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Dioxiranes Are The Active Agents in Ketone-Catalyzed Epoxidations with Oxone

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SUPPORTING INFORMATION

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General Experimental

NMR data were collected on a Varian Unity-400 (400 MHz ^{1}H, 376.3 MHz ^{19}F, 100.6 MHz ^{13}C), or a Varian Unity-500 (500 MHz ^{1}H, 125.8 MHz ^{13}C) in the University of Illinois School of Chemical Sciences Varian/Oxford Instrument Center for Excellence in NMR laboratory. ^{1}H NMR spectra were obtained in deuteriochloroform ($CDCl_3$) with either tetramethylsilane (TMS, $\delta = 0.00$ for ^{1}H) or chloroform ($\delta = 7.26$ for ^{1}H) as an internal reference unless otherwise stated. ^{13}C NMR spectra were proton decoupled and in $CDCl_3$ with either TMS ($\delta = 0.00$ for ^{13}C) or chloroform ($\delta = 77.0$ for ^{13}C) as an internal reference unless otherwise stated. Chemical shifts are reported in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplet), br (broad), app. (apparent) and exch (D_2O exchangeable); coupling constants, *J*, are reported in Hertz (Hz); integration is provided; and assignments of individual resonances are supported in most cases by the following NMR experiments: APT/DEPT, COSY, or HETCOR. Data are presented in the form: chemical shift (multiplicity, coupling constants, integration and assignments where relevant). Infrared spectra (IR) were recorded KBr pellets on a Mattson Galaxy 5020 spectrometer. Peaks are reported in units of cm^{-1} with the following relative intensities: s (strong, 67 - 100 %), m (medium, 34 - 66 %), w (weak, 0 - 33 %) and br (broad). Mass spectra were obtained through the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois. Low-resolution fast atom bombardment (FAB) spectra were

obtained on a VG ZAB-SE spectrometer in magic bullet (3/1, dithiothreitol/dithioerythitol) or 3-nitrobenzyl alcohol. Data are reported in the form *m/z* (intensity relative to base = 100). Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory.

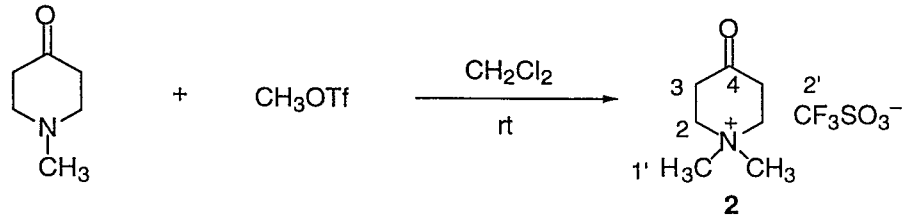
Isotope ratios were obtained by FI on a Finnigan -MAT 731 spectrometer. Each compound labelled with O-18 was analyzed along with the natural abundance material. The O-18 enrichment was obtained by subtracting the O-18 abundance in the natural sample from that in the O-18 enriched sample.

Analytical capillary gas chromatography (GC) was performed using Hewlett Packard 5890 gas chromatographs fitted with a flame ionization detector (H_2 carrier gas, 1 mL/min). The column used was HP–5 50–m cross-linked 5 % phenyl methyl silicone gum phase. The injector temperature was 225 °C, the detector temperature was 300 °C. Retention times (t_R) and integrated ratios were obtained from Hewlett Packard 3393A integrators.

Melting points (mp) were determined in vacuum-sealed capillaries on a Thomas-Hoover capillary melting point apparatus and are corrected.

The solvents used in reactions were reagent grade and distilled from the indicated drying agents under a nitrogen atmosphere: tetrahydrofuran (THF): sodium metal/benzophenone ketyl; acetonitrile, dichloromethane (CH_2Cl_2), P_2O_5. The solvents used for extraction and chromatography were technical grade and distilled from the indicated drying agents: hexane: $CaCl_2$; ethyl acetate (EtOAc): K_2CO_3. All solvents used for recrystallization were distilled. Unless otherwise noted, all reactions were performed in oven- and/or flame-dried glassware under an atmosphere of dry nitrogen or argon.

