Reactions of Arylmethanethiols with 1,4-Disubstituted 1,3-Butadiynes

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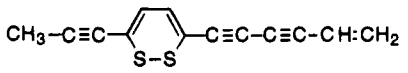
Owing to our interest in the synthesis and bioactivity of 1,2-dithiacyclohexa-3,5-dienes [1,2-dithiins, *e.g.* thiarubrine A (**1**) and thiarubrine B (**2**)], we are investigating the reactions of thiols with enediynes, polyenynes, and polyalkynes under various experimental conditions.[1–9] Efficient syntheses of a wide variety of natural and unnatural 1,2-dithiins[2–11] and a study of structure–activity relationships (SAR) will help in gaining a better understanding of the mechanisms involved in the cleavage of DNA by 1,2-dithiins[6] and enediyne antitumor agents such as the calicheamicins and neocarzinostatin.[12–18]



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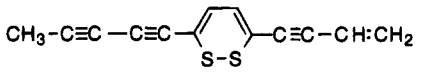

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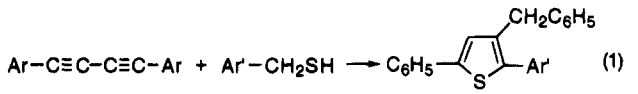
It has been reported that benzenethiol[10a] reacts with 1,4-diphenyl-1,3-butadiyne (**3a**) in ethanol/sodium hydroxide to give (*Z*)-1,4-diphenyl-1-(phenylthio)but-1-en-3-yne and 1,4-diphenyl-1,4-(diphenylthio)buta-1,3-diene and that phenylmethanethiol (**4a**) reacts with 1,3-butadiynes in ethanol/potassium hydroxide[10b,c] or in *N,N*-dimethylformamide/potassium hydroxide[11] to give (*Z,Z*)-1,4-bis[(phenylthio)methyl]-1,3-butadienes which are precursors to 1,2-dithiins. We observed[7] that equimolar amounts of diyne **3a** and thiol **4a** react in dimethyl sulfoxide/potassium hydroxide to give the thiophene **5a** (66%). Similarly, (4-methylphenyl)- (**4b**), (3-chlorophenyl)- (**4c**), and 2-furylmethanethiol (**4d**) react with **3a** to give the corresponding thiophenes **5b** (59%), **5c** (54%), and **5d** (64%). In ethanol/sodium hydroxide **3a** reacts stereospecifically with **4a**, **4b**, and **4c** to give the corresponding 1:1 nucleophilic addition products [(*Z*)-1,4-diphenyl-1-[(arymethyl)thio]but-1-en-3-ynes **6a** (69%), **6b** (76%), and **6c** (85%)] which cyclize to the respective thiophenes **5a** (80%), **5b** (90%), and **5c** (85%) in DMSO/KOH.



(1)

3a Ar = C_6H_5
3b Ar = 2-thienyl
3c Ar = 3-thienyl

4a Ar' = C_6H_5
4b Ar' = 4-$CH_3C_6H_4$
4c Ar' = 3-ClC_6H_4
4d Ar' = 2-furyl
4e Ar' = 4-FC_6H_4
4f Ar' = 2-thienyl

5a Ar' = C_6H_5
5b Ar' = 4-$CH_3C_6H_4$
5c Ar' = 3-ClC_6H_4
5d Ar' = 2-furyl

The large number of reports in recent years concerning the synthesis of thiophenes and their derivatives attest to the current interest and importance of these compounds in biology, chemistry, industry, and medicine.[19–22] Thus, the reaction in eq 1 is valuable for the facile synthesis of uniquely substituted thiophene oligomers. The reaction of **4a**, **4c**, **4d**, and (4-fluorophenyl)methanethiol (**4e**) with 1,4-bis(2-thienyl)butadiyne (**3b**) affords the respective 2,2′-bithiophenes **7a** (65%), **7b** (51%), **7c** (74%), and **7d** (66%). Similarly, the reaction of **3b** and (2-thienyl)methanethiol (**4f**) gave the 2,2′:5′,2″-terthiophene derivative **8** (71%). 2,2′-Bithiophene and 2,2′:5′,2″-terthiophene and their derivatives are of interest in the chemistry of organic conducting polymers[23,24] and for their wide range of photobiological effects.[25–28]

In order to evaluate the influence of position three of the thiophene ring, 1,4-bis(3-thienyl)butadiyne (**3c**) was prepared and reacted with thiols **4c**, **4e**, and **4f** to afford

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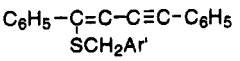
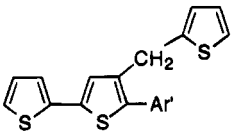
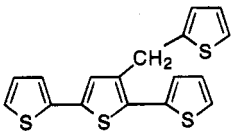


6a Ar' = C_6H_5
6b Ar' = 4-$CH_3C_6H_4$
6c Ar' = 3-ClC_6H_4



7a Ar' = C_6H_5
7b Ar' = 3-ClC_6H_4
7c Ar' = 2-furyl
7d Ar' = 4-FC_6H_4



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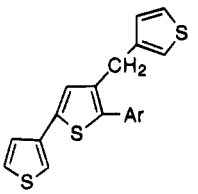
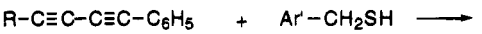
the 2,3′-bithiophenes **9** (59%) and **10** (69%), and the 2,2′:5′,3″-terthiophene **11** (68%), respectively.



