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Thiol Radical Addition to Alkynes. Sulfanyl Radical Addition and Hydrogen Atom Abstraction Relative Reaction Rates.

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Abstract. 2-(Toluenesulfanyl)- **1** and 2-(benzenesulfanyl)-phenylacetylene **10** reacted with benzenethiol and toluenethiol, respectively, in the presence of AIBN at 84 and 154 °C to give products deriving from vinyl radicals **2** which undergo hydrogen abstraction reaction and 5-*ortho* and 5-*exo* cyclization onto both the adjacent phenyl rings in competition with the β-fragmentation. Definitive evidence has been obtained that alkanesulfanyl radical addition to the alkyne triple bond is a non-reversible process, whereas arenesulfanyl radicals add in a reversible mode. Competing experiments involving several alkynes towards benzenethiol and benzeneethanethiol radical addition have been performed in order to determine the relative rate constants of the sulfanyl radical addition to the alkyne triple bond (k_I) and the hydrogen abstraction reaction by the resulting vinyl radicals (k_H). The k_I values are mainly determined by the vinyl radical stabilization provided by the C-(α) vinyl radical substituent, whereas the k_H values seem to be mainly determined by polarity factors. An unexpected different behavior between α-propyl and α-long-chain substituents is discussed in terms of different hybridization of the vinyl radical.

Keywords: β-fragmentation; vinyl radical; sulfanyl radical addition; hydrogen abstraction.

Sulfanyl radicals add to alkynes leading to the corresponding β-sulfanylvinyl radicals,[1,2] which can undergo cyclization onto aromatic[3] and heteroaromatic[4] rings, alkene double bonds[5] and heteroatom-containing multiple bonds,[6,7] in competition with the hydrogen abstraction reaction (HA-reaction) leading to thiol/alkyne adducts. Although the formation of thiol/alkyne adducts is well documented,[2,8] little is known about some relevant mechanistic aspects of this two-step reaction. In particular, the factors governing both the sulfanyl radical addition to the alkyne triple bond and the subsequent HA-reaction by resulting β-sulfanylvinyl radicals are still unexplored. Moreover, little is known about the importance of the reversibility of the sulfanyl radical addition. We have previously suggested[5,7] that arenesulfanyl radical addition occurs in a reversible manner, whereas the alkanesulfanyl radical addition should be a non-reversible process, due to the greater strength of the vinylic carbon-sulfur bond.[9] However, our suggestion was rather speculative, because no quantitative data were available in the literature about the importance of the vinylic carbon-sulfur bond scission in β-sulfanylvinyl radical chemistry.[10]

RESULTS AND DISCUSSION

In order to obtain evidence about the reversibility of the sulfanyl radical addition to the alkyne triple bond we investigated the fate of β-(benzenesulfanyl)-β-(toluenesulfanyl)vinyl radicals **2** which were generated from both benzenesulfanyl radical addition to (toluenesulfanyl)phenylacetylene **1** (Method A) and toluenesulfanyl radical addition to (benzenesulfanyl)phenylacetylene **10** (Method B). Sulfanyl radicals were generated at two different temperatures (84 °C and 154 °C) with the thiol/AIBN method (see Experimental Section)

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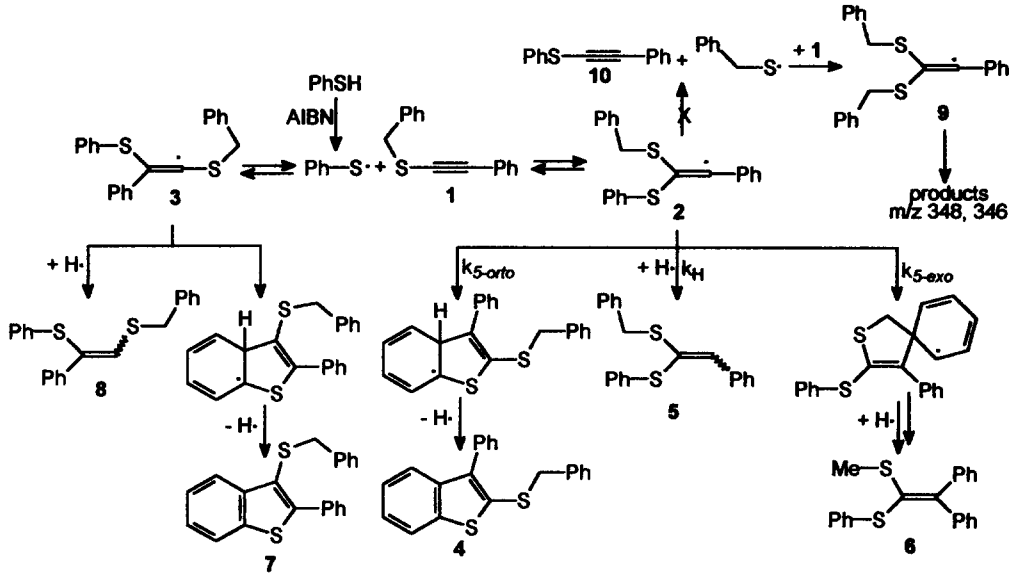
Radicals **2** were expected to undergo several kinds of reactions: 1) the hydrogen abstraction reaction, leading to the adduct **5**; 2) both 5-(π-*endo*)*ortho* and 5-(π-*exo*)*exo* cyclizations, leading to the benzothiophene derivative **4** and the 1,4-phenyl migration product **6**,[5] respectively; 3) β-fragmentation of the vinylic carbon-sulfur bond leading to either toluenesulfanyl or benzenesulfanyl radicals. We reasoned that the formation of toluenesulfanyl radicals could be detected under the Method A conditions through trapping by alkyne **1** (Scheme 1), whereas the formation of benzenesulfanyl radicals could be detected under the Method B conditions through trapping by the alkyne **10** (Scheme 2). So, in the first case we looked for possible products deriving from the vinyl radical **9**, and in the second case for products deriving from vinyl radicals **14** and/or **15**.

