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Synthesis of an Achiral Isomer of Lipoic Acid As an Anchor Group for SAM Formation on Gold Surfaces

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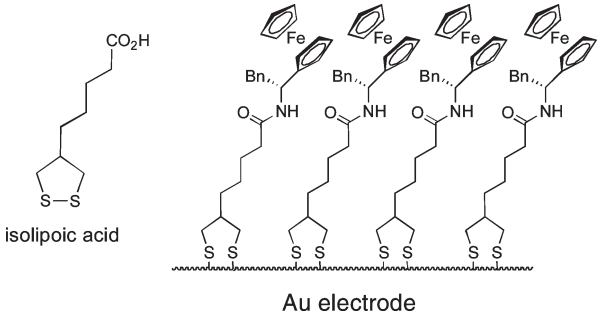

Isolipoic acid, a symmetrical and achiral isomer of the commonly used α-lipoic acid, has previously been overlooked as a tether group for the formation of self-assembled monolayers (SAMs). Here its ready synthesis through a new route and its functionalization with ferrocenyl groups for redox-active SAM formation on gold electrodes are described.

The chemical modification of surfaces is intertwined with many areas of nanoscience. As far as the formation of self-assembled monolayers (SAMs) on gold surfaces is concerned,[1] the chiral compound α-lipoic (thioctic) acid **1** has often been chosen as a starting material for the synthesis of functional (e.g., photo-, redox-, or analyte-responsive) monolayers (Figure 1).[2,3] This is due to its commercial availability, the ease in which it can be derivatized, and the fact that as a cyclic disulfide, it has been identified as a more stable anchor group on gold than related thiols.[2h−j] The examples of SAMs based on derivatives of α-lipoic acid tend to be racemic mixtures; the naturally occurring (*R*)-enantiomer **2** is less widely available. However, the use of a racemic mixture of disulfides for SAM formation would become an issue when surface chirality, a topic of growing importance and interest within nanoscale chemistry,[4] is identified as a factor in the property or behavior of a monolayer. At present, functionalized gold surfaces containing enantiopure molecules tend to be based on thiols rather than disulfides, for example, in amino acid[5] and cyclodextrin[6] based systems.

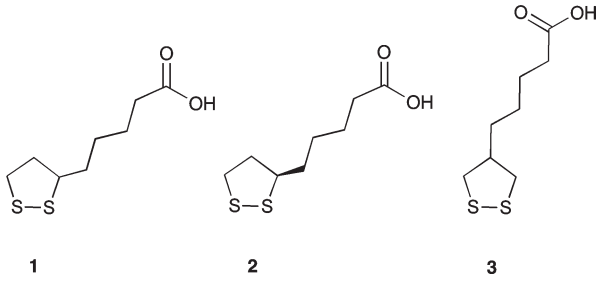

FIGURE 1. Structures of α-lipoic acid (**1** and **2**) and isolipoic acid **3**.

As part of our ongoing interest in developing electrochemical chiral sensors,[7] we looked for alternatives to **1** that would allow appropriately functionalized chiral units to be anchored to a surface via a robust but achiral disulfide linker. Isolipoic acid **3** is a known compound and was identified as a good candidate. However, as far as we are aware, its use in the formation of monolayers has been limited to one previous example,[8] probably due to the laborious procedure reported for its preparation.[9] Here we report an improved procedure for its synthesis from cheap starting materials and its ready modification, allowing it to be a convenient achiral alternative to the ubiquitous **1** for the formation of functional disulfide-based SAMs.

(1) For a general review of SAMs on metal surfaces, see: Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M. *Chem. Rev.* **2005**, *105*, 1103.

