

IMINO-ETHER

REARRANGEMENTS

A Thesis presented by

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To my Parents and Barbara

ABSTRACT

The preparation and pyrolysis of a large number of N-acylimidates is described. The unusual products formed can be rationalised by either a six centre [1,5] sigmatropic rearrangement, or by a four centre transition state.

Though these routes are not mutually exclusive, the experimental data points to the latter postulate as the major pathway for pyrolysis.

The x-ray crystallographic structure of the N-acylimidates was determined for the first time, and the geometry about the carbon - nitrogen double bond also supports the four centre mechanism.

Also synthetic work on an N-thioacyl imidate is described, with particular attention to the attempted synthesis of dithiobenzamide.

Acknowledgements

I thank my supervisor Professor Sir Derek Barton for the privilege of working for him, and his encouragement and guidance at all times.

Thanks also go to Dr. S. Prabhakar with whom many useful discussions were held.

The excellent analytical service of Mr. K.I. Jones and his staff, and the mass spectral data supplied by Mrs. J. Lee are acknowledged.

Also Mr. A.P. Coleman and his staff are thanked for their technical assistance.

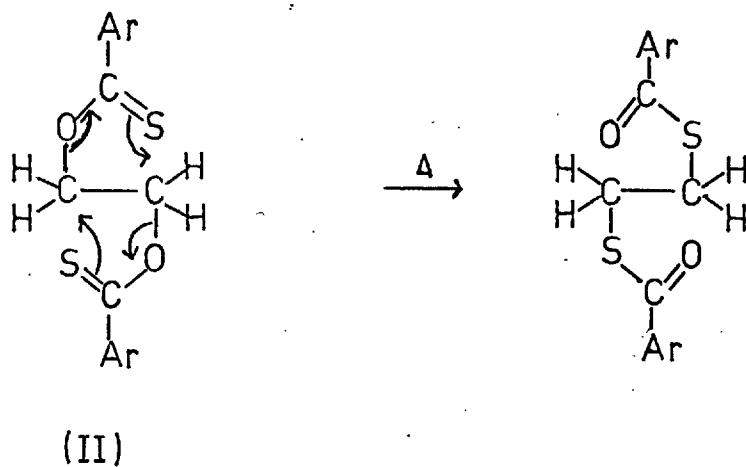
The X-ray crystallographic structure determination was carried out by Mr. D.J. Williams.

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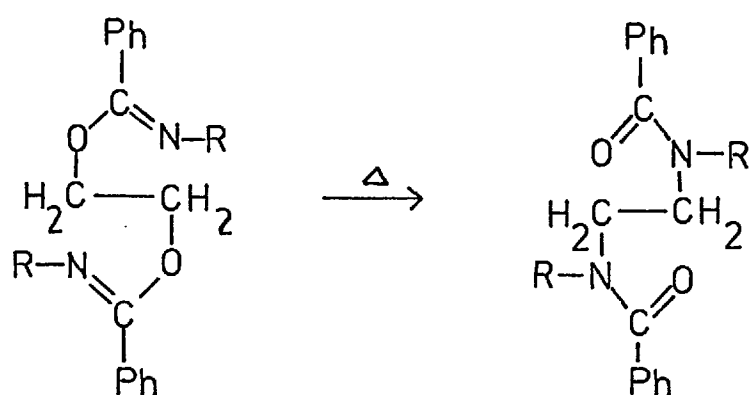
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DISCUSSION

Work was initiated with a goal of diamino-sugar synthesis, from dihydroxy sugars, by application of a thermal rearrangement of dithionesters (II)¹ to their nitrogen analogues.



The initial compound (VIa) had been synthesised¹, and shown to undergo rearrangement (Scheme 1).

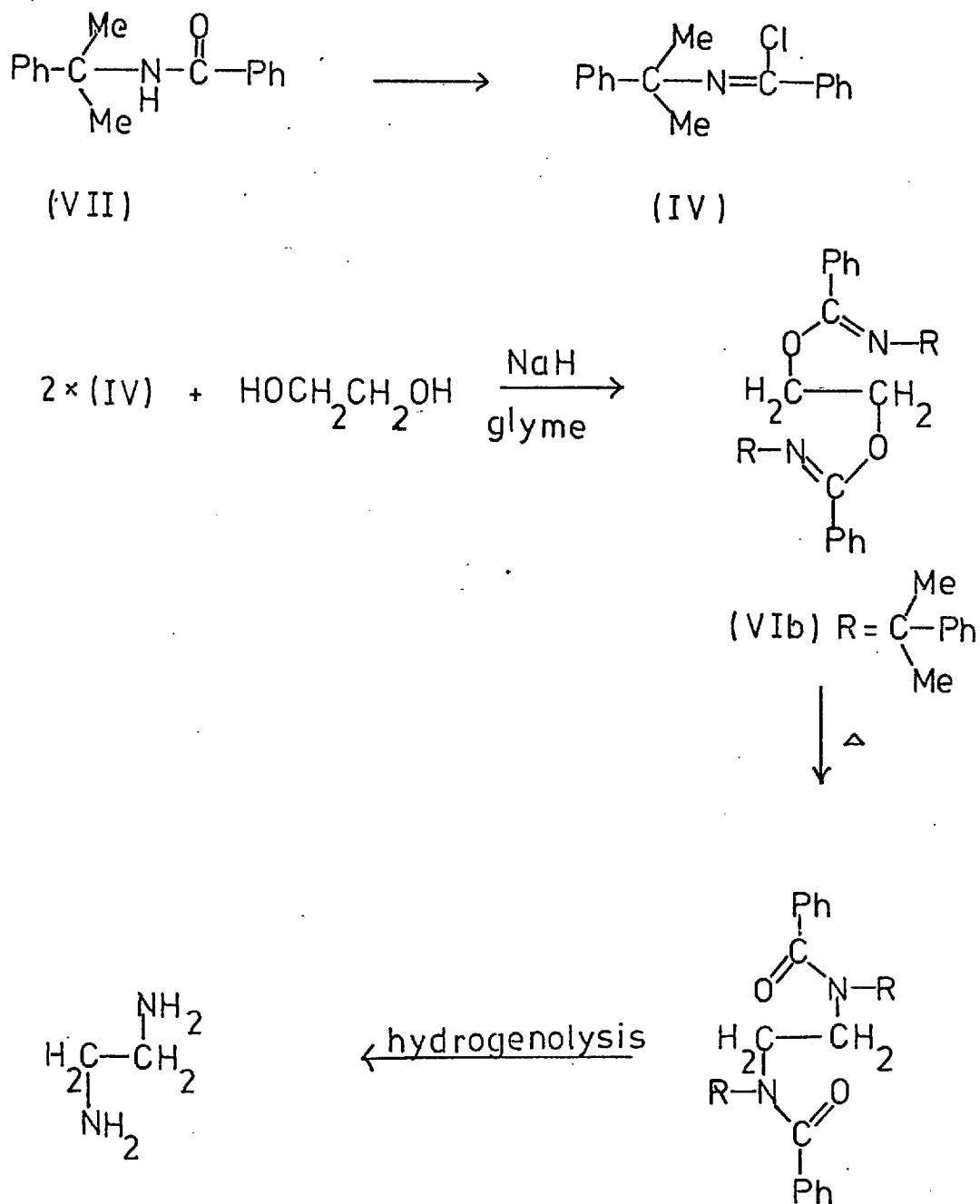


(VIa) R = Ph

(VIb) R = $\begin{array}{c} \text{CH}_3 \\ | \\ \text{C}-\text{Ph} \\ | \\ \text{CH}_3 \end{array}$

SCHEME 1

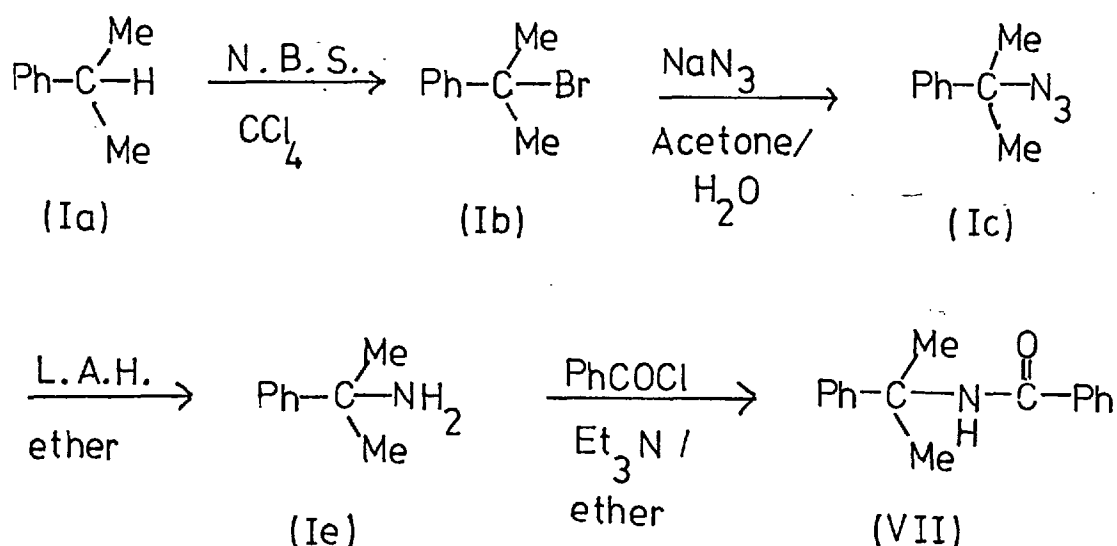
However to apply this to the synthesis of amino sugars, a grouping which was readily hydrogenolysable was required, as a substituent on the nitrogen. Such a moiety is the "cumyl" residue, and synthesis of the compound (VIb) was undertaken (Scheme 2).



SCHEME 2

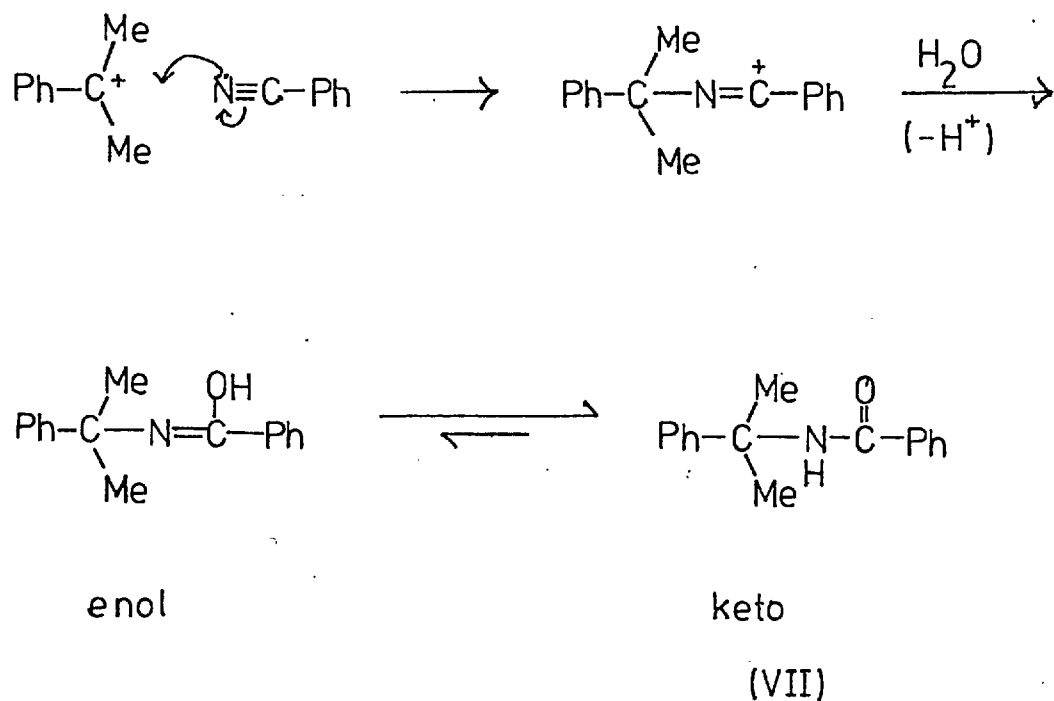
Also (Scheme 2) could be monitored by using a benzyl group substituted on the nitrogen as a "simple model".

N-cumylbenzamide (VII) was prepared by a novel route, (Scheme 3) as opposed to the literature method², from benzoylation of the amine (Ie), resulting from nitration of cumene and reduction of the nitro product, or using the Hofmann reaction, treating 2-phenyl-2-methylpropionamide with sodium hypobromite.



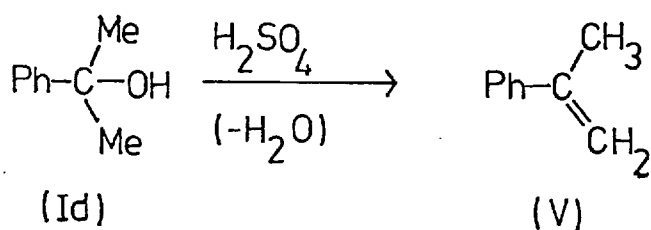
SCHEME 3

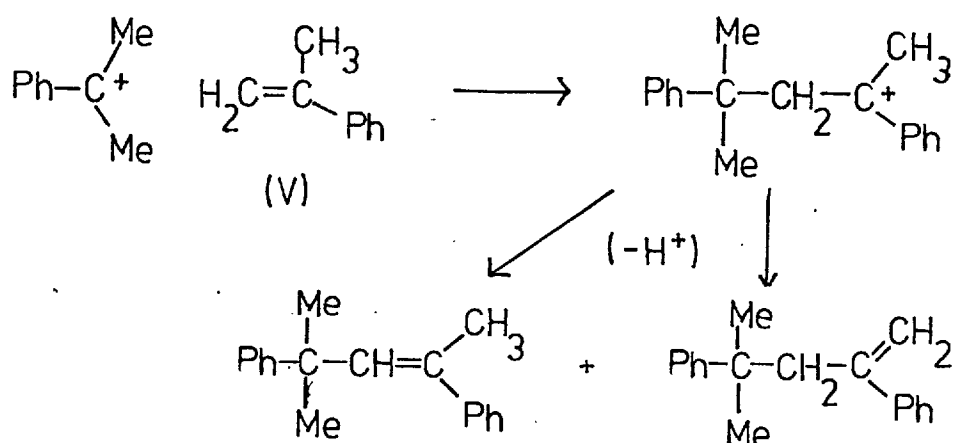
The overall yield in this 4 stage synthesis was rather low (ca. 9%), and so before further work was carried out, synthesis of (VII) was attempted by the Ritter reaction³, involving nucleophilic addition of a nitrile to a carbonium ion, in the presence of sulphuric acid, subsequent dilution with water yielding the amide (Scheme 4).



SCHEME 4

Reactions of this nature all failed, only materials corresponding to α -methyl styrene (V) and benzonitrile being observed (t.l.c.). A review article⁴, stated that the Ritter reaction between α -methyl styrene and acrylonitrile was unsuccessful, the α -methyl styrene being a stronger nucleophile than the nitrogen of acrylonitrile, hence resulting in dimer formation⁵ (Scheme 5).

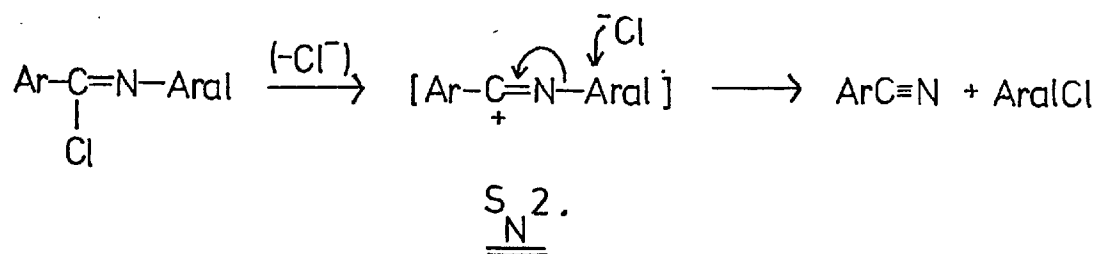
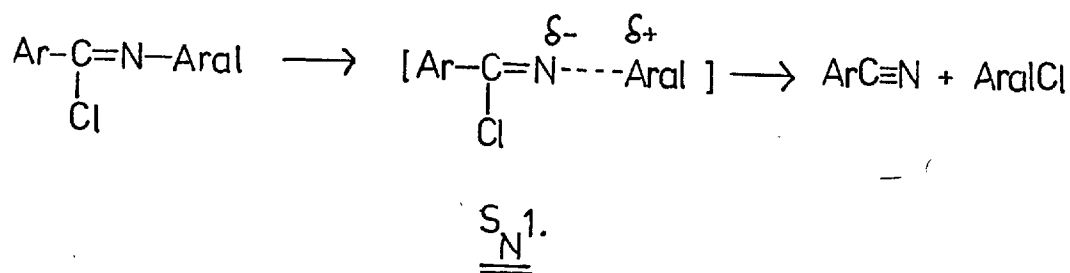
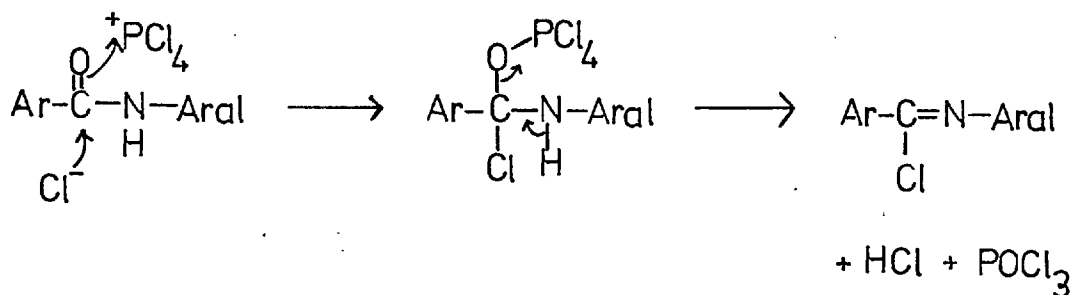


SCHEME 5

These pentenes would have virtually the same R_f as α -methyl styrene and thus, this accounts for the observed apparent lack of reaction between benzonitrile and 2-phenyl-propan-2-ol (Id).

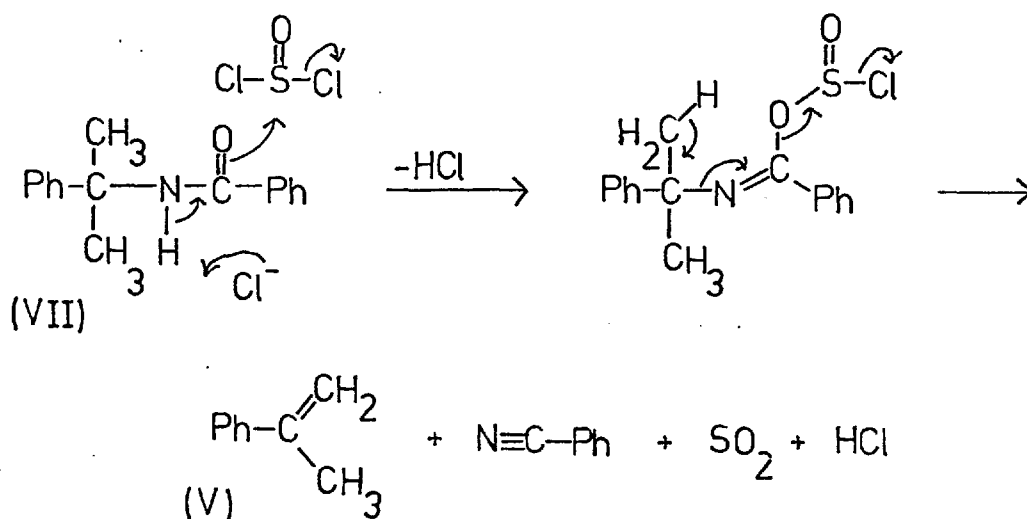
Reverting back to (Scheme 2), the chloro compound (IV) had to be synthesised, and treatment of the amide (VII) with thionyl chloride⁶ was carried out. The required imidoyl halide (IV) was not observed, instead benzonitrile and α -methyl styrene (t.l.c.) were formed. These are the expected products of the von Braun reaction^{6,7} on a secondary amide, which is conducted using excess phosphorus pentachloride, and is considered to be a nucleophilic attack at a saturated carbon, giving the imidoyl halide as an intermediate, with subsequent breakdown of this via

an S_N1 or S_N2 process (Scheme 6), resulting in cleavage products.

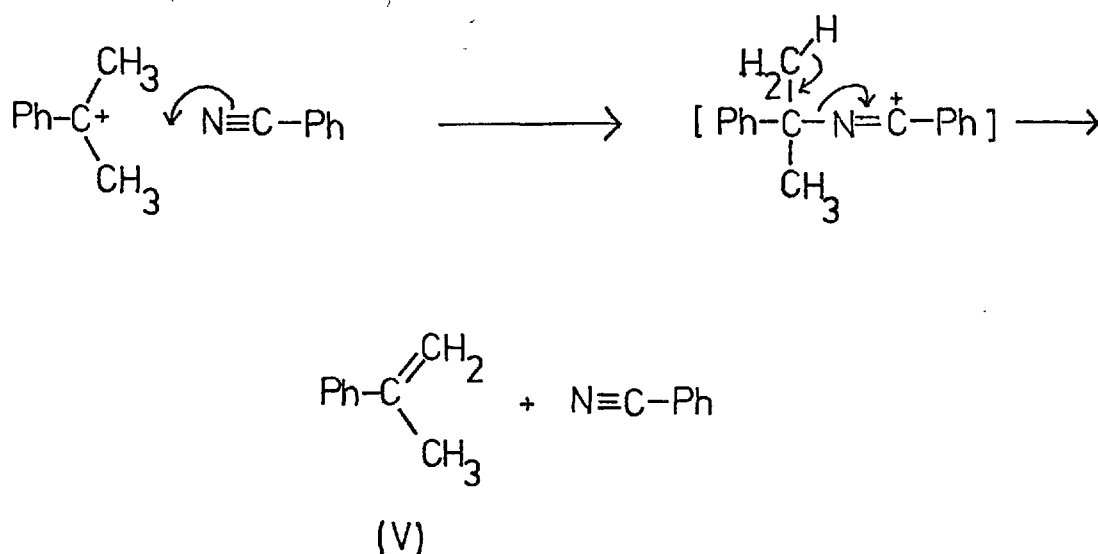


SCHEME 6

The S_N1 route is obviously favoured when the Aralkyl group will yield a stable carbonium ion, as in the case considered where Aral. is the cumyl group, and thus leading to ready collapse of the intermediate imidoyl halide. However another intermediate may be written in this instance, accounting for the non appearance of imidoyl halide.

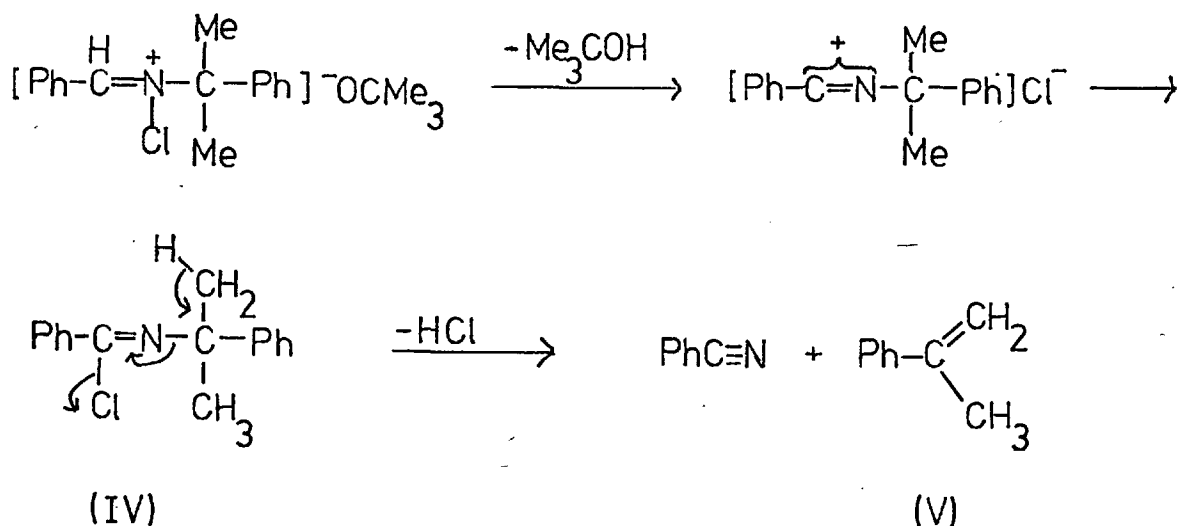
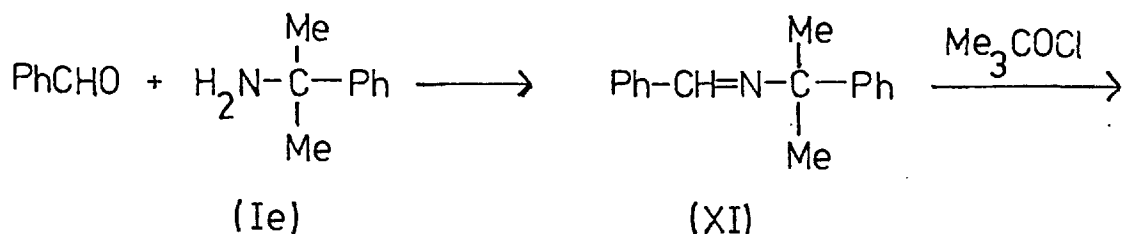


Reconsideration of the Ritter reaction³ at this point brings further evidence to bear, in that there may be initial attack by the nitrile, to give the intermediate, as required, but the thermodynamics of the system are such that subsequent elimination occurs, rather than attack by water.



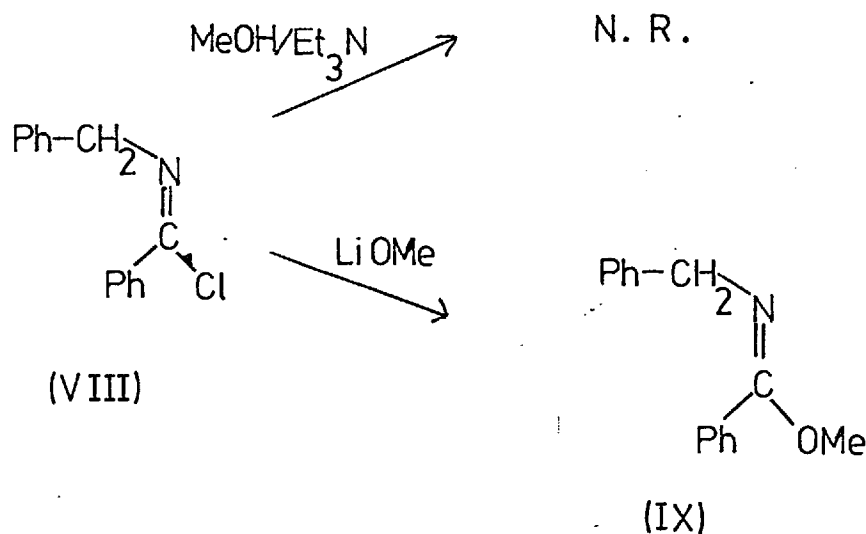
The reaction of the Schiff Base (XI), from the condensation of benzaldehyde and 2-amino-2-phenyl propane (Ie), with *t*-butyl hypochlorite⁸ cannot be considered in the same way but whether it was the imidoyl halide (IV) which

collapsed down too readily to permit isolation, or decomposition of an intermediate, could not be determined.

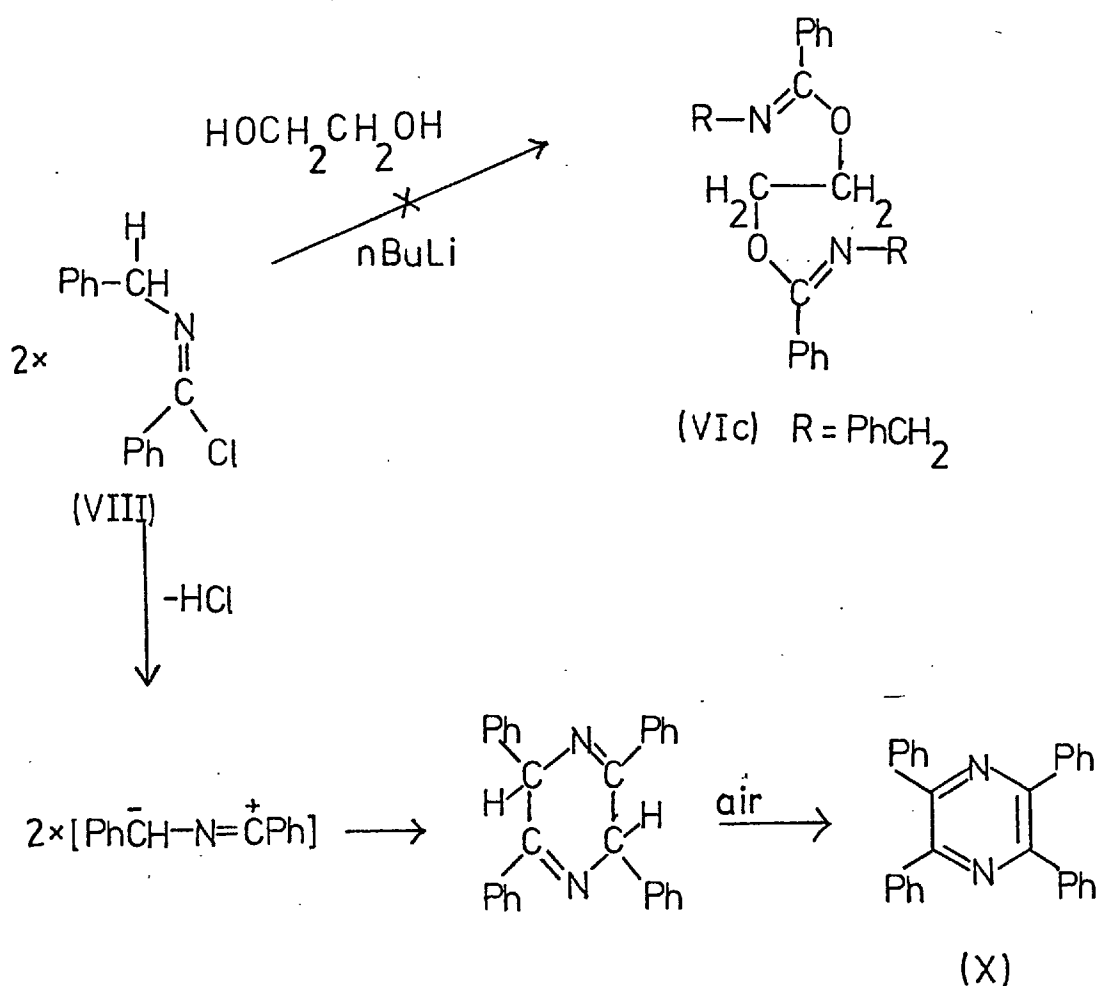


Thus the experimental data would indicate that the cumyl residue was giving undue difficulty in the synthetic work, and so the simpler N-benzyl-benzimino-chloride (VIII) was investigated, preparing it from N-benzyl benzamide and phosphorus pentachloride^{9,10}. Initial reactions were carried out to elucidate the ease with which (VIII) reacted with methanol, to give the imidate (IX), but reaction with methanol and triethylamine failed. Instead the methoxide ion was required, generating it from lithium and methanol, to yield imidate

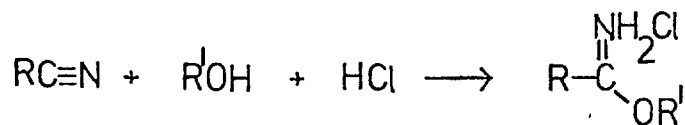
(IX), characterised by the methylene (δ 4.6) and methoxy (δ 4.0) singlets in the N.M.R., ν $>C=N$, 1670 cm^{-1} , and analysis.



This work substantiated the preparation of the diimide (VIa) which required the generation of the anion of ethylene glycol for reaction with N-phenyl benzimidoyl chloride¹¹. An analogous synthesis of diimide (VIc) was undertaken, but using n-butyl lithium to prepare the dianion of ethylene glycol, and reacting this with the imidoyl halide (VIII). However the desired product (VIc), could not be isolated, instead tetraphenyl pyrazine (X) was found, m^+/e 384, analysis indicating only C,H,N present, and m.pt. This is easily explained by the dimerisation of a 1,3 dipole, formed from the imidoyl halide (VIII), the non aromatic product readily oxidising with air on work up¹¹.

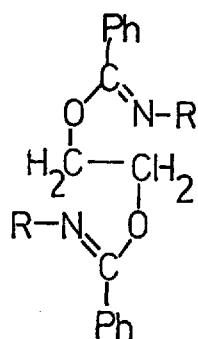
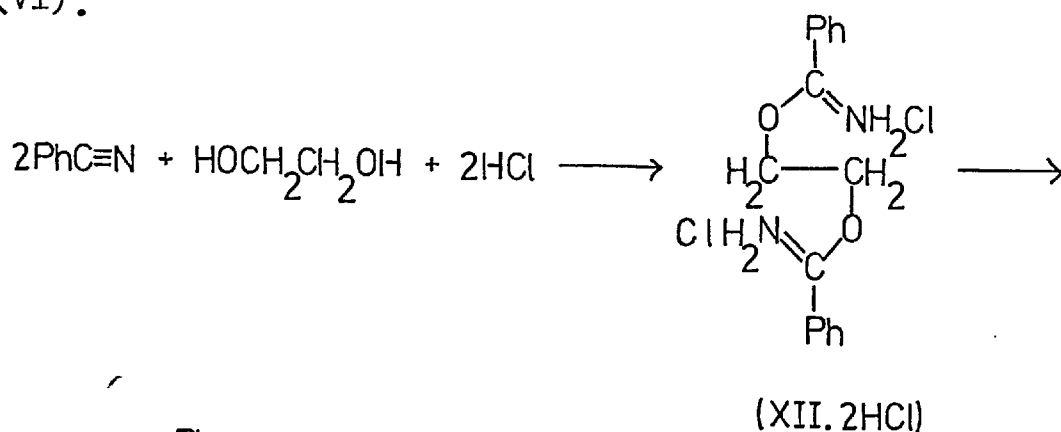


This setback in the formation of diimide (VIc) prompted an alternative approach to synthesis, using the Pinner method^{12,13,14} which consists of condensing an alcohol and a nitrile in anhydrous conditions, in the presence of hydrogen chloride.

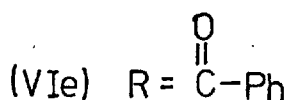
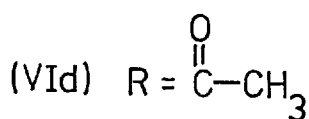


It was thought that incorporation of a diol, instead of the alcohol might furnish the required diimide hydrochloride (XII.2HCl), and that this could be modified

on the nitrogen subsequently, giving general structure (VI).

