CONFORMATION OF 5-NITRO-TETRAHYDRO-1,3-OXAZINES BY N.M.R. AND DIPOLE MOMENTS*

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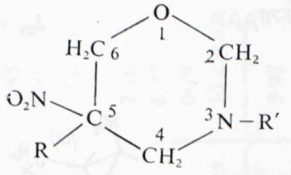
Abstract—N.M.R. and dipole moment data indicate that the molecules of 5-nitro-tetrahydro-1,3-oxazines substituted with alkyls at the C_5 and nitrogen atoms exist in the chair conformation with the axial nitro group. The position of the alkyl at the nitrogen atom varies: Me and Et are axial, while t-Bu and cyclohexyl are equatorial. Substitution of the hydrogen atom for an alkyl at the C_5 results in rapid ring inversion at room temperature.

PREVIOUS dipole moment study[1] on 5-nitrotetrahydro-1,3-oxazines



where R = simple alkyl and R′ = cyclohexyl, indicated that the molecules exist in the chair conformation with the nitro and cyclohexyl groups axial and equatorial, respectively. Further investigations on this class of compounds by means of N.M.R. and dipole moments led to conformational assignments for much larger variety of substituents.

The N.M.R. spectra (60 Mc) of the compounds examined are presented in Table 1 and Fig. 1 (the ring methylene groups are arbitrarily designated by the letters: α, β and γ).

If R = alkyl, the N.M.R. spectrum of the ring protons consists of three quartets, each corresponding to an individual methylene group in the ring (Fig. 1). The quartets indicate the presence of three AB two-spin systems, resulting from non-equivalence of the protons within each methylene group.

In the spectra of the compounds with R = H, the quartets collapse and the only observable splitting results from spin–spin interactions of the α- and β-methylene groups with the hydrogen atom at the C_5.

* Paper LXVII in the series "Aliphatic Nitro Compounds."

[1] D. Gürne and T. Urbański, *J. Chem. Soc.* 1912 (1959); *Roczniki Chem.* **34**, 881 (1960).

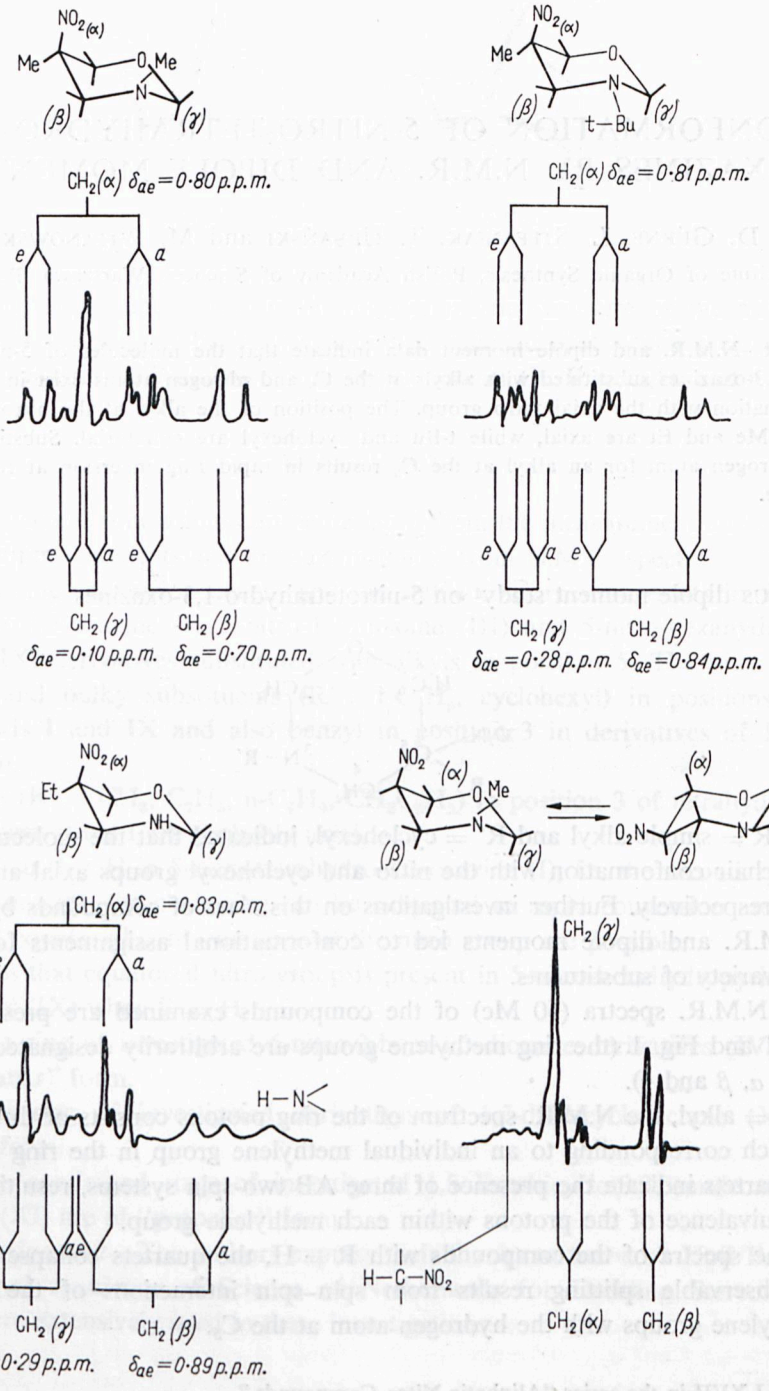
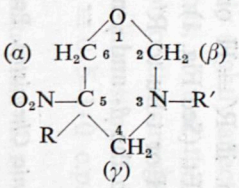

