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EPOXIDATION OF SILYL ENOL ETHERS, PHTHALIDES, AND ENOL ESTERS BY DIMETHYLDIOXIRANE.

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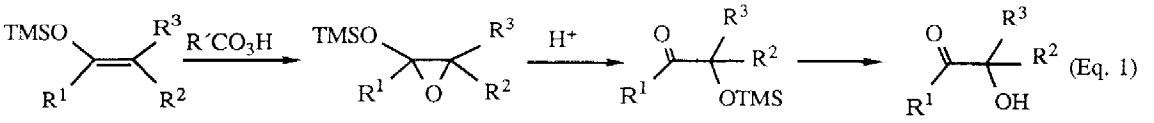
Abstract: The corresponding pure epoxides were isolated in excellent yields, prepared via epoxidation by dimethyldioxirane.

The peracid oxidation of silyl enol ethers **1**, the Rubottom reaction [1], is a widely used method for the preparation of α-hydroxy carbonyl compounds **4** via hydrolysis of the isolable α–trimethylsilyloxy carbonyl derivatives **3**. Rearrangement of the intermediary α-trimethylsilyloxy epoxides **2** has been postulated as the mechanistic course for the formation of these synthetically useful α–hydroxylated carbonyl substrates (Eq. 1).



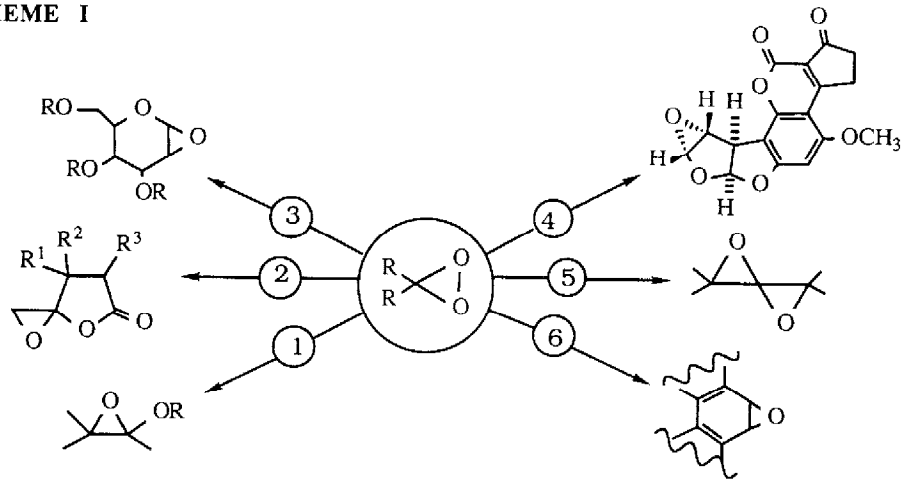
(Eq. 1)

1 **2** **3** **4**

Although examples of such epoxides **2** were previously detected or even isolated [2,3], in one case also an X-ray structure determination was reported [4], only very recently [5] it was shown that epoxidation by dimethyldioxirane constitutes a general method for the synthesis of such labile epoxides; however, no mention was made of their isolation. These preliminary results prompt us to report on the isolation and characterization of the labile α-silyloxy epoxides **2a,b** and the related oxides of the phthalides **5a,b** and enol ester **5c**, all interesting building blocks for organic synthesis.

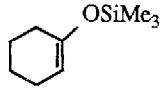
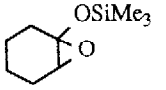
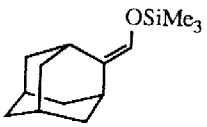
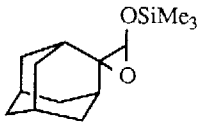
Dioxirane (as ketone solution [6]), an oxidant that is efficient in transferring oxygen, selective in its reactivity, and mild towards the oxidized products [7], was shown (Scheme 1) to convert enol ethers [8] ①, γ-methylene-γ-butyrolactones [9] ②, sugar-derived dihydropyrans [10] ③, and aflatoxin B_1 [11] ④ to their expected epoxides, allenes [12] to their dioxides ⑤, and polycyclic arenes [13] to their oxides ⑥, as portrayed in Scheme I. Indeed, dimethyldioxirane transformed the silyl enol ethers **1a,b** to the corresponding labile α-silyloxy epoxides **2a,b**; the pure products were isolated in high yield (Table 1). Attempts to prepare [3] the epoxide **2a**, using the neutral N-sulfonyloxaziridine, led to rearrangement products.

SCHEME I



The simple and convenient epoxidation procedure consisted of adding rapidly a solution of dimethyldioxirane (10-30% molar excess) in acetone [14] (ca. 0.1-0.12 M), dried over molecular sieves (4Å) at -20 °C, to a cooled (-40 °C), stirred solution of silyl enol ethers **1** (0.67 - 0.80 mmol) in abs. CH_2Cl_2 (10 ml) under N_2. The stirring was continued until complete consumption (Table 1) of the starting material and the solvent removed in vacuum at 0 °C, yielding the new α-silyloxy epoxides **2** in high purity (IR, NMR).

