Regio- and Stereo-selectivity of the First [3 + 2] Cycloaddition of Carbonyl Oxide to Electron-poor Alkenes. Bidirectionality of the 1,3-Dipole

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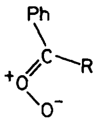
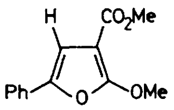
The carbonyl oxide (**1**), derived from the 2,3,7-trioxabicyclo[2.2.1]heptene (**3**) by thermal rearrangement, yields, as major products, methyl 1,2-dioxolane-4-carboxylate (**8**) and the novel tricyclic biperoxide (**4**) (whose structure was established by *X*-ray diffraction), by reaction with methyl acrylate and the acrylate (**3**) respectively, whereas it yields 5-ethoxy-1,2-dioxolane (**9**) with ethyl vinyl ether.

Recently, we have reported the presence of a carbonyl oxide intermediate in dye-sensitized photo-oxygenation of some 2-methoxyfurans.[1] This method represents a convenient alternative to ozonolysis of alkenes for the production of the 1,3-dipolar specie;[2] ozonolysis has such limitations that until now [3 + 2] cycloadditions of carbonyl oxides to electron-poor alkenes have not been observed.†

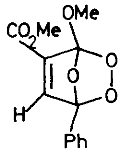
We have now elucidated the mechanism of formation of the carbonyl oxide (**1**) by carrying out the tetraphenylporphyrin sensitized photo-oxygenation of the furan (**2**) in deuteriochloroform at −60 °C, which leads to the 2,3,7-trioxabicyclo[2.2.1]heptene (**3**).‡ Compound (**3**) converts, at −20 °C within 3 h, to the same products obtained when the reaction was carried out in nitromethane,[1] so confirming that the carbonyl oxide (**1**) arises from the cleavage of the peroxide (**3**) and excluding the alternative possibility that it is directly



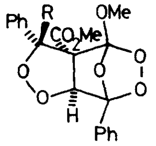
(**1**)



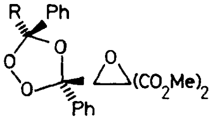
(**2**)



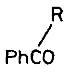
(**3**)



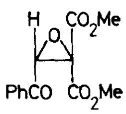
(**4**)



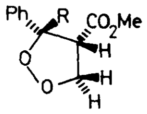
(**5**)



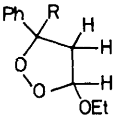
(**6**)



(**7**)



(**8**)



(**9**)

R = CH=C(CO$_2$Me)$_2$

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† 1,2-Dioxolanes are formed upon ozonolysis of alkoxy-1-alkenes, but not from alkyl-1-alkenes; the high dipolarophilicity of the aldehydes produced *in situ* and the reduced dipolarophilicity of the alkenes towards the carbonyl oxide lead to the predominance of ozonide products.[3] Carbonyl oxides can also be generated by singlet oxygen oxidation of diazoalkanes or by reaction of carbenes with oxygen. However, [3 + 2] cycloaddition to alkenes was not observed as other reactions were preferred.[4]

‡ *endo*-Peroxide (**3**) exhibited satisfactory ^{1}H and ^{13}C n.m.r. spectral data. By addition of methanol pre-cooled at −60 °C it leads quantitatively to the α-methoxy hydroperoxide obtained when the reaction was carried out in methanol.[1]

formed from a transition state of the reaction of singlet oxygen with the furan (**2**).[1]

With the apolar carbon tetrachloride[5] as solvent, silica gel chromatography, carried out after 3 h, led to the isolation of 3,4,8,9,10-pentaoxatricyclo[5.2.1.$0^{2,6}$]decane (**4**)§ (53%) (m.p. 59—61 °C from n-hexane/diethyl ether) and 1,2,4-trioxolane (**5**)§ (16%) (m.p. 118—119 °C from n-hexane/diethyl ether), in addition to the ethylene (**6**)[1] (9%) and the epoxide (**7**)[1] (2%)¶ which were the major products when the reaction was carried out in nitromethane or deuteriochloroform. It is evident that compounds (**4**) and (**5**), whose structures were confirmed by *X*-ray analysis†† (Figures 1 and 2), are formed by the cycloaddition of the carbonyl oxide (**1**) to the double bond of the *endo*-peroxide (**3**) and to the ketone group of the epoxide (**7**) respectively.‡‡ Compound (**4**) is the first example of a biperoxide tricyclic system of this type; the only previous example of an *X*-ray structure determination of a compound containing the 1,2,4-trioxolane structural unit present in (**5**) was for a disordered structure.[6]