NO2(α)
Me
O Me
N
(β)
(γ)
CH2(α) δae=0·80 p.p.m.
e
a
CH2 (γ)
δae=0·10 p.p.m.
CH2 (β)
δae=0·70 p.p.m.
NO2(α)
Me
O
N
t—Bu
(β)
(γ)
CH2(α) δae=0·81 p.p.m.
CH2 (γ)
δae=0·28 p.p.m.
CH2 (β)
δae=0·84 p.p.m.
NO2(α)
Et
O
NH
(β)
(γ)
CH2(α) δae=0·83 p.p.m.
H—N
CH2 (γ)
δae=0·29 p.p.m.
CH2 (β)
δae=0·89 p.p.m.
NO2
(α)
O Me
N
(β)
(γ)
O2N
Me
H—C—NO2
CH2 (γ)
CH2(α)
CH2(β)

FIG. 1.

TABLE 1. N.M.R. SPECTRA OF 5-NITRO-TETRAHYDRO-1,3-OXAZINES

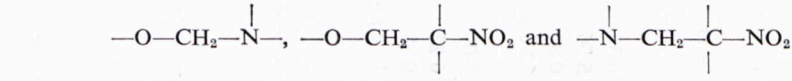
(τ — value in p.p.m.; *a* — axial, *e* — equatorial, *J* — coupling constant in c.p.s.)



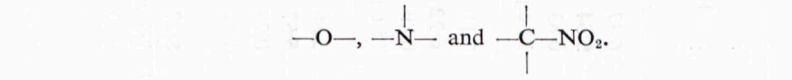
	R	—CH_3	—CH_2CH_3	—CH_3	—CH_3	—CH_2CH_3	—$CH_2CH_2CH_3$	—H	—H
	R′	—CH_3	—CH_3	—CH_2CH_3	—C(—CH_3)(—CH_3)—CH_3	—H	—H	—CH_3	—$CH_2C_6H_5$
α–CH_2	*a*	6·43	6·42	6·43	6·51	6·37	6·38		
	e	**5·63**	**5·62**	**5·55**	**5·70**	**5·54**	**5·56**	5·95	5·90
	δ_{ae}	0·80	0·80	0·88	0·81	0·83	0·82		
	J	12 c.p.s.	12 c.p.s.	12 c.p.s.	12 c.p.s.	12 c.p.s.	12 c.p.s.		
β–CH_2	*a*	7·22	7·20	7·16	7·27	7·11	7·09		
	e	**6·52**	**6·56**	**6·37**	**6·42**	**6·22**	**6·21**	6·63	6·55
	δ_{ae}	0·70	0·64	0·79	0·85	0·89	0·88		
	J	12·5 c.p.s.	12 c.p.s.	13 c.p.s.	12·5 c.p.s.	15 c.p.s.	15 c.p.s.		
γ–CH_2	*a*	6·05	6·05	5·97	5·96	5·86	~5·80 (broadened)	5·83	5·72
	e	**5·95**	**5·95**	**5·79**	**5·68**	**5·57**			
	δ_e	0·10	0·10	0·18	0·28	0·29			
	J	9 c.p.s.	9 c.p.s.	9 c.p.s.	9 c.p.s.	10 c.p.s.			
R		8·51	8·15 *J*=7·3 c.p.s. 9·13	8·53	8·50	8·27 *J*=7·3 c.p.s. 9·13	8·77—8·28 9·02	5·5	5·5
R′		7·66	7·68	7·43 *J*=7·1c.p.s. ·93	8·87	7·63	7·77	7·47	6·10 2·70

