Unsymmetrical Dialkyl Sulfides for Self-Assembled Monolayer Formation on Gold: Lack of Preferential Cleavage of Allyl or Benzyl Substituents

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Received August 3, 1998. Revised Manuscript Received August 19, 1998

Five unsymmetrical sulfides and one unsymmetrical disulfide were synthesized for self-assembled monolayer (SAM) formation on gold electrodes. Each compound contained a dinitrobenzyl ester group at the end of a primary alkyl chain as one sulfide arm, with an allyl, methyl, or cyanobenzyl group for the other arm. Cyclic voltammetry (CV) of the resulting SAMs showed no evidence for differential cleavage of allyl or cyanobenzyl sulfide groups relative to methyl, contrary to expectations if sulfide cleavage accompanied the self-assembly process.

Introduction

Self-assembled monolayers (SAMs) are formed when molecules spontaneously adsorb on a surface to form an ordered, single-molecule-thick sheet. Recently, much interest has been generated in SAMs formed from sulfur-containing compounds covalently bound to the surfaces of gold and other metals.[1] Among the molecules of interest are thiols (R−S−H),[2] disulfides (R−S−S−R),[3,4] and sulfides (R−S−R).[5,6]

Thiols are believed to bind to gold in an oxidation/reduction process, forming a thiolate (R−S) species, perhaps with the formation of dihydrogen or water.[1] SAMs formed from symmetrical disulfides appear nearly identical to those originating from thiols, suggesting a reductive cleavage of the disulfide to produce two thiolate species.[3,4,7] Similar conclusions can be drawn from phase separations[8] or differential exchange[9] observed in SAMs formed from unsymmetrical disulfides.

The question is more difficult with sulfides. Sulfur XPS,[10,11] Fourier transform infrared reflection−absorption spectroscopy (FT-IRRAS),[10] and electrochemical evidence[10] suggest that thiol and sulfide SAMs are indistinguishable, implying that sulfides, like thiols and disulfides, bind as thiolates to gold surfaces. This is consistent with a surface-enhanced Raman study indicating that sulfides cleave to thiolates upon adsorption on silver.[12] On the other hand, sulfide and thiol SAMs give rise to distinct XP spectra for carbon and different electrochemical blocking behavior.[13] Ellipsometry and contact angle measurements suggest differences between SAMs formed from sulfides and the analogous thiols in some cases[14,15] although not in others.[14] Mass spectroscopy studies can detect intact sulfides being released from sulfide SAMs, but there are also apparent signals from thiolate or disulfide species, which complicate the interpretation.[11,16,17] It has recently been emphasized that the reliability of any sulfide SAM study depends on the use of purified sulfides, due to the preferential adsorption of any thiol and disulfide contaminants onto the gold surface.[13,14,17]

Adsorption of sulfides as thiolates requires that one substituent arm of the sulfide be cleaved. Certain substituents should be lost preferentially: a cleavage pathway with radical, cationic, or anionic character would be expected to remove substituents with relatively stable fragments (such as allyl or benzyl) more easily than substituents lacking such stabilization (such as a primary alkyl or methyl). We tested this idea by preparing SAMs of unsymmetrically substituted sulfides in which a primary alkyl substituent—as part of a short (**3**, **7**) or long (**11**, **15**) chain—competed for cleavage with an allyl (**7**, **15**) or methyl (**3**, **11**) substituent. The primary alkyl substituent ended in a dinitrophenyl group (attached as an ester) to serve as an electrochemi-