9 Ar = 3-ClC_6H_4
10 Ar = 4-FC_6H_4
11 Ar = 2-thienyl

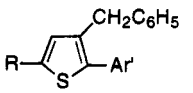
The addition of thiol to an unsymmetrical 1,4-disubstituted butydiyne may occur at two different positions which can lead to regioisomeric products. In order to explore the regiochemistry of the reaction, 1-methoxy-5-phenyl-2,4-pentadiyne (**3d**)[29,30] and 2-methyl-6-phenyl-3,5-hexadiyn-2-ol (**3e**) were prepared[29,31] and reacted with thiols **4a**, **4d**, and (3-methylphenyl)methanethiol (**4g**, eq 2). With both **3d** and **3e**, nucleophilic addition occurred regioselectively at the carbon leading to the resonance-stabilized carbanion of the 1:1 addition product (eq 3) which subsequently cyclizes to the corresponding thiophene.

The stereospecific nucleophilic addition of thiols to dialkynes to form cis enyne thioethers proceeds in a stepwise manner.[32-36] Thiophene formation probably occurs via anionic cyclization of the enyne thioether. The resonance-stabilized benzyl carbanion (eq 3) in the enyne thioether adds to the carbon–carbon triple bond to form the intermediate which leads to the thiophene (eq 4).



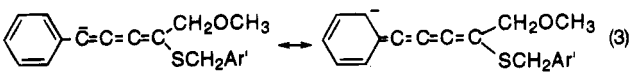
3d R = CH_3OCH_2
3e R = $(CH_3)_2C(OH)$

4a Ar' = C_6H_5
4d Ar' = 2-furyl
4g Ar' = 3-$CH_3C_6H_4$



(2)

5e R = CH_3OCH_2, Ar' = C_6H_5
5f R = $(CH_3)_2C(OH)$, Ar' = C_6H_5
5g R = CH_3OCH_2, Ar' = 2-furyl
5h R = $(CH_3)_2C(OH)$, Ar' = 2-furyl
5i R = CH_3OCH_2, Ar' = 3-$CH_3C_6H_4$
5j R = $(CH_3)_2C(OH)$, Ar' = 3-$CH_3C_6H_4$



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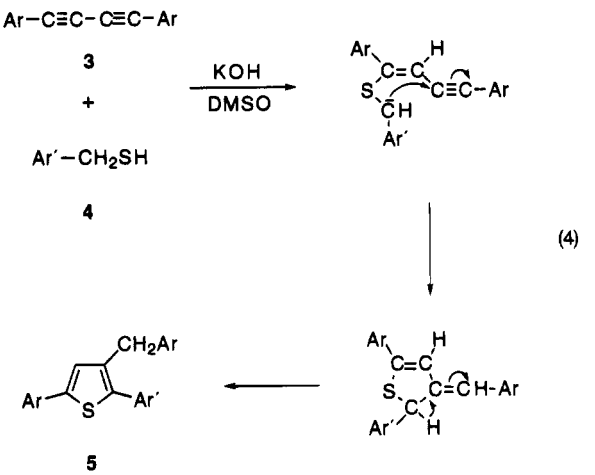

(4)

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The facile one-step or two-step procedures described above for the synthesis of thiophenes, 2,2′- and 2,3′-bithiophenes, and 2,2′:5′,2″- and 2,2′:5′,3″-terthiophenes are easily modified for selective preparation of a wide variety of thiophene analogues including oligothiophenes.

Experimental Section

Microanalyses were performed by Robertson Microlit Laboratories, Inc., Madison, NJ. HRMS were obtained at 70 eV. CIMS (2-methylpropane) and EIMS were obtained at an ionization potential of 70 or 100 eV. ^1H (300 and 500 MHz) and ^{13}C NMR (75.4 and 125.7 MHZ) spectra were recorded in $CDCl_3$. Analytical TLC was performed on Analtech Uniplate 10- × 20-cm (250-μm thick) silica gel GF prescored glass plates, which were developed with hexanes or 10:1 hexanes/ethyl acetate. The plates were visualized by UV. Flash column chromatography was performed on 40 g of 225–400-mesh silica gel.

Compounds **5a–5d**, **5f–5h**, **6a–6c**, **7a–7d**, and **8–11** were shown to be greater than 97% pure by ^1H NMR.

Phenylmethanethiol (**4a**) and **2-furylmethanethiol** (**4d**) are commercially available. **(4-Methylphenyl)-** (**4b**),[37] **(3-chlorophenyl)-** (**4c**),[38] and **(3-methylphenyl)methanethiol** (**4g**)[38] were prepared as previously described. **(4-Fluorophenyl)methanethiol** (**4e**) was prepared (80%)[38] from (4-fluorophenyl)chloromethane: bp 76–78 °C/10 mmHg; ^1H NMR δ 1.74 (t, J = 8 Hz, 1 H), 3.66 (d, J = 8 Hz, 2 H), 6.36 (dd, J = 9.9 Hz, 2 H), 7.25 (dd, J = 9.9 Hz, 2 H); ^{13}C NMR δ 27.9 (SCH_2), 115.2

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(d, J = 21 Hz), 123.3 (d, J = 7 Hz), 136.6, 158.5 (d, J = 245 Hz) (C_6H_4). **(2-Thienylphenyl)methanethiol (4f)** was prepared (80%)[39,40] from (2-thienyl)chloromethane.

