PART A

CARBONIUM ION REARRANGEMENTS IN THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE

PART B

N. M. R. STUDIES OF STEREOISOMERISM IN SOME CARBONYL DERIVATIVES

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
Floie Marie Vane
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ABSTRACT

PART A

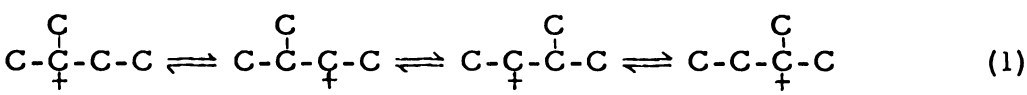
CARBONIUM ION REARRANGEMENTS IN THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE

PART B

N.M.R. STUDIES OF STEREOISOMERISM IN SOME CARBONYL DERIVATIVES

by Floie Marie Vane

PART A: Products from carbonium ion reactions frequently have been explained by rearrangements of tertiary and secondary carbonium ions to less stable carbonium ions. In the study of the reaction of C^{14}-labeled t-amyl chloride with aluminum chloride, a rate of 1.55 was observed for C-2 $\rightleftharpoons$ C-3/C-1 $\rightleftharpoons$ C-4 equilibration.[1] It was suggested that 87% of the reaction proceeded through 1 which equilibrates C-2, C-3 and C-1, C-4 and 13% through 2 which equilibrates C-1, C-4 only.



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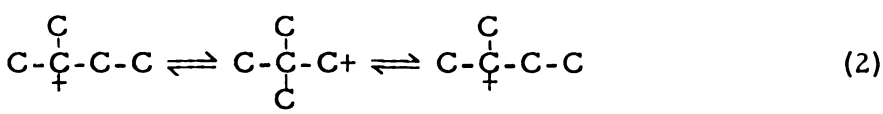

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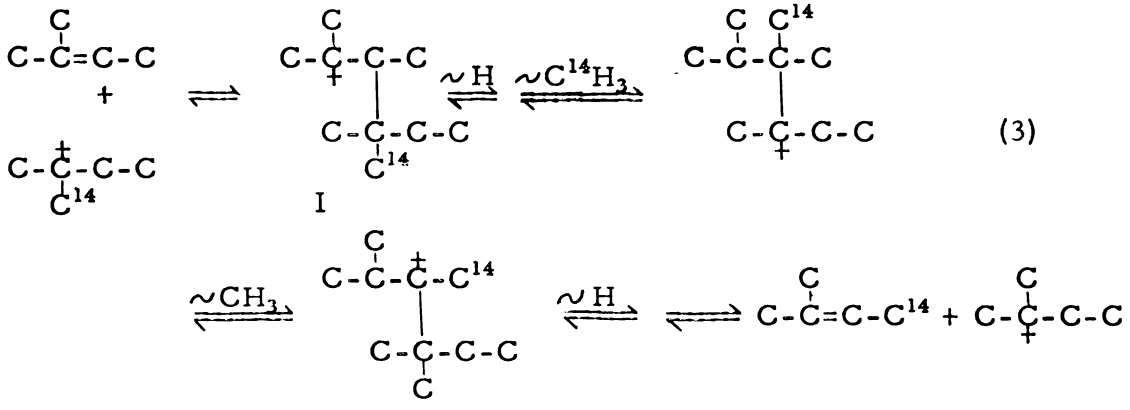
An alternate explanation for 2 would be a bimolecular reaction (3) which does not invoke rearrangement to a primary carbonium ion.



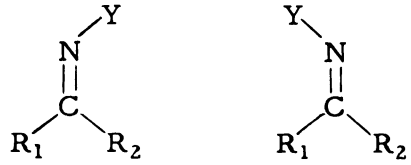
(3)

Bimolecular paths in the reactions of t-amyl chloride-1-C^{13} and t-amyl chloride-2-C^{13} with aluminum chloride were verified by identification (mass spectrometry) of dilabeled t-amyl chloride and hexyl chlorides in the reaction products. The data support I (3) as the first intermediate formed by the attack of t-amyl cation on a C_5 olefin. This C_{10} carbonium ion may undergo fast and reversible rearrangements to other C_{10} carbonium ions. The C_{10} unit, which disproportionates into an olefin and a tertiary carbonium ion, may lead to two C_5 units or a C_4 and a C_6 unit. Calculations of statistical isotopic distribution suggest that each t-amyl species has undergone an average of one bimolecular reaction resulting in complete equilibration of the methyl and partial equilibration of the non-methyl carbon atoms. No scrambling between methyl and non-methyl carbon atoms was detected.

The volatile products from the reaction of 1.74 g. of t-amyl chloride with 0.080 g. of aluminum chloride at 0° for five minutes are 68.2% t-amyl chloride, 16.7% t-butyl chloride, 5.7% 3-chloro-2-methylbutane, 4.2% 2-chloro-2-methylpentane, 1.5% 3-chloro-3-methylpentane, and 3.8% of the corresponding hydrocarbons. The percent recovery of volatile products and the percent t-amyl chloride in the volatile fraction increased with 1) increase in the ratio t-amyl chloride/aluminum chloride, 2) decrease in temperature, and 3) decrease in

reaction time. After five minutes the reaction appears to stop. The apparent termination of the reaction may involve deactivation of the catalyst by highly unsaturated polymers.

PART B: Problems associated with syn-anti isomers (II, III) of



II III

2,4-dinitrophenylhydrazones (DNP's), ortho-, meta- and para-nitrophenylhydrazones, semicarbazones and thiosemicarbazones were studied by nuclear magnetic resonance spectroscopy.

Hydrogens, cis and trans to Y usually resonate at different frequencies. Assignments of syn and anti isomers (syn refers to the isomer having Y cis to the smaller group) were made by comparing the equilibrium ratios of 2-butanone, 2-pentanone, methyl isopropyl ketone and methyl t-butyl ketone DNP's.

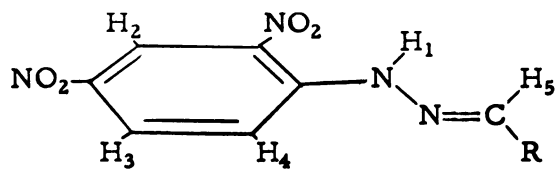
In methylene bromide and chloroform solutions, aldehydic and β-hydrogens are deshielded (hydrogens cis to Y resonate at lower fields than those trans) and α-hydrogens are shielded. The isomer chemical shift differences are 30-45 cps for aldehydic hydrogens and 0-10 cps for α- and β-aliphatic hydrogens. Acetaldehyde, benzyl ethyl ketone and ethyl cyclopropyl ketone DNP's show two resonances for each aromatic hydrogen of the 2,4-dinitrophenyl ring.

Hydrogen bonding of the N-H of the syn isomer of acetaldehyde DNP to the solvent leads to greater syn:anti ratios in the better hydrogen-bonding solvents. In addition two N-H resonances are observed in

pyridine, dimethyl sulfoxide and dimethylformamide solutions of acetaldehyde DNP.

Formation of aldehyde DNP's is kinetically controlled and leads to the syn isomer.

The following long-range spin-spin coupling constants were observed in DNP's (4): $J_{H_1H_3} = 0.7$ cps, $J_{H_1H_4} = 0.2$ cps, and $J_{H_1H_5} = 0.8$ cps.



(4)

Reference

1. J. D. Roberts, R. E. McMahon and J. S. Hine, J. Am. Chem. Soc., 72, 4237 (1950).

PART A

CARBONIUM ION REARRANGEMENTS IN THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE

PART B

N.M.R. STUDIES OF STEREOISOMERISM IN SOME CARBONYL DERIVATIVES

By

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PART A

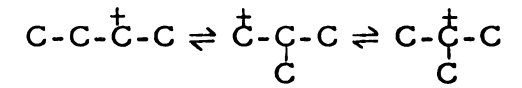
CARBONIUM ION REARRANGEMENTS IN THE REACTION OF t-AMYL CHLORIDE WITH ALUMINUM CHLORIDE

INTRODUCTION

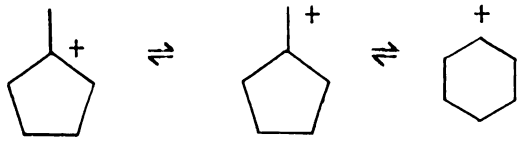
The action of Lewis acids on organic compounds is a common method for generating carbonium ions. Investigation of the nature and properties of these carbonium ions has been the object of many investigators.

In the study of alkyl halides and isoparaffins in the presence of aluminum halides, Bartlett, Condon and Schneider[1] observed 1) equilibration of the alkyl halide with olefins, 2) addition of alkyl halides to olefins, 3) rapid halogen-hydrogen exchange between alkyl halides and alkanes, 4) isomerization and Wagner-Meerwein rearrangements of alkyl halides, and 5) production of products which could not be explained by simple combinations of starting materials. Pines and co-workers studied the isomerizations of alkanes with a variety of catalysts. In addition to Lewis acids, promotors such as acid and olefins,[2,3] oxygen,[4,5] light,[5,6] water,[7] or alkyl halides,[8] were necessary for isomerization. In the condensation of alkyl halides with ethylene in the presence of Lewis acids, Schmerling[9] observed that the rate increased in the order: primary halides < secondary halides < tertiary halides. Schneider and Kennedy[10,11,12] studied the alkyl fluoride-boron trifluoride induced isomerizations of hydrocarbons.

Often, products were explained by rearrangements of tertiary and secondary carbonium ions to primary carbonium ions, e.g., the isomerization of n-butane to isobutane[7] (1a) and methylcyclopentane to cyclohexane[3] (2a). In the reaction of C^{14}-labeled t-amyl chloride with aluminum chloride, Roberts, McMahon and Hine[13] obtained a rate of 1.55 for C-2 $\rightleftharpoons$ C-3/C-1 $\rightleftharpoons$ C-4. Equilibration



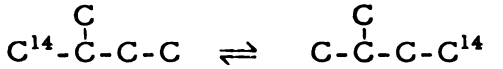
(1a)



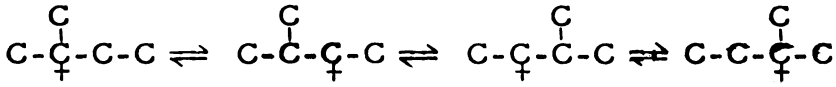
(2a)

of C-2 and C-3 (3a) should proceed twice as fast as equilibration of C-1 and C-4 (4a) if the only path of isomerization was 5a. To explain the observed value they suggested that 87% of the rearrangement

(3a)

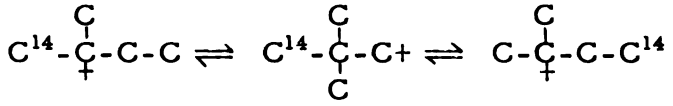


(4a)



(5a)

proceeds through 5a and 13% through 6a which effects only C-1, C-4 exchange.

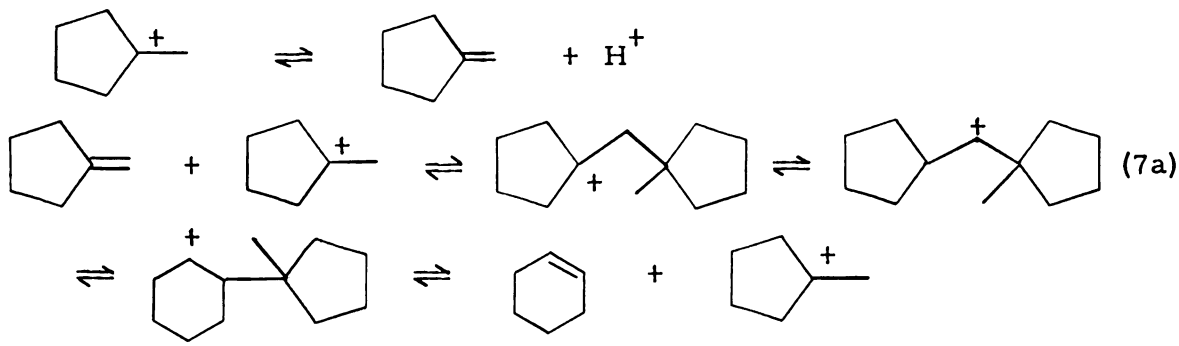


(6a)

Calculations[14] have shown that the activation energy necessary for rearrangements of tertiary to primary and secondary to primary carbonium ions should be at least 33 and 22 kcal., respectively. These values warrant examination of alternate mechanisms not involving primary carbonium ions.

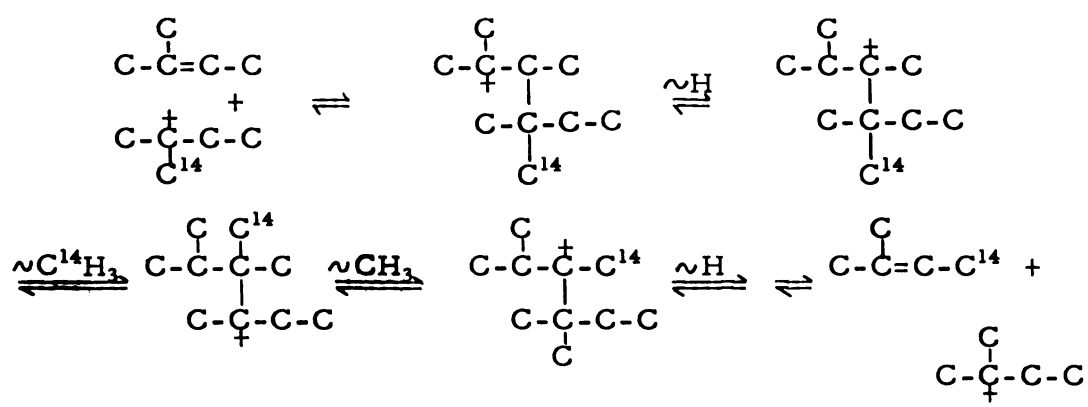
Disproportionation reactions have been invoked to explain products which were not multiples of starting reactants.[1, 9, 10, 11, 12, 15] Similarly, reaction of a methylcyclopentyl cation with its olefin, ring enlargement, and disproportionation (7a) would lead to cyclohexane

without intervention of a primary carbonium ion intermediate. The isomerization of n-butane to isobutane and the faster C-1, C-4 exchange in t-amyl chloride can also be explained by bi-



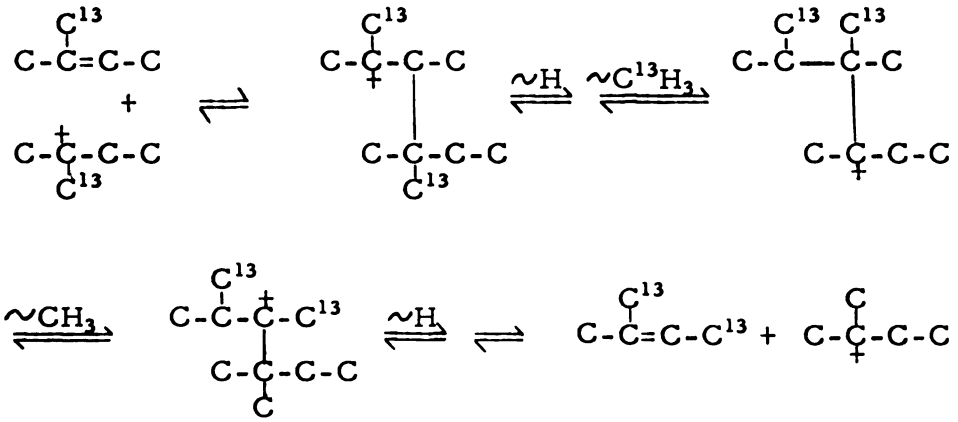
(7a)

molecular reactions. Reaction sequence 8a results in C-1 ⇌ C-4 equilibration but not C-1 ⇌ C-3. C_{10} units, as in 8a, have been proposed to explain formation of t-butyl and hexyl chlorides from the action of aluminum chloride on t-amyl chloride[1] and formation of isobutylene and hexenes from sulfuric acid treatment of isoamylenes.[15]



(8a)

The purpose of this investigation was to study quantitative and qualitative effects of temperature, time and concentration upon the reaction of t-amyl chloride and aluminum chloride. It was hoped that bimolecular reactions would be verified by identification of dilabeled products which should result when two C^{13}-labeled t-amyl species combine (9a).



(9a)

RESULTS

1. Reactions of t-Amyl Chloride with Aluminum Chloride

The products of the reaction of t-amyl chloride with aluminum chloride consist of a volatile portion and a brown polymeric residue. Tables Ia-IIIa summarize the effect of time, temperature and concentration on the recovered products. The qualitative composition of the products is practically unaffected by time, temperature and concentration. Table Ia indicates that the carbonium ion formed undergoes many rapid reactions. The reaction appears to stop after five minutes. Bimolecular reactions decrease, as expected, at low temperatures (Table IIa). An increase in aluminum chloride concentration greatly reduces the amount of the volatile fraction collected and decreases the percentage of t-amyl chloride in the product.

Additions of 2-methyl-2-butene (1.8-22%) to the reaction of t-amyl chloride with aluminum chloride produced little change in the product composition. Saturation of the t-amyl chloride with hydrogen chloride or water, or exposure of the aluminum chloride to the atmosphere for 10 min. had no effect on the reaction. When the volatile portion of the reaction products was removed and fresh t-amyl chloride was reacted with the remaining brown residue, the t-amyl chloride was recovered quantitatively. The above findings suggest that the polymer is involved in the deactivation of the aluminum chloride which causes the apparent termination of the reaction.

If formation of t-butyl and hexyl chlorides occurs by disproportionation of a C_{10} unit, equimolar amounts of the two are expected. However, the yield of t-butyl chloride is greater than that of the hexyl chlorides (Tables Ia-IIIa). Table IVa contains the product analyses of the reactions of aluminum chloride with t-butyl chloride, 3-methyl-3-chloropentane, and mixtures of chlorides. The table reflects the more

Table Ia. The Reaction of t-Amyl Chloride with Aluminum Chloride[a] at 0°: Effect of Reaction Time[b]

Time:	5 sec.[c]	5 sec.	30 sec.	3.5 min.	5 min.	7 min.	15 min.	25 min.
% Recovery (volatile fraction)	87	91	86	78	72	71	72	63
% Composition (wt/wt) of recovered product								
isobutane	t	t	t	0.2	0.4	0.6	0.3	0.2
isopentane	0.3	0.7	1.1	1.9	2.7	2.9	2.4	2.0
t-butyl chloride	1.2	2.4	3.9	15.0	16.7	20.2	18.5	21.8
2-methylpentane	t	t	t	0.4	0.6	0.6	0.6	0.6
3-methylpentane	t	t	t	0.2	0.2	0.3	0.3	0.2
t-amyl chloride	93.7	90.7	83.0	71.5	68.2	62.8	65.5	62.1
3-chloro-2-methylbutane	4.0	5.5	10.2	5.6	5.7	5.4	5.2	4.8
2-chloro-2-methylpentane	0.3	0.5	1.1	3.4	4.2	4.8	4.5	5.2
3-chloro-3-methylpentane	0.1	0.2	0.7	1.7	1.5	2.2	2.7	2.4

[a] The mole ratio, t-amyl chloride/aluminum chloride, was 28.

[b] All reactions were quenched with N, N-dimethylaniline.

[c] The reaction temperature was -37°.

[t] Only a trace was present (< 0.2%).

Table IIa. The reaction of t-Amyl Chloride with Aluminum Chloride[a] for 1.5 min.: Effect of Temperature

Temperature:	-61°	-35°	0°	22°	50°
% Recovery (volatile fraction)	89	88	72	72	66
% Composition (wt/wt) of recovered product					
isobutane	--	t	0.4	0.9	0.6
isopentane	0.3	0.4	2.7	3.5	2.8
t-butyl chloride	1.3	1.4	16.7	17.2	18.1
2-methylpentane	--	--	0.6	0.6	0.8
3-methylpentane	--	--	0.2	0.3	0.2
t-amyl chloride	93.7	91.8	68.2	63.7	61.7
3-chloro-2-methylbutane	4.7	5.7	5.7	7.0	8.3
2-chloro-2-methylpentane	t	0.4	4.2	4.7	4.0
3-chloro-3-methylpentane	t	0.2	1.5	2.3	3.5

[a]The mole ratio, t-amyl chloride/aluminum chloride, was 28.

[t]Only a trace was present (< 0.2%).

Table IIIa. The Reaction of t-Amyl Chloride with Aluminum Chloride at 0° for 1.5 min.: Effect of Concentration

t-Amyl Cl/$AlCl_3$(mole)	190	43	33	26	15
% Recovery (volatile fraction)	97	94	97	76	59
% Composition (wt/wt) of recovered product					
isobutane	t	t	0.2	0.9	2.7
isopentane	0.3	0.6	1.7	5.0	6.4
t-butyl chloride	0.3	2.6	10.7	19.1	30.8
2-methylpentane	--	--	t	0.5	1.5
3-methylpentane	--	--	t	0.4	0.5
t-amyl chloride	97.7	90.2	77.7	64.1	47.4
3-chloro-2-methylbutane	1.7	5.9	5.8	5.0	3.1
2-chloro-2-methylpentane	t	0.5	1.9	3.7	5.8
3-chloro-3-methylpentane	t	0.2	1.9	1.3	1.6

[t]Only a trace was present (< 0.2%).

Table IVa. The Reactions of t-Butyl Chloride and Methylpentyl Chlorides with Aluminum Chloride[a] at 0°.

Reacting Halide(s):	C_3C-Cl		$(C\text{-}C)_2C$(Cl)-C		C_3C-Cl + C_2C(Cl)-C-C-C		C_3C-Cl + C_2C(Cl)-C-C + C_2C(Cl)-C-C-C	
Reaction Time:	0	5 min.	0	5 min.	0	5 min.	0	5 min.
% Composition (wt/wt) of recovered product								
isobutane	--	2.0	--	0.04	--	1.0	--	1.7
isopentane	--	0.2	--	0.09	--	0.2	--	2.7
t-butyl chloride	100	87.4	--	2.3	43	45.7	18	30.0
2-methylpentane	--	t	--	1.6	--	1.9	--	0.8
3-methylpentane	--	t	--	1.3	--	0.7	--	0.4
t-amyl chloride	--	4.5	--	4.4	--	7.7	67	47.1
3-chloro-2-methylbutane	--	0.5[c]	--	0.4	--	0.7	--	4.2
2-chloro-2-methylpentane	--	t	--	40.3	57	25.1	15	9.2
2-chloro-2, 3-dimethylbutane	--	5.4	--	--	--	b	--	b
3-chloro-3-methylpentane	--	t	100	40.3	--	15.6	--	4.2
% Recovery (volatile product)		73		75		62		78

[a] The mole ratio, alkyl halide/aluminum chloride, was about 28.
[b] The presence of small amounts of 2-chloro-2, 3-dimethylbutane cannot be excluded.
[c] The presence of small amounts of isooctane cannot be excluded.
[t] Only a trace was present (< 0.1%).

rapid disappearance of t-amyl chloride and hexyl chlorides than t-butyl chloride. Condon[16] also made this observation and suggested that the methylpentenes polymerized faster than isobutene.

The absence of isopropyl and n-propyl chlorides in the reaction products of t-amyl chloride and their stability under the reaction conditions (Table Va), indicate that the C_{10} unit is not disproportionating into C_3 and C_7 units. Similarly, the absence of 1- and 2-chlorobutane, which are stable under the reaction conditions, implies that the C_{10} unit does not disproportionate to the 2-butyl cation and a C_6 olefin.

2. Reactions of C^{13}-Labeled t-Amyl Chlorides with Aluminum Chloride

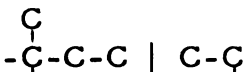
Analysis of t-amyl chloride. Table VIa summarizes the product composition of the reactions of t-amyl chloride-1-C^{13} and t-amyl chloride-2-C^{13} with aluminum chloride at 0° for 5 min.

To verify that the starting C^{13}-labeled chlorides had the label only at the designated carbon, the chlorides and the alcohols from which they were prepared were analyzed by mass spectrometry and proton n.m.r.

The mass spectrum of a labeled compound can, in principle, furnish information on the fraction of labeled molecules (isotopic analysis) and the position of labels in the molecules.

The parent ions in the spectra of both t-amyl chloride and t-amyl alcohol are too small to calculate the isotopic composition. A satisfactory alternative in the chloride spectrum, the $C_5H_{11}^+$ ion, is subject to interference in the labeled species from $C_5H_{10}^+$ and $C_5H_9^+$. The lower appearance potential of $C_5H_{10}^+$ eliminated the possibility of removing the interference. At the same time, $C_5H_{10}^+$ intensity is too low at ionization voltages below the appearance potential of $C_5H_{11}^+$ to permit using it as a basis for an isotopic analysis. A satisfactory analysis was derived from the 70-volt spectrum by assuming that $C_5H_{11}^+$, $C_5H_{10}^+$

Table Va. The Reactions of Propyl + t-Amyl Chlorides, and Butyl + t-Amyl Chlorides with Aluminum Chloride[a] at 22°

Reacting Halide:								
Reaction Time:	0	5 min.	0	5 min.	0	5 min.	0	5 min.
Selected products, % (wt/wt)								
2-chloropropane	14.4	21.7	--	1.0	--	--	--	--
1-chloropropane	--	--	12.0	20	--	--	--	--
2-chlorobutane	--	--	--	--	12.2	25.6	--	1.5
1-chlorobutane	--	--	--	--	--	--	10.5	25.4
t-amyl chloride	85.6	22.4	88.0	23.5	87.8	22.2	89.5	23.2

[a] The mole ratio, alkyl halides/aluminum chloride, was about 10.

