PART I

THE FORMATION OF BENZYNE IN A FRAGMENTATION REACTION

Part II

A STUDY OF RESTRICTED ROTATION ABOUT THE N-CO BOND BY NMR

by

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PART I

THE FORMATION OF BENZYNE IN A FRAGMENTATION REACTION

PREFACE

The first part of this work was undertaken in order to investigate the possibility of benzyne formation via a carbonium ion precursor. The second part has been devoted to a study of the restricted rotation about nitrogen-carbonyl bonds using nuclear magnetic resonance.

I would like to express my sincere thanks to my research directors, Dr. Robert R. Fraser and Dr. Frank A. L. Anet, for their invaluable help and suggestions during the course of these investigations.

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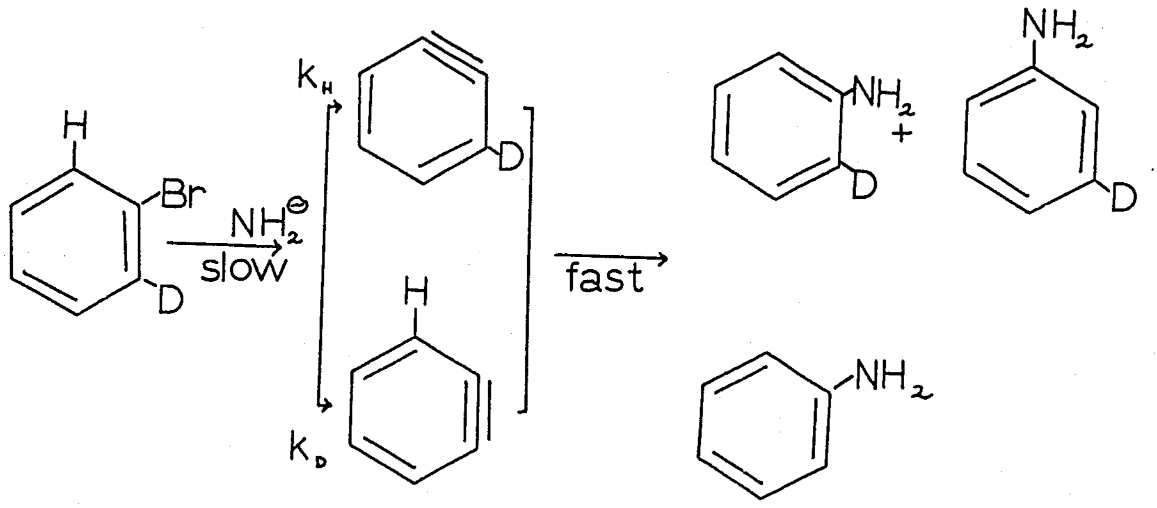
ABSTRACT

The deamination reaction of 2-aminotriphenylcarbinol in 97% formic acid had been studied in order to investigate the possibility of benzyne formation via a carbonium ion precursor. Product analysis showed that a small but significant amount of benzophenone was formed, which indicated some fragmentation. While this evidence strongly suggests that the other fragment was benzyne, no direct proof of this has been obtained.

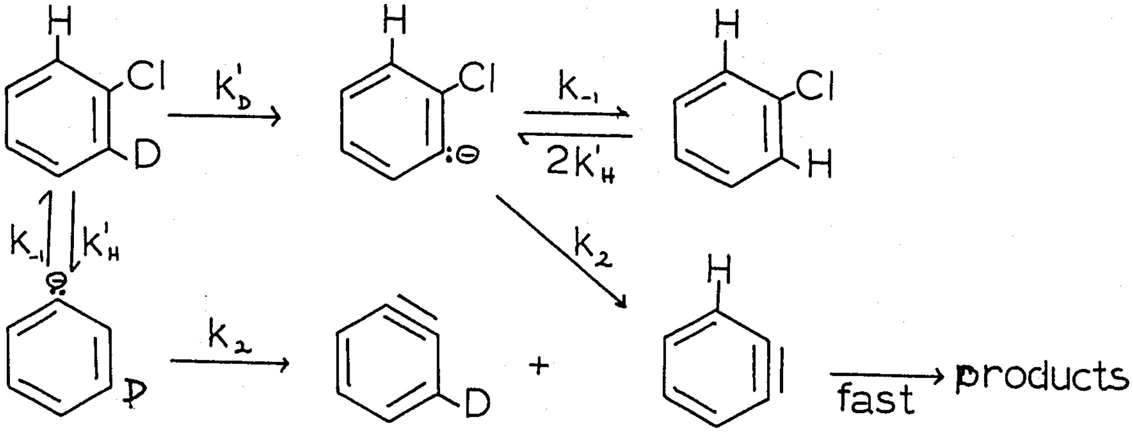
INTRODUCTION

The existence of benzyne has become well established in the last ten years. A triple bond in a benzene-type ring was first suggested by Roberts and co-workers (1,2,3) to explain the amination reaction of halobenzenes. The products of these reactions are independent of the nature of the halogen substituent or solvents used. Substituent groups do not change the rate of reactions. All these facts are in accordance with the postulated benzyne intermediate. The mechanism was elucidated by kinetic studies (4,5) and deuterium exchange experiments (2).

The mechanism proposed and subsequently proved for the amination of bromobenzene (2) involves a concerted elimination as follows:

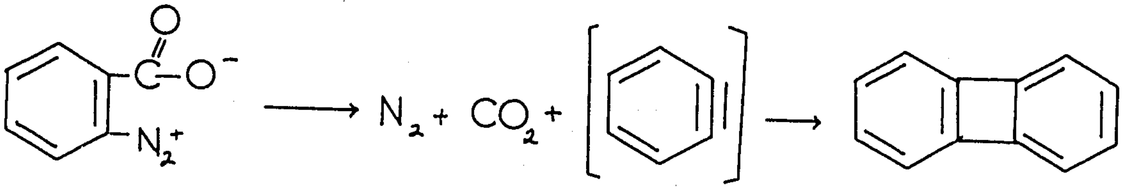


Chlorobenzene, however, is found to undergo a two-step elimination reaction according to the scheme shown:



These mechanisms were established on the basis of the observed kinetic isotope effect. If the loss of a halide ion is relatively easy, the concerted mechanism is followed; otherwise proton removal precedes the rate controlling step.

Following this discovery of benzyne, numerous analogous reactions were reported, and these are summarized in several reviews.(6-12). All these reactions involve a carbanion precursor of benzyne. A different route may have been followed in the thermal decomposition of benzenediazonium-2-carboxylate (13):

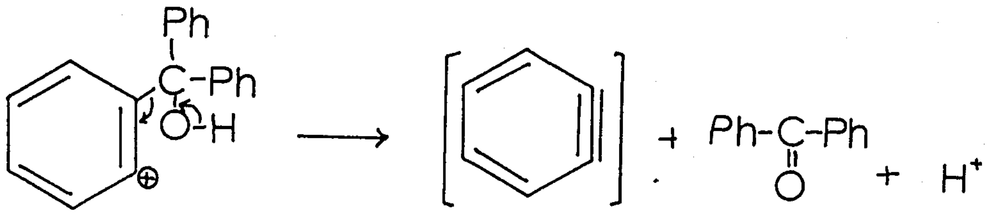


The presence of benzyne was indicated by the isolation of biphenylene, as well as addition products when the reaction was carried out in the presence of furan and anthracene.

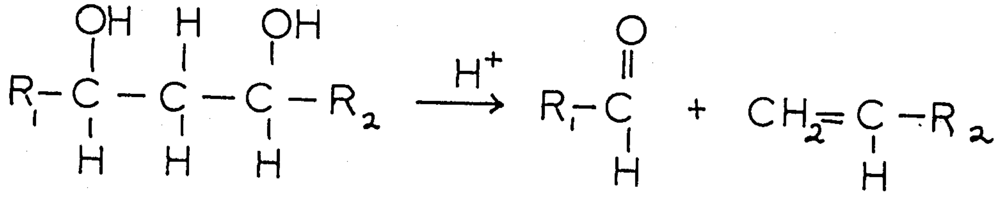
More recently other investigators (14-21) made use of similar methods for benzyne generation. Friedman and Logullo (23) reported that fragmentation of suitably <u>ortho-</u>disubstituted benzenes under aprotic conditions gave very good yields of benzyne.

Spectroscopic evidence (24,25) had also been obtained for the existence of benzyne. In this study the benzyne was generated by flash photolysis of benzenediazonium-2-carboxylate.

In the above two reactions it is unlikely that the first step of transition state would involve a negatively charged entity. The aim of the present work was to investigate whether benzyne could be formed by fragmentation of the appropriate carbonium ion, i.e.

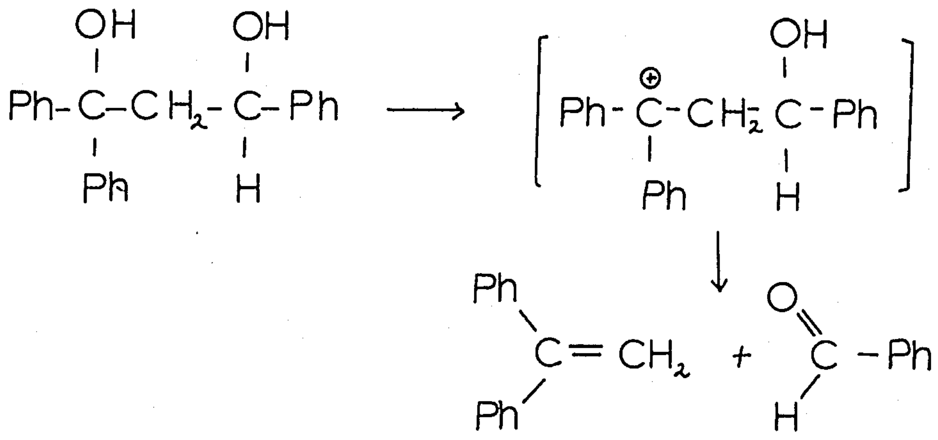


It is well known that fragmentation of a substituted 1,3-diol into a ketone and an olefin proceeds through a carbonium ion intermediate (26).



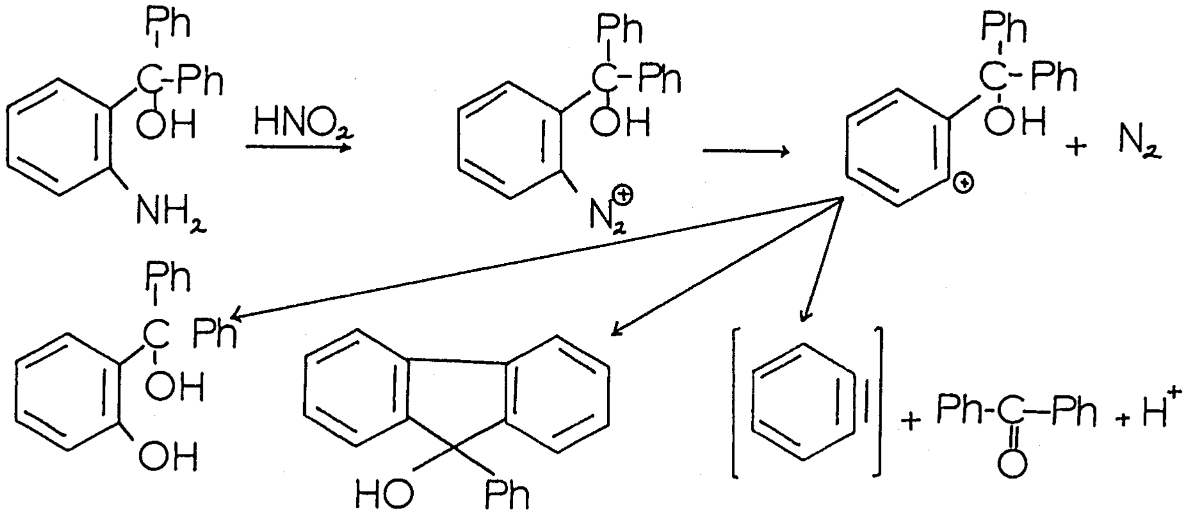
$$R_1-\underset{H}{\overset{OH}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-R_2 \xrightarrow{H^+} R_1-\underset{H}{\overset{\overset{O}{\|}}{C}} + CH_2=\underset{H}{C}-R_2$$

Aromatic substitution at the carbon atom where the carbonium ion is formed stabilizes this ion, thus controlling the direction of carbon-carbon bond cleavage.



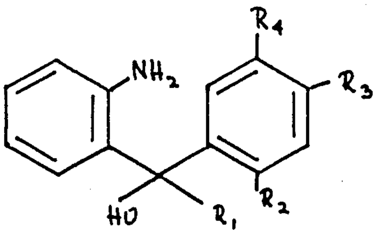
It seems possible that a similar reaction could take place in an aromatic system. Diazonium salt decompositions occurring in acidic media are known to follow a heterolytic mechanism (27), producing an aromatic carbonium ion.

A suitable way of generating a carbonium ion which could yield benzyne and a stable ion upon fragmentation was thought to be the following:



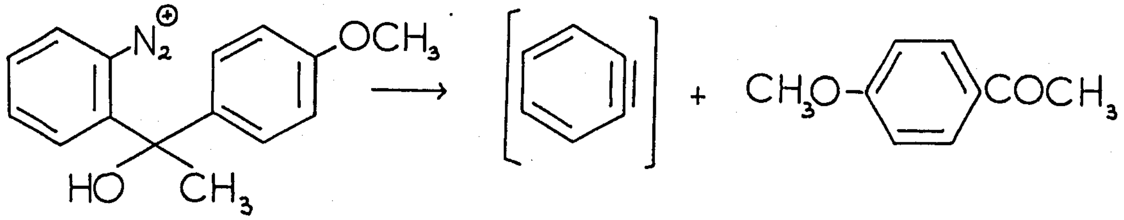
Undoubtedly ring closure would be a competitive reaction, but some fragmentation might take place.

While this work was in progress, Stiles and Sisti (28) reported an identical study with negative results. They diazotized a series of substituted amino alcohols of the type I:



	R_1	R_2	R_3	R_4
a.,	C_6H_5	H	H	H
b.,	$4\text{-}CH_3OC_6H_4$	H	CH_3O	H
c.,	$2\text{-}CH_3C_6H_4$	CH_3	H	H
d.,	$2,4\text{-}(CH_3)_2C_6H_3$	CH_3	CH_3	H
e.,	$2,5\text{-}(CH_3)_2C_6H_3$	CH_3	H	CH_3
f.,	CH_3	H	H	H
g.,	C_2H_5	H	H	H
h.,	CH_3	H	CH_3O	H
i.,	CH_3	CH_3	CH_3	H
j.,	CH_3	CH_3	CH_3O	CH_3

and found the reaction products to be phenols, fluorenols and rearranged ketones. Only in one instance did they isolate a product (p-methoxyacetophenone) in about 0.3% yield that indicated bond cleavage:



No explanation was offered as to why this particular compound should undergo fragmentation, in contrast to b.

