although several methods are available for the selective lactonization.[14,15] 1,4-Butanediol (**34**) was converted to γ-butyrolactone (**35**) in 66% yield. Six- and seven-membered lactones, **37** and **39**, were obtained by treatment of 1,5-pentanediol (**36**) and 1,6-hexanediol (**38**) with 2 equiv of PCMP, respectively.

A precipitate was gradually formed during the course of the oxidation, and most of the oxidant consumed could be precipitated from the reaction mixture by concentration or by dilution with hexane. A precipitate recovered was subjected to oxidation with hydrogen peroxide to generate PCMP in about 70% yield based on the starting PCMP. The active oxygen contained in the PCMP regenerated was almost the same as that in the original PCMP. Thus, treatment of **13** with the regenerated PCMP gave epoxy alcohol **14** in 90% yield (Table I, run 7).

In summary, the PCMP which can be easily prepared from CMP and hydrogen peroxide was found to be effective for the oxidation of olefins to epoxides and secondary alcohols to ketones as well as α,ω-diols to lactones.

Experimental Section

Melting points were determined with a Yanagimoto capillary melting point apparatus. All melting points are uncorrected. Infrared (IR) spectra were measured with a Jasco Model A-202 spectrometer. ^1H and ^{13}C NMR were measured with JEOL PMX-60 and a Hitachi R-90H spectrometers in $CDCl_3$ by using Me_4Si as the internal standard, respectively. GLC analysis was carried out with a Yanagimoto G1800 apparatus employing a thermal conductivity detector. The yields of products were estimated from the peak areas by using an internal standard technique.

Preparation of Tris(cetylpyridinium) 12-Molybdophosphate $[\pi\text{-}C_5H_5N^+(CH_2)_{15}CH_3]_3(PMo_{12}O_{40})^{3-}$ (CMP). To a solution of cetylpyridinium chloride, $\pi\text{-}C_5H_5N^+(CH_2)_{15}CH_3Cl^-$ (3.0 g, 8.4 mmol), in distilled water (70 cm^3) was added dropwise 12-molybdophosphoric acid, $H_3PMoO_{40}{\cdot}nH_2O$ (5.1 g, ca. 2.8 mmol), in distilled water (10 cm^3) to form immediately a yellow precipitate (CMP). After stirring was continued for 2 h, the resulting precipitate was filtered off, washed several times with distilled water, and dried in vacuo to give CMP in 90–95% yield: IR (KBr) 3400, 2900, 2850, 1630, 1480, 1460, 1060, 950, 870, 790 cm^{-1}. Anal. Calcd for $C_{63}H_{114}N_3Mo_{12}O_{40}P$: C, 27.65; H, 4.21; N, 1.54. Found: C, 27.57; H, 4.54; N, 1.44.

Preparation of PCMP. To aqueous 35% hydrogen peroxide (50 cm^3) was added CMP (5 g, 1.8 mmol), and the mixture was stirred at 40–45 °C for 48 h. The suspended solution was cooled to room temperature to give a fine pale yellow to white precipitate. After centrifuging, the precipitate was washed repeatedly with distilled water and dried in vacuo to give PCMP in 70–75% yield by weight based on the starting CMP. The active oxygen contained in PCMP was estimated to be 2.3–2.5 mmol per gram of PCMP by iodometry: IR (KBr) 3400, 2900, 2850, 1630, 1480, 1460, 1165, 1070, 990, 865, 590, 540 cm^{-1}; ^{13}C NMR ($Me_4Si/CDCl_3$) δ 145.5, 144.2, 128.6, 62.6, 31.6, 29.8, 29.4, 29.2, 26.3, 22.7, 14.1.

