Synthesis and Structure of Functionalized Derivatives of the Cleft-Shaped Molecule Dithiosalicylide

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Introduction

Conformationally rigid molecules whose structures define cavities and clefts have potential uses as receptors,[1−3] catalysts,[4,5] and as molecular building blocks in the construction of new materials.[6] Dithiosalicylides are a class of conformationally well-defined, cleft-shaped molecules.[7,8] NMR[7] and X-ray crystallographic[8] studies have shown that dithiosalicylide (**1**) adopts a boat conformation where the aromatic rings form a shallow "v-shaped" pocket in which the dihedral angle between the aromatic rings is approximately 65 °.[8] Although dithiosalicylides are not conformationally locked, as is the case for the structurally related Kagan's ether[1,2] and Troeger's base[3] compounds, the inversion barrier between the enantiomeric boat conformations is quite high (∼25 kcal/mol).[7]

As part of investigations[9−11] into the chemistry of 3*H*-1,2-benzodithiol-3-one 1-oxide and related compounds, we recently developed a simple preparation of dithiosalicylide from 3*H*-1,2-benzodithiol-3-one (**2**).[12,13] Treatment of **2** with triphenylphosphine provides good yields of **1**, presumably via dimerization of a benzothietan-2-one (**3**) or ketene (**4**) intermediate (Scheme 1).[14] We describe here the application of this protocol to the preparation of dithiosalicylide analogs that present larger cavities than the parent compound and to several analogs that may be amenable to further functionalization. In addition, we present the crystal structures of two dithiosalicylides that show that the compounds form discrete, self-included dimers and that interactions between the dimers give rise to interesting supramolecular structures.

Results and Discussion

The 3*H*-1,2-benzodithiol-3-ones (**5**) used in these studies were prepared by conversion of the appropriately substituted anthranilic acid derivatives (**6**) to the corresponding thiosalicylic acid analogs (**7**),[15] followed by cyclization using thiolacetic acid in sulfuric acid (Scheme 2).[16] In each case, treatment of **5** with triphenylphosphine in methylene chloride at room temperature affords good yields of the corresponding dithiosalicylide analogs (**8**) (Scheme 2). Consistent with the notion (Scheme 1) of negative charge developing on sulfur in the transition state of the triphenylphosphine-mediated dimerization reaction, we observe that **5b** reacts more rapidly than either **5a** or **2**.

With the aim of preparing functionalizable dithiosalicylides, we sought to brominate the methyl positions of **8a**. Accordingly, treatment of **8a** with *N*-bromosuccinimide (NBS) in carbon tetrachloride yields a mixture of brominated analogs that are separable by careful silica gel column chromatography and recrystallization. With careful control of conditions, it is possible to obtain the monobrominated cleft (**9**) and the dibrominated cleft (**10**) in 30% and 27% recovered yields respectively (Scheme 3).

Because the dithiosalicylide-forming reaction described here (Scheme 1) involves dimerization of triphenylphosphine-activated 3*H*-1,2-benzodithiol-3-ones, it is possible to prepare assymetrically functionalized clefts by this method. For example, treatment of a 1:1 mixture of **5b** and **5c** with triphenylphosphine in methlylene chloride at 24 °C affords **11**, **8b**, and **8c** in approximately equal yields. These products are separable by careful column chromatography. Using this approach, the asymmetric clefts **11**−**14** were prepared.

Crystals of dithiosalicylides **8c** and **11** suitable for X-ray analysis were obtained by dissolving each compound in a mixed solvent system (ethyl acetate:hexane for **11** and chloroform:ethanol for **8c**) and allowing slow evaporation to dryness. As shown in Figure 1, each molecule contains a well-defined v-shaped pocket with dihedral angles between the planes of their aromatic units of 56.6° (**8c**) and 62.2° (**11**), similar to the parent dibenzo derivative **1**.[8] Notably, elaboration of **1** has increased the size of each cleft such that the entrance to each pocket approaches nanometer dimensions as demonstrated by "upper rim" H···H (8.29 Å) and H···Br (8.16 Å) separations for **8c** and **11**, respectively, which are greater than those H···H separations (6.43 and 6.69 Å) of **1**.

