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Highly Selective Sulfoxidation of Allylic and Vinylic Sulfides by Hydrogen Peroxide Using a Flavin as Catalyst

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A highly chemoselective oxidation of allylic and vinylic sulfides to the corresponding sulfoxides has been developed using flavin **1** as the oxidation catalyst and hydrogen peroxide as the terminal oxidant. The sulfoxides were formed in good to excellent yields in a highly selective manner even when an excess of the oxidant was used. Sulfone formation was completely suppressed to <0.5% (in one single case 1.5% sulfone was detected). No epoxidation of double bonds or interference with other functional groups was observed under the reaction conditions. The general applicability was demonstrated by the selective oxidation of various allylic and vinylic sulfides having different electronic properties. A number of functionalities including hydroxy, acetoxy, amino, silyloxy, and formyl groups are tolerated under these mild reaction conditions.

Introduction

Organosulfur compounds are versatile intermediates in organic synthesis and useful for the preparation of biologically and medically important products.[1] In particular, sulfoxides and sulfones have been extensively used for carbon−carbon bond forming reactions,[2] rearrangements,[3] and eliminations.[4] When different functional groups are present in a molecule, it can be difficult to transform one of them without interfering with the other. It is therefore of great interest to chemoselectively synthesize these compounds. Organic sulfides having a nucleophilic double bond present in the molecule are examples of such compounds. The sulfur moiety can easily be oxidized by electrophilic oxidants, but special conditions are required to chemoselectively obtain sulfoxides without sulfone formation or epoxidation of the double bond.

There is a significant difference in the nucleophilicity of the sulfide compared to the sulfoxide,[5] and although some methods have been developed for selective oxidation to sulfoxides,[6] further improvement of this chemoselective reaction is desirable. A variety of the existing methods have the disadvantage of being expensive, using toxic chemicals, or suffering from moderate selectivity. In particular, for the oxidation of sulfides containing double bonds only one thorough investigation with regard to the scope of substrates has been published.[7] Recently, Koo and co-workers reported on the oxidation of allylic sulfides using a trirutile-type solid oxide catalyst.[8] Several allylic sulfides were oxidized to the corresponding sulfoxides without formation of epoxides. Sulfone formation, however, could in none of the cases be completely avoided, even when equimolar amounts of the oxidant were used.

These results prompted us to examine the use of a biomimetic flavin system, previously developed in our

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(1) General Reviews: (a) Metzner, P.; Thuillier, A. *Sulfur Reagents in Organic Synthesis*; Academic Press: London, 1994. (b) Drabowicz, J.; Kielbasinski, P.; Mikolajczyk, M. In *The chemistry of sulphones and sulphoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; Wiley: Chichester, U.K., 1988; pp 233−378. (c) Gundermann, K.-D.; Hümke, K. In *Methoden der Organischen Chemie (Houben-Weyl) Organische Schwefel-Verbindungen*; Klamann, D., Ed.; Thieme: Stuttgart, New York, 1985; Vol. E11, Teil 1. (d) Page, P. C. B., Ed. *Organosulfur Chemistry I*; Springer: Berlin, 1999. (e) Page, P. C. B., Ed. *Organosulfur Chemistry II*; Springer: Berlin, 1999.

(2) Solladie, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 6, p 148.

(3) (a) Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 2100. (b) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147. (c) De Lucchi, O.; Miotti, U.; Modena, G. *Org. React.* **1991**, *40*, 157. (d) Braverman, S. In *The chemistry of sulphones and sulphoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; Wiley: Chichester, U.K., 1988; pp 717−758.

(4) (a) Hofmann, J. E.; Wallace, T. L.; Schriesheim, A. *J. Am. Chem. Soc.* **1964**, *86*, 1561. (b) De Groot, A.; Jansen, B. J. M.; Reuvers, J. T. A.; Tedjo, E. M. *Tetrahedron Lett.* **1981**, *22*, 4137.

(5) Bonchio, M.; Conte, V.; De Conciliis, M. A.; Di Furia, F.; Ballistreri, F. P.; Tomaselli, G. A.; Toscana, R. M. *J. Org. Chem.* **1995**, *60*, 4475−4480.

(6) For examples, see: (a) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287−1290. (b) Ali, M. H.; Stevens, W. C. *Synthesis* **1997**, 764−768. (c) Batigalhia, F.; Zaldini-Hernandes, M.; Ferreira, A. G.; Malvestiti, I.; Cass, Q. B. *Tetrahedron* **2001**, *57*, 9669−9676. (d) Suárez, A. R.; Rossi, L. I.; Martin, S. E. *Tetrahedron Lett.* **1995**, *36*, 1201−1204. (e) Ravikumar, K. S.; Bégué, J.-P.; Bonnet-Delpon, D. *Tetrahedron Lett.* **1998**, *39*, 3141−3144. (f) Fraile, J. M.; García, J. I.; Lázaro, B.; Mayoral, J. A. *J. Chem. Soc., Chem. Commun.* **1998**, 1807−1808. (g) Iranpoor, N.; Firouzabadi, H.; Pourali, A.-R. *Tetrahedron* **2002**, *58*, 5179−5184. (h) Raghavan, P. S.; Ramaswamy, V.; Upadhya, T. T.; Sudalai, A.; Ramaswamy, A. V.; Sivasanker, S. *J. Mol. Catal., A* **1997**, *122*, 75−80. (i) Martin, S. E.; Rossi, L. I. *Tetrahedron Lett.* **2001**, *42*, 7147−7151. (j) Orito, K.; Hatakeyama, T.; Takeo, M.; Suginome, H. *Synthesis* **1995**, 1357−1358. (k) Breton, G. W.; Fields, J. D.; Kropp, P. J. *Tetrahedron Lett.* **1995**, *36*, 3825−3828. (l) Arterburn, J. B.; Nelson, S. L. *J. Org. Chem.* **1996**, *61*, 2260−2261.

(7) For the sulfoxidation of some terminally unsaturated sulfides, see: (a) Ravikumar, K. S.; Bégué, J.-P.; Bonnet-Delpon, D. *Tetrahedron Lett.* **1998**, *39*, 3141−3144. (b) Ravikumar, K. S.; Zhang, Y. M.; Bégué, J.-P.; Bonnet-Delpon, D. *Eur. J. Org. Chem.* **1998**, 2937−2940.

(8) Choi, S.; Yang, J.-D.; Ji, M.; Choi, H.; Kee, M.; Ahn, K.-H.; Byeon, S.-H.; Baik, W.; Koo, S. *J. Org. Chem.* **2001**, *66*, 8192−8198.

