

STRUCTURAL STUDIES BY NUCLEAR MAGNETIC RESONANCE—XI

CONFORMATIONS AND CONFIGURATIONS OF OXIME O-METHYL ETHERS

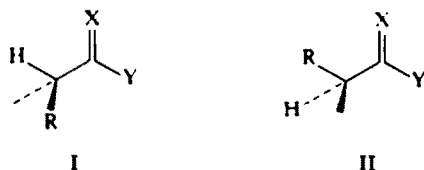
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(Received in U.S.A. 14 June 1966; accepted for publication 19 July 1966)

Abstract—Conformations and configurations were assigned to several aldehyde and ketone oxime O methyl ethers from analysis of their 60-Mc. NMR spectra. Interpretation of the data from the *cis*-isomers (methoxy *cis* to hydrogen) of the aldehyde derivatives in terms of rotamers I and II, whereby a single bond eclipses the double bond, led to the following conclusions: For α -mono-substituted derivatives, when R was varied from methyl to t-butyl, ΔH° for I \rightarrow II varied from +390 to +4,500 cal/mole. A similar range was obtained for α,α -disubstituted derivatives. Interpretation of the data from the *trans*-isomers led to the conclusion that, whereas I is the only significant rotamer for α,α -disubstituted derivatives, for α -mono-substituted I and III are equally important.

INVESTIGATIONS concerning rotational isomerism about single bonds joining sp^3 to sp^2 hybridized carbon atoms have showed that, when X is carbon (Y = hydrogen)³ or oxygen (Y = hydrogen, methyl, ethyl or halogen),⁴ the stable rotamers are I and II, whereby a single bond eclipses the double bond. No studies have been reported when X is a substituted nitrogen.



Our interests in problems arising from restricted rotation about single, double and partial double bonds, and particularly in the general problem of the relative stabilities of I and II as functions of R, X and Y, have led us to examine the NMR spectra of oxime O-methyl ethers (X = NOME). Because of configurational isomerism about the C=N double bond, these compounds are suitable models to study the relative stabilities of I and II not only when the tetrahedral carbon is *cis* to the lone electron pair, but also when it is *cis* to the methoxy group. In the latter case, I and II may be sufficiently destabilized to make II and IV competitive in stability with I and II. Cyclopropanecarboxaldehyde⁵ and ethyl α,α -difluoro- and α,α -dichloroacetates⁶

¹ Fellow of the Alfred P. Sloan Foundation.

² Lubrizol Fellow, 1964-65.

³ A. A. Bothner-By and H. Günther, *Disc. Faraday Soc.* **34**, 127 (1962), and Ref. cited therein.



⁴ G. J. Karabatsos and N. Hsi, *J. Amer. Chem. Soc.* **87**, 2864 (1965), and Ref. cited therein.

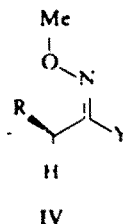
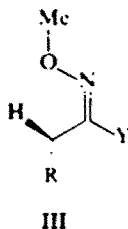
⁵ L. S. Bartell and J. P. Guillory, *J. Chem. Phys.* **43**, 647 (1965). It was suggested, Ref. 4, that in the liquid phase cyclopropanecarboxaldehyde may exist in conformations I and II.

⁶ T. L. Brown, *Spectrochim. Acta* **18**, 1615 (1962).

TABLE I. CHEMICAL SHIFTS (τ -VALUES) OF OXIME O-METHYL ETHERS

R ₁	R ₂	R ₃	NOMe	Solvent	H ₁		H ₂ (CH ₃)		H ₃ (CH ₃)		H ₄ (CH)		H ₅ (CH ₃)		OCH ₃	
					cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans
H		Me		Neat	2.70	3.35	8.27	8.27							6.20	6.27
H		Me		CCl ₄	2.77	3.45	8.25	8.21							6.23	6.32
H		Me		C ₆ H ₆	2.98	3.55	8.47	8.55							6.20	6.26
H		CH ₃ CMes		Neat	2.65	3.39			7.75	7.93					6.18	6.13
H		CH ₃ CMes		CCl ₄	2.73	3.45			7.84	7.99					6.29	6.25
H		CH ₃ CMes		C ₆ H ₆	2.73	3.33			7.77	8.04					6.16	6.13
H		CH ₃ ph		Neat	2.58	3.28			6.37	6.60					6.18	6.13
H		CH ₃ ph		CCl ₄	2.67	3.37			6.40	6.57					6.22	6.13
H		CH ₃ ph		C ₆ H ₆	2.77	3.33			6.42	6.72					6.18	6.12
H		CHMe ₂		Neat	2.77	3.61					6.92	7.57	8.99	8.93	6.20	6.14
H		CHMe ₂		CCl ₄	2.87	3.72					7.03	7.62	8.99	8.93	6.31	6.25
H		CHMe ₂		C ₆ H ₆	2.90	3.67					6.90	7.75	9.17	9.12	6.18	6.17
H		CHEt ₂		Neat	2.98	3.73					7.16	7.92			6.18	6.15
H		CHEt ₂		CCl ₄	2.98	3.80									6.30	6.26
H		CHEt ₂		C ₆ H ₆	2.85	3.73					6.97	8.03			6.18	6.18
H		CH(CMe ₂) ₂		Neat										6.20	6.20	
H		CH(CMe ₂) ₂		CCl ₄	2.83										6.25	6.25
H		CH(CMe ₂) ₂		C ₆ H ₆	2.53										6.20	6.20
H				Neat	3.13	4.15									6.23	6.14
H				CCl ₄	3.03	4.25									6.30	6.21
H				C ₆ H ₆	3.15	4.28									6.21	6.12
H				Neat	2.75	3.53					6.85	7.40			6.23	6.18
H				C ₆ H ₆	2.70	3.53					6.75	7.50			6.17	6.13
H				Neat	2.82	3.65									6.22	6.18