Stiles and Sisti decomposed these compounds in aqueous 10% sulfuric acid. If a solvent of lower nucleophilicity were to be used, the lifetime of the carbonium ion intermediate would be prolonged and thus the probability of electron shift necessary for benzyne formation enhanced. On the basis of this reasoning our diazotizations were carried out in acetic and formic acid media, both solvents of lower nucleophilicity. (29)

METHODS AND RESULTS

2-Aminotriphenylcarbinol, the starting material for the diazotization reaction was synthesized by reacting methyl anthranilate with phenyl magnesium bromide. In our hands the reported method (35) gave 2-(N-methylamino)-triphenylcarbinol as the major product and only minor amounts of the primary aminocarbinol were obtained. It was found, however, that the addition of magnesium bromide to the reaction mixture greatly enhanced the yield of the desired product.

The decomposition of the diazonium salts of 2-aminotriphenylcarbinol was studied in two solvents. Treatment of the amine with sodium nitrite in glacial acetic acid resulted in diazotization followed by decomposition which was accompanied by gas evolution. The infrared spectrum of the crude product was very complex. It contained a small absorption peak at 1664 cm^{-1}, characteristic of aromatic ketones (22,30). However, the strongest peaks observed at 1530 cm^{-1} and 1250 cm^{-1}, also appeared in the spectrum of 2-aminotriphenylcarbinol treated with hot glacial acetic acid.

A similar control experiment showed that no reaction occurs between formic acid and 2-aminotriphenylcarbinol; therefore, formic rather than acetic acid was employed as reaction medium subsequently.

The neutral products of diazotization in formic acid were separated by elution chromatography. Table 1 summarizes

TABLE I.

Products Isolated from the Diazotization of 2-Aminotriphenylcarbinol in Formic Acid.

Compound	Yield (in grams)	Eluent composition (% benzene in ligroin)	Volume (in ml.)	Melting Point (in °C)	
				Observed	Literature
9-Phenylfluorene	0.139	10	150	143.31	144.3 (31)
Hydrocarbon X	0.017	40	100	199-204.5	-
Benzophenone	0.008	65	250	230-235*	232-237*(32)
2-phenylbenzophenone	0.086	70	250	82-84	85-87 (33)
9-Phenylfluorenol	0.880	100	550	85-87	85-87 (34)

*m.p. of the 2,4-dinitrophenylhydrazone derivative taken.

the results of this experiment. The compounds isolated were characterized on the basis of their infrared and ultraviolet spectra. Mixed melting points were taken with authentic samples.

A possible source of by-products is the reduction of various intermediates or end products by formic acid. To check this point, the major product, 9-phenylfluorenol was boiled in 97% formic acid. This yielded an amorphous material, not identical with any of the deamination products.

One of the products was identified as benzophenone. This indicates that fragmentation did in fact occur. Attempts to obtain a more direct proof of benzyne formation by isolating addition products from furan and thiophene with the benzyne intermediate were prevented by the instability of these compounds in formic acid.

Diazotization of 2-amino-4'4"-dimethoxytriphenylcarbinol in formic acid could not be attempted, since these two compounds were found to react even at low temperatures.

EXPERIMENTAL

A Leitz hot stage microscope was used for determining all the melting points. All melting points reported are uncorrected and the values quoted from the literature are those given in the methods of preparation employed. The infrared spectra were recorded on a Perkin-Elmer Infracord using 0.1 mm. sodium chloride cells. Ultraviolet spectra were taken on a Beckman DU recording spectrophotometer.

MATERIALS

2-Aminotriphenylcarbinol

2-Aminotriphenylcarbinol was synthesized by a modified method of Baeyer and Villiger (35).

The Grignard reagent was prepared from bromobenzene (16.3 ml.; 0.15 mole) and magnesium (3.1 g.; 0.15 mole) in anhydrous diethyl ether (27 ml). Magnesium bromide (0.5 g., dried at 120° for 24 hr.) was added to a solution of methyl anthranilate (6.5 g.; 0.045 mole) in ether (5.6 ml.) The suspension was slowly added to the cooled Grignard reagent. A red precipitate was formed at once, which turned yellow after stirring for half an hour at room temperature. The reaction mixture was cooled in an ice bath and was hydrolyzed by adding a solution of ammonium chloride (10%). The hydrolyzed mixture was extracted with ether. The ether solution yielded 6.88 g. of 2-aminotriphenylcarbinol (57% yield, m.p. 117-119°). After recrystallization from benzene the carbinol melted at 120.3 - 121.1° (lit. 120-121°).

Previous attempts in which no magnesium bromide was used gave erratic yields (0-20%) of 2-aminotriphenylcarbinol. The large amounts of white crystalline material (60%) isolated from the tarry reaction mixture had a melting point of 172-174° after recrystallization from ethanol. The compound was identified as 2-(N-methylamino)-triphenylcarbinol on the basis of the Hinsberg test, NMR spectrum and analysis (calcd. for $C_{20}H_{19}ON$: C=83.0, H=6.62, N = 4.84; found: C=82.8, H=6.22, N=4.29). N-methylation of 2-aminotriphenylcarbinol gave a product (m.p. 170-173°) having an identical infrared spectrum. Mixed melting point of the two showed no depression.

9-Phenylfluorene

This compound was prepared by the method of Ullmann and Wurstemberger (36), m.p. 145-146° (lit. 144.5°).

2-Phenylbenzophenone

The method of Bradsher (31) was followed in the preparation of this compound, m.p. 85-87° (lit. 86-87°).

9-Phenylfluorenol

This fluorenol was prepared as described by Kliegl (34), m.p. 85-87° (lit. 85-87°).

2-Amino-4'4"-dimethoxytriphenylcarbinol

The aminocarbinol was synthesized following the method of Iganaki (40). It was purified by dissolving in ether and precipitating as the amine hydrochloride by bubbling hydrogen chloride gas through the solution. The aminehydrochloride was treated with dilute sodium hydroxide solution and extracted with ether. Shiny platelets were obtained from the ether solution, m.p. 64-66° (lit. 103°). In spite of the analytical results (calcd. for $C_{21}H_{21}O_3N$: C = 75.2, H = 6.27; found: C = 71.7, H = 6.97), both the NMR and infrared spectra indicated that the compound isolated had the correct structure.

PRELIMINARY INVESTIGATIONS

2-Aminotriphenylcarbinol and Acetic Acid

At room temperature 2-aminotriphenylcarbinol dissolved very slowly in glacial acetic acid. After completely dissolving and standing for 5 minutes, the clear solution was cooled and neutralized with a 10% solution of sodium hydroxide. The ether extract of this solution yielded a white solid upon evaporation. The infrared spectrum of this material differed from that of 2-aminotriphenylcarbinol by having a broad shoulder at 1640 cm^{-1}. When the treatment was repeated using boiling acetic acid, a pale crystalline compound was obtained (m.p. 135-137°). The infrared spectrum changed completely: both the hydroxy and amino peaks disappeared and new, very intense bands appeared at 1530 cm^{-1} and 1250 cm^{-1}. No structural investigation of this product was undertaken.

2-Aminotriphenylcarbinol and Formic Acid

An identical treatment of the aminocarbinol in formic acid did not produce spectral changes. Boiling formic acid appeared to react with 2-aminotriphenylcarbinol, hence heating in formic acid prior to diazotization was avoided in the experiments.

DIAZOTIZATIONS

Diazotization of 2-Aminotriphenylcarbinol in Acetic Acid

2-Aminotriphenylcarbinol (0.46 g.; 0.0016 mole) was dissolved in glacial acetic acid (4.5 ml.) at 40°. The reaction mixture was cooled in an ice bath and a solution of sodium nitrite (0.46 g.) in water (4.5 ml.) was added. The diazonium salt thus formed was decomposed (without isolating it) on a steam bath. The cooled solution was then neutralized with sodium hydroxide solution (10%) and extracted with ether. The dark, syrupy product (0.41 g.) showed a complex infrared spectrum, containing a weak band at 1664 cm^{-1}. The lack of intense absorption in this region and the obvious complication of starting material reacting with solvent indicated further efforts to identify and purify the product to be undesirable.

Diazotization of 2-Aminotriphenylcarbinol in Formic Acid

The 2-aminotriphenylcarbinol (4.75 g., 0.017 mole) was dissolved in formic acid (97%, 45 ml.) at room temperature. The light yellow solution was cooled in an ice-salt bath. A solution of sodium nitrite (2.7 g., 0.019 mole) in water (4 ml.) was added and the reaction vessel was heated on a steam bath. After ten minutes the evolution of gases ceased. Then the solution was cooled and neutralized with sodium hydroxide solution (10%), followed by extraction with ether. After evaporating the ether, a solid residue (3.15 g.) remained.

CHROMATOGRAPHY OF THE REACTION MIXTURE

The crude reaction mixture was dissolved in a small amount of benzene and absorbed on the top of a column of activated alumina (60 g.). The eluents used were ligroin (b.p. 40-60°) and benzene in various proportions, added in 50 ml. aliquots. The solvents were evaporated in a rotary evaporator connected to a water suction pump. The crystalline compounds isolated are listed in Table 1. in order of their elution. They were identified as follows:

9-Phenylfluorene

Mixed melting point with an authentic sample of 9-phenylfluorene (m.p. 145°) did not show depression. The ultraviolet spectra of the two samples were identical.

Hydrocarbon X

The compound melted over the range 198.8-204.5° after several recrystallizations from benzene-petroleum ether. It was found to be insoluble in ethanol, petroleum ether and diethyl ether. The ultraviolet spectrum in

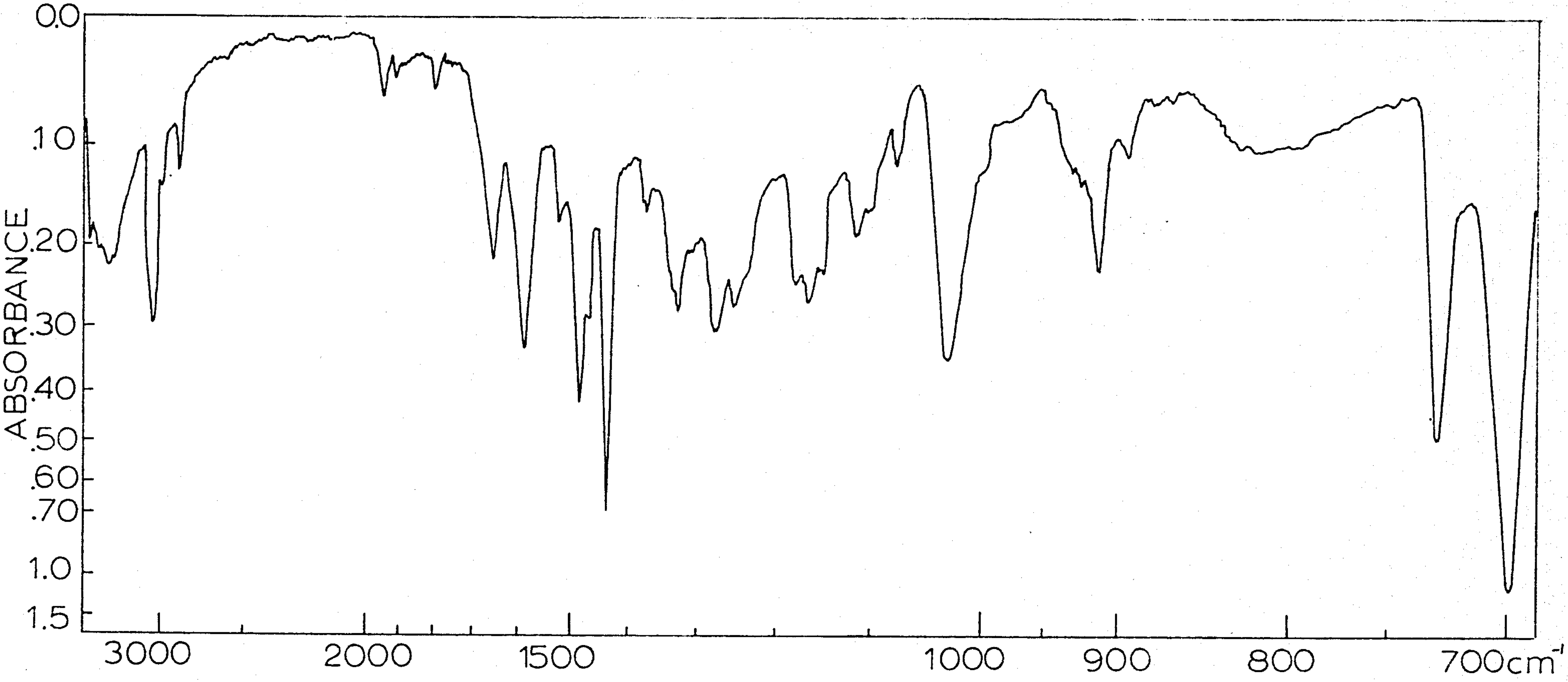


FIG.1 - INFRARED SPECTRUM OF A CARBONTETRACHLORIDE SOLUTION (5%) OF THE CRUDE DEAMINATION PRODUCT OF 2-AMINOTRIPHENYLCARBINOL IN FORMIC ACID.

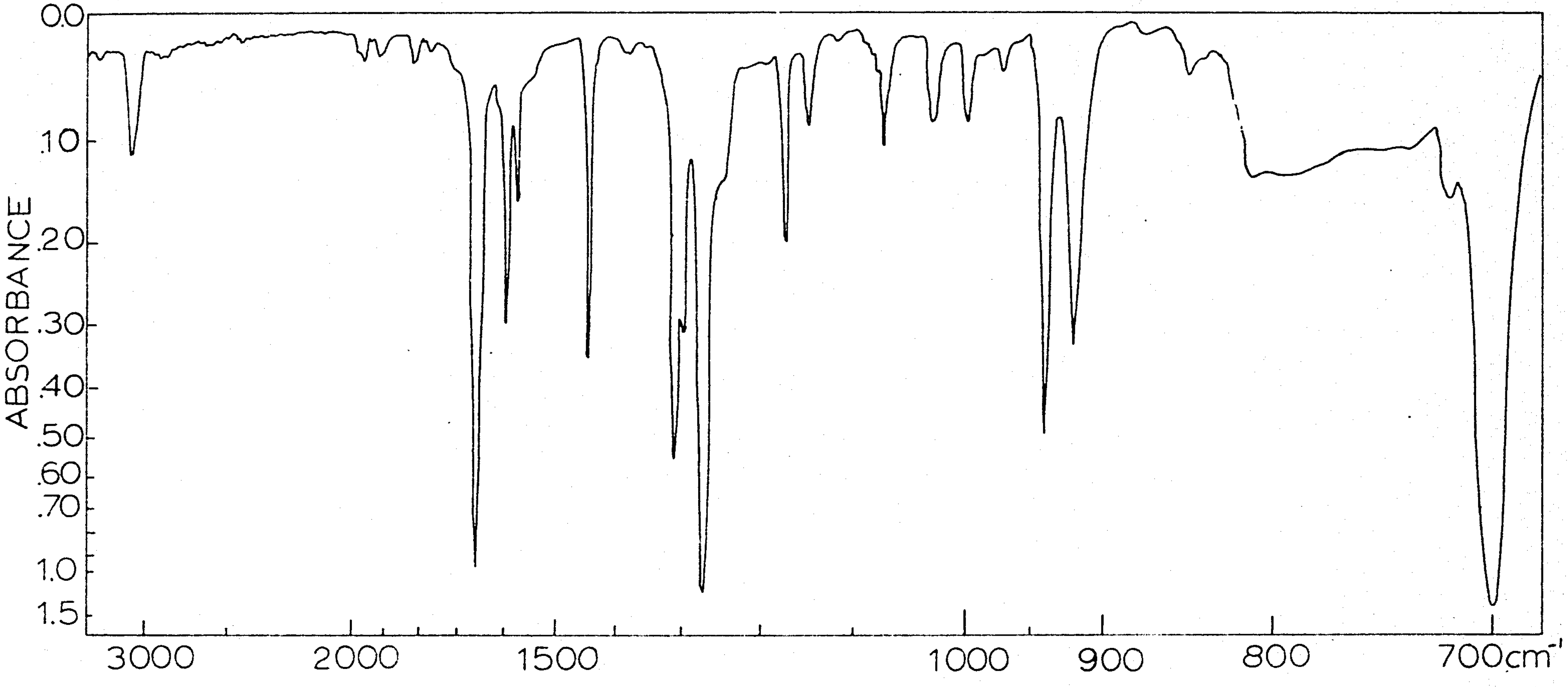


FIG.2 - INFRARED SPECTRUM OF BENZOPHENONE IN CARBONTETRACHLORIDE SOLUTION (5%).

