

Surface-Mediated Reactions. 8. Oxidation of Sulfides and Sulfoxides with *tert*-Butyl Hydroperoxide and OXONE¹

Paul J. Kropp,* Gary W. Breton, John D. Fields, Jesse C. Tung, and Brian R. Loomis

Contribution from the Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27599-3290

Received November 18, 1999

Abstract: Silica gel and alumina have been found to mediate the oxidation of sulfides and sulfoxides with (CH₃)₃COOH and OXONE. With all combinations except (CH₃)₃COOH/alumina, sulfides were oxidized with reasonably good selectivity to sulfoxides. These studies afforded insights into the mechanisms of surface-mediated processes. Adsorption studies, combined with the effect of partial silylation of silica gel, indicate that oxidation of sulfides by (CH₃)₃COOH/silica gel occurs at least predominantly via nucleophilic attack by the sulfide on (CH₃)₃COOH, which is activated by being bound to isolated silanol sites on the silica gel surface (Scheme 2), whereas oxidation of sulfoxides involves nucleophilic attack by (CH₃)₃COOH on the sulfoxide, which is activated by being bound to associated silanol sites (Scheme 3). Oxidation of sulfoxides by (CH₃)₃COOH/alumina involves attack of (CH₃)₃COO⁻ on the sulfoxide bound to free Al⁺ sites on the surface (Scheme 4B). Mediation of oxidation by OXONE involves instead activation by its being dispersed on the surface of the adsorbent, providing contact between KOSO₂OOH, the oxidizing component, and the substrate. With silica gel, binding involves the associated silanol sites (Scheme 5). It is proposed that this is a general model for surface mediation of inorganic salts.

The surfaces of silica gel and alumina have proven to be remarkably versatile mediators of chemical reactivity. However, despite numerous useful synthetic applications,² little is known about the mechanisms through which these surfaces mediate reactivity. We report here the novel application of silica gel and alumina to mediate the oxidation of sulfides and sulfoxides by *tert*-butyl hydroperoxide and provide insight into the mechanisms of these processes.³ Comparison is made with the role of these surfaces in mediating the oxidation of sulfides and sulfoxides by OXONE.

Results and Discussion

***tert*-Butyl Hydroperoxide.** Although numerous reagents have been employed for the oxidation of sulfides,⁴ there is a continuing need for ones that are efficient, selective, and environmentally responsible. One oxidant that meets the last criterion, along with being inexpensive and safe to handle even in large quantities,^{5,6} is *tert*-butyl hydroperoxide [(CH₃)₃COOH]. However, used alone it is a poor oxidizing agent. Thus treatment of dibutyl sulfide (**1a**) with (CH₃)₃COOH afforded only very slow oxidation to the corresponding sulfoxide **2a** (Table 1). However, in the presence of silica gel oxidation occurred rapidly to afford sulfoxide **2a** with minimal over-oxidation to sulfone

3a.^{7,8} Treatment of sulfide **1a** with 2.0 mol equiv of (CH₃)₃COOH in the presence of silica gel afforded sulfone **3a** in high yield, which could also be obtained by oxidation of sulfoxide **2a** (Table 2). Thus selective oxidation to either the sulfoxide or sulfone could be attained by simple stoichiometric control.

Despite the usual sensitivity of silica gel to moisture,⁹ similar results were obtained using either anhydrous or the less expensive 70% aqueous (CH₃)₃COOH. Besides being environmentally benign, silica gel is recyclable; comparable results were obtained using silica gel that had been previously used and recycled five times.

Similar results were obtained with the aryl analogues **1b,c** and **2b,c** (Table 3) and 4-methylthiane (**4**) (Table 4). Despite being surface-mediated, oxidation over silica gel showed no obvious steric effect; partial oxidation of sulfide **4** afforded the

(5) (CH₃)₃COOH is commercially available, has high thermal stability, and is safer to handle than CH₃CO₃H or HOOH because of its much lower sensitivity to decomposition catalyzed by trace metallic impurities.⁶ Moreover, its byproduct of oxidation, (CH₃)₃COH, is easily removed from reaction mixtures by distillation or rotary evaporation, obviating the need for aqueous workup as required for the traditionally used peroxyacid oxidants. This is particularly useful since the products of many oxidations are water soluble.

(6) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63–73.

(7) To provide qualitative rate data, oxidations were terminated prior to total conversion. For preparative purposes, complete oxidation can be effected by using longer reaction times or employing a small excess of oxidant.

(8) Oxidation with 30% aqueous HOOH gave lower yields of sulfoxide **2a** or sulfone **3a**. The use of lower ratios of silica gel to (CH₃)₃COOH afforded slower oxidation. Tung, J. C. Unpublished results.

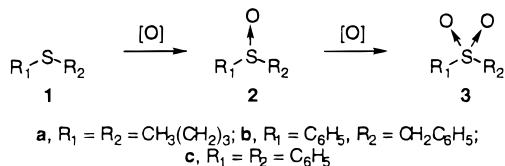
(9) See, for example: (a) Kropp, P. J.; Daus, K. A.; Tubergen, M. W.; Kepler, K. D.; Wilson, V. P.; Craig, S. L.; Baillargeon, M. M.; Breton, G. W. *J. Am. Chem. Soc.* **1993**, *115*, 3071–3079. (b) Kropp, P. J.; Crawford, S. D. *J. Org. Chem.* **1994**, *59*, 3102–3112. (c) Kropp, P. J.; Breton, G. W.; Craig, S. L.; Crawford, S. D.; Durland, W. F., Jr.; Jones, J. E., III; Raleigh, J. S. *J. Org. Chem.* **1995**, *60*, 4146–4152.

