JOC*Note*

Orthogonally Functionalized Oligomers for Controlled Self-Assembly

Austen K. Flatt, Yuxing Yao, Francisco Maya, and James M. Tour*

Department of Chemistry and Center for Nanoscale Science and Technology, MS 222, Rice University, 6100 Main Street, Houston, Texas 77005

tour@rice.edu

Received December 15, 2003

Abstract: The synthesis of molecules terminated with complementary thiol-protecting groups is described. The target compounds contain functionalities on one end known to form self-assembled monolayers on metal surfaces while at the other end an intact thioacetate is present whereby self-assembly may again occur after an in situ deprotection. Self-assembly data is reported for selected compounds to assess their efficacy in surface adhesion.

We recently reported the advantages of using the mononitro thiol−thioacetate terminated oligo(phenylene ethynylene) (OPE) (**1**) for use in the NanoCell, a functioning molecular memory device.[1] We report here the synthesis of this and other related molecules. The structures of the target compounds **1**−**6** are shown in Figure 1. We have designed these compounds to allow for self-assembly of the molecules via the free thiol[2,3] or nitrile[4] while protecting the other sulfur atom as a thioacetate to ensure molecular directionality and to inhibit cross-linking if self-assembled monolayer (SAM) assembly on nanorods is desired. Following initial assembly, the acetate can be removed with NH_4OH or acid to afford the thiolate or thiol, respectively, which can be assembled onto another metallic material.[5] For the mononitro compounds **1** and **6**, this affords a monolayer with all the nitro groups oriented in the same direction, a result made possible only by the orthogonal protection scheme outlined here.[6]

To exploit the orthogonally functionalized approach, the syntheses were accomplished with the use of a Boc-protected sulfur atom that could be deprotected using trifluoroacetic acid (TFA) to afford the free thiol,[7] leaving the thioacetate moiety on the other end intact.

The synthesis of the *S*-Boc-protected intermediate **7** is shown in Scheme 1. Treatment of 1,4-diiodobenzene with *tert*-butyllithium at −78 °C, followed by the addition of sulfur,[8] and quenching with di(*tert*-butyl)dicarbonate (Boc_2O) afforded the desired compound **7** in moderate yield.

The synthesis of the mononitro compound **1** is shown in Scheme 2. Diazotization of 4-bromo-2-nitroaniline[9] followed by iodination afforded the desired aryl iodide **8**, which was selectively coupled with trimethylsilylacetylene to give **9**[3] in high yield. Compound **9** was coupled with 1-ethynyl-4-thioacetylbenzene[8] to afford **10**. Deprotection of the alkyne using tetrabutylammonium fluoride[8] afforded the terminal alkyne **11**, which was coupled with **7** to give the orthogonally protected **12** in moderate yield. Chemoselective cleavage of the Boc group using TFA in anisole and methylene chloride yielded the target molecule **1** with the nitro group exclusively at the 3′-position oriented toward the thiol.

To examine the effects of the nitro group on the electrical characteristics of the series of molecules, the unfunctionalized compound **2** was synthesized. The synthesis of **2** is shown in Scheme 3 and began by coupling **13**[10] with 1-ethynyl-4-thioacetylbenzene[8] to afford the desired product **14**. The alkyne was then deprotected to afford **15**. Without the addition of AcOH and Ac_2O, the acetate was also lost. Compound **15** was then coupled with **7** to give **16**. Treatment of **16** with TFA afforded the target molecule **2** in fair yield. Also shown in Scheme 3 is the synthesis of the more soluble diethyl-derivatized compound **3**, accomplished by coupling 1-ethynyl-4-thioacetylbenzene[8] with **17** to give **18**. Intermediate **18** was then deprotected to give the alkyne **19**, which was coupled with **7** to give **20**. Chemoselective deprotection of **20** using TFA afforded the target compound **3**.

