Mechanistic Aspects of Oxygen Transfer by *gem*-Dialkylperoxonium Ions

A. J. Bloodworth* and T. Melvin

Department of Chemistry, University College London, 20 Gordon Street, London WC1H OAJ, U.K.

John C. Mitchell*

Department of Chemistry, City of London Polytechnic, 31 Jewry Street, London EC3N 2EY, U.K.

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Monocyclic *gem*-dialkylperoxonium ion **2** has been generated from the reaction of 1-bromo-4-hydroperoxy-4-methylpentane (**1**) with silver tetrafluoroborate or trifluoroacetate, and related bicyclic ion **4** has been formed from the reaction of 5-hydroperoxycyclooctene (**3**) with *N*-bromosuccinimide. These species have been shown to oxidize efficiently both dialkyl sulfoxides and methyl phenyl sulfide. Reaction with thianthrene 5-oxide afforded X_{Nu} values of 0.10 for **2** and 0.72 for **4**, while competition reactions with $(p\text{-}XC_6H_4)_2SO$ (X = Me, H, F, and Cl) yielded Hammett ρ values (versus σ) of -0.83 ± 0.11 and -1.77 ± 0.58. These results indicate that *gem*-dialkylperoxonium ion salts, $R^1R^2O^+\text{–}OH,X^-$, are electrophilic oxygen transfer reagents, tunable to some extent by choice of R^1, R^2, and X, but provide no evidence of deprotonation to the corresponding dioxygen ylide under the conditions studied.

Oxygen atom transfer reactions are of wide interest to both the chemical and biological communities. Recently, attention has been focused on metal-free, peroxide-containing reagents which are believed to transfer oxygen by heterolytic mechanisms, for example, (i) carbonyl oxides (formed in the ozonolysis of alkenes or by the photooxidation of diazo compounds),[1] (ii) perepoxides (formed by singlet oxygenation of alkenes),[2] (iii) dioxiranes,[3] and (iv) models for the activity of flavin monooxygenase enzymes[4] (including α-azohydroperoxides).[5]

In recent communications,[6-8] we presented evidence for the existence and oxygen transfer ability of a further class of such peroxy reagents, the *gem*-dialkylperoxonium ions, $R^1R^2O^+\text{–}OH$. (We have introduced the term *gem* to differentiate these dialkylperoxonium ions from the isomeric *vic* species $HR^1O^+\text{–}OR^2$.) Our results at that time gave a clear demonstration of oxygen atom transfer to both sulfides and sulfoxides, but little could be said about the nucleophilic versus electrophilic character, and hence selectivity, of the new species.[8,9]

In this paper we give full details of our previous work, describe two separate attempts to characterize mechanistically the oxygen atom transfer reactions between *gem*-dialkylperoxonium ions and sulfur-centered substrates, and compare the selectivity of our reagents with other reported oxygen atom transfer species.

Results and Discussion

Evidence for *gem*-Dialkylperoxonium Ions. As previously described,[8] *gem*-dialkylperoxonium ion **2** was generated by treatment of 1-bromo-4-hydroperoxy-4-methylpentane (**1**) with either silver tetrafluoroborate or silver trifluoroacetate; and *gem*-dialkylperoxonium ions **4a** and **4b** were generated by reaction of 5-hydroperoxycyclooctene (**3**) with *N*-bromosuccinimide (Scheme I). The isomeric ions **4a** and **4b** were formed in a ratio of about 3:1 and exhibited parallel chemistry.[7a,b] In the remainder of this paper, we will refer to this mixture as ion **4** and will use only the major component to represent this mixture. It seems reasonable to assume that there are no major mechanistic differences between the two species, but it should be remembered that the results presented herein are for the mixture.

In the absence of any added oxygen atom trap, peroxonium ion **2** quantitatively afforded cyclic peroxide 3,3-dimethyl-1,2-dioxane by rearrangement and deprotonation. In contrast, peroxonium ion **4** transferred oxygen to the associated succinimide ion, and equimolar amounts of *N*-hydroxysuccinimide and bicyclic ether were produced (Scheme II).

When a sulfur-containing substrate was introduced into each reaction mixture, the fate of the intermediate was dramatically altered. For peroxonium ion **2**, incorporation of methyl phenyl sulfoxide completely suppressed the formation of cyclic peroxide. Instead, cyclic ether 1,1-dimethyltetrahydrofuran was produced together with an equimolar amount of methyl phenyl sulfone (Scheme III). Treatment of the sulfoxide with a mixture of bromo hydroperoxide **1** and trifluoroacetic acid under comparable conditions produced no appreciable amount of sulfone, thus ruling out protonated hydroperoxide as the active oxidant. The *exact* correlation between the yield of cyclic ether and that of sulfone, and the evidence presented previously[6,10] for the parallel formation of a trialkylperoxonium ion analogous to **2**, provide a powerful case that ion **2** is the oxygen transfer reagent in this system (Scheme III).

