Free-Radical Addition of Heteroarenethiols and Heteroarylmethanethiols to Hexyne and Phenylacetylene. Chemical Behavior of the Transient β-Sulfanylvinyl Radicals

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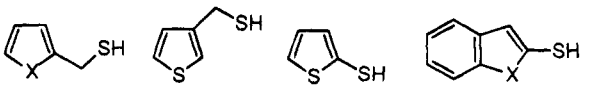
The free-radical reaction of a number of heteroarenethiols (including 2-thiophene-, 2-benzo[*b*]furan-, and 2-benzo[*b*]thiophenethiol) and heteroarylmethanethiols (including 2-furyl-, 2-thienyl-, and 3-thienylmethanethiol) with hex-1-yne and phenylacetylene has been investigated in benzene solution both at 100 °C in the presence of AIBN and at room temperature in the presence of BEt_3/O_2. Under both of these conditions the above thiols generally furnished transient 2-sulfanylvinyl radicals through regioselective addition of corresponding sulfanyl radicals to the terminal alkyne carbon, but 2-benzo[*b*]furanthiol failed to react with either alkyne in the presence of BEt_3/O_2 and unexpectedely gave 2-(ethylsulfanyl)benzo[*b*]furan to a significant extent. The produced 2-(2-heteroarylsulfanyl)vinyl radicals largely preferred to undergo intermolecular H-abstraction reaction rather than intramolecular 5-endo cyclization onto the heteroaryl moiety of the 2-sulfanyl substituent. The 2-[(2-thienylmethyl)sulfanyl]- and, especially, 2-[(2-furylmethyl)sulfanyl]vinyl radicals, besides H-abstraction, promptly underwent intramolecular 5-exo cyclization to give spiro radicals that interestingly underwent β-scission of their respective C–S and C–O bond resulting in ring cleavage of the original heteroaryl group. The 2-[(3-thienylmethyl)sulfanyl]vinyl radicals did not exhibit any similar 5-exo cyclization, but did undergo a 6-endo cyclization to a very slight extent.

In previous studies[1,2] we have investigated the free-radical reactions of benzenethiol with various phenyl- and alkylacetylenes. These reactions, carried out at 90–100 °C in the presence of azoisobutyronitrile (AIBN) involve the intervention of 1-phenyl- and 1-alkyl-2-(phenylsulfanyl)vinyl radicals arising from regioselective addition of phenylsulfanyl radicals to carbon–carbon triple bonds. Linear, sp-hybridized 1-phenyl radicals were shown to exhibit a pronounced preference to undergo H-transfer from benzenethiol from the side trans to PhS. The corresponding bent (and rapidly interconverting) sp^2-hybridized 1-alkyl radicals displayed a similar trend which was however dependent upon both the size of the 1-alkyl substituent and that of the substituent cis to either of the radical centers. Moreover, these intermediates displayed some propensity to undergo an intramolecular cyclization reaction in a stereoelectronically unfavored 5-endo fashion[3] leading to benzo[*b*]thiophene products.

On this basis we subsequently succeeded in devising a useful synthetic entry to 3- (and 2,3-di-) substituted benzothiophenes employing the thermal reaction of diphenyl disulfide with alkynes promoted by di-*tert*-butyl peroxide.[4] Very recently, we have also performed a study of related additions of phenethyl, allyl, and benzyl mercaptans to monosubstituted acetylenes.[5] The ensuing 2-(alkylsulfanyl)vinyl radicals were found to exhibit, besides hydrogen abstraction from the thiol present, a variety of attractive decomposition processes. In particular, the 2-(benzylsulfanyl)vinyl radicals readily rearranged to (vinylsulfanyl)methyl radicals via a novel 1,4-migration of the aryl group from sulfanylmethyl to the vinyl carbon. The rearranged radicals were formed through intramolecular addition of their vinylic precursors to the adjacent aromatic ring in a stereoelectronically favored 5-exo mode,[3] followed by ring opening of the resulting spirocyclohexadienyl intermediate.

Here, we report our results from a study of the radical additions of 2-thiophene- (**4**), 2-benzo[*b*]furan- (**5**), and benzo[*b*]thiophenethiol (**6**) to hex-1-yne and phenylacetylene. We were interested in investigating the chemical reactivity and synthetic potential of corresponding 2-(heteroarylsulfanyl)-substituted vinyl radicals. Their possible intramolecular cyclization might, in principle, offer a novel synthetic approach to the construction of the respective thieno-fused heteroarene ring system. Considerable attention has been devoted to the chemical investigation of 2-alkane- and 2-arene-sulfanylvinyl radicals, but to our knowledge the 2-(heteroarylsulfanyl)-substituted members are still unexplored.

We also report our results from a concomitant study of the radical addition of 2-furyl- (**1**), 2-thienyl- (**2**), and 3-thienylmethanethiol (**3**) to same alkyne substrates. The possible 2-(heteroarylmethylsulfanyl)vinyl radical intermediates were believed to furnish new examples of 1,4-migration of the five-membered 2- (and 3-) heteroayl groups, similar to those already encountered with aryl groups in the analogous 2-(benzylsulfanyl)vinyl species.



1 (X=O) **2** (X=S) **3** **4** **5** (X=O) **6** (X=S)

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(1) Benati, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2103.
(2) Benati, L.; Capella, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1305.
(3) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. Beckwith, A. L. J.; Easton, C. J.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980**, 482.
(4) Benati, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1659.
(5) Benati, L.; Capella, L.; Montevecchi, P. C.; Spagnolo, P. *J. Org. Chem.* **1994**, *59*, 2818.

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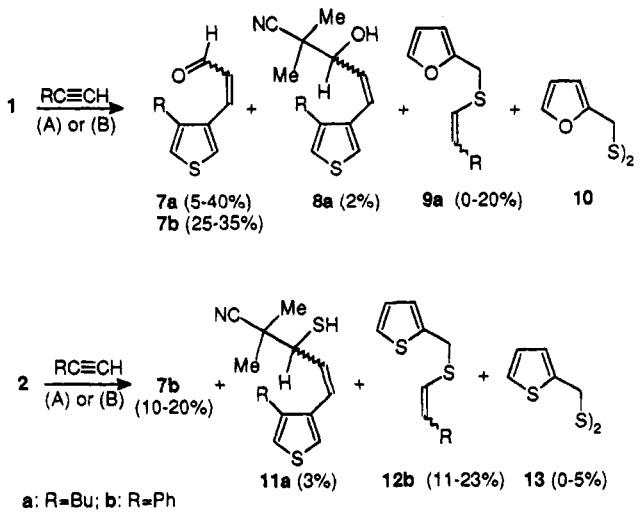
Scheme 1



