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SOLVOLYSIS OF BRIDGEHEAD-SUBSTITUTED BICYCLO[2.2.0]HEXANES (1)

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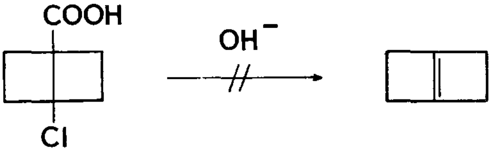
While working out conditions for the preparation of 4-chlorobicyclo-[2.2.0]hexane-1-carboxylic acid (I) (2), the lability of the chloroacid in basic solution was noted. We have now examined its solvolysis as part of a general program of research on reactivity and rearrangements of strained bicyclic compounds and because halodecarboxylation of I might afford (but has not) the interesting strained olefin bicyclo[2.2.0]hexene-1,4 (II). Although the preferred course of halodecarboxylation is generally trans (3) and the method of synthesis requires the chlorine and carboxyl of I to be cis (2), Vaughan, et al., have observed that cis-2-bromocyclopentane carboxylate actually gives more cyclopentene than the trans on basic solvolysis (4). The latter result is consistent with either a non-concerted process or a concerted cis-elimination via co-planar leaving groups (5) but in either case encouraged the hope of preparing II in this way.



I II

The anion of I was solvolyzed at 40.0° in water and in 80% ethanol, each 1.0 M in sodium hydroxide, and gave first-order kinetics to 100% reaction. In water k_1 is 2.5×10^{-4} sec^{-1} (half-life 46 min.) and in 80% ethanol k_1 is 1.5×10^{-6}. In 80% ethanol 1.0 M in perchloric acid there is no reaction ($k_1 < 6 \times 10^{-8}$). The effect of solvent polarity on the rate shows that the solvolysis is S_N1 in nature and that the carboxylate anion does not participate in the rate-determining step (3,6).

From aqueous solvolysis we isolated a mixture of acids in essentially quantitative yield; gas chromatography of the methyl esters (prepared with diazomethane) indicated the presence of four products in the ratio 70:23:5:2. The major acid (III) after purification had m.p. 97-100° and composition $C_7H_{10}O_3$* and consumed one mole of hydrogen on reduction over palladium, giving dihydro-III, m.p. 93.5-94.5°. Spectra of III-methyl ester, $\nu_{CO}^{CCl_4}$ 1735 cm^{-1}, indicated the presence of a tertiary hydroxyl group α to the carbomethoxyl (doublet -OH absorption at 3603 and 3545 cm^{-1} in dilute carbon tetrachloride solution)(7) and a terminal methylene (ν^{CCl_4} 3077, 884 cm^{-1}; τ 5.18, 2H, broad singlet). The structure of III was then established (8) by reduction of dihydro-III-methyl ester with lithium aluminum hydride followed by cleavage of the resulting crude diol with periodic acid, giving finally 3-methylcyclopentanone, identified by comparison with an authentic sample. The next two products (IV + V), though not individually characterized, were shown to be diolefinic acids with the same carbon skeleton as III by hydrogenation to 3-methylcyclopentane carboxylic acid (glpc comparison; stereochemistry unknown) and independently by preparing a similar mixture by dehydrating III. The last product could not be obtained in sufficient quantity for identification.

We may use the solvolysis rate found for I to estimate a rate for the corresponding chlorohydrocarbon, and compare the estimated rate with a prediction for a localized (classical) model. Vaughan, et al. (4), have solvolyzed several β-bromo acid anions having structures such that the carboxylate anion cannot participate in the transition state (e.g. 2-bromobicyclo[2.2.2]octane-1-carboxylate) and find rate accelerations of 11-42 fold over the corresponding halide without the carboxylate group; taking an intermediate value of 25, we estimate the rate for 1-chlorobicyclo[2.2.0]hexane (VI) (9) in 80% ethanol at 40° to be 6×10^{-8}. Assuming a simple additivity of I-strain, we can predict the rate for a classical model by dividing the observed rate for

