Conformation and Reactivity in 2-Chlorocyclobutanones: the Rearrangement of 7-*exo*-Chloro-7-isopropylbicyclo[3,2,0]hept-2-en-6-one

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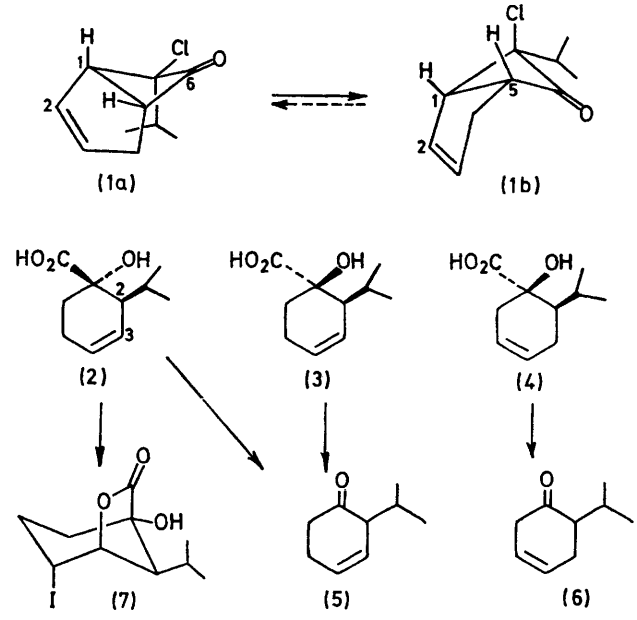
Summary Because of conformational effects in the cyclobutanone ring, 7-*exo*-chloro-7-isopropylbicyclo[3,2,0]-hept-2-en-6-one rearranges abnormally on base treatment and gives three hydroxycyclohexenecarboxylic acids: a possible mechanism involves ketol rearrangements.

THE stereospecific ring-contraction of 2-halogenocyclobutanones with aqueous base, recently reviewed by Conia and Salaun,[1] proved invaluable for establishing the relative stereochemistry of several chloroketen–cyclopentadiene adducts:[2] the reaction has recently been re-examined.[3]

We now report that the 7-*exo*-chloro-adduct (1) from chloroisopropylketen behaves anomalously with 2N-NaOH, because of the difficulty of achieving the equatorial chloro-group conformation required for ring contraction:[1] in conformation (1a) the 7-*endo*-isopropyl group and *endo*-4-H interact unfavourably.† Instead of the expected bicyclo-[3,1,0]hexene-*exo*-carboxylic acid, the adduct (1) slowly gives three isomeric hydroxy-acids (2), (3), and (4), in a ratio of 30:20:50 (50%; 95% of total acids) together with 2-isopropyltropone (18%.)[5] The structures for these acids follow from reactions outlined in Scheme 1. Dihydro-derivatives of acids (3) and (4) were identical, but different from dihydro-(2): the former had the same relative stereochemistry at C-1 and C-2. Further, all dihydro-derivatives after conversion into the corresponding 1,2-glycols gave 2-isopropylcyclohexanone upon periodate cleavage, showing that all three acids had the same carbon-skeleton.

The position of the double-bond in each acid was established by similar periodate cleavage without prior hydrogenation. Acids (2) and (3) gave the same non-conjugated cyclohexenone shown to be (5) by its ready isomerisation to 2-isopropylcyclohex-2-enone (λ_{max} 235 nm; 1 olefinic proton, δ 6·69). In the same manner acid (4) gave a different non-conjugated cyclohexenone (6), which isomerised with base to 2-isopropylcyclohex-4-enone (λ_{max} 227 nm; 2 olefinic protons δ 6·00, 6·95).‡ Finally the relative



SCHEME 1.