(2) For some representive examples of α-lipoic acid tethers on gold surfaces, see: (a) Klajn, R.; Fang, L.; Coskun, A.; Olson, M. A.; Wesson, P. J.; Stoddart, J. F.; Grzybowski, B. A. *J. Am. Chem. Soc.* **2009**, *131*, 4233. (b) Zhao, L. Y.; Davis, J. J.; Mullen, K. M.; Chmielewski, M. J.; Jacobs, R. M. J.; Brown, A.; Beer, P. D. *Langmuir* **2009**, *25*, 2935. (c) Beer, P. D.; Davis, J. J.; Drillsma-Milgrom, D. A.; Szemes, F. *Chem. Commun.* **2002**, 1716. (d) Marois, J. S.; Morin, J. F. *Langmuir* **2008**, *24*, 10865. (e) Faragher, R. J.; Schwan, A. L. *J. Org. Chem.*, **2008**, *73*, 1371 and references cited therein. (f) Thavarungkul, P.; Dawan, S.; Kanatharana, P.; Asawatreratanakul, P. *Biosens. Bioelectron.* **2007**, *23*, 688. (g) Qian, X.; Li, J.; Nie, S. *J. Am. Chem. Soc.* **2009**, *131*, 7540. (h) Sharma, J.; Chhabra, R.; Andersen, C. S.; Gothelf, K. V.; Yan, H.; Liu, Y. *J. Am. Chem. Soc.* **2008**, *130*, 7820. (i) Chow, E.; Hibbert, D. B.; Gooding, J. J. *Anal. Chim. Acta* **2005**, *543*, 167. (j) Zhang, S.; Cardona, C. M.; Echegoyen, L. *Chem. Commun.*, **2006**, 4461 and references cited therein. (k) Abad, J. M.; Gass, M.; Bleloch, A.; Schiffrin, D. J. *J. Am. Chem. Soc.*, **2009**, *131*, 10229 and references cited therein. (l) Davis, J. J.; Orlowski, G, A.; Rahman, H.; Beer, P. D. *Chem. Commun.*, **2010**, *46*, 54−63 and references cited therein.

(3) Derivatives of **1** have also been used to functionalise quantum dots, see for example: (a) Susumu, K.; Uyeda, H. T.; Medintz, I. L.; Pons, T.; Delehanty, J. B.; Mattoussi, H. *J. Am. Chem. Soc.* **2007**, *129*, 13987. (b) Mulrooney, R. C.; Singh, N.; Kaur, N.; Callan, J. F. *Chem. Commun.* **2009**, 686.

(4) (a) For a recent special issue on nanoscale chirality, see: Amabilino, D. B. *Chem. Soc. Rev.*, **2009**, *38*, 669 and references cited therein. (b) Parschau, M.; Passerone, D.; Rieder, K. H.; Hug, H. J.; Ernst, K. H. *Angew. Chem., Int. Ed.*, **2009**, *48*, 4065 and references cied therein.

(5) Nakanishi, T.; Matsunaga, M.; Nagasaka, M.; Asahi, T.; Osaka, T. *J. Am. Chem. Soc.*, **2006**, *128*, 13322 and references cited therein.

(6) Xu, C. H.; Ng, S. C.; Chan, H. S. O., *Langmuir*, **2008**, *24*, 9118 and references cited therein.

(7) (a) Willener, Y.; Joly, K. A.; Moody, C. J.; Tucker, J. H. R. *J. Org. Chem.* **2008**, *73*, 1225. (b) Laurent, P.; Miyaji, H.; Collinson, S. R.; Prokes, I.; Moody, C. J.; Tucker, J. H. R.; Slawin, A. M. Z. *Org. Lett.* **2002**, *4*, 4037.

(8) Fabianowski, W.; Coyle, L. C.; Weber, B. A.; Granata, R. D.; Castner, D. G.; Sadownik, A.; Regen, S. L. *Langmuir* **1989**, *5*, 35.