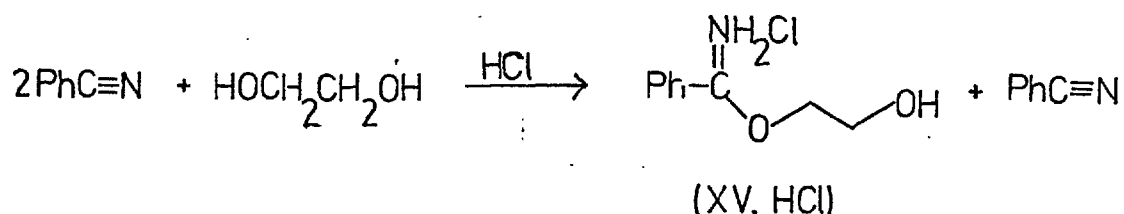


(VI)

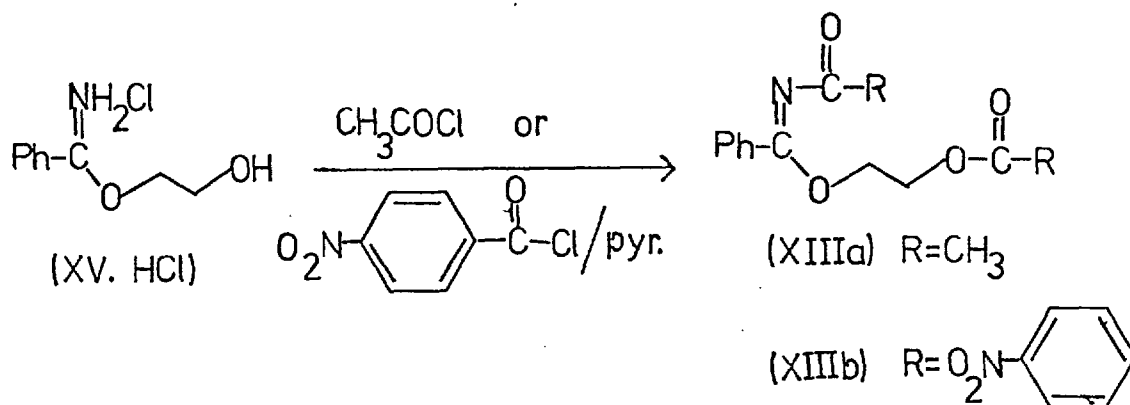


Preliminary work did indeed give the diimideate hydrochloride (XII.2HCl), from benzonitrile and ethylene glycol, the product being characterised as the free imideate (XII). This was carried out by partitioning the hydrochloride (XII.2HCl) between ether and cold aqueous bicarbonate. The free imideate (XII), on evaporation of the ether, and crystallisation, showed the presence of $>\text{C}=\text{N}$ - (I.R. ν 1640 cm^{-1}), an ether linkage (I.R. ν 1100 cm^{-1}) and analysed correctly. The hydrochloride (XII.2HCl) was then acetylated, using acetic anhydride and pyridine, to give (VIId), which was considered to be a suitable model for the interconversion pyrolysis (Scheme I). The product was an oil unfortunately, and did not permit characterisation, being unstable to moisture,

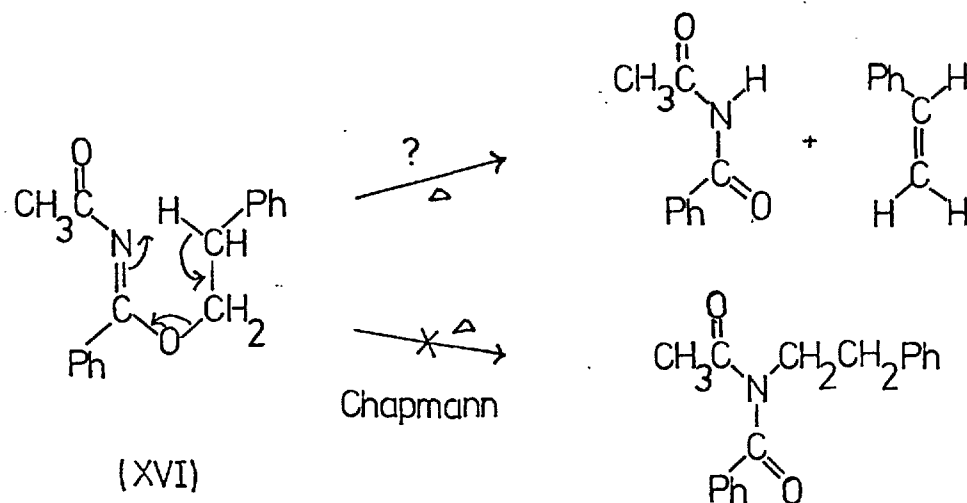
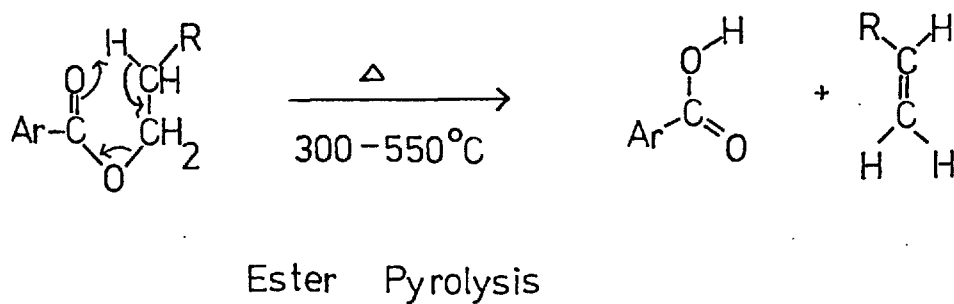
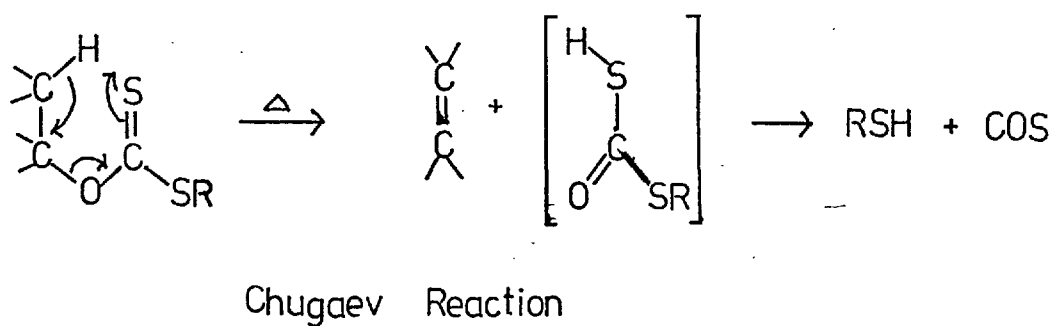
but showed the expected methylene singlet for a symmetrical compound (N.M.R.). This, hopefully could easily be surmounted by benzoylating (XII.2HCl), to yield (VIe), the extra aromatic residues enhancing the chance of crystallisation. Repreparation of the hydrochloride (XII.2HCl) failed though, giving rise to the halfway product (XV.HCl) instead - also characterised as the free imidate, which showed the presence of a broad hydroxyl (ν 3240 cm^{-1}), masking the normal narrow N-H stretch of free imidates in the I.R.. The N.M.R. showed only 5 aromatic protons, and two methylene signals (multiplets). The required mass ion of 165 was found for $\text{C}_9\text{H}_{11}\text{NO}_2$ and it was analysed correctly. Repetition of the reaction subsequently, using all possible variations of conditions, including the employment of solvents gave solely the hydrochloride (XV.HCl).



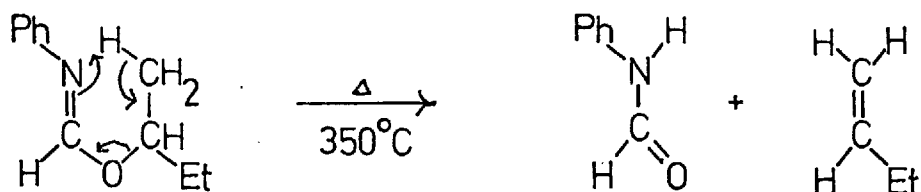
The structure of the half imidate (XV) was further substantiated by reaction with p-nitrobenzoyl chloride to give the di-p-nitrobenzoate (XIIIb), which was fully characterised. Acetylation of (XV.HCl) again gave rise to an oil, which was assumed to be (XIIIa).



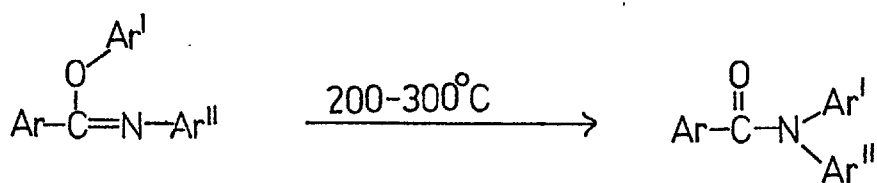
Concurrent with this work on diimides of type (VI), a half model (XVI) was synthesised, from benzonitrile and β -phenethyl alcohol, by the Pinner route, and acetylated. It was hoped that this might undergo a 6-membered rearrangement, as outlined, similar to the rearrangement of the diimide in (Scheme 1). This would parallel the Chugaev Rearrangement¹⁵ of xanthate esters, possessing a β -hydrogen, and pyrolysis of esters^{15a}.



There was also a reference in the literature to a very similar rearrangement, where N-phenyl-sec-butyl formimide, instead of undergoing the Chapman rearrangement^{17,18} had actually accomplished the required reaction, and so this was quite feasible.



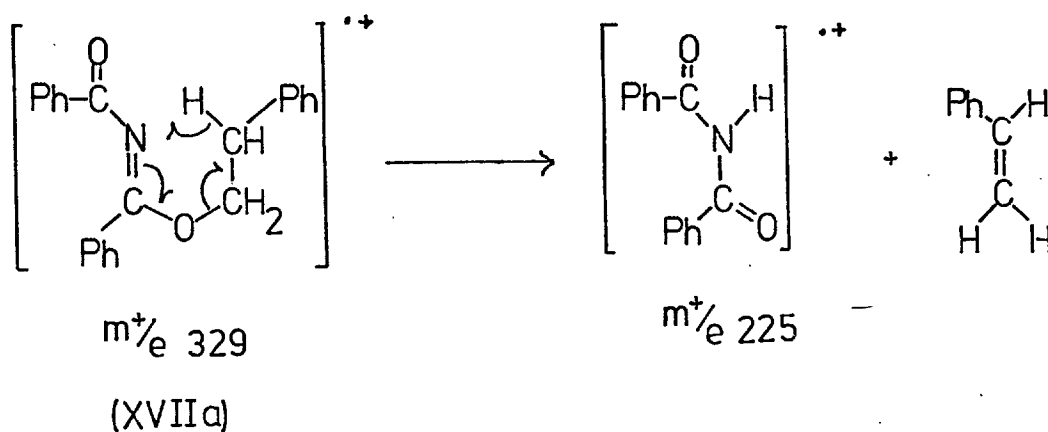
The N-acetyl imide (XVI) was also an oil, and so was not fully characterised. However preliminary pyrolysis at 180°C gave no indication of styrene, although new products were appearing (t.l.c.). Another possibility was the Chapman Rearrangement^{17,18} which aryl imides undergo, but only one product would be expected here, and also the temperature was rather low.



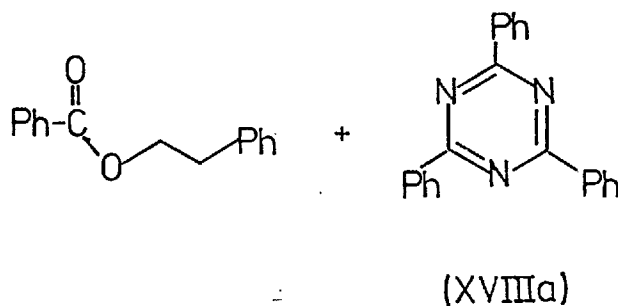
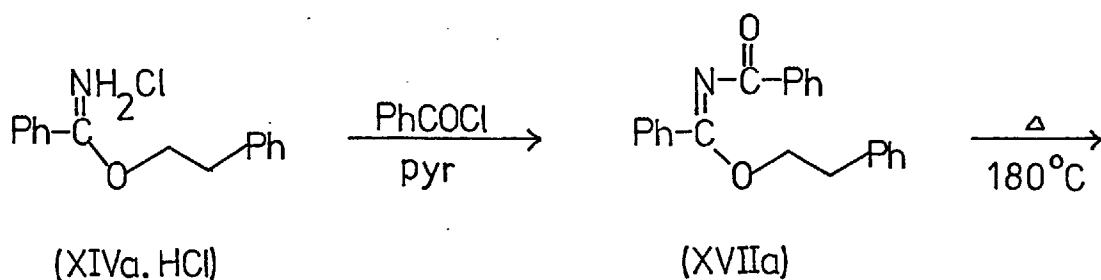
Chapmann Rearrangement.

Clarification of this pyrolysis was carried out by N-benzoylation of the imide hydrochloride (XIVa), to give a crystalline N-benzoyl benzimide (XVIIa), which was fully characterised, showing I.R. ν 1660, 1640 cm^{-1} , characteristic of the conjugated >C=N-C=O group. N.M.R., 15 aromatic protons, two being deshielded by the anisotropy

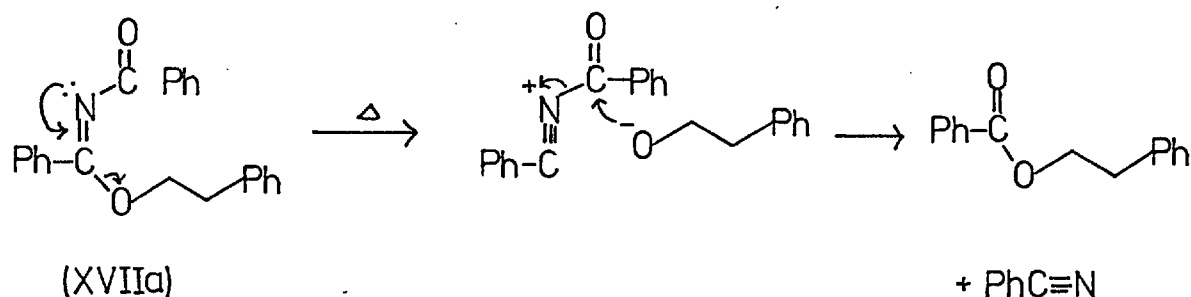
of the carbonyl group as expected, and two methylene triplets, the one adjacent to the oxygen being at lower field. The required mass ion of m^+/e 329 for $C_{21}H_{19}NO_2^-$ was found, with the presence of a benzoyl residue (m^+/e 105) and loss of a 104 unit (styrene) arising from the McLafferty rearrangement.



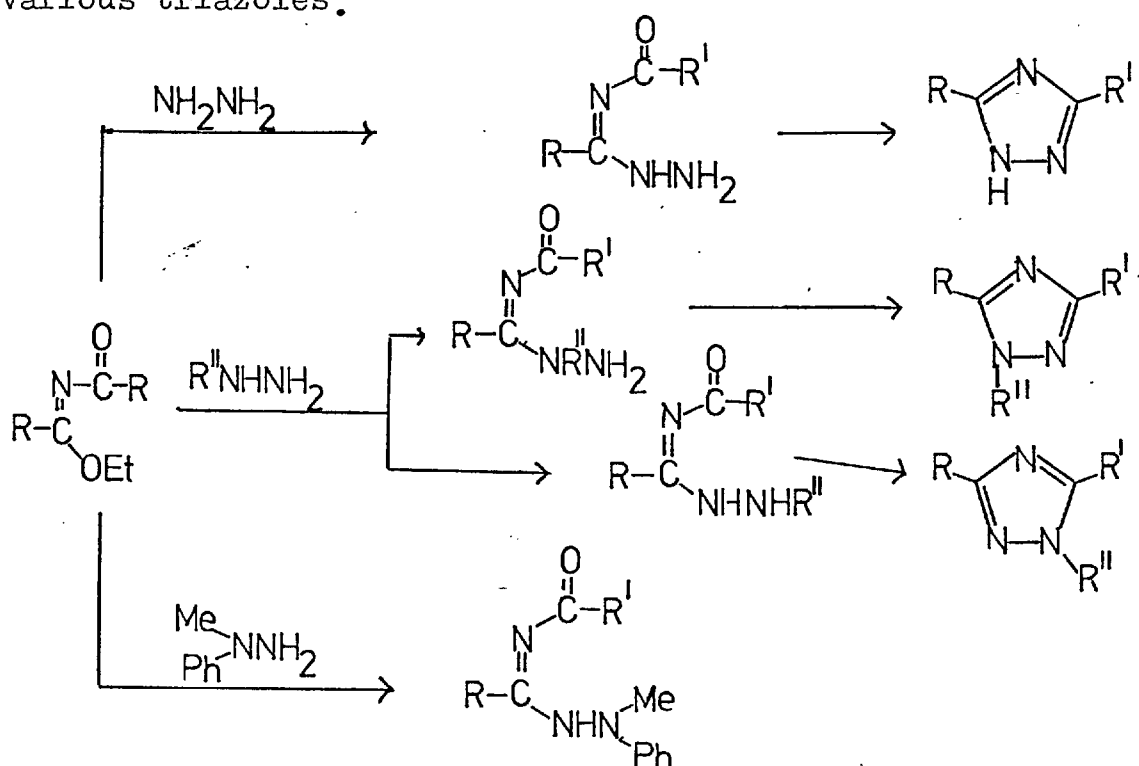
Pyrolysis of (XVIIa) gave β -phenethyl benzoate and 2,4,6-triphenyl-1,3,5-triazine (XVIIIa).



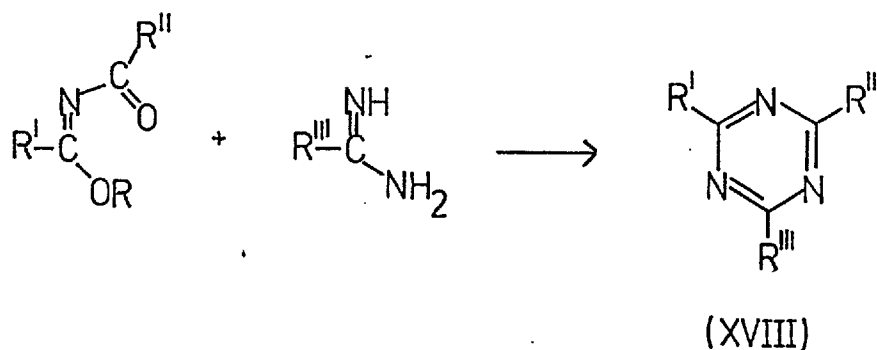
This pyrolysis can readily be explained by the polarisation, and cleavage of the ether link in (XVIIa), and subsequent attack on the carbonyl group by the alkoxy group, to yield ester and nitrile, the latter trimerising at the reaction temperature.



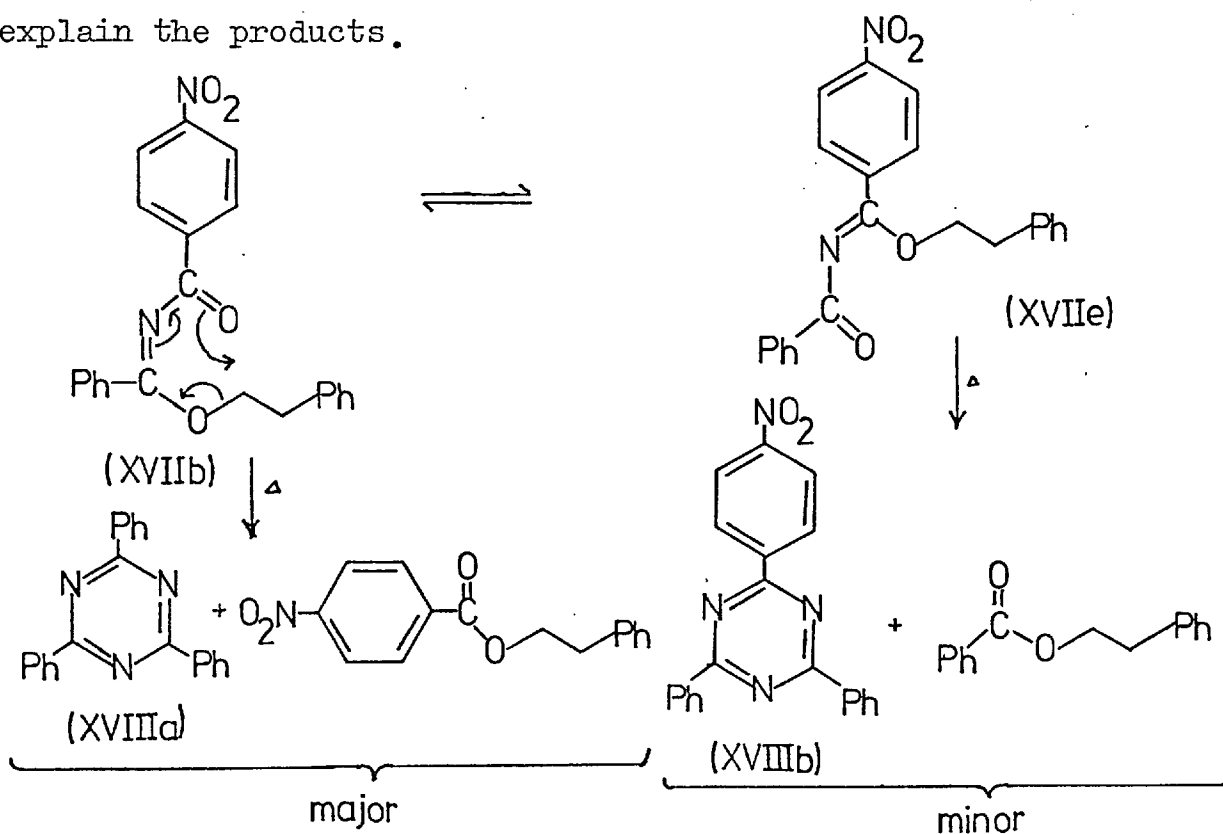
Reference to the literature indicated that N-acyl imidates (XVII) as a class of compounds were known, being first prepared in the late 19th century,^{19,20} however subsequent references are very few, and the chemistry of these compounds, apart from hydrolysis was virtually unknown, although the parent imidates (XIV) and derivatives have been widely studied and reviewed.¹⁴ Baccar and Barras²¹ had studied their reaction with hydrazines, to give various triazoles.



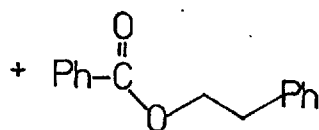
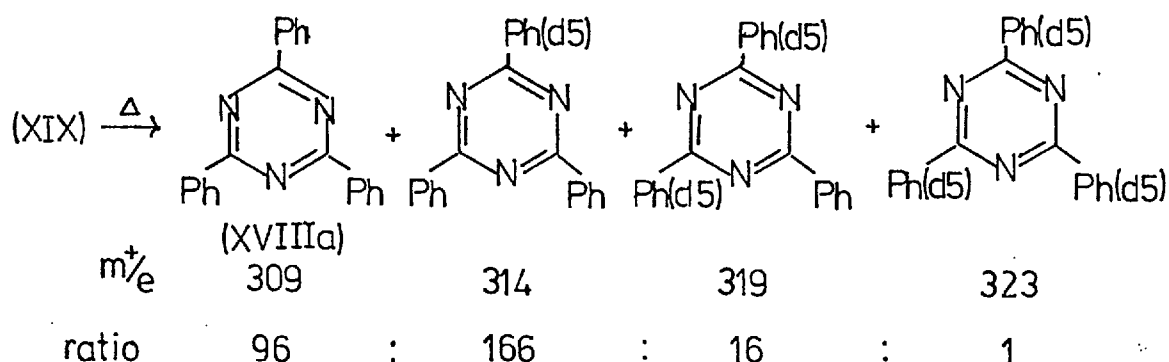
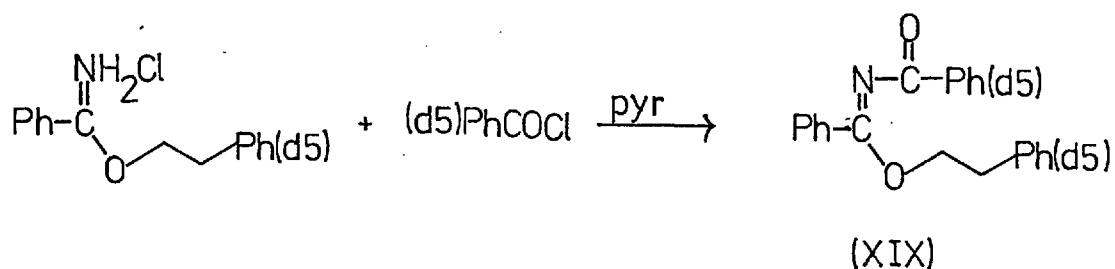
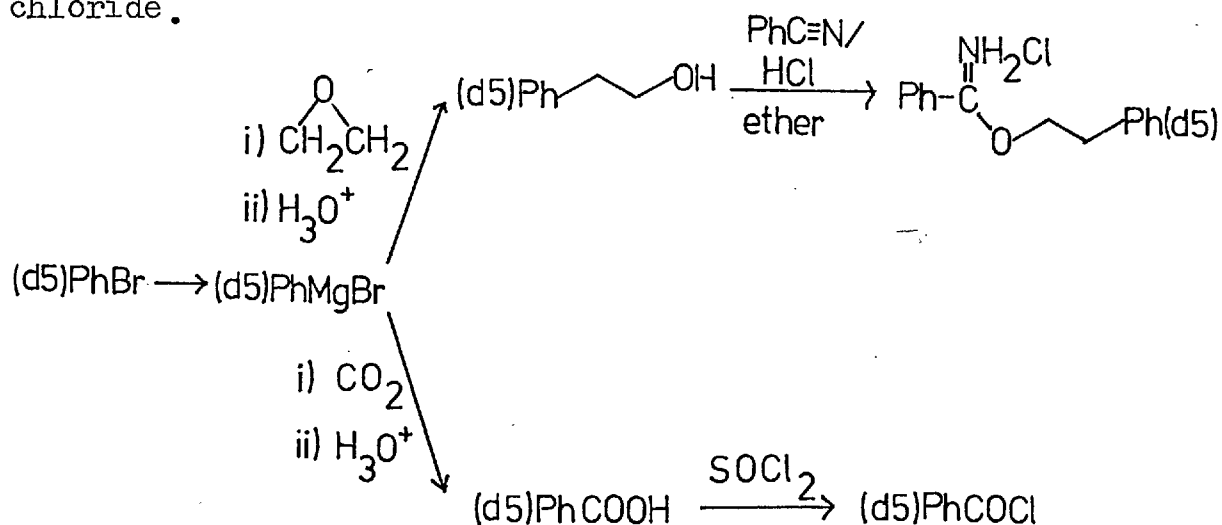
Bader²² had condensed N-acyl imidates with amidines, to give trisubstituted s-triazines, bearing three different substituents.



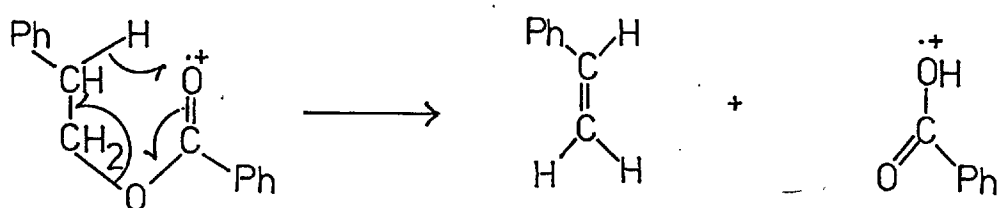
Bearing in mind the formation of triazine (XVIIIa) from pyrolysis, and the fact that the parent imidates (XIV) readily trimerise^{23,24} to yield triazines (XVIII), the reaction was studied further by pyrolysing the N-p-nitro benzoyl benzimidate (XVIIb). This would hopefully yield triazine (XVIIIa) and β -phenethyl-p-nitro benzoate, substantiating the proposed collapse of imidates to ester and nitrile. Unexpectedly two triazines, and two esters were obtained on pyrolysis, and a [1,5] sigmatropic rearrangement stage, prior to pyrolysis, was suggested to explain the products.



This prepyrolysis rearrangement partially accounts for the formed products, as 2,4,6-tri-p-nitrophenyl-1,3,5-triazine (XVIIIId) should be formed rather than triazine (XVIIIb). As the p-nitrophenyl group might adversely affect the formation of triazine (XVIIIId), the d-10 imidate (XIX) was prepared, using conventional Grignard reactions on d-5-bromobenzene, to give d-5- β -phenethyl alcohol, and d-5-benzoic acid, which was converted to the acid chloride.



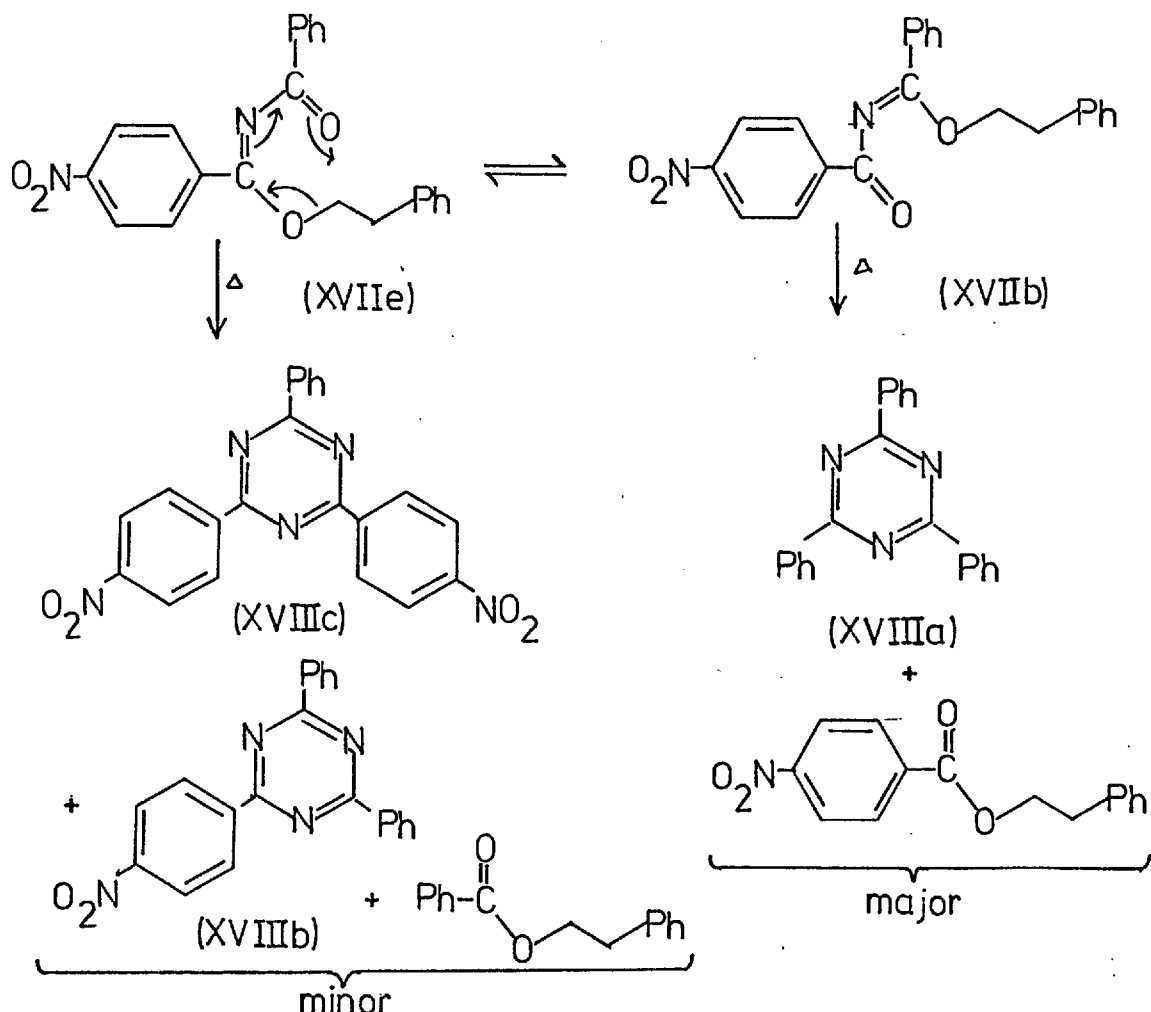
The mass spectral evidence showed that all possible triazines were produced on pyrolysis, although not in the statistical distribution required for a complete equilibrium prior to pyrolysis. The β -phenethyl benzoate could not be examined in the mass spectrometer as there was no parent peak, due to a facile McLafferty rearrangement.



To substantiate the prepyrolysis interconversion proposal, N-benzoyl- β -phenethyl-p-nitrobenzimidate (XVIIe), the product obtained from the [1,5] sigmatropic rearrangement, was synthesised from p-nitrobenzonitrile and β -phenethyl alcohol, by the Pinner method, giving the hydrochloride (XIVe.HCl), and on benzylation (XVIIe) was formed.

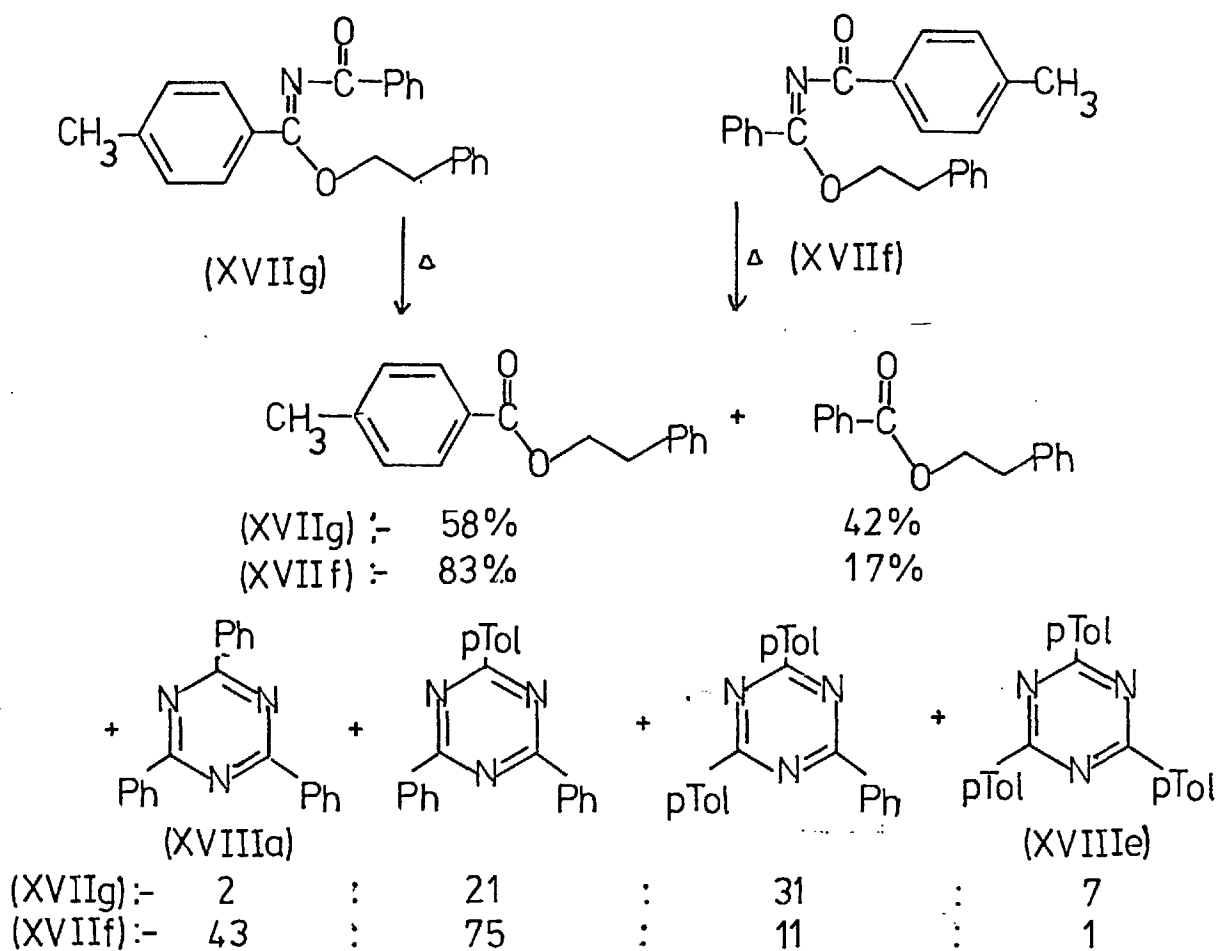
Pyrolysis of (XVIIe) gave all four products, as with the pyrolysis of (XVIIb), with the triazine (XVIIIa) and β -phenethyl-p-nitrobenzoate predominating again. This result would indicate that, if this prepyrolysis interconversion was true, the imidate (XVIIb) was more labile to pyrolysis than imidate (XVIIe), and this was borne out, as the pyrolysis temperature, and time, were greater for (XVIIe). Also produced in the pyrolysis of (XVIIe)

was 2,4-di-p-nitrophenyl-6-phenyl-1,3,5-triazine (XVIIIc).

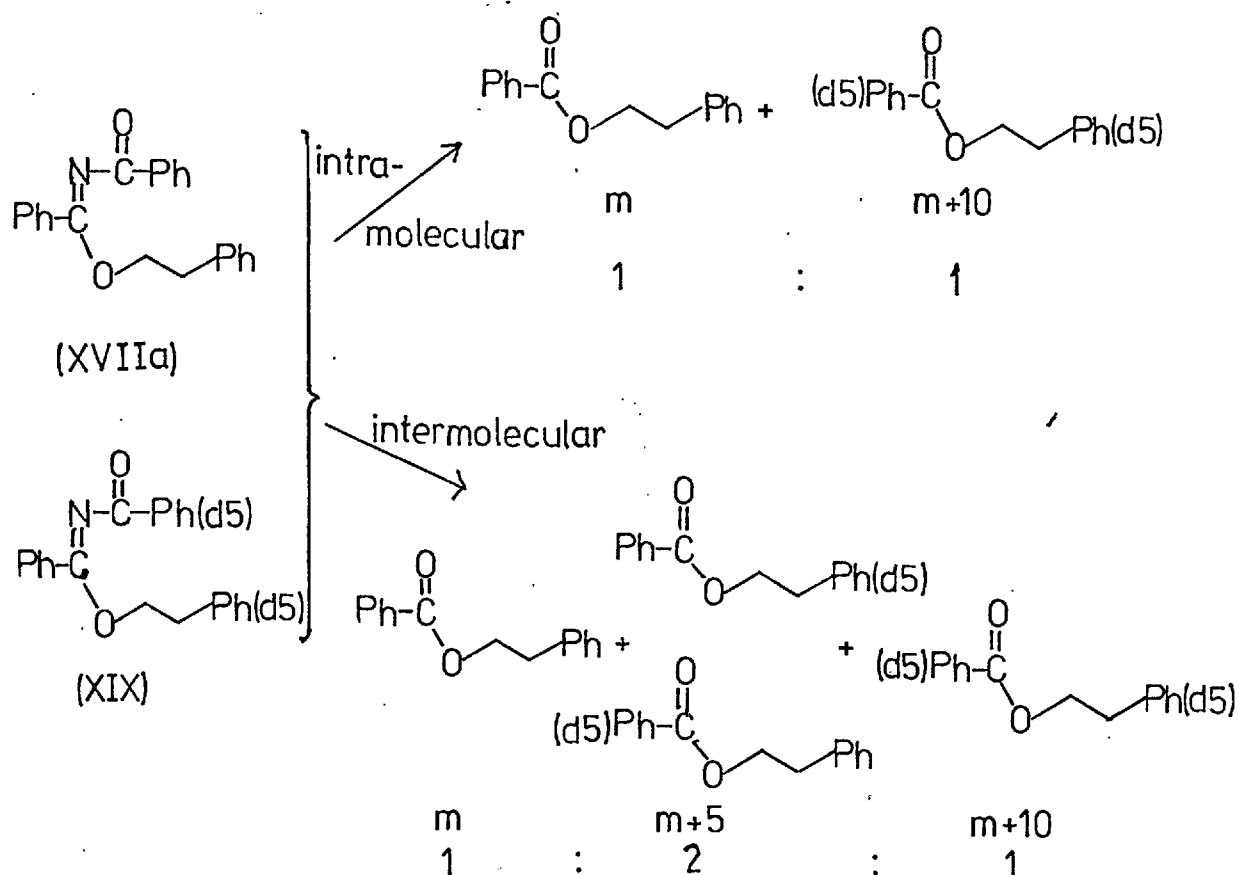


Evidence for the interconversion of imidates (XVIIb), and (XVIIe) was sought by N.M.R. and I.R. spectroscopy of the pyrolysate, before isolation of products, but none was found. This was not surprising, as any imidate formed on interconversion would only be there in trace amounts, and this system was not ideal for N.M.R. study. A better pair of imidates for this interconversion study, would be the p-tolyl analogues (XVIIIf), (XVIIIg), both synthesised using the Pinner method, with acylation of the chlorides, as hopefully any interconversion would be easily monitored by the shift of the methyl group in the

N.M.R. Unfortunately all that could be seen on pyrolysing N-acyl imidates (XVIIIf) and (XVIIIg) for increasing intervals of time was a gradual production of pyrolysis products. Here again the mass spectral evidence indicated that all possible triazines were formed, confirming the deuterium work on imidate (XIX).