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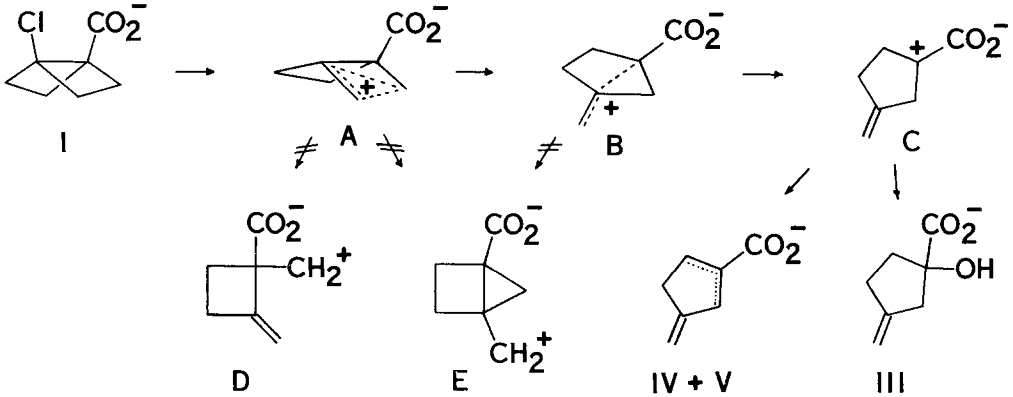
*Satisfactory analyses were obtained for all new compounds characterized.

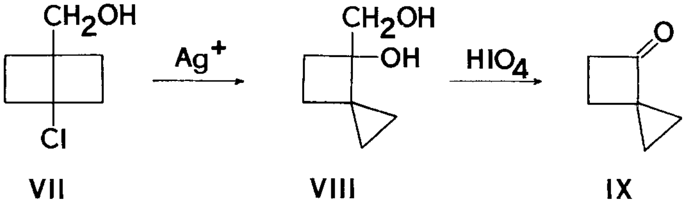
1-chloro-1-methylcyclobutane (10) by the factor by which the latter compound is slower than tert-butyl chloride (13.5); in this way, we predict for VI a rate of 3 x 10^{-7}. The fair agreement of the two values indicates that the observed rate for I is about "normal", or that whatever σ-delocalization occurs in the transition state does not dramatically affect the rate.

On the other hand the products observed from solvolysis of I seem most satisfactorily rationalized as proceeding from delocalized intermediate cations:



Rearrangement to ion C clearly requires more than one step, and failure to observe products derived from localized ions D and E despite the strongly nucleophilic environment argues against their inclusion in the scheme.

Although we do not yet have rate data, we find the silver-assisted solvolysis of 1-hydroxymethyl-4-chlorobicyclo[2.2.0]hexane (VII) takes a different course, with the 1,2 rather than the 2,3 bond migrating. Carbinol VII was prepared by diborane reduction of I (11) and solvolyzed in aqueous silver nitrate at room temperature. The proximate product, glycol VIII, was not purified but was oxidized directly with periodic acid to give spiro[2.3]hexan-4-one IX, isolated in about 80% yield.



The structure of IX follows uniquely from its composition and spectroscopic properties. The infrared spectrum indicated cyclopropane C-H at 3086 cm^{-1} and a cyclobutanone carbonyl at 1776 cm^{-1}, while the nmr spectrum consisted of two sets of AA'BB' multiplets with band centers at approximately 7.0 (C-5), 7.8 (C-6), 8.75 and 8.95 (C-2, C-3) τ. Other bands in the infrared spectrum of IX occurred at 1445 (m), 1414 (m), 1389 (m), 1333 (s), 1238 (m), 1149 (m), 1116 (m), 1049 (s), 1042 (s), 1011 (w), 977 (s) and 864 (m) cm^{-1}. Despite the large number of steps from commercially-available starting material, this route appears the best available to the interesting (12) 4-substituted spirohexane system.

Further studies on the transformations of these and related compounds are in progress, and will be reported in forthcoming papers.

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