was confirmed by GC and GC–MS using an authentic sample (Research Plus) as reference (SPB-1 column, 30 m, 0.32-mm i.d. 0.25-μm coating at 260 °C; retention time 26.4 min). The MS displayed peaks at m/z (relative intensity) 402 (24), 384 (100), 369 (47), 367 (13), 351 (36), 300 (28), 299 (33), 273 (38), 271 (69), and lower m/z steroidal clusters. Similar oxidation of cholesterol in a homogeneous solution gave small amounts of many products.

We have shown that a steroidal manganese(III) porphyrin catalyst intercalated in a synthetic bilayer is capable of the hydroxylation of hydrocarbons in moderate yields. This assembly also selectively hydroxylated cholesterol at carbon 25. The O_2/ascorbic acid/manganese porphyrin system has been shown in other studies to generate an oxomanganese(IV) porphyrin as the reactive intermediate.[12b,13] The selectivity observed here must be due to the enforced proximity of the tertiary hydrogen at C-25 to the incipient manganyl group of the oxidized catalyst (1) at the catalytic center (Figure 1), precisely the motif that has been revealed in the X-ray crystal structure of the enzyme–substrate complex of cytochrome P-450_{cam}.[14]

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Use of the Brønsted Relationship To Detect a Mechanistic Shift for Reaction of 2-(Methylthio)ethyl Chloride with Thiophenoxide Anions

Summary: The linear Brønsted plot for reaction of thiophenoxide ions with 2-(methylthio)ethyl chloride in DMSO changes slope for highly deactivated thiophenoxides, thus suggesting a mechanism change. Attack of a neutral nucleophile on an anionic electrophile may be involved.

Table I. Second-Order Rates for Reactions of ArS^- Ions with $MeSCH_2CH_2Cl$ (1) and *n*-Butyl Chloride in DMSO at 25 °C

		10^3k_2 (M^{-1} s^{-1})	
ArS^-, Ar =	pK_a[a]	1[b]	*n*-BuCl[c]
4-$MeOC_6H_4$	11.2	95.4 ± 2.4	105 ± 20 (100)
C_6H_5	10.3	41.8 ± 0.2	44.2 (42.6)
2-naphthyl	9.5	26.6 ± 1.5	25.6 ± 0.6 (25.4)
4-BrC_6H_4	9.0	18.3 ± 2.8	(13.3)
3-ClC_6H_4	8.57	12.1 ± 1.1	
2-ClC_6H_4	8.5	13.7 ± 0.5	9.01 (8.77)
3-$CF_3C_6H_4$	8.1	9.86 ± 0.20	7.54 ± 0.60 (5.78)
2,4,5-$Cl_3C_6H_2$	6.00	8.62 ± 0.86	1.04 ± 0.18 (0.852)
4-$NO_2C_6H_4$	5.5	22.9 ± 3.1	0.313 ± 0.029 (0.279)
C_6Cl_5	3.3	23.8 ± 6.7	0.099 ± 0.0045 (0.0581)

[a] From ref 2. [b] Rates were run as pseudo first order by following the disappearance of the thiophenoxide by UV as described in ref 1. [c] The values in parentheses are from ref 2.

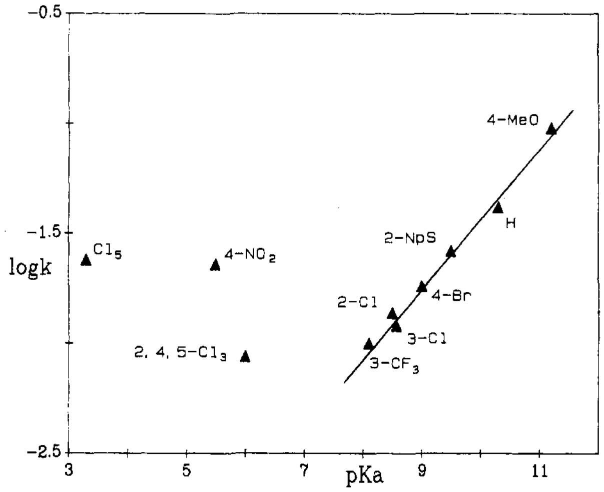

Figure 1. Brønsted plot for reaction of 2-(methylthio)ethyl chloride (1) with thiophenoxide anions in DMSO.