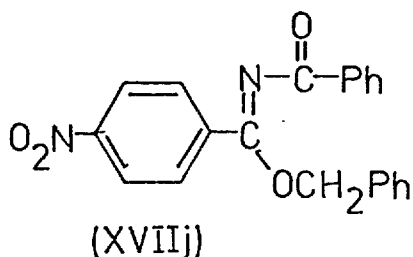
Evidence was also being sought, as to the nature of the pyrolysis, whether inter or intramolecular. In theory copyrolysis of imidates (XIX) and (XVIIa), and mass spectral analysis of the β -phenethyl benzoate should give the required data (Scheme 7).



Further consideration shows this to be impractical on two accounts

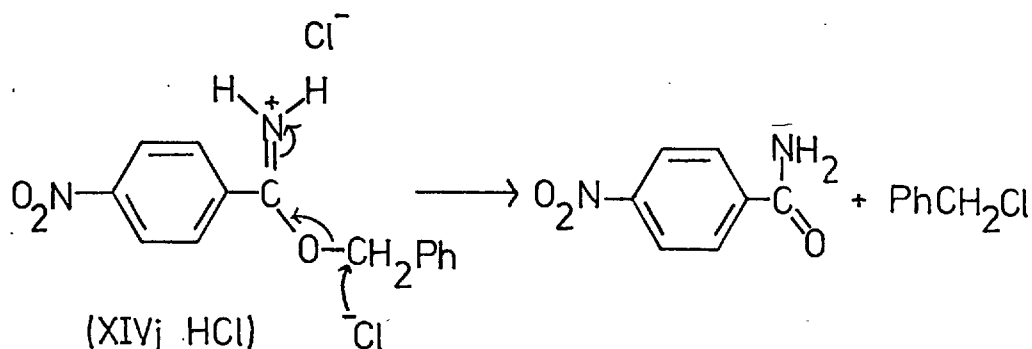
- i) The proposed prepyrolysis interconversion would affect imidate (XIX).
- ii) β -phenethyl benzoate gives no mass ion.

Reconsideration shows a suitable model to be (XVIIj).



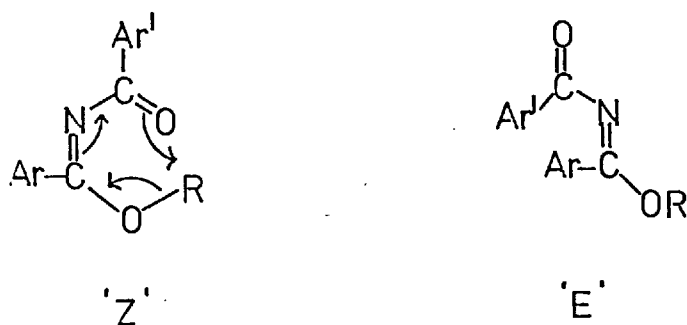
Here, isolation of benzyl benzoate from the copyrolysis of (XVIIj) and its d-10 analogue, should yield the data required. The N-acyl imidate (XVIIj) was synthesised and characterised, but the overall yield in the reaction was

very poor, due to formation of p-nitrobenzamide as well as the imidate hydrochloride (XIVj.HCl) in the Pinner synthesis. Minor modifications were made on the Pinner synthesis, by lowering the reaction temperature, using excess alcohol, and changing the solvent, but still p-nitrobenzamide was produced. This product can be rationalised as arising from a nucleophilic attack on the formed hydrochloride, by chloride ion, the driving force being the ability of the benzyl group to stabilise a partial positive charge.



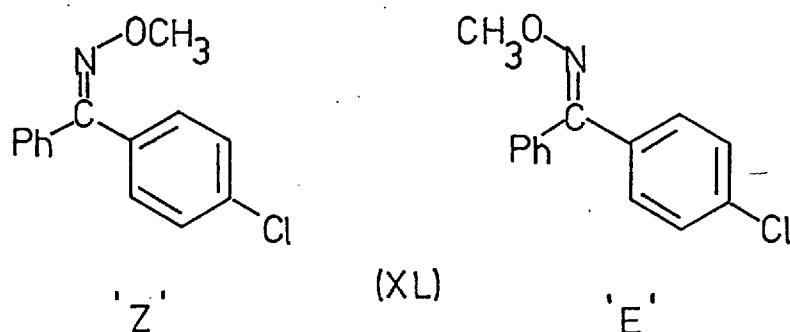
Naturally if the N-acyl imidate (XVIIj) is to be used as a deutero model, a high yield in synthesis is required, and so another model was sought.

Other aspects of work were also under consideration, a major one being the conformation of the acyl residue about the double bond, because only the 'Z' conformation yields itself to undergo the [1,5] sigmatropic re-arrangement.

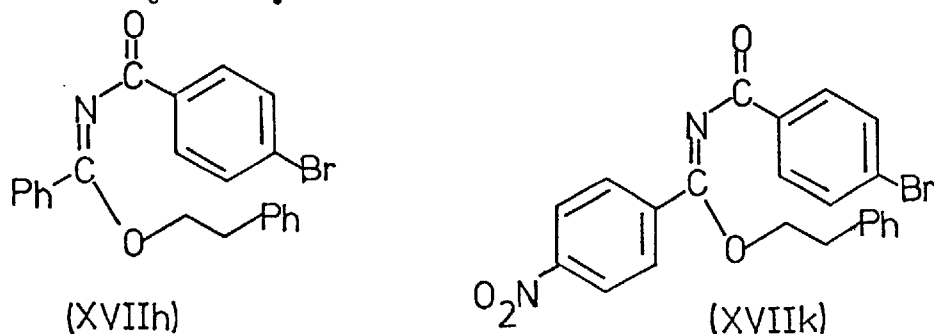


(XVII)

Imidate (XVIIc) would appear to fit in between these two materials for relative ease of isomerisation, and so variable temperature studies were undertaken. However, there was no indication of any line broadening, or appearance of a second signal over the temperature range - 50 to + 160°C. This was unexpected, and perhaps the imidates (XVII) are of a fixed configuration, akin to oxime ethers (XL)²⁷, the two forms of which are known, and show no interconversion even at 200°C²⁷.

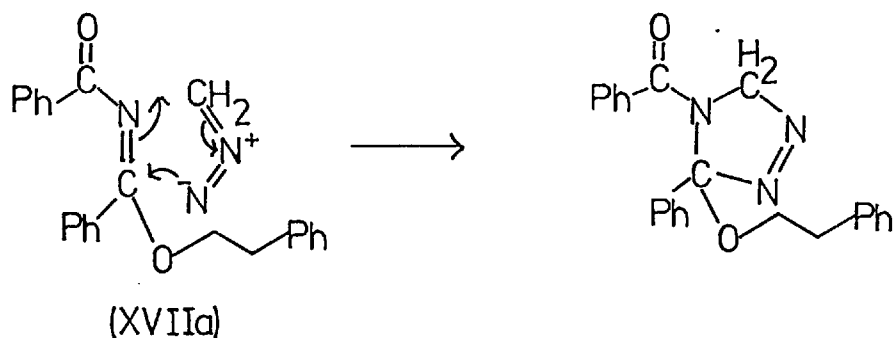


To assign the configuration about the double bond, in N-acyl imidates, suitable heavy atom derivatives (XVIIh), (XVIIk) were prepared, but although the parent compounds possessed good morphology, these materials did not give suitable crystals.

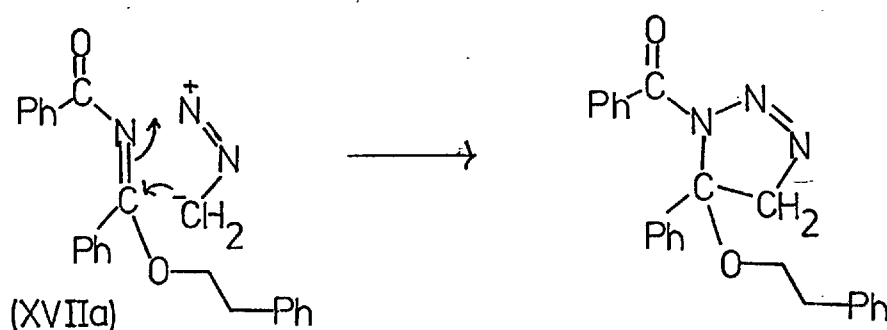


The N-acyl imidates, as a group of compounds, could also be expected to undergo 1,3 cyclo-addition reactions to

the carbon-nitrogen double bond^{30,31}, and maybe act as a diene or dienophile for the Diels-Alder reaction.

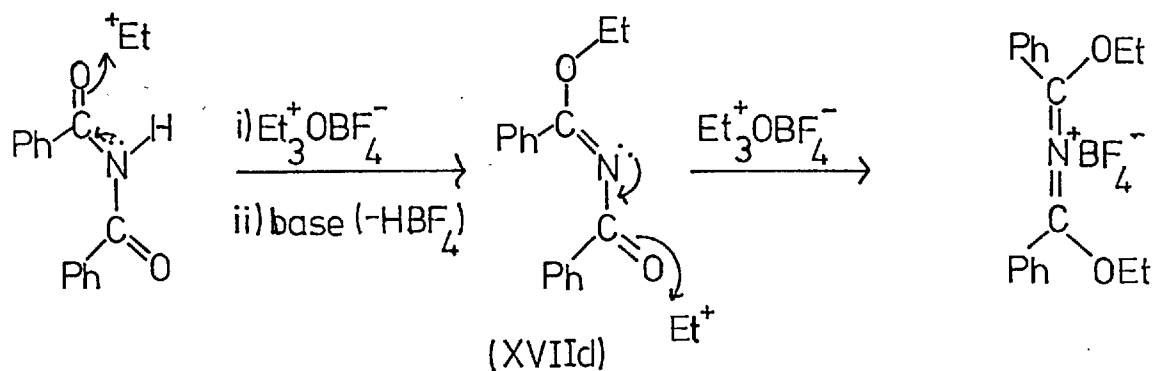


or

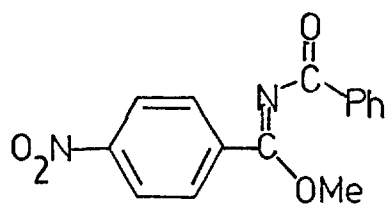


This was not found however, the reaction with diazomethane yielding starting imide (XVIIa) and polymethylene, rather than 1,2,3 or 1,2,4-triazolines, phenyl azide also failed to react. Likewise, reactions of (XVIIa) with cyclopentadiene and tetracyanoethylene failed to show any Diels-Alder adduct.

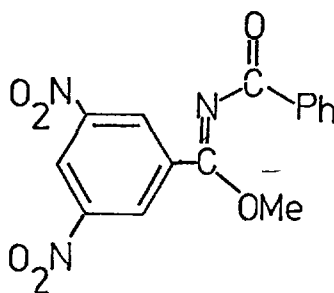
Another possible reaction is 'O' ethylation, using triethyloxonium tetrafluoroborate³², where the imide (XVIIId) can be considered the intermediate in dialkylation of dibenzamide, which would yield the unknown linear "azaallenic system"



Unfortunately here again no reaction of imidate (XVIIId) was observed with ethyl Meerwein's salt in dichloromethane. Further work was now carried out on a suitable model for deuterium studies, to determine whether the reaction was inter or intra molecular. In place of the benzyl-p-nitrobenzimidate (XVIIJ), the methyl derivative (XVIIr) was synthesised. This material was an oil unfortunately, and so the 3,5-dinitrobenzimidate (XVIIIm) was prepared instead.

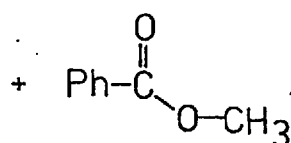
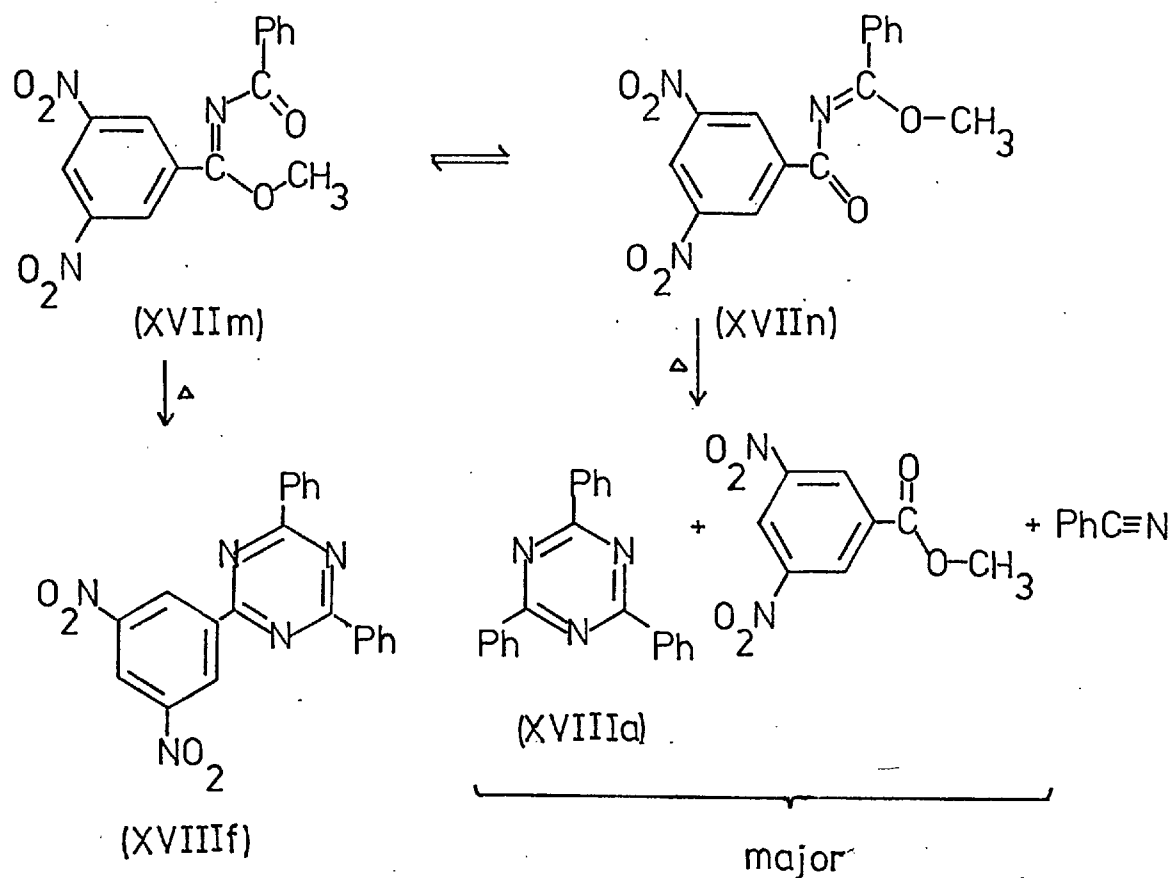


(XVIIr)



(XVIIIm)

Pyrolysis of this imidate (XVIIIm), (Scheme 8) gave unexpectedly virtually no methyl benzoate, instead the predominant products were methyl-3,5-dinitrobenzoate, and the triphenyl triazine (XVIIIa). There was however a band which corresponded to a mixture of benzonitrile, methyl benzoate and 2,4-diphenyl-6-(3',5'-dinitrophenyl)-1,3,5-triazine (XVIIIf), and although the triazine portion was easily removed, the benzonitrile and methyl benzoate were never successfully separated, even by use of silver nitrate impregnated silica gel t.l.c. plates.

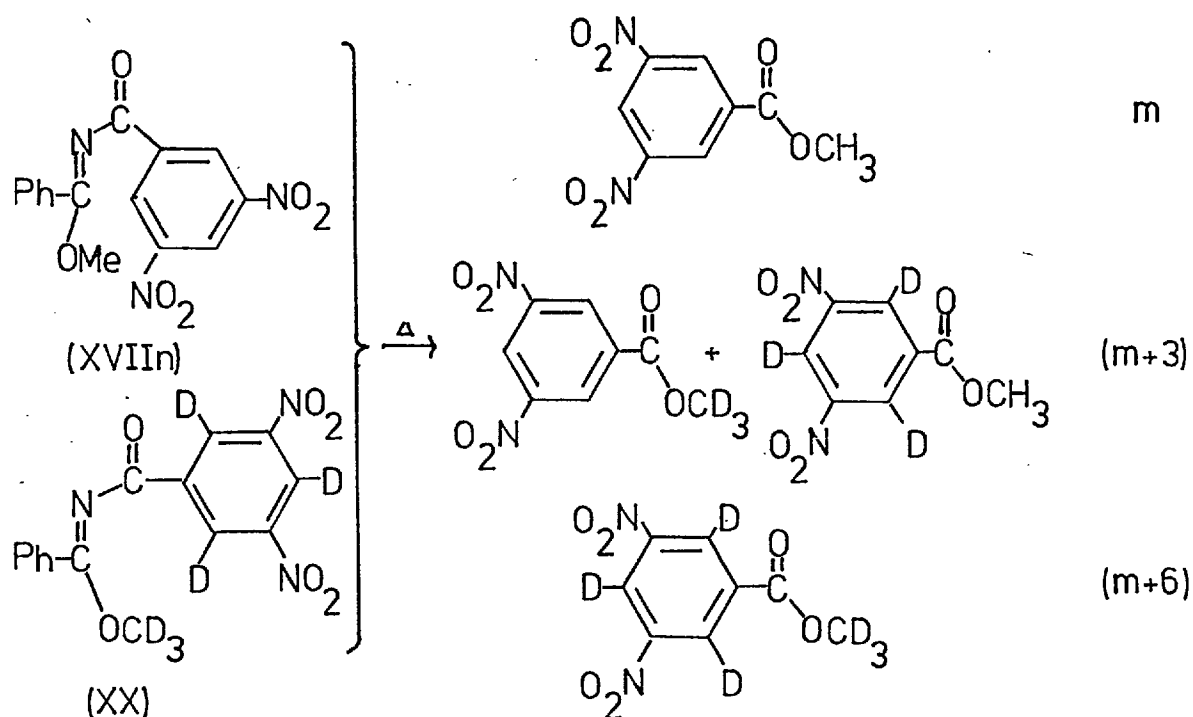


SCHEME 8

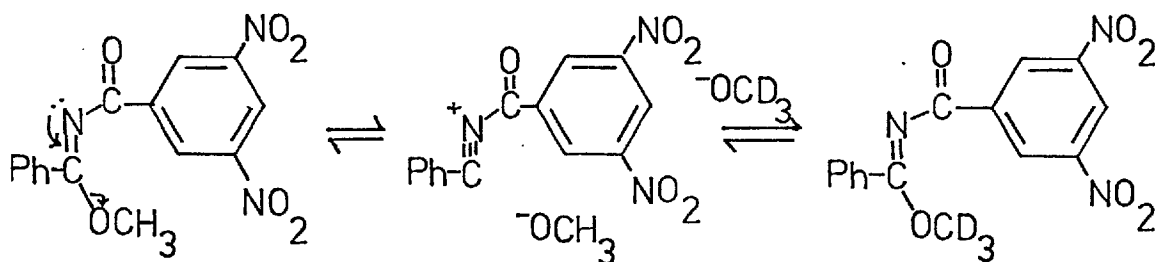
The predominance of methyl-3,5-dinitrobenzoate in the pyrolysis immediately indicates that this system is amenable to study for prepyrolysis interconversion to imidate (XVIIIn), and also that this latter compound (XVIIIn) could be the ideal model for deuterium studies. Synthesis of imidate (XVIIIn), and pyrolysis, indicated the same products as for the pyrolysis of (XVIIIm), (Scheme 8), in very similar yields.

Consequently imidate (XVIIIm) was studied for prepyrolysis interconversion to (XVIIIn), by heating samples, in sealed tubes, for increasing lengths of time, but here again N.M.R. only indicated the gradual production of pyrolysis products. The study was even undertaken in a flow apparatus (see experimental), with the hope of

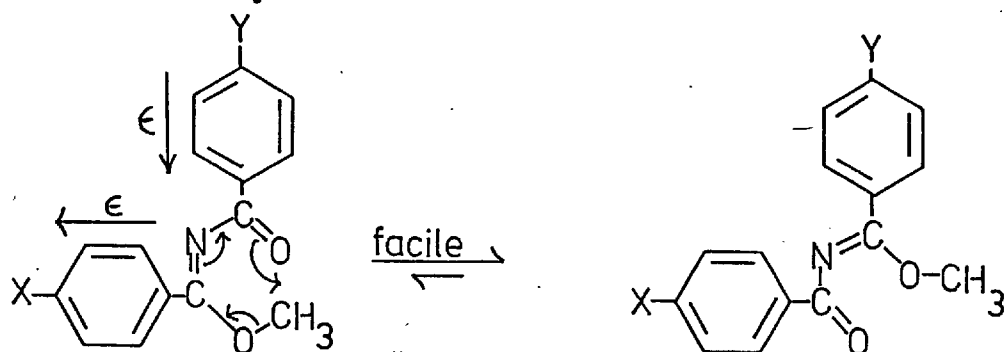
flushing out the imidate (XVIIIn) before it could pyrolyse, but there was no trace of imidate (XVIIIn). The deuterio analogue of imidate (XVIIIn), (XX), was prepared and the copyrolysis of (XXVIIIn) and (XX) carried out in the flow apparatus, isolating the methyl-3,5-dinitrobenzoate from the cold part of the apparatus. This would hopefully eliminate any possible exchange of alkoxy groups in the esters, although this is unknown in the literature³³. The mass spectrum of this ester showed m , $(m+3)$, $(m+6)$ in a 1:2:1 ratio, clearly indicative of an intermolecular rearrangement.



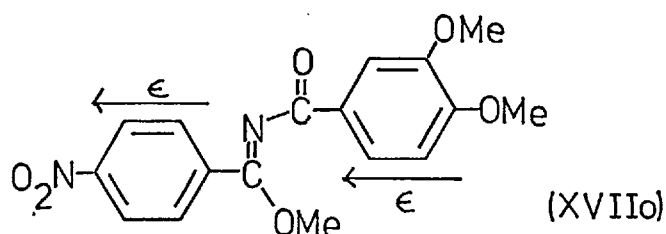
However the possibility of alkoxy exchange in the imidates themselves must not be precluded, as it would theoretically yield an identical result, and the pyrolysis itself could be intramolecular.



Consideration of the aromatic substituents, coupled with the pyrolysis products of N-acyl imidates (XVII), led to the preparation of a further imide, with the hope of seeing the prepyrolysis interconversion. It would seem that the more electron withdrawing the substituent is on Ar, the greater is the proportion of ester arising from the pyrolysis of the interconversion imide. Consequently if this electron flow is aided by electron donating substituents in Ar¹, the ease of interconversion should be enhanced.

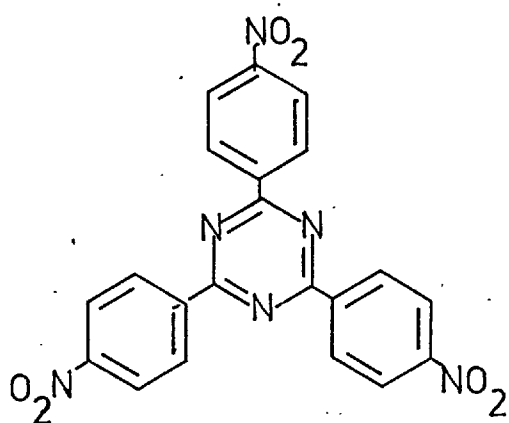


To test this hypothesis, N-3,4-dimethoxybenzoyl-methyl-p-nitrobenzimidate (XVIIo) was synthesised and pyrolysed.

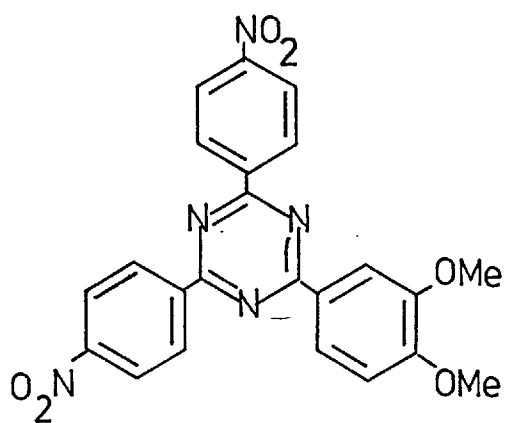


This did indeed give methyl-p-nitrobenzoate on pyrolysis, along with veratronitrile, as the main products. This was the first time a major amount of any nitrile had been isolated, and raises the question whether the triazines are formed by "acid catalysed" trimerisation of free nitriles produced on pyrolysis? No methyl-3,4-dimethoxy-benzoate was detected, but running concurrently

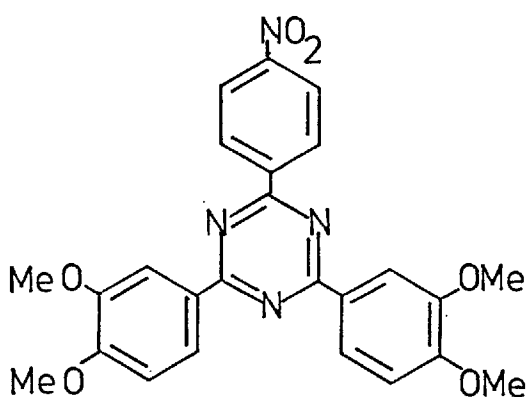
with the two major bands were small amounts of triazines. The mass spectrum showed ions corresponding to 474, 459, 444, 429 ($459, 429 \gg 474, 444$) for the fraction of higher R_f , and ions 489, 474, 459, 444 ($474, 444 \gg 489, 459$) for the lower R_f triazine. The possible triazine structures are depicted below:-



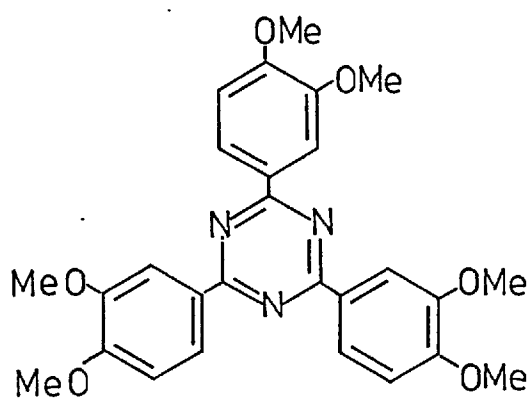
(XVIIIId)

 $m^+_{/e} 444$ 

(XVIIIIf)

 $m^+_{/e} 459$ 

(XVIIIIf)

 $m^+_{/e} 474$ 

(XVIIIIf)

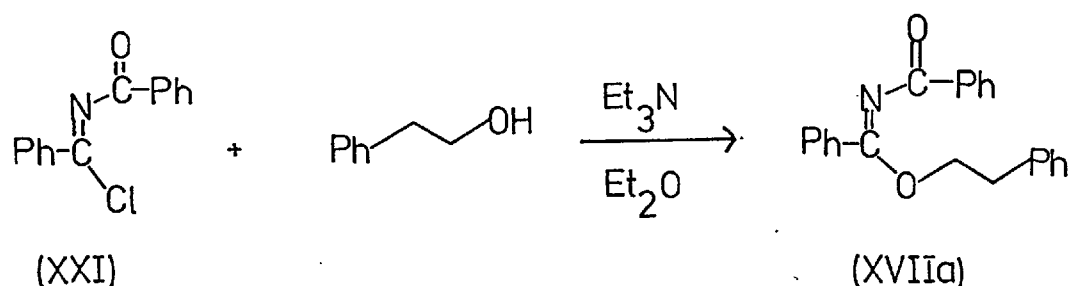
 $m^+_{/e} 489$

Unfortunately it is impossible to say unequivocally whether all four triazines are present, as both anisole³⁴ and aromatic nitro compounds³⁴ show loss of a fragment measuring 30 mass units in the mass spectrum. The latter fact was shown independently from the mass spectrum of authentic tri-p-nitrophenyl triazine (XVIIIId) (m^+/e 444, 414).

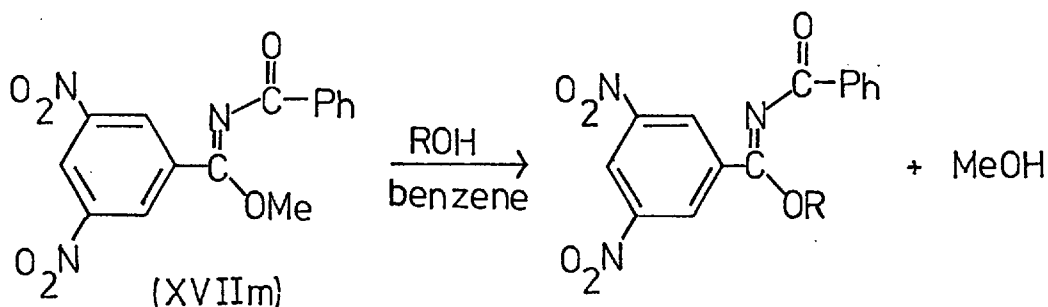


The proposed [1,5] sigmatropic rearrangement prior to pyrolysis should occur with retention of configuration at the migrating carbon^{34a}. This should be easily demonstrated by isolation of the requisite ester from pyrolysis of an imidate prepared from an optically active alcohol, and showing it to have the same rotation as the authentic ester.

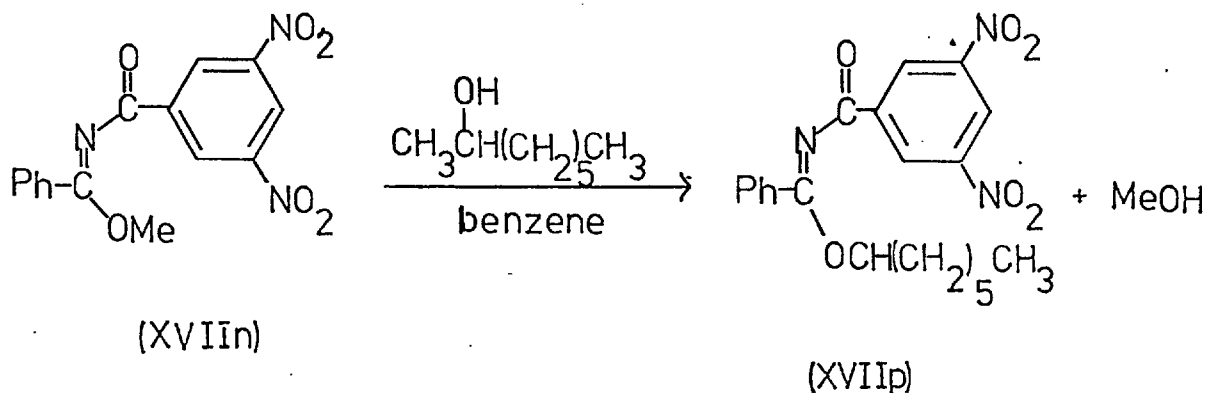
Suitable secondary alcohols are octan-2-ol or cholestanol. Early on, the Pinner synthesis of the appropriate imidate hydrochlorides had been attempted, but with little success. Also the alternative mode of preparation from N-benzoyl-phenylimino chloride (XXI) and cholestanol was tried, but without success, although reaction of (XXI) with β -phenethyl alcohol, in the presence of triethylamine, gave the imidate (XVIIa), identical in all respects to that prepared from benzoylation of the imidate hydrochloride (XIVa).



However the facile exchange between ethoxy and methoxy groups, which occurred on crystallisation of imidate (XVIIIm) from chloroform containing ethanol, (ca. 1% used as stabiliser) offers a potential new route to the synthesis of imidates from sterically hindered, or highly insoluble alcohols.



Initially the exchange was carried out between imidate (XVIIIn) and octan-2-ol, by codistillation of benzene and methanol, and the crystalline imidate (XVIIIp) was fully characterised.

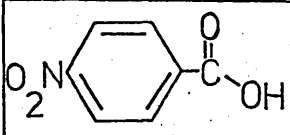
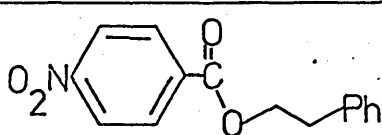
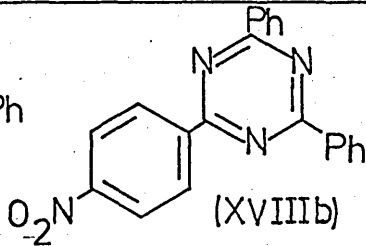
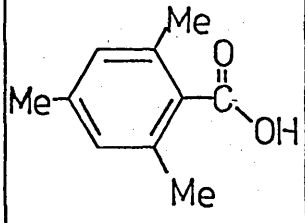
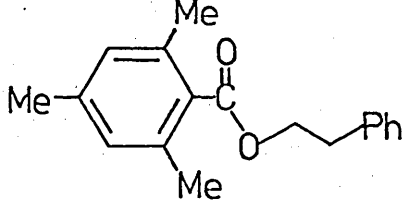
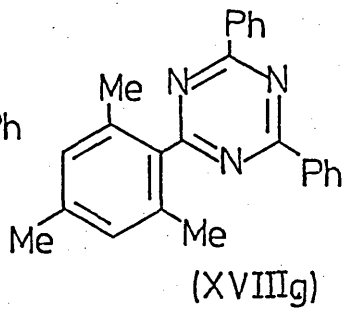
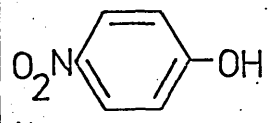
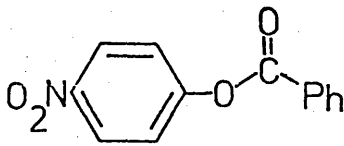
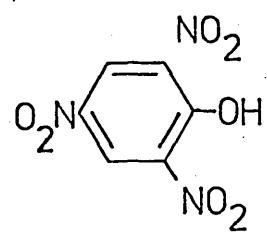
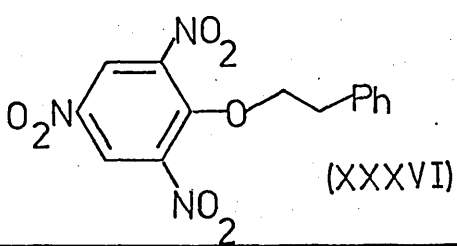


This inability to crystallise these imidates was a hindrance, but the work using d-octan-2-ol was still carried out, and the imidate (XVIIq*), characterised by its mass ion, pyrolysed. The 3,5-dinitro ester produced had $[\alpha_D] + 26.8^\circ$ (m.pt. $43.5-50^\circ\text{C}$ constant), as compared with the authentic d-2-octyl-3',5'-dinitrobenzoate $[\alpha_D] + 32^\circ$ (m.pt. $50.5 - 53^\circ\text{C}$). This is not unequivocal evidence for the prepyrolysis interconversion as the [1,5] sigmatropic rearrangement does involve oxygen exchange, the acyl oxygen in the imidate becoming the ether oxygen in the ester produced on pyrolysis. This latter point could easily be demonstrated by the use of an oxygen - 18 label on the carbonyl, and subsequent determination of its position in the pyrolysis ester, and is discussed later.

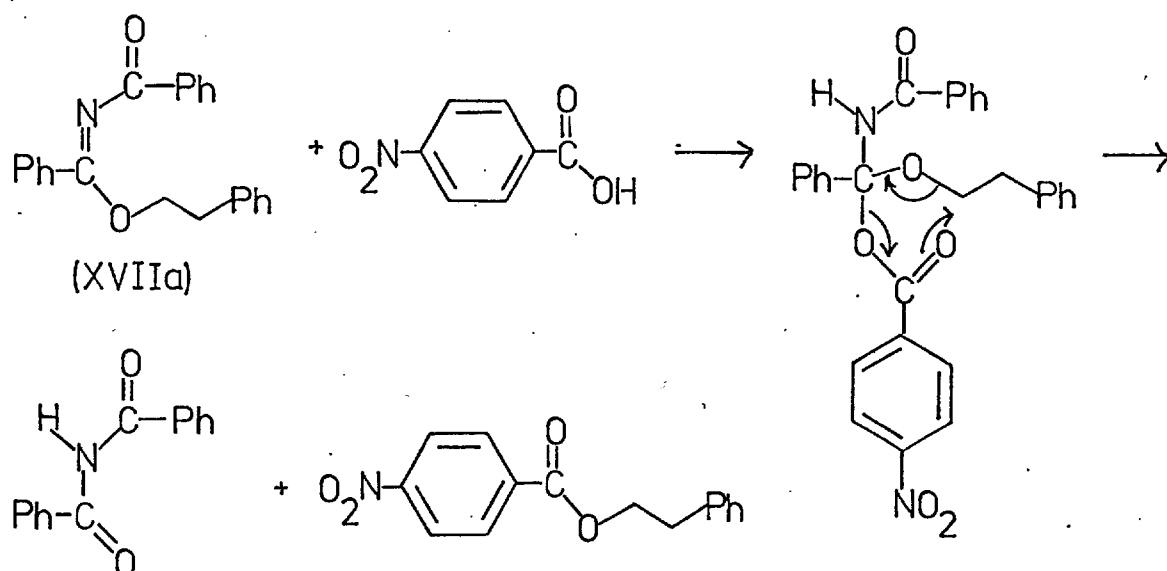
Early on, work had been carried out to see whether the pyrolysis of the imidate (XVIIa) was enhanced, or retarded by acid or base, and other additives. However monitoring reactions containing β -phenethyl alcohol or diisopropyl ethylamine at 190°C (using boiling decalin in a kinetic flask) failed to show enhancement of reaction rate, when compared with a blank (t.l.c. and product isolation). Also acetic acid, boron trifluoride and triethylamine (15-20mg) were pyrolysed with imidate (XVIIa), (200mg), but only at 100°C in a sealed tube. In every case t.l.c. showed no pyrolysis and the starting imidate (XVIIa) was recovered.