With several OPEs synthesized, we focused on making the aliphatic thiol−thioacetate-derivatized molecule **4**[11] as shown in Scheme 4. Although the synthesis did not require the use of a Boc-protected intermediate, this compound was needed as a control for electrical testing. Commercially available 1,12-dibromododecane was converted to the dithioacetate using potassium thioacetate in DMF[12] to afford **21**.[13] The dithioacetate was deprotected using NaOH in acetone to give the dithiol **22**.[14] The dithiol was then monoprotected using 1 equiv of acetic anhydride in pyridine and methylene chloride to afford the target molecule **4**.

In an effort to synthesize similar molecules with alternative metal bonding groups, we turned our focus to synthesizing **5** (Scheme 5). Compound **5** allows for self-assembly via the thiolate (after deprotection) with the resulting SAM terminated with amino groups that could

(1) Tour, J. M.; Cheng, L.; Nackashi, D. P.; Yao, Y.; Flatt, A. K.; St. Angelo, S. K.; Mallouk, T. E.; Franzon, P. D. *J. Am. Chem. Soc.* **2003**, *125*, 13279−13283.
(2) Ulman, A. *Chem. Rev.* **1996**, *96*, 1533−1554.
(3) Tour, J. M.; Rawlett, A. M.; Kozaki, M.; Yao, Y.; Jagessar, R. C.; Dirk, S. M.; Price, D. M.; Reed, M. A.; Zhou, C.-W.; Chen, J.; Wang, W.; Campbell, I. *Chem. Eur. J.* **2001**, *7*, 5118−5134.
(4) Steiner, U. B.; Caseri, W. R.; Suter, U. W. *Langmuir* **1992**, *8*, 2771−2777.
(5) Cai, L.; Yao, Y.; Yang, J.; Price, D. W., Jr.; Tour, J. M. *Chem. Mater.* **2002**, *14*, 2905−2909.
(6) Tour, J. M. *Molecular Electronics: Commercial Insights, Chemistry, Devices, Architecture and Programming*; World Scientific: River Edge, NJ,, 2003.
(7) Ohkanda, J.; Lockman, J. W.; Kothare, M. A.; Qian, Y.; Blaskovich, M. A.; Sebti, S. M.; Hamilton, A. D. *J. Med. Chem.* **2002**, *45*, 177−188.
(8) Pearson, D. L.; Tour, J. M. *J. Org. Chem.* **1997**, *62*, 1376−1387.
(9) Wilson, G. J.; Hunt, F. C. *Aust. J. Chem.* **1983**, *36*, 2317−2326.
(10) Lavastre, O.; Ollivier, L.; Dixneuf, P. H. *Tetrahedron* **1996**, *52*, 5495−5504.
(11) Bain, C. D.; Troughton, E. B.; Tao, Y. T.; Evall, J.; Whitesides, G. M.; Nuzzo, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 321−335.
(12) Zheng, T.-C.; Burkart, M.; Richardson, D. E. *Tetrahedron Lett.* **1999**, *40*, 603−606.
(13) Kushmerick, J. G.; Holt, D. B.; Pollack, S. K.; Ratner, M. A.; Yang, J. C.; Schull, T. L.; Naciri, J.; Moore, M. H.; Shashidhar, R. *J. Am. Chem. Soc.* **2002**, *124*, 10654−10655.
(14) Hall, W. P.; Reid, E. E. *J. Am. Chem. Soc.* **1947**, *65*, 1466−1468.

10.1021/jo035821b CCC: $27.50
Published on Web 02/04/2004

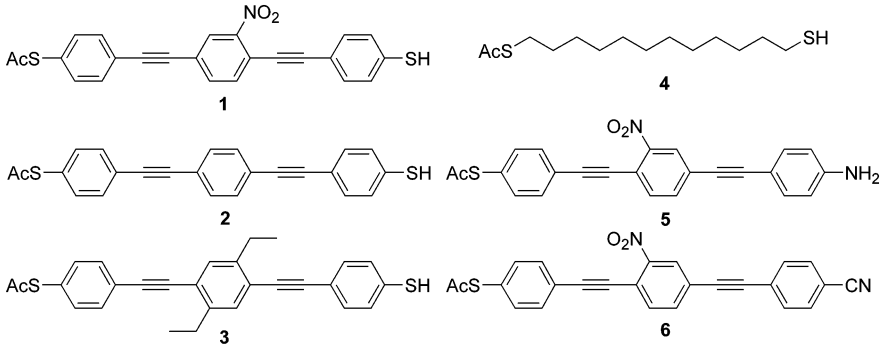


FIGURE 1. Structures of the target compounds **1**−**6**.

