The Conformational Analysis of Saturated Heterocycles. Part LXVII.[1] 2-Alkyl-3,6-dihydro-2*H*-1,2-oxazines and 3-Alkyl-3,4-dihydro-1*H*-2,3-benzoxazines

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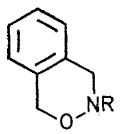
Low temperature n.m.r. studies of the title compounds indicate that nitrogen inversion is slowed. Peak area measurements show that 2-methyl substituents prefer the equatorial position by a factor of *ca.* 10 : 1 and 2-t-butyl substituents by a considerably larger factor. This considerable equatorial preference is due in part to lone pair–lone pair repulsion in the 2-axial conformers. The conclusions from n.m.r. are compared with measured and calculated dipole moments.

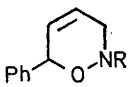
THE conformational analysis of dihydro-1,2-oxazines has previously received little attention. There are considerable differences in conformational behaviour between the hexahydro-[2] and the tetrahydro-pyridazines:[3] the former possess mixtures of *ee*, *ea*, and *aa* conformations, while the latter prefer the *ea* conformation (*cf.* ref. 4). In view of this, we have now extended our study of the tetrahydro-1,2-oxazines[5] to some dihydro-analogues.

Variable temperature n.m.r. studies on perfluoro-3,6-dihydro-2-methyl-1,2-oxazine had disclosed no signals attributable to different conformers.[6] Previous quantitative work has been limited to a dipole moment study of 3,4-dihydro-2,3-benzoxazine (1) in dioxan by Lumbroso and Pifferi[7] who conclude that it exists as 75% (1a) and 25% (1b).

We have now prepared four *N*-alkyl derivatives of dihydro-1,2-oxazine (2)—(5) and examined their conformations by n.m.r. and dipole moment studies.



(1) R = H
(2) R = Me
(3) R = Bu^t



(4) R = Me
(5) R = Bu^t
(6) R = H
(7) R = CMe_2CN

Preparation of Compounds.—The monocyclic compounds (4) and (5) were prepared from the NH-analogue (6).[8] Methylation was carried out by the method of ref. 9 for the conversion of *ON*-dimethylhydroxylamine into *ONN*-trimethylhydroxylamine whereas the t-butyl group was introduced by the reaction of the Strecker product (7) with methylmagnesium iodide (*cf.* ref. 10). In the bicyclic series, the methyl derivative was made by a known[11] procedure, while the t-butyl compound was prepared by an adaptation of the previously mentioned Grignard reaction.

EXPERIMENTAL

3,6-Dihydro-2-methyl-6-phenyl-1,2-oxazine.—3,6-Dihydro-6-phenyl-1,2-oxazine[8] (0·1 mol, 16·1 g) and methyl iodide (0·05 mol, 7·1 g) in ether (150 ml) were kept for four days at 20°. The filtered solution was treated with anhydrous potassium carbonate (10 g). After filtration, the ether was removed and the residue chromatographed on neutral alumina with dry ether as eluant. The residue (4·5 g, 39%) distilled to give the *dihydro-oxazine*, b.p. 60° at 0·05 mmHg (Found: C, 74·9; H, 7·4; N, 7·7. $C_{11}H_{13}NO$ requires C, 75·3; H, 7·5; N, 8·0%).

2-Methyl-2-(3,6-dihydro-6-phenyl-1,2-oxazin-2-yl)propionitrile.—Acetone (0·1 mol, 5·8 g) was added dropwise at 0° to 3,6-dihydro-6-phenyl-1,2-oxazine hydrochloride (0·1 mol, 19·8 g) and potassium cyanide (0·1 mol, 6·5 g) in water (165 ml). The mixture was subsequently stirred for 3 h, and extracted with ether (4 × 50 ml). Evaporation of the dry (Na_2SO_4) extracts and fractional distillation of the residue gave the *amino-nitrile* (18·2 g, 80%), b.p. 108—111° at 1 mmHg (Found: C, 72·8; H, 6·9; N, 11·8. $C_{14}H_{16}N_2O$ requires C, 73·6; H, 7·1; N, 12·2%), δ (CCl_4) 7·28 (5H, s), 5·90 (2H, s), 5·12—5·40 (1H, m), 3·35—3·52 (2H, m), 1·44 (3H, s), and 1·28 (3H, s).

