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DIMETHYLDIOXIRANE EPOXIDATION OF ALKENES BEARING TWO ELECTRON DONATING SUBSTITUENTS.

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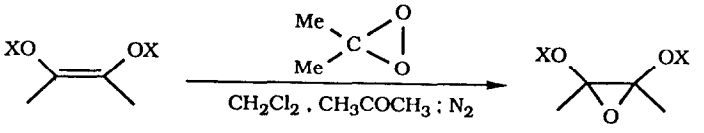
Abstract: Various enol-type alkenes, such as 2,3-dimethylbenzodioxin (**1**), O-tetrabenzyl glycal (3), 1,2-bis(trimethylsilyloxy)cycloalkenes (**9**) were transformed in excellent yields to their labile epoxides by dimethyldioxirane (as acetone solution); the silyl ketene acetal **5** and 2-methyl-3-trimethylsilyloxybenzo[b]furan (7) gave the corresponding epoxide rearrangement products.

Enol ethers [1] and silyl enol ethers [2] are easily oxidized by electrophilic oxygen transfer reagents, e.g. peracids. The resulting epoxides readily undergo acid-catalyzed rearrangement to give the corresponding α-alkoxy or α-silyloxy ketones. Only in limited cases, especially when hindered enol-type alkenes are employed, the labile epoxides can be isolated [1,3].

Dimethyldioxirane [4] (as acetone solution [5]), an efficient and rapidly developing oxidant, performs under strictly neutral conditions. It was shown that this novel epoxidizing agent converts enol ethers [6], 2,3-dimethylbenzofurans [7], silyl enol ethers [8], enol esters and lactones [9], and enol phosphates [10] to their corresponding epoxides, which are difficult to prepare through classical routes.

Recently we demonstrated that dimethyldioxirane also epoxidizes even electron-poor alkenes such as α,β-unsaturated acids, esters and ketones[11]. These epoxidations were extended to β-oxo enol ethers [12] and flavones [13], substrates which possess at the same time electron-donating and electron-accepting substituents.

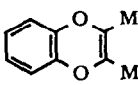
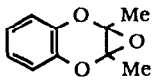
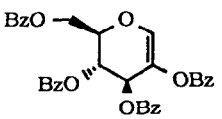
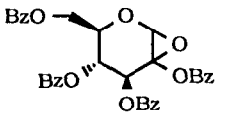
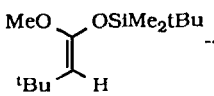
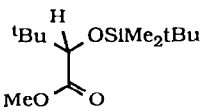
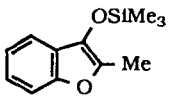
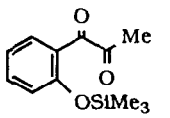
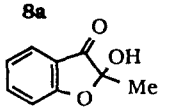
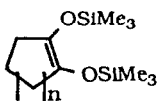
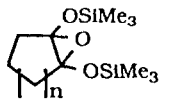
To date little if any work on the epoxidation of the highly reactive alkenes with two electron-donating substituents, particularly alkoxy and silyloxy groups, have been reported [14]. Dimethyldioxirane should be particularly suited in view of its mild nature for such hydrolytically labile substrates and thermally sensitive epoxides derived thereof (Eq. 1). Indeed, as revealed in Table 1, most of these extremely labile epoxides (Entries



(Eq. 1)

1,2,5) can be prepared by dimethyldioxirane epoxidation, isolated, and spectrally characterized. In some cases (Entries 3,4) the epoxides could be inferred through the rearrangement products that were isolated instead.

Table 1 : Oxidation [a] of Olefins with Two Electron-Donating Substituents by Dimethyldioxirane (as Acetone Solution).

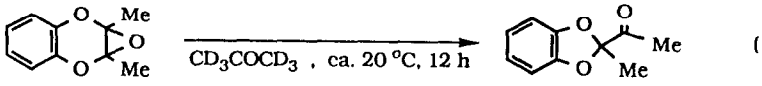
Entry	Substrate	Reaction Conditions	Product	Yield (%) [b]	Ref. [c]
1.	 **1**	-70 °C, 1.0 h -50 °C, 0.5 h -30 °C, 0.5 h	 **2**	ca. 100 [d]	15
2.	 **3**	-20 °C, 2.0 h	 **4**	ca. 100 [d]	16
3.	 **5**	-40 °C, 1.0 h	 **6**	ca. 100 [d]	17
4.	 **7**	-70 °C, 1.0 h -50 °C, 0.5 h -30 °C, 0.5 h	 **8a**  **8b**	72 28	18 19
5.					
	9a, n=1 **9b**, n=2	-30 °C, 3.0 h -30 °C, 3.0 h	**10a**, n=1 **10b**, n=2	97 98	20 21

[a] In CH_2Cl_2 / CH_3COCH_3 under N_2 atmosphere. [b] Yield of isolated pure product after evaporation (distillation) of the solvents but rigorous purification was not possible in view of the labile nature of these epoxides. [c] Selected spectral data of products **2, 4, 6, 8, 10** are given in Refs. 15-21 ; IR data were recorded on a Perkin-Elmer 1420 instrument ; ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were run on a Bruker WM 200, chemical shifts refer to C_6D_6 or CD_3COCD_3. [d] Estimated by ^1H NMR.

