

50°, the isolated hydrocarbon product is nearly pure VIII (>95%). While this represents a useful synthetic method for preparation of VIII, it is not yet clear to what extent these reductions in the anhydrous media, which result in higher yields of tricyclic hydrocarbon, involve concerted reactions or prior ionizations.

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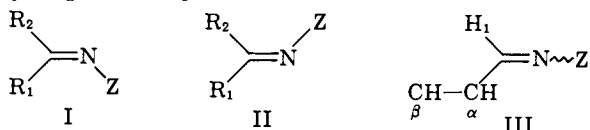
RECEIVED JUNE 21, 1963

Structural Studies by Nuclear Magnetic Resonance.

III. *syn-anti* Assignments from Solvent Effects

Sir:

N.m.r. is becoming progressively more important in the elucidation of structural problems arising from restricted rotation around double bonds. We can assign structures to I and II provided, when R₁ is methyl or hydrogen the equilibrium ratio I/II increases as R₂



changes from methyl to ethyl to isopropyl to *t*-butyl.¹

Table I summarizes results pertinent to *syn-anti* structural assignment. The notation H₁, H_α, H_β is shown in III. Shielded (+) means that hydrogens when *cis* to Z resonate at higher magnetic fields than when *trans*; deshielded (−) denotes the reverse. All spectra were taken with an A-60 Varian Associates n.m.r. spectrometer.

Z	Solvent	H ₁	H _α ^o	H _β
−NH ₂	<i>a, b</i>	−	+	−
−NHCH ₃	<i>a, b, i</i>	−	+	+
−NHC ₆ H ₄ X (<i>p</i>)	<i>a, b, c, f</i>	−	+	+
X=H, Cl, CH ₃				
−NHC ₆ H ₄ NO ₂ (<i>o</i>)	<i>f, i</i>	−	+	−
−NHC ₆ H ₄ NO ₂ (<i>p</i>)	<i>f, i</i>	−	+	<i>l</i>
−NHC ₆ H ₃ (NO ₂) ₂	<i>d, e, f, g, h, i, j, k</i>	−	+	−
−NHCONH ₂	<i>e, f</i>	−	+	<i>l</i>
−NHCSNH ₂	<i>e, f</i>	−	+	−
−OH ^m	<i>a, b, c, f, g</i>	−	−	+
−OTs	<i>b, c</i>	−	−	+
−N(CH ₃) ₂	<i>a, b, i</i>	<i>n</i>	−	+
−NCH ₂ C ₆ H ₅	<i>a, b, c</i>	<i>n</i>	+	+
Nitrosamines	<i>a, b, c, f</i>	+	+	+

^a Neat. ^b Carbon tetrachloride. ^c Benzene. ^d Methylene chloride. ^e Chloroform. ^f Methylene bromide. ^g Nitrobenzene. ^h Pyridine. ⁱ Dimethyl sulfoxide. ^j Dimethylformamide. ^k Tetramethylurea. ^l In most unsymmetrical compounds Δν is zero. ^m W. D. Phillips, *Ann. N. Y. Acad. Sci.*, **70**, 817 (1958); E. Lustig, *J. Phys. Chem.*, **65**, 491 (1961), and observations from our laboratories. ⁿ Only one aldehyde derivative isomer. ^o Values computed from α-methyl and α-methylene hydrogens.

Regardless of solvent used, H₁ is strongly deshielded (Δν = 15–60 c.p.s.) and it can be confidently used to assign *syn* and *anti* structures. Assignments from H_α and H_β are complicated because structural changes in R₁ and R₂, or changes in solvent, frequently reverse the resonances of *cis* and *trans* hydrogens, e.g., α-methine hydrogens are deshielded; benzyl (H_α) hydrogens of nitrophenylhydrazones are deshielded; H_α of acetaldehyde 2,4-dinitrophenylhydrazone and thiosemicarbazone is deshielded in dimethyl sulfoxide, dimethylformamide, acetone, and tetramethylurea; in benzene H_β's

(1) For equilibrium values see G. J. Karabatsos, J. D. Graham, and F. M. Vane, *J. Am. Chem. Soc.*, **84**, 753 (1962); G. J. Karabatsos, B. A. Shapiro F. M. Vane, J. S. Fleming, and J. S. Ratka, *ibid.*, in press.

are always shielded. Assignments, therefore, based on arguments from analogy must be made cautiously. The nitrosamine assignments² should be reversed.