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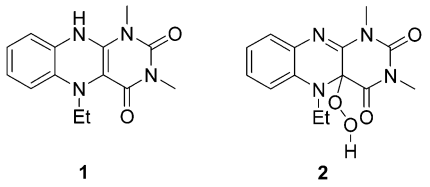
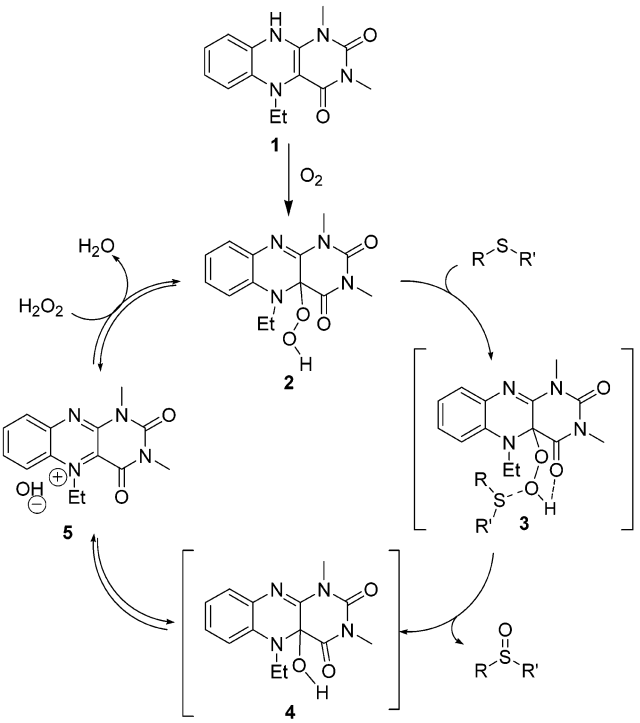
CHART 1



1 **2**

SCHEME 1



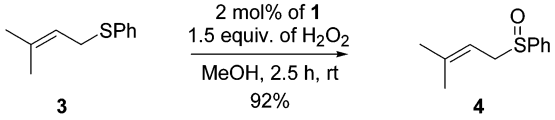
group,[9] in the sulfoxidation of allylic and some vinylic sulfides without overoxidation to sulfone or epoxide formation. The same system has been used in studies on heteroatom oxidations by our group.[9] On the basis of the results obtained for oxidation of tertiary amines to amine oxides,[9a] a triple catalytic system for the dihydroxylation of olefins using hydrogen peroxide as the terminal oxidant has been developed.[10] The *N*,*N*,*N*-1,3,5-trialkylated flavin **1** serves as a catalyst precursor which is activated by molecular oxygen to give hydroperoxy flavin **2** (Chart 1). Hydroperoxide **2** transfers its electrophilic oxygen to the substrate, and is readily reoxidized by hydrogen peroxide to maintain the catalytic cycle (Scheme 1).

Herein, we report a mild procedure for the highly chemoselective sulfoxidation of various allylic and some vinylic sulfides using environmentally benign hydrogen peroxide as terminal oxidant. An advantage with the present system is that the hydrogen peroxide can be kept at a low concentration by slow addition, leading to even milder conditions.

(9) (a) Bergstad, K.; Bäckvall, J.-E. *J. Org. Chem.* **1998**, *63*, 6650−6655. (b) Minidis, A. B. E.; Bäckvall, J.-E. *Chem.—Eur. J.* **2001**, *7*, 297−302.

(10) (a) Bergstad, K.; Jonsson, S. Y.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1999**, *121*, 10424−10425. (b) Jonsson, S. Y.; Adolfsson, H.; Bäckvall, J.-E. *Org. Lett.* **2001**, *3*, 3463−3466. (c) Jonsson, S. Y.; Färnegårdh, K.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2001**, *123*, 1365−1371.

SCHEME 2



3 **4**

Results and Discussion

Oxidation of Various Allylic Sulfides with Different Electronic Properties. To use hydrogen peroxide as terminal oxidant for the selective sulfoxidation of allylic substrates, suitable reaction conditions have to be found. Hydrogen peroxide is known to be a nucleophilic oxidant; therefore, it is not surprising that the uncatalyzed reaction of hydrogen peroxide with sulfides is very slow.[9b] To selectively oxidize sulfides to their corresponding sulfoxides, the hydroperoxide has to be moderately electrophilic to prevent further oxidation of the sulfoxide to a sulfone or interfere with double bonds present in the molecule.

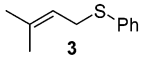
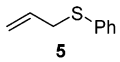
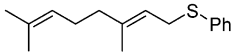
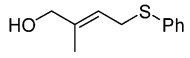
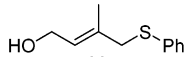
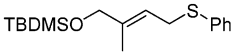
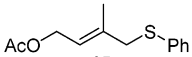
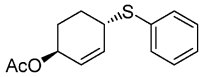
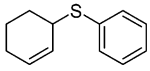
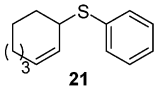
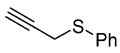
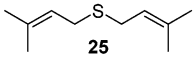
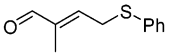
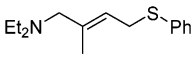
The catalytic cycle (Scheme 1)[9b] is initiated by the generation of the electrophilic and reactive hydroperoxide intermediate **2**[11] from **1** and molecular oxygen. The hydroperoxide **2** transfers an oxygen atom to the sulfide to give sulfoxide and hydroxyflavin intermediate **4**. Elimination of OH^- from **4** produces the aromatic 1,4-diazine **5**. The latter intermediate becomes the catalytic species that activates and reacts with hydrogen peroxide to give the flavin hydroperoxide **2**. The advantage of the *N*,*N*,*N*-1,3,5-trialkylated flavin system (Scheme 1) over the *N*,*N*,*N*-3,5,10-trialkylated analogues often used is that the elimination of OH^- from **4** to give **5** is favored due to aromatization.

Using the electron-rich phenyl prenyl sulfide (**3**) as a model compound, we adopted a previously established procedure for the sulfoxidation of saturated sulfides.[9b] Only a small amount of flavin catalyst **1** was employed (2 mol %), and a minor excess of the oxidant H_2O_2 (1.5 equiv) was used. Methanol was chosen as the solvent, and no inert conditions such as dry solvent or argon atmosphere were required. With this catalytic system sulfide **3** was oxidized to sulfoxide **4** in 92% isolated yield with remarkable selectivity (>99.5%) with respect to both the sulfur moiety and the double bond; neither sulfone nor epoxide formation could be detected (Scheme 2). It was not necessary to strictly control the amount of hydrogen peroxide to avoid overoxidation, which shows that the flavin system is highly selective for sulfoxidation.

To demonstrate the generality and scope of this methodology, a variety of allylic sulfides containing various functional groups were oxidized to the corresponding sulfoxides under these reaction conditions (Table 1). Allyl phenyl sulfide (**5**) and geranyl phenyl sulfide (**7**) were oxidized to the corresponding sulfoxides in high yields (Table 1, entries 2 and 3). No overoxidation products or epoxides were formed in either case. In particular for **7** this is noteworthy since it has two trisubstituted and therefore very nucleophilic double bonds. Also the even more electron-rich double bonds in sulfides **9**, **11**, **13**, and **15** were not attacked under the

(11) One reviewer considered participation of a dioxirane intermediate as an alternative mechanism. Such a mechanism seems less likely in our case.