Views depicting the crystal structures of **8c** and **11** are shown in Figure 1c,d. Both molecules assemble such that they form self-included dimers held together by offset face-to-face [plane-to-plane distances: 3.36 (**8c**), 3.43 Å (**11**)] and tilted T edge-to-face $\pi-\pi$ interactions [ring center−ring center distances: 5.37 (**8c**), 5.37 Å (**11**)].[17] The self-inclusion exhibited by the unsymmetric cleft **11**

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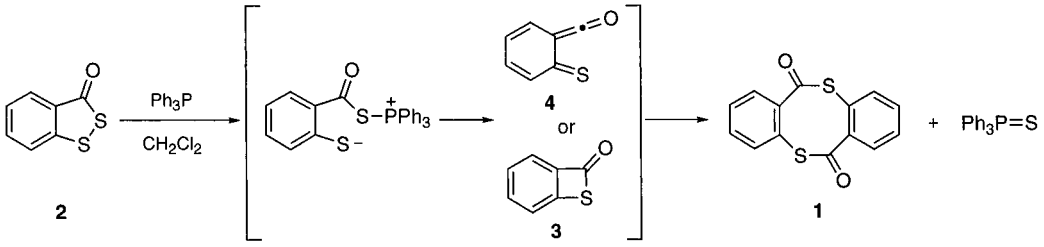
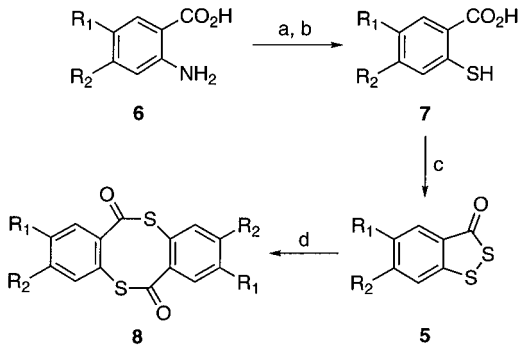
Scheme 1

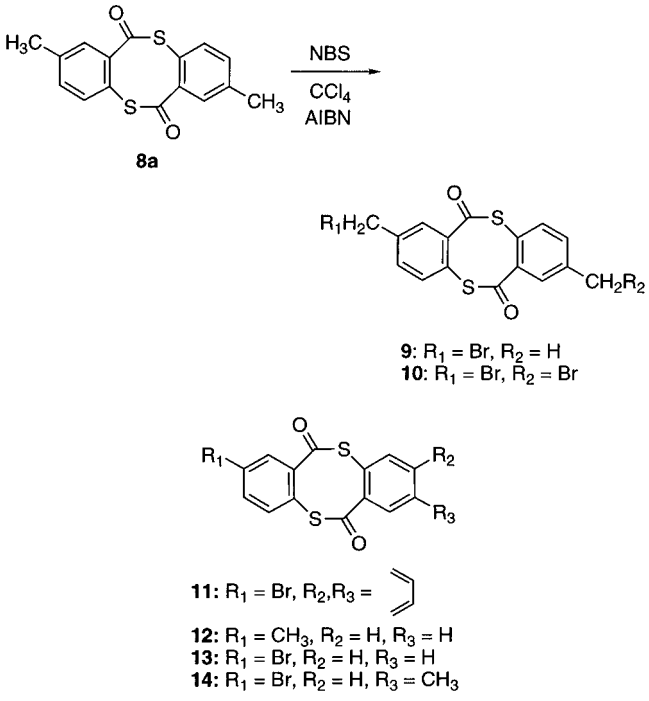


Scheme 2[a]



[a] Reagents: (a) $NaNO_2$–HCl, Na_2S; (b) Zn, HOAc, reflux 8 h; (c) H_2SO_4, CH_3COSH 60 °C; (d) Ph_3P.

Scheme 3



displays selectivity, with the naphthyl, rather than the bromo, substituent residing within the cleft. Neighboring dimers in both structures interact *via* offset face-to-face π–π interactions [plane-to-plane distances: 3.48 and 3.60 Å (**8c**), 3.62 and 3.67 Å (**11**)], which give rise to infinite supramolecular layered arrays.