SCHEME 1. Synthesis of the *S*-Boc Intermediate 7

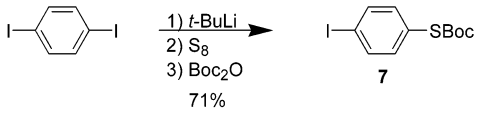


TABLE 1. Chemical Self-Assembly Data for Compounds 1, 2, and 4 in THF for 40 min

	thickness (nm)	
compd	found[a]	calcd[b]
1	2.5	2.3
2	2.1	2.3
4	2.2	1.8

[a] Value measured by ellipsometry with ca. ± 0.2 nm error in the measurement. [b] The theoretical thickness calculated by molecular mechanics including the Au−S bond and a tilt angle of 20° for the OPEs[17]and 33° for the alkane.[2,18]

then form coordination compounds with metallic nanorods and nanoparticles. Alkyne **23**[15] was coupled with **9** to afford the desired compound **24**. Intermediate **24** was then deprotected to give **25** and coupled with 1-iodo-4-thioacetylbenzene[8] to afford the target compound **5** in fair yield.

Also shown in Scheme 5 is the synthesis of the nitrile-terminated OPE **6**, produced in order to take advantage of the known bonding interactions between nitriles and metals.[4,16] The alkyne **26**[16] was coupled with **9** to give **27**, followed by deprotection to afford the alkyne **28**. Compound **28** was then coupled with 4-iodothioacetylbenzene[8] to yield the target compound **6**.

With the completed molecules in hand, we carried out SAM formation on gold for compounds **1**, **2**, and **4**. Using ellipsometry, we compared the observed and theoretical thicknesses (Table 1) to assess monolayer formation. Immersion times were limited to 40 min, due to the rapid assembly of thiols on gold compared to thioacetates.[5,17] Assembly data for all three compounds are close to the predicted values. Self-assembly data obtained corroborate with our previous published data.[1]

In conclusion, we have synthesized several new orthogonally functionalized compounds for controlled self-assembly applications. Thiol−thioacetate derivatized OPEs were accessed via a convenient Boc protection−deprotection scheme to afford the free thiol in the presence of a thioacetate. Self-assembly studies revealed effective monolayer formation of selected compounds on gold.