Subsequently, "catalysis" by p-nitrobenzoic acid was attempted on imidate (XVIIa), and enhanced reaction rate

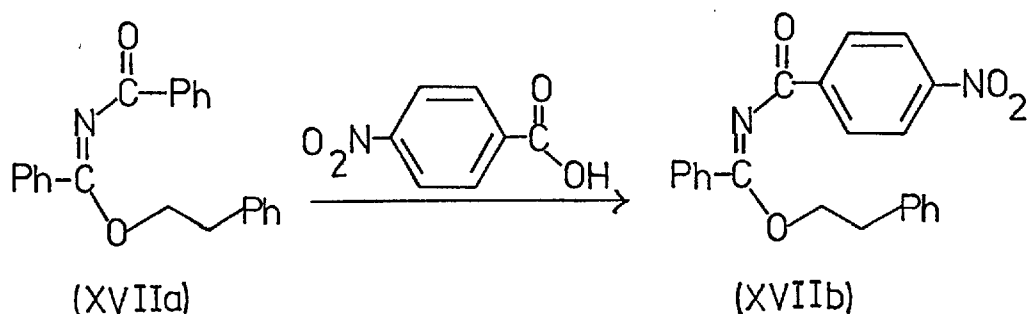
was obvious (t.l.c.), and also the production of two new products. Other "acid catalysts" were employed, and all showed enhancement in the rate of production of triazine (XVIIIa) and β -phenethyl benzoate, as well as being incorporated in the reaction, to give new products summarised below.

"Catalyst"	Time hrs.	Temp. °C	New Products
	4	210	  (XVIIIb)
	20	210	  (XVIIIg)
	17½	210	
	1	145	 (XXXVI)

These results are difficult to explain with just one mode of attack. In "catalysis" reaction (1) the ester formation may be looked on simply as addition, followed by a rearrangement.

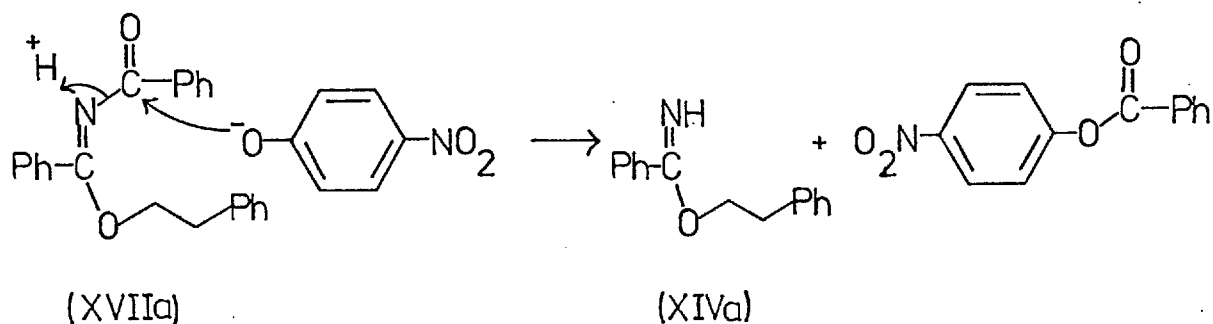


But the triazine formation is inexplicable unless replacement of the acyl function on nitrogen is envisaged.



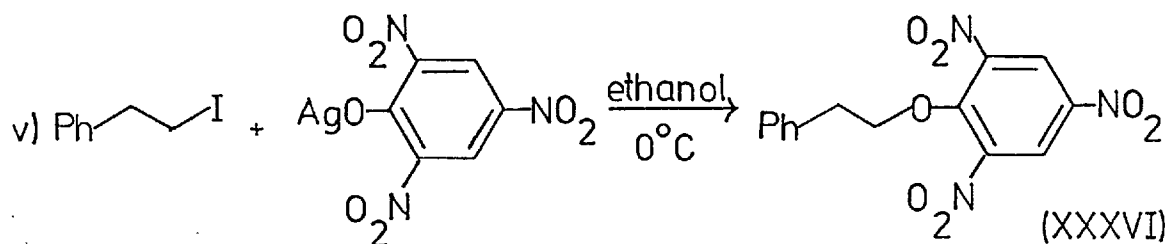
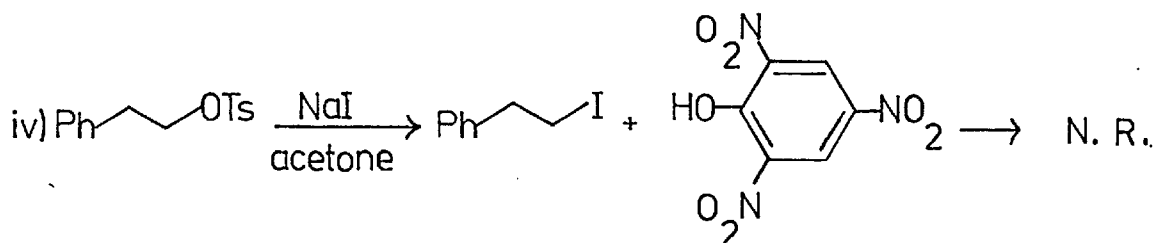
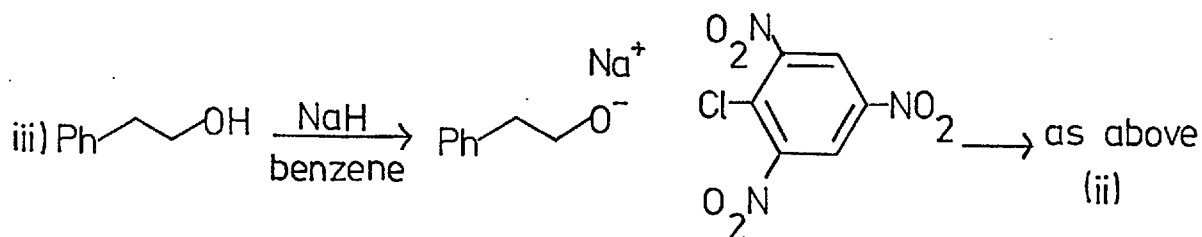
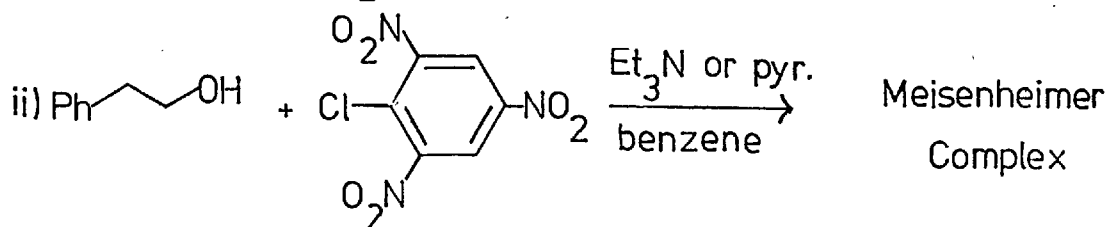
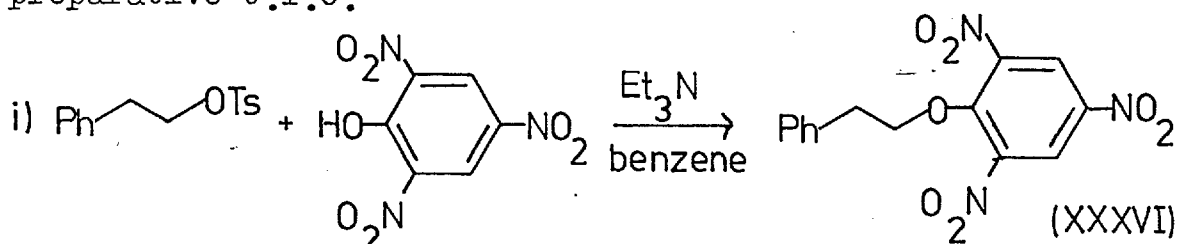
A sterically hindered acid, such as mesitoic acid, might be thought not to undergo this "catalysis", but although a slightly greater reaction time was required, the analogous products resulted.

The "catalysis" with *p*-nitrophenol was unexpected, but must be explained as arising from attack at the carbonyl group of the acyl residue.



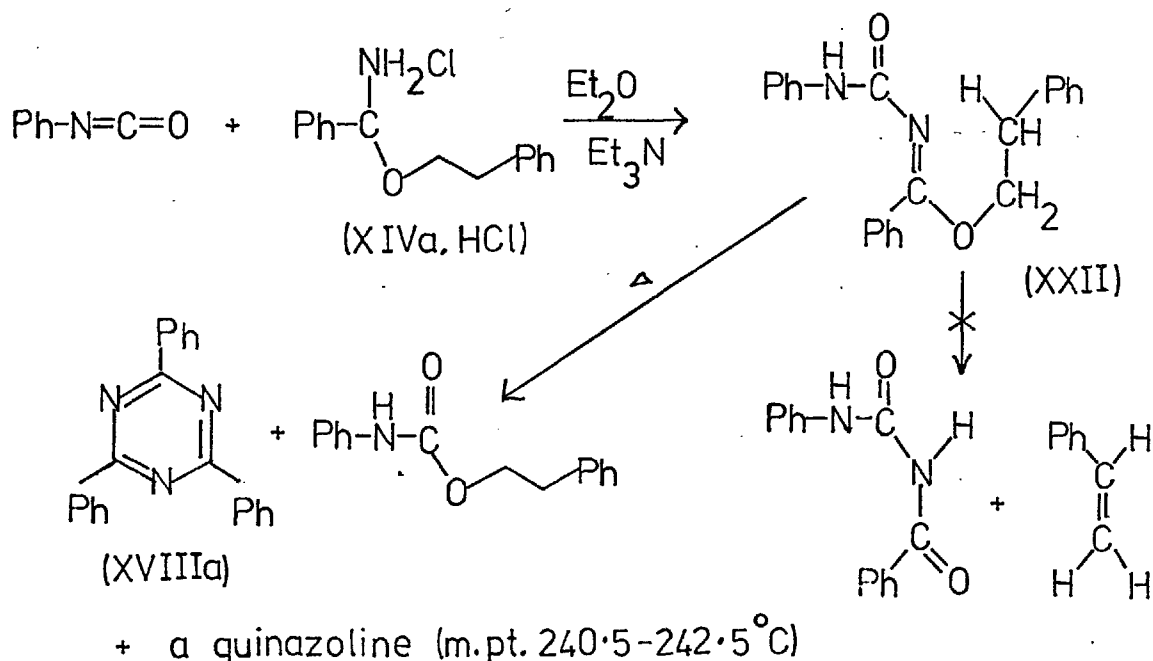
However the facility of pyrolysis in the presence of picric acid remains a complete mystery, as pyrolysis of the imidate (XVIIa) alone is only truly evident after 24 hours at 145°C .

Unexpectedly, the picryl ether (XXXVI) was unknown in the literature, and so an authentic sample was prepared. This was not quite so simple as may be thought, and several syntheses were attempted, eventually (XXXVI) was obtained using the initial synthesis (i) on a larger scale, and separating the product, in poor yield, by preparative t.l.c.



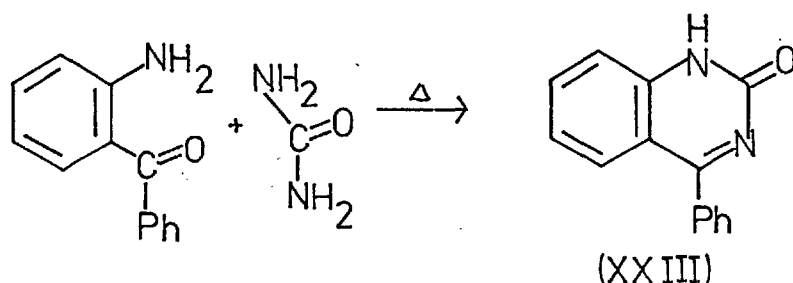
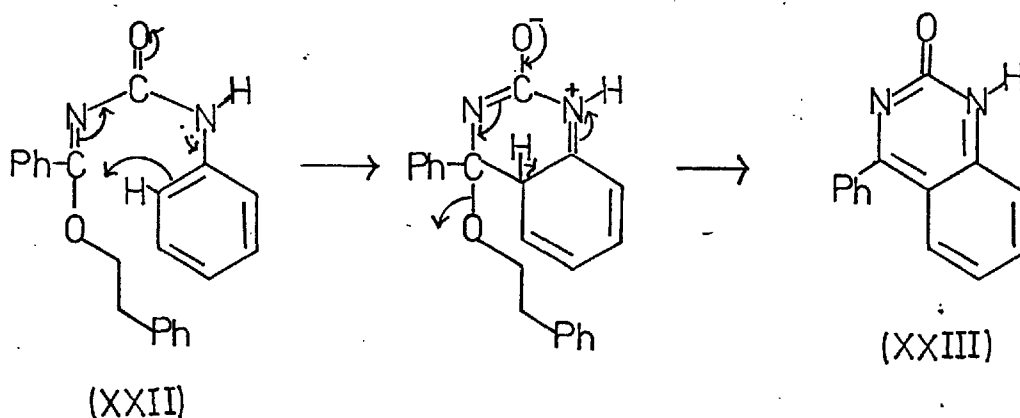
Only the reactions (i) and (v) showed the required product, reactions (ii) and (iii) gave immediate bright red colourations, which were attributed to Meisenheimer complexes³⁵, which on the addition of acid just regenerated starting material. In reaction (iv) a precipitate was noticed, indicating that the 1-iodo-2-phenyl-ethane had probably formed, but the subsequent addition of picric acid gave none of the desired ether. This however prompted the authentic synthesis of the iodide, and reaction with silver picrate (v).

At this juncture, a reference to the reaction of phenyl isocyanate with imidate hydrochlorides³⁶ was thought to be worth investigation, as the products might undergo pyrolysis to yield styrene.



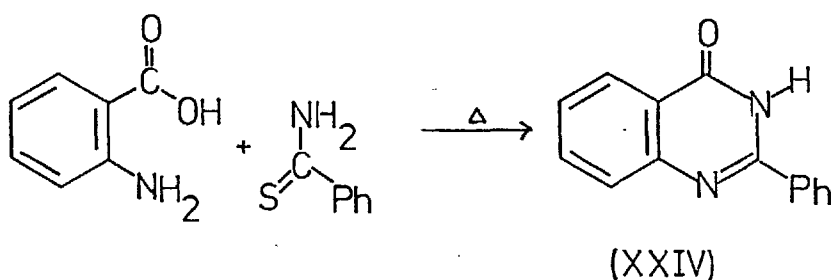
This did not occur, but instead, 2,4,6-triphenyl-1,3,5-triazine (XVIIIa) and β -phenethyl-N-phenyl urethane were

formed, paralleling the pyrolysis of imidates. Also present was an unidentified product, which, after analysis was considered to be a quinazoline³⁷, and 1,2-dihydro-4-phenyl-2-oxoquinazoline (XXIII) could conceivably be produced.

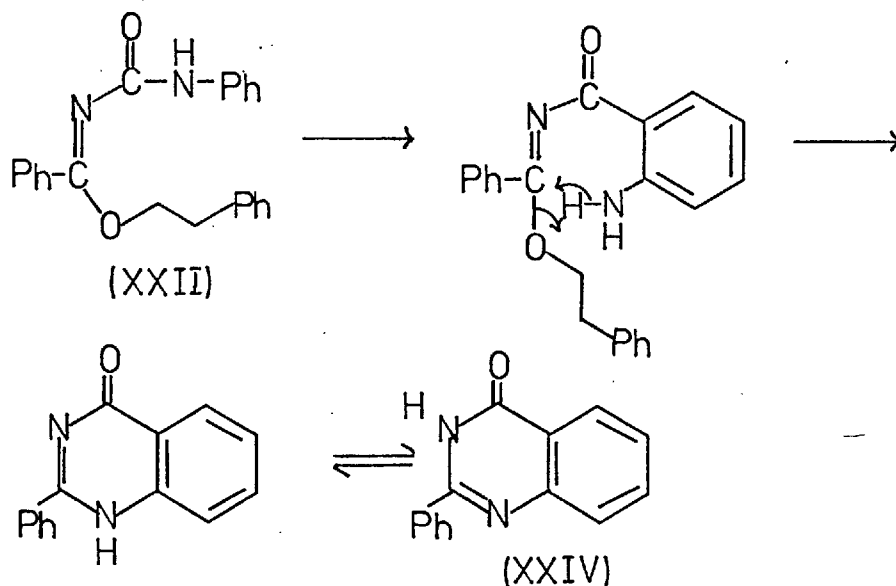


The literature melting point for (XXIII) was 250-251°C³⁷, which was rather high, and synthesis of (XXIII) from 2-aminobenzophenone and urea³⁷ showed it was not the pyrolysis product.

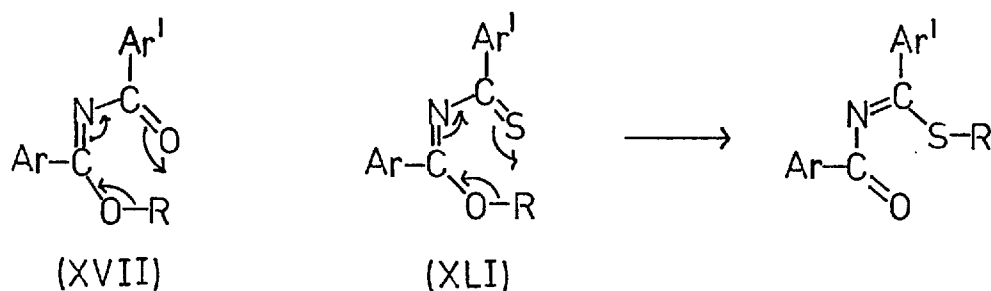
The other possible alternative structure, from a consideration of melting point was 2-phenyl-4-oxoquinazoline (XXIV)³⁸, and synthesis of this from anthranilic acid and thiobenzamide proved it to be identical to the quinazoline from pyrolysis of (XXII).



This is more difficult to explain mechanistically, as any mechanism involving the production of aniline, and subsequent recombination is unlikely. A suitable rationale is forthcoming if an initial Fries type rearrangement³⁹ occurs, with subsequent ring closure.

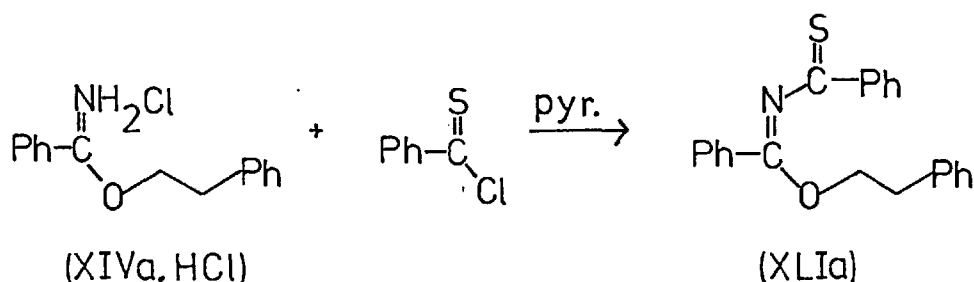


No further work on this topic was undertaken, instead further evidence for the [1,5] sigmatropic rearrangement of *N*-acyl imidates (XVII), prior to pyrolysis was sought, using the sulphur analogue (XLI).

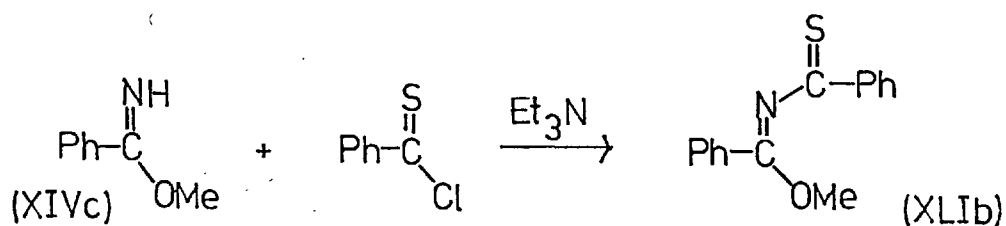


If (XLI) could be synthesised, a consideration of the bond energies indicates that the [1,5] sigmatropic rearrangement would be very labile, and hopefully this would facilitate the isolation of the prepyrolysis interconversion isomer.

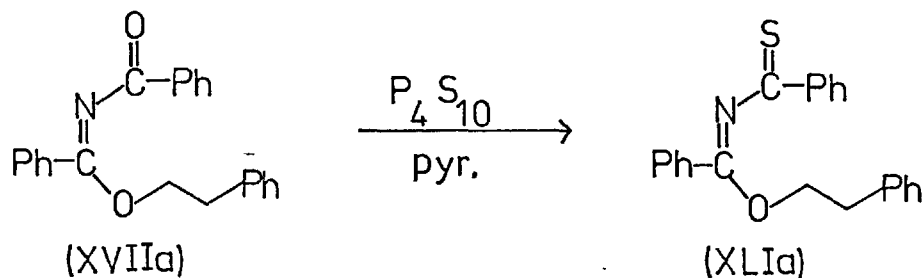
The obvious synthesis of the model (XLI) employs the reaction of the imidate hydrochloride (XIVa.HCl) with thiobenzoyl chloride⁴⁰. This reaction was very complex (t.l.c.) only benzamide being isolated and characterised.



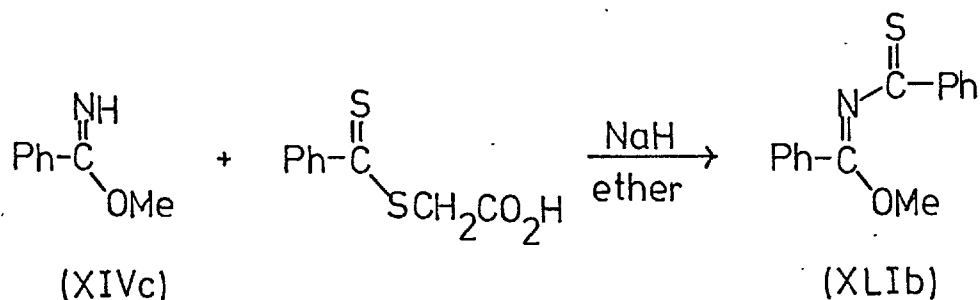
In case the pyridine was decomposing the thiobenzoyl chloride, the reaction was repeated on the free imidate (XIVc), under nitrogen, using triethylamine as base, but again no evidence of the required product was found.



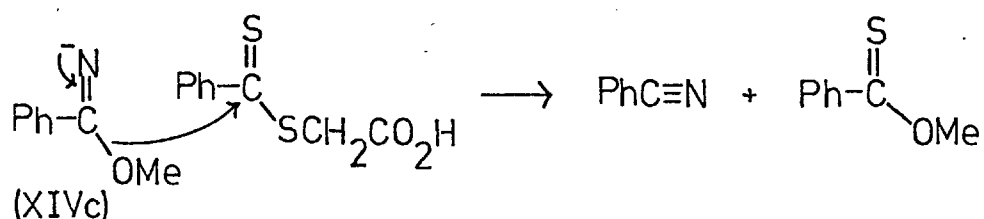
Also treatment of the N-acyl imidate (XVIIa) with phosphorus pentasulphide⁴¹ should result in thionation, but this also failed, starting material being present.



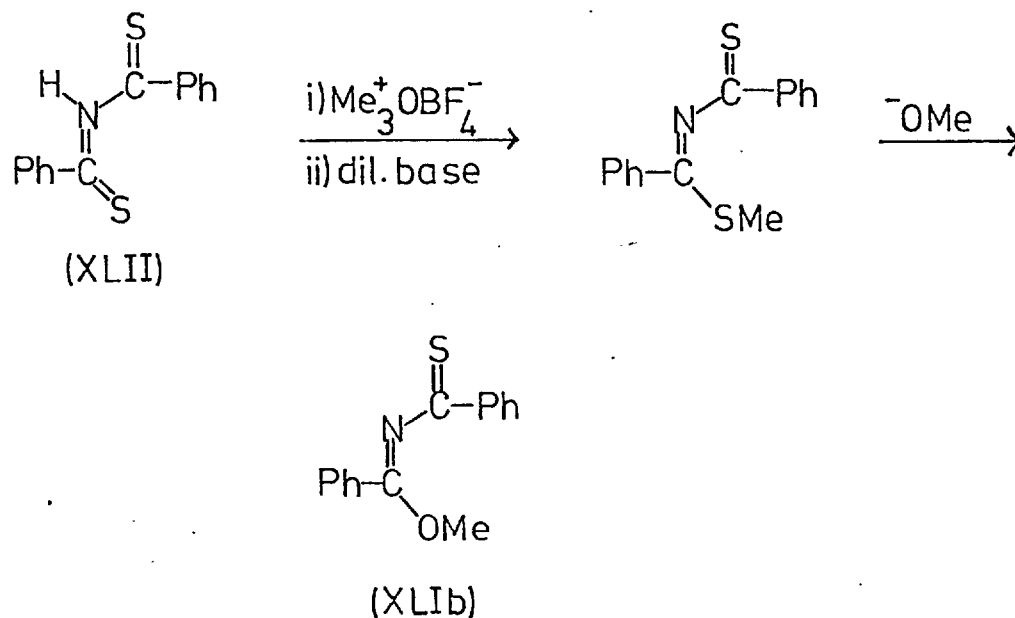
The possibility of thioacylating a free imidate with phenyl thioglycolic acid⁴² was next investigated.



The anion of the imidate (XIVc) was formed using sodium hydride, and reacted with phenyl thioglycolic acid. The resultant products, after removal of the sodium salt, were methyl thionbenzoate and benzonitrile, which were explained by collapse of the anion of (XIVc) to benzonitrile and attack by methoxide on the thioglycolic acid.

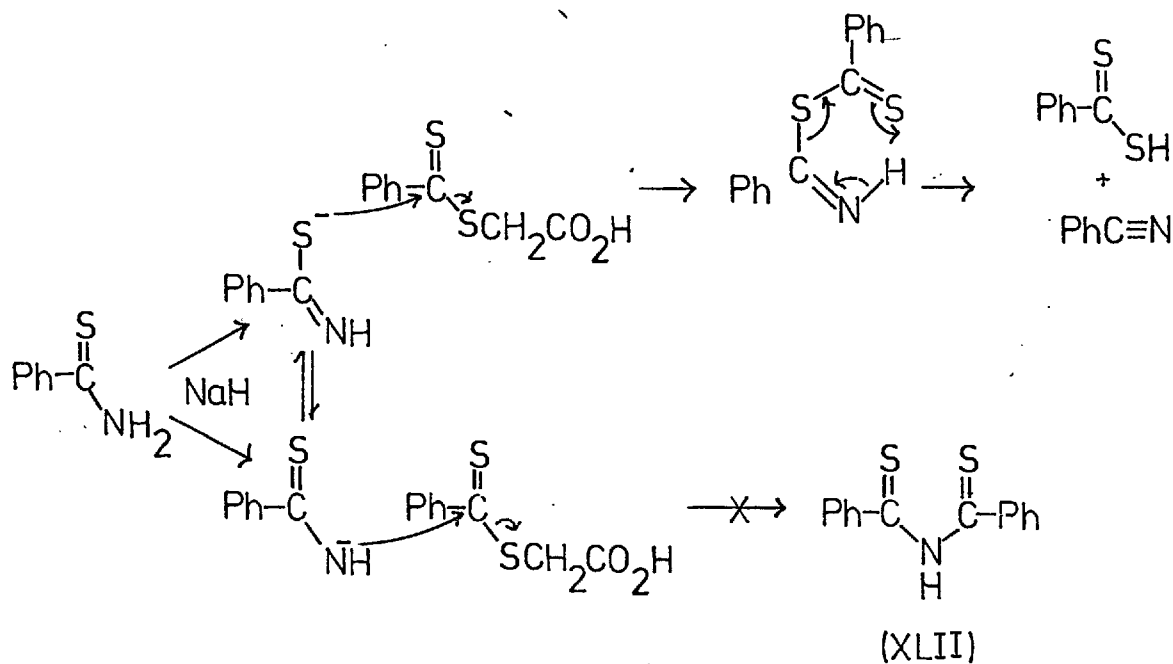


As this direct route to synthesis had failed, a synthesis using dithiobenzamide (XLII) was attempted.

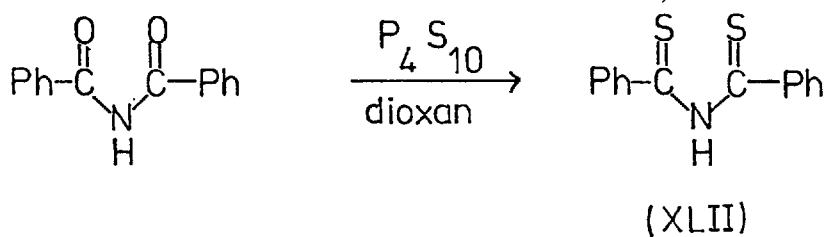


However a literature search showed that dithiobenzamide (XLII) was itself unknown, although monothiodibenzamide (XXVIII) was known⁴³.

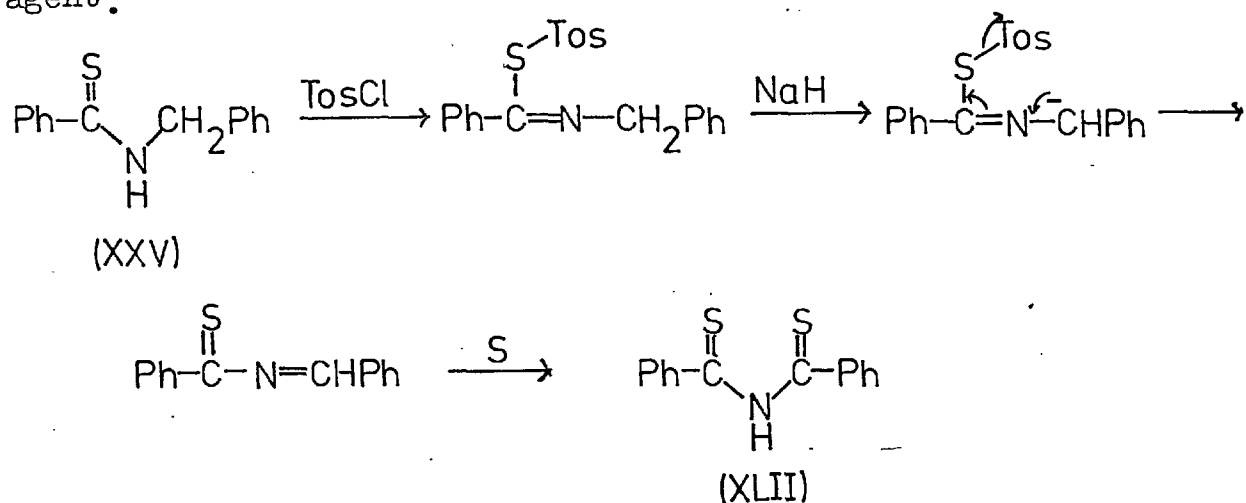
Initially thiobenzamide was reacted with sodium hydride, to give the anion, and this was subsequently reacted with phenyl thioglycolic acid. The t.l.c. was very complex, showing 6 spots active to palladous chloride, and considering the electron distribution of the anion, it is obvious that attack can occur through sulphur as well as nitrogen.



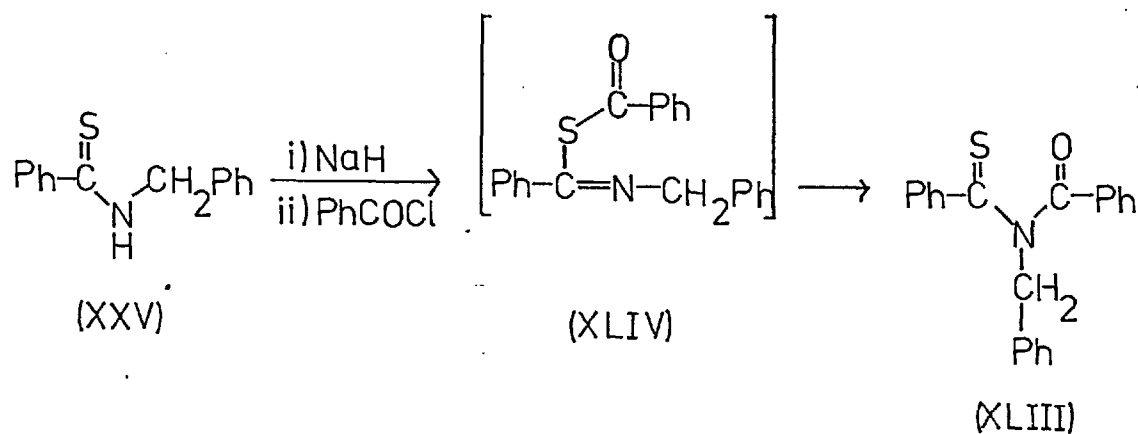
The thionation of dibenzamide, using phosphorus pentasulphide was also attempted, without success, although some reaction had occurred.



A less direct synthetic route, using N-thiobenzoyl benzylamine (XXV), synthesised from benzylamine and sulphur^{44,45}, was now undertaken. This involved tosylation on the sulphur, subsequent elimination by forming the anion, and final treatment with a sulphurising agent.



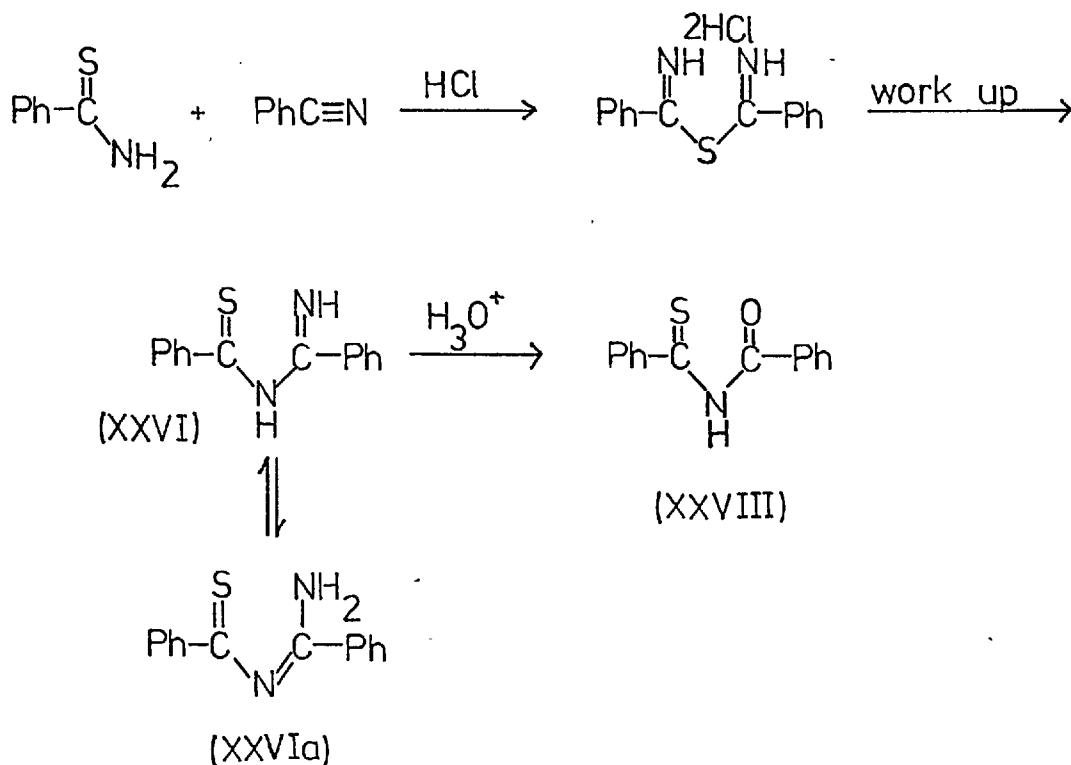
Initial reactions with tosyl chloride failed completely,⁴⁶ but there was a reference to benzoylation on the sulphur, by formation of the anion of (XXV) with sodium, and subsequent reaction of the sodium salt with benzoyl chloride. This also failed, using tosyl chloride, and so the literature preparation was undertaken. The product was shown to be the amide (XLI) rather than the structure (XLIV), given in the literature.



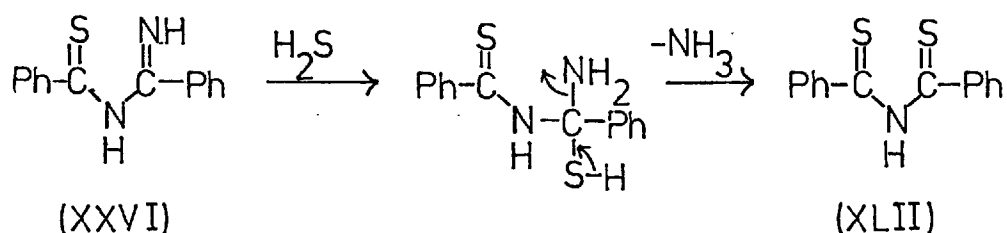
The evidence for this was twofold, firstly there was no infrared absorption attributable to the carbon-nitrogen double bond, and secondly from quantitative U.V. studies⁴⁷, these showed a weak absorption λ_{max} 470 nm ($\log \epsilon$ 2.297), which was attributed to the $n \rightarrow \pi^*$ transition of $>\text{C}=\text{S}$. This was substantiated by the orange colouration of the product (XLIII).

Naturally the reaction of (XXV) with excess sulphur, and the preparation of (XLII) from benzylamine with excess sulphur, were attempted, but only *N*-thiobenzoyl benzylamine (XXV) was isolated, although t.l.c. did show the presence of one other material.

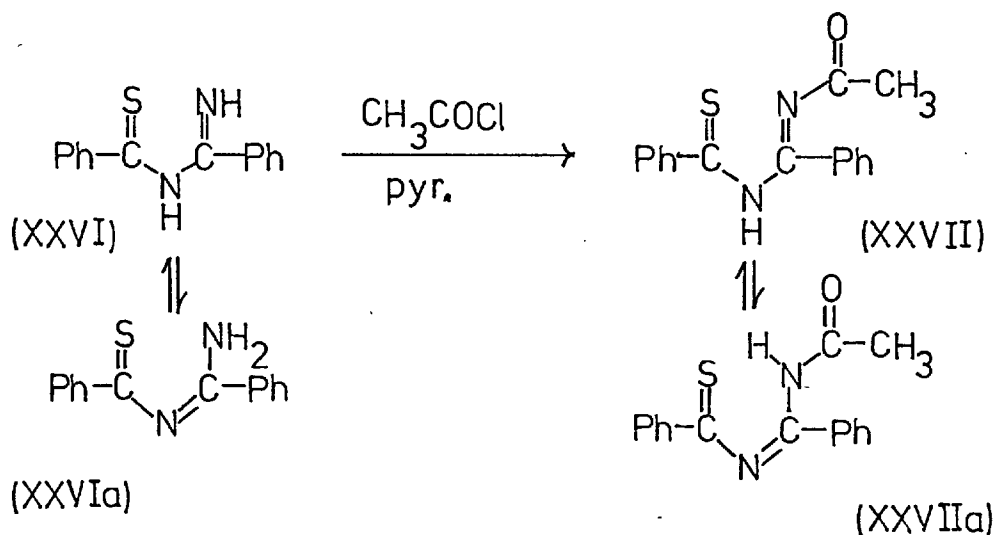
Next reactions on *N*-thiobenzoyl benzamidine (XXVI), prepared from thiobenzamide and benzonitrile in the presence of HCl, and liberation of the free base from the hydrochloride, and monothiodibenzamide (XXVIII), obtained by acid hydrolysis of (XXVI) were studied.