For peroxonium ion **4**, incorporation of methyl phenyl sulfide completely suppressed the formation of *N*-hydroxysuccinimide, giving instead equimolar amounts of methyl phenyl sulfoxide and succinimide (Scheme IV). Neither starting hydroperoxide **3** nor *N*-hydroxysuccinimide oxidized the sulfide under the same conditions.[11]

(1) (a) Sawaki, Y.; Kato, H.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *103*, 3832. (b) Adam, W.; Haas, W.; Sieker, G. *J. Am. Chem. Soc.* **1984**, *106*, 5020. (c) Ando, W.; Miyazak, H.; Kohmoto, S. *Tetrahedron Lett.* **1979**, 1317.

(2) Schaap, A. P.; Recher, S. G.; Faler, G. R.; Villasenor, S. R. *J. Am. Chem. Soc.* **1983**, *105*, 1691.

(3) Murray, R. W.; Jeyaraman, R.; Pillay, M. K. *J. Org. Chem.* **1987**, *52*, 746.

(4) (a) Branchaud, B. P.; Walsh, C. T. *J. Am. Chem. Soc.* **1985**, *107*, 2153. (b) Oae, S.; Asada, K.; Yoshimura, T. *Tetrahedron Lett.* **1983**, *24*, 1265. (c) Ball, S.; Bruice, T. C. *J. Am. Chem. Soc.* **1979**, *101*, 4017.

(5) Baumstark, A. L. *Bioorg. Chem.* **1986**, *14*, 326.

(6) Porter, N. A.; Mitchell, J. C. *Tetrahedron Lett.* **1983**, *24*, 543.

(7) (a) Bloodworth, A. J.; Courtneidge, J. L.; Eggelte, H. J. *J. Chem. Soc., Chem. Commun.* **1983**, 1267. (b) Courtneidge, J. L. Ph.D. Dissertation, University of London, 1982.

(8) Bloodworth, A. J.; Melvin, T.; Mitchell, J. C. *J. Org. Chem.* **1986**, *51*, 2612.

(9) DiFuria, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853.

(10) Mitchell, J. C.; Heaton, S.; Porter, N. A. *Tetrahedron Lett.* **1984**, *25*, 3769.

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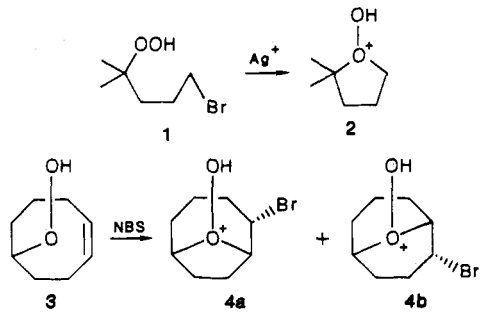
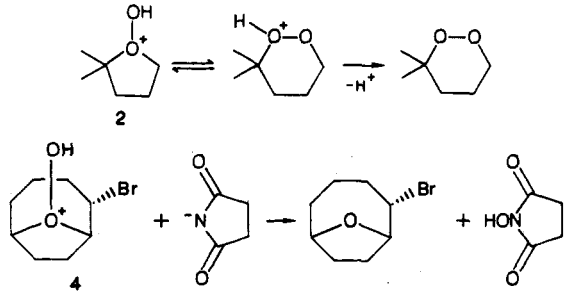
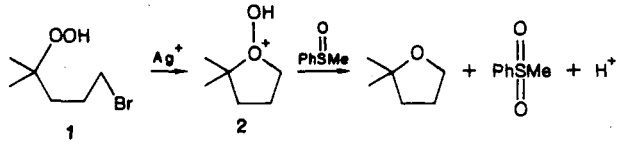
Scheme I



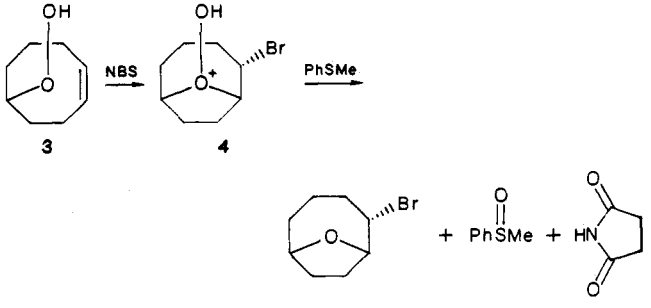
Scheme II



Scheme III



Scheme IV

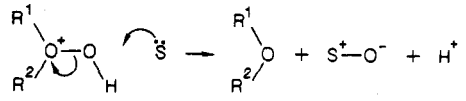


This fact and the evidence presented previously[7] for the parallel formation of an analogous trialkylperoxonium ion firmly point to *gem*-dialkylperoxonium ion **4** as the oxidant.