Table VIa. The Reactions of C^{13}-Labeled t-Amyl Chlorides with Aluminum Chloride at 0° for 5 min.

Reacting Halide	1-C^{13}	2-C^{13}
Wt. of t-amyl chloride (g.)	1.0	1.0
Wt. of aluminum chloride (g.)	0.047	0.047
% Recovery (volatile fraction)	52	52
% Composition (wt/wt) of recovered product		
isobutane	t	t
isopentane	0.9	1.2
t-butyl chloride	21.6	21.0
2-methylpentane	0.4	0.2
3-methylpentane	0.2	0.1
t-amyl chloride	62.4	66.6
3-chloro-2-methylbutane	4.1	3.6
2-chloro-2-methylpentane	7.4	5.3
3-chloro-3-methylpentane	2.0	1.5

[t]Only a trace was present (< 0.1%).

and $C_5H_9^+$ are all produced with the same isotopic distribution. The intensities of these ions in the t-amyl alcohol spectrum are considerably lower than in the chloride spectrum; moreover, these peaks may also include contributions from oxygen-containing ions. Therefore, isotopic analysis of the labeled alcohols was made by attributing the peak at mass 59($C_3H_7O^+$) to the unlabeled species and that at 60 to the labeled. Good agreement of the alcohol analysis with the chlorides supports and justifies the procedure.

	1-C^{13}	2-C^{13}
Alcohol, % labeled	43.0	57.6
Chloride, % labeled	43.0	57.7

The mass spectrum of a labeled molecule can be used to locate the label only if the relevant decomposition paths are known and if the atoms of the molecule do not lose their identity before decomposition. Spectra of the 1-C^{13}- and 2-C^{13}-labeled species clearly define certain primary decomposition steps and show that no rearrangement precedes these steps. Table VIIa contains the partial spectra of t-amyl chloride unlabeled, 1-C^{13}, and 2-C^{13}, corrected for natural abundance of heavy isotopes and for the contribution of unlabeled t-amyl chloride. Table VIIIa contains corresponding data for the t-amyl alcohols. Table IXa shows derived label-retention values in $C_4H_8X^+$ and $C_3H_6X^+$, formed by respective loss of CH_3 and C_2H_5 from the parent ions. In the chlorides, $C_4H_8Cl^+$, $C_4H_7Cl^+$ and $C_4H_6Cl^+$ were assumed to have the same retention. The same assumption was made for $C_3H_6Cl^+$, $C_3H_5Cl^+$ and $C_3H_4Cl^+$. In the alcohols, interference from other ions is evidently very small and was neglected. Thus, respective intensities at masses 73 and 74 were attributed to unlabeled and labeled $C_4H_8OH^+$, and those at 59 and 60 to unlabeled and labeled $C_3H_6OH^+$. Evidently, $C_4H_8X^+$ and $C_3H_6X^+$

Table VIIa. Partial Mass Spectra of t-Amyl Chlorides

Mass	Ion[a]	Relative Intensity		
		Unlabeled	1-C^{13}	2-C^{13}
69	$C_5H_9^+$	2.9	0.0	0.0
70	$C_5H_{10}^+$	16.5	2.5	2.6
71	$C_5H_{11}^+$	100.0	16.3	16.2
72	. . .	0.0	100.0	100.0
75	$C_3H_4Cl^+$	1.2	0.5	0.0
76	$C_3H_5Cl^+$	54.8	1.2	1.5
77	$C_3H_6Cl^+$	92.6	57.8	59.3
78	. . .	0.1	92.3	98.2
89	$C_4H_6Cl^+$	0.4	0.1	0.0
90	$C_4H_7Cl^+$	1.4	0.8	0.2
91	$C_4H_8Cl^+$	15.8	8.0	1.6
92	. . .	0.1	8.1	16.4
105	$C_5H_{10}Cl^+$	0.1	0.1	0.0
106	$C_5H_{11}Cl^+$ (parent)	0.1	0.1	0.1
107	. . .	. . .	0.2	0.1

[a]Unlabeled ions only are listed.

Table VIIIa. Partial Mass Spectra of t-Amyl Alcohols

Mass	Ion[a]	Relative Intensity		
		Unlabeled	$1\text{-}C^{13}$	$2\text{-}C^{13}$
59	$C_3H_7O^+$	100.0	b	b
60	. . .	0.0	100.0	100.0
69	$C_5H_9^+$	0.7	0.0	0.0
70	$C_5H_{10}^+$	1.6	0.5	0.5
71	$C_5H_{11}^+$	6.0	1.1	1.0
72	. . .	0.2	7.0	5.3
73	$C_4H_9O^+$	56.2	26.9	0.0
74	. . .	0.0	27.9	57.2
87	$C_5H_{11}O^+$	0.1	0.0	0.0
88	$C_5H_{12}O^+$ (parent)	0.0	0.0	0.1
89	. . .	0.0	0.0	0.0

[a] Unlabeled ions only are listed.

[b] Assumed zero.

Table IXa. Label Retention in Selected Ions

Ion	t-Amyl Chloride		t-Amyl Alcohol	
	$1\text{-}C^{13}$	$2\text{-}C^{13}$	$1\text{-}C^{13}$	$2\text{-}C^{13}$
$C_4H_8X^+$	51%	100%	51%	100%
$C_3H_6X^+$	99	100	100	100

in the spectra of both the chloride and the alcohol are formed solely by loss of the original CH_3 and C_2H_5 groups on the tertiary carbon atom. The data gave assurance that the starting chlorides contained only the desired isotopic species and that the methods of purification and analysis were acceptable.

The pertinent mass-spectral results on the t-amyl chlorides recovered from the reactions with aluminum chloride are given in Table Xa. The data do not distinguish directly between C-3 and C-4; therefore, these positions are grouped together under % label distribution. To identify individual isotopic species, distinction between C-3 and C-4 is necessary. The fact that no label is found in C-2 from the reaction of the 1-C^{13} chloride is strong evidence that no label is present in C-3, but all of it (34.6%) is in C-4. Analogously, the finding that no label is in C-1 from the reaction of the 2-C^{13} chloride implies that no label is in C-4, but all of it (50.8%) is in C-3. Corroborative evidence is afforded by proton n.m.r. The spectrum of t-amyl chloride recovered from the reaction of the 1-C^{13} chloride shows C^{13} satellites for the gem-dimethyl protons (τ = 8.47) and the methyl protons (τ = 8.97) of the ethyl group ($J_{C^{13}H}$ in both cases is about 130 cps). No excess label was detected in C-3.

On the basis of mass-spectral and proton n.m.r. data, the isotopic results of t-amyl chloride can be summarized as follows:

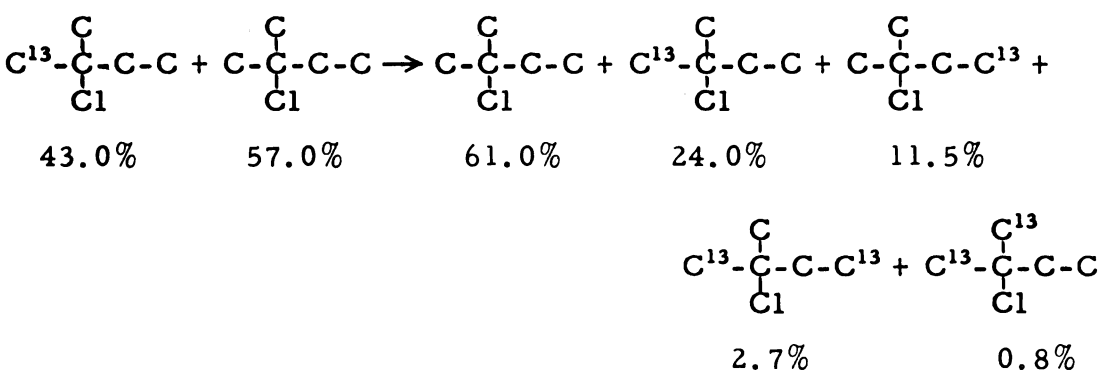
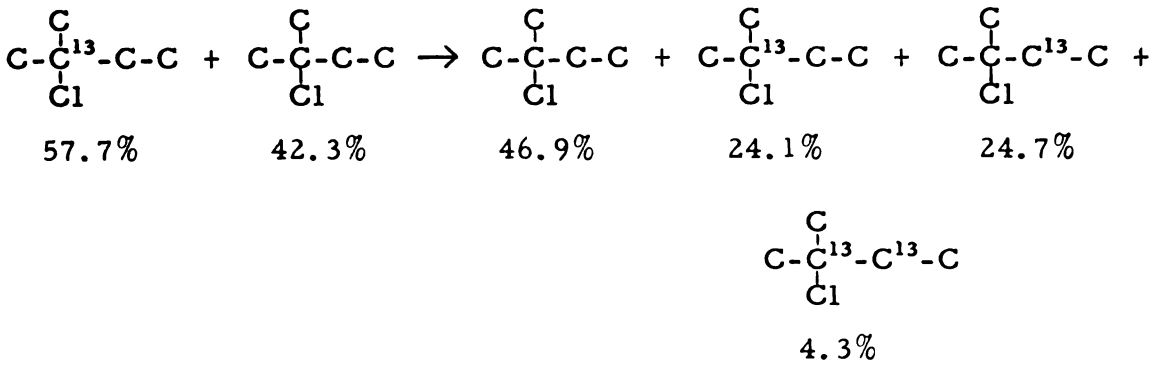


Table Xa. Isotopic Composition of t-Amyl Chlorides from Mass-Spectral Analysis

Reaction Time:	0		5 min.					
	$C_5H_{11}^+$	% label[a]	$C_5H_{11}^+$	$C_4H_8Cl^{+b}$	$C_3H_6Cl^{+b}$	% label	% label distribution in position	
							1, 1'	2	3 & 4
t-amyl chloride-1-C^{13}		43.0				42.5	65.4	0	34.6
unlabeled (% molecules)	57.0		61.0	31	30.0				
monolabeled	43.0		35.5	66	68.2				
dilabeled	0.0		3.5	3	1.8				
t-amyl chloride-2-C^{13}		57.7				57.4	0	49.2	50.8
unlabeled	42.3		46.9	0.0	47.8				
monolabeled	57.7		48.8	94	52.2				
dilabeled	0.0		4.3	6	0.0				

[a] The % label denotes the number of labeled atoms per 100 molecules.

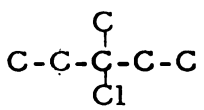
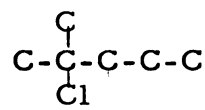
[b] The isotopic composition was computed on the basis of labeled molecules only (contribution of unlabeled t-amyl chloride removed).



Label retention of the recovered t-amyl chlorides agrees with the label content of starting materials. The data imply that C-1, C-4 and C-2, C-3 equilibration has been reached (the small deviations observed are probably within experimental error).

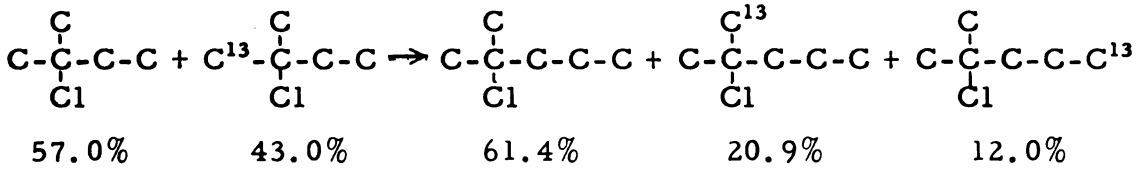
Analysis of hexyl and t-butyl chlorides. The presence of the hexyl chlorides in small quantities prevented individual isolation, but evaluation of the isotopic composition of each chloride was possible as a consequence of their fragmentation patterns. The $C_4H_8Cl^+$ region (parent-less-ethyl, masses 90 and 91) is hit heavily by 3-chloro-3-methylpentane and lightly by 2-chloro-2-methylpentane; conversely, the $C_3H_6Cl^+$ region (parent-less-propyl, masses 76 and 77) is hit heavily by 2-chloro-2-methylpentane and lightly by 3-chloro-3-methylpentane. These differences are apparent in the partial mass spectra shown in Table XIa. By neglecting the contributions of the 2-chloro isomers in the $C_4H_nCl^+$ region and of the 2-chloro isomer in the $C_3H_nCl^+$ region, the label content in the ethyl groups of the 3-chloro isomer and in the propyl group of the 2-chloro isomer can be estimated. As in the case of the t-amyl chlorides, the parent peak is very small and the over-all label content in the molecules was calculated from the $C_6H_n^+$ peaks, on the assumption again that each $C_6H_{13}^+$, $C_6H_{12}^+$ and $C_6H_{11}^+$ fragment ion has the same isotopic enrichment as the original hexyl chloride molecules. Also, the assumptions made in the t-amyl chlorides regarding the $C_4H_nCl^+$ and

Table XIa. Partial Mass Spectra of Hexyl Chlorides

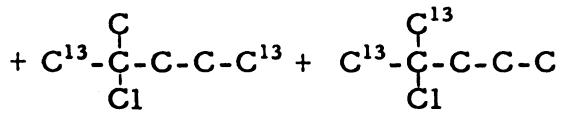
m/e		
105	3.4	7.8
104	0.7	0.5
91	191.0	5.0
90	122.3	1.4
85	100.0	100.0
84	26.5	68.1
77	3.9	149.6
76	3.2	65.3

$C_3H_nCl^+$ ions were presumed to be valid in the hexyl chlorides. Proton n.m.r. showed again that the methyl carbons had not equilibrated with C-2, C-3 or C-4. The hexyl chlorides obtained from the 1-C^{13} chloride had all the label in the methyl groups and none in C-2, C-3 and C-4. Table XIIa summarizes the pertinent mass-spectral results of the hexyl chlorides recovered from the 5 min. reaction. In addition to the above approximations and assumptions, the decomposition of the hexyl chlorides into hexenes and hydrogen chloride upon standing may cause the label distribution values to be in serious error.

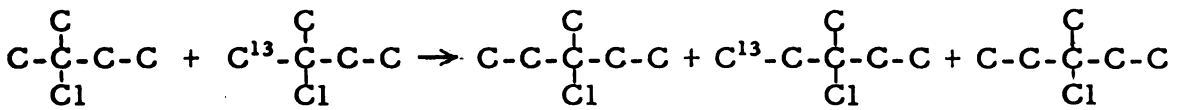
Isotopic results of the hexyl chlorides by mass-spectral and proton n.m.r. data are summarized as follows:



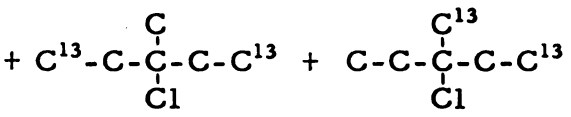
57.0% 43.0% 61.4% 20.9% 12.0%



3.9% 1.8%



57.0% 43.0% 61.4% 23.4% 9.5%



2.5% 3.2%

Since C-3 and C-4 of 2-chloro-2-methylpentane are not distinguishable by mass spectrometry, evaluation of each individual isotopic species from the 2-C^{13} compound is not possible.

Table XIIa. Isotopic Composition of Hexyl Chlorides from Mass-Spectrometry Analysis

Reacting t-Amyl Chloride	1-C^{13}			2-C^{13}		
Isotopic Composition of Hexyl Chlorides	$C_6H_{13}^+$	$C_4H_8Cl^+$	$C_3H_6Cl^+$	$C_6H_{13}^+$	$C_4H_8Cl^+$	$C_3H_6Cl^+$
Unlabeled (% molecules)	61.4	73.1	73.9	39.9	51.8	71.5
Monolabeled	32.9	25.3	24.8	45.3	42.0	28.5
Dilabeled	5.7	1.6	1.8	13.8	6.2	0.0
Trilabeled	0.0	0.0	0.0	1.0	0.0	0.0
Labels/100 ions	44.3	28.5	28.4	75.9	54.4	28.5
Label Distribution in						
3-chloro-3-methylpentane						
% in positions 1, 2, 4, 5		71.3			56.7	
% in positions 1', 3		28.7			43.3	
2-chloro-2-methylpentane						
% in positions 3, 4, 5		35.9			62.5	
% in positions 1, 1', 2		64.1			37.5	
Isomer Distribution						
% 3-chloro-3-methylpentane		19.0			17.2	
% 2-chloro-2-methylpentane		81.0			82.8	

The over-all label content (44.3%) in the hexyl chlorides obtained from the reaction of the 1-C^{13} chloride agrees with the starting t-amyl chloride (43.0%). The methyl groups of the hexyl chlorides from the 1-C^{13} chloride have equilibrated (small deviations are probably within experimental error).

The label content (75.9%) in the hexyl chlorides obtained from the reaction of t-amyl chloride-2-C^{13} (57.7%) is lower than what would be statistically expected (57.7 x 3/2 = 86.6%). Furthermore, C-2 and C-3 have not attained equilibrium.

Inability to collect t-butyl chloride in sufficient purity prevented their meaningful isotopic analysis.

Some calculated distributions of label. The degree to which either all carbon atoms in the sample or specific groups of atoms equilibrate is determined by the rearrangements undergone by the carbonium ions. According to the proposed mechanisms a C_{10} carbonium ion, as shown in 8a and 9a, is the intermediate involved in the formation of both dilabeled t-amyl chloride and hexyl chlorides. Formation of these products requires rearrangements of the carbonium ion before disproportionation; these rearrangements can result either in complete or partial equilibration of the carbon atoms. The experimental results exclude equilibration of the six methyl carbon atoms with the four carbon atoms inside the chain; thus, the only equilibrations possible are those among the six methyl carbon atoms, or those among the four non-methyl carbon atoms.

Two separate calculations of label distribution were carried out. Method A is based on the assumption that the six methyl carbon atoms, or the four non-methyl carbon atoms, of the C_{10} unit become statistically distributed and the C_{10} unit subsequently disproportionates into two units. The smaller units recombine and the process is repeated until all methyl groups, or all non-methyl groups, are statistically distributed throughout

all the molecules. Method B is based on the assumption that after the original statistical distribution and disproportionation, the smaller units do not recombine further and the reaction stops.

The percentage of dilabeled, monolabeled and unlabeled t-amyl molecules formed by Method A from 2-chloro-2-methylbutane-2-C^{13} (57.7% monolabeled and 42.3% unlabeled molecules) was calculated by p^2, $2p(1-p)$ and $(1-p)^2$, respectively, where p is the percent of labeled carbon atoms (0.577/2). Similarly, the percentage of trilabeled, dilabeled, monolabeled and unlabeled t-amyl and t-hexyl molecules formed from the same process, was calculated by p^3, $3p^2(1-p)$, $3p(1-p)^2$ and $(1-p)^3$, respectively. The percentage of trilabeled, dilabeled, monolabeled and unlabeled t-amyl and t-hexyl molecules formed by Method A from 2-chloro-2-methylbutane-1-C^{13} (43.0% monolabeled and 57.0% unlabeled molecules) was calculated by p^3, $3p^2(1-p)$, $3p(1-p)^2$ and $(1-p)^3$, respectively, where $p = 0.43/2$.

The percentage of dilabeled, monolabeled and unlabeled t-amyl and t-hexyl molecules formed by Method B from 1-C^{13} and 2-C^{13}-labeled 2-chloro-2-methylbutane was found by Ap^2, $[Bp^2 + Cp(1-p)]$ and $[Dp^2 + Ep(1-p) + F(1-p)^2]$, respectively. The fraction of labeled molecules (p) is 0.43 for the 1-C^{13}-labeled t-amyl chloride and 0.577 for the 2-C^{13}-labeled t-amyl chloride. A, B, and D are the probabilities that a dilabeled, monolabeled and unlabeled t-amyl or t-hexyl molecule, respectively, are formed if two labeled units combine, scramble and disproportionate. C and E are the probabilities that a monolabeled and an unlabeled t-amyl or t-hexyl molecule, respectively, are formed when a labeled molecule combines with an unlabeled molecule. F is the probability of forming an unlabeled molecule when two unlabeled molecules unite. A + B + D must equal 1; C + E must equal 2; and F is 1.

The calculated values are compared in the experimental values in Table XIIIa.

Table XIIIa. Comparison of Some Calculated Values of Isotopic Composition with Experimental Values of Recovered t-Amyl and Hexyl Chlorides from the Reactions of 1-C^{13}- and 2-C^{13}-Labeled t-Amyl Chlorides with Aluminum Chloride

	1-C^{13}					2-C^{13}				
	$\%C_0$	$\%C_1$	$\%C_2$	$\%C_3$	% over-all label	$\%C_0$	$\%C_1$	$\%C_2$	$\%C_3$	% over-all label
t-Amyl Chloride										
Method A	62.9	31.6	5.3	0.3	43.0	50.6	41.1	8.3	0.0	57.7
Method B	60.7	35.6	3.7	0.0	43.0	47.9	46.6	5.6	0.0	57.7
Experimental	61.0	35.5	3.5	0.0	42.5	46.9	48.8	4.3	0.0	57.7
Hexyl Chlorides										
Method A	62.9	31.6	5.3	0.3	43.0	36.0	43.9	17.8	2.4	86.6
Method B	60.7	35.6	3.7	0.0	43.0	30.1	53.3	16.7	0.0	86.6
Experimental	61.4	32.9	5.7	0.0	43.3	39.9	45.3	13.8	1.0	75.9

DISCUSSION

The carbonium ions will be represented as free ions, but most likely they are associated with the tetrachloroaluminate ion. Isotope effects (C^{12} versus C^{13}) are small and will be neglected in the discussion. All rearrangements will be represented as 1, 2-Wagner-Meerwein shifts. 1, 3-Shifts, which have been postulated in similar rearrangements[15, 17] are ignored because the results in the present system are identical with two 1, 2-shifts. The results afford the following comments and conclusions.

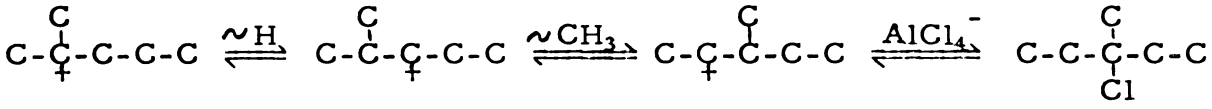
Formation of hydrocarbons in the reactions of aluminum chloride with t-butyl, t-amyl and hexyl chlorides must occur by a hydride transfer from a hydride donor to the carbonium ion (10a). The most probable source of hydride is a heavy olefin that is eventually converted to polymer and/or the polymer itself. This highly unsaturated polymer probably causes the deactivation of the aluminum chloride.

$$\begin{array}{c} C \\ | \\ C\text{-}\overset{+}{C}\text{-}C\text{-}C \end{array} + RH \rightleftharpoons \begin{array}{c} C \\ | \\ C\text{-}C\text{-}C\text{-}C \end{array} + R^{+} \qquad (10a)$$

The simplest and most reasonable path leading to 3-chloro-2-methylbutane is 11a, an intramolecular path that is supported by the

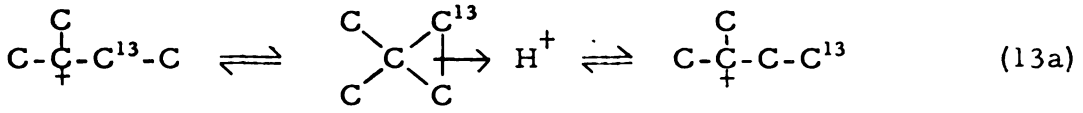
$$\begin{array}{c} C \\ | \\ C\text{-}\overset{+}{C}\text{-}C\text{-}C \end{array} \overset{\sim H}{\rightleftharpoons} \begin{array}{c} C \\ | \\ C\text{-}C\text{-}\overset{+}{C}\text{-}C \end{array} \overset{AlCl_4^-}{\rightleftharpoons} \begin{array}{c} C \\ | \\ C\text{-}C\text{-}C\text{-}C \\ \quad\quad | \\ \quad\quad Cl \end{array} \qquad (11a)$$

appearance of the secondary chloride at low temperatures (Table Ia). Path 12a, similar to 11a, represents the equilibration of 2-chloro-2-methylpentane and 3-chloro-3-methylpentane.



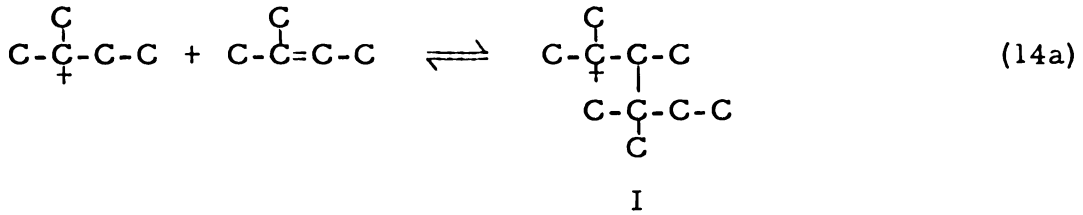
(12a)

Protonated cyclopropanes, as in 13a, do not intervene as intermediates because they would cause methyl and non-methyl scrambling.



