Addition of Heteroaromatic Thiols to Electron-Rich Alkenes: A Reversed Hetero Ene Reaction

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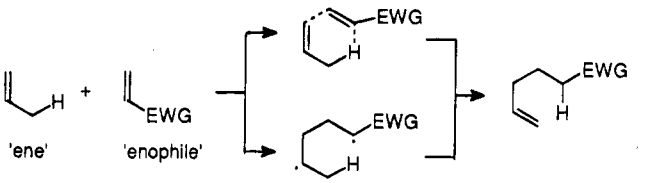
Benzothiophenethiol **1a** reacted with styrene to give thiol **2a**, which resulted from a "reversed hetero ene reaction". When the reaction was carried out in the presence of radical precursors, products deriving from radical addition to the styrene double bond of both thiols **1a** and **2a** were formed. The reaction of **1a** with butyl vinyl ether (BVE) gave the α,β-unsaturated dithioester **23a**, deriving from the "ene reaction product" **22a** through elimination of butanol. Similar behavior was exhibited by benzofuranthiol **1b**, which reacted with styrene to give thiol **2b** and with BVE to give the thionoester **23b**. Both dithio- and thionoesters **23a,b** were trapped as Diels–Alder adducts. In contrast, thiophenethiol **1c** did not react with styrene and reacted with BVE to give an electrophilic 1:1 adduct. Ene reaction of thiols **1a,b** occurred only with electron-rich olefins. In agreement, **1a** did not react with hex-1-ene and methyl acrylate and reacted with dimethyl maleate to give a nucleophilic adduct.

The ene reaction occurs between an alkene having an allylic hydrogen (an "ene") and a compound containing an electron-deficient double bond (an "enophile") to form a σ-bond with migration of the ene double bond and 1,5-hydrogen shift. From a mechanistic standpoint the ene reaction is related to the Diels–Alder reaction, since both reactions can be concerted, proceeding through cyclic transition states involving six electrons.[1] However, not all the ene reactions are concerted, some of these proceeding through a stepwise mechanism involving a diradical intermediate[2] (Scheme 1). In all cases, ene reactions occur only under drastic conditions, their activation energy being higher than that for an analogous Diels–Alder reaction. Ene reactions can be Lewis acid catalyzed, and in these cases occur under milder conditions through either a concerted or a stepwise zwitterionic mechanism.[3]

Ene reactions can be divided into "all-carbon" ene reactions, in which the enophile is an alkene substituted with electron-withdrawing groups, and "hetero" ene reactions, in which hetero enophiles, including carbonyl and thiocarbonyl compounds, imines, nitroso compounds, hydrazines, azo compounds, and dioxygen, are employed.[1] In contrast, there appear to be very few "hetero" ene reactions involving hetero ene components. The known examples are confined to thermal cyclization of olefinic ketones through an intramolecular ene reaction of the corresponding enols (the so-called "Conia reaction"), which occurs generally at very high temperatures (>300 °C).[4]

We report herein examples of thermal ene reactions occurring under mild conditions (ca. 80 °C) with a hetero

Scheme 1



ene reagent in which the benzylic function is replaced with a thiol group, i.e., a vinyl thiol. Vinyl thiols generally exist in the more stable tautomeric form as thioketones, which should be considered as enophiles rather than enes. The thiol function can be preserved when the double bond is a part of an aromatic ring. We reasoned that when weakly aromatic rings are considered, the double bond might have enough alkenic bond character to allow the corresponding arenethiol to behave as an "ene". Thus, we have taken into account the reactions of benzothiophenethiol **1a** and benzofuranthiol **1b** with simple alkenes (styrene, hex-1-ene, butyl vinyl ether (BVE), methyl acrylate, and dimethyl maleate) to obtain evidence for intermolecular hetero ene reactions.

Results and Discussion

Benzothiophenethiol **1a** reacted with styrene in benzene solution at 85 °C to give a complex reaction mixture. Column chromatography allowed for the separation of the adducts **5a** (10%) and **12a** (15%), methyl sulfides **9a** (1–2%) and **16a** (3–5%), the hydroxy derivative **17a** (5%), the ketone **18a** (5%), and the disulfide **13a** (40%). In addition, GC–MS analysis revealed the formation of noticeable amounts of benzaldehyde.

The reaction was repeated in the presence of AIBN, but this radical precursor did not significantly modify the reaction products pattern. In spite of this finding, the regiochemistry of adduct **5a** indicates that a radical mechanism took place involving regioselective addition

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(1) Ene reactions have been extensively reviewed; see the following: Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1990; pp 241–261. Snider, B. B. Ene Reactions with Alkenes as Enophiles and Oppolzer, W. Metallo-ene Reactions In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, Chapters 1.1 and 1.2.

(2) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476. Stephenson, L. M.; Orfanopoulos, M. *J. Org. Chem.* **1981**, *46*, 2200. Nahm, S. H.; Cheng, H. N. *J. Org. Chem.* **1986**, *51*, 5093.

(3) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. Snider, B. B.; Ron, E. *J. Am. Chem. Soc.* **1985**, *107*, 8160.

(4) Brocard, J.; Moinet, G.; Conia, J. M. *Bull. Soc. Chim. Fr.* **1972**, 1711. Mandville, G.; Leyendecker, F.; Conia, J. M. *Bull. Soc. Chim. Fr.* **1973**, 963. Leyendecker, F.; Drouin, J.; Conia, J. M. *Tetrahedron Lett.* **1974**, 2931. Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1. Bortolussi, M.; Bloch, R.; Conia, J. M. *Bull. Soc. Chim. Fr.* **1975**, 2727. Conia, J. M.; Lange, G. L. *J. Org. Chem.* **1978**, 43, 564.

