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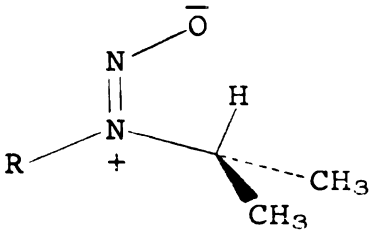
ABSTRACT

STEREOCHEMICAL STUDIES OF NITROSAMINES, OXIMES AND N-SUBSTITUTED HYDRAZONES BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

by Robert Arthur Taller

Nuclear magnetic resonance spectroscopy was used to study the configurations and conformations of N-nitrosamines, oximes, N-methylhydrazones, N,N-dimethylhydrazones, and phenylhydrazones.

It was observed that whereas α-methyl, α-methylene, and β-methyl protons of the nitrosamines resonate at higher magnetic fields when cis than when trans to the nitroso oxygen, α-methine protons resonate at lower fields. This difference is attributed to the greater stability of I, whereby the methine proton eclipses the nitrogen-nitrogen bond. The nature of the association between benzene and nitrosamine was deduced



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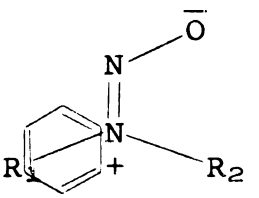

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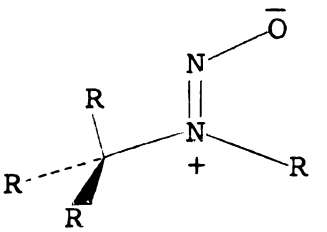

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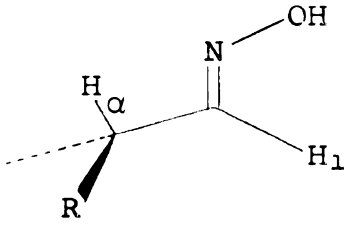
by observing the proton resonance shifts of groups R_1 and R_2 as a function of benzene concentration. These studies showed that the benzene molecule interacts with the partially positive nitrogen atom in a way that places the ring closer to the trans than to the cis protons (II). Changes in the chemical shifts of the trans isomers are consistent with the assumption that the minimum energy conformations are those in which the nitrogen-nitrogen bond is eclipsed with a substituent on the tetrahedral carbon (III).

The spin-spin coupling interactions between H_1 and H_α of aldoximes (IV) were studied as functions of temperature and solvent. The data were interpreted in terms of rotamers



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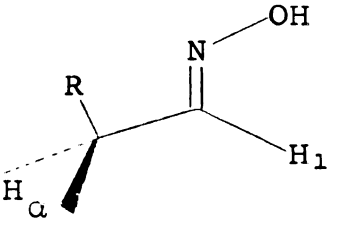

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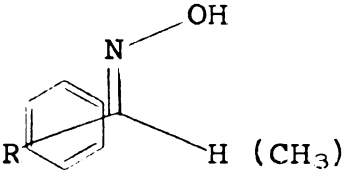

VI

where a single bond eclipses the carbon-nitrogen double bond (IV and V). In all cases IV is stabler than V. The effect of benzene on the chemical shifts was interpreted in terms of VI, whereby the benzene molecule interacts with the sp^2 hybridized carbon of the oxime and is situated anti to the hydroxyl group.

The stable conformations about the nitrogen-nitrogen single bond of aldehyde and ketone N-methylhydrazones was found

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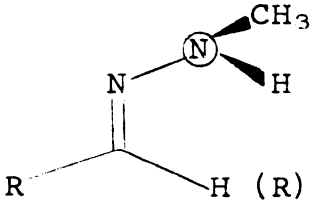

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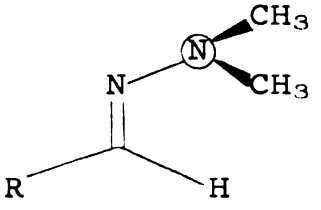

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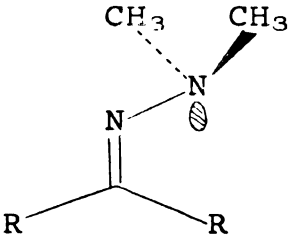

IX

to be VII. That of aldehyde N,N-dimethylhydrazones was the analogous conformation VIII. As a result of nonbonded interactions ketone N,N-dimethylhydrazones assume conformation IX.

The effect of solvent on the chemical shifts of phenylhydrazones led to the conclusion that extensive self-association and hydrogen bonding between phenylhydrazone and solvent exists. Plausible structures of these hydrogen-bonded complexes are suggested.

STEREOCHEMICAL STUDIES OF NITROSAMINES, OXIMES AND N-SUBSTITUTED HYDRAZONES BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

By

Robert Arthur Taller

A THESIS

Submitted to
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for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

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The author wishes to express his sincere appreciation to Professor G. J. Karabatsos for his guidance, encouragement, and friendship during the course of this investigation.

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Appreciation is extended to his parents for their understanding and financial assistance during the years of his education.

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INTRODUCTION

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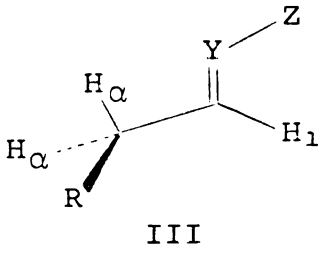
Geometrical or configurational isomers arising from restricted rotation about double bonds (1,2,3) and partial double bonds (4,5,6,7) can be effectively studied by nuclear magnetic resonance spectroscopy (n.m.r.). A proton in group R_1 as well as in group R_2, for example, may resonate at different magnetic fields when Z is cis (I) or trans (II) to it. As a result of this magnetic nonequivalence two R_1 signals may be observed, one for each geometrical isomer.

I (cis) II (trans)

The relative field position of these two signals will vary with X (carbon, nitrogen), Y (nitrogen, oxygen) or Z (hydrogen, oxygen, substituted nitrogen). For example, whereas in one particular compound R_1 may resonate at a higher field (shielded) when cis (I) than when trans (II) to Z, in another the reverse might be true (8).

Conformational isomers can be studied by observing discrete changes in spin-spin coupling constants (9,10) and in chemical shifts (11). For example, the important conformations of a tetrahedral carbon bonded to a trigonal carbon may be determined by measuring changes in the spin-spin coupling constant, $J_{H_1H_\alpha}$, with temperature and solvent. Assuming $J_t > J_g$ (12), where J_t is the trans coupling (dihedral angle $\sim 180^\circ$) and J_g is the gauche coupling (dihedral angle $\sim 60^\circ$),



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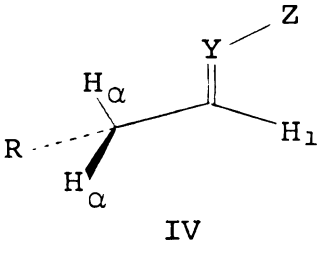

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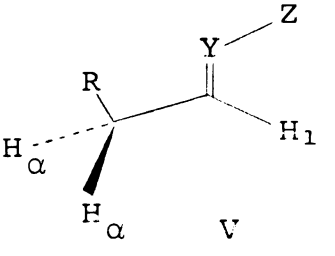

V

the averaged coupling should be temperature independent if III, IV and V are energetically equivalent. If V is more stable than III or IV, the coupling should increase with increase in temperature, and if it is less stable, the coupling should decrease (10). In the absence of spin-spin coupling between protons in group R_1 with protons in group R_2 (I) conformational data may be obtained from chemical shifts. Although this requires knowledge of the anisotropic effects of the carbon-nitrogen and the nitrogen-nitrogen double bonds, intelligent guesses can be made by comparison of these with other isoelectronic groups (11,13).

Additional information regarding configurational and conformational isomers may be obtained from the variations of chemical shifts (8,14,15,16,17) and to a smaller extent coupling constants (18,19) with solvent. These variations are generally attributed to changes in the dielectric constant of the solvent (20) or to solvent association with substrate. With respect to association two distinct interactions leading to chemical shift changes can occur. One type of interaction leads to the "hydrogen bond shift," whereby the hydroxyl proton signals of alcohols (21) and

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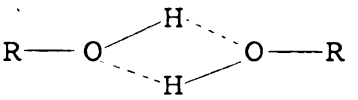
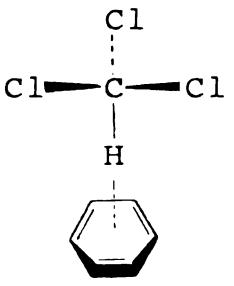
carboxylic acids (22) appear at lower fields when these compounds are associated than when they are unassociated. This is an example of an n-donor association, that is, hydrogen bonding between the lone pair electrons of the donor species



VI

with the protons of the acceptor molecule (VI). The chemical shift of the unassociated species can be obtained by dilution with an inert solvent. A second type of interaction arises from association of a proton (15) or polar molecule (17, 22, 23) with an aromatic nucleus. For example, when chloroform is diluted with benzene (VII), the proton signal progressively shifts toward high field as the benzene concentration increases. This high field shift can be attributed to the large



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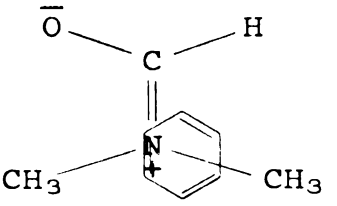

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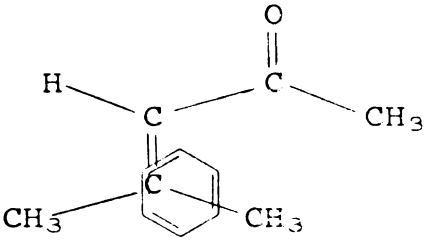

IX

induced diamagnetism resulting from circulation of the π-electrons of the aromatic ring. Association between benzene and N,N-dimethylformamide (VIII) and between benzene and mesityl oxide (IX) lead to similar results (22, 23). These

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interactions lead to the "π-donor association shifts," which in most cases are upfield shifts.

In order to understand the factors that influence: (a) syn-anti isomerism about double bonds and partial double bonds; (b) the relative stability of the conformations of a tetrahedral carbon bonded to a trigonal carbon; (c) the anisotropic effects of hetero-atoms bonded to a carbon-nitrogen or nitrogen-nitrogen double bond; and (d) the effect of solvents on chemical shifts and coupling constants, the following systems were studied.

A. Nitrosamines. A preliminary study of three nitrosamines by the author (24) showed that the previously reported assignments (7) were incorrect. To further elucidate nitrosamine-solvent association and to assess the important conformations of these compounds, ten additional nitrosamines were studied.

B. Oximes. Phillips (1) assigned structures to the syn and anti forms of several oximes and concluded that the only isolable form of aldoximes is the anti form. Lustig (2) reported that isomers of ketoximes could only be observed in aromatic solvents. He also postulated that magnetic non-equivalence was due to the oxygen atom. Saitô (25), on the other hand, attributed the anisotropy of the hydroxylamino group to the lone pair electrons of the nitrogen atom. A series of aldoximes and ketoximes were prepared in order

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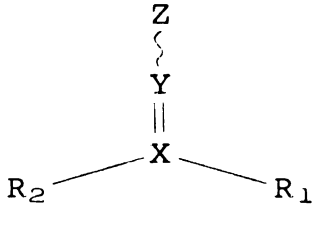
to understand the anisotropic contributions of the hydroxylamino group and to elucidate the conformations of these compounds. The effect of solvents on the chemical shifts and spin-spin coupling constants were also studied.

C. N-Methylhydrazones and N,N-Dimethylhydrazones. These compounds were prepared in order to understand the factors controlling syn-anti isomerism and to determine conformational preference about the nitrogen-nitrogen single bond.

D. Phenylhydrazones. Although syn and anti assignments were previously reported (24), the effect of solvents (aromatic and aliphatic) on the chemical shifts that could possibly reveal the degree and type of association in solution was not examined.

The following conventions will be used throughout this thesis: The syn isomer has Z cis to the smaller alkyl group (X). For example, the syn isomer of butanone oxime has the methyl and hydroxylamino groups cis to each other. The notation used to distinguish the various protons is shown in XI, each proton being referred to as cis or trans with respect to Z.



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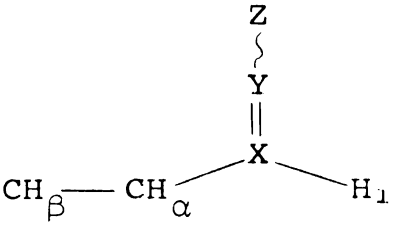
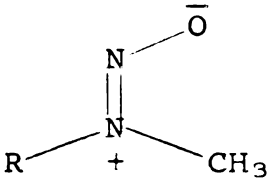


XI

PART A--N-NITROSAMINES

Results

Figure 1 shows the n.m.r. spectra of dimethyl, methyl ethyl, methyl isopropyl and methyl t-butyl nitrosamines. Table 1 summarizes the chemical shifts and syn/anti ratios of several nitrosamines. The chemical shifts are accurate to ± 0.03 p.p.m. The accuracy in chemical shift differences between cis and trans protons is ± 0.01 p.p.m. The syn/anti ratios were determined by integration of peak areas and are accurate to ± 5%. The syn/anti assignments are based on the assumption that the ratio Ia/IIa increases as R changes from ethyl to isopropyl to t-butyl.



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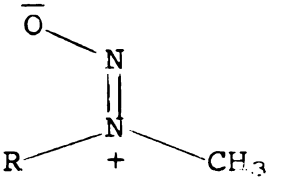

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Two observations are pertinent to the ensuing discussion on conformations: (a) In $R(CH_3)NNO$ the resonance of the trans-β-methyl of the R group shifts to lower fields as R changes from ethyl (τ = 8.62) to isopropyl (τ = 8.58) to t-butyl (τ = 8.46). In $R[CH(CH_3)_2]NNO$ the resonance of the trans-α-methine shifts to higher fields by 0.3-0.4 p.p.m. as R changes from methyl (τ = 5.15) to benzyl (τ = 5.43) to isopropyl (τ = 5.74).

Table 2 contains the differences in chemical shifts of cis and trans protons. A positive (+) $\Delta\delta$ means that cis

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protons resonate at higher fields than trans; a negative reverse. The important points are: (a) Whereas α-methyl and α-methylene protons resonate at higher fields when cis than when trans to the nitroso oxygen, α-methine protons resonate at lower fields (negative $\Delta\delta$). (b) While positive $\Delta\delta$ values are smaller in benzene than in carbon tetrachloride--with diisopropyl nitrosamine the notable exception--negative $\Delta\delta$ values are larger in benzene. (c) The $\Delta\delta$ values for α-methyl, α-methylene and β-methyl vary over small ranges, while those for α-methine vary over larger ranges.

Table 3 summarizes Δ^{γ} (ν in benzene $-\nu$ in carbon tetrachloride) values obtained from the data in Table 1. The important points are: (a) $\Delta\nu$ values are higher for the trans than for the cis protons, except for the β-methyl of diisopropyl nitrosamine which is smaller. Nitrosamines thus behave similarly to amides (16,22,26,27,28), but opposite to compounds having the structure $R_1R_2C{=}NNHX$ (see Parts C and D). (b) As the size of R_1 and R_2 of dialkylnitrosamines increases the $\Delta\nu$ values for cis-α-methine are very small and decrease as the R of $R[CH(CH_3)_2]NNO$ increases in size.

Table 4 shows the effect of various solvent on the chemical shifts of methyl ethyl nitrosamine. Figure 2 shows the variation of the chemical shifts of methyl ethyl nitrosamine with benzene as the solvent. Figure 3 compares the effect of dilution on the chemical shifts of methyl ethyl and methyl-t-butyl nitrosamine. When carbon tetrachloride or dimethyl sulfoxide

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are used as solvents, dilution has practically no effect on the chemical shifts. Table 5 contains the ultraviolet spectral values of several nitrosamines in cyclohexane.

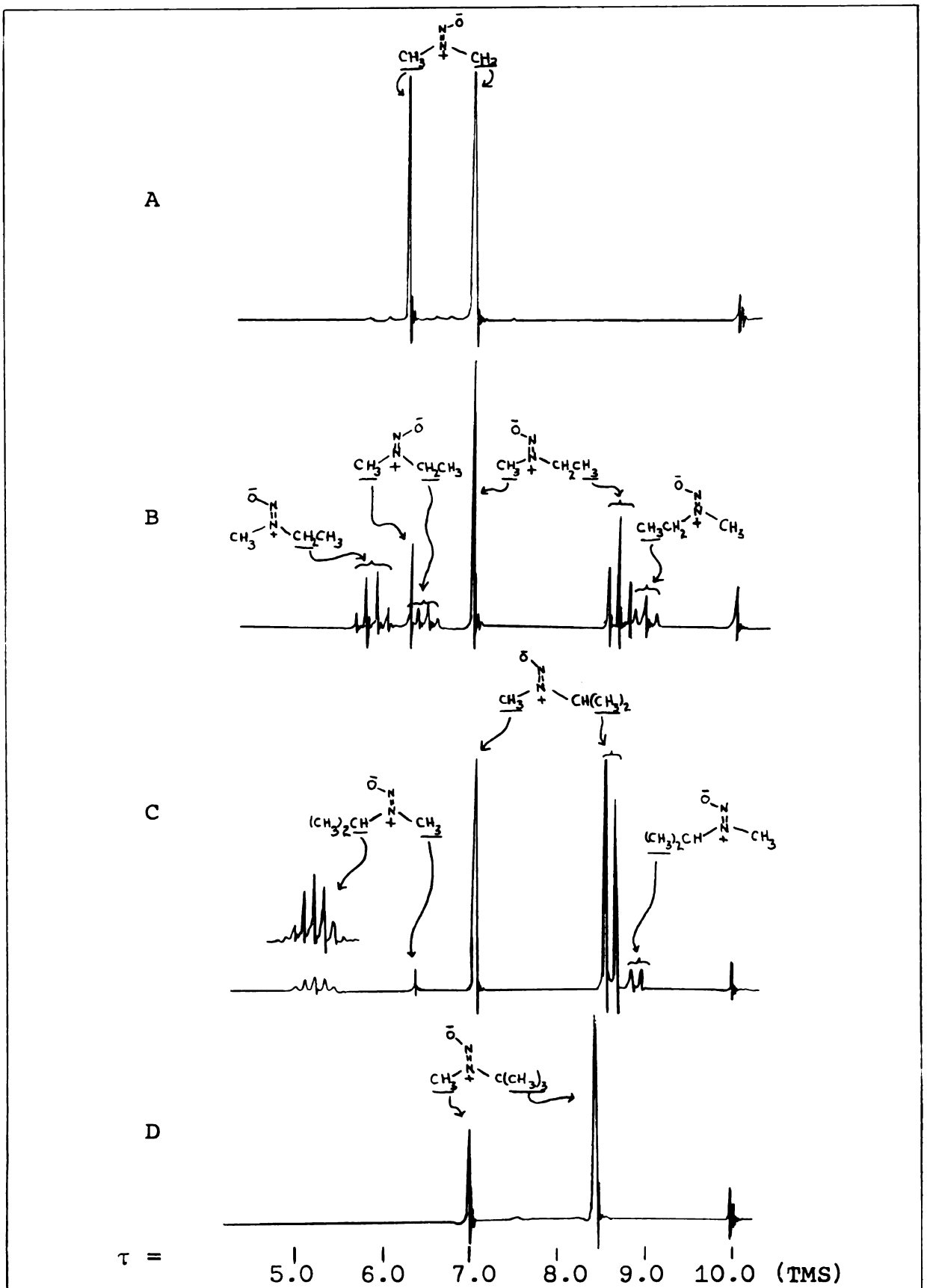


Figure 1. Neat n.m.r. spectra of dimethyl nitrosamine (A), methyl ethyl nitrosamine (B), methyl isopropyl nitrosamine (C), and methyl t-butyl nitrosamine (D).

Table 1. Chemical Shifts (τ-Values) of Nitrosamines

R_1R_2NNO	$\alpha(CH)$	$\alpha(CH_2)$	$\alpha(CH_3)$		$\beta(CH_3)$		Percent syn/anti[a]
			cis	trans	cis	trans	

Table 1. Chemical Shifts (τ-Values) of Nitrosamines

R_1R_2NNO			$\alpha(CH)$		$\alpha(CH_2)$		$\alpha(CH_3)$		$\beta(CH_3)$		Percent[a]
R_1	R_2	Solvent	cis	trans	cis	trans	cis	trans	cis	trans	syn/anti
CH_3	CH_3	Neat					6.98	6.23			
CH_3	CH_3	CCl_4					7.04	6.24			
CH_3	CH_3	C_6H_6					7.60	7.04			
CH_3	CH_2CH_3	Neat			6.41	5.83	7.00	6.28	8.98	8.67	78/22
CH_3	CH_2CH_3	CCl_4			6.48	5.85	7.07	6.29	8.95	8.62	73/27
CH_3	CH_2CH_3	C_6H_6			6.91	6.49	7.54	7.01	9.42	9.26	79/21
CH_3	$CH(CH_3)_2$	Neat	4.97	5.17			7.05	6.34	8.88	8.59	89/11
CH_3	$CH(CH_3)_2$	CCl_4	4.97	5.15			7.13	6.38	8.91	8.58	89/11
CH_3	$CH(CH_3)_2$	C_6H_6	5.12	5.60			7.52	6.99	9.41	9.15	90/10
CH_3	$C(CH_3)_3$	Neat					7.03			8.46	100/0
CH_3	$C(CH_3)_3$	CCl_4					7.11			8.46	100/0
CH_3	$C(CH_3)_3$	C_6H_6					7.44			8.91	100/0
CH_3	$(CH_2)_3CH_3$	Neat			6.44	5.87	7.02	6.28			79/21
CH_3	$(CH_2)_3CH_3$	CCl_4			6.53	5.91	7.08	6.30			78/22
CH_3	$(CH_2)_3CH_3$	C_6H_6			6.86	6.45	7.51	6.96			77/23
CH_3	$CH_2C_6H_5$	Neat			5.21	4.72	7.15	6.41			74/26
CH_3	$CH_2C_6H_5$	CCl_4			5.28	4.70	7.14	6.33			79/21
CH_3	$CH_2C_6H_5$	C_6H_6			5.64	5.26	7.56	6.99			78/22
CH_3	C_6H_5	Neat					6.68				100/0
CH_3	C_6H_5	CCl_4					6.62				100/0

Continued

R_1R_2NNO R_1	R_2	Solvent	α(CH_2) cis	α(CH_2) trans	α(CH_2) cis	α(CH_2) trans	α(CH_3) cis	α(CH_3) trans	β(CH_3) cis	β(CH_3) trans	Percent syn/anti[a]
CH_3	C_6H_5	C_6H_6					7.19				100/0
CH_2CH_3	$CH_2C_6H_5$	Neat			5.22[b]	4.77[b]			9.18	8.81	50/50

Table 1 - Continued

R_1R_2NNO			α(CH)		α(CH_2)		α(CH_3)		β(CH_3)		Percent
R_1	R_2	Solvent	cis	trans	cis	trans	cis	trans	cis	trans	syn/anti[a]
CH_3	C_6H_5	C_6H_6					7.19				100/0
CH_2CH_3	$CH_2C_6H_5$	Neat			5.22[b] (6.58)[b]	4.77[b] (5.98)[b]			9.18	8.81	50/50
CH_2CH_3	$CH_2C_6H_5$	CCl_4			5.28[b] (6.58)[b]	4.76[b] (5.93)[b]			9.08	8.67	53/47
CH_2CH_3	$CH_2C_6H_5$	C_6H_6			5.57[b] (6.85)[b]	5.22[b] (6.42)[b]			9.50	9.20	55/45
$CH_2C_6H_5$	$CH(CH_3)_2$	Neat	5.10	5.45	5.22	4.78			9.10	8.70	84/16
$CH_2C_6H_5$	$CH(CH_3)_2$	CCl_4	5.13	5.43	5.30	4.75			9.02	8.58	82/18
$CH_2C_6H_5$	$CH(CH_3)_2$	C_6H_6	5.23	5.82	5.54	5.16			9.36	9.01	88/12
CH_2CH_3	C_6H_5	Neat			5.99	5.54			8.97	8.78	~96/4
CH_2CH_3	C_6H_5	CCl_4			5.99	5.47			8.85		~97/3
CH_2CH_3	C_6H_5	C_6H_6			6.39				9.26		
$CH_2C_6H_5$	C_6H_5	CCl_4			4.84						~100/0
$CH_2C_6H_5$	C_6H_5	C_6H_6			5.15						~100/0
$CH(CH_3)_2$	C_6H_5	Neat	4.87	5.06					8.94	8.68	57/43
$CH(CH_3)_2$	C_6H_5	CCl_4	4.88	4.97					8.82	8.55	64/36
$CH(CH_3)_2$	C_6H_5	C_6H_6	4.92	5.28					9.17	8.95	58/42
$CH(CH_3)_2$	$CH(CH_3)_2$	CCl_4	5.11	5.74					8.85	8.48	
$CH(CH_3)_2$	$CH(CH_3)_2$	C_6H_6	5.19	6.25					9.20	8.82	

[a] Syn is the isomer having R_1 cis to the oxygen.

[b] Methylene of the ethyl group.

Table 2. $\Delta\alpha^{gas}(CH_3 - CH_2)$ Values, in p.p.m. of Nitrosamines

R_1R_2NNO		$\alpha(CH_3)$			$\alpha(CH_2)$			$\alpha(CH)$			$\beta(CH_3)$		
R_1	R_2	Neat	CCl_4	C_6H_6	Neat	CCl_4	C_6H_6	Neat	CCl_4	C_6H_6	Neat	CCl_4	C_6H_6
CH_3	CH_3	+0.75	+0.80	+0.56									

Table 2. $\Delta\delta^{a}(\delta_{cis} - \delta_{trans})$ Values, in p.p.m., of Nitrosamines

R_1R_2NNO		$\alpha(CH_3)$			$\alpha(CH_2)$			$\alpha(CH)$			$\beta(CH_3)$		
R_1	R_2	Neat	CCl_4	C_6H_6	Neat	CCl_4	C_6H_6	Neat	CCl_4	C_6H_6	Neat	CCl_4	C_6H_6
CH_3	CH_3	+0.75	+0.80	+0.56									
CH_3	CH_2CH_3	+0.72	+0.78	+0.53	+0.58	+0.63	+0.42				+0.31	+0.33	+0.16
CH_3	$(CH_2)_3CH_3$	+0.74	+0.78	+0.55	+0.57	+0.62	+0.41						
CH_3	$CH(CH_3)_2$	+0.71	+0.75	+0.53	.			-0.20	-0.18	-0.48	+0.29	+0.33	+0.26
CH_3	$CH_2C_6H_5$	+0.74	+0.81	+0.57	+0.50	+0.58	+0.38						
CH_2CH_3	C_6H_5				+0.45	+0.52					+0.19		
CH_2CH_3	$CH_2C_6H_5$				+0.60	+0.65	+0.43				+0.37	+0.41	+0.30
					(+0.45)[b]	(+0.52)[b]	(+0.35)[b]						
$CH(CH_3)_2$	$CH(CH_3)_2$							c	-0.63	-1.06	c	+0.37	+0.38
$CH(CH_3)_2$	$CH_2C_6H_5$				+0.44	+0.55	+0.38	-0.35	-0.30	-0.59	+0.40	+0.44	+0.35
$CH(CH_3)_2$	C_6H_5							-0.21	-0.09	-0.36	+0.26	+0.27	+0.22

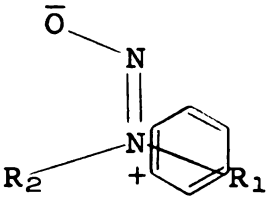
[a] Positive value means that the proton *cis* to the N-$\overline{O}$ group resonates at higher magnetic field than when *trans*; a negative value denotes the reverse.

[b] Methylene of benzyl group.

[c] Compound is a solid.

Discussion

Solvent Effects--The greater upfield shift of the trans over the cis proton resonances when the solvent is changed from carbon tetrachloride to benzene suggests stereospecific association between benzene and the nitrosamine. Structure IIIa, whereby the benzene is attracted by the positive charge



IIIa

on the nitrogen and repelled by the negative charge on the oxygen, is the most attractive formulation of this association. All the data support IIIa. For example: (a) Figure 2 shows that on dilution with benzene the trans proton shifts upfield more rapidly than the cis. (b) Table 3 shows that the $\Delta\nu$ values of alkyl methyl nitrosamines decrease as the alkyl group is changed from methyl to t-butyl. The increase in the size of R should decrease the equilibrium constant for 1. Figure 3 also supports structure IIIa in that the

$$R_1CH_3NNO + C_6H_6 \rightleftharpoons R_1CH_3NNO\cdot C_6H_6 \qquad 1$$

resonances of ethyl methyl nitrosamine shift upfield more rapidly than those of methyl t-butyl nitrosamine. Further support for structure IIIa is shown in Table 4. Alkyl

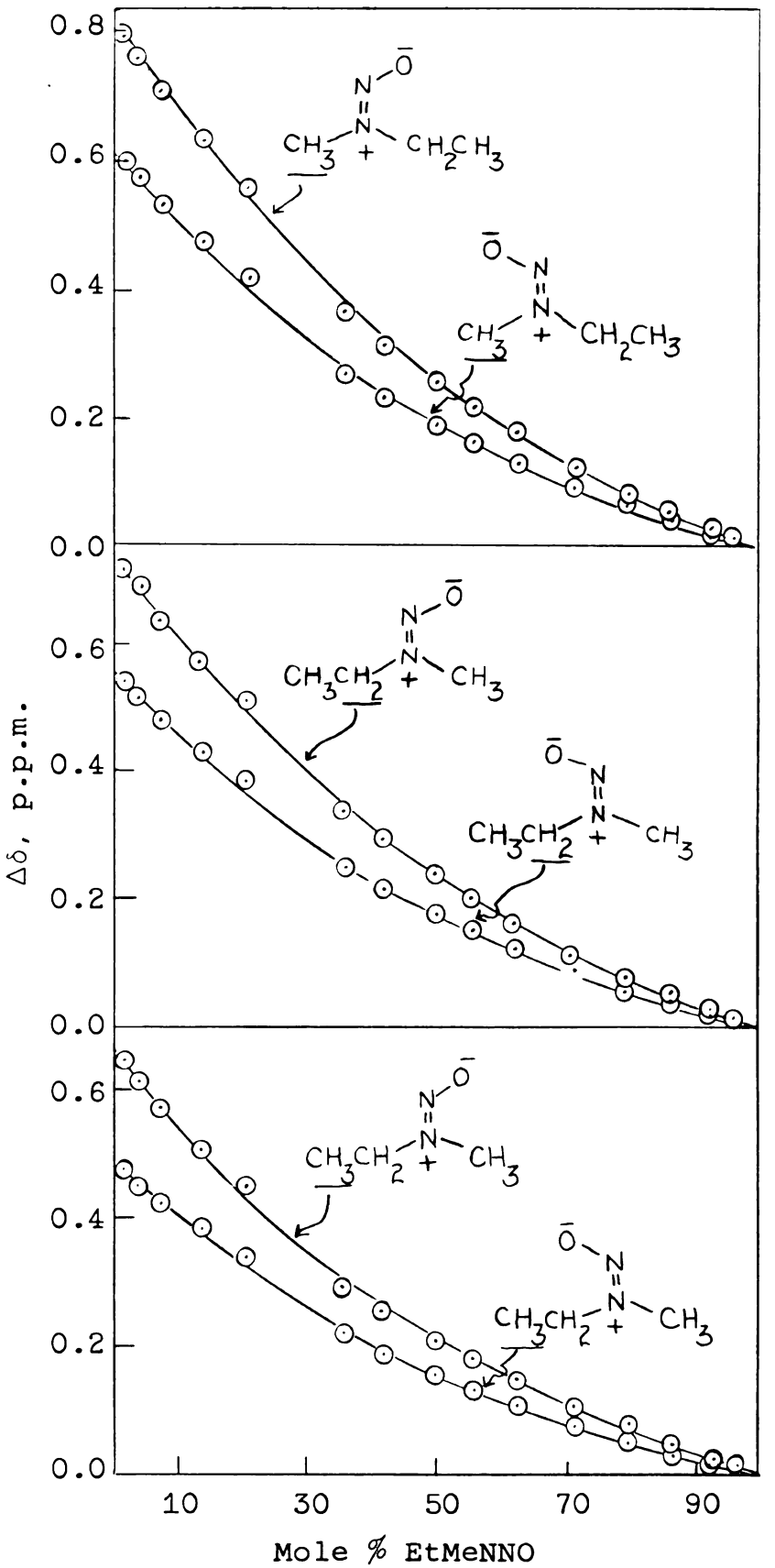


Figure 2. The upfield shift of the proton resonances of methyl ethyl nitrosamine on dilution with benzene.

