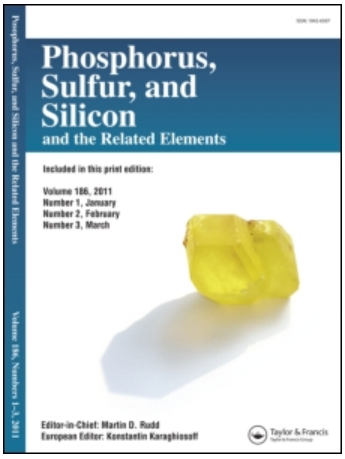

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Pier Carlo Montevecchi[a]; Maria Luisa Navacchia[a]
[a] Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Bologna, Italy

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THIOL MEDIATED 5-(π-*ENDO*)*ORTHO* VINYL RADICAL CYCLIZATIONS

PIER CARLO MONTEVECCHI* and MARIA LUISA NAVACCHIA

Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy

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The radical reaction of benzenethiol with alkynes **1a-o** carried out at 154 °C affords a mixture of thiol/alkyne adduct **3** and benzothiophene **5**, deriving from vinyl radical intermediates **2** through hydrogen abstraction and 5-(π-*endo*)*ortho*cyclization onto the adjacent thiophenyl ring, respectively. This latter reaction occurs through the reversible formation of cyclohexadienyl radical intermediates **4** which can evolve to **5** to an extent largely depending on the reaction conditions employed. The 5-*ortho* cyclization is governed both by stereoelectronic factors, which favor the cyclization of p-centered, linear α-arylvinyl radicals **2a-f**, and polar factors, which favor the cyclization of α-EWG substituted vinyl radicals **2c,n,o**.

Keywords: Sulfanyl radicals; thiols; radical cyclization; alkynes; benzothiophenes

INTRODUCTION

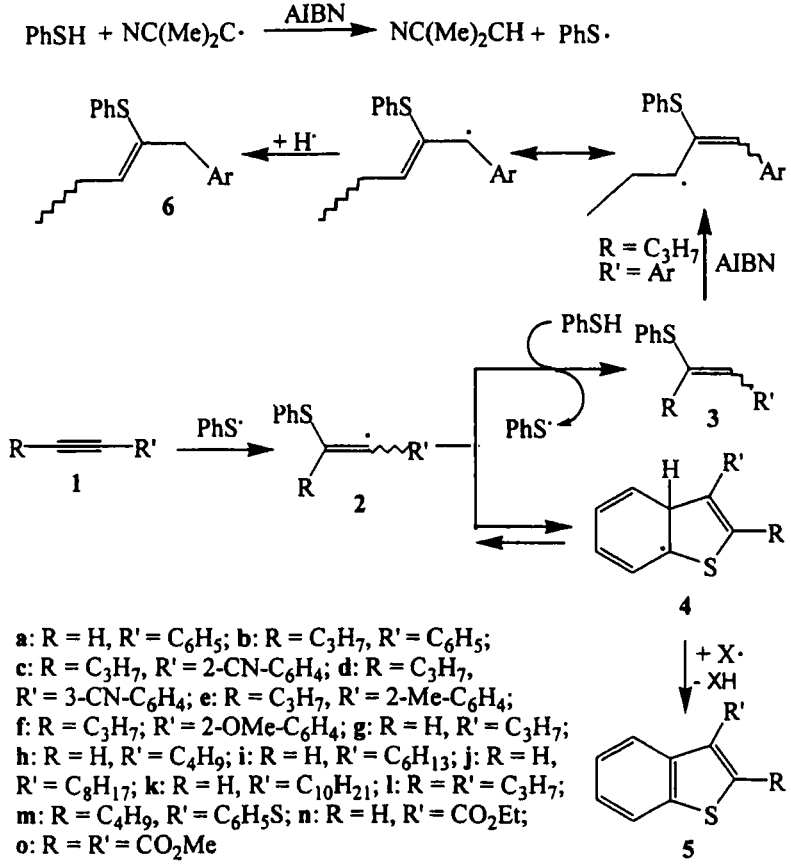
Since a few years we have interested in thiol-mediated cyclizations and rearrangements of β-sulfanylvinyl radicals.[1] We have shown that these species can undergo cyclization onto aromatic[2] and heteroaromatic[3] rings, alkene double bonds[4,5] and heteroatom-containing multiple bonds[6,7] in competition with the hydrogen abstraction reaction, leading to thiol/alkyne adducts,[8,9] and the 1,5-hydrogen migration[5].

As for the cyclization onto the benzene ring, we have previously explored the importance of steric and stereoelectronic factors in governing the 5-*exo* cyclization, which can occur in competition with the 6-*ortho* cyclization in both (π-*exo*) and (π-*endo*) mode.[2]

* Corresponding Author.

In prosecution of our researches on the thiol-mediated β-sulfanylvinyl radical chemistry, we have undertaken a study of the 5-(π-*endo*)*ortho* cyclization onto aromatic rings, a rather unexplored reaction.[10]

For this work we selected the vinyl radicals **2**, which were generated at high temperature (154 °C) through benzenesulfanyl radical addition to the alkyne **1**triple bond, and we explored the effect of both α- and β-substituents on the rate of the 5-(π-*endo*)*ortho* cyclization onto the adjacent thiophenyl ring. This reaction, leading to the benzothiophene derivative **5**, was expected to occur in competition with the hydrogen abstraction reaction, leading to the thiol/alkyne adduct **3** (Scheme 1).



a: R = H, R' = C_6H_5; **b**: R = C_3H_7, R' = C_6H_5;
c: R = C_3H_7, R' = 2-CN-C_6H_4; **d**: R = C_3H_7,
R' = 3-CN-C_6H_4; **e**: R = C_3H_7, R' = 2-Me-C_6H_4;
f: R = C_3H_7; R' = 2-OMe-C_6H_4; **g**: R = H, R' = C_3H_7;
h: R = H, R' = C_4H_9; **i**: R = H, R' = C_6H_{13}; **j**: R = H,
R' = C_8H_{17}; **k**: R = H, R' = $C_{10}H_{21}$; **l**: R = R' = C_3H_7;
m: R = C_4H_9, R' = C_6H_5S; **n**: R = H, R' = CO_2Et;
o: R = R' = CO_2Me