The conclusion is that, if R = alkyl, the conformation of the ring is fixed, but if R = H, rapid inversion of the ring occurs and results in averaging the signals within each methylene group.

The spectral assignments for each individual methylene group are based on the spin–spin interaction effects observed in compounds with alternatively R = H and R′ = H (Fig. 1). In the latter case, only the broadening of the signals of the neighbouring methylene group is observed because of the exchange of the NH protons between the molecules. The relative positions of the signals are



going upfields, which is in agreement with what should be expected from the deshielding effect, decreasing in the series:



Conformational assignments from the N.M.R. spectra are based on the relative chemical shifts between the signals within each methylene group in the ring. According to the existing data[2] on the effect of diamagnetic anisotropy of single bonds in cyclohexane in the chair conformation, the signal of an axial proton should be about 0·40 p.p.m. upfields relative to that of the corresponding equatorial proton. The diamagnetic anisotropies of C—N and C—O bonds should be smaller but of the same order of magnitude as that of the C—C bond. The relative chemical shift within an axial-equatorial pair of protons (δ_{ae}) should not be affected by a neighbouring equatorial substituent since it is symmetrically disposed with respect to the two protons. An axial substituent at the neighbouring carbon atom should change δ_{ae}; if it is an alkyl, the expected effect is a substantial decrease in δ_{ae}.

The values of δ_{ae} in the N.M.R. spectra of the compounds examined here (Table 1) show some important regularities:

(i) the δ_{ae} values for the α- and β-methylene groups are much larger than the value for the γ-methylene group.

(ii) δ_{ae} for the α-methylene groups is fairly constant at 0·84±0·04 p.p.m.

(iii) δ_{ae} for the β-methylene groups is 0·87±0·02 p.p.m. if R′ = H or t-Bu, but decreases to 0·72±0·08 p.p.m. if R′ = Me or Et. (See Fig. 1).

(iv) δ_{ae} for the γ-methylene group is 0·28–0·29 p.p.m. if R′ = H or t-Bu, and decreases to 0·14±0·04 p.p.m. if R′ = Me or Et. (See Fig. 1).

(v) the average decrease in δ_{ae} on passing from R′ = H or t-Bu to R′ = Me or Et is nearly identical (0·15–0·16 p.p.m.) for both the β- and γ-methylene groups.

[2] L. M. Jackman, *Applications of* N.M.R. *Spectroscopy in Organic Chemistry*. Pergamon Press, London (1959).

None of the twelve theoretically possible boat forms[1] can account for these regularities. However, assumption of the chair conformation of the ring leads to the following conformational assignments:

(a) the NO_2 group is axial in each case (R = alkyl is equatorial).

(b) R′ = Me, Et is axial, while R′ = t-Bu is equatorial. This is presented in Fig. 2.

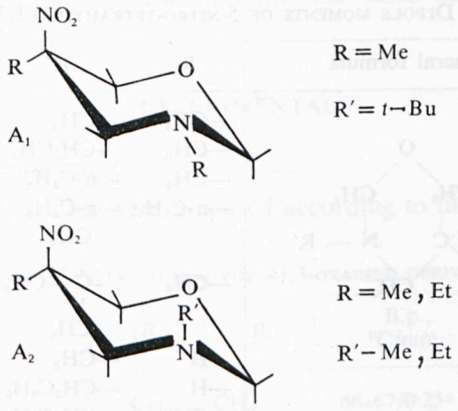


FIG. 2.