Experimental Section

Chemicals were purchased from the following suppliers: absolute ethanol, McCormick Distilling Co.; NaOH, $NaHCO_3$, Na_2SO_4, H_2SO_4, HCl, Fisher Chemical Company; 3-amino-2-naphthoic acid, Fluka Chemical Co. All other chemicals were purchased from Aldrich Chemical Co. Thin-layer chromatography was performed on silica gel plates, 0.25 mm, with F_{254} fluorophore (Aldrich), and visualization of compounds was achieved with UV light at 254 or 360 nm. Column chromatography was performed using 230-400 mesh silica gel (Merck) with technical-grade solvents that were distilled prior to use. High resolution mass spectrometry was performed at the Midwest Centre for Mass Spectrometry (University of Nebraska–Lincoln), and elemental analysis was performed at M-H-W Laboratories (Phoenix, AZ). Intensity data for crystallographic studies were collected on Enraf-Nonius CAD-4 diffractometers at 298 K. All crystallographic calculations were conducted using the NRCVAX program package[18] locally implemented on an IBM-compatible pentium-based PC. Packing diagrams were constructed with the aid of RES2INS.[19]

General Procedure for the Synthesis of Substituted 3*H*-1,2-Benzodithiol-3-ones (5). To a stirred suspension of the appropriate anthranilic acid derivative (165 mmol) in water (85 mL) and concd HCl (33 mL) at 5 °C was added dropwise a solution of $NaNO_2$ (11.4 g, 165 mmol) in water (45 mL) and the solution maintained at 5 °C. Crushed ice was added to the reaction mixture periodically during addition to keep the temperature below 5 °C. Meanwhile, $Na_2S{\cdot}9H_2O$ (43.7 g, 182 mmol) and sublimed sulfur (5.8 g, 181 mmol) were dissolved in water (48 mL) by heating and made alkaline by addition of 10 M NaOH (17 mL), and the resulting alkaline disulfide solution was cooled to 5 °C in an ice bath. The cold diazo solution was added to the alkaline disulfide solution dropwise with crushed ice added periodically to maintain the temperature below 5 °C. Following addition of the diazo solution, the mixture was stirred at 24 °C until evolution of N_2 gas stopped. Concentrated HCl was added to the solution until precipitation of the crude product as a yellow solid was complete. The precipitate was collected and boiled in a saturated solution of $NaHCO_3$ (400 mL). After being boiled for 15 min, the mixture was filtered to remove the insoluble material, and concd HCl was added to the filtrate until the crude product precipitated out as a yellow solid. Excess concd HCl was added to the mixture until precipitation was complete, and the precipitate was isolated by filtration. This material was boiled in absolute EtOH (150 mL) for 15 min and filtered and the filtrate concentrated under reduced pressure to yield the 2,2′-dithiosalicylic acid derivative (approximately 90% pure).

The 2,2′-dithiosalicylic acid derivative was mixed with Zn dust (10 g) in glacial CH_3COOH (150 mL) and refluxed for 48 h. The mixture was then cooled and filtered. The solid collected in this manner was boiled in 5 M NaOH (300 mL). After being boiled for 30 min, the undissolved solid was removed by filtration and the clear filtrate acidified with concd HCl until the crude product precipitated out as a yellow solid. Concentrated HCl was added to the mixture until the precipitation was complete. The precipitate was collected and boiled in EtOH (125 mL) and

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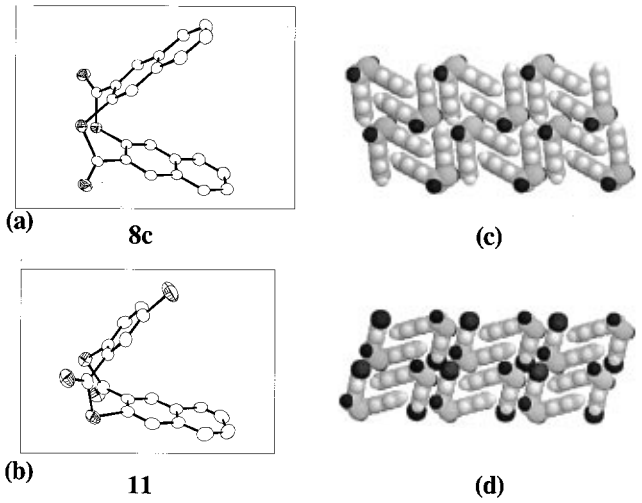

Figure 1.

filtered and the filtrate concentrated under reduced pressure to yield the thiosalicylic acid derivative (**7**) contaminated with a small amount of elemental sulfur. This material was directly carried on to the next step.

