Chemistry of Sulfenic Acids. 3. Studies of Sterically Hindered Sulfenic Acids Using Flash Vacuum Pyrolysis

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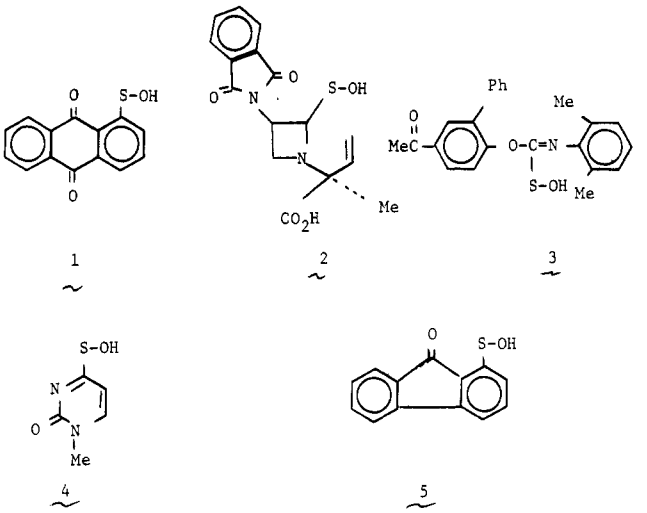
Flash vacuum pyrolysis (FVP) of sulfoxides containing β-hydrogen atoms affords sulfenic acids (RSOH) in good concentration under conditions where they are stable. The application of this technique to the synthesis and study of sterically hindered sulfenic acids **12a–e** is described. The principal or primary reaction of simple sulfenic acids prepared in this manner is dehydration to thiosulfinates **13** (eq 1). Steric inhibition to dehydration (eq 1) appears to only be of importance for 2-methyl-2-propanesulfenic acid (**12a**) which was trapped in good yield with methyl propiolate to afford **16a**. 2,4,6-Tri-*tert*-butylbenzenesulfenic acid (**12e**) appears to be destabilized as a consequence of interaction between the SOH and adjacent *tert*-butyl groups. In the pyrolysis section of the apparatus, **12e** decomposes to phenol **21** and aryl radical **22**, which reacts further. Thermolysis of sulfoxides generates the sulfenic acids **12a–e** in very low concentration at any one time. The products of sulfenic acids generated in this way result from secondary reactions of the corresponding thiosulfinates.

The importance of sulfenic acid (RSOH) intermediates in mechanistic organic sulfur chemistry is well recognized.[1,2] There is growing awareness that these species are involved in regulating the catalytic activity of certain enzyme systems.[3] Despite numerous attempts to isolate sulfenic acids, only a few very special examples are known. Several are derivatives of 1-anthraquinone sulfenic acid (**1**, Chart I), first prepared by Fries in 1912.[4] In 1974 Chou and co-workers isolated a stable penicillin (azetidinone) sulfenic acid (**2**).[5] The X-ray structure of (2-phenyl-4-acetylphenoxy)[(2,6-dimethylphenyl)imino]methanesulfenic acid (**3**) has been described.[6] 1-Methyluracil-4-sulfenic acid (**4**),[7] 2-methyl-2-propanesulfenic acid,[8] and various protein sulfenic acids[3,9] are claimed to be stable in solution.

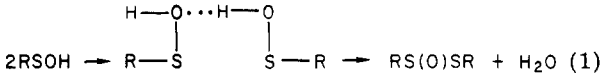
The stability of sulfenic acids **1–4** has been attributed to electronic and intramolecular hydrogen bonding effects, although the closely related 9-oxofluorene-1-sulfenic acid (**5**) could not be isolated.[10]

Steric effects may also play some role in stabilizing **1–4** and have been suggested as primarily responsible for the stability of 2-methyl-2-propanesulfenic acid in solution. In proteins the SOH group may reside in clefts in the globular protein. This and related structural features in 2-methyl-2-propanesulfenic acid may inhibit the attack of various substrates on the sulfenic acid. In simple sulfenic acids this means disrupting the intermolecular formation

Chart I



of complex **6**, believed to be a prerequisite for thiosulfinate formation (eq 1).[1,2,11,12]



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We describe in this paper the application of the flash vacuum pyrolysis (FVP) technique to the synthesis and study of sulfenic acids. This technique has been used to investigate the influence of steric hindrance on sulfenic acid reactivity.

Synthesis of Sulfenic Acids. Sulfenic acid chemistry is not well understood. High sulfenic acid reactivity and scarcity of preparation conditions convenient for study have hindered investigation of these species. The principal reactions of sulfenic acids are seldom observed directly. Much of our knowledge has been derived indirectly, via rationalization of end reaction products.[2]

The principal reaction of sulfenic acids appears to be thiosulfinate formation (eq 1).[1,2,11,12] Thiosulfinates [RS(O)SR] are labile and thermally disproportionate, via free radicals, to disulfides (RSSR) and thiosulfonates (RSO_2SR)

(1) Part 2: Davis, F. A.; Jenkins, R. H., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 7967.
(2) For leading references on the chemistry of sulfenic acids see: (a) Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, *17*, 65. (b) Hogg, D. R., *Compr. Org. Chem.* **1979**, *4*, 261. (c) Davis, F. A.; Rizvi, S. Q. A.; Ardecky, R.; Gosciniak, D. J.; Friedman, A. J.; Yocklovich, S. G., *J. Org. Chem.* **1980**, *45*, 1650. (d) Davis, F. A.; Friedman, A. J., Naidr, U. K. *J. Am. Chem. Soc.* **1978**, *100*, 2844.
(3) Allison, W. A. *Acc. Chem. Res.* **1976**, *9*, 293.
(4) (a) Fries, K. *Chem. Ber.* **1912**, *45*, 2965. (b) Bruice, T. C.; Markiw, P. T. *J. Am. Chem. Soc.* **1957**, *79*, 3150. (c) Jenny, W., *Helv. Chim. Acta* **1958**, *41*, 326.
(5) Chou, T. S.; Burgtorf, J. R.; Ellis, A. L.; Lammert, S. R.; Kukolja, S. P. *J. Am. Chem. Soc.* **1974**, *96*, 1609.
(6) Kato, K. *Acta Crystallogr., Sect. B*, **1972**, *B28*, 55.
(7) Pal, B. C.; Uziel, M.; Doherty, D. G.; Cohn, W. W. *J. Am. Chem. Soc.* **1969**, *91*, 3634.
(8) Davis, K. E.; Shelton, J. R. *Int. J. Sulfur Chem.* **1973**, *8*, 197.
(9) Costa, M.; Peccim, L.; Pensa, B.; Cannella, C. *Biochem. Biophys. Res. Commun.* **1977**, *78*, 596. Lin, W. S.; Gaucher, G. M.; Armstrong, D. A.; Lal, M. L. *Can. J. Chem.* **1976**, 54, 242. Lin, W. S.; Armstrong, D. A.; Gaucher, G. M. *Can. J. Biochem.* **1975**, *53*, 298.
(10) Kharasch, N.; Bruice, T. C. *J. Am. Chem. Soc.* **1951**, *73*, 3240.
(11) Davis, F. A.; Yocklovich, S. G.; Baker, S. G. *Tetrahedron Lett.* **1978**, 97.
(12) Block, E.; O'Conner, J. *J. Am. Chem. Soc.* **1974**, *96*, 3921, 3929.

0022-3263/81/1946-3467$01.25/0

(eq 2).[13] Thiosulfinates and thiosulfonates are also sus-

$$2RS(O)SR \rightarrow RSSR + RSO_2SR \quad (2)$$

$$RS(O)SR + H_2O \rightarrow RSO_2H + RSH \quad (3)$$

$$RSO_2SR + H_2O \rightarrow RSO_2H + RSOH \quad (4)$$

ceptible to nucleophilic attack. With water, for example, sulfinic acids (RSO_2H, eq 3 and 4) are formed.[2,14] Note that water is formed in the dehydration of sulfenic acids (eq 1).

