# m-Chloroperbenzoic Acid Oxidation of Dioxins and Dihydrodioxins

Luigi Lopez,* Vincenzo Calò and Michele Fiorentino
Dipartimento di Chimica, Università di Bari, via Amendòla 173, 71026 Bari, Italy

The m-chloroperbenzoic acid (MCPBA) oxidation of dihydrodioxins affords, in high yield, ethylene glycol dibenzoates, via unstable epoxy diethers. These elusive intermediates have been characterized chemically and by ^{1}H n.m.r. spectroscopy. In contrast, the MCPBA oxidation of 2,3,5,6-tetraphenyl-p-dioxin fails to give the corresponding (Z)-stilbenediol dibenzoate but yields instead benzil.

As part of our work on the photosensitized oxygenation of electron-rich p-dioxins and dihydro-p-dioxins induced by electron-acceptors such as 9,10-dicyanoanthracene (DCA),[1] 2,4,6-tetrabromocyclohexadien-1-one (TBCHD),[2] and tetrachloro-p-benzoquinone,[3] we have studied the chemical oxidation of the same substrates with tris(p-bromophenyl)-ammoniumyl tetrafluoroborate,[4] peroxomolybdenum(VI), or chromium(VI) complexes,[5] TBCHD,[6] and m-chloroperbenzoic acid (MCPBA). Here we report the results obtained in the MCPBA oxidation of the dihydrodioxins (1a—c) and the dioxin (2).


(1)   (2)
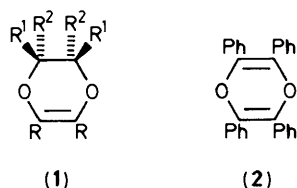
a; R = Ph; $R^1 = R^2 = H$
b; R = p - MeOC$_6$H$_4$, $R^1 = R^2 = H$
c; R = $R^1 = $ Ph, $R^2 = $ H

Results and Discussion

MCPBA (99%; 1 equiv.) was added to deuteriochloroform (CDCl$_3$) solutions of the dihydrodioxins (1a—c) (10^{-1}M) synthesized as reported in the Experimental section. The reactions, when followed by ^{1}H n.m.r. on an XL-200 Varian instrument, showed the formation both of the corresponding diesters (5a—c) and the intermediates, presumably the epoxy diethers (3a—c). Use of an excess of MCPBA (>2 equiv.) effected complete reaction, both starting material and intermediates being absent. The conversion of vinylene diethers into the corresponding dibenzoates (5a—c) (Table), occurs presumably via the intermediacy of unstable epoxy diethers (3a—c), which undergo facile nucleophilic ring-opening with MCPBA and/or in part with traces of water (moist MCPBA) leading respectively to the hydroxy peresters (4a—c), or to the trans-glycols (6a—c) which are easily converted into (4a—c) by reaction with MCPBA. Ring-opening of (4a—c) affords (5a—c) plus m-chlorobenzoic acid (Scheme 1).

Similar reactions have been carried out, on a preparative scale, in chloroform (spectroscopic grade), dry methylene chloride, and dry acetonitrile both with 1 equiv. of MCPBA in order to try and isolate the elusive intermediates (3a—c) and/or directly with an excess of MCPBA to synthesize (5a—c). Attempts to isolate the intermediates, particularly (3a), afforded only the hydrolysis product, benzil (8). As far as we know, Wasserman's[7] attempt to characterize an epoxy diether is the only one reported, and he described in a note the conversion of the unstable compound (3a) into the corresponding stable and isolable diol (6a). Although we do not exclude its formation (see

(1a–c)

(3a–c)   (4a–c)   (5a–c)

(6a–c)
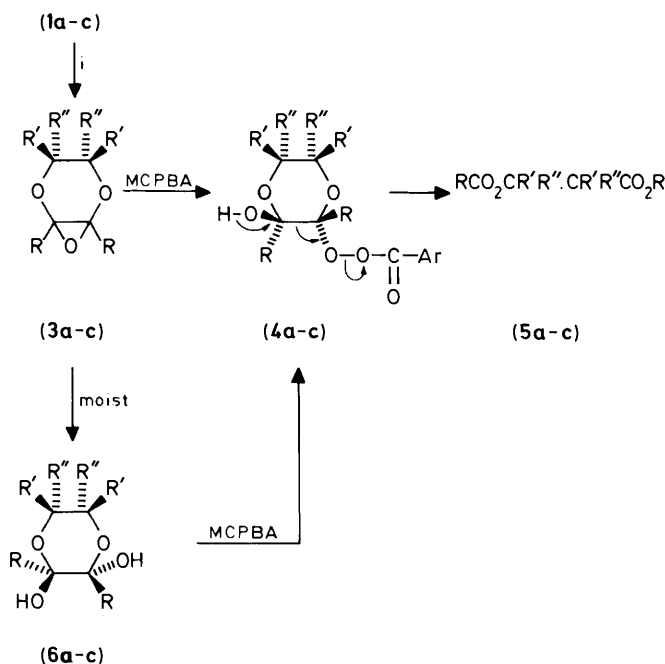
Scheme 1.