TABLE 1. Oxidation of Various Allylic Sulfides with the Flavin Catalyst−H_2O_2 System[a]

Entry	Sulfide	Sulfoxide	H_2O_2 (equiv)	Yield of Sulfoxide (%)
1	 **3**	**4**	1.5	92
2	 **5**	**6**	1.5	88
3	 **7**	**8**	1.5	76
4	 **9**	**10**	1.5	77
5	 **11**	**12**	1.5	74
6	 **13**	**14**	1.5	87
7	 **15**	**16**	1.5	96
8	 **17**	**18**	1.5	80
9	 **19**	**20**	1.5	84
10	 **21**	**22**	1.5 2	72 86[b,c]
11	 **23**	**24**	1.5	75[b]
12	 **25**	**26**	1.5	85[d]
13	 **27**	**28**	1.5 4	65 77[b,c]
14	 **29**	**30**	1.5	86

[a] Unless otherwise noted, the reactions were performed using 0.018 equiv of **1** in MeOH at rt. Reaction times vary from 2.5 to 3 h. [b] The reaction was run overnight. [c] The reaction was run with 0.04 equiv of **1**. [d] The reaction was run at 0 °C; 1.5% sulfone was formed.

reaction condition (Table 1, entries 4−7). Comparing sulfides **9** and **11**, the position of the electron-donating methyl group on the double bond does not affect their reactivity toward oxidation. The sulfide **13** tolerated the condition applied, but quenching the reaction with sodium dithionite destroyed the product formed, and therefore, an alternative workup was used (see the Experimental Section). Sulfide **17**, synthesized from *trans*-1-acetoxy-4-chloro-2-cyclohexene,[12] was oxidized to a 1:1 diastereomeric mixture of the corresponding sulfoxides **18**. Compounds **19** and **21** containing unsubstituted cycloalkene moieties were as well cleanly transformed to sulfoxides **20** and **22**, respectively. In the case of **21** the yield could be slightly increased by using 2 equiv of hydrogen peroxide and 0.04 equiv of the catalyst and running the reaction overnight.

Phenyl propargyl sulfide (**23**) (Table 1, entry 11) was transformed to sulfoxide **24** by the flavin catalytic system, although a slightly lower yield (75%) was obtained. Also in this case no other oxidation products could be detected.

As expected, electron-rich allylic sulfides were oxidized faster than their electron-deficient counterparts. The oxidation of diprenyl sulfide (**25**) under standard conditions gave a high yield of sulfoxide contaminated with small amounts of the corresponding sulfone as a side product, the sulfoxide-to-sulfone ratio being 98:2. Lowering the temperature to 0 °C improved the sulfoxide-to-sulfone ratio to 98.5:1.5. It is noteworthy that a catalyst loading of only 1 mol % was enough to perform the reaction equally well. On the other hand, sulfide **27**, having an α,β-unsaturated carbonyl moiety and being less electron-rich on the sulfur, needed modified conditions to be oxidized. Running the reaction overnight employing 0.04 equiv of **1** and 4 equiv of hydrogen peroxide gave 77% isolated yield without the formation of sulfone, whereas using the standard conditions gave 65% sulfoxide **28** after 3 h. It is noteworthy that no epoxide was formed, although the double bond is more electrophilic and might be susceptible to hydrogen peroxide attack.

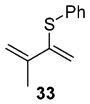
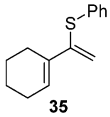
Since amines also can be oxidized to their corresponding *N*-oxides using the catalytic flavin system,[9b] it was of interest to investigate how sulfide **29** acts under these reaction conditions. It is well-known that tertiary amines react faster than secondary amines, but the competitive behavior of a tertiary amine vs a thioether using flavins has not been studied so far. The sole product in the catalytic oxidation of **29** was sulfoxide **30**, which was obtained in 86% isolated yield after 3 h. No *N*-oxide could be detected when the reaction was followed by NMR spectroscopy.

Oxidation of Vinylic Sulfides to the Corresponding Sulfoxides. Attempts to apply the developed conditions to vinylic substrates proved to be moderately successful using 2 mol % flavin **1**. When phenyl vinyl sulfide (**31**) was allowed to react with hydrogen peroxide under the standard conditions (Table 2, entry 1), after 3 h only 24% of the sulfide was converted to sulfoxide. With the use of 0.04 equiv of **1** and 4 equiv of hydrogen peroxide an isolated yield of 60% was obtained.

1,3-Dienic systems influence the flavin-catalyzed process even more. The oxidation of sulfides **31** and **33** led to conversions of only 11% and 12%, respectively, after 3 h under standard conditions. Also in these cases an increase of the amounts of catalyst and oxidant yielded sulfoxides in better yields as exemplified by oxidation of **31** to **32** (Table 2, entry 1). Using the H_2O_2·urea complex

(12) Bäckvall, J.-E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676−3686.

TABLE 2. Oxidation of Vinylic Sulfides with the Flavin Catalyst−H_2O_2 System

Entry	Sulfide	Sulfoxide	H_2O_2 (equiv)	Conv. (%)	Yield of Sulfoxide (%)
1	 **31**	**32**	1.5	24[a]	n.d.[b]
			4	75[c]	60
2	 **33**	**34**	1.5	11[a]	n.d.
			10	74[d]	53
3	 **35**	**36**	1.5	12[a]	n.d.
			10	80[d,e]	60

[a] The reactions were performed using 0.02 equiv of **1** in MeOH at rt. Reaction times vary from 2.5 to 3 h. [b] nd = not determined. [c] The reaction was run for 24 h using 0.04 equiv of **1**. [d] The reaction was run for 48 h using 0.04 equiv of **1** and H_2O_2·urea complex. [e] The reaction was run at 35 °C.

as the oxidant source for the oxidation of the vinylic sulfides (Table 2, entries 2 and 3) gave better results, presumably because of better solubility and increased stability of the oxidant.

Due to the longer reaction times (and elevated temperature in the case of **35**) the vinylic sulfoxides could react further, once formed, which serves as an explanation for the somewhat lower yields. In addition, the flavin hydroperoxide might decompose if the sulfide reacts too slowly.[13] Nevertheless, the chemoselectivity of the catalytic process was not affected by the changed conditions. Neither sulfone nor epoxide formation was observed. Frontal orbital theory can be used to explain the different behavior of this class of compounds. Compared to that of allylic sulfides, the HOMO of the vinylic sulfides is, due to conjugation with the double bond, significantly lowered. Therefore, the high chemoselectivity observed in the case of allylic sulfides, which is explained by a good orbital overlap of the LUMO of the hydroperoxy flavin **2** and the HOMO of the allylic sulfides, is decreased in going to vinylic sulfides. This effect is even more pronounced for the 1,3-dienic sulfides where the electrons are delocalized over the whole unsaturated system. (Diphenyl sulfide, in which the electrons are delocalized over two aromatic rings, gave only 13% conversion under standard conditions.) The high chemoselectivity of the flavin-catalyzed sulfoxidation, associated with a moderate reactivity of the flavin hydroperoxide, leads to a slow conversion with these less reactive vinylic substrates.