Sulfenic acids have been prepared in two ways: (a) the hydrolysis of a sulfenyl derivative (eq 5)[15-17] and (b) the thermolysis of sulfinyl derivatives (eq 6-8).[17-19] The

$$RSX + H_2O \rightarrow RSOH + HX \quad (5)$$

$$X = Cl, Br, NR_2, SR, OSiMe_3$$

$$RS(O)CR_2CR_2H \rightarrow RSOH + R_2C{=}CR_2 \quad (6)$$

$$RS(O)N{=}CHAr \rightarrow RSOH + ArCN \quad (7)$$

$$RS(O)SCHR_2 \rightarrow RSOH + R_2C{=}S \quad (8)$$

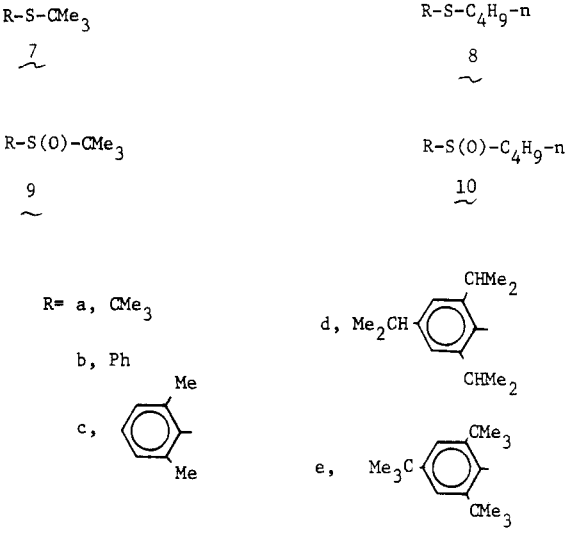
former results in complex mixtures of products generally including disulfide, thiosulfonate, and sulfinic and sulfonic acids.[14-16] Although sulfenic acids are believed to be intermediates in these reactions, they have never been isolate or detected. The products of eq 5 are believed to arise as illustrated in equations 1-4.[15-17] Reaction of the media and/or reagents needed to generate the sulfenic acid limits the usefulness of this procedure (eq 5).

The thermolysis of sulfinyl derivatives, sulfoxides (eq 6), sulfinimines (eq 7),[19] and thiosulfinates (eq 8)[20] is much more attractive. The thermolysis can be carried out in the absence of water under conditions where the reaction media will not react with the sulfenic acid or its reaction products. Furthermore, in sulfoxide pyrolysis (eq 6) the alkene is essentially inert and easily disposed of.

The mechanism for the thermal rearrangement of sulfinyl derivatives to sulfenic acid is believed to involve a stereospecific cis elimination via a concerted or nearly concerted transition state.[2d,21] Unfortunately, at temperatures (80-200 °C) where these reactions proceed at reasonable rates the concentration of the sulfenic acid at any one time is very small. Furthermore, these reaction temperatures preclude isolation of the labile sulfenic acids and many of their reaction products.

For the exploration of sulfenic acid chemistry new methods of synthesis must be developed. These methods must avoid conditions where the sulfenic acid and/or reaction products are subject to high temperatures for extended periods of time or conditions under which they react with the media. The ideal method should also afford the sulfenic acids in good concentration under conditions where they are stable.

Chart II



The flash vacuum pyrolysis (FVP) technique[1,11,22,23] appears to be a useful method for preparing sulfenic acids and for studying their chemistry. FVP is a controlled pyrolysis. The substrate (sulfoxide) comes in contact with the hot zone for very short periods of time (ca. 10^{-3} s), and the product (sulfenic acid) is immediately deposited on a cold finger cooled to liquid nitrogen temperatures (-196 °C). Since the pyrolysis is carried out in the gas phase, inter- or bimolecular reactions of the sulfenic acid (i.e., eq 1) should be minimized. Because the sulfenic acids are collected at -196 °C they should be both stable and collectable in high concentration. Microwave studies of sulfenic acids generated by FVP have been described by Block and co-workers.[23]

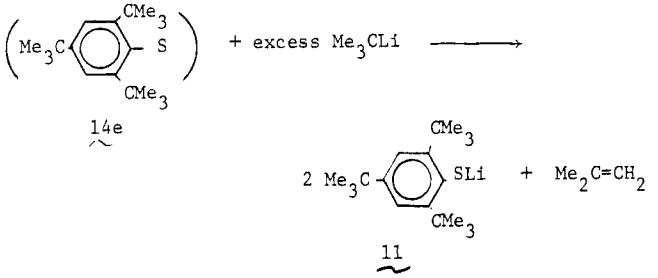
Syntheses of Sulfoxides. Although almost any sulfoxide containing a β-hydrogen can, in principle, be used to generate sulfenic acids by FVP (eq 6), it is desirable to use *tert*-butyl sulfoxides for several reasons. First, as a consequence of both steric bulk and the statistically greater number of β-hydrogen atoms, *tert*-butyl sulfoxides form sulfenic acids at lower temperatures.[17,24] This is advantageous since a lower pyrolysis temperature minimizes secondary reactions of the sulfenic acids in the gas phase. Second, we have noted that *tert*-butyl sulfoxides have a somewhat higher vapor pressure than other, less hindered, sulfoxides. It is critical to have the sulfoxides in the gas phase and in the pyrolysis section prior to rearrangement to the sulfenic acids and alkene (eq 6).

A variety of methods can be used to prepare unhindered aryl *tert*-butyl sulfides. These include reaction of *tert*-butyl alcohol in the presence of sulfuric acid[8] or phosphorus oxychloride-ferric chloride[25] with an aryl thiol. However, these methods do not work well for hindered aryl *tert*-butyl sulfides, either giving low yields or no yield at all. A procedure that we have found useful in synthesizing sterically hindered sulfides is the reaction of *tert*-butyllithium with a disulfide (eq 9). Good to excellent yields of sulfides **7a-d** (Chart II) were prepared in this manner.

$$Me_3CLi + ArSSAr \rightarrow Me_3CSAr + ArSLi \quad (9)$$

(13) Koch, P.; Ciuffarin, E.; Fava, A. *J. Am. Chem. Soc.* **1970**, *92*, 5971. Kice, J. L.; Large, G. B. *Tetrahedron Lett.* **1965**, 3537.
(14) Kice, J. L.; Rogers, T. E. *J. Am. Chem. Soc.* **1974**, *96*, 8009, 8015. Hogg, D. R.; Stewart, J. *J. Chem. Soc., Perkin Trans. 2* **1974**, 43.
(15) Sulfenyl halides: Vinkler, E.; Kivernyi, F. *Int. J. Sulfur Chem.* **1973**, *8*, 111. Kharasch, N.; King, W.; Bruice, T. C. *J. Am. Chem. Soc.* **1955**, *77*, 931. Reference 10.
(16) Disulfides: Hogg, D. R.; Stewart, J. *J. Chem. Soc., Perkin Trans. 2*, **1974**, *436*. Hogg, D. R.; Robertson, A. *Tetrahedron Lett.* **1974**, 3783.
(17) Sulfenate esters: (a) Davis, F. A.; Friedman, A. J. *J. Org. Chem.* **1976**, *41*, 897. (b) Ciuffarin, E.; Gambarotta, S.; Isola, M.; Senatore, L. *J. Chem. Soc., Perkin Trans. 2* **1978**, 554.
(18) Sulfoxides: See ref 1, 8, 11. Emerson, D. W.; Craig, A. P.; Potts, I. W., Jr. *J. Org. Chem.* **1967**, *32*, 102. Jones, D. N.; Hill, D. N.; Lewton, D. A.; Shippard, C. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1574.
(19) Sulfinimines: See ref 2b and 17a.
(20) Thiosulfinates: See ref 12.
(21) Janssen, J. W. A.; Kwart, H. *J. Org. Chem.* **1977**, *42*, 1530.
(22) For a recent monograph on the FVP technique see: Brown, R. F. C. "Pyrolytic Methods in Organic Chemistry"; Academic Press: New York, 1980.
(23) Block, E.; Penn, R. E.; Revelle, L. K. *J. Am. Chem. Soc.* **1979**, *101*, 2200. Penn, R. E.; Block, E.; Revelle, L. K. *Ibid.* **1978**, *100*, 3622.
(24) Emerson, D. W.; Kornski, T. J. *J. Org. Chem.* **1969**, *34*, 4115.
(25) Micha-Screttas, M.; Screttas, C. G. *J. Org. Chem.* **1977**, *42*, 1462.

