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Synthesis of Symmetrical and Unsymmetrical Alkyl Disulfides with Attached Flavin Analog for Formation of Self-Assembled Monolayers on Gold

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Abstract: We describe a general procedure for the synthesis of symmetrical and unsymmetrical disulfides with an attached flavin analog. Self-assembled monolayers of these disulfides on gold have potential applications as pH sensors and electrocatalysts. The use of a self-assembled monolayer prepared from one of these disulfides in probing the pH of solutions is reported.

Keywords: Flavins, electrochemistry

Introduction

Long-chain, terminally functionalized alkanethiols ($HS(CH_2)_nX$) or alkyl disulfides ($X(CH_2)_nSS(CH_2)_nX$) absorb spontaneously on gold surfaces to form self-assembled monolayers (SAMs).[1] Monolayers with a large variety of terminal groups X have been studied extensively as fundamental models of organic surfaces and have found applications in a wide range of scientific and technological areas.[2] SAMs with redox-active components are particularly useful as model systems for studying the interfacial microenvironments that influence electron transfer[3] and have potential applications in electrocatalysis,[4] sensors,[5] and electrochemical devices such as organic light-emitting diodes[6] and ion-gates.[7]

We are interested in studying SAMs with flavin analogs as the redox-active terminal group. Flavoenzymes are important enzymes that catalyze a wide range of electrochemical reactions in biological systems.[8] The electrochemical properties of flavin (the redox-active moiety of flavoenzymes) are governed by non-covalent interactions (including π-stacking, hydrophobic effects, hydrogen bonding, and electrostatic interactions)[9] between flavin and the apoprotein to which it is bound. The redox potential of flavin varies by at least 600 mV in different apoproteins. In the absence of apoproteins, flavins (e.g. flavin adenine dinucleotides, FAD, or mononucleotide, FMN) and analogs (e.g. **1**)[10] undergo two reversible 1e$^-$ reduction steps with overlapping potentials in aqueous solutions (Scheme I). The formal potential of **1** dissolved in aqueous solution

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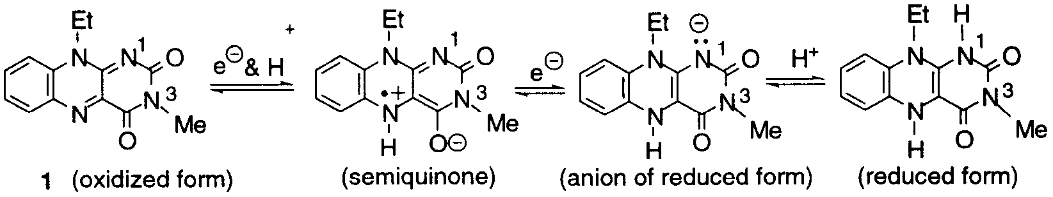
is linearly related to pH with a slope of -0.057 V (pH unit)$^{-1}$ up to pH 6.7 (Figure 1).[11] The slope decreases to -0.027 V (pH unit)$^{-1}$ at higher pH values. Similar relationships are observed for FAD and FMN.[12] The change in slope at pH 6.7 is attributed to dissociation of the N^1-proton in the reduced form.

Scheme I



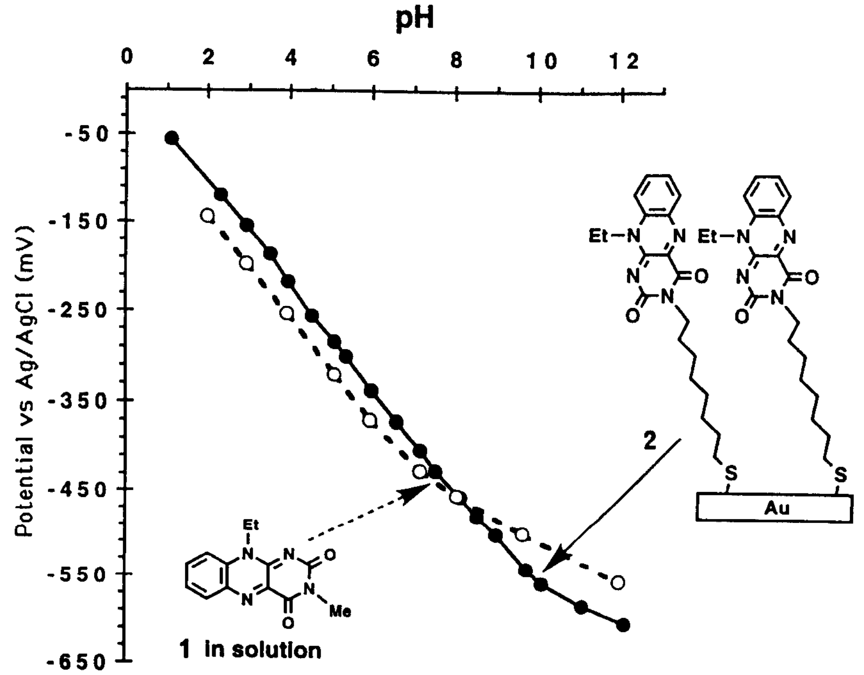
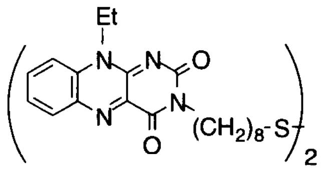
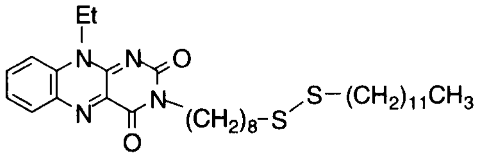


