

The Conformation of Mono- and Di-*N*-methyl *trans*-Decahydroquinazolines*

Wilfred L. F. Armarego,^A Richard A. Y. Jones,^B Alan R. Katritzky,^B
David M. Read^B and Roger Scattergood^B

^A Medical Chemistry Group, John Curtin School of Medical Research,
Australian National University, Canberra, A.C.T. 2600.

^B School of Chemical Sciences, University of East Anglia,
Norwich, NR4 7TJ, England.

Abstract

The conformational equilibria of the title compounds all involve substantial contributions from conformers with both lone pairs axial and with one pair axial and one equatorial.

One of us recently¹ used the geminal coupling constants of the C2 protons to deduce that the lone pairs in *trans*-decahydroquinazolines had the following orientations: unsubstituted: 1-*eq*, 3-*eq*; 1-methyl: 1-*ax*, 3-*eq*; 3-methyl: 1-*eq*, 3-*ax*; 1,3-dimethyl: 1-*ax*, 3-*ax*. However, these conclusions appeared incompatible with those reached at East Anglia for the conformational equilibria of 1,3-dialkylhexahydropyrimidines as measured by dipole moments^{2,3} (and recently confirmed by n.m.r. chemical shift measurements^{4,5}) and for 1-alkylhexahydropyrimidines as measured by dipole moments and infrared band shapes.⁶

Moreover, it has been shown⁷ that the J_{gem} criterion is not valid when structural changes adjacent to the CH₂ group occur.[†]

We therefore measured the dielectric constant, specific volume and dipole moment of 1-methyl-, 3-methyl- and 1,3-dimethyl-*trans*-decahydroquinazoline (Tables 1 and 2). The conformers with both lone pairs equatorial are expected to be of high energy² and the contributions from these conformers are therefore neglected. We assume that the moments of the individual conformers (a)–(c) of (1)–(3) are those calculated (cf.²) for the corresponding conformers in the hexahydropyrimidine series (Table 3). Using

* Part LXXI of 'The Conformational Analysis of Saturated Heterocycles' (Part LXX, Baker, V. J., Katritzky, A. R., and Majoral, J.-P., *Tetrahedron*, in press). Part XXII of 'Quinazolines' (Part XXI, Armarego, W. L. F., and Reece, P. A., *J. Chem. Soc., Perkin Trans. 1*, in press.)

† Chemical shift differences are also unreliable as conformational criteria; see refs. 7 and 8.

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³ Blackburne, I. D., Duke, R. P., Jones, R. A. Y., Katritzky, A. R., and Record, K. A. F., *J. Chem. Soc., Perkin Trans. 2*, 1973, 332.

⁴ Riddell, F. G., and Williams, D. A. R., *Tetrahedron Lett.*, 1971, 2073.

⁵ Eliel, E. L., Kopp, L. D., Dennis, J. E., and Evans, S. A., Jr, *Tetrahedron Lett.*, 1971, 3409.

⁶ Cook, M. J., Jones, R. A. Y., Katritzky, A. R., Moreno Mañas, M., Richards, A. C., Sparrow, A. J., and Trepanier, D. L., *J. Chem. Soc., Perkin Trans. 2*, 1973, 325.

⁷ Halls, P. J., Jones, R. A. Y., Katritzky, A. R., Snarey, M., and Trepanier, D. L., *J. Chem. Soc., B*, 1971, 1320.

⁸ Crabb, T. A., Chivers, P. J., Jones, E. R., and Newton, R. F., *J. Heterocycl. Chem.*, 1970, 7, 635.

