Carbon-13 T_1 Study of Aldehydes and Aldehyde Oximes

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The ^{13}C spin lattice (T_1) parameters for some aldehydes and their oxime derivatives have been examined and interpreted in terms of self association and segmental motion. The strength of the hydrogen bonding in the oximes was examined by a temperature-dependence study of T_1. Some evidence was found to support an earlier proposal that the *E* (*anti*) isomer participates less effectively in hydrogen bonding than the *Z* (*syn*) isomer.

OXIMES have been the subject of many studies, in particular those related to the determination of structural details [1-4] and self association.[5-9] Traditionally, i.r. Raman, and ^1H n.m.r. spectroscopy have been the main tools used in such investigations. More recently ^{13}C and ^{15}N nuclear magnetic resonance spectroscopy [10-15] have been employed. Both ^{13}C and ^{15}N chemical shifts are sensitive to the geometry of the molecule and are different for the two geometric isomers of aldehyde oximes (Figure 1).

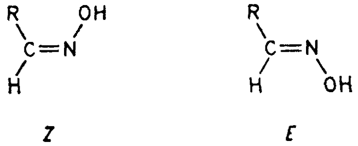


FIGURE 1 Geometric isomers of aldehyde and ketone oximes

In measuring isomer ratios from ^{13}C or ^{15}N spectra, differences between the spin–lattice relaxation times (T_1) and nuclear Overhauser effects (n.O.e) between the isomers can cause anomalous peak intensities. Roberts *et al.*[13] have used relaxation reagents to overcome this problem.

Whilst T_1 variations are a nuisance in determining isomer ratios, they potentially contain information about the relative importance of hydrogen-bonded interactions involving the two isomers. Thus the dipolar contribution (T_1^{DD}) to T_1 is a function of molecular mobility; association *via* hydrogen bonding decreases the mobility of the molecule as a whole, due to its increased effective mass. Information about hydrogen bonding in oximes is of interest because Caldeira and Gil [9] have explained the anomalous isomer ratio (*ca.* 65 : 35 in favour of isomer *Z*) for acetaldehyde oxime in terms of decreased participation in hydrogen bonding by isomer *E*. This is supposed to arise because there is steric hindrance between the methyl group and the second oxime molecule (see Figure 2).

We report here the room temperature ^{13}C T_1 values of several aldehydes and their oxime derivatives and the variation with temperature of T_1 values for the oximes. The results are discussed in terms of the extent of hydrogen bonding in the two isomers of the oximes and segmental motion along the carbon chains.

EXPERIMENTAL

Aldehydes were obtained from commercial sources and purified in the appropriate manner prior to investigation by n.m.r. spectroscopy. Oximes were prepared from the aldehydes and a 20% excess of hydroxylamine hydrochloride in 15% aqueous sodium hydroxide at 60—70 °C. The oximes were distilled under reduced pressure or recrystallised, as appropriate, before investigation by n.m.r. spectroscopy.

Proton-decoupled ^{13}C n.m.r. spectra at natural abundance were obtained on a Varian CFT 20 instrument using an 8-mm variable-temperature probe. For routine spectra at room temperature samples were diluted to 1.5M with $CDCl_3$ and $SiMe_4$ was used as an internal reference. In the variable-temperature experiments a saturated solution of the oxime in $CDCl_3$ or the pure liquid oxime were used. In the first case the solvent was used as the lock-reference signal, and in the second an external deuteriated solvent in a concentric capillary tube was used. The aldehyde solutions were purged with N_2 gas to remove dissolved oxygen. The oxime carbons, having T_1 values considerably less than 20 s are little affected by the small amounts of dissolved oxygen that might be present.

The ^{13}C T_1 values for protonated carbon atoms were obtained using the fast inversion-recovery pulse sequence [16] for the oximes and the progressive saturation sequence [17] for the more slowly relaxing aldehydes. T_1 Values were calculated from the slope of the semi-logarithmic plot of ($I_\infty - I_\tau$) against τ. Values of E_A, the activation energy governing the temperature dependence of T_1, were obtained from an unweighted least-squares analysis of the dependence of $\ln T_1$ for a given carbon atom on the reciprocal of the absolute temperature. This treatment assumes a constant percentage deviation in T_1 which is calculated in the analysis.

