Kurzmitteilungen / Short Communications

Dimethyldioxirane Epoxidation of β-Oxo Enol Ethers

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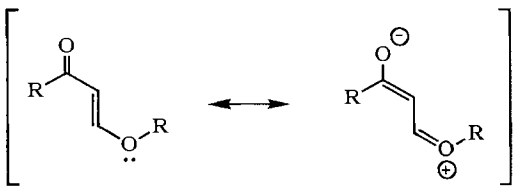
Received May 28, 1990

Key Words: Epoxidation / Dioxirane, dimethyl- / Enol ethers, β-oxo

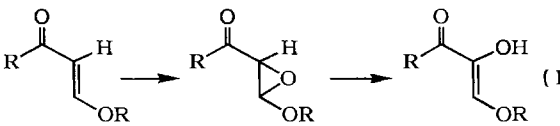
The synthesis of the epoxides **2a–f** by epoxidation of the β-oxo enol ethers 2,2-dimethyl-3(2*H*)-furanone (**1a**), (*Z*)-2-(ethoxymethylene)cyclohexanone (**1b**), and 3-alkoxy-5,5-dimethyl-2-cyclohexenones **1c–f** with dimethyldioxirane is reported. These labile epoxides (stable below 0°C) were isolated and characterized spectroscopically (IR, ^1H, and ^{13}C NMR). Warming up to room temperature led to decomposition to afford complex product mixtures. When the epoxidation of 3-ethoxy-5,5-dimethyl-2-cyclohexenone (**1c**) was conducted above 0°C, the epoxide **2c** afforded the rearrangement product 3-ethoxy-2-hydroxy-5,5-dimethyl-2-cyclohexenone (**3**).

The carbonyl group of a conjugated enone is known to decrease the electron density of the C=C bond. Thus, these olefins are considerably less susceptible towards electrophilic addition than alkyl- or aryl-substituted ones. Due to the low reactivity of these substrates towards electrophilic epoxidizing agents, either no epoxidations take place even under insisting conditions, or side reactions lead to products other than the desired epoxides. A frequently encountered side reaction is the Baeyer-Villiger oxidation[1], commonly performed by peroxy acids, occasionally with hydrogen peroxide. Consequently, α,β-unsaturated carbonyl compounds are usually converted into the corresponding epoxides by other methods, e.g. by oxidation with alkaline hydrogen peroxide, known as the Weitz-Scheffer reaction[2] or by elimination of hydrogen halides from halohydrin precursors[3].

In contrast, an alkoxy or aryloxy substituent increases the electron density of the C=C bond, and consequently enol ethers[4] are easily oxidized by electrophilic oxygen transfer reagents (e.g. peroxy acids). The resulting epoxides readily undergo acid-catalyzed rearrangement to give the corresponding α-alkoxy ketones; thus, such peroxy acid epoxidations have only limited success. In β-oxo enol ethers **1** the carbon–carbon double bond bears both the electron-accepting oxo and the electron-donating alkoxy group in such a way that conjugation results in a relatively unreactive substrate towards electrophilic as well as nucleophilic epoxidizing agents. It is, therefore, not surprising that epoxides of β-oxo enol ethers are hardly known[5], despite the fact that they should serve as useful building blocks in organic synthesis. A further complication is their propensity towards rearrangement, which is expected to afford the 3-alkoxy-2-hydroxy-2-enones **3** [Eq. (1)], a class of reductone-like[6] compounds, which is difficult to obtain. Certainly, the usual epoxidizing agent such as peroxy acids can hardly be used for the transformation **1** → **2**, and it is easily recognized that a successful epoxidation of β-oxo enol ethers **1** require an oxidant which is efficient in transferring oxygen, selective in its reactivity, and mild towards the oxidized product. A powerful and selective oxidant for this purpose, which performs under strictly neutral conditions, is dimethyldioxirane[7] (as acetone solution[8]). Such demanding epoxidations, which lead to sensitive epoxides, were recently achieved on enol ethers[9], silyl enol ethers[10], enol esters[11], α,β-unsaturated ketones, acids, esters, and lactones[12], and allenes[13]. In this communication we report that, indeed, β-oxo enol ethers **1** may be conveniently converted into their hitherto unknown epoxides in high (>95%) yields.



