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Oxidative Coupling of Methyl Phenyl Sulfide via Sulfonium Formation Using an Oxovanadium Complex

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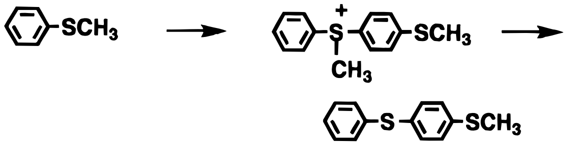
There is considerable interest in direct oxidation as a means of synthesizing sulfoxides. Numerous catalysts have been utilized as oxygenase-like models[1] in the formation of sulfoxides by the oxidation of sulfide compounds with oxygen. The mechanism likely involves a one-electron transfer process.

Traditionally, sulfonium compounds have been synthesized[2] with low conversion by the alkylation of the sulfides with iodoalkanes in the presence of an equimolar amount of silver salt, by the protonation of sulfoxides, and by the treatment of alkyl sulfoxides with alkyl Grignard reagents.

Recently, we reported that *N,N'*-ethylenebis(salicylideneaminato)oxovanadium undergoes a two-electron transfer at 0.5 V (vs Ag/AgCl) through disproportionation in the presence of acids.[3] Oxovanadium acetylacetonate (VO(acac)$_2$) could be employed as a two-electron mediator in the oxidation of an aryl sulfide (ca. 1.0−2.0 V vs Ag/AgCl) because of its suitably high redox potential (1.1 V vs Ag/AgCl).

In this paper, we report that unsymmetric arylalkylsulfonium salts can be synthesized by the oxygen-mediated oxidative coupling of the arylsulfides catalyzed by an oxovanadium complex (eq 1). Of note is the use of the abundant, inexpensive oxidant, oxygen, as a raw material. The reaction involves not only a new catalytic system for oxidation of sulfides by an electron-transfer analogous to that of an oxidase model but also the direct formation of unsymmetric aryl sulfides via sulfonium cations. We believe that a two-electron transfer relay system from the sulfide to oxygen leads to oxidative coupling yielding the sulfonium compounds without sulfoxide or sulfone formation.



(1)

The oxidative coupling of an aryl sulfide with oxygen to form the corresponding sulfonium cation by an electron transfer can be catalyzed with VO(acac)$_2$ in the presence of tetrabutylammonium perchlorate, trifluoromethanesulfonic acid, or trifluoroacetic anhydride in dichloromethane.[4] In the presence of VO(acac)$_2$, the reaction is accompanied by quantitative oxygen uptake.[5] For each mole of oxygen consumed, 2.0 mol of product is generated.

The combination of 500 MHz COSY ^{1}H- and ^{13}C-NMR and IR spectroscopy permitted identification of the sulfonium structure.[6] In the NMR spectra, signals (^{1}H-NMR: 3.65 ppm; ^{13}C-NMR: 28.4 ppm) attributed to the adjacent methyl group appeared at lower field than those due to the neutral methylthio group (2.45 and 14.6 ppm, respectively).

The demethylation (eq 1) of methylphenyl-4-(methylthio)phenylsulfonium perchlorate (2 g, 5.7 mmol) was carried out in pyridine (15 mL) at reflux temperature for 1 h. The demethylation proceeds quantitatively, resulting in the formation of methyl 4-(phenylthio)phenyl sulfide (1.27 g) in 96% yield.[7] After the oxidative coupling, the reaction mixture was neutralized with excess pyridine (100 mL) and then refluxed for 1 h. This one-pot synthesis resulted in the same product (yield 98%) (Table 1). However, the oxidative coupling of cyclopropyl phenyl sulfide did not proceed, presumably because of elimination of a labile methyne proton after the oxidation. Diphenyl sulfide was not oxidized, presumably due to its higher oxidation potential (1.7 V). The alkyl-substituted arylmethyl sulfides with a lower oxidation peak potential also produced the corresponding aryl sulfides. The electron-donating alkyl substituents promote the coupling reaction because the reaction proceeds through electrophilic substitution.

Methyl phenyl sulfide shows an irreversible oxidation peak potential of 1.5 V (vs Ag/AgCl) (Figure 1). The isolated sulfonium cation (methylphenyl-4-(methylthio)-phenylsulfonium perchlorate) is oxidized at a higher potential of 1.9 V.[8] Incorporation of the sulfonium group into the phenylene ring results in an increase in the oxidation potential due to electron withdrawal. It was concluded that the dimerized sulfonium cation was not oxidized by the oxovanadium catalyst because oxygen

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† PREST, JRDC-Investigator 1992−1994.

[1] Riley, D. P.; Smith, M. R.; Correa, P. E. *J. Am. Chem Soc.* **1988**, *110*, 177.