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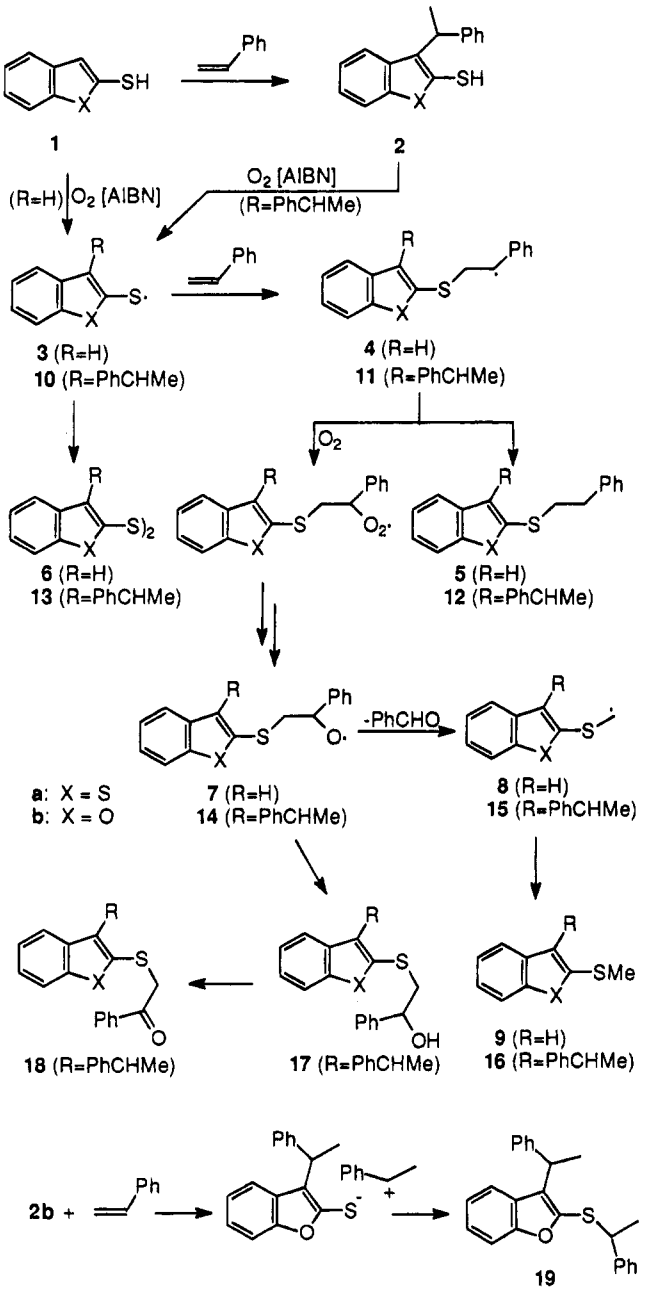
Scheme 2



of thiyl radical **3a** to the styrene double bond. Radical addition of thiyl radicals to the alkene double bond occurs readily, although in a reversible manner.[5] Thus, intermediate benzyl radical **4a** could abstract a hydrogen atom to give adduct **5a** or could be trapped by dioxygen to give the alkoxy radical **7a** (Scheme 2). β-Scission of radical **7a** afforded benzaldehyde with elimination of methylthio radical **8a**, from which methyl sulfide **9a** arose by hydrogen abstraction. Intermediate thiyl radical **3a** could be generated from dioxygen through an oxidation/deprotonation process. Dioxygen-promoted radical addition of arenethiols to alkynes has been previously reported.[6] To prevent any radical initiation, the reaction was repeated in the absence of both AIBN and dioxygen. Under these conditions none of the **5a** or **9a** products were formed, the thiol **2a** (racemic mixture) being the exclusive reaction product (ca. 80% yield).

The formation of thiol **2a** led us to infer that this compound could be responsible for products **12a**, **13a**, **16a**, **17a**, and **18a** through dioxygen (or AIBN) promoted formation of the intermediate thiyl radical **10a**. In fact, dimerization could lead to the disulfide **13a**, whereas addition to the styrene double bond could lead to the benzyl radical **11a**, which either afforded the adduct **12a** by hydrogen abstraction or was trapped by dioxygen thus leading to the alkoxy radical **14a**. In contrast to the analogous radical **7a**, two kinds of reactions seem to have opened for radical **14a**: β-scission with formation of benzaldehyde and methylthio radical **15a**, from which methyl sulfide **16a** was formed, or hydrogen abstraction giving the hydroxy derivative **17a**, from which its oxidation product **18a** was formed (Scheme 2).