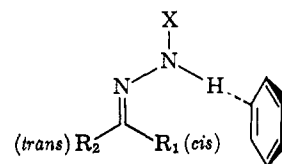
We wish to present a general method for assigning *syn* and *anti* structures, and to comment on the structure of some substrate–solvent association complexes. In aromatic solvents *cis* and *trans* hydrogens resonate at higher fields than they do in aliphatic solvents. From the fact that the degree of upfield shift differs for *cis* and *trans* hydrogens we can assign *syn-anti* structures. Table II summarizes Δν values (Δν = ν in aromatic solvent − ν in aliphatic solvent) compiled from derivatives of three aliphatic aldehydes, six aliphatic ketones, and acetophenone. We have used benzene, chlorobenzene, and alkylbenzenes as aromatic solvents, and acetone, dimethyl sulfoxide, carbon tetrachloride, chloroform, methylene bromide, and methylene chloride as aliphatic solvents.

TABLE II^a

Z	Δν(α-CH ₃)		Δν(α-CH ₂)		Δν(β-CH ₃)	
	<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>
−NHC ₆ H ₅ ^b	20–32	3–7	22–39	3.5–7	14–17	2.4–5
−NHC ₆ H ₄ CH ₃ (<i>p</i>) ^b	18–23	2–5			15.6 ^e	3.0 ^e
−NHC ₆ H ₄ Cl(<i>p</i>) ^b	22–38	7–13		7.2 ^e	15.6 ^e	4.2 ^e
−NHC ₆ H ₄ NO ₂ (<i>o</i>) ^c	28–38	5–21	34.8 ^f	18.6 ^f	22.8 ^e	12–14
−NHC ₆ H ₄ NO ₂ (<i>m</i>) ^c	38–47	15–16			24.0 ^e	7.8 ^e
−NHC ₆ H ₃ (NO ₂) ₂ ^c	43–55	16–23	27.0 ^f	15–18	27.6 ^e	9.6 ^e
−NHC ₆ H ₂ (NO ₂) ₂ ^c	38–60	24–38	37.8 ^f	25.2 ^f	27–36	10–19
−NHC ₆ H ₄ CO ₂ H(<i>o</i>) ^c	24–32	11–26				
−NHC ₆ H ₄ CO ₂ H(<i>p</i>) ^{c,e}	38.8	8.4				
−NHCH ₃ ^{b,g}	21.6	4.2				
−NHCSNH ₂ ^d	42.5	29.4	70.8	36.0	37.2	21.0
−N(CH ₃) ₂ ^{b,h}	3.0	1.2				
−NCH ₂ C ₆ H ₅ ^{b,c}	12.0	9.6				
−OH ^b	3–5	9.6–10.5	1.2 ^e	9.0 ^e	11–26	11–26
Nitrosamines ^b	18–28	29–41	22.8 ⁱ	34.8 ⁱ	24–35	28–36

^a All Δν values are in c.p.s. Sample concentrations varied from 5–10%. Wherever a range for Δν is given, the low Δν (*cis*) values correspond to the low Δν (*trans*) values. ^b Δν values were computed from spectra in benzene and carbon tetrachloride. ^c Δν values were computed from spectra in benzene and methylene bromide. ^d Δν values were computed from spectra of butanone thiosemicarbazone in benzene and chloroform. ^e Values from butanone derivative. ^f Values from phenylacetone derivative. ^g Values from acetaldehyde derivative. ^h Values from methyl isopropyl ketone derivative. ⁱ Values from N-nitrosomethyl-ethylamine.

Compounds of the structure =NNHX have Δν (*cis*) > Δν(*trans*). Increase in the acidity of the NH, or decrease in R₁ and R₂ size, results in larger Δν values. In the absence of the NH hydrogen (Z = −N(CH₃)₂, −NCH₂C₆H₅) Δν's are small and the difference between Δν(*cis*) and Δν(*trans*) negligible. We interpret the results in terms of the hydrogen-bonded complex IV. Nitrobenzene behaves as acetone and dimethyl sulfoxide do; apparently the NH hydrogen bonds with the nitro group and not with the phenyl ring.



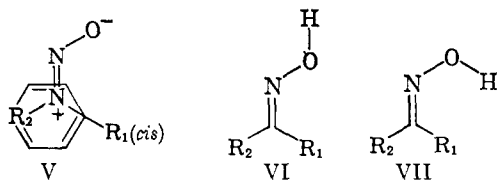
IV

For nitrosamines Δν(*cis*) < Δν(*trans*). We propose an unsymmetrical association complex (V) analogous to the one suggested for amides.³ Repulsions between oxygen and benzene force the ring closer to R₂ than R₁. We predict that alkyl nitrites will behave similarly.