Scheme 1



The reaction of benzenethiol with alkyne **1** (Method A) gave, at both temperatures, a mixture constituted by isomeric benzothiophenes **4** and **7**, the methyl sulfide **6**, and isomeric thiol/alkyne adducts **5** and **8** (Scheme 1 and Table 1) in addition to diphenyl disulfide and some phenyl benzyl sulfide [$PhCH_2SPh$]. The source of this latter product is unclear. Products **4**-**6** were those expected from the vinyl radical **2**, whereas products **4** and **7** were derived from the radical **3**, in turn generated by non-regioselective sulfanyl radical addition to both alkynic carbons of **1** (Scheme 1). Supporting evidence for the intermediacy of the radical **3** in the formation of products **7** and **8** arose from reaction of toluenethiol with a ten-fold excess of the alkyne **10** (Method B; see later). Under these conditions radical **3** could not be formed and, as a consequence, products **7** and **8** were not found in the reaction mixture.

GC-MS analysis of the reaction mixture carried out at 154 °C showed trace amounts (< 0.5% relative yield) of a compound at m/z 348 (M^+), which was probably derived from toluenesulfanyl radical addition to alkyne **1** through the intermediacy of the radical **9** (Scheme 1). Toluenesulfanyl radicals were expected from **2** by β-scission of the $PhCH_2S$-vinyl carbon bond. No traces of this product could be observed in the reaction carried out at 84 °C. These findings indicate that the β-fragmentation reaction, with displacement of toluenesulfanyl radicals, cannot compete with the hydrogen abstraction reaction and both the 5-*exo* and the 5-*ortho* cyclizations onto the phenyl ring, at least up to 150 °C. On this basis we can state that alkanesulfanyl radical addition to the alkyne triple bond is an irreversible process up to 150 °C. From the relative yield of products **4** and **6** (Table 1) we can estimate the 5-(π-*endo*)*ortho* cyclization relative rate constant with respect to the 5-(π-*endo*)*exo* cyclization [$k_{5\text{-}ortho}/k_{5\text{-}exo}$ = 0.09 at 84 °C and 0.38 at 154 °C).

Scheme 2

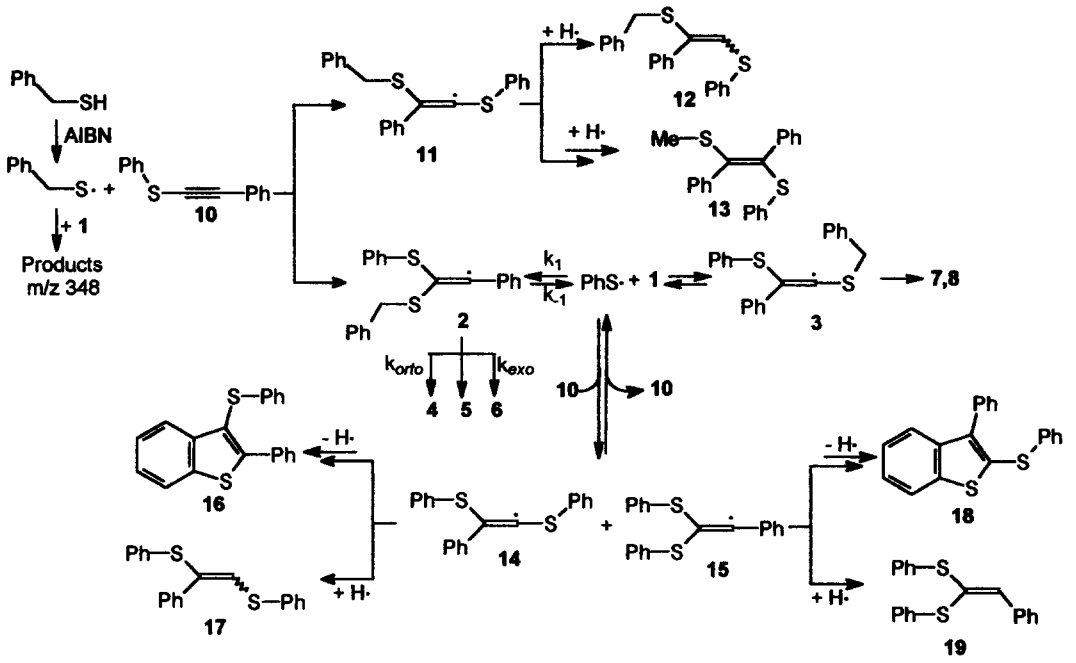


Table 1

Relative yields, %, of reaction products **4-8, 12, 13, 16-19** obtained from the reaction of benzenethiol with alkyne **1** (1.5 equiv.) and from the reaction of toluenethiol with alkyne **10** (1.5 equiv.). In square brackets the relative yields obtained by using a ten-fold excess of alkyne **10**.

		Reaction products relative yields, %								
Alkyne	Conditions	**4**	**5**	**6**	**7**	**8**	**12**	**13**	**16 + 18**	**17 + 19**
1	PhSH, 84 °C	1.7	40	19	3.3	35				
1	PhSH, 154 °C	7	36	18	8	32				
10	$PhCH_2SH$, 84 °C	1 [1]	16 [3]	5 [2]	1	6	10 [16]	4 [4]	21[a] [53][b]	38[a] [21][a]
10	$PhCH_2SH$, 154 °C	[<0.5]	[2]	[<0.5]			[5]	[<0.5]	[82][b]	[10][c]

a) 4:1 isomeric mixture; b) 10:1 isomeric mixture; c) 2:1 isomeric mixture.