1



1 **2** **3** (Eq. 1)

Results and Discussion

The various β-oxo enol ethers **1a–f** were transformed by dimethyldioxirane quantitatively into the corresponding epoxides **2a–f** [Eq. (1)]. The results are given in Table 1, in which are stated the yields, the temperature, and time of epoxidation. The long reaction times and excess dimethyldioxirane (cf. Table 1) were necessary for achieving total conversion of the relatively unreactive β-oxo enol ethers **1**, especially since low temperatures (−20°C or 0°C) were required for preventing decomposition of the labile epoxides **2**.

Epoxides **2** were stable enough, at least below 0°C, for measuring their spectra, but they decomposed readily above 0°C, which thus precluded their rigorous purification for elemental analyses. In the IR spectra the absorption at $\tilde{\nu}$ = 1630–1600 cm^{-1} of the β-oxo enol ethers **1** disappeared and that at $\tilde{\nu}$ = 1685–1660 cm^{-1} experienced a hypsochromic shift to $\tilde{\nu}$ = 1725–1775 cm^{-1}. The ap-

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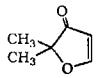
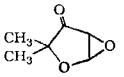
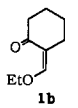
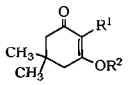
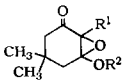
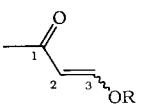
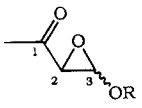
Table 1. Dimethyldioxirane[a] oxidation of β-oxo enol ethers **1a–f** to the epoxides **2a–f**

β-Oxo enol ether	Conditions	Epoxide	Yield (%)[b]
 **1a**	0° C, 23 h[c]	 **2a**	ca. 100[d]
 **1b**	-20° C, 11.5 h	 **2b**	ca. 100
			
1c (R^1=H ; R^2 = Et)	-20° C, 26h	**2c** (R^1=H ; R^2 = Et)	98
1d (R^1=H ; R^2 = n-Bu)	-20° C, 11h	**2d** (R^1=H ; R^2 = n-Bu)	99
1e (R^1=H ; R^2 = Ph)	-20° C, 24h[c]	**2e** (R^1=H ; R^2 = Ph)	97
1f (R^1=Me; R^2 = Et)	-20° C,17h[c]	**2f** (R^1=Me; R^2 = Et)	ca. 100

[a] 0.06–0.09 M in CH_2Cl_2/CH_3COCH_3 under N_2. – [b] Yield of isolated product after removal of the solvent (0°C/15 Torr), but rigorous purification was not possible in view of decomposition of these epoxides above 0°C. – [c] The dimethyldioxirane solution was added in two portions. – [d] 86% conversion, all others complete conversion of the starting material.

Table 2. Characteristic ^{13}C-NMR signals[a] for β-oxo enol ethers **1** and epoxides **2**

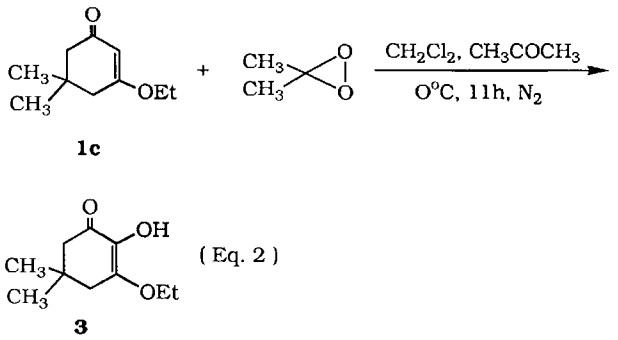



β-Oxo enol ether	^{13}C Shifts[b] Epoxide C-1	C-2	C-3		^{13}C Shifts[c] Epoxide C-1	C-2	C-3
1a	207.7	104.6	176.3	**2a**	207.4	52.7	80.8
1b	199.8	115.0	156.9	**2b**	203.7	64.0	84.3
1c	199.5	101.3	176.1	**2c**	204.8	58.9	88.0
1d	199.6	101.5	176.4	**2d**	204.7	59.0	88.1
1e	194.4	104.9	176.7	**2e**	203.7	58.9	87.6
1f	198.6	113.7	169.5	**2f**	205.2	65.9	89.9

[a] At room temperature (ca. 20°C). – [b] 250 MHz, $CDCl_3$. – [c] 200 MHz, C_6D_6.

pearance of the characteristic epoxide proton signals at δ = 2.9–4.9 and the characteristic ^{13}C-NMR resonance lines (cf. Table 2) of the C-2 and C-3 epoxide carbon atoms at δ = 52–66 and 80–90 confirm the structure assignment of the epoxides **2**. Particularly supportive are the upfield shifts of 40–50 ppm for the C-2 and 70–95 ppm for the C-3 epoxide versus olefin carbon atoms (cf. Table 2).