General Procedure for Epoxidation of Olefins and Allylic Alcohols. To a stirred solution of PCMP (480 mg) containing about 1 mmol of active oxygen in chloroform (10 cm^3) were added dropwise olefins (1.0 mmol) at room temperature. After removal of the precipitate by centrifugation and filtration, the products were isolated by MPLC (on silica gel hexane:ethyl acetate = 5:1 eluent). The spectral data of the products agreed with those of authentic samples and literature values.[16,17]

Spectral Data for 4:[16] ^{13}C NMR ($Me_4Si/CDCl_3$) δ 134.8 (d), 134.7 (d), 61.7 (d), 60.6 (d), 51.9 (t), 50.9 (d), 46.4 (d), 44.6 (d), 43.9 (d), 31.0 (t); ^1H NMR ($Me_4Si/CDCl_3$) δ 6.15 (d, 2 H), 3.17 (t, 1 H), 3.00 (d, 1 H), 2.82 (m, 2 H), 2.55 (m, 1 H), 1.85 (q, 1 H), 1.55 (m, 2 H), 1.30 (d, 1 H), 1.22 (t, 1 H); IR (NaCl) 3045, 2980, 2900, 1460, 840, 760 cm^{-1}.

Spectral Data for 5:[9] ^{13}C NMR ($Me_4Si/CDCl_3$) δ 132.0 (d), 129.4 (d), 53.3 (d), 50.9 (d), 49.1 (d), 41.8 (d), 39.8 (d), 38.5 (d), 31.4 (t), 29.0 (t); ^1H NMR ($Me_4Si/CDCl_3$) δ 5.65 (m, 2 H), 3.04 (d, 2 H), 2.76 (d, 2 H), 2.47 (m, 2 H), 2.27 (m, 2 H), 1.40 (d, 1 H), 0.78 (d, 1 H); IR (NaCl) 3150, 2960, 1720, 1450, 1370, 1220, 850, 708 cm^{-1}.

Spectral Data for 6:[17] ^{13}C NMR ($Me_4Si/CDCl_3$) δ 61.6 (d), 58.5 (d), 48.8 (d), 48.6 (d), 48.4 (d), 44.6 (d), 39.9 (d), 39.1 (d), 29.6 (t), 26.9 (t); ^1H NMR ($Me_4Si/CDCl_3$) δ 3.60–3.30 (m, 2 H), 3.18 (t, 2 H), 2.80–2.33 (m, 4 H), 1.97–1.60 (t, 2 H), 1.60–1.16 (t, 1 H), 0.92 (t, 1 H); IR (NaCl) 2950, 1450, 1390, 1220, 850 cm^{-1}.

General Procedure for Oxidation of Alcohols and Diols. To a stirred solution of PCMP (480 mg) in benzene (20 cm^3) were added dropwise alcohols or diols (1.0 mmol), and then the mixture was stirred under reflux for 2–6 h. The isolation and identification of products were carried out in a manner similar to that described above.

Spectral Data for 29: ^{13}C NMR ($Me_4Si/CDCl_3$) δ 214.7 (s), 62.6 (t), 55.4 (d), 44.9 (t), 21.4 (t), 16.8 (t), 13.7 (q), 11.7 (q); ^1H NMR ($Me_4Si/CDCl_3$) δ 3.66 (d, 2 H), 3.54 (s, 1 H), 2.82–2.20 (m, 1 H), 2.43 (t, 2 H), 1.70–1.16 (m, 4 H), 0.89 (t, 3 H), 0.86 (t, 3 H); IR (NaCl) 3450, 2925, 1700, 1455, 1370, 1030 cm^{-1}.

Spectral Data for 31: ^{13}C NMR ($Me_4Si/CDCl_3$) δ 221.2 (s), 69.3 (t), 49.6 (s), 34.5 (d), 21.1 (q), 19.8 (q); ^1H NMR ($Me_4Si/CDCl_3$) δ 3.50 (s, 2 H), 3.26–2.82 (m, 1 H), 2.58 (s, 1 H), 1.17 (s, 6 H), 1.05 (d, 6 H); IR (NaCl) 3450, 2950, 1685, 1460, 1370, 1020 cm^{-1}.