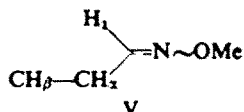
H			2.88	3.73	CCl ₄						6.32	6.27
H				3.62	C ₆ H ₆						6.15	6.13
Me	Me	Neat			CCl ₄	8.22	8.20					6.25
Me	Me	CCl ₄			CCl ₄	8.25	8.21					6.29
Me	Me	C ₆ H ₆			C ₆ H ₆	8.37	8.39					6.18
Me	Et	Neat			CCl ₄	8.24	8.22					6.22
Me	Et	CCl ₄			CCl ₄	8.27	8.23		7.83		6.21	6.30
Me	Et	C ₆ H ₆			C ₆ H ₆	8.31	8.33		7.88		6.28	6.12
Me	Neopentyl	Neat			CCl ₄	8.18	8.16	7.75	7.93	8.96	6.17	6.25
Me	Neopentyl	CCl ₄			CCl ₄	8.23	8.18	7.82	7.98		6.27	6.33
Me	Neopentyl	C ₆ H ₆			C ₆ H ₆	8.20	8.37	7.76	7.97		6.11	6.19
Me	Benzyl	Neat			CCl ₄	8.32	8.33	6.33	6.57		6.12	6.13
Me	Benzyl	CCl ₄			CCl ₄	8.33	8.30	6.39	6.61		6.17	6.17
Me	Benzyl	C ₆ H ₆			C ₆ H ₆	8.35	8.37	6.38	6.63		6.09	6.11
Me	i-Pr	Neat			Neat	8.29	8.29				6.27	6.27
Me	i-Pr	CCl ₄			CCl ₄	8.30	8.29	6.65	7.58	8.96	6.27	6.27
Me	i-Pr	C ₆ H ₆			C ₆ H ₆	8.33	8.38	6.68	7.58	8.94	6.28	6.30
Me	ph	Neat			C ₆ H ₆	7.88		6.54	7.62	9.04	6.18	6.18
Me	ph	CCl ₄			CCl ₄	7.84					6.02	6.18
Me	ph	C ₆ H ₆			C ₆ H ₆	7.92					6.05	6.23
Et	Et	Neat			Neat						6.04	6.18
Et	Et	CCl ₄			CCl ₄							6.22
Et	Et	C ₆ H ₆			C ₆ H ₆							6.29
i-Pr	i-Pr	Neat			CCl ₄							6.13
i-Pr	i-Pr	CCl ₄			C ₆ H ₆							6.23
i-Pr	i-Pr	C ₆ H ₆			Neat			6.95	7.51	8.89	6.30	6.30
i-Pr	i-Pr	CCl ₄			CCl ₄			7.02	7.55	8.92		
i-Pr	i-Pr	C ₆ H ₆			C ₆ H ₆			6.87	7.56	8.89		
i-Pr	Benzyl	Neat			Neat							6.18
i-Pr	Benzyl	CCl ₄			CCl ₄			6.73	7.58	8.98	6.15	6.13
i-Pr	Benzyl	C ₆ H ₆			C ₆ H ₆			6.70	7.60	9.10	6.17	6.17
i-Pr	ph	Neat			CCl ₄			6.47	7.22	8.89	6.18	6.17
i-Pr	ph	CCl ₄			C ₆ H ₆			6.55	7.26	8.90	6.08	6.24
i-Pr	ph	C ₆ H ₆			CCl ₄			6.54	7.24	8.82	6.12	6.28
i-Pr	ph	C ₆ H ₆			C ₆ H ₆					8.83	6.08	6.22



have been reported to have two-fold (I and IV minima) rather than threefold barriers to rotation.

RESULTS

Chemical shifts. Table 1 summarizes the chemical shifts of few representative oxime-O-methylethers. The rotation used to distinguish various protons is shown in V. Each proton is referred to as *cis* or *trans* with respect to the methoxy group. Assign-






ments of hydrogens as *cis* or *trans* are based on arguments given previously. The chemical shifts, calculated from first order spectral analysis, are accurate to ± 0.03 ppm, except those of ethyl, isopropyl, cyclopentyl and diethylcarbinyl groups, whose accuracy is less.

Table 2 summarizes the difference in the chemical shifts of *cis* and *trans* protons, $\Delta\delta$, which are accurate to ± 0.001 ppm. A positive $\Delta\delta$ means that *cis* protons resonate at higher fields than *trans*, a negative reverse. The pertinent points are: (a) H_1 resonates at lower fields when *cis* to the methoxy than when *trans* ($\Delta\delta \sim -0.8$ ppm). (b) In carbon tetrachloride or in neat liquid α -methyl protons resonate at slightly higher fields when *cis* than when *trans*. Addition of benzene causes the signals to cross over. (c) α -Methylene and α -methine protons resonate at appreciably lower fields when *cis* than when *trans*. $\Delta\delta$ values of α -methine protons are comparable in magnitude to those of H_1 . In all cases, except H_1 of the acetaldehyde derivative, $\Delta\delta$ values are more negative in benzene than in carbon tetrachloride.

Table 3 summarizes several $\Delta\nu$ ($\nu_{\text{in benzene}} - \nu_{\text{in carbon tetrachloride}}$) values. A negative $\Delta\nu$ means that a proton resonates at a lower field in benzene than in carbon tetrachloride, a positive reverse. The most striking feature of the data is the lower field absorption of so many protons in benzene, which generally causes upfield shifts, than in carbon tetrachloride. The features pertinent to subsequent discussion are: (a) Benzene shifts both *cis* and *trans* H_1 downfield, except those of the acetaldehyde and cyclopropane carboxaldehyde derivatives; *cis* are shifted more than *trans*. (b) Both *cis* and *trans* α -methyl protons are shifted upfield, except *cis* of the methyl *t*-butyl ketone derivative. (c) Whereas *cis* α -methylene and α -methine protons are shifted downfield, *trans* are shifted upfield. Notable exception is the *trans* α -methine of the *di-t*-butylacetaldehyde derivative. (d) Both *cis* and *trans* β -methyl protons are shifted upfield, except *cis* of the ethyl group of the ethyl *t*-butyl ketone derivative. (e) Methoxy groups are shifted downfield.