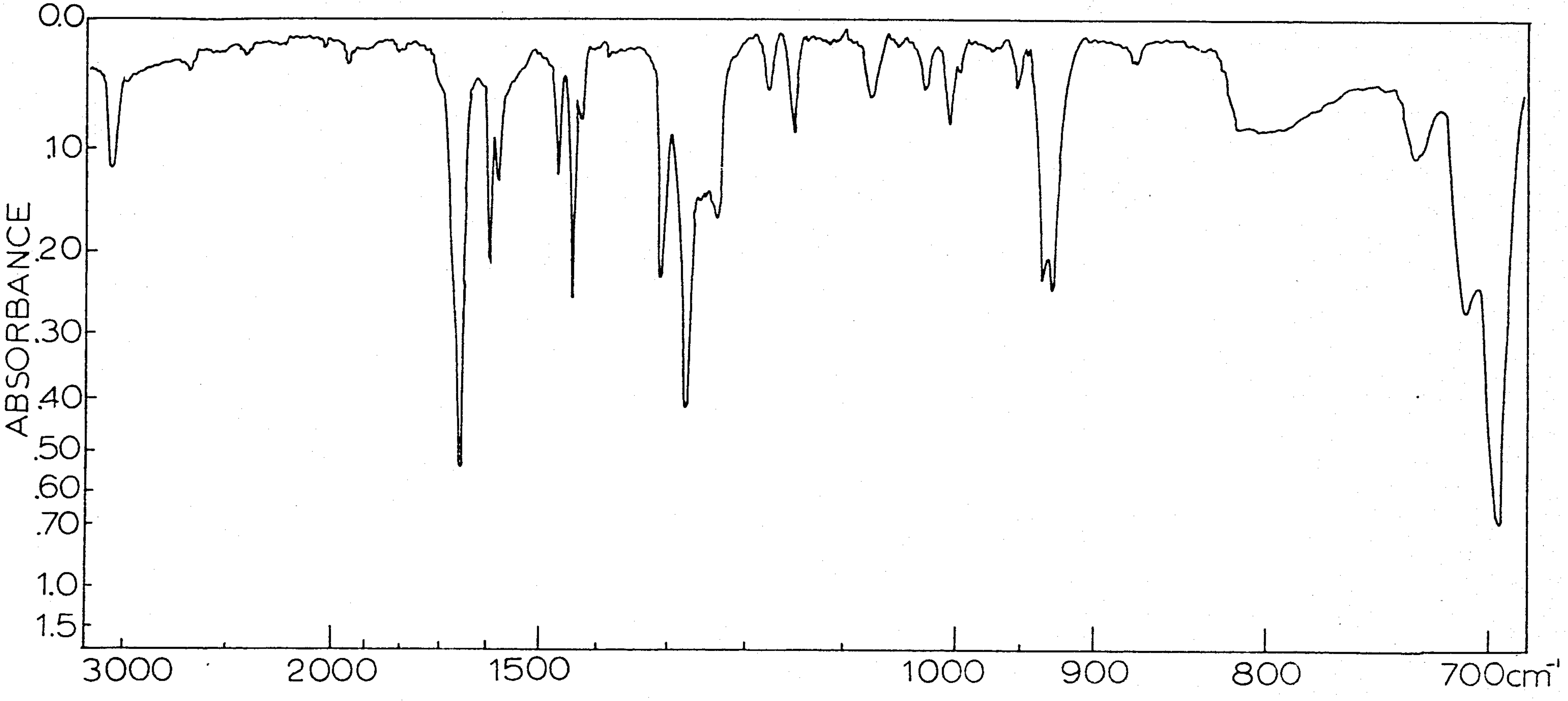


FIG. 3 - INFRARED SPECTRUM OF 2-PHENYLBENZOPHENONE IN CARBONTETRACHLORIDE SOLUTION (3.54%).

cyclohexane indicated a complex aromatic fused ring system, possibly 9,9-diphenylfluorene (38,39), 9,9'-spirobifluorene (40), or some other large molecule containing a fluorene type skeleton. Structure identification was not attempted, since the yield of this product was very small.

Benzophenone

The infrared spectrum of this viscous, pale yellow liquid was identical with that of an authentic sample of benzophenone. Mixed melting point of the 2,4-dinitrophenylhydrazone derivative prepared from this oil and authentic benzophenone-2,4-dinitrophenylhydrazone did not show melting point depression (m.p. 232-237°). Thus it was concluded that the fraction was benzophenone with traces of impurities which prevented crystallization of that relatively low melting compound (m.p. 49°).

2-Phenylbenzophenone

The infrared spectrum and melting point of this compound were identical with those of an authentic sample of 2-phenylbenzophenone, prepared by the method of Bradsher (31).

9-Phenylfluorenol

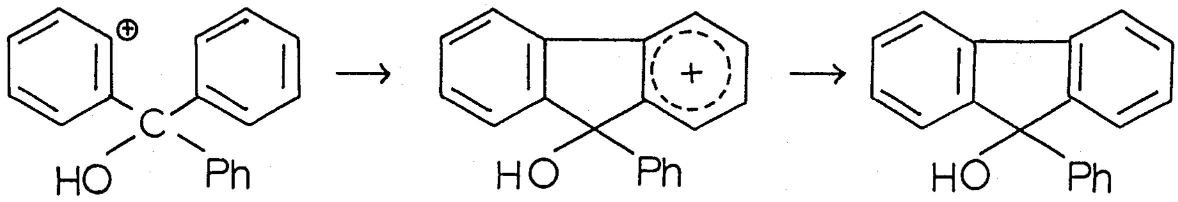
The infrared and ultraviolet spectra were identical with those taken of an authentic sample of 9-phenylfluorenol. Mixed melting point of the two samples did not show depression (85-87°).

The Reaction of 9-Phenylfluorenol and Formic Acid

9-Phenylfluorenol (0.0244 g.) was dissolved and boiled in formic acid (5 ml.; 97%). The solution, which was pale orange at first, turned colorless as a white precipitate formed. The amorphous white material was regained after an attempted recrystallization from benzene-ligroin mixture. The product could not be resolved by repeated elution chromatography to give a compound having a sharp melting point (m.p. observed 170-178°). The ultraviolet spectrum of the material taken in cyclohexane solution was similar to, but not identical with that of "Hydrocarbon X".

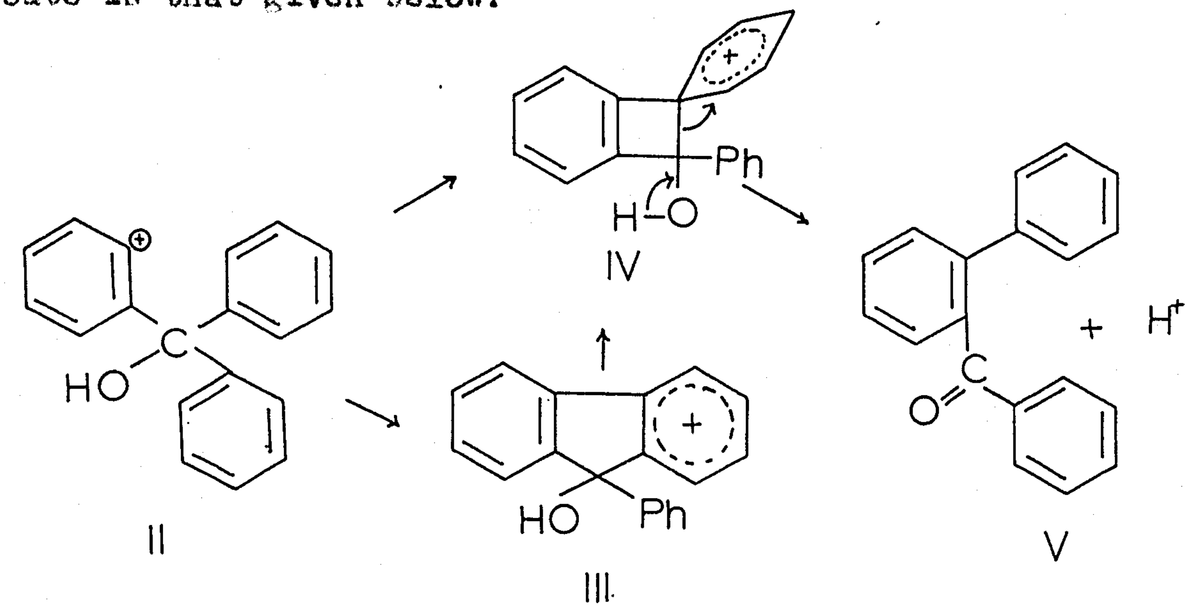
DISCUSSION

Our results do not differ greatly from those published by Stiles (28), except for the isolation of very small amounts of fragmentation and reduction products. As seen from Table 1., diazotization of 2-aminotriphenylcarbinol in formic acid gave five neutral products. The main product is 9-phenylfluorenol which arises from ring closure, as shown below:



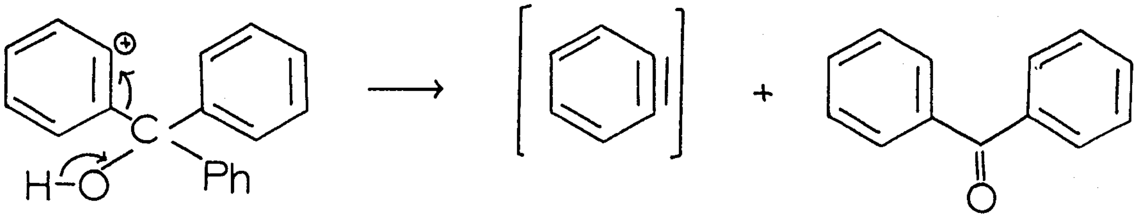
The small amount of 9-phenylfluorene is probably a reduction product due to the formic acid medium. It was shown that the 9-phenylfluorene is not a reaction product of 9-phenylfluorenol and formic acid. It is possible that some of the starting material was reduced to 2-aminotriphenylmethane and diazotization of this amine yielded 9-phenylfluorene. This possibility was not tested experimentally.

The mechanism proposed by Stiles may be followed in the formation of 9-phenylbenzophenone. The carbonium ion formed by the loss of nitrogen rearranges to give a cyclic intermediate (IV). This intermediate then would give rise to the ketone (V). A schematic representation of this route is that given below:



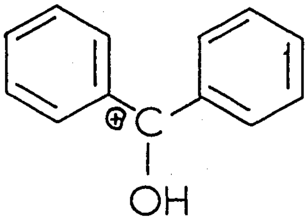
Carbonium ion (II) may cyclize to give either (IV) directly, or (III) which then rearranges into (IV). The carbonium ion (IV) then loses a proton giving the ketone (V). It may seem unnecessary to postulate a strained transition state involving a four membered ring. However, the structure of the ketones formed in the study of Stiles requires a 1,3-shift, and it is reasonable to expect that the same bonds would be broken and formed here too, regardless of the different solvent used.

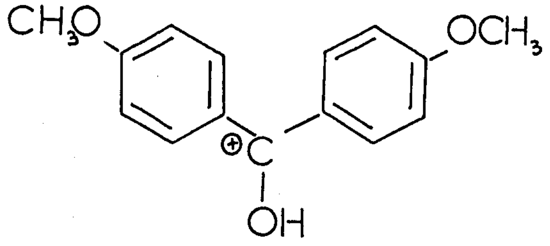
A small fraction of the reaction does proceed by the anticipated route:

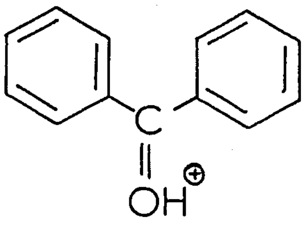


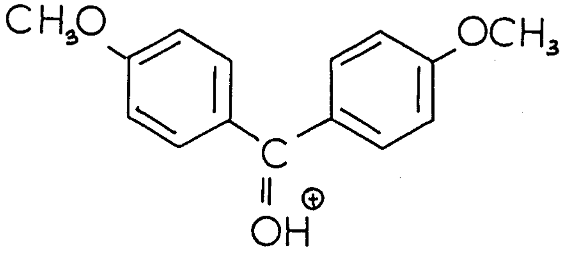
The benzyne formed has very short lifetime. It is attacked by the solvent carboxylate ions or any other nucleophile present. The identity of the final product is not known and its yield must be almost negligible. It is not surprising therefore that it had not been isolated from the reaction mixture.

Formic acid appears to favour benzyne formation more than aqueous sulfuric acid does. An obvious way to promote fragmentation further is to stabilize the carbonium ion fragmentation-product by electron donating groups. Thus, 2-amino-4'4"-dimethoxytriphenylcarbinol would give rise to carbonium ion VII whose stability is expected to be greater than that of VI.


VI


VII

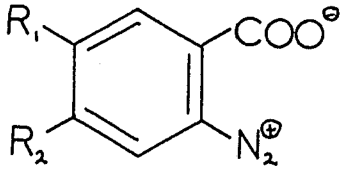

VIII


IX

These carbonium ions are actually the protonated ketones VIII and IX. The pK_{BH^+} values are -6.16 and -4.39 for VIII and IX respectively (37). Thus IX is considerably more stable than VIII.

Unfortunately, while the p-methoxy substituent increases the stability of the carbonium ion intermediate, it also enhances the reactivity of the starting material towards formic acid.

Stiles and co-workers (21) recently proved that the pyrolysis of substituted anthranilic acid diazonium carboxylates produce benzyne (X). The nature of the intermediate had been unequivocally established by showing that positions 1 and 2 are equivalent.



X

	R_1	R_2
a.	H	I
b.	I	H
c.	H	F
d.	H	NO_2

The type of fragmentation in this present investigation and that reported by Stiles are very closely related. The first step is most likely loss of nitrogen in both cases, followed by decarboxylation or carbon-carbon bond fission. In either instance a carbonium ion is the precursor of benzyne.

CLAIMS TO ORIGINAL FINDINGS

1. The use of magnesium bromide in Grignard reactions.
2. The detection of fragmentation in the deamination reaction of 2-aminotriphenylcarbinol.

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PART II

A STUDY OF RESTRICTED ROTATION ABOUT THE N-CO BOND BY NMR.

