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PYROLYSIS OF ANILINO NITRILES
AND ANILINO ACIDS

THESIS

SUBMITTED TO THE UNIVERSITY OF GLASGOW
IN FULFILMENT OF THE REGULATIONS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

FEBRUARY 1955

WILLIAM C. BAIN

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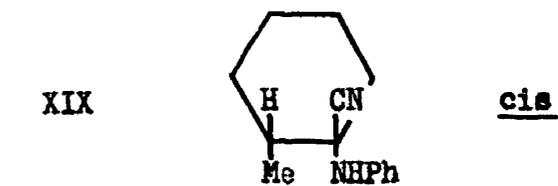
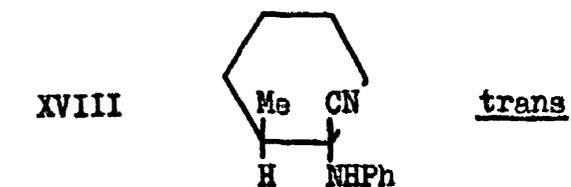
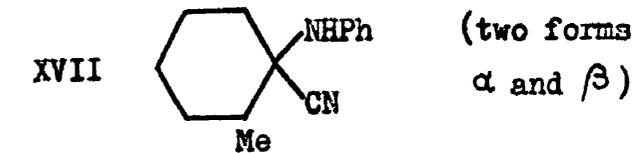
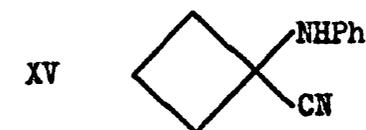
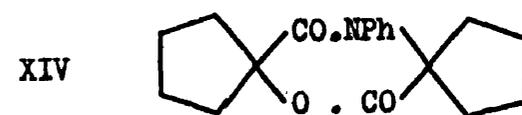
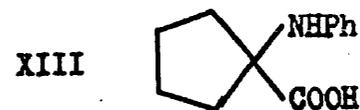
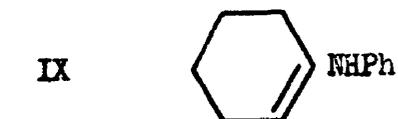
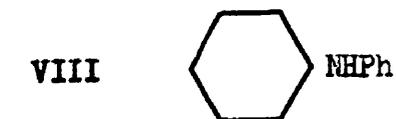
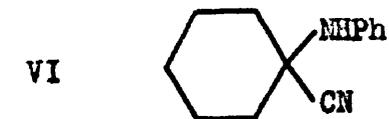
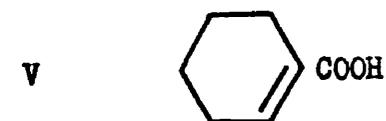
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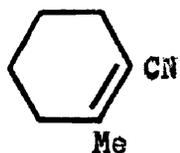
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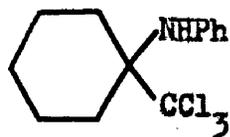
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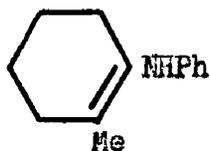
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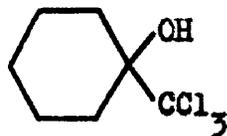
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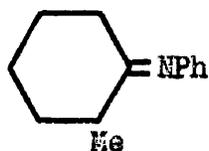
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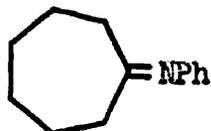
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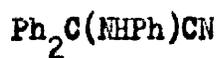
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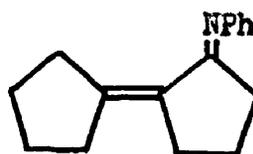
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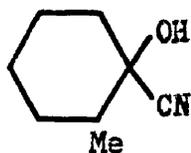
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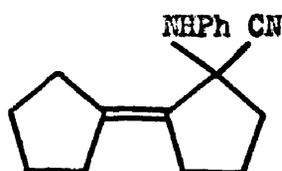
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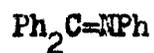
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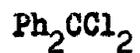
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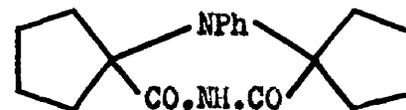
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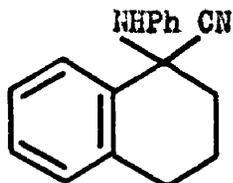
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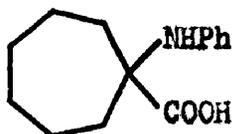
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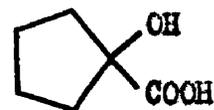
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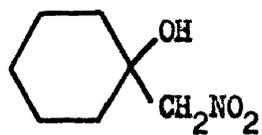
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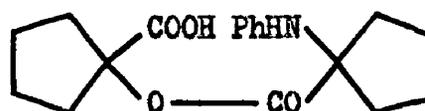
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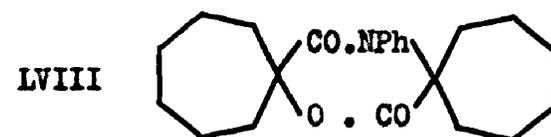
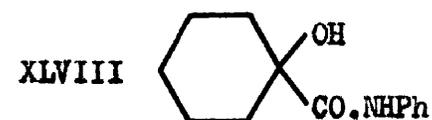
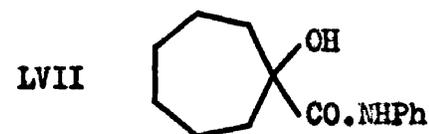
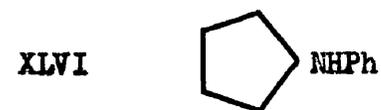
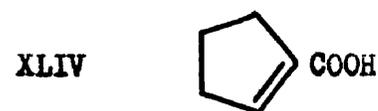
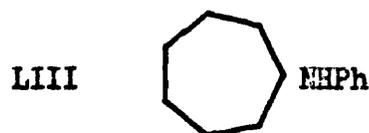
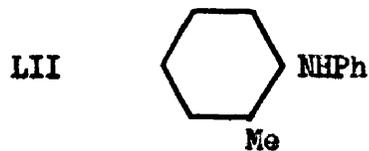
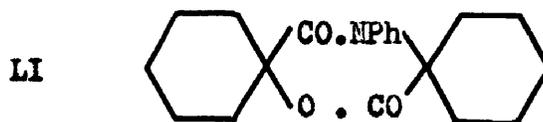
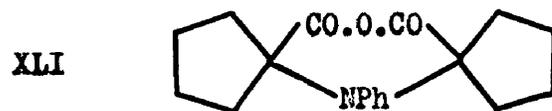


XXIX



XXXIX





S U M M A R Y

The pyrolyses of anilino nitriles and anilino acids, derived from $C_4 - C_7^*$ alicyclic ketones have been carried out.

The C_5 , C_6 , and C_7 anilino nitriles, as well as both geometric isomers of the C_6 anilino nitrile with a 2-methyl substituent (C_α and C_β) have been found to undergo primary reversible dissociation into hydrogen cyanide and the corresponding anil. The yields of hydrogen cyanide and anil are almost theoretical, except from the C_5 compound, which undergoes partial secondary decomposition into aniline and (2-cyclopentylidene)cyclopentylidene)aniline. The rates of decomposition have been measured under constant though arbitrary conditions. α -Anilino- α -cyanodiphenylmethane has also been pyrolysed and it too has been found to give hydrogen cyanide and anil. It has been concluded from this, and also from consideration of the pyrolysis of the geometric isomers of 1-anilino-1-cyano-2-methylcyclohexane, that the hydrogen atom that combines with the cyano group to eliminate hydrogen cyanide is likely to come from the anilino group (i.e., C/N elimination), rather than from the ring (i.e., C/C elimination).

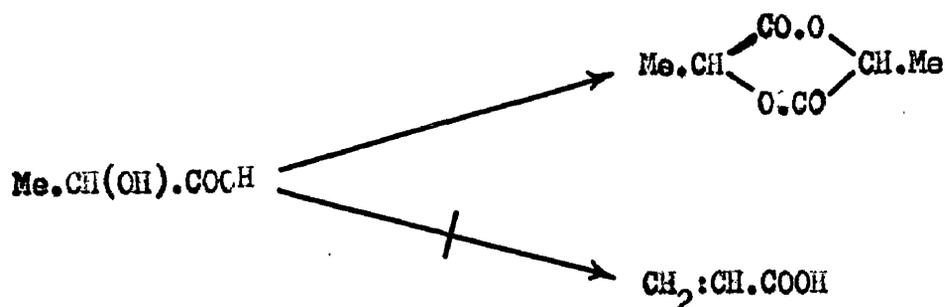
The C_5 , C_6 , and C_7 anilino acids obtained by hydrolysis of the anilino nitriles all decompose thermally to give aniline and the corresponding unsaturated acid. The yield is by no means theoretical, however, and increases with ring size. Other products of decomposition have been isolated and identified and their probable origin discussed. These products are of the same functional group structure for the three ring sizes, the effect of ring size being to vary the yields of products rather than the main reaction route.

Thus, although from the literature it would appear that the C_5 and C_6 compounds give completely different types of pyrolysis products, it has been found in the present work that products are of the same functional group structure.

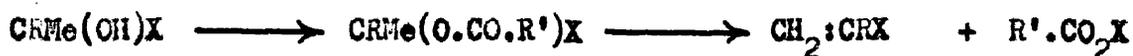
* Here and throughout this thesis the subscripts of the letter C refer to the number of atoms in the ring.

GENERAL INTRODUCTION

It has long been known that direct thermal dehydration of lactic acid (obtainable in large quantities by fermentation processes) gives rise to lactide and not commercially useful acrylic acid.



β -Hydroxypropionic acid gives the desired acrylic acid, but is not readily available. Burns, Jones & Ritchie (1935 (1)) showed that the dehydration of I could be carried out in good yield, though indirectly, by acetylation or benzoylation of the hydroxyl group of the nitrile, ester or substituted amide, followed by vapour phase pyrolysis of this derivative (450-500°C).



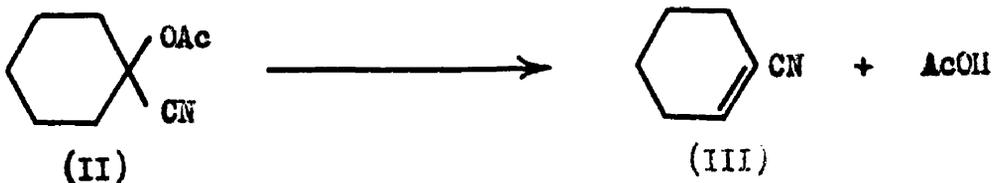
(I)

where R = H, or Me; X = CN, CO₂Alk, CO.NHAc (not, however, CO₂H) ;

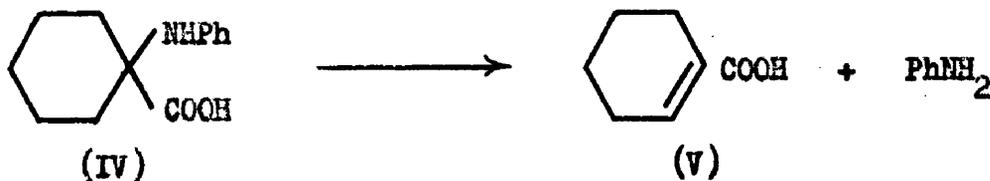
R' = Me or Ph.

The following pyrolytic scissions have also been recorded.

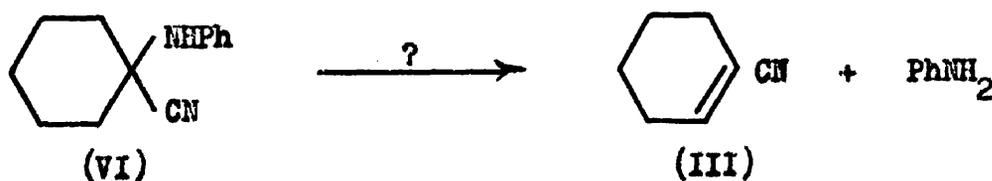
(a) 1-acetoxy-1-cyanocyclohexane (II) into acetic acid and 1-cyanocyclohexene (III) (vapour phase, 450°C (1)).



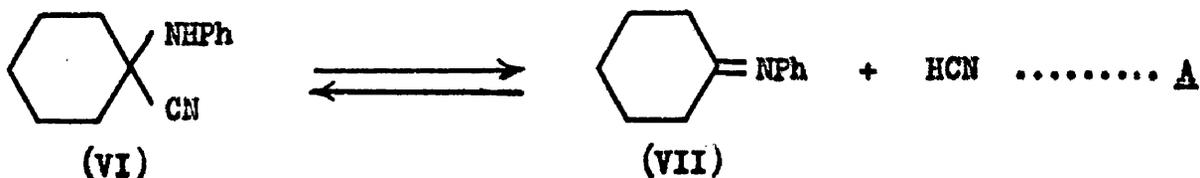
(b) 1-anilino-1-carboxycyclohexane (IV) into aniline and 1-carboxycyclohexene (V) (simple distillation (2)).



It therefore seemed worth while to investigate the possibility that pyrolysis of 1-anilino nitriles (which are readily available by reaction of aniline and hydrogen cyanide with ketones) might provide an alternative simple and cheap general route to olefinic nitriles, which are of considerable industrial importance. For example, it would be expected from reactions (a) and (b) above that 1-anilino-1-cyanocyclohexane (VI) would give, on pyrolysis, aniline and 1-cyanocyclohexene (III).

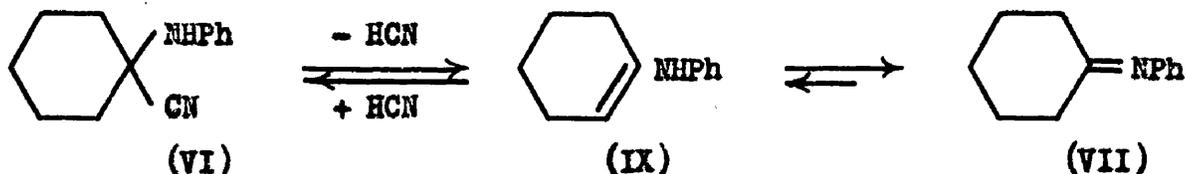


On attempted vapour phase pyrolysis of VI, no significant scission was observed (3), the product being mainly unchanged material along with traces of hydrogen cyanide (up to 600°C). It has recently been shown (4) that the anilino nitrile VI, heated at ca. 245°C, in a static system in a stream of nitrogen to carry off the hydrogen cyanide, gives hydrogen cyanide and cyclohexylideneaniline (VII), the reaction being reversible.



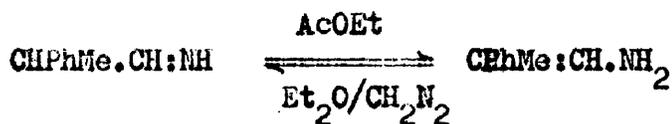
The anil VII was recognised by (a) hydrolysis to aniline and cyclohexanone, (b) addition of hydrogen cyanide at room temperature to regenerate the anil VII, (c) catalytic hydrogenation to N-cyclohexylaniline (VIII). Reaction (b) shows the dissociation A to be reversible and explains the failure to obtain permanent scission in the vapour phase reactor previously employed (3) - the anil VII would recombine with the hydrogen cyanide as the pyrolysate left the reactor, leaving the anilino nitrile VI, irrespective of how far the dissociation had taken place at the furnace temperature.

The mechanism of reaction A is of interest as hydrogen cyanide could be eliminated either as shown above (C/N elimination), or via a labile vinylamine IX, by C/C elimination, thus:-



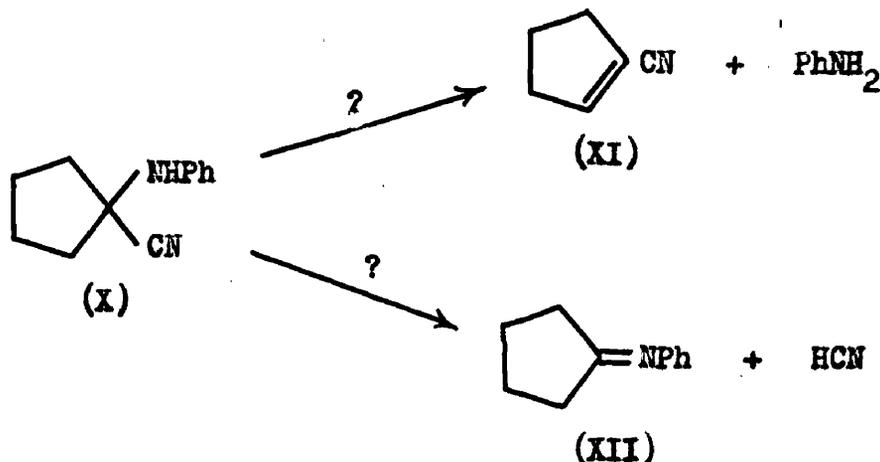
Stable vinylamines are in general readily obtainable only where the nitrogen atom is fully substituted,* and thus the anil VII and the vinylamine IX will probably exist in tautomeric equilibrium with VII predominating. It is thus not possible to affirm that, simply because the anil VII is isolated, C/N elimination must have occurred. This problem is further discussed later in the light of the results of the present investigations.

* Seher (5), however, found the following imine-enamine pair to be capable of independent existence.

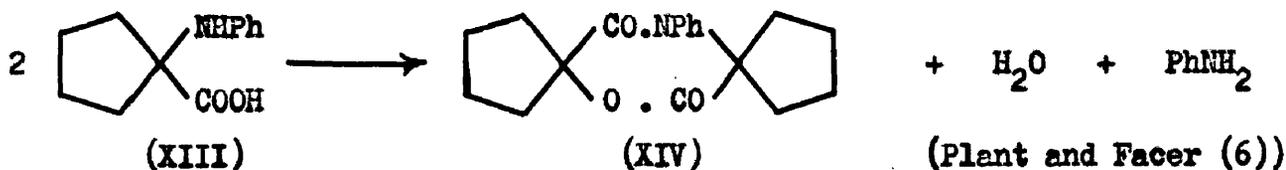
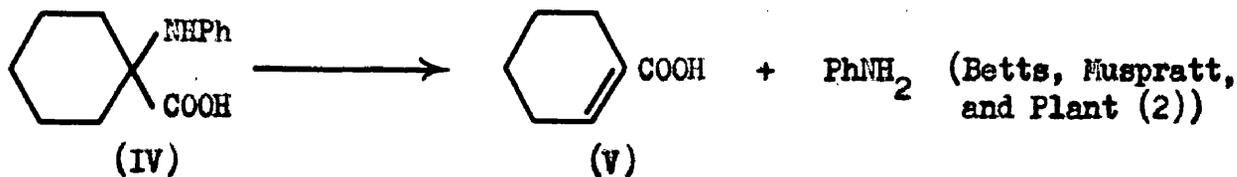


OBJECTS OF RESEARCHPyrolysis of Anilino Nitriles

It seemed possible that, owing to the different intervalency angles in the C_5 and C_6 compounds, the pyrolysis of 1-anilino-1-cyanocyclopentane (X) might give the corresponding unsaturated nitrile XI and aniline, thus following a route analogous to the pyrolysis of 1-anilino-1-carboxycyclohexane (IV) mentioned above.



This view was at first sight supported in some measure by the observation of Plant and Facer (6) that X "decomposes on distillation with the formation of some aniline", which suggests the concurrent formation of the unsaturated nitrile XI. The probability that the C_5 and C_6 anilino nitriles might give different products on pyrolysis was also supported by the fact that according to the literature the corresponding anilino acids do give different products on pyrolysis.

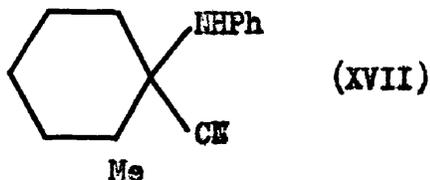


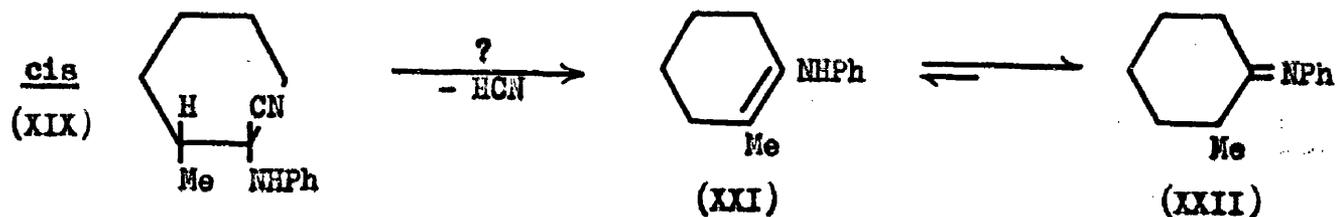
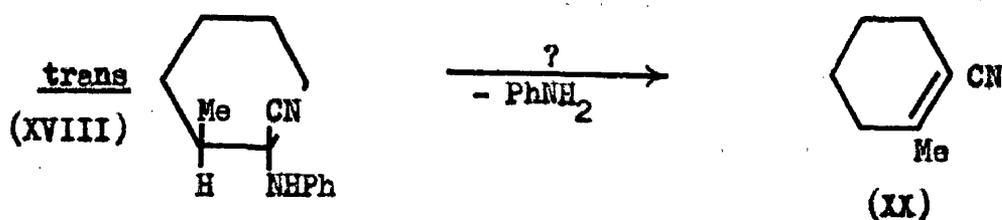
Betts, Muspratt & Plant (2) recorded that the C_6 anilino acid IV gives on pyrolysis the unsaturated acid V and aniline, while Plant & Facer (6) recorded that the C_5 acid XIII gives the curious lactone-lactam structure XIV, named by Plant & Facer (6) as the lactone of 1-1'-hydroxycyclopentane-1'-carboxylylanilinocyclopentane-1-carboxylic acid and in American Abstracts (7) as 13-phenyl-6-ox-13-azadispiro (4.2.4.2) tetradecane-7,14-dione. For convenience, such structures will be called lactone-lactams throughout this thesis. The unsaturated acid V was identified by means of its dibromo derivative. The structure XIV was not completely proved by Plant & Facer (6) and was deduced from (a) its elementary analysis, (b) the fact that it was not basic and (c) that it dissolved slowly in alkali and was reprecipitated slowly by dilute acid. It also did not react with ammonia or aniline at high temperature.

It seemed desirable also to extend the investigations to the C_4 and C_7 compounds, i.e. by pyrolysis of 1-anilino-1-cyanocyclobutane (XV) and 1-anilino-1-cyanocycloheptane (XVI) in order to investigate further the effect of ring size on the pyrolysis route.

Pyrolysis of 1-Anilino-1-cyano-2-methylcyclohexane.

As the dehydration of alcohols is facilitated by β -substitution it was thought that elimination of the hydrogen atom from the C_6 anilino nitrile VI might occur more readily in the presence of a 2-methyl substituent, i.e. by pyrolysing 1-anilino-1-cyano-2-methylcyclohexane (XVII). There is the complication here of cis-trans isomerism.

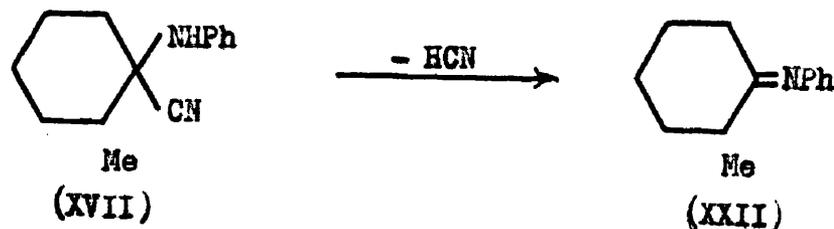




(cis and trans have here, arbitrarily and for convenience, been made to refer to the methyl and anilino groups). Thus, as before, it appears formally possible that, if the same type of carbon/carbon (C/C) elimination occurs (assuming that C/C elimination occurs at all), one geometrical isomer would give the unsaturated nitrile XX and the other the anil XXII. The products obtained from a given isomer would depend on whether the elimination was cis or trans, but Barton (8) has found consistent cis elimination in vapour-phase pyrolysis of various esters and accounts for this as being due to a four-centre transition state. This and the further complications of the above scheme are discussed later in the light of the results obtained.

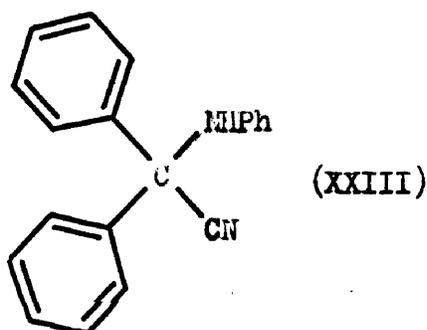
Pyrolysis of α -Anilino- α -cyanodiphenylmethane (XXIII).

In the above simplified scheme carbon/carbon (C/C) elimination has been assumed. Carbon/nitrogen (C/N) elimination, however, appears equally possible, thus giving the anil directly.



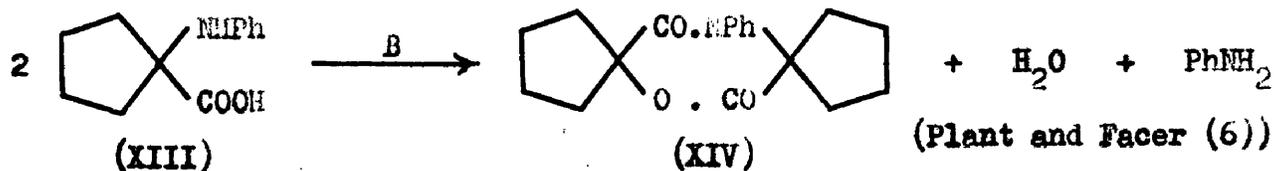
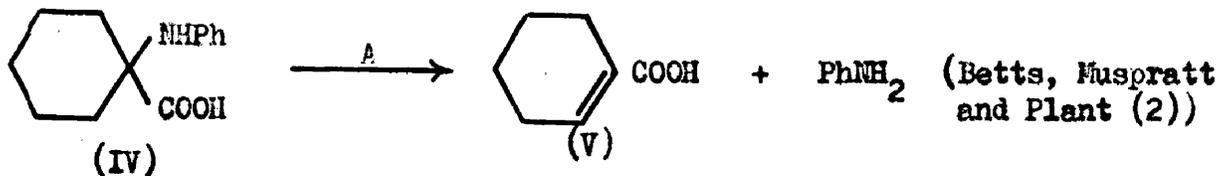
In this case the cis and trans isomers XIX and XVIII should both yield the anil XXII (see, however, the fuller discussion on p.25).

Direct evidence for C/N elimination was not available, but has now been obtained (see p.31) by pyrolysis of a compound with which C/C elimination is not possible, i.e., where both 2-positions are fully blocked (have no hydrogen atom attached) viz., α -anilino- α -cyanodiphenylmethane (XXIII).



Pyrolysis of C₅, C₆, and C₇ Anilino Acids.

The pyrolysis of the C₅, and C₆ anilino acids have, as mentioned on p.5, been recorded in the literature.



It seemed desirable to confirm these results as other products (e.g., an anil) might also be formed, (especially as the yields of the products V and XIV are not recorded), and also extend the work to the pyrolysis of the C₇ acid to see whether it followed route A or B or both.

PREPARATION OF COMPOUNDS FOR PYROLYSIS.

Ketones. cyclopentanone, cyclohexanone, 2-methylcyclohexanone, and cycloheptanone were obtained from stock of chemical suppliers. The cyclobutanone had to be prepared from pentaerythritol by the method of Roberts and Sauer (9). (see p.14).

1-Anilino Nitriles.

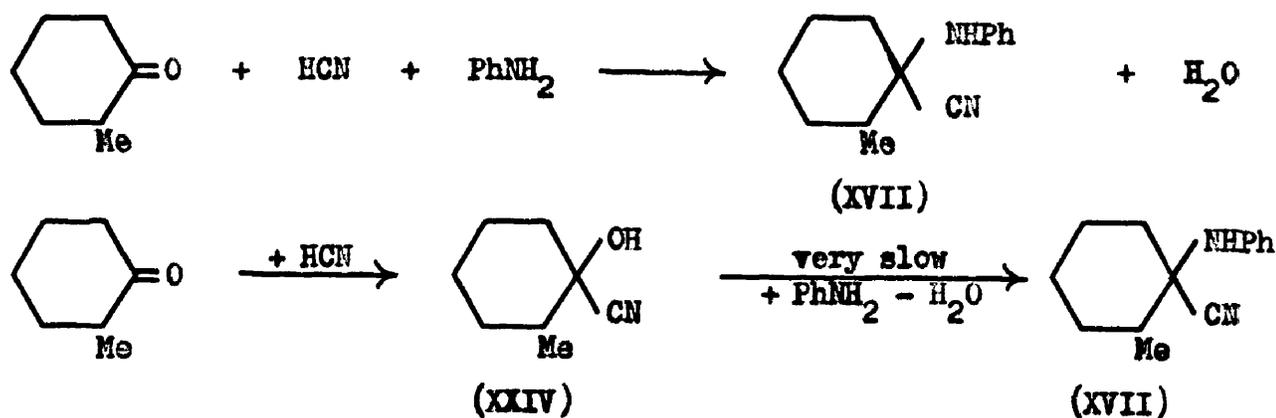
The C_4 , C_5 , C_6 and C_7 anilino nitriles (XV, X, VI, XVI) were prepared using an adaptation of the method of Mulder (10), consisting of the addition of an excess of hydrogen cyanide to an equimolecular mixture of aniline and the appropriate ketone. The anilino nitriles crystallised from a suitable solvent in good yield.

1-Anilino-1-cyano-2-methylcyclohexane, α - and β -forms (XVII α and β).

The method used in this preparation was the same, but since this product was a mixture of the geometric isomers (arbitrarily designated the α - and β - forms) separation was necessary - first by fractional crystallisation from benzene and then from petroleum. Two forms were isolated, the α - form (less soluble in benzene than the β -form) m.p. 124-125 $^{\circ}$, and β -form m.p. 84-86 $^{\circ}$. These two forms correspond to those isolated by Bukhsh, Desai, Hunter and Hussain (11) (m.p. 126 $^{\circ}$ and 88 $^{\circ}$) by a different method, consisting of the addition of acetic acid and potassium cyanide to a mixture of aniline and 2-methylcyclohexanone. They then fractionally crystallised the product from benzene and *n*-hexane followed by hand-picking of crystals. This made the method unsuitable for preparation of the comparatively large quantity required for pyrolysis (ca. 30 g.).

Initial attempts to prepare the β -form (XVII β) were unexpectedly made difficult by the fact that piperidine was used as catalyst in early experiments. This method gave a small amount of the cyanohydrin, 1-cyano-1-hydroxy-2-methyl-cyclohexane (XXIV), which separated as a solid. This interference with the desired

course of the reaction was confirmed in a control experiment in which a mixture of equivalent amounts of aniline and 2-methylcyclohexanone was divided into two equal portions, to one of which piperidine was added. On adding the same excess of hydrogen cyanide to each, the one without piperidine solidified after three hours, but the other remained liquid even after standing for several weeks. The reason for this is probably that piperidine acts as a basic catalyst (piperidine being a stronger base than aniline) to convert the ketone preferentially to the cyanohydrin XXIV which, as is discussed later (p.16), reacts only very slowly with aniline.

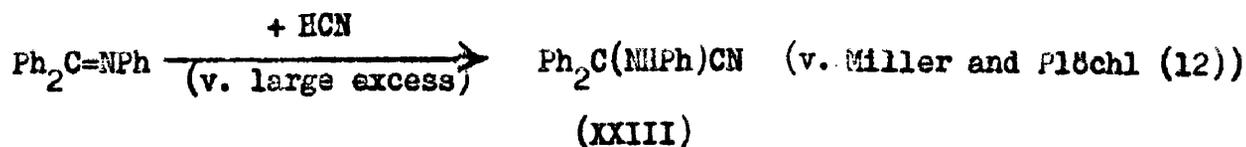
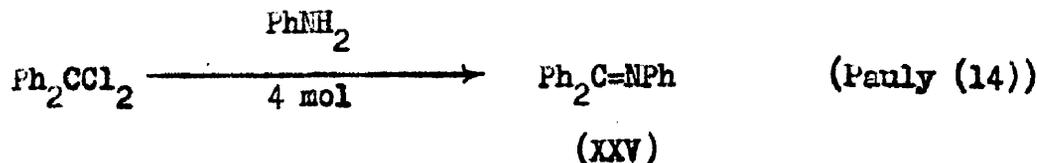
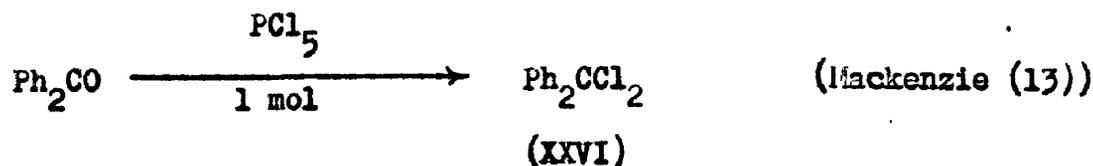


The above also applies to the unsubstituted rings (e.g., preparation of 1-anilino-1-cyanocyclohexane).

Preparation of α -Anilino- α -cyanodiphenylmethane (XXIII).

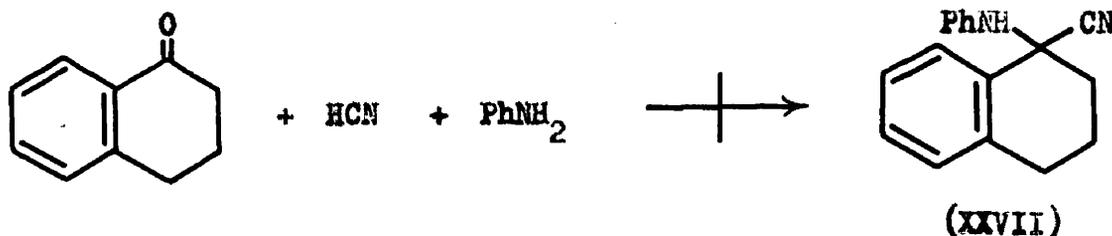
The method used for the C₄, C₅, C₆ and C₇ anilino nitriles was unsuccessfully tried using benzophenone in place of the alicyclic ketone. The aniline/hydrogen cyanide/benzophenone mixture did not solidify even after standing for several weeks.

