\text{onset, CACI}} = 169$ °C). 1:2 BTMAAOC has a T_{onset} that is approximately 30 °C higher than 1:2 CAOC, with the only structural difference between the two ILs being the nature of the cation. In comparison, 1:2 CAGE and 1:2 BTMAAGE, whose structures differ in the same way (cholinium vs. BTMA cation), have T_{onset} values that are nearly identical. This suggests that the thermal decomposition behaviour of these systems is governed by more complex rules than a simple direct correlation between the decomposition temperature and the structural complexity of the IL structure.

In order to better understand the thermal decomposition of 1:2 BTMAAOC isothermal TGA measurements were performed using four different temperatures: 50 °C, 70 °C, 90 °C, 110 °C. For each measurement, the sample was held at 30 °C for 10 min to remove residual moisture, then heated quickly (10–20 °C/min) to the desired temperature, which was then maintained for 20 hours. The data is shown in Figure 7.14.

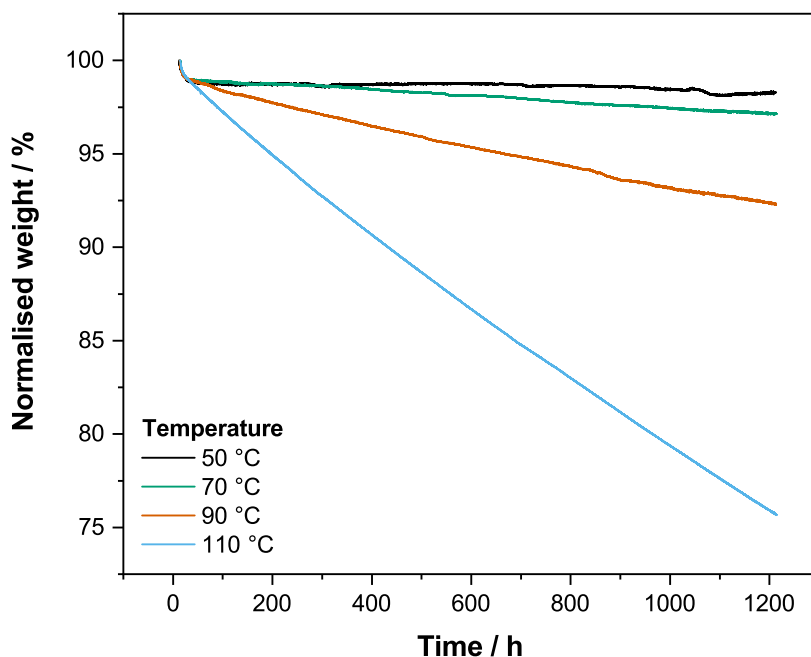


Figure 7.14. Isothermal TGA data for 1:2 BTMAAOC

It has been reported that the onset temperature T_{onset} (calculated above) can overestimate the stability of a system.^{147,148} An alternative to this involves calculating a different temperature parameter, $T_{0.01/10 \text{ h}}$, which represents the temperature at which 1% of the sample decomposes over a time period of 10 h. Other values can be used, here 0.01% and 10 h were chosen as these are commonly reported in the literature.^{147–150} This is calculated according to equations 7.1 and 7.2, according to the method proposed by MacFarlane *et al.*:^{147,148}

$$t_{1-x} = \frac{100 \times x}{k} \quad (7.1)$$

$$t_{0.99} = a \times e^{(-T/b)} \quad (7.2)$$

where $x = 0.01$ (for a 1% extent of decomposition) and $t_{0.99} = 1/k$.

The isothermal decomposition curves of 1:2 BTMAAOC are linear at all four temperatures, suggesting that the decomposition follows zero-order or pseudo zero-order kinetics. A linear fit was performed in order to determine the rate constant k (equal to the slope of the graph) for the isothermal decompositions. The rate constants were used to calculate $t_{0.99}$ for each isothermal temperature. These values were then fitted according to equation 7.2 (Figure 7.15). $T_{0.01/10 \text{ h}}$ was calculated to be 137 °C (410 K), which is approximately 40 °C lower than T_{onset} .

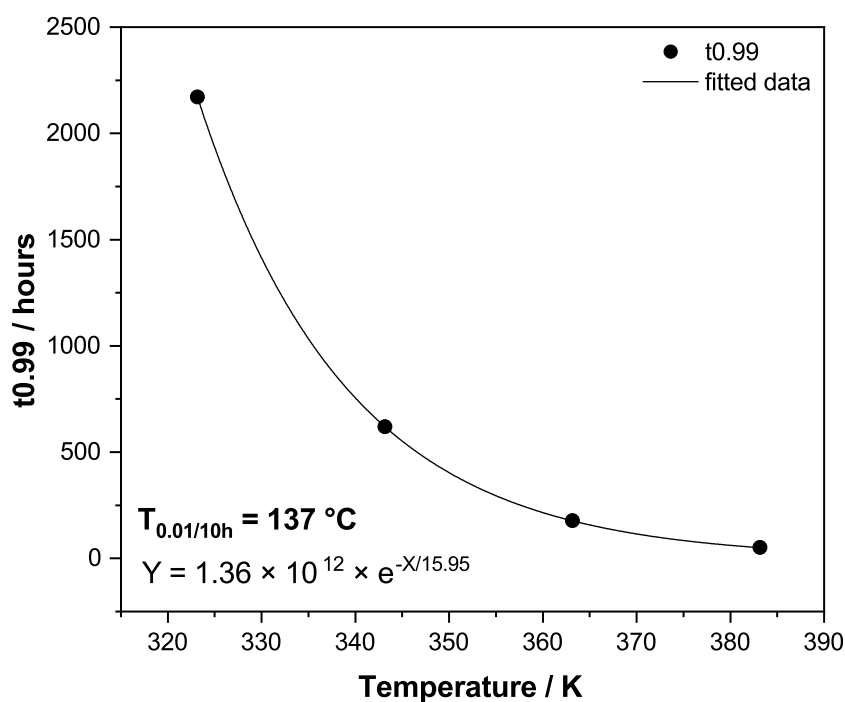


Figure 7.15. Analysis of $t_{0.99}$ for the isothermal decomposition of 1:2 BTMAAOC

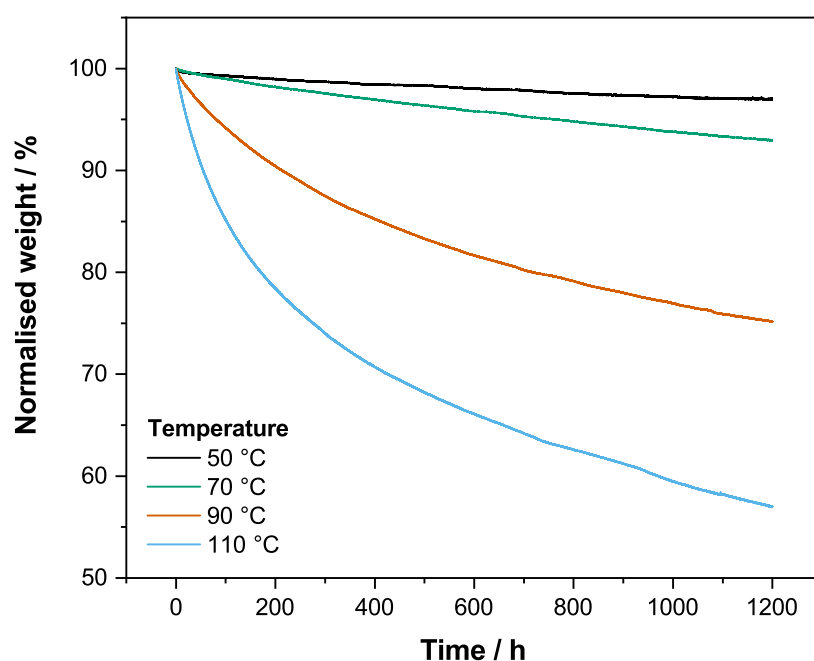


Figure 7.16. Isothermal TGA data for 1:2 CAOC

The kinetic analysis shown for 1:2 BTMAAOC was not performed for the other ILs, as these showed more complex decompositions. For example, the isothermal TGA data obtained for 1:2 CAOC is given in Figure 7.16. The curves are not linear, like in the case of 1:2 BTMAAOC, but instead they have a parabolic shape, indicating that the decomposition kinetics cannot be

approximated using a zero-order reaction rate. This suggests that the decomposition of 1:2 CAOC is more complex and requires further work in order to elucidate its mechanism. Future work using mass spectrometry combined with TGA analysis (TGA-MS) to analyse the nature of the decomposition products could provide valuable information about the decomposition pathway.

Chapter 8

Summary and outlook

The previous chapters have presented data on six different ionic liquids (ILs): 1:2 butyltrimethylammonium and octanoate (BTMAAOC), 1:2 choline and octanoate (CAOC), 1:2 butyltrimethylammonium and geranate (BTMAAGE), 1:2 choline and 2-octenoate (CA2OE), 1:2 choline and citronellate (CACI) and 1:2 choline and geranate (CAGE). The structures of the six 1:2 ILs are shown in Figure 8.1 for easy referencing. These systems were chosen in order to probe the effect that different structural moieties have on the properties of the ILs. Throughout this work and in this chapter, the colours red and blue are used to highlight structural differences (added structural complexity) relative to the structure of 1:2 BTMAAOC, the IL with the simplest structure (depicted entirely in black in Figure 8.1). Red indicates changes in the cation structure, while blue is used to indicate changes in the anion structure. The structure of the cation was varied by either including or excluding a terminal hydroxyl group. This hydroxyl group can engage in hydrogen bonding with the headgroups of the acid/anion species and its presence was expected to lead to systems with increased ordering (with the opposite being true when it is absent). The structure of the carboxylic acid / anion was varied in two ways, by changing the number of branching methyl groups and/or the number of C-C double bonds present in the alkyl chain. The inclusion of either or both of these features was expected to increase the fluidity of the ILs (specifically of the nonpolar regions), resulting in systems with a lower degree of ordering.

In each chapter, the thermal behaviour of the ILs was investigated using differential scanning calorimetry (DSC) and dynamic mechanical analysis (DMA). The viscosity of each IL (except

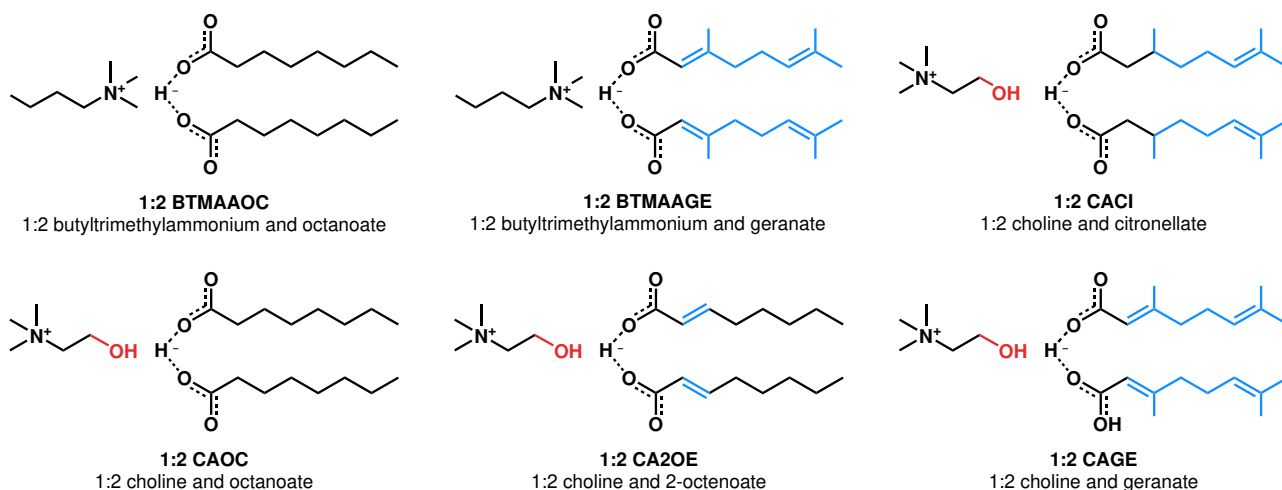


Figure 8.1. Structures of the 1:2 ILs discussed in this work

for 1:2 CA2OE) was also measured across a range of temperatures. Polarised-light microscopy (PLM) and small- and wide-angle X-ray scattering (SAXS and WAXS) measurements were also used to understand the structuring of each system and how this changes with increasing temperature.

Figure 8.2 describes the main characteristics of the liquid crystalline (LC) mesophases exhibited by these systems: the type of LC phase and the d -spacing (the size of the repeating unit) extracted from small-angle X-ray scattering data. The water content of the 'dry' ILs is also reported where relevant; this was measured using Karl-Fischer titration after drying the sample under high vacuum for at least 24 h at room temperature. The three structural features (hydroxyl group, double bonds, branching groups) have been designated as structural feature (SF) I, II and III respectively, to make it easier to indicate which ILs contain which structural features in Figure 8.2.

Using X-ray scattering, all of the 1:2 ILs (except for 1:2 CACI) have been shown to exhibit a liquid crystalline (LC) phase with a lamellar bilayer structure, which collapses to an isotropic liquid phase upon heating. Table 8.1 (the same as Table 7.4 in Chapter 7) shows the temperatures of the LC-to-isotropic transition for all 1:2 ILs in this work, derived from five different techniques. These temperatures differ not only between ILs (as a result of changes in cation and anion structure), but also between techniques (for the same IL). Care was taken to ensure the samples are as dry as possible for all measurements and, where possible, the same heating rates were used across measurements. Discrepancies are, however, unavoidable, most likely due to the different samples containing different amounts of moisture.

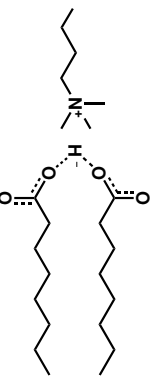
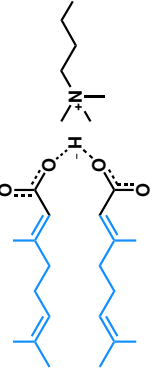
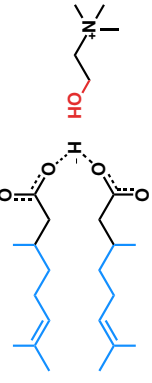
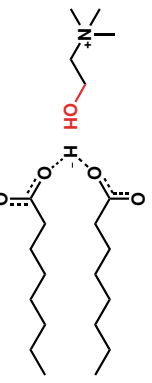
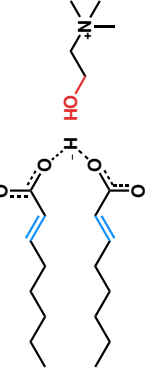
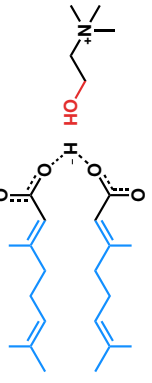
 1:2 BTMAAOC - Contains none of the SF I / II / III (simplest IL structure) - Hygroscopic, 8 mol% water - Two LC structures (two sets of peaks) - Predominant LC structure: fluid lamellar L_α, $d = 20.3 \text{ \AA}$ - Other LC structure: lamellar bilayers, $d = 24.2 \text{ \AA}$	 1:2 BTMAAGE - Contains two of the SF I / II / III - Hygroscopic, 13 mol% water - Two LC structures - Predominant LC structure: L_α bilayers, $d = 19.6 \text{ \AA}$ - Other LC structure: possibly lamellar, $d = 61.6 \text{ \AA}$	 1:2 CACI - Contains three of SF I / II / III - Low water content, 2 mol% - Isotropic liquid at all investigated temperatures, with segregated polar / nonpolar nandomains
 1:2 CAOC - Contains one of SF I / II / III - Low water content, 2 mol% - Only one LC structure, L_α bilayers, $d = 22.4 \text{ \AA}$	 1:2 CA2OE - Contains two of the SF I / II / III - Hygroscopic, 8 mol% water - Multiple LC mesophases present - Predominant LC structure: disordered L_β bilayers, $d = 20.9 \text{ \AA}$ - Other mesophases: unknown geometry, larger d-spacings (58–66 $\text{\AA}$)	 1:2 CAGE - Contains three of the SF I / II / III - Hygroscopic, 8 mol% water - Only one LC structure — L_α bilayers, $d = 22.4 \text{ \AA}$ - Water thought to be accommodated by polar region of bilayer

Figure 8.2. The 1:2 ILs discussed in this work, the structural features (SFs) they contain and an overview of their liquid crystalline mesophases

Table 8.1. Temperatures of the liquid crystal to isotropic liquid transitions for all 1:2 ILs in this work. Above these transition temperatures, the ILs are in the isotropic liquid phase, which is comprised of distinct polar and nonpolar nanodomains.

Ionic Liquid	Temperature / °C				
	DSC ^a	PLM ^b	DMA ^c	Viscosity ^d	SAXS ^e
1:2 CAGE	−10	n/a	2	n/a	5–15
1:2 CACI	−10	n/a	−2	n/a	< 5
1:2 CA2OE	12	25	n/a [*]	n/a	5–15
1:2 BTMAAGE	24	27	15	< 25	25–35
1:2 CAOC	52	60	57	50–55	50–55
1:2 BTMAAOC	17	25	37 ^{**}	35–40	35

^a On heating ^b Temp. of birefringence loss ^c Tan δ peak on cooling at $f = 1$ Hz

^d Temp. above which IL shows Newtonian flow behaviour

^e Temp. at which sharp LC peak disappears

^{*} Not observed ^{**} Tan δ peak on heating

1:2 CACI is the only IL that did not show a LC phase at the studied temperatures. However, based on DSC data, on the appearance of the IL at low temperatures, and on comparisons with 1:2 CAGE (which has a very similar structure), it is possible that 1:2 CACI may exhibit a liquid crystalline mesophase at temperatures below −15—−20 °C. SAXS and WAXS measurements performed between 5–55 °C indicated that 1:2 CACI has an isotropic liquid structure over this temperature range. X-ray scattering measurements could not be performed at lower temperatures and so the nature of 1:2 CACI at low temperatures could not be confirmed or investigated in more detail. The nature of the constituent species in the ILs was found to affect both the breadth of the temperature window over which the LC mesophase is stable and the temperature of the LC-isotropic transition (Table 8.1). The simplest ILs in terms of structure are 1:2 BTMAAOC and 1:2 CAOC, which contain the [(octanoate)₂H][−] anion. The linear, saturated anion means that the alkyl tails can pack efficiently, with strong Van der Waals interactions between neighbouring alkyl chains, giving rise to ILs with stable lamellar L_α bilayers. Comparing these two systems, the only structural difference is the nature of the cation, namely the presence of a hydroxyl group in the cholinium cation of 1:2 CAOC and the absence thereof

in the BTMA cation of 1:2 BTMAAOC.

The LC phase of 1:2 CAOC is more stable than that of 1:2 BTMAAOC, with a larger LC window and a higher LC-isotropic transition temperature. This is attributed to the ability of the hydroxyl group to form hydrogen bonds with the anion headgroups, with adjacent hydroxyl groups and with any residual water present in the system. These increased intermolecular interactions lead to a more thermally stable bilayer. Additionally, 1:2 CAOC reached a lower level of moisture when dried under high vacuum, while 1:2 BTMAAOC appears to be strongly hygroscopic and harder to remove moisture from. As the cation of 1:2 BTMAAOC does not contain a hydroxyl group, it is thought that the $[(\text{octanoate})_2\text{H}]^-$ anions form hydrogen bonds with the water instead. It is possible that the hygroscopic nature of the ILs, particularly of those containing BTMA cations, stems, at least in part, from a need for hydrogen-bonding interactions that help form and/or stabilise the liquid crystal bilayers.

One main difference between these ILs is that liquid crystalline 1:2 CAOC showed a single lamellar bilayer structure (d -spacing of) while the scattering profile of 1:2 BTMAAOC showed two sets of peaks, thought to be associated with two different lamellar LC structures. The main structure found in 1:2 BTMAAOC (most intense set of scattering) peaks is a fluid lamellar L_α phase with a d -spacing of approximately 20.3 Å. The other, lower-intensity, set of scattering peaks is associated with a secondary lamellar LC structure, with a slightly larger d -spacing of 24.2 Å. This phase is thought to comprise only a small amount of the IL and it is not believed to have a strong influence on its properties. The reason for the existence of this phase is unknown and requires further investigation.