Attempts to extend this procedure (eq 9) to the synthesis of *tert*-butyl 2,4,6-tri-*tert*-butylphenyl sulfide (**7e**) were unsuccessful. Addition of an excess of *tert*-butyllithium to 2,4,6-tri-*tert*-butylphenyl disulfide (**14e**) gave a quantitative yield of 2,4,6-tri-*tert*-butylbenzenethiol. Emission of a gas, presumably isobutene, was noted. Evidently, steric hindrance to attack of the *tert*-butyllithium at the S–S bond in **14e** forces the lithium reagent to function as a reducing agent. The ability of *tert*-butyllithium to act as a reducing agent with trialkylboranes has been reported,[26] but the reaction with **14e** appears to be the first example with an organosulfur compound. With *n*-butyllithium, **14e** was unreactive, affording less than 10% of the thiol **11**, and none of the *n*-butyl sulfide **8e**. *n*-Butyl

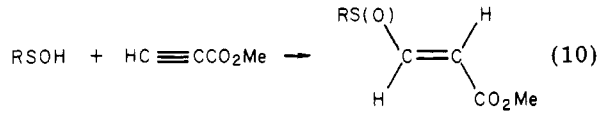


2,4,6-tri-*tert*-butylphenyl sulfide (**8**) was prepared in good yield by treatment of the corresponding thiol with sodium hydride followed by *n*-butyl bromide.

Oxidation of sulfides **7b–e** and **8b–e** with *m*-chloroperbenzoic acid (*m*-CPBA) gave the corresponding sulfoxides **9b–e** and **10b–e** in excellent yields. All new sulfoxides gave satisfactory elemental analysis and had IR and NMR spectra consistant with their structures.

Characterization of Sulfenic Acids. Sulfenic acids possess few spectral features that can be used in their identification. Although NMR was used in studying sulfenic acid **12a**, no absorption attributable to the SOH proton could be assigned.[8]

Short of actual isolation of a stable sulfenic acid, one of the best methods for determining their presence is trapping with an alkene or alkyne. Methyl propiolate has been the reagent most commonly used to trap sulfenic acids (eq 10).[2,8,11,12,17a] The *trans*-vinyl sulfoxide **16** is formed ex-



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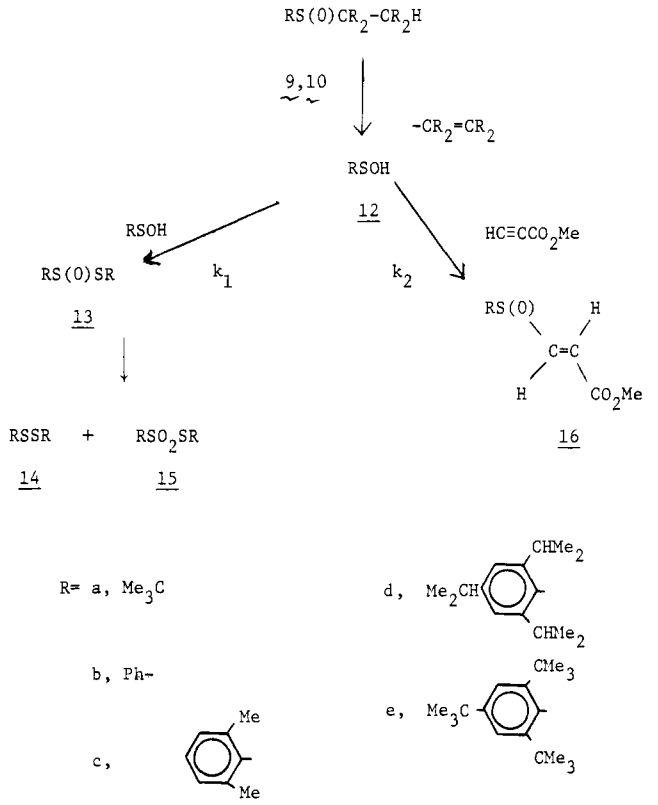
clusively, resulting from a stereospecific cis addition of the sulfenic acid to the alkyne. Addition of a sulfenic acid to an alkene (eq 10) has been shown to be the reverse of sulfoxide pyrolysis (eq 6).[21]

Usually the trapping of sulfenic acids is carried out under thermolysis conditions. The sulfinyl derivatives (eq 6–8) are heated in solution with the alkyne or alkene. These conditions maximize trapping of the sulfenic acid (eq 10). Bimolecular reactions of the sulfenic acid (i.e., thiosulfinate formation, eq 1) are minimized because the concentration of the sulfenic acid at any one time is very small.

A method is required to estimate the influence of structural variations on the reactivity or stability of sulfenic acids. We propose to use the vinyl sulfoxide/thiosulfinate

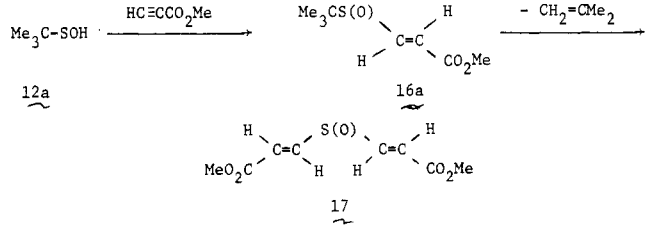
Scheme I



(16/13) ratio (Scheme I) for this purpose.

There is compelling evidence that the primary or principal reaction of simple sulfenic acids is thiosulfinate formation (eq 1).[1,2,11,12] If some structural change is made in the sulfenic acid which inhibits formation of **6**, and therefore the thiosulfinate **13** (i.e., stabilizes the sulfenic acid), then the vinyl sulfoxide **16** will be formed in the presence of methyl propiolate. Thiosulfinate **13** will be formed at some rate k_1 and vinyl sulfoxide **16** at some rate k_2 (Scheme I). While both k_1 and k_2 will be dependent upon the reaction conditions and the molecular structure of the sulfenic acid, k_2 will be less so than k_1, on the basis of the principle of microscopic reversibility (vide supra). Recall that formation of **16** is simply the reverse of sulfoxide pyrolysis (eq 6), and the latter has been shown to be insensitive to structural changes in the sulfenic acid.[8,24] While the reverse of eq 10 (vinyl sulfoxide pyrolysis) has not been described, evidence is presented here and elsewhere[1] that the ratio of **16**/**13** can be used as an approximate measure of sulfenic acid reactivity.

Thermolysis of Sulfoxides. Thermolysis of sulfoxides **9** and **10** affords good yields of sulfenic acids **12a–d**. This is supported by the isolation of vinyl sulfoxides **16a–d** in



excellent yields when the thermolysis of **9c–d** is carried out in the presence of methyl propiolate (Table I, entries 1 and 3).[2d,8] Under similar conditions 2-methyl-2-propanesulfenic acid (**12a**) affords sulfinyl *trans,trans*-diacrylate (**17**).[8] Although the vinyl sulfoxide **16a** was a proposed intermediate, it could not detected.

(26) Hubbard, J. L.; Kramer, G. W. *J. Organomet. Chem.* **1978**, *156*, 81 and references cited therein.

(27) For a discussion of α-disulfoxides and sulfenyl sulfinates in the rearrangement of sulfinyl radicals to thiosulfonates see: Chau, M. M.; Kice, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 7711.