The reaction of toluenethiol with 1.5 molar equivalents of alkyne **10** (Method B), carried out at 84 °C, led to a complex reaction mixture. In addition to products **4-6**, expected from radical **2**, and products **12,13**, expected from the regioisomeric radical **11** through 5-(*π-exo*)*exo* cyclization and hydrogen abstraction, respectively, column chromatography furnished alkyne **1**, adduct **8**, an inseparable mixture of benzothiophenes **16** and **18** and an inseparable mixture of (benzenethiol/alkyne **10**) adducts **17** and **19** (Scheme 2 and Table 1). Regioisomeric benzothiophenes **16,18** and adducts **17,19** were identified by GC-MS analysis. Structural assignment was not possible owing to difficulties in their chromatographic separation. These products were expected from radicals **14,15**, in turn generated by non-regioselective benzenesulfanyl radical addition to the alkyne **10** triple bond, through 5-(*π-endo*)*ortho* cyclization and hydrogen abstraction, respectively (Scheme 2). Compelling evidence for products **16-19** was obtained from an independent experiment. Radicals **14,15**, when generated by reacting at 84 °C for 2h a fluorobenzene solution of benzenethiol, alkyne **10** (1.5 molar equivalents) and AIBN (0.2 molar equivalents), gave compounds **16-19** as the only products in the same ratio as obtained from toluenethiol and alkyne **10**. In addition to the above

products, the reaction of toluenethiol with alkyne **10** gave small amounts of benzothiophene **7** and isomeric products at m/z 348, as detected by GC and GC-MS analysis.

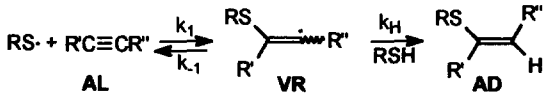
The formation of products **7,8,16-19** showed that the radical **2**, in competition with the formation of products **4-6**, can undergo C-S bond scission with formation of the alkyne **1** by displacement of benzenesulfanyl radicals. These latter can be trapped by alkyne **1** to give products **4-6** and **7,8** through the intermediacy of vinyl radicals **2** and **3**, respectively, whereas trapping by alkyne **10** can give radicals **14,15**, from which products **16-19** arise. Finally, trapping of toluenesulfanyl radical by the alkyne **1** eventually gives products at m/z 348 (Scheme 2). In the light of these results we can state that, different from the alkanesulfanyl radical addition, the arenesulfanyl radical addition to the alkyne triple bond is a reversible process.

In order to minimize the formation of cross-over products arising from sulfanyl radical trapping by the alkyne **1**, the reaction was repeated at 84 °C and 154 °C by using a ten-fold excess of alkyne **10**. GC and GC-MS analysis of the reaction mixtures showed the formation of products **4-6,12,13,16-19** and the absence of products at m/z 348 and products **7,8** (Table 1, numbers in square brackets). So, we can infer that, under these conditions, both toluenesulfanyl radicals and benzenesulfanyl radicals were quantitatively captured by the alkyne **10**. This result allowed us to calculate the relative rate constant of the β-scission reaction (k_{-1}) with respect to the 5-*exo* cyclization onto the phenyl ring through the ratio between products (**16** + **17** + **18** + **19**) and the 1,4-phenyl migration product **6** [$k_{-1}/k_{5\text{-}exo} \geq 200$ (154°C) and $k_{-1}/k_{5\text{-}exo} \cong 30$ (84°C)].

A further goal of our mechanistic investigation was to study the factors governing the sulfanyl radical addition to the alkyne triple bond and the subsequent HA-reaction by the resulting β-sulfanylvinyl radicals. For this purpose we have studied the substituent effect on the corresponding relative rate constants, k_1 and k_H. The k_1 and k_H values were calculated through competitive experiments involving the thiol radical addition to several alkynes.

The general reaction pathway for the thiol radical addition to the alkyne triple bond is depicted in Scheme 3. Sulfanyl radicals, produced at 85 °C with the thiol/AIBN method, add to the alkyne (**AL**) leading to the corresponding vinyl radical (**VR**), from which the thiol/alkyne adduct (**AD**) is formed by HA-reaction.

Scheme 3



For two competing alkynes $\mathbf{AL}_A$ and $\mathbf{AL}_B$ the kinetic equations are:

$$\frac{\delta[AD]_A}{\delta t} = k_{H(A)} \cdot [VR]_A \cdot [RSH] \qquad \frac{\delta[AD]_B}{\delta t} = k_{H(B)} \cdot [VR]_B \cdot [RSH] \qquad (1)$$

In the steady-state assumption equations (1) become:

$$\frac{\delta[AD]_A}{\delta t} = \frac{k_{H(A)} \cdot k_{1(A)} \cdot [AL]_A \cdot [RS\cdot]}{k_{-1(A)} + k_{H(A)} \cdot [RSH]} \qquad \frac{\delta[AD]_B}{\delta t} = \frac{k_{H(B)} \cdot k_{1(B)} \cdot [AL]_B \cdot [RS\cdot]}{k_{-1(B)} + k_{H(B)} \cdot [RSH]} \qquad (2)$$

In the light of the fact that alkanesulfanyl radicals (R = alkyl) add to the alkyne triple bond in an irreversible manner ($k_{-1} << k_H$), whereas the arenesulfanyl radical addition is a reversible process ($k_{-1} > k_H$), from equations (2) we can obtain equations (3) and (4) for the alkanethiol and the arenethiol radical addition, respectively.

$$\frac{[AD]_A}{[AD]_B} = \frac{k_{1(A)}}{k_{1(B)}} \frac{[AL]_A}{[AL]_B} \qquad (3) \qquad \frac{[AD]_A}{[AD]_B} = \frac{k_{1(A)}}{k_{1(B)}} \cdot \frac{k_{-1(B)}}{k_{-1(A)}} \cdot \frac{k_{H(A)}}{k_{H(B)}} \cdot \frac{[AL]_A}{[AL]_B} \qquad (4)$$