⁷ G. J. Karabatos and R. A. Taller, *J. Amer. Chem. Soc.* **86**, 4373 (1964) and previous papers in the series.

TABLE 2. $\delta_{110} - \delta_{100}$ ($\Delta\delta$), IN PPM, OF OXIME O-METHYL ETHERS*

R ₁	R ₂	$\Delta\delta(\text{H}_1)$		$\Delta\delta(\alpha\text{-CH}_2)$		$\Delta\delta(\alpha\text{-CH})$		$\Delta\delta(\beta\text{-CH}_2)$		$\Delta\delta(\text{OCH}_3)$	
		Neat	C ₆ H ₆	Neat	C ₆ H ₆	Neat	C ₆ H ₆	Neat	C ₆ H ₆	Neat	C ₆ H ₆
H	Me	-0.65	-0.57	+0.01	-0.08					0.00	-0.06
H	Et	-0.83								+0.06	
H	Pr	-0.78								+0.08	+0.04
H	(CH ₂) ₄ Me	-0.78	-0.82							+0.07	+0.05
H	i-Bu	-0.74	-0.80							+0.06	+0.04
H	Neopentyl	-0.74			0.25					+0.05	+0.03
H	Benzyl	-0.70			-0.18					+0.05	+0.06
H	i-Pr	-0.84			-0.23					+0.06	+0.01
H	sec-Bu	-0.85	-0.93							+0.05	+0.01
H	CH(Me)CH(Me)Et	0.84								+0.08	0.00
H	sec-Pentyl	-0.83	-0.88							+0.02	0.00
H	CH(Et)(CH ₂) ₃ Me	-0.81								+0.03	0.00
H		-1.02	-1.13							+0.03	0.00
H		-0.78	0.85							+0.05	+0.04
H		-0.83								+0.04	+0.02
Me	Me			+0.02	-0.02						0.00
Me	Et			+0.02	-0.02					+0.04	+0.07
Me	Pr			+0.01	-0.02						-0.01
Me	CH ₂ CHMe ₂			+0.02	-0.09						-0.02
Me	CH ₂ CMc ₂			+0.02	-0.17						-0.05
Me	CH ₂ ph			-0.01	-0.02						-0.08
Me	CHMe ₂			0.00	-0.05						0.01
Me	ph										0.00
Et	Et				-0.10						-0.16
Et	ph										-0.14
n-Pr	ph										-0.17
i-Pr	CHMe ₂										-0.18
i-Pr	CH ₂ ph				-0.24						-0.13
i-Pr	ph										-0.16

* Negative values mean that the *cis* to the methoxy proton resonates at a lower magnetic field than the *trans*; positive the reverse. † *Cis* values for the methoxy group are those of the isomer having OCH₃ *cis* to R₁. ‡ γ -Methyl.

TABLE 3. $\nu_{\text{in benzene}}^{\text{---}\nu_{\text{in carbon tetrachloride}}}$ ($\Delta\nu$)^a IN C/S OF OXIME O-METHYL ETHERS

R ₁	R ₁ R ₂ C=NOMe		Δν(H ₁)		Δν(α-CH ₂)		Δν(α-CH ₂)		Δν(α-CH) ^a		Δν(β-CH ₂)		Δν(OCH ₃) ₂	
	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans	cis	trans
H	+12.6	+6.0	+13.2	20.4									-1.8	-3.6
H		-1.8												
H		-3.0												
H	-5.4	-1.8					+8.4 ^b						-7.8	-6.6
H	-4.8	-1.2					+12.6 ^b						-9.0	-7.8
H		-7.2					+6.6 ^b						-8.4	-7.2
H		-2.4					-4.2						-7.8	-7.2
H		-3.0					+9.0						-2.4	-0.6
H	-7.2	-1.2											-7.8	-4.8
H		-6.0											-8.4	-5.4
H	-7.8	-4.2											-9.0	-6.6
H		-4.8											-7.2	-4.8
H	-18.0												-9.0	-7.8
H	+7.2	+1.8											-3.0	
H		-6.6											-5.4	-5.4
H													-10.2	-8.4
Me														
Me														
Me														
Me														
Me														
Me														
Me														
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i-Pr														
i-Pr														
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^a Positive values mean that resonance in benzene is at higher field; negative the reverse.




^b ν in benzene $\rightarrow \nu$ neat.

The half-widths, 0.6–0.9 c/s, of *cis*-H₁ differ noticeably from those, 1.2–1.7 c/s, of *trans*-H₁ in the temperature range –30° to 90°. Similar broadening and differences observed in formaldoxime O-methyl ether were shown to arise from incomplete quadrupole⁸ wash-out of J_{H₁CN}.

syn | *anti* Isomers. In Table 4 we have summarized *syn* and *anti* percentages, whose accuracy is about ±5%, and free energy differences between these isomers at 40°.