[2] Roush, D. M.; Price, E. M.; Templeton, L. K.; Templeton, D. H.; Heathcock, C. H. *J. Am. Chem. Soc.* **1979**, *101*, 2971. Yamamto, K.; Shouji, E.; Nishide, H.; Tsuchida E. *J. Am. Chem. Soc.* **1993**, *115*, 5819. Anderson, K. K.; Caret, R. L.; Karup-Nielsen, I. *J. Am. Chem. Soc.*, **1974**, *96*, 8020.

[3] Yamamoto, K.; Oyaizu, K.; Iwasaki, N.; Tsuchida, E. *Chem. Lett.* **1993** 1223. Tsuchida, E.; Yamamoto, K.; Oyaizu, K.; Iwasaki, N.; Anson, F. C. *Inorg. Chem.* **1994,** *33***.** 1056.

[4] A typical procedure for this catalytic reaction is as follows: VO(acac)$_2$ (0.066 g, 5 mmol/L), trifluoromethanesulfonic acid (0.075 g, 10 mmol/L), trifluoroacetic anhydride (2.1 g, 0.2 mol/L), and tetrabutylammonium perchlorate (3.42 g, 0.2 mol/L) were dissolved in CH_2Cl_2 (40 mL) in a closed vessel maintained at 20 °C. The mixture was stirred for 1 h under a dry argon atmosphere before the reaction. The atmosphere in the vessel was then replaced with oxygen. A solution of methyl phenyl sulfide (1.24 g, 0.2 mol/L) in CH_2Cl_2 (10 mL) was added. The reaction was carried out for 40 h under an oxygen atmosphere with constant stirring at 20 °C. Methyl phenyl sulfide and methyl phenyl sulfoxide were not detected in the reaction mixture by gas chromatography. The mixture was poured into ether (300 mL) to precipitate the product. Methylphenyl-4-(methylthio)phenylsulfonium perchlorate was isolated after extraction of the precipitate with CH_2Cl_2 (3.2 g, 94%).

[5] Oxygen consumption was determined as follows: The vanadyl catalyst and acids were dissolved in CH_2Cl_2 in a closed vessel maintained at 20 °C and were mixed for 1 h under a dry argon atmosphere until a steady state was reached. A similar vessel equipped with a manometer and a burette was connected to it with a tube. The atmosphere in the vessel was replaced by oxygen. The whole instrument was kept airtight. A solution of aryl sulfide in CH_2Cl_2 was added. Tetrachloroethane was carefully added from a burette to the second vessel to keep the pressure at 1 atm. Oxygen consumption was measured from the net amount of the tetrachloroethane added during the reaction.

[6] Methylphenyl-4-(methylthio)phenylsulfonium perchlorate: IR (KBr, cm^{-1}) 3002, 2922, 1088, 812, 743, 680, 625; ^{13}C-NMR (CDCl$_3$, 500 MHz 119.7, 126.4, 127.2, 129.5, 130.2, 131.4, 134.6, 148.9 14.6, 28.4; ^{1}H-NMR (CDCl$_3$, 500 MHz 7.36, 7.58, 7.63, 7.79, 7.63 (9H, m); 2.45, 3.65 (6H). Anal. Calcd for $C_{14}H_{15}S_2ClO_4$: C, 48.48; H, 4.36. Found: C, 48. 40; H, 4.38.

[7] Methyl 4-thiophenoxyphenyl sulfide: IR (KBr, cm^{-1}) 3056, 2919, 1580, 1476, 1437, 810, 739, 689; ^{1}H-NMR (500 MHz, CDCl$_3$) 7.29−7.01 (9H, m); 2.28 (3H); ^{13}C-NMR (500 MHz, CDCl$_3$) 126.7, 127.2, 129.1 130.2, 131.4, 132.2, 136.7, 138.2, 15.6. Anal. Calcd for $C_{13}H_{12}S_2$: C, 67.2; H, 5.21. Found: C, 66.8; H, 5.28.

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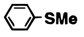
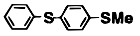
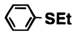
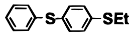
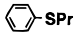
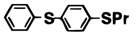
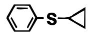
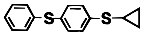
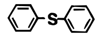
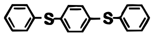
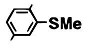
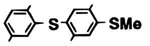
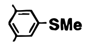
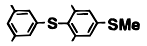
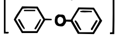
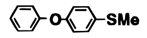
Table 1. Oxidative Coupling of Thioanisol Derivatives Catalyzed by VO(acac)$_2$ Followed by Demethylathion

Reactant	Epa (V)[a]	Product	Yield (%)[b]	MS (m/e)
	1.5		100	232
	1.4		94	246
	1.5		100	250
	1.3		trace	258
	1.7		0	-
	1.2		100	289
	1.2		100	289
Me-S-Me 	1.3 -		8	216

