Tetrahedron Letters,Vol.31,No.3,pp 331-334,1990 0040-4039/90 $3.00 + .00
Printed in Great Britain Pergamon Press plc

DIMETHYLDIOXIRANE EPOXIDATION OF α,β–UNSATURATED KETONES, ACIDS AND ESTERS.

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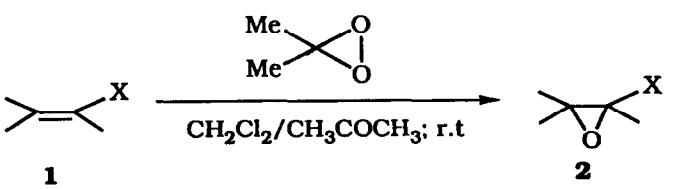
Abstract: The corresponding epoxides were isolated in excellent yields via oxygen transfer by dimethyldioxirane (as acetone solution) .

α,β–Unsaturated[1] ketones and esters are difficult to epoxidize by peracid or metal-catalyzed methods. The use of alkaline hydrogen peroxide is generally preferred, but usually proceeds non-stereospecifically. However, tungstate-catalyzed epoxidations with aqueous hydrogen peroxide allows [2] preparing some epoxides of α,β-unsaturated acids stereospecically under buffered conditions. Similarly, t-butyl hydroperoxide and an alkyllithium in dry tetrahydrofuran [3] was shown to epoxidize esters and sulfones in a stereo- and regiospecific manner.

Dimethyldioxirane (as acetone solution [4]), an efficient oxygen transfer agent [5] permits converting γ-methylene-γ-butyrolactones [6], sugar-derived dihydropyrans [7], silyl enol ethers [8], and aflatoxin B_1 [9] to their expected epoxides , allenes [10] to their dioxides, and polycyclic arenes [11] to their oxides unter strictly neutral conditions. Although this stereospecific oxidant [12] is expected to act as an electrophilic epoxidizing reagent and is indeed as such confirmed[13], in its propensity to oxidize heteroatoms, e.g. sulfides to sulfoxides *versus* sulfoxides to sulfones, using the thianthrene oxide probe [14], dioxiranes show a slight preference for the latter process, which speaks for distinct nucleophilic character. As a matter of fact, the present preliminary results demonstrate that dimethyldioxirane epoxidizes α,β-unsaturated ketones, acids and esters **1** to the epoxides **2** (Eq. 1) in excellent yields (Table 1).

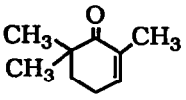
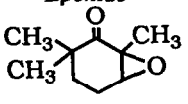
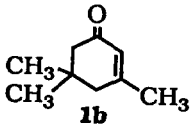
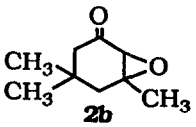
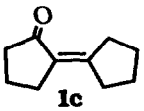
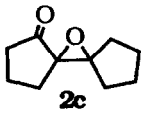
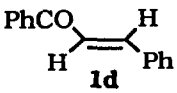
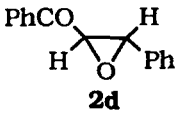
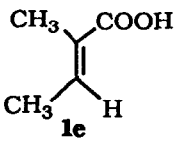
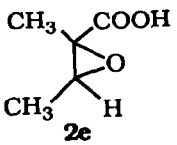
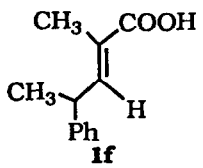
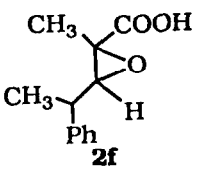
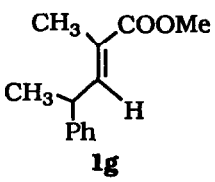
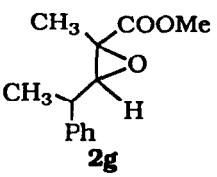
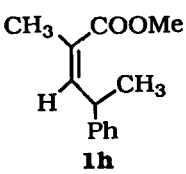
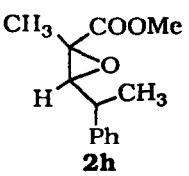


1 **2**

a-d : X = COR; e,f : X = CO_2H; g,h : X = CO_2Me

The general epoxidation procedure consisted of adding rapidly at room temperature a solution of dimethyldioxirane (10-30% molar excess) in acetone (0.08-0.11M), dried over molecular sieves (4 Å) at -20 °C,

Table 1: Dimethydioxirane Epoxidation [a] of α,β-Unsaturated Ketones, Acids and Esters.

Substrate	Time (h)	Epoxide	Yield (%) [b]	Ref. [c]
 **1a**	24	 **2a**	90	15
 **1b**	20	 **2b**	86	16
 **1c**	20	 **2c**	94	17
 **1d**	18	 **2d**	97	18
 **1e**	23	 **2e**	93	19
 **1f**	20	 **2f**	96 (70:30) [d]	20
 **1g**	16	 **2g**	98 (70:30) [d]	21
 **1h**	20	 **2h**	99 (62:38) [d]	22

[a] In CH_2Cl_2/CH_3COCH_3. [b] Yield of isolated pure product. [c] Selected spectral data of the epoxides 2 are given in the Refs. 15-22; IR data were obtained on a Perkin Elmer 1420 instrument, ^1H NMR (250 MHz) and ^{13}C NMR (63 MHz) spectra were run on a Bruker WM 250, referring chemical shifts to Me_4Si. [d] Mixture of diastereomers.

to a stirred solution of the α,β–unsaturated substrates **1** (0.42-1.05 mmol) in absolute CH_2Cl_2 (10 mL). After stirring for ca. 12h, a new quantity of dimethyldioxirane (10-30% molar excess) was added and stirring continued until complete consumption (Table 1) of the starting material. The solvent was removed in vacuo, yielding the epoxides in high purity (NMR).