Nuclear Overhauser effects were obtained from the ratio of peak intensities (measured by integration) in the presence of proton decoupling to those in the absence of decoupling.

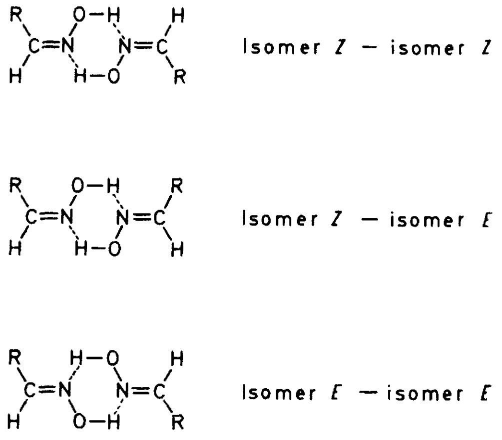
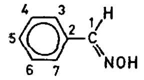
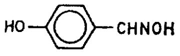
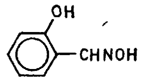
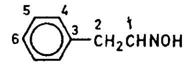


FIGURE 2 Self association in aldehyde oximes

TABLE 1

^{13}C Shifts for some aromatic aldehyde oximes: values given in p.p.m. from $SiMe_4$ *

Compounds		^{13}C Shift						
		C-1	C-2	C-3	C-4	C-5	C-6	C-7
		151.1 (40.9)	132.0 (4.4)	128.9 (0.5)	127.4 (1.5)	130.2 (4.0)		
		149.6 (41.3)	125.0 (5.3)	128.9 (3.8)	116.6 (0.0)	159.1 (4.8)		
		152.9 (43.8)	116.6 (4.4)	156.7 (4.7)	116.6 (0.8)	131.3 (5.4)	120.1 (−0.5)	130.8 (2.8)
	Z	150.9	31.7	136.3	128.9	128.9	126.9	
	E	150.9	35.9	136.8	128.9	128.9	126.7	

* $\delta_{aldehyde} - \delta_{oxime}$ in parentheses.

The gated decoupling facility was used for the latter set of measurements. A pulse delay of at least ten times the longest T_1 value was used.

RESULTS AND DISCUSSION

Chemical Shifts.—The ^{13}C chemical shifts for most of the aldehydes and oximes examined in this study have been reported previously.[13] Chemical shifts for the aromatic oximes which were not included in the earlier report are given in Table 1, together with the observed difference in shift from the corresponding aldehyde. The ^{13}C chemical shifts are also given for phenylacetaldehyde oxime, since our values differ from the earlier ones [13] in that the chemical shifts of both C-3 and C-6 were found to be slightly different in isomers Z and E.

Spin–Lattice Relaxation and Nuclear Overhauser Effects.—The values of the nuclear Overhauser effects for the oximes are given in Table 2. The percentage mean derivation, σ_N, was calculated for the n.O.e. of each carbon, and pooling the values of σ_N gives an overall value of 8% as the uncertainty of an individual estimate of the n.O.e. The maximum value [18] for a proton-decoupled carbon nucleus is 2.987 when the dipole–dipole mechanism is the only significant contribution to the ^{13}C spin-lattice relaxation, the dipolar contribution to T_1 being related to the n.O.e. by expression (1).

TABLE 2

N.O.e. for oximes

	C-1	C-2	C-3	C-4	C-5
MeCHNOH Z	2.7	2.3			
MeCHNON E	2.6	2.7			
EtCHNOH Z	2.7	2.7	2.5		
EtCHNOH E	2.9	2.8	2.7		
PrCHNOH Z	2.6	3.0	2.9	2.8	
PrCHNON E	2.8	2.9	2.7	2.9	
PhCHNOH E	3.1		2.8	2.8	3.0

$$T_1^{DD} = 1.987\ T_1/(\text{n.O.e.} - 1) \qquad (1)$$

The low values of the n.O.e. for C-1 in both isomers of acetaldehyde oxime and Z isomers of propionaldehyde oxime and butyraldehyde oxime are most probably due to paramagnetic relaxation caused by traces of metal ions in solution; this has been shown to be significant in ^{15}N T_1 measurements of oximes.[15,19] Since co-ordination of the metal undoubtably occurs on the nitrogen or oxygen atoms, only C-1 is sufficiently close to the paramagnetic centre to be relaxed by this mechanism. The only other contribution to T_1 which might be significant in these molecules is spin rotation (T_1^{SR}), and that is most likely to be observed for the methyl groups of the smallest derivatives, acetaldehyde oxime and propionaldehyde oxime. The particularly low n.O.e. values for the methyl carbons of the Z isomers of these oximes indicate appreciable T_1^{SR} contributions due to the effective free rotation of these groups [4] as discussed below.

