

STRUCTURES AND REACTIONS OF SOME SIMPLE
ORGANIC ACIDS AND THEIR METAL COMPLEXES
IN AQUEOUS SOLUTIONS

by

BENJAMIN BRYAN SMITH

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Chemistry Department,
Imperial College,
London, S.W.7.

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ABSTRACT

Proton resonance spectra of some $\alpha\beta$ -unsaturated mono-, di- and tricarboxylic acids have been measured in aqueous solution as a function of pH. Information about the ionisation sequences of the di- and tricarboxylic acids has been deduced, and the chemical shifts have been explained qualitatively.

Measurements have been made on the isomerisation of cis aconitic acid as a function of pH and temperature. Approximate half lives and final equilibrium ratios of the isomers are reported.

The complexes formed by cobalt(II) with some $\alpha\beta$ -unsaturated carboxylic acids have been studied by means of their contact shift spectra. In some cases, the formation of chelates is indicated.

Some addition reactions of $\alpha\beta$ -unsaturated acids with amines and thioglycollic acid have been followed by proton resonance spectra. The products have been characterised, where possible, by their proton resonance spectra and, in some cases, by the spectra of their complexes with cobalt(II).

A number of aminopolycarboxylic acids have been prepared, and their complexes with nickel(II) and cobalt(II) studied by means of their contact shift spectra. Assignments have been made, where possible, and the structures of the complexes are discussed. The large shifts of the protons in the five and six membered chelate rings in nickel(II) complexes have been explained in terms of isotropic contact shifts, and an approximate correlation between

the observed N - CH shifts and the Ni - N - C - H dihedral angles has been derived. Differences in shifts between the nickel(II) and cobalt(II) complexes have been attributed mainly to a pseudo-contact contribution to the shifts in the latter complexes, and an approximate estimate of this effect has been obtained.

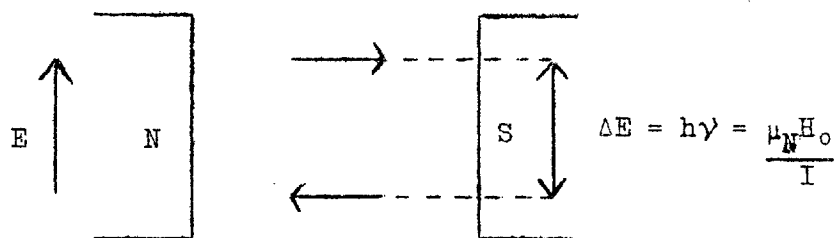
CHAPTER I
INTRODUCTION.

Nuclear Magnetic Resonance (n.m.r.)^{1,2}

Since this thesis is largely concerned with the measurement of n.m.r. spectra, the main features of this technique are outlined below. Several isotopic nuclei possess magnetic moments (μ_N), which have values which are small (of the order of $1/1000$ th of the electronic magnetic moment, μ_e), but characteristic of the particular species. In a magnetic field, the interaction energy of the nucleus with the field depends on the orientation of the nucleus and is quantised, only certain energies being allowed, corresponding to different orientations of the nucleus. The number of permitted orientations is $(2I + 1)$, where I is the nuclear spin quantum number.

The most important nucleus, and the one whose n.m.r. spectra are studied in the present work, is the proton, i.e. the nucleus of the hydrogen atom. For the proton (represented as H^1), there are two possible orientations in a field, corresponding to alignment of the nucleus with (low energy), or against (high energy) the field; here $I = \frac{1}{2}$, usually expressed by saying that the spin of the proton is $\frac{1}{2}$. In the diagram (see overleaf), ΔE is the energy difference between the two levels in the field of strength H_0 . The resonance frequency, ν , given by

$$\nu = \frac{\mu_N^H}{hI} \text{-----} (1)$$



is the frequency of the radiation needed to induce transitions between them. In this work, the frequency was fixed at 56 45 mcs./sec. (1 mcs./sec. = 10^6 cs./sec.), for which protons come to resonance at an H_0 value of about 13,236 gauss; the field is changed linearly, slightly, to cover the spectra. Generally, for magnetic fields of the order of 10,000 gauss, resonance frequencies for other nuclei lie in the radio frequency region (1-100 mcs./sec.).

Some other nuclei (e.g. F^{19} , P^{31}) have $I = \frac{1}{2}$ and behave like the proton, except that their magnetic moments, and hence their resonance conditions, are different. Many nuclei have $I > \frac{1}{2}$, in which case the number $(2I + 1)$ of energy levels, in a magnetic field, is greater than two. If the energy of such a nucleus depends only on interaction with the magnetic field, the levels are equally spaced, and transitions only occur between adjacent levels, so that the above formula still applies. However, when $I > \frac{1}{2}$, a nucleus also possesses a nuclear electric quadrupole moment (represented by the symbol Q), which arises from a non spherically symmetrical charge distribution. This can interact strongly with electric field

gradients at the nucleus, and the above formula does not strictly apply. Some nuclei (e.g. C^{12} , O^{16}) have $I = 0$ and zero magnetic moments.

When placed in a magnetic field, a collection of equivalent nuclei (considered to have $I = \frac{1}{2}$ for simplicity) in a macroscopic sample come to thermal equilibrium with their surroundings and adopt a Boltzmann distribution, so that the number in the upper level is very slightly less than the number in the lower energy level. This results in a net absorption of radio frequency radiation, since in the applied R.F. radiation, transitions are equally likely upwards or downwards.³ The process of absorption tends to equalise the population of the two levels but the absorption condition (an excess in the lower level) is maintained by relaxation processes.

Spin-lattice relaxation.^{4,5} In addition to the applied field H_0 , a nucleus experiences local magnetic dipole fields (up to approximately 15 gauss) from nearby magnetic nuclei, both in the same molecule and in neighbouring molecules. The thermal motions of the molecules in liquid samples make the local fields fluctuate over a wide frequency range. The most intense components of the fluctuating fields are at frequencies of about 10^{10} - 10^{11} cs./sec., but some weak components are at the resonance frequency, and it can be shown that these induce transitions downward with a greater probability than upward.⁶ A nucleus in the upper level is said to "relax" to the lower level, the energy ΔE being given up as extra thermal energy to the surroundings (the "lattice"). This "spin-lattice relaxation" process allows the collection of nuclei in a

sample to come to thermal equilibrium when a magnetic field is applied, and still maintains a greater population in the lower level in the presence of applied R.F. radiation at the resonance frequency.

The efficiency of the process is expressed in terms of a characteristic spin-lattice relaxation time T_1 , which is the time required for all but $\frac{1}{e}$ of the equilibrium excess number in the upper level to drop to the lower level. Since the transitions also reduce the lifetime of a nucleus in any one level, T_1 also represents the average lifetime. When this is long, it follows from the Uncertainty Principle ($\Delta E \Delta t = h$) that each level will be sharply defined, hence ΔE is sharply defined, and the absorption line(s) can be very narrow. This is often the case for diamagnetic liquids, T_1 often lying in the range 1 to 100 seconds. In diamagnetic solids, due to the much greater restriction on molecular motions, T_1 can be much longer and is sometimes of the order of hours, although the lines are very broad due to other causes (see below). For nuclei with quadrupole moments, interaction of the quadrupole with fluctuating field gradients provides another method of spin-lattice relaxation, giving very short relaxation times T_1 , and consequently, broad lines.

Spin-spin relaxation,^{4,5} which can be characterised by a spin-spin relaxation time T_2 , involves a direct exchange of an amount of energy, ΔE , between a nucleus in an upper level and one in the lower level. This again broadens the resonance line due to

a shortening of the time spent in one level. The effect is greatest in solids (i.e. T_2 smallest) where nuclei are in fixed positions. Broadening of the lines is then also produced by the direct effect local fields of neighbouring magnetic nuclei which, since they are held in "rigid" lattice positions, are not averaged to zero as they are in liquids. In general, line widths are proportional to $(\frac{1}{T_1} + \frac{1}{T_2})$; the latter term is sometimes written as $\frac{1}{T_2}$, to include contributions from local fields and field inhomogeneities.

Chemical Shifts. When a diamagnetic molecule is placed in a magnetic field H_0 , the electrons develop an induced circulation about the field axis such as to generate a magnetic field opposing the applied field. This induced diamagnetic circulation (and hence the diamagnetic moment) is proportional to the strength of the applied field and is the origin of diamagnetism in molecules. A nucleus in the molecule experiences the induced field in addition to that of the applied field such that,

$$H_{(\text{nucleus})} = H_0 (1 - \sigma) \text{ -----(2)}$$

where $H_{(\text{nucleus})}$ is the field at the nucleus, and σ is a dimensionless shielding factor, which depends on the precise chemical environment of the nucleus. Thus, nuclei in different chemical environments will come to resonance at different values of the applied field (or frequency) and the resulting separations in line positions, called chemical shifts, are proportional to the applied field H_0 . They are given by,

$$\delta = \frac{H - H_{\text{reference}}}{H_{\text{reference}}} = \frac{\nu - \nu_{\text{reference}}}{\nu_{\text{reference}}} \text{ -----(3)}$$

where $H(\nu)$ is the resonance position of the nucleus, and $H_{\text{reference}}$ ($\nu_{\text{reference}}$) is the resonance position of some arbitrarily chosen reference. δ is usually expressed in parts per million (p.p.m.) or sometimes directly in frequency units as $(\nu - \nu_{\text{reference}})$. The reference substance is a convenient standard against which the resonance lines of other substances are compared; to eliminate bulk susceptibility effects it is used as an internal reference, being dissolved in the sample. For protons, tetramethylsilane (T.M.S.) is mainly used; its line position (in p.p.m.) is arbitrarily taken as 10.00 to define the τ scale. In aqueous solutions the methyl resonance of t-butanol ($\tau = 8.75$)⁷ is often used.

An important contribution to the shielding of a nucleus comes from the electrons of its own atom. The shielding depends on neighbouring groups in the molecule, partly because they affect the electron density round the nucleus, and partly because their presence affects the potential field in which the electrons move and restricts their circulation. Usually, the restriction of circulation depends on the orientation of the molecule in the applied field. It is possible to measure the resultant anisotropy of the shifts (e.g. for C^{13} in a single crystal of calcite, $CaCO_3$),⁸ but for molecules in solution, the observed shifts are averages over all molecular orientations.

Another contribution to the shielding is the small additional fields at a nucleus which come from the induced circulations in other groups in the molecule. These fields average

to zero in solution, unless the groups themselves are magnetically anisotropic, which they usually are. The resulting "long range shielding" can be calculated knowing the distance and orientation of the groups, and the magnitude of their induced moments (expressed in terms of their principal susceptibilities). A particular case is that of aromatic groups, whose anisotropy arises from induced "ring currents" in molecular orbitals spread over several atoms. Long range shielding effects are no greater than about 1-2 p.p.m., and are noticeable mainly with proton resonances, for which the range of shifts is fairly small, since the hydrogen atom has only one 1s electron.

Spin-Spin Coupling. In addition to chemical shifts, n.m.r. lines frequently show fine structure (splittings), arising from interactions between non-equivalent nuclei (of different types, or the same type but with different chemical shifts) in the same molecule. These interactions are independent of the magnetic field and are proportional to the product of the magnetic moments of the interacting nuclei; they usually arise from a coupling of the nuclear spins via nuclear spin-electron spin interactions, which are transmitted by electron spin-electron spin interactions through the chemical bonds linking the nuclei. The splittings are usually expressed as J cycles/sec. (cps.) and may be either positive or negative; a positive coupling means that the antiparallel arrangement of nuclear spins is more stable than the parallel.

The number of lines produced in a group of equivalent

nuclei of type A by another of type B, in the same molecule, is $(2n_B I_B + 1)$, where n_B is the number of equivalent nuclei in group B with spin I_B . Similarly, the number of lines produced in group B is $(2n_A I_A + 1)$. The relative intensities of the lines are given by the corresponding binomial coefficients. The above is the case for first order splittings and only applies strictly when $\delta \gg J$. When $\delta \approx J$, the spectrum becomes more complex, and must be analysed by more exact mathematical methods;⁹ several of the results are tabulated.^{10,11}

Chemical Exchange.^{12,13,14} Chemical exchange frequently affects the observed values of both chemical shifts and splittings. In the absence of exchange, a sample containing two molecular species can show two sets of sharp lines, one set from each species. The same is observed with slow exchange between the species, i.e. when the frequency of exchange is much less than the frequency separations between the lines from a given group in the two species. For rapid exchange, in which the frequency of the exchange is much greater than the frequency separations, only one set of lines is observed, each representing weighted averages of the shifts and splittings over the two species. If the exchange rate is increased from slow to rapid, the separate lines from a given group first broaden, then coalesce to a broad band, which finally sharpens to the averaged line(s). These intermediate shapes can be compared with those calculated for different chemical lifetimes, from which the latter can be estimated.

Exchange processes can be either intermolecular, such as between $R.COOH$ and $R.COO^-$, or intramolecular, such as between the rotational isomers resulting from restricted rotation about a single bond. In the latter case, rotation is usually fast enough at room temperature to preclude the observation of separate lines from each rotational isomer of a molecule. In some intermolecular exchanges, spin-spin splittings are averaged to zero if the bonding between the nuclei is broken during the exchange. Similarly, splittings can be artificially removed by inducing one nucleus to "jump" between its levels at a rate fast compared with the coupling constant, J cps. This is the basis of the double resonance (or spin decoupling) technique which is very useful in the analysis of spectra. Also, splittings from nuclei with electric quadrupoles (e.g. N^{14}) are often averaged out because of the short relaxation time T_1 , which prevents the nucleus spending a long enough time in one level.

Paramagnetic n.m.r. Spectra.¹⁵

So far only the spectra of diamagnetic samples have been considered. The presence of paramagnetic ions has a profound effect on the sharp resonance lines of a diamagnetic liquid. Since μ_e is of the order of 10^3 times as large as μ_N , the fluctuating magnetic fields due to paramagnetic ions are relatively intense, and can provide a very effective method of spin-lattice relaxation. The consequent shortening of the nuclear T_1 may result in considerable broadening of the resonance lines. The effect on the nuclear T_1 depends on the magnitude of the electron spin-lattice relaxation

time, T_{1e} . Ions such as high spin Mn(II), Cr(III) and Fe(III) (and also molecular oxygen), for which T_{1e} is longer than the correlation time ($\approx 10^{-11}$ sec.) for molecular motions, are very efficient in shortening the nuclear T_1 , and hence in broadening the resonance lines of nuclei in the same sample. These effects are particularly marked for nuclei in molecules bonded as ligands to the paramagnetic ions, partly because they are closer to the unpaired electron(s), and partly because a fractional unpaired electron can be transmitted to their own atoms through the bonds, by delocalisation for example. The lines of such nuclei are usually too broad to be observed.

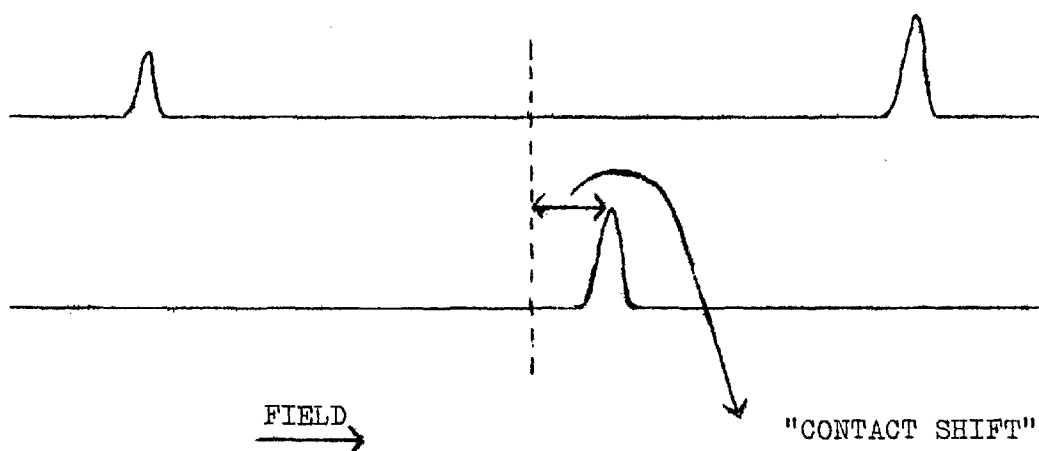
With some ions, in particular high spin Co(II) and Ni(II), the T_{1e} is extremely short, and can be shorter than the correlation time for molecular motions so that the local field is averaged out before the ion moves appreciably, and the fluctuating field is less intense. These ions have less effect in shortening the T_1 of nuclei in the same sample, whose resonances, although broadened, can be observed quite sharply even in solutions in which the metal ions have concentrations of several molar. Even when the nuclei are in ligands bonded to such ions, their resonances can be observed. They are broader than those of non-bonded species (since they are closer to, and also coupled directly to, the unpaired electron(s)), but not so broad as to obscure the observation that the lines of these ligand nuclei are often greatly displaced from their positions in the diamagnetic ligand.

These displacements are produced by one or both of two effects, namely, contact shifts and pseudocontact shifts.

Isotropic hyperfine contact shifts.^{16,17} These are called isotropic as they are not dependent on the orientation of the molecule with respect to the field, and are thus not averaged out by random reorientation in liquids. The interaction responsible for producing contact shifts occurs between the nucleus and a fractional unpaired electron spin, which is present in an orbital having s character of the atom containing the nucleus. Only s orbitals have a finite electron density at the nucleus; the interaction is often called Fermi contact interaction. Unpaired electron density in the orbitals of the ligand atom results from transmission from the metal ion via the bonding electrons, either by spin polarisation or delocalisation or both. The mechanism is roughly analogous to nuclear spin-spin coupling.

Since the electron spin resonance (e.s.r.) spectra of paramagnetic complexes frequently show splittings due to this contact interaction between the electron and nuclear spins in the ligands, it might be expected that, in a complex (containing one unpaired electron for simplicity), the unpaired electron would produce a doublet splitting of the n.m.r. line from each of the non-equivalent groups of nuclei, which would be extremely large (up to 100 mcs./sec. is found for the e.s.r. splittings). However, this splitting would be partially averaged out due to the short T_{1e} , usually leaving lines too broad to be seen. However, when T_{1e} is extremely short,

as in the cases of Co(II) and Ni(II) ions, the averaging can be almost complete, and since the nuclear T_1 is then not greatly shortened, this results in observably sharp lines for the nuclei in the complex, as shown below for one line (i.e. one group of nuclei).



The observed line is a weighted average of the expected two split components. Equally intense components would average to the diamagnetic position. However, the components would be of unequal intensity because at thermal equilibrium the lower of the electron energy levels is populated about 1% more than is the upper level. Hence the observed position, being a weighted average, is displaced from the corresponding diamagnetic position in the direction of the more intense component, and by an amount proportional to the splitting.

The displacements (contact shifts) are sometimes measured relative to the position of the corresponding diamagnetic compound

to allow for the effects of diamagnetic shielding. They can be either upfield or downfield depending on whether the fractional unpaired electron spin on the proton is positive or negative (i.e. whether the upfield or downfield component is more intense). The preferred alignment, in a magnetic field, of the unpaired electron on the metal ion is taken as positive, but the fractional unpaired electron spin density on nuclei in the ligand can be either positive or negative, depending on the mechanism of transmission. The above diagram corresponds to a fractional negative spin density on the ligand nucleus.

The magnitude of the shift depends on the size of the spin density induced on the atom containing the nucleus, and thus for any one type of nucleus, it also depends on the bonds between the metal ion and the group containing the nuclei. Thus, it is sensitive to molecular structure. The sign of the spin density also depends on the molecular structure. Non-equivalent nuclei (giving separate lines in the spectrum of the diamagnetic ligand) in a ligand give different contact shifts, whose magnitude can be as much as several hundred p.p.m. relative to the corresponding diamagnetic complex. These large shifts correspond to no more than 0.1 of an unpaired electron delocalised over the ligand; in the hydrogen atom, with one whole unpaired electron in the $1s$ orbital, the interaction corresponds to a shift of about 10^4 p.p.m..

For a given group of nuclei in a given complex, the magnitude of the observed shift (since it depends on the weighted

average of two components which differ by a Boltzmann factor) is proportional to the applied field and inversely proportional to the absolute temperature. For a paramagnetic ground state complex which follows the Curie law, the contact shift is given by,

$$\frac{\Delta H}{H_0} = - A \frac{\gamma_e}{\gamma_N} \frac{g \beta S (S+1)}{3 k T} \quad \text{-----} \quad (4)$$

where ΔH is the displacement (in field units), H_0 is the applied field, γ_e and γ_N are given by μ_e/h and μ_N/h respectively, g is a proportionality factor representing the magnetic moment of the complex, β is the Bohr magneton, S is the total spin quantum number ($S = 1$ for Ni(II), $S = 3/2$ for Co(II)), and T is the absolute temperature. A is the hyperfine coupling constant, equivalent to the splitting that would be observed.

Contact shifts have been observed for several types of magnetic nuclei in paramagnetic complexes. In the present work only proton contact shifts are studied. In different environments these may result from different mechanisms for the transmission of electron spin density. For C-H protons in an unsaturated group (in which the C atoms have sp^2 hybridisation), the unpaired electron is often (though not always) delocalised through the π system, which is shown by an alternation of the signs of spin density along the group (i.e. by an alternation of the direction of the shifts). For these systems a quantitative relationship (derived from e.s.r. spectra) exists between A (obtained from the contact shifts) and the spin density on each carbon atom of a conjugated system. The

elegant work of Phillips and coworkers on Ni(II) complexes of aminotroponeimines is worthy of mention.^{15,18} For C-H protons in aliphatic systems (in which the C atom is sp^3 hybridised), no quantitative relationship between the shift and the spin density is yet known, but the shifts are sensitive to the geometry of the molecule. The mechanism may involve delocalisation over σ bonds, since the shifts are in one direction only, and also are rapidly attenuated along an aliphatic C skeleton; their spatial dependence suggests that the mechanism may be analogous to the spin-spin coupling between protons in aliphatic groups. For protons in N-H bonds, the situation appears to be similar; the shifts are less likely to be averaged out by exchange with solvent protons than in labile diamagnetic systems because they are so large.

Pseudocontact shifts.^{16,17,19,20} These involve the combined actions of electron spin-orbit interaction, (electron orbit-nuclear spin) dipolar coupling and (electron spin-nuclear spin) dipolar coupling. A nucleus in a paramagnetic complex experiences a magnetic field arising from the induced paramagnetic moment on the metal ion. In solution, due to random reorientation, this magnetic field averages to zero unless the metal ion has an anisotropic magnetic moment. When this is so (e.g. high spin Co(II)), the nucleus experiences a residual net field. The effect is analogous to the long range shielding in diamagnetic high resolution n.m.r., which arises from groups which have anisotropic diamagnetic induced moments. Like long range shielding, this residual field

can be calculated, and is given by,

$$\frac{\Delta H}{H_0} = - \frac{\beta^2 \cdot S(S+1)}{27kTd^3} \cdot (3 \cos^2 \alpha - 1)(g_{\parallel} - g_{\perp})(g_{\parallel} + 2g_{\perp}) \text{----(5)}$$

where d is the distance between the proton and the paramagnetic metal ion, $g_{\parallel}$ and $g_{\perp}$ are g -factors representing the values (which can be determined experimentally) of the magnetic moment of the complex aligned parallel and perpendicular to the field direction respectively, α is the angle between the axis of symmetry of the complex and the radius vector from the metal atom to the proton, and the other symbols have their usual meaning.

For octahedral complexes, it has usually been found that the pseudo-contact contribution to the contact shift for Ni(II) is zero or small. The ground state of Ni(II) ($3d^8$), in an octahedral environment, would not be expected to exhibit any significant paramagnetic anisotropy, and this is confirmed by measurements of the static susceptibility of Ni(II) complexes. Octahedral Co(II) ($3d^7$) might be expected to give rise to anisotropy in view of its "unbalanced" d orbitals, and indeed, this is found to be so from magnetic susceptibility measurements on Co(II) complexes. The presence of pseudocontact contributions can be deduced by n.m.r. spectra in several ways:¹⁵

(a) By comparison of the spectra of Ni(II) and Co(II) complexes with the same ligand, provided they have the same conformations and structures. Assuming that the transmission of electron spin density occurs by the same mechanism in both cases,

it would be expected that the relative shifts for the same protons would be in the same ratios. If this is found not to be the case then the differences can be attributed to pseudocontact shifts in the Co(II) complexes.

(b) By comparison of solid and solution spectra.

Isotropic contact shifts of a paramagnetic complex are the same in both solid and solution phases, whereas pseudocontact shifts are not. This method is, however, limited due to the severe nuclear dipole-dipole broadening of the resonances in solids

(c) The two processes involve different dependences of the nuclear T_1 and T_2 on the magnitudes of the observed shifts.

The pseudocontact shift is essentially a magnetic field effect, transmitted through space, and is thus not related to the electronic structure and bonding in complexes. However, it is sensitive to the geometrical arrangement of nuclei relative to the metal ion, and depends on distances and angles.

Hence although the contributions of contact and pseudocontact effects are often difficult to distinguish, both are sensitive to the geometry of a ligand and thus, so are the observed shifts. The fact that the observed shifts are very large is useful in that small structural changes can be detected, provided the lines are not too broad. Also, exchange processes (for example, between free and bound ligand) are less likely to average out the line positions than in diamagnetic spectra.

In certain cases (e.g. the Ni(II) aminotroponeimineates)^{15,18}

there exists a rapid equilibrium between a diamagnetic (planar) species and a paramagnetic (tetrahedral) species; the observed shifts are then weighted averages of the diamagnetic and paramagnetic complexes. These cases become apparent since the observed shift is not simply inversely proportional to the absolute temperature, but involves a more complicated temperature dependence.

CHAPTER II

Part A. Proton Resonance Spectra of Some Olefinic

Acids in Aqueous Solution.

This investigation was undertaken as part of a broader study of the effects of diamagnetic and paramagnetic metal ions on $\alpha\beta$ -unsaturated carboxylic acids. The spectra of a number of unsaturated acids have been measured, in aqueous solution, as a function of pH; the chemical shifts provide some information about the ionisation sequences. Previously, other workers have measured the spectra of some of the acids and/or their esters in various solvents.²¹⁻³⁵ (See also Tables). Of particular note is the work of Jackman and Wiley,²⁴⁻²⁶ who pioneered the use of n.m.r. in assigning configurations to pairs of geometrical isomers of olefinic derivatives. Recently, Collin and Sternhell³¹ have measured the spectra of a few of the acids and their potassium salts in D₂O, but no detailed study as a function of pH appears to have been done.

Experimental.

The spectra were recorded at 56.45 mcs./sec. on a Varian 4311 spectrometer at $22 \pm 1^\circ\text{C}$. Since the spectrometer does not have a field-frequency locking system, it is not stable enough to allow calibrated recorder paper to be used. Each spectrum was calibrated by the sideband technique, t-butanol ($\sim 1\%$) being used as the internal reference. Chemical shift positions are the average of

at least six determinations for each sample (of different pH) for each acid. The error in the shifts is about ± 0.01 p.p.m.; they were converted into τ values, taking τ of t-butanol as 8.75.⁷ Coupling constant error is ± 0.2 cycles/sec.. The concentrations of the acids were 0.15 M except for the less soluble fumaric acid (0.04 M) and monoethyl fumarate (0.08 M). Preliminary experiments with several of the acids indicated no appreciable concentration dependence of the shift or couplings over a concentration range of 0.04 M to 0.25 M. pHs were measured at $20 \pm 1^\circ\text{C}$ with a Cambridge bench type pH meter, using a miniature glass and calomel electrode assembly. A small glass cell was constructed to allow the measurement of small quantities of solution (ca. 0.5 ml.). The required pH was obtained by the addition of KOH or HCl before diluting to the required concentration, and about 15 - 30 samples (at different pH) of each acid of the same concentration were used.

Materials. Fumaric acid, maleic acid, trans crotonic acid and methacrylic acid (α -methyl acrylic acid) were obtained from B.D.H. Ltd., and mesaconic acid, citraconic acid, itaconic acid and $\beta\beta'$ -dimethylacrylic acid from L. Light and Co.. They were used as supplied, their n.m.r. spectra being taken as sufficient criteria of purity.

Cis crotonic acid was prepared according to Hatch and Nesbitt.³⁶ Yield 4 g. (32%), b.p. $170-172^\circ$ (lit.^{36,37} $169-170^\circ$).

Trans aconitic acid was prepared by dehydrating citric acid.³⁸ Yield 38 g. (22%), m.p. $191-194^\circ$ (lit.³⁹ $194-198^\circ$).

Analysis. Calculated for $C_6H_6O_6$: C 41.38, H 3.45, O 55.17.

Found: C 41.60, H 3.47, O 54.92

Cis aconitic anhydride was prepared from trans aconitic acid by a modified literature method.⁴⁰ Trans aconitic acid, in an evacuated flask, was heated to about 140° on an oil bath and maintained at 135 – 145° for about one hour. During the heating, the white solid melted to give a dark brown liquid and a colourless liquid condensed on the cooler, upper parts of the flask, forming a white solid. After removal from the oil bath and cooling, the contents of the flask were refluxed with benzene for about five minutes. The benzene extract was separated and, on cooling, deposited white, needle-shaped crystals. Further extractions of the brown residue gave more product, which was recrystallised from benzene and dried in vacuo. Yield 6 g (40%), m.p. 70 – 72° (lit.³⁹ 74°).

Analysis. Calculated for $C_6H_4O_5$: C 46.15, H 2.56, O 51.29

Found: C 46.05, H 2.39, O 51.07

The product, dissolved in H_2O , gave an n.m.r. spectrum consistent with cis aconitic acid only; also the pH values of the solutions, containing known amounts of added alkali, showed that a tribasic acid was present.

Monoethyl maleic acid was prepared as the potassium salt.⁴¹ Yield 33 g. (70%), m.p. $\sim 180^\circ$ (dec.) (lit.^{41,42} $\sim 180^\circ$ (dec.)).

Analysis. Calculated for $C_6H_7O_4K$: C 39.54, H 3.88, O 35.12

Found: C 39.23, H 3.77, O 34.90

Monoethyl fumaric acid. After abortive attempts,^{41,42} the

pure product was obtained from the isomerisation of monoethyl maleic acid using $\text{S}_2\text{O}_3^{=}$ as catalyst.⁴³ Dilute HCl was added slowly with stirring to a solution of potassium monoethyl maleate (27.3 g.) and sodium thiosulphate (37.2 g.) in H_2O (300 ml.) till the pH was about 2-3. The cloudy solution was allowed to stand at room temperature for 48 hours, after which time n.m.r. analysis showed isomerisation to be complete. Acidification to pH 1-2 and several extractions with ether (200 ml.) gave the crude yellow product (17 g., 63%), which gave a negative test for thiosulphate. It was purified by dissolving in a small quantity of H_2O , dissolution being effected by adding potassium carbonate. The sulphur was centrifuged off and acidification (pH $\sim$ 1) and cooling in ice- H_2O gave white crystals. This procedure was repeated several times to remove all the sulphur and the final product dried in vacuo. Yield 7 g. (26%), m.p. 66-70° (lit.³⁹ 70°).

Analysis. Calculated for $\text{C}_6\text{H}_8\text{O}_4$: C 50.00, H 5.60, O 44.40

Found : C 48.93, H 5.37, O 43.60

The literature methods^{41,42} resulted in mixtures of products and the above procedure proved to be far more suitable.

In all the prepared compounds, the absence of extraneous peaks in the n.m.r. spectra, together with the analyses, were taken as sufficient criteria of purity.

Results and Discussion.

The formulae of the acids studied are shown in Tables 1 (monocarboxylic acids) and 4 (di- and tricarboxylic acids), which give the experimental values of the shifts of the unionised acids and the fully ionised acids. Coupling constants are listed in Tables 2 (monocarboxylic acids) and 5 (di- and tricarboxylic acids). The ratios of the shifts to the splittings (i.e. δ/J) were usually large enough for the spectra to be analysed by a first order approach, although non equivalent protons in the group $\text{H}-\text{C}=\text{C}-\text{H}$ (cis or trans) were always treated as an AB pair.

The protons in the $-\text{COOH}$ groups are not seen separately since they exchange rapidly with those of the solvent (H_2O) to give a single line, whose position, a weighted average of the shifts in the two types of environment, is close to the position for H_2O itself at any given pH. The rapid exchange involves all the carboxyl and carboxylate sites, hence the observed shifts and coupling constants are weighted averages of those of the acid and the anion(s). As the pH is increased over the ranges in which the carboxyl groups ionise, the proportion of anion(s) increase, and the observed values alter; this is particularly noticeable in the shifts, which usually move upfield (i.e. to higher τ values) with increasing pH. The shifts, plotted as functions of pH, are shown in Figures 1 and 2 for the monocarboxylic acids and Figures 3 and 4 for the di- and tricarboxylic acids. For a monocarboxylic acid, equal amounts of acid and anion will be present when the pH of the

Table 1. Monocarboxylic Acids. Chemical Shifts(in p.p.m.) of the Unionised and Ionised
Forms.

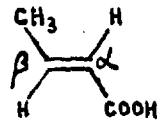
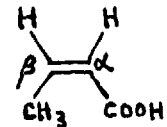
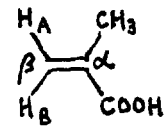
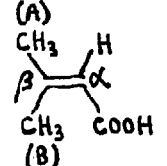
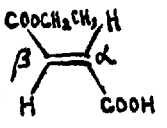
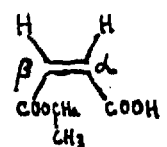
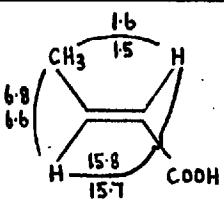
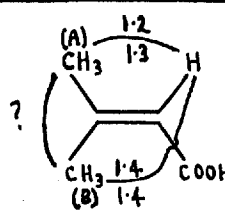
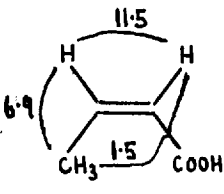
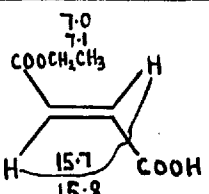
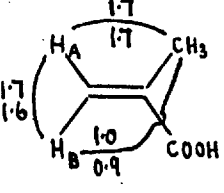
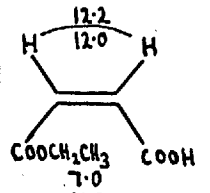
FORMULA	PROTON TYPE	τ_{ACID}	τ_{IONISED}	$\Delta\tau$	MIDPOINT OF S/pH CURVE	pK(x°C)	REFERENCE
 TRANS CROTONIC	H _α	4.08	4.15	0.07	≈ 4.6	4.69(25°) ³⁹	26
	H _β	2.91	3.35	0.44	4.75		27
	CH ₃	8.09	8.18	0.09	≈ 4.7		28 30 31 35
 CIS CROTONIC	H _α	4.14	4.18	0.04	/	4.41(18°) ⁵⁹	26
	H _β	3.49	3.91	0.42	/		27
	CH ₃	7.93	8.13	0.20	4.55		28 30
 METHACRYLIC	H _A	4.26	4.65	0.39	4.50	4.66(18°) ⁵⁹	25
	H _B	3.88	4.33	0.45	4.40		26
	CH ₃	8.08	8.12	0.04	≈ 4.4		28 29
 ββ'-DIMETHYLACRYLIC	H _α	4.25	4.35	0.10	≈ 5.2	5.12(25°) ³⁹	23
	CH ₃ (A)	8.06	8.21	0.15	5.15		25
	CH ₃ (B)	7.88	8.07	0.19	5.15		26 28 31
 MONOETHYL FUMARATE	H _α	3.13	3.09	-0.04	≈ 3.3	3.40(25°) ⁴¹	
	H _β	3.13	3.50	0.37	3.35		
	CH ₂	5.70	5.74	0.04	≈ 3.3		
	CH ₃	8.69	8.70	0.01	≈ 3.3		
 MONOETHYL MALEATE	H _α	3.49	3.39	-0.10	≈ 3.0	3.08(25°) ⁴¹	
	H _β	3.63	4.18	0.55	3.00		
	CH ₂	5.72	5.82	0.10	≈ 3.0		
	CH ₃	8.71	8.73	0.02	≈ 3.0		

Table 2. Monocarboxylic Acids. Coupling Constants.^a

FORMULA	REFERENCE	FORMULA	REFERENCE
 TRANS CROTONIC	26 27 28 30 31	 $\beta\beta'$-DIMETHYLACRYLIC	23 25 26 28 31
 CIS CROTONIC^b	26 27 28 30	 MONOETHYL FUMARATE	
 METHACRYLIC	25 26 28	 MONOETHYL MALEATE	

^a Coupling constants (the coupled protons are indicated by the curved lines) are in cycles/sec.. The upper values refer to the unionised acid and the lower values to the fully ionised acid.

^b The values are for the unionised acid.

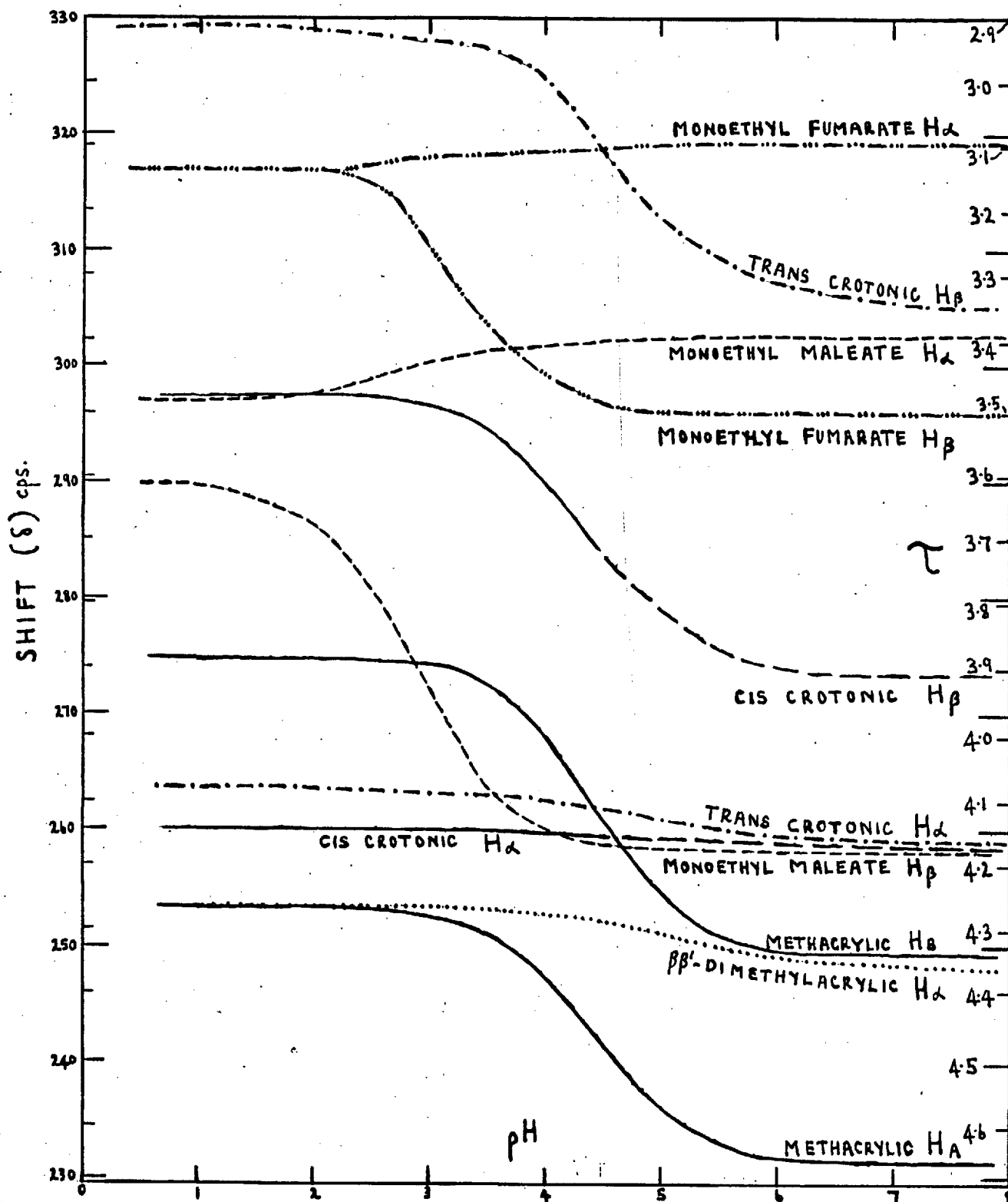


Figure 1. Monocarboxylic Acids. Chemical shifts, in cycles/sec., on the low field side of t-butanol, for the olefinic CH protons. τ values are also indicated.

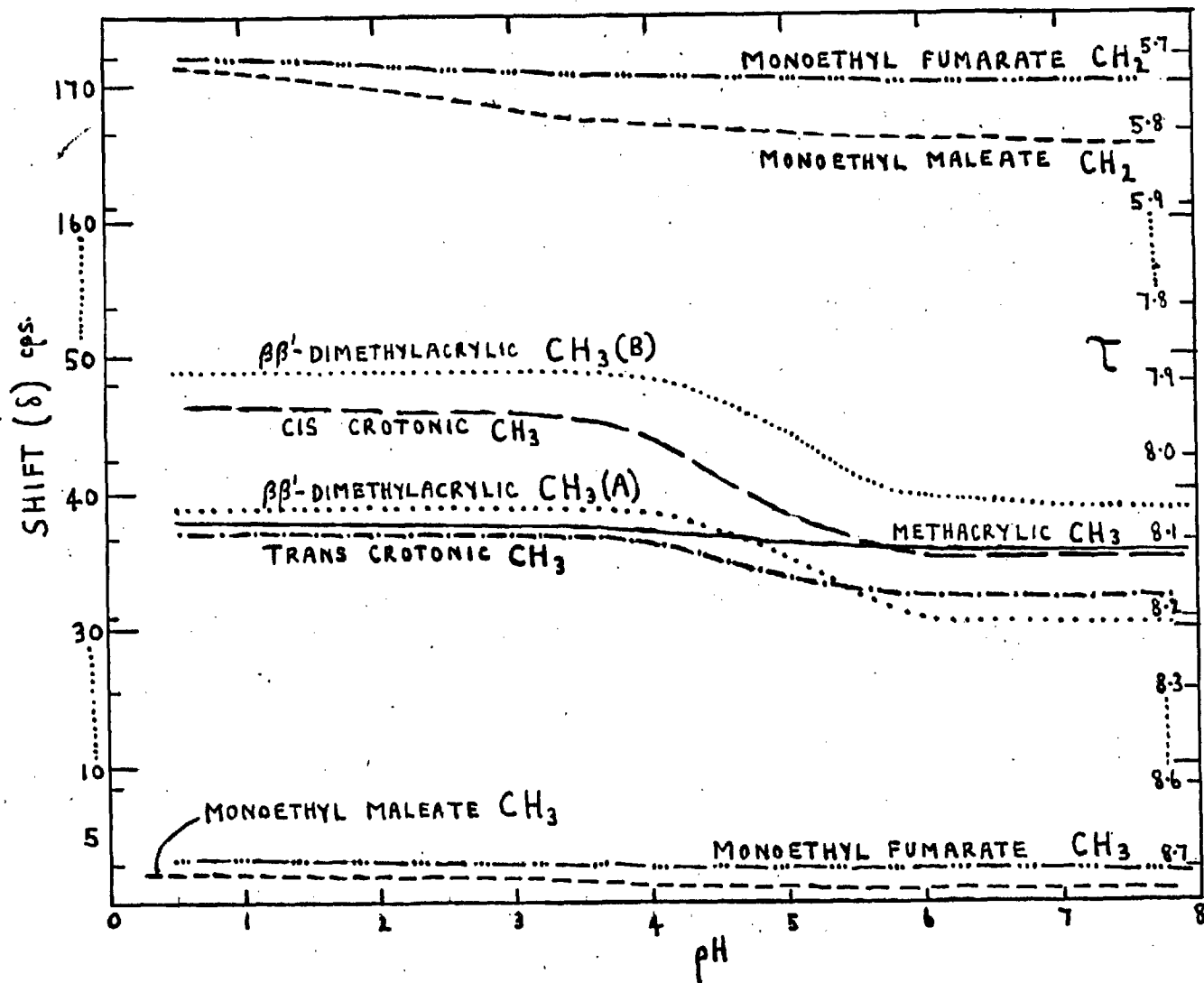


Figure 2. Monocarboxylic Acids. Chemical shifts, in cycles/sec., on the low field side of t-butanol, for the CH₃ and CH₂ protons. τ values are also indicated.

solution is equal to the pK value, hence the midpoint of the step in the plotted curve should occur at this value of the pH, which was generally found to be so (Table 1), within the limits set by errors in the shifts and temperature differences. The shifts in the iso (=cis) crotonate anion, whose ABX₃ spectrum was not first order, were estimated, knowing the values derived from the approximately first order spectra of the unionised acid (pH $\approx$ 1) and of a solution at pH $\sim$ 4, in which the relative amounts of acid and anion were calculated from the known pK value

Assignments. Several of the acids contain two olefinic protons or two methyl groups, to which the correct lines in the spectra had to be assigned, although often only as confirmation of those reported in earlier measurements of the acids and/or their esters.

One criterion, first demonstrated by Jackman and Wiley,²⁴⁻²⁶ is that the long range shielding of a carboxyl group causes a group in the cis position to be less shielded (i.e. to have a lower τ value) than an equivalent trans group. For example, this allows the assignment of the methyl groups in $\beta\beta'$ -dimethylacrylic acid, and of the β protons in the cis and trans crotonic acids.

In the latter acids, the assignments are confirmed by a more general criterion, the H-CH₃ coupling constant, which is greater for the β proton since this is vicinal to the methyl protons. Although the smaller coupling constants across the group

$$\text{H}-\overset{\textstyle |}{\underset{\textstyle |}{\text{C}}}=\overset{\textstyle |}{\underset{\textstyle |}{\text{C}}}-\text{H}$$
 often differ for cis and trans arrangements, they

depend on other factors and are not always a reliable indication of stereochemistry.

Recently, the assignment of the high field CH_3 resonance in $\beta\beta'$ -dimethylacrylic acid $\left(\begin{array}{c} \text{(trans)} \\ \text{CH}_3 \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{CH}_3 \quad \text{COOH} \\ \text{(cis)} \end{array} \right)$ to the trans CH_3 group has been confirmed by measurement of the nuclear Overhauser effect.⁴⁴ The intensity of the $=\text{C}^{\text{H}}$ line was increased by saturation of the high field CH_3 line, but not by saturation of the low field one; since both methyls are spin coupled about equally to the $=\text{C}^{\text{H}}$ proton, the effect must depend on direct dipole-dipole interaction, which will be greater for the CH_3 closer to this proton.

Another criterion, which is apparent from the curves in Figure 1, and has been noticed previously,⁴⁵ is that the shift difference between acid and anion is much smaller for an α proton than for a β proton. [It should be remembered that the α and β lines may cross over in going from acid to anion.]

Monocarboxylic acids - unionised There are negligible amounts of the anions present in solutions of pH below about 2, and the values of the shifts and coupling constants represent those of the unionised acids. It is known that the substituent groups attached to an olefin have approximately additive effects on the shifts of the olefin protons, since correlation tables can be compiled.⁴⁶⁻⁴⁸ Recently, Pascual, Meier and Simon have shown that the shifts in many olefin derivatives are given by the empirical

relation,⁴⁹

$$\delta_H = 5.28 + \sum_i Z_i$$

where δ_H is the shift in p.p.m., measured downfield from T.M.S. as zero, and Z_i is the additive contribution from a group i . The values of Z_i which they give for the groups concerned in the present work are given in Table 3, together with the calculated shift values, which are seen to agree fairly well with the observed shifts.

Some explanations of how the groups affect the shifts have been indicated elsewhere.^{50,51} The shift of an olefinic proton is determined by shielding by the electrons immediately around it, which depends on the electron density, and partly by long range shielding - there is always an appreciable contribution from the olefin group itself.

The common substituent in all the acids is the carboxyl group, whose contributions, which are fairly large, can (as for any other group) be regarded as the result of three or four effects.

(a) Inductive. The group attracts electrons and reduces the electron density around the protons.

(b) Conjugation. The π electrons of the olefin and carbonyl groups are delocalised; the ground state of the acids can be represented as a resonance hybrid of the two canonical structures.

