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Attempts at Vinyl Radical Carbonylation through Cyclization onto Carbonyl and Cyano Groups

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Abstract. Sulfanylvinyl radicals **4-6, 16**, produced from toluenesulfanyl radical addition to alkynes **1-3**, **15**, gave only products arising from cyclization onto the thiophenyl ring and H-abstraction. No products were obtained deriving from possible 5-membered cyclization onto the esteric or thioesteric carbonyl group. Similar results were obtained from toluenesulfanyl radical addition to alkynyl nitriles **20** and **24**, which did not provided any evidence for 5- or 6-membered vinyl radical cyclization onto the aliphatic cyano group. In contrast, both toluenesulfanyl- and benzenesulfanyl- vinyl radicals **32** and **37a** smoothly cyclize onto the aromatic cyano group leading to ketones **35** and **39**. This protocol represents a novel indirect radical carbonylation and provides a useful synthetic approach to indenones.

Recent developments in organic synthesis have led to the insertion of radical steps in planning of synthetic strategies. Carbon-carbon[1] (alkenes, alkynes, aromatic rings), carbon-nitrogen[2] (imines, hydrazones, nitriles) and nitrogen-nitrogen[3] (azides) multiple bonds have been used as radical acceptors. At present, an important goal of organic chemists is to achieve the direct or indirect radical carbonylation[4] by intramolecular addition of carbon-centred radicals to a carbonyl function or to its synthetic equivalents, such as hydrazones[2b,d,f] and nitriles.[2c,d] Alkyl radical cyclization onto the carbonyl group of aldehydes[5] and esters[6] has been reported. However, synthetically reliable results have been obtained only with thio- and seleno esters[7] and acyl germanes.[8] The problem for a direct carbonylation seems to be the reversibility of the alkyl radical addition step and then the presence of a good leaving group (as a sulfanyl, selenyl or germyl radical) is believed to be essential. On the contrary, no data seem to be available concerning the addition of vinyl radicals to carbonyl groups. Moreover, although vinyl radical addition to nitriles has been recently reported,[9] no synthetic approach has been attempted. This in spite of the fact that nitriles might be good synthetic equivalents for ketones owing to their easy availability and easy hydrolysis of intermediate imines.

We report here results obtained from our attempts to achieve direct and indirect vinyl radical carbonylation through cyclization onto carbonyl and cyano groups. Vinyl radicals were generated through a well-established protocol[10] by toluenesulfanyl radical addition to suitable alkynes having a carbonyl or a cyano group in the side chain. Toluenesulfanyl-promoted vinyl radicals having a radical acceptor R in the side chain can in principle undergo cyclization onto the R function and 5-(π-endo)exo cyclization onto the arenesulfanyl group eventually leading to the 1,4-aryl migration product (Scheme 1).[10] This latter reaction has been used in several instances as relative clock to study the vinyl radical cyclization onto a number of radical acceptors, including CC double bonds and aromatic rings. In competition with the above reactions, H-abstraction and 6-ortho cyclization generally occur leading to thiol/alkyne adducts and benzothiopyrans, respectively (Scheme 1).

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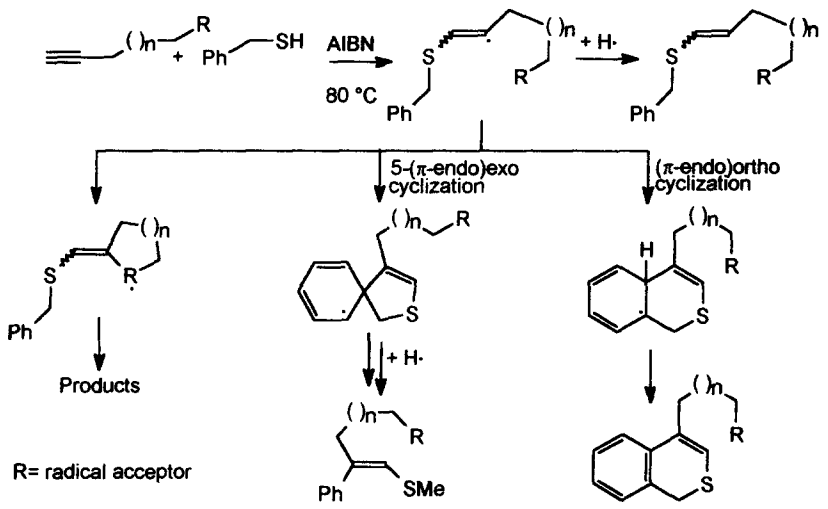
Scheme 1



RESULTS AND DISCUSSION

Reactions were carried out by reacting equimolar amounts of the appropriate alkyne and toluenethiol in boiling fluorobenzene[11] in the presence of AIBN. The reaction mixtures were analysed by ^{1}H NMR and GC-MS and then chromatographed on silica gel. Yields of reaction products, reported in Schemes 2 and 3, are based on reacted alkyne, which was generally recovered in ca. 35-40%. Structural assignment to reaction products arose from ^{1}H (and ^{13}C, when appropriate) NMR, MS and HRMS analysis.

Vinyl radicals **4** and **16**, obtained from butynyl trimethylacetate **1** and phenylpropynyl trimethylacetate **15**, seemingly underwent no π-endo nor π-exo 5-membered cyclization onto the esteric carbonyl group, although the possible oxy radical intermediates might evolve by loss of a fairly stable *tert*-butyl radical. The 1,4-phenyl migration products **10** and **18**, benzothiopyrans **13** and **19**, and the H-abstraction products **7** and **17** were exclusively formed. (Scheme 2).