(13a)

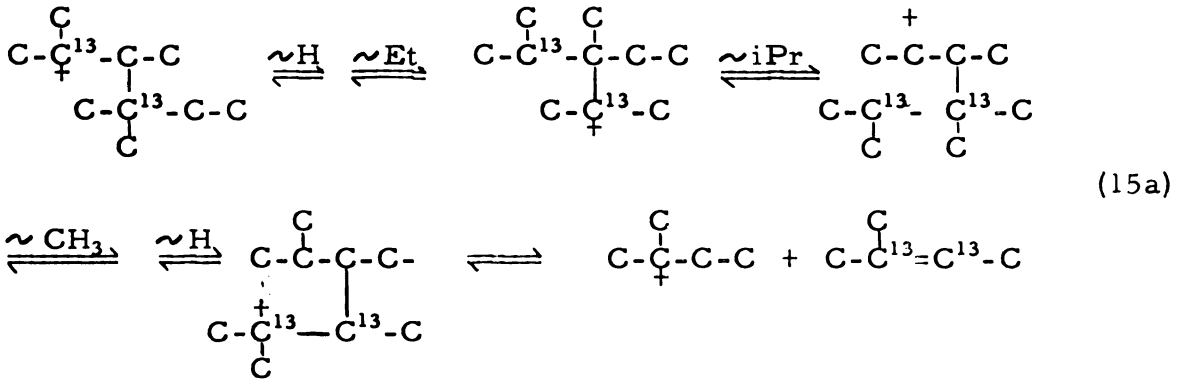
The occurrence of bimolecular reactions was verified by identification of dilabeled species in the products. The data are explicable on the assumption that I(14a), the first bimolecular intermediate, is capable of undergoing fast and reversible rearrangements to other C_{10}



(14a)

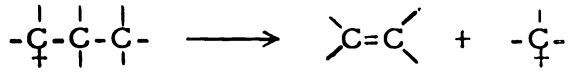
I

carbonium ions. During these rearrangements the six methyl carbon atoms attain statistical distribution faster than the four non-methyl carbon atoms (Table XIIIa). The faster equilibration of methyl carbon atoms can be seen by inspection of reactions such as 9a which effects methyl equilibration only and others such as 15a which simultaneously effect methyl and non-methyl equilibration.



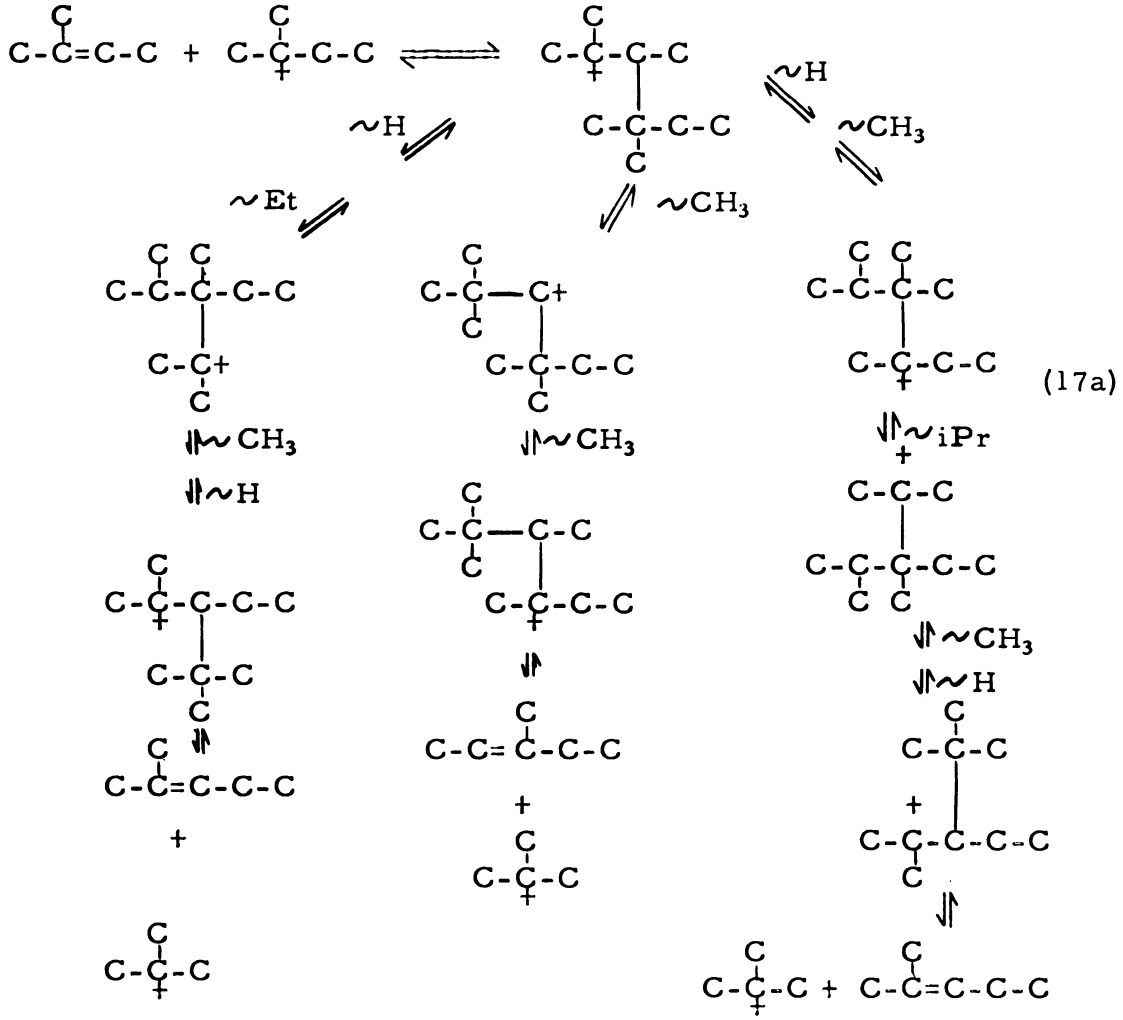
(15a)

Absence of 1- and 2-propyl chlorides, 1- and 2-butyl chlorides, and 1-, 2- and 3-pentyl chlorides in the products (Table Ia) indicates that disproportionation (16a) results in the formation of tertiary carbonium ions only. Apparently, under the experimental conditions of



(16a)

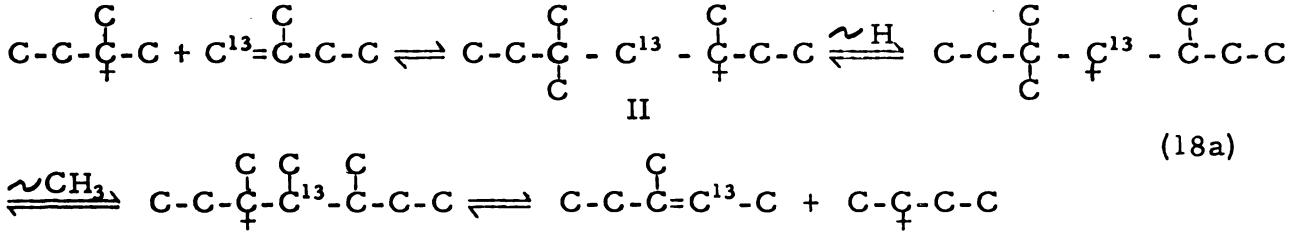
this work, fission to an olefin and a secondary carbonium ion is more expensive energetically than rearrangement to a carbonium ion which undergoes fission to an olefin and a tertiary carbonium ion. Therefore, C_{10} carbonium ions may lead to two C_5 species or a C_4 and a C_6 species as in 17a.



(17a)

Secondary reactions between C_5 and C_4 or C_5 and C_6 units undoubtedly occur to some extent, but their results neither detract nor add anything significant to the discussion of the t-amyl cation.

Reaction sequences such as 18a must be excluded because the

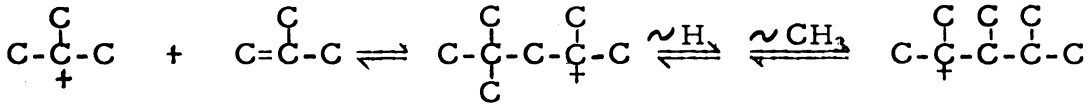


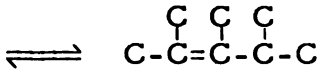
(18a)

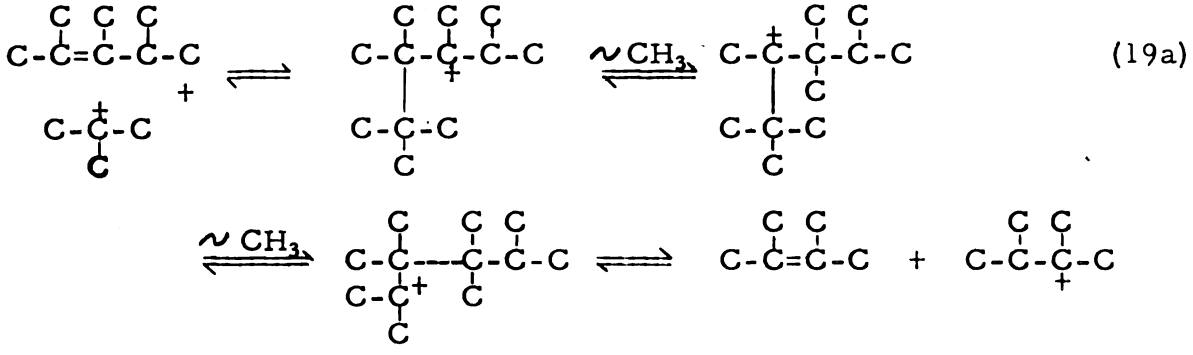
hexyl chlorides obtained from the reaction of t-amyl chloride-1-C^{13} have incorporated negligible amounts of label in C-2, C-3 and C-4. Whitmore and Mosher[15] found that 3, 5, 5-trimethyl-2-heptene (olefin analog of II in 18a) upon treatment with sulfuric acid leads only to isoamylenes.

The relative contributions of bimolecular and unimolecular reactions to the over-all isotope-position rearrangement in the t-amyl system can not be assessed with any degree of accuracy for two reasons: 1) complete isotope-position equilibration has been achieved under the experimental conditions, and 2) the necessary assumption that the nonmethyl carbon atoms equilibrate during each bimolecular reaction is not true.

t-Butyl chloride, in contrast to t-amyl chloride, gives mainly the 2-chloro-2, 3-dimethylbutane. All reasonable reaction sequences lead preferentially to the 2, 3-dimethylbutyl system rather than the 2- or 3-methylpentyl system (19a).







(19a)

A termolecular reaction would be the most reasonable path for formation of t-amyl chloride from t-butyl chloride and should entail simultaneous formation of a C_7 species. Unidentified peaks in the chromatogram (Fig. 2a) of the reaction products could be C_7 compounds.

Disproportionation of a C_{12} unit from the reaction of 3-chloro-3-methylpentane and aluminum chloride could lead to t-butyl chloride and a C_8 species, or t-amyl chloride and a C_7 species.

EXPERIMENTAL

1. The Reactions of t-Amyl Chloride with Aluminum Chloride

In a 25-ml. side-arm flask equipped with a 10 inch glass-spiral column and distillation head connected to a vacuum system was placed 1.75 g. (0.016 mole) of t-amyl chloride (purified by distillation). The flask was immersed in an ice bath. To the magnetically-stirred t-amyl chloride was added 0.078 g. (0.0006 mole) of anhydrous aluminum chloride (Baker and Adamson, reagent grade). At the end of 5 min. the reaction was quenched by injection of 73 μl. (0.0006 mole) of N, N-dimethylaniline. Immediately the ice bath was removed and the volatile portion of the reaction mixture was pulled under vacuum into two traps immersed in liquid air. The amount of liquid collected was 1.26 g. (72% yield based on weight).

All reactions followed the above procedure with changes in reaction time, temperature, and reactant concentrations. In many instances N, N-dimethylaniline was not added; the yield and product composition were unchanged.

2. Product Analysis

Small amounts (0.5-1.5 μl.) of the collected product were injected into a Perkin-Elmer Vapor Fractometer, Model 154. The columns used were 5-30% Silicon Oil on Celite and the column temperatures were about 80°. The vapor phase chromatograms of the reaction products of t-amyl chloride, t-butyl chloride and 3-methyl-3-chloropentane with aluminum chloride are shown in Figs. 1a, 2a and 3a. The individual components were identified by comparison of their retention times with those of authentic samples. Correlation of the area weight of the peaks

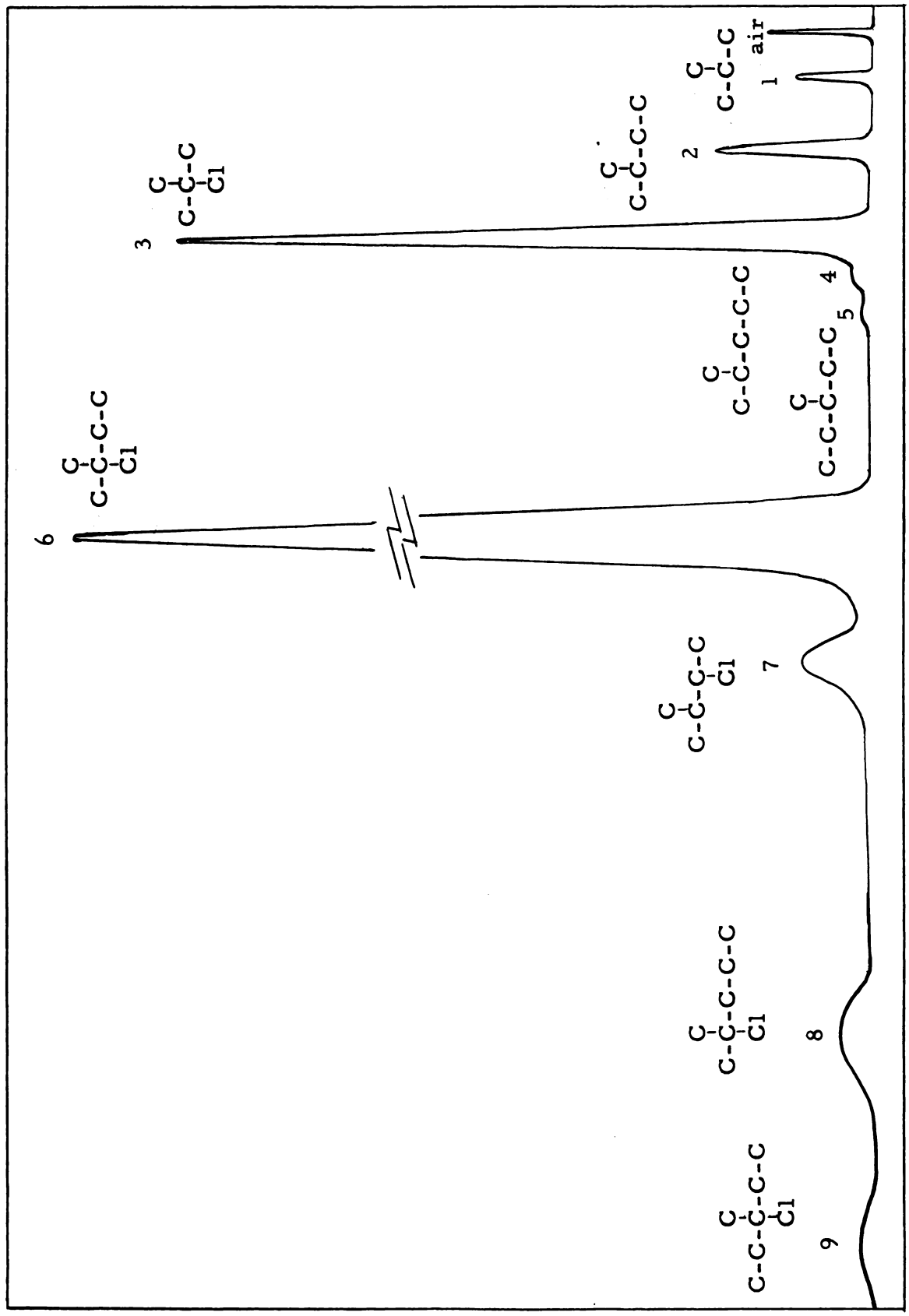


Fig. 1a. The v. p. chromatogram of the products from the reaction of 1.74 g. of t-amyl chloride with 0.080 g. of aluminum chloride at 0° for 5 min.

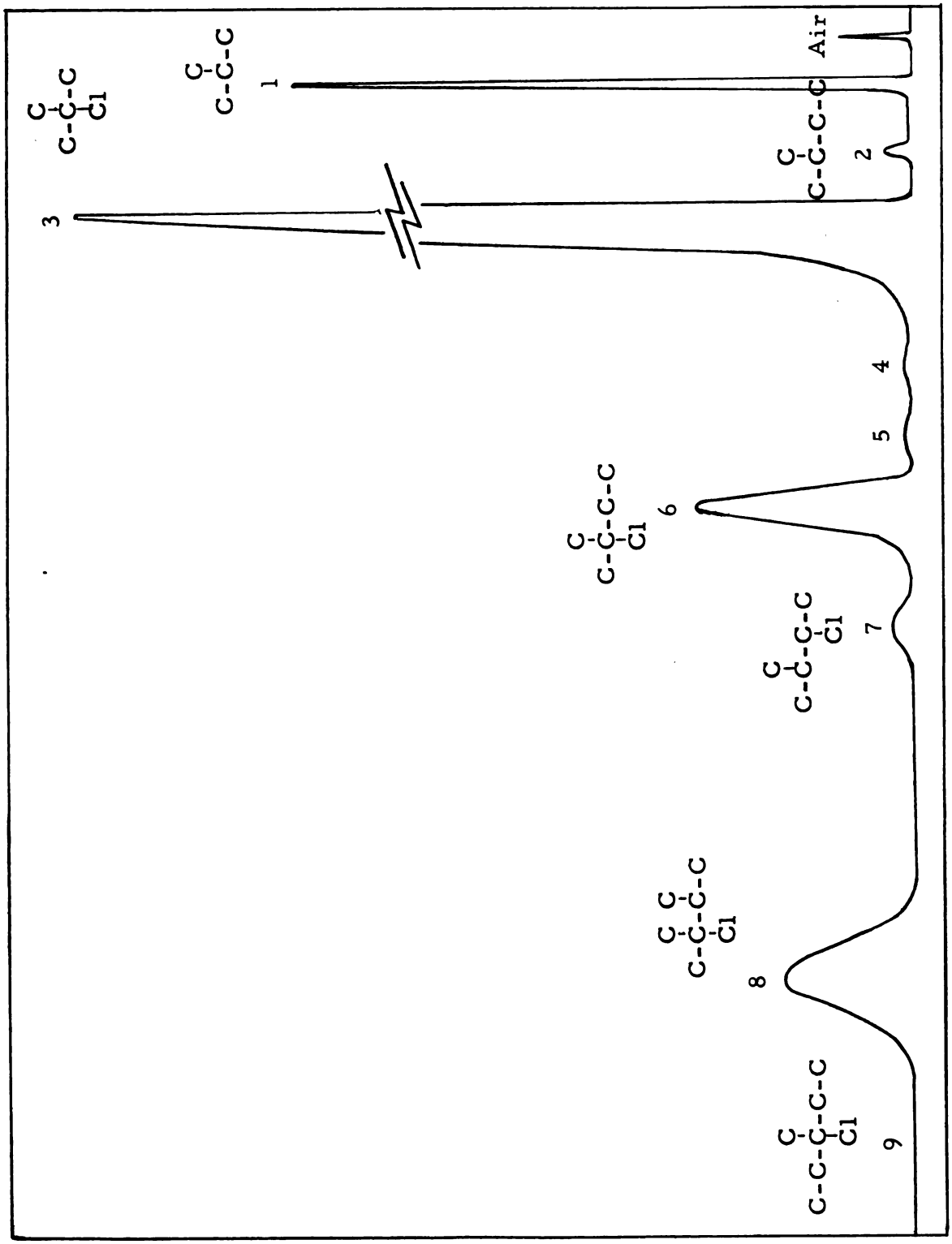


Fig. 2a. The v.p. chromatogram of the products from the reaction of 1.69 g. of t-butyl chloride with 0.087 g. of aluminum chloride at ρ^{o} for 5 min.

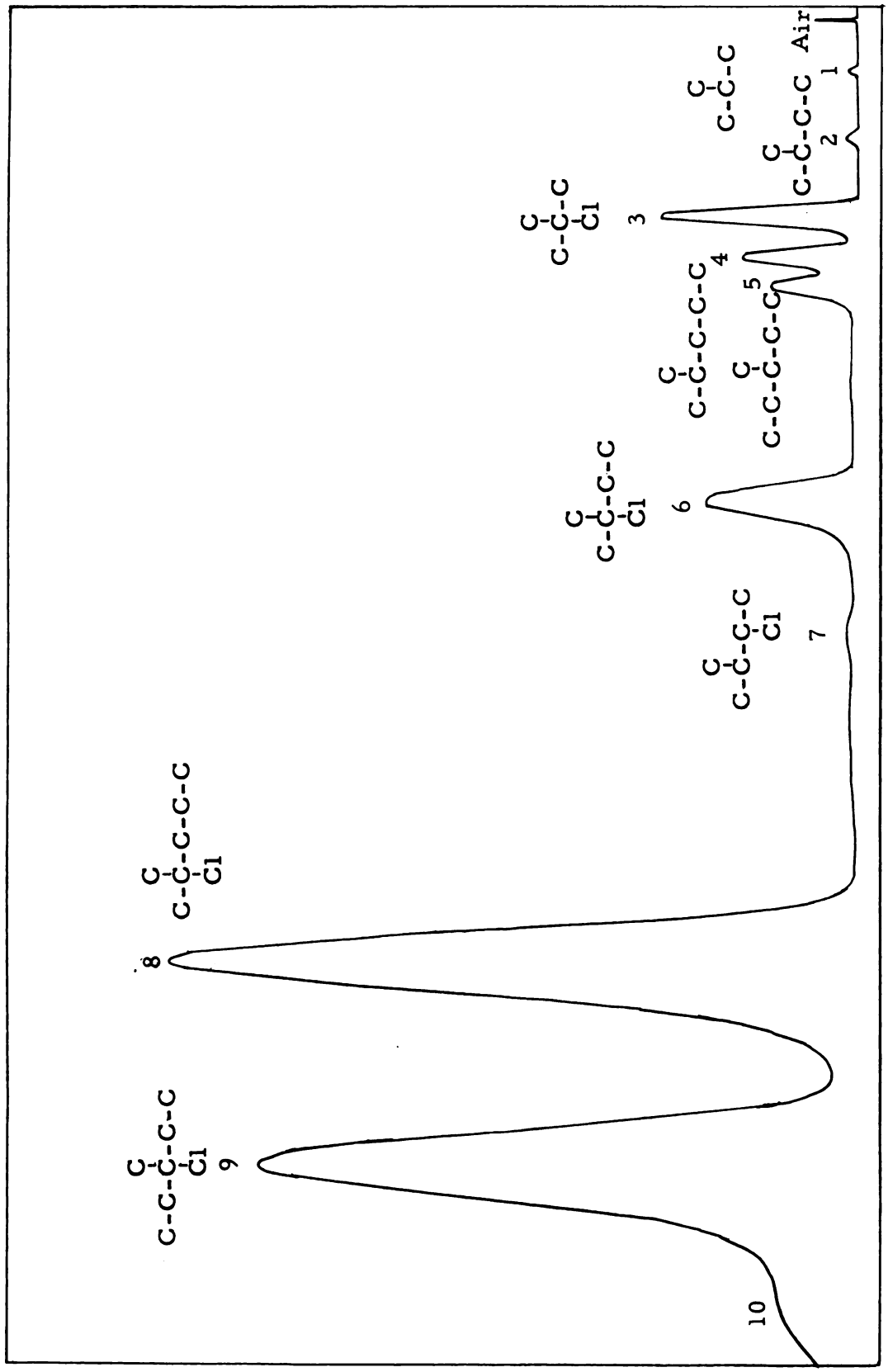


Fig. 3a. The v. p. chromatogram of the products from the reaction of 1.78 g. of 3-chloro-3-methylpentane with 0.073 g. of aluminum chloride at 0° for 5 min.

to component weight allowed the quantitative determination of the reaction components. The error involved (standard deviation) did not exceed ± 10%.

Reaction products of t-amyl chloride. Peaks 1, 2, 3, 4, 5, 6, 8 and 9 (Fig. 1a) were identified by comparison of the vapor phase chromatography (v.p.c.) retention times with known compounds. Attempts to prepare 3-chloro-2-methylbutane by chlorination of the alcohol gave a mixture of two chlorides (10:1 ratio) corresponding to peaks 6(t-amyl chloride) and 7. In some runs the presence of amylenes could be detected between peaks 2 and 3. Occasionally, a trace of t-amyl alcohol would appear directly before peak 6. If a sample of the reaction mixture was passed through the chromatograph at a high amplitude, an unidentified peak could be seen between peaks 7 and 8, another after peak 9 and several with very high retention times. The peak between 7 and 8 did not correspond to the hexyl alcohols, 3-chloropentane, or 1-chloro-2-methylbutane. Isooctane (2,2,4-trimethylpentane) falls on top of peak 7 and 3-chloro-2,3-dimethylbutane comes immediately after peak 8. Isopropyl chloride which would appear after peak 2 and 2-chlorobutane which would appear between 5 and 6 could not be detected in the reaction products. n-Propyl chloride falls on peak 3.