2-t-Butyl-3,6-dihydro-6-phenyl-1,2-oxazine.— 2-Methyl-2-(3,6-dihydro-6-phenyl-1,2-oxazin-2-yl)propionitrile (0·05 mol, 11·2 g) in dry ether (100 ml) was added dropwise at 0° to methylmagnesium iodide (0·17 mol) in ether (74 ml). The mixture was heated under reflux for 1 h and added to saturated ammonium chloride (200 ml). The ether layer was dried (Na_2SO_4) and evaporated. The residue was fractionally distilled to give the *dihydro-oxazine* (8·1 g, 74%), b.p. 74—75° at 0·05 mmHg (Found: C, 76·7; H, 8·5; N, 6·8. $C_{14}H_{19}NO$ requires C, 77·3; H, 8·8; N, 6·5%), $\nu_{max.}$ (film) 1360—1390, 1215—1250 [$C(Me)_3$], 1170, 880, 720—760, and 695 cm^{-1}.

[1] Part LXVI, V. J. Baker, I. D. Blackburne, A. R. Katritzky, R. A. Kolinski, and Y. Takeuchi, *J.C.S. Perkin II*, 1974, 1563.
[2] R. A. Y. Jones, A. R. Katritzky, D. L. Ostercamp, K. A. F. Record, and A. C. Richards, *J.C.S. Perkin II*, 1972, 34.
[3] R. A. Y. Jones, A. R. Katritzky, K. A. F. Record, and R. Scattergood, *J.C.S. Perkin II*, 1974, 406.
[4] J. E. Anderson, *J. Amer. Chem. Soc.*, 1969, **91**, 6374.
[5] R. A. Y. Jones, A. R. Katritzky, S. Saba, and A. J. Sparrow, *J.C.S. Perkin II*, 1974, 1554.
[6] J. Lee and K. G. Orrell, *Trans. Faraday Soc.*, 1965, **61**, 2342.
[7] H. Lumbroso and G. Pifferi, *Bull. Soc. chim. France*, 1969, 3401.
[8] O. Wichterle and S. Svastal, *Coll. Czech. Chem. Comm.*, 1951, **16**, 33 (*Chem. Abs.*, 1952, **46**, 2070d).
[9] L. W. Jones and R. T. Major, *J. Amer. Chem. Soc.*, 1928, **50**, 2742 (*Chem. Abs.*, 1928, **22**, 4461).
[10] (*a*) F. Kuffner and W. Koechlin, *Monatsh.*, 1962, **93**, 476; (*b*) N. J. Leonard and F. P. Hauck, jun., *J. Amer. Chem. Soc.*, 1957, **79**, 5279.
[11] G. Pifferi, P. Consonni, and E. Testa, *Gazzetta*, 1966, **96**, 1671.

3,4-*Dihydro*-3-*methyl*-2,3-*benzoxazine*.—This was prepared by the method of Pifferi [11] and had b.p. 49° at 0·15 mmHg (lit.,[11] 70—75° at 0·4 mmHg).

2-*Methyl*-2-(3,4-*dihydro*-2,3-*benzoxazin*-3-*yl*)*propionitrile*.—Acetone (0·1 mol. 5·81 g) was added dropwise at 0° to 3,4-dihydro-2,3-benzoxazine hydrochloride [11] (0·1 mol, 17·2 g) and potassium cyanide (0·1 mol, 6·51 g) in water (170 ml). The mixture was stirred for 3 h at room temperature. The gummy solid was filtered off, washed with water, and crystallized from n-hexane to give the *aminonitrile* (14·0 g, 69%), m.p. 63—64° (Found: C, 70·8; H, 7·2; N, 13·7. $C_{12}H_{14}N_2O$ requires C, 71·2; H, 7·0; N, 13·8%), $\nu_{max.}$ (Nujol) 2225 (C≡N), 805, and 750 cm^{-1}, δ ($CDCl_3$) 7·0—7·4 (4H, m), 4·97 (2H, s), 4·08 (2H, s), and 1·60 (6H, s).