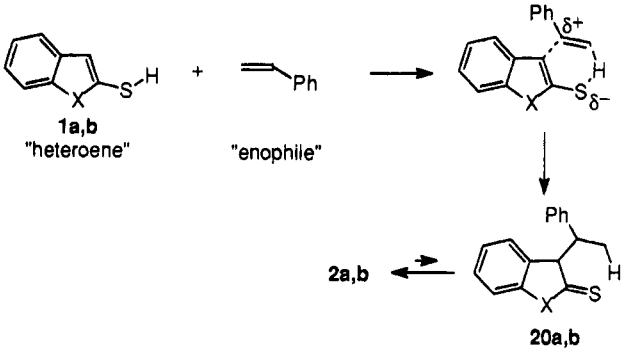
Similar results were obtained from benzofuranthiol **1b**. Reaction with styrene at 85 °C in the presence of dioxygen gave a complex mixture from which methyl sulfide **16b** (10%) and disulfide **13b** (35%) could be isolated together with a 1:1 inseparable mixture of the isomeric adducts **12b** and **19**. Moreover, the same reaction repeated in the absence of oxygen only gave the thiol **2b** (ca. 75%) as a racemic mixture. Sulfides **12b** and **16b**, analogous to sulfides **12a** and **16a**, arose from thiol **2a** through radical intermediate **11a**, whereas adduct **19** might be attributable to initial proton transfer from thiol **2b** to the styrene double bond, followed by nucleophilic attack of the resulting thiolate at the intermediate benzyl cation (Scheme 2).

Thus, it can be concluded that both thiols **1a** and **1b** react with styrene in nonradical conditions to give thiols **2a** and **2b**, which can be considered the tautomeric forms of dithioester **20a** and thionoester **20b**, respectively. Actually, compounds **20a,b** were expected from the ene reaction between styrene (the "enophile") and the α,β-unsaturated thiols **1a,b** ("enes") (Scheme 3).

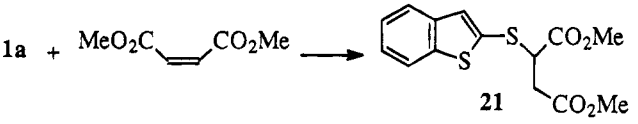
However, the route leading to **20a,b** (and then to thiols **2a,b**) presents some peculiar differences with respect to the classical "ene reaction". First of all, the regiochemistry of attack on the carbon–carbon double bond is reversed, the 1,5-hydrogen shift occurring toward the terminal alkenic carbon atom. Moreover, thiol **1a** did not react in nonradical conditions with 1-hexene and methyl acrylate (alkenes less electron rich than styrene), whereas reaction with dimethyl maleate (a highly electron deficient olefin) exclusively gave the nucleophilic 1:1 adduct **21** (Scheme 4).

These findings led us to suggest that the driving force of hetero ene reactions involving thiols **1a,b** is the proton

Scheme 3

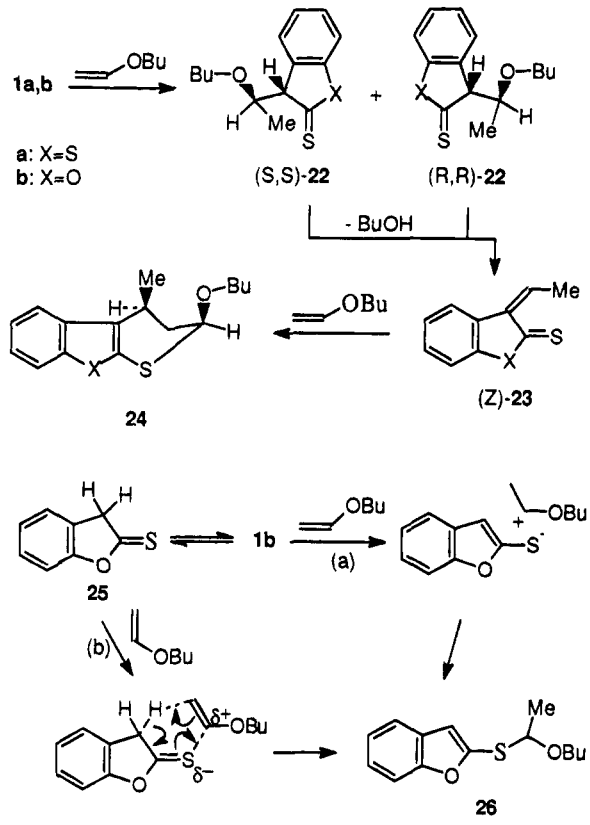


Scheme 4

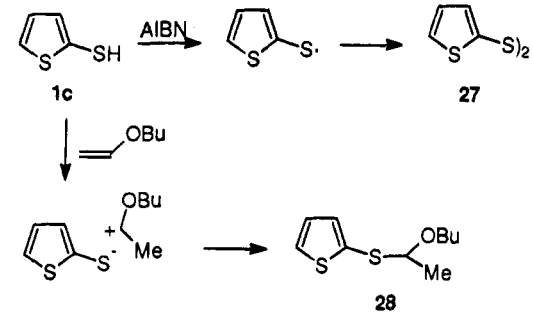


(5) Griesbaum, K. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 273.
(6) Benati, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2103.

Scheme 5



Scheme 6



transfer between the sulfur atom and the alkenic carbon atom. Thus, we claim that a concerted mechanism takes place through a six-membered cyclic transition state in which the C–H bond is more developed than the C–C bond (that is, an incipient carbocation is formed on the enophile). This situation is opposed to that of the "all-carbon" ene reactions, which require electron-poor enophiles and occur through transition states in which the new C–C bond is more highly developed than the C–H one (that is, an incipient carbanion is formed on the enophile). To stress this reversed polarity, we will refer to our reactions as "reversed hetero ene reactions".