Reaction products of t-butyl chloride. Identification of peaks 1, 2, 3, 6, 7, 8 and 9 (Fig. 2a) was made by comparing retention times with known compounds. The presence of 1-chloro-3-methylpentane (peak 9) implies the presence of 2-chloro-2-methylpentane under peak 8. Peaks 4 and 5 and two peaks beyond 9 were unidentified.

Reaction products of 3-chloro-3-methylpentane. Peaks 1 through 9 (Fig. 3a) were identified by comparison of their retention times with known compounds. Peak 10 and two peaks beyond 10 were not identified.

3. Preparations of Reference Compounds

t-Amyl chloride, t-butyl chloride, isopropyl chloride, 2-chlorobutane, n-propyl chloride, 1-chloro-3-methylbutane, 2-methyl-2-butene, isobutene, isopentane and isobutane were commercially available. 2-Methylpentane and 3-methylpentane were gifts from American Oil Research Labs., Whiting, Indiana.

2-Methyl-2-pentanol. A solution of 28.4 g. (0.20 mole) of methyl iodide in 50 ml. of anhydrous ether was added to 5.2 g. (0.22 mole) of magnesium over a period of 30 min. The solution was refluxed for 30 min. on a steam bath. A solution of 15.5 g. (0.18 mole) of 2-pentanone in 75 ml. of anhydrous ether was added dropwise to the above solution in an ice bath. The solution was stirred for 2 hrs. and allowed to stand overnight. Sixty-five ml. of a cold, saturated ammonium chloride solution was added to the Grignard complex. The ether layer was separated and the aqueous layer was washed with ether. The combined ether layers were washed with cold water and dried over magnesium sulfate. The ether was removed and 14.0 g. (0.14 mole, 78%) of crude alcohol was obtained. V.p.c. showed the presence of a slight ether impurity. The crude alcohol was converted directly into the chloride.

2-Chloro-2-methylpentane. In a 50-ml. flask connected directly to a distillation head were placed 4.0 g. (0.039 mole) of 2-methyl-2-pentanol and 7.0 ml. (0.080 mole) of conc. hydrochloric acid. The magnetically stirred mixture was heated with an oil bath and the fraction boiling from 85-100° was collected. After the chloride was washed with a 10% sodium bicarbonate solution and with water, it was dried over magnesium sulfate. The product weighted 2.0 g. (0.017 mole, 42%) and v.p.c. showed the presence of two small impurities (probably olefins). The chloride was distilled and the fraction boiling at 29°/29 mm. was used for mass-spectral analysis.

3-Methyl-3-pentanol. The Grignard procedure for the preparation of 2-methyl-2-pentanol was repeated using 3-pentanone. Identical amounts were used and a yield of 75% was obtained. V.p.c. showed a small ether impurity.

3-Chloro-3-methylpentane. The procedure for the preparation of 2-chloro-2-methylpentane was followed using 4.0 g. (0.039 mole) of 2-methyl-2-pentanol and 7.0 ml. (0.080 mole) of conc. hydrochloric acid. The fraction (2.6 g., 0.022 mole, 55%) boiling between 85 and 95° was collected. The chloride was distilled and the fraction boiling at 29°/28 mm. was collected for mass-spectral analysis.

3-Methyl-2-butanol. In a 300 ml. three-necked flask fitted with a stirrer, reflux condenser, and a dropping funnel were placed 0.73 g. (0.020 mole) of lithium aluminum hydride and 125 ml. of anhydrous ether. In the dropping funnel were placed 5.6 g. (0.065 mole) of methyl isopropyl ketone and 20 ml. of anhydrous ether. The solution was added dropwise over a period of 30 min. and stirring was continued with reflux for one hour. To the solution was added dropwise 2 ml. of water, followed by 2 ml. of 10% sodium hydroxide and 1 ml. of water. The solution was stirred with reflux for one hour. The ether solution was removed and dried over magnesium sulfate. After removal of the ether, 4.53 g. (0.050 mole, 77%) of alcohol remained. Minor ether and ketone impurities were shown by v.p.c.

3-Chloro-2-methylbutane. The above mixture of 3-methyl-2-butanol was treated with conc. hydrochloric acid according to the 2-chloro-2-methylpentane preparation. In addition to the main product (t-amyl chloride), v.p.c. showed the presence of 3-chloro-2-methylbutane, unreacted alcohol and methyl isopropyl ketone.

2,3-Dimethyl-2-butanol. The procedure for the preparation of 2-methyl-2-pentanol was followed using 5.3 g. (0.22 mole) of magnesium,

28.4 g. (0.20 mole) of methyl iodide and 17.2 g. (0.20 mole) of methyl isopropyl ketone. After the ether was removed, v.p.c. showed that the mixture (24.5 g.) contained the alcohol (~50%), ether and unreacted ketone. Approximate yield was 60%.

2-Chloro-2,3-dimethylbutane. The above solution of 2,3-dimethyl-2-butanol, ether and methyl isopropyl ketone was treated with 30.0 ml. (0.34 mole) of conc. hydrochloric acid (see preparation of 2-chloro-2-methylpentane) and the fraction boiling 52-94° was collected. In addition to the chloride (~40%) v.p.c. showed that the mixture contained ether, methyl isopropyl ketone and two unidentified low retention compounds.

3-Pentanol. In a 300-ml. three-necked flask equipped with a stirrer, reflux condenser and a dropping funnel, 3.8 g. (0.10 mole) of lithium aluminum hydride was added to 15 ml. of anhydrous ether. To the above mixture 8.6 g. (0.10 mole) of 3-pentanone in 50 ml. of anhydrous ether was added over a period of 30 min. After stirring for 20 min., the solution, immersed in an ice bath, was hydrolyzed with 35 ml. of 10% sodium hydroxide. After the solution was stirred for 1.5 hrs., the ether layer was removed and the aqueous layer was extracted three times with ether. The combined ether extracts were washed three times with water and dried over magnesium sulfate. After most of the ether was removed, 8.8 g. of the alcohol-ether mixture was found by v.p.c. to contain 80% of 3-pentanol (~0.080 mole, ~80%).

3-Chloropentane. A mixture of 2.0 g. of the above 3-pentanol-ether solution and 7.0 ml. of conc. hydrochloride acid was heated and the fraction boiling from 75-90° was collected. The presence of 70% of 3-chloropentane, 30% of the unreacted alcohol and a trace of ether was shown by v.p.c.

4. Syntheses of C^{13}-Labeled Compounds

t-Amyl alcohol-1-C^{13}. In a 300-ml. three-necked flask were placed 3.64 g. (0.15 mole) of magnesium and sufficient anhydrous ether to cover the magnesium. A solution of 2.0 g. (0.014 mole) of unlabeled methyl iodide in 7 ml. of anhydrous ether was added through a dropping funnel to initiate the reaction. After the reaction had started, 17.0 g. (0.12 mole) of methyl iodide-C^{13} in 50 ml. of anhydrous ether was added over a period of 1.5 hrs. After the solution had refluxed one hour over a steam bath, 10.4 g. (0.14 mole) of methyl ethyl ketone in 50 ml. of anhydrous ether was added over a period of one hour. The Grignard complex was hydrolyzed with 50 ml. of a saturated ammonium chloride solution. The ether layer was removed and the aqueous portion was washed with ether. The combined ether solutions were washed with water and dried over magnesium sulfate. After removal of the ether, approximately 7.8 g. (0.089 mole, 66%) of t-amyl alcohol-1-C^{13} was obtained. The alcohol was purified with a Beckman Megachrom before conversion to the chloride.

t-Amyl chloride-1-C^{13}. A mixture of 6.8 g. (0.077 mole) of t-amyl alcohol-1-C^{13} and 24.0 ml. (0.30 mole) of conc. hydrochloric acid was heated and the fraction distilling from 65-82° was collected. Approximately 7.9 g. (0.074 mole, 96%) of the chloride was obtained. The t-amyl chloride-1-C^{13} was purified with a Beckman Megachrom before mass-spectral analysis and before reaction with aluminum chloride.

t-Amyl alcohol-2-C^{13}. The Grignard procedure used for the preparation of the 1-C^{13} alcohol was followed using 11.0 g. (0.46 mole) of magnesium, 65.0 g. (0.46 mole) of methyl iodide and 9.6 g. (0.11 mole) of methyl propionate-1-C^{13}. After removal of the majority of the ether, 14.4 g. of an ether and alcohol ($\sim$ 53%, $\sim$ 0.087 mole) mixture

was obtained. Approximate yield of the crude alcohol was 80%. The ether-alcohol mixture was separated with a Beckman Megachrom before conversion to the chloride.

t-Amyl chloride-2-C^{13}. A solution of 6.2 g. (0.071 mole) of t-amyl alcohol-2-C^{13} and 18.0 ml. (0.22 mole) of conc. hydrochloric acid was distilled and the fraction boiling from 65-82° was collected. The chloride which weighed 7.3 g. (0.069 mole, 98%) contained small amounts of amylenes as shown by v.p.c. t-Amyl chloride-2-C^{13} was purified with a Beckman Megachrom before mass-spectral analysis and reaction with aluminum chloride.

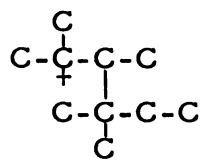
5. Isotope Analysis

Analyses of the C^{13}-labeled compounds were preformed with a Consolidated Model 21-103C Mass Spectrometer by Seymour Meyerson of the Research and Development Department, American Oil Company, Whiting, Indiana.

The n.m.r. spectra were taken with a Model V4300-2 Varian Associates high resolution n.m.r. spectrometer at 60 Mc.

SUMMARY

Bimolecular paths in the reactions of t-amyl chloride-1-C^{13} and t-amyl chloride-2-C^{13} with aluminum chloride were verified by identification (mass spectrometry) of dilabeled t-amyl chloride and hexyl chlorides in the reaction products. The data support I as the first intermediate formed by the attack of t-amyl cation on a C_5 olefin.



I

This C_{10} carbonium ion may undergo fast and reversible rearrangements to other C_{10} carbonium ions. The C_{10} unit, which disproportionates into an olefin and a tertiary carbonium ion, may lead to two C_5 units or a C_4 and a C_6 unit. Calculations of statistical isotopic distribution suggest that each t-amyl species has undergone an average of one bimolecular reaction resulting in complete equilibration of the methyl and partial equilibration of the non-methyl carbon atoms. No scrambling between methyl and non-methyl carbon atoms was detected.

The volatile products from the reaction of 1.74 g. of t-amyl chloride with 0.080 g. of aluminum chloride at 0° for 5 min. are 68.2% t-amyl chloride, 16.7% t-butyl chloride, 5.7% 3-chloro-2-methylbutane, 4.2% 2-chloro-2-methylpentane, 1.5% 3-chloro-3-methylpentane and 3.8% of the corresponding hydrocarbons. The percent recovery of volatile products and the percent t-amyl chloride in the volatile fraction increased with 1) increase in the ratio t-amyl chloride/aluminum chloride, 2) decrease in temperature, and 3) decrease in reaction time.

After five minutes the reaction appears to stop. The apparent termination of the reaction may involve deactivation of the catalyst by highly unsaturated polymers.

PART B

N.M.R. STUDIES OF STEREOISOMERISM IN SOME CARBONYL DERIVATIVES

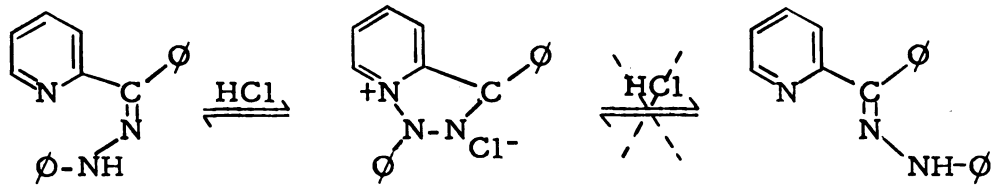
INTRODUCTION

The possibility of stereoisomerism about the carbon-nitrogen double bond in phenylhydrazones has long been recognized.[18] A survey of the literature reveals that the majority of the reported isolations of syn and anti isomers occurs when there is an α-substituent which is capable of hydrogen bonding with the N-H group. Geometric isomers of α-halo 2,4-dinitrophenylhydrazones (DNP's), α-alkoxy DNP's,[19] α-carbonyl DNP's,[20,21,22] furfural DNP[23,24] and 2-acylpyridine phenylhydrazones[25] have been reported. Aromatic DNP's such as those of acetophenone,[26] benzaldehyde[27] and ethyl benzoyl acetate[28] have been isolated in syn and anti forms, but examples of aliphatic derivatives are very limited. Gordon[29] has observed two bands on a chromatographic column for 2-butanone DNP. Three forms of acetaldehyde DNP melting at 168.5°, 156-57° and 149° were obtained by Bryant.[31] Bryant suggested that the two higher melting forms were the stable and unstable isomers, while the 149° form was a mixture of the two. Ingold and coworkers[32] isolated two forms of acetaldehyde DNP melting at 146° and 162°. van Duin[30] separated aldehyde DNP isomers by chromatography. The melting point of the major acetaldehyde DNP was 167-68° and that of the unstable was 93-4°. Laws and Sidgwick,[33] isolated the isomers of acetaldehyde phenylhydrazones.

Various methods have been used to obtain evidence for the existence of stereoisomers. Melting points are not a reliable criterion because they are sensitive to impurities. Furthermore, DNP's can exist in different crystalline forms whose melting points may be different.[33,34,35,36]

Ramirez and Kirby,[19] from differences in the N-H infrared absorbtion band and ultraviolet absorption maxima, were able to assign syn and

anti structures to α-halo and α-alkoxy DNP's. Bredereck,[24] with the aid of dipole moment studies, identified the stabler, higher melting form of substituted furfural DNP's as the syn-hydrogen isomer. Kuhn and Munzing,[25] through isolation of a 8-aza-indozolium salt from one of the isomers of 2-benzoyl pyridine phenylhydrazone, were able to establish the isomeric configurations (1b)

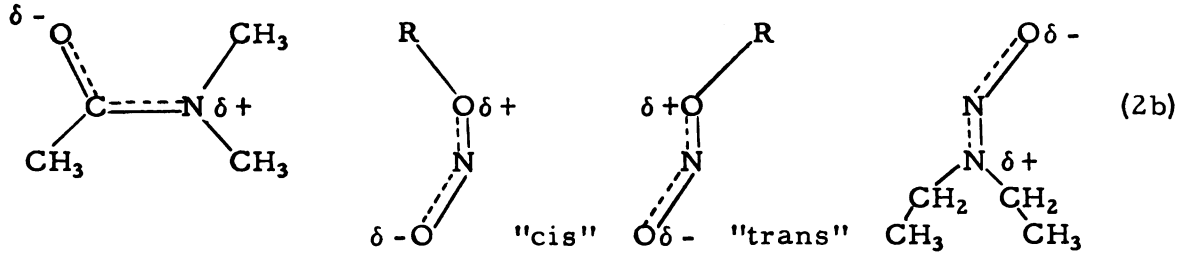


(1b)

Recently, nuclear magnetic resonance (n.m.r.) spectroscopy has become a valuable tool in the study of hindered rotation. The main areas of study have been hindered rotation about single bonds, about partial double bonds and about double bonds.

N.m.r. studies of hindered rotation about single bonds are difficult because one must determine whether the nonequivalence of the hydrogens should be ascribed to slow rotation, or to rapid rotation in which the time-averaged environment of each hydrogen, or group of hydrogens, is different.[37]

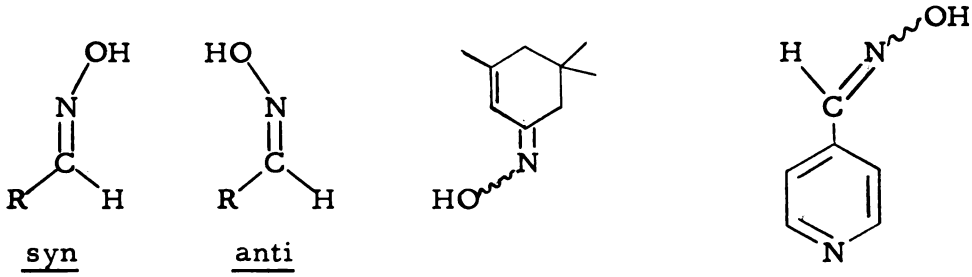
Hindered rotation about partial double bonds is exemplified by amides,[38-44] nitrites[45,46,47] and nitrosamines.[48] The two nonequivalent N-CH_3 groups of N, N-dimethylacetamide (2b-I) appear as a doublet.



I II III (2b)

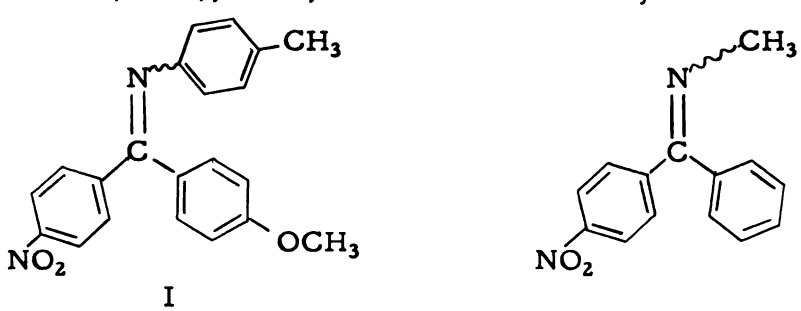
Doubling of α-hydrogens in the n.m.r. spectra of alkyl nitrites has been studied at low temperatures. The doubling is again attributed to partial double bond character which allows the molecules to exist in cis and trans rotational isomers (2b-II). Studies of N, N-diethyl nitrosamine reveal two quartets for the methylene protons and two triplets for the methyl protons (2b-III).

Relatively high barriers of rotation about double bonds simplify studies on geometric isomers. In addition to the well-studied carbon-carbon double bonds, isomerism of carbon-nitrogen double bonds in oximes and imines has been investigated. Phillips[49] observed two aldehydic resonances in propionaldoxime and assigned the low field triplet to the syn form (3b-I, R=$CH_2CH_2CH_3$). Lustig[50] applied n.m.r.



(3b)

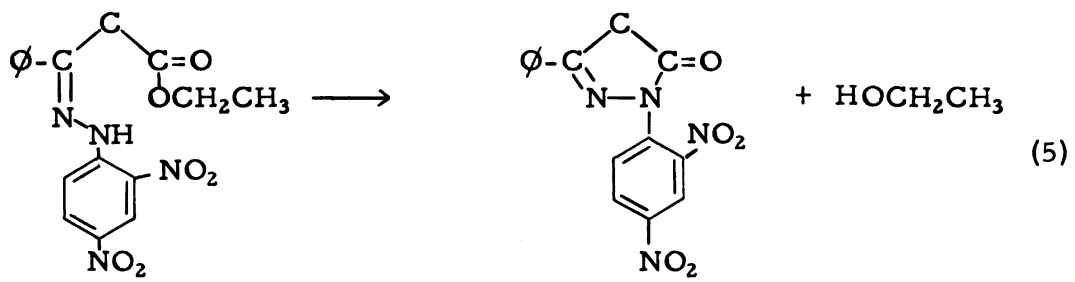
spectroscopy to the study of ketooximes. The isomers of isophorone (3b-II) and isonicotinaldehyde oximes (3b-III) have been observed by Slomp and Wecter,[51] and Mosher and co-workers,[52] respectively. Curtin and Hauser,[53] studying the stereoisomerism of imines, observed two resonances for the phenyl-methyl and phenyl-methoxy protons in p-methoxy, p'-nitrobenzophenone p-tolylimine (4b-I). p-Nitrobenzophenone methyl imine (4b-II), also, exhibited two methyl resonances.



(4b)

In the n.m.r. spectra of oximes, nitrites and nitrosamines, but not in amides, the hydrogens in close vicinity of the oxygen were assigned to the low field resonances.

Application of n.m.r. to other C=N compounds such as DNP's and semicarbazones (SC's) has been limited. In 1959 Curtin[54] used n.m.r. to distinguish between the DNP's and SC's of aldehydes and of ketones. Difference in the n.m.r. spectra of the isomers of ethyl benzoylacetate DNP allowed Silverstein and Shoolery[28] to assign the absolute configuration of each isomer. In their attempts to identify the isomers by cyclization to pyrazolines, they obtained identical rate constants for both isomers; therefore, they concluded that isomerization was much faster than cyclization (5).



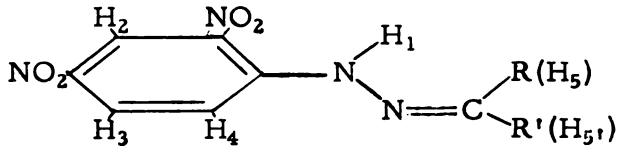
(5)

The purpose of the present investigation was to extend n.m.r. studies of C=N isomerism to 2,4-dinitrophenylhydrazones, the mono-nitrophenylhydrazones, semicarbazones and thiosemicarbazones.

RESULTS

1. Chemical Shifts

2,4-Dinitrophenylhydrazones (DNP's). Table Ib lists the chemical shifts of aldehyde and ketone DNP's in methylene bromide. The aromatic, aldehydic and N-H hydrogens are numbered as in 6b.



(6b)

In symmetrical DNP's (R = R') only one isomer is possible, but the two groups, R and R', are magnetically nonequivalent and usually resonate at different frequencies. The two possible stereoisomers of unsymmetrical DNP's are designated as syn and anti, syn referring to the isomer which has the 2,4-dinitrophenyl group cis to the smaller group. Assignment of syn-anti structures to the isomers was based on equilibrium values (Table Xb). When one R is methyl and the other isopropyl or t-butyl, only one isomer is present. From steric considerations the syn configuration was assigned to these isomers. On this assumption the minor peaks in the spectra of 2-butanone DNP (Fig. 1b) and 2-pentanone DNP were assigned to the anti isomer. Isomer compositions of semicarbazones (Tables XIb and XIIb), thiosemicarbazones (Table XIb) and aldehyde DNP's (Table Xb) support this assignment.

Two sets of aromatic hydrogen resonances are observed when one of the R groups is hydrogen or contains a phenyl or cyclopropyl group. In addition ethyl cyclopropyl ketone DNP, which was not assigned

Table Ib. Chemical Shifts[a] of Equilibrated Solutions of 2,4-Dinitrophenylhydrazones in Methylene Bromide

DNP	H_1	H_2	H_3	H_4	H_5	$H_{5'}$	∅	α-CH or α-CH_2	α-CH_3	β-CH_2	β-CH_3 or γ-CH_3
Formaldehyde	-1.10	0.93	1.63	2.07	2.73	3.23	----	----	----	----	----
Acetaldehyde	-1.00	.98 (.93)	1.70 (1.63)	2.10 (2.08)	2.35	(2.84)	----	----	7.82 (7.85)	----	----
Propionaldehyde	-1.00	.98	1.70	2.08	2.35	(3.05)	----	7.50[m]	----	----	8.78 (8.70)
n-Butyraldehyde	-0.98	.97	1.71	2.13	2.37	(3.03)	----	7.54[m]	----	8.32[m]	8.80[m]
Isobutyraldehyde	-0.97	.97	1.70	2.10	2.40	?	----	7.25[m]	----	----	8.78 (8.75)
Acetone	-0.92	1.02	1.75	2.12	----	----	----	----	7.78 7.86	----	----
2-Butanone	-0.98	0.98	1.73	2.10	----	----	----	7.50	7.87 (7.82)	----	8.77 (8.72)
2-Pentanone	-0.92	1.00	1.75	2.13	----	----	----	7.57	7.92 (7.85)	8.33[m]	9.03
Methyl isopropyl ketone	-0.95	0.95	1.72	2.08	----	----	----	7.27	7.91	----	8.79
Methyl t-butyl ketone	-0.90	.98	1.73	2.10	----	----	----	----	7.90	----	8.73
3-Pentanone	-1.13	.98	1.73	2.10	----	----	----	7.53	----	----	8.77 8.80
Diisopropyl ketone	-1.22	1.02	1.75	2.12	----	----	----	7.08	----	----	8.70 8.80

Continued

Table Ib - Continued

DNP	H_1	H_2	H_3	H_4	H_5	$H_{5'}$	ϕ	α-CH or α-CH_2	α-CH_3	β-CH_2	β-CH_3 or γ-CH_3
Phenylacetone	-0.95	0.98	1.72	2.08	----	----	2.73	6.25 (6.19)	7.97 (7.81)	----	----
Dibenzyl ketone	-1.13	1.02	1.72	2.07	----	----	2.70	6.13 6.20	----	7.13[m]	----
Benzylacetone	-0.90	1.03	1.68	2.22	----	----	2.67	7.13[m]	7.91 (7.87)	7.13[m]	----
Benzyl ethyl ketone	-1.15	0.97 (1.02)	1.71 (1.72)	2.08 (2.05)	----	----	2.73	6.21[b] (6.13)	7.54[c] (7.42)	----	8.86 (8.75)
Ethyl cyclopropyl ketone[d]	-1.25 (-0.78)	1.22 (1.23)	1.95 (1.98)	2.33 (2.40)	----	----	----	e	e	e	e

[a] Internal standard was tetramethylsilane (τ = 10.00). The numbering corresponds to 6b. The chemical shifts of the minor isomer (anti) are placed in parentheses.