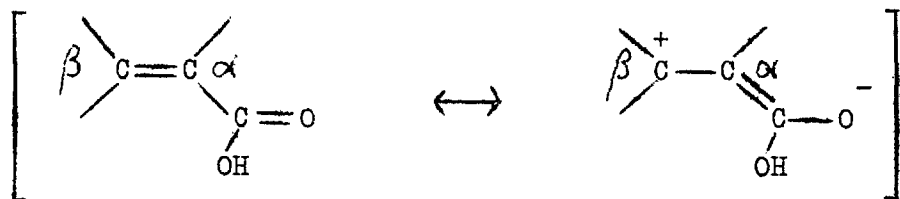
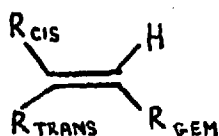


Table 3. Monocarboxylic Acids. Calculated and Observed

Chemical Shifts (in p.p.m.) for Olefinic Protons.



$$\delta_{\text{H}} = 5.28 + \sum_i Z_i$$

SUBSTITUENT R	Z _i	FOR R		REFERENCE	
	GEM	CIS	TRANS		
-H	0	0	0	49	
-CH ₃	0.44	-0.26	-0.29		
-COOH (SOLO)	1.00	1.35	0.74		
-COOH (CONJ.)	0.69	0.97	0.39		
-COOR' (SOLO)	0.84	1.15	0.56		
-COOR' (CONJ.)	0.68	1.02	0.33		
-CH ₂ COOH	—	-0.1	-0.2	PRESENT WORK	
-COO ⁻ (SOLO)	0.93	0.91	0.33		
-COO ⁻ (CONJ.)	0.76	0.60	-0.16		
-CH ₂ COO ⁻	—	-0.2	-0.3		
ACID	PROTON TYPE	UNIONISED		IONISED	
		τ _{CALC.}	τ _{OBS.}	τ _{CALC.}	τ _{OBS.}
TRANS CROTONIC	H _α	3.98	4.08	4.05	4.15
	H _β	2.93	2.91	3.37	3.35
CIS CROTONIC	H _α	4.01	4.14	4.08	4.18
	H _β	3.54	3.49	3.95	3.91
METHACRYLIC	H _A	4.24	4.26	4.65	4.65
	H _B	3.66	3.88	4.10	4.33
ββ'-DIMETHYLACRYLIC	H _α	4.27	4.25	4.34	4.35
MONOETHYL FUMARATE	H _α	3.01	3.13	2.94	3.09
	H _β	3.07	3.13	3.44	3.50
MONOETHYL MALEATE	H _α	3.70	3.49	3.63	3.39
	H _β	3.65	3.63	4.20	4.18

This conjugation should be most developed when the groups are coplanar. There is a change in the electron density distribution, particularly at the β carbon atom. Also, the removal of π electrons from the olefin group must alter its long range shielding effect. (The shifts in vinyl derivatives can be explained satisfactorily by conjugation effects,⁵⁰ and in the case of trans nitropropene, the effect of conjugation with the $-\text{NO}_2$ group on the π electron distribution has been calculated,⁵² and found to leave positive charge on the β carbon atom)

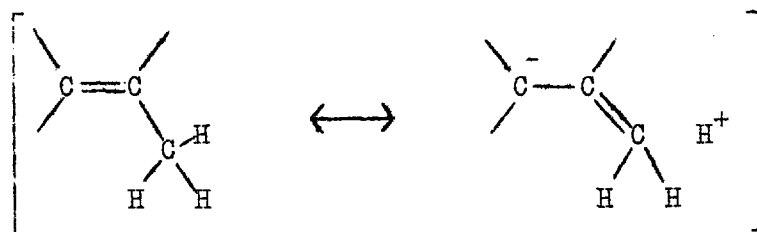
(c) Long range shielding. Protons which are roughly in the same plane as the carboxyl group experience a shift to lower fields, which is greater the closer they are to it. The effect is evident in the differences between cis and trans β protons, but it must be quite large at the α proton also.

(d) Another possible effect is that the internal electric field arising from the electric dipole moment in the molecule can alter the shielding, either by producing electron displacements^{53,54} or by inhibiting the diamagnetic electron circulations.⁵⁵ It is difficult to distinguish this effect from the others, since little attention has been given to it so far.

The above effects, which tend to make the olefin protons in the acids occur at relatively low τ values, together comprise the carboxyl group contribution, whose total value (at a given position) seems to be fairly constant.

In the acids where the second substituent is a methyl

group, the changes in the $=C-H$ shifts can be ascribed to this CH_3 . Its contributions are considerably smaller than those of the carboxyl. When attached to an olefin, a CH_3 group is weakly electron releasing. Its inductive effect is opposite to that of carboxyl, as also is its conjugation effect, which can be represented by

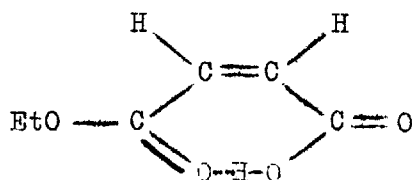


This could explain the increase in shielding which a methyl group produces on the distant olefin proton. Since the increase is almost the same for cis and trans arrangements, there seems to be little change in the long range shielding effects at this position when CH_3 replaces $=C-H$, but these may contribute to the decrease in shielding of the proton on the same carbon atom as the methyl group.

In the acids, the β protons (relative to the carboxyl groups) show a considerable range of shifts since they can be cis or trans to carboxyl and α or β relative to methyl. The α protons cover a smaller range since they differ only by the effects of one or two β methyls.

The contributions of two substituents on an olefin are not completely independent, particularly when both have large effects, as in the monoesters (and in the di- and tricarboxylic

acids mentioned later), which have two carboxyl groups. The decreases in shielding are considerably less than would be found if each group had the same effect as in the methyl acids. There must be a limit to the removal of electrons from the olefin group, and the displacement by one carboxyl will limit those available to the other. This is explicitly allowed for in the tabulated contributions; the values for COOH (conj.) and COOR (conj.) must be used to give satisfactory agreement with the observed shifts. The long range shielding effects, however, seem to be little changed. In the fumarate ester, the conjugated carboxyl and ester groups have almost identical overall effects since the proton τ values are nearly (if not exactly) the same, and agree well with the calculated values. In the maleate ester, the τ values differ slightly and are both lower than the calculated ones. Possibly some intramolecular hydrogen bonding increases the tendency of the groups to be coplanar, thus increasing their long range shielding effects.



The τ values of the methyl protons in the acids are lower than those for methyls attached to simple olefins, presumably due to the extra electron withdrawal by the carboxyl groups. In the crotonic acids and $\beta\beta'$ -dimethylacrylic acid, the differences arising from the carboxyl long range shielding are evident.

The τ values for the CH_2 and CH_3 groups in the esters are both slightly lower than in ethyl esters of saturated acids, possibly because of long range shielding by the olefin group.

Monocarboxylic acids - anions. In solutions of pH above about 8, the amounts of unionised acids will be negligibly small and the shift and splitting values are those of the fully ionised acids (anions).

It was found that the olefin proton shifts could again be fitted to the formula, giving the COO^- group the additive contributions shown in Table 3. The lower values, compared with COOH , merely express the fact that the shifts have (usually) moved upfield on ionisation. The $\Delta\tau$ changes relative to the acids are given in column 5 of Table 1.

One reason why COO^- is less effective than COOH in deshielding olefin protons is that its inductive effect is different, since its negative charge tends to repel electrons. Also, the conjugation shown with COOH , which places negative charge on the group, will be considerably inhibited with COO^- . However, since the difference between contributions at cis and trans β positions is about the same for both groups, their long range shielding effects seem to be about the same, at least at the β position. This does not necessarily mean that their intrinsic anisotropies are the same; the COO^- group, being less conjugated with the olefin, has less tendency to stay coplanar with it. (If its average orientation is more out of plane than for COOH , its similar effect

indicates a greater intrinsic anisotropy.)

The large differences, $\Delta\tau$, for the β protons probably result from the increase in electron density at the β carbon, resulting from the decrease in conjugation. The $\Delta\tau$ values for the α protons are considerably smaller, and are smaller than the changes ($\Delta\tau \approx 0.22$) in the α protons in aliphatic carboxylic acids. Banwell and Sheppard⁵⁰ suggested that the relative insensitivity of such protons to the substituent α to them results from a balance of factors of opposing signs. In this case, the change in inductive effect should increase the shielding, but changes in conjugation and long range shielding could produce small effects in either direction. The greater π electron density in the olefin group should increase its long range deshielding effect.

The shifts in the monoesters were used to calculate values for the contributions from a conjugated COO^- group, which has a smaller deshielding effect than a conjugated COOH . In both esters the $\Delta\tau$ values for the β protons are similar to those in the other acids; however, there are small downfield shifts ($\Delta\tau \approx 0.1, 0.04$ for maleic and fumaric esters respectively) for the α protons. Possibly the reduced conjugation by the $-\text{COO}^-$ allows the ester group to increase its conjugation, which could decrease the shielding of the proton β to it (i.e. the α proton) sufficiently to outweigh the other effects.

The methyl groups in the anions are all more shielded

than in the acids, since the electron density in the anion is greater; again the difference is smallest for the α group (in methacrylic acid).

Coupling Constants (Table 2). The values are similar to those found in previous measurements on substituted olefins^{47,56}

The values, which are probably positive, for cis (11-12 cycles/sec.) and trans (15-16 cycles/sec.) pairs of olefinic protons are lower than those found in simple olefins. It is well known⁵⁷ that a substituent produces a decrease in these coupling constants roughly in proportion to its electronegativity. The values are only slightly altered in the anions, suggesting that the COO^- group differs only slightly from the COOH group.

The vicinal $\text{H}-\underset{\text{CH}_3}{\text{C}}=$ coupling constants, and those in the ethyl groups, also have typical values and are probably positive.

The $\text{H}-\text{C}=\text{C}-\text{CH}_3$ coupling constants are smaller and their signs not certain. Their magnitudes are not a reliable indication of stereochemistry.

Fumaric, mesaconic, itaconic and trans aconitic acids.

These are considered together since the ionisations of their carboxyl groups overlap. In both the acids ($\text{pH} < 2$) and fully ionised anions ($\text{pH} > 8$), the olefinic proton shifts (Tables 4 and 6) are given fairly closely by the formula, again using "conjugated" values for the COOH and COO^- groups (except in itaconic acid). The published table does not include $-\text{CH}_2\text{COOH}$ and $-\text{CH}_2\text{COO}^-$ groups, but values were derived from the data for itaconic acid; they are

Table 4. Di- and Tricarboxylic Acids. Chemical Shifts

(in p.p.m.) of the Unionised and Fully Ionised Forms.

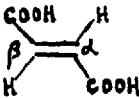
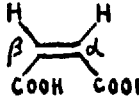
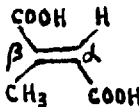
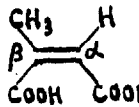
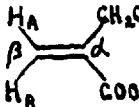
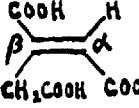
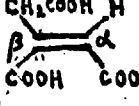
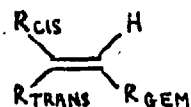
FORMULA	PROTON TYPE	τ_{ACID}	τ_{IONISED}	$\Delta\tau$	MIDPOINT OF S/pH CURVE			pK $a = 18^\circ C, b = 25^\circ C$			REF.
					STEP 1	STEP 2	STEP 3	pK_1	pK_2	pK_3	
 FUMARIC	H	3.14	3.49	0.35	3.65	—	—	⁵⁸ 3.02 (b)	⁵⁸ 4.38 (b)	—	24 25 26 32 34 35
 MALEIC	H	3.55	3.98	0.43	1.95	5.95	—	⁵⁸ 1.92 (b)	⁵⁸ 6.23 (b)	—	24 25 26 32 34 35
 MESACONIC	H_α	3.20	3.52	0.32	4.0	—	—	³⁹ 3.07 (b)	⁵⁹ 4.82 (a)	—	24 26 30 31
	CH_3	7.82	8.05	0.23	3.8	—	—	—	—	—	—
 CITRACONIC	H_α	4.00	4.48	0.48	5.75	—	—	³⁹ 2.42 (b)	⁵⁹ 6.17 (a)	—	24 26 30 31
	CH_3	7.91	8.08	0.17	2.55	5.85	—	—	—	—	—
 ITACONIC	H_A	4.09	4.61	0.52	4.4	—	—	³⁹ 3.85 (b)	³⁹ 5.45 (b)	—	29
	H_B	3.62	4.14	0.52	4.45	—	—				
	CH_2	6.57	6.84	0.27	4.8	—	—				
 TRANS ACONITIC	H_α	2.99	3.40	0.41	4.1	—	—	³⁹ 2.8 (b)	³⁹ 3.5 (b)	—	—
	CH_2	6.13	6.56	0.43	3.75	—	—				
 CIS ACONITIC	H_α	3.60	4.36	0.76	≈ 2.0	≈ 4.5	≈ 6.5	⁶⁵ 1.95 (b)	—	—	—
	CH_2	6.50	6.91	0.41	≈ 1.8	≈ 4.5	≈ 6.5				

Table 5. Di- and Tricarboxylic Acids. Coupling Constants.^a

FORMULA	REF.	FORMULA	REF.
FUMARIC		ITACONIC	33
MALEIC^b	33	TRANS ACONITIC	
MESACONIC	26 30 31	CIS ACONITIC	
CITRACONIC	26 30 31		

^a Coupling constants are in cycles/sec.. The upper values refer to the unionised acid and the lower values to the fully ionised acid. ^b Value from reference 33.

Table 6. Di- and Tricarboxylic Acids. Calculated and Observed Chemical Shifts (in p.p.m.) for Olefinic Protons.



$$\delta_{\text{H}} = 5.28 + \sum Z_i$$

SUBSTITUENT R	Z _i FOR R			REFERENCE
	GEM	CIS	TRANS	
-H	0	0	0	49
-CH ₃	0.44	-0.26	-0.29	
-COOH (SOLO)	1.00	1.35	0.74	
-COOH (CONJ.)	0.69	0.97	0.39	
-COOR' (SOLO)	0.84	1.15	0.56	
-COOR' (CONJ.)	0.68	1.02	0.33	
-CH ₂ COOH	—	-0.1	-0.2	PRESENT WORK
-COO ⁻ (SOLO)	0.93	0.91	0.33	
-COO ⁻ (CONJ.)	0.76	0.60	-0.16	
-CH ₂ COO ⁻	—	-0.2	-0.3	

ACID	PROTON TYPE	UNIONISED		IONISED	
		τ _{CALC.}	τ _{OBS.}	τ _{CALC.}	τ _{OBS.}
FUMARIC	H	3.06	3.14	3.36	3.49
MALEIC	H	3.64	3.55	4.12	3.98
MESACONIC	H	3.35	3.20	3.65	3.52
CITRACONIC	H	3.90	4.00	4.38	4.48
ITACONIC	H _A	4.08	4.09	4.61	4.61
	H _B	3.57	3.62	4.11	4.14
TRANS ACONITIC	H	3.26	2.99	3.66	3.40
CIS ACONITIC	H	3.74	3.60	4.32	4.36

fairly small and similar to those quoted for other CH_2X groups.

The shifts can be interpreted as for the mono acids. On ionisation, the inductive effects will alter and the conjugation, which, even in the acids, is less than in the methyl mono acids, will be further reduced. However, the long range shielding effects should not alter greatly. All the shifts move upfield on ionisation, and $\Delta\tau$ (Table 4) for all the olefinic protons are fairly large because each is β to a carboxyl.

In fumaric acid the two carboxyl groups are equivalent. The two $=\text{CH}$ protons are equivalent in the acid and in its dianion, and they appear equivalent, giving one line, in solutions where the acid is partly ionised, because of the rapid hydrogen exchange. The closeness of the macroscopic ionisation constants ($\text{pK}_1 = 3.02$, $\text{pK}_2 = 4.38$ at 25°C)⁵⁸ shows that the ionisations overlap, and only one step is seen in the curve of shift against pH (Figure 3), which lies close to that for the β proton in monoethyl fumarate. If the hydrogen exchange were very slow, the spectrum of the monoanion, $\begin{array}{c} \text{COOH} \quad \text{H} \\ \beta \quad \quad \alpha \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \quad \text{COO}^- \end{array}$, would be expected to be similar to that of the monoester anion, in which H_α had shifted to lower τ and H_β to higher τ . The average value of H_α and H_β in the ester $\left(\frac{\tau_\alpha + \tau_\beta}{2} = 3.30 \right)$ is close to the shift of the monoanion, which may be taken as that of the middle of the step ($\tau = 3.31$), although the anion concentration does not rise above 71%.

In mesaconic acid, $\begin{array}{c} \text{COOH} \quad \text{H} \\ \beta \quad \quad \alpha \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{CH}_3 \quad \quad \text{COOH} \end{array}$, the two carboxyl groups

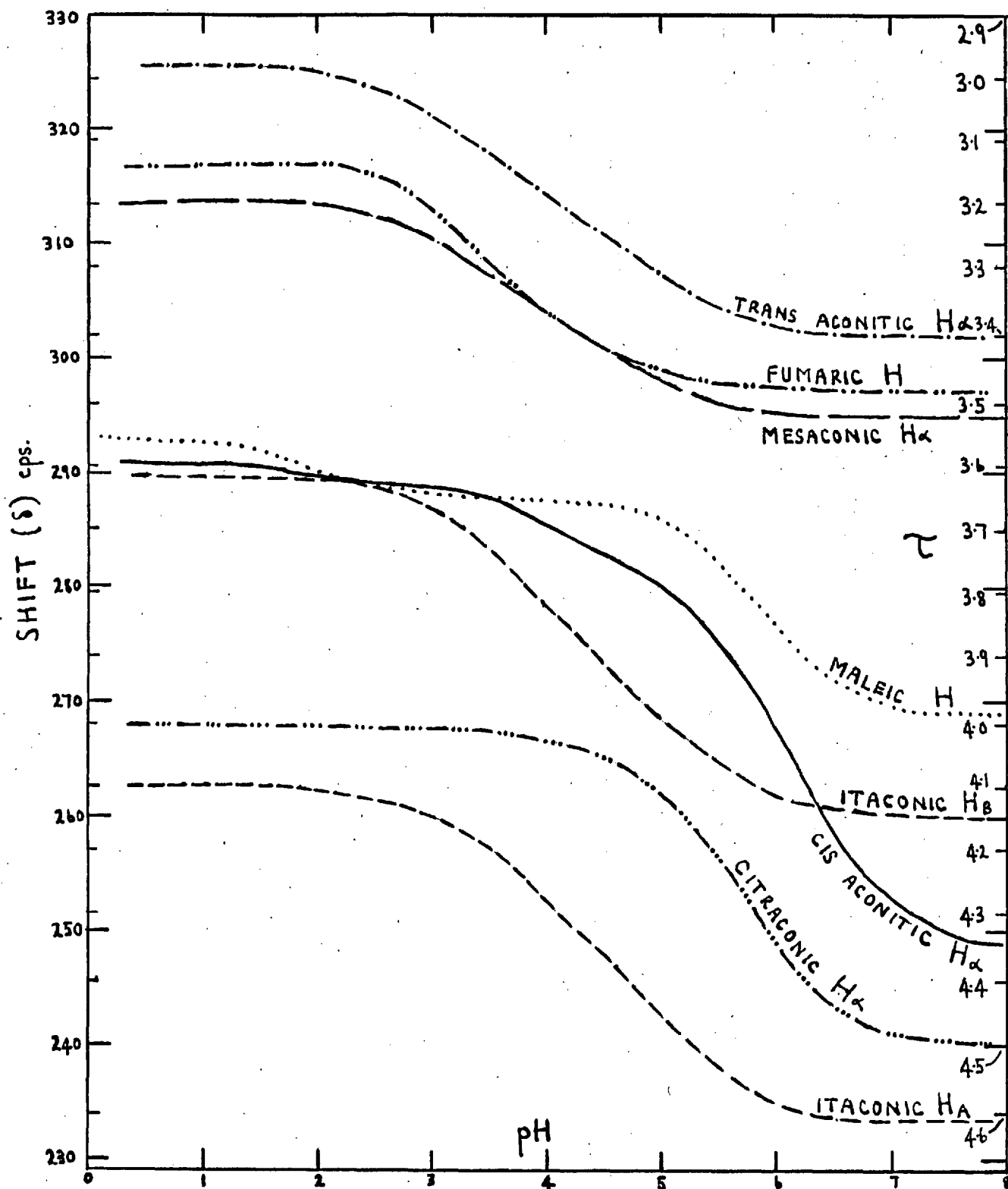
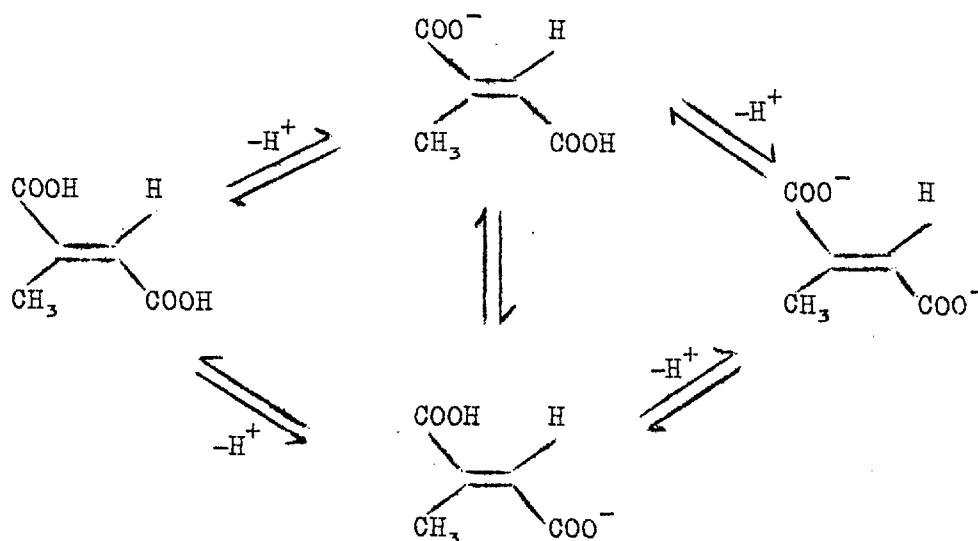


Figure 3. Di- and Tricarboxylic Acids. Chemical shifts, in cycles/sec on the low field side of t-butanol, for the olefinic CH protons.

τ values are also indicated.

are not equivalent. The macroscopic ionisation constants ($pK_1 = 3.07$ at 25°C ,³⁹ $pK_2 = 4.82$ at 18°C ⁵⁹) are fairly close so their ionisations overlap and neither value represents the acid strength of one group alone.

The equilibria are



Each step can be represented by a "microscopic" ionisation constant; to determine these, it is necessary to follow the extent of the ionisation of each group separately. This is not possible since both the olefin and methyl (Figure 4) curves show only one step, and each shift will be affected by both carboxyls. However, the greater effect should come from the distant carboxyl, so the fact that the midpoint of the CH_3 curve is at a lower pH (3.6) than that of H_α (4.0) suggests that the α carboxyl reaches a given degree of ionisation at a lower pH than the β carboxyl. The $\Delta\tau$ value for H_α is about the same as in fumaric acid, and $\Delta\tau$ for the

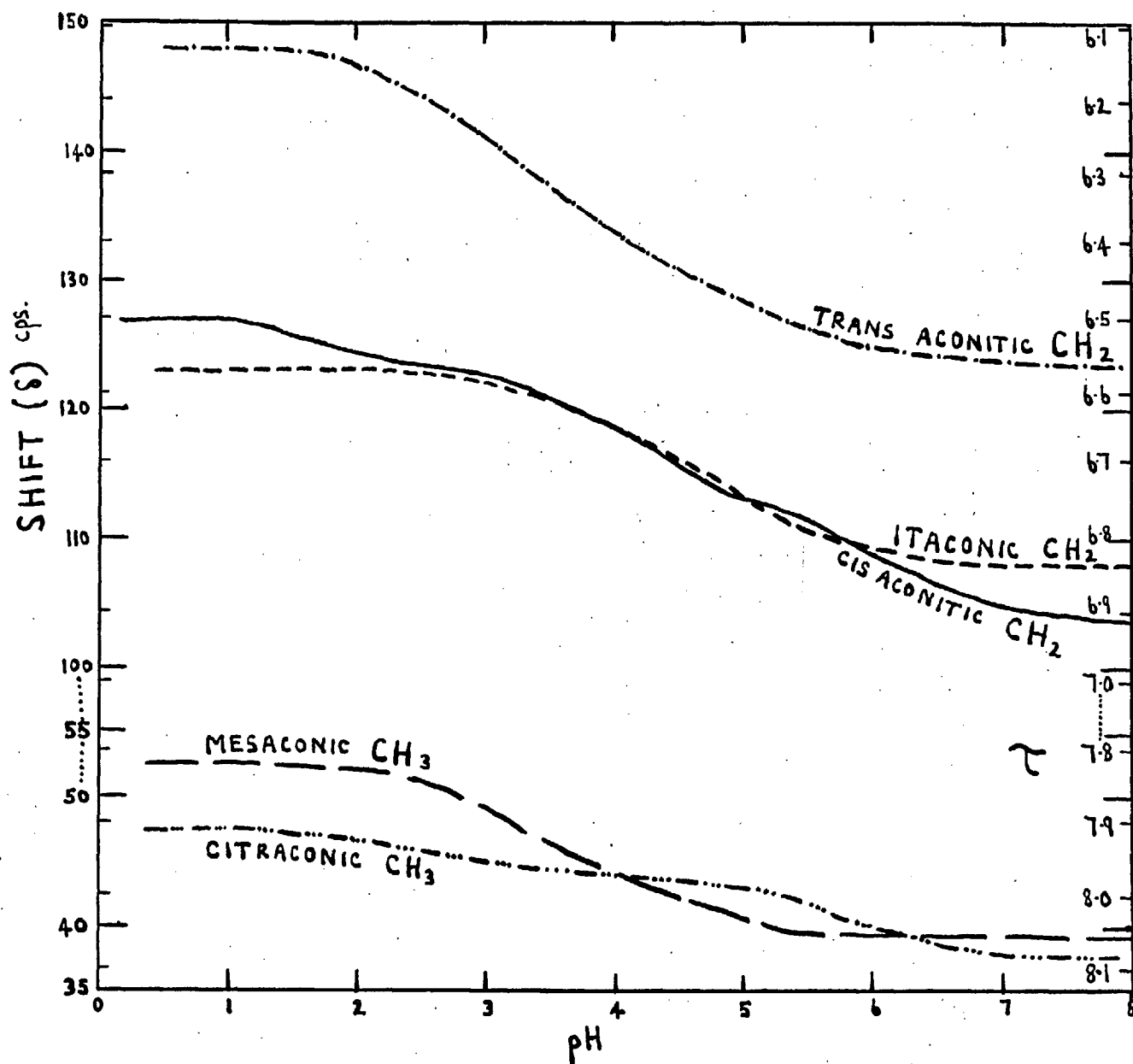
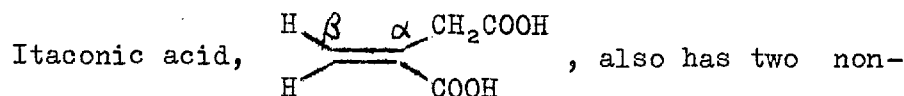


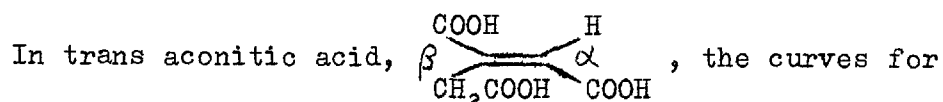
Figure 4. Di- and Tricarboxylic Acids. Chemical shifts, in cycles/sec., on the low field side of *t*-butanol, for the CH_3 and CH_2 protons. τ values are also indicated.

methyl group is similar to other β methyl groups.



equivalent carboxyls whose ionisations overlap (macroscopic $\text{pK}_1 = 3.85$, $\text{pK}_2 = 5.45$ at 25°C).³⁹ Again the curves show only one step, which will include the effects of both carboxyls.

However, the step for the CH_2 protons ($\Delta\tau = 0.27$), which is similar to that for the CH_2 protons in propionic acid ($\Delta\tau = 0.22$), is expected to result mainly from the ionisation of the carboxyl attached to it, and the (almost equal) steps of the olefinic protons should result mainly from the ionisation of the α carboxyl. The midpoints (olefinic protons = 4.4, $\text{CH}_2 = 4.8$) indicate that the latter carboxyl is the stronger acid.

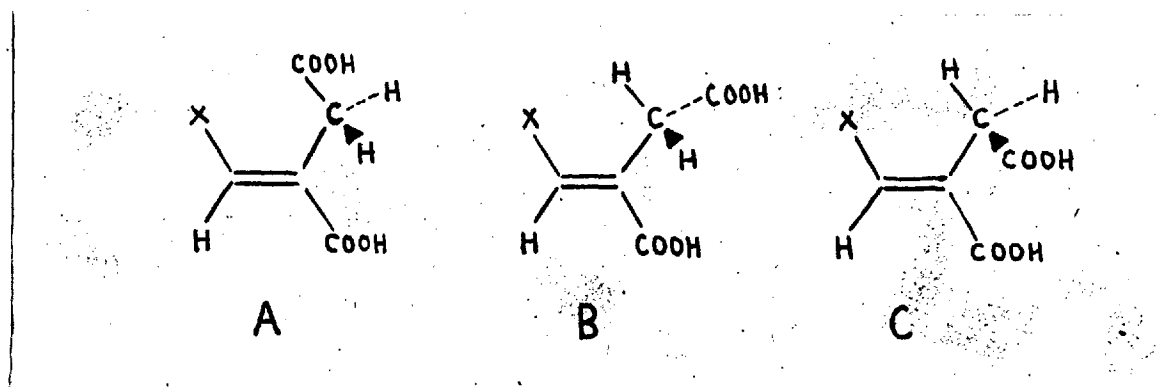


both $=\text{CH}$ and CH_2 protons show one step only, indicating that all three ionisations overlap. Hence the value of pK_3 (macroscopic), which does not seem to be recorded, must lie fairly close to those of pK_1 and pK_2 ($= 2.8$ and 3.5 at 25°C respectively).³⁹ The step for H_α is about the same as for fumaric and mesaconic acids, and is attributed mainly to the ionisation of the β carboxyl group. The midpoint is at $\text{pH} \approx 4.1$, suggesting that the α carboxyl is not the first to ionise, since the midpoint for the CH_2 curve is at $\text{pH} \approx 3.75$. The CH_2 shift will depend on both its own carboxyl and the α carboxyl; presumably this is why its step ($\Delta\tau = 0.43$) is larger than that in itaconic acid.

The coupling constants are of the expected order of magnitude. The couplings across the group $H - C = C - C - H$ deserve comment; for the acids their values are:

mesaconic acid	$J_{trans} = 1.6$ cycles/sec.
trans aconitic acid	$J_{trans} = 0.6$
itaconic acid	$\begin{cases} J_{trans} \approx 0.6 \\ J_{cis} \approx 1.0. \end{cases}$

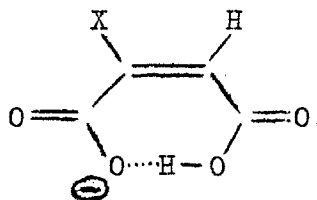
One reason for the relatively low values in trans aconitic acid and itaconic acid could be the conformation for the side chain. It is known^{57,60} that these coupling constants depend on the dihedral angle, ϕ , between the $H - C = C$ plane and the $=C - C - H$ plane, and are largest (about -2 cycles/sec.) when $\phi \sim 60-120^\circ$ and least (approximately zero) when $\phi \approx 0^\circ$ or 180° . Their measured values are weighted averages over rotational isomers, which may be written as



In itaconic acid ($X = H$), repulsions between the carboxyl groups are minimised in conformation A, but the side chain carboxyl can also avoid the other groups, particularly in trans aconitic acid

(X = COOH), in conformations B or C, in which one C - H has $\phi \sim 180^\circ$.

Maleic, citraconic and cis aconitic acids. These acids each have two cis carboxyl groups between which a strong intramolecular hydrogen bond can form when one is ionised.

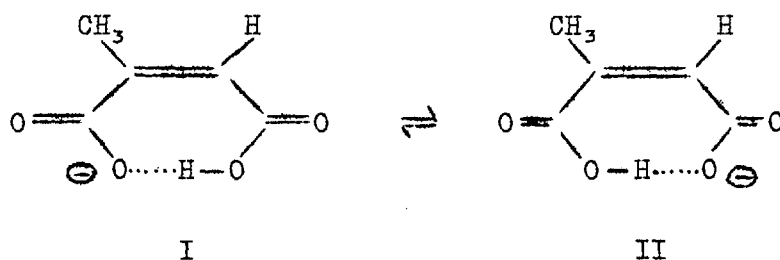


In the solid state, the hydrogen maleate anion (X = H) is almost planar and the hydrogen may be midway between the oxygens;⁶¹ the presence of a strong hydrogen bond in aqueous solution also is indicated by infrared spectroscopy.⁶² The stabilisation of the monoanion in this way accounts satisfactorily for the greater acidity for loss of the first proton, and weaker acidity for loss of the second, relative to fumaric acid.^{63,64} The ionisation constants ($pK_1 = 1.92$, $pK_2 = 6.23$ at 25°C)⁵⁸ are different enough to allow separate steps, whose midpoints occur at pH values (1.95 and 5.95) close to the pK , to be seen in the curve for the olefin protons. The rapid hydrogen exchange results in one averaged line for these, which, in the acid, lies between those for the monoethyl maleate. The step over the first ionisation is small (0.1 p.p.m.) and the line position ($\tau = 3.55$) represents the monoanion (which will be almost 100% of the species present). The mean value of the shifts in the monoester anion ($\frac{3.38+4.18}{2} = 3.78$) is higher than

this, suggesting an additional deshielding contribution in the hydrogen maleate. A reasonable explanation of this observation has been given recently (see footnote 13b to ref. 34); the strong hydrogen bonding in the monoanion holds the carboxyl groups in fixed coplanar orientations, in which their long range deshielding contributions are greater. Ionisation of the hydrogen from the hydrogen bond gives the dianion, in which repulsion between the carboxylate groups probably prevents them being coplanar. The second step is fairly large; the shift in the dianion is about 0.14 lower than the "calculated" value.

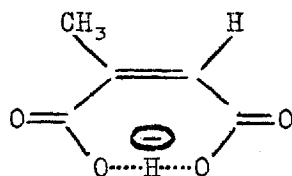
In citraconic acid, $\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \beta \\ \diagup \\ \text{COOH} \end{array} = \begin{array}{c} \text{H} \\ \diagup \\ \alpha \\ \diagdown \\ \text{COOH} \end{array}$, the two carboxyl groups

are not equivalent and, as in maleic acid, the macroscopic ionisation constants are considerably different ($\text{pK}_1 = 2.42$, $\text{pK}_2 = 6.17$ at 25°C).³⁹ The loss of one proton from the acid produces the monoanion; if this contains an unsymmetrical hydrogen bond, it could be regarded as a mixture of two species in equilibrium, the equilibrium being brought about mainly by means of a fast intramolecular hydrogen exchange.



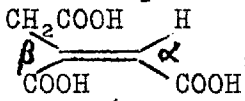
Over the first ionisation, $\Delta\tau$ for H_α is very small (about 0.01); this could be interpreted as indicating that the main

species is II and that the α carboxyl was the stronger of the two groups in the acid. The first step $\Delta\tau$ for the CH_3 (about 0.06) is smaller than for the methyl groups which are β to carboxyls in the monoacids, but a smaller change would be expected since the long range deshielding should be greater due to the greater coplanar orientation in the monoanion. However, instead of being regarded as weighted averages over I and II, the shifts could equally well arise from the single structure with a symmetrical hydrogen bond.



III

Whatever the structure of the monoanion may be, the hydrogen bonding is absent in the dianion; the carboxylate groups are probably not coplanar, and their long range shielding is reduced. The second $\Delta\tau$ for H_α (about 0.47) is as large as the overall change in maleic acid and (almost) as in the monoethyl maleate. The second $\Delta\tau$ for the methyl (about 0.11) is greater than the first, and its overall change is nearly the same as in cis crotonic acid. The coupling constant, $J(\text{H}-\text{CH}_3)$, has the expected value.

In cis aconitic acid, , the small $\Delta\tau$ found for both H_α (about 0.04) and the CH_2 (about 0.07) over the range of the first ionisation ($\text{pK}_1 = 1.95$ at 25°C)⁶⁵ resemble those in citraconic acid, and it is probable that the monoanion has the

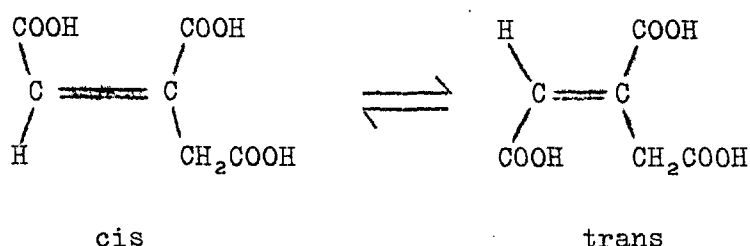
same structural possibilities as discussed for citraconic, with CH_3 replaced by CH_2COOH . Both curves show slight inflexions at about pH 5.5, suggesting that there is a central step with a midpoint at about 4.5, which may be attributed mainly to the ionisation of the $-\text{CH}_2\text{COOH}$ group. The final steep step for H_α , with a midpoint at a pH of about 6-7, would then represent the loss of the strongly hydrogen-bonded hydrogen. The overall $\Delta\tau$ (0.41) for the CH_2 protons is larger than that in itaconic acid (0.27), since they will be affected by the group β to them. The overall $\Delta\tau$ for H_α (0.76) is particularly large; possibly in the anion repulsions between the three carboxylate groups cause the side chain to adopt an average orientation, in which its COO^- group produces an increased shielding of H_α .

The value of $J_{(\text{H}-\text{CH}_2)}$ increases on going to the fully ionised anion by more than was found in the other acids; this also indicates a change in the orientation of the side chain.

In the above discussion, changes in the solvation of the species by H_2O have not been considered, since little work has so far been done on their effects on such spectra.

Part B. The Isomerisation of Cis and Trans
Aconitic Acids.⁶⁶

It has long been recognised that cis aconitic acid readily isomerises to the trans form in aqueous solution,^{67,68}



the equilibrium lying in favour of the more stable trans. Malachowski⁶⁸ noted that the proportion of the trans acid in an equilibrium mixture was about 85%, and decreased slightly with dilution and increasing temperature. Krebs and Eggleston⁶⁹ found that isomerisation occurred most readily under both extremely acidic and basic conditions, and that the cis isomer was relatively inert in neutral and slightly alkaline solutions. They also reported that the equilibrium mixture contained more than 30% of the cis isomer from the isomerisation of the trans acid under certain conditions. The relative inertness of the cis form in neutral and slightly alkaline solutions was later confirmed by Ambler and Roberts.⁷⁰

Proton resonance provides a particularly useful method for this type of study, since separate lines are seen from each isomer in the same solution, and their relative amounts are obtained directly from the intensities (areas). This investigation was undertaken with the aim of obtaining information about the pH and

temperature dependence of the isomerisation rate, and of the ratio of isomers in the final equilibrium mixtures. The effects of certain metal ions on the equilibria were also investigated.

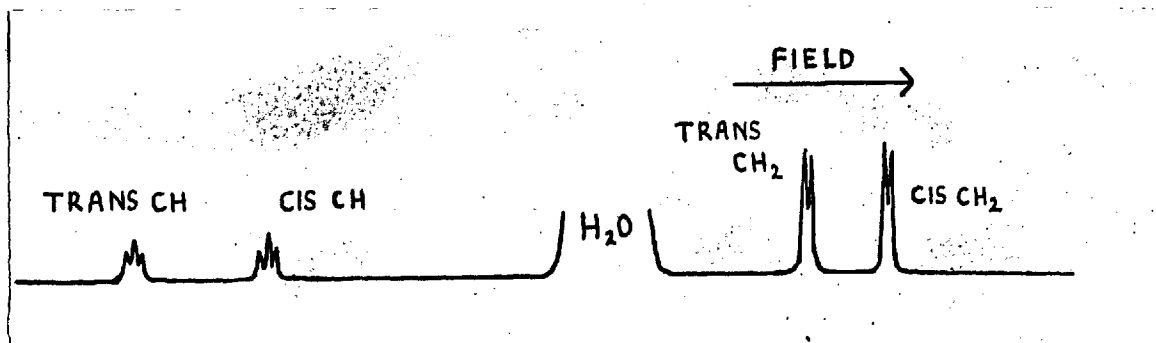
Experimental.

0.2M solutions of the cis isomer were used throughout, and the required pH obtained by the addition of HCl or NaOH. Isomerisations of the trans isomer (0.2 M solutions) gave identical final equilibrium ratios to those obtained in the cis isomerisations, but all rates were measured for the latter. The initial pH values were measured with a Cambridge pH meter at $20 \pm 1^\circ\text{C}$. The temperatures of $20 \pm 1^\circ$, $60 \pm 1^\circ$, and $100 \pm 1^\circ$ were obtained using oil baths, and in the case of the higher temperatures, where the rate of isomerisation is faster, the reaction was quenched in ice- H_2O before recording the spectra. Areas under the lines were measured by counting squares, as the electronic integration available proved to have no appreciable advantage.

Results and Discussion.

An attempt was made to determine whether the features of the aconitic acid isomerisation are also common to the maleic acid $\rightleftharpoons$ fumaric acid isomerisation. However, after heating solutions of maleic acid of various pHs at 100° for one week, very little isomerisation had taken place. Also, since the maleic $\rightleftharpoons$ fumaric equilibrium lies almost completely towards fumaric acid, the amounts of maleic at equilibrium are too small for the n.m.r. method to be a suitable method for detecting them.

It is clear that the isomerisation of the cis isomer is readily followed from the growth of the trans isomer CH and CH₂ resonances or the decrease of the cis CH and CH₂ ones. A typical spectrum is illustrated below



The CH₂ resonances were selected as being more suitable for area measurements. Table 7 illustrates the estimated half lives for the isomerisation (columns 2, 5 and 8) and the percentage of the cis isomer in the final equilibrium mixture (columns 3, 6 and 9) for the pH range 0 $\rightarrow$ 14 at 20°, 60° and 100°C. Temperature, as expected, has a profound effect on the rate of isomerisation. Increasing the acidity below pH 1 has no effect on the rate, whereas increasing the alkalinity above pH 13 causes a large rate increase. It is apparent that the cis isomer is very inert in the slightly alkaline and neutral pH regions, confirming the previous observations;^{69,70} as expected, in the pH range 7 $\rightarrow$ 11 there was no appreciable isomerisation at 20° after one month. At 100° some decarboxylation occurred on prolonged heating in the pH range 2 $\rightarrow$ 4.

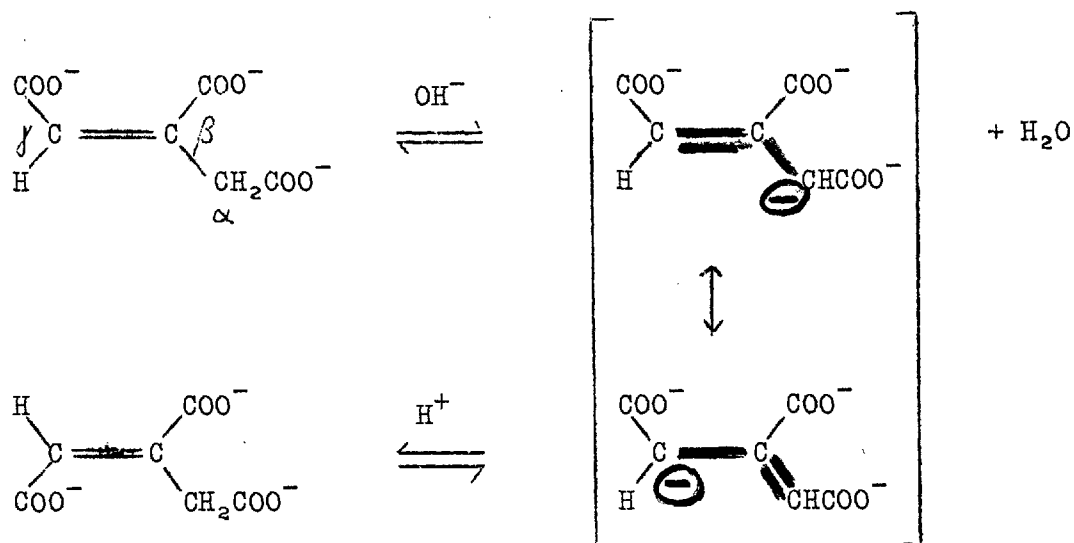
Table 7. The Isomerisation of Cis Aconitic Acid.

20°C			60°C			100°C		
pH	HALF LIFE $t_{1/2}$ MINUTES	PERCENTAGE OF CIS IN FINAL SOLUTION	pH (20°C)	HALF LIFE $t_{1/2}$ MINUTES	PERCENTAGE OF CIS IN FINAL SOLUTION	pH (20°C)	HALF LIFE $t_{1/2}$ MINUTES	PERCENTAGE OF CIS IN FINAL SOLUTION
<0	4,800	4 ± 2	<0	7	5 ± 2	0.1	3	5 ± 2
0.2	4,800	5 ± 2	0.5	7	6 ± 2	1.0	3	6 ± 2
1.0	4,100	5 ± 2	1.0	7	6 ± 2	2.5	5	30 ± 5
2.5	7,500	20 ± 5	2.5	105	30 ± 5	4.0	11	30 ± 5
4.1	48,000	26 ± 5	4.1	250	36 ± 5	6.9	680	13 ± 3
6.9	—	—	6.9	6900	13 ± 2	8.5	780	12 ± 3
8.5	—	—	8.5	—	—	11.3	740	12 ± 3
11.3	—	—	11.3	—	—	13.2	2	5 ± 2
13.5	960	6 ± 2	13.2	80	9 ± 3	>14	<<1	5 ± 2
>14	6	13 ± 3						

The dashes in the table indicate that estimates were not possible for these solutions because of the extremely slow isomerisation.

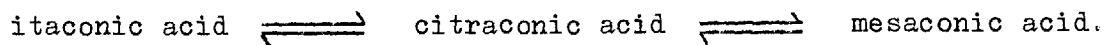
Possible mechanisms for the isomerisation are as follows.

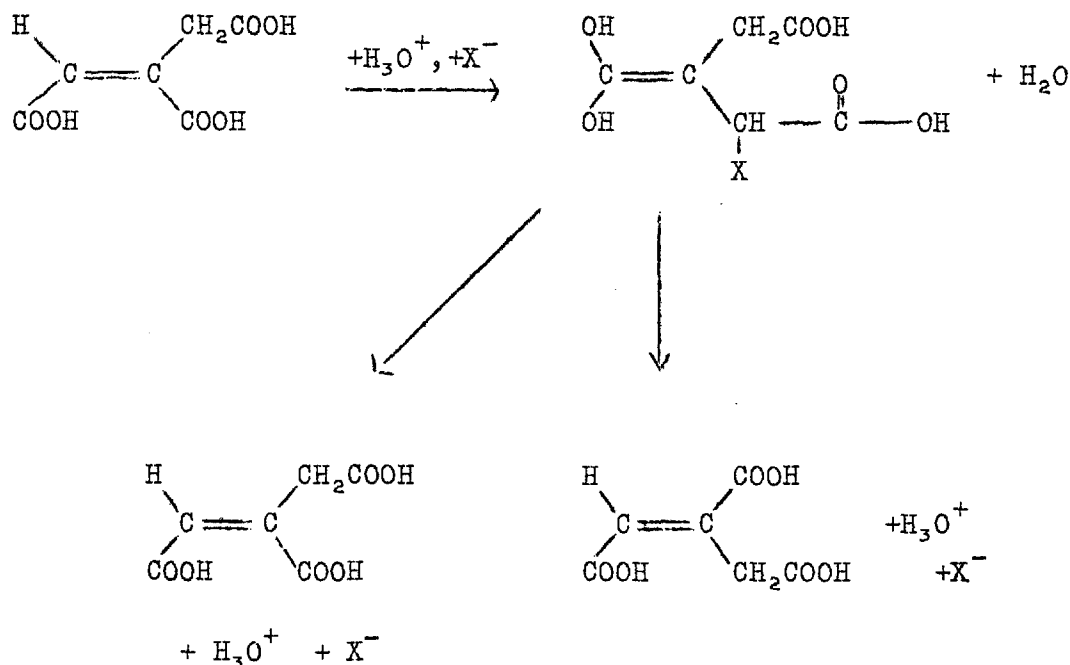
(1) Base catalysed.



A rate determining first step would support the observations. The mechanism essentially involves an uncoupling of the π electrons in the $\beta\gamma$ -double bond thus facilitating rotation about the σ bond, with the formation of the more thermodynamically stable trans isomer.

The mechanism is analogous to the well known base catalysed tautomerism between $\alpha\beta$ - and $\beta\gamma$ -unsaturated acids,⁷¹ e.g.



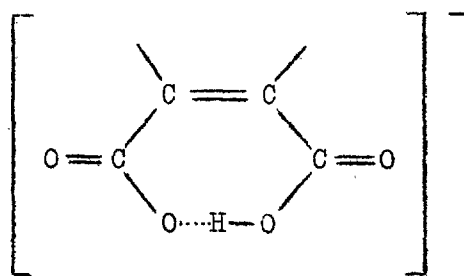
(2) Acid catalysed.⁷²

The first step is considered to be rate determining. However, the observation that the rate does not increase below pH 1 suggests that other mechanisms or steps could be important.

The final equilibrium ratios of the isomers show considerable variation, depending on the pH and temperature. The most striking feature of these is the percentage of the cis isomer in the solutions in the pH range of about 2 $\rightarrow$ 5. In some cases the cis percentage appears to exceed 30%. This agrees with the proportion of cis observed by Krebs and Eggleston⁶⁹ in certain solutions, though they pointed out that their values were of uncertain accuracy. The percentage of cis decreases outside the pH range 2 $\rightarrow$ 5 and appears to reach a minimum in the extreme acid and alkaline regions. No

definite trend of the final equilibrium ratio is noticeable with increasing temperature, in contrast to the observations of Malachowski.⁶⁸

The formation of an intramolecular hydrogen bonded mono-anion chelate with the cis isomer, in the pH range $2 \rightarrow 5$, is a possible explanation for the higher proportion of the cis isomer in the equilibrium solutions. e g.



This structure will be most important in the pH range $2 \rightarrow 5$.

Finally, the effect of the presence of certain metal ions on the equilibria was investigated. It had been hoped that metal ions would alter the rates of isomerisation and/or the final equilibrium ratios by virtue of their complexing abilities. The stronger chelating possibilities of cis aconitic acid might have been expected to influence the equilibria in its favour. However, solutions of cis aconitic acid containing Ag(I), Mg(II), Cd(II), Hg(II), Zn(II), Al(III) and Co(II) ions at various pHs and temperatures showed no appreciable difference in rates or equilibrium ratios from those of the free acids, although measurements were hampered by precipitation in many cases and were largely restricted to low pHs.