On the basis of the above results, reactions of thiols **1a,b** with BVE, an electron-rich olefin, were also considered to obtain further evidence of reversed hetero ene reactions. Thiol **1a** reacted with a 5-fold excess of BVE to yield almost quantitative amounts of thiopyran **24a** (Scheme 5). Formation of thiopyran **24a** is ascribable to the initial reversed hetero ene reaction leading to intermediate **22a**. Thermal elimination of *n*-butanol should lead to the α,β-unsaturated dithioester **23a**, which can be trapped by a second molecule of BVE to give the Diels–Alder adduct **24a**. When the same reaction was repeated in the presence of equimolar amounts of BVE, noticeable amounts of starting thiol **1a** (50%) were recovered, the adduct **24a** being obtained as the major reaction product (80%) together with minor amounts of an unidentified compound at *m/z* 192 (M^+). This finding indicates that the Diels–Alder reaction favorably competes with the reversed hetero ene reaction leading to **22a**. Similarly, thiol **1b** reacted with BVE to give the Diels–Alder adduct **24b** (50%), which was accompanied by the unexpected formation of adduct **26** (30%) (Scheme 5).

The occurrence of Diels–Alder reactions between α,β-unsaturated thiocarbonyl compounds **23a,b** and BVE is relevant from a mechanistic standpoint. In fact, although Diels–Alder reactions of α,β-unsaturated thioketones and thioaldehydes with electron deficient alkenes have been reported,[7] only a few Diels–Alder reactions of α,β-unsaturated thiono and dithio esters are known, the only examples being confined to the dimerization reaction by [4 + 2] cycloaddition.[8]

Diastereomerically pure adducts **24a,b** were obtained in a highly stereospecific fashion. The ^{1}H NMR spectrum clearly showed the C(1)–H and C(3)–H bonds of the thiopyran ring to be in the equatorial position, as indicated by coupling constant values with C(2)–H methylenic protons (see Experimental Section). Obviously, methyl and butoxy groups lie in the axial position. Such a configuration can only arise from a stereospecific Diels–Alder addition of BVE to the (*Z*)-isomer (*Z*)-**23a,b**, which, therefore, must be formed in a highly stereoselective fashion. Assuming that enantiomeric mixtures of (*R,R*)- and (*S,S*)-**22a,b** arise from the stereospecific hetero ene reaction between BVE and thiols **1a,b**, the most reasonable route leading to (*Z*)-**23a,b** would involve an intramolecular thermal *syn*-elimination of butanol through a four-membered cyclic transition state. Indeed, eliminations proceeding through a four-membered E*i* mechanism are rather rare,[9] and to our knowledge, *syn*-elimination of alcohol from ethers having a β-hydrogen atom are unprecedented.

As far as the adduct **26** is concerned, an ionic stepwise mechanism (Scheme 5, path a), analogous to that leading to adduct **19** (see Scheme 2) and to adduct **28** (see Scheme 6), could be confidently claimed. However, competition between the ionic stepwise addition and the ene reaction should be favored by enhancing the aromatic character of the heteroaromatic ring on passing from benzofuranthiol **1b** to benzothiophenethiol **1a**. On the contrary, we did not find any products deriving from electrophilic addition of thiol **1a** to the BVE double bond. Moreover, we have found that thiol **1b**, owing to its low aromaticity, exists in equilibrium with thionoester **25** as a 50:50 tautomeric mixture. Thus, it might be suggested that both thiol **1b** and dithioester **25** can behave as ""hetero enes" with the "enophile" BVE: **25** might lead to **26** through a stepwise (or concerted) hetero ene reaction in which the thiocarbonyl function is part of a hetero ene reagent (Scheme 5, path b).

Unlike thiols **1a,b**, thiophenethiol **1c** did not react with styrene under nonradical conditions. This finding can

(7) Metzner, P. *Synthesis* **1992**, 1185. Saito, T.; Karakasa, T.; Fujii, H.; Furuno, E.; Suda, H.; Kobayashi, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1359.

(8) Gosselin, P.; Masson, S.; Thuillier, A. *Tetrahedron Lett.* **1980**, *21*, 2421. Hoffmann, R.; Hartke, K. *Chem. Ber.* **1980**, *113*, 919.

(9) Examples of a four-membered E*i* *syn*-elimination include hydrometallo-elimination from organometallic compounds (Lau, K. S. Y.; Becker, Y.; Huang, F.; Baezinger, N.; Stille, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 5664. Baudin, J. B.; Julia, M.; Rolando, C. *Tetrahedron Lett.* **1984**, *25*, 3203) and conversion of epoxides to olefins (Sonnet, P. E. *Tetrahedron* **1980**, *36*, 557).

be related to the higher aromatic character of thiophene, compared with benzothiophene and benzofuran, which prevents the occurrence of the "ene reaction". Moreover, thiol **1c** reacted with BVE under nonradical conditions to give the electrophilic adduct **28** in good yield. In this case, protonation of the double bond could occur as result of the high basicity of BVE, but once again the highly aromatic character of **1c** prevented the ene reaction from occurring; thus, an ion-pair mechanism (leading to the electrophilic adduct **28**) took place instead of a concerted one (Scheme 6). When the reaction was carried out in the presence of dioxygen (and/or AIBN), the adduct **28** was accompanied by minor amounts of disulfide **27**.