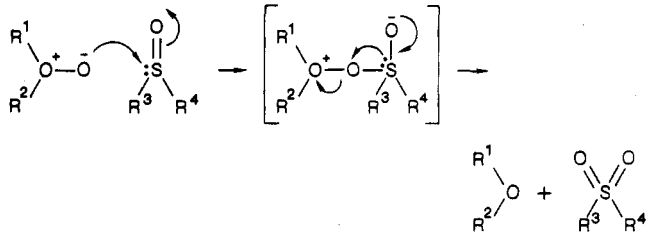
Evidence was similarly obtained for oxygen atom transfer from a *gem*-dialkylperoxonium ion based on naphthopyran.[8] However, this system suffered the disadvantage that the hydroperoxide precursor had to be generated in situ from hydrogen peroxide, thus adding to the potential complications of any mechanistic investigation. Hence, we restricted our mechanistic studies to the systems yielding ions **2** and **4**.

Mechanistic Studies. *gem*-Dialkylperoxonium ions, $R^1R^2O^+$–OH, bear an obvious resemblance to protonated hydrogen peroxide, H_2O^+–OH,[12] and so electrophilic oxygen transfer[9] to nucleophilic substrates was readily envisaged (Scheme V). Interest here lies in the influence of the groups R^1 and R^2 upon the electrophilicity of the ions. It is also possible to envisage the process of deprotonation, by the counterion or by a basic site in the substrate, to afford the corresponding dioxygen ylide, $R^1R^2O^+$–O^-. The ylide would be expected to participate in nucleophilic oxygen transfer[9] to substrates like sulfoxides (Scheme VI) by analogy with the chemistry of carbonyl oxides[1] and perepoxides.[2] As described below, we have used two different approaches to probe these mechanistic pathways for peroxonium ions **2** and **4**.

Scheme V



Scheme VI



Our first approach was based on the method introduced by Adam et al. to provide a chemical means of differentiating between carbonyl oxides and dioxiranes.[1b,13] The electrophilic versus nucleophilic nature of these and various other oxygen transfer reagents was examined by using thianthrene 5-oxide, a substrate incorporating both nucleophilic sulfide and electrophilic sulfoxide sites for oxygen uptake. Product distributions from oxidation of this compound were used to calculate X_{Nu}, a parameter reflecting oxygen transfer character and ranging from 0.0 (completely electrophilic) to 1.0 (totally nucleophilic). As expected, basic solutions of hydrogen peroxide scored 1.00 on this scale, while acidic solutions scored 0.06.[1b]

When our peroxonium intermediates **2** and **4** were generated in the presence of the Adam probe, X_{Nu} values of 0.10 and 0.72, respectively, were obtained. For the purposes of discussion and comparison, these results are presented in Table I along with some data presented by Adam et al. for other oxidants.

The low X_{Nu} value for peroxonium ion **2** is unremarkable in that it seems to confirm the expected similarity of *gem*-dialkylperoxonium ions and protonated hydrogen peroxide (Scheme V). Since strong acid (HBF_4 or HO_2CCF_3) is generated during the course of the silver salt reactions, it would have been surprising if any significant amount of the deprotonated form of **2** were produced, thereby raising the value of X_{Nu} by switching attack to the sulfoxide site (Scheme VI). Conversely, it was tempting to ascribe the much higher X_{Nu} value of peroxonium ion **4** to the formation of an appreciable concentration of the dioxygen ylide, a result in keeping with the greater basicity of the associated counterion, succinimide anion. However, there are puzzling aspects of such an interpretation, such as the question of how *N*-hydroxysuccinimide is formed in the absence of added substrate and of why no sulfone

(11) The inclusion of galvinoxyl in the reaction mixture had no effect, militating against a free-radical chain mechanism for the oxidation.

(12) (a) Alder, R. W.; Whiting, M. C. *J. Chem. Soc.* **1964**, 4707. (b) Christe, K. O.; Wilson, W. W.; Curtis, E. C. *Inorg. Chem.* **1979**, *18*, 2578. (c) Olah, G. A.; Berrier, A. L.; Surya Prakash, G. K. *J. Am. Chem. Soc.* **1982**, *104*, 2373.

(13) (a) Adam, W.; Durr, H.; Haas, W.; Lohray, B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 101. (b) Values of X_{Nu} as high as 0.85 have now been reported for isolated dimethyldioxirane: Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800.

Table I. Nucleophilic Character (X_{Nu}) of Oxygen Transfer Agents Derived with Thianthrene 5-Oxide[a]

conditions	oxidizing species[b]	X_{Nu}[c]	total yield,[c] %
1. H_2O_2, 1 M NaOH, PhH	HOO^-	1.0	0.25
2. $R^1C(=N_2)R^2$, $^1O_2$, CH_2Cl_2	$R^1R^2C{=}O^+{-}O^-$		
a. R^1 = *t*-Bu, R^2 = Me		0.96	0.77
b. R^1 = *t*-Bu, R^2 = H		0.92	0.83
c. R^1 = Ph, R^2 = Ph		0.89	7.76
3. 3, NBS, CH_2Cl_2	4	0.72	19
4. R^1COR^2, KSO_5H, CH_2Cl_2/H_2O			
a. R^1 = Me, R^2 = Me		0.67	10.1
b. R^1 = *t*-Bu, R^2 = Me		0.64	5.33
c. R^1 = *t*-Bu, R^2 = H		0.57	5.04
5. *m*-CPBA, CH_2Cl_2	*m*-CPBA	0.36	27.0
6. 1, AgX, CH_2Cl_2	2		
a. X = BF_4		0.10	37
b. X = O_2CCF_3		0.10	34
7. H_2O_2, 1 M HCl, Et_2O	$H_2O^+{-}OH$	0.06	3.27