SCHEME 1

RESULTS AND DISCUSSION

Reactions were carried out in bromobenzene solution with equimolar amounts of the appropriate alkyne **1a-o**, benzenethiol and azobis*iso*butyronitrile (AIBN) under different reaction conditions. Following conditions of Method A a bromobenzene solution of benzenethiol and AIBN was slowly added within 3 h with a syringe pump to a boiling bromobenzene solution of the alkyne **1b-f,i-k**. Following conditions of Method B benzenethiol and AIBN were rapidly added to a boiling bromobenzene solution of the alkyne **1a-c,j,k,m,o**, and the resulting solution was refluxed for 1h. Following conditions of Method C a bromobenzene solution of benzenethiol, AIBN and the alkyne **1a-c,g-l,n** was heated in a sealed tube at 154°C for 1 h. Moreover, following conditions of Method D, alkynes **1a,b** and benzenethiol were reacted in bromobenzene at 154 °C for 1h in a sealed tube without AIBN. Subsequent work up followed by silica gel flash chromatography of the resulting crudes (see Experimental Part) generally separated mixtures constituted by the appropriate thiol/alkyne adduct **3** (Z/E mixture) and the benzothiophene **5**, as evidenced by ^{1}H NMR and GC-MS analyses. The relative yields of the reaction products **3** and **5** (70–80% overall yields, based on reacted alkyne; 40–50% based on starting alkyne) are reported in the Table. A repeated column chromatography of these mixture allowed for the separation of small amounts of pure products **3a-o** and **5a-f,i-k,m-o**. The previously unknown adducts **3c-f,i-k** and benzothiophenes **5b-f,i-k,m,o** could be characterized on the basis of ^{1}H nmr and ms spectral data and elemental analysis. Benzothiophenes **5g,h,l**, which were formed in small amounts, could be detected only in the gc-ms spectrum.

TABLE Adducts **3** and benzothiophene **5** relative yields, % from reactions of benzenethiol (1 mol equiv) with alkynes **1a-o** (1 mol equiv) carried out in refluxing bromobenzene in the presence of AIBN (1 mol equiv) with the syringe pump tecnique (Method A), in refluxing bromobenzene in the presence of AIBN (1 mol equiv) (Method B), in a sealed tube at 154°C in the presence of AIBN (1 mol equiv) (Method C) and in a sealed tube at 154°C in the absence of AIBN (Method D)

Entry	*Alkyne*	*R*	*R'*	*Adduct 3/benzothiophene 5 relative yield ratio, % (Method)*
1	**1a**	H	C_6H_5	85:15 (B), 99:1 (C), 99:1 (D)
2	**1b**	C_3H_7	C_6H_5	65:35 (A)[a], 70:30 (B)[a], 84:16 (C)[a], 88:12 (D)

Entry	*Alkyne*	*R*	*R'*	*Adduct 3/benzothiophene 5 relative yield ratio, % (Method)*
3	**1c**	C_3H_7	2-CNC_6H_4	28:72 (A)[a], 25:75 (B)[a], 85:15(C)[a]
4	**1d**	C_3H_7	3-CN-C_6H_4	67:33 (A)[a]
5	**1e**	C_3H_7	2-Me-C_6H_4	73:27 (A)[a]
6	**1f**	C_3H_7	2-OMe-C_6H_4	67:27 (A)[a]
7	**1g**	H	C_3H_7	99:1 (C)
8	**1h**	H	C_4H_9	99:1 (C)
9	**1i**	H	C_6H_{13}	83:17(A), 96:4 (C)
10	**1j**	H	C_8H_{17}	83:17 (A), 96:4 (B), 96:4 (C)
11	**1k**	H	$C_{10}H_{21}$	85:15 (A), 97:3 (B), 99:1 (C)
12	**1l**	C_3H_7	C_3H_7	99:1 (C)
13	**1m**	C_4H_9	C_6H_5S	80:2 (B)
14	**1n**	H	CO_2Et	50:50 (C)
15	**1o**	CO_2Me	CO_2Me	10:90 (B)

a. Adduct **3** was contaminated with isomeric adduct **6**(ca. 3:1 **4/6** yield ratio)

Column chromatography of the reaction mixture resulting from alkynes **1b-f** gave, in addition to adducts **3b-f** and benzothiophenes **5b-f**, unidentified products which were assigned the structure of the rearranged adducts **6b-f** on the basis of the ^1H nmr and gc-ms spectral analysis (Scheme 1). A full characterization was not possible owing to the impossibility of obtaining pure samples. ^1H nmr analysis of the corresponding reaction mixtures showed adducts **3b-f** and **6b-f** to be present in a ca. 3:1 ratio. The formation of regioisomeric adducts **6b-f** probably resulted from a 2-cyanopropyl radical promoted post-isomerization of the first formed adduct **3b-f** through intermediacy of an allyl radical (Scheme 1). This suggestion was supported by an independent experiment which showed that the adduct **3b** was converted to **6b** upon heating in refluxing bromobenzene in the presence of AIBN (1 equiv) (30% conversion yield).

As mentioned above, the adduct **3** and the benzothiophene **5** were the expected products deriving from the vinyl radical intermediate **2** through a chain process: hydrogen abstraction from benzenethiol leads to the adduct **3** (chain propagation), whereas 5-(π-*endo*)*ortho* cyclization onto the adja-

cent phenyl ring leads to the cyclohexadienyl radical **4**. In turn, **4** can give the benzothiophene **5** through hydrogen abstraction by some radical species (chain termination) (Scheme 1). Vinyl radicals **2** were in turn derived from regioselective benzenesulfanyl radical addition to the alkyne **1** triple bond. The radical mechanism was proved by reacting the alkyne **1b** and benzenethiol in refluxing bromobenzene in the absence of any radical initiator (dioxygen or AIBN). Under these conditions starting **1b** was recovered unchanged after 2 h.

