A new Procedure for Olefin Oxiranation by Peroxybenzimidic Acid; Synthesis of some Carbohydrate-precursor Oxirans and other Epoxides

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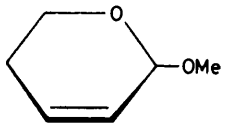
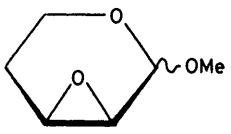
Synthesis of *cis*- and *trans*-2-methoxy-3,4-epoxytetrahydropyrans (4) and (5), 3,4-anhydro-1,2-isopropylidene-β-DL-arabinopyranose (6), and the *cis*- and *trans*-2-methoxy-3,4-epoxytetrahydrofurans (7) and (8), which are carbohydrate-precursor oxirans, using a new procedure of oxiranation with peroxybenzimidic acid and potassium carbonate as the basic catalyst is described. The method has been extended to the oxiranation of several olefins such as indene (9), oct-1-ene (10), *trans*-β-methylstyrene (11), allyl alcohol (12), and chroman-4-one (13). In all cases, the method appears to be efficient and produces the oxirans in excellent yields after short reaction times.

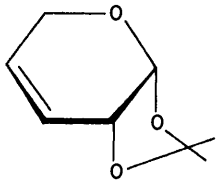
OXIRANS are important in sugar chemistry because of their high reactivity towards numerous nucleophiles which permits the introduction into sugar structures of a wide variety of substituents [1] of chemical and biological importance. In the course of our work on the synthesis of sugar and nucleoside antibiotic analogues from non-carbohydrate precursors,[2] we wished to synthesize the five oxiran derivatives (4)—(8) of the pyranic and furanic unsaturated compounds (1)—(3), in order to build sugar-like structures by the introduction of various groups,



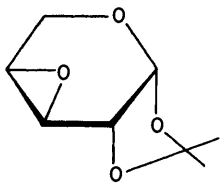
(1)



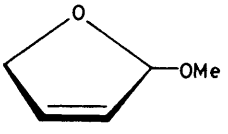
(4) *cis*
(5) *trans*



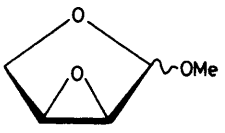
(2)



(6)



(3)



(7) *cis*
(8) *trans*

such as the hydroxy-, azido-, or amino-groups, *via* the nucleophilic opening of these oxirans. Among the oxiranation methods, that in which the substrates are unsaturated compounds and the oxidants are hydrogen peroxide or peroxy-acids has been utilized for the synthesis of a number of carbohydrate or sugar-precursor oxirans.[3,4] In our series of unsaturated compounds, we observed that these methods gave, in most cases, low yields and undesired isomers or olefin degradation. The only method which succeeded in synthesing the expected oxirans was that of Payne,[5] slightly modified by Ferrier and Prasad,[6] in which the oxidizing agent is peroxybenzimidic acid, generated in the reaction medium by benzonitrile–hydrogen peroxide in the presence of a basic catalyst such as sodium hydrogen carbonate; but only moderate yields were obtained after long reaction times (2 days to several weeks).

To synthesize large quantities of oxirans, it was necessary to increase the yield of the reaction and to decrease the reaction time. We solved these problems by replacing the usual catalysts [5,7] of the Payne reaction with potassium carbonate. The present report describes the application of this new procedure to the synthesis of some sugar-precursor non-carbohydrate oxirans and its extention to the production of several more common epoxides.

RESULTS AND DISCUSSION

Oxiranation with benzonitrile–hydrogen peroxide must be carried out under conditions in which there is a good equilibrium between the rate of formation of the peroxybenzimidic acid and the rate of its degradation into benzamide and oxygen by its further reaction with hydrogen peroxide. Payne has shown that the optimum pH for oxiranation is 8, but we observed that pH values <8.5 and >10 led to slow epoxidation with low yield. So we performed the oxiranation under intermediate pH values by the slow addition of hydrogen peroxide to a suspension of potassium carbonate in the methanolic olefin which contained benzonitrile. The initial pH was *ca.* 9 and reached 9.5—9.7 by the end of the reaction because of the progressive dissolution of the catalyst.

