Substituent Effects on the Formation and Equilibration of *trans*-1,2-Dibromocyclohexanes

By P. L. BARILI, G. BELLUCCI, G. BERTI,* F. MARIONI, A. MARSILI, and I. MORELLI
(*Istituti di Chimica organica e Chimica farmaceutica, Università di Pisa, 56100 Pisa, Italy*)

Summary Ratios of diaxial to diequatorial dibromides ranging from 15·7 to 0·76 for the kinetic and from 1·7 to more than 100 for the thermodynamic products have been observed for the bromination products of some cyclohexenes substituted in the 3- and 4-position with groups of different size and polarity.

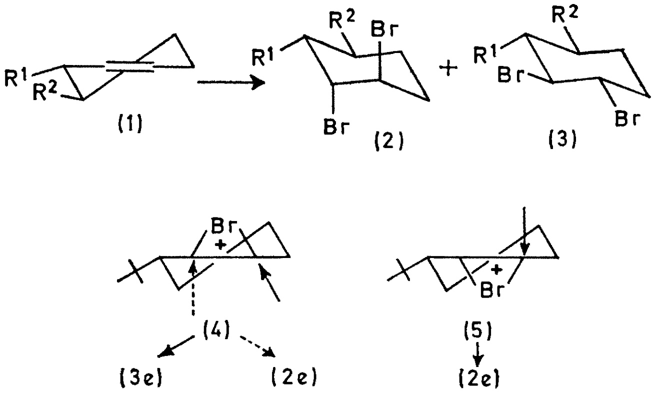
IT is generally assumed that the addition of electrophiles to cyclohexene derivatives gives the corresponding *trans*-diaxial products[1] preferentially. However, 3- and 4-substituted cyclohexenes (**1**) add bromine in chloroform to produce, as well as the diaxial (**2**), the diequatorial dibromides (**3**); the ratios (**2**) : (**3**) appear to depend on the size, position, and polarity of the substituent (see Table). Analyses were carried out by an n.m.r. method (integration of the signals corresponding to the protons α to bromine), and by g.l.p.c. [except for (**2e**) and (**3e**) which equilibrate at the temperature of the injection block]; the two techniques gave identical results.

Alkene	Ratio[a] (**2**) : (**3**)	$k_1 \times 10^5$ (s^{-1})	$(\mathbf{3}) \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} (\mathbf{2})$[b] $k_{-1} \times 10^5$ (s^{-1})	K_{393}
(**1a**; $R^1 = H$, $R^2 = Me$)	6·7	1·95	1·1	1·8
(**1b**; $R^1 = H$, $R^2 = Bu^t$)	15·7	2·4	1·4	1·7
(**1c**; $R^1 = H$, $R^2 = CO_2Me$) ..	9·0	2·35	0·9	2·6
(**1d**; $R^1 = Me$, $R^2 = H$)	3·5	1·95	0·9	2·2
(**1e**; $R^1 = Bu^t$, $R^2 = H$)	0·76	180	—	>99

[a] Products of the bromination in $CHCl_3$ at 0°.
[b] Thermal equilibration of neat liquid at 120° under N_2.

3-Substituted cyclohexenes yield higher amounts of diequatorial dibromides than the corresponding 4-substituted compounds; this is particularly evident in the case of the 3-t-butyl derivative (**1e**) which gives (**3e**) as the major product. This can be interpreted in terms of a steric effect of the substituent, which shields the *cis*- more than the *trans*-side of the ring and causes preferential formation of the *trans*-bromonium ion (**4**). On the other hand, the diaxial dibromide (**2e**) can be derived either from the *cis*-ion (**5**) by attack of the anion on C-1, or from the *trans*-ion (**4**) by attack on C-2, the latter process being again severely hindered by the steric effect of the vicinal alkyl substituent; attack on C-1 will therefore also be favoured in this case, leading to the diequatorial isomer (**3e**). These hypotheses are supported by previous results showing that (**1e**) reacts with peroxyacids to give a 9 : 1 ratio of *trans*- to *cis*-epoxide[2] (which can be considered as models for the bromonium ions) and adds hypochlorous acid to produce 45% diaxial and 55% diequatorial chlorohydrins.[3]

The dibromides (**2**) and (**3**) can readily and cleanly be thermally equilibrated, probably through the intramolecular mechanism suggested by Grob and Winstein.[4] The Table gives the K values for the (**3**) ⇄ (**2**) equilibria at 120°. The diaxial dibromide predominates in all cases because of the dipole–dipole repulsion.[5] The polarity of the substituent on C-4, more than its size, apparently influences the equilibrium, but only in a limited way. However, the size of the substituent on C-3 has a dramatic influence on the diaxial–diequatorial ratio at equilibrium, which corresponds to more than 99 : 1 (probably *ca.* 99·8 : 0·2) for the 3-t-butyl dibromides; also, the rate (k_1) of the diequatorial–diaxial conversion is almost 100 times higher for the 3-t-butyl than for the 3-methyl derivative. While these data cannot be justified by assuming an undistorted, perfectly staggered, chair conformation of the t-butylcyclohexane ring, in which the distance between an axial or equatorial substituent and one of the methyl groups of the adjacent equatorial t-butyl group would be exactly the same, recent calculations by Altona and Sundaralingam[6] indicate a considerable distortion of the geometry around the t-butyl group for the most stable conformation of t-butylcyclohexane: the non-bonding interactions are modified in such a way as to make a substituent on the vicinal carbon less hindered in the axial than in the equatorial position. However, the high preference of (**2e**) over (**3e**) cannot be explained only on the basis of these steric terms. Pasto and Rao[7] found that in the equilibrium between the *cis*- and *trans*-forms of 2-t-butylcyclohexanol the former (axial OH) is favoured by 0·55 kcal mol^{-1} at 298°K; even considering the preference of the diaxial (**2b**) over the diequatorial dibromide (**3b**) in the 4-t-butylcyclohexane system



($-\Delta G_{393} = 0{\cdot}41$ kcal mol^{-1}), one is far from accounting for the more than 3·6 kcal mol^{-1} by which (**2e**) is more stable than (**3e**). An increase in the dipole–dipole interaction term in (**3e**) could perhaps contribute to its destabilization. The n.m.r. spectrum of (**2e**) does not support its existence in a twist–boat conformation, since the half-band width of the unresolved signal corresponding to the protons α to Br 4·5 Hz at 60 MHz) is consistent with their being both approximately equatorial.

This work was supported by a grant from the Consiglio Nazionale delle Ricerche.

(*Received, August 6th,* 1970; *Com.* 1309).

[1] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, 1965, p. 99.
[2] J.-C. Richer and C. Freppel, *Canad. J. Chem.*, 1968, **46**, 3709.
[3] J.-C. Richer and C. Freppel, *Tetrahedron Letters*, 1969, 4411.
[4] C. A. Grob and S. Winstein, *Helv. Chim. Acta*, 1952, **35**, 782.
[5] Ref. 1, p. 159.
[6] C. Altona and M. Sundaralingam, *Tetrahedron*, 1970, **26**, 925.
[7] D. J. Pasto and R. D. Rao, *J. Amer. Chem. Soc.*, 1969, **91**, 2790.