Table I. Thermolysis of Sulfoxides

entry	sulfoxide	conditions	time, h	temp, °C	products (% yield)[a]
1	**9c**	5% $HC{\equiv}CCO_2Me$/PhMe	12	100	**16c** (84)
2	**9d**	PhH	12	78	**14d** (82)
3		5% $HC{\equiv}CCO_2Me$/PhH	12	78	**16d** (85)
4		PhMe + 10% PhSMe	24	110	**14d** (70)
5	**10d**	PhMe	136	110	**10d** (48), **14d** (20)
6	**13d**	PhH	17	78	**13d** (5), **14d** (73)
7	**10e**	PhMe	50	110	**10e** (37), **14e** (31)
8		5% $HC{\equiv}CCO_2Me$/PhMe	50	110	**10e** (39), **14e** (15)[b]

[a] Isolated yields unless otherwise noted. [b] Complex mixture of product also detected. See text.

Table II. Flash Vacuum Pyrolysis (FVP) of Sulfoxides

entry	sulfoxide	FVP temp, °C	conditions[a]	products (% yield)[b]
1	**9a**	175		**9a** (67), **13a** (2)
2		340		**13a** (93)
3		360	$HC{\equiv}CCO_2Me$	**13a** (10), **16a** (40)
4		340	5% $HC{\equiv}CCO_2Me$/PhMe	**13a** (7), **16a** (70)
5	**9b**	620		**13b** (58), **14b** (6), **15b** (10)
6		620	5% $H{\equiv}CCO_2Me$/PhMe	**13b** (58), **14b** (6), **15b** (8)
7	**9c**	520	5% $HC{\equiv}CCO_2$/PhMe	**13c** (65), **14c** (15), **15c** (8)
8	**9d**[c]	360		decomposed in the sample inlet
9	**10d**[c]	380		**10d** (10), **13d** (58), **14d** (6), **15d** (6)
10		380	5% $HC{\equiv}CCO_2Me$/PhMe	**10d** (17), **13d** (57), **14d** (16), **15d** (10)
11	**10e**[c]	290		**21** (23), **23** (5),[d] **26** (20),[d] **27** (15)[d]

[a] See Experimental Section. [b] Isolated yields unless otherwise noted. [c] Entrain pyrolysis technique used. [d] Gas chromatographic yields.

Attempts to trap 2,4,6-tri-*tert*-butylbenzenesulfenic acid (**12e**) under these conditions with methyl propiolate were unsuccessful. At least 15 compounds were indicated by GLC, and the NMR indicated the absence of **16e** (Table I, entry 8). The sulfoxide **10e** was recovered in 39% yield, and disulfide **14e** was isolated in 15% yield. Our inability to trap this sulfenic acid may be related to its greater steric bulk in the region of the SOH group as compared with sulfenic acids **12a–d**.

In the absence of trapping reagents, arenesulfenic acids, generated under thermolysis conditions, afford disulfides (RSSR), thiosulfonates (RSO_2SR), and sulfinic acids (RSO_2H).[2d] These products have been rationalized as arising via disproportionation of the initially formed thiosulfinate (eq 2). Arenesulfenic acids have also been shown to form sulfinic acids as per eq 11.[2d] Benzenesulfenic acid (**12b**), for example, affords disulfide **14b** (56%), thiosulfonate **15b** (44%), and sulfinic acid (trace).[2d] By contrast, sterically hindered sulfenic acids **12d** and **12e** react almost exclusively to form the corresponding disulfides **14d,e** (Table I, entries 5, 7, and 8).

$$2RSOH \rightarrow RSO_2H + RSH \qquad (11)$$

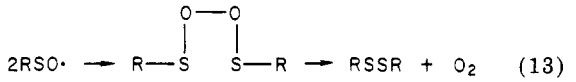
The disappearance of oxygen from the products of these sulfenic acids may be explained in several ways. Homolytic cleavage of the S–OH bonds in **12d,e** would give thiyl (ArS·) and hydroxyl radicals, respectively. Dimerization of these thiyl radicals would give disulfides **14d,e**. Since thermolysis of **9d** and **10d** (precursors of sulfenic acid **12d**) in the presence of methyl propiolate gave good yields of the trapped sulfenic acid **16d**, this possibility is unlikely. Furthermore, FVP of **10d** gave thiosulfinate **13d** in greater than 58% yield (Table II, entry 9).

Reaction of **12d,e** according to eq 12 would also form

$$2RSOH \rightarrow RSSR + H_2O_2 \qquad (12)$$

disulfides. Recently we reported that 2-pyridine- and pentafluorobenzenesulfenic acids react according to eq 12.[1] However, the fact that 2,4,6-triisopropylbenzenesulfenic acid (**12d**) can be trapped and gives thiosulfinate **13d** makes a sequence such as this also unlikely. Furthermore, attempts to detect H_2O_2 by carrying out the thermolysis of **9d** in the presence of sulfides (formation of the sulfoxide or sulfone) were unsuccessful (Table I, entry 4).

Disproportionation of thiosulfinates to disulfides and thiosulfonates (eq 2) is believed to occur via intermediate thiyl (RS·) and sulfinyl (RSO·) radicals.[12,28] Two sulfinyl radicals combine to give α-disulfoxides [RS(O)S(O)R] or sulfenyl sulfinates [RS(O)OSR] which rearrange to thiosulfonates.[29] For sulfenic acids **12d,e** steric hindrance may prevent formation of these intermediates, resulting in the less hindered disulfenyl peroxide **18**, which extrudes molecular oxygen as shown (eq 13). Indeed, thermolysis of



(13)

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2,4,6-triisopropylphenyl 2,4,6-triisopropylbenzenethiosulfinate (**13d**) gives the disulfide **14d** in greater than 73% yield (Table I, entry 6). Phenyseleninyl radicals (PhSeO·) are reported to react in a related manner (eq 13).[28]

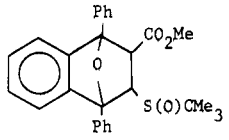
FVP of Sulfoxides. FVP of sulfoxides **9a–c** and **10d** with condensation of the pyrolyzate on the cold finger cooled to −196 °C affords the corresponding sulfenic acids **12a–d** in good to moderate yields (Scheme I). These sulfenic acids are stable under the FVP conditions. The corresponding, labile thiosulfinates, **13a–d**, are isolated in good yield on thawing of the cold trap (Table II, entries 2, 5, 7, 10). The small amounts of disulfide **14** and thiosulfonate **15** also observed result from disproportionation of **13** on workup (Scheme I). Contrast the product distribution observed for thermolysis of sulfoxides (Table I) with that for FVP of sulfoxides (Table II). Note that under the thermolysis conditions thiosulfinates **13** are not detected.

Trapping of sulfenic acids **12a–d** on the cold finger by codepositing a methyl propiolate–toluene solution was successful only for 2-methyl-2-propanesulfenic acid (**12a**).

(28) Kice, J. L.; Lee, T. W. S. *J. Am. Chem. Soc.* **1978**, *100*, 5094.
(29) FVP of phenyl benzyl sulfoxide at 550 °C affords a 70% yield of phenyl benzenethiosulfonate ($PhSO_2SPh$) and 60% 1,2-diphenylethane.

A 69–73% yield of vinyl sulfoxide **16a** was isolated as a thermally labile oil by using preparative TLC. Note that **16a** has previously been suggested as an intermediate in the formation of **17**.[8]

Although a satisfactory elemental analysis could not be realized for **16a** because of its thermal lability, the NMR and IR spectra clearly support the proposed structure. IR absorptions at 1730 and 1081 cm^{-1} are characteristic of the C=O and S=O functional groups, respectively. In the proton NMR the *tert*-butyl group of **16a** is observed at δ 1.3 (s, 9 H), and the characteristic AB quartet of the trans vinyl protons is observed at δ 6.3 and 7.7 (J = 15 Hz), respectively.[2d] Isolation of Diels–Alder adduct **19** on heating **16a** with 1,3-diphenylisobenzofuran is additional support for the proposed structure of **16a**.



19

A greater yield of **16a** was isolated by using a solution of methyl propiolate in toluene rather than pure methyl propiolate on the cold finger to trap **12a** (40% vs. 70%, (Table II, entries 3 and 4). These results are consistent with the suggestion of Shelton and Davis that polar and aromatic solvents stabilize sulfenic acids.[8a] Presumably this solvent interferes with formation of hydrogen bonded species **6**, believed necessary for thiosulfinate formation (eq 1).