Sir: We recently demonstrated that *p*-aminothiophenoxide reacts with 2-(methylthio)ethyl chloride (1) or 2-(phenylthio)ethyl brosylate in dimethyl sulfoxide (DMSO) by a direct displacement S_N2 mechanism.[1] On the other hand, solvolysis of these derivatives in DMSO proceeds by neighboring sulfur participation to give a cyclic sulfonium ion (a k_Δ mechanism).[1] In this paper we report that a series of seven highly nucleophilic thiophenoxide anions undergo reaction with 1 in DMSO to provide second-order rate constants, Table I, which give a linear Brønsted plot,[2] Figure 1. The log k values for reaction of the same seven nucleophiles also plot linearly against log k values for their S_N2 reaction with *n*-butyl chloride, Table I.[2] With the β-thioethyl substrates, we anticipated a break from the linear relationship with weakly nucleophilic thiophenoxide ions because at some point the first-order k_Δ process should be faster than the second-order S_N2 reactions. We did indeed find a break in the linear relationship but, surprisingly, the weakest thiophenoxide nucleophiles react *more* rapidly, indicating that some mechanism other than k_Δ is involved, Figure 1.

The thiophenoxides with pK_a values less than 8.1 still follow second-order kinetics. The calculated pseudo-first-order rates for the least reactive anions are still more than an order of magnitude greater than the measured first-order rate for 1 in DMSO in the absence of any thiophenoxide ion ($k = 8.5 \times 10^{-5}$ s^{-1}). The rate *increase* observed for the 4-nitro- and pentachlorothiophenoxide ions, Figure 1, is not predicted by either the normal S_N2 process or by the neighboring sulfur-assisted process. With regard to the mechanism, it is instructive to note that the deviating substrates follow second-order kinetics and *give substitution products expected for an S_N2 process.*

The most logical explanation for the break in the Brønsted plot, Figure 1, is that there has been a change in mechanism to some bimolecular substitution process other than that followed by the seven more nucleophilic thiophenoxide anions. The mechanism must account for a nucleophilic reactivity order which is the inverse of the intrinsic nucleophilicity of the thiophenoxide ions! Since

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(1) Sedaghat-Herati, M. R.; Harris, J. M.; McManus, S. P. *J. Org. Chem.* **1988**, *53*, 2539.
(2) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3223. See also: Bordwell, F. G.; Cripe, T. A.; Hughes, D. L. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; Advances in Chemistry 215; American Chemical Society, Washington, DC, 1987; Chapter 9.

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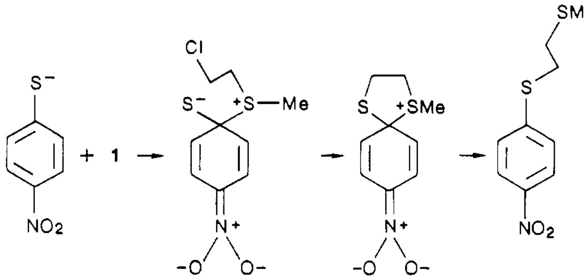
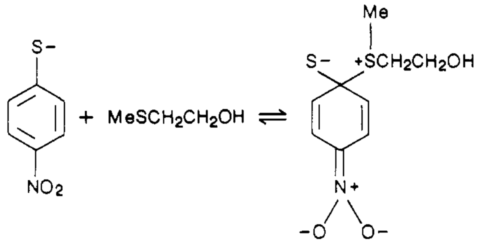
3894 *J. Org. Chem.* **1988**, *53*, 3894-3896

the anomalous reaction only occurs when strong electron-withdrawing groups are substituted on the aryl nucleus, involvement of the aryl ring is suggested. Recent studies have reminded us of the high nucleophilicity of the sulfur atom in 1.[3-5] Thus a *possible* mechanism for the anomalous nucleophiles involves attack by the sulfur of 1 on the electrophilic thiophenoxide aromatic ring by an S_NAr mechanism,[6] eq 1. Provided that the first step of the mechanism is rate-determining, this mechanism predicts the observed reactivity trend of faster rates as the thiophenoxide anions are substituted with stronger electron-withdrawing groups. A rapid second step is anticipated since it involves a favorable ring closure to a five-membered ring.[7] The rate of the third step is more difficult to estimate. We attempted to find evidence for the mechanism by substituting $MeSCH_2CH_2OH$ for the chloride 1 in the reaction with *p*-nitrothiophenoxide in DMSO, but we observed no UV evidence for complex **2**, eq 2. This may be because it is reversibly formed in a fast reaction, which, of course, would be consistent with a fast third step in eq 1.[8]



(1)



(2)

Alternatively, we have considered rate-limiting formation of the dimer of 1,[3,4] i.e., $MeSCH_2CH_2S^+(Me)CH_2CH_2Cl^-$, which could subsequently react with the thiophenoxide ions by displacement of 1 and give the observed S_N2 product. However, in the absence of thiophenoxide ion, 1 (at a concentration of 0.4 M) is stable at 25 °C in DMSO-d_6 for at least 12 h as determined by NMR.