For oximes Δν's are small and Δν(*cis*) < Δν(*trans*). This striking difference between oximes and compounds

(2) C. E. Looney, W. D. Phillips, and E. L. Reilly, *ibid.*, **79**, 6136 (1957).

(3) J. V. Hatton and R. E. Richards, *Mol. Phys.*, **8**, 253 (1960); **5**, 139, 153 (1962).



of the $=\text{NNHX}$ structure indicates that the conformation of aliphatic oximes in benzene is VI, not VII. Microwave spectroscopy has shown⁴ that the conformation of formaldoxime in the gas phase is VI. For $=\text{NNHX}$ compounds conformation IV is preferred over the one which is analogous to VI, because of unfavorable interactions between X and R₁ in VI.

Acknowledgment.—We thank the United States Atomic Energy Commission for financial support, Grant AT(11-1)-1189.

(4) I. N. Levine, *J. Mol. Spectry*, **8**, 276 (1962).

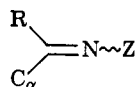
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RECEIVED MAY 25, 1963

Structural Studies by Nuclear Magnetic Resonance. IV. Conformations of *syn-anti* Isomers from Chemical Shifts and Spin-Spin Coupling Constants

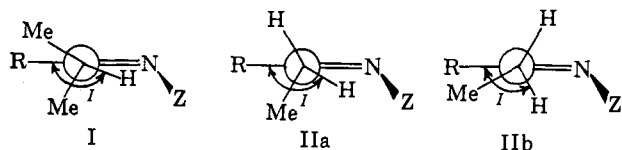
Sir:

We reported¹ in our n.m.r. studies on structural assignments to *syn* and *anti* isomers that α -methyl hydrogens when *cis* to Z resonate at higher fields (*shielded*) than when *trans*; for α -methylene hydrogens the chemi-



cal shift difference between *cis* and *trans* hydrogens is smaller than it is for α -methyl hydrogens, and in many cases this difference is zero; α -methine hydrogens when *cis* to Z resonate at *appreciably lower fields* (*deshielded*) than when *trans*. In this respect α -methine hydrogens behave as hydrogens directly bonded to the imino carbon.²

This puzzling behavior of α -hydrogens is explicable from conformational considerations. Because of steric interactions between Z and isopropyl when *cis* to each other, the preferred conformation of the isopropyl group might be I ($I \sim 180^\circ$ or slightly smaller). Conformation I places the methine hydrogen in or near the $\text{C}=\text{N}-\text{Z}$



plane and explains the similarity in behavior between methine and hydrogens directly bonded to the imino carbon (deshielded). The angle I will depend on the size of R, *i.e.*, as R increases in size I will increase and approach 180° . As I increases, the methine hydrogen will become more deshielded. Our data support this hypothesis, *e.g.*, in oximes ($\text{Z} = \text{OH}$), when $\text{R} = \text{H}$, $\tau(\text{trans}) = 7.55$ and $\tau(\text{cis}) = 6.87$; when $\text{R} = \text{Me}$, $\tau(\text{trans}) = 7.52$ and $\tau(\text{cis}) = 6.55$. From similar arguments the important conformations of the ethyl group

(1) G. J. Karabatsos, R. A. Taller, and F. M. Vane, *J. Am. Chem. Soc.*, **85**, 2326 (1963).

(2) We also observed the same behavior in nitrosamines. In cases such as oximes where all α -hydrogens are deshielded (*cis* lower than *trans*), we find the same trend; *i.e.* α -methine hydrogens are more deshielded (0.7–1.0 p.p.m. in carbon tetrachloride) than α -methyl hydrogens (0.03–0.05 p.p.m. in carbon tetrachloride).

should be those where I varies from 180° (IIa) to 125° (IIb).

We could test further the above hypothesis by measuring $J_{\text{H}_\alpha\text{H}_\beta}$ for *cis* (III) and *trans* (V) isomers provided $J_{\text{H}_\alpha\text{H}_\beta}$ were a function of the dihedral angle, as J is



in ethane derivatives.³

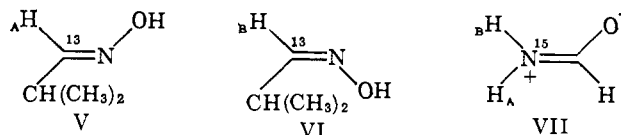
The data summarized in Table I are consonant with the advanced explanation. As expected from a dihedral angle of about 180° , J_{cis} for isopropyl compounds is large (7.6 c.p.s.). For ethyl compounds II_a predicts J_{cis} larger than J_{cis} for methyl compounds, while II_b predicts the reverse. The data indicate that both II_a and II_b are important contributors, but do not allow assignment of relative contributions. J 's, especially J_{trans} of oximes, are solvent dependent. In addition, J_{trans} of oximes depends on concentration, *e.g.*, J_{trans} of isobutyraldoxime = 6.55, 6.35, 6.30 c.p.s. in carbon tetrachloride solutions of 20%, 10%, and 5% concentration, respectively. Preliminary temperature studies also show that J_{cis} of isobutyraldoxime (neat) decreases by 0.10 c.p.s. and J_{trans} by about 0.20 c.p.s. as the temperature is raised from 38° to about 70° . These results are easily understood in terms of self-association and hydrogen bonding between solute and solvent.

