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OXIDATIONS BY METHYL TRIFLUOROMETHYL DIOXIRANE. EPOXIDATION OF ENOL ETHERS

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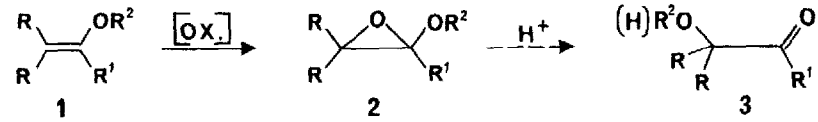
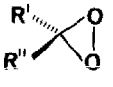
Abstract. Isolated methyl trifluoromethyl dioxirane **4b** has been employed to achieve the rapid, low temperature epoxidation of enol ethers, such as alkoxy(aryl)methylidene adamantanes **1a-e** and methoxy(2-naphthyl)methylidene 2-bornane **1f**, affording the corresponding spirooxiranes in excellent (92-97%) yields.

Recently, spirooxiranes have attracted much attention in our and other laboratories because of their possible involvement as intermediates or side-products in s.e.t. *chain oxygenations*,[1] *as well as oxidation by metal peroxides*,[2] of hindered enol ethers.[3] It is recognized that, when peroxyacid (e.g., MCPBA = *m*-Cl-$C_6H_4CO_3H$) epoxidation procedures are applied to the direct synthesis of alkoxy oxiranes (epoxyethers) **2**,[4] or of strained oxaspiroalkanes,[5,6] one is often faced with only limited (if any) success. This is because the initially formed oxirane **2** can easily undergo acid-catalyzed rearrangement to give α-alkoxy or α-hydroxy ketones **3** (eq.1);[7] it may also *suffer from further oxidation, yielding products which formally derive from cleavage of C=C bonds in* **1**.[2,8]



1 **2** **3**

The key to our search for a suitable epoxidation agent came from the remarkable progresses recorded in the field of dioxirane chemistry. These reactive cyclic peroxides **4** are generated in the reaction of potassium peroxomonosulfate (caroate) with ketones;[9] either *in situ*[10] or as isolated entities,[11] dioxiranes have been shown to be capable of performing selective oxidations on a variety of organic substrates.



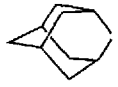
4a,b

a : $R' = R'' = CH_3$
b : $R' = CH_3$, $R'' = CF_3$

Dialkyl dioxiranes can be isolated, as dilute solutions in the parent ketone, by low-temperature distillation from the ketone-caroate reaction mixture.[11] We have recently reported on the isolation of methyl trifluoromethyl dioxirane **4b** (Mello dioxirane).[12] Then, as in the case of **4a**,[13] this new dioxirane could be fully characterized by a combination of spectroscopic techniques (including ^{17}O nmr).[12] It was observed that *in epoxidations, as well as in* other oxidations (e.g., oxidation of alkanes), Mello dioxirane **4b** exhibits a reactivity by far exceeding that already outstanding recorded for **4a**.[12] We now report that this novel reagent is eminently suited to the conversion of *hindered* enol ethers (e.g., **1a-f**) into the corresponding epoxides under quite mild conditions. Pertinent examples are collected in Table 1; most of the spirooxiranes listed therein had never been previously described as isolated pure compounds. The starting materials, i.e. alkoxy(aryl)methylidene adamantanes **1a-e** and methoxy(2-naphthyl)methylidene 2-bornane **1f**, were obtained according to a general procedure devised by Schaap,[3] starting with the appropriate ester ArCOOR and either adamantanone or *dl*-camphor (for **1f**).[14]

TABLE 1. Epoxidation of Enol Ethers by Methyl Trifluoromethyl Dioxirane (**4b**).[a]

1a-f ⟶ 2a-f

Compound	R, R	^{1}R	^{2}R	Reaction time, min	Epoxide[b] yield, %	Ref.[c]
a		Ph	Me	4	94[e]	15
b	//	1-Nap[d]	Me	5	97	16
c	//	2-Nap[d]	Me	5	94	17
d	//	Ph	CH_2Ph	5	93	18
e	//	Ph	Ph	6	92	19
f		2-Nap[d]	Me	5	92[f]	20

[a] In CH_2Cl_2/CF_3COCH_3 at -20°. [b] Isolated yields (unless noted otherwise) at ≥ 96% conversion of the starting material. [c] Selected characteristic data for each of the 3-alkoxy-3-(aryl)spiro[oxirane-2,2'-adamantane]'s **2a-e** and for 3-methoxy-3-(2-naphthyl)spiro[oxirane-2,2'-bornane] **2f** are reported in the Refs. and Notes section (mp's and bp's are given in °C, not corrected); gc/ms and ir data were obtained by using a Hewlett-Packard (GC 5890 A/ MSD 5970 B) and Perkin-Elmer (FT IR 1710) instrument, respectively; ^{1}H-nmr (200 MHz) and ^{13}C-nmr (50.309 MHz) spectra were run on a Varian XL200 spectrometer, referring chemical shifts to Me_4Si. [d] Nap=naphthyl. [e] From gc/ms and ^{1}H-nmr analysis of solutions. [f] As a ca. 50:50 mixture of two diastereomeric *exo*- and *endo*-spirooxiranes, both having the *Z* configuration (cf., ref. 14); noteworthy, epoxidation of **1f** with MCPBA (CH_2Cl_2, -20°) gives a *ca.* 4:1 (*endo/exo*) mixture of the same diastereomers (in some 80% overall yield).

