Formation of 1,5-Dimethylbicyclo[3,2,1]octan-8-one by Zinc Dehalogenation

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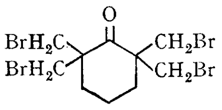
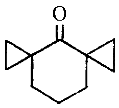
The reaction of 2,2,6,6-tetra(bromomethyl)cyclohexanone (I) with zinc in aqueous methanol has been shown to lead to the dispiro-compound (II) and the monospiro-compound (III).[1] In this reaction we report the formation of the bicyclic ketone (IV) in 5 and 10% yield respectively, together with (II) and (III), when an equivalent amount of the di- or mono-sodium salt of ethylenediaminetetra-acetic acid is added to the reaction medium. The appearance of a band at 1740 cm.$^{-1}$ in the crude reaction product on infrared analysis indicated formation of a new ketone.

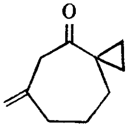
The crude reaction product was distilled, and then treated with aqueous potassium permanganate to remove the olefin (III). The product was then treated with Girard's reagent, and the derivative of (IV) was hydrolysed with dilute hydrochloric acid to regenerate the ketone. The ketone (II) does not form carbonyl derivatives under normal conditions.[1] The ketone was purified by repeated sublimation to m.p. 140—142°, and was readily identified as (IV) by n.m.r. and analytical analysis. Singlets appeared at 1·05 (6H), 1·72 (6H), and a slightly split peak appeared at 2·22 p.p.m. (4H). The 2,4-dinitrophenylhydrazone exhibited m.p. 189—190°, and the n.m.r. showed a pair of singlets at 1·04 and 1·08 (6H), a singlet at 1·76 (6H), and a broad multiplet at 2·35—2·70 p.p.m. (4H), along with the normal aromatic pattern.



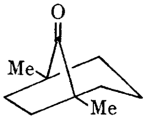
(I)



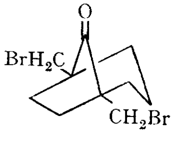
(II)



(III)



(IV)



(V)

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Separation of the singlet for the methyl groups of (IV) into a definite pair of singlets on formation of the dinitrophenylhydrazone is a valuable aid in structure confirmation of the otherwise symmetrical molecule. Geometrically, only one of the methyl groups is in close proximity to the face of the aromatic ring, and hence is shielded.

Tetrasodium ethylenediaminetetra-acetate has been used in zinc dehalogenation–cyclization reactions with considerable success, two outstanding examples being found in Applequist's synthesis of spiropentane[2] and McGreer's synthesis of spirohexane.[3] Zinc dehalogenation of (I) in the presence of Na_4-EDTA or acetic acid produced no (IV), but (II) and (III) were formed in different ratios along with the endocyclic isomer of (III). The addition of Na_3-EDTA to the reaction yielded only (II) and (III) in the same ratio as in its absence [(II)/(III) = 1·5].

Zinc dehalogenation of 2,2,5,5-tetra(bromomethyl)cyclopentanone in the presence of the disodium salt of EDTA did not yield any bicyclic ketone. It seems quite possible that the ketone (IV) arises from a protonated carbonyl intermediate whose conformation is geometrically oriented as to allow 1,5-cyclization to compete with 1,3-cyclization and ring expansion, the two probable initial reactions leading to ketones (II) and (III) respectively.[4] No evidence for formation of 2,2,6,6-tetramethylcyclohexanone was found, indicating that reduction of the bromomethyl groups occurs after formation of the intermediate (V).

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[2] D. E. Applequist, G. F. Fanta, and B. W. Henrikson, *J. Org. Chem.*, 1958, **23**, 1715.
[3] D. E. McGreer, *Canad. J. Chem.*, 1960, **38**, 1638.
[4] P. Leriverend and J. M. Conia, *Bull. Soc. chim. France*, 1966, **1**, 116.