Synthesis of the *cis*- and *trans*-tetrahydropyrans (4) and (5) [carbohydrate nomenclature: methyl 2,3-anhydro-4-deoxy-α-(*cis*) and -β-(*trans*)-DL-erythropento-pyranoside [8]) had been previously described by Sweet and Brown,[9] who epoxidized 2-methoxy-5,6-dihydro-2*H*-pyran (1) with *m*-chloroperoxybenzoic acid in 7 days with 80% yield (Table 1). The *trans*-isomer was preferentially obtained (*cis* : *trans* ratio, 1 : 9) because of the presence of an allylic methoxy-group, which is known to favour a *trans*-oxiran formation.[10] This synthetic

method was not valuable in our work because we wished to prepare the *cis*-isomer. The *cis*-isomer had been obtained in consistent yield from compound (1) by Chmielewski and Zamojski [11] who used peroxybenzimidic acid, which gave a ratio of *cis* : *trans* of 13 : 7. The predominance of the *cis*-isomer is because iminoperoxy-acids have a lower stereospecificity than peroxy-acids and because, with this oxidant, an anomeric methoxy-group favours the formation of *cis*-oxirans.[12] However, the reaction time was *ca.* 2—3 weeks and the yield of pure product *ca.* 58%. With our procedure we obtained the same *cis* : *trans* ratio in 1.30 h with 94% yield of the pure epoxides (4) and (5) (Table 1).

With 3,4-dideoxy-1-*O*,2-*O*-isopropylidene-α-DL-*glycero*-pent-3-enopyranose (2),[13] oxiranation by the benzonitrile–hydrogen peroxide–potassium carbonate method led to 3,4-anhydro-1-*O*,2-*O*-isopropylidene-β-DL-arabino-pyranose (6) with high yields (95%) in short reaction times (1.30 h) (Table 1). The *arabino*-configuration of the only product was determined by chemical degradation which consisted of oxiran opening by sodium azide followed by acidic methanolic cleavage of the isopropylidene group, and an attempt at diacetal formation between the two hydroxy-groups at C-2 and C-3 with acetone. The lack of acetalization showed the *trans*-configuration of these two groups and consequently the *arabino*-configuration of the oxiran (6).

Compound (3) [14] has been epoxidized in excellent yield with our procedure to give a mixture of the *cis*- and *trans*-2-methoxy-3,4-epoxytetrahydrofurans (7) and (8), with a ratio of *ca.* 3 : 2, respectively. These compounds, which are precursors of furanic carbohydrate analogues related to a tetrose-type structure are, in sugar nomenclature, methyl 2,3-anhydro-α- and -β-DL-erythrofuranosides. The synthesis of these oxirans was not possible with peroxy-acids, because not only are alkoxy-dihydrofurans decomposed into furan by acids, but also they are sensitive to peracids which lead, in some cases, to ethylenic lactones.[15] Therefore, in an attempt to epoxidize compound (3) with *m*-chloroperbenzoic acid we obtained a mixture of several ethylenic products, lactones, and ethylenic lactones and only traces of the β-epoxide. The determination of the anomeric configurations of the two oxirans (7) and (8) was not directly possible by n.m.r. spectroscopy because, as in the case of 2,3-anhydro-nucleosides with the furanic structure,[16] the spectra of both α- and β-anomers present a sharp singlet for the anomeric proton resonance which indicates a coupling constant of $J_{1,2} < 0.5$ Hz. The anomeric configurations were determined by ^{1}H n.m.r. spectroscopy after chemical degradation which consisted of oxiran opening by sodium azide followed by benzoylation.*

In order to compare our oxiranation procedure with the general method of Payne we also prepared the five oxirans (4)—(8) with sodium hydrogen carbonate as the basic catalyst. Results are reported in Table 1.

