Substitution *vs.* Rearrangement in 7-Chloro-7-methylbicyclo[3,2,0]hept-2-en-6-ones. The Importance of C-7 Stereochemistry

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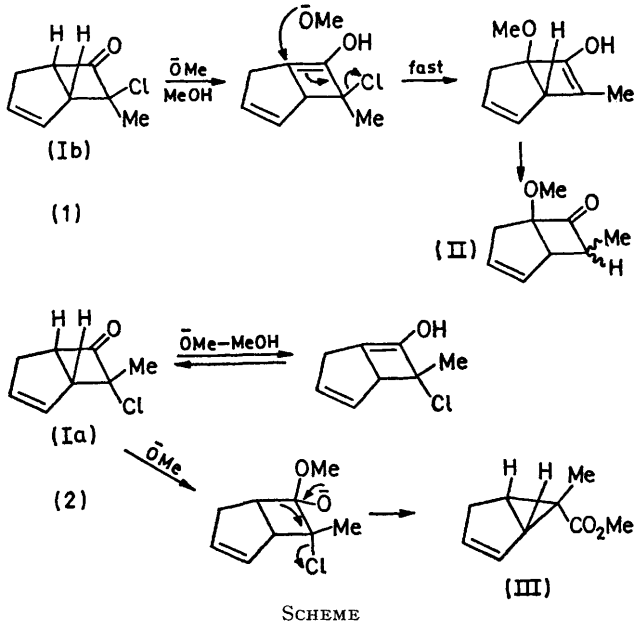
Summary The chloromethylketen adducts of cyclopentadiene undergo competitive stereospecific substitution and rearrangement reactions with nucleophilic bases which depend upon the base strength and the C-7 stereochemistry of the starting material.

CHLOROCYCLOBUTANONES have been utilized for a large number of synthetic schemes.[1] This report describes stereospecific rearrangements of the chloromethylketen adducts of cyclopentadiene (Ia, Ib)[2] dependent upon their C-7 stereochemistry.

Treatment of the individual isomers (Ia) and (Ib) with lithium methoxide in methanol gave two distinct reactions. At room temperature, (Ib) rapidly and quantitatively gives a C-7 epimeric mixture of 5-methoxy-7-methylbicyclo-[3,2,0]but-2-en-6-ones (II). At a slower rate, (Ia) rearranges stereospecifically to *endo*-6-methoxycarbonyl-*exo*-6-methylbicyclo[3,1,0]hex-2-ene (III). These results can be rationalized by mechanisms 1 and 2 (Scheme).



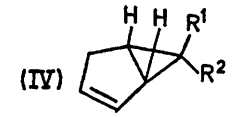
SCHEME

In mechanism 1, the rate determining step is the formation of the enol of (Ib). This is followed by a fast S_N2' reaction to give a methoxy-substituted enol which ketonizes to (II). The fact that this substitution occurs rapidly with the 7-*exo*-chloro-compound but not with the 7-*endo*-chloro-isomer is in accord with the known stereochemistry of this reaction where the attacking nucleophile is *syn* to the leaving group.[3] Unable to follow this pathway, (Ia) undergoes a comparatively slow semibenzilic acid rearrangement (mechanism 2). The stereospecificity of the semibenzilic acid rearrangement of α-chlorocyclobutanones to cyclopropane carboxylic acids has been demonstrated.[4]

In support of these mechanisms, we have followed these reactions with n.m.r. spectroscopy using deuteriated lithium methoxide in CD_3OD. Using less than one equivalent of base with (Ib), we observed a rapid formation of (II) with the C-7 methyl group of the products appearing as singlets. The 7-*endo*-methyl isomer of (II) (δ 1·0 p.p.m.) is formed preferentially (as predicted by ease of protonation) but subsequent equilibration results in an epimeric mixture favouring the 7-*exo*-methyl isomer (δ 1·2 p.p.m.) in *ca.* 6:4 ratio.† N.m.r. integration indicates the absence of C-5 proton exchange of unchanged starting material signifying that the methoxide addition to the enol is faster than ketonisation. The formation of (II) from (Ib) is in accord with literature reports of related α,α-dichloro- and α-chlorocyclobutanones.[5-7]‡ However, in these examples, an analysis of the significance of the stereochemistry of the leaving group was not attempted.

Similar reaction with (Ia) showed a rapid loss of the C-5 proton n.m.r. signal followed by the formation of product (III). N.m.r. integration indicated complete exchange of the C-5 proton of both product and starting material showing that ketonization is faster than product formation.

Upon treatment with aqueous lithium hydroxide, the *endo*-chloro-isomer (Ia) rearranges stereospecifically to the *endo*-carboxylic acid (IVa) (m.p. 94—94·5°, 83%). Similar treatment of the *exo*-chloro-isomer (Ib) produces a product mixture from which the *exo*-carboxylic acid (IVb) (m.p. 75—75·5°, 60%) can be sublimed. The use of LiOD in D_2O produced acids (IVa) and (IVb) with no incorporation of deuterium at carbon as indicated by n.m.r. integration. Thus it appears that aqueous hydroxide ion does not promote enolization of (Ia) or (Ib) at a rate competitive with the semibenzilic acid rearrangement.



a, $R^1 = Me$; $R^2 = CO_2H$

b, $R^1 = CO_2H$; $R^2 = Me$

In utilizing α-halogenocyclobutanones for synthetic purposes, two determining factors that must be considered are the nature of bases and nucleophiles in the reaction media (already shown to be strategic)[5] and the stereochemistry of the halide (a determining factor in the synthesis of 2-alkyltropones from I).[8]

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† The configurations are based on the chemical shifts of *exo- vs. endo*-methyl protons at C-7 in the n.m.r. spectra; in related compounds that of the latter appears at higher field (see W. T. Brady, F. H. Parry, tert., and J. D. Stockton, *J. Org. Chem.*, 1971, **36**, 1486).

‡ In using mixtures of (Ia) and (Ib), other investigators failed to observe significant amounts of (II).[7] Under their experimental conditions, we found that the individual isomers (Ib) and (Ia) produced (II) and (III), respectively.

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