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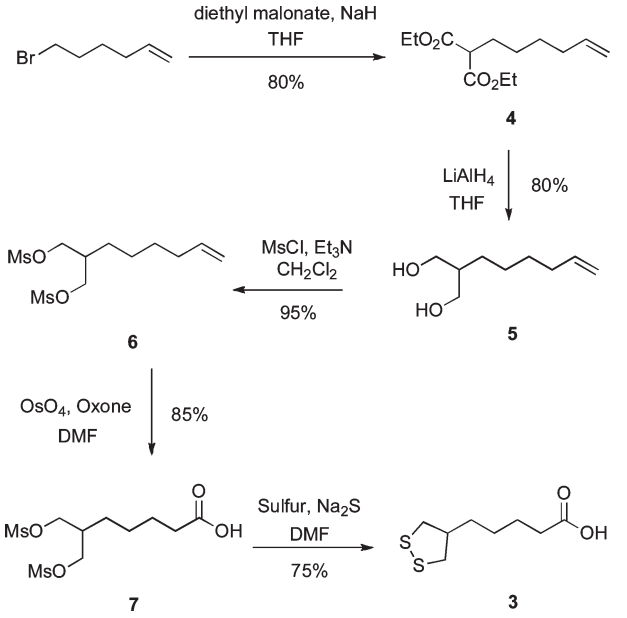
SCHEME 1. Synthetic Scheme for the Preparation of Isolipoic Acid 3



The first step in its synthesis (Scheme 1) involved a nucleophilic substitution between diethyl malonate and 6-bromo-1-hexene, which gave the malonate **4** in 80% yield. While purification by flash column chromatography was necessary on a small scale, this could be replaced by a distillation on a larger scale. This was followed by the reduction of the diester into the diol **5**, which could once again be purified by distillation, in good yield (80%). The diol could then be converted into a dimesylate, and product **6** was obtained in 95% yield after flash column chromatography. It is interesting to note that this is the only purification by chromatography required in this route. The terminal olefin could then be oxidized, using a catalytic amount of osmium tetroxide in the presence of oxone,[10] to provide the carboxylic acid **7**, in 85% yield. The crude product was judged sufficiently pure to be engaged in the final step, treatment with sulfur and sodium sulfide hydrate, to give the desired isolipoic acid **3**, in 75% yield after trituration. The first four steps of the synthesis were reproducible in multigram scale, with the final reaction proceeding readily on the gram scale.[11]

With isolipoic acid **3** now in hand, we decided to test its reactivity and ability to form SAMs through reaction with the known[7a] chiral ferrocenylamine **8** in the presence of the amide coupling agent PyBOP to form the amide **9** in good yield (Scheme 2, also see ESI). As a comparison, the reaction was repeated with carboxylic acids **1** and **2** to form the corresponding amides **10** (as a mixture of diastereomers) and **11**, also in good yields.

A series of SAMs of **9** on gold were then prepared by immersing clean polycrystalline gold electrodes in dichloromethane solutions ([**9**] = ca. 1.5 mM). Representative cyclic voltammograms in dichloromethane at different scan rates

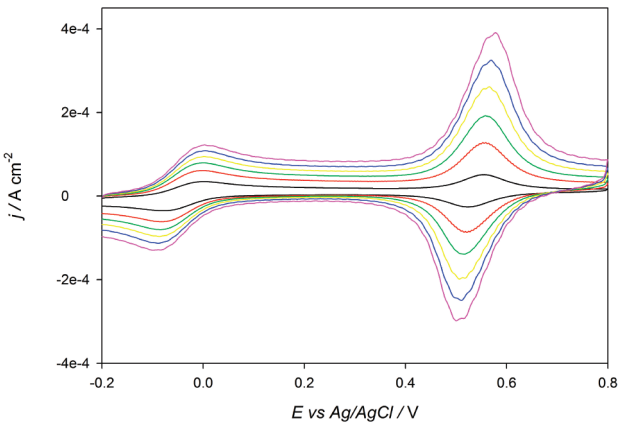
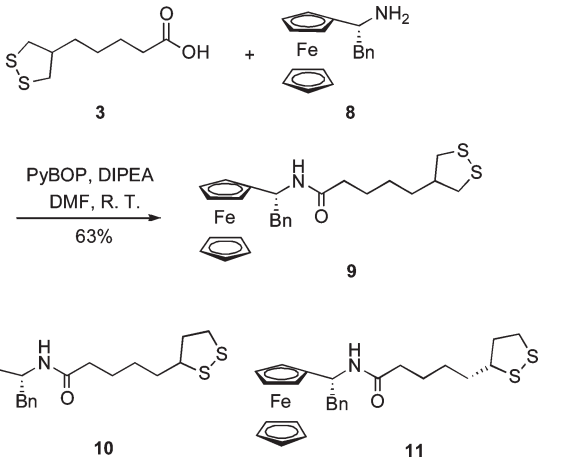