It may be argued that FVP of sulfoxides **9** and **10** leads not to the sulfenic acids and alkene (eq 6) but rather to some heterogenously catalyzed radical reaction affording sulfinyl radicals (RSO·) which react in some manner to give the observed products. Since sulfinyl radicals afford thiosulfonates **15**[29] and since these products are minor ones in the FVP of **9** and **10**, this possibility is unlikely (Table II). The best evidence that sulfenic acids are formed under FVP conditions is the trapping of 2-metyl-2-propanesulfenic acid (**12a**) with methyl propiolate to give **16a** (Table II, entries 3 and 4).

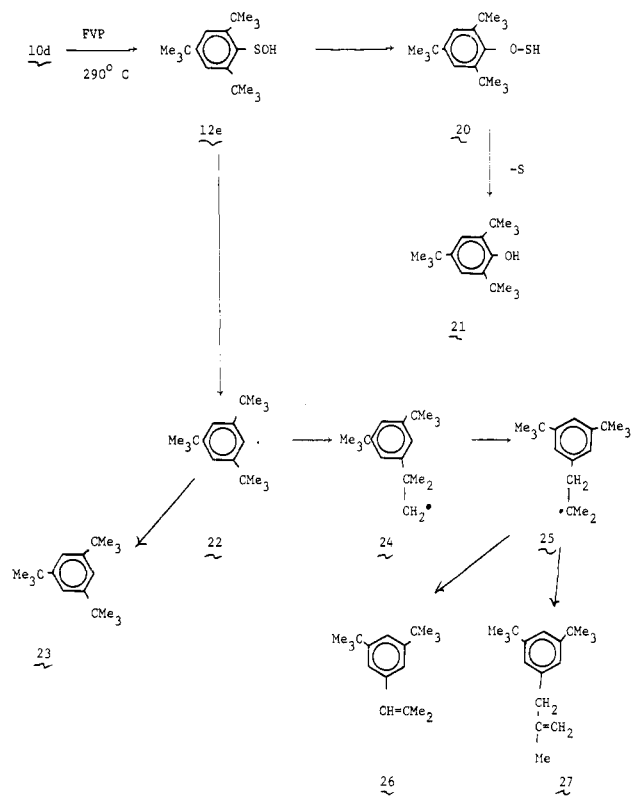
The possibility that sulfoxides **9** and **10** are rearranging in the sample chamber to sulfenic acids to any significant extent is also improbable. This would require that the thiosulfinates **13** survive the temperatures of the pyrolysis section (300–600 °C) and is most unlikely. Furthermore, starting material can be isolated on the cold-finger trap with low pyrolysis temperature.

Rearrangement in the sample chamber to the sulfenic acid was observed for *tert*-butyl 2,4,6-triisopropylphenyl sulfoxide (**9d**). This was indicated by isolation of disulfide **14d** and thiosulfonate **15d** from the sample chamber. In **9d** the increase in steric interactions between the *tert*-butyl and adjacent isopropyl groups probably accounts for the increased thermal lability of this sulfoxide. This problem has been alleviated by using the more thermally stable *n*-butyl sulfoxide **10d** in our FVP experiments (Table II, entries 9 and 10).

The inability to trap sulfenic acids **12b–d** with methyl propiolate on the cold finger suggests that the steric hindrance in the region of the SOH group is not sufficient to inhibit thiosulfinate formation (eq 1). The possibility that steric hindrance also inhibits trapping of the sulfenic acid (eq 10) is unlikely since under thermolysis conditions these sulfenic acids were trapped in excellent yields (Table I).

If any arenesulfenic acid can be stabilized by steric hindrance alone it should be 2,4,6-tri-*tert*-butylbenzenesulfenic acid (**12e**). In sulfenic acid **12e**, Drieding and CPK models suggest that the SOH group is more hindered than in sulfenic acids **12a–d**. However, these models also reveal considerable steric interaction between the SOH and the adjacent *tert*-butyl groups.

Scheme II



FVP of *n*-butyl 2,4,6-tri-*tert*-butylphenyl sulfoxide (**10e**) occurs at 290 °C, the lowest of any of the sulfoxide FVP temperatures, reflecting steric conjestion about the SO group in **12e**. The reaction produces a complex mixture devoid of sulfur (Scheme II; Table II, entry 11).

GLC of the reaction mixture reveals the presence of at least nine products. 2,4,6-Tri-*tert*-butylphenol (**21**) was isolated in 23% yield by preparative TLC and identified by comparison with an authentic sample. Three other major products (and a variety of minor ones) were isolated by TLC. The major products were isolated in the ratio of 1:4:3 and a combined yield of 40%. The first product of this mixture was identified as 2,4,6-tri-*tert*-butylbenzene (**23**) by comparison with an authentic sample.

The two other major products of this mixture were tentatively identified as 1-(3,5-di-*tert*-butylphenyl)-2-methylpropene (**26**) and 3-(3,5-di-*tert*-butylphenyl)-2-methylpropene (**27**) on the basis of their IR, NMR, and mass spectra and the chemistry reported in the literature.

Consistent with the proposed structures, **26** and **27** have very similar mass spectra. They display molecular ions at m/e 244, M – Me ions at m/e 229, and base ions at m/e 57 (C_4H_9). Absorption in the IR spectra of **26** and **27** is observed at 3080, 1650, and 880 cm^{-1}, consistent with the presence of the CH=C alkene functionality. The 250-MHz ^1H NMR of the mixture provides additional support for the proposed structures. Methyl absorptions are observed at δ 1.7, 1.86, and 1.9 and methylene absorption at δ 6.3 (ArCH=C).

The formation of these products may be rationalized by assuming formation of the 2,4,6-tri-*tert*-butylbenzene radical via homolytic cleavage of the C–SOH bond of **12e** (Scheme II). Radical **22** is reported to rearrange first to the neopentyl radical **24**[30] and then to the tertiary radical

25.[31] Loss of a hydrogen atom from **25** would afford **26** and **27**, with the more conjugated **26** predominating (Scheme II). It is important to note that disulfide **14e** is not a product of the flash vacuum pyrolysis of sulfoxide **10e**, and products **21**, **23**, **26**, and **27** are not detected in the thermolysis of this sulfoxide.

We believe that in both instances, FVP and thermolysis of **10e**, 2,4,6-tri-*tert*-butylbenzenesulfenic acid (**12e**) is formed. This conclusion is supported by the fact that thermolysis and FVP of sulfoxides **9a–c** and **10d** afford in every case the corresponding sulfenic acids (Tables I and II). At the lower thermolysis temperature (110 °C) **12e** apparently reacts in a manner similar to 2,4,6-triisopropylbenzenesulfenic acid (**12d**) to afford the corresponding disulfide (eq 13). The much higher FVP temperature (290 °C) causes **12e** to decompose in two ways in the pyrolysis section of the FVP apparatus: the first leads to phenol **21**, possibly via an intermediate such as **20**, and the second to the 2,4,6-tri-*tert*-butylphenyl radical (**22**). This radical reacts as outlined in Scheme II. Elemental sulfur was also detected in the FVP of **10e** and is consistent with these results. Undoubtedly, increased interaction between the SOH and the adjacent *tert*-butyl groups in **12e** is responsible for the enhanced reactivity of this sulfenic acid.

The GC/MS of the products of the FVP of **10e** indicated, in addition to the major products outline in Scheme II, the presence of di-*n*-butyl disulfide and di-*tert*-butylbenzene (<1–2%).

Conclusions. FVP of alkyl and aryl sulfoxides containing β-hydrogen atoms with condensation of the pyrolyzate on a cold finger cooled to −196 °C affords sulfenic acids (RSOH) in good to moderate yields. These sulfenic acids are stable under the conditions of FVP. This is supported by the isolation of thiosulfinates [RS(O)SR] in good yield and by trapping experiments with methyl propiolate. The fact that thermally labile thiosulfinates are the principal products of the sulfenic acids generated in this way provides compelling evidence that the primary reaction of simple sulfenic acids is dehydration to thiosulfinates (eq 1).

