Intramolecular Hydrogen Bonding in *trans*-2-Halogenocyclohexanols, and Enthalpy Differences between the Chair Conformations

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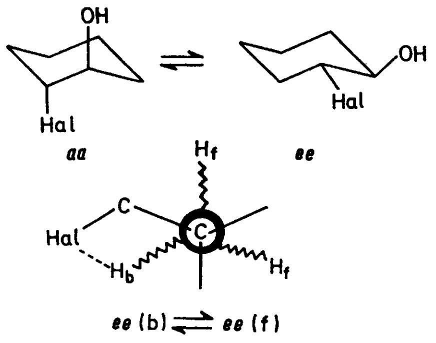
Summary Infrared studies show that in non-polar solvents at 25° the *ee*-forms of *trans*-2-halogenocyclohexanols are largely but not completely hydrogen bonded: the *ee*(bonded)- and *aa*-forms do not differ greatly in thermochemical stability.

THE *ee*- and *aa*-conformations of *trans*-2-halogenocyclohexanols are readily distinguished by i.r. spectrometry, which reveals the presence or absence of intramolecular hydrogen bonding.[1] In a recent quantitative study[2] of simple halogenohydrins in CS_2 solution, the enthalpy differences between the chair forms were evaluated on the basis that bonding is *complete* in the *ee*-conformations. This appeared questionable on general grounds, especially since the spectrum of a fixed *ee*-halogenohydrin has a distinct shoulder on the high-frequency side of the main O–H stretching band.[3] To test this point the four new steroids (I)—(IV)[4] shown in the Scheme were examined: the results were then used in a re-investigation of simple halogenocyclohexanols (V) and (VI).



SCHEME

Compounds were examined at spectral slit-width 2·5 cm^{-1} in 1 cm cells as dilute solutions in CCl_4(253—348 K) and CS_2 (253—309K). The following positions (ν_{max}, cm^{-1}) and, in parentheses, areas (A, percentages of total absorption) refer to the components of the O–H absorptions at 288K.

	Compound	Solvent	ν_{max} (A)	ΔH^0(J mol^{-1}) *ee*(f) ⇌ *ee*(b)	
(I)	2*β*-Bromo-5α-androstan-3α-ol	CCl_4	3620(100)		
(II)	3*β*-Bromo-5α-androstan-2α-ol	CCl_4	3625(1) 3613(8) 3583(91)	−11,500 ± 2000	
		CS_2	3603(8) 3573(92)	−17,000 ± 3000	
(III)	2*β*-Iodo-5α-androstan-3α-ol	CCl_4	3618(100)		
(IV)	3*β*-Iodo-5α-androstan-2α-ol	CCl_4	3618(11) 3606(4) 3569(86)	− 8000 ± 1000	
		CS_2	3603(5) 3582(11) 3558(84)	−11,000 ± 1500	
				aa ⇌ *ee*(b) corrected	apparent
(V)	*trans*-2-Bromocyclohexanol	CCl_4	3620(9) 3603(3) 3580(88)	−2100 ± 2000	−8000
		CS_2	3611(8) 3597(3) 3577(89)	+5300 ± 3000	−12,000[a]
(VI)	*trans*-2-Iodocyclohexanol	CCl_4	3619(13) 3604(2) 3568(85)	−7600 ± 2000	−8000
		CS_2	3606(14) 3588(5) 3559(81)	+4500 ± 3000	−7100[b]

[a] Ref. 2 gives −8000. [b] Ref. 2 gives *ca.* −9500.

Two of the steroids, (I) and (III), showed "single" bands (thus resembling 5α-androstan-3α-ol[5]) throughout the temperature range studied: these compounds therefore remain in the expected *aa*-arrangement. (That this probably corresponds to various particular conformations, related by rotation of the C–OH bond, is immaterial for the present purpose.) Analysis (Dupont 310 curve resolver) of the O–H absorption of the *ee*-compounds (II) and (IV) gave components (Scheme) with about 70% Lorentzian character. With each compound the main band corresponds to the bonded form *ee*(b) and the minor ones to the free forms *ee*(f). The latter become more important as the temperature is increased, and a quantitative study led to the ΔH^0 figures shown.

From these results it follows that the highest-frequency band of a halogenocyclohexanol, (V) or (VI), represents overlapping absorption of *aa* and *ee*(f)-forms. Separation of the contributions was based on the assumption that the position of the *ee*(f) ⇌ *ee*(b) equilibrium at a particular temperature is the same as that of the steroidal analogue (II) or (IV). In this way the total O–H absorptions were divided between the *aa*-forms (one band) and the *ee*-forms (three bands), and the enthalpy differences between the *aa*- and the *ee*(b)-forms were obtained from the temperature dependence of the appropriate absorptions. The results are subject to rather wide limits of uncertainty since the procedure involves assessing the differences between small areas, and making certain assumptions in the theoretical treatment.[4] The main conclusion is that the enthalpies of the forms are closer than is suggested by "apparent" ΔH^0 values [based on the notion that the *ee*-form is entirely in the *ee*(b)-conformation[2]]. Thus destabilisation of the *aa*-form by steric factors and of the *ee*(b)-form by dipole–dipole interaction leads to a balance of thermochemical stabilities.

The half-height widths (*ca.* 25 Hz) of the >C*H*–Hal and >C*H*–OH signals of compounds (V) and (VI) (at 100 MHz and 30° in CCl_4) show that diequatorial forms predominate, but give little guide as to the relative concentrations of diequatorial and diaxial forms ([*ee*(b)] + [*ee*(f)]/[*aa*]). To obtain these from the i.r. data requires knowledge of the forms' integrated absorption coefficients. Attempts to evaluate the coefficients by the standard procedure[6] were unsatisfactory; although accurate relative concentrations could not therefore be obtained they appear to be in the range 7—12 for CCl_4 and CS_2 solutions at 25°. In view of the present results entropy effects must be important in leading to the predominance of diequatorial forms.

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