Experimental Section

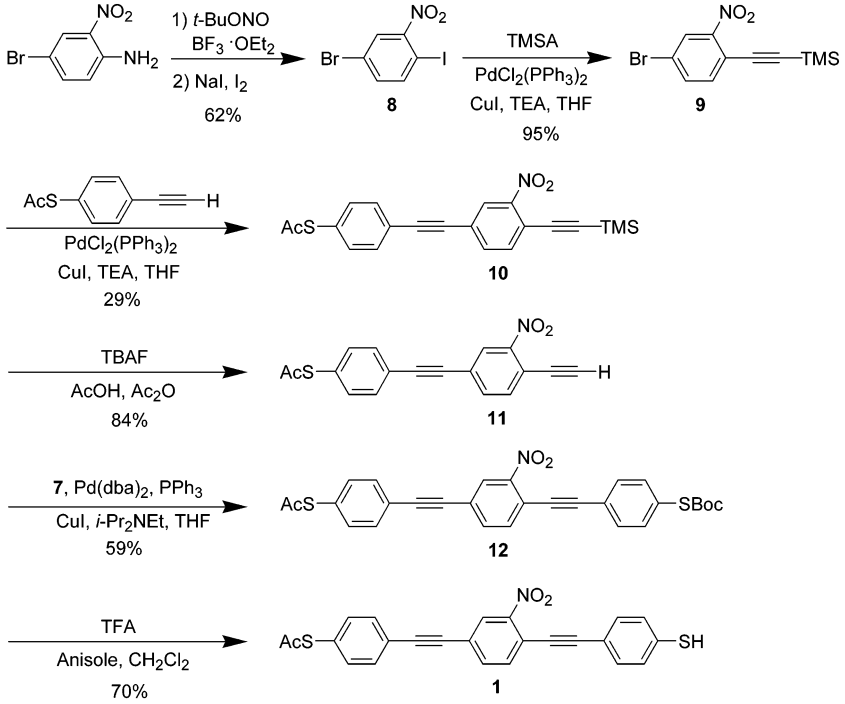
Thioacetic Acid *S*-[4-[4-(4-mercaptophenylethynyl)-3-nitrophenylethynyl]phenyl] Ester (1). To a 50 mL round-bottom flask containing a stir bar were added **12** (0.25 g, 0.47 mmol), CH_2Cl_2 (6.0 mL), anisole (0.5 mL), and TFA (1.0 mL). The reaction was allowed to stir at room temperature for 4 h. EtOAc (25 mL) was then added and washed with water (3×). The organic layer was dried using anhydrous $MgSO_4$, and the solvent was removed in vacuo. The residue was dissolved in a minimum amount of CH_2Cl_2, and hexanes were then added. Care was taken to evaporate only the CH_2Cl_2 on the rotary evaporator. The solid was filtered, washed with hexanes, and purified by flash chromatography on silica gel (CH_2Cl_2) to afford the product as an orange solid (0.125 g, 70%): mp 105−108 °C; FTIR (KBr) 2564, 2209, 1709, 1587, 1539, 1503, 1398, 1343, 1270, 1119, 1094, 1014, 953, 826, 620, 597, 526 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 1.5 Hz, 1H), 7.71 (dd, J = 8.1, 1.5 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.58 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 3.58 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.4, 149.6, 135.5, 134.6, 134.5, 134.0, 132.8, 132.5, 129.5, 129.0, 127.9, 123.9, 123.4, 119.4, 118.5, 98.9, 92.9, 88.6, 85.5, 30.6; HRMS calcd for $C_{24}H_{15}NO_3S_2$ 429.0493, found 429.0496.

Thioacetic Acid *S*-[4-[4-(4-mercaptophenylethynyl)-phenylethynyl]phenyl] Ester (2). To a 100 mL round-bottom flask containing a stir bar were added **16** (0.56 g, 1.16 mmol), CH_2Cl_2 (18 mL), anisole (1.5 mL), and TFA (3.0 mL). The reaction was allowed to stir at room temperature for 4 h upon which time an orange precipitate had formed. Hexanes (50 mL) was added, and the solid was filtered, washed with hexanes, and purified by flash chromatography on silica gel (3:1 CH_2Cl_2/hexanes) to afford the product as a white solid (0.29 g, 65%): mp 190 °C dec; FTIR (KBr) 2567, 2209, 1920, 1708, 1689, 1584, 1512, 1479, 1403, 1351, 1304, 1267, 1118, 1094, 1014, 947, 837, 822, 619, 596, 543, 524, 506, 448, 415 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.6 Hz, 2H), 7.50 (m, 4H), 7.40 (d, J = 8.6 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 3.54 (s, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 134.5, 132.39, 132.38, 131.8, 131.7, 129.1, 128.5, 124.5, 123.5, 122.9, 120.3, 91.1, 90.9, 90.7, 89.7, 30.5; HRMS calcd for $C_{24}H_{16}OS_2$ 384.0643, found 384.0636. Anal. Calcd: C, 74.97; H, 4.19. Found: C, 74.68; H, 4.12.

