A VERY SIMPLE OXIDATION OF OLEFINS AND KETONES WITH UHP - MALEIC ANHYDRIDE

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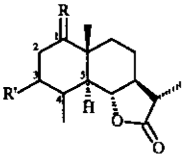
Abstract - The oxidation of olefins and ketones to oxiranes and esters, respectively, is carried out with the UHP (urea-hydrogen peroxide complex) - maleic anhydride system in a mild and very simple procedure.

The epoxidation of olefins with peroxyacids (MCPBA, PBA, 3,5-DNPBA, PAA, TFPAA, MPPA and monoperoxymaleic acid) is a very important reaction in organic synthesis.[1] Recently, Heaney *et al.*[2] have shown that magnesium monoperoxypthalate (MMPP), as well as the complex urea-hydrogen peroxide (UHP), together with acetic and trifluoroacetic anhydrides in the presence of a buffer (disodium hydrogen phosphate)[3] are alternatives to the use of *m*-chloroperoxybenzoic acid (MCPBA)[4] or other peroxy acids prepared from concentrated (85-90%) aqueous solutions of hydrogen peroxide.

In this paper we present the results obtained in the oxidation of olefins and ketones to oxiranes and esters, respectively, with peroxymaleic acid prepared from UHP and maleic anhydride.

The results obtained in the oxidation of olefins are given in Table I. It can be observed that the yields are moderate to high and the use of a buffer is unnecessary, except in the case of geraniol in which the reaction must be stopped at 50% conversion to avoid obtaining a complex mixture of maleates. However, the addition of 3 equivalents of anhydrous sodium carbonate allows the corresponding epoxides to be isolated. Cyclohexene afforded very poor yields even with the addition of a buffer, the main product results from the attack of maleic acid on the initially formed epoxide. The terminal olefins with a smaller nucleophility such as 1-heptene and 1-octen-3-ol react more slowly but the yield is good and comparable to those of Heaney *et al.*[3] using UHP-trifluoroacetic anhydride. A similar situation arises in the epoxidation of cholesterol, in which the yield and selectivity are higher. Finally, the selectivity obtained in the epoxidation of certain olefins (see penultimate entry in Table I) is markedly greater than those afforded by the use of MCPBA (4:1 against 2.7:1 respectively).[5]

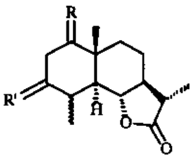
Table I

olefin	time (h)	yield (%)[a]
2-methyl-3-buten-2-ol (**1**)	4	72
1-octen-3-ol (**2**)	20	76 (55:45; threo:erythro)[b]
1-heptene (**3**)	12[c]	71
linalool (**4**)	5[c]	75 [2-methyl-5-(2'-propyl-2'-hydroxy)-2-vinyltetrahydrofuran][6]
geraniol (**5**)	3.5[c]	33 (2,3-epoxide), 9 (6,7-epoxide)[d]
		12 (2,3-epoxide), 14 (6,7-epoxide), 31 (2,3 - 6,7-epoxide)[e]
geranyl acetate (**6**)	6	77 (6,7-epoxide)
trans-stilbene (**7**)	20	80
cholesterol (**8**)	2	76 (α-epoxide)
limonene (**9**)	3	73 (*cis:trans* mixture of epoxides)
cyclohexene (**10**)	3[c]	23[b]
		
R = O; R' = H; $\Delta^{4(5)}$ (**11**)	4	82 (α:β; 5:1)
R = α-H; β-OTBS; R' = H; $\Delta^{3(4)}$ (**12**)	4	80(α)
R = H,H; R' = H; $\Delta^{2(3)}$; 4α-Me (**13**)	5	90(α)
R = R' = H; $\Delta^{1(2)}$; 4β-Me (**14**)	5	85(α)
R = α-H, β-OTBS; R' = β-OH; $\Delta^{4(5)}$ (**15**)	3	85(β:α; 4:1)[f]
R = α-H, β-OTBS; R' = α-OH; $\Delta^{4(5)}$ (**16**)	2	85(α)

a) Isolated yield. b) Determined by nmr from reaction mixture. c) Reaction was carried out at 0°C. d) Reaction was stopped at *ca* 50% conversion. e) Solid anhydrous Na_2CO_3 was added. f) (β:α ; 2.7:1) with MCPBA.[5]