Analogously, vinyl radical **5** and **6**, obtained from butynyl thioacetate **2** and thiobenzoate **3**, only gave the 1,4-migration products **11** and **12** and the adducts **8** and **9**, besides minor amounts of the thiopyran **14**. No products which might have derived from π-exo cyclization onto the thioester carbonyl group and subsequent facile β-scission of the possible oxy radical intermediates through C-S bond fragmentation were obtained. (Scheme 2)

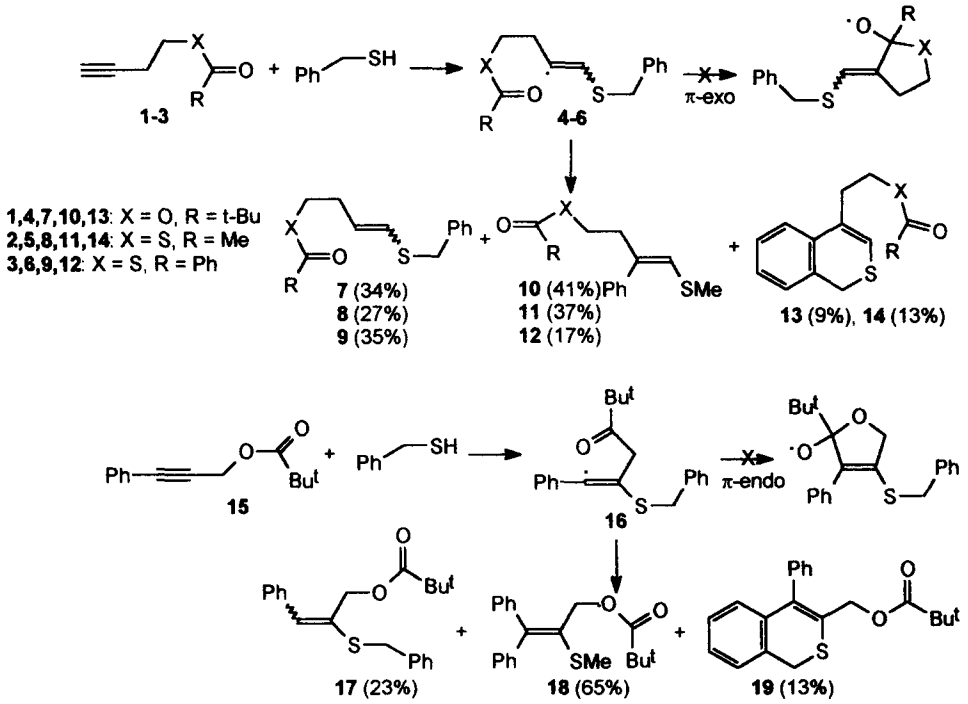
It can be therefore inferred that the failure of sulfanylvinyl radicals **4-6**, **16** to undergo direct carbonylation was presumably due to limiting kinetic rather than thermodynamic factors. Namely, the lack of sulfanyl vinyl radical addition to the carbonyl group rather than the reversibility of the addition process itself was the determining reason for unsuccessful carbonylation.

Attempts to achieve indirect carbonylation by vinyl radical addition to the cyano group led to contradictory results. Reaction of toluenethiol with cyanopentyne **20** and cyanomethyl propynyl ether **24** furnished the expected H-abstraction products **21** and **25**, the 1,4-aryl migration products **22** and **26** and the thiopyrans **23** and **27**, whereas no products ascribable to 5- (or 6-) membered cyclization onto the aliphatic cyano group were obtained (Scheme 3). In contrast, reaction of toluenethiol with 2-cyanodiphenylacetylene **28a** gave, after silica gel chromatography, the ketone **35** in significantly good yields besides minor amounts of a mixture of polar, unidentified compounds. Ketone **35** was likely formed by hydrolysis of the imine **34**

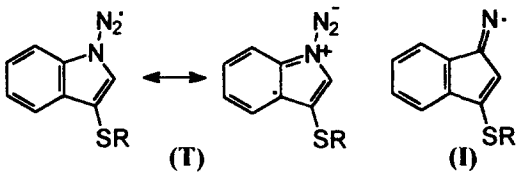
upon chromatographic conditions. The imine **34** was in turn derived from vinyl radical **32**, which exclusively underwent cyclization onto the aromatic cyano group to give the iminyl radical **33** (Scheme 3). No products deriving from the regioisomeric vinyl radical **29a** could be found. This finding was somewhat surprising because alkanesulfanyl radical addition to the CC triple bond of diarylacetylenes is expected to be non-regioselective and, as we have previously shown,[10c] non-reversible.

More satisfactory results were obtained from the reaction of the acetylene **28a** with benzenethiol (PhSH) which gave the imine **38**, and then the ketone **39**, in synthetically useful yield (65%) as the exclusive product deriving from radical **37a** (Scheme 4). Similarly to the above reaction, no product was obtained from the regioisomeric vinyl radical **36a**, but in this case this finding can be likely ascribable to the fact that benzenesulfanyl radicals add to alkyne triple bonds in a reversible manner.[10c]

Scheme 2



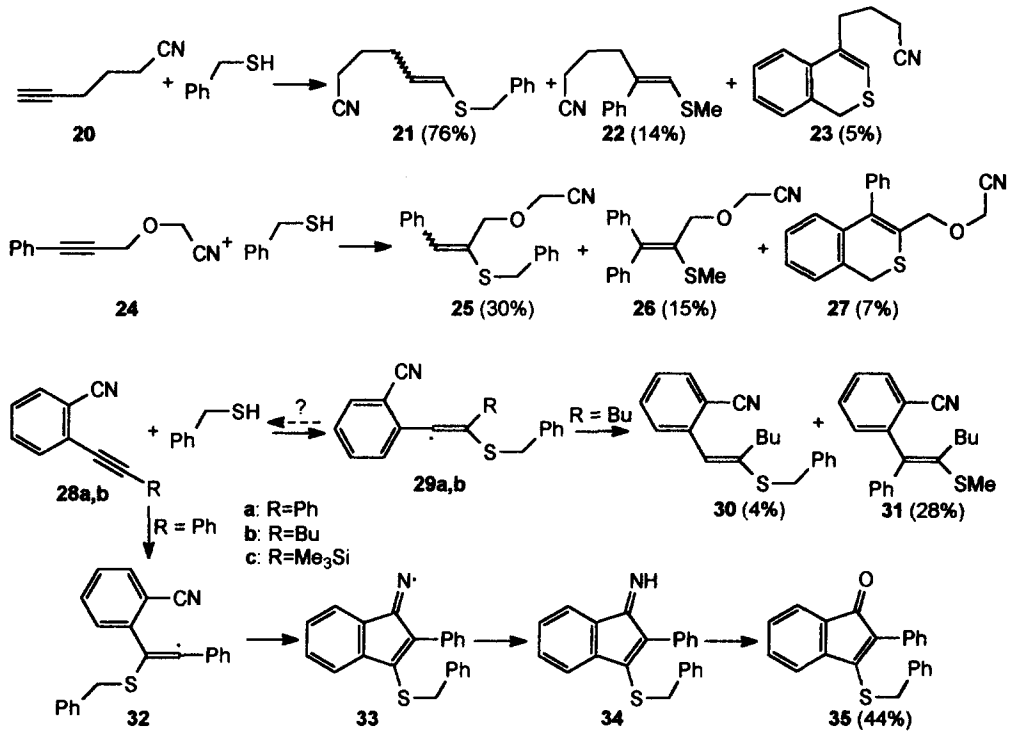
The different reactivity of the aromatic nitrile **28a** and the aliphatic ones **20** and **24** towards vinyl radical attack parallels our previous evidence obtained from a related study of vinyl radical cyclizations onto the azido group. We have recently reported[3a] that sulfanylvinyl radicals, produced under comparable conditions, undergo smooth 5-cyclization onto aromatic azides, but appear to be unreactive towards the aliphatic ones.