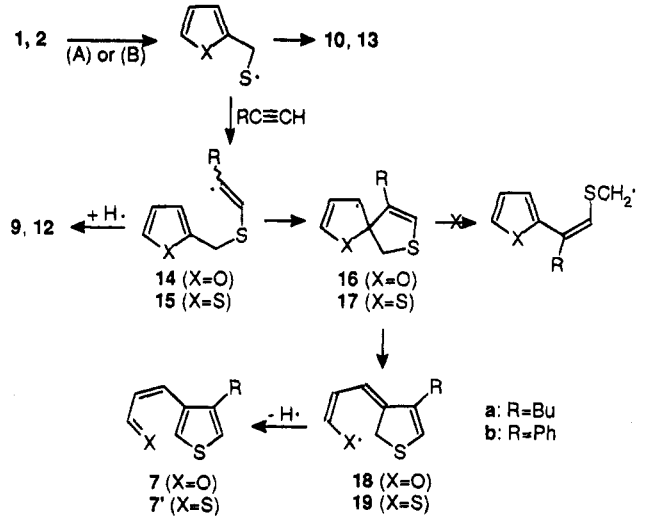
(A): Procedure A; (B): Procedure B

Results and Discussion

The present reactions were carried out in a benzene solution by using a 0.1 M concentration of the appropriate thiol **1**–**6** and a 5-fold excess of hex-1-yne or phenylacetylene under two different experimental conditions, i.e. at 100 °C in the presence of AIBN for 2 h (procedure A) and at room temperature in the presence of triethylborane and oxygen (air) for 1 h (procedure B).[6] The crude reaction mixtures were directly analyzed by GC–MS and/or subjected to column chromatography. The identification of the isolated products was generally performed by ^{1}H NMR and MS spectral analyses.

2-Furylmethanethiol (**1**) reacted with hex-1-yne in the presence of AIBN (procedure A) to give a complex mixture, from which the thienylacrolein (**7a**) and the thienyl hydroxy nitrile **8a** (formally ascribable to further reaction of **7a** with 2-cyano-2-propyl radicals arising from AIBN) could be isolated in very low yield (Scheme 1). Under analogous conditions, the thiol **1** when reacted with phenylacetylene gave the corresponding thienylacrolein (**7b**) in 25% yield, in addition to trace amounts of the vinyl sulfide **9b** and the disulfide **10** (Scheme 1). When performed according to the BEt_3/O_2 method (procedure B), the two reactions above also furnished the acrolein products **7a,b**, but to a remarkably higher extent. Under these circumstances, hex-1-yne also gave significant amounts of the vinyl sulfide adduct **9a** (Scheme1). Comparable results were obtained with 2-thienylmethanethiol (**2**). In fact, in the presence of AIBN, the thiol **2** when reacted with hex-1-yne furnished small amounts of the thienyl mercaptonitrile **11a** [possibly resulting from further reaction of transient thienylthioacrolein (**7'a**) (*vide infra*) with 2-cyano-2-propyl radicals] and the disulfide **13** along with a complex mixture of unidentifiable products (Scheme 1). However, both in the presence of AIBN and of BEt_3/O_2, the thiol **2** upon reaction with phenylacetylene led to significant amounts of the thienylacrolein (**7b**) and additionally gave the vinyl sulfide **12b** to a similar extent (Scheme 1). All the above reaction products **7**–**13** can be easily derived from the initially formed (2-furyl- and 2-thienylmethyl)-sulfanyl radicals (Scheme 2).

Scheme 2



These sulfanyl radicals, besides affording a small amount of disulfide products **10** and **13** by dimerization, could add to the terminal carbon of the alkyne substrate to furnish the expected sulfanylvinyl radicals **14a,b** and **15a,b**. Hydrogen abstraction reaction of these intermediates could give the adducts **9a,b** and **12a,b**, whereas a 5-exo cyclization to the *ipso* 2-position of the sulfanyl heteroaromatic ring would initially form the spiro radicals **16a,b** and **17a,b**. These cyclized species **16a,b** and **17a,b** could then lead to the observed aldehydes **7a,b** and (transient) thioaldehydes **7'a,b** through β-cleavage of the respective C–X bond, thus affording the fairly resonance-stabilized radicals **18** and **19** and, finally, the eventual H-abstraction reaction of the latter (Scheme 2).

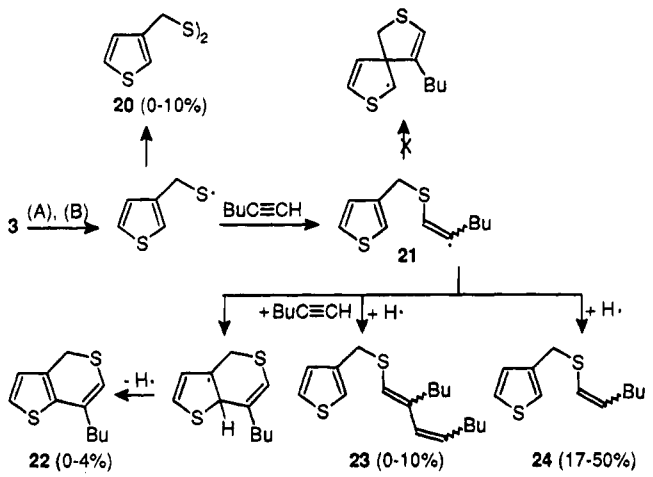
The resulting reactive thioaldehydes **7'a,b** could suffer (extensive) decomposition into unidentifiable products and, in part, conversion into the oxo derivatives **7a,b** by formal hydrolysis. Therefore, similarly to their 2-(benzylsulfanyl)vinylic analogs, the radicals **14** and **15** may promptly exhibit intramolecular 5-exo cyclization, but in such cases the cyclized products **16** and **17** would avoid β-scission of their C–CH_2 bond that, in principle, might have led to 1,4-migration of the respective 2-heteroaryl group from sulfanylmethyl to vinyl carbon. The postulated rearrangement of vinyl radicals **14** and **15** to radicals **18** and **19** is noteworthy since it could provide unprecedented instances of homolytic addition to thiophene and furan nuclei resulting in ring cleavage of these heteroarenes.

Under the conditions of procedure A, in the presence of hex-1-yne 3-thienylmethanethiol (**3**) led to the sulfide adduct **24** and the disulfide **20** in 20% and 10% yields, respectively, as the exclusive identifiable products (Scheme 3). The same reaction, performed by using a very low concentration of the thiol reactant (which was achieved through very slow addition of the thiol to the alkyne) furnished the 1:2 thiol–alkyne adduct **23** in 10% yield together with little amounts of the cyclized thienothiopyran **22** in addition to the compounds **24** (17%) and **20** (4%) (Scheme 3).