Increasing the structural complexity of the anion species has generally resulted in systems with less stable LC phases. 1:2 CAGE and 1:2 CACI are the most structurally complex ILs, with their anions containing both double bonds and branching methyl groups. Despite the fact that both 1:2 CAGE and 1:2 CACI contain cholinium cations, which form hydrogen bonds with the anion headgroups, the LC phases of these ILs are only stable up to very low temperatures. The DSC profiles of 1:2 CAGE and 1:2 CACI are nearly identical, each showing a peak at -10°C upon heating that is thought to correspond to the LC-isotropic transition. For 1:2 CAGE, SAXS data recorded at 5°C shows that the IL has a lamellar LC structure; this disappears at 10°C , giving way to an isotropic liquid structure. A single set of peaks was observed, with a d -spacing that is very close to double the size of the $[(\text{geranate})_2\text{H}]^-$ anion; this suggests that,

much like 1:2 CAOC, 1:2 CAGE can accommodate residual water within the bilayer. For 1:2 CACI, only an isotropic liquid structure was observed in the SAXS data. However, due to its similarity to 1:2 CAGE and the fact that their DSC profiles are nearly identical, it is thought that 1:2 CACI may also show a LC phase at low temperatures. The decreased stability of the LC mesophases in these ILs is attributed to poor packing of the anion chains, as a result of the steric hindrance caused by the double bonds and branching groups. This is analogous to the way lipid bilayers become more fluid (less ordered) when these structural features are introduced into the alkyl chains.^{52,53}

The two remaining ILs are 1:2 BTMAAGE and 1:2 CA2OE, which have structures with an intermediate degree of complexity. 1:2 BTMAAGE contains geranic acid / geranate anions and/or complex $[(\text{geranate})_2\text{H}]^-$ anions (double bonds and branching methyl groups) and a BTMA cation (no hydroxyl group). Initially, this IL was expected to have the least ordered structure, as the packing of the alkyl tails was thought to be more disrupted than in ILs like 1:2 CAOC and 1:2 BTMAAOC. Additionally, the lack of a hydroxyl group on the cation was expected to lead to weaker anion-cation interactions. Contrary to these expectations, 1:2 BTMAAGE exhibited liquid crystalline structuring, with its SAXS profiles showing two different sets of peaks, associated with two liquid crystalline mesophases. The predominant phase present in 1:2 BTMAAGE has a lamellar bilayer structure with a d -spacing of 19.6 Å. This is maintained up to 25 °C and collapses to an isotropic liquid structure at higher temperatures. A second LC phase, comprising only a small amount of the sample, was also observed; this too has a lamellar structure, but with a much larger d -spacing of approximately 61.6 Å (roughly three times the length of a single bilayer).

Both of the LC phases observed for 1:2 BTMAAGE are maintained to a higher temperature than the LC phase of 1:2 CAGE. While it was initially thought that the hydroxyl group of 1:2 CAGE would lead to an increase in the stability of the LC phase (compared to 1:2 BTMAAGE, where this hydroxyl group is missing), it appears that the more complex interactions and molecular arrangements (leading to the formation of multiple mesophases) present in 1:2 BTMAAGE may increase the thermal stability of the LC arrangements.

A similar behaviour is observed for 1:2 CA2OE, which contains 2-octenoic acid / 2-octenoate anions and/or $[(2\text{-octenoate})_2\text{H}]^-$ anions (linear, unsaturated — one double bond) and a cholinium cation (hydroxyl group). The SAXS profile of 1:2 CA2OE also shows the presence of two

lamellar LC phases. The predominant phase (associated with the highest-intensity scattering peaks) is a disordered L_β lamellar gel phase. The increased anion-cation hydrogen bonding and the lack of sterically demanding branching groups in 1:2 CA2OE were initially thought to lead to a more stable LC phase, but, unexpectedly, the main bilayer structure of 1:2 CA2OE collapses at a lower temperature than in the case of 1:2 BTMAAGE.

In addition to the peaks associated with this main LC phase, several low- q , low-intensity peaks can be observed in the scattering profile of 1:2 CA2OE. These are thought to arise from one or more LC phases present in 1:2 CA2OE; no currently known LC structure could be found that would match the relative positions of these peaks. This is thought to be because the peaks are not necessarily associated with the same LC phase, but rather are the result of a coexistence of multiple LC phases with different preferred repeat spacings (as indicated by a slight asymmetry in the WAXS peak). As was the case for 1:2 BTMAAGE, these phases are thought to constitute only a small amount of the IL. The reason for their existence is unknown at the moment and requires further study.

Both 1:2 BTMAAGE and 1:2 CA2OE appear to have more complex LC structures than the other ILs discussed in this work and should be studied in more detail in the future. In to a principal lamellar bilayer phase, both of these ILs show the presence of other LC structures, which appear to be more thermally stable (i.e. maintained to higher temperatures) than the LC phases exhibited by all other ILs, except 1:2 CAOC. Based on the relative intensity of the scattering peaks, these phases are thought to comprise only a small proportion of the ILs but should nonetheless be studied in more detail.

8.1 Future work

This work has investigated the structure-property relationships in CAGE-like ILs, showing that the nature of the constituent species in an IL has a strong effect on the molecular arrangement and structuring present in the system. This, in turn, affects the physicochemical properties of the IL, such as its thermal behaviour and viscosity. X-ray scattering measurements have shown that the ILs in this work form ordered liquid crystalline phases, which seem to be strongly affected by the amount of moisture present in the system. Future work is needed in order to understand the intermolecular interactions (anion-cation, anion-water and cation-water) that

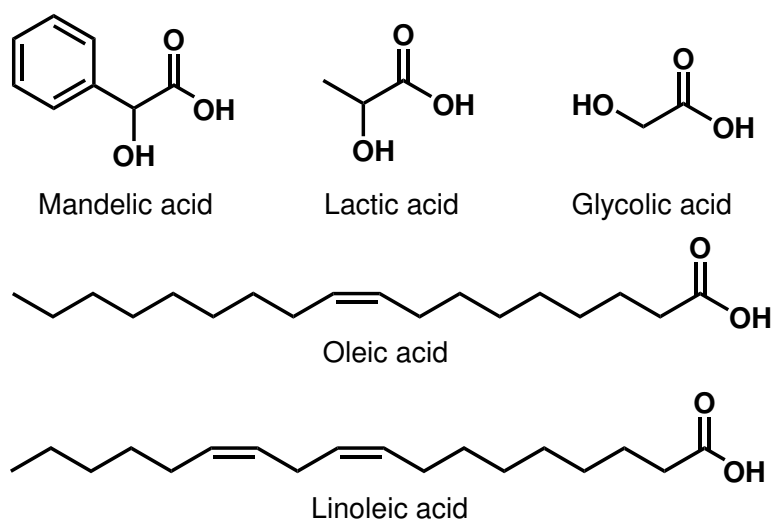


Figure 8.3. Carboxylic acid species that could be used in future for the synthesis of 1:2 CAGE-like ILs

occur in these systems and that lead to the formation of these liquid crystalline structures. An overview of possible future experiments and techniques that would lead to an improved understanding of 1:2 CAGE and of similar systems is presented in this section.

Synthesising and analysing new systems

- **Studying systems with different constituent species** to expand the scope of the structure-property relationships. Some examples are given in Figure 8.3. Alpha-hydroxy acids (mandelic, lactic, glycolic) are commonly used in skincare as chemical peeling agents, and may therefore aid in the process of skin permeation. However, their irritation potential may be higher than that of other acids. Additionally, mandelic acid also contains a phenyl group, so it would provide an understanding of how aromatic CAGE-like systems would behave. Fatty acids (oleic and linoleic) are structurally similar to the lipids that make up the skin stratum corneum, so they may have improved interactions with the skin barrier.
- **Investigating systems with varying ratios** of cation salt to carboxylic acid. The 1:1 systems corresponding to the 1:2 ILs in this work were also synthesised, with their DSC profiles shown in Appendix B. Most of these systems are solid up to relatively high temperatures, but do not form well-defined crystals. X-ray scattering and/or powder diffraction would be useful in determining their molecular arrangements; comparison with the molecular arrangements of 1:2 ILs could provide insight into the role played by the additional equivalent of carboxylic acid

present in the 1:2 systems.

Molecular Dynamics (MD) simulations

- **Theoretical analysis of scattering patterns.** MD simulations can be used to compute theoretical scattering patterns for a system. This allows for a much broader investigation than experimental work, as it required no synthesis. For systems that have been synthesised and for which experimental scattering patterns can be obtained, MD simulations can be used in tandem with experimental data to understand the origin of the observed peaks and the nature of the interactions present in the system.^{128,151}
- **Investigating IL-water interactions.** MD can be used to simulate IL-water mixtures with various compositions and gain an understanding of the interactions that occur in these systems. The effects of ethanol or of other hydrogen-bonding species on the IL structure can also be investigated. Additionally, the intermolecular interactions and molecular packing of IL mixtures can be investigated using simulations without requiring extensive experimental work.
- **Studying the dynamics of viscous flow.** In this work, DMA data showed that all 1:2 ILs, with the exception of 1:2 CA2OE, undergo a thermally activated relaxation. Based on the calculated parameters, this is thought to proceed via an intermolecular diffusive process. MD simulations could be used to identify the possible minimum energy configurations involved in the thermally activated relaxation process.¹⁰⁸

Pharmaceutically relevant experiments

- **Investigating the thermal stability of the 1:2 ILs.** The thermal stability of 1:2 CAGE is a potential issue when it comes to the use of this IL in pharmaceutical formulations that require long-term storage. Exposure to heat — even temperatures as low as 15–20 °C — causes 1:2 CAGE to change from colourless to yellow, initially, then further to an orange-brown colour. For 1:2 CAGE to be of commercial use, it is imperative that both the reason for this change and the effect of the decomposition products on the IL properties are thoroughly understood. Techniques such as NMR, infrared spectroscopy, mass spectrometry and gas chromatography could help identify the decomposition products. Additionally, investigating the thermal stability of some CAGE-like systems could help identify an alternative system that has the same

pharmaceutically relevant properties (e.g. transdermal delivery) as 1:2 CAGE, alongside an improved thermal stability. From the ILs in this work, a promising candidate is 1:2 CACl. This IL is the most similar to 1:2 CAGE in terms of structure and properties, but has the advantage of remaining colourless when heated.

- **Measuring the transdermal delivery potential.** Similar to the 2019 study of Tanner *et al.*,³⁵ Franz diffusion cell experiments could be used to understand the potential of these 1:2 systems in delivering a model solute across a barrier (usually porcine skin).
- **Assessing protein stability in IL solutions.** The use of ILs for the dissolution and stabilisation of proteins is a main topic of interest in the field.¹⁵² In particular, 1:2 CAGE has been shown to improve the stability and delivery of insulin.^{11,27} The stability of insulin and of other proteins in the 1:2 ILs presented in this work can be investigated using a number of techniques, such as fluorescence spectroscopy, circular dichroism, dynamic light scattering, etc. Most of these techniques cannot be performed in neat IL solutions, so aqueous IL-buffer mixtures are most likely necessary. MD simulations can complement experimental studies by investigating the IL-protein interactions that would occur in a neat IL-protein solution. MD simulations can also be used to understand the interaction of an IL with smaller solutes (model drugs) which could provide a basis for their use as solvents or excipients in the field of drug delivery.

Chapter 9

Synthesis and Methods

The synthesis of ILs and DESs differs from traditional organic synthesis in a few specific ways, which will be briefly discussed here. For a comprehensive guide to ionic liquid synthesis and purification, several excellent resources are available in the literature.^{18,153–155} In classical organic synthesis, the desired product is usually purified at the end of the process. As a result, conditions such as elevated temperatures and lower-purity starting materials can be used in order to optimise the duration or cost of the reaction, with the resulting contaminants being removed relatively easily. Commonly, purification methods rely on differences between the desired product and the impurities, such as differences in physical state (filtration), polarity (chromatography), volatility (distillation), and solubility (liquid-liquid extraction and crystallisation).¹⁵⁶

In the case of ionic liquids and deep eutectic solvents, many of these techniques are difficult or impossible to perform. The contaminants present in an IL or DES are usually excess starting materials, residual solvents, or decomposition products. In the vast majority of cases, these kinds of impurities are soluble in / miscible with the IL or DES, and so cannot be removed by filtration. In some cases, however, a suitable solvent can be found that causes the impurity to precipitate; this can then be removed by filtration.¹⁵⁴ Isolating ILs/DESs through distillation is also not possible in most cases, due to the low vapour pressure exhibited by these systems. While the distillation of some ILs has been reported in the literature, this required elevated temperatures and ultra-high vacuum conditions, making this technique unsuitable for use as a routine purification method.^{157,158} Chromatography, commonly used for the purification of organic compounds, can be useful on a small scale; however, ILs and DESs are often synthesised

in large amounts, in order to be used as solvents. In these cases, chromatography would require the use of large quantities of the stationary and mobile phases, leading to increased costs and waste.

The two most common purification methods for ILs and DESs are crystallisation and liquid-liquid extraction. Crystallisation is useful in the purification of some IL systems (such as imidazolium halides), but is generally not applicable, as ILs are designed to have low melting points. Similarly, DESs are characterised by a significant decrease in the melting points of their components, and so are not well-suited to crystallisation. Liquid-liquid extraction can be used when the contaminants are soluble in a solvent that does not dissolve the IL. Aqueous washes can remove hydrophilic contaminants, such as excess metal halides, from hydrophobic ILs,^{159,160} while organic solvents can be used to remove hydrophobic impurities (as long as the solvent and IL are immiscible).^{154,161,162} In the case of DESs, liquid-liquid extraction is not as useful as it is for ILs. ILs are ionic compounds (salts), with a well-defined stoichiometry that is maintained by electrostatic interactions; washing an IL with a solvent will not affect the cation:anion ratio. DESs, on the other hand, are not compounds but mixtures. Washing with a solvent will inevitably lead to the partial removal of one or more of the DES components along with the impurities. This will alter the composition of the DES and affect its behaviour and properties, leading to a system that is not reproducible and to inconsistent, unreliable results. Because purification of the final system is extremely difficult, the most common approach to synthesising high-purity ILs and DESs is to purify the starting materials and then proceed with the synthesis in a manner that minimises additional contaminants (e.g. low temperatures).

The purpose of this work is to investigate the structure-property relationships in CAGE and CAGE-like systems. For the measured properties to be an accurate representation of reality, the purity of the synthesised systems had to be as high as possible. To achieve this, all starting materials were purchased with a purity > 98% where possible and purified before use as stated below. The synthesis and storage conditions were also controlled in order to minimise thermal decomposition, and contaminants such as coloured impurities and excess solvent were removed at the end of the process. A general overview of the starting material purification and the synthetic routes follows, with particular emphasis on the steps taken to improve the purity of the final systems.

9.1 Purification of Starting Materials

Cholinium bicarbonate

Cholinium bicarbonate was purchased as an approximately 80 wt% aqueous solution, with the specification sheet listing the concentration as 75–85 wt%. In the literature synthesis of 1:2 CAGE, the aqueous cholinium bicarbonate is used as received.⁹ For this work, it was necessary to know the exact concentration of the solution, to ensure that the ratio of the starting materials is accurate in the synthesis of cholinium-based ILs.

To calculate the exact concentration, the cholinium bicarbonate solution was titrated with a 3 M aqueous HCl solution to $\text{pH} \simeq 7$. The concentration of the cholinium bicarbonate solution was calculated to be 77.9 wt% (used as 78 wt% in all future stoichiometry calculations).

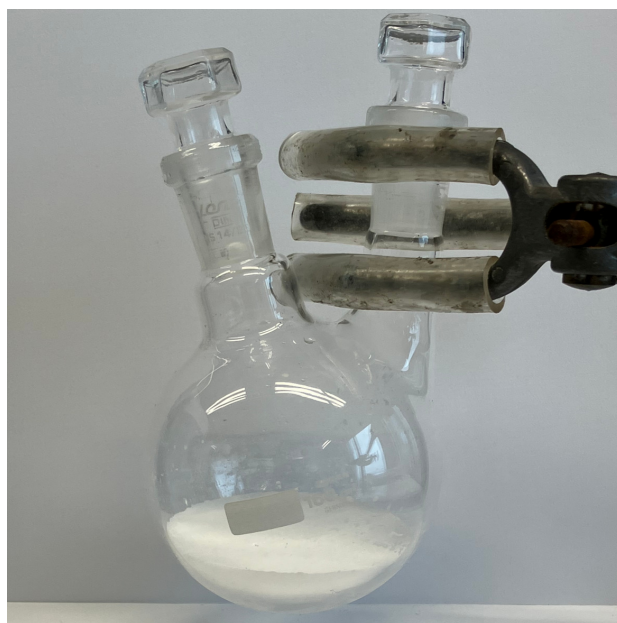
Geranic acid

Geranic acid is only sold by major suppliers as 'technical grade' geranic acid, which has a purity of 85 % by weight. The main impurity in this is nerolic acid, which is the *Z*-isomer of 3,7-dimethylocta-2,6-dienoic acid (geranic acid is the *E*-isomer). Additional impurities cause the viscous liquid to have a yellow colour (Figure 9.1a). Zakrewsky *et al.* purify this acid from an acetone solution containing 70 wt% geranic acid and 30 wt% acetone.⁹ This is cooled to -78°C in order to crystallise the *E*-isomer of the acid. The supernatant is then decanted and the entire procedure is repeated 5–7 times.

Using this method in our lab, it was found that separating the pure acid was difficult, as it often crystallised alongside the acetone solution if left to cool for too long. Additionally, even though the melting point of pure geranic acid is given in the literature as 21°C ,¹⁶³ the low temperature used by Zakrewsky *et al.* (-78°C , achieved using cardice)⁹ was indeed necessary in order to observe crystallisation. Our hypothesis is that this behaviour might be caused by the formation of hydrogen bonds between the ketone group of acetone (HBA) and the acidic proton of geranic acid (HBD). In practice, if the mixture was removed from the cardice bath too early (to prevent the entire mixture crystallising) some of the pure geranic acid would still be liquid and would be decanted alongside the acetone. If the mixture was allowed to completely solidify, it then had to be partially melted in order to decant the liquid acetone solution; this introduced



(a) Technical grade (85 wt%), as received.



(b) Purified through consecutive crystallisations from hexane.

Figure 9.1. Geranic acid at room temperature.

a high degree of human error and resulted in some of the acid melting and being lost. Both cases led to significant losses in the amount of pure geranic acid recovered after purification. The full procedure (5–7 crystallisations) also took several days and required the use of large amounts of solvent and cardice (relative to the amount of acid obtained at the end). If this procedure were to be used on an industrial scale, it would most likely require optimisation in order to improve the yield and reduce time, solvent and energy consumption.

To improve this procedure, a more optimal solvent — one that can dissolve the impurities and nerolic acid, but does not crystallise alongside the pure geranic acid — needed to be identified. *n*-Hexane was found to be the best for this application; the acid crystallised out of solution at a higher temperature ($-20\text{ }^{\circ}\text{C}$, achieved using a freezer), while the solvent remained liquid and retained the impurities in solution. In our lab, the acid was crystallised four times from a solution containing 40 wt% hexane (50 % by volume). Pure geranic acid was obtained as a white crystalline solid (Figure 9.1b), with a melting point of $22\text{ }^{\circ}\text{C}$ as measured by DSC. Single-crystal X-ray crystallography was used to confirm that the E-isomer was obtained (Figure 9.2). Additionally, the hexane used in the crystallisation process was recovered (using a rotary evaporator) and reused in subsequent crystallisations.

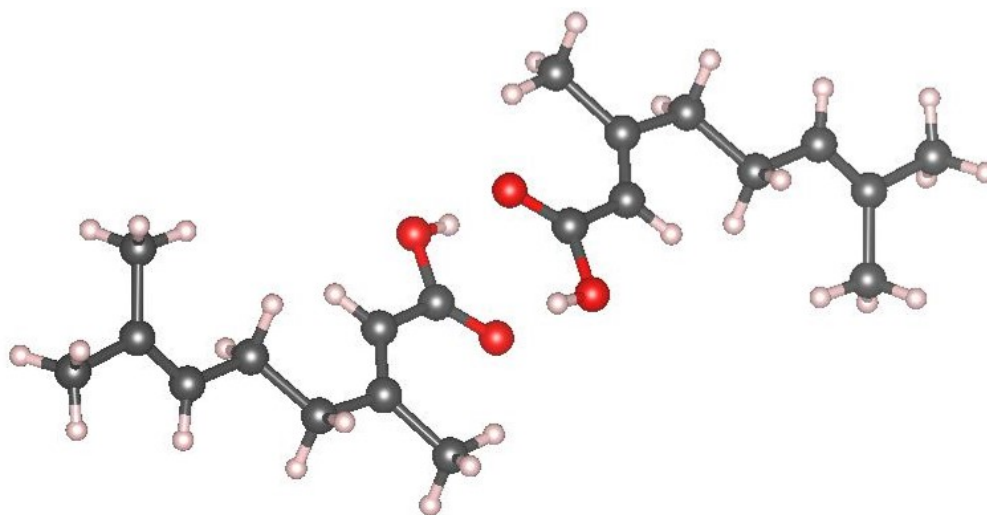
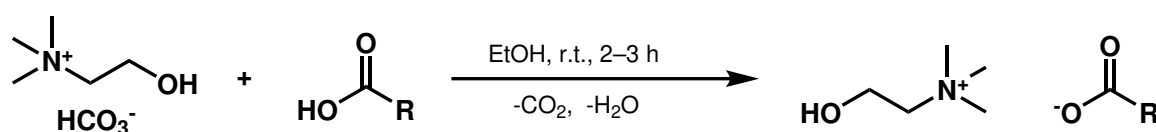


Figure 9.2. Crystal structure of geranic acid, recrystallised from hexane, obtained by single-crystal X-ray crystallography. Two molecules are shown. Because a different purification method was used compared to the literature (recrystallisation from hexane, rather than acetone) the crystal structure was recorded in order to confirm that this afforded the E-isomer of 3,7-dimethylocta-2,6-dienoic acid (i.e. geranic acid).

