Conjugative Effects in Furan *syn*-Diepoxides. Crystal and Molecular Structure of Methyl 3,5,7-Trioxatricyclo[4.1.0.$0^{2,4}$]heptane-1-carboxylate

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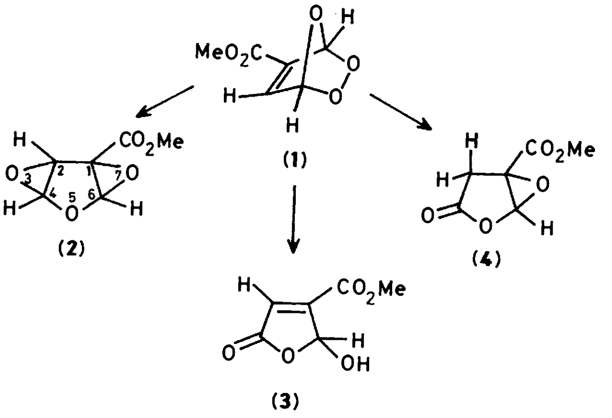
The stereochemistry of the title compound (**2**), a furan diepoxide derivative, has been defined in detail by means of an *X*-ray crystal structure analysis. Triclinic crystals in space group $P\bar{1}$ have lattice parameters $a = 4.1979(4)$, $b = 13.948(1)$, $c = 5.7324(4)$ Å, $\alpha = 92.462(7)$, $\beta = 103.070(7)$, $\gamma = 91.136(8)$°, and $Z = 2$. The structure was solved by direct methods and refined by full-matrix least-squares calculations to $R = 0.048$ with 948 observed reflections. The two epoxy rings are in *syn* configuration, the five-membered ring is strictly planar and there are evidences of a π electron conjugation between the epoxy rings through a $2p$ orbital of the interconnecting oxygen atom. A suggestion for the interpretation of the reaction of crystal decay has been provided by the scrutiny of the difference electron density map.

Recently some of us have reported that thermal conversion at 35 °C of methyl 2,3,7-trioxabicyclo[2.2.1]hept-5-ene-5-carboxylate (**1**) leads, in good yield, to methyl 3,5,7-trioxatricyclo-[4.1.0.$0^{2,4}$]heptane-1-carboxylate (**2**), when chloroform was used as solvent, and to methyl 2-hydroxy-5-oxo-2,5-dihydrofuran-3-carboxylate (**3**), when acetone was used. In both solvents some methyl 3-oxo-2,6-dioxabicyclo[3.1.0]hexane-5-carboxylate (**4**) was obtained.[1]



Scheme.

If the diepoxide (**2**) is formed by a rearrangement of the peroxide (**1**), the two epoxy groups have *syn* configuration. Besides getting confirmation of this point, an *X*-ray crystallographic analysis of (**2**) has been carried out in order to obtain accurate stereochemistry, in view of its structural relationship with crotepoxide, a *syn* diepoxide which displays significant inhibitory activity against Lewis lung carcinoma and Walker intramuscolar carcinoma.[2]

Results and Discussion

Figure 1 shows a perspective view of the molecule with the atom-labelling scheme. The Table lists the final atomic positional parameters. The structure determination confirms the stereochemistry of the molecule assigned on the basis of mechanistic considerations. The two epoxy rings are *syn* with respect to the five-membered ring. Neglecting the substituents at C(1) and C(2), the trioxatricycle displays a mirror symmetry plane running through O(5) and the midpoint of the C(1)–C(2) bond. The differences, indeed, between the corresponding geometrical parameters fall in the range of a few times the standard deviations and are hardly significant.

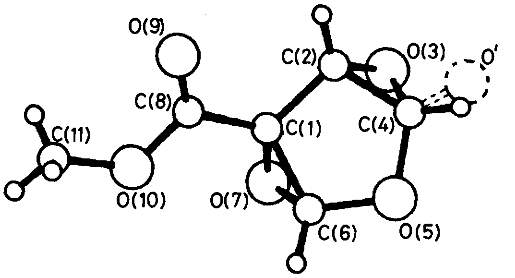


Figure 1. Perspective view of the molecule showing the atom-labelling scheme. Dashed lines refer to the extra atom O′