In connection with the relative stabilities of *syn* and *anti* isomers we examined the UV spectra of several oxime O-methyl ethers and we are presenting some pertinent

TABLE 4. *syn* and *anti* PERCENTAGES AND ΔF_{40°} VALUES FOR *syn* → *anti* OF OXIME O-METHYL ETHERS^a

R ₁ R ₂ C=NOMe		% <i>syn</i> ^b	% <i>anti</i>	ΔF _{40°} (Kcal/mole)
R ₁	R ₂			
H	Me	48	52	-0.06
H	Et	54	46	+0.10
H	n-Pr	61	39	0.28
H	(CH ₂) ₃ Me	58	42	0.20
H	i-Bu	58	42	0.20
H	Neopentyl	64	36	0.36
H	Benzyl	51	49	0.02
H	i-Pr	76	24	0.71
H	sec-Bu	71	29	0.55
H	CH(Me)CH(Me)Et	69	31	0.48
H	sec-Pentyl	71	29	0.55
H	CH(Et)(CH ₂) ₃ Me	65	35	0.38
H	CH(CMe ₂) ₂	100	0	
H		54	46	0.10
H		68	32	0.46
H		74	26	0.65
Me	Et	81	19	0.90
Me	n-Pr	72	28	0.58
Me	i-Bu	74	26	0.64
Me	Neopentyl	76	24	0.71
Me	Benzyl	71	29	0.56
Me	i-Pr	86	14	1.1
Me	t-Bu	100	0	
Et	i-Pr	63	37	0.33
Et	t-Bu	100	0	
Me	Ph	98	2	2.4
Et	ph	84	16	1.0
n-Pr	ph	80	20	0.85
i-Pr	ph	39	61	-0.28
Benzyl	i-Pr	60	40	0.25

^a Data from neat liquids.

^b *syn* is the isomer having the methoxy group *cis* to R₁.

⁸ B. L. Shapiro, S. J. Ebersole and R. M. Kopehik, *J. Mol. Spectr.* 11(4), 326 (1963).

data in Table 5. Derivatives of the aliphatic carbonyl compounds show no strong absorption above 220 $m\mu$. In the series alkyl phenyl ketone oxime O-methyl ethers, as the alkyl group is varied from methyl to ethyl to isopropyl, the percentages of the *cis*-phenyl isomers increase from 2% to 16% to 61%, while both λ_{\max} and ϵ decrease.

TABLE 5. UV SPECTRA OF SOME OXIME O-METHYL ETHERS IN CYCLOHEXANE





$R_1R_2C=NOMe$ R_1 R_2	$\lambda_{\max} m\mu$	$\epsilon \times 10^4$
H ph	263	13.8
Me ph	252	10.8
Et ph	248*	8.5
n-Pr ph	248*	7.7
i-Pr ph	236 ^b	5.0

* Weak shoulder at about 262 $m\mu$.

^b Weak shoulder at about 247 $m\mu$.

Spin-spin coupling. Table 6 summarizes the effect of temperature (-30° to 90°) on J_{H_1, H_2} , whose precision from several measurements is estimated as ± 0.03 c/s, of several *cis* H_1 -methoxy isomers, to which we will refer henceforth as the *syn* isomers.

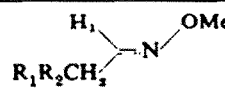



TABLE 6. SPIN-SPIN COUPLING CONSTANTS OF NEAT LIQUID

$R_1R_2CH_2$		$H_1 \text{---} N \text{---} OMe$						
R_1	R_2	-30°	0°	J_{H_1, H_2} 40°	(c.p.s.) 50°	70°	90°	
H	H	5.90	5.90	5.87				
H	Me	5.92	5.87	5.80	5.75			
H	Et	6.05	6.02	5.90	5.80			
H	n-Pentyl	6.10	6.00	5.95	5.90	5.86	5.82	
H	n-Pentyl	6.00*	5.95*	5.90*	5.85*	5.82*		
H	i-Pr	6.40	6.38	6.30	6.20	6.20	6.20	
H	t-Bu	6.85	6.85	6.83	6.80	6.60	6.50	
H	ph	6.60		6.55	6.55	6.50	6.40	
Me	Me	6.18	6.05	6.00	5.90	5.80		
Me	Et	7.10	6.90	6.55	6.45	6.45	6.30	
Me	sec-Bu	7.25	7.20	6.95	6.80	6.80	6.75	
Et	Et	7.95	7.75	7.35	7.20	7.15	7.00	
Et	n-Bu	8.10	7.90	7.65	7.40	7.30	7.20	
t-Bu	t-Bu	10.40*	10.35	10.25	10.15	10.05	10.00	
		8.70	8.50	7.85	7.70	7.55	7.40	
		8.15*	7.75*	7.60*	7.45*	7.20*		
		7.30	7.00	6.55	6.45	6.35	6.20	
		6.15	6.05	5.75	5.65	5.60	5.55	

* From a 10% CCl_4 soln.

All $J_{H_1H_\alpha}$'s decrease with increase in temperature, except $J_{H_1H_\alpha}$ of acetaldehyde oxime O-methyl ether that remains constant. $J_{H_1H_\alpha}$ of the cyclopropanecarboxaldehyde derivative suffers the largest decrease, about 15%, in the range -30° to 90° . These couplings increase with increase of solvent polarity (Table 7), except $J_{H_1H_\alpha}$ of the phenylacetaldehyde derivative that decreases, and $J_{H_1H_\alpha}$ of the acetaldehyde derivative that remains constant.

TABLE 7. EFFECT OF SOLVENT POLARITY ON $J_{H_1H_\alpha}$ OF 

		$J_{H_1H_\alpha}$ (c.p.s.)	
R_1	R_2	cyclohexane (40°)*	acetonitrile (40°)*
H	H	5.88	5.90
H	Me	5.70	5.90
H	Et	5.95	6.15
H	n-Bu	6.00	6.15
H	i-Pr	6.30	6.50
H	t-Bu	6.90	6.90
H	ph	6.65	6.55
Me	Me	5.80	6.05
Me	Et	6.60	6.95
Me	sec-Bu	7.00	7.35
Et	Et	7.35	7.80
Et	n-Bu	7.65	8.05
t-Bu	t-Bu	10.35	10.45
		7.50	8.30
		6.50	7.05
		5.80	6.15

* 10% solns.