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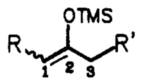
Use of Difference NOE Experiments To Assign the Geometry of Trimethylsilyl Enol Ethers

Thomas H. Keller, Edward G. Neeland, and Larry Weiler*

Department of Chemistry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1Y6

Received August 22, 1986

During the course of our investigations on 14-membered ring keto lactones, we synthesized a number of trimethylsilyl (Me_3Si) enol ether derivatives of the ketone carbonyl. The most widely used method for assigning the geometry of trimethylsilyl enol ethers is ^{13}C NMR spectroscopy. Heathcock et al. have demonstrated that the allylic carbon 3 (see **A**) of an *E* trimethylsilyl enol ether resonates 5–6 ppm upfield from the *Z* isomer.[1]



A

However, this method suffers from two shortcomings: First, both isomers must be available to assign the geometry with confidence.[2] Second, in highly functionalized molecules, it can be challenging to identify the allylic carbon of interest. Furthermore, Friedrich et al. have prepared both trimethylsilyl enol ethers of cyclodecanone and their ^{13}C NMR spectra appear to violate Heathcock's generalization.[3]

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[1] Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

[2] Barillier, D.; Strobel, M. P.; Morin, L.; Paquer, D. *Tetrahedron* **1983**, *39*, 767.

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0022-3263/87/1952-1870$01.50/0

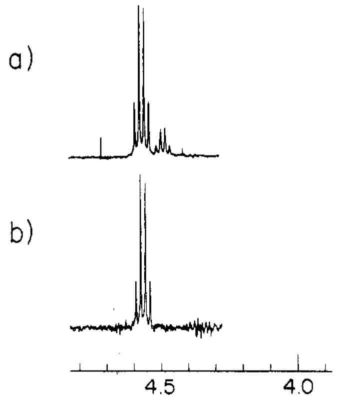
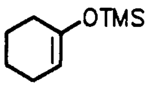


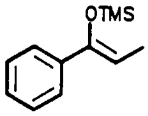
Figure 1. (a) ^{1}H NMR spectrum (400 MHz) of the vinyl protons of a 4:1 mixture of **3a** and **3b**. (b) Difference NOE spectrum obtained by irradiation of the Me$_3$Si signals at δ 0.14 in the mixture.

The nuclear Overhauser effect (NOE) has been used successfully to uniquely determine the geometries of methyl enol ethers.[4] We now report the application of difference NOE's in the assignment of the geometry of silyl enol ethers. Analysis of molecular models of an E trimethylsilyl enol ether such as **1** indicates that the vinylic and silyl methyl protons overlap at closest approach and are 2–3 Å apart at the maximum. These interatomic distances are sufficiently close that irradiation of either set of protons should exhibit an NOE enhancement[5] in the other, thereby demonstrating the E double-bond geometry.

To test this hypothesis, we prepared the trimethylsilyl enol ethers **1** and **2** of cyclohexanone and propiophenone.[1,6]



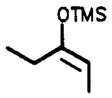
1



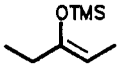
2

Separate irradiation of the silyl methyl protons in each isomer led to the selective enhancement of protons syn to the Me$_3$Si protons in the difference NOE experiment.[7] For the enol either **1**, only the vinylic and the allylic C-6 protons showed enhanced NOE's. For **2**, the ortho aromatic protons and the vinyl methyl protons were enhanced.

A 4:1 mixture, by ^{1}H NMR, of the E and Z isomers of 3-[(trimethylsilyl)oxy]-2-pentene (**3a**, **3b**)[1] provided an even more convincing example of the usefulness of difference NOE's in the assignment of trimethylsilyl enol ether geometries. The NMR spectrum of the vinyl protons in the mixture is shown in Figure 1a. The two quartets are readily visible at δ 4.50 and 4.58—with the major isomer at lower field. The simultaneous irradiation of the silyl methyl protons of both isomers led to exclusive enhancement of the vinylic quartet of the major isomer (Figure 1b), which must be the E isomer **3a**.