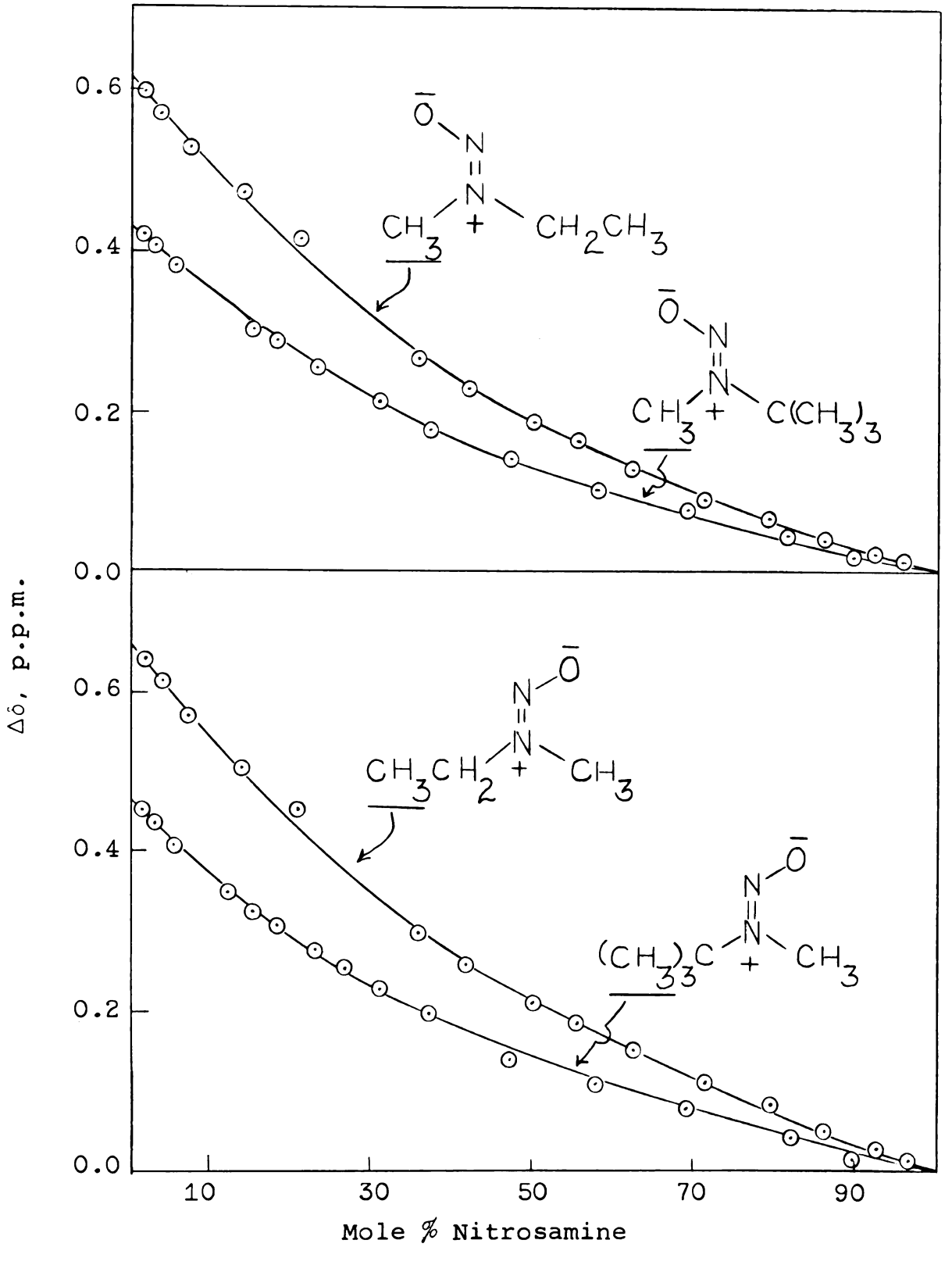


Figure 3. The upfield shifts of the proton resonances of methyl ethyl nitrosamine and methyl t-butyl nitrosamine on dilution with benzene.

Table 3. $\Delta\nu$ (ν in benzene − ν in carbon tetrachloride) Values, in c.p.s., of Nitrosamines

Table 3. Δ^{γ}($^{\gamma}$ in benzene - $^{\gamma}$ in carbon tetrachloride) Values, in c.p.s., of Nitrosamines

R_1R_2NNO		α(CH_3)		α(CH_2)		α(CH)		β(CH_3)	
R_1	R_2	cis	trans	cis	trans	cis	trans	cis	trans
CH_3	CH_3	32.4	48.0						
CH_3	CH_2CH_3	28.2	43.2	25.8	38.4			28.2	38.4
CH_3	$(CH_2)_3CH_3$	25.8	39.6	19.8	32.4				
CH_3	$CH(CH_3)_2$	23.4	36.6			9.0	27.0	30.0	34.2
CH_3	$C(CH_3)_3$	19.8							33.0
CH_3	$CH_2C_6H_5$	25.2	39.6	21.6	33.6				
CH_3	C_6H_5	34.2							
CH_2CH_3	$CH_2C_6H_5$			17.4 (16.2)[a]	27.6 (29.4)[a]			25.2	31.8
CH_2CH_3	C_6H_5			24.0				24.6	
$CH_2C_6H_5$	$CH(CH_3)_2$			14.4	24.6	6.0	23.4	20.4	25.8
$CH_2C_6H_5$	C_6H_5			18.6					
$CH(CH_3)_2$	$CH(CH_3)_2$					2.4	30.6	21.0	20.4
$CH(CH_3)_2$	C_6H_5					2.4	18.6	21.0	24.0

[a]Methylene of the ethyl group.

Table 4. Solvent Effects on the Chemical Shifts of Methyl Ethyl Nitrosamine

Solvent	α(CH$_2$) cis	α(CH$_2$) trans	α(CH$_3$) cis	α(CH$_3$) trans	β(CH$_3$) cis	β(CH$_3$) trans
			7.07	6.29	8.95	8.62

Table 4. Solvent Effects on the Chemical Shifts of Methyl Ethyl Nitrosamine

Solvent	$\alpha(CH_2)$		$\alpha(CH_3)$		$\beta(CH_3)$	
	cis	trans	cis	trans	cis	trans
Carbon tetrachloride	6.48	5.85	7.07	6.29	8.95	8.62
Cyclohexane	6.53	5.92	7.14	6.39		
Acetone	6.42	5.82	7.01	6.28	8.97	8.67
Dimethyl sulfoxide	6.44	5.86	7.02	6.31	9.01	8.71
Methanol		5.82	6.94		8.92	8.63
Benzene	6.91	6.48	7.54	7.01	9.42	9.26
Toluene	6.90	6.43	7.53	6.95	9.37	9.19
o-Xylene	6.92	6.44	7.54	6.94	9.37	9.16
m-Xylene	6.88	6.41	7.51	6.92	9.35	9.15
p-Xylene	6.88	6.41	7.51	6.90	9.34	9.14
iso-Durene	6.91	6.42	7.51	6.91	9.34	9.12
Chlorobenzene	6.67	6.18	7.28	6.67	9.20	8.97
Bromobenzene	6.72	6.22	7.32	6.71	9.24	9.02
Iodobenzene	6.73	6.21	7.32	6.69	9.24	9.01
m-Dichlorobenzene	6.60	6.06	7.19	6.53	9.13	8.86
Anisole		6.32	7.40	6.82	9.29	9.09
N,N-Dimethylaniline		6.44		6.94	9.37	9.17
Nitrobenzene	6.36	5.81	6.93	6.27	8.94	8.66
Pyridine	6.50	5.99	7.07	6.46	9.12	8.88
Phenol	6.85	6.55	7.43	7.01	9.36	9.21

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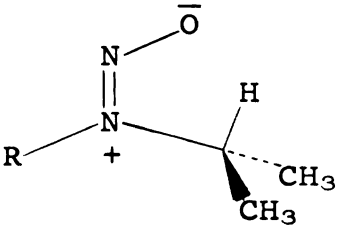
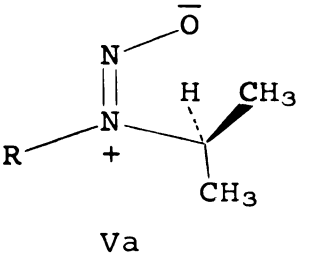
substituted benzenesdo not shift the resonances of the trans protons to as high fields as benzene does. On the basis of steric interactions this trend is anticipated.

Conformations--Since the protons of R_1 and R_2 do not couple to a measurable extent, the important conformation of R_1 and R_2 must be deduced from chemical shift data. Information on the anisotropic contribution of the NNO group could simplify conformational assignments. However, in the absence of this information, a comparison of the NNO group with other groups having similar anisotropic characteristics is necessary. From the similar behavior of the chemical shifts of the nitrosamines and the $R_1R_2C{=}NZ$ compounds it is reasonable to assume that the anisotropic effects of the two groups are qualitatively similar. Previous work in this laboratory (24) showed that the region in the C=NZ plane is deshielded with respect to the region above and below the plane. The ensuing discussion of conformations will be based on the assumption that the region in the NNO plane is also deshielded with respect to the region above and below the plane.

Pertinent conformations of the cis groups can be deduced, with some certainty, only from the isopropyl group. Of the two conformations IVa and Va only the eclipsing structure IVa



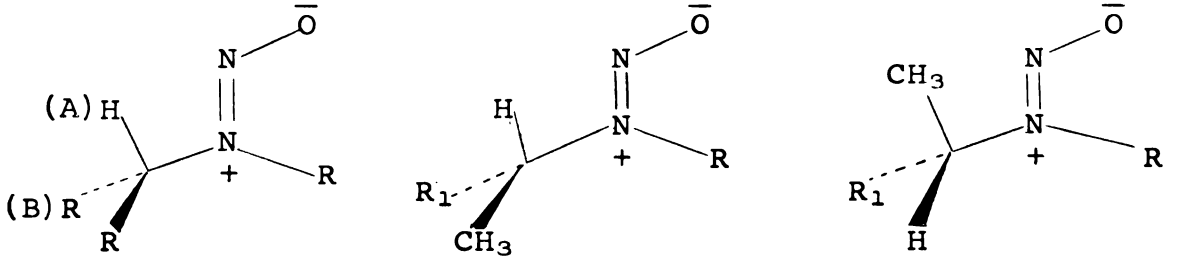
IVa



Va

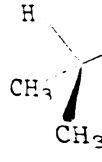
is consistent with the results. Conformation IVa explains the fact that α-methine protons, compared to α-methyl and α-methylene, resonate at lower fields when cis than when trans to the oxygen. Conformation IVa also explains the small $\Delta\nu$ values for the cis-α-methine, because the methine is farthest away from the associated benzene and should experience a smaller anisotropic effect.

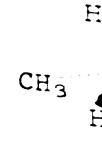
To deduce the conformations of the trans group two assumptions must be made: Firstly, that the group R eclipses the nitrogen-nitrogen double bond VIa and secondly that region A



VIa VIIa VIIIa

in the plane of the NNO group is deshielded with respect to region B. The first assumption is based on evidence regarding rotational isomerism about sp^2-sp^3 carbon-carbon bonds (29). On the basis of these assumptions it will be shown that when R is methyl VIIa is more stable than VIIIa, and that the ratio VIIa/VIIIa decreases as R changes from methyl to isopropyl. Considering the conformation of methyl t-butyl nitrosamine, IXa, of methyl isopropyl nitrosamine, Xa, XIa' and XIa'', and of methyl ethyl nitrosamine, XIIa', XIIa'' and XIIIa, if Xa is energetically comparable to XIa and XIIa to XIIIa then in





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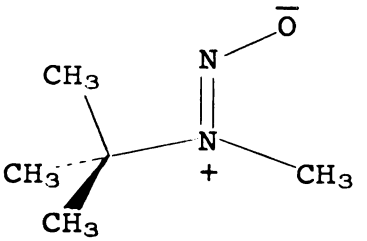
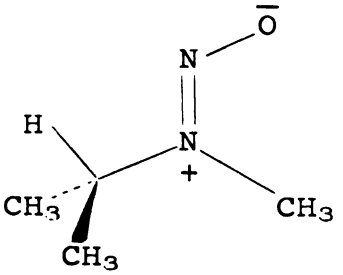
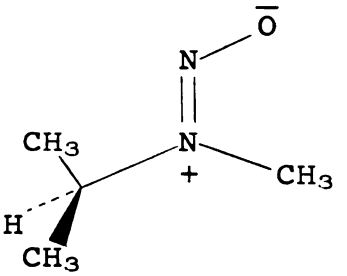


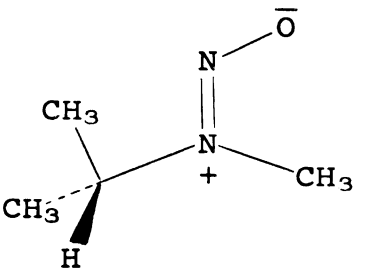
IXa



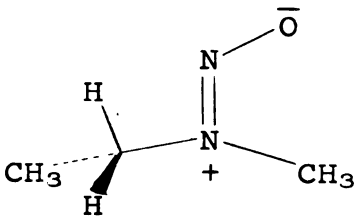
Xa



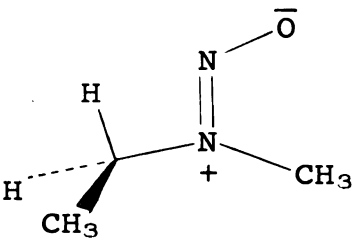
XIa'



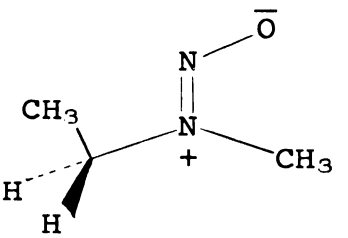
XI_a''



XIIa'



XIIa''



XIIIa

all three compounds the methyl groups should spend one-third of the time at region A and two-thirds of the time at region B. Therefore, the <u>trans</u>-β-methyls of all these compounds should resonate at approximately the same field. If Xa is favored over XIa and XIIa over XIIIa, then the methyl groups should spend one-third of the time at region A in the <u>t</u>-butyl compound IXa and progressively less than one-third in the isopropyl and ethyl compounds. In this case the <u>t</u>-butyl should be at

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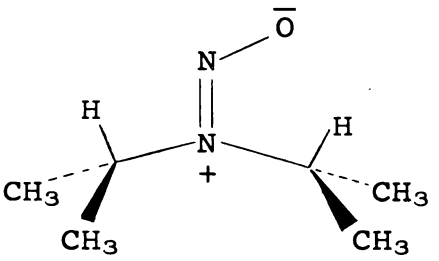
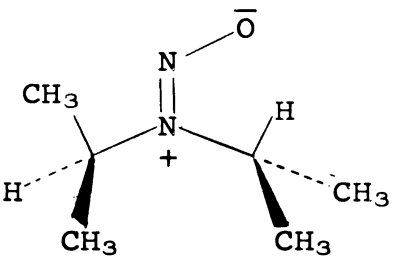
lower field than the isopropyl and the isopropyl at lower field than the ethyl. The data (Figure 1) adequately support the last hypothesis.

The important conformers of the diisopropyl nitrosamine are XIVa and XVa. Due to severe methyl interactions in XIVa



XIVa



XVa

the ratio XVa/XIVa should be larger than the ratio XIa/Xa. Comparison of the chemical shifts of diisopropyl nitrosamine and methyl isopropyl nitrosamine supports this conclusion. (a) The <u>trans</u>-α-methine of diisopropyl nitrosamine should be shifted upfield with respect to that of the methyl isopropyl nitrosamine (in carbon tetrachloride the shift is 0.59 p.p.m., Table 1). The <u>trans</u>-β-methyl should be shifted downfield (in carbon tetrachloride the shift is -0.10 p.p.m.). (c) The $\Delta\nu$ value for <u>trans</u>-α-methine should be larger for diisopropyl than for methyl isopropyl nitrosamine. Table 3 shows that the $\Delta\nu$ value for <u>cis</u>-α-methine decreased from 9.0 to 2.4 c.p.s. due to a decrease in complex stability, whereas the <u>trans</u>-α-methine increased from 27.0 to 30.6 c.p.s. (d) The $\Delta\nu$ value of the <u>trans</u>-β-methyl should decrease more rapidly

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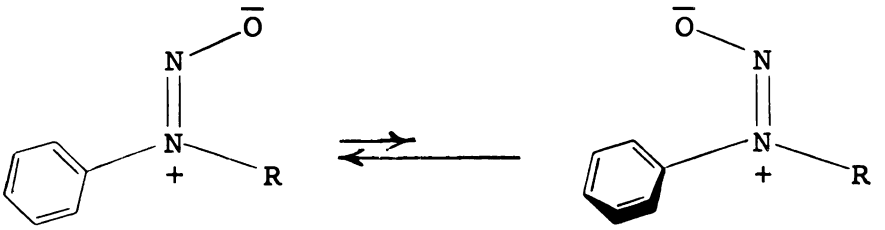
than that of the corresponding cis-β-methyl in going from methyl isopropyl to diisopropyl nitrosamine. Table 3 shows that the corresponding decreases are 12.8 and 9.0 c.p.s. The change of the trans-β-methyl is large enough to result in Δ^{γ} cis (21.0 c.p.s.) > Δ^{γ} trans (20.4 c.p.s.) for diisopropyl nitrosamine.

Syn/anti Isomers--The syn/anti isomer ratios of nitrosamines are comparable to those of $R_1R_2C{=}NZ$ compounds (3). Table 1 shows that the ethyl, benzyl and n-butyl groups have the same effective size. The phenyl group, on the other hand, has a large effective size. In isomer XVIIa the loss of overlap is large enough to shift the equilibrium in favor of XVIa. When R is methyl only the cis-methyl isomer is observed.



XVIa XVIIa

The possibility of rapid isomer interconversion is excluded by the fact that both isomers are observed when R is ethyl or isopropyl. The ultraviolet spectra (Table 5) show a decrease of λ_{max} from 275 mμ (R = CH_3, CH_2CH_3) to 250 mμ (R = isopropyl). Apparently when R is isopropyl the interactions between phenyl and isopropyl in XVIa are sufficiently large to cause loss of overlap between phenyl and the NNO group. The 224 mμ band (R = isopropyl) could be the absorption of isomer XVIIIa.

Table

R·R	
R_1	
CH_3	
CH_3	
(CH_3)	
CH_3	
CH_3CH	
(CH_3)	

[a] In

Table 5. Partial Ultraviolet Spectra of Nitrosamines in Cyclohexane[a]

R_1R_2NNO		λ_{max}(mμ)	ε x 10^3
R_1	R_2		
CH_3	CH_3	232	5.87
CH_3	CH_2CH_3	233	5.79
$(CH_3)_2CH$	$(CH_3)_2CH$	235	6.23
CH_3	C_6H_5	274	7.02
CH_3CH_2	C_6H_5	275	6.77
$(CH_3)_2CH$	C_6H_5	250 224	5.53 7.69

[a]In 95% ethanol a hypsochromic shift occurs of about 3-5 mμ.

PART B--OXIMES

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Results

The n.m.r. spectra of acetone, 2-butanone, methyl isopropyl ketone and methyl t-butyl ketone oximes are shown in Figures 4 and 5. Table 6 contains the chemical shifts, which are accurate to ± 0.03 p.p.m., of aldoximes and ketoximes. The differences between the chemical shifts of cis and trans protons are summarized in Tables 7 and 8. $\Delta\delta$ Values were obtained from the chemical shift data in Table 6. A positive (+) $\Delta\delta$ value means that protons resonate at higher field when cis than when trans to the hydroxyl group. A negative (-) value denotes the reverse. The interesting points are:
(a) H_1 resonates at lower field when cis to the hydroxyl group than when trans. The $\Delta\delta$ value is approximately -0.7 p.p.m.
(b) In contrast to H_1, cis-α-methyl protons, in neat liquid or in carbon tetrachloride solution, resonate at slightly lower fields than or at the same field as the trans-α-methyl protons. The $\Delta\delta$ value is approximately 0 to -0.05 p.p.m. The notable exception is acetophenone, which has a $\Delta\delta$ of -0.22 p.p.m.
(c) α-Methylene and α-methine protons also have negative $\Delta\delta$ values. Generally α-methine $\Delta\delta$ values, -0.90 p.p.m., are larger than H_1 $\Delta\delta$ values, which are -0.70 p.p.m. (d) In every case, except for acetophenone, $\Delta\delta$ values are more negative in benzene than in the neat liquid or carbon tetrachloride solution.
(e) β-Methyls, with the exception of di-t-butyl ketone oxime, have very small $\Delta\delta$ values.

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Tables 9 and 10 summarize $\Delta\nu$(ν in benzene - ν in carbon tetrachloride or neat) values of aldoximes and ketoximes respectively. A positive (+) $\Delta\nu$ value means that protons resonate at higher field in benzene than in the neat liquid or carbon tetrachloride solution. A negative value means the reverse. The important points are: (a) In most cases benzene shifts both cis and trans-H_1 upfield; the trans protons, however, show a greater upfield shift than the corresponding cis protons. The exceptions are cyclopentanecarboxaldehyde oxime where the cis-H_1 shifts downfield ($\Delta\nu$ = -1.2 c.p.s.), and the cis-H_1 of t-butylacetaldehyde oxime ($\Delta\nu$ = 0.0 c.p.s.). (b) The cis and trans α-methyl protons are shifted upfield. (c) α-Methylenes have positive $\Delta\nu$ values, with t-butylacetaldehyde being the notable exception, for both cis and trans protons. trans-α-Methines have positive $\Delta\nu$ values, whereas cis-α-methines have negative. The cis-α-methine of isopropyl t-butyl ketone oxime, whose $\Delta\nu$ is +22.2 c.p.s., is the notable exception. (e) Both the cis and trans β-methyl protons are shifted upfield, except the cis-β-methyl of isopropyl t-butyl ketone oxime and the trans-β-methyl of di-t-butyl ketone oxime.

Tables 11 and 12 summarize the syn/anti isomer ratios and the free energy differences between the two isomers of aldoximes and ketoximes. There seems to be little correlation between group size and isomer stability. In acetaldehyde oxime the supposedly sterically unfavorable anti isomer predominates.

Table 13 summarizes the effect of temperature on the spin-spin coupling constants ($J_{H_1H_\alpha}$) of oxime isomers in which the

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hydroxyl is cis to the aldehydic proton (syn isomer). The precision from several measurements is about ± 0.03 c.p.s. All coupling constants decrease with increase in temperature, with acetaldehyde oxime showing the smallest change. Cyclopentanecarboxaldehyde oxime shows the largest decrease from -30° to $+90^{\circ}$C. Table 14 shows the decrease in coupling with increase of solvent polarity. Figures 7, 8 and 9 show the effect of dilution on the spin-spin coupling constants of the syn isomers of acetaldehyde, propionaldehyde and isobutyraldehyde oxime respectively. Table 15 summarizes the effect of temperature on the spin-spin coupling constants, $J_{H_1H_\alpha}$ of the anti isomers i.e., those in which the hydroxyl is trans to the aldehydic proton. The notable differences between $J_{H_1H_\alpha}$ (anti) and $J_{H_1H_\alpha}$ (syn) are: (a) $J_{H_1H_\alpha}$ (anti) increases abruptly in changing from a monosubstituted to a disubstituted acetaldehyde oxime. (b) Whereas $J_{H_1H_\alpha}$(anti) of the disubstituted derivatives decrease with increase in temperature, those of the monosubstituted derivatives behave erratically. (c) As evidenced from Table 16 $J_{H_1H_\alpha}$ (anti) increases with increasing solvent polarity.

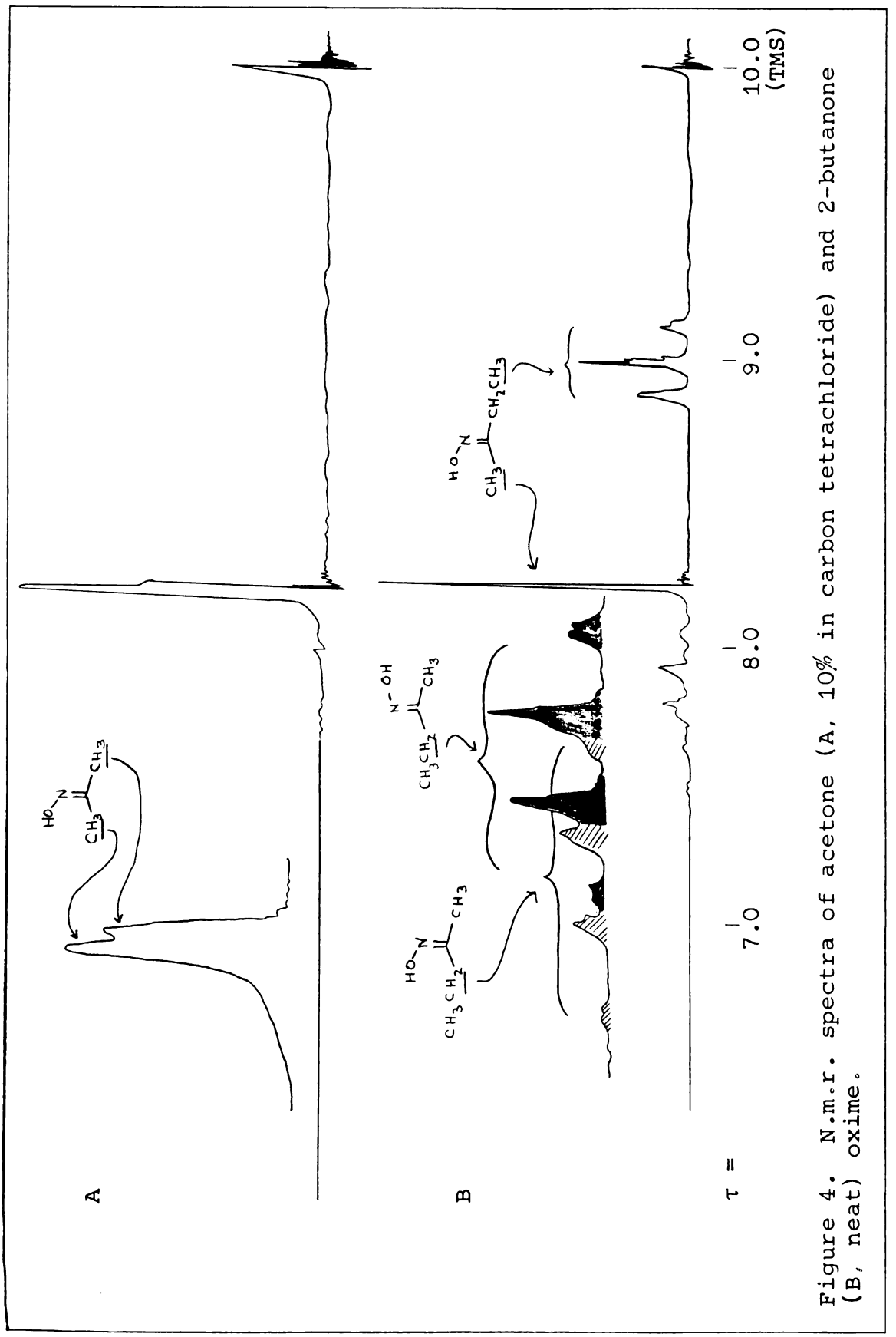


Figure 4. N.m.r. spectra of acetone (A, 10% in carbon tetrachloride) and 2-butanone (B, neat) oxime.

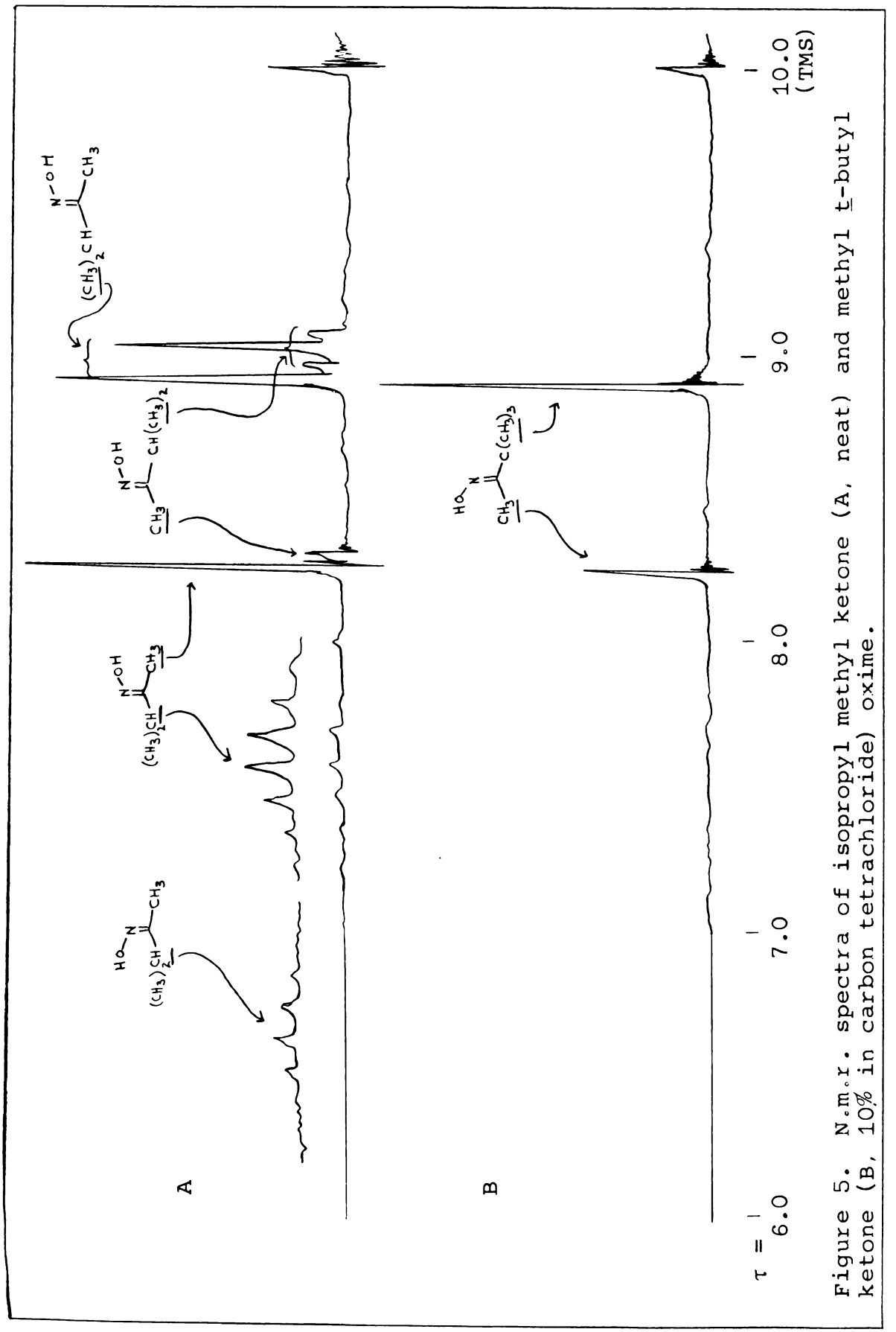


Figure 5. N.m.r. spectra of isopropyl methyl ketone (A, neat) and methyl t-butyl ketone (B, 10% in carbon tetrachloride) oxime.