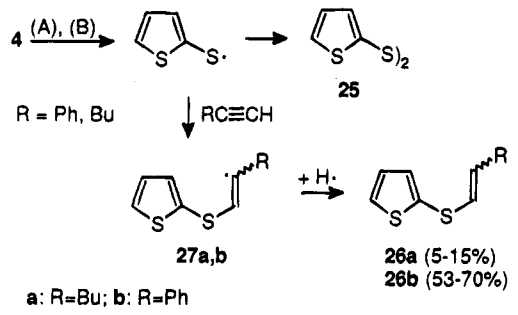
Conversely, the corresponding reaction in the presence of BEt_3/O_2 gave the sulfide **24** (50%) and the thiopyran

(6) Triethylborane is known to undergo autoxidation in the presence of oxygen resulting in the production of ethyl radicals owing to homolytic substitution at boron atom. This system has recently found some use as a mild initiator of homolytic processes involving C- and S-centered radicals. (See: Baciocchi, E.; Muraglia, E. *Tetrahedron Lett.* **1993**, *34*, 5015. Ichinose, Y.; Wakamatsu, K.; Nozaki, K.; Birbaum, J.-L.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1987**, 1647.)

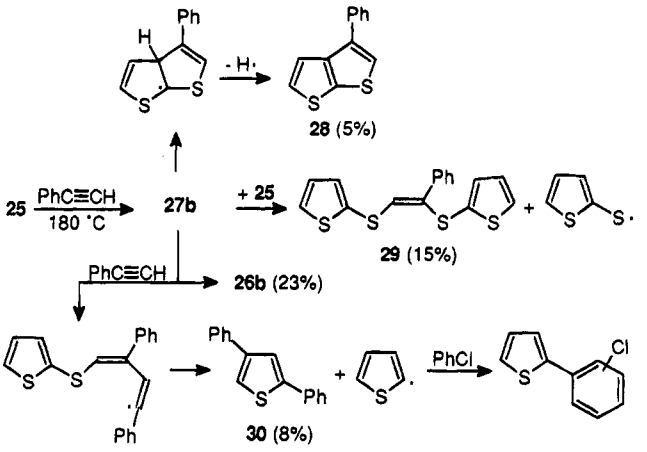
Scheme 3



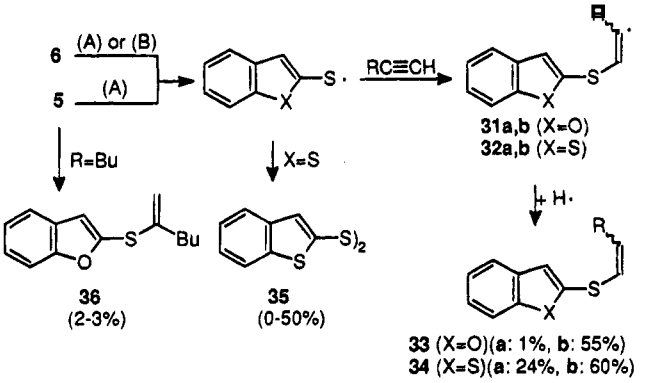
Scheme 4



Scheme 5



Scheme 6



22 (4%) as the only isolable products (Scheme 3). In light of these findings, it therefore appears that the intermediate 2-[(3-thienylmethyl)sulfanyl]vinyl radical **21** is largely prone to undergo intermolecular addition to another alkyne unit and/or H-abstraction reaction, but, unlike its congeners **14** and **15**, is essentially reluctant to perform an intramolecular 5-exo cyclization. Moreover, it appears that radical **21** shows some tendency to cyclize in a 6-endo mode to give the thiopyran **22**. The chemical behavior of the radical **21**, as compared with the radicals **14** and **15** [and the previous (2-phenylsulfanyl)-substituted ones] can be ascribed to the reports that the radical reactivity of the 3-position of the thiophene ring is markedly lower than that of the 2-position of both the thiophene[7] and furan[8] rings as well as being slightly lower than that of the benzene ring.[7]

Following procedure A and B, 2-thiophenethiol (**4**) was treated with the two usual alkynes to give the disulfide **25** and varying amounts of the addition products **26a** [15%(A)−5%(B)] and **26b** [70%(A)−53%(B)] (Scheme 4). No evidence for any possible 5-endo cyclization product of the ensuing 2-(2-thienylsulfanyl)vinyl radicals **27a,b** could be obtained from these reactions.

In an additional experiment the radical reaction of the disulfide **25** with phenylacetylene was investigated at 180 °C in chlorobenzene. Under these drastic conditions (and in the absence of any effective H-donor) the intermediate radical **27b** was able to yield the cyclized product **28**, but to a very small extent. In such a case the radical **27b** preferentially led to the sulfide **26b**, the bis-sulfide **29** (due to an S_H2 reaction with the disulfide **25**), and 2,4-diphenylthiophene (**30**). The latter compound was probably formed through the outlined mechanism, which was substantiated by the observed trapping (GC−MS) of the eventually displaced 2-thienyl radical by chlorobenzene solvent (Scheme 5).

Similar to 2-thiophenethiol (**4**), its benzo derivative **6** reacted with hex-1-yne and phenylacetylene under conditions of both procedures A and B to give the H-abstraction products **34a,b** of the corresponding sulfanylvinyl radicals **32a,b** while providing no evidence for any cyclization product of these intermediates (Scheme 6). Thus, with the above 2-(2-heteroarylsulfanyl)-substituted vinylic radicals **27** and **32** unfavorable stereoelectronic factors could play a major role in preventing the 5-endo cyclization process. This fact could be particularly true for the radicals **32** which failed to cyclize onto the 3-position of the 2-benzothienyl moiety, although this position is highly susceptible to homolytic attack.[9]

The AIBN-induced reaction of 2-benzo[*b*]furanthiol (**5**) with phenylacetylene led to the sulfide adduct **33b** (55%) as the only isolable product (Scheme 6). This reaction suggests that, like the congeners **27** and **32**, the 1-phenyl-2-(2-benzofurylsulfanyl)vinyl radical **31b** should be hindered from undergoing an unfavorable 5-endo cyclization and is further discouraged by the expectedly poor reactivity of the benzofuryl 3-position. On the other hand, inconclusive evidence concerning the chemical behavior of the corresponding 1-butylvinyl radical **31a** was furnished by the analogous reaction of the thiol **5** in the presence of hex-1-yne. This reaction gave much tarry

(7) Camaggi, C. M.; Leardini, R.; Tiecco, M.; Tundo, A. *J. Chem. Soc. (B)* **1970**, 1683. Tiecco, M.; Tundo, A. *Int. J. Sulfur Chem.* **1973**, *8*, 295.