Figure 1. The pH dependence of the redox potential (E$^{0'}$) of isoalloxazine of **2** in a self-assembled monolayer on gold (filled circles) compared with **1** (1mM) dissolved in aqueous buffer solution (open circles).

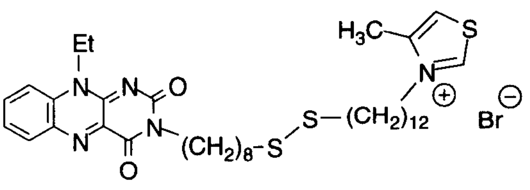
SAMs with attached flavin analogs may serve as model systems for studying microenvironmental effects on the redox properties of flavin.[13] They also have potential applications in electrocatalysis and sensors.[14,15] We developed a convenient procedure for the synthesis of symmetrical disulfide **2** with an attached isoalloxazine moiety (the heterocyclic ring system of flavin). In a recent communication,[11] we reported the formation and electrochemical studies of the SAMs of this disulfide on gold. At shown in figure 1, the inflection point of the redox potential – pH plot of **2** is at pH 10. This indicates a pK_a value of about 10 for the *N*-1 proton of the reduced isoalloxazine of **2** in SAMs --a 1000 fold increase in the acid dissociation constant (K_a) when compared to that of **1** free in solution which has a pK_a value of 6.7. This leads to a linear change in redox potential of about 600 mV over a pH range of 10. In this paper, we describe the detailed procedure for the synthesis of disulfide **2** and the use of the SAMs from this disulfide to probe pH of solutions. In addition, this general synthetic procedure is very useful for preparing unsymmetrical disulfides. We describe herein the synthesis of unsymmetrical disulfides **3** and **4** as examples. Our interest in **4**, containing a thiazolium and a flavin moiety arises from the potential use of its SAM on gold in catalyzing the one-pot synthesis of methyl esters from aldehydes.[14] In solution, the thiazolium ion reacts with aldehydes to form a reactive intermediate[16] which can be readily oxidized by flavins.[14, 17] The oxidized intermediate then reacts with methanol yielding the desired ester and regenerating the thiazolium catalyst. The reduced flavin can then be regenerated efficiently at an electrode. The use of unsymmetrical disulfide **4** may ensure close proximity between the thiazolium and flavin catalysts, thus promoting efficient oxidation of the reactive intermediate by flavin. Furthermore, immobilization of **4** on gold by formation of SAM may allow efficient regeneration of flavin at the gold electrode.