[b] -$\underline{CH_2}\phi$

[c] $\underline{CH_2}CH_3$

[d] Syn-anti structures were not assigned. The minor isomer is in parentheses.

[e] Chemical shift was not determined.

[m] Complex multiplet.

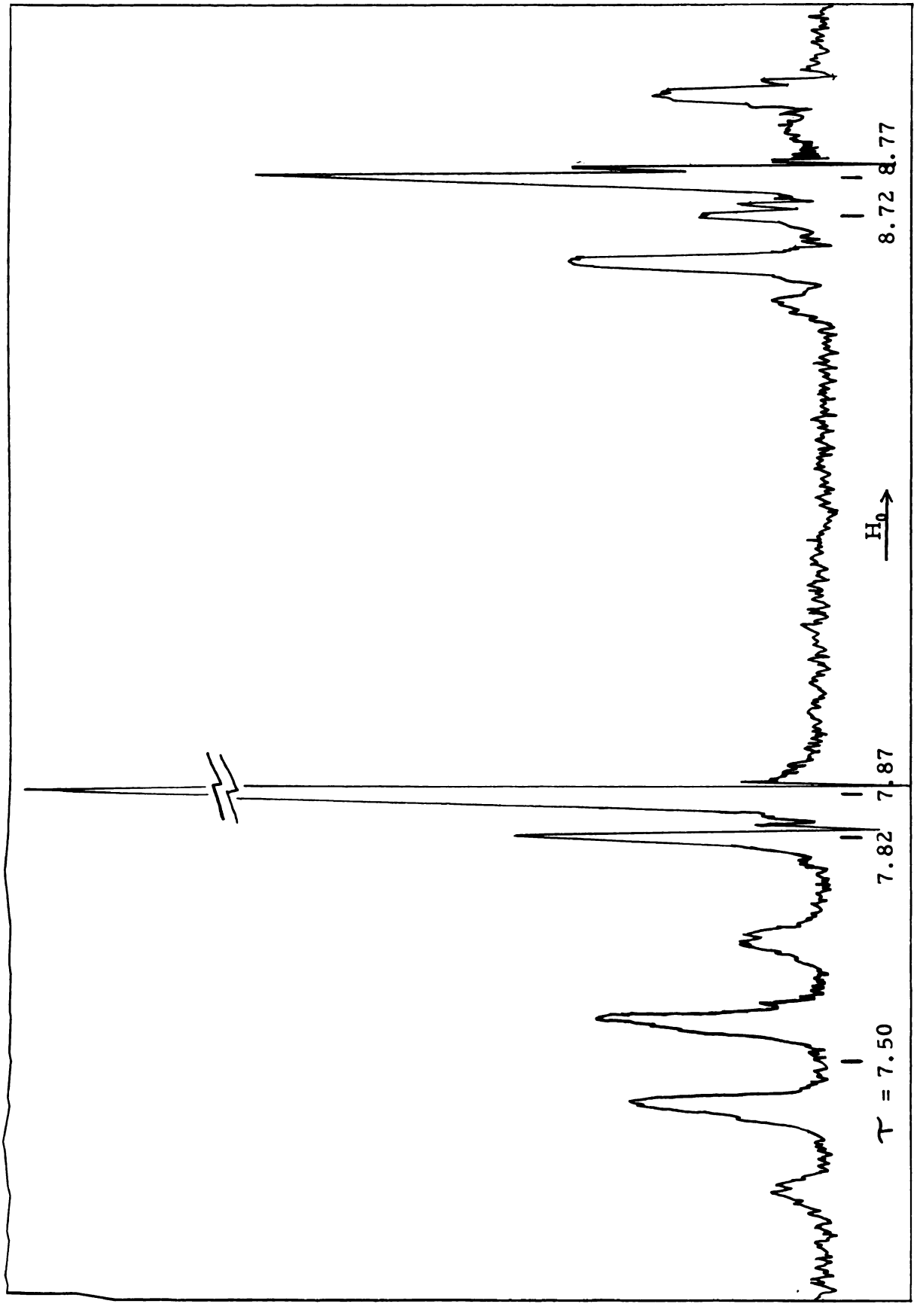


Fig. 1b. N.m.r. spectrum of 2-butanone 2,4-dinitrophenylhydrazone in methylene bromide.

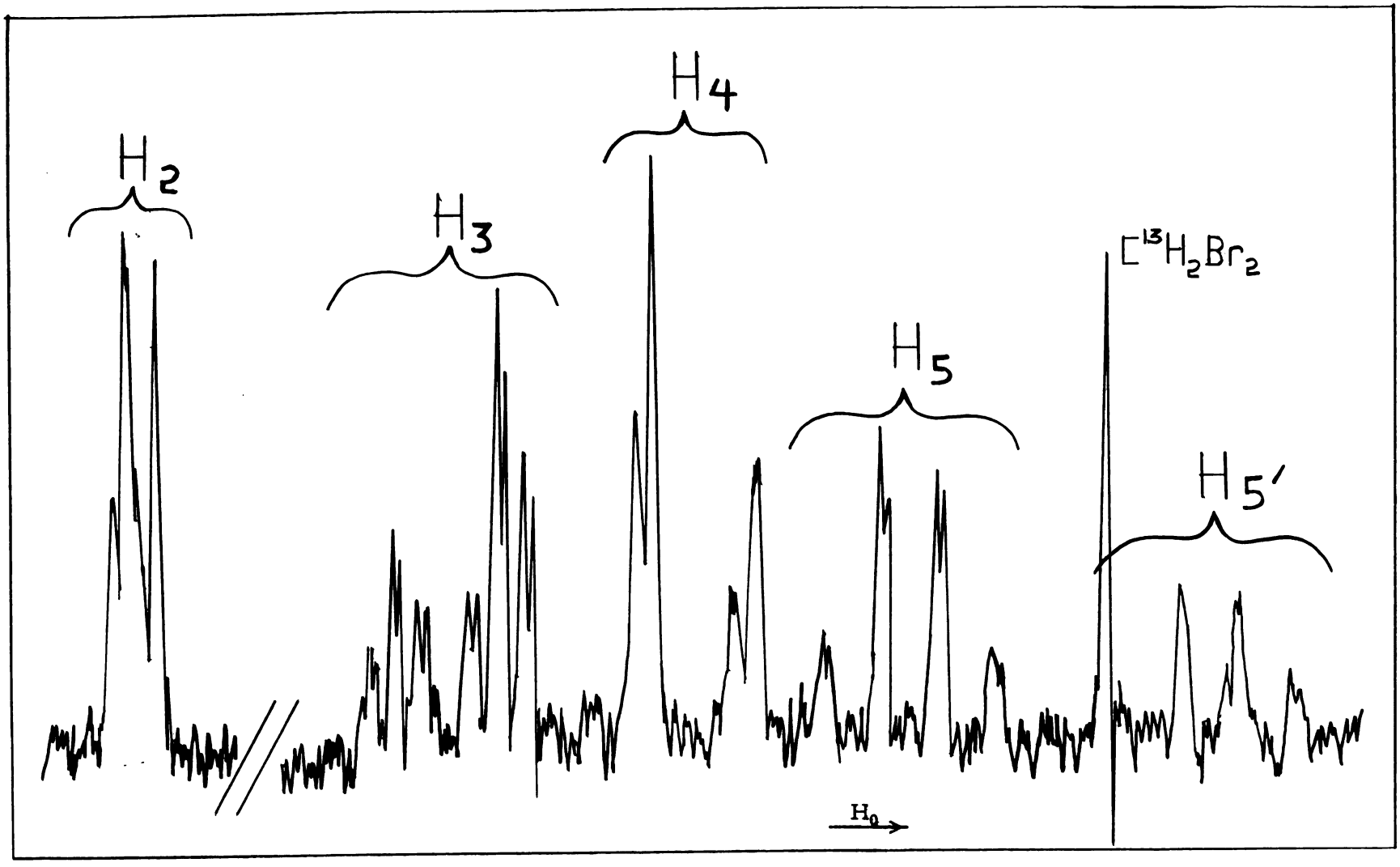


Fig. 2b. N.m.r. spectrum of the aromatic and aldehydic hydrogens of an equilibrated methylene bromide solution of acetaldehyde 2,4-dinitrophenylhydrazone. (The numbering corresponds to 6b. τ values are listed in Table Ib.)

syn-anti structures, has two H_1 resonance signals. Fig. 2b contains the partial n.m.r. spectrum of an equilibrated solution of acetaldehyde DNP. Low anti isomer concentrations prevented the observation of two sets of aromatic hydrogens in the n.m.r. spectra of propionaldehyde, n-butyraldehyde, isobutyraldehyde and phenylacetone DNP's. Although the presence of a second doublet for the β-CH_3 of isobutyraldehyde DNP indicated the presence of 5% of the anti isomer, only one aldehydic doublet could be observed, because the signal to noise ratio was too low.

The chemical shifts of the alkyl hydrogens, H_2, H_3, and H_4 are fairly consistent, but H_1 varies significantly. When the 2,4-dinitrophenyl group is cis to a group larger than methyl (3-pentanone, diisopropyl ketone, dibenzyl ketone and benzyl ethyl ketone DNP's), H_1 resonates at a lower field.

Tables IIb, IIIb, IVb and Vb list the chemical shifts of formaldehyde, acetaldehyde, 2-butanone and 3-pentanone DNP's, respectively, in various solvents. Aromatic and alkyl hydrogens are relatively solvent independent, whereas H_1 and H_5 are appreciably solvent dependent. Two H_1 resonances are observed for acetaldehyde DNP in dimethyl sulfoxide, dimethylformamide and pyridine.

Table 6b shows the small variation in the chemical shifts of DNP hydrogens over the available concentration range.

Mononitrophenylhydrazones. Table VIIb contains the chemical shifts of para-nitrophenylhydrazones (p-NP's), meta-nitrophenylhydrazones (m-NP's) and ortho-nitrophenylhydrazones (o-NP's). The numbering corresponds to 7b. Figs. 3b and 4b show the aromatic hydrogens of acetone p-NP and acetone o-NP, respectively. The aromatic hydrogens of m-NP's were complex and were not resolved. Assignment of the

Table IIb. Chemical Shifts[a] of Formaldehyde 2,4-Dinitrophenylhydrazone in Various Solvents

Solvent	H_1	H_2	H_3	H_4	H_5	$H_{5'}$	$\Delta\delta$[f]
CH_2Br_2	-1.10	0.93	1.63	2.07	2.73	3.23	30.0
$CHCl_3$	-1.13	0.85	1.63	2.05	s	s	s
ϕNO_2	-1.08	1.10	s	s	s	s	s
Dioxane	-1.12	1.02	1.67	2.12	2.73	3.30	34.3
Acetone	-1.32	1.02	1.60	2.00	2.42	3.17	45.5
DMSO[b]	-1.50	1.13	1.62	2.10	2.37	3.13	48.0
TMU[c]	-1.50	1.10	1.62	2.03	2.23	3.18	57.0
DMF[d]	-1.50	1.10	1.62	s	2.40	3.19	47.5
Pyridine	-1.57	1.00	s	s	s	s	s
TFA[e]	----	0.72	1.53	1.95	3.07	----	0

[a]Internal standard was tetramethylsilane (τ = 10.00). Numbering corresponds to 6b.

[b]Dimethyl sulfoxide.

[c]Tetramethylurea.

[d]Dimethylformamide.

[e]Trifluoroacetic acid.

[f]Distance (cps) between H_5 and $H_{5'}$.

Table IIIb. Chemical Shifts[a] and anti/syn Ratios of Acetaldehyde 2,4-Dinitrophenylhydrazone in Various Solvents

Solvent	H_1	H_2	H_3	H_4	H_5	$H_{5'}$	$\Delta\delta$ [g]	α-CH_3	$\Delta\delta$ [h]	anti/syn
CH_2Br_2	-1.00	0.98 (0.93)	1.70 (1.63)	2.10 (2.08)	2.35	2.84	-30	7.82 (7.85)	+2.4	33/67
$CHCl_3$	-1.07	0.87 (0.84)	1.71 (1.63)	2.11 (2.08)	2.46	2.96	-30	7.83 (7.89)	+3.6	31/69
$\not\emptyset NO_2$	-0.97	1.10	s	s	s	s	s	7.91 (7.93)	+2.3	34/66
Dioxane	-1.00	1.03 (0.99)	1.70 (1.65)	2.17 (2.12)	2.37	2.93	-34	7.92 (7.96)	+1.6	26/74
Acetone-d_6	-1.17	1.05 (1.02)	1.67 (1.62)	2.08	2.10	2.83	-44	7.88 (7.86)	-1.2	29/71
DMSO-d_6 [b]	-1.30 (-0.87)	1.20 (1.15)	1.73 (1.65)	2.23 (2.21)	2.03	2.80	-46	7.95 (7.93)	-0.9	14/86
TMU[c]	-1.37	1.12 (1.07)	1.63 (1.56)	2.23 ?	1.85	?	?	7.93 (7.88)	-3.0	17/83
DMF[d]	-1.33 (-1.15)	1.10 (1.06)	1.67 ?	s	s	s	s	7.88 (7.86)	-1.4	18/82
Pyridine	-1.40 (-1.00)	s	s	s	s	s	s	8.01 (8.09)	+5.5	21/79
Quinoline	-0.87	s	s	s	s	s	s	8.29 (8.42)	+8.0	27/73
TFA[e]	----	0.77	1.50	2.22	1.80	----	0	7.48	0	----

[a] Internal standard was tetramethylsilane (τ = 10.00). The numbering corresponds to 6b. Chemical shifts of the anti isomer are placed in parentheses; [b] Dimethyl sulfoxide; [c] Tetramethylurea; [d] Dimethylformamide. [e] Trifluoroacetic acid; [g] Chemical shift (cps) of H_5 from $H_{5'}$. (Negative sign indicates that H_5 is at a lower field than $H_{5'}$); [h] Chemical shift (cps) of syn methyl from anti methyl. (Negative sign indicates that the syn methyl is at lower fields.) [s] Solvent interference.

Table IVb. Chemical Shifts[a] and anti/syn Ratios of 2-Butanone 2,4-Dinitrophenylhydrazone in Various Solvents

Solvent	H_1	H_2	H_3	H_4	α-CH_2	α-CH_3	$\Delta\delta$[f]	β-CH_3	$\Delta\delta$[g]	anti/syn
CH_2Br_2	-0.98	0.98	1.73	2.10	7.50	7.87 (7.82)	+3.5	8.78 (8.72)	-3.0	17/83
$CHCl_3$	-1.00	0.92	1.70	2.07	7.48	7.89 (7.82)	+5.0	8.75 (8.72)	-2.4	18/82
ϕNO_2	-0.88	1.07	s	s	7.55	7.97 (7.88)	+5.4	8.82 (8.77)	-2.5	16/84
Dioxane	-0.92	1.03	1.73	2.17	s	7.93 (7.87)	+4.0	8.80 (8.75)	-2.5	16/84
Acetone-d_6	-0.97	1.08	1.68	2.08	7.46	7.85 (7.82)	+1.9	8.79 (8.72)	-4.0	23/77
DMSO-d_6[b]	-0.80	1.17	1.67	2.18	7.52	7.92 (7.86)	+3.0	8.83 (8.78)	-2.0	20/80
TMU[c]	-0.87	1.13	1.62	2.10	s	s	s	8.83 h	h	s
DMF[d]	-0.97	1.03	s	s	s	7.83 (7.81)	+1.5	8.80 (8.75)	-3.0	18/82
Pyridine	-0.92	0.98	s	s	7.57	8.08 (7.93)	+9.0	8.87 h	h	7/83
TFA[e]	----	0.72	1.38	2.58 (2.57)	6.77	7.11 (7.05)	+3.4	7.58 (7.65)	+4.0	30/70

[a]Internal standard was tetramethylsilane (τ = 10.00). The numbering corresponds to 6b. Chemical shifts of the anti isomer are placed in parentheses; [b]Dimethyl sulfoxide; [c]Tetramethylurea; [d]Dimethylformamide; [e]Trifluoroacetic acid; [f]Chemical shift (cps) of syn α-CH_3 from anti α-CH_3. (Positive sign indicates that the syn α-CH_3 is at higher fields); [g]Chemical shift (cps) of the syn β-CH_3 from anti β-CH_3. (Negative sign indicates that the syn β-CH_3 is at lower fields); [h]Inability to distinguish the anti isomer may be caused by its low concentration.
[s]Solvent interference.

Table Vb. Chemical Shifts[a] of 3-Pentanone 2,4-Dinitrophenylhydrazone in Various Solvents

Solvent	H_1	H_2	H_3	H_4	α-CH_2	$\Delta\delta$[d]	β-CH_3	$\Delta\delta$[e]
CH_2Br_2	-1.12	1.00	1.73	2.08	7.50	0	8.75 8.79	2.4
$CHCl_3$	-1.17	0.98	1.73	2.00	7.55	0	8.77	0
Acetone	-1.17	1.03	1.63	2.00	s	s	8.73 8.78	2.5
DMSO[b]	-0.97	1.17	1.63	2.15	s	s	8.83 8.85	0.6
Pyridine	-1.13	0.95	s	s	7.62 7.67	3.0	8.41 8.50	4.8
TFA[c]	----	0.73	1.43	2.61	6.72 6.76	2.4	8.41 8.50	5.4

[a]Internal standard was tetramethylsilane (τ = 10.00). The numbering corresponds to 6b.

[b]Dimethyl sulfoxide; [c]Trifluoroacetic acid; [d]Chemical shift difference (cps) between the two α-CH_2's; [e]Chemical shift difference (cps) between the two β-CH_3's.

[s]Solvent interference.

Table VIb. Concentration Studies of Some 2,4-Dinitrophenylhydrazones[a]

Solvent	Conc.[b]	H_1	H_2	H_3	H_4	α-CH_2	α-CH_3	β-CH_3
2-Butanone DNP								
DMSO[c]	6.3%	-0.80	1.17	1.67	2.18	s	s	8.83
"	2.0	-0.82	1.14	1.64	2.14			8.83
CH_2Br_2	7.1	-0.98	0.98	1.73	2.10	7.50	7.87	8.78
"	3.3	-0.96	0.95	1.71	2.08	7.50	7.87	8.78

Solvent	Conc.	H_1	H_2	H_3	H_4	H_5	$H_{5'}$
Formaldehyde DNP							
DMSO	13%	-1.50	1.13	1.62	2.10	2.37	3.13
"	2	-1.51	1.08	1.57	2.01	2.37	3.13

[a] Internal standard was tetramethylsilane (τ = 10.00). The numbering corresponds to 6b.

[b] Concentration computed from weights.

[c] Dimethyl sulfoxide.

[s] Solvent interference.

Table VIIb. Chemical Shifts[a] of para-, meta- and ortho-Nitrophenylhydrazones

p-NP	Solvent	H_1	H_2	H_3	H_4	$H_{4'}$	α-CH or α-CH_2	α-CH_3	β-CH_3
Acetaldehyde	CH_2Br_2	?	1.93	3.05	2.76	(3.22)	----	7.96 (8.04)	----
Acetone	CH_2Br_2	2.48	1.93	3.00	----	----	----	7.92 8.05	----
2-Butanone	CH_2Br_2	2.37	1.93	2.98	----	----	7.63 (7.67)	8.07 (7.96)	8.87
Methyl isopropyl ketone	CH_2Br_2	2.27	1.92	2.93	----	----	7.42	8.10 (8.03)	8.87
3-Pentanone	CH_2Br_2	2.20	1.92	2.95	----	----	7.61 7.65	----	8.83
3-Pentanone	DMSO[b]	0.15	1.93	2.83	----	----	7.58 7.64	----	8.88 8.92
3-Pentanone	Acetone	0.83	1.90	2.80	----	----	s	----	8.85 8.90
Diisopropyl ketone	CH_2Br_2	2.07	1.93	2.93	----	----	7.02 7.31	----	8.83 8.85
Phenylacetone	CH_2Br_2	2.35	1.93	2.95	----	----	6.38 (6.33)	----	8.17 (7.95)

Continued

Table VIIb - Continued

m-NP[c]	Solvent	α-CH or α-CH_2	α-CH_3	β-CH_3
Acetaldehyde	CH_2Br_2	----	7.95 (8.04)	----
Acetone	CH_2Br_2	----	7.93 8.07	----
2-Butanone	CH_2Br_2	7.65 (7.70)	8.11 (7.97)	8.87
Methyl isopropyl ketone	CH_2Br_2	7.38	8.11 (7.68)	8.88
Phenylacetone	CH_2Br_2	6.31 (6.27)	8.17 (8.09)	----

o-NP	Solvent	H_1	H_2	H_3	H_4	H_5	α-CH or α-CH_2	α-CH_3	β-CH_3
Acetaldehyde[d]	CH_2Br_2	-0.67	----	----	----	----	----	7.94 (7.98)	----
Acetone[d]	CH_2Br_2	-0.53	----	----	----	----	----	7.87 7.97	----
2-Butanone[d]	CH_2Br_2	-0.50	----	----	----	----	7.62	8.03 (7.93)	8.79 (8.85)
Methyl isopropyl ketone[d]	CH_2Br_2	-0.40	----	----	----	----	7.40	7.98 (7.96)	8.82
3-Pentanone	CH_2Br_2	-0.83	1.83	2.10	2.47	3.22	7.54	----	8.77 8.80
3-Pentanone	DMSO[b]	-0.70	1.85	2.12	2.35	3.13	s	----	8.83 8.85
3-Pentanone	Acetone	-0.81	1.81	2.03	2.42	3.21	s	----	8.77 8.82

Continued

Table VIIb - Continued

	Solvent	H_1	α-CH_2	β-CH_3
Phenylacetone[d]	CH_2Br_2	-0.63	6.31 (6.27)	8.17 (8.09)

[a]Internal standard was tetramethylsilane (τ = 10.00). The numbering corresponds to 7b. The chemical shifts of the anti isomer are placed in parentheses.

[b]Dimethyl sulfoxide.

[c]The chemical shifts of H_1 and of the aromatic hydrogens were not calculated.

[d]The chemical shifts of the aromatic and aldehydic hydrogens were not calculated.

[s]Solvent interference.

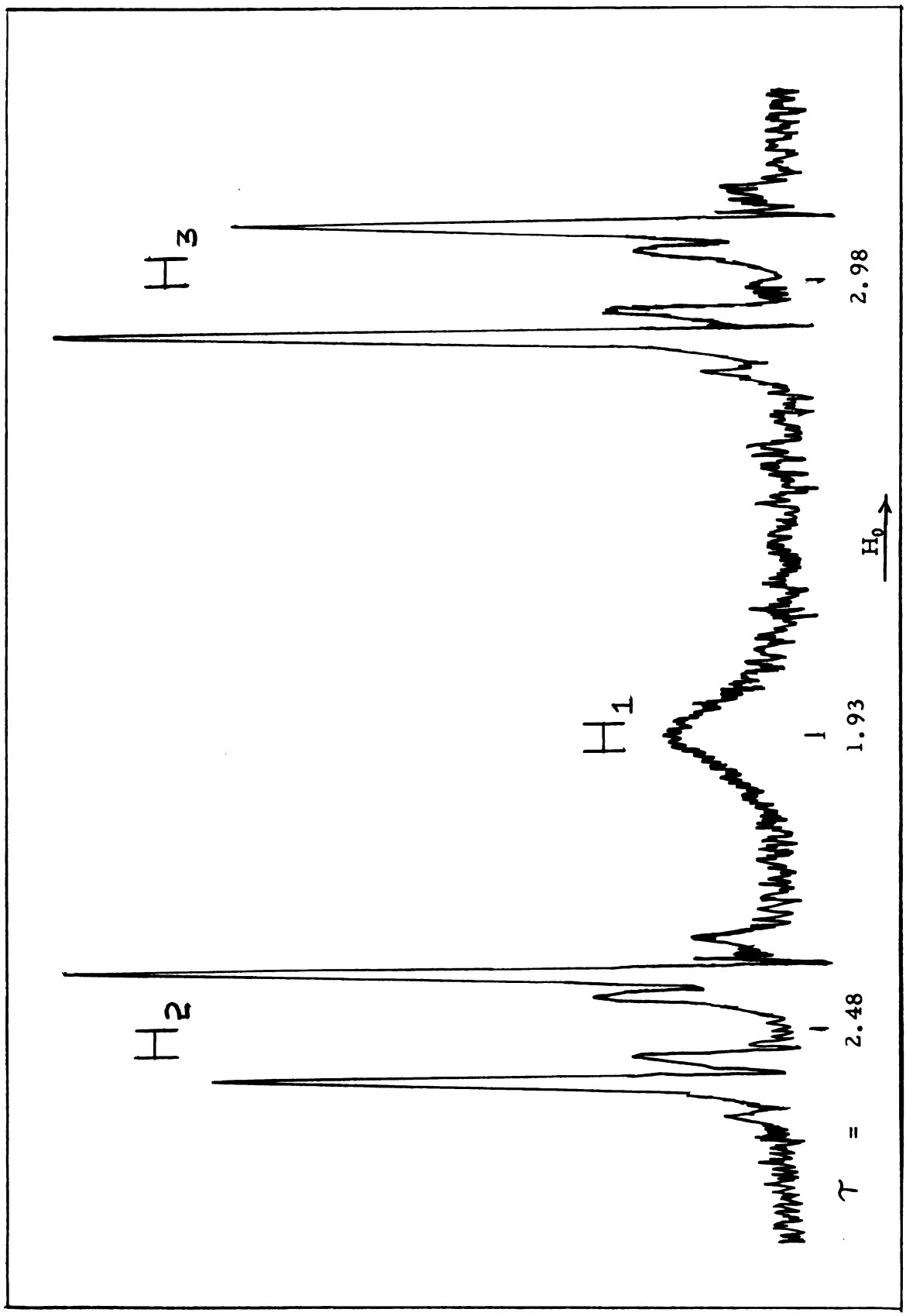


Fig. 3b. N.m.r. spectrum of aromatic and N-H hydrogens of acetone para-nitrophenylhydrazone in methylene bromide. (Numbering corresponds to 6b).