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ABSTRACT

The NMR spectra of certain N-substituted acetanilides and N-carboxy-ethylenimines were examined over a range of temperatures. The type of hybridization of the nitrogen atom in acetanilides cannot be established on the basis of their NMR spectra alone. Temperature dependence of the NMR spectra of N-substituted carboxy-ethylenimines strongly indicates sp^3 hybridization of the nitrogen atom in these molecules.

INTRODUCTION

The Use of Nuclear Magnetic Resonance in Rate Studies

Nuclear magnetic resonance spectroscopy is a very useful tool in studying rate processes. The slope and width of absorption lines are intimately related to time dependent structural changes.

The mathematical basis for determining rates from NMR spectra was developed by Gutowsky, Anderson and others. (1-4)

The simplest type of rate process is the exchange of individual nuclei between two positions or sites. If the exchange rate is slow, the spectrum consists of two separate signals; if it is rapid, only one signal appears in the averaged position. The above statement can be expressed in a mathematical form.

In order to observe sharp lines in the absence of exchange, a large value of T_2 is required. We shall assume equal populations, p_A and p_B, and lifetimes τ_A, τ_B at sites A and B:

$$p_A = p_B = \frac{1}{2} \qquad \tau_A = \tau_B = 2\tau$$

The resonance line centered on the mean frequency is described by the line shape function $g(\nu)$, which is given as: (5)

$$g(\nu) = K \frac{\tau(\nu_A - \nu_B)^2}{[\frac{1}{2}(\nu_A + \nu_B) - \nu]^2 + 4\pi^2\tau^2(\nu_A - \nu)^2(\nu_B - \nu)^2} \qquad (1)$$

where K is a normalizing factor and the frequency ν is measured in cycles per second. The resonance frequency of the line arising from nuclei at site A is designated as ν_A, and ν_B is associated with nuclei at site B. The function $g(\nu)$ depends only on the product $\tau|\nu_A - \nu_B|$. At very large values of τ

$$\frac{g(\nu)}{\nu_A - \nu_B} \approx \frac{K(\nu_A - \nu_B)}{4\pi^2\tau(\nu_A - \nu)^2(\nu_B - \nu)^2} \tag{2}$$

while as $\tau \to 0$

$$g(\nu) \approx \frac{K\tau(\nu_A - \nu_B)^2}{[\frac{1}{2}(\nu_A - \nu_B) - \nu]^2} \tag{3}$$

but at $\nu = \frac{\nu_A + \nu_B}{2}$

$$g(\nu) \approx \frac{K}{\pi^2\tau(\nu_A - \nu_B)} \tag{4}$$

Thus in the first case the spectrum consists of two lines, at ν_A and ν_B, but at small τ the signal gives a sharp maximum at $\frac{\nu_A + \nu_B}{2}$. A graphical representation for various values of $2\pi\tau(\nu_A - \nu_B)$ is given in Fig. 1. (5)

An expression for peak separation is easily found from equation (1) by differentiating with respect to ν and determining the maximum and minimum. Thus:

$$\text{separation of peaks} = \left[(\nu_A - \nu_B)^2 - \frac{1}{2\pi^2\tau^2}\right]^{\frac{1}{2}} \tag{5}$$

At very large τ the separation of peaks is $(\nu_A - \nu_B)$, therefore the above expression may be rewritten as:

$$\frac{1}{2\tau} = \pi \left[\frac{(\text{separation of peaks at large}\,\tau)^2 - (\text{separation of peaks})^2}{2} \right] \tag{6}$$

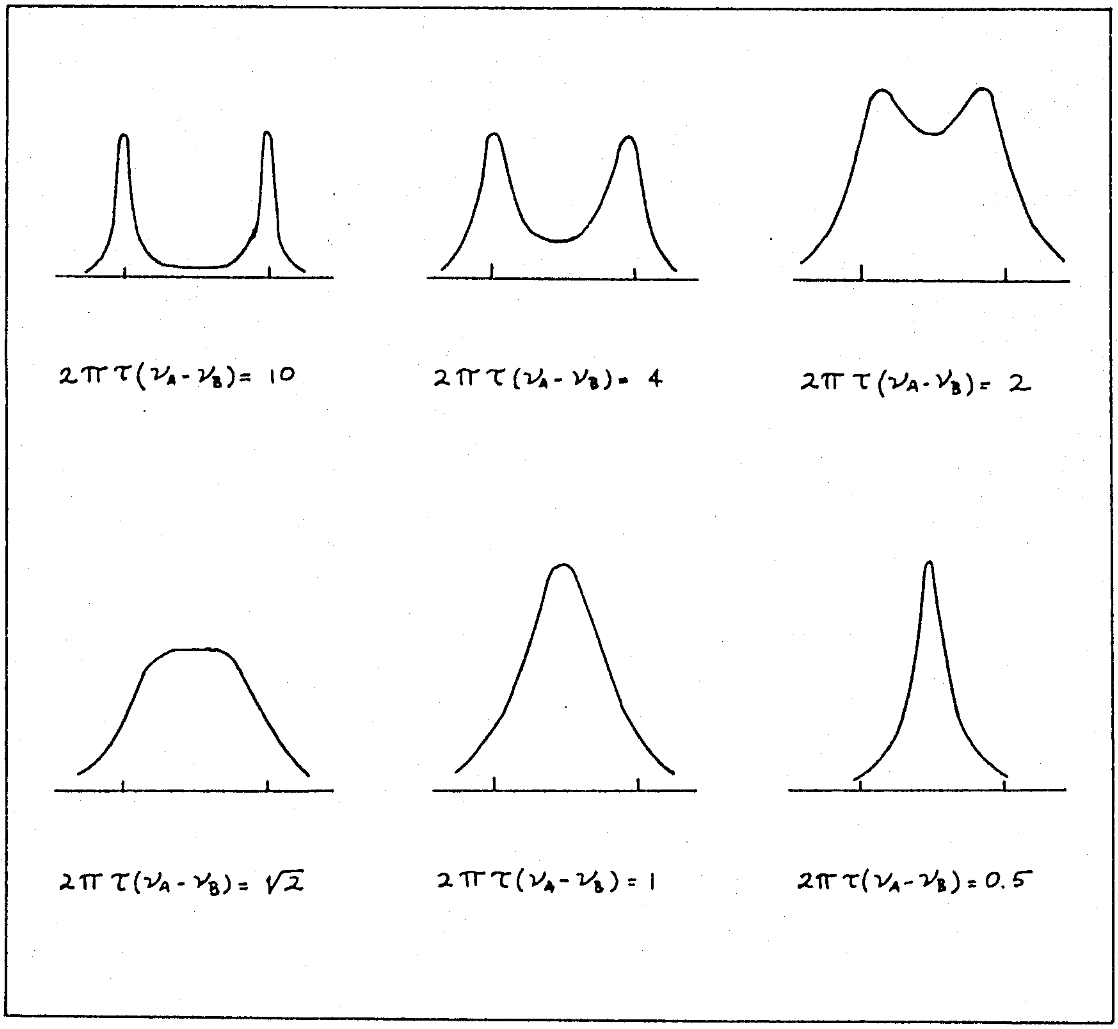


FIG. 1

Change of $\sigma(\nu)$ for increasing exchange rate between two positions with equal populations. Taken from Reference (5), p.223.

This equation may be utilized for the determination of τ as long as

$$\tau > \frac{\sqrt{2}}{2\pi(\nu_A - \nu_B)} \qquad (7)$$

The two peaks coalesce at $\tau = \frac{\sqrt{2}}{2\pi(\nu_A - \nu_B)}$. The temperature at which this takes place is defined as the coalescence temperature. Thus, the measurement of ν_A, ν_B and the coalescence temperature is sufficient for determining τ, unless the signal width is relatively large in comparison with ($\nu_A - \nu_B$). In this case, the relaxation time T_2 must be taken into account. The simple equation defining the intensity of absorption (V) is:

$$V = -\frac{1}{4}\gamma H_1 M_0 \frac{\tau(\omega_A - \omega_B)^2}{[\frac{1}{2}(\omega_A + \omega_B) - \omega]^2 + \tau^2(\omega_A - \omega)^2(\omega_B - \omega)^2} \qquad (8)$$

where:

γ = magnetogyric ratio

H_1 = oscillating magnetic field

M_0 = equilibrium value of the macroscopic moment, M

ω = angular frequency of field H_1

ω_A, ω_B = Larmor frequency of the corresponding nuclei

When T_2 must be included, this equation no longer applies, for τ becomes

$$\tau^{-1} = (T_2')^{-1} - (T_2)^{-1} \qquad (9)$$

The equation describing the intensity of absorption (V) in this case is equation (10), derived by Gutowsky and Holm.(4)

$$V = \frac{\gamma H_1 M_0 (1+\tau/T_2)P + QR}{P^2 + R^2} \qquad (10)$$

where:

$$P = \tau\left\{\left(\frac{1}{T_2}\right)^2 - \left[\frac{1}{2}(\omega_A+\omega_B)-\omega\right]^2 + \frac{1}{4}(\omega_A-\omega_B)^2\right\} + \frac{1}{T_2}$$

$$Q = \tau\left[\frac{1}{2}(\omega_A+\omega_B)-\omega-\frac{1}{2}(p_A-p_B)(\omega_A-\omega_B)\right]$$

$$R = \left[\frac{1}{2}(\omega_A+\omega_B)-\omega\right]\left(1+\frac{2\tau}{T_2}\right) + \frac{1}{2}(p_A-p_B)(\omega_A-\omega_B)$$

and all the other symbols have their usual meaning.

The expressions above were developed for rate processes involving a change in population of two sites. If the process is temperature dependent, then the typical first order rate equation is used.

$$k = k_0 e^{-E_a/RT} \qquad (11)$$

The rate constant k is inversely proportional to the lifetime of nuclei at any one site,

$$k = \frac{1}{2\tau} \qquad (12)$$

Thus,

$$\log \frac{1}{2\pi\tau(\nu_A-\nu_B)} = \log \frac{k}{\pi(\nu_A-\nu_B)} - \frac{E}{2.3RT} \qquad (13)$$

and a plot of $\frac{1}{2\pi\tau(\nu_A-\nu_B)}$ vs T^{-1} gives a straight line having slope E_a.

Spin multiplets may be collapsed by a similar mechanism. The coalescence temperature does not have the same precise meaning in this case, but it does give an indication of the rate.

Moment Analysis

The theory of moment analysis was developed by Anderson and McConnell (7). Their method offers means of analysing very complex or poorly resolved NMR spectra. This approach can be utilized in the absence of saturation, field inhomogeneities or nonlinear sweep. The analysis requires that the spectrum be divided into basic groups of multiplets, a, b, c... etc. The moment method calculates the multiplet moments of these basic groups. The multiplet moment (Ma) of a group a is defined as:

$$(M_a)^\tau = \frac{\sum_{mn} (\nu_{mn})^\tau L_{mn}}{\sum_{mn} L_{mn}} \qquad (14)$$

where ν_{mn} are the transition frequencies in group a and L_{mn} the corresponding line intensities. If all groups have the same width, the intensity may be taken as the line height; otherwise the area under the absorption line is measured.

Basic groups of multiplets, a, b, c... etc., arise if the nuclei within the molecule can be divided into groups A, B, C... etc., so that the multiplet a corresponds to magnetic transitions in group A only. Nuclei within a multiplet have chemical shifts of the same order as the coupling constants involved.

For a molecule containing only one basic group A, all nuclei have the same spin and magnetogyric ratio. Thus the moment equations are:

$$M_1 = N^{-1}\sum_i \Delta\nu_i = 0 \tag{15}$$

$$M_2 = N^{-1}\sum_i (\Delta\nu_i)^2 \tag{16}$$

$$M_3 = N^{-1}\sum_i (\Delta\nu_i)^3 \tag{17}$$

$$M_4 = N^{-1}\left[\sum_i (\Delta\nu_i)^4 + \tfrac{2}{3}I(I+1)\sum_{i<j}(\Delta\nu_i - \Delta\nu_j)^2 J_{ij}^2\right] \tag{18}$$

where

$$\Delta\nu_i = \nu_i - \langle\nu\rangle \tag{19}$$

The observable mean resonance frequency of the multiplet a is $\langle\nu\rangle$ and thus $\Delta\nu_i$ is the chemical shift. These equations show that the first three moments are not influenced by exchange coupling (i.e. indirect spin-spin coupling).

For a single basic multiplet containing two chemical groups with N_1 nuclei in group 1 and N_2 nuclei in group 2, (group 1 being displaced from the mean by $\Delta\nu_1$ and group 2 by $\Delta\nu_2$) the first moment equation is obviously:

$$N_1\Delta\nu_1 + N_2\Delta\nu_2 = 0 \tag{20}$$

The second moment is then expressed as:

$$\langle(\Delta\nu)^2\rangle = \frac{N_1 N_2}{(N_1+N_2)^2}\;(\Delta\nu_1 + \Delta\nu_2)^2 \tag{21}$$

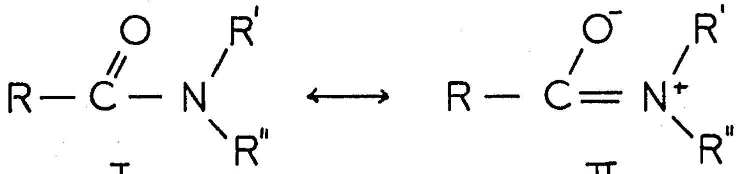
Thus, by measuring the second moment, the magnitude of the chemical shift is easily determined. Similarly, the fourth moment equation becomes:

$$\sum_{i}^{N_1}\sum_{j}^{N_2} J_{ij}^2 = \frac{3N_1N_2\langle(\Delta\nu)^2\rangle}{2I(I+1)(N_1+N_2)}\left\{\frac{\langle(\Delta\nu)^4\rangle}{\langle(\Delta\nu)^2\rangle^2} - \frac{N_1^3+N_2^3}{N_1N_2(N_1+N_2)}\right\} \qquad (22)$$

This equation gives the mean-square coupling constant and is independent of the coupling constant between nuclei in the same group.

Restricted Rotation in Amides

Partial double bond character of the C-N bond of aliphatic amides was first postulated by Pauling.(8) He predicted that resonance structure II should give an important contribution to the ground state of those amides.



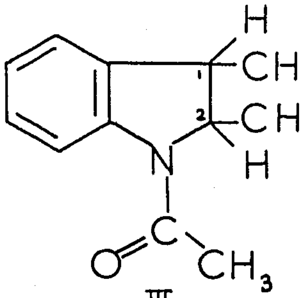
I   II

X-ray studies of amides showed that the RCONR' groups are planar. The observed C-N bond distance (9), 1.32 Å, corresponds to a bond order of 1.8. Microwave spectra confirmed the contraction of "normal" C-N bond length (10). This bond shortening is due partly to contraction of the atomic radii which are determined by their state of hybridization, and partly to some double bond character of the C-N bond.

Phillips (11), and Gutowsky and Holm (4) were the first investigators using NMR spectroscopy to demonstrate restricted rotation in amides. Due to the nonequivalence of the two N-methyl groups of dimethylformamide and dimethylacetamide they observed two N-methyl lines in the spectra. The splitting was found to be proportional to the applied field strength, and thus is a chemical shift rather than a simple spin-spin splitting (5). On raising the temperature, the two lines coalesce. Assuming that T_2 is independent of the rate of reorientation and change in temperature, the rotational energy barrier can be calculated for these amides by measuring their NMR spectra over a range of temperatures.