The δ_{ae} of 0·28 p.p.m. for the γ-methylene group if R′ = H or an equatorial alkyl t-Bu here may be regarded as the normal value for the tetrahydrooxazine ring, because the other substituents are remote and should not exert any appreciable effect; the equatorial alkyl should not affect the δ_{ae}, either.

An axial substituent R′ (methyl or ethyl) decreases equally the values of δ_{ae} for the γ- and β-methylene groups. In neither case is the δ_{ae} for the α-methylene group appreciably affected.

The high values of δ_{ae} for both the α- and β-methylene groups can be explained only by the presence of an axial nitro group. Should the reverse be true, the δ_{ae} would have been lowered to about 0·15 p.p.m. by the axial alkyl, as it is the case with the γ-methylene group quartet. Nearly identical δ_{ae} values for both the α- and β-methylene groups suggest that the nitro group is oriented symmetrically with respect to these groups. Since the over-all effect is a remarkable increase in δ_{ae} and the equatorial protons are closer to the NO_2 group than are the axial ones, the former are probably strongly deshielded and the latter only slightly affected. It seems that the NO_2 plane is perpendicular to the C_2–C_5 axis, so that the equatorial α- and β-protons lie near the plane, i.e. in the region of the strongest deshielding.[3]

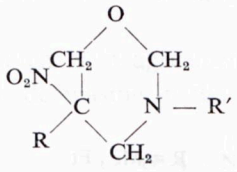
It is an interesting fact that all equatorial protons are slightly coupled to each other (J = 0·5–1·0 c.p.s.), as indicated by slight splitting or broadening of

[3] A. C. Huitric and W. F. Trager, *J. Org. Chem.* **27**, 1926 (1962).

their signals. This may be a result of coplanarity of the C—H and C—C bonds joining each individual pair of equatorial protons in the chair conformation of the ring.

Results of dipole moment measurements for a number of 5-nitrotetrahydro-1,3-oxazines are given in Table 2.

TABLE 2. DIPOLE MOMENTS OF 5-NITRO-TETRAHYDRO-1,3-OXAZINES

General formula	R	R′	μ,D
	—CH_3	—CH_3	4·02
	—CH_3	—CH_2CH_3	3·95
	—CH_3	—n-C_4H_9	4·04
	—n-C_3H_7	—n-C_4H_9	4·04
	—CH_3	—$C(CH_3)_3$	4.53
	—H	—CH_3	3·42
	—H	—$CH_2C_6H_5$	3·36
	—CH_3	—$CH_2C_6H_5$	4.11

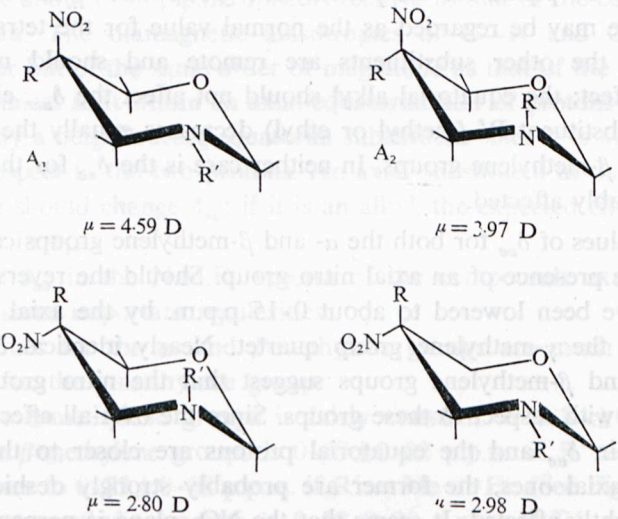


FIG. 3. Calculated values of dipole moments.

Theoretical values of dipole moments were calculated for the four combinations of the positions of R and R′ in the chair conformation (Fig. 3).

They were calculated by using the group moment 3·5 D for the nitro group (this value corresponds better to non-aromatic nitro compounds than does the

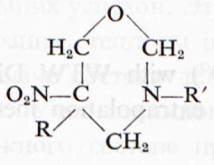
3·25 D previously accepted) and the bond moments C—O 0·86 D (bond length 1·43 Å) and C—N 0·45 D (bond length 1·47 Å) and the C—N—C and C—O—C angles 111° and 110°42′, respectively. Good agreement is observed between the values observed and calculated for the conformations postulated previously from the N.M.R. data: 'A_1' for R′ = t-Bu and 'A_2' for R′ = Me, Et; the values for R = H and R′ = methyl or benzyl may be readily explained by rapid ring inversion resulting in an intermediate value between those given in Fig. 3.