Table 8 summarizes the effect of temperature (-30° to 90°) on $J_{H_1H_\alpha}$ of the *trans* H_1 -methoxy isomers, to which we will refer to as the *anti* isomers. Several features of the data are worth noting and comparing with those of the data for the *syn* isomers (Table 6). Firstly, there is an abrupt increase in $J_{H_1H_\alpha}$ in changing from monosubstituted acetaldehyde oxime O-methyl ethers to disubstituted, so that all $J_{H_1H_\alpha}$'s of the disubstituted derivatives are larger than those of the monosubstituted. Secondly, whereas $J_{H_1H_\alpha}$'s of the disubstituted derivatives decrease with increase in temperature, $J_{H_1H_\alpha}$'s of the monosubstituted behave irregularly. And thirdly, whereas the couplings of the disubstituted derivatives increase with increase of solvent polarity (Table 9), those of the monosubstituted decrease slightly or remain unchanged, except $J_{H_1H_\alpha}$ of phenylacetaldehyde oxime O-methyl ether that increases. To summarize: $J_{H_1H_\alpha}$'s of disubstituted acetaldehyde oxime O-methyl ethers behave similarly to those of the *syn* isomers, while those of monosubstituted do not.

TABLE 8. SPIN-SPIN COUPLING CONSTANTS OF NEAT LIQUID







$\begin{array}{c} R_1R_2CH_2 \\ \\ H_1 \\ \\ =N-OMe \end{array}$		$\begin{array}{c} R_1R_2CH_2 \\ \\ H_1 \\ \\ =N-OMe \end{array}$					
R ₁	R ₂	J _{H₁H₂} (c/s)					
		-30°	0°	40°	50°	70°	90°
H	H	5.62	5.50	5.57			
H	Me	5.35	5.48	5.55	5.45		
H	Et	5.40	5.45	5.50	5.45	5.45	
H	n-Pentyl	5.40	5.45	5.50	5.40	5.55	5.50
H	i-Pr	5.42	5.50	5.60	5.55	5.50	5.60
H	t-Bu	5.88	5.91	5.96	5.90	5.95	5.95
H	ph	5.30	5.40	5.50	5.50	5.40	5.45
Me	Me	7.30	7.35	7.35	7.20	7.15	
Me	Et	7.75	7.78	7.65	7.60	7.50	7.45
Me	sec-Bu	8.05	8.10	8.00	7.90	7.90	7.85
Et	Et	8.35	8.25	8.15	8.00	8.00	7.85
Et	n-Bu	8.35	8.35	8.25	8.15	8.10	8.05
		9.10	9.10	9.00	8.75	8.70	8.55
		7.20	7.05	7.00	6.85	6.80	6.75
		7.30	7.23	7.20	7.10	7.05	7.00

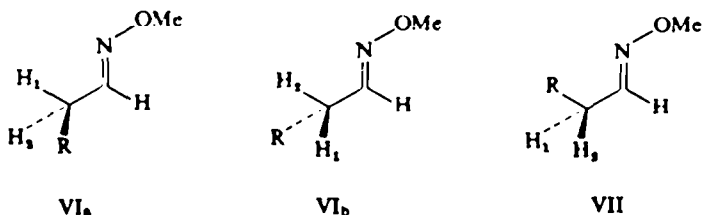
TABLE 9. EFFECT OF SOLVENT POLARITY ON J_{H₁H₂} OF

$\begin{array}{c} R_1R_2CH_2 \\ \\ H_1 \\ \\ =N-OMe \end{array}$		$\begin{array}{c} R_1R_2CH_2 \\ \\ H_1 \\ \\ =N-OMe \end{array}$	
R ₁	R ₂	J _{H₁H₂} (c/s)	
		Cyclohexane (40°) ^a	Acetonitrile (40°) ^a
H	H	5.70	5.60
H	Me	5.50	5.50
H	Et	5.60	5.50
H	n-pentyl	5.60	5.60
H	i-Pr	5.65	5.55
H	t-Bu	6.10	6.00
H	Ph	5.50	5.70
Me	Me	7.30	7.40
Me	Et	7.70	7.80
Me	sec-Bu	8.10	8.25
Et	Et	8.30	8.40
Et	n-Bu	8.20	8.40
		8.80	9.25
		7.00	7.30
		7.20	7.40

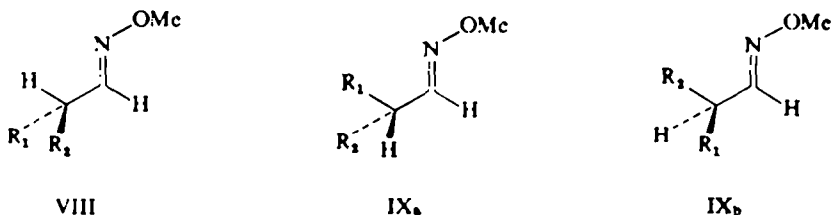
^a 10% solns.

DISCUSSION

Conformations of the syn isomers. Assuming that the stable conformations of the *syn* isomers are eclipsing (I and II), the relative stabilities of rotamers I and II can be qualitatively assessed from the dependence of J_{H_1, H_a} 's on temperature. Assuming $J_t > J_g$, where J_t is the *trans* coupling and J_g the *gauche*, J_{H_1, H_a} of monosubstituted



derivatives should be temperature independent if VI_a, VI_b and VII are energetically equivalent. If VI_a is more stable than VII, the coupling should decrease with increase in temperature; and if less stable, it should increase. Similarly, for disubstituted derivatives the coupling should be temperature independent if VIII, IX_a and IX_b are energetically equivalent. If VIII is more stable than IX_a, the coupling should decrease with increase in temperature; and if less stable, it should increase. We conclude that in all cases examined the more stable rotamer is the one where the hydrogen is eclipsing the double bond.



