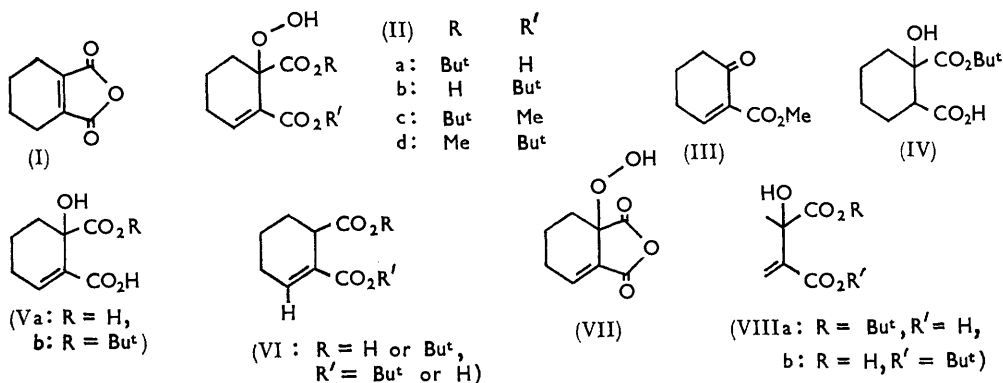


### 627. The Autoxidation of Dialkylmaleic Anhydrides.

By J. E. BALDWIN, D. H. R. BARTON, and J. K. SUTHERLAND.

The autoxidation of representative dialkylmaleic anhydrides in *t*-butyl alcohol containing potassium *t*-butoxide has been shown to be comparable with the known autoxidations of ketone and of ester carbanions.

IN recent years the autoxidation of ketonic carbanions with oxygen-potassium *t*-butoxide has been shown to be a synthetically useful procedure.<sup>1-6</sup> In all cases the initial product is a hydroperoxide. The reaction has recently been extended to the autoxidation of ester anions.<sup>7</sup> In connection with our studies on nonadrides,<sup>8</sup> we examined the possibility of degrading dialkylmaleic anhydrides by autoxidation of their derived carbanions. Although the procedure eventually proved unsatisfactory for nonadride degradation, we carried out some studies on model compounds which may be of more general interest.



Autoxidation of the anhydride (I) in *n*-potassium *t*-butoxide gave, after rapid consumption of one mole of oxygen, a crystalline acid (40%), C<sub>12</sub>H<sub>18</sub>O<sub>6</sub>, further characterised as its (mono-)methyl ester. This acid contained a hydroperoxide grouping. Its methyl

<sup>1</sup> Barton, Pradhan, Sternhell, and Templeton, *J.*, 1961, 255; cf. Arigoni, Barton, Corey, and Jeger, *Experientia*, 1960, **16**, 41.

<sup>2</sup> Bailey, Barton, Elks, and Templeton, *Proc. Chem. Soc.*, 1960, 214; *J.*, 1962, 1578.

<sup>3</sup> Baldwin, Barton, Faulkner, and Templeton, *J.*, 1962, 4743.

<sup>4</sup> Davis and Weedon, *Proc. Chem. Soc.*, 1960, 182.

<sup>5</sup> Hanna and Ourisson, *Bull. Soc. chim. France*, 1961, 1945; Lavie, Glotter, and Shvo, *Tetrahedron*, 1963, **19**, 1377.

<sup>6</sup> Camerino, Patelli, and Sciaky, *Gazzetta*, 1962, 676, 693.

<sup>7</sup> Abramoff and Sprinzak, *Proc. Chem. Soc.*, 1962, 150; Gersmann, Nieuwenhuis, and Bickel, *ibid.*, p. 279; Gersmann, Nieuwenhuis, and Bickel, *Tetrahedron Letters*, 1963, 1383.

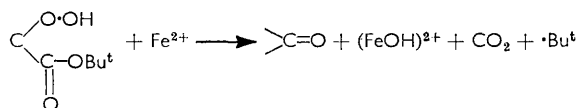
<sup>8</sup> Baldwin, Barton, Bloomer, Jackman, Rodriguez-Hahn, and Sutherland, *Experientia*, 1962, **18**, 345.