We claimed that resonance stabilisation of the cyclized triazenyl radical of type (**T**) by unpaired electron delocalization onto the indole ring should provide the driving force for the observed cyclization onto aromatic azides. However, it seems that a similar resonance stabilisation can be hardly provided for the corresponding iminyl radical intermediate of type (**I**).[12] So, at present we have no definite explanation to justify the observed high different reactivity of aliphatic and aromatic nitriles (and azides). It could be an attractive suggestion to infer that vinyl radical additions to electron poor nitriles (and azides as well) are SOMO/LUMO controlled, so the conjugated aryl ring, by lowering the LUMO orbital energy, would ease the interaction with the SOMO orbital of the weakly electrophilic[10d] vinyl radical.

Our findings indicate that the aromatic cyano group can effectively act as a radical synthetic equivalent of the carbonyl group. Our protocol would represent a useful synthetic approach to indenones starting from 2-cyanodiarylacetylenes. However, with (2-cyanophenyl)alkylacetylenes this protocol was predicted to be of no utility owing to the unfavourable sulfanyl radical addition regiochemistry, which is governed by the stability of the ensuing 1-phenylvinyl radical.[10] In agreement, the reaction of 1-(2-cyanophenyl)hexyne **28b** with toluenethiol gave only products **30** and **31** arising from radical **29b**, which was formed by regioselective sulfanyl radical addition to the alkyl-substituted acetylene carbon (Scheme 3).

Scheme 3

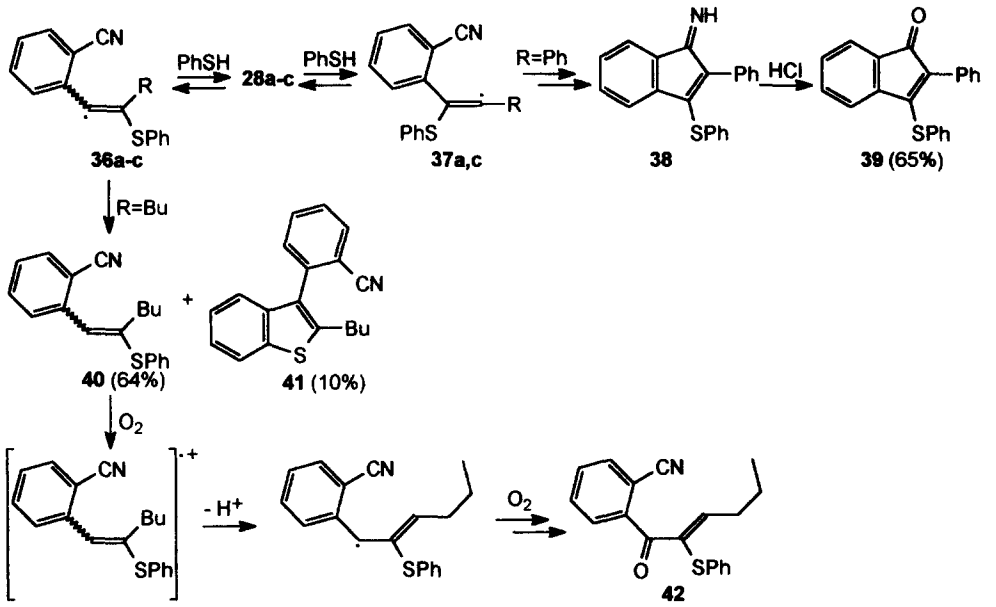


Analogous results were obtained from the reaction of **28b** with benzenethiol, which led to chromatographic separation of the adduct **40** and benzothiophene **41**. This latter compound was derived from intermediate radical **36b** by 5-ortho cyclization onto the adjacent thiophenyl ring. Benzothiophene **41** presents a C1 molecular symmetry, as evidenced by the presence of diasteromeric methylenic protons in the ^{1}H NMR spectrum.[13] In addition to the adduct **40** and benzothiophene **41** chromatography also isolated the ketosulfide **42** (10%). This product was not originally present in the crude reaction mixture; it might be formed upon column chromatography possibly through a dioxygen-promoted oxidation.[14] The easy air oxidation of related vinyl sulfides has already been reported,[15] but formation of ketosulfide products involving no migration of the

sulfanyl group and instead migration of the alkene double bond is unprecedented. A possible mechanism for the formation of **42** is depicted in Scheme 4.