Enthalpy differences between the two rotamers of individual compounds could be determined by either of two approaches. Eq. (1) expresses the coupling of acetaldehyde oxime O-methyl ether in terms of J_t and J_g . Eq. (2) expresses the coupling

$$J_{\text{obs.}} = \frac{1}{2}(J_t + 2J_g) \quad (1)$$

$$J_{\text{obs.}} = p(J_t + J_g)/2 + (1 - p)J_g \quad (2)$$

$$J_{\text{obs.}} = pJ_t + (1 - p)J_g \quad (3)$$

of the monosubstituted derivatives, where p is the fractional population of VI and $(1 - p)$ that of VII. And Eq. (3) expresses the couplings of the disubstituted derivatives, where p is the fractional population of VIII and $(1 - p)$ that of IX.

A direct approach involves the simultaneous evaluation of J_t , J_g and ΔH° for each substituted acetaldehyde derivative as follows: For monosubstituted derivatives these quantities could be evaluated from Eq. (5) and for disubstituted derivatives from Eq.

(7). This approach requires $\Delta S^\circ = 0$ for the

$$K_{\text{eq. (monosubstituted)}} = 2(1 - p/p) \quad (4)$$

$$\Delta H_{(\text{monoo})}^\circ = -RT \ln (J_t + J_g - 2J_{\text{obs.}})/(J_{\text{obs.}} - J_g) \quad (5)$$

$$K_{\text{eq. (disubstituted)}} = (1 - p)/2p \quad (6)$$

$$\Delta H_{(\text{di})}^\circ = -RT \ln \frac{1}{2}(J_t - J_{\text{obs.}})/(J_{\text{obs.}} - J_g) \quad (7)$$

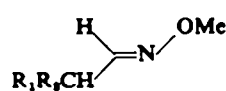
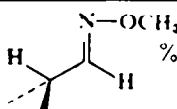




equilibrium between rotamers. This assumption is hardly justified in cases where R is other than methyl; e.g. rotation of a *t*-butyl group should be much more hindered in II than in I.

A second approach involves the evaluation of J_t and J_g independently of ΔH° . If we assumed that *di-t*-butylacetaldehyde oxime O-methyl ether exists solely in VIII, then its $J_{\text{obs.}}$ is J_t . J_g then can be calculated from Eq. (1). These values can be checked by assuming that the *t*-butylacetaldehyde derivative also exists solely in VI. From Eq. (8), which expresses its

$$J_{\text{obs. (tBu)}} = \frac{1}{2}(J_t + J_g) \quad (8)$$

coupling, and (1) we can thus calculate J_t and J_g . Rotamer populations can then be calculated from Eq. (2) and (3), and ΔH° values from plots of $\log K$ vs $1/T$. As mentioned⁴ an error would arise from the assumption that J_t and J_g are the same for the acetaldehyde, monosubstituted acetaldehyde and disubstituted acetaldehyde derivatives. This error could be diminished by applying a 0.4 c/s correction for each

TABLE 10. ROTAMER POPULATIONS OF 

							
R_1	R_2	-30°	0°	40°	50°	70°	90°
H	Me	77	76	74	73		
H	Et	80	79	76	74		
H	<i>n</i> -Pentyl	81	79	78	76	75	74
H	<i>i</i> -Pr	89	88	86	84	84	84
H	<i>t</i> -Bu	100	100		99	94	91
H	ph	88		85	85	83	79
Me	Me	47	45	44	43	42	
Me	Et	58	55	51	50	50	48
Me	<i>sec</i> -Bu	60	59	56	54	54	53
Et	Et	68	66	61	59	58	57
Et	<i>n</i> -Bu	71	68	65	62	60	59
<i>t</i> -Bu	<i>t</i> -Bu	99	98	97	96	95	94
		78	76	68	66	64	62
		71*	66*	64*	63*	59*	
		61	57	51	50	49	47
		46	45	42	40	39	39

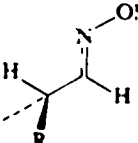



* In 10% soln in CCl_4 .

alkyl or aryl substituent, i.e., by increasing J_{obs} of each monosubstituted derivative by 0.4 c/s and of each disubstituted by 0.8 c/s, as was done with the aldehydes.^{4,10} We thus calculate $J_t = 11.3$ c/s and $J_g = 3.2$ c/s from both *t*-butyl and *di*-*t*-butyl-acetaldehyde oxime O-methyl ethers. The small variation at low temperatures of the coupling constants of these two compounds and the insensitivity of these constants to solvent polarity strengthen the assumption that the two compounds exist mainly in VI and VIII.

In Table 10 are summarized rotamer populations that were calculated from Eqs. (2) and (3). ΔH° values, evaluated from plots of $\log K$ vs $1/T$, are summarized in Table 11. These values are probably reliable to $\pm 30\%$. In addition to errors of probably 5–10% that are introduced by experimental uncertainties in J_{obs} and temperature control, appreciable but presently undeterminable errors may be introduced by disregarding the contributions to J_{obs} from torsional oscillations and excited vibrational states, and by using only one set of J_t and J_g for *all* monosubstituted and one set for *all* disubstituted acetaldehyde derivatives.

