Large Preference for Equatorial Iodine in 2-Isopropyl-5-iodo-1,3-dioxans

By NICOLAS J. KOTITE, MARIA HARRIS, and MOSES K. KALOUSTIAN*

(Department of Chemistry, Fordham University, Bronx, New York 10458, *and Chemistry Department, American University of Beirut, Lebanon)*

Summary The configurational equilibria of diastereoisomeric 2-isopropyl-5-iodo-1,3-dioxans heavily favour the equatorial iodides at room temperature in all solvents studied: ΔG^0, $-1{\cdot}92$ (C_6H_{12}), $-1{\cdot}35$ (C_6H_6), $-1{\cdot}43$ ($CHCl_3$), and $-0{\cdot}95$ kcal mol^{-1} (MeCN).

VERY little is known about the conformational preferences of the iodo group in alicyclic systems, and there is virtually no knowledge of such preferences in heterocyclic systems. In cyclohexyl iodide, the iodo group has a mild equatorial preference (ΔG^0 $-0{\cdot}43$ kcal mol^{-1}).[1]

We here report the conformational analysis of a 5-iodo-substituted 1,3-dioxan, a model heterocyclic ring which has provided a fruitful framework for the study of the interplay of polar and van der Waals interactions.[2]

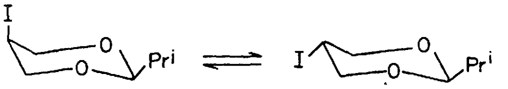
The anancomeric *cis*- and *trans*-2-isopropyl-5-iodo-1,3-dioxans (**1**) and (**2**) were equilibrated in the presence of Amberlyst-15 catalyst at room temperature; the results are summarized in the Table.

TABLE

Solvent	$-\Delta G_0$/kcal mol^{-1}	$-G^0{}_{cyc}$/kcal mol^{-1}
C_6H_{12}	1·92 ± 0·05	—
C_6H_6	1·35 ± 0·04	—
$CHCl_3$	1·43 ± 0·04	0·43
MeCN	0·95 ± 0·04	—

The equatorial iodides are favoured in all four solvents and, as expected,[3] the increase in the relative proportions of the more polar axial isomers (**1**) parallels the increase in the polarity of the solvent; the trend is similar to that of 5-bromo-, 5-chloro-, and 5-fluoro-1,3-dioxans.[4] The conformational energy of the iodo group in cyclohexane (1·92 kcal mol^{-1}) is the largest value reported to date for a monoatomic group in six-membered alicycles or heterocycles.

Since all four carbon–halogen dipole moments are quite similar (2·2—2·3 D), the greater preference observed for equatorial iodide as compared to the corresponding bromides in identical solvents, and comparison with the known conformational energy of iodocyclohexane, strongly suggest the presence of appreciably repulsive I · · · O non-bonded interactions in (**1**) (I · · · O *ca.* 3·49 Å). In the *cis*-2-isopropyl-5-halogeno-1,3-dioxans, as X varies from F to Cl to Br to I, the X · · · O non-bonded interactions gradually change from attractive (X=F) to repulsive (X=I), which is in marked contrast to those of the cyclohexyl halides,[5] where the conformation energies are small and constant.[6]



(1) (2)

FIGURE. Configurational equilibria in 2-isopropyl-5-iodo-1,3-dioxans.

Compound (**2**) was synthesized from *cis*-2-isopropyl-5-toluene-*p*-sulphonyloxy-1,3-dioxan and NaI in Me_2CO (sealed tube, 120 °C, 4 h, 28·5% isolated yield); compound (**1**) was best obtained† by equilibration of (**2**) in MeCN over Amberlyst-15 catalyst [(**2**)/(**1**) *ca.* 4)], followed by preparative g.l.c. (6ft, 15% Carbowax on Chromosorb W 40/60, 110 °C).‡

We thank the Arts and Sciences Research Council of the American University of Beirut for financial support, Rohm and Haas for a generous sample of Amberlyst-15, and Dr. P. B. Hill (American Health Foundation) for the use of his analytical gas chromatograph.

(*Received*, 25*th July* 1977; *Com.* 761.)

† Reaction of *trans*-2-isopropyl-5-toluene-*p*-sulphonyloxy-1,3-dioxan with NaI, under a variety of conditions, yielded (**2**) as the predominant product.

‡ The 1,3-dioxans gave satisfactory spectral and elemental analyses.

[1] J. A. Hirsch, 'Topics in Stereochemistry,' eds. N. L. Allinger and E. L. Eliel, Vol. 1, Interscience, New York, 1967, p. 204 and references cited therein.
[2] M. K. Kaloustian, N. Dennis, S. Mager, S. A. Evans, F. Alcudia, and E. L. Eliel, *J. Amer. Chem. Soc.*, 1976, **98**, 956; E. L. Eliel and D. Kandasamy, *J. Org. Chem.*, 1976, **41**, 3899.
[3] M. K. Kaloustian, *J. Chem. Educ.*, 1974, **51**, 777.
[4] R. J. Abraham, H. D. Banks, E. L. Eliel, O. Hofer, and M. K. Kaloustian, *J. Amer. Chem. Soc.*, 1972, **94**, 1913.
[5] N. S. Zefirov, L. G. Gurvich, A. S. Shashkov, M. Z. Krimer, and E. A. Vorob'eva, *Tetrahedron*, 1976, **32**, 1211.
[6] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Wiley, New York, 1965, pp. 45—46.