The results obtained in the oxidation of ketones, carried out under similar conditions to the epoxidations although with a 1:3:9 ratio of equivalents substrate:anhydride:UHP in dichloromethane or 1,2-dichloroethane, are given in Table II. The results obtained for cyclic ketones (cyclopentanone, cyclohexanone, etc.) are comparable for both methods but in several cases, the conversions with UHP-maleic anhydride are low although with moderate yields; special mention should be made of the case of benzophenone which undergoes no reaction, in contrast with the results obtained with monoperoxymaleic acid prepared from aqueous hydrogen peroxide (90%).[1c] Variations in the proportions of the reagents and an increase in temperature or reaction times did not lead to improved results.

Table II

ketone	**time (h)**	**yield (%) (lactone or ester)[a]**
cyclopentanone **(17)**	8[b]	68
cyclohexanone **(18)**	10	87
2-methylcyclohexanone **(19)**	10	84 (6-hydroxyheptanoic acid lactone)
cycloheptanone **(20)**	10	64
cyclooctanone **(21)**	5 days	(45)[c] (67)[d]
2-cyclohexen-1-one **(22)**	12	46 (enol lactone)
acetophenone **(23)**	48	93 (33)[c](70)[d] (phenyl acetate)
tert-butylmethylketone **(24)**	48	81 (89)[c] (*tert*-butyl acetate)
2-octanone **(25)**	48	93 (10)[c](71)[d] (hexyl acetate)
benzophenone **(26)**	-	70[d]
		
R = H,H; R' = O; 4α-Me **(27)**	24	91 (57)[c] (3,4 O-insertion)
R = O; R' = H,H; 4β-Me **(28)**	24	88 (45)[c] (1,10 O-insertion)

a) Isolated yield. b) Reaction was carried out at 0°C. c) Yield based upon conversion (in parentheses). d) Yields obtained with peroxymaleic acid from 90% aqueous hydrogen peroxide solution.[1c]

In all the cases studied the migratory aptitudes are in good accordance with the expected for the Baeyer-Villiger reaction.[7] It is noteworthy that the reaction of 2-cyclohexen-1-one generates with moderate yield the corresponding enol lactone, which complements the applicability of the UHP complex since in the above-mentioned work of Heaney[3] the epoxidation of the double bond of 2-cyclohexen-1-one is carried out in alkaline medium.

Summarizing, we believe that the system UHP-maleic anhydride presents some advantages over other previously used methods in the epoxidation of olefins and in certain cases in the Baeyer Villiger oxidation of ketones, since the use of buffers is generally not required, and because of its low cost,[8] easy experimental handling and the fact that the subproducts of the reaction (urea and maleic acid) are readily removed by filtration because of their low solubility in the solvents employed.

ACKNOWLEDGEMENTS

L. Astudillo is indebted to the A. I. E. T. I. Foundation for a fellowship.

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage and are uncorrected. ^{1}H-Nmr (200 MHz) and ^{13}C-Nmr (50 MHz) spectra were measured on a Bruker WP-200SY with $CDCl_3$ as solvent. Ir spectra were recorded on a Shimadzu IR-408 spectrophotometer in $CHCl_3$. Mass spectra were measured on a VG Micromass ZAB-2F. The optical rotations were measured on a Perkin-Elmer polarimeter, model 241 at 20-30^0 C in $CHCl_3$ in *ca* 0.5% concentrations. Column chromatography was carried out using Merck silica gel 60 (0.065-0.2 mm). Dichloromethane and 1,2-dichloroethane were dried over CaH_2 and distilled before use.

Epoxidation of olefins

To a well-stirred suspension of the complex UHP (9 mmol, 847 mg) in dry dichloromethane (5 ml), solid maleic anhydride was added (4.5 mmol, 442 mg). The mixture was kept for 5 min at room temperature with stirring, the olefin (3 mmol) was then added slowly, either neat or dissolved in dry dichloromethane (5 ml), a copious white precipitate forming over time. The reaction mixture was stirred for the time shown in Table I, and diluted with dichloromethane. Solid sodium hydrogen carbonate was added. The mixture was filtered slowly through a short column of neutral alumina (Merck, activity II).[9] After removing the solvent at reduced pressure the products were purified by flash chromatography, distillation or direct crystallization. In some cases reactions were buffered by addition of solid anhydrous sodium carbonate (3 mmol per mmol of substrate) just before addition of olefin, and some reactions were conducted at 0^{0}C (see Table I). Identification of products was done by direct comparison of their physical and spectroscopic data with authentic samples prepared according to standard procedures or to those reported in the literature.[1a,1g,10] Selected values are given for epoxides of **12**, **13**, and **14**.