In view of the fact that a trimethylsilyl group, like an aryl group, can provide effective resonance stabilisation to vinyl radicals,[16] we attempted to extend the scope of the above vinyl radical carbonylation by using 2-cyanophenyl(trimethylsilyl)acetylene **28c** as the alkyne precursor (Scheme 4). However, the reaction of benzenethiol with the alkyne **28c** provided no evidence at all for any vinyl radical product. Probably, with alkyne **28c** steric hindrance strongly discouraged the reversible addition of benzenesulfanyl radicals to either alkyne carbon atom.[17] Similarly to benzenethiol, toluenethiol hardly reacted with the alkyne **28c** to give very small amounts of possible sulfanyl adducts, which however were only detected by GC-MS analysis.

Scheme 4



CONCLUSIONS

Results obtained from our sulfanyl radical-promoted vinyl radicals indicate that the aromatic cyano group can behave as an effective synthetic equivalent of the keto function in intramolecular radical cyclizations, as evidenced by the reaction of 2-cyanodiphenylacetylene **28a** with both toluene- and benzenethiols. In fact, intermediate vinyl radicals **32** and **37a** smoothly cyclized onto the cyano group leading to indenone derivatives **35** and **39** by subsequent hydrolysis of imino products **34** and **38** under chromatographic conditions. In contrast, vinyl radicals produced from aliphatic nitriles **20** and **24** exclusively underwent H-abstraction and cyclization onto the thiophenyl ring. These findings provided evidence of a highly different reactivity of aliphatic and aromatic nitriles, possibly as a consequence of the different easy of the frontier molecular orbital approach between the electron poor cyano group and the weakly electrophilic vinyl radical. Finally, attempts to achieve direct vinyl radical carbonylation through intramolecular addition to esteric and thioesteric carbonyl groups failed: upon our conditions radicals **4-6, 16** underwent preferential cyclization onto the thiophenyl ring and H-abstraction.

EXPERIMENTAL SECTION

Starting Materials. Benzenethiol, toluenethiol and cyanopentyne **20** are commercially available.

But-1-yn-4-yl trimethylacetate **1** [oil; ^{1}H NMR δ 1.20 (9H, s), 1.95 (1H, t, J = 2.5 Hz), 2.5 (2H, dt, Jd = 2.5 Hz, Jt = 7 Hz), 4.15 (2H, t, J = 7 Hz); MS m/z 154 (M^+, 10), 115 (10), 85 (90), 57 (100). Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15; O, 20.75. Found: C, 70.4; H, 9.1%] and *1-phenylpropyn-3-yl trimethylacetate* **15** [oil; ^{1}H NMR δ 1.20 (9H, s), 4.85 (2H, s), 7.2-7.4 (5H, m); MS m/z 216 (M^+, 10), 160 (100), 131 (60), 115 (80), 114 (85), 57 (100). Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46; O, 14.79. Found: C, 78.0; H, 7.5%] were obtained as oily products in nearly quantitative yields by reacting for 1 h at room temperature under nitrogen a THF solution (100 mL) of equimolar amounts (20 mmoles) of trimethylacetyl chloride and the appropriate sodium alcoholate, in turn obtained from buthynol or phenylpropynol, respectively, and sodium hydride in anhydrous THF.

But-1-yn-4-yl thioacetate **2** [oil; ^{1}H NMR δ 2.02 (1H, t, 2.5 Hz), 2.35 (3H, s), 2.48 (2H, dt, Jd = 2.5 Hz, Jt = 7 Hz), 3.04 (2H, t, J = 7 Hz); MS m/z 128 (M^+, 10), 127 (90), 113 (90), 86 (60), 85 (60), 43 (100). Anal. Calcd. for C_6H_8OS: C, 56.22; H, 6.29; O, 12.48; S, 25.01. Found: C, 56.38; H, 6.32; S, 24.87%] and *but-1-yn-4-yl thiobenzoate* **3** [oil; ^{1}H NMR δ 2.05 (1H, t, J = 2.6 Hz), 2.58 (2H, dt, J_d = 2.6 Hz, J_t = 6.7 Hz), 3.36 (2H, t, J = 6.7 Hz), 7.1- 8 (5H, m); MS m/z 190 (M^+, 15), 189 (60), 105 (100), 77 (100), 51 (85). Anal. Calcd. for $C_{11}H_{10}OS$: C, 69.44; H, 5.30; O, 8.41; S, 16.85. Found: C, 69.70; H, 5.33; S, 16.77%] were obtained in ca. 90-95% yield by stirring at room temperature for 3 h an acetone solution (100 mL) of equimolar amounts of butynyl tosylate and thioacetic or thiobenzoic acid, respectively, in the presence of anhydrous sodium carbonate. Butynyl tosylate was prepared as described in the literature[18] and used without further purification.

Cyanomethyl 1-phenylpropyn-3-yl ether **24** [oil; MS m/z 171 (M^+, 20), 170 (10), 115 (100), 103 (50); IR ν_{MAX} 2215 cm^{-1}. Anal. Calcd. for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18; O, 9.35. Found: C, 77.40; H, 5.32%] was obtained as an oil in 54% yield by heating at 80 °C for 6 h a THF solution of sodium 1-phenylpropynoate (20 mmol) and bromoacetonitrile (40 mmol). The title product was separated by silica gel column chromatography.

2-Cyanodiphenylacetylene **28a** [oil; MS m/z 203 (M^+, 100), 176 (15); IR ν_{Max} 2220 cm^{-1}. Anal. Calcd. for $C_{15}H_9N$: C, 88.65; H, 4.46; N, 6.89. Found: C, 88.90; H, 4.48%], *1-(2-cyanophenyl)hex-1-yne* **28b** [^{1}H NMR δ: 0.9 (3H, t, J = 7.5 Hz), 1.4-1.7 (4H, m), 2.5 (2H, t, J = 7.5 Hz), 7.2-7.7 (4H, m); MS m/z 183 (M^+, 40), 182 (60), 168 (100), 141 (60), 140 (100), 127 (40), 113 (40); IR ν_{Max} 2220 cm^{-1}. Anal. Calcd. for $C_{12}H_{13}N$: C, 85.21; H, 7.15; N, 7.64. Found: C, 85.47; H, 7.11%] and *1-(2-cyanophenyl)-2-(trimethylsilyl) acetylene* **28c** [^{1}H NMR δ: 0.3 (9H, s), 7.3-7.7 (4H, m); MS m/z 199 (M^+, 10), 184 (100), 154 (10); IR ν_{Max} 2220 cm^{-1}. Anal. Calcd. for $C_{12}H_{13}NSi$: C, 72.31; H, 6.57; N, 7.03; Si, 14.09. Found: C, 72.10; H, 6.60%] were obtained by the procedure reported in the literature[19] for the preparation of disubstituted alkynes from halobenzenes and terminal acetylenes. According to this procedure, a solution of 2-bromobenzonitrile (20 mmol) and tetrakis(triphenylphosphine)palladium[20] $Pd(PPh_3)_4$ (1 mmol, 1.16 gr) in piperidine (30 mL) was stirred at room temperature under nitrogen atmosphere for 15 min, then a solution of the appropriate terminal acetylene (phenylacetylene, trimethylsilylacetylene, or hex-1-yne) (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 off and the crude product chromatographed on silica gel column to give **28a,c** in ca. 85% yield, and **28b** in 58% yield.