FIGURE 2. Cyclic voltammograms of **9** recorded in dichloromethane (0.1 M TBA·PF_6 as supporting electrolyte and dmfc as internal reference) at different scan rates (100, 300, 500, 704, 909, and 1111 mV s^{-1}, respectively black, red green, yellow, blue, and pink).

SCHEME 2. Synthesis of Chiral Disulfides 9, 10, and 11



are presented in Figure 2. The redox processes clearly seen at positive potentials versus Ag/AgCl are ascribed to the Fc^+/Fc couple for **9** ($E^{\circ\prime}$ = 578 mV vs decamethylferrocene internal reference at 500 mV s^{-1}). The appearance and peak separation (< 60 mV) of these redox waves are indicative of a surface-bound species; this was confirmed by the peak current intensity being proportional to the scan rate (see ESI for more details).[12]

Similar cyclic voltammograms to **9** in both DCM and water were observed for SAMs of **10** and **11**, which were prepared by using identical procedures. In addition, surface coverages (with respect to geometric area and obtained from the charge under the ferrocene oxidation peaks, assuming a one-electron oxidation process) were similar for SAMs of all three compounds (ranges 3.0−4.4 × 10^{-10}, 3.0−4.3 × 10^{-10}, and 2.3−4.0 × 10^{-10} mol cm^{-2} for **9**, **10**, and **11**, respectively) and similar to those for a related compound in the literature.[2c] These results indicate that in these three systems, the surface packing densities are not adversely affected by the position of the alkyl chain; rather the bulky ferrocene and benzyl groups are likely to have the major influence on the surface organization of these

(10) Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124*, 3824.

(11) Following evidence for some polymerization of **3** at elevated temperatures, it was found easier to carry out the final step in gram rather than multigram quantitities.

(12) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications*; Wiley: New York, 1980; Chapter 12.

monolayers. SAMs of each compound gave similar stability profiles after stirring in a dichloromethane solution of electrolyte over a time scale of 1 h.[13]

To summarize, we have prepared the symmetrical disulfide **3** through a readily accessible procedure. Our studies indicate that it is a convenient alternative to α-lipoic acid as a stable anchor group for SAMs, and it is expected to be a particularly attractive choice when surface-bound arrays of homochiral or achiral molecules are required.

Experimental Section

Diethyl 2-(Hex-5-enyl)malonate (4). Diethyl malonate (10.62 mL, 70.0 mmol) was added, over 40 min, to a stirred suspension of sodium hydride (2.80 g of a 60% w/w mixture in mineral oil; 70.0 mmol) in THF (170 mL), at 0 °C. The resulting colorless solution was stirred at 0 °C for 15 min, then at room temperature for 30 min before being cooled again to 0 °C. A solution of 6-bromo-1-hexene (8.50 mL, 63.6 mmol) in THF (80 mL) was then added over 5 min, and the resulting reaction mixture was heated at reflux for 18 h. After cooling to room temperature, the reaction mixture was quenched by addition of water (25 mL). Ethyl acetate (100 mL) and water (200 mL) were added and the layers separated. The aqueous layer was extracted with ethyl acetate (2 × 100 mL). The combined organic extracts were washed with brine (200 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure. Vacuum distillation afforded the title compound (12.28 g, 80%) as a colorless oil: bp 116−120 °C at 3 mbar (lit.[14] bp 143−145 °C at 15 mmHg); (found: C, 64.5; H, 9.2; $C_{13}H_{22}O_4$ requires C, 64.4; H, 9.2%); (found: MH^+, 243.1594; $C_{13}H_{22}O_4 + H$ requires 243.1596); ν_{max} ($CHCl_3$) 3078, 2984, 2933, 2861, 1726, 1640, 1464, 1446, 1392, 1371, 1337, 1300, 1256, 1240, 1178, 1157, 1122, 1096, 1028, 916, 860 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 5.77 (1H, tdd, J = 16.9, 10.1, 6.7 Hz, CH_2=C<u>H</u>), 4.87−5.06 (2H, m, C<u>H</u>$_2$=CH), 4.19 (4H, q, J = 7.1 Hz, OC<u>H</u>$_2$CH$_3$), 3.30 (1H, t, J = 7.5 Hz, CH_2C<u>H</u>), 2.04 (2H, m, CH_2), 1.89 (2H, dd, J = 15.4, 7.6 Hz, CH_2), 1.30−1.48 (4H, m), 1.26 (6H, t, J = 7.1 Hz, OCH$_2$C<u>H</u>$_3$); δ_C (100 MHz; $CDCl_3$) 169.5 (C), 138.5 (CH), 114.5 (CH_2), 61.2 (CH_2), 52.0 (CH), 33.4 (CH_2), 28.5 (CH_2), 28.4 (CH_2), 26.7 (CH_2), 14.1 (CH_3); m/z (ES) 265 ([M + Na]$^+$, 100%), 243 (4, [M + H]$^+$).