1,4-Diphenyl-1,3-butadiyne (3a) was prepared (80%) from phenylethyne as previously described.[41] **1,4-Bis(2-thienyl)-1,3-butadiyne (3b)** and **1,4-bis(3-thienyl)-1,3-butadiyne (3c)** were obtained from 2- and 3-ethynylthiophene which were prepared from 2- and 3-(2,2-dibromoethenyl)thiophene, respectively.[42]

Preparation of 1-Methoxy-5-phenyl-2,4-pentadiyne (3d).[29,30] Bromine (12.1 g, 75.6 mmol) was added to a mixture of ice–water (35 g) and 10 M aqueous NaOH solution (17.4 mL, 0.174 mol). Phenylethyne (7 g, 68.6 mmol) in THF (5 mL) was added dropwise to the mixture at 0 °C. After being stirred for 6 h at rt, the mixture was poured into a saturated aqueous NH_4Cl solution (50 mL) and extracted (3 × 30 mL) with ether. The combined extracts were washed with saturated NaCl aqueous solution until the washings were ≈pH 7 and dried ($MgSO_4$), and the solvent was removed to give a residue which was 1-bromo-2-phenylethyne: ^{1}H NMR ($CDCl_3$) δ 7.2–7.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 58, 79.5, 132, 137, 138, 142. Butanamine (12.84 g, 0.176 mol) was added to a mixture of NH_2OH·HCl (4.19 g, 0.061 mol) and CuCl (71.4 mg, 0.78 mmol) under N_2 at 0 °C. This mixture was stirred for 10 min at 0 °C and then slowly added to a solution of methyl propargyl ether (2.415 g, 34.5 mmol) in EtOH (70 mL) at 15 °C. A solution of bromophenylethyne (5.675 g, 31.3 mmol) in EtOH (35 mL) was added during 3.5 h to the stirred mixture. After being stirred for 1 h longer, the reaction mixture was poured into water (100 mL) and extracted (3 × 50 mL) with hexanes. The combined extracts were washed with saturated NH_4Cl aqueous solution (50 mL), dried ($MgSO_4$), and concentrated to afford a yellow liquid (3.32 g) which was purified by chromatography on silica gel (230–400 mesh) first using hexanes and then 3:1 hexanes/acetone to give **3d** (2.14 g, 40.3%): IR (neat, cm^{-1}) 3059 w, 2990 w, 2931 m, 2823 m, 2241 m, 1444 m, 1353 s, 1186 m, 1102 s; ^{1}H NMR ($CDCl_3$) δ 3.4 (s, 3 H), 4.2 (s, 2 H), 7.3–7.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 57.4, 59.9, 70.8, 73.2, 76.6, 78.6, 121, 128, 129, 132.

Preparation of 2-Methyl-6-phenyl-3,5-hexadiyn-2-ol (3e). Compound **3e** was synthesized from 1-bromo-2-phenylethyne and 2-methyl-1-but-3-yn-2-ol using the procedure described above for the preparation of **3d**.[29–31] Compound **3e** was purified by chromatography on silica gel (230–400 mesh) first using hexanes then 3:1 hexanes/acetone;: mp 59–60 °C (lit.[31a] mp 56 °C); IR ($CHCl_3$, cm^{-1}) 3594 m, 3155 m, 2983 m, 2254 s, 1466 m, 1381 m, 1164 m, 1099 m; ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 6 H), 2.57 (s, 1 H), 7.2–7.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 30.7, 65.6, 73.1, 78.6, 86.7, 121.4, 127.6, 128.3, 132.5.

General Procedure for the Synthesis of 2,5-Diaryl-3-(phenylmethyl)thiophenes 5. 2-(2-Furyl)-5-phenyl-3-(phenylmethyl)thiophene (5d). A flask equipped with a magnetic stirbar, a rubber septum port, a solid addition funnel, and a water condenser topped with a T tube leading to a source of N_2 was charged with a mixture of 2-furylmethanethiol (114 mg, 1.0 mmol) and KOH (58 mg, 1.0 mmol) in DMSO (15 mL). 1,4-Diphenylbutadiyne (**3a**, 200 mg, 1.0 mmol) was added slowly in small portions. After addition of **3a**, the reaction mixture was stirred at rt for 1 h. TLC analysis (hexanes) showed the absence of **3a**. Ether (50 mL) was added to the reaction solution, and this reaction mixture was poured to a mixture of ice (15 g) and saturated NH_4Cl solution (15 mL). The organic layer was washed with saturated NaCl solution (25 mL) and dried (4 Å molecular sieves 10 h), the volatile materials were removed *via* rotatory evaporator, and the residue was chromatographed (hexanes, R_f = 0.20). Recrystallization from 1:5 ether/ethanol gave light yellow crystals of **5d** (200 mg, 64%, mp 89–90 °C): HREIMS m/z 316.0895, calcd m/z for $C_{21}H_{16}OS$ 316.0921; IR (KBr, cm^{-1}) 3553 m, 3447 s, 3414 s, 2919 w, 2356 w, 1948 w, 1617 w, 1592 m, 1490 m, 1449 m, 1330 w, 1205 w, 1026 w, 998 m, 871 w, 853 w, 797 w, 754 m, 725 vs, 687 s, 639 m; ^{1}H NMR δ 4.15 (s, 2 H), 6.40–6.44 (m, 2 H), 6.99 (s, 1 H), 7.21–7.35 (m, 8 H), 7.43 (m, 1 H), 7.52–7.55 (2 H); ^{13}C NMR δ 35.4 (SCH_2), 106.3, 111.6, 125.4, 126.2, 126.4, 127.5, 127.8, 128.3, 128.5, 128.8, 133.3, 137.3, 139.9, 141.6, 142.0, 148.8; UV (CH_3CN) λ_{max} (log ϵ) = 332 (4.21).