(1) Part 7: Foti, C. J.; Fields, J. D.; Kropp, P. J. *Org. Lett.* **1999**, *1*, 903–904.

(2) For reviews, see: (a) *Preparative Chemistry Using Supported Reagents*; Laszlo, P., Ed.; Academic: San Diego, 1987. (b) *Solid Supports and Catalysts in Organic Synthesis*; Smith, K., Ed.; Ellis Horwood: New York, 1992. (c) Clark, J. H. *Catalysis of Organic Reactions by Supported Inorganic Reagents*; VCH: New York, 1994. (d) Kabalka, G. W.; Pagni, R. M. *Tetrahedron* **1997**, *53*, 7999–8605.

(3) For a preliminary report of a portion of these studies, see: Breton, G. W.; Fields, J. D.; Kropp, P. J. *Tetrahedron Lett.* **1995**, *36*, 3825–3828.

(4) *Syntheses of Sulphones, Sulphoxides and Cyclic Sulphides*; Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester, 1994.

Table 1. Oxidation of Sulfide **1a** with (CH₃)₃COOH^a

adsorbent	solvent	time, h	yield, % ^b		
			1a	2a	3a
none	CDCl ₃	24	49	45	
SiO ₂	CH ₂ Cl ₂	0.5	1	88	7
SiO ₂	CF ₃ C ₆ H ₅	0.5		92	5
SiO ₂ ^c	CH ₂ Cl ₂	0.5	7	83	10
SiO ₂ ^d	CH ₂ Cl ₂	0.5	3	86	4
SiO ₂ ^e	CH ₂ Cl ₂	0.5	7	86	6
SiO ₂ (OSiMe ₃) ^f	CH ₂ Cl ₂	0.5	8	80	4
SiO ₂ ^g	CH ₂ Cl ₂	4		19	81
Al ₂ O ₃	CH ₂ Cl ₂	4	37	13	47
Al ₂ O ₃ (neut) ^h	CH ₂ Cl ₂	4	75	18	2
Al ₂ O ₃ (C ₅ H ₅ N) ⁱ	CH ₂ Cl ₂	4	76	18	

^a Conducted using 1.0 mol equiv of 70% aqueous (CH₃)₃COOH according to the standard procedure with solvent described in the Experimental Section unless otherwise indicated. ^b Isolated yields except for the run conducted in CDCl₃ solution, in which case the reaction mixture was analyzed by ¹H NMR spectroscopy relative to an internal standard. ^c Run on a 6.0-mmol scale with silica gel that had been previously used and recycled five times. ^d Anhydrous solution of (CH₃)₃COOH in decane used. ^e Fisher S-157. ^f Partially silylated as described in the Experimental Section. ^g 2.0 mol equiv of (CH₃)₃COOH used. ^h Pretreated with 0.08 mmol/g (0.20 mmol) of CH₃SO₃H in 5 mL of CH₂Cl₂. ⁱ Pretreated with 0.08 mmol/g (0.20 mmol) of pyridine in 5 mL of CH₂Cl₂.

Table 2. Oxidation of Sulfoxide **2a** with (CH₃)₃COOH^a

adsorbent	yield, %	
	2a	3a
none ^b	96	
SiO ₂	1	93
SiO ₂ (OSiMe ₃) ^c	50	24
Al ₂ O ₃	6	92
Al ₂ O ₃ (neut) ^d	97	3
Al ₂ O ₃ (C ₅ H ₅ N) ^e	80	20
Al ₂ O ₃ ^f	83	16

^a Conducted for 4 h according to the standard procedure with CH₂Cl₂ as solvent unless otherwise indicated. ^b Run in CDCl₃ solution for 24 h; analyzed by ¹H NMR spectroscopy relative to diphenylmethane as an internal standard. ^c Partially silylated as described in the Experimental Section. ^d Pretreated with 0.08 mmol/g (0.20 mmol) of CH₃SO₃H in 5 mL of CH₂Cl₂. ^e Pretreated with 0.08 mmol/g (0.20 mmol) of pyridine in 5 mL of CH₂Cl₂. ^f Reverse order of addition; (CH₃)₃COOH added before sulfoxide **2a**.

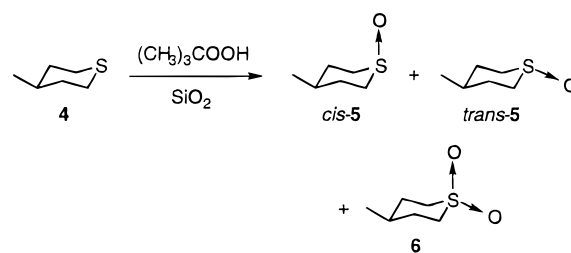
Table 3. Oxidation of Sulfides **1b,c** and Sulfoxides **2b,c** with (CH₃)₃COOH/Silica Gel^a

substrate	time, h	yield, %		
		1	2	3
1b	1	5	93	tr ^b
2b	6		5	95
1c	6	8	73	14
2c	24		tr ^b	95

^a Conducted according to the standard procedure with CH₂Cl₂ as solvent. ^b Trace.