Initially the reaction of excess H_2S on amidine (XXVI) was studied in various solvents, but no new sulphur containing products appeared (t.l.c.), instead sulphur precipitated out of the reaction.



When the reaction was conducted in acetic anhydride, a new spot (t.l.c.) appeared, but this was attributed to the acetylation product (XXVII), and was subsequently prepared.

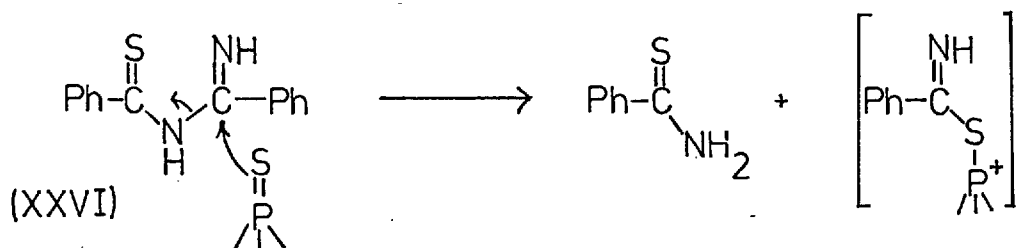


The structure (XXVII) for the product was proposed, as the N.M.R. of (XXVI) showed two distinct >NH protons, tending to rule out structure (XXVIa), although the position of the hydrogens is of minor importance.

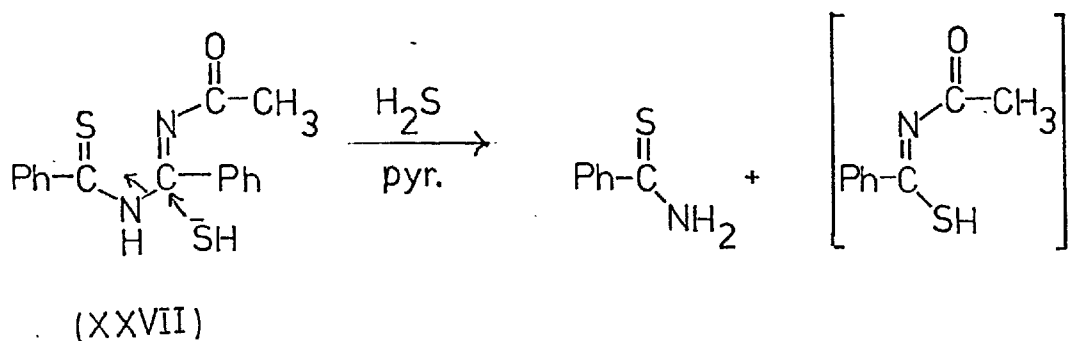
Acylation on sulphur has been disproved, and the compound possessed a weak $n \rightarrow \pi^*$ transition of >C=S anyway (U.V.).

Although two separate protons can be seen for (XXVI), a structure (XXVIIa) would be possible after acetylation, and this latter structure fits the I.R. data for the carbonyl (ν 1720 cm^{-1}) and carbon-nitrogen double bond (ν 1645 cm^{-1}); which seem unconjugated, when compared with N-acyl imidates (XVII), I.R. ν 1660, 1640 cm^{-1} .

However its reaction with H_2S is more easily explained by the conjugated structure (XXVII), discussed subsequently. The amidine (XXVI) was next treated with phosphorus pentasulphide in dioxan, to yield two sulphur containing new compounds, however isolation of the major component showed it to be thiobenzamide, which would arise by cleavage of the carbon-nitrogen single bond concomittantly with attack by phosphorus pentasulphide.

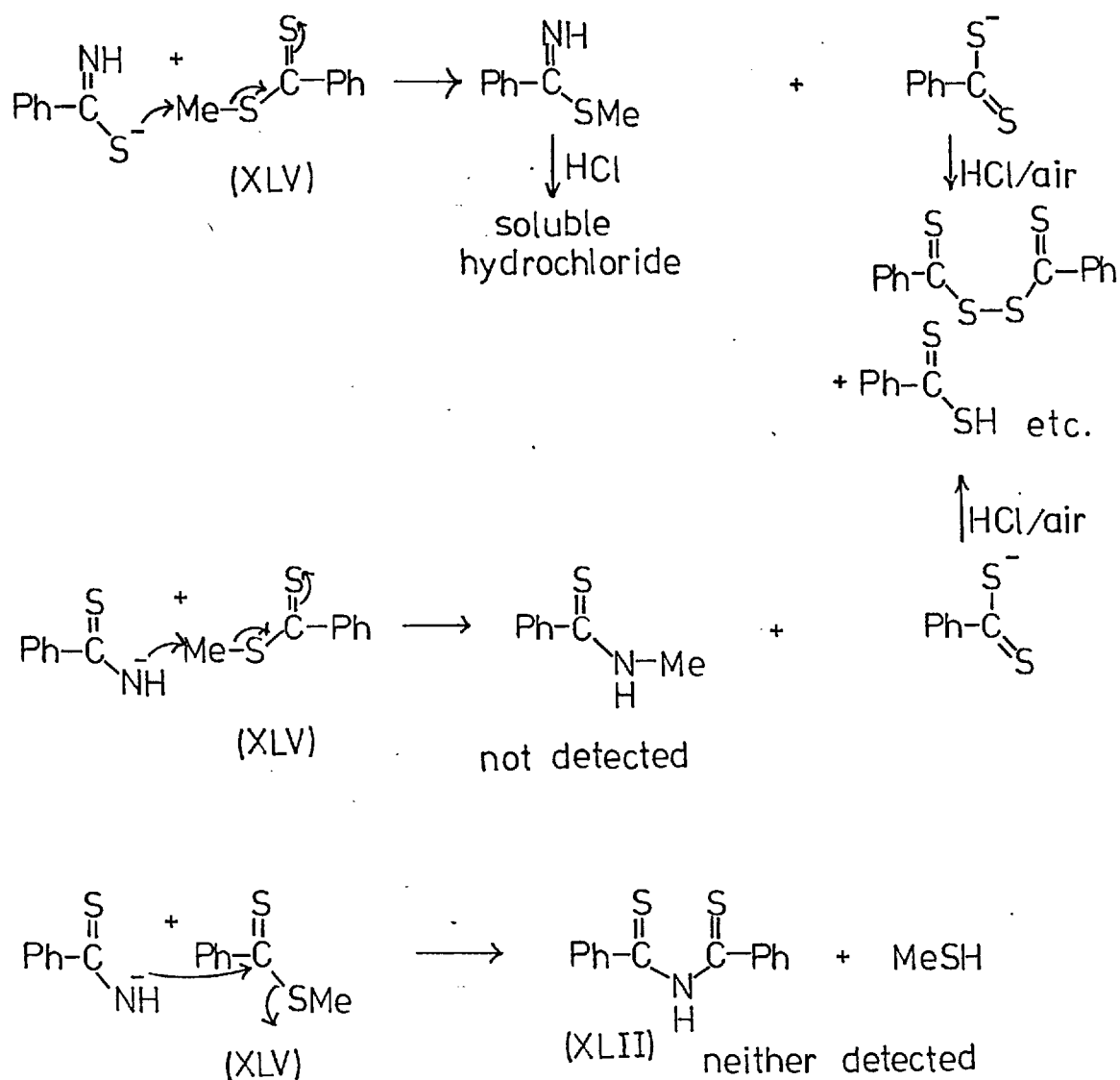


Finally reaction of N-acetyl-N-thiobenzoyl-benzamidine (XXVII) with H_2S was investigated, using pyridine as solvent. This again produced thio-benzamide, presumably in an analagous fashion to the reaction of P_4S_{10} with the parent amidine (XXVI).



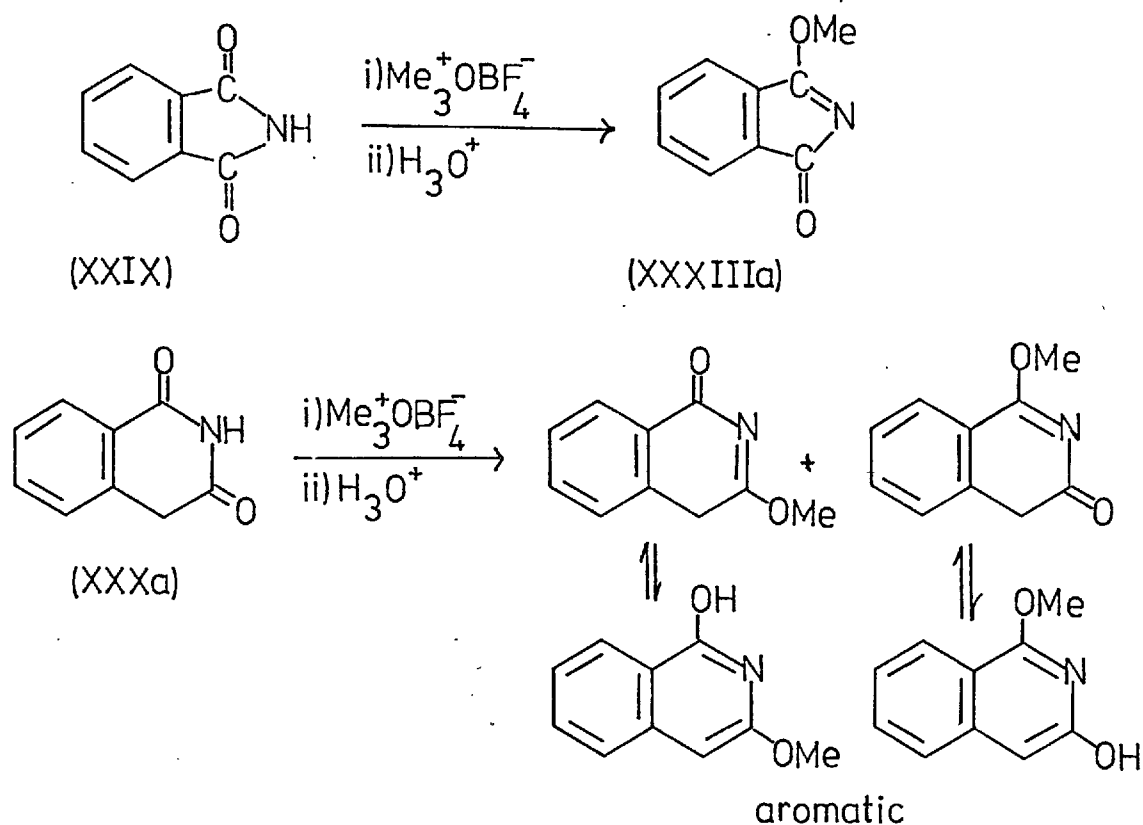
Monothiodibenzamide (XXVIII) was also treated with phosphorus pentasulphide, but although a reaction was apparent, no new sulphur containing spots could be detected (t.l.c./PdCl₂).

A last attempt at the synthesis of dithiobenzamide (XLII) was made, by reacting the anion of thiobenzamide with methyl dithiobenzoate (XLV). However the attack apparently proceeded through the sulphur (Scheme 9), as on acid work up only dithiobenzoyl disulphide, along with other oxidation products (or mass spectral fragmentation products) was detected.



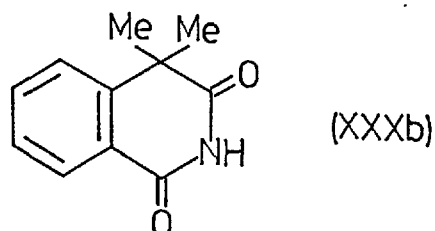
SCHEME 9

Consideration of the stereochemistry of imidates (XVII) at the carbon-nitrogen double bond, led to the attempted synthesis of models with a fixed configuration, for comparison of the methoxyl shift in N.M.R.

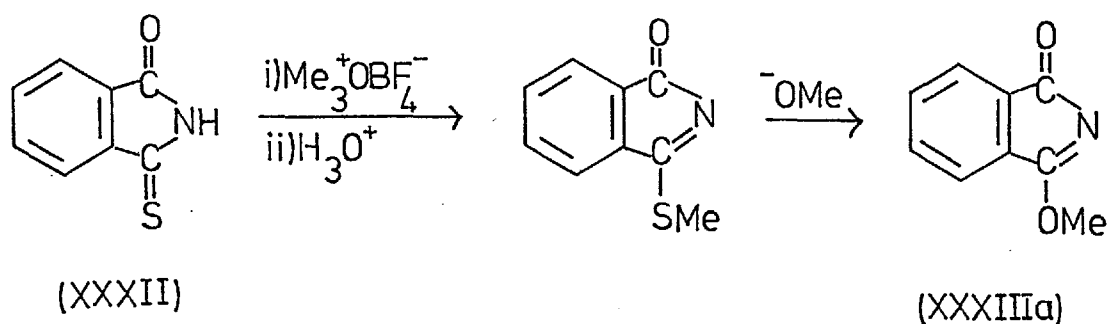


Both phthalimide (XXIX) and homophthalimide (XXXa) were treated with trimethyloxonium tetrafluoroborate in dichloromethane, hopefully to give the 'O' alkylated products, paralleling the reaction with amides. The reaction was inhomogeneous, and unreacted starting material was recovered in both cases. On further consideration of the homophthalimide reaction, it was obvious that this was a poor choice, for although preferential attack on one carbonyl could be hoped for, it is probable that either of the products would rearrange spontaneously to the aromatic tautomer. A much better

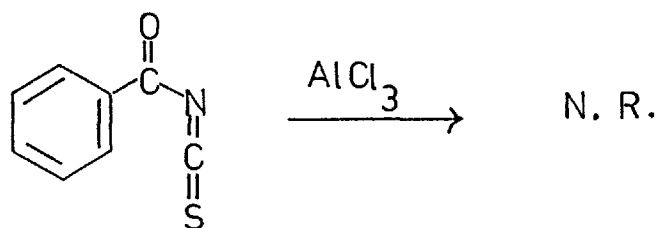
model would have been the dimethyl derivative (XXXb), where rearrangement to the preferred aromatic system was impossible.

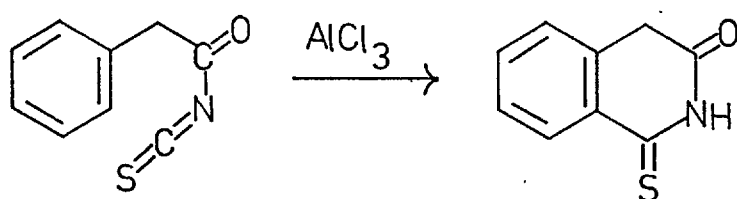


Monothiophthalimide (XXXII) was next studied, with the idea that methylation on sulphur would be facilitated, and then subsequent attack by methoxide would yield the model of known stereochemistry (XXXIIIa).

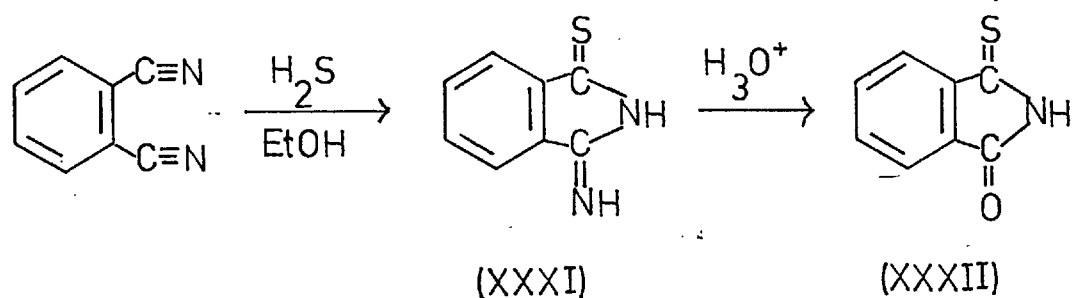


The preparation of (XXXII) was now undertaken, but the initial literature citation⁴⁸, for the cyclisation of benzoyl isothiocyanate was found not to occur when the original literature was referred to⁴⁹. The presence of electron donating substituents being necessary to afford cyclisation, the reaction only being generally applicable to synthesis of six membered rings.

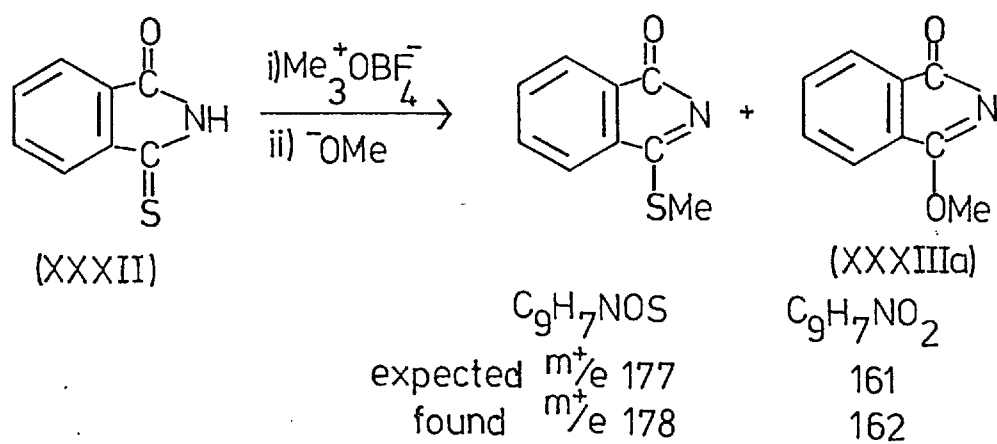




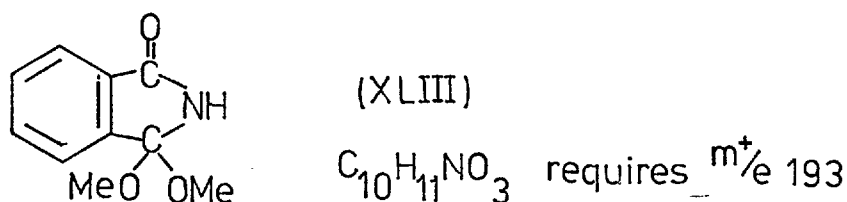
Instead the conventional route, involving the acid hydrolysis of 1-imino-3-thioisoindoline (XXXI)⁵⁰, was used to synthesise (XXXII).



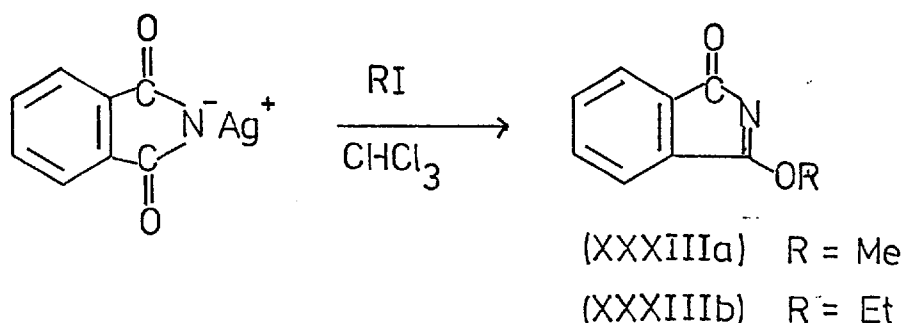
The methylation of (XXXII) with methyl Meerwein's salt was monitored by the disappearance of the red colouration, but unfortunately on work up phthalimide was obtained. Due to the obvious instability of the methylated intermediate, the reaction was repeated, and immediately treated with excess methoxide. The resultant solid, from evaporation of solvent showed 4 spots on t.l.c., but the mass spectrum was unusual, in the fact that the expected ions were not found, instead, ions of mass one unit greater were observed.



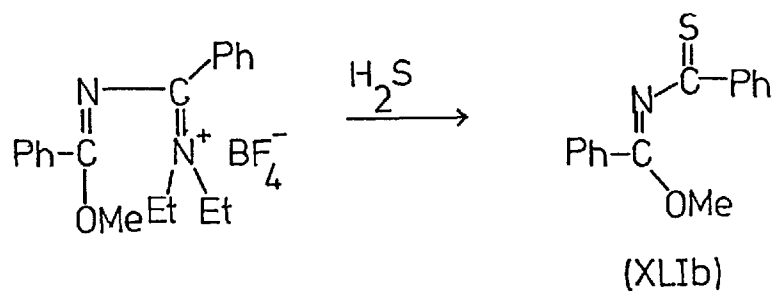
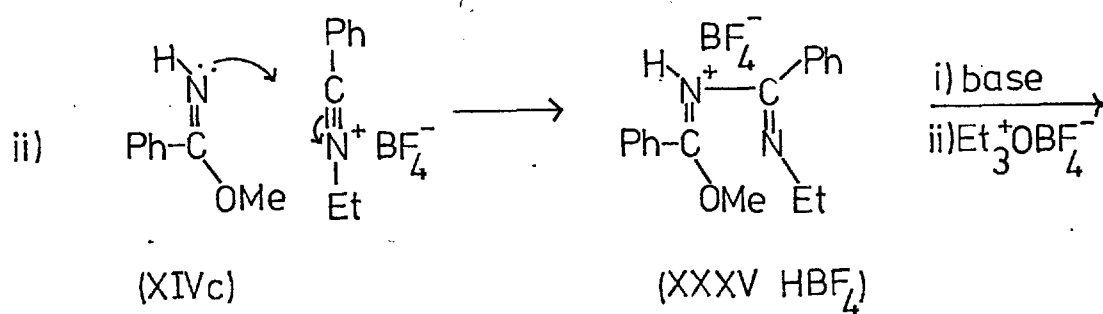
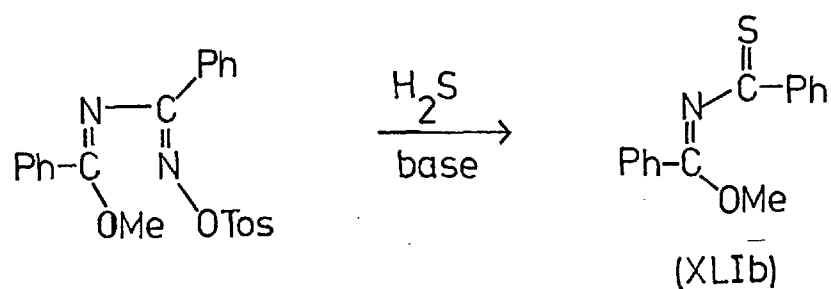
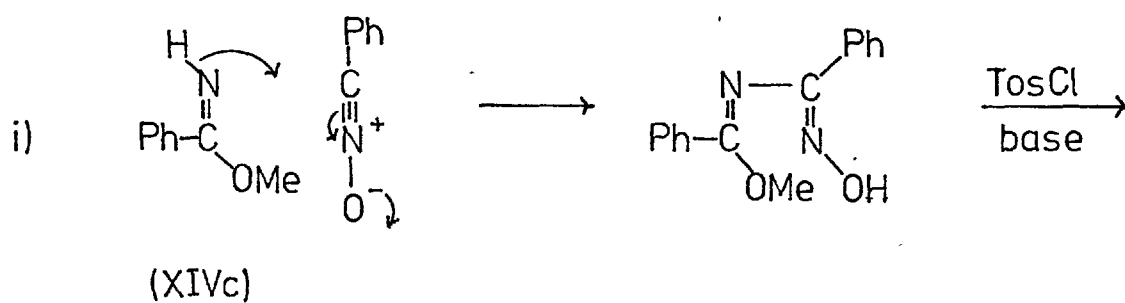
From the presence of -OH or >NH stretch (I.R.) and methoxyl protons (δ 3.35 N.M.R.), integrating to show the possible presence of the dimethylated product (XLIII), it was decided to leave the study of this reaction.



Instead a literature reference⁵¹ to the preparation of (XXXIIIb) from silver phthalimide and ethyl iodide was investigated. However the practical details were vague, and although the silver salt was dried to constant weight, the main product isolated on removal of the silver iodide was phthalimide. Although with methyl iodide small quantities of an oil were found, which could possible have been the required product.

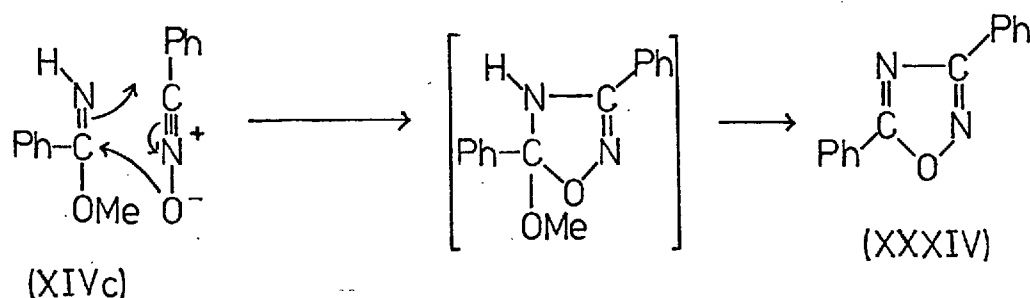


These attempted syntheses of a model with known stereochemistry, for N.M.R. comparison with imidate (XVIIc) were now abandoned, instead further approaches to the synthesis of a sulphur analogue (XLI) were tried (Scheme 10).

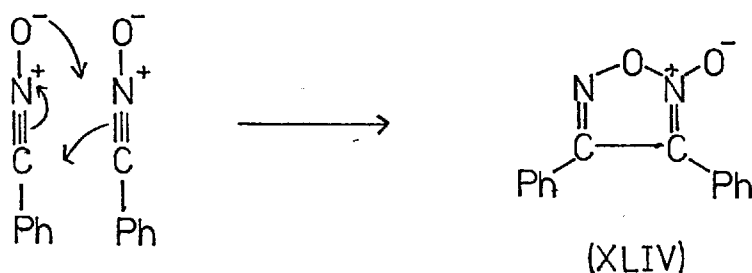


SCHEME 10

This involved the preparation of an intermediate, which would be labile to attack by H_2S , and the first idea (Scheme 10, (i)) involved the reaction of free imidate with a nitrile oxide. The reaction of benzo-hydroxamoyl chloride with methyl benzimidate (XIVc), in the presence of triethylamine, proceeded instantaneously to give a crystalline product. Unfortunately this was 3,5-diphenyl-1,2,4-oxadiazole (XXXIV), resulting from 1,3 dipolar addition of the nitrile oxide to the carbon-nitrogen double bond, with elimination of methanol, rather than the straight addition product required.



This was characterised by the m.pt., with reference to the literature⁵², and the mass spectrum. The other possible product (XLIV), resulting from dimerisation of benzonitrile oxide, was present in trace quantities (m^+/e 238), but this does not fragment by loss of oxygen in the mass spectrometer⁵³.



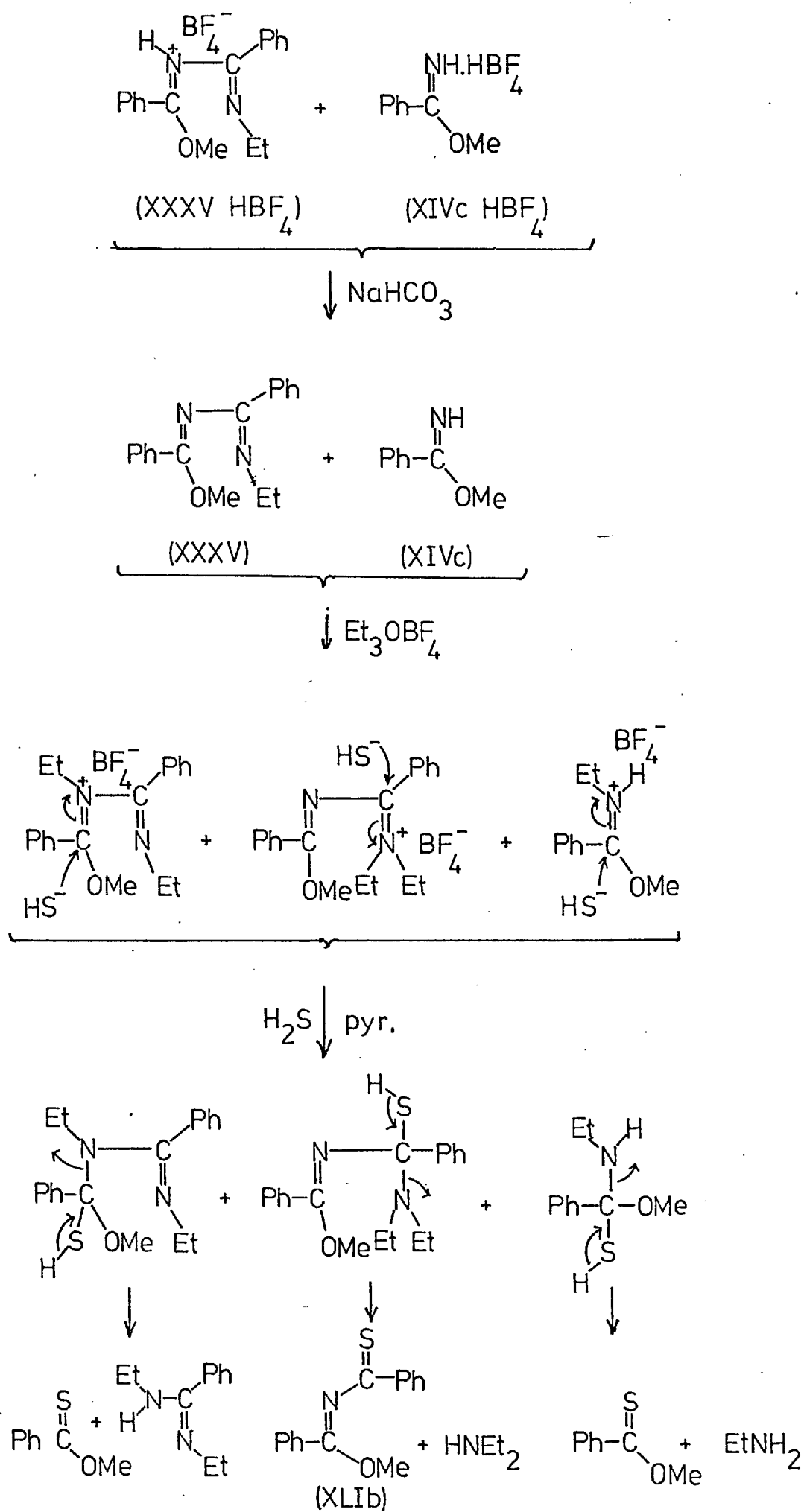
Further confirmation was gained from the work of two Belgians⁵⁴, who had carried out an identical reaction to give (XXXIV).

The ability of the free imidates (XIV), to undergo 1,3 dipolar reactions, whilst the N-acyl substituted compounds (XVII) appear not to, is interesting, and would warrant further research. From preliminary considerations it would seem likely that the carbonyl group has a certain polarising effect on the electrons of the nitrogen, and this may be the reason for the non-reactivity of (XVII).

The reaction of imidate (XVIIc) with N-ethyl benzonitrilium salt (Scheme 10, (ii)) was now investigated, there being no possibility of 1,3 dipolar addition, and indeed the required fluoroborate salt (XXXV.HBF₄) was obtained.

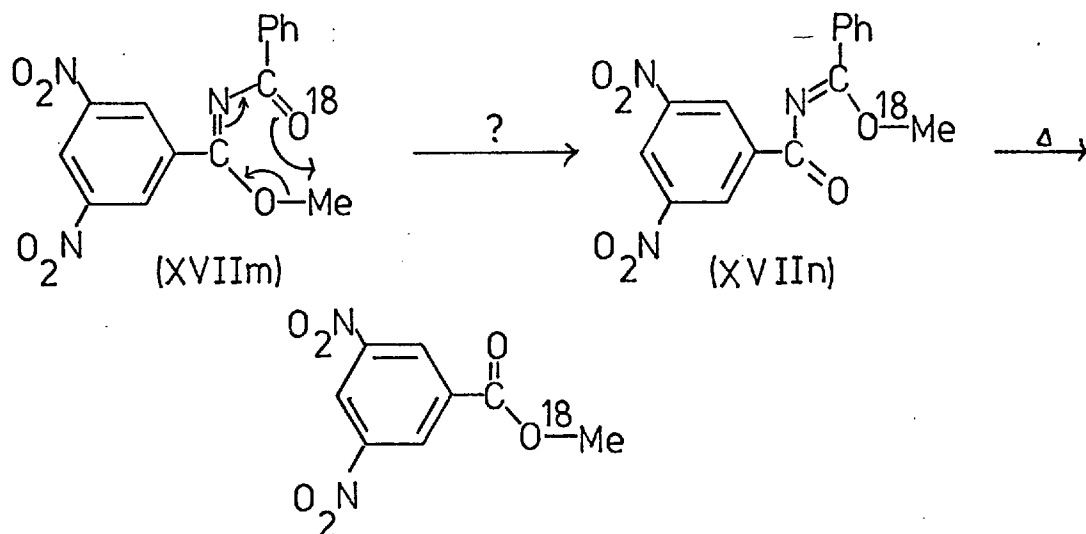
However due to difficulties of purification, it was decided to work on the crude product [(XXXV.HBF₄) and (XIVc.HBF₄)] The mixture of free bases was liberated and treated with ethyl Meerwein's salt, and this in turn treated with H₂S. No reaction was immediately apparent, but the addition of pyridine yielded one non polar product. This was methyl thionbenzoate, and its production could be rationalised from both components of the mixture (Scheme 11).

SCHEME 11

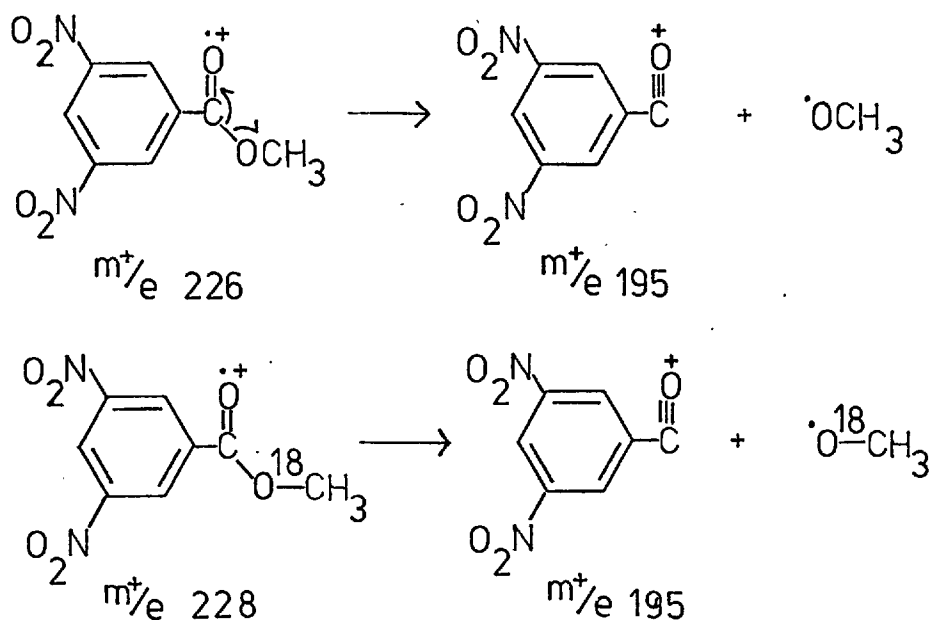


The imidate fluoroborate ($\text{XIVc} \cdot \text{HBF}_4$) was independantly shown to yield methyl thionbenzoate, as in (Scheme 11), and as the position of ethylation in (XXXV) could not be specified, no further work was undertaken.

The final work carried out was an oxygen-18 labelling study on the *N*-acyl imidate (XVIIIm), as this would give conclusive evidence concerning the proposed prepyrolysis interconversion, on isolation of the methyl-3,5-dinitrobenzoate and mass spectral determination of the position of the labelled oxygen.

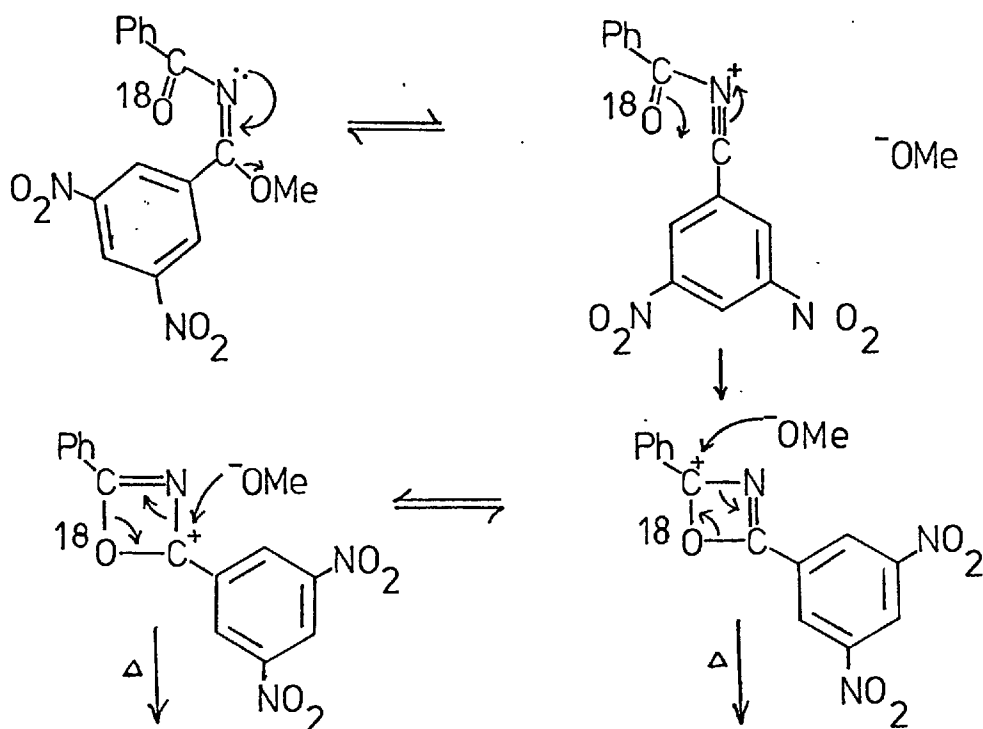


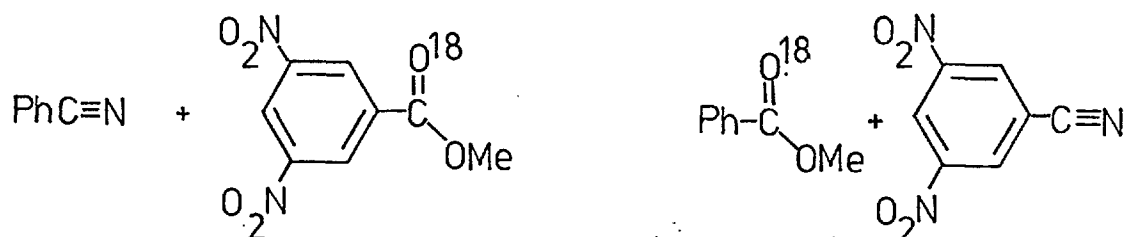
After overcoming difficulties in the synthesis of labelled benzoyl chloride from benzotrichloride and O^{18} -water (40%), the labelled imidate was obtained and pyrolysed. The required ester was isolated by preparative t.l.c. and analysed by mass spectrometry. Methyl esters undergo α -cleavage in the mass spectrometer⁵⁵, and so the O^{18} label would be expected to fragment to leave a common breakdown peak of $m^+/e=195$.