When the dimethyldioxirane epoxidation of 3-ethoxy-5,5-dimethyl-2-cyclohexenone (**1c**) was carried out at 0°C instead of –20°C, 3-ethoxy-2-hydroxy-5,5-dimethyl-2-cyclohexenone (**3**) was isolated in 99% yield [Eq. (2)] rather than the epoxide **2c**. That enol **3** is indeed the thermal rearrangement product of the epoxide **2c** has been demonstrated beyond doubt by allowing a solution of the authentic epoxide **2c** to warm up in the NMR tube to room temperature. Identical ^{1}H- and ^{13}C-NMR spectra were observed as in the direct oxidation **1c**→**3** at 0°C.



1c **3** (Eq. 2)

Our present results clearly demonstrate that epoxidation of β-oxo enol ethers **1** with dimethyldioxirane permits the formation and isolation of the labile epoxides **2** in high yields. Although epoxides of α-oxo enol ethers are well known[14], epoxides **2** are the first isolated and spectroscopically characterized examples of β-oxo enol ethers, which are now readily and conveniently available for synthetic purposes.

It is surprising that dioxiranes can epoxidize electronically activated as well as deactivated olefins, in this case the relatively reluctant β-oxo enol ethers **1**. Such ambiphilic[15] behavior, i.e. the display of electrophilic as well as nucleophilic character depending on the electron demand of the substrate, is typical for radicals[16], and we suspect that the actual oxygen transfer agent is the dioxyl diradical, derived from cleavage of the peroxide bond in the dioxirane. Theoretical work[17], thermochemical estimates[18], and microwave structural data[19] all imply that peroxide bond homolysis in dioxiranes should be rather facile (activation energy probably less than 15 kcal/mol) and thus accessible at the presented epoxidation conditions.

We thank the *Degussa AG* (Frankfurt, F.R.G.) for a generous gift of Caroate (potassium peroxomonosulfate). Financial support by the *Deutsche Forschungsgemeinschaft* (SFB 347 "Selektive Reaktionen Metall-aktivierter Moleküle"), and the *Fonds der Chemischen Industrie* is gratefully appreciated.

Experimental

Instrumentation and Materials: IR: Perkin-Elmer 1420. – ^{1}H, ^{13}C NMR: Bruker WM 250 (250 MHz), WM 200 (200 MHz); $CDCl_3$ or C_6D_6 as solvent and standard. – All solvents were purified following standard methods. Acetone and water were doubly distilled from EDTA. Potassium peroxomonosulfate, as the triple salt $2\,KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, was used as received from Degussa. 2,2-Dimethyl-3(2*H*)furanone (**1a**) was purchased from Aldrich Chemical Co. The β-oxo enol ethers **1b–f** were prepared following literature procedures[19]. – The isolated dimethyldioxirane was prepared in acetone (0.06–0.09 M), as previously described by us[8b]. The dimethyldioxirane was collected within 10–15 min at ca. 50 Torr, the peroxide content determined by oxidation of methyl phenyl sulfide to its sulfoxide, the latter quantified by ^{1}H NMR.

Epoxidation of β-Oxo Enol Ethers: A solution of dimethyldioxirane in acetone (0.06–0.09 M), which was dried with molecular sieves (4 Å) at –20°C, was added under N_2 rapidly to a cooled, stirred solution of the β-oxo enol ethers **1a–f** (0.65–1.04 mmol) in absol. CH_2Cl_2 (10 ml) (for specific conditions cf. Table 1). The stirring was continued usually until complete consumption of the

β-oxo enol ether **1a–f** (monitored by TLC), the solvent removed in vacuo (0°C, 15 Torr), and the hitherto unknown epoxides **2a–f** obtained in high purity (IR, NMR). Warming up to room temperature caused decomposition, thus preventing rigorous purification of these labile epoxides for elemental analyses.