[a] V vs Ag/AgCl in CH$_3$CN [b] Determined by GC

consumption was not observed in the same reaction of the sulfonium compound. The redox potential ($E_{1/2}$) of VO(acac)$_2$, which is ascribed to the redox couple between V(IV)/V(V), is 1.1 V in dichloromethane. In an anaerobic acidic environment, two reversible redox couples were observed at very close potentials (1.4 and 1.6 V) via cyclic voltammetry and can be assigned to V(III)/V(IV) and V(IV)/V(V), respectively.[9] This result supports the idea that a two-electron transfer is facilitated due to the small potential separation between the two redox couples.[10]

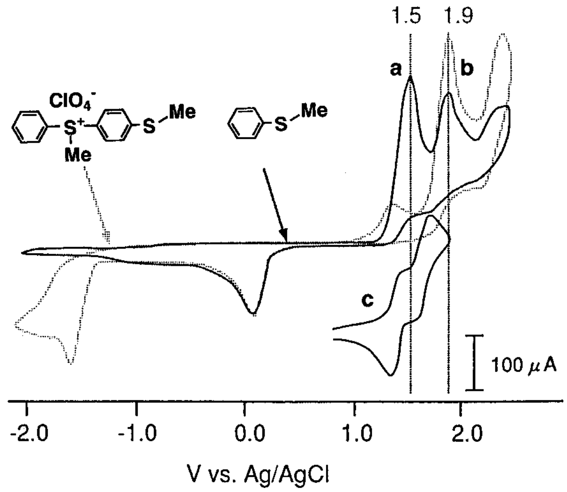
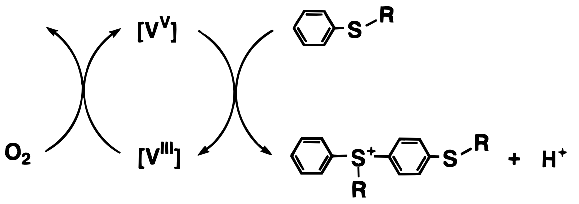


Figure 1. Cyclic voltammetry of methyl phenyl sulfide (2 mmol/L) (a), methylphenyl-4-(methylthio)phenyl sulfonium perchlorate (2 mmol/L) in CH$_2$Cl$_2$ (b), and VO(acac)$_2$ (2 mmol/L) under anaerobic conditions in CH$_2$Cl$_2$ in the presence of trifluoromethanesulfonic acid (10 mmol/L) and trifluoroacetic anhydride (0.2 mol/L) (c). Scanning rate 50 mV/s, Pt electrode (28.3 mm^2).

Scheme 1



The oxidative coupling of methyl phenyl sulfide with oxygen occurs through two redox couples that bridge the large potential gap between oxygen and aryl sulfides. The oxovanadium catalyst acts as an excellent electron mediator in the catalytic reaction. The catalyst is activated by oxidation with oxygen to a high-valent vanadyl(V) species. The resulting active cationic species[11] of methyl phenyl sulfide derived from its oxidation by the activated vanadyl catalyst reacts electrophilically with the benzene ring of the sulfide to form the dimerized sulfonium cation accompanied by proton elimination. The resulting vanadium(III) species is reoxidized to vanadyl(V) by oxygen (Scheme 1).

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[8] Electrochemical measurements were carried out in a two-compartment cell kept under a dry argon atmosphere. A platinum disk (28.3 mm^2) and platinum wire (ϕ = 0.2 mm, 200 mm) were used as working and auxiliary electrodes, respectively. The reference electrode consisted of an Ag/AgCl electrode in CH$_2$Cl$_2$ solution containing 0.1 mol/L tetrabutylammonium tetrafluoroborate. The electrode potential was determined at 0.21 V vs NHE by adjustment with a ferrocene−ferrocenium(+) redox couple. Cyclic voltammograms were measured in CH$_2$Cl$_2$ solution containing 0.1 M TBABF$_4$.

[9] Bonadis, J. A.; Butler, W. M.; Percoraro, V. L.; Carrano, C. *Inorg. Chem.* **1987**, *26*, 1218. Bonadis et al. have reported the redox properties of VO(salen) in an acidic atmosphere and provided evidence for what they considered to be the disproportionation of VO(salen) to VO(salen)$^+$-(V) and a vanadium(III) species. Yamamoto, K.; Tsuchida, E.; Nishide, H.; Jikei, M.; Oyaizu, K. *Macromolecules* **1993**, *26*, 3432.

[10] Rechardson, D. E.; Taube, H. *Inorg. Chem.* **1981**, 20, 1278. $M - e = M^+{:}E_1^o$, $M^+ - e = M^{2+}{:}E_2^o$, $[M^+]/[M][M^{2+}] = \exp[(E_2^o - E_1^o)\text{-}25.69]$ at 298 K. On the basis of this equation decrease of the ($E_2^o - E_1^o$) results in a decrease of [M$^+$]. This means that the two-electron transfer is facilitated at the small potential separation.

[11] It is presumed that the reaction proceeds via formation of a vanadium−sulfide dication complex through a two-electron transfer. However, the structure of active sulfide species has not yet been identified.