2,5-Diphenyl-3-(phenylmethyl)thiophene (5a): mp 94–95 °C (lit.[7] mp 94–95 °C).

2-(4-Methylphenyl)-5-phenyl-3-(phenylmethyl)thiophene (5b) was chromatographed (hexanes, R_f = 0.24) and recrystallized from methanol to give colorless crystals (200 mg, 59%, mp 107–108 °C): HRCIMS m/z 340.1266, calcd for $C_{24}H_{20}S$ 340.1285; IR (KBr, cm^{-1}) 3060 w, 3010 w, 2928 w, 1947 w, 1596 w, 1485 m, 1450 m, 1427 m, 1028 w, 846 m, 837 w, 764 m, 720 vs, 687 vs; ^{1}H NMR δ 2.34 (s, 3 H), 4.01 (s, 2 H), 7.15 (m, 1 H), 7.18–7.34 (m, 12 H), 7.52 (m, 2 H); ^{13}C NMR δ 21.2 (CH_3), 34.7 (SCH_2), 125.4, 126.0, 126.2, 127.2, 127.4, 128.7, 128.9, 129.3, 131.2, 134.1, 136.6, 137.4, 138.6, 140.9, 141.9; UV (CH_3CN) λ_{max} (log ϵ) = 313 (3.78).

2-(3-Chlorophenyl)-5-phenyl-3-(phenylmethyl)thiophene (5c) was chromatographed (hexanes, R_f = 0.35) and recrystallized from methanol to give colorless crystals (190 mg, 54%, mp 80–81 °C): HRCIMS m/z 360.0722, calcd for $C_{23}H_{17}ClS$ 360.0739; IR (KBr, cm^{-1}) 3062 w, 3029 w, 2917 w, 1948 w, 1593 m, 1560 m, 1481 m, 1452 m, 1407 w, 1075 w, 975 w, 891 w, 843 w, 756 vs, 693 vs; ^{1}H NMR δ 4.00 (s, 2 H), 7.06 (s, 1 H), 7.15–7.35 (m, 11 H), 7.46 (m, 1 H), 7.53–7.55 (m, 2 H); ^{13}C NMR δ 34.7 (SCH_2), 125.5, 126.2, 126.3, 126.4, 127.1, 127.5, 128.4, 128.5, 128.8, 129.0, 129.7, 133.9, 134.4, 135.9, 136.7, 137.7, 140.4, 143.0; UV (CH_3CN) λ_{max} (log ϵ) = 313 (3.79).

3-Benzyl-5-(methoxymethyl)-2-phenylthiophene (5e). Chromatography (silica gel, hexane/ether = 100/15) gave 140 mg of **5e** (43.7%): HRCIMS m/z 294.1080, calcd for $C_{19}H_{18}OS$ 294.1078; IR (neat, cm^{-1}) 3058 w, 3025 m, 2923 m, 2821 m, 1599 m, 1494 m, 1450 s, 1380 m, 1140 m, 1088 s 760 s, 701 s; ^{1}H NMR ($CDCl_3$) δ 3.8 (s, 3 H), 3.99 (s, 2 H), 4.5 (s, 2 H), 6.7 (s, 1 H), 7.1–7.5 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 34, 58, 69, 126, 127.4, 128.3, 128.4, 129.1, 129.6, 134.3, 135.6, 138, 138.3, 140.8. Anal. Calcd for $C_{19}H_{18}OS$: C, 77.55; H, 6.12. Found: C, 77.29; H, 6.20.

3-Benzyl-5-(2-hydroxy-2-propyl)-2-phenylthiophene (5f): HRCIMS m/z 308.1246, calcd for $C_{20}H_{20}OS$ 308.1235; IR ($CHCl_3$, cm^{-1}) 3590 m, 3424 b, 3027 m, 2977 s, 2927 m, 2250 s, 1560 m, 1494 m, 1454 m, 1371 m, 1322 m, 1159 s, 908 vs, 734 vs; ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 6 H), 2.4 (s, 1 H), 3.9 (s, 2 H), 6.7 (s, 1 H), 7.1–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 31.9, 34.7, 71.2, 125, 125.9, 127.3, 128.4, 128.8, 129, 135.3, 137.5, 140.9, 152.4.