Epoxide **2a**: 131 mg (ca. 100% yield at 86% conversion) was obtained by following the above procedure at 0°C for 23 h, in which a total of 35 ml (2.17 mmol) of a 0.062 M solution of dimethyldioxirane [added in two portions, the second (20 ml, 1.24 mmol) after 8 h] and 117 mg (1.04 mmol) of 2,2-dimethyl-3(2*H*)-furanone (**1a**) were used. – IR (CCl_4): $\tilde{\nu}$ = 1775 (s) cm^{-1}, 1370 (m), 1215 (m), 1150 (s), 1095 (s), 995 (w), 850 (m). – ^1H NMR (200 MHz, C_6D_6): δ = 1.01 (s, 3H), 1.18 (s, 3H), 2.90 (d, *J* = 1.45 Hz, 1H), 4.83 (d, *J* = 1.45 Hz, 1H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 24.6, 26.3, 52.8, 80.8, 83.1, 207.4.

Epoxide **2b**: 168 mg (ca. 100% yield) was obtained by following the above procedure at −20°C for 11.5 h, in which a total of 20 ml (1.20 mmol) of a 0.06 M solution of dimethyldioxirane and 152 mg (0.99 mmol) of (*Z*)-2-(ethoxymethylene)cyclohexanone (**1b**) were employed. – IR (CCl_4): $\tilde{\nu}$ = 2940 (m) cm^{-1}, 1725 (s), 1445 (m), 1380 (m), 1250 (m), 1220 (m), 1190 (m), 1130 (s), 1100 (s), 1005 (m), 930 (w). – ^1H NMR (200 MHz, C_6D_6): δ = 0.97 (t, *J* = 7.1 Hz, 3H), 1.29–1.53 (m, 4H), 1.70–2.06 (m, 3H), 2.26–2.36 (m, 1H), 3.32–3.56 (m, 2H), 4.37 (d, *J* = 0.8 Hz, 1H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 15.2, 23.7, 24.7, 28.2, 41.7, 64.1, 65.3, 84.3, 203.7.

Epoxide **2c**: 162 mg (98% yield) was obtained by following the above procedure at −20°C for 26 h, in which a total of 15 ml (1.34 mmol) of a 0.089 M solution of dimethyldioxirane and 152 mg (0.90 mmol) of 3-ethoxy-5,5-dimethyl-2-cyclohexenone (**1c**) were used. – IR (CCl_4): $\tilde{\nu}$ = 2980 (m) cm^{-1}, 1730 (s), 1390 (m), 1360 (m), 1280 (m), 1230 (m), 1150 (m), 1080 (m), 980 (w), 940 (w). – ^1H NMR (200 MHz, C_6D_6): δ = 0.62 (s, 3H), 0.68 (s, 3H), 0.93 (t, *J* = 7.0 Hz, 3H), 1.63–1.79 (m, 1H), 1.99–2.07 (m, 2H), 2.34 (d, *J* = 13.3 Hz, 1H), 3.03–3.11 (m, 1H), 3.22–3.31 (m, 1H), 3.49 (s, 1H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 14.5, 27.6, 30.3, 33.2, 42.2, 48.5, 58.9, 59.1, 88.0, 204.8.

Epoxide **2d**: 150 mg (99% yield) was obtained by following the above procedure at −20°C for 11 h, in which a total of 13 ml (1.03 mmol) of a 0.079 M solution of dimethyldioxirane and 140 mg (0.71 mmol) of 3-(butyloxy)-5,5-dimethyl-2-cyclohexenone (**1d**) were used. – IR (CCl_4): $\tilde{\nu}$ = 2980 (s) cm^{-1}, 1730 (s), 1470 (m), 1375 (m), 1350 (m), 1220 (m), 1165 (m), 1145 (m), 1080 (m), 980 (w). – ^1H NMR (200 MHz, C_6D_6): δ = 0.63 (s, 3H), 0.69 (s, 3H), 0.77 (t, *J* = 7.1 Hz, 3H), 1.11–1.42 (m, 4H), 1.63–1.81 (m, 2H), 2.04 (d, *J* = 14.4 Hz, 1H), 2.34 (d, *J* = 13.3 Hz, 1H), 3.02–3.13 (m, 1H), 3.22–3.33 (m, 1H), 3.49 (s, 1H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 13.9, 19.4, 27.7, 30.4, 31.7, 33.2, 42.3, 48.6, 59.0, 63.3, 88.1, 204.7.