In summary, contrary to peroxy acids, dimethyldioxirane (as acetone solution) is an efficient oxygen transfer reagent, yielding labile epoxides that are not readily accessible via classical routes. The preparatively useful feature of this report is that the dioxirane reagent epoxidizes even α,β-unsaturated carbonyl compounds when an excess of the reagent, longer reaction times, and elevated temperatures are used.

Acknowledgements: We thank Interox-Chemie GmbH (Munich, F.R.G.) for a generous gift of Curox (potassium peroxomonosulfate). Financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully appreciated.

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15. **2a**: IR (CCl_4): 1710 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 1.02 (s, CH_3), 1.11 (s, CH_3), 1.28-1.38 (m, 1H), 1.40 (s, CH_3), 1.75-2.22 (m, 3H), 3.37-3.38 (m, 1H).-

^{13}C NMR (63 MHz, $CDCl_3$): δ = 16.2, 20.7, 24.8, 25.3, 30.0, 41.7, 57.5, 61.0, 209.7.

16. **2b**: IR (CCl_4): 1730 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 0.92 (s, CH_3), 1.02 (s, CH_3), 1.43 (s, CH_3), 1.68-1.74 (m, 1H), 1.78-1.84 (m, 1H), 2.05-2.11 (m, 1H), 2.59-2.65 (m,1H), 3.05 (br.s, 1H).-

^{13}C NMR (63 MHz, $CDCl_3$): δ = 24.0, 27.8, 30.8, 36.1, 42.8, 48.0, 61.4, 64.3, 207.9.

17. **2c**: IR (CCl_4): 1760 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 1.55-2.01 (m, 9H), 2.06-2.27 (m, 3H), 2.34-2.43 (m, 2H).-

^{13}C NMR (63 MHz, $CDCl_3$): δ = 17.9, 24.9, 25.4, 27.3, 29.5, 31.9, 37.2, 67.9, 76.7, 173.2.

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19. **2e**: IR (CCl_4): 3400, 1715 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 1.38 (d, J = 5.39 Hz, CH_3), 1.53 (s, CH_3), 3.35 (q, J = 5.39 Hz, 1H), 10.06 (br.s, 1H).-

^{13}C NMR (63 MHz, $CDCl_3$): δ = 12.8, 13.2, 57.4, 58.6, 176.7.

20. **2f**: IR (CCl_4): 3400, 1720 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 1.34 and 1.48 (d,J = 7.18 and 6.91Hz, CH_3; minor and major), 1.56 and 1.65 (s, CH_3; major and minor), 2.59-2.76 (m, 1H), 3.28 and 3.33 (d, J = 9.44 and 9.43 Hz, 1H; minor and major), 7.15-7.36 (m, 5H), 9.90 (br.s,1H).-

^{13}C NMR (63 MHz, $CDCl_3$), major: δ = 13.4, 19.3, 38.5, 58.5, 67.1, 126.9, 127.1, 128.9, 141.4, 176.5; minor: δ = 13.0, 16.9, 38.4, 58.1, 67.0, 127.0, 127.2, 128.7, 142.2, 176.4.

21. **2h**: IR (CCl_4): 1745 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 1.35 and 1.50 (d, J = 7.20 and 6.93 Hz, CH_3; minor and major), 1.58 and 1.67 (s, CH_3; major and minor), 2.63-2.76 (m, 1H), 3.27 and 3.31 (d,J=9.63 and 9.51 Hz, 1H; minor and major), 3.69 and 3.72 (s, OCH_3; major and minor), 7.20-7.37(m,5H).- ^{13}C NMR (63 MHz, $CDCl_3$), major: δ = 13.9, 19.3, 38.6, 52.6, 58.7, 67.0, 127.0, 127.2, 128.8, 141.7, 171.6; minor: δ = 13.5, 17.0, 38.5, 52.5, 58.2, 66.7, 126.9, 127.2, 128.6, 142.5, 171.7.

22. **2g**: IR (CCl_4): 1770 cm^{-1}.-

^1H NMR (250 MHz, $CDCl_3$): δ = 1.29 and 1.48 (d, J = 7.16 and 6.88 Hz, CH_3; minor and major), 1.51 and 1.60 (s, CH_3; major and minor), 2.59-2.80 (m,1H), 2.99 and 3.03 (d, J = 2.83 and 2.84 Hz, 1H; major and minor), 3.72 and 3.82 (s, OCH_3; major and minor), 7.11-7.36 (m,5H).- ^{13}C NMR (63 MHz, $CDCl_3$), major: δ = 18.9, 19.4, 38.4, 52.3, 60.5, 69.0, 127.1,127.2, 128.7,141.9,170.4; minor: δ = 16.9, 19.5, 38.3, 52.5, 60.3, 68.7, 126.9, 127.0, 128.6, 142.6, 170.5.

(Received in Germany 9 October 1989)