(8) Benati, L.; La Barba, N.; Tiecco, M.; Tundo, A. *J. Chem. Soc. (B)* **1969**, 1253.

(9) Martelli, G.; Spagnolo, P.; Tiecco, M.; Tundo, A. *J. Chem. Soc., Perkin Trans. 1* **1972**, 556.

Scheme 7

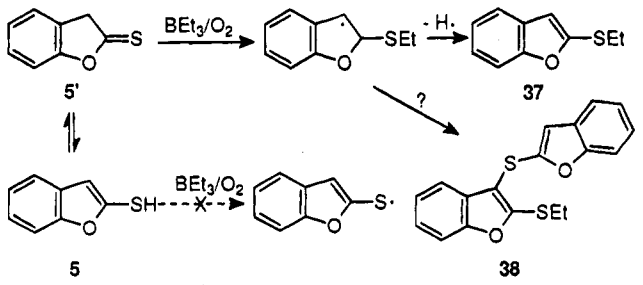


Table 1. Isomer Ratios[a] of (*Z*)- and (*E*)-Vinyl Sulfides Obtained from Radical Addition of the Thiols 1–6 to Hex-1-yne and Phenylacetylene

			Z/*E* isomer ratio	
thiol	alkyne	vinyl sulfide	A[b]	B[c]
1	hex-1-yne	9a		65:35
2	phenylacetylene	12b	80:20	85:15
3	hex-1-yne	24a	70:30	60:40
4	hex-1-yne	26a	50:50	60:40
4	phenylacetylene	26b	70:30	90:10
5	phenylacetylene	33b	95:5	
6	hex-1-yne	34a	50:50	65:35
6	phenylacetylene	34b	90:10	90:10

[a] Isomer ratios determined by ^{1}H NMR spectral analysis. [b] Isomer ratio referring to reaction carried out according to procedure A. [c] Isomer ratio referring to reaction carried out according to procedure B.

material and, to a slight extent, a 1:2 mixture of the adduct **33a** and its regioisomer **36**, whose source is unknown (Scheme 6). Our further objective to investigate these radical reactions using the BEt_3/O_2 procedure was frustrated by the fact that under these circumstances the thiol **5**, in the presence of either alkyne, gave no evidence of any sulfanylvinylic radical product, but furnished 2-(ethylsulfanyl)benzo[*b*]furan **37** in 22–24% yield instead, along with minor amounts (5–6%) of an unknown compound which, according to MS and ^{1}H NMR spectral evidence, probably was the benzofuran derivative **38** (Scheme 7). The initial intervention of the ethyl radical initiator in the formation of the benzofuran **37** and the unknown compound was clearly suggested by the finding that the same reactions carried out in the absence of oxygen (in order to avoid the initial occurrence of the ethyl radical from BEt_3) resulted in substantial suppression of the two above products.

The apparent failure of thiol **5** to react with our alkynes under these latter conditions was possibly a consequence of its peculiar tendency to equilibrate with the thione tautomer **5'** (^{1}H NMR spectroscopy actually showed that in benzene solution, at room temperature, the two tautomeric forms **5** and **5'** were present in ca. 1:1 ratio). The tautomer **5'** might have been preferentially removed by the ethyl radical owing to preferred attack at the sulfur atom of its weak thiocarbonyl group (Scheme 7).

As described throughout this paper, our thiol reactions with hex-1-yne and phenylacetylene usually resulted in the formation of 1:1 thiol/alkyne adducts to a varying degree. The observed vinylic adducts normally occurred as isomeric mixtures of the *Z*- and *E*-isomers. The determined *Z*/*E* ratios are collected in Table 1. The data in Table 1 evidently point to a general tendency of the thiols **1–6** to add to the alkynes in a trans-stereoselective fashion (preferentially giving *Z*-adducts). Such stereochemical evidence is fairly consistent with that previously provided by similar radical reactions of benzenethiol (and alkanethiols) with various alkynes.[1,2]

In conclusion, both in the presence of AIBN and BEt_3/O_2, the heteroarylmethanethiols **1–3** reacted with phenylacetylene and hex-1-yne to give transient 2-sulfanylvinyl radicals **14**, **15**, and **21** whose decomposition mode was dependent upon both the nature of the heteroaryl moiety of the sulfanyl substituent and its S-susbtituted position. In addition to intermolecular H-abstraction, [(2-thienylmethyl)sulfanyl]vinyl (**15**) and [(2-furylmethyl)-sulfanyl]vinyl radicals (**14**) promptly underwent intramolecular 5-exo cyclization to form the corresponding spiro radicals **16** and **17**, which in turn suffered preferential β-scission of the C–X bond interestingly resulting in ring cleavage of the original heteroaryl group.

Instead, the 3-thienyl derivative **21** was highly reluctant to perform a similar 5-exo cyclization reaction but was able to cyclize in a 6-endo mode. 2-Thiophene- (**4**) and 2-benzo[*b*]thiophenethiol (**6**) also reacted with hex-1-yne and phenylacetylene to afford the corresponding 2-sulfanylvinyl radicals **27** and **32** largely prone to undergo H-abstraction reaction rather than intramolecular 5-endo cyclization. Finally, a peculiar behavior was encountered with 2-benzo[*b*]furanthiol (**5**), in that this thiol furnished no apparent reaction with hex-1-yne or phenylacetylene in the presence of BEt_3/O_2, whereas with phenylacetylene, in the presence of AIBN, smoothly afforded the expected vinylic radical **31b** which strictly behaved like its analogs **27** and **32**.

Experimental Section

Furylmethanethiol (**1**) phenylacetylene, hex-1-yne, AIBN, and triethylborane (1.0 M pentane solution) were commercially available. Thiols **2**,[10] **3**,[11] **4**,[12] **5**,[13] and **6**[14] were prepared as described in the literature.

Disulfides **10**,[15] **13**,[16] and **25**,[17] thienothiophene **28**,[18] and diphenylthiophene **30**[19] were identified by GC–MS spectral comparison with authentic specimens. Structural assignment to the new reaction products generally arose from ^{1}H NMR and MS spectral analysis and elemental analysis. Compounds **8a**, **11a**, **29**, **38**, and the isomeric mixture of **33a** and **36** were identified by ^{1}H NMR, MS, and HRMS; elemental analysis was not performed owing to the small amounts of isolated product or to some difficulties in obtaining pure samples. Thiine **22** was not isolated; its identification arose from GC–MS analysis and from examination of the ^{1}H NMR spectrum of a mixture of **22** and **24**.

Column chromatography was performed on Merck silica gel (0.040–0.063 particle size) by gradual elution with light petroleum (bp 40–70 °C) and diethyl ether.