[a] All entries except 3 and 6 (this work) taken from ref 1b. [b] The species considered to be primarily responsible for the products observed. [c] Calculated as described in ref 1b.

was produced when methyl phenyl sulfide was used as the oxygen atom trap (Scheme IV). It was confirmed independently that methyl phenyl sulfoxide is a markedly less successful trap for 4 than is the sulfide, a reversal of the situation found for carbonyl oxides and perepoxides. The behavior of the X_{Nu} scale, particularly in midrange, is far from clear, and, as we shall discuss later, values of 0.6–0.7 can be achieved by reagents that other evidence indicates are preferentially electrophilic.

We decided to seek further evidence concerning the mechanism of oxygen transfer from our reagents by using an approach based on the Hammett $\sigma\rho$ correlation. This technique has been applied previously to investigate the mechanisms of oxidations by carbonyl oxides,[1a] perepoxides,[2] and dioxiranes.[3]

Sulfoxides were selected as the substrates for this study. They are able to undergo both nucleophilic and electrophilic oxygen transfer and, therefore, provide the clearest indicator of the preferred mechanism for the oxidant under scrutiny.

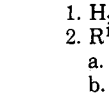
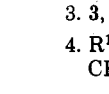
When our intermediates 2 and 4 were generated in the presence of para-substituted aryl sulfoxides $(p\text{-}XC_6H_4)_2SO$ (X = Me, H, F, and Cl), ρ values of -0.83 ± 0.11 and -1.77 ± 0.58 respectively were obtained. These results and similar data for other oxidants are listed in Table II.

That the ρ values are negative clearly indicates that peroxonium ions 2 and 4 are both behaving as electrophilic oxygen transfer reagents toward sulfoxides. This would seem to dispel the idea, prompted by the X_{Nu} results above, that there might be present an appreciable concentration of the deprotonated form of ion 4. This form would presumably have a positive ρ value comparable to those of the carbonyl oxide and perepoxide in Table II. Thus, the relatively high X_{Nu} (0.72) for ion 4 ($\rho = -1.77$) remains unexplained, but it should be noted that dimethyldioxirane generated in situ exhibits parallel behavior, scoring 0.67 on the Adam scale[13b] (Table I) while having a ρ value of −0.76 (Table II).

It must be conceded that the possibility of some single electron transfer (SET) character in these peroxonium ion oxygen transfer reactions cannot be ruled out. Correlations against σ^+ were inferior to those against σ for both 2 and 4, but the use of such evidence to dismiss SET character has recently been called into question.[14]

(14) Miller, A. E.; Bischoff, J. J.; Bizub, C.; Luminoso, P.; Smiley, S.; *J. Am. Chem. Soc.* **1986**, *108*, 7773.

Table II. Hammett ρ Values for Various Oxygen Transfer Reagents from Oxidations of Sulfoxides

oxygen atom donor	sulfoxide	solvent	Hammett ρ value	ref
1. $PhCO^{\cdot}OO^-$	XC_6H_4SOPh	dioxane/H_2O	+0.71	*a*
2. 	XC_6H_4SOMe	PhH	+0.52	*b*
3. $R_2C{=}O^+{-}O^-$	$(XC_6H_4)_2SO$	PhH	+0.26	*c*
4. 	XC_6H_4SOMe	MeCOMe	−0.76	*d*
5. 2	$(XC_6H_4)_2SO$	PhH	−0.83	*e*
6. $RCO^{\cdot}OOH$	$(XC_6H_4)_2SO$	PhH	−1.06	*c*
7. 4	$(XC_6H_4)_2SO$	CH_2Cl_2	−1.77	*e*

[a] Taken from ref 9. [b] Taken from ref 2. [c] Taken from ref 1a. [d] Taken from ref 3. [e] Present study.

Conclusions

The results show that *gem*-dialkylperoxonium ions 2 and 4 are electrophilic oxygen transfer reagents and provide no evidence that deprotonation occurs to give the corresponding dioxygen ylides under the conditions studied. The origin of the relatively high X_{Nu} value on the thianthrene 5-oxide scale for peroxonium ion 4 remains obscure, but similar behavior has been noted for dimethyldioxirane. Both the X_{Nu} and Hammett ρ values indicate that species 2 and 4 have different selectivities, thereby supporting the concept that *gem*-dialkylperoxonium ion reagents, $R^1R^2O^+{-}OH,X^-$, might be tunable to some extent through choice of the alkyl groups R^1 and R^2 and counterion X. The electrophilic nature of species 2 and 4 and their relationship to known oxidants (Tables I and II) serve to indicate which types of substrates should undergo oxygen transfer most successfully with *gem*-dialkylperoxonium ions.