3-Benzyl-2-(2-furyl)-5-(methoxymethyl)thiophene (5g). Chromatography (silica gel, 100:30 hexanes/ether) gave **5g** (215.3 mg, 64.5%): HRCIMS m/z 284.0885, calcd for $C_{17}H_{16}O_2S$ 284.0871; IR (neat, cm^{-1}) 3025 w, 2924 s, 2822 m, 1496 s, 1450 s, 1372 s, 1147 s, 1087 vs, 735 vs; ^{1}H NMR ($CDCl_3$) δ 3.3 (s, 3 H), 4.1 (s, 2 H), 4.4 (s, 2 H), 6.3 (m, 2 H), 6.6 (s, 1 H), 7.1–7.4 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 35.1, 57.5, 68.8, 106.7, 111.4, 125.96, 128.32, 128.38, 129.5, 135.9, 138.9, 139.9, 141.5, 148.6.

3-Benzyl-2-(2-furyl)-5-(2-hydroxy-2-propyl)thiophene (5h) was prepared in 69% yield: HRCIMS m/z 298.1, calcd for $C_{18}H_{18}O_2S$ 298.1027; IR ($CHCl_3$, cm^{-1}) 2427 b, 2027 m, 2977 s, 2926 m, 1600 m, 1496 s, 1452 s, 1369 s, 1157 s, 909 vs, 733 vs, 650 s; ^{1}H NMR ($CDCl_3$) δ 1.65 (s, 6 H), 2.5 (b, 1 H), 4.15 (s, 2 H), 6.41–6.46 (m, 2 H), 6.71 (s, 1 H), 7.24–7.46 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 31.75, 35.22, 71.09, 106.5, 111.4, 125.2, 125.98, 126.64, 128, 135.9, 140, 141.4, 148.75, 152.4.

3-Benzyl-5-(methoxymethyl)-2-(3-methylphenyl)thiophene (5i): HRCIMS m/z 308.1236, calcd for $C_{20}H_{20}OS$ 308.1235; IR(neat, cm^{-1}) 3025 m, 2922 s, 1601 s, 1451 s, 1380, 1140 s, 1089 s, 907 m, 845 m, 785 s, 703 s; ^{1}H NMR ($CDCl_3$) δ 2.3 (s, 3 H), 3.3 (s, 3 H), 3.9 (s, 2 H), 4.5 (s, 2 H), 6.7 (s, 1 H), 7.1–7.3 (M, 9 H); ^{13}C NMR ($CDCl_3$) δ 21.2, 34.5, 57.6, 69, 125.6, 126.1, 128.1, 128.3, 128.5, 129.4, 129.9, 134.1, 135.4, 137.9, 138.8, 139.4, 140.8. Anal. Calcd for $C_{20}H_{20}OS$: C, 77.92; H, 6.49. Found: C, 77.79; H, 6.67.

3-Benzyl-5-(2-hydroxy-2-propyl)-2-(3-methylphenyl)thiophene (5j): HRCIMS m/z 222.1409, calcd for $C_{21}H_{22}OS$ 322.1391; IR (neat, cm^{-1}) 3384 b, 3026 s, 2974 vs, 2921 s, 1603 s, 1492 s, 1451 s, 1370 s, 1160 s, 880 m, 845 m, 784 s, 701 vs; ^{1}H NMR ($CDCl_3$) δ 1.3 (s, 1 H, 1.6 (s, 6 H), 2.3 (s, 3 H), 3.9 (s, 2 H), 6.7 (s, 1 H), 7.1–7.3 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 21.3, 31.9, 34.7, 71.2, 125, 125.8, 126.1, 128.1, 128.3, 128.5, 129.9, 134.2, 135.3, 137.5, 138, 141, 152. Anal. Calcd for $C_{21}H_{22}OS$: C, 78.26; H, 6.83. Found: C, 78.50; H, 6.60.

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General Procedure for the Synthesis of the 1:1 Addition Products. (Z)-1,4-Diphenyl-1-(phenylthio)methyl]but-1-en-3-yne (6a). A flask equipped with a magnetic stirbar, a rubber septum port, rubber septum, and a water condenser topped with a T tube leading to a source of N_2 was charged with a mixture of 1,4-diphenyl-1,3-butadiyne (**3a**, 200 mg, 1.0 mmol), sodium hydroxide (40 mg, 1.0 mmol) in ethanol (20 mL). Phenylmethanethiol (**4a**, 0.12 g, 1.0 mmol) was added via syringe to the flask. After the addition, the reaction mixture was refluxed for 2 h with stirring. TLC analysis (hexanes) showed the absence of **3a**. The reaction mixture was cooled to rt. Ether (40 mL) was added, and the mixture was poured into a mixture of ice (20 g) and saturated NH_4Cl solution (20 mL). The organic layer was washed with 20 mL of saturated NaCl solution and dried (4-Å molecular sieves 10 h), the volatile materials were removed *via* rotatory evaporator, and the residue was chromatographed (silica gel, 80 g, 225–400 mesh, hexane, $R_f = 0.13$) to give a colorless liquid (220 mg, 69%): HRCIMS m/z 326.1133, calcd for $C_{23}H_{18}S$ 326.1128; IR (CCl_4, cm^{-1}); ^1H NMR δ 3.84 (s, 2 H), 6.02 (s, 1 H), 7.11–7.13 (m, 5 H), 7.25–7.31 (m, 6 H), 7.41–7.43 (m, 4 H); ^{13}C NMR δ 37.2 (CH_2S), 87.6, 97.5 ($-C\equiv C-$), 110.3, 123.4, 126.8, 127.8, 128.1, 128.2, 128.3, 128.6, 128.7, 131.3, 127.5, 138.6, 148.9; UV (CH_3CN) λ_{max} (log ϵ) = 334 (3.53).