Reaction of Thiols 1–6 with Hex-1-yne and Phenylacetylene. Method A. A solution of the appropriate thiol **1–6** (2 mmol), alkyne (hex-1-yne or phenylacetylene, 10 mmol), and AIBN (0.2 mmol) in benzene (20 mL) was heated in a sealed tube at 100 °C for 2 h. The solvent was removed, and the residue was analyzed by GC–MS and was then chromatographed on silica gel column.

Method B. To a solution of the appropriate thiol **1–6** (2 mmol) and alkyne (hex-1-yne or phenylacetylene, 10 mmol)

(10) Cagniant, P. *C. R. Hebd. Seances Acad. Sci.* **1949,** *229*, 1342.
(11) Cagniant, P.; Cagniant, D. *Bull. Soc. Chim. Fr.* **1977**, 2597.
(12) Houff, W. H.; Schuetz, R. D. *J. Am. Chem. Soc.* **1953,** *75*, 6316.
(13) Wierzbick, M.; Kirsh, G.; Cagniant, D.; Liebermann, M.; Schafer, T. W. *Eur. J. Chem. Chim. Ther.* **1977,** *12*, 557.
(14) Schuetz, R. D.; Fredericks, W. L. *J. Chem. Soc. (C)* **1970,** 2433.
(15) Harpp, D. N.; Smith, R. A. *J. Org. Chem.* **1979,** *44*, 4140.
(16) Mieloszynski, J. L.; Aberkane, O.; Schneider, M.; Paquer, D.; Born, M.; Parc, G. *Sulfur Lett.* **1988,** *8*, 31.
(17) Ponticello, G. S; Habecker, C. N.; Varga, S. L.; Ptzenberger, S. M. *J. Org. Chem.* **1989,** *54*, 3223.
(18) Spagnolo, P.; Testaferri, L.; Tiecco, M.; Martelli, G. *J. Chem. Soc., Perkin Trans. 1* **1972,** *1*, 93.
(19) Wymberg, H.; Van Driel, H.; Kellog, R. M.; Buter, J. *J. Am. Chem. Soc.* **1967,** *89*, 3487.

in benzene (20 mL) triethyl borane (1 M pentane solution, 20 mL)) was added at room temperature in an open flask. The reaction mixture was stirred for 2 h; the solvent was then removed; and the residue was analyzed by GC–MS and was chromatographed.

From 2-Furylmethanethiol (1) and Hex-1-yne. Method A. Chromatography gave (*E*)-1-(4-*n*-butyl-3-thienyl)-5-cyano-5-methylpent-1-en-3-ol (**8a**) (ca. 5–10 mg, 2–3%), (E)-3-(4-n-butyl-3-thienyl)propenal [(E)-**7a**] (20 mg, 5%) and a mixture of unidentifiable products. **8a**: ^{1}HNMR δ = 0.95 (3H, t, J = 5 Hz), 1.3–1.5 (4H, m), 1.35 (3H, s), 1.45 (3H, s), 1.5–1.7 (2H, m), 2.0 (1H, br d, J = 2.7 Hz), 2.60 (2H, t, J = 7.0 Hz), 4.1 (1H, dd, J_1 = 7.3 Hz, J_2 = 2.7 Hz; collapsing to d, J = 2.7 Hz upon irradiation at δ 6.15), 6.15 (1H, dd, J_1 = 15.5 Hz, J_2 = 7.3 Hz), 6.68 (1H, d, J = 15.5 Hz), 6.95 (1H, br d, J = 3.0 Hz), 7.45 (1H, d, J = 3.0 Hz); MS m/z (rel intensity) 263 (M^+, 15), 196 (40), 195 (100), 111 (20); HRMS calcd for $C_{15}H_{21}NOS$ 263.13439; found 263.13460. (*E*)-**7a**: ^{1}H NMR δ = 0.95 (3H, t, J = 7.5 Hz), 1.3–1.6 (4H, m), 2.70 (2H, t, J = 7.5 Hz), 6.60 (1H, dd, J_1= 7.5 Hz J_2= 16 Hz; collapsing to doublet, J = 16 Hz, upon irradiation at δ 9.65 Hz), 7.00 (1H, br d, J = 3.0 Hz), 7.42 (1H, d, J = 16 Hz), 7.6 (1H, d, J = 3.0 Hz), 9.64 (1H, d, J = 7.5 Hz); MS m/z (rel intensity) 194 (M^+, 90), 151 (100), 137 (25), 123 (80), 97 (30), 79 (30), 45 (60). Anal. Calcd for $C_{11}H_{14}OS$: C, 68.00; H, 7.26; O, 8.23; S, 16.50. Found: C, 68.15; H, 7.30; S, 16.40.

Method B. Chromatography gave an inseparable mixture of (*E*)- and (*Z*)-2-furylmethyl hex-1-en-1-yl sulfide [(*E*)- and (*Z*)-**9a**] (80 mg, 20%; *Z*/*E* ratio 65:35) and (*E*)-propenal (*E*)-**7a** (86 mg, 22%) and (*Z*)-propenal [(Z)-**7a**] (70 mg, 18%). **9a**: ^{1}HNMR δ = 0.90 (3H, t, J = 7 Hz), 1.2–1.4 (4H, m), 2.0–2.2 (2H, m), 3.85 (2H, s), 5.60 (1H, A part of an ABX_2 system, J_{AB} = 9 Hz, J_{AX} = 7 Hz), 5.74 (1H, A′ part of an A′B′X′$_2$ system, $J_{A'B'}$ = 15 Hz, $J_{A'X'}$ = 6.7 Hz), 5.93 (1H, B′ part of an A′B′X′$_2$ system, $J_{A'B'}$ = 15 Hz, $J_{B'X'}$ = 1.2 Hz), 5.96 (1H, B part of an ABX_2 system, J_{AB} = 9 Hz, J_{AX} = 1.2 Hz), 6.20 (1H, m), 6.35 (1H, m), 7.40 (1H, m); MS m/z (rel intensity) 196 (M^+, 20), 81 (100), 53 (20). Anal. Calcd. for $C_{11}H_{16}OS$: C, 67.30; H, 8.22; O, 8.15; S, 16.33. Found: C, 67.45; H, 8.18; S, 16.40. (*Z*)-**7a**: ^{1}H NMR δ = 0.90 (3H, t, J = 7.5 Hz), 1.2–1.7 (4H, m), 2.6 (2H, t, J = 7.5 Hz), 6.20 (1H, dd, J_1= 11 Hz, J_2= 7.9 Hz), 7.01 (1H, m), 7.4 (1H, m), 7.45 (1H, dd, J_1= 11 Hz, J_2= 1 Hz), 10.0 (1H, dd, J_1= 7.9 Hz, J_2= 1 Hz; collapsing to doublet, J = 1 Hz upon irradiation at δ 6.2); MS m/z (rel intensity) 194 (M^+, 50), 151 (100), 123 (60).