Experimental Section

Unless otherwise indicated, NMR spectra were recorded with a Varian XL 200 spectrometer for solutions in $CDCl_3$. ^1H NMR spectra (60 MHz) were obtained with a JEOL PMX 60 instrument and 20-MHz ^{13}C NMR spectra with a Varian CFT 20 spectrometer. Infrared spectra were measured with a Perkin-Elmer 983 instrument. Mass spectra were obtained by using a VG 7070 F/H mass spectrometer plus Finnigan INCOS data system. *p*-Tolyl sulfone and phenyl sulfone were prepared by potassium permanganate oxidation of the sulfoxides. *p*-Fluorophenyl sulfoxide was prepared by the method of Granoth et al.[15] and purified by distillation. Benzyl methyl sulfoxide was prepared by periodate oxidation of the sulfide.[16] All other sulfides, sulfoxides, and sulfones were commercial samples, which were recrystallized until shown to be pure by analytical HPLC. Thianthrene 5-oxide, thianthrene 5,5-dioxide, thianthrene 5,10-dioxide, and thianthrene 5,5,10-trioxide were prepared by the methods of Gilman and Swayampati.[17] 1,8-Bis(bromomethyl)naphthalene was prepared by the method of Bockelheide et al.[18] All other reagents were commercial samples used without further purification.

Chromatography. Analytical HPLC was performed by using a Waters M6000 pump, Pye Unicam PU 4025 variable-wavelength detector at 254 nm, and Rheodyne injector valve. For Hammett analysis, a 10 cm × 4.5 mm silica gel (5 μm) column was used with a 20% EtOAc/petroleum ether solvent system flowed at 1.5 mL/min. For X_{Nu} analysis, serial 10 cm × 4.5 mm and 25 cm × 4.5 mm silica gel (5 μm) columns were used with a 25% Et-

(15) Granoth, C. D.; Kalir, A.; Paleh, Z. *J. Chem. Soc. C* **1969**, 2424.
(16) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282.
(17) (a) Gilman, H.; Swayampati, D. R. *J. Am. Chem. Soc.* **1955**, *77*, 5944. (b) Gilman, H.; Swayampati, D. R. *J. Am. Chem. Soc.* **1955**, *77*, 3387.
(18) Rohrback, W. D.; Gerson, F.; Mockel, R.; Bockelheide, V. *J. Org. Chem.* **1984**, *49*, 4128.

OAc/petroleum ether solvent system flowed at 3.0 mL/min. Integrals were obtained directly from a Hewlett-Packard 3390A reporting integrator interfaced to the detector.

Preparation of Peroxonium Ion Precursors. 1-Bromo-4-methyl-4-hydroperoxypentane (1). A solution of 2-methyl-4-penten-2-ol (6.3 g, 63 mmol) and benzoyl peroxide (2.0 g, 8.3 mmol) in benzene (100 mL) was cooled to 0 °C. Hydrogen bromide was bubbled through the mixture and the acidic solution stirred at ambient temperature overnight. The solution was neutralized ($NaHCO_3$) and the organic phase separated and dried ($MgSO_4$). Solvent was removed at reduced pressure and the residue taken up in hexane and filtered to remove unreacted benzoyl peroxide. The hexane solution was chromatographically separated on silica gel to yield 2,5-dibromo-2-methylpentane (9.6 g, 62%) as a colorless oil. ^1H NMR was in good agreement with reported values.[19] ^{13}C NMR: 29.71, 33.17, 34.20, 45.89, 66.27 ppm.

A solution of 85% aqueous hydrogen peroxide (0.3 g) in diethyl ether (10 mL) was dried ($MgSO_4$). 2,5-Dibromo-2-methylpentane (1.0 g, 4.1 mmol) was added and the solution cooled to −78 °C. Silver tetrafluoroborate (1.0 g, 5.1 mmol) was added in one portion and the solution stirred for 0.5 h. The solution was neutralized and the organic phase separated and dried. Preparative liquid chromatography (10% EtOAc in hexane, 12 × 1 in. silica gel column) gave the hydroperoxy bromide in 30% yield. ^1H NMR: 1.22 (s, 6 H), 1.50–2.15 (m, 4 H), 3.43 (t, J = 7 Hz, 2 H), 7.92 (s, 1 H) ppm. ^{13}C NMR: 23.91, 27.29, 34.31, 36.74, 82.11 ppm. Anal. Calcd: C, 36.59; H, 6.66. Found: C, 36.61; H, 6.82.

