Tetrahedron Letters No. 28, pp. 1981-1986, 1963. Pergamon Press Ltd.
Printed in Great Britain.

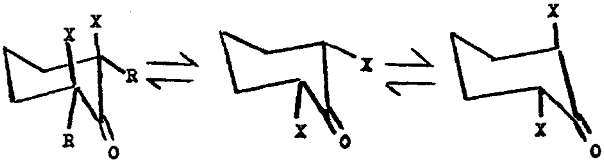
THE BROMINATION OF BICYCLO(3.2.1)OCTANONE-3.
AN EXAMPLE OF AN α,α'-DIAXIAL DIBROMOCYCLOHEXANONE.(1)

C.W. Jefford
Chemistry Department
Temple University
Philadelphia 22, Pa.

B. Waegell
Institut de Chimie
2 rue Goethe
Strasbourg, France

(Received 28 June 1963; in revised form 10 September 1963)

The interplay of steric and electronic factors in the determination of the configuration of α-halo and α,α'-dihalocyclohexanones is well recognized. (2,3) In the two kinds of equilibria (I$\rightleftarrows$II, II$\rightleftarrows$III) depicted below the existence of the diaxial conformer I is usually prohibited because of the severe 1,3 diaxial interaction between the halogen atoms. The diaxial dihalogen configuration (I) is only achieved when steric factors are inoperative; for example Corey (3) has reported that dibromination of 2,6-dimethylcyclohexanone gave the 2,6-dibromo derivative of configuration IV.



I R = H

IV R = CH_3

X = Br

II

III

X = Halogen in all cases

We wish to report the first example of an α,α'-diaxial dibromocyclohexanone in which both steric and electronic factors are equally determinative. The bromination of bicyclo(3.2.1)octanone-3 (Va)(4) with pyridinum perbromide in tetrahydrofuran proceeded rapidly (5 minutes). Two major products were obtained in nearly quantitative yield, a monobromo (Vb) and a dibromo derivative (Vc) in 2:3 ratio. (5) Some physical properties of Va, Vb and Vc are assembled in tables I and II.

TABLE I

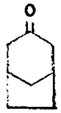
Compound(6)	m.p.	U.V		I.R.	
		λ_{max}	ϵ	$\nu_{C=O}$	
Va	139°	280 mμ	19(d)	1711 cm^{-1}	(f)
Vb	48	315	105(d)	1715	(f)
		313	96(e)	1715	(e)
Vc	88	342	195(d)	1725	(f)
		341	190(e)	1722	(e)

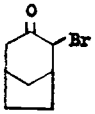
The solvents used were cyclohexane (d), acetonitrile (e) and chloroform (f).

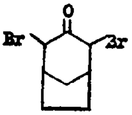
Overall inspection of the spectral results in Table I indicates that the bromine atoms in both Vb and Vc must be axial (7,8). Moreover, the spectral data are sensibly invariant to solvent polarity which thereby rules out conformational equilibrium for the bromo derivatives. In other words, the cyclohexane moieties of Vb and Vc do not adopt boat forms. However, the value of 1725 cm^{-1} is somewhat large and it could be indicative of the *trans* dibromo configuration (*axial-equatorial*) for Vc, notwithstanding the contraindication provided by the ultra-violet spectral data.

TABLE II

Calculated and Measured Dipole Moments





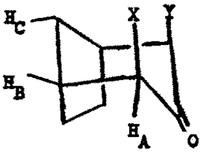


	Va	Vb ax.	eq.	Vc eq.eq.	ax.ax.	ax.eq.
Calcd. (9)	-	3.62,	4.23	4.82	4.98	3.90
					4.37 (10)	
Measured	3.11	3.71			4.20	

Benzene was used as solvent. Values are in Debye units.

This ambiguity is also encountered on comparing the measured dipole moment of Vc with those calculated for the three possible configurations (Table II). Although, if mutual induction between the two axial C-Br bonds of the diaxial configuration for Vc is taken into account then the calculated dipole moment is 4.37 D which is reasonably close to the measured value of 4.20 D (10). Incidentally, both sets of evidence in Tables I and II unequivocally substantiate the axial configuration for 2-bromobicyclo(3.2.1)-octanone-3 (Vb).