Reaction Products. Structural assignments to reaction products generally arose by ^{1}H NMR, IR, and MS spectral data in addition to elemental analysis or HRMS. 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 generally recorded at 200 MHz (unless otherwise stated) in $CDCl_3$ solutions using Me_4Si as internal standard. Mass spectra were determined by the electron impact method. Yields of reaction products are based on reacted starting alkyne, unless otherwise stated.

Reactions with α-Toluenethiol. General Procedure. A solution of the appropriate alkyne (4 mmol), α-toluenethiol (0.44 mL, 4 mmol) and AIBN (130 mg, 0.8 mmol) in fluorobenzene (40 mL) was refluxed for 3 h. The reaction mixture was analyzed by ^{1}H NMR and GC-MS and then chromatographed.

From But-1-yn-4-yl trimethylacetate 1. Chromatography gave unreacted thiol, unreacted alkyne **1** (40%, as determined by ^{1}H NMR analysis of the reaction mixture), *1H-4-(β-trimethylacetoxyethyl)-2-benzothiopyran* **13** (60 mg, 9%) [MS m/z 276 (M^+, 10), 174 (100), 173 (80); ^{1}H NMR δ 1.15 (9H, s), 2.9 (br t, J= 7 Hz), 3.85 (2H, s), 4.20 (2H, t; collapsing to singlet upon irradiation at δ 2.9), 6.35 (1H, brs; collapsing to singlet upon irradiation at δ 2.9), 7.3 (5H, m); HRMS calcd for $C_{16}H_{20}O_2S$ 276.397; found 276.397], a 1:1 Z/E mixture of *1-(benzylthio)-4-(trimethylacetoxy)but-1-ene* **7** (225 mg, 34 %) [MS m/z 278 (M^+, 2), 176 (30), 91 (100), 85 (100), 57 (70); ^{1} H NMR δ 1.15 (9H, s), 2.4 (2H, m), 3.84 (1H, s), 3.86 (1H, s), 4.03 (1H, t, J=7Hz; collapsing to singlet upon irradiation at δ 2.4), 4.06 (1H, t, J=7Hz, collapsing to singlet upon irradiation at δ 2.4), 5.53 (0.5H, dt, Jd = 10 Hz, Jt = 7 Hz), 5.59 (0.5H, dt, Jd = 15 Hz, Jt = 7 Hz), 6.02 (0.5H, dt, Jd = 15 Hz, Jt = 1 Hz), 6.04 (0.5H, dt, Jd = 10 Hz, Jt = 1 Hz), 7.2-7.3 (5H, m). Anal. Calcd. for $C_{16}H_{22}O_2S$: C, 69.03; H, 7.96; O, 11.49; S, 11.52. Found: C, 69.25; H, 8.00; S, 11.45%], and *1-(methylthio)-2-phenyl-4-(trimethylacetoxy)but-1-ene* **10** (270 mg, 41%) [MS m/z 278 (M^+, 2), 176 (100), 161 (95), 127 (95), 115 (90), 57 (100); ^{1}H NMR δ 1.15 (9H, s), 2.22 (3H, s), 2.78 (2H, t, J = 7 Hz), 4.05 (2H, t, J = 7 Hz), 6.02 (1H, s), 7.2-7.4 (5H, m). Anal. Calcd. for $C_{16}H_{22}O_2S$: C, 69.03; H, 7.96; O, 11.49; S, 11.52. Found: C, 69.30; H, 7.97; S, 11.46%].

From But-1-yn-4-yl thioacetate 2. Chromatography gave unreacted thiol, unreacted alkyne **2** (45%, as determined by ^{1}H NMR analysis of the reaction mixture), *1H-4-(β-thioacetoxyethyl)-2-benzothiopyran* **14** (70 mg, 13%) contaminated with small amounts of unidentified products [^{1}H NMR δ 2.32 (3H, s); superimposed to a 2H multiplet); 2.85 (2H, m); 3.72 (2H, s); 6.35 (1H, brs; collapsing to singlet upon irradiation at δ 2.85), 7.2-7.4 (5H, m); MS, m/z 250 (M^+, 10), 173 (100); HRMS calcd for $C_{13}H_{14}OS_2$ 250.384; found 250.384], a 1:1 Z/E mixture of *1-(benzylthio)-4-(thioacetoxy)but-1-ene* **8** (150 mg, 27%) [MS m/z 176 (M^+- MeCOSH, 30), 91 (100), 85 (60); ^{1}H NMR δ 2.30 (6H, s), 2.35 (4H, m), 2.85 (4H, t), 3.85 (4H, s), 5.45-5.65 (2H, m; collapsing to doublets at δ 5.52, J = 10 Hz, and δ 5.58, J = 15 Hz, upon irradiation at δ 2.35), 6.0 (2H, m), 7.2-7.5 (10H, m). Anal. Calcd. for $C_{13}H_{16}OS_2$: C, 61.86; H, 6.39; O, 6.34; S, 25.41. Found: C, 62.05; H, 6.42; S, 25.30%], *1-(methylthio)-2-phenyl-4-(thioacetoxy)but-1-ene* **11** (205 mg, 37%) [MS m/z 252 (M^+, 10), 176 (50), 161 (100); ^{1}H NMR δ 2.25 (3H, s), 2.30 (3H, s), 2.65-2.9 (4H, AA'BB' system), 6.05 (1H, t, J = 1.0 Hz), 7.2-7.4 (5H, m). Anal. Calcd. for $C_{13}H_{16}OS_2$: C, 61.86; H, 6.39; O, 6.34; S, 25.41. Found: C, 61.7; H, 6.41; S, 25.25%] and a fraction (80 mg) of unidentified products.