All non-hydrogen atoms are spread over four planes: the five-membered ring, the two epoxy rings and the methoxycarbonyl fragment. The strict planarity (maximum displacement 0.008 Å) of the five-membered ring is a requirement of fusion with the two epoxy rings. They form two symmetrical but not perfectly isosceles triangles inclined at 108.3(3) and 108.6(3)° to the plane of the five-membered ring. The apical oxygen atoms make a short O(3) ··· O(7) contact, 2.653(2) Å. The carbon–oxygen bonds in the epoxy rings can be divided in two sets. C(2)–O(3) and C(1)–O(7) [1.464(2) and 1.444(2) Å], farther from O(5), show lengths comparable with those found in epoxy rings of other molecules,[3] whereas C(4)–O(3) and C(6)–O(7) [1.393(3) and 1.404(3) Å], which face O(5), are significantly shorter. This discrepancy gives clear evidence of a π electron bonding interaction between O(5) and the epoxy rings. This effect can be included among those quoted in the literature as 'pseudo-conjugation' or 'hyperconjugation' and is due to the unsaturated character of the three-membered rings (*e.g.* the cyclopropane ring) and to their ability to provide conjugative interactions.[4,5] If O(5) is pictured as being sp^2 hybridized, its $2p$ orbital, whose axis is perpendicular to the five-membered ring, overlaps effectively with the adjacent roughly parallel C–O bent-bonds of the epoxy rings. The effect of this interaction

Table. Fractional atomic co-ordinates with estimated standard deviations in parentheses

	x	y	z
C(1)	0.386 0(6)	0.729 9(2)	0.331 5(4)
C(2)	0.253 1(6)	0.706 4(2)	0.069 4(4)
O(3)	−0.054 9(5)	0.650 1(2)	0.018 7(4)
C(4)	0.240 7(6)	0.603 5(2)	0.044 9(5)
O(5)	0.359 1(5)	0.562 4(1)	0.264 4(3)
C(6)	0.444 0(6)	0.637 3(2)	0.439 8(4)
O(7)	0.184 3(4)	0.692 3(1)	0.481 9(3)
C(8)	0.588 5(6)	0.818 3(2)	0.414 3(4)
O(9)	0.702 1(6)	0.865 9(2)	0.284 7(4)
O(10)	0.629 1(5)	0.836 8(1)	0.648 6(3)
C(11)	0.833 6(8)	0.918 8(2)	0.748 7(5)
H(C2)	0.298(6)	0.751(2)	−0.036(5)
H(C4)	0.298(7)	0.559(2)	−0.068(5)
H(C6)	0.617(6)	0.616(2)	0.572(5)
H(111)	0.803(8)	0.966(2)	0.682(6)
H(112)	0.833(8)	0.936(2)	0.898(6)
H(113)	1.026(8)	0.914(2)	0.759(6)
O′	0.102(5)	0.568(2)	−0.117(4)

affects the bond lengths formed by O(5) whose mean value [1.399(2) Å] is slightly shorter than the oxygen–carbon single-bond length (1.43 Å). It is intermediate between the values found in furan[6] (1.362 Å) and in tetrahydrofuran[7] [1.428(3) Å] and compares well with that found in dibenzofuran[8] [1.404(3) Å]. The C(1)–C(2) bond length [1.499(3) Å] is close to the single C(sp^3)–C(sp^2) bond length and is significantly longer than C(2)–C(4) and C(1)–C(6) [average 1.446(3) Å]. These are even shorter than both the single C(sp^2)–C(sp^2) bond length (1.48 Å) and the C–C bond commonly found in epoxy rings.[3] Thus, all these findings indicate π electron conjugation between the two epoxy groups through the interconnecting oxygen atom. This effect, specific for the *syn* diepoxide, is expected to lower its enthalpy relative to the *anti* isomer.

Protruding from the face opposite the epoxy rings, the bonds C(2)–H(2), C(4)–H(4), C(6)–H(6) and C(1)–C(8) form an average angle of 27(2)° (range 26—29°) with the plane of the five-membered ring. This value is exactly half-way between those expected for the sp^3(55°) and sp^2(0°) hybridization of the intra-ring carbon atoms.

The fragment C(1)–C(8)–O(9)–O(10)–C(11) is planar within 0.020 Å as a consequence of the partial double-bond character of C(8)–O(10) as indicated by its length [1.329(2) Å]. The length C(1)–C(8) [1.481(3) Å] is typical of a single C(sp^2)–C(sp^2) bond. The methyl group at C(11) is in a staggered conformation with respect to C(8)–O(10) bond. The torsion angle C(2)–C(1)–C(8)–O(9) [−13.1(4)°] is that which optimizes the intramolecular contact O(9) $\cdots$ H(C2) [2.65(2) Å].