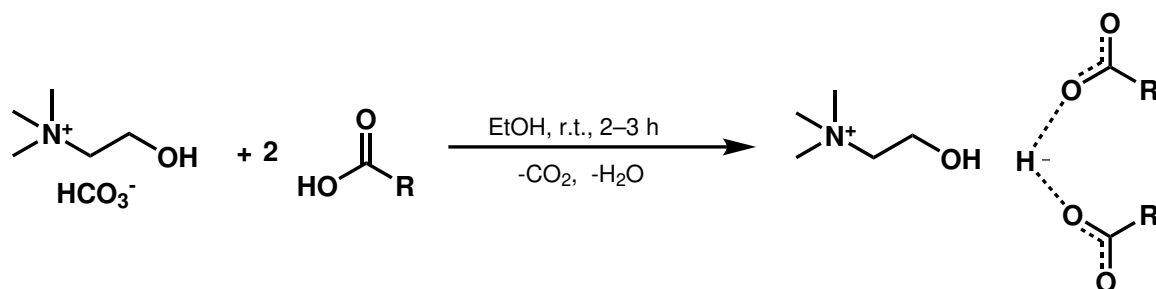
Other carboxylic acids

Citronellic acid (94%) and 2-octenoic acid (98%, TCI) were purified before use by vacuum distillation. Octanoic acid (99%) was used as received, without further purification.

9.2 Synthesis of cholinium-based ILs



Scheme 9.1. Synthesis of 1:1 ILs containing a cholinium cation



Scheme 9.2. Synthesis of 1:2 ILs containing a cholinium cation

The systems containing a cholinium cation were synthesised according to a modified literature

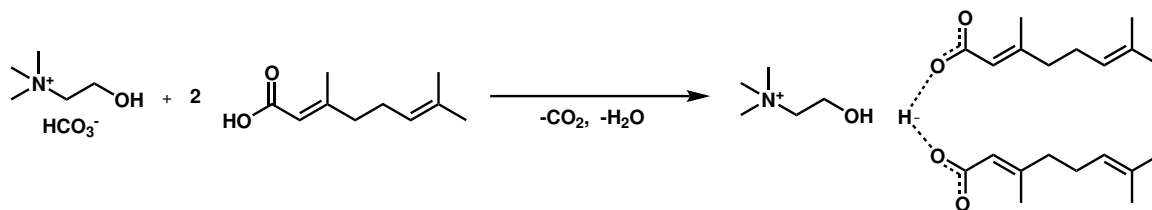
procedure⁹ by the total (Scheme 9.1) or partial (Scheme 9.2) neutralisation of the appropriate carboxylic acid with cholinium bicarbonate. In this synthetic route, an ethanol solution of the carboxylic acid is added dropwise to the aqueous cholinium bicarbonate. While in the literature procedure no additional solvent is used, here ethanol is added in order to reduce the viscosity of the two starting materials and improve mixing. The reaction mixture is then stirred at room temperature for a few hours to ensure that the reaction is complete. During the reaction, the bicarbonate anion deprotonates the acid, leading to the formation of carbonic acid and a carboxylate anion. The carbonic acid then rapidly decomposes to form carbon dioxide and water, which are removed from the reaction mixture under reduced pressure, along with the solvent. In the case of the 1:1 systems, the acid is fully neutralised, affording the cholinium carboxylate salt. For the 1:2 systems, the synthesis uses two equivalents of acid and only one equivalent of cholinium bicarbonate. In this case, half of the quantity of acid is converted into the carboxylate, while the other half remains protonated.

A 2020 paper by Mann *et al.* reported the synthesis of CAGE-Oct, a system related to CAGE, in which one equivalent of geranic acid was replaced with one equivalent of octanoic acid.¹³ They showed that there is no evidence of the acid existing as a free species in this system; instead, a statistical distribution of $[(\text{geranate})\text{H}(\text{octanoate})]^-$, $[(\text{geranate})_2\text{H}]^-$, and $[(\text{octanoate})_2\text{H}]^-$ anions was observed. These anions formed hydrogen-bonded clusters with the cholinium cation, in which protons were shared and rapidly exchanged. The CAGE-Oct system analysed by Mann *et al.* is synthesised using two equivalents of acid, and so is analogous to 1:2 CAGE, where not all of the acid is deprotonated. Based on the findings of Mann *et al.* and on our own data, which will be discussed in later chapters, it is assumed that an extended $[\text{carboxylate}_2\text{H}]^-$ anion (Scheme 9.2) is formed in all of the 1:2 ILs discussed in this work. It should be noted, however, that the systems are more dynamic than the images shown here would suggest, with the hydrogen-bonding networks breaking apart and re-forming constantly, and with the protons being shared and exchanged between the different species present in each system.

Synthesis of CAGE ILs

The two choline-and-geranate systems in this work (1:1 CAGE and 1:2 CAGE) were synthesised using the method outlined above with some additional modifications, particularly in the last step of the procedure - removing the solvent and drying the final product. The synthesis of 1:2

CAGE is shown in Scheme 9.3.



Scheme 9.3. Synthesis of 1:2 CAGE from cholinium bicarbonate and geranic acid

The literature procedure involves removing excess solvent on a rotary evaporator, followed by drying for 48 h in a vacuum oven; both steps are run at a temperature of 60 °C.⁹ In our lab, it was observed that drying 1:2 CAGE at elevated temperatures results in a colour change, going from colourless to yellow to orange, depending on the temperature and the amount of time. Figure 9.3a shows a freshly prepared sample of 1:2 CAGE that was dried under vacuum at 40 °C for 36 h. We also observed that once this process starts, the colour of the sample continues to intensify and darken even when the heat source is removed. Figure 9.3b shows a sample of 1:2 CAGE that was heated to 40 °C for 24 h (giving it a yellow colour) and then allowed to sit at room temperature for 6 months. During this time, the colour of the sample changed from yellow to dark orange and finally to the dark brown / black seen here. Zakrewsky *et al.* do not report observing this colour change in their initial study,⁹ but a photograph of a yellow-coloured sample of 1:2 CAGE is included in a subsequent publication from the same authors.³⁰ Koppisch *et al.* also reported a behaviour consistent with our observations: 1:2 CAGE (dried at 50 °C for 12–16 h) showed a yellow colour, which darkened when the sample was stored at room temperature for months.³¹

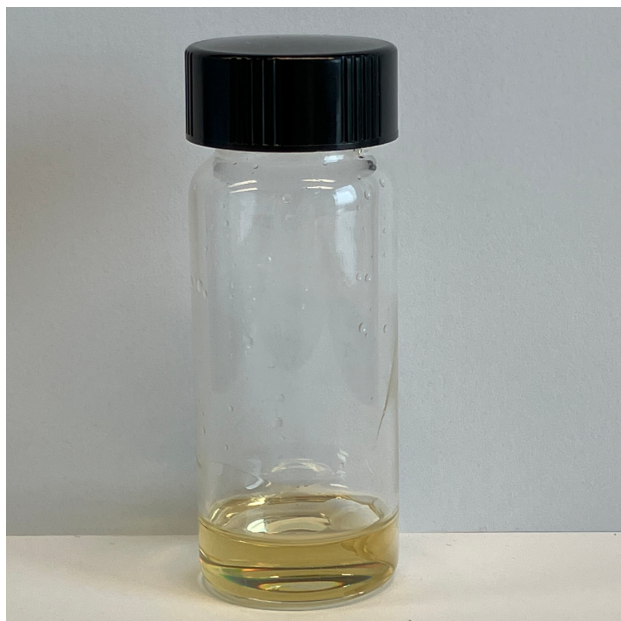
The presence of coloured impurities in ILs is a well-known phenomenon. These chromophores cause the ILs to have a yellow, orange, or red colour (when they should be colourless) and are often caused by the use of excessive heating when synthesising the ILs, although their exact nature is unknown.^{155,164} Such impurities occur even when the IL is otherwise apparently pure (e.g. by NMR or HPLC), and so are thought to exist in extremely small concentrations, which are undetectable using most analytical techniques.¹⁶⁴ Still, these concentrations are sufficient to cause an intense colouring of the ILs, which can interfere with optical spectroscopy measurements. The synthesis of 'spectroscopic grade' ILs has been explored in numerous publications, and often involves the thorough purification of starting materials, as well as decolorisation of the final IL.^{154,155,164} The impurities in 1:2 CAGE may be similar to those seen in other ILs and,

as has been shown, purifying the starting materials and reducing the reaction temperature does lead to a colourless product. However, the freshly-synthesised IL can still become coloured if it is heated, either during the drying step or during storage. This suggests that the coloured impurities are not by-products of the neutralisation reaction, but rather products of thermal decomposition.

The mechanisms responsible for the formation of these impurities are not yet known. The thermal stability of DESs containing choline chloride and various carboxylic acids has been studied by Binnemans *et al.*, who found that these decompose through an esterification reaction between the hydroxyl group of the cholinium cation and the carboxylic acid group.¹⁶⁵ This reaction is very slow at room temperature, but can be accelerated by heating. No details are given in this publication about the formation of coloured impurities in any of the studied systems. While this esterification is a possible decomposition pathway for 1:2 CAGE, it is unlikely to be the predominant reaction at room temperature, as there is no evidence of free acid being present in the system. At room temperature, 1:2 CAGE consists of a cholinium cation and an extended $[(\text{geranate})_2\text{H}]^-$ anion, with extensive hydrogen bonding and rapid proton exchange occurring between these species.¹³

We have observed that purified geranic acid remained colourless upon heating and upon long-term storage at room temperature. When other cholinium ILs were heated, 1:2 CACl and 1:2 CAOC remained colourless, while 1:2 CA2OE took on a yellow colour. One structural aspect that may play a role here is the saturation of the C2–C3 bond of the acid / anion. This bond is saturated in 1:2 CACl and 1:2 CAOC, but unsaturated in 1:2 CA2OE and 1:2 CAGE. This results in the presence of a conjugated system (an α – β unsaturated carboxylic acid) which increases the reactivity of the β -carbon. Still, it is unknown what role, if any, this feature plays in the formation of coloured impurities; more work is necessary in order to understand this phenomenon.

In order to prevent the colour change, future samples of 1:2 CAGE were dried at room temperature for 24 h and stored in a freezer ($-20\text{ }^\circ\text{C}$). Additionally, to reduce the temperature of the mixture during the neutralisation reaction, the addition of the acid was done at $0\text{ }^\circ\text{C}$, over an ice bath, and the mixture was then allowed to warm to room temperature while stirring. 1:2 CAGE prepared using this method is colourless (Figure 9.4a) and remains colourless for an extended period of time (> 6 months) if stored at $-20\text{ }^\circ\text{C}$ (Figure 9.4b). Despite the lack



(a) 1:2 CAGE dried at 40 °C for 36 h.



(b) 1:2 CAGE dried at 40 °C for 24 h, then stored at room temperature for 6 months.

Figure 9.3. 1:2 CAGE dried under vacuum at 40 °C.



(a) Freshly prepared 1:2 CAGE, dried at room temperature.



(b) 1:2 CAGE, dried at room temperature, after being stored at −20 °C for 6 months.

Figure 9.4. 1:2 CAGE prepared without heating.

of additional heating, this method was effective in drying the sample. The water content of freshly dried 1:2 CAGE, measured using a volumetric Karl-Fischer titrator, was 0.3–0.5 wt%. Zakrewsky *et al.* did not report the water content of their sample, so a direct comparison is not possible. However, Jorge *et al.* report following the same synthetic procedure and achieving a water content of 2.2 wt%¹⁶⁶ — significantly higher than the one measured in our lab. It should be pointed out here that 1:2 CAGE is hygroscopic and will absorb moisture when handled under atmospheric conditions.³¹ A sample of freshly dried 1:2 CAGE was left open to air in our lab showed a water content of approximately 11 wt% after one month.

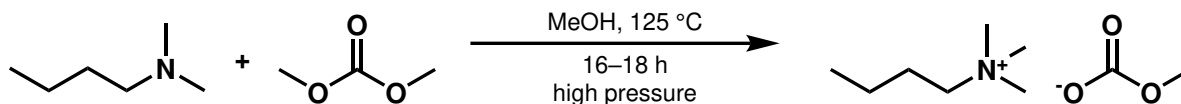
1:1 CAGE was synthesised under the same conditions. A similar colour change (from white to yellow/orange) was observed on heating and, more slowly, when stored at room temperature for extended periods of time. All other cholinium-based systems were synthesised and dried at room temperature, and no obvious colour change was observed. All systems synthesised in this work were stored in a $-20\text{ }^{\circ}\text{C}$ freezer in order to prevent any potential thermal decomposition and were handled under dry conditions when possible. Details of the synthetic procedures and full characterisations of the systems are given in Section 9.4.

9.3 Synthesis of butyltrimethylammonium-based systems

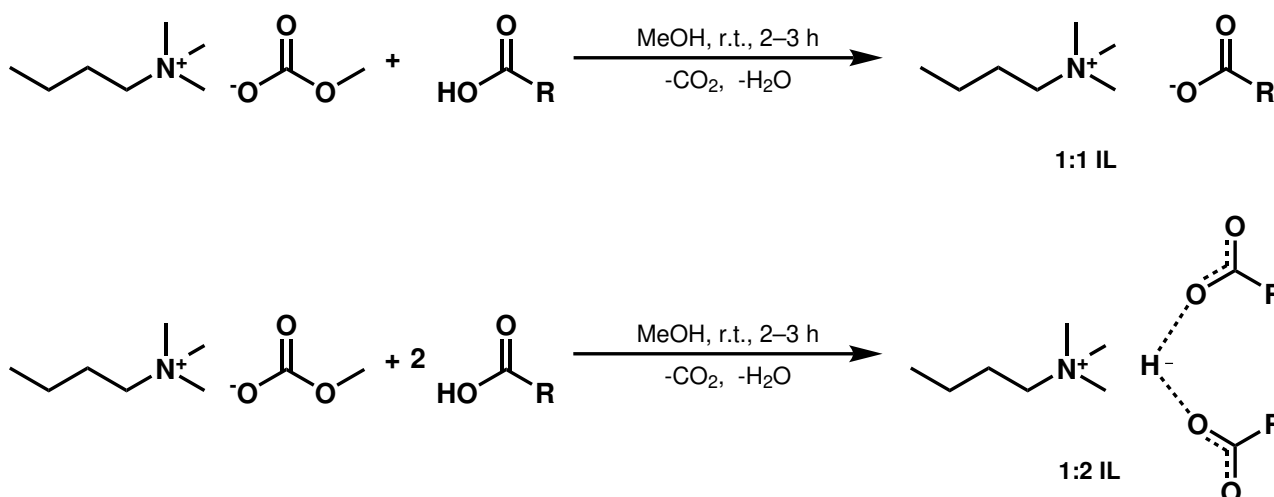
Systems containing a butyltrimethylammonium (BTMA) cation are synthesised using a two-step process, in which a cation precursor is synthesised, then reacted with the appropriate carboxylic acid to afford the final 1:1 or 1:2 IL (Scheme 9.4). In the first step, butyltrimethylamine, excess dimethylcarbonate, and methanol are loaded into a pressure tube, sealed, and stirred at $125\text{ }^{\circ}\text{C}$. The excess of dimethylcarbonate and the high temperature are necessary for the methylation reaction to proceed to completion. Consequently, the pressure tube is required to prevent evaporation, as the reaction temperature is higher than the boiling point of the starting materials and solvent.

The mixture is allowed to react until complete consumption of the starting amine is observed by ^1H NMR (usually 16–18 h). The resulting BTMA methylcarbonate is not isolated and is instead immediately reacted with the carboxylic acid. In a similar reaction to the one described for cholinium-based systems, the methylcarbonate anion deprotonates (some or all of) the acid, affording the desired system. The side-product (carbonic acid monomethyl ester)

Step 1: High-pressure synthesis of the BTMA cation



Step 2: Synthesis of the 1:1 IL (top) or 1:2 IL (bottom) via acid-base neutralisation



Scheme 9.4. Synthesis of systems containing a butyltrimethylammonium (BTMA) cation

rapidly decomposes to methanol and carbon dioxide, which are easily removed under reduced pressure alongside excess dimethylcarbonate and residual solvent.

This high-pressure route is useful because the synthesis can be performed on a large scale, with good yields and without needing to isolate the intermediate cation precursor. However, the high temperature used in the first step causes the cation precursor, and therefore the final product, to have a yellow colour. For the 1:1 salt, coloured contaminants are removed by dissolving the salt in methanol, stirring this solution with activated charcoal, filtering, then passing it through a reverse-phase silica column and a 0.2 μm filter.^{154,155} The same purification procedure cannot be used for the 1:2 IL. If any free acid is present in the system this can be retained by the charcoal and/or silica, resulting in a final product that no longer contains equimolar amounts of cation, anion, and acid. To avoid this, the 1:2 IL is synthesised from the purified 1:1 salt, which is thoroughly dried on a Schlenk line, weighed, and mixed with an equimolar amount of the carboxylic acid, in methanol. The 1:2 IL can then be isolated by removing the excess solvent under reduced pressure, followed by drying on a Schlenk line. Both the 1:1 and 1:2 ILs obtained in this way are NMR-pure, despite a fainter yellow colouring persisting in some

samples.

9.4 General experimental procedures

9.4.1 General considerations

All reagents were purchased from Merck or VWR, unless otherwise stated. Starting materials were used as received unless a purification procedure is given below. Solvents were of HPLC-grade purity, used without further purification. Purified Type 2 water was obtained from a Sartorius Arium® Advance EDI system. Activated charcoal Norit SX ultra (SIGMA-ALDRICH) was used for decolourisation purposes.

The synthesised ILs were dried on a Schlenk line with an end vacuum of approximately $8\text{--}10 \times 10^{-3}$ mbar. Glindemann PTFE sealing rings (SIGMA-ALDRICH) were used with ground glass joints to avoid the use of vacuum grease. Water content after drying was determined via volumetric Karl Fischer titration using a V20 Volumetric Karl Fischer Titrator (Mettler-Toledo).

Elemental analysis was performed on a ThermoFlash 2000 CHN analyser (Thermo Fisher) through the London Metropolitan University service. Mass spectra were recorded using electrospray ionisation on an LCT Premier mass spectrometer (Waters). Fourier-transform infrared spectroscopy (FTIR) measurements were run on a Spectrum 100 FTIR (Perkin-Elmer) equipped with an ATR accessory. Samples were loaded and measured in air and at ambient temperatures.

The measured CHN values were considered to be within acceptable limits if they were within 0.4% of the theoretical values. In the case of larger deviations, these are explicitly mentioned and explained if possible. If the measured values can be attributed to an IL system containing a single type of impurity (e.g. water, solvent, or an excess of either carboxylic acid or ammonium salt), then the formula of this system is given. Otherwise, it is likely that the system contains more than one type of impurity (including impurities of an unknown nature, such as ones present in the starting materials) and the exact composition cannot be determined.

NMR spectra were recorded on 400 MHz Bruker spectrometers. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet,

sxt = sextet, m = multiplet), coupling constant in Hz, integration, assignment. ^{13}C NMR spectra were recorded with complete proton decoupling. In the assignment, protons and methyl groups attached to the n^{th} carbon are represented as $\text{C}(n)\text{H}_x$ and $\text{C}(n)\text{Me}_x$, where x is the number of protons or methyl groups, respectively.

Over the course of this work, each synthesis has been performed multiple times according to the general procedures detailed below. Representative syntheses are then given for each system. It should be noted that in our lab, ‘room temperature’ is consistently lower than the standard ambient temperature of 25 °C and usually varies between 15–20 °C.

9.4.2 General procedure A: synthesis of cholinium ILs

To one equivalent of cholinium bicarbonate (80 wt% in water) was added dropwise a solution of carboxylic acid in ethanol. One or two equivalents of the acid were used for the synthesis of 1:1 and 1:2 systems, respectively. The reaction mixture was stirred at room temperature for 2–3 h. CO_2 evolution was observed upon addition and for the first 15–30 min of stirring. The solvent was removed under reduced pressure and the resulting viscous oil was dried in vacuo for 24 h at room temperature to afford the desired 1:1 or 1:2 cholinium IL.