When the reaction was repeated with methyl acrylate as the solvent at −20 °C, in addition to (**4**) (4%), (**5**) (5%), (**6**) (14%), and (**7**) (23%), the dioxolane (**8**)§ (22%)§§ was isolated as a liquid by silica gel chromatography, showing that [3 + 2] cycloaddition with electron-poor alkenes is a general reaction of the carbonyl oxide (**1**). The stereochemistry of the dioxolane (**8**) was assigned by comparing the ^{1}H n.m.r. spectrum with that of the dioxolane (**4**). No evidence for any regio- or stereo-isomer was observed in spite of the fact that steric hindrance should favour the formation of the regioisomer. However, with a total yield of *ca.* 70%, it is incorrect to speak of regio- and stereo-specificity.

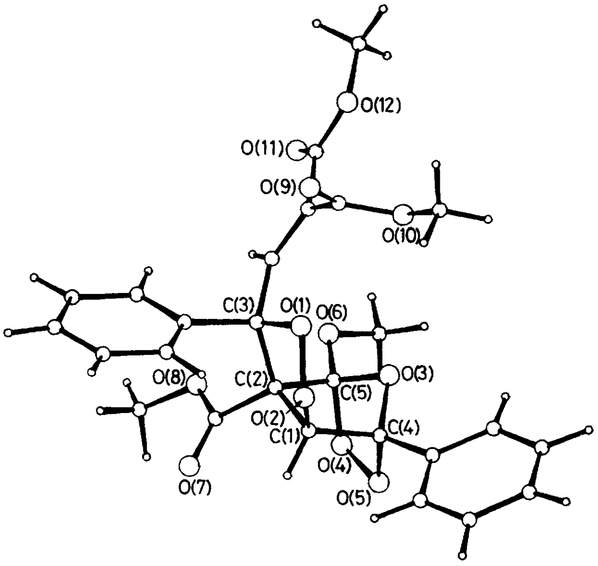

Figure 1. Molecular structure of the tricyclodecane (**4**). Relevant bond lengths (Å) and angles (°): O(1)–O(2) 1.476(4), O(1)–C(3) 1.424(5), C(2)–C(3) 1.598(4), C(1)–C(2) 1.530(6), C(1)–O(2) 1.424(4), C(2)–C(5) 1.533(6), C(1)–C(4) 1.535(6), O(3)–C(5) 1.409(5), O(3)–C(4) 1.410(5), O(4)–C(5) 1.456(4), O(5)–C(4) 1.456(4), O(4)–O(5) 1.479(4); O(2)–O(1)–C(3) 105.0(4), O(1)–O(2)–C(1) 104.7(4), O(2)–C(1)–C(2) 107.9(5), C(1)–C(2)–C(3) 101.6(5), C(2)–C(3)–O(1) 103.1(5), C(2)–C(1)–C(4) 102.8(5), C(1)–C(2)–C(5) 98.6(5), C(2)–C(5)–O(3) 104.6(5), C(5)–O(3)–C(4) 96.5(5), O(3)–C(4)–C(1) 103.6(5), O(3)–C(5)–O(4) 103.2(5), C(5)–O(4)–O(5) 102.8(4), O(4)–O(5)–C(4) 101.8(5), O(5)–C(4)–O(3) 101.6(5).