2



3



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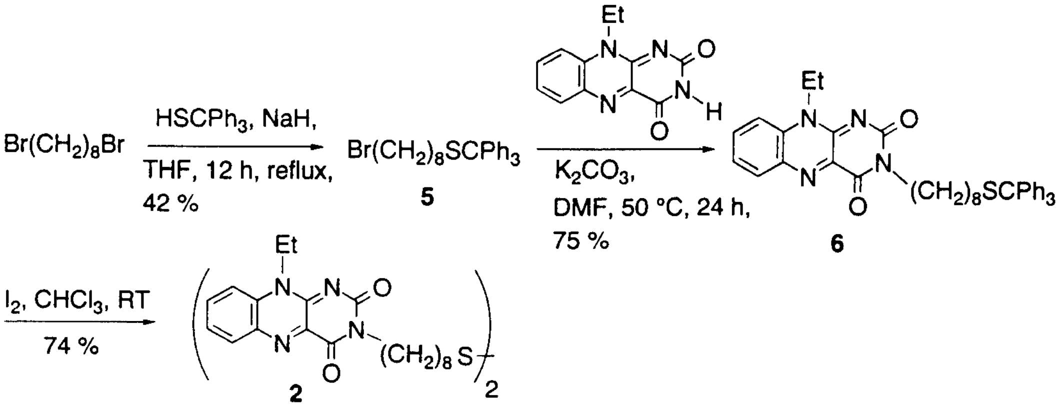
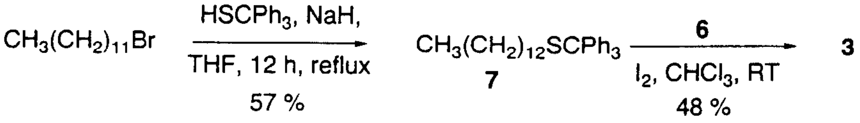
Results and Discussion

In order to avoid thiol oxidation in solution by the isolloxazine group, the more stable disulfides (**2-4**) were synthesized. The synthetic approach of **2** is outlined in Scheme II. Mono-substitution of 1,8-dibromooctane with triphenylmethyl mercaptan in the presence of sodium hydride gave 8-bromo-1-(*S*-trityl)mercaptooctane (**5**). Deprotonation of the *N*-3 proton of 10-ethylisoalloxazine[10] by potassium carbonate followed by *N*-alkylation with **5** yielded the key intermediate **6**. Compound **6** can be converted readily to symmetrical disulfide **2** by iodine coupling[18] of the tritylmercapto- group. Iodine coupling of **6** with other tritylmercapto- compounds such as **7** (Scheme III) yielded unsymmetrical disulfide **3**. The unsymmetrical disulfide **4** consisting of both thiazolium and isoalloxazine moieties was obtained by oxidative coupling of intermediate **6** with **8** to generate the unsymmetrical disulfide **9**, followed by nucleophilic substitution of **9** by 4-methylthiazole (Scheme IV).

Scheme II

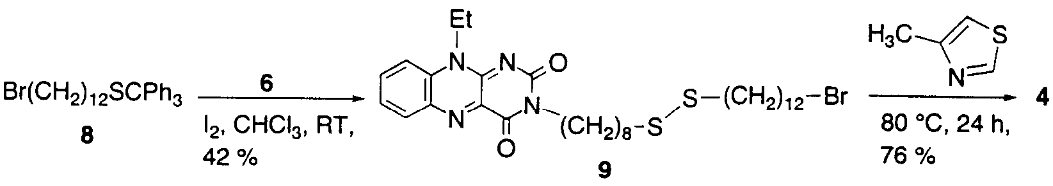


Scheme III



$$\mathrm{CH_3(CH_2)_{11}Br} \xrightarrow[\text{THF, 12 h, reflux, 57 \%}]{\mathrm{HSCPh_3,\ NaH,}} \underset{\mathbf{7}}{\mathrm{CH_3(CH_2)_{12}SCPh_3}} \xrightarrow[\mathrm{I_2,\ CHCl_3,\ RT,\ 48\ \%}]{\mathbf{6}} \mathbf{3}$$

Scheme IV



Characterization of SAMs from disulfides 2-4 by cyclic voltammetry

The redox properties of the SAMs from disulfides **2-4** were determined by cyclic voltammetry in buffer solutions. A representative cyclic voltammogram of a SAM from **2** at high pH is shown in Figure 2. The flavin moieties in these SAMs are stable to repeated cycling, no observable changes in redox potential or peak currents occur for at least 20 cycles after attaining steady state (Figure 3). The surface coverage of the flavin moiety in the SAMs from **2**-**4** was calculated by integrating the area under the oxidation or reduction peak and determined to be approximately 4.6 x 10^{-10} mol/cm^2, 2.4 x 10^{-10} mol/cm^2, and 2.1 x 10^{-10} mol/cm^2 respectively. In the case of **3** and **4**, these values are consistent with the flavin moieties covering half of the monolayer surface in SAMs from **3** and **4**, and the dodecyl chains or the thiazolium moieties covering the other half. Detailed studies of the redox and catalytic properties of a SAM from **4** are underway.