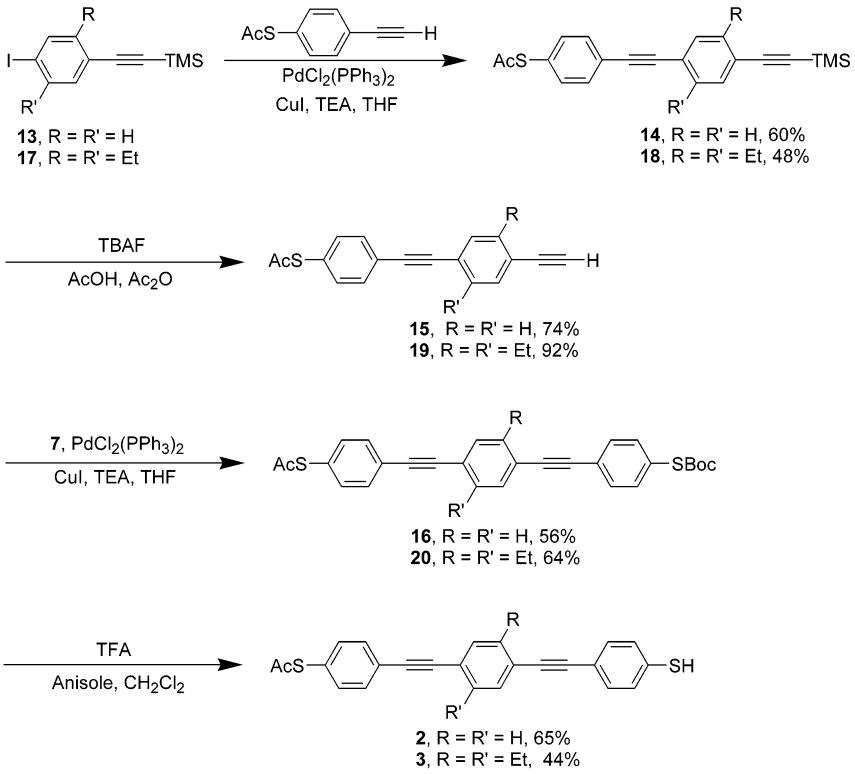
Thioacetic Acid *S*-[4-[2,5-diethyl-4-(4-mercaptophenylethynyl)phenylethynyl]phenyl] Ester (3). Compound **20** (0.228 g, 0.4 mmol) was dissolved in CH_2Cl_2 (5 mL) followed by addition of anisole (0.5 mL) and TFA (1 mL). The reaction was stirred at room temperature for 4 h. The mixture was dissolved in EtOAc, and water (20 mL) was added. The organics were extracted with EtOAc (3×) and dried over anhydrous $MgSO_4$

(15) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, *8*, 627−630.
(16) Dirk, S. M.; Tour, J. M. *Tetrahedron* **2003**, *59*, 287−293.
(17) Tour, J. M.; Jones, L., II; Pearson, D. L.; Lamba, J. S.; Burgin, T. P.; Whitesides, G. W.; Allara, D. L.; Parikh, A. N.; Atre, S. *J. Am. Chem. Soc.* **1995**, *117*, 9529−9534.
(18) Mbindyo, J. K. N.; Mallouk, T. E.; Mattzela, J. B.; Kratochvilova, I.; Razavi, B.; Jackson, T. N.; Mayer, T. S. *J. Am. Chem. Soc.* **2002**, *124*, 4020−4026.

SCHEME 2. Synthesis of the Mononitro Compound 1



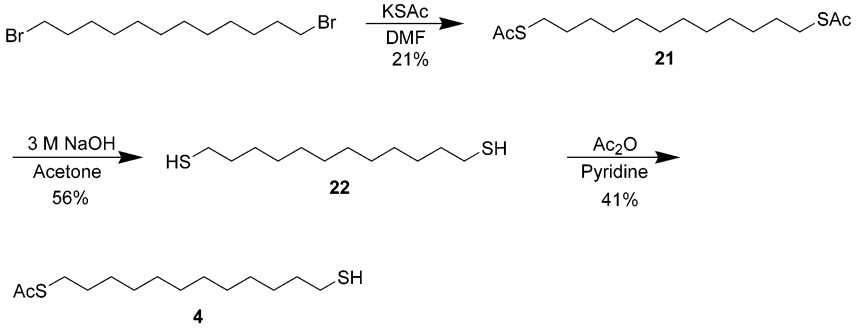
SCHEME 3. Synthesis of Compounds 2 and 3