Table 1. Measurements of dielectric constants and specific volume at 25° in cyclohexane for *trans*-decahydroquinazoline derivatives

w is the weight fraction, ϵ_1 and ϵ_{12} are the dielectric constants for solvent and solution respectively, and v_1 and v_{12} are the corresponding specific volumes

Deriv- ative	$10^6 \times$ w	$10^6 \times$ $(\epsilon_{12} - \epsilon_1)$	$10^6 \times$ $(v_1 - v_{12})$	Deriv- ative	$10^6 \times$ w	$10^6 \times$ $(\epsilon_{12} - \epsilon_1)$	$10^6 \times$ $(v_1 - v_{12})$
1,3-Dimethyl	1550	1203	326	1-Methyl	3899	5633	956
	1738	1384	369	(continued)	4532	6529	1136
	2183	1760	483	3-Methyl	1673	1564	393
	4654	3772	990		2586	2389	601
1-Methyl	1026	1428	243		4244	4093	1019
	2219	3172	554		6071	5749	1493
	3530	5021	866		6784	6370	1594

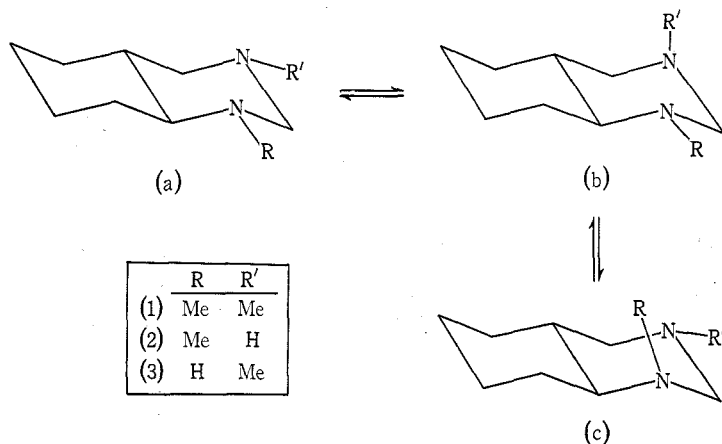
Table 2. Dipole moments in cyclohexane at 25° for *trans*-decahydroquinazoline derivatives

Derivative	$d\epsilon/dw$	$-dv/dw$	$TP_{2\infty}$	ϵ^P	μ (D)
1,3-Dimethyl	0.82 ± 0.01	0.21 ± 0.01	79.08	50.42	1.18 ± 0.01
1-Methyl	0.95 ± 0.01	0.24 ± 0.01	76.07	44.53	1.24 ± 0.02
3-Methyl	1.45 ± 0.01	0.25 ± 0.01	94.42	44.53	1.56 ± 0.01

Table 3. Calculated conformational equilibria for the *trans*-decahydroquinazoline derivatives

Deriv- ative	Predicted moments μ			Observed moment μ (D)	Lone pairs axial (%)
	<i>eq-eq</i>	<i>ax-eq</i>	<i>eq-ax</i>		
1,3-Dimethyl	1.54 ± 0.1	0.88 ± 0.1	0.88 ± 0.1	1.18	40 ± 15
1-Methyl	1.85 ± 0.1	0.94 ± 0.1^A	1.18 ± 0.1^B	1.56	60 ± 15^C
3-Methyl	1.85 ± 0.1	0.94 ± 0.1^A	1.18 ± 0.1^B	1.24	25 ± 15^C

^A H_{ax} , ^B H_{eq} , ^C Calculated by use of the value of 0.94 D for the moment of the *ax-eq* conformer.



equation (1) we can calculate the mole fractions of the di-*N*-lone pair axial conformer (a) (Table 3):

$$\mu_{\text{obs}}^2 = n_1(1 \cdot 54)^2 + (1 - n_1)(0 \cdot 88)^2 \quad (1)$$

The accuracy of the result is limited by the assumption that the dipole moments are unaffected by the fused cyclohexane ring. Errors of $\pm 0 \cdot 1$ D in the calculated moments yield ranges of $\pm 15\%$ in the percentages of di-*N*-lone pair axial conformer found. Thus the proportions of this conformer for the 1,3-dimethyl (1) and 1-methyl (2) compounds are not significantly different from that (54%) for 1,3-dimethylhexahydropyrimidine.³ However, there is a significant increase in the axial-equatorial conformer population in the 3-methyl (3) as compared to the 1-methyl (2) derivative: this reflects the more crowded environment at the 1-position (due to *syn*-axial interactions with H 4a and H 8).

This paper points out again the danger of using J_{gem} values of CH_2 protons α to a nitrogen atom to deduce the conformation of the *N*-lone pair.

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