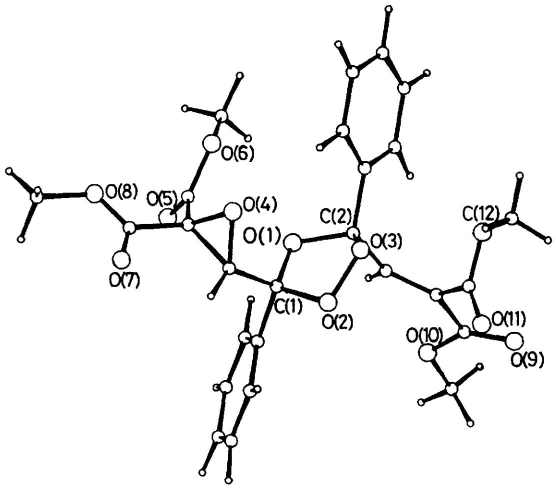

Figure 2. Molecular structure of the trioxolane (**5**). Relevant bond lengths (Å) and angles (°): O(1)–C(1) 1.382(5), O(1)–C(2) 1.440(3), C(1)–O(2) 1.449(4), O(2)–O(3) 1.468(3), O(3)–C(2) 1.417(5); C(2)–O(1)–C(1) 107.3(3), O(1)–C(1)–O(2) 106.0(3), C(1)–O(2)–O(3) 102.1(3), O(2)–O(3)–C(2) 100.0(2), O(3)–C(2)–O(1) 102.7(3).

The bidirectionality of the 1,3-dipole was established by carrying out the reaction with ethyl vinyl ether as solvent; in addition to (**6**) (11%), the dioxolane (**9**)§ (84%) was obtained; this was isolated as a liquid by filtration on silica gel. The stereochemistry of the dioxolane (**9**) has not been established

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§ All new compounds isolated exhibited satisfactory spectroscopic and analytical data.

¶ No evidence for regio- or stereo-isomers of (**4**) or (**5**) was observed; if present at all their yields must be at least 10 or 20 times smaller than those of the observed cycloadducts. However, with a total yield of *ca.* 80%, it is incorrect to speak of regio- and stereo-specificity.

†† *Crystal data* for (**4**): $C_{26}H_{24}O_{12}$, M = 528.45, monoclinic, space group $P2_1/c$ (no. 14), a = 8.720(4), b = 14.128(8), c = 22.297(9) Å, β = 112.96(3)°, U = 2529(5) Å^3, Z = 4, D_c = 1.39 g cm^{-3}, μ(Cu-K_α) = 9.05 cm^{-1}, θ = 1—75°. The final conventional and weighted R-factors were 0.077 and 0.095 respectively for 2403 independent observed reflections [$I > 3\sigma(I)$] and 343 parameters. (**5**): $C_{26}H_{24}O_{12}$, M = 528.45, monoclinic, space group $P2_1/c$ (no. 14), a = 11.808(1), b = 10.538(7), c = 21.629(3) Å, β = 99.08(1)°, U = 2658(2) Å^3, Z = 4, D_c = 1.32 g cm^{-3}, μ(Cu-K_α) = 8.61 cm^{-1}, θ = 1—70°. The final conventional and weighted R-factors were 0.057 and 0.078 respectively for 2109 independent observed reflections [$I > 3\sigma(I)$] and 343 parameters.

Intensity data for the compounds (**4**) and (**5**) were collected on an Enraf-Nonius CAD4 diffractometer with ω/θ scan mode, using Cu-K_α radiation. Structures were solved by direct methods and refined by full-matrix least-squares technique with $w^{-1} = \sigma^2(F_o)$, where σ was taken from counting statistics. Non-hydrogen atoms were refined with anisotropic thermal parameters. H atoms were located by stereochemical criteria and held constant in the refinement. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

‡‡ In the light of the present results, we re-examined the mixture of the reaction in nitromethane;[1] under these conditions only trace amounts of (**4**) and (**5**) were detectable. Evidently the polar solvent stabilizes the polar carbonyl oxide (**1**) promoting its formation to the detriment of peroxide (**3**). On the other hand, the small yield of (**5**) may be due to the negative influence of solvent polarity on the [3 + 2] cycloaddition of the carbonyl oxide which leads to the apolar species (**5**),[5] this reaction being supplanted by the formation of the dipolar intermediates which lead to (**6**) and (**7**).[1] The results obtained in deuteriochloroform support these hypotheses.

§§ When carbon tetrachloride was used as the solvent, the yield of (**8**) was lower.

as the spectral data obtained were inadequate. Chemical experiments to determine the stereochemistry are in progress.

The aforementioned trapping experiments of the carbonyl oxide represent a convenient start to investigations, into both the mechanistic and synthetic fields, on the little known 1,3-dipolar species[2] which has attracted much attention as a model for mono-oxygenase enzymes.[7]

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