Conclusion

We have shown that a flavin-catalyzed oxidation with hydrogen peroxide as the terminal oxidant can be used in a highly efficient and chemoselective sulfoxidation of various allylic and vinylic sulfides. A number of functional groups are tolerated in the sulfoxidation of allylic sulfides, including tertiary amines, which demonstrates the mildness of the procedure. In all cases allylic sulfoxides were obtained in high to excellent yields under mild reaction conditions and short reaction times, whereas vinylic substrates require a slightly modified procedure.

Experimental Section

General Methods. ^{1}H (400 or 300 MHz) and ^{13}C (100 or 75 MHz) NMR spectra were recorded in $CDCl_3$ using residual solvent as internal standard. Chemical shifts (δ) are reported in parts per million, and coupling constants (J) are given in hertz. IR spectra were obtained using an FT-IR instrument, and the samples were examined as neat films on NaCl plates. Only the strongest/structurally most important peaks (cm^{-1}) are listed. Mass spectra were recorded using a GC−MS instrument with a 15 m × 0.32 mm column. Silica gel 60 (240−400 mesh) was used for flash chromatography, and analytical thin-layer chromatography was performed on precoated silica gel 60-F_{254} plates. Unless otherwise noted, all chemicals were obtained from commercial suppliers and used without further purification. All reactions were performed at room temperature unless otherwise noted. Phenyl sulfide compounds were prepared by the reaction of the corresponding halides (either chloride or bromide) with thiophenol in acetone in the presence of K_2CO_3, and diprenyl sulfide (**25**) was prepared by the reaction of prenyl bromide with $Na_2S·xH_2O$ in EtOH.

Sulfide 9.[14,15] To a solution of triethylaluminum (2.71 g, 23.8 mmol, 1.0 M solution in hexanes, 23.8 mL) was added dropwise at 0 °C a solution of thiophenol (3.6 mL, 35.7 mmol) in benzene (12 mL). After the mixture was stirred for 30 min at room temperature 1-methyl-1-vinyloxirane (1 g, 11.9 mmol) was added over 35 min. Aqueous workup with cold diluted hydrochloric acid followed by column chromatography (pentane/EtOAc, 85:15) afforded 98% sulfide **9** (2.26 mg, 11.6 mmol) as a mixture of *Z*- and *E*-isomers in a ratio of 8:2 and 98% yield. The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41−7.19 (m, 5 H), 5.50−5.42 (m, 1 H), 3.94 (s, 2 H), 3.57−3.54 (dd, J = 8.0, 0.8 Hz, 2 H), 1.79 (app m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.1, 135.7, 131.6, 129.0, 127.1, 122.9, 61.9, 32.4, 21.4. The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41−7.19 (m, 5 H), 5.62−5.55 (m, 1 H), 3.99 (s, 2 H), 3.60−3.57 (m, 2 H), 1.61 (br s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.7, 136.4, 130.2, 128.9, 126.5, 120.6, 68.3, 31.8, 13.7.

Sulfide 11.[16] A mixture of (*E*)- and (*Z*)-4-acetoxy-2-methyl-2-butenyl phenyl sulfide (**15**) (0.230 mg, 0.97 mmol) was allowed to react with a 2 M solution of NaOH (160 mg, 4 mmol in 2 mL of H_2O) in ethanol. After 1 h 15 mL of brine was added and the mixture washed with 3 × 15 mL of dichloromethane. The combined organic phases were dried over $MgSO_4$, filtered, and evaporated. Flash chromatography with pentane/EtOAc (2:1) gave a mixture of *E*/*Z*-isomers (*E*:*Z* = 3.4:1) of sulfide **11** (150 mg, 0.77 mmol) in 77% yield as a colorless oil. The following are data for the *E*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.18 (m, 5H), 5.44−5.40 (m, overlap with *Z*-isomer signal, 1H), 4.08 (d, J = 7.0 Hz, 2H), 3.50 (s, 2H), 1.8 (d, J = 0.4 Hz, 3H). The following are data for the *Z*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.18 (m, 5H), 5.52−5.48 (m, overlap with *E*-isomer signal, 1H), 3.80 (d, J = 7.0 Hz, 2H), 3.51 (s, 2H), 1.89 (br d, J = 1.2 Hz, 3H).

Sulfide 13.[8] To a stirred solution of sulfide **9** (194 mg, 1 mmol) and imidazole (204 mg, 3 mmol) in DMF (2.5 mL) was added *tert*-butyldimethylsilyl chloride (226 mg, 1.5 mmol).

(13) (a) Mager, H. I. X.; Berends, W. *Tetrahedron* **1976**, *32*, 2303−2312. (b) Smith, S. B.; Bruice, T. C. *J. Am. Chem. Soc.* **1975**, *97*, 2875−2881. (c) Venkataram, U. V.; Bruice, T. C. *J. Chem. Soc., Chem. Commun.* **1984**, 899−900. (d) Bruice, T. C.; Miller, A. *J. Chem. Soc., Chem. Commun.* **1980**, 693−694. (e) Iwata, M.; Bruice, T. C.; Carrell, H. L.; Glusker, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 5036−5044.

(14) Mori, I.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron* **1984**, *40*, 4013−4018.

(15) Yasuda, A.; Takahashi, M.; Takaya, H. *Tetrahedron Lett.* **1981**, *22*, 2413−2416.

(16) Moiseenkov, A. M.; Veselovsky, V. V.; Makarova, Z. G.; Zhulin, V. M.; Smit, W. A. *Tetrahedron Lett.* **1984**, *25*, 5929−5932.

After 22 h the reaction mixture was poured into 5 mL of water, and the resulting mixture was extracted with 2 × 15 mL of chloroform. The combined organic layers were dried over Na_2SO_4. Sulfide **13** (284 mg, 0.96 mmol) was obtained as a mixture of *E*- and *Z*-isomers in a ratio of 1:2.6 in 96% yield. The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36−7.15 (m, overlap with *E*-isomer signal), 5.41−5.33 (m, 1H), 4.0 (s, overlap with *E*-isomer signal, 2H), 3.58 (d, overlap with *E*-isomer signal, J = 10 Hz, 2H), 1.74 (br s, 3H), 0.89 (s, overlap with *E*-isomer signal, 9H), 0.05 (s, 6H). The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36−7.15 (m, overlap with *Z*-isomer signal, 5H), 5.62−5.54 (m, 1H), 3.99 (s, overlap with *Z*-isomer signal, 2H), 3.58 (d, overlap with *Z*-isomer signal, 2H), 1.55 (br s, 3H), 0.89 (s, overlap with *Z*-isomer signal, 9H), 0.04 (s, 6H).

Sulfide 15. This sulfide was prepared from 4-acetoxy-1-chloro-2-methyl-2-butene[12] and thiophenol using the procedure described in ref 17 for reaction with 4-acetoxy-1-chloro-2-butene. Sulfide **15** (435 mg, 1.84 mmol) was obtained as a mixture of *E*- and *Z*-isomers in a ratio of 3.6:1 in 96% yield. The following are data for the *E*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.20 (m, overlap with *Z*-isomer signal, 5H), 5.4−5.35 (m, 1H), 4.52 (d, J = 6.8 Hz, 2H), 3.5 (s, 2H), 2.01 (s, 3H), 1.83 (br m, 3H). The following are data for the *Z*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.4−7.17 (m, overlap *E*-isomer signal, 5H), 5.44−5.4 (m, 1H), 4.25 (d, J = 7.2 Hz, 2H), 3.55 (s, 2H), 1.99 (s, 3H), 1.9 (br m, 3H). The sulfide was characterized by hydrolysis to the known[16] alcohol **11**.