The activation energy for the β-scission reaction (ΔG^*_{-1}) depends on the following factors: 1) the vinylic carbon-sulfur bond strength, in turn depending on the nature of the R substituent (alkyl or aryl);[9] 2) the nature of R' and R" substituents, which in principle can affect the stability of the starting alkyne (**AL**), the vinyl

radical (**VR**), and the transition state as well. As the transition state for radical addition to the CC triple bond is later, and resembles the vinyl radical intermediate,[2,3] we reasoned that R' and R" substituents should stabilize (or destabilize) both the transition state and the vinyl radical in the same way. On this basis we could assume that: 1) the sulfanyl radical addition rate constant ratio, $k_{1(A)}/k_{1(B)}$, is independent of the nature of the sulfanyl substituent R; 2) the β-scission rate constant, k_{-1}, is dependent on the nature of the sulfanyl substituent R, but independent of the nature of vinyl radical substituents R' and R". From $k_{-1(A)}/k_{-1(B)} = 1$ equation (4) becomes:

$$\frac{[AD]_A}{[AD]_B} = \frac{k_{1(A)}}{k_{1(B)}} \cdot \frac{k_{H(A)}}{k_{H(B)}} \cdot \frac{[AL]_A}{[AL]_B} \qquad (5)$$

On this basis, from equation (3) we could obtain the sulfanyl radical addition relative rate constants through competing experiments involving alkanethiol radical addition (R = alkyl). The obtained $k_{1(A)}/k_{1(B)}$ values were set in equation (5), from which we could obtain the HA-relative rate constants ($k_{H(A)}/k_{H(B)}$) through competing experiments involving arenethiol radical addition (R = Ph).

Table 2

Entry	Alkyne	R'	R"	k_1	k_H
1	1-pentyne	H	propyl	1	1
2	1-octyne	H	hexyl	5.5	0.24
3	1-decyne	H	octyl	5.5	0.24
4	1-dodecyne	H	decyl	5.5	0.26
5	t-butylacetylene	H	t-butyl	0.43	1.6
6	phenylacetylene	H	phenyl	27	1.1
7	ethyl propiolate	H	CO_2Et	12[a]	< 0.001[b]
8	4-octyne	propyl	propyl	0.5	0.50
9	5-decyne	butyl	butyl	0.6	0.45

[a]Determined from competitive reaction with phenylacetylene in the presence of benzeneethanethiol through the benzene derivative **20** and **21** yield ratio (see Scheme 3). No thiol/alkyne adduct was formed in detectable yield. [b]3-(Ethoxycarbonyl)benzothiophene **22** was also formed in 2% relative yield.

Competitive experiments were carried out under *pseudo* first-order conditions by reacting at 85 °C a solution of the appropriate thiol [benzenethiol (R = Ph) or benzeneethanethiol (R = $PhCH_2CH_2$)] and AIBN (0.2 molar equiv) in an appropriate mixture of neat alkynes $\mathbf{AL}_A$ and $\mathbf{AL}_B$ (see Experimental Section). GC-MS analysis of the resulting reaction mixtures detected the formation of the corresponding thiol/alkyne adducts $\mathbf{AD}_A$ and $\mathbf{AD}_B$ as the almost exclusive reaction products, except in the case of ethyl propiolate (Table 2, entry 7). From the adduct yield ratios ($[\mathbf{AD}]_A/[\mathbf{AD}]_B$), which were determined by GC and ^{1}H NMR analysis of the reaction mixtures, we calculated the k_1 and k_H relative rate constants through equations 3 and 5 (Table 2).

With terminal alkynes, as expected,[2,8] the sulfanyl radical addition occurred exclusively at the C(1) carbon atom (Table 2, entries 1-7). Moreover, according to the general evidence that thiols add to the alkyne triple bond in a *trans* stereoselective mode,[2,8] the thiol/alkyne adduct (**AD**) was preferentially (or almost exclusively) formed as Z-isomer in all cases examined.

From the values reported in Table 2 we can see that both R' and R" alkyne substituents affect the sulfanyl radical addition relative rate constants (k_1). The expected great reactivity of phenylacetylene, as compared with n-pentyne (entries 1,6), should be due to the stabilization provided by the benzene ring to the resulting vinyl radical (**VR**, R' = H, R" = Ph) through unpaired electron delocalization.

In contrast, the greater reactivity of 1-octyne, 1-decyne and 1-dodecyne, as compared with 1-pentyne (Table 2, entries 1-4), was unexpected. Like the parent vinyl radical (**VR**, R' = R" = H), and different from α-phenyl vinyl radicals, which are sp-hybridized, linear ones, α-alkyl substituted vinyl radicals are believed to

exist in two rapidly interconverting (E) and (Z) forms[11] with a structure intermediate between a bent, sp^2-hybridized, and a linear, sp-hybridized, structure.[12] The observed effect of the size of the alkyl substituent in determining the different reactivity of alkylacetylenes would suggest that α-long-chain-alkyl-substituted vinyl radicals (R" = hexyl, octyl, decyl) are more stable than the corresponding α-propyl-substituted one, possily as a consequence of a greater sp^2 character of the unpaired electron containing orbital.

The lower reactivity of oct-4-yne and 5-decyne, as compared with 1-pentyne (Table 2, entries 1,8,9), should be a consequence of the steric hindrance determined by the n-propyl and n-butyl group, respectively, to the sulfanyl radical approach. Steric effects determined by a bulky R" substituent might also be responsible for the low reactivity exhibited by *tert*-butylacetylene (Table 2, entry 5). It is worth noting that it is generally believed[1,2] that the radical addition to terminal alkylacetylenes occurs regioselectivity to the C(1) carbon atom only due to more favorable steric factors. However, the value observed for 4-octyne showed that the n-propyl group, as compared with the hydrogen atom, exerts only a slight steric effect ($k_1 = 0.5$). So, the sulfanyl radical addition to 1-pentyne would occur at both carbon atoms [$k_1(C1)/k_1(C2) = 2$] if steric effects were the only (or the main) factor determining the regioselectivity. This finding indicates that the regioselective radical addition to terminal alkylacetylenes is mainly governed by stabilization effects provided by the α-alkyl substituent. In agreement with the above suggestion, the different stability of α-hydrogen and α-alkyl-substituted vinyl radicals could be a consequence of a different sp^2 character of the unpaired electron containing orbital.