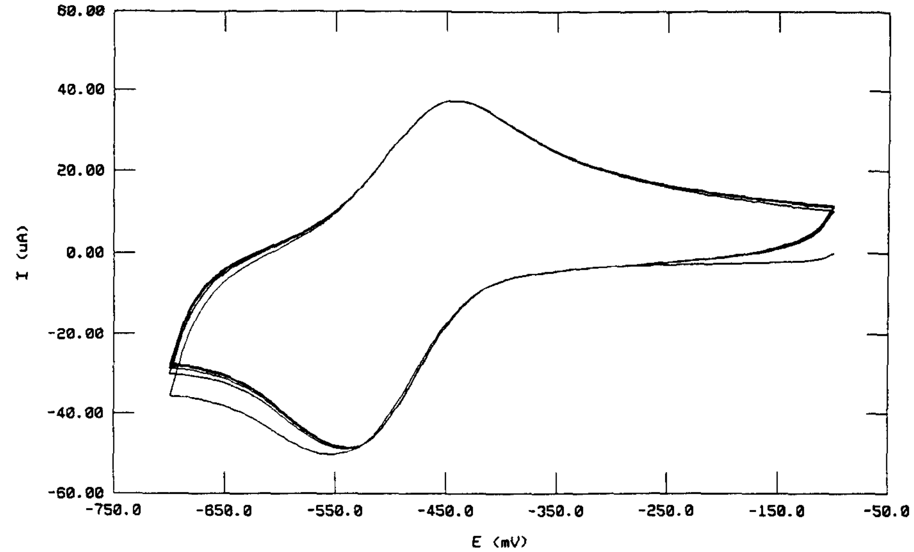


Figure 2. Cyclic voltammogram of a SAM from **2** in an aqueous buffer solution at pH 9.02 (first cycle and steady state cycle). Scan rates are 0.1 Vs^{-1}.

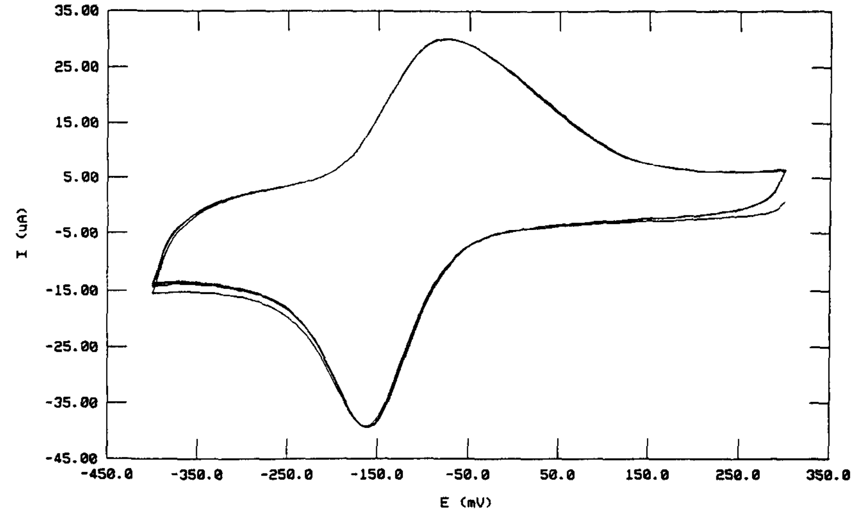


Figure 3. Cyclic voltammogram of a SAM from **2** in an aqueous buffer solution at pH 2.3 (first cycle and steady state cycles). Scan rates are 0.1 Vs^{-1}.

SAMs from 2 as pH probe

The linear change in redox potential of about 600 mV over a pH range of 10 allows the use of a SAM from **2** as a sensitive probe of pH. We determined the redox potentials of the monolayer in several unbuffered electrolyte solutions by cyclic voltammetry (Table 1). The pH values of the solutions can be determined from the redox potentials of **2** in SAM using the calibration plot in Figure 1 or calculated from the equation $E^{0'}$ vs Ag/AgCl (mV) = -57pH + 9. The pH values calculated from the redox potentials agree with the values measured with a combination pH electrode and pH meter.

Table 1. Determination of pH of electrolyte solutions from redox potential of a monolayer of **2**.