Sulfide 17. *cis*-1-Acetoxy-4-chlorocyclo-2-hexene[12] (698 mg, 4 mmol) was allowed to react with thiophenol (0.62 mL, 6 mmol) and K_2CO_3 (1.10 g, 8 mmol) in 20 mL of refluxing acetone overnight. Water was added, and the mixture was extracted with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. After removal of the solvent in vacuo the residue was purified by flash chromatography (pentane/EtOAc, 90:10) to give sulfide **17** (800 mg, 3.2 mmol) in 81% yield as a pale yellow oil. GC−MS: m/z 248 $[M]^+$ (2), 189 $[M - AcO]^+$ (15), 188 $[M - AcOH]^+$ (47), 139 $[M - C_6H_5S]^+$ (18), 110 $[C_6H_5SH]^+$ (49), 79 (100), 77 $[C_6H_5]^+$ (52). IR (film): 3035, 2949, 1732, 1242, 739, 692 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50−7.35 (m, 2H), 7.34−7.20 (m, 3H), 6.00 (dd, J = 10.2, 3.9, 1H), 5.81 (ddd, J = 10.2, 3.9, 1.5 Hz, 1H), 5.26−5.18 (m, 1H), 3.88−3.80 (m, 1H), 2.25−2.06 (m, 2H), 2.03 (s, 3H), 1.80−1.64 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 134.6, 132.1, 131.9, 128.9, 127.8, 127.2, 66.9, 43.3, 25.6, 25.1, 21.2.

Propargyl Phenyl Sulfide (23).[8,18] Sodium hydroxide (1.5 g, 37.5 mmol) and thiophenol (2.3 mL, 22.5 mmol) were stirred in water (20 mL) for 25 min, after which the reaction mixture was cooled to 0 °C and propargyl bromide (3.35 g, 80% solution in toluene, 22.5 mmol) in benzene (25 mL) was added dropwise. Tetrabutylammonium bromide (0.73 g, 2.25 mmol) was added, and the mixture was stirred vigorously for 2.5 h. The organic phase was separated, washed with water (2 × 12 mL) and then brine (12 mL), and dried over $MgSO_4$, and solvents were removed in vacuo. Sulfide **23** was obtained in 90% yield (2.99 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.24 (m, 5H), 3.6 (d, J = 2.8 Hz, 2H), 2.25 (t, J = 2.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.4, 130.5, 129.4, 127.4, 80.3, 72.0, 23.0.

4-Chloro-3-methyl-2-butenyl Phenyl Sulfide (37). To a stirred solution of 4-hydroxy-3-methyl-2-butenyl phenyl sulfide[14,15] (**9**) (194 mg, 1 mmol) in 3 mL of dry dichloromethane was added triethylamine (279 μL, 2 mmol). The solution was cooled in an ice bath, after which methanesulfonyl chloride (155 μL, 2 mmol) was added dropwise. The solution was stirred overnight at room temperature. The reaction mixture was concentrated in vacuo and the residue diluted with diethyl ether and washed with 5 mL of water and 5 mL of brine. The organic phase was dried over Na_2SO_4. Filtration through silica afforded 1.54 g (91%) of the product as a mixture of *E*- and *Z*-isomers (pale yellow oil). The following are data for the *E*- + *Z*-isomers. GC−MS: m/z 212 $[M]^+$ (77), 214 $[M]^+$ (29), 177 $[M - Cl]^+$ (16), 176 $[M - HCl]\bullet^+$ (20), 110 $[C_6H_5S]\bullet^+$ (100). The following are data for the *Z*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.19 (m, 5H), 5.55−5.50 (m, 1H), 3.88 (s, 2H), 3.58−3.55 (dd, J = 0.9, 8.1 Hz, 2H), 1.84 (app q, J = 0.9, 1.5, 1.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 135.4, 130.8, 129.0, 126.7, 125.5, 42.8, 32.1, 21.7. The following are data for the *E*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.19 (m, 5H), 5.70−5.40 (m, 1H), 3.98 (s, 2H), 3.52 (d, overlap with the *Z*-isomer signal, 2H), 1.64 (app t, J = 0.9, 0,6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 135.4, 130.9, 129.0, 126.8, 125.6, 51.6, 32.3, 14.3.

Sulfide 29. A mixture of 4-chloro-3-methyl-2-butenyl phenyl sulfide (851.5 mg, 4 mmol), diethylamine (8.36 mL, 80 mmol), potassium carbonate (1.9 g, 14.4 mmol), and sodium iodide (0.5 g, 3.3 mmol) in acetonitrile was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, and the residue was diluted with 50 mL of saturated aqueous sodium carbonate solution and washed with 3 × 70 mL of dichloromethane. The combined organic layers were dried over Na_2SO_4, and the solvent was removed in vacuo. Sulfide **29** (106.2 mg, 0.43 mmol) (yellow oil) was obtained as a mixture of *E*- and *Z*-isomers in a ratio of 4:1 in 85% yield. The following are data for the *E*- + *Z*-isomers. GC−MS: m/z 250 $[M + H]^+$ (15), 249 $[M]^+$ (9), 234 $[M - CH_3]^+$ (31), 178 $[M - N(C_2H_5)_2 + H]\bullet^+$ (18), 177 $[M - N(C_2H_5)_2]^+$ (88), 176 $[M - HN(C_2H_5)_2]\bullet^+$ (100), 140 $[M - C_6H_5S]^+$ (42), 135 $[C_6H_5SC_2H_2]^+$ (33), 110 $[C_6H_5S]\bullet^+$ (6), 86 $[(C_2H_5)_2NCH_2]^+$ (25), 72 $[(C_2H_5)N(C_2H_4)]^+$ (32). The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36−7.32 (m, 2H), 7.30−7.23 (m, 2H), 7.21−7.15 (m, 1H), 5.49−5.43 (m, 1H), 3.65−3.62 (d, J = 7.7 Hz, 2H), 2.88 (br s, 2H), 2.42−2.35 (q, J = 7.2 Hz, 4H), 1.75 (d, J = 1.2 Hz, 3H), 1.01−0.96 (t, J = 7.0, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 136.8, 130.0, 128.9, 126.2, 122.8, 53.7, 46.9, 31.8, 23.0, 11.9. The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36−7.32 (m, 2H), 7.30−7.23 (m, 2H), 7.21−7.15 (m, 1H), 5.49−5.43 (m, 1H), 3.60−3.57 (d, J = 7.2, 2H), 2.86 (br s, 2H), 2.41−2.34 (q, J = 7.2 Hz, 4H), 1.61 (br s, 3H), 0.97−0.92 (t, J = 7.2, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 130.2, 128.8, 126.3, 122.8, 61.7, 46.6, 32.1, 15.1, 11.5.