The influence of structural modifications on sulfenic acid reactivity can be estimated by the vinyl sulfoxide/thiosulfinate (**16**/**13**) ratio (Scheme I). This method indicates steric hindrance to be only of importance in stabilizing 2-methyl-2-propanesulfenic acid (**12a**) toward thiosulfinate formation. 2,4,6-Tri-*tert*-butylbenzenesulfenic acid (**12e**) appears to be destabilized as a consequence of steric interactions between the adjacent *tert*-butyl groups and the SOH functionality.

While our results do not rule out the possibility that steric effects may play some role in stabilizing protein sulfenic acids, they do suggest that electronic and/or hydrogen bonding effects may be of more importance. Indeed, the introduction of a 4-nitro group into benzenesulfenic acid (**12b**; i.e., 4-nitrobenzenesulfenic acid) gives a vinyl sulfoxide/thiolsulfinate ratio of 0.22.[1] It is likely that electronic and/or hydrogen bonding effects are primarily responsible for the stability of sulfenic acids **1–4**, and work is currently underway to ascertain this.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^{1}H NMR spectra were measured on Varian A-60A and Varian HR-250 (250 MHz) NMR spectrometers. GS/MS data were obtained on a Finnigan 4000 GC/MS using a 6 ft × $^1/_4$ in., 3% OV-17 on Anakorm Q (90/100–mesh), glass column. Gas chromatographic analyses were performed on a Perkin-Elmer 900 gas chromatograph with a 6 ft × $^1/_8$ in., 3% OV-17 on Anakorm Q (90/100–mesh) column. The analyses were determined by comparison of peak areas with standard solutions of the reaction products. Analyses were performed at least twice and the results averaged. Elemental analyses were obtained from Micro-Analyses Inc. Solvents were purified by literature methods.

Synthesis of Disulfides. Di-*tert*-butyl disulfide (**14a**) and diphenyl disulfide (**14b**) were purchased from Aldrich Chemical Co. 2,6-Xylyl disulfide (**14c**)[32] and 2,4,6-triisopropylphenyl disulfide (**14d**)[33] were prepared according to literature methods. 2,4,6-Tri-*tert*-butylphenyl disulfide (**14d**) was prepared by using the procedure described by Rundel[34] with the following modifications.

1,2,3-Tri-*tert*-butylbenzene (Frinton; 49.2 g, 0.2 mol) was brominated in trimethyl phosphate according to the procedure of Pearson et al.[35] In our hands yields were improved when a 4-mol excess of Br_2 was used and the reaction time increased to 72 h. The orange-yellow semisolid crystallized from ethanol as colorless plates: 36 g (55%); mp 176–167 °C (lit.[34] mp 171.5–173.5 °C).

2,4,6-Tri-*tert*-butylphenylmagnesium bromide was prepared as previously described from 16.3 g (0.5 mol) of the bromide and 1.2 g of magnesium in dry THF.[34] Formation of the Grignard reagent was slow and required refluxing for 8 h, at which time freshly sublimed sulfur (1.8 g, 0.05 mol) was added. After refluxing for 8 h in an N_2 atmosphere, the reaction mixture was cooled to room temperature and 1.0 g (0.024 mol) of lithium aluminum hydride slowly added. The solution was refluxed for 1 h, cooled, and hydrolyzed with a saturated solution of NH_4Cl, followed by extraction with ether (2 × 250 mL). The ether solution was washed with water (3 × 250 mL) followed by oxidation of the thiol to the disulfide **14d** by dropwise addition of a saturated solution of potassium ferrocyanide (25 g of $K_3[Fe(CN)_6]$ in 250 mL of 10% NaOH solution). After the ether solution was dried over $MgSO_4$, the solvent was removed under vacuum to give a yellow solid which was crystallized from ethyl acetate, affording 8.3 g (60%) of **14e**, mp 230–232 (lit.[34] mp 233–234 °C).

Synthesis of *tert*-Butyl Aryl Sulfides (7b–e) from *tert*-Butyllithium and Aryl Disulfides. In a 100-mL three-necked flask equipped with a magnetic stir bar and nitrogen and syringe inlets was placed 0.0042 mol of the appropriate disulfide **14** in 24 mL of dry *n*-pentane. The reaction mixture cooled to −78 °C in a dry ice–acetone bath and 6 mL of a 1.7 M solution of *tert*-butyllithium (Aldrich) added via syringe. The solution was then stirred at room temperature for 2 h under N_2, at which time the reaction mixture cooled again to −78 °C and cautiously hydrolyzed by dropwised addition of H_2O. The aqueous phase was separated from the *n*-pentane solution and acidified to afford the thiols corresponding to **14**. After the *n*-pentane solution was dried over anhydrous $MgSO_4$, the solvent was removed under vacuum to give the crude *tert*-butyl aryl sulfides **7** which were oxidized to the corresponding sulfoxides, **9**, without further purification unless otherwise noted.

***tert*-Butyl 2,6-Xylyl Sulfide (7c).** This compound was obtained as a yellow, viscous oil (85%) in greater than 95% purity by NMR ($CDCl_3$): δ 1.3 (s, 9 H, CMe_3), 2.6 (s, 6 H, Me), 7.15 (s, 3 H).

***tert*-Butyl 2,4,6-Triisopropylphenyl Sulfide (7d).** This sulfide was obtained as an oil contaminated with the corresponding thiol (approximately 25%). The thiol was oxidized to the disulfide **14d** by being dissolved in 100 mL of methanol containing 2.0 g of triethylamine and 2.0 g of I_2.[36] After the mixture stirred overnight, 100 mL of H_2O was added to the reaction mixture followed by extraction with ethyl ether (3 × 50 mL). The ether solution was washed with water (3 × 50 mL) and 10% Na_2SO_3

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solution (3 × 50 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent under vacuum gave a clear oil which distilled at 75–76 °C (0.1 torr). The sulfide, **7d**, solidified in the receiver: 80% yield; mp 31–32 °C; NMR ($CDCl_3$) δ 1.2 (m, 27 H, Me), 2.9 (quintuplet 1 H, CH), 4.15 (quintuplet 2 H, CH), 7.0 (2 H).

Anal. Calcd for $C_{19}H_{32}S$: C, 78.08; H, 10.96. Found: C, 78.25; H, 11.11.

Preparation of *n*-Butyl Aryl Sulfides (8d,e). In a 100-mL three-necked flask equipped with a magnetic stir bar, reflux condenser, dropping funnel, and N_2 inlet was placed 3.0 g (57% in mineral oil) of sodium hydride (Aldrich) in 25 mL of dry tetrahydrofuran. The reaction was cooled to 0 °C, and 0.0018 mol of 2,4,6-triisopropyl- or 2,4,6-tri-*tert*-butylbenzenethiol (prepared by lithium aluminum hydride reduction of **14d,e**) in 25 mL of tetrahydrofuran were added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and 5.0 mL of *n*-butyl bromide added dropwise. The reaction mixture was stirred at room temperature for 8 h, 100 mL of water was slowly added, and the solution was extracted with $CHCl_3$ (3 × 25 mL). After the chloroform solution was dried over anhydrous $MgSO_4$, the solvent was removed under vacuum to give the crude sulfides **8d,e** as oils.

***n*-Butyl 2,4,6-triisopropylphenyl sulfide (8d)**: bp 111–114 °C (0.15 torr); 0.45 g (85%); yellow oil; NMR ($CDCl_3$) δ 0.7–1.7 (m, 9 H, CH_3CH_2), 1.25 (s, 6 H, Me), 1.35 (s, 11 H, Me), 2.35–3.4 (m, 2 H CH), 4.0 (heptet, 1 H, CH, J = 7 Hz), 7.05 (s, 2 H).

***n*-Butyl 2,4,6-Tri-*tert*-butylphenyl Sulfide (8e).** This compound was obtained in a 90% yield and was sufficiently pure to be oxidized: NMR ($CDCl_3$) δ 0.7–2.7 (m, 9 H), 1.3 (s, 9 H, Me), 1.6 (s, 18 H, Me), 7.35 (s, 2 H).

