

Efficient synthesis of thioamide terminated molecular wires

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Received 13 July 2006; revised 31 August 2006; accepted 7 September 2006

Available online 29 September 2006

Abstract—Bis-thioamide terminated ‘molecular wires’ are formed in a high yield under mild conditions from readily synthesised bis-nitrile terminated molecules and aqueous ammonium sulfide in DMF.

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A fundamental question in molecular electronics is the conductivity characteristics of potential ‘molecular wires’ such as oligo(phenylene ethynylene)s (OPEs), in particular when bound between metal electrodes. Recently, methods have been developed with the potential to make conductance measurements on single molecules and the methods and results have been reviewed.¹ Most measurements so far have used thiol terminated molecular wires to link between two gold electrodes.^{1,2} Although measurements on poorly conducting *n*-alkanedithiols show a reasonable agreement between different methods, the same is not true of unsaturated wires such as OPEs, where the conductivity of similar wires varies by several orders of magnitude. Indeed, the conductivity of individual molecules is found to vary substantially using the same measurement method^{3a} and even with time (stochastic switching).^{3b,c,d} For thiol terminated unsaturated wires (unlike the saturated series), it is likely that conductance is dominated by the gold–sulfur contact. Theoretical and experimental studies indicate that small changes in the hybridisation state of sulfur, or how it binds to the gold surface have dramatic effects on the ‘contact resistance’.^{3c,4}

An anchoring group which displays less variation in conductance is crucial for future studies, and the ultimate goal is one which does not provide a significant barrier to electron transport.

A comparison between molecular wires differing only in the contact groups is also important to allow separation of the effects on conductivity of the junctions and the

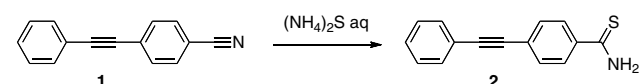
rest of the wire. Currently single examples of the use of pyridyl⁵ and isonitrile⁶ contact groups provide the only published variation from thiol terminated wires in the measurement of single molecule conductivity.

Thiols have other disadvantages as the anchoring group. Free thiols rapidly dimerise and in situ deprotection of thioacetates is usually adopted. Unfortunately, the thioacetate group has a poor stability under the reaction conditions usually used to synthesise molecular wires such as Sonogashira⁷ coupling of terminal alkynes with aryl bromides.^{8,9}

Herein, we report the preparation of two-terminal primary-thioamide substituted OPEs as potential molecular wires. We felt that the thioamide group had many potential advantages over sulfide as a contacting terminus: thioamides should be easily generated from cyanide groups which are stable to the reaction conditions for OPE synthesis; they are easily handled species which are not prone to rapid dimerisation; and contact resistance of the thioamide group should not suffer from the same sensitivity to sulfur rehybridisation as observed for thiols, and may display a two-point binding to a gold surface.¹⁰ We are aware of only one report on the use of thioamide as an anchoring group in the formation of a self assembled monolayer (SAM) on a gold surface.¹¹

The preparation of thioamides by thionation of aryl nitriles using ammonium sulfide in methanol has been reported to occur either at room temperature or under microwave irradiation.¹² We initially sought to apply this method to the conversion of a model nitrile terminated bis-arylalkyne **1**¹³ to the corresponding thioamide **2** (Table 1). The poor solubility of **1**, and most other potential molecular wires, in methanol prompted a

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Table 1. Conversion of aryl nitrile **1** to arylthioamide **2**


| Entry | Equivalent (NH ₄) ₂ S | Solvent | Temp (°C) | Time (h) | Yield ^a 2 (%) |
|-------|--|---------|-----------|----------|---------------------------------|
| 1 | 1.25 | EtOH | 80 | 24 | 10 |
| 2 | 3.0 | EtOH | 80 | 18 | 40 |
| 3 | 5.0 | EtOH | 20 | 30 | 88 |
| 4 | 10.0 | EtOH | 20 | 18 | 89 |
| 5 | 10.0 | DMF | 20 | 0.5 | 89 |
| 6 | 3.0 | DMF | 20 | 0.5 | 88 |
| 7 | 1.5 | DMF | 20 | 1.0 | 92 |