Part C. Complexes of the Olefinic Carboxylic Acids

With Metal Ions.

An olefinic carboxylic acid can interact with metal ions through its carboxyl group(s) or double bond or both, but usually the carboxyl groups are involved. With inert metals, several complexes have been isolated, such as the cobaltic complexes of the type $[(\text{NH}_3)_5\text{Co}^{\text{III}} - \text{O} - \text{COC} = \underset{\text{R}_1}{\text{C}} - \underset{\text{R}_2}{\text{C}} - \text{COOH}]^{2+}\text{X}_2^-$.⁷³ The formation of labile complexes with several metal ions in (aqueous) solutions have been studied by pH titration and other methods; such measurements give the stepwise stability constants whose values are relatively low ($\log K, \approx 1.5-3$), showing that the complexes formed are not very stable (relative to the aquo ions).

Recent studies have indicated that Cu(I) and Ag(I) ions can coordinate to some extent to the double bond of certain unsaturated acids.^{74,75} Some olefin-bonded complexes have been isolated.⁷⁶

Since the n.m.r. spectra of both acids and olefins are known to be affected by bonding to metals, it was hoped that some information could similarly be obtained for the olefinic acids.

Complexes with diamagnetic metal ions.

The protons in a ligand bonded to a diamagnetic metal ion are usually more shielded than in the acidic form of the ligand but less than in the free anion. This is indicated partly by measurements on solutions in which the ligands, although labile, were known to be almost entirely complexed,^{77,78} and also by the spectrum of $(\text{NH}_3)_5\text{Co}^{\text{III}} - \text{OCOCH} = \text{CH} - \text{COOH}$ (maleate and fumarate)⁷⁹ in which

the CH protons nearest to the metal ion have greater τ values than the others. Similarly, in bonded olefins, the protons are more shielded than those in the free olefin.^{80,81}

Unfortunately, in the present work, little indication of the effects of diamagnetic metal ions could be found. It was necessary to use solutions which were moderately concentrated (~ 0.2 M) in the acid in order to observe the resonances clearly, and when the pH was raised sufficiently to ionise the acids, the metal ion precipitated as the hydroxide (or hydroxy complex).

The acids used were trans crotonic, citraconic, methacrylic, maleic and cis aconitic; they were dissolved together with an equivalent (1:1) amount of a soluble salt of the metal, and made up to the required pH and a concentration of 0.2 M. The results are summarised briefly below.

- (1) With Al(III), the acids at $\text{pH} < 2$ showed the same spectra as the free acids; at $\text{pH} > 2$ precipitation occurred.
- (2) With Cd(II), the acids showed the same spectra as the free acids at pHs below 4. At pH 4 - 6 a very slight shift (3 - 4 cycles/sec.) of the olefinic protons to low field was observed, but this was considered to be hardly significant. Precipitation occurred on prolonged standing.
- (3) With Mg(II), cis aconitic acid, in the pH range 4 - 7, gave a very small shift to low field (3 - 4 cycles/sec.) which was again considered to be hardly significant. At lower pHs no shifts were observed.

(4) With Ag(I), spectra identical to the free acids were observed at $\text{pH} \leq 3$; at $\text{pH} > 3$ precipitation occurred.

(5) With Hg(II) (as the $\text{Hg}(\text{NO}_3)_2$ salt), over the pH range $0 \rightarrow 12$, there was addition to the double bond of all the acids, presumably giving products of the type

$$\begin{array}{c} \text{CH} - \text{CH} - \text{COOH} \\ | \quad | \\ \text{HgX} \quad \text{OH} \end{array} \quad (\text{X} = \text{NO}_3).$$

Complexes with Co(II) ion.

In these, the interaction of the ligand with the Co(II) ion produces contact shifts which are larger and could be observed more readily than the small changes found for diamagnetic complexes.

A wider range of acids was studied; 1:1 solutions of the acid and a Co(II) salt were prepared and adjusted to the required pH with concentrations of 0.2 M.

At low pH (0 - 2), the spectra of all the acids show only small changes from the shift positions found for the free acids under the same conditions; there is a slight paramagnetic broadening (due to the shortening of T_1) which obscures the smaller splittings of the lines, but, as expected, there is little evidence of any complexing of ligand to the Co(II) ion. However, as the pH is increased further, and the acids become ionised, all the lines move progressively to lower fields and become considerably broader; this behaviour is analogous to that found for the spectra of aliphatic alcohols to which Co(II) is progressively added⁸² This continues until $\text{pH} \approx 7$ at which value some precipitation of cobaltous hydroxide (or hydroxy complex) begins. A typical spectrum is illustrated in Figure 5 and all the spectra at $\text{pH} \approx 7$ are indicated

in Figure 6 together with the shift positions of the free ligands (anions) at the same pH; the line positions of the olefinic protons are very sensitive to small changes in pH. The large downfield shift of the lines with increasing pH is good evidence for complex formation, as the free acids themselves show a much smaller upfield shift over the same pH range.

Since Co(II) has no large affinity for double bonds,⁸³ it is likely that the role of metal-double bond interaction here is small, and the relatively large shifts can be attributed to contact shifts arising from the appearance of slight electron spin density at the protons in the ligands when the carboxylate groups are bonded to Co(II). The fact that the olefinic, methylene and methyl protons all shift to lower field indicates that they all have a small positive spin density induced on them. This suggests that the mechanism involves direct delocalisation of electrons from Co(II) to oxygen and then through the σ bonds. If the transmission were through π bonds, an alternation of shift is expected, and the methyl groups should also then be shifted considerably in the direction opposite to the $\text{C} = \overset{\text{H}}{\text{C}}$ protons which they replace; their smaller shifts in the same direction indicate σ delocalisation, being attenuated through one more bond. The magnitude of the shift for a given type of proton in different acids will depend partly on the strengths of the Co - O bonds. Because there is rapid exchange of ligand among its various states of combination, the observed lines are weighted averages of the various species present, i.e. the free

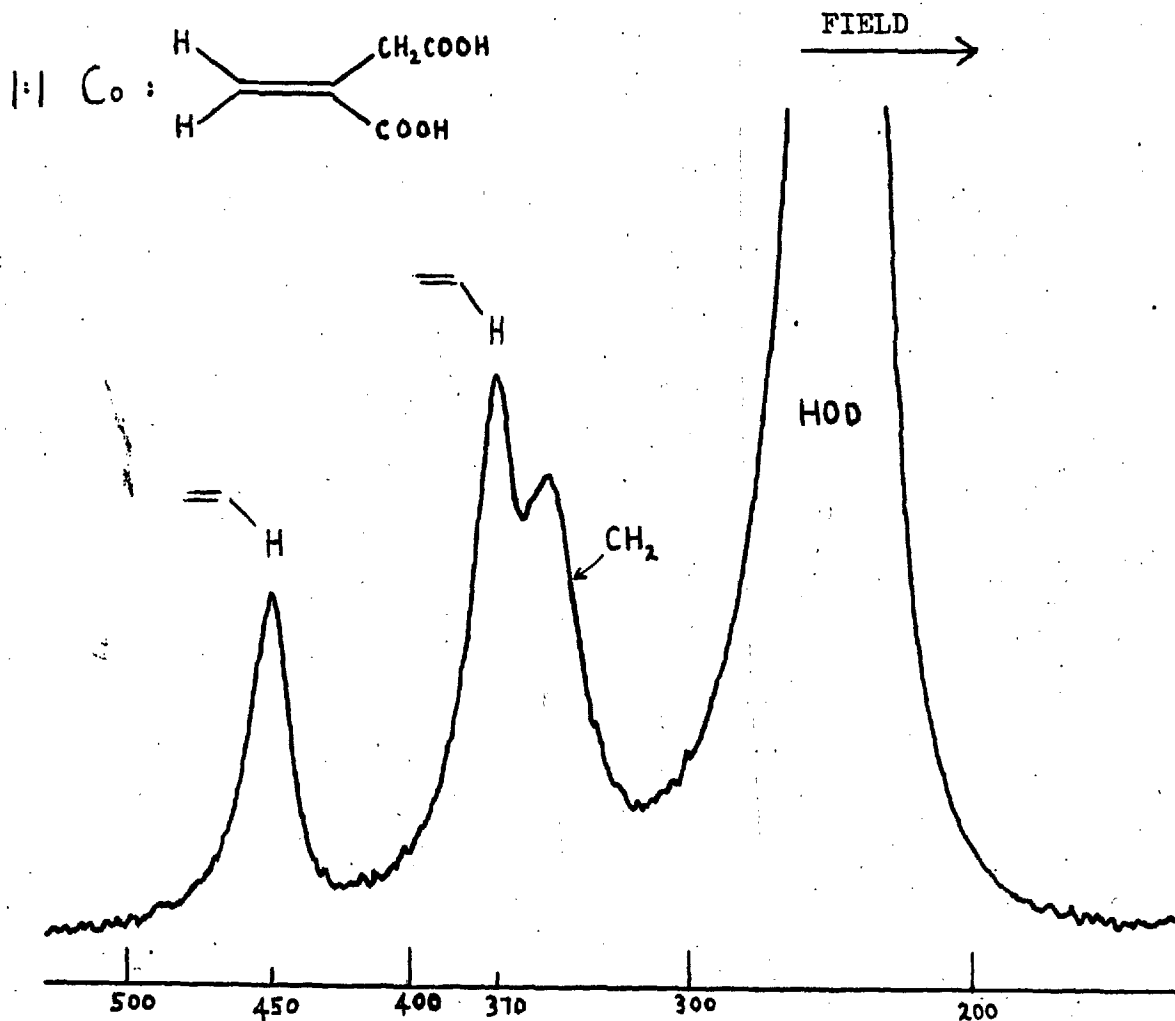


Figure 5. Typical spectrum of the 1:1 complex of Co(II) with itaconic acid at pH-7. The scale is in cycles/sec. on the low field side of t-butanol (zero).

ligand acid, its various anions, and its complexes with Co(II) in the possible ratios 1:1, 1:2, etc.. At pH ~ 7 the free ligands will be mostly ionised; it is not possible to estimate the relative amounts of the other species accurately since the stability constants are not known. However, in each case the main species present is probably a labile 1:1 complex, since (a) in all cases, increasing the ligand concentration above the 1:1 ratio at the same pH (~ 7) caused the lines to move upfield towards the diamagnetic positions, as would be expected for lines which are weighted averages if the additional ligand remained free and did not form higher complexes, and (b) an increase in the relative concentration of Co(II) at the same pH caused no appreciable difference in the line positions, but only increased the paramagnetic broadening. Hence the given spectra provide a rough indication of the shifts in 1:1 complexes.

The assignments of the lines were made by comparing their intensities or by following the shifts from the "diamagnetic" position as the extent of complex formation was increased.

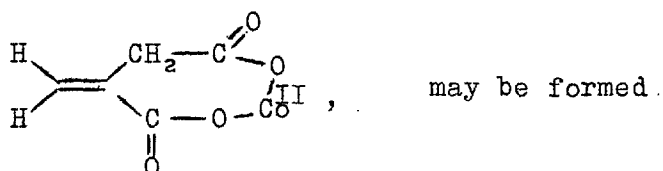
Trans crotonic, $\beta\beta'$ -dimethylacrylic and methacrylic acids are all monodentate ligands (assuming that the double bond is not involved). In the first two, the olefin protons show a fairly large shift downfield; in crotonic acid, H_α and H_β have different shifts and possibly H_α is the lower of the two. In methacrylic acid, H_A and H_B show smaller shifts (as would be expected for olefin protons β to a carboxyl group) and lie close to the HOD line. The methyl shifts are smaller and appear to be the same for the two

groups in the $\beta\beta'$ -dimethylacrylic acid.

Monoethyl fumaric and monoethyl maleic acids give small shifts also, and presumably act as monodentate ligands. The relatively large splittings can still be resolved with these ligands; the complete AB pattern is seen in the fumaric ester but only one half is visible for the maleic ester - presumably the other half is obscured by the HOD line

Fumaric and mesaconic acids will almost certainly function as monodentate ligands, and their shifts are similar to those in the mono-carboxylate acids. The two protons in the fumaric complex will be made to appear equivalent by the rapid ligand exchange.

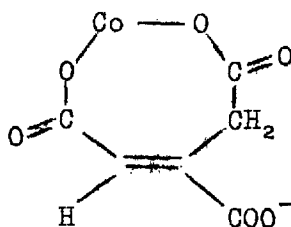
In itaconic acid, the CH_2 protons (assigned as the broadest and highest field of the three lines in Figures 5 and 6) occur at considerably lower fields than do the CH_3 protons in the monodentate acids. This suggests that they receive some unpaired electron density through the side chain carboxyl, indicating that the metal ion is bound preferentially to the $-\text{CH}_2\text{COOH}$ or that a chelate ring,



In the methacrylic, $\beta\beta'$ -dimethylacrylic and itaconic acid cases, if the spin density is transmitted only through the bonds, it would be expected that the shift difference (arising from long range shielding by the carboxylate group(s)) between H_A and H_B ($\text{CH}_3(\text{A})$, and $\text{CH}_3(\text{B})$ in $\beta\beta'$ -dimethylacrylic) would be the same as in the

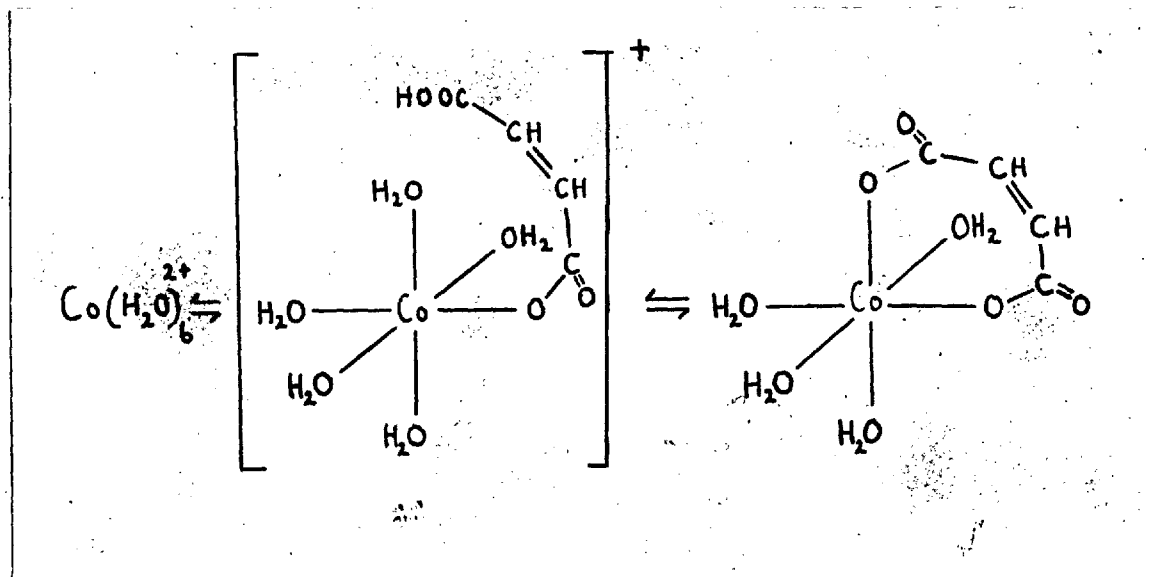
diamagnetic anions. This may be so for the methacrylic case as the shift difference is quite close in the diamagnetic anion and the paramagnetic complex. However, the appearance of one sharp line for both CH_3 groups in the $\beta\beta'$ -dimethylacrylic complex, and the much larger shift difference between H_A and H_B in the itaconic complex than in the diamagnetic anion, suggests the presence of some other effect in addition to the long range shielding; this could be a pseudocontact shift from the Co(II) (which is transmitted through space).

Trans aconitic acid shows a small low field shift in the pH range $0 \rightarrow 3$, followed by a much larger shift at higher pH. The large CH_2 shift again suggests the formation of a chelate, with either a seven membered ring as above, or else, as may be indicated by the relatively large value for the shift of the olefin proton, an eight membered ring.



Maleic acid. In the pH range $0 \rightarrow 3$, the olefinic protons show a small shift to low field. This can be interpreted as due to the formation of a labile one ended complex during the ionisation of the first carboxyl group; the two $=\text{CH}$ protons in this complex appear equivalent due to the rapid ligand exchange. In the pH range

3 $\rightarrow$ 7, a much larger low field shift develops; this is consistent with the formation of a chelate when the second carboxyl group ionises.



The greater shift for this complex relative to the monodentate ones may be the result of contributions coming from two carboxyl groups. (The greater stability of such a complex is due to the chelate effect and does not necessarily imply stronger bonding.)

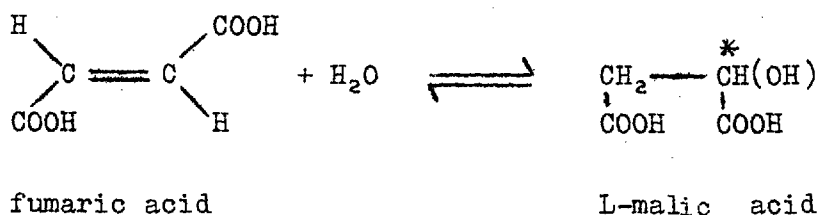
Citraconic acid exhibits very similar behaviour to that of maleic acid; a small downfield shift in the pH range 0 $\rightarrow$ 4, followed by a large shift as the second carboxyl group ionises. This can be explained in the same way as maleic acid. The larger shift (at pH $\sim$ 7) of the olefinic proton compared with maleic acid may indicate the formation of a more strongly bonded chelate, which is not surprising in view of the electron donating capabilities of the CH₃ group. The CH₃ protons give a much smaller shift to low fields.

Cis aconitic acid exhibits similar behaviour to maleic and citraconic acids. The formation of a chelate with the cis carboxylates is again likely, but in this case the ligand is potentially tridentate and the rather large CH_2 shift suggests that the $-\text{CH}_2\text{COO}^-$ group does in fact form a second chelate ring with Co(II) .

CHAPTER III

Addition Reactions of Some Simple Olefinic Acids

The original purpose of this work was to investigate the hydration of fumaric acid. The enzyme fumarase is highly specific for catalysing the reactions in the equilibrium,⁸⁴



which take place in the neutral pH region. This catalysis is believed⁸⁵ to involve activation of the fumaric acid double bond at the enzyme surface, by both a basic and an acidic group, whose pK values are believed to correspond to those of an imidazole and carboxyl group respectively.

Recently, the non-enzymatic hydration of fumaric acid in the neutral pH region has been studied,⁸⁶ and it was hoped that it might be possible to produce a non-enzymatic catalysis of the hydration, which might help to explain the enzyme mechanism. Proton resonance spectra provide a useful means of following such reactions involving simple molecules in aqueous solution.

Aqueous solutions of fumaric acid, in the pH range 5 - 9, were heated at 100⁺1°C for several hours in the presence of potential catalysts. Some of these were metal salts since one possible catalytic process would be the attack by a metal-bonded H₂O molecule

on a fumaric acid molecule which, if also coordinated to the metal, could be both activated by polarisation and also held in a favourable position adjacent to the H_2O ; a mechanism such as this explains the Ru(III) catalysed hydration of acetylene.⁸⁷ Other catalysts were amino acids and imidazole, which could possibly form unstable intermediates whose subsequent hydrolysis by H_2O would produce malic acid. The spectra showed that no malic acid could be detected under these conditions. However, it was noticed that other (slow) reactions of the amino acids and imidazole with fumaric acid were taking place. These proved to be simple addition reactions; their study was extended to include other α/β -unsaturated acids and other additive reagents, but much of the work concerned fumaric acid because the products could possibly be analogous to intermediates in the hydration. A further point of interest is that, when amino acids are used, the products are potentially useful chelating agents for metal ions. The reactions are conveniently divided into three classes, namely, those involving the formation of (A) C - N bonds, (B) C - S bonds and (C) C - O bonds.

A. Reactions involving the formation of C - N bonds.

This class included reactions of fumaric acid with several amino acids and imidazole (Table 8), and of glycine with other olefinic acids (Table 9). In some cases reaction was extremely slow and even prolonged heating at 100° gave only small amounts of the products.

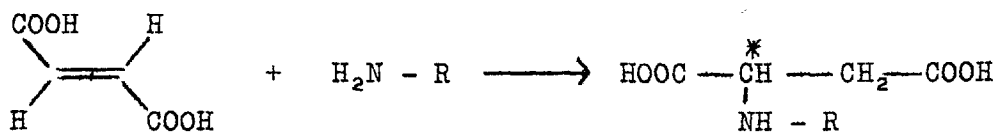
Experimental.

Aqueous solutions containing the unsaturated acid and the other reactant were heated, usually at $100\pm 1^\circ\text{C}$ in the neutral pH region (pH 5 - 9). Concentrations in the range 0.2 M to 1.0 M were used; usually equimolar amounts of the reactants were taken. The proton resonance spectra of the mixtures were recorded at 22°C at various time intervals, using t-butanol ($\sim 1\%$) as internal reference. The reactions were conveniently followed by observing (at the normal probe temperature, $\sim 22^\circ\text{C}$) the decrease in the intensities of the resonance lines of the reactants and the appearance of new product lines, all of which (except with imidazole) are from aliphatic CH protons and lie on the high field side of the H_2O line. The products were characterised, where possible, by their proton resonance spectra (at 22°C), and also, for those which are chelating agents, by their Co(II) contact shift spectra.

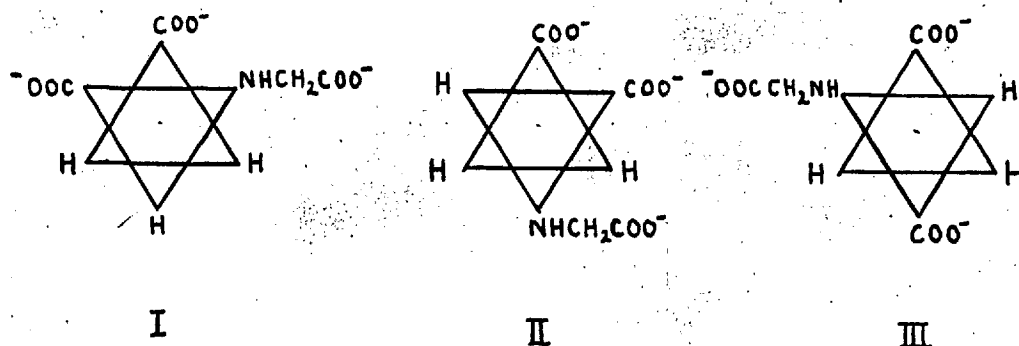
Results and Discussion.

Fumaric acid with glycine, α -alanine and β -alanine.

In the proton resonance spectra of the partially reacted mixtures, some lines of the aliphatic CH groups of the products are obscured by overlapping lines from the unreacted amino acids; however, the spectra are consistent with those expected from the simple addition products.



With glycine ($R = -CH_2COOH$), the product (N-carboxymethyl aspartic acid) gives a spectrum which is approximately first order at $pH \approx 1$ and $pH \approx 9$, and is not obscured by other lines. The $-CH-CH_2-$ group gives an approximately AX_2 spectrum in which the coupling constant, $J_{H-CH_2} = 5.8 \pm 0.5$ cycles/sec. at both pHs. This value suggests that, of the three possible rotational isomers,



II and III may be more heavily populated than I. This would be expected from a consideration of the electrostatic and steric interactions of the three negatively charged carboxylate groups.

With (DL) α -alanine ($R = -\overset{*}{\underset{CH_3}{CH}} - COOH$) and β -alanine ($R = -CH_2CH_2COOH$), the reactions were very slow and the samples always contained the unreacted amino acid. The instrumental resolution was not good enough to separate their lines from those of the products; however, the lines which could be seen suggest that AX_2 groups are present, with $J_{CH-CH_2} \approx 6$ cycles/sec. in both

Table 8. Addition Reactions of Fumaric Acid with Amines.^a

NAME AND FORMULA	RELATIVE RATE	PRODUCT	SPECTRUM		PREVIOUS REF.
			DIAMAG.	Co (ii).	
$\text{H}_2\text{N}-\text{CH}_2-\text{COOH}$ GLYCINE	SLOW $t_{1/2} > 2 \text{ days.}$	$\text{HOOC}-\overset{*}{\text{CH}}-\text{CH}_2-\text{COOH}$ $\quad \quad $ $\quad \quad \text{NH}-\text{CH}_2-\text{COOH}$	FIG. 7A	FIG. 8b	90
$\begin{array}{c} \text{CH}_3 \\ \\ \text{H}_2\text{N}-\overset{*}{\text{CH}}-\text{COOH} \end{array}$ α -ALANINE	VERY SLOW $t_{1/2} > 2 \text{ days.}$	$\text{HOOC}-\overset{*}{\text{CH}}-\text{CH}_2-\text{COOH}$ $\quad \quad $ $\quad \quad \text{NH}-\overset{*}{\text{CH}}-\text{COOH}$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}_3$	FIG. 7B	FIG. 8d	88 89
$\text{H}_2\text{N}-\text{CH}_2\text{CH}_2\text{COOH}$ β -ALANINE	VERY SLOW $t_{1/2} > 2 \text{ days.}$	$\text{HOOC}-\overset{*}{\text{CH}}-\text{CH}_2-\text{COOH}$ $\quad \quad $ $\quad \quad \text{NH}-\text{CH}_2\text{CH}_2\text{COOH}$	FIG. 7C	FIG. 8e	
$\begin{array}{c} \text{H} \\ \\ \text{HC} \quad \text{N} \quad \text{CH} \\ \quad \quad \\ \text{HC} \quad \text{N} \\ \quad \quad \\ \text{IMIDAZOLE} \end{array}$	MODERATE $t_{1/2} \sim 24 \text{ hrs.}$	$\text{HOOC}-\overset{*}{\text{CH}}-\text{CH}_2-\text{COOH}$ $\quad \quad $ $\quad \quad \text{N}$ $\quad \quad \diagup \quad \diagdown$ $\quad \quad \text{C} \quad \text{C}$ $\quad \quad \quad $ $\quad \quad \text{N} \quad \text{N}$	FIG. 7D	-	
$\begin{array}{c} \text{CH}=\text{C}-\text{CH}_2\text{CH}-\text{COOH} \\ \quad \\ \text{N} \quad \text{NH} \\ \quad \\ \text{CH} \quad \text{NH} \end{array}$ HISTIDINE	$t_{1/2} \gg 2 \text{ days.}$	—	-	-	
$\text{H}_2\text{N}-\text{CH}_3$ METHYLAMINE	$t_{1/2} \gg 2 \text{ days.}$	—	-	-	

Addition Reaction of Maleic Acid with Glycine.^a

GLYCINE	FAST $t_{1/2} \sim 12 \text{ hrs.}$	AS FOR FUMARIC	FIG. 7	FIG. 8	90
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^a Reactions carried out at 100°C and pH~9.

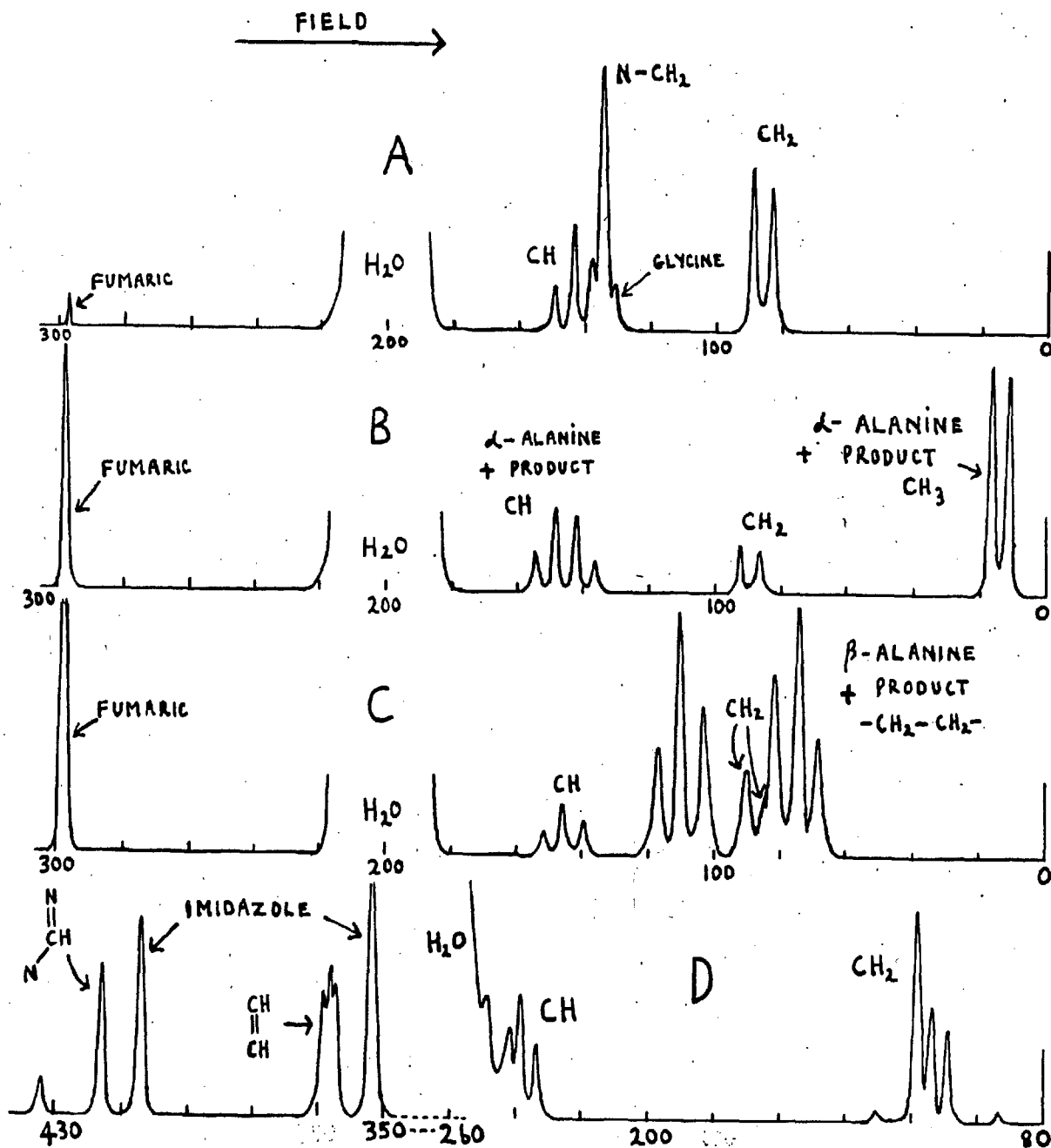


Figure 7. Spectra of reaction mixtures of fumaric acid with (A) glycine, (B) α -alanine, (C) β -alanine, and (D) imidazole at pH-9. Shifts are in cycles/sec. on the low field side of t-butanol. In (D), a large excess of imidazole was used; this accounts for the low position of the H₂O line. (The scale is also displaced at 260 cycles/sec..)

cases, similar to the glycine product.

The products from glycine and β -alanine contain one asymmetric carbon atom and are probably racemic mixtures of the D and L forms. With α -alanine, which already has an asymmetric carbon, the product is probably a mixture of the four possible optical isomers; these isomers have previously been prepared from the condensation of aspartic acid with α -bromopropionic acid.^{88,89} N-carboxymethyl aspartic ester has also been conveniently prepared recently by the reaction of glycine with monoethyl maleic ester.⁹⁰

Since the products are imino tricarboxylic acids they are potentially useful chelating agents for metal ions. Compounds of this type, when complexed to Ni(II) or Co(II), exhibit very large contact shifts of the protons contained in the ligand(s),⁹¹ which are discussed in chapters IV and V. They can provide a better method for characterising the species in the mixtures, since their lines, although broad, have different shifts and often do not overlap. The value of the method is increased if the pH of the solutions is controlled; the imino acids are tetradentate and can form Co(II) complexes (containing two or three chelate rings) at pH values which are too low to allow the formation of the less stable complexes of the (bidentate) amino acids. To illustrate this, Figure 8a shows the proton resonance spectrum of a mixture of glycine and fumaric acid in which the reaction is only partly complete and which therefore contains only a small quantity of the product. Addition of Co(II) ions to the solution and adjustment of the pH to about 3 - 4 gives

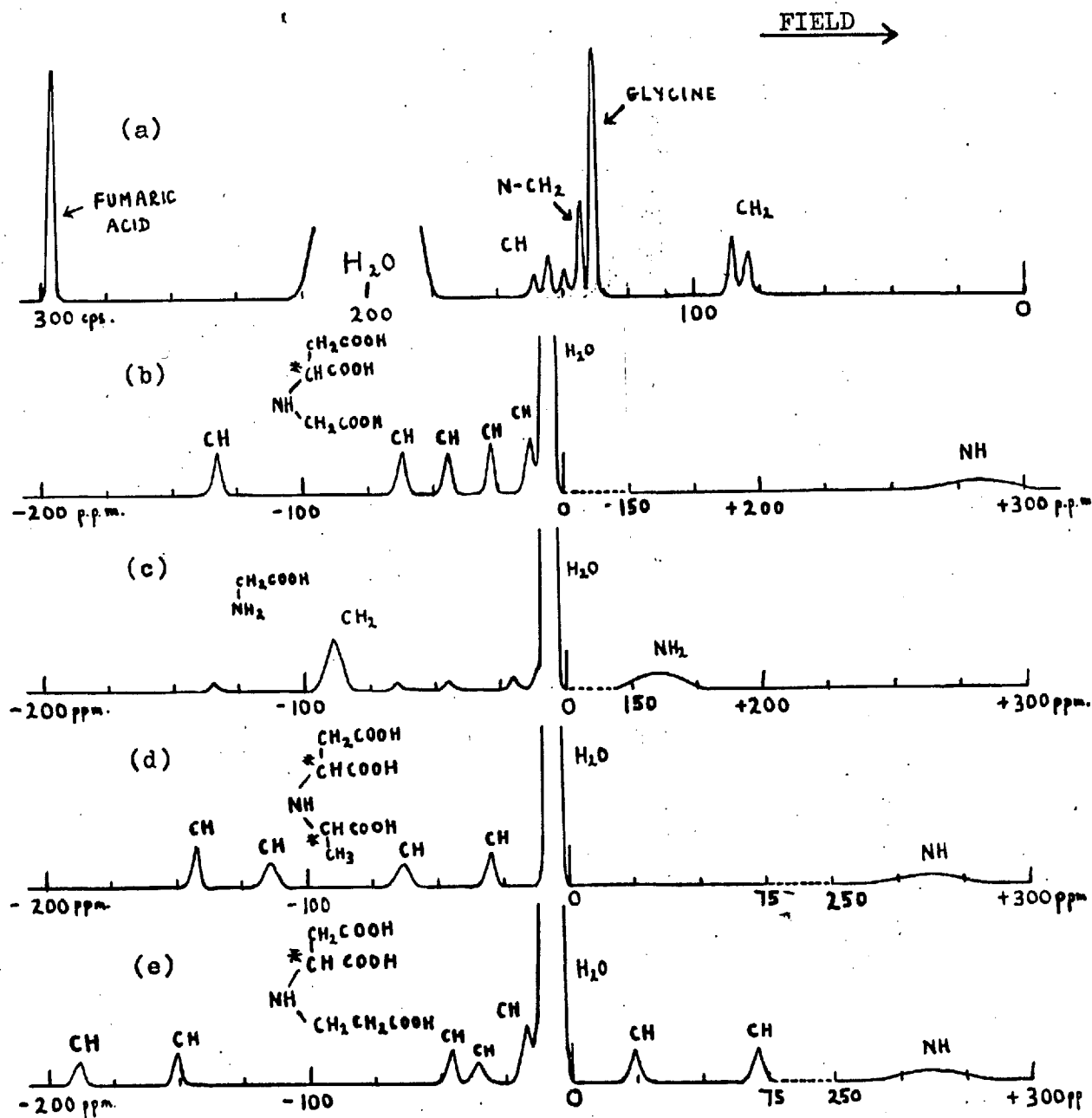
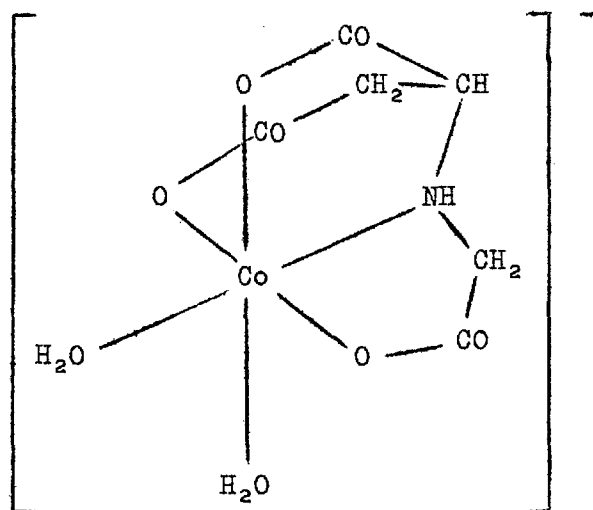


Figure 8. (a) Spectrum of fumaric acid-glycine reaction mixture at pH 9. (b) Co(II) contact shift spectrum of (a) at pH ~3-4. (c) Co(II) contact shift spectrum of (a) at pH ~7. (d) and (e) Co(II) contact shift spectra of fumaric acid- α -alanine and β -alanine reaction mixtures at pH ~3-4 respectively. For full explanation see text.

the contact shift spectrum shown in Figure 8b. This spectrum is similar to those obtained previously⁹¹ with amino acids and imino carboxylic acids, which show very broad high field lines from N - H protons and sharper lines (usually on the low field side of H₂O) from C - H protons. In this particular case, the very broad high field line at approximately 280 p.p.m. (16,000 cycles/sec., relative to t-butanol) is characteristic of a proton attached to an imino nitrogen atom which is bound to Co(II). The sharper low field lines are typical of C - H protons contained in a five or six membered chelate ring of a Co(II) complex; the four observed - probably each represent one C - H proton, with one missing line hidden by the intense H₂O band. Addition of more Co(II) to the solution has no appreciable effect, and it is likely that the complex present is a 1:1 species, whose possible structure is indicated below.



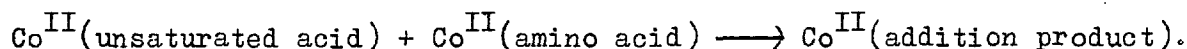
A "mixed" complex containing both the product ligand and glycine may also exist (see chapter V).

Although glycine is present in large excess, no lines of the Co(II) - glycine chelate complexes are observed at pH 3 - 4, since these, which contain only single five membered chelate rings, are not sufficiently stable to form at this pH. In contrast, at pH $\approx$ 7, they are formed, and the contact shift spectrum then consists mainly of two intense lines, one very broad high field line (from -NH₂) at about 160 p.p.m. (9,000 cycles/sec.) and one sharper low field line (from -CH₂) at about 90 p.p.m. (5,100 cycles/sec.), which are known to come from mixtures of the 1:1, 1:2 and 1:3 Co(II)/glycine chelates.⁹¹ Some other very weak lines are present which correspond approximately to the lines present at pH 3 - 4, but they are largely obscured by the intense line at $\sim$ 90 p.p.m.

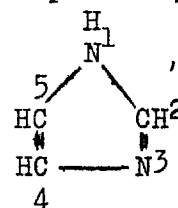
The situation is similar for the reaction mixtures with both α -alanine and β -alanine. At pH 3 - 4, contact shifts, which can be attributed to the complexes of the products, are obtained (Figures 8d and 8e), whereas at pH $\approx$ 7 the major lines correspond to those of Co(II) complexes with α -alanine and β -alanine respectively (see chapter V). The spectra of the products contain many lines and others are probably obscured by the H₂O resonance, which makes a full assignment difficult. However, the very broad high field line at about 265 - 280 p.p.m. (15,000 - 16,000 cycles/sec.) is a good indication of the presence of the imino group in the complex.

It would also be possible to use contact shift spectra as a convenient way of following the course of an addition reaction,

provided that the product and at least one reactant gave spectra, and that the lines did not overlap. After suitable time intervals, samples of the reaction mixture would be "quenched" (if necessary), Co(II) added to them, and the spectra recorded. Also, a continuous record could be made of a reaction of the type:

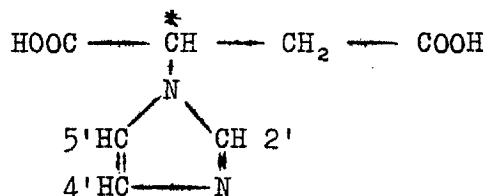


Imidazole, histidine and methylamine. Imidazole,



reacts relatively readily with fumaric acid at 100° and $\text{pH} \approx 9$.

The spectrum of the main product (Figure 7d) is consistent with the structure



The $-\text{CH}-\text{CH}_2-$ group gives an ABC pattern on the high field side of H_2O . The main low field lines of the product are close to those of imidazole, as would be expected for the addition compound. The weak line at the lowest field may represent another product, whose structure is not known.

The reactions of methylamine and histidine with fumaric acid under mildly alkaline conditions ($\text{pH} \approx 9$) were extremely slow. After several days at 100° , the spectra of both reaction mixtures showed weak high field lines, but the reactions were not followed further. The methylamine product is probably N-methyl aspartic acid,

while histidine could add to the double bond through either the NH_2 group or the imidazole $>\text{NH}$. The enormous difference in the reaction rates of imidazole and histidine with fumaric acid may be due to the steric effects of the large histidine molecule.

Maleic acid and glycine react readily at 100° under mildly alkaline conditions; they give the same product as with fumaric acid, but the reaction is considerably faster and some isomerisation also occurs. Presumably the other compounds would also give products similar to those from fumaric acid, but more readily.

Glycine with methacrylic, trans crotonic, itaconic and citraconic acids. Prolonged heating at 100° at $\text{pH} \approx 1 - 2$ gave no observable reaction, and heating at $\text{pH} \leq 1$ for several days produced slight hydration in all cases. At $\text{pH} \approx 9$, crotonic acid reacts readily with glycine giving a product whose spectrum (Figure 9) is consistent with the structure shown in Table 9. A first order analysis of the spectrum at $\text{pH} \approx 11$ is not possible, but J_{AB} ($= 15.7^{+0.3}$ cycles/sec.) is estimated approximately from the "AB" part of the "ABXY₃" pattern. At $\text{pH} \approx 1$, the $-\text{CH}-\text{CH}_2-$ group appears to give an AX_2 type spectrum and $J_{\text{H}-\text{CH}_2}$ ($= 6.4^{+0.3}$ cycles/sec.) can be estimated from the " AX_2Y_3 " pattern. The lines expected for the

possible product, $\text{HN} \begin{array}{l} \text{CH}_2-\text{CH}_3 \\ | \\ \text{CH}-\text{COOH} \\ * \\ \text{CH}-\text{COOH} \end{array}$, were not observed, so little, if any, of it was formed.

The product, which was required for contact shift spectra studies (see chapters IV and V), was isolated as follows. A solution

Table 9. Addition Reactions of Glycine with Unsaturated Acids.^a

NAME AND FORMULA	RELATIVE RATE	PRODUCT	SPECTRUM		PREVIOUS REF.
			DIAMAG.	Co (II).	
$\begin{array}{c} \text{CH}_3 \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{COOH} \end{array}$ CROTONIC ACID	MODERATE $t_{1/2} \sim 24 \text{ hrs.}$	$\begin{array}{c} \text{CH}_3 - \overset{*}{\text{CH}} - \text{CH}_2 - \text{COOH} \\ \\ \text{NH} - \text{CH}_2 - \text{COOH} \end{array}$	FIG. 9A	FIG. 10a	92
$\begin{array}{c} \text{H} \quad \text{CH}_3 \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{COOH} \end{array}$ METHACRYLIC ACID	VERY SLOW $t_{1/2} \gg 2 \text{ days}$	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 - \overset{*}{\text{CH}} - \text{COOH} \\ \\ \text{NH} - \text{CH}_2 - \text{COOH} \end{array}$	FIG. 9C	FIG. 10b	
$\begin{array}{c} \text{H} \quad \text{CH}_2\text{COOH} \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{COOH} \end{array}$ ITACONIC ACID	SLOW $t_{1/2} > 2 \text{ days}$	$\begin{array}{c} \text{CH}_2 - \text{COOH} \\ \\ \text{CH}_2 - \overset{*}{\text{CH}} - \text{COOH} \\ \\ \text{NH} - \text{CH}_2 - \text{COOH} \end{array}$	FIG. 9B	-	
$\begin{array}{c} \text{CH}_3 \quad \text{H} \\ \diagdown \quad \diagup \\ \text{C} = \text{C} \\ \diagup \quad \diagdown \\ \text{COOH} \quad \text{COOH} \end{array}$ CITRACONIC ACID	VERY SLOW $t_{1/2} \gg 2 \text{ days}$	$\begin{array}{c} \text{CH}_2 - \text{COOH} \\ \\ \text{CH}_3 - \overset{*}{\text{C}} - \text{COOH} \\ \\ \text{NH} - \text{CH}_2 - \text{COOH} \end{array}$	FIG. 9D	FIG. 10c	

^a Reactions carried out at 100°C and pH-9.

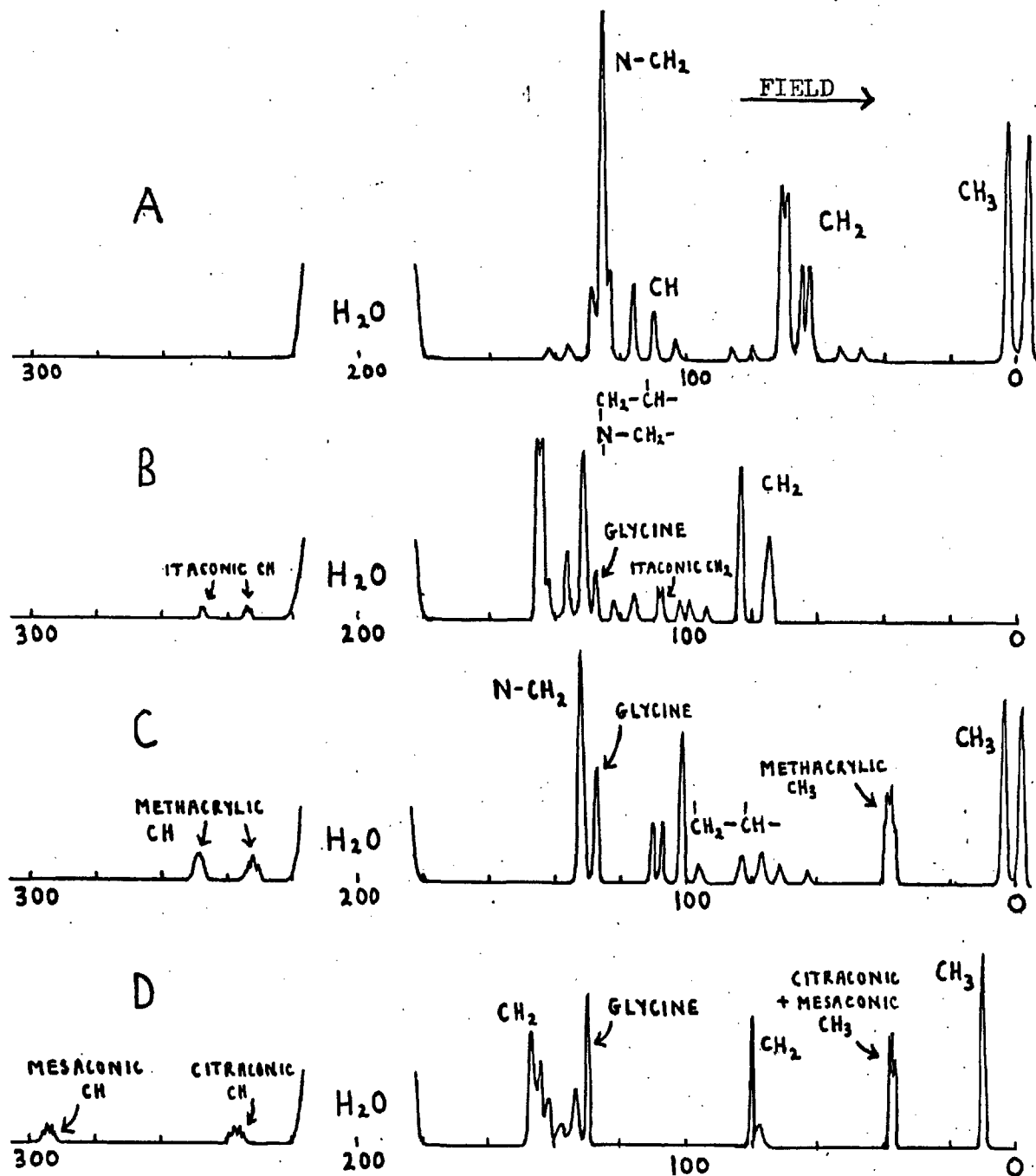


Figure 9. Spectra of reaction mixtures of glycine with (A) crotonic acid, (B) itaconic acid, (C) methacrylic acid, and (D) citraconic acid at pH 9. Shifts are in cycles/sec. on the low field side of t-butanol.

containing glycine and excess crotonic acid in the presence of $\text{Ba}(\text{OH})_2$ ($\text{pH} \approx 9$) was heated at 100° till the reaction had reached completion (about 24 hours). The barium ion was removed by precipitating BaSO_4 with dilute sulphuric acid; after centrifugation, the resulting yellow solution was pumped to dryness in vacuo. Leaching of the brown residue gave a white powder which was the crude product. It was purified by washing with absolute ethanol several times and finally recrystallising from hot water. (Yield, 70%).