$R_1R_2C{=}NOH$ R_1 R_2	Solvent	H_1 cis	H_1 trans	$\alpha(CH_2)$ cis	$\alpha(CH_2)$ trans	$\alpha(CH_3)$ cis	$\alpha(CH_3)$ trans	$\alpha(CH)$ cis	$\alpha(CH)$ trans	$\beta(CH_3)$ cis	$\beta(CH_3)$ trans	NOH
H CH_3	Neat	2.60	3.19			8.18	8.21					-0.02
	10% C_6H_6	2.79	3.53			8.42	8.57					

Table 6. Chemical Shifts (τ-Values) of Aldoximes and Ketoximes.

$R_1R_2C{=}NOH$		Solvent	H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		NOH
R_1	R_2		cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	
H	CH_3	Neat	2.60	3.19			8.18	8.21					-0.02
H	CH_3	10% C_6H_6	2.79	3.53			8.42	8.57					
H	CH_2CH_3	Neat	2.65	3.36		7.77[b]						8.97	-0.13
H	CH_2CH_3	10% C_6H_6	2.73	3.60		7.94[b]					9.27	9.23	
H	$(CH_2)_2CH_3$	Neat	2.67	3.35		7.78[b]							-0.26
H	$(CH_2)_2CH_3$	10% C_6H_6	a	3.53		7.93[b]							
H	$CH_2CH(CH_3)_2$	Neat	2.64	3.30		7.85[b]							-0.26
H	$CH_2CH(CH_3)_2$	10% C_6H_6	a	3.45	7.80	8.12							
H	$CH_2C(CH_3)_3$	Neat	2.59	3.26	7.75	7.98							
H	$CH_2C(CH_3)_3$	10% C_6H_6	2.59	3.41	7.74	8.10							
H	$CH_2C_6H_5$	10% CCl_4	2.58	3.18	6.30	6.50							
H	$CH_2C_6H_5$	10% C_6H_6	a	3.27	6.36	6.73							
H	$CH(CH_3)_2$	Neat	2.73	3.52					6.87	7.58	8.98	8.95	-0.13
H	$CH(CH_3)_2$	10% C_6H_6	2.76	3.73					6.80	7.83	9.17	9.17	
H	$CH(CH_3)CH_2CH_3$	Neat	2.79	3.56					6.93	7.71	8.99	8.96	-0.07
H	$CH(CH_3)CH_2CH_3$	10% C_6H_6	a	3.72					6.86	7.88	9.16	9.16	
H	$CH(CH_3)(CH_2)_2CH_3$	Neat	2.80	3.56					7.02	7.63	9.00	8.96	-0.28
H	$CH(CH_3)(CH_2)_2CH_3$	10% C_6H_6	a	3.72					6.94	7.76	9.15	9.15	

Continued

Table 6 - Continued

R_1R_2C-NOH R_1	R_2	Solvent	H_1 cis	H_1 trans	α(CH_2) cis	α(CH_2) trans	α(CH_3) cis	α(CH_3) trans	α(CH)		β(CH_3)		NOH

Table 6 - Continued

R_1R_2C=NOH R_1	R_2	Solvent	H_1 cis	H_1 trans	$\alpha(CH_2)$ cis	$\alpha(CH_2)$ trans	$\alpha(CH_3)$ cis	$\alpha(CH_3)$ trans	$\alpha(CH)$ cis	$\alpha(CH)$ trans	$\beta(CH_3)$ cis	$\beta(CH_3)$ trans	NOH
H	$CH(CH_2CH_3)_2$	Neat	2.86	3.60					7.10	7.98			-0.10
H	$CH(CH_2CH_3)_2$	10% C_6H_6	a	3.78					7.05	8.07			
H	$CH(CH_2CH_3)(CH_2)_3CH_3$	Neat	2.87	3.61					6.97	7.88			-0.07
H	$CH(CH_2CH_3)(CH_2)_3CH_3$	10% C_6H_6	a	3.75					6.88	7.93			
H	$CH[CH(CH_3)_2]_2$	Neat	2.82	3.57					7.10[b]	8.30[b]			0.20
H	$CH[CH(CH_3)_2]_2$	10% C_6H_6	a	3.71						8.75[b]			
H		Neat	2.70	3.39					6.73	7.37			-0.02
H		10% C_6H_6	2.68	3.56					6.60	7.52			
H		Neat	2.75	3.54									0.17
H		10% C_6H_6	a	3.65									
CH_3	CH_3	10% CCl_4					8.11	8.12					
CH_3	CH_3	10% C_6H_6					8.28	8.36					
CH_3	CH_2CH_3	Neat			7.60	7.78	8.16	8.16			8.94	8.94	
CH_3	CH_2CH_3	10% C_6H_6			7.67	7.99	8.24	8.34			9.11	9.11	
CH_3	$CH(CH_3)_2$	Neat					8.17	8.22	6.49	7.45	8.97	8.92	
CH_3	$CH(CH_3)_2$	10% C_6H_6					8.23	8.39	6.36	7.64	9.14	9.08	

Continued

Table [illegible] - Continued

$R_1R_2C{=}NOH$ R_1	R_2	Solvent	H$_\perp$ cis	H$_\perp$ trans	$\alpha(CH_2)$ cis	$\alpha(CH_2)$ trans	$\alpha(CH_3)$ cis	$\alpha(CH_3)$ trans	$\alpha(CH)$ cis	$\alpha(CH)$ trans	$\beta(CH_3)$ cis	$\beta(CH_3)$ trans	NOH
CH_3	$C(CH_3)_3$	10% CCl_4					8.15				8.84		

Table 6 - Continued

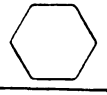
R_1R_2C=NOH		Solvent	H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		NOH
R_1	R_2		cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	
CH_3	$C(CH_3)_3$	10% CCl_4					8.15					8.84	
CH_3	$C(CH_3)_3$	10% C_6H_6					8.18					9.01	
CH_3CH_2	CH_2CH_3	Neat			7.60	7.75					8.91	8.91	0.18
CH_3CH_2	CH_2CH_3	10% C_6H_6			7.66	7.98					9.04	9.04	
$(CH_3)_2CH$	$C(CH_3)_3$	10% CCl_4							7.40		8.68[c]	8.86[d]	0.03
$(CH_3)_2CH$	$C(CH_3)_3$	10% C_6H_6							7.77		8.58[c]	8.98[d]	
$(CH_3)_3C$	$C(CH_3)_3$	10% CCl_4									8.73	8.57	0.17
$(CH_3)_3C$	$C(CH_3)_3$	10% C_6H_6									8.80	8.53	
CH_3	C_6H_5	10% CCl_4					7.71	7.93					-0.13
CH_3	C_6H_5	10% C_6H_6					7.86	8.00					
CH_3CH_2	C_6H_5	50% CCl_4			7.17	7.42					8.88	8.88	-0.55
CH_3CH_2	C_6H_5	10% C_6H_6			7.22	7.58					8.93	8.93	
$CH_3CH_2CH_2$	C_6H_5	50% CCl_4			7.17	7.17							
$CH_3CH_2CH_2$	C_6H_5	10% C_6H_6			7.18	7.18							
CH_3	$CH_2C_6H_5$	50% CCl_4			6.24	6.49	8.20	8.20					0.00
CH_3	$CH_2C_6H_5$	10% C_6H_6			6.29	6.61	8.27	8.37					

[a] Solvent interference.
[b] Center of multiplet.
[c] β-Methyl of isopropyl group.
[d] β-Methyl of t-butyl group.

Table 7. Δδ (cis − δ trans) Values, in p.p.m., of Aldoximes.

$R_1R_2C{=}NOH$		H		α(CH_2)		α(CH_2)		α(CH)		β(CH_2)	
R_1	R_2	Neat	C_6H_6[a]	Neat	C_6H_6[a]	Neat	C_6H_6[a]	Neat	C_6H_6[a]	Neat	C_6H_6[a]

Table 7. $\Delta\delta$(δ *cis* - δ *trans*) Values, in p.p.m., of Aldoximes.

R_1R_2C=NOH		H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$	
R_1	R_2	Neat	C_6H_6[a]	Neat	C_6H_6[a]	Neat	C_6H_6[a]	Neat	C_6H_6[a]	Neat	C_6H_6[a]
H	CH_3	-0.59	-0.74			-0.03	-0.15				
H	CH_2CH_3	-0.71	-0.87								+0.04
H	$(CH_2)_2CH_3$	-0.68									
H	$CH_2CH(CH_3)_2$	-0.66		-0.32							
H	$CH_2C(CH_3)_3$	-0.67	-0.82	-0.23	-0.36						
H	$CH_2C_6H_5$	-0.60		-0.20	-0.37						
H	$CH(CH_3)_2$	-0.79	-0.97					-0.71	-1.03	+0.03	0.00
H	$CH(CH_3)CH_2CH_3$	-0.77						-0.78	-1.02	+0.03	0.00
H	$CH(CH_3)(CH_2)_2CH_3$	-0.76						-0.61	-0.82	+0.04	0.00
H	$CH(CH_2CH_3)_2$	-0.74						-0.88	-1.02		
H	$CH(CH_2CH_3)(CH_2)_3CH_3$	-0.74						-0.91	-1.05		
H	$CH[CH(CH_3)_2]_2$	-0.75						-1.20			
H		-0.69	-0.88					-0.64	-0.92		
H		-0.79									

[a] 10% Solutions.

Table 8. $\Delta\delta$ (δ *cis* - δ *trans*) Values, in p.p.m., of Ketoximes.

$R_1R_2C=NOH$	$\alpha(CH_2)$	$\alpha(CH_3)$	$\alpha(CH)$	$\beta(CH_3)$
	* Neat	* Neat	* Neat	* Neat

Table 8. $\Delta\delta$ (δ *cis* - δ *trans*) Values, in p.p.m., of Ketoximes.

R_1R_2C=NOH		α(CH_2)		α(CH_3)		α(CH)		β(CH_3)	
R_1	R_2	* Neat or # CCl_4	C_6H_6[a]	* Neat or # CCl_4	C_6H_6[a]	* Neat or # CCl_4	C_6H_6[a]	* Neat or # CCl_4	C_6H_6[a]
CH_3	CH_3			#-0.01[b]	-0.08				
CH_3	CH_2CH_3	*-0.18	-0.32	* 0.00	-0.10			* 0.00	0.00
CH_3	$CH(CH_3)_2$			*-0.05	-0.16	*-0.96	-1.28	*+0.05	+0.06
CH_3CH_2	CH_2CH_3	*-0.15	-0.32					* 0.00	0.00
$(CH_3)_3C$	$C(CH_3)_3$							#+0.16[b]	+0.27
CH_3	C_6H_5			#-0.22[b]	-0.14				
CH_3CH_2	C_6H_5	#-0.25[c]	-0.36					# 0.00[c]	0.00
$CH_3CH_2CH_2$	C_6H_5	# 0.00[c]	0.00						
CH_3	$CH_2C_6H_5$	#-0.25[c]	-0.32	# 0.00[c]	-0.10				

[a] 10% Solution

[b] 10% Solution

[c] 50% Solution

$R_1R_2C{=}NOH$	H_1	$\alpha(CH_2)$	$\alpha(CH_3)$	$\alpha(CH)$	$\beta(CH_3)$

Table 9. $\Delta^{\nu a}$($^{\nu}$ in benzene - $^{\nu}$ neat) Values, in c.p.s., of Aldoximes.

R_1R_2C=NOH		H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$	
R_1	R_2	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans
H	CH_3	+11.4	+20.4			+14.4	+21.6				
H	CH_2CH_3	+ 4.8	+14.4		+10.2						+15.6
H	$(CH_2)_2CH_3$		+10.8		+ 9.0						
H	$CH_2CH(CH_3)_2$		+ 9.0		+15.0						
H	$CH_2C(CH_3)_3$	+ 0.0	+ 9.0	- 0.6	+ 7.2						
H	$CH_2C_6H_5$[b]		+ 5.4	+ 3.6	+13.8						
H	$CH(CH_3)_2$	+ 1.8	+12.6					- 4.2	+15.0	+11.4	+13.2
H	$CH(CH_3)CH_2CH_3$		+ 9.6					- 4.2	+10.2	+10.2	+12.0
H	$CH(CH_3)(CH_2)_2CH_3$		+ 9.6					- 4.8	+ 7.8	+ 9.0	+11.4
H	$CH(CH_2CH_3)_2$		+10.8					- 3.0	+ 5.4		
H	$CH(CH_2CH_3)(CH_2)_3CH_3$		+ 8.4					- 5.4	+ 3.0		
H	$CH[CH(CH_3)_2]_2$		+ 8.4						+24.0		
H		- 1.2	+10.2					- 7.8	+ 9.0		
H			+ 6.6								

[a] Positive value means that the proton resonance in benzene is at higher field; a negative value means the reverse.

[b] 10% carbon tetrachloride solution.

Table 10. $\Delta\nu_{OH}$(ν in benzene- ν in carbon tetrachloride[b] or neat[c]) values, in c.p.s., of Ketoximes.

Table 10. $\Delta^{\gamma a}$($^{\gamma}$ in benzene- $^{\gamma}$ in carbon tetrachloride[b] or neat[c]) Values, in c.p.s., of Ketoximes.

R_1R_2C=NOH		α(CH_2)		α(CH_3)		α(CH)		β(CH_3)	
R_1	R_2	cis	trans	cis	trans	cis	trans	cis	trans
CH_3	CH_3[b]			+10.2	+14.4				
CH_3	CH_2CH_3[c]	+ 4.2	+12.6	+ 4.8	+10.8			+10.2	+10.2
CH_3	$CH(CH_3)_2$[c]			+ 3.6	+10.2	- 7.8	+10.5	+10.2	+ 9.6
CH_3	$C(CH_3)_3$[b]			+ 1.8					+10.2
CH_3CH_2	CH_2CH_3[c]	+ 3.6	+13.8					+ 7.8	+ 7.8
$(CH_3)_2CH$	$C(CH_3)_3$[b]					+22.2		- 6.0[d]	+ 6.6[e]
$(CH_3)_3C$	$C(CH_3)_3$[b]							+ 4.2	- 2.4
CH_3	C_6H_5[b]			+ 9.0	+ 4.2				
CH_3CH_2	C_6H_5[b]	+ 3.0	+ 9.6					+ 3.0	+ 3.0
$CH_3CH_2CH_2$	C_6H_5[b]	+ 0.6	+ 0.6						
CH_3	$CH_2C_6H_5$	+ 3.0	+ 7.2	+ 4.2	+10.2				

[a] Positive value means that the proton resonance in benzene is at higher field; a negative value means the reverse.

[b] Carbon tetrachloride.

[c] Neat.

[d] β-Methyl of isopropyl group.

[e] β-Methyl of t-butyl group.

Table 11. *syn*/*anti* Ratios and $\Delta F^{o}_{40^{o}}$ Values for *syn* ⟶ *anti* of Aldoximes.

$R_1R_2C{=}NOH$ R_1	R_2	Solvent	Percent *syn*	Percent *anti*	$\Delta F^{o}_{40^{o}}$ (Kcal/mole)
H	CH_3	Neat	39	61	-0.27
H	CH_2CH_3	Neat	56	44	0.15
H	$(CH_2)_2CH_3$	Neat	54	46	0.10
H	$CH_2CH(CH_3)_2$	Neat	52	48	0.05
H	$CH_2C(CH_3)_3$	Neat	61	39	0.27
H	$CH_2C_6H_5$	10% CCl_4	55	45	0.12
H	$CH(CH_3)_2$	Neat	73	27	0.61
H	$CH(CH_3)CH_2CH_3$ [a]	Neat	70	30	0.51
H	$CH(CH_3)(CH_2)_2CH_3$	Neat	67	33	0.43
H	$CH(CH_2CH_3)_2$	Neat	67	33	0.43
H	$CH(CH_2CH_3)(CH_2)_3CH_3$	Neat	67	33	0.43
H	$CH[CH(CH_3)_2]_2$	Neat	71	29	0.55
H		Neat	64	36	0.35
H		Neat	70	30	0.51

[a] *syn*/*anti* Ratio 71/29 after heating sample to 150°.

Table 12. *syn*/*anti* Ratios and $\Delta F^{o}_{40^{o}}$ Values for *syn* ⟶ *anti* of Ketoximes.

$R_1R_2C{=}NOH$ R_1	R_2	Solvent	Percent *syn*	Percent *anti*	$\Delta F^{o}_{40^{o}}$ (Kcal/mole)
CH_3	CH_2CH_3	Neat	74	26	0.64
CH_3	$CH(CH_3)_2$	Neat	91	9	1.41
CH_3	$C(CH_3)_3$	10% CCl_4	100	0	
$(CH_3)_2CH$	$C(CH_3)_3$	10% CCl_4	100	0	
CH_3	C_6H_5	10% CCl_4	94	6	1.68
CH_3CH_2	C_6H_5	50% CCl_4	92	8	1.49
CH_3	$CH_2C_6H_5$	50% CCl_4	74	26	0.64

Table 13 Spin-Spin Coupling Constants of Aldoximes (syn isomer) at Various Temperatures.

Table 13. Spin-Spin Coupling Constants of Aldoximes (syn isomer) at Various Temperatures.

R_1R_2CH		$J_{H_1H_\alpha}$ (c.p.s.)									
R_1	R_2	-30°[a]	0°[a]	40°	50°	60°	70°	90°	110°	130°	150°
H	H	6.00	5.93	5.94	5.89		5.88	5.86			
H	CH_3	6.15	6.01	5.85	5.79		5.79	5.79			
H	CH_2CH_3	6.42	6.31	6.10	6.08		6.07	6.00			
H	$CH(CH_3)_2$	6.55	6.53	6.42	6.37		6.36	6.47			
H	$C(CH_3)_3$	7.30	7.19	7.10	6.96		6.98	6.88			
H	C_6H_5[b]	6.69	6.53	6.49	6.46	6.39	6.48				
CH_3	CH_3	6.80	6.64	6.33	6.18		6.07	5.97			
CH_3	CH_2CH_3	7.90	7.55	7.19	7.00		6.87	6.79	6.75	6.71	6.56
CH_3	$(CH_2)_2CH_3$	7.95	7.79	7.38	7.09		6.97	6.86			
CH_3CH_2	CH_2CH_3	8.72	8.48	8.08	7.90		7.72	7.56			
CH_3CH_2	$(CH_2)_3CH_3$	8.75	8.59	8.15	7.95		7.79	7.73			
$(CH_3)_2CH$	$CH(CH_3)_2$		8.50	8.42	8.20		8.18	8.08			
		7.89	7.51	7.12	6.93		6.76	6.66			
		6.50	6.32	6.15	6.00		5.87	5.76			

[a] All aldoximes measured at -30° and 0° were diluted with carbon tetrachloride (50% v/v) to reduce the viscosity.

[b] 10% w/v in carbon tetrachloride.

Table 14. The Effect of Solvent Polarity on the Spin-Spin Coupling Constants of Aldoximes (syn isomer).

R_1R_2CH		$J_{H_1H_\alpha}$ (c.p.s.)		
R_1	R_2	Neat (40°)	Cyclohexane (40°)[a]	Acetonitrile (40°)[a]
H	H	5.94	5.91	5.91
H	CH_3	5.85	5.79	5.74
H	CH_2CH_3	6.10	6.11	6.09
H	$CH(CH_3)_2$	6.42	6.45	6.44
H	$C(CH_3)_3$	7.10	7.08	6.93
H	C_6H_5	6.49	b	6.41
CH_3	CH_3	6.33	6.02	6.01
CH_3	CH_2CH_3	7.19	6.96	6.85
CH_3	$(CH_2)_2CH_3$	7.38	7.13	7.03
CH_3CH_2	CH_2CH_3	8.08	7.74	7.73
CH_3CH_2	$(CH_2)_3CH_3$	8.15	7.92	7.85
$(CH_3)_2CH$	$CH(CH_3)_2$	8.42	8.18	8.08
		7.12	6.86	6.89
		6.15	5.71	5.93

[a] 10% solutions.

[b] Sample insoluble in cyclohexane.

Table 15. Spin-Spin Coupling Constants of Aldoximes (anti isomer) at Various Temperatures.

R_1R_2CH–$C(H_1)$=N–OH	$J_{H_1H_\alpha}$ (c.p.s.)

Table 15. Spin-Spin Coupling Constants of Aldoximes (anti isomer) at Various Temperatures.

R_1R_2CH		$J_{H_1H_\alpha}$ (c.p.s.)									
R_1	R_2	-30°[a]	0°[a]	40°	50°	60°	70°	90°	110°	130°	150°
H	H	5.56	5.49	5.51	5.54		5.53	5.50			
H	CH_3	5.33	5.38	5.49	5.43		5.47	5.46			
H	CH_2CH_3	5.36	5.50	5.47	5.45		5.52	5.53			
H	$CH(CH_3)_2$	5.41	5.47	5.52	5.53		5.57	5.59			
H	$C(CH_3)_3$	5.84	5.92	5.82	5.92		5.91	5.90			
H	C_6H_5[b]			5.45	5.50	5.44	5.50				
CH_3	CH_3	7.22	7.35	7.33	7.11		7.20	7.12			
CH_3	CH_2CH_3	7.70	7.78	7.80	7.55		7.61	7.59	7.60	7.72	7.56
CH_3	$(CH_2)_2CH_3$	7.51	7.78	7.83	7.62		7.64	7.65			
CH_3CH_2	CH_3CH_2	8.30	8.16	8.22	8.10		8.08	8.07			
CH_3CH_2	$(CH_2)_3CH_3$	8.18	8.30	8.31	8.18		8.16	8.15			
$(CH_3)_2CH$	$CH(CH_3)_2$	8.53	8.80	8.69	8.62		8.60	8.58			
		7.25	7.26	7.20	7.02		7.00	6.93			
		7.36	7.15	7.27	7.17		7.12	7.09			

[a] All aldoximes measured at -30° and 0° were diluted with carbon tetrachloride (50% v/v) to reduce the viscosity.

[b] 10% w/v in carbon tetrachloride.

Table 16. The Effect of Solvent Polarity on the Spin-Spin Coupling Constants of Aldoximes (anti isomer).

R_1R_2CH		$J_{H_1H_\alpha}$ (c.p.s.)		
R_1	R_2	Neat (40°)	Cyclohexane (40°)[a]	Acetonitrile (40°)[a]
H	H	5.51	5.53	5.68
H	CH_3	5.49	5.51	5.52
H	CH_2CH_3	5.47	5.57	5.59
H	$CH(CH_3)_2$	5.52	5.67	5.61
H	$C(CH_3)_3$	5.82	5.82	5.95
H	C_6H_5	5.45	b	5.56
CH_3	CH_3	7.33	7.22	7.24
CH_3	CH_2CH_3	7.80	7.68	7.77
CH_3	$(CH_2)_2CH_3$	7.83	7.78	7.86
CH_3CH_2	CH_2CH_3	8.22	8.20	8.34
CH_3CH_2	$(CH_2)_3CH_3$	8.31	8.26	8.36
$(CH_3)_2CH$	$CH(CH_3)_2$	8.69	8.55	8.72
		7.20	6.96	7.29
		7.27	7.21	7.38

[a] 10% solutions.

[b] Sample insoluble in cyclohexane.

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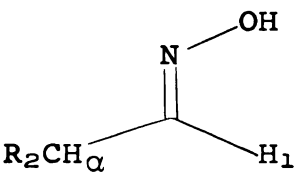
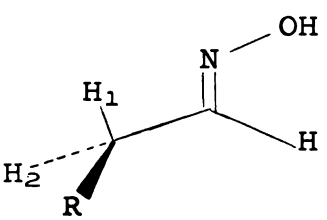
Discussion

Conformations of the syn Isomers--The relative stability of the rotamers of the syn isomers of aldoximes can be qualitatively assessed from the dependence of $J_{H_1H_\alpha}$ (Ib) on temperature, provided the following two assumptions are correct.

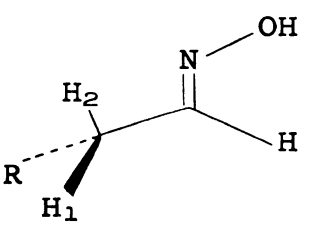


Ib

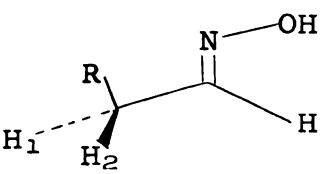
(a) The minimum energy conformations are IIb, IIIb and IVb, Vb, whereby a single bond eclipses the double bond. Several



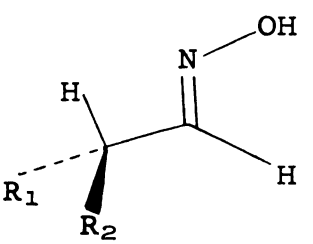
IIb



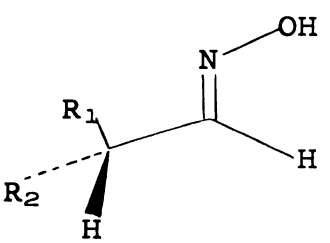
IIb'



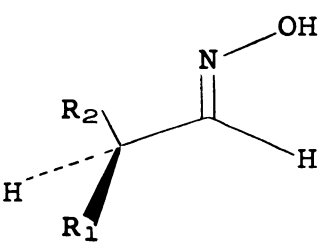
IIIb



IVb



Vb



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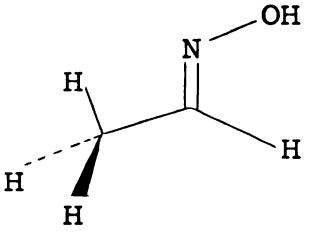
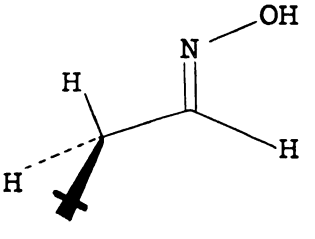
studies on rotational isomerism about single bonds joining sp^3 to a sp^2 hybridized carbon atoms have shown this to be true (9,10,29,30). (b) $J_t > J_g$ (12), where J_t is the <u>trans</u> coupling (dihedral angle = 180°) and J_g the gauche (dihedral angle = 60°). On the basis of these assumptions, if IIb and IIIb are energetically equivalent, $J_{H_1H_\alpha}$ should be temperature independent. If IIb is more stable than IIIb, this coupling should decrease with increase in temperature; and if less stable, it should increase. Similarly, if IVb and Vb are energetically equivalent the coupling should be temperature independent. If IVb is more stable than Vb, the coupling should decrease with increase in temperature; and if less stable, it should increase. For <u>all</u> the <u>syn</u> isomers examined, the most stable rotamer is the one in which the <u>hydrogen</u> eclipses the double bond.

The enthalpy differences between the various rotamers may be determined as follows. Equation <u>1</u> expresses the coupling of acetaldehyde oxime (VIb) in terms of J_t and J_g. Equation <u>2</u>



VIb



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VIIb

expresses the couplings of the monosubstituted oximes, where X is the fractional population of IIb and (1 - X) that of IIIb.

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$$J_{obs.} = 1/3(J_t + 2J_g) \qquad 1$$

$$J_{obs.} = X(J_t + J_g)/2 + (1 - X)J_g \qquad 2$$

$$J_{obs.} = XJ_t + (1 - X)J_g \qquad 3$$

Equation 3 expresses the couplings of the disubstituted oximes, where X is the fractional population of IVb and (1 - X) that of Vb. If it is assumed that at -30° t-butylacetaldehyde oxime exists solely in conformation VIIb, J_t and J_g can be calculated from equations 1 and 4. Rotamer populations can then be calculated from equations 2 and 3, and ΔH^o values from

$$J_{obs.(t\text{-butyl})} = 1/2(J_t + J_g) \qquad 4$$

plots of log K vs 1/T.

Use of the same J_t and J_g for monosubstituted and disubstituted acetaldehyde oximes would introduce some error in the ΔH^o values. To minimize this error a 0.4 c.p.s. correction should be applied for each alkyl or aryl substituent (31,32). Thus the observed coupling of monosubstituted compounds should be increased by 0.4 c.p.s. and that of the disubstituted by 0.8 c.p.s. This procedure gives J_t = 13.0 c.p.s. and J_g = 2.4 c.p.s.

Table 17 contains the rotamer populations calculated from equations 2 and 3. Table 18 summarizes the ΔH^o values, which are probably reliable to ± 30%, obtained from plots of log K vs 1/T (Figure 6).

The ΔH^o values in both cyclic and acyclic series become more positive as the alkyl group R increases in size. This

Table 17. Rotamer Population of Aldoximes (syn isomer).

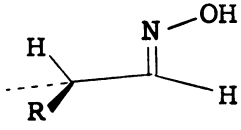
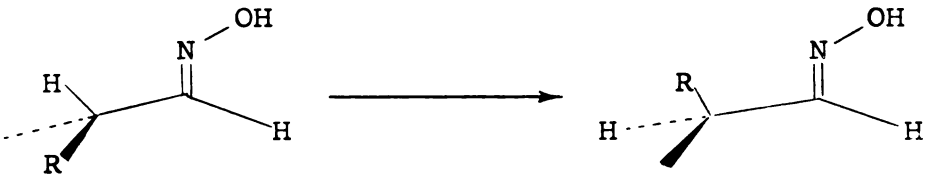
R_1R_2CH		 %									
R_1	R_2	-30°	0°	40°	50°	60°	70°	90°	110°	130°	150°
H	CH_3	78	76	72	71		71	71			
H	CH_2CH_3	83	81	77	77		77	75			
H	$CH(CH_3)_2$	86	85	83	82		82				
H	$C(CH_3)_3$	100	98	96	93			92			
H	C_6H_5	88	85	85	84	83					
CH_3	CH_3	49	48	45	43		42	41			
CH_3	CH_2CH_3	60	56	53	51		50	49	49	48	47
CH_3	$(CH_2)_2CH_3$	60	58	54	52		51	50			
CH_3CH_2	CH_2CH_3	67	65	61	60		58	56			
CH_3CH_2	$(CH_2)_3CH_3$	68	66	62	60		58	58			
$(CH_3)_2CH$	$CH(CH_3)_2$		65	64	62		62	61			
		59	56	52	50		49	48			
		46	44	43	42		40	39			

Table 18. ΔH° Values Obtained from Plots of log K vs 1/T.