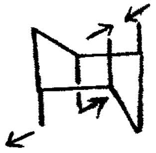
Finally, recourse to NMR spectroscopy dispelled the uncertainties surrounding the probable structure of Vc. The NMR spectra of the bromo derivatives Vb and Vc are complex. The proton H_A in Vb shows an octet, whereas H_A in Vc appears as a quartet. This multiplicity can be explained on the basis of long range nuclear spin-spin coupling (11). The double irradiation technique or the so called "spin decoupling" method (12) was applied to Vb and Vc and permitted the deduction and confirmation of their structures unambiguously.



Va Y=X=H

Vb Y=H, X=Br

Vc Y=X=Br



VI

In particular, for Vc, the long range coupling between H_A and H_C was found to be 1.8 cps, while the coupling between H_A and H_B amounted to 3 cps. These values together with the original quartet pattern exhibited by H_A are consistent only with the geometry and symmetry displayed by the diaxial dibromo arrangement Vc (11, 13).

The establishment of the α,α'-diaxial dibromocyclohexanone structure (exemplified by Vc) now poses the question of its unexpected existence. An explanation is fittingly found in terms of the "Reflex Effect" (14). Recently, it has been shown that repulsion between axial substituents on the bottom side of a cyclohexane chair causes axial substituents on the top side to come closer together (VI). Thus in 3,3,5,5 -tetramethylcyclohexanone (VII) axial substituents at C_2 and C_6 experience greater steric constraint than those in cyclohexanone itself (15). Comparison of bicyclo(3.2.1) octanone-3 (Va) with VII reveals that the ethane bridge "pinches" the cyclohexanone moiety so that axial substituents adjacent to the carbonyl function are tilted away from each other and consequently become less encumbered (16); accordingly the bulky diaxial dibromo configuration of Vc finds good accommodation.

A full account of this work will be published elsewhere.

Acknowledgements. We wish to express our thanks to Dr. A. Melera, Varian Associates, Zurich, Switzerland for the spin-decoupling experiments and to Professor G. Ourisson and Dr. J.M. Lehn for helpful discussions. We are particularly indebted to Professor G. Ourisson for the provision of laboratory facilities.

NOTES AND REFERENCES

1. C.W. Jefford, B. Waegell, J. Gunsher and J. Waslyn, presented at the XIXth IUPAC Congress, Abstracts A, p. 136. London, July 10-17, 1963.

2. E.J. Corey, J. Am. Chem. Soc., 75, 2301,3297 (1953).

3. E.J. Corey, T.H. Topie and W.A. Wozniak, J. Am. Chem. Soc., 77, 5415 (1955)

4. C.W. Jefford, Proc. Chem. Soc., 64, (1963).

5. These conditions may well be kinetic ones. A third product was isolated in trace amounts. It appears to be the trans dibromo derivative.

6. All compounds reported gave acceptable analyses.

7. R.N. Jones, D.A. Ramsey, F. Herling and K. Dobriner, J. Am. Chem. Soc., 74, 2828 (1952).

8. R.C. Cookson, J. Chem. Soc., 282 (1954).

9. Allinger's method was followed. N.L. Allinger, M. DaRooge, M.A. Miller and B. Waegell, J. Org. Chem., 28, 780 (1963).

10. Induction was assumed between the two C-Br bonds. N.L. Allinger, J. Allinger, L.A. Freiberg, R.F. Czaja and N.A. LeBel, J. Am. Chem. Soc., 82, 5876 (1960).

11. J.I. Musher, Molecular Physics, 6, 93 (1963) and references cited therein.

12. J.D. Baldeschwieler and E.W. Randall, Chem. Rev., 63, 81 (1963).

13. J. Meinwald and Y.C. Meinwald, J. Am. Chem. Soc., 85, 2514 (1963).

14. C. Sandris and G. Ourisson, *Bull. Soc. chim. France,* 1524 (1958).

15. B. Waegell and G. Ourisson, *Bull. Soc. chim. France,* 495, 496, 503 (1963).

16. B. Waegell, P. Pouzet and G. Ourisson, to appear in *Bull. Soc. chim. France*.