As evidenced by results reported in the Table, the benzothiophene **5** / adduct **3** yield ratio is strongly determined by the experimental reaction conditions and the nature of both α- and β-vinyl radical substituents as well.

According to the postulated radical mechanism, the relative yield of benzothiophene **5** was found to be dependent on the thiol concentration. Low thiol hydrogen donor concentrations, obtained with the syringe pump technique (Method A), generally favored the formation of benzothiophene **5** by disfavoring the competing hydrogen abstraction reaction leading to **3**, as expected (Table, entries 2,3,10,11). However, the **5/3** ratio increased 4–5 times with α-alkylvinyl radicals **1j,k** on passing from Method B to Method A (entries 9–11), while a small increase (1.1–1.2 times) was observed with α-arylvinyl radicals **2b,c** (Table, entries 2,3). In these latter cases it can be inferred that vinyl radical **2b,c** can abstract the hydrogen atom from a source different from the thiol, possibly from the cyclohexadienyl radical intermediate **4b,c**.

Comparison of results obtained under Method B and Method C conditions (Table, entries 1,2,3,10,11) shows that the **5/3** ratio was strongly lowered by carrying out the reaction in a sealed tube instead of in refluxing bromobenzene. This different trend could be ascribed to the air dissolved in the bromobenzene solution when the reaction was carried out in a sealed tube. Actually, benzenesulfanyl radicals can be easily produced from benzenethiol by a dioxygen-promoted reaction.[11,12] In agreement, we found that benzenethiol reacted with alkynes **1a** and **1b** in a sealed tube at 154 °C in the absence of AIBN (Method D) leading to results strictly comparable to those obtained in the presence of AIBN (Method C) (Table, entries 1,2). Also, we found that the yield of benzothiophene **5a** increased in a roughly linear way with the concentration of AIBN. Reactions of **1a** carried out in refluxing bromobenzene in the presence of 0.25, 0.75 and 1.0 molar equivalents of AIBN gave adduct **3a** and benzothiophene **5a** in 96:4, 88:12 and 85:15 yield ratio, respectively.

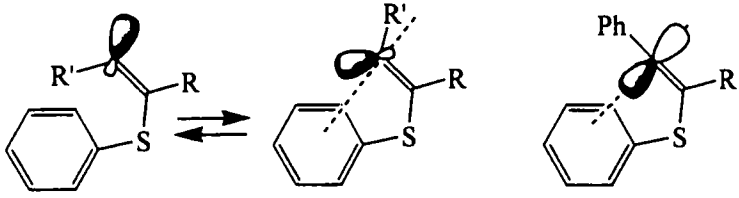
These findings could be explained according to the reaction mechanism if we assumed that the formation of the cyclohexadienyl radical **4**, precursor of the benzothiophene **5**, occurs in a reversible manner. In this suggestion an increase of the AIBN concentration should result in an increased steady concentration of radical species (X.) which can effectively remove the radical **4** from the equilibrium through hydrogen atom abstraction reaction (chain termination) (Scheme 1).

As for the effect of vinyl radical substituents, it can be observed that the replacement of a β-hydrogen with an alkyl group favors the formation of the benzothiophene derivative **5**, as evidenced by the behavior exhibited by radicals **2a** and **2b** (Table, entries 1,2). This finding is likely due to steric effects which disfavor the competing hydrogen abstraction reaction by disfavoring the approach of the hydrogen donor. We have previously reported that radical **2b** abstracts a hydrogen atom 2 times slower than the parent radical **2a** at 80 °C.[9]

Similarly, it would appear that an increase in lengthiness of the α-alkyl side chain favors the cyclization reaction (Table, entries 7–11). Also in these cases the observed increase of the benzothiophene **5** yield on passing from R = propyl, butyl (entries 7,8) to R = hexyl, octyl, decyl entries 9–11) could be due to the fact that, for an unclear reason, radicals **2i-k** abstract the hydrogen atom slower than radicals **2g,h**.[9]

Under conditions of Method B (refluxing bromobenzene in the presence of AIBN) the relative yields of the benzothiophene derivative **5** increased from 3–5% for R = alkyl (Table, entries 10,11) to 15–30% for R = phenyl (Table, entries 1,2), 20% for R = benzenesulfanyl (Table, entry 13) and 90% for R = methoxycarbonyl (Table, entry 15). Moreover, in spite of the finding that the reactions carried out in a sealed tube generally gave the benzothiophene derivative **5** in lower yields, ethyl propiolate **1n** reacted under conditions of Method C to give the benzothiophene **5n** in 50% relative yield. Finally, we found that a 2-cyano substituent present in the α-phenyl ring strongly increased the yield of the corresponding benzothiophene, as evidenced by comparison of entries 2 and 3 (Table). A similar effect was not exhibited by other 2-substituents (Table, entries 5,6) nor by a cyano group in 3-position (Table, entry 4). Since we have reported[9] that α-alkylvinyl radicals **2i-k** abstract the hydrogen atom from benzenethiol 4 times slower than radical **2a** and 2 times slower than radical **2b**, the greater **5/3** yield ratio observed for radicals **2a,b**, as compared with radicals **2i-k**, must be attributed to an effective capability of the α-phenyl substituent in

promoting the vinyl radical cyclization. This effect, previously observed in related 5-(π-*endo*)*endo* cyclizations onto the alkene double bond,[4] might be due to the more favorable stereoelectronic conditions expected for α-aryl-substituted vinyl radicals **2a,b**, which are the sp-hybridized, linear ones, as compared with α-alkyl-substituted vinyl radicals **2i-k**, which are the sp^2-hybridized, interconverting ones[1]. In fact, according to the Baldwin-Beckwith rules[13] for radical cyclizations, the transition state for a 5-*endo-trig* cyclization is achieved when the unpaired electron containing orbital and the CC double bond form an angle of 109°. This situation should be better achieved for a linear vinyl radical, rather than for a bent vinyl radical (Scheme 2).