To a stirred suspension of the thiosalicylic acid derivative (**7**, 11.9 mmol) in concd H_2SO_4 (25 mL) at 24 °C under N_2 was added thiolacetic acid (1.87 mL, 26.2 mmol) over a period of 10 min. The mixture was placed in an oil bath preheated to 60 °C and stirred for 4 h. The dark mixture was then poured over crushed ice and allowed to stand at 24 °C for 30 min. The precipitate so obtained was triturated with boiling $CHCl_3$ (2 × 100 mL), the resulting $CHCl_3$ solution filtered, and the filtrate extracted with saturated $NaHCO_3$ (2 × 100 mL) and water (2 × 100 mL). The organic layer was dried over Na_2SO_4 and the solvent removed under reduced pressure to yield the crude product (**5**), which was subsequently purified by column chromatography.

5-Methyl-3*H*-1,2-benzodithiol-3-one (5a). The yellow solid was purified by flash chromatography on silica gel with hexane−EtOAc (6:1) to yield **5a** as a yellow solid (64% yield from 5-methylanthranilic acid). This material was recrystallized from EtOAc−hexane to form fine yellow needles: mp 78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.52−7.46 (m, 2H), 7.75 (s, 1H), ^{13}C NMR (500 MHz, $CDCl_3$) δ 20.7, 124.1, 126.9, 129.3, 134.9, 135.9, 145.4, 193.6; IR ($CHCl_3$) 3032, 1675, 1221 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_8H_6OS_2$ 181.9860, found 181.9863. Anal. Calcd for $C_8H_6O_2S$: C, 52.72; H, 3.32. Found: C, 52.90; H, 3.49.

5-Bromo-3*H*-1,2-benzodithiol-3-one (5b). The yellow solid was purified by flash chromatography on silica gel with with hexane−EtOAc (8:1) to yield **5b** as a yellow solid (38% yield from 5-bromoanthranilic acid). This material was recrystallized from EtOAc−hexane to form light yellow needles: mp 114−115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 8.6 Hz, 1H), 7.73 (dd, J = 1.9 Hz, 8.6 Hz, 1H), 8.08 (d, J = 1.9 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) 119.7, 125.7, 129.9, 131.0, 136.3, 146.9, 191.9; HRMS (EI) *m*/*z* calcd for $C_7H_3OS_2Br$ 245.8808, found 245.8813. Anal. Calcd for $C_7H_3OS_2Br$: C, 34.16; H, 1.23. Found: C, 34.30; H, 1.32.

3*H*-1,2-Naphthodithiolan-3-one (5c). The reddish yellow powder (prepared as described above except stirred for only 45 min in the thiolacetic acid reaction) was purified by flash chromatography on silica gel with hexane−EtOAc (6:1) to yield **5c** as a reddish yellow solid (48% yield from 3-amino-2-naphthoic acid). This material was recrystallized from EtOAc−hexane to form reddish yellow crystals: mp 147−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (m, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 8.04 (s, 1H), 8.54 (s, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 122.5, 126.7, 127.0, 127.2, 128.3, 129.9, 130.2, 130.5, 135.8, 140.0, 194.0; HRMS (EI) *m*/*z* calcd for $C_{11}H_6OS_2$ 217.986, found 217.9853. Anal. Calcd for $C_{11}H_6OS_2$: C, 60.55; H, 2.77. Found: C, 60.70; H, 2.59.

General Procedure for the Synthesis of Dithiosalicylides 1 and 8. The appropriate 3*H*-1,2-benzodithiol-3-one (3.84 mmol) and triphenylphosphine (1.01 g, 3.84 mmol) were stirred in CH_2Cl_2 (30 mL) under N_2 at 24 °C. When TLC indicated that the reaction was nearly complete (~160 h), the turbid yellow mixture was evaporated to dryness under reduced pressure to obtain the crude product. Reaction times can be decreased with use of excess triphenylphosphine. Because the triphenylphosphine sulfide byproduct of this reaction migrates close to the dithiosalicylide products on silica gel, it was desirable to convert the triphenylphosphine sulfide to the more polar triphenylphosphine oxide prior to column chromatography. Accordingly, glycidol (2.6 mL, 38.6 mmol) and CF_3COOH (3.0 mL, 39 mmol) were added to a solution of the crude reaction product in benzene (25 mL), and the mixture was heated at 55 °C until all triphenylphosphine sulfide was converted to triphenylphosphine oxide[20] as indicated by TLC. This workup procedure does not affect the yield of the desired product. The solution was then cooled, diluted with EtOAc (30 mL), and extracted with saturated $NaHCO_3$ (2 × 50 mL) and water (2 × 50 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to yield a thick oil that was subsequently purified by column chromatography.