1,1-Dimethyl-4-oxopiperidinium Trifluoromethanesulfonate (2)



2

A 50-mL, round-bottom flask equipped with a magnetic stir bar was charged with a solution of 1-methyl-4-piperidone (1.13 g, 10 mmol) in CH_2Cl_2 (30 mL). The solution was cooled to 0 °C and MeOTf (1.6 mL, 14.1 mmol, 1.4 equiv) was added via syringe. The cooling bath was removed and the reaction mixture was stirred at rt for 4 h. Removal of solvent in vacuo afforded a white solid which was recrystallized (EtOAc/CH_3CN, 10/1) to provide 2.03 g (73%) of **2** as white plates.

Analytical data for **2**:

mp: 134-5 °C (CH_3CN/EtOAc)

^{1}H NMR: (400 MHz, CD_3CN)

3.70-3.67 (m, 4 H, HC(2)), 3.24 (s, 6 H, HC(1')), 2.72-2.69 (m, 4 H, HC(3)).

^{13}C NMR: (100 MHz, CD_3CN)

200.60 C(4)), 121.88 (q, J = 318, C(2')), 61.88 C(2)), 52.47 C(1')), 35.78 C(3)).

IR: (KBr)

1727 (s), 1724 (s), 1489 (w), 1482 (w), 1454 (w), 1416 (w), 1286 (s), 1279 (s), 1261 (s), 1252 (s), 1222 (m), 1171 (s), 1160 (s), 1157 (s), 1089 (s).

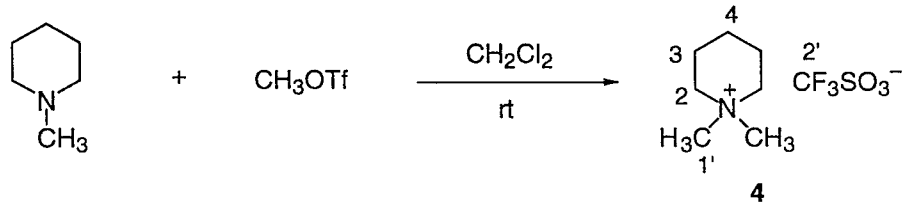
MS: (FAB)

130 (M^++2, 19), 129 (M^++1, 16), 128 (M^+, 100).

Analysis: $C_8H_{14}NF_3O_4S$ (MW 277.31)

Calcd:	C, 34.66;	H, 5.09;	N, 5.05.
Found:	C, 34.55;	H, 5.11;	N, 4.79.

1,1-Dimethylpiperidinium Trifluoromethanesulfonate (4)



4

A 50-mL, round-bottom flask equipped with a magnetic stir bar was charged with a solution of 1-methylpiperidine (1.0 g, 10 mmol) in CH_2Cl_2 (30 mL). The solution was cooled to 0 °C and MeOTf (1.7 mL, 15 mmol, 1.5 equiv) was added via syringe. The cooling bath was removed and the reaction mixture was stirred at rt for 4 h. Removal of solvent in vacuo afforded a white solid which was recrystallized (EtOAc/CH_3CN, 15/1) to provide 2.01 g (76%) of **4** as white plates.

Analytical data for **2**:

mp: 258-9 °C (CH_3CN/EtOAc)

^{1}H NMR: (400 MHz, D_2O)

3.16 (t, J = 6.0, 4 H, HC(2)), 2.92 (s, 6 H, HC(1')), 1.71-1.70 (m, 4 H, HC(3)), 1.47 (qn, J = 6.1, 2 H, HC(4)).

^{13}C NMR: (100 MHz, D_2O)

119.36 (q, J = 316.6, C(2')), 62.59 C(2)), 51.24 C(1')), 20.08 C(4)), 19.54 C(3)).

IR: (KBr)

1486 (m), 1472 (m), 1463 (m), 1270 (s), 1225 (s), 1158 (s), 1146 (s), 1030 (s), 926 (m).

MS: (FAB)

115 (M^++1, 8), 114 (M^+, 100).

Analysis: $C_8H_{16}NF_3O_3S$ (MW 263.28)

Calcd:	C, 36.50;	H, 6.13;	N, 5.32;	F, 21.65.
Found:	C, 36.68;	H, 6.25;	N, 5.19;	F, 21.42.

Determination of O-18 Enrichment in H_2O General Procedure

Dicyclohexylcarbodiimide (Aldrich) was dissolved in dry cyclohexane and filtered to remove the insoluble impurities, and the cyclohexane was evaporated under vacuum. The purified dicyclohexylcarbodiimide (0.206 g, 1.0 mmol, 1 equiv) was dissolved in dry THF (2 mL) and to this was added $H_2{}^{18}O$ (0.21 mL, 11.6 mmol, 11.6 equiv) and camphorsulfonic acid (1 mg, 0.0043 mmol, 0.004 equiv). After being stirred for 1 h, the crystalline DCU was filtered off, washed with THF, dried under vacuum and sent for mass spectrometric analysis of O-18 enrichment.