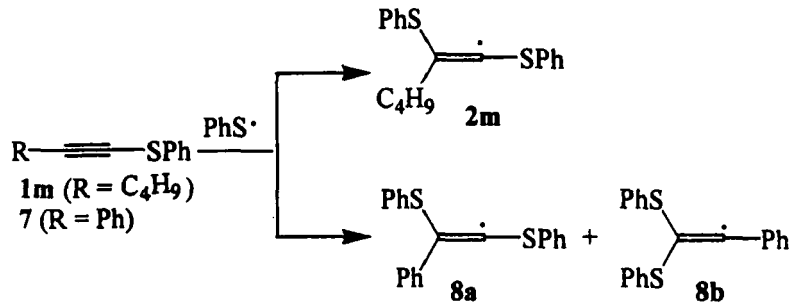


sp^2-hybridized, intercoverting radicals p-hybridized, linear radicals

SCHEME 2

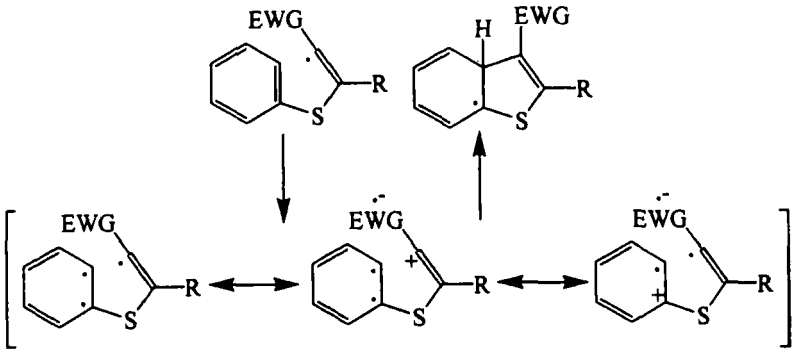
Also the apparent effect of the α-sulfur atom in favoring the cyclization reaction would be explained in terms of favorable stereoelectronic factors if we assumed a linear structure for this radical. This suggestion was strongly supported by the evidence that benzenesulfanyl radical addition to 1-(phenylthio)hex-1-yne **1m** gave the α-(phenylthio)vinyl radical **2m** in a regioselective mode, whereas the addition to 2-(phenylthio)phenylacetylene **7** gave a mixture of regioisomeric α-(phenylthio)- (**8a**) and α-phenyl- (**8b**) vinyl radicals.[9] This behavior indicates that the sulfur atom, like the phenyl ring, can stabilize the vinyl radical through unpaired electron delocalization, this pointing to a linear structure (Scheme 3).

The strong effect of the α-(2-cyanophenyl) substituent in favoring the vinyl radical cyclization (Table, entry 3) can not be explained only in terms of stereoelectronic factors. We believe that in the case of radical **2c** polar factors can play an important role. On the other hand, polar factors must be also invoked to explain the high yield of the benzothiophene



SCHEME 3

derivatives **5n,o** observed in the case of radicals **2n,o** (Table, entries 14,15). As we have previously shown[2], the addition of vinyl radicals to the benzene ring is governed by SOMO/HOMO frontier molecular orbital interaction. The presence of an α-EWG substituent should enhance the cyclization rate by increasing the electrophilic character of the vinyl radical, that is by stabilizing the transition state through the canonical forms depicted in Scheme 4.



SCHEME 4

It must be pointed out that a great electrophilic character of the vinyl radical should favor the formation of the benzothiophene derivative **5** both by increasing the cyclization reaction rate and by disfavoring the competing hydrogen abstraction reaction. In fact, according to the Roberts' state-

ment,[14] the hydrogen abstraction from benzenethiol by electrophilic radicals is expected to be disfavored since electrophilic sulfanyl radicals are displaced. This suggestion is supported by our previous finding[9] that radical **1n** abstracts the hydrogen atom from benzenethiol at 80 °C 10^3 times slower than radical **1a**.

Finally, it is worth to note that benzothiophenes **5c,e,f**, showed diastereomeric methylenic protons in the ^{1}H nmr spectrum. This finding indicates the presence of a C1 molecular symmetry, probably arising from restricted rotation around the CC single bond between the C-3 carbon atom and the 2-substituted phenyl ring.

This atropoisomerism, already observed in the related 2-butyl-3-(2-cyanophenyl)benzothiophene,[7] is not present in the parent benzothiophene **5b** nor in the 3-(3-cyanophenyl)derivative **1d**. Spectra performed in DMSO at high temperature showed the atropoisomerism is present even at 140 °C. Semiempirical calculations gave a rotational barrier ≥ 26 Kcal/mol.

CONCLUSIONS

The radical reaction of benzenethiol with alkynes **1a-o** carried out at 154 °C affords a mixture of benzothiophene **5** and thiol/alkyne adduct **3** in a ratio dependent on the reaction conditions employed and the nature of the vinyl radical substituents. Notwithstanding that this reaction has no synthetic utility owing to experimental difficulties in the chromatographic separation of reaction products **3** and **5** and, in several cases, to the low yields of the benzothiophene derivative **5**, it provides a useful tool for understanding factors governing the 5-(π-*endo*)*ortho* cyclization of vinyl radicals onto the benzene ring.

We have shown that the 5-*ortho* cyclization is a reversible reaction, so that the yield of benzothiophene **5** depends on the capability of the cyclohexadienyl radical intermediate to evolve to product **5**, in turn depending on the reaction conditions employed. Moreover, we have shown that stereoelectronic factors favor the cyclization of p-centered, linear α-arylvinyl radicals **2a-f**, whereas polar factors favor the cyclization of α-EWG substituted vinyl radicals **2c,n,o** as a consequence of the enhanced electrophilic character.

EXPERIMENTAL SECTION

Column chromatography was performed on silica gel (0.040–0.063 particle size) by gradual elution with light petroleum (b.p. 40–70 °C)-diethyl ether. ^{1}H NMR spectra were recorded at 200 MHz in $CDCl_3$ solutions using Me_4Si as internal standard. Mass spectra were determined by the electron impact method.