TABLE I

Compound	Solvent (Concd., 5–10%)	$J_{\text{H}_\alpha\text{H}_\beta}$ (<i>cis</i>)	$J_{\text{H}_\alpha\text{H}_\beta}$ (<i>trans</i>)
MeHC=N-NHC ₃ H ₇ (NO ₂) ₂	b, c, d, e, f	5.60 ± 0.05	5.40 ± 0.05
MeHC=N-NHC ₃ H ₇ (NO ₂) ₁	g, h	5.50 ± 0.05	5.30 ± 0.05
EtHC=N-NHC ₃ H ₇ (NO ₂) ₂	b	5.4 ± 0.1	5.0 ± 0.1
<i>i</i> -PrHC=N-NHC ₃ H ₇ (NO ₂) ₂	b	7.6 ± 0.1	4.9 ± 0.1
MeHC=N-NH ϕ	g, i, k, l	5.75 ± 0.05	5.55 ± 0.05
MeHC=N-NH ϕ	m	5.80 ± 0.05	5.60 ± 0.05
EtHC=N-NH ϕ	a	5.2 ± 0.1	5.2 ± 0.1
<i>i</i> -PrHC=N-NH ϕ	a, i, k, n	7.6 ± 0.1	5.0 ± 0.1
MeHC=N-NC ₃ H ₇ NO ₂ (o)	b	5.50 ± 0.05	5.30 ± 0.05
MeHC=N-NHMe	a, i	5.80 ± 0.05	5.50 ± 0.05
MeHC=N-NHMe	k, l	5.80 ± 0.05	5.60 ± 0.05
MeHC=N-NHCONH ₂	b	5.80 ± 0.05	5.50 ± 0.05
MeHC=N-NHCSNH ₂	b	5.80 ± 0.05	5.50 ± 0.05
MeHC=N-OH	a, b, i, k	5.80 ± 0.05	6.30 ± 0.05
MeHC=N-OH	e, g, l	5.75 ± 0.05	6.10 ± 0.05
EtHC=N-OH	a	5.75 ± 0.05	6.10 ± 0.05
EtHC=N-OH	b, k, l	5.75 ± 0.05	5.90 ± 0.05
EtHC=N-OH	g	5.75 ± 0.05	6.00 ± 0.05
<i>i</i> -PrHC=N-OH	a	7.65 ± 0.05	6.65 ± 0.05
<i>i</i> -PrHC=N-OH	g	7.60 ± 0.05	6.15 ± 0.05
<i>i</i> -PrHC=N-OH	k	7.55 ± 0.05	6.30 ± 0.05
<i>i</i> -PrHC=N-OH	l	7.50 ± 0.05	6.0 ± 0.1

^a Neat. ^b Methylene bromide. ^c Nitrobenzene. ^d Dioxane. ^e Pyridine. ^f Dimethylformamide. ^g Acetone. ^h Quinoline. ⁱ Benzene. ^k Carbon tetrachloride. ^l Dimethyl sulfoxide. ^m Methanol. ⁿ Isodurene.

Exceptionally high J_{trans} values for oximes⁴ result in $J_{\text{trans}} > J_{\text{cis}}$ for acetaldoxime and propionaldoxime. We find $J_{\text{C}^{13}\text{H}_\alpha}$ (V) = 162 ± 2 c.p.s. and $J_{\text{C}^{13}\text{H}_\beta}$ (VI) = 174 ± 2 c.p.s. From the dependence of $J_{\text{C}^{13}\text{H}}$ on the % s-character of the carbon atomic orbitals we conclude



that the imino carbon orbital in $\text{C}-\text{H}_\beta$ has more s

(3) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Phys. Chem.*, **64**, 1793 (1960).

(4) Our studies confirm the correctness of oxime assignments by W. P. Phillips, *Ann. N. Y. Acad. Sci.*, **70**, 817 (1958); E. Lustig, *J. Phys. Chem.*, **65**, 491 (1961).