General Procedure for the Chemoselective Oxidation of Allylic Sulfides to the Corresponding Sulfoxides Using the Flavin−H_2O_2 System. To a stirred solution of the allylic sulfide (0.5 mmol) in methanol (1.5 mL) at room temperature was added flavin **1** (2.7 mg, 0.01 mmol, 2 mol %, if not indicated differently). After 1 min under air atmosphere 30% aqueous hydrogen peroxide (0.75 mmol, 1.5 equiv) was added to the solution in one portion, leading to a color change from red to yellow. The resulting mixture was stirred at room temperature for the specified amount of time, and sodium dithionite was added. Workup method A: Water (20 mL) was added, and the mixture was extracted with 3 × 15 mL of dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. Workup method B: The reaction mixture was diluted with 40 mL of diethyl ether, and the organic phase was washed with 3 × 20 mL of water. The organic layer was dried over Na_2SO_4 and filtered. After removal of the solvent in vacuo the residue was purified by flash chromatography.

Oxidation of Phenyl Prenyl Sulfide (3):[8] Sulfoxide 4.[8,19] The reaction time was 2.5 h. Workup was made according to method B. Flash chromatography with pentane/EtOAc (3:1) afforded sulfoxide **4** (82 mg, 0.46 mmol) in 92% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60−7.57 (m, 2H), 7.50−7.46 (m, 3H), 5.10−5.03 (m, 1H), 3.56−3.48 (m, 2H), 1.71

(17) Bäckvall, J.-E.; Sellén, M.; Nyström, J.-E. *Acta Chem. Scand.* **1988**, *B42*, 397−402.

(18) Donkerwood, J. G.; Gordon, A. R.; Johnstone, C.; Kerr, W. J.; Lange, U. *Tetrahedron* **1996**, *52*, 7391−7420.

(19) Binns, M. R.; Haynes, R. K.; Katsifis, A. G.; Schober, P. A.; Vonwiller, S. C. *J. Am. Chem. Soc.* **1988**, *110*, 5411−5423.

(s, 3H), 1.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 142.4, 131.1, 129.0, 124.5, 111.2, 56.8, 26.0, 18.1.

Oxidation of Allyl Phenyl Sulfide (5):[20] **Sulfoxide 6.**[6b,21] The reaction time was 2.5 h. Workup was made according to method A. Flash chromatography with pentane/EtOAc (1:4) afforded sulfoxide **6** (74 mg, 0.44 mmol) in 88% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62−7.56 (m, 2H), 7.54−7.44 (m, 3H), 5.61 (ddt, J = 17.2, 9.6, 7.6 Hz, 1H), 5.32 (ddd, J = 9.6, 1.2, 1.2 Hz, 1H), 5.18 (ddd, J = 17.2, 1.2, 1.2 Hz, 1H), 3.53 (dd, J = 12.8, 7.6 Hz, 1H), 3.46 (dd, J = 12.8, 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 131.0, 128.9, 125.2, 124.2, 123.8, 60.8.

Oxidation of Geranyl Phenyl Sulfide (7):[8] **Sulfoxide 8.**[8] The reaction time was 3 h. Workup was made according to method B. Flash chromatography with pentane/EtOAc (65:35) afforded an isomeric mixture of sulfoxide **8** (101 mg, 0.38 mmol) in 76% yield as a pale yellow oil. The following are data for isomer A. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64−7.56 (m, 2H), 7.52−7.44 (m, 3H), 5.09−5.00 (m, 2H), 3.64−3.44 (m, 2H), 2.02 (br s, 4H), 1.68 (s, 3H), 1.59 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 132.1, 131.1, 129.9, 124.6, 123.8, 110.9, 56.7, 39.9, 26.5, 25.8, 17.8, 16.6. The following are data for isomer B. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64−7.56 (m, 2H), 7.52−7.44 (m, 3H), 5.09−5.00 (m, 2H), 3.64−3.44 (m, 2H), 1.97−1.89 (m, 4H), 1.74 (d, J = 1.2 Hz, 3H), 1.67 (d, J = 0.8 Hz, 3H), 1.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6, 143.6, 131.1, 129.1, 124.5, 123.8, 110.9, 56.7, 32.3, 26.5, 23.7, 17.8, 16.6.

Oxidation of Sulfide 9: Sulfoxide 10.[8] The reaction time was 2 h. Workup was made according to method B. Flash chromatography with pentane/EtOAc (1:1) afforded *E*- and *Z*-isomers (1:2.6) of sulfoxide **10** (80.5 mg, 0.38 mmol) in 77% yield as a yellow oil. The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61−7.58 (m, 2H), 7.56−7.46 (m, 3H), 5.45−5.37 (m, 1H), 4.0 (s, 2H), 3.62−3.58 (m, 2H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5, 145.3, 131.3, 129.2, 124.5, 110.9, 67.6, 55.9, 14.0. The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61−7.58 (m, 2H), 7.56−7.46 (m, 3H), 5.02−4.98 (m, 1H), 3.97 (s, 2H), 3.77−3.70 (m, 2H), 1.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 143.2, 131.3, 129.2, 124.3, 112.7, 61.5, 54.8, 22.7.

Oxidation of Sulfide 11:[16] **Sulfoxide 12.**[22] The reaction time was 3 h and 20 min. Workup was made according to method A. Flash chromatography with pentane/EtOAc (4:1) afforded the *E*- and *Z*-isomers (4:1) of sulfoxide **12** in 74% yield as a colorless oil. The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62−7.47 (m, 5H), 5.50−5.46 (m, 1H), 4.16−4.12 (m, 2H), 3.48 and 3.39 (AB pattern, J_{AB} = 12.4, 2H), 2.16 (br s, 1H), 1.8 (br s, 3H). The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67−7.44 (m, 5H), 6.05−5.0 (m, 1H), 3.97 (br m, 2H), 3.76 and 3.42 (AB pattern, J_{AB} = 17 Hz, 2H), 2.55 (br s, 1H), 1.71 (br s, 3H).

Oxidation of Sulfide 13: Sulfoxide 14.[8] The reaction time was 3 h. Workup was made according to method B without quenching. Flash chromatography with pentane/EtOAc (5:1) afforded the *E*- and *Z*-isomers (1:3.3) of sulfoxide **14** (135 mg, 0.43 mmol) in 87% yield as a yellow oil. The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62−7.55 (m, 2H), 7.51−7.44 (m, 3H), 5.37−5.31 (m, 1H), 3.97 (s, 2H), 3.68−3.53 (m, 2H), 1.39 (s, 3H), 0.86 (s, 9H), 0.035 (d, J = 1.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.3, 144.5, 131.1, 129.0, 124.6, 110.0, 67.7, 56.2, 25.9, 21.4, 13.8, −5.33. The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62−7.55 (m, 2H), 7.51−7.44 (m, 3H), 5.18−5.09 (m, 1H), 3.84 (s, 2H), 3.68−3.53 (m, 2H), 1.25 (s, 3H), 0.86 (s, 9H), 0.02 (d, J = 0.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.5, 143.4, 131.2, 129.1, 124.5, 112.2, 61.8, 55.8, 25.9, 21.4, 18.5, −5.25.