There is only one reference to α -anilino- α -cyanodiphenylmethane (XXIII) in the literature. v. Miller and Plöchl (12) prepared it by addition of hydrogen cyanide to the anil (diphenylmethylene)aniline (XXV), which was prepared from benzophenone via dichlorodiphenylmethane (XXVI).



The overall yield of the anilino nitrile XXIII from benzophenone was 47% of theory.

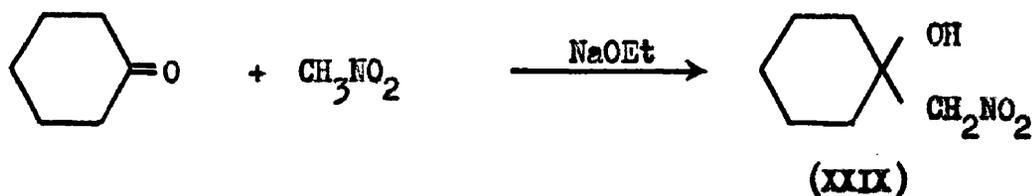
Attempted Preparation of α -Anilino- α -cyanotetralin (XXVII).



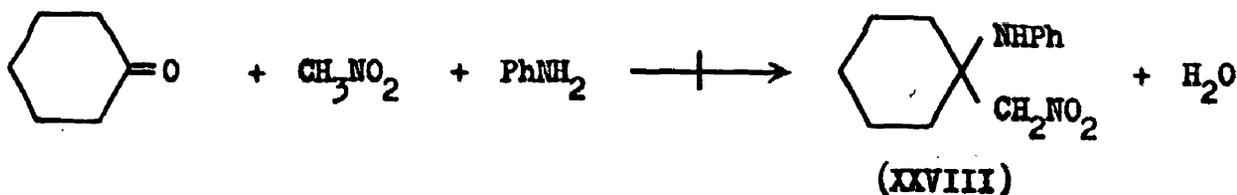
The anilino nitrile XXVII was of interest because of its aromatic and its part-saturated ring. When the preparation from α -tetralone was attempted by the method used for the C_n anilino nitriles, no yield of XXVII was obtained. This is not surprising in view of the very high dissociation constant (8.06) observed by Lapworth and Manske (15) for the cyanohydrin of α -tetralone. The stability of the anilino nitriles, as shown later (p. 21) appears to be related to the dissociation constants of the corresponding cyanohydrins.

Attempted Preparation of 1-Anilino-1-(nitromethyl)cyclohexane (XXVIII).

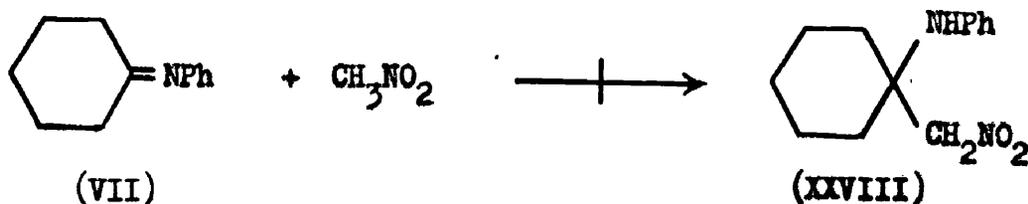
Frazer and Kon (16) described the preparation of 1-hydroxy-1-(nitromethyl)-cyclohexane (XXIX) by alkali-catalysed reaction of cyclohexanone with nitromethane.



The preparation of the anilino compound XXVIII was attempted by mixing equimolecular quantities of aniline, nitromethane and cyclohexanone to see whether the type of preparation used for the C_n anilino nitriles could be extended to one using nitromethane in place of hydrogen cyanide (as appears to occur in the preparation of XXIX, the $-\text{CH}_2\text{NO}_2$ group taking the part of the $-\text{CN}$ group.).

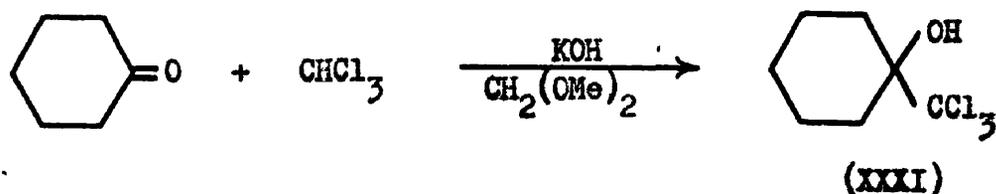


This was unsuccessful, as was the attempted preparation of XXVIII by the addition of nitromethane to cyclohexylideneaniline (VII).

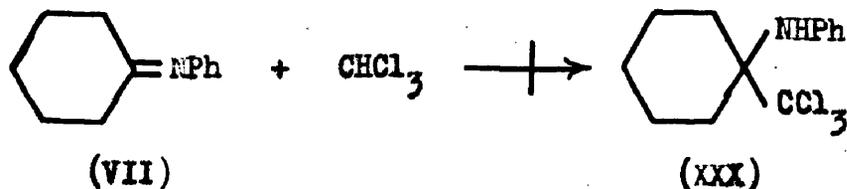
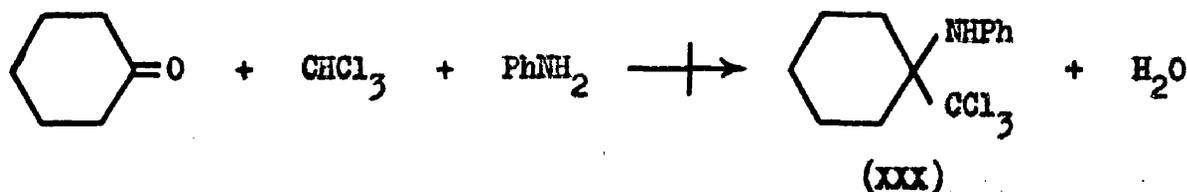


Attempted Preparation of 1-Anilino-1-(trichloromethyl)cyclohexane(XXX).

A similar addition to that shown by Frazer and Kon (16) has been described by Weizmann (17) where chloroform is used in place of nitromethane, giving 1-hydroxy-1-(trichloromethyl)cyclohexane (XXXI).

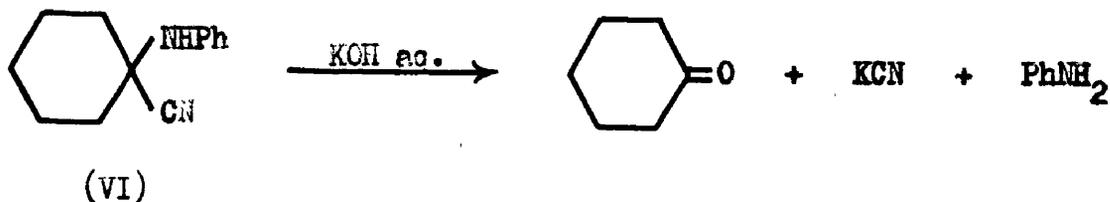


Similar preparations to the ones described under the previous heading, using chloroform in place of nitromethane, were tried but without success.



Preparation of l-Anilino-carboxylic acids.

Attempted alkaline hydrolysis of the cyano group of l-anilino-1-cyano-cyclohexane (VI) does not give the corresponding amide or acid, but simply causes the molecule to revert to aniline, cyclohexanone and alkali cyanide.



Direct hydrolysis of the cyano group using hot 50% sulphuric acid was not attempted, because Bucherer and Barsch (18) although they isolated the desired anilino acid, found that resinous material was formed during the period of heating. A two stage hydrolysis was preferred, in which the intermediate amide is isolated, (described by Plant and Facer (6) for the C₅ nitrile X and Betts, Muspratt and

Plant (2) for the C₆ nitrile VI.) This method was successfully applied to the C₇ nitrile XVI. The first stage of the hydrolysis occurs readily by solution of the nitrile in concentrated sulphuric acid followed by treatment with water. The second stage occurs less readily, especially with the C₆ nitrile, which requires stirring and refluxing with boiling concentrated hydrochloric acid for twelve hours.

One observed peculiarity of these anilino acids, which is not recorded in the literature, was that all three have wide melting-point ranges (15-17°). Even after several recrystallisations of the acids from benzene or acetone their melting points did not change appreciably. This does not appear to be caused by impurities, since equivalent weight determinations and micro-analysis results corresponded well with the theoretical values. A measurement of the loss of weight of the C₆ acid at 160° for thirty minutes showed that some decomposition had taken place. It is therefore likely that the rather discrepant melting point ranges observed represent decomposition temperatures rather than true melting points, although the time required for melting point determinations is much less than thirty minutes. The method of determining melting points by preheating the liquid bath to 10° below the temperature at which melting begins, was tried; but this made little difference to the ranges observed.

Preparation of cycloButanone.

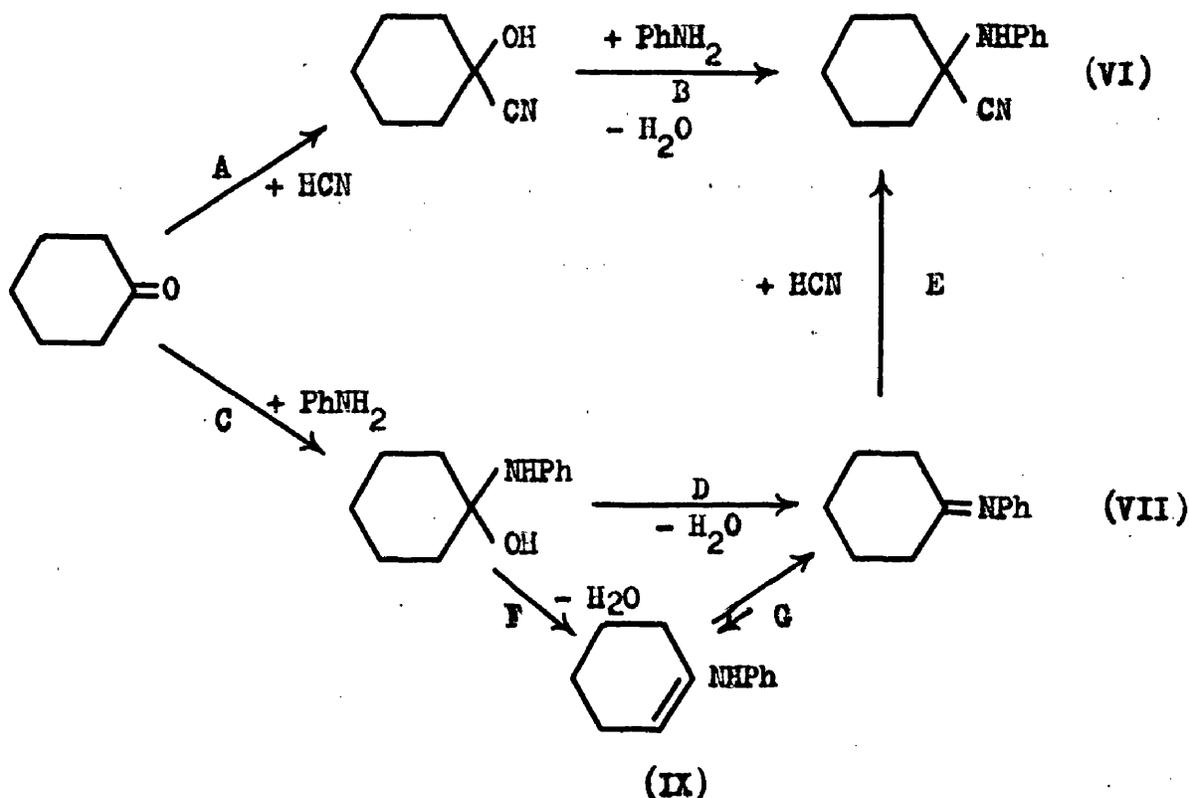
This ketone is rather inaccessible. The most useful preparative methods are (i) from pentaerythritol as starting point (Roberts and Sauer (9); used in the present work); and (ii) from the reaction of keten with diazomethane (Kaarsemaker and Coops (19)). The chief disadvantage of the former method is that it is long and tedious and the yield is low. (Roberts and Sauer recorded a 40% overall

yield, but in the present work it was found to be 5% although it would probably have been greater had a more efficient continuous extractor been available, as the method requires two continuous extractions.) The chief disadvantage of the latter method is the difficulty of obtaining sufficient diazomethane: N-nitrosodimethylurethane (or other suitable nitroso compound) is not readily obtainable in the large amount required (1-2 kg.).

The method of Roberts and Sauer involves the following reactions:-

- 1) Phosphorus tribromide was prepared from red phosphorus and bromine.
- 2) Lead tetraacetate was prepared from red lead, acetic acid and acetic anhydride.
- 3) Pentaerythrityl tetrabromide was obtained by reaction of pentaerythritol with phosphorus tribromide, according to the method of Schurink (20). A more recently published method of Herzog (21) is even less suited to the preparation of a large quantity of pentaerythrityl tetrabromide.
- 4) Methylenecyclobutane was obtained by reaction of pentaerythrityl tetrabromide with zinc in the presence of zinc bromide and aqueous ethanol.
- 5) Methylenecyclobutane was hydroxylated with performic acid to 1-(hydroxymethyl)-1-cyclobutanol which was isolated by continuous extraction with methylene chloride.
- 6) Finally the 1-(hydroxymethyl)-1-cyclobutanol was oxidised with lead tetraacetate to cyclobutanone, the product again being isolated by continuous extraction with methylene chloride.

The identity of the cyclobutanone obtained was confirmed by preparation of the semicarbazone and 2:4-dinitrophenylhydrazone, and also by the infra-red absorption spectrum, which was compared with that recorded by Roberts and Sauer (9).

Reaction Route Followed in the Preparation of Anilino Nitriles

At first sight the route appears to be that via the cyanohydrin (A-B).

The objection to this is that cyanohydrins react only very slowly with aniline at room temperature (e.g., cyclopentanone cyanohydrin, when mixed with an equivalent quantity of aniline, gives a homogeneous mixture which even when seeded with a few crystals of 1-anilino-1-cyanocyclopentane does not solidify until it has been standing for several months. cycloHexanone cyanohydrin reacts even more slowly.)

The reaction of aniline, ketone (C₄, C₅, C₆ and C₇) and hydrogen cyanide, on the other hand, is very rapid; water separates from the mixture within a few minutes and the product solidifies within a few hours.

Thus B appears unlikely to be one of the reactions occurring, and this eliminates route A-B from consideration.

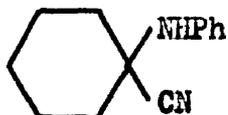
The route C-D-E is a much more probable alternative. The reaction E is found to be very rapid. The anil VII reacts readily and rapidly at room temperature to form the anilino nitrile VI. The reaction C-D is supported by the fact that Sapiro and P'eng (22) recorded that aniline and cyclohexanone reacted without a catalyst at room temperature and atmospheric pressure after 2 hours to the extent of 10.3% to give the anil VII. If this reaction (C-D) is reversible the equilibrium will be displaced by reaction of the anil VII with hydrogen cyanide, thus making the conversion of cyclohexanone to anil quicker. Thus, since reaction B is very slow, reaction C-D fairly rapid, and reaction E rapid and complete, the most likely overall route is C-D-E (and/or C-F-G-E, which amounts to the same thing, since the vinylamine IX and anil VII will be in equilibrium).

RESULTS AND DISCUSSIONPYROLYSIS OF 1-ANILINO NITRILESOutline of Experimental Methods and Results Obtained.Pyrolysis of Anilino Nitriles X, VI, XVII α , XVII β , and XVI.

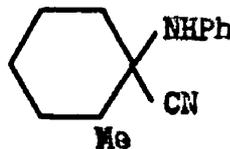
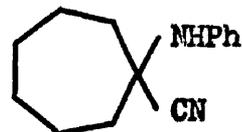
These pyrolyses were done in a stream of nitrogen, using the same weight (15g.) of each anilino nitrile. The conditions of pyrolysis were standardised as far as possible by (a) constant temperature of heating bath, (b) constant rate of flow of nitrogen, and (c) use of constant weight of material.



(X)



(VI)

(XVII α)(XVII β)

(XVI)

(a) The temperature control was $\pm 5^\circ$ at 200° and 250° . The "Simmerstat" control used was not very sensitive and was not independent of mains voltage.

(b) The rate of nitrogen flow could be kept at 13.5 ± 0.5 cc./min. by regulation of the reducing valve on the nitrogen cylinder.

(c) The use of a constant weight of material is not ideal, since the lower the molecular weight, the greater the theoretical amount of hydrogen cyanide available for elimination. If, in order to obviate this effect, the same fraction of a gram molecule is taken for each pyrolysis, the volume of liquid present would increase with molecular weight, which would retard removal of hydrogen cyanide. In either case the volume of liquid present will be constantly varying during pyrolysis since there will be a difference in density between the liquid anilino nitrile and anil, to say nothing of the free hydrogen cyanide dissolved in the liquid, which will,

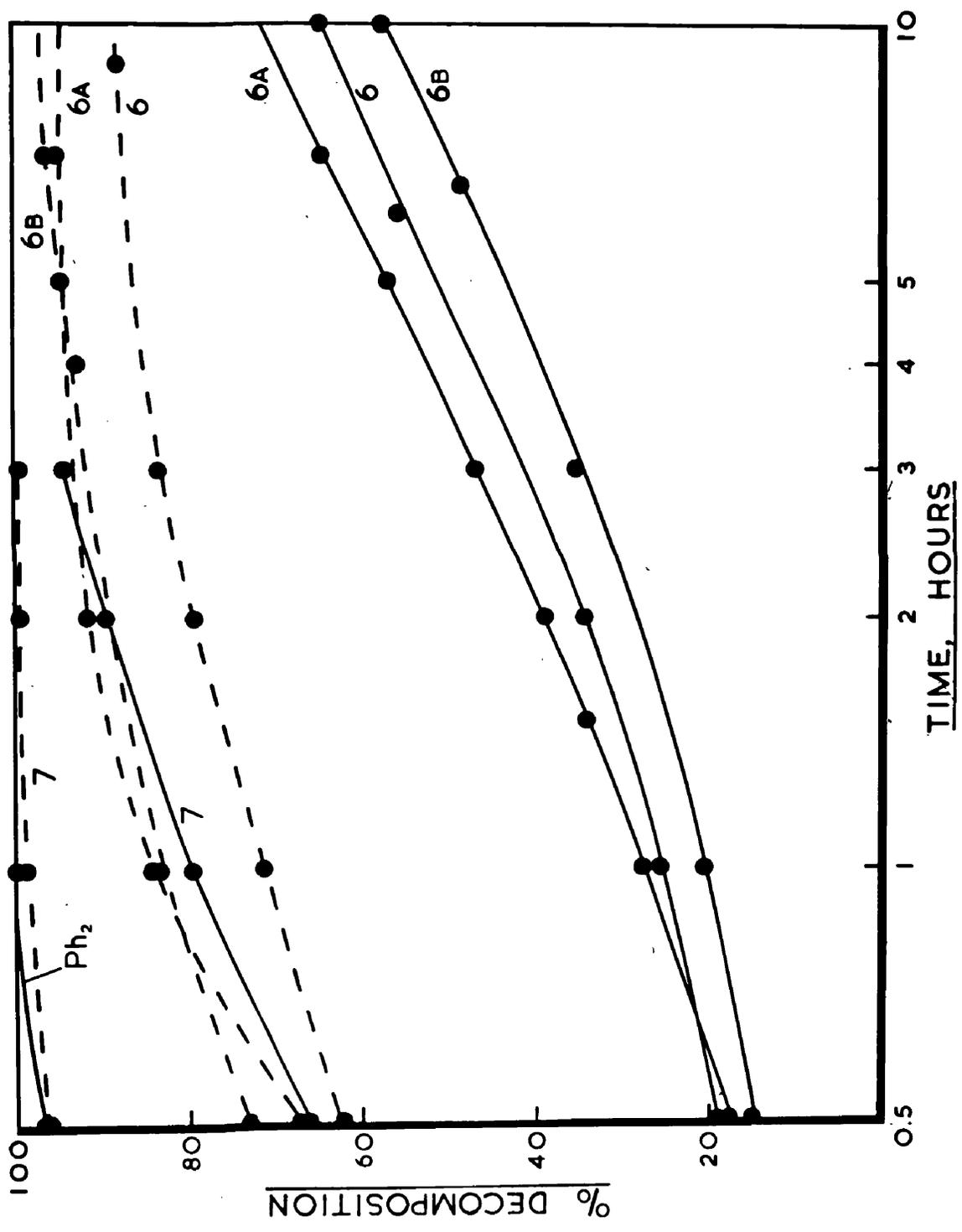


FIGURE I

FIGURE I

Pyrolysis of Anilino Nitriles

Full Line 200°
Broken Line 250°

- 6 1-anilino-1-cyanocyclohexane
6A 1-anilino-1-cyano-2-methylcyclohexane, α -form
6B " " " β -form
7 1-anilino-1-cyanocycloheptane
Ph₂ α -anilino- α -cyanodiphenylmethane

Notes. (a) The time scale is logarithmic in order to make the curves easier to distinguish, and has no kinetic significance.

(b) The reversal of decomposition order (6B, 6, 6A, at 200° and 6, 6A, 6B, at 250°) is probably caused by experimental error, cf. Table II, p. 43.

TABLE I

Pyrolysis of Anilino Nitriles
% of Theory of Hydrogen Cyanide Eliminated

Time hrs.	C ₅		C ₆		C _α		C _β		C ₇	
	200°	250°	200°	250°	200°	250°	200°	250°	200°	250°
½	26.8	58.6	18.9	62.3	17.7	67.1	15.0	73.3	66.1	96.
1	38.0	77.5	25.8	71.2	28.0	84.2	20.7	83.3	79.6	98.
1½					34.4					
2	47.5	79.6	34.6	79.3	39.0	91.8			89.7	99.
3				83.2	47.0		35.5		94.2	99.
3½			45.0							
4	60.3							92.9		
5					57.0	94.5				
6	64.8	80.2	55.8							
6½							48.2			
7					64.3	94.8		96.2		
9	68.7			87.8						
10			64.7				57.6			
45					94.2					
130					95.2					

however, presumably be small, at the elevated temperature of the experiment. This assumes that the reaction is unidirectional, which is nearly true for the anilino nitriles VI, XVII α , XVII β , and XVI. On the whole the best compromise seemed to be to use the same weight of anilino nitrile for each pyrolysis. The hydrogen cyanide eliminated was determined by trapping in alkali solution and titrating the alkali cyanide against silver nitrate. The rate of elimination of hydrogen cyanide was followed by renewing the alkali solution and titrating the solution removed.

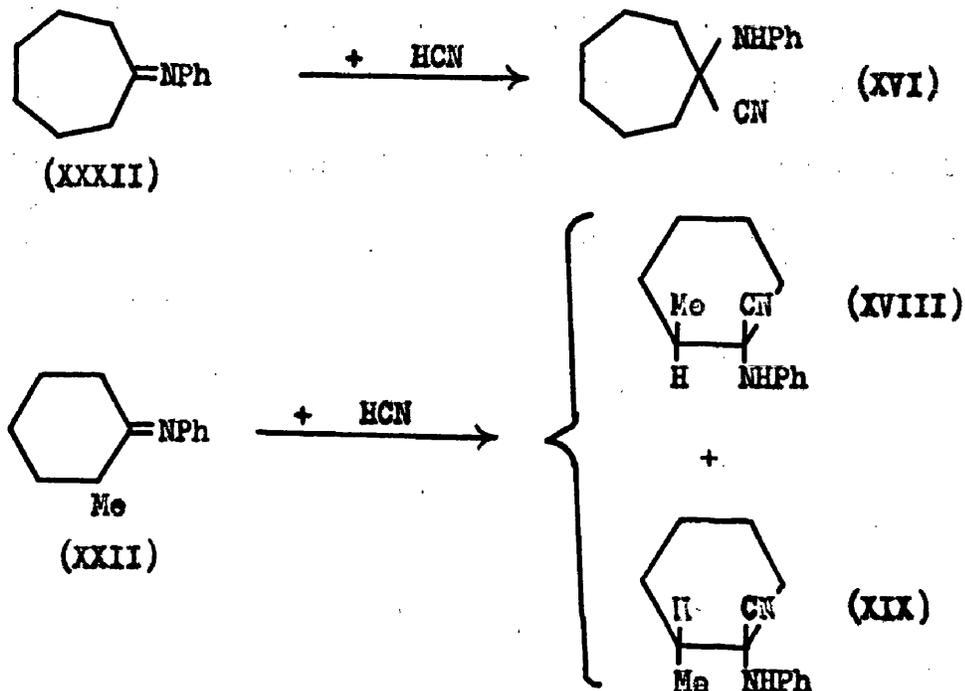
Products of Pyrolysis of Anilino Nitriles VI, XVII α , XVII β , and XVI.

The products of pyrolysis of these four anilino nitriles are hydrogen cyanide (ca. 95-99% of theory), and the corresponding anil (ca. 80% of theory after purification). The anil was isolated by vacuum distilling the pyrolysis residue, (i.e., crude anil), after all or nearly all the hydrogen cyanide had been eliminated. This avoids the complication of the elimination of hydrogen cyanide during distillation: some of this hydrogen cyanide would re-combine with the anil on cooling, thus contaminating the distillate with the original anilino nitrile.

The time required for the complete elimination of hydrogen cyanide (see Fig. I and Table I) varied from 3 - 130 hours but did not appear to affect the yield of anil obtained. In all cases there was a small amount (ca. 1g.) of tarry residue which had a carbylamine-like smell.

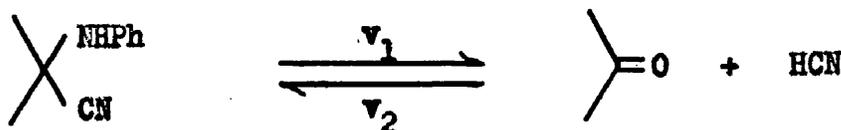
The cycloheptylideneaniline (XXXII) and 2-methylcyclohexylideneaniline (XXII) were identified by (a) almost quantitative acid hydrolysis to aniline and the original ketone, (b) addition at room temperature of hydrogen cyanide (quantitative) to yield (from anil XXXII) the original anilino nitrile XVI; and (from anil XXII)

a mixture of the geometric isomers XVII α and XVII β , with the former predominating.



Rates of Elimination of Hydrogen Cyanide from the Anilino Nitriles Pyrolysed.

These rates are plotted in Fig. I and recorded in Tables I and II. No conclusions with regard to the kinetics of the reaction can be drawn from these graphs since the rate of elimination of hydrogen cyanide will depend not only on the rates of forward and back reactions v_1 and v_2 , but also on the influence of the stream of nitrogen which continuously displaces the hydrogen cyanide.



This latter effect will vary in spite of constant rate of nitrogen flow since the amount of free hydrogen cyanide is much greater towards the beginning of the reaction than towards the end. Thus the actual rate of hydrogen cyanide

elimination will depend on the unpredictable "sweeping out" effect of the nitrogen. Nevertheless, since the rate of nitrogen flow has been kept constant, the results obtained can be used for comparing the rates of decomposition. Owing to the inaccuracies caused by variations in rate of flow, temperature, and even atmospheric pressure (the variation due to this will be much less than the other errors) only a very large difference in rate can be considered significant. Such a difference is here encountered when we pass from the C_6 to the C_7 compound, the latter compound eliminating hydrogen cyanide much more readily than the former. This increase in rate with ring expansion is parallel to the increased cyanohydrin dissociation-constant observed on passing from cyclohexanone to cycloheptanone (Prelog (23)).

The C_5 anilino nitrile decomposes at a higher rate than the C_6 anilino nitriles, which is again in accordance with Prelog's results. Here, however, elimination of hydrogen cyanide is not theoretical (ca. 80%) and the mechanism is complicated by the formation of by-products and products of secondary pyrolysis (considered later). The C_4 anilino nitrile XV as shown in Table II, decomposes considerably more slowly than the C_6 compound VI; of the anilino nitriles investigated it is the slowest in eliminating hydrogen cyanide. Unfortunately, Prelog's series of dissociation constants does not include a value for the C_4 cyanohydrin, and no reference to this constant can be traced.

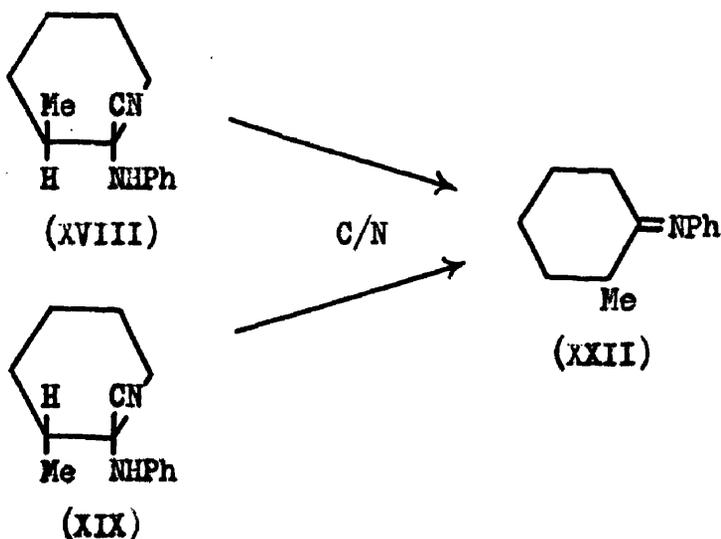
The anilino nitrile derived from benzophenone has the fastest rate of decomposition observed for any of the anilino nitriles pyrolysed. The elimination of hydrogen cyanide is theoretical and the very fast rate shows the influence of the phenyl groups.

Pyrolysis of 1-Anilino-1-cyanocycloheptane (XVI). The yield of hydrogen cyanide was almost theoretical, and that of the purified anil high (99.4 and

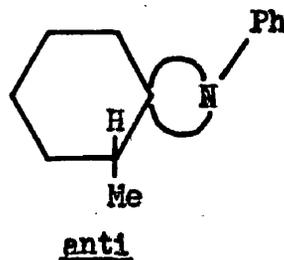
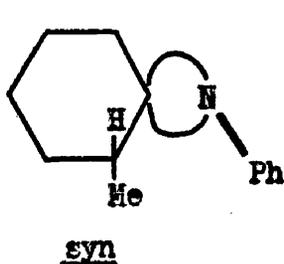
85% respectively). A very small amount of tarry residue was formed.

Pyrolysis of α - and β -forms of 1-Anilino-1-cyano-2-methylcyclohexane (XVIII α and β)

As mentioned above, it was at first thought that the two geometric isomers of 1-anilino-1-cyano-2-methylcyclohexane might pyrolyse to different products. This was found not to be so, however: both give almost theoretical yields of hydrogen cyanide (α -form, 95%; β -form, 96%) and high yields of anil (α -form, 80%; β -form, 82%). The simplest explanation (though not necessarily the correct one) is that the cyano group is eliminated along with a hydrogen atom from the -NH- portion of the anilino group (i.e., C/N elimination) - not with a hydrogen atom from the 2-position (-CHMe-) or the 6-position (-CH₂-) (i.e., C/C elimination).



There is the further possible complication that the anil XXII may exist as two geometric isomers (possibly mutually interconvertible), by analogy with the syn-anti isomerism of oximes.

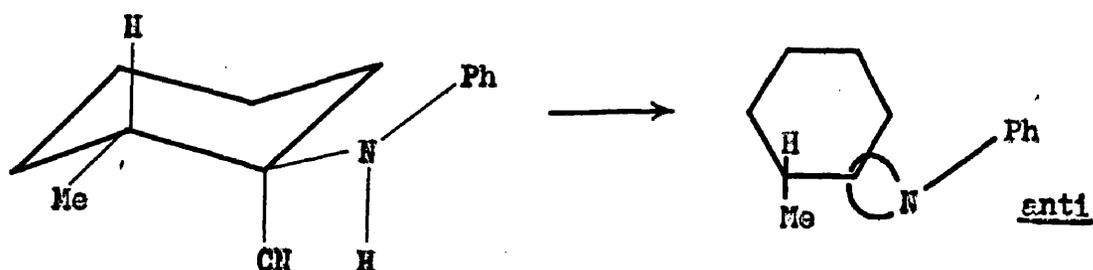
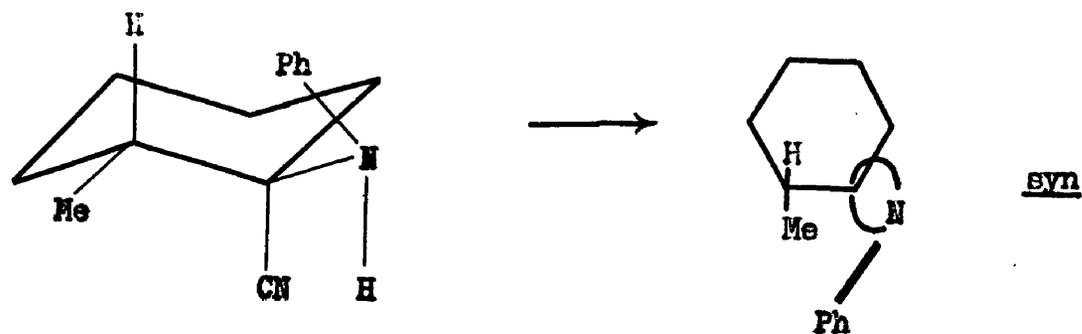


Manchot and Furlong (24) isolated two forms (yellow and red) of ethyl o-hydroxybenzylidene-p-aminobenzoate. The red form was less stable than the yellow and was converted to it at 83°.

Hassel (25) has discussed various possible forms of cyclohexane and its derivatives. On applying these ideas to the present work it appears that the cis- and trans- forms of XVII will each give a mixture of the syn- and anti- forms of the anil. The assumptions made are (i) that C/N elimination occurs (arguments are advanced later in favour of this), (ii) that the cyano group and hydrogen atom combine to eliminate hydrogen cyanide when they are closest together, and (iii) that the reversal of the bond structure of the nitrogen atom occurs (this is the normal behaviour of an amine $NR_1R_2R_3$, which cannot be separated into optical isomers).

The above idea is shown* for the trans-form (κ -anilino, ϵ -cyano, κ -methyl, ϵ -hydrogen) and it will be seen that it can give either a syn- or anti-form of the anil.

* Only the "chair" forms are considered since the "boat" form is not favoured either theoretically or experimentally (Hassel (25)).