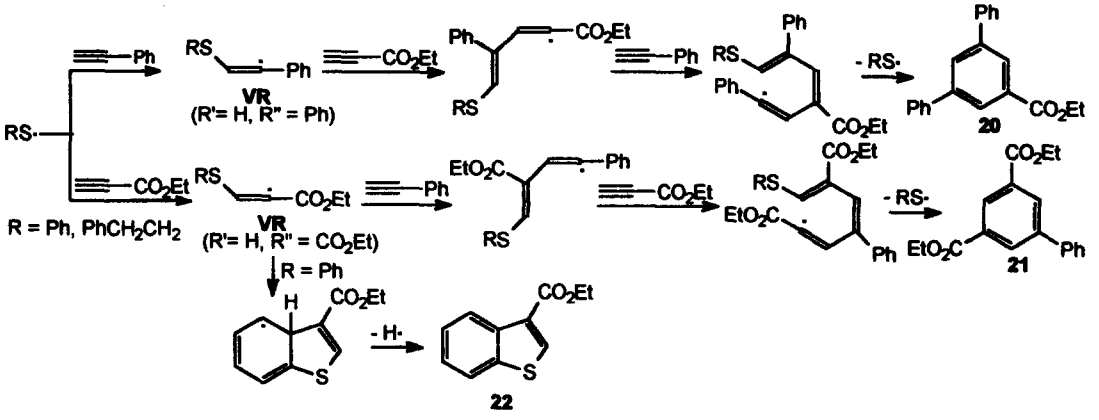
For the HA-reaction relative rate constants, we found that the replacement of a hydrogen atom with a n-propyl or a n-butyl group decreases the k_H value (Table 2, entries 1,8,9), probably as a consequence of the greater steric hindrance to the approach of the thiol hydrogen donor, which comes from the side opposite to the sulfur atom. From Table 2, entries 1-7, the α-substituent plays a notable role, which can be explained in terms of polar factors. According to the Roberts' statement,[13] we believe the hydrogen abstraction reaction is a disfavored process when both the attacking radical and the displaced radical show the same philicity.[14] Since sulfanyl radicals, which are displaced from thiol, are electrophilic in character, the HA-reaction will be preferred by decreasing the electrophilic character of the vinyl radical. On this basis, it is not surprising that α-phenyl- and α-short-chain-alkyl substituted vinyl radicals abstract the hydrogen atom faster than the α-long-chain-alkyl substituted ones because these latter are expected to be more electrophilic owing to the greater sp^2 character.

The importance of polar factors is strongly supported by the finding that the α-(ethoxycarbonyl)vinyl radical (**VR**, R' = H, R" = CO_2Et), a linear and strongly electrophilic one, abstracts the hydrogen atom at the lowest rate ($k_H < 1x10^{-3}$) (Table 2, entry 7). This alkyne showed a peculiar reactivity. A competitive experiment carried out with benzeneethanethiol (0.1 mmol) in the presence of phenylacetylene (10 mmol) and ethyl propiolate (20 mmol) under the usual reaction conditions gave a complex reaction mixture, constituted of the thiol/phenylacetylene adduct (**AD**, R = $PhCH_2CH_2$, R' = H, R" = Ph), 1,3-diphenyl-5-(ethoxycarbonyl) benzene **20** and 1-phenyl-5-di(ethoxycarbonyl)benzene **21** besides minor amounts of unidentified products. No propiolate/thiol adduct (**AD**, R = $PhCH_2CH_2$, R' = H, R" = CO_2Et) was found. The formation of products **20** and **21** can be easily explained through the addition/addition/addition/cyclization sequential process involving as key steps the addition of the poorly electrophilic α-phenyl-substituted vinyl radical to the electron-poor propiolate triple bond and the addition of the strongly electrophilic α-(ethoxycarbonyl)vinyl radical to the electron-rich phenylacetylene triple bond (Scheme 4). This is an unprecedented example of an umpolung effect in vinyl radical chemistry. This reaction was repeated under more dilute conditions in fluorobenzene solvent (see Experimental Section). Under these conditions products **1** and **2** were obtained as the almost exclusive reaction products in 52:48 relative yields; from this ratio the k_1 value for ethyl propiolate was calculated (Table 2, entry 7).

The competitive experiment carried out in the presence of benzenethiol in neat alkyne mixture gave major amounts of the phenylacetylene/thiol adduct, besides minor amounts of products **20** and **21** and unidentified products. The reaction was repeated in fluorobenzene solution to give the phenylacetylene/thiol adduct (**AD**; R = Ph, R' = H, R" = Ph) and 3-(ethoxycarbonyl)benzothiophene **22** in a 98:2 yield ratio together with only trace amounts (detected by GC-MS) of the propiolate/thiol adduct (**AD**; R = Ph, R' = H, R" =

CO_2Et). The benzothiophene derivative **22** was derived from the vinyl radical (**VR**; R = Ph, R' = H, R" = CO_2Et) through 5-(π-*endo*)*ortho* cyclization (Scheme 4).

Scheme 4



CONCLUSIONS

The β-(benzenesulfanyl)-β-(toluenesulfanyl)vinyl radical **2**, generated from both benzenesulfanyl radical addition to (toluenesulfanyl)phenylacetylene **1** and toluenesulfanyl radical addition to (benzenesulfanyl)-phenylacetylene **10**, can cyclize onto both the thiophenyl radical acceptor in a 5-(π-*endo*)*ortho* and 5-(π-*exo*)*exo* mode, leading to the benzothiophene derivative **4** and the 1,4-aryl migration product **6**, respectively ($k_{5\text{-}ortho}/k_{5\text{-}exo}$ = 0.09 at 84 °C and 0.38 at 154 °C). Our findings indicate that the addition of alkanesulfanyl radicals to the alkyne triple bond is a non-reversible process, whereas the addition of arenesulfanyl radicals is a reversible one ($k_{-1}/k_{5\text{-}exo} \geq 200$ at 154 °C and $\cong 30$ at 84 °C).