The dependence of ΔH° on the α -carbon substituent closely parallels that observed with aldehydes. For example, in the acyclic compounds ΔH° becomes more positive in changing R from methyl to *t*-butyl. ΔH° of the diethyl derivative is more positive

TABLE 11

ΔH° for	ΔH° (cal/mole)
 $RCH_2CH=NOMe$	
R	
Me	+380
Et	+570
n-Pentyl	+590 (~500°)
i-Pr	+650
t-Bu	+4,500
ph	+1,200
$R_1R_2CHCH=NOMe$	
R ₁ R ₂	
Me Me	+300
Et Et	+700
t-Bu t-Bu	+4,400
	+1,200 (~800°)
	+780
	+450

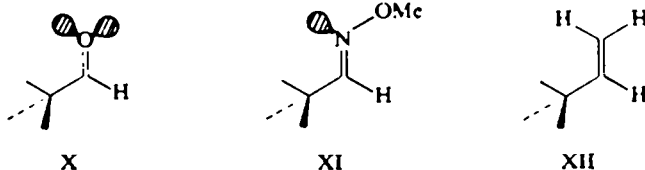
* From 5% soln in CCl_4 .

¹⁰ It is assumed that the substituent effect on J_{H_1, H_α} is the same as was in aliphatic aldehydes. By comparing the J values of the acetaldehyde, propionaldehyde and cyclohexanecarboxaldehyde derivatives (Table 6) we conclude that this effect must be greater than 0.15 c/s.

than that of the monoethyl; that of the cyclohexyl is similar to that of the dimethyl rather than of the diethyl; and that of the cyclopropyl¹¹ is more positive than that of the cyclopentyl, which in turn is more positive than that of the cyclohexyl.¹²

The effect of solvent polarity on rotamer population supports further the proposed conformations. Because of the higher dipole moment of VI over VII and VIII over IX (R = alkyl), the ratios VI|VII and VIII|IX increase (J_{obs} increases) with increase of solvent polarity. As expected,¹² phenylacetaldehyde oxime O-methyl ether shows opposite behavior. The arguments previously applied⁴ against bisecting conformations (III and IV) can also be applied here. The most cogent argument provided by our data against III and IV is the increase of J_{obs} with increase of solvent polarity. Since III would have a higher dipole moment than IV, increase of solvent polarity should decrease J_{obs} (assume $J_c > J_d$).

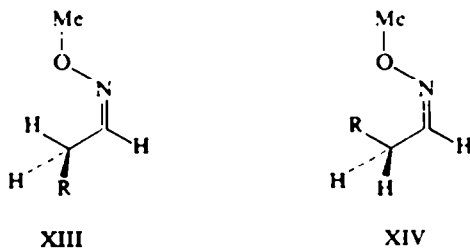
It is worth pointing out that the rotamer populations of the oxime O-methyl ethers closely parallel those of olefins¹³ rather than those of aldehydes,⁴ although from structural considerations (X–XII) the reverse might have been expected. Whereas II



is generally more stable than I for aldehydes, the reverse is true for olefins and oxime O-methyl ethers. Although the source of these differences is not clear, electron density and availability at X might be the controlling factor. This point will be considered in subsequent publications in conjunction with the effect of Z (= NZ) on the relative stabilities of I and II.

Conformations of the anti isomers. Since a quantitative interpretation of the coupling constants of the *anti* isomers is impossible, we will present several qualitative interpretations and point out the limitations of each.

Monosubstituted derivatives. If XIII and XIV were the only rotamers of the *anti*



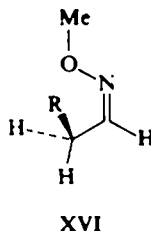
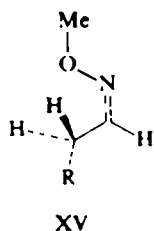
isomers, the coupling constants would increase with increased solvent polarity when R is alkyl and decrease when R is phenyl. The observed trend (Table 9) is opposite.

¹¹ Although we have assumed that the cyclopropyl derivative has three-fold barrier to rotation, our present data do not exclude the possibility that the barrier may be two-fold.

¹² For interpretation of these observations the reader should refer to Ref. 4.

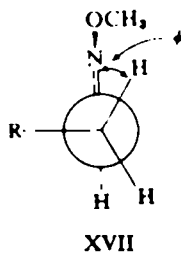
¹³ A. A. Bothner-By, C. Naar-Colin and H. Günther, *J. Amer. Chem. Soc.* **84**, 2748 (1962).

Furthermore, judging from the magnitudes of J_{obs} 's and their dependence on temperature, ΔH° between XIII and XIV would be zero, except when R is t-butyl. Such a conclusion is unreasonable. We are forced therefore to consider XV and XVI.

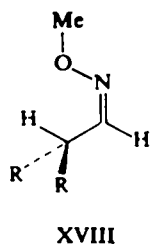


Since XV would have the higher dipole moment and lower coupling, increase of solvent polarity should decrease J_{obs} , except again J_{obs} of the phenylacetaldehyde derivative. The data agree reasonably with this interpretation, although the variation of J_{obs} with solvent polarity is too small. From the magnitudes and temperature dependence of J_{obs} , ΔH° between XV and XVI should be about zero, except when R is t-butyl, in which case XVI would be more stable. Again this conclusion seems unreasonable. The data are best interpreted in terms of XIII and XV as the important rotamers. Since XV would have slightly higher dipole moment than XIII, increased solvent polarity should decrease J_{obs} only slightly. The nondependence of the relative stabilities of the rotamers on R, except when R is t-butyl is also understandable.

We finally wish to point out that our data do not rigorously exclude conformations where ϕ is other than 0° or 60° (XVII).



Disubstituted derivatives. *A priori* considerations lead to the conclusion that, regardless of the size of R, the most stable rotamer should be XVIII. The large J_{obs} and their increase with increased solvent polarity support this conclusion.