9.4.3 General procedure B: synthesis of 1:1 BTMA ILs

One equivalent of N,N-dimethylbutylamine was placed in a pressure tube (CambridgeGlass) and to it was added one equivalent of dimethylcarbonate in methanol. The pressure tube was sealed and the reaction mixture was stirred at 125 °C for 16 h until ^1H NMR showed complete consumption of the starting amine. The mixture was allowed to cool to room temperature and one equivalent of the carboxylic acid was added dropwise. The mixture was stirred for 3–4 h at room temperature. Activated charcoal was then added and the mixture was stirred at room temperature for 3 days. The charcoal was removed by gravity filtration, followed by filtration through a 0.2 μm PTFE membrane and then by passing through a C18 column. The solvent was removed under reduced pressure and the resulting viscous oil was dried in vacuo for 24 h at room temperature to afford the desired 1:1 IL.

9.4.4 General Procedure C: synthesis of 1:2 BTMA ILs

One equivalent of the 1:1 DES (synthesised according to general procedure B) was dissolved in methanol. To this was added dropwise a solution of one equivalent of carboxylic acid in methanol. The mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure and the resulting viscous oil was dried in vacuo for 24 h at room temperature to afford the desired 1:2 IL.

9.4.5 Experimental Details

1:2 CAGE

Geranic acid (16.87 g, 100.3 mmol, 2 equiv.) in ethanol was added dropwise to an 78 wt% aqueous solution of choline bicarbonate (10.62 g, 50.15 mmol) cooled to 0 °C in an ice bath. The mixture was allowed to warm to room temperature and stirred for 2–3 h. The solvent was removed under reduced pressure and the resulting IL was dried in vacuo for 24 hour at room temperature. The desired IL was obtained as a colourless viscous oil (21.68 g, 49.3 mmol, 98% yield).

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 1.56 & 1.64 (s, 6 H, Ger-C(7)Me₂), 1.94–2.14 (m, 14 H, overlap of Ger-C(4,5)H₂ and Ger-C(3)Me), 3.12 (s, 9 H, Ch-NMe₃), 3.39–3.46 (m, 2 H, Ch-C(1)H₂), 3.81–3.90 (m, 2 H, Ch-C(2)H₂), 5.01–5.10 (m, 2H, Ger-C(6)H), 5.56 (s, 2H, Ger-C(2)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 17.5 & 17.7 (Ger-C(7)Me₂), 25.4 (Ger-C(3)Me), 25.8 (Ger-C(5)), 39.9 (Ger-C(4)), 53.1 (Ch-NMe₃), 55.1 (Ch-C(2)), 67.2 (Ch-C(1)), 121.6 (Ger-C(2)), 123.7 (Ger-C(6)), 131.1 (Ger-C(7)), 149.7 (Ger-C(3)), 169.8 (Ger-C(1));

FTIR (ATR, ν_{max} / cm^{-1}): 3034, 2963, 2911, 2857, 1691, 1640, 1550, 1437, 1390, 1375, 1310, 1227, 1149, 1087, 1001, 956, 867, 819, 691;

ESI⁺ m/z 104.11 (M⁺, 100%);

ESI[−] m/z 167.10 (M[−], 100%);

Elem. analysis (CHN): Found C, 68.13; H, 10.83; N, 3.20 %. Calc. for C₂₅H₄₅NO₅ C, 68.30; H, 10.32; N, 3.19 %.

1:2 CACI

1:2 CACI was synthesised according to general procedure A, from 78 wt% aqueous choline bicarbonate (14.57 g, 68.8 mmol) and citronellic acid (23.41 g, 137.5 mmol, 2 equiv.). The desired IL was obtained as a colourless viscous oil (29.47 g, 66.4 mmol, 97% yield).

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.83 (d, $J = 6$ Hz, 6 H, Cit-C(3)Me), 1.00–1.34 (m, 4 H, Cit-C(2)H₂), 1.55 & 1.63 (s, 6 H, Cit-C(7)Me₂), 1.72–1.99 (m, 8 H, Cit-C(4,5)H₂), 1.99–2.08 (m, 2 H, Cit-C(3)H), 3.11 (s, 9 H, Ch-NMe₃), 3.38–3.43 (m, 2 H, Ch-C(1)H₂), 3.80–3.88 (m, 2 H, Ch-C(2)H₂), 5.07 (m, 2 H, Cit-C(6)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 17.5 (Cit-C(7)Me), 19.8 (Cit-C(3)Me), 25.1 (Cit-C(4/5)), 25.5 (Cit-C(7)Me), 29.8 (Cit-C(4/5)), 35.8 (Cit-C(2)), 44.1 (Cit-C(3)), 53.1 (Ch-NMe₃), 55.0 (Ch-C(2)), 67.2 (Ch-C(1)), 124.8 (Cit-C(6)), 130.3 (Cit-C(7)), 175.0 (Cit-C(1));

FTIR (ATR, ν_{max} / cm^{-1}): 3029, 2962, 2913, 2851, 1698, 1567, 1451, 1377, 1286, 1199, 1084, 953, 865, 822, 720;

ESI⁺ m/z 104.11 (M^+ , 100%)

ESI[−] m/z 169.12 (M^- , 100%);

Elem. analysis (CHN): Found C, 68.07; H, 11.41; N, 2.96 %. Calc. for C₂₅H₄₉NO₅ C, 67.68; H, 11.13; N, 3.16 %.

1:2 CAOC

1:2 CAOC was synthesised according to general procedure A, from 78 wt% aqueous choline bicarbonate (22.02 g, 104.0 mmol) and octanoic acid (30.12 g, 208.8 mmol, 2 equiv.). The desired IL was obtained as a colourless viscous gel (37.95 g, 96.9 mmol, 93% yield).

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.84 (t, $J = 7.0$ Hz, 6 H, Oct-C(8)H₃), 1.14–1.29 (m, 16 H, Oct-C(4,5,6,7)H₂), 1.42 (p, $J = 7.2$ Hz, 4 H, Oct-C(3)H₂), 2.00 (t, $J = 7.4$ Hz, 4 H, Oct-C(2)H₂), 3.10 (s, 9 H, Ch-NMe₃), 3.37–3.43 (m, 2 H, Ch-C(1)H₂), 3.79–3.86 (m, 2 H,

Ch-C(2)H₂);

¹³C{¹H} NMR (100 MHz, DMSO-d₆, δ in ppm) 13.9 (Oct-C(8)), 22.1 (Oct-C(7)), 25.5 (Oct-C(6)), 28.6 (Oct-C(5)), 29.0 (Oct-C(4)), 31.3 (Oct-C(3)), 36.2 (Oct-C(2)), 53.1 (Ch-NMe₃), 55.0 (Ch-C(2)), 65.6 (Ch-C(1)), 174.4 (Oct-C(1));

FTIR (ATR, $\nu_{\max}$ / cm⁻¹): 3032, 2950, 2922, 2853, 1702, 1565, 1465, 1386, 1265, 1227, 1197, 1090, 1004, 952, 863, 726;

ESI⁺ m/z 104.11 (M⁺, 100%);

ESI⁻ m/z 143.11 (M⁻, 100%);

Elem. analysis (CHN): Found C, 63.66; H, 11.02; N, 3.77 %. Calc. for C₂₁H₄₅NO₅ C, 64.41; H, 11.58; N, 3.58 %. The measured values for C and H are outside of the range corresponding to analytical purity ($\pm 0.4\%$). Possible reasons for this include the presence of residual moisture or solvent in the final IL sample or a small deviation in the stoichiometry of the constituents (theoretically, the IL is thought to contain cholinium, octanoate and octanoic acid in a 1:1:1 ratio). However, no formula could be found that would correspond to the measured CHN values. It is possible that the impurities present in the IL are a combination of several factors, including excess moisture and/or solvent, excess cholinium bicarbonate or octanoic acid being used in the synthesis, and/or the presence of impurities in the starting materials (and therefore in the final product).

1:2 CA2OE

1:2 CA2OE was synthesised according to general procedure A, from 78 wt% aqueous choline bicarbonate (13.09 g, 61.8 mmol) and 2-octenoic acid (17.55 g, 123.4 mmol, 2.0 equiv.). The desired IL was obtained as a colourless viscous oil (23.64 g, 61.0 mmol, 99% yield).

¹H NMR (400 MHz, DMSO-d₆, δ in ppm) 0.86 (t, $J = 7.0$ Hz, 6 H, 2Oct-C(8)H₃), 1.18–1.42 (m, 12 H, 2Oct-C(5,6,7)H₂), 2.07 (q, $J = 7.3$ Hz, 4 H, 2Oct-C(4)H₂), 3.12 (s, 9 H, Ch-NMe₃), 3.39–3.45 (m, 2 H, Ch-C(1)H₂), 3.78–3.87 (m, 2 H, Ch-C(2)H₂), 5.71 (d, $J = 15.5$ Hz, 2 H, 2Oct-C(2)H), 6.49 (dt, $J = 15.4, 7.0$ Hz, 2 H, 2Oct-C(3)H);

¹³C{¹H} NMR (100 MHz, DMSO-d₆, δ in ppm) 13.9 (2Oct-C(8)), 21.9 (2Oct-C(7)), 27.7 (2Oct-C(6)), 30.8 (2Oct-C(5)), 31.2 (2Oct-C(4)), 53.1 (Ch-NMe₃), 55.1 (Ch-C(2)), 67.1 (Ch-C(1)),

127.0 (2Oct-C(2)), 142.9 (2Oct-C(3)), 168.9 (2Oct-C(1));

FTIR (ATR, $\nu_{\max}$ / cm^{-1}): 3032, 2957, 2926, 2874, 2858, 1695, 1652, 1556, 1479, 1466, 1377, 1261, 1206, 1127, 1090, 984, 956, 867, 675;

ESI⁺ m/z 104.11 (M^+ , 100%);

ESI⁻ m/z 141.09 (M^- , 100%);

Elem. analysis (CHN): Found C, 64.85; H, 11.01; N, 4.00 %. Calc. for $\text{C}_{21}\text{H}_{41}\text{NO}_5$ C, 65.08; H, 10.66; N, 3.61 %.

1:2 BTMAAGE

1:2 BTMAAGE was synthesised according to general procedure C, from 1:1 BTMAAGE (13.23 g, 46.7 mmol) and geranic acid (7.85 g, 46.7 mmol, 1.0 equiv.). The desired IL was obtained as a light-yellow viscous gel that melts in the hand (20.66 g, 45.7 mmol, 98% yield).

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) δ 0.92 (t, $J = 7.4$ Hz, 3 H, BTMA-C(4) H_3), 1.28 (sxt, $J = 7.4$ Hz, 2 H, BTMA-C(3) H_2), 1.56 (s, 6 H, Ger-C(7)Me), 1.59–1.71 (m, 8 H, overlap of BTMA-C(2) H_2 and Ger-C(7)Me), 1.90–2.10 (m, 14 H, overlap of Ger-C(4,5) H_2 and Ger-C(3)Me), 3.06 (s, 9 H, BTMA-NMe₃), 3.25–3.34 (m, 2 H, BTMA-C(1) H_2), 5.02–5.11 (m, 2 H, Ger-C(6)H), 5.60 (s, 2 H, Ger-C(2)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) δ 13.5 (BTMA-C(4)), 17.5 & 17.6 (Ger-C(7)Me₂), 19.2 (BTMA-C(3)), 24.0 (BTMA-C(2)), 25.4 (Ger-C(3)Me), 25.8 (Ger-C(4/5)), 39.9 (Ger-C(4/5)), 52.0 (BTMA-NMe₃), 65.0 (BTMA-C(1)), 122.2 & 123.7 (Ger-C(6) and Ger-C(2)), 131.0 (Ger-C(7)), 148.4 (Ger-C(3)), 169.6 (Ger-C(1));

FTIR (ATR, $\nu_{\max}$ / cm^{-1}): 3031, 2964, 2922, 2876, 1645, 1566, 1487, 1442, 1376, 1224, 1152, 1104, 975, 873, 818, 739, 696;

ESI⁺ m/z 116.14 (M^+ , 100%);

ESI⁻ m/z 167.11 (M^- , 100%);

Elem. analysis (CHN): Found C, 71.85; H, 11.01; N, 3.84 %. Calc. for $\text{C}_{27}\text{H}_{49}\text{NO}_4$ C, 71.80; H, 10.93; N, 3.10 %.

1:2 BTMAAOC

1:2 BTMAAOC was synthesised according to general procedure C, from 1:1 BTMAAOC (34.15 g, 131.6 mmol) and octanoic acid (18.99 g, 131.7 mmol, 1.0 equiv.). The desired IL was obtained as a light-yellow viscous gel (44.02 g, 109.1 mmol, 83% yield).

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.85 (t, $J = 7.0$ Hz, 6 H, Oct-C(8) H_3), 0.93 (t, $J = 7.4$ Hz, 3 H, BTMA-C(4) H_3), 1.13–1.34 (m, 18 H, overlap of BTMA-C(3) H_2 & Oct-C(4,5,6,7) H_2), 1.42 (p, $J = 7.2$ Hz, 4 H, Oct-C(3) H_2), 1.59–1.70 (m, 2 H, BTMA-C(2) H_2), 2.00 (t, $J = 7.4$ Hz, 4 H, Oct-C(2) H_2), 3.06 (s, 9 H, BTMA- NMe_3), 3.25–3.34 (m, 2 H, BTMA C(1) H_2);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 13.5 (Oct-C(8)), 13.9 (BTMA-C(4)), 19.1 (BTMA-C(3)), 22.1 (Oct-C(7)), 24.0 (BTMA-C(2)), 25.7 (Oct-C(6)), 28.7 (Oct-C(5)), 29.0 (Oct-C(4)), 31.1 (Oct-C(3)), 36.4 (Oct-C(2)), 52.0 (BTMA- NMe_3), 65.0 (BTMA-C(1)), 175.6 (Oct-C(1));

FTIR (ATR, ν_{max} / cm^{-1}): 3024, 2962, 2929, 2850, 1702, 1637, 1576, 1491, 1466, 1380, 972, 913, 722;

ESI $^+$ m/z 116.14 (M^+ , 100%);

ESI $^-$ m/z 143.11 (M^- , 100%);

Elem. analysis (CHN): Found C, 68.27; H, 13.04; N, 3.48 %. Calc. for $\text{C}_{23}\text{H}_{49}\text{NO}_4$ C, 68.44; H, 12.24; N, 3.47 %. The measured value for hydrogen is outside of the range corresponding to analytical purity ($\pm 0.4\%$). This cannot be explained by an excess of moisture/solvent or by a deviation in the 1:2 stoichiometry of the starting materials and so a formula cannot be provided that would correspond to the measured CHN values. It is possible that the IL contains more than one kind of impurity or that it contains unknown impurities, such as ones present in the starting materials.

1:1 CAGE

Geranic acid in ethanol was added dropwise to an 78 wt% aqueous solution of choline bicarbonate cooled to 0 °C in an ice bath. The mixture was allowed to warm to room temperature and stirred for 2–3 h. The solvent was removed under reduced pressure and the resulting viscous oil was dried in vacuo for 24 h at room temperature. The desired IL was obtained as a white

hygroscopic solid (10.21 g, 37.6 mmol, 96% yield), m.p. 110–170 °C, with some decomposition.

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 1.56 & 1.63 (s, 3 H, Ger-C(7)Me₂), 1.86–1.95 (m, 5 H, overlap of Ger-C(4/5)H₂ and Ger-C(3)Me), 1.99–2.07 (m, 2 H, Ger-C(4/5)H₂), 3.14 (s, 9 H, Ch-NMe₃), 3.40–3.48 (m, 2 H, Ch-C(1)H₂), 3.82–3.92 (m, 2 H, Ch-C(2)H₂), 5.03–5.12 (m, 1 H, Ger-C(6)H), 5.56 (s, 1 H, Ger-C(2)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 17.2 & 17.5 (Ger-C(7)Me₂), 25.5 (Ger-C(3)Me), 26.0 (Ger-C(5)), 39.7 (Ger-C(4)), 53.1 (Ch-NMe₃), 54.9 (Ch-C(2)), 67.4 (Ch-C(1)), 124.2 (Ger-C(2)), 126.9 (Ger-C(6)), 130.7 (Ger-C(7)), 141.5 (Ger-C(3)), 171.0 (Ger-C(1));

FTIR (ATR, ν_{max} / cm^{-1}): 3025, 2963, 2918, 2850, 1640, 1559, 1392, 1368, 1307, 1180, 1146, 1090, 1010, 955, 870, 821, 779, 702;

ESI⁺ m/z 104.11 (M⁺, 100%);

ESI[−] m/z 167.11 (M[−], 100%);

Elem. analysis (CHN): Found C, 64.32; H, 10.96; N, 5.02 %. Calc. for C₁₅H₂₉NO₃ C, 66.38; H, 10.77; N, 5.16 %. The measured value for carbon is significantly higher than the theoretical value, which could be due to the presence of residual moisture in the sample. Calculated values for C₁₅H₂₉NO₃ (H₂O)_{0.5} C, 64.25; H, 10.78; N, 5.00 % are within the range corresponding to analytical purity ($\pm 0.4\%$) compared to the theoretical values.

1:1 CACI

1:1 CACI was synthesised according to general procedure A, from 78 wt% aqueous choline bicarbonate (8.54 g, 40.3 mmol) and citronellic acid (6.86 g, 40.3 mmol, 1 equiv.). The desired IL was obtained as a white hygroscopic solid (10.58 g, 38.7 mmol, 96% yield), m.p. 102–112 °C.

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.80 (d, $J = 6$ Hz, 3 H, Cit-C(3)Me), 0.97–1.32 (m, 2 H, Cit-C(2)H₂), 1.55 (s, 3 H, Cit-C(7)Me), 1.63 (m, 4 H, overlap of Cit-C(7)Me and Cit-C(3)H), 1.69–1.99 (m, 4 H, Cit-C(4,5)H₂), 3.12 (s, 9 H, Ch-NMe₃), 3.39–3.46 (m, 2 H, Ch-C(1)H₂), 3.81–3.89 (m, 2 H, Ch-C(2)H₂), 5.07 (m, 1 H, Cit-C(6)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 17.5 ((Cit-C(7)Me), 20.2 (Cit-C(3)Me), 25.3 (Cit-C(4/5)), 25.5 (Cit-C(7)Me), 30.4 (Cit-C(4/5)), 37.2 (Cit-C(2)), 46.9 (Cit-C(3)), 53.1 (Ch-

NMe₃), 54.9 (Ch-C(2)), 67.4 (Ch-C(1)), 125.1 (Cit-C(6)), 130.0 (Cit-C(7)), 175.3 (Cit-C(1));

FTIR (ATR, $\nu_{\max}$ / cm⁻¹): 3023, 2957, 2919, 2847, 1564, 1489, 1447, 1368, 1316, 1140, 1086, 1007, 951, 863, 826, 724;

ESI⁺ m/z 104.11 (M⁺, 100%);

ESI⁻ m/z 169.12 (M⁻, 100%);

Elem. analysis (CHN): Found C, 64.95; H, 11.59; N, 5.86 %. Calc. for C₁₅H₃₁NO₃ C, 65.89; H, 11.43; N, 5.12 %.

1:1 CAOC

1:1 CAOC was synthesised according to general procedure A, from 78 wt% aqueous choline bicarbonate (8.84 g, 41.7 mmol) and octanoic acid (6.02 g, 41.7 mmol, 1 equiv.). The desired IL was obtained as a colourless viscous gel (9.94 g, 40.2 mmol, 96% yield).

¹H NMR (400 MHz, DMSO-d₆, δ in ppm) 0.85 (t, J = 7.0 Hz, 3 H, Oct-C(8)H₃), 1.13–1.30 (m, 8 H, Oct-C(4,5,6,7)H₂), 1.39 (p, J = 7.2 Hz, 2 H, Oct-C(3)H₂), 1.83 (t, J = 7.2 Hz, 2 H, Oct-C(2)H₂), 3.14 (s, 9 H, Ch-NMe₃), 3.41–3.47 (m, 2 H, Ch-C(1)H₂), 3.81–3.89 (m, 2 H, Ch-C(2)H₂);

¹³C{¹H} NMR (100 MHz, DMSO-d₆, δ in ppm) 14.4 (Oct-C(8)), 22.6 (Oct-C(7)), 27.1 (Oct-C(6)), 29.3 (Oct-C(5)), 29.9 (Oct-C(4)), 31.9 (Oct-C(3)), 39.1 (Oct-C(2)), 53.5 (Ch-NMe₃), 55.3 (Ch-C(2)), 67.9 (Ch-C(1)), 176.5 (Oct-C(1));

FTIR (ATR, $\nu_{\max}$ / cm⁻¹): 3025, 2952, 2924, 2853, 1570, 1480, 1466, 1380, 1304, 1091, 1008, 955, 920, 865, 723;

ESI⁺ m/z 104.11 (M⁺, 100%);

ESI⁻ m/z 143.11 (M⁻, 100%);

Elem. analysis (CHN): Found C, 62.18; H, 11.89; N, 6.09 %. Calc. for C₁₃H₂₉NO₃ C, 63.12; H, 11.82; N, 5.66 %.