EXPERIMENTAL

Preparation of the compounds

The following compounds were prepared according to the literature (Table 3):

TABLE 3. 5-NITRO-TETRAHYDRO-1,3-OXAZINE DERIVATIVES

General formula	R	R′	B.p., °C/mm	M.p., °C	Ref.
	CH_3	CH_3	66–67/0·25[a]	—	4
	C_2H_5	CH_3	84–85/0·4	—	4
	C_2H_5	H	68–69/0·1	—	4,6
	n-C_3H_7	H	86–87/0·6[b]	—	7
	H	$CH_2C_6H_5$	—	52	5
	CH_3	CH_2CH_3	73–74/0·5	—	4
	CH_3	n-C_4H_9	92–94/0·2	—	4
	n-C_3H_7	n-C_4H_9	107–108/0·3	—	8
	CH_3	$CH_2C_6H_5$	—	66–68	9

[a] n_D^{20} 1·4712.
[b] Not reported until now.

3-Methyl-5-nitro-tetrahydro-1,3-oxazine (R = H, R′ = Me). 5-Hydroxymethyl-3-methyl-5-nitro-tetrahydro-1,3-oxazine[8,10] (17·6 g, 0·1 mole) was mixed with methanolic 6% solution of sodium (39 g, 0·1 gram atom), warmed to 40° on a water bath, and cooled. Methanol was then distilled off *in vacuo*. A stoichio-

[4] Z. Eckstein, P. Gluziński, W. Hofman and T. Urbański, *J. Chem. Soc.* 489 (1961).
[5] T. Urbański and D. Gürne, *Roczniki Chem.* **28**, 175 (1954); *ibid.* **34**, 315 (1960).
[6] E. L. Hirst, J. K. N. Jones, S. Minahan, F. W. Ochyński, A. T. Thomas and T. Urbański, *J. Chem. Soc.* 924 (1947).
[7] T. Urbański and H. Piotrowska, *Roczniki Chem.* **29**, 379 (1955).
[8] M. Senkus, *U. S. Pat.* 2,447,822 (1948).
[9] D. Gürne and T. Urbański, *Roczniki Chem.* **31**, 855 (1957).
[10] T. Urbański, D. Gürne, I. Szczerek and M. Mordarski, *Bull. Acad. Polon. Sci., Ser. sci. chim.* (in press).

metric proportion of hydroxylamine hydrochloride in a little amount of water was added to the residue. The mixture was extracted with ether, the extract dried and evaporated. The residual oil was very slowly distilled under 0·01 mm. Temperature of the bath should not exceed 40°. The yield was 1·5 g.

3-tert-*Butyl*-5-*methyl*-5-*nitro*-*tetrahydro*-1,3-*oxazine* (R = Me, R′ = t-Bu). 2-Methyl-2-nitropropan-1,3-diol (13·5 g, 0·1 mole) and t-butylamine (7·3 g, 0·1 mole) were mixed with 30% aqueous formaldehyde (11 ml, 0·11 mole). The temperature of the mixture rose to 60°. After cooling, the mixture was left overnight. The crystalline product was then filtered and recrystallized from ethanol; yield 14 g (70%), m.p. 88–89°. (Found: N, 14·2. $C_9H_{18}N_2O_3$ requires: N, 13·9%).

Purity of the substances was also verified by N.M.R. signal intensities.

N.M.R. spectra

The N.M.R. spectra were measured at 60 Mc with Varian V–4300 C spectrometer. The temperature was 27±0·3°. Carbon tetrachloride solutions (about 5% w/v) and tetramethylsilane internal standard were used. Chemical shifts were measured by the audio sideband superposition method with an error of ±0·5 c.p.s. The shifts are reported in τ-values (TMS standard = 10,00 p.p.m.).

Dipole moments

Dipole moments were measured in CCl_4 solutions (20°) with WTW Dipolmeter Type DM 01 by the heterodyne-beat method. The extrapolation method of Le Fèvre and Vine was employed.