3-*t*-*Butyl*-3,4-*dihydro*-2,3-*benzoxazine*.— 2-Methyl-2-(3,4-dihydro-2,3-benzoxazin-3-yl)propionitrile (0·05 mol, 10·1 g) in ether (100 ml) was added at 0° to methylmagnesium iodide (0·17 mol) in ether (74 ml). The mixture was heated under reflux for 1 h and decomposed with a saturated solution of ammonium chloride (200 ml). The ether layer was separated and dried (Na_2SO_4). The ether was evaporated and the residue fractionally distilled to give the *dihydrobenzoxazine* (7·5 g, 78%), b.p. 63—64° at 0·04 mmHg (Found: C, 75·5; H, 8·7; N, 7·5. $C_{12}H_{17}NO$ requires C, 75·3; H, 9·0; N, 7·3%), $\nu_{max.}$ (film) 1360—1385, 1190—1265 [$C(Me)_3$], 925, 860, 805, 775, and 740 cm^{-1}.

Physical Measurements.—These were measured in Norwich on a Varian HA 100 spectrometer and at the Harwell National Laboratory on a Varian HR 220 spectrometer. Temperatures were measured with a standard methanol sample. The solvent in each case was $CDCl_3$–$CFCl_3$ (1 : 1). Chemical shifts were measured from Me_4Si as internal standard. Dipole moments were measured as previously described [12] in cyclohexane solution at 25°.

TABLE 1

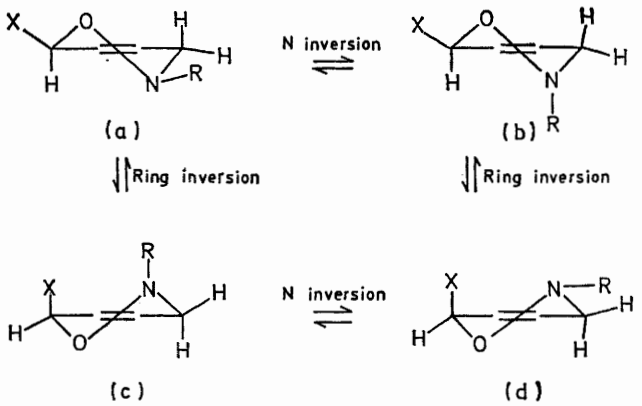
Calculated and observed dipole moments (D) for compounds (2)—(5)

Compound	Calculated	Observed
(2)	0·84	0·97
(3)	0·54	0·90
(4)	1·23	1·17
(5)	1·06	1·24

The measured dipole moments are recorded in Table 1. Additional data are deposited as Supplementary Publication No. SUP 21127 (4 pp.).*

RESULTS AND DISCUSSION

N.m.r. Spectra.—Room temperature n.m.r. spectral data for the bicyclic compounds (2) and (3) are recorded in Table 2: they indicate rapid inversion both of the ring and at the nitrogen atom. Variable temperature n.m.r. spectra for (2) and (3) pass through a coalescence point (Table 3), and show at low temperature the peaks recorded in Table 4. Specifically, the NCH_2 and OCH_2 peaks, originally singlets, are now each AB patterns, but the *N*-methyl peak remains a singlet. This is consistent with slowing of *either* ring inversion *or* nitrogen inversion. The spectra are not consistent with the slowing of *both* nitrogen and ring inversion *unless* there is an overwhelming preponderance of one form in the conformational equilibrium *or* chemical shift differences between all stereochemically non-equivalent protons in the two conformations are negligible. In the t-butyl compound it is likely that there will indeed be only an insignificant proportion of the t-butyl axial conformer; nevertheless the similar behaviour of the two compounds and the following line of reasoning led us to reject this as the sole explanation of the spectral behaviour. The free energy of activation at coalescence is 11·2 ± 0·3 kcal mol^{-1} for both compounds (Table 3). This compares with values of 13·7 kcal mol^{-1} for nitrogen inversion in tetrahydro-2-methyl-1,2-oxazine.[13] The barrier to ring inversion in cyclohexenes [14] is only *ca.* 5 kcal mol^{-1} compared with values of *ca.* 10 kcal mol^{-1} in cyclohexanes,[15] so it is likely that the observed low temperature spectra reflect slow nitrogen inversion, and are due to time-averages of type (2a) ⇌ (2c). No information is available regarding the population of the individual conformers, because the pairs (2a) ⇌ (2c) and (2d) ⇌ (2b) are mirror images of each other and therefore energetically identical. (A recent report [16] suggests that the inversion barrier in 3,3,5-trimethyl-3,6-dihydro-1,2-dioxin is 11 kcal mol^{-1}. This surprisingly high value may be due to steric interactions of the 5-methyl group with 6-H_2, and 4-H with the 3-methyl groups in the transition state.)