Oxidation of 15: Sulfoxide 16.[16] The reaction time was 3 h and 20 min. Workup was made according to method A. Flash chromatography with pentane/EtOAc (1:1) afforded the *E*- and *Z*-isomers (5.4:1) of sulfoxide **16** in 96% yield as a white powder. The following are data for the *E*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62−7.47 (m, 5H), 5.39−5.33 (m, 1H), 4.62−4.48 (m, 2H), 3.51 and 3.39 (AB pattern, J_{AB} = 16.6 Hz, 2H), 2.03 (s, 3H), 1.78 (br m, 3H). The following are data for the *Z*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65−7.49 (m, 5H), 5.69−5.63 (m, 1H), 4.38−4.24 (m, 1H), 3.71 and 3.54 (AB pattern, J_{AB} = 16.8 Hz, 2H), 2.0 (s, 3H), 1.8 (br s, 3H).

Oxidation of Sulfide 17: Sulfoxide 18. The reaction time was 3.5 h. Workup was made according to method A. Flash chromatograph with pentane/EtOAc (1:1) afforded sulfoxide **18** (106 mg, 0.40 mmol) in 80% yield as a pale yellow oil in a nonseparable diastereomeric mixture of 1:1. A 20% yield of 4-acetoxy-2-cyclohexenyl phenyl sulfide (**17**) (30 mg, 0.10 mmol) could be recovered. The following are data for diastereomers A + B: GC−MS: m/z 250 $[M - CH_2]^+$ (37), 125 $[C_6H_5SO]^+$ (100), 109 $[C_6H_5S]^+$ (12), 77 $[C_6H_5]^+$ (49). IR (film): 3066, 2930, 1732, 1243, 748, 690 cm^{-1}. The following are data for diastereomer A. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65−7.60 (m, 2H), 7.53−7.48 (m, 3H), 6.00 (ddd, J = 10.4, 4.0, 1.6 Hz, 1H), 5.47 (ddd, J = 10.4, 4.0, 0.8 Hz, 1H), 5.24−5.16 (m, 1H), 3.38−3.32 (m, 1H), 2.28−1.70 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 141.7, 132.5, 131.5, 129.1, 125.1, 124.7, 66.0, 62.2, 25.2, 21.1, 17.6. The following are data for diastereomer B. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.58 (m, 2H), 7.54−7.48 (m, 3H), 6.08 (ddd, J = 10.0, 3.2, 2.0 Hz, 1H), 5.82 (ddd, J = 10.0, 3.2, 1.2 Hz, 1H), 5.25−5.16 (m, 1H), 3.46−3.38 (m, 1H), 2.28−1.55 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 141.6, 133.2, 131.3, 129.0, 125.1, 124.1, 66.8, 60.8, 25.9, 19.9, 17.6.

Oxidation of 2-Cyclohexenyl Phenyl Sulfide (19):[23] **Sulfoxide 20.**[24] The reaction time was 2.5 h. Workup was made according to method A. Flash chromatography with pentane/EtOAc (1:4) afforded sulfoxide **20** (88 mg, 0.42 mmol) in 84% yield as a yellow oil in a nonseparable diastereomeric mixture of 55:45. The following are data for the first diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.54 (m, 2H), 7.49−7.42 (m, 3H), 6.11−6.05 (m, 1H), 5.61−5.54 (m, 1H), 3.35−3.28 (m, 1H), 2.34−1.40 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 135.1, 130.8, 128.8, 124.7, 119.3, 61.3, 24.5, 23.2, 19.8. The following are data for the second diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.54 (m, 2H), 7.49−7.42 (m, 3H), 5.99−5.93 (m, 1H), 5.15−5.08 (m, 1H), 3.27−3.21 (m, 1H), 2.34−1.40 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 135.1, 131.1, 128.7, 125.1, 119.9, 62.9, 24.8, 21.3, 18.8.

Oxidation of 2-Cyclooctenyl Phenyl Sulfide (21):[25] **Sulfoxide 22.**[26] Sulfide **21** (109 mg, 0.50 mmol) was reacted with 30% aqueous hydrogen peroxide solution (112 μL, 1.00 mmol) using flavin **1** (5.4 mg, 0.02 mmol) as catalyst for 2.5 h at room temperature. Workup was made according to method A. Flash chromatography with pentane/EtOAc (65:35) afforded sulfoxide **22** (102 mg, 0.43 mmol) in 86% yield as a pale yellow oil in a nonseparable diastereomeric mixture of 78:22. The following are data for the first diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65−7.40 (m, 5H), 5.76−5.68 (m, 1H), 5.54−5.65 (m, 1H), 3.60−3.48 (m, 1H), 2.10−1.18 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 134.0, 130.9, 128.8, 124.9, 123.4, 63.3, 28.6, 28.2, 26.4, 26.1, 24.9. The following are data for the second diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65−7.40 (m, 5H), 5.84−5.72 (m, 1H), 5.48−5.40 (m, 1H), 3.70−

(20) Arnau, N.; Moreno-Mañas, M.; Pleixats, R. *Tetrahedron* **1993**, *49*, 11019−11028.

(21) Antoniak, D. J.; Ridley, D. D.; Smal, M. A. *Aust. J. Chem.* **1980**, *33*, 2635−2651.

(22) (a) Nederlof, P. J. R.; Moolenar, M. J.; de Waard, E. R.; Huisman, H. O. *Tetrahedron Lett.* **1976**, *36*, 3175−3178. (b) van der Laan, R.; Moolenaar, M. J.; de Koning, H.; Huisman, H. O. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 220−225.

(23) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208−1217.

(24) Hua, D. H.; Venkataraman, S.; Chan-Yu-King, R.; Paukstelis, J. V. *J. Am. Chem. Soc.* **1988**, *110*, 4741−4748.

(25) Hardinger, S. A.; Fuchs, P. L. *J. Org. Chem.* **1987**, *52*, 2739−2749.

(26) Whitesell, J. K.; Carpenter, J. F.; Yaser, H. K.; Machajewski, T. *J. Am. Chem. Soc.* **1990**, *112*, 7653−7659.

3.56 (m, 1H), 2.10−1.18 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 133.5, 130.6, 128.7, 124.4, 121.6, 61.9, 30.3, 28.2, 26.5, 26.1, 25.3.

Oxidation of Propargyl Phenyl Sulfide (23): Sulfoxide 24.[27] The reaction time was 21 h. Workup was made according to method B. Flash chromatography with pentane/EtOAc (9:1) afforded sulfoxide **24** (61.8 mg, 0.38 mmol) in 76% yield as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72−7.69 (m, 2H), 7.55−7.51 (m, 3H), 3.70−3.57 (dq, AB pattern, J_{AB} = 19.4 Hz, J_4 = 2.8 Hz, 2H), 2.33 (t, J = 2.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 131.9, 129.2, 124.6, 76.5, 72.9, 47.9.