The room temperature T_1 values for the aldehydes and oximes are given in Table 3. In all cases studied the T_1 values for the aldehydes are longer by a factor of 2—8 than those for the corresponding oximes. This is understandable if there is extensive hydrogen bonding in the oximes, but not the aldehydes. Association by hydrogen bonding increases the effective mass and volume of the molecular unit, and this slows down the molecular rotational diffusion and increases the rot-

TABLE 3

Room temperature T_1 values in seconds for aldehydes and oximes

	C-1	C-2	C-3	C-4	C-5	C-6	C-7
MeCNO	21	26					
MeCHNOH Z	5.3	10.3					
MeCHNOH E	5.2	8.6					
Et_2CHO	*a*	28	23				
EtCHNOH Z	3.7	5.5	5.4				
EtCHNOH E	3.8	5.2	4.2				
PrCHO	*a*	16	21	16			
PrCHNOH Z	2.1	2.8	3.7	4.4			
PrCHNOH E	2.7	2.6	3.5	4.3			
Me_2CHCHO	*a*	32.7	18				
$Me_2CHCHNOH$ Z	2.3	3.5	2.2				
$Me_2CHCHNOH$ E	2.0	3.8	2.5				
PhCHO	13	*a*	11	11	8.5		
PhCHNOH E	1.5	*a*	1.3	1.4	0.65		
p-$HOC_6H_4\cdot CHO$	4.0	*a*	3.5	3.5	*a*		
p-$HOC_6H_4\cdot CHNOH$ E	2.1	*a*	1.7	1.6	*a*		
o-$HOC_6H_4\cdot CHNOH$ E	1.4	*a*	*a*		0.90	1.2	1.5
$PhCH_2CHNOH$ Z	1.5	1.8	*a*	3.8	3.8	1.2 [b]	
$PhCH_2CHNOH$ E		1.1	*a*				

[a] Too long to measure. [b] ^{13}C Resonances for the two isomers are coincident.

ational diffusion time constant, τ_c. An increase in τ_c causes a decrease in T_1^{DD} by virtue of the relationship (2),[20] which is appropriate for purely dipolar $^{13}C\{^1H\}$

$$NT_1^{DD} = \frac{1}{h^2\gamma_C^2\gamma_H^2 r_{C-H}^6\tau_c} \qquad (2)$$

relaxation in an isotropically reorienting molecule at the limit of extreme narrowing (N is the number of protons attached to the relaxing nucleus, γ_C,γ_H are the magnetogyric ratios of carbon and hydrogen, respectively and, r_{C-H} is the carbon–hydrogen bond distance). Unfortunately the change in T_1^{DD} is not simply related to the change in molecular mass and volume, but is also dependent on the microviscosity ($f_r\eta$) of the medium according to Gierer and Wirtz[21] modification of the Stokes–Einstein[22] expression [equation (3) in which

$$\tau_c = \frac{V_m{}^* f_r \eta}{kT} \qquad (3)$$

$V_m{}^*$ is the molecular volume, T the absolute temperture, k Boltzmann's constant, η the macroscopic viscosity, and f_r the microviscosity factor]. The dependence on the unknown microviscosity factor means that values of T_1^{DD} cannot be used to compare the extent of hydrogen bonding in different solutions. However it is valid to use T_1^{DD} values to compare hydrogen bonding in isomers of an oxime present in the same solution. In practice, T_1^{DD} values for corresponding carbon atoms in different isomers of a given oxime were found to be the same, within experimental error, except for C-1 of butyraldehyde oxime [T_1^{DD} = 2.6(Z); 3.0(E)], C-2 of acetaldehyde oxime [T_1^{DD} = 15.7(Z); 10.1(E)], and C-3 of propionaldehyde oxime [T_1^{DD} = 7.2(Z); 4.9(E)]. Only the results for butyraldehyde oxime reflect hydrogen-bonding difference; the results for the other two compounds are again indicative of methyl group rotation.

