Displacement Reactions on 7-Halogenonorbornanones

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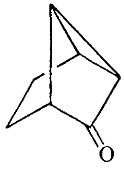
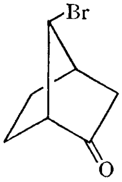
IN the course of investigations directed towards a synthesis of the tricyclic ketone (I) we have discovered two reactions of 7-halogenonorbornanones which appear to be of both preparative and mechanistic significance.

The first reaction is a displacement with inversion of configuration at C-7. The readily available *syn*-7-bromonorbornanone (II)[1] reacted with lithium chloride in refluxing dimethylformamide[2] to give *anti*-7-chloronorbornanone (III) as major product. The latter could be obtained pure by g.l.c. and was identical with an authentic sample prepared by a more circuitous route. S_N2 Displacements at C-7 in norbornane are rare: they are expected to be disfavoured as a consequence of the low C-1, C-7, C-4 bond angle (93°)[3] and of steric hindrance by the *exo*-hydrogens at C-5 and C-6 to the incoming nucleophile. Although we have some evidence that the carbonyl group may play a rôle in facilitating displacement in the present instance, *cf.* high reactivity of α-halogeno-ketones in S_N2 reactions, this possiblity requires further investigation.

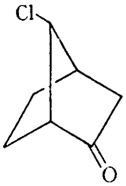
The second reaction is a displacement with retention of configuration at C-7. Treatment of the *anti*-chloro-ketone (III) with methanolic potassium hydroxide gave the *anti*-7-methoxy-ketone (IV)[4] as sole isolable product. Under the conditions used, *syn*-7-chloronorbornanone is recovered unchanged and the rate difference between the two epimeric chloro-ketones is estimated to be greater than 10^5. We ascribe the high reactivity of (III) in this reaction to participation of the enolate ion (V),[5] leading to (I) as a transient species, which subsequently reacts with methoxide ion to give (IV), *cf.* (VI).[6]



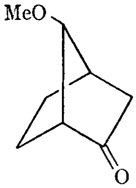
(I)



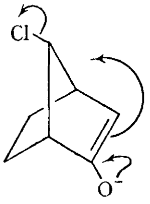
(II)



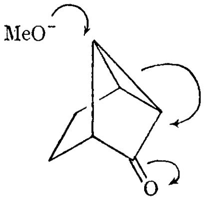
(III)



(IV)



(V)



(VI)

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[1] L. H. Zalkow and A. C. Oehlschlager, *J. Org. Chem.*, 1964, **29**, 1625; R. R. Sauers and J. A. Beisler, *ibid.*, p. 210.

[2] A. J. Parker, *Quart. Rev.*, 1962, **16**, 163; J. D. Hutchinson and W. M. Weaver, *J. Amer. Chem. Soc.*, 1964, **86**, 261.

[3] G. A. Sim, *J. Chem. Soc.*, 1965, 5974.

[4] Identified by comparison with material prepared by an unambiguous route, S. C. Lewis and G. H. Whitham, unpublished work.

[5] High reactivity of 7-*anti*-toluene-*p*-sulphonyloxynorbornanone in acetolysis has recently been similarly explained in terms of participation of the enol. P. G. Gassman and J. L. Marshall, forthcoming publication. We thank Professor Gassman for this information prior to publication.

[6] Absence of product derived from attack at C-4 is attributed to poor overlap of the C-3–C-4 bond with the π-orbital of the carbonyl group.