$R_1R_2CHCH{=}NOH$		
R_1	R_2	ΔH° (cal/mole)
H	CH_3	+720
H	CH_2CH_3	+750
H	$CH(CH_3)_2$	+520
H	$C(CH_3)_3$	+3900
H	C_6H_5	+740
CH_3	CH_3	+550
CH_3	CH_2CH_3	+610
CH_3	$(CH_2)_2CH_3$	+670
CH_3CH_2	CH_2CH_3	+720
CH_3CH_2	$(CH_2)_3CH_3$	+710
$(CH_3)_2CH$	$CH(CH_3)_2$	+460
		+700
		+460

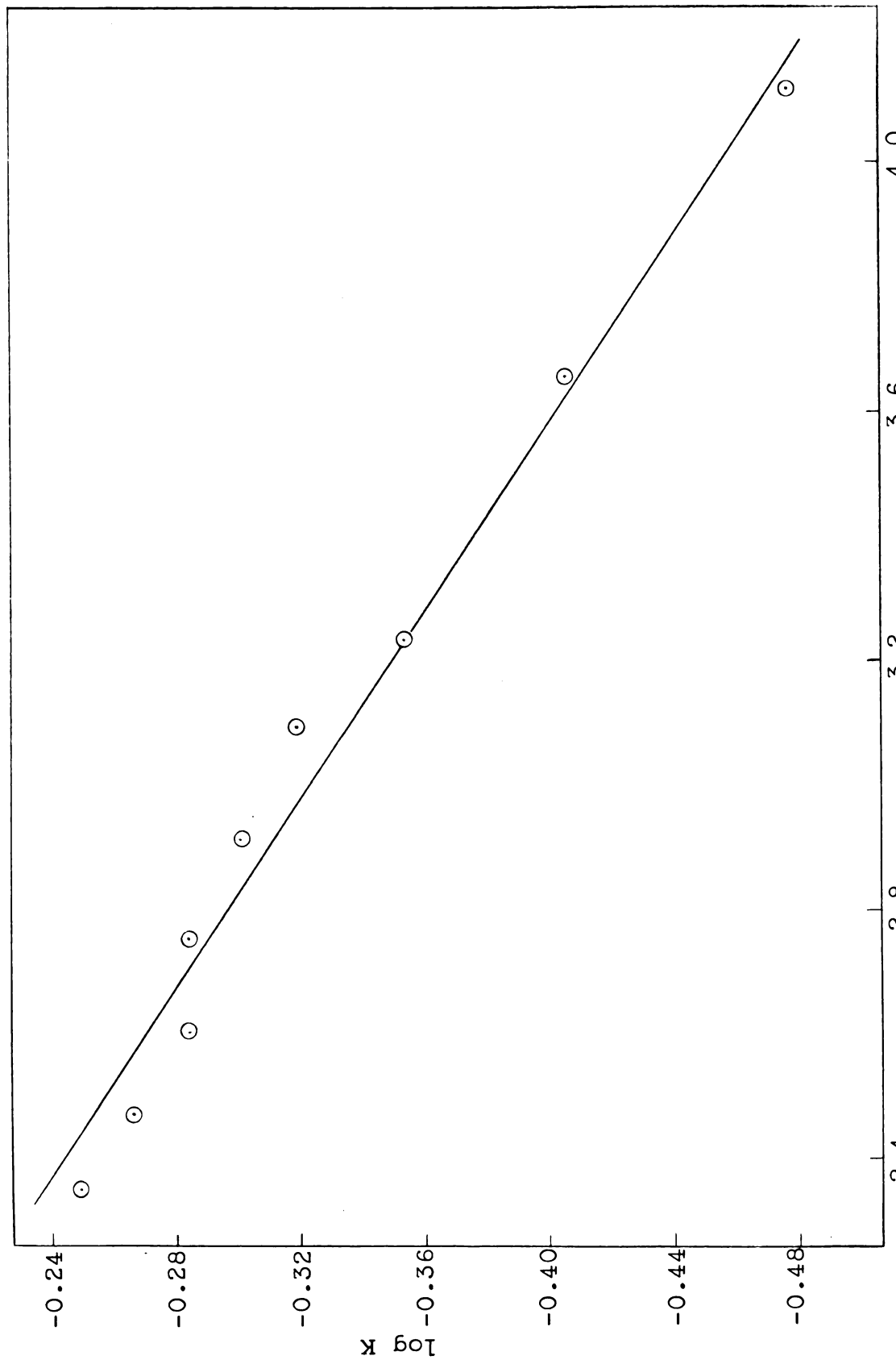
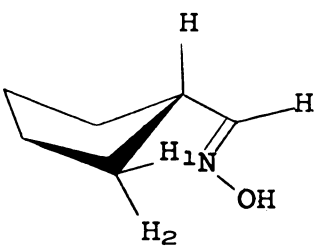
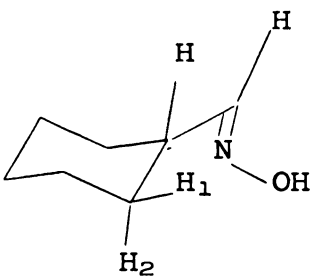


Figure 6. ΔH^{o} plot for 2-methylbutyraldehyde oxime (syn isomer).

trend parallels that observed with aldehydes (10a). The more positive ΔH^{o} value of cyclopentanecarboxaldehyde oxime over cyclohexanecarboxaldehyde oxime may be rationalized as follows. In the cyclopentyl case, because of less puckering of the ring the nitrogen is closer to H_2 (VIIIb) than it is in the cyclohexyl case (IXb). The difference in interaction energies is



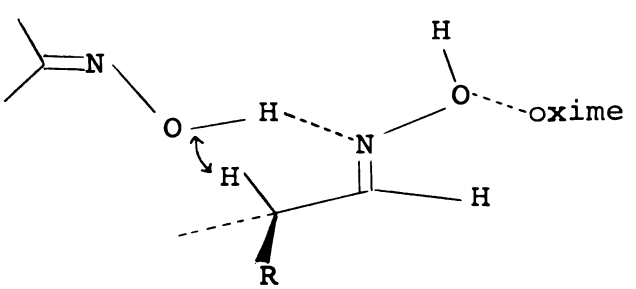
VIIIb



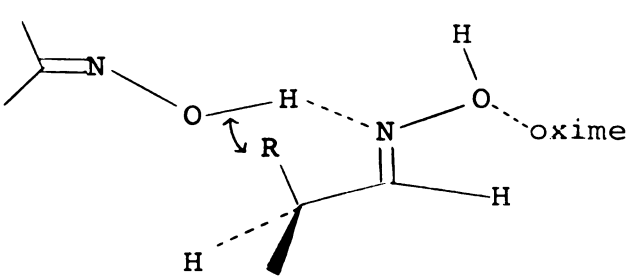
IXb

apparently large enough to lead to the observed result.

The decrease of the observed coupling constants on dilution with either polar or nonpolar solvents is probably caused by the decrease in the strong intermolecular hydrogen bonding (33,34) that exists in the neat liquid. Strong hydrogen bonding should favor Xb over XIb. As the intermolecular hydrogen



Xb

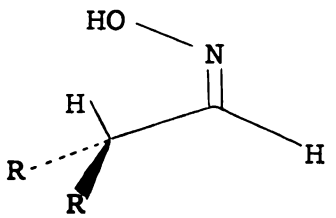


XIb

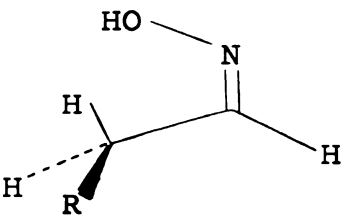
bonding is decreased by dilution with solvent, the decrease in

the ratio Xb/XIb decreases the coupling. The effect of solvent dilution on coupling is shown in Figures 7, 8 and 9.

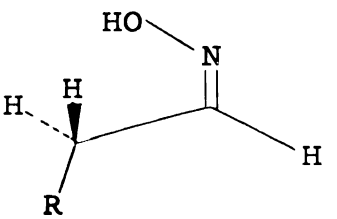
Conformations of the anti Isomers--From the effect of temperature on the coupling constants of the anti isomers it is evident that no quantitative conclusions regarding rotamer stability can be drawn. A few qualitative trends, however, are worth pointing out. For example, the abrupt increase in coupling in going from monosubstituted to disubstituted oximes suggests that XIIb is the most stable rotamer of the disubstituted oximes. The erratic behavior of the coupling of the



XIIb



XIIIb



XIVb

monosubstituted oximes indicates that in addition to XIIIb rotamer XIVb might be present in large quantities.

Chemical Shifts--The $\Delta\delta$ values summarized in Tables 7 and 8 show that protons cis to the hydroxyl group are generally deshielded with respect to those that are trans. Saitô and Nukada (25) attributed these differences to the anisotropic effect of the lone electron pair on the nitrogen. In view of the finding (35,36), which is consistent with other work on similar systems (37), that XVb is the conformation of formaldoxime, it is conceivable that the anisotropy of the lone

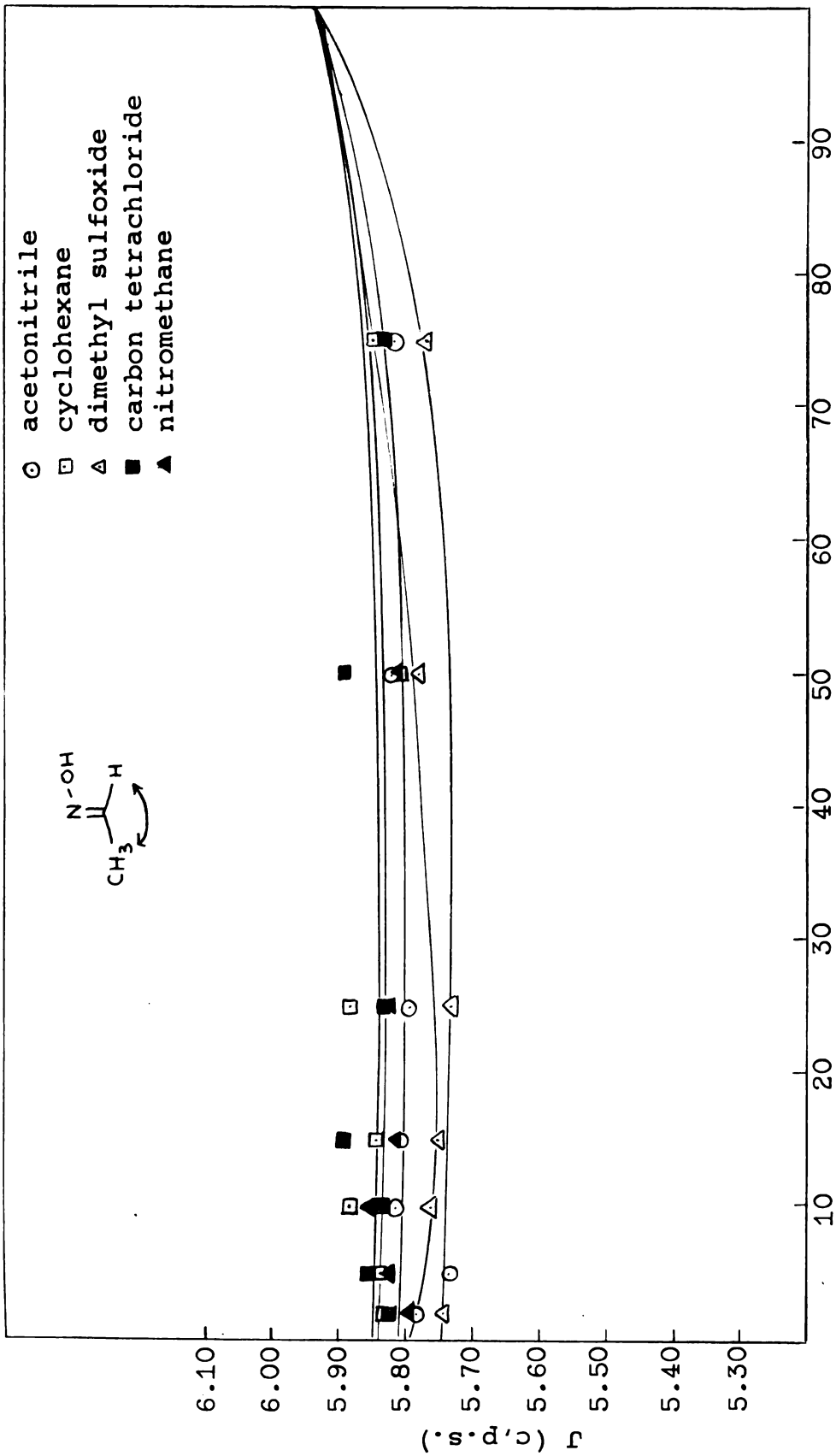


Figure 7. Effect of solvent dilution on the spin-spin coupling constant of acetaldehyde oxime ($J_{H_1H_\alpha}$, <u>syn</u> isomer).

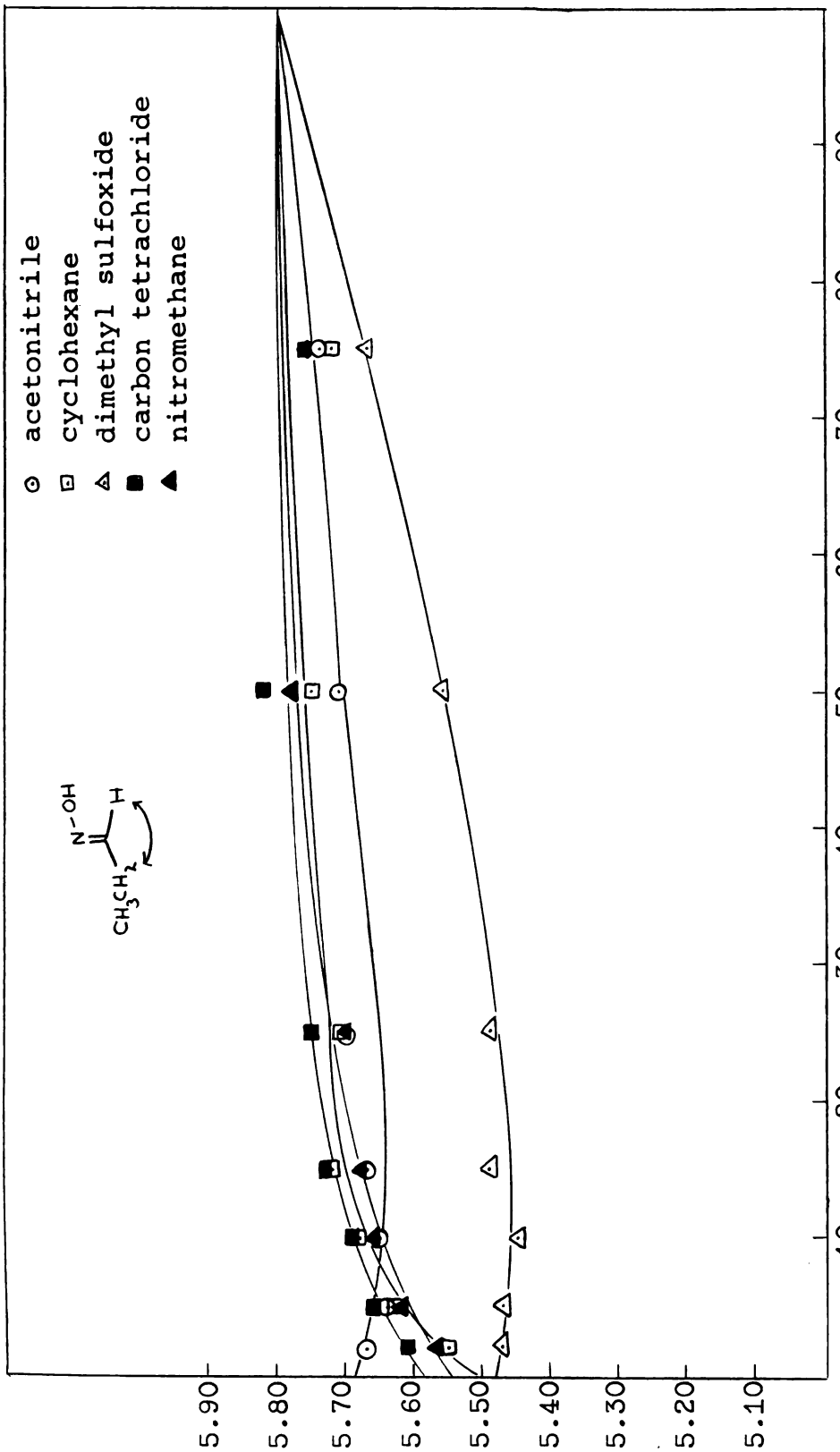


Figure 8. Effect of solvent dilution on the spin-spin coupling constant of propionaldehyde oxime ($J_{H_1H_\alpha}$, syn isomer).

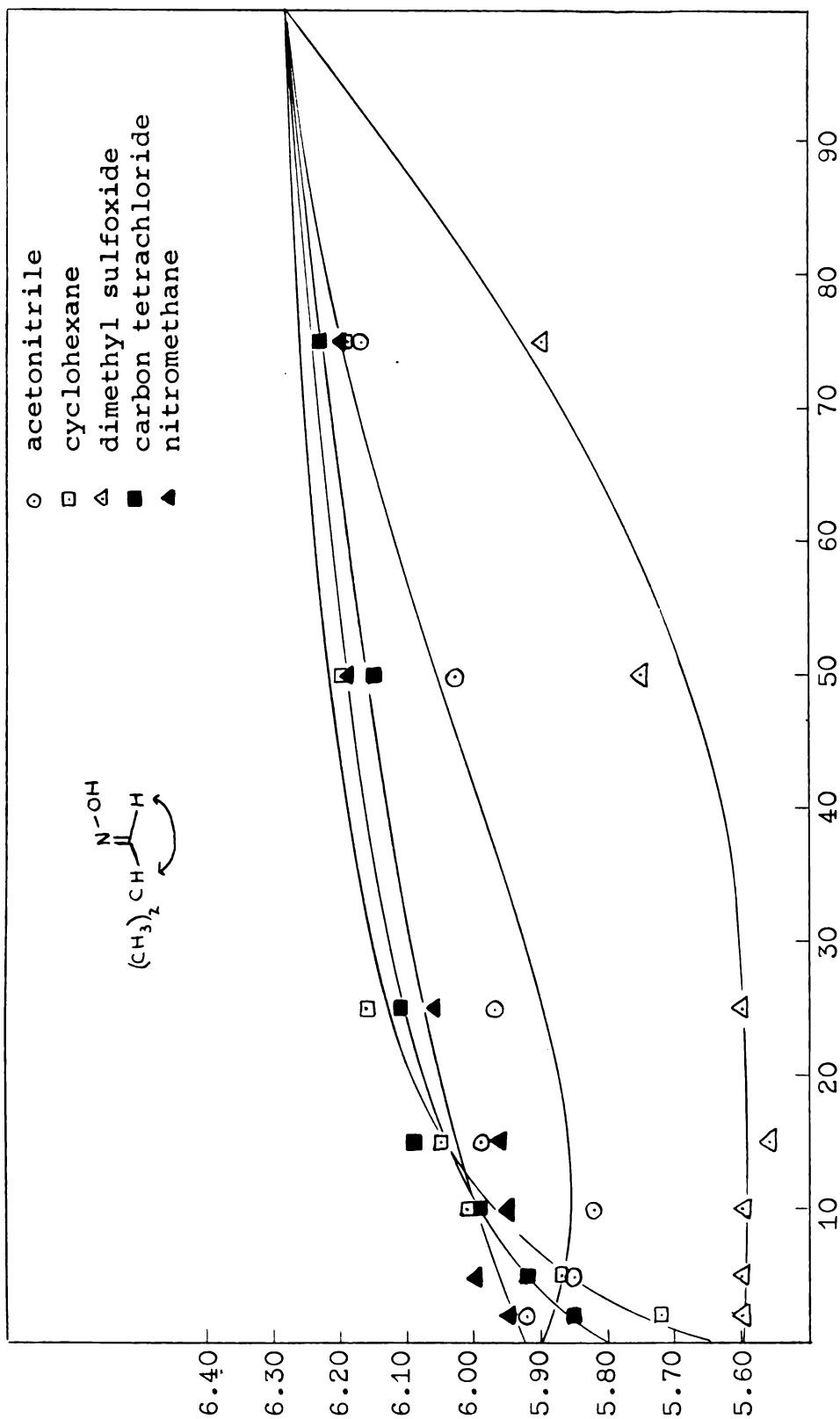
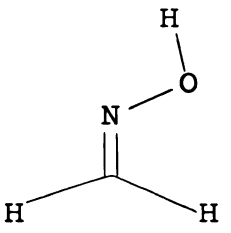


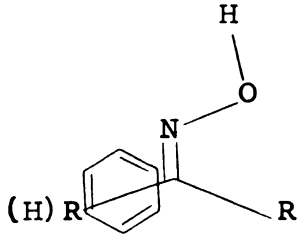
Figure 9. Effect of solvent dilution on the spin-spin coupling constant of isobutyraldehyde oxime ($J_{H_1H_{\alpha'}}$ syn isomer).



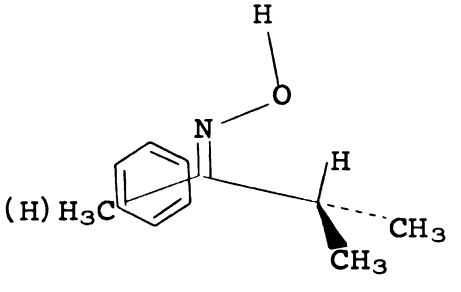
XVb

electron pairs on the oxygen, that are close to the cis group protons, rather than that of the nitrogen lone pair causes these differences. Regardless of the cause of these differences, the observed variations in $\Delta\delta$ values, e.g., about zero, -0.2 p.p.m. and -1.0 p.p.m. for α-methyl, α-methylene and α-methine protons respectively, are not surprising. As pointed out in the section on conformations, the average time spent by each proton in various positions greatly depends on the degree of substitution at the α-carbon.

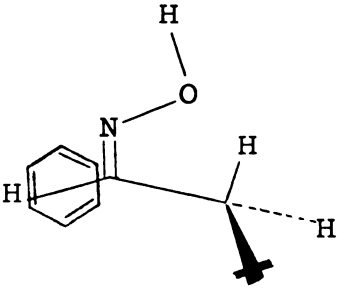
Solvent Effects--Tables 9 and 10, and Figure 10, show that trans protons undergo a larger upfield shift than the corresponding cis protons on dilution with benzene. Association between benzene and oxime as in XVIb, whereby the benzene is



XVIb



XVIIb



XVIIIb

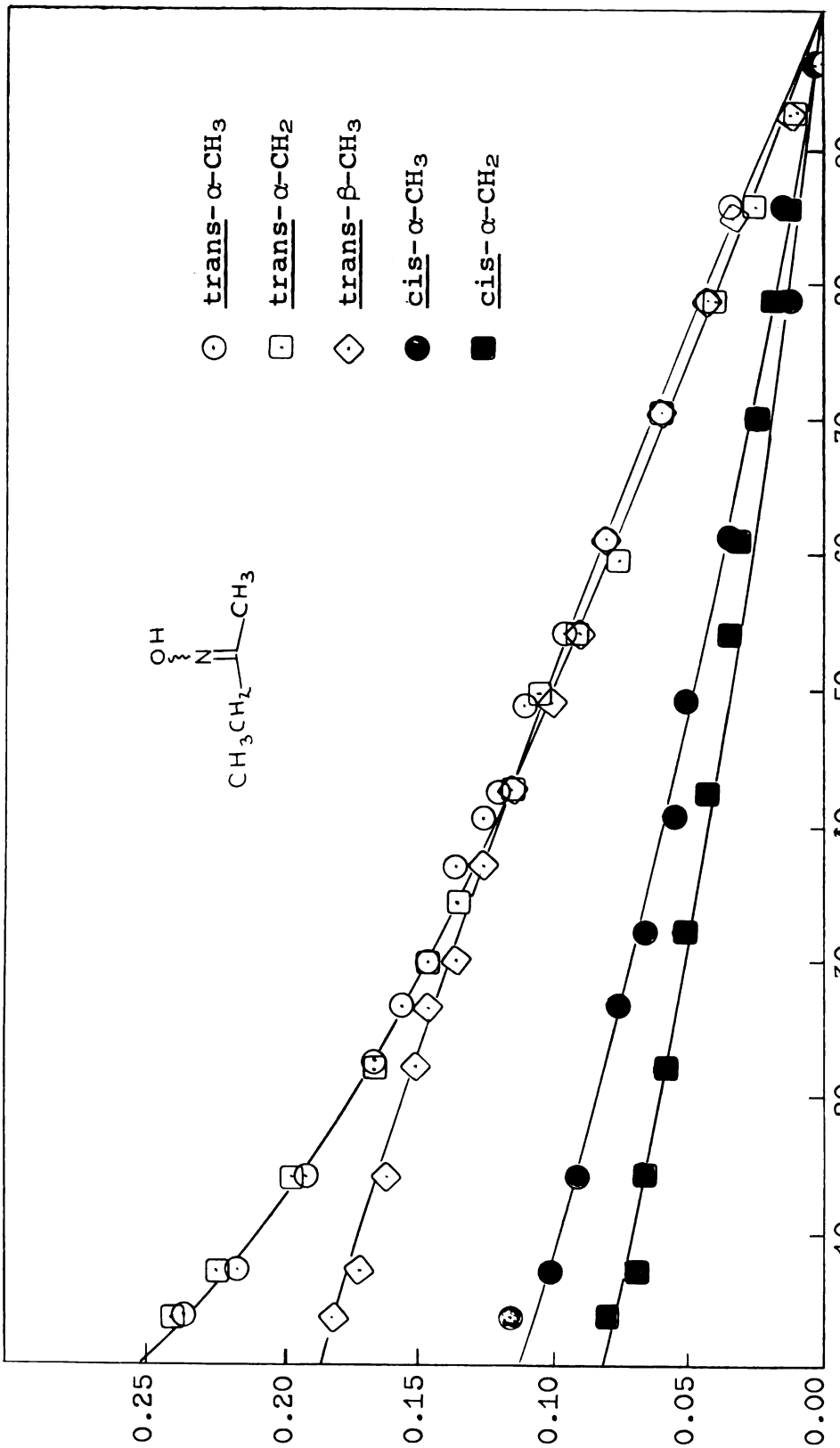


Figure 10. Effect of benzene on the chemical shifts of butanone oxime.

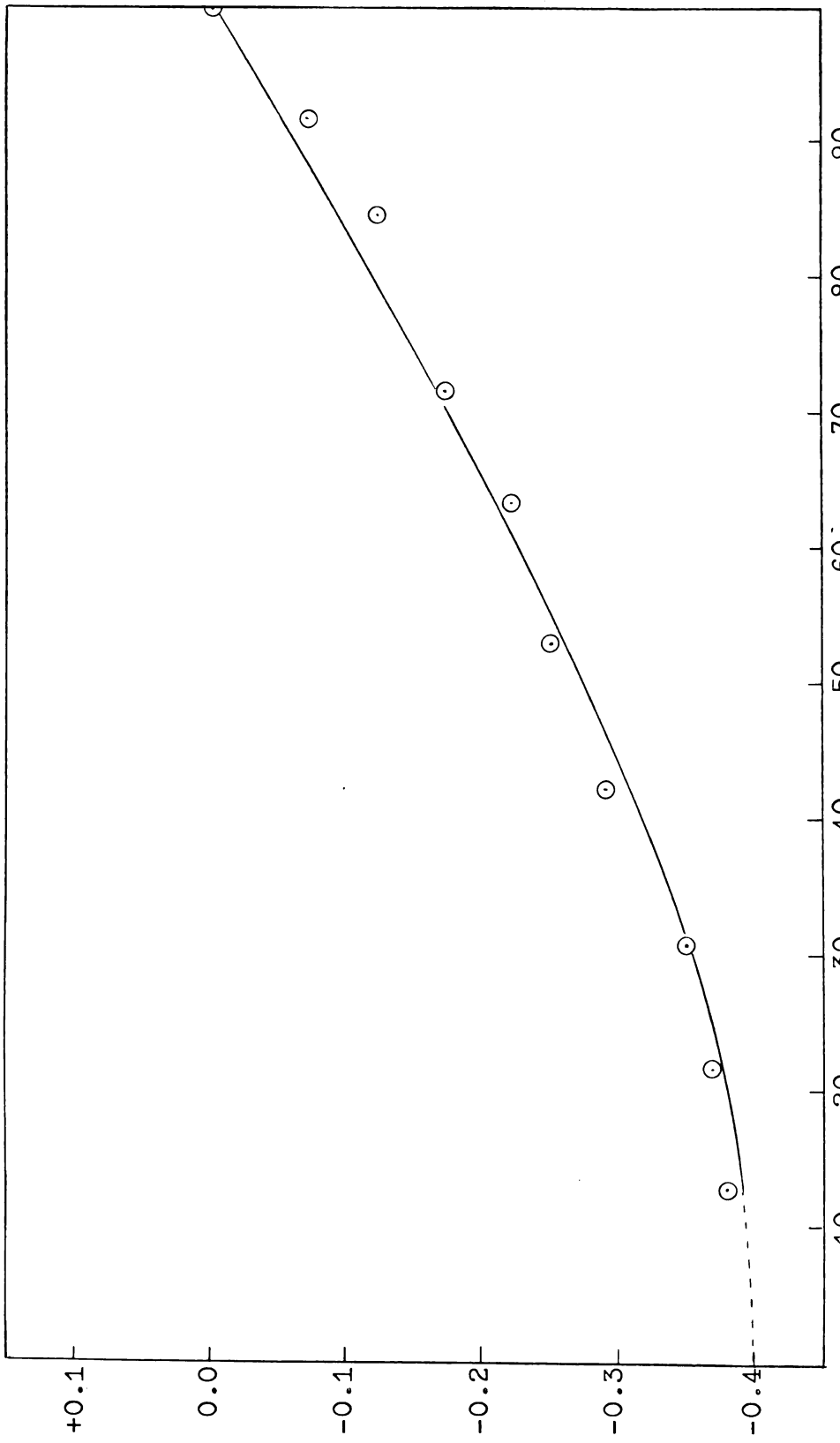
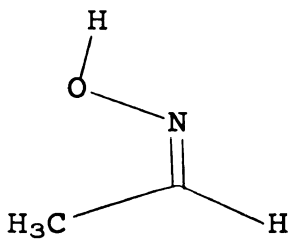


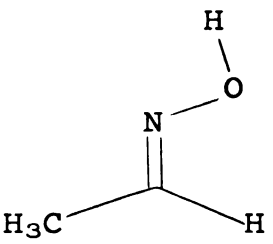
Figure 11. Effect of benzene dilution on the NOH chemical shift of ethyl methyl ketoxime.

attracted by the positive charge on the sp^2 hybridized carbon and repelled by the hydroxyl lone electron pairs (23), adequately rationalizes this fact. The deshielding, Figure 11, rather than the expected shielding of the hydroxyl proton, as well as the deshielding of cis-α-methine protons, XVIIb, and cis-α-methylene protons of t-butylacetaldehyde oxime, XVIIIb, are in good agreement with this formulation.

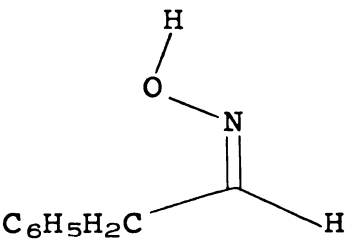
syn/anti Isomers--The greater stability of XIXb over XXb and the almost equal distribution of isomers XXIb and XXIIb



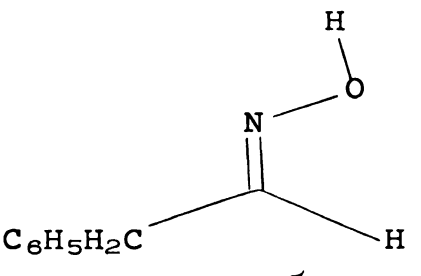
61%
XIXb



39%
XXb



45%
XXIb



55%
XXIIb

indicate that the attractive forces of the nonbonded interactions are quite important in these, as well as in other (38), cases.

PART C--N,N-DIMETHYLHYDRAZONES AND N-METHYLHYDRAZONES

Results

The chemical shifts of N,N-dimethylhydrazones and N-methylhydrazones are found in Tables 19 and 20, respectively. The most apparent difference between the two is the absence of trans isomers in the aldehyde N,N-dimethylhydrazone series. The n.m.r. spectra of acetone, 2-butanone and methyl isopropyl ketone N,N-dimethylhydrazones, are shown in Figures 12 and 13; those of acetone, 2-butanone, methyl isopropyl ketone and methyl t-butyl ketone N-methylhydrazones in Figures 14 and 15. Tables 21 and 22 summarize the differences between the chemical shifts of cis and trans protons of N,N-dimethylhydrazones and N-methylhydrazones, respectively. A positive $\Delta\delta$ value means that protons cis to the N,N-dimethylamino or N-methylamino group resonate at higher field than trans; a negative value denotes the reverse. Whereas the α-methyl groups of N-methylhydrazones have positive $\Delta\delta$ values, those of N,N-dimethylhydrazones have negative.

Tables 23 and 24 summarize the $\Delta\nu$(ν in benzene - ν in carbon tetrachloride) values of N,N-dimethylhydrazones and N-methylhydrazones, respectively. Positive values mean that protons resonate at higher field in benzene; negative values denote the reverse. The important points are: (a) $\Delta\nu$ values are larger for N-methylhydrazones than for N,N-dimethylhydrazones. (b) For N-methylhydrazones the cis protons have considerably larger $\Delta\nu$ values than the corresponding trans. The syn/anti ratios of the aldehyde and ketone N-methylhydrazones are summarized in Table 26.

Table 25 contains the spin-spin coupling constants and half-widths of aldehyde N-methylhydrazones. The half-widths of the anti isomers, where the N-methylamino group is trans to the aldehydic proton, are considerably smaller than those of the syn isomers. The effect of temperature on the spin-spin coupling constants, $J_{H_1H_\alpha}$, of the syn aldehyde N,N-dimethylhydrazones and N-methylhydrazones, are summarized in Tables 27 and 29, respectively; and the effect of solvent polarity in Tables 28 and 30. Decrease in temperature, or increase in solvent polarity, increases these couplings. All recorded spin-spin coupling values, whose precision is about ± 0.03 c.p.s., are averages of at least three spectral sweeps.