Scheme 1), we have been unable to isolate and fully characterize (6a). It seems likely however that (6a) will be readily hydrolysed to (2d), consistent with our results for the MCPBA oxidation of (1a) in acetonitrile and other solvents. After the disappearance of (1a) in the reaction mixture we added several drops of aqueous methanol[7] and, following the reaction by gas chromatography, observed a decrease in the peak corresponding to the unisolated intermediate and the formation of (8). In a similar reaction, without the addition of aqueous methanol, we observed the conversion of the same intermediate into (5a). Similarly, (3a) was isolated by semi-preparative h.p.l.c. on a reverse-phase column with a mobile phase (acetonitrile–water, 70:30 v/v). The fractions eluted (gas chromatographically pure) were reduced to small volume and then extracted with diethyl ether. The combined extracts were dried and evaporated to dryness. The product was rapidly analysed by ^{1}H n.m.r. with the aim of fully characterizing the epoxy diether (3a). Unfortunately, (3a) undergoes partial isomerization into 2-benzoyl-2-phenyl-1,3-dioxolane (7) during work-up; the latter then undergoes hydrolysis to give (8) [equation (1)].
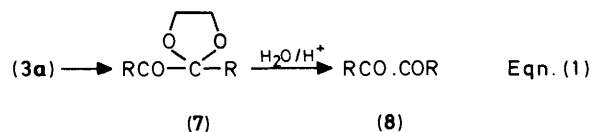

(3a) → RCO—C—R $\xrightarrow{H_2O/H^+}$ RCO.COR   Eqn. (1)

(7)   (8)

Substrates	Products*b* (yields %)	M.p. (°C)	ν/cm⁻¹	¹H n.m.r. δ(CDCl₃)
(1a)	(5a) (90)	72—73	1 712	4.668
(1b)	(5b) (90)	117—118	1 730	4.606 (s)
(1c)	(5c) (95)	247—248	1 708	6.459 (s)
(2)	(8)*c*	94	1 670	8.7—7.249 (m)

a $\geqslant$ 2 Equivalents of MCPBA. *b* The yields are on the isolated products. Consistent elemental analyses and mass spectra are also available. *c* Since 2 equiv. of (8) results from (2) the yield is expressed as (8)/2 × (2) × 100.

Product (7), prepared independently[8] has the same R_t value as the incompletely characterized intermediate; its spectral properties are consistent with the carbonyl structure. An important feature in the ¹H n.m.r. spectra of the isomeric systems is the methylene proton absorption. In both isomers, it appears as a well resolved (AA'BB') system with different chemical shifts and half-widths.[9] In product (7), not detected in the deuteriochloroform reaction mixture followed by ¹H n.m.r., the two symmetrical multiplets fall in the range δ 4.152—4.112, whereas the peripheral methylene protons in the intermediate (3a) appear in the range δ 3.770—3.585. The different chemical shifts and widths are in accord with the structures of the two isomers. The width difference is, apparently, a result of the increased mobility of the five-membered *vs.* the six-membered ring.[10] On this basis we can claim that (8) is formed from (7) which arises from the isomerization of (3a). Conversion of the h.p.l.c. isolated product, by reaction with MCPBA, into (2a) provides further support for the unstable intermediate being an oxirane. In a similar oxidation of (1c) we observed in the ¹H n.m.r. spectrum a singlet at δ 6.469 [similar to that found in a pure sample of (5c)[11]] a singlet at δ 5.544 (starting material), and two doublets centred at δ 5.150 and 4.913 attributable to the intermediate oxirane product (3c). These last signals disappear with an excess of MCPBA. In the MCPBA oxidation of (1b) the two singlets at δ 4.664 and 3.846, in the ratio of 4:6, indicate the formation of (5b).[12]