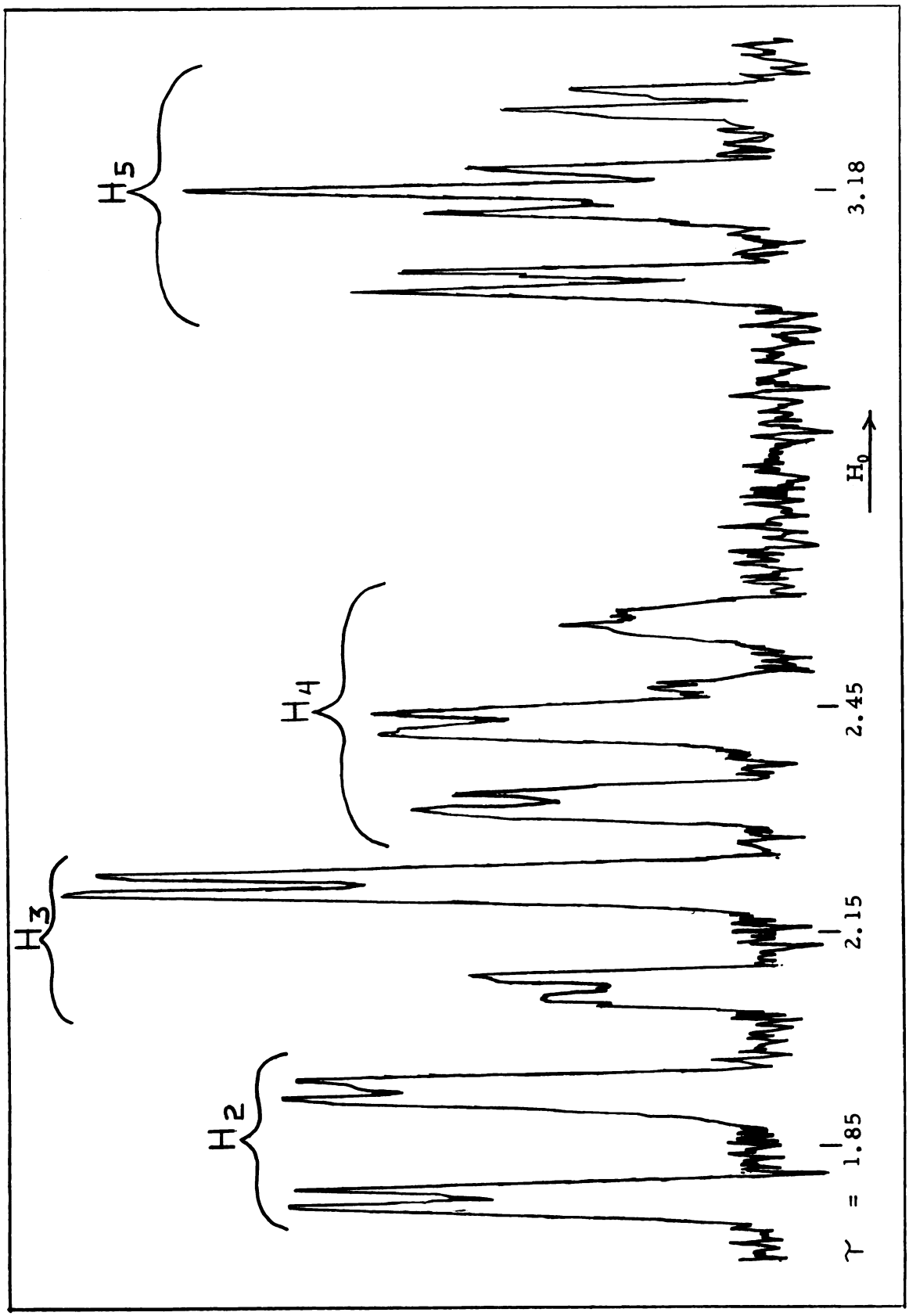
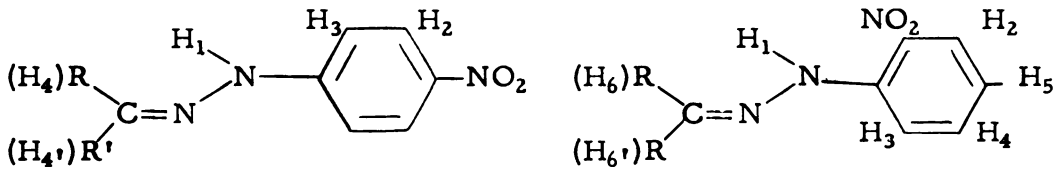


Fig. 4b. N.m.r. spectrum of the aromatic hydrogens of acetone ortho-phenylhydrazone in methylene bromide. (Numbering corresponds to 7b).



(7b)

aromatic hydrogens was made by assuming that the hydrogen at lowest fields was the hydrogen ortho to the nitro group. Chemical shifts were calculated using first order approximations. As in DNP's, acetaldehyde o-NP developed a second set of aromatic hydrogens upon equilibration.

Semicarbazones and Thiosemicarbazones. Tables VIIIb and IXb summarize the chemical shifts of SC's and TSC's, respectively. The N-H and NH_2 resonances were not calculated. Cis and trans hydrogens of TSC's become equivalent in trifluoroacetic acid. Traces of trifluoroacetic acid caused the two methyl singlets of acetone TSC in methylene bromide and chloroform to coalesce. Addition of sulfuric acid to acetone TSC in methylene bromide broadened the peaks but did not cause them to coalesce.

2. Isomer Chemical Shift Differences

Tables Xb, XIb and XIIb contain the $\Delta\delta$'s of the nitrophenylhydrazones in methylene bromide, the $\Delta\delta$'s of SC's and TSC's in chloroform, and the $\Delta\delta$'s of TSC's in trifluoroacetic acid, respectively. For convenience the values are reported in cps. For the unsymmetrical derivatives, a positive sign signifies that the hydrogens cis to the derivative group are at higher fields (higher τ) than the corresponding trans hydrogens. A negative sign indicates the reverse. For example, in the spectrum of 2-butanone DNP, the minor α-CH_3 and β-CH_3 peaks occur at lower fields than the major peaks. On the assumption that the major isomer is the syn isomer (2,4-dinitrophenyl group is cis to the methyl),

Table VIIIb. Chemical Shifts[a] of Semicarbazones

SC	Solvent	H_5[c]	$H_{5'}$[d]	-Ø	α-CH or α-CH_2	α-CH_3	β-CH_2 or β-CH_3	γ-CH_3
Acetaldehyde	CH_2Br_2	3.00	(3.53)	----	----	8.07 (8.12)	----	----
Acetone	TFA[c]	----	----	----	----	7.23 7.32	----	----
	$CHCl_3$	----	----	----	----	8.00 8.15	----	----
2-Butanone	TFA	----	----	----	6.95 (7.00)	7.33 (7.27)	8.56	----
	$CHCl_3$	----	----	----	7.71	8.12 (8.03)	8.90	----
Methyl isopropyl ketone	TFA	----	----	----	6.67	7.37 (7.33)	8.55 (8.58)	----
	$CHCl_3$	----	----	----	7.50	8.15	8.92	----
2-Pentanone	TFA	----	----	----	7.03[m]	7.35 (7.27)	8.10[m]	8.87 8.93
	$CHCl_3$	----	----	----	7.77[m]	8.15 (8.04)	8.42[m]	9.07 9.10
3-Pentanone	TFA	----	----	----	6.92 6.99	----	8.55 8.57	----
	$CHCl_3$	----	----	----	7.72	----	8.92	----
Diisopropyl ketone	TFA	----	----	----	6.42 6.72	----	8.50 8.54	----
	$CHCl_3$	----	----	----	7.02 7.35	----	8.87 8.89	----

Continued

Table VIIIb - Continued

SC	Solvent	H_5[c]	$H_{5'}$[d]	-Ø	α-CH or α-CH_2	α-CH_3	β-CH_2 or β-CH_3	γ-CH_3
Acetophenone	TFA	----	----	2.12[m]	----	6.92 (7.00)	----	----
Phenylacetone	TFA	----	----	----	5.67 (5.69)	7.33 (7.40)	----	----

[a]Internal standard was tetramethylsilane (τ = 10.00).

[b]Trifluoroacetic acid.

[c]Aldehydic hydrogen of the syn isomer.

[d]Aldehydic hydrogen of the anti isomer.

[m]Complex multiplet.

[s]Solvent interference.

Table IXb. Chemical Shifts[a] *of Thiosemicarbazones*

Table IXb. Chemical Shifts[a] of Thiosemicarbazones

TSC	Solvent	H_5[d]	$H_{5'}$[e]	α-CH_2	α-CH_3	β-CH_2	β-CH_3	γ-CH_3
Acetaldehyde	$CHCl_3$	s	s	----	8.01 (8.06)	----	----	----
"	DMSO[b]	2.52	(3.23)	----	8.08 (8.05)	----	----	----
Acetone	$CHCl_3$	----	----	----	7.96 8.05	----	----	----
"	CH_2Br_2	----	----	----	7.94 8.01	----	----	----
"	CH_2Br_2 + TFA[c]	----	----	----	7.96	----	----	----
"	CH_2Br_2 + H_2SO_4	----	----	----	7.94 8.01	----	----	----
"	$\not{\text{O}}NO_2$	----	----	----	8.01 8.09	----	----	----
"	DMSO	----	----	----	8.03 8.07	----	----	----
"	Pyridine	----	----	----	8.12 8.16	----	----	----
"	TFA	----	----	----	8.22	----	----	----
2-Butanone	$CHCl_3$	----	----	7.65	8.04 (7.98)	----	8.88 (8.85)	----
"	TFA	----	----	7.80	8.12	----	8.83	----

Continued

Table IXb - Continued

TSC	Solvent	H_5[d]	$H_{5'}$[e]	α-CH_2	α-CH_3	β-CH_2	β-CH_3	γ-CH_3
2-Pentanone	$CHCl_3$	----	----	7.72	8.03 (7.99)	8.42[m]	----	9.07[m]
3-Pentanone	$CHCl_3$	----	----	7.65	----	----	8.86 8.88	----
	TFA	----	----	7.78	----	----	8.87	----

[a]Internal standard was tetramethylsilane (τ= 10.00).

[b]Dimethyl sulfoxide.

[c]Trifluoroacetic acid.

[d]Aldehydic hydrogen of the syn isomer.

[e]Aldehydic hydrogen of the anti isomer.

[m]Complex multiplet.

[s]Solvent interference.

Table XIb. Proton Chemical Shift Differences[a] and $\frac{J_{gem}}{J_{vic}}$ Ratios of Bromomethanes. Bromide

Table Xb. Isomer Chemical Shift Differences[a] and anti/syn Ratios of Nitrophenylhydrazones in Methylene Bromide

		Aldehyde hydrogen	α-CH or α-CH_2	α-CH_3	β-CH_2 or β-CH_3	γ-CH_3	anti/syn
Formaldehyde	DNP	30.0	----	----	----	----	----
	p-NP	34.5[f]	----	----	----	----	----
Acetaldehyde	DNP	-30.0	----	+2.3	----	----	33/67
	o-NP	?	----	+2.6	----	----	43/57
	m-NP	?	----	+5.6	----	----	40/60
	p-NP	-28.0	----	+5.3	----	----	35/65
Propionaldehyde	DNP	-43.0	m	----	-5.0	----	22/78
n-Butyraldehyde	DNP	-40.0	m	----	m	m	13/87
Isobutyraldehyde	DNP	?	m	----	-2.0	----	5/95
Acetone	DNP	----	----	4.5	----	----	----
	o-NP	----	----	5.5	----	----	----
	m-NP	----	----	8.6	----	----	----
	p-NP	----	----	7.8	----	----	----
2-Butanone	DNP	----	0	+3.5	-2.4	----	17/83
	o-NP	----	0	+5.0	-2.0	----	15/85
	m-NP	----	+2.8	+8.0	0	----	13/87
	p-NP	----	+2.5	+7.0	0	----	19/81
2-Pentanone	DNP	----	0	+4.0	m	0	14/86
Methyl isopropyl ketone	DNP	----	d	d	d	----	0/100
	o-NP	----	e	+1.5	e	----	8/92
	m-NP	----	e	+5.5	e	----	3/97
	p-NP	----	e	+4.1	e	----	0/100
Methyl t-butyl ketone	DNP	----	d	----	d	----	0/100

Continued

Table Xb – Continued

Table Xb - Continued

		Aldehyde hydrogen	α-CH or α-CH_2	α-CH_3	β-CH_2 or β-CH_3	γ-CH_3	anti/syn
3-Pentanone	DNP	----	0	----	2.4	----	----
	o-NP	----	0	----	2.0	----	----
	p-NP	----	2.7	----	0	----	----
Diisopropyl ketone	DNP	----	0	----	5.5	----	----
	p-NP	----	17.0	----	1.4	----	----
Phenylacetone	DNP	----	-3.5	+10.0	----	----	15/85
	o-NP	----	-2.5	+11.7	----	----	14/86
	m-NP	----	-2.0	+14.3	----	----	14/86
	p-NP	----	-2.8	+13.0	----	----	16/84
Dibenzyl ketone	DNP	----	3.5	----	----	----	----
Benzylacetone	DNP	----	m	+2.6	m	----	15/85[c]
Benzyl ethyl ketone	DNP	----	$CH_2\phi$ -4.6 CH_2CH_3 +7.5	----	+6.6	----	45/55[b]

[a] The distance (cps) of hydrogens cis to the derivative group from those trans. A positive sign indicates that cis hydrogens are at higher fields than trans hydrogens. No sign is given for symmetrical derivatives.

[b] The anti isomer is cis to the ethyl group.

[c] Ratio was obtained in nitrobenzene.

[d] Only one isomer present.

[e] Concentration of anti isomer was too low to determine Δδ.

[f] Dimethyl sulfoxide.

[m] Complex multiplet prevented the determination of Δδ.

Table XIb. Isomer Chemical Shift Differences and anti/syn Ratios of Semicarbazones and Thiosemicarbazones in Chloroform[a]

		Aldehyde hydrogen	α-CH or α-CH_2	α-CH_3	β-CH_2 or β-CH_3	γ-CH_3	anti/syn
Acetaldehyde	SC	-31[c]	----	+3.6[c]	----	----	43/57[c]
"	TSC	s	----	+3.0	----	----	26/74
Acetone	SC	----	----	9.0	----	----	----
"	TSC	----	----	5.8[b]	----	----	----
"	"	----	----	4.0[c]	----	----	----
"	"	----	----	5.0[d]	----	----	----
"	"	----	----	2.5[e]	----	----	----
"	"	----	----	1.3[f]	----	----	----
"	"	----	----	0	----	----	----
2-Butanone	SC	----	0	+5.8	0	----	15/85
"	TSC	----	0	+3.4	-2.0	----	17/83
2-Pentanone	SC	----	0	+6.2	m	-2.5	14/86
"	TSC	----	0	+2.6	m	m	20/80
Methyl isopropyl ketone	SC	----	g	g	g	----	0/100
3-Pentanone	SC	----	0	----	0	----	----
"	TSC	----	0	----	1.3	----	----
Diisopropyl ketone	SC	----	19.7	----	1.3	----	----

[a]The distance (cps) of hydrogens cis to the derivative group from those trans. A positive sign indicates that the cis hydrogens are at higher fields than the trans hydrogens. No sign is given for symmetrical derivatives.

[b]Methylene bromide; [c]Nitrobenzene; [d]Pyridine; [e]Dimethyl sulfoxide; [f]Trifluoroacetic acid; [g]Only one isomer present.

[m]Complex multiplet prevented the determination of $\Delta\delta$.

Table XIIb. Isomer Chemical Shift Differences[a] and anti/syn Ratios of Semicarbazones in

Table XIIb. Isomer Chemical Shift Differences[a] and anti/syn Ratios of Semicarbazones in Trifluoroacetic Acid

SC	α-CH	α-CH_2	α-CH_3	β-CH_2	β-CH_3	γ-CH_3	anti/syn
Acetone	----	----	5.0	----	----	----	----
2-Butanone	----	+3.2	+4.2	----	0	----	22/78
2-Pentanone	----	0	+4.3	m	----	+3.3	29/71
Methyl isopropyl ketone	0	----	+2.8	----	+2.3	----	14/86
3-Pentanone	----	3.8	----	----	1.4	----	----
Diisopropyl ketone	19.0	----	2.7	----	----	----	----
Acetophenone[b]	----	----	+4.5	----	----	----	95/5
Phenylacetone[b]	----	-1.3	+4.0	----	----	----	84/16

[a] The distance (cps) of hydrogens cis to the derivative group from those trans. A positive sign indicates that the cis hydrogens are at higher fields than the trans hydrogens. No sign is given for symmetrical derivatives.

[b] The $\Delta\delta$'s and the anti/syn ratios were assigned assuming that the major isomer had the derivative group cis to the aromatic ring.

[m] Complex multiplet prevented the determination of $\Delta\delta$.

the α-CH_3 has a positive $\Delta\delta$. The β-CH_3 has a negative $\Delta\delta$, because it resonates at a lower field when cis to the phenyl group (anti isomer).

Generally, α-hydrogens are shielded (positive $\Delta\delta$) while aldehydic and β-hydrogens are deshielded (negative $\Delta\delta$). β-Hydrogens of SC's and 2-butanone DNP in trifluoroacetic acid, β-$CH_2(CH_2\emptyset)$ and β-CH_3 of benzyl ethyl ketone DNP and α-CH_2 of phenylacetone nitrophenylhydrazones are exceptions. In trifluoroacetic acid the minor isomer peaks of SC's of acetophenone and phenylacetone resonate at higher fields than the major peaks. The methyls of DNP, o-NP and TSC of acetaldehyde are deshielded in carbonyl solvents (dimethyl sulfoxide, tetramethylurea, dimethylformamide and dimethyl formamide and acetone). The methyls of acetaldehyde p-NP and all the 2-butanone derivatives are shielded in the carbonyl solvents.

A decrease of about 0.5 cps in $\Delta\delta$'s of acetone DNP in methylene bromide, and acetone SC and TSC in chloroform was noted when the spectra of warmed solutions were compared to those of cooled solutions.

3. Equilibration and Stability of the Derivatives

The isomer ratios of some unsymmetrical nitrophenylhydrazones changed with time to a constant value. Most SC's, TSC's and aliphatic ketone DNP's had equilibrated by the time the spectra were taken. The n.m.r. of fresh solutions of acetaldehyde, propionaldehyde, n-butyraldehyde, benzyl ethyl ketone and phenylacetone DNP's showed the presence of one isomer; upon standing the second isomer (anti) appeared. Fig. 5b shows the equilibration of acetaldehyde DNP in methylene bromide. The anti aromatic and aldehyde resonances appeared simultaneous with the anti methyl peaks. The time required for equilibration depended on the solvent, and it decreased as the melting point of the crystals decreased (Table XIIIb). Figs. 6b and 7b contain the partial n.m.r. spectra of benzyl ethyl ketone DNP in a freshly prepared solution and an equilibrated solution, respectively.

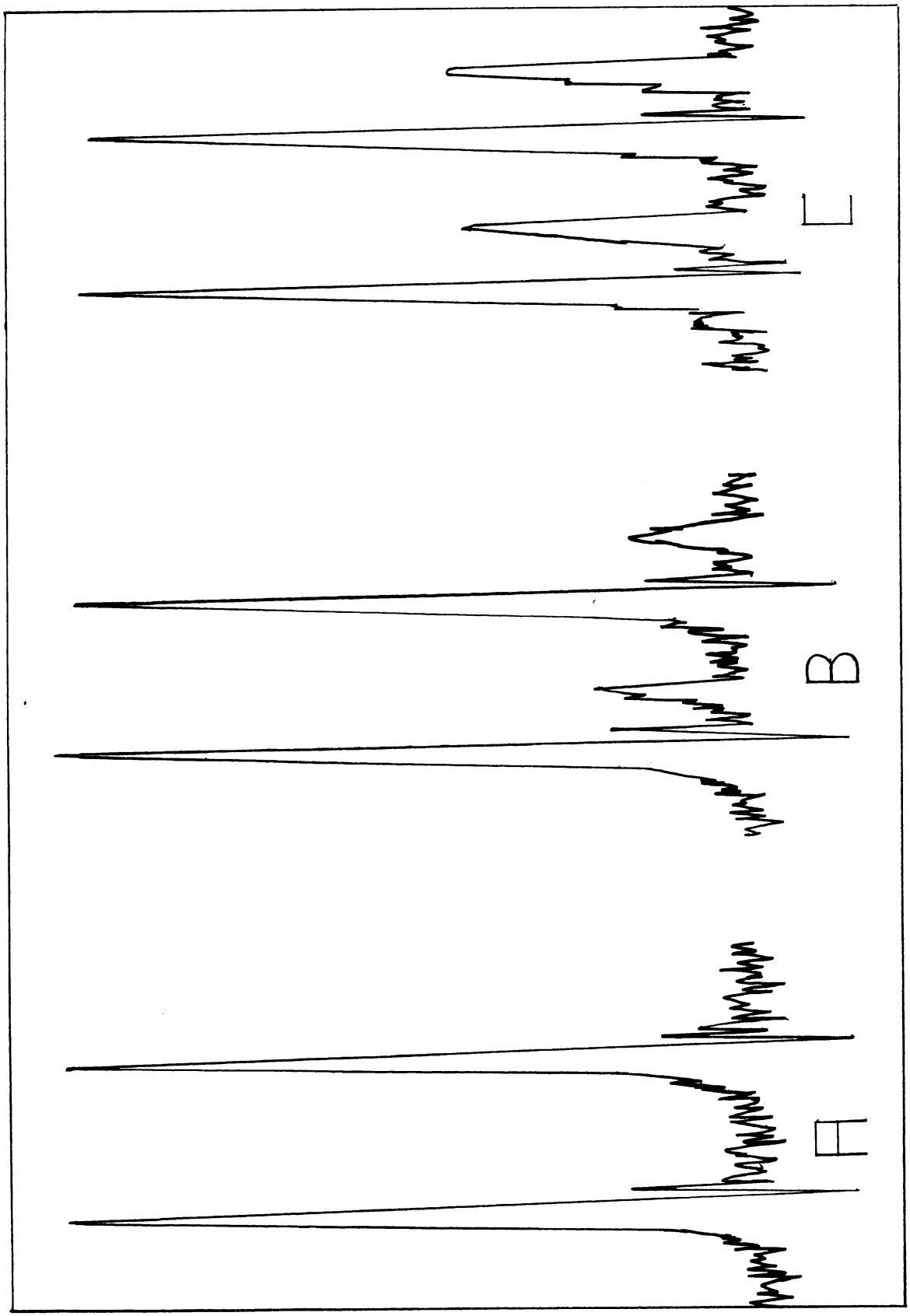


Fig. 5b. N.m.r. spectra of the methyl peaks of acetaldehyde 2,4-dinitrophenylhydrazone in methylene bromide: (A) freshly prepared solution, (B) solution after five hours, (C) equilibrated solution.