Similar studies of N-aryl amides (4,12) on the other hand, showed no such effect.

Anet and Muchowsky (13) were the first investigators to observe restricted rotation about a carbon-nitrogen bond in a cyclic amide. They studied the NMR spectrum of N-acetyl-2,3-dimethyl indoline (III), and found a small, low field aromatic hydrogen peak beside the main aromatic region. The proton at position 2 gave a broad band at much lower field than expected.



III

Upon heating to 70°, the low field band disappeared and the H(2) spectrum was resolved into a sharp multiplet. This effect would be expected if there were restricted rotation about the carbon-nitrogen bond. The double bond is stabilized through conjugation with the benzene ring, so that the carbonyl group becomes coplanar with the phenyl ring. The molecule can exist in two conformations, depending on the orientation of the carbonyl group. Due to the magnetic anisotropy of the carbonyl group, the neighbouring aromatic hydrogen and H(2) are shifted to lower field. Hydrogen bonding between the carbonyl group and H(2) or the ortho-hydrogen of the phenyl ring would also lower the frequency of these proton resonance signals. (14,15)

Thus it seemed desirable to exmine some other related systems to investigate the possibility of establishing a correlation between the rotational energy barrier and electronic or steric factors. Various N-substituted arylamides and ethylenimines were selected for this study.

EXPERIMENTAL

MATERIALS

N-Phenylacetanilide

This compound was prepared from commercially available diphenylamine, following the method of Kaufman (16). Colorless crystals were obtained, m.p. 100-103° (lit.102-104°).

N-i-Propylacetanilide

N-i-Propylaniline was prepared by the method of Emerson and Neuman (17). The aniline was acetylated as described by Hickinbottom (18). Colorless crystals were obtained, m.p. 35° (lit. 38°).

N-t-Butylacetanilide

No satisfactory method was found in the literature for the preparation of N-t-butylaniline, therefore the following synthetic route was devised:

t-Butylamine (15 ml.; 0.143 mole) and 15 ml. anhydrous ether was placed in a 350 ml. three-necked flask, equipped with a stirring magnet, dropping funnel, condenser with drying tube, and a serum cap. n-Butyl lithium (20 ml. of a 15.2% solution in hexane; 0.047 mole), commercially obtained from Foote Co., was slowly injected through the serum cap with a syringe. Then bromobenzene (4.2 ml.) in ether was added through the dropping funnel. The solution was stirred under reflux for about five hours. Water was then added slowly, with cooling, to extract the inorganic material. The organic solution was dried over anhydrous sodium sulfate and the hexane distilled off. The residue was distilled under vacuum and the t-butylaniline collected at 86°/1 mm. The yield was 2.81 g. (47%).

The amine was reacted with acetic anhydride to obtain N-t-butylacetanilide (19). Recrystallization from ligroin gave colorless crystals, m.p. 54°(lit.55°).

Ethylenimine Derivatives

The preparations described by Bestian (20) were employed in the synthesis of the following compounds:

N-acetylethylenimine, b.p. 28°/2 mm. (lit. 42°/20 mm.)
N-carbomethoxyethylenimine, b.p. 63°/22 mm. (lit. 60°/21 mm.)
N-(dimethylamidocarboxy)-ethylenimine, b.p. 24°/0.1 mm. (lit. 79°/11 mm.)

Certain small scale preparations were also carried out, without isolating the intermediate products, as described below.

N-Carbomethoxyethylenimine

2-Chloroethylamine hydrochloride (1 g.) was dissolved in water (3.5 ml.) and added to a solution of sodium hydroxide (1 g.) in water (3.5 ml.) in a test tube. The reaction mixture was kept at 80° for three minutes, then quickly cooled. Methyl chloroformate (1.05 ml.; 1.5 times the theoretical amount) was added and the mixture was shaken for a few minutes. The urethane formed was extracted with methylene dichloride, and the extract was transferred to an NMR tube. The solvent was evaporated and the sample redissolved in the appropriate solvent chosen for low temperature studies.

Prolonged heating at any stage of the preparation led to isomerisation.

N-(Dimethylamidocarboxy)-ethylenimine

This compound was prepared in a similar manner, using N,N-dimethylcarbamyl chloride instead of methyl chloroformate. The N,N-dimethylcarbamyl chloride was synthetized by the method of Hantzsch (21), b.p. 25°/0.5 mm. (lit. 165°/760 mm.)

N-Carbomethoxy-2,2-dideuteroethylenimine

The same small scale preparation was carried out as that described above, using 2-chloro-2,2-dideuteroethylamine hydrochloride as the starting material for the ethylenimine.

2-Chloro-2,2-dideuteroethylamine Hydrochloride

A modified form of the method of Weissbach and Sprinson (22) was utilized. An ethereal solution of lithium aluminium deuteride (1.06 g.; 0.025 mole) was placed in a 100 ml. three-necked flask, equipped with a magnetic stirrer, a reflux condenser with a drying tube, and a small conical flask connected to the third neck by tygon tubing. Glycine ethyl ester hydrochloride (2.135 g.; 0.020 mole) was added from the small flask to the reaction vessel at a rate sufficient to maintain the ether reflux. After all of the hydrochloride was added, the reaction mixture was stirred for an additional half hour. Then the excess lithium aluminum deuteride was decomposed with a small amount of 5% sodium hydroxide solution and the reaction mixture transferred into a continuous extractor. The reaction mixture was extracted for 48 hours with ether, containing 6 ml. of 20% hydrochloric acid. The ether was evaporated and the residual amine hydrochloride was crystallized from hot absolute ethanol by the addition of dry ether. The yield was 320 mg. (62%).

All compounds synthetized were identified on the basis of their IR spectra as well as by comparing their physical constants with those recorded in the literature.

Measurement

All NMR spectra were taken on a Varian V-4302 high resolution spectrometer at 60 Mc/sec. Care was taken to set the radio frequency power well below saturation level and to select a pure absorption mode in order to obtain the correct intensities for moment analysis.

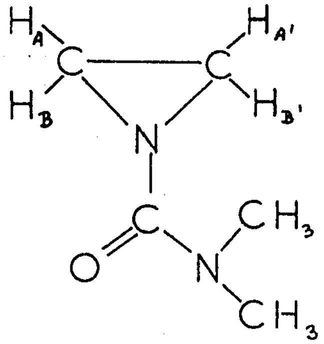
Solutions for low temperature measurement were prepared in the NMR tubes. The tube containing the sample and a small amount of tetramethyl silane was immersed into an acetone-Dry Ice cooling bath. The suitable gaseous solvent was condensed directly into this mixture. No effort was made to determine the concentration of these solutions.

For low temperature measurements the samples were cooled by boiling off liquid nitrogen and passing the cold gas into the spinner jacket. The temperature was controlled by regulating the rate of heating of the liquid nitrogen. The temperature was measured by a copper-constantan thermocouple, with the reference junction at 0°. These readings were converted into degrees centigrade on the basis of the standard calibration table for this thermocouple, as given by Roeser and Wensel, National Bureau of Standards. (23) Direct calibration showed that all voltage readings had to be corrected by -0.5mv. within the temperature range studied.

For moment analysis, measurements were made by placing a millimeter grid on the spectrum and recording intensities as "heights" relative to an arbitrary base line. These values were fed into an IBM 650 computer which was programmed to calculate M_2, M_3 and M_4. Calculations were made on spectra taken in different solvents, at increasing and decreasing magnetic fields and with various sweep rates.

Moment Analysis Calculations

The moment analysis for spectra A - H were carried out on the basis of the following assignment:



Equation (18) was used, with $N_1 = N_2 = 2$. Thus

$$(J_{AB}^2 + J_{AB'}^2)^{\frac{1}{2}} = \left[\frac{2(M_4 - M_2^2)}{M_2}\right]^{\frac{1}{2}}$$

where the values of M_2 and M_4 were obtained from the computer results.

RESULTS

N-i-Propylacetanilide

The spectrum of N-i-propylacetanilide in carbon-tetrachloride consists of a methyl doublet (8.90, 8.89 τ), a single methyl line (8.6 τ) and a complex aromatic peak (2.74 τ). No spectral changes were observed upon increasing the temperature to 65°. (Fig. 2.)

N-t-Butylacetanilide

N-t-butylacetanilide gives a straightforward NMR spectrum. There is a low field aromatic band (2.72 τ), a methyl peak at 8.45 τ, and a sharp absorption line at 8.67 τ corresponding to the t-butyl group. A carbon-tetrachloride solution of the compound was cooled to -20°, and the spectrum was taken with and without added benzene. In no case was there any change in shape or relative intensity of the methyl peaks. (Fig. 3.)

N-Phenylacetanilide

Two peaks are present in the NMR spectrum of N-phenylacetanilide. The low field broad band at 2.83 τ is due to ten protons of the phenyl rings, while the methyl group gives rise to a sharp line at 8.09 τ. (Fig. 4.)

Low temperature measurements on a carbondisulfide solution of the compound showed a gradual peak broadening in the aromatic region. At -92° the spectrum shows two distinct but complex peaks. The "coalescence temperature" is about -8°. (Fig. 5.)

ETHYLENIMINE DERIVATIVES

N-Acetylethylenimine

The spectrum of N-acetylethylenimine in vinyl chloride consists of two closely spaced lines at 7.92 τ and 7.85 τ for the methyl and methylene peaks respectively. (Fig. 6.) These assignments are based on relative intensities of the two peaks. Broadening of both lines was observed below -119°. The ring protons gave a much broader band than the methyl protons, but no splitting occurred. The addition of toluene to the vinyl chloride solution did not cause any change in the spectrum.

N-Carbomethoxyethylenimine

The spectrum of N-carbomethoxyethylenimine taken in vinyl chloride solution contains a methylene line at 7.79 τ and a sharp methoxy peak at 6.36 τ. (Fig. 7.) Upon cooling, the former broadens and finally splits into a closely spaced, strongly overlapping broad doublet at about -86°. Addition of toluene reduces the chemical shift between these two lines, and only broadening was detected within the temperature range measured (down to -117°).

The spectrum of N-carbomethoxy-2,2-dideuteroethylenimine was identical with that of the undeuterated one, except for the methylene peak intensity, which in this case corresponded to two protons only.

N-(Dimethylcarboxamido)-ethylenimine

The spectrum of this urea was examined in a variety of solvents. In freon ($CHClF_2$) no spectral changes could be detected down to -150°. The spectrum in vinyl chloride was the same as in other solvents: an N-methyl doublet centered around 7.10 τ and a broad methylene singlet at 7.96 τ were found. (Fig. 8.) The methylene peak had split into a doublet at -85° (the separation of maxima being 2.06 cps.; Fig. 9b). The coalescence temperature can be taken as about -77°.

Addition of toluene greatly enhanced the splitting. The coalescence temperature remained essentially the same (about -75°), but the peak separation increased to 9.3 cps. at -88°. The peak pattern was found to be roughly a quartet. (Fig. 9c.) Similar solvent effects were observed using styrene, ethylbenzene and furan. (Fig. 9d.)

The resolution permitted moment analysis in these cases. Three solvent systems were chosen for such measurement, and the results are summarized in Table I.

The chemical shifts are very different in each case, but fairly consistent coupling constants are obtained, regardless of the solvent used. The large deviation in the value of $(J_{AB}^2 + J_{AB'}^2)^{1/2}$ calculated for spectrum G is probably due to erroneous intensity measurements.

TABLE 1

Moment Analysis Results for N-(Dimethylcarboxamido)-ethylenimine

Spectrum Number	M_2 Linear Units	M_4 Linear Units	Conversion Factor	M_4 $(cps)^4$	M_2 $(cps)^2$	$2(M_2)^{\frac{1}{2}}$	$\left[\frac{2(M_4-M_2)}{M_2}\right]^{\frac{1}{2}}$	Mean $(J^2_{AB}+J^2_{AB'})^{\frac{1}{2}}$
A*	4.62	60.66	1.39	84.3	6.42	5.06	3.67	3.96
B*	6.28	126.5	1.39	175.8	8.73	5.90	4.26	
C†	19.05	661.5	1.43	946.0	27.2	10.42	3.89	3.92
D†	19.57	684.9	1.39	952.0	27.2	10.42	3.94	
E‡	10.64	245.8	1.28	314.6	13.6	7.38	4.37	4.31**
F‡	10.19	235.0	1.40	329.0	14.2	7.54	4.24	
G‡	18.04	703.5	1.07	752.6	19.3	8.78	6.27	
H‡	12.86	363.8	1.27	462.0	16.4	8.10	4.32	

* Solvent is vinyl chloride
† Solvent is vinyl chloride with toluene added
‡ Solvent is furan
** Mean value calculated excluding value from spectrum G. Including G the mean value is 4.80