Conclusions

We have shown that benzothiophenethiol **1a** and benzofuranthiol **1b** react under nonradical conditions with electron-rich alkenes to give products deriving from a "reversed hetero ene reaction" in which these aromatic thiols behave as "hetero ene" reagents. Reaction with styrene led to thiols **2a,b**, tautomeric forms of the "ene reaction" products **20a,b**. Moreover, reaction with BVE gave α,β-unsaturated dithioester **23a** or thionoester **23b**, resulting from the ene products **22a** and **22b**, respectively, through stereoselective thermal *syn*-elimination of butanol. Compounds **23a,b** were isolated as the Diels–Alder adducts with the BVE dienophile. In contrast, thiol **1a** did not react with 1-hexene or methyl acrylate, whereas reaction with dimethyl maleate afforded the nucleophilic adduct **21**.

Finally, thiophenethiol **1c** did not react with styrene, due to its highly aromatic character, while it did react with BVE to give the Markovnikov adduct **28** through an ionic stepwise mechanism.

Experimental Section

Structural assignment to the reaction products was generally made on the basis of ^1H (^{13}C) NMR and MS spectral data in addition to elemental analysis. Identification of compounds **9a** and **16a**, separated in small amounts, arose from ^1H NMR, GC–MS, and HRMS analysis. Compounds **12b** and **19** were obtained as an inseparable mixture and, therefore, are not fully characterized.

NMR spectra were recorded in $CDCl_3$ solutions at 200 MHz (unless otherwise stated) with tetramethylsilane as the internal standard. Column chromatography was carried out on silica gel (0.040–0.063 μm particle size) by gradual elution with light petroleum ether (bp 40–70 °C)/diethyl ether. Mass spectra were recorded by the electron impact method on a VG 7070E instrument.

Starting Materials. All the alkenes employed were commercialy available. Thiols **1a**,[10] **1b**,[11] and **1c**[12] were obtained as described in the literature [^1H NMR **1a** δ = 3.70 (1H, s), 7.2–7.4 (3H, m), 7.6–7.8 (2H, m); **1b** (tautomeric mixture with **25**) δ = 3.70 (0.5H, s; collapsed upon D_2O shake), 4.25 (1H, s), 6.80 (0.5H, s), 7.15–7.5 (4H, m)].

Reaction of Thiols 1a,b with Styrene and Dioxygen. A solution of the appropriate thiol **1a,b** (2 mmol) and styrene (10 mmol) in benzene (20 mL) was heated in a sealed tube at 85 °C for 2 h. The resulting reaction mixture was analyzed by GC-MS, the solvent was evaporated off, and the residue was chromatographed.

From Benzothiophenethiol 1a. Chromatography gave benzothien-2-yl 2-phenylethyl sulfide (**5a**) (55 mg, 10%) [^1H NMR δ = 1.9–2.0 (2H, m), 3.1–3.2 (2H, m), 7.1–7.4 (8H, m), 7.6–7.8 (2H, m); MS *m/z* (rel inten) 270 (M^+, 60), 166 (50), 105 (100). Anal. Calcd for $C_{16}H_{14}S_2$: C, 71.07; H, 5.22; S, 23.71. Found: C, 71.3; H, 5.25; S, 23.55]; 3-(1-phenylethyl)-benzothien-2-yl 2-phenylethyl sulfide (**12a**) (110 mg, 15%) [^1H NMR δ = 1.84 (3H, d, J = 8 Hz), 2.9–3.05 (2H, m), 3.1–3.2 (2H, m), 5.10 (1H, q, J = 8 Hz), 7.1–7.5 (13H, m), 7.75 (1H, d, J = 8 Hz); MS *m/z* (rel inten) 374 (M^+, 80), 105 (100). Anal. Calcd for $C_{24}H_{22}S_2$: C, 76.96; H, 5.92; S, 17.12. Found: C, 77.25; H, 5.95; S, 17.0]; benzothien-2-yl methyl sulfide (**9a**) (5 mg, 1–2%) [^1H NMR δ = 2.60 (s), 7.2–7.8 (m); MS *m/z* (rel inten) 180 (M^+, 90), 165 (100), 121 (50); HRMS calcd for $C_9H_8S_2$ 180.00675, found 180.00690]; 3-(1-phenylethyl)benzothien-2-yl methyl sulfide (**16a**) (17 mg, 4%) [^1H NMR δ = 1.8 (3H, d, J = 7.7 Hz), 2.5 (3H, s), 4.98 (1H, q, J = 7.7 Hz), 7.2–7.8 (9H, m); MS *m/z* (rel inten) 284 (M^+, 100), 269 (70), 221 (40), 165 (20), 91 (30); HRMS calcd for $C_{17}H_{16}S_2$ 284.06935, found 284.06950]; 3-(1-phenylethyl)benzothien-2-yl 2-hydroxy-2-phenylethyl sulfide (**17a**) (40 mg, 5%) (1:1 diastereomeric mixture) [^1H NMR δ = 1.80 (1.5H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 5.05), 1.85 (1.5H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 5.05), 2.55 (0.5 H, broad signal), 2.65 (0.5 H, broad signal), 3.0 (0.5H, A part of an ABX system, J_{AB} = 13 Hz, J_{AX} = 7.5 Hz), 3.05 (0.5H, A' part of an A'B'X' system, $J_{A'B'}$ = 13 Hz, $J_{A'X'}$ = 7.5 Hz), 3.25 (0.5H, B' part of an A'B'X' system $J_{A'B'}$ = 13 Hz, $J_{B'X'}$ = 3.3 Hz), 3.28 (0.5H, B part of an ABX system J_{AB} = 13 Hz, J_{BX} = 3.3 Hz), 4.70 (0.5H, br m), 4.85 (0.5H, br m), 5.05 (1H, two quartets superimposed upon each other, J = 7 Hz), 7.1–7.5 (13H, m), 7.7–7.8 (1H, m); MS *m/z* (rel inten) 390 (M^+, 50), 372 (3), 204 (20), 269 (30), 221 (25), 180 (20), 107 (60), 91 (100); IR ν_{max} 3620 (sh), 3550 (br). Anal. Calcd for $C_{24}H_{22}OS_2$: C, 73.81; H, 5.68; O, 4.10; S, 16.42. Found: C, 74.0; H, 5.65; S, 16.3], benzoylmethyl 3-(1-phenylethyl)benzothien-2-yl sulfide (**18a**) (40 mg, 5%) [^1H NMR δ = 1.70 (3H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 5.0), 4.25 (2H, AB system, J_{AB} = 9 Hz, inner lines separation = 4 Hz), 5.0 (1H, q, J = 7 Hz), 7.0–8.0 (14 H, m); MS *m/z* (rel inten) 388 (M^+, 50), 268 (70), 267 (90), 253 (75), 105 (100), 91 (50), 77 (70). Anal. Calcd for $C_{24}H_{20}OS_2$: C, 74.19; H, 5.19; O, 4.12; S, 16.50. Found: C, 74.5; H, 5.15; S, 16.4], and bis(3-(1-phenylethyl)-benzothien-2-yl) disulfide **13a** (200 mg, 40%) (1:1 diastereomeric mixture) [^1H NMR (300 MHz) δ = 1.55 (1.5H, d, J = 7 Hz; collapsing to singlet upon irradiation at δ 5.0), 1.65 (1.5H, d, J = 7 Hz; collapsing to singlet upon irradiation at δ 5.0), 5.0 (1H, q, J = 7 Hz), 6.8–7.8 (9H, m); MS *m/z* (rel inten) 538 (M^+, 15), 340 (30), 269 (30), 207 (59), 149 (40), 129 (40), 105 (100), 91 (90), 77 (60), 57 (70). Anal. Calcd for $C_{32}H_{26}S_4$: C, 71.33; H, 4.86; S, 23.80. Found: 71.5; H, 4.90; S, 23.65].