Analysis: Calculated for $\text{C}_6\text{H}_{11}\text{NO}_4$: C 44.70, H 6.88, N 8.69.

Found: C 45.15, H 6.71, N 8.56.

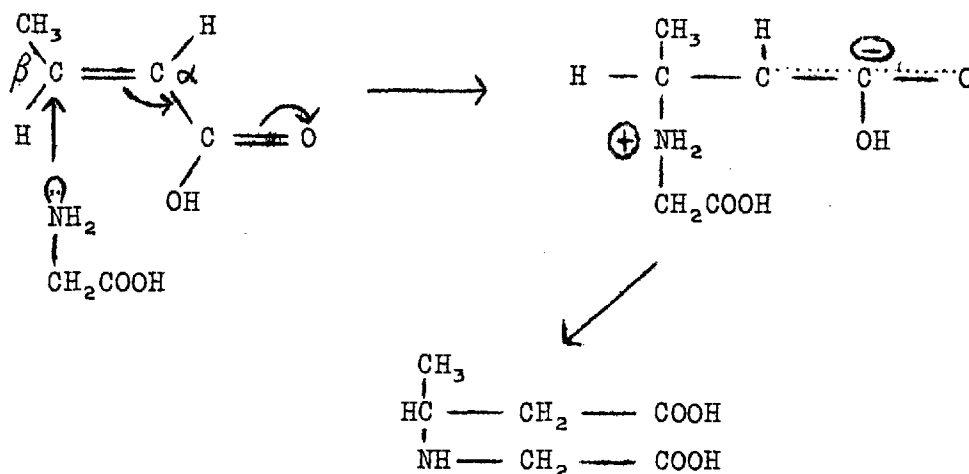
The analysis and n.m.r. spectrum were sufficient indication of purity. The compound is probably a racemic mixture. Previously, it had been prepared by the reaction between the sodium salts of glycine and crotonic acid.⁹²

Compared with crotonic acid, the addition is slower with itaconic acid and slower still with methacrylic. The spectra of the reaction mixtures are complex and overlap with the lines of the reactants, but they again suggest, as with crotonic, that the nitrogen has added only to the β - carbon of the olefinic acid.

With citraconic acid, the nitrogen appears to have added only to the carbon carrying the CH_3 group. With itaconic and citraconic acids, a little of the isomeric mesaconic acid was produced during the reactions.⁷¹ Previously, amines have been observed to add to $\alpha\beta$ -unsaturated acids or their esters forming β -alkyl amino products.⁹³⁻⁹⁶

The addition of Co(II) to the reaction mixtures and adjustment of pH gave contact shift spectra in all cases (Figure 10). Although the low field (relative to t-butanol) spectra are somewhat complex and not easily assigned, the appearance of a very broad field line between about 180 p.p.m. and 350 p.p.m. in each case indicates the presence of an imino group. The complexes of the crotonic product with Co(II) (and also with Ni(II)) are dealt with more fully in chapter V (Ni(II) in chapter IV).

The increase of rate with pH, and the preferential addition to the more positive of the olefin carbon atoms in the monobasic acids, suggests that the reactions involve nucleophilic addition as indicated in the scheme below.⁹⁷



The molecules are drawn in the acid forms, although at $\text{pH} \approx 9$ they will be mainly in the anionic forms. The rates increase with pH, due to the increasing concentration of the nucleophilic $\text{R} - \text{NH}_2$ species; they also decrease with increasing steric hindrance arising from substituent groups. Attack at the β carbon is preferred because

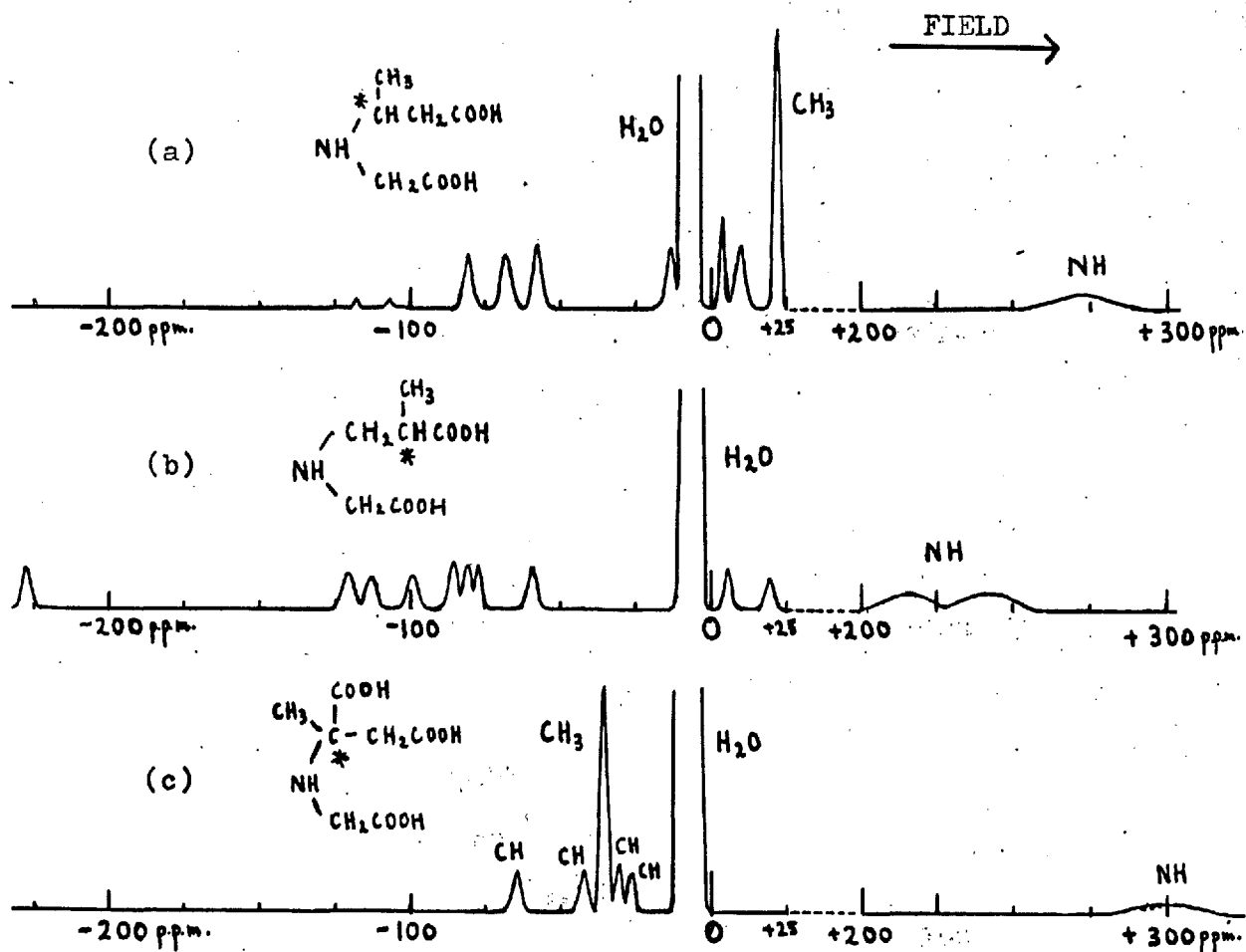


Figure 10. Co(II) contact shift spectra at pH-3-4 of (a) crotonic acid-glycine reaction mixture, (b) methacrylic acid-glycine reaction mixture, and (c) citraconic acid-glycine reaction mixture. Shifts are in p.p.m. relative to t-butanol.

the conjugation with the carboxyl group places the greater fractional positive charge on this, and also because this gives an intermediate with more resonance stabilisation.

When the reactions were carried out under acidic conditions (i.e. $\text{pH} \approx 1 - 2$), they were extremely slow and an equilibrium was established,



which lies well towards the reactant side. When solutions of the products (obtained at $\text{pH} \approx 9$) at $\text{pH} \approx 1 - 2$ were heated at 100° the reactants were regenerated and the above equilibrium established - no hydration was observed. Prolonged heating of the acids at $\text{pH} \approx 1$ resulted in a little hydration.

B. Reactions involving the formation of C - S bonds.

Addition reactions of thioglycollic acid ($\text{HS} - \text{CH}_2 - \text{COOH}$) with several unsaturated acids were studied at $\text{pH} 1 - 2$ and at $\text{pH} \approx 7$ in the same way as for the amino acids. At $\text{pH} > 7$, thioglycollic acid is fairly easily oxidised to dithioglycollic acid in the presence of air at room temperature; air was not excluded from the solutions, but at $\text{pH} \leq 7$ the oxidation is very slow and may be neglected. The reactants used and the products formed are summarised in Table 10. The reactions are all of the type

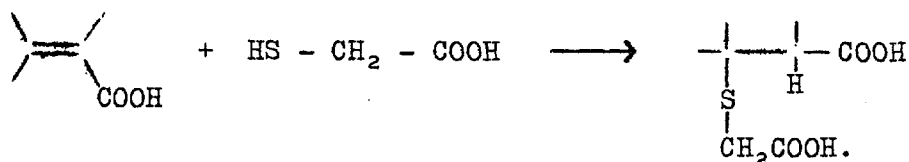
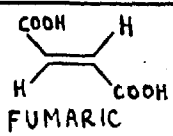
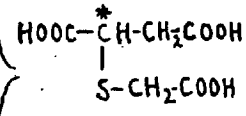
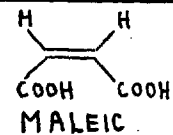
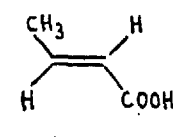
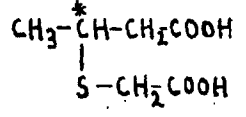
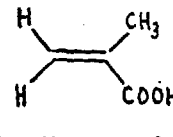
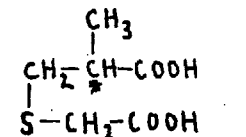
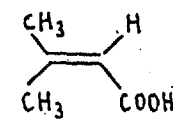
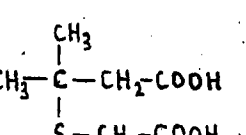
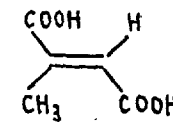
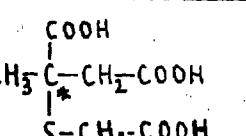
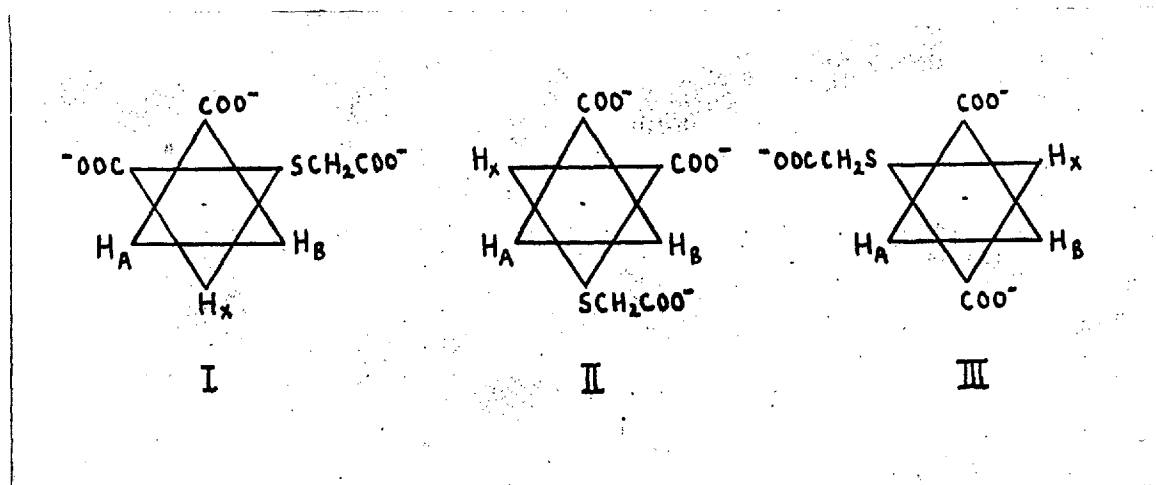
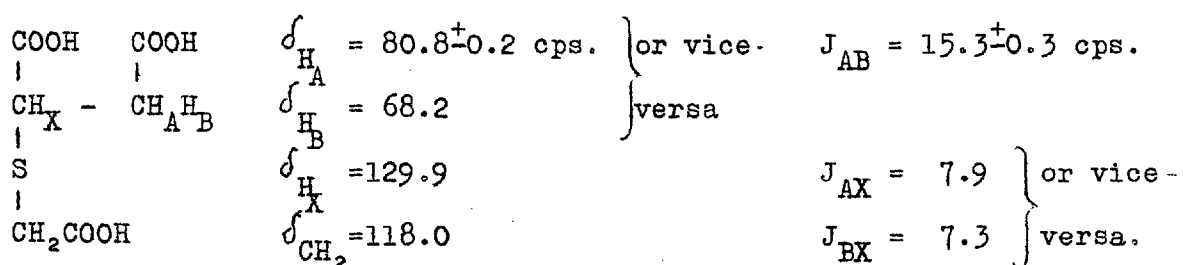


Table 10. Addition Reactions of Thioglycollic Acid,
 $\text{HS-CH}_2\text{-COOH}$, with Unsaturated Acids.

NAME AND FORMULA	CONDITIONS		RELATIVE RATE	PRODUCT	SPECTRUM	PREVIOUS REF.
	pH	T°C.				
 FUMARIC	2	20	SLOW		FIG. 11	99
	2	100	FAST			
 MALEIC	7	20	SLOW			
	2	20	VERY FAST ^a			
 CROTONIC	7	20	VERY FAST ^b		FIG. 12a	100
	1-2	100	SLOW			
	7	100	FAST			
 METHACRYLIC	1-7	20	VERY SLOW		FIG. 12b	100 101
	1-2	100	SLOW			
 $\beta\beta'$ -DIMETHYLACRYLIC	7	100	SLOW		FIG. 12d	
	1-2	100	VERY SLOW			
 MESACONIC	1-2	100	VERY SLOW		FIG. 12c	
	7	100	SLOW			

^a $t_{1/2}$ ~ 100 mins.. ^b $t_{1/2}$ ~ 60 mins..

Maleic acid reacts considerably faster than fumaric acid; both acids give the same product, which will probably be a racemic mixture. The proton resonance spectrum (Figure 11) is fairly simple; the $-\text{CH}-\text{CH}_2-$ group gives an ABX pattern, and a complete analysis of the spectrum was possible.⁹⁸ The shifts (relative to t-butanol) and coupling constants at $\text{pH} \approx 9$ are given below; the latter are probably all positive.



The values of J_{AX} and J_{BX} indicate that rotamers II and III are both more heavily populated than I. This would be expected since, in II and III, the electrostatic and steric interactions between the bulky, negatively charged groups are minimised.

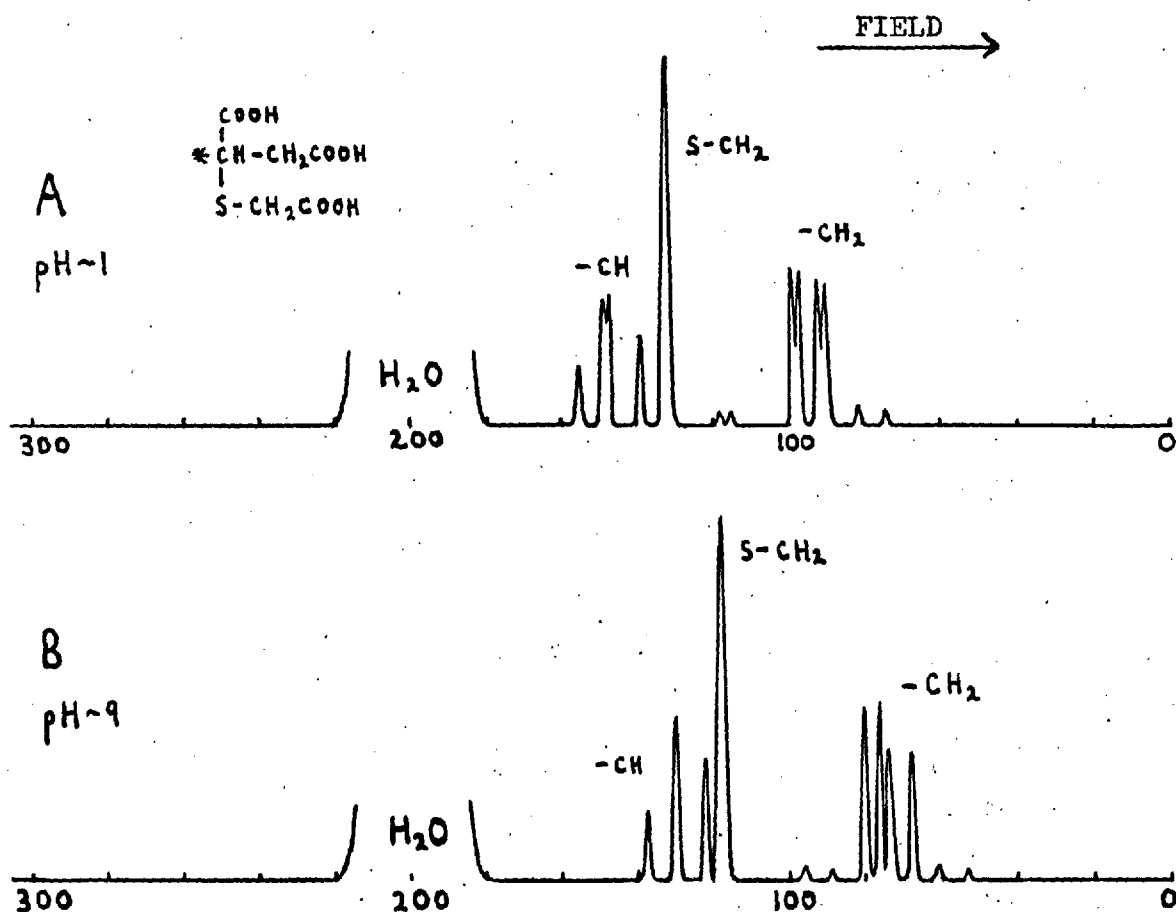


Figure 11. Spectra of the product from the reaction between maleic (fumaric) acid and thioglycollic acid at (A) pH~1 and (B) pH~9. Shifts are in cycles/sec. on the low field side of t-butanol.

With crotonic, methacrylic and $\beta\beta'$ -dimethylacrylic acids, the reactions were slower, and the spectra (Figure 12) of the products appear to be consistent with the structures given in Table 10, which would result from addition of the sulphur to the β carbon atom. With mesaconic acid (Figure 12c), the main product seems to have sulphur attached to the carbon carrying the methyl group, though the complex spectrum also suggests the presence of other products or decomposition products or both.

Previously, some of the products have been prepared by similar addition reactions and condensation reactions.⁹⁹⁻¹⁰¹

With the fumaric acid and crotonic acid addition products, attempts were made to observe the spectra of the Co(II) complexes, although these would be expected to be much less stable than those formed by the nitrogen containing analogues. On addition of Co(II) to the solutions of the products, they slowly formed brown precipitates and no spectra were observed. It seems likely that decomposition occurred to give cobalt sulphide.

The addition of thioglycollic acid to $\alpha\beta$ -unsaturated acids resembles the additions of amino acids in being faster the higher the pH, and also in the preference for β -attack. This suggests that a similar mechanism may operate, i.e. nucleophilic attack by the anion RS^- at the β carbon atom (of an unsymmetrically substituted double bond). The reactions would be expected to be faster since sulphur has a greater intrinsic nucleophilic reactivity than amino nitrogen.¹⁰²

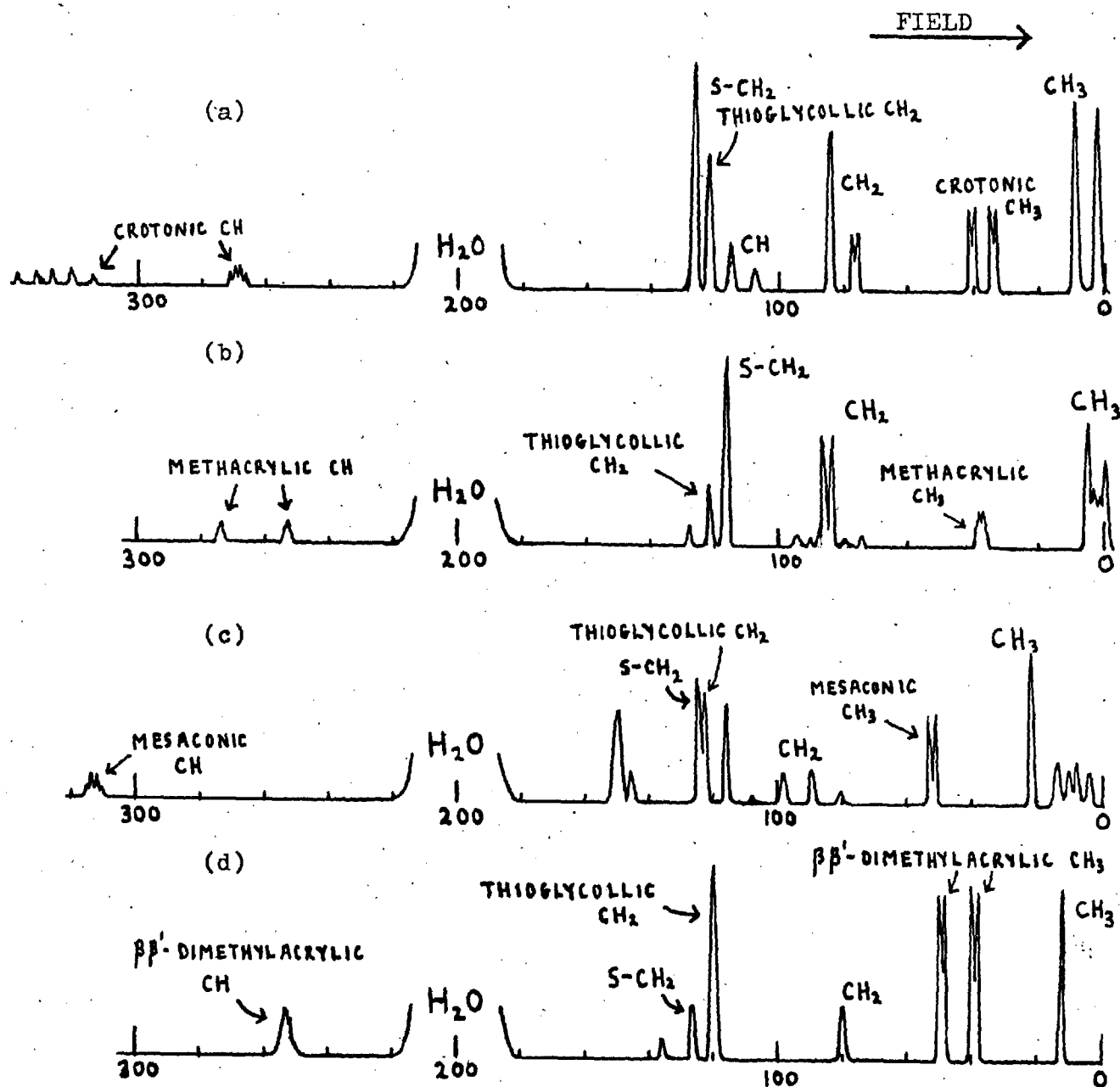
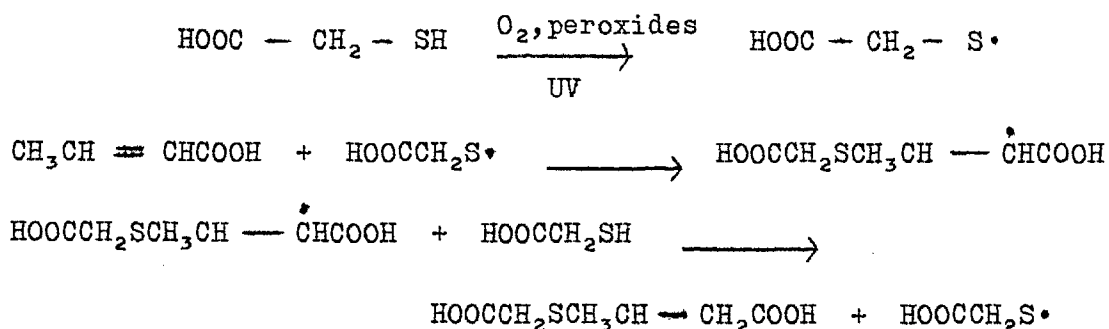


Figure 12. Spectra of reaction mixtures of thioglycolic acid with (a) crotonic acid, (b) methacrylic acid, (c) mesaconic acid, and (d) $\beta\beta'$ -dimethylacrylic acid at pH-1-2. Shifts are in cycles/sec. on the low field side of *t*-butanol.

Some of the additions are also fairly fast in acidic solutions, and it is possible that a free radical mechanism could be involved as follows:¹⁰³ (e.g. for the addition to crotonic acid)



In the absence of kinetic studies it is uncertain whether one or both mechanisms operate.

The effect of metal ions. The effects of some diamagnetic metal ions on the thioglycollic addition reactions at various pHs were investigated in the hope of finding catalytic effects. The metal ions tried were Zn(II), Ag(I), Hg(II), Al(III), Mg(II), Na(I), Ca(II) and Cd(II). With Ag(I) and Hg(II), the measurements were hampered by precipitation of solid products. The others mostly showed small effects; however, in acid solutions (pH $\approx$ 2), Zn^{2+} gave a considerable enhancement of the reaction rates of all the additions, which was most marked for the slower reactions. For example, the presence of 0.2 M Zn^{2+} in a 0.2 M reaction mixture of crotonic acid and thioglycollic acid accelerated the rate by at least a factor of ten. The rate depends on the concentration of the Zn^{2+} , and was also found to depend on the anion present, $\text{SO}_4^{=}$ producing a considerable enhancement of the reactions, whereas

Cl^- , NO_3^- and ClO_4^- had little or no effect. Hence the catalytic effect of ZnSO_4 is due partly to the Zn^{2+} ion and partly to the sulphate anion (which would be present mainly as HSO_4^- at this pH). For 0.2 M (with respect to both reactants) solutions of all the reaction mixtures except maleic and fumaric acids, the presence of 0.2 M ZnSO_4 accelerated the rate by at least a factor of 20; for maleic acid, the rate was approximately doubled.

The mechanism of this catalysis in acidic solution is not easily explained. Zn(II) is not known to add to the double bonds of mono-olefins to form π type complexes,¹⁰⁴ and at pH 2 the only expected effect would be a weak one-ended interaction with the carboxyl groups. Possibly interaction of Zn(II) ions with the unsaturated acid carboxyl group(s) activates the double bond, although other metal ions would also complex with $-\text{COO}^-$. The catalytic effect of sulphate (or more likely HSO_4^-) is not understood. If the free radical mechanism applies, it is even more difficult to envisage how Zn(II) and HSO_4^- could act as catalysts; although some metal ions do act as free radical initiators (in redox reactions),¹⁰⁵ Zn(II) is not known to act in this way.

In contrast, at $\text{pH} \approx 7$, ZnSO_4 has a marked negative catalytic effect; this may be due to the formation of Zn(II) chelates with the sulphur group of thioglycollic acid at this pH,¹⁰⁶ thus inhibiting the addition.

Few definite conclusions can be made except that a detailed study of the kinetics would be worthwhile.

Attempts were made to cleave the C - S bond in the addition compounds using (a) alkali and (b) Hg(II) under various conditions, in the hope that malic acid would be formed. However, all attempts using the quoted methods¹⁰⁷ proved unsuccessful, perhaps largely due to the formation of solid Hg(II) adducts. Hydration was only observed on prolonged heating of the olefinic acids under acidic conditions ($\text{pH} \leq 1$).

C. Reactions involving the formation of C - O bonds.

This class included the reactions of $\alpha\beta$ -unsaturated acids with both water and formic acid. Formic acid, $\text{H} - \text{C} \begin{array}{l} \nearrow \text{O} \\ \searrow \text{OH} \end{array}$, has been observed to add to olefinic acids under acidic conditions.¹⁰⁸ H_2O will add slowly to fumaric acid in the neutral pH region,⁸⁶ but much faster in strong alkaline conditions or when catalysed by strong acids.

Prolonged heating (several days) of the unsaturated acids with both formic acid (as its anion) and water at $100^\circ \pm 1^\circ\text{C}$, in the neutral pH region (pH 5 - 9), gave no apparent reaction.

CHAPTER IV

Proton Contact Shift Spectra of Complexes of Ni(II) with Aminopolycarboxylic Acids in Aqueous Solutions.

Since contact shift spectra provide a useful method for analysing certain organic reaction mixtures (as was demonstrated in the preceding chapter), it was decided to study more fully the spectra of the complexes formed by Co(II) and Ni(II) with chelating ligands of structures similar to the addition products obtained in chapter III. In some cases, the spectra can provide useful information about the structures of the complexes formed and the nature of the metal-ligand bonding. The ligands used were restricted to those able to form five and six membered chelate rings since these are known to give the most stable complexes.¹⁰⁹ Previously, complexes of a few monocarboxylic amino acids and EDTA derivatives with Co(II) and Ni(II) have been studied,⁹¹ but little other work has been done with aliphatic ligands such as these, in contrast to the many studies made in recent years on the Co(II) and Ni(II) complexes of unsaturated ligands.¹⁷ Some proton resonance studies of some of the present aliphatic ligands with diamagnetic metals have been made; of particular interest are those involving Co(III),¹¹⁰ Mo(VI)¹¹¹ and Tl(III).¹¹²

Experimental.

The solutions were prepared by dissolving weighed amounts of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and the ligand in H_2O , to give known concentrations in the range 0.25 M to 0.5 M with respect to both the metal ion and

the ligand. It was found that variation of concentration had a negligible effect on the position of the lines, provided the metal/ligand ratio and pH were kept constant. The line positions of a particular species also usually do not vary greatly with pH, but in order to control the amounts of 1:1 or 1:2 complexes present, the pH was adjusted by addition of sodium carbonate and was measured using Universal Indicator Paper (± 0.5 pH unit). In cases where the intense H_2O resonance obscured part of the spectrum, the measurements were usually repeated in D_2O , using anhydrous $NiCl_2$. The samples were contained in 5 mm. o.d. thin-walled tubes; these were not made to spin, partly because the homogeneity obtained without spinning is better than the half widths of even the sharpest lines, and partly because the ionic solutions generate bad spinning sidebands, particularly with the high R.F. power levels used. The spectra were recorded at 56.45 mcs./sec. at $22 \pm 1^\circ C$, using t-butanol ($\sim 1\%$) as internal reference. The lines are generally broad and, in order to observe them clearly above the noise level, it was necessary to use higher R.F. power levels than are used with normal diamagnetic samples. This makes the samples more sensitive to the probe temperature and to vibrations, and the base line often showed instabilities and drifting. Also, since the spectrometer is not stable enough to use calibrated chart paper, the line separations had to be measured by the sideband technique. The line positions in each spectrum are the averages of at least six consecutive determinations (three increasing and three decreasing field). A few measurements were also made at 100 mcs./sec..

The error in the contact shifts varies from about ± 0.2 p.p.m. for the sharpest lines to about ± 10 p.p.m. for those which are very broad and only just visible above the noise. All line positions are given in p.p.m. and referred to *t*-butanol as zero. The contact shifts should strictly be measured relative to the line positions of the equivalent protons in a closely similar diamagnetic complex, but all the diamagnetic aliphatic CH groups lie close together and the differences are almost negligible compared with the large contact shifts.

Materials. $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and sodium carbonate (both "Analar") were obtained commercially. Anhydrous NiCl_2 was prepared by heating the hexahydrate at 120°C for several hours [Several of the names given for the ligands do not follow the I.U.P.A.C. nomenclature, but are used since they indicate the differences between the ligands.]

Glycine, N-methyl glycine, NN'-dimethylglycine, α -alanine, CC'-dimethylglycine, iminodiacetic acid, N-methyl iminodiacetic acid, nitritotriacetic acid and β -alanine were obtained commercially. They were used as supplied; their proton resonance spectra confirmed that they were pure.

N-ethyl iminodiacetic acid was prepared by an analogous method to that given for the N-methyl derivative,¹¹³ i.e. by the reaction of ethylamine with chloroacetic acid. (Yield, 55%).

Analysis. Calculated for $\text{C}_6\text{H}_{11}\text{NO}_4$: C 44.70, H 6.88, N 8.69.

Found: C 44.98, H 7.00, N 8.57

Imino - α - propionic acetic acid was prepared as directed¹¹⁴

as the hydrochloride from α -alanine and chloroacetic acid. The initial product was found to be a mixture of the required compound and nitrilo - α - propionic diacetic acid. A good separation of these two was effected by dissolving the mixture in ethanol, adding ether, and cooling in an ice-water mixture. The imino derivative precipitated out and was filtered off and dried in vacuo. Evaporation of the filtrate gave the nitrilo derivative. The n.m.r. spectrum of the imino compound showed the presence of a very small quantity of some other compound, but the product was taken as sufficiently pure for use. (Yield, 22%).

Imino - di - α - propionic acid was prepared in poor yield (16%) from DL - α - alanine and DL - α - bromopropionic acid.¹¹⁵ The product was found to contain a small amount of another product (probably the nitrilo - tri - α - propionic acid). Attempts to remove this impurity using ion-exchange methods proved unsuccessful, but its amount was not large enough to contribute greatly to the main spectra.

Nitrilo - α - propionic diacetic acid (which was also obtained as a by-product in the preparation of imino - α - propionic acetic acid), nitrilo - di - α - propionic acetic acid and nitrilo - tri - α - propionic acid were best prepared as the monopotassium salts from various reactions of glycine or DL - α - alanine with chloroacetic acid or DL - α - bromopropionic acid.¹¹⁶ The α and di - α derivatives were very hygroscopic and difficult to handle. The α and tri - α derivatives gave the expected n.m.r. spectra; impurities were seen

to be present, but their amounts were not large enough to interfere with the main spectra. The di- α derivative contained more impurity. (Yields, 55%, 60% and 19% respectively.)

Imino - di - β - propionic acid was prepared by hydrolysing the dipropionitrile derivative (obtained commercially) with $\text{Ba}(\text{OH})_2$.¹¹⁷ (Yield, 85%).

Analysis. Calculated for $\text{C}_6\text{H}_{11}\text{NO}_4$: C 44.70, H 6.88, N 8.69.

Found: C 34.98, H 5.88, N 5.97.

The analytical figures do not agree; however, the organic part of the sample appears to be mainly the required ligand, and an A_2B_2 spectrum only was obtained. The original dinitrile appears pure, giving only an A_2B_2 proton spectrum. The product sample gives a spectrum which, over the pH range 1 - 12, shows no sign of another product (except for a very weak single line). Its spectrum, measured in solution in CF_3COOH , shows also a broad line expected from the two NH protons in the protonated form, $\text{H}_2\text{N}^+ \begin{matrix} \nearrow \text{CH}_2\text{CH}_2\text{COOH} \\ \searrow \text{CH}_2\text{CH}_2\text{COOH} \end{matrix}$. The area of this line relative to the CH_2 lines is about 1:4.4. The contact shift spectra give no indication of other likely complexing ligands.

Nitrilo - tri - β - propionic acid was prepared from β -alanine and β - bromopropionic acid by a method analogous to that for nitrilo - β - propionic diacetic acid.¹¹⁸ (Yield, 29%). The product was contaminated with a little NaCl, but its n.m.r. spectrum showed that it was otherwise pure enough for use.

Imino - β - propionic acetic acid was prepared by hydrolysing

the monocyanoethyl derivative which was prepared from glycine and acrylonitrile.¹¹⁹ The product crystallised as the dihydrate. (Yield, 74%).

Analysis. Calculated for $C_5H_{13}NO_6$: C 32.78, H 7.15, N 7.64.

Found: C 33.15, H 7.23, N 7.56.

Imino - α - propionic - β - propionic acid was prepared by the same method, using DL - α - alanine.¹¹⁹ (Yield, 78%).

Analysis. Calculated for $C_6H_{11}NO_4$: C 44.70, H 6.88, N 8.69.

Found: C 44.60, H 6.89, N 8.59.

Imino - β - butyric acetic acid was prepared from crotonic acid and glycine as described in chapter III (page 84).

N -2- hydroxyethyl iminodiacetic acid was prepared from ethanolamine and chloroacetic acid by the same method used for N - methyl iminodiacetic acid.¹¹³ (Yield, 44%).

Analysis. Calculated for $C_6H_{11}NO_5$: C 40.67, H 6.26, N 7.91.

Found: C 40.49, H 6.21, N 7.68.

Nitrilo - β - propionic diacetic acid was obtained in good yield (82%) by the reaction between β -alanine and chloroacetic acid.¹¹⁸

Analysis. Calculated for $C_7H_{11}NO_6$: C 40.97, H 5.40, N 6.83.

Found: C 40.61, H 5.29, N 6.80.

Nitrilo - di - β - propionic acetic acid was prepared by the addition of glycine to acrylic acid. $Ba(OH)_2$ was added to an equimolar solution of glycine and acrylic acid till the pH was about 9 - 10, and the solution kept at 40°C for 48 hours. N.m.r. analysis showed that no acrylic acid was present, the reaction having gone to

completion. The Ba was removed with dilute sulphuric acid and the filtrate evaporated to a viscous syrup in vacuo. Trituration of the syrup with ethanol and warming gave a white powder, which was the crude product. It was recrystallised twice from hot water and dried in vacuo. (Yield, 31%).

Analysis. Calculated for $C_8H_{13}NO_6$: C 43.84, H 5.97, N 6.39.

Found: C 43.50, H 6.15, N 6.19.

The n.m.r. spectrum of the product corresponded to the required product only. It is interesting to note that this product was always the only one isolated from reaction mixtures of glycine and acrylic acid of varying concentrations and at different temperatures. Under no conditions was it possible to isolate the imino β -propionic acetic acid; however, this acid was the only product obtained from the reaction of glycine with acrylonitrile, followed by hydrolysis of the nitrile product, as mentioned earlier.

Several of the preparations mentioned above, performed according to methods in the literature, gave mixtures containing appreciable amounts of several similar products; these could presumably all be separated by ion exchange processes, although the method did not prove very successful. It is not certain whether all the products reported previously have been free from impurities. Generally, the proton resonance spectra of the ligands showed that they were sufficiently pure ($> 95\%$) for use, whether or not they had been analysed. Also, with several of the same ligands samples, the spectra of their complexes with Tl(III) have recently been

measured in this laboratory;¹¹² these spectra, in all cases, confirmed that impurities were absent or present only in small amounts.

Several ligands, which are usually mentioned later in the text, contain one or more asymmetric carbon atoms and must be mixtures of the various optical isomers; no attempt was made to isolate these.

Results and Discussion.

A. General.

Before dealing with the spectra it is convenient to consider some general topics concerning the complexes.

1. Species present in solution. It is assumed that all the complexes are monomeric. Most of the ligands are tridentate or tetradentate; hence the samples contain mainly 1:1 or 1:2 complexes or mixtures of these. (Of course, the ligand carboxyl groups must lose their protons before coordinating to the metal.) When the stability constants are known, the relative amounts present can be estimated knowing the concentrations and pH. Often the 1:1 and 1:2 complexes give separate spectra which can be identified since the 1:1 lines diminish and the 1:2 lines increase as the pH of a 1:2 sample is increased. [An example of such changes is shown in Figure 13 but usually only the spectra of 1:1 and/or 1:2 complexes alone are given.] Some hydroxy complexes will also be present at higher pHs.

2. Coordination number and shape. It is assumed in all the complexes that the Ni(II) is bonded to six ligand atoms, either

N or O (including H_2O), arranged octahedrally or nearly so. This is generally found for $Ni(II)$ with this type of ligand, and is confirmed by the visible colours of the solutions, the pale green with the 1:1 complexes in which five O atoms and one N atom are bonded, and the pale blue with the 1:2 complexes in which four O atoms and two N atoms are bonded. It is also assumed that the $Ni(II)$ has the high spin d^8 electron configuration with two unpaired electrons; in an octahedral complex these are expected¹²⁰ to give rise to magnetic moments of about 2.9 - 3.3 B.M.. This was confirmed for some of the complexes by measuring their susceptibilities in solution using the method of Evans.¹²¹

3. Isomerism. Several of the complexes studied can give isomers.

(a) Geometric isomers, resulting from different spatial arrangements of the bonded chelate rings, and of the methyl substituents in them, are potentially most numerous for the complexes of iminodiacetic acid (IDA) and its derivatives.

(b) "One ended" complexes, in which one end of a chelating group is not bonded to the metal, are always possible, and are definitely present in some 1:2 complexes.

(c) Optical isomers are present when the ligands are themselves asymmetric; D and L isomers give identical n.m.r. spectra (in an optically inactive solvent) but diastereoisomers, which are formed with 1:2 complexes, can give different spectra.

4. Structural parameters. No X-ray crystallographic study appears to have been made on any of the complexes studied here, though, in any case, the structures of inorganic complexes in solution are not necessarily the same as those in the crystalline state. The Ni - N and Ni - O bond distances are probably close to those found in other complexes, but the structures of the chelate rings are less certain. In some complexes,¹²² the five membered ring is slightly puckered; in others, where more than one ring is formed, it is more puckered, and the construction of scale molecular models of, for example, IDA complexes, suggests that in these the five membered rings are puckered, and this is supported by proton resonance spectra of diamagnetic complexes,¹¹⁰⁻¹¹² and by the present work. Six membered rings are expected to be very much puckered, as is found for β -alanine chelate rings.¹²³ In order to estimate the structures of the complexes studied, scale models were used, both of the space filling (Courtauld) and skeletal (Dreiding) types.

5. Exchange processes often produce considerable simplification of the appearance of n.m.r. spectra; their effects on the proton resonance of diamagnetic EDTA complexes have been thoroughly discussed by Reilley.^{124,125} There are several possibilities.

(a) If both the Ni - O and Ni - N bonds are sufficiently labile, overall exchange of the ligand molecules on and off the metal would be fast relative to the differences in shifts between the free and complexed ligands. This is often the case with diamagnetic complexes, but in the present study the shift differences are very large and

overall exchange is often "slow" relative to this n.m.r. time scale. Hence separate lines are seen from free ligand, from 1:1, and from 1:2 complexes. Nickel is the least labile of divalent ions of the first row transition metals; however, the overall exchange is fast enough to produce equilibrium mixtures of the various species (and isomers) within a few seconds (usually) of preparing the solutions.

(b) The Ni - O bond has a relatively short lifetime; hence the O atoms rapidly dissociate from and coordinate to the metal ion; but the Ni - N bond has a long lifetime and, since the N atom does not become free, "umbrella inversion" of its bond configuration does not occur. While the group is open ended, restricted rotation about the single bonds occurs, and some averaging of the line positions results, but protons in chelate rings can still give rise to separate lines. Usually only one Ni - O bond will be open at a time. Since Ni - N bonds are stronger than Ni - O, it is considered unlikely that Ni - O lifetimes are longer than Ni - N lifetimes. The fact that contact shift lines from the NH protons are seen supports the assumption that the nitrogen stays coordinated. They cannot be exchanging with the H₂O faster than 10^5 times/sec.; however, the exchange rate of free NH groups, which result if the Ni - N bond opens, is much faster.¹²⁶

(c) Both types of bond have long lifetimes (i.e. they are regarded as permanent). This could give rise to separate line positions from all the magnetically non-equivalent protons in the ligands.

(d) Configurational changes within the ligands are usually fast. If the ligand group is free, or bonded at one end only, restricted rotation occurs about all the (single) bonds. During the time that the ligand is bonded rigidly at both ends, rapid interconversion among the various conformations of the chelate ring will occur, as far as steric hindrances allow; conformational motions are severely restricted when a ligand such as IDA forms two fused chelate rings

If one group of a polydentate ligand becomes temporarily free by opening of an Ni - O bond, the other chelate rings become less rigid and their conformational flexibility is increased. Interconversion of cis and trans isomers is possible since, when the free carboxyl coordinates again, it can do so either to the original site or to another. The latter process involves displacement of coordinated H₂O. The former may also do so if H₂O had replaced the ligand oxygen, but there may not have been time for this if the group had only been free for a very short time; in this case, the group may not have had time for restricted rotation.

6. Position of the H₂O line. This is a weighted average of the positions of the coordinated H₂O and free H₂O in the bulk solvent, since there is rapid exchange of protons between these two sites. In the absence of other competing ligands, it has recently been shown that¹²⁷ the addition of Ni(II) ions makes the H₂O line shift downfield, linearly with Ni(II) concentration, and from this, that the proton contact shift for the coordinated H₂O has been calculated to be 489 cycles/sec. (adjusted to correspond to 56.45 mcs./

sec. used here), i.e. -8.52 p.p.m. at 40°C, assuming Ni(II) is six coordinate. From this value, it is easily calculated that at 40°C the shifts are expected to be about -0.48 p.p.m. for 0.5 M solutions and -0.24 p.p.m. for 0.25 M solutions; these agree fairly well with the values of -0.50 p.p.m. and -0.25 p.p.m. at 22°C measured independently here. When the bound H₂O molecules are displaced by a chelating ligand, the observed H₂O line, whose position is again proportional to the ratio of bound H₂O to free H₂O, moves upfield towards the Ni(II)-free H₂O position. It is clear that the number of sites in the complex occupied by H₂O can be estimated from the position of the H₂O line, knowing the concentration of Ni(II). However, the estimate is not accurate, partly because the shifts were not large, and partly because the contact shift of coordinated H₂O depends on the other ligands present, and also because the free H₂O position is affected by the presence of bulky ions (which alter the hydrogen bonded structure).

B. Assignments and Discussion of Spectra.

A typical series of spectra (for the 1:1 and 1:2 complexes with MIDA) is shown in Figure 13. In the following sections, discussion of the equivalence and non-equivalence of protons will refer to their contact (or pseudocontact) shifts⁷. Since these arise from the metal atom, either through the bonds or through space, their values, particularly for CH₂ groups in chelate rings, depend on the spatial position of the protons relative to the metal. The differences in shifts due to long range (diamagnetic) shielding by

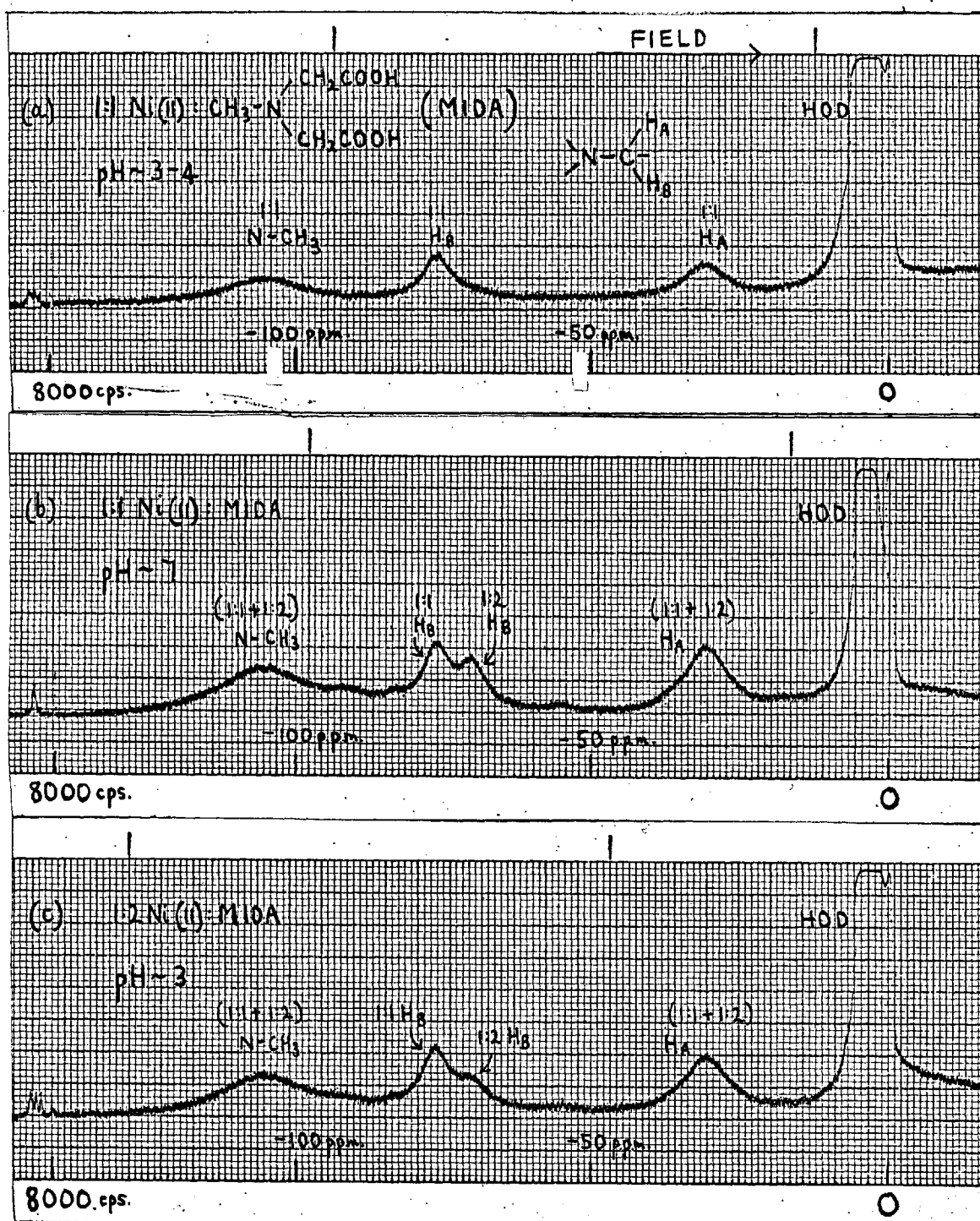


Figure 13. Typical contact shift spectra of the complexes of Ni(II) with N-methyl iminodiacetic acid in D_2O . Contact shifts are in p.p.m. on the low field side of t-butanol.