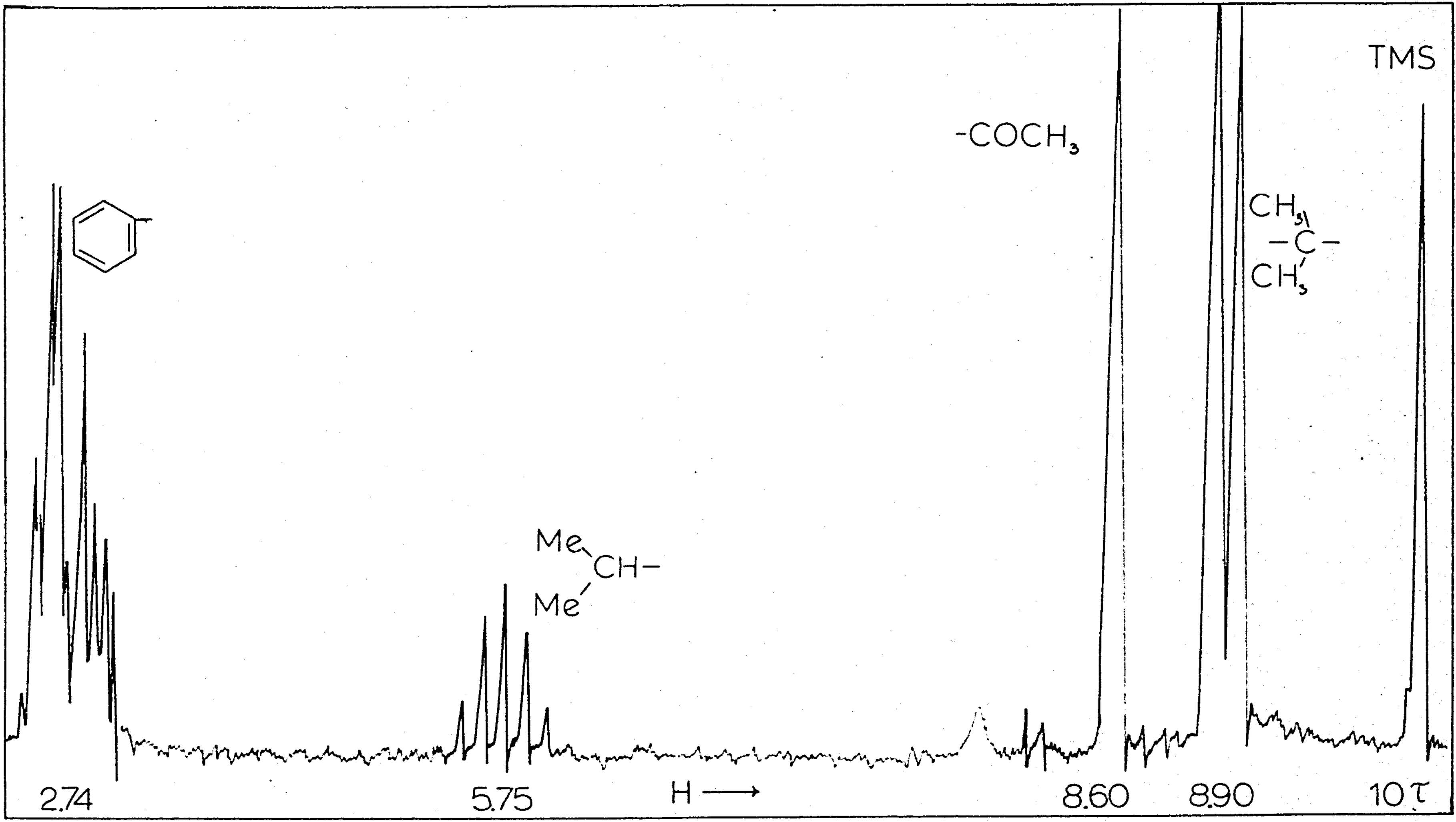


FIG. 2 - NMR SPECTRUM OF N-i-PROPYLACETANILIDE IN CARBONTETRACHLORIDE SOLUTION AT 65°

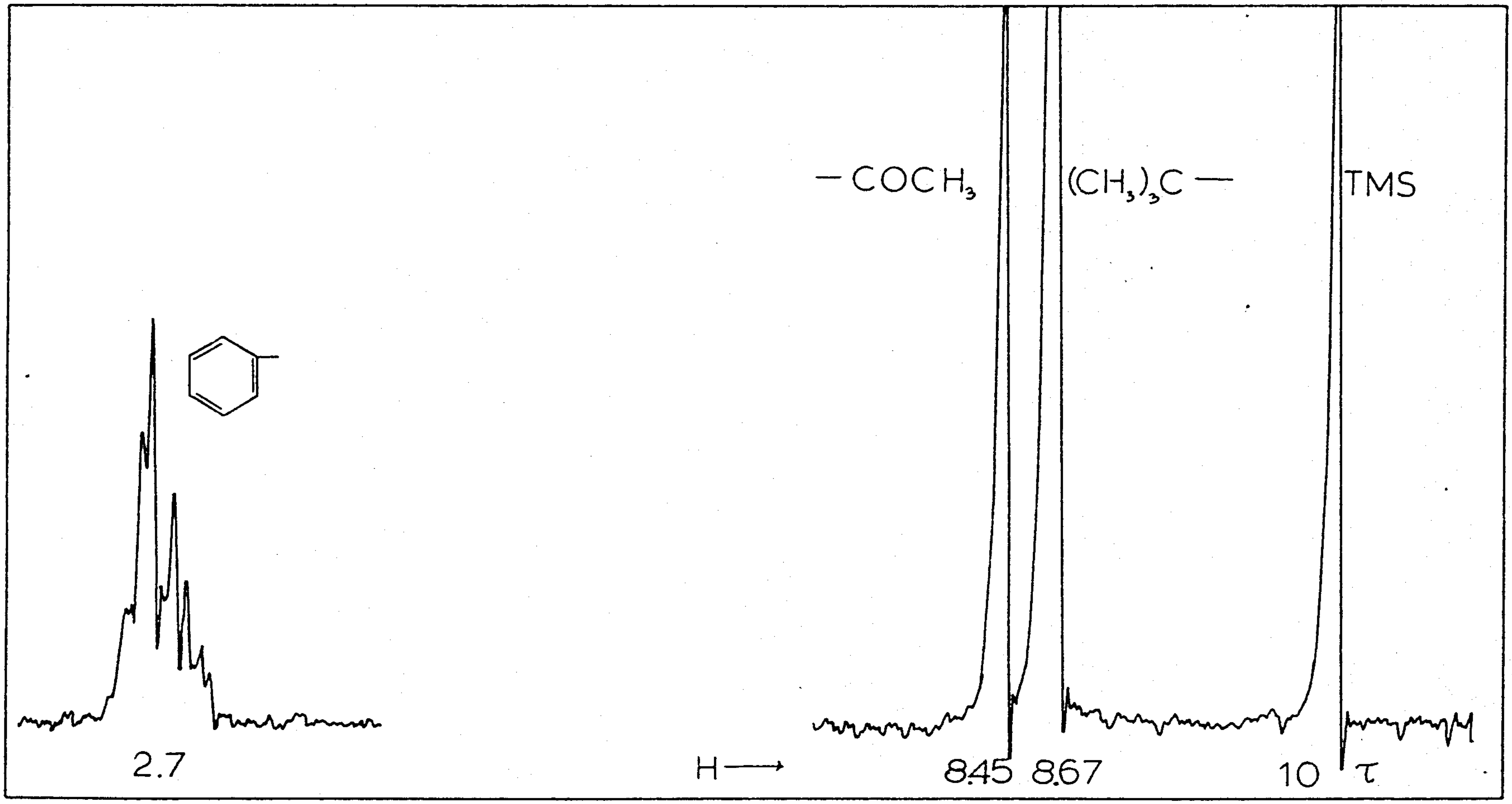


FIG. 3 - NMR SPECTRUM OF N-t-BUTYLACETANILIDE IN CARBONTETRA-CHLORIDE SOLUTION AT ROOM TEMPERATURE.

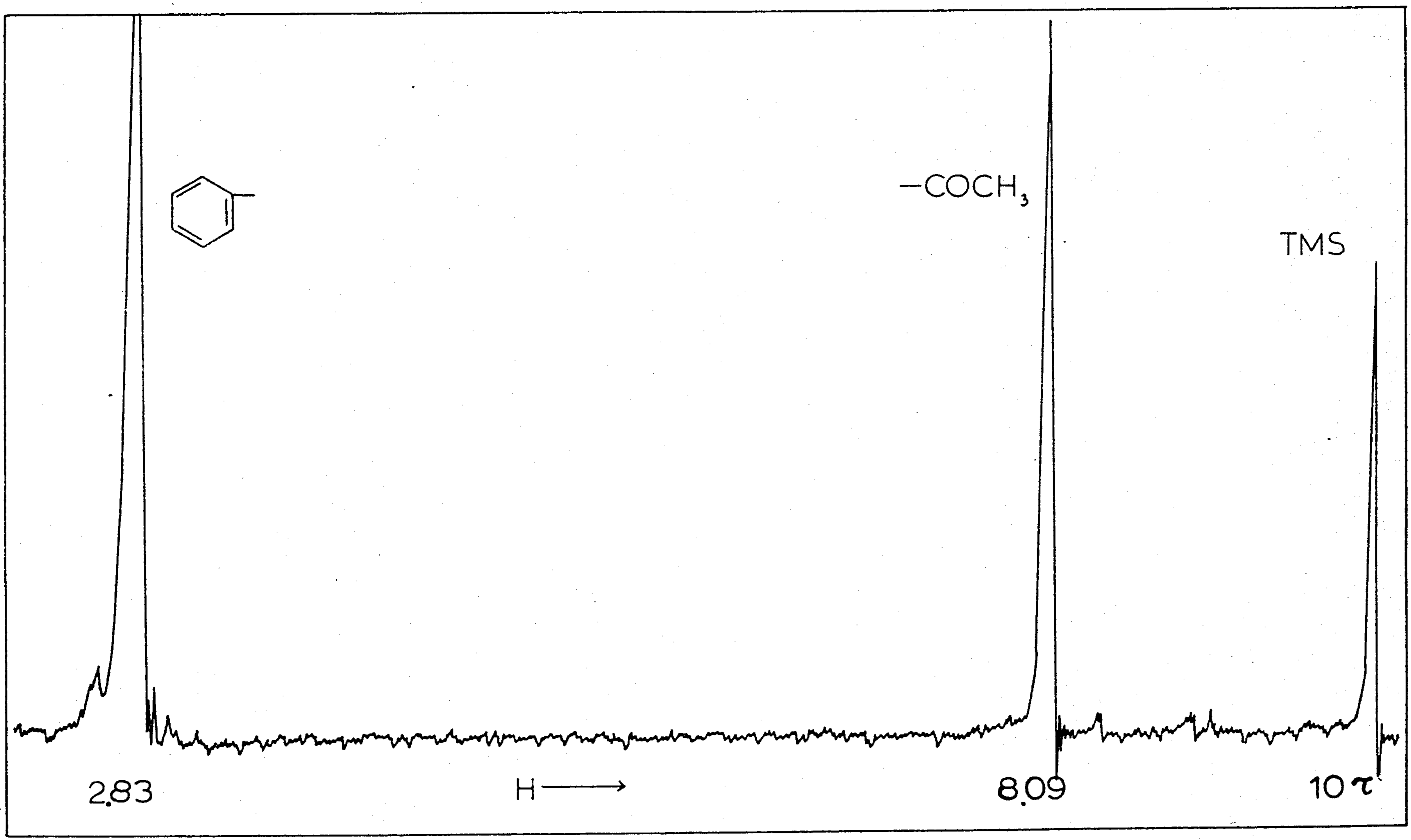


FIG 4 - NMR SPECTRUM OF N-PHENYLACETANILIDE IN CARBONDISULFIDE SOLUTION AT ROOM TEMPERATURE.

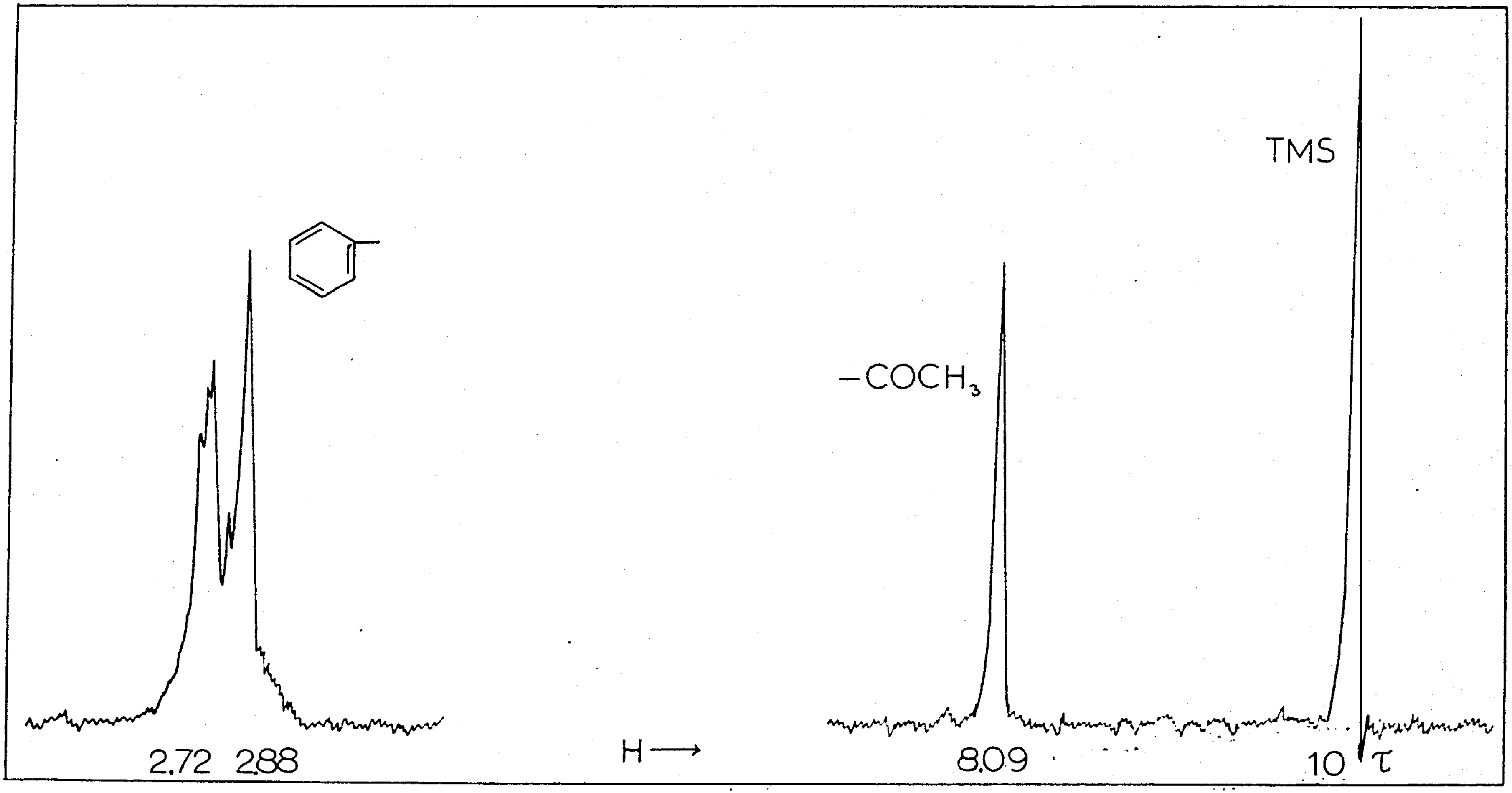


FIG. 5 - NMR SPECTRUM OF N-PHENYLACETANILIDE IN CARBONDISULFIDE SOLUTION AT -105°

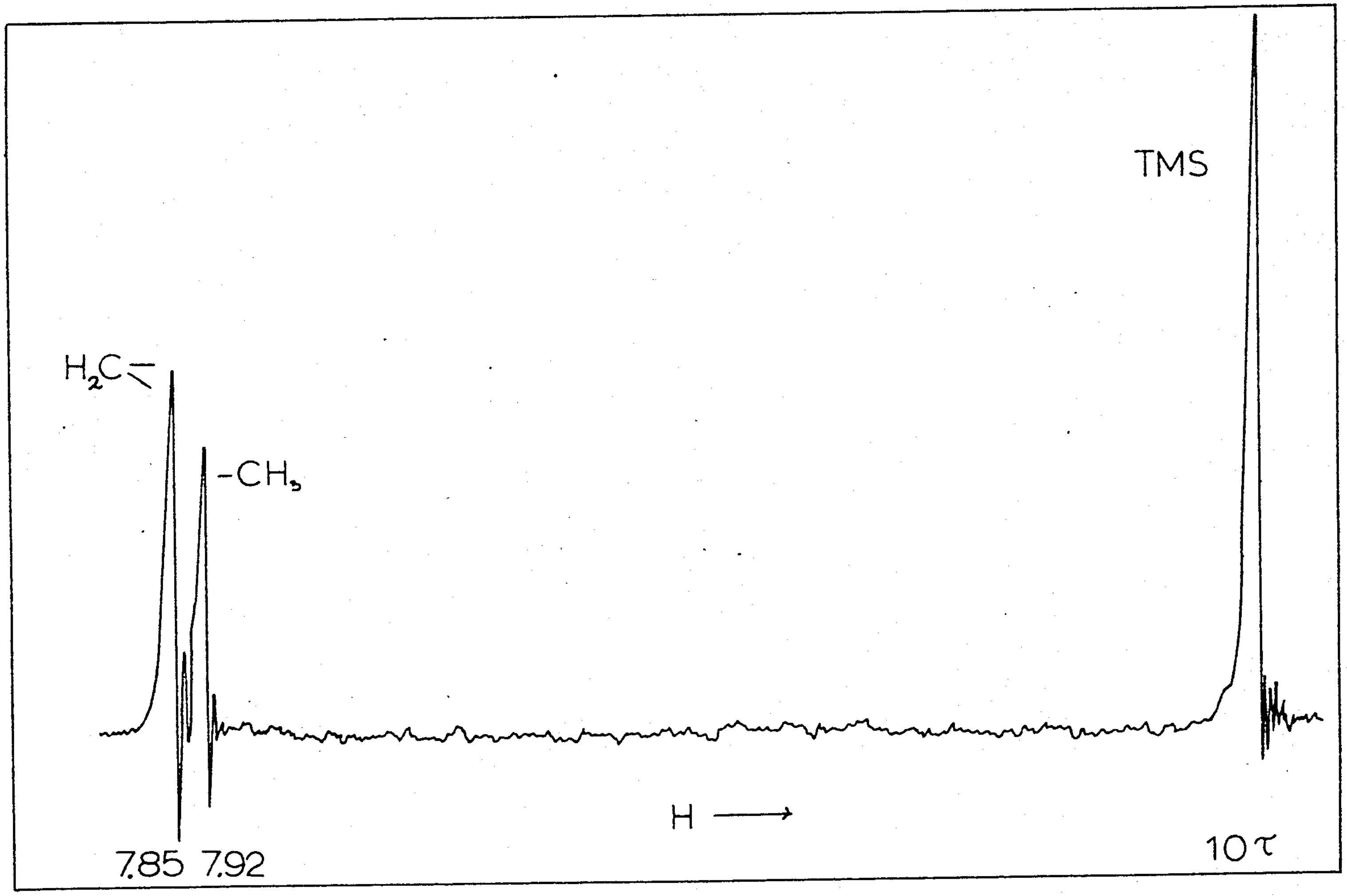


FIG. 6 - NMR SPECTRUM OF N-ACETYLETHYLENIMINE IN VINYL CHLORIDE SOLUTION.