This was not realised, instead, both peaks at m^+/e 197 and 195 were present, ratio ca. 1:4, but with only a total O^{18} content of 30%. This meant that $\frac{2}{3}$ of the total O^{18} label was present on the carbonyl grouping, and whilst the imidates (XVII) might undergo, to some extent, a [1,5] sigmatropic rearrangement, the main reaction route is different.

A four centred transition state was thus proposed to explain the reaction products, and occurrence of the O^{18} label on the carbonyl of the methyl-3,5-dinitrobenzoate.





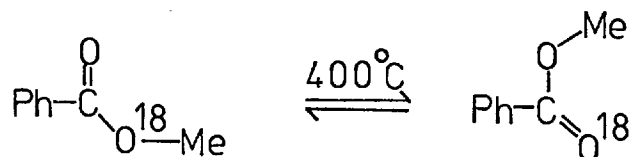
This also explains the loss of $\frac{1}{4}$ of the total O^{18} activity on pyrolysis, as if the methyl benzoate had been examined, the missing 10% of O^{18} label would hopefully have been located.

This four centre reaction does not involve the alkoxy unit of the imidate in any inversion at the carbon, and consequently the experiment with imidate (XVIIId*), prepared from d-octan-2-ol, though still valid, is obviously rendered superfluous.

Also the four centre mechanism produces ester and nitrile direct, the latter presumably trimerising to give a triazine, accounting for the isolation of veratronitrile on pyrolysis of imidate (XVIIIo).

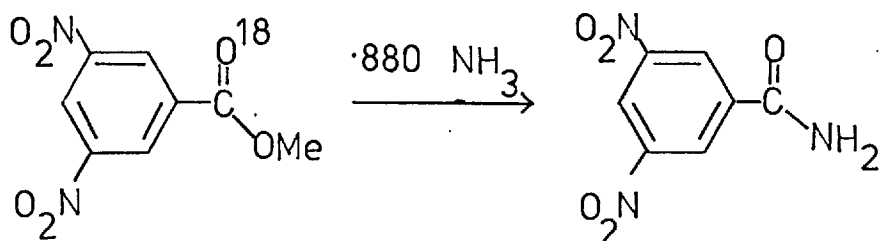
The deuterium labelling experiments, involving copyrolysis of imidate (XVIIIn) and its d-6 analogue (XX) are still accountable (page 34), but obviously the postulation of the alkoxy exchange is occurring, and thus the intramolecular 4 centre rearrangement would appear intermolecular, due to prior exchange/loss of methoxyl and trideuteromethoxyl groupings. This is also backed up by the observation that one alkoxy unit can be exchanged for another, as in the preparation of the 2-octyl imidate (XVIIIq) from methoxy imidate (XVIIIn).

The above statements are made with a slight reservation, as it is known⁵⁶ that methyl benzoate (labelled O¹⁸ on the ether oxygen) will rearrange at 400°C, although there was no trace of rearrangement at 250°C.



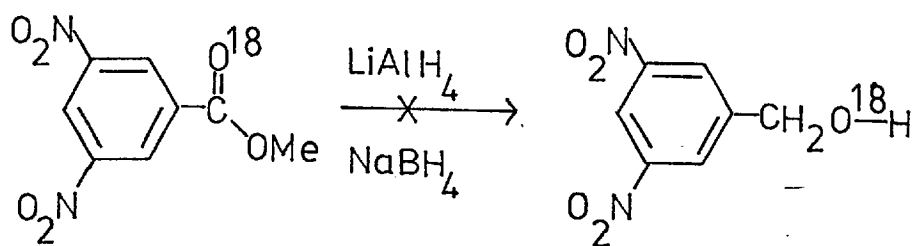
Consequently it cannot be said that no rearrangement of the O¹⁸ ester would occur at 230°C, though this is unlikely. Methyl benzoate (carbonyl O¹⁸) was prepared independently, and shown to undergo α -cleavage without rearrangement in the mass spectrometer.

Naturally the mass spectral evidence alone was not considered sufficient, and the methyl-3,5-dinitrobenzoate was converted to the amide. This showed a virtually identical amount of O¹⁸ to be still present on the carbonyl (20% overall, $\frac{2}{3}$ total O¹⁸ label in the ester), confirming the mass spectral study on the ester.

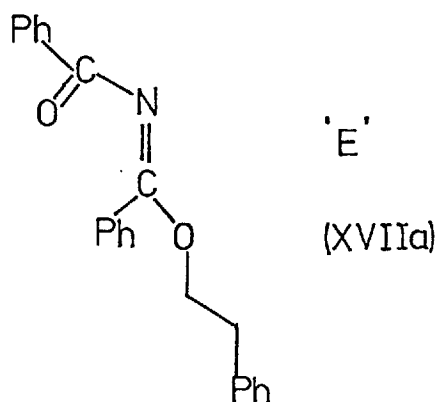


The amide derivative was chosen, as acid or base hydrolysis of the ester, to the acid, would lead to O¹⁸ exchange with water⁵⁷.

The reduction of the methyl-3,5-dinitrobenzoate, to the corresponding alcohol, with lithium aluminium hydride or sodium borohydride^{58,59} was attempted, but the expected alcohol was not obtained, instead there was a deep blue or red colouration (depending on the temperature) in the reaction. This was attributed to a Meisenheimer complex³⁵, and subsequent treatment with acid regenerated the starting materials (t.l.c.).

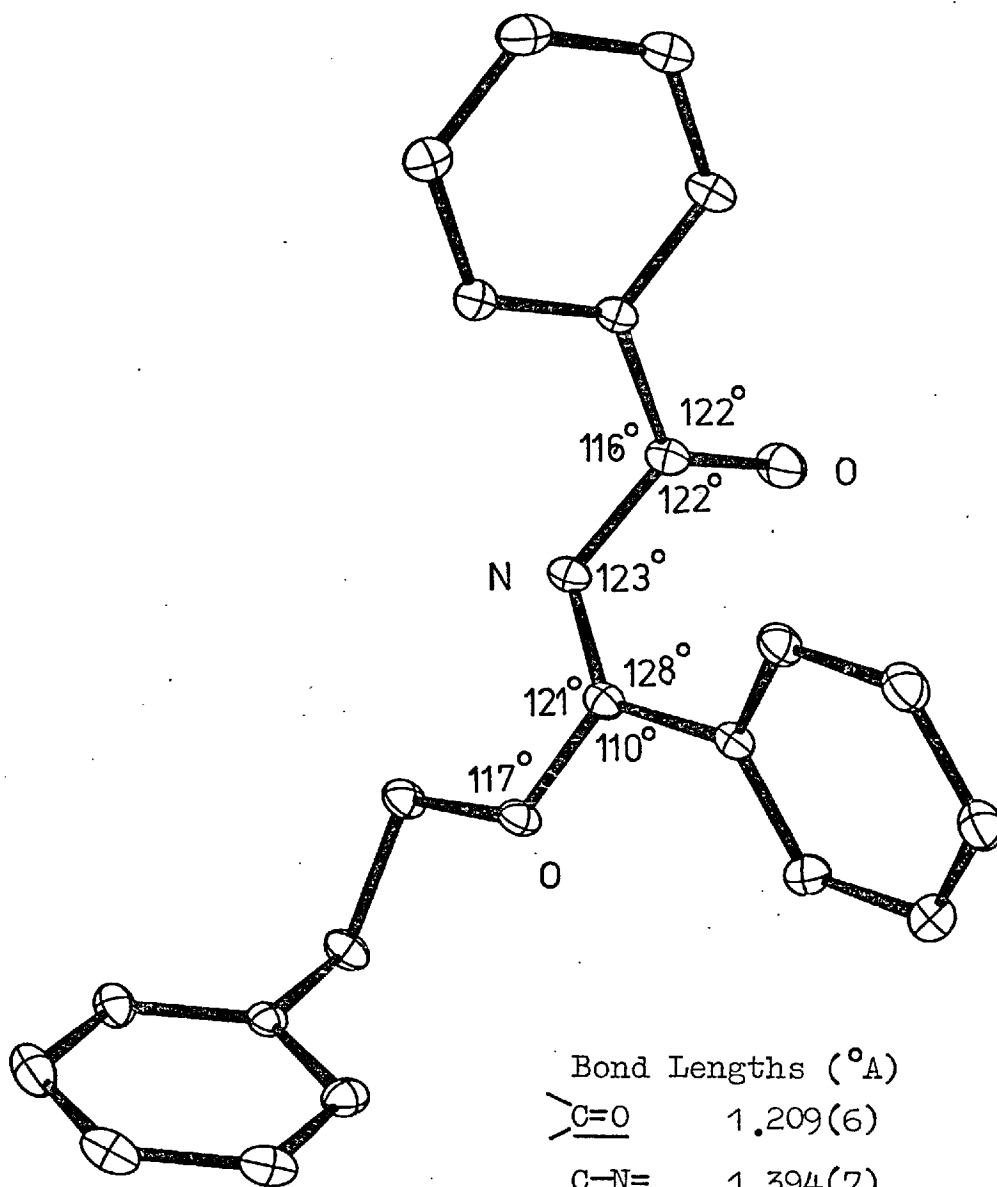


The final evidence in opposition to the proposed [1,5] sigmatropic rearrangement of *N*-acyl imidates came from the x-ray crystallographic structure of imidate (XVIIa), which showed conclusively that the carbonyl group was on the opposite side of the carbon-nitrogen double bond to the ether link.



The full x-ray structure is depicted on the next page.

Perspective view of N-acyl imidate (XVIIa).



Bond Lengths (°A)	
$\text{C}=\text{O}$	1.209(6)
$\text{C}-\text{N}=\text{C}$	1.394(7)
$\text{C}=\text{N}-$	1.272(5)
$-\text{N}=\text{C}-\text{O}-$	1.343(6)
$\text{C}=\text{O}-\text{C}=\text{O}$	1.459(5)

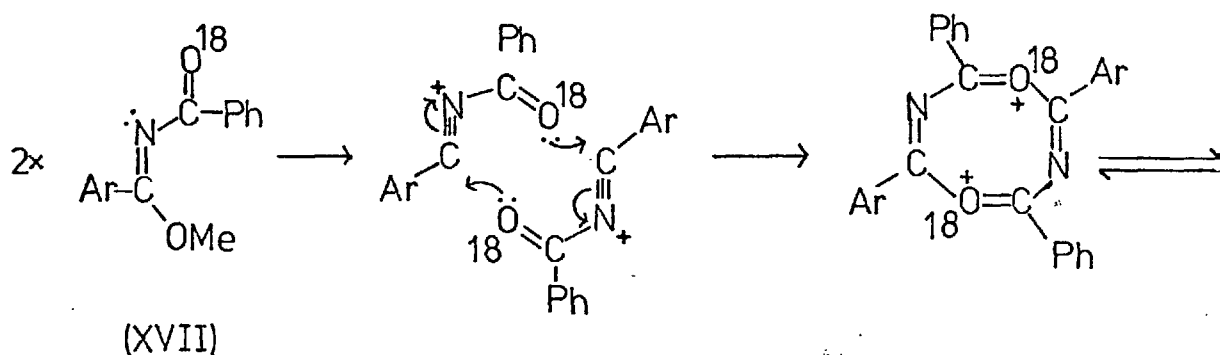
Ref. C.K.Johnson (1965) ORTEP. ORNL-3794, Oak Ridge
National Laboratory, Tennessee.

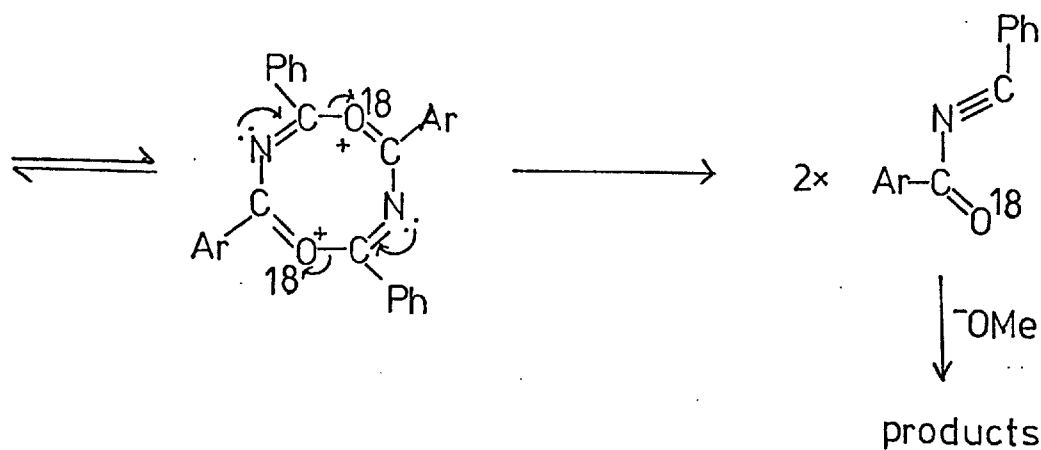
CONCLUSIONS

The initial proposition of a [1,5] sigmatropic rearrangement of imidates (XVII), prior to pyrolysis, was shown by oxygen - 18 labelling studies not to occur to any great extent. This was borne out by the configuration at the carbon-nitrogen double bond, found by x-ray crystallographic studies, which showed the carbonyl and ether oxygens to be on opposite sides, thus making approach impossible. The possibility of the acyl group "flipping over" on heating was unlikely as there was just one methoxyl resonance for the imidate (XVIIc) over the temperature range -50 to +160°C.

Instead the products produced on pyrolysis can be explained by a 4 centre transition state. This latter mechanism is in agreement with the inability to observe an inversion at the carbon of imidate (XVIIq*), prepared from d-octan-2-ol, and also necessitates the oxygen - 18 label to be on the carbonyl of the ester produced, as found experimentally.

The four centred mechanism of rearrangement does require a highly strained transition state, and a bimolecular process would be equally acceptable and also account for the products, as the order of reaction was not measured.





The work on the sulphur analogue (XLI), which would hopefully have substantiated the [1,5] sigmatropic rearrangement postulate was thus not required. However the failure to prepare the model (XLI) and dithio-benzamide (XLII), by numerous pathways, leaves scope for further investigation.

EXPERIMENTAL

Unless otherwise stated the following data apply to experiments described in this section. Melting points were determined on a Kofler block and are uncorrected. I.R. spectra were recorded on a Unicam SP200 as nujol mulls. N.M.R. spectra were recorded with a Varian T.60., using deuteriochloroform with tetramethylsilane as an internal reference, and the following abbreviations were used to describe the data:- s = singlet; d = doublet, t = triplet, q = quartet; m = multiplet. Mass spectra were recorded with a Perkin Elmer 270 low resolution (routine spectra) or an A.E.I. MS9 high resolution spectrometer, and all composition data were obtained by measuring the mean peak heights. Ultra violet spectra were recorded on a Unicam SP 800 spectrophotometer in ethanol. Rotations were measured on a Perkin Elmer 141 polarimeter, and are for chloroform solutions.

Petroleum ether refers to the fraction b.pt. 60-80°C.

Benzene and ether were dried over sodium wire. Pyridine was distilled from, and stored over potassium hydroxide pellets. Chloroform was shaken with water and distilled from phosphorus pentoxide to remove the ethanol.

Thin layer (t.l.c.) and preparative t.l.c. (1 mm) plates were prepared from Merck Silica Gel GF 254.

EXPERIMENTAL

Preparation of α - bromocumene⁶⁰ (Ia)

Equimolar quantities of cumene and N-bromosuccinimide were refluxed in carbon tetrachloride for 4 hours. After cooling, the succinimide was filtered off and the product used without further purification as the material decomposed on column chromatography, using silica gel/pet. ether.

Preparation of α -azidocumene (Ic)

To a solution of sodium azide (4g, in water/acetone) at room temperature, crude α -bromo-cumene (4g) in acetone, was slowly added, with vigorous stirring. The reaction was worked up by pouring onto ice/H₂O and extracting with ether, washing with water. This crude extract was shown to contain azide (IR $\vee$ 2160cm.⁻¹) but almost certainly the alcohol (Id) and styrene (V) were present. Here again purification was impossible due to decomposition on t.l.c.

Preparation of α -aminocumene (Ie)

A solution of the crude azide (Ic) (.7g in anhydrous ether) was added dropwise to L.A.H. (.7g, , in 25ml dry ether) with vigorous stirring. Excess L.A.H. was decomposed by the dropwise addition of ethyl acetate. After addition of aqueous sodium hydroxide the ether layer was retained and extracted with dil. HCl. The amine (.2g, 33% theor.)

was then reliberated by neutralisation with sodium hydroxide and extraction with ether.

Preparation of N-cumylbenzamide (VII)

To the amine (Ie) (•2g) in ether, benzoyl chloride (•2ml, excess) was added with stirring followed by triethylamine (•16ml), and the whole left overnight. The hydrochloride was filtered off and partitioned between water/dichloromethane. The dichloromethane was combined with the ether filtrate and this was stirred with sodium hydroxide until the excess benzoyl chloride was destroyed. After washing the organic layer with water the amide (VII) (•1g, 28%) was obtained. M.Pt. 158-159°C Lit. 159°C ² (ethanol) m^+/e 239 found for $C_{16}H_{17}NO$.

Attempted preparation of the amide (VII) from α -Bromocumene (Ib) and benzonitrile using a Friedel Crafts Catalyst.⁶¹

To a mixture of benzonitrile (1.5g) and anhydrous aluminium chloride (3.3g) in anhydrous ether (20ml), dry HCl gas was vigorously passed for 1 hour. To this mixture, under reflux, (Ib) (1.9g) in ether was added dropwise while still passing HCl slowly. After 8 hours refluxing, the whole was allowed to stand overnight, before pouring onto ice. The dichloromethane extract showed no amide (VII) by t.l.c.

Preparation of dimethyl phenyl carbinol (Id) Grignard reaction.

Bromobenzene (1.56g) was added dropwise, to a stirred suspension of Magnesium (.24g) in ether (20ml), so that the reaction refluxed steadily. To the Grignard, acetone (1.16g, twice theoretical) was added with cooling, and the whole refluxed for a few minutes. The product (.5g 37%) was obtained by pouring onto ice and extracting with ether. T.l.c. showed two spots, but this was to be expected as the carbinol (Id) would readily dehydrate to give α -methylstyrene (v). (Scaled up reactions gave 65% yield).

Attempted Ritter Reaction^{3,4,62} on the carbinol (Id), with benzonitrile.

i) The crude alcohol (Id) (.4g) was added dropwise to a mixture of glacial acetic acid (5 ml) containing benzonitrile (.34g) and conc. sulphuric acid (.6ml). The whole was allowed to stir overnight before pouring onto ice, and neutralising with sodium carbonate. The ether extract showed no amide (VII) t.l.c., only a spot corresponding to α -methylstyrene (V).

ii) A mixture of the alcohol (Id) (1.32g) and benzonitrile (1.03g) was treated dropwise with 1.0ml conc. sulphuric acid, keeping the temperature at 20-30°C. The whole was then stirred

vigorously on an oil bath for 1 hour at 65°C before pouring onto water. The crystals formed were filtered off, but recrystallisation from water showed them to be benzamide M.Pt. 132°C Lit. M.Pt. 128-129.5°C⁶³ and I.R. of authentic sample.

Preparation of N-benzyl-benziminobchloride⁹ (VIII)

To a stirred suspension of phosphorus pentachloride (16.2g) in dry benzene (50ml) N-benzyl benzamide (16g) was added portionwise. The whole was then stirred for 2 hours at room temperature, before heating briefly on a steam bath, to obtain a homogeneous solution. The whole was then distilled to give the imino chloride (13.9g, 80% theory) B.Pt. 130°C.0.5mm Hg Lit. B.Pt.120°C.3mm.¹⁰ IR. ν 1670, 1460, 900 cm.⁻¹.

(Ref.⁹ quotes B.Pt. 104° 60mm. but the later ref.¹⁰ is in better agreement).

Attempted preparation of N-benzyl-methyl benzimidate (IX)

To a solution of the iminobchloride (VIII) (.46g) in dry methanol (2.5ml) triethylamine (.2g) was added, and the whole allowed to stir for five hours. T.l.c. showed several spots, but on work up by pouring onto ice and extracting with benzene the N.M.R. showed no major methoxy peak.

Preparation of N-benzyl-methyl benzimidate (IX)

The imino chloride (VIII) (.5g) was added to a large excess of lithium methoxide in methanol, and the whole allowed to

stir overnight, t.l.c. ($\text{Al}_2\text{O}_3/\text{CH}_2\text{Cl}_2$) showed one major spot of slightly higher Rf than starting material, and this was obtained as an oil by pouring the reaction onto ice and extracting with benzene.

N.m.r. δ 7.5, 10H (2s); δ 4.6, 2H_s; δ 4.0, 3H_s. IR.

ν 1670, 1600, 1460, 1280, 1130 cm^{-1} .

Found C 80.24%; H 6.69%; N 6.20%, $\text{C}_{15}\text{H}_{15}\text{NO}$ requires C 79.97%; H 6.71% N 6.27%.

Reaction of the iminochloride (VIII) with the dianion of ethylene glycol.

i) To ethane diol (.056ml, .062g), lithium (.014g) was added and the whole stirred. To this dianion the imino chloride (.46g) was added and the whole stirred at room temperature. T.l.c. showed only the presence of N-benzyl benzamide.

As the formation of the dianion was not very practicable by this method, n-butyl lithium was used for its generation.

ii) To ethane diol (1.12ml) in dry dimethyl acetamide (20ml), n-butyl lithium (30ml of 13.14% sol'n, .71g/ml) was added dropwise with stirring. To this the imino chloride (7g, slightly less than theory) was added dropwise. The addition proceeded with the production of a deep red colouration, and after two hours the reaction was poured onto ice. Extraction with benzene gave a red oil (ν 1620-1660 cm^{-1} broad) which, with methanol precipitated a yellow solid.

IR ν 1470, 1400, 790, 710 cm^{-1} m^+/e 384. Recrystallisation from dichloromethane gave colourless crystals. M.Pt. 252-253 $^{\circ}\text{C}$ Found. C 87.22%; H 7.20%; N 5.46% $\text{C}_{28}\text{H}_{20}\text{N}_2$ Requires C 87.47%; H 7.29%; N 5.24%. N.m.r. δ 7.2-7.8, indicated that all protons were aromatic, and thus the material was tetraphenyl pyrazine (X) lit. m.pt. 246 $^{\circ}\text{C}$.¹¹

Reaction of N-Cumyl-benzamide (VII) with thionyl chloride

To the amide (VII) (0.48g) in benzene (1ml) thionyl chloride (.32ml) was added, and the whole heated on a water bath with stirring for 1½ hours, whereupon the reaction appeared homogeneous. The excess thionyl chloride was flushed off with benzene under vacuum, to yield an oil which showed two spots on t.l.c. ($\text{CH}_2\text{Cl}_2/\text{SiO}_2$). These had identical R_f 's to benzonitrile and α -methyl styrene, confirmed by IR (ν 2270, 1500, 1460 cm^{-1}).

The reaction of the ketimine (XI) with t-butylhypochlorite.⁸

A solution of 2-amino-2-phenyl-propane (VI) (0.5g) and benzaldehyde (0.4g) was refluxed in ethanol for 30mins. All solvent was removed by rotary evaporation, and then high vacuum to yield an oil (.8g) IR ν 1650 cm^{-1} which was assumed to be the required Schiff Base. To the Schiff Base (0.08g) in ether (5ml) t-butyl hypochlorite (.4g, excess) was added, and the whole refluxed. T.l.c. showed the presence of benzonitrile, benzaldehyde and unreacted starting material,

confirmed by I.R. (ν , 2270, 1700, 1650cm^{-1}), as this reaction was not progressing smoothly further work was not attempted.

Preparation of ethane diol dibenzimidate hydrochloride (XII.2HCl)^{12,13}.

To a mixture of benzonitrile (10.3g, 0.1mole) and ethylene glycol (0.05 mole) at 0°C , dry HCl gas was passed until the weight increase was 3.65g (.1 mole). This was refrigerated overnight before triturating with anhydrous ether, to yield a solid hydrochloride, unstable to moist air. (Yield $< 10\%$ - leave at 0°C longer).

Acetylation of the imidate hydrochloride (XII.2HCl).

To the crude hydrochloride (.58g) in dry pyridine (2ml) at 0°C acetic anhydride (.18g) was added, and the whole allowed to stir overnight, warming up to room temperature. The crude product as an oil was obtained by pouring onto ice and extracting with ether, removing the last traces of pyridine under vacuum. Preliminary spectral evidence would indicate that the product was the N-acetyl benzimidate of ethylene glycol monoacetate (XIII).

Repeat preparation of the diimidate hydrochloride (XII, 2HCl) and acetylation.

The hydrochloride was prepared as before and characterised as the free imine (XII) by partitioning the hydrochloride between ice cold sodium bicarbonate and ether. Evaporation of the ether gave a colourless oil, which crystallised from ether m.pt.

97-98°C. I.R. ν 1620, 1355, 1080, 760, 690 cm^{-1} .

Found C 71.88%; H 6.08%; N 10.48%; $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_2$ requires C 71.68%; H 6.01%; N 10.44%.

Acetylation as before gave an unstable oil (3 spots t.l.c. $\text{CH}_2\text{Cl}_2/\text{Al}_2\text{O}_3$) with the desired spectral data. I.R. ν 1740, 1670, 1280-1240 1130 cm^{-1} . N.m.r. δ 7.1-7.8, 10Hm; δ 4.4, 4H; δ 2.1, 6Hs., as expected for a symmetrical molecule.

Repetition of the reaction with ethylene glycol subsequently failed, giving the mono imide hydrochloride (XV.HCl), as experienced when the reaction was first carried out.

The free imine (XV) was liberated as above and crystallised from CH_2Cl_2 /ether to give colourless crystals m.pt. 75-95°C. m^+/e 165 I.R. ν 3220, 1630, 1460, 1070, 700 cm^{-1} . Found C 65.19%; H 6.87%; N 8.28%. $\text{C}_9\text{H}_{11}\text{NO}_2$ requires C 65.44%; H 6.71%; N 8.48%.

Preparation of Ethyleneglycol mono-p-nitrobenzoate-N-p-nitrobenzoyl-benzimidate (XIIIb)

To the imide hydrochloride (XV.HCl) in dry pyridine (10ml) at 0°C p-nitrobenzoyl chloride (1.11g) was added and the whole stirred for 36 hours, allowing to warm to room temperature. The reaction was then poured onto ice/water, and the solid precipitate taken into dichloromethane.

Evaporation of solvent yielded a yellow solid, recrystallisation

(benzene) gave M.Pt. $166-168^{\circ}\text{C}$. m^{+}/e 463. I.R. ν 1725, 1670, 1650, 1530, 1325 1280 cm^{-1} . N.m.r. δ 8.3, 8H; δ 7.5, 5H; δ 4.9, 4Hs. Found C 59.72%; H 3.79%; N 8.91%. $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_8$ requires C 59.61%; H 3.70%; N 9.07%.

Preparation of β -phenethylbenzimidatehydrochloride (XIVa.HCl)^{12,13}

To a mixture of β -phenethyl alcohol (12.2g) and benzonitrile (10.3g) at 0°C , dry HCl gas was passed, until there was a weight increase of 3.65g (just over). The whole was refrigerated (0°C) for 48 hours whereupon trituration with anhydrous ether gave colourless crystals (16g, 38%) of the hydrochloride.

I.R. ν 1640, 1465, 1390, 880, 740, 700 cm^{-1} .

Preparation of N-acetyl- β -phenethylbenzimidate (XVI).

To the hydrochloride (XIVa.HCl) (8.72g) in pyridine (30ml) at 0°C , acetic anhydride (3.4g) was added, and the whole allowed to stir for 24 hours at room temperature. The imidate (XIV) was obtained as an oil, by pouring onto ice, extracting with ether, and removing all solvent. I.R. ν 1720, 1640, cm^{-1} . N.m.r. δ 7.4-7.6, 10H m; δ 4.5, 2Ht; δ 3.2, 2Ht. m^{+}/e 267. The material was too unstable to purify and analyse.

Preparation of N-benzoyl- β -phenethyl benzimidate (XVIIa)^{19,21}

To the hydrochloride (XIVa.HCl) (2.6g) in pyridine (10ml) at

0°C benzoyl chloride (1.4g) was added, and the whole allowed to stir overnight at room temperature. The product was obtained as an oil after pouring into ice/water and extracting with ether. This crystallised from ether (yield, 60% pure) M.Pt. 79-80°C I.R. $\checkmark$ 1665, 1645, 1280 cm^{-1} ., N.M.R. δ 8.0-8.2, 2Hm; δ 7.2-7.6, 13Hm; δ 4.6, 2Ht; δ 3.2, 2Ht. m^+/e 329 Found C 80.33%; H 5.71%; N 4.19%. $\text{C}_{22}\text{H}_{19}\text{NO}_2$ requires C 80.22%; H 5.81%; N 4.25%.

Pyrolysis of N-benzoyl- β -phenethyl benzoate (XVII a)

From preliminary experiments in a sealed capillary tube, under Nitrogen, the starting material had completely disappeared in ca. 24 hours at 196°C. 435mg of (XVIIa) in a sealed tube under Nitrogen, were pyrolysed for 44 hours at 196°C and the products separated by preparative t.l.c.

(benzene/petrol 1:1, SiO_2) showing three major components.

Band 1 (22mg) + 20mg solid partially insoluble in CH_2Cl_2 , the solvent used for application of material to prep. plate.

This recrystallised from dichloromethane to give colourless plates M.Pt. 238°C m^+/e 309 and was shown to be 2,4,6-triphenyl-1,3,5-triazine⁶⁴ (XVIIa) by preparation of an authentic sample⁶⁴ M.Pt. 238°C M.M.Pt. 238°C Lit M.Pt.⁶⁴ 232°C I.R. $\checkmark$ 1538 cm^{-1} .

Band 2 (Rf ca. 0.4) 206mg.

This was β -phenethyl benzoate, from comparison with an authentic sample prepared from equimolar amounts of β -phenethyl alcohol and benzoyl chloride in pyridine. I.R.

ν 1720, 1280 cm^{-1} N.M.R. δ 7.9-8.1, 2Hm; δ 7.2-7.6, 8Hm; δ 4.5, 2Ht; δ 3.05, 2Ht.

Band 3 (origin) 109mg.

This contained some unreacted starting material as well as dibenzamide, which probably came from hydrolysis¹⁴. The presence of dibenzamide was also confirmed by synthesis of an authentic sample⁶³ from benzoyl chloride and benzamide. M.Pt. 145°C., Lit. m.pt.⁶³ 144°C. I.R. match. ν 3250, 1700, 1510, 1470, 1230, 1120, 720 cm^{-1} . Thus overall recovery from plate was 81%.

Preparation of N-p-nitrobenzoyl- β -phenethyl benzimidate (XVIIb)

From reaction of p-nitrobenzoyl chloride with the hydrochloride (XIVa.HCl) as for (XVIIa) but using CH_2Cl_2 to extract the product on workup, to yield yellow crystals from benzene (55% theory, pure) M.Pt. 126-128°C m^+/e 374. I.R. ν 1660, 1640, 1540, 1350, 1280, 850, 730, 710 cm^{-1} . N.M.R. δ 8.3-7.9, 4Hm; δ 7.2-7.4, 10Hm; δ 4.65, 2Ht; δ 3.15, 2Ht. Found C 70.46%; H 4.95%; N 7.31% $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_4$ requires C 70.58%; H 4.85%; N 7.48%.

Pyrolysis of N-p-nitrobenzoyl- β -phenethyl benzimidate (XVIIb)

472mg of (XVIIb) were pyrolysed for 23 hours in a sealed tube under nitrogen to yield five bands on preparative t.l.c.

(benzene/petrol 1:1, SiO_2).

Band 1 Rf. 0.65 (1.0mg)

This was 2,4,6-triphenyl-1,3,5-triazine m^+/e 309, comparative t.l.c. and I.R.

Band 2 Rf. 0.43 (4.5mg)

This recrystallised from dichloromethane to give pale yellow plates, M.Pt. $226-7^\circ\text{C}$. m^+/e 354, I.R. ν 1540, 1460, 1420, 1380, 1340 cm^{-1} . From this evidence it was deduced that the material was 2,4-diphenyl-6-p-nitrophenyl-1,3,5-triazine⁶⁵ (XVIIIb) Lit M.Pt.⁶⁵ 218°C .

Band 3 11mg.

This was β -phenethyl benzoate. Comparison of I.R. and N.M.R. with authentic sample.

Band 4 (42mg)

This was a yellow solid, which crystallised from alcohol m.pt. $60-61^\circ\text{C}$. I.R. ν 1725, 1530, 1350, 1280 cm^{-1} . N.M.R.

δ 8.2, 4Hd; δ 7.3, 5Hs; δ 4.6, 2Ht; δ 3.1, 2Ht. This proved to be β -phenethyl-p-nitrobenzoate, identical with an authentic sample, prepared from β -phenethyl alcohol and p-nitrobenzoyl chloride in pyridine, M.Pt. $61.5-62.5^\circ\text{C}$. M.M.Pt. $60-61^\circ\text{C}$. Lit.M.Pt. $62-63^\circ\text{C}$ ⁶⁶.

Band 5 (origin) 380mg.

This contained basically starting material, and amides from

hydrolysis. Further preparative t.l.c. (benzene/ethyl acetate 2:1, SiO_2) showed 3 bands, the middle of which was shown to be p-nitrobenzoyl benzamide I.R. comparison with authentic sample⁶⁷ prepared from benzamidine hydrochloride⁶⁸ and p-nitro benzoyl chloride, hydrolysing the intermediate N-acyl benzamidine with dilute HCl. M.Pt. 175-177°C. Lit 174°C⁶⁷ (Methanol).

It was obvious that pyrolysis of the imidate (XVIIb) was incomplete in this case and so the experiment was repeated, but in a kinetic flask, using decalin (B.Pt. 191°C) in the outer flask, and keeping the reaction melt (476 mg) under a balloon of nitrogen for 130 hours, this gave products identical to the five bands above.

i) 20mg ii) 54mg iii) 30mg iv) 300mg v) 50mg.

Preparation of N-d5-benzoyl- β -d5-phenethyl benzimidate (XIX)

a) d5-benzoyl chloride^{69 70}

To the Grignard from Magnesium (120mg) and d5-bromobenzene (810mg) in ether (5ml), benzene (5ml) was added and the whole stirred at 0°C whilst CO_2 was passed onto the surface for 2 hours. The d5-benzoic acid was obtained by normal acid/alkali work up, and refluxed with thionyl chloride (5 fold excess) with traces of D.M.F. in benzene (5ml) for 1 hour, to yield d5-benzoyl chloride (210mg 30%).

b) d5- β -phenethyl alcohol⁷¹

Onto the Grignard, from Magnesium (120mg) and d-5-bromobenzene (810mg) in T.H.F. (5ml), at 0°C, a large excess of ethylene oxide (dried by passage over soda-lime) was passed. The whole was allowed to stir for 1 hour, raising to room temperature, and then boiling briefly. The jellied mass was poured onto ice/dil HCl, and after extraction with dichloromethane, preparative t.l.c. (benzene/ethyl acetate 2:1, SiO₂) afforded the alcohol (224mg 35%).

c) Pinner synthesis to form imidate hydrochloride (XIVa. HCl-d5).

Prepared from benzonitrile (182mg) and d-5-alcohol (224mg) as for preparation of (XIVa), except that due to the small weight of HCl required excess was used. Yield 460mg (100%).

d) d-5-Benzoylation of d-5-imidate hydrochloride to give the imidate (XIX).

As for (XVIIa), from 460mg d-5-hydrochloride, and 210mg d-5-benzoyl chloride (less than theory).

The pyridine was removed by washing with dilute acid at 0°C during work up, to give (XIX) 80mg (17%) M.Pt. 78-79.5°C.

Authentic m.pt. 79-80°C. m⁺/e 339, as required for C₂₂H₉D₁₀NO₂ (No 334, 329 ions).

e) Pyrolysis of N-d5-benzoyl-d5-β-phenethyl benzimidate (XIX)

80mg of (XIX) were pyrolysed for 87 hours at 192°C in a sealed tube under nitrogen, and the products separated by preparative t.l.c., as for the pyrolysis of non-deuterated

sample (XVIIa).

Band 1. 13.6mg was 2,4,6-triphenyl-1,3,5-triazine showing m^+/e , 309,314,319,324, ratio 96:166:16:1 -from peak height measurement.

Band 2. ca. 60mg. - β -phenethyl benzoate. This showed no mass ion, due to a ready McLafferty rearrangement c f. authentic sample.

Attempted reaction of N-benzoyl- β -phenethyl benzimidate (XVIIa) with diazomethane.