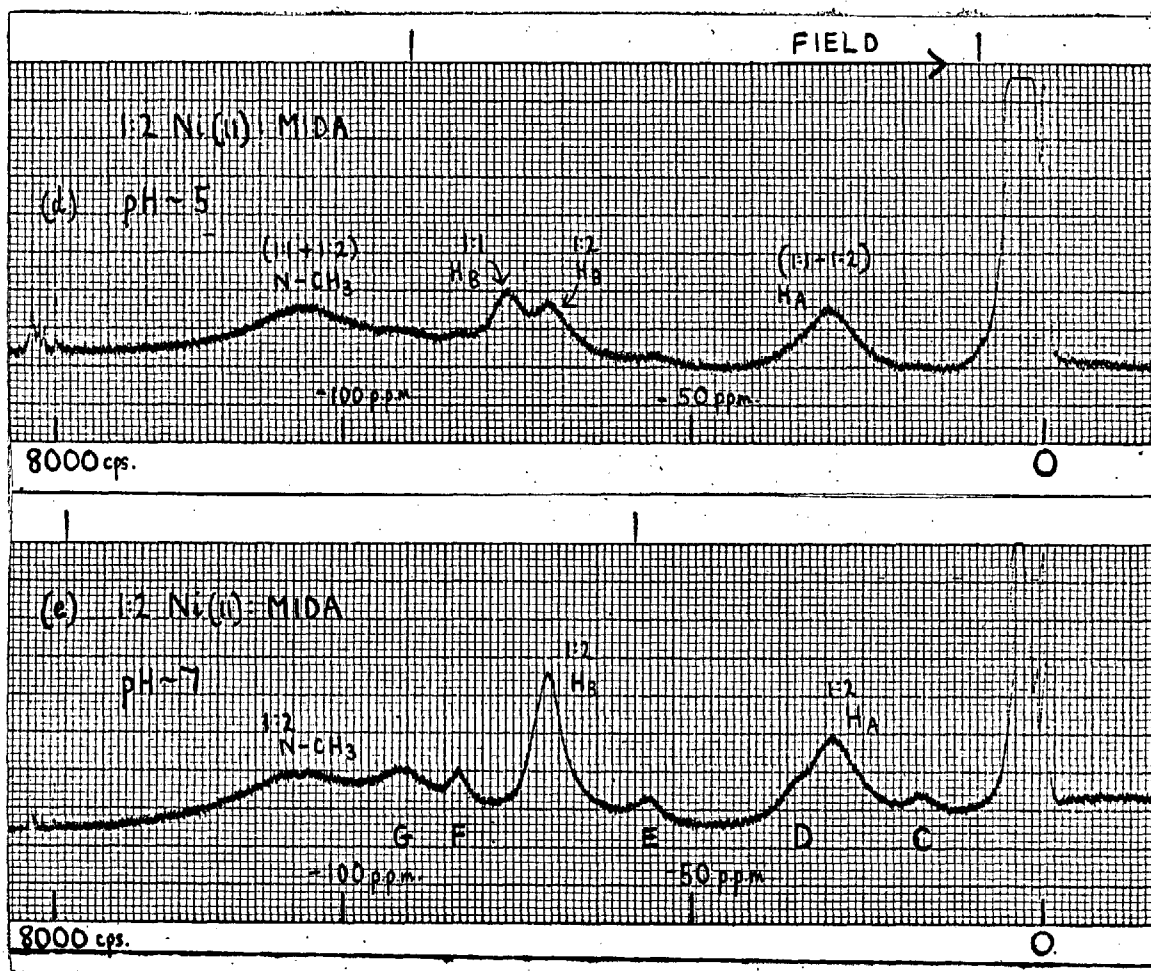


Figure 13 (cont.). Typical contact shift spectra of the complexes of Ni(II) with N-methyl iminodiacetic acid in D_2O . Contact shifts are in p.p.m. on the low field side of t-butanol (cycles/sec. are also indicated). The lines C,D,E,F and G (in spectrum (e)) are attributed to a small amount of an isomer of the 1:2 complex (see text). Some of these lines are also visible in spectra (b) and (d).

other groups, which are important in diamagnetic complexes,¹¹⁰ will, of course, be present, but they are negligibly small relative to the large shifts and broad lines. However, the effect of the other ligand groups can often be discussed similarly in the dia- and paramagnetic cases, since the position and symmetry of other ligand groups can alter the preferred conformations of a chelate ring by steric interactions.

Bidentate ligands forming one five membered chelate ring.

The spectra of 1:1 complexes of some bidentate ligands are shown in Figure 14; they have been measured and assigned previously,⁹¹ but are given here since they are helpful in discussing the other complexes.

The NH protons are assigned to the lines on the high field side since these are absent in D₂O solutions. They are very broad and difficult to see above the noise level; they are discussed briefly (p. 148) after the discussion of the CH lines. The assignments of the CH lines, shown on the spectra, can often be made from their relative intensities (areas).

With glycine (Figure 14a), there is one line for the CH₂ protons, so that these are equivalent or nearly so. One explanation is that the ring is planar (and rigid), in which case the protons would be equivalent.

If the five membered ring is puckered and rigid, two separate lines from the "axial" and "equatorial" CH₂ protons might be expected, since their contact shifts depend on the angles the CH bonds make with the C - N - Ni plane (i.e. the dihedral angles).

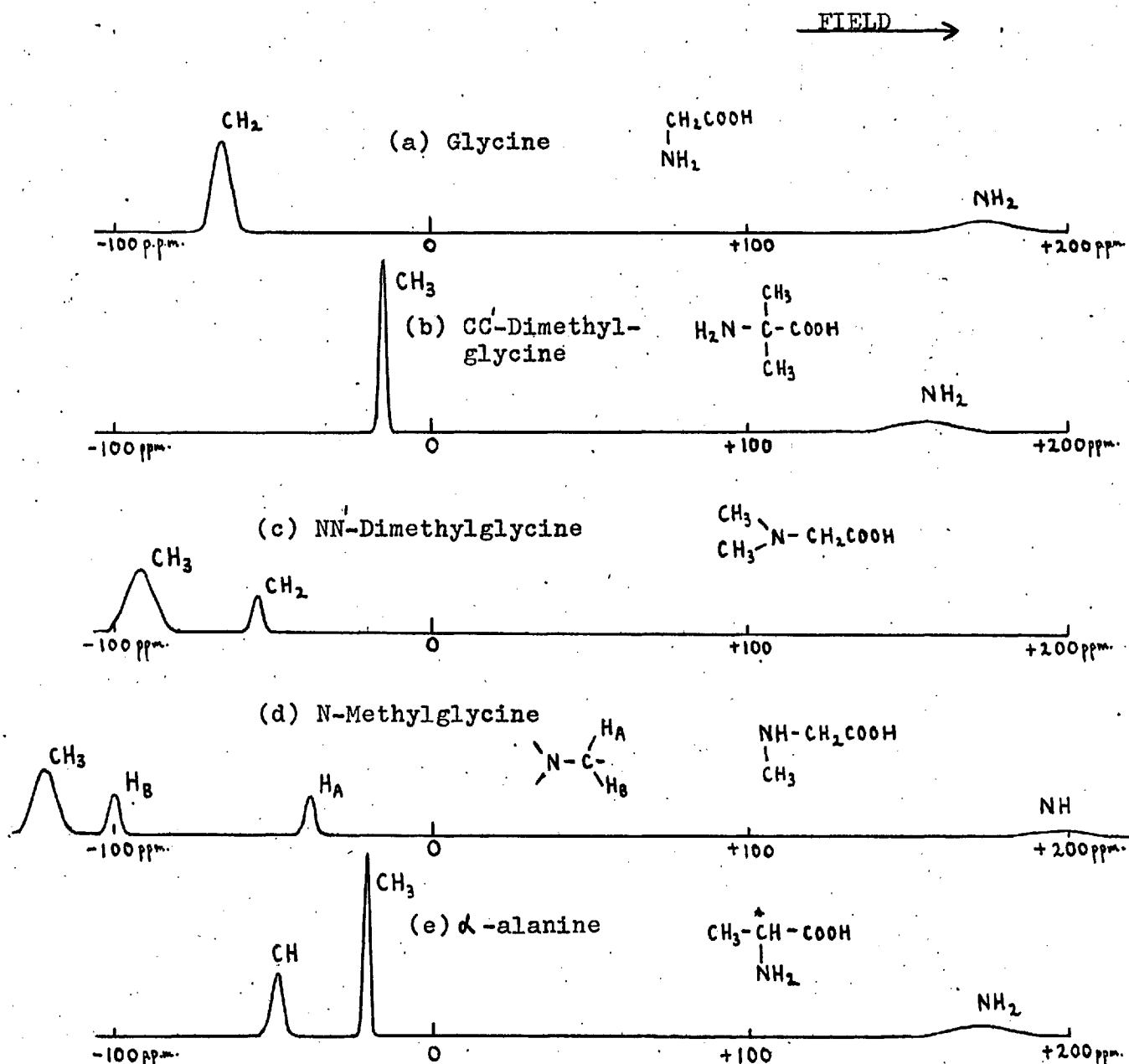
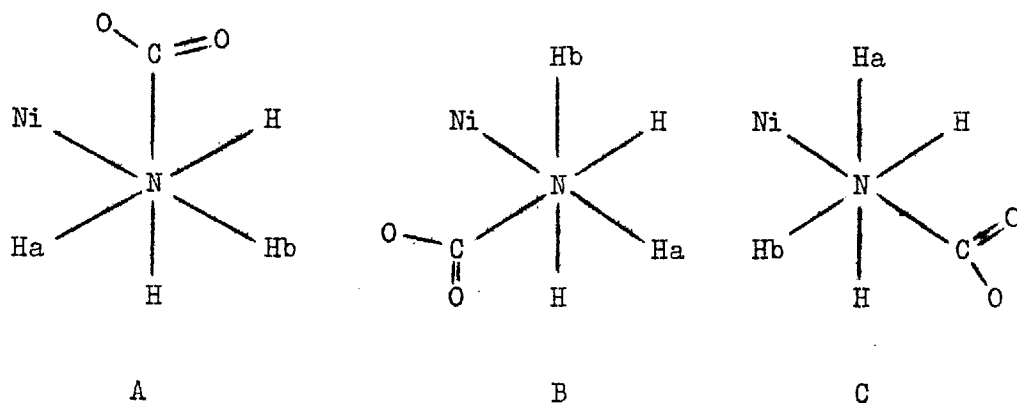


Figure 14. Spectra of 1:1 complexes of Ni(II) with bidentate ligands. Contact shifts are in p.p.m. relative to t-butanol.

However, a single line could again be observed from a puckered ring if the two protons were made equivalent. This could result from rapid motion of the chelate ring between two conformations, in which the protons had effectively interchanged positions, and which would have equal residence times, due to the symmetry of the ligand and the rest of the complex. (The situation is similar to that given below for rotamers A and B if the carboxylate is assumed to be bonded to the metal, although the change in dihedral angle would be less than the 120° shown.)

A second cause of equivalence could be lability of the Ni - O bond. This would allow the ligand to spend part of the time in the "one-ended" state, and in this condition restricted rotation can occur about the C - N bond.¹²⁴ In this case, considering the rotamers shown below (depicted looking down the N - C bond), the



symmetry of the groups at the ends of the bond makes rotamers A and B equivalent, and Ha and Hb are also equivalent in C. Hence they become equivalent, relative to the metal, if rotation occurs.

Similar alternatives can be given to explain the equivalence of the two methyl groups in CC'-dimethyl glycine (Figure 14b) and in NN'-dimethyl glycine (Figure 14c). In the latter case, the complex is weaker than glycine ($\log K, = 4.82$ and 5.86 respectively),¹²⁸ and a larger amount of free ligand is observable in the spectrum. Methyl groups might be expected to increase the stability of the complexes by virtue of their electron donating capabilities, and the decrease is probably due to their steric effects. As expected, the shift of a methyl group on the carbon atom of a five membered ring is considerably less than that of a methyl group attached to the coordinated nitrogen atom.

With N-methyl glycine (sarcosine) (Figure 14d), two CH lines are observed, presumably one from each of the CH₂ protons. If the ring was rigidly planar, the CH₂ protons would be expected to be almost equivalent; their difference would be due to the change in the long range shielding on replacing NH by N - CH₃, but this is negligible relative to contact shifts. It is reasonable to suppose that steric interaction between the CH₃ and the coordinated H₂O tends to make the ring stay puckered. If it is rigid, the CH₂ protons are not equivalent. If it is flexible, one conformation would be preferred and their average environments (and shifts) differ. If the lability of the Ni - O bond allows rotation about the N - CH₂ bond, they would still differ on the average since the three rotamers of the one-ended form are not equivalent (since one of the N - H protons has been replaced by CH₃).

With α -alanine, the ring again is expected to be more stable if puckered.

With all the ligands, increasing the ligand concentration so that the ratio of ligand to metal ion was 2:1, produced, at $\text{pH} \approx 7$, a marked broadening of all the lines observed in the spectra. Also, all the lines moved slightly (of the order of a few p.p.m.) towards the t-butanol. The observed lines probably represent weighted averages of 1:1, 1:2 and (possibly) 1:3 Ni(II) chelates, due to rapid exchange between them. With N-methyl glycine, a doubling of the CH lines is apparent. The fact that exchange with the free ligand was also occurring was noticed in the broadening of the free ligand lines, which are fairly sharp when free ligand is present with the 1:1 complexes at lower pH. In some cases, the averaging between the complex species was incomplete, resulting in broad asymmetrical lines.

Below $\text{pH} \approx 4$, no lines consistent with chelate formation were seen, although the Ni(II) would be expected to complex weakly with the carboxylate groups giving one-ended species with small contact shifts. These weak one-ended complexes are probably present in very small concentration at $\text{pH} \approx 7$ also. In the pH range 5 - 7, the observed CH lines from the chelates showed a small shift to low field with increasing pH.

Tridentate ligands which can form two five membered chelate rings. These ligands (after the acidic protons have been displaced) form stable 1:1 and 1:2 Ni(II) complexes of the general formulae

NiL^0 and NiL_2^{2-} over the pH range 4 - 7.

Iminodiacetic acid (IDA), $\text{NH} \begin{array}{l} \text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{array}$. The spectrum of the 1:1 complex (Figure 15a) consists of one very broad high field N - H line and two low field lines of equal intensity, each of which comes from two CH protons. One possible explanation is that each line represents the CH_2 group in one ring of the complex, implying that the two five membered rings are different; this could arise if one chelate ring were rigidly bonded and the other carboxyl were free, but the stability constant of the 1:1 complex ($\log pK_1 = 8.2$)¹²⁸ is considerably greater than that for glycine ($\log K_1 = 5.9$)¹²⁸ showing that both rings are closed, at least for most of the time. Another explanation is that each line represents the two CH_2 groups in cis and trans isomers (Figure 16a). However, in these, the environment of the CH_2 groups (relative to the nickel) seems too similar to produce the observed difference, even if there is a marked anisotropy of the nickel, which is unlikely. Also, the isomers would each have to be equally stable to be present in equal amount, yet the models suggest that the trans one should be less stable since the C - N - C bond angle is probably strained. The models do show that the rings are likely to be puckered (Figure 16a), suggesting - the preferred explanation - that the two protons in each CH_2 group are non-equivalent relative to the Ni(II), each line coming from one proton in each CH_2 group; the assignment to H_A and H_B is discussed later.

Unfortunately, the width of the lines (half height

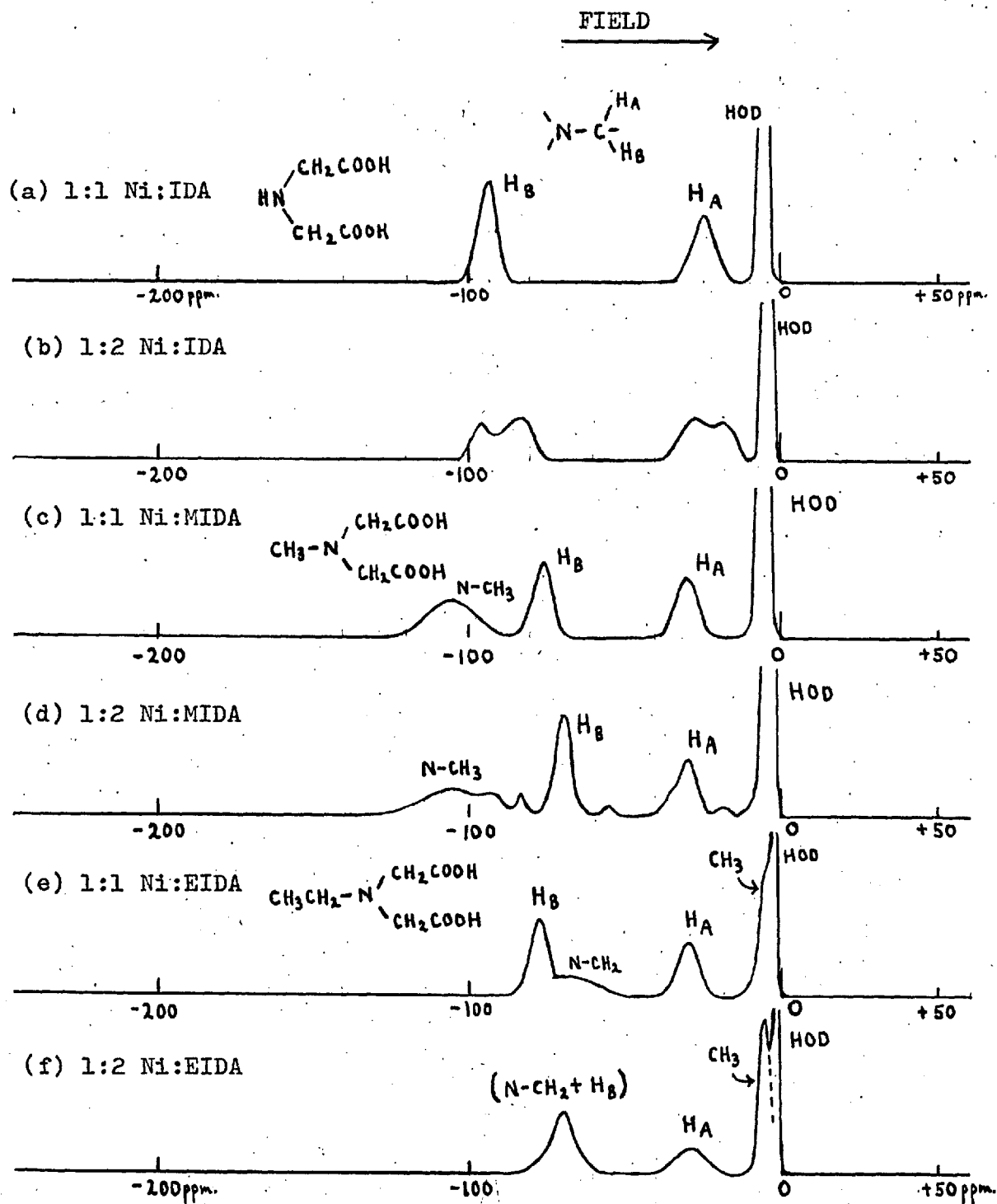
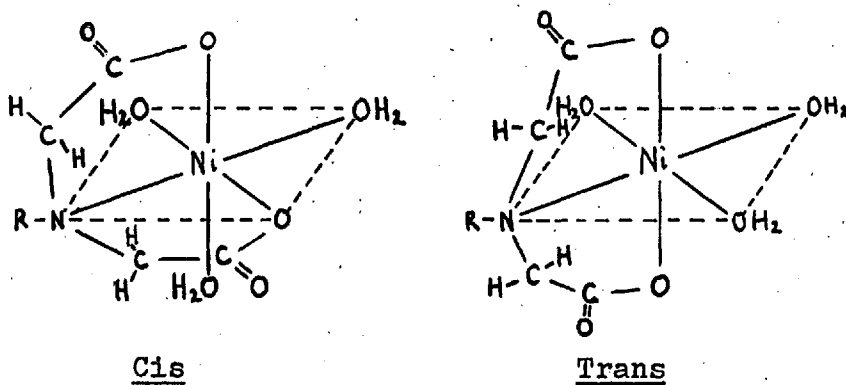


Figure 15. Spectra of Ni(II) complexes of IDA derivatives.

Contact shifts are in p.p.m. relative to t-butanol.

(a) 1:1 Ni(II):IDA derivatives



(b) 1:2 Ni(II):IDA derivatives

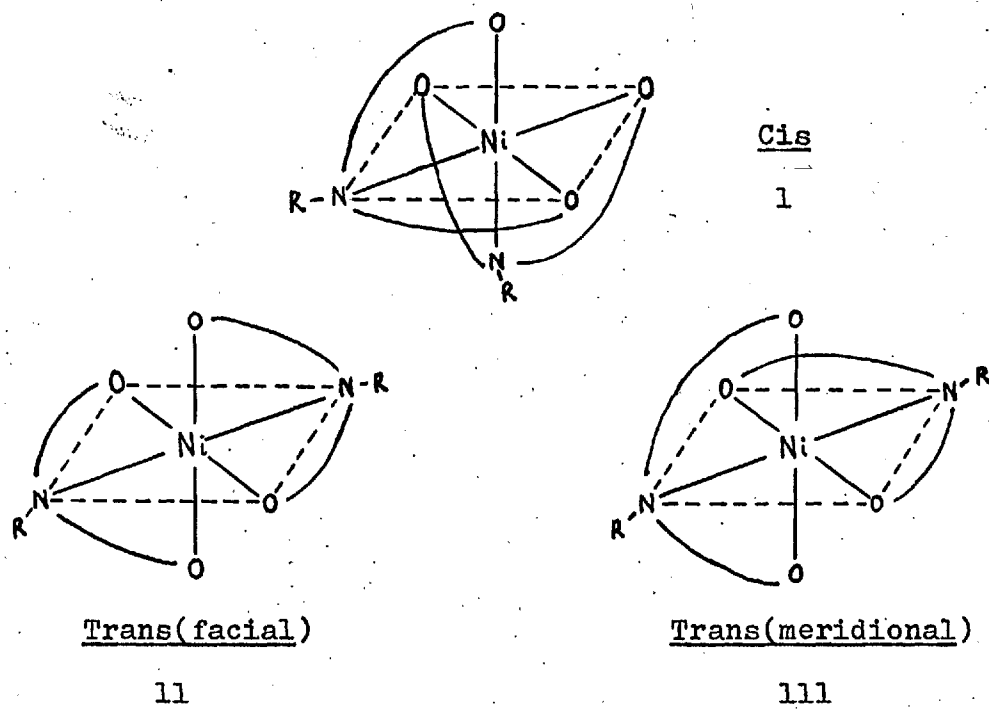


Figure 16. Possible isomers of (a) 1:1 and (b) 1:2 Ni(II) complexes with IDA derivatives.

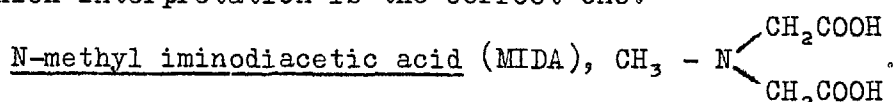
≈ 375 cycles/sec. and ≈ 285 cycles/sec. for those at about -24 p.p.m. and -93 p.p.m. respectively) does not allow observation of the geminal coupling constant (expected to lie in the range $15 - 20$ cycles/sec.), which would confirm the non-equivalence of the CH_2 protons. A similar non-equivalence does give observable splitting in the proton resonance spectra of complexes of IDA with the diamagnetic metal Tl(III) .¹¹²

The cis isomer, if more stable, should be the major (or only) species present, but the presence of the trans isomer could be undetected, either if its spectrum coincided with that of the cis (within the widths of the lines), or if lability of the $\text{Ni} - \text{O}$ bonds allows fast interconversion between the isomers. In both isomers, the two rings would probably be rigid whilst they were bonded (case 5c), but conformational motion would not remove the non-equivalence in the CH_2 groups in either, nor (when one $\text{Ni} - \text{O}$ bond breaks), would restricted rotation about the $-\text{N} - \text{CH}_2$ bond, since there are three different groups (Ni , $-\text{CH}_2$ and H) at the nitrogen end of the bond. If only the cis isomer is present, its two CH_2 groups appear equivalent; this is possible with a rigid structure but conformational lability could have this effect.

When the ratio of Ni(II) to IDA is $1:2$ and the pH is adjusted to ≈ 7 , the spectrum in Figure 15b is obtained. The doubling of the lines is due to the presence of $1:2$ complexes only. This is expected at this pH from the values of the stability constants, and confirmed by (1) the colour of the solution, which

was blue in contrast to the green for the 1:1 complex, (2) by the absence of free ligand, and (3) by the HOD position, which corresponds to that of Ni(II)-free H₂O, since all the sites on the Ni(II) are occupied by ligand atoms. The possible structures of the complex are shown in Figure 16b, where N - O = N.CH₂.COO and R = H. In the trans (facial) isomer, II, the plane of symmetry through the two N atoms makes all the CH₂ pairs identical, and a spectrum consisting of two equally intense lines would be expected. Scale models suggest that in each of the other two isomers, I and III, the CH₂ groups are in slightly different environments relative to the nickel atom. It is perhaps unlikely that isomer III would be formed in any appreciable quantity; the Dreiding model suggests that the rings are strained, and Cooke¹¹⁰ has recently pointed out that this isomer is expected to involve considerable C - N - C angle strain. In support of this, he has prepared and characterised the 1:2 Co(III) complexes of IDA, and found that only isomers I and II could be obtained. If isomer III is not considered, the observed spectrum, which consists of two doubled lines, could be ascribed to a mixture of isomers I and II. Although the doubled lines could not be resolved completely, it does seem that the inner line in each doublet is broader (and more intense) than the outer. Two interpretations are possible: (1) the broader pair of lines could represent the cis isomer (I), the greater width being due to unresolved smaller non-equivalence of the two sets of CH₂ groups in this isomer; (2) each doublet could represent the non-equivalent CH₂ groups in

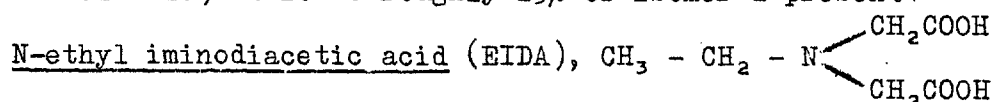
the cis isomer (i.e. two different CH_2 pairs), and the broadening arises from overlapping of the CH_2 groups of the isomer II (i.e. one CH_2 pair), which is present in smaller amount, with the inner line of each doublet. It would be expected that the main pair of lines are close for both isomers I and II, since in each of them, the IDA groups are themselves in the cis configuration. It is not possible to say which interpretation is the correct one.



In the spectrum of the 1:1 complex (Figure 15c), by comparison with the 1:1 complexes of IDA and N-methyl glycine, the lines at about -30.5 p.p.m. and -76.5 p.p.m. are assigned as due to the AB pair protons of the CH_2 groups, and the broader line at about -106 p.p.m. to the CH_3 group. As with IDA, although cis and trans isomers are possible, only one set of lines is observed. This indicates that only one isomer is present or that both are, but their lines overlap or are averaged out by rapid interconversion. As before, the trans isomer is expected to be the less stable.

The spectrum shown in Figure 15d is ascribed to the 1:2 complexes only, using the same criteria which were given for the IDA complexes. The lines at about -30 p.p.m., -70 p.p.m. and -106 p.p.m. are assigned as due to CH_2 pairs and the CH_3 group. Among the isomers shown ($\text{R} = \text{CH}_3$), II would be expected to be preferred, since in I, the cis isomer, there would be considerable steric repulsion between the two CH_3 groups, and III would again involve considerable C - N - C angle strain. The fact that II would give rise to only one AB pair for the CH_2 groups is consistent

with the two intense lines at -30 p.p.m. and -70 p.p.m.. Five other small lines are also observed (though more may be obscured by the three intense lines); they do not seem to be due to another ligand as impurity since analogous lines are not present in the Co(II) sample, and the diamagnetic spectrum of the ligand shows only the lines expected for MIDA. They could be ascribed to either isomer I or III, in each of which four lines from two different CH_2 pairs and one CH_3 line would be expected. Probably I would be favoured; hence the 1:2 sample may contain a mixture of the isomers I and II. If this is so, the relative intensities of the lines (though these are not too reliable) indicate roughly 15% of isomer I present.

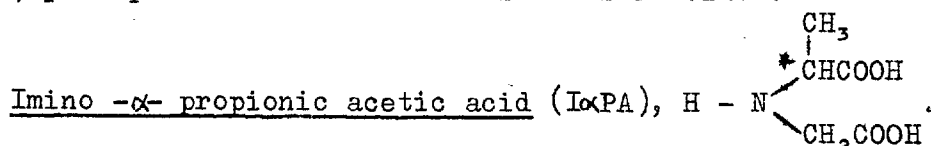


In the spectrum of the 1:1 complex (Figure 15e), the lines at -28.5 p.p.m. and -78 p.p.m. are assigned as the CH_2 AB pairs in the five membered rings, and the very broad line at about -68 p.p.m. to the $\text{N} - \text{CH}_2$ group, by comparison with MIDA. The sharper line at about -5 p.p.m., which is partially obscured by the HOD resonance, is assigned as the CH_3 group. As with IDA and MIDA, the possibility of cis and trans isomers exists.

The 1:2 complex (Figure 15f) shows only a three line spectrum. The lines at -29.5 p.p.m. and -70 p.p.m. are assigned to the CH_2 pairs in the rings. The intensity of the -70 p.p.m. line and its broad base indicate that it overlaps with another broad line, which is assigned as the $\text{N} - \text{CH}_2$ group; the groups must have nearly the same shift value, since the appearance of the line was the same

at 100 mcs./sec.. The relatively sharp line at -6 p.p.m. is assigned as the CH_3 group. The fact that only one CH_2 pair is observed suggests that the complex is in fact isomer II (with $\text{R} = -\text{CH}_2\text{CH}_3$). The absence of other lines indicates that isomers I and III are not present. This would be expected because of the larger steric repulsion between the bulky ethyl groups in isomer I than between the CH_3 groups in the cis 1:2 MIDA complex. As before, III is thought unlikely because of the angle strain. Hence, it is suggested that the 1:2 complex formed in this case is exclusively isomer II, in which the ethyl group steric interactions and the C - N - C angle strain are minimised.

The effect of variation of pH in the range 4 - 7 is similar for all three cases (i.e. IDA, MIDA and EIDA), and was studied more fully with EIDA. No appreciable difference in the spectrum of the 1:1 complex is observed, though a little 1:2 is formed at about pH 7. The 1:2 solution consists of a mixture of 1:1 and 1:2 complexes at about pH 5 and, as the pH is increased to about 7, the 1:1 complex decreases and finally disappears. Above pH 7, hydroxide (or hydroxy complexes) precipitated in both the 1:1 and 1:2 solutions.



In the spectrum of the 1:1 complex (Figure 17a), the CH_2 pair is assigned to the line at -18.5 p.p.m. together with one of the other two lines at -79 p.p.m. and -102.5 p.p.m.; the other line of the latter two represents the single CH; the exact assignment is discussed

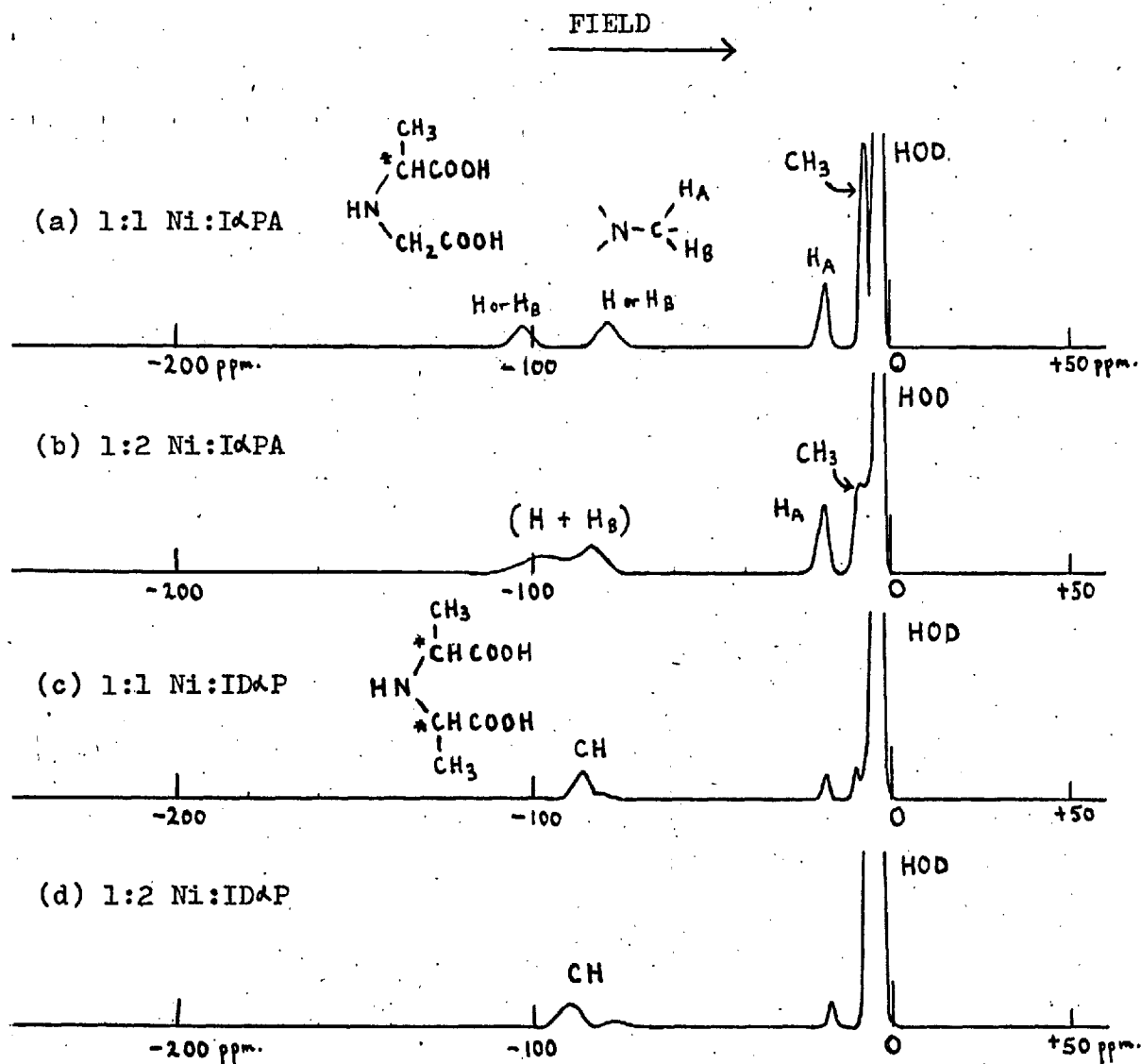
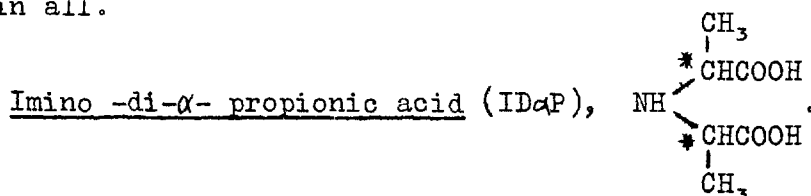


Figure 17. CH Spectra of Ni(II) complexes of IΔPA and IDΔP.

Contact shifts are in p.p.m. relative to t-butanol.

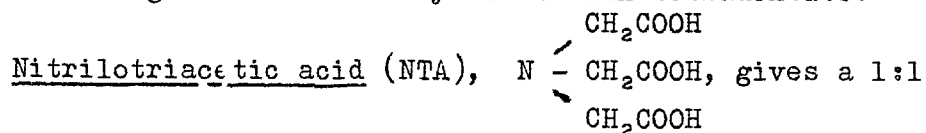
later. The CH_3 group lies close to the HOD line (-7.5 p.p.m.). There is no indication of different isomers, although more are possible. In addition to the trans (expected to be unstable), there are two possible cis isomers, with the CH_3 group either inside, between the rings, or (more likely) on the outside of them. Each isomer would, of course, be a 1:1 mixture of D and L forms, since the ligand contains an asymmetric carbon atom, but these would give the same spectrum.

The spectrum of the 1:2 complexes is shown in Figure 17b (for a solution in which the criteria mentioned before all showed that only 1:2 complexes were present). Again there appears to be one CH_3 line (although its reduction in intensity could suggest that in fact it is doubled, with half completely hidden under the HOD line) and three CH lines; the outer two are fairly broad, which may be the result of overlapping, unresolved lines from isomers. Many isomers are possible. The non-equivalence of the two rings would alone give rise to two isomers from structure III. When allowance is also made for the asymmetric carbon atoms and the spatial position of the CH_3 group, structures I and II each are the basis of four complexes of formula $\text{Ni}(\text{DL})$, four of $\text{Ni}(\text{LL})$ and four of $\text{Ni}(\text{DD})$, and structure III could give two of each of these formulae, making thirty isomers in all.



The spectrum of the 1:1 complex shows a line at -86 p.p.m. (Figure 17c) which can be attributed to the CH protons. It is uncertain whether the other very small lines present are due to impurities or isomers. Unfortunately, no CH_3 line could be observed, presumably being obscured by the HOD line. The ligand is presumably a mixture of meso and active DD and LL forms and would be expected to give both spatial and optical isomers for the 1:1 complex. For the cis structure, there are DD, LL, and two non-equivalent DL isomers (with the CH_3 groups both inside or both outside) from the meso form. The trans form can give DD, LL and one DL isomer. It is not known which may be present. The spectrum of the 1:2 complexes is similar to the 1:1, although rather broader; again no CH_3 line is seen. There is no indication of which of the many possible isomers are present.

Tetradentate ligands which can form three five membered chelate rings. With Ni(II) , these form 1:1 complexes (e.g. NiL^-) which are stable over a wide range of pH; hydroxy complexes may form above $\text{pH} \sim 8$. Some 1:2 complexes are probably formed although, in these, the two ligands are unlikely to be both tetradentate.



complex whose spectrum is illustrated in Figure 18a. The one broad line seems to represent all the CH_2 protons. Models show that when all three carboxyls are bonded the three rings are not equivalent. Two of them appear to be in the configuration of the trans structure

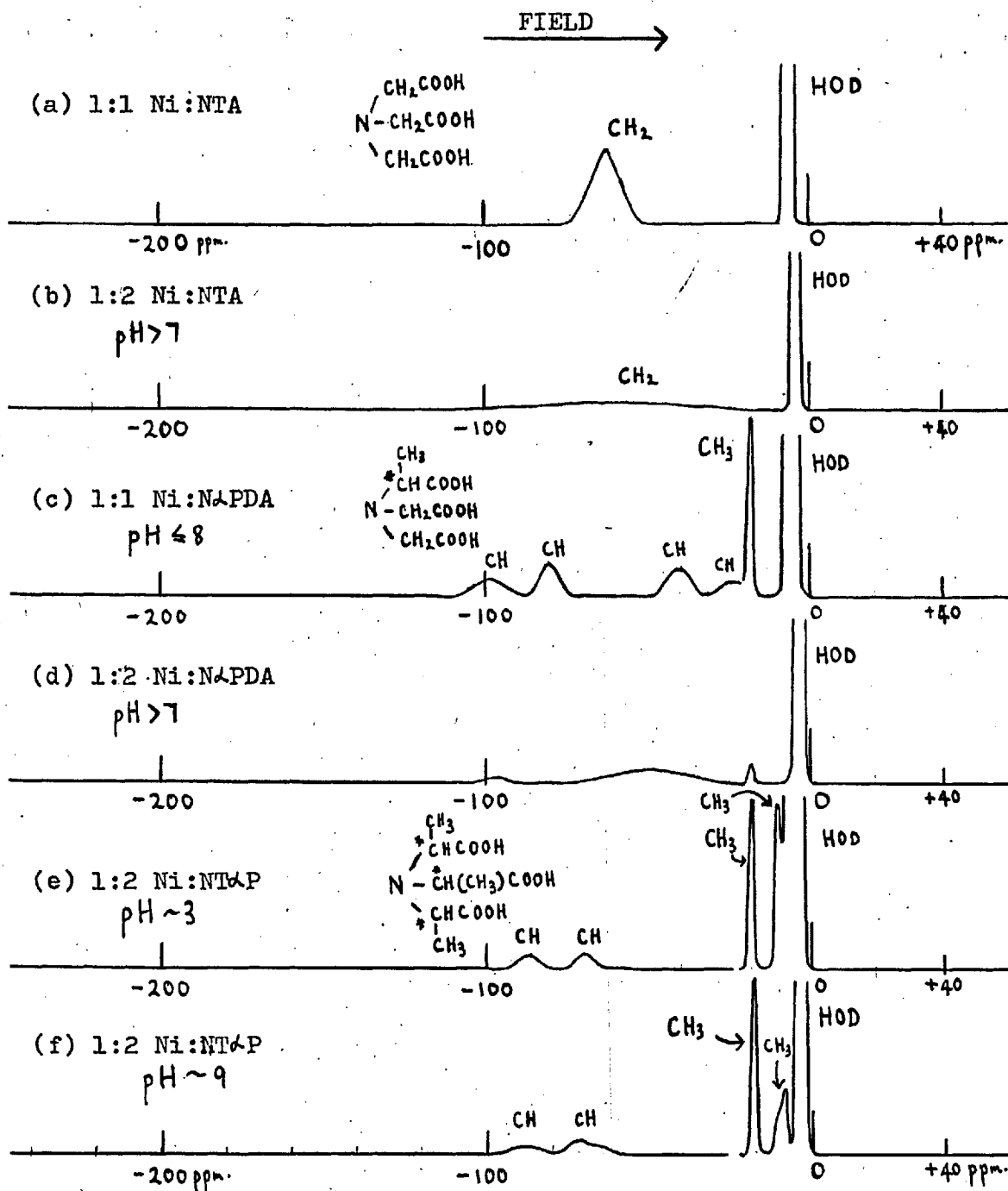
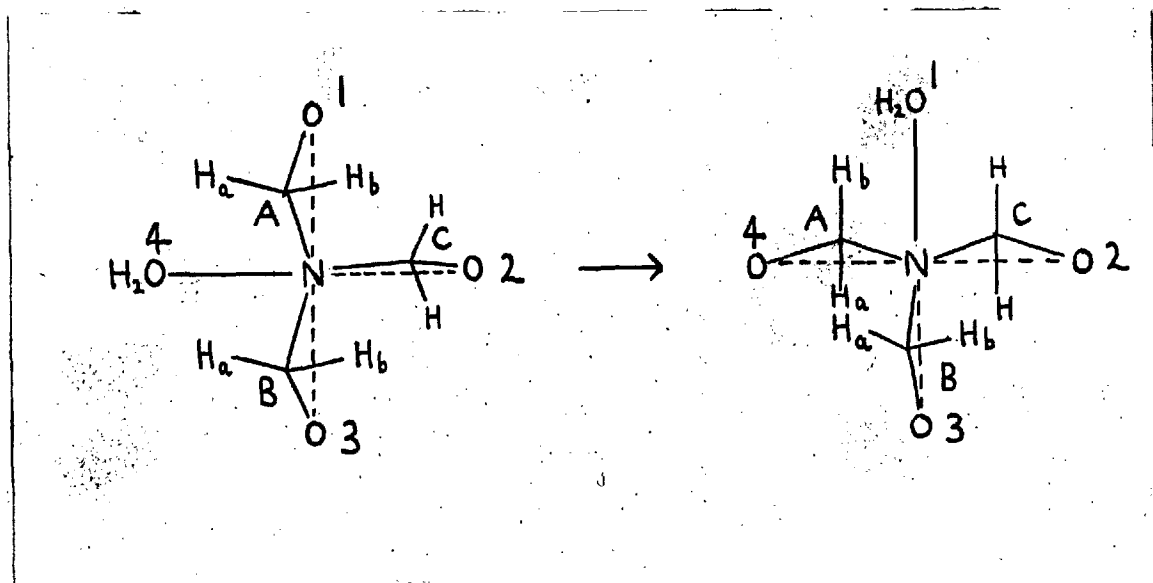


Figure 18. Spectra of Ni(II) complexes of NTA, NAPDA and NTAP. Contact shifts are in p.p.m. relative to t-butanol. In (c), (e) and (f), the signal/noise ratio is reduced at -20 p.p.m..

for an IDA group, and are rigid and strained, while the third is less strained and more mobile (see below). The models may give a false impression of the flexibility of the rings, but it seems unlikely that conformational rearrangements, making the three rings equivalent (on the average), are possible whilst the groups are all coordinated, especially when the steric interactions between the rings are also considered. The observed equivalence could more plausibly arise from lability of the Ni - O bonds.

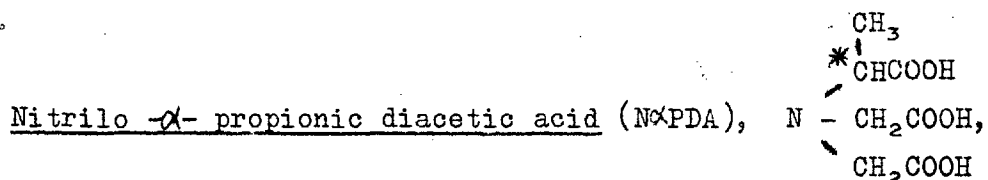
Suppose one of the strained rings (A, say) opens and reforms by displacing H₂O at position 4, H₂O taking its place at position 1. The ring B is now mobile, and C and A strained, but H_a and H_b in ring A have interchanged environments. A succession of bond migrations



will interchange the two CH₂ on each ring; the symmetry of the three rings and the bonding sites ensures that on the average each CH proton spends an equal time in the different environment, so all are equivalent. This mechanism does not require rotation about the

C - N bonds (apart from the torsional motion over $< 60^\circ$). It is probable that when group A (say) is "free", it can undergo restricted rotation, and since rings B and C can become equivalent by converting to the less strained arrangement of the cis IDA (Figure 16a), the A group CH_2 protons become equivalent. However, complete averaging would not occur unless the three rings are made equivalent by the bond migration suggested above. The ligand is probably tetradentate for most of the time since the stability constant ($\log K_1 = 11.3$)¹²⁸ is considerably greater than that for $\text{Ni}(\text{IDA})^0$ ($\log K_1 = 8.2$).¹²⁸

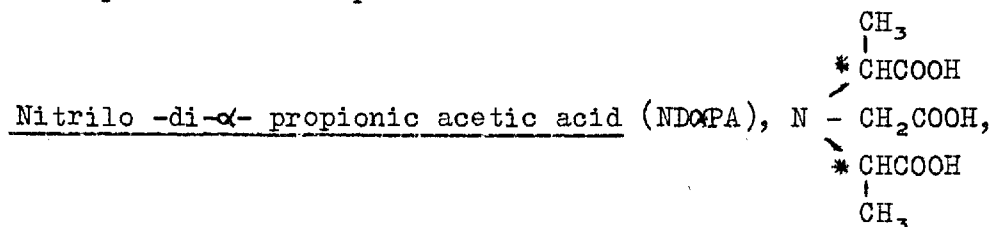
The spectrum of the 1:2 solution at low pH (4 - 6) is identical with that of the 1:1 complex. At pH > 7 , the solution becomes blue and the line becomes very broad and is only just visible (Figure 18b). Presumably a 1:2 complex is formed, with two nitrogen atoms coordinated. Several isomers are possible, some with one ligand tetradentate and the other bidentate with two groups free, and some with both ligands tridentate, each with one free group. Exchange between the free and bound positions could make the observed line very broad. Overall exchange between 1:1 and 1:2 species is also possible.



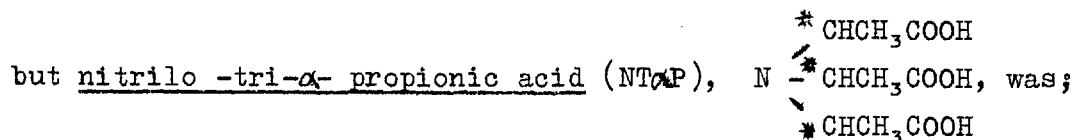
forms a 1:1 complex whose spectrum is shown in Figure 18c at pH ≤ 8 . Four equally intense low field lines are visible and one relatively sharp, intense line (the CH_3). The 1:1 complex should contain three five membered rings, one being asymmetric because it contains the

CH₂ group. This will affect the preferred conformations of the other rings, and the environments in which the protons in the two CH₂ groups are placed by the bond migration are not equivalent, hence different pairs of lines are expected for each CH₂ group. It appears that each CH proton does in fact give rise to a separate line, assuming that one missing line is obscured by the HOD resonance. A similar situation is present in the 1:1 Tl(III) : NαPDA complex, which gives rise to two different AB pairs.¹¹² The exact assignment of the CH lines is discussed later.

At pH ≤ 7, the 1:2 solution gives a spectrum identical with that of the 1:1 complex; above pH 7, the solution becomes deep blue and over the range pH 7 to 8 the spectrum changes (i.e. over a small pH range) to give one broad band (Figure 18d). As with NTA, a 1:2 complex is probably formed with two nitrogen atoms coordinated to the metal; the broadening may be due to exchange between free and bound positions for the ligand groups. Overall ligand exchange with the 1:1 species is also possible.



could not be made pure enough to be useful in this investigation,



it is probably a mixture of several optical isomers. Each of the three asymmetric carbon atoms can have either the D or L configuration.