Epoxidation with H_2O (90% O-18) Representative Procedure

A 10-mL, round-bottom flask equipped with a magnetic stir bar was charged with a solution of promoter **2** (28.0 mg, 0.1 mmol, 1 equiv) in CH_3CN (1.5 mL) and H_2O (90% O-18, 1.0 mL). The mixture was cooled to 0 °C and stirred for 1 h and then EDTA (1 mg), olefin **1** (15.8 mg, 0.10 mmol) were added. The solution was then treated with a solid mixture of Oxone (61.4 mg, 0.10 mmol, 1 equiv) and $NaHCO_3$ (22 mg, 0.26 mmol, 2.6 equiv) in 4 portions each over 2 h. The progress of the reaction was monitored by removing approximately 0.1 mL of the reaction mixture and analyzing the aliquots by GC (HP-5, 180°C, isothermal). After one additional hour at 0 °C the reaction was complete. The reaction mixture was extracted with CH_2Cl_2 (3 x 6 mL) and the aqueous layer was carefully drawn off and saved. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (Et_2O/pentane, 15/1) to afford 16.5 mg (91%) of epoxide **3** which was shown by mass spectrometry to contain 34±1% O-18. The aqueous layer was distilled to give 578 mg of H_2O whose O-18 labeling lavel was determined to be 86±1%.

Control 1: Epoxidation in the Absence of Promoter

Following the representative procedure of epoxidation, a solution of olefin **1** (15.6 mg, 0.10 mmol) and EDTA (1 mg) in CH_3CN (1.5 mL) and H_2O (1.0 mL) was cooled to 0 °C. Then a

solid mixture of Oxone (61.0 mg, 0.10 mmol, 1 equiv) and $NaHCO_3$ (22 mg, 0.26 mmol, 2.6 equiv) was added in 4 portions each over 2 h. After an additional hour, GC analysis (HP-5, 180° C, isothermal) showed only 0.8% conversion. Work up provided 15.0 mg (96%) of recovered olefin **1**.

Control 2: Epoxidation in the Presence of 1,1-Dimethylpiperidinium Triflate (4)

Following the representative procedure of epoxidation, a solution of **4** (31.1 mg, 0.12 mmol, 1 equiv), olefin **1** (18.6 mg, 0.12 mmol) and EDTA (1 mg) in CH_3CN (1.5 mL) and H_2O (1.0 mL) was cooled to 0 °C. Then a solid mixture of Oxone (72.0 mg, 0.12 mmol, 1 equiv) and $NaHCO_3$ (26 mg, 0.32 mmol, 2.6 equiv) was added in 4 portions each over 2 h. After an additional hour GC analysis (HP-5, 180° C, isothermal) showed only 0.7% conversion. Work up provided 17.0 mg (91%) of recovered olefin **1**.

Control 3: Epoxide 3 under the Reaction Conditions

Following the representative procedure of epoxidation, a solution of epoxide **3** (18.5 mg, 0.11 mmol, 1 equiv) and EDTA (1 mg) in CH_3CN (1.5 mL) and H_2O (90% O-18, 1.0 mL) was cooled to 0 °C. Then a solid mixture of Oxone (65.0 mg, 0.11 mmol, 1 equiv) and $NaHCO_3$ (24 mg, 0.29 mmol, 2.6 equiv) was added in 4 portions each over 2 h. After an additional hour, work up provided 17.0 mg (92%) of epoxide **3** which was shown by mass spectromety to contain no O-18 above natural abundance.

Incoporation of O-18 into Promoter 2

Three, flame-dried, round-bottomed flasks equipped with magnetic stir bars were all charged with CH_3CN (0.3 mL) and H_2O (90% O-18, 0.2 mL) at 0 °C. The promoter **2** (8 mg) was added to each flask and the mixtures in the three flasks were stirred for 10 min, 30 min, 60 min, respectively. After the indicated time, the solvents were removed under vacuum at 0 °C and

the solid residues were dried and sent for mass spectrometric analysis. It was found the ^{18}O enrichment was 63% after 10 min, 74% after 30 min and 86% after 60 min.