During the last steps of the least-squares refinement of the atomic positions, it was observed that the position of H(4) was stereochemically incorrect. A difference electron density map, calculated at this stage without a contribution by H(4), showed two peaks, close in space and in weight, clearly emerging above the background. One of them was at the expected position for the hydrogen atom, whereas the second fulfilled the geometrical requirements of an oxygen atom bound to (C4) through one of its sp^2 orbitals. This finding has been interpreted in terms of cleavage of the epoxy bond C(2)–O(3) and the formation at C(4) of a ketone. This reaction would account for crystal decay observed during the exposure to X-ray radiation. This peak was included, designated O′, among the atoms to be refined with an isotropic thermal factor and a fixed occupancy factor of 0.2, based on the peak height. The crystal packing (Figure 2) shows no short van der Waals contacts between the molecules of the title compound, while computation of the intermolecular distances involving O′ reveals that only two are slightly less than the sum of the van der Waals radii. In particular, O′ forms two distances, 2.60(1) Å long, with O(5) and O′ at $\bar{x},\bar{y},\bar{z}$ and shifted by one cell along b. Thus, at least for a small percentage, the crystal lattice can accommodate the product of the reaction. The crystallographic analysis, hence, provides evidence that the first step, at least, of the degradation process induced by radiation consists of the conversion of (**2**) into the isomer (**4**).

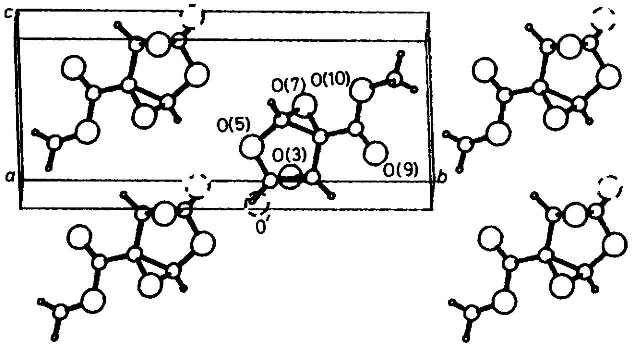


Figure 2. Crystal packing viewed along **a**. Dashed lines refer to the extra atom O′

Experimental

The compound was prepared as described in ref. 1. A well formed crystal, obtained by evaporation of an anhydrous chloroform solution at low temperature under nitrogen atmosphere, was sealed in a Lindemann capillary.

Crystal Data.—$C_6H_6O_5$, $M = 158.1$. Triclinic, $a = 4.197\,9(4)$, $b = 13.948(1)$, $c = 5.732\,4(4)$ Å, $\alpha = 92.462(7)$, $\beta = 103.070(7)$, $\gamma = 91.136(8)°$, $V = 326.5$ Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred reflections), filtered Cu-K_α radiation ($\lambda = 1.5418$ Å), space group $P\bar{1}$, $Z = 2$, $D_x = 1.61$ g cm^{-3}. Crystal dimensions 0.2 × 0.3 × 0.5 mm, $F(000) = 164$, μ(Cu-K_α) = 12.1 cm^{-1}.

Data Collection and Processing.—CAD4 diffractometer, ω–θ scan mode, θ(max.) = 76°, room temperature, 948 unique observed reflections [$I_o \geqslant 3\sigma(I_o)$] out of the total of 1 363 measured. Three standard reflections ($-1\ -2\ 4$, $0\ -4\ 3$, $1\ 5\ -2$), monitored throughout the data collection to check electronic and crystal stability, showed a systematic decrease of intensity with time which reached *ca.* 20% at the end of data collection. A linear correction for the radiation damage was applied together with the Lorentz and polarization factors. Absorption was neglected.

Structure Analysis and Refinement.—The structure was solved by direct methods, through a straightforward application of MULTAN 78.[9] The E-map with the highest figure of merit showed all non-hydrogen atoms. The hydrogen atoms and the additional O′ atom were successively located by difference Fourier syntheses. Full-matrix least-squares minimized $\Sigma w(\Delta F)^2$, where $w = 1/\sigma^2(F)$. 129 refined parameters included overall scale factors, positional parameters of all atoms, anisotropic thermal parameters for non-hydrogen atoms and isotropic for hydrogen atoms and O′, and a correction for secondary extinction [g coefficient = $1.87(5) \times 10^{-5}$]. Final R and R_w values for the observed reflections were 0.048 and 0.073. The final difference electron density synthesis showed no peak $\geqslant \pm 0.2$ e Å^{-3}. Atomic scattering factors were taken from ref. 10. All calculations were performed by the Enraf–Nonius system of programs (SDP)[11] on a PDP 11/34 computer. Lists of thermal parameters and observed and calculated structure factors can be obtained from F. G.

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