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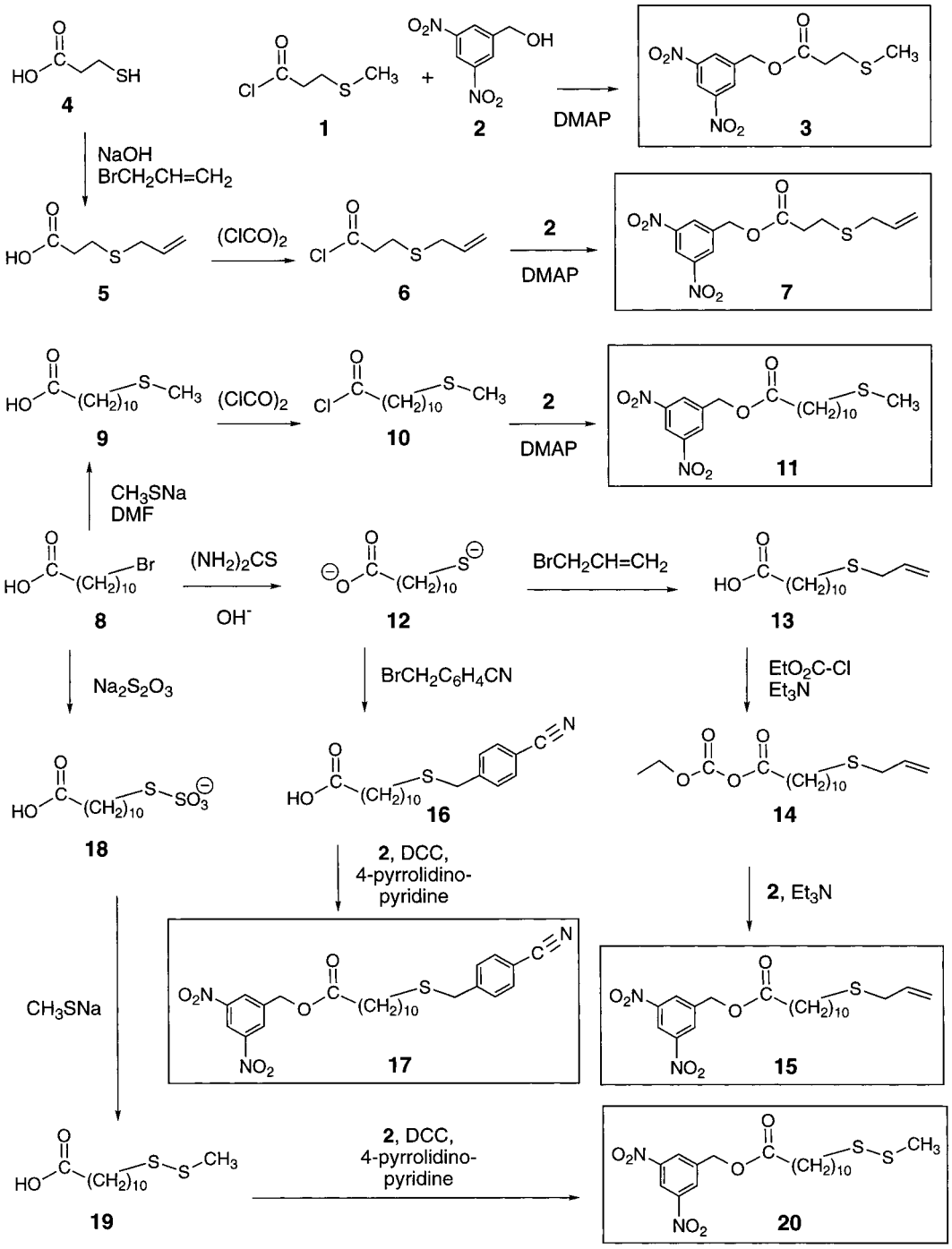
10.1021/cm980553x CCC: $15.00
Published on Web 12/01/1998

Scheme 1. Synthesis of Sulfides 3, 7, 11, 15, and 17, and Disulfide 20



cal reporter for cyclic voltammetry (CV) studies. Substantial sulfide cleavage upon adsorption should result in relatively high retention of the dinitrophenyl reporter group in the SAM when the second sulfide substituent is the reactive allyl group, compared to when the second substituent is methyl. We also prepared a sulfide with a cyanobenzyl substituent (**17**), to compete against the long-chain primary alkyl substituent, and a methyl disulfide derivative (**20**), to provide a reference SAM.

Identification of a preferentially cleaved sulfide substituent (such as allyl) during SAM formation could lead to a new family of useful SAM precursors. Such sulfides could be used in place of the alternative thiols, which are less stable and can be difficult to work with.

Synthesis

The short-chain sulfides **3** and **7** and the long-chain methyl sulfide **11** were synthesized by esterification of the corresponding acid chlorides, as shown in Scheme 1. 3-Methylthiopropanoyl chloride (**1**) was commercially available; acid chlorides **6** and **10** were prepared by treating the corresponding acids **5** and **9** with oxalyl chloride. Acid **5** was prepared by allylating thiol **4**, while acid **9** was prepared by thiomethylation of 10-bromoundecanoic acid (**8**). Bromo acid **8** was also converted with thiourea to thiolate **12**, which was allylated to **13** or benzylated to **16**. The long-chain allyl sulfide **15** was prepared in better purity from **13** through the mixed anhydride **14** rather than through the acid chloride. The

