Conformational Effects in the Reaction of 2-Monochlorocyclobutanols with Base: Ring-contraction *versus* Hydride Shift

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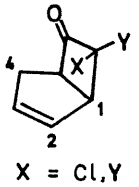
Summary 2-Monochlorocyclobutanols, treated with base, either ring-contract or undergo a hydride shift: conformational analysis explains the observed course of reaction.

STEREOSPECIFIC, base-catalysed ring contraction of certain 2,2-dichlorocyclobutanols involved the chlorine atom *trans* to the hydroxyl group; a bent cyclobutane ring with the diequatorial arrangement of these groups was suggested for the reaction pathway.[1] For *cis*-2-monochlorocyclobutanols where the diequatorial arrangement cannot be achieved, we now report two distinct modes of reaction: either stereospecific ring-contraction to cyclopropane carboxaldehydes, or a hydride shift leading to cyclobutanones.



(I) X = Cl, Y = H
(II) X = Cl, Y = Me
(III) X = Me, Y = Cl

The addition of monochloroketens to cyclopentadiene provided a useful source of the intermediate monochlorocyclobutanones. Thus, monochloroketen gave exclusively the 7-*endo*-chloroketone (I)[2] whilst methylchloroketen yielded both the 7-*endo*- and 7-*exo*-chloro-derivatives[3]

[respectively (II) and (III)], separable by chromatography. Borohydride reduction of these α-chloroketones was markedly affected by the C–Cl dipole, which directed attack on the opposite face of the cyclobutanone to that linked to the chloro-group (see Table). In the *exo*-chloro-

Borohydride reduction of bicyclo[3,2,0]hept-2-en-6-ones

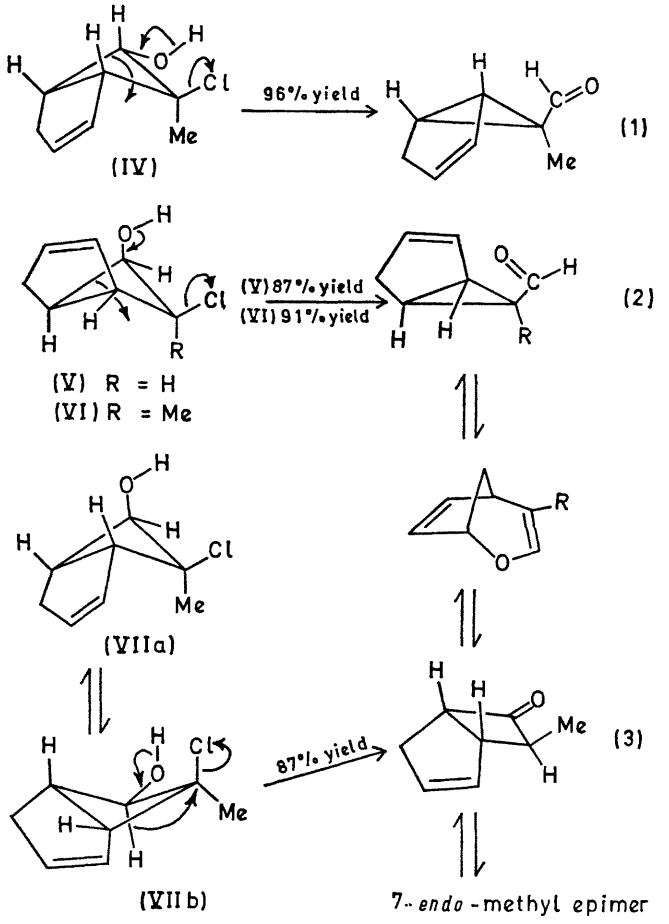
Ketone	Yield	% *endo*-Alcohol	% *exo*-Alcohol
(I)	96	100	0
(II)	93	100	0
(III)	97	22	78
7,7-Dichlorobicyclo-(3,2,0)hept-2-en-6-one	94	81	19

ketone (III), this effect reverses the normal preference for *exo*-face attack in the bicyclo[3,2,0]hept-2-en-6-one system,[1,4] whilst for the *endo*-chloroketones (I and II) steric and dipole effects combine to produce the *endo*-alcohols exclusively.[2]† It was difficult to separate the epimeric alcohols derived from (III), but low-temperature crystallisation gave the *exo*-alcohol (VII, m.p. 44°; 97% pure) and the *endo*-alcohol (IV; 91% pure) as an oil.

All alcohols reacted rapidly and stereospecifically with strong aq. KOH, and the course of the reactions are outlined in Equations (1—3). In the ring-contraction reactions, only one aldehyde signal was observed in the n.m.r. spectrum of each product, while stereochemistry was clearly indicated by the fact that each *endo*-aldehyde was in equilibrium with its 2-oxabicyclo[3,2,1]octa-3,6-diene valence-bond tautomer.[5]‡ For characterisation, and as a further check on the stereospecificity of the reaction, the aldehydes were oxidised to the corresponding crystalline acids (Ag_2O) which were then analysed as methyl esters (g.l.c.).

Ring-contraction of (IV) is unexceptional, as the chloro- and hydroxy-groups can achieve the *trans*-diequatorial arrangement known to be required in the dichloro-series[1] (Equation 1). For the 7-*endo*-chloro-6-*endo*-alcohols (V and VI), ring-contraction is again observed and with inversion occurring at C-7 in the rearrangement a reaction path involving an equatorial chlorine and an axial hydroxyl group seems most likely. (Equation 2.) The diequatorial arrangement of the reacting groups is not, therefore, mandatory in this reaction.

A remarkable change in mechanism was observed when the 7-*exo*-chloro-6-*exo*-alcohol was treated with base. In this case, no aldehyde was detected, but instead the equilibrium mixture of 7-*endo*- and 7-*exo*-methylbicyclo[3,2,0]-hept-2-en-6-ones (66% *endo*-epimer) was obtained. A hydride shift was shown to have occurred (as in Equation 3), rather than elimination of HCl to give the enol as intermediate, because after a short reaction time in D_2O–KOD and examination of the ketones by n.m.r. the signal of the methyl group for the 7-*exo*-methyl ketone was a doublet (therefore 7-*endo*-hydrogen rather than deuterium), whereas for the 7-*endo*-methyl ketone the methyl appeared as a singlet. Thus the latter compound was formed by deuteriation of the enolate anion derived from undeuteriated 7-*exo*-methyl ketone.



We suggest that ring-contraction, normally the favoured reaction course, is not observed with the latter alcohol because the required conformation with an equatorial chloro-group (VIIa) produces a bad interaction between the 7-*endo*-methyl group and the C-4 *endo*-hydrogen atom. The preferred conformation with both hydroxyl and methyl groups equatorial (VIIb) is nicely set up for the observed hydride shift. [Such a pathway is not available for alcohol (IV) where the same bad interaction is present in the ring-contraction]. Thus, conformational considerations, well established for cyclohexanes, appear to be of use in considering the reactivity of cyclobutanes, even in rather inflexible systems.

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† Stereochemical assignments will be dealt with in a later publication.
‡ By n.m.r. ($CDCl_3$) the product of alcohol (VI) contained 82% of aldehyde valence-bond tautomer.

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