Alkynes **1a,b,g-l,n,o** and azobisisobutyronitrile (AIBN) were commercially available. The alkyne **1m**[17] was obtained in 90% yield by refluxing for 2h an anhydrous THF solution (50 ml) of diphenyl disulfide (15 mmol) and lithium hexenide (15 mmol), in turn obtained from butyl lithium and hex-1-yne.

GENERAL PROCEDURE FOR THE PREPARATION OF ALKYNES 1c,f

Alkynes **1c-f** were obtained according to the procedure reported in the literature[15] for the preparation of disubstituted alkynes from halobenzenes and terminal acetylenes. A solution of the appropriate bromobenzene derivative (2-bromobenzonitrile, 3-bromobenzonitrile, 2-bromoanisole and 2-bromotoluene) (20 mmol) and tetrakis(triphenylphosphine)palladium[16] [$Pd(PPh_3)_4$] (1 mmol, 1.16 gr) in piperidine (30 ml) was stirred at room temperature under nitrogen atmosphere for 15 min, then a solution of 1-pentyne (20 mmol) in piperidine (20 ml) was added. The reaction mixture was stirred for 6 h at ca. 30 °C under nitrogen, then extracted with diethyl ether and washed several times with an ammonium chloride saturated solution. The organic layer was separated and dried, the solvent was evaporated and the crude product chromatographed on silica gel column to give the corresponding alkyne.

1-(2-Cyanophenyl)pent-1-yne 1c

This compound was obtained in 85% yield as a colorless oil; ir: ν CN 2220 cm^{-1}; ^{1}H nmr: δ 1.1 (3H, t, J = 7 Hz), 1.7 (2H, sextuplet, J = 7 Hz), 2.50 (2H, t, J = 7 Hz), 7.2–7.7 (4H, m); ms: m/z 169 (M^+, 95), 168 (100), 154 (100), 140 (80), 127 (40), 113 (30). *Anal.* Calcd. for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.40; H, 6.56; N, 8.25.

1-(3-Cyanophenyl)pent-1-yne 1d

This compound was obtained in 78% yield as a colorless oil; ir: ν CN 2220 cm^{-1}; ^1H nmr: δ 1.0 (3H, t, J = 7 Hz), 1.6 (2H, sextuplet, J = 7 Hz), 2.35 (2H, t, J = 7 Hz), 7.2–7.7 (4H, m); ms: m/z (rel. intensity) 169 (M^+, 95), 168 (100), 154 (100), 140 (100), 127 (100), 113 (80). *Anal.* Calcd. for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.42; H, 6.57; N, 8.25.

1-(2-Methylphenyl)pent-1-yne 1e

This compound was obtained in 68% yield as a colorless oil; ^1H nmr: δ 1.05 (3H, t, J = 7 Hz), 1.65 (2H, sextuplet, J = 7 Hz), 2.42 (3H, s, superimposed to 2H, t, J = 7 Hz), 7.1–7.4 (4H, m); ms: m/z (rel. intensity) 158 (M^+, 100), 143 (90), 128 (90), 115 (90). *Anal.* Calcd. for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 90.80; H, 8.94.

1-(2-Metoxyphenyl)pent-1-yne 1f

This compound was obtained in 70% yield as a colorless oil; ^1H nmr: δ 1.0 (3H, t, J = 7 Hz), 1.6 (2H, sextuplet, J = 7 Hz), 2.4 (2H, t, J = 7 Hz), 3.8 (3H, s), 6.85 (2H, m), 7.15–7.4 (2H, m); ms: m/z (rel. intensity) 174 (M^+, 90), 131 (50), 115 (100), 91 (60). *Anal.* Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10; O, 9.18. Found: C, 82.95; H, 8.12.

GENERAL PROCEDURE FOR THE REACTION OF BENZENETHIOL WITH ALKYNES 1b-f,i-k. METHOD A

A bromobenzene solution (5 ml) of benzenethiol (0.20 ml, 2 mmol) and AIBN (330 mg, 2 mmol) was added within 3 h with a syringe pump to a boiling bromobenzene solution (15 ml) of the appropriate alkyne **1b-f,i-k** (2 mmol). The resulting solution was refluxed for additional 30 min. The reaction mixture was cooled, washed twice with NaOH 10% and once with water, the organic layer was dried over Na_2SO_4 and the solvent evaporated. The organic residue was chromatographed on silica gel column to separate a mixture consisting of unreacted alkyne **1b-f,i-k** and reaction products **3b-f,i-k, 5b-f,i-k** and **6b-f**. This mixture was weighted and analyzed by gc-ms and ^1H nmr to determine the yield of the unreacted alkyne

(35–50%) and the relative yields of reaction products (70–80% overall yields, based on reacted alkyne; relative yields are reported in the Table). Repeated column chromatography of the above mixtures allowed for the separation of pure samples of the adduct **3b**[8a] and the hitherto unknown adducts **3c-f,i-k** and benzothiophenes **5b-f,i-k**.

2-Propyl-3-phenylbenzo[b]thiophene 5b

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.7 (2H, sextuplet, J = 7 Hz), 2.8 (2H, t, J = 7 Hz), 7.2–7.8 (9H, m); ms: m/z (rel. intensity) 252 (M^+, 65), 223 ($M^+ - C_2H_5$, 100), 221 (70). *Anal.* Calcd. for $C_{17}H_{16}S$: C, 80.90; H, 6.39; S, 12.71. Found: C, 81.14; H, 6.41.

2-Propyl-3-(2-cyanophenyl)benzo[b]thiophene 5c

This compound was obtained as colorless oil; ^{1}H nmr: δ 1.0 (3H, t, J = 7 Hz), 1.6–1.8 (2H, m), 2.80 (1H, ABXY system, J_{AB} = 14.5; J_{BX} = 8.5; J_{BY} = 7.0; J_{AX} = 8.7; J_{AY} = 6.5 Hz; inner lines separation 20 Hz), 7.2–7.9 (8H, m); ms: m/z (rel. intensity) 277 (M^+, 50), 248 ($M^+ - C_2H_5$, 100), 246 (40). *Anal.* Calcd. for $C_{18}H_{15}NS$: C,77.94; H,5.45; N, 5.05; S, 11.56. Found: C, 78.15; H, 5.46; N, 5.04.