6*H*,12*H*-Dibenzo[*b*,*f*][1,5]dithiocin-6,12-dione (1). Flash chromatography on silica gel eluted with hexane−EtOAc (8:1) provided **1** as a white solid (74%). This material was recrystallized from CH_2Cl_2−hexane to give white crystals: mp 174−176°C, °C (lit.[10e] mp 175−176 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (m, 4H), 7.25 (m, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 197.3, 142.5, 135.6, 131.2, 131.0, 126.5, 125.2 (corresponds with literature data[11a]).

2,8-Dimethyl-6*H*,12*H*-dibenzo[*b*,*f*][1,5]-dithiocin-6,12-dione (8a). Flash chromatography on silica gel eluted with hexane−EtOAc (8:1) provided **8a** as a white solid (74%). This material was recrystallized from EtOAc−hexane to give white crystals: mp 188−189 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.28 (s, 6H), 7.04 (m, 4H), 7.21 (m, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 21.2, 122.1, 127.2, 131.8, 135.6, 142.0, 142.6, 198.3; HRMS (EI) *m*/*z* calcd for $C_{16}H_{12}O_2S_2$ 300.0279, found 300.0280. Anal. Calcd for $C_{16}H_{12}O_2S_2$: C, 63.99; H, 4.03. Found: C, 63.74; H, 4.27.

2,8-Dibromo-6*H*,12*H*-dibenzo[*b*,*f*][1,5]dithiocin-6,12-dione (8b). Compound **8b** was prepared as described above, except the reaction was complete at ~140 h. Flash chromatography on silica gel eluted with hexane−EtOAc (8:1) provided **8b** as a white solid (72%). This material was recrystallized from EtOAc−hexane to give colorless crystals: mp 223−224 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H), 7.26 (s, 1H), 7.39−7.47 (m, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 123.9, 126.2, 129.7, 134.5, 137.1, 143.6, 194.7; HRMS (EI) *m*/*z* calcd for $C_{14}H_6O_2S_2Br_2$ 427.8176, found 427.8171.

Dinaphtho[2,3-*c*:2′,3′-*g*][1,5]dithiocin-7,15-dione (8c). Flash chromatography on silica gel eluted with EtOAc provided **8c** as a white solid (48%). This material was recrystallized from EtOH−$CHCl_3$−hexane to give colorless cubic crystals: mp 324−325 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, 4H), 7.65 (m, 2H), 7.77 (m, 2H), 7.80 (s, 2H), 7.88 (s, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 120.9, 127.4, 128.1, 128.5, 128.6, 128.6, 133.1, 133.6, 136.8, 139.8, 197.9; HRMS (EI) *m*/*z* calcd $C_{22}H_{12}O_2S_2$ 372.0279, found 372.0267. Anal. Calcd for $C_{22}H_{12}O_2S_2$: C, 70.96; H, 3.25. Found: C, 68.23; H, 3.47. Single crystals for X-ray diffraction studies were obtained by slowly evaporating to dryness (~3 days) a 10:10:1 solution of EtOH−$CHCl_3$−hexane containing analytically pure crystallized **8c** (10 mg). Crystal data for **8c**: triclinic, space group *P*-1, a = 9.851(2) Å, b = 9.899(2) Å, c = 10.212(2) Å, α = 78.300(2)°, β = 85.990(2)°, γ = 63.940(2)°, U = 875.8(3) Å^3, ρ_{calcd} = 1.41 g cm^{-3}, $2\theta_{max}$ = 120°, Cu Kα radiation (λ = 1.540 60 Å) for Z = 2. Least-squares refinement based on 2377 reflections with $I_{net} > 2.0\sigma(I_{net})$ (out of 2591 unique reflections) and 235 parameters on convergence gave a final value of R = 0.038 (refinement based on F).[21]