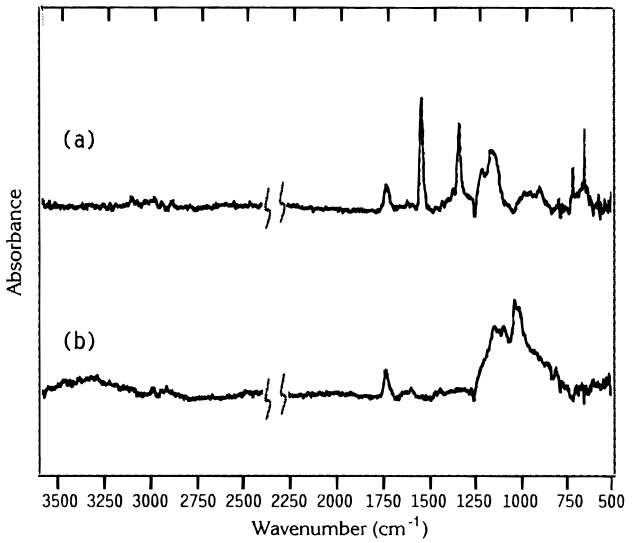


Figure 1. (a) FT-IRRAS spectrum of a SAM freshly derived from compound **3**. (b) FT-IRRAS spectrum of a SAM derived from compound **3** after reduction at −0.5 V for 15 s in an O_2-free environmment.

cyanobenzyl sulfide **17** and the disulfide **20** were best prepared, albeit in low yield, by DCC-catalyzed esterification of the corresponding acids **16** and **19**. Acid **19** was prepared from **8** by thiomethylation of the corresponding Bunte salt **18**.

Results and Discussion

When cyclic voltammetric measurements of SAMs with dinitrophenyl substituents were attempted starting from the open circuit potential, there were no obvious waves. However, when SAM electrodes were held at −0.5 V vs SCE for 15 s and then scanned anodically from this potential, oxidation waves were observed. To investigate this behavior further, we performed FT-IRRAS measurements before and after the reduction at −0.5 V. The FT-IRRAS spectrum of SAM **3**, after thorough rinsing with ethanol and drying in the N_2 glovebox housing the FTIR spectrometer, is shown in Figure 1a. A second rinsed and dried slide of SAM **3** was placed in an aqueous solution in an oxygen-free N_2 glovebox. Its potential was held at −0.5 V for 15 s; it was then removed from solution before the potential clamp was removed to avoid back-oxidation and allowed to dry in the glovebox for about 6 h. Its FT-IRRAS spectrum is shown in Figure 1b.

The peak at 1740 cm^{-1} represents the ester carbonyl and is present both before (Figure 1a) and after (Figure 1b) reduction. The vibrations in Figure 1a at 1555 and 1349 cm^{-1} are characteristic of NO_2 stretching. After 15 s of reduction, Figure 1b shows that these absorptions are essentially absent. Instead, there is a small NH_2 deformation around 1600 cm^{-1} in conjunction with a broad band around 3300 cm^{-1}, indicating the formation of a primary amine. These results are consistent with the known electrochemical reduction of dinitrobenzenes to phenylenediamines.[18] As a control, we treated a hexadecanethiol SAM to the same reducing regimen under atmospheric conditions and examined its FT-IRRAS spectrum in the 3300 cm^{-1} region for evidence of hydration or other nonspecific alteration of the SAM; there was no peak. We conclude that the cyclic voltammograms that we observed from the dinitrophenyl-substituted compounds are derived from oxidation[19] of the aniline groups formed during the initial reduction period.

Table 1. Cyclic Voltammetry of SAMs Made from Unsymmetrical Sulfides DNB−$O_2C(CH_2)_nS$−R or Disulfide DNB−$O_2C(CH_2)_nS$−S−R on Gold Electrodes

compd	n	R	$E^{\circ\prime}$ (V)	Q (μC)	Γ (nmol/cm^2)	ΔE_p (mV)
3	2	CH_3	−0.138	86	0.57	62
7	2	$CH_2CH{=}CH_2$	−0.018	34	0.23	88
11	10	CH_3	0.044	31	0.21	584
15	10	$CH_2CH{=}CH_2$	0.010	24	0.16	160
17	10	4-cyanobenzyl	0.091	19	0.13	694
20	10	SCH_3	0.027	60	0.40	340

Figure 2 shows the cyclic voltammograms of SAMs made from the five sulfides and the disulfide, and Table 1 shows the corresponding electrochemical data. The formal potential, $E^{\circ\prime}$, is similar for all of the compounds (as expected because they all are dinitrophenyl derivatives). The surface coverage values, Γ, calculated from the total charge, Q, under the appropriate voltammetric reduction wave after subtraction of the residual current, are smaller for SAMs from the allyl-substituted sulfides compared to SAMs from the methyl-substituted sulfides in both the short-chain (**3** vs **7**) and long-chain (**11** vs **15**) cases. Among the three long-chain sulfides, the cyanobenzyl derivative **17** gave rise to the lowest coverage. Coverage resulting from the unsymmetrical disulfide **20** was better than all the sulfides except **3**. The SAMs derived from the compounds with longer alkyl chains exhibited greatly decreased electron-transfer rates,[20,21] as indicated by the larger values of ΔE_p (peak separation) compared with values for the shorter chain sulfides.