The ready cleavage of the double bond of cyclic vinylene diethers with MCPBA and the mechanism operating are supported by previous reports on the perbenzoic oxidation of alkoxy epoxides,[13] and the MCPBA oxidation of cyclic enol-ethers[14] and azasteroids.[15] Surprisingly, the MCPBA oxidation of (2) does not lead to the corresponding (*Z*)-stilbene diol dibenzoate (12), a normal cleavage product of the intermediate dioxetane (11) arising from the DCA-sensitized
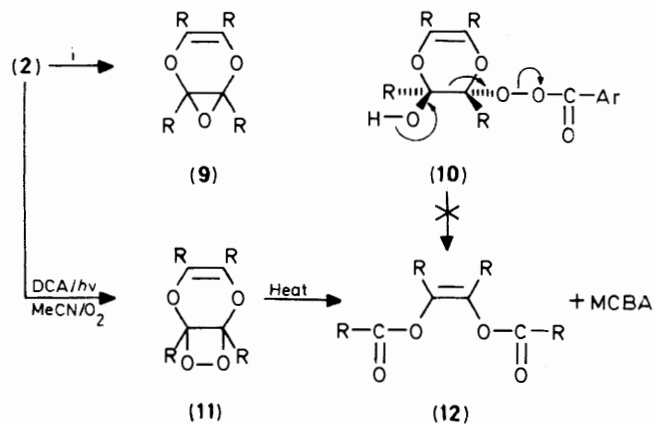

Scheme 2.

photo-oxygenation of (2);[1] instead, it affords 2 equivalents of benzil as the sole reaction product (see Scheme 2).

A similar result has been obtained by Scaiano *et al.*[12] in the u.v. irradiation of an oxygenated benzene solution of (2). The authors suggested a mechanism involving the formation of singlet oxygen which reacted with (2) to give the dihydrodioxin (11). The subsequent fragmentation yielded two equivalents of (8) with no trace of (7). This result could be better accommodated by a different mechanism involving the formation of ozone which upon reaction with (2) would lead to (8), as observed in the ozonation of (2) [equation (2)]. Our results

$$(2) \xrightarrow[\text{benzene}]{O_3} \qquad \text{Eqn. (2)}$$

for the MCPBA oxidation of (1d) can be explained in at least three different ways: (i) fast isomerization of the intermediate (9) into (13) which, in the protic medium, yields two equivalents of (8); (ii) formation of the diepoxide (14) whose fragmentation would lead to a similar result; and finally (iii) an improbable fragmentation of (10) into (8) [equations (3)—(5)]: work is in progress to define the mechanism operating.
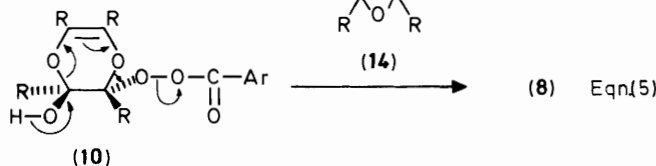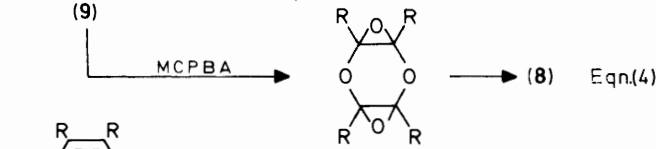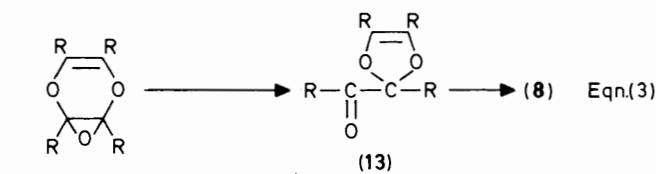
Experimental

M.p.s were determined on an electrochemical apparatus and are uncorrected. Infrared spectra (KBr discs) were taken on a Perkin-Elmer 681 spectrometer. The ¹H n.m.r. spectra (CDCl₃) were recorded by using a Varian XL-200 MHz instrument. G.c. analyses were run on a Hewlett-Packard model 5750 instrument using columns of 15 × 0.25 ft packed with 10% SP2100 Supelcoport on Chromosorb GAW-DMCS. Mass spectra were taken on a Kratos MS80 instrument. H.p.l.c. analyses were run on a Perkin-Elmer series 3B using an analytical C-18 reverse-phase column. A semi-preparative C-18 Perkin-Elmer column has been used for the isolation of (3a).