Similarly the other three possible forms (trans $\epsilon\kappa\epsilon\kappa$; cis $\kappa\epsilon\epsilon\kappa$; and cis $\epsilon\kappa\kappa\epsilon$) can each give both syn- and anti- forms of the anil.

There is a further possibility that the anil could exist in more than two forms; but since the exact structures for cyclohexane rings containing carbonyl groups (and thus also for those containing anil groups) are not yet known (Hassel (25)) this possibility will not be considered here.

There was no experimental evidence for different anils being formed from the α - and β -forms of the anilino nitrile XVII. The infra-red absorption spectra were virtually identical (Fig. V) and the chief physical constants were identical within the limits of experimental error.

If there were any difference between the two anils it would be expected that the infra-red absorption spectra would show some difference, since in the spectra of the original anilino nitriles XVII α and β there are considerable differences.

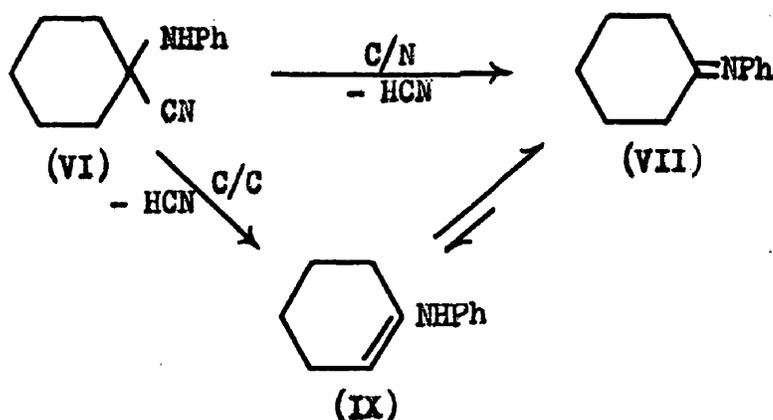
	n_D^{20} Δ	d_4^{20} Δ
anil from α -form	1.5504	0.9902
	0.0004	0.0004
anil from β -form	1.5508	0.9898

It is of course possible that the anil as isolated consists of an equilibrium mixture of interconvertible syn- and anti-forms. On this basis, even although the α - and β -forms gave different initial proportions of syn- and anti-forms of the anil, the same equilibrium mixture would be obtained from both α - and β -forms of the anilino nitrile XVII, provided that the velocity of interchange of syn- and anti-forms is rapid.

In the following discussion it will be assumed that the anilino nitriles XVII α and β give the same anil or equilibrium mixture of anils.

Possibility of C/C and C/N Elimination in the Pyrolysis of Anilino Nitriles.

It was mentioned earlier that the anil can be considered as coming from either C/N or C/C elimination from the anilino nitrile, e.g.

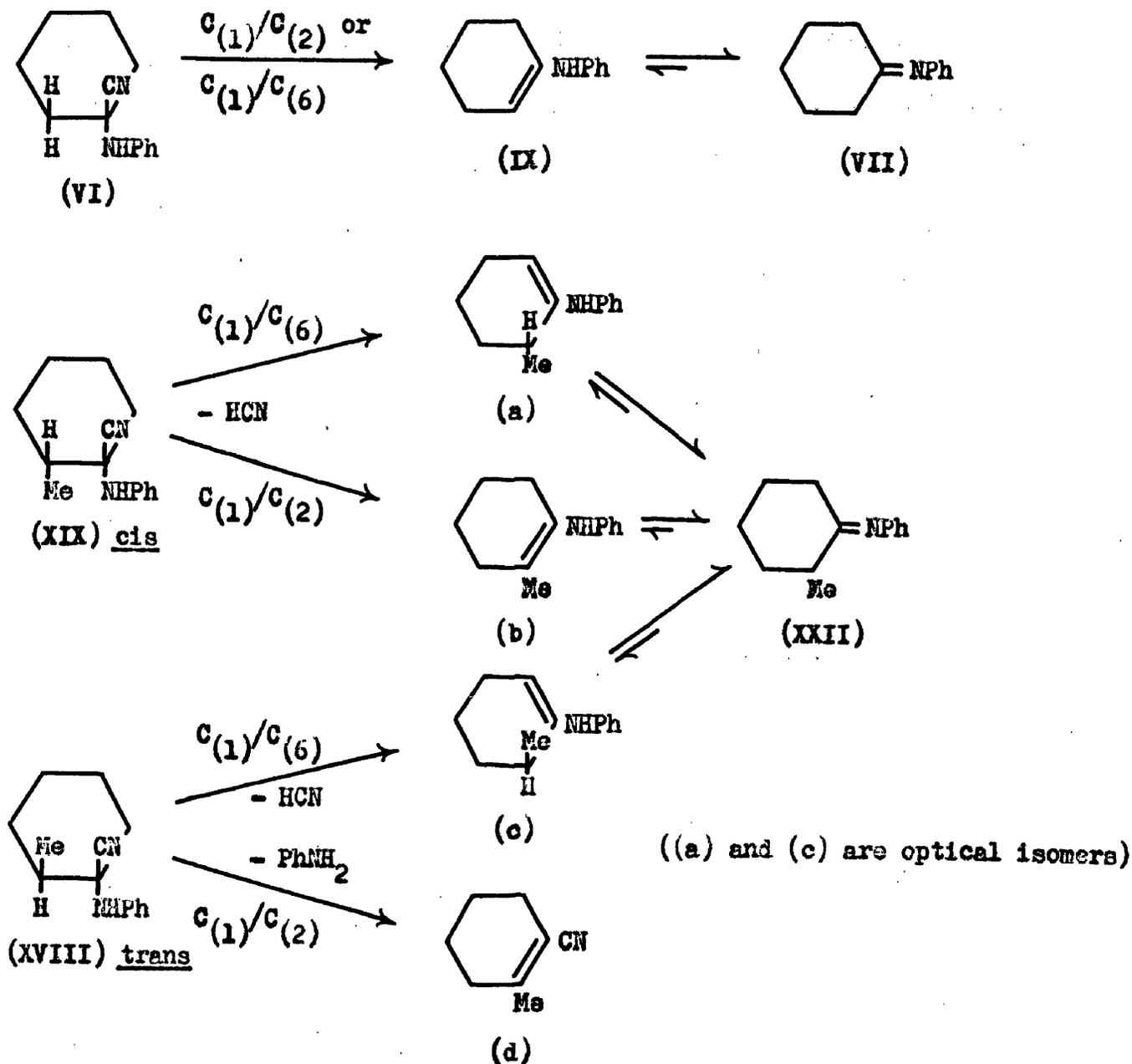


Thus for the C_6 anilino nitrile without a 2-methyl substituent the anil is obtained no matter which route is followed, for although the isolation of the anil VII at first sight favours the C/N route it is clear that the C/C route can give the same product. Barton (8) has obtained evidence favouring consistent cis elimination in certain homogeneous vapour phase reactions.

The following scheme assumes that consistent cis elimination occurs*

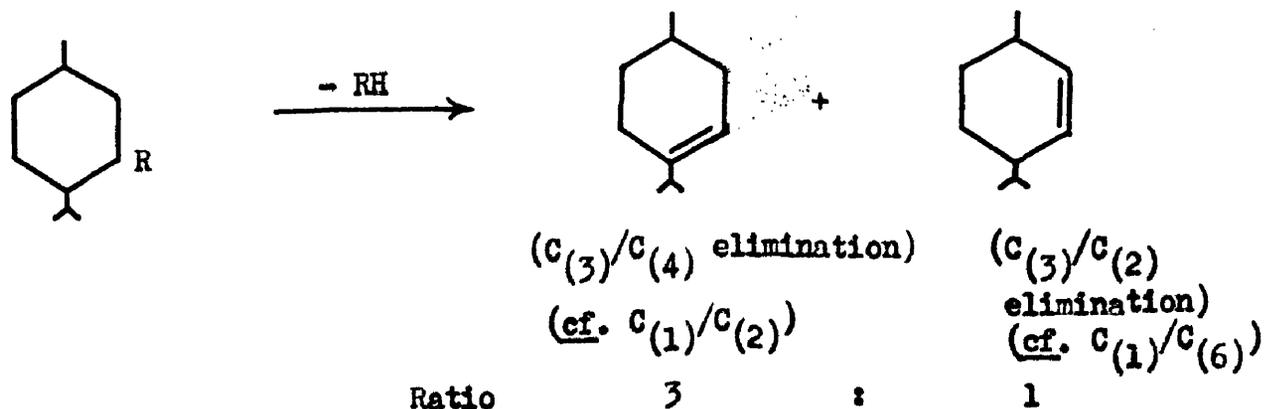
(If consistent trans elimination occurs, the general conclusions are still valid):-

Scheme A



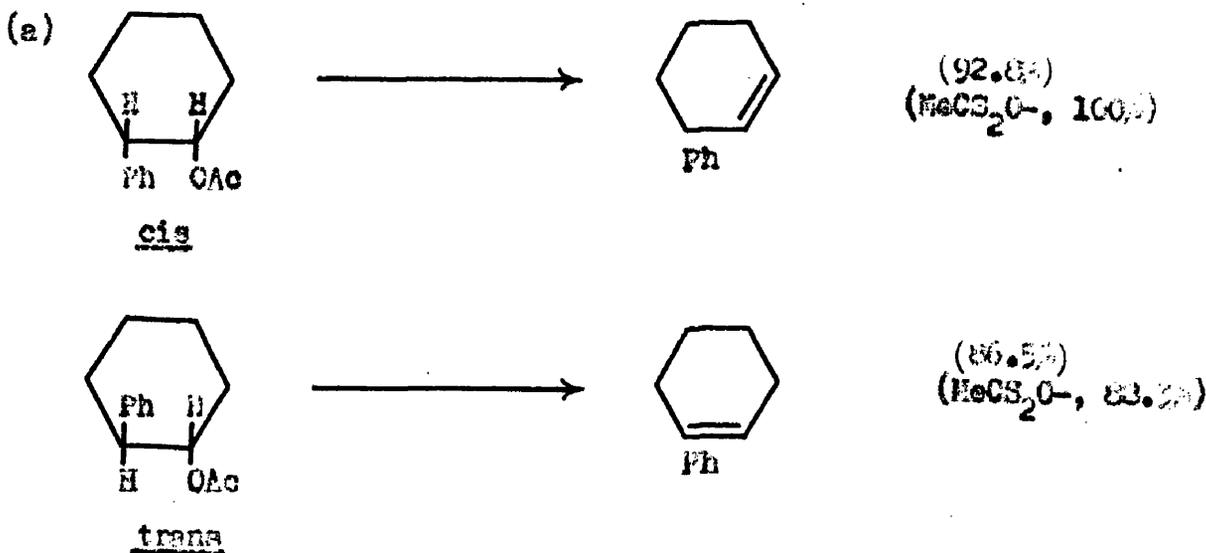
* Here and elsewhere planar forms of the cyclohexane rings have been shown where there appears to be no difference in the conclusion arrived at from consideration of these, and the "chair" form with ϵ and κ substituents described by Hassel (25).

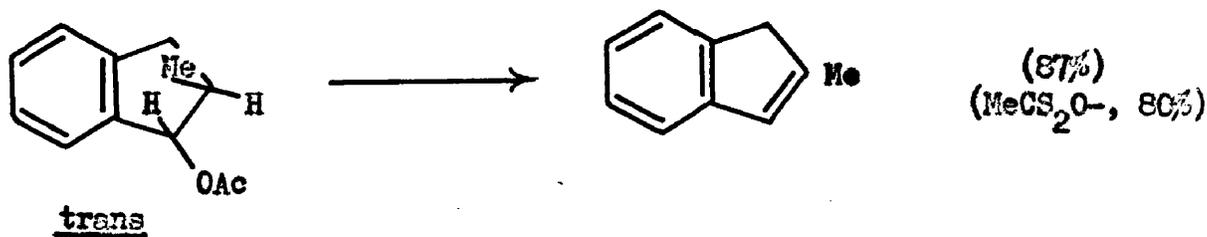
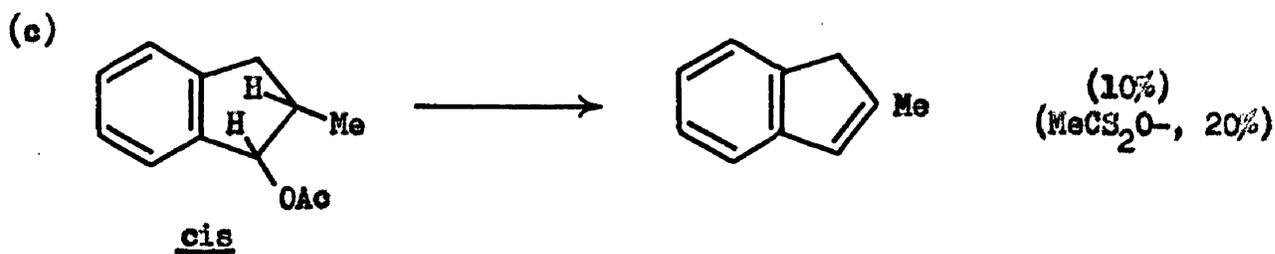
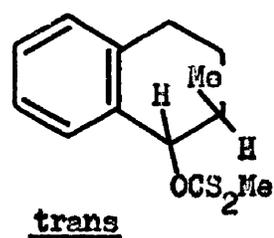
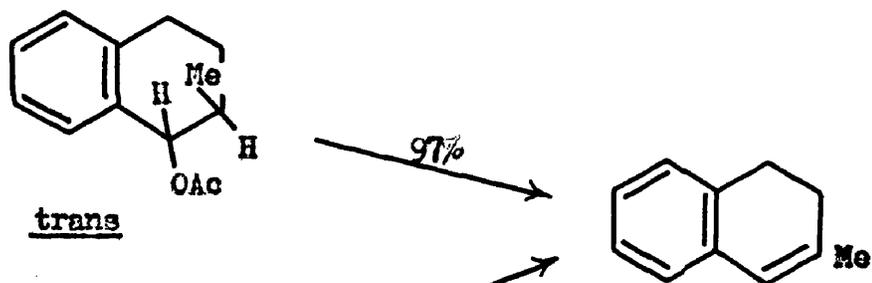
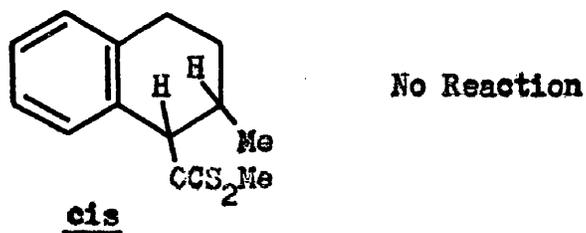
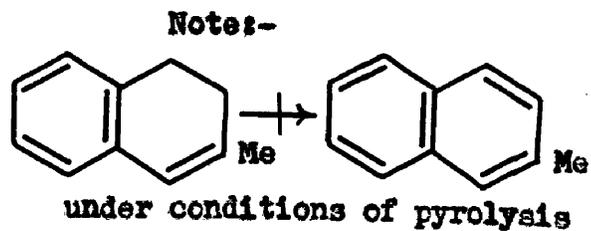
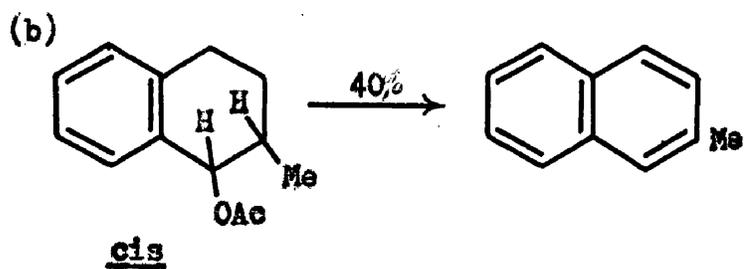
In the above scheme, the possibility of concurrent $C_{(1)}/C_{(2)}$ and $C_{(1)}/C_{(6)}$ elimination is considered. This is likely, in view of several analogous pyrolyses of (-) menthyl esters recorded in the literature.



(R=Cl, Barton, Head and Williams, (26); R=OBz, *idem*, (27); R=OAc, McNiven and Read, (28).)

Similar results for the pyrolysis of several acetates and xanthates were also recorded by Alexander and Mudrak, (29):-





Apart from one minor exception*, all the above reactions exhibit cis elimination, whether in the vapour phase (acetates) or liquid phase (xanthates). This suggests that cis elimination may also occur in the liquid phase pyrolysis of the anilino nitriles described in this thesis.

Scheme A shows that, with the anilino nitrile VI there are two possible C/C eliminations ($C_{(1)}/C_{(2)}$ and $C_{(1)}/C_{(6)}$) giving the same product. When the 2-methyl group is introduced, hydrogen cyanide can be eliminated by $C_{(1)}/C_{(6)}$ elimination from both cis- and trans- forms, but by $C_{(1)}/C_{(2)}$ elimination only from the cis- form. This leaves, as a possibility, the $C_{(1)}/C_{(2)}$ elimination of aniline from the trans- form.

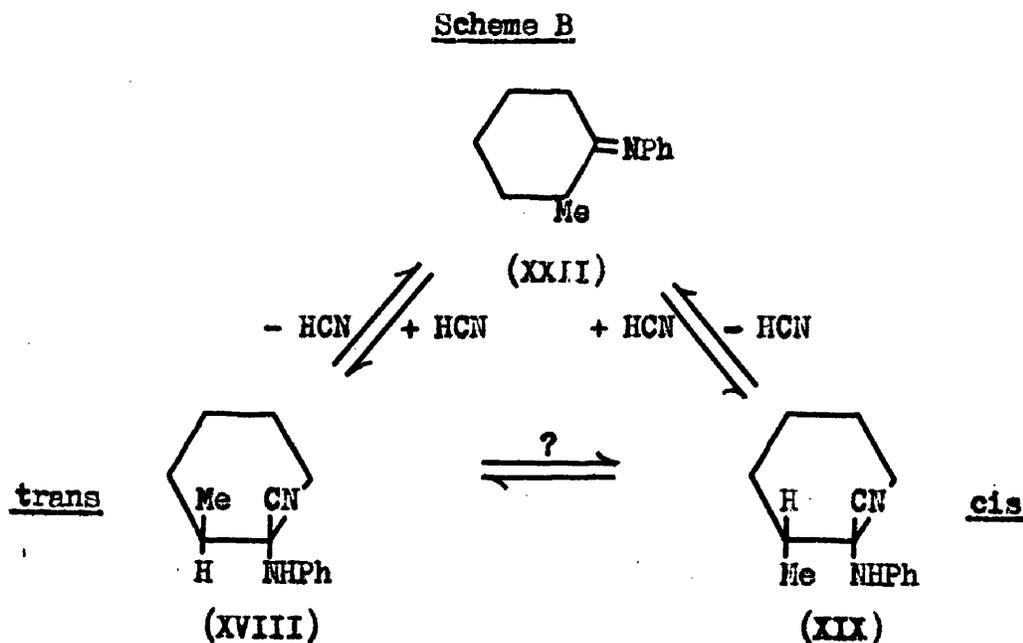
Because of the electron-repelling properties of the methyl group, it is likely that $C_{(1)}/C_{(2)}$ will predominate over $C_{(1)}/C_{(6)}$ elimination. The results of Barton, and Alexander and Mudrak, where the isopropyl and phenyl groups have a similar effect, support this conclusion.

Since the cis- and trans-forms (XIX and XVIII) are found to give the same products, it is likely that C/N elimination occurs for all the anilino nitriles. This conclusion is valid unless the elimination changes from cis with the cis- form to trans in the trans-form, which is very unlikely in view of the consistent cis elimination found by the authors mentioned above.

The hypothesis of C/N elimination is further supported by the results obtained for the pyrolysis of d-anilino- d - cyanodiphenylmethane. This readily eliminates hydrogen cyanide to form the anil in spite of the fact that C/C elimination is structurally excluded.

* This exception is the one noted under (b) where the acetate gives 2-methylnaphthalene instead of the expected 2-methyl-3:4-dihydronaphthalene.

There is further no evidence that the more labile of the isomers XVIII and XIX is converted into the other, at temperatures below that at which hydrogen cyanide is eliminated, i.e., there is nothing to support the alternative possibility that the single pair of products observed (hydrogen cyanide and anil) is produced by $C_{(1)}/C_{(2)}$ elimination from what is effectively a single isomer (XVIII or XIX) rather than by two C/N eliminations, leading to identical end-products. In this connection it should be noted that there are two different methods (Scheme B) by which the one form can be converted into an equilibrium mixture of both; a direct interconversion, possible but unlikely, and an indirect interconversion.



The indirect interconversion, however, necessitates the initial breakdown of the anilino nitrile into anil and hydrogen cyanide, so that this type of interconversion does not affect the results or conclusions drawn.

The above scheme B gives some idea of what must occur: and it will be seen that it is really impossible to pyrolyse the pure isomer (XVIII or XIX) since this type of indirect interconversion must be taking place during the pyrolysis.

This occurs, of course, only because the product of pyrolysis of both cis- and trans- forms is the anil - if other products were formed for either cis or trans the interconversion would no longer be possible and the other product would be isolated in place of the anil. Thus the general conclusions arrived at above still hold although any investigations into reaction rate processes (not undertaken in the present work) would have to take the indirect conversion into account.

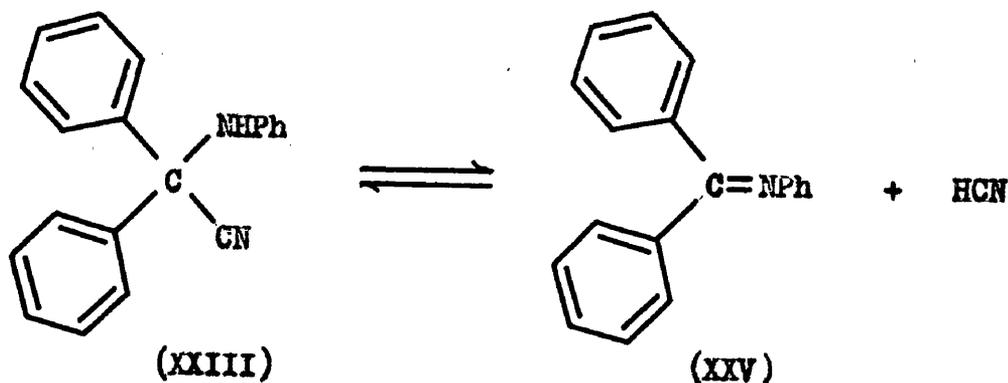
Rates of Elimination of Hydrogen Cyanide.

As will be seen from Table II (p. 43) the rates of elimination of hydrogen cyanide from anilino nitriles XVIII and XIX are greater than that of the unmethylated compound VI. This effect is slight, however, when compared with the large increase in rate for the decomposition of the C₇ anilino nitrile XVI, although it is outside the range of experimental error. The increase in rate on changing from VI to XVIII or XIX tends to indicate a C/C mechanism and could be a manifestation of the effect mentioned before (i.e. easier elimination of the β -hydrogen atom caused by the methyl group). A C/C mechanism must, however, give rise to different products from the pyrolysis of XVIII and XIX (unless the elimination changes from cis to trans, which is unlikely) and the slight increase in rate of elimination is therefore probably caused by the steric influence of the methyl group on the spacial relation of the anilino and cyano groups.

Pyrolysis of α -Anilino- α -cyanodiphenylmethane (XXIII).

The pyrolysis of anilino nitrile XXIII gives hydrogen cyanide (100%) and (diphenylmethylene)aniline (XXV) (98%). The rate of decomposition is shown in Tables I and II and in Fig. I, and it will be seen that this occurs with extreme readiness. XXIII is in fact the most readily decomposed of the anilino nitriles investigated. This pyrolysis at least proves that C/N elimination can occur,

since no C/C elimination is here possible, the carbon atoms in the 2-(or β -) position being fully substituted.



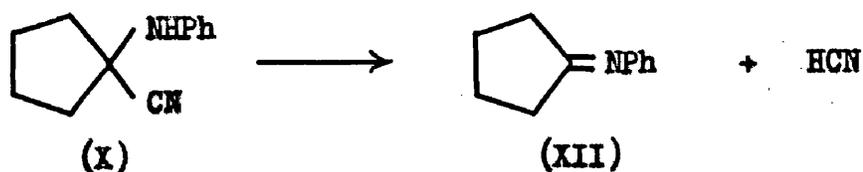
The extreme readiness with which decomposition occurs suggests that this route will be followed, at least partly, in the pyrolysis of the other anilino nitriles, although the phenyl groups appear to have a profound influence over the rate of decomposition of the anilino nitrile XXIII, making it faster even than the rapidly decomposing C_7 anilino nitrile XVI.

The greater part of the evidence therefore suggests that C/N elimination is the one which occurs, at least to a very large extent, in the pyrolysis of the anilino nitriles.

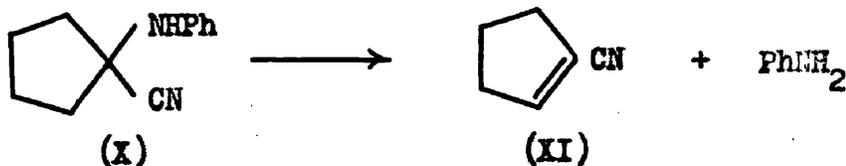
Pyrolysis of 1-Anilino-1-cyanocyclopentane (X).

Preliminary experiments in pyrolysing this compound gave somewhat puzzling results. Pyrolysis for six hours at 230° in a stream of nitrogen gave aniline (34% of theory), (aniline was noted by Plent and Facer (6)), and hydrogen cyanide (65% of theory). The fact that these figures add up to 99% is fortuitous, as will be clear from the later discussion.

The elimination of hydrogen cyanide suggests the following primary scission:-



Similarly elimination of aniline suggests the following primary scission:-



However, neither the anil XII nor the unsaturated nitrile XI could be isolated from the reaction mixture. Aniline (b.p. 183°) was the lowest boiling component of the pyrolysate, whereas the boiling point of the nitrile XI at 760 mm. is ca. 150° , (calculated from boiling points given by Cook and Linstead (30) ($69^{\circ}/15$ mm., $81^{\circ}/30$ mm.) from the well-known formula $\log p = A - B/T$ (where p = pressure, T = absolute temperature, and A and B are constants)). Hence, there can be practically none of the unsaturated nitrile XI present.

A fraction was obtained, b.p. $75 - 220^{\circ}/12$ mm., which at the time showed no further separation on redistillation; but it is now clear that it actually contained some cyclopentylideneaniline (XII).

A large amount of tarry material was also formed in this pyrolysis. It was later considered that the failure to obtain the anil could be due to its decomposing during the long pyrolysis period; and further experiments were therefore performed in which the heating time was much shorter. Obviously, however, the hydrogen cyanide had to be eliminated as quickly as possible in order to get a reasonable conversion of anilino nitrile to anil. This can be effected in two ways - (a) by performing the pyrolysis under vacuum, thus removing

the volatile hydrogen cyanide rapidly but leaving the anil, and (b) by making the nitrogen stream as rapid as possible (any cooling effect this would have would tend to reduce the rate of decomposition of the anil, while still maintaining a rapid removal of hydrogen cyanide - hence the cooling effect is no great disadvantage). These methods proved equally successful.

To prevent hydrogen cyanide from entering the vacuum line (during the vacuum distillation of the pyrolysate), and also to determine its amount, two traps containing aqueous potassium hydroxide were used. The solution has to be concentrated in order that it should have a reasonably low vapour pressure, thus avoiding too much water passing on to the low temperature trap.

Method (a) gave hydrogen cyanide (58% of theory) and anil XII (45% of theory) on pyrolysis for three hours at 190°. The anil XII was recognised by hydrolysis, addition of hydrogen cyanide, and hydrogenation, as with the other anils examined.

This amount of anil decomposed appears to represent establishment of equilibrium, since 57.3% hydrogen cyanide was evolved during the two hours under vacuum and only another 1.0% during the next hour. This was confirmed by the fact that during the ensuing distillation of the pyrolysate (lasting about $\frac{1}{4}$ hour) a further 21.4% hydrogen cyanide was eliminated. This is caused by removal of the anil during distillation, thus displacing the equilibrium just as when hydrogen cyanide is being removed.

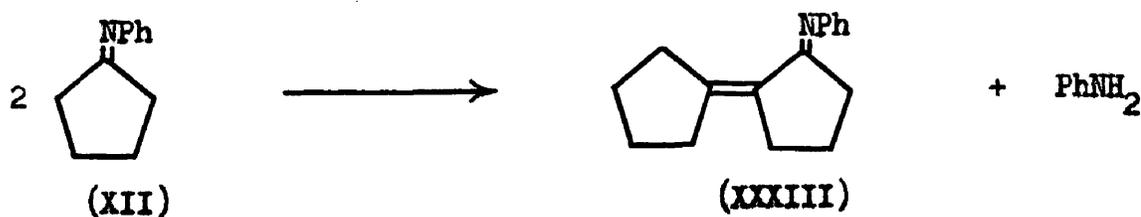
Method (b) gave hydrogen cyanide (50.5% of theory) and cyclopentylidene-aniline (XII) (48% of theory).

It thus appears that if the heating period is not too prolonged, hydrogen cyanide and anil are formed just as with the C₆ and C₇ anilino nitriles.

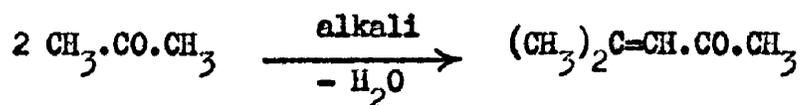
Products of Prolonged Heating of 1-Anilino-1-cyanocyclopentane (X).

There still remains the problem of why aniline is formed when the heating is prolonged: and this problem was in fact tackled before the above-mentioned short-time heating experiments were done. It was at that time desired to test the stability of the anil XII on prolonged heating. The anil was synthesised via the diethyl acetal by the method used by Hoch (31) for the preparation of a number of anils. These did not, however, include XII, which is not described in the literature. (This anil later proved identical with the one produced by pyrolysis, the infra-red absorption spectra being the same). The C₆ and C₇ anils (VII, XXII and XXXII) are quite stable on prolonged heating, and no difficulty is experienced in isolating them from the pyrolysates (e.g., XVII α gave an 80% yield of anil on heating for 20 hours at 250° or 117 hours at 200°).

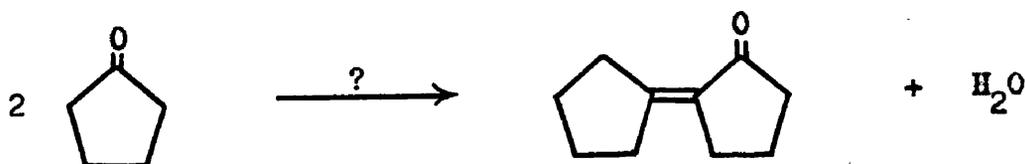
On heating the C₅ anil XII for six hours at 230° aniline, (2-cyclopentylidene-cyclopentylidene)aniline (XXXIII) and a tarry residue were formed, which explains the formation of aniline in the original pyrolysis of the anilino nitrile X.



This type of reaction is analogous to the aldol condensation of acetone:-



Wallach (32) observed a similar aldol-type condensation of cyclopentanone at room temperature, in presence of an alkaline catalyst (sodium methoxide), thus:-



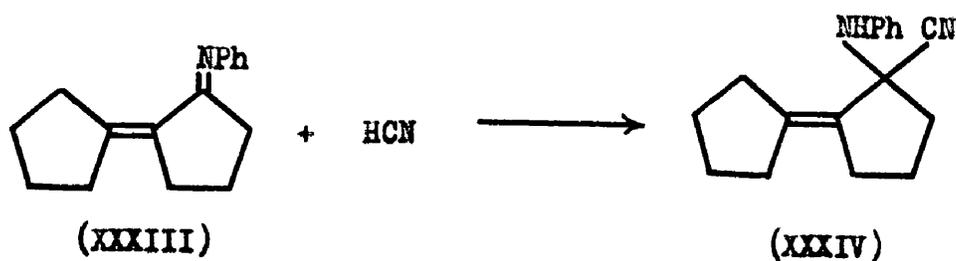
It is conceivable that the reaction might occur without a catalyst at higher temperatures and pressures.

It is interesting to note here that Wallach (32) states that cyclopentanone, cyclohexanone and cycloheptanone condense at different rates - cyclopentanone extraordinarily quickly, cyclohexanone only slowly and incompletely, and cycloheptanone still more slowly. This is in accordance with the present work, where C_6 and C_7 anils VII and XXXII are stable to heat and the C_5 anil XII condenses to aniline and XXXIII.

The (2-cyclopentylidenecyclopentylidene)aniline (XXXIII) was identified by quantitative acid hydrolysis to aniline and 2-cyclopentylidenecyclopentanone. The latter was characterised by its oxime (described by Wallach (32)) and 2:4-dinitrophenylhydrazone. It does not give a crystalline compound on addition of hydrogen cyanide, as do the other anils VII, XII, XXXII, which regenerate the original anilino nitriles. Nevertheless, it appears to add hydrogen cyanide (about 50% of theory)^{*}, this being eliminated again on heating. Owing to the difficulty of totally removing all excess of hydrogen cyanide at room temperature a gravimetric method was adopted for measuring the hydrogen cyanide retained by anil XXXIII. As much as possible of the excess of hydrogen cyanide was removed at room temperature in vacuo and the hydrogen cyanide retained was weighed. All the hydrogen cyanide was recovered by heating at 250° for 23 hours in a stream of nitrogen. Some combination had undoubtedly occurred, but it does not appear to give the anilino nitrile XXXIV, which by analogy with X would be expected to be

* assuming that one molecule of hydrogen cyanide adds on to one of XXXIII.