Longer alkyl chains are expected to encourage the formation of denser SAMs than shorter alkyl chains, due to increased interchain van der Waals attractions.[22] However, we did not see such a trend. In fact, the higher Γ values for the shorter sulfides (**3** and **7**) compared to the analogous longer sulfides (**11** and **15**) suggested that the shorter chains promoted higher surface coverages. (An alternative explanation is that the long-chain sulfides were less completely reduced than the short-chain sulfides during the 15-s preliminary reduction process, so the density of observable electroactive groups in the long-chain SAMs was less than the actual alkyl chain density. This seems unlikely, however, since we saw no comparable evidence of incomplete coverage or reduction for the long-chain disulfide **20**, as discussed below.)

Binding site positions in the gold lattice restrict a monolayer of alkanethiols to a density of about 0.77 nmol/cm^2;[1] with a bulky tail group such as, for example,

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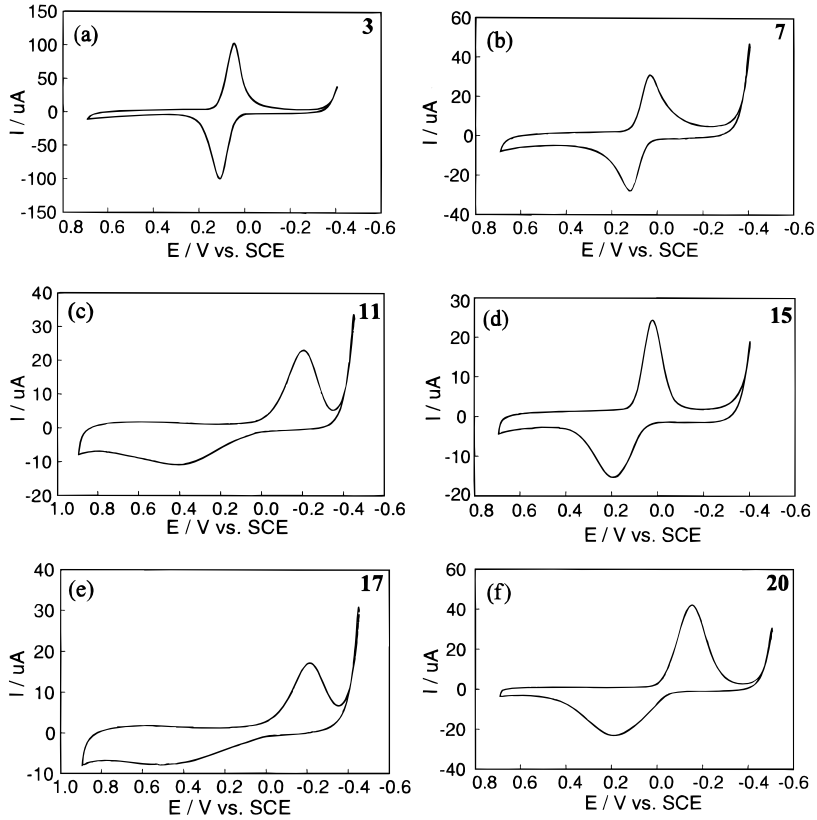

Figure 2. Cyclic voltammograms of SAMs derived from the following sulfides and disulfide: (a) compound **3**, (b) compound **7**, (c) compound **11**, (d) compound **15**, (e) compound **17**, (f) compound **20**.

ferrocene, the full-coverage density falls to about 0.45 nmol/cm^2.[23] Apparent surface coverages of SAMs derived from sulfides with allyl and benzyl substituents (**7**, **15**, and **17**) were much lower than this (0.13−0.23 nmol/cm^2), and the long-chain methyl sulfide (**11**) did not fare any better (0.21 nmol/cm^2). Only the short-chain methyl sulfide (**3**) gave rise to a relatively dense monolayer (0.57 nmol/cm^2).