5-Hydroperoxycyclooctene (3). 5-Bromocyclooctene[20] (10 g, 53 mmol) in dry DMSO (5 mL) was added over 15 min to sodium cyanide (5.75 g, 117 mmol) dissolved in DMSO (25 mL) at 90 °C. The mixture was stirred at 100 °C for 3 h, allowed to cool, and poured into water (200 mL). Diethyl ether (3 × 50 mL) was used to extract the alkyl cyanide, and the combined extracts were washed with water (200 mL) and dried with $MgSO_4$. The solvent was removed at reduced pressure, and the crude 5-cyanocyclooctene was obtained in 97% yield. ^{13}C NMR: 23.52, 25.16, 27.10, 28.09, 29.45, 32.31, 128.61, 129.03, 130.71 ppm. IR: 2230, 1728 cm^{-1}. The 5-cyanocyclooctene was then stirred with potassium hydroxide and hydrogen peroxide according to the method of Hartley for the conversion of alkyl cyanides to carboxylic acids[21] to give 5-cyclooctenecarboxylic acid as a white solid in 83% yield. ^1H NMR: 1.4–3.0 (m, 11 H), 5.5–6.0 (t, 2 H), 8.0–9.0 (br s, 1 H) ppm. ^{13}C NMR: 27.91, 29.72, 31.63, 33.09, 35.25, 47.06, 133.31, 134.35, 187.57 ppm. IR: 1701 (C=O) cm^{-1}. Oxalyl chloride (15 mL, 17 mmol) was then added to the acid (5.5 g, 3.5 mmol) in anhydrous benzene (100 mL) under nitrogen. Dimethylformamide (0.3 mL) was added and the solution stirred for 4 h at room temperature. The solvent was removed at reduced pressure and the acid chloride purified by distillation to give 5-cyclooctenecarbonyl chloride as a clear liquid (92%). ^{13}C NMR: 23.48, 25.51, 27.31, 29.38, 31.12, 55.20, 128.78, 130.72, 177.46 ppm. IR: 1793 cm^{-1}. The acid chloride (1.0 g, 5.3 mmol) was treated with *N*-hydroxypyridine-2-thione sodium salt (0.9 g, 6.0 mmol) in anhydrous ether (125 mL) containing a few crystals of DMAP according to the method of Barton and Crich[22] to give the *O*-acyl thiohydroxamate as a stable yellow crystalline ester (mp 63–64 °C dec) in 60% yield. ^1H NMR: 1.2–3.2 (m, 11 H), 5.5–5.9 (m, 2 H), 6.3–7.7 (m, 3 H), 8.0–8.3 (m, 1 H) ppm. ^{13}C NMR: 25.80, 25.84, 27.73, 29.34, 41.16, 112.59, 129.24, 130.92, 133.41, 137.52, 137.63, 172.77, 175.97 ppm. IR: 1787, 1601 cm^{-1}. Anal. Calcd: C, 63.85; H, 6.51; N, 5.32; S, 12.17. Found: C, 63.39; H, 6.59; N, 5.45; S, 11.85. The thione ester (2.5 g, 10 mmol) was then dissolved in ether (100 mL) and added in small portions along with a solution of 1,1-diethylpropanethiol[22] (1.6 g, 12 mmol) in ether (75 mL) to a flask containing diethyl ether (75 mL) saturated with oxygen and fitted with a CO_2/acetone condenser. The reaction vessel was irradiated with a 500-W tungsten lamp during the addition of reagents, further addition being made as the yellow color dissipated. Upon complete addition and color loss, the solvent was removed at reduced pressure and the resulting mixture dissolved in pentane (10 mL) and cooled to 0 °C. The hydroperoxide was extracted into ice-cold aqueous sodium hydroxide (4 M, 5 × 10 mL) and washed with pentane. The aqueous fraction was then acidified (HCl), and cold dichloromethane (2 × 25 mL) was added to extract the hydroperoxide. The solution was dried ($MgSO_4$) and the solvent removed at reduced pressure to give 5-hydroperoxycyclooctene in 55% yield. ^1H NMR: 1.40–2.40 (m, 10 H), 4.00 (m, 1 H), 5.66 (m, 2 H), 8.13 (br s, 1 H) ppm. ^{13}C NMR: 22.33, 25.31, 25.72, 31.62, 31.82, 86.84, 129.76, 129.89 ppm. Anal. Calcd: C, 67.56; H, 9.94. Found: C, 67.29; H, 9.81. Spectroscopic and analytical data have been previously reported for this hydroperoxide by an alternative synthesis.[7b]

Standard Reaction Conditions for the Formation and Trapping of Peroxonium Ion Intermediates. Reaction of 1-Bromo-4-methyl-4-hydroperoxypentane with Silver Tetrafluoroborate in the Presence of Para-Substituted Aryl Sulfoxides. 1-Bromo-4-methyl-4-hydroperoxypentane (0.05 g, 0.26 mmol) was dissolved in anhydrous benzene (350 mL) and mixed with phenyl sulfoxide (0.708 g, 3.5 mmol) and either *p*-tolyl sulfoxide (0.806 g, 3.5 mmol), *p*-chlorophenyl sulfoxide (0.949 g, 3.5 mmol), or *p*-fluorophenyl sulfoxide (0.833 g, 3.5 mmol) in a round-bottomed flask cooled to 0 °C. Silver tetrafluoroborate (0.16 g, 8.2 mmol) was added to the solution, and the mixture was allowed to warm to room temperature and stirred for 1 h. The solution was then filtered through a sintered glass funnel containing a short pad of silica to remove the silver salts and the filtrate concentrated at reduced pressure. Analytical HPLC was used to determine extent of oxidation of incorporated sulfoxides.