(Z)-1,4-Diphenyl-1-[[(4-methylphenyl)thio]methyl]but-1-en-3-yne (6b) was chromatographed (silica gel, 80 g, 225–400 mesh, hexanes, $R_f = 0.10$) to give a yellow liquid (220 mg, 76%): HRCIMS m/z 340.1295, calcd for $C_{24}H_{20}S$ 340.1285; IR (CCl_4, cm^{-1}) 3024 vs, 2923 vs, 2862 s, 2191 w, 1895 w, 1800 w, 1596 s, 1512 vs, 1485 vs, 1443 vs, 1380 w, 1311 m, 1285 m, 1218 m, 1180 m, 1107 m, 1071 m, 1027 s, 913 s, 875 m; ^1H NMR δ 2.24 (s, 3 H), 3.83 (s, 2 H), 6.02 (s, 1 H), 7.01–7.02 (m, 4 H), 7.28–7.32 (m, 6 H), 7.43–7.48 (m, 4 H); ^{13}C NMR δ 21.0 (CH_3), 37.0 (CH_2S), 87.6, 97.5 ($-C\equiv C-$), 110.1, 123.4, 127.9, 128.1, 128.2, 128.3, 128.6, 128.9, 131.3, 134.4, 136.4, 138.7, 149.2; UV (CH_3CN) λ_{max} (log ϵ) = 334 (3.92).

(Z)-1,4-Diphenyl-1-[[(3-chlorophenyl)thio]methyl]but-1-en-3-yne (6c) was chromatographed (silica gel, 80 g, 225–400 mesh, hexanes, $R_f = 0.11$) to give yellow liquid (270 mg, 77%): HRCIMS m/z 360.0745, calcd for $C_{23}H_{17}ClS$ 360.0739; IR (CCl_4, cm^{-1}); ^1H NMR δ 3.66 (s, 2 H), 5.92 (s, 1 H), 6.87–6.94 (m, 1 H), 6.97 (s, 1 H), 6.99–7.16 (m, 2 H), 7.18–7.23 (m, 6 H), 7.28–7.31 (m, 2 H), 7.36–7.39 (m, 2 H); ^{13}C NMR δ 36.6 (CH_2S), 67.4, 97.6 ($-C\equiv C-$), 111.0, 123.2, 126.8, 127.0, 127.8, 128.2, 128.4, 128.7, 128.8, 129.4, 131.3, 133.8, 138.3, 139.7, 148.1; UV (CH_3CN) λ_{max} (log ϵ) = 332 (3.99).

General Procedure for the Cyclization of the Intermediate 1:1 Addition Products. 2,5-Diphenyl-3-(phenylmethyl)thiophene (5a). A flask equipped with a magnetic stirbar, a rubber septum port, and a water condenser topped with a T tube leading to a source of N_2 was charged with a mixture of KOH (25 mg, 0.46 mmol) in DMSO (10 mL). 1,4-Diphenyl-1-[(phenylthio)methyl]but-1-en-3-yne (**6a**, 150 mg, 0.46 mmol) was added slowly. After the addition of the alkyne, the reaction mixture was stirred at rt for 1 h. TLC analysis (hexanes) showed the absence of **6a**. Ether (40 mL) was added to the reaction solution and this reaction mixture was poured into a mixture of ice (15 g) and saturated NH_4Cl solution (15 mL). The organic layer was washed with saturated NaCl solution (25 mL) and dried (4 Å molecular sieves 10 h), the volatile materials were removed *via* rotatory evaporator, and the residue was chromatographed (225–400 mesh, hexanes) to give colorless crystals (120 mg, 80%, mp 94–95 °C (lit.[7] mp 94–95 °C).

Cyclization of **6b** gave **5b** which was chromatographed (225–400 mesh, hexanes) to give colorless crystals (120 mg, 90%, mp 107–108 °C).

Cyclization of **6c** gave **5c** which was chromatographed (225–400 mesh, hexanes) to give colorless crystals (170 mg, 85%, mp 80–81 °C).

5'-Phenyl-4'-(2-thienylmethyl)-2,2'-bithiophene (7a) was prepared from **4a** (0.11 mL, 0.9 mmol), KOH (50 mg, 0.9 mmol) in DMSO (15 mL), and 1,4-bis(2-thienyl)-1,3-butadiyne (**3b**, 200 mg, 0.9 mmol) using the general procedure described above. The residue was chromatographed (hexanes, $R_f = 0.17$). Recrystallization from methanol gave colorless crystals (200 mg, 65%, mp 70–71 °C): HRCIMS m/z 338.0235, calcd for $C_{19}H_{14}S_3$ 338.0257; IR (CCl_4, cm^{-1}) 2953 s 1203 vs, 1174 s, 1057 m; ^1H NMR δ 4.12 (s, 2 H), 6.78 (m, 1 H), 6.90–6.96 (m, 2 H), 7.04 (s, 1 H), 7.10–7.15 (m, 3 H), 7.31–7.38 (m, 3 H), 7.44–7.46 (m, 2H); ^{13}C NMR δ 29.1 (CH_2), 123.5, 123.8, 124.3, 124.9, 126.4, 126.8, 127.7, 128.6, 129.0, 133.5, 135.7, 136.0, 137.1, 138.0, 143.6; UV (CH_3CN) λ_{max} (log ϵ) = 324 (3.87).