We prepared the disulfide **20** to provide a qualitative "reference" for these results. The disulfide should undergo S−S cleavage to give a mixed SAM of electroactive dinitrophenyl-derived alkylthiolate groups and inert methylthiolate groups. If all sites are filled, the adsorbed electroactive thiolates would give rise to an apparent coverage of about 0.38 nmol/cm^2. These results are in line with the observed coverage being 0.40 nmol/cm^2.

If sulfide cleavage occurred during a radical, cationic, or anionic chemisorption process for SAM formation, then we would expect the more-reactive allyl and benzyl groups to be preferentially cleaved compared to methyl groups from primary alkyl sulfides, leading to a relatively higher surface coverage of retained electroactive groups. However, as noted above for both the short-chain and long-chain sets, this was not the case. The low absolute surface coverage values from all of the sulfides (with the possible exception of **3**) also seem more consistent with an adsorption process without cleavage, such that the inert alkyl group occupies space in the SAM alongside the dinitrophenyl-containing chain. Alternatively, cleavage could occur after the sulfides have physisorbed to the surface, so that steric effects of both sulfide substituents influence the final surface density. In either case, the low coverage from the sulfide with the sterically most demanding group, cyanobenzyl, and the relatively high coverages from the sterically undemanding methyl sulfides suggest steric control of the assembly process.

If cleavage occurred during a subsequent chemisorption to make a thiolate SAM, the low levels of apparent coverage from **7**, **15**, and **17** (that is, about half the coverage from the disulfide **20**) would require some cleavage of the primary alkyl substituents bearing the reporter groups. This implies that there would not be much preference for cleaving allyl or benzyl groups over primary alkyl groups (contrary to expectations for a radical, cationic, or anionic process) nor, at least in the case of **11**, would there be much preference for cleaving methyl (as would be expected for a sterically demanding process such as an S_N2 displacement). The absence of highly preferential cleavage is supported by an FT-IRRAS spectrum of the SAM from sulfide **17**, which has a cyano reporter group on the benzyl substituent. The spectrum showed the presence of the cyano group (2229 cm^{-1}), indicating that exclusive cleavage of the benzyl−sulfur bond does not occur during SAM formation from **17**.

Conclusions

Cyclic voltammetry of SAMs formed from five dinitrophenyl-substituted unsymmetrical sulfides showed no evidence for marked differential cleavage of allyl or cyanobenzyl groups relative to methyl, as might be expected for a typical dissociation process. The rather low apparent surface coverage of SAMs formed from

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these sulfides, as well as the observation in one SAM of both terminal groups from an unsymmetrical sulfide, is consistent with a SAM comprised of intact sulfides.

Experimental Section

Self-Assembled Monolayer Preparation. Glass microscope slides were cleaned by sonication in successive baths of piranha solution, distilled water, and 2-propanol and were then coated by thermal evaporation with 50 Å of chromium, followed by 1500 Å of gold, as previously described.[5] The resulting gold electrodes were immersed in 1 mM acetonitrile solutions of the sulfides or disulfide for about 24 h and then were rinsed thoroughly with acetonitrile.

Cyclic Voltammetry. Cyclic staircase voltammetric measurements (step size = 1 mV) were made in a three-electrode cell with an EG&G Model 283 potentiostat/galvanostat employing Model 270 Electrochemistry Analysis Software (Princeton Applied Research Corp.) running on an IBM-compatible 486 computer. The reference electrode was an EG&G Saturated Calomel Electrode (SCE) separated from the working electrode compartment by a Luggin capillary; all potentials discussed in this paper are referenced to this SCE. The counter electrode was a platinum wire spiral. The SAM-modified gold substrates constituted the working electrodes. The supporting electrolyte was aqueous phosphate buffer (Aldrich) at pH 7.2.

FT-IRRAS. Fourier transform infrared reflection−absorption spectroscopy measurements were carried out using a Bruker IFS 66 FTIR spectrometer housed in a N_2 glovebox. The spectrometer was equipped with a Graseby-Specac grazing angle reflection accessory and a liquid-N_2-cooled MCT detector. All spectra were obtained using *p*-polarized light incident upon the modified gold substrate at an angle of 86°. Background spectra were obtained from a freshly prepared bare gold surface.