Reaction of 1-Bromo-4-methyl-4-hydroperoxypentane with Silver Salts in the Presence of Thianthrene 5-Oxide. 1-Bromo-4-methyl-4-hydroperoxypentane (0.082 g, 0.42 mmol) was dissolved in dichloromethane (25 mL) containing thianthrene 5-oxide (0.156 g, 0.67 mmol) and cooled to 0 °C. Silver trifluoroacetate (0.16 g) or silver tetrafluoroborate (0.26 g) was added in one portion and the mixture stirred for 0.5 h. The mixture was then filtered through a short silica pad and the filtrate concentrated at reduced pressure. The reaction products were identified by analytical HPLC. Retention times were as follows: for thianthrene 5-oxide, 3.46 min; for thianthrene 5,5-dioxide, 3.75 min; for thianthrene 5,10-dioxide, 7.35 min; for thianthrene 5,5,10-trioxide, 9.22 min; for *p*-nitrophenyl sulfone (internal standard), 3.05 min.

Reaction of 5-Hydroperoxycyclooctene with *N*-Bromosuccinimide in the Presence of Para-Substituted Aryl Sulfoxides. 5-Hydroperoxycyclooctene (6.05 g, 0.35 mmol) was dissolved in dichloromethane (350 mL) and mixed with phenyl sulfoxide (0.708 g, 3.5 mmol) and either *p*-tolyl sulfoxide (0.806 g, 3.5 mmol), *p*-chlorophenyl sulfoxide (0.949 g, 3.5 mmol), or *p*-fluorophenyl sulfoxide (0.833 g, 3.5 mmol). *N*-Bromosuccinimide (0.063 g, 0.35 mmol) was added to the solution and the mixture stirred for 1.5 h. The mixture was then concentrated at reduced pressure and analytical HPLC used to determine extent of oxidation of incorporated sulfoxides.

Reaction of 5-Hydroperoxycyclooctene with *N*-Bromosuccinimide in the Presence of Thianthrene 5-Oxide. 5-Hydroperoxycyclooctene (0.1 g, 0.7 mmol) was dissolved in dichloromethane (25 mL) containing thianthrene 5-oxide (0.16 g, 0.7 mmol). *N*-Bromosuccinimide (0.125 g, 0.7 mmol) was added in one portion and the mixture stirred for 1 h. The solution was then concentrated at reduced pressure and the product distribution determined by analytical HPLC.

Reaction of 1,8-Bis(bromomethyl)naphthalene with Hydrogen Peroxide in the Presence of Benzyl Methyl Sulfoxide. 1,8-Bis(bromomethyl)naphthalene (0.3 g, 1 mmol) was dissolved in anhydrous ether (12.5 mL) containing either 1, 2, or 3 mmol of benzyl methyl sulfoxide. Hydrogen peroxide (86%, 0.05 g, 3 mmol) was mixed with another portion of anhydrous ether (12.5 mL), dried over $MgSO_4$, and filtered. Silver tetrafluoroborate (0.5 g, 2 mmol) was added to each of the dibromide/sulfoxide solutions at 0 °C. The hydrogen peroxide solutions were then added and stirred for 90 s, after which time triphenylphosphine (0.5 g, 2 mmol) in ether (15 mL) was added to the solutions. After 1 min, the mixture was filtered and dried with $MgSO_4$ and the solvent removed at reduced pressure. The pyran and sulfone products were analyzed by ^1H NMR versus authentic samples.

Determination of Hammett and X_{Nu} Parameters. X_{Nu} parameters were calculated according to the method of Adam,[1b]

(19) House, H. O. *J. Org. Chem.* **1974**, *39*, 3102.
(20) Ziegler, K.; Wilms, H. *Justus Liebigs Ann. Chem.* **1950**, *567*, 1.
(21) Hartley, D. *J. Chem. Soc.* **1962**, 4722.
(22) Barton, D. H. R.; Crich, D. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1603.

by using thianthrene 5,5-dioxide, 5,10-dioxide, and 5,5,10-trioxide concentrations as determined by calibrated integrals obtained from HPLC analysis of the reaction mixtures. For Hammett parameters, relative rates of oxidation (k_X/k_H) were determined by HPLC analysis of the competition reaction mixtures containing either *p*-methyl-, *p*-chloro-, or *p*-fluoro-substituted phenyl sulfoxides and the parent unsubstituted phenyl sulfoxide. Calibrated integrals were used to determine the relative yields of sulfones from which the following k_X/k_H values were calculated, taking the mean of at least three independent measurements: for peroxonium ion **2**, k_X/k_H (substituent) = 2.22 (*p*-Me), 1.00 (*p*-H), 0.74 (*p*-F), 0.49 (*p*-Cl); for peroxonium ion **4**, 1.99 (*p*-Me), 1.00 (*p*-H), 1.05 (*p*-F), 0.07 (*p*-Cl). Assuming a Hammett linear free energy relationship,[23] plots of log (k_X/k_H) versus 2σ gave ρ values of -0.83 ± 0.11 ($R = 0.98$) for peroxonium ion **2** and -1.77 ± 0.58 ($R = 0.91$) for peroxonium ion **4**.