α-Epoxide from 12 - mp 97-99 ^{0}C (hexane) ; $[\alpha]_D + 23.7^0$; ir 1770 cm $^{-1}$ (γ-lactone); ^{1}H-nmr δ 3.89 (1H, dd, J= 9.7 and 9.7 Hz, H-6), 3.33 (1H, dd, J= 6.4 and 6.4 Hz, H-1), 2.95 (1H, d, J= 2.9 Hz, H-3), 1.43 (3H, s, H-15), 1.21 (3H, d, J= 7.0 Hz, H-13), 0.91 (3H, s, H-14) ; ms (m/z) 380 (M$^+$), 365 , 323 .

α-Epoxide from 13 - mp 154-156^{0}C (hexane-CH_2Cl_2) ; [α]$_D$ +12.2^0 ; ir 1775 cm^{-1} (γ–lactone) ; ^{1}H-nmr δ 3.73 (1H, dd, J= 10.4 and 10.5 Hz, H-6), 3.21 (1H, m, H-2), 3.07 (1H, dd,J= 3.5 and 2.6 Hz, H-3), 1.32 (3H, d, J= 6.8 Hz, H-15), 1.20 (3H, d, J= 6.7 Hz, H-13); ms (m/z) 250 (M$^+$), 235 , 217.

α-Epoxide from 14 - mp 141-143^{0}C (hexane-CH_2Cl_2) ; [α]$_D$ +55^0 ; ir 1770 cm^{-1} (γ–lactone) ; ^{1}H–nmr δ 3.97 (1H, dd, J= 9.7 and 9.6 Hz, H-6), 3.15 (1H, dd, J= 4.2 and 3.2 Hz, H-2), 2.83 (1H, d, J= 4.2 Hz, H-1), 1.21 (3H,d, J= 6.8 Hz, H-13), 1.00 (3H, d, J= 7.4 Hz, H-15), 0.98 (3H, s, H-14) ; ms (m/z) 250 (M$^+$), 232.

Oxidation of ketones

This was carried out in an identical experimental procedure to the epoxidations of olefins although with a 1:3:9 molar ratio substrate:anhydride:UHP in dichloromethane or 1,2-dichloroethane. Identification of esters or lactones was done by direct comparison with commercially available samples or samples prepared according to literature procedures.[7,11] Data are given for lactones derived from ketones **22**, **27**, and **28**.

ε–Enol lactone from 22 - Purified by flash chromatography with CH_2Cl_2 -hexane 1:1 as eluent. Ir 1740 (ε-lactone), 1660, 1630 cm^{-1} (enol lactone) ; ^{1}H-nmr δ 6.34 (1H, ddd, J= 6.6, 1.4, and 1.3 Hz, -CH=CH-O-), 5.36 (1H, dd, J= 6.6 and 6.3 Hz , -CH=CH-O-), 2.68 (2H, dd, J= 6.2 and 6.6 Hz, -O-CO-CH$_2$-), 2.32 (2H, m, -CH=CH-CH$_2$), 2.07 (2H, m, -CH$_2$); ^{13}C-nmr δ 172.15 (-COO), 139.77 (-O-CH=CH-), 113.13 (-OCH=CH), 32.77 (-CO-CH$_2$-), 24.48 (-CH$_2$-CH=CH-), 23.06 (-CH$_2$-) ; ms (m/z) 112 (M$^+$), 84, 55.

ε- Lactone from (27) - mp 158-160^{0}C (hexane-CH_2Cl_2) ; [α]$_D$ -28.6^0 ; ir 1770 (γ-lactone), 1720 (ε–lactone); ^{1}H-nmr δ 4.86 (1H, m, H-4), 3.84 (1H, dd, J= 9.9 and 9.8 Hz, H-6), 1.54 (3H, d, J= 7.5 Hz, H-15), 1.24 (3H, d, J= 6.8 Hz, H-13), 1.20 (3H, s, H-14) ; ms (m/z) 266 (M$^+$), 251, 222, 178, 163.

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Received, 5ht November, 1992