The results for butyraldehyde oxime suggest that in this case hydrogen bonding is less important for isomer E. Presumably, this is due to steric hindrance between the alkyl group and the second oxime molecule, as Caldeira and Gil[9] suggested for acetaldehyde oxime. That the effect is not noticeable in acetaldehyde oxime or propionaldehyde oxime suggests it may be less important than Caldeira and Gil believed, requiring the presence of a bulky alkyl group before it is detectable. Caldeira and Gil[9] mostly based their conclusions on changes in the $E:Z$ isomer ratio of acetaldehyde oxime on changing the temperature, solvent, or concentration of the oxime solution. Both their approach and ours rely on observations of differences which are unfortunately close to experimental error.

In Z-acetaldehyde oxime T_1^{DD} for the methyl carbon is 2.5 times the value for the methine carbon; the corresponding ratio in the E isomer is 1.6. Similar effects are shown in propionaldehyde oxime where the ratios are 1.7 for the Z isomer and 1.2 for the E isomer. Comparison with the theoretical ratios of 0.33 for a completely rigid molecule[20] and 3.0 for a completely freely rotating methyl group[23] indicates that independent methyl group rotation is important in all these oximes, but more pronounced in the Z isomers. This is in agreement with the observed n.O.e. values and is consistent with a microwave study[4] of acetaldehyde oxime in which the barrier to methyl group rotation was found

TABLE 4

Dependence of oxime T_1 values on temperature

MeCHNOH Z	C-1	C-2	C-3	C-4	C-5
64 °C	11.3	24.1			
48	7.40	10.4			
33	5.25	8.66			
18	2.99	6.45			
10	2.66	5.25			
E_A/kJ mol^{-1}	21.8	20.1			
	±1.3	±3.8			
σ_T	4.7%	14%			
MeCHNOH E					
64 °C	12.8	22.2			
48	7.19	10.2			
33	4.47	7.51			
18	3.15	5.99			
10	2.46	4.73			
E_A/kJ mol^{-1}	23.8	20.9			
	±1.7	±3.3			
σ_T	7.0%	14%			
EtCHNOH Z					
80 °C	7.84	6.58	8.23		
60	4.78	5.98	5.66		
40	3.56	4.96	5.16		
20	1.76	2.59	4.50		
E_A/kJ mol^{-1}	20.5	13.0	7.9		
	±2.1	±3.3	±2.1		
σ_T	6.1%	13%	7.4%		
EtCHNOH E					
80 °C	5.16	6.95	6.43		
60	5.30	6.81	6.01		
40	4.22	5.21	4.71		
20	1.85	3.11	2.93		
E_A/kJ mol^{-1}	14.6	11.7	11.3		
	±5.4	±2.9	±2.5		
σ_T	21%	11%	8.9%		
PrCHNOH Z					
95 °C	9.91	8.09	9.61	13.2	
81	5.91	6.76	7.29	9.74	
67	3.84	4.60	5.60	7.36	
49	2.78	2.98	4.74	5.66	
35	1.38	1.75	2.77	4.18	
16	0.587	0.996	1.52	2.15	
E_A/kJ mol^{-1}	30.5	24.3	20.1	19.2	
	±1.7	±0.8	±1.7	±1.3	
σ_T	8.2%	4.6%	6.8%	5.9%	
PrCHNOH E					
95 °C	5.68	8.11	9.65	9.48	
81	6.21	6.24	7.09	9.39	
67	3.94	4.39	5.08	6.89	
49	2.45	2.87	3.96	5.87	
35	1.43	1.79	2.52	3.24	
16	0.641	0.922	1.28	2.53	
E_A/kJ mol^{-1}	25.9	24.2	21.7	16.3	
	±2.5	±0.4	±1.3	±1.7	
σ_T	16%	2.6%	5.8%	9.3%	
PhCHNOH E					
80 °C	2.62	[a]	3.06	3.35	2.11
60	1.52		1.46	1.87	0.95
40	0.98		1.09	1.12	0.75
20	0.40		0.45	0.50	0.29
E_A/kJ mol^{-1}	26.4		25.9	26.8	2.68
	±2.1		±3.3	±1.3	±3.8
σ_T	6.9%		11%	3.5%	13%