1:1 CA2OE

1:1 CAOC was synthesised according to general procedure A, from 78 wt% aqueous choline bicarbonate (8.50 g, 51.5 mmol) and 2-octenoic acid (7.32 g, 51.5 mmol, 1 equiv.). The desired IL was obtained as a colourless viscous oil (12.53 g, 51.1 mmol, 99% yield).

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.85 (t, $J = 7.0$ Hz 3 H, 2Oct-C(8) H_3), 1.17–1.38 (m, 6 H, 2Oct-C(5,6,7) H_2), 1.99 (q, $J = 7.1$ Hz, 2 H, 2Oct-C(4) H_2), 3.13 (s, 9 H, Ch-NMe $_3$), 3.41–3.46 (m, 2 H, Ch-C(1) H_2), 3.82–3.88 (m, 2 H, Ch-C(2) H_2), 5.58 (d, $J = 15.3$ Hz, 1 H, 2Oct-C(2)H), 6.21 (dt, $J = 15.3, 7.0$ Hz, 1 H, 2Oct-C(3)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 14.0 (2Oct-C(8)), 22.0 (2Oct-C(7)), 28.2 (2Oct-C(6)), 30.9 (2Oct-C(5)), 31.1 (2Oct-C(4)), 53.1 (Ch-NMe $_3$), 55.0 (Ch-C(2)), 67.4 (Ch-C(1)), 131.8 (2Oct-C(2)), 137.8 (2Oct-C(3)), 170.0 (2Oct-C(1));

FTIR (ATR, ν_{max} / cm^{-1}): 3024, 2956, 2925, 2876, 2854, 1653, 1559, 1480, 1463, 1373, 1279, 1242, 1137, 1088, 980, 951, 870, 709;

ESI $^+$ m/z 104.11 (M^+ , 100%);

ESI $^-$ m/z 141.09 (M^- , 100%);

Elem. analysis (CHN): Found C, 63.02; H, 10.20; N, 5.29 %. Calc. for C $_{13}$ H $_{27}$ NO $_3$ C, 63.64; H, 11.09; N, 5.71 %. The measured values for carbon and hydrogen are outside of the range corresponding to analytical purity ($\pm 0.4\%$). These values cannot be explained by an excess of moisture/solvent or by a deviation in the 1:1 stoichiometry of the starting materials and so a formula cannot be provided that would correspond to the measured CHN values. It is possible that the IL contains more than one kind of impurity or that it contains unknown impurities, such as ones present in the starting materials.

1:1 BTMAAGE

1:1 BTMAAGE was synthesised according to general procedure B. The cation was synthesised using the high-pressure route, from N,N-dimethylbutylamine (10.23 g, 101.1 mmol) and dimethylcarbonate (22.1 g, 245.3 mmol, 2.4 eq.), and reacted with geranic acid (17.01 g, 101.1 mmol, 1 equiv.). BTMAAGE 1:1 was obtained as an off-white solid (25.99 g, 91.7 mmol,

91% yield), m.p. 149–152 °C.

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.93 (t, $J = 7.4$ Hz, 3 H, BTMA-C(4) H_3), 1.29 (sxt, $J = 7.4$ Hz, 2 H, BTMA-C(3) H_2), 1.56 (s, 3 H, Ger-C(7)Me), 1.69–1.68 (m, 5 H, overlap of Ger-C(7)Me and BTMA-C(2) H_2), 1.83–1.92 (m, 5 H, overlap of Ger-C(4/5) H_2 and Ger-C(3)Me), 1.97–2.06 (m, 2 H, Ger-C(4/5) H_2), 3.07 (s, 9 H, BTMA-NMe $_3$), 3.27–3.35 (m, 2 H, BTMA-C(1) H_2), 5.04–5.12 (m, 1 H, Ger-C(6)H), 5.40 (s, 1 H, Ger-C(2)H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, DMSO- d_6 , δ in ppm) 13.5 (BTMA-C(4)), 17.1 (Ger-C(3)Me), 17.5 (Ger-C(7)Me), 19.2 (BTMA-C(3)), 24.1 (BTMA-C(2)), 25.5 (Ger-C(7)Me), 26.1 (Ger-C(4/5)), 39.7 (Ger-C(4/5)), 52.0 (BTMA-NMe $_3$), 64.9 (BTMA-C(1)), 124.3 (Ger-C(6)), 128.5 (Ger-C(2)), 130.5 (Ger-C(7)), 138.9 (Ger-C(3)), 170.2 (Ger-C(1));

FTIR (ATR, ν_{max} / cm^{-1}): 3014, 2966, 2921, 2877, 1644, 1563, 1489, 1447, 1379, 1357, 1305, 1164, 1097, 1061, 1028, 976, 913, 875, 821, 740;

ESI $^+$ m/z 116.14 (M^+ , 100%);

ESI $^-$ m/z 167.11 (M^- , 100%);

Elem. analysis (CHN): Found C, 71.87; H, 11.79; N, 4.93 %. Calc. for $\text{C}_{17}\text{H}_{33}\text{NO}_2$ C, 72.03; H, 11.74; N, 4.94 %.

1:1 BTMAAOC

BTMAAOC 1:1 was synthesised according to general procedure B. The cation was synthesised using the high-pressure route, from N,N-dimethylbutylamine (22.23 g, 219.7 mmol) and dimethylcarbonate (46.38 g, 514.9 mmol, 2.3 eq.), and reacted with octanoic acid (31.69 g, 219.7 mmol, 1.0 eq.). BTMAAOC 1:1 was obtained as an off-white powder (51.36 g, 198.0 mmol, 90% yield), m.p. 162–168 °C.

^1H NMR (400 MHz, DMSO- d_6 , δ in ppm) 0.85 (t, $J = 6.7$ Hz, 3 H, Oct-C(8)Me), 0.93 (t, $J = 7.3$ Hz, 3 H, BTMA-C(4) H_3), 1.10–1.41 (m, 12 H, overlap of BTMA-C(3) H_2 & Oct-C(4,5,6,7) H_2 & Oct-C(3) H_2), 1.59–1.69 (m, 2 H, BTMA-C(2) H_2), 1.72 (t, 2 H, $J = 7.4$ Hz, Oct-C(2) H_2),

3.07 (s, 9 H, BTMA-NMe₃), 3.27–3.35 (m, 2 H, BTMA-C(1)H₂);

¹³C{¹H} NMR (100 MHz, DMSO-d₆, δ in ppm) 13.5 (Oct-C(8)), 14.0 (BTMA-C(4)), 19.2 (BTMA-C(3)), 22.2 (Oct-C(7)), 24.1 (BTMA-C(2)), 26.6 (Oct-C(6)), 28.9 (Oct-C(5)), 29.5 (Oct-C(4)), 31.4 (Oct-C(3)), 38.7 (Oct-C(2)), 52.1 (BTMA-NMe₃), 64.9 (BTMA-C(1)), 174.6 (Oct-C(1));

FTIR (ATR, $\nu_{\max}$ / cm⁻¹): 3014, 2953, 2922, 2850, 1574, 1499, 1462, 1375, 977, 914, 726;

ESI⁺ m/z 116.14 (M⁺, 100%);

ESI⁻ m/z 143.11 (M⁻, 100%);

Elem. analysis (CHN): Found C, 70.09; H, 12.97; N, 5.46 %. Calc. for C₁₅H₃₃NO₂ C, 69.45; H, 12.82; N, 5.40 %. The measured value for carbon is outside of the range corresponding to analytical purity ($\pm 0.4\%$). This cannot be explained by an excess of moisture/solvent or by a deviation in the 1:1 stoichiometry of the starting materials and so a formula cannot be provided that would correspond to the measured CHN values. It is possible that the IL contains more than one kind of impurity or that it contains unknown impurities, such as ones present in the starting materials.

9.5 Physicochemical Measurements

9.5.1 X-ray Scattering Measurements

Small-angle X-ray scattering (SAXS) and wide-angle X-ray scattering (WAXS) measurements were run at the Diamond Light Source synchrotron (Didcot, Oxfordshire) on the I22⁷⁸ and DL-SAXS beamlines.

Samples run on the I22 beamline were loaded into polycarbonate capillaries, sealed, and measured using an X-ray energy of 18 keV (corresponding to a wavelength of 0.69 Å) and a sample-to-detector distance of 1–5 m. The beamline was equipped with a Pilatus P3-2M detector for SAXS measurements and a custom Pilatus3-2M-DLS-L detector for WAXS measurements.

Samples run on the DL-SAXS beamline were loaded into glass capillaries, sealed, and measured using a Genix3D Mo Micro-Source with an energy of 17.8 keV (corresponding to a wavelength of

0.70 Å). The sample-to-detector distance was 70 mm, giving access to a q -range of 0.05–2.3 Å⁻¹.

Silver behenate (lattice parameter 58.38 Å) was used to calibrate the data.¹⁶⁷ Sample temperature was controlled using a water recirculator fitted to the capillary holder and a thermocouple inserted into the holder. This allowed access to a temperature range of 5–60 °C. Sample temperature was set and maintained for 3 min before measuring. The recorded 2D images were integrated to 1D scattering plots using the Data Analysis WorkbeNch (DAWN) software. The data was then analysed using Origin (2020) software.

9.5.2 Polarising Microscopy (PLM)

Images were taken using a QICAM fast-1394 CCD camera (QImaging, Canada) connected to a Nikon Eclipse E600 polarisation microscope, fitted with 4x and 10x objective lenses. Images were captured using a custom-made LabVIEW program and analysed using ImageJ software.¹⁶⁸

9.5.3 Differential Scanning Calorimetry (DSC)

Thermal transition points were measured on a DSC 1 STARe or a DSC 3 STAR (both Mettler Toledo) equipped with a liquid nitrogen cooling system. Samples were weighed and sealed in aluminium crucibles inside a glove box. Samples were heated and subsequently cooled at a rate of 5 °C min⁻¹. First-order transition temperatures are given as the peak maximum and glass transition temperatures are determined using the midpoint method.

9.5.4 Dynamic Mechanical Analysis (DMA)

DMA spectra were recorded under a nitrogen atmosphere on a PerkinElmer DMA 8000 instrument with liquid nitrogen cooling. For each measurement, a fresh stainless-steel plate (30.0 mm x 14.0 mm x 0.5 mm, PerkinElmer) was cleaned with ethanol, dried in an oven, and folded in half along the crease line to form a pocket, which the sample was then loaded into. The pocket was placed in the instrument in a three-point bending configuration. The storage modulus (M') and loss tangent ($\tan \delta = M'' / M'$) were recorded at variable frequencies with a scanning temperature of 4 K min⁻¹. The temperature range for each sample was selected based on DSC thermograms. It should be noted here that the stress applied by this method is not a pure

shear stress; instead, the mechanical modulus presently measured is a combination of both the shear and the bulk modulus.^{102,106–108}

9.5.5 Thermogravimetric Analysis (TGA)

Thermogravimetric analysis (TGA) measurements with variable heating rates were performed on a Pyris1 TGA (PerkinElmer) equipped with a microbalance. For all measurements, nitrogen was used as a carrier gas, with a flow rate of 20–60 mL min⁻¹. For each sample, 2–10 mg were loaded on a platinum pan and left to equilibrate at 30 °C for 10 min, in order to remove residual moisture. The sample was then heated to 350 °C using a heating rate of 5, 10, 15 or 20 °C min⁻¹.

For some samples, isothermal TGA measurements were also performed, following a similar procedure. 2–5 mg of sample were loaded on a platinum pan and allowed to equilibrate at 30 °C for 10 min, in order to remove residual moisture. Then, the sample was rapidly heated to the desired temperature (50, 70, 90 or 110 °C) using a heating rate of 20 °C min⁻¹ and held at this temperature for 1200 min (20 h).

9.5.6 Rheology Measurements

Viscosity was measured under inert, dry, nitrogen conditions (to avoid moisture uptake of the samples) using a MCR 301 rheometer (Anton Paar) with cone-plate geometry. The measuring probe was a CP50-1 cone with a gap size of 0.101 mm.

For dynamic viscosity measurements, the studied range was 25–105 °C with a 5 °C step. For each temperature 30 points were measured with shear rates ranging from 50 to 150 s⁻¹. In the isotropic liquid phase, samples showed Newtonian flow behaviour and therefore the values for each temperature were averaged across the range of shear rates.

For samples with high viscosities that showed shear-thinning behaviour, dynamic viscosity could not be measured. Instead, steady-shear oscillation measurements were run between 25–70 °C with oscillating frequencies of 0.01–100 rad s⁻¹. The complex viscosity (η^*), storage (E') and loss (E'') moduli, and loss tangent ($\tan \delta = E''/E'$) were measured for each sample.

9.5.7 Solid-state NMR measurements

Spectra were recorded on a Bruker 600 MHz spectrometer. Each sample was packed into a disposable rotor insert inserted into a 4 mm zirconium rotor and sealed with a Kel-F cap (all purchased from Bruker). Care was taken to ensure an even sample packing, with no air gaps. The rotor was placed in the probe and inserted into the NMR spectrometer. Samples were spun at the magic angle $\theta_{\text{m}} = 54.74^\circ$ at a frequency of 5 kHz. Data was collected using Bruker TopSpin software, while data analysis was performed using MestReNova (2020) software.

Bibliography

- (1) Mikulic, *Pharmaceutical Market: Worldwide Revenue 2001-2023*, Statistic, 2024.
- (2) Y. H. Bae and K. Park, *Advanced Drug Delivery Reviews*, 2020, **158**, 4–16.
- (3) J. Gao, J. M. Karp, R. Langer and N. Joshi, *Chemistry of Materials*, 2023, **35**, 359–363.
- (4) D. Etit, S. Meramo, Ó. Ögmundarson, M. K. Jensen and S. Sukumara, *Current Opinion in Biotechnology*, 2024, **87**, 103100.
- (5) *Code of Federal Regulations, Title 21*.
- (6) P. Hinderliter and S. A. Saghir, in *Encyclopedia of Toxicology*, ed. P. B. T. Wexler, Academic Press, Oxford, Third Edition, 2014, pp. 849–855.
- (7) M. R. Prausnitz and R. Langer, *Nature Biotechnology*, 2008, **26**, 1261–1268.
- (8) M. S. Alqahtani, M. Kazi, M. A. Alsenaidy and M. Z. Ahmad, *Frontiers in Pharmacology*, 2021, **12**, 618411.
- (9) M. Zakrewsky, K. S. Lovejoy, T. L. Kern, T. E. Miller, V. Le, A. Nagy, A. M. Goumas, R. S. Iyer, R. E. Del Sesto, A. T. Koppisch, D. T. Fox and S. Mitragotri, *Proceedings of the National Academy of Sciences*, 2014, **111**, 13313–13318.
- (10) A. Banerjee, K. Ibsen, Y. Iwao, M. Zakrewsky and S. Mitragotri, *Advanced Healthcare Materials*, 2017, **6**, 1601411.
- (11) A. Banerjee, K. Ibsen, T. Brown, R. Chen, C. Agatemor and S. Mitragotri, *Proceedings of the National Academy of Sciences*, 2018, **115**, 7296–7301.
- (12) K. N. Ibsen, H. Ma, A. Banerjee, E. E. L. Tanner, S. Nangia and S. Mitragotri, *ACS Biomaterials Science & Engineering*, 2018, **4**, 2370–2379.

- (13) S. K. Mann, M. K. Devgan, W. T. Franks, S. Huband, C. L. Chan, J. Griffith, D. Pugh, N. J. Brooks, T. Welton, T. N. Pham, L. L. McQueen, J. R. Lewandowski and S. P. Brown, *The Journal of Physical Chemistry B*, 2020, **124**, 4975–4988.
- (14) J. Takeda, Y. Iwao, M. Karashima, K. Yamamoto and Y. Ikeda, *ACS Biomaterials Science & Engineering*, 2021, **7**, 595–604.
- (15) M. Devgan, Ph.D. Thesis, Imperial College London, London, 2021.
- (16) J. P. Hallett and T. Welton, *Chemical Reviews*, 2011, **111**, 3508–3576.
- (17) T. Welton, *Biophysical Reviews*, 2018, **10**, 691–706.
- (18) B. Clare, A. Sirwardana and D. R. MacFarlane, in *Ionic Liquids*, ed. B. Kirchner, Springer, Berlin, Heidelberg, 2010, vol. 290, pp. 1–40.
- (19) J. C. Araque, J. J. Hettige and C. J. Margulis, *The Journal of Physical Chemistry B*, 2015, **119**, 12727–12740.
- (20) K. Shimizu, A. A. H. Pádua and J. N. Canongia Lopes, *The Journal of Physical Chemistry B*, 2010, **114**, 15635–15641.
- (21) R. D. Rogers and G. Gurau, *Proceedings of the National Academy of Sciences*, 2018, **115**, E10999.
- (22) Q. M. Qi and S. Mitragotri, *Journal of Controlled Release*, 2019, **311–312**, 162–169.
- (23) T. Hattori, H. Tagawa, M. Inai, T. Kan, S.-i. Kimura, S. Itai, S. Mitragotri and Y. Iwao, *Scientific Reports*, 2019, **9**, 20191.
- (24) P. Karande, A. Jain, K. Ergun, V. Kispersky and S. Mitragotri, *Proceedings of the National Academy of Sciences*, 2005, **102**, 4688–4693.
- (25) Q. M. Qi, M. Duffy, A. M. Curreri, J. P. R. Balkaran, E. E. L. Tanner and S. Mitragotri, *Advanced Functional Materials*, 2020, **30**, 2004257.
- (26) R. Yang, T. Wei, H. Goldberg, W. Wang, K. Cullion and D. S. Kohane, *Advanced Materials*, 2017, **29**, 1606596.
- (27) E. E. Tanner, K. N. Ibsen and S. Mitragotri, *Journal of Controlled Release*, 2018, **286**, 137–144.
- (28) A. Vaidya and S. Mitragotri, *Journal of Controlled Release*, 2020, **327**, 26–34.

- (29) K. Peng, Y. Shi, A. LaBarbiera and S. Mitragotri, *ACS Biomaterials Science & Engineering*, 2023, **9**, 2838–2845.
- (30) M. Zakrewsky, A. Banerjee, S. Apte, T. L. Kern, M. R. Jones, R. E. D. Sesto, A. T. Koppisch, D. T. Fox and S. Mitragotri, *Advanced Healthcare Materials*, 2016, **5**, 1282–1289.
- (31) J. R. Greene, K. L. Merrett, A. J. Heyert, L. F. Simmons, C. M. Migliori, K. C. Vogt, R. S. Castro, P. D. Phillips, J. L. Baker, G. E. Lindberg, D. T. Fox, R. E. Del Sesto and A. T. Koppisch, *PLoS ONE*, 2019, **14**, 1–22.
- (32) J. Ko, A. Mandal, S. Dhawan, M. Shevachman, S. Mitragotri and N. Joshi, *Bioengineering & Translational Medicine*, 2021, **6**, e10191.
- (33) M. Shevachman, A. Mandal, K. Gelston, S. Mitragotri and N. Joshi, *Global Challenges*, 2022, **6**, 2200064.
- (34) G. M. Neville, A.-M. Dobre, G. J. Smith, S. Micciulla, N. J. Brooks, T. Arnold, T. Welton and K. J. Edler, *Advanced Functional Materials*, 2024, **34**, 2306644.
- (35) E. E. L. Tanner, A. M. Curreri, J. P. R. Balkaran, N. C. Selig-Wober, A. B. Yang, C. Kendig, M. P. Fluhr, N. Kim and S. Mitragotri, *Advanced Materials*, 2019, **31**, 1901103.
- (36) C. M. Chism, S. Plash, D. Zuckerman, G. S. Dasanayake, M. Bennett, S. K. Tripathi, S. D. Pedigo and E. E. L. Tanner, *ACS Applied Engineering Materials*, 2023, **1**, 23–31.
- (37) H. Albadawi, Z. Zhang, I. Altun, J. Hu, L. Jamal, K. N. Ibsen, E. E. L. Tanner, S. Mitragotri and R. Oklu, *Science Translational Medicine*, 2021, **13**, eabe3889.
- (38) M. Freemantle, *Chemical & Engineering News*, 1998, **76**, 32–37.
- (39) W. Silva, M. Zanatta, A. S. Ferreira, M. C. Corvo and E. J. Cabrita, *International Journal of Molecular Sciences*, 2020, **21**, 7745.
- (40) S. Koutsoukos, F. Philippi, F. Malaret and T. Welton, *Chemical Science*, 2021, **12**, 6820–6843.
- (41) P. A. Hunt, C. R. Ashworth and R. P. Matthews, *Chemical Society Reviews*, 2015, **44**, 1257–1288.
- (42) K. Dong, S. Zhang and J. Wang, *Chemical Communications*, 2016, **52**, 6744–6764.
- (43) P. A. Hunt, *Topics in Current Chemistry*, 2017, **375**, 59.