Comparison between alkanethiol and arenethiol radical addition relative rates has been proven to be a useful tool for determinig the relative rate constants of both the sulfanyl radical addition to the alkyne triple bond and subsequent hydrogen abstraction by the resulting vinyl radical. Our results indicate that sulfanyl radical addition is governed by steric effects and, mainly, by stabilization of the vinyl radical provided by the C(α)-substituent. Steric effects also affect the hydrogen abstraction reaction which is mainly governed by polar factors. In particular, α-ethoxycarbonyl-substituted vinyl radicals, electrophilic in character, showed a high reluctance of undergoing hydrogen abstraction reaction from the thiol hydrogen donor. Long side chain alkylacetylenes add sulfanyl radicals faster than 1-pentyne (k_H = 5.5). In contrast, the resulting α-long-chain-alkyl-substituted vinyl radicals abstract the hydrogen atom at a lower rate (k_H = 0.25) than the α-propyl vinyl radical. This finding suggests a greater sp^2 character, and a greater stabilization and more electrophilic character, for the former radicals.

EXPERIMENTAL SECTION

Benzenethiol, α-toluenethiol and all the alkynes employed for competitive experiments were commercially avilable. (Toluenesulfanyl)phenylacetylene **1**[15] and (benzenenesulfanyl)phenylacetylene **10**[16] were prepared in 75-80% yield by treating a THF solution of sodium phenylacetylide with dibenzyl disulfide or diphenyl disulphide, respectively. Column chromatography was performed on silica gel (0.040-0.063 particle size) by elution with light petroleum (b.p. 40-70 °C)-diethyl ether. ^1H 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.

Reaction of benzenethiol with (toluenesulfanyl)phenylacetylene 1 (Method A). A solution of benzenethiol (220 mg, 2 mmol), (toluenesulfanyl)phenylacetylene **1** (670 mg, 3 mmol), and AIBN (166 mg, 1 mmol; 66 mg, 0.4 mmol, for reactions carried out in fluorobenzene) in bromobenzene (or fluorobenzene) (20 mL) was refluxed for 30 min (2 h for reactions carried out in fluorobenzene), afterwards the solvent was evaporated off and the residue analyzed by GC-MS and GC to determine the relative yields of the reaction products (see Table 1). Column chromatography of the mixture obtained from the reaction carried out in bromobenzene separated the following compounds: 1) *2-(benzylthio)-3-phenylbenzo[b]thiophene* **4**, colourless oil (35 mg, 0.10 mmol, 5%) [^{1}H NMR δ 3.80 (2H, s), 7.2-7.6 (14H, m); MS m/z 332 (M^+, 20), 241 (40), 240 (40), 91 (100); HRMS calcd. for 332.06935; found 332.0695]; 2) mixture of (E)- and (Z)-*1-phenyl-2-(benzylthio)-2-(phenylthio)ethylene* **5**, colourless oil (185 mg, 0. 55 mmol, 27%) [^{1}H NMR δ 3.91 (0.4H, s), 4.03 (1.6H, s), 6.55 (0.2H, s), 7.0-7.6 (16 H, m); MS m/z 334 (M^+, 40), 165 (90), 134 (100), 91 (70); HRMS calcd. for $C_{21}H_{18}S_2$ 334.08500; found 334.0853]; 3) *1,2-diphenyl-2-(methylthio)-2-(phenylthio)ethylene* **6**, colourless oil (90 mg, 0.27 mmol, 13%) [^{1}H NMR δ 2.15 (3H, s), 7.0-7.6 (15H, m); MS m/z 332 (M^+, 70), 225 (50), 210 (100), 178 (60), 165 (60); HRMS calcd. for $C_{21}H_{18}S_2$ 334.08500; found 334.0855]; 4) *3-(benzylthio)-2-phenylbenzo[b]thiophene* **7**, colourless oil (40 mg, 0.12 mmol, 6%) [^{1}H NMR δ 4.00 (2H, s), 7.0-7.6 (14H, m); MS m/z 332 (M^+, 20), 241 (40), 240 (40), 91 (100); HRMS calcd. for $C_{21}H_{16}S_2$ 332.06935; found 332.0690]; 5) mixture of (E)- and (Z)-*1-phenyl-1-(phenylthio)-2-(benzylthio)ethylene* **8**, colourless oil (160 mg, 0.48 mmol, 24%) [^{1}H NMR δ 3.90 (0.4H, s), 3.98 (1.6H, s), 6.45 (0.2H, s), 6.75 (0.8H, s), 7.0-7.6 (15H, m); MS m/z 334 (M^+, 20), 134 (90), 91 (100); HRMS calcd. for $C_{21}H_{18}S_2$ 334.08500; found 334.0854].