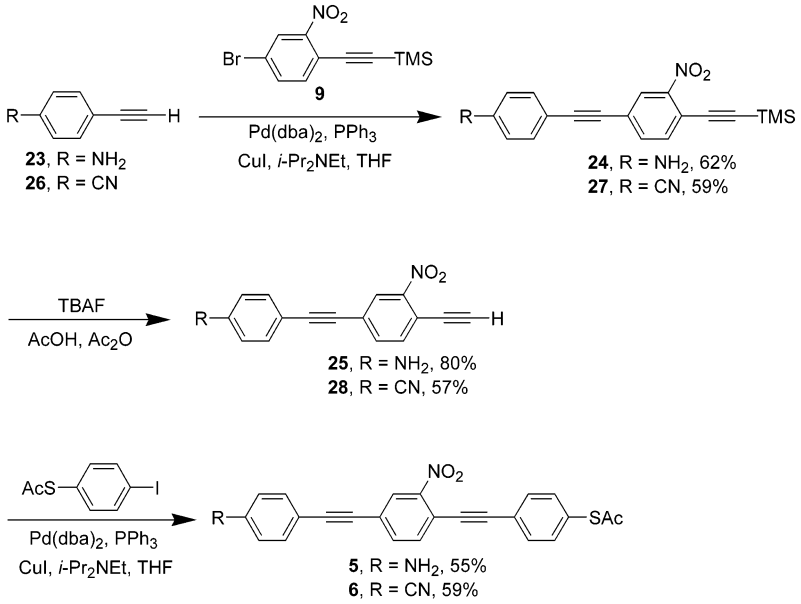
followed by removal of the solvent in vacuo. Flash chromatography (1:1 hexane/CH_2Cl_2) afforded the desired product (0.080 mg, 44%) as a sticky light brown residue: IR (KBr) 3679, 3019, 2968, 2870, 2402, 2209, 1704, 1593, 1495, 1404, 1359, 1216, 1119, 950, 828, 794, 750, 670, 616 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (m, 3H), 7.44 (m, 5H), 7.28 (m, 2H), 3.55 (s, 1H), 2.86 (m, 4H), 2.46 (s, 3H), 1.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 143.8, 143.6, 137.4, 134.4, 132.2, 132.1, 131.8, 131.5, 128.2, 124.8, 122.8, 122.2, 93.9, 93.8, 90.1, 88.7, 46.7, 30.4, 29.9, 27.3, 14.9; HRMS calcd for $C_{28}H_{24}OS_2$ 440.1269, found 440.1270.

Thioacetic Acid *S*-(12-Mercaptododecyl) Ester (4).[11] To a 50 mL round-bottom flask containing a stir bar were added **22** (0.20 g, 0.85 mmol), CH_2Cl_2 (5.0 mL), pyridine (5.0 mL), and acetic anhydride (0.08 mL). The reaction was allowed to stir at room temperature overnight. The next day, the reaction was concentrated in vacuo. The residue was dissolved in CH_2Cl_2 and purified by flash chromatography on silica gel (CH_2Cl_2) to afford the product as a white solid (0.10 g, 41%): mp 32−34 °C; FTIR (KBr) 2919, 2851, 1697, 1471, 1435, 1355, 1135, 1114, 959, 717, 638 cm^{-1};. ^1H NMR (400 MHz, $CDCl_3$) δ 2.85 (t, J = 8.3 Hz, 2H), 2.51 (quart, J = 8.3, 7.2 Hz, 2H), 2.31 (s, 3H), 1.60 (m, 4H),

SCHEME 4. Synthesis of the Aliphatic Compound 4



SCHEME 5. Synthesis of the Amine (5) and Nitrile (6) Orthogonally Functionalized Thioacetate Compounds



1.34−1.25 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 34.5, 31.1, 29.93, 29.90, 29.85, 29.6, 29.51, 29.47, 29.2, 28.8, 25.1; HRMS calcd for $C_{14}H_{28}OS_2$ 276.1582, found 276.1587. Anal. Calcd: C, 60.81; H, 10.21. Found: C, 61.01; H, 10.30.

