Strained Systems: Cubane

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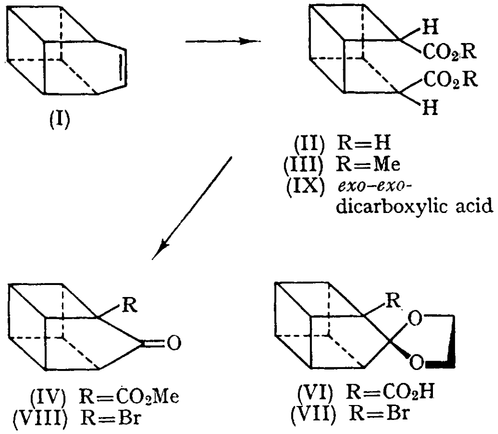
RECENTLY we reported the simple synthesis of pentacyclic hydrocarbon (I) from the cyclooctatetraene–maleic anhydride adduct.[1] We report a convenient conversion of (I) into the penultimate intermediate of Eaton and Cole's synthesis of cubane.[2]

Treatment of (I) with osmium tetraoxide provided in 75% yield a *cis*-diol, m.p. 140·5°[3] (isopropylidene derivative, 79·5°) which was smoothly oxidized with an excess of Jones reagent to afford the *endo–endo*-dicarboxylic acid (II),[4] m.p. 222·5° ν_{max} (Nujol) 3200—2500 cm.$^{-1}$, 1710. τ (pyridine) $-3{\cdot}83$ (2H, s), 6·37 (4H, m), 6·55 (2H, m) and 7·02 (2H, m). The above structure and stereochemistry of (II) is supported by the easy formation of an anhydride, m.p. 193°; ν_{max}(CHCl$_3$) 1810 (w) 1785, and 1740; τ (deuteriochloroform) 6·20 (6H, m) and 6·50 (2H, m). The dimethyl ester (III), m.p. 94°, of (II) underwent an intramolecular Dieckmann condensation on treatment with methylsulphinyl carbanion at 0° for 20 min. to provide in 85% yield a keto-ester (IV), m.p. 46°, ν_{max}(CHCl$_3$) 1770, 1725, τ (deuteriochloroform) 6·10 (3H, m) 6·20 (3H, s), 6·37 (3H, m), and 6·77 (1H, t).[5] In contrast, sodium methoxide treatment of (III) converted it into the *exo–exo*-isomer (V), m.p. 82°, presumably through (IV). Ketalization followed by alkaline hydrolysis converted (IV) quantitatively into the ketal acid, (VI), m.p. 125°.



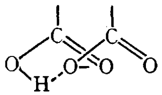
(I)

(II) R=H
(III) R=Me
(IX) *exo-exo*-
dicarboxylic acid

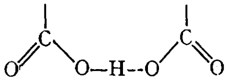
(IV) R=CO$_2$Me
(VIII) R=Br

(VI) R=CO$_2$H
(VII) R=Br

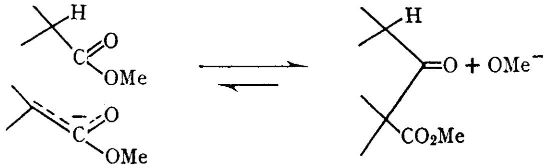
The modified Hunsdiecker reaction[6] of (VI) afforded the corresponding bromide (VII) and



(II)′



(X)



(III)′

chloride in 65% and 20% yields, respectively. Hydroloysis of (VII) gave a bromo-ketone (VIII). All physical properties of (VII) and (VIII) are identical to those reported by Eaton and Cole.[2] Since (VIII) has already been converted into cubane,[2] the above transformation completes a synthesis of cubane from cyclo-octatetraene.

The dissociation constants of (II) deserve comment. While pK_1 and pK_2 of the *exo–exo*-dicarboxylic acid (IX),[7] m.p. 261°, obtained from (V), are normal (4·22 and 5·27 in water), the *endo–endo* isomer (II) where the two carboxyl groups are extraordinarily congested exhibits unexpected pK values, 5·01 and 7·17 (water). One might expect the ΔpK of (II) to be at least greater than 5 since racemic di-t-butylsuccinic acid (X) showed ΔpK = 9·54.[8] The small ΔpK of (II) should be caused mainly by destabilization of the monoanion in view of a relatively large pK_1.[9] We tentatively suggest that because of the special geometrical arrangement of the monoanion the two carbonyl groups are oriented face to face as shown in (II)′, thus inducing a large dipole–dipole interaction. Those of the mono-anion of (X) could avoid such an interaction. Detailed studies on this unusual behaviour are under way.

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[1] S. Masamune, H. Cuts, and M. G. Hogben, *Tetrahedron Letters*, 1966, 1017; see also W. G. Dauben and D. L. Whalen, *ibid.*, p. 3743.

[2] P. E. Eaton and T. W. Cole, Jr., *J. Amer. Chem. Soc.*, 1964, **86**, 3157. For a second synthesis, see J. C. Barborak, L. Watts, and R. Pettit, *ibid.*, 1966, **88**, 1328.

[3] All new compounds reported herein melted with a range of less than one degree.

[4] The term "*endo*" is used with respect to the centre of the cube type molecule. The application of the Lemieux–Johnson oxidation to (I) resulted in the complete destruction of nuclear carbon–carbon bonds. As noted before in ref. 1, single carbon–carbon bonds of molecules of this type exhibit so-called double bond character. We found also that bromine reacts with the parent system. The *endo–endo*-dicarboxylic acid (II) decomposed at its melting point. Identical results were obtained from separate crystallizations from water, dioxan, and chloroform, and after hydrolysis of the anhydride.

[5] Although the keto-ester (IV) is extremely sensitive to alkali, the success of the Dieckmann condensation is due to an equilibrium which is controlled mainly by the relative basicity of methoxide and anion (III)′. Since no proton is available in the system to protonate (III)′, and since methoxide is the weaker base, the equilibrium is shifted to the right-hand side of the above equation.

[6] S. J. Cristol and W. C. Firth, Jr., *J. Org. Chem.*, 1961, **26**, 280.

[7] We have also isolated the *endo–exo*-dicarboxylic acid (XI), m.p. 251°(dimethyl ester, m.p. 73°), and established the stereochemistry of all three possible stereoisomers (II, IX, and XI) on the basis of chemical transformations, chemical equivalence and non-equivalence of the respective methoxycarbonyl and corresponding hydroxymethyl groups.

[8] L. Eberson, *Acta Chem. Scand.*, 1959, **13**, 211.

[9] Most dicarboxylic acids with large ΔpK values exhibit pK_1 2·5—3·5. (H. C. Brown, D. H. McDaniel and O. Hafliger, "Determination of Organic Structures by Physical Methods", ed. E. A. Braude and F. C. Nachod, Academic Press, New York, 1955; ch. 14, pp. 624–625.) The solvation effect in the mono- and di-anion of (II) will be discussed in a later publication.