The reaction was repeated in the presence of AIBN (0.4 mmol). GC–MS and TLC comparison with the reaction mixture obtained in the absence of AIBN did not reveal any differences.

From Benzofuranthiol 1b. Chromatography gave a 50:50 inseparable mixture of isomeric 3-(1-phenylethyl)benzofuro-2-yl 2-phenylethyl sulfide (**12b**) and 3-(1-phenylethyl)benzofuro-2-yl 1-phenylethyl sulfide (**19**) (45 mg, 10% overall yield) [MS *m/z* (rel inten) 358 (M^+, 20), 105 (100); HRMS calcd for $C_{24}H_{22}OS$ 358.13914, found 358.13950], 3-(1-phenylethyl)benzofur-2-yl methyl sulfide (**16b**) (35 mg, 10%) [^1H NMR δ = 1.8 (3H, d, J = 7.5 Hz), 2.50 (3H, s), 4.55 (1H, q, J = 7.5 Hz), 7.0–7.5 (9H, m); MS *m/z* (rel inten) 268 (M^+, 40), 253 (50), 105 (100). Anal. Calcd for $C_{17}H_{16}OS$: C, 76.08; H, 6.01; O, 5.96; S, 11.95. Found: C, 76.4; H, 6.05; S, 11.9], and bis(3-(1-phenylethyl)-benzofur-2-yl) disulfide (**13b**) (200 mg, 35%) [^1H NMR (300 MHz) δ = 1.55 (1.5H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 4.50), 1.65 (1.5H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 4.50), 4.50 (1H, q, J = 7 Hz), 7.1–7.5 (9H, m); MS *m/z* (rel inten) 506 (M^+, 25), 253 (100), 178 (15). Anal. Calcd for $C_{32}H_{26}O_2S_2$: C, 75.86; H, 5.17; O, 6.32; S, 12.66. Found: C, 76.10; H, 5.20; S, 12.6]. Subsequent chromatography of the mixture of adducts **12b** and **19** gave two fractions containing these compounds in variable amounts [^1H NMR (300 MHz) **12b** δ = 1.8 (3H, d, J = 7.3 Hz), 2.85–2.95 (2H, m), 3.1–3.2 (2H, m, collapsing to singlet at δ 3.15 upon irradiation at δ 2.9), 4.55 (1H, q, J = 7.3 Hz, collapsing to singlet upon irradiation at δ 1.8), 7.0–7.5 (14H, m); **19** (1:1 diastereomeric mixture) δ = 1.40 (1.5H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 4.35), 1.60 (1.5H, d, J = 7 Hz,

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collapsing to singlet upon irradiation at δ 4.35), 1.70 (3H, d, J = 7 Hz, collapsing to singlet upon irradiation at δ 4.55), 4.35 (1H, m), 4.55 (1H, m), 7.0–7.5 (14H, m)].

The reaction was repeated in the presence of AIBN (0.4 mmol). GC–MS and TLC comparison with the reaction mixture obtained in the absence of AIBN did not reveal any differences.

