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1-HALOBICYCLO[2.2.2]OCTANES

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The commonly used methods for the preparation of 1-halobicyclooctane derivatives, i.e., (i) the Hunsdiecker reaction of bicyclo[2.2.2]octane-1-carboxylic acids[1] and (ii) the halogenation of bicyclo[2.2.2]octan-1-ols with Lucas reagent[2], presented severe limitations to their synthetic utility. This fact, coupled with the intrinsic theoretical interest in reactions at bridgehead carbon atoms, prompted us to investigate the preparation and reactions of this series of compounds.

We wish now to report the facile synthesis of 1-halobicyclo[2.2.2]octanes from the corresponding 1-hydroxy and 1-methoxy derivatives. We have found that the thermal reaction of 4-methylbicyclo[2.2.2]octan-1-ol (Ia) with a sample of undistilled phosphorus oxychloride afforded 1-chloro-4-methylbicyclo[2.2.2]octane*) (Ic), m.p. 76-77°. As expected, when the reaction was effected in the presence of polyphosphoric acid with freshly-distilled phosphorus oxychloride or thionyl chloride, both yield (75 - 80%) and degree of purity of Ic were improved. This method is not limited, however, to the preparation of chloro compounds, but can be extended to other halo derivatives, as illustrated by the synthesis of 1-bromo-4-methylbicyclo[2.2.2]octane (Id). Treatment of carbinol Ia with phosphorus tribromide and polyphosphoric acid afforded compound Id, m.p. 92-93°, [lit.[3] 92-94°], in 77 % yield.

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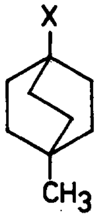
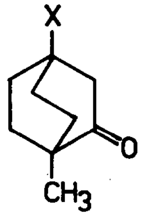
* Satisfactory elemental analyses and consistent infrared and n.m.r. spectra were obtained for all compounds reported herein.



Ia, X = OH Id, X = Br

Ib, X = OMe Ie, X = $OPOCl_2$

Ic, X = Cl



IIa, X = OH

IIb, X = OMe

In view of the fact that acid-catalyzed cleavages of C-O bonds at bridgehead carbon atoms presumably involve carbonium ion intermediates, it appeared reasonable to extend this reaction to an alkoxy derivative. As expected, 1-methoxy-4-methylbicyclo[2.2.2]octane (Ib) was easily converted under identical reaction conditions to the same chloro derivative Ic, in 75 % yield. On the other hand, treatment of Ia with freshly-distilled phosphorus oxychloride in the absence of polyphosphoric acid gave the expected dichlorophosphate (Ie), m.p. 39-40°, in 80 % yield. The structure of Ie was established by an examination of its spectral data. The infrared spectrum was consistent with structure Ie; its n.m.r. spectrum (CCl_4) showed a singlet of 3 methyl protons at 0.83 ppm. and a multiplet of 12 methylene protons at 1.9 ppm.

Starting compounds Ia and Ib were prepared from the corresponding 1-hydroxy (IIa) and 1-methoxy-4-methylbicyclo[2.2.2]octan-3-ones (IIb), in 75 - 78 % yield by a modified Wolff-Kishner method, the details of which will be reported later. The procedure employed here afforded considerably higher yields than previously published methods[3,4].

Further studies intended to exploit this method of substitution of various functional groups on bridgehead carbon atoms are now in progress[5]. Details, including spectral data for these compounds and further examples, will appear in a subsequent publication.

References

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3 H.D.Holtz and L.M.Stock, J.Am.Chem.Soc. 86, 5183 (1964) ; the authors are grateful to Prof.L.M.Stock for a copy of part of the Ph.D. thesis of Dr. Holtz.

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5 After this paper had been prepared for publication, the work of K.Suzuki and K.Morita [J.Org.Chem. 32, 31 (1967)] appeared, in which the synthesis of 1-halobicyclo[2.2.2]octanes from 1-methoxy or 1-hydroxy derivatives by the use of inorganic halides or acyl halides in the presence of stannic chloride, are reported. The facility and yields of the method described by the above mentioned authors are quite similar to those reported in this paper.