Electrolyte Solution	$E^{0'}$ (mV)	pH calculated from $E^{0'}$ [a]	pH measured[b]
0.2 M HOAc	-141±5	2.6±0.1	2.76
0.1 M NaOAc	-444±5	7.9±0.1	7.84
0.1 M NaH_2PO_4	-256±5	4.7±0.1	4.71
0.1 M Na_2HPO_4	-525±5	9.4±0.1	9.37

[a] $E^{0'}$ vs Ag/AgCl (mV) = -57(pH) + 9. [b] The pH values of solutions are measured using a Corning mV/pH meter (model 350) with a combination electrode.

Summary

The general procedure we developed provides a convenient route for the synthesis of symmetrical and unsymmetrical disulfides with an attached flavin analog. The SAMs prepared from these disulfides contain a flavin moiety that can be used to probe the pH of solutions accurately. Currently, we are exploring the use of SAM patterning techniques to fabricate a pH microsensor that contains an internal microreference as well as the flavin sensing domain. We are also exploring the use of flavin derivatized monolayers on gold in electrocatalysis and the tuning of its redox potential by controlling its microenvironment in SAMs.

Experimental

Materials and General Methods: Melting points were determined on a Melt-Temp apparatus and are uncorrected. All nuclear magnetic resonance (NMR) spectra were measured on a GE QE-300 in $CDCl_3$ and are reported in δ (ppm) downfield from tetramethyl silane or using known chemical shifts of solvents as reference. High resolution mass spectrum analyses were determined by the mass spectrometry facility at University of California, Riverside, USA. Microanalysis was performed by Roberston Microlit Laboratories, Inc. Madison, NJ. Tetrahydrofuran (THF) is dried and distilled over sodium before used.

Gold-coated silicon wafers were prepared by thermal deposition of a 25 Å layer of chromium (to enhance the adhesion), followed by a 500 Å layer of gold (99.99%). The gold-coated wafers were washed sequentially with ethanol, water, ethanol, and chloroform. SAMs were prepared by immersing the wafer in 20 mL of a dilute solution (1.0-0.02 mM) of disulfides in acetonitrile at room temperature for more than 50 hours. The modified surfaces were then rinsed repeatedly with ethanol, chloroform and dried under a slow stream of argon.

Cyclic Voltammetry. The formal potential ($E^{0'}$) of the bound isoalloxazine moiety was determined from the mean value of the cathodic and anodic peak potentials in cyclic voltammograms. All experiments were done using a conventional three-electrode cell, with the SAM-modified gold surface as the working electrode. A platinum wire was used as counter electrode, and Ag/AgCl (containing aqueous solution of 3 M NaCl and saturated AgCl: EG&G filling solution for reference electrode M400) as reference electrode. Unbuffered solutions were preprared by dissolving electrolytes in water. The pH values of all solutions were determined by a Corning mV/pH meter 350 (Corning high performance combination electrode No. 476390) before use in experiments. Electrochemical experiments were performed using an EG&G potentiostat/galvanostat model 263A, controlled by EG&G M270 electrochemical PC software to record and analyze data. Solutions were purged with argon to remove oxygen, and the argon atmosphere was maintained over the solution during the measurements. All experiments were done at room temperature (25 °C).

Synthesis

3-{8-[8-(10-Ethyl-2,4-dioxo-4,10-dihydro-2*H*-benzo[*g*]pteridin-3-yl)-octyldisulfanyl]-octyl}-10-ethyl-10*H*-benzo[*g*]pteridine-2,4-dione (2). Compound **6** (0.95 g, 1.51 mmol) was dissolved in 50 mL of chloroform and a separate solution of 1.12 g of iodine in 150 mL of chloroform was prepared. The two solutions were mixed and stirred for 10 minutes. The solution was decanted into a separatory funnel and washed with 50 mL of 0.1 M sodium thiosulfate and 50 mL of water. The reaction flask contained a black tar that was dissolved in a 150 mL of a 1/1/1 mixture of chloroform/methanol/water and added to a separatory funnel. The solution was washed with 50 mL of 0.1 M sodium thiosulfate and 50 mL of water. The chloroform layer was separated, combined with the first extraction and dried with magnesium sulfate. The solvent was removed *in vacuo*. The product was purified by radial chromatography (silica plate 2 cm thick, solvent 2 % MeOH/$CHCl_3$) to give 0.43 g (0.56 mmol, 74 % yield) of product. ^{1}H-NMR (300 MHz, $CDCl_3$) 8.35 (2H, J = 8.3, 1.5 Hz, dd), 7.90 (2H, J = 7.3, 7.3, 1.5 Hz, ddd), 7.59-7.67 (4H, overlapping resonances), 4.78 (4H, J = 7.3 Hz, q), 4.10 (4H J = 7.3 Hz, t), 2.65 (4H, J = 7.3 Hz, t), 1.51 (6H, J = 7.3 Hz, t), 1.7-1.2 (24H, overlapping resonances); ^{13}C-NMR (75 MHz, $CDCl_3$) 159.2, 155.4, 148.4, 137.3, 135.8, 135.3, 133.4, 132.3, 126.1, 114.7, 41.9, 39.9, 39.0, 29.1, 28.9, 28.3, 27.6, 26.7, 14.0, 12.1. HRMS (FAB): calcd for $C_{40}H_{51}N_8O_4S_2$ $(M + H)^+$: 771.3474, obsd. 771.3462.