Reaction of Thiophenethiol 1c with BVE and Dioxygen. A solution of thiol **1c** (2 mmol), BVE (10 mmol), and AIBN (0.4 mmol) in benzene (20 mL) was heated in a sealed tube for 2 h. The reaction mixture was chromatographed to afford disulfide **27**[13] (35 mg, 15%) and 1-butoxyethyl 2-thienyl sulfide (**28**) (350 mg, 80%) [^{1}H NMR δ = 0.95 (3H, t, J = 7.5 Hz), 1.3–1.7 (4H, m), 1.45 (3H, d, J = 6.8 Hz), 3.44 (1H, dt, J_d = 9.5 Hz, J_t = 6.5 Hz), 3.95 (1H, dt, J_d = 9.5 Hz, J_t = 6.5 Hz), 4.68 (1H, q, J = 6.8 Hz), 7.0 (1H, m), 7.15 (1H, m), 7.40 (1H, m); MS m/z (rel inten) 216 (M^+, 5), 116 (35), 101 (60), 71 (30), 57 (100), 45 (95). Anal. Calcd for $C_{10}H_{16}OS_2$: C, 55.51; H, 7.45; O, 7.39; S, 29.64. Found: C, 55.25; H, 7.50; S, 29.5].

Reaction of Thiols 1a-c with Styrene. A degassed solution of the appropriate thiol **1a-c** (2 mmol) and styrene (10 mmol) in benzene (20 mL) was refluxed for 2 h. The reaction mixture was extracted with 10% aqueous NaOH; TLC and GC–MS analyses showed that no products were present in the organic layer at an appreciable extent. The aqueous layer was acidified with 1:1 HCl/water and extracted with diethyl ether, the solvent was evaporated off, and the residue was chromatographed.

From Benzothiophenethiol 1a. Chromatography gave a 1:1 inseparable mixture (360 mg) of starting thiol **1a** (40%) and 3-(1-phenylethyl)benzo[*b*]thiophene-2-thiol (**2a**) (80%) [^{1}H NMR δ = 1.84 (3H, d, J = 7.2 Hz), 3.5 (1H, s, collapsing upon D_2O shake), 5.0 (1H, q, J = 7.2 Hz, collapsing to a singlet upon irradiation at δ 1.84), 7.1–7.5 (7H, m), 7.6–7.8 (2H, m); MS m/z (rel inten) 270 (M^+, 100), 225 (80), 221 (50), 192 (50), 166 (25); HRMS calcd for $C_{16}H_{14}S_2$ 270.05370, found 270.05340]. The mixture of thiols **2a** and **1a** was dissolved in benzene (20 mL) and treated at room temperature with equimolar amounts of DDQ (340 mg, 1.5 mmol) for 15 min. The reaction mixture was filtered and the filtrate chromatographed to give the corresponding disulfides **13a** and benzothien-2-yl disulfide [mp 111–112 °C; ^{1}H NMR δ = 7.3–7.4 (3H, m), 7.6–7.8 (2H, m); MS m/z (rel inten) 330 (M^+, 25), 165 (100), 121 (50)].

From Benzofuranthiol 1b. Chromatography gave 3-(1-phenylethyl)benzo[*b*]furan-2-thiol (**2b**) as an oil (380 mg, 75%) [^{1}H NMR δ = 1.85 (3H, d, J = 7 Hz), 3.55 (1H, s), 4.55 (1H, q, J = 7 Hz, collapsing to a singlet upon irradiation at δ 1.85), 7.1–7.5 (9H, m); MS m/z (rel inten) 254 (M^+, 100), 239 (70), 176 (70), 105 (30); HRMS calcd for $C_{16}H_{14}OS$ 254.07654, found 254.07690]. Thiol **2b** was dissolved in benzene (20 mL) and treated with DDQ (340 mg, 1.5 mmol) as described above to give disulfide **13b**.

From Thiophenethiol 1c. Chromatography gave unreacted thiol **1c** in ca. 85% yield as the only separable product.

Reaction of Thiols 1a-c with Butyl Vinyl Ether. A degassed solution of the appropriate thiol **1a-c** (2 mmol) and butyl vinyl ether (10 mmol) in benzene (20 mL) was refluxed for 2 h. The reaction mixture was extracted with aqueous 10% NaOH, the benzene layer was separated, the solvent was evaporated off, and the residue chromatographed. The aqueous layer was acidified with 1:1 HCl/water and extracted with diethyl ether; TLC and GC–MS analysis showed that no products were present.

From Benzothiophenethiol 1a. Chromatography gave 1-methyl-3-butoxybenzo[*b*]thiopheno[2,3-*b*]dihydrothiopyran (**24a**) (520 mg, 90%) [^{1}H NMR δ = 0.9 (3H, t, J = 7 Hz), 1.3–1.7 (4H, m), 1.55 (3H, d, J = 7 Hz, collapsing to a singlet upon irradiation at δ 3.4), 2.30 (1H, A part of an ABXY system, J_{AB} = 14 Hz, J_{AX} = 5.8 Hz, J_{AY} = 3 Hz), 2.50 (1H, B part of an ABXY system, J_{AB} = 14 Hz, J_{BX} = 4 Hz, J_{BY} = 3 Hz), 3.45 (2H, m), 3.85 (1H, dt, J_d = 9 Hz, J_t = 6.5 Hz), 5.15 (1H, dd, J_1 = J_2 = 3 Hz), 7.1–7.35 (2H, m), 7.55 (1H, br d, J = 8 Hz), 7.70 (1H, br d, J = 8 Hz); ^{13}C NMR δ = 13.7 (CH_3), 19.2 (CH_2), 20.5 (CH_3), 27.0 (CH), 31.5 (CH_2), 37.8 (CH_2), 70.0 (OCH_2), 82.3 (OCHS), 120.0 (=CH), 121.7 (=CH), 123.0 (=CH), 124.0 (=CH), 127.5 (>C<), 129.5(>C<), 137.5 (>C<), 139.5 (>C<); MS m/z (rel inten) 292 (M^+, 30), 266 (15), 192 (60), 166 (50), 121 (40), 101 (60), 57 (95), 45 (100). Anal. Calcd for $C_{16}H_{20}OS_2$: C, 65.71; H, 6.89; O, 5.47; S, 21.93. Found: C, 65.5; H, 6.85; S, 22.0]. The reaction was repeated in the presence of equimolar amounts of BVE and worked up as described above. Upon acidification and extraction with diethyl ether, thiol **1a** was recovered in ca. 50% yield from the aqueous layer. Column chromatography of the organic layer gave an unidentified product (20 mg) at m/z 192 (M^+) (GC–MS) and thiopyran **24a** (200 mg, 70%).