The general epoxidation procedure is attractively simple: first, 0.4 to 0.8 M solutions of dioxirane **4b** in 1,1,1-trifluoro-2-propanone CF_3COCH_3 (bp 22°) are obtained employing the procedure and equipment described;[13] then, to a cool (-20° to -10°) and stirred solution of the enol ether (0.1-0.2 mmol) in dry CH_2Cl_2 (5-10 ml), also containing 0.2-0.3 g of buffer agent Na_2HPO_4 in suspension, an aliquot of a standard[13] solution of **4b** is quickly added, so that the molar ratio of dioxirane to enol ether is *ca.* 1:1. Within 4-6 min the reaction is complete (gc or gc/ms monitoring); the suspended buffer salt is filtered off and the solvent removed *in vacuo*, yielding the almost pure epoxyether. The latter can be further purified by recrystallization and/or by performing column chromatography (silica gel, silanized) at 0-8°C. Just spirooxirane **2a** resisted preliminary attempts of isolation from solution; however, gc/ms and nmr spectra showed that this methoxy oxirane was also formed in high yield (Table 1). By contrast, attempted epoxidation of **1a** with MCPBA in dry CH_2Cl_2 (at 0° and at -20°, 2 to 6 h) gave only α-hydroxy ketone **3a** (in **3**: R,R = adamantylidene, ^{1}R = Ph; yield > 90%),[21] the rearrangement product of **2a**. We notice that, by using dimethyl dioxirane (**4a**) solutions, the epoxidation of enol ethers **1a-g** can also be performed obtaining only slightly lower yields, but requiring significantly longer reaction times. As an example, epoxidation of **1c** by **4a** in CH_2Cl_2-acetone, under conditions practically identical to those given above, required *ca.* 4 h for complete consumption of the enol ether, affording **2c** in 88% yield.

We also find that either dioxirane **4a** or **4b** can be usefully employed in the epoxidation of other enol ethers, e.g. simple and substituted 2,3-dihydropyrans. For instance, upon reaction of **4b** with 2,3-dihydropyran under the given conditions, the corresponding epoxide **5** [4c] could be obtained in high (>92%) yield (nmr analysis of solutions in $CDCl_3/CF_3COCH_3$, at -20°).[22]

Enlightening cases were recently reported showing that dimethyl dioxirane permits the efficient synthesis of sensitive compound such as oxaspiropentanes and 1,4-dioxaspiropentanes, not contaminated by products deriving from unwanted isomerization and/or rearrangements.[5,6] The results reported herein provide yet another case where epoxidation via dioxirane is demonstrated to function as a useful substitute for conventional methods.

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14) All of the enol ethers yielded correct ^1H-, ^{13}C nmr, ir, and ms spectra; **1a** : mp 94-95°; **1b** : mp 102-103°; **1c** : mp 68°; **1d** : mp 49°; **1e** : mp 110°; **1f** : bp 160-163°/0.005 mm; the latter (having the *Z* configuration) was obtained as a single stereoisomer by column chromatography (silica gel) of a ca. 90:10 mixture of *Z/E* stereoisomers (gc/ms, and ^1H nmr analysis).

15) **2a**: ^{1}H nmr (CD_2Cl_2) d 1.2-2.1 (m, 14H), 3.15 (s, 3H), 7.30-7.45 (m, 5H); ^{13}C nmr (CD_2Cl_2) d 26.84, 31.62, 32.32, 32.44, 34.42, 34.72, 35.24, 36.46, 37.20, 52.33 (OCH_3), 80.50 [oxirane ring (=ox. rg) C], 92.50 (ox. rg. C), 127.85, 127.94, 128.36, 129.14; ms m/z (rel.intensity = r.i.) 270 (2, M), 238 (39), 211 (30) [adamantylidene(Ad)>$^{\pm}$Ph)], 105 (100), 91 (21), 77 (45); ir (CH_2Cl_2) 920 cm^{-1} (oxirane stretching = ox. str.).