Table XIIIb. Time Studies of the Equilibration of Acetaldehyde 2,4-Dinitrophenylhydrazones

Nitrobenzene Time	anti/syn	Pyridine Time	anti/syn	Methylene Bromide Time	anti/syn
Acetaldehyde DNP, m.p. = 164-65°					
0.5 hr.	0/100	0.1 hr.	0/100	0.1 hr.	0/100
11.5 hrs	+/100	8.5 hrs.	15/85	8.8 hrs.	19/81
1 day 2 hrs.	4/96	11.3 hrs.	19/81	9.5 hrs.	25/75
3 days 10 hrs.	17/83	1 day 6.7 hrs.	21/79	1 day 7 hrs.	28/72
5 days 8 hrs.	19/81			2 days	30/70
11 days	28/72			3 days 10 hrs	34/66
Acetaldehyde DNP, m.p. = 145-47°					
		0.2 hr.	+/100	0.2 hr.	+/100
		1.5 hrs.	8/92	2.5 hrs.	11/89
		4.0	12.5/87.5	7.5	28/72
		6.0	20/80	13.0	32/68

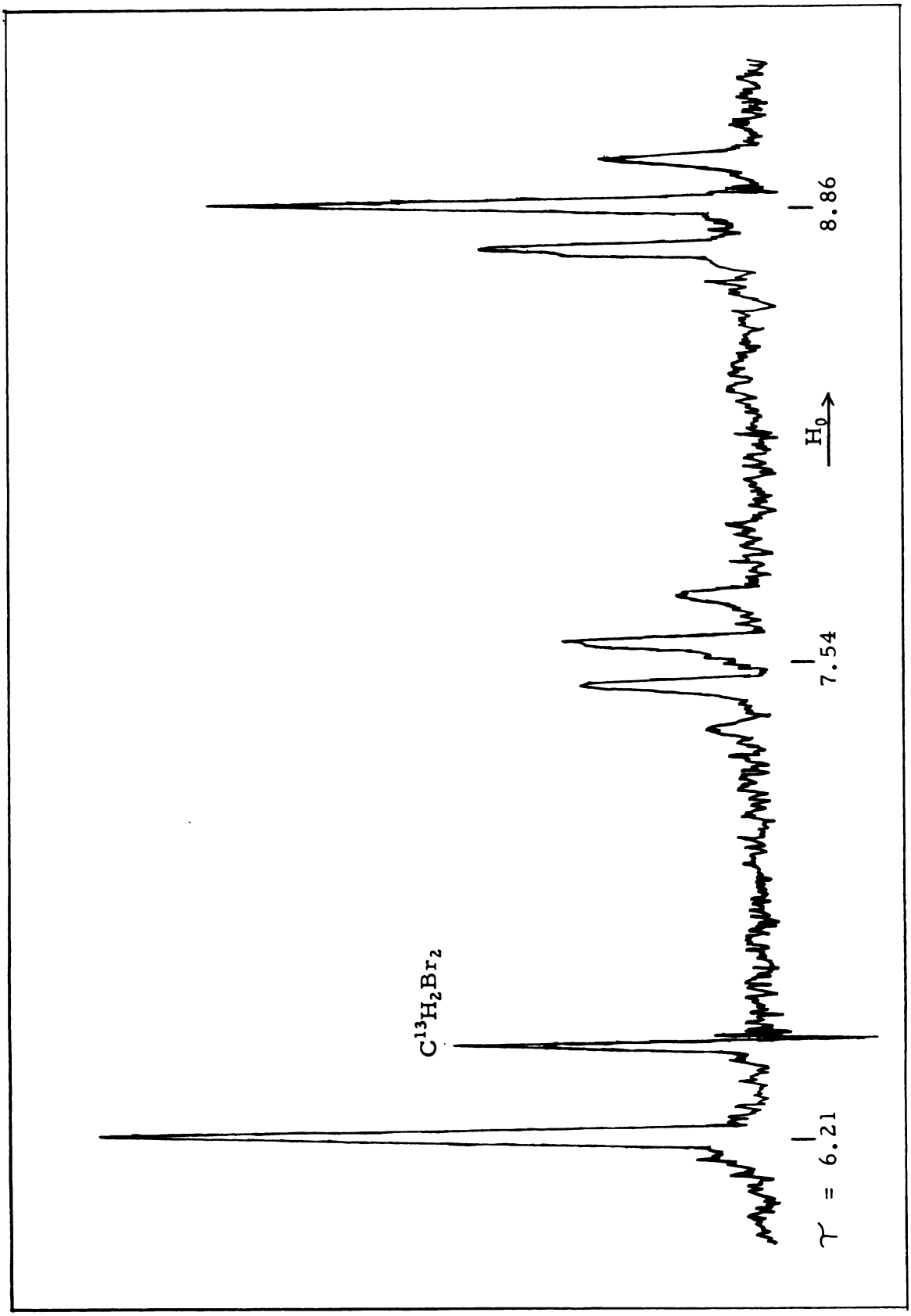


Fig. 6b. N.m.r. spectrum of a freshly prepared solution of benzyl ethyl ketone 2,4-dinitrophenylhydrazone in methylene bromide.

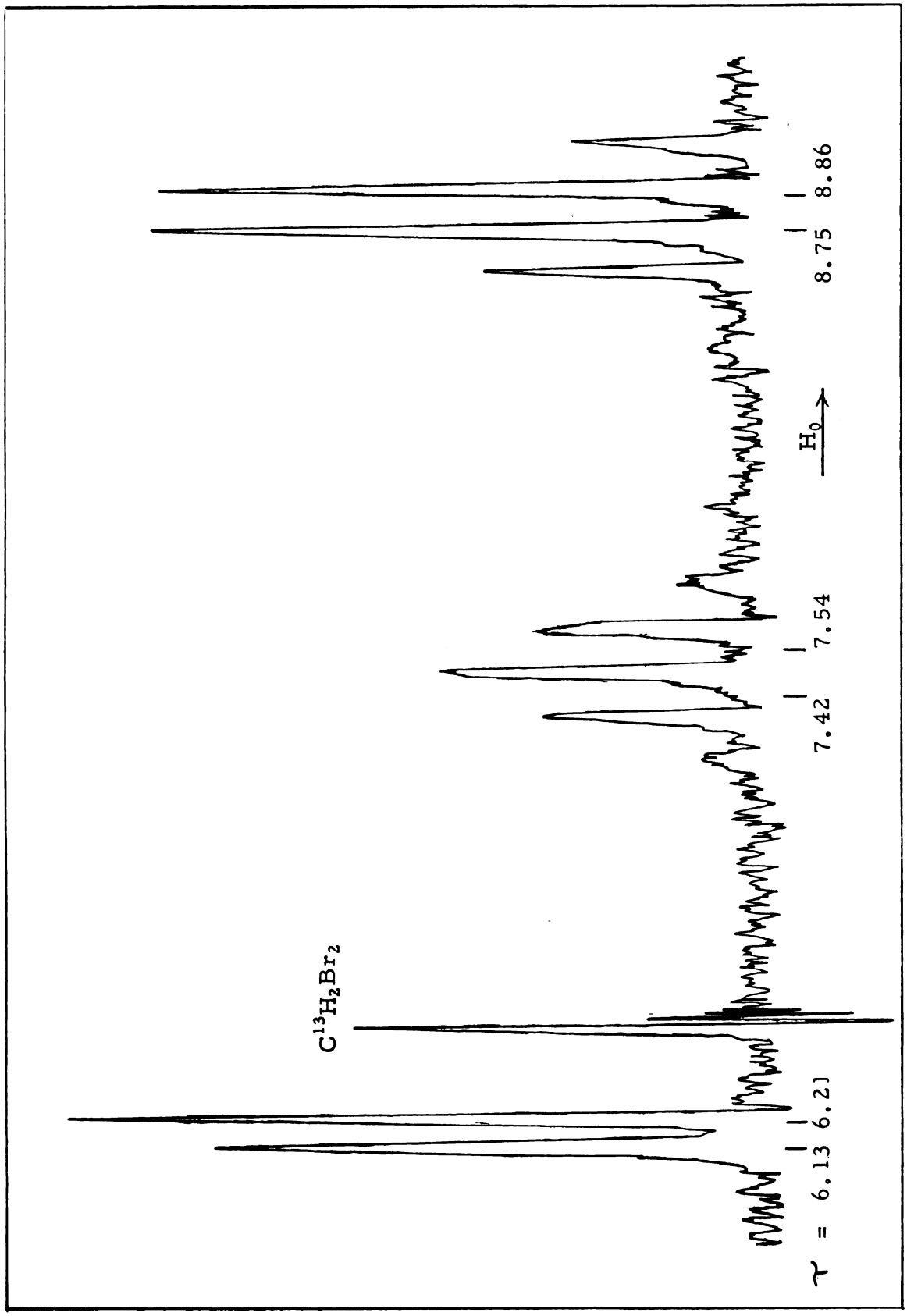


Fig. 7b. N.m.r. spectrum of an equilibrated solution of benzyl ethyl ketone 2,4-dinitrophenylhydrazone in methylene bromide.

The equilibration is acid-catalyzed. Some solutions of acetaldehyde DNP, which were prepared in the absence of acid, did not equilibrate after standing at room temperature for 10 days. Addition of traces of acid to these solutions effected equilibration within several hours.

When the solvent was removed under reduced pressure from equilibrated acetaldehyde solutions, the crystals melted over a wider range and 10-15° lower than the original crystals. When these lower melting crystals were redissolved, the n.m.r. showed the presence of 20-25% of the anti isomer.

Attempts to obtain pure anti isomer crystals of acetaldehyde DNP by fractional crystallization from methylene bromide-n-heptane solutions resulted in the separation of a mixture (melting point = 87-105°) which contained 85% anti and 15% syn. On standing solutions of this mixture reached the same anti/syn ratios as the syn isomer.

Acetaldehyde crystals were obtained that melted at 145-46°, 157-58°, 160-61° and 165-66°. The n.m.r. spectra of the latter three crystals contained one isomer (methyl doublet at τ = 7.82 in methylene bromide). The low-melting crystals showed the presence of less than 5% of the anti isomer.

In solution nitrophenylhydrazones did not isomerize to the azo form; phenylhydrazones have been reported to isomerize.[55]

DNP, o-NP, SC and TSC crystals are stable indefinitely, whereas some m-NP and p-NP crystals decomposed to a dark oil after standing for several days. In general, solutions of all the derivatives were stable. Occasionally, decomposition to starting ketones was observed in trifluoroacetic acid solutions of SC's.

4. Spin-Spin Coupling Constants

Table XIVb lists aldehydic, aromatic and N-H coupling constants (J's) of several nitrophenylhydrazones. The complex spectra of the aromatic hydrogens of m-NP's were not analyzed.

H_1 of DNP's couples strongly with H_3 and H_5, weakly with H_4, and not at all with H_2 and $H_{5'}$. These couplings disappear upon exchange with D_2O as illustrated in Figs. 8b and 9b. The couplings also disappear in tetramethylurea, dimethylformamide and trifluoroacetic acid. Addition of traces of acid and water to dimethyl sulfoxide did not destroy the coupling. The broadness of H_4 of formaldehyde DNP in comparison with H_4 of acetone DNP and the broadness of $H_{5'}$ in comparison with H_5 of N-deuterated formaldehyde DNP imply that there is a small coupling ($\sim$ 0.2 cps) between H_4 and $H_{5'}$.

H_1 of o-NP's also couples selectively with the ortho hydrogen, one meta hydrogen (H_4), and the aldehydic hydrogen of the syn isomer. Coupling of H_1 with aromatic hydrogens is not observed in formaldehyde p-NP in dimethylsulfoxide, but the H_1 does couple with the cis aldehydic hydrogen.

5. Benzene Anisotropy Calculations

The bond lengths and angles used to calculate the distance of hydrogens from the phenyl ring are listed in Table XVb. The lettering corresponds to 8b.

In the absence of data on bond lengths and angles of DNP's values were estimated by comparing similar compounds.[56] The following comments are pertinent to the calculations: 1) The most inaccurate value is that of "e". The only reported N-N bond lengths (1.46 $\pm$ .02Å) are in hydrazine, α,α- and α,β-dimethylhydrazine. 2) For simplification angles "ad" and "bd" were assumed to be 120° in the syn and anti

Table XIVb. Spin-Spin Coupling Constants[a]

DNP's	Solvent	J_{12}	J_{13}	J_{14}	J_{15}	$J_{15'}$	J_{23}	J_{24}	J_{34}	$J_{55'}$
Formaldehyde	CH_2Br_2	0	0.7	0.2	0.8	0	2.6	0.4	9.7	11.0
"	Dioxane	0	0.7	b	1.0	0	2.5	0.4	9.8	11.3
"	DMSO[d]	0	0.7	b	0.8	0	2.6	0.4	9.6	11.2
"	Acetone	0	0.7	b	0.8	0	2.6	0.4	9.7	11.2
"	DMF[e]	0	0	s	0	0	2.6	0.4	9.9	11.2
"	TMU[f]	0	0	0	0	0	2.6	0.4	9.6	11.4
Acetaldehyde	CH_2Br_2	0	0.8	b	0.7	0	2.5	0.4	9.8	----
Propionaldehyde	"	0	0.7	b	0.7	c	2.6	0.4	9.8	----
Isobutyraldehyde	"	0	0.7	b	0.6	c	2.5	0.4	9.7	----
Acetone	"	0	0.7	0.3	----	----	2.5	0.5	9.7	----
2-Butanone	"	0	0.7	0.3	----	----	2.5	0.4	9.6	----
3-Pentanone	"	0	0.7	0.2	----	----	2.5	0.4	9.6	----

o-NP[h]	Solvent	J_{13}	J_{14}	J_{16}	J_{23}	J_{24}	J_{25}	J_{34}	J_{35}	J_{45}
Acetaldehyde	Acetone	0.2	0.6	0.7	0.5	1.6	8.4	8.7	1.6	6.5
Methyl isopropyl ketone	CH_2Br_2	0.2	0.6	----	0.5	1.5	8.4	8.6	1.7	6.6
3-Pentanone	CH_2Br_2	0.4	0.6	----	0.5	1.8	9.0	9.0	1.7	7.0

p-NP	Solvent	J_{12}	J_{13}	J_{23}	J_{14}	$H_{14'}$	$J_{44'}$
Formaldehyde	DMSO[d]	0[g]	0[g]	9.5	0.8	0	12.0
Acetone	CH_2Br_2	0[g]	0[g]	9.5	----	----	----

[a] J values are in cps. The numbering corresponds to 6b and 7b. J values listed as zero are < 0.1 cps from observed line-widths; [b] Broad signal; [c] Concentration of the anti isomer was too small to determine the J. [d] Dimethyl sulfoxide; [e] Dimethylformamide; [f] Tetramethylurea; [g] H_2 and H_3 form an A_2B_2 system. The peak heights and widths were identical; [h] J_{12}, J_{15} and $J_{16'}$ are < 0.1 cps.

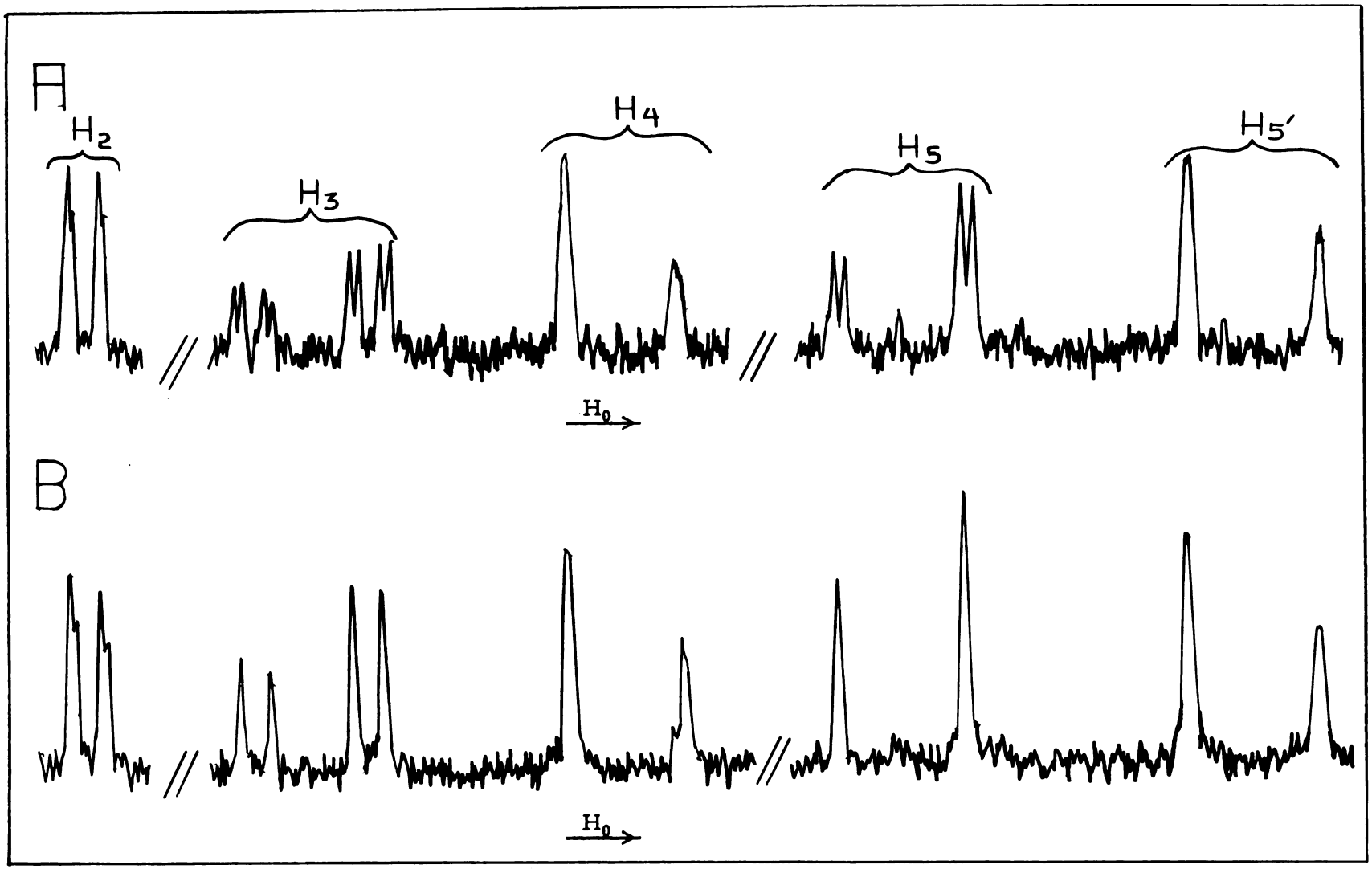


Fig. 8b. N.m.r. spectra[53] of (A) formaldehyde 2, 4-dinitrophenylhydrazone in methylene bromide and (B) formaldehyde 2, 4-dinitrophenylhydrazone exchanged with D_2O in methylene bromide (Numbering corresponds to 6b).

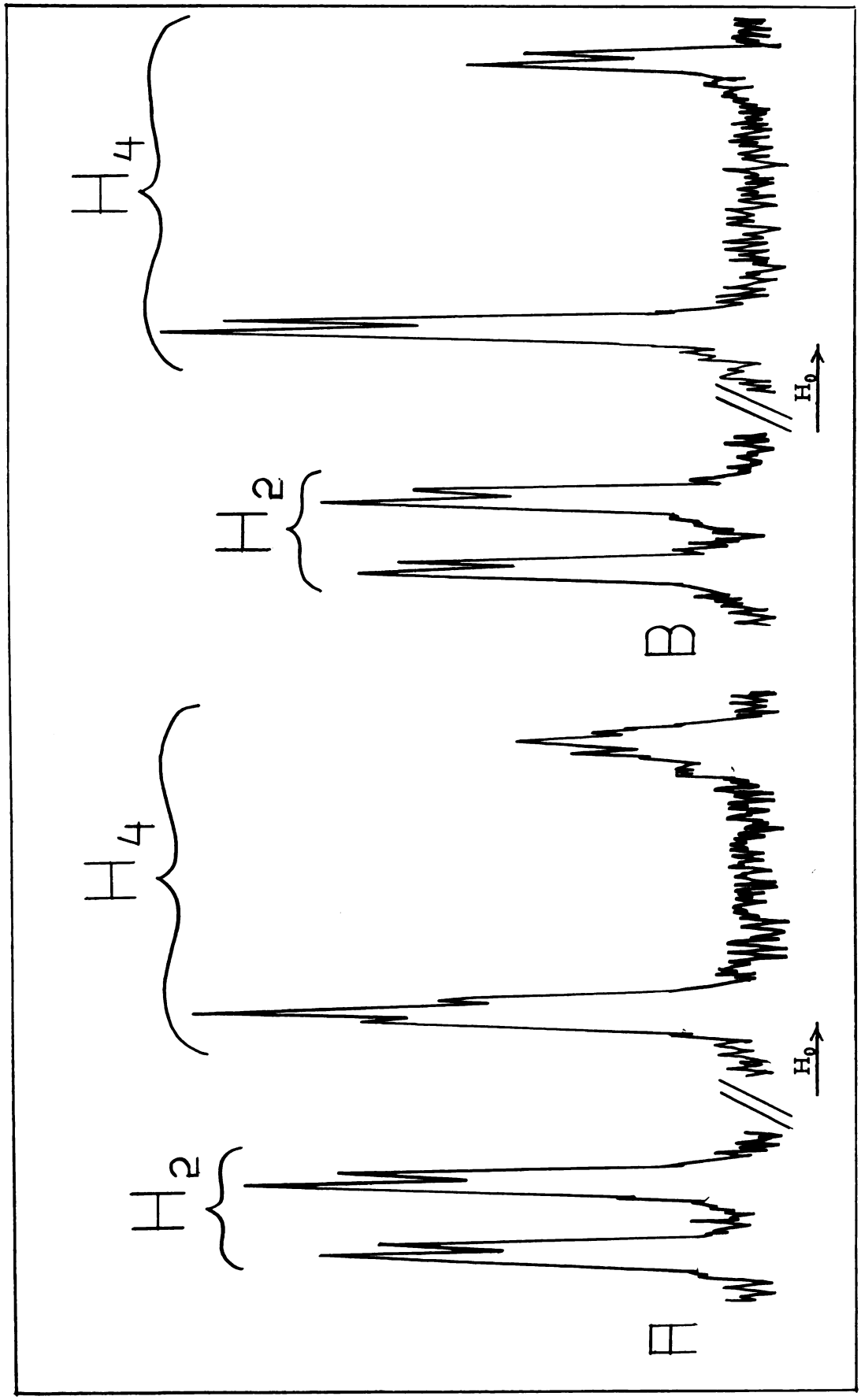
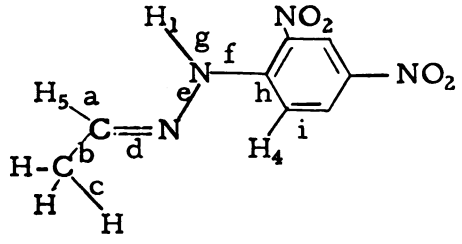


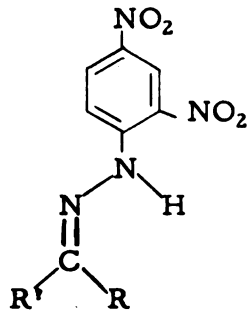
Fig. 9. N.m.r. spectra[53] of H_2 and H_4 of (A) acetone 2,4-dinitrophenylhydrazone in methylene bromide and (B) acetone 2,4-dinitrophenylhydrazone exchanged with D_2O in methylene bromide (Numbering corresponds to 6b).

Table XVb. Bond Lengths and Angles Used in the Anisotropy Calculations

Bond Lengths	Bond Angles
a . . . 1.08Å	bc . . . 109.5°
b . . . 1.50	bd . . . 120
c . . . 1.10	ad . . . 120
d . . . 1.29	de . . . 112
e . . . 1.45	ef . . . 124
f . . . 1.37	
g . . . 1.04	
h . . . 1.39	
i . . . 1.08	



(8b)



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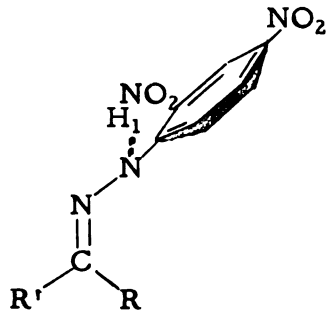
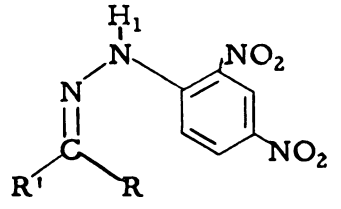


II



III

(9b)

isomers. This assumption may introduce an error of five degrees when the 2,4-dinitrophenyl group is cis to a methyl. 3) A planar trigonal nitrogen with a N-N-C angle ("ef") of 124° was assumed. The increase of four degrees over 120° was made by comparison of trimethylamine (108°) to diethylamine (112°). 4) Hydrogen bonding of the H_1 to the ortho-nitro group restricts rotation about bond "f". 5) The (averaged) position of the methyl hydrogens was estimated to be in the center of the triangle formed by the three hydrogens. 6) The distances of H_5 and methyl hydrogens along the p and z axes of the benzene ring were calculated for conformations I and II (Fig. 9b), where the z axis is normal to the plane of the aromatic ring at its center and the p axis is in the plane of the ring. Conformation III is sterically impossible when R is methyl. When R is hydrogen, its distance from H_4 is only about 0.8 Å.

δ values, obtained from Johnson and Bovey's nuclear shielding values,[57] are listed in Table XVIb. A positive δ represents a shielding effect (shift to higher fields) of the benzene ring on the hydrogens and a negative δ, a deshielding effect.

Table XVIb. Calculated Shielding Values for cis and trans Aldehydic and Methyl Protons[a]

	R = H	R' = H	R = CH_3	R' = CH_3
Conformation I				
p(Å)	5.13	5.83	5.51	6.53
z "	0	0	0	0
(ppm)	-0.218	-0.138	-0.159	-0.087[b]
Conformation II				
p(Å)	3.63	3.29	5.12	5.87
z "	1.45	3.17	1.30	1.38
(ppm)	-0.120	-0.154	+0.091	-0.110[b]

[a]Values are in ppm.