5'-(3-Chlorophenyl)-4'-(2-thienylmethyl)-2,2'-bithiophene (7b) was chromatographed (hexanes, $R_f = 0.21$) and crystallized from methanol to give light yellow crystals (250 mg, 73%, mp 94–95 °C): HRCIMS m/z 371.9887, calcd for $C_{19}H_{13}ClS_3$ 371.9867; IR (CCl_4, cm^{-1}) 3072 w, 2908 w, 1591 vs, 1564 s, 1482 s, 1429 s, 1230 m, 1189 w, 1097 m, 1042 w, 1004 w, 883 m, 834 vs, 801 vs; ^1H NMR δ 4.10 (s, 2 H), 6.78–6.79 (m, 1 H), 6.91 (dd, $J = 3$, 5 Hz, 1 H), 6.97 (dd, $J = 3$, 5 Hz, 1 H), 7.03 (s, 1 H), 7.13–7.17 (m, 3 H), 7.28–7.31 (m, 3 H), 7.44 (s, 1 H); ^{13}C NMR δ 29.1 (CH_2), 123.7, 123.9, 124.5, 125.0, 126.4, 126.8, 127.1, 127.8, 129.0, 129.8, 134.4, 135.3, 136.1, 136.4, 136.8, 143.2; UV (CH_3CN) λ_{max} (log ϵ) = 329 (3.58).

5'-(4-Fluorophenyl)-4'-(2-thienylmethyl)-2,2'-bithiophene (7d) was chromatographed (hexanes, $R_f = 0.13$) and then recrystallized from methanol to give colorless crystals (216 mg, 66%, 89–90 °C): HRCIMS m/z 356.0190, calcd for $C_{19}H_{13}FS_3$ 356.0163; IR (CCl_4, cm^{-1}) 3073 w, 2910 w, 1601 m, 1506 vs, 1463 w, 1430 w, 1231 vs, 1150 m, 1095 w, 883 vs, 801 vs, 769 vs; ^1H NMR δ 4.09 (s, 2 H), 6.79 (m, 1 H), 6.93 (dd, $J = 3$, 5 Hz 1 H), 7.00 (dd, $J = 3$, 5 Hz, 1 H), 7.04 (s, 1 H), 7.02 (t, $J = 3$ Hz, 2 H), 7.08–7.16 (m, 2 H), 7.20 (d, $J = 5$ Hz, 1 H), 7.40–7.43 (m, 2 H); ^{13}C NMR δ 29.1 (CH_2), 115.7 (d, $J = 23$ Hz), 123.6, 123.9, 124.4, 124.9, 126.3, 126.9, 127.8, 129.6, 130.8 (d, $J = 8$ Hz), 135.8, 136.2, 136.8, 137.0, 143.5, 162.44 (d, $J = 248$ Hz); UV (CH_3CN) λ_{max} (log ϵ) = 326 (3.69).

5'-(2-Furyl)-4'-(2-thienylmethyl)-2,2'-bithiophene (7c) was chromatographed (hexanes, $R_f = 0.15$) and then recrystallized from methanol to give colorless crystals (220 mg, 74%, 45–46 °C): HRCIMS m/z 328.0082, calcd for $C_{17}H_{12}OS_3$ 328.0050; IR (CCl_4, cm^{-1}) 3116 m, 3074 m, 2910 w, 2847 w, 1586 m, 1496 vs, 1431 vs, 1381 m, 1296 w, 1226 vs, 1156 s, 1111 w, 1078 m, 1026 vs, 1000 m, 964 w; ^1H NMR δ 4.24 (s, 2 H), 6.40 (s, 2 H), 6.79–6.80 (m, 1 H), 6.88–6.89 (m, 1 H), 6.90–6.96 (m, 2 H), 7.10–7.14 (m, 3 H), 7.40 (s, 1 H); ^{13}C NMR δ 23.6 (CH_2), 107.1, 111.7, 123.6, 123.8, 124.4, 125.0, 126.4, 126.8, 127.1, 127.7, 135.3, 136.3, 136.8, 141.7, 142.5, 148.1; UV (CH_3CN) λ_{max} (log ϵ) = 346 (3.62).

3'-(2-Thienylmethyl)-2,2':5',2''-terthiophene (8) was chromatographed (hexanes, $R_f = 0.17$) and then recrystallized from methanol to give yellowish liquid (230 mg, 71%); HRCIMS m/z 343.9843, calcd for $C_{17}H_{12}S_4$ 343.9821; IR (CCl_4, cm^{-1}) 3075 s, 2924 s, 1784 w, 1728 m, 1586 w, 1505 s, 1431 vs, 1383 s, 1229 vs, 1114 m, 1077 m, 1043 s; ^1H NMR δ 4.21 (s, 2 H), 6.79–6.80 (m, 1 H), 6.89–6.91 (m, 1 H), 6.94–6.95 (m, 1 H), 6.98 (s, 1 H), 7.01–7.02 (s, 1 H), 7.10–7.15 (m, 4 H), 7.25–7.26 (m, 1 H); ^{13}C NMR δ 29.4 (CH_2), 123.7, 123.9, 124.4, 125.0, 125.8, 126.2, 126.5, 126.8, 127.6, 127.7, 130.6, 135.0, 135.6, 136.7, 136.8, 142.9; UV (CH_3CN) λ_{max} (log ϵ) = 345 (3.97).