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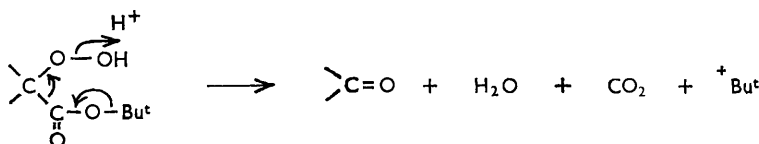
ester showed a triplet at  $2.52 \tau$  ( $J = 4$  c./sec.) corresponding to one vinyl proton. The nuclear magnetic resonance spectrum confirmed the presence of one  $\text{CO}_2\cdot\text{Me}$  and one  $\text{CO}_2\text{Bu}^t$  grouping. The presence of the t-butyl group was, of course, already expected from the molecular composition of the compound. Clearly, the acid must be either (IIa) or (IIb).

Treatment of the methyl ester [(IIc) or (IId)] with ferrous ion gave methyl 2-oxocyclohex-1(6)-enecarboxylate (III), characterised as its 2,4-dinitrophenylhydrazone. The ultraviolet spectrum of the 2,4-dinitrophenylhydrazone was identical with that reported<sup>9</sup> for the derivative of the corresponding ethyl ester. The ester (III) must be formed according to the Haber-Weiss scheme,<sup>10</sup> as shown.



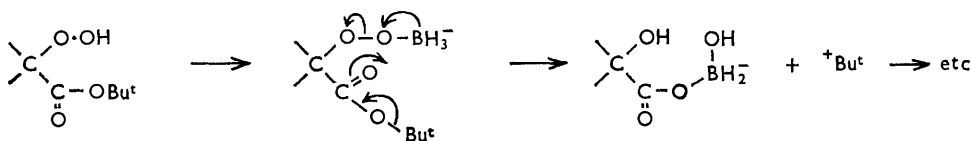
This degradation not only proves that the hydroperoxide must be (IIa), but it also provides a convenient route to the esters of 2-oxocyclohex-1(6)-enecarboxylic acids, which are not easy to obtain otherwise.<sup>9</sup>

On warming the hydroperoxide (IIa) with dilute sulphuric acid cyclohex-2-enone was obtained. This cationic degradation must involve the following process:



This generates 2-oxocyclohex-1(6)-enecarboxylic acid the decarboxylation of which, by tautomerism to 2-oxocyclohex-5-enecarboxylic acid, presents no difficulty.

Catalytic hydrogenation of (IIa) gave the saturated monoester (IV), whereas reduction with sodium borohydride afforded the dicarboxylic acid (Va). The reduction of the hydroperoxide group to hydroxyl is not unexpected, but the concomitant hydrolysis of the t-butyl ester under such mild conditions requires a specific explanation. The stability of (IV) under alkaline conditions excludes a simple intramolecular attack of neighbouring carboxylate anion on the ester function, accounting for the rapid hydrolysis. The hydroperoxide (IIa) was recovered unchanged after extended treatment with N-sodium hydroxide. The results could be explained by the following scheme:



We have, however, not studied this interesting hydrolysis in detail. Reduction of the hydroperoxide (IIa) with iodide ion gave the hydroxy-ester (Vb) which gave a complex boron-containing compound on reduction with borohydride under identical conditions.

The hydroperoxide (IIa) could, in principle, be formed by autoxidation of the anion of the anhydride followed by ring-opening by attack of butoxide ion, or by prior ring-opening followed by autoxidation of the resultant t-butyl ester. We were able to obtain evidence in favour of the former mechanism in the following way. Treatment of tetrahydrophthalic anhydride (I) with N-potassium t-butoxide for 30 minutes under nitrogen gave the expected mono-ester (VI) showing one vinyl proton [triplet at  $\tau 2.80$  ( $J = 4$  c./sec.)] in its nuclear magnetic resonance spectrum. This compound autoxidised at only half the

<sup>9</sup> Brenner, *J. Org. Chem.*, 1961, **26**, 22, and references there cited.

<sup>10</sup> See Uri, *Chem. Rev.*, 1952, **50**, 375.

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rate of tetrahydrophthalic anhydride (I) itself, and gave an inferior yield of the hydroperoxide (IIa). The small amount of the latter which is formed may arise from reversion of (VI) to (I) by the normal autoxidation.