From But-1-yn-4-yl thiobenzoate 3 Chromatography gave unreacted thiol, unreacted alkyne **3** (40%, as determined by ^{1}H NMR analysis of the reaction mixture), a 1:1 E/Z mixture of *1-(benzylthio)-4-(thiobenzoyloxy)but-1-ene* **9** (260 mg, 35%) [^{1}H NMR δ 2.36-2.54 (4H, m), 2.9-3.2 (4H, m), 3.85 (4H, s), 5.60 (1H, dt, Jd = 10 Hz, J_t = 7.0 Hz), 5.65 (1H, dt, J_d = 15, J_t = 7.0 Hz), 6.3 (1H, dt, J_d = 10, J_t = 1.5 Hz), 6.7(1H, dt, J_d = 15, J_t = 1.5 Hz), 7.2-8.0 (10H, m); MS m/z 314 (M^+, 0.5), 105 (70), 91 (100), 85 (80), 77 (50).). Anal. Calcd. for $C_{18}H_{18}OS_2$: C, 68.75; H, 5.77; O, 5.09; S, 20.39. Found: C, 69.0; H, 5.8; S, 20.25%] and *1-(methylthio)-2-phenyl-4-(thiobenzoyloxy)but-1-ene* **12** (130 mg, 17%) [^{1}H NMR δ 2.25 (3H, s), 2.8 (2H, tt, J_1 = 7.5 , J_2 = 1.0 Hz), 3.0 (2H, m), 6.1 (1H, t, J = 1.0 Hz), 7.2-8.0 (5H, m); MS m/z 314 (M^+, 1), 176 (50), 161 (100), 105 (80), 77 (75).). Anal. Calcd. for $C_{18}H_{18}OS_2$: C, 68.75; H, 5.77; O, 5.09; S, 20.39. Found: C, 68.8; H, 5.80; S, 20.30%]. GC-MS and ^{1}H NMR analysis of the crude detected **9** and **12** as only reaction products.

From 1-Phenylpropyn-3-yl trimethylacetate 15. Chromatography gave unreacted thiol, unreacted alkyne **15** (300 mg, 35%), *1,1-diphenyl-2-(methylthio)-3-(trimethylacetoxy)prop-1-ene* **18** (575 mg, 65%) [^{1}H NMR δ 1.25 (9H, s), 2.20 (3H, s), 4.75 (2H, s), 7.1-7.4 (10H, m); MS m/z 340 (M^+, 40), 292 (20), 255 (20), 191 (100), 57 (65). Anal. Calcd. for $C_{21}H_{24}O_2S$: C, 74.08; H, 7.10; O, 9.39; S, 9.42. Found: C, 74.23; H, 7.14; S, 9.35%],

(Z)-*2-(benzylthio)-1-phenyl-3-(trimethylacetoxy)prop-1-ene* (Z)-**17** (200 mg, 23%) [^{1}H NMR δ1.25 (9H, s), 3.97 (2H, s), 4.80 (2H, s), 6.8 (1H, s), 7.1-7.4 (10H, m); MS m/z 340 (M^+, 15), 238 (10), 147 (85), 91 (100), 57 (50). Anal. Calcd. for $C_{21}H_{24}O_2S$: C, 74.08; H, 7.10; O, 9.39; S, 9.42. Found: C, 74.25; H, 7.15; S, 9.37%. The ^{1}H NMR spectrum showed signals at δ 4.05 (s), 4.82 (s) and 6.73 (s) ascribable to the E-isomer], and *1H-3-(trimethylacetoxymethyl)-4-phenyl-2-benzothiopyran* **19** (115 mg, 13 %) [^{1}H NMR δ 1.25 (9H, s), 3.90 (2H, s), 4.65 (2H, s), 7.1-7.4 (9H, s); MS m/z 338 (M^+, 40), 235 (100), 57 (50); HRMS calcd for $C_{21}H_{22}O_2S$ 338.468; found 338.468].

From 5-Cyanopent-1-yne 20. Chromatography gave unreacted thiol (35%, as determined by ^{1}H NMR analysis of the reaction mixture) and a fraction constituted by adducts **21** (1:1 Z/E ratio), methyl sulfide **22** and (possible) thiopyran **23** in a 85:15:5 ratio (400 mg, 80% overall yield based on reacted thiol). The presence of **23** was deduced from the ^{1}H NMR spectrum which showed, in addition to signals of compounds **21** and **22**, signals at δ 2.75 (t, J = 7 Hz), 3.75 (s) and 6.3 (s), and from GC-MS analysis showing a peak at m/z 215 (M^+, 20). Repeated column chromatography of this fraction led to the separation of some pure *1-(benzylthio)-5-cyanopent-1-ene* **21** [^{1}H NMR δ 1.7 (2H, q, J = 7 Hz), 2.2 (4H, m), 3.95 (2H, s), 5.49 (0.5H, dt, J_d = 10 Hz, J_t = 7 Hz), 5.51 (0.5H, dt, J_d = 15 Hz, J_t = 7 Hz), 5.98 (0.5H, dt, J_d = 15 Hz, J_t = 1 Hz), 6.03 (0.5H, dt, J_d = 10 Hz, J_t = 1 Hz), 7.2-7.4 (5H, m). MS m/z 217 (M^+, 20), 91 (100); HRMS calcd for $C_{13}H_{15}NS$ 217.093; found 217.093] and *5-cyano-2-phenyl-1-(methylthio)pent-1-ene* **22** [H NMR δ 1.7 (2H, q, J = 7 Hz); 2.2 (2H, m; superimposed to a 3H singlet due to SMe group), 2.64 (2H, br t, J = 7 Hz), 6.08 (1H, br s; collapsing to singlet upon irradiation at δ 2.64), 7.2-7.4 (10H, m); MS m/z 217 (M^+, 80), 163 (60), 161 (50), 129 (50), 115 (100), 91 (30); HRMS calcd for $C_{13}H_{15}NS$ 217.093; found 217.093].