16) **2b**: mp 110-111° (n-hexane); ^{1}H nmr ($CDCl_3$) d 1.05-2.3 (m, 14H), 3.12 (s, 3H), 7.45-8.40 (m, 7H); ^{13}C nmr ($CDCl_3$) d 27.14-36.92 (Ad, 9 C resonances), 52.50 (OCH_3), 76.31(ox.rg. C), 92.66 (ox. rg. C), 124.83-133.84 (1-Nap, 10 C resonances); ms m/z (r i.) 320 (17.7, M) 288 (13.3), 261 (14.3) (Ad>$^{\pm}$ Nap), 186 (73), 155 (100), 91 (7.6), 79 (8.8); ir(KBr) 1220, 930 cm^{-1} (ox. str.).

17) **2c**: mp 99-100°C (petroleum ether); ^{1}H nmr ($CDCl_3$) d 1.2-2.25 (m, 14H), 3.23 (s, 3H), 7.49-7.95 (m, 7H); ^{13}C nmr ($CDCl_3$) d 26.96-36.71 (Ad 9 C resonances), 52.57 (OCH_3), 76.25 (ox. rg. C), 92.72 (ox. rg. C) 125.42-133.35 (2-Nap, 10 C resonances); ms m/z (r.i.) 320 (16.3, M), 288 (20.3), 261 (25.8), 186 (7.4), 155 (110), 127 (35.7), 91 (8.4), 79 (8.8); ir(KBr) 1261, 933 cm^{-1} (ox. str.), etc.

18) **2d**: mp 83° (ligroin); ^{1}H nmr ($CDCl_3$) d 1.52-2.80 (m, 14H), 4.65 (s, 2H), 7.23-8.00 (m, 10H); ^{13}C nmr ($CDCl_3$) d 26.80-38.74 (Ad, 9 C resonances), 52.11, 64.00 (ox.rg. C), 90.28 (ox. rg. C), 127.08-132.09 (Ph and Ph', 8 C rsns); ms m/z (r i.) 346 (0, M), 255 (2) [M-91($PhCH_2$)], 211 (10), 105 (100), 91 (19), 77 (20); ir(KBr) 1260, 970, 940 cm^{-1} (ox. str.), etc.

19) **2e**: mp 86-87° (n-heptane); ^{1}H nmr ($CDCl_3$) d 1.40-2.32 (m, 14H), 6.95-755 (m, 10H); ^{13}C nmr ($CDCl_3$) d 27.18-36.54 (Ad, 9 C resonances), 65.83 (ox. rg. C), 74.12 (ox. rg. C), 118.05-155.54 (Ph and Ph', 8 C resonances); ms m/z (r. i.) 332 (0, M), 239 (6) [M-93(PhO)] , 227 (21), 211 (58), 105 (100), 91 (22), 77 (47); ir(KBr) 1259, 958, 940 cm^{-1} (ox. str.), etc.

20) *endo*-**2f**: ^{1}H nmr ($CDCl_3$) d 0.87 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.09-1.67 (m, 7H), 3.27 (s, 3H, OCH_3), 7.47-7.90 (m, 7H); ^{13}C nmr ($CDCl_3$) d 11.34 ($^{10'}CH_3$), 19.17 and 19.86 ($^{9'}CH_3$ and $^{8'}CH_3$), 27.56, 30.86, 37.35, 44.36, 49.01, 49.27, 52.29 (OCH_3), 80.36 (ox. rg. C), 89.30 (ox. rg. C), 124.91-133.80 (2-Nap, 10 C resonances); ms m/z (r. i.) 322 (2, M), 211 (5) (2'-bornylidene>$^{\pm}$Nap), 186 (57), 155 (100), 127 (32), 41 (11).

exo-**2f**: ^{1}H nmr ($CDCl_3$) d 0.87 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.09-1.67 (m, 7H), 3.245 (s, 3H), 7.47-7.90 (m, 7H); ^{13}C nmr ($CDCl_3$) d 12.45 ($^{10'}CH_3$), 19.35 and 21.95 ($^{9'}CH_3$ and $^{8'}CH_3$), 28.00, 29.45, 32.40, 36.55, 44.30, 47.50, 52.43, 80.36, 89.30, 124.90-133.75 (2-Nap, 10 C resonances).

21) **3a**: mp 161-163° (EtOH); ^{1}H nmr ($CDCl_3$) d 1.38-2.65 (m, 14H), 2.13 (br. s, 1H), 7.30-8.01 (m, 5H); ^{13}C nmr ($CDCl_3$) d 199.64 (C=O), etc; ir(KBr) 3480, 3450 (OH str.), 1672 cm^{-1} (C=O str.), etc.; anal. Calcd for $C_{17}H_{20}O_2$, C 79.65; H, 7.86 %. Found C, 78.97; H, 8.02 %.

22) **5**: ^{1}H nmr ($CDCl_3/CF_3COCH_3$) d 1.40-2.10 (m, 4H), 3.12 (m, 1H, epoxide C-H), 3.54 (m, 2H), 4.74 (apparent d, J = 2.55 Hz, epoxide C-H); ^{13}C nmr ($CDCl_3/CF_3COCH_3$) d 20.12, 22.10, 51.50, 62.66, 76.90 (^{2}C).

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