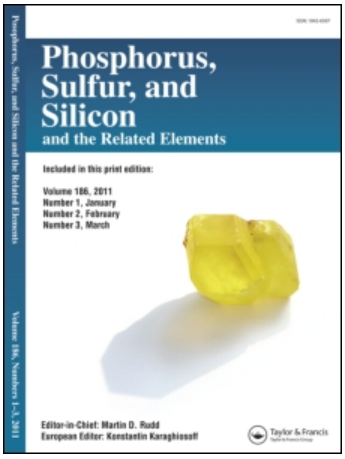

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POLYDENTATE S_NX_M (X = S,O,N) LIGANDS BY SELECTIVE REDUCTION OF ORGANOSULFUR HETEROCYCLES WITH TRIBUTYLTIN HYDRIDE

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POLYDENTATE S_NX_M (X = S,O,N) LIGANDS BY SELECTIVE REDUCTION OF ORGANOSULFUR HETEROCYCLES WITH TRIBUTYLTIN HYDRIDE

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(Received 15 July 1996; Revised 5 September 1996; In final form 5 September 1996)

Acyclic tetradentate organosulfur ligands of the type S_2X_2 (where X = S,O,N) can be efficiently prepared by selective desulfurization of bis(1,3-dithiolanes) and bis(1,3-dithianes); bis(1,3-oxathiolanes); and bis(thiazolidines) with two equivalents of tri-*n*-butyltin hydride. This is a very versatile procedure as many dialdehydes and diketones (or their synthetic equivalents) are available for elaboration into bis(thioheterocycles) by reaction with 1,2-ethane- and 1,3-propanedithiols, mercaptoethanol or mercaptoethylamine, and their varied structural features can be incorporated into S_2X_2 ligands. The net result of the procedure is the controlled formal monoalkylation of dithiols to form compounds **1** (X = S); and the alkylation of the less nucleophilic heteroatom (O or N) of mercaptoethanol or mercaptoethylamine to form **1** (X = O,N).

Keywords: Organosulfur heterocycles; tributyltin hydride; dithiols; chelators

INTRODUCTION

Tetradentate ligands containing S_2X_2 donor atoms (where X = S,O,N) have considerable utility as chelators to a variety of metal ions,[1] or as precursors to polydentate macrocyclic compounds.[2] We report here the preparation of tetradentate dithiols **1** (R′ = H) of the S_2X_2 type, by a procedure which also allows for the synthesis of penta- and higher dentate ligands. The strategy for the preparation of S_2X_2 ligands **1** is based on the selective reductive cleavage of one

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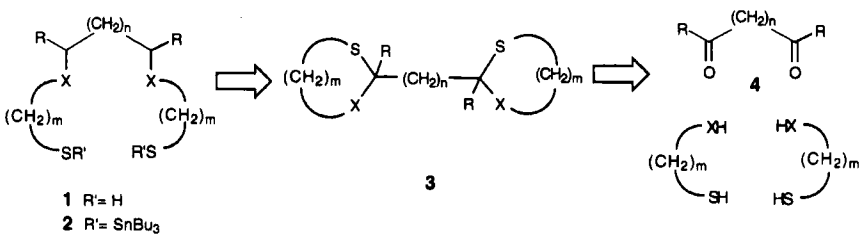
C-S bond in each ring of bis(1,3-thiaheterocyclic) compounds **3**, which are available in generally high yield from the reaction of dialdehydes or diketones **4** (or synthetic equivalents of these), and the appropriate dithiols, mercaptoalcohols, or mercaptoamines.



RESULTS AND DISCUSSION

Requisite for this approach is the availability of reagents capable of effecting the required selective reductive desulfurization. While there are many reagents capable of cleaving the C-S bond, few are capable of discriminating one C-S bond in molecules where several are present.[3] We have reported that organotin hydrides can be selective desulfurization agents,[4] and the present work extends this to the reduction of C-S bonds in bis(1,3-dithiolanes; -dithianes; -oxathiolanes; and -thiazolidines) to produce polydentate ligands **1**.[5] The reactions appear to be radical processes, as they are initiated by 2,2′-azobisisobutyronitrile (AIBN) and inhibited by hydroquinone or galvinoxyl.