Tables 35 and 35 contain the ultraviolet spectral data of N,N-dimethylhydrazones and N-methylhydrazones, respectively. Whereas aldehyde and ketone N-methylhydrazones have similar λ_{max} and ε values, aldehyde and ketone N,N-dimethylhydrazones do not.

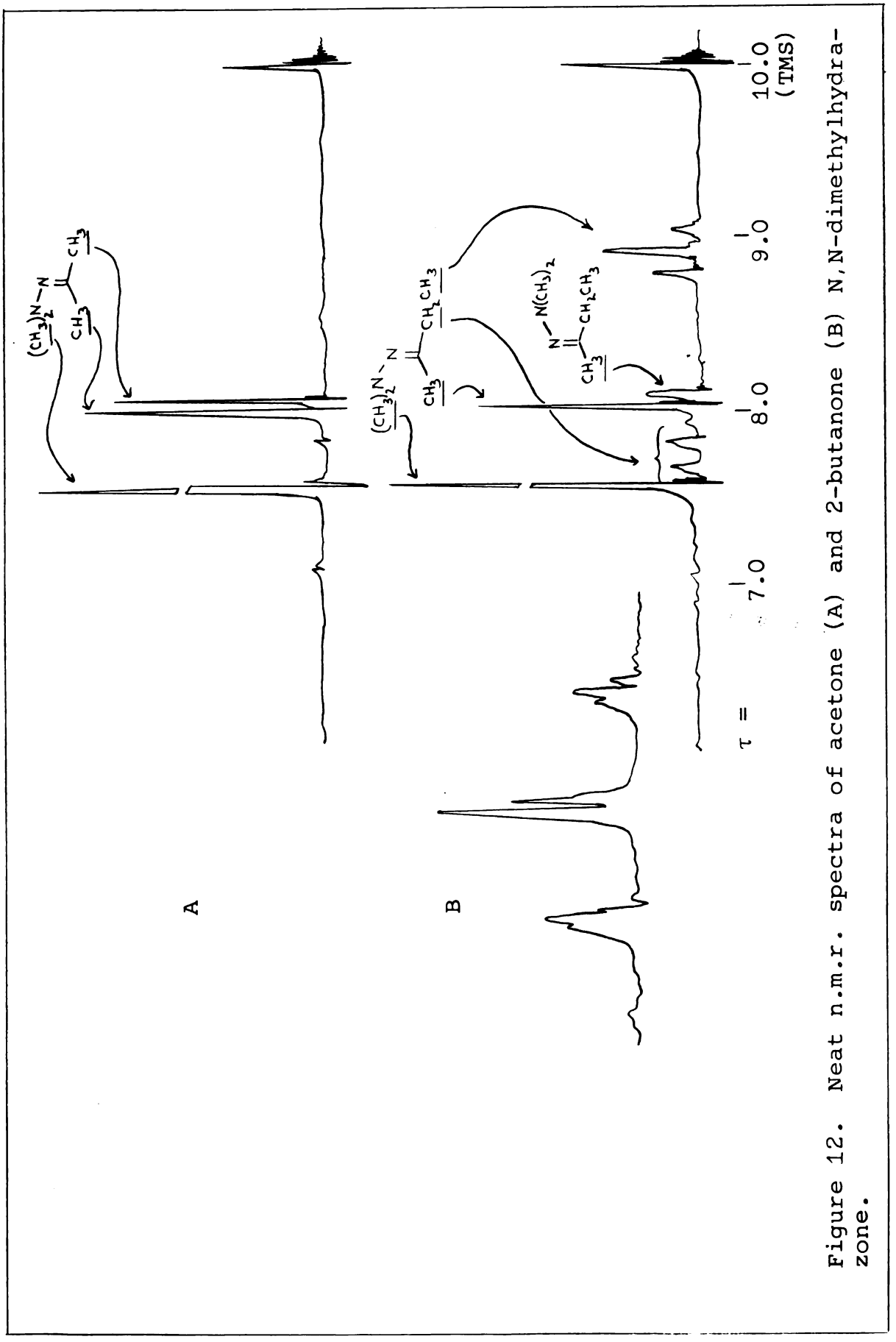


Figure 12. Neat n.m.r. spectra of acetone (A) and 2-butanone (B) N,N-dimethylhydrazone.

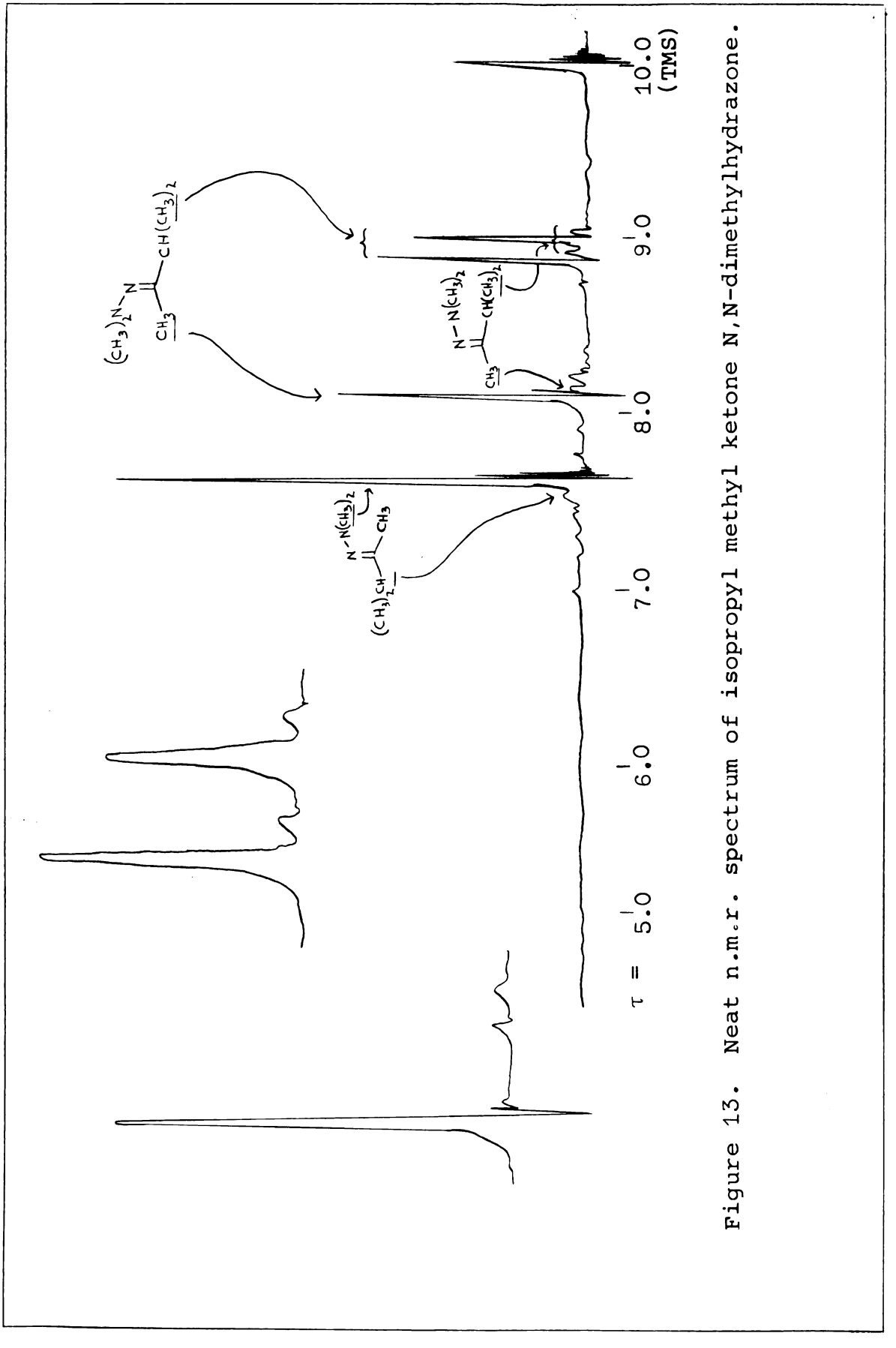


Figure 13. Neat n.m.r. spectrum of isopropyl methyl ketone N,N-dimethylhydrazone.

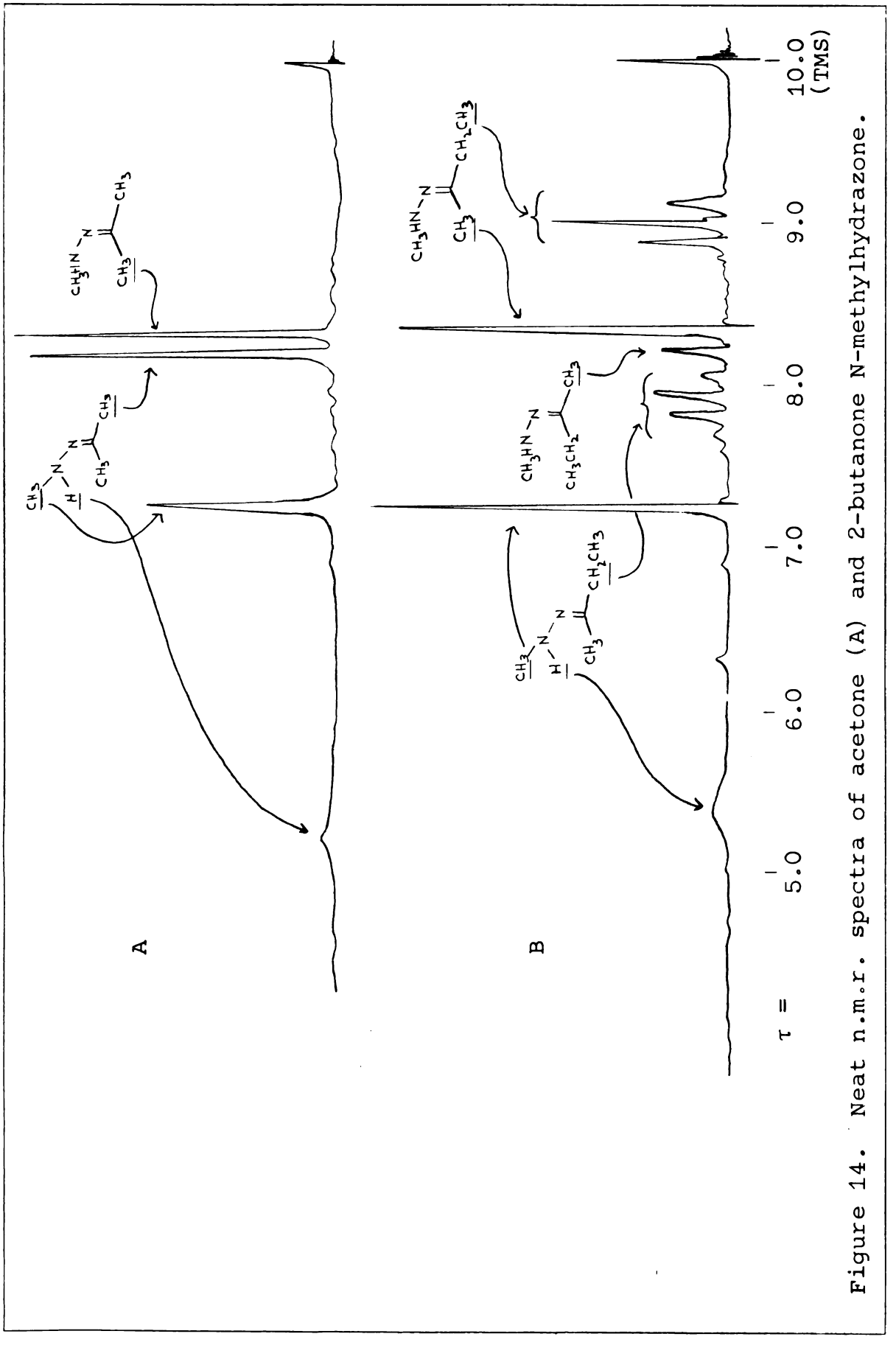


Figure 14. Neat n.m.r. spectra of acetone (A) and 2-butanone N-methylhydrazone.

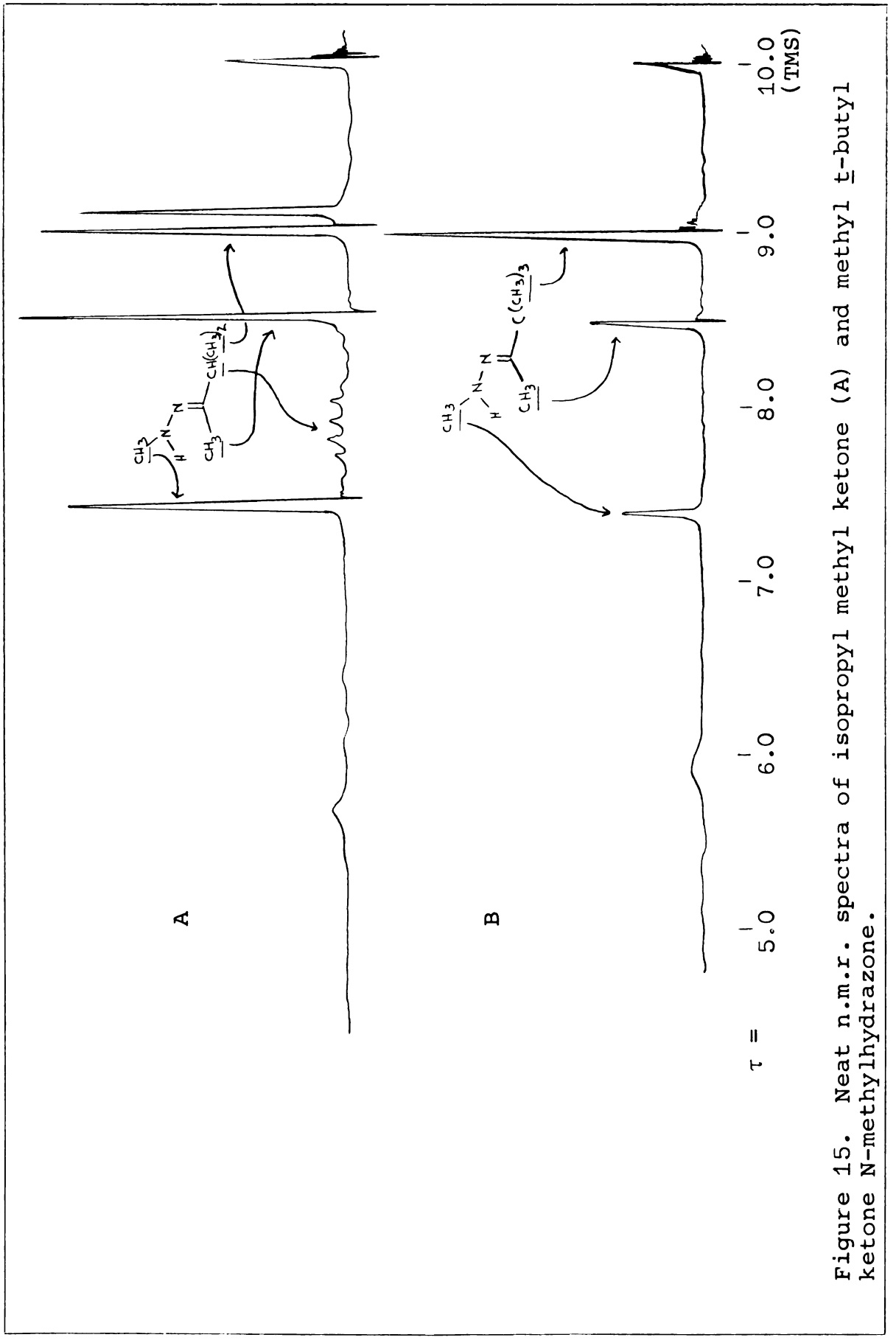


Figure 15. Neat n.m.r. spectra of isopropyl methyl ketone (A) and methyl t-butyl ketone N-methylhydrazone.

Table 19. Chemical Shifts (τ-Values) of Aldehyde and Ketone N,N-Dimethylhydrazones

$R_1R_2C{=}NN(CH_3)_2$			H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		$N(CH_3)_2$
R_1	R_2	Solvent	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis
H	CH_3	Neat	3.47					8.20					7.38
H	CH_3	10% CCl_4	3.51					8.17					7.36
H	CH_3	10% C_6H_6	3.66					8.20					7.48
H	CH_2CH_3	Neat	3.48			7.83						9.01	7.37
H	CH_2CH_3	10% CCl_4	3.53			7.87						8.98	7.36
H	CH_2CH_3	10% C_6H_6	3.60			7.88						9.01	7.46
H	$CH_2C(CH_3)_3$	Neat	3.46			7.94							7.35
H	$CH_2C(CH_3)_3$	10% CCl_4	3.50			7.95							7.34
H	$CH_2C(CH_3)_3$	10% C_6H_6	3.50			7.84							7.45
H	$CH(CH_3)_2$	Neat	3.57							7.67		8.99	7.38
H	$CH(CH_3)_2$	10% CCl_4	3.64							7.64		8.97	7.37
H	$CH(CH_3)_2$	10% C_6H_6	3.64							7.67		8.96	7.46
H	$CH(CH_2CH_3)_2$	Neat	3.69							7.97			7.35
H	$CH(CH_2CH_3)_2$	10% CCl_4	3.71							7.93			7.35
H	$CH(CH_2CH_3)_2$	10% C_6H_6	3.75							7.88			7.46
H		Neat	3.64										7.39
H		10% CCl_4	3.66										7.38

Continued

Table 19 - Continued

$R_1R_2C{=}NN(CH_3)_2$			H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		$N(CH_3)_2$
R_1	R_2	Solvent	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis
H		10% C_6H_6	3.64										7.46
CH_3	CH_3	Neat					8.09	8.16					7.67
CH_3	CH_3	10% CCl_4					8.12	8.16					7.67
CH_3	CH_3	10% C_6H_6					8.28	8.28					7.61
CH_3	CH_2CH_3[a]	Neat				7.87	8.14	8.20				8.99	7.69
CH_3	CH_2CH_3	10% CCl_4				7.86	8.14	8.17				8.96	7.69
CH_3	CH_2CH_3	10% C_6H_6				7.94	8.25	8.28			9.16	9.02	7.60
CH_3	$CH(CH_3)_2$[b]	Neat					8.17	8.27		7.63	9.04	8.99	7.69
CH_3	$CH(CH_3)_2$	10% CCl_4					8.18	8.27		7.61	9.01	8.97	7.69
CH_3	$CH(CH_3)_2$	10% C_6H_6					8.25	8.31		7.62	9.16	9.00	7.60

[a]Percent syn = 82, percent anti = 18; syn is the isomer having the $N(CH_3)_2$ group cis to R_1.

[b]Percent syn = 93, percent anti = 7.

Table 20. Chemical Shifts (τ-Values) of Aldehyde and Ketone N-Methylhydrazones

$R_1R_2C{=}NNHCH_3$			H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		$(N\text{-}CH_3)$		NH
R_1	R_2	Solvent	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	
H	CH_3	Neat	3.18	3.58			8.36	8.22					7.32	7.16	4.44
H	CH_3	10% CCl_4	3.26	3.62			8.38	8.19					7.28	7.12	
H	CH_3	10% C_6H_6	3.52				8.76	8.28					7.48	7.16	
H	CH_2CH_3	Neat	3.19	3.76		7.83						9.01	7.32	7.17	4.82
H	CH_2CH_3	10% CCl_4	3.28	3.80		7.84						8.98	7.29	7.14	
H	CH_2CH_3	10% C_6H_6	3.48			7.88					9.25	9.04	7.48	7.20	
H	$CH_2C(CH_3)_3$	Neat	3.19	3.58		7.96							7.30	7.17	4.85
H	$CH_2C(CH_3)_3$	10% CCl_4	3.24			7.99							7.26	7.14	
H	$CH_2C(CH_3)_3$	10% C_6H_6	3.38			7.90							7.49	7.18	
H	$CH(CH_3)_2$	Neat	3.29	3.88					7.65		9.04	8.98	7.33	7.19	4.66
H	$CH(CH_3)_2$	10% CCl_4	3.36						7.65		9.03	8.98	7.29	7.17	5.17
H	$CH(CH_3)_2$	10% C_6H_6	3.50						7.64		9.22	8.99	7.47	7.18	
H	$CH(CH_2CH_3)_2$	Neat	3.40	3.92					8.04				7.30	7.15	4.31
H	$CH(CH_2CH_3)_2$	10% CCl_4	3.47						8.04				7.26	7.15	
H	$CH(CH_2CH_3)_2$	10% C_6H_6	3.60						7.96				7.47	7.15	
H		Neat	3.35	3.78									7.33	7.20	4.50
H		10% CCl_4	3.39										7.29	7.17	

Continued

Table 20 - Continued

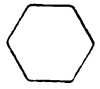
$R_1R_2C{=}NNHCH_3$			H_1		$\beta(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		$(N\text{-}CH_3)$		NH
R_1	R_2	Solvent	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	
H		10% C_6H_6	3.49										7.49	7.17	
CH_3	CH_3	Neat					8.34	8.20					7.25		5.17
CH_3	CH_3	10% CCl_4					8.36	8.16					7.21		
CH_3	CH_3	10% C_6H_6					8.70	8.23					7.17		
CH_3	CH_2CH_3	Neat				7.88	8.35	8.22				9.01	7.24		5.33
CH_3	CH_2CH_3	10% CCl_4				7.88	8.39	8.20				8.99	7.20		
CH_3	CH_2CH_3	10% C_6H_6			8.24	7.90	8.70	8.22			9.24	9.00	7.17		
CH_3	$CH(CH_3)_2$	Neat					8.40	8.31		7.64		9.01	7.24		5.34
CH_3	$CH(CH_3)_2$	10% CCl_4					8.42	8.28		7.62		8.98	7.19		
CH_3	$CH(CH_3)_2$	10% C_6H_6					8.70	8.27		7.62	9.24	8.98	7.17		
CH_3	$C(CH_3)_2$	Neat					8.40					8.95	7.22		5.59
CH_3	$C(CH_3)_2$	10% CCl_4					8.41					8.96	7.17		
CH_3	$C(CH_3)_2$	10% C_6H_6					8.66					8.91	7.17		

Table 21. $\Delta\delta$(δ *cis* - δ *trans*)[a] Values, in p.p.m., of Ketone N,N-Dimethylhydrazones

$R_1R_2C{=}NN(CH_3)_2$		$\alpha(CH_3)$		$\beta(CH_3)$		$N(CH_3)_2$	
R_1	R_2	Neat	C_6H_6	Neat	C_6H_6	Neat	C_6H_6
CH_3	CH_3	-0.07	0.00			0.00	0.00
CH_3	CH_2CH_3	-0.06	-0.03	0.00	+0.14	0.00	0.00
CH_3	$CH(CH_3)_2$	-0.10	-0.06	+0.05	+0.16	0.00	0.00

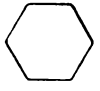
[a]Positive value means that the proton *cis* to the $N(CH_3)_2$ group resonates at higher magnetic field than when *trans*; a negative value denotes the reverse.

Table 22. $\Delta\delta$(δ *cis* - δ *trans*)[a] Values, in p.p.m., of Aldehyde and Ketone N-Methylhydrazones

$R_1R_2C{=}NNHCH_3$		H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\beta(CH_3)$		$(N\text{-}CH_3)$	
R_1	R_2	Neat	C_6H_6	Neat	C_6H_6	Neat	C_6H_6	Neat	C_6H_6	Neat	C_6H_6
H	CH_3	-0.40				+0.14	+0.48			+0.16	+0.32
H	CH_2CH_3	-0.57							+0.21	+0.15	+0.28
H	$CH_2C(CH_3)_3$	-0.39								+0.13	+0.31
H	$CH(CH_3)_2$	-0.59						+0.06	+0.23	+0.14	+0.29
H	$CH(CH_2CH_3)_2$	-0.52								+0.15	+0.32
H		-0.43								+0.13	+0.32
CH_3	CH_3					+0.14	+0.47				
CH_3	CH_2CH_3			+0.34		+0.13	+0.48		+0.24		
CH_3	$CH(CH_3)_2$					+0.09	+0.43		+0.26		

[a]Positive value means that the proton *cis* to the $NHCH_3$ group resonates at higher magnetic field than when *trans*; a negative value denotes the reverse.

Table 23. $\Delta\nu$ (ν in benzene - ν in carbon tetrachloride)[a] Values, in c.p.s., of Aldehyde and Ketone N,N-Dimethylhydrazones

$R_1R_2C{=}NN(CH_3)_2$		H_1	$\alpha(CH_2)$	$\alpha(CH_3)$		$\alpha(CH)$	$\beta(CH_3)$		$N(CH_3)_2$
R_1	R_2	cis	trans	cis	trans	trans	cis	trans	cis
H	CH_3	+9.0			+1.8				+7.2
H	CH_2CH_3	+4.2	+0.6					+1.8	+6.0
H	$CH_2C(CH_3)_3$	0.0	-6.6						+6.6
H	$CH(CH_3)_2$	0.0				+1.8		-0.6	+5.4
H	$CH(CH_3CH_2)_2$	+2.4				-3.0			+6.6
H		-1.2							+4.8
CH_3	CH_3			+9.6	+7.2				-3.6
CH_3	CH_2CH_3		+4.8	+6.6	+6.6		+12.0	+3.6	-5.4
CH_3	$CH(CH_3)_2$			+4.2	+2.4	+0.6	+ 9.0	+1.8	-5.4

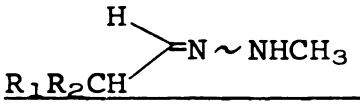
[a]Positive value means that the proton resonance in benzene is at higher field; a negative value denotes the reverse.

Table 24. $\Delta\nu$(ν in benzene - ν in carbon tetrachloride)[a] Values, in c.p.s., of Aldehyde and Ketone N-Methylhydrazones

$R_1R_2C{=}NNHCH_3$		H_1		$\alpha(CH_2)$		$\alpha(CH_3)$		$\alpha(CH)$		$\beta(CH_3)$		$(N\text{-}CH_3)$	
R_1	R_2	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans
H	CH_3	+15.6				+22.8	+ 5.4					+12.0	+ 2.4
H	CH_2CH_3	+12.0			+ 2.4					+16.2	+ 3.6	+11.4	+ 3.6
H	$CH_2C(CH_3)_3$	+ 8.4			- 5.4							+13.8	+ 2.4
H	$CH(CH_3)_2$	+ 8.4							- 0.6	+11.4	+ 0.6	+10.8	+ 0.6
H	$CH(CH_2CH_3)_2$	+ 7.8							- 4.8			+12.6	0.0
H		+ 6.0										+12.0	0.0
CH_3	CH_3					+20.4	+ 4.2					- 2.4	
CH_3	CH_2CH_3			+21.6	+1.2	+18.6	+ 1.2			+15.0	+ 0.6	- 1.8	
CH_3	$CH(CH_3)_2$					+16.8	- 0.6		0.0	+15.6	0.0	- 1.2	
CH_3	$C(CH_3)_3$					+15.0					-3.0	0.0	

[a] Positive value means that the proton resonance in benzene is at higher field; a negative value denotes the reverse.

Table 25. Spin-spin Coupling Constants and Half Widths of Aldehyde N-Methylhydrazones[a]



R_1	R_2	J(syn)	Half width(syn)	J(anti)	Half Width(anti)
H	H	5.38	1.35	5.67	1.05
H	CH_3	5.12	1.50	5.10	1.15
H	$C(CH_3)_3$	6.20	1.80	5.50	1.30
CH_3	CH_3	5.21	1.30	5.00	
CH_3CH_2	CH_2CH_3	6.50	1.50		
		5.00	1.45	5.30	

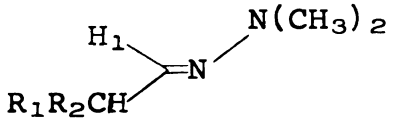
[a]Neat Samples.

Table 26. Syn/anti Ratios of Aldehyde and Ketone N-Methylhydrazones[a]

$R_1R_2C{=}NNHCH_3$		Percent	Percent
R_1	R_2	syn	anti
H	CH_3	73	27
H	CH_2CH_3	83	17
H	$CH_2C(CH_3)_3$	83	17
H	$CH(CH_3)_2$	96	4
H	$CH(CH_2CH_3)_2$	95	5
H		90	10
CH_3	CH_2CH_3	83	17
CH_3	$CH(CH_3)_2$	96	4
CH_3	$C(CH_3)_3$	100	0

[a]Neat Samples.

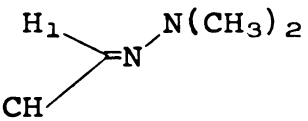
Table 27. Spin-Spin Coupling Constants of Aldehyde N,N-Dimethylhydrazones (syn isomer) at Various Temperatures

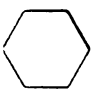


R_1	R_2	$J_{H_1H_\alpha}$ (c.p.s.)[a] -30°	0°	$+44^\circ$	$+70^\circ$
H	H	5.33	5.31	5.32	5.26
H	CH_3	5.16	5.12	5.10	5.00
H	$C(CH_3)_2$	6.24	6.24	6.22	6.11
CH_3	CH_3	5.35	5.25	5.12	5.08
CH_3CH_2	CH_2CH_3	6.82	6.52	6.33	6.10
		5.24	5.16	5.00	4.77

[a]Neat samples.

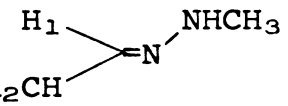
Table 28. The Effect of Solvent Polarity on the Spin-Spin Coupling Constants and Half Widths of Aldehyde N,N-Dimethylhydrazones (syn isomer)

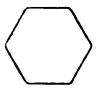


R_1	R_2	$J_{H_1H_\alpha}$ (c.p.s.) Neat (44°)	Cyclohexane (44°)[a]	Acetonitrile (44°)[a]	Half Width[b,c] (c.p.s.) (44°)
H	H	5.32	5.30	5.37	1.79
H	CH_3	5.10	5.00	5.30	1.81
H	$C(CH_3)_3$	6.22	6.10	6.25	1.76
CH_3	CH_3	5.12	4.96	5.50	1.89
CH_3CH_2	CH_2CH_3	6.33	6.24	6.80	1.78
		5.00	4.80	5.50	1.90

[a]10% solutions; [b]Neat; [c]Half width of tetramethylsilane = 0.40 c.p.s.

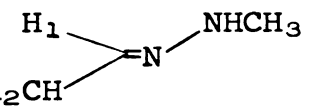
Table 29. Spin-Spin Coupling Constants of Aldehyde N-Methylhydrazones (syn isomer) at Various Temperatures



		$J_{H_1H_\alpha}$(c.p.s.)[a]				
R_1	R_2	-30°	0°	+43°	+60°	+80°
H	H	5.50	5.36	5.38	5.20	
H	CH_3	5.33	5.15	5.12	5.10	5.05
H	$C(CH_3)_2$[b]	6.25	6.20	6.20	6.16	6.08
CH_3	CH_3	5.34	5.23	5.21	5.06	4.98
CH_3CH_2	CH_2CH_3[b]	6.87	6.66	6.50	6.31	6.14
	b	5.20	5.13	5.00	4.93	4.88

[a]Neat samples.
[b]Approximately 50% carbon tetrachloride.