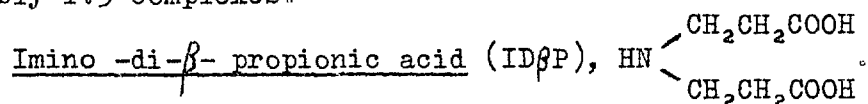
In the solution with 1:2 ratios, but at $\text{pH} \approx 3$ (Figure 18e), the complexes present will probably be a mixture of isomers of the 1:1 ratio. The complexes Ni(DDD) and Ni(LLL) should give identical spectra, with only one CH and one CH_3 line. These could well be represented by one of the smaller broad lines and one of the sharper stronger lines respectively. For the complexes Ni(DDL) and Ni(DLL) , another set of lines would be expected, but containing two methyl lines and two CH lines (since, of the three methyl groups, two are in different environments from the third, and likewise the CH). If these were not appreciably different, they could overlap, giving the other CH and CH_3 observed in Figure 18e. The DDD and LLL isomers would be expected to be more stable since, in these, steric repulsion between the rings is minimised.

When the pH is increased, the colour of the solution changes from green to blue, indicating that 1:2 complexes are being formed, containing two Ni - N bonds. Some of the lines are noticeably doubled (Figure 18f), indicating the presence of isomers. The difference from the 1:1 is small and it is possible that the ligand is tridentate, since steric repulsions will be considerable in any tetradentate structure, and would be less if one chelate group was free.

Ligands giving only six membered chelate rings. The differences between the complexes of the ligands with one, two and three $\text{CH}_2\text{CH}_2\text{COO}$ groups are very similar to the differences with one, two and three CH_2COO groups; it is possible that the imino ligands, with two attached groups, which give the most detailed spectra, and

~~these~~, are analogous in the two cases.

β - alanine, $\text{NH}_2 - \text{CH}_2 - \text{CH}_2 - \text{COOH}$, gives a 1:1 complex whose spectrum, which has been previously reported,⁹¹ is illustrated in Figure 19a. There is also a broad line at about +178 p.p.m. (absent in D_2O) which is assigned as the NH protons. The stability constant ($\log K_1 = 4.6$)¹²⁸ shows that this complex, with a six membered ring, is less stable than the glycine complex with a five membered ring ($\log K_1 = 5.9$);¹²⁸ probably the Ni - O bond is more labile, and the six membered ring, which is considerably puckered,¹²³ has more conformational flexibility than a five membered ring. This freedom of movement allows the protons in a CH_2 group to interconvert and appear equivalent. The assignments have been reported previously;⁹¹ the broad line at -166.5 p.p.m. is assigned to the - N - CH_2 group by analogy with the large shift for the N - CH_2 in the Ni(II) complex with $\text{NH}_2 - \text{CH}_2 - \text{CH}_2 - \text{NH}_2$, and the sharper line at +8 p.p.m. is assigned to the - $\text{CH}_2 - \text{COO}$ group by analogy with the small upfield shift in the complex with malonate, $^-\text{OOC} - \text{CH}_2 - \text{COO}^-$. When the concentration of the ligand is increased, the lines are broadened, indicating rapid exchange involving 1:1, 1:2 and possibly 1:3 complexes.



The spectrum of the 1:1 complex (Figure 19b) shows four lines. These could come from cis and trans isomers, but, as with the IDA complex, it is probable that lability of the Ni - O bonds would allow them to interconvert rapidly and separate lines would not be seen. Also, the

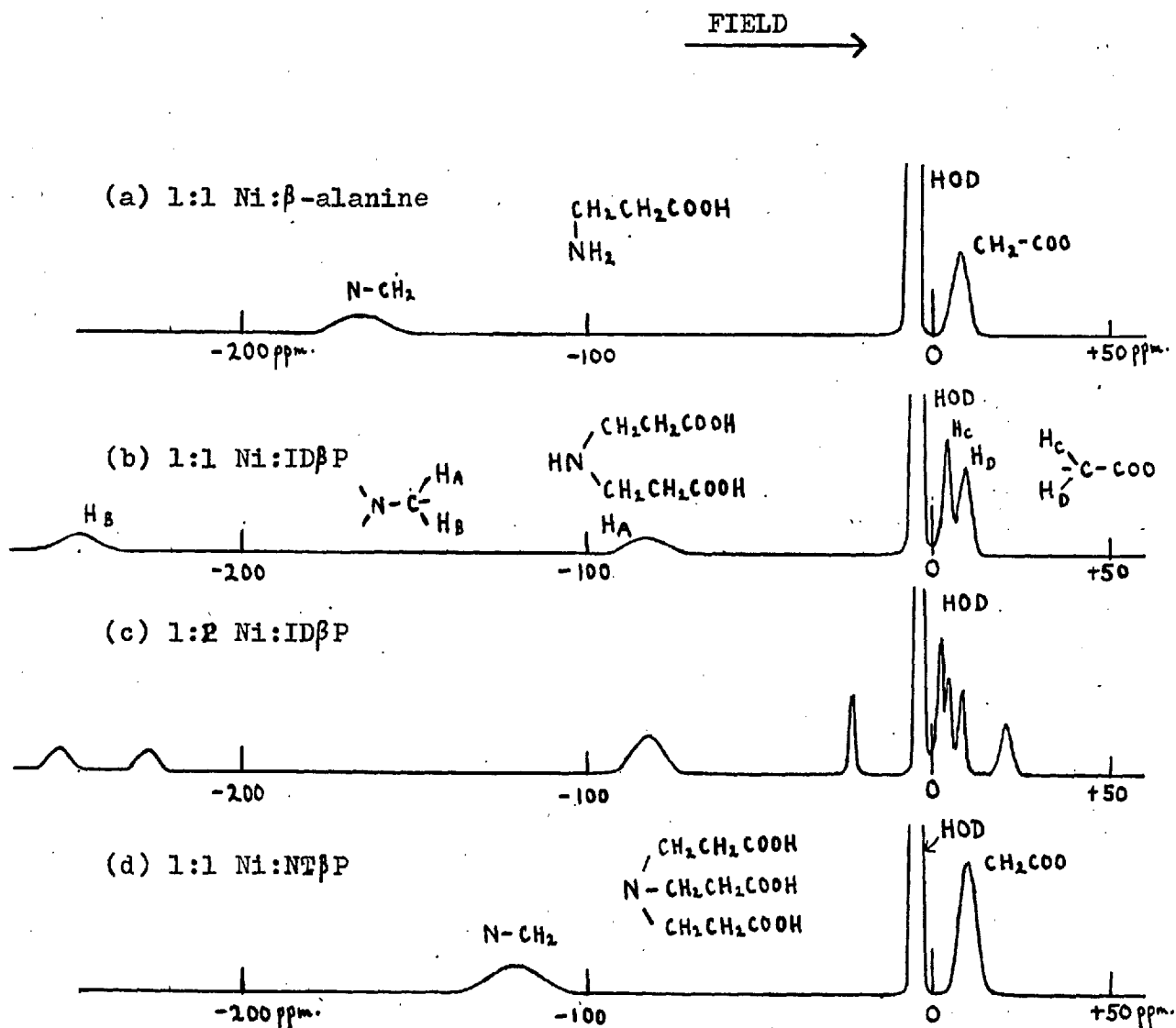


Figure 19. CH Spectra of Ni(II) complexes of β-alanine, IDβP and NTβP. Contact shifts are in p.p.m. relative to t-butanol.

two rings should be equivalent. Models confirm the X-ray data¹²³ and indicate that the rings are considerably puckered, and it seems reasonable to assign the two low field lines to the two non-equivalent protons of the N - CH₂ groups, and the two high field (sharper) lines to the two non-equivalent protons in each CH₂ - COO group.

There are eight lines in the spectrum of the 1:2 complex (Figure 19c); i.e. as with IDA, there are twice as many lines as in the 1:1 complex. Probably the doubling can be explained in the same way, as arising from a mixture of isomers; the intensities of the lines, which don't appear to be equal, seem to rule out the presence of only one isomer, in which the rings are not all equivalent. In this case, the isomer analogous to the trans meridional structure III would not be relatively unstable since there is less angle strain.

The free ligand lines in the solutions, under some conditions, are fairly strong since the complexes are less stable than the IDA ones; also, the free ligand lines are broadened when the pH is ~ 5 - 7, indicating that the overall ligand exchange rate is moderately fast.

The spectrum of the 1:1 complex of nitrilo -tri-β- propionic acid (NTβP),
$$\text{N} \begin{array}{c} \diagup \text{CH}_2\text{CH}_2\text{COOH} \\ \text{---} \text{CH}_2\text{CH}_2\text{COOH} \\ \diagdown \text{CH}_2\text{CH}_2\text{COOH} \end{array}$$
 (Figure 19d) is very similar to that of the 1:1 β-alanine complex and by comparison, the low and high field CH lines are assigned to the N - CH₂ and CH₂ - COO groups respectively. Hence, as with NTA, the three rings are equivalent; this is likely to result from the Ni - O bonds migration. The

construction of models suggests that, although there is less angle strain than with NTA, there would be considerable steric crowding if three rings formed together, and it is possible that one is free on the average. This is supported by its stability constant ($\log K_1 = 5.8$)¹²⁹ which is not larger than that of the ID β P complex ($\log K_1 = 6.2$)¹²⁸.

With concentration ratios of 1:1, sharp free ligand lines are also visible, so exchange between bound and unbound ligand must be fairly slow; but increasing the concentration of the ligand produces a broadening of the lines, and this may be due to exchange between free and bound ligand groups, or to ligand exchange between 1:1 and 1:2 species.

Tridentate ligands forming one five membered and one six membered rings. Imino - β - propionic acetic acid (I β PA), $\text{NH} \begin{cases} \text{CH}_2\text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{cases}$.

The spectrum of the 1:1 complex (Figure 20a) shows four lines; however, the one at -74 p.p.m. probably represents two CH protons since its intensity is about twice that of the other low field lines, and its shape is unsymmetrical. The lines can be assigned as if one species is present; cis and trans isomers are possible but would interconvert rapidly. By comparison with the two imino acids already discussed (IDA and ID β P), each of the three CH₂ groups is expected to give two lines. The relatively sharp line at +9 p.p.m. appears to represent two protons and is assigned to the CH₂ - COO protons in the six membered ring. The line at -74 p.p.m. is clearly seen to consist of two broad bands which, together with the lines at -135 p.p.m.

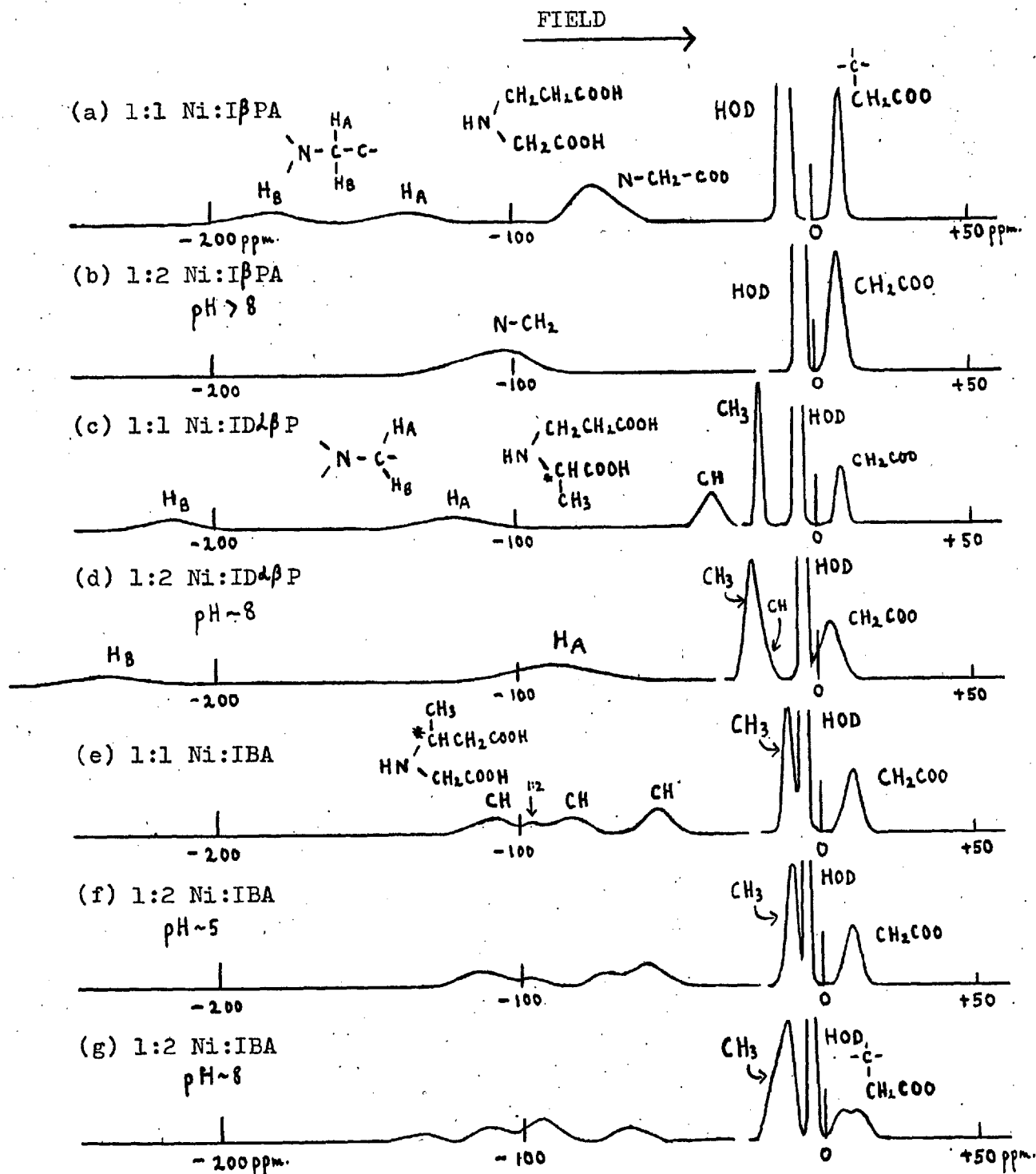
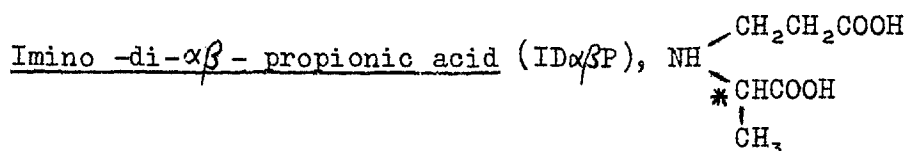


Figure 20. CH Spectra of Ni(II) complexes of I β PA, ID Δ β P and IBA. Contact shifts are in p.p.m. relative to t-butanol. The break in the base lines indicates a reduced signal/noise ratio for the higher field lines.

and -180 p.p.m., represent the N - CH₂ groups. The line at -180 p.p.m. can be assigned to one of the N - CH₂ protons in the six membered ring, and one of the lines at $\sim$ -74 p.p.m. is very likely to come from one proton in the five membered ring CH₂. If the line at -135 p.p.m. is assigned to the six membered ring CH₂, as suggested by comparison with other six membered ring line positions, then the second overlapping line comes from the five membered ring CH₂ group, suggesting that this ring may be nearly planar on the average.

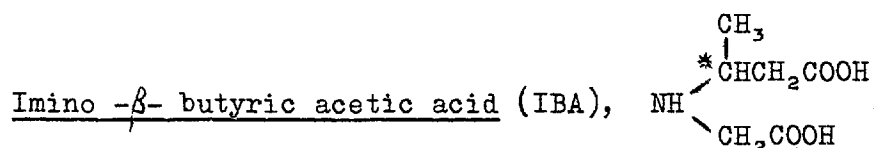
In the 1:2 sample at pH > 8 only two lines are seen (Figure 20b) at -106 p.p.m. and +7 p.p.m.; the solution is blue and probably the major species is a 1:2 complex. However, the band at $\sim$ -106 p.p.m. is very broad, and the line at +7 p.p.m. is also markedly broader than in the 1:1 complex, suggesting that exchange processes, possibly including ligand exchange, may be averaging out the non-equivalences within the CH₂ groups. The line at + 7 p.p.m. is assigned to the CH₂ - COO group in the six membered ring; the band at $\sim$ -106 p.p.m. is asymmetrical and consists of at least two overlapping bands, one from each of the two N - CH₂ groups.



The spectrum of the 1:1 complex (Figure 20c) can be assigned similarly to the previous complex. The lines at about +8 p.p.m. and at -122, -214 p.p.m. are attributed to the CH₂ - COO and the CH₂ - N groups respectively in the six membered ring; the remaining two lines then represent the CH₃ and CH protons in the five membered ring.

Again, any isomers are not distinguished.

In the 1:2 sample at pH $\sim$ 8, the blue colour and the absence of free ligand indicate that the major species present is (are) the 1:2 complex(es). The spectrum (Figure 20d) shows only four lines, but they are broader and the intensities suggest that the single CH proton is obscured by the CH₃ line. The other lines are assigned as indicated. The broadening may result from exchange processes, or from unresolved doubling of the lines due to the differences expected between the isomers — as with the 1:2 complexes of I_oPA, many isomers are possible.



The spectra, at various pHs, are illustrated in Figure 20e - g. The 1:1 spectrum, which is similar to the two previous cases, is very difficult to assign. The relatively sharp lines near the t-butanol can be assigned as the CH₃ group (-11 p.p.m.) and the CH₂ group in the six membered ring (+ 10 p.p.m.). If the weak line at about -96 p.p.m. (Figure 20e) is assigned to the 1:2 complex, the other three lines can be assigned to the remaining three CH protons. In the 1:2 solution, on increasing the pH from 5 to 7, one of the lines moves downfield (-73 p.p.m. to -83 p.p.m.), possibly because the butyric carboxyl is ionising. There is also a doubling of the two relatively sharp lines near t-butanol in the 1:2 complex, which is undoubtedly present at pH 8 (blue colour of the solution, absence of free ligand and HOD line position), and this probably indicates

the presence of isomers.

Ligands which may form two five membered and one six membered rings. These ligands are potentially tetradentate, but in 1:2 complexes they may behave as if they were N-substituted IDA derivatives with the six membered ring group free.

N -2- hydroxyethyl iminodiacetic acid (HEIDA),

$$\text{HOCH}_2\text{CH}_2\text{N} \begin{cases} \text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{cases}$$
 It is convenient to consider the 1:2 complex first. Over the pH range 5 - 10, it gives the same three-line spectrum (shown for pH $\approx$ 8 in Figure 21c), which is very similar to that for the 1:2 complex with N-ethyl iminodiacetic acid (EIDA) (Figure 15f, page 120). This suggests that the hydroxyethyl groups are not bound to the Ni(II) in the 1:2 complex. The assignment of lines is then similar to that given for EIDA. The CH₂ groups in the acetate five membered rings give lines at -28 p.p.m. and -70.5 p.p.m. The intensity of the latter line and its broad base suggest that it represents two broad lines overlapping; the other is assigned to the N - CH₂ group in the uncomplexed hydroxyethyl group, and the relatively sharp line at about -8 p.p.m. is assigned as the CH₂ - OH group. (There was no sign of doubling of the overlapping lines even in spectra recorded at 100 mcs./sec.). The OH proton (when in H₂O solution) is not seen; it will be in fast exchange with the H₂O protons and, in any case, its shift is expected to be small. There is no indication of the presence of isomers; the possibilities are probably the same as discussed for the EIDA complex.

In contrast, compared with the spectrum of the 1:1 complex

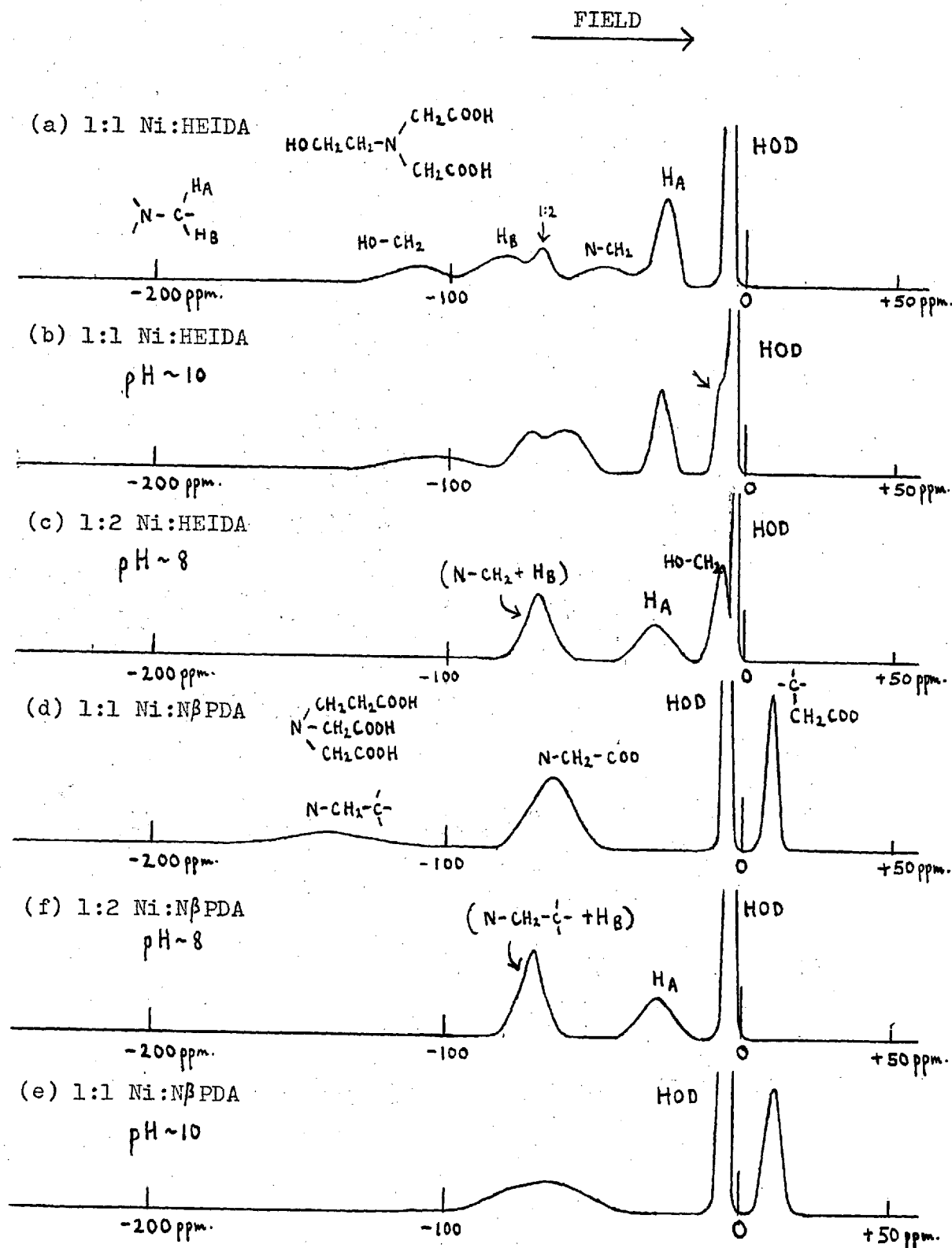
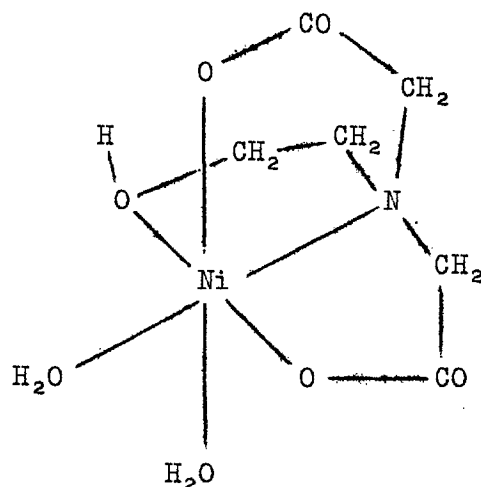


Figure 21. Spectra of Ni(II) complexes of HEIDA and N β PDA.

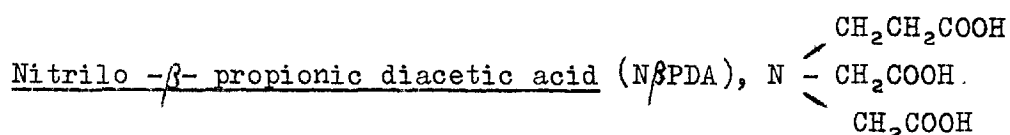
with EIDA (Figure 15e), the lines of the spectrum of the 1:1 complex with HEIDA (Figure 21a) are considerably broader, and the one at -110 p.p.m. is much lower than any in the other complex. A reasonable explanation is that the hydroxyl group is bound to the Ni(II), at least for part of the time. There is evidence from pH titrations and the stability constants derived therefrom,¹³⁰ that this ligand forms more stable complexes than does IDA, presumably because the hydroxyethyl group does also form a weak chelate ring.



A possible assignment is that the acetate CH_2 groups give the sharper line at -28 p.p.m. and the broader line at -80 p.p.m.. The two other broad lines (at -50 and -110 p.p.m.) then represent the two CH_2 groups of the hydroxyethyl group; the $\text{O} - \text{CH}_2$ protons would be expected to be those having a bigger shift (of -110 p.p.m.) if OH is bonded to the Ni(II) . The broadness of the lines indicates that the $\text{Ni} - \text{OH}$ bond is labile; if the hydroxyl group is non-bonded for part of the time, the spectrum is an average over tri- and

tetradentate complexes; this would broaden the acetate CH_2 lines as well.

The pH titrations¹⁴⁴ show that when the pH rises above 9, the 1:1 complex can lose a proton from either the coordinated OH group or one of the two coordinated H_2O molecules; the pK for this step is 10.83. Although there is some indication (Figure 21b) of a different spectrum in the pH region 8 - 10, precipitation of hydroxy complexes (or hydroxide) occurs as would be expected since the n.m.r. samples have a concentration (0.5 M) much greater than those used in the pH titrations (10^{-4} to 10^{-5} M).

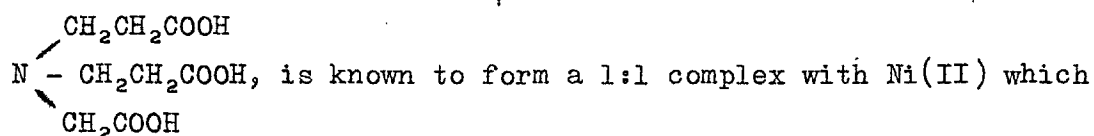


This ligand is known to form 1:1 complexes with transition metals which are more stable than those with IDA,¹²⁹ presumably because of the formation of the third six membered ring in addition to the two stable five membered rings. The structure can be less strained than with NTA, since the two five membered rings can be cis to each other; in fact its stability constant ($\log K_1 = 11.4$)¹²⁸ is almost the same as that for the NTA complex. The six membered ring would be expected to be less stable than the five membered ones; lability of its $\text{Ni} - \text{O}$ bond would make the two protons in each CH_2 group equivalent. In the spectrum (Figure 21d), the lines at about +10 p.p.m. and -133 p.p.m. probably represent the six membered ring CH_2COO and $\text{N} - \text{CH}_2$ groups respectively. The rather broad line at -63 p.p.m. is about twice as intense as the others, and seems to represent all

the CH_2 protons in the five membered rings. Non-equivalence in each CH_2 group would be expected; it may be that these rings are labile. When the pH is increased from 8 to 10 the spectrum changes (Figure 21e), and the green coloured solution changes to a deeper, intense green. Possibly this is due to the ionisation of the complexed H_2O molecules, giving hydroxy complexes.

At pH 8, the 1:2 complex is the main species and the Ni(II) is fully complexed (by the usual criteria). The spectrum (Figure 21f) is similar to those of the 1:2 complexes of EIDA and HEIDA; presumably the propionic chain is not bonded to the Ni(II) . The assignment would be similar, with the band at -70 p.p.m. representing overlapping lines; in this case, however, the propionic CH_2COO protons are missing. Presumably they lie under the HOD line, but this could not be resolved, even at 100 mcs./sec. (nor could the -70 p.p.m. band).

A ligand which may form one five and two six membered chelate rings. Nitrilo -di- β - propionic acetic acid ($\text{ND}\beta\text{PA}$),



probably contains one five membered and two six membered rings.¹²⁹

The spectrum of the 1:1 complex at $\text{pH} \sim 6$ (Figure 22a) contains five lines. The two overlapping relatively sharp lines at about +8 p.p.m. are assigned to the $\text{CH}_2 - \text{COO}$ protons, and the very broad lines at -106 p.p.m. and -158 p.p.m. are assigned to the $\text{N} - \text{CH}_2$ protons in the six membered rings. The six membered rings would be

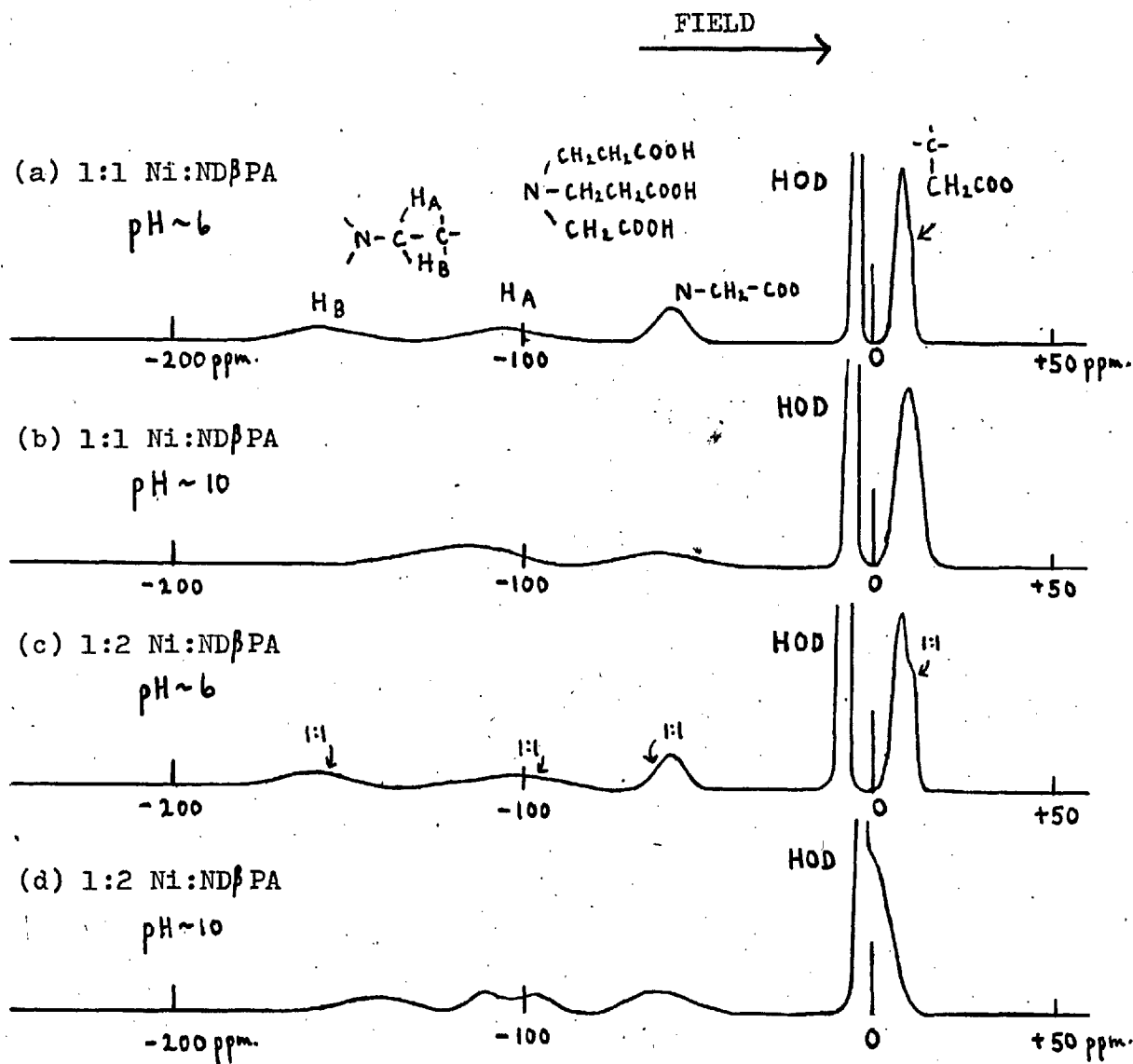


Figure 22. Spectra of Ni(II) complexes of NDβPA.

Contact shifts are in p.p.m. relative to t-butanol.

expected to be in slightly different environments but can become equivalent. The observation of one line (-58.5 p.p.m.) for the CH_2 protons in the five membered ring is not surprising, for the group can be in a symmetrical environment and they can become equivalent by conformational or rotational movement (the latter following Ni - O lability). A complex containing one five membered ring is less rigid than one containing two, and easier internal motion would be expected. The change in the spectrum in the pH range 8 - 10 (Figure 22b) can be ascribed to the reasons given previously for HEIDA and ~~Nppa~~.

In the 1:2 solution, the spectrum at pH ~ 6 (Figure 22c) is that of the 1:1 complex. As the pH is increased, the solution becomes greenish-blue in colour, and a markedly broader different spectrum results (Figure 22d). The presence of a considerable amount of free ligand at pH 9 - 10 and the broadness of the lines suggests that the solution contains a mixture of 1:1 and 1:2 complexes, which are exchanging with each other fairly rapidly. In the 1:2 complex, presumably one of the six membered rings becomes free.

NH Resonances. The NH lines are generally very broad and difficult to measure; since their positions do not vary much with the structure of the complexes, they have not been discussed in assigning the spectra. Also, they were absent from most of the spectra, which were measured in D_2O . Their positions for some of the complexes studied are shown in Figure 23. They all have large shifts to high field. For NH_2 groups (in monochelate ligands),

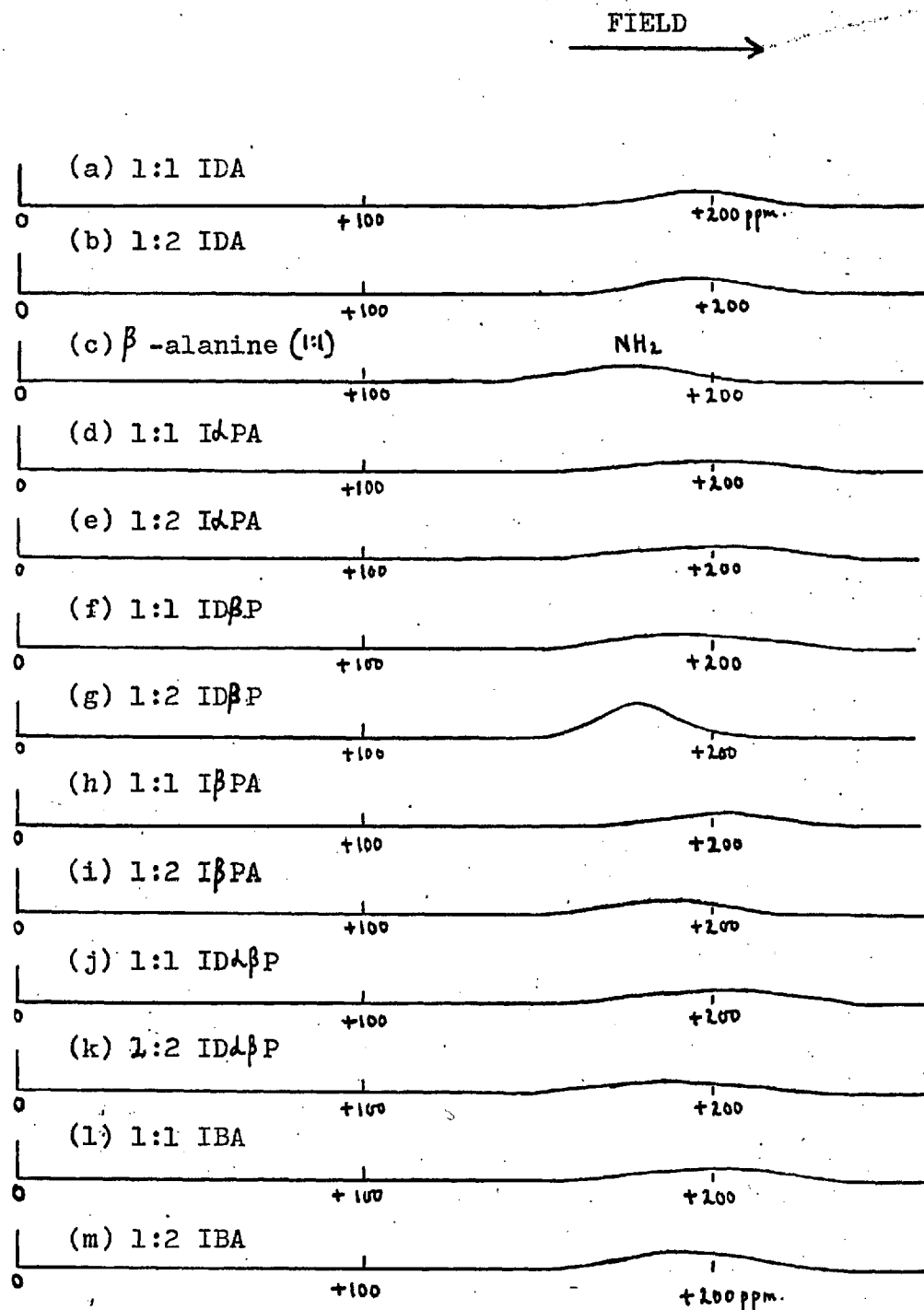


Figure 23. Spectra of NH resonances of Ni(II) complexes. Contact shifts are in p.p.m. on the high field side of t-butanol.

the values are in the range +160 to +200 p.p.m. for both five and six membered chelate rings. For imino NH groups in complexes of IDA derivatives (with two five membered chelate rings), the values are about +200 p.p.m.. In some cases, the values in 1:2 complexes are lower than those in the 1:1; in mixtures containing 1:1 and 1:2 complexes, the lines usually overlap and are not resolved. Even when isomers are possible and are indicated by the CH part of the spectrum, the NH lines are usually too broad to show a doubling.

Since the NH proton lines can be observed separately, it follows that the rate of exchange of these protons with the solvent H_2O is no more than about $1/(2\pi \times 10,000) \text{ sec.}^{-1}$. As already mentioned, this supports the assumption that the nitrogen atoms are not very labile. When a nitrogen atom becomes free, the rate of proton exchange is expected to be similar to that in amines, which is very rapid, and this would provide an effective mechanism for proton exchange if the Ni - N bonds were open for long.

C. Interpretation.

Summary of the shift values for the Ni(II) - amino-acid complexes. The observed ranges of shift values can be summarised as follows.

- | | | |
|--------------------------------------|--------------------------------|----------------------|
| 1. In 5 membered chelate rings, | $\underline{CH}$ protons | - 20 to -100 p.p.m.. |
| 2. In 6 membered chelate rings, | $\underline{CH} - N$ | - 80 to -240. |
| | $\underline{CH} - COO$ | 0 to + 20. |
| 3. In 5 membered chelate rings, | $N - \underline{CH}_3$ | - 90 to -120. |
| | $N - \underline{CH}_2 - CH_2X$ | - 70 to - 80. |
| 4. In 5 or 6 membered chelate rings, | $N - C - \underline{CH}_3$ | - 4 to - 20. |
| 5. In 5 or 6 membered chelate rings, | $N - \underline{H}$ | +160 to +200. |

Previous measurements⁹¹ had shown that in Ni(II) amine complexes, the N - CH shifts are as large as those found here; however, in Ni(II) complexes of carboxylic acids, the shifts are considerably smaller, within about ± 15 p.p.m.. The above facts suggest that the main contribution to the shifts comes through the coordinated nitrogen atom.

The large variation in shifts for the N - C^H protons suggests that they depend on the structures of the rings, and in fact there does seem to be a correlation between the shifts and the dihedral angle (ϕ) between the N - C^H plane and the Ni^N - N - C plane. These dihedral angles were estimated from Dreiding models (Table 11). The values are not expected to be accurate since the models have the same distances for all bonds of the same type, and equal values for Ni - O and Ni - N bonds (≈ 2.1 Å; although these distances are in fact both approximately 2.1 Å). Also, all the angles at saturated carbon and nitrogen atoms are the same ($109^\circ 28'$), and all the angles at the metal are 90° . X-ray studies show that these distances and (especially) angles are not constant. As a consequence, for example, the five membered glycine type ring is puckered slightly in $[\text{Ni}(\text{glycine})_2]^\circ$ ¹²², but apparently more so in $[\text{Ni}(\text{histidine})_2]^\circ$ ¹³¹ in $[\text{Ni} \cdot \text{H}_2\text{EDTA} \cdot \text{H}_2\text{O}]^\circ$ ¹³² there are rings both slightly and considerably puckered. Unfortunately, the X-ray studies have not located the hydrogen atoms, and, in any case, structures of complexes in the crystalline solid are often not the same as those in solution. Thus the models are probably as good a way as any to

Table 11. Dihedral Angles for N-C-H Protons in Five and Six Membered Chelate Rings of Ni(II) Complexes.

CHELATE RINGS	FORMULA	PROTON TYPE	SHIFT p.p.m.	RANGE OF SHIFTS	DIHEDRAL ANGLE ϕ
FIVE MEMBERED RIGID	$\begin{array}{c} \text{HN} \diagup \text{CH}_A\text{H}_B\text{COOH} \\ \text{CH}_A\text{H}_B\text{COOH} \end{array}$	H _A	-24	H _A - 20-30	~ 95°
		H _B	-93		
	$\begin{array}{c} \text{CH}_3-\text{N} \diagup \text{CH}_A\text{H}_B\text{COOH} \\ \text{CH}_A\text{H}_B\text{COOH} \end{array}$	H _A	-30.5	H _B - 70-100	~ 145°
		H _B	-76.5		
	$\begin{array}{c} \text{CH}_3\text{CH}_2\text{N} \diagup \text{CH}_A\text{H}_B\text{COOH} \\ \text{CH}_A\text{H}_B\text{COOH} \end{array}$	H _A	-28.5		
		H _B	-78		
SIX MEMBERED RIGID	$\begin{array}{c} \text{HN} \diagup \text{CH}_A\text{H}_B\text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{array}$	H _A	-135	H _A - 80-140	~ 50°
		H _B	-180		
	$\begin{array}{c} \text{HN} \diagup \text{CH}_A\text{H}_B\text{CH}_2\text{COOH} \\ \text{CHCOOH} \\ \text{CH}_3 \end{array}$	H _A	-122	H _B - 180-250	~ 170°
		H _B	-214		
	$\begin{array}{c} \text{HN} \diagup \text{CH}_A\text{H}_B\text{CH}_2\text{COOH} \\ \text{CH}_A\text{H}_B\text{CH}_2\text{COOH} \end{array}$	H _A	-83		
		H _B	-247		
PROLINE	$\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \quad \\ \text{CH}_2 \quad \text{CH}_X-\text{COOH} \\ \text{(A)} \diagdown \text{NH} \end{array}$	H _A	-77		140°
		H _A	-145		20°
		H _X	-60		135°
HISTIDINE	$\begin{array}{c} \text{CH}_2-\text{CH}_X-\text{COOH} \\ \quad \\ \text{N} \quad \text{NH}_2 \end{array}$	H _X	-171		150°

obtain rough estimates of angles; the model structures do agree fairly well with those determined by X-rays.

The most reliable estimates are expected to be those obtaining fused rings, since these make the structures fairly rigid, apart from molecular vibrations over small displacements. For five membered rings, this applies to IDA derivatives, whose CH_2 protons give a large and a small shift. Since the trans structure appears to be more strained, it is assumed that they have the cis one (Figure 16a). In this structure, the largest values of the dihedral angles which seem possible without undue strain are 95° (H outside) and 145° (H inside); since the rings have some flexibility, the observed shifts probably are averages over a smaller angular difference than this. This is allowed for by a broad circle in the diagram (Figure 24). When the rings carry a CH_3 group, this is likely to be on the outside position, leaving the C - H inside; the spectra show only the larger shift value and this is assigned to $\phi \approx 145^\circ$. Variations of shifts among IDA derivatives (-70 to -110 p.p.m. for the larger shift) are probably partly due to variations in ϕ .

With six membered rings, the largest shifts and separations are found with tridentate ligands; these are expected to be fairly rigid, especially in 1:2 complexes, whereas single six membered rings are more labile and three such rings are fairly crowded sterically. The angles measured for the N - CH_2 protons are about 50° (H inside) and 170° (H outside), assigned to the shifts of about -100 p.p.m. and

-220 p.p.m. respectively. Some support for this is the absence of the larger shift when one of these CH protons is replaced by a CH₃ group which is expected to occupy an outside position.

CH shifts reported previously for histidine and proline complexes⁹¹ have been included. In both complexes, the five membered ring is expected to be rigid, and in the proline complex, where rigidity is due to the C - N bond being part of a five membered heterocyclic ring, angles can be measured for the two N - CH₂ protons in this ring.

When plotted against ϕ , the shifts lie roughly on a curve (Figure 24). The variation shown is also consistent with the shifts found for flexible groups, whose observed values will be averaged over the range covered in the movement, and can be calculated when the averaging occurs between equivalent environments, since the residence times will be equal. For N - CH₃ groups, the shift (in p.p.m. and negative in sign) should be given by

$$S_{\text{average}} = 1/3 S(\phi=180) + 2/3 S(\phi=60) = 1/3 \cdot 240 + 2/3 \cdot 50 = 113,$$

agreeing with the observed values (average of three = 108). The lower value (-70 to -80 p.p.m.) for N - CH₂X groups could arise because the X group is expected (for steric reasons) to occupy preferentially the position trans to the Ni - N bond, so that the CH₂ protons spend more time in gauche positions ($\phi = 60^\circ$).

A CH₂ group in a five membered ring, moving between equivalent positions, should give a shift of $1/2 (S_A + S_B)$, where S_A and S_B are the shifts each proton has in the two positions. The shift of

KEY

P = Proline
 H = Histidine
 5 = 5-membered rings (rigid)
 6 = 6-membered rings (rigid)
 Av.5 = Averaged 5-membered rings

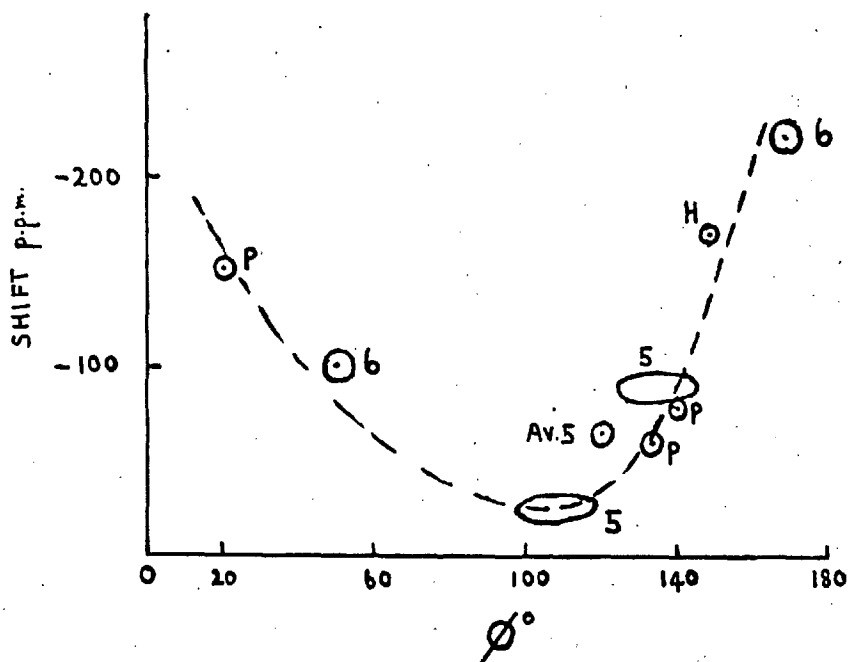


Figure 24. Dependence of observed N-C-H contact shifts on the dihedral angle (ϕ).

about -60 p.p.m. observed for glycine and NN'-dimethyl glycine agree with this for $S_A \approx 20$ and $S_B \approx 100$, but they could equally well result from the averaging over a smaller range of ϕ , or for planar rings ($\phi = 120^\circ$). In a flexible six membered ring, the N - CH₂ shift should be $1/2(220 + 100) = 160$, agreeing roughly with the observed values for single N - CH₂ lines.

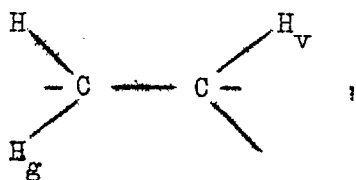
Hence the observed N - CH shifts are at least consistent with the angular variation shown in Figure 24. It must be remembered, however, that this is based on angles, none of which are known experimentally (even when the structure of a complex is known), and on assignments of shifts to particular CH protons which have not all been confirmed experimentally

D. Origin of the Shifts.

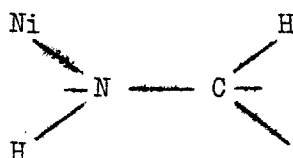
The observed variation can not easily be explained by the pseudocontact mechanism. Protons would then feel an averaged magnetic field from the Ni(II) atom, directly through space. The magnitude and direction of their shifts would depend on $1/(\text{Ni} - \text{H distance})^3$ and also on the angle between the Ni - H direction and the bond axes at the Ni(II). However, in several structures (e.g. that for the imino - β - propionic acetic complex), it appears that the N - CH protons with similar distances and angles relative to the Ni(II), have shifts which differ too much to be explained this way. Also, although the large shift of NH protons may be expected, since they are close to the Ni(II), it is unlikely that none of the N - CH protons would show shifts in the same direction, since some of them

can make similar angles to the Ni(II) axes.