2-Propyl-3-(3-cyanophenyl)benzo[b]thiophene 5d

This compound was obtained as colorless oil; ^{1}H nmr: δ 1.0 (3H, t, J = 7 Hz), 1.6–1.8 (2H, m), 2.8 (2H, t, J = 7 Hz), 7.2–7.9 (8H, m); ms: m/z (rel. intensity) 277 (M^+, 50), 248 ($M^+ - C_2H_5$, 100), 246 (30). *Anal.* Calcd. for $C_{18}H_{15}NS$: C,77.94; H,5.45; N, 5.05; S, 11.56. Found: C, 78.12; H, 5.46; N, 5.06.

2-Propyl-3-(2-methylphenyl)benzo[b]thiophene 5e

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7.5 Hz), 1.65 (2H, sextuplet, J = 7.5 Hz), 2.05 (3H, s), 2.67 (2H, ABX_2system, J_{AB} = 14.5 Hz, J_{AX} = 7.3; inner line separation 4.2 Hz), 7.1–7.9 (8H, m); ms: m/z (rel. intensity) 266 (M^+, 80), 237 ($M^+ - C_2H_5$, 100), 222 (50), 221 (70). *Anal.* Calcd. for $C_{18}H_{18}S$: C,81.15; H, 6.81; S, 12.04. Found: C, 81.0; H, 6.79.

2-Propyl-3-(2-methoxyphenyl)benzo[b]thiophene 5f

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.6 (2H, m), 2.72 (2H, ABX_2 system, J_{AB} = 14.5 Hz, $J_{AX} = J_{BX}$ = 7 Hz, inner line separation 2.7 Hz), 3.72 (3H, s), 6.6–7.6 (8H, m); ms: m/z (rel. intensity) 282 (M^+, 85), 253 (M^+- C_2H_5, 100), 237 (30), 221 (40). *Anal.* Calcd. for $C_{18}H_{18}OS$: C, 76.56; H, 6.42; O, 5.66; S, 11.35. Found: C, 76.78; H, 6.44.

3-Hexylbenzo[b]thiophene 5i

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.2–1.5 (6H, m), 1.7 (2H, quintuplet, J = 7 Hz); 2.8 (2H, t, J = 7 Hz), 7.1 (1H, s), 7.2–7.5 (4H, m); ms: m/z (rel. intensity) 218 (M^+, 80), 148 (M^+-C_5H_{12}, 80), 147 (M^+-C_5H_{13}, 100). *Anal.* Calcd. for $C_{14}H_{18}S$: C, 77.01; H, 8.31; S, 14.68. Found: C, 77.24; H, 8.33.

3-Octylbenzo[b]thiophene 5j

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.2–1.5 (10H, m), 1.7 (2H, quintuplet, J = 7 Hz); 2.8 (2H, t, J = 7 Hz), 7.1 (1H, s), 7.2–7.5 (4H, m); ms: m/z (rcl. intensity) 246 (M^+, 20), 148 (M^+-C_7H_{14}, 60), 147 (M^+-C_7H_{15}, 100). *Anal.* Calcd. for $C_{16}H_{22}S$: C, 77.99; H, 9.00; S, 13.01. Found: C, 78.20; H, 9.03.

3-Decylbenzo[b]thiophene 5k

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.2–1.5 (14H, m), 1.7 (2H, quintuplet, J = 7 Hz); 2.8 (2H, t, J = 7 Hz), 7.1 (1H, s), 7.2–7.5 (4H, m); ms: m/z (rcl. intensity) 274 (M^+, 20), 148 (M^+-C_9H_{18}, 80), 147 (M^+-C_9H_{19}, 100). *Anal.* Calcd. for $C_{18}H_{26}S$: C, 78.77; H, 9.55; S, 11.68. Found: C, 79.0; H, 9.58.

1-(2-Cyanophenyl)-2-(phenylthio)pent-1-ene 3c

This compound was obtained as colorless oil (1:1 E/Z mixture); ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.5–1.8 (2H, m), 2.2–2.5 (2H, m), 6.40 (0.5H, s), 6.90 (0.5H, s), 7.1–7.9 (9H, m); ms: m/z (rcl. intensity) 279 (M^+, 100), 236

(60), 140 (40), 135 (45), 116 (40), 109 (40), 87 (70), 65 (30). *Anal.* Calcd for $C_{18}H_{17}NS$: C, 77.38; H, 6.13; N, 5.01; S, 11.48. Found: C, 77.60; H, 6.15; N, 4.99.

1-(3-Cyanophenyl)-2-(phenylthio)pent-1-ene 3d

This compound was obtained as colorless oil (1:1 E/Z mixture); ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.5–1.8 (2H, m), 2.2–2.5 (2H, m), 6.30 (0.5H, s), 6.70 (0.5H, s), 7.1–7.9 (9H, m); ms: m/z (rcl. intensity) 279 (M^+, 100), 236 (60), 140 (40), 135 (45), 116 (40), 109 (40), 87 (70), 65 (30). *Anal.* Calcd. for $C_{18}H_{17}NS$: C, 77.38; H, 6.13; N, 5.01; S, 11.48. Found: C, 77.55; H, 6.15; N, 5.03.

1-(2-Methylphenyl)-2-(phenylthio)pent-1-ene 3e

This compound was obtained as colorless oil (1:1 E/Z mixture); ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.5–1.8 (2H, m), 2.3 (3H, s) superimposed to 2.2–2.5 (2H, m), 6.6 (0.5H, s), 6.8 (0.5H, s), 7.0–7.6 (9H, m); ms: m/z (rel. intensity) 268 (M^+, 100), 237 (40), 221 (35), 129 (90), 117 (70), 115 (55), 105 (30). *Anal.* Calcd. for $C_{18}H_{20}S$: C, 80.54; H, 7.51; S, 11.95. Found: C, 80.75; H, 7.53

1-(2-Methoxyphenyl)-2-(phenylthio)pent-1-ene 3f

This compound was obtained as colorless oil (1:1 E/Z mixture); ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.5–1.8 (2H, m), 2.2–2.4 (2H, m), 3.75 (1.5H, s), 3.85 (1.5H, s), 6.6–7.6 (10H, m); ms: m/z (rel. intensity) 284 (M^+, 70), 241 (40), 159 (50), 131 (75), 115 (60), 91 (100), 77 (60), 65 (40), 51 (40), 40 (45). *Anal.* Calcd. for $C_{18}H_{20}OS$: C, 76.01; H, 7.09; O, 5.62; S, 11.27. Found: C, 76.25; H, 7.11.