To the imidate (100mg) in ether (2.5ml) at 0°C diazomethane⁷² (5ml of ether sol'n) was added and the whole allowed to stir in a stoppered flask. After 24 hours there was no change in t.l.c., and the starting imidate was recovered (.I.R. of crystals). Even after 2 weeks only the imidate and polymethylene could be detected.

Preparation of N-benzoyl-methyl benzimidate²⁰ (XVIIc).

The hydrochloride (XIVc.HCl) (15.5g 90% theory) was obtained from benzonitrile (10.3g) and methanol (3.2g) and benzoylated in the usual way. To give an oil (80% theory) used without further purification I.R. ν 1680-1640 broad, 1460, 1280, 870, 710 cm^{-1} N.M.R. δ 7.9-8.1, 2Hm; δ 7.2-7.7, 8Hm; δ 4.0, 3Hs.

Preparation of N-benzoyl-ethyl benzimidate²⁰ (XVIIId)

The hydrochloride (XIVd.HCl) (13.2g., 70% theory) was obtained from benzonitrile (10.3g) and ethanol (4.6g) and benzoylated

in the usual manner to give an oil. This eventually crystallised from ethanol m.pt. 60-63°C lit. m.pt. ²⁰ 65°C. I.R. ν 1680, 1670, 1280, 1070, 880 cm^{-1} . N.M.R. δ 7.9-8.1, 2Hm: δ 7.2-7.7, 8Hm: δ 4.5, 2Hq: δ 1.5, 3Ht.

Reaction of N-benzoyl-ethylbenzimidate (XVIIId) with triethyl-oxonium tetra-fluoroborate.

The Meerwein salt was prepared according to the literature procedure³², and its activity confirmed by ethylation of N-benzyl benzamide. [collapse of CH_2 doublet δ 4.6 to singlet at δ 5.2, with introduction of ethyl group δ 4.3 (CH_2), q, δ 1.35 (CH_3), t.]

Reaction of equimolar quantities of Meerwein salt and imidate (XVIIId) in dichloromethane at room temperature, gave no crystalline fluoroborate salt, unchanged starting material being recovered (I.R.).

Preparation of N-benzoyl- β -phenethyl-p-nitro benzimidate (XVIIe).

To a solution of p-nitrobenzonitrile⁷³ (prepared by dehydration of the amide with POCl_3) (148mg) and β -phenethyl alcohol in dry ethanol free chloroform (10ml) at 0°C, dry HCl was slowly passed for 30mins. The whole was refrigerated overnight, and the hydrochloride (190mg, 62%) was obtained by removal of the chloroform and trituration with ether. (Longer refrigeration, ca. 4 days gave yields of 90%).

Benzoylation in the usual manner afforded the imidate (XVIIe), yellow crystals from CH_2Cl_2 /ether (40%) M.pt. 124-126°C m^+/e 374 IR. ν 1660, 1600, 1535, 1350, 1270 cm^{-1} N.M.R.

δ 3.15, 2Ht: δ 4.65, 2Ht: δ 7.2-8.2 14Hm. Found C 70.55%: H 4.89%: N 7.23% $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_4$ requires C 70.58%: H 4.85%: N 7.48%.

Pyrolysis of N-benzoyl- β -phenethyl-p-nitrobenzimidate (XVIIe).

400mg of imidate (XVIIe) were pyrolysed under nitrogen in a sealed tube at 220°C for 20 hours, to give three bands on preparative t.l.c. (benzene/petrol 3:1, SiO₂) as well as a small amount of insoluble material.

Band 1. less than 10mg

This was 2,4-diphenyl-6-p-nitro-phenyl-1,3,5-triazine (XVIIIb) m⁺/e 354, same Rf. as previous sample.

Band 2. (110mg)

This was a mixture, but trituration with ether washed out β -phenethyl benzoate, (N.M.R. I.R. t.l.c.) to leave a solid identical with the insoluble material from preparative t.l.c. application. This showed m⁺/e 399, as the base peak (M.Pt.

>230°C) and was assigned the structure 2,4-di-p-nitrophenyl-6-phenyl-1,3,5-triazine (XVIIIc) rather than 2,4,6 tri-p-nitrophenyl-1,3,5-triazine (XVIIIId) which was synthesised independently and shown to have m⁺/e 444.

Band 3. (140mg)

This was β -phenethyl-p-nitrobenzoate (I.R. t.l.c. m.mpt.) after recrystallisation from ethanol.

Preparation of 2,4,6-tri-p-nitrophenyl-1,3,5-triazine (XVIIIId)²³

The hydrochloride (XIVb.HCl) (85%) was obtained by passage of HCl into p-nitro-benzonitrile and methanol, in chloroform in the usual manner. The free imidate was liberated by partitioning between ice cold sodium bicarbonate and chloroform, and crystallised from CHCl₃/Et₂O to give pale yellow needles m.pt. 95-95.5°C. lit. 93°C²³ N.M.R. δ 8.4-7.7,

4Hm; δ 3.95, 3Hs. Trimerisation of the imidate (100mg) was accomplished by heating on a steam bath with glacial acetic acid (60mg) for 4 hours. The resultant solid (40mg) was washed with hot water and methanol and dried in vacuo. I.R. ν 1540, 1350, 1110, 895, 840, 755 cm^{-1} m^+/e 444 for $\text{C}_{21}\text{H}_{12}\text{N}_6\text{O}_6$. m.pt. $> 230^\circ\text{C}$.

Preparation of N-p-toluoyl- β -phenethylbenzimidate (XVIIIf)

This was prepared as usual from the imidate hydrochloride (XIVa.HCl) (7.85g) and toluoyl chloride (4.65g), to give colourless crystals (7.5g, 70%) from ether, m.pt. $100-101^\circ\text{C}$. I.R. ν 1660, 1640, 1280, 1155, 1080 cm^{-1} . N.M.R. δ 8.0-7.6, 2Hd; δ 7.6-7.0, 12Hm; δ 4.65, 2Ht; δ 3.2, 2Ht; δ 2.4, 3Hs. Found C 80.35%; H 6.20%; N 4.06%. $\text{C}_{23}\text{H}_{21}\text{NO}_2$ requires C 80.44%; H 6.16%; N 4.08%.

Pyrolysis of N-p-toluoyl- β -phenethyl benzimidate (XVIIIf)

400mg of (XVIIIf) were pyrolysed at 222°C in a sealed tube under Nitrogen for 18 $\frac{1}{2}$ hours, to yield 3 fractions on preparative t.l.c. (benzene/petrol 1:1, SiO_2).

Band 1. 51mg. A mixture of all possible triazines.

m^+/e 309, 323, 337, 351 ratio 43:75:11:1 (from peak heights)

Band 2. 260mg. A mixture of β -phenethyl benzoate (17%) and β -phenethyl-p-methyl benzoate (83%) (from N.M.R.) I.R. shows a trace of nitrile (ν 2250 cm^{-1}).

Band 3. 34mg at origin - amide nature.

Total recovery of material was 87%.

Preparation of N-benzoyl- β -phenethyl-p-toluoimide (XVIIIg)

To a solution of p-tolunitrile (11.7g) and β -phenethyl alcohol (11.2g) in dry ether (ca. 30ml) at 0°C , dry HCl gas was

passed until the weight increase was 3.65g. The stoppered flask was stored at 0°C overnight to yield the hydrochloride (XIVg.HCl) (7g, 26%) on filtration (obviously longer storage at 0°C is required). Benzoylation in the usual manner gave the imide (XVIIg) as colourless crystals from ether/petrol M.Pt. 67.5-69°C. I.R. ν 1660, 1640, 1460, 1280 cm^{-1} .

N.M.R. δ 7.7-8.0, 2Hm; δ 7.5-6.8, 12Hm; δ 4.5, 2Ht; δ 3.15, 2Ht; δ 2.3, 3Hs. Found C 80.36%; H 6.22%; N 3.95%. $\text{C}_{23}\text{H}_{21}\text{NO}_2$ requires C 80.44%; H 6.16%; N 4.08%.

Pyrolysis of N-benzoyl- β -phenethyl-p-toluoimide (XVIIg)

This was done as for (XVIIIf).

Band 1. (44mg)

A mixture of all possible triazines m^+/e 309, 323, 337, 351 ratio 2:21:33:7.

Band 2. (296mg)

This was a mixture of β -phenethyl benzoate (41%) and β -phenethyl-p-methyl benzoate (59%) from N.M.R. I.R. shows a trace of nitrile (ν 2250 cm^{-1}) also present.

Band 3. (34mg) - origin, amide in nature.

The total recovery of material from preparative t.l.c. was 92%.

Preparation of 2,4,6-tri-p-tolyl-1,3,5-triazine (XVIIe)⁷⁴

From the chlorosulphonic acid catalysed trimerisation of p-tolunitrile Yield 80%. M.Pt. 286-288°C Lit. 278-279°C (toluene)⁶⁵, m^+/e 351 as expected for $\text{C}_{24}\text{H}_{21}\text{N}_3$ fragmenting solely to m^+/e 117. N.M.R. δ 2.5 for Methyl. I.R. ν 1610, 1585, 1520, 1415, 1380, 865, 810, 780 cm^{-1} .

Preparation of N-p-bromobenzoyl- β -phenethyl-benzimide (XVIIh)

From p-bromobenzoyl chloride (2.5g) and the imidate hydrochloride (XIVa.HCl) as normal. Crystals from CHCl_3 /Ether (2.5g, 50%). M.Pt. $93.5-94.5^\circ\text{C}$ m^+/e 408 I.R. ν 1660, 1645, 1280, 1080 cm^{-1} . N.M.R. δ 7.9-7.2, 14Hm; δ 4.4, 2Ht; δ 3.15, 2Ht. Found C 64.66%; H 4.48% Br 19.88%; N 3.44%. $\text{C}_{22}\text{H}_{18}\text{BrNO}_2$ requires C 64.73%; H 4.41%; Br 19.61%; N 3.43%.

Preparation of N-benzoyl-benzyl-p-nitrobenzimidate (XVIIj)

Preparation of the imidate hydrochloride (XIVj.HCl) by passage of HCl gas into ethanol free chloroform, at 0°C and refrigeration, as usual, gave a precipitate, which on filtering off proved to be p-nitrobenzamide. Evaporation of the chloroform filtrate and trituration with ether, did however afford the hydrochloride (13% theory). Benzoylation of this hydrochloride gave the imidate M.Pt. $98.5-100^\circ\text{C}$ (CHCl_3 /ether) m^+/e 360 I.R. ν 1680, 1660, 1535, 1350, 1280 cm^{-1} N.M.R. δ 8.2-7.3, 14Hm; δ 5.5, 2Hs. Found C 69.78%; H 4.51%; N 7.50%; $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_4$ requires C 69.99%; H 4.48%; N 7.77%.

Preparation of N-p-bromobenzoyl- β -phenethyl-p-nitrobenzimidate (XVIIk).

From p-bromobenzoylation of the imidate hydrochloride (XIVe.HCl) as normal. Crystals from CHCl_3 / Et_2O . M.Pt. $102-103^\circ\text{C}$. I.R. ν 1680-1640, 1530, 1350 cm^{-1} . N.M.R. δ 8.3-7.2, 13Hm; δ 4.7, 2Ht; δ 3.2, 2Ht. Found C 58.30%; H 3.91%; N 5.98%. $\text{C}_{22}\text{H}_{17}\text{BrN}_2\text{O}_4$ requires C 58.28%; H 3.75%; N 6.18%.

Preparation of N-benzoyl-methyl-3,5-dinitrobenzimidate (XVIIIm).

3,5-dinitrobenzonitrile was prepared by dehydration of the amide⁷³ (80%) m.pt. $129-131^\circ\text{C}$, lit. m.pt. $129-130^\circ\text{C}$ (ethanol)⁷⁵. Benzoylation of the imidate hydrochloride (XIVm.HCl)

(87%, crystalline from CHCl_3 after 5 days) prepared as for hydrochloride (XIVe.HCl), afforded a yellow oil which crystallised on addition of ether. The crude spectral data showed the required material to be present. However crystallisation, $\text{CHCl}_3/\text{Et}_2\text{O}$, for analysis gave a material m.pt. $140-152^\circ\text{C}$ which analysed incorrectly. The mass spectrum of this material showed m^+/e 329 and 343 which was attributed to an ethoxy residue, arising due to facile replacement of methoxy by ethoxy by the ethanol present in chloroform. Crystallisation of a new sample from ethanol free CHCl_3 /ether gave yellow crystals (50%) M.Pt. $165-166.5^\circ\text{C}$. I.R. ν 3200, 1680, 1660, 1550, 1350, cm^{-1} rest v. complex N.M.R. δ 9.2-8.7, 3Hm; δ 8.2-8.0, 2Hm; δ 7.7-7.4, 3Hm; δ 4.15, 3Hs. Found C 54.85%; H 3.42%; N 12.77%. $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_6$ requires C 54.72%; H 3.37%; N 12.76%.
Pyrolysis of N-benzyl-methyl-3,5-dinitrobenzimidate (XVIIIm)

400mg of (XVIIIm) were pyrolysed at 210°C for 40 hours in a sealed tube under Nitrogen to give 4 bands on preparative t.l.c. (benzene/petrol 1:1, SiO_2) and a small amount of insoluble material.

Band 1. (Rf 0.6) 6mg, was 2,4,6-triphenyl-1,3,5-triazine m.m.pt. $236-237^\circ\text{C}$. m^+/e 309.

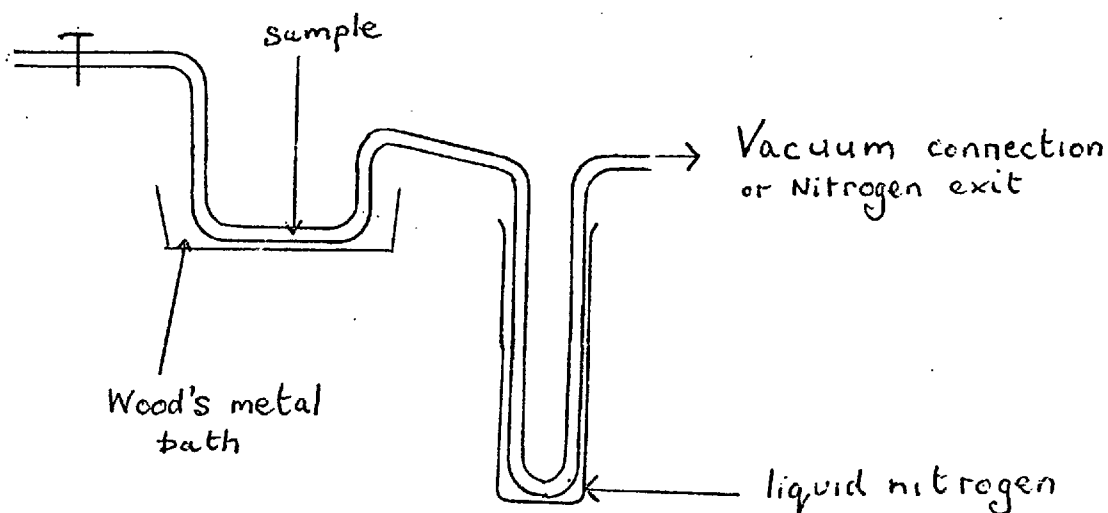
Band 2. (Rf. 0.36) 56mg. a mixture of benzonitrile and methyl benzoate (I.R. and N.M.R.) along with some solid material, which was separated by washing with petroleum ether. This solid was identical to insoluble material m^+/e 399. M.Pt. ca. 270°C (sublimed), CH_2Cl_2 /petrol.

Hence probably 2,4-diphenyl-6-dinitrophenyl-1,3,5-triazine (XVIIIf) (Insufficient sample for microanalysis). The separation of benzonitrile, and methyl benzoate was attempted on silver nitrate impregnated plates, but unfortunately failed.

Band 3. (172mg) Rf 0.11 This was methyl-3,5-dinitrobenzoate m.pt. $108-108.5^{\circ}\text{C}$, by comparison with an authentic sample, m.pt. $107-107.5^{\circ}\text{C}$ m.m.pt. $107.5-108^{\circ}\text{C}$ (benzene/petrol) lit. m.pt. 107.8°C ⁷⁶.

Band 4. (65mg) - origin - not investigated.

Pyrolysis of (XVIIIm) was also carried out under nitrogen flow, and in vacuum, in the apparatus depicted, but no proposed pyrolysis intermediates were detected at 205°C .



Preparation of N-3,5-dinitrobenzoyl-methyl-benzimidate (XVIIIn).

From the imidate hydrochloride (XIVc.HCl) (580mg) and 3,5-

dinitrobenzoyl chloride (850mg) as usual, to give white fluffy crystals from ether. M.Pt. 112-114°C (550mg, 50%) m^+/e 329. I.R. ν 3200, 1645, (br.) 1550, 1350, 1300, 1100, 940, 715 cm^{-1} . N.M.R. δ 9.2, 3Hs; δ 7.8-7.2, 5Hm; δ 4.2, 3Hs. Found C 54.69%; H 3.40%; N 12.79%. $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_6$ requires C 54.72%; H 3.37%; N 12.76%.

Pyrolysis of N-3,5-dinitrobenzoyl-methyl-benzimidate (XVIIIn)

400mg were pyrolysed at 203°C for 11 hours in a sealed tube under nitrogen to give 6 bands on preparative t.l.c. (benzene/petrol 1:1, SiO_2).

Band 1. (8mg) triazine (XVIIIa) m.pt. 236.5-237°C m.m.pt. 237-238°C.

Band 2. (10mg) triazine (XVIIIf) m^+/e 399 m.pt. 270° (sublimed). Found C 63.10%; H 3.50%; N 17.36%, $\text{C}_{21}\text{H}_{13}\text{N}_5\text{O}_4$ requires C 63.16%; H 3.28%; N 17.54%.

Band 3. (36mg) mainly benzonitrile (I.R.), some ester.

Band 4. (13mg) mainly methyl benzoate (I.R.), some nitrile.

Band 5. (183mg) methyl-3,5-dinitrobenzoate m.pt. 106-107.5° m.m.pt. 107-107.5°C.

Preparation of N-d3-3,5-dinitrobenzoyl-d3-methyl-benzimidate (XX).

i) d-5-benzoic acid (718mg, 57%) was prepared as in the preparation of deuterio imidate (XIX) on a millimolar scale.

ii) Nitration.⁷⁷ To d-5-benzoic acid (635mg) and conc. H_2SO_4 (3ml), fuming nitric acid (1ml. S.G 1.54) was added dropwise, keeping the temperature between 70-90°C. After standing overnight, the whole was heated for 4 hours on a

steam bath. This mono nitrated product was treated again with fuming nitric acid (.75ml) and heated for 3 hours on a steam bath, and 3 hours on an oil bath (140°C). The cooled product was poured onto ice and the product filtered off, washing with water. Yield 502mg (50%, as lit.)⁷⁷.

M.Pt. 203-207°C m⁺/e 215. for $C_7H_3D_3N_2O_6$.

iii) Acid chloride

The deuterio acid (500mg) was refluxed with thionyl chloride (900mg) in benzene (5ml) with a trace of D.M.F., as normal to give the acid chloride (267mg, 50%) from petrol.

iv) The deuterio imidate hydrochloride (XIVe.HCl) (1.734g, 99%) was prepared from benzonitrile (1.03g) and deuterio methanol (400mg 1.1 equiv.) as normal, and acylation with the prepared acid chloride afforded the d-6-imidate (XX)

M.Pt. 108.5-111°C m⁺/e 335 for $C_{15}H_5D_6N_3O_6$.

Copyrolysis of N-3,5-dinitrobenzoyl-methyl-benzimidate (XVIIIn) and deuterio analogue (XX).

100mg of a 1:1 mixture of imidates was pyrolysed under Nitrogen flow, in the apparatus previously explained, for 2 hours at 290-300°C. Preparative t.l.c. of material in the cold trap, (benzene/petrol, 1:1 SiO₂) gave two main bands, as required.

Ester band. (25mg) methyl-3,5-dinitrobenzoate m.pt. 107-107.5°C m.m.pt. 106-107.5°C m⁺/e 226, 229, 232 ratio 1:2:1 demonstrating that the pyrolysis was intermolecular.

Preparation of N-3,4-dimethoxybenzoyl-methyl-p-nitrobenzimidate (XVIIIo).

Veratroyl chloride was prepared as normal from the acid, obtained by oxidation of veratraldehyde with potassium permanganate⁷⁸.

The imidate hydrochloride (XIVb.HCl) (216.5mg), was treated with veratroyl chloride (200.5mg) for 1 hour (overnight reaction gave the required product, but it was contaminated with an amide (I.R.)) in pyridine, to give yellow crystals (210mg, 61% theory) M.Pt. 133.5-135°C (benzene/petrol) m^+/e 344, I.R. ν 1680, 1660, 1540, 1360 cm^{-1} , rest very complex). N.M.R. δ 8.3-7.5, 6Hm; δ 6.8-7.2, 1Hd; δ 4.1, 3Hs; δ 3.95, 6Hs. Found C 59.66%; H 4.68%; N 7.94% $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_6$ requires C 59.30%; H 4.68%; N 8.14%.

Pyrolysis of N-3,4-dimethoxybenzoyl-methyl-p-nitrobenzimidate (XVIIo).

400mg of imidate (XVIIo) were pyrolysed for $7\frac{3}{4}$ hours at 210°C in a sealed tube, under nitrogen and preparative t.l.c. (benzene/ethyl acetate 2:1, SiO_2) gave two main bands.

Band 1. (135mg). Treatment of the oil with ethanol gave a small amount of precipitate showing, m^+/e 474, 459, 444, 429.

The remainder was methyl-p-nitrobenzoate. M.Pt. 91-93°C m.m.pt. 90-92°C. lit. m.pt. 96°C⁷⁹ (ethanol).

Band 2. Again some ethanol insoluble material, showing m^+/e 489, 474, 459, 444. The remainder was veratronitrile (I.R.) m.pt. 62-63°C m.m.pt. 62-64°C. Compared with an authentic sample⁸⁰ m.pt. 63-64°C lit 66-67°C⁸⁰.

Attempted preparation of cholestanyl benzimidate hydrochloride.

Cholestan-3 β -ol⁸¹, (388mg) and benzonitrile (103mg) in ether (40ml) were treated with HCl gas, in the usual manner, but after storage at 0°C for 3 days, no imidate hydrochloride could be detected. The reaction was repeated using chloroform (ethanol free) and dioxan as solvents, and even storage

of up to 4 weeks gave no product, cholestanol being obtained (I.R., t.l.c.) on removal of solvent and trituration with ether.

Reactions of cholestane-3 β -ol with N-benzoyl-benziminochloride (XXI).

The iminochloride (XXI) was prepared⁸² by treatment of dibenzamide with phosphorus pentachloride to give colourless crystals m.pt. 85.5-86.5°C lit. m.pt.⁸² 87°C (petrol).

i) Cholestanol (195mg) in glyme (5ml) was refluxed with 24mg NaH (washed with hexane to remove paraffin oil) for 2 hours. After cooling, the imino chloride (122mg) was added and after stirring for 15 minutes, the excess Sodium Hydride was destroyed with t-butanol. After filtration, a solid was obtained on evaporation m.pt. >250°C showing m⁺/e 388, 105 but apart from this it did not seem to be the required material.

ii) Cholestane-3 β -ol (190mg) and N-benzoyl benziminochloride (122mg) with triethylamine (50mg) were refluxed overnight, after filtration and removal of solvent trituration with ether gave more triethylamine hydrochloride (I.R.) but the only material to be characterised was cholestanol, although there was indication (t.l.c.) that a new product was partially formed.

Reaction of β -phenethyl alcohol and N-benzoyl benziminochloride

A solution of iminochloride (XXI) (243mg), β -phenethyl alcohol (122mg) and triethylamine (101mg) in glyme (5ml) was refluxed overnight. Removal of solvent, and trituration with ether gave triethylamine hydrochloride, the filtrate was

Concentrated to give the imide (XVIIa) m^+/e 329, I.R. and N.M.R. match. m.pt. $73-76^{\circ}$ m.m.pt. $74-77^{\circ}$. but in very poor yield.

Reaction of N-3,5-dinitrobenzoyl-methyl-benzimide (XVIIIn) with octan-2-ol.

The imide (329mg) and octan-2-ol (130mg) in benzene (80ml) was heated so that the benzene slowly distilled (ca. 3 hours). The residual oil was crystallised by addition of ether, to show the required crude product. This product was freed of amide contamination by taking up into cold chloroform (ethanol free) and filtering.

Crystallisation (CHCl_3 /ether) gave the pure material (XVIIp) m.pt. $103-107^{\circ}\text{C}$ m^+/e 427. I.R. ν 3200, 1670, 1650, 1555 cm^{-1} (rest very complex). N.M.R. δ 9.2, 3Hs;

δ 7.6-7.4, 5Hm; δ 5.6-5.1, 1Hm; δ 2.0-0.8, ca. 16H.

Found C 61.74%; H 5.87%; N 10.01%. $\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}_6$ requires C 61.82%; H 5.90%; N 9.83%.

Pyrolysis of N-3,5-dinitro benzoyl-2-octyl-benzimide (XVIIp).

400mg of (XVIIp) were pyrolysed for 1 hour at 210°C in a sealed tube under nitrogen to give two major bands on preparative t.l.c. (benzene/petrol 1:1, SiO_2).

Band 1. Triazine (XVIIIa) (by comparative t.l.c.) m.m.pt.

Band 2. (72mg) 2-octyl-3', 5'-dinitrobenzoate, by comparison with authentic sample, distilled using a Kugelrohr apparatus, to remove unreacted octan-2-ol. I.R. ν 3200, 1725, 1560, 1360, 1290, 1180, 730 cm^{-1} N.M.R. δ 9.2, 3Hm; δ 5.6-5.0, 1Hm; δ 2.2-0.6, 16Hm. Yields were very low due to charring on pyrolysis.

Reaction of N-benzoyl-methyl-3,5-dinitrobenzimidate (XVIIIm) with octan-2-ol.

Slow distillation of benzene, from the reaction mixture, as in the preparation of imidate (XVIIp) gave unchanged starting material. To overcome this the benzene was continually distilled off, using a Soxhlet apparatus containing calcium hydride to remove the methanol which codistills.

Overnight reflux of imidate (XVIIIm) (260mg) with octan-2-ol (130mg, 1.2 equivalents) gave a yellow oil on removal of benzene. I.R. ν 3150, 1660, 1640, 1540, 1320 920 cm^{-1} . N.M.R. δ 7.9-8.2, 2Hm; δ 7.4-7.7, 3Hm; δ 5.3 (br.), 1Hm; δ 0.6-2.0, ca. 16H. m^+/e 427. This material however did not crystallise.

Pyrolysis of N-benzoyl-2-octyl-3',5'-dinitrobenzimidate (XVIIId).

391mg of crude imidate were pyrolysed for 16 hours at 176°C under nitrogen. The reaction showed extensive charring, but lower temperature or less time, showed incomplete reaction. Preparative t.l.c. (benzene/petrol 1:1, SiO_2) gave 3 main bands.

Band 1. 4.0mg. - 2,4,6-triphenyl-1,3,5-triazine, comparative t.l.c. m.pt. 236°-238°C: m.m.pt. 236-237°C.

Band 2. (84mg) 2-octyl-3',5'-dinitro benzoate (N.M.R., I.R. comparison).

Band 3. (22mg) methyl-3,5-dinitrobenzoate, m.pt. 106-106.5°C m.m.pt. 106-107°C. (I.R. and N.M.R.). This arose due to the presence of the methyl imidate (XVIIIm).

Reaction of imidate (XVIIIm) with d-octan-2-ol.

Soxhlet exchange, as for imidate (XVIIIg), overnight gave

the required imidate (XVIIq^{*}) as an oil, I.R., N.M.R. identical to (XVIIq).

Pyrolysis of N-benzoyl-d-2-octyl-3',5'-dinitro benzoate (XVIIq^{*}).

The crude imidate (XVIIq^{*}) (3.15g) was pyrolysed in a sealed tube under nitrogen at 176°C for 16 hours. To give 2-octyl-3',5'-dinitro benzoate (230mg) after prep t.l.c. (benzene/petrol 1:1, SiO₂) m.pt. 43.5-50°C (constant) $[\alpha_D] = + 26.8^\circ$.

Authentic d-2-octyl-3',5'-dinitro benzoate m.pt. 50.5-53°C (ethanol) gave $[\alpha_D] + 32^\circ$.

Experiments on "catalysis" of imidate pyrolysis - see discussion

These were done in a sealed tube, using ca. 10% (by weight) of the so called catalyst, in the normal manner, examining the pyrolysis by t.l.c. for enhancement of reaction rate, and new products, with reference to pyrolysis of the imidate alone.

Pyrolysis of N-benzoyl-β-phenethyl-benzimidate (XVIIa) and p-nitro benzoic acid.

180mgs of the mixture (10:1) were pyrolysed at 210°C for 4 hours, in a sealed tube, under nitrogen, giving rise to the normal pyrolysis products and two other materials, which were separated by preparative t.l.c. (benzene/petrol 1:1, SiO₂).

Triazine fraction, (1.5mg) this was 2,4-diphenyl-6-p-nitro-phenyl-1,3,5-triazine (XVIIIb) m⁺/e 354, comparative t.l.c.

Ester fraction (28mg) this was β-phenethyl-p-nitro benzoate m.pt. 59.5-60°C m.m.pt. 59.5-60.5°C (ethanol) and I.R. match.

Pyrolysis of N-benzoyl-β-phenethyl-benzimidate (XVIIa) and

Mesitoic acid.

190mg of the mixture (10:1) were pyrolysed at 210°C in a sealed tube under nitrogen for 20 hours. Again two new materials were produced, and these were separated by preparative t.l.c. (benzene/petrol 1:1, SiO₂).

Triazine fraction (< 1mg). This showed m⁺/e 351, and from the breakdown pattern (247, 145) the material was assumed to be 2,4-diphenyl-6-(2',4',6'-trimethyl-phenyl)-1,3,5-triazine (XVIIIg).

Ester fraction (101.5mg). This was a mixture of β-phenethyl benzoate (80%) and β-phenethyl-mesitoate (20%)
I.R. ∨ 1720, 1285 N.M.R. δ 3.0, +δ 4.55, 2 triplets;
δ 2.1-2.4 methyl;

An authentic sample of β-phenethyl-mesitoate⁸³ was prepared from mesitoyl chloride and β-phenethyl alcohol, and purified by distillation using the Kugelrohr apparatus.

N.M.R. δ 2.1-2.4, 9Hm; δ 3.0, 2Ht; δ 4.55, 2Ht;
δ 6.8, 2H br.s.; δ 7.25, 5Hs. I.R. ∨ 1725, 1280 cm.⁻¹.

The N.M.R. of an authentic mixture of β-phenethyl-benzoate (80%) and β-phenethyl mesitoate matched exactly with the pyrolysis fraction.

Pyrolysis of N-benzoyl-β-phenethyl-benzimidate (XVIIa) and p-nitrophenol.

200mg of a (10:1) mixture were pyrolysed at 210°C in a sealed tube under nitrogen for 17½ hours, one new product was apparent, and this was separated by preparative t.l.c. (benzene/petrol, 1:1, SiO₂)

The new product ran virtually concurrent with β-phenethyl benzoate, but treatment of this fraction with petrol

enabled the ester to be washed out. The product was recrystallised m.pt. $142-142.5^{\circ}\text{C}$ (benzene/petrol) I.R.

ν 1740, 1600, 1530, 1350, 1270, 1215, 1070 cm^{-1} .

This proved to be p-nitrophenyl benzoate lit m.pt.⁸⁴ 142°C m.m.pt. $142.5-143^{\circ}\text{C}$ with an authentic sample from benzoyl chloride and p-nitrophenol.

Pyrolysis of N-benzoyl- β -phenethyl-benzimidate (XVIIa) with picric acid.

190mg of the mixture (10:1) were pyrolysed for 1 hour at 145°C and the one new product isolated by preparatory t.l.c. (benzene petrol 1:1, SiO_2). This again came out mixed with β -phenethyl benzoate, and was thought to be an ether (I.R. ν 1100 cm^{-1}) after re-separation by t.l.c. Pyrolysis on a larger scale, (imidate (250mg) and picric acid (175mg) (molar equivalents)) for 2 hours at 140°C afforded a much greater yield of ester and ether by preparative t.l.c. (ethyl acetate, SiO_2). The ether was a yellow oil, which on treatment with ether solidified. Recrystallisation gave crystals, m.pt. $72.5-74^{\circ}\text{C}$. m^+/e 333. N.M.R. δ 8.8, 2Hs; δ 7.2, 5Hs; δ 4.4, 2Ht; δ 3.1, 2Ht. I.R. ν 1610, 1540, 1350, 1100, 970, 720 cm^{-1} . Found C 50.71%; H 3.45%; N 12.54%. $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_7$ requires C 50.46%; H 3.33%; N 12.61%, proving it to be β -phenethyl-picryl ether (XXXVI).

Attempted preparations of β -phenethyl-picryl ether (XXXVI)

i) β -Phenethyl tosylate (276mg) and picric acid (229mg, dried) were refluxed in benzene (10ml) with triethyl amine (101mg), overnight. T.l.c. (benzene, SiO_2) indicated a trace of the required product, but this did not increase

with time.

ii) Picryl chloride was prepared according to the literature⁸⁵ from pyridine picrate and phosphorus oxychloride m.pt. 79-81°C lit. m.pt.⁸⁵ 79-81°C. I.R. $\checkmark$ 3100, 1610, 1560, 1360, 1070, 950, 940, 740, 735 cm^{-1} .

To picryl chloride (62mg) and β -phenethyl alcohol (30.5mg) in benzene (5ml), pyridine (20mg) was added, there was an immediate red colouration. After stirring overnight, dil. HCl was added and the reaction extracted with benzene, but t.l.c. showed no reaction (benzene/ SiO_2). Similarly the reaction using triethylamine, in place of pyridine failed.

iii) To sodium hydride (48mg of 50% suspension), in benzene (5ml), β -phenethyl alcohol was added. To this, after 5 minutes, picryl chloride (124mg) in benzene (ca. 3ml) was added dropwise. There was an immediate red colouration, which persisted overnight, and work up, as for (ii) above, showed no reaction, t.l.c. (benzene, SiO_2) and I.R.

iv) 1-iodo-2-phenyl-ethane was prepared from β -phenethyl alcohol, potassium iodide, and orthophosphoric acid⁸⁶, purifying the product by column chromatography (benzene, SiO_2). I.R. $\checkmark$ 1600, 1500, 1460, 1220, 1175, 760, 710 cm^{-1} . N.M.R. δ 7.2, 5Hs; δ 3.4-3.0 4H. (2 triplets superimposed). To 1-iodo-2-phenyl-ethane (222mg) in ethanol (4ml) at 0°C, silver picrate⁸⁷ was added and the whole stirred overnight. T.l.c. (benzene, SiO_2) again indicated the formation of β -phenethyl-picryl ether.

The ether was eventually prepared according to route (i),

using preparative t.l.c. to separate it. M.pt. 72.5-73.5°C m.m.pt. with sample from pyrolysis 73-74°C.

Preparation of N¹-phenyl-carboxamido-β-phenethyl-benzimidate³⁶
(XXII).

To the imidate hydrochloride (XIVa) (261.5mg) and triethylamine (101mg) in glyme (5ml), phenyl isocyanate (119mg) was added and the whole stirred overnight. The reaction was then poured onto ice/water, and extracted with chloroform, to yield a crystalline product (181mg, 52%) from ether m.pt. 102-104°C I.R. ν 3250, 1665, 1650, 1600, 1540, 1250, 1130, 700 cm^{-1} . N.M.R. δ 7.8-6.8, 16Hm, (D_2O exch.); δ 4.5, 2Ht; δ 3.1, 2Ht. Found C 76.59%; H 5.85%; N 8.22%. $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_2$ requires C 76.72%; H 5.85%; N 8.13%. m^+/e 344.

Pyrolysis of N¹-phenyl-carboxamido-β-phenethyl-benzimidate
(XXII).

400mg of (XXII) were pyrolysed in a sealed tube under nitrogen at 218°C for 1½ hours to give six bands on preparative t.l.c. (benzene/petrol 1:1, SiO_2).

Band 1. 11mg, was 2,4,6-triphenyl-1,3,5-triazine m^+/e 309, m.pt. 237°C m.m.pt. 238°C.

Bands 2 + 3. (minor) 26mg. Not investigated.

Band 4. (170mg). This proved to be β-phenethyl-N-phenyl urethane, m.pt. 79.5-80.5°C m.m.pt. 78.5-79.5°C, by comparison with an authentic sample, (m.pt. 76.5-78.5°C lit. 79-80°C⁸⁸ (ethanol)) prepared^{88,89} by briefly heating equimolar amounts of phenyl isocyanate and β-phenethyl alcohol on a steam bath, and crystallising the solid mass from ethanol. I.R. ν 3370, 1700, 1600 cm^{-1} . N.M.R. δ 8.2; 1H (br), D_2O exchange; δ 7.6-7.0, 10H m; δ 4.4,

2Ht; δ 3.0, 2Ht.

Band 5. (47mg) - not investigated.

Band 6. (145mg) this showed m^+/e 222 m.pt. 241-242°C (CHCl₃). Found C 75.78%; H 4.72%; N 12.81% C₁₄H₁₀N₂O requires C 75.66%; H 4.54%; N 12.6%. This data would indicate the material to be a quinazoline³⁷.

Preparation of 1,2-dihydro-4-phenyl-2-oxoquinazoline³⁷ (XXIII)

A mixture of 2-amino benzophenone (2g) and urea (1g) were heated with vigorous stirring at ca. 195°C on an oil bath, until the material solidified (ca. 40mins.). The cake was crystallised from ethanol m.pt. 261-262°C (some change 250-260°C) lit.³⁷ 250°C m^+/e 222. I.R. ν 3100-2800 br.

Preparation of 2-phenyl-4-oxoquinazoline (XXIV)³⁸

Anthranilic acid (1.37g) and thiobenzamide⁹⁰ (1.37g) were heated on an oil bath (135-160°C) for 2 hours with stirring. The cooled product was dissolved in cyclohexane, and the crystals recrystallised from ethanol m.pt. 240-242°C Lit.³⁸ 235°C. M^+/e 222. This was identical with fraction 6 from pyrolysis, m.m.pt. 239-241°C. I.R. ν 3200, 3140, 3070, 1660, 1605, 1100, 950, 780, 700 cm.⁻¹. U.V. λ 217, (log ϵ 4.34); λ 236, (log ϵ 4.42); λ 290, (log ϵ 4.15); λ 317 in fl.⁹¹

Preparation of thiobenzoyl chloride

To the Grignard (from Magnesium (2.4g) and bromobenzene (15.7g) in ether (50ml)) prepared under nitrogen, benzene (50ml) was added, and the whole cooled to 0°C (ice/salt bath). To this Carbon Disulphide (9.1g, 8ml, 0.12 mole) was added dropwise, and the whole stirred overnight.