From 2-Furylmethanethiol (1) and Phenylacetylene. Method A. Chromatography gave 2-furylmethyl disulfide (**10**, 2–3 mg), 1-phenyl-3-cyano-3-methyl-1-butene (40 mg), a mixture of possible (Z)- and (*E*)-2-furylmethyl β-stiryl sulfide [(*Z*)- and (*E*)-**9b**] (2–3 mg), as evidenced by GC–MS analysis [GC–MS m/z (rel intensity) 216 (M^+, 20), 134 (20), 81 (100)], and (*E*)-3-(4-phenyl-3-thienyl)propenal [(*E*)-**7b**] (100 mg, 25%): ^{1}HNMR δ = 6.53 (1H, dd, J_1= 16 Hz, J_2= 7.8 Hz), 7.2–7.8 (8H, m), 9.53 (1H, d, J = 7.8 Hz); MS m/z (rel intensity) 214 (M^+, 15), 185 (100), 184 (30). Anal. Calcd for $C_{13}H_{10}OS$: C, 72.87; H, 4.70; O, 7.47; S, 14.96. Found: C, 73.10; H, 4.75; S, 15.05.

Method B. Chromatography gave (*E*)-propenal [(*E*)-**7b**, 50 mg, 12% and (*Z*)-propenal (*Z*)-**7b**, 90 mg, 21%]: ^{1}H NMR δ = 6.2 (1H, dd, J_1= 11.5 Hz, J_2= 8 Hz), 7.3–7.6 (8H, m), 10.15 (1H, d, J = 8 Hz, collapsing to s upon irradiation at δ 6.2); MS m/z (rel intensity) 214 (M^+, 20), 185 (100), 184 (40).

From 2-Thienylmethanethiol (2) and Hex-1-yne. Method A. Chromatography gave 2-thienylmethyl disulfide (**13**, 13 mg, 5%) and (*E*)-1-(4-*n*-butyl-3-thienyl)-5-cyano-5-methylpent-1-ene-3-thiol (**11a**, 15 mg, 3%): ^{1}H NMR δ = 0.95 (3H, t, J = 7.5 Hz), 1.45 (3H, s) and 1.50 (3H, s), superimposed to 1.3–1.7 (4H, m), 1.90 (SH, d, J = 6 Hz, collapsing to singlet upon irradiation at δ 3.5), 2.55 (2H, t, J = 7 Hz), 3.50 (1H, dd, J_1 = 8 Hz, J_2= 6 Hz), 6.0 (1H, dd, J_1 = 15 Hz, J_2 = 8 Hz), 6.50 (1H, d, J = 15 Hz), 6.9 (1H), 7.3 (1H); MS m/z (rel intensity) 279 (M^+, 20), 246 (20), 211 (100), 178 (40), 177 (40), 97 (25); HRMS calcd for $C_{15}H_{21}NS_2$ 279.11154; found 279.11185.

From 2-Thienylmethanethiol (2) and Phenylacetylene. Method A. Chromatography gave a 80:20 Z/E mixture of (*Z*)- and (*E*)-2-thienylmetyl β-styryl sulfide [(*Z*) and (*E*)-**12b**] (50 mg, 11%), (*E*)-Aldehyde (*E*)-**7b** (40 mg, 10%), and tarry materials. **12b**: ^{1}H NMR δ = 4.20 (2H, s), 6.27 (0.8H, A part of an AB system, J = 10.5 Hz), 6.47 (0.8H, B part of an AB system, J = 10.5 Hz), 6.57 (0.2H, A′ part of A′B′ system, J = 15 Hz), 6.73 (0.2H, B′ part of an A′B′ system, J = 15 Hz), 6.9–7.0 (3H, m), 7.2–7.5 (5H, m); MS m/z (rel intensity) 232 (M^+, 10), 97 (100). Anal. Calcd for $C_{13}H_{12}S_2$: C, 67.20; H, 5.21; S, 27.60. Found: C, 67.55; H, 5.18; S, 27.70.

Method B. Chromatography gave a 85:15 mixture of the adducts (*Z*)- and (*E*)-**12b** (105 mg, 23%), a ca. 2:1 mixture of (*Z*)- and (*E*)-**7b** (90 mg, 20%), and tarry materials.

From 2-Thiophenethiol (4) and Hex-1-yne. Method A. Chromatography gave a 50:50 mixture of (*Z*)- and (*E*)-2-thienyl hex-1-en-1-yl sulfide [(*Z*)- and (*E*)-**26a**] (55 mg, 14%) and 2-thienyl disulfide **25** (50 mg, 22%). **26a**: [^{1}H NMR δ = 0.9 (3H, t, J = 7 Hz), 0.95 (3H, t, J = 7 Hz), 1.2–1.5 (8H, m), 2.10 (2H, dt, J_d = J_t = 7 Hz), 2.25 (2H, dt, J_d = J_t=7 Hz), 5.63 (1H, dt, J_d = 9.5 Hz, J_t = 7 Hz), 5.76 (1H, A part of an ABX_2 system, J_{AB} = 15 Hz, J_{AX} = 7 Hz; collapsing to A part of an AB system upon irradiation at δ 2.1), 6.05 (1H, B part of an ABX_2 system, J_{AB} = 15 Hz, J_{BX} = 1 Hz; collapsing to B part of an AB system upon irradiation at δ 2.1), 6.07 (1H, dt, J_d = 9.5 Hz, J_t = 1 Hz), 6.9–7.4 (3H, m); MS m/z (rel intensity) 198 (M^+, 100), 155 (50), 121 (60), 116 (50). Anal. Calcd for $C_{10}H_{14}S_2$: C, 60.56; H, 7.11; S, 32.33. Found: C, 60.70; H, 7.15; S, 32.50.

Method B. Chromatography gave a 60:40 mixture of (*Z*)- and (*E*)-**26a**, (20 mg, 5%) and disulfide **25** (185 mg, 80%).

From 2-Thiophenethiol (4) and Phenylacetylene. Method A. Chromatography gave a 70:30 mixture of (*Z*) and (*E*)-2-thienyl β-styryl sulfide (**26b**) (300 mg, 70%) and a mixture of unidentified products (20 mg). **26b**: ^{1}H NMR δ (*Z*-isomer) = 6.40 (1H, A part of an AB system, J = 11 Hz), 6.50 (1H, B part of an AB system, J = 11 Hz), 7.0–7.6 (8H, m); ^{1}H NMR δ (*E*-isomer) = 6.52 (1H, A part of an AB system, J = 15.5 Hz), 6.8 (1H, B part of an AB system, J = 15.5 Hz), 7.0–7.6 (8H, m); MS m/z (rel intensity) 218 (M^+, 90), 185 (60), 184 (60), 170 (50). Anal. Calcd for $C_{12}H_{10}S_2$: C, 66.01; H, 4.62; S, 29.37. Found: C, 65.75; H, 4.65; S, 29.25.