1-(Phenylthio)oct-1-ene 3i

This compound was obtained as colorless oil (1:1 E/Z mixture); ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.2–1.5 (8H, m), 2.2 (2H, m), 5.85 (0.5H, dt, J_d = 9.5 Hz; J_t = 7 Hz); 6.0 (0.5H, B part of an ABX system, J_{AB}= 15 Hz, J_{AX} = 6.5 Hz), 6.14 (0.5H, A part of an AB system, J_{AB} = 15 Hz), 6.2 (0.5

H, dt, J_d 9.5 Hz, J_t= 2 Hz), 7.1–7.5 (5H, m); ms: m/z (rel. intensity) 220 (M^+, 50), 149 (100), 116 (70), 110 (70), 69 (80). *Anal.* Calcd. for $C_{14}H_{20}S$: C, 76.30; H, 9.15; S, 14.55. Found: C, 76.05; H, 9.13.

(Z)- 1-(Phenylthio)dec-1-ene (Z)-3j

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.1–1.5 (12H, m), 2.2 (2H, br q, J = 7.5 Hz), 5.82 (1H, dt, J_d = 9.5 Hz; J_t = 7.5 Hz); 6.18 (1H, dt, J_d9.5 Hz, J_t = 1.5 Hz), 7.1–7.5 (5H, m); ms: m/z (rcl. intensity) 248 (M^+, 20), 149 (100), 116 (70), 110 (100), 83 (70). *Anal.* Calcd. for $C_{16}H_{24}S$: C, 77.36; H, 9.74; S, 12.91. Founds C, 77.13; H, 9.71.

(E)- 1-(Phenylthio)dec-1-ene (E)-3j

This compound was obtained as colorless oil; ^{1}H nmr: δ 0.85 (3H, t, J = 7 Hz), 1.1–1.4 (12H, m), 2.15 (2H, q, J = 7.5 Hz), 6.0 (1H, B part of an ABX system, J_{AB} = 15 Hz, J_{AX} = 7.5 Hz), 6.13 0 (1H, A part of an AB system, J_{AB} = 15 Hz), 7.1–7.5 (5H, m); ms: m/z (rel. intensity) 248 (M^+, 20), 149 (100), 116 (70), 110 (00), 83 (70). *Anal.* Calcd. for $C_{16}H_{24}S$: C, 77.36; H, 9.74; S, 12.91. Found: C, 77.52; H, 9.76

1-(Phenylthio)dodec-1-ene 3k

This compound was obtained as colorless oil (1:1 E/Z mixture); ^{1}H nmr: δ 0.9 (3H, t, J = 7 Hz), 1.2–1.6 (16H, m), 2.2 (2H, m), 5.85 (0.5 H, dt, J_d = 9.5 Hz; J_t = 7 Hz); 6.0 (0.5H, B part of an ABX system, J_{AB}= 15 Hz, J_{AX} = 6.5 Hz), 6.14 (0.5H, A part of an AB system, J_{AB} = 15 Hz), 6.2 (0.5 H, dt, J_d 9.5 Hz, J_t= 2 Hz), 7.1–7.5 (5H, m); ms: m/z (rel. intensity) 276 (M^+, 40), 149 (100), 147 (60), 116 (80), 110 (70), 97 (80), 83 (50). *Anal.* Calcd. for $C_{18}H_{28}S$: C, 78.20; H, 10.21; S, 11.60. Found: C, 78.43; H, 10.24.

Gc-ms and ^{1}H nmr analysis of the reaction mixtures obtained from alkynes **1b-f** showed, together with products **3b-f** and **5b-f**, the presence of isomeric adducts which were tentatively assigned the structure of (E)- and (Z)-**6b-f** (ca. 3:1 isomeric ratio, as evidenced by integrals of singlets at δ 3.4–3.5 in the ^{1}H nmr spectrum). The **3/5** ratio was found to be ca. 3:1.

Subsequent column chromatography of these reaction mixtures separated, together with pure samples of products **3b-f** and **5b-f**, a ca. 1:1 isomeric mixture constituted by adducts **3b-f** and the possible adducts **6b-f**, which were not fully characterized.

1-Phenyl-2-(phenylthic)pent-2-ene **6b** (E- and Z- mixture) showed peaks at δ 1.0 (3H, t, J = 7 Hz), 2.2–2.5 (2H, m), 3.4 (1.5H, br s), 3.5 (0.5H, br s), 5.87 (0.75H, t, J = 7 Hz), 5.98 (0.25H, t, J = 7 Hz) and 7.1–7.5 (10H, m) in the ^{1}H nmr spectrum and the molecular ion at m/z 254 in the gc-ms spectrum.

1-(2-Cyanophenyl)-2-(phenylthio)pent-2-ene **6c** (E- and Z- mixture) showed peaks at δ (200 MHz) 1.0 (3H, t, J = 7 Hz), 2.4 (2H, m), 3.7 (1.5H, br s), 3.8 (0.5H, br s), 6.0 (0.75H, t, J = 7 Hz), 6.1 (0.25H, t, J = 7 Hz) and 7.1–7.9 (9H, m) in the ^{1}H nmr spectrum and the molecular ion at m/z 279 in the gc-ms spectrum.

1-(3-Cyanophenyl)-2-(phenylthio)pent-2-ene **6d** (E- and Z- mixture) showed peaks at δ 1.0 (3H, t, J = 7 Hz), 2.4 (2H, m), 3.4 (1.5H, br s), 3.5 (0.5H, br s), 5.9 (0.75H, t, J = 7 Hz), 6.0 (0.25H, t, J = 7 Hz) and 7.1–7.9 (9H, m) in the ^{1}H nmr spectrum and the molecular ion at m/z 279 in the gc-ms spectrum.