TABLE 1

Synthesis of the oxirans (4)—(8)

	K_2CO_3			$NaHCO_3$			Literature			
Substrate	Yield (%)	Time (h)	Isomers (%)	Yield (%)	Time (h)	Isomers (%)	Method	Yield (%)	Time (h)	Isomers (%)
(1)	94	1.30	α, 65 β, 35	58 [a]	500	α, 65 β, 35	*m*-$ClC_6H_4CO_3H$	80 [b]	160	α, 10 β, 90
(2)	95	1.30	α, 0 β, 100	76	48	α, 0 β, 100				
(3)	94	2	α, 60 β, 40	72	48	α, 60 β, 40				

[a] Ref. 11. [b] Ref. 9.

It is clear that with our procedure, not only are the reaction times greatly reduced, but the yields are strongly increased. Evidently, when the *cis*- and *trans*-isomers are obtained together, their ratio is the same as that in the method with sodium hydrogen carbonate as catalyst, because the mechanism of oxiranation is similar. An interesting characteristic of the procedure is that it can be applied to large-scale preparations of oxirans because of its simplicity; so we have prepared compounds (4) and (5) from 500 g of the olefin (1) in a one-pot reaction.

To investigate the scope of application of our epoxidation method, we prepared oxirans of compounds (9)—(13) and compare the results with those of Payne's method and with other reported methods in Table 2. In all cases we found that oxiranation by peroxybenzimidic acid with potassium carbonate as catalyst leads to higher yields and lower reaction times than that using sodium hydrogen carbonate except, however, for chromone. Likewise, yields are often higher than those obtained with other methods reported in the literature.

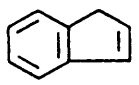
TABLE 2

Oxiranation of compounds (9)—(13)

	K_2CO_3		$NaHCO_3$		Literature	
Substrate	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)	Reference
(9)	90	2	80	48	80	17 [a]
(10)	92	2.5	62	48	87	18 [b]
(11)	93	2	56	48	85	19 [c]
(12)	80—85	2.5	76	24	83	20 [d]
(13)	76	2	74	6	39	21 [e]

[a] Perbenzoic acid. [b] Trifluoroperacetic acid. [c] Hydroperoxy ethers. [d] Chlorohydrin. [e] H_2O_2–NaOH.

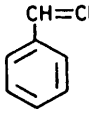
* The chemical degradation will be reported in a subsequent paper.



(9)

$Me[CH_2]_5CH=CH_2$

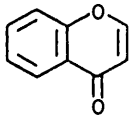
(10)



(11)

$CH_2=CH-CH_2OH$

(12)



(13)

The above compounds were obtained in racemic form, but only one enantiomer (D or L) is drawn for each of them

EXPERIMENTAL

^1H N.m.r. spectra were obtained at 60 MHz using a Perkin-Elmer R24B spectrometer. All the spectra were recorded in $CDCl_3$ with chemical shifts (δ) given downfield from $SiMe_4$ as the internal standard. T.l.c. was conducted on precoated Merck plates (Kieselgel $60F_{254}$) and developed with phosphomolybdic acid. Preparative column chromatography was conducted also with precoated Merck plates (Kieselgel $60F_{254}$) and ethyl acetate–hexane mixtures were used as eluant. I.r. spectra were recorded with a Beckman Acculab 4 spectrometer and refractive indexes measured on an OPL refractomer. Elemental analyses were performed by the ' Serviçe central de microanalyse du centre National de la Recherche Scientifique de Lyon '. All the known epoxides that we obtained gave physical characteristics which are identical with those reported in the literature.