2-(Hex-5-enyl)propane-1,3-diol (5). A solution of diester **4** (12.26 g, 50.6 mmol) in THF (80 mL) was added, at 0 °C, to a stirred suspension of lithium aluminum hydride (3.84 g, 101 mmol) in THF (220 mL). The reaction mixture was stirred at 0 °C for 30 min, and then at room temperature for 3 h. The mixture was then diluted with THF (150 mL) and cooled to 0 °C. Water (3.8 mL), aqueous sodium hydroxide solution (2 M; 5.7 mL), and water (3.8 mL) were added successively and the resulting mixture was stirred vigorously at room temperature overnight. The mixture was then filtered through Celite, washing with ethyl acetate. The solvents were removed under reduced pressure and the resulting oil was purified by vacuum distillation to give the title compound (6.40 g, 80%) as a colorless oil: bp 108−112 °C at 3 mbar (lit.[15] bp 92−93 °C at 3 mmHg); (found: C, 68.0; H, 11.6; $C_9H_{18}O_2$ requires C, 68.3; H, 11.5); (found: M + Na^+, 181.1199; $C_9H_{18}O_2$ + Na requires 181.1205); ν_{max} ($CHCl_3$) 3628, 3515, 3078, 3011, 2931, 2860, 1640, 1602, 1465, 1418, 1240, 1028, 916, 639 cm^{-1}; δ_H (400 MHz; $(CD_3)_2CO$) 5.81 (1H, tdd, J = 17.0, 10.2, 6.7 Hz, CH_2=C<u>H</u>), 4.87−5.05 (2H, m, C<u>H</u>$_2$=CH), 3.52−3.67 (6H, m, C<u>H</u>$_2$OH), 2.00−2.12 (2H, m, C<u>H</u>$_2$), 1.56−1.67 (1H, m, CH), 1.26−1.45 (6H, m, CH_2); δ_C (100 MHz; $(CD_3)_2CO$) 140.8 (CH), 115.7 (CH_2), 65.5 (CH_2), 44.9 (CH), 35.4 (CH_2), 31.1 (CH_2), 29.5 (CH_2), 28.4 (CH_2); m/z (ES) 223 (100%), 181 (40, [M + Na]$^+$).