Table 30. The Effect of Solvent Polarity on the Spin-Spin Coupling Constants of Aldehyde N-Methylhydrazones (syn isomer)[a]

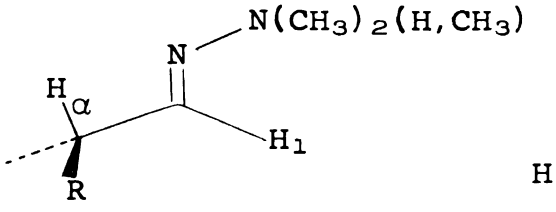


		$J_{H_1H_\alpha}$(c.p.s.)		
R_1	R_2	Neat (43°)	Cyclohexane (43°)[b]	Acetonitrile (43°)[b]
H	H	5.38	5.33	5.42
H	CH_3	5.12	5.06	5.24
H	$C(CH_3)_3$	6.20	6.20	6.25
CH_3	CH_3	5.21	4.87	5.32
CH_3CH_2	CH_2CH_3	6.50	6.31	6.70
		5.00	4.77	5.30

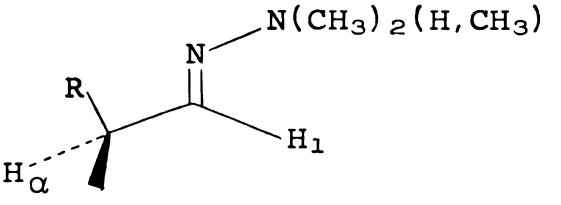
[a]Spin-spin coupling constant of acetaldehyde = 2.90 c.p.s.
[b]10% solutions.

Discussion

Conformations of the syn Isomers--The relative stability of rotamers Ic and IIc can be determined from the dependence



Ic

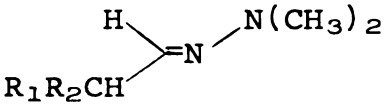


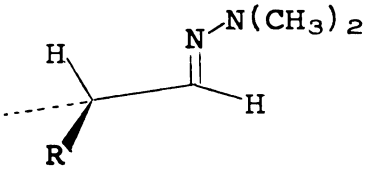
IIc

of $J_{H_1H_\alpha}$ on temperature, as discussed in the oxime section (Part B). The trans, dihedral angle = 180°, and gauche, dihedral angle = 60°, spin-spin coupling constants were calculated from the acetaldehyde and t-butylacetaldehyde derivatives. They are J_t = 10.6 c.p.s. and J_g = 2.7 c.p.s. for the N,N-dimethylhydrazones, and J_t = 10.5 c.p.s. and J_g = 2.8 c.p.s. for the N-methylhydrazones.

The rotamer populations of the N,N-dimethylhydrazones and N-methylhydrazones are found in Tables 31 and 33, respectively. The ΔH° values, which were obtained by plotting log K vs 1/T, are listed in Tables 32 and 34. Representative plots are shown in Figures 16 and 17. The trends in ΔH° values are similar to those of the oximes. For example, α,α-dimethyl derivatives have smaller ΔH° values and larger percentages of alkyl eclipsed rotamers than the α,α-diethyl derivatives. Similarly the ΔH° values of cyclohexanecarboxaldehyde derivatives are closer to those of dimethyl rather than diethyl α,α-disubstituted derivatives.

Table 31. Rotamer Population of Aldehyde N,N-Dimethylhydrazones (syn isomer)





%

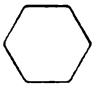
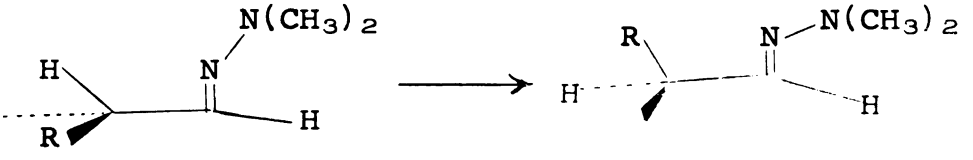
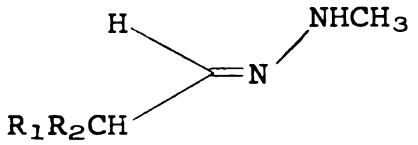
R_1	R_2	-30°	0°	+44°	+70°
H	CH_3	73	72	71	69
H	$C(CH_3)_3$	99.7	99.7	99.5	97
CH_3	CH_3	44	43	41	40
CH_3CH_2	CH_2CH_3	62	59	56	53
		42	41	39	36

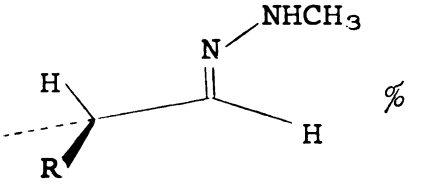
Table 32. ΔH° Values Obtained from Plots of log K vs 1/T



$R_1R_2CHCH{=}NN(CH_3)_2$		
R_1	R_2	ΔH°(cal/mole)
H	CH_3	+ 290
H	$C(CH_3)_3$	+4600
CH_3	CH_3	+ 280
CH_3CH_2	CH_2CH_3	+ 650
		+ 390

Table 33. Rotamer Populations of Aldehyde N-Methylhydrazones (syn isomer)

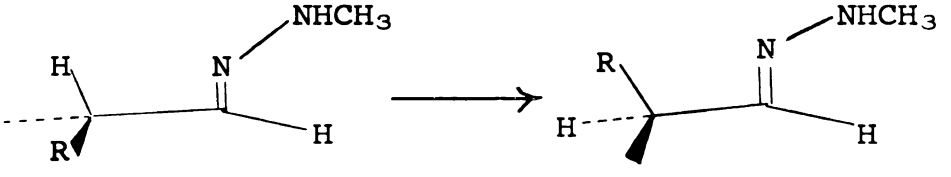




%

R_1	R_2	-30°	0°	+43°	+60°	+80°
H	CH_3	76	71	71	70	69
H	$C(CH_3)_3$	100	99	99	98	96
CH_3	CH_3	43	42	42	40	39
CH_3CH_2	CH_2CH_3	63	60	58	56	54
		42	41	39	38	37

Table 34. ΔH° Values Obtained from Plots of log K vs 1/T



$R_1R_2CHCH{=}NNHCH_3$		
R_1	R_2	ΔH° (cal/mole)
H	CH_3	+550
H	$C(CH_3)_3$	+3900
CH_3	CH_3	+290
CH_3CH_2	CH_2CH_3	+560
		+330

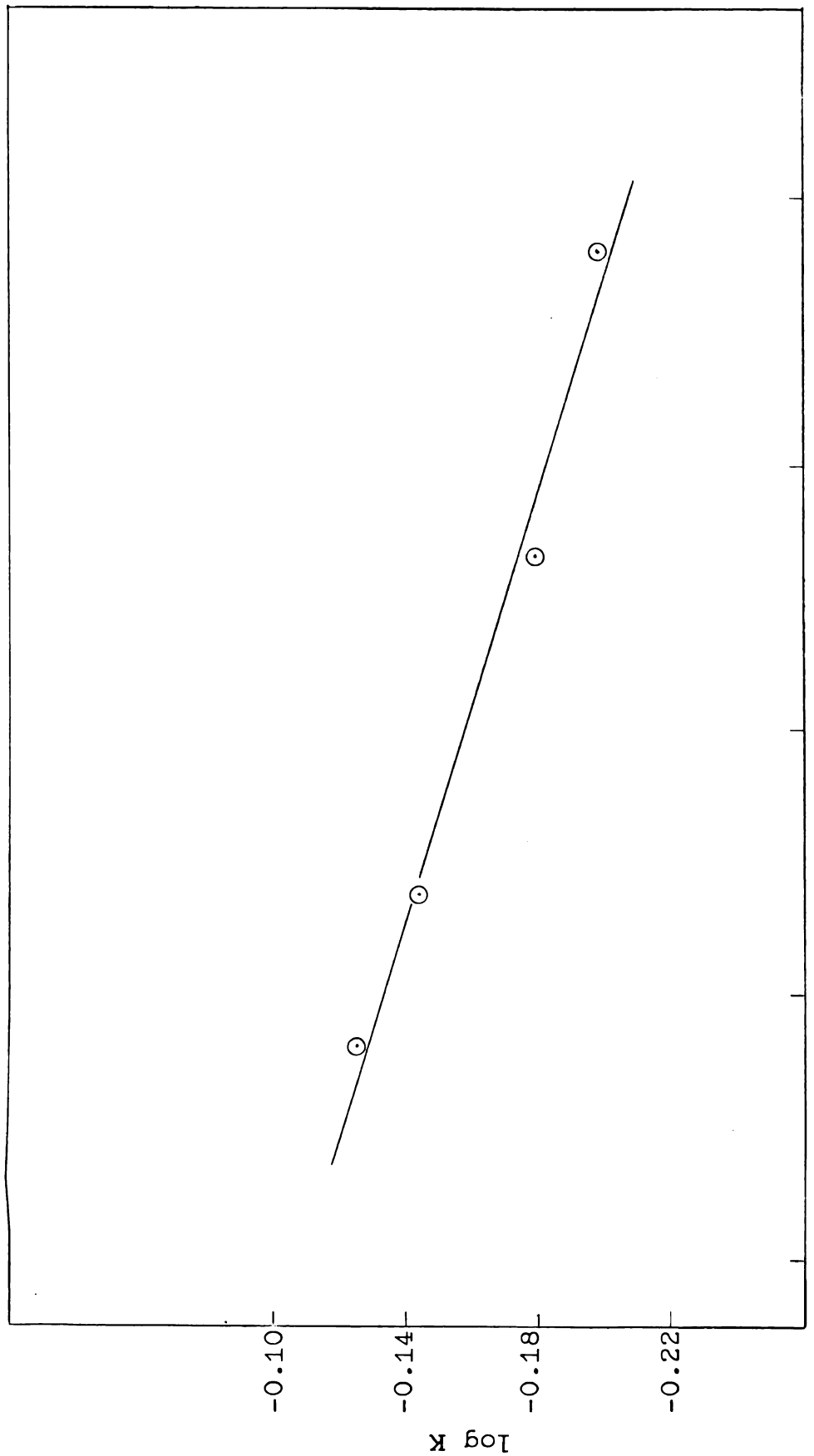


Figure 16. ΔH^{o} plot for isobutyraldehyde N,N-dimethylhydrazone (syn isomer).

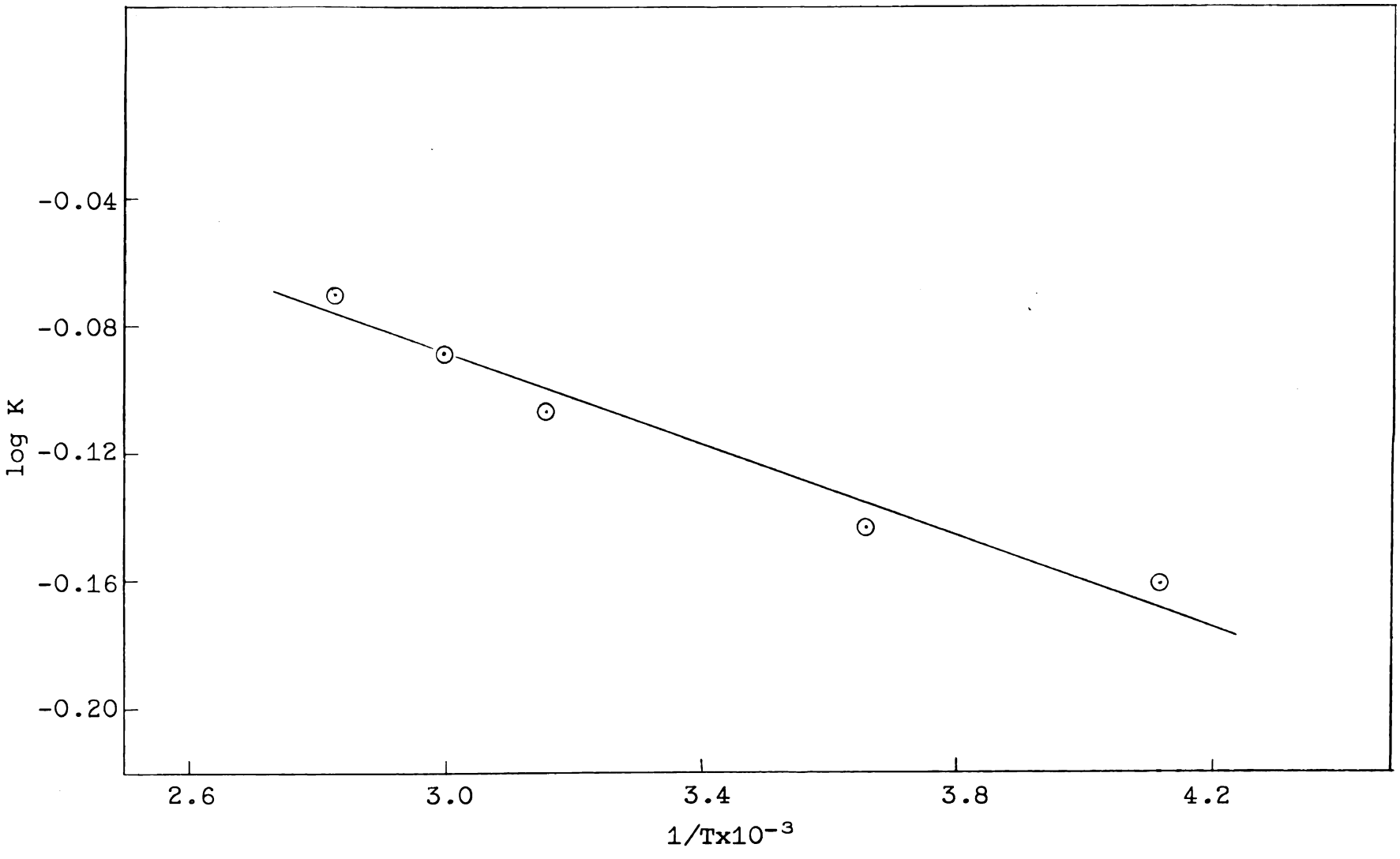
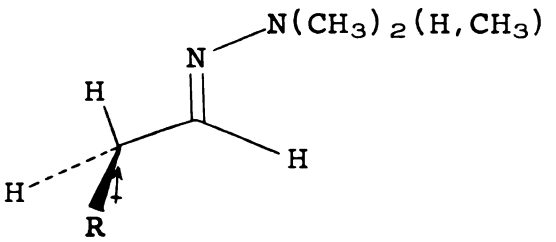
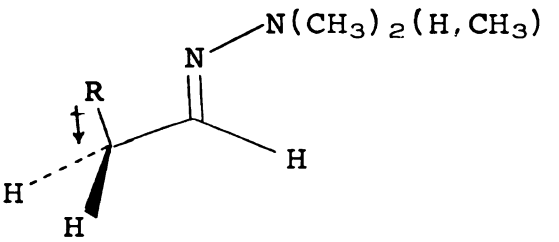


Figure 17. ΔH^{o} plot for cyclohexanecarboxaldehyde N-methylhydrazone (<u>syn</u> isomer).

The effect of solvent polarity on the coupling constants further supports the assumption that the important minimum energy conformations are eclipsed rather than bisecting. The observed increase of these couplings with increase of solvent polarity fits IIIc and IVc, but not Vc and VIc. Had Vc and VIc been the important conformations, increase in solvent

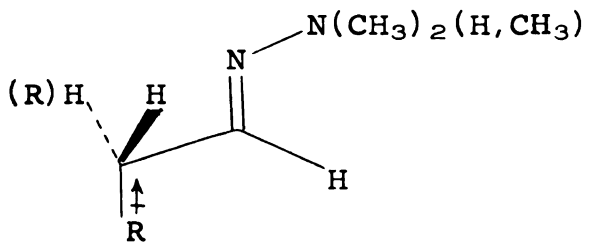


IIIc

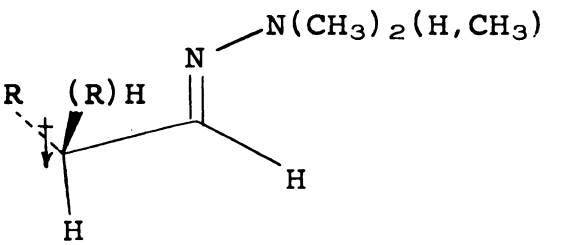


IVc

polarity would increase the ratio Vc/VIc and lead to a decrease in coupling, as J_{120^o} should be smaller than $J_{\underline{cis}}$.

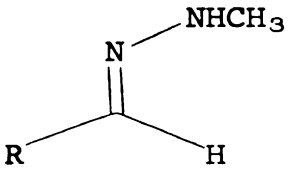


Vc

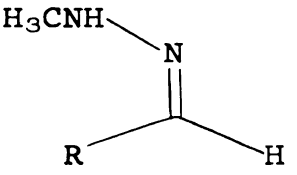


VIc

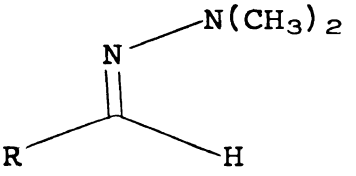
The Effect of Conformations about the Nitrogen-Nitrogen Single Bond on Chemical Shifts and Long Range Spin-Spin Coupling Constants--As mentioned, whereas of aldehyde N-methylhydrazones both the syn, VIIc, and the anti, VIIIc, isomers are present in solution, only the syn, IXc, isomer of aldehyde N,N-dimethylhydrazones is detectable. Furthermore, the syn



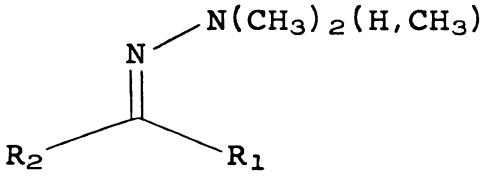
VIIc



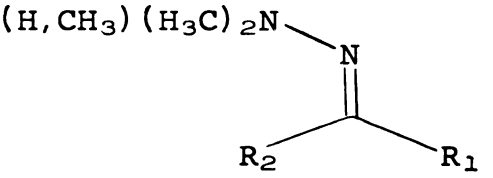
VIIIc



IXc



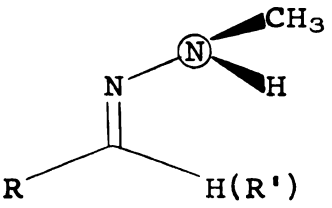
Xc



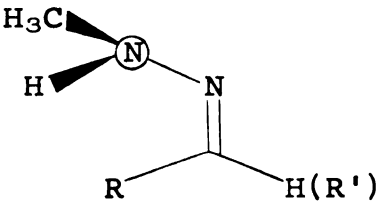
XIc

Xc, and the anti, XIc, isomers of both ketone N-methyl and N,N-dimethylhydrazones are present in solution. These facts can be explained by steric interactions that result in conformational preferences about the nitrogen-nitrogen single bond. The explanation and support of it are outlined below.

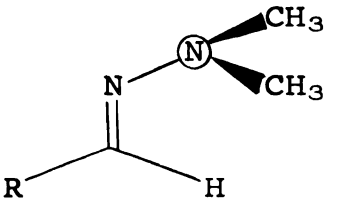
Whereas both syn, XIIc, and the anti, XIIIc, isomers of N-methylhydrazones can exist in the depicted conformations, where the unshared pair of electrons in both isomers are



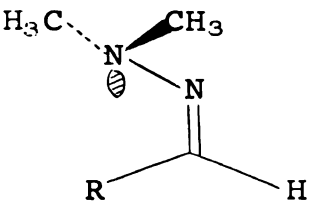
XIIc



XIIIc



XIVc



XVc

parallel to and overlap with the π-orbitals of the double bond, only the syn, XIVc, isomer of N,N-dimethylhydrazones can assume such conformations. In the anti, XVc, isomer, because of strong nonbonded interactions between R and methyl, rotation about the nitrogen-nitrogen bond might force the compound to a conformation where the unshared electrons are orthogonal to the π-orbitals of the double bond. The ensuing loss of overlap energy would thus explain the greater stability of XIVc over XVc. The above explanation can be tested by ultraviolet spectroscopy, since it implies that aldehyde N,N-dimethylhydrazones will have conformation XIVc and ketone N,N-dimethylhydrazones conformation XVc.

The ultraviolet spectra of aldehyde and ketone N-methylhydrazones (Table 36) are similar; e.g., λ_{max} (95% ethanol) = 229 mμ ($\varepsilon = 5.0 \times 10^3$). Aldehyde N,N-dimethylhydrazones have λ_{max} (95% ethanol) = 239 mμ ($\varepsilon = 5.7 \times 10^3$). These are the $\pi \rightarrow \pi^*$ transitions. The increase from 229 mμ to 239 mμ is probably due to the inductive effect of the second methyl substituent in N,N-dimethylhydrazone. In the ketone N,N-dimethylhydrazone, a lower energy transition appears, which has λ_{max} (cyclohexane) = 274 mμ ($\varepsilon = 8.2 \times 10^2$); λ_{max} (95% ethanol) = 268 mμ ($\varepsilon = 8.2 \times 10^2$); and λ_{max} (H_2O) = 253 mμ ($\varepsilon = 7.8 \times 10^2$). From its solvent dependence (39) it appears to be an $n \rightarrow \pi^*$ transition. Apparently as the lone pair electrons of the N,N-dimethylhydrazone becomes orthogonal with the π-orbitals of the double bond the $\pi \rightarrow \pi^*$ transition shifts to lower wavelengths and is masked by the absorption of the solvent.

Table 35. Ultraviolet Spectral Values of Aldehyde and Ketone N,N-Dimethylhydrazones

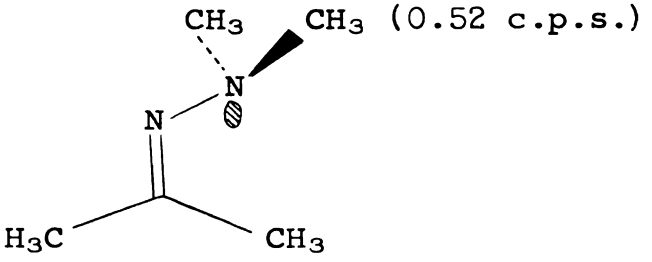
$R_1R_2C{=}NN(CH_3)_2$ R_1	R_2	Solvent	λ_{max} (mμ)	ε
H	CH_3	Cyclohexane	240.8	6.8×10^3
H	CH_3	95% Ethanol	239.0	5.7×10^3
H	CH_3	H_2O	231.0	1.2×10^3
CH_3	CH_3	Cyclohexane	266.0	6.0×10^2
CH_3	CH_3	95% Ethanol	265.0	7.6×10^2
CH_3	CH_3	H_2O	256.0	3.9×10^2
CH_3	CH_2CH_3	Cyclohexane	274.0	8.2×10^2
CH_3	CH_2CH_3	95% Ethanol	268.0	8.2×10^2
CH_3	CH_2CH_3	H_2O	253.0	7.8×10^2

Table 36. Ultraviolet Spectral Values of Aldehyde and Ketone N-Methylhydrazones

$R_1R_2C{=}NNHCH_3$ R_1	R_2	Solvent	λ_{max}(mμ)	ε
H	CH_3	Cyclohexane	230.0	$4.5x10^3$
H	CH_3	95% Ethanol	228.0	$4.6x10^3$
H	CH_2CH_3	Cyclohexane	228.0	$4.1x10^3$
H	CH_2CH_3	95% Ethanol	229.0	$5.0x10^3$
CH_3	CH_3	Cyclohexane	229.0	$1.9x10^3$
CH_3	CH_3	95% Ethanol	226.0	$4.6x10^3$
CH_3	CH_3	Acetonitrile	229.0	$5.3x10^3$
CH_3	CH_2CH_3	Cyclohexane	228.0	$1.4x10^3$
CH_3	CH_2CH_3	95% Ethanol	228.0	$4.9x10^3$

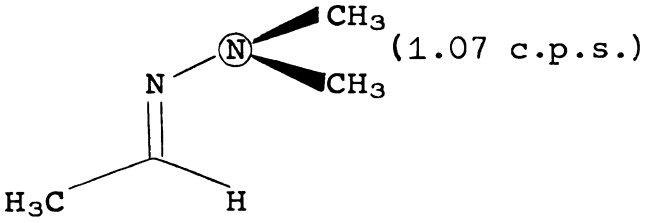
Stereospecificity of Long Range Spin-Spin Coupling--

Acetone N,N-dimethylhydrazones, conformation **XVIc**, shows zero coupling between the N-methyl and the α-methyl protons, as judged from signal half-widths of 0.50 c.p.s. These half-widths are the same as those of tetramethylsilane under identical instrumental conditions. When the N,N-dimethylamine group is in conformation **XIVc**, then coupling between such protons is detectable. For example, the half-width of the α-methyl signal of acetaldehyde N,N-dimethylhydrazone, **XVIIc**, is 1.01 c.p.s. Since in both ketone and aldehyde N-methylhydrazones the N-methylamino group has the same conformations as in aldehyde N,N-dimethylhydrazones, similar coupling are anticipated. The half-widths recorded in **XVIIIc** through **XXc** support this deduction.



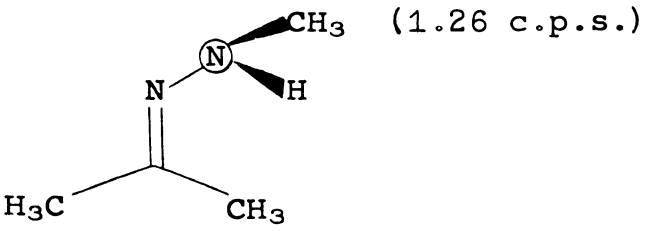
(0.50 c.p.s.)

XVIc



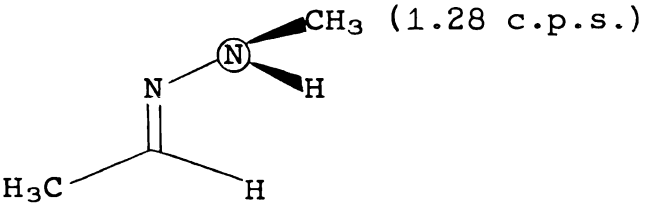
(1.01 c.p.s.) (1.79 c.p.s.)

XVIIc



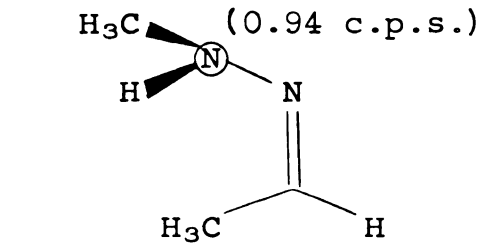
(1.15 c.p.s.)

XVIIIc



(1.03 c.p.s.)

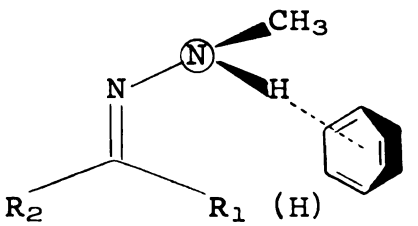
XIXc



XXc

Chemical Shifts--The above observations concerning differences in nitrogen-nitrogen single bond conformations are further supported by the chemical shift data. For example, whereas the α-methyl protons of N-methylhydrazones resonate at higher fields when cis than when trans to the N-methylamino group (Table 22), those of N,N-dimethylhydrazones resonate at lower fields (Table 21).

Solvent Effects--The larger upfield shift of the cis over the trans protons of N-methylhydrazones on dilution with benzene (Table 24) can be interpreted in terms of XXIc. Figures 18 through 23 show the effect of solvent dilution on ketone and



XXIc

aldehyde derivatives. The inability of N,N-dimethylhydrazones to form such an association complex explains the relatively small effect of benzene on their chemical shifts (Table 23).

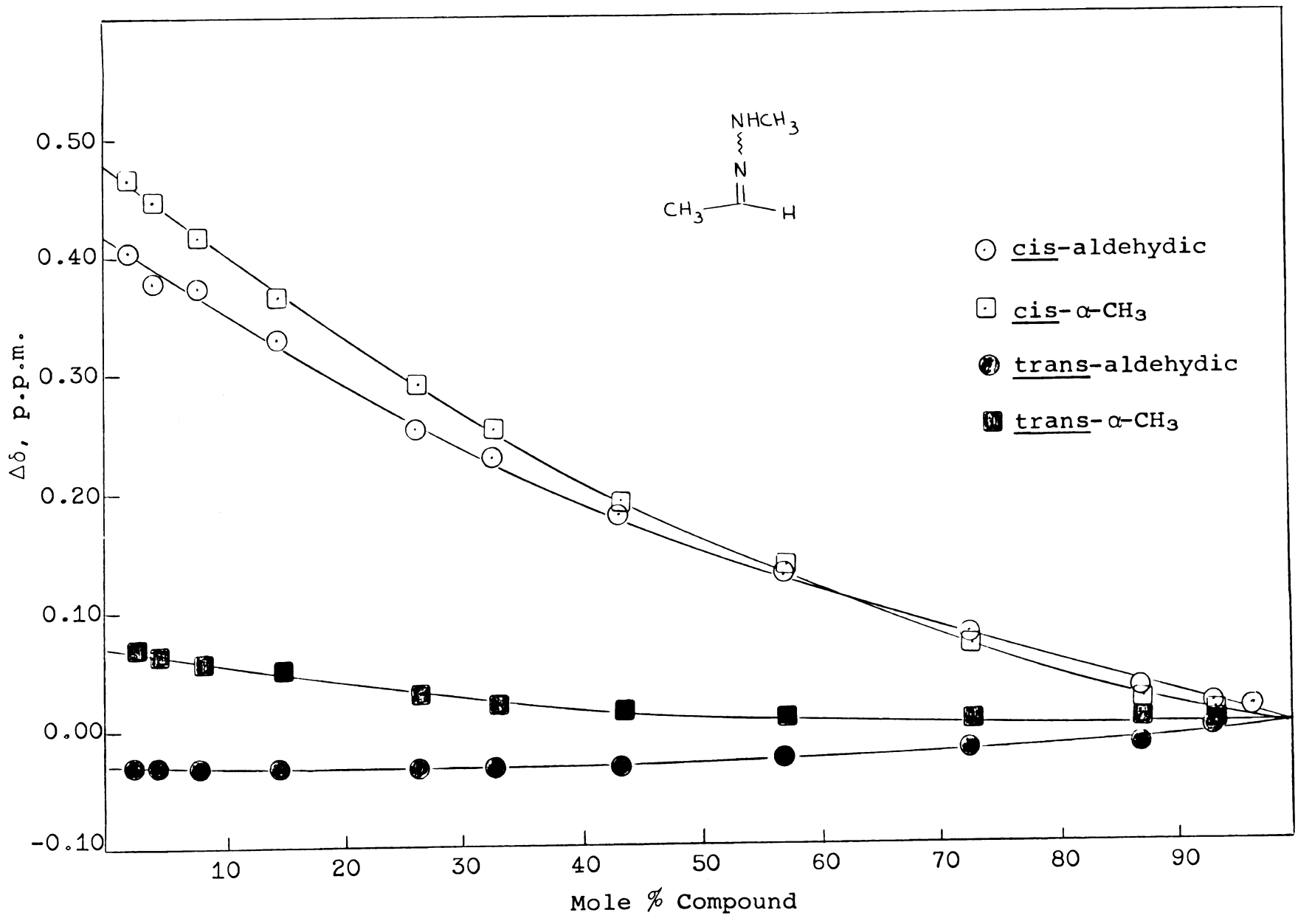


Figure 18. Effect of benzene on the chemical shifts of acetaldehyde N-methylhydrazone.