General Procedure for Oxiranations.—To a vigorously stirred suspension of olefin (1 mol), benzonitrile (1.5 mol), and potassium carbonate (25 g) in methanol (250—450 ml) was added hydrogen peroxide (40% v/v; 2.5 mol) as drops until the starting material had disappeared. During the addition, the temperature was maintained at *ca.* 25—30 °C with a cold water-bath. When the reaction was complete, the mixture was stirred for a further 0.5 h at 40 °C to destroy the excess of benzonitrile. It was then treated with 5% palladium-on-charcoal (300 mg) at the same temperature to decompose the excess of hydrogen peroxide. The mixture was treated with just sufficient hydrochloric acid to neutralize the potassium carbonate and then kept for 1.5 h at −10 °C. The insoluble material was removed by filtration and washed with pentane–diethyl ether (1 : 1, 100 ml). The filtrate was treated according to either Procedure A or B.

Procedure A.—The filtrate was diluted with ethyl acetate (300 ml) and methanol, and was distilled under atmospheric pressure as an azeotropic mixture with ethyl acetate. The remaining aqueous solution was extracted with ethyl acetate (5 × 100 ml), the solvent was evaporated under atmospheric pressure, and the residue was distilled in the case of compounds (4), (5), (7), (8), epoxyindene, and glycidol or purified by column chromatography for compound (6) and epoxychromone.

Procedure B.—The filtrate was extracted with pentane for 5 h. The solvent was removed by evaporation and the product was distilled. This procedure was used for the extraction of 1,2-epoxyoctane and α-methyl-β-phenylethylene oxide.

3,4-*Anhydro*-1-O,2-O-*isopropylidene*-β-DL-*arabinopyranose* (6) gave n_D^{20} 1.4570; R_F 0.60 (ethyl acetate–hexane, 1 : 1); $\nu_{max.}$ 1 380 and 1 390 cm^{-1} (CMe_2); δ 1.38 and 1.50 (6 H, 2s, 2 × Me), 3.25 (2 H, s, 3-, 4-H), 4.17 and 3.38 (2 H, 2d, $J_{5,5'}$ −13 Hz, 5-, 5'-H), 4.26 (1 H, d, $J_{1,2}$ 4.7 Hz, 2-H), and 5.28 (1 H, d, $J_{1,2}$ 4.7 Hz, 1-H) (Found: C, 55.7; H, 7.15. $C_8H_{12}O_4$ requires C, 55.81; H, 6.98%).

cis-2-*Methoxy*-3,4-*epoxytetrahydrofuran* (7) gave n_D^{20} 1.4455; R_F 0.2—0.3 (ethyl acetate–hexane, 1 : 1); b.p. 64 °C/25 mmHg; $\nu_{max.}$ 2 860 (OMe) and 860 and 815 cm^{-1} (oxiran); δ 3.50 (3 H, s, OMe), 3.73 (2 H, s, 2-, 3-H), 3.78 (1 H, d, $J_{4,4'}$ −11 Hz, 4-H), 4.15 (1 H, d, $J_{4,4'}$ −11 Hz, 4'-H), and 5.02 (1 H, s, 1-H) (Found: C, 51.65; H, 6.8. $C_5H_8O_3$ requires C, 51.70; H, 6.90%).

trans-2-*Methoxy*-3,4-*epoxytetrahydrofuran* (8) gave n_D^{20} 1.4365; R_F 0.60—0.65 (ethyl acetate–hexane, 1 : 1); b.p. 90 °C/25 mmHg; $\nu_{max.}$ 2 860 (OMe) and 860 and 815 cm^{-1} (oxiran); δ 3.40 (3 H, s, OMe), 3.62 and 3.75 (2 H, 2d, $J_{2,3}$ 3 Hz, 2-, 3-H), 4.00 and 3.75 (2 H, 2d, $J_{4,4'}$ −11 Hz, 4-, 4'-H), and 4.93 (1 H, s, 1-H) (Found: C, 52.0; H, 7.05. $C_5H_8O_3$ requires C, 51.70; H, 6.90%).

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