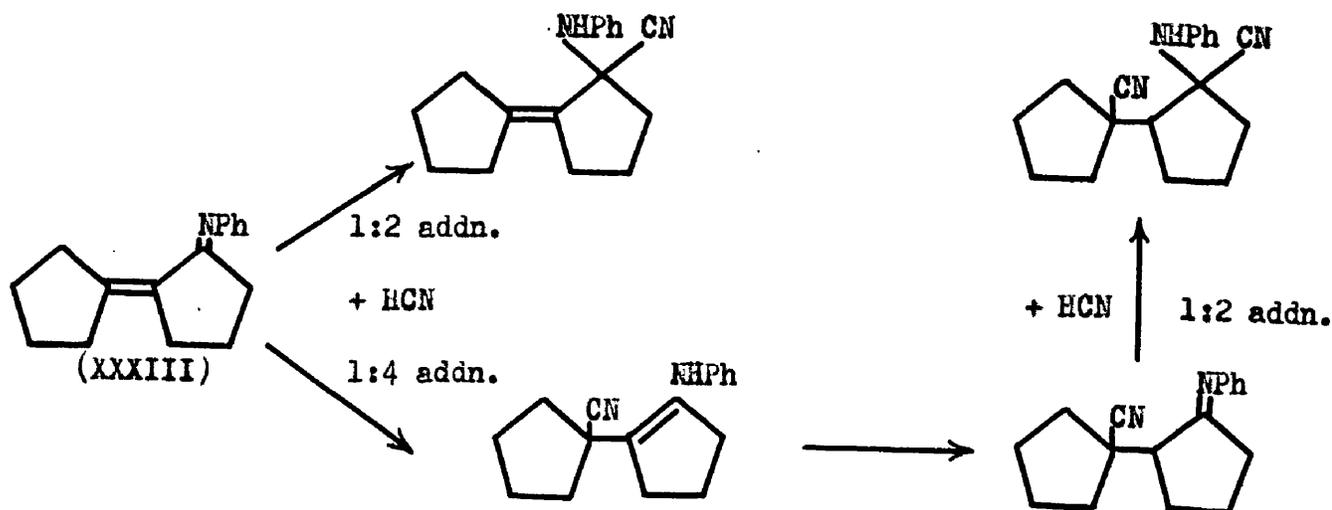
a solid.



Non-theoretical Elimination of Hydrogen Cyanide from 1-Anilino-1-cyano-cyclopentane (X).

It will be seen from p. 81 and Table I (p. 19) that at 150, 200, and 250° the elimination of hydrogen cyanide from the anilino nitrile X is about 80% of theory, and that the reaction appears to stop at this stage. This figure should be compared with 95-99% for the other anilino nitriles VI, XVIIa and β and XVI.

This non-theoretical elimination cannot of course be explained by the further condensation of the primary product, cyclopentylideneaniline, mentioned above, as hydrogen cyanide is not involved in this secondary reaction. It was at first thought that hydrogen cyanide might add on to the conjugated unsaturated anil XXXIII to give a product which might not re-eliminate hydrogen cyanide, thus:-



As mentioned previously, however, the product formed by addition of hydrogen cyanide to XXXIII, regenerates the amount of hydrogen cyanide originally added, if it is heated at 250° in a current of nitrogen. Although this evolution is somewhat slower than that shown by the original anilino nitrile X, the fact that evolution of hydrogen cyanide virtually stops after ca. 80% has still to be explained.

After an 80.2% elimination at 150° , which appears to be the maximum (or very near it) at that temperature, a further amount of hydrogen cyanide is obtained on raising the temperature to 300° , bringing the total up to 93.2% (which is very near to the 95-96% obtained from the C_6 and C_7 anilino nitriles). This shows that there are two distinct reactions involved - first, the primary scission to anil and hydrogen cyanide; second, some other reaction which gives a product which retains nitrile groups at 150° but which eliminates hydrogen cyanide at 300° .

Such a product has now been isolated from the tarry residue from the pyrolysis by distillation and crystallisation. The compound (A) is sharp-melting (m.p. 138°), dissolves in dilute hydrochloric acid, and is reprecipitated by dilute alkali. On prolonged boiling with alcoholic potassium hydroxide the solution gives a positive test for cyanide ion, (cf. the anilino nitriles, which give aniline, ketone and cyanide). The base does not give a reaction for primary or secondary amine and the reaction for tertiary aromatic amine is also negative. This behaviour recalls the base isolated by Drew (33) from the pyrolysis of 2-anilino-2-cyanopropane (obtained from acetone, aniline, and hydrogen cyanide). The solution of A in hydrochloric acid gives a precipitate with chloroplatinic acid (characteristic of an amine) and also a precipitate with potassium ferrocyanide (characteristic of a tertiary amine). It may be

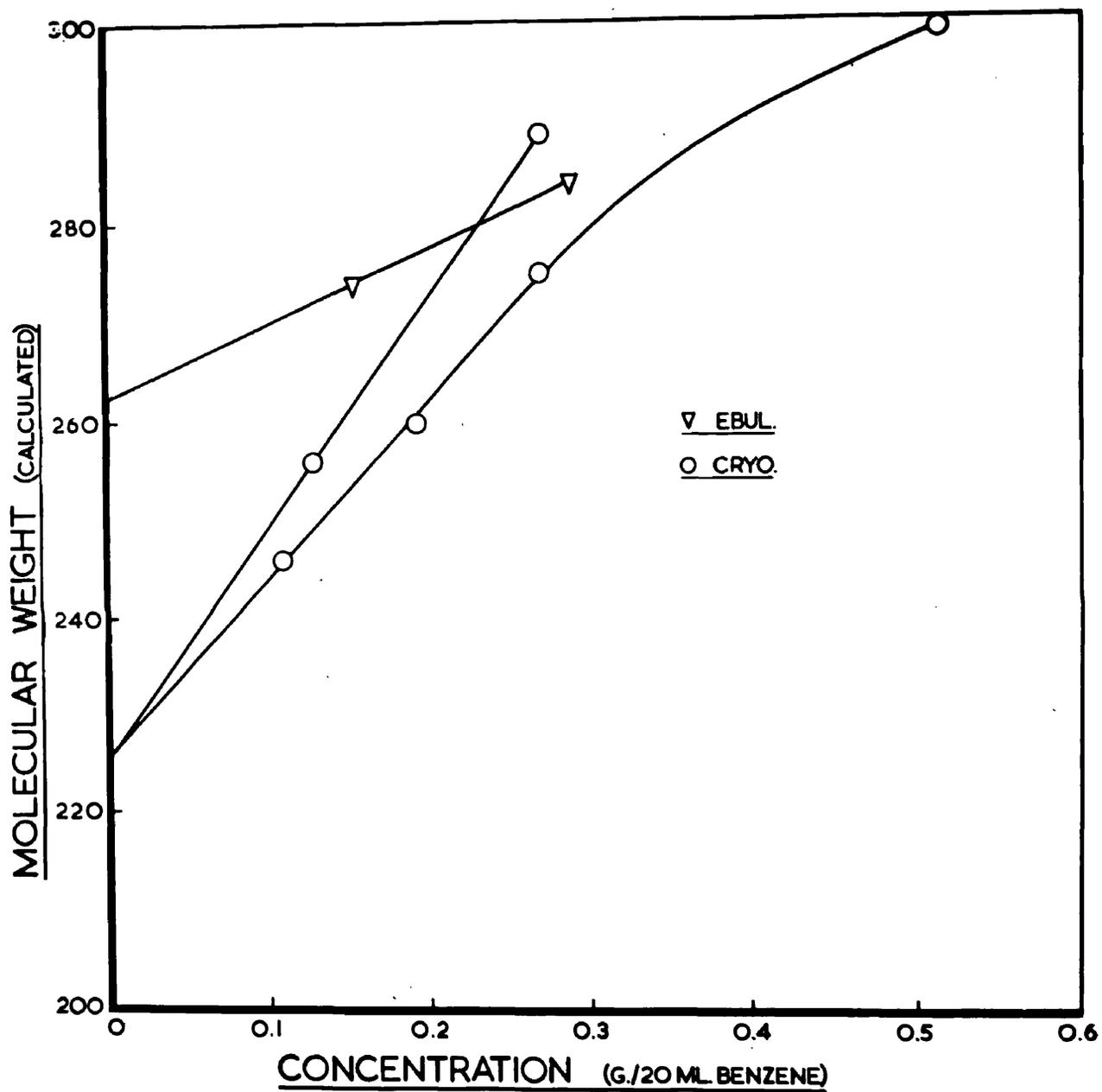


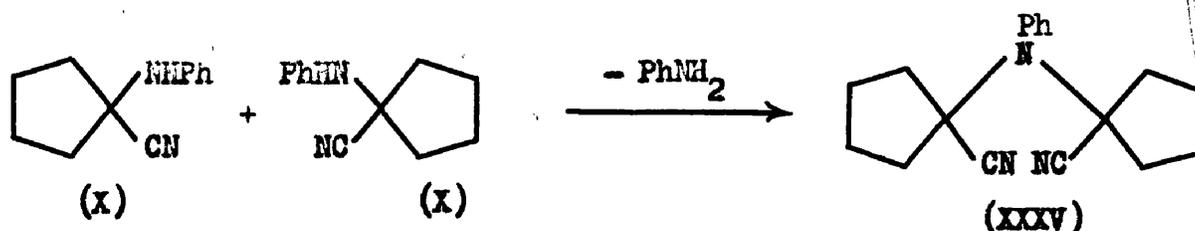
FIGURE II

FIGURE II

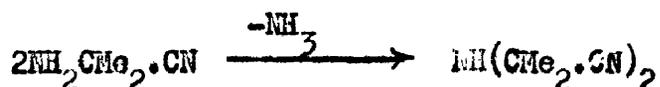
Molecular Weight of Compound, (A), m.p. 138°,
from Pyrolysis of 1-Anilino-1-cyanocyclopentane

(the two cryoscopic determinations are duplicates)

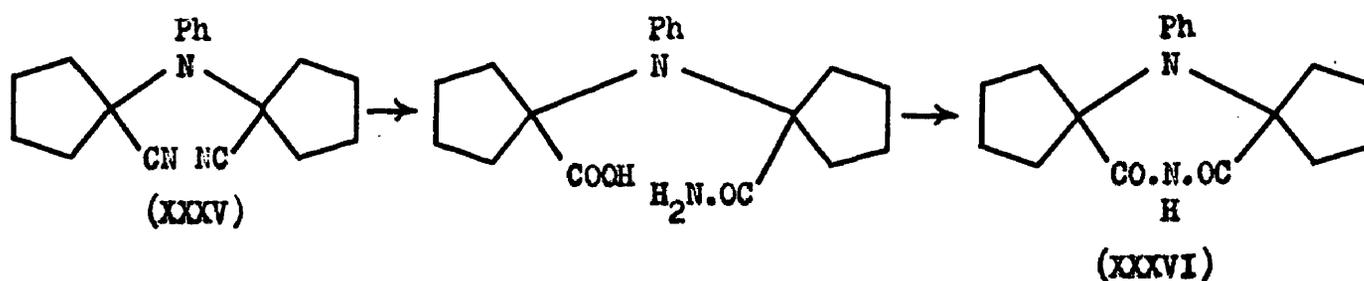
assumed, then, that the compound A contains at least two nitrogen atoms - one in a tertiary amine group, the other in a cyano group. The equivalent weight determined by ignition of the platinichloride is 288, but the molecular weight determined in benzene (cryoscopic) has the value 230. This last determination is somewhat in doubt as the molecular weight varies considerably with concentration (see Fig. II). This variation is of a much greater order than the normal slight variation due to the non-ideality of solutions. This variation might be due to association, though in this case 230 would be a maximum value, since the true molecular weight would be less than the observed if association occurs. If the boiling point of the compound is taken as an indication of molecular weight, and for the same type of compound this is generally true, then the compound A should have a molecular weight considerably greater than 225, since its boiling point is about 50° higher at 3 mm. than that of the unsaturated anil. XXIII M.S. 225. Microanalysis (see p.83) suggests the formula $C_{6n}H_{7n}N_n$ and if $n=3$, the molecular weight is 279. This value agrees with experimental values for the equivalent of 283 (micro-titration) and 288 (ignition of platinichloride). A determination of nitrile groups (by determining the ammonium chloride formed by hydrolysis of A with concentrated hydrochloric acid) gave a value of 281 (assuming one nitrile group per molecule). The molecular formula thus corresponds to two molecules of the original anilino nitrile X minus aniline; and the following reaction appears to be a formal possibility:-



This would account for the presence of a tertiary basic group and also the presence of a nitrile group. A similar reaction has been described by Dubsky and Wensink (34) *viz.*, the heating of 2-amino-2-cyanopropane to give bis-(α -cyanoisopropyl)amine.



The formula XXXV does not entirely explain the properties of A on acid hydrolysis, which gives an amount of ammonium chloride corresponding to only one nitrile group. This could be explained by assuming a ring formation on hydrolysis.



The objection to this is that the hydrolysis product is water soluble (neutral) whereas the compound XXXVI would be expected to be insoluble.

Compound A is quite stable to heat at 200° : under conditions in which the original anilino nitrile XII decomposes to the extent of 65%, virtually no A (< 0.4%) had decomposed. In another similar experiment at 300° hydrogen cyanide was given off (see Experimental section) in amount which indicated an equivalent weight of 350 (i.e., 350 g. of A gives 1 g. mol hydrogen cyanide). If the formula XXXV is indeed correct it is difficult to see why, if XXXV eliminates hydrogen cyanide at all, it should not eliminate two molecules of hydrogen cyanide, thus giving an equivalent weight of 140.

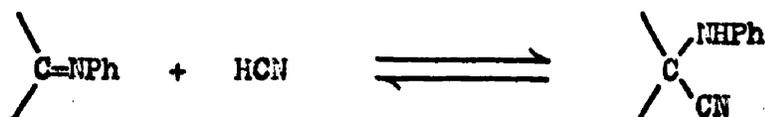
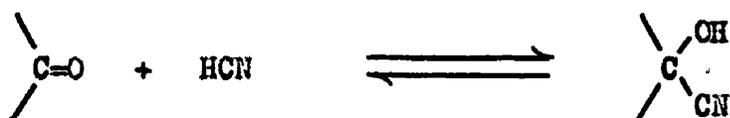
It can be seen then that, although the identity of the compound A is not

yet clear, its properties of hydrogen cyanide elimination (none at 200° and a considerable amount at 300°) correspond to and account for the non-theoretical elimination of hydrogen cyanide from 1-anilino-1-cyanocyclopentane (X) at 200° and about theoretical elimination at 300° .

Analogy Between C=O and C=NPh Groups

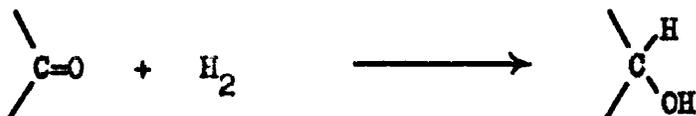
It is interesting to note here that there is a close analogy between the C=O group and the C=NPh group. This is evidenced by the following:-

(a) Addition of Hydrogen Cyanide:-

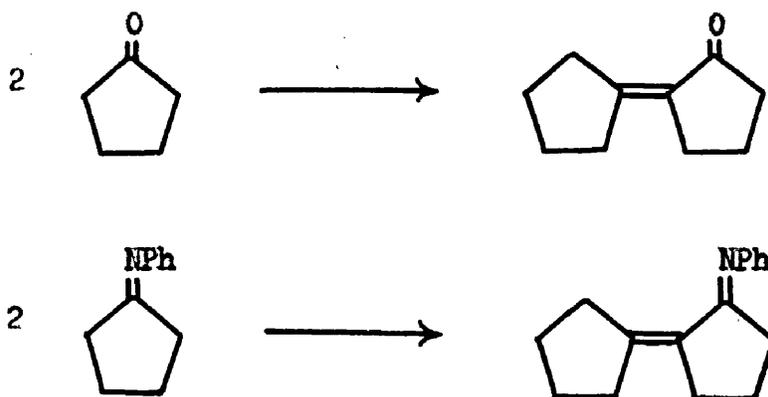


In both cases the reaction is reversible, although the ketone reaction requires a trace of alkali as catalyst and the anil reaction appears to occur spontaneously.

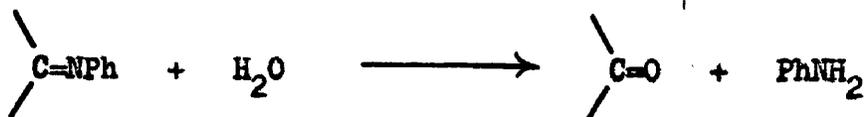
(b) Hydrogenation:-



(c) Aldol-type Condensation (cf. p.35):-



The = NPh group thus appears to react much as the = O atom, and in reactions (a) and (b) the -NHPh group formed corresponds to the -OH group. There is, of course, no analogy for the acid hydrolysis:-

Pyrolysis of 1-Anilino-1-cyanocyclobutane (XV).

Only a small amount (ca. 8 g.) of this compound was available and since the former controlled experiments in hydrogen cyanide elimination required the use of 15 g. of the sample, a semi-micro technique was adopted. The apparatus used was similar to the first one, though smaller in scale and a microburette was used for the cyanide titration (for fuller description see p.84).

As it was desired to measure the rate of elimination of hydrogen cyanide (if any) from the C₄ anilino nitrile relative to the other anilino nitriles, all the anilino nitriles prepared were subjected to pyrolysis in this apparatus. The amount of material required in the apparatus was 0.3 g. and the time chosen

TABLE II

Pyrolysis of Anilino Nitriles

Semi-micro Scale

<u>Anilino Nitrile</u>	<u>mean</u> <u>%HCN</u>	<u>duplicates</u>	
C ₄	38	36.4	38.7
C ₅	65	66.3	64.2
C ₆	49	50.8	48.2
C _α	57	55.3	58.6
C _β	56	56.8	55.3
C ₇	92	91.4	92.3
diphenyl-	97	96.8	97.0

for relative measurements was ten minutes. The reproducibility of results was determined by duplicate determinations, and the results were found to be reproducible to 3%. These have the valuable effect of confirming the previous macro-scale results. The semi-micro are in fact more accurate than the macro results, since it was much easier to control the nitrogen flow-rate and the temperature for the ten minutes of the run, than for the ten hours or more required for the macro-scale work. The results (Table II) agree quite well with those obtained in the macro-scale experiments. The elimination of hydrogen cyanide is much faster in the semi-micro pyrolysis because, although the temperature and rate of flow of nitrogen are the same as in the macro experiments, the weight of sample is only 1/50th of the weight in the macro pyrolysis; the rate of flow of nitrogen per unit weight of material is therefore actually much faster, and the equilibrium will thus be displaced more quickly.

The C₄ anilino nitrile is the slowest to decompose of all the anilino nitriles tested. This was unexpected, in view of the rise in rate of decomposition in passing from the C₆ to C₅ compounds. The value of the dissociation constant for the C₄ cyanohydrin is not recorded in the literature, so that no analogy can here be drawn as with the other anilino nitriles.

The total elimination of hydrogen cyanide from the C₄ anilino nitrile is ca. 70%. Since cyclobutanone exists (presumably in a strained state) there seems no particular reason why the anil should not exist as well, especially in view of the analogy between the C=O and C=NPh groups, noted above. If the ring can be strained to accommodate the C=O double bond, it can presumably also be strained to accommodate the C=NPh double bond. In view of the elimination of hydrogen cyanide it therefore seems likely that cyclobutylidene-aniline is a primary product of this pyrolysis. It is also possible that because

of the non-theoretical elimination of hydrogen cyanide and the elimination of aniline, the anilino nitrile XV gives products similar to those of the C₅ anilino nitrile.

Further work on the anilino nitrile XV would have involved the preparation of cyclobutanone on a reasonably large scale (to obtain ca. 100 g.). This could only be done by using efficient specially constructed continuous extractors in the Roberts and Sauers (9) method of preparation or (which would probably be better and more convenient though still difficult) using the method of Kaarsemakers and Coops (19) (reaction of keten with diazomethane). The chief difficulty is in obtaining sufficient diazomethane. This makes the method either expensive or tedious, but the method seems more promising than that of Roberts and Sauer, which, in our hands, gave a low yield.

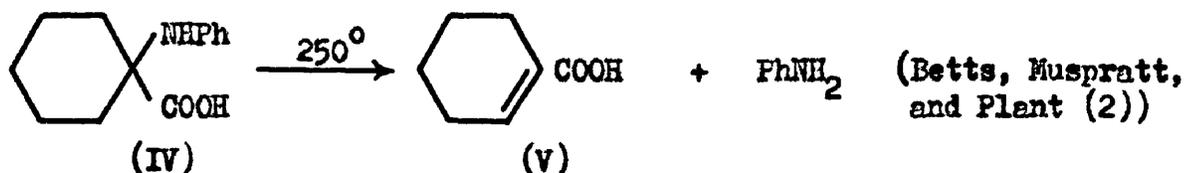
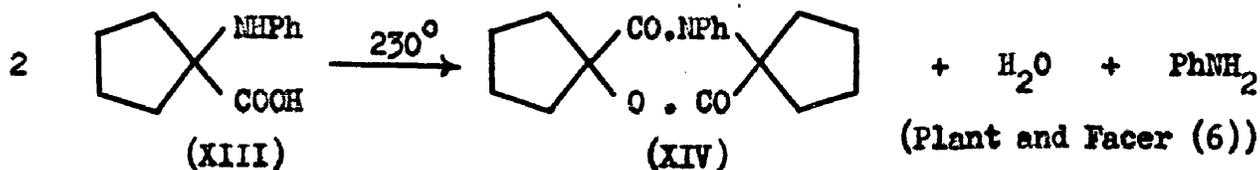
TABLE III

Pyrolysis of Anilino Acids

<u>Product</u>	<u>% yield of theory</u>			<u>% by weight</u>		
	C ₅	C ₆	C ₇	C ₅	C ₆	C ₇
aniline	39	54	65	17.5	23.2	26.0
unsaturated acid	7.1	36	52	3.9	21.5	31.1
1-hydroxyanilide	3.9	6.4	3.9	3.9	6.4	3.9
lactone-lactam	21	13	10.5	<u>15.0</u>	<u>10.1</u>	<u>8.0</u>
				<u>40.3</u>	<u>61.2</u>	<u>69.0</u>

PYROLYSIS OF 1-ANILINOCARBOXYLIC ACIDS.

The pyrolyses of the C₅ and C₆ anilino acids XIII and IV are described in the literature, though yields are not recorded:-



These pyrolyses were repeated and extended to the C₇ acid XXXVII, using a static system (250°; 1 hour) similar to that used for the anilino nitriles, but omitting the stream of nitrogen. The weight of starting material was ca. 50-80 g. The products and yields obtained are recorded in Table III.

It will be seen from Table III that although the products mentioned by Plant et al. (2, 6) are indeed formed, all the anilino acids studied gave products of the same structural type, as follows:-

Aniline

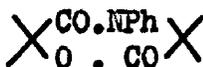
Unsaturated acid



1-Hydroxyanilide



Lactone-lactam



The impression derived from the earlier literature (2, 6) that the C_5 and C_6 anilino acids decompose by entirely different routes is thus deceptive. It will nevertheless be seen from Table III that there is a variation of yield on changing the ring size. The most striking difference is the low yield of unsaturated acid from the pyrolysis of the C_5 anilino acid.

Isolation and Identification of Products.

- (1) Aniline. This was isolated by vacuum distillation and identified by conversion to acetanilide.
- (2) Unsaturated Acids. These were also isolated by vacuum distillation and were identified by their melting points and those of their dibromo derivatives.
- (3) 1-Hydroxyanilides. These were isolated by fractional crystallisation of the residue obtained after distillation of aniline and unsaturated acid. They were identified as follows:-

(a) Hydrolysis gave aniline and the corresponding hydroxy acid, the latter being identified by melting point and mixed melting point with the product obtained by hydrolysis of the corresponding cyanohydrin. (b) There are two values recorded in the literature for the melting point of the C_6 hydroxyanilide and the value obtained agrees well with one of these and fairly well with the other. (c) The three hydroxyanilides were synthesised from the corresponding ketones by reaction with hydrogen cyanide and hydrolysis of the cyanohydrin, followed by reaction of the hydroxy acid with aniline. Mixed melting point determinations were done and in no case was a depression of melting point obtained. Infra-red absorption spectra also showed that the synthetic and pyrolytic hydroxyanilides were identical. (d) Their identification was confirmed by microanalysis.

(4) Lactone-lactams. These were also isolated by fractional crystallisation of the pyrolysis residue.

Identification. It has been clearly shown by infra-red absorption spectra that the three (C_5 , C_6 , C_7) lactone-lactams have the same functional-group structure. If, therefore, the lactone-lactam structure proposed by Plant is correct, all three have this type of structure. It has been found that all three have similar chemical properties, but that the C_6 and C_7 compounds are more inert (e.g. the C_5 compound dissolves slowly in dilute alkali, whereas the C_6 and C_7 compounds require warm alkali and even then dissolve slowly). The molecular formulae of the three compounds have been confirmed by molecular weight determinations and microanalyses.

There remains, however, the problem of whether the structure proposed by Plant is indeed correct. No evidence against this structure has been found, and some evidence has been found in favour of it. Plant supports his view of the structure by (a) elementary analysis, (b) the fact that it dissolves slowly in dilute alkali and is reprecipitated slowly by dilute acid (a characteristic of a lactone), (c) the fact that it is not basic, and (d) the fact that it does not react with aniline or dry ammonia at elevated temperatures. Properties (a), (b), and (c) have been confirmed in the present work, and further evidence favouring the structure XIV has been obtained as follows:-

(e) The microanalyses and molecular weights agree well with the calculated values. This provides strong evidence for the ring structure because on increasing the ring size from five to six and six to seven the formula rises by $2 \times CH_2$, thus suggesting that there are two saturated alicyclic rings in each molecule, thus:-

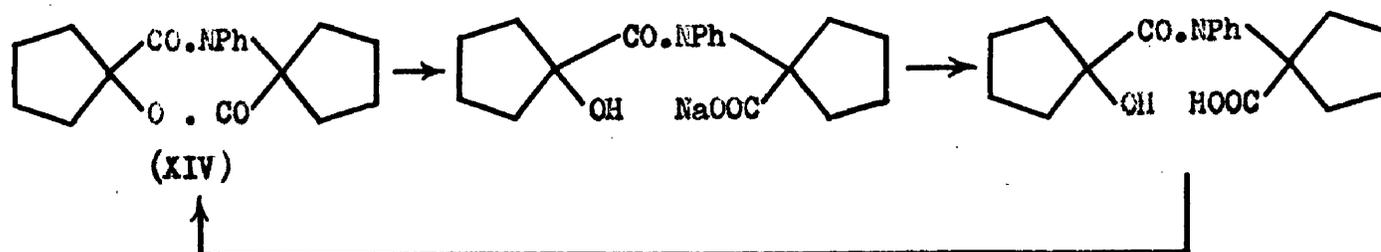


(The following apply to the C₅ lactone-lactam)

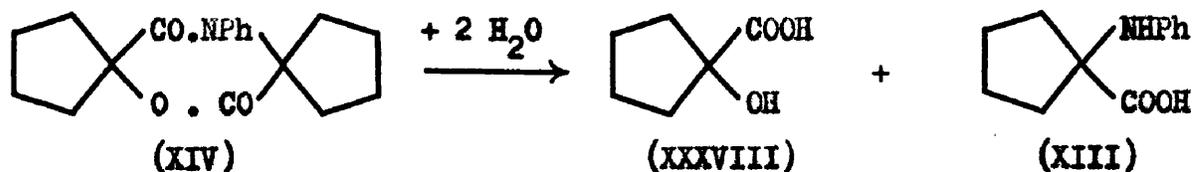
(f) The equivalent weight was determined by dissolving a weighed amount in an excess of warm dilute standard alkali, and back-titrating the excess of alkali.

(Found: 306, C₁₈H₂₁O₃N requires 299 (for monoacidic base)).

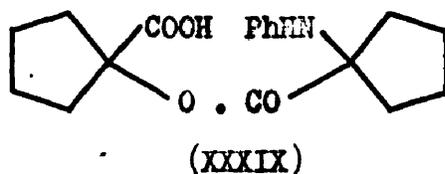
(g) Reprecipitation from alkaline solution by dilute acid occurs in a rather peculiar manner. A sticky paste is first precipitated which slowly becomes solid on standing. This solid is the original lactone-lactam (identified by melting point and mixed melting point). The initial precipitation as a paste can be accounted for by assuming that the paste is a mixture of lactone-lactam and free hydroxy acid: the latter on standing re-esterifies itself completely, thus:-



(h) A hydrolysis of the lactone-lactam with boiling alkali for three hours has no further effect and addition of acid merely reprecipitates the original lactone-lactam as before. Acid hydrolysis was attempted in the hope that the lactone-lactam would hydrolyse to 1-hydroxycyclopentanecarboxylic acid (XXXVIII) and 1-anilino-cyclopentanecarboxylic acid (XIII):-



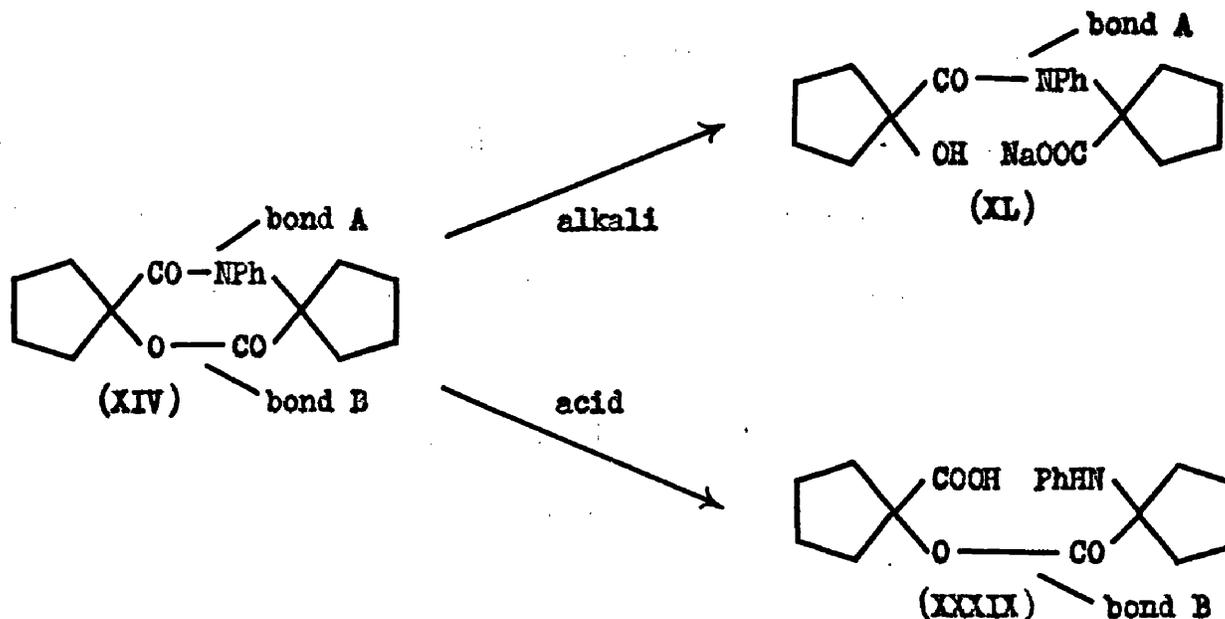
Only a trace of the hydroxy acid XXXVIII was found, however, and none of the anilino acid XIII. The main product was a new compound which is believed to have the structure XXXIX, a partial hydrolysis product.



This structure was deduced from the following:-

- (i) Like the original anilino acid XIII it dissolves in both dilute sulphuric acid and dilute alkali; thus, it contains both acidic and basic groups (-COOH and -NHPh). It is, however, not so readily soluble in dilute sulphuric acid as the anilino acid XIII and it requires heating or prolonged agitation in an excess of dilute sulphuric acid to effect solution. It is just as readily soluble in alkali as the anilino acid XIII.
- (ii) Its solution in dilute sulphuric acid gives a precipitate with nitrous acid, which indicates a secondary amine group.
- (iii) On heating above its melting point water is evolved, and the original lactone-lactam is regenerated (recognised by melting point, mixed melting point, and infra-red absorption spectrum).
- (iv) Its equivalent weight was determined by dissolving in standard alkali and back titrating with standard acid. (Found: 316. XXXIX requires 317).
- (v) It gave a positive result on testing for nitrogen.

Thus it can be seen that the lactone-lactam XIV can be only partially hydrolysed:-



The question which arises is why the hydrolysis stops at this point.

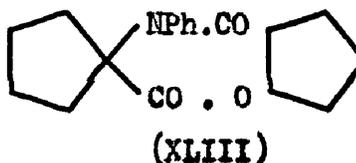
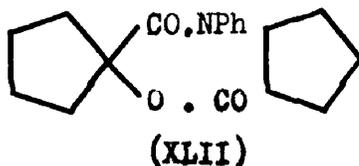
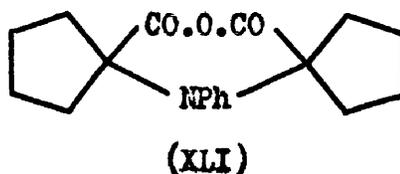
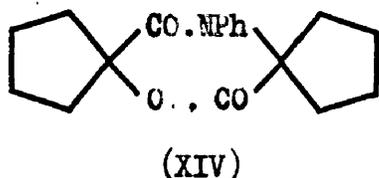
It is well known that tertiary alcohols are difficult to esterify, and that the esters once formed are difficult to hydrolyse.

Similar considerations apply to acids whose carboxyl groups are attached to a tertiary carbon atom. It will be seen that the bond B is formed (formally) from a tertiary alcohol and an acid whose α -carbon atom is tertiary. It is not surprising, therefore, that this bond does not hydrolyse, as both hindering effects are present. Similar considerations will apply to the bond A in the compound XL.

The reason why the bond A or B is attacked in the first place is presumably that strain present (possibly caused by the bulky substituents) in the heterocyclic ring renders the bond more open to attack. Once the bond is broken, however, the strain will no longer be present and the remaining bond will be extremely difficult to hydrolyse for the reason stated.

Consideration of Structure of Lactone-lactam.

There are four possible structures for the lactone-lactam (as it has been called up to now), which merit consideration. They are all, of course, isomeric, as follows:-

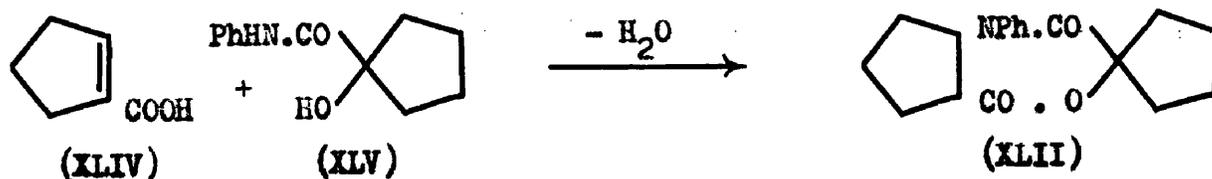


The structure XIV has already been discussed at length. The structure XLI was also considered by Plant, but he considered it less likely than XIV because XLI would be expected to be basic (owing to the tertiary amino group present), whereas the compound isolated showed no basic properties. This is not quite conclusive, however, as sterically hindered tertiary amines (e.g., triphenylamine) do not show basic properties. The present work provides additional evidence against this structure.