Methanesulfonic Acid 2-Methanesulfonyloxymethyloct-7-enyl Ester (6). Methanesulfonyl chloride (12.46 mL, 161 mmol) was added over 15 min to a stirred solution of diol **5** (6.37 g, 40.2 mmol) and triethylamine (28.0 mL, 201 mmol) in CH_2Cl_2 (350 mL), at 0 °C. The reaction mixture was stirred at 0 °C for a further 30 min and then at room temperature for 3 h. Water (300 mL) was added and the layers wereseparated. The aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic extracts were washed with brine (300 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel, eluting with ethyl acetate−light petroleum (1:2) to give the title compound (12.0 g, 95%) as a light yellow oil: (found: C, 41.8; H, 7.0; $C_{11}H_{22}O_6S_2$ requires C, 42.0; H, 7.1); (found: M + Na^+, 337.0750; $C_{11}H_{22}O_6S_2$ + Na requires 337.0755); ν_{max} ($CHCl_3$) 2933, 2861, 1468, 1346, 1332, 1172, 1004, 977, 950, 934, 847, 834, 784, 745 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 5.71−5.85 (1H, m, CH_2=C<u>H</u>), 4.92−5.06 (2H, m, C<u>H</u>$_2$=CH), 4.24 (4H, m, CHC<u>H</u>$_2$O), 3.04 (6H, s, SO_2Me), 2.11−2.21 (1H, m, CH_2C<u>H</u>), 2.02−2.11 (2H, m, CH_2), 1.40 (6H, s, CH_2); δ_C(100 MHz; $CDCl_3$) 138.3 (CH), 114.8 (CH_2), 68.2 (CH_2), 38.1 (CH), 37.3 (CH_3), 33.4 (CH_2), 28.6 (CH_2), 26.8 (CH_2), 25.9 (CH_2); m/z (ES) 337 ([M + Na]$^+$, 100%).

Carboxylic Acid (7). Osmium tetroxide (1.24 mL of a 2.5% w/w solution in tBuOH, 0.099 mmol) was added to a stirred solution of olefin **6** (3.10 g, 9.86 mmol) in DMF (65 mL), and the resulting solution was stirred for 5 min. Oxone (24.2 g, 39.4 mmol) was then added in three portions, over 20 min, and the resulting mixture was stirred vigorously for a further 3.5 h. Sodium sulfite (18.6 g) was added, and the resulting beige mixture was stirred for a further 1.5 h. Water (200 mL), aqueous hydrochloric acid solution (2 M; 50 mL), and ethyl acetate:ether (1:1, 200 mL) were added and the layers separated. The aqueous layer was extracted with ethyl acetate:ether (1:1, 150 mL). The combined organic extracts were washed with brine (200 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the title compound (2.78 g, 85%) as a white solid. The crude carboxylic acid was used as such for the next step.

Isolipoic Acid (3). Sulfur (273 mg, 8.51 mmol) and sodium sulfide hydrate (2.05 g, 8.51 mmol) were added to a stirred solution of carboxylic acid **7** (2.83 g, 8.51 mmol) in DMF (85 mL), and the resulting reaction mixture was heated at 85 °C for 4.5 h. The mixture was then cooled to room temperature, water (200 mL) and ether (200 mL) were added, and the layers were separated. The aqueous layer was extracted with ether (2 × 100 mL). The combined organic extracts were washed with brine (250 mL) and dried ($MgSO_4$) and solvents were removed under reduced pressure. The resulting yellow solid was triturated from hexane, to afford the title compound (1.32 g, 75%) as yellow needles: mp 70−72 °C (lit.[9] mp 68−70 °C); (found: M − H^-, 205.0357; $C_8H_{14}O_2S_2$ − H requires 205.0357); ν_{max} (neat) 2929, 2855, 1695, 1461, 1411, 1302, 1260, 1210, 943, 746, 712 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.25 (2H, dd, J = 11.0, 6.6 Hz, CH_2), 2.80 (2H, dd, J = 11.0, 6.6 Hz, CH_2), 2.54 (1H, sept, J = 6.6 Hz, CH_2C<u>H</u>-($CH_2S)_2$), 2.36−2.40 (2H, m, CH_2), 1.63−1.71 (2H, m, C<u>H</u>$_2$), 1.50−1.56 (2H, m, CH_2), 1.41−1.47 (2H, m, CH_2); δ_C(100 MHz; $CDCl_3$) 179.7 (C), 47.5 (CH), 43.9 (CH_2), 33.8 (CH_2), 33.4 (CH_2), 27.9 (CH_2), 24.5 (CH_2); m/z (ES) 205 ([M − H]$^-$, 27%), 171 (100).