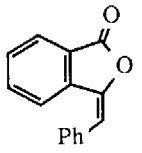
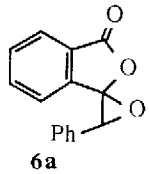
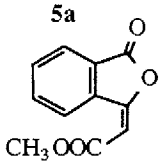
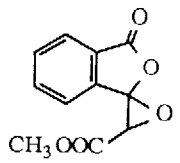
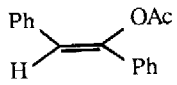
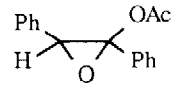
Table 1 *Epoxidation [a] of the Enol Silyl Ethers* ***1a,b*** *to the Epoxides* ***2a,b*** *by Dimethyldioxirane.*

Substrate	Conditions	α-Silyloxy epoxide	Yield(%) [b]	Ref.[c]
 **1a**	- 40 °C, 3h	 **2a**	99	15
 **1b**	-40 °C, 3h	 **2b**	98	16

[a] In CH_2Cl_2/CH_3COCH_3 at -40 °C. [b] Yield of isolated product. [c] Selected spectral data of the α-silyloxy epoxides **2** are given in the Refs. 15 and 16; IR data were obtained on a Perkin Elmer 1420 instrument, ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were run on a Brucker WM 200, referring chemical shifts to Me_4Si.

As an extension of this useful epoxidation, the phthalides **5a,b** and the enol ester **5c** (Table 2) were treated with the dimethyldioxirane reagent. The pure epoxides **6a-c** were also isolated in high yields (Table 2). While the more sensitive α-silyloxy epoxides **2** had to be prepared at subambient temperatures (-40 °C), the epoxidation of the phthalides **5a,b** and the enol ester **5c** needed to be performed [17] at elevated temperature (+ 20 °C). Epoxide **6a** was detected in negligible amounts when the epoxidation of phthalide **5a** was carried at -20 °C.

Table 2 *Epoxidation[a] of Phthalides 5a,b and Enol Ester 5c to their Epoxides 6 by Dimethyldioxirane*

Substrate	Time (h)	Epoxide	Yield (%)[b]	Ref.[c]
 **5a**	4.0	 **6a**	85	18
 **5b**	12.0	 **6b**	93	19
 **5c**	7.0	 **6c**	84	20

[a] In CH_2Cl_2/CH_3COCH_3 at room temperature. [b] Yield of isolated product. [c] Selected spectral data of the epoxides **6** are given in Refs. 18-20; IR data were recorded 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.

Significant was the observation that addition of 1,1,1-trifluoroacetone promoted epoxidation under conditions at which the dimethyldioxirane was ineffective. Presumably oxygen exchange afforded the much more reactive methyl(trifluoromethyl)dioxirane (Mello's dioxirane) [8,21] which subsequently promoted epoxidation of this more sluggish substrate. It is conceivable that a catalytic cycle can be devised in which CF_3COCH_3 may serve as mediator in the oxygen transfer between dimethyldioxirane and less reactive oxygen acceptors.

In contrast to peroxy acids and N-sulfonyloxaziridines, dimethyldioxirane (as acetone solution) is an efficient oxygen transfer reagent, permitting the isolation of sensitive epoxides under extremely mild (neutral) conditions. The new and encouraging feature of the present report is that the dioxirane reagent can be conveniently used at elevated temperature ($\geq 20\ ^oC$) to epoxidize even electron-deficient double bonds [17].

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14. The concentration of the dimethyldioxirane reagent is important ! Using concentrations less than 0.08 M, the α-silyloxy ketones **3** were isolated instead of the desired epoxides **2**.
15. **2a**: IR (CCl_4): 1220, 960, 850 cm^{-1}; ^1H NMR (200 MHz, C_6D_6): δ = 0.29 (s, 9H), 1.02-1.39 (m, 4H), 1.56-1.64 (m, 2H), 1.97-2.12 (m, 2H), 3.11-3.14 (m,1H); ^{13}C NMR (50 MHz, C_6D_6): δ = 1.3, 20.1, 21.0, 25.3, 31.5, 59.8, 82.0.
16. **2b**: IR (CCl_4): 1250, 970, 840 cm^{-1}; ^1H NMR (200 MHz, C_6D_6): δ = 0.26 (s, 9H), 1.32-2.23 (m, 14H), 4.67 (s, 1H); ^{13}C NMR (50 MHz, C_6D_6): δ = 0.20, 27.5, 28.2, 30.7, 34.0, 34.3, 35.1, 35.5, 36.4, 37.0, 68.0, 82.5.
17. Dimethyldioxirane epoxidizes α,β-unsaturated carbonyl compounds when an excess of the reagent and longer reaction times are used; Adam, W. ; Hadjiarapoglou, L.; Nestler, B. *to be published.*
18. **6a**: m.p.: 132-133 °C ($CHCl_3$- pet. ether); IR (CCl_4): 1810 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 4.64 (s, 1H), 7.38-7.94 (m, 9H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 64.3, 90.0, 121.5, 125.7, 127.6, 127.9, 128.4, 128.7*, 129.1, 130.1*, 131.5, 131.8, 134.9, 142.7, 166.7; * extraneous resonances.
19. **6b**: m.p.: 153-155 °C ($CHCl_3$ - pet. ether); IR (CH_2Cl_2): 1800, 1760 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 3.38 (s, CH_3), 4.40 (s, 1H), 7.67-7.84 (m, 3H), 7.92-8.04 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 53.1, 58.1, 87.4, 124.3, 125.8, 128.6, 132.1, 135.1, 139.5, 165.6, 171.9.
20. **6c**: m.p.: 61-62 °C ($CHCl_3$ - pet. ether); IR (CCl_4): 1775 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.90 (s, CH_3), 4.16 (s, 1H), 7.31-7.43 (m, 8H), 7.44-7.52 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.6, 65.6, 85.6, 116.7*, 124.7*, 125.7, 127.0, 127.6*, 128.1, 128.5*, 128.6, 128.7, 129.1, 133.1, 135.5, 168.8; * extraneous resonances.
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