From 1-Phenylpropyn-3-yl cyanomethyl ether 24. . Chromatography gave unreacted alkyne **24** (45%, as determined by ^{1}H NMR analysis of the reaction mixture), an unknown product at m/z 233 (M^+) (30 mg, 6%) and an inseparable mixture of adducts **25** (ca. 2:1Z/E ratio), methyl sulfide **26** and thiopyran **27** [^{1}H NMR δ 3.97 (2H, s), 4.15 (2H, s), 4.22 (2H, s), 7.1-7.5 (9H, m); GC-MS 293 (M^+, 100), 292 (60), 235 (80)] in 27:58:14 ratio (350 mg, 54% overall yield). Further elution gave 60 mg of an intractable mixture. Repeated chromatography of the main fraction led to separation of some pure *2-(benzylthio)-1-(phenyl)propen-3-yl cyanomethyl ether* **25** [^{1}H NMR δ (Z-isomer) 4.04 (2H, s); 4.24 (2H, s), 4.33 6.78 (1H, s), 7.1-7.5 (10H, m); ^{1}H NMR δ (E-isomer) 4.07 (2H, s), 4.26 (2H, s), 4.34 (2H, s), 6.7 (1H, s), 7.1-7.5 (10H, m); MS m/z 295 (M^+, 10), 147 (50), 91 (100); HRMS calcd for $C_{18}H_{17}ONS$ 295.103; found 295.103] and *1,1-diphenyl-2-(methylthio)propen-3-yl cyanomethyl ether* **26** [^{1}H NMR δ 2.28 (3H, s), 4.22 (2H, s), 4.35 (2H, s), 7.1-7.5 (10H, m); MS m/z 295 (M^+, 60), 223 (20), 191 (100); HRMS calcd for $C_{18}H_{17}ONS$ 295.103; found 295.103].

From 2-Cyanodiphenylacetylene 28a. Chromatography gave unreacted thiol, unreacted alkyne **28a** (240 mg, 30%) and *3-(benzylthio)-2-phenylinden-1-one* **35** (440 mg, 48%) [red solid, m.. p. 94-96 °C; MS m/z 328 (M^+, 20), 237 (15), 165 (10), 91 (100); ^{1}H NMR δ 3.90 (2H, s), 7.0-7.5 (14H, m); ^{13}C NMR δ 37 (CH_2), 120, 122, 127.7, 128.2, 128.25, 128.7, 128.9, 129.4, 129.7 (q), 130.3, 131.2 (q), 131.4 (q), 133.4, 136 (q), 144 (q), 154.2 (q), 194 (CO); IR ν_{MAX} 1700 cm^{-1}. Anal. Calcd. for $C_{22}H_{16}OS$: C, 80.45; H, 4.91; O, 4.87; S, 9.76. Found: C, 80.7; H, 4.93; S, 9.71%]. This product was absent in the reaction mixture. The ^{1}H NMR spectrum of the crude showed, in addition to aromatic protons, a signal at δ 3.35 ascribable to the imine **34**. Further elution gave a mixture of intractable products (240 mg).

From 1-(2-Cyanophenyl)hex-1-yne 28b. Chromatography gave starting alkyne **28b** (280 mg, 38%), an inseparable 80:10:10 mixture (360 mg, 47% overall yield) of methyl sulfide **31**, an unknown product [GC-MS, m/z 305 (M^+, 20), 248 (30), 91 (100)], and *2-(benzylthio)-1-(2-cyanophenyl)hex-1-ene* **30** (ca. 1:1 Z/E ratio)[^{1}H NMR δ: 0.8 (3H, t, J = 7 Hz), 0.9 (3H, t, J = 7 Hz), 1.1-1.7 (8H, m), 2.35 (2H, t, J = 7 Hz), 2.48 (2H, t, J = 7 Hz), 3.90 (2H, s), 4.1 (2H, s), 6.4 (1H, s), 6.72 (1H, s), 7.1-7.7 (18H, m); GC-MS m/z 307 (M^+, 10), 160 (20), 91 (100)] and a fraction constituted by inseparable, unidentifiable products (140 mg). Repeated

chromatography of the above mixture led to the separation of some pure *1-(2-cyanophenyl)-2-(methylthio)-1-phenylhex-1-ene* **31** [^{1}H NMR δ 0.75 (3H, t, J = 7 Hz), 1.2 (2H, m), 1.5 (2H, m), 2.12 (3H, s), 2.25 (2H, t), 7.2-7.8 (9H, m); MS m/z 307 (M^+, 100), 292 (30), 244 (40), 236 (50), 230 (60), 217 (60), 216 (40); HRMS calcd for $C_{20}H_{21}NS$ 307.139; found 307.139]

1-(2-Cyanophenyl)-2-(trimethylsilyl)acetylene 28c. GC-MS and TLC analysis of the reaction mixture showed the presence on unreacted thiol and alkyne **28c** in addition to dibenzyl disulfide and trace amounts of two isomeric products at m/z 323 (M^+, 5), 232 (20), 91 (80), 73 (100).

Reactions with Benzenethiol. General Procedure. A solution of benzenethiol (0. 40 mL, 4 mmol) in fluorobenzene (5 mL) was slowly added with a syringe pump within 3 h to a boiling solution of the appropriate alkyne (4 mmol) and AIBN (130 mg, 0.8 mmol) in fluorobenzene (40 mL). The reaction mixture was refluxed for a further 1 h, then analyzed by ^{1}H NMR and chromatographed.

