An Epoxidation *cis* to Two Allylic Benzoyloxy-groups

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Direct epoxidation of tri-*O*-benzoylcyclopentene-3,5/4-triol proceeds in the same stereochemical sense as that of the parent triol, which yields 1,2-anhydrocyclopentane-1,2,3,5/4-pentol.

WHEREAS epoxidation with peracids normally proceeds *cis* to an allylic hydroxy-group,[1] acylation of that hydroxy-group usually reverses this stereochemical preference.[1,2] We desired both epoxides (2a) and (3a) derived from the known olefin (1a). Posternak *et al.*[3] reported that epoxidation of cyclopentenetriol (1a) gave the epoxide (3a); epoxidation of the tribenzoate (1b) seemed a promising route to (2a).

RESULTS AND DISCUSSION

The tribenzoate (1b), like various 3,6-diacyloxycyclohexenes,[4] was resistant to peracids under standard conditions, but with pertrifluoroacetic acid in a polar solvent (sulpholane) at 80 °C, in the presence of a base powerful enough to deprotonate trifluoroacetic acid but not pertrifluoroacetic acid (anhydrous Na_2HPO_4), the epoxidation was successful. Debenzoylation of this epoxide product, however, yielded a material identical with the product of direct epoxidation of (1a); likewise, benzoylation of this latter product yielded a material identical to that from epoxidation of (1b).

a; R = H
b; R = PhCO
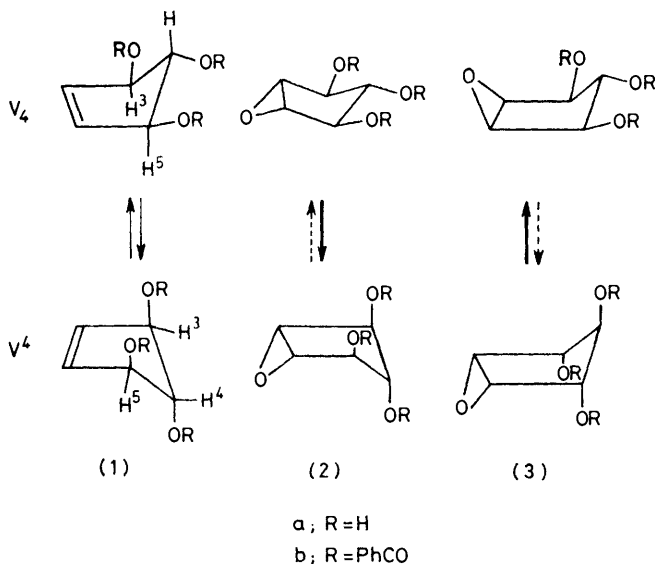
Evidence that both epoxides have structure (3) and not structure (2) comes from two sources. (*i*) Examination of the AB_2 † system formed by H^3, H^4, and H^5 in

† In all compounds the protons on positions 1 and 2 resonate as a sharp singlet; irradiation of this singlet in the case of epoxide (3b) results in only minor changes in the AB_2 system. This absence of vicinal coupling can be attributed to dihedral angles close to 90°.

the ^1H n.m.r. spectra of compounds (1a and b) and their epoxidation products revealed that the changes in both chemical shift and coupling constants on epoxidation supported structure (3). Spectra of the benzoylated derivatives were examined in $CDCl_3$ with $SiMe_4$ as internal standard, and those of the deprotected compounds in D_2O with sodium 3-trimethylsilylpropane-1-sulphonate as internal standard, both at 100 MHz.

Epoxidation of the olefin (1a) results in an upfield shift of the allylic protons of 0.5 p.p.m. and of the homoallylic proton of 0.4 p.p.m.; epoxidation of the olefin (1b) results in an upfield shift of 0.4 p.p.m. for the allylic protons and 0.1 p.p.m. for the homoallylic proton. The systematic study by Ali *et al.*[5] indicates that in various fused cyclopentenes, epoxidation results in an upfield shift of a homoallylic proton *cis* to an epoxy-group by 0.38 ± 0.13 p.p.m. (five cases) but of a *trans*-homoallylic proton by 0.15 ± 0.04 p.p.m. (four cases), and an upfield shift of a *trans*-allylic proton by 0.58 ± 0.15 p.p.m. (nine cases) but of a *cis*-allylic proton by 0.24 ± 0.17 p.p.m. (nine cases).

The coupling constant ($J_{3,4} = J_{4,5}$) for olefin (1b) was 2.9 Hz, which increased to 5.8 Hz on epoxidation; that for olefin (1a) was 5.0 Hz, which increased to 6.4 Hz on epoxidation. Steyn and Sable[6] showed that, like other systems with the bicyclo[3.1.0]hexane skeleton, the six-membered ring in cyclopentene oxides showed a strong preference for the boat conformation. The two envelope conformations of substituted cyclopentenes, by contrast, are normally comparably favoured. Coupling constants in the V_4 conformation are high because of an almost 180° dihedral angle; they are low in the V^4 conformation because of an almost 90° dihedral angle.[6] Therefore, conversion of olefin (1) to epoxide (2) should decrease the coupling constant, but conversion to epoxide (3) should increase it, as observed.