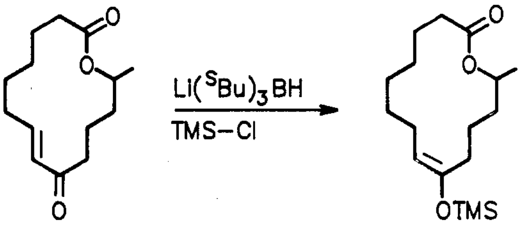


3a



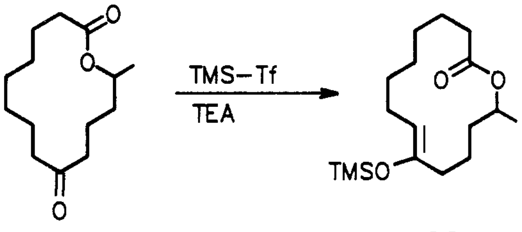
3b

The application of this difference NOE procedure to the macrocyclic trimethylsilyl enol ethers **6a** and **6b** gave unambiguous and quick results, subsequently confirmed by ^{13}C NMR studies on both isomers. The E isomer **6a** was produced by a 1,4-reduction of the α,β-unsaturated ketone **4** with lithium tri-*sec*-butylborohydride followed by trapping with trimethylsilyl chloride (Me$_3$SiCl); E:Z = 97:3. The Z trimethylsilyl enol ether **6b** was prepared by treating the saturated ketone **5** with trimethylsilyl triflate and triethylamine;[8] E:Z = 6:94.[9] On irradiation of the Me$_3$Si protons at δ 0.16 in **6a**, only the vinyl signal at δ 4.45 is enhanced, whereas irradiation of the Me$_3$Si protons at δ 0.15 in **6b** gave enhanced NOE's in the signals at δ 2.05 and 2.25 and no enhancement of the vinyl signal at δ 4.43. These results clearly proved that isomer **6a** had the E geometry and that **6b** had the Z geometry.[10]



4

6a



5

6b

Finally, we reexamined the NMR data for the [(trimethylsilyl)oxy]cyclodecenes. There are conflicting data in the original report,[3] and these compounds may be exceptions to Heathcock's rule. On treatment with refluxing TEA/Me$_3$SiCl,[11] cyclodecanone gave two trimethylsilyl enol ethers in a ratio of 95:5. From a difference NOE, the major isomer was proven to have the E geometry. From the known allylic carbon resonances of both isomers, the ^{13}C NMR showed the major compound did not violate Heathcock's rules for distinguishing between the E and Z isomers of trimethylsilyl enol ethers.

Experimental Section

The ^{1}H NMR spectra were recorded on a Bruker WH-400 spectrometer with an Aspect 2000 data system. The ^{13}C NMR spectra were obtained on a Varian XL-300 spectrometer. Difference NOE experiments were performed as follows. A set of eight scans was accumulated and stored while irradiating (DP = 35L) at 30 ppm (off resonance). The irradiation frequency was then centered on the signal due to the Me$_3$Si protons and a further

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(4) (a) Mersh, J. D.; Sanders, J. K. M. *Tetrahedron Lett.* **1981**, *22*, 4029. (b) Schilling, G.; Klosterhalfen, B. *Org. Magn. Reson.* **1979**, *12*, 605. (c) Huet, J.; Fabre, O.; Zimmerman, D. *Tetrahedron* **1981**, *37*, 3739.

(5) Bell, R. A.; Saunders, J. K. *Can. J. Chem.* **1970**, *48*, 1114.

(6) Propiophenone upon treatment with LDA/Me$_3$SiCl gives mainly the Z trimethylsilyl enol ether.

(7) (a) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703. (b) Gupta, R. K.; Koenig, S. H.; Redfield, A. G. *J. Magn. Reson.* **1972**, *7*, 66.

(8) Emde, H.; Gotz, A.; Hofmann, K.; Simchen, G. *Liebigs Ann. Chem.* **1981**, 1634.

(9) A discussion of these results will be published subsequently.

(10) The major isomer from treating **5** with Me$_3$SiOTf/TEA was the $\Delta^{8,9}$ isomer by comparison with the minor isomer from the 1,4-reduction of **4**.