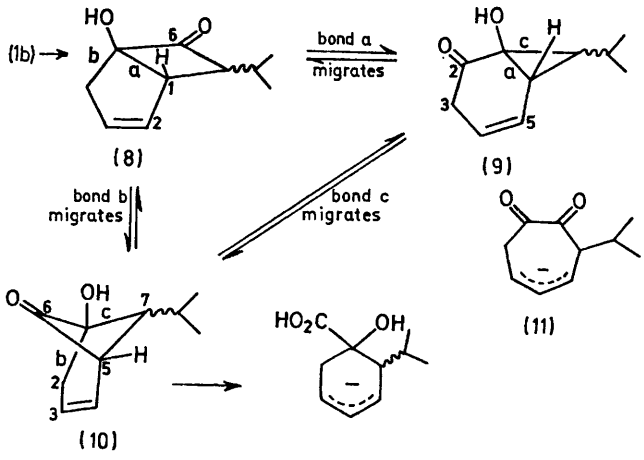
stereochemistry of these acids at C-1 and C-2 was demonstrated by their behaviour with Na_2CO_3–I_2. Acid (2) reacted completely within 8 min to give iodo-lactone (7), whilst in contrast acids (3) and (4) gave only partial reaction after 24 h.§ In a half-chair conformation of these

† The size of the *endo*-substituent in (1) appears critical: the 7-*endo*-methyl and -ethyl adducts ring-contract normally. In the case of related cyclobutanols, a 7-*endo*-methyl substituent is sufficient to divert the normal ring-contraction.[4]

‡ The non-conjugated cyclohexenones were only characterised spectroscopically: other compounds mentioned here had satisfactory analyses.

§ Iodolactonisation was used to separate acid (2) from acids (3) and (4). Treatment of lactone (7) with zinc–methanol regenerated (2).

acids the axial carboxylate anion required for iodolactonisation is only readily attained when the neighbouring isopropyl group is *cis* and pseudoequatorial. This stereochemistry we therefore assign to acid (2).



SCHEME 2.

Rearrangement in deuterium oxide–NaOD gave hydroxy-acids (2), (3), and (4), containing *four* non-exchangeable deuterium atoms per mole, located by the ^{1}H n.m.r. spectra at C-2 (1D), C-6 (2D), and the allylic methylene group (C-3 or C-5; 1D).

It is difficult to suggest mechanisms to account for the pattern of labelling which would not also lead to double-bond isomers of the acids observed.¶ Tentatively we favour Scheme 2, where the initially formed ketol (8)[6] equilibrates with ketols (9) and (10). The last-named resembles other bridged, $\beta\gamma$-unsaturated cyclobutanones which Wenkert has shown to open *via* the allyl anion.[7] This scheme does require selective deuteriation of the enol of (9) at C-3 rather than C-5, which further implies moderately rapid conversion of (9) into (10) and thence into ring-opened products. Evidence for the intervention of ketol rearrangements was obtained from the behaviour of the related spiro-adduct (1; but with bismethylene at C-4): under similar conditions it yielded epimeric tricyclic ketols (9; but bismethylene at C-3) (ν_{max} 1665 cm^{-1}) in 15% yield. Further comment on the above mechanisms is reserved for the full paper.

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¶ The alternative opening of either ketol (8) or (9) to the anion (11), followed by protonation and benzylic acid rearrangement would be expected to lead to extensive deuteriation and other double-bond isomers of the observed acids unless the benzylic acid rearrangement was unusually fast.

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[3] D. L. Garin and K. L. Canmalk, *J.C.S. Chem. Comm.*, 1972, **333**.
[4] P. R. Brook and A. J. Duke, *Chem. Comm.*, 1970, **652**.
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[6] The formation of 5-substituted derivatives by nucleophilic displacement on these chloroketen adducts is now well established: see ref. 3, and V. R. Fletcher and A. Hassner, *Tetrahedron Letters*, 1970, 1071; W. T. Brady and J. P. Hieble, *J. Org. Chem.*, 1971, **36**, 2033, P. D. Bartlett and T. Ando, *J. Amer. Chem. Soc.*, 1970, **92**, 7518.
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