One point of general interest is the specificity of attack of the *t*-butoxide anion upon the hydroperoxide-anhydride (VII). Although other factors may be involved, this could also be a further example of nucleophilic attack upon a carbonyl group being greatly facilitated by an  $\alpha$ -hydroperoxide grouping, a phenomenon to which we earlier directed attention.<sup>3</sup>

Dimethylmaleic anhydride gave, on autoxidation under the usual conditions, the crystalline alcohol (VIIIa or VIIIb). The constitution was assigned on the basis of its ultraviolet, infrared, and nuclear magnetic resonance spectrum [peaks at  $\tau$  3.56 (1 proton), 4.00 (1 proton), 8.46 (3 protons), and 8.56 (9 protons)]. The alternative (VIIIa) is preferred on the theoretical grounds summarised in the above paragraph.

## EXPERIMENTAL

Melting points were taken on a Kofler hot-stage apparatus. Ultraviolet spectra were taken in ethanol and infrared spectra in chloroform. Nuclear magnetic resonance spectra were determined at room temperature on approx. 10% w/v solutions in deuteriochloroform, using tetramethylsilane as internal standard.

*Autoxidation of Cyclohexene-1,2-dicarboxylic Acid Anhydride (I).*—The anhydride (1.0 g.), in *n*-potassium *t*-butoxide in *t*-butyl alcohol (63 ml.), was agitated with oxygen (1 mol. uptake). The acidified (acetic acid) solution was concentrated to small volume *in vacuo* at room temperature, diluted with water, and extracted with ether. Crystallisation of the product from benzene-ether afforded the *hydroperoxide* (IIa) (460 mg.), m. p. 154—155° (decomp.),  $\nu_{\max}$ . 3400, 3000—2700, 1715, and 1685  $\text{cm}^{-1}$  (Found: C, 55.2; H, 6.85%; Equiv., 252 (base), 290 (iodometric).  $\text{C}_{12}\text{H}_{18}\text{O}_6$  requires C, 55.8; H, 7.05%; Equiv., 258). Treatment with diazomethane gave the *methyl ester* (IIc), m. p. 80—81° (from *n*-pentane),  $\lambda_{\max}$ . 215  $\text{m}\mu$  ( $\epsilon$  10,000),  $\nu_{\max}$ . 3500, 1715, and 1640  $\text{cm}^{-1}$  (Found: C, 57.35; H, 7.4.  $\text{C}_{13}\text{H}_{20}\text{O}_6$  requires C, 57.6; H, 7.4%).

*Acid-catalysed Degradation of the Hydroperoxide (IIa).*—The hydroperoxide (264 mg.) in 4*N*-sulphuric acid (12 ml.) was heated to 95° for 3 min. and steam-distilled into aqueous 2,4-dinitrophenylhydrazine sulphate. Chromatography on Bentonite-Celite gave cyclohex-2-enone 2,4-dinitrophenylhydrazone (189 mg.), identified by m. p., mixed m. p., and infrared spectrum. The methyl ester (IIId), treated in the same way, gave a similar yield of the cyclohex-2-enone derivative.

*Catalytic Hydrogenation of the Hydroperoxide (IIa).*—The hydroperoxide (475 mg.) in ethyl acetate (100 ml.) was hydrogenated over 5% palladised charcoal (240 mg.) until saturated (2 mol. uptake). Crystallisation of the product from ethyl acetate-light petroleum (b. p. 60—80°) gave the *t*-butyl ester (IV) (342 mg.), m. p. 97—99°,  $\nu_{\max}$ . 3500, 1715, and 1700  $\text{cm}^{-1}$  (Found: C, 59.0; H, 8.3.  $\text{C}_{12}\text{H}_{20}\text{O}_5$  requires C, 59.0; H, 8.25%).

*Reduction of the Hydroperoxide (IIa) with Sodium Borohydride.*—The hydroperoxide (74 mg.) in 0.1*N*-aqueous sodium hydroxide (4 ml.) (pH adjusted to 9—10) was treated with sodium borohydride (210 mg.) in the minimum of water for 12 hr. at room temperature. Acidification (dilute hydrochloric acid), extraction into ether, and crystallisation from ethyl acetate-methanol gave the *hydroxy-dicarboxylic acid* (Va) (45 mg.), m. p. 175—180° (decomp.),  $\lambda_{\max}$ . 217  $\text{m}\mu$  ( $\epsilon$  8000),  $\nu_{\max}$ . 1720 and 1695  $\text{cm}^{-1}$ . This compound was characterised (ethereal diazomethane) as its *dimethyl ester*, m. p. 91—92° [from light petroleum (b. p. 60—80°)],  $\lambda_{\max}$ . 223  $\text{m}\mu$  ( $\epsilon$  5000) (Found: C, 56.2; H, 6.7.  $\text{C}_{16}\text{H}_{14}\text{O}_5$  requires C, 56.05; H, 6.6%).