(11) House, H. O.; Czuba, L. J.; Gall, M.; Olmstaed, H. O. *J. Org. Chem.* **1969**, *34*, 2324.

eight scans stored (on resonance). After approximately 100 cycles of this acquisition sequence, two 16K data blocks of on-resonance and off-resonance spectra resulted. Subtraction of the 16K data blocks produced the difference NOE spectrum. $CDCl_3$ stored over K_2CO_3 was used in the initial NMR experiments, but hydrolysis of some of the enol ethers was observed and C_6D_6 was found to be a more suitable solvent. The NMR spectra were calibrated vs. $CHCl_3$ at δ 7.24 or C_6D_6 at δ 7.15.

The trimethylsilyl enol ethers **1**, **2**, **3a**, and **3b** were prepared according to published procedures (see above). All reactions were carried out in flame-dried glassware under a N_2 atmosphere. Ratios of enol ethers were determined by capillary GC on a 12-m SE-30 or Carbowax column.

(*E*)-9-[(Trimethylsilyl)oxy]-8-tetradecen-13-olide (6a). The enone **4** (50 mg, 0.21 mmol) was dissolved in 5 mL of THF and the resultant mixture cooled to −78 °C. Lithium tri-*sec*-butylborohydride (0.21 mL, 0.21 mmol) was then injected in one portion. After being stirred at −78 °C for 15 min, a filtered mixture of Me_3SiCl (0.053 mL, 0.42 mmol) and Et_3N (0.030 mL, 0.21 mmol) in 1 mL of THF was added. The reaction mixture was allowed to warm to room temperature, evaporated, and flash chromatographed on silica gel, eluting with hexane–ethyl acetate (9:1, v/v). The appropriate fractions were evaporated to afford 33 mg of a 97:3 mixture of **6a** and **6b** and 29 mg of the 1,2-reduction products.

6a: ^1H NMR (400 MHz, $CDCl_3$) δ 0.18 (s, 9 H), 1.25 (d, 3 H, J = 7 Hz), 1.30–1.75 (m, 13 H), 1.85–2.05 (m, 2 H), 2.15–2.50 (m, 3 H), 4.48 (dd, 1 H, J = 5.0, 11.2 Hz), 4.93 (m, 1 H, J = 3.5, 7, 10.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.41 (q), 20.26 (q), 22.57 (t), 24.44 (t), 25.49 (t), 25.54 (t), 25.58 (t), 26.16 (t), 26.87 (t), 28.17 (t), 30.56 (t), 35.21 (t), 35.81 (t), 69.23 (d), 107.42 (d), 151.97 (s), 173.69 (s); MS, M^+ = 312.2119, calcd for $C_{17}H_{32}O_3Si$ 312.2120.

(*Z*)-9-[(Trimethylsilyl)oxy]-8-tetradecen-13-olide (6b). Trimethylsilyl triflate (93.9 mg, 0.42 mmol) was added dropwise to a solution of ketone **5** (100 mg, 0.42 mmol) and Et_3N (34 mg, 0.33 mmol) in 5 mL of dry ether at 0 °C. The reaction mixture was stirred overnight at room temperature and then diluted with ether, washed with ice-cold aqueous NH_4Cl, dried ($MgSO_4$), and filtered, and the solvent was evaporated. The crude product was filtered through a short silica gel column to yield 97 mg (94%) of four isomeric silyl enol ethers in a ratio of 85:5:4:6 (**6b**:**6a**:**6c**:**6d**).[12]

6b: ^1H NMR (400 MHz, $CDCl_3$) δ 0.15 (s, 9 H), 1.17 (d, 3 H, J = 6.5 Hz), 1.18–2.10 (m, 16 H), 2.25 (m, 2 H), 4.40 (t, 1 H, J = 8 Hz), 5.05 (m, 1 H, J = 3.5, 6.5, 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.63 (q), 13.67 (q), 21.0 (t), 24.47 (t), 24.67 (t), 27.31 (t), 28.40 (t), 28.62 (t), 33.30 (t), 34.36 (t), 34.69 (t), 69.23 (d), 109.65 (d), 149.76 (s), 173.87 (s); MS, M^+ = 312.2119, calcd for $C_{17}H_{32}O_3Si$ 312.2120.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada for financial support of this work.