SCHEME In (a)—(d) X = H for (1)—(3), X = Ph for (4)—(7).

The spectra of the monocyclic *N*-methyl and *N*-t-butyl compounds (4) and (5) are recorded in Table 2 (for room temperature spectra) and Table 4 (for low temperature spectra). Of the considerable changes

* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1973, Index issue. Items less than 10 pp. are supplied as full-size copies.

[12] R. J. Bishop, L. E. Sutton, D. Dineen, R. A. Y. Jones, A. R. Katritzky, and R. J. Wyatt, *J. Chem. Soc.* (*B*), 1967, 493.

[13] F. G. Riddell, J. M. Lehn, and J. Wagner, *Chem. Comm.*, 1968, 1403.

[14] F. A. L. Anet and M. Z. Haq, *J. Amer. Chem. Soc.*, 1965, **87**, 3147.

[15] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Wiley, New York, 1965, p. 41.

[16] M. L. Kaplan and G. N. Taylor, *Tetrahedron Letters*, 1973, 295.

appearing in the low temperature spectra, the splitting of the *N*-methyl peak into two at low temperatures is the most significant. Again, the spectral changes are consistent with the slowing of *either* ring inversion *or* nitrogen inversion, but not both (subject to the same proviso as above). We again suppose that nitrogen inversion is the slower.

TABLE 2

Room temperature n.m.r. data [a]

R	Me [b]	Bu^t [c]
3-Alkyl-3,4-dihydro-2,3-benzoxazines		
δ_R	2·67 (3H, s)	1·70 (9H, s)
$\delta_{H(1)}$	4·80 (2H, s)	4·92 (2H, s)
$\delta_{H(4)}$	3·70 (2H, s)	3·95 (2H, s)
$\delta_{aromatic}$	6·9—7·1 (4H, m)	7·05—7·2 (4H, m)
2-Alkyl-3,6-dihydro-6-phenyl-1,2-oxazines [b]		
δ_R	2·58 (3H, s)	1·02 (9H, s)
$\delta_{H(3)}$	3·11—3·25 (2H, m)	3·21—3·34 (2H, m)
$\delta_{H(4,5)}$	5·83 (2H, s)	5·80 (2H, s)
$\delta_{H(6)}$	5·22—5·39 (1H, m)	5·15—5·30 (1H, m)
$\delta_{aromatic}$	7·22 (5H, s)	7·22 (5H, s)

[a] At 60 MHz. [b] In CCl_4. [c] In $CDCl_3$.

TABLE 3

Coalescence data [a]

OCH_2	NCH_2
3,4-Dihydro-3-methyl-2,3-benzoxazine [b]	
T_c 277 K	
J 15 Hz	
$\Delta\nu$ 25 Hz	Not calculable
$\Delta G_c^{\ddagger}$ 11·5 kcal mol^{-1}	
3-t-Butyl-3,4-dihydro-2,3-benzoxazine [c]	
T_c 271 K	T_c 268 K
J 15 Hz	J 15 Hz
$\Delta\nu$ 59·8 Hz	$\Delta\nu$ 41·9 Hz
$\Delta G_c^{\ddagger}$ 10·8 kcal mol^{-1}	$\Delta G_c^{\ddagger}$ 10·9 kcal mol^{-1}

[a] $\Delta G_c^{\ddagger} = 4{\cdot}57\ T_c\ \{9{\cdot}97 + \log[T_c/(\delta\nu^2 + 6J^2)^{\frac{1}{2}}]\}$ [J. M. Lehn, F. G. Riddell, B. J. Price, and I. O. Sutherland, *J. Chem. Soc.* (*B*), 1967, 387]. [b] Measured in $CFCl_3$–$CDCl_3$ (1 : 1) at 100 MHz. [c] Measured in $CFCl_3$–$CDCl_3$ (1 : 1) at 220 MHz.