The equivalent weight of XLI would be 150, whereas the value found for the compound isolated is 306. Also, the structure XLI would not account for the properties described under (h) above.

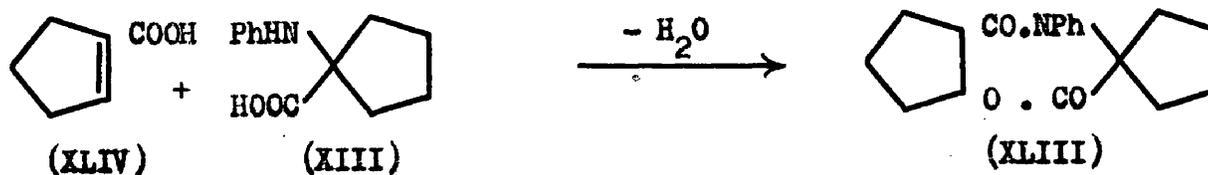
The structures XLII and XLIII both require the formation of a seven-membered ring which, though possible, seems less likely than the six-membered ring required by XIV and XLI. The compound XLII could conceivably be formed by addition of the

unsaturated acid XLIV to the hydroxyanilide XLV, (both pyrolysis products):-



When this reaction was tried (actually using the C_6 compounds) under conditions similar to those used for the original pyrolyses, the only products were unchanged unsaturated acid and hydroxyanilide.

The compound XLIII could be formed by addition of the unsaturated acid XLIV to the anilino acid XIII itself:-



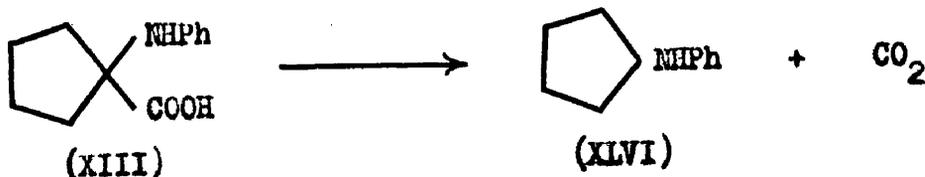
This mode of addition seems unlikely, but there appears to be no way of verifying this under the conditions of pyrolysis as the anilino acid XIII alone would give the lactone-lactam, so that its isolation would be inevitable in a test experiment whether the above reaction occurred or not.

Thus it appears that the structure XIV originally proposed by Plant (6) is the most likely. The structure XLI can be rejected; but from the evidence obtained the structures XLII and XLIII are possible, as their chemical properties would be very similar to those of XIV, all three being lactone-lactams.

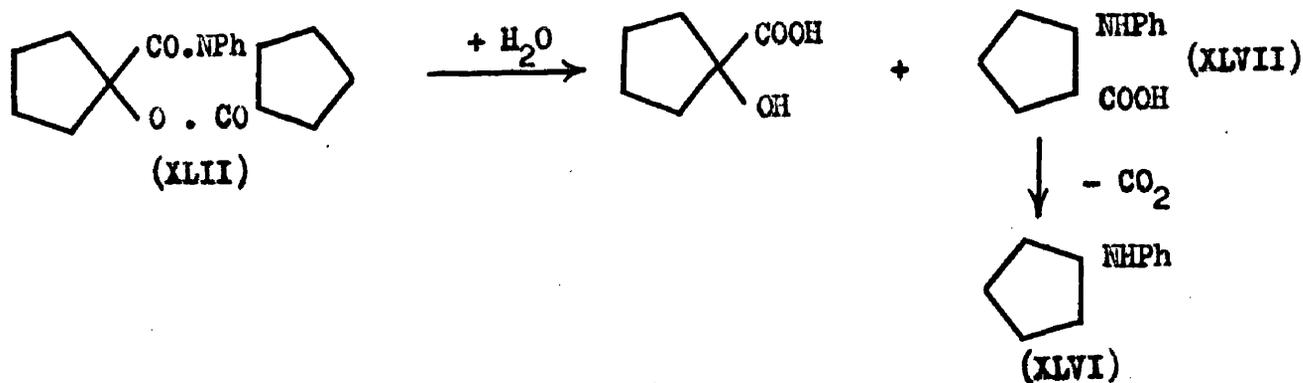
The isolation of even the small amount of l-hydroxy acid from the lactone-lactam hydrolysis suggests that structure XLIII is not correct, but it does not rule out structure XLII. Only the isolation of the l-anilino acid would be

conclusive here.

In a test experiment it was found that the original C₅ anilino acid XIII gives cyclopentylaniline (XLVI) on prolonged boiling with dilute sulphuric acid:-



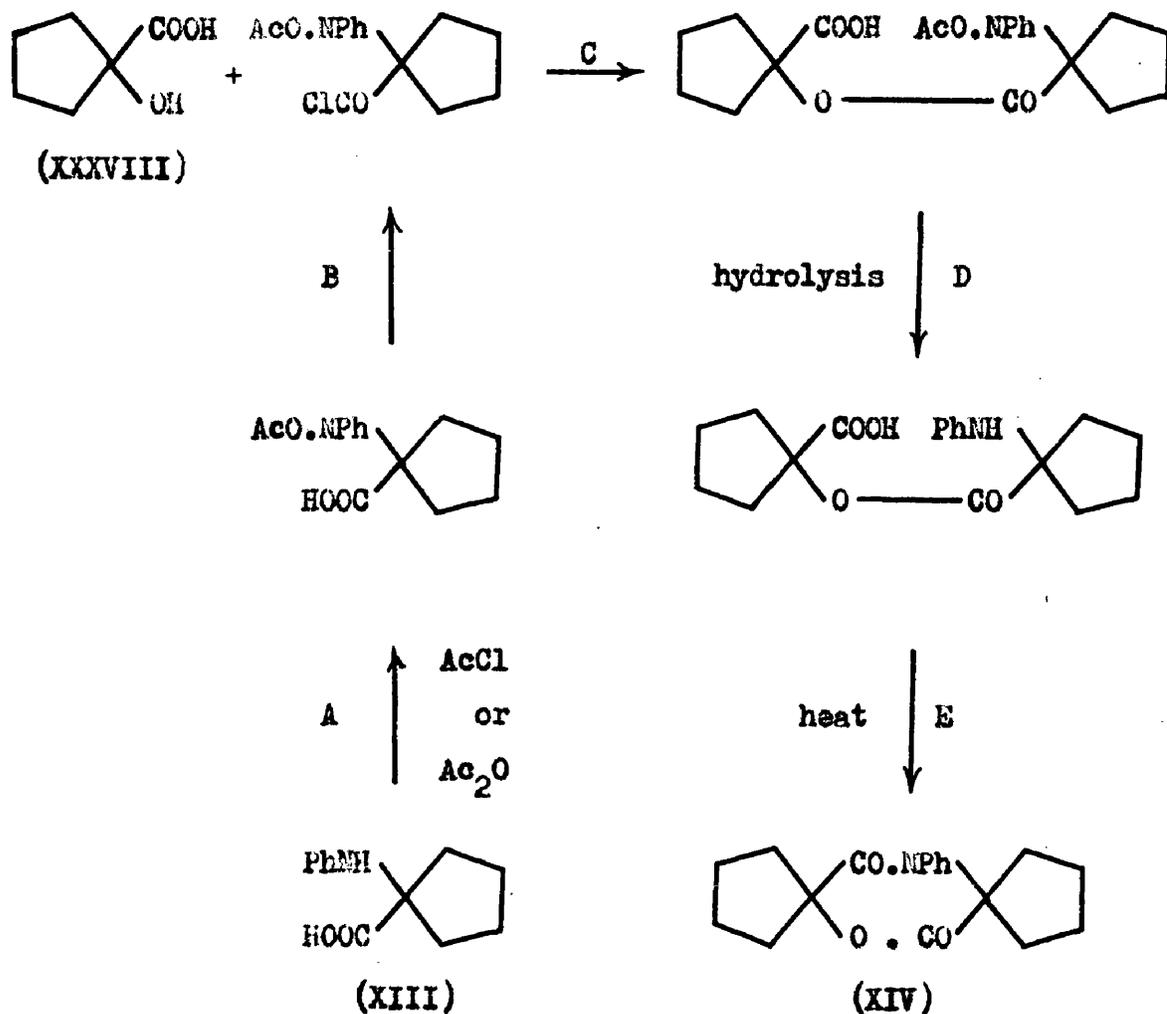
From the hydrolysis of the C₅ lactone-lactam XIV, a trace of cyclopentyl-aniline was formed, This, however, is not conclusive proof of the previous existence of the anilino acid XIII in the hydrolysate, since the 2-anilino acid XLVII produced by hydrolysis of XLII could also decarboxylate, thus:-



Thus it appears that even although the lactone-lactam could be completely hydrolysed (unless under very mild conditions, which seems to be impossible in view of the "tertiary effect" mentioned before), this would not give conclusive proof of its structure.

An unequivocal synthesis of the lactone-lactam XIV appears to be extremely difficult in view of the tertiary groups involved. The starting point would presumably be the hydroxy acid XXXVIII and the anilino acid XIII. A synthesis

on the following lines was attempted but without success:-

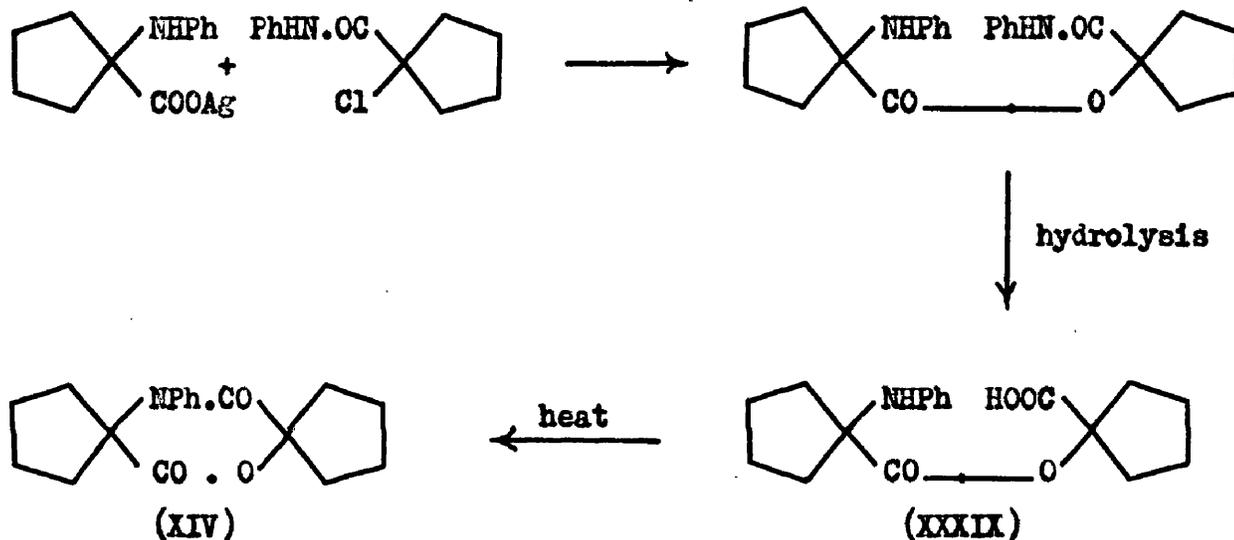


The hydrolysis at stage D should not hydrolyse the ester group owing to the tertiary effect mentioned before. The reaction E is, if the ideas on the structure of the lactone-lactam are correct, one which is found to occur readily.

The reaction A, although recorded by Plant (6), was found to give only a minute yield of the acetyl derivative (only a few milligrams were isolated) using either acetyl chloride or acetic anhydride. The main product of attempted acetylation is a neutral compound (the acetyl derivative is acidic owing to the carboxyl group) which was not further investigated. This method of synthesis was abandoned because of this and also because the reaction C might not occur because

of steric hindrance.

Another method of synthesis which suggested itself was a silver salt esterification. This method often succeeds in esterifying tertiary acids or alcohols where other methods fail.



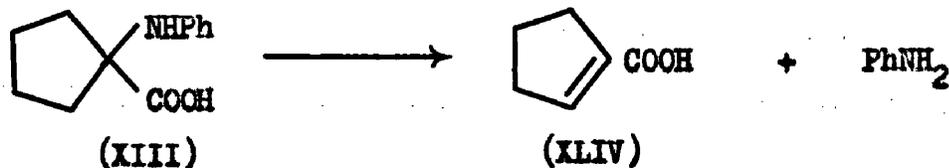
The silver salt of the anilino acid XIII was found to be unstable, however, - it deposits metallic silver on standing, and the method is thus not promising. It is also possible that the bulky -NPh and -CONPh groups would prevent the combination of the chloride and silver salt.

Origin of the Products in the Pyrolysis of the Anilino Acids.

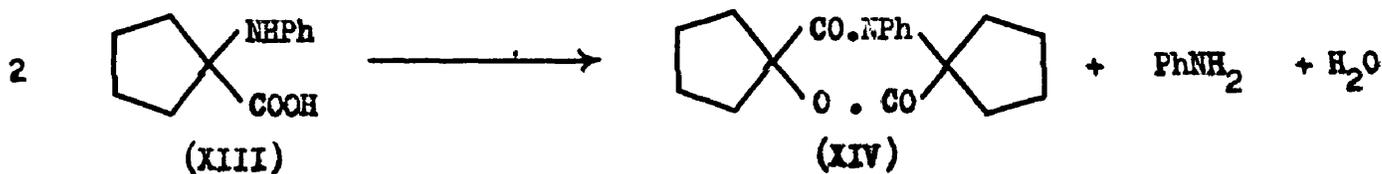
As the products of the three anilino acids (C_5 , C_6 and C_7) are of the same functional group structure (though differing in amount) the discussion will be illustrated by using only one ring-size (viz., 5). The conclusions will of course apply to all the ring sizes.

Aniline and Unsaturated Acid.

The presence of aniline is accounted for by the primary scission of the anilino acid to unsaturated acid and aniline, thus:-



The amount of aniline (see Table III) is, however, too great to be wholly accounted for in this way, especially for the C₅ and C₆ compounds; but this excess of aniline can be accounted for by the following formation of the lactone-lactam (of which more may be formed than is shown in the Table, since there are crystallisation losses):-

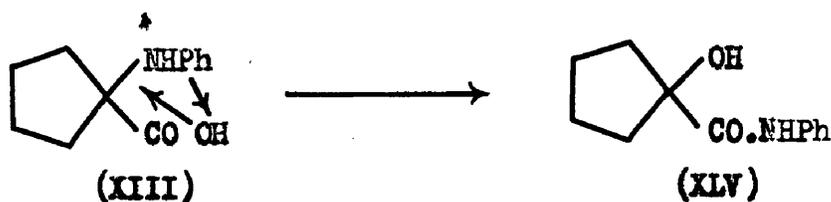


In the pyrolyses a small amount of water was always formed.

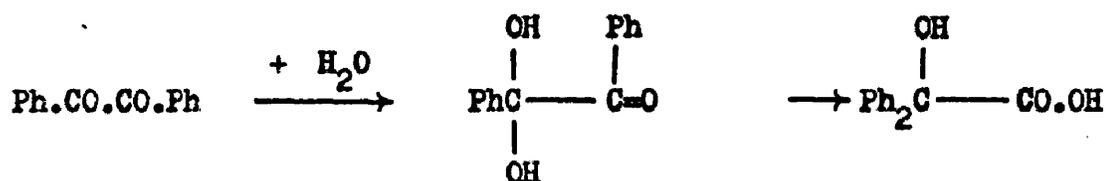
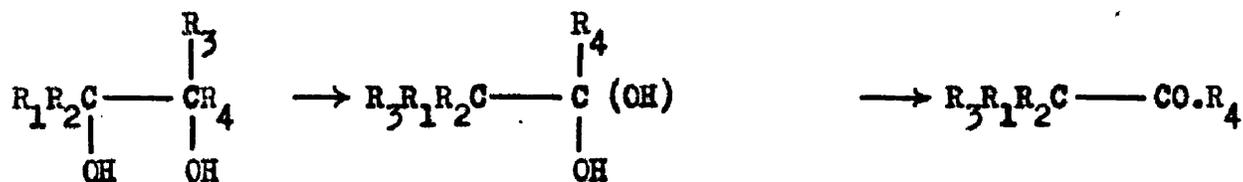
The formation of the hydroxyanilide does not, of course, account for any of the liberated aniline, since it is isomeric with the original anilino acid.

Hydroxyanilide.

This was an entirely unexpected product, and it is difficult to account for its presence. A direct rearrangement of the anilino acid is one possible explanation, thus:-

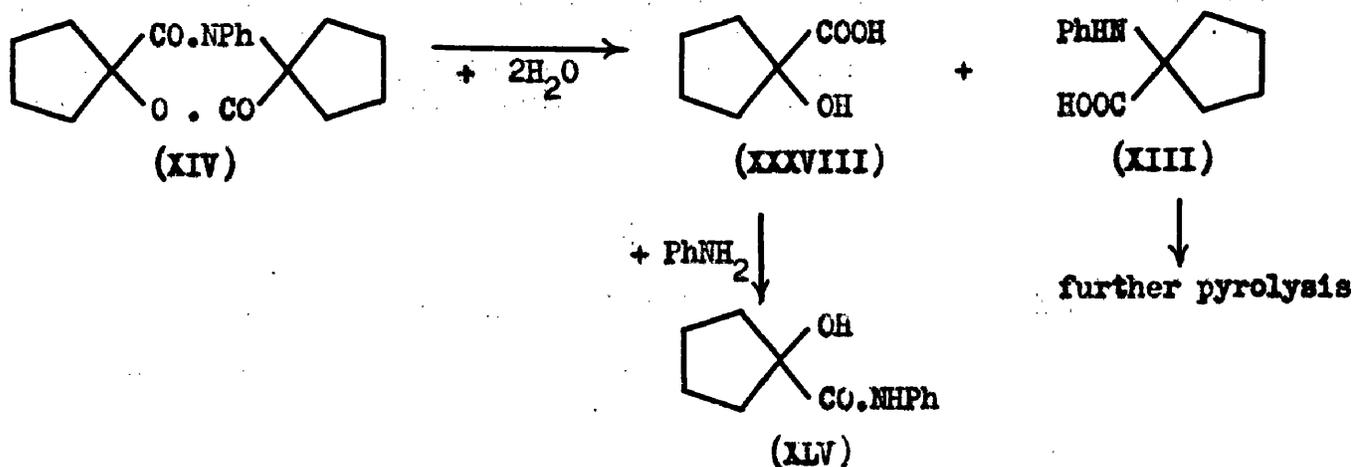


This reaction bears some resemblance to other types of rearrangement, e.g., the pinacol-pinacone and benzilic acid rearrangements:-



In both these rearrangements the net result is that the hydroxyl group and the R₃ (or phenyl) group change places. Since such rearrangements usually require acidic or basic catalysts, some experiments were done with the C₆ anilino acid to see if rearrangement could be brought about catalytically at room temperature. Phosphoric acid in ether and boron trifluoride in ether were tried as catalysts, but no hydroxyanilide was formed. Thus the direct rearrangement lacks experimental proof, though it remains a possibility.

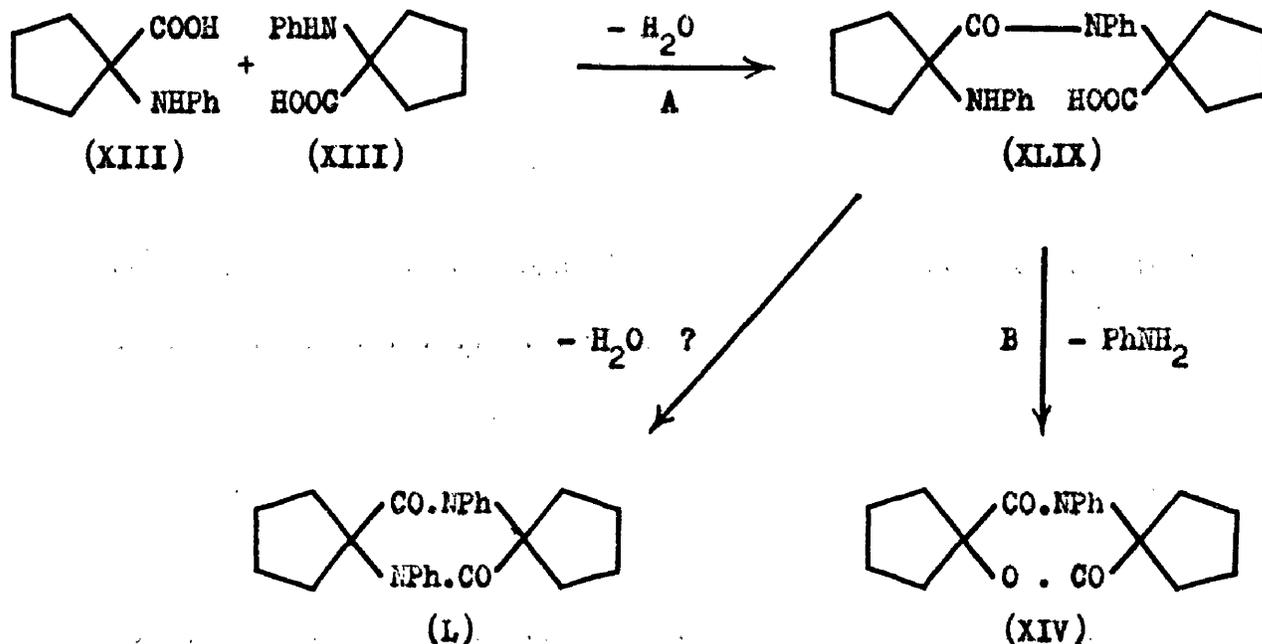
There is the further possibility that the hydroxyanilide is formed by some indirect route, e.g., from the lactone-lactam, thus:-



The water and aniline required by this scheme are both present in the mixture while it is being pyrolysed, as they are products of formation of the lactone-lactam. Nevertheless, in a test experiment the lactone-lactam was found not to decompose when heated under reflux with water and aniline at the original pyrolysis temperature. This appears to eliminate the possible occurrence of the above reaction.

The hydroxyanilide (C_6 , XLVIII) is stable to heating at the pyrolysis time and temperature used for the anilino acid. This shows that the hydroxyanilide cannot be the only primary product of pyrolysis; and if it is, in fact, one of several primary products, the other reaction routes must compete with formation of hydroxyanilide. In other words, the heat-stability of the hydroxyanilide eliminates the possibility that the rearrangement to anilide is the sole primary reaction.

Lactone-lactam. The formation of the lactone-lactam is almost as difficult to account for as the hydroxyanilide. The following reaction appears a formal possibility:-



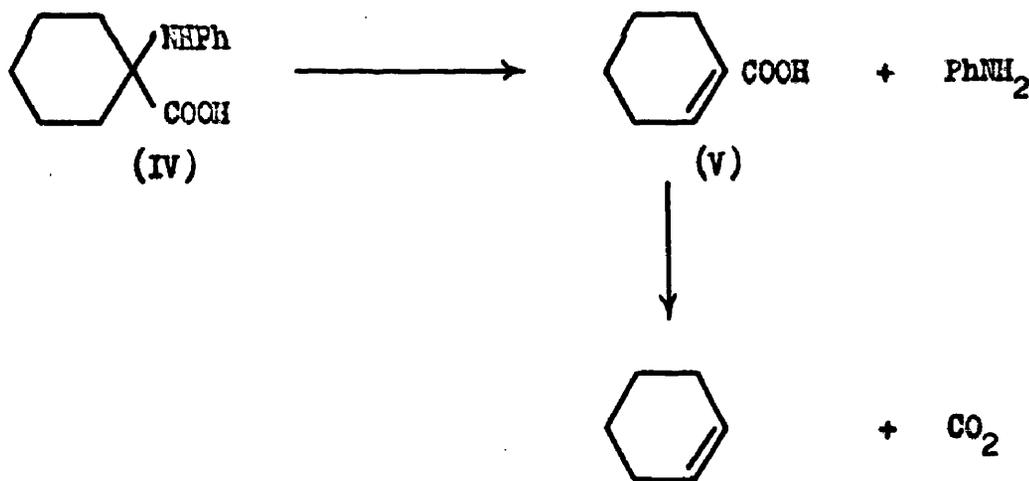
Reaction A is quite normal, being the formation of substituted amide from amine plus acid. Reaction B seems, however, to be a rather curious method of forming an ester linkage. It is indeed difficult to see why XLIX does not eliminate a further molecule of water in the same manner as reaction A to form the substituted diketopiperazine L. It may be that steric factors forbid this, since phenyl and cyclopentyl (-hexyl or -heptyl) rings are so bulky.

Another hypothesis for the formation of the lactone-lactam is that put forward on page 51, which, however, was not supported experimentally, and in any case would lead to an isomeric form of the lactone-lactam (i.e., XLII).

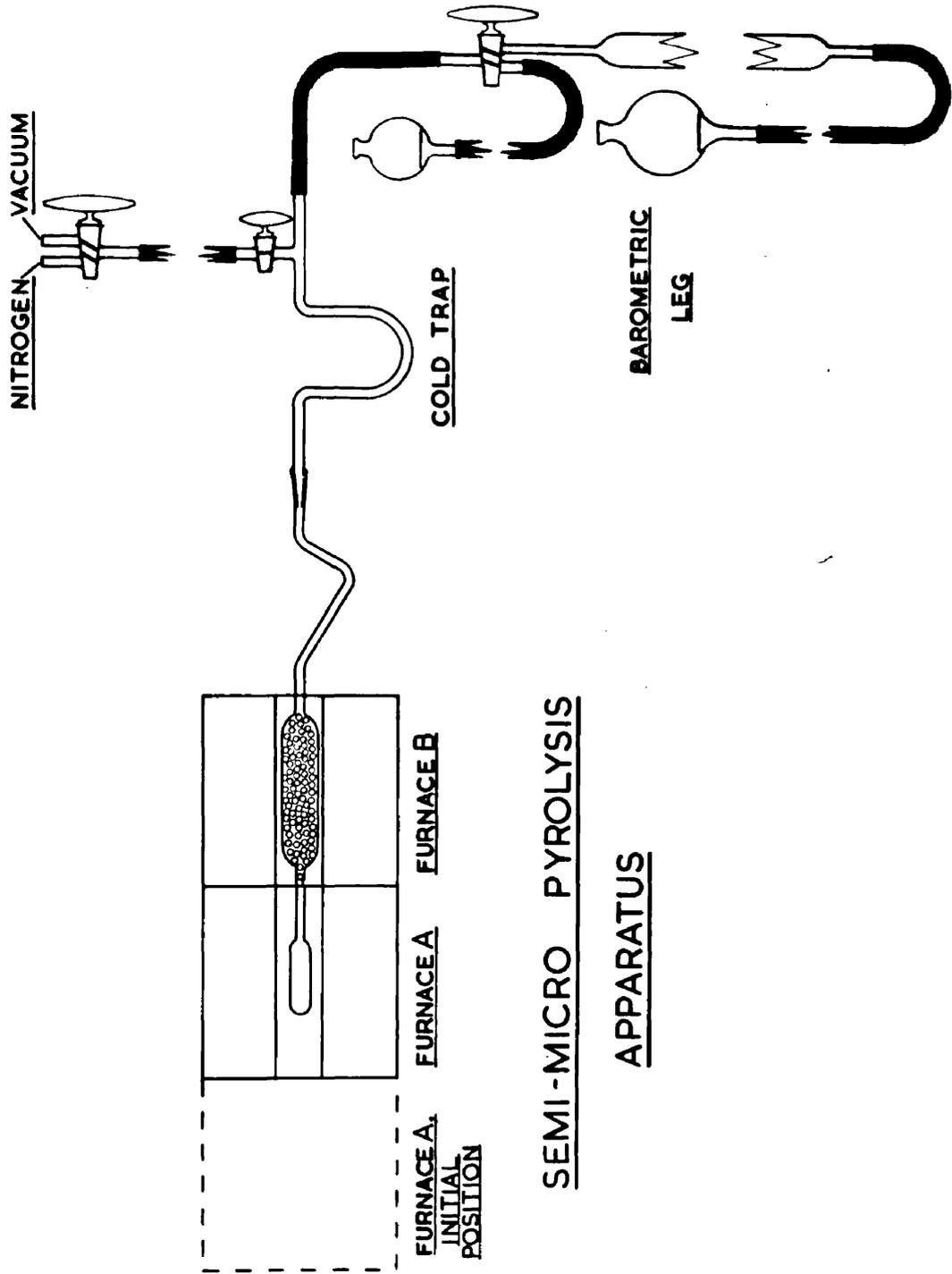
High Temperature Pyrolysis of 1-Anilinocyclohexanecarboxylic Acid (IV).

The acid IV was pyrolysed at 500° in a flow reactor to see whether the yield of cyclohexanecarboxanilide (XLVIII) was increased by increasing the temperature and decreasing the contact time. None of the hydroxyanilide XLVIII could be detected in the pyrolysate, however, and the main products were benzene, cyclohexene, aniline, carbon dioxide, carbon monoxide and hydrogen (see p.96).

The aniline, cyclohexene and carbon dioxide can be explained by the primary scission of IV to aniline and cyclohexene-1-carboxylic acid (V), followed by secondary pyrolysis of V to give carbon dioxide and cyclohexene, thus:-



The benzene and hydrogen can be accounted for by the pyrolytic dehydrogenation of some of the cyclohexene to give benzene and hydrogen, although the amount of hydrogen (see p.96) is only about half the theoretical amount based on the benzene formed. This dehydrogenation of cyclohexene has been found to occur during the pyrolysis of cyclohexyl acetate (540-550° ; Burns, Jones and Hitchie (1))



SEMI-MICRO PYROLYSIS

APPARATUS

FIGURE III

TABLE IV

Pyrolyses in Semi-micro Flow Reactor

Compound	IV C ₆ anilino acid	V C ₆ unsaturated acid	LI C ₆ lactone- lactam	XLVIII C ₆ hydroxy- anilide	XIII C ₅ anilino acid
ml. of gas formed (N.T.P.)	26	29	38	17.5	21.5
gas formed; % of theory	85	54	92*	57	66
gas analysis CO	7.9	4.1	23.0	16.5	15.0
CO ₂	17.7	28.5	13.7	1.6	11.6
% of theory CO	13.7	4.3	36.4*	23.7	22.2
CO ₂	30.6	30.0	21.7*	2.3	17.2
Ratio CO:CO ₂	0.446	0.144	1.68	10.3	1.29

* assuming that one molecule of LI gives two molecules of gas.



The carbon monoxide (ca. 30% of theory) could not at the time be accounted for; but it was thought that it might come from the secondary pyrolysis of the hydroxyanilide XLVIII, and/or the lactone-lactam LI. This was supported by the results obtained from the pyrolyses described under the next heading.

Pyrolyses in Semi-micro Flow Reactor.

Because of the small amounts of hydroxyanilide XLVIII and lactone-lactam LI available, a semi-micro pyrolysis apparatus (see p.99 and Fig. III) was devised. It will be seen from the results (Table IV) that all three low temperature pyrolysis products (unsaturated acid V, hydroxyanilide XLVIII, and lactone-lactam LI) give carbon monoxide on pyrolysis. The unsaturated acid V does not give sufficient to account for the amount present in the high-temperature pyrolysis of the anilino acid IV. It seems therefore that the carbon monoxide comes mainly from the secondary pyrolysis of the hydroxyanilide XLVIII and lactone-lactam LI.

At 250° for one hour the anilino acid IV gives very little gas, which shows that the formation of carbon dioxide and carbon monoxide is mainly a high temperature reaction.

The lactone-lactam LI gives amounts of carbon monoxide and carbon dioxide of the same order. The latter presumably comes from the lactone group and the former from either the lactone or the lactam group.

The hydroxyanilide XLVIII gives almost wholly carbon monoxide, and this

accords with its structure which seems unlikely to be able to form carbon dioxide. This decomposition of the hydroxyanilide possibly explains the failure to isolate it in the high-temperature pyrolysis (macro-scale) of the anilino acid IV.

EXPERIMENTALPREPARATION OF COMPOUNDS FOR PYROLYSIS1-Anilino Nitriles.

The anilino nitriles were very readily prepared from the corresponding ketones by the following method (except for the anilino nitrile from benzophenone, for which a special method had to be employed: see p.66).

The ketone (1 mol) and aniline (1 mol) were mixed in a large flask (at least five times the total volume of liquid) and hydrogen cyanide (1.5 mol) was added. The homogeneous mixture became cloudy after a few seconds and the heat liberated in the reaction was sufficient to boil the excess of hydrogen cyanide. After 1-3 hours the contents of the flask were solid. The anilino nitrile crystallised from ethanol or petroleum (60-80°)/benzene in good yield.

When impure the anilino nitriles discoloured on standing. A pure sample did not discolour even when exposed to light and air for several months. (Drew (33) implied that light and air should be excluded in order to avoid discolouration).

The following anilino nitriles were prepared by this method:-

1-Anilino-1-cyanocyclobutane (XV): colourless needles (m.p. 62-63°) from petroleum (60-80°)/benzene; yield, 70% of theory. (Found: C, 76.9; H, 6.9. $C_{11}H_{12}N_2$ requires C, 76.7; H, 7.0%).

1-Anilino-1-cyanocyclopentane (X): colourless prisms (m.p. 56-57°) from ethanol; yield, 79% of theory. (Lit. (6), m.p. 58°).

1-Anilino-1-cyanocyclohexane (VI): colourless prisms (m.p. 74-75°) from ethanol; yield, 75% of theory. (Lit. (4), m.p. 75°).

1-Anilino-1-cyanocycloheptane (XVI): colourless prisms (m.p. 85-86°) from ethanol; yield, 78% of theory. (Found: C, 78.8; H, 8.6; N, 13.3. $C_{14}H_{18}N_2$ requires C, 78.5;

H, 8.5; N, 13.1%).

Preparation of 1-Anilino-1-cyano-2-methylcyclohexane, α - and β - forms

(XVII α and β).