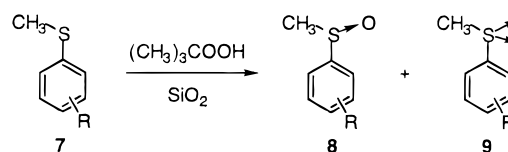
diastereomeric sulfoxides **5** in a cis/trans ratio similar to that obtained previously by solution-phase oxidation of sulfide **4** with (CH₃)₃COOH at 50 °C for 100 h.¹⁰ Finally, a study of substituent

(10) Johnson, C. R.; McCants, D., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 1109–1114.

Table 4. Oxidation of 4-Methylthiane (**4**) with (CH₃)₃COOH/Silica Gel^a

equiv ^b	yield, %		
	4	5	6
1.0		81 ^c	9
2.0			83

^a Conducted for 4 h according to the standard procedure with CH₂Cl₂ as solvent. ^b [(CH₃)₃COOH]/[**4**]. ^c cis-5/trans-5 = 0.59 at 25% conversion.

Table 5. Oxidation of Sulfides **7** with (CH₃)₃COOH/Silica Gel^a

R	time, min	yield, %		
		7	8	9
4-OCH ₃	5	4	94	2
H	15	3	94	3
3-OCH ₃	20	3	95	2
4-NO ₂	30	7	89	4

^a Conducted according to the standard procedure with CH₂Cl₂ as solvent.

effects revealed the following relative rates of oxidation of the phenyl sulfides **7**: R = 4-OCH₃ > R = H > R = 3-OCH₃ > R = 4-NO₂ (Table 5).

Somewhat different behavior was observed over alumina, which afforded slow oxidation of sulfide **1a** (Table 1) but readily mediated the oxidation of sulfoxide **2a** to sulfone **3a** (Table 2). Similarly, oxidation of thianthrene 5-oxide (**10**) over alumina gave principally the sulfone **11**, whereas over silica gel the bissulfoxide **12** was the major product (Table 5).

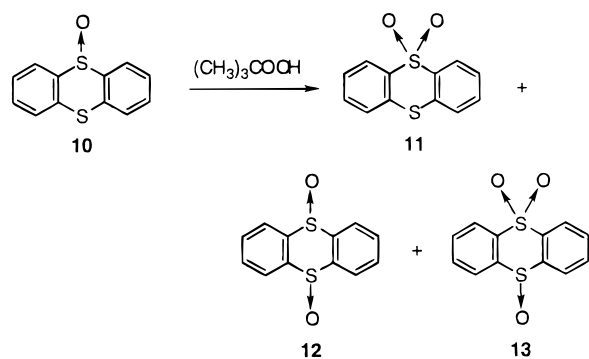
OXONE. This commercial oxidant consists of a 2:1:1 mixture of the active ingredient KOSO₂OOH, along with KHSO₄ and K₂SO₄, respectively. Although reactive toward a variety of functional groups, it has received relatively little use in organic synthesis because it is only soluble in very polar solvents, thus usually necessitating the use of aqueous conditions.¹¹ It has been reported, however, that OXONE dispersed on “wet alumina” suspended in organic solvents effects oxidation of phenyl alkyl sulfides to the corresponding sulfoxides and sulfones.¹² We have found that oxidation of sulfide **1a** and sulfoxide **2a** occurs equally well whether the OXONE is dispersed on either alumina or silica gel (Table 7).¹³

Solvent-Free Oxidations. Surface-mediated reactions have traditionally been conducted using a stirred suspension of the

(11) Kennedy, R. J.; Stock, A. M. *J. Org. Chem.* **1960**, *25*, 1901–1906.

(12) Greenhalgh, R. P. *Synlett* **1992**, 235–236. See also: Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Epifano, F.; Rosati, O. *Synlett* **1996**, 767–768.

(13) We have found that the need to add water varies from batch to batch of OXONE, which is hygroscopic. Thus the reagent might better be described as “moist” OXONE supported on alumina or silica gel.

Table 6. Oxidation of Thianthrene 5-Oxide (**10**) with (CH₃)₃COOH^a

catalyst	yield, %		distribution, %			X _{SO} ^b
	10	11–13	11	<i>cis</i> - 12	<i>trans</i> - 12	
SiO ₂	12	81	19	4	59	0.31
Al ₂ O ₃	39	58	79			0.83

^a Conducted as described in the Experimental Section. ^b (**11** + **13**)/(**11** + **13**) + (**12** + **13**); see ref 24.