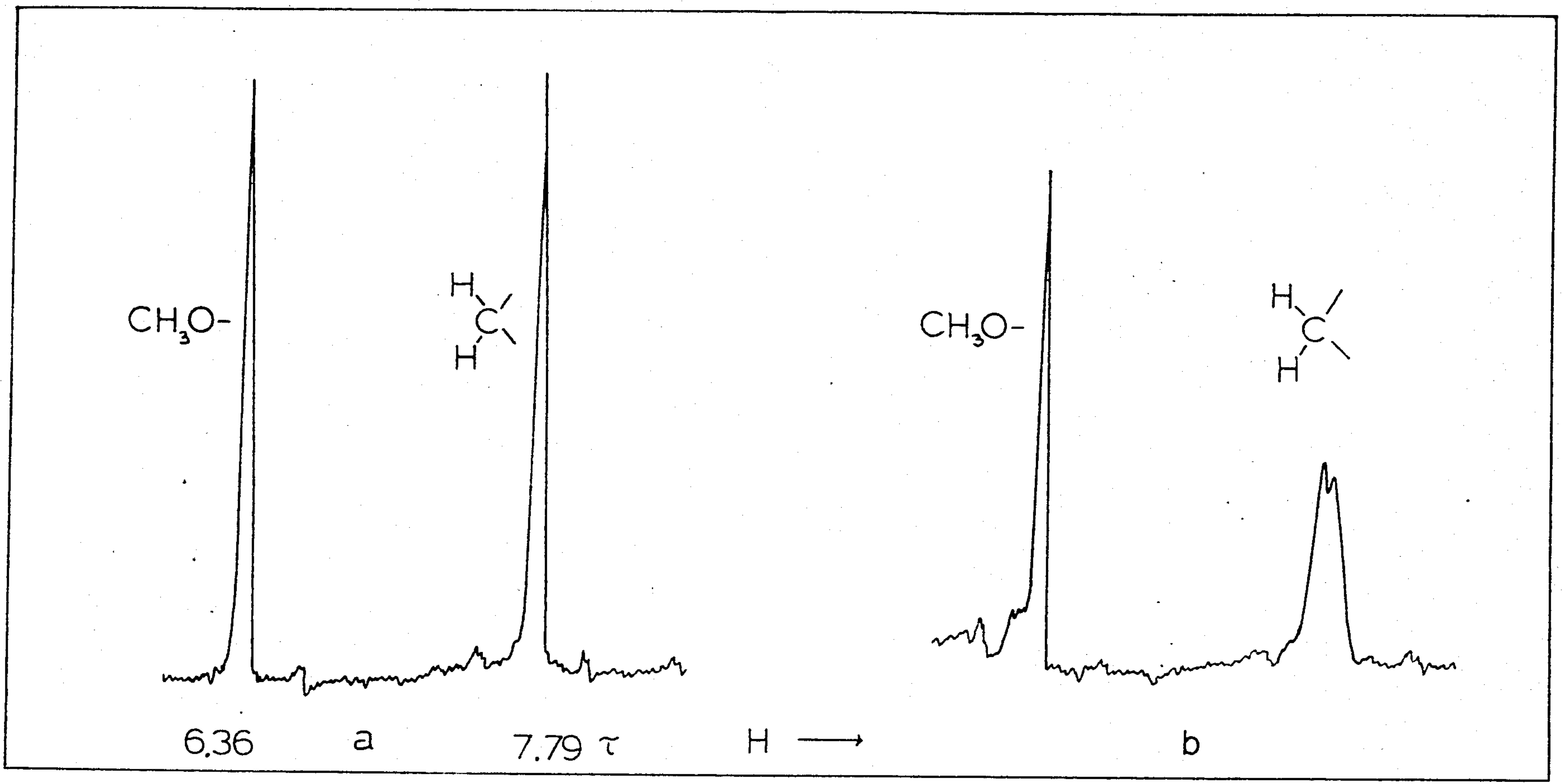


FIG.7 - NMR SPECTRUM OF N-CARBOMETHOXYETHYLENIMINE IN VINYL CHLORIDE SOLUTION: a. AT -72° b. AT -98°.

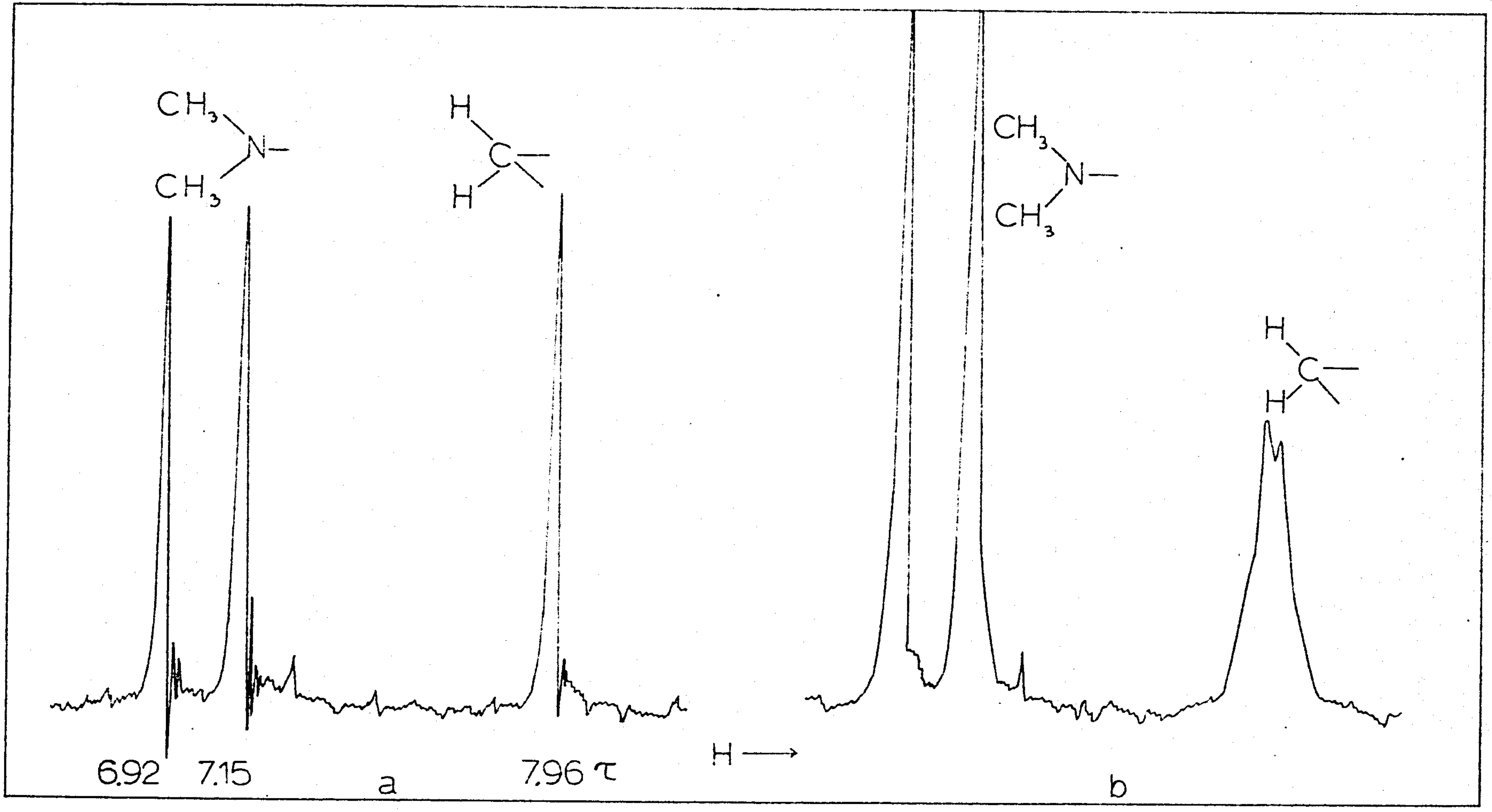


FIG.8- NMR SPECTRUM OF N-(DIMETHYLCARBOXAMIDO)-ETHYLENIMINE IN VINYL CHLORIDE: a. AT -44° b. AT -90°

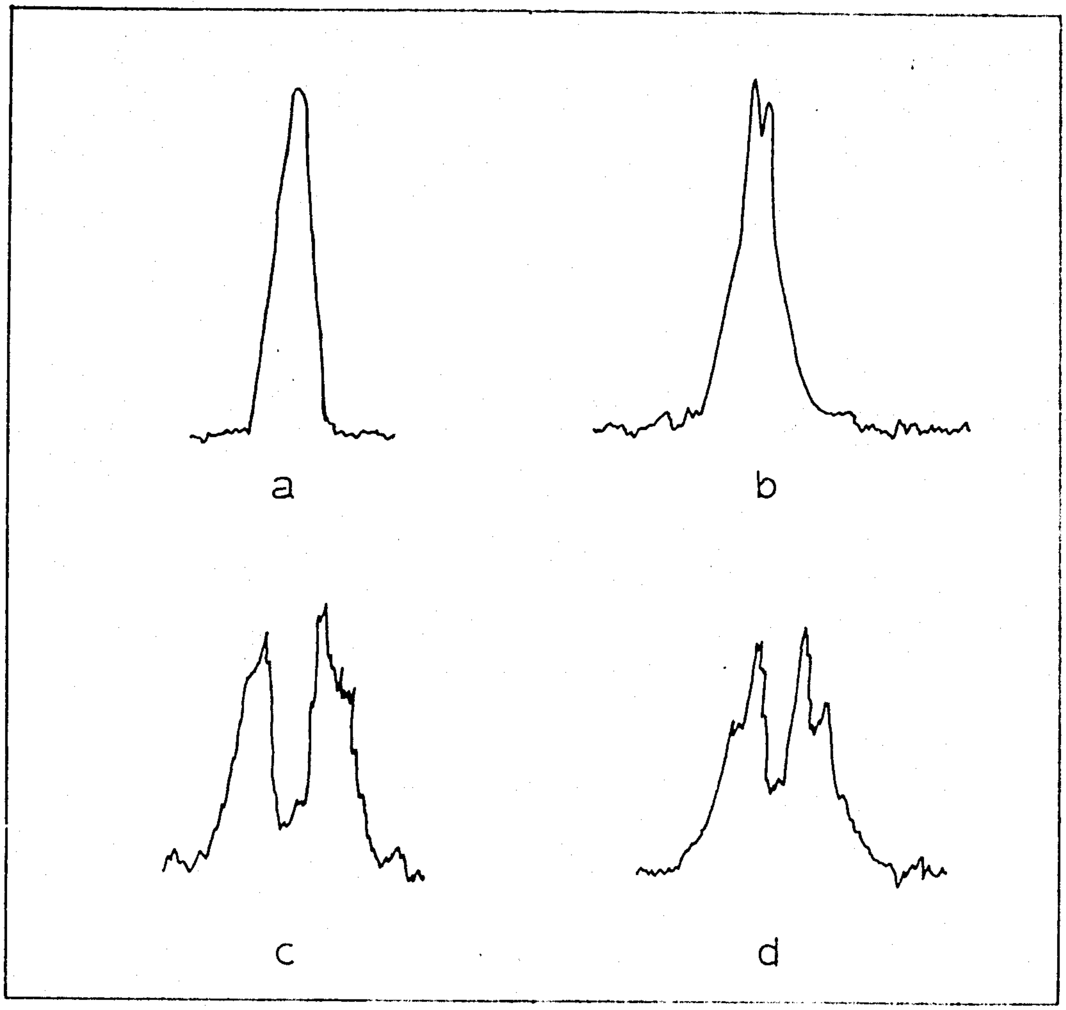


FIG.9 - RING PROTON RESONANCE OF
N-(DIMETHYLCARBOXAMIDO)-ETHYLENIMINE

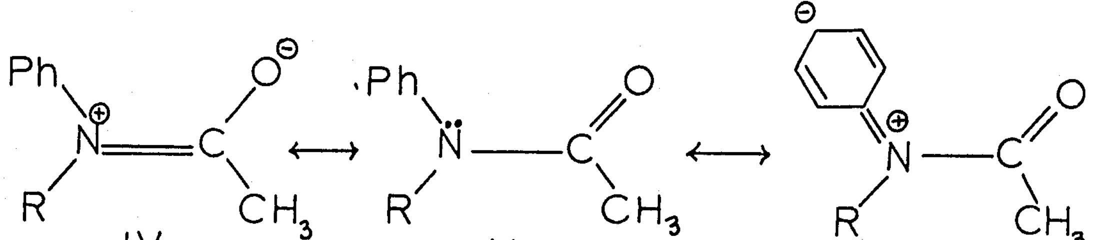
a. in freon at -100°
b. in vinyl chloride at -90°
c. in vinyl chloride with added toluene at -92°
d. in furan at -97°

DISCUSSION

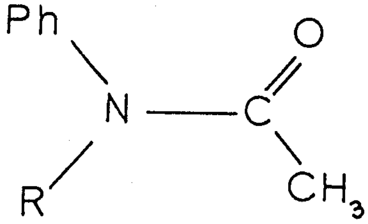
N-Substituted Acetanilides

The object of this study was to examine the effect of various R substituents on the NMR spectra of compounds in the series of Ph-N(R)-CO-CH_3. Earlier workers (4,10) have shown that the nitrogen atom in aliphatic amides is close to sp^2 hybridized. In contrast, it is known that the nitrogen atom of aniline is nearly sp^3 hybridized (31).