Materials.—2,3-Diphenyl-2,3-dihydro-*p*-dioxin (m.p. 93 °C), 2,3-bis(*p*-methoxyphenyl)-2,3-dihydro-*p*-dioxin (m.p. 102 °C), *cis*-2,3,5,6-tetraphenyl-2,3-dihydro-*p*-dioxin (m.p. 165 °C), and 2,3,5,6-tetraphenyl-*p*-dioxin (m.p. 214 °C) were prepared by reported methods.[17,18] MCPBA by (Fluka) was purified as reported in ref. 19. Deuteriochloroform (Aldrich) Gold Label and chloroform (C. Erba) spectroscopic grade was used as received. Acetonitrile (C. Erba) was purified by distillation with CaH₂ and P₂O₅ and stored over molecular sieves. Dichloro-methane (C. Erba) was purified by standard procedures.

General Procedure for the MCPBA Oxidation of 2,3-Dihydro-dioxins.—To a stirred acetonitrile solution of (1a) (0.238 g, 0.1 mol), was added *m*-chloroperbenzoic acid (0.5 g, *ca.* 3 equiv.).

The disappearance of the starting material and the elusive intermediate (3a), tested by h.p.l.c., t.l.c., and g.c., occurs within 3 h. The solution was poured in water, extracted with diethyl ether, washed with sodium hydrogen carbonate (10%), and then dried (Na$_2$SO$_4$). The solution was reduced to small volume and the residue, adsorbed on a silica gel column was chromatographed with hexane–diethyl ether (5:1, v/v) as eluant. The crude reaction product (2a) (0.240 g, 90%) was not further purified but characterized spectroscopically and by comparison with an authentic sample. Crystallization from ethanol gave pure (5a), m.p. 72—73 °C and consistent elemental analysis. Similar reactions carried out in dichloromethane and chloroform afforded the same reaction product with yields in the range 85—90%.

Similar procedures have been followed for the MCPBA oxidation of (1b) and (1c). The physical and spectroscopic data are reported in the Table.

m-*Chloroperbenzoic Acid Oxidation of* (2).—To a stirred chloroform solution of (2) (0.388 g, 0.1 mol) was added MCPBA (0.5 g, *ca.* 3 equiv.). A fast conversion of the starting material into (8) was revealed by g.c. and t.l.c. As reported above, the residue was adsorbed on silica gel and chromatographed to give the crude product (8) (0.38 g) which was characterized spectroscopically and by comparison with an authentic commercial sample (Aldrich).

Ozonolysis of (2).—A benzene solution of (2) at 0 °C was treated with ozone from a micro-Supelco ozonator. Following the reaction by g.c., we observed, within 30 min, complete disappearance of (2) and formation of (8) as the sole reaction product. Characterization of the latter was by i.r. spectroscopy.

References
1 L. Lopez, unpublished work.
2 L. Lopez and V. Calò, *J. Chem. Soc., Chem. Commun.*, 1984, 1266.
3 L. Lopez and A. P. Schaap, unpublished work.
4 L. Lopez and F. Ciminale, *Tetrahedron Lett.*, in the press.
5 R. Curci, L. Lopez, and L. Troisi, unpublished work.
6 L. Lopez and V. Calò, *Synthesis*, 1984, 224.
7 H. H. Wasserman and J. Saito, *J. Am. Chem. Soc.*, 1975, **97**, 905.
8 R. K. Sumerbell and D. R. Berger, *J. Am. Chem. Soc.*, 1959, **81**, 633.
9 J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution Nuclear Magnetic Resonance Spectroscopy,' Pergamon Press, New York, 1965, vol. 1, pp. 399—423.
10 B. Fuchs, *Tetrahedron Lett.*, 1970, 1747.
11 K. B. Wiberg and K A. Saegebarth, *J. Am. Chem. Soc.*, 1957, **79**, 6256.
12 A. P. Schaap, K. A. Zaklika, B. Kaskar, and L. W.-Fung, *J. Am. Chem. Soc.*, 1980, **102**, 389.
13 C. L. Stevens and J. J. De Young, *J. Am. Chem. Soc.*, 1954, **76**, 718.
14 I. J. Borowitz, G. J. Williams, L. Gross, and R. Repp, *J. Org. Chem.*, 1968, **33**, 2013.
15 A. P. Schaap, J. J. Bonet, and L. Lopez, unpublished results.
16 M. V. George, Ch. V. Kumar, and I. C. Scaiano, *J. Phys. Chem.*, 1979, **83**, 2452.
17 R. K. Summerbell and D. R. Berger, *J. Am. Chem. Soc.*, 1957, **79**, 6504.
18 W. Madelung and M. Oberwegner, *Justus Liebigs Annalen*, 1936, **526**, 195.
19 N. N. Schwartz and J. H. Blumbergs, *J. Org. Chem.*, 1964, **29**, 1976.