Table 7. Oxidation of Sulfide **1a** and Sulfoxide **2a** with OXONE^a

substrate	adsorbent	time, h	yield, %		
			1a	2a	3a
1a		4	100		
1a	SiO ₂	1	7	88	5
1a	SiO ₂ (OSiMe ₃) ^b	1	64	22	
2a	SiO ₂	16		14	86
2a	SiO ₂ (OSiMe ₃) ^b	16		96	
1a	Al ₂ O ₃	4	6	89	4
1a	Al ₂ O ₃ (neut) ^c	4	5	95	
1a	Al ₂ O ₃ (C ₅ H ₅ N) ^d	4	6	78	16
2a	Al ₂ O ₃	16		11	89
2a	Al ₂ O ₃ (neut) ^c	16		54	42
2a	Al ₂ O ₃ (C ₅ H ₅ N) ^d	16			98

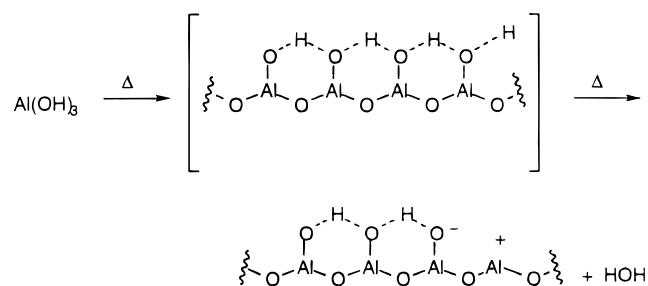
^a Conducted according to the standard procedure with CH₂Cl₂ as solvent unless otherwise indicated. ^b Partially silylated as described in the Experimental Section. ^c Pretreated with 0.08 mmol/g (0.20 mmol) of CH₃SO₃H in 5 mL of CH₂Cl₂. ^d Pretreated with 0.08 mmol/g (0.20 mmol) of pyridine in 5 mL of CH₂Cl₂.

Table 8. Solvent-Free Oxidation of Sulfide **1a** and Sulfoxide **2a** with (CH₃)₃COOH/Silica Gel^a

substrate	(CH ₃) ₃ COOH	time, s	yield, %		
			1a	2a	3a
1a	anhydrous	^b	2	88	6
1a	anhydrous	40	4	78	14
1a	70% aqueous	40	5	86	6
2a	70% aqueous	80		5	91
2a	70% aqueous ^c	80		10	90

^a Conducted according to the standard solvent-free procedure described in the Experimental Section with microwave heating unless otherwise indicated. ^b Maintained at 25 °C for 0.5 h. ^c Sulfoxide **2a** and (CH₃)₃COOH adsorbed to separate 1.25-g samples of silica gel that were combined and mixed by tumbling prior to heating.

adsorbent in an organic solvent.² Although the choice of solvent can affect the rate or selectivity of reaction,⁹ indicating that the solvent can play a role, it has become increasingly evident that a solvent is frequently unnecessary.² Indeed, direct adsorption of sulfide **1a**, followed by (CH₃)₃COOH, onto silica gel with tumbling at 25 °C resulted in formation of sulfoxide **2a** in 0.5 h (Table 8), the same time required for oxidation in the presence of CH₂Cl₂. Reaction time was dramatically reduced to 40 s by microwave irradiation. Although microwave-assisted reactions are normally conducted with moistened adsorbent to facilitate

Scheme 1

heating, sulfide **1a** exhibited similar rates of oxidation with either anhydrous or aqueous (CH₃)₃COOH, whether the silica gel was pretreated with additional water or not. However, the amount of over-oxidation to sulfone **3a** decreased with increasing amounts of water.¹⁴

Supported reagents have traditionally been prepared by evaporating a solution of the reagent on the adsorbent and solvent-free reactions conducted by first evaporating a solution of the substrate on the supported reagent. We have found that evaporative deposition is unnecessary. Simply mixing the neat reagent and substrate with the adsorbent is adequate. It is not even critical that initial coverage of the surface be uniform; a split run in which sulfoxide **2a** and (CH₃)₃COOH were initially adsorbed to separate portions of silica gel that were then mixed afforded sulfone **3a** in a yield comparable to that obtained by the conventional procedure (Table 8).

Mechanisms. A. Surface Structures. γ -Alumina is prepared by flash calcination of hydrated aluminas (Scheme 1).¹⁵ Although the initially formed surface is totally hydroxylated, at the temperatures required for the preparation some chemisorbed water is subsequently lost through condensation of adjacent OH groups, leaving oxide ions in the outermost layer and exposed aluminum ions in the next lower layer.¹⁶ Thus activated alumina is amphoteric, containing basic and Lewis acidic sites in close proximity, along with residual OH groups. The involvement of O⁻ sites in surface-mediated processes can be probed by neutralization with acid and Al⁺ sites by complexation with pyridine.¹⁷

The surface of silica gel consists of silanol groups that fall into two classes.¹⁶ The majority of the groups have O–O distances of approximately 500 pm, well beyond the limit for internal hydrogen bonding, and are thus isolated (**14**). For silica gel that has been equilibrated at 120 °C, approximately 15% of the silanol sites are geminal and hence sufficiently close to form hydrogen-bonded chains through interaction with adjacent groups (**15**).¹⁸ Little attention has been given to which sites are involved in the adsorption of various types of substrates and in various types of surface-mediated reactivity.¹⁹ However, the

(14) Solvent-free oxidation of sulfide **1a** with (CH₃)₃COOH/alumina or OXONE over either silica gel or alumina gave inferior results.

(15) Diddams, P. In *Solid Supports and Catalysts in Organic Synthesis*; Smith, K., Ed.; Ellis Horwood and PTR Prentice Hall: New York, 1992; p 13.