3,5-Dinitrobenzyl 3-(Methylthio)propanoate (3). 3-(Methylthio)propanoyl chloride (0.50 g, 3.6 mmol), *N,N*-(dimethylamino)pyridine (DMAP, 0.044 g, 0.36 mmol), and 3,5-dinitrobenzyl alcohol (**2**, 0.71 g, 3.6 mmol) were dissolved in 20 mL of dry CH_2Cl_2. The reaction mixture was refluxed for 12 h, treated with 5% HCl, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated by rotary evaporation to give an oil (0.91 g, 84%). Purification by column chromatography (petroleum ether/EtOAc 7/3) gave 0.78 g (72%) of **3** as a light yellow oil: TLC (petroleum ether/EtOAc 7/3) R_f 0.45; IR (KBr) 3096, 2910, 1736, 1596, 1544, 1345, 1246, 1164 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.02 (1H, s), 8.59 (2H, s), 5.35 (2H, s), 2.80 (4H, m), 2.15 (3H, s). Anal. Calcd for $C_{11}H_{12}N_2O_6S$: C, 44.00; H, 4.03; N, 9.33; S, 10.68. Found: C, 44.02; H, 3.93; N, 9.17; S, 10.41.

3,5-Dinitrobenzyl 3-(Allylthio)propanoate (7). 3-Mercaptopropanoic acid (**4**, 0.82 mL, 9.4 mmol) and NaOH (0.75 g, 19 mmol) in 10 mL of distilled H_2O were added dropwise to a solution of allyl bromide (0.98 mL, 11 mmol) in 20 mL of EtOH at room temperature. After the reaction mixture was stirred overnight and the ethanol was removed by rotary evaporation, the crude product was extracted with EtOAc, dried over $MgSO_4$, and concentrated by rotary evaporation to give 1.3 g (96%) of 3-(allylthio)propanoic acid[24] (**5**): TLC (CH_2Cl_2/EtOAc/AcOH 33/33/1) R_f 0.78; ^1H NMR ($CDCl_3$) δ 5.79 (1H, m), 5.12 (2H, m), 3.18 (2H, d), 2.74 (2H, t), 2.66 (2H, t).

Oxalyl chloride (0.14 mL, 1.6 mmol) was added to **5** (0.20 g, 1.4 mmol) in 20 mL of dry CH_2Cl_2. The reaction mixture was stirred for 18 h at room temperature. Solvent and excess oxalyl chloride were removed by rotary evaporation to give 0.22 g (99%) of 3-(allylthio)propanoyl chloride (**6**): IR 2929, 1794 cm^{-1}.

3,5-Dinitrobenzyl alcohol (**2**, 0.27 g, 1.4 mmol) and DMAP (17 mg, 0.14 mmol) were added to **6** (0.22 g, 1.4 mmol) in 20 mL of dry CH_2Cl_2 at room temperature. The reaction mixture was stirred for 1 day, treated with 5% HCl, and extracted with CH_2Cl_2; the extract was dried over $MgSO_4$ and concentrated by rotary evaporation to give 0.23 g (52%) of crude product, which was purified by column chromatography (hexane/EtOAc 8/2) to give 0.19 g (44%) of **7** as a light yellow oil: TLC (petroleum ether/EtOAc 7/3) R_f 0.56; IR (KBr) 3091, 2922, 1743, 1543, 1345, 1242, 1145, 916, 807, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.01 (1H, s), 8.59 (2H, s), 5.78 (1H, m), 5.36 (2H, s), 5.10 (2H, m), 3.17 (2H, d), 2.77 (4H, m). Anal. Calcd for $C_{13}H_{14}N_2O_6S$: C, 47.85; H, 4.32; N, 8.58; S, 9.83. Found: C, 47.84; H, 4.45; N, 8.41; S, 9.68.

3,5-Dinitrobenzyl 11-(Methylthio)undecanoate (11). 11-Bromoundecanoic acid (**8**, 5.00 g, 18.9 mmol) and dry triethylamine (2.63 mL, 18.9 mmol) were dissolved in 100 mL of dry DMF, and then $NaSCH_3$ (1.98 g, 28.3 mmol) was added at 0 °C. The reaction mixture was heated to 65 °C and stirred overnight. Treatment with 5% HCl resulted in a white precipitate which was recrystallized from water to give 3.96 g (90%) of 11-(methylthio)undecanoic acid (**9**): mp 39−40 °C (lit.[25] 43−45 °C); IR (KBr) 2923, 2851, 2677, 1703, 1462, 1431, 1292, 938, 723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.50 (2H, t), 2.37 (2H, t), 2.11 (3H, s), 1.62 (4H, m), 1.43−1.35 (12H, m).