TABLE 4

Low temperature [a] (*ca.* −80°) n.m.r. chemical shifts (δ) for 3-alkyl-3,4-dihydro-2,3-benzoxazines (2) and (3) and 2-alkyl-3,6-dihydro-6-phenyl-1,2-oxazines (4) and (5)

Compd.	OCH_2	NCH_2	NMe	NBu^t	Aromatic
(2)	5·17 4·79 [b]	3·94 3·81 [b]	2·82		7·00—7·28
(3)	5·10 4·83 [b]	4·08 3·87 [b]		1·22	7·00—7·23

Compd.	OCH	NCH_2	NMe	NBu^t	Olefinic	Aromatic
(4)	6·0—6·15	3·3—3·48	2·78		5·52	7·40
			2·68		5·88—5·96	
(5)	5·95—6·1	3·25—3·65		1·16	5·45	7·40
				0·84	5·85—5·95	

[a] In $CDCl_3$–$CFCl_3$ (1 : 1) at 220 MHz. [b] $^2J_{ae}$ 15 Hz.

TABLE 5

Estimated conformer dipole moments (D) for compounds (2)—(5)

Compound	Conformer and moment (a)	(b)	(c)	(d)
(2)	0·51	1·65	≡(b)	≡(a)
(3)	0·54	1·63	≡(b)	≡(a)
(4)	1·05	1·96	1·58	0·93
(5)	1·08	1·94	1·52	0·87

TABLE 6

Cartesian co-ordinates of ring atoms in 3-alkyl-3,4-dihydro-2,3-benzoxazines and 2-alkyl-3,6-dihydro-6-phenyl-1,2-oxazines

	Atom no.	*X*	*Y*	*Z*
Benzoxazine	1	0	0	0
	2	0·836	−1·065	0·460
	3	2·004	−1·160	−0·395
	4	2·92	0	0
	5	2·155	1·325	0
	6	0·765	1·325	0
Oxazine	1	0	0	0
	2	0·84	−1·10	0·36
	3	2·053	−1·13	−0·45
	4	2·981	0	0
	5	2·159	1·29	0
	6	0·822	1·29	0
Equatorial position at C(1)	*a*	−0·834	0·019	0·682
Axial position at C(1)		−0·386	−0·175	−1·01

[a] Ref. 18.

Dipole Moments.—We have calculated the dipole moments of the various conformers (Table 5) by making the following assumptions.

(i) The geometry of the dihydro-1,2-oxazine ring was estimated as follows. The four-carbon fragment was assumed to be planar and to have the following dimensions: =C–C,[17] 153 pm; C=C, 133·7 pm in the monocyclic series [17] and 139 pm in the bicyclic; [17] C–C–C, 122·5° in the monocyclic series [18] and 120° in the bicyclic The C–O and C–N bond lengths [17] were taken as 143 and 147 pm respectively. This leaves four independent variables (two Cartesian co-ordinates of the oxygen and nitrogen atoms) and five undetermined dimensions (the four remaining bond angles and the N–O bond length). The co-ordinates were adjusted to give all the bond angles as near as possible to 110° [19] and the N–O bond length close to 146 pm.[20,*] The best approximation is shown in Table 6.

(ii) The group moment of the benzene ring in (2) and (3) was taken from that of tetralin [21] (0·52 D), acting in the plane of the ring and bisecting it.

(iii) The group moment of the double bond in (4)

* *Cf.* 145·6 pm reported for the N–O bond length (F. G. Riddell, P. Murray Rust, and J. Murray Rust, *Tetrahedron*, 1974, **30**, 1087).

[17] 'Handbook of Chemistry and Physics,' ed. R. C. Weast, The Chemical Rubber Co., Cleveland, 1970, 51st edn., pp. F-154, F-155.

[18] E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505.

[19] *Cf.* I. D. Blackburne, R. P. Duke, R. A. Y. Jones, A. R. Katritzky, and K. A. F. Record, *J.C.S. Perkin II*, 1973, 332.

[20] P. A. Giguère and I. D. Liu, *Canad. J. Chem.*, 1952, **30**, 948.

[21] A. L. McClellan, 'Tables of Experimental Dipole Moments,' Freeman, San Francisco, 1963.

and (5) was taken from that of cyclohexene [22] (*ca.* 0·3 D) acting in the plane of the double bond and bisecting it at right angles.