Oxidation of Sulfides 7 and 8 to Sulfoxides 9 and 10. In a 250-mL three-necked flask equipped with a magnetic stir bar and dropping funnel was placed 0.0096 mol of the appropriate sulfide in 100 mL of $CHCl_3$. *m*-Chloroperbenzoic acid (1.94 g, 0.0096 mol, of 85% puriety) was added dropwise in 25 mL of $CHCl_3$ at 0 °C. After the reaction mixture was allowed to warm to room temperature and stirred for an additional 0.5 h, the solution was washed with 5% Na_2SO_3 solution (2 × 50 mL), 5% $NaHCO_3$ solution (2 × 50 mL), and water (2 × 50 mL). After the mixture was dried over anhydrous $MgSO_4$, the solvent was removed under vacuum and the crude sulfoxide purified by chromatography on silica gel.

***tert*-Butyl 2,6-xylyl sulfoxide (9c)** was obtained by elution with *n*-pentane followed by ether: oil; 1.8 g (90%); IR (film) 1050 cm^{-1} (s, S=O); NMR ($CDCl_3$) δ 1.3 (s, 9 H, CMe_3), 2.1 (s, 3 H, Me), 2.8 (s, 3 H, Me), 7.0–7.3 (m, 3 H). A satisfactory elemental analysis could not be obtained.

***tert*-Butyl 2,4,6-Triisopropylphenyl Sulfoxide (9d).** Elution with 10% ethyl acetate 90% *n*-hexane gave 2.3 g (70%) white crystals: mp 80.5–82 °C; IR (KBr) 1060 cm^{-1} (s, S=O); NMR ($CDCl_3$) δ 0.65–1.15 (m + s, 27 H), 2.0–3.5 (m, 2 H), 4.3–4.8 (m, 1 H), 6.6–7.0 (m, 2 H).

Anal. Calcd for $C_{22}H_{38}OS$: C, 71.70; H, 10.06. Found: C, 71.97; H, 10.00.

***n*-Butyl 2,4,6-Triisopropylphenyl Sulfoxide (10d).** Elution with 10% ether–90% *n*-hexane gave 1.8 g (59%) of white crystals: mp 49–50 °C; IR (KBr) 10.40 cm^{-1} (s, S=O); NMR ($CDCl_3$) δ 0.7–2.0 (m, 9 H, *n*-Bu), 1.2 (d, 6 H, J = 5 Hz), 1.4 (d, 12 H, Me, J = 8 Hz) 3.05 (heptet, 2 H, CH, J = 8 Hz), 4.1 (heptet, 1 H, CH, J = 7 Hz), 7.25 (s, 2 H).

Anal. Calcd for $C_{19}H_{32}OS$: C, 74.01; H, 10.39. Found: C, 73.83; H, 10.25.

***n*-Butyl 2,4,6-Tri-*tert*-butylphenyl Sulfoxide (10e).** Elution with 10% ether–90% *n*-hexane gave 1.5 g (44%) of white crystals: mp 96–97 °C [sublimed at 60–65 °C; mp 105 °C (0.1 torr)]; IR (KBr) 1080 cm^{-1} (s, S=O); NMR ($CDCl_3$) δ 0.7–3.5 (m, 9 H, Bu), 1.35 (s, 9 H, CMe_3), 1.6 (s, 18 H, CMe_3), 7.2–7.5 (m, 2 H).

Anal. Calcd for $C_{22}H_{38}OS$: C, 75.35; H, 10.93; S, 9.15. Found: C, 75.74; H, 10.90; S, 9.21.

Thermolysis of Sulfoxides 9c,d and 10d,e and Thiosulfinate 13d. Typically, 0.0008 mol of the sulfoxide or thiosulfinate (Table I) was placed in a 25-mL single-necked flask equipped with a magnetic stir bar, reflux condenser, and nitrogen inlet in 10 mL of the appropriate solvent (Table I). After the mixture was refluxed under nitrogen for the specified time period (the course of the reaction was monitored by TLC for the disappearance of sulfoxide or thiosulfinate), the solvent was removed under vacuum. The reaction mixture was purified by preparative TLC on silica gel.

Methyl *trans*-[(2,6-Xylyl)sulfinyl]acrylate (16c). Development with 1:1 ether–*n*-pentane gave an 84% yield of white crystals: mp 98–99 °C; IR (KBr) 1720 (C=O), 1080 cm^{-1} (s, S=O); NMR ($CDCl_3$) δ 2.5 (s, 6 H, Me), 3.8 (s, 3 H, OMe, AB q), 6.7 (d, 1 H, J = 15 Hz), 7.7 (d, 1 H, J = 15 Hz), 7.1 (m, 3 H).

Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.49; H, 5.92. Found: C, 60.45; H, 5.97.

Methyl *trans*-[(2,4,6-Triisopropylphenyl)sulfinyl]acrylate (16d). Development with 1:1 ether–*n*-pentane gave an 82% yield white crystals: mp 110–113 °C; IR (KBr) 1720^{-1} (s, C=O), 1080 cm^{-1} (S=O); NMR ($CDCl_3$) δ 1.2 (d, 18 H, J = 7 Hz), 2.9 (m, 1 H), 3.8 (s, 3 H, OMe), 3.8 (m, 2 H, AB q), 6.7 (d, 1 H, J = 15 Hz), 7.7 (d, 1 H, J = 15 Hz), 7.1 (s, 2 H).

Anal. Calcd for $C_{19}H_{28}O_3S$: C, 67.86; H, 8.33. Found: C, 67.71; H, 8.31.

Flash Vacuum Pyrolysis (FVP) of Sulfoxides 9 and 10. The appropriate sulfoxide, typically 150–250 mg, is placed in the sample chamber. The sample chamber is heated with a heating tape maintained at 10–15 °C lower than the melting point of the sulfoxide. The preheat section of the pyrolysis chamber is maintained at a temperature approximately 25 °C above the melting point of the sulfoxide. The pyrolysis chamber temperature is set at the minimum temperature where most of the sulfoxide reacts and is determined by trial and error.

Isolation of Products from the FVP of Sulfoxides. After completion of the FVP experiment the vacuum is disengaged and the system flushed with dry nitrogen gas. The liquid N_2 is removed from the cold-finger Dewar, and the products which had collected on the cold-finger are washed into a receiver. The products were analyzed by preparative TLC (silica gel), GLC, GC/MS, or column chromatography on Florisil (Table II).

FVP of Di-*tert*-butyl Sulfoxide (9a). Preparative TLC (elution with 1:1 benzene–$CHCl_3$) gave **13a**,[12] and elution with ether gave **16a**.

Methyl *trans*-(*tert*-butylsulfinyl)acrylate (16a): oil; 70% yield; IR (film) 1730 cm^{-1} (s, C=O), 1080 (s, S=O); NMR ($CDCl_3$) δ 1.3 (s, 9 H, CMe_3), 3.8 (s, 3 H, OMe, Ab q), 6.3 (d, 1 H, J = 15 Hz), 7.7 (d, 1 H, J = 15 Hz).

Adduct of 16a and 1,3-Diphenylisobenzofuran (19). In a 10-mL single-necked flask equipped with a magnetic stir bar, reflux condenser, and nitrogen inlet were placed 0.2 g (0.001 mol) of methyl *trans*-(*tert*-butylsulfinyl)acrylate (**16a**) and 0.28 g (0.001 mol) of 1,3-diphenylisobenzofuran (Aldrich) in 5 mL of dry benzene. After the mixture was heated at reflux for 4 h, the solvent was removed under vacuum and the resulting oil chromatograph on Florisil. Elution with 1:1 ether–$CHCl_3$ gave 0.14 g (30%) of white crystals: mp 139–141 °C; IR (KBr) 1720 (C=O), 1050 (S=O); NMR ($CDCl_3$) δ 1.1 (s, 9 H, CMe_3), 3.2 (s, 3 H, OMe, AB q), 3.8 (d, 1 H, J = 4 Hz), 4.15 (d, 1 H, J = 4 Hz), 7.2–8.0 (m, 14 H).