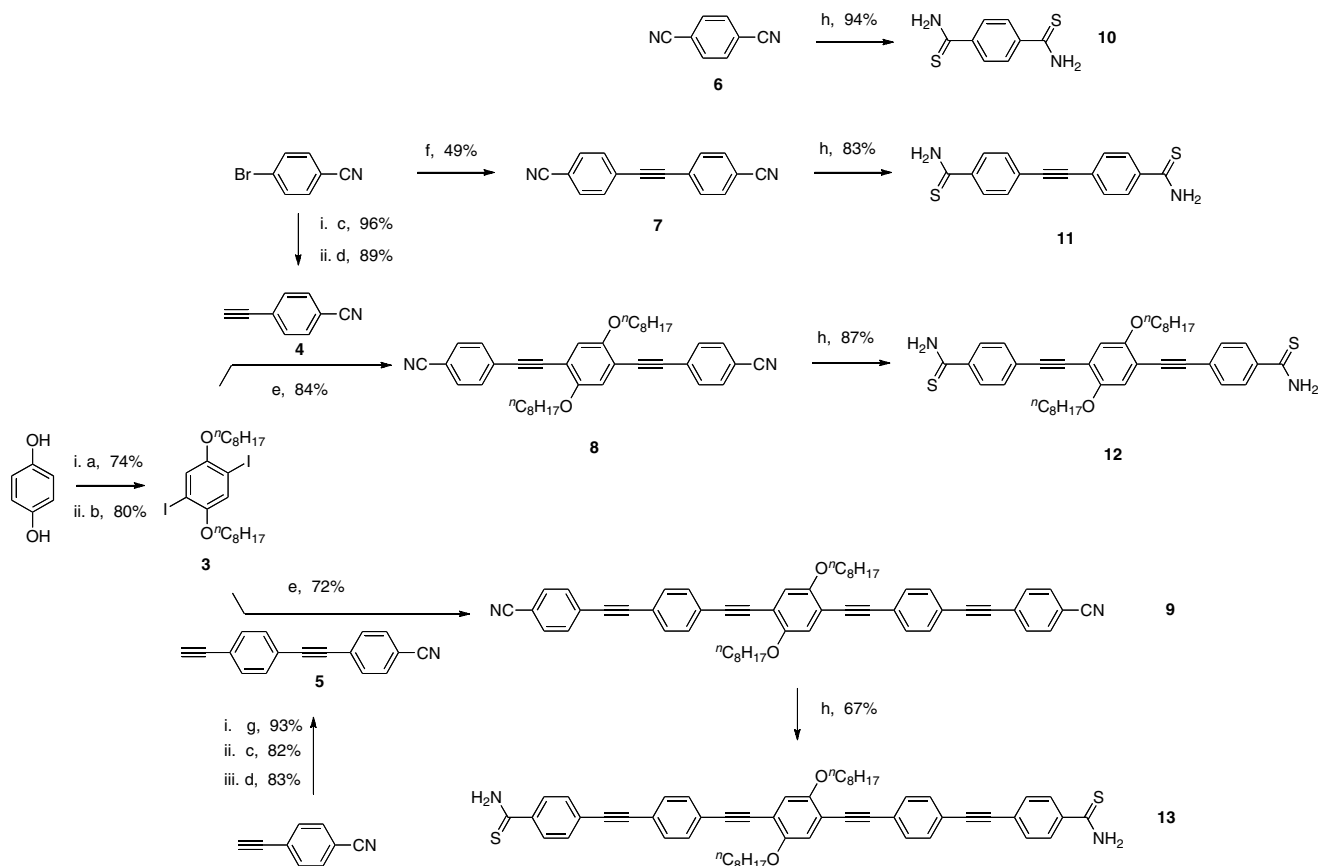
^a Isolated yield.

change to ethanol for the solvent but under these conditions there was no reaction at room temperature and heating to reflux, or use of microwave heating, resulted in significant decomposition (Table 1, entry 1). We have previously observed the susceptibility of OPEs to nucleophilic attack by thiolate. Pleasingly, increasing the amount of ammonium sulfide allowed the isolation of **2** in a good yield (entries 2–4). However, long reaction times prompted the investigation of DMF as the solvent

and we were delighted to observe a clean and high yielding conversion to thioamide **2** in less than an hour with only 1.5 equiv of (NH₄)₂S (entries 5–7).