- (44) K. Fujita, D. R. MacFarlane and M. Forsyth, *Chemical Communications*, 2005, 4804–4806.
- (45) P. A. Hunt, *The Journal of Physical Chemistry B*, 2007, **111**, 4844–4853.
- (46) H. Abe, T. Takekiyo, M. Shigemi, Y. Yoshimura, S. Tsuge, T. Hanasaki, K. Ohishi, S. Takata and J.-i. Suzuki, *The Journal of Physical Chemistry Letters*, 2014, **5**, 1175–1180.
- (47) H. Abe, Y. Yoshiichi, T. Hirano, T. Ohkubo and H. Kishimura, *Journal of Molecular Liquids*, 2022, **367**, 120383.
- (48) T. L. Greaves and C. J. Drummond, *Chemical Reviews*, 2008, **108**, 206–237.
- (49) J. Dupont, *Accounts of Chemical Research*, 2011, **44**, 1223–1231.
- (50) L. K. Saunders, H. Nowell, P. R. Raithby and C. C. Wilson, *CrystEngComm*, 2016, **18**, 5916–5929.
- (51) J. A. Berrocal, F. Di Meo, M. García-Iglesias, R. P. J. Gosens, E. W. Meijer, M. Linares and A. R. A. Palmans, *Chemical Communications*, 2016, **52**, 10870–10873.
- (52) G. Van Meer, D. R. Voelker and G. W. Feigenson, *Nature Reviews Molecular Cell Biology*, 2008, **9**, 112–124.
- (53) M. Cebecauer, in *Methods in Membrane Lipids*, ed. D. M. Owen, Springer New York, New York, NY, 2015, vol. 1232, pp. 7–17.
- (54) A. P. Abbott, G. Capper, D. L. Davies, R. K. Rasheed and V. Tambyrajah, *Chemical Communications*, 2003, 70–71.
- (55) J. Płotka-Wasyłka, M. De La Guardia, V. Andruch and M. Vilková, *Microchemical Journal*, 2020, **159**, 105539.
- (56) J. Afonso, A. Mezzetta, I. M. Marrucho and L. Guazzelli, *Green Chemistry*, 2023, **25**, 59–105.
- (57) D. O. Abranches and J. A. Coutinho, *Annual Review of Chemical and Biomolecular Engineering*, 2023, **14**, 141–163.
- (58) E. L. Smith, A. P. Abbott and K. S. Ryder, *Chemical Reviews*, 2014, **114**, 11060–11082.
- (59) Y. Marcus, *ACS Sustainable Chemistry & Engineering*, 2017, **5**, 11780–11787.
- (60) C. Florindo, F. S. Oliveira, L. P. N. Rebelo, A. M. Fernandes and I. M. Marrucho, *ACS Sustainable Chemistry & Engineering*, 2014, **2**, 2416–2425.

- (61) R. Craveiro, I. Aroso, V. Flammia, T. Carvalho, M. Viciosa, M. Dionísio, S. Barreiros, R. Reis, A. Duarte and A. Paiva, *Journal of Molecular Liquids*, 2016, **215**, 534–540.
- (62) D. A. Alonso, A. Baeza, R. Chinchilla, G. Guillena, I. M. Pastor and D. J. Ramón, *European Journal of Organic Chemistry*, 2016, **2016**, 612–632.
- (63) A. Skulcova, A. Russ, M. Jablonsky and J. Sima, *BioResources*, 2018, **13**, 5042–5051.
- (64) J. A. Coutinho and S. P. Pinho, *Fluid Phase Equilibria*, 2017, **448**, 1.
- (65) M. A. R. Martins, S. P. Pinho and J. A. P. Coutinho, *Journal of Solution Chemistry*, 2019, **48**, 962–982.
- (66) F. Guthrie, *Proceedings of the Physical Society of London*, 1884, **6**, 124–146.
- (67) L. J. Kollau, M. Vis, A. Van Den Bruinhorst, R. Tuinier and G. De With, *Journal of Molecular Liquids*, 2020, **302**, 112155.
- (68) Y. Koga, P. Westh, K. Nishikawa and S. Subramanian, *The Journal of Physical Chemistry B*, 2011, **115**, 2995–3002.
- (69) L. J. B. M. Kollau, M. Vis, A. Van Den Bruinhorst, A. C. C. Esteves and R. Tuinier, *Chemical Communications*, 2018, **54**, 13351–13354.
- (70) C. M. Jeffries, J. Ilavsky, A. Martel, S. Hinrichs, A. Meyer, J. S. Pedersen, A. V. Sokolova and D. I. Svergun, *Nature Reviews Methods Primers*, 2021, **1**, 70.
- (71) C. D. Putnam, M. Hammel, G. L. Hura and J. A. Tainer, *Quarterly Reviews of Biophysics*, 2007, **40**, 191–285.
- (72) T. Li, A. J. Senesi and B. Lee, *Chemical Reviews*, 2016, **116**, 11128–11180.
- (73) S. P. Meisburger, W. C. Thomas, M. B. Watkins and N. Ando, *Chemical Reviews*, 2017, **117**, 7615–7672.
- (74) T. Bizien, D. Durand, P. Roblina, A. Thureau, P. Vachette and J. Pérez, *Protein & Peptide Letters*, 2016, **23**, 217–231.
- (75) F. Peyronel, A. G. Marangoni and D. A. Pink, *Food Research International*, 2020, **129**, 108846.
- (76) B. Różycki and E. Boura, *Biophysical Chemistry*, 2022, **288**, 106843.
- (77) P. Willmott, *An Introduction to Synchrotron Radiation: Techniques and Applications*, Wiley, 2011.

- (78) A. J. Smith, S. G. Alcock, L. S. Davidson, J. H. Emmins, J. C. Hiller Bardsley, P. Holloway, M. Malfois, A. R. Marshall, C. L. Pizzey, S. E. Rogers, O. Shebanova, T. Snow, J. P. Sutter, E. P. Williams and N. J. Terrill, *Journal of Synchrotron Radiation*, 2021, **28**, 939–947.
- (79) S. T. Hyde, in *Handbook of Applied Surface and Colloid Chemistry*, ed. K. Holmberg, Wiley, Chichester Weinheim, 2001.
- (80) A. Triolo, O. Russina, H.-J. Bleif and E. Di Cola, *The Journal of Physical Chemistry B*, 2007, **111**, 4641–4644.
- (81) A. Triolo, O. Russina, R. Caminiti, H. Shirota, H. Y. Lee, C. S. Santos, N. S. Murthy and E. W. Castner, Jr, *Chemical Communications*, 2012, **48**, 4959.
- (82) J. E. Hallett, D. W. Hayward, P. Bartlett and R. M. Richardson, *Liquid Crystals*, 2014, **41**, 1791–1802.
- (83) N. J. Brooks, F. Castiglione, C. M. Doherty, A. Dolan, A. J. Hill, P. A. Hunt, R. P. Matthews, M. Mauri, A. Mele, R. Simonutti, I. J. Villar-Garcia, C. C. Weber and T. Welton, *Chemical Science*, 2017, **8**, 6359–6374.
- (84) F. Philippi, D. Rauber, B. Kuttich, T. Kraus, C. W. M. Kay, R. Hempelmann, P. A. Hunt and T. Welton, *Physical Chemistry Chemical Physics*, 2020, **22**, 23038–23056.
- (85) K. Qian, R. E. Winans and T. Li, *Advanced Energy Materials*, 2021, **11**, 2002821.
- (86) S. Koutsoukos, J. Avila, N. J. Brooks, M. Costa Gomes and T. Welton, *Physical Chemistry Chemical Physics*, 2023, **25**, 6316–6325.
- (87) C. Tschierske, *Angewandte Chemie International Edition*, 2013, **52**, 8828–8878.
- (88) G. S. Ginsburg, D. Atkinson and D. M. Small, *Progress in Lipid Research*, 1984, **23**, 135–167.
- (89) A. S.I., K. Pal, S. Kralj and S. Thomas, in *Nanofabrication for Smart Nanosensor Applications*, Elsevier, 2020, pp. 295–321.
- (90) K. Goossens, K. Lava, C. W. Bielawski and K. Binnemans, *Chemical Reviews*, 2016, **116**, 4643–4807.
- (91) Z. Huang, P. Qi, Y. Liu, C. Chai, Y. Wang, A. Song and J. Hao, *Physical Chemistry Chemical Physics*, 2019, **21**, 15256–15281.

- (92) S. Hassan, W. Rowe and J. T. Tiddy, in *Handbook of Applied Surface and Colloid Chemistry*, ed. K. Holmberg, Wiley, Chichester Weinheim, 2001.
- (93) I. Dierking, *Textures of Liquid Crystals*, Wiley, 1st edn., 2003.
- (94) G. Tiddy, *Physics Reports*, 1980, **57**, 1–46.
- (95) M. Dreja, *Chemical Communications*, 1998, 1371–1372.
- (96) In *Strategies to Modify the Drug Release from Pharmaceutical Systems*, ed. M. L. Bruschi, Woodhead Publishing, Cambridge, Waltham, Kidlington, 2015, pp. 87–194.
- (97) S. Koutsoukos, F. Philippi, D. Rauber, D. Pugh, C. W. M. Kay and T. Welton, *Physical Chemistry Chemical Physics*, 2022, **24**, 6453–6468.
- (98) I. R. Nichols, C. M. Hamadani, C. M. Chism, A. N. Hunter, H. Ahmad, K. Wontor, A. E. Williams, P. Vashisth, N. I. Hammer, S. Kundu and E. E. L. Tanner, *Advanced Therapeutics*, 2023, **6**, 2200096.
- (99) F. Oliviero and L. Punzi, in *Synovial Fluid Analysis and The Evaluation of Patients With Arthritis*, ed. B. F. Mandell, Springer International Publishing, Switzerland, 2022, pp. 79–90.
- (100) A. Saupe, *Journal of Colloid and Interface Science*, 1977, **58**, 549–558.
- (101) A. Dobre, S. Koutsoukos, F. Philippi, D. Rauber, C. W. M. Kay, O. Palumbo, M. M. Roessler and T. Welton, *Physical Chemistry Chemical Physics*, 2024, **26**, 8858–8872.
- (102) F. Philippi, D. Rauber, O. Palumbo, K. Goloviznina, J. McDaniel, D. Pugh, S. Suarez, C. C. Fraenza, A. Padua, C. W. M. Kay and T. Welton, *Chemical Science*, 2022, **13**, 9176–9190.
- (103) D. Rauber, F. Philippi, D. Schroeder, B. Morgenstern, A. J. P. White, M. Jochum, T. Welton and C. W. M. Kay, *Chemical Science*, 2023, **14**, 10340–10346.
- (104) G. W. Kamykowski, in *Handbook of Transition Metal Polymerization Catalysts*, ed. R. Hoff and R. T. Mathers, Wiley, First Edition, 2010, pp. 563–566.
- (105) H. A. Barnes, *A Handbook of Elementary Rheology*, University of Wales, Institute of Non-Newtonian Fluid Mechanics, 2000.
- (106) O. Palumbo, F. Trequattrini, F. M. Vitucci and A. Paolone, *The Journal of Physical Chemistry B*, 2015, **119**, 12905–12911.

- (107) O. Palumbo, F. Trequattrini, G. Appetecchi, L. Conte and A. Paolone, *Journal of Molecular Liquids*, 2017, **243**, 9–13.
- (108) O. Palumbo, A. Paolone, D. Rauber, C. Kay, F. Philippi and T. Welton, *Journal of Alloys and Compounds*, 2022, **919**, 165860.
- (109) O. Palumbo, A. Paolone, F. Philippi, D. Rauber and T. Welton, *International Journal of Molecular Sciences*, 2023, **24**, 11046.
- (110) M. Kalichevsky, E. Jaroszkiewicz, S. Ablett, J. Blanshard and P. Lillford, *Carbohydrate Polymers*, 1992, **18**, 77–88.
- (111) R. Hagen, L. Salmén, H. Lavebratt and B. Stenberg, *Polymer Testing*, 1994, **13**, 113–128.
- (112) Z. Lei, W. Xing, J. Wu, G. Huang, X. Wang and L. Zhao, *Journal of Thermal Analysis and Calorimetry*, 2014, **116**, 447–453.
- (113) K. L. Ngai and D. J. Plazek, *Rubber Chemistry and Technology*, 1995, **68**, 376–434.
- (114) *Anelastic Relaxation in Crystalline Solids*, ed. A. Nowick and B. Berry, Elsevier, 1972.
- (115) G. Cannelli, R. Cantelli, F. Cordero and F. Trequattrini, *Physical Review B*, 1997, **55**, 14865–14871.
- (116) M. Sha, X. Ma, N. Li, F. Luo, G. Zhu and M. D. Fayer, *The Journal of Chemical Physics*, 2019, **151**, 154502.
- (117) A. F. Bouarab, J.-P. Harvey and C. Robelin, *Physical Chemistry Chemical Physics*, 2021, **23**, 733–752.
- (118) J. C. Dyre and N. B. Olsen, *Physical Review E*, 2004, **69**, 042501.
- (119) A. I. I. Tyler, R. V. Law and J. M. Seddon, in *Methods in Membrane Lipids*, Springer New York, New York, 2015, vol. 1232.
- (120) R. A. Gonçalves, Y.-M. Lam and B. Lindman, *Molecules*, 2021, **26**, 3946.
- (121) Z.-J. Chen and R. Stark, *Solid State Nuclear Magnetic Resonance*, 1996, **7**, 239–246.
- (122) J. Fejzo, A. Krezel, W. M. Westler, S. Macura and J. L. Markley, *Journal of Magnetic Resonance*, 1991, **92**, 651–657.
- (123) J. F. Nagle and S. Tristram-Nagle, *Biochimica et Biophysica Acta (BBA) - Reviews on Biomembranes*, 2000, **1469**, 159–195.

- (124) B. A. Lewis and D. M. Engelman, *Journal of Molecular Biology*, 1983, **166**, 211–217.
- (125) J. N. A. Canongia Lopes and A. A. H. Padua, *Journal of Physical Chemistry B*, 2006, **110**, 3330–3335.
- (126) H. K. Kashyap, J. J. Hettige, H. V. R. Annapureddy and C. J. Margulis, *Chemical Communications*, 2012, **48**, 5103–5105.
- (127) H. V. R. Annapureddy, H. K. Kashyap, P. M. De Biase and C. J. Margulis, *The Journal of Physical Chemistry B*, 2010, **114**, 16838–16846.
- (128) N. S. Elstone, K. Shimizu, E. V. Shaw, P. D. Lane, L. D’Andrea, B. Demé, N. Mahmoudi, S. E. Rogers, S. Youngs, M. L. Costen, K. G. McKendrick, J. N. Canongia Lopes, D. W. Bruce and J. M. Slattery, *The Journal of Physical Chemistry B*, 2023, **127**, 7394–7407.
- (129) G. L. Burrell, N. F. Dunlop and F. Separovic, *Soft Matter*, 2010, **6**, 2080.
- (130) T. Yamada, P. A. Bonnaud, S. Tejima and J.-i. Fujita, *Chemical Physics Letters*, 2023, **816**, 140387.
- (131) N. Bloembergen, *Nuclear Magnetic Relaxation*, Springer Netherlands, Dordrecht, 1948.
- (132) T. H. Kim, MIT Department of Physics, 2008.
- (133) A. G. Cook, J. L. Wardell and C. T. Imrie, *Chemistry and Physics of Lipids*, 2011, **164**, 118–124.
- (134) H. Tokuda, K. Hayamizu, K. Ishii, M. A. B. H. Susan and M. Watanabe, *The Journal of Physical Chemistry B*, 2004, **108**, 16593–16600.
- (135) H. Tokuda, K. Hayamizu, K. Ishii, M. A. B. H. Susan and M. Watanabe, *The Journal of Physical Chemistry B*, 2005, **109**, 6103–6110.
- (136) H. Tokuda, K. Ishii, M. A. B. H. Susan, S. Tsuzuki, K. Hayamizu and M. Watanabe, *The Journal of Physical Chemistry B*, 2006, **110**, 2833–2839.
- (137) Z. K. Koi, W. Z. N. Yahya, R. A. Abu Talip and K. A. Kurnia, *New Journal of Chemistry*, 2019, **43**, 16207–16217.
- (138) P. Barthen, W. Frank and N. Ignatiev, *Ionics*, 2015, **21**, 149–159.
- (139) F. Philippi, D. Rauber, K. L. Eliassen, N. Bouscharain, K. Niss, C. W. M. Kay and T. Welton, *Chemical Science*, 2022, **13**, 2735–2743.
- (140) R. Centore, A. Roviello and A. Sirigu, *Liquid Crystals*, 1988, **3**, 1525–1534.

- (141) H. R. Kricheldorf, M. Rabenstein and G. Schwarz, *Journal of Polymer Science Part A: Polymer Chemistry*, 2000, **38**, 3019–3027.
- (142) H. T. Srinivasa, *Molecular Crystals and Liquid Crystals*, 2019, **680**, 10–19.
- (143) B. Borah, G. R. Acharya, D. Grajeda, M. S. Emerson, M. A. Harris, A. Milinda Abeykoon, J. Sangoro, G. A. Baker, A. J. Nieuwkoop and C. J. Margulis, *Journal of the American Chemical Society*, 2023, **145**, 25518–25522.
- (144) A. Alfutimie, R. Curtis and G. J. Tiddy, *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 2015, **465**, 99–105.
- (145) A. Alfutimie, R. Curtis and G. J. Tiddy, *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 2014, **456**, 286–295.
- (146) C. V. Kulkarni, *Langmuir*, 2011, **27**, 11790–11800.
- (147) K. J. Baranyai, G. B. Deacon, D. R. MacFarlane, J. M. Pringle and J. L. Scott, *Australian Journal of Chemistry*, 2004, **57**, 145–147.
- (148) T. J. Wooster, K. M. Johanson, K. J. Fraser, D. R. MacFarlane and J. L. Scott, *Green Chemistry*, 2006, **8**, 691–696.
- (149) M. T. Clough, K. Geyer, P. A. Hunt, J. Mertes and T. Welton, *Physical Chemistry Chemical Physics*, 2013, **15**, 20480.
- (150) Y. Cao and T. Mu, *Industrial & Engineering Chemistry Research*, 2014, **53**, 8651–8664.
- (151) D. W. Bruce, C. P. Cabry, J. N. Canongia Lopes, M. L. Costen, L. D’Andrea, I. Grillo, B. C. Marshall, K. G. McKendrick, T. K. Minton, S. M. Purcell, S. Rogers, J. M. Slatery, K. Shimizu, E. Smoll and M. A. Tesa-Serrate, *The Journal of Physical Chemistry B*, 2017, **121**, 6002–6020.
- (152) P. Bharmoria, A. A. Tietze, D. Mondal, T. S. Kang, A. Kumar and M. G. Freire, *Chemical Reviews*, 2024, **124**, 3037–3084.
- (153) C. M. Gordon, M. J. Muldoon, M. Wagner, C. Hilgers, J. H. Davis and P. Wasserscheid, in *Ionic Liquids in Synthesis*, ed. P. Wasserscheid and T. Welton, Wiley, First Edition, 2007, pp. 7–55.
- (154) A. J. McIntosh, J. Griffith and J. Gräsvik, in *Application, Purification, and Recovery of Ionic Liquids*, ed. O. Kuzmina and J. P. Hallett, Elsevier, Amsterdam, 2016.