Bukhsh et al. (11) described the isolation of the two geometric isomers of XVII from the solid mixture obtained from reaction of aniline, 2-methylcyclohexanone and aqueous potassium cyanide in the presence of an excess of acetic acid. They simply designated these the A- and B- forms, without attempting to specify their absolute configuration. The method of separation they described was crystallisation of the mixture, first from benzene, in which the higher-melting A-form (m.p. 126°) was less soluble than the lower-melting B-form, and then from n-hexane, followed by hand separation of the two shapes of crystal (A-form, plates; B-form, soft needles). Further crystallisation of the soft needles from n-hexane yielded the pure B-form, m.p. 83°. The A-form had the lesser solubility in both solvents.

This method of separation was successfully adapted to the reaction product of 2-methylcyclohexanone, aniline, and hydrogen cyanide:-

The product of the reaction (1.32 molar scale) was crystallised from 400 ml. benzene and the following fractions were obtained:-

<u>Fraction</u>	<u>Yield g.</u>	<u>m.p.</u>	
(i)	91	114-126°	on standing overnight - heavy prisms.
(ii)	40	80-87°	on further standing for 2 days, light fluffy needles.
(iii)	29	81-121°	on standing a further 3 days.
(iv)	75	83-124°	on reducing volume of solution to 150 ml. and standing overnight.
(v)	<u>31</u> up to 110° <u>266</u> (94%)		on total evaporation of benzene - sticky solid.

Fractions (iii) and (iv) were combined and recrystallised from 150 ml. benzene to give (vi), 68 g., m.p. 110-125°. The filtrate from this crystallisation gave, after total evaporation of benzene, (vii), 35 g., m.p. 65-85°. Fractions (ii) and (vii) were combined and recrystallised from 700 ml. light petroleum (60-80°) to give (viii), 16 g., m.p. 80-125° and (ix), 37 g., m.p. 84-86° (Lit. (11), for B-form of XVII, 83°). The product (ix) was obtained by decanting the petroleum solution from the solid (viii), after the solution had stood for 4 hours. The decanted solution was allowed to stand overnight, giving the crystals (ix).

Further crystallisations of the fraction (i) from benzene gave pure XVIIId, 53 g., m.p. 124-125° (Lit. (11), m.p. 126°).

Bukhsh et. al. (11), applied their method on a small scale (0.05 mol) and the percentage yields were not stated.

Initial attempts to prepare the β -form were unexpectedly made difficult by the fact that piperidine (0.5 g.) was used as a catalyst. This gave a small amount of 1-cyano-1-hydroxy-2-methylcyclohexane (XXIV) which separated as a solid, m.p. 48-55°, \underline{M} (cryo. in benzene) = 144. (Calc. for $C_8H_{13}ON:\underline{M}$ = 139). A pure specimen of XXIV, prepared from 2-methylcyclohexanone and hydrogen cyanide, had m.p. 50-59°. (This substance has previously been recorded (35) only in the liquid state.)

The large melting point range may be caused by partial dissociation into ketone and hydrogen cyanide. The presence of XXIV caused the reaction mixture containing XVII α and XVII β to remain partly liquid, and in early experiments only XVII α could be isolated. This interference with the desired course of the reaction was confirmed in a control experiment:-

Aniline (93 g., 1 mol) and 2-methylcyclohexanone (112 g., 1 mol) were mixed and the mixture divided into two equal portions. Piperidine (0.5 g.) was added

to one portion and hydrogen cyanide (29 ml., 0.75 mol) added to each. The mixture that did not contain piperidine solidified after 1½ hours, but the other was only partly solid after several weeks.

The infra-red absorption spectra of the anilino nitriles are shown in Figs. IV and V.

Preparation of α -Anilino- α -cyanodiphenylmethane (XXIII).

An attempt was made to prepare anilino nitrile XXIII by the method used for the others, but this was unsuccessful. Even after standing for four weeks at room temperature, the mixture did not deposit any solid.

The method of v. Miller and Plöchl (12) was used.

Benzophenone (106.5 g., 0.586 mol) was treated with phosphorus pentachloride (122 g., 0.586 mol) to give α : α -dichlorodiphenylmethane (XXVI), b.p. 185°/25 mm. (120.5 g., 0.508 mol, 87% of theory).

The dichloro compound XXVI, (120.5 g., 0.508 mol) reacted with aniline (189 g., 2.03 mol) to give (diphenylmethylene)aniline (XXV) (100.5 g., 0.391 mol, 77% of theory) light-yellow prisms, m.p. 114-115° from petroleum. (Lit. (12), m.p. 112-113°).

The anil XXV, (74 g., 0.288 mol) was treated with a large excess of hydrogen cyanide (ca. 200 ml., 5 mol) to give α -anilino- α -cyanodiphenylmethane (XXIII), (58 g., 0.204 mol, 71% of theory), colourless prisms, m.p. 144-145° from petroleum (60-80°)/benzene. (Lit. (12) m.p. 146.5°).

The anilino nitrile XXIII gave a brilliant red colour with concentrated sulphuric acid, this being in agreement with the observation of v. Miller & Plöchl (12).

The overall yield of the anilino nitrile XXIII from benzophenone was 47.5% of theory; yields are not quoted in the literature.

Attempted Preparation of α -Anilino- α -cyanotetralin.

α -Tetralone (5.0 g., 0.034 mol) and aniline (3.2 g., 0.034 mol) were mixed and hydrogen cyanide (2.0 ml., 0.052 mol) added. No solid separated from the mixture even after several weeks.

Preparation of cyclobutanone.

The method of Roberts and Sauer (9) was used.

Pentaerythritol (750 g., 5.52 mol) was treated with phosphorus tribromide (3 kg., 11.08 mol) (prepared in 95% yield from red phosphorus and bromine), according to the method of Schurink (20) to give pentaerythrityl tetrabromide (834 g., 2.15 mol, 39% of theory) m.p. 159-160° (Lit. (20), 163°). The pentaerythrityl tetrabromide was crystallised from carbon tetrachloride (2 l.) instead of using the continuous extraction, and crystallisation from ethanol described: this is not practicable owing to the amount of ethanol (24 l.) which would be required for ca. 800 g. of product.

Pentaerythrityl tetrabromide (678 g., 1.75 mol) was treated with zinc (476 g., 7.3 g. atom) in the presence of water, ethanol and zinc bromide. This gave methylenecyclobutane (65 g., 0.954 mol, 54.4% of theory), which was used without purification for the next stage.

Methylenecyclobutane (65 g., 0.954 mol) was hydroxylated with formic acid and hydrogen peroxide to give 1-(hydroxymethyl)cyclobutanol (28.6 g., 0.280 mol, 29.4% of theory) b.p. 100-104°/11 mm. (Roberts and Sauer (9) recorded 93°/5 mm.).

1-(hydroxymethyl)cyclobutanol (28.6 g., 0.280 mol) was oxidised with lead tetraacetate to give cyclobutanone (7.9 g., 0.113 mol, 40.3% of theory) b.p. 98-102°; 2:4-dinitrophenylhydrazone, m.p. 144-145°; semicarbazone 210-214° d. (Lit. (9), m.ps. 146-146.5° and 206-207° d., respectively). The infra-red absorption spectrum is

shown in Fig. VII: it is almost identical with that recorded by Roberts and Sauer (9).

1-Anilinocarboxylic Acids.

The anilino acids were prepared by the method of Plant and Facer (6) and Betts, Muspratt and Plant (2).

The anilino nitrile was dissolved in concentrated sulphuric acid and after two days was poured on to crushed ice. On making the solution alkaline with ammonium hydroxide solution the amide was precipitated, which on hydrolysis with concentrated hydrochloric acid (the C₅ anilino amide required 1 hour, the C₆ and C₇ anilino amides required 12 hours) gave the 1-anilinocarboxylic acid.

The following anilino acids were prepared by this method:-

1-Anilinocyclopentanecarboxylic acid crystallised from xylene in prisms, m.p. 150-162°, yield 63% of theory (Found: C, 70.4; H, 7.4; N, 6.8. Equivalent, 205.0. Calc. for C₁₂H₁₅O₂N: C, 70.2; H, 7.4; N, 6.8%. Equivalent (monobasic acid), 205.2.).

1-Anilinocyclohexanecarboxylic acid crystallised from benzene in very fine needles, m.p. 123-140°, yield 55% of theory (Found: C, 71.4; H, 7.7; N, 6.3. Equivalent, 218.1. Calc. for C₁₃H₁₇O₂N: C, 71.2; H, 7.8; N, 6.4%. Equivalent (monobasic acid), 219.3). (Betts, Muspratt and Plant (2) recorded m.p. 142°. Bucherer and Barsch (18) recorded m.p. 158°; yields not recorded).

1-Anilinocycloheptanecarboxylic acid crystallised from benzene in prisms, m.p. 143-158°, yield 78% of theory (Found: C, 72.0; H, 8.0; N, 6.3. Equivalent 234.0. C₁₄H₁₉O₂N requires C, 72.1; H, 8.2; N, 6.0%. Equivalent (monobasic acid) 233.3). The intermediate amide, 1-anilinocycloheptanecarboxylamide separated from ethanol in colourless needles m.p. 141-142° (Found: C, 72.2; H, 9.1; N, 12.0.

$C_{14}H_{20}ON_2$ requires C, 72.4; H, 8.7; N, 12.1%.

The infra-red absorption spectra of the anilino acids are shown in Fig. VI.

Attempted Preparation of 1-Anilino-1-(nitromethyl)cyclohexane.

cyclohexanone (49 g., 0.5 mol), aniline (46.5 g., 0.5 mol) and nitromethane (30.5 g., 0.5 mol) were mixed and allowed to stand at room temperature for three weeks. No solid separated although there appeared to be a small amount of water formed.

Another experiment using equimolecular amounts of cyclohexylideneaniline and nitromethane was also unsuccessful.

Attempted Preparation of 1-Anilino-1-(trichloromethyl)cyclohexane.

Similar experiments to the above, using chloroform in place of nitromethane gave no solid product.

PYROLYSIS OF 1-ANILINONITRILESPyrolysis Method

A static method was used in which the compound was heated to a predetermined temperature. A stream of nitrogen was passed through to drive off the volatile hydrogen cyanide, and the high boiling components were returned to the reactor by a reflux condenser.

The apparatus was a semi-micro distillation flask (25 ml.) in a Wood's metal bath heated by an electric hot-plate controlled by a "Simmerstat". The temperature of the metal bath could be controlled to $\pm 5^{\circ}$. The outlet from the distillation flask was connected to a wash-bottle containing an excess of sodium hydroxide solution. The cyanide absorbed was titrated against 0.1 N silver nitrate solution with addition of ammonium hydroxide and potassium iodide (indicator) (36). Test experiments showed that even large excesses of sodium hydroxide did not affect the results of titrations. Test experiments also showed that only one wash-bottle was necessary to absorb all the hydrogen cyanide. To facilitate direct comparison of the various results, the same quantity of initial material (15 g.) was used in each experiment, and the rate of flow of nitrogen (measured by a flowmeter) was maintained at 13.5 ± 0.5 c.c./min. during all the pyrolyses by adjustment of the reducing valve on the nitrogen cylinder.

The anilino nitriles pyrolysed by this method were 1-anilino-1-cyanocyclopentane (X), 1-anilino-1-cyanocyclohexane (VI), 1-anilino-1-cyanocycloheptane (XVI), 1-anilino-1-cyano-2-methylcyclohexane (α and β forms: XVII α and β), and α -anilino- α -cyanodiphenylmethane (XXIII).

All of these except the C₅ nitrile (X), gave an almost theoretical yield of

TABLE I

Pyrolysis of Anilino Nitriles

% of Theory of Hydrogen Cyanide Eliminated

Time hrs.	C ₅		C ₆		C _α		C _β		C ₇	
	200°	250°	200°	250°	200°	250°	200°	250°	200°	250°
½	26.8	58.6	18.9	62.3	17.7	67.1	15.0	73.3	66.1	96.2
1	38.0	77.5	25.8	71.2	28.0	84.2	20.7	83.3	79.6	98.8
1½					34.4					
2	47.5	79.6	34.6	79.3	39.0	91.8			89.7	99.4
3				83.2	47.0		35.5		94.2	99.4
3½			45.0							
4	60.3							92.9		
5					57.0	94.5				
6	64.8	80.2	55.8							
6½							48.2			
7					64.3	94.8		96.2		
9	68.7			87.8						
10			64.7				57.6			
45					94.2					
130					95.2					

aniline and the corresponding anil. The results for hydrogen cyanide elimination are shown in Table I, and the results for VI, XVI, XVII α and β , and XXIII are plotted in Fig. I. (p.19).

Pyrolysis of 1-Anilino-1-cyano-2-methylcyclohexane α -form (XVII α).

This gave hydrogen cyanide and (2-methylcyclohexylidene)aniline (XXII), yield 85% of theory from 250° pyrolysis; b.p. 143-146°/15 mm., n_D^{20} 1.5504, d_4^{20} 0.9902. (Lit. (31), b.p. 143-146°/12 mm., 149-150°/18 mm.; Lit. (37), b.p. 152-153°/14 mm.)

Hydrolysis:-

10.57 G. of the anil XXII were added to 100 ml. of 2N hydrochloric acid and stirred for five minutes. The mixture was extracted with three 50 ml. portions of ether. After removal of the ether by distillation the residual liquid was dissolved in 50 ml. ethanol (free from carbonyl compounds) and made up to 100 ml. Two 2 ml. portions of this solution were taken and their ketone content determined by the method of Iddles (38). (The method consisted of weighing the 2:4-dinitrophenylhydrazone produced by reaction of the ketone with a saturated solution of 2:4-dinitrophenylhydrazine in 2N hydrochloric acid).

The acid solution from the ether extraction was boiled for a few minutes to expel residual ether and, after making up to 250 ml. with 2N hydrochloric acid, the aniline content was determined by the method of Siggia (39) using 50 ml. portions for titration against sodium nitrite solution with potassium iodide/starch paper as indicator.

The results of the determinations were as follows:-

2-methylcyclohexanone 95.1, 95.7% (m.p. of 2:4-dinitrophenylhydrazone and mixed m.p. with sample prepared from the original 2-methylcyclohexanone, 134-135° (Lit., m.p. 136°))

aniline 98.4, 99.0%

Addition of Hydrogen Cyanide:-

10 ml. hydrogen cyanide (large excess) reacted vigorously with 4.25 g. of the anil XXII to yield, after evaporation of the hydrogen cyanide, 4.84 g. (98.6% of theory) of a mixture of the α - and β -forms of 1-anilino-1-cyano-2-methylcyclohexane (XVII α and β), m.p. 70-80°.

In another similar experiment 4.63 g. of the anil XXII gave, after fractional crystallisation of the residue from benzene, 2.99 g. (57% of theory) of XVII α , m.p. 121-124°. This shows the α - is produced in greater amount than the β -form.

Hydrogenation:-

11.03 G. of the anil XXII dissolved in ethyl acetate with the addition of 0.1 g. platinum dioxide reacted with 1320 c.c. (reduced to N.T.P.) of hydrogen (99% of theory; time required ca. 3 hours), to yield the crude amine. Distillation gave 9.94 g. (89% of theory) of pure N-(2-methylcyclohexyl)aniline, (LII) b.p. 147-149°/13 mm. (b.p. recorded (40) as 146-152°/15 mm.)

Reaction of the amine LII with sodium nitrite in dilute hydrochloric acid gave a yellow oil which soon solidified. Crystallisation from ethanol gave pale-yellow prisms of N-nitroso-(2-methylcyclohexyl)aniline (Found: C, 71.6; H, 8.0; N, 13.0. $C_{15}H_{18}ON_2$ requires C, 71.5; H, 8.3; N, 12.8%), m.p. 106-107°.

The benzoyl derivative prepared by the Schotten-Baumann method had m.p. 89-90° (prisms from ethanol). (Found: C, 81.8; H, 7.5; N, 4.7. $C_{20}H_{23}ON$ requires C, 81.9; H, 7.9; N, 4.8%).

The amine LII gave a brilliant red colour with a mixture of nitric acid: sulphuric acid: water in the ratio 1:9:10. (This colour reaction was described by Fouque (41) for cyclohexylaniline.)

Pyrolysis of 1-Anilino-1-cyano-2-methylcyclohexane, β -form. (XVII β).

This gave hydrogen cyanide and (2-methylcyclohexylidene)aniline (XXII: 82% of theory from 250° pyrolysis), b.p. 140-143°/12 mm., n_D^{20} 1.5508, d_4^{20} 0.9898. The infra-red absorption spectrum of this anil XXII is shown in Fig. V and is practically identical with that of the anil from the α -form (XVII α).

Pyrolysis of 1-Anilino-1-cyanocycloheptane (XVI).

This gave hydrogen cyanide and cycloheptylideneaniline (XXXII; yield 85% of theory from 250° pyrolysis), b.p. 152-154°/13 mm., n_D^{20} 1.5568, d_4^{20} 1.0024. (Found: C, 83.7; H, 9.5; N, 7.8. $C_{13}H_{17}N$ requires C, 83.4; H, 9.2; N, 7.5%).

Hydrolysis:-

This was carried out as for the anil XXII and the results were as follows:-

cycloheptanone 94.6, 94.0% (m.p. and mixed m.p. of 2:4-dinitrophenylhydrazone, 144-145° (Lit. 148°))

aniline 98.9, 99.3%

Addition of Hydrogen Cyanide:-

Hydrogen cyanide reacted very violently with the pure anil XXXII, and ether was added to moderate the reaction. 10 ml. of hydrogen cyanide were added to 6.313 g. of the anil XXXII to yield, after evaporation of the ether and excess of hydrogen cyanide, 7.127 g. (98.6% of theory) of the anilino nitrile XVI, m.p. and mixed m.p. 84-86°.

Hydrogenation:-

This was carried out as for the anil XXII, as follows:-

16.41 G. of the anil XXXII reacted with 1910 c.c. (reduced to N.T.P.) of hydrogen (102% of theory), to yield the crude amine. Distillation gave pure N-cycloheptylaniline (LIII) b.p. 168-170°/18 mm., n_D^{20} 1.5616, d_4^{20} 0.9989 (Lit. (42),

b.p. 156-157°/11 mm.)

The N-nitroso derivative was a light-yellow oil which, unlike the corresponding derivative of the amine LII, did not crystallise.

The benzoyl derivative crystallised from petroleum (60-80°) in prisms, m.p. 106-107° (Found: C, 81.9; H, 7.6; N, 5.2. $C_{20}H_{23}ON$ requires C, 81.9; H, 7.9; N, 4.8%).

The acetyl derivative crystallised from ethanol/water in prisms, m.p. 51-53° (Found: C, 78.0; H, 9.4; N, 6.4. $C_{15}H_{21}ON$ requires C, 77.9; H, 9.2; N, 6.1%).

The amine LIII, unlike the others obtained (XLVI, LII and VIII), did not give the colour reaction described by Fouque (41).

Pyrolysis of 1-Anilino-1-cyanocyclopentane (X).

Preliminary Experiment. 59.0 G. of X were pyrolysed for six hours at 230° (bath) in a stream of nitrogen (rate of flow not measured). The hydrogen cyanide eliminated was 63.1% of theory after 2 hours, and 64.6% of theory after 6 hours. Distillation of the residue at atmospheric pressure gave aniline, (10.0 g., 34% of theory), b.p. 182-183°/751 mm. (Lit. 183°/760 mm.).

The aniline was identified:-

- (i) by conversion to acetanilide (m.p. and mixed m.p. 113-114°, Lit. 114°) under anhydrous conditions (necessary to avoid hydrolysis of any anil which might be present).
- (ii) by determination of the amine group by titration with N hydrochloric acid using congo red as indicator. (Equivalent weight: 93.2. Calc. for C_6H_7N : 93.1).
- (iii) by refractive index measurement.

	n_D^{17}	
distilled aniline	1.5845	(Lit. n_D^{20} 1.5863)
liquid obtained	1.5840	

No fraction boiling lower than aniline was obtained and further distillation of the residue under vacuum gave only a fraction of wide boiling range, 75-220°/12 mm., and a tarry residue which did not crystallise from benzene.

Method (a) - Vacuum Pyrolysis. 40 G. of the anilino nitrile were refluxed under a pressure of 14 mm. using a water condenser. A trap containing potassium hydroxide solution (1:1) was inserted in the vacuum line and the amount of hydrogen cyanide eliminated was determined.

Total time (hours)	Temperature	% Hydrogen cyanide eliminated during each hour	Total % hydrogen cyanide
1	140°	13.3	13.3
2	190°	44.0	57.3
3	190°	1.0	58.3

The residue was light-yellow and weighed 33.4 g. (97.6% of theory based on the 58.3% elimination of hydrogen cyanide).

Distillation of this residue, using an aqueous alkali trap in the vacuum line, gave 20.3 g. of a liquid, b.p. 121-124°/7 mm. A further 21.4% of hydrogen cyanide was eliminated during the distillation. Redistillation of the liquid gave pure cyclopentylideneaniline (XII), b.p. 122°/7 mm., n_D^{20} 1.5648, d_4^{20} 1.0173 (Found: C, 82.7; H, 7.9; N, 8.6. $C_{11}H_{13}N$ requires C, 83.0; H, 8.2; N, 8.8%).

The infra-red absorption spectrum is shown in Fig. V.

The anil XII was a colourless liquid which on exposure to air (1-2 days) became brown and finally formed a black tar. The other anils, VII, XXII, and XXXII, underwent a similar decomposition, though more slowly.

The anil XII was identified by the following methods:-

Hydrolysis. This was carried out as for the anils XXII and XXXII, and the results were as follows:-

cyclopentanone 94.0%, 94.0% (m.p. and mixed m.p. of 2:4-dinitrophenylhydrazone, 144-145°, (Lit. 146°))

aniline 99.8%, 100.7%

Addition of Hydrogen Cyanide. 6.20 G. of XII reacted vigorously with hydrogen cyanide to give 7.06 g. (97.4% of theory) of 1-anilino-1-cyanocyclopentane (X), m.p. and mixed m.p. 55-57°.

Hydrogenation. 15.5 G. of XII reacted with 2090 c.c. (corrected to N.T.P.) of hydrogen (95% of theory) to yield the crude amine. Distillation gave pure cyclopentylaniline (XLVI), 12.7 g. (81% of theory), b.p. 139-140°/13 mm., n_D^{20} 1.5670, d_4^{20} 1.0084. The acetyl derivative crystallised from ethanol/water in prisms, m.p. 95-96° (Lit. (42), b.p. (amine) 137°/12 mm., m.p. (acetate) 96°).

Like the amines LII and VIII, the amine XLVI gave the colour reaction described by Fouque (41) (cf. pp. 72, 74).

Method (b) - Rapid Nitrogen-Flow. 100 G. of X were pyrolysed for two hours at 200°. During the first hour the stream of nitrogen was slow (14 c.c./min.) and during the second hour it was very much faster; the hydrogen cyanide eliminated being 14.7% and 36.2% respectively (total 50.5% of theory). The residue was distilled at this stage, no attempt being made to obtain the highest possible yield of hydrogen cyanide as in previous experiments. By taking an aliquot portion of the contents of the alkali trap, the amount of hydrogen cyanide eliminated during distillation could be measured.

Distillation gave (i) 0.9 g., b.p. 110-121°/7 mm., (ii) 51.0 g. of crude

cyclopentylideneaniline, b.p. 121-133°/7 mm. and (iii) a very viscous residue.

The hydrogen cyanide eliminated during distillation was 18.7% of theory.

Synthesis of cyclopentylideneaniline (XII).

This was carried out before XII was isolated by pyrolysis of the anilino nitrile X, and the object was to find the stability of XII to heat. It was prepared by the method which Hoch (31) applied to the synthesis of a number of anils, not, however, including XII.

cyclopentanone Diethylacetal (LIV). Attempts to prepare this compound by the method of Boesekin and Telligen (43) gave mainly high-boiling material and none of the desired product. The method was the reaction of cyclopentanone, ethyl orthoformate, ethanol, and dry hydrogen chloride. The method of Levina et al. (44) was more successful:-

cyclopentanone (86 g., 1 mol) was mixed with ethyl orthoformate (148 g., 1 mol) and one drop of conc. sulphuric acid added. After standing for 45 min. the mixture was neutralised with sodium ethoxide and distilled to give cyclopentanone diethylacetal (LIV), b.p. 67-69°/24 mm. (121 g., 0.75 mol, 76% of theory) (Lit. (43), b.p. 63-65°/20 mm.)

cyclopentylideneaniline (XII). The acetal LIV (30.3 g., 0.191 mol) was mixed with aniline (26.8 g., 0.288 mol) and the mixture slowly distilled using a column, as described by Hoch (31). The amount of ethanol formed was 13.1 ml. (56% of theory). Distillation of the residue gave cyclopentylideneaniline (XII), b.p. 133°/13 mm., n_D^{20} 1.5646 (10.1 g., 0.063 mol, 33% of theory), cf. b.p. 122°/7 mm., n_D^{20} 1.5648 for the anil XII from pyrolysis. The infra-red absorption spectrum of the synthetic anil XII is shown in Fig. V, and is almost identical with that of the anil XII from the pyrolysis of the anilino nitrile X.

Pyrolysis of cyclopentylideneaniline (XII).

This was carried out in order to test the heat-stability of the C₅ anil XII (cf. p.35).

The anil XII (21.2 g., 0.133 mol) was heated at 230° for 6 hours (the temperature and duration of one of the previous pyrolyses of 1-anilino-1-cyanocyclopentane (X)). Distillation of the residue gave (i) aniline (3.8 g., 0.041 mol, 6.1% of theory), b.p. 80-83°/17 mm. (identified by conversion to acetanilide), (ii) a fraction (7.2 g.), b.p. 83-178°/17-3 mm., (iii) (2-cyclopentylidene)cyclopentylidene)aniline (XXXIII) (3.5 g., 0.0155 mol, 23% of theory), b.p. 178-182°/3 mm. (Found: C, 85.9; H, 8.8. C₁₆H₁₉N requires C, 85.3; H, 8.5%) and (iv) a tarry residue (4.8 g.). Pyrolysis loss = 1.9 g.

(2-cyclopentylidene)cyclopentylidene)aniline (XXXIII) was a very viscous light-yellow liquid which crystallised on standing. When the liquid was exposed to air, it became brown after about an hour and finally formed a black tar. This effect was much more rapid with the solid (which would have a large surface area compared with the liquid) and it was not practicable to recrystallise it.

The identity of the anil XXXIII was confirmed by hydrolysis to aniline and 2-cyclopentylidene)cyclopentanone (LV) :-

Aniline 1.020 G. of XXXIII were stirred for 5 minutes with 50 ml. warm 2N hydrochloric acid. After being cooled, the liquid was extracted with 25 ml. of ether to remove the water-insoluble unsaturated ketone LV and made up to 100 ml. with 2N hydrochloric acid. 10 ml. portions were titrated against 0.1 N bromate/bromide by the method of Siggia (45).

aniline 100.0, 100.8%.

Ketone. 1.182 G. of XXXIII were dissolved in 30 ml. ethanol, 10 ml. 2N

hydrochloric acid added, and the mixture made up to 100 ml. with ethanol. Portions (5 ml.) of this solution were taken for ketone determination by the method of Iddles *et al.* (38).

2:4-dinitrophenylhydrazone of the ketone LV 96.5, 96.6%

2-cycloPentylidenecyclopentanone (LV) was isolated (0.8 g.) by hydrolysing an ethereal solution of the anil XXXIII (1.5 g.) with dilute hydrochloric acid. The ether layer was separated and the ether distilled off. The oxime crystallised from ethanol in needles, m.p. 122-123°. (Lit. (32), m.p. 123-124°; (46), m.p. 123°; (47), m.p. 122-123°). The 2:4-dinitrophenylhydrazone crystallised from glacial acetic acid in deep-red prisms m.p. 220° d. (Found: C, 58.5; H, 5.3; N, 17.0. $C_{16}H_{18}O_4N_4$ requires C, 58.2; H, 5.5; N, 17.0%).

Addition of Hydrogen Cyanide to (2-cycloPentylidenecyclopentylidene)aniline
(XXXIII)

The anil XXXIII (2.618 g.) was weighed in an evacuated (<1 mm.) flask, the flask having been evacuated through an attached stopcock. After releasing the vacuum, hydrogen cyanide (ca. 1 ml.) was added and the flask re-evacuated for $\frac{1}{2}$ hour. The flask was reweighed under vacuum: the amount of hydrogen cyanide retained was 0.1563 g. (50% of theory). The weighing of the flask under vacuum avoids possible error caused by hydrogen cyanide vapour.

The mixture was then heated at 250° in a stream of nitrogen, and the hydrogen cyanide was eliminated as follows:-

Total time (hours)	HCN eliminated (% of 0.1563 g.)
$\frac{1}{2}$	63.2
2	74.0
23	100.5
47	101.5

Thus the amount of hydrogen cyanide retained (0.1563 g.) is eliminated on heating at 250° for 23 hours.

The fact that the percentage of hydrogen cyanide retained is 50 is probably fortuitous, since in a similar experiment, though with an evacuation pressure of 5 mm., 81% of theory of hydrogen cyanide was retained.

Pyrolysis of 1-Anilino-1-cyanocyclopentane (X) Under the Standard Conditions Used for the C₆, C_α, β, and C₇ Anilino Nitriles.

This gave a 68.7% yield of hydrogen cyanide at 200° and 80.2% at 250°.

The latter is almost the maximum yield because 79.6% hydrogen cyanide is eliminated during the first two hours and only 0.6% during the next four.

The residue from the 250° pyrolysis gave the following fractions on distillation:-

- (i) 1.8 g. 76-79°/15 mm., aniline (48% of theory).
- (ii) 1.6 g. 79-132°/15 mm., intermediate fraction.
- (iii) 3.2 g. 132-135°/15 mm., cyclopentylideneaniline (25% of theory).
- (iv) 0.9 g. 135-184°/15-4 mm., intermediate fraction.
- (v) 1.1 g. 184-186°/4 mm., (2-cyclopentylidenecyclopentylidene)aniline (XXXIII) (12% of theory).
- (vi) 2.5 g. tarry residue.

Hydrogen cyanide accounted for 1.7 g., and the pyrolysis loss was 2.2 g.

The fraction (v) solidified on standing, and its solution in dilute hydrochloric acid in ethanol gave a red precipitate of the 2:4-dinitrophenylhydrazone of 2-cyclopentylidenecyclopentanone (LV) with 2:4-dinitrophenylhydrazine solution.

Pyrolysis of 1-Anilino-1-cyanocyclopentane (X) at 150° and 300°.

5 G. of X were heated in a fast stream of nitrogen (55 c.c./min.) at 150° for

96 hours followed by 24 hours at 300°. The hydrogen cyanide eliminated was as follows:-

Time (hours)	½	1	2	4	9	24	48	72	96
% HCN	20.2	27.7	37.3	47.1	57.4	69.8	78.2	80.1	80.2

The temperature was then raised to 300°.

Time (further hours)	0	½	1	3	7	24
% HCN, total	80.2	87.7	90.6	92.4	92.8	93.2

The residue was a hard black glassy solid.

These results indicate that there is formed during the pyrolysis a constituent containing nitrile groups, this being fairly stable at 150° but not at 300°.

Compound m.p. 138° (A) from Pyrolysis of 1-Anilino-1-cyanocyclopentane (X).

The compound A was initially isolated from the combined tarry residues from a number of pyrolyses of the anilino nitrile X:-

52 G. of the residues were distilled to give (i) a fraction b.p. 160-207°/0.7 mm., 12 g., and (ii) a fraction b.p. 207-220°/0.7 mm., 8 g. Fraction (ii) was a sticky glassy solid when at room temperature. On addition of petroleum (60-80°) it gave a crystalline solid, m.p. 130-136° (4.5 g.). Two recrystallisations from petroleum (60-80°)/benzene gave colourless prisms m.p. 137-138°, (A) (1.5 g.).

In a pyrolysis of the anilino nitrile X, (163 g.) in a current of nitrogen (ca. 50 c.c./min.) at 220° for two hours, the hydrogen cyanide eliminated was 53.4% of theory. The yield of crude A, b.p. 211-220°/0.6 mm., was 8 g. (4.9% by weight) and this gave, after crystallisation from petroleum (60-80°)/benzene, 2.1 g. of A, m.p. 137-138°, (1.3% by weight).

A much improved yield of A was obtained by refluxing the anilino nitrile X (250 g.) for 9 hours at 185-215° (thermometer in liquid; water condenser).

The amount of hydrogen cyanide escaping (measured by connecting the top of the condenser to an alkali trap) was only 1.4% of theory. The residue was distilled to give an initial fraction b.p. $80^{\circ}/10$ mm. to $212^{\circ}/1$ mm. (presumably aniline, cyclopentylideneaniline (XII) and (2-cyclopentylidenecyclopentylidene)aniline (XXXIII)) followed by 40 g. (16% by weight) of crude A, b.p. $212-226^{\circ}/1$ mm. (a sticky, glassy, light-brown substance) which when crystallised from petroleum ($60-80^{\circ}$)/benzene gave 30 g. (12% by weight) slightly impure A, m.p. $135-137^{\circ}$. Two further recrystallisations gave 23.3 g. (9.3% by weight) of pure A, colourless prisms, m.p. $137-138^{\circ}$. The distillation residue was a hard black tar.

The infra-red absorption spectrum of A is shown in Fig. IX. The only definite assignment is the nitrile group at 2230 cm^{-1} .

Properties of Compound m.p. $137-138^{\circ}$ (A). A had the following general properties. It was insoluble in cold or hot water but dissolved in dilute hydrochloric acid and was reprecipitated by dilute sodium hydroxide (m.p. and mixed m.p. of reprecipitated compound, $137-138^{\circ}$).

The solution of A in dilute hydrochloric acid (solution g) did not react with sodium nitrite solution. The mixture gave no turbidity and no colouration when added to either an alkaline solution of β -naphthol or sodium hydroxide solution. This indicates the absence of primary and secondary amine and tertiary aromatic amine. The solution g gave a white precipitate with potassium ferrocyanide solution; this is characteristic of a tertiary amine. The solution g also gave a precipitate with chloroplatinic acid solution (characteristic of an amine).

On heating a few mg. of A in a test-tube, hydrogen cyanide was evolved (tested for with copper acetate/benzidine acetate paper). When 200 mg. of A were refluxed for one hour with 12 ml. alcoholic potassium hydroxide solution (methanol: water: potassium hydroxide ::10:1:1), the solution gave a positive result on testing for

cyanide ion (Prussian blue test).

On boiling with conc. hydrochloric acid for two hours, A apparently hydrolysed since the solution then gave no precipitate on making alkaline with sodium hydroxide solution; and even when the solution was slowly neutralised no precipitate was obtained.