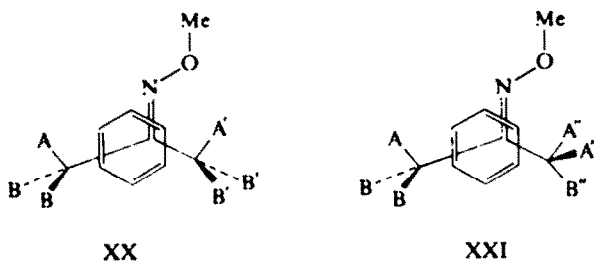


Chemical shifts. As in so many other compounds of the general structure XIX, region A is deshielded with respect to B (both A and B in the plane of the molecule). Our interpretation that XVIII is the most stable rotamer of the *anti* disubstituted



derivatives finds further support in the fact that, whereas *cis* and *trans* α -methyl protons resonate at about the same field, *cis* α -methine protons resonate at appreciably lower fields than *trans*.

Interpretation of solvent effects. The striking feature of the chemical shifts is the effect of benzene on them; i.e. whereas some resonances are shifted upfield, several are shifted downfield (Table 3). Any interpretation of this effect requires specific orientation of benzene by interaction with the solute. The data are adequately interpretable in terms of XX and XXI, whereby the benzene is attracted by the positive



charge on the sp^2 -hybridized carbon and is closer to the group that is *trans* to methoxy. The *s-trans* conformation about the N—O bond is chosen in accordance with formaldoxime¹⁴ and with p—p lone pair electron repulsions.¹⁵ Models XX and XXI require that the methoxy be deshielded in benzene, as is indeed the case. Positions A and A', and to a lesser extent A'' and B'', would be deshielded, whereas B and B' would be shielded. Since *cis*- α -methine protons spend most time in A' it is understandable that they are shifted downfield by benzene. The only *trans*- α -methine that spends all time in A is that of *di-t*-butylacetaldehyde derivative and it is indeed the only *trans*- α -methine that is shifted downfield. Consistent with the proposed models¹⁶ is the small downfield shift of *cis*- α -methylene protons, thus further supporting the conclusions drawn from spin-spin coupling that XIII and XV are significantly populated. Finally, the fact that the only *cis*- α -methyl and *cis*- β -methyl protons shifted downfield by benzene are those of methyl and ethyl *t*-butyl ketone derivatives suggests XXI as the model for these compounds. It is expected that when the *trans* group is *t*-butyl repulsive interactions between B and B' in XX will force the *cis* group to assume a bisecting conformation.

¹⁴ I. N. Levine, *J. Chem. Phys.* **38**, 2326 (1963).

¹⁵ N. L. Owen and N. Sheppard, *Proc. Chem. Soc.* **264** (1963).

¹⁶ Our interpretation should not be construed as implying a one to one solvent-solute complex.

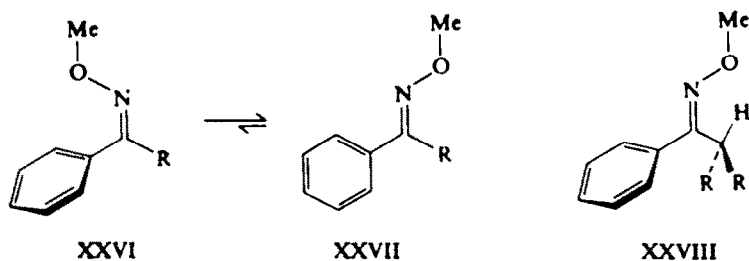
syn-anti *Isomers*. The greater stability of XXII over XXIII is another case demonstrating the importance of attractive forces between two groups, when at



least one group has available polarizable electrons. The greater stability of XXIV over XXV when X = Y = Cl,¹⁷ Br,¹⁸ F,¹⁹ X = Me, Y = Cl,²⁰ Br,²¹ CN²² has been established.



The large dependence of the ratio XXVI|XXVII on R is best understood in terms of methoxy-phenyl interactions in XXVI that force the phenyl out of conjugation



with the C=N, and in terms of phenyl-R interactions in XXVII. As R increases in size the latter interactions force the phenyl out of conjugation with the C=N. Thus, when R is isopropyl complete loss of conjugation (XXVIII) forces the equilibrium in favor of XXVI. The UV spectra amply justify this argument.

EXPERIMENTAL

Preparation of oxime O-methyl ethers. To an aqueous soln of 0.1 mole aldehyde or ketone, 0.11 mole methoxylamine hydrochloride and 0.11 mole AcONa \cdot 3H₂O was added 95% EtOH until the soln cleared. After 20 hr reflux the soln was extracted 3 times with ether. The ether layer was washed 3 times with 5% NaHCO₃ aq, once with water and dried. Distillation gave the oxime ether in 50–70% yield. The oxime ethers are clear, sweet smelling liquids that boil 10–20° higher than the corresponding carbonyl compounds.

NMR spectra were determined at 60 Mc. on a Model A-60 spectrometer (Varian Associated Palo Alto, Calif.). Undegassed solutions were used with TMS as internal reference.

UV spectra were taken with a Cary 14 recording spectrophotometer.

Acknowledgement—We thank the United States Atomic Energy Commission for financial support Grant COO-1189-15.

¹⁷ K. S. Pitzer and J. L. Hollenberg, *J. Amer. Chem. Soc.* **76**, 1493 (1954).

¹⁸ J. M. Dowling, P. G. Puranik, A. G. Meister and S. I. Miller, *J. Chem. Phys.* **26**, 233 (1957).

¹⁹ N. C. Craig and E. A. Entemann, *J. Amer. Chem. Soc.* **83**, 3047 (1961).

²⁰ R. A. Beaudet, *J. Chem. Phys.* **40**, 2705 (1964).

²¹ P. S. Skell and R. G. Allen, *J. Amer. Chem. Soc.* **80**, 5997 (1958).

²² J. N. Butler and R. D. McAlpine, *Canad. J. Chem.* **41**, 2487 (1963).