It is more likely that some fractional unpaired electron is placed on the nitrogen atom, and is transmitted via the bonding electrons into orbitals containing hydrogen 1s character, where contact interaction with the protons can occur. One mechanism for the transmission is spin polarisation, involving a slight uncoupling of electron spins in the σ bonds; this can explain the sign alternation between the NH and N - CH protons but not the angular variation. The latter can result from another mechanism involving direct overlap between orbitals of atoms which are not adjacent. Probably both mechanisms contribute to the shifts. The situation seems to be analogous to the problem of spin coupling between aliphatic protons. In the group

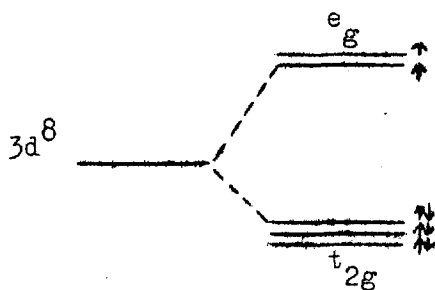


the proton H produces a slight unpairing of the electron spin in its CH bond; this unpairing is then transmitted into the other bonds where contact interaction with the protons occurs. The geminal coupling between H and H_g is large and negative; the vicinal coupling between H and H_v is fairly large, positive, and depends on the dihedral angle. In the complexes, Ni(II) is bonded to tetrahedral nitrogen; a fractional unpaired electron gets directly into the Ni - N bond, and its effect is transmitted by the electrons to give



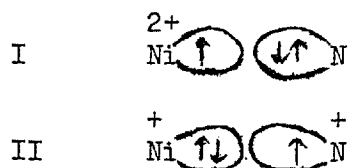
negative spin density on the NH protons and positive spin density (whose magnitude depends on ϕ) on the N - CH protons. The theoretical interpretation of spin coupling is incomplete, but it probably involves processes similar to these mentioned above, which will now be given in more detail.

Some fractional unpaired electron can appear on the nitrogen as follows. Octahedrally coordinated Ni(II) has two groups of 3d orbitals, the three t_{2g} orbitals (lower energy), whose lobes point between the ligands, and the two e_g orbitals (higher energy), whose lobes point towards the ligands. There are eight 3d electrons of which six are in the three t_{2g} and the two e_g orbitals each contain one unpaired electron, i.e.



The unpaired electrons are aligned preferentially in the direction of the applied magnetic field; they are said to have a positive spin direction. In the Ni - N bond, the nitrogen lone pair, which is situated in one of the N sp^3 orbitals, is directed towards one of the lobes of an e_g orbital. Covalent σ bonding between the atoms

will involve a transfer of electrons from the nitrogen to the nickel; this will be favoured for the nitrogen electron whose spin is anti-parallel to that of the electron in the nickel e_g orbital. This will leave a slight excess of positive electron spin on the nitrogen orbital, i.e. in the same direction as the applied field.

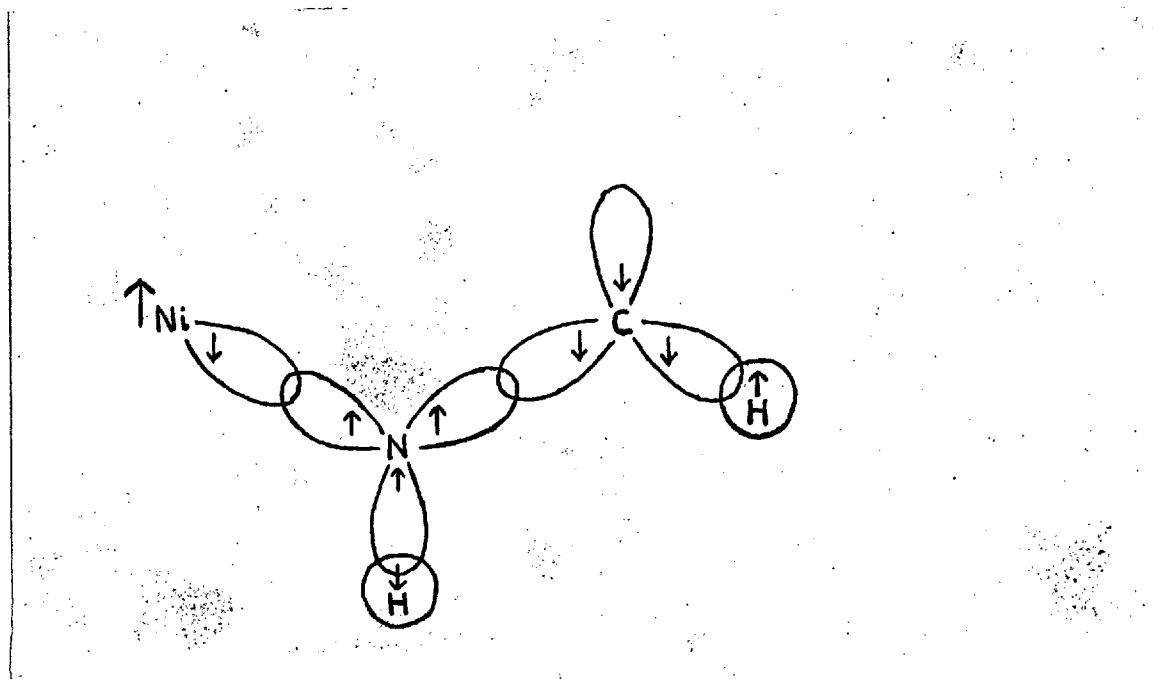


This positive spin density on the nitrogen can result from only a slight σ electron transfer, and the contribution to the ground state of the extreme structure represented by II may be only a few per cent.

The above description has only considered σ bonding; however, it should be noted that it has recently been suggested from e.s.r. evidence,^{133,134} that apparently small values of spin densities on atoms bonded to transition metal ions may result from cancellation of spin densities of opposite signs, transferred by σ and π mechanisms, involving e_g and t_{2g} orbitals respectively. It will be assumed here that the shifts arise from a net positive spin density on the nitrogen σ orbital, but there is no direct evidence for this.

Spin polarisation is one mechanism by which the spin density can be transmitted to the other atoms in the ligand; it involves a slight unpairing of the electrons in the σ bonds of the N - C skeleton. Positive spin density in one of the nitrogen sp^3 orbitals would tend to stabilise positive spin direction for the other three

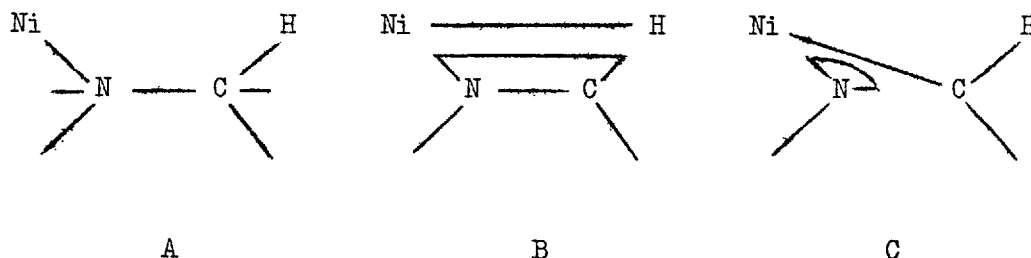
electrons in the sp^3 orbitals. Since the electrons in the bonds have antiparallel spins, this means that the hydrogen 1s electron in the NH bond would favour an antiparallel orientation. This gives rise



to a small negative spin density on the hydrogen atom; hence its resonance occurs upfield. Similarly, there is expected to be a negative spin density in the sp^3 orbital of the carbon next to the nitrogen, and a positive spin density on the hydrogen atom attached to this carbon, explaining the observation of low field C - H shifts; however, this mechanism would still predict an alternation of upfield and downfield shifts along an aliphatic group (bonded only to nitrogen), which is not observed; nor does it predict an angular dependence.

It is likely that another mechanism, involving direct overlap of orbitals of non-adjacent atoms, is also important. This

mechanism could well be similar to that responsible for (diamagnetic) spin coupling between vicinal protons.^{135,136} The ground state of the group is represented mainly by the structure A, but there are also small contributions from structures such as B and C, in which



there is direct overlap between "non bonded" atoms, which can place unpaired spin density from the Ni - N bond into the hydrogen 1s orbital. The contributions of these unconventional pairing schemes can be very small; their importance obviously depends on the dihedral angle but the calculations are very difficult. The effects of this mechanism should also fall off with increasing number of bonds away from the nitrogen, but it would always give positive spin densities.

The differences in shifts between equivalent types of N - CH protons in different complexes can be due to

- (a) differences in ϕ values; these can easily result from conformational changes due to steric interactions between ligands, and can explain the changes between 1:1 and 1:2 complexes, and between isomers;
- (b) differences in Ni - N bond strengths; the stronger the bond the greater the shift is expected to be. This may explain the range

of N - CH₃ shift values;

(c) differences in bond angles which alter the spin polarisation;

(d) differences in the pseudocontact contribution, since octahedral Ni(II) complexes do have anisotropic magnetic moments.¹³⁷

CH protons which are further away from the nitrogen have smaller shifts to which all three mechanisms can contribute (they all fall off with distance). With five membered chelates, the sign alternation expected for spin polarisation is not observed; the shifts are all to low field, agreeing with overlap. Angular dependence is not apparent (except with proline) and, in any case, could be due to pseudocontact effects.

Also, there will certainly be effects from the - COO⁻ group which have not yet been considered. The group does not seem to transmit unpaired spin very effectively; in six membered rings, the small upfield shift for the CH₂COO protons suggests that they receive a small negative spin density, which must presumably be present in the five membered rings, cancelling out part of the full effect from the nitrogen.

It is interesting to compare the contact shift spectra with the proton resonance spectra of Tl(III) complexes of the same ligands.¹¹² In these, the values of the Tl - H spin coupling constants for the CH protons follow a similar pattern to the contact shifts in showing non-equivalences and in angular dependence. Both phenomena probably depend in similar ways on the transmission of spin interactions through σ bonds.

NH protons. The differences between different complexes, and between 1:1 and 1:2 complexes, are probably due to changes in bond strength. It is surprising that Ni - OH protons have downfield shifts, as already mentioned for coordinated H₂O; they can also be observed directly for coordinated CH₃OH in methanolic solutions of Ni(II) salts at -60°C.¹³⁸ The change in sign may be due to a difference in bond hybridisation; nitrogen will be nearly tetrahedral and sp³ hybridised; the oxygen forms only three bonds and its orbitals could have more s character with an angle closer to 120°. The spin interactions across an H₂X group are known to be very sensitive to such changes, the geminal coupling in a CH₂ group being positive in some olefins, and could well change sign from tetrahedral N to trigonal O.

Line widths. There are several contributions to the widths. Firstly, the presence of the paramagnetic Ni(II) ion will shorten the proton T₁ in two ways. One effect is the dipole-dipole interaction between electron and proton spins coming directly through space; this will fall off as 1/R³. The other is the interaction of the proton with the unpaired spin density which is present on its hydrogen atom; this should decrease in proportion to the contact shift. Secondly, the line widths will be affected if the protons are involved in exchange processes whose rates are of the same order of magnitude as the separations between the shifts. Thirdly, lines can appear broad if they contain unresolved overlapping lines, for example from isomers. It is difficult to interpret the widths; some

of the lines are so broad that they can hardly be observed and exchange effects can not be ruled out without studies of the effect of temperature. Exchange effects probably explain the great width of the NH lines, and of the CH lines in some 1:2 samples at high pH. The increase of CH line width with shift is fairly general, but in some complexes where exchange and isomers are unlikely, such as the 1:1 IDA complex, the widths of the lines are not proportional to contact shift and must be due mostly to the dipolar shortening of T_1 . T_1 values were not measured; they are difficult to measure since they are short, e.g. $\sim 10^{-2} - 10^{-4}$ cycles/sec. (from the line widths).

CHAPTER V

Proton Contact Shift Spectra of Co(II) Complexes of Aminopolycarboxylic Acids in Aqueous Solutions.

This chapter describes a study of the complexes formed by Co(II) with the aminocarboxylic and polycarboxylic acids studied in chapter IV, and with some additional ligands. The contact shift spectra were studied, in the same way as Ni(II), as a function of pH and concentration, and, in addition, some samples were measured at different temperatures. Some complexes ("mixed" complexes) containing two different ligands were also measured.

Experimental.

The same procedure was adopted as described in the preceding chapter, but, in addition, the Co(II) solutions were deoxygenated with nitrogen to prevent oxidation to Co(III). Also, anhydrous CoSO₄ or CoCl₂ was used when D₂O was the solvent. For measurements carried out at other than room temperature ($22 \pm 1^\circ\text{C}$), a Varian variable temperature unit was used; the sample temperature is then known to about $\pm 2^\circ\text{C}$.

Materials. In addition to the materials used in the preceding chapter, NN'-diethyl glycine and N-acetyl glycine were obtained commercially. Some of the addition products whose contact shift spectra were mentioned in chapter III, were also re-examined.

Results and Discussion.

A. General.

Several of the general topics discussed for Ni(II) apply

as well to Co(II) complexes.

Again only monomeric complexes are considered. The relative amounts of 1:1 and 1:2 complexes present can either be seen from the spectrum, or estimated if the stability constants are known. Co(II) ion usually forms weaker complexes with a given ligand than does Ni(II), since the bonds to the metal are weaker, and, in particular, the complexes with six membered chelate rings are less stable with Co(II).

It is also assumed that the coordination about the Co(II) is approximately octahedral. In support of this, - the colours of the solutions were similar to those found in similar complexes to arise from d - d transitions in the high spin ($3d^7$) electron configuration, pale pink for the 1:1 complexes (with one bonded nitrogen atom) and a more intense purple for the 1:2 complexes (with two bonded nitrogen atoms). The intense blue or purple colour which would indicate the presence of tetrahedral complexes was usually absent, except in some alkaline solutions. In some cases, the octahedral assumption was also supported by measurement of the magnetic moments (using the Evans method¹²¹). Octahedral high spin Co(II) complexes usually give magnetic moments in the range 4.7 - 5.2 B.M.,^{139,140} whereas tetrahedral ones give values in the range 4.4 - 4.7 B.M..^{139,140}

Regarding isomers, and structural parameters, the remarks given for Ni(II) apply equally to Co(II).

Exchange processes will also have similar effects for the

two metal ions. Co - N and Co - O bonds generally seem more labile than the corresponding bonds to nickel,¹⁴¹ but the overall ligand exchange is not usually fast enough to average out the difference between 1:1, 1:2 and free ligand.

The position of the H₂O line is again a weighted average, but at 40°C the contact shift for the coordinated H₂O (assuming Co(H₂O)₆²⁺) has been calculated¹²⁷ to be -3880 cycles/sec. (for 56.45 mcs./sec.), i.e. -68.7 p.p.m., considerably greater than that for Ni(II). The observed shift of the H₂O line at 40°C should then be about -1.93 p.p.m. and -3.86 p.p.m. for 0.25 M and 0.5 M solutions. The shifts measured here at 22°C were -1.83 p.p.m. and -3.38 p.p.m. respectively. If allowance is made for the increase of contact shift with decrease of temperature, the difference between the two sets of values becomes even greater; it may arise partly because different anions were used (ClO₄⁻ at 40°C, SO₄⁼ in the present work), since SO₄⁼ can also complex to Co²⁺, and also because the average coordination number of Co²⁺ in water may decrease with temperature - there is some evidence for this.¹⁴² The present values were used, since they were determined at the same temperature as the other solutions; the H₂O line position (in 0.5 M solution) is then expected to shift upfield by about 32 cycles/sec. for each molecule of H₂O replaced by another ligand atom (and proportionately less for the 0.25 M solutions), hence the number of sites on the Co(II) occupied by other ligand atoms can be estimated roughly,¹⁴³ subject to the sources of error mentioned before.

In discussing the spectra, the word "equivalence" refers to the contact shifts, as discussed for Ni(II). However, in Co(II) complexes, the contributions from pseudocontact effects, coming directly through space from anisotropic magnetic moments on the metal atom, are likely to be relatively more important than for Ni(II), and in interpreting the shifts (see later, after the assignments), the spatial position of the protons relative to the metal is especially important. For a given ligand, the shifts for Co(II) complexes are generally similar to those for Ni(II), and the differences can often be attributed to pseudocontact shifts with Co(II).

One marked difference between the spectra of Co(II) and Ni(II) is that Co(II) spectra usually have much sharper lines than the corresponding Ni(II) ones, as indicated in the typical spectrum (Figure 25). This is useful in that it enables more definite assignments to be made, partly because there is less overlapping, and partly because line intensities can be measured more readily. The Ni(II) spectra are so broad in some cases that it is extremely difficult to make assignments. The sharper Co(II) lines probably result from a longer nuclear T_1 (i.e. a shorter electron T_{1e}) than for Ni(II).

B. Assignments and Discussion of Spectra.

Bidentate ligands forming one chelate ring. With N-acetyl glycine and NN'-diethyl glycine, no separate spectra could be observed under any conditions, probably because the inductive, mesomeric and/or steric effects of the N - COCH₃ and N $\begin{matrix} \nearrow \text{CH}_2\text{CH}_3 \\ \searrow \text{CH}_2\text{CH}_3 \end{matrix}$ groups make the complexes unstable enough to allow fast overall ligand

exchange. The spectra of the 1:1 complexes of the other ligands, which have been reported previously,⁹¹ are illustrated in Figure 26, together with the assignments, which are largely self explanatory. The spectra are very similar to those obtained with Ni(II), and the same interpretations can be applied. However, with the N-methyl and NN'-dimethyl complexes, the CH₃ lines have a smaller shift than the CH lines, in contrast to the Ni(II) case. This is probably due to the Co(II) pseudocontact shift, since the structures of the complexes with both metal ions would be expected to be similar. It is also worth noting that in the α -alanine complex (Figure 26e), and in complexes with other unsymmetrical glycine derivatives, the NH₂ group gives a doublet line; the two lines must each be due to an N - H proton, made non-equivalent possibly by the pseudocontact effects.

Tridentate ligands which can form two five membered rings.

IDA. The spectra of the 1:1 and 1:2 complexes of IDA are illustrated in Figure 27. The 1:1 spectrum is similar to that obtained with Ni(II) and is assigned in the same way. There is no indication of cis and trans isomers. The width of even the sharpest line in these complexes (half width $\approx$ 150 cycles/sec.) prevents the observation of spin-spin splitting within the CH₂ group.

The 1:2 complex gives only one "set" of lines, which could arise from one isomer only (II), but it might be expected that isomers (possibly I and II in Figure 16b) might be present, as suggested for Ni(II). If so, their separate lines are averaged out because of

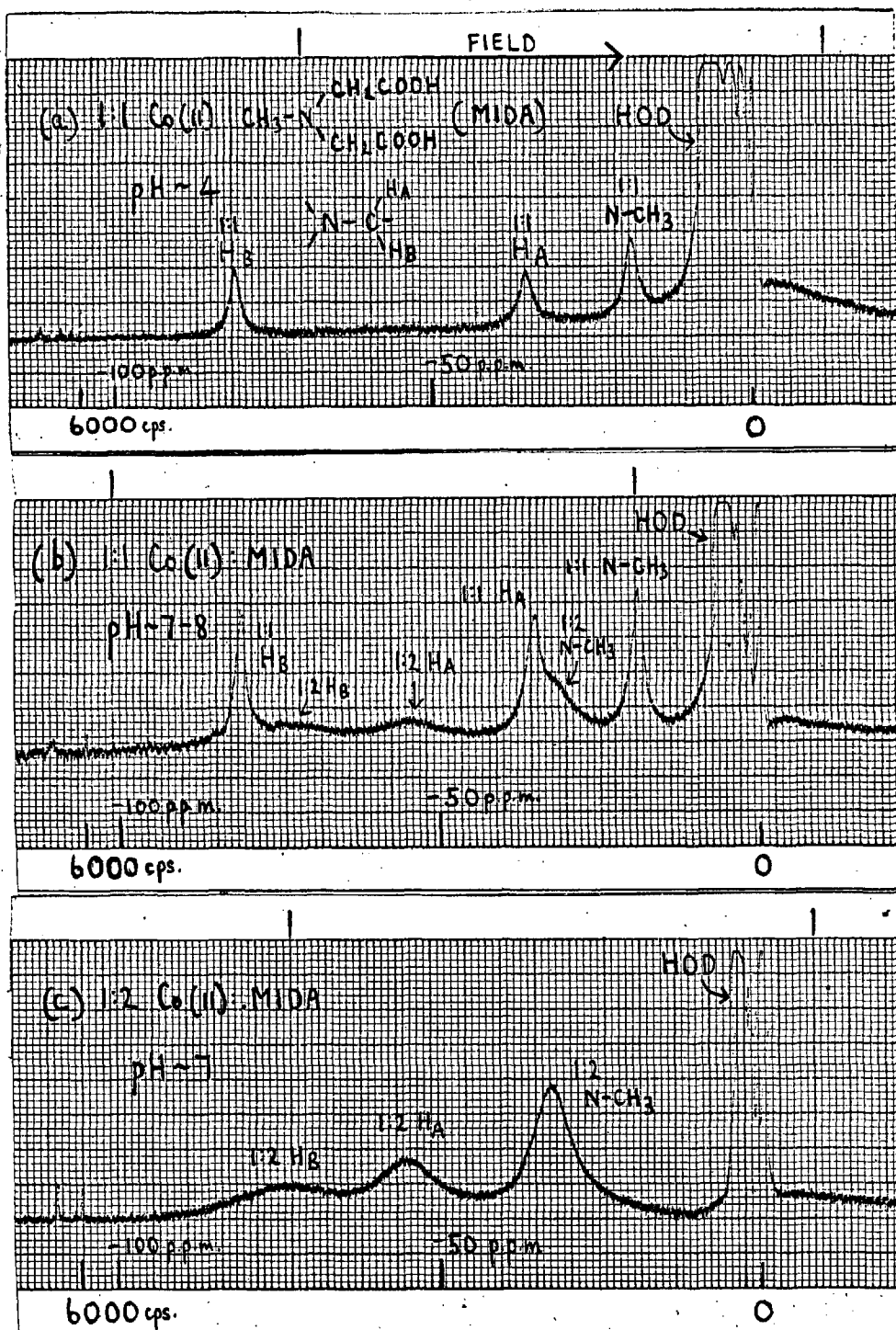


Figure 25. Typical contact shift spectra of the complexes of Co(II) with N-methyl iminodiacetic acid in D_2O . Contact shifts are in p.p.m. on the low field side of t-butanol.

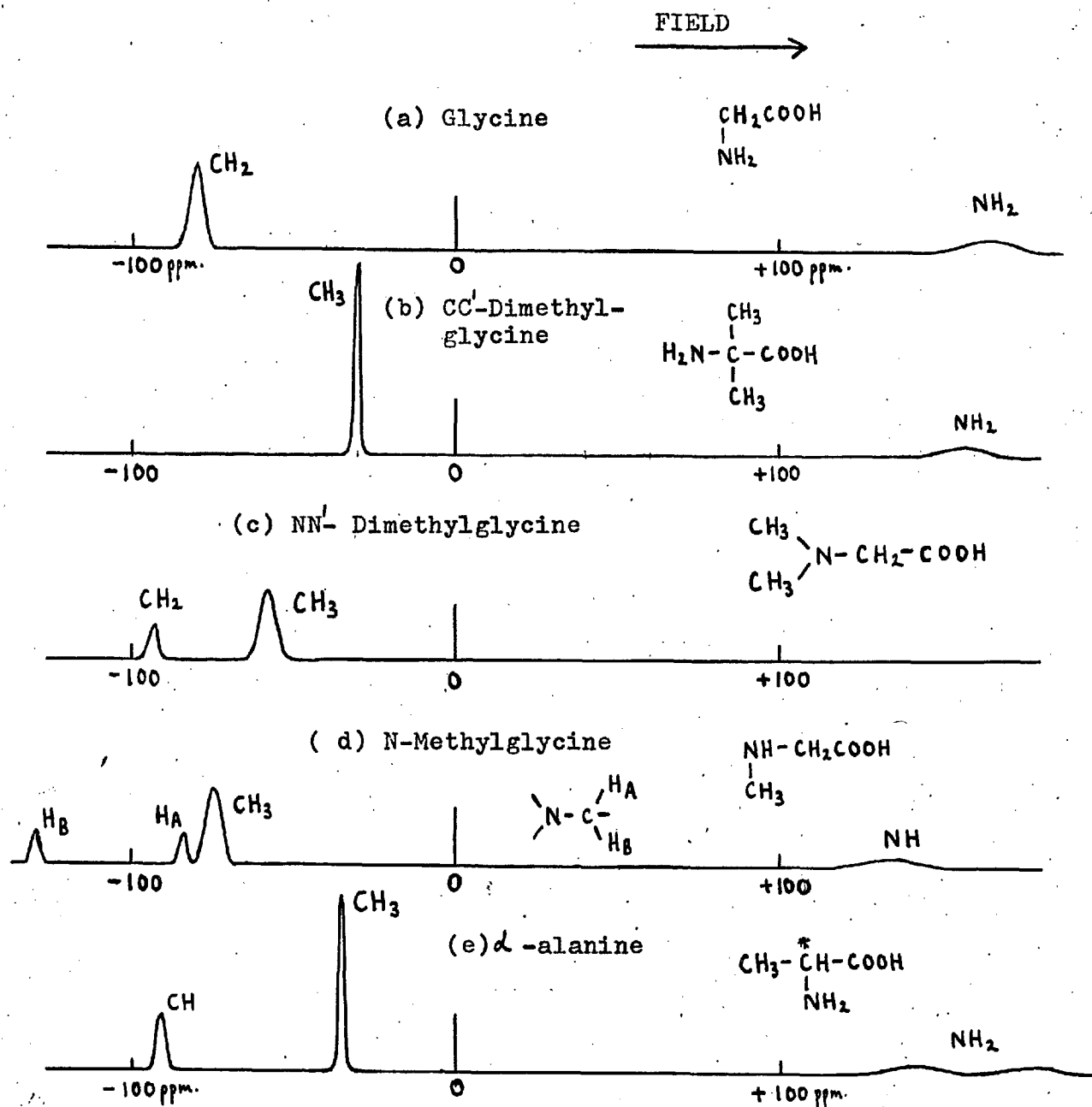


Figure 26. Spectra of 1:1 complexes of Co(II) with bidentate ligands. Contact shifts are in p.p.m. relative to t-butanol.

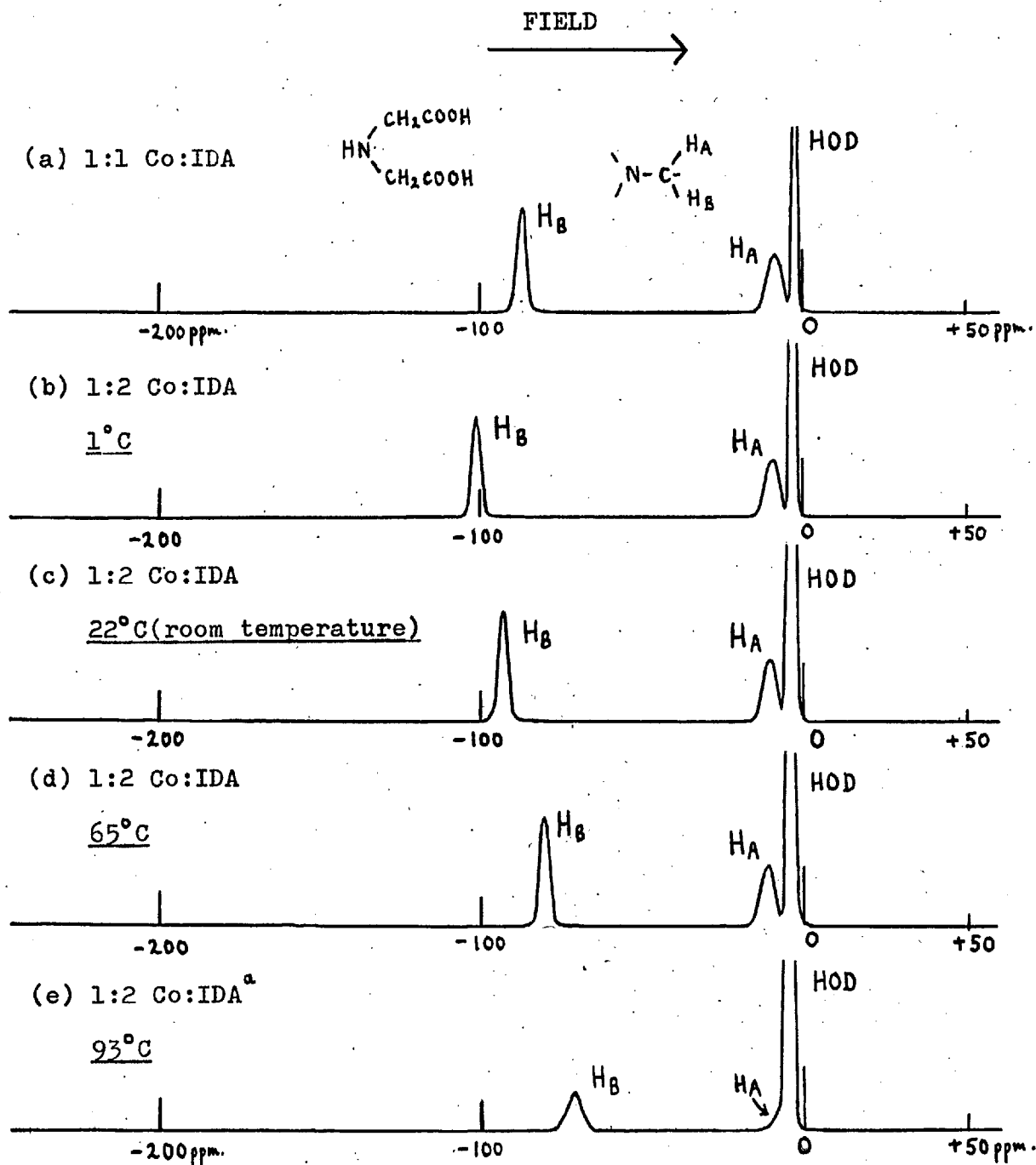


Figure 27. CH Spectra of Co(II) complexes of IDA at various temperatures. Contact shifts are in p.p.m. on the low field side of t-butanol.^a Small amount of solid precipitated during measurement.

the greater lability of the Co(II) complexes compared with the Ni(II) ones. When the temperature of the 1:2 complex is altered, the CH lines shift as illustrated in Figure 27b-e. Both contact and pseudocontact shifts should be inversely proportional to the absolute temperature, and this behaviour is observed, showing that if chemical equilibria (e.g. between isomers) are present, then either their position of equilibrium does not change much over the temperature range 274 - 366°A, or the isomer lines are close together. Alteration of temperature could also affect line positions and shapes by altering the rates of the various exchange processes which may be present sufficiently to bring them into the same order of magnitude as frequency separations. In this case, no significant narrowing or broadening of the lines was observed.

MIDA. The assignments of the 1:1 complex were made by comparing its spectrum (Figure 28a) with that of the N-methyl glycine complex, and from the line intensities. At pH 8, the 1:1 sample shows the three additional small broad lines of the 1:2 complex are also present (Figure 28b), showing that, at room temperature, ligand exchange between the complexes is slow relative to the frequency separations.

The spectrum of the 1:2 complex alone, at room temperature, is assigned similarly as shown (Figure 28c). The broadness of the three lines probably results from exchange processes; this idea is supported by measuring the spectrum at different temperatures. As the temperature is decreased the exchange processes would slow down,

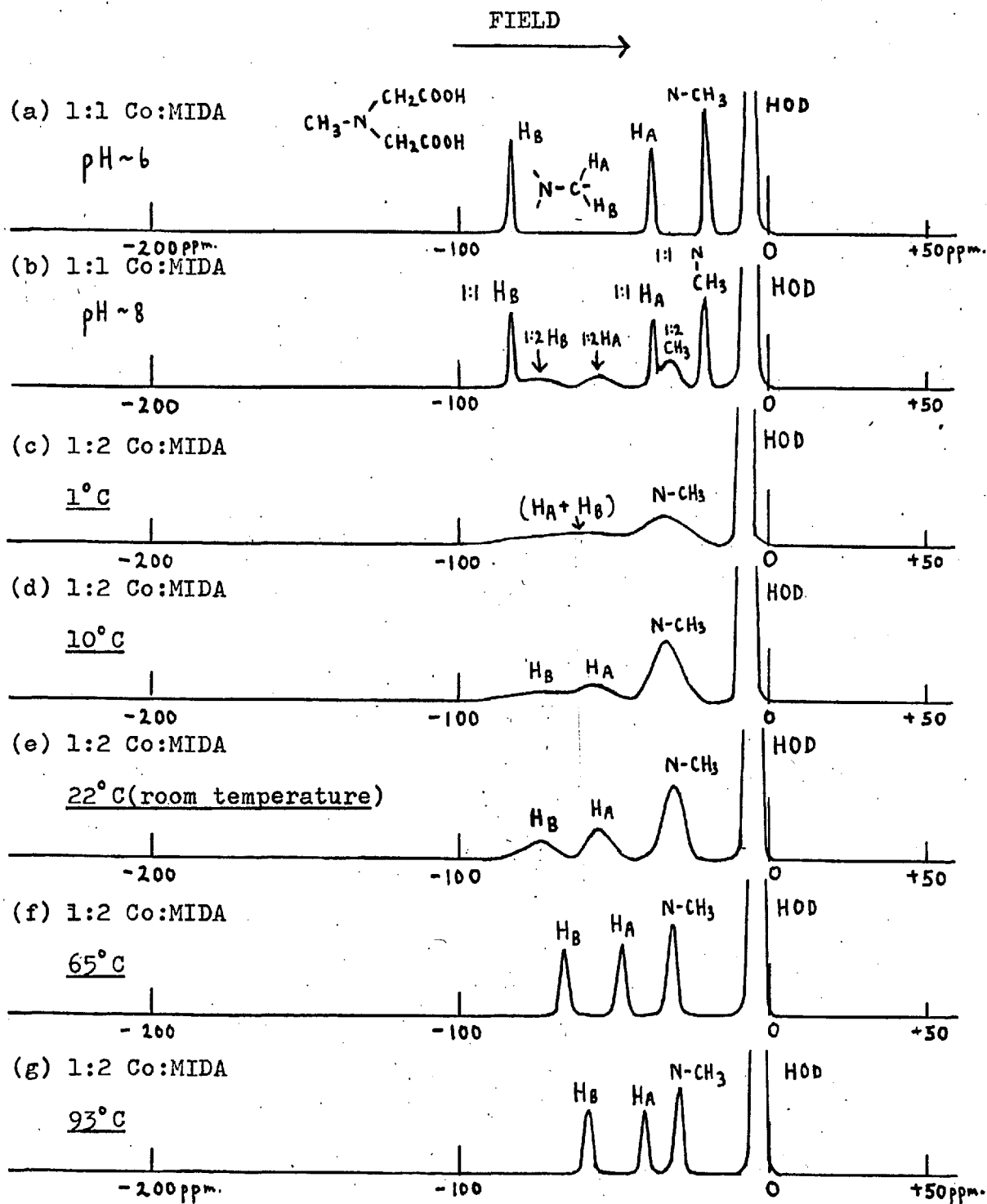


Figure 28. Spectra of Co(II) complexes of MIDA at various temperatures. Contact shifts are in p.p.m. on the low field side of t-butanol.

and all three lines become much broader and overlap more. At higher temperatures, where the exchange would be faster, the three lines are considerably sharper. The changes are not due to exchange with free ligand, which would make the lines broaden with increasing temperature. The decrease in shifts with increasing temperature is approximately that expected from their dependence on $1/T$ abs. Possibly one of the exchange processes involved is the interconversion among cis and trans isomers. It was not possible (due to freezing) to cool the solutions sufficiently to make the interconversion slow enough to allow separate lines to be seen, when it should have been possible to estimate the relative amounts of the isomers and perhaps to identify the separate species. Separate sets of lines are observed in the corresponding 1:2 solutions with Ni(II), presumably because the complexes are less labile.

EIDA. In the spectrum of the 1:1 solution at pH 6 (Figure 29a), the lines at -32 p.p.m. and -80.5 p.p.m. are assigned to the AB pairs in the two five membered rings. The high field lines at +28 p.p.m. and +39.5 p.p.m. are assigned as the N - CH₂ and -CH₃ groups respectively. The HOD line position (-300 cycles/sec. in 1:1 solutions at pH 6 - 8) indicates that three molecules of H₂O are bound to each Co(II) ion. Small amounts of three other lines are attributed to the 1:2 complex, since they disappear when more Co(II) is added, and increase in intensity as the pH is raised. The spectra of the 1:2 solutions (Figure 29b) confirm this; at pH 7 - 8, the presence of only a very small amount of free ligand

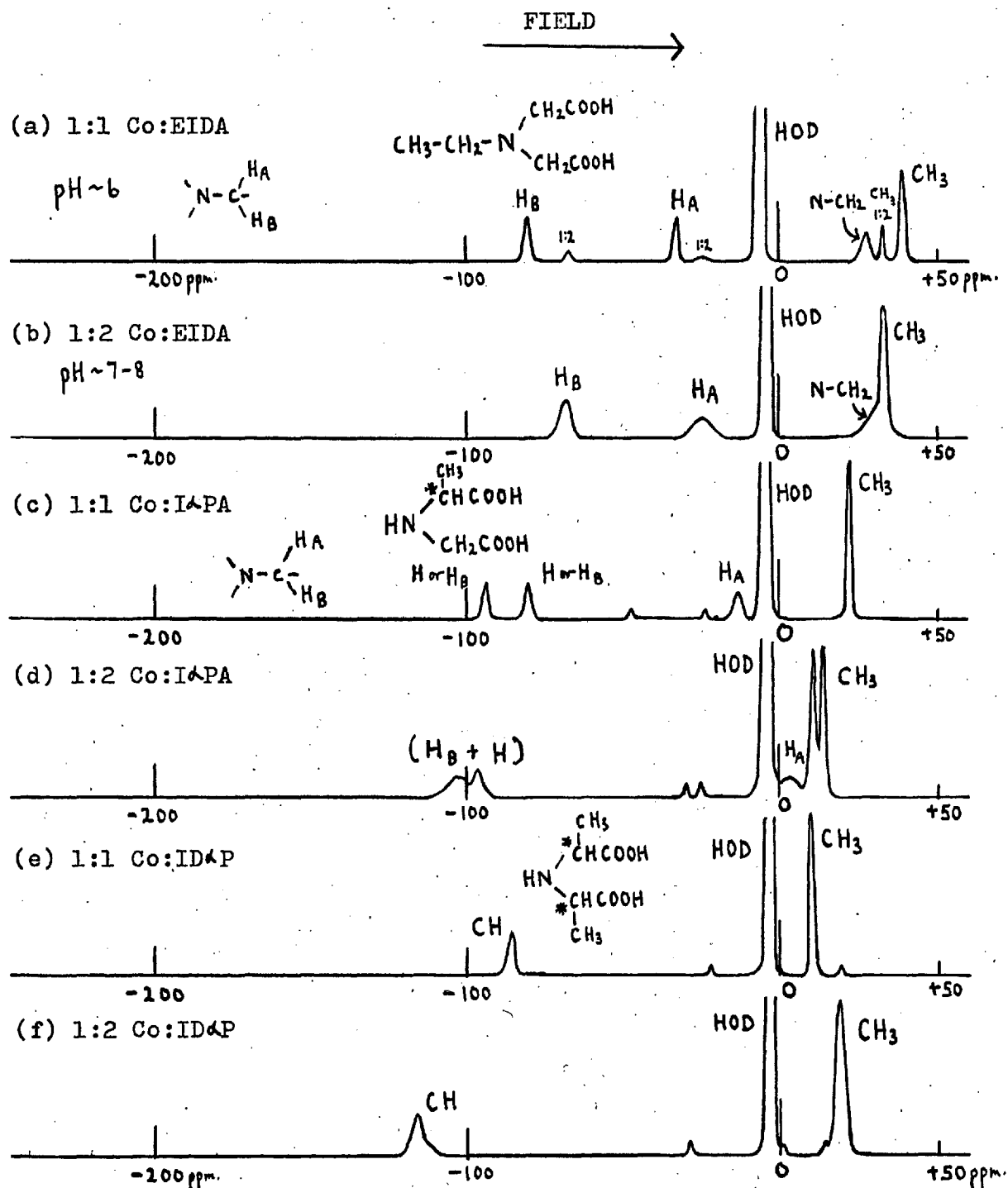


Figure 29. CH Spectra of Co(II) complexes of EIDA, IAPA and IDAP. Contact shifts are in p.p.m. relative to *t*-butanol.

and the position of the HOD line (which corresponds approximately to that of Co(II)-free H_2O , ~ -200 cycles/sec.) show that all the Co(II) sites are occupied by ligand. The assignments are made as before; the high field line clearly consists of two overlapping lines. The broadness of the lines probably results from exchange processes, possibly involving isomers, as suggested for the MIDA complex. The $N - CH_2CH_3$ protons lie at considerably higher field than the $N - CH_3$ in the MIDA complex, and both groups are higher than they are in the corresponding Ni(II) complexes. There is probably a pseudocontact contribution in the Co(II) complexes - this is discussed later.

IAPA. The spectrum of the 1:1 complex (Figure 29c) is similar to that of the Ni(II) complex, although the CH_3 line lies on the high field side of water. The assignment of CH lines is not certain; possibly the line with the small shift is one of the CH_2 pair, as suggested for Ni(II). As with Ni(II), there is no indication of the presence of the several possible isomers. Some additional weak lines are observed, probably from the small amount of impurity present in the ligand. As the pH of the 1:1 solution is increased, four new lines appear due to a small amount of the 1:2 complex.

The spectrum of the 1:2 complex (Figure 29d) contains two relatively sharp CH_3 lines of approximately equal intensities; the other lines are broad, but measurement of the spectrum at 100 mcs./sec. did just resolve the lowest of the three lines into

two, again of roughly equal intensities, and it is possible that the others are unresolved double lines. The doubling of lines is presumably due to the presence of isomers, or to non-equivalent rings in either one major isomer, or group of isomers (possibly DD, DL) in equilibrium. Many isomers are possible; observed doublings may represent differences between a set of DL isomers and a set of [(DD) + (LL)] isomers.

IDoP. The ligand is probably a mixture of meso and active (DD + LL) forms and, as mentioned for Ni(II), could give rise to several isomeric 1:1 complexes of both cis and trans types. The 1:1 spectrum (Figure 29e) shows only two fairly sharp lines for the CH and CH₃ protons; nothing can be deduced about the isomers. Small additional lines are probably due to impurities in the ligand.

In the 1:2 complex (Figure 29f), there is a doubling of the CH line; the broad CH₃ line may be doubled but could not be resolved. Many isomers are possible, but it is not possible to conclude which ones are present. It is worth noting that the corresponding Ni(II) 1:1 and 1:2 complexes gave only one CH line.

Tetradentate ligands which can form three five membered chelate rings. NTA. The spectra are similar to those discussed for Ni(II). The single line observed (Figure 30b) for the 1:1 complex can be attributed to averaging by bond migration following lability of the Co - O bonds. The spectrum of the 1:1 complex was measured at three other temperatures in the range 0 - 100°C (roughly the limits for aqueous solutions). With increasing temperature, the shift of the line decreases as expected; it also becomes broader. Possibly

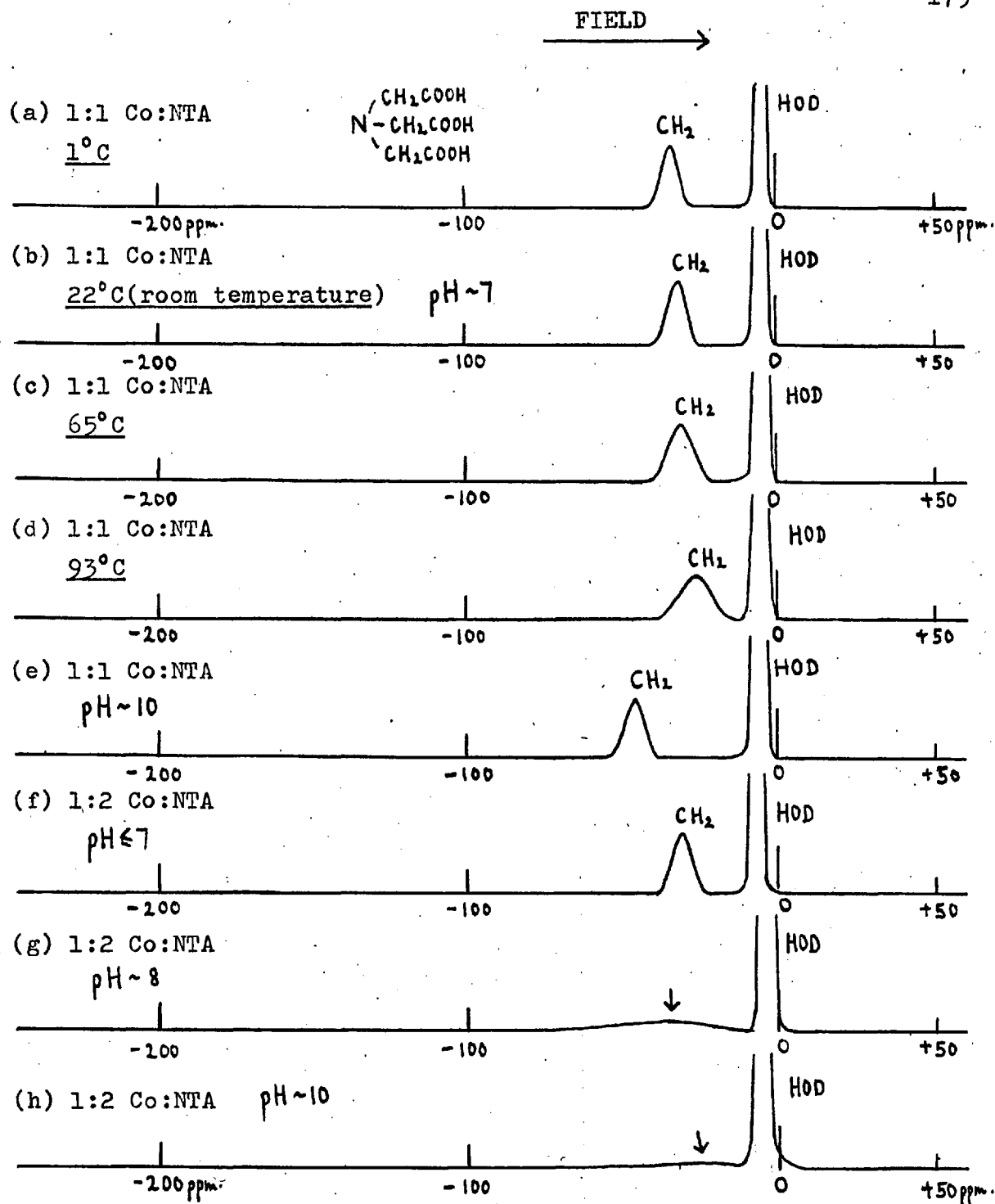


Figure 30. Spectra of Co(II) complexes of NTA at various temperatures. Contact shifts are in p.p.m. relative to t-butanol.

this is due to the increasing rate of overall ligand exchange. The large increase in shift observed for the 1:1 complex in the pH range 8 - 10, and the accompanying colour change from red to deep purple-blue, may represent the formation of a hydroxy complex.

In the 1:2 solutions (Figure 30f-h), the line is slightly broader than in the 1:1 at pH 7, but becomes very broad as the pH is increased to 8, and the solution has a purple-blue colour again. Presumably a 1:2 complex is formed, with two nitrogen atoms bonded, and the broadness is due to exchange between the isomers of the 1:2 complex as the $-\text{CH}_2\text{COO}^-$ groups move between free and bound positions. Exchange with free ligand may also occur, but the position of the line does not appear to move inwards appreciably before it becomes broad.

NCPDA. The spectrum of the 1:1 complex in the pH range 6 - 8 (Figure 31a) shows a line from each CH proton and one sharp, intense CH_3 line, similar to the Ni(II) complex. The non-equivalences arise from the asymmetric surroundings in which each $-\text{CH}_2\text{COO}$ group is placed, whether or not there is bond migration, although this is likely. At higher pH (8 to 10), the blue colour and broader lines suggest the formation of a different complex, probably a hydroxy complex.

The 1:2 solutions below pH 7 show a spectrum identical to that of the 1:1 complex, and the fact that the lines are relatively sharp and that the excess free ligand present also has sharp lines, shows that overall ligand exchange is slow. As the pH is increased,

all the lines broaden and move inwards, and the free ligand broadens considerably, indicating that, in this case, there is an increasing rate of exchange between the complexed and free ligand, which was not certain for the NTA complex. At pH ~ 9 , although no precipitation occurred, no lines are visible except possibly a very broad band hidden by the HOD line.

NTxP. The spectra of the 1:1 and 1:2 solutions (Figure 3ld and e) are complicated by the presence of small amounts of impurities. However, the main lines can be assigned to CH₃ and CH protons in the NTxP. There are several lines of each type, showing that isomers are certainly present, but it is not possible to conclude which ones or to estimate their relative amounts.

The spectra of the 1:2 solutions at pH ≥ 8 contain relatively sharp lines, in contrast to the severe exchange broadening observed with NTA and N α PDA; possibly with this ligand, in whose 1:1 complexes there is expected to be considerable steric hindrance, it is more favourable for it to be tridentate, in which case the tetradentate/bidentate isomer is absent.

ND α PA contained larger amounts of impurity and the spectra of 1:1 and 1:2 solutions showed many lines. The only conclusion that could be reached was that several isomers of complexes of the main ligand appeared to be present, as would be expected.