With an efficient method in hand to convert aryl nitriles to thioamides, we prepared a series of π -conjugated oligo(phenylene ethynylene) molecular wires with two-terminal nitrile functionality via iterative Sonogashira cross-coupling (Scheme 1).

1,4-Diiodo-2,5-di-*n*-octyloxybenzene (**3**) was prepared according to the previously reported procedures¹⁴ and coupled with 4-ethynylbenzonitrile¹⁵ (**4**) to afford bis-nitrile **8**.¹⁶ 4-((4-Ethynylphenyl)ethynyl)benzonitrile (**5**)¹⁷ was prepared by chemoselective Sonogashira coupling between 4-ethynylbenzonitrile and 1-bromo-4-iodobenzene at ambient temperature; coupling of the resultant aryl bromide with trimethylsilylacetylene under identical conditions except that the temperature was increased to 70 °C; and protodesilylation with K₂CO₃/MeOH furnished **5**. Sonogashira coupling of 2 equiv of **5** with core diiodide **3** comprised a straightforward and high yielding synthesis of the bis-nitrile terminated compound **9**. Compounds **8** and **9** were obtained in high purity after flash chromatography of the crude product following



Scheme 1. Reagents and conditions: (a) ⁿC₈H₁₇Br (2.5 equiv), KOH (2.5 equiv), ⁿBu₄N⁺Br⁻ (9 mol %), 80 °C, 16 h; (b) Hg(OAc)₂ (2.5 equiv), CH₂Cl₂, rt, 12 h; (c) trimethylsilylacetylene (1.2 equiv), PdCl₂(PPh₃)₂ (5 mol %), CuI (10 mol %), triethylamine (3.0 equiv), benzene, 70 °C, 16 h; (d) K₂CO₃ (10 equiv), MeOH, CH₂Cl₂, rt 30 min; (e) PdCl₂(PPh₃)₂ (10 mol %), CuI (20 mol %), triethylamine (6.0 equiv), THF, rt, 16 h; (f) 4-ethynylbenzonitrile (1.0 equiv), PdCl₂(PPh₃)₂ (5 mol %), CuI (10 mol %), triethylamine (3.0 equiv), benzene, 70 °C, 16 h; (g) 1-bromo-4-iodobenzene (1.0 equiv), PdCl₂(PPh₃)₂ (5 mol %), CuI (10 mol %), triethylamine (3.0 equiv), THF, rt, 16 h; (h) (NH₄)₂S (6.0 equiv of a 50% wt aqueous solution), DMF, rt, 30 min.

precipitation from the reaction mixture with water, representing an important practical improvement upon the use of earlier described molecular wires incorporating labile protecting groups on sulfur. The '2-ring' analogue 4,4'-(ethyne-1,2-diyl)dibenzonitrile (**7**) is known¹⁸ and displays a good solubility in common organic solvents without the necessity for *n*-alkoxy substituents. Hence **7** was simply obtained via cross-coupling between 4-bromobenzonitrile and 4-ethynylbenzonitrile.

Compounds **7–9**, together with commercially available 1,4-dicyanobenzene (**6**), constitute a suitable array of precursor molecules to the desired bis-thioamide terminated molecular wires.¹⁹

The conditions developed for thioamide synthesis above were applied to bis-nitriles **6–9** and 3 equiv of ammonium sulfide was found to be optimal for the clean thio-amination of each nitrile group. Hence, the conversion to bis-thioamide terminated molecular wires **10–13** was effected under mild conditions in good to excellent yields (Scheme 1).¹⁶

In summary, we have demonstrated the first synthesis of bis-thioamide terminated molecular wires to be straightforward, clean and high yielding. Studies on the electrical characteristics of these molecules will be reported elsewhere.

Acknowledgements

We thank the EPSRC for funding this work through an adventurous chemistry research Grant No. EP/C528824/1.