(16) For descriptions of current models for the surfaces of alumina and silica gel, see: (a) Knözinger, H. In *The Hydrogen Bond. III. Dynamics, Thermodynamics and Special Systems*; Schuster, P., Zundel, G., Sandorfy, C., Eds.; North-Holland: Amsterdam, 1976; Chapter 27. (b) Dufour, P.; Houtman, C.; Santini, C. C.; Nédéz, C.; Basset, J. M.; Hsu, L. Y.; Shore, S. G. *J. Am. Chem. Soc.* **1992**, *114*, 4248–4257.

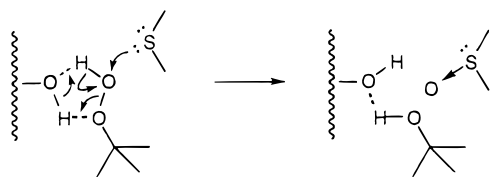
(17) For a review of the quenching of Al⁺ sites on alumina surfaces, see: Knözinger, H. *Adv. Catal.* **1976**, *25*, 184–271. The A540 Fisher alumina used in the current study has 0.08 mmol/g of strongly basic sites and, presumably, an equivalent number of Al⁺ sites. Foti, C. J. Unpublished results.

(18) Sindorf, D. W.; Maciel, G. E. *J. Am. Chem. Soc.* **1983**, *105*, 1487–1493.

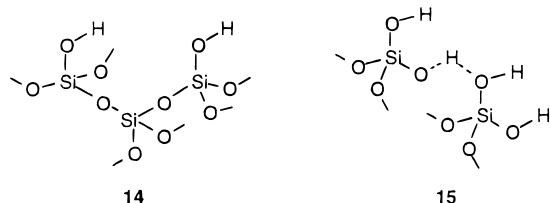
Table 9. Adsorption onto Silica Gel and Alumina^a

substrate	adsorbent	adsorption, %	
		substrate	(CH ₃) ₃ COOH
	SiO ₂		88
	SiO ₂ (OSiMe ₃) ^b		71
	Al ₂ O ₃		79
1a	SiO ₂	82 ^c	81 ^c
1a	SiO ₂ (OSiMe ₃) ^b	29	80
1a	Al ₂ O ₃	tr ^d	78
2a	SiO ₂	99	70
2a	SiO ₂ (OSiMe ₃) ^b	64	25
2a	Al ₂ O ₃	20	49
3a	Al ₂ O ₃	6	75

^a Conducted using 1.0 mmol of substrate/2.5 g of alumina as described in the Experimental Section unless otherwise indicated. ^b Partially silylated as described in the Experimental Section. ^c Analyzed 5 min after the addition of (CH₃)₃COOH. ^d Trace.

Scheme 2

hydrogen-bonded silanol groups are more acidic (pK_a 5–7) than their isolated counterparts (pK_a 9.5) and react preferentially with hexamethyldisilazane,²⁰ affording a convenient method for probing their involvement.



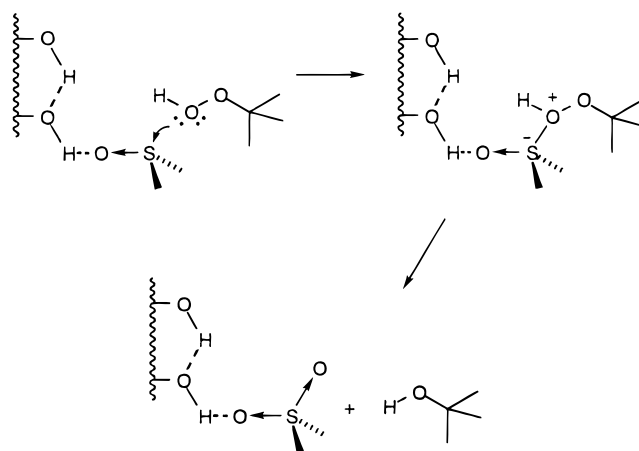
B. tert-Butyl Hydroperoxide. Under the conditions used, (CH₃)₃COOH was substantially adsorbed from solution onto the silica gel surface (Table 9). Since the extent of adsorption was almost identical onto silica gel that had been partially silylated, adsorption evidently occurs predominantly at the isolated sites — presumably because there it can occur via reciprocal hydrogen bonding, in which both the silanol group and the hydroperoxide each serve as a hydrogen bond donor and acceptor (Scheme 2), without disrupting existing hydrogen bonding as would be required at the associated sites.²¹ The resulting complex is poised for nucleophilic attack by the sulfide at the surface–solution interface (electrophilic oxidation²²), resulting in two proton shifts and the transfer of an oxygen atom to the sulfide (Scheme 2). As expected for a process centered at the isolated sites, partial silylation of the silica gel had no significant effect on the rate of oxidation of sulfide **1a** (Table 1). Electrophilic oxidation is supported by the value of 0.31 for X_{SO} observed on oxidation of thianthrene 5-oxide (**10**) (Table 6),²³ as well as by the relative rates of oxidation of the substituted sulfides **7**: R = 4-OCH₃ > R = H > R = 3-OCH₃ > R = 4-NO₂ (Table 5).

(19) See, however, ref 9.

(20) Sindorf, D. W.; Maciel, G. E. *J. Phys. Chem.* **1982**, *86*, 5208–5219.