From Benzofuranthiol 1b. Chromatography gave 1-methyl-3-butoxybenzo[*b*]furano[2,3-*b*]dihydrothiopyran (**24b**) (270 mg, 50%) [^{1}H NMR δ = 0.9 (3H, t, J = 7 Hz), 1.2–1.6 (4H, m), 1.5 (3H, d, J = 7.4 Hz), 2.35 (2H, dd, J_1 = J_2 = 4 Hz), 3.25 (1H, tq, collapsing to triplet, J = 4 Hz, upon irradiation at δ 1.5), 3.4 (1H, dt, J_d = 9 Hz, J_t = 7 Hz), 3.85 (1H, dt, J_d = 9 Hz, J_t = 7 Hz), 5.20 (1H, t, J = 4 Hz), 7.1–7.2 (2H, m), 7.35–7.45 (2H, m); ^{13}C NMR δ = 13.7 (CH_3), 19.2 (CH_2), 20.5 (CH_3), 26.0 (CH), 31.5 (CH_2), 37.8 (CH_2), 70.2 (OCH_2), 84.0 (OCHS), 110.5 (=CH), 114.5(>C<), 118.0 (=CH), 122.3 (=CH), 122.4 (=CH), 128.5 (>C<), 144.5 (>C<), 154.5 (>C<); MS m/z (rel inten) 276 (M^+, 30), 176 (90), 101 (70), 57 (80), 45 (100). Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29; O, 11.58; S, 11.60. Found: C, 69.7; H, 7.256; S, 11.55] and benzofur-2-yl 1-butoxyethyl sulfide (**26**) (150 mg, 30%) [^{1}H NMR δ = 0.95 (3H, t, J = 7 Hz), 1.2–1.6 (4H, m), 1.6 (3H, d, J = 6 Hz), 3.45 (1H, dt, J_d = 9.5 Hz, J_t = 6.2 Hz), 3.96 (1H, dt, J_d = 9.5 Hz, J_t = 6.2 Hz), 4.94 (1H, q, J = 6 Hz), 6.90 (1H, s), 7.15–7.55 (4H, m); MS m/z (rel inten) 250 (M^+, 10), 150 (30), 121 (20), 101 (70), 57 (90), 45 (100). Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67,17; H, 7.25; O, 12.78; S, 12.81. Found: C, 67.3; H, 7.20; S, 12.75].

From Thiophenethiol 1c. Chromatography gave sulfide **28** (365 mg, 85%).

Reaction of Benzothiophenethiol 1a with Dimethyl Maleate. A degassed solution of thiol **1c** (2 mmol) and dimethyl maleate (10 mmol) in benzene (20 mL) was refluxed for 2 h. The reaction mixture was extracted with 10% aqueous NaOH, the benzene layer was separated, the solvent was evaporated off, and the residue was chromatographed to give 1,2-bis(methoxycarbonyl)ethyl benzothien-2-yl sulfide (**21**) (185 mg, 60%) [^{1}H NMR δ = 2.80 (1H, A part of an ABX system, J_{AB} = 17 Hz, J_{AX} = 6 Hz), 3.01 (1H, B part of an ABX system, J_{AB} = 17 Hz, J_{BX} = 9 Hz), 3.66 (3H, s), 3.72 (3H, s), 4.0 (1H, dd, J_1 = 9 Hz, J_2 = 6 Hz), 7.30 (2H, m), 7.40 (1H, s), 7.70 (2H, m); MS m/z (rel inten) 310 (M^+, 70), 279 (15), 250 (35), 165 (100), 134 (40), 121 (85). Anal. Calcd for $C_{14}H_{14}O_4S_2$: C, 54.18; H, 4.55; O, 20.62; S, 20.66. Found: C, 54.0; H, 4.50; S, 20.55]. The aqueous layer was acidified with 1:1 HCl/water and extracted with diethyl ether; the organic layer was separated, the solvent was evaporated off, and the residue was chromatographed to give starting thiol **1a** (50%).

Reaction of Benzothiophenethiol 1a with Methyl Acrylate in 1-Hexene. A degassed solution of thiol **1a-c** (2 mmol) and the appropriate alkene (10 mmol) in benzene (20 mL) was refluxed for 2 h. The reaction mixture was extracted with 10% aqueous NaOH; TLC and GC–MS analyses showed that no products were present in the organic layer. The aqueous layer was acidified with 1:1 HCl/water and extracted with diethyl ether, the solvent was evaporated, and the residue was chromatographed to give starting thiol **1a** in ca. 85% yield as the only separable product.

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