Reaction of α-toluenethiol with (benzenesulfanyl)phenylacetylene 10 (Method B). A solution of toluenethiol (250 mg, 2 mmol), (benzenesulfanyl)phenylacetylene **10** (630 mg, 3 mmol), and AIBN (66 mg, 0.4 mmol) in fluorobenzene (20 mL) was refluxed for 2h and worked up as described for Method A. GC-MS and GC analysis of the reaction mixture detected the formation of compounds **4-8,12,13,16-19** (relative yields are reported in Table 1), alkyne **1**, diphenyl disulfide, dibenzyl disulfide, phenyl benzyl disulfide and three isomeric, unidentified products at m/z 348 (M^+). Subsequent column chromatography gave: 1) an inseparable mixture of unreacted alkyne **10** and alkyne **1**; 2) a mixture of diphenyl disulfide, dibenzyl disulfide and phenyl benzyl disulfide (120 mg; 30% overall yield); 3) trace amounts of benzothiophene **4**; 4) adduct **5** (60 mg, 0.18 mmol, 9%); 5) methyl sulfide **6** (15 mg, 0.04 mmol, 2%); 6) adduct **8** (20 mg, 0.06 mmol, 3%); 7) mixture of (E)- and (Z)-*1-phenyl-1-(benzylthio)-2-(phenylthio) ethylene* **12**, colourless oil (35 mg, 0.1 mmol, 5%) [^{1}H NMR δ 3.95 (2H, s), 6.52 (0.5H, s), 6.78 (0.5H, s), 7.0-7.6 (15 H, m); MS m/z 334 (M^+, 50), 210 (20), 165 (80), 134 (100), 91 (60); HRMS calcd. for $C_{21}H_{18}S_2$ 334.08500; found 334.0847]; 8) *1,2-diphenyl-1-(methylthio)-2-(phenylthio)ethylene* **13**, colourless oil (13 mg, 0.04 mmol, 2%) [^{1}H NMR δ 2.15 (3H, s), 7.0-7.6 (15H, m); MS m/z 334 (M^+, 50), 210 (100), 178 (40); HRMS calcd. for $C_{21}H_{18}S_2$ 334.08500; found 334.0846]; 9) an inseparable mixture of isomeric benzothiophenes **16** and **18** (90 mg, 0.28 mmol, 14%)[^{1}H NMR δ 7.0-7.6 (aromatic protons); GC-MS, m/z 318 (M^+, 100), 240 (59)]; 10) an inseparable mixture of isomeric adducts **17** and **19** (120 mg, 0.38 mmol, 19%) [^{1}H NMR δ 7.0-7.6 (aromatic protons); GC-MS m/z 320 (M^+, 40) 211 (100) 178 (50)].

The reaction was repeated by refluxing for 30 min (2 h for the reaction carried out in fluorobenzene) a bromobenzene (or fluorobenzene) solution (10 mL) of toluenethiol (60 mg, 0.5 mmol), (benzenesulfanyl)-phenylacetylene **10** (1.05 g, 5 mmol), and AIBN (83 mg, 0.5 mmol; 166 mg, 0.1 mmol, for the reaction carried out in fluorobenzene). The resulting reaction mixture was worked up as described above. GC-MS analysis showed the absence of products **7,8** and the unknown products at m/z 348. The relative yields of products **4-8,16-19** were calculated by GC analysis and are reported in Table 1 in square brackets.

Competitive Experiments. General Procedure. A solution of the appropriate thiol [benzenethiol (R=Ph) or benzeneethanethiol (R=$PhCH_2CH_2$)] (0.1 mmol) and AIBN (17 mg, 0.1 mmol) in an appropriate mixture of two alkynes was heated in a sealed tube at 85 °C for 30 min, then the excess alkyne was evaporated off and the residue analyzed by GC and ^1H NMR to determine the adduct yield ratios. The following alkyne mixtures were employed: 1-pentyne (1.97 mL; 20 mmol)/phenylacetylene (0.22 mL; 2 mmol); 1-octyne (2.95 mL; 20 mmol)/phenylacetylene (0.22 mL; 2 mmol); 1-decyne (3.6 mL; 20 mmol)/phenylacetylene (0.22 mL; 2 mmol); 1-dodecyne (4.23 mL; 20 mmol)/phenylacetylene (0.22 mL; 2 mmol); 1-pentyne (0.39 mL; 4 mmol)/5-decyne (0.72 mL; 4 mmol); 1-pentyne (0.39 mL; 4 mmol)/4-octyne (0.58 mL; 4mmol); 1-pentyne (0.39 mL; 4 mmol)/*tert*-butylacetylene (0.49 mL; 4 mmol).

The thiol/alkyne adducts were formed in each case as the almost exclusive reaction products, except the case of ethyl propiolate.. The following alkyne/thiol adducts were detected by GC-MS and ^1H NMR analysis of the vinylic proton region: **AD** (R = $PhCH_2CH_2$, R' = H, R" = Ph),[17] **AD** (R = $PhCH_2CH_2$, R' = H, R" = t-Bu),[17] **AD** (R = $PhCH_2CH_2$, R' = R" = propyl),[17] **AD** (R = $PhCH_2CH_2$, R' = H, R" = propyl) [$\delta_{(Z)\text{-isomer}}$ 5.6 (dt, J_d = 9.5 Hz, J_t = 7.1 Hz), 5.93 (dt, J_d = 9.5 Hz, J_t = 1.7 Hz); $\delta_{(E)\text{-isomer}}$ 5.73 (dt, J_d = 17.0 Hz, J_t = 7.1 Hz), 5.9 (d, J = 17.0 Hz], **AD** (R = $PhCH_2CH_2$, R' = H, R" = hexyl) [$\delta_{(Z)\text{-isomer}}$ 5.6 (dt, J_d = 9.5 Hz, J_t = 7.1 Hz), 5.92 (dt, J_d = 9.5 Hz, J_t = 1.0 Hz)], **AD** (R = $PhCH_2CH_2$, R' = H, R" = octyl) [$\delta_{(Z)\text{-isomer}}$ 5.6 (dt, J_d = 9.5 Hz, J_t = 7.0 Hz), 5.9 (dt, J_d = 9.9 Hz, J_t = 1.0 Hz)], **AD** (R = $PhCH_2CH_2$, R' = H, R" = decyl) [$\delta_{(Z)\text{-isomer}}$ 5.6 (dt, J_d = 9.5 Hz, J_t = 7.0 Hz), 5.91 (dt, J_d = 9.9 Hz, J_t = 1.2 Hz)], **AD** (R = $PhCH_2CH_2$, R' = R" = butyl) [$\delta_{(E)\text{- and }(Z)\text{-mixture}}$ 5.4 (t, J = 7 Hz), 5.65 (t, J = 7 Hz)], **AD** (R=Ph, R' = H, R" = Ph)[8a] **AD** (R=Ph, R' = H, R" = t-Bu),[8a] **AD** (R = Ph, R' = R" = propyl)[8a] **AD** (R=Ph, R' = R" = butyl),[8a] **AD** (R=Ph, R' = H, R" = propyl),[8a] **AD** (R=Ph, R' = H, R" = hexyl),[18] **AD** (R=Ph, R' = H, R" = octyl),[19] and **AD** (R=Ph, R' = H, R" = decyl).[20] Adduct (**AD**, R = $PhCH_2CH_2$, R' = H, R" = CO_2Et) was not detected. Adduct (**AD**, R = Ph, R' = H, R" = CO_2Et) was formed in trace amounts and detected only by GC-MS spectral comparison with an authentic specimen.[21]