Anal. Calcd for $C_{28}H_{28}O_4S$: C, 73.04; H, 6.09. Found: C, 72.94; H, 5.84.

FVP of *tert*-Butyl Phenyl Sulfoxide (9b). Preparative TLC (elution with 1:1 $CHCl_3$–benzene) gave **14b**,[2d] **15d**,[2d] and **13b**.[13]

FVP of *tert*-Butyl 2,5-Xylyl Sulfoxide (9c). Preparative TLC (elution with 1:1 *n*-pentane–ether) gave **14c**,[32] **15c**, and **13c**.

2,6-Xylyl 2,5-xylenethiosulfonate (15c) had the following properties: mp 115–117 °C; IR (KBr) 1330, 1160 cm^{-1} (s, SO_2); NMR ($CDCl_3$) δ 2.25 (s, 6 H, Me), 2.5 (s, 6 H, Me), 7.0–7.4 (m, 6 H).

Anal. Calcd for $C_{16}H_{18}O_2S_2$: C, 62.74; H, 5.92. Found: C, 62.71; H, 5.93.

2,6-Xylyl 2,6-xylenethiosulfinate (13c) had the following properties: mp 89–90 °C; IR (KBr) 1100 cm^{-1} (s, S=O); NMR ($CDCl_3$) δ 2.15 (d, 12 H, Me), 7.2 (m, 6 H).

Anal. Calcd for $C_{16}H_{18}OS_2$: C, 66.20; H, 6.21. Found: C, 66.23; H, 6.13.

FVP of *n*-Butyl 2,4,6-Triisopropylphenyl Sulfoxide (10d). Preparative TLC (elution with 1:1 *n*-pentane–ether) gave **14d**,[33] **15d**,[37] **13d**,[37] and **10d**.

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FVP of *n*-Butyl 2,4,6-Tri-*tert*-butylphenyl Sulfoxide (10e). Preparative TLC, on elution first with *n*-pentane, gave the fraction consisting of **23**, **26**, and **27**, which were further analyzed by GLC and GLC/MS. The fraction consisting of these compounds had the following properties: IR (film) 3080 (s, =CH), 1650 (s, C=C), 880 (s, CH=C) cm^{-1}; 220-MHz NMR ($CDCl_3$) δ 81.3 (s, CMe_3) 1.7 (s, 3 H, Me), 1.86 (s, 3 H, Me), 1.9 (s, 3 H, Me), 3.3 (s, 2 H, CH_2), 4.75 and 4.8 (d, 2 H, $=CH_2$), 6.3 (s, 1 H, CH=C), 7.0-7.3 (m). The mass spectrum of the compound proposed as **1-(3,5-di-*tert*-butylphenyl)-2-methylpropene (26)** was as follows: *m/z* (relative intensity) 244 (4, M) 229 (8), 131 (6), 115 (5), 91 (7), 77 (4), 57 (100), 55 (15), 41 (50). The mass spectrum of the compound proposed as **3-(3,5-di-*tert*-butylphenyl)-2-methylpropene (27)** was as follows: *m/z* (relative intensity) 224 (7, M), 229 (19), 131 (6), 115 (6), 91 (6), 77 (5), 57 (100), 41 (47).

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Registry No. 7a, 107-47-1; **7b**, 3019-19-0; **7c**, 16463-11-9; **7d**, 78089-43-7; **8d**, 78089-44-8; **8e**, 78089-45-9; **9a**, 2211-92-9; **9b**, 4170-71-2; **9c**, 66713-28-8; **9d**, 78089-46-0; **10d**, 78089-47-1; **10e**, 78089-48-2; **13a**, 31562-40-0; **13b**, 1208-20-4; **13c**, 66713-32-4; **13d**, 989-39-9; **14a**, 110-06-5; **14b**, 882-33-7; **14c**, 2905-17-1; **14d**, 20875-34-7; **14e**, 19715-27-6; **15b**, 1212-08-4; **15c**, 66713-33-5; **15d**, 1062-30-2; **16a**, 66713-31-3; **16c**, 66713-30-2; **16d**, 78089-49-3; **19**, 66741-04-6; **21**, 732-26-3; **23**, 1460-02-2; **26**, 72215-86-2; **27**, 72215-85-1; 1,2,3-tri-*tert*-butylbenzene, 40782-34-1; 2,4,6-tri-*tert*-butylphenyl bromide, 3975-77-7; 2,4,6-tri-*tert*-butylbenzenethiol, 961-39-7; 2,4,6-triisopropylbenzenethiol, 22693-41-0.

Synthesis, Conformation, and Complexation Behavior of 2,9,18,25-Tetraoxa[8,8](1,4)naphthalenophane†

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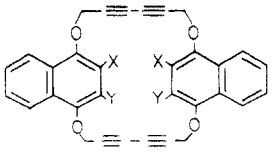
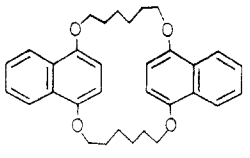
The synthesis of the title compound is described. Evidence is presented for its preferential "face-edge" conformation. Charge-transfer complexation proves to be a classical $\pi-\pi$ interaction with the "face-edge" conformation. There is no evidence for inclusion complexation. Attempted synthesis of substituted analogues of the title compound is described, including novel transformations in the 1,2,4-trisubstituted and 1,2,3,4-tetrasubstituted naphthalene series.

Introduction

We report the preparation and charge-transfer complexation behavior of (1,4)naphthalenophanes **1** and **2**. We have previously shown[3] that the analogous (1,4)-benzenophane **9**, approximating a 3.5 × 4 Å box, is too narrow to accommodate intracavity hosts. Rather it forms π complexes via a flattened conformation wherein the two aromatic rings are coplanar. It seemed to us that fusion of benzo lips onto **9**, forming (1,4)naphthalenophanes such as **1** and **2**, with their increased bite could circumvent these difficulties. A number of interesting transformations were encountered in the development of routes to functionalized derivatives of **1** such as **1a** and **1b**. These are reported here as is the charge-transfer complexation behavior of **2**.



1 X=Y=H
1a X=COOCH$_3$, Y=H
1b X=Y=-CH$_2$OAc
1c X=CH$_2$OAc, Y=H



2

Results and Discussion

Preparation of (1,4)Naphthalenophanes 1 and 2. Our initial plan was to prepare the naked phane **1** and to functionalize it or its hydrogenated derivatives at the 2 and 2′ positions. Linking these functionalities would then enforce a syn conformation upon the molecule. Cupric acetate oxidation of 1,4-bis(propynyloxy)naphthalene[2] afforded a difficultly soluble mixture of products. Peaks due to **1** (35% yield) could be identified in the mixture by their characteristic upfield shifts[3] but separation of **1** from the mixture was thwarted by its insolubility. Catalytic reduction of the crude mixture afforded cyclophane **2** in 28% overall yield, thus confirming the assignments made above.

Conformation of 2. The syn face-face conformation of **2** is not consistent with its NMR spectra. The data suggest that both the anti and edge-face conformations play an important role in defining the structure of **2**. The marked upfield shift of protons of C2 and C3, δ 5.84 as compared with δ 6.67 in 1,4-bis(1-propyloxy)naphthalene, defines a "cyclization shift" Δ_{cyc}[3] of 0.83 ppm. This may be compared with Δ_{cyc} for the analogous benzenophanes[3] of 0.3–0.5 ppm. Yoshino et al.[28] have studiked several [3.3](1,4)naphthalenophanes. An ArH Δ_{cyc} of 1.5 ppm was observed for a [3.3](1,4)naphthaleno(9,10)-anthracenophane.[28] *syn*-[3.3](1,4)Naphthalenophane is reported to have a Δ_{cyc} of 0.23 ppm; the anti conformer has a Δ_{cyc} of 1.15 ppm.[29] Otsubo et al.[4] have described the preparation of a series of [3.3] mixed arenophanes. The

† *Chemical Abstracts* name: 2,9,18,25-tetraoxapentacyclo[24.6.2.2^{10,12}.0^{11,16}.0^{27,32}]tetratriacontadeca-(10,12,14,16,26,28,30,32,33,35)-ene.

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