Compound **9** (0.50 g, 2.1 mmol) was dissolved in 50 mL of dry CH_2Cl_2; oxalyl chloride (0.23 mL, 2.6 mmol) was added and the mixture was stirred overnight. Excess oxalyl chloride was removed under vacuum to give 0.53 g (2.1 mmol) of 11-(methylthio)undecanoyl chloride (**10**) as a yellow oi: IR (CH_2Cl_2) 3070, 2935, 1796, 1405, 1300, 700 cm^{-1}. This acid chloride was dissolved in 25 mL of dry CH_2Cl_2. Alcohol **2** (0.43 g, 2.1 mmol) and DMAP (26 mg, 0.21 mmol) were added, and the reaction mixture was stirred for 1 day and then treated with 5% HCl and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and concentrated by rotary evaporation to give 0.65 g (73%) of a crude product; purification by column chromatography (petroleum ether/EtOAc 7/3) gave 0.54 g (60%) of **11**, a light yellow oil: TLC (petroleum ether/EtOAc 7/3) R_f 0.81; IR (KBr) 3049, 2922, 2856, 1735, 1543, 1475, 1342, 1225, 1168, 1030, 729 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.03 (1H, s), 8.55 (2H, s), 5.30 (2H, s), 2.44 (4H, m), 2.10 (3H, s), 1.65 (2H, m), 1.58 (2H, m), 1.23−1.26 (12H, m). Anal. Calcd for $C_{19}H_{28}N_2O_6S$: C, 55.32; H, 6.84; N, 6.79; S, 7.77. Found: C, 55.60; H, 7.12; N, 6.65; S, 7.74.

3,5-Dinitrobenzyl 11-(Allylthio)undecanoate (15). 11-Bromoundecanoic acid (**8**, 2.0 g, 7.5 mmol), thiourea (0.632 g, 8.30 mmol), and 30 mL of DMSO were warmed slightly to attain solution and then stirred for 12 h at room temperature. To this reaction mixture was added 113 mL of 10% NaOH. The reaction mixture was stirred for 30 min in an ice bath. Allyl bromide (1.30 mL, 15.1 mmol) was then added slowly. The mixture was stirred overnight and then acidified with concentrated HCl to pH 2 to give 1.63 g (84%) of a white precipitate of 11-(allylthio)undecanoic acid (**13**): TLC (hexane/EtOAc 7/3) R_f 0.2; IR ($CDCl_3$) 3300−2500 (broad), 2909, 2665, 1695, 1430, 1290, 1223, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.77 (1H, m), 5.10 (2H, m), 3.12 (2H, d), 2.47 (2H, m), 2.35 (2H, m), 1.58 (4H, m), 1.40−1.27 (12H, m).

Compound **13** (0.511 g, 1.98 mmol) and triethylamine (0.28 mL, 2.0 mmol) were dissolved in 20 mL of dry THF. Ethyl chloroformate (0.21 mL, 2.2 mmol) was slowly added at 0 °C and the mixture was stirred for 1.5 h in an ice bath. The resulting solution of mixed anhydride **14** was treated with alcohol **2** (0.39 g, 2.0 mmol) and triethylamine (0.28 mL, 2.0 mmol) and stirred for 1 day. After removal of solvent, the crude product was purified by column chromatography (CH_2Cl_2/hexane 6/4) to give 0.109 g (13%) of **15**: TLC (hexane/EtOAc 7/3) R_f 0.54; IR (KBr) 2928, 1745, 1543, 1343, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.01 (1H, s), 8.55 (2H, s), 5.78 (1H, m), 5.30 (2H, s), 5.10 (2H, m), 3.12 (2H, m), 2.45 (4H, m), 1.67 (2H, m), 1.52 (2H, m), 1.45−1.26 (12H, m). Anal. Calcd for $C_{21}H_{30}N_2O_6S$: C, 57.52; H, 6.90; N, 6.39; S, 7.31. Found: C, 57.72; H, 6.85; N, 6.24; S, 6.98.

3,5-Dinitrobenzyl 11-[(4-Cyanobenzyl)thio]undecanoate (17). 11-Bromoundecanoic acid (**8**, 1.2 g, 4.5 mmol), thiourea (0.38 g, 5.0 mmol), and 18 mL of DMSO were warmed slightly to attain solution and then stirred overnight at room temper-

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ature. To this reaction mixture, 68 mL of 10% NaOH was added, and the mixture was stirred for 30 min in an ice bath. 4-Cyanobenzyl bromide (1.00 g, 5.1 mmol) was then added slowly. The mixture was stirred overnight and then diluted with 400 mL of water and filtered. The filtrate was acidified with concentrated HCl to pH 2 to give 1.35 g (90%) of a white precipitate of 11-[(4-cyanobenzyl)thio]undecanoic acid (**16**): mp 85−86.5 °C; IR ($CDCl_3$) 3276, 2919, 2850, 2238, 1725, 1605, 1411, 1165, 847 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60 (2H, d), 7.42 (2H, d), 3.72 (2H, s), 2.36 (4H, m), 1.62 (2H, m), 1.53 (2H, m), 1.42−1.25 (12H, m).