(21) For a proposed similar cyclic hydrogen-bonded interaction of (CH₃)₃COOH with alcohols, see: Dankleff, M. A. P.; Curci, R.; Edwards, J. O.; Pyun, H.-Y. *J. Am. Chem. Soc.* **1968**, *90*, 3209–3218.

(22) By convention, the mechanisms of oxidation reactions are characterized in terms of the mode of action of the oxidant.

Scheme 3

In principle, oxidation of sulfoxides to sulfones could occur via an analogous mechanism. However, under the reaction conditions sulfoxide **2a** was quantitatively adsorbed to the surface (Table 9). Adsorption at the more acidic, associated sites apparently activates the sulfoxide for nucleophilic attack by unbound (CH₃)₃COOH (Scheme 3) since partial silylation of these sites substantially reduced the rate of oxidation (Table 2). Hence, there is a reversal in mechanism, from electrophilic to nucleophilic,²² on going from sulfide to sulfoxide.

Oxidation of sulfide **1a** by (CH₃)₃COOH occurred only sluggishly over alumina and afforded substantial over-oxidation to sulfoxide **2a** (Table 1), while oxidation of sulfoxide **2a** occurred readily (Table 2). In both cases neutralization substantially quenched oxidation. Hence the active species in the predominant pathway for each oxidation is apparently (CH₃)₃COO[−], formed by reaction of (CH₃)₃COOH with O[−] sites of the basic alumina. This is consistent with the X_{SO} value of 0.83 obtained on oxidation of thianthrene 5-oxide (**10**) (Table 6), which is quite different from the value of 0.31 observed for (CH₃)₃COOH/silica gel but in the range (0.5–1.0) exhibited by nucleophilic oxidants in solution.²³ Oxidation of sulfoxide **2a** was also substantially quenched by adsorption of pyridine to the alumina. Hence the sulfoxide is apparently activated toward nucleophilic attack by (CH₃)₃COO[−] through adsorption to the Al⁺ sites (Scheme 4B), in analogy with its activation toward nucleophilic attack by (CH₃)₃COOH on adsorption to the associated sites of silica gel.²⁴

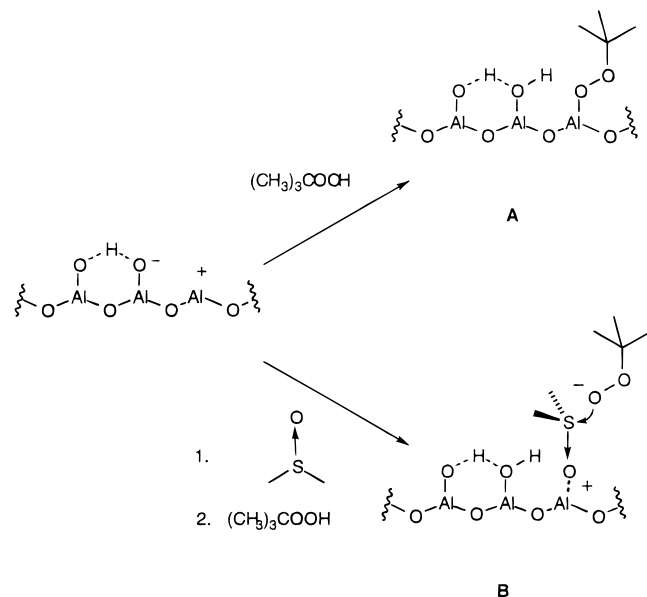
The order of addition to alumina is critical; adsorption of (CH₃)₃COOH first substantially quenched oxidation of sulfoxide **2a** (Table 2). This is undoubtedly due to association of the initially formed (CH₃)₃COO[−] with the Al⁺ sites (Scheme 4, A), both rendering the anion unavailable for reaction and blocking the Al⁺ sites from adsorption by the sulfoxide.²⁵ Little attention has previously been given to the order of addition of the reagent and substrate in surface-mediated reactivity. Most often the reagent is adsorbed first, which is deleterious in this case.

(23) Thianthrene 5-oxide (**10**) has been proposed as a model system for differentiating between nucleophilic and electrophilic oxidation: Adam, W.; Golsch, D. *J. Org. Chem.* **1997**, *62*, 115–119. Nucleophilic oxidants typically display X_{SO} values >0.5 and electrophilic oxidants values <0.5.

(24) Only 20% of sulfoxide **2a** was adsorbed (Table 9), corresponding to coverage of all of the Al⁺ sites.¹⁷ However, since sulfone **3a** is less strongly adsorbed, it will equilibrate with remaining sulfoxide **2b**, permitting further oxidation.

(25) See: (a) Leffler, J. E.; Miller, D. W. *J. Am. Chem. Soc.* **1977**, *99*, 480–483. (b) Rebek, J.; McCready, R. *Tetrahedron Lett.* **1979**, *45*, 4337–4338.