General Procedure for the Synthesis of Ferrocenyl Amides. *N*,*N*-Diisopropylethylamine (0.52 mmol, 4.0 equiv) and the desired carboxylic acid (0.20 mmol, 1.5 equiv) were added to a solution of primary amine **8** (0.13 mmol, 1.0 equiv) in DMF (5.5 mL). The mixture was stirred for 5 min, and then a solution of

(13) Prelimimary ellipsometry studies indicate that monolayer thickness values for SAMS of **9**, **10**, and **11** are within experimental error of one another. Further detailed studies on these and related systems are planned in due course.

(14) Salomon, R. G.; Coughlin, D. J.; Ghosh, S.; Zagorski, M. G. *J. Am. Chem. Soc.* **1982**, *104*, 998.

(15) Juang, T. M.; Leu, Y. J.; Hsu, C. S. *Mol. Cryst. Liq. Cryst. Sci. Technol., Sect. A* **1993**, *237*, 223.

PyBOP (0.26 mmol, 2.0 equiv) in DMF (2.5 mL) was added by cannula. The reaction mixture was stirred at room temperature overnight, then ethyl acetate (35 mL) and water (35 mL) were added and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were washed with brine (60 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel.

Ferrocenyl Isolipoic Amide (9). Amide **9** was obtained from the reaction of isolipoic acid **3** (44 mg, 0.21 mmol) with primary amine **8** (43 mg, 0.14 mmol). The crude product was purified by column chromatography on silica gel, eluting with ethyl acetate−light petroleum (1:4) to give the title compound (44 mg, 63%) as an orange oil: (found: M + Na^+, 516.1112; $C_{26}H_{31}FeNOS_2$ + Na requires 516.1089); $[\alpha]^{25}_D$ −32.8 (*c* 0.82, $CHCl_3$); ν_{max} ($CHCl_3$) 3436, 3089, 3065, 3011, 2931, 2859, 2293, 2256, 1710, 1667, 1604, 1505, 1455, 1441, 1418, 1373, 1240, 1106, 1080, 1029, 1002, 290, 860 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 7.17−7.29 (3H, m, ArH), 7.09−7.15 (2H, m, ArH), 5.53 (1H, d, *J* = 8.6 Hz, FcCHNH), 5.19 (1H, dt, *J* = 8.6, 5.8 Hz, FcCHNH), 4.04−4.18 (9H, m, FcH), 3.13−3.25 (3H, m, CH_2, CHHPh), 2.88−2.93 (1H, m, CHHPh), 2.75 (2H, dd, *J* = 11.0, 6.7 Hz, CH_2), 2.43−2.54 (1H, m, CH), 2.05−2.19 (2H, m, CH_2), 1.42−1.65 (4H, m, CH_2), 1.24−1.32 (2H, m, CH_2); δ_C (100 MHz; $CDCl_3$) 171.2 (C), 137.7 (C), 129.4 (CH), 128.2 (CH), 126.4 (CH), 90.2 (C), 68.7 (CH), 67.8 (CH), 67.6 (CH), 66.8 (CH), 66.4 (CH), 48.8 (CH), 47.5 (CH), 43.91 (CH_2), 43.88 (CH_2), 42.2 (CH_2), 36.5 (CH_2), 33.4 (CH_2), 27.9 (CH_2), 25.6 (CH_2); *m*/*z* (ES) 516 ([M + Na]$^+$, 100%).