(iv) The group moment of the '*N*-alkylpiperidine' systems were taken from those of *N*-methyl- and *N*-t-butyl-piperidines (0·77 and 0·70 D respectively) [12] acting at angles of 56·5 [12] and 61·2° [23] respectively from the axis bisecting the CNO angle.

(v) The group moment of the 'ether' system (CON) was taken from that of tetrahydropyran (1·55 D) and bisecting the CON angle.[21]

(vi) The N–O bond moment was assumed to have a value of 0·26 D acting from nitrogen to oxygen.[5]

(vii) The group moment of the phenyl substituent in (4) and (5) was taken from that of phenylcyclohexane [12] (0·62 D).

Conformational Isomerism in the Monocyclic Series.—In this monocyclic series the four conformations (a)—(d) are all energetically different from each other. We have neglected conformation (c), which has two *syn*-diaxial groups. If nitrogen inversion is slower than ring inversion then the two *N*-methyl signals observed at 193 K (relative intensities 87 : 13) must be due to conformers (4a) and (4b) + (4d) respectively. In principle we could assess the relative populations of the two minor conformers (4b) and (4d) from dipole moment measurements, but for reasons set out below these are less reliable than we would wish. The following argument suggests that the minor conformer (4b), with the *N*-methyl group axial and the phenyl group equatorial, is more important than (4d).

At 193 K the t-butyl compound (5) shows two t-butyl signals of relative intensities *ca.* 95 : 5. These are assigned to conformers (5a) and (5b) + (5d) respectively, but it is probable that (5b), with an axial t-butyl group, will be negligibly populated so the 5% minor signal arises solely from (5d). If we now assume that the equilibrium constant [(5a)]/[(5d)] is the same as [(4a)]/[(4d)], that is that the conformational behaviour of the phenyl group is independent of the *N*-alkyl substituent, we can deduce that the percentages of (4b) and (4d) are 8·4 and 4·6 respectively at 193 K (Table 6). Unfortunately these values depend rather critically on the intensity ratio of the t-butyl signals and this cannot be measured with high accuracy: an error of ±1% is barely significant in the 95% preponderance of (5a), but leads to a change in the [(4b)] : [(4d)] ratio from 7·4 : 5·6 to 9·4 : 3·6.

For comparison between the n.m.r. and dipole moment measurements we need to extrapolate the conformer populations from 193 to 298 K (by assuming all ΔS^0 values to be zero), but in so doing the errors in the relative proportions of minor conformers become exaggerated. The results of this extrapolation are shown in Table 7 and the dipole moments calculated for (4) and (5) using these proportions and the calculated conformer moments are compared with the observed moments in Table 1. The agreement is good for the methyl compound but rather poor for the t-butyl.* Possible reasons for the discrepancy are discussed below.

Conformational Isomerism in the Bicyclic Series.—In the bicyclic compounds (2) and (3) there are only two energetically different conformers, having the nitrogen substituent equatorial [(a) ≡ (d)] or axial [(b) ≡ (c)]. In principle the conformational equilibrium can be determined from dipole moment measurements using equation

TABLE 7

Conformer populations at 193 and 298 K (%)

Compound	193 K [a]				298 K [b]			
	(a)	(b)	(c)	(d)	(a)	(b)	(c)	(d)
(2)	91	9	≡(b)	≡(a)	82	18	≡(b)	≡(a)
(3)	100	0 [c]	≡(b)	≡(a)	100	0	≡(b)	≡(a)
(4)	87	8·4	0 [c]	4·6	73	16	0	11
(5)	95	0 [c]	0 [c]	5	87	0	0	13

[a] From n.m.r. areas, assuming [(4a)]/[(4d)] = [(5a)]/[(5d)] and [(2a)]/[(2b)] = [(4a)]/[(4b)]. [b] Extrapolated from 193 K values, assuming $\Delta S^0 = 0$. [c] Assumed.