3-(8-Dodecyldisulfanyl-octyl)-10-ethyl-10*H*-benzo[*g*]pteridine-2,4-dione (3). 12-(*S*-Trityl)mercaptododecane (**7**) (1.09 g, 2.45 mmol) and 0.447 g (0.711 mmol) of 10-ethyl-3-[8-(*S*-trityl) mercaptooctane]isoalloxazine (**6**) were dissolved in 20 mL of chloroform and 10 mL of methanol. Iodine (1.11 g) was dissolved in 40 mL of a 50/50 mixture of methanol and chloroform. The iodine mixture was added to the reaction mixture and allowed to stir for 20 minutes. Chloroform (300 mL) was added to the solution and then extracted with 50 mL of 0.5 N sodium thiosulfate, water (3 x 50 mL portions), and dried over magnesium sulfate. The solvent was removed *in vacuo*. The crude product was purified by column chromatography (silica, 2 % MeOH/$CHCl_3$) and crystallized in ethanol to give 0.20 g (0.341 mmol, 48 % yield) of product. mp 125-127 °C; ^1H-NMR (300 MHz, $CDCl_3$) 8.34 (1H, J = 7.8, 1.0 Hz, dd), 7.91 (1H, J = 7.3, 7.3, 1.5 Hz, ddd), 7.61-7.68 (2H, overlapping resonances), 4.79 (2H, J = 6.8 Hz, q), 4.11 (2H, J = 7.6 Hz, t), 2.67 (4H, J = 7.3 Hz, t), 1.8-1.1 (32H, overlapping resonances), 1.52 (3H, J = 7.3 Hz, t), 0.87 (3H, J = 6.8 Hz, t); ^{13}C-NMR (75 MHz, $CDCl_3$) 159.4, 155.5, 148.6, 137.3, 135.9, 135.5, 133.5, 132.4, 126.2, 114.9, 42.0, 40.1, 39.3, 31.8, 29.6, 29.5, 29.3, 29.2, 29.1, 29.0, 28.5, 28.4, 27.7, 26.8, 22.6, 14.0, 12.3. HRMS (FAB): calcd for $C_{32}H_{51}N_4O_2S_2$ $(M + H)^+$: 587.3453, obsd. 587.3441.

3-{12-[8-(10-Ethyl-2,4-dioxo-4,10-dihydro-2*H*-benzo[*g*]pteridin-3-yl)-octyldisulfanyl]-dodecyl}-4-methyl-thiazol-3-ium bromide (4). 12-Bromododecyl 8-(10-ethylisoalloxazine)octyl disulfide (**9**) (0.27 g, 0.41 mmol) was dissolved in 3 mL of 4-methylthiazole and heated to 90 °C for 18 h. After cooling the solution to room temperature, the excess 4-methylthiazole was removed *in vacuo*. A total of 10 mL of ethyl acetate was added and the crude product was sonicated. A total of 0.238 g (0.31 mmol, 76 % yield) of a yellow solid was recovered after filtration. mp 125-127 °C; ^1H-NMR (300 MHz, $CDCl_3$) 11.52 (1H, s), 8.33 (1H, J = 8.3 Hz, d), 7.92 (1H, J = 7.3 Hz, t), 7.79 (1H, s), 7.62-7.7 (2H, overlapping resonances), 4.80 (2H, J = 6.8 Hz, q), 4.72 (2H, J = 7.6 Hz, t), 2.67 (4H, J = 7.3 Hz, t), 2.64 (3H, s), 2.0-1.25 (35H, overlapping resonances). HRMS (FAB): calcd for $C_{36}H_{54}N_5O_2S_3$ (M^+): 684.3440, obsd 684.3424.