Thioacetic Acid *S*-[4-[4-(4-Aminophenylethynyl)-2-nitrophenylethynyl]phenyl] Ester (5). See the general coupling procedure. Used were **25** (0.78 g, 2.97 mmol), 1-iodo-4-thioacetylbenzene[8] (0.91 g, 3.27 mmol), $Pd(dba)_2$ (0.09 g, 0.15 mmol), PPh_3 (0.16 g, 0.60 mmol), CuI (0.06 g, 0.30 mmol), THF (20 mL), and *i*-Pr_2NEt (2 mL, 12 mmol). The reaction was stirred at room temperature for 15 h. The mixture was then poured into water and extracted with EtOAc (2×). The combined organics were washed with brine (2×) and dried over anhydrous $MgSO_4$. The crude materials were purified by flash chromatography on silica gel (12:24:1 hexane/CH_2Cl_2/EtOAc). The collected fractions were concentrated to about 5 mL and then diluted with hexanes; the formed precipitates were filtered to give **5** as orange crystals (0.67 g, 55%): mp 181−183 °C; FTIR (KBr) 3447, 3366, 2214, 2194, 1710, 1626, 1600, 1534, 1518, 1477, 1399, 1348, 1289, 1268, 1121, 1088, 1015, 957, 895, 835, 823, 617, 556, 527 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.18 (d, J = 1.7 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.82 (dd, J = 8.1, 1.5 Hz, 1H), 7.69 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H), 6.73 (d, J = 8.6 Hz, 2H), 5.25 (s, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 193.7, 151.2, 150.2, 135.9, 135.6, 135.4, 134.0, 133.1, 130.4, 127.3, 125.9, 123.3, 115.9, 114.5, 107.6, 97.4, 97.3, 87.1, 85.8, 31.2; HRMS calcd for $C_{24}H_{16}N_2O_3S$ 412.0882, found 412.0879. Anal. Calcd: C, 69.89; H, 3.91; N, 6.79. Found: C, 69.99; H, 3.89; N, 6.71.

Thioacetic Acid *S*-[4-[4-(4-Cyanophenylethynyl)-2-nitrophenylethynyl]phenyl] Ester (6). See the general coupling procedure. Used were **28** (0.35 g, 1.29 mmol), 1-iodo-4-thioacetylbenzene[8] (0.39 g, 1.41 mmol), $Pd(dba)_2$ (0.04 g, 0.06 mmol), PPh_3 (0.07 g, 0.26 mmol), CuI (0.03 g, 0.13 mmol), THF (5 mL), and *i*-Pr_2NEt (0.9 mL, 5.2 mmol). The reaction was stirred at room temperature overnight. The mixture was then diluted with EtOAc/THF (50/50 mL), washed with water (1×) and brine (1×), and dried over anhydrous $MgSO_4$. Flash chromatography on silica gel (CH_2Cl_2) and concentration of the collected fractions in vacuo to about 30 mL followed by filtration gave **6** as an orange solid (0.32 g, 59%): mp 154−156 °C; FTIR (KBr) 2360, 2338, 2222, 1708, 1599, 1538, 1520, 1398, 1341, 1270, 1125, 1091, 960, 830, 611, 554 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.39 (d, J = 1.6 Hz, 1H), 7.99 (dd, J = 8.1, 1.6 Hz, 1H), 7.95 (m, 3H), 7.82 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 192.7, 149.3, 136.0, 135.0, 134.6, 132.7, 132.4, 132.3, 129.8, 127.7, 126.1, 122.8, 122.2, 118.3, 117.1, 111.7, 97.4, 91.7, 90.5, 86.0, 30.4; HRMS calcd for $C_{25}H_{14}N_2O_3S$ 422.0725, found 422.0715.

Acknowledgment. This work was supported by DARPA, ONR, and the Department of Commerce, NIST. The NSF, CHEM 0075728, provided partial funds for the 400 MHz NMR. We thank Dr. Ian Chester of FAR Research, Inc., for trimethylsilylacetylene.

Supporting Information Available: General experimental procedure for the Castro-Stephens/Sonogashira protocol, experimental procedures for compounds **7**−**27**, NMR data for all new compounds, and monolayer preparation data. This material is available free of charge via the Internet at http://pubs.acs.org.

JO035821B