For complexes such as these, and those of the asymmetric IDA derivatives, which appear to exist in various optical isomeric

forms, a complete study is only possible if the highly pure ligands are available, and preferably if measurements could be made at 100 mcs./sec. or even higher frequencies, to separate lines which are close together. Unfortunately, the small amounts of impurity in some of the present ligands were difficult to remove; also some of the lines were probably obscured by the HOD resonance.

Ligands which form only six membered rings. β -alanine forms a weaker complex with Co(II) than it does with Ni(II)— ($\log \beta_2 = 7$, and $\log K_1 = 4.63$, $\log K_2 = 3.40$, $\log \beta_2 = 8.03$ respectively).¹²⁸ The spectrum of the 1:1 complex (Figure 32a) shows two very weak lines at about -21.5 p.p.m. and -155.5 p.p.m., which are assigned as the CH_2COO and $\text{N} - \text{CH}_2$ groups respectively, in the same way as the corresponding Ni(II) complex; in contrast to the Ni(II) complex, the CH_2COO line is on the low field side of water. The remarks about lability made for the Ni(II) complex apply equally to the Co(II) one. Increasing the concentration of the ligand appeared to have little effect on the appearance of the spectrum, apart from a possible slight broadening; there may be rapid exchange involving 1:1, 1:2 and possibly 1:3 complexes .

IDSP. The spectrum of the 1:1 complex (Figure 32b) shows four lines, as was observed for the corresponding Ni(II) complex; however, in contrast to the Ni(II) complex, the intensities do not appear to be equal. It may be that isomers are present, though the appearance of separate lines from them would not be expected in view of the lability of the Co - O bonds.

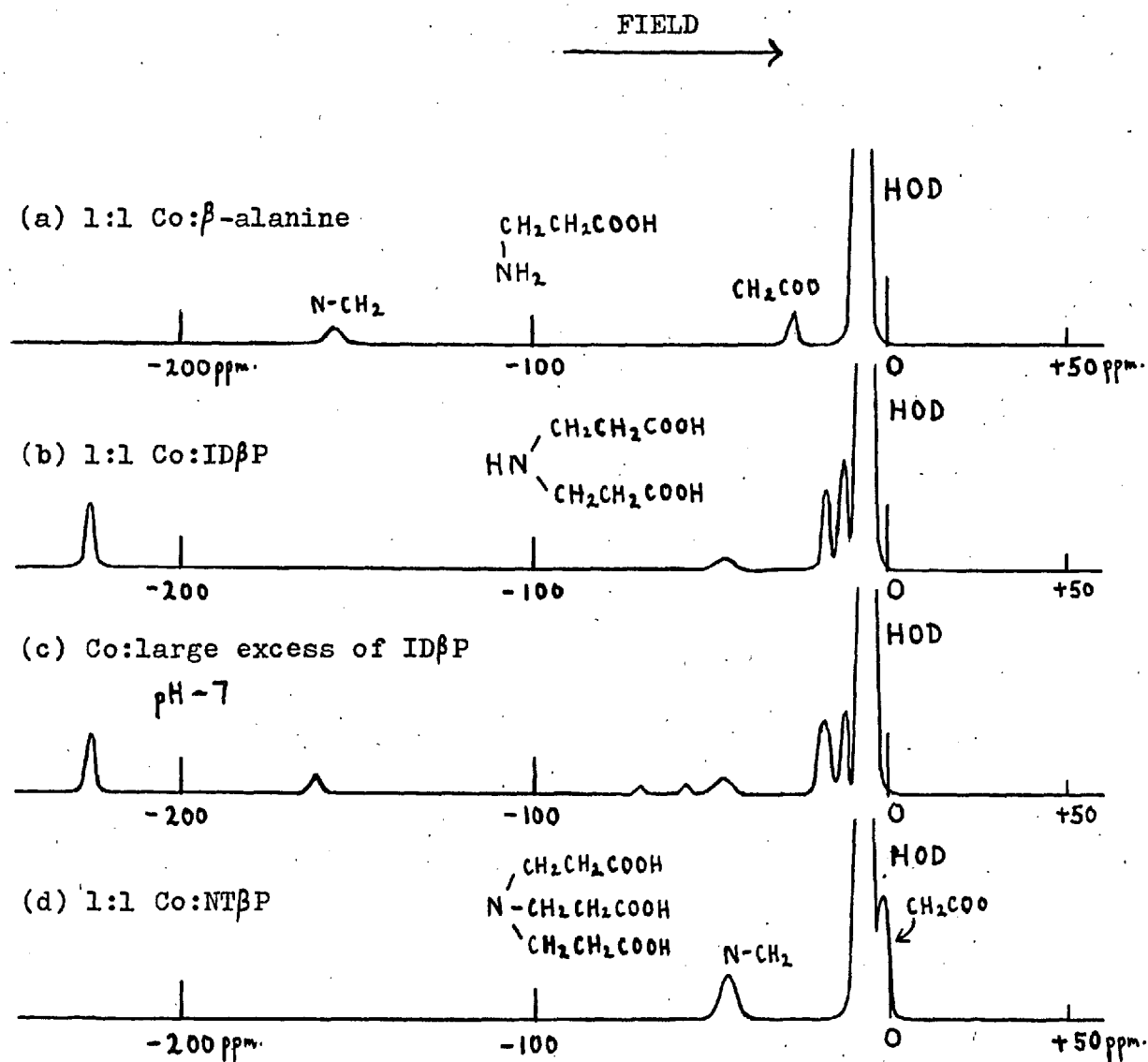


Figure 32. CH Spectra of Co(II) complexes of β-alanine, IDβP and NTβP. Contact shifts are in p.p.m. relative to t-butanol.

The spectrum of the 1:2 solution at pH 7 was identical to that of the 1:1 complex. However, as the ligand concentration was further increased (at pH $\sim$ 7), some additional small lines appeared, and the intensities of the original four lines altered slightly; with a large excess of ligand, one of the new lines became moderately strong (Figure 32c). Possibly isomers are present, but with such a large excess of ligand, the small lines may be due to impurities.

NTBP. The 1:1 complex gives a spectrum consisting of two broad lines (Figure 32d), assigned as indicated. The complex is fairly weak ($\log K_1 = 4.8$),¹²⁸ being no more stable than that with IDBP ($\log K_1 = 4.92$),¹²⁸ probably due to strong steric interference between the three $\text{CH}_2\text{CH}_2\text{COO}^-$ groups, if all bonded to the metal. It is possible that one of them is mainly free; exchange between this and the others could account for the broadness of the lines, and could also explain the fairly small values of the shifts.

Ligands which can form one five and one six membered chelate rings. IGPA. The spectrum of the 1:1 complex (Figure 33a) shows six relatively sharp lines of approximately equal intensities, suggesting that all six protons are non-equivalent, similar to the five non-equivalences found for the Ni(II) complex. Possible assignments are shown in the Figure. When the pH of a 1:2 solution is increased from 7 to 10, a new set of six lines develops, which must represent the 1:2 complex. At pH $\approx$ 10, the width of the lines (three of them are very broad) and their displacement towards

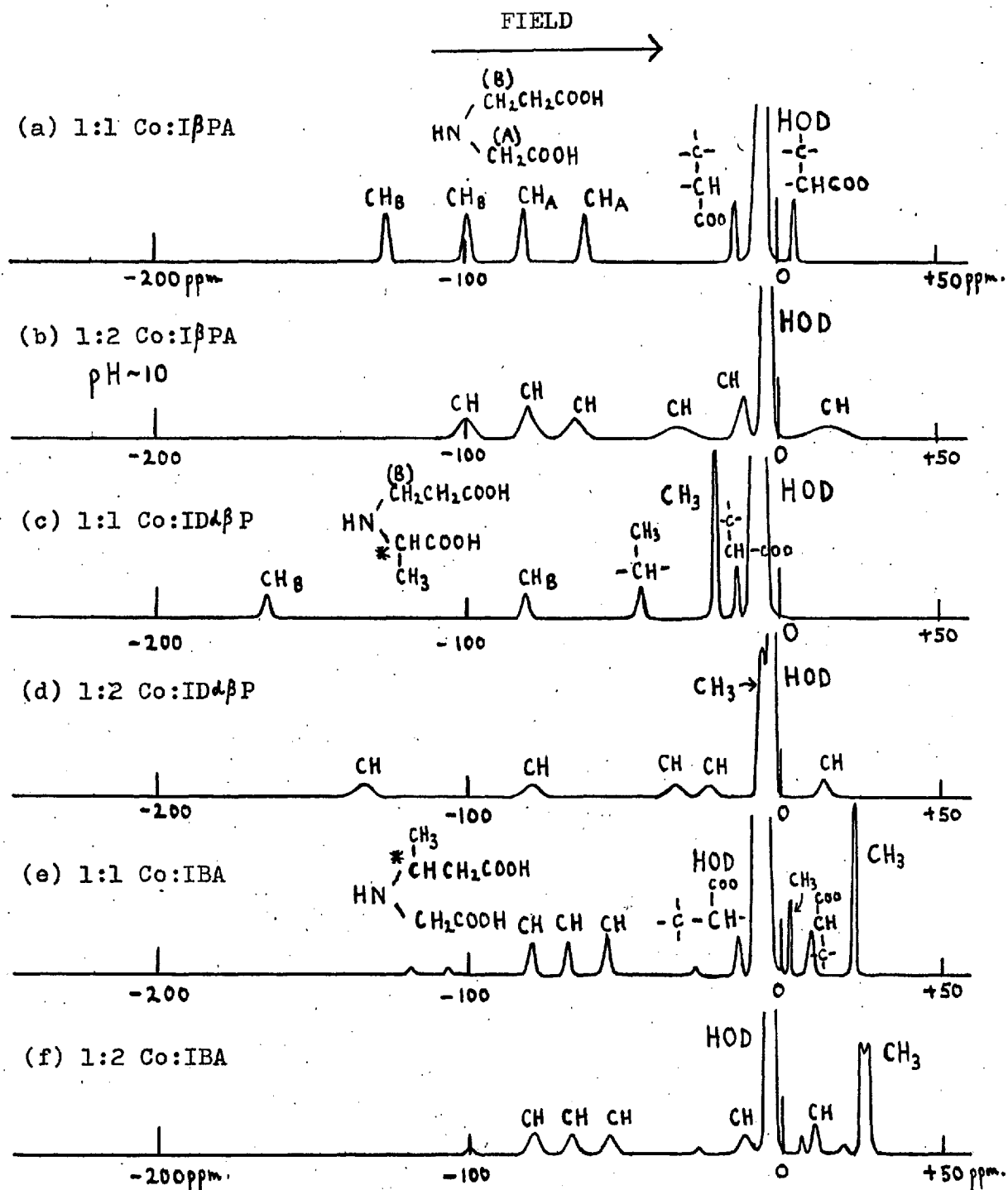


Figure 33. CH Spectra of Co(II) complexes of I β PA, ID $\alpha\beta$ P and IBA. Contact shifts are in p.p.m. relative to t-butanol. In (e), the signal/noise ratio is reduced for the high field CH_3 .

t-butanol, suggests that overall ligand exchange is becoming faster. The HOD line position indicates that no H_2O molecules are bound to the Co(II) ,

ID~~ox~~SP. In the 1:1 complex (Figure 33c), four small lines (of equal intensities) and one CH_3 line are observed; probably the five CH protons are non-equivalent, with the missing line obscured by the HOD or free ligand resonances; it could not be detected even when the spectrum was recorded at 100 mcs/sec..

The spectrum of the 1:2 complex (Figure 33d) does contain five lines, corresponding to all the non-equivalent CH protons; the CH_3 line is partly obscured by the HOD line. All the lines are fairly broad; this may indicate the presence of isomers, since several are possible, but doubling of the lines was not found. The broadening could also result from ligand exchange.

IBA. The spectrum of the 1:1 complex contains seven main lines and some additional very small lines (Figure 33e), whose intensities differ somewhat. All the five CH protons are presumably non-equivalent, as suggested in the two preceding cases; if only one species is present, six lines (one for the CH_3) would be expected. The ligand appears to be pure (analysis and n.m.r. spectrum); possibly cis and trans type isomers are present, the two relatively sharp high field lines (at +3.5 p.p.m and +23.5 p.p.m.) perhaps representing CH_3 groups in two isomers.

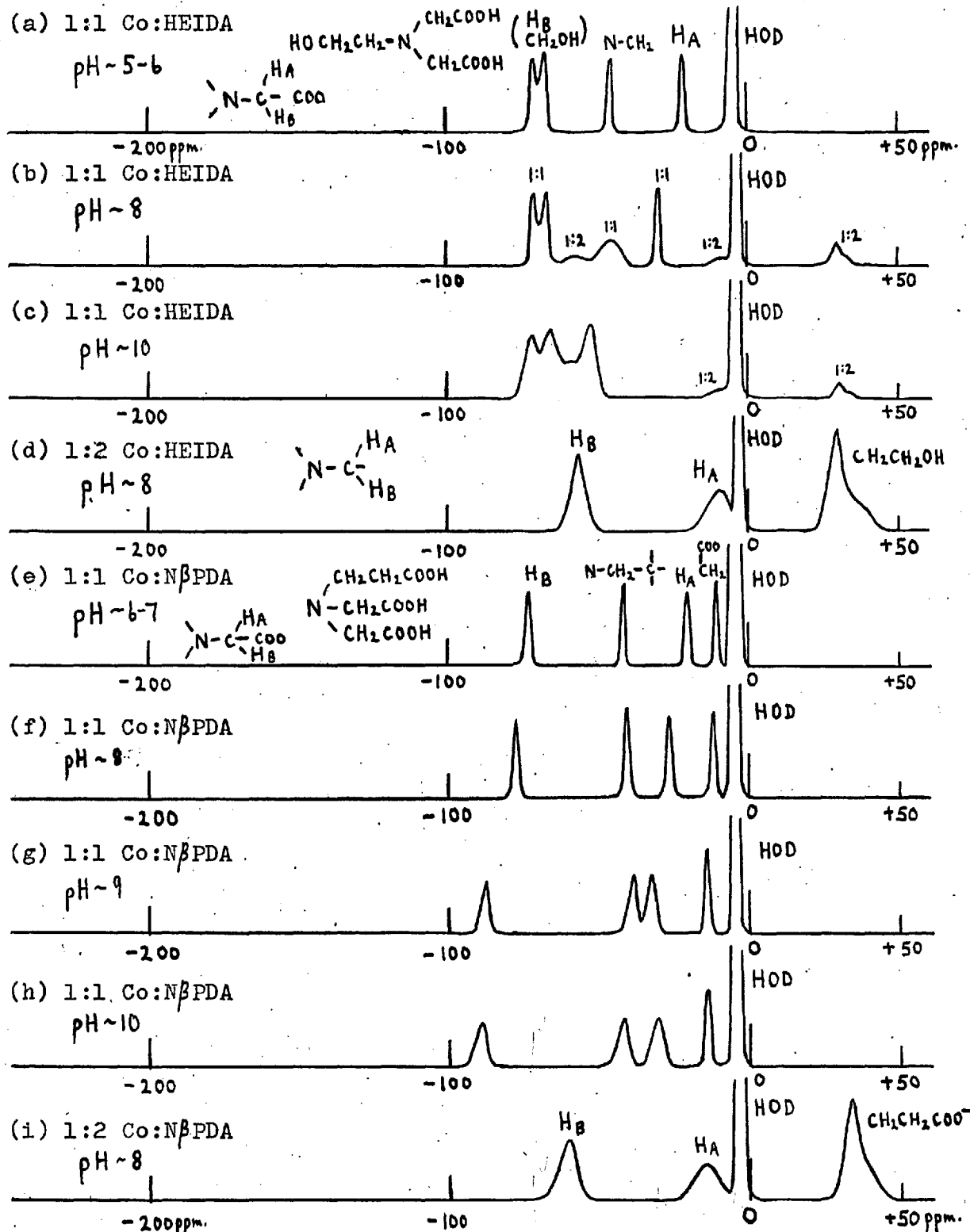
In the 1:2 solution at pH 8, six main lines and some other very weak lines appear to be present, all of them broadened due to

exchange and/or overlapping. The intense CH_3 line is doubled, suggesting differences between isomers, possibly of the types DD ($\equiv$ LL) and DL ($\equiv$ LD). The HOD line position indicates that all the Co(II) sites are occupied by ligand atoms.

The spectra of both the Co(II) and Ni(II) 1:1 complexes of the above three ligands show separate lines for all the CH protons, and a doubling of the CH_3 lines in the 1:2 complexes.

Ligands which can form two five and one six membered chelate rings HEIDA. The Co(II) complexes behave as do the Ni(II) ones. It is convenient to consider the 1:2 complex first. Its spectrum (Figure 34d) is very similar to that of the 1:2 complex with EIDA, suggesting that, as might be expected, the $-\text{CH}_2\text{CH}_2\text{OH}$ groups are free, and not coordinated through the hydroxyl. These two CH_2 groups are assigned to the overlapping lines at high field, and the low field lines represent the CH_2 pairs in the (equivalent) five membered rings. The spectrum is unchanged at $\text{pH} \sim 10$; there is no coordinated H_2O to ionise, although, even if it did, the effect on the spectrum would be small.

In the 1:1 solution at $\text{pH} 5 - 6$, the spectrum (Figure 34a) is that of the 1:1 complex, which differs markedly from that of the 1:1 EIDA in having no high field lines. There are four lines (of equal intensities), two of which (probably at -20 p.p.m., and one of the pair at about -70 p.p.m.) must arise from the CH_2 pairs in the five membered IDA rings. The other two at -43 p.p.m. and about -70 p.p.m. are assigned to the N - CH_2 and O - CH_2 protons of



Contact shifts are in p.p.m. relative to t-butanol.

the $\text{N-CH}_2\text{.CH}_2\text{.OH}$ group respectively. Their low field shift suggests that the OH group is coordinated, as suggested previously.¹³⁰ Other evidence that the ligand is coordinated at four Co(II) sites is provided by the HOD line position (-260 ± 2 cycles/sec.), whose downfield shift of 60 cycles/sec. is approximately one third of the value found for a solution of $\text{Co(H}_2\text{O)}_6^{2+}$ at the same concentration. The OH proton is not seen separately since it will exchange rapidly with H_2O ; the averaged H_2O line position will be affected by the OH shift, but not to a large extent.

As the pH is increased to about 10, lines from the 1:2 complex (Figure 34c) appear and grow more intense, but, in addition, the lines from the 1:1 complex become broader and alter their positions; also, the colour of the solution changes from red to a very deep red-blue. As was suggested previously for the corresponding Ni(II) complex, this behaviour is probably associated with ionisation of another proton from the complex, which is shown by the pH titration (giving a pK of 9.8 for the process).¹⁴⁴ The ionisation could represent loss of the hydroxyl proton (giving a more strongly coordinated but nevertheless labile five membered $\text{CH}_2\text{CH}_2\text{O}^-$ ring), or of one of the protons on a complexed H_2O molecule, or both. The resulting complex could be tetrahedral, as suggested by the intense blue colour of the solution, which is expected for tetrahedral Co(II) complexes. The HOD line position (-185 cycles/sec. at $\text{pH} \sim 10$) is also higher than the value for completely coordinated, octahedral Co(II) in H_2O ; this could indicate tetrahedral Co(II) if it gives an upfield contact shift.

NBPDA. This behaves similarly to the previous ligand. The 1:2 spectrum (Figure 34i) is almost the same, and again resembles that of the 1:2 Co(II): EIDA. It is very likely that the $-\text{CH}_2\text{CH}_2\text{COO}^-$ group is free, and the assignments are the same as for the 1:2 HEIDA complex.

In the 1:1 solution at $\text{pH} \sim 6 - 7$, the ligand is probably tetradentate, with the propionic carboxyl (which must be ionised at this pH) coordinated also, at least for part of the time, since all the lines lie on the low field side and the HOD position is that expected for only two coordinated H_2O molecules. Two of the four lines come from the CH_2 pairs in the five membered rings, and two from the different CH_2 groups in the $-\text{CH}_2\text{CH}_2\text{COO}^-$ unit; a possible assignment is shown. As with HEIDA, increasing the pH of the 1:1 solution gives changes in the line widths and positions, the colour of the solution becomes an intense red-blue, and the HOD line position is unusually high. It is again possible that a hydroxy complex (which may be tetrahedral) is formed; in this case, it must only result from loss of a proton from coordinated H_2O .

A ligand which can form one five and two six membered chelate rings. ND/PA. The spectrum of the 1:1 complex (Figure 35a) at $\text{pH} \leq 8$ shows five equally intense lines. If the two propionic groups are identical, only one line is expected from the five membered ring CH_2 protons, and the other four must represent non-equivalent protons in each CH_2 group of a six membered ring. The carboxyl groups must all be ionised at $\text{pH} \sim 6$; yet as the pH

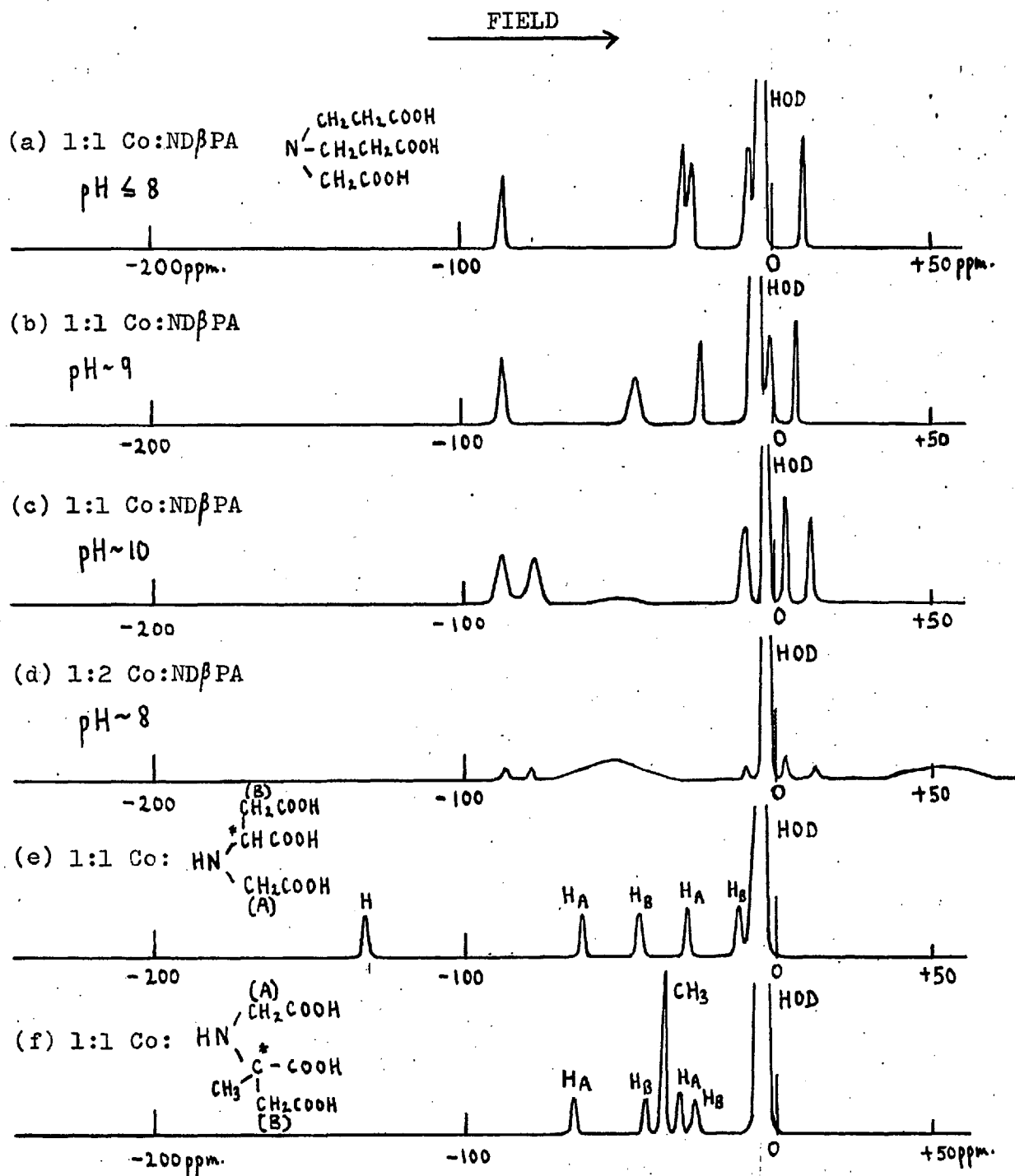
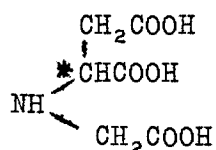


Figure 35. CH Spectra of Co(II) complexes of ND β PA, fumaric-glycine and mesaconic-glycine reaction mixtures. Contact shifts are in p.p.m. relative to t-butanol.

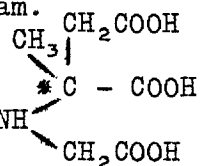
is increased above ~ 8 , the lines become broader and their positions alter as shown (Figure 35b and c). The solution colour is a deep red-blue; presumably a hydroxy complex is formed, which may be tetrahedral.

The 1:2 complex appears to show only two broad lines (Figure 35d) possibly as a result of exchange of groups between chelate and "one ended" states. The line at high field must represent the "open ended" group(s).

The addition products of glycine with fumaric and mesaconic acids. Figure 35e shows the spectrum of the 1:1 complex formed by the addition product of glycine and fumaric acid, which is



The two five membered rings would be expected to give separate lines for the three CH protons, and it would also be expected that the other CH_2 protons should be non-equivalent because they are attached to an asymmetric carbon atom. The six membered ring in this case would be expected to be more rigid than an $\text{N} - \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COO}$ ring, because it is fused to a five membered chelate ring. Four equally intense lines are observed and, in some measurements, a fifth line at about -12.7 p.p.m. seems to be evident on the side of the HOD line; thus each proton gives a separate line. A tentative assignment is shown on the diagram.



The other addition product has the formula $\text{NH} \text{---} * \text{CHCOOH}$, and the spectrum of its 1:1 complex is shown in Figure 35f. Again each

CH proton gives one line and the CH_3 gives another. A tentative assignment is shown.

Both addition products, in H_2O solution, show a broad line in the high field region +200 p.p.m. to +350 p.p.m., which shows that they contain coordinated imino NH groups.

Complexes with mixed ligands. Complexes of this type are quite important since they are sometimes invoked as intermediates in catalytic processes. Since contact shifts are large, they might be used to study their formation.

In a solution containing equal amounts of Co(II) , IDA and MIDA, in the proportions 1:1:1, statistically the following situation would be expected.

Complex:	Co(IDA)_2^{2-}	$\text{Co(IDA)(MIDA)}^{2-}$	Co(MIDA)_2^{2-}
Percentage:	25%	50%	25%

Figure 36 illustrates the spectrum of the 1:1:1 mixture at different temperatures. Lines corresponding to the 1:2 complexes of IDA and MIDA can be assigned as indicated, and the three additional low field lines clearly visible can be attributed to the mixed complex; the presence of a third high field NH line also shows that a mixed complex has been formed. Since the broadness and overlapping of the lines does not allow a reliable estimate of the relative amounts of the three complexes to be made, measurements were made at various temperatures to find the conditions giving the sharpest lines. Although sharper lines were obtained at higher

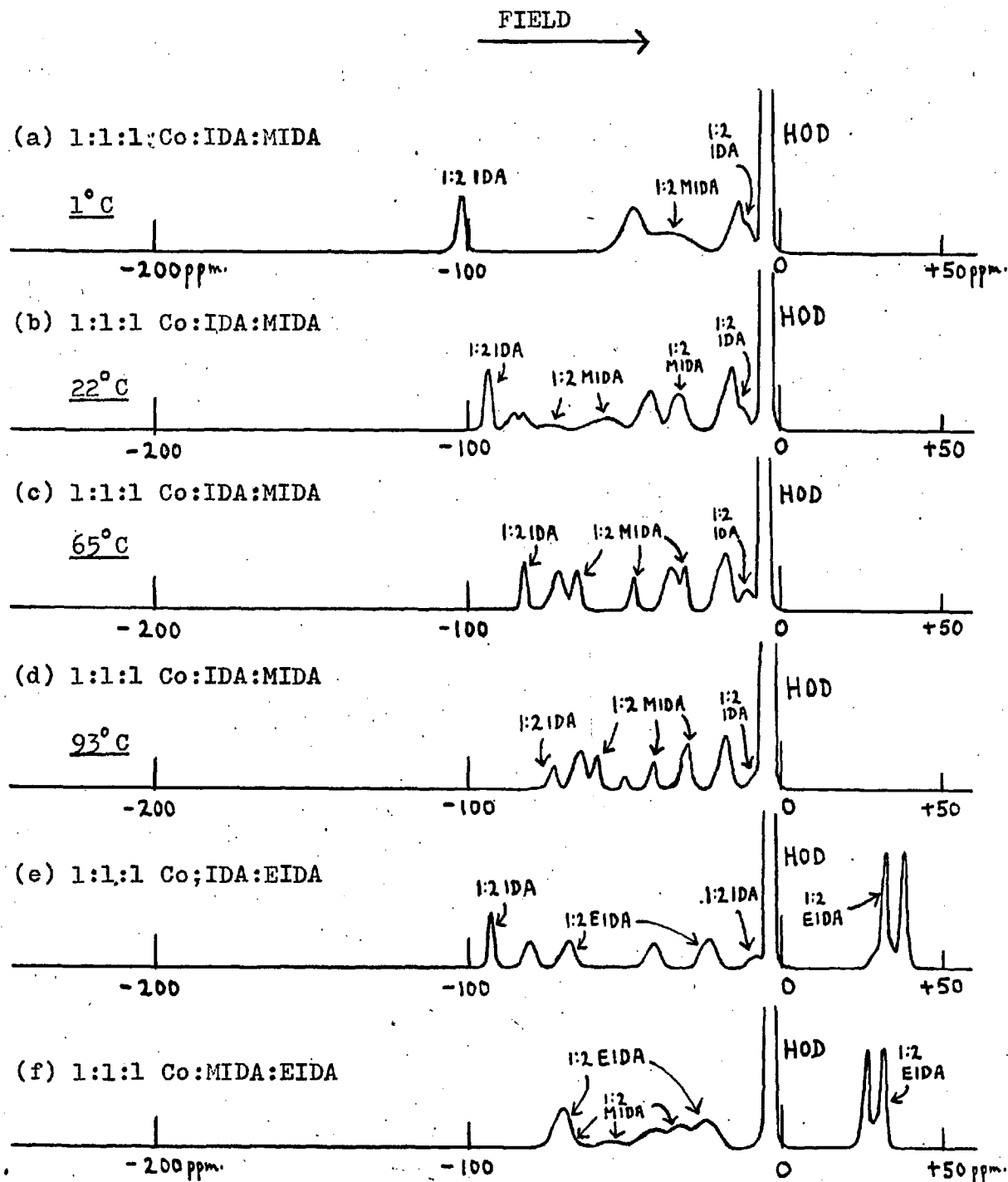


Figure 36. CH Spectra of "mixed" complexes of Co(II) with IDA, MIDA and EIDA. Contact shifts are in p.p.m. relative to t-butanol.

temperatures, overlapping still occurs and no reliable estimate of the species present is possible. However, there does appear to be more of the mixed complex present than of the 1:2 IDA and MIDA.

In the case of a solution containing Co(II), IDA and EIDA (1:1:1), the spectrum (Figure 36e) shows the presence of Co(IDA)_2 , Co(EIDA)_2 (as indicated) and some other lines, which are ascribed to Co(IDA)(EIDA) . It is possible that some other lines may be overlapping. Consideration of the relatively sharp high field lines is more helpful. The line at +32 p.p.m. represents the $\text{N} - \text{CH}_2 - \text{CH}_3$ group in the complex Co(EIDA)_2 , while the line at +38 p.p.m. is assigned as the $\text{N} - \text{CH}_2 - \text{CH}_3$ group in the mixed complex Co(IDA)(EIDA) . The fact that they have approximately equal intensities indicates that there is about twice as much mixed complex as Co(EIDA)_2 present. The low field lines also indicate that approximately equal amounts of Co(IDA)_2 and Co(EIDA)_2 are present. Thus, probably the statistically expected distribution of complexes is present.

Similar measurements on a solution containing 1:1:1 ratios of Co(II), MIDA and EIDA, suggest that the statistical distribution is again present; in the low field spectrum (Figure 36f) there is considerable overlapping.

NH Resonances. The NH lines, although sharper than those of the corresponding Ni(II) complexes, are very broad and fairly difficult to measure; they have not been discussed in the assignment of the spectra since their broadness is not very helpful in this

connection. Their positions for some of the spectra are illustrated in Figure 37. They all have large shifts to high field. The values for NH_2 groups in five membered rings (in bidentate ligands) lie in the range from +130 p.p.m. to +180 p.p.m. (Figure 26). No line could be seen for the β -alanine complex, possibly because of its low stability. For imino NH groups in complexes of IDA derivatives, the values are considerably higher (+240 p.p.m. to 310 p.p.m.). In some cases, the values of the 1:2 complexes are lower than those in the 1:1. In some mixtures containing 1:1 and 1:2 complexes, both lines can be seen, but in others, the lines are not resolved. There is some indication that when isomers are possible, as suggested by the low field CH part of the spectrum, the NH lines also show a doubling or extra width.

The remarks about NH proton exchange made for the corresponding Ni(II) complexes apply equally to the Co(II) ones.

C. Interpretation.

The shifts are roughly similar in magnitude and direction to those of the corresponding Ni(II) complexes. The NH lines occur at high field, most of the CH lines are at low field, and the two protons in CH_2 groups in chelate rings are often non-equivalent. In five membered rings, the CH protons cover a wider range, being lower in monochelate glycine derivatives, and higher or lower in IDA derivatives. In six membered chelates, the N - CH protons tend to occur upfield and the CH_2COO downfield relative to the positions

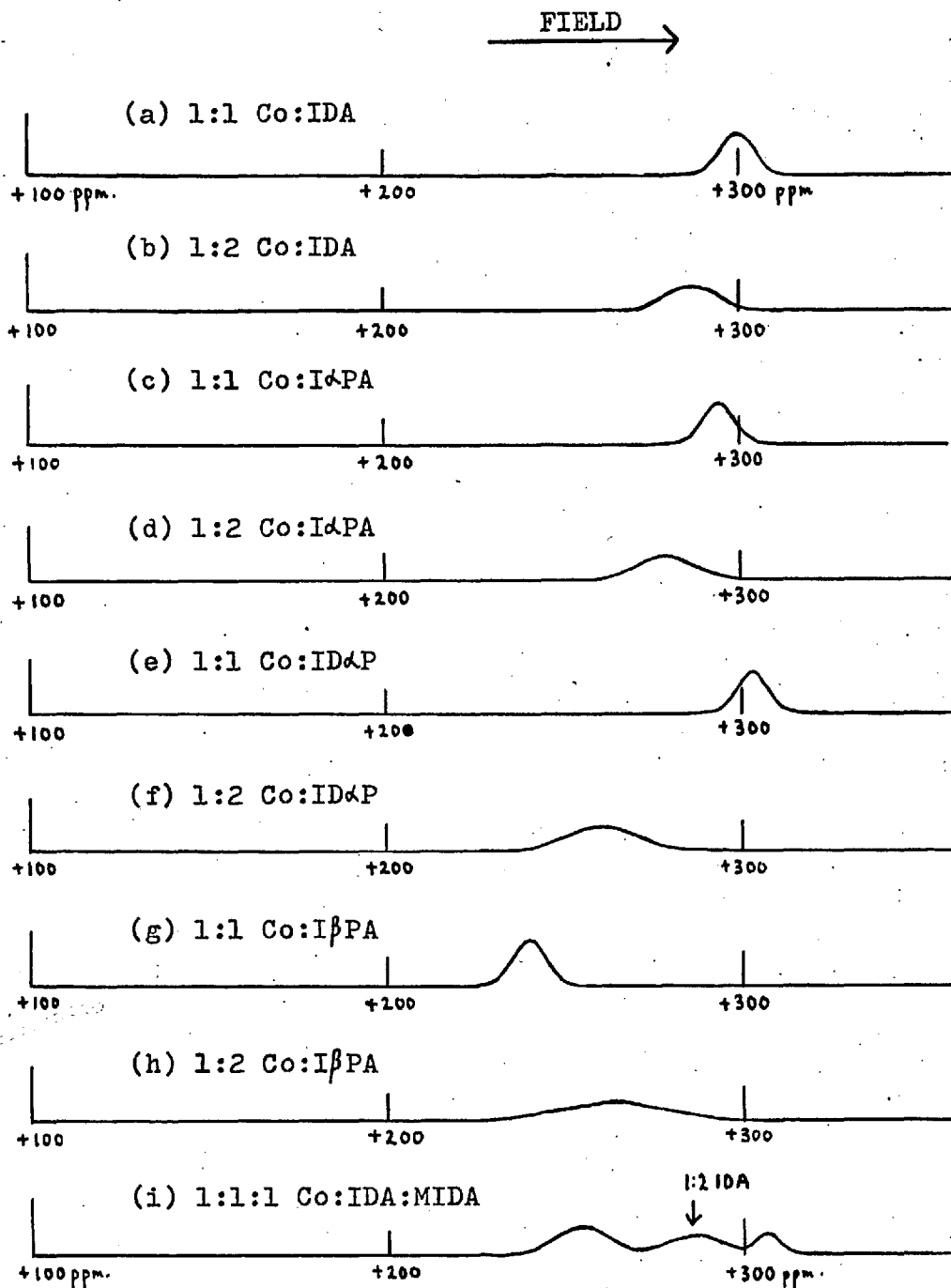


Figure 37. NH Resonances of Co(II) complexes of IDA, IDPA, IDAP, I β PA and a "mixed" IDA:MIDA complex. Contact shifts are in p.p.m. on the high field side of t-butanol.

in the Ni(II) complexes. One marked difference is that N - CH₃ groups occur at higher fields by about 40 - 80 p.p.m., and in NCH₂CH₂X groups (attached to IDA), even the protons in the CH₂X group (when non-bonded) are shifted upfield by about 40 p.p.m..

The similarity of patterns suggests that there is still an important contribution from the contact shift, arising from the transmission of unpaired spin to the protons by the two mechanisms discussed for Ni(II), with the accompanying angular dependence. However, these mechanisms appear to decrease sharply with distance, and would not be expected to produce the relatively large upfield shift of the NCH₂CH₂X protons. This shift can be explained qualitatively in terms of pseudocontact shifts. These have been found to be important in several previous studies of shifts in Co(II) complexes, in particular that by Happe and Ward on pyridine adducts of Co(II) acetylacetonates,¹⁴⁵ in which the cobalt is in an environment similar to that in the present complexes. Following the usual procedure, it is assumed that for Ni(II) and Co(II) complexes of the same ligand, whose structures are assumed to be the same, the shift difference for a remote proton is due entirely to the pseudocontact effect in the Co(II) complex. From this, the g-factor term is calculated, and used to derive the pseudocontact shifts for all the other protons. In the present case, the remote protons are taken to be those in the CH₃ group in the 1:1 complex with N-ethyl IDA. As indicated by space-filling models, it is assumed that steric hindrance makes this group spend most of the

time in the orientation with the C - C bond parallel to the Co - N bond (Figure 38).

The pseudocontact shift is given by the expression,

$$\frac{\Delta H}{H_0} = \left[\frac{-\beta^2 \cdot S(S+1)}{27kT} \right] \left[(g_{\parallel} - g_{\perp})(g_{\parallel} + 2g_{\perp}) \right] \left[\frac{3\cos^2\alpha - 1}{d^3} \right]$$

(numerical term) (g-factors term) (geometrical term)

where $g_{\parallel}$ and $g_{\perp}$ are the g-factors parallel and perpendicular respectively to the Co - N axis, and the other symbols have the meaning given previously (p. 20). Assuming that the complex has tetragonal symmetry, with all four oxygen atoms equivalent, [although this is not strictly correct since two of them are from ligand carboxyls], using Dreiding models, values of d and α (the angle between the direction of a proton from the cobalt and the Co - N axis) can be measured and the geometrical factor calculated. To allow approximately for the free rotation of the CH_3 group, this factor was calculated at six positions, 60° apart, and the average found ($= + 0.015$). Hence

$$\begin{aligned} \text{(averaged) shift} &= + 45 \text{ p.p.m.} = \left[\begin{array}{c} \text{numerical} \\ \text{term} \end{array} \right] \left[\begin{array}{c} \text{g-factors} \\ \text{term} \end{array} \right] (0.015) \\ \therefore 3000 &= \left[\begin{array}{c} \text{numerical} \\ \text{term} \end{array} \right] \left[\begin{array}{c} \text{g-factors} \\ \text{term} \end{array} \right] \end{aligned}$$

For the N - CH_2 protons in the same complex, if it is assumed that they are held rigidly in the conformation shown, the geometrical factor is +0.0255, giving a pseudocontact shift of +76.5. These protons also receive a contact shift of about -50 since they make a dihedral angle of 60° with the Co-N bond, assuming the same

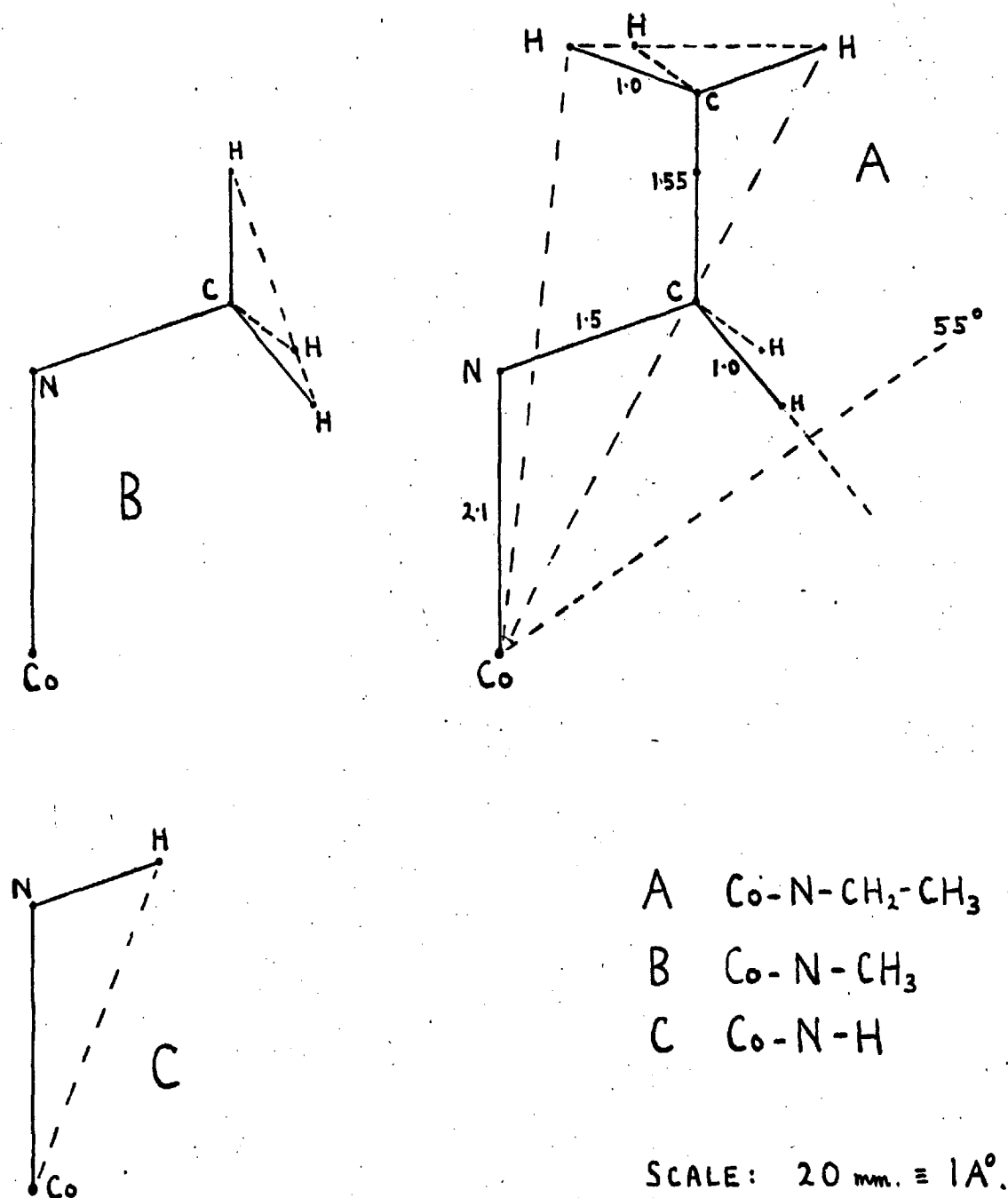


Figure 38. Diagrammatic representation of (A) Co-N-CH₂-CH₃, (B) Co-N-CH₃ and (C) Co-N-H groups in 1:1 Co(II) complexes.

relation as for Ni(II). The total shift should be +26.5, which is fairly close to the measured value of $\sim +30.5$ (for all three $\text{NCH}_2\text{CH}_2\text{X}$ complexes). For N - CH_3 groups in general, the pseudocontact contribution will be averaged over rotation of the CH_3 group; the approximate average value calculated is +74. The differences between the Co- NCH_3 and Ni - NCH_3 positions in complexes with these ligands are about +36, +47 and +86, of the same order of magnitude. In six membered chelate rings, the N - CH proton, whose dihedral angle and contact shift are both large, is calculated to have a fairly large and positive pseudocontact contribution; this agrees with the smaller low field shifts found in the Co(II) complexes. The CH_2COO protons both have α close to or below 55° and are predicted to have small negative pseudocontact shifts, which again agrees with their positions below the H_2O line.

The predictions are less satisfactory with five membered chelate rings. In IDA complexes, the α values are about $40 - 45^\circ$ and a fairly large positive shift is expected, yet the line positions are roughly the same as those in the Ni(II) complexes. It seems difficult to strain the rings sufficiently to get α values close to 55° , for which the pseudocontact contribution is zero. In several glycine derivatives (with one chelate ring), the CH protons are at lower field than in the Ni(II) complexes, as if there is a negative pseudocontact contribution.

For NH protons, a constant contribution of +270 is predicted; this seems to be too large, and the differences between imino NH

and amino NH_2 groups and the non-equivalence of the two NH_2 protons, are not explained on this simple model. Possibly better agreement would be found if two simplifications were corrected. One, already mentioned, is that the complexes do not have tetragonal symmetry, since the bonded H_2O and carboxyl oxygens are not equivalent; hence three g -factors should be used to describe the anisotropy. The pseudocontact contribution would then not necessarily be greatest along the Co-N axis, and could also vary between complexes with one chelate ring (one bonded carboxyl) and complexes with two. Apparently, however, few, if any, determinations of the three g -values for complexes of this type have been made. The second oversimplification in the simple model is that it assumes that the pseudocontact field contributions arise from a point magnetic dipole centred on the cobalt nucleus,¹⁷ whereas the unpaired electrons are spread out, at least over the metal d orbitals. The error would be greatest for the NH protons since these are the nearest. It does seem necessary, nonetheless, to include fairly large pseudocontact contributions (they are about eight times those found by Happe and Ward¹⁴⁵) to explain the large shifts of N - CH_2X protons. These contributions are, of course, sensitive to the geometric arrangement of the protons, and like the contact shifts, will change with small changes in ring conformations, as, for example, between 1:1 and 1:2 complexes.

Some of the differences between Co(II) and Ni(II) complexes could also arise from other factors, such as the

following.

(1) Differences in structure. These are expected to be fairly small.

The bond lengths to O and N are slightly longer for Co(II) than for Ni(II), and the ring conformations can differ somewhat; in the histidine complexes,¹³¹ the dihedral angles differ by up to 10° .

In calculating distances and angles from Dreiding models, it was assumed that the structures were the same for a given ligand.

(2) Differences in bond strengths and lability. The stability

constants of Co(II) complexes are usually smaller than those of the corresponding Ni(II) ones;¹²⁸ this is largely the effect of weaker bonding to the nitrogen,¹⁴⁶ and it might be expected that this atom would carry less unpaired electron density in Co(II) complexes.

It is also found that Co(II) complexes are more labile than Ni(II),¹⁴¹ and it is possible that the averaging of shifts due to ligand lability occurs more readily, especially with six membered chelates, which are fairly weak.

(3) Differences in electronic structure. In the approximately octahedral environments in these complexes, the electron configuration for the seven 3d electrons of Co(II) is usually high spin, differing from Ni(II) in having one empty t_{2g} orbital. This could accept p or π type electrons from the bonded N or O atoms, leaving more unpaired spin density on these atoms (in p orbitals) than with Ni(II). This has been suggested to explain the larger H_2O contact shift with Co(II);¹²⁷ it may contribute to the NH shifts but does not seem to have large effects on the CH protons (which are in σ

orbitals).

The explanation of the NH line positions is, in fact, less certain than for the Ni(II) complexes. The contact shift should be large but if the pseudocontact contribution is, in fact, very large and positive, the contact contribution must be negative. The differences between imino NH and NH₂ groups seem to be fairly characteristic; they may be related to the dihedral angles between the NH bond and the Co - O bonds, suggesting that π overlap with the t_{2g} may be involved. This would also explain the non-equivalence of NH₂ protons. As with Ni(II), it is still uncertain why the H₂O protons are shifted downfield and the NH ones upfield.

The sharpness of the shifted lines in the Co(II) complexes, relative to those with Ni(II), has already been mentioned; it presumably arises from a longer T_1 , due to a shorter electron T_{1e} for Co(II), as has been found in other complexes.¹⁴⁷ The main contribution to T_1 is probably the electron dipole-nuclear dipole interaction since the line widths are greater for the protons closer to the Co(II).

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