The dithio acid was liberated by pouring onto ice/HCl and extracted with benzene, this was extracted with sodium hydroxide to give the sodium salt, from which the acid was liberated on neutralisation, and extracted with benzene. The acid was then added dropwise to refluxing thionyl chloride (36g, .3 mole) in benzene (50ml) with a trace of D.M.F. After removing the benzene the acid chloride (2g) was distilled as a purple oil B.pt. 80°C , 0.7mm. Lit. $60-65^{\circ}\text{C}$, 0.2mm⁴⁰.

Reaction of thiobenzoyl chloride with β -phenethyl-benzimidate hydrochloride (XIVa.HCl).

To the hydrochloride (521mg) in pyridine (ca. 1ml) at 0°C , thiobenzoyl chloride (313mg) was added dropwise, and the whole stirred overnight. The reaction was poured onto ice and extracted with chloroform, removing solvent and pyridine under vacuum, after drying over Na_2SO_4 . The only material isolated was benzamide (I.R.), t.l.c. benzene/petrol showed a complex reaction.

Reaction of thiobenzoyl chloride with methyl benzimidate (XIVc).

To a mixture of imidate (135mg), and triethylamine (101mg) in dry ether (5ml) at 0°C , under nitrogen, thiobenzoyl chloride was added. After stirring overnight, the reaction was filtered, evaporation gave a red oil, which was basically unreacted imidate (I.R.). T.l.c. was again complex.

Treatment of N-benzoyl- β -phenethyl-benzimidate (XVIIa) with phosphorus pentasulphide.

To the imidate (329mg) in dry pyridine (4ml) at 0°C phosphorus

pentasulphide (222mg, 5 equiv.) was added, and the whole stirred overnight, the reaction was then poured onto vigorously stirred petrol, and filtered. After evaporation of solvent the crude oil was shown to be mainly starting material, crystallisation (ether) gave dibenzamide (I.R.) a minor hydrolysis product.

Reaction of methyl benzimidate (XIVc) with phenyl thioglycolic acid.

The free imidate was prepared from the imidate hydrochloride (XIVc.HCl) as normal. To methyl benzimidate (135mg) in ether (5ml) sodium hydride (200mg, 50% dispersion, 4 equivalents) was added and the whole stirred, hydrogen being evolved briskly. After ca. 1 minute, phenylthioglycolic acid (212mg) was added and the whole stirred overnight. Filtration, gave a yellow oil which on evaporation proved to be methyl thionbenzoate with some nitrile (ν 2260 cm^{-1}) m^+/e 152. I.R. ν 1600, 1460, 1280, 1240, 770, 700 cm^{-1} . N.M.R. δ 8.0-8.3, 2Hm; δ 7.3-7.7, 5Hm (due to nitrile aromatics); δ 4.25, 3Hs.

Reaction of thiobenzamide with phenyl thioglycolic acid.

To thiobenzamide (137mg) in fresh dry T.H.F. (5ml) at room temperature, Sodium Hydride (70mg, ca. 50% dispersion, $1\frac{1}{2}$ equiv.) was added, and the whole stirred. When effervescence had ceased, phenyl thioglycolic acid (212mg) was added and the whole stirred overnight, before pouring onto petroleum ether. T.l.c. showed 6 spots, all active to palladous chloride, and a nitrile stretch (ν 2260 cm^{-1}) was evident from I.R.

Attempted preparation of dithiobenzamide from dibenzamide, using P_2S_5 .

A mixture of P_2S_5 (111mg., $1\frac{1}{4}$ equiv.) and dibenzamide (225mg) was stirred in refluxing dry dioxan⁹² (2ml) for 1 hour before pouring onto petroleum ether. The filtrate gave a viscous oil, no trace m^+/e 257, instead m^+/e 313, 225.

Preparation of N-thiobenzoyl benzylamine^{44,45} (XXV)

A mixture of benzylamine (5.35g, .05 mole) and sulphur (2g, .065 mole) was heated at reflux (180°C) for 45 mins. on a Wood's metal bath, after cooling the whole was triturated with pet. ether (80-100) and filtered. The solid was recrystallised from petrol (80-100) m.pt. 81.0-83.5°C, lit.⁴⁰ 84-85°C (yield 3.7g, 67%). I.R. ν 3300, 1530, 1500, 1400, 1335, 1200, 1075, 950 cm^{-1} . N.M.R. δ 7.8-7.5, 2Hm; δ 7.4-7.2, 8Hm; δ 4.95 2Hd, cannot see $>N-H$, but on D_2O exchange, methylene doublet collapses to a singlet.

Reaction of benzylamine with excess sulphur.

Benzylamine (5.35g) was refluxed with Sulphur (4g, $2\frac{1}{2}$ equiv.), as above. T.l.c. showed one extra spot (active to palladous chloride) but continued heating did not increase this, and work up of the reaction as above gave solely N-thiobenzoyl benzylamine.

Preparation of N-thiobenzoyl benzamidine^{93,94} (XXVI)

A solution of thiobenzamide (1.03g) and benzonitrile (.773g) in ether (35ml), at 0°C, was saturated with dry HCl gas, and kept at room temperature for five days. The initial yellow solution quickly turned red, and deposited an oil, which eventually crystallised. This crude hydrochloride was partitioned between ether/ $KHCO_3$, liberating the free

imine, and thiobenzamide contaminant. The required hydrochloride (orange crystals) was acquired by addition of ethanolic HCl to the dried ether solution. After filtration the free base was liberated, as before, and the red oil crystallised from benzene m.pt. $75.5-76^{\circ}\text{C}$, lit.⁹⁴ $73-74^{\circ}\text{C}$. I.R. ν 3350, 1600 (br), 1420-1360, 1220, 1060, 800, 780, 720, 700 cm^{-1} . N.M.R. δ 8.5-8.3, 2Hm; δ 8.2-7.8, 2Hm; δ 7.6-7.2, 6Hm; δ 6.7 br, + δ 8.5-10, ca. 2N-H which disappeared on D_2O exchange.

Reaction of N-thiobenzoyl-benzamidine (XXVI) with H_2S .

To the amidine hydrochloride (XXVI.2HCl) (50mg) in formamide (1ml) H_2S was slowly passed, and the reaction stoppered. After 12 hours the orange colour disappeared, to give a new spot (t.l.c. benzene/EtOAc, 2:1) unactive to palladous chloride, and a precipitate (3 days) which was characteristic of sulphur.

Reaction of N-thiobenzoyl-benzamidine (XXVI) with H_2S , in acetic anhydride.

Passage of H_2S , as above (50mg (XXVI) in 2ml Ac_2O) gave no colour change, but t.l.c. (benzene/EtOAc 2:1 SiO_2) showed complete reaction. Preparative t.l.c. indicated that this could be acetylation.

Reaction of N-thiobenzoyl-benzamidine (XXVI) with P_2S_5 .

A mixture of amidine (XXVI) (120mg) and P_2S_5 (111mg, $2\frac{1}{2}$ equiv.) in dioxan (2ml) was stirred at room temperature, for 48 hours, t.l.c. (benzene/ethyl acetate 2:1, SiO_2) showed two new spots active to palladous chloride. The reaction was then poured into pet. ether and the filtrate

purified by preparative t.l.c.. The more polar material was proved to be thiobenzamide I.R. ν 3360, 1600, 1330, 1130 cm^{-1} . matches authentic, m^+/e 137, comparative t.l.c.

Preparation of N-acetyl-N'-thiobenzoyl-benzamidine (XXVII)

To the amidine (XXVI) (240mg) in pyridine (2.5ml) at 0°C ., acetyl chloride (78.5mg, .071ml) was added, and the whole stirred overnight, before pouring onto ice/dil. HCl, and extracting with dichloro-methane. This was dried with Na_2SO_4 and evaporated, to yield a red/brown oil, which, on treatment with anhydrous ether afforded a red solid (60% theor. crude). Recrystallisation, CHCl_3 /ether gave two crystal forms - orange and red. These showed identical Rf. (benzene/ethyl acetate 2:1), I.R. solution spectra (CHCl_3) ν 1720, 1645, 1450, 1380 cm^{-1} (CHCl_3) and qualitative U.V. ethanol. m^+/e 282, m.pt. $142-146^\circ\text{C}$. Found C 67.92%; H 4.99%; N 9.74%. $\text{C}_{16}\text{H}_{14}\text{N}_2\text{SO}$ requires C 68.08%; H 5.00%; N 9.92%.

Reaction of N-acetyl-N'-thiobenzoyl-benzamidine (XXVII) with H_2S .

To the amidine (XXVII) (30mg) in pyridine 1ml, H_2S was slowly passed, for 2 hours. Overnight, this gave an orange solution, which showed 2 new spots t.l.c. (benzene/ethyl acetate 2:1). This seemed identical to the reaction of P_2S_5 on the amidine (XXVI) and preparative t.l.c. gave thiobenzamide, comparative t.l.c., I.R. (CHCl_3). The less polar material was also obtained, m^+/e 147/148 m.pt. $230-240^\circ\text{C}$. subl. This does not correspond to acetamide, or

N-acetyl benzamide, which are possible products.

Preparation N-thiobenzoyl-benzamide (XXVIII)⁴³

To the amidine hydrochloride (XXVI.2HCl) (690mg) in acetone/water (1:1) dilute hydrochloric acid (5ml, 2N) was added and the whole left unstoppered overnight. This should have given deep red prisms, but instead, an oil was present, which was extracted with CCl_4 to give the required product. M.pt. $103-106^\circ\text{C}$, Lit. 117°C ⁴³ benzene/petrol (150mg pure, 28% theory). I.R. ν 1725, 1695, 1600, 1525 - 1460 (br) 1240, 725 cm^{-1} .

Reaction of N-thiobenzoyl-benzamide (XXVIII) with phosphorus penta-sulphide.

The amide (XXVIII) (50mg) and P_2S_5 (9mg., 1 equiv.) were stirred overnight in dioxan (1ml). Dioxan itself appeared to slowly decompose (XXVIII) but none of the reaction products were active to palladous chloride spray (t.l.c. benzene/petrol 1:1, SiO_2).

Preparation of methyl-dithio-benzoate (XXIX)⁹⁵

Dithiobenzoic acid was prepared and purified, as in the preparation of thiobenzoyl chloride, from Bromobenzene (15.7g). To the sodium salt of dithiobenzoic acid in neutral water, dimethyl sulphate (12.6g, 1 equiv.) was added, and the whole stirred for 3 hours at room temperature. The precipitated red oil was extracted with ether and distilled, to give dithio ester (2g, ca 13% theor.) B.pt. $115-118^\circ\text{C}$, 3mm Hg. I.R. ν 1450, 1240, 1055, 995, 775, 700 cm^{-1} . N.M.R. δ 8.2-7.9, 2Hm; δ 7.6-7.2, 3Hm; δ 2.7, 3Hs.

Reaction of thiobenzamide with methyl dithiobenzoate (XXIX)

To thiobenzamide (137mg) in dry xylene (2ml), sodium hydride (50mg, 60% disp'n., slight excess) was added, and the whole warmed to ca. 75°C on an oil bath with stirring, effervescence was observed, and the white sodium salt precipitated out. After cooling, the dithio ester (XXIX) (168mg) was added, and the whole stirred overnight. No reaction (t.l.c. benzene/petrol 1:1, SiO₂). The whole was then warmed to ca. 100°C on an oil bath, whereupon the white precipitate turned red. This product was filtered off, and partitioned between ether/dil. HCl, to give a deep red oil, N.M.R. showed no methyl protons. However the mass spectrum showed m⁺/e 306, 242, 154., indicative of Ph-^SC-S-S-C^S-Ph and other oxidation or breakdown products. The filtrate was unreacted dithio ester (90mg) by N.M.R. and I.R.

Attempted S-Tosylation of N-thiobenzoyl-benzylamine⁴⁶ (XXV)

To the amine (XXV) (227mg) in dry xylene (1ml), sodium hydride (50mg of 57% dispersion) was added, and the whole heated to reflux, with stirring. The precipitated sodium salt was quickly filtered off and washed with benzene and then stirred with Tosyl chloride (190mg) in xylene (1.2ml). T.l.c. showed no new sulphur containing spot after 3 days, and so the temperature was raised to ca. 70°C. The reaction was then filtered, evaporation of the filtrate gave a white crystalline solid I.R. ν 3300, 1640, 1145 cm.⁻¹, N.M.R. 4.65, methylene doublet. This was indicative of N-benzoyl-benzylamine lit. m.pt. 105-106°C⁹⁶, recrystallised sample

m.pt. 103-105°C, arising by simple oxidation.

S-Benzoylation of N-thiobenzoyl-benzylamine⁴⁶

Reaction of the sodium salt of the amine (XXV), prepared from sodium hydride as above, rather than sodium metal⁴⁶, with benzoyl chloride (140mg, 1 equiv.) in dry xylene (1.2ml) gave an instantaneous orange colour, with the evolution of heat. After 1 hour the mixture was filtered, and the filtrate evaporated to give orange crystals (alcohol) m.pt. 103-105°C, lit.⁴⁶ 106°C. I.R. ν 1675, 1600, 1340-1200 (complex) 980, 780, 740, 705 cm^{-1} N.M.R. δ 5.7, 2Hs; δ 6.8-7.8, 15H.m. U.V. λ 226nm (log ϵ 4.276); 240.5nm (log ϵ 4.132); λ 307.5nm (log ϵ 3.997); λ 324nm (shoulder) (log ϵ 3.975); λ 470nm (log ϵ 2.297). This material was N-benzoyl-N-thiobenzoyl benzylamine, and not the required S-benzoylated product. - See discussion.

Reaction of Phthalimide (XXIX) with trimethyl oxonium tetra fluoroborate.

An inhomogeneous mixture of Meerwein salt⁹⁷ (260mg) and phthalimide (259mg) was stirred in dichloromethane (10ml). After 2 days the precipitate was filtered off, and shown to be unreacted phthalimide (I.R.).

Reaction of Homophthalimide (XXXa) with trimethyl oxonium tetrafluoroborate.

Homophthalimide was prepared as the literature route^{98,99}, by chromic acid oxidation of indene, to give homophthalic acid, dehydration to give the anhydride, and reaction of this with ammonia.

Homophthalimide (161mg) and Meerwein salt (148mg) were

stirred in dichloromethane (5ml) for 2 days, filtration yielded unreacted homophthalimide.

Preparation of monothiophthalimide⁵⁰ (XXXII)

A suspension of phthalonitrile (5g) in ethanol (40ml) was stirred for nine hours with a solution of sodium sulphide (10g) in water (10ml), previously saturated with H_2S . Addition of water precipitated the orange 1-imino-3-thioisoindoline (XXXI) which was filtered off. (XXXI) (200mg) was then heated with dil. HCl (5ml, 2N) on a steam bath for 10 minutes, precipitating the imide (XXXII), filtration and crystallisation from benzene, gave red needles (18% theory, lit⁵⁰ 22% overall) m.pt. 175-176.5°C, lit. m.pt. 177°C⁵⁰. I.R. ν 3220, 1740, 1720, 1300, 1125, 990, 790, 705 cm^{-1} .

Attempted S-methylation of monothiophthalimide (XXXII)

To (XXXII) (81.5mg) in dry dichloromethane (2ml) methyl Meerwein salt (74mg, 1 equiv.) was added and the whole stirred at room temperature for 3 hours, until the red colouration had virtually disappeared. The whole was poured onto ice/ $NaHCO_3$ and extracted with dichloromethane, to give phthalimide (I.R.).

Attempted preparation of 3-methoxy isoindoline (XXXIIIa)

Reaction of monothiophthalimide (XXXII) with Meerwein salt, was carried out as above, until the solution had decolourised. The solvent was then removed under vacuum, and the white/orange solid treated with sodium methoxide in methanol (23mg Na. in 2.5ml dry methanol, 2 equiv.). The resulting yellow solution showed 1 major spot, unreactive to palladous

chloride, and 4 minor spots t.l.c. (benzene/EtOAc 2:1 SiO_2). Spectral data after removing methanol showed the presence of OMe (δ 3.35, N.M.R.), but also $>\text{NH}$ or $-\text{OH}$ stretch (I.R.). The Mass Spectrum showed m^+/e 178, 162.

Attempted O-Alkylation of silver phthalimide^{51,100}

Silver phthalimide, prepared from potassium phthalimide and silver nitrate¹⁰¹, was dried to constant weight (70°C in vacuo). To silver phthalimide (1.27g) in chloroform (5ml), ethyl iodide (.78g) was added and the whole stirred in the dark for 4 weeks. The precipitated silver iodide was filtered off, and washed with dry chloroform.

Evaporation gave mainly phthalimide. Attempted O-methylation also failed, again giving phthalimide, although a small amount of oil (ca. 50mg) showed m^+/e 163, 161, 146 (loss Me), 130, loss (OMe). I.R. $\checkmark$ 1560 cm^{-1} (as literature⁵¹ for XXXIIIb) N.M.R. δ 3.9 (OMe?).

The work was repeated in chloroform, and benzene, but no significant yield of the isoindoline (XXXIII) could be obtained.

Reaction of benzonitrile oxide with methyl benzimidate(XIVc)

To benzohydroxamoyl chloride¹⁰² (155mg) and methyl benzimidate (135mg) in dry ether (2ml), triethylamine (101mg) was added, and the whole stirred at room temperature.

There was an immediate precipitation (Et_3NHCl) but the reaction was stirred for 2 hours before filtration and crystallisation of the product from ether. Recrystallisation (petrol) gave colourless crystals, m.pt. $106-109^\circ\text{C}$ m^+/e 222. I.R. $\checkmark$ 1610, 1560, 1130, 1070, 793, 725, 690 cm^{-1} N.M.R. δ 8.4-8.1, 4Hm; δ 7.7-7.4, 6Hm. This evidence

indicated that the product was 3,5-diphenyl-1,2,4-oxadiazole (XXXIV) lit m.pt. ¹⁰² 108°C.

Reaction of N-ethyl-benzonitrilium salt, with methyl benzimidate (XIVc)

Benzonitrile (490mg) and ethyl Meerwein salt (900mg) were refluxed in dry dichloromethane (10ml), to give the nitrilium salt, which was used in situ.

To the imidate (XIVc), (135mg, 1m mole), the nitrilium salt (1 equiv., ca. 2ml of CH_2Cl_2 sol'n.) was added, and the whole stoppered. Standing overnight, precipitated fine needles, but filtration of these indicated them to be the fluoroborate salt of (XIVc). The filtrate, however on removal of the dichloromethane, and trituration with ether, gave a precipitate (ca. 150mg). This was obviously a mixture (N.M.R. δ 4.32, δ 4.4 two OMe peaks) but repeated crystallisation ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$) afforded pure adduct (XXXV. HBF_4). M.pt. 161.5-166.5°C, I.R. ν 3270, 1670, 1620, 1460, 1320, 1090 (br), 710 cm^{-1} . Found C 57.46%; H 5.40%; N 7.83%; $\text{C}_{17}\text{H}_{19}\text{BF}_4\text{N}_2\text{O}$ requires C 57.66%; H 5.37%; N 7.91%.

Reaction of Hydrogen Sulphide on impure(XXXV).

Due to the difficulty of purifying the imidate adduct (XXXV), work was carried out on the crude product. 500mg of the crude fluoroborate salt, was partitioned between dichloromethane and ice cold sodium bicarbonate, liberating the free imines (XXXV) and (XIVc). To this mixture (373mg) in dry dichloromethane (5ml), ethyl Meerwein (373mg) was added, to further ethylate the imines. After stirring

overnight, H_2S was passed through the reaction mixture for two hours, and again left overnight. T.l.c. showed all polar material (i.e. fluoroborate salts still present), addition of pyridine (1ml) caused an immediate yellow colouration, showing one non polar spot (yellow) (t.l.c. benzene/ethyl acetate 2:1, SiO_2). Isolation of this by preparative t.l.c. showed it to be methyl thion-benzoate. I.R. ν 1600, 1460, 1320, 1280, 1240, 1065, 785, 700 cm^{-1} . N.M.R. δ 8.3-8.0, 2Hm; δ 7.6-7.2, 3Hm; δ 4.25, 3Hs, as obtained in earlier reactions.

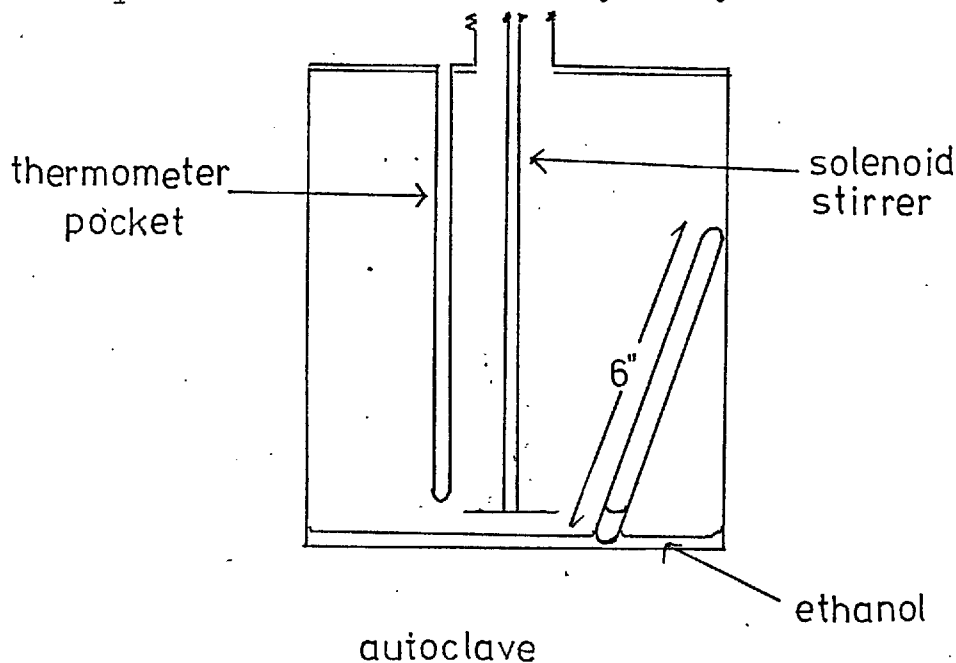
Reaction of methyl benzimidate (XIVc) alone, with ethyl Meerwein, and subsequent treatment with H_2S , in the presence of pyridine also gave methyl thionbenzoate, and so the reaction sequence was abandoned.

Preparation of N-benzoyl-methyl-3,5 dinitro benzoate (XXVIIIm) O^{18} labelled.

i) Preparation of benzoyl chloride - O^{18} ¹⁰³

Benzotrichloride (390mg) and $\text{H}_2 \text{O}^{18}$ (36 μl .) (42% O^{18}) were sealed, under vacuum, in a Carius tube. This tube was placed in an autoclave containing some ethanol, and the whole heated to ca. 200°C for 24 hours, giving a positive pressure to offset to some extent the pressure generated in the Carius tube. After cooling the benzoyl chloride was used without purification. Some difficulty was experienced here, with Carius tubes breaking, and it is imperative to get a good seal, at a reasonable distance from the cold end, so as not to create too large a temperature gradient, and introduce striations in the glass. The ratio

of liquid volume to air was ca. 10:1.



ii) Reaction of benzoyl chloride - O^{18} with imidate hydrochloride (XIVm.HCl).

To the hydrochloride (XIVm.HCl) (840mg) in pyridine (4ml). The acid chloride- O^{18} (450mg - estimated) was added, and the whole stirred overnight. Work up in the usual manner gave the O^{18} imidate (XVIIIm) m.pt. 163-165.5°C authentic m.pt. 165-166.5°C m.m.pt. 163-166°C m^+/e 329, 331 ratio ca. 60:40 (39% O^{18} incorporation).

Pyrolysis of N-(O^{18} -benzoyl)-methyl-3,5-dinitrobenzoate (XXVIIIm).

126mg of O^{18} -imidate (XVIIIm) were pyrolysed in a sealed tube under nitrogen at 230°C for 16 hours and the products separated by preparative t.l.c. (benzene petrol 1:1, SiO_2) to give methyl-3,5-dinitrobenzoate (62.5mg) m^+/e 228, 226 ratio ca. 3:7 (32% O^{18} incorporation) and m^+/e 197, 195 ratio ca. 1:4 (21% O^{18} incorporation in this fragment i.e.

$\frac{2}{3}$ retained) m.pt. of ester = 106.5-108°C m.m.pt. 106-107.5°C authentic m.pt. 107.5-108.5°C.

Repetition of the reaction, starting from benzotrichloride and H_2O^{18} gave O^{18} -imidate (XXVIIIm) (43% O^{18}) m.pt. 160-163.5°C and pyrolysis of 50mg as above gave methyl-3,5-dinitrobenzoate (24mg) m.pt. 104.5-106.5°C (benzene/petrol) m^+/e 228, 226 ratio ca. 1:2 (34.5% O^{18} incorporation) and m^+/e 197, 195 ratio ca. 1:4 (23.5% O^{18} incorporation in this fragment). Thus showing very good agreement of results.

Attempted reduction of methyl-3,5-dinitrobenzoate with Lithium Aluminium Hydride¹⁰⁴.

To a solution of ester (113mg) in T.H.F. (5ml) at -70°C (cardice/ether) bath a suspension of L.A.H. (38mg) in T.H.F. (5ml) was added dropwise. There was an immediate blue colour, and after 3 hours the reaction mixture was poured onto ice/HCl and extracted with dichloromethane. T.l.c. (benzene/ethyl acetate 2:1, SiO_2) showed mainly unreacted ester, confirmed by I.R.

Attempted reduction of methyl-3,5-dinitrobenzoate with Sodium Boro-hydride⁵⁹.

To a mixture of sodium borohydride (9.4mg) and ester (90mg) in diglyme (2.5ml). (The reaction solution went blue immediately) anhydrous aluminium chloride (11.2mg) was added portionwise, keeping at room temperature. After 3 hours stirring the blue colour persisted, and work up by pouring onto ice/HCl and extraction with CH_2Cl_2 indicated that the ester was still largely present (t.l.c. benzene/ethyl acetate 2:1, SiO_2) although 3 new spots

appeared.

Preparation of 3,5-dinitro-benzamide, from methyl-3,5-dinitrobenzoate - O^{18}

The O^{18} -ester (10mg) was stirred at room temperature with .880 ammonia (0.5ml) for $2\frac{1}{2}$ hours, before neutralising with HCl, and extracting with ethylacetate. This extract was separated on thin t.l.c. plates (benzene/ethyl acetate 1:2 SiO_2) showing 1 major band Rf 0.5. The 3,5-dinitro-benzamide m.pt. $182-185^{\circ}C$. lit. m.pt. $183^{\circ}C^{106}(H_2O)$ gave m^+/e 213, 211 ratio ca. 1:4, showing 20% O^{18} incorporation.

Preparation of methyl benzoate, carbonyl- O^{18} labelled^{56,105} (2-oxapropiophenone-1 - O^{18})

Benzoyl chloride (O^{18}) (281mg) was added to sodium methoxide in methanol (138mg in 10ml methanol, 3 equivalents) and the whole stirred at room temperature for 1 hour. The whole was poured onto ice and extracted with dichloromethane, washing with water. The product was purified by prep. t.l.c. (benzene/petrol 1:1, SiO_2). I.R. $\checkmark$ 1720, 1690, 1285, 1110, 720 cm^{-1} .

Mass ions 138, 136 ratio ca. 4:6 showed 43% O^{18} incorporation. fragments 107, 105 ratio ca. 4:6 showed 42% O^{18} incorporation in this fragment.

X-ray crystallographic structure determination on N-benzoyl-
β-phenethyl benzimidate (XVIIa).

The crystals of N-acyl imidate are clear triclinic rhombs,
P $\bar{1}$, $a = 11.3958(6)$, $b = 9.1297(5)$, $c = 11.0422(7)$ °A.

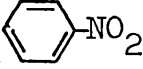
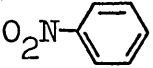
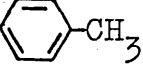
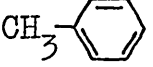
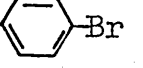
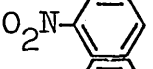
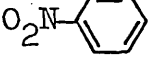
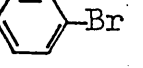
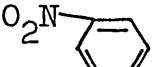
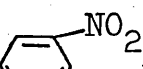
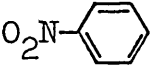
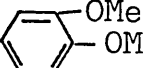
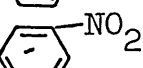
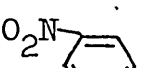
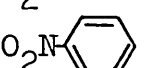
$\alpha = 116.864(5)$, $\beta = 118.014(5)$, $\gamma = 68.670(5)$,
2 mols/ cell. Intensities of 3,380 reflections were measured
on a Siemens diffractometer with Cu-K $_{\alpha}$ radiation
and of these 136 were reckoned unobserved. The structure
was solved by the symbolic - addition procedure and refined
to a current $R = 0.074$. A perspective view of the
molecule, along with the atomic dimensions is shown in
the discussion.

Appendix 1 (fold out)

Appendix 1.

N-Acyl imidates prepared, general structure:- $\text{Ar}-\text{C}(\text{OR})=\text{N}-\text{C}(=\text{O})-\text{Ar}^1$

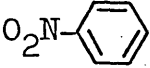
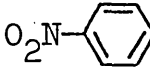
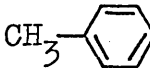
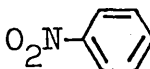
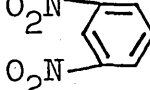
(XVII)

XVII	Ar	Ar ¹	R	m. pt.(°C)	yield (%)
a	Ph	Ph	CH ₂ CH ₂ Ph	79-80	60
b	Ph		CH ₂ CH ₂ Ph	126-128	55
c	Ph	Ph	Me	oil	80(crude)
d	Ph	Ph	Et	60-63	
e		Ph	CH ₂ CH ₂ Ph	124-126	40
f	Ph		CH ₂ CH ₂ Ph	100-101	70
g		Ph	CH ₂ CH ₂ Ph	67.5-69	
h	Ph		CH ₂ CH ₂ Ph	93.5-94.5	
j		Ph	CH ₂ Ph	98.5-100	
k			CH ₂ CH ₂ Ph	102-103	
m		Ph	Me	165-166.5	50
n	Ph		Me	112-114	50
o			Me	133.5-135	61
p	Ph		2-octyl	103-107	
q		Ph	2-octyl	oil	
r		Ph	Me	oil	

Appendices 2 and 3 (fold out).

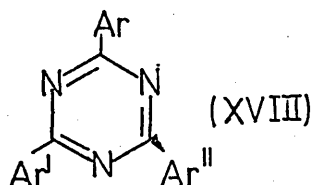
Appendix 2.

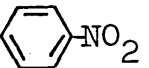
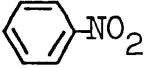
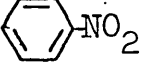
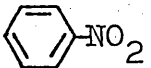
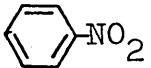
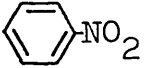
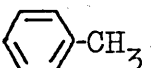
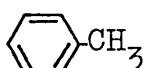
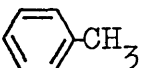
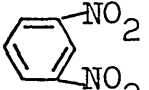
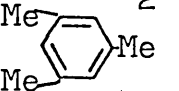
Iminoether hydrochlorides, general structure: $-\text{Ar}-\text{C}(\text{NH}_2\text{Cl})(\text{OR})$
(XIV)

XIV	Ar	R	solvent	yield (%)
a	Ph	$\text{CH}_2\text{CH}_2\text{Ph}$	none	38
b		Me	CHCl_3	85
c	Ph	Me	none	90
d	Ph	Et	none	70
e		$\text{CH}_2\text{CH}_2\text{Ph}$	CHCl_3	62 (up to 90% with longer time)
g		$\text{CH}_2\text{CH}_2\text{Ph}$	ether	26 (need longer at 0 C)
j		CH_2Ph	CHCl_3	13 (amide impurity)
m		Me	CHCl_3	87 (5 days)

Appendix 3.

Triazines of general structure:-

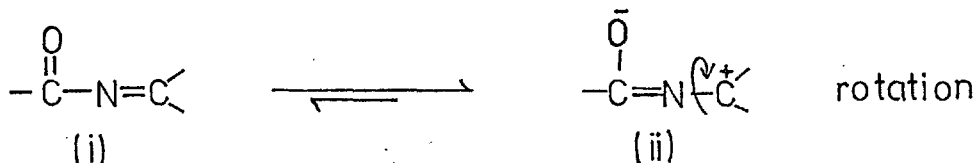


XVIII	Ar	Ar'	Ar''	m. pt. (°C)	comments
a	Ph	Ph	Ph	238	lit. 232°C ⁶⁴
b	Ph	Ph		226	lit. 218°C ⁶⁵
c	Ph			230	m/e 399
d				230	m/e 444
e				286-288	lit. 278-9°C ⁶⁵
f	Ph	Ph		ca. 270	sublimed
g	Ph	Ph			m/e 351

Carbon-nitrogen double bond isomerisations.

In the discussion it is assumed that N-acyl imidates (XVII) are stable to inversion at the carbon-nitrogen double bond, there being no observation of two methoxyl signals for (XVIIc) in the N.M.R., and hence only the one (E) form present.

There is however the theoretical possibility that inter-conversion takes place, but that it is too rapid to be observed, even at -50 C. This would necessitate a large contribution from the 1,4-dipolar structure (ii) of the conjugated $\overset{\text{O}}{\text{C}}=\text{N}=\text{C}$ system (i), which is unfortunately ruled out when the X-ray structure is looked at.



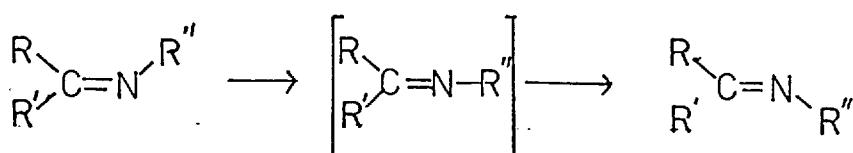
Instead the molecule appears to be orientated to minimise interactions of the aryl rings, with the net result that system (i) is non-planar, making π overlap impossible. The reason for the preference of this apparently unfavoured structure is unknown, as is the reason for lack of observation of isomerisation. Thus as previously stated the imidates (XVII) must be more akin to oximes etc., where there is a hetero-atom adjacent to the nitrogen, and no isomerisation at the carbon-nitrogen double bond is observed.

N.M.R. studies on various carbon-nitrogen double bond systems have been undertaken²⁷, and Table 1 shows calculated energies of activation for the isomerisations.

Structure	E_a , kcal/mole
$(CF_3)_2C=NC(F)_2$	13
$Ph\overset{H}{C}=NPh$	16-17
$p-XC_6H_4$ $\quad \quad \quad \diagdown$ $\quad \quad \quad C=NC_6H_4Y-p$ $\quad \quad \quad \diagup$ $p-X'C_6H_4$	17-20
$(CH_3)_2C=NPh$	21
$p-XC_6H_4$ $\quad \quad \quad \diagdown$ $\quad \quad \quad C=NCH_3$ $\quad \quad \quad \diagup$ $p-XC_6H_4$	25-27
$p-ClC_6H_4$ $\quad \quad \quad \diagdown$ $\quad \quad \quad C=NX$ $\quad \quad \quad \diagup$ Ph	no interconversion
$X = Br, Cl, OH, OMe.$	

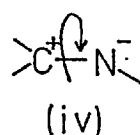
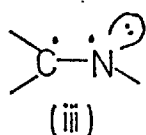
Table 1

It is postulated²⁷ that the mode of inversion for N-aryl or N-alkyl imines is by a lateral shift mechanism, which entails the substituent on one side of the nitrogen atom changing to the other, and it is akin to the umbrella inversions of amines.

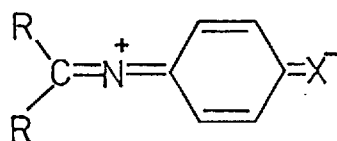


lateral shift

Homolytic cleavage of the carbon- nitrogen bond (iii) is unfeasible, an energy of ca. 50 kcal/mole being required¹⁰⁷ and heterolytic cleavage(iv), coupled with rotation, though explaining the isomerisations is considered unlikely.



This was from a consideration of Hammett plots, where the para substituents on the nitrogen ring had a far greater effect than substituents on the carbon aryl rings



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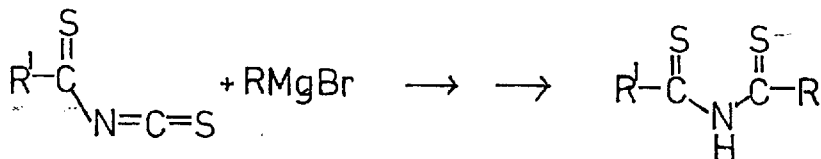
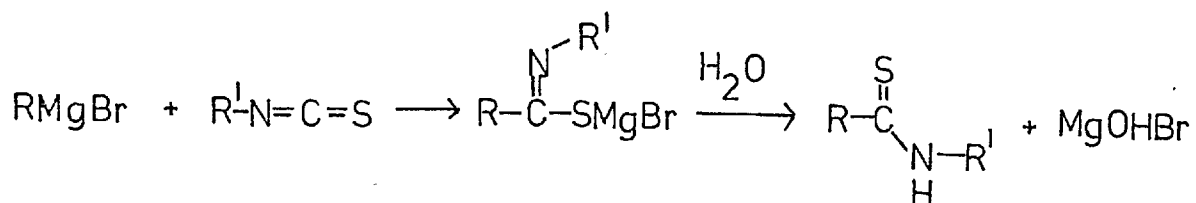
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SUPPLEMENT

Consideration of the chemistry of isothiocyanates¹, and their reaction with Grignard reagents, yielding thioamides, gives rise to the postulate that thionacyl isothiocyanates², might undergo a parallel reaction.

Hence if $R = R' = \text{Ph}$, dithiobenzamide (XLII) would be the product.

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