*Reduction of the Hydroperoxide (IIa) with Iodide Ion.*—The hydroperoxide (200 mg.) in chloroform (10 ml.) was shaken with 10% aqueous potassium iodide (10 ml.) containing acetic acid (3 drops) for 5 min. at room temperature. The organic layer was separated and washed with aqueous sodium pyrosulphite. Crystallisation of the product from benzene-light petroleum (b. p. 60—80°) gave the *t*-butyl ester (Vb) (130 mg.), m. p. 127—128°,  $\nu_{\max}$ . 3400 and 1710  $\text{cm}^{-1}$  (Found: C, 59.45; H, 7.4.  $\text{C}_{12}\text{H}_{18}\text{O}_5$  requires C, 59.5; H, 7.45%).

*Ferrous Ion-catalysed Decomposition of the Hydroperoxide Methyl Ester (IIc).*—Ferrous ammonium sulphate [2.90 ml. of a solution from 4.096 g. in water (50 ml.) with 4*N*-hydrochloric acid (one drop)] was added to the ester (100 mg.) during 1 hr. at 0° and stirred for a further

hour. Dilution with water and extraction into ether gave a gum having  $\lambda_{\max}$  269 ( $\epsilon$  3800) and 327  $m\mu$  ( $\epsilon$  1700),  $\nu_{\max}$  1725, 1660, and 1620  $\text{cm}^{-1}$ . This furnished the 2,4-dinitrophenylhydrazone of methyl 2-oxocyclohex-1(6)-enecarboxylate (III). Purified by chromatography over Bentonite-Celite in benzene, this had m. p. 200–206° (from chloroform-benzene),  $\lambda_{\max}$  254 ( $\epsilon$  13,600) and 370  $m\mu$  ( $\epsilon$  23,200) (Found: C, 50.05; H, 4.45; N, 16.65.  $\text{C}_{14}\text{H}_{14}\text{N}_4\text{O}_6$  requires C, 50.3; H, 4.2; N, 16.75%).

*Preparation and Autoxidation of the Ester (VI).*—The anhydride (I) (282 mg.) in *n*-potassium t-butoxide in t-butyl alcohol (10 ml.) under nitrogen was set aside for 30 min. at room temperature. Acidification with acetic acid, removal of most of the solvent *in vacuo*, dilution with water, and extraction into ether gave the ester (VI) (335 mg.), m. p. 127–128° [from benzene-light petroleum (b. p. 60–80°)],  $\lambda_{\max}$  217  $m\mu$  ( $\epsilon$  8000),  $\nu_{\max}$  1710, 1690, and 1650  $\text{cm}^{-1}$  (Found: C, 63.55; H, 8.0.  $\text{C}_{12}\text{H}_{18}\text{O}_4$  requires C, 63.7; H, 8.0%).

The anhydride (I) (100 mg.) was treated with potassium t-butoxide under nitrogen as above for 1 hr. Autoxidation of this solution proceeded at half the rate for the anhydride (I) and the yield of hydroperoxide (IIa) was much lower (13 mg.). This result was confirmed by autoxidation of the mono-ester (VI) (53 mg.) to give the hydroperoxide (10 mg.). Again the rate of autoxidation was about half that for the anhydride (I) under the same conditions.

*Autoxidation of Dimethylmaleic Anhydride.*—The anhydride (550 mg.) was oxygenated as for the anhydride (I) (see above). Crystallisation of the product from benzene-light petroleum (b. p. 60–80°) gave the hydroxy-ester (VIIIa) (103 mg.), m. p. 104–105°,  $\lambda_{\max}$  210  $m\mu$  ( $\epsilon$  4700),  $\nu_{\max}$  3400, 1720, 1690, and 1625  $\text{cm}^{-1}$  (Found: C, 55.55; H, 7.55%; Equiv., 204.  $\text{C}_{10}\text{H}_{16}\text{O}_5$  requires C, 55.55; H, 7.4%; Equiv., 216).

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