1-(2-Methylphenyl)-2-(phenylthio)pent-2-ene **6e** (E- and Z- mixture) showed peaks at δ 1.0 (3H, t, J = 7 Hz), 2.3 (3H, s), superimposed to 2.2–2.5 (2H, m), 3.4 (1.5H, br s), 3.5 (0.5H, br s), 5.65 (0.75H, t, J = 7 Hz), 6.0 (0.25H, t, J = 7 Hz) and 7.1–7.6 (9H, m) in the ^{1}H nmr spectrum and the molecular ion at m/z 268 in the gc-ms spectrum.

1-(2-Methoxypheny)(phenylthio)pent-2-ene **6f** (E- and Z- mixture) showed peaks at δ 1.0 (3H, t, J = 7 Hz), 2.2–2.4 (2H, m), 3.5 (1.5H, br s), 3.55 (0.5H, br s), 3.85 (2.25H, s), 3.9 (0.75H, s), 5.8 (0.75H, t, J = 7 Hz), 6.05 (0.25H, t, J = 7 Hz) and 6.6–7.6 (9H, m) in the ^{1}H nmr spectrum and the molecular ion at m/z 284 in the gc-ms spectrum.

GENERAL PROCEDURE FOR THE REACTION OF BENZENETHIOL WITH ALKYNES 1a-c,j,k,m,o. METHOD B

A bromobenzene solution (5 ml) of AIBN (330 mg, 2 mmol) and benzenethiol (0.22 ml, 2 mmol) was rapidly added to a boiling bromobenzene solution (15 ml) of the appropriate alkyne **1a-c,j,k,m,o** (2 mmol). The

resulting mixture was refluxed for 1 h, and then worked up as described in Method A. Silica gel chromatography separated a mixture consisting of unreacted alkyne **1a-c,j,k,m,o**, adducts **3a-c,j,k,m,o** and **6b-f** and benzothiophene **5a-c,j,k,m,o**. This mixture was weighted and analyzed by gc-ms and ^{1}H nmr to determine the yield of the unreacted alkyne **1a-c,j,k,m,o** (45–55%) and the relative yields of reaction products **3a-c,j,k,m,o, 5a-c,j,k,m,o** and **6b-f** (70–80% overall yields, based on reacted alkyne; relative yields are reported in the Table). Repeated column chromatography of the mixtures obtained from alkynes **1a,m,o** allowed for the separation of pure samples of the previously reported adducts **3a**,[8a] **3m**,[18] and **3o**[20] and benzothiophene **5a**[10] and the hitherto unknown benzothiophenes **5m** and **5o**.

2-Butyl-3-(phenylthio)benzo[b]thiopene 5m

This product was obtained as colorless oil; ^{1}H nmr: δ 0.9 (2H, t, J = 7 Hz), 1.2–1.7 (4H, m), 3.10 (2H, t, J = 7 Hz), 7.0–7.5 (5H, m); ms: m/z (rel. intensity) 298 (M^+, 100), 255 (M^+-CH_3CH_2, 60), 222 (60), 221 (50), 147 (40). *Anal.* Calcd. for $C_{18}H_{18}S_2$: C, 72.43; H 6.08; S, 21.49. Found: C, 72.20; H 6.10.

2,3-Bis(methoxycarbonyl)benzo[b]thiophene 5o

This product was obtained as colorless oil; ^{1}H nmr: δ 3.9 (3H, s), 4.0 (3H, s), 7.0–8.0 (4H, m); ms: m/z (rel. intensity) 250 (M^+, 80), 219 (M^+- OCH_3, 100), 189 (50). *Anal.* Calcd. for $C_{12}H_{10}O_4S$: C, 57.59; H, 4.03; 0, 25.57; S, 12.81. Found: C, 57.75; H, 4.05.

GENERAL PROCEDURE FOR THE REACTION OF BENZENETHIOL WITH ALKYNES 1a-c,g-l,n. METHOD C

A bromobenzene solution of the appropriate alkyne **1a-c,g-l,n** (2 mmol), AIBN (330 mg, 2 mmol), and benzenethiol (0.22 ml, 2 mmol) was heated at 154 °C for 1 h in a sealed tube and then worked up as described for Method A. Reaction mixtures obtained from alkynes **1a-c,i-k** were directly analyzed by GC, GC-MS and ^{1}H NMR to determine the adduct

3/benzothiophene **5** yield ratio (see Table). Gc-ms analysis of reaction mixtures from alkynes **1g,h,l** detected the formation of adducts **3g,h,l** and possible benzothiophenes **5g** [GC-MS, m/z (rel. intensity) 176 (M^+, 20), 147 (100)], **5h** [GC-MS, m/z (rel. intensity) 190 (M^+, 15), 147 (100] and **5l** [GC-MS, m/z (rel. intensity) 218 (M^+, 50), 189 (100)] (**3/5** ratio = ca. 99:1). Column chromatography of the above reaction mixtures led to the separation of the previously reported adducts **3g**,[8b] **3h**,[8a] and **3l**[8a] in 55, 50 and 60% yield, respectively (yields based on starting alkyne). The reaction mixture obtained from alkyne **1n** was chromatographed on silica gel column to give the previously reported adduct **3n**[19] (25%) and benzothiophene **5n**[10] (25%) (yields based on starting alkyne **1n**).

GENERAL PROCEDURE FOR THE REACTION OF BENZENETHIOL WITH ALKYNES 1a,b. METHOD D

A bromobenzene solution of the appropriate alkyne **1a,b** (2 mmol) and benzenethiol (0.22 ml, 2 mmol) was heated at 154 °C for 1 h in a sealed tube and then directly analyzed. Gc-ms and ^1H nmr showed the formation of products **3a** and **5a** in 99:1 ratio and in 70% overall yield (based on starting alkyne) and products **3b** and **5h** in 88:12 ratio and in 40% overall yield (based on starting alkyne), respectively.

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