Reaction of ethyl propiolate with benzeneethanethiol in the presence of phenylacetylene. Benzeneethanethiol (R = $PhCH_2CH_2$) (14 mg, 0.1 mmol) was reacted under conditions of General Procedure in an ethyl propiolate (390 mg, 4 mmol)/phenylacetylene (200 mg, 2 mmol) mixture. GC-MS analysis of the resulting reaction mixture showed the presence of the thiol/phenylacetylene adduct (**AD**, R = $PhCH_2CH_2$-, R' = H, R" = Ph), 1,3-diphenyl-5-(ethoxycarbonyl)benzene **20** and 1-phenyl-5-bis(ethoxycarbonyl)benzene **21** together with unidentified products. This reaction was repeated by reacting at 85°C for 2h a fluorobenzene solution (10 mL) of ethyl propiolate (1.96 g, 20 mmol), phenylacetylene (1.0 g, 10 mmol), benzeneethanethiol (138 mg, 1 mmol) and AIBN (166 mg, 1 mmol). GC-MS and ^1H NMR analysis of the reaction mixture showed the formation of the benzene derivatives **20** and **21** as the almost exclusive products in a 52:48 ratio. Subsequent column chromatography on a silica gel column allowed for the separation of *1,3-diphenyl-5-(ethoxycarbonyl)benzene* **20**, colourless oil (100 mg, 0.34 mmol, 34%) [^1H NMR δ 1.4 (3H, t, J = 7 Hz), 4.45 (2H, q, J = 7 Hz), 7.1-7.5 (10H, m), 7.95 (1H, t, J = 2 Hz), 8.23 (2H, d, J = 2 Hz); IR ν_{max}($CHCl_3$) 1710 cm^{-1}; MS, m/z 302 (M^+, 100), 257 (70), 229 (40), 228 (80), 226 (40); HRMS calcd. for $C_{21}H_{18}O_2$ 302.13068; found 302.1309] and *1-phenyl-3,5-bis(ethoxycarbonyl)benzene* **21**, colourless oil (95 mg, 0.32 mmol, 32%) [^1H NMR δ 1.4 (6H, t, J = 7 Hz), 4.45 (4H, q, J = 7 Hz), 7.1-7.5 (5H, m), 8.43 (2H, d, J = 2 Hz), 8.64 (1H, t, J = 2 Hz); IR ν_{max}($CHCl_3$) 1710 cm^{-1}; MS, m/z 298 (M^+, 80), 253 (100), 225 (40), 197 (40), 151 (70); HRMS calcd. for $C_{18}H_{18}O_4$ 298.12051; found 298.1208].

Reaction of ethyl propiolate with benzenethiol in the presence of phenylacetylene. Benzenethiol (R = Ph) (11 mg, 0.1 mmol) was reacted under conditions of General Procedure in an ethyl propiolate (390 mg, 4 mmol)/phenylacetylene (204 mg, 2 mmol) mixture. GC-MS analysis showed the formation of a complex mixture mainly constituted by the thiol/phenylacetylene adduct (**AD**, R = Ph, R' = H, R" = Ph) together with minor amounts of benzene derivatives **20** and **21** and other unidentified products. This reaction was repeated by reacting at 85°C for 2h a fluorobenzene solution (10 mL) of ethyl propiolate (1.96 g, 20 mmol), phenylacetylene (1.0 g, 10 mmol), benzenethiol (110 mg, 1 mmol) and AIBN (166 mg, 1 mmol). GC-MS and ^1H NMR analysis of the reaction mixture showed the formation of the phenylacetylene/thiol adduct (**AD**, R =

Ph, R' = H, R" = Ph) as the almost exclusive product, together with small amounts of 3-(ethoxycarbonyl)-benzothiophene **22** [(**AD**, R = Ph, R' = H, R" = Ph)/**3** = 98:2] and trace amounts of the propiolate/thiol adduct (**AD**, R = Ph, R' = H, R" = CO_2Et) [(**AD**, R = Ph, R' = H, R" = Ph)/ (**AD**, R = Ph, R' = H, R" = CO_2Et) > $1 \cdot 10^3$].

Reaction of ethyl propiolate with benzenethiol. A fluorobenzene solution (10 mL) of ethyl propiolate (0.98 g, 10 mmol), benzenethiol (110 mg, 1 mmol) and AIBN (33 mg, 0.2 mmol) was heated in a sealed tube at 85°C for 2h, then the solvent and the excess alkyne were evaporated off and the residue chromatographed on silica gel column to give the thiol/alkyne adduct (**AD**, R' = H, R" = CO_2Et) (20 mg, 10%)[21] and *3-(ethoxycarbonyl)benzo[b]thiophene* **22**, colourless oil (160 mg, 0.78 mmol, 78%) [^{1}H NMR δ 1.4 (3H, t, J = 7 Hz), 4.4 (2H, q, J = 7 Hz), 7.3-7.5 (2H, m), 7.85 (2H, d, J = 8 Hz), 8.37 (1H, s), 8.60 (1H, d, J = 8 Hz); ν_{max}($CHCl_3$) 1715 cm^{-1}; MS m/z 206 (M^+, 40), 161 (100), 89 (40); HRMS calcd. for $C_{11}H_{10}O_2S$, 206.0401; found 206.0404].

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