- (155) S. Koutsoukos, J. Becker, A. Dobre, Z. Fan, F. Othman, F. Philippi, G. J. Smith and T. Welton, *Nature Reviews Methods Primers*, 2022, **2**, 49.
- (156) W. L. Armarego, in *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Eighth Edition, 2017, pp. 1–70.
- (157) M. J. Earle, J. M. Esperança, M. A. Gilea, J. N. Canongia Lopes, L. P. Rebelo, J. W. Magee, K. R. Seddon and J. A. Widegren, *Nature*, 2006, **439**, 831–834.
- (158) A. W. Taylor, K. R. J. Lovelock, A. Deyko, P. Licence and R. G. Jones, *Physical Chemistry Chemical Physics*, 2010, **12**, 1772.
- (159) J. G. Huddleston, H. D. Willauer, R. P. Swatloski, A. E. Visser and R. D. Rogers, *Chemical Communications*, 1998, 1765–1766.
- (160) A. E. Visser, R. P. Swatloski and R. D. Rogers, *Green Chemistry*, 2000, **2**, 1–4.
- (161) J. R. Harjani, R. D. Singer, M. T. Garcia and P. J. Scammells, *Green Chem.*, 2009, **11**, 83–90.
- (162) J. Marek, P. Stodulka, J. Cabal, O. Soukup, M. Pohanka, J. Korabecny, K. Musilek and K. Kuca, *Molecules*, 2010, **15**, 1967–1972.
- (163) P. A. Stadler and P. Oberhänsli, *Helvetica Chimica Acta*, 1959, **42**, 2597–2603.
- (164) M. J. Earle, C. M. Gordon, N. V. Plechkova, K. R. Seddon and T. Welton, *Analytical Chemistry*, 2007, **79**, 758–764.
- (165) N. Rodriguez Rodriguez, A. Van Den Bruinhorst, L. J. B. M. Kollau, M. C. Kroon and K. Binnemans, *ACS Sustainable Chemistry & Engineering*, 2019, **7**, 11521–11528.
- (166) L. R. Jorge, L. K. Harada, E. C. Silva, W. F. Campos, F. C. Moreli, G. Shimamoto, J. F. B. Pereira, J. M. Oliveira, M. Tubino, M. M. D. C. Vila and V. M. Balcão, *Frontiers in Pharmacology*, 2020, **11**, 243.
- (167) T. Blanton, T. Huang, H. Toraya, C. Hubbard, S. Robie, D. Louër, H. E. Göbel, G. Will, R. Gilles and T. Raftery, *Powder Diffraction*, 1995, **10**, 91–95.
- (168) C. A. Schneider, W. S. Rasband and K. W. Eliceiri, *Nature Methods*, 2012, **9**, 671–675.
- (169) S. Vyazovkin, A. K. Burnham, J. M. Criado, L. A. Pérez-Maqueda, C. Popescu and N. Sbirrazzuoli, *Thermochimica Acta*, 2011, **520**, 1–19.
- (170) N. Sbirrazzuoli, *Thermochimica Acta*, 2013, **564**, 59–69.

- (171) S. Vyazovkin, *Isoconversional Kinetics of Thermally Stimulated Processes*, Springer Cham, Switzerland, 2015.
- (172) M. Burkeyev, Y. Tazhbayev, A. Bolatbay, Y. Minayeva, S. Davrenbekov, Y. Nassikhatuly, A. Kovaleva, K. Kutzhanova and A. Kazhmuratova, *Journal of Chemistry*, 2022, **2022**, ed. M. Pitsikalis, 1–8.
- (173) J. Meng, Y. Pan, F. Yang, Y. Wang, Z. Zheng and J. Jiang, *Materials*, 2021, **14**, 2560.
- (174) D. H. Zaitsau and A. Abdelaziz, *Journal of Molecular Liquids*, 2020, **313**, 113507.
- (175) M. E. Brown, *Journal of thermal analysis*, 1997, **49**, 17–32.
- (176) A. K. Galwey, *Journal of Thermal Analysis and Calorimetry*, 2007, **87**, 601–615.
- (177) H. L. Friedman, *Journal of Polymer Science Part C: Polymer Symposia*, 2007, **6**, 183–195.
- (178) M. J. Starink, *Journal of Materials Science*, 2007, **42**, 483–489.
- (179) C. Xu and Z. Cheng, *Processes*, 2021, **9**, 337.
- (180) P. Budrugaec, *Journal of Thermal Analysis and Calorimetry*, 2002, **68**, 131–139.

Appendix A

Differential scanning calorimetry (DSC) data for 1:2 ILs

Table A.1. DSC data for the 1:2 ILS. T_g is the temperature of the glass transition, T_c is the temperature of the cold crystallisation, T_m is the temperature of the endothermic melting transition and T_{L-L} is the temperature of the liquid crystal to isotropic transition. All temperatures are measured during the heating cycle. The enthalpy values are calculated as the area under the curve. The entropy values are calculated by dividing the enthalpy by the transition temperature (in Kelvin).

IL	$T_g / ^\circ\text{C}$	$T_c / ^\circ\text{C}$	$T_m / ^\circ\text{C}$	$\Delta H_m / \text{kJ mol}^{-1}$	$\Delta S_m / \text{J mol}^{-1} \text{K}^{-1}$	T_{L-L}	$\Delta H_{L-L} / \text{kJ mol}^{-1}$	$\Delta S_{L-L} / \text{J mol}^{-1} \text{K}^{-1}$
1:2 BTMAAOC	-95	-34	-20	2.59 ± 0.18	10.24 ± 0.69	17	1.62 ± 0.03	5.59 ± 0.10
1:2 CAOC	-95	-35	-28	1.37 ± 0.04	5.57 ± 0.15	52	1.20 ± 0.01	3.69 ± 0.03
1:2 BTMAAGE	-78	n/a	n/a	n/a	n/a	24	1.89 ± 0.03	6.35 ± 0.11
1:2 CA2OE	-90	-23	-3-4	could not integrate		12	0.90 ± 0.03	3.16 ± 0.11
1:2 CACl	-80	n/a	n/a	n/a	n/a	-10	0.93 ± 0.01	3.53 ± 0.04
1:2 CAGE	-83	n/a	n/a	n/a	n/a	-14	0.37 ± 0.01	1.40 ± 0.02

Appendix B

DSC data for 1:1 ILs and neat acids

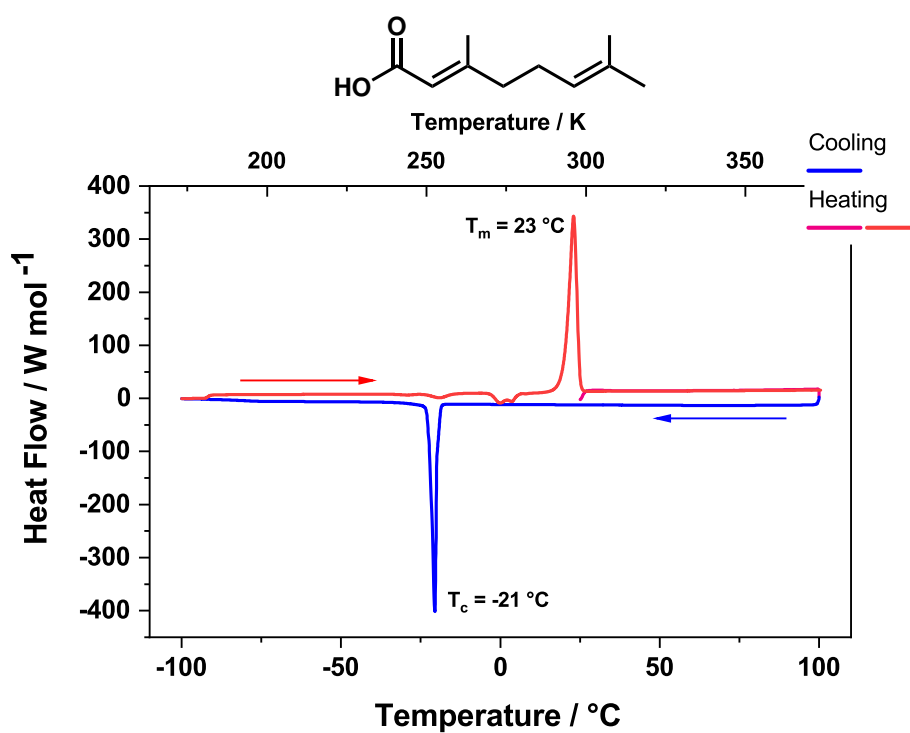


Figure B.1. DSC traces of geranic acid, collected using a heating and cooling rate of $5^{\circ}\text{C}/\text{min}$

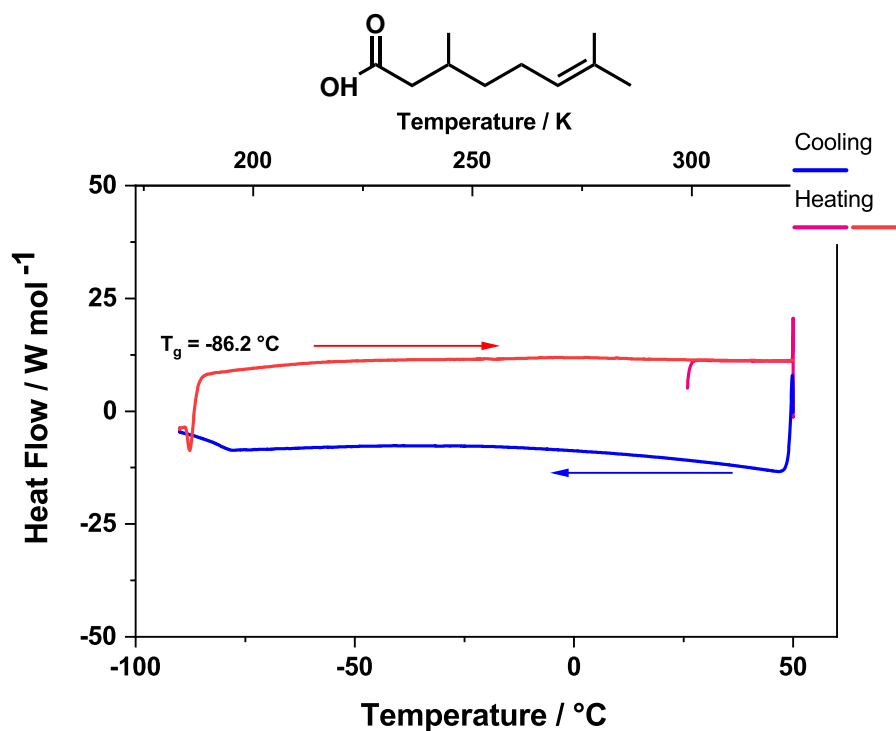


Figure B.2. DSC traces of citronellic acid, collected using a heating and cooling rate of 5 °C/min

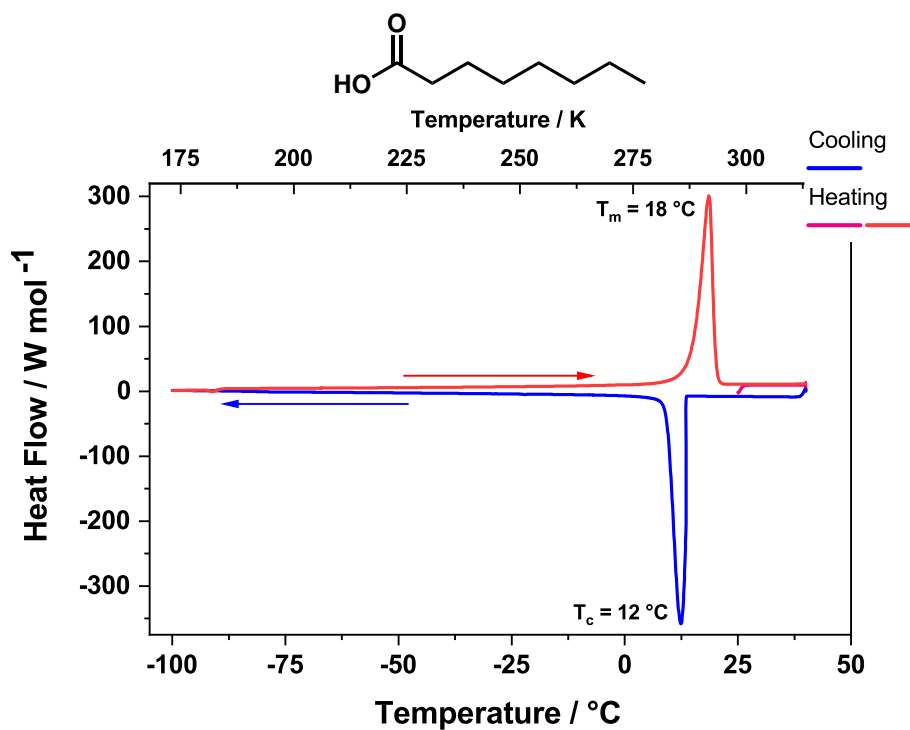


Figure B.3. DSC traces of octanoic acid, collected using a heating and cooling rate of 5 °C/min

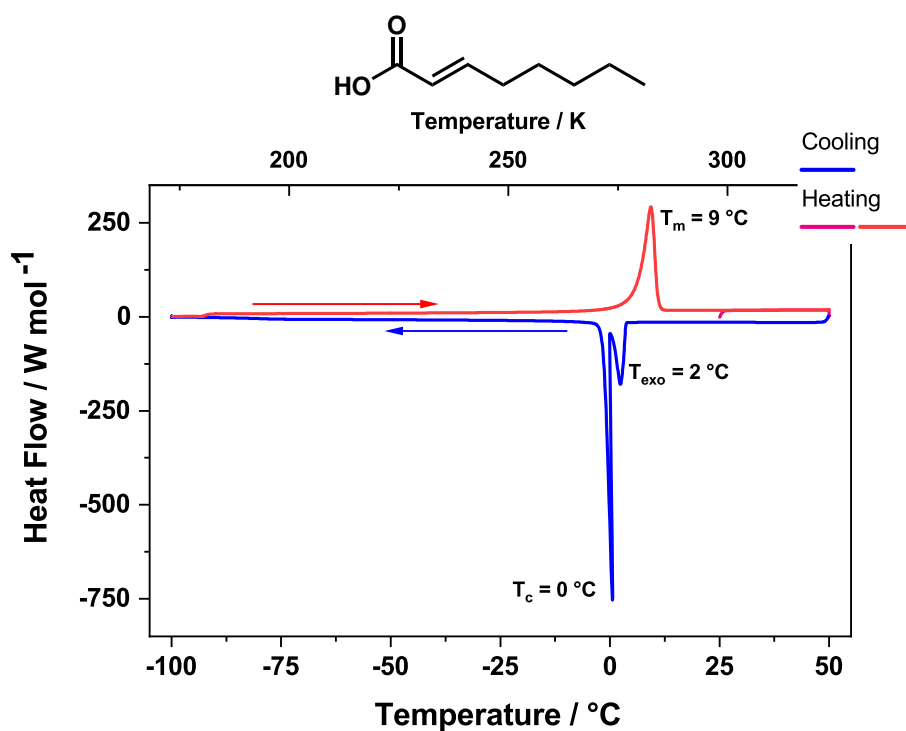


Figure B.4. DSC traces of 2-octenoic acid, collected using a heating and cooling rate of 5 °C/min

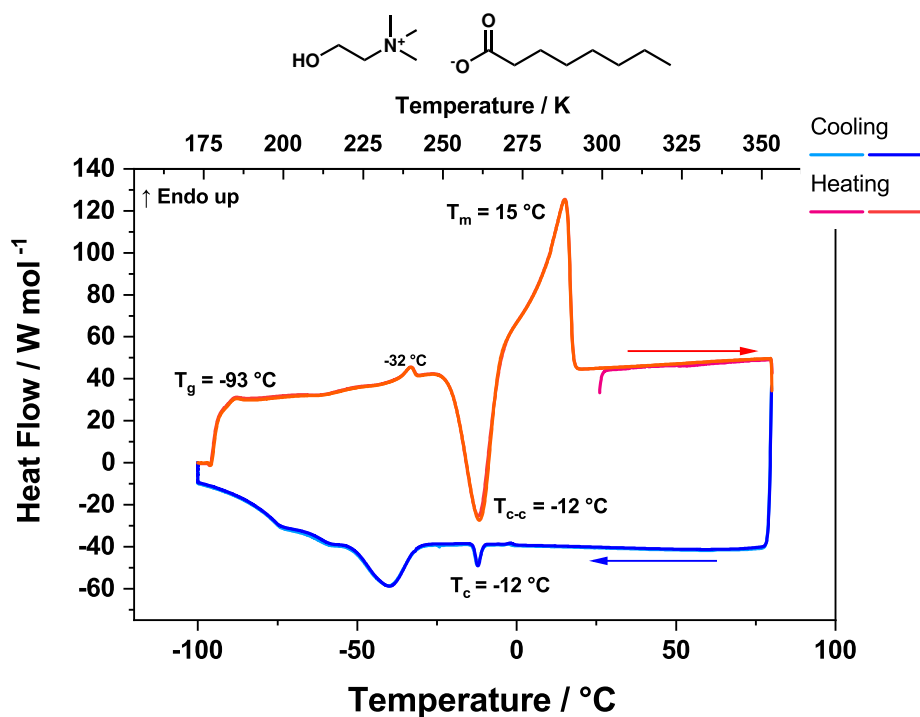


Figure B.5. DSC traces of 1:1 choline and octanoate (CAOC), collected using a heating and cooling rate of 5 °C/min

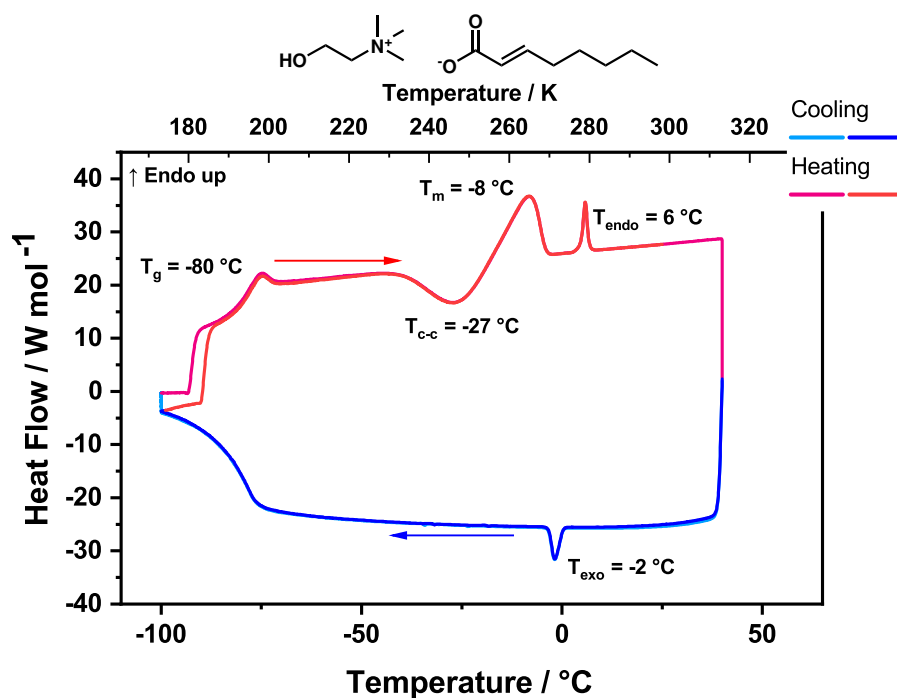


Figure B.6. DSC traces of 1:1 choline and 2-octenoate (CA2OE), collected using a heating and cooling rate of 5 °C/min

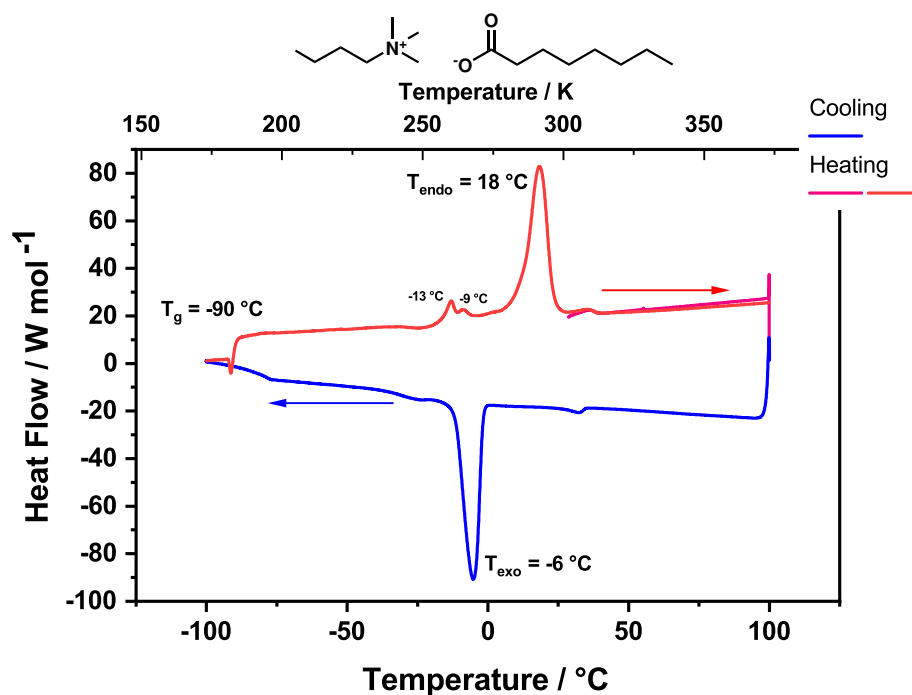


Figure B.7. DSC traces of 1:1 butyltrimethylammonium and octenoate (BTMAAOC), collected using a heating and cooling rate of 5 °C/min