A third mechanistic possibility is a shift to a single electron transfer (SET) process involving the sulfonium ion formed by the k_Δ mechanism.[9-12] Bordwell and Harrelson have shown[13] that primary alkyl chlorides have reduction potentials which are too low for SET reaction with ArS^-, but the intermediate sulfonium ion could well have a sufficiently positive reduction potential. Two problems are apparent with this proposed mechanism. First, one would expect the oxidation potentials of the thiophenoxides to be roughly proportional to Hammett σ values of the ring substituents, so that the *p*-nitro and pentachloro derivatives would probably have less negative oxidation potentials than the trichloro derivative and should thus react more slowly by the SET mechanism. Secondly, this mechanism would appear to require rate-limiting formation of the sulfonium ion, a fact we ruled out above.

Future work will concentrate on elucidating this previously unobserved mechanism for reaction of nucleophiles with 2-(alkylthio)ethyl derivatives.

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[5] Toward methyl iodide in methanol, diethyl sulfide has a *n* value about 4 units less than thiophenoxide (cf. Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319). In DMSO, pentachlorothiophenoxide is about 3 orders of magnitude less nucleophilic than thiophenoxide (cf. Table I). Thus, we can estimate that 1 is only slightly less nucleophilic than the highly deactivated thiophenoxide ions.

[6] March, J. *Advanced Organic Chemistry*, 3rd ed.; New York: John Wiley and Sons, 1985; pp 576–8.

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[8] We are not aware of an example of an attack of a neutral nucleophile on a aromatic anion to form a Meisenheimer complex (e.g. see, Terrier, F. *Chem. Rev.* **1982**, *82*, 77). However, there is evidence for Meisenheimer complex formation by attack of a dianionic nucleophile on a trianionic aromatic substrate, cf. Crampton, M. R. *J. Chem. Soc., Perkin Trans 2* **1978**, 343. The referees have suggested that the pentachloro derivative ought to show steric retardation to ring attack. Also, the slight excess of thiol used in these reactions may provide a pathway for attack by 1 on the neutral thiol in addition to attack on thiophenoxide anion.

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Dual Hydrogen Bond Association of (*R*,*R*)-*N*,*N*'-Diisopropyltartramide with (*S*,*S*)-9,10-Dimethyl-9,10-dihydrophenanthrene-9,10-diol

Summary: (*S*,*S*)-9,10-Dimethyl-9,10-dihydrophenanthrene-9,10-diol (**2**) associates more strongly with (*R*,*R*)-*N*,*N*'-diisopropyltartramide (**1**) than its enantiomer through dual hydrogen bonds in nonaqueous media. The X-ray crystal structure of the 1:1 complex of (*S*,*S*)-**2** and (*R*,*R*)-**1** identified the interaction of these species as two sets of hydrogen bonds between the gauche hydroxyls of (*S*,*S*)-**2** and two amide carbonyls of (*R*,*R*)-**1**.

Sir: The enantiomers of 1,2-diols undergo enantioselective association with (*R*,*R*)-*N*,*N*'-diisopropyltartramide (**1**) through hydrogen bonds in nonaqueous media. In our previous resolution of a series of enantiomers of 1-phenyl-2-alkyl-1,2-ethanediols using (*R*,*R*)-**1** as the chiral mobile-phase additive in silica gel chromatography, dual hydrogen bonds of (*R*,*R*)-**1** and gauche hydroxyls of diol enantiomers were proposed as the mode of association responsible for the observed enantioselection although the bonding sites in (*R*,*R*)-**1** remained obscure.[1] In the present study, the dual hydrogen bond association of (*R*,*R*)-**1** with a 1,2-diol is clearly demonstrated by an X-ray crystal analysis of the complex of (*R*,*R*)-**1** with (*S*,*S*)-9,10-dimethyl-9,10-dihydrophenanthrene-9,10-diol (**2**)[2] and the

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