Ferrocenyl (±)-α-Lipoic Amide (10). Amide **10** was obtained from the reaction of (±)-α-lipoic acid **1** (41 mg, 0.20 mmol) with primary amine **8** (40 mg, 0.13 mmol). The crude product was purified by column chromatography on silica gel, eluting with ethyl acetate−light petroleum (1:4) to give the title compound (48 mg, 75%) as a mixture of diastereomers as an orange oil: (found: M + Na^+, 516.1126; $C_{26}H_{31}FeNOS_2$ + Na requires 516.1089); $[\alpha]^{25}_D$ −25.3 (*c* 0.96, $CHCl_3$); ν_{max} ($CHCl_3$) 3436, 3089, 3065, 3010, 2932, 2859, 1711, 1666, 1505, 1455, 1441, 1367, 1313, 1242, 1183, 1106, 1080, 1046, 1028, 1001, 910, 823 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 7.17−7.30 (3H, m, ArH), 7.07−7.15 (2H, m, ArH), 5.61 (1H, d, *J* = 8.6 Hz, FcCHNH), 5.18 (1H, dd, *J* = 14.2, 8.6 Hz, FcCHNH), 4.00−4.19 (9H, m, FcH), 3.47−3.58 (1H, m), 3.07−3.20 (3H, m, CH_2, CHHPh), 2.85−2.97 (1H, m, CHHPh), 2.38−2.48 (1H, m), 2.06−2.20 (2H, m), 1.84−1.93 (1H, m), 1.54−1.70 (4H, m), 1.28−1.45 (2H, m); δ_C (100 MHz; $CDCl_3$) 171.3 (C), 137.6 (C), 129.4 (CH), 128.1 (CH), 126.4 (CH), 90.1 (C), 68.6 (CH), 67.7 (CH), 67.5 (CH), 66.8 (CH), 66.2 (CH), 56.31 (CH), 56.26 (CH), 48.8 (CH), 42.4 (CH_2), 40.2 (CH_2), 38.4 (CH_2), 36.6 (CH_2), 34.60 (CH_2), 34.56 (CH_2), 28.7 (CH_2), 25.40 (CH_2), 25.36 (CH_2); *m*/*z* (ES) 516 ([M + Na]$^+$, 100%).

Ferrocenyl (*R*)-(+)-1,2-Dithiolane-3-pentamide (11). Amide **11** was obtained from the reaction of (*R*)-(+)-1,2-dithiolane-3-pentanoic acid **2** (101 mg, 0.49 mmol) with primary amine **8** (100 mg, 0.33 mmol). The crude product was purified by column chromatography on silica gel, eluting with ethyl acetate−light petroleum (1:4) to give the title compound (108 mg, 67%) as an orange oil: (found: M + Na^+, 516.1115; $C_{26}H_{31}FeNOS_2$ + Na requires 516.1089); $[\alpha]^{21}_D$ +22.2 (*c* 1.03, $CHCl_3$); ν_{max} ($CHCl_3$) 3672, 3436, 3089, 3011, 2932, 2859, 1666, 1604, 1505, 1455, 1441, 1240, 1106, 1046, 1028, 1001, 913, 823 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 7.20−7.32 (3H, m, ArH), 7.10−7.17 (2H, m, ArH), 5.65 (1H, d, *J* = 8.6 Hz, FcCHNH), 5.21 (1H, dt, *J* = 8.6, 6.1 Hz, FcCHNH), 4.04−4.18 (9H, m, FcH), 3.49−3.61 (1H, m), 3.07−3.25 (3H, m), 2.93 (1H, dd, *J* = 13.8, 7.8 Hz), 2.36−2.51 (1H, m), 2.06−2.23 (2H, m), 1.84−1.97 (1H, m), 1.52−1.75 (4H, m), 1.28−1.46 (2H, m); δ_C (100 MHz; $CDCl_3$) 171.4 (C), 137.6 (C), 129.4 (CH), 128.1 (CH), 126.4 (CH), 90.1 (C), 68.6 (CH), 67.7 (CH), 67.5 (CH), 66.7 (CH), 66.2 (CH), 56.3 (CH), 48.8 (CH), 42.3 (CH_2), 40.2 (CH_2), 38.4 (CH_2), 36.6 (CH_2), 34.6 (CH_2), 28.7 (CH_2), 25.4 (CH_2); *m*/*z* (ES) 516 ([M + Na]$^+$, 100%).

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Supporting Information Available: SAM preparation and electrochemistry data for SAMs recorded in DCM and water. This material is available free of charge via the Internet at http://pubs.acs.org.