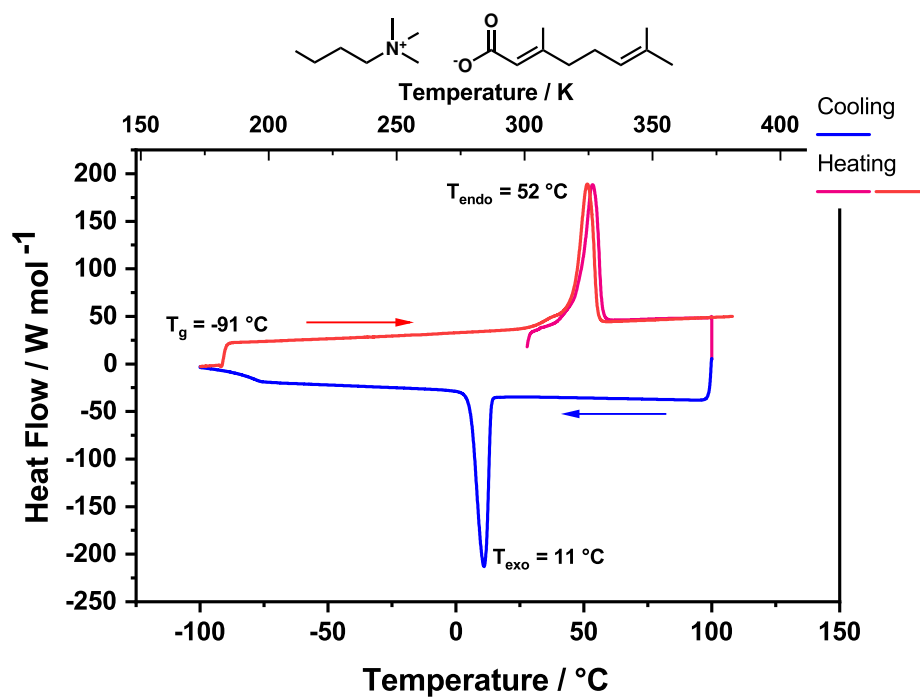


Figure B.8. DSC traces of 1:1 butyltrimethylammonium and geranate (BTMAAGE), collected using a heating and cooling rate of 5 °C/min

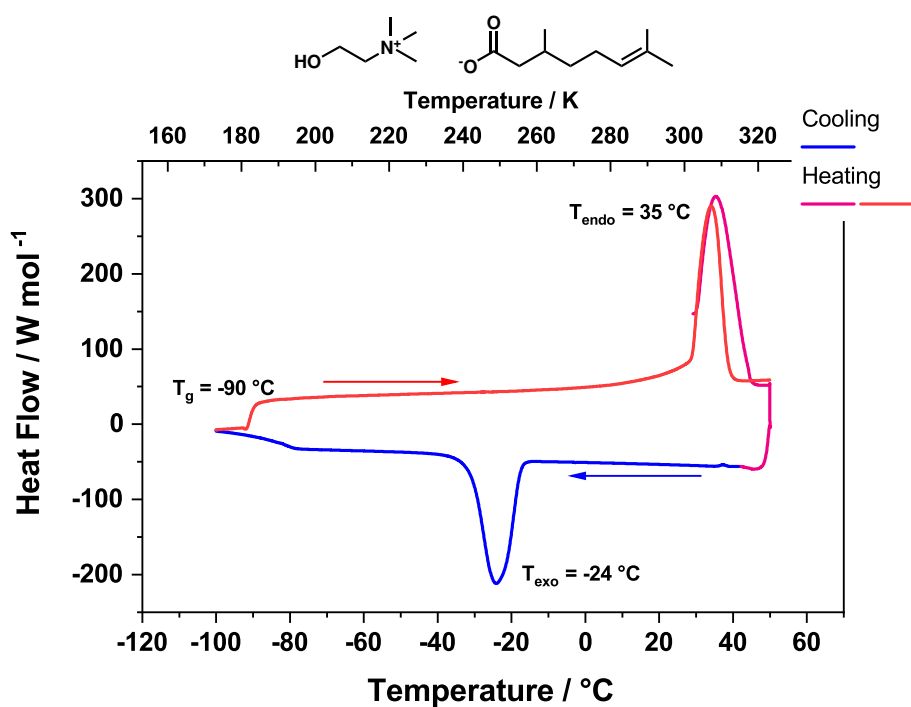


Figure B.9. DSC traces of 1:1 choline and citronellate (CACI), collected using a heating and cooling rate of 5 °C/min

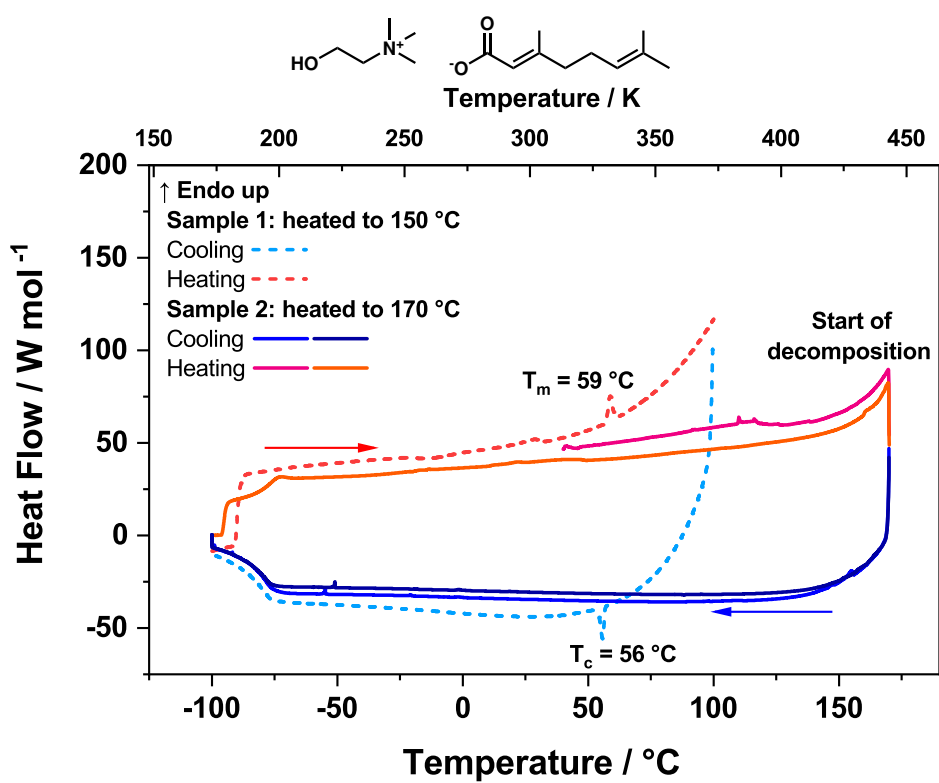


Figure B.10. DSC traces of 1:1 choline and geranate (CAGE), collected using a heating and cooling rate of 5 °C/min

Appendix C

Dynamic viscosity measurements

This data was partially published in Reference [101]

Table C.1 shows the average viscosity values at each temperature, as well as the relative deviation of viscosity δ with respect to the fitting data (Equation C.1).

$$\delta = \frac{100(\eta_{exp} - \eta_{calc})}{\eta_{calc}} \quad (C.1)$$

where η_{exp} is the experimental viscosity and η_{calc} is the viscosity obtained from the VFT fit (Equation 2.7).

Table C.1. Experimental viscosities of the 1:2 ILs. δ is calculated according to Equation C.1

T / K	BTMAAOC		CAOC		BTMAAGE		CACI		CAGE	
	η / mPa s	δ / %	η / mPa s	δ / %	η / mPa s	δ / %	η / mPa s	δ / %	η / mPa s	δ / %
298.15	—	—	—	—	891.64	0.1	865.80	−0.1	1134.25	0.05
303.15	—	—	—	—	616.94	−0.3	617.624	0.2	801.84	−0.2
308.15	—	—	—	—	441.07	−0.1	448.96	0.09	583.83	0.1
313.15	—	—	—	—	323.61	0.2	333.31	0.02	433.34	0.2
318.15	150.30	−0.004	—	—	242.74	0.5	251.91	−0.1	327.11	0.06
323.15	115.83	−0.005	—	—	184.91	0.4	193.13	−0.6	251.19	−0.1
328.15	90.82	0.04	177.89	0.07	143.30	0.2	151.21	−0.5	196.42	−0.1
333.15	72.14	−0.1	141.66	−0.2	113.00	0.2	120.28	−0.2	156.08	0.06
338.15	58.28	0.001	114.89	0.1	90.35	0.2	96.52	−0.3	125.15	−0.2
343.15	47.70	0.2	94.21	0.5	73.10	−0.06	78.55	−0.2	101.86	−0.2
348.15	39.35	−0.02	77.29	−0.1	59.80	−0.4	64.74	0.002	83.87	−0.08
353.15	32.86	−0.05	64.28	−0.3	49.51	−0.6	53.97	0.4	69.74	−0.06
358.15	27.73	0.004	54.03	−0.2	41.48	−0.7	45.58	1	58.61	0.08
363.15	23.60	−0.008	45.89	0.04	34.92	−1	38.64	1	49.59	0.02
368.15	20.25	−0.003	39.15	0.02	29.65	−2	32.94	1	42.37	0.1
373.15	17.51	−0.02	33.64	−0.007	25.40	−2	28.54	2	36.45	0.1
378.15	15.24	−0.07	29.22	0.4	21.81	−3	24.78	3	31.52	−0.01

Appendix D

Isoconversional kinetic analysis of 1:2 BTMAAOC

Further analysis on the decomposition of 1:2 BTMAAOC was performed following the isoconversional method. The kinetic analysis of TGA data has been studied extensively, and there are many publications that present a thorough overview of the field and methods that have been developed through the years. In particular, the reader is directed to references [169–171]. These served as the basis for the following section, which summarises the relevant theory to the analysis performed in this work.

For any material, the decomposition reaction proceeds at a rate given by the basic reaction rate equation

$$\frac{d\alpha}{dt} = k(T)f(\alpha) \quad (\text{D.1})$$

where t is the reaction time and T is the temperature. $f(\alpha)$, also called the reaction model, is a mathematical function that describes the reaction mechanism. α is the conversion, calculated as

$$\alpha = \frac{m_0 - m_t}{m_0 - m_f} \quad (\text{D.2})$$

where m_0 is the initial sample mass, m_f is the mass of the residue obtained at the end of the measurement, and m_t is the sample mass at a given time t .

$k(T)$ is the rate constant, whose temperature-dependence can be described by the Arrhenius

law

$$k(T) = A \exp\left(-\frac{E}{RT}\right) \quad (\text{D.3})$$

where R is the ideal gas constant, A is the pre-exponential factor, E is the activation energy.

Combining equations D.1 and D.3, the rate of decomposition can be expressed as

$$\frac{d\alpha}{dt} = A f(\alpha) \exp\left(-\frac{E}{RT}\right) \quad (\text{D.4})$$

or, considering a linear heating rate $\beta = dT/dt$, this can be rewritten as

$$\frac{d\alpha}{dT} = \frac{A}{\beta} f(\alpha) \exp\left(-\frac{E}{RT}\right) \quad (\text{D.5})$$

The aim of kinetic analysis is to determine parameters A and E associated with the thermal decomposition of a material. Several different methods have been developed for this purpose, the most common of which are isoconversional methods. These rely upon the isoconversional principle which states that at a constant conversion α the reaction model $f(\alpha)$ is constant and the reaction rate $d\alpha/dt$ depends only on temperature. Such methods are often referred to as 'model-free', as they do not require any knowledge of the reaction mechanism. This has proven extremely useful for materials such as polymers and ionic liquids^{172–174}, which tend to have complex decomposition processes. It should be noted that the activation energy calculated in this way corresponds to the global process of decomposition, which may involve multiple reaction steps, as well as other processes (e.g. evaporation). Because of this, it is referred to as an 'apparent' activation energy.^{170,175,176}

Model-free isoconversional methods fall into a number of different categories, with the main ones being differential methods (e.g. the Friedman method)^{171,177} and integral methods (e.g. the Kissinger-Akahira-Sunose method).^{169,171,172} While differential methods have the advantage that they can be applied to any heating program (not just ones with a constant heating rate), they are best suited to differential data, such as the heat flow recorded by differential scanning calorimetry (DSC). When used for TGA measurements (integral-type data), they require the data to be smoothed, which can introduce systematic errors to the calculation of E and A . Integral methods, on the other hand, are better suited to integral-type data, such as TGA, but rely on assumptions that can break down in specific cases. Integral methods are based on equation D.4, which can be rearranged and integrated over time to give an integral form of the

reaction model $f(\alpha)$, denoted as $g(\alpha)$:

$$g(\alpha) = \int_0^\alpha \frac{d\alpha}{f(\alpha)} = A \int_0^t \exp\left(-\frac{E}{RT}\right) dt \quad (\text{D.6})$$

For a linear heating rate $\beta = dT/dt$ $g(\alpha)$ can be expressed in terms of temperature

$$g(\alpha) = \frac{A}{\beta} \int_{T_0}^T \exp\left(-\frac{E}{RT}\right) dT \quad (\text{D.7})$$

where T_0 is the initial temperature of the sample at time t_0 . The integral

$$I(E, T) = \int_{T_0}^T \exp\left(-\frac{E}{RT}\right) dT \quad (\text{D.8})$$

is known as the temperature integral and does not have an analytical solution. Instead, it is replaced with an approximation

$$I(E, T) \approx S(T) - S(T_0) \quad (\text{D.9})$$

$$S(T) \approx \int_0^T \exp\left(-\frac{E}{RT}\right) dT \quad (\text{D.10})$$

$S(T_0)$ is the integral from zero to T_0 , corresponding to the process that may occur before the initial temperature is reached. In traditional integral methods, $S(T_0)$ is assumed to be zero, i.e. assuming that no decomposition occurs before the measurement starts.¹⁷¹ While this is suitable for most materials, Starink *et al.* suggest that, in order to avoid this assumption breaking down and introducing significant errors into the calculation, the initial temperature T_0 must be at least 50–70 °C lower than the temperature at which the decomposition becomes apparent (here, this is considered to be the onset temperature, T_{onset}).¹⁷⁸ There are several 'traditional' integral methods, all of which approximate the temperature integral in slightly different ways. These include the Ozawa-Flynn-Wall, Starink, and Kissinger-Akahira-Sunose (KAS) methods.¹⁷¹ Xu *et al.* have shown that, for ILs, these three integral methods result in similar E values¹⁷⁹ and Vyazovkin *et al.* suggest that the KAS and Starink methods should be used over the OFW method, which is significantly less accurate.¹⁶⁹ In accordance with this, the present work uses the KAS method in calculating the activation energy associated with IL thermal decomposition. The KAS method relies on the equation

$$\ln\left(\frac{\beta_i}{T_{\alpha,i}^2}\right) = C - \frac{E_\alpha}{RT_{\alpha,i}} \quad (\text{D.11})$$

where the α subscript refers to a given extent of conversion and the i subscript denotes one of

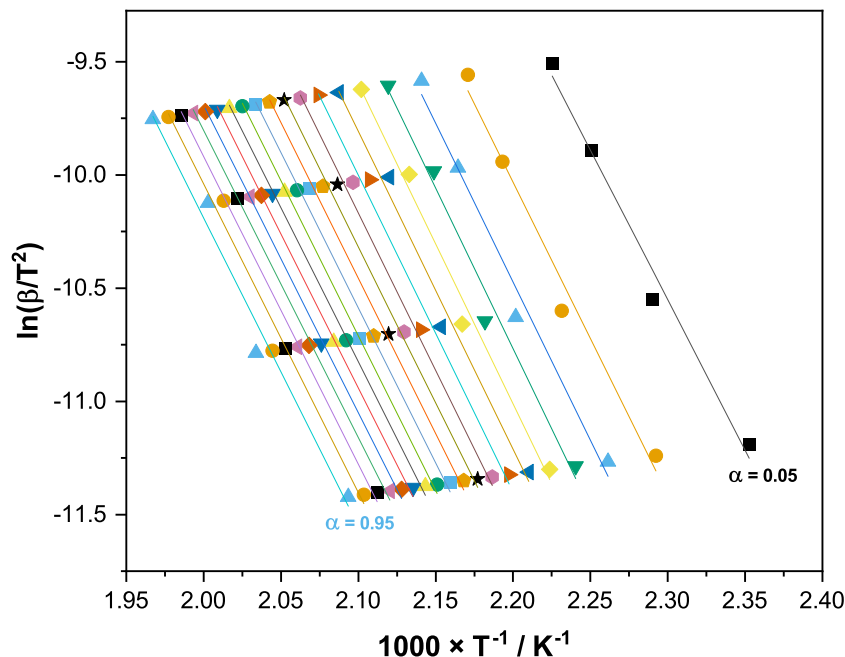


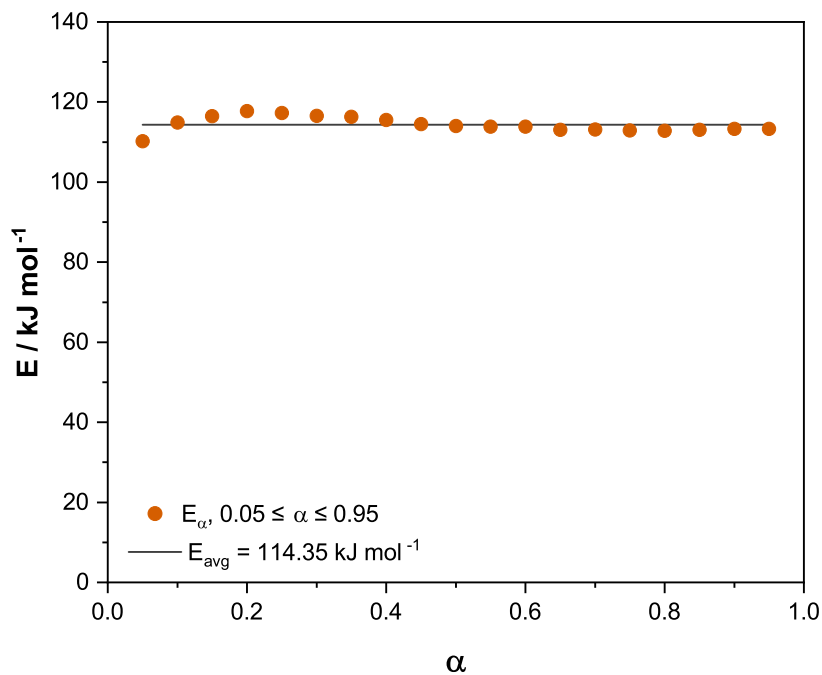
Figure D.1. Kissinger-Akahira-Sunose plot for 1:2 BTMAAOC. Conversion values are between 0.05 and 0.95, with a step of 0.05. The heating rates are 2.5, 5, 10, and 15 °C min⁻¹.

several heating rates. C is a constant. Plotting isoconversional values of $\ln(\beta_i/T_{\alpha,i}^2)$ against $1/T$ for several different heating rates results in a straight line of slope $-E_\alpha/R$. The dependence of E on the extent of conversion α can be determined in this way.

Figure D.1 shows the KAS plot for 1:2 BTMAAOC, based on TGA data obtained using four different heating rates (2.5, 5, 10 and 15 °C/min). In order to analyse the raw TGA data (sample mass and sample temperature) specific conversion values were chosen between 0.05–0.95, with a step of 0.05. For each thermogram, the temperatures T_α at these specific conversions were determined by cubic spline interpolation using OriginLab (2020) software. Each set of four isoconversional points was linearly fitted and the activation energy E_α was calculated from the slope (Table D.1). The variation of E with conversion is shown in Figure D.2. The KAS method relies on the assumption that E is roughly constant across the whole range of α values. According to Vyazovkin *et al.*, this method (like any 'traditional' integral method) is not suitable for processes where the difference between the maximum (E_α^{max}) and minimum (E_α^{min}) values calculated for E_α constitutes more than 20–30% of the average E_α value.¹⁶⁹ In such cases, the use of more complex integral methods or of the Friedman differential method can yield consistent results despite the large variation.^{171,180} For 1:2 BTMAAOC, $E_\alpha^{max} - E_\alpha^{min} = 7.57 \text{ kJ mol}^{-1}$, or approximately 6.6% of the average E_α value of $114.35 \text{ kJ mol}^{-1}$ (solid line in Figure D.2).

Table D.1. Activation energies E_a calculated using the KAS method for 1:2 BTMAAOC

α	E_α	R^2	α	E_α	R^2
0.05	110.2	0.98	0.55	113.8	0.98
0.10	114.9	0.98	0.60	113.8	0.97
0.15	116.4	0.98	0.65	113.0	0.97
0.20	117.8	0.98	0.70	113.2	0.97
0.25	117.2	0.98	0.75	112.9	0.97
0.30	116.5	0.98	0.80	112.8	0.97
0.35	116.3	0.98	0.85	113.1	0.97
0.40	115.5	0.98	0.90	113.3	0.97
0.45	114.5	0.98	0.95	113.3	0.97
0.50	114.0	0.98	E_{avg}	114.4	

**Figure D.2.** Variation of the activation energy E_α (KAS method) with the extent of conversion α for 1:2 BTMAAOC