(*ii*) The epoxide was opened with HCl in methanol, and the resulting material was titrated with periodic acid. Opening of cyclopentene epoxides with HCl has been shown to proceed with Walden inversion and without rearrangement.[7] The product from epoxide (2a) should not react with periodate, since the hydroxy-groups are all *trans* and anchored,[8] whereas that from epoxide (3a) should react with 3 mol of the reagent.

In aqueous solution, buffered at pH 7.0 with 10mM sodium phosphate, the products from the cyclopentene-triol epoxide immediately took up 0.95 mol equiv. of periodate; thereafter a further 1.55 mol equiv. were consumed during 2 h. After 10 h, 2.95 mol equiv. of

periodate had been consumed. Such behaviour in the cyclohexane series is characteristic of the disposition of three hydroxy-groups on the same side of the molecule which can form a tridentate complex with periodate.[9,10] Such a tridentate structure is possible only with the products from epoxide (3a).

Epoxide (3a) has no effect on the α-L-arabinofuranosidases of *Monilinia fructigena*, or on yeast invertase. The inertness of the latter enzyme, a β-D-fructofuranosidase rather than an α-glucosidase, is surprising in view of the alkylation of a carboxylate group in its active site by conduritol B epoxide.[11] Conduritol B epoxide bears a similar structural relationship to an α-glucopyranoside as epoxide (3a) does to a β-fructofuranoside.

EXPERIMENTAL

Olefins (1a) *and* (1b).—The procedure of Gaoni[12] was followed, with the following improvements. Separation of the isomers formed on allylic bromination of *E*-3,4-dibenzoyloxycyclopentene was unnecessary, since all plausible S_N1 routes from either isomer would give the desired tri-*O*-benzoylcyclopentene-3,5/4-triol. Omission of this separation step improved the yield from the dibenzoyloxycyclopentene from 13.5 to 76%. De-*O*-benzoylation was achieved with 33mM barium methoxide in methanol (18 h, 4 °C) in 81% yield (*cf.* 50% with methanolic ammonia[12]).

1,2-*Anhydrocyclopentane*-1,2,3,5/4-*pentol*.—This compound was made by the method of Posternak *et al.*[3] (except that *m*-chloroperbenzoic acid was substituted for perbenzoic acid), a product (64%) of m.p. 126—128 °C being obtained.

An identical product, m.p. 128—129 °C after recrystallisation from ethanol, was obtained in 79% yield by debenzoylation of epoxide (3b) with 33mM barium methoxide in methanol. After 18 h at 4 °C, solid CO_2 was added, the barium carbonate was filtered off, the filtrate was evaporated, and the residue was triturated with dry acetone.

3,4,5-*Tri-O-benzoyl*-1,2-*anhydrocyclopentane*-1,2,3,5/4-*pentol*.—Tribenzoate (1b) (0.90 g) and anhydrous disodium hydrogenphosphate (3.0 g) in sulpholane (tetrahydrothiophen 1,1-dioxide) (20 ml) were stirred at 80 °C, and a mixture of sulpholane (1.25 ml), trifluoroacetic anhydride (1.25 ml), and 83% aqueous hydrogen peroxide (0.25 ml) was added dropwise during 30 min. After reaction for a further 1 h at 80 °C, the mixture was cooled, taken up in dichloromethane, washed with water, dried with anhydrous magnesium sulphate, and evaporated at 22 °C under filter-pump vacuum. The epoxidation of the sulpholane solution of reactants and products was then repeated twice. After the

third epoxidation this sulpholane solution, now containing no unreacted olefin, was diluted with water (500 ml), and extracted with light petroleum (b.p. 30—40 °C) (10 × 500 ml). The organic extracts were dried ($MgSO_4$) and evaporated, and the semi-solid residue was recrystallised from methanol to give the *product* (0.42 g, 45%), m.p. 169—170 °C (Found: C, 70.35; H, 4.5. $C_{26}H_{20}O_7$ requires C, 70.25; H, 4.5%); δ(60 MHz, CCl_4, relative to $SiMe_4$) 4.0 (2 H, s, epoxy-CH), 5.5—6.0 (3 H, AB_2 m, methine CH), 7.5 (9 H, br s, *m*- and *p*-benzoate), and 8.2 (6 H, br m, *o*-benzoate).

The same compound was produced by treating crude epoxide (3a) from epoxidation of olefin (1a) (45 mg) with pyridine (0.6 ml) and benzoyl chloride (0.3 ml) for 16 h at 22 °C. After the addition of a few drops of water to destroy the excess of benzoyl chloride, the mixture was taken up in dichloromethane, which was subsequently washed with water, dilute HCl, and saturated $NaHCO_3$. The organic phase was dried with $MgSO_4$, evaporated, and the residue was recrystallised to give a product, m.p. 169—170 °C, n.m.r. as above (75 mg, 45%).

Ring-opening and Periodate Titration.—Epoxide (3a) (1.32 mg) was dissolved in 11M HCl in methanol (*ca.* 2 ml) and left at 22 °C for six days. The solution was evaporated at room temperature, and the syrup taken up in water (10.0 ml). This solution (100 µl) was injected into 10^{-4}M sodium periodate in 10mM sodium phosphate buffer, pH 7.0 (5 ml), and the absorbance followed at 223 nm. Optical-density changes were calibrated with tartaric acid, and were monitored discontinuously, to avoid u.v.-induced over-oxidation.

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