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[12] Isomers **6c** and **6d** were the $\Delta^{9,10}$ silyl enol ethers.

3,3-Difluorocyclobutene. Synthesis and Reaction with Diazomethane

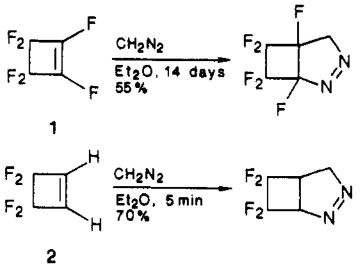
William R. Dolbier, Jr.,* and Dheya M. Al-Fekri[1]

Department of Chemistry, University of Florida, Gainesville, Florida 32611

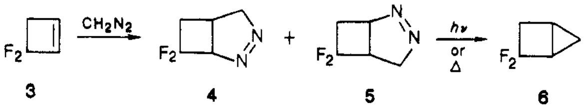
Received August 18, 1986

Recently, Chambers and co-workers completed a systematic study of the effects of fluorine and perfluoroalkyl substituents on the reactivity and regiochemistry of alkenes in their reactions with diazomethane.[2] From their results, they concluded that the reactivity of such alkenes increases with increasing presence of perfluoroalkyl groups as follows: $(R_F)_2C{=}C(R_F)_2 \gg (R_F)_2C{=}CFR_F \gg (R_F)_2C{=}CF_2$, $R_FCF{=}CFR_F$, and $CF_3CH{=}CHCF_3 > CF_3CF{=}CHCF_3 \gg CF_3CF{=}CFCF_3$

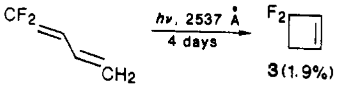
While perfluoroalkenes of the type $R_FCF{=}CFR_F$, including perfluorocyclohexene, were found to be essentially unreactive, perfluorocyclopentene and perfluorocyclobutene (**1**) underwent reaction, albeit reluctantly. In an earlier study,[3] we found that 3,3,4,4-tetrafluorocyclobutene (**2**) as expected from the Chambers study was considerably more reactive than **1**, providing further evidence that *vinyl* fluorine substituents are not enhancing to the dipolarophilicity of olefins.



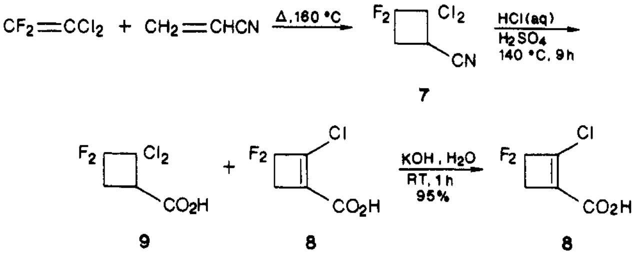
We were interested in the unsymmetrically fluorine-substituted pyrazolines **4** and **5** in the hope that they might act as precursors to 2,2-difluorobicyclopentane (**6**).



Therefore, a synthesis of 3,3-difluorocyclobutene (**3**) was required. Initially, a photochemical scheme involving the photolysis of 1,1-difluoro-1,3-butadiene was envisaged.



Indeed, small amounts of the desired product could be obtained, but the method was deemed inappropriate for synthesis of gram quantitites of **3**. Our method of choice for the synthesis of **3** began with the regiospecific [2 + 2] cycloaddition of 1,1-dichloro-2,2-difluoroethylene with acrylonitrile, which proceeded almost quantitatively.[4]



Acidic hydrolysis of the adduct **7** led to a mixture of carboxylic acid products comprised largely of cyclobutene **8**, plus some **9**. The crude mixture was converted cleanly to 2-chloro-3,3-difluorocyclobutene carboxylic acid (**8**) by treatment with base.

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[1] Taken from the Ph.D. Dissertation of D.M.A.-F., University of Florida, 1985.

[2] Bryce, M. R.; Chambers R. D.; Taylor, G. *J. Chem. Soc., Perkin Trans. 1* **1984**, 509.

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