Oxidation of Diprenyl Sulfide(25):[28] **Sulfoxide 26.**[8] The reaction time was 2.5 h at 0 °C. Workup was made according to method A. Flash chromatography with pentane/EtOAc (1:4) afforded sulfoxide **26** (79 mg, 0.425 mmol) in 85% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.27−5.18 (m, 2H), 3.45−3.30 (m, 4H), 1.77 (s, 6H), 1.68 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 111.4, 49.8, 25.9, 18.4.

Oxidation of Sulfide 27:[29] **Sulfoxide 28.**[8] Sulfide **27** (96 mg, 0.50 mmol) was reacted with 30% aqueous hydrogen peroxide solution (112 μL, 1.00 mmol) using flavin **1** (5.4 mg, 0.02 mmol) as catalyst for 3 h at room temperature. Workup was made according to method A. Flash chromatography with pentane/EtOAc (1:1) afforded sulfoxide **28** (81 mg, 0.385 mmol) in 77% yield as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.35 (s, 1H), 7.60−7.52 (m, 2H), 7.52−7.44 (m, 3H), 6.37 (dt, J = 8.1, 1.5 Hz, 1H), 3.92 (dd, J = 12.9, 8.1 Hz, 1H), 3.71 (dd, J = 12.9, 8.1 Hz, 1H), 3.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 145.1, 142.3, 138.0, 131.5, 129.2, 123.9, 55.6, 9.4.

Oxidation of Sulfide 29: Sulfoxide 30. The reaction time was 3.5 h. Workup was made according to method B. Flash chromatography with pentane/EtOAc (4:1) afforded sulfoxide **30** (97 mg, 0.37 mmol) in 86% yield as a yellow oil. The following are data for the *Z*- + *E*-isomers. MS: *m*/*z* calcd for $C_{15}H_{24}NSO$ (M^+ + H) 266.1573, found 266.1585. The following are data for the *Z*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.58 (m, 2H), 7.51−7.47 (m, 3H), 5.30−5.23 (m, 1H), 3.64−3.57 (m, 2H), 2.84 (s, 2H), 2.38−2.33 (q, J = 7.2 Hz, 4H), 1.44 (app s, 3H), 0.93 (t, J = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 143.6, 131.1, 129.1, 124.6, 112.5, 61.7, 56.4, 46.7, 23.5, 11.8. The following are data for the *E*-isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61−7.58 (m, 2H), 7.51−7.47 (m, 3H), 5.30−5.23 (br m, 1H), 3.69−3.65 (m, 2H), 2.72−2.71 (d, J = 4 Hz, 2H), 2.35−2.29 (q, J = 7.2 Hz, 4H), 1.76 (app s, 3H), 0.96−0.92 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 143.7, 131.1, 129.1, 124.6, 114.3, 56.1, 54.1, 46.8, 15.4, 11.9.

General Procedure for the Chemoselective Oxidation of Vinylic Sulfides to the Corresponding Sulfoxides Using the Flavin−H_2O_2 System. To a stirred solution of the vinylic sulfide (0.5 mmol) in methanol (1.5 mL) at room temperature was added flavin **1** (5.4 mg, 0.02 mmol, if not indicated differently). After 1 min under air atmosphere the specified amount of hydrogen peroxide was added to the solution in one portion, leading to a color change from red to yellow. The resulting mixture was stirred at room temperature or 35 °C for the specified amount of time and quenched by addition of sodium dithionite (0.2 g, 1.1 mmol). Water (20 mL) was added, and the mixture was extracted with 3 × 15 mL of dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered. After removal of the solvent in vacuo the residue was purified by flash chromatography.

Oxidation of Vinyl Phenyl Sulfide (31):[30] **Preparation of Sulfoxide 32.**[6b] Sulfide **31** (68 mg, 0.50 mmol), 30% aqueous hydrogen peroxide (224 μL, 2.00 mmol), and flavin **1** (5.4 mg, 0.02 mmol) were reacted for 24 h at room temperature. Flash chromatography with pentane/EtOAc (1:1) afforded sulfoxide **32** (45 mg, 0.30 mmol) in 60% yield as a yellow oil. A 14% yield of **31** (10 mg, 0.07 mmol) could be recovered. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63−7.56 (m, 2H), 7.52−7.44 (m, 3H), 6.67 (dd, J = 16.4, 9.6 Hz, 1H), 6.17 (d, J = 16.4, 1H), 5.87 (d, J = 9.6, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 142.9, 131.2, 129.4, 124.5, 120.6.

Oxidation of 3-Methyl-2-phenylthio-1,3-butadiene (33):[31] **Sulfoxide 34.**[31] Sulfide **33** (88 mg, 0.50 mmol), urea hydrogen peroxide addition complex (475 mg, 5.00 mmol), and flavin **1** (5.4 mg, 0.02 mmol) were reacted for 48 h at room temperature. Flash chromatography with pentane/EtOAc (1:1) afforded sulfoxide **34** (51 mg, 0.265 mmol) in 53% yield as a yellow oil. A 16% yield of **33** (14 mg, 0.08 mmol) could be recovered. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66−7.58 (m, 2H), 7.47−7.36 (m, 3H), 6.18 (s, 1H), 5.80 (s, 1H), 5.21 (s, 1H), 5.05 (s, 1H), 1.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.6, 143.7, 137.5, 131.2, 129.0, 125.6, 116.2, 114.8, 22.1.

Oxidation of 1-(1-Phenylthiovinyl)cyclohexene (35):[31] **Sulfoxide 36.**[31] Sulfide **35** (108 mg, 0.50 mmol), urea hydrogen peroxide addition complex (475 mg, 5.00 mmol), and flavin **1** (6.8 mg, 0.025 mmol) were reacted for 48 h at 35 °C. Flash chromatography with pentane/EtOAc (4:1) afforded sulfoxide **36** (70 mg, 0.30 mmol) in 60% yield as a yellow oil. A 26% yield of **35** (30 mg, 0.13 mmol) could be recovered. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.58 (m, 2H), 7.46−7.36 (m, 3H), 6.02 (s, 1H), 6.00−5.96 (m, 1H), 5.65 (s, 1H), 1.40−2.30 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 144.1, 131.5, 131.0, 129.1, 128.9, 125.5, 112.2, 27.7, 25.3, 22.2, 21.6.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **17**, **18**, **24**, **26**, and **28**−**30**. This material is available free of charge via the Internet at http:pubs.acs.org.

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(27) Skattebøl, L.; Boulette, B.; Solomon, S. *J. Org. Chem.* **1967**, *32*, 3111−3114.
(28) Takabe, K.; Katagiri, T.; Tanaka, J. *Tetrahedron Lett.* **1971**, *12*, 1503−1506.
(29) Nederlof, P. J. R.; Moolenaar, M. J.; De Waard, E. R.; Huisman, H. O. *Tetrahedron* **1978**, *34*, 2205−2207.
(30) van der Schaaf, P. A.; Kolly, R.; Kirner, H.-J.; Rime, F.; Mühlebach, A.; Hafner, A. *J. Organomet. Chem.* **2000**, *606*, 65−74.
(31) Bäckvall, J.-E.; Ericsson, A. *J. Org. Chem.* **1994**, *59*, 5850−5851.