Scheme 4



C. Solvent-Free Oxidations. Presumably the oxidations of sulfide **1a** and sulfoxide **2a** in the absence of solvent (Table 8) occur via analogous mechanisms. The split run in which sulfoxide **2a** and (CH₃)₃COOH were adsorbed to separate portions of silica gel indicates that substantial migration occurs on the surface.²⁶ Since similar, although slower, oxidation occurred without heating, the effect of microwave irradiation is most likely simply thermal.²⁷

D. OXONE. Amazingly, simple mixing of solid OXONE with moist silica gel or alumina, either as a suspension in CH₂Cl₂ or solvent-free, apparently results in its dispersion, or at least dispersion of the active component KOSO₂OOH, on the surface of the adsorbent, facilitating oxidation. A small amount of water must be present to facilitate adsorption,²⁸ as well as promote heating when microwave irradiation is used. Although a suspension of moist OXONE in CH₂Cl₂ will effect oxidation of sulfide **1a** without an adsorbent present,¹ reaction is substantially faster in the presence of silica gel. Moreover, silylation of the associated sites of silica gel slowed the oxidation of sulfide **1a** and quenched that of sulfoxide **2a** (Table 7). Thus, when present, silica gel is involved — through adsorption at the associated sites (Scheme 5),²⁹ facilitating contact between the reactants for electrophilic oxidation. Sulfoxide **2a** underwent substantially slower oxidation than sulfide **1a** with OXONE over both silica gel and alumina (Table 7), as expected from both its weaker nucleophilicity and its higher degree of adsorption to the surfaces (Table 9).

Oxidation of sulfide **1a** by OXONE/alumina was insensitive to either neutralization of the O⁻ sites or the presence of pyridine, which complexes with the Al⁺ sites (Table 7). On the other hand, oxidation of sulfoxide **2a** was partially quenched by neutralization but accelerated by the presence of pyridine

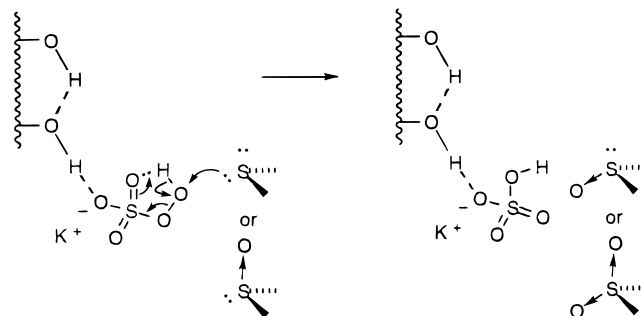
(26) For a summary of other studies showing mobility of molecules on the surfaces of silica gel and alumina, see: Worrall, D. R.; Williams, S. L.; Wilkinson, F. *J. Phys. Chem. B* **1997**, *101*, 4709–4716.

(27) Also, see: Raner, K. D.; Strauss, C. R.; Vyskoc, F.; Mokbel, L. *J. Org. Chem.* **1993**, *58*, 950–953.

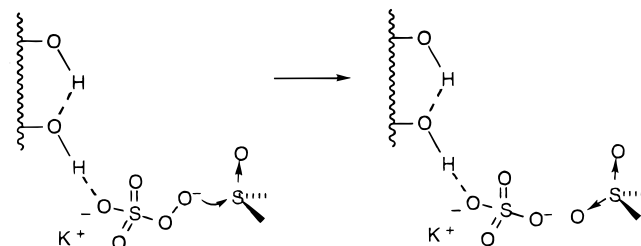
(28) The role of water in facilitating reactions involving solid reagents has been attributed to breakup of the crystal lattice: (a) Carpino, L. A.; Sau, A. C. *J. Chem. Soc., Chem. Commun.* **1979**, 514. (b) Tanaka, M.; Koyanagi, M. *Synthesis* **1981**, 973–975. (c) Hirano, M.; Yakabe, S.; Monobe, H.; Morimoto, T. *Can. J. Chem.* **1977**, *75*, 1905–1912.

(29) Alternatively, adsorption might be viewed as involving OXONE and adsorbed water at the associated sites.

Scheme 5



Scheme 6



(Table 7). Oxidation in this case evidently involves competing reaction of the sulfoxide with KOSO₂OOH as in Scheme 5 and with KOSO₂OO⁻ as in Scheme 6. Neutralization quenches the latter process, which is faster. Treatment of the alumina with pyridine quenches competitive binding of the sulfoxide with Al⁺ sites, which normally slows oxidation. This contrasts with oxidation by (CH₃)₃COOH/alumina, which involves attack of (CH₃)₃COO⁻ on sulfoxide bound to Al⁺ sites (Scheme 4B) and is accelerated by the binding. Being surface-bound itself, KOSO₂OO⁻ is unable to react with bound sulfoxide.

Concluding Remarks

In summary, oxidation of sulfides to sulfoxides occurs readily with (CH₃)₃COOH over silica gel or with OXONE over either silica gel or alumina; reaction is fastest with (CH₃)₃COOH over silica gel, whereas the greatest selectivity is afforded by OXONE over neutralized alumina. Oxidation of sulfoxides to sulfones occurs with both (CH₃)₃COOH and OXONE over either silica gel or alumina but more rapidly with (CH₃)₃COOH.