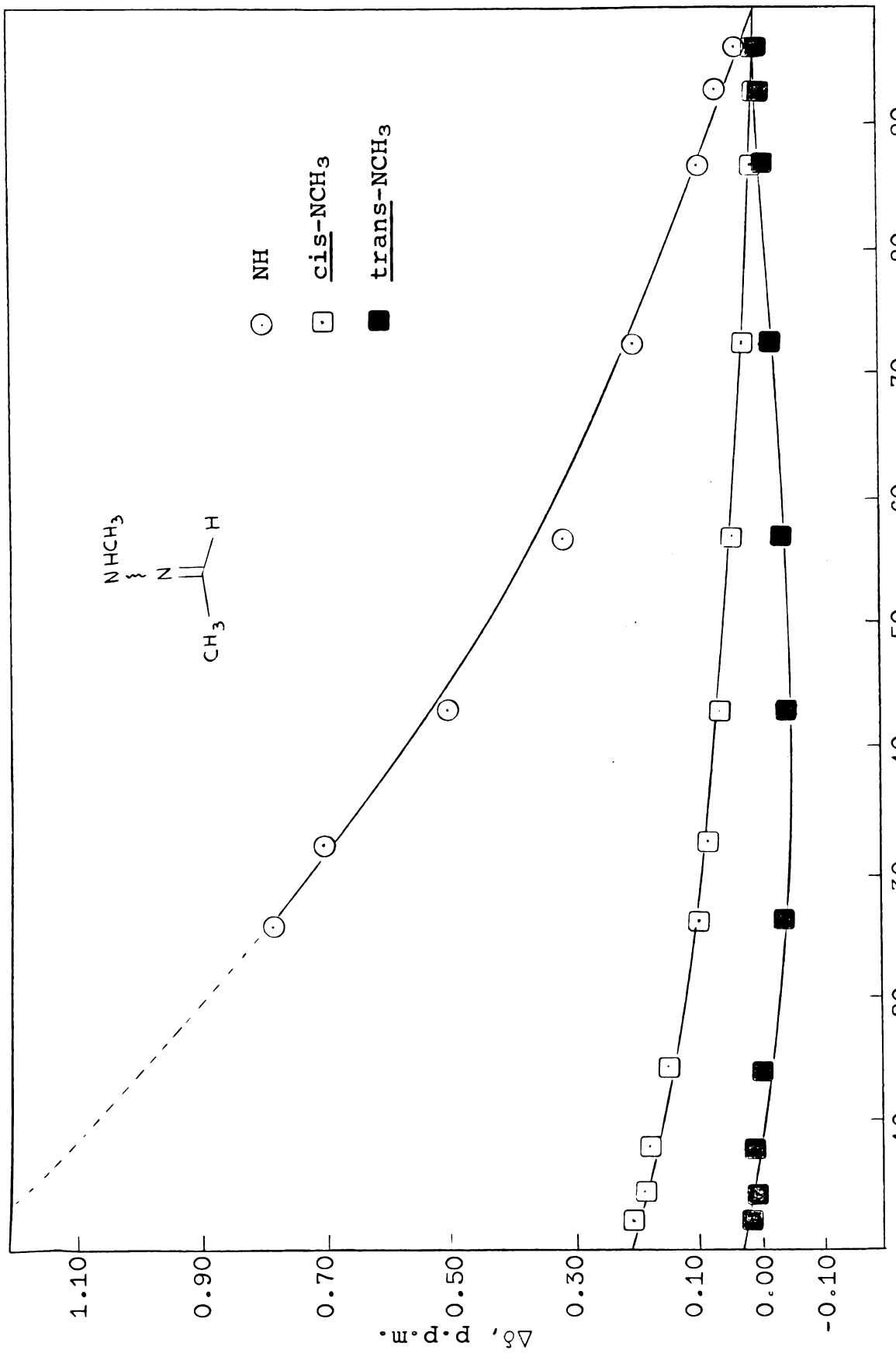


Figure 19. Effect of benzene on NH and $\underline{NCH_3}$ resonances of acetaldehyde N-methylhydrazone.

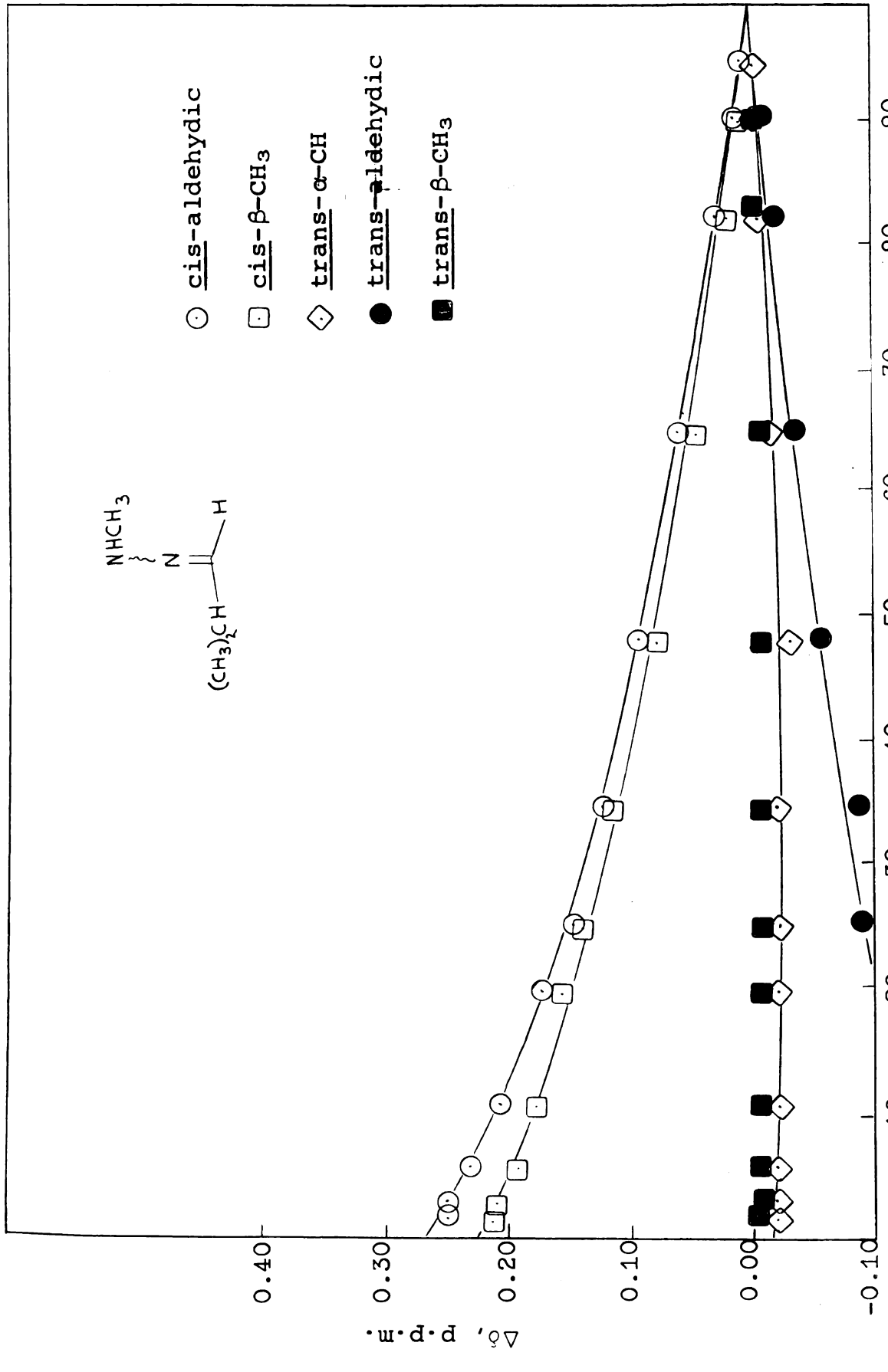


Figure 20. Effect of benzene on the chemical shifts of isobutyraldehyde N-methylhydrazone.

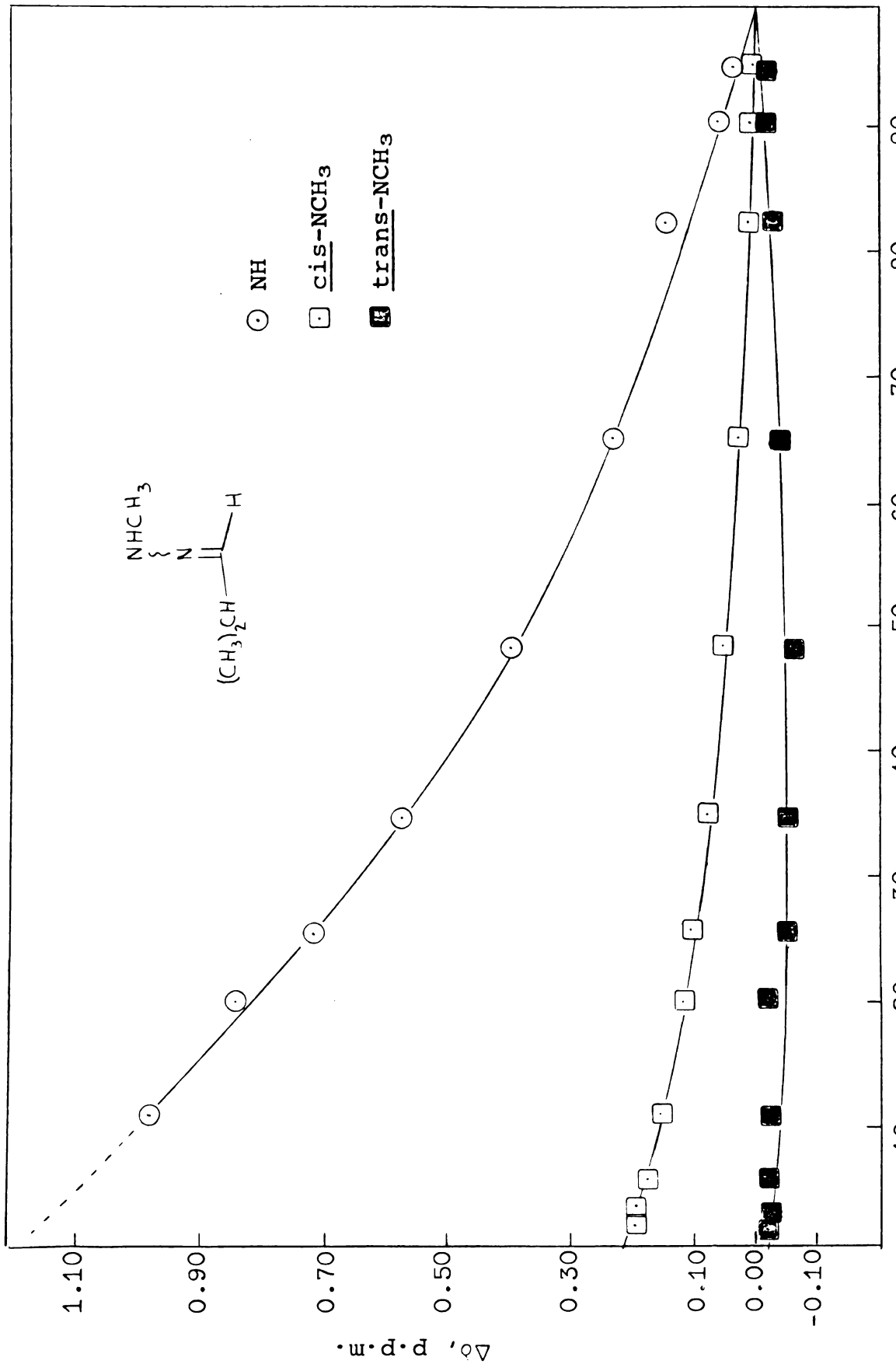


Figure 21. Effect of benzene on NH and NCH_3 resonances of isobutyraldehyde N-methylhydrazone.

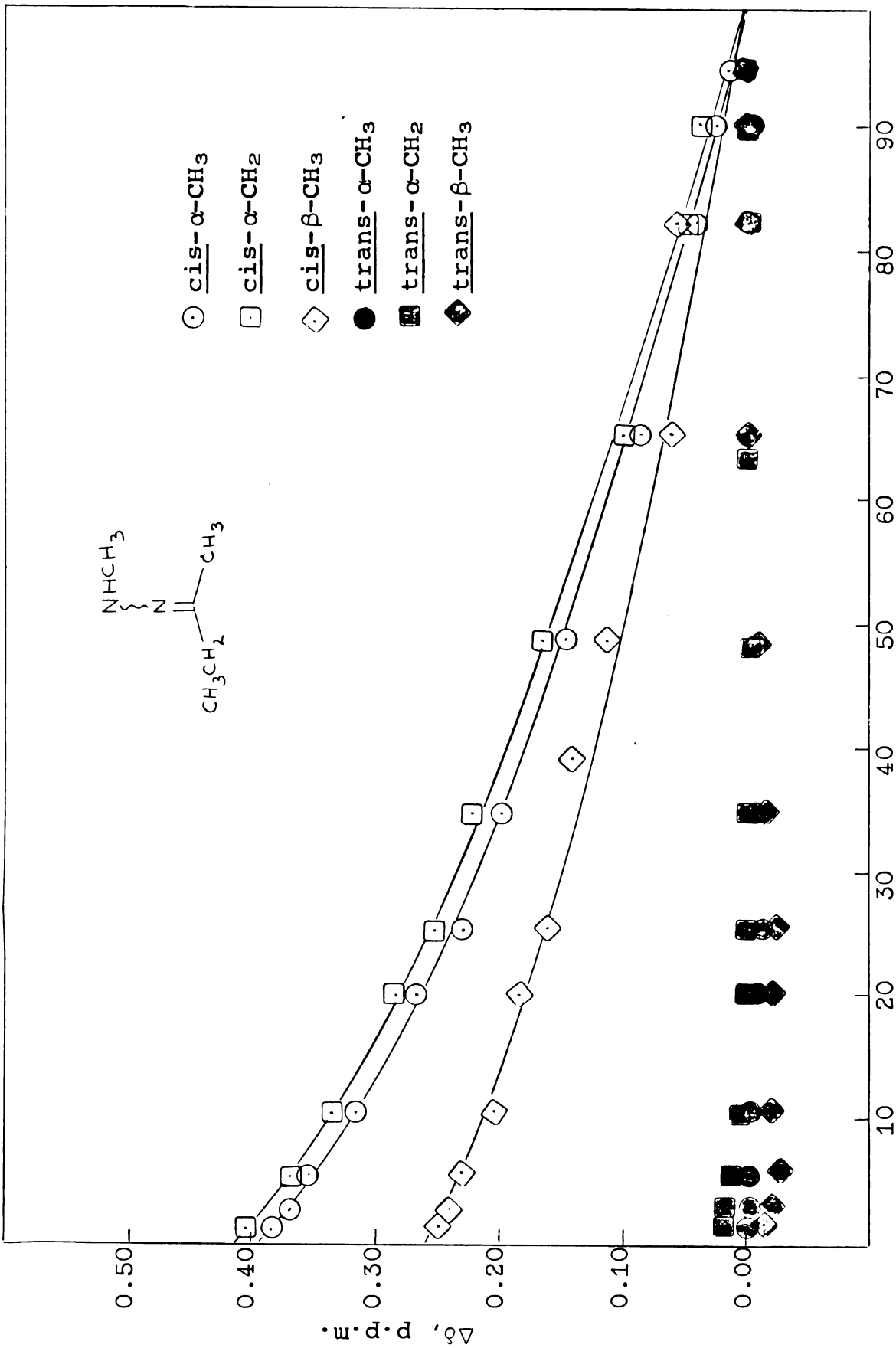


Figure 22. Effect of benzene on the chemical shifts of 2-butanone N-methylhydrazone.

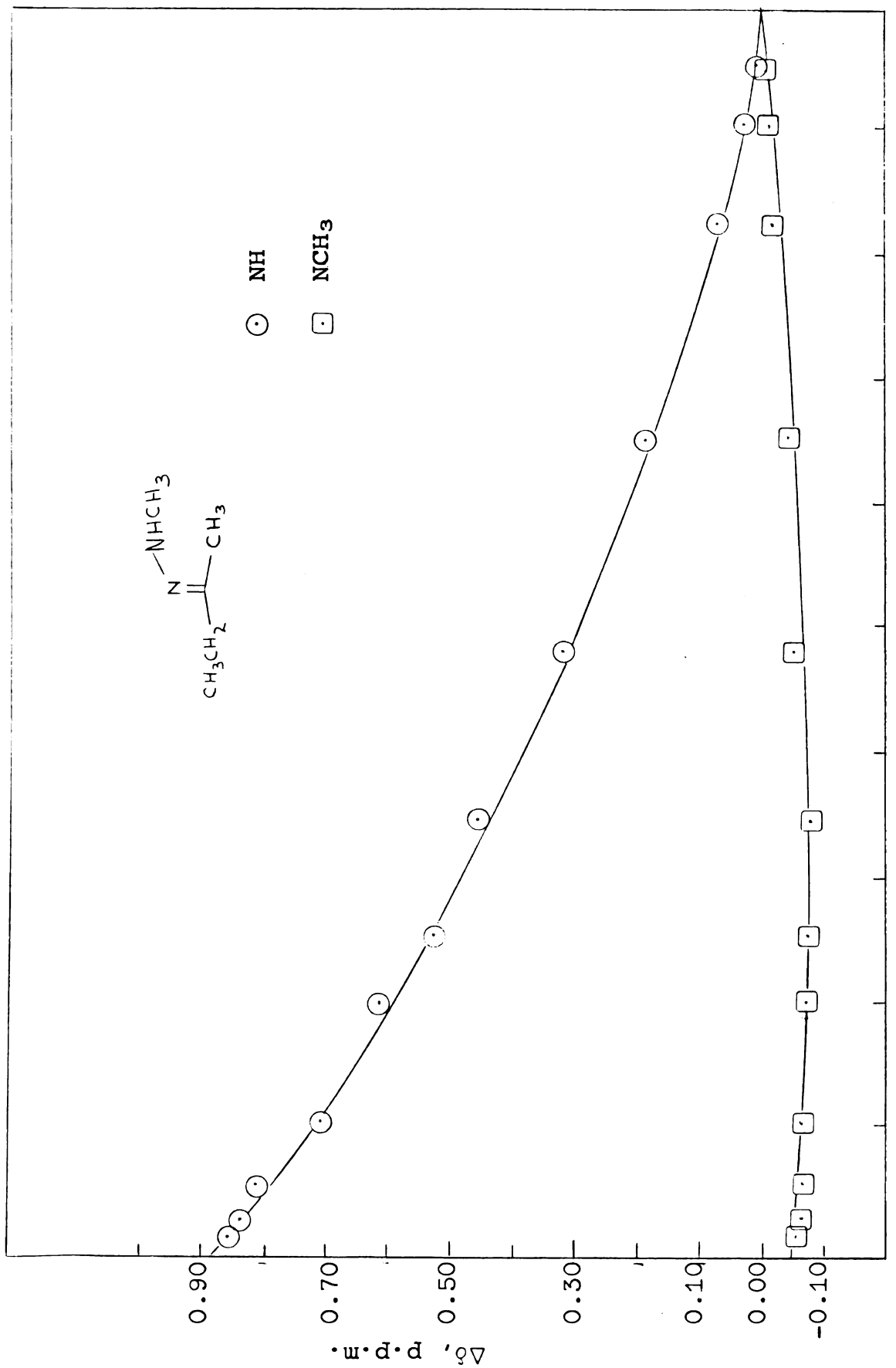


Figure 23. Effect of benzene on NH and $\underline{NCH_3}$ resonances of 2-butanone N-methylhydrazone.

PART D--PHENYLHYDRAZONES

Results

Previous studies showed that both cis and trans hydrogens of phenylhydrazones resonate at higher magnetic fields in benzene than in aliphatic solvents (24). The upfield shift of the cis-hydrogens is, however, three to six times larger than the corresponding trans. A comparison of the spectra of 2-butanone phenylhydrazone, neat, in benzene and in carbon tetrachloride is shown in Figure 24. Table 37 summarizes $\Delta\nu$ values ($\Delta\nu = \nu$ in benzene $- \nu$ in carbon tetrachloride) obtained from previous work (24). The effect of various solvents on the chemical shifts of 2-butanone phenylhydrazone is shown in Table 38. Note that methyl benzoate, nitrobenzene, pyridine, and 2,4-dimethylpyridine behave as nonaromatic solvents.

Figure 25 shows the effect of dilution on the cis-α-methyl and cis-β-methyl hydrogens of 2-butanone phenylhydrazone. The dilution curves indicate that the chemical shift of the α-methyl hydrogen is more sensitive to dilution than that of the β-methyl. Also, whereas on dilution with benzene the chemical shifts move upfield, on dilution with carbon tetrachloride and dimethyl sulfoxide they move downfield. Figure 26 shows the effect of dilution on the resonances of trans-α-methyl and trans-β-methyl hydrogens. These resonances are less sensitive to dilution than those of the cis. In contrast to the cis-hydrogens, trans-hydrogens resonate at lower magnetic fields when diluted with benzene. Figure 27 shows the effect of dilution on the chemical shifts of methyl t-butyl ketone

phenylhydrazone. These shifts are less sensitive to dilution than those of 2-butanone phenylhydrazone.

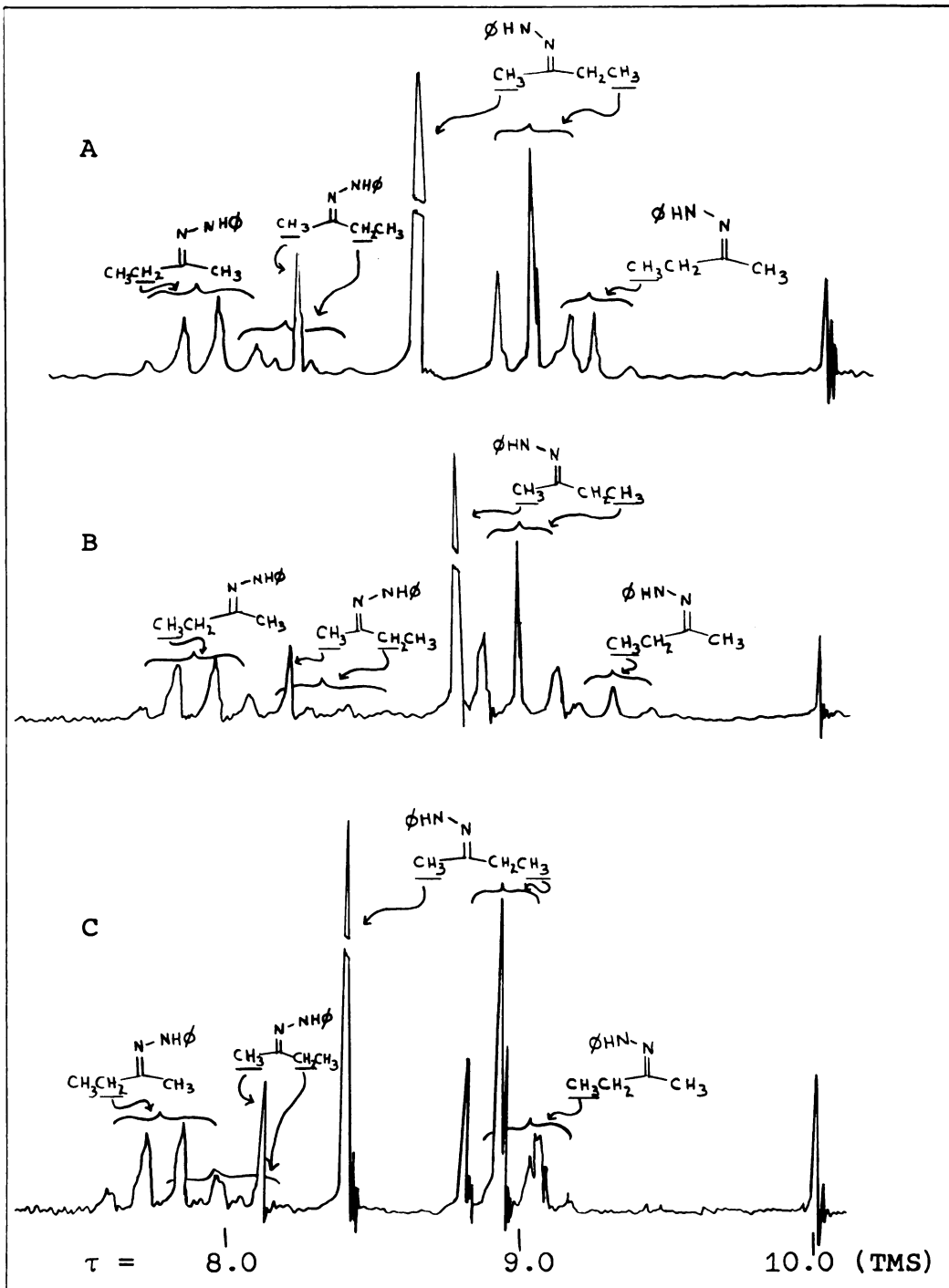


Figure 24. Nuclear magnetic resonance spectrum of 2-butanone phenylhydrazone: A, neat; B, 5 mole % in benzene; C, 5 mole % in carbon tetrachloride.

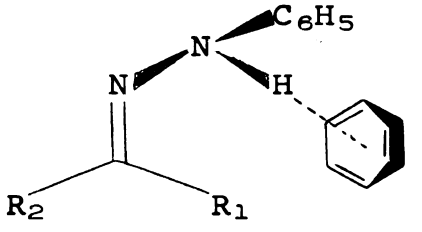
Table 37. $\Delta\nu$ (ν in benzene - ν in carbon tetrachloride) Values, in c.p.s., of Pnenylhydrazones

$R_1R_2C{=}NNHC_6H_5$		$\alpha(CH_3)$		$\alpha(CH_2)$		$\alpha(CH)$	$\beta(CH_3)$	
R_1	R_2	cis	trans	cis	trans	trans	cis	trans
H	CH_3	37.8	15.0					
H	CH_2CH_3				4.8		18.8	4.8
H	$CH(CH_3)_2$					1.8	13.8	3.0
CH_3	CH_3	21.6	4.8					
CH_3	CH_2CH_3	22.2	4.8	21.6	7.2		16.2	2.4
CH_3	$CH(CH_3)_2$	20.4	3.0			4.8	15.0	2.4
CH_3	$C(CH_3)_3$	21.0						2.4
CH_3	$CH_2CH(CH_3)_2$	19.8	3.0				11.4[a]	3.0[a]
CH_3	$CH_2C_6H_5$	25.2	6.6	21.0	3.6			
CH_3	C_6H_5	31.8						

[a]Values for γ-CH_3

Discussion

Solvent Effects--The large difference between $\Delta\nu$ (cis) and $\Delta\nu$ (trans) (Table 37) and the dependence of the chemical shifts on the concentration of phenylhydrazone in benzene (Figures 25, 26, 27), can be interpreted in terms of a stereospecific and reversible association between benzene and phenylhydrazone. The data suggest a hydrogen bonded species, whereby the benzene molecule associates with the anilino hydrogen (Id). Evans (40), Bottini and Nash (41) and Wepster (42) have independently shown that the trivalent nitrogen of aniline is



Id

pyrimidal. Complex Id is consistent with all the data. For example, since R_1 is closer than R_2 to the aromatic ring center, $\Delta\nu$ (cis) is greater than $\Delta\nu$ (trans); because of steric interaction between benzene and R_1, cis-β-methyls will assume conformations which places them farther away than cis-H_α from the ring. Hence, $\Delta\nu$ (cis-H_α) is greater than $\Delta\nu$ (cis-H_β).

Conformation IId can be excluded for the following reasons: Firstly, it is not favored because of unfavorable interactions between the phenyl group and the protons.

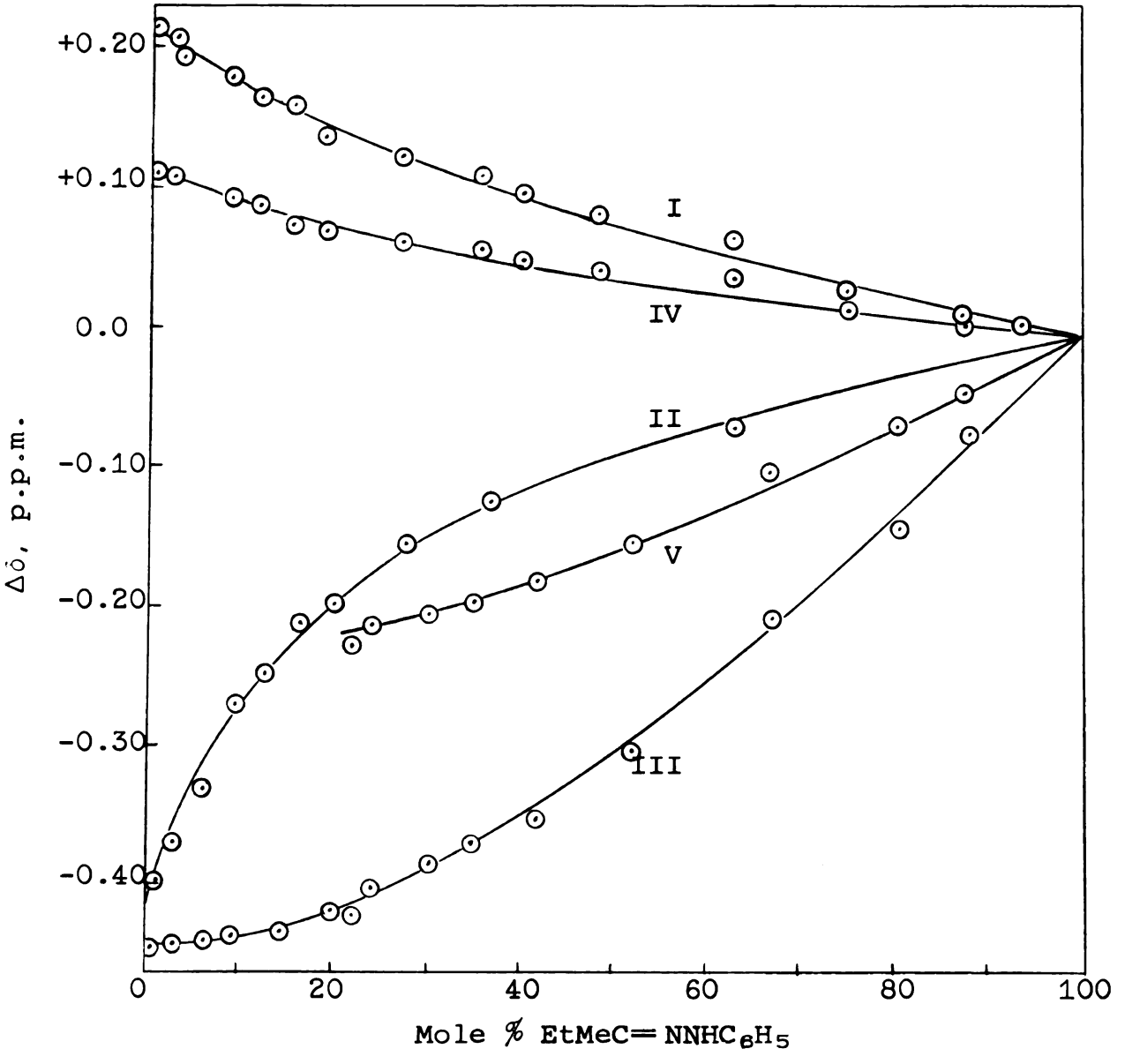


Figure 25. Effect of dilution on the chemical shifts of butanone phenylhydrazone: I, cis-α-methyl in benzene; II, cis-α-methyl in carbon tetrachloride; III, cis-α-methyl in dimethyl sulfoxide; IV, cis-β-methyl in benzene; V, cis-β-methyl in dimethyl sulfoxide.