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Notes

Stereochemical Control in the Synthesis of 2,5-Disubstituted Tetrahydrofurans

Robert L. Mulholland, Jr., and A. Richard Chamberlin*

Department of Chemistry, University of California, Irvine, California 92717

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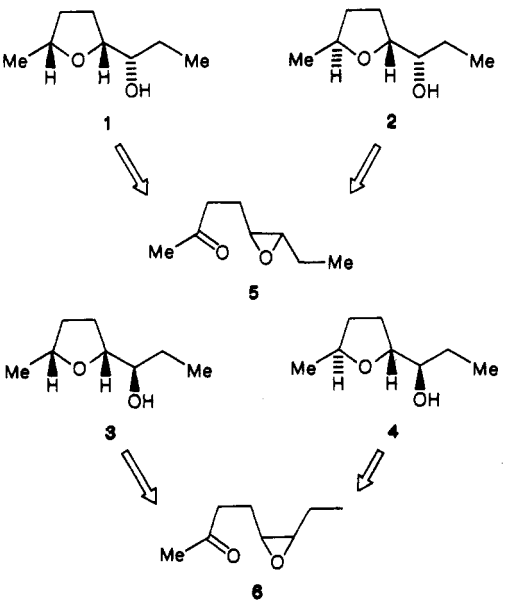
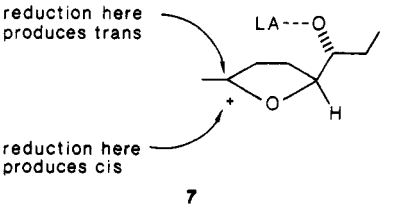
The synthesis of polyether antibiotics and other complex targets containing oxacyclic subunits has led to the development of many procedures for constructing substituted tetrahydrofurans.[1] Despite several notable examples of stereoselection in the synthesis of 2,5-disubstituted tetrahydrofurans, a completely satisfactory general method of stereochemical control has yet to be reported. One noteworthy example was demonstrated by Kishi, where cyclization of a hydroxy epoxide with the relative stereochemistry *predetermined* yielded a *trans*-2,5-tetrahydrofuran.[2] In the process of addressing the general problem of substituted tetrahydrofuran formation, we have found a new method of constructing these ring systems that appears to be particularly promising for the stereoselective formation of the especially troublesome[3] 2,5-trans derivatives such as **2** and **4**.

We originally sought a method that might allow complete stereochemical control (in a *predictable* direction) at each of three centers in the hydroxy tetrahydrofuran diastereomers **1**-**4**.[4] The general plan was to effect an electrophilic epoxide opening with carbonyl participation, followed by either inter- or intramolecular reduction of the resulting carbonium ion. Control of the tetrahydrofuran stereochemistry would thus derive from the choice of reduction mode (inter → cis tetrahydrofuran and intra → trans tetrahydrofuran), while the relative stereochemistry of the resultant alcohol group would simply depend upon



whether the cis or trans epoxide was cyclized (opening of protonated epoxides by internal or external nucleophiles generally proceeds with inversion).[5]



The first obstacle presenting itself in the intermolecular cyclization/reduction was the necessity of finding a source of hydride compatible with the acidic conditions necessary to initiate cyclization. Fortunately, trialkylsilanes survive mild Lewis and protic acid conditions and are known to reduce simple cationic intermediates related to **7** (i.e., reduction of ketals to ethers).[6]

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(2) (a) Fukuyama, T.; Vransic, B.; Negri, D. P.; Kishi, Y. *Tetrahedron Lett.* **1978**, 2741. (b) Nakata, T.; Kishi, Y. *Tetrahedron Lett.* **1978**, 2745.

(3) See ref 1c for examples of difficulties in forming 2,5-trans tetrahydrofurans stereoselectively.

(4) This particular set of diastereomers was chosen because all are known compounds, distinguishable by NMR: Porter, N. A.; Zuraw, P. J. *J. Org. Chem.* **1984**, *49*, 1345. We did experience some problems in the workup and isolation because of water solubility and volatility.

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(6) (a) Lancelin, J.-M.; Zollo, P. H. A.; Sinay, P. *Tetrahedron Lett.* **1983**, *24*, 4833. (b) Doyle, M. P.; DeBruyn, D. J.; Kooistra, D. A. *J. Am. Chem. Soc.* **1972**, *94*, 3659. (c) Kursandov, D. N.; Parnes, Z. N.; Loim, N. M. *Synthesis* **1974**, 633.

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