General Procedure for the Synthesis of Unsymmetrical Dithiosalicylides 11−14. Equal portions of two 3*H*-1,2-benzodithiol-3-ones (0.83 mmol of each) and triphenylphosphine (477

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(21) The author has deposited atomic coordinates for **8c** and **11** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

mg, 1.8 mmol) were stirred in CH_2Cl_2 (20 mL) under N_2 at 24 °C. When all starting material was consumed as indicated by TLC, the turbid yellow mixture was evaporated to dryness under reduced pressure to yield the crude product. Glycidol (550 μL, 8.3 mmol) and CF_3COOH (639 μL, 8.3 mmol) were added to a solution of the crude reaction product in benzene (10 mL), and the mixture was heated at 55 °C until all triphenylphosphine sulfide was converted to triphenylphosphine oxide as indicated by TLC. The solution was cooled, diluted with EtOAc (25 mL), and extracted with saturated $NaHCO_3$ (2 × 25 mL) and water (2 × 25 mL). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to yield a thick oil that was subsequently purified by column chromatography.

2-Methyl-6*H*,12*H*-dibenzo[*b*,*f*][1,5]dithiocin-6,12-dione (12). Flash chromatography on silica gel eluted with hexane−EtOAc (10:1) provided **12** as a yellow-white solid (28%). Compounds **8a** and **1** were obtained in 24% and 26% yields, respectively. This material was recrystallized from EtOAc−hexane to give white crystals: mp 139−140 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 (s, 3H), 7.03 (m, 2H), 7.20 (d, J = 7.6 Hz, 1H), 7.25 (m 2H), 7.35 (m, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 21.2, 122.0, 125.4, 126.6, 127.2, 131.0, 131.2, 131.8, 135.6, 135.7, 142.1, 142.4, 142.8, 197.7, 198.0; HRMS (EI) m/z calcd $C_{15}H_{10}O_2S_2$ 286.0122, found 286.0121. Anal. Calcd for $C_{15}H_{10}O_2S_2$: C, 62.93; H, 3.52. Found: C, 63.00; H, 3.45.

2-Bromo-6*H*,12*H*-dibenzo[*b*,*f*][1,5]dithiocin-6,12-dione (13). Flash chromatography on silica gel eluted with hexane−EtOAc (10:1) provided **13** as a white solid (35%). Compounds **8b** and **1** were obtained in 26% and 23% yields, respectively. This material was recrystallized from EtOH−hexane to give white crystals: mp 198−199 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.2 (d, J = 7.6 Hz, 1H), 7.25 (m, 1H), 7.32 (m, 1H), 7.37−7.42 (m, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 124.3, 124.8, 125.6, 126.6, 129.4, 131.4, 131.5, 134.0, 135.8, 136.8, 142.3, 143.7, 195.6, 196.3; HRMS (EI) m/z calcd for $C_{14}H_7O_2S_2Br$ 349.9071, found 349.9079. Anal. Calcd for $C_{14}H_7O_2S_2Br$: C, 48.01; H, 2.02. Found: C, 48.20; H, 2.18.

2-Bromo-8-methyl-6*H*,12*H*-dibenzo[*b*,*f*][1,5]dithiocin-6,-12-dione (14). Flash chromatography on silica gel eluted with hexane−EtOAc (12:1) provided pure **14** as a white solid (25%). Compounds **8a** and **8b** were also obtained in 28% and 24% yields, respectively. This material was recrystallized from EtOH−hexane to give white crystals: mp 215−216 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 3H), 7.06 (s, 1H), 7.11 (m, 1H), 7.21 (m, 1H), 7.24 (s, 1H), 7.38 (m, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 21.2, 121.5, 124.4, 125.7, 127.3, 129.6, 132.2, 134.0, 135.7, 136.9, 142.2, 142.5, 144.0, 196.3, 196.7; HRMS (EI) m/z calcd for $C_{15}H_9O_2S_2Br$ 363.9227, found 363.9231. Anal. Calcd for $C_{15}H_9O_2S_2Br$: C, 49.46; H, 2.49. Found: C, 49.60; H, 2.32.