Quantitative Determinations of Properties of A. (i) Microanalysis, Found: C, 77.60; H, 7.69; N, 15.37; Calc. for $C_{6n}H_{7n}N_n$; C, 77.38; H, 7.58; N, 15.04%.

(ii) A cryoscopic determination (benzene) of the molecular weight gave a value of 230. There was, however, a large variation of molecular weight (calculated) with concentration (Fig. II p.39). An ebullioscopic determination (benzene) gave a value of 263 and the concentration effect was much smaller (Fig. II). A Rast determination gave a value of 264.

(iii) The equivalent weight of the base A was determined by ignition of the platinichloride, giving values of 287, 290, (0.3549 g. platinichloride (dried for 8 hours at 100°) gave 0.0704 g. platinum; 0.4059 g. gave 0.0800 g. platinum). Another determination by titration on the micro-scale gave a value of 283.

(iv) Nitrile groups were determined by hydrolysing A with conc. hydrochloric acid and measuring the amount of ammonium chloride formed:-

1.1260 G. of A were hydrolysed with 25 ml. conc. hydrochloric acid and after being refluxed for six hours the mixture was cooled and made up to 100 ml. with water. Portions (5 ml.) of this solution were taken for determination of ammonia, using the distillation part of a semi-micro Kjeldahl apparatus. The values obtained for the molecular weight (assuming one nitrile group per molecule) were 277, 281. Another similar determination with two hours reflux gave values, 281, 281.

(v) On heating 300 mg. of A at 200° (under the conditions described for the

TABLE II

Pyrolysis of Anilino Nitriles

Semi-micro Scale

<u>Anilino Nitrile</u>	<u>mean</u> <u>H₂CN%</u>	<u>duplicates</u>	
C ₄	38	36.4	38.7
C ₅	65	66.3	64.2
C ₆	49	50.8	48.2
C _α	57	55.3	58.6
C _β	56	56.8	55.3
C ₇	92	91.4	92.3
diphenyl-	97	96.8	97.0

pyrolysis of 1-anilino-1-cyanocyclobutane (XV); see p.84), very little hydrogen cyanide was evolved after one hour, but on raising the temperature to 300° the amount was considerable.

Temperature	Time (hours)	% Hydrogen cyanide
200°	1	2
300°	further 1	74
"	" 1	77
"	" 1	78

The percentage yields of hydrogen cyanide are based on a molecular weight of 279 ($C_{18}H_{21}N_3$) and assume one cyano group per molecule.

The probable formula for A was thus $C_{18}H_{21}N_3$, since the microanalysis suggested $C_{6n}H_{7n}N_n$, and the various molecular weight and equivalent weight determinations (except for the seemingly anomalous cryoscopic molecular weight value) agreed with the value $279 = C_{18}H_{21}N_3$. There was also one substituted amino group and one hydrolysable nitrile group per molecule.

Pyrolysis of 1-Anilino-1-cyanocyclobutane (XV).

Owing to the small amount of the anilino nitrile XV available, a semi-micro method with 300 mg. of substance was used for comparing its rate of hydrogen cyanide elimination with those of the other anilino nitriles. The apparatus and pyrolysis method were similar to the standard method used (see p.70) except that the scale was less and a micro-burette was used for titrations. The temperature was kept at $200 \pm 2^\circ$, the rate of flow of nitrogen was 13.5 ± 0.5 c.c./min, and the duration of each pyrolysis was ten minutes. The results of the determinations, including those for the C_5 , C_6 , C_α , C_β , and C_7 and diphenylmethylene anilino nitriles, are given in Table II.

Another pyrolysis was done at 250° using 4.5 g. of XV with a rate of nitrogen

flow of 50 c.c./min. During the first 30 min. 49.6% of theory of hydrogen cyanide was eliminated, and during the second 30 min. 8.9%, making the total 58.6%. 0.2 G. of aniline b.p. 78-80°/13 mm. was isolated from the residue by distillation, leaving a black tarry residue. The aniline was recognised by infra-red absorption spectrum (see Fig. IX) and by conversion to acetanilide, m.p. and mixed m.p. 113-114°.

Pyrolysis of α -Anilino- α -cyanodiphenylmethane (XXIII).

This pyrolysis was done under the same conditions as the C₆ and C₇ anilino nitriles (macro scale).

The products were:-

Temperature	Time (hours)	Hydrogen cyanide eliminated, % of theory	Yield of (diphenylmethylene)-aniline (XXV) % of theory
200°	0.5	96.8	
	1	99.8	
	2	100.3	98.0
250°	0.5	100.4	
	1	100.6	97.1

Both pyrolysis residues were light-yellow and melted at 114-115° either alone or mixed with (diphenylmethylene)aniline (XXV) obtained as an intermediate in the preparation of the anilino nitrile XXIII; (see p.66) which was light-yellow and melted at 114-115°.

TABLE III

Pyrolysis of Anilino Acids

<u>Product</u>	<u>% yield of theory</u>			<u>% by weight</u>		
	C ₅	C ₆	C ₇	C ₅	C ₆	C ₇
aniline	39	54	65	17.5	23.2	26.0
unsaturated acid	7.1	36	52	3.9	21.5	31.1
l-hydroxyanilide	3.9	6.4	3.9	3.9	6.4	3.9
lactone-lactam	21	13	10.5	<u>15.0</u>	<u>10.1</u>	<u>8.0</u>
				<u>40.3</u>	<u>61.2</u>	<u>69.0</u>

P Y R O L Y S I S O F 1-ANILINOCARBOXYLIC ACIDS

These pyrolyses were done at 250° for one hour in a static system similar to that used for the anilino nitriles except that the nitrogen stream was omitted and a larger quantity of material (ca. 50-80 g.) was used. A summary of products and yields for the C₅, C₆, and C₇ anilino acids is given in Table III.

Pyrolysis of 1-Anilino-cyclopentanecarboxylic Acid (XIII).

50.0 G. of the anilino acid XIII were heated for 1 hour at 250° and the residue distilled to give 9.90 g. of a mixture b.p. 150-210° (containing water, aniline and cyclopentene-1-carboxylic acid (XLIV)) and a residue (i). The distillate b.p. 150-210° and also the residue (i) did not give a precipitate on testing with 2:4-dinitrophenylhydrazine solution in dilute hydrochloric acid/ethanol. This shows the absence of cyclopentanone and cyclopentylideneaniline. The water was recognised by removing the droplets with a pipette, removing the aniline by shaking several times with benzene and testing with anhydrous copper sulphate. The aniline was separated from the acid XLIV by extraction with dilute hydrochloric acid. The amount (7.0 g.) was determined by sodium nitrite titration (39). The residue from the hydrochloric acid extraction was the crude acid XLIV, fraction (ii), 0.36 g.

The distillation residue (i) (39.4 g.) was extracted with dilute sodium carbonate to give a solution (iii) and a residue (iv). The solution (iii) was made acid with dilute hydrochloric acid to precipitate 1.76 g. of the crude acid XLIV, m.p. 112-121°, (v). Fractions (ii) and (v) were combined and recrystallised from petroleum to give prisms of the pure acid XLIV m.p. 120-121° (Lit. (30), m.p. 121°). The dibromo derivative crystallised from acetic acid/water in prisms,

m.p. 133-134° (Lit., (48), m.p. 133°).

The residue (iv) was extracted with dilute hydrochloric acid to give a solution (vi) and a residue (vii). The solution (vi) contained 2.95 g. aniline, determined by sodium nitrite titration (39).

The residue (vii) was dried under vacuum and crystallised from 150 ml. benzene to give 1.55 g. of crystals (viii), m.p. 167-169°, and a filtrate (ix). The crystals (viii) were recrystallised from benzene to give plates of pure 1-hydroxycyclopentanecarboxanilide (XLV) m.p. 169-170°, 1.17 g. (Found: C, 69.9, H, 7.4; N, 7.1. $C_{12}H_{15}O_2N$ requires C, 70.2; H, 7.4; N, 6.8%). The infra-red absorption spectrum is given in Fig. VII. Its identity was confirmed by hydrolysis and synthesis (see below).

The filtrate (ix) was heated to 60° and an equal volume of petroleum (60-80°) added. After ten hours the crystals (x), 12.4 g., m.p. 130-144°, were filtered off (leaving filtrate (xi)), and recrystallised from 300 ml. petroleum (60-80°)/100 ml. benzene. This gave 7.48 g. of crude lactone-lactam XIV, m.p. 136-144°. Two further crystallisations from petroleum (60-80°)/benzene gave the pure C_5 lactone-lactam XIV, prisms, m.p. 143-144°, 2.5 g. (Found: C, 72.4; H, 7.1; N, 4.7, \underline{M} (cryo. in benzene), 295. Calc. for $C_{18}H_{21}O_3N$: C, 72.2; H, 7.1; N, 4.7%. \underline{M} . 299) (Plant and Facer (6) recorded m.p. 142°).

The filtrate (x) was evaporated to dryness leaving 6.4 g. of a tarry residue which was not further investigated.

Hydrolysis of 1-Hydroxycyclopentanecarboxanilide (XLV).

0.64 G. of XLV were refluxed for 4 hours with conc. hydrochloric acid, and the mixture evaporated to dryness. The solid residue was extracted with three 20 ml. portions of ether, and the ether evaporated off to give crude 1-hydroxycyclo-

pentanecarboxylic acid (XXXVIII), m.p. 98-101° (0.31 g., 76% of theory).

Crystallisation from benzene gave colourless water-soluble plates m.p. 103-104° (Lit., (35), m.p. 103°). This product gave no depression of melting point when mixed with the acid XXXVIII prepared by hydrolysis of cyclopentanone cyanohydrin.

The ether-insoluble portion of the hydrolysate was aniline hydrochloride. (0.37 g., 92% of theory) m.p. and mixed m.p. 196-198° (Lit. 198°). Its identity was confirmed by conversion to acetanilide (m.p. and mixed m.p. 113-114°), by liberating the aniline from the hydrochloride with alkali and reacting the aniline with acetic anhydride.

Synthesis of 1-Hydroxycyclopentanecarboxanilide (XLV).

1-Cyanocyclopentanol (prepared from reacting cyclopentanone with hydrogen cyanide) (35 g., 0.340 mol.) was refluxed with conc. hydrochloric acid (according to the method of Bucherer and Brandt (49)) to give 1-hydroxycyclopentanecarboxylic acid (XXXVIII) which crystallised from benzene in water-soluble plates, m.p. 103-104° (Lit. (35). m.p. 103°).

The hydroxy acid XXXVIII (2.8 g., 0.022 mol) was refluxed at 200° with aniline (4.2 g., 0.045 mol) for five minutes. After being cooled, the mixture solidified and was shaken with dilute hydrochloric acid followed by water. Recrystallisation from benzene gave the pure anilide XLV (1.3 g., 0.0063 mol. 29% of theory), m.p. 169-170°, either alone or mixed with the anilide XLV prepared by pyrolysis.

Properties of Lactone-lactam (XIV).

The melting point, microanalysis and molecular weight are given on p.87. XIV dissolved readily in warm dilute sodium hydroxide (more slowly, ca. 12 hours, in cold) and was reprecipitated (m.p. and mixed m.p. 143-144°) on making the solution

acid with dilute sulphuric acid. It reprecipitated first as a sticky paste which on standing became solid.

Equivalent Weight Determination. 0.3848 G. of XIV were dissolved in 50 ml. of 0.0976N sodium hydroxide by heating on the steam bath for 25 minutes. The solution was cooled and titrated (phenolphthalein as indicator) against hydrochloric acid solution (50 ml. 0.0976N sodium hydroxide \equiv 51.35 ml. hydrochloric acid), titre = 36.15 ml. A correction had to be applied because of the reaction of the alkali with carbon dioxide from the air during the period on the steam bath. This correction was determined by a blank estimation: 50 ml. of 0.0976N sodium hydroxide were heated for 25 minutes as before. After being cooled the solution was titrated against the hydrochloric acid solution, titre = 49.40 ml. The difference between the standardisation and the blank determination was $51.35 - 49.40 = 1.95$ ml. The amount of 0.0976N sodium hydroxide used for hydrolysis is thus equivalent to $(49.40 - 36.15)$ ml. = 13.25 ml. of the hydrochloric acid solution \equiv 12.90 ml. 0.0976N sodium hydroxide. Thus the corrected equivalent weight is $0.3848 \times 1000/12.90 \times 0.0976 = 306$; the uncorrected equivalent weight was 267. ($C_{18}H_{21}O_3N$ requires 299).

The correction applied will tend to be somewhat too great owing to the fact that during the heating on the steam-bath, the average concentration of the alkali will be higher in the blank than in the actual determination. This probably explains the slightly high value obtained for the equivalent weight.

Hydrolysis.

Alkaline Hydrolysis. 0.72 G. of the lactone-lactam XIV were refluxed with 10% sodium hydroxide solution for three hours. On making the solution acid with dilute sulphuric acid, 0.69 g. of XIV (m.p. and mixed m.p. $143-144^\circ$) were obtained.

Acid Hydrolysis. 2.8 G. of XIV were refluxed for 20 hours with 50 ml. 4N sulphuric acid. The solution was filtered to remove unchanged XIV, 1.06 g. (m.p. and mixed m.p. 143-144°), brought to ca. pH 5 using dilute sodium hydroxide, and the precipitate formed crystallised from benzene to give diamond-shaped prisms of l'-carboxycyclopentyl l-anilinocyclopentanecarboxylate (XXXIX) m.p. 148-155° d. (Found: C, 68.5; H, 7.1; N, 4.5. $C_{18}H_{23}O_4N$ requires C, 68.1; H, 7.3; N, 4.4%). A very small amount (ca. 2 mg.) of l-hydroxycyclopentanecarboxylic acid (XXXVIII), was formed (m.p. and mixed m.p. 103-104°). The infra-red absorption spectrum is given in Fig. VIII.

The structure of XXXIX was deduced from the following properties:-

- (i) It was acid to litmus, even after several recrystallisations from benzene.
- (ii) It gave a positive result on testing for nitrogen.
- (iii) The equivalent weight was determined by dissolving in an excess of standard sodium hydroxide and back-titrating with standard alkali. (Found: 316, $C_{18}H_{23}O_4N$ (monobasic acid) requires 317). Unlike the equivalent determination of the lactone-lactam XIV (which is, of course, a hydrolysis), this could be done rapidly at room temperature and thus the correction required for XIV is avoided.
- (iv) XXXIX dissolved readily in dilute sodium hydroxide and with difficulty in dilute sulphuric acid. The latter solvent was here much less efficient than for the C_5 anilino acid, XIII.
- (v) The solution of XXXIX in dilute sulphuric acid gave a light-yellow oily precipitate with sodium nitrite solution.
- (vi) 0.2801 G. of XXXIX were heated to 250° in a small test tube for five minutes. Droplets of water (recognised by the blue colour with anhydrous copper

sulphate) condensed in the upper portion of the tube. Crystallisation of the residue from benzene gave 0.05 g. of the original lactone lactam XIV, recognised by its m.p. and mixed m.p. (143-144°) and also by its infra-red absorption spectrum (Fig. VIII).

Pyrolysis of 1-Anilinocyclohexanecarboxylic Acid (IV).

The C₆ anilino acid IV was pyrolysed, and the products isolated and identified, in the same way as for the C₅ anilino acid XIII (see p.86). The products and yields are given in Table III. The products had the following properties:-

Unsaturated Acid. cyclohexene-1-carboxylic acid had b.p. 123-126°/7 mm. m.p. 29-31° (Lit. (2), m.p. 29-31°), and its identity was confirmed by preparation of the dibromo derivative which crystallised from petroleum (60-80°) in prisms m.p. 144-145° (Lit. (2), m.p. 144°), and by an equivalent weight determination (Found: 125. Calc. for C₇H₁₀O₂ (monobasic acid): 126).

1-Hydroxyanilide. 1-Hydroxycyclohexanecarboxanilide (XLVIII) crystallised from benzene in plates, m.p. 174-175° (Found: C, 71.3; H, 7.8; N, 6.5. M, (ebul. in benzene), 216, 214. Calc. for C₁₃H₁₇O₂N: C, 71.2; H, 7.8; N, 6.4%, M, 219.) (Lit. (50), m.p. 175°; (18), m.p. 167°).

Acid hydrolysis of XLVIII gave aniline hydrochloride (59% of theory), m.p. and mixed m.p. 196-198°, and 1-hydroxycyclohexanecarboxylic acid (LVI) (51% of theory), which crystallised from benzene in water-soluble plates, m.p. 107-108° (Found: C, 58.3; H, 8.4. Calc. for C₇H₁₂O₃ : C, 58.3; H, 8.4%) (Lit. (49), m.p. 108°). There was no depression of melting point when a sample of this hydrolysis product was mixed with a sample of LVI prepared by hydrolysis of the cyanhydrin of cyclohexanone. The latter sample crystallised from benzene in water-soluble plates, m.p. 107-108° (Found: C, 58.2; H, 8.6. Calc. for C₇H₁₂O₃: C, 58.3; H, 8.4%).

The anilide XLVIII was synthesised in a way similar to that used for the C_5 anilide (see p. 88). The synthetic anilide crystallised from benzene in plates (Found: C, 70.9; H, 7.7; N, 6.1. Calc for $C_{15}H_{17}O_2N$: C, 71.2; H, 7.8; N, 6.4%) m.p. 174-175°, either alone or mixed with the anilide XLVIII from the pyrolysis. The infra-red absorption spectra of both the synthetic and pyrolytic products XLVIII are given in Fig. VII: the spectra are almost identical.

Lactone-lactam. The C_6 lactone-lactam LI crystallised from petroleum (60-80°)/benzene in prisms, m.p. 157-158° (Found: C, 73.7; H, 7.7; N, 4.5. M, (cryo. in benzene) 330, 331. $C_{20}H_{25}O_3N$ requires C, 73.4; H, 7.7; N, 4.3%. M, 327). The infra-red absorption spectrum is given in Fig. VIII, and is very similar to that of the C_5 lactone-lactam in the 1400-2000 cm^{-1} region. The lactone-lactam LI was less readily soluble in warm dilute alkali than the C_5 lactone-lactam XIV.

Pyrolysis of 1-Anilino-cycloheptanecarboxylic Acid (XXXVII).

The C_7 anilino acid XXXVII was pyrolysed, and the products isolated and identified in the same way as for the C_5 and C_6 anilino acids. The products and yields are given in Table III. The products had the following properties:-

Unsaturated Acid. cycloheptene-1-carboxylic acid crystallised from petroleum (60-80°) in needles, m.p. 50-51° (Lit. (51), m.p. 51-53°). (Found: C, 68.4; H, 8.9. Equivalent weight, 140. Calc. for $C_8H_{12}O_2$: C, 68.5; H, 8.6%. Equivalent weight 140).

1-Hydroxyanilide. 1-Hydroxycycloheptanecarboxanilide (LVII) crystallised from benzene in plates, m.p. 171-172° (Found: C, 72.4, H, 8.1; N, 6.3. $C_{14}H_{19}O_2N$ requires C, 72.1; H, 8.2; N, 6.0%). The infra-red absorption spectrum is given in Fig. VII.

Acid hydrolysis of LVII gave aniline hydrochloride (93% of theory), m.p. and mixed m.p. 196-198°, and 1-hydroxycycloheptanecarboxylic acid (38% of theory), which after drying at 80° under 2 mm. pressure, to remove water of crystallisation, was crystallised from benzene in water-soluble plates, m.p. 78-79°. (Lit. (52), m.p. 78°). There was no depression of melting point when a sample of this hydrolysis product was mixed with a sample (m.p. 78-79°) prepared by hydrolysis of the cyanhydrin of cycloheptanone.

The anilide LVII was synthesised in a way similar to that used for the C₅ and C₆ anilides. The synthetic anilide LVII crystallised from benzene in plates, m.p. 171-172° either alone or mixed with the anilide LVII from pyrolysis.

Lactone-lactam. The C₇ lactone-lactam LVIII crystallised from petroleum (60-80°)/benzene in prisms, m.p. 132-133°. (Found: C, 74.2; H, 7.9; N, 4.3. C₂₂H₂₉O₃N requires C, 74.3; H, 8.2; N, 3.9%). The infra-red absorption spectrum is given in Fig. VIII and is very similar to the C₅ and C₆ lactone-lactams in the 1400-2000 cm.⁻¹ region. The lactone-lactam LVIII was less readily soluble in warm dilute alkali than the C₅ lactone-lactam XIV.

Attempted Reaction of cycloHexene-1-carboxylic acid (V), and 1-Hydroxycyclohexanecarboxanilide (XLVIII).

The unsaturated acid V (1.23 g.) was heated under reflux with an equimolecular quantity of the anilide XLVIII (2.14 g.) to 260° for one hour. The only products were unchanged material, viz., (i) the unsaturated acid V, (0.96 g., 78% of the original; m.p. and mixed m.p. 29-31°) isolated by extraction of the mixture with dilute sodium carbonate and precipitation of V from this solution by making it acid with dilute sulphuric acid, and (ii) the hydroxyanilide XLVIII (1.86 g., 87% of the original; m.p. and mixed m.p. 174-175°), isolated by crystallising

from benzene the residue from the sodium carbonate extraction.

Prolonged Acid Hydrolysis of 1-Anilinocyclopentanecarboxylic Acid (XIII).

0.60 G. of the anilino acid XIII was refluxed with 25 ml. 4N sulphuric acid for 50 hours. After the solution was made alkaline with dilute sodium hydroxide, an emulsion was precipitated: this was extracted with ether to give, after evaporation, 0.13 g. of cyclopentylaniline (XLVI) recognised by preparation of the acetyl derivative, m.p. and mixed m.p. (with the derivative of XLVI prepared as described on p.76) 95-96° (Lit. (42), m.p. 96°).

Prolonged Hydrolysis of C₅ Lactone-lactam XIV to cyclopentylaniline.

5.47 G. of XIV were refluxed with 100 ml. 4N sulphuric acid for 20 hours. The solution was made alkaline with dilute sodium hydroxide and the emulsion formed was extracted with ether. Evaporation of the ether gave 0.15 g. of cyclopentylaniline (XLVI), recognised by preparation of the acetyl derivative, m.p. and mixed m.p. 95-96° (Lit. (42), m.p. 96°).

Attempted Synthesis of the C₅ Lactone-lactam.

(i) Preparation of the Acetyl Derivative of 1-Anilinocyclopentanecarboxylic Acid (XIII) (Plant and Facer (6)).

The acid XIII (4 g.) was refluxed with 60 ml. benzene and acetic anhydride (5 ml.) for 7 hours. The benzene was removed under vacuum and the residue crystallised from acetone/petroleum, and then from acetone. This gave 0.02 g. of the acetyl derivative, colourless prisms, m.p. 183-194° d. (Lit. (6), m.p. 195°). The acetyl derivative dissolved, as expected, in dilute sodium hydroxide solution but not in dilute sulphuric acid even on warming (contrast the anilino acid XIII, which dissolved in both). Evaporation of the filtrates from the

acetone/petroleum and acetone crystallisations gave a large amount of a neutral by-product.

An acetylation using acetyl chloride was no more successful:-

4.23 G. of XIII was heated for one hour with 30 ml. acetyl chloride, after which it had completely dissolved. After evaporation of most of the acetyl chloride the mixture was crystallised as before. The yield of the acetyl derivative was 0.01 g., m.p. 180-190° d. Again a large amount of the neutral by-product was formed.

(ii) Preparation of Silver Salt of 1-Anilinocyclopentanecarboxylic Acid (XIII).

A neutral solution of the ammonium salt of the acid XIII (2.72 g.) was prepared by dissolving it in an excess of ammonia solution and boiling to remove the excess of ammonia. The calculated amount of silver nitrate (2.11 g.) was added and the silver salt was filtered off. This proved to be unstable, since it became shiny-black after a few hours owing to the formation of metallic silver.

Attempted Catalytic Rearrangement of 1-Anilinocyclohexanecarboxylic Acid (IV).

0.2 G. of the acid IV were dissolved in 20 ml. ether and 6 ml. phosphoric acid was added as catalyst (mixture (i)). Another similar mixture was made up but containing 0.18 g. of the acid IV and 0.02 g. of 1-hydroxycyclohexanecarbox-anilide (XLVIII) in place of the 0.2 g. of the acid IV (mixture (ii)). Both mixtures, which were homogeneous, were kept at room temperature for 15 days, after which they were poured into 20 ml. water and placed on the steam bath to evaporate the ether. Mixture (ii) gave crystals of the hydroxyanilide XLVIII (0.019 g., m.p. and mixed m.p. 174-175°); but mixture (i) gave a clear solution. This shows that there had been no detectable conversion of the acid IV to hydroxyanilide XLVIII.

A similar experiment using boron trifluoride as catalyst also gave no hydroxyanilide XLVIII.

Stability to Heat of 1-Hydroxycyclohexanecarboxanilide (XLVIII).

2.60 G. of XLVIII were heated to 250° for one hour: no decomposition had taken place, the product being 2.60 g., m.p. and mixed m.p. 174-175°.

Attempted Reaction of the C₅ Lactone-lactam XIV with Aniline and Water.

The lactone-lactam XIV (1.078 g., 0.0036 mol) was heated under reflux to 250° for one hour with aniline (0.979 g., 0.015 mol) and water (0.3 g., 0.017 mol). The residue was dissolved in 15 ml. benzene and extracted with hydrochloric acid to remove the aniline: no precipitate or crystals were formed, showing the absence of the hydroxyanilide XLV.

High Temperature (500°) Pyrolysis of 1-Anilinocyclohexanecarboxylic Acid (IV) in a Flow Reactor.

The original object of this pyrolysis was to find whether, during the pyrolysis of IV, the yield of 1-hydroxycyclohexanecarboxanilide (XLVIII) was increased by raising the temperature and reducing the contact time. This was not so, however, and none of the anilide XLVIII was isolated from the pyrolysate.

The acid IV (89.0 g., 0.407 mol; in pellet form) was pyrolysed during three hours in a flow reactor at 500°. 10.9 L. of gas (10.2 l. at N.T.P.) were collected, which gave the following analysis (Hempel):-

	CO ₂	CO	H ₂
	27.4%	29.4%	12.0%
	26.5%	29.2%	10.7%
mol	0.123	0.133	0.052

The 70.2 g. of pyrolysis residue were distilled:-

(a) At atmospheric pressure, to give 12.1 g. of a liquid b.p. 68-82°. After drying (magnesium sulphate) and redistillation, this gave 10.1 g., b.p. 77-79° (fraction (i)).

(b) Under vacuum, to give

- | | | |
|-------|---------|--------------------|
| (ii) | 0.9 g. | b.p. 45-86°/28 mm. |
| (iii) | 26.8 g. | b.p. 86-92°/28 mm. |

The residue was tarry and did not give crystals on addition of benzene - this suggests the absence of the hydroxyanilide XLVIII. The residue and also the fractions (ii) and (iii) gave a negative result on testing for ketone with 2:4-dinitrophenylhydrazine solution in ethanol/dilute hydrochloric acid. This denoted the absence of cyclohexanone (and also of cyclohexylideneaniline (VII)). The residue was not further investigated.

Fraction (i). This fraction (b.p. 77-79°) proved to be a mixture of cyclohexene (b.p. 83°) and benzene (b.p. 80°): separation by distillation was impracticable. The mixture (i) decolourised bromine in carbon tetrachloride instantaneously.

cycloHexene. This was recognised by oxidation of a portion of the mixture with alkaline permanganate solution to give adipic acid, m.p. and mixed m.p. 151-152°.

Benzene. The identification of the benzene proved troublesome since the cyclohexene gave resinous products on nitration, or on attempted preparation of the aroylbenzoic acid by reaction with phthalic anhydride in carbon disulphide. The following method was satisfactory:- 3 ml. of the mixture (i) was treated with bromine (while cooling in an ice bath to avoid loss of benzene) until it was very slightly yellow. The yellow colour was removed by adding one drop of the original mixture (i), and the benzene was distilled off in a semi-micro

distillation flask, leaving 1:2-dibromocyclohexane. 0.5 ml. of benzene, n_D^{20} 1.5010 (Lit. for benzene, n_D^{20} 1.5011) was obtained, and its identity confirmed by preparation of m-dinitrobenzene, m.p. and mixed m.p. 87-88° (Lit. 89°).

The original mixture had n_D^{20} 1.4655 which indicated that the ratio of cyclohexene: benzene was 2:1. (The values recorded in the literature are cyclohexene n_D^{20} 1.4465 and benzene, n_D^{20} 1.5011, which by interpolation gave 34.8% benzene).

The above was confirmed by the infra-red absorption spectra (Fig. IX) of the mixture (i), and a control mixture containing benzene: cyclohexene in the ratio 2:1 (n_D^{20} 1.4651).

Aniline. This was identified by conversion to acetanilide (m.p. and mixed m.p. 113-114°) and determined by titration with 0.1 N bromate/bromide (45) which indicated a purity of 96%.

The following is a summary of the identified products from 0.407 mol of the anilino acid IV:-

	g.	mol	% of theory
carbon dioxide	5.0	0.123	30
carbon monoxide	3.4	0.133	33
hydrogen	0.1	0.052	6.4*
<u>cyclohexene</u>	8.1	0.099	24
benzene	4.0	0.051	12.5
aniline	25.7	0.277	68

* This value assumes that one molecule of IV gives two molecules of hydrogen (i.e. that the hydrogen is produced from dehydrogenation of cyclohexene to give benzene).

Pyrolysis in Semi-micro Flow Reactor.

These pyrolyses were done in order to find the origin of the carbon monoxide in the high temperature pyrolysis of the C₆ anilino acid IV.

The apparatus is shown in Fig. III (p.61). It consisted essentially of a tube closed at one end and connected at the other to a barometric leg by means of which about 80% of the gas in the apparatus could be transferred to the sample tube. The reaction tube was heated by two furnaces A and B both at the same temperature. Furnace B heated the reaction chamber which was packed with glass beads (ca. 3 mm. dia.). The substance for pyrolysis (300 mg.) was introduced into the end of the tube and the glass beads added, which were prevented from falling into the compound by a constriction in the tube. The apparatus was then filled with nitrogen by repeated evacuation and introduction of nitrogen. With furnace B in the position shown and furnace A in the initial position both furnaces were allowed to come up to the working temperature 540° during two hours, after which the furnace A was moved to the working position. The gas evolved was collected at atmospheric pressure and the barometric leg was adjusted during pyrolysis to collect the gas at approximately atmospheric pressure. At the end of the pyrolysis, which lasted about ten minutes, the apparatus was removed from the furnaces and allowed to cool for twenty minutes. The total volume of gas evolved during pyrolysis was measured by the difference between the initial and final volume readings on the gas burette, and the level of the mercury in the collecting limb of the burette was brought down to 130 ml. before closing the stopcock thus collecting ca. 80% of the gas in the apparatus. It would be possible to collect almost 100% of the gas in the apparatus by use of a sampling tube, but this was not found necessary as the 80% transfer gave more than sufficient

TABLE IV

Pyrolyses in Semi-micro Flow Reactor

Compound	IV C ₆ anilino acid	V C ₆ unsaturated acid	LI C ₆ lactone- lactam	XLVIII C ₆ hydroxy- anilide	XIII C ₅ anilino acid
ml. of gas formed (N.T.P.)	26	29	38	17.5	21.5
gas formed; % of theory	85	54	92*	57	66
gas analysis CO	7.9	4.1	23.0	16.5	15.0
CO ₂	17.7	28.5	13.7	1.6	11.6
% of theory CO	13.7	4.3	36.4*	23.7	22.2
CO ₂	30.6	30.0	21.7*	2.3	17.2
Ratio CO:CO ₂	0.446	0.144	1.68	10.3	1.29

* assuming that one molecule of LI gives two molecules of gas.

gas for two analyses. By measuring the total volume of the apparatus (29 ml.) the amount of gases evolved could be calculated.

The Sleigh apparatus (53) was found to be accurate and reliable for gas analyses, and suitable for the small amounts available 8.5 - 9 ml. could be analysed to $\pm 0.2\%$.

The results are given in Table IV.