In addition to providing convenient, environmentally benign methods for the oxidation of sulfides and sulfoxides, the present studies have afforded significant insights into the mechanistic aspects of surface-mediated behavior. Mediation by silica gel has been found to involve principally either the isolated or associated sites, depending on the reagent and substrate. Also, despite the common concept of a “supported reagent”, either the reagent or the substrate may be the bound species involved in reaction. Similarly, the O⁻ and Al⁺ sites of alumina may be involved or not. Thus each surface-mediated reaction requires individual mechanistic analysis. Depending on the mechanism, the order of adsorption to the surface may be critical for optimal results, as in the oxidation of sulfoxides with (CH₃)₃COOH/alumina. It has also been shown that surface-mediated reactions can be conducted by simple mixing of the adsorbent, reagent, and substrate in the dry state followed by appropriate heating, without any use of solvent except to extract the product from the adsorbent — thereby extending the flexibility and environmental friendliness of these reactions. Our studies in the fascinating realm of surface-mediated reactivity continue,

including pursuing spectroscopic evidence for the mechanisms proposed here.

Experimental Section

Standard Procedure with Solvent. Into a 25-mL round-bottomed flask was weighed 2.5 g of Merck 10181 silica gel or Fisher A540 alumina that had been equilibrated with the atmosphere at 120 °C for at least 48 h. The flask was stoppered and the contents allowed to cool to 25 °C. For oxidations with OXONE, 0.5 mL of water was added and the adsorbent was tumbled on a rotary evaporator at atmospheric pressure until uniformly free-flowing.³⁰ A solution of 1.0 mmol of sulfide or sulfoxide in 5 mL of CH₂Cl₂ was added with stirring followed by 137 μL (1.0 mmol) of 70% aqueous (CH₃)₃COOH or 462 mg of OXONE (1.5 mmol of KOSO₂OOH). The slurry was stirred at 25 °C for the specified amount of time. The adsorbent was then removed by vacuum filtration and washed with 100 mL of ethyl acetate. The combined organic fractions were washed with 30 mL of a saturated, aqueous solution of FeSO₄, dried several hours over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was chromatographed through silica gel by elution with 4:1 hexanes–ethyl acetate.

Standard Solvent-Free Procedure. Into a 25-mL round-bottomed flask was weighed 2.5 g of Merck 10181 chromatographic silica gel that had been equilibrated with the atmosphere at 120 °C for at least 48 h. The flask was stoppered and the contents allowed to cool to 25 °C. The substrate was added without solvent and the resulting mixture tumbled on a rotary evaporator at atmospheric pressure until uniformly free-flowing. The oxidant was then added and the mixture again tumbled. After being heated for the specified period of time,³¹ the mixture was allowed to cool to 25 °C and was washed with 100–200 mL of ethyl acetate. The adsorbent was collected by vacuum filtration and the filtrate concentrated under reduced pressure. The residue was weighed and analyzed by ¹H NMR spectroscopy.

Partial Oxidation of Tetrahydro-4-methyl-2H-thiopyran (4). Oxidation was conducted according to the standard procedure over SiO₂ with 0.25 equiv of (CH₃)₃COOH. The ratio of the diastereomeric sulfoxides **5** was determined by integration of the diagnostic signals at δ 3.18 (*trans*-**5**) and 2.88 (*cis*-**5**).

(30) The need for this step varied from batch to batch of OXONE.

(31) Microwave heating was conducted using a commercial 500-W Little Litton oven.

Oxidation of Thianthrene 5-Oxide (10). Oxidations were conducted for 24 h according to the standard procedure except that the product mixture was dissolved in CH₂Cl₂ and analyzed by HPLC (5-μm LiChrosorb S 60 column, 1% CH₃OH in CH₂Cl₂, flow rate of 1 mL/min, UV detection at 254 nm) relative to a known amount of thianthrene added as an internal standard.

Adsorption Studies. Into a 25-mL round-bottomed flask was weighed 2.5 g of Merck 10181 chromatographic silica gel or Fisher A540 chromatographic alumina that had been equilibrated to the atmosphere at 120 °C for at least 48 h. The flask was stoppered, and the contents allowed to cool to 25 °C. A solution of 1.0 mmol each of substrate and diphenylmethane, as an internal standard, in 5 mL of CH₂Cl₂ was added to the flask with stirring. After 5 min 137 μL (1.0 mmol) of 70% aqueous (CH₃)₃COOH was added. The slurry was stirred at 25 °C for 20 min, after which a 250-μL aliquot was removed from the supernatant liquid, evaporated to dryness, and analyzed by ¹H NMR spectroscopy.

Silylation of Silica Gel. In a modification of the procedure by Maciel,²⁰ 20.0 g of Fisher S-157 silica gel that had been equilibrated with the atmosphere at 120 °C for at least 48 h was weighed into a 200-mL round-bottomed flask. The flask was then stoppered and the contents allowed to cool to 25 °C. A solution of 3.0 mL (14.2 mmol) of hexamethyldisilazane in 40 mL of toluene was added and the resulting slurry was mixed slowly on a rotary evaporator at 25 °C for 20 h. The solvent was then removed under aspirator pressure at 65 °C for 1.5 h and then 0.5 mmHg at 120 °C for 1.5 h. After being equilibrated with the atmosphere at 120 °C for at least 48 h, the silylated silica gel was weighed. The increase in weight for several runs was 1.45–1.57 g, corresponding to 102–110% silylation of the available associated silanol sites.

Acknowledgment. Generous financial support by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the University of North Carolina at Chapel Hill/Hoechst Celanese Corporation Discovery Awards Program is gratefully acknowledged, as is a PPG Summer Internship awarded to B.R.L.

Supporting Information Available: Description of starting sulfides and characterization of products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA9940569