Epoxide **2e**: 145 mg (97% yield) were obtained by following the above procedure at −20°C for 24 h, in which a total of 25 ml (1.85 mmol) of a 0.074 M solution of dimethyldioxirane [added in two portions, the second (10 ml, 0.74 mmol) after 12 h] and 140 mg (0.65 mmol) of 5,5-dimethyl-3-phenoxy-2-cyclohexenone (**1e**) were used. – IR (CCl_4): $\tilde{\nu}$ = 2970 (m) cm^{-1}, 1730 (s), 1595 (m), 1375 (m), 1350 (m), 1230 (s), 1170 (m), 1060 (m), 970 (m), 700 (m). – ^1H NMR (200 MHz, C_6D_6): δ = 0.56 (s, 3H), 0.70 (s, 3H), 1.62–1.84 (m, 2H), 2.04–2.32 (m, 2H), 3.52 (s, 1H), 6.81–7.19 (m, 5H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 27.3, 30.0, 33.5, 41.5, 48.3, 58.9, 87.6, 119.7, 124.1, 129.8, 153.8, 203.7.

Epoxide **2f**: 160 mg (ca. 100% yield) were obtained by following the above procedure at −20°C for 17.0 h, in which a total of 22 ml (1.96 mmol) of a 0.089 M solution of dimethyldioxirane [added in two portions, the second (10 ml, 0.89 mmol) after 13 h] and 148 mg (0.81 mmol) of 3-ethoxy-2,5,5-trimethyl-2-cyclohexenone (**1f**) were used. – IR (CCl_4): $\tilde{\nu}$ = 2990 (m) cm^{-1}, 1735 (s), 1460 (m), 1400 (m), 1380 (m), 1360 (m), 1220 (m), 1150 (m), 1110 (m), 1095 (s), 985 (w), 940 (w). – ^1H NMR (200 MHz, C_6D_6): δ = 0.65 (s, 6H), 1.01 (t, *J* = 7.0 Hz, 3H), 1.54 (s, 3H), 1.63–1.76 (m, 2H), 1.98 (d, *J* = 14.1 Hz, 1H), 2.42 (dd, J_1 = 0.74 Hz, J_2 = 13.4 Hz, 3H), 3.36–3.51 (m, 2H). – ^{13}C NMR (50 MHz, C_6D_6): δ = 10.4, 15.4, 27.5, 30.4, 32.4, 41.3, 48.4, 61.2, 65.9, 89.9, 205.2.

3-Ethoxy-2-hydroxy-5,5-dimethyl-2-cyclohexenone (**3**) was obtained in 99% yield from the reaction of 20 ml (1.03 mmol) of a 0.051 M solution of dimethyldioxirane and 128 mg (0.76 mmol) of 3-ethoxy-5,5-dimethyl-2-cyclohexenone (**1c**) at 0°C for 11 h. – IR (CCl_4): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 2960 (m), 1680 (w), 1620 (s), 1370 (m), 1345 (m), 1290 (s), 1230 (m), 1180 (s), 1150 (m), 1050 (m). – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.09 (s, 6H), 1.36 (t, *J* = 7.02 Hz, 2H), 2.32 (s, 2H), 2.39 (s, 2H), 4.36 (q, *J* = 7.02 Hz, 2H), 5.33 (br. s, 1H). – ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.7 (q), 28.4 (q), 32.2 (s), 41.5 (t), 66.2 (t), 131.2 (s), 151.0 (s), 193.9 (s).

CAS Registry Numbers

1a: 35298-48-7 / **1b**: 128445-74-9 / **1c**: 6267-39-6 / **1d**: 128445-75-0 / **1e**: 72035-56-4 / **1f**: 29769-81-1 / **2a**: 128445-76-1 / **2b**: 128470-33-7 / **2c**: 128445-77-2 / **2d**: 128445-78-3 / **2e**: 128445-79-4 / **2f**: 128445-80-7 / **3**: 128445-81-8 / dimethyldioxirane: 74087-85-7

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