2-(3-Chlorophenyl)-5-(3-thienyl)-3-(3-thienylmethyl)-thiophene (9) was prepared from 1,4-bis(3-thienyl)-1,3-butadiyne (**3c**) as described above using thiol **4c**. The residue was chromatographed (silica gel, 40 g, 225–400 mesh, hexanes, $R_f = 0.10$) and then recrystallized from methanol to give colorless crystals (200 mg, 59%, mp 77–78 °C): HRCIMS m/z 371.9882, calcd for $C_{19}H_{13}ClS_3$ 371.9868; IR (CCl_4, cm^{-1}) 3108 w, 3070 w, 2924 w, 2851 w, 1747 w, 1593 vs, 1564 vs, 1535 w, 1482 vs, 1454 s, 1403 s, 1341 w, 1296 w, 1253 m, 1221 w, 1198 m, 1097 s, 1081 vs, 1017 w, 985 m, 938 w, 879 s; ^1H NMR δ 3.94 (s, 2 H), 6.88–6.89 (m, 2 H), 6.98 (s, 1 H), 7.22–7.31 (m, 7 H), 7.42 (s, 1 H); ^{13}C NMR δ 29.7 (CH_2), 119.6, 121.1, 125.7, 125.8, 126.3, 126.4, 127.0, 127.4, 127.9, 128.8, 129.7, 134.3, 135.0, 135.4, 135.7, 137.0, 137.8, 140.7. UV (CH_3CN) λ_{max} (log ϵ) = 312 (4.14). Anal. Calcd for $C_{19}H_{13}ClS_3$: C, 61.21; H, 3.39. Found: C, 61.07; H, 3.60.

2-(4-Fluorophenyl)-5-(3-thienyl)-3-(3-thienylmethyl)-thiophene (10) was prepared from **3c** as described above using thiol **4e**. The residue was chromatographed (silica gel, 40 g, 225–400 mesh, hexanes, $R_f = 0.11$) and recrystallized from methanol to give colorless crystals (230 mg, 69%, mp 103–104 °C): HRCIMS m/z 356.0160, calcd for $C_{19}H_{13}FS_3$ 356.0163; IR (CCl_4, cm^{-1}) 3112 w, 3053 w, 2908 w, 2850 w, 1891 w, 1756 w, 1649 w, 1603 m, 1560 w, 1530 m, 1505 vs, 1465 m, 1402 w, 1298 w, 1226 vs, 1158 vs, 1095 w, 1081 w, 1015 w, 967 w, 938 w; ^1H

NMR δ 3.92 (s, 2 H), 6.87–6.89 (m, 2 H), 6.98 (s, 1 H), 7.02–7.06 (m, 2 H), 7.23–7.24 (m, 2 H), 7.27–7.28 (m, 1 H), 7.30–7.31 (m, 1 H), 7.35–7.38 (m, 2 H); ^{13}C NMR δ 29.6 (CH_2), 115.5 (d, J = 22 Hz), 119.4, 121.0, 125.7, 125.8, 126.1, 126.3, 128.0, 130.0, 130.6 (d, J = 8 Hz), 135.2, 136.1, 136.4, 137.3, 141.0, 162.2 (d, J = 247 Hz); UV (CH_3CN) λ_{max} (log ϵ) = 309 (3.65). Anal. Calcd for $C_{19}H_{13}FS_3$: C, 64.04; H, 3.65. Found: C, 63.75; H, 3.72.

3-(3-Thienylmethyl)-5-(3-thienyl)-2,2′-bithiophene (11) was prepared from **3c** as described above using thiol **4f.** The residue was chromatographed (silica gel, 40 g, 225–400 mesh, hexanes, R_f = 0.10). Recrystallization from methanol gave colorless crystals (220 mg, 68%, mp 98–99 °C): HREIMS m/z 343.9826, calcd for $C_{17}H_{12}S_4$ 343.8821; IR (CCl_4, cm^{-1}) 3113 m, 3073 m, 2911 s, 2805 m, 1788 w, 1748 w, 1658 w, 1537 m, 1509 s, 1463 s, 1427 vs, 1463 vs, 1400 vs, 1384 vs, 1351 m, 1296 m, 1252 s, 1217 s, 1199 s, 1182 s, 1151 m, 1080 vs, 1049 w, 999 m, 938 m; ^{1}H NMR δ 4.08 (s, 2 H), 6.93–6.95 (m, 3 H), 7.03 (m, 1 H), 7.09 (m, 1 H), 7.23–7.33 (m, 5 H); ^{13}C NMR δ 30.1 (SCH_2), 119.5, 121.2, 125.4, 125.7, 125.9, 126.3, 126.4, 127.5, 128.1, 129.9, 135.0, 135.6, 137.1, 137.2, 140.5; UV (CH_3CN) λ_{max} (log ϵ) = 330 (4.33).

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Supplementary Material Available: ^{1}H NMR spectra of **5a–5d**, **5f–5h**, **6a–6c**, **7a–7d**, and **8–11** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.