From 2-Cyanodiphenylacetylene 28a. Chromatography gave unreacted thiol, unreacted alkyne **28a** (285 mg; 35%), and *2-phenyl-3-(phenylthio)inden-1-one* **39** (530 mg, 65%) [red solid, m.p. 99-100 °C; MS m/z 314 (M^+, 90), 281 (60), 205 (90), 176 (100); IR ν_{Max} 1700 cm^{-1}(CO); ^{13}C NMR δ 121.6, 122, 127.8, 128.05, 128.1, 128.9, 129.1, 129.8, 130.2 (q), 130.6 (q), 130.7 (q), 131.5, 133.4, 135.5 (q), 142 (q), 152 (q), 193 (CO).. Anal. Calcd. for $C_{21}H_{14}OS$: C, 80.22; H, 4.49; O, 5.09; S, 10.20. Found: C, 80.54; H, 4.51; S, 10.15%] and a mixture of unidentified products (100 mg).

From 1-(2-Cyanophenyl)hex-1-yne 28b. Chromatography gave starting alkyne **28b** (180 mg, 25%), *1-(2-cyanophenyl)-2-(phenylthio)hex-1-ene* **40** (2:1 Z/E mixture) (385 mg, 44%) [^{1}H NMR δ(Z-isomer) 0.8 (3H, t, J=7.3 Hz), 1.2 (2H, sextuplet, J=7.3 Hz), 1.5 (2H, m), 2.3 (2H, t, J=7.3 Hz), 6.9 (1H, s), 7.2-7.8 (9H, m); MS m/z 293 (M^+, 30), 250 (100), 236 (30); δ(E-isomer) 0.8 (3H, t, J=7.3 Hz), 1.2 (2H, sextuplet, J=7.3 Hz), 1.6 (2H, m), 2.35 (2H, t, J=7.3 Hz), 6.4 (1H, s), 7.2-7.8 (9H, m); MS m/z 293 (M^+, 30), 250 (100), 236 (30). Anal. Calcd. for $C_{19}H_{19}NS$: C, 77.77; H, 6.53; N, 4.77; S, 10.93. Found: C, 78.00; H, 6.56; S, 10.88%], *2-butyl-3-(2-cyanophenyl)benzo[b]thiophene* **41** (85 mg, 10%) contaminated with some (E)-adduct [^{1}H NMR δ 0.8 (3H, t, J = 7 Hz), 1.25 (2H, m), 1.6 (2H, m), 2.73 (1H, A part of an ABXY system; J_{AB} = 15 Hz, J_{AX} = 8.5 Hz, J_{AY} = 6.9 Hz), 2.87 (1H, B part of an ABXY system; J_{AB} = 15 Hz, J_{BX} = 8.9 Hz, J_{BY} = 6.0 Hz), 7.2-7.9 (aromatic protons); GC-MS m/z 291 (M^+, 70), 248 (100), 246 (50), 204 (30); HRMS calcd. for $C_{19}H_{17}NS$ 291.108; found 291.108], *1-(2cyanobenzoyl)-1-(phenylthio)pent-1-ene* **42** (90 mg, 10%; this product was absent in the reaction mixture) [oil; ^{1}H NMR δ 1.0 (3H, t, J = 7.3 Hz), 1.6 (2H, sextuplet, J = 7.3 Hz), 2.58 (2H, q, J = 7.3 Hz; collapsing to doublet upon irradiation at δ 2.6; collapsing to triplet upon irradiation at δ 7.0), 7.0 (1H, t, J=7.3 Hz), 7.1-7.6 (9H, m); MS m/z 307 (M^+, 50), 198 (60), 197 (60), 182 (70), 130 (95), 102 (100); HRMS calcd. for $C_{19}H_{17}NOS$ 307.1031; found 307.1035); IR ν_{Max} 2220, 1700 cm^{-1}], and an unknown products (70 mg) which was absent in the reaction mixture [^{1}H NMR δ 0.75 (3H, t, J = 7 Hz), 1.2-1.5 (4H, m), 2.1 (1H, A part of an ABX_2 system, J_{AB} = 17.5 Hz, J_{AX} = 7.3 Hz), 2.5 1 (1H, A part of an ABX_2 system, J_{AB} = 17.5 Hz, J_{BX} = 7.1 Hz), 7.3-8.2 (aromatic protons); GC-MS m/z 233 (10), 176 (100), 149 (80); IR ν_{Max} 2225 cm^{-1}(CN)].

From 1-(2-Cyanophenyl)(trimethylsilyl)acetylene 28c. GC-MS and TLC analysis of the reaction mixture showed the presence on unreacted thiol and alkyne **28c** in addition to diphenyl disulfide.

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11. Fluorobenzene is a convenient solvent for radical reactions, owing to its low toxicity.
12. On the other hand, we have recently evidenced (see ref. 10d) that the cyclization rate of vinyl radicals is not largely dependent on the resonance stabilization of radical adducts.
13. In particular, the allylic methylene exhibited a well defined ABXY system, with J_{AB} = 15 Hz. The source of the observed atropoisomerism is believed to arise from restricted rotation around the CC single bond between the C-3 carbon atom and the 2-cyanophenyl ring. Semiempirical calculations provide evidence that the molecule arranges itself with the 2-cyanophenyl ring perpendicular to the benzothiophene plane, with a ca. 26 Kcal/mol rotational barrier. This value is quite high and is in agreement with ^{1}H NMR data, which show the atropisomers to be still present at 100 °C.
14. However, in a repeated chromatography or on standing at the air no further oxidation of **41** was observed.
15. For vinyl sulfides oxidation see: Benati, L.; Montevecchi, P. C.; Nanni, D.; Spagnolo, P. *Tetrahedron Lett.*, **1993**, *34*, 3595; Capella, L.; Montevecchi, P. C.; Nanni , D. *J. Org. Chem.*, **1994**, *59*, 7379.
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17. Similarly, in a independent experiment we observed that no addition products were formed from phenyl(trimethylsilyl)acetylene and benzenethiol under the reaction conditions employed. In contrast, reaction of benzenethiol with aryl(trimethylsilyl)acetylene having a fairly good radical acceptor in 2-position, such as an azido function, smoothly lead to cyclization products. (These results will be published elsewhere).
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