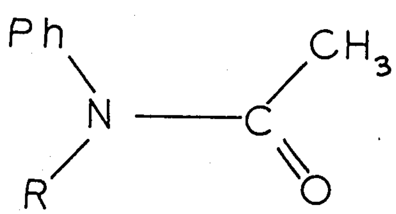
Therefore, in molecules containing the basic unit Ph-N(R)-CO-CH_3, structure IV should give a much more important contribution to the ground state resonance hybrid than VI. As a result of a significant contribution of structure IV to the resonance hybrid, the molecule should exist in two conformations, VII and VIII.



IV V VI



VII



VIII

NMR is a potentially suitable tool for detecting the position of equilibrium between the two conformers and determining the rate constant for the interconversion of conformers. The necessary requirements, for such measurement to be made, are:

1. The less stable conformation must have a sufficiently large population to allow detection by NMR. Generally, a minimum of 1 to 10% is required.

2. The NMR spectra of the conformations must differ enough to permit observation, and the change of one conformation to the other must result in the interchange of at least two non-superimposable lines of the spectra. If the spectrum observed is shown to be a superposition of spectra of two conformations, a maximum value for the rate constant can be estimated (6) from equation (23):

$$\frac{k}{\pi} = \left[\frac{\delta^2 - \Delta^2}{2}\right]^{\frac{1}{2}} \tag{23}$$

where Δ is the frequency separation of peak maxima,
and δ the chemical shift.

When the observed spectrum is an averaged one, the value of ν may be unknown. If ν is zero, no conclusion can be drawn about the presence or absence of energy barriers. If ν is judged to be large on the basis of other considerations, a minimum value of the rate constant may be postulated but its value is very uncertain.

3. The rate constant for the conversion of one conformation to the other must be of the order of $1/2\pi\nu$ sec^{-1} (see

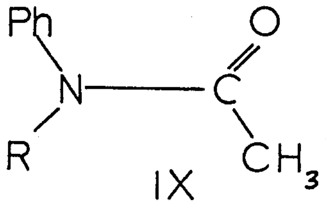
p.5) within the temperature range at which high resolution NMR spectra can be taken (-150° to 250°). Measurements at various temperatures are necessary to evaluate the activation energy and rate constant.

Previous work showed that no change takes place in the NMR spectrum of N-methylacetanilide upon temperature variation (4). However, more complex systems where the nitrogen is incorporated into a fused ring system, such as N-acetyl derivatives of *cis*-and *trans*-2,3-dimethylindolines (13) and the alkaloid strychnospermine (32), do show restricted rotation about the N-CO bond.

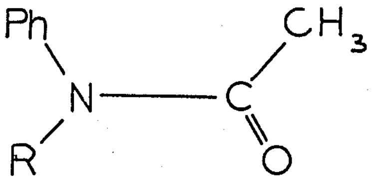
In order to investigate the effect of the size of the R group, studies were made when R was isopropyl, t-butyl and phenyl. Only in the last case was restricted rotation shown in the NMR spectra. The broad phenyl resonance peak observed at room temperature separated into two complex peaks of equal intensity below 8°. There were no low field proton resonances analogous to those found in the spectrum of N-acetyl-2,3-dimethylindoline (13), but this is to be expected, as here the phenyl groups cannot become coplanar with the amide group.

The NMR spectra of N-isopropyl and N-t-butylacetanilide did not change within the temperature range -20° to 80°. By analogy with N-phenylacetanilide there should be restricted rotation in these compounds. It is unlikely that the NMR spectra of the two possible conformers IX and

X would be identical.



IX



X

It seems more likely that these compounds exist essentially in one conformation, interconverting to another conformation to an extent of less than 5%. The relative stability of IX and X would probably depend primarily upon the size of R. For methyl, IX is the more likely, for all the others, X is the more probable conformation. The induced field of the carbonyl group of IX may cause some low field shifts of the ortho proton resonance of the phenyl group, but no such effect is expected for X.

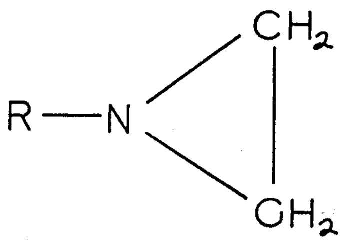
In summary, the NMR results obtained suggest sp^2 hybridization of the nitrogen in compounds of the type $Ph-N(R)-CO-CH_3$.

Ethylenimine Derivatives

Our knowledge of the geometry of ethylenimine is based on results obtained from microwave spectroscopy (40, 41, 42). Turner and coworkers found the carbon-carbon distance to be 1.480 Å (42). This is much shorter than the normal $C_{sp^3}-C_{sp^3}$ bond length, 1.526 ± 0.002 Å (18) and closely corresponds to the $C_{sp^2}-C_{sp^2}$ bond distance. The carbon-nitrogen bond length in ethylenimine is 1.488 Å, slightly longer than the $C_{sp^3}-N$ distance in aliphatic amines (e.g. methylamine has a carbon-nitrogen bond length of 1.474 ± 0.005 Å (24).) Therefore, the ethylenimine ring approximates to an equilateral triangle. The nature of bonding compatible with C-C-C interatomic angles of 60° had been investigated by Coulson (38). He put forward a concept of "bent" bonds to account for the observed bond lengths and bond strength in cyclopropane. He found that maximum overlap of bonding orbitals can be achieved if the orbitals participating in the ring form an angle of 104° at the carbon atom. The bonding would be intermediate in type between an "end-wise" sigma bonding overlap and a "side-wise" pi overlap. The similar geometry of ethylenimine suggests "bent" bonds in this heterocyclic ring also. The hybridization of the nitrogen would be analogous to that of the carbon atoms. For a favourable orbital overlap the p character of the carbon-carbon and carbon-nitrogen bond forming orbitals must increase. In confirmation of this, the H-C-H bond angle has been found to be 116.7° (42), which indicates that the orbitals not involved in the ring skeleton have considerable amount of s character (22).

The above considerations predict that the nitrogen in ethylenimine should be different from the tetrahedrally hybridized nitrogen of ammonia and aliphatic amines (31). The type of hybridization of the nitrogen is reflected by its rate of inversion. Recently, the rate of inversion for the N,N-dibenzylmethylamine in aqueous solution had been determined to be $2 \pm 1 \times 10^5$ sec^{-1} (36). This is very fast: as expected for an sp^3 hybridized nitrogen.

The inversion rates of several N-substituted ethylenimines were measured by Bottini and Roberts (28). Typical rate constants for inversion at the coalescence temperature for XI are listed in Table 2. The observed temperature dependence of the spectra shows that electronic effects are very important. The transition state to inversion is presumably planar and would be stabilized by double bond character of the nitrogen-carbonyl carbon bond. The hybridization of this bond is a function of both the inductive and the resonance effect of the substituents. The inductive substituent constant, σ^I, had been measured by Taft for several substituents (16). Certain of these are given in Table 3. The positive values indicate inductive electron withdrawal and the negative values show electron release. The values of σ^I for $-CON(CH_3)_2$ and $-CO_2CH_3$ had not been measured, but it is reasonable to expect that the order for RCO follows that of R, i.e. that the σ^{I} values increase in the order $-COCH_3$, $-CON(CH_3)_2$, $-CO_2CH_3$.



XI

TABLE 2

Coalescence temperature and inversion rate of N-substituted ethylenimines.

Substituent group R in IX.	Solvent	Coalescence temperature °C	k(sec^{-1})	Reference
Et		108	60	28
CH_2Ph		105	60	28
Ph		-60	42	28
$CON(CH_3)_2$	vinyl chloride toluene	-77		*
$COOCH_3$	"	-86		*
$COCH_3$	"	-119		*

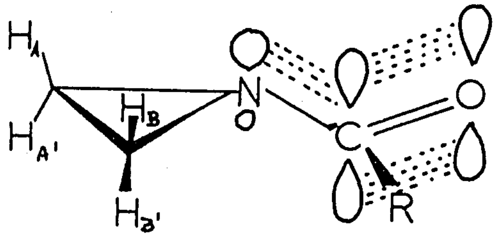
*This work.

TABLE 3

Inductive Substituent Constants (16)

Substituent	σ^I	Substituent	σ^I
Me	-0.05	$N(CH_3)_2$	0.10
Et	-0.05	OCH_3	0.25
CH_2Ph	0.04	CH_3CO	0.28
Ph	0.10		

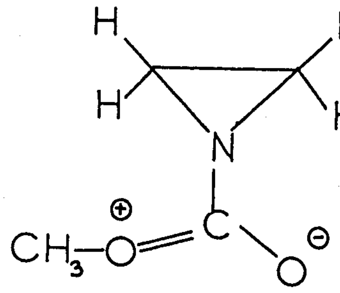
The inductive effect of COR groups creates a slight positive charge on the nitrogen, resulting in a stronger bonding of electrons, i.e. increased _s_ character of the lone orbital. An unsymmetrical overlap would result between its lobes and the carbonyl electron cloud (XII), lending partial double bond character to that bond.

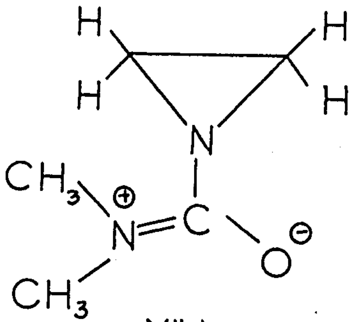


XIII

Therefore, the more electron withdrawing the substituent group on the nitrogen, the more it stabilizes the transition state for inversion. The limiting case is that of complete sp^2 hybridization, where the planar state is no longer a transition state but the ground state of the molecule. This is well demonstrated in aliphatic amides. The energy barriers to rotation and inversion in formamide had been measured to be 18- 3 kcal.mole^{-1} (17) and about 1 kcal. mole^{-1} (33) respectively. Thus, formamide is a rigid, nearly planar molecule at room temperature. The weak interaction between the nitrogen lone pair and the carbonyl bond in ethylenimine is not sufficient to inhibit rotation about the carbon-nitrogen bond, but may be expected to increase the energy barrier to inversion.

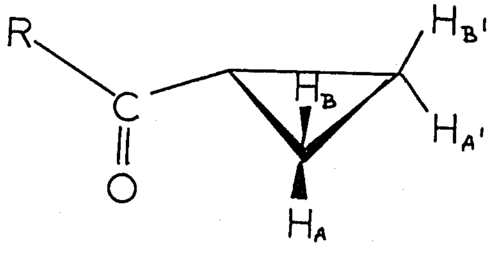
So far we have considered inductive effects alone, which account for the general trend of decreasing coalescence temperature in Table 3, but not for the order within the COR series. Here, resonance must also be taken into account. Cross conjugation decreases the double bond character of the nitrogen-carbonyl bond in the urethane (XIII) and urea (XIV), but this type of resonance contribution is not important for the N-acetyl derivative.


XIII

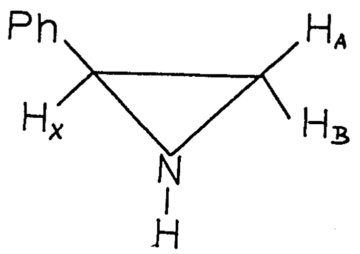

XIV

The significance of these structures is demonstrated by the well defined doublet observed for the N-methyl resonance in XIV at room temperature. The splitting of the N-methyl line at room temperature is analogous to that observed in aliphatic amides. This is interpreted as being due to double bond character of that nitrogen-carbonyl bond. Consequently, the carbonyl-ring nitrogen bond becomes almost sp^3 hybridized, and splitting of the ethylenic ring proton resonance line at low temperature must be caused by a decreased rate of inversion at the ring nitrogen. This is a unique example of the two types of barrier to internal motion being demonstrated in the same molecule.

The magnitude of coupling constants of ethylenic protons in N-(dimethylcarboxamido)-ethylenimine and the appearance of the spectrum at low temperature closely correspond to the theoretical spectrum AA'BB', calculated by Wiberg and Nist for coupling constants $J_{AB}=2$, $J_{AB'}=1$, $J_{AA'}=4$, $J_{BB'}=4$ cps. (30). The spectrum found cannot be matched by any theoretical spectra calculated for much larger J_{AB} or $J_{AB'}$. This is expected for the system XV which would show a time averaged single ring proton resonance at room temperature. At very low temperatures, when the lifetime of the conformers becomes detectable by NMR, an AA'BB' type absorption pattern is observed, for the carbonyl group interacts more strongly with protons in one side of the ring (H_A, $H_{A'}$) than with the other protons (H_B, $H_{B'}$).



XV



XVI

There is also good agreement with the coupling constants for 2-phenylethylenimine (XVI), calculated by Brois (19). He found J_{AX}=3.1, J_{BX}=6.0 and J_{AB}= 0.6 cps.

Additional evidence for the nature of internal motion of N-substituted ethylenimines was obtained by Anet (34), who repeated the measurements of Traylor (33) in various solvent systems. Anet found the coalescence temperature of methanesulfonyl-ethylenimine to vary between -35° to -40°, depending on the solvent used. At low temperatures the ring protons form a typical A_2B_2 spectrum, found in the ethylenimine systems. The higher inversion barrier in this case is expected. The electron negativity of the sulfonyl group increases the p character of the nitrogen orbital participating in the sulphur-nitrogen sigma bond. Thus, the non-bonding orbital of the nitrogen acquires more s character, raising the barrier to inversion.

A similar measurement done on N-nitroso-ethylenimine in vinyl chloride showed no spectral change down to -160° (34), whereas the NMR spectra of some aliphatic nitrosamines in aromatic solvents (39) indicate a significant amount of double bond character of the nitrogen-nitrogen bond at room temperature. A possible explanation is that the ethylenimine ring structure fixes the C-N-C bond angle. This diminishes the steric inhibition of rotation around the N-N bond, in comparison with the "open" aliphatic compounds.

Earlier workers assumed that in ethylenimine the nitrogen has a pure tetrahedral configuration, with the lone electron pair constituting the fourth bond. For alkyl substituents this is probably valid, but in more complex molecules intermediate states of hybridizations may be involved. The present results suggest that electron-withdrawing CRO substituents give some *s* character to the 2p orbital of the nitrogen and shorten the N-CRO bond. However, orbital overlap in ethylenimines is less favourable than in aliphatic amides and hence rotation about the nitrogen-carbonyl bond is not hindered.

CLAIMS TO ORIGINAL RESEARCH

1. New method of preparation of N-t-butylaniline.
2. Modification of the method of preparation of 2,2-dideuteroethylenimine.
3. Synthesis of N-carbomethoxy-2,2-dideuteroethylenimine.
4. Observation of spectral changes upon lowering the temperature for the following compounds:

    N-phenylacetanilide

    N-carbomethoxyethylenimine

    N-(dimethylamidocarboxy)-ethylenimine
5. Moment analysis of the ethylenic hydrogen peak of N-(dimethylamidocarboxy)-ethylenimine for obtaining approximate coupling constants.

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