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- Typical procedures. 4,4'-(2,5-Bis(octyloxy)-1,4-phenylene)bis(ethyne-2,1-diyl)dibenzonitrile (**8**). To a stirred solution of 1,4-diiodo-2,5-bis(octyloxy)benzene (**3**) (586.4 mg, 1.0 mmol), PdCl₂ (17.7 mg, 0.1 mmol), PPh₃ (52.5 mg, 0.2 mmol) and CuI (38.1 mg, 0.2 mmol) in THF (5 mL) was added a solution of 4-ethynylbenzonitrile (254 mg, 2.0 mmol) (**4**) in THF (10 mL) followed by triethylamine (0.84 mL, 6.0 mmol). The mixture was stirred in the dark at room temperature for 16 h before pouring onto H₂O (150 mL), extraction with CH₂Cl₂ (2 × 150 mL), drying over MgSO₄ and concentration in vacuo. Purification by column chromatography (SiO₂, eluted with 2:1 CH₂Cl₂–hexane) gave the *title compound* (**8**) as an off-white solid (492 mg, 84%) mp 104–107 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.57 (4H, d, *J* = 8.7 Hz), 7.52 (4H, d, *J* = 8.7 Hz), 6.94 (2H, s), 3.96 (4H, t, *J* = 6.3 Hz), 1.81–1.74 (4H, m), 1.50–1.42 (4H, m), 1.34–1.14 (16H, m), 0.80 (6H, t, *J* = 7.3 Hz) ppm. ¹³C NMR (100.5 MHz, CDCl₃): δ = 154.10 (s), 132.25 (d), 132.20

(d), 128.49 (s), 118.69 (s), 117.05 (d), 114.03 (s), 111.77 (s), 93.64 (s), 90.49 (s), 69.84 (t), 31.99 (t), 29.54 (t), 29.50 (t), 29.48 (t), 26.27 (t), 22.85 (t), 14.26 (q) ppm. IR (solid): $\nu = 2227$ (w), 2198 (w), 1600 (w), 837 (s) cm^{-1} . LRMS (EI): $m/z = 584$ (M^+ , 100%), 360 (76%). Microanalysis. $\text{C}_{40}\text{H}_{44}\text{O}_2\text{N}_2$ requires: C, 82.15; H, 7.58; N, 4.79. Found: C, 82.12; H, 7.30; N, 4.74.

4,4'-(2,5-Bis(octyloxy)-1,4-phenylene)bis(ethyne-2,1-diyl)dibenzothioamide (12). To a stirred solution of **4,4'-(2,5-bis(octyloxy)-1,4-phenylene)bis(ethyne-2,1-diyl)dibenzonitrile (8)** (117.3 mg, 0.2 mmol) in DMF (5 mL) was added ammonium sulfide (0.16 mL of a 50% wt aqueous solution, 1.2 mmol) and the resultant green solution was stirred at room temperature for 30 min. The solution was then poured onto H_2O (100 mL) and extracted with EtOAc (150 mL) before washing with H_2O (100 mL), drying over MgSO_4 and concentration in vacuo. Purification by column chromatography (SiO_2 , eluted with 1:1 hexane–EtOAc) gave the *title compound (12)* as a yellow solid (114.0 mg, 87%). Mp 198–202 °C (from ethanol). ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$): $\delta = 10.00$ (2H, br s), 9.61 (2H, br s), 8.02 (4H, d, $J = 8.5$ Hz), 7.58 (4H, d, $J = 8.5$ Hz), 7.27 (2H, s), 4.13 (4H, t, $J = 6.0$ Hz), 1.81 (4H, pentet, $J = 7.5$ Hz), 1.56 (4H, pentet, $J = 7.5$ Hz), 1.45–1.25 (16H, m), 0.88 (6H, t, $J = 7.0$ Hz) ppm. ^{13}C NMR (100.5 MHz, $(\text{CD}_3)_2\text{SO}$): $\delta = 198.81$ (s), 153.21 (s), 138.85 (s), 130.56 (d), 127.64 (d), 125.09 (s), 116.63 (d), 113.18 (s), 94.23 (s), 88.39 (s), 68.89 (t), 31.15 (t), 30.63 (t), 28.71 (t), 28.67 (t), 25.53 (t), 22.04 (t), 13.87 (q) ppm. IR (solid): $\nu = 3299$ (w, br), 3156 (w, br), 1643 (m), 1410 (m), 842 (s) cm^{-1} . LRMS (ES^+): $m/z = 653$ ($\text{M}+\text{H}^+$). Microanalysis. $\text{C}_{40}\text{H}_{48}\text{N}_2\text{O}_2\text{S}_2$ requires: C, 73.58; H, 7.41; N, 4.29. Found: C, 73.70; H, 7.43; N, 4.10.