Compound **16** (0.20 g, 0.60 mmol), DCC (0.124 g, 0.60 mmol), alcohol **2** (0.119 g, 0.60 mmol), and 4-pyrrolidinopyridine (9 mg, 0.06 mmol) were dissolved in 20 mL of dry CH_2Cl_2. The reaction mixture was stirred for 1.5 h and then cooled to −5 °C to precipitate *N*,*N*-dicyclohexylurea, which was removed by filtration. The filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography (hexane/EtOAc 8/2) followed by recrystallization from diethyl ether at −5 °C to give 57 mg (19%) of **17** as off-white crystals: mp 48−49 °C; IR (KBr) 3089, 2928, 2853, 2224, 1737, 1605, 1543, 1344, 1165, 729 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.00 (1H, s), 8.55 (2H, s), 7.60 (2H, d), 7.42 (2H, d), 5.31 (2H, s), 3.72 (2H, s), 2.42 (4H, m), 1.67 (2H, m), 1.53 (2H, m), 1.42−1.25 (12H, m). Anal. Calcd for $C_{26}H_{31}N_3O_6S$: C, 60.80; H, 6.08; N, 8.18; S, 6.24. Found: C, 61.23; H, 6.29; N, 7.88; S, 6.25.

3,5-Dinitrobenzyl 11-(Methyldithio)undecanoate (20). 11-Bromoundecanoic acid (**8**, 2.0 g, 7.5 mmol) was dissolved in 17 mL of methanol. Water (7 mL) was added slowly until a slight turbidity developed. The mixture was refluxed while sodium thiosulfate pentahydrate (2.34 g, 9.43 mmol) in 5 mL of water was added over 15 min. After 6 h, the mixture was cooled and concentrated by rotary evaporation to a milky solution of **18**. Water (20 mL) was added, the mixture was cooled to 0 °C, sodium thiomethoxide (0.529 g, 7.54 mmol) in 3.5 mL of water was added, and the mixture was stirred for 1 h. Addition of 5% HCl precipitated 11-(methyldithio)undecanoic acid (**19**) as a white solid (1.78 g, 90%): mp 112.5−114 °C; IR (KBr) 3200−2700 (br), 2921, 2851, 1715, 1462, 1238, 1198, 1034 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.72 (2H, t), 2.39 (3H, s), 2.18 (2H, t), 1.62 (2H, m), 1.47 (2H, m), 1.36−1.25 (12H, m).

Compound **19** (0.50 g, 1.9 mmol), DCC (0.391 g, 1.89 mmol), alcohol **2** (0.375 g, 1.89 mmol), and 4-pyrrolidinopyridine (28 mg, 0.19 mmol) were dissolved in 50 mL of dry CH_2Cl_2. The reaction mixture was stirred for 1 day. DMAP (12 mg, 0.095 mmol) was then added. After 1 day, the reaction mixture was put in the freezer to precipitate dicylcohexylurea, which was removed by filtration. The filtrate was concentrated by rotary evaporation and treated with 5% HCl, which was then extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude product was purified twice by column chromatography (hexane/EtOAc 4/1, then CH_2Cl_2) followed by trituration with hexane to give 53 mg (6%) of **20** as a yellow oil: TLC (hexane/EtOAc 7/3) R_f 0.42 and (CH_2Cl_2) R_f 0.71; IR (KBr) 3099, 2922, 2850, 1743, 1545, 1463, 1344, 1159 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.0 (1H, s), 8.55 (2H, s), 5.31 (2H, s), 2.68 (2H, t), 2.44 (2H, t), 2.41 (3H, s), 1.68 (4H, m), 1.35−1.20 (12H, m). Anal. Calcd for $C_{19}H_{28}N_2O_6S_2$: C, 51.33; H, 6.35; N, 6.30; S, 14.43. Found: C, 51.53; H, 6.33; N, 6.20; S, 14.25.

Acknowledgment. We thank Mr. Montray Leavy for performing the reduction of the hexadecanethiol SAM. This work was supported by the National Science Foundation and the State of Mississippi through the Mississippi EPSCoR Project.

CM980553X