(i) where $N_{(a)}$ and $N_{(b)}$ are the mole fractions of conformers (a) and (b), and $\mu_{(a)}$ and $\mu_{(b)}$ their calculated dipole moments. Inserting the values recorded in Table 5 gives $N_{(a)}$ 0·70 for the *N*-methyl compound and 0·75 for the t-butyl. These values seem unnaturally small, especially for the t-butyl compound in which one would expect a negligible proportion of the axial conformer. Again, therefore, the dipole moment data seem suspect and particularly so for the t-butyl compound (3), as for the monocyclic t-butyl compound (5).

$$\mu^2_{obs} = N_{(a)}\mu^2_{(a)} + N_{(b)}\mu^2_{(b)} \qquad (i)$$

An alternative approach makes use of the n.m.r. data for the monocyclic compounds. We may suppose that the equilibrium constant [(2a)]/[(2b)] is the same as [(4a)]/[(4b)], that is, that the conformational equilibrium at nitrogen is unaffected by the presence of an equatorial 6-phenyl group or by the fused benzene ring. The second assumption is only crude, because the differing carbon–carbon bond lengths do change the ring geometry significantly. The results of these calculations, however, are recorded in Table 7, together with extrapolated populations for 298 K.

The comparison of observed and calculated dipole

* In fact, excellent agreement between the n.m.r. and dipole moment data results if the populations of the (d) and (b) conformers are interchanged. However, we reject this conclusion because it seems completely unreasonable that the *N*-t-butyl group should exist to a significant extent in the axial position and yet that there should be no pseudoaxial phenyl. Models suggest that the steric interactions of an axial *N*-t-butyl in the present series are more severe than in hexahydropyrimidines, in which it seems there is no significant axial *N*-t-butyl concentration.

[22] An average value from reported values of 0·21 D in heptane, W. D. Kumler, R. Boikess, P. Bruck, and S. Winstein, *J. Amer. Chem. Soc.*, 1964, **86**, 3126, and 0·42 D in CCl_4, C.-Y. Chen, R. J. W. Le Fèvre, and K. M. S. Sundaram, *J. Chem. Soc.*, 1965, 553.

[23] R. A. Y. Jones, A. R. Katritzky, P. G. Lehman, A. C. Richards, and R. Scattergood, *J.C.S. Perkin II*, 1972, 41.

moments, using these populations, is presented in Table 1 and, as for the monocyclic compounds, it can be seen that the comparison is (just) acceptable for the methyl compound but very poor for the t-butyl.

Errors.—In the monocyclic series the n.m.r. data leave no doubt but that the *N*-methyl compound exists largely, and the *N*-t-butyl overwhelmingly, in a single conformation. The doubts lie in the proportions of the minor conformers. We do not claim that the values for these in Table 7 are highly precise, only that it is likely that both conformers (4b) and (4d) are significantly populated whereas the sole minor conformer of the t-butyl compound is probably (5d). Whence, then, arise the discrepancies between the n.m.r. and dipole moment data? The agreement for the methyl compound is remarkably good, considering the many assumptions made in calculating the dipole moments. We suggest that the greater discrepancy in the t-butyl values arises from a considerable distortion of the molecule: the nitrogen equatorial bond almost eclipses the 3-pseudo-axial bond and severe non-bonded interactions are likely with an undistorted t-butyl group. Some of the other assumptions required to interpret the dipole moment data may also be responsible for the discrepancies.

In the bicyclic series the quantitative conclusions of Table 7 are less certain, since they are derived from n.m.r. data only by extrapolation from the monocyclic compounds. The greater divergence between n.m.r. values and calculated dipole moments is therefore hardly surprising.

Conclusions.—The equilibrium [(4a)]/[(4b)] indicates that in the dihydro-1,2-oxazines a 2-methyl group prefers the equatorial position with ΔG^0 *ca.* 0·9 kcal mol^{-1}. This value is not highly accurate, but it is certainly significantly smaller than the corresponding value for tetrahydro-2-methyl-1,2-oxazine [5] for which the ΔG^0 value is 1·9 kcal mol^{-1}.

This behaviour is similar to that of 4-substituents in cyclohexenes, as compared to 1-substituents in cyclohexane, for which the ΔG^0 (Me) values are *ca.* 1·0 [24] and 1·7 [25] kcal mol^{-1} respectively. It seems likely that in the dihydro-oxazines the equilibrium position arises from a balance between lone-pair–π-bond repulsions in the equatorial conformer and strong lone-pair–lone-pair repulsions in the axial one.[5]

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[24] B. Rickborn and S.-Y. Lwo, *J. Org. Chem.*, 1965, **30**, 2212.
[25] Ref. 14, p. 43.