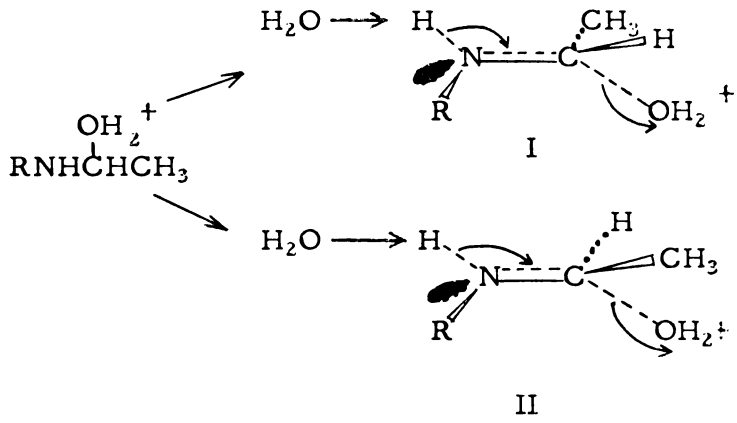
[b]Values had to be estimated as Johnson and Bovey's nuclear shielding table[6] contained values only for p = 0→5.56Å.

DISCUSSION

1. syn-anti Isomerization

The presence of only the syn isomer in the n.m.r. spectra of fresh solutions of aldehyde and some ketone DNP's, and the later appearance of the anti isomer, indicate that the crystalline form is the syn isomer. The immediate presence of both isomers in aliphatic DNP, SC and TSC solutions is attributed either to existence of both isomers in the crystalline form or to rapid syn-anti equilibration. The sharp melting point of the original crystals and the lower, wide melting-point range of the crystals remaining after solvent removal argue in favor of rapid equilibration.

Since the anti acetaldehyde DNP was found to be more soluble than the syn, it was still possible that the preparation leads to both isomers but only the syn isomer crystallizes out of solution. However, quantitative yields were obtained from the acid and acid-free preparations of acetaldehyde DNP. In addition to the above evidence, the stability of the anti isomer to recrystallization suggests that formation of the DNP's is kinetically controlled. The rate-determining step in the acid-catalyzed formation of DNP's[58] and SC's[59] is attack of hydrazine or semicarbazide on the carbonyl. The second step, which leads to products, involves the loss of water. If the transition states for the formation of the isomers of acetaldehyde can be visualized as in (10b), the steric interactions of the CH_3 and R groups in II may sufficiently increase the activation energy to prevent formation of the anti isomer.



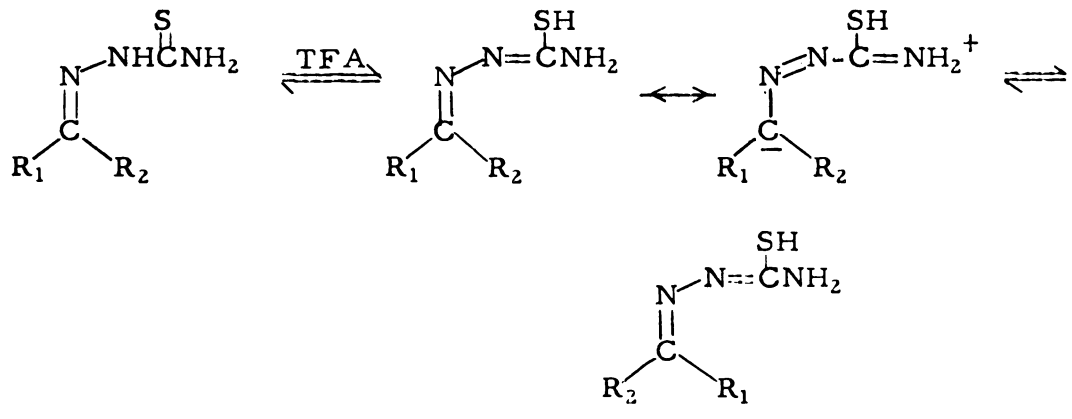
I

II

(10b)

The appearance of one methyl signal (syn isomer) in the n.m.r. of the high melting acetaldehyde crystals (157-58°, 160-61° and 165-66°) and only a trace of the anti isomer in the low melting crystals (145-46°) suggest that the previously reported[31,32] isomers that melted at 146-49°, 156-57 and 167-69° were also the syn isomer. Lowering of the melting points may be due to traces of impurities or the presence of small amounts of the anti isomer. Although pure anti acetaldehyde DNP was not obtained, the mixture of 85% anti·15% syn did melt in a range close to that obtained by van Duin[30] for the anti isomer.

The greater sensitivity (Table IXb) of TSC's over SC's to trifluoroacetic acid (TFA) may be due to enolization of TSC's, but not SC's, in TFA. Enolization should be more favorable for the sulfur-carbon double bond, which is less stable than a carbon-oxygen double bond. In the enolized form the activation energy of rotation could be sufficiently lowered by resonance (11b), so that rotation is too fast for n.m.r. to differentiate between cis and trans hydrogens. Comparison

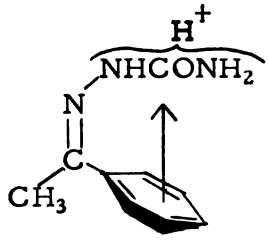


(11b)

of the chemical shifts of the SC's with TSC's in chloroform and trifluoroacetic acid (Tables VIIIb and IXb) support the above suggestion. In chloroform the chemical shifts of SC's and TSC's differ by < 0.1 ppm. In trifluoroacetic acid α-hydrogens of SC's resonate at fields 0.75 ppm lower than in chloroform, while α-hydrogens of TSC's resonate at fields 0.25 ppm higher than in chloroform. The high field shift of α-hydrogens of TSC's would be expected from the negative charge placed on the carbonyl carbon in the resonance form of 11b. Protonation of the SC must be causing an inductive withdrawal of electrons which results in the shift of lower fields. Addition of traces of sulfuric acid to TSC's in methylene bromide, in contrast to trifluoroacetic acid, must be protonating the TSC rather than simply promoting enolization.

N.m.r. differentiates between the cis and trans hydrogens of ketone DNP's in trifluoroacetic acid, but not between the cis and trans hydrogens of aldehyde DNP's (Tables II-V). Apparently, aldehyde DNP's isomerize very fast in trifluoroacetic acid.

The observance of the minor isomer peaks of acetophenone and phenylacetone SC's at high fields (the minor isomer peaks of phenylacetone nitrophenylhydrazones are at low fields) may reflect a solvent change of $\Delta\delta$'s or a change in anti/syn ratios. A favorable interaction between the aromatic ring and a protonated derivative group may increase the stability of the anti isomer (12b).



(12b)

2. Hydrogen Bonding

Hydrogen bonding of H_1 of DNP's to the ortho nitro group is inferred from 1) the low field H_1 resonance of DNP's and o-NP's relative to p-NP's in a poor hydrogen-bonding solvent (methylene bromide), and 2) the greater solvent dependence of H_1 in p-NP's than in DNP's and o-NP's.

The increase of syn:anti ratios and the lower H_1 resonance of acetaldehyde DNP (Table IIIb) with better hydrogen-accepting solvents imply that H_1 is hydrogen bonded, not only to the ortho nitro group, but also, to the solvent. The following data imply that steric effects influence the degree of solvent hydrogen bonding: 1) H_1's of aldehyde DNP's resonate at lower fields than those of methyl ketone DNP's. 2) The anti H_1 of acetaldehyde DNP resonates at higher fields than the syn H_1. 3) H_1 resonances of 2-butanone and 3-pentanone DNP's vary less (0.2 ppm) with solvent changes than those of acetaldehyde and formaldehyde DNP's (0.5 ppm).

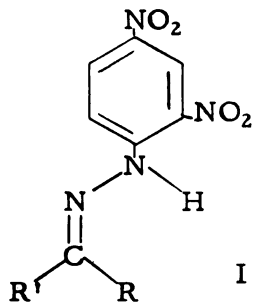
Carbonyl solvents (dimethyl sulfoxide, tetramethylurea, acetone and 'dimethylformamide) shift H_1 to lower fields and reverse the appearance of the methyl peaks of acetaldehyde DNP. Apparently, these solvents, while hydrogen bonding to H_1, either exert a strong anisotropy effect on the affected hydrogens or greatly alter the conformations of the molecule.

3. Anisotropy Effects

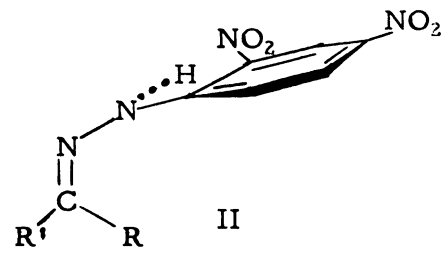
The main cause of the nonequivalence between cis and trans hydrogens is not known, because there are many anisotropic bonds and groups present and many conformations available to the molecules. The phenyl rings of nitrophenylhydrazones and the carbonyls of carbazones cannot be the sole causes, because the nonequivalence is also

observed in hydrazones, oximes, nitrites, nitrosamines and amides. No simple correlation of shielding and deshielding effects was observed in these compounds.[60] Hydrogens comparable to the aldehydic hydrogen of aldehyde derivatives are deshielded in all cases studied except amides. No uniform effect is found for the α- and β-hydrogens.

Variation of the isomer chemical shift difference ($\Delta\delta$'s) with the different derivatives and with solvents indicates that the phenyl and the carbonyl groups are contributing to the anisotropy effect. Calculations (Table XVIb) of the nuclear shielding values for hydrogens of conformation I, assuming that the phenyl ring is the sole contributor to the non-equivalence, predict a greater deshielding effect on the cis hydrogens than on the trans. $\Delta\delta$ for the aldehydic hydrogen = -0.218-(-0.138) = -0.080 ppm. $\Delta\delta$ for the α-CH_3 = -0.159-(-0.087) = -0.072 ppm. Shielding effects are predicted for the cis aldehydic hydrogen relative to the trans hydrogen ($\Delta\delta$ = +0.201 ppm) and for the cis α-CH_3 relative to the trans in conformation II. Averaging of conformations I and II



I



II

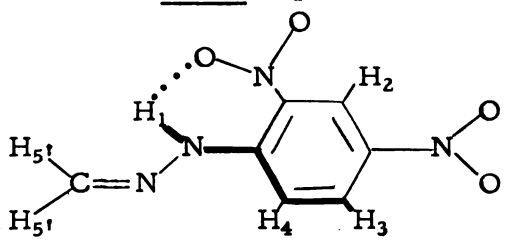
gives $\Delta\delta$ = -0.023 ppm for aldehyde protons and $\Delta\delta$ = +0.065 ppm for methyl protons. Although the signs are in agreement with experimental values ($\Delta\delta$ = -0.5 ppm for aldehydic hydrogens and +0.05 ppm for α-hydrogens), the magnitude of $\Delta\delta$ for the aldehydic hydrogen is in error. This may signify that the anisotropic contribution of the phenyl ring is important for α- and β-hydrogens but that another factor, such as the anisotropy of the nitrogen-nitrogen bond, is important for

aldehydic hydrogens. However, the assumption that a 2,4-dinitrophenyl ring has the same anisotropic effect as benzene and the equal averaging of conformations I and II may make the correlation of calculated and experimental shielding values for α-CH_3 fortuitous.

The magnitude of $\Delta\delta$'s depends upon the difference of the magnetic environments of the cis and trans hydrogens and the rate of rotation about the C=N bonds. The variation of the $\Delta\delta$'s of the DNP SC and TSC of acetone with temperature changes indicate that $\Delta\delta$'s observed at room temperature are not maximum values. Therefore, the variation of $\Delta\delta$ for different derivatives and in different solvents may be ascribed to one of, or a combination of the following: 1) conformational differences, 2) anisotropy effects of the associated solvent molecules, or 3) variation in the rates of isomerization.

4. Spin-Spin Coupling

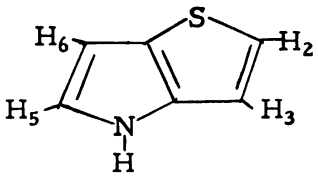
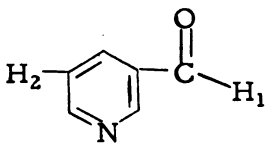
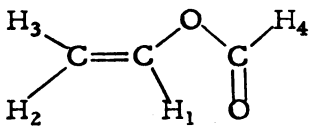
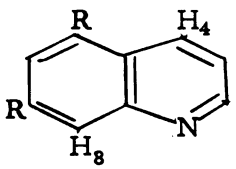
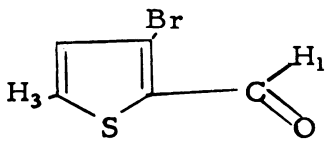
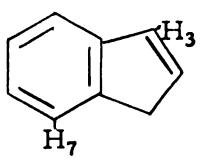
The selective coupling of H_1 of DNP's and o-NP's with one of the meta hydrogens illustrates the angle dependence of spin-spin coupling. Hydrogen bonding of H_1 to the ortho nitro group places H_1 and H_3 of DNP's or H_4 of o-NP's in a trans coplanar conformation (13b). Similar



(13b)

transoid couplings have been previously reported and are summarized in Table XVIIb. Evidently, the hydrogen bond between H_1 and a ortho nitro group is not necessary for H_1 to couple selectively with a cis aldehydic hydrogen.

Table XVIIb. Long-Range Coupling Constants Illustrating the Angle Dependence of Spin-Spin Coupling

Compound	J(cps)	Reference
	$J_{25} = \pm 1.3$ $J_{36} = \pm 0.5$	61
	$J_{12} = 0.44 \pm 0.05$	62
	$J_{14} = \pm 0.6 \pm 0.05$ $J_{24} = \pm 1.7 \pm 0.1$ $J_{34} = \pm 0.8 \pm 0.1$	63
 R = Cl or CH_3	$J_{48} = 0.8$	64
	$J_{13} = 1.1$	65
	$J_{37} = 0.7$	66

EXPERIMENTAL

1. Nuclear Magnetic Resonance Spectra

All n.m.r. spectra were taken with a Varian A-60 n.m.r. spectrometer at approximately 35° on undegassed samples. Tetramethylsilane was the internal reference standard (assigned τ of 10.00). Chemical shifts were measured with sweep widths of 1000, 500 and 250 cps. Spin-spin coupling constants and isomer chemical shift differences ($\Delta\ \delta$'s) were obtained from spectra recorded with 100 and 50 cps sweep widths. The internal chemical shift accuracy of a n.m.r. spectrum is $\pm$ 0.02 ppm.

2. Solvents

Acetone, chloroform, dioxane, dimethylformanide and nitrobenzene were purified by distillation of commercially available materials. Dimethyl sulfoxide was obtained from Crown Zellerback. Pyridine, methylene bromide and quinoline were obtained from Matheson Coleman and Bell. Dimethyl sulfoxide-d_6 and acetone-d_6 were purchased from Merck, Sharp and Dohme of Canada, limited.

3. Carbonyl Reagents

Benzyl ethyl ketone was obtained from Chemical Intermediates Research Laboratories, benzylacetone from Aldrich Chemical Co., formaldehyde from Matheson Coleman and Bell, phenylacetone from Perrigo Co. and propiophenone from Eastman Organic Chemicals. Acetone was purified by the sodium iodide compound.[67] All other ketones and aldehydes were purified by distillation of commercially

available compounds. Purities were checked by n.m.r. and gas chromotography.

4. Dinitrophenylhydrazones

The majority of the 2,4-dinitrophenylhydrazones were prepared according to the method of Shriner, Fuson and Curtin.[68] The diglyme procedure of H. J. Shine[69] was utilized for the preparation of the DNP's of propionaldehyde and n-butyraldehyde which appeared sensitive to strong acid catalysis. In some cases the diethyl ether of diethylene glycol was substituted for the dimethyl ether because of availability. Acetaldehyde DNP was also prepared using phosphoric acid.[70] The melting points are listed in Table XVIIIb. The following are typical preparations.

Acetone DNP. To 1.0 g. (0.005 mole) of 2,4-dinitrophenylhydrazine (Eastman Organic Chemicals) was added 5 ml. of conc. sulfuric acid. Water (~8 ml.) was added dropwise until solution was complete. Addition of 25 ml. of 95% ethanol to the solution was followed by addition of 1.0 g. (0.017 mole) of acetone in 20 ml. of 95% ethanol. The solution was allowed to stand at room temperature until crystallization occurred. The yellow crystals were separated by filtration and were recrystallized twice from water-ethanol solutions. (m.p. = 126-27°)

Propionaldehyde DNP. To a solution of 1.0 g. (0.005 mole) of 2,4-dinitrophenylhydrazine in 30 ml. of diglyme was added 1.0 g. (0.017 mole) of propionaldehyde. Precipitation was induced by addition of water. Care was taken not to add excess water because unreacted 2,4-dinitrophenylhydrazine would also precipitate. After filtration the yellow-orange crystals were recrystallized twice from water-ethanol solutions. (m.p. = 150-51°)

Table XVIIIb. Melting Points of 2,4-Dinitrophenylhydrazones[a]

DNP	Observed Melting Point	Reported Melting Points Ref. 71	Ref. 72
Formaldehyde	165-66°	166°	155, 167°
Acetaldehyde	145-46, 157-58, 160-61	147, 168	146, 163.5-4.5
Propionaldehyde	150-51	154	---
Isobutyraldehyde	181-83	182	187
n-Butyraldehyde	120	122	123
Acetone	126-27	126	128
2-Butanone	114-15	117	115
3-Pentanone	153-54	156	156
Methyl isopropyl ketone	119	117	117
2-Pentanone	143	144	141
Methyl t-butyl ketone	125-26	125	117
Diisopropyl ketone	96	95	94-8
Phenylacetone	153	156	156
Benzylacetone	127-28	---	131-32
Benzyl ethyl ketone	133-4	---	140-41
Dibenzyl ketone	107-8	100	---
Ethyl cyclopropyl ketone	163	---	---

[a]Melting points were obtained on a melting point block.

Acetaldehyde DNP. To a solution of 1.0 g. (0.023 mole) of acetaldehyde in 5 ml. of 95% ethanol was added 20 ml. (0.005 mole) of a 0.25 M phosphoric acid-ethanol solution of 2,4-dinitrophenylhydrazine. The gold crystals were removed by filtration and recrystallized twice from water-ethanol solution. (m.p. = 145-46°)

5. Mononitrophenylhydrazones

The procedure of Shriner, Fuson and Curtin[68] was followed in the preparation of the p-nitrophenylhydrazones. Table XIXb lists the melting points of the mononitrophenylhydrazones. The following are typical preparations of ortho-, meta- and para-nitrophenylhydrazones.

Acetone p-NP. A mixture of 1.0 g. (0.007 mole) of p-nitrophenylhydrazine (Eastman Organic Chemicals), 1.0 g. (0.017 mole) of acetone and 10 ml. of 95% ethanol was heated to boiling, and a drop of glacial acetic acid was added. The dark gold crystals were separated and recrystallized from a water-ethanol solution. (m.p. = 148.5-49.5°)

3-Pentanone o-NP. To a solution of 0.5 g. (0.003 mole) of ortho-nitrophenylhydrazine-hydrochloride (Aldrich Chemical Co.), 3 ml. of water and 3 ml. of conc. sulfuric acid was added 10 ml. of 95% ethanol and 0.5 ml. (0.005 mole) of 3-pentanone. Water was added until the ortho-nitrophenylhydrazone precipitated. After heating to dissolve the precipitate, the solution was cooled. The orange-red crystals were removed and recrystallized from 95% ethanol. (m.p. = 57°)

2-Butanone m-NP. The procedure for the preparation of 3-pentanone ortho-nitrophenylhydrazone was followed using 0.5 g. (0.003 mole) of meta-nitrophenylhydrazone-hydrochloride (Aldrich Chemical Co.) and 0.5 ml. (0.004 mole) of 2-butanone. (m.p. = 97-8°)

Table XIXb. Melting Points of Mononitrophenylhydrazones[a]

	o-PN		m-NP		p-NP	
	Obs.	Lit.	Obs.	Lit.	Obs.	Lit.
Formaldehyde	----	----	----	----	177°	181°
Acetaldehyde	118-19°	124°	----	142°	126	128.5
Acetone	68	70	120°	----	148-49	149
2-Butanone	74	73	97-8	99.5	125	128-29
Methyl Isopropyl ketone	60-1	----	76	----	102-4	107(103.5)
3-Pentanone	57	60	----	----	138	144
Diisopropyl ketone	----	----	----	----	145	----
Phenylacetone	98	----	112-14	----	142-43	----

[a]Melting points were obtained on a melting point block. Literature values from Ref. 72.

6. Semicarbazones and Thiosemicarbazones

The semicarbazones were prepared according to the procedure of Shriner, Fuson and Curtin[73] and the thiosemicarbazones according to Cheronis and Entrikin.[74] For water-insoluble carbonyl compounds a water-ethanol mixture was used as solvent. Table XXb lists the melting points.

Acetone SC. One ml. (0.014 mole) of acetone, 1.0 g. (0.009 mole) of semicarbazide hydrochloride (Matheson Coleman and Bell) and 1.5 g. (0.018 mole) of sodium acetate were dissolved in 10 ml. of water in a test tube and vigorously shaken. The test tube was placed in a beaker of boiling water to dissolve the white precipitate. As the solution cooled white crystals appeared and were collected by filtration. The semicarbazone was recrystallized twice from water. (m.p. = 187°)

Acetone TSC. To 1.0 g. (0.11 mole) of thiosemicarbazide (Eastman Organic Chemicals) and 1.0 g. (0.017 mole) of acetone in a test tube was added a solution of 2.0 g. (0.024 mole) of sodium acetate in 15 ml. of water. The solution was warmed for a minute and then allowed to cool. The white crystals were filtered and recrystallized twice from water. (m.p. = 179°)

7. Equilibration and Fractional Crystallization of Acetaldehyde DNP

A solution of acetaldehyde DNP in methylene bromide was heated on a steam bath (one to two days) until syn-anti equilibrium was reached. The progress of equilibration was checked by removing samples and integrating the methyl signals in the n.m.r. spectrum. After cooling n-heptane was added causing precipitation. The crystals were removed and more n-heptane was added. The process was repeated until further addition of n-heptane gave no precipitation. The solvent of the

Table XXb. Melting Points of Semicarbazones and Thiosemicarbazones[a]

	Semicarbazones		Thiosemicarbazones	
	Obs.	Lit.	Obs.	Lit.
Acetaldehyde	b	162°[c]	145-46°	146°[d]
Acetone	187°	187[c]	179	179[d]
2-Butanone	148	146[c] 148[d]	96	----
2-Pentanone	101	110[c]	78	----
Methyl isopropyl ketone	111-4	113[c], 114[d]		
3-Pentanone	137-38	139[c]	86	----
Diisopropyl ketone	155-56	160[c]		
Acetophenone	198	198[c]		
Phenylacetone	187	198[c]		

[a]Melting points were obtained on a melting point block.

[b]Crystals were not obtained. Solutions were made by extraction from the oil with methylene bromide.

[c]Literature values from Ref. 73.

[d]Literature values from Ref. 74, p. 663.

heptane-rich solution was removed by evaporation (water aspirator pressure).

The first crystals were mainly the syn isomer while the last were mainly the anti. Attempts to purify further the anti-enriched mixture failed. Table XXIb shows a typical attempt to separate the isomers.

Table XXIb. Fractional Crystallization of Acetaldehyde 2,4-Dinitrophenylhydrazone

Fraction	% anti	Melting Point
1	2	157-58°
2	3-5	154-56
3	21	152-54
4	30	92-94
5	85	89-93

Other solvent pairs, such as alcohol-water and ethyl acetate-cyclohexane, failed to produce results as good as those obtained from methylene bromide-heptane.

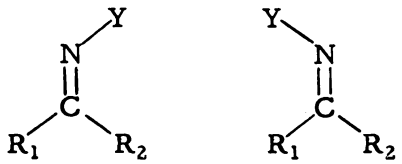
Heating of ethanol solutions of acetaldehyde DNP (syn isomer), in the presence or absence of acid, did not effect isomerization.

Isomerization by prolonged heating of acetaldehyde crystals (syn) resulted in slight decomposition; a small amount of the anti isomer was detected.

Attempts to selectively crystallize the anti isomer by addition of anti-enriched crystals to equilibrated solutions were unsuccessful.

SUMMARY

The magnetic nonequivalence of hydrogens cis and trans to Y permitted the nuclear magnetic resonance study of stereoisomerism



about the C=N bond in 2,4-dinitrophenylhydrazones, para-, meta- and ortho-nitrophenylhydrazones, semicarbazones and thiosemicarbazones. The chemical shift difference between hydrogens cis and trans to Y is 30-45 cps for aldehydic hydrogens, 0-10 cps for α-hydrogens and 0-5 cps for β-hydrogens. Generally, aldehydic hydrogens and β-hydrogens are deshielded (hydrogens cis to Y are at lower fields), while α-hydrogens are shielded. Solvent effects on the isomer chemical shift difference are important.

Kinetically-controlled formation of the aldehyde 2,4-dinitrophenylhydrazones leads to the syn isomer (Y is cis to the smaller R group). Equilibration occurs with time and it is acid catalyzed. Isomer ratios at equilibrium agree with steric predictions.

The N-H's of 2,4-dinitrophenylhydrazones and ortho-nitrophenylhydrazones hydrogen bond to the ortho nitro group. Additional hydrogen bonding between the N-H and solvent of acetaldehyde 2,4-dinitrophenylhydrazone causes a decrease of anti/syn equilibrium ratios, a low field shift of N-H resonances, and in some solvents, a reversal in the appearance of the syn and anti methyl resonances.

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