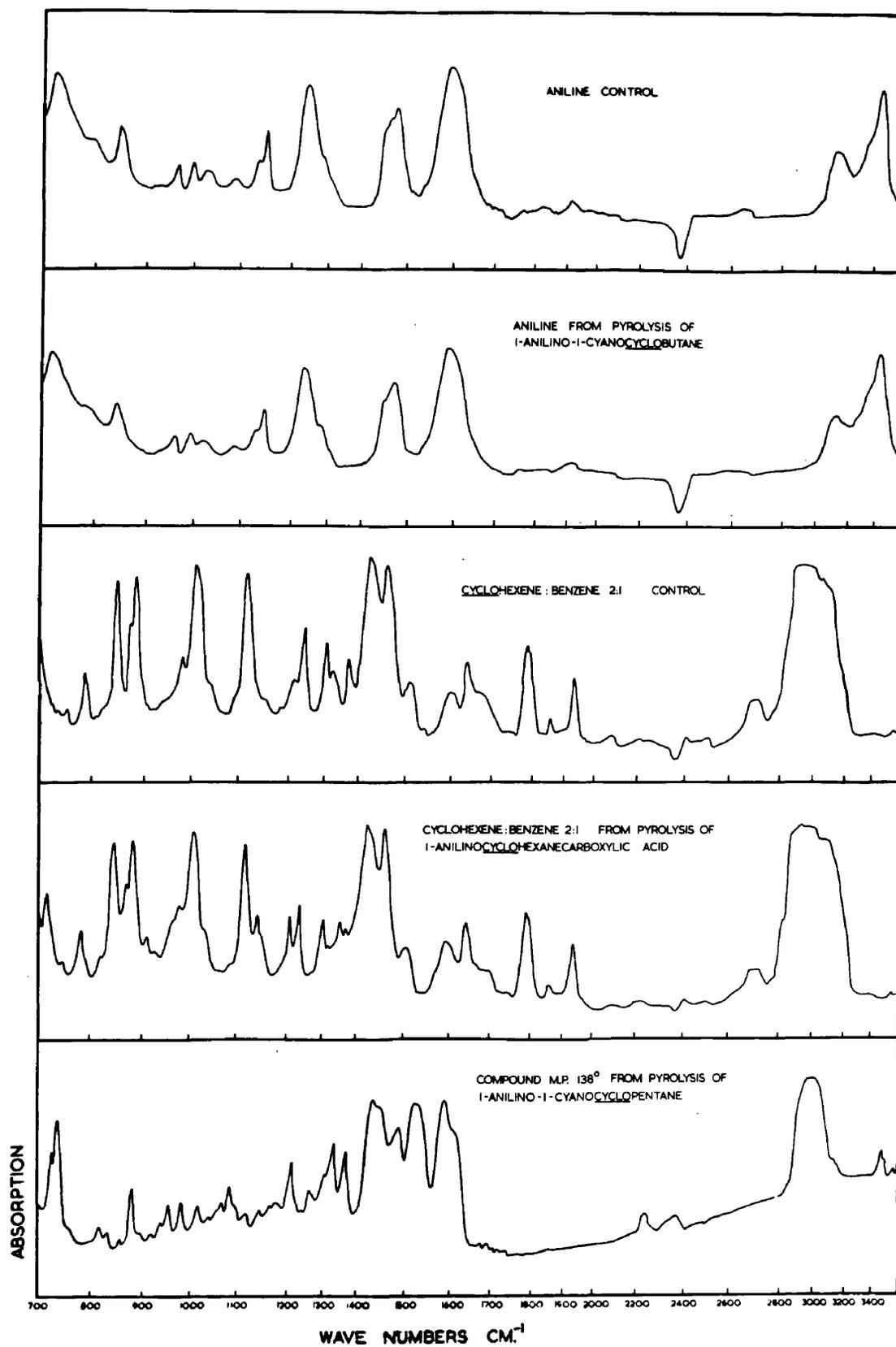


FIGURE IX

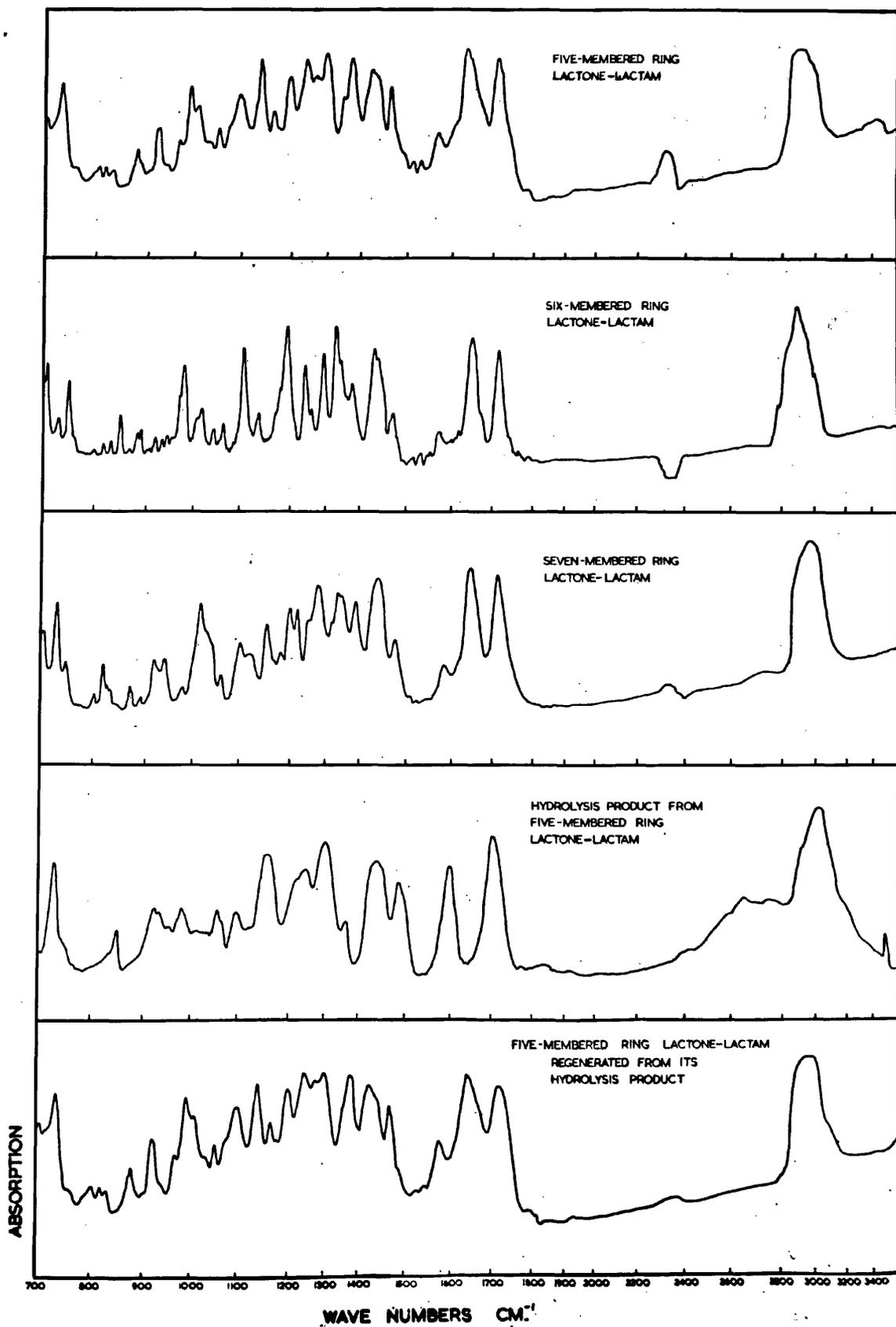


FIGURE VIII

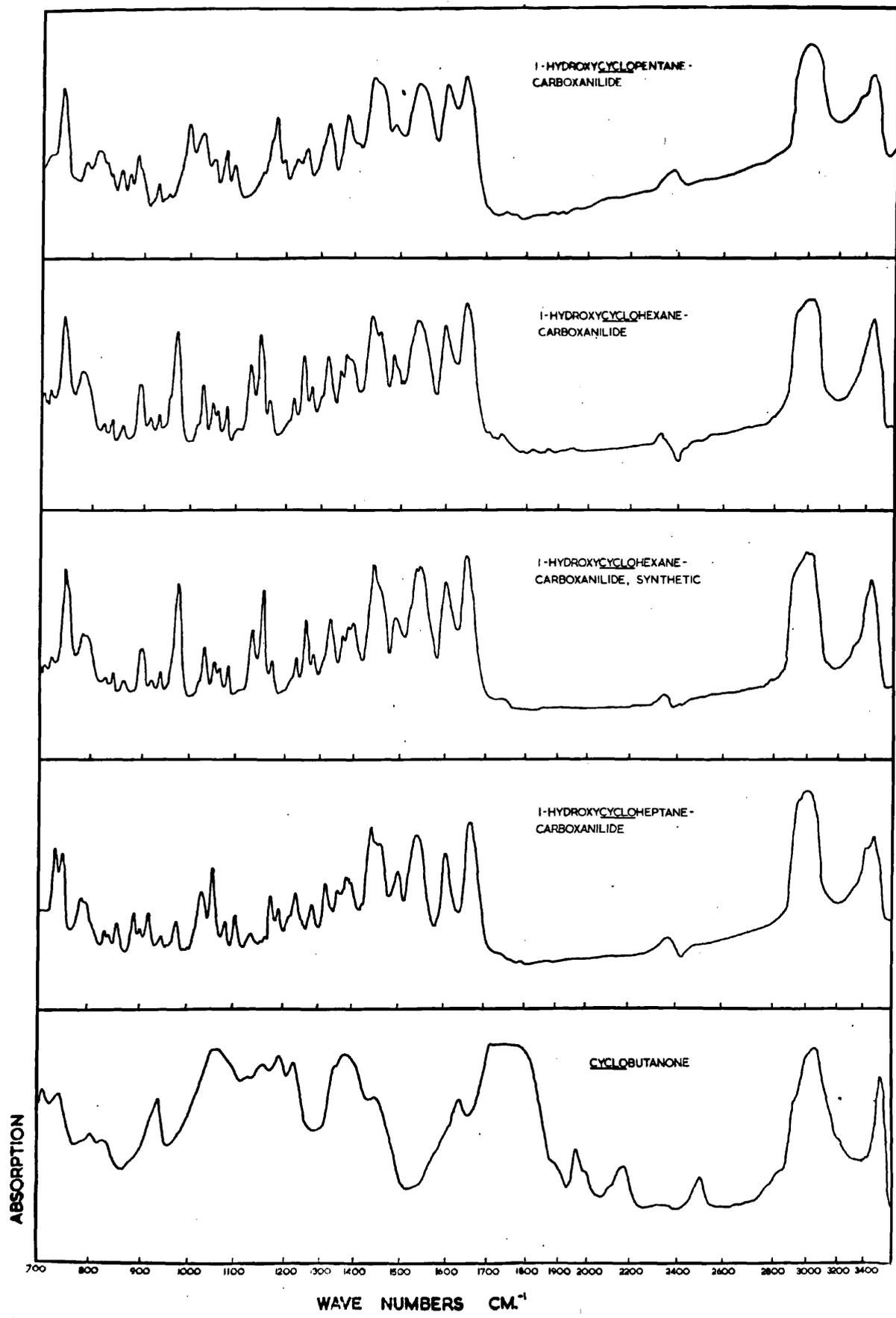


FIGURE VII

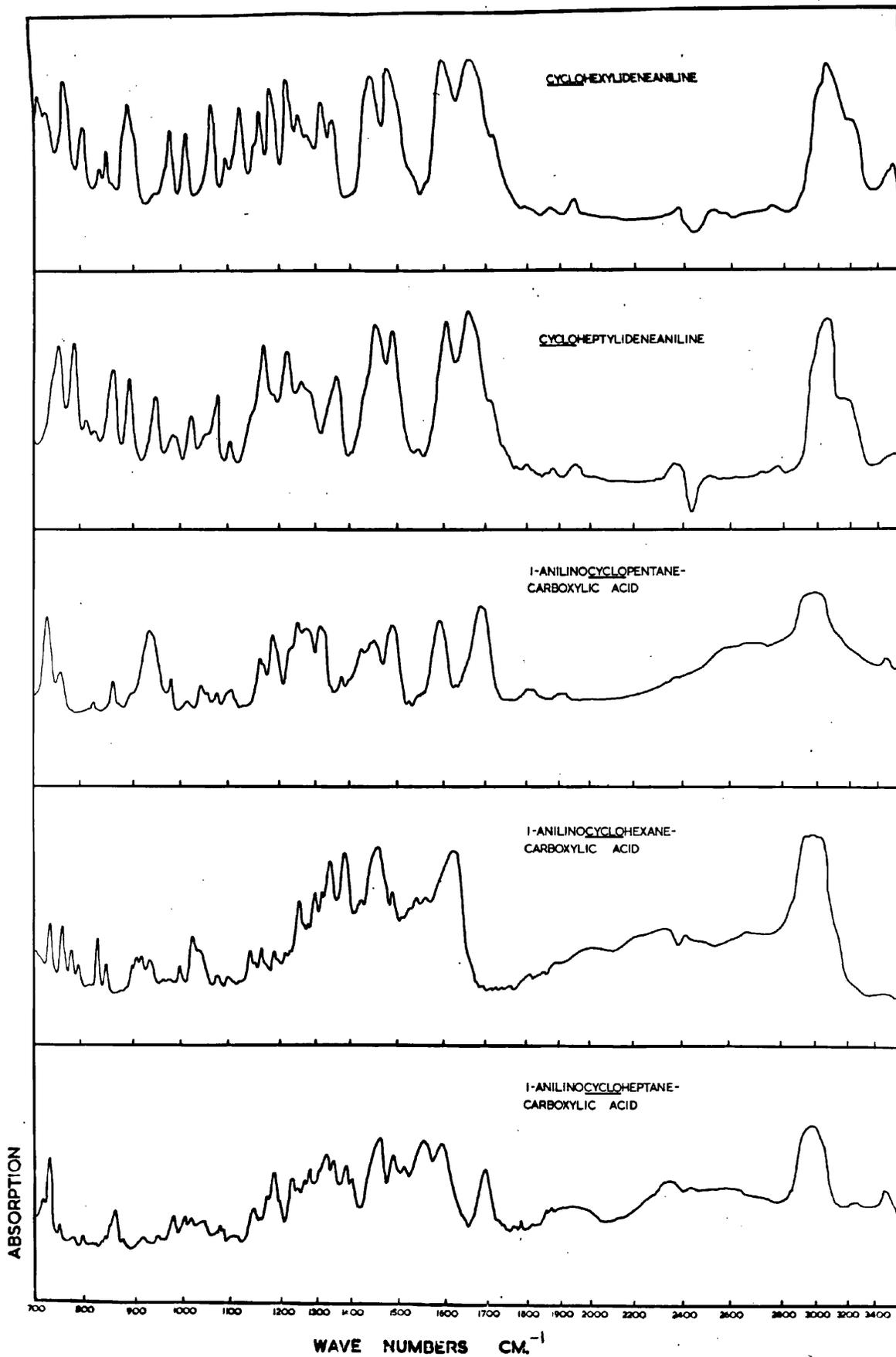


FIGURE VI

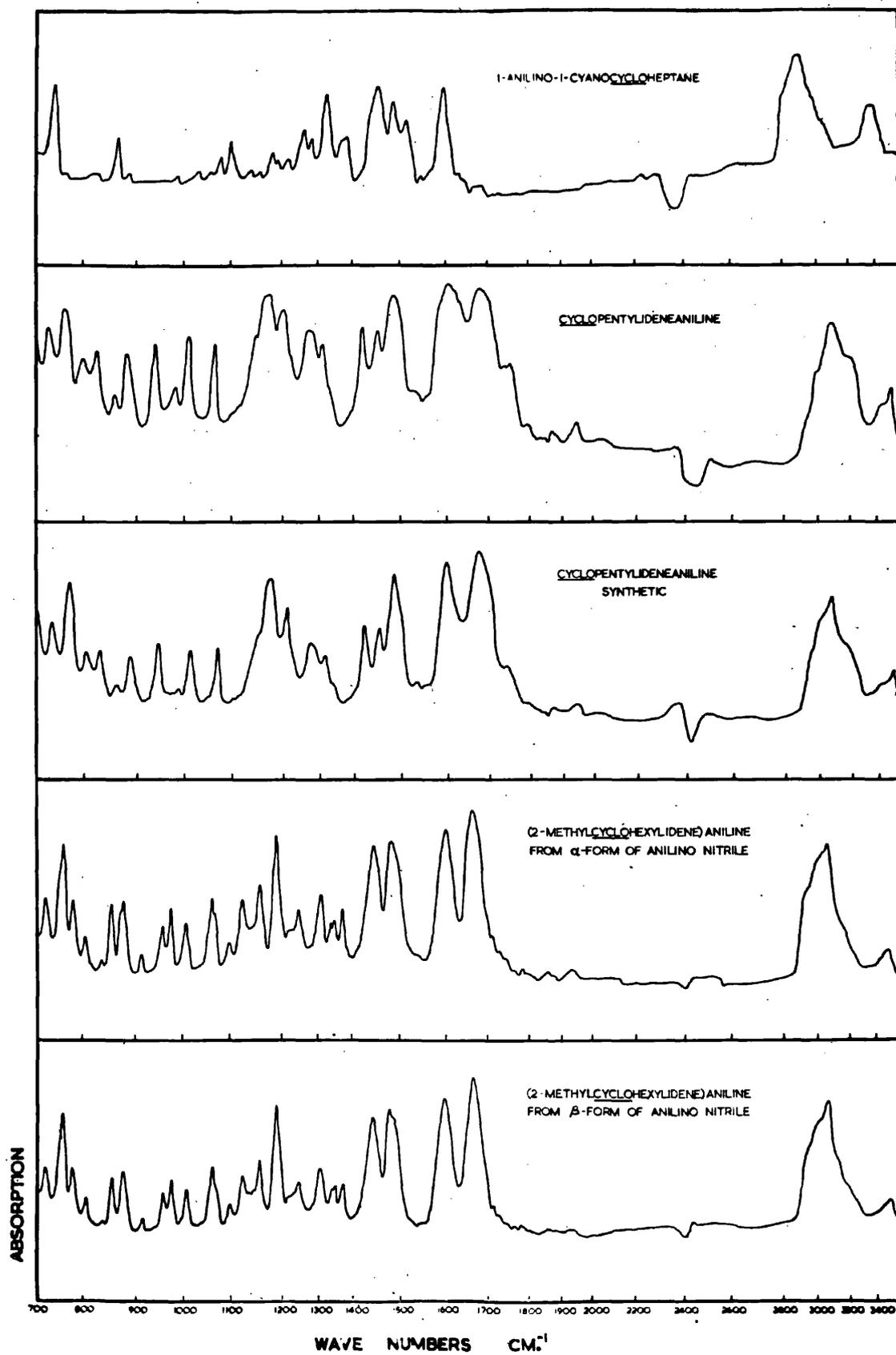


FIGURE V

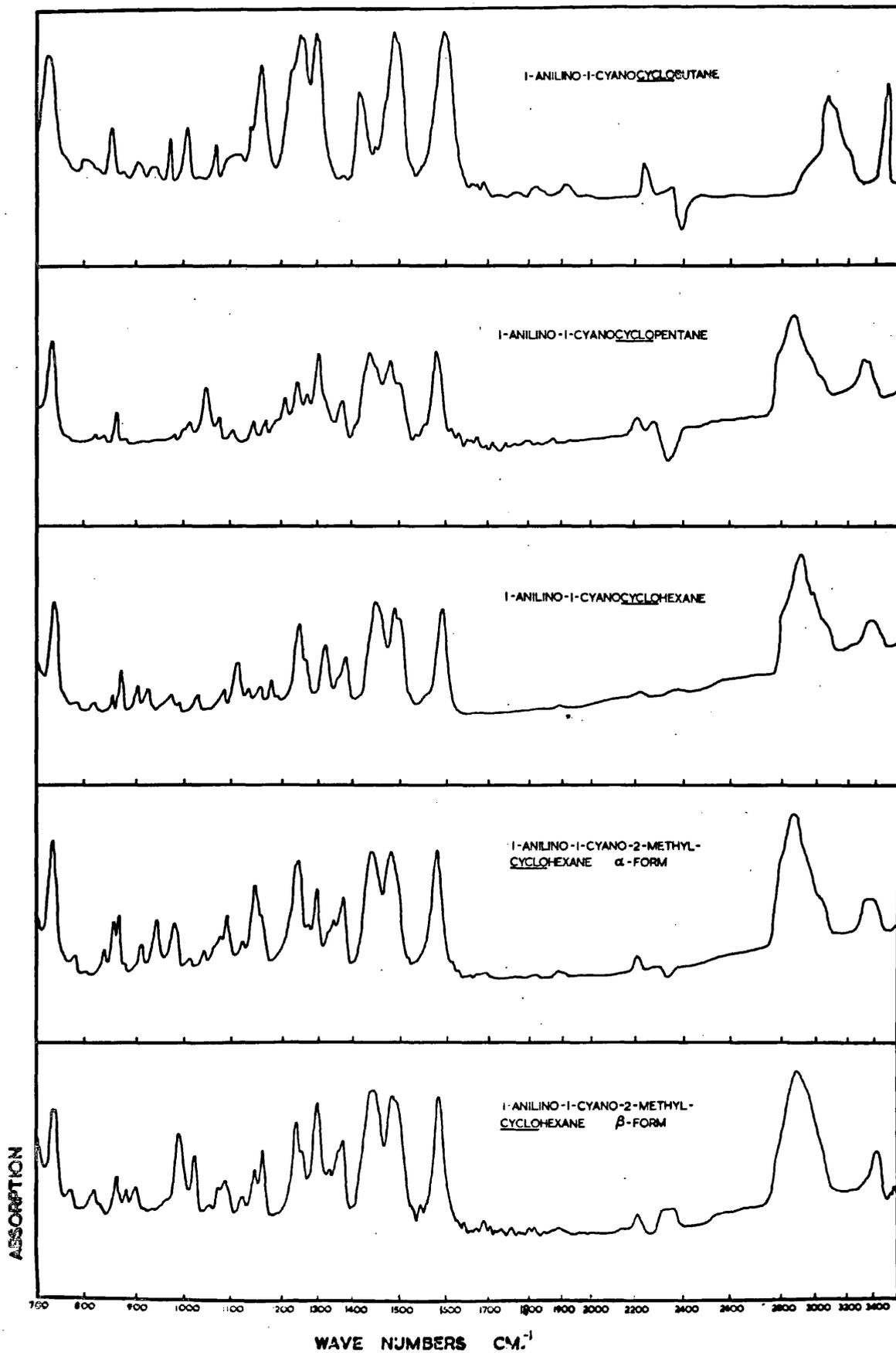


FIGURE IV

FIGURES IV - IX

Infra-red Absorption Spectra

All the spectra were done in nujol suspension except the following :-

Fig. IV	1-anilino-1-cyanocyclobutane	liquid capillary (melted solid)
" V	<u>cyclopentylideneaniline</u>	liquid cell
" V	" synthetic	" "
" V	2-methylcyclohexylideneaniline from α -form of anilino nitrile	" "
" V	do. from β -form of anilino nitrile	" "
" VI	<u>cyclohexylideneaniline</u>	" "
" VI	<u>cycloheptylideneaniline</u>	" "
" VII	<u>cyclobutanone</u>	" "
" IX	aniline control	" "
" IX	aniline from pyrolysis of 1-anilino-1-cyanocyclobutane	" "
" IX	<u>cyclohexene/benzene</u> 2:1, control	" "
" IX	do. from pyrolysis of 1-anilinocyclohexanecarboxylic acid	" "

INFRA-RED ABSORPTION SPECTRAAnilino Nitriles (Figs. IV and V).

The spectra are similar in the region 1400-1700 cm.^{-1} . The C_4 anilino nitrile shows a difference in the region 1400-1500 cm.^{-1} , the 1420 cm.^{-1} band being much weaker than the 1490 cm.^{-1} band.

The α - and β - forms of 1-anilino-1-cyano-2-methylcyclohexane are discussed later (p. 104).

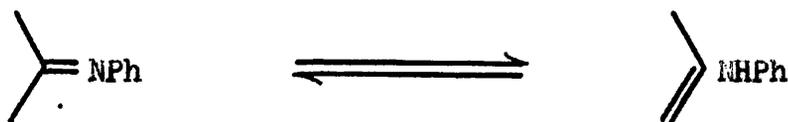
Assignments:-

- 3350-3450 cm.^{-1} NH of anilino group.
- 2210-2220 cm.^{-1} Nitrile group. This is a weak band and scarcely appears at all in the spectra of the C_6 and C_7 anilino nitriles. It is most prominent for the C_4 anilino nitrile.
- 1590-1610 cm.^{-1} Unassigned. This band is of too high a wave number and is too strong to be assigned to the anilino group.

Anils (Figs. V and VI).

These all show what appears to be a characteristic double band in the region 1600-1680 cm.^{-1} , the separation being ca. 75 cm.^{-1} . The synthetic and pyrolytic C_5 anils have almost identical spectra. The anils from the α - and β - forms of 1-anilino-1-cyano-2-methylcyclohexane have also almost identical spectra, showing that both forms give the same anil.

All the spectra of the anils have a band at ca. 3500 cm.^{-1} , corresponding to a NH bond. This indicates that the anils exist partly in the enamine form.

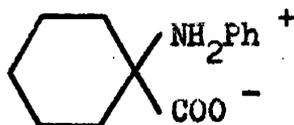


Assignments:-

- 3500 cm.^{-1} NH group.
 1700 cm.^{-1} Unassigned.
 1620 cm.^{-1} Substituted imine.

Anilino Acids (Fig. VI).

These spectra differ considerably from one another. The spectra of the C_5 and C_7 acids resemble one another more than either does the spectrum of the C_6 acid. The C_6 acid, unlike the C_5 and C_7 acids, has no acid $\text{C}=\text{O}$ band (1700-1730 cm.^{-1}), but has a very strong carboxylate ion band (1620 cm.^{-1}). This shows that, in the solid state, the C_6 acid exists almost wholly in the ionised form:-



This effect may correspond with the fact that the C_6 acid is difficult to crystallise from organic solvents (it tends to supersaturate or form a gel), while the C_5 and C_7 acids crystallise comparatively well.

Assignments:-

- 1715 cm.^{-1} (C_5 and C_7) Acid $\text{C}=\text{O}$.
 1620 cm.^{-1} (C_6) Carboxylate ion.

Hydroxyanilides (Fig. VII).

The spectra are very similar in the region 1450-1750 cm.^{-1} , showing that they have the same double-bond structure. The spectra of the synthetic and pyrolytic C_6 hydroxyanilides are almost identical.

Assignments:-

3500 cm.⁻¹ Hydroxyl group.

1660 cm.⁻¹ Amide group.

Lactone-lactams (Fig. VIII).

These spectra are very similar in the region 1400-1800 cm.⁻¹ showing that they have the same double-bond structure. The two main bands (1640 and 1720 cm.⁻¹) have not been assigned.

cyclobutanone (Fig. VII).

This spectrum is almost identical with that for cyclobutanone recorded by Roberts and Sauer (9).

Hydrolysis Product from C₅ Lactone-lactam (Fig. VIII).

This shows an acid and/or ester band at 1710 cm.⁻¹

C₅ Lactone-lactam Regenerated from its Hydrolysis Product (Fig. VIII).

This spectrum is almost identical with the original.

Aniline Control and Aniline from Pyrolysis of 1-Anilino-1-cyanocyclobutane (Fig. IX).

These spectra are practically identical.

cyclohexene/Benzene Mixture (Fig. IX).

The control mixture of cyclohexene/benzene (2:1) gives almost the same spectrum as the product from the high temperature pyrolysis of 1-anilino-cyclohexanecarboxylic acid.

Compound m.p. 138° from Pyrolysis of 1-anilino-1-cyanocyclopentane (Fig. IX).

The only clear assignment is the nitrile band at 2220 cm.⁻¹

1-Anilino-1-cyano-2-methylcyclohexane, α - and β - forms.

The author is indebted to Mr. W. H. T. Davison, Dunlop Research Centre, for the following results and observations:-

Configuration of Isomers of 1-Anilino-1-cyano-2-methylcyclohexane.

Experimental

(LiF prism, NH stretching absorptions only).

A and B stand for the appropriate isomers. (α and β respectively) C for the unmethylated compound, D for diphenylamine.

1. Crystals (as paraffin mulls,)

- B 3403 cm.⁻¹ (unbonded NH); m.p. 86°; very soluble in CCl₄.
 A 3361 cm.⁻¹ (bonded NH); m.p. 126°; very slightly soluble in CCl₄.
 C 3357 cm.⁻¹ (bonded NH); m.p. 76°; very soluble in CCl₄.

2. Solutions in CCl₄

Equimolar solutions, in 0.2 cm. cells.

- B 3436 cm.⁻¹ (unbonded NH) and possible 3357 cm.⁻¹ (bonded NH).

The relative intensity of the bonded to unbonded bands is less than 0.1.

- A 3432 cm.⁻¹ (unbonded NH) and 3357 (bonded NH) band of 0.3 relative intensity.

- C 3421 cm.⁻¹ (unbonded) and 3342 (bonded) band of 0.2 relative intensity.

- D 3436 cm.⁻¹ (unbonded) only.

3. Solutions in acetone/CCl₄ (1:4 in 0.01 cm. cell)

- B unresolved broad absorption at 3395 cm.⁻¹

- A unresolved broad absorption at 3376 cm.^{-1}
- C unresolved broad absorption at 3372 cm.^{-1}
- D absorption at 3371 cm.^{-1} (bonded) with small shoulder at 3435 (unbonded).

4. Solutions in ether/ CCl_4

All solutions were equimolar and examined in mixed solvents (1:4) in a 0.01 cm. cell.

- B 3431 (unbonded), 3357 cm.^{-1} (bonded) relative intensity of bonded to unbonded absorptions 0.95
- C 3414 (unbonded), 3343 cm.^{-1} (bonded) relative intensity 2.5.
- D 3434 (unbonded), 3345 cm.^{-1} (bonded) relative intensity 2.5.
- A 3426 (unbonded), 3349 cm.^{-1} (bonded) relative intensity 1.8.

Discussions and Conclusions

The approach of the investigation is based upon the assumption (which appears to be substantiated from an examination of an atomic model) that the isomer in which the methyl is adjacent to the anilino group will give greater steric blocking to the anilino group than either the other isomer, or the unmethylated compound. The investigation becomes one therefore of determining the relative amounts of hydrogen bonding in the two isomers and the unmethylated compound (C).

In every experiment B shows less hydrogen bonding than A. Furthermore, A and C have similar bonding behaviour in experiments 2, 3 and 4.

The only anomaly is in the case of crystals of C which, although showing spectroscopic evidence of bonding, have a low m.p. and good solubility, being similar to diphenylamine (m.p. 54°). A possible explanation is that crystals of A exhibit "infinite chain" association while crystals of C and D associate in dimers.

It appears, therefore, that isomer B exhibits rather more hindrance to hydrogen bonding than does isomer A. In this case it is probable that B is the isomer in which the methyl is adjacent to the anilino group.

REFERENCES

- (1) Burns, R., Jones, D.T., & Ritchie, P.D., J. chem. Soc., 1935, 400, 714.
- (2) Betts, L.B., Muspratt, R., & Plant, S.G.P., J. chem. Soc., 1927, 1310.
- (3) Ritchie, P.D., unpublished observations, 1934.
- (4) Drew, E.W., & Ritchie, P.D., Chem. & Ind. (Rev.), 1952, 1104.
- (5) Seher, A., Arch. Pharm., Berl., 1951, 284, 371.
- (6) Plant, S.G.P. & Facer, J.E., J. chem. Soc., 1925, 2039.
- (7) Chemical Abstracts, Collective Formula Index, (1920-46), p. 1288.
- (8) Barton, D.H.R., J. chem. Soc., 1949, 2174.
- (9) Roberts, J.D., & Sauer, C.W., J. Amer. chem. Soc., 1949, 71, 3925.
- (10) Mulder, A., Rec. Trav. chim. Pays-Bas, 1907, 26, 180.
- (11) Bukhsh, M.W., Desai, R.D., Hunter, R.F., & Hussain, M., J. chem. Soc., 1936, 1159.
- (12) v. Miller, W., & Plöchl, J., Ber. dtsh. chem. Ges., 1892, 25, 2056.
- (13) Mackenzie, J.E., J. chem. Soc., 1896, 69, 987.
- (14) Pauly, C., Liebigs Ann., 1877, 187, 199.
- (15) Lapworth, A., & Manske, R.H.F., J. chem. Soc., 1928, 2548.
- (16) Frazer, H.B. & Kon, G.A.R., J. chem. Soc., 1934, 604.
- (17) Weizmann, C., Bergmann, E., & Sulzbacher, M., J. Amer. chem. Soc., 1948, 70, 1189.
- (18) Bucherer, H.T., & Barsch, H., J. prakt. Chem., 1934, 140, 162.
- (19) Kaarsemaker, S., & Coops, J., Rec. Trav. chim. Pays-Bas, 1951, 70, 1033.
- (20) Schurink, H.B., Org. Synth., 1937, 17, 73.
- (21) Herzog, H.L., Org. Synth., 1951, 31, 82.
- (22) Sapiro, R.H., & Peng, S., J. chem. Soc., 1938, 1171.
- (23) Prelog, V., J. chem. Soc., 1950, 423.
- (24) Manchot, W., & Furlong, J.R., Ber. dtsh. chem. Ges., 1909, 42, 3030, 4383.
- (25) Hassel, A., Research, Lond., 1950, 3, 504. Quart. Rev. chem. Soc., Lond., 1953, 7, 221.
- (26) Barton, D.H.R., Head, A.J., & Williams, R.J., J. chem. Soc., 1952, 453.
- (27) Barton, D.H.R., Head, A.J., & Williams, R.J., J. chem. Soc., 1953, 1715.
- (28) McNiven, H.L., & Read, J., J. chem. Soc., 1952, 2067.
- (29) Alexander, E.R., & Mudrak, A., J. Amer. chem. Soc., 1950, 72, 1810, 3194, 1951, 73, 59.
- (30) Cook, A.H., & Linstead, R.P., J. chem. Soc., 1934, 959.
- (31) Hoch, J., C.R. Acad. Sci., Paris, 1934, 199, 1429.

- 32) Wallach, O., Ber. dtsh. chem. Ges., 1896, 29, 2964; 1897, 30, 1095.
- 33) Drew, E.W., M.Sc. Thesis, London University, 1953.
- 34) Dubsky, J.V., & Wensink, W.D., Ber. dtsh. chem. Ges., 1916, 49, 1134.
- 35) v. Auwers, K., & Krollpfeiffer, F., Ber. dtsh. chem. Ges., 1915, 48, 1393.
- 36) Cumming, A.C., & Kay, S.A., "Quantitative Chemical Analysis", Oliver & Boyd, London, 9th Edn., p. 178.
- 37) Grammaticakis, P., Bull. Soc. chim. Fr., 1949, 16, 144.
- 38) Iddles, H.A., Low, A.W., Rosen, B.D., & Hart, Industr. Engng Chem. (Anal.) 1939, 11, 102.
- 39) Siggia, S., "Quantitative Organic Analysis", Wiley & Sons, Inc., New York, 1st Edn., p. 71.
- 40) Kranzlein, G., & Corell, M., Chem. Abstr., 1921, 15, 380. (Ger. P. 483205, Nov. 20th 1925).
- 41) Fouque, A.G., Ann. Chim., 1921, 15, 330.
- 42) Leovenich, J., Utsch. H., Holdrickx, P., and Shaefer, E., Ber. dtsh. chem. Ges., 1929, 62, 3103.
- 43) Boesekin, J., & Telligen, F., Rec. Trav. chim. Pays-Bas, 1938, 57, 135.
- 44) Levina, R.Y., Kulikov, S.G., & Parshikov, N.G., Chem. Abstr., 1941, 35, 6931.
- 45) Siggia, S., "Quantitative Organic Analysis", Wiley & Sons, Inc., New York, 1st Edn., p. 111.
- 46) Venus-Danilova, E.D., Chem. Abstr., 1937, 31, 665.
- 47) Zelinski, N.D., & Shukin, N.I., Chem. Abstr., 1931, 25, 2420.
- 48) Urion, M., Ann. Chim., 1934, 1, 46.
- 49) Bucherer, H.T., & Brandt, W., J. prakt. Chem., 1934, 140, 136.
- 50) Passerini, M., Chem. Abstr., 1924, 18, 245.
- 1) Buchner, E., & Jacobi, A., Ber. dtsh. chem. Ges., 1898, 31, 401.
- 2) Buchner, E., Ber. dtsh. chem. Ges., 1897, 30, 1949.
- 3) Sleigh, S.W., J. Soc. chem. Ind., Lond., 1937, 15, 430.