8-Bromo-1-(*S*-trityl)mercaptooctane (5). 1,8-Dibromooctane (7.37 g, 27.1 mmol) and 0.83 g of (60 % in mineral oil) sodium hydride was dissolved in 30 mL of tetrahydrofuran. Triphenylmethyl mercaptan (1.86 g, 6.74 mmol) dissolved in 10 mL of tetrahydrofuran was added dropwise. The solution was brought to reflux overnight. The solvent was removed *in vacuo* . The crude product was dissolved in methylene chloride, washed with water, saturated sodium chloride solution, and dried with sodium sulfate. The solvent was evaporated and the crude compound was placed in the freezer to solidify. The solid was placed on a suction filter, the excess 1,8-dibromooctane began to melt upon warming to room temperature and left the product as residue on the filter funnel. This was done twice and the crude product was crystallized in hexane to obtain 1.34 g (2.87 mmol, 42 % yield) of product. mp 86 °C; ^1H-NMR (300 MHz, $CDCl_3$) 7.40 (6H, J = 7.8 Hz, d), 7.30-7.18 (9H, overlapping resonances), 3.38 (2H, J = 6.8 Hz, t), 2.13 (2H, J = 7.3 Hz, t), 1.82 (2H, m), 1.41-1.16 (10H, overlapping resonances); ^{13}C-NMR (75 MHz, $CDCl_3$) 145.14, 129.65, 127.78, 126.51, 66.47, 33.83, 32.78, 31.98, 28.92, 28.57, 28.51, 28.06. HRMS (FAB): calcd for $C_{27}H_{31}SKBr^+$ (M + K)$^+$: 505.0967, obsd 505.0988.

10-Ethyl-3-(8-tritylsulfanyl-octyl)-10*H*-benzo[g]pteridine-2,4-dione (6). A total of 2.08 g (4.45 mmol) of 8-bromo-1-(*S*-trityl)mercaptooctane (**5**), 1.04 g (4.29 mmol) 10-ethylisoalloxazine, 1.5 g of potassium carbonate, and 30 mL of DMF were heated at 60 °C for 14 hours. The solution was cooled and the DMF was removed by distilling under vacuum. The crude product was dissolved in 50 mL of chloroform, washed with water (4 x 50 mL portions), and dried over magnesium sulfate. The solvent was removed *in vacuo*. The product was purified by column chromatography (silica, 2 % MeOH/$CHCl_3$) to give 2.99 g (3.19 mmol, 74 % yield) of product. mp 180-184 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) 8.33 (1H, J = 7.8, 1.5 Hz, dd), 7.90 (1H, J = 7.3, 1.5 Hz, td), 7.6-7.7 (2H, m), 7.40 (6H, J = 7.3 Hz, d), 7.3-7.17 (9H, overlapping resonances), 4.78 (2H, J = 7.3 Hz, q), 4.09 (2H J = 7.3 Hz, t), 2.11 (2H, J = 7.3 Hz, t), 1.8-1.1 (12H, overlapping resonances), 1.51 (3H, J = 7.3 Hz t). ^{13}C-NMR (75 MHz, $CDCl_3$) 159.3, 155.4, 148.4, 145.0, 137.1, 135.8, 135.3, 133.3, 132.2, 129.5, 127.6, 126.3, 126.1, 114.8, 66.3, 42.0, 39.9, 31.9, 28.93, 28.87, 28.78, 28.5, 27.6, 26.7, 12.1. HRMS (FAB): calcd for $C_{39}H_{41}N_4O_2S$ (M + H)$^+$: 629.2950, obsd 629.2983.

12-(*S*-Trityl)mercaptododecane (7). Triphenylmethyl mercaptan (2.45 g, 8.88 mmol), 2.49 g (10.0, mmol) of 1-bromododecane, 2.08 g of sodium hydride (60% in mineral oil) and 50 mL of tetrahydrofuran was refluxed overnight. The solution was filtered and the solvent was evaporated. The crude product was dissolved in 50 mL of methylene chloride. The solution was washed with water (3 x 50 mL portions), dried with magnesium sulfate and the solvent was removed *in vacuo*. The crude yellow product was recrystallized in hexane to give 1.82 g of crude product. The filtrate was reduced in volume two more times to recover an additional 1.39 g. The crude products were combined and recrystallized a second time to yield 2.24 g (5.04 mmol, 57 % yield) of product. mp 43-48 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) 7.41 (6H, J = 7.3 Hz, d), 7.3-7.18 (9H, overlapping resonances), 2.13 (2H, J = 7.32 Hz, t), 1.38-1.16 (20H, overlapping resonances), 0.87 (3H, J = 6.8 Hz, t); ^{13}C-NMR (75 MHz, $CDCl_3$) 145.2, 129.7, 127.7, 126.5, 66.5, 32.1, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 29.0, 28.7, 22.7, 14.1.