Method B. Chromatography gave a 90:10 mixture of sulfide adducts (*Z*)- and (*E*)-**26b**, (230 mg, 53%).

From 4-Thienylmethanethiol (3) with Hex-1-yne. Method A. Chromatography gave a 70:30 *Z*/*E* mixture of 3-thienylmethyl hex-1-en-1-yl sulfide (**24**) (70 mg, 17%) and 3-thienylmethyl disulfide (**20**) (30 mg, 12%). **24**: ^{1}H NMR δ = 0.90 (3H, t, J = 7.5 Hz), 1.2–1.5 (4H, m), 1.95–2.15 (2H, m), 3.85 (2H, s), 5.55 (0.7H, A part of an ABX_2 system, J_{AB} = 9.5 Hz, J_{AX} = 7 Hz), 5.66 (0.3H, A′ part of an A′B′X′$_2$ system, $J_{A'B'}$ =15 Hz, $J_{A'X'}$ = 7 Hz), 5.88 (0.7H, B part of an ABX_2 system, J_{AB} = 9.5 Hz , J_{AX} = 1 Hz), 5.88 (0.3H, B′ part of an A′B′X′$_2$ system, $J_{A'B'}$ =15 Hz, $J_{A'X'}$ = 1 Hz), 7.0–7.15 (2H, m), 7.2–7.3 (1H, m); MS m/z (rel intensity) 212 (M^+, 40), 97 (100). Anal. Calcd for $C_{11}H_{16}S_2$: C, 62.21; H, 7.59; S, 30.20. Found: C, 62.35; H, 7.63; S, 30.05. **20**: ^{1}H NMR δ = 3.6 (2H, s), 6.95–7.10 (2H, m), 7.2–7.3 (1H, m); MS m/z (rel intensity) 258 (M^+, 5), 193 (15), 97 (100). Anal. Calcd for $C_{10}H_{10}S_4$: C, 45.76; H, 5.38; S, 48.86. Found: C, 45.85 ; H, 5.45; S, 48.5.

The reaction was repeated by adding slowly (3 h) with a syringe pump a solution of thiol **3** (2 mmol) and AIBN (2 mmol) in benzene (5 mL) to a boiling solution of hex-1-yne (1 mL) and AIBN (0.2 mmol) in benzene (20 mL). The reaction mixture was refluxed for further 3 h and then worked up in the usual manner. Chromatography gave an isomeric mixture of the adduct **23** (50 mg, 9%), a ca. 1:3 mixture (85 mg, 20% overall yield) of the thienothiine **22** and the adducts (*Z*) and (*E*)-***24*** in 70:30 ratio. **23**: ^{1}H NMR δ = 0.85 (3H, t, J = 7 Hz), 0.90 (3H, t, J = 7 Hz), 1.2–1.5 (8H, m), 1.95–2.20 (4H, m), 3.50 (2H, s), 5.58 (0.6H, dt, J_d = 9.5 Hz, J_t = 7 Hz), 5.66 (0.4H, dt, J_d = 15 Hz, J_t = 7 Hz), 5.85 (1H, br s), 5.99 (0.4H, dt, J_d = 15 Hz, J_t = 1 Hz), 6.02 (0.6H, dt, J_d = 9.5 Hz, J_t = 1 Hz), 6.85–7.00 (2H, m), 7.15–7.25 (1H, m); GC–MS m/z (rel intensity) 294 (M^+, 30), 179 (30), 135 (30), 123 (30), 97 (100). HRMS calcd for $C_{17}H_{26}S_2$ 294.14760; found 294.14732. **22**: GC–MS m/z 210 (M^+, 100), 209 (90), 167 (80), 134 (50); ^{1}H NMR showed the vinylic proton at δ = 5.80, t, J = 1 Hz; collapsing to singlet upon irradiation at δ 2.1.

Method B. Chromatography gave a ca. 1:10 inseparable mixture (230 mg, 55% overall yield) of thiine **22** and the adducts (*Z*) and (*E*)-**24** in 60:40 ratio.

From 2-Benzo[*b*]furanthiol (5) and Hex-1-yne. Method A. Chromatography gave a fraction (18 mg, 4%) constituted by a 80:20 mixture of the adducts (*Z*) and (*E*)-**33a** and the regioisomeric adduct **36** in 1:2 ratio: ^{1}H NMR δ = 0.9 (3H, t), 1.2−1.6 (4H, m), 2.1−2.3 (2H, m), 5.0 and 5.15 (=C**H$_2$**, br singlets), 5.78 (A part of an ABX_2 system, J_{AB} = 9 Hz, J_{AX} = 7 Hz, $-CH_2CH{=}CH_{cis}$), 5.95 (A′ of an A′B′X′$_2$ system, $J_{A'B'}$ = 15 Hz, $J_{A'X'}$ = 7 Hz, $-CH_2CH{=}CH_{trans}$), 6.08 (B′ of an A′B′X′$_2$ system, $J_{A'B'}$ = 15 Hz, $J_{B'X'}$ = 0 Hz), 6.16 (B part of an ABX_2 system, J_{AB} = 9 Hz, J_{BX} = 1Hz), 6.8 (0.7H, s), 7.0 (1.3H, s), 7.2−7.6 (4H, m)]. GC−MS analysis showed two chromatographic peaks in ca. 2:1 ratio due to compound **36** [MS *m*/*z* (rel intensity) 232 (M$^+$, 50) 190 (30), 150 (100)], the unresolved isomers (*Z*)- and (*E*)-**33a** [MS *m*/*z* (rel intensity) 232 (M$^+$, 100), 189 (70), 150 (30)], and a large amount of unidentifiable tarry material.

Method B. Chromatography gave 2-(ethylsulfanyl)benzo[*b*]furan (**37**) (65 mg, 18%), probable 2-(ethylsulfanyl)-3-(2-benzo[*b*]furylsulfanyl)benzo[*b*]- furan (**38**) (20 mg, 6%), and large amounts of unidentifiable solid polimeric products. **37**: ^{1}H NMR δ = 1.35 (3H, t, *J* = 7.5 Hz), 2.98 (2H, q, *J* = 7.5 Hz), 6.80 (1H, s), 7.2−7.35 (2H, m), 7.4−7.6 (2H, m); MS *m*/*z* (rel intensity) 178 (M$^+$, 100, 150 (70), 149 (70), 121 (70). Anal. Calcd for $C_{10}H_{10}OS$: C, 67.38; H, 5.65; O, 8.98; S, 17.99. Found: C, 67.50; H, 5.60; S, 17.90. **38**: ^{1}H NMR δ = 1.35 (3H, t, *J* = 7.5 Hz), 3.10 (2H, q, *J* = 7.5 Hz), 6.80 (1H, s), 7.1−7.7 (8H, m); HRMS calcd for $C_{18}H_{14}O_2S_2$ 326.04352; found 326.04303.