4,4'-(4,4'-(2,5-Bis(octyloxy)-1,4-phenylene)bis(ethyne-2,1-diyl)bis(4,1-phenylene))bis(ethyne-2,1-diyl)dibenzonitrile (9) was prepared as for **8** as a white solid mp 167–168 °C. ^1H NMR (400 MHz, CDCl_3): $\delta = 7.58$ (4H, d, $J = 8.5$ Hz), 7.53 (4H, d, $J = 8.5$ Hz), 7.48–7.43 (8H, m), 6.95 (2H, s), 3.97 (4H, t, $J = 6.5$ Hz), 1.78 (4H, pentet, $J = 6.8$ Hz), 1.56–1.44 (6H, m), 1.36–1.16 (14H, m), 0.80 (6H, t, $J = 7.0$ Hz) ppm. ^{13}C NMR (100.5 MHz, CDCl_3): $\delta = 153.98$ (s), 132.29 (2 × d), 131.92 (d), 131.80 (d), 128.20

(s), 124.46 (s), 122.16 (s), 118.65 (s), 117.14 (d), 114.21 (s), 111.92 (s), 94.72 (s), 93.65 (s), 89.69 (s), 88.67 (s), 69.89 (t), 32.01 (t), 29.58 (t), 29.56 (t), 29.51 (t), 26.29 (t), 22.87 (t), 14.28 (q) ppm. IR (solid): $\nu = 2199$ (w, br), 1595 (m), 834 (s) cm^{-1} . LRMS (MALDI-TOF): $m/z = 784$ (M^+ , 100%). Microanalysis. $\text{C}_{56}\text{H}_{52}\text{O}_2\text{N}_2$ requires: C, 85.68; H, 6.68; N, 3.57. Found: C, 85.41; H, 6.63; N, 3.49.

4,4'-(4,4'-(2,5-Bis(octyloxy)-1,4-phenylene)bis(ethyne-2,1-diyl)bis(4,1-phenylene))bis(ethyne-2,1-diyl)dibenzothioamide (13) was prepared as for **12** except that it was protected from light during the reaction, purification and storage. It was isolated as a yellow solid mp 203–205 °C. ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$): $\delta = 10.01$ (2H, br s), 9.64 (2H, br s), 8.01 (4H, d, $J = 8.5$ Hz), 7.70 (4H, d, $J = 8.8$ Hz), 7.68 (4H, d, $J = 8.8$ Hz), 7.62 (4H, d, $J = 8.5$ Hz), 7.26 (2H, s), 4.12 (4H, t, $J = 6.3$ Hz), 1.81 (4H, pentet, $J = 7.3$ Hz), 1.56 (4H, pentet, $J = 7.8$ Hz), 1.45–1.25 (16H, m), 0.88 (6H, t, $J = 7.0$ Hz) ppm. ^{13}C NMR (100.5 MHz, $(\text{CD}_3)_2\text{SO}$): $\delta = 198.87$ (s), 153.21 (s), 139.15 (s), 131.87 (d), 131.51 (d), 130.99 (d), 127.70 (d), 124.57 (s), 123.04 (s), 122.11 (s), 116.64 (d), 113.17 (s), 94.36 (s), 91.10 (s), 90.92 (s), 88.49 (s), 68.91 (t), 31.22 (t), 28.81 (t), 28.74 (2 × t), 25.61 (t), 22.13 (t), 13.96 (q). IR (solid): $\nu = 3367$ (w, br), 3268 (w, br), 1721 (w), 1625 (w), 1213 (m, br), 833 (s) cm^{-1} . LRMS (ES^-): $m/z = 851$ ($\text{M}-\text{H}^+$, 100%). Microanalysis. $\text{C}_{56}\text{H}_{56}\text{N}_2\text{O}_2\text{S}_2$ requires: C, 78.83; H, 6.62; N, 3.28. Found: C, 78.80; H, 6.57; N, 3.23.

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19. Calculations²⁰ indicate that nitrile terminated molecular wire **6**, between gold electrodes, should have a large zero bias conductance (close to the conductance quantum) due to the close alignment of the LUMO with the Fermi level of gold allowing near-resonant-tunnelling through the LUMO. Although nitriles are not expected to bind strongly enough to gold to be useful as 'fixed' molecular wires, we are investigating the use of **6–9** in dynamic conductance experiments.
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