12-Bromo-1-(*S*-trityl)mercaptododecane (8). A total of 20.81 g (63.4 mmol) of dibromododecane, 3.98 g (14.4 mmol) of triphenylmethyl mercaptan, 4.00 g of sodium hydride (60% in mineral oil) and 80 mL of THF were refluxed over 24 hours. The solution was filtered after cooling to room temperature and the solvent was removed *in vacuo*. The crude product was dissolved in 75 mL of ether and washed with water (5 x 75 mL portions). The solvent was dried with magnesium sulfate and removed *in vacuo*. The yellow oil was dissolved in 100 mL of hexane and placed in the freezer. The solution was cooled overnight and the white solid was filtered and allowed to dry (11.01 g). The solid was recrystallized twice more in hexane and 4.01 g of crude product was purified by column chromatography (silica, 5 % ethyl acetate/hexane) to give 2.7 g (5.16 mmol, 36 % yield) of product. mp 86-88 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) 7.41 (6H, *J* = 7.8 Hz, d) 7.3-7.17 (9H, overlapping resonances), 3.40 (2H, *J* = 7.1 Hz, t), 2.13 (2H, *J* = 7.3 Hz, t), 1.85 (2H, m), 1.5-1.1 (18H, overlapping resonances); ^{13}C-NMR (75 MHz, $CDCl_3$) 145.2, 129.6, 127.7, 126.45, 66.5, 33.7, 32.8, 32.1, 29.4, 29.3, 29.1, 29.0, 28.7, 28.6, 28.2.

3-[8-(12-Bromo-dodecyldisulfanyl)-octyl]-10-ethyl-10*H*-benzo[*g*]pteridine-2,4-dione (9). 10-Ethyl-3-[8-(S-trityl)mercaptooctane) isoalloxazine (**6**) (0.59 g, 0.94 mmol), and 0.51 g (0.98 mmol) of **8** were dissolved in 15 mL of chloroform and 10 mL of methanol. Iodine (0.66 g) was dissolved in 30 mL of a 50/50 mixture of chloroform and methanol and added to the first solution. The solution was stirred for 15 minutes and 300 mL of chloroform was added. The solution was washed with 50 mL of 0.5 N $Na_2S_2O_4$, water (3 x 50 mL portions), and dried with magnesium sulfate. The solvent was removed *in vacuo* and the crude product was purified by column chromatography (silica, 2 % MeOH/$CHCl_3$) to give 0.19 g (0.25 mmol, 26 %) of symmetrical disulfide **2** and 0.28 g (0.42 mmol, 42 % yield) of product **9** which was recrystallized in ethanol for elemental analysis. mp 109-110°C; ^{1}H-NMR (300 MHz, $CDCl_3$) 8.34 (1H, *J* = 7.7 Hz, d), 7.90 (1H, *J* = 7.3 Hz, t), 7.6-7.7 (2H, overlapping resonances), 4.79 (2H, *J* = 7.3 Hz, q), 4.11 (2H, *J* = 7.6 Hz, t), 3.41 (2H, *J* = 6.8 Hz, t), 2.67 (4H, *J* = 7.3 Hz, t), 1.87-1.1 (35H, overlapping resonances); ^{13}C-NMR (75 MHz, $CDCl_3$) 159.4, 155.5, 148.6, 137.4, 136.0, 135.4, 133.5, 132.4, 126.2, 114.9, 42.1, 40.1, 39.3, 33.8, 32.8, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.7, 28.5, 28.2, 27.7, 26.9, 12.3. HRMS (FAB): calcd for $C_{32}H_{50}N_4O_2S_2Br$ $(M + H)^+$:665.2558, obsd 665.2562. Anal. Calcd for $C_{32}H_{49}N_4O_2S_2Br$: C, 57.73%; H, 7.42%. Found: C, 57.83%; H, 7.62%.

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