[a] Too long to be measured.

to be 7 677 ± 209 *J* mol^{-1} in isomer *E* and only 1 568 ± 125 *J* mol^{-1} in isomer *Z*. Levy and Nelson[10] have observed differences in T_1 values for the C-1 and C-3 carbon atoms in acetone oxime and the C-1 methyl carbons in the two isomers of ethyl methyl ketone oxime. They suggested that when the methyl group is *anti* to the NO*H* group (*e.g.* in isomer *E*) a conformational well is available for methyl rotation. This is not true when the methyl group is *syn* to the NO*H* group (*e.g.* isomer *Z*) and the methyl group spins more freely, giving a longer T_1 value. Our observation of this effect in propionaldehyde oxime contrasts with the experience of Levy and Nelson[10] who found no significant difference in the T_1 values of the ethyl carbons in the two isomers of ethyl methyl ketone oxime.

In the aromatic aldehydes and oximes and in phenylacetaldehyde oxime there is evidence of phenyl-ring rotation about an axis through C-2 and C-5 (C-3 and C-6 in phenylacetaldehyde oxime). Using the equation of Allerhand *et al.*,[24] the tumbling ratio, ρ, for phenyl group rotation can be calculated from the ratio of the average T_1 for the *ortho* and *meta* carbon atoms divided by the T_1 for the *para* carbon atom. The value of ρ is 1.9 for benzaldehyde, 4.7 for benzaldehyde oxime, 2.6 for *o*-hydroxybenzaldehyde oxime, and 9.3 for both isomers of phenylacetaldehyde oxime. The difference in T_1 values for the CH_2 group of the two phenylacetaldehyde oxime isomers suggests different degrees of segmental motion of the benzylic moieties. This is not detectable in the aromatic ring because of the coincidences in chemical shift. The results in Table 3 show that independent segmental motion along the carbon chain is more important in the aliphatic oximes than their parent aldehydes. For example T_1^{DD} values of the methine carbons in the oximes are less than or equal to those of the methylene carbons, whereas in the aldehydes the methine carbon relaxation times are longer than those of the methylene carbons. For a completely rigid molecule T_1^{DD} for the CH carbon should be twice that for the CH_2 carbon. The apparently decreased segmental motion in the aldehydes is probably due to their increased rate of molecular tumbling; as τ_c for rotational diffusion becomes shorter, independent motions such as segmental and methyl group rotation become less apparent.[20]

The activation energies obtained from the variation of T_1 values with temperature are given in Table 4. Because the n.O.e. values were found to be independent of temperature over the range studied, it was not necessary to specifically calculate the dipolar contribution (T_1^{DD}) to obtain the slope of the rate–temperature plot. The activation energies provide a measure of the resistance to molecular reorientation by both internal and intermolecular motions. When molecular association *via* hydrogen bonding is present, some modes of molecular motion require disruption of the hydrogen bonds prior to molecular reorientation. This is reflected in an increased value for the activation energy. For the oximes studied here the E_a values for the aldehydic (C-1) carbon atoms fall in the range 15 ± 5 to 31 ± 2 kJ mol^{-1} which is characteristic of hydrogen-bonded systems.[25,26] For a given aliphatic oxime isomer, E_A decreases monotonically along the carbon chain as lower energy internal modes of reorientation such as segmental motion and methyl group rotation become appreciable. As with T_1 values, E_A values can only be compared meaningfully between the isomers of a single oxime. In general, E_A values for comparable carbon atoms are the same within experimental error for the two isomers, but butyraldehyde oxime is once more the exception. For this oxime a significantly lower E_A for C-1 of isomer *E* reinforces the idea that this isomer participates less in hydrogen bonding.

In summary, we have found several features of the ^{13}C spin relaxation of oximes that lend support to other evidence of a considerable degree of hydrogen-bonding between the nitrogen lone pair and the hydroxy-proton of a neighbouring molecule. These include the relatively large E_A values for molecular reorientation characteristic of other hydrogen-bonded systems;[26] short T_1 values compared to the parent aldehydes, and segmental motion characteristic of aliphatic molecules anchored at one end. We have not been able to confirm the contention of Caldeira and Gil[9] that self-association is more extensive in one isomer than the other for acetaldehyde oxime, however this effect should and does appear to be more pronounced in butyraldehyde oxime.

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