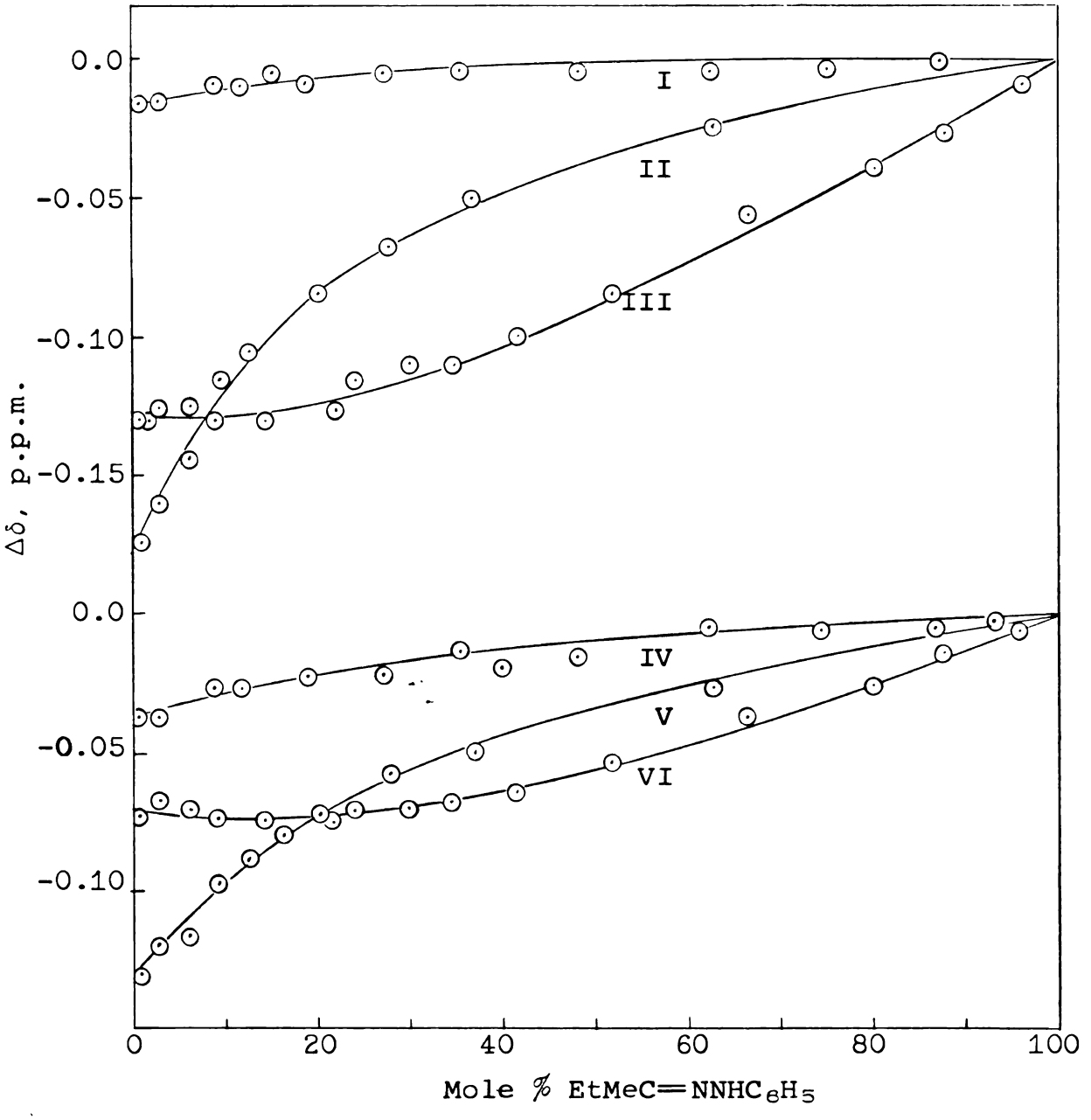


Figure 26. Effect of dilution on the chemical shifts of butanone phenylhydrazone: I, trans-α-methyl in benzene; II, trans-α-methyl in carbon tetrachloride; III, trans-α-methyl in dimethyl sulfoxide; IV, trans-β-methyl in benzene; V, trans-β-methyl in carbon tetrachloride; VI, trans-β-methyl in dimethyl sulfoxide.

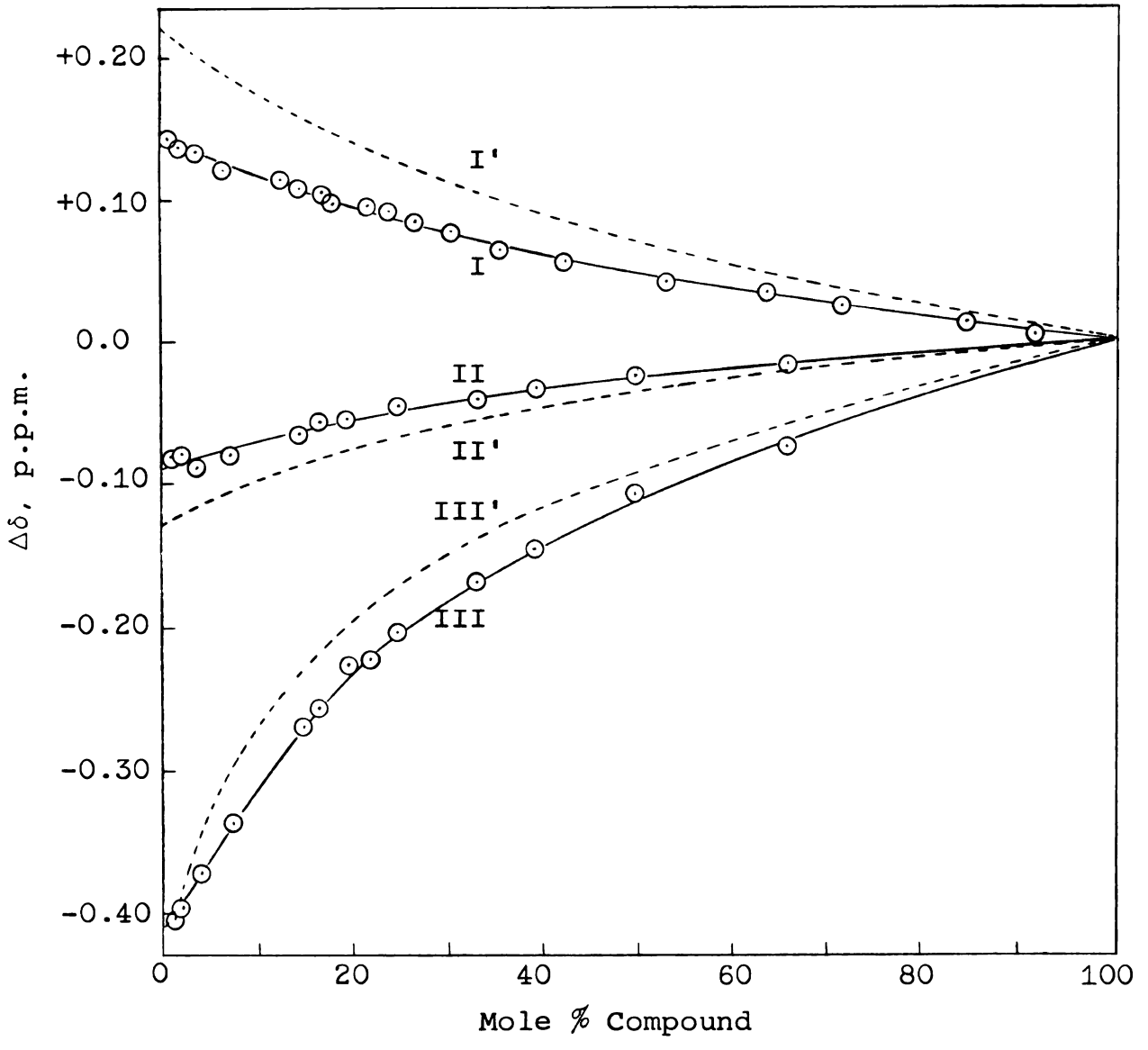
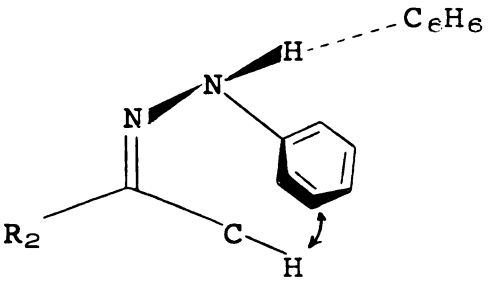


Figure 27. Effect of dilution on the chemical shifts of methyl t-butyl ketone phenylhydrazone: I, cis-α-methyl in benzene; II, trans-β-methyl in carbon tetrachloride; III, cis-α-methyl in carbon tetrachloride; I', cis-α-methyl of butanone phenylhydrazone in benzene; II', trans-β-methyl of butanone phenylhydrazone in carbon tetrachloride; III', cis-α-methyl of butanone phenylhydrazone in carbon tetrachloride.



IId

Secondly, if it was an important contributor, in all solvents capable of hydrogen bonding with the anilino proton the cis-H_α (methyl) and trans-H_α (methyl) should be shielded by 0.3 p.p.m. and 0.1 p.p.m., respectively (43,44). The other conformations available by rotation about the nitrogen-nitrogen bond do not accommodate the large $\Delta\nu$ (cis)--$\Delta\nu$ (trans) values and are thus discarded as important contributors.

When toluene, xylenes, or isodurene are substituted for benzene the upfield shift of the cis-hydrogens progressively decreases (Table 38). This can be explained as a decrease in the stability of complex Id, i.e., the equilibrium for 1 is greater than that for 2. The data support this explanation.

$$R_1R_2{=}NNH\emptyset + C_6H_6 \rightleftharpoons R_1R_2{=}NNH\emptyset \cdot C_6H_6 \qquad 1$$

$$R_1R_2{=}NNH\emptyset + \text{isodurene} \rightleftharpoons R_1R_2{=}NNH\emptyset \cdot \text{isodurene} \qquad 2$$

For example, the resonance of the cis-H_α in a 1:1 (mole/mole) mixture of benzene-isodurene (τ = 8.74) is closer to that in benzene (τ = 8.77) than to that in isodurene (τ = 8.65).

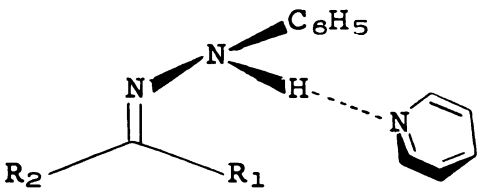
In solvents having two sites available for hydrogen bonding with the anilino hydrogen competition is expected between

Table 38. Solvent Effects[a] on the Chemical Shifts of Butanone Phenylhydrazone

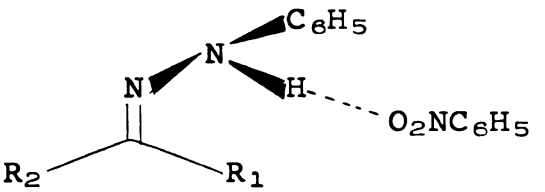
Solvent	α-CH_3 cis	α-CH_3 trans	β-CH_3 cis	β-CH_3 trans
Benzene	8.77	8.20	9.30	8.97
Toluene	8.73	8.20	9.25	8.97
o-Xylene	8.72	8.22	9.22	8.97
m-Xylene	8.72	8.22	9.22	8.97
p-Xylene	8.70	8.20	9.22	8.95
Isodurene	8.65	8.22	9.18	8.95
Anisole	8.62	8.13	9.19	8.96
N,N-Dimethylaniline	8.72	8.22	9.24	8.98
Fluorobenzene	8.55	8.14	9.14	8.95
Chlorobenzene	8.55	8.15	9.17	8.97
Bromobenzene	8.55	8.15	9.16	8.96
Iodobenzene	8.52	8.14	9.14	8.96
m-Dichlorobenzene	8.44	8.12	9.19	8.95
Methylbenzoate	8.30	8.05	9.14	8.86
Nitrobenzene	8.17	8.00	8.93	8.88
Pyridine	8.27	8.04	9.11	8.91
Dimethyl sulfoxide	8.22	8.10		8.95
Acetone	8.20			8.91
Benzene-Chlorobenzene(1:1, m./m.)	8.65	8.19	9.23	8.89
Benzene-Acetone (1:1,m./m.)	8.35			8.93
Benzene-Pyridine (1:1, m./m.)	8.43	8.10	9.24	8.94
Benzene-Dimethyl sulfoxide (1:1, m./m.)	8.24	8.09	9.01	8.94
Benzene-Nitrobenzene (1:1, m./m.)	8.41	8.08	9.19	8.94
Benzene-Isodurene (1:1, m./m.)	8.74		9.23	8.97

[a]Concentration 5 mole percent; values are in τ.

π-donor and n-donor association. From the parallel behavior of nitrobenzene, methyl benzoate, and pyridine to that of acetone, dimethyl sulfoxide, and methanol (Table 38) it is concluded that association occurs with the lone electron pairs of the heteroatoms rather than with the π-electrons of the rings. IIId and IVd predict no shielding of the cis-hydrogens by the aromatic ring current.

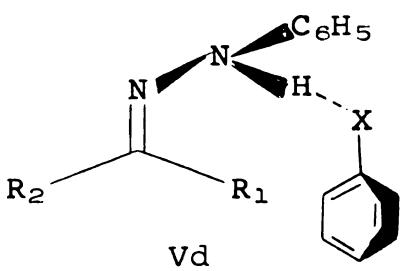


IIId



IVd

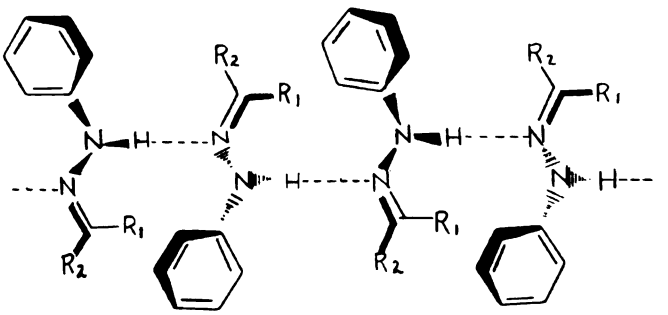
Halobenzenes compete more effectively than benzene for the anilino hydrogen, as judged by the fact that in a 1:1 (mole/mole) mixture of benzene-chlorobenzene the resonance of cis-H_α (τ = 8.65) is closer to that in chlorobenzene (τ = 8.55) than to that in benzene (τ = 8.77). Thus hydrogen bond formation occurs at the halogen atom site rather than with the π-electrons of the ring. In contrast to pyridine and nitrobenzene, the halobenzenes strongly shield the cis-hydrogens. This difference is anticipated, as seen by comparing IIId and IVd with Vd.



Vd

The strong solvent dependence of the cis-H_α resonance in pure as well as in mixed solvents provided a measure of the relative solvent basicity towards the anilino proton. The relative strengths of these hydrogen bonds for the solvents examined are: dimethyl sulfoxide > acetone > pyridine > nitrobenzene > chlorobenzene > benzene > isodurene.

From the dilution results (Figures 25,26,27) and the above discussion, VId is suggested as the general structure of liquid phenylhydrazones. Structure VId explains the larger



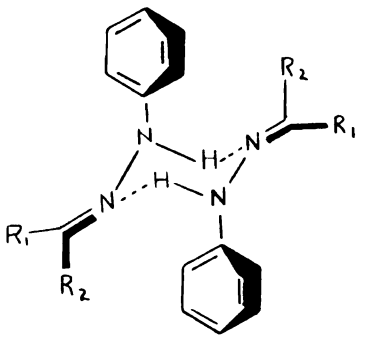
VId

upfield shift of cis over trans-hydrogens and of cis-H_α over cis-H_β with increase in the concentration of phenylhydrazone in aliphatic solvents. It also accommodates the unusual downfield shift of trans-hydrogens in benzene, since the two phenyl groups will exert a stronger shielding effect than a single benzene ring (Id).

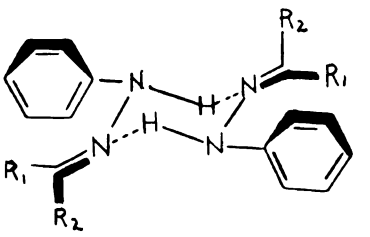
The shapes of the dilution curves indicate that whereas hydrogen bonding between dimethyl sulfoxide and phenylhydrazone is stronger than phenylhydrazone self-association, hydrogen

bonding between carbon tetrachloride or benzene with the phenylhydrazone is weaker. The sharper change in the chemical shift of 2-butanone phenylhydrazone as compared to that of methyl t-butyl ketone phenylhydrazone (Figure 27) implies that increase in the size of R_2 weakens self-association (VId) and favor solvent competition for the anilino hydrogen.

Cyclic dimers and trimers that are alternative structures to VId are not consistent with the data. For example, VIId



VIId



VIIId

predicts that in aliphatic solvents increase in the concentration of phenylhydrazone should lead to stronger shielding of trans rather than cis-hydrogens. Structure VIIId, which has the same severe steric interactions as IId, is excluded by the results from dilution studies.

EXPERIMENTAL

A. Preparation of N-Nitrosamines

Most of the nitrosamines were prepared from commercially available amines. N-nitrosodimethylamine and N-nitroso-N-phenylbenzylamine were purchased from Eastman Organic Chemicals.

Amines were obtained from the following sources: methyl-n-butylamine, diisopropylamine, N-isopropylaniline, N-methylbenzylamine, methylisopropylamine from K & K Laboratories, Inc.; N-isopropylbenzylamine from Aldrich Chemical Co., Inc.; methylethylamine hydrochloride, benzylamine from Eastman Organic Chemicals; tert-butylamine, N-ethylaniline from Matheson Coleman & Bell.

Methyl-tert-butylamine and N-ethylbenzylamine were prepared by lithium aluminum hydride reduction of tert-butylformamide and benzylacetamide. Since the nitrosamines were prepared by well-known methods (45,46), only a limited number of synthetic procedures are described. Table 39 contains the boiling and melting points of the N-nitrosamines.

Preparation of tert-Butylformamide. To a 300-ml., three-necked, round-bottomed flask equipped with a Tru-bore stirrer, reflux condenser and pressure equalized dropping funnel was added 30 g. (0.41 mole) of tert-butylamine and 70 ml. of m-xylene. The flask was placed in an ice bath and 18 g. (0.38 mole) of formic acid (98%) was added dropwise over a thirty minute period. When the addition was completed the ice bath was replaced by a heating mantle and the material

Table 39. Boiling Points and Melting Points of N-nitrosamines

N-nitrosamine	Obs.° C	Lit. ° C
N-nitrosodimethylamine	-----	153 (747 mm.)[a]
N-nitrosomethylethylamine	49.5 (9.5 mm.)	163 (747 mm.)[b]
N-nitrosomethylisopropylamine	58.5-59 (9.0 mm.)	-----
N-nitrosomethyl-n-butylamine	67 (6.0 mm.)	199-201[c]
N-nitrosomethyl-tert-butylamine	37-38 (1.5 mm.)	-----
N-nitrosodiisopropylamine	m.p. 46-47	194-195, m.p. 46[c]
N-nitroso-N-methylaniline	69-69.5 (0.7 mm.)	128 (19 mm.)[c]
N-nitroso-N-ethylaniline	73.5-74 (0.8 mm.)	133 (19 mm.)[c]
N-nitroso-N-isopropylaniline	86.5-87.5 (1.4 mm.)	-----
N-nitroso-N-methylbenzylamine	83.5-84 (10.7 mm.)	-----
N-nitroso-N-ethylbenzylamine	89.5 (0.7 mm.)	-----
N-nitroso-N-isopropylbenzylamine	94 (0.8 mm.)	-----
N-nitroso-N-phenylbenzylamine	m.p. 57-58	m.p. 58[c]

[a]Literature value from reference 46.

[b]Literature value from reference 48.

[c]F. K. Beilstein, "Handbuch der Organischen Chemie," Springer-Verlag OGH., Berlin, reference 49.

was then heated to reflux. After overnight reflux the reaction mixture was allowed to cool to room temperature. A water trap was then inserted between the condenser and the flask to collect the water carried over with the refluxing xylene. When approximately 10 ml. of water was collected, the remaining xylene and unreacted formic acid were removed under vacuum. No attempt was made to purify the tert-butylformamide. The yield of crude tert-butylformamide was 30.0 g. (80%); reported (45) b.p. 65° (1 mm.).

Preparation of Methyl-tert-butylamine hydrochloride. Into a two liter, three-necked, round-bottomed flask fitted with a reflux condenser, Tru-bore stirrer and pressure equalized dropping funnel was placed 48.0 g. (1.25 mole) of lithium aluminum hydride and 600 ml. of anhydrous ethyl ether. The flask was then placed in an ice bath and a drying tube was attached to the top of the condenser to eliminate moisture. To the rapidly stirred mixture was added during a one hour period, a solution of 30.0 g. (0.30 mole) of tert-butylformamide in 100 ml. of anhydrous ethyl ether. After the addition was completed the grey suspension was stirred overnight at room temperature and then held at reflux for six hours. Work-up consisted of adding 40 ml. of water, followed by 200 ml. of 2N sodium hydroxide to the cooled solution. The ether layer was decanted from the white solid and dried over anhydrous magnesium sulfate. Anhydrous hydrogen chloride was then bubbled through the dried ethyl ether extract until all

the amine hydrochloride precipitated (1 hour). The white solid was filtered and dried under vacuum. The yield of methyl-tert-butylamine hydrochloride was 29.5 g. (80%), m.p. 251°; reported (45), m.p. 252-254°.

Preparation of N-nitrosomethyl-tert-butylamine. A solution of 29.5 g. (0.24 mole) of methyl-tert-butylamine hydrochloride, 23 ml. of glacial acetic acid and 53 ml. of water was added to a 300-ml., three-necked, round-bottomed flask fitted with a reflux condenser, Tru-bore stirrer and pressure equilized dropping funnel. To the stirred reaction mixture 45.5 g. (0.66 mole) of sodium nitrite dissolved in 76 ml. of water was added over a thirty minute period. During the addition the reaction mixture was maintained at 25-30°. After stirring at room temperature for thirty minutes, 90 ml. of 10 N sodium hydroxide was added to the cooled solution. The material was extracted with five 10 ml. portions of ethyl ether, dried over anhydrous magnesium sulfate and concentrated. Fractionation yielded a yellow liquid, b.p. 37-38° (1.5 mm.), 18.56 g. (67%); reported (45), b.p. 66° (5 mm.).

Preparation of Benzylacetamide. Freshly distilled benzylamine (15.0 g., 0.14 mole) and reagent grade glacial acetic acid were refluxed for four hours in a 100-ml. round-bottomed flask fitted with a four inch air condenser wrapped with asbestos tape. Distillation of the white semi-solid yielded a white solid, b.p. 119-121 (0.6 mm.), m.p. 61-62°, 7.42 g. (36%); reported (47), m.p. 60.4-61.4°.

Preparation of N-Ethylbenzylamine. Into a 500-ml., three-necked, round-bottomed flask fitted with a reflux condenser, Tru-bore stirrer and pressure equilized dropping funnel was placed 3.79 g. (0.10 mole) of lithium aluminum hydride and 200 ml. of anhydrous ethyl ether. To the stirred mixture, cooled in an ice bath, was added 7.40 g. (0.049 mole) of benzylacetamide dissolved in 100 ml. of anhydrous ethyl ether. After the addition was completed, the mixture was refluxed for 16 hours. The reaction mixture was hydrolized with 10 ml. of water followed by 50 ml. of 2 N sodium hydroxide. The amine was extracted with ethyl ether and dried over anhydrous magnesium sulfate. Anhydrous hydrogen chloride was bubbled through the anhydrous ether solution yielding a white solid, m.p. 184°, 6.80 g. (88%); reported (48), m.p. 184°.

Preparation N-nitroso-N-ethylbenzylamine. A solution of 6.80 g. (0.04 mole) of N-ethylbenzylamine hydrochloride and 15 ml. of glacial acetic acid was added to a 100-ml., three-necked, round-bottomed flask equipped with a Tru-bore stirrer, reflux condenser and a pressure equalized dropping funnel. To the stirred mixture was added 8.30 g. (0.12 mole) of sodium nitrite dissolved in 20 ml. of water. The pot temperature was maintained below 10° during the addition. The mixture was then stirred at room temperature for three hours, cooled (ice bath), neutralized with 30 ml. of 10 N sodium hydroxide, extracted with ethyl ether, and dried over anhydrous potassium carbonate. Fractionation yielded a yellow liquid, b.p. 89.5 (0.7 mm.), 4.0 g. (67%).

B. Preparation of Aldoximes and Ketoximes

Oximes were prepared by reacting the freshly distilled aldehyde or ketone with hydroxylamine hydrochloride and a suitable base (50). A large number of aldehydes and ketones were commercially available materials. 3-Methyl-2-isopropyl-butyraldehyde, cyclopentane carboxaldehyde and 3,3-dimethyl-butyraldehyde were prepared in this laboratory (51). Acetaldehyde oxime and 2-butanone oxime were purchased from Matheson Coleman & Bell. Acetophenone, and 2-methylpropional-dehyde oximes were purchased from Eastman Organic Chemicals. 2,4,4-Trimethyl-3-pentanone and 2,2,4,4-tetramethyl-3-pentanone oximes were obtained from Merck Sharp & Dohme Research Lab.

Two oxime preparations are described below. Tables 40 and 41 summarize the melting and boiling points of the aldoximes and ketoximes.

Preparation of Cyclohexanecarboxaldehyde oxime. Into a 500-ml. round-bottomed flask equipped with a reflux condenser were placed 10.0 g. (0.14 mole) of hydroxylamine hydrochloride, 40.0 g. (0.70 mole) of potassium hydroxide pellets and 200 ml. of 95% ethanol. Cyclohexanecarboxaldehyde (10.0 g., 0.08 mole) was then added dropwise via the condenser. The reaction mixture was heated and maintained at reflux for 1.5 hours. The solution was then poured onto 250 ml. of water, extracted with ethyl ether and dried over anhydrous potassium carbonate. Fractionation yielded a

Table 40. Boiling Points and Melting Points of Aldoximes

Aldehyde	Obs.° C	Lit. ° C
Acetaldehyde	m.p. 47	47[a]
Propionaldehyde	68-69 (48 mm.)	77 (100 mm.)[a]
Butyraldehyde	83 (44 mm.)	152 (715 mm.)[a]
3-Methylbutyraldehyde	90-91 (40 mm.) m.p. 49-50	161 (759 mm.)[a] m.p. 48.5
3,3-Dimethylbutyraldehyde	80 (13 mm.)	-----
Phenylacetaldehyde	m.p. 98-98.5	98.5[a]
2-Methylpropionaldehyde	-----	140[a]
2-Ethylbutyraldehyde	71-73 (6 mm.)	-----
3-Methyl-2-isopropylbutyraldehyde	87-88 (15 mm.)	-----
2-Methylbutyraldehyde	89-90 (40 mm.)	149-151 (749 mm.)[a]
2-Methylvaleraldehyde	61 (2.5 mm.)	-----
2-Ethylhexanal	83 (1.6 mm.)	-----
Cyclopentanecarboxaldehyde	69-70 (1.8 mm.)	-----
Cyclohexanecarboxaldehyde	69-73 (2.8 mm.)	m.p. 90-91[a]

[a]Literature values from reference 48.

Table 41. Boiling Points and Melting Points of Ketoximes

Ketone	Obs. ^{o} C	Lit. ^{o} C
Acetone	m.p. 58	m.p. 59[a,b]
2-Butanone	150-152	152[a]
3-Methyl-2-butanone	161-162	157-158[a]
3,3-Dimethyl-2-butanone	m.p. 74-75.5	74[b]
3-Pentanone	72-73 (12 mm.)	165[a]
2,2,4-Trimethyl-3-pentanone	143-144	141[a]
2,2,4,4-Tetramethyl-3-pentanone	159.5-161	-----
Acetophenone	58-59	60[a]
Propiophenone	105-106 (2.5 mm.) m.p. 53-54	165 (38 mm.)[a] m.p. 53-54
Butyrophenone	109-110 (2 mm.) m.p. 49-50	m.p. 50[a]
Phenylpropanone	142-144 (15 mm.)	m.p. 68-70[a]

[a]Literature values from reference 48.

[b]Literature values from reference 50.

colorless liquid, b.p. 69-73 (2.8 mm.), 7.47 g. (74%).

Preparation of 3,3-Dimethylbutyraldehyde oxime. Into a 50-ml. round-bottomed flask fitted with a reflux condenser were placed 2.5 g. (0.039 mole) of hydroxylamine hydrochloride, 10 ml. of 10% sodium hydroxide and 1.0 g. (0.0096 mole) of 3,3-dimethylbutyraldehyde. The reaction mixture was refluxed for 11 hours, cooled, saturated with sodium chloride, extracted with three 10 ml. portions of ethyl ether, and dried over magnesium sulfate. Fractionation yielded a colorless liquid, b.p. 80 (13 mm.), 0.71 g. (62%).

C. Preparation of N-Methylhydrazones and N,N-Dimethylhydrazones

A modified procedure of Braddock and Willard (52) was used to prepare the substituted hydrazones. When pure, hydrazone derivatives are colorless pungent smelling liquids. Analysis (n.m.r., u.v.) of the low molecular weight aldehyde N-methylhydrazones must be completed immediately after their preparation, since they turn yellow and then form crystals on standing in the refrigerator. Aldehyde hydrazones are known to dimerize at room temperature (53). Tables 42 and 43 summarize the boiling points of the N-methylhydrazones and N,N-dimethylhydrazones. The two preparations given below illustrate the procedure used.

Preparation of 3,3-Dimethylbutyraldehyde-N,N-dimethylhydrazone. Into a 25-ml., two-necked, round-bottomed flask

Table 42. Boiling Points of N-Methylhydrazones

Carbonyl Compound	Obs. b.p. ^{o} C
Acetaldehyde	104
Propionaldehyde	110-111
3,3-Dimethylbutyraldehyde	70 (25 mm.)
2-Methylpropionaldehyde	130-131
2-Ethylbutyraldehyde	98 (30 mm.)
Cyclohexanecarboxaldehyde	70 (4 mm.)
Acetone	116
2-Butanone	129
3-Methyl-2-butanone	140
3,3-Dimethyl-2-butanone	50 (20 mm.)

Table 43. Boiling Points of N,N-Dimethylhydrazones

Carbonyl Compound	Obs. b.p. ^{o} C
Acetaldehyde	91.5
Propionaldehyde	111-112
3,3-Dimethylbutyraldehyde	65 (50 mm.)
2-Methylpropionaldehydr	108
2-Ethylbutyraldehyde	148-152
Cyclohexanecarboxaldehyde	78 (6 mm.)
Acetone	79
2-Butanone	113
3-Methyl-2-butanone	65-68 (60 mm.)

with a reflux condenser, drying tube and rubber syringe cap was added 5.0 g. (0.03 mole) of barium oxide, and a solution of 1.0 g. (0.01 mole) of 3,3-dimethylbutyraldehyde in 10 ml. of absolute ethanol. To the cooled solution 1.0 g. (0.016 mole) of dimethylhydrazine was added with a hypodermic syringe. After the initial exothermic reaction subsided, the reaction mixture was refluxed for one hour. The material was then cooled, filtered, extracted with additional ethanol and dried over anhydrous magnesium sulfate. Fractionation yielded a colorless liquid, b.p. 65 (50 mm.), 0.80 g. (56%).

Preparation of Cyclohexanecarboxaldehyde-N-methylhydrazone. Into a 25-ml., two-necked, round-bottomed flask fitted with a reflux condenser, drying tube and a rubber syringe cap was added 7.6 g. (0.05 mole) of barium oxide and a solution of 0.92 g. (0.02 mole) of methylhydrazine in 5 ml. of anhydrous ethyl ether. A solution of 1.96 g. (0.02 mole) of cyclohexanecarboxaldehyde in 5 ml. of ethyl ether was added with a hypodermic syringe. The reaction mixture was allowed to stand overnight, filtered, extracted with ethyl ether and dried over anhydrous magnesium sulfate. Distillation yielded a yellow liquid, b.p. 70 (4 mm.), 1.2 g. (47%).

D. Preparation of Phenylhydrazones

2-Butanone phenylhydrazone, b.p. 106-107 (2.2 mm.) and 3,3-dimethyl-2-butanone phenylhydrazone, b.p. 96 (0.7 mm.) were prepared according to well-known procedures (54,55).

E. Solvents

Benzene-d_6 was purchased from Merck Sharp & Dohme of Canada Limited. Carbon tetrachloride, benzene and cyclohexane were purified by well-known procedures (54,55). Acetonitrile and dimethylsulfoxide were dried over calcium hydride and distilled. All purified solvents were stored over molecular sieves in glass stoppered bottles.

F. Spectra

Nuclear magnetic resonance spectra were determined at 60 Mc. on a Varian Associates Model A-60 Analytical Spectrometer. Undegassed samples were run in thin walled glass A-60 tubes using tetramethylsilane as the internal reference. Coupling constants (J values) were recorded at 50 c.p.s. sweep width. Recorded coupling constants are the average of at least three spectral sweeps taken from low to high field strength and vice versa. Temperature studies were carried out using a Varian Associates V-6040 Variable Temperature Controller. Temperatures are accurate to $\pm 2^{o}$ C. Ultraviolet spectra were taken on a Cary 14 Recording Spectrophotometer (Applied Physics Corporation).

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