S_4 Ligands[9]

The reductions of bis(1,3-dithiolanes) and bis(1,3-dithianes) **3a–3h** with two equivalents of tri-*n*-butyltin hydride (abbreviated hereafter as TBTH) in refluxing benzene in the presence of AIBN as initiator are summarized in the **Table**. We observed the selective cleavage of only one of the geminal C-S bonds in each heterocyclic ring of **3** with no over-reduction to hydrocarbons when the stoichiometry of **3** to organotin hydride was controlled at 1:2 to produce the bis(tributyltin sulfides) **2** in excellent yields. The reactions were monitored by the ^{1}H NMR changes in several signals: the disappearance of Bu_3SnH; the disappearance of the thioacetal methine (in **3a**, **b**, **e**, **f**) and the rise of the reduction product methylene (or methine from reduction of thioketals **3c**, **d**, **g**, **h**); and the .5–.7 ppm upfield shift (in benzene) which the methylene protons adjacent to sulfur in heterocycles **3** undergo on reduction to acyclic products **2**. The results are consistent with a process where tributyltin radical attacks sulfur

TABLE Reduction of bis(1,3-Dithianes, -Oxathiolanes, and -Thiazolidines) with two equivalents of TBTH

Heterocycles **3**					*Products*				
	R	*X*	*m*	*n*	*3 to 2 (R' = $SnBu_3$)*			*2 to 1 (R' = H)*	
						reaction time (h)	*% Yield*[a]		*% Yield*[b]
3a	H	S	2	1	**2a**	15	96	**1a**[7]	66
3b	H	S	3	1	**2b**	15	97	**1b**[7]	85
3c	CH_3	S	2	1	**2c**	15	98	**1c**	82
3d	CH_3	S	3	1	**2d**	8	97	**1d**	96
3e	H	S	2	2	**2e**	12	97	**1e**	84
3f	H	S	3	2	**2f**	15	98	**1f**	77
3g	CH_3	S	2	2	**2g**	14	80	**1g**	74
3h	CH_3	S	3	2	**2h**	6	90	**1h**	80
3i	H	S	2	0	**2i**	20	—[c]	**1i**[7,21]	17
3j	H	S	3	0	**2j**	25	—[c]	**1j**[8]	78
3k	H	O	2	1	**2k**	30	65	**1k**	40
3l	CH_3	O	2	1	**2l**	28	82	**1l**	74
3m	H	O	2	2	**2m**	34	75	**1m**	67
3n	CH_3	O	2	2	**2n**	40	95	**1n**	82
3o	CH_3	N	2	2	**2o**	16	92	**1o**	—

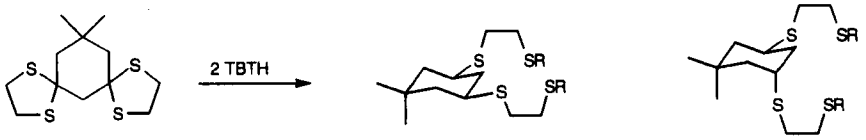
[a]crude yield; [b]based on bis(heterocycles) **3**; [c]intermediates **2** not isolated.

on heterocycles **3** with the cleavage of the C-S bond leading to the more stable carbon radical.[4a] Subsequent hydrogen atom abstraction from TBTH yields tetravalent carbon and propagates the radical process by concomitant formation of a tributylstannyl radical.

We were unable to purify bis(tributylstannyl sulfides) **2** for elemental analysis as these decomposed on attempted distillation or chromatography. The yields reported for **2** in the **Table** are for the crude products. Bis(tributylstannyl sulfides) **2** were destannylated by passing these through columns of silica gel to produce dithioetherdithiols **1** in good yields. While we have selected to destannylate **2** to the dithiols, procedures have been developed for the direct alkylation[10] or acylation[11] of organotin sulfides to other products. The reduction of **3c**, **3d**, **3g