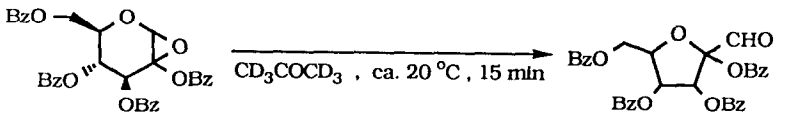
The general epoxidation procedure consisted of adding rapidly a stock solution of dimethyldioxirane (ca. 0.1 M) in acetone, to a stirred, cooled solution of the appropriate substrate in absolute CH_2Cl_2 (10 ml) under a N_2 atmosphere. The stirring was continued until complete consumption of the starting material (cf. Table 1), the solvent and excess dimethyldioxirane removed by distillation (-30 °C / 0.01 Torr or 0 °C / 15 Torr) to afford the pure epoxides or the rearrangement products, as confirmed by IR, ^1H and ^{13}C NMR spectral data.

Furan epoxides constitute a class of unknown compounds of great biological interest, which are postulated as cytotoxic intermediates in the oxidative metabolism [22] .Since the related benzo[b]furan epoxides could very recently be prepared by dimethyldioxirane epoxidation [7], the same procedure was employed for the epoxidation of the 2-methyl-3-trimethylsilyloxybenzo[b]furan (**7**). Unfortunately, only the rearrangement products **8a,b** were isolated in 72 and 28 % relative yields. Attempts to detect the corresponding epoxide by ^1H and ^{13}C NMR failed even at -78 °C.

Although epoxide **2** could be isolated in pure form by distillation of the solvent (-20 °C / 0.01 Torr), when left at ca. 20 °C, it rearranged into the corresponding 2-acetyl-2-methyl-1,3-benzodioxolane (**11**) [23] (Eq.2). Similarly, epoxide **4** was also produced, but it was more labile since at ca. 20 °C it rearranged into the aldehyde **12** already within 15 min (Eq. 3).



2 **11** (Eq. 2)



4 **12** (Eq. 3)

In summary, we have shown that isolated dimethyldioxirane (as acetone solution) is an efficient oxygen transfer agent, which permits the preparation and isolation of sensitive epoxides under mild conditions.

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15. **2**: ^{1}H NMR (200 MHz, CD_3COCD_3, -20 °C): δ = 1.71(s, 6H), 6.86-6.98(m, 4H).- ^{13}C NMR (50 MHz, CD_3COCD_3, -20 °C): δ = 15.8, 84.8, 116.1, 122.5, 138.1.-
16. **4**: ^{1}H NMR (200 MHz, CD_3COCD_3 , -20 °C): δ = 3.46-3.82 (m, 4H), 4.15-4.25 (m, 1H), 4.44-4.87 (m, 7H), 4.99-5.08 (m, 1H), 5.37 (d, J = 0.90 Hz, 1H), 7.17-7.36 (m, 20H) .- ^{13}C NMR (50 MHz, CD_3COCD_3, -20 °C): δ = 65.1, 66.7, 68.7, 71.8, 73.3, 73.6, 78.8, 79.1, 82.0, 126.4, 126.6, 126.7, 127.2, 135.9, 136.8, 136.9, 137.0 .-
17. **6**: b.p.= 100 °C / 0.01 Torr / Kugelrohr .- IR(CCl_4): ν = 2980 cm^{-1}, 1770, 1750, 1270, 1260, 1130, 875, 850.- ^{1}H NMR (200 MHz, C_6D_6 , 20 °C): δ = -0.02 (s, 3H), 0.03 (s, 3H), 0.89 (s, 9H), 0.90 (s, 9H), 3.66 (s, 3H), 3.87 (s, 1H) .- ^{13}C NMR (50 MHz, C_6D_6 , 20 °C): δ = -5.3, -5.0, 18.8, 26.2, 26.3, 35.9, 51.7, 80.1, 173.3.-
18. **8a**: ^{1}H NMR (200 MHz, CD_3COCD_3, -20 °C): δ = 0.34 (s, 9H), 2.41 (s, 3H), 7.1-7.8 (m, 4H).- ^{13}C NMR (50 MHz, CD_3COCD_3, -20 °C): δ = 1.5, 25.6, 119.6, 122.3, 125.2, 130.9, 136.8, 157.3, 195.4, 201.4.-
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20. **10a**: IR (CCl_4): ν = 2990 cm^{-1}, 1500, 1320, 1270, 1255, 1055, 895, 870.- ^{1}H NMR (200 MHz, C_6D_6, 20 °C): δ = 0.23-0.29 (m, 18H), 1.16-1.29 (m, 2H), 1.65-1.94 (m, 4H).- ^{13}C NMR (50 MHz, C_6D_6, 20 °C): δ = 1.6, 18.3, 30.8, 90.8.-
21. **10b**: IR(CCl_4): ν = 2960 cm^{-1},1250, 1220, 1100, 935, 905, 840 .- ^{1}H NMR (200 MHz, C_6D_6 , 20 °C): δ = -0.06-0.02 (m, 18H), 0.88-0.97 (m, 4H), 1.54-1.57 (m, 2H), 1.70-1.74 (m, 2H).- ^{13}C NMR (50 MHz, C_6D_6 , 20 °C): δ = 1.4, 21.4, 32.6, 85.4.-
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