2-Bromo-6*H*,12*H*-naphthobenzo[*b*,*f*][1,5]dithiocin-6,12-dione (11). Flash chromatography on silica gel eluted with hexane−EtOAc (12:1) provided **11** as a white solid (22%). Compounds **8b** and **8c** were also obtained in 33 and 30% yields, respectively. This material was recrystallized from $CHCl_3$−hexane to give white crystals: mp 284 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, J = 8.3 Hz, 1H), 7.27 (m, 1H) 7.41 (d, J = 2.1 Hz, 1H), 7.60 (m, 2H), 7.78 (m, 2H), 7.83 (m, 1H), 7.91 (s, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 120.8, 123.7, 125.8, 127.5, 128.2, 128.7, 128.9, 129.0, 129.6, 133.2, 133.5, 134.3, 136.9, 137.1, 139.0, 144.4, 196.3, 196.4; HRMS (EI) m/zcalcd for $C_{18}H_9O_2S_2Br$ 399.9227, found 399.9234. Single crystals for X-ray diffraction studies were obtained by slowly evaporating to dryness (∼3 days) a 10:1 solution of $CHCl_3$−hexane containing analytically pure crystallized **11** (10 mg). Crystal data for **11**: triclinic, space group P-1, a = 8.974(2) Å, b = 9.776(5) Å, c = 10.029(5) Å, α = 89.19(3)°, β = 89.13(3)°, γ = 67.33(3)°, U = 811.7(6) Å^3, ρ_{calcd} = 1.64 g cm^{-3}, $2\theta_{max}$ = 46°, Mo Kα radiation (λ = 0.710 69 Å) for Z = 2. Least-squares refinement based on 1674 reflections with $I_{net} > 2.0\sigma(I_{net})$ (out of 2250 unique reflections) and 208 parameters on convergence gave a final value of R = 0.066 (refinement based on F).[21]

2-(Bromomethyl)-8-methyl-6*H*,12*H*-dibenzo[*b*,*f*][1,5]-dithiocin-6,12-dione (9) and 2,8-Bis(bromomethyl)-6*H*,12*H*-dibenzo[*b*,*f*][1,5]dithiocin-6,12-dione (10). Compound **8a** (300 mg, 1.0 mmol) and NBS (crystallized from EtOAc, 356 mg, 1.9 mmol) were dissolved in CCl_4 (20 mL) and heated to reflux. When the solution reached reflux, a catalytic amount of AIBN was added and refluxing was continued for 8 h under N_2. The solution was then cooled and evaporated to dryness under reduced pressure. The resulting yellowish-white solid was dissolved in $CHCl_3$ (20 mL) and extracted with water (2 × 30 mL). The organic phase was dried over Na_2SO_4, solvent removed under reduced pressure, and the yellow solid purified by flash chromatography on silica gel with 12:1 hexane EtOAc to isolate **10**, which elutes first off the column (recovered yield: 30%) and **9** (recovered yield: 27%). Both were recrystallized from EtOAc−hexane to give white crystals. Compound **9**: mp 129-130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.29 (s, 3H), 4.31−4.36 (m, 2H), 7.05 (m, 2H), 7.22 (m, 1H), 7.25 (m, 2H), 7.31 (m, 1H) ; ^{13}C NMR (500 MHz, $CDCl_3$) δ 21.2, 30.8, 121.8, 125.3, 127.0, 127.2, 131.2, 132.0, 135.6, 136.1, 141.3, 142.2, 143.2, 197.2, 197.5; HRMS (EI) m/z calcd for $C_{16}H_{11}O_2S_2Br$ 377.9384, found 377.9398. Compound **10**: mp 165-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.30−4.36 (m, 4H), 7.24 (m, 2H), 7.26 (m, 2H), 7.31 (s, 1H), 7.33 (s, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 30.7, 125.1, 127.0, 131.4, 136.2, 141.6, 142.8, 196.4; HRMS (EI) m/z calcd for $C_{16}H_{10}O_2S_2Br_2$ 455.8489, found 455.8492. Anal. Calcd for $C_{16}H_{10}O_2S_2Br_2$: C, 42.12; H, 2.21. Found: C, 42.12; H, 2.01.

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Supporting Information Available: Complete X-ray data and methods for **8c** and **11** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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