This reaction was repeated under nitrogen atmosphere. Chromatography gave sulfide **37** (ca. 10 mg, 3%), trace amounts of bis-sulfide **38**, a yellow unknown product (60 mg, 20%), and unidentified material Unknown: mp = 215−217 °C, ^{1}H NMR δ = 7.2−7.7 (aromatic protons); MS *m*/*z* (rel intensity) 296 (M$^+$, 65), 266 (100), 237 (40), 205 (25), 150 (20); HRMS calcd for $C_{16}H_8O_2S_2$ 295.9965732; found 295.9962461.

From 2-Benzo[*b*]furanthiol (5) and Phenylacetylene. Method A. Chromatography gave (*Z*)-2-benzo[*b*]furyl β-styryl sulfide (*Z*)-**33b**: mp 73−74 °C (pentane/ether) (275 mg, 55%); ^{1}H NMR δ = 6.55 (1H, A part of an AB system, J_{AB} = 10.5 Hz), 6.66 (1H, B part of an AB system, J_{AB} = 10.5 Hz), 6.90 (1H, d, *J* = 1 Hz), 7.2−7.6 (4H, m); MS *m*/*z* (rel intensity) 252 (M$^+$, 100), 219 (40), 191 (35), 121 (60), 77 (80). Anal. Calcd for $C_{16}H_{12}OS$: C, 76.16; H, 4.79; O, 6.34; S, 12.71. Found: C, 76.45; H, 4.80; S, 12.65.

Method B. Chromatography gave the sulfide **37** (ca. 20%) and the bis-sulfide **38** (ca. 5%) as the only identifiable products.

From 2-Benzo[*b*]thiophenethiol (6) and Hex-1-yne. Method A. Chromatography gave a 50:50 mixture of (*Z*)- and (*E*)-2-benzo[*b*]thienyl hex-1-en-1-yl sulfide [(*Z*) and (*E*)-**34a**] (120 mg, 24%) and 2-benzo[*b*]thienyl disulfide (**35**) (mp = 111−112 °C, 165 mg, 50%). **34a**: ^{1}H NMR δ = 0.90 (3H, t, *J* = 7 Hz), 0.95 (3H, t, *J* = 7 Hz), 1.2−1.5 (8H, m), 2.15 (2H, dt, J_d = J_t = 7 Hz), 2.25 (2H, dt, J_d = J_t = 7 Hz), 5.79 (1H, dt, J_d = 9 Hz, J_t = 7 Hz), 5.98 (1H, A part of an ABX_2 system, J_{AB} = 14.5 Hz, J_{AX} = 7 Hz), 6.17 (1H, B part of an ABX_2 system, J_{AB} = 14.5 Hz, J_{BX} = 1 Hz), 6.23 (1H, dt, J_d = 9 Hz, J_t = 1 Hz), 7.2−7.4 (3H, m), 7.6−7.8 (2H, m); MS *m*/*z* (rel intensity) 248 (M$^+$, 100), 205 (30), 172 (40), 166 (40). Anal. Calcd for $C_{14}H_{16}S_2$: C, 67.69; H, 6.49; S, 25.82. Found: C, 67.85, H, 6.45; S, 25.70. **35**: ^{1}H NMR δ = 7.3−7.4 (3H, m), 7.6−7.8 (2H, m); MS *m*/*z* (rel intensity) 330 (M$^+$, 25), 165 (100), 121 (50). Anal. Calcd for $C_{16}H_{10}S_4$: C, 58.15; H, 3.05; S, 38.81. Found: C, 58.35 , H, 3.10 ; S, 38.6.

Method B. Chromatography gave a 65:35 mixture of the adducts (*Z*)- and (*E*)-**34a** (90 mg, 18%), disulfide **35** (120 mg, 35%), and unidentifiable products.

From 2-Benzo[*b*]thiophenethiol (6) and Phenylacetylene. Method A. Chromatography gave a 90:10 mixture of (*Z*)- and (*E*)- 2-benzo[*b*]thienyl β-styryl sulfide [(*Z*) and (*E*)-**34b**] (310 mg, 60%) and unidentifiable material. **34b**: ^{1}H NMR δ (*Z*-isomer) = 6.52 (1H, A part of an AB system, *J* = 10.5 Hz), 6.60 (1H, B part of an AB system, *J* = 10.5 Hz), 7.2−7.8 (9H, m); (E-isomer) 6.7 (1H, A part of an AB system, *J* = 16 Hz), 6.88 (1H, B part of an AB system, *J* = 16 Hz), 7.2−7.8 (9H, m); MS *m*/*z* (rel intensity) 268 (M$^+$, 100), 235 (70), 234 (60). Anal. Calcd for $C_{16}H_{12}S_2$: C, 71.60; H, 4.51; S, 23.89. Found: C, 71.75; H, 4.55; S, 24.00.

Method B. Chromatography gave a 90:10 mixture of adducts (*Z*)- and (*E*)-**34b** (370 mg, 70%) and a mixture of unidentifiable products.

Reaction of 2-Thienyl Disulfide (25) with Phenylacetylene. A solution of disulfide **25** (230 mg, 1 mmol) and phenylacetylene (2 mL) in chlorobenzene (20 mL) was heated in a sealed tube for 5 h. The solvent was removed under reduced pressure. Chromatography of the residue gave a fraction containing three isomeric products that probably were *o*, *m*, and *p*-2-thienylchlorobenzene [GC−MS *m*/*z* (rel intensity) 196,194 (M$^+$, 100), 115 (20)], 3-phenylthieno[2,3-*b*]-thiophene (**28**) (20 mg, 5%); a 85:15 *Z*/*E* mixture of 2-thienyl β-styryl sulfide **26b** (100 mg, 23%); 2,4-diphenylthiophene **30** (40 mg, 8%), and α,β-bis(2-thienylsulfanyl)styrene (**29**) (100 mg, 15%) (1:1 *Z*/*E* isomeric mixture) [^{1}H NMR δ = 6.50 (0.5H, s), 6.8−7.7 (12H, m), 7.80 (0.5H, s); MS *m*/*z* (rel intensity) 332 (M$^+$, 75), 306 (40), 217 (80), 184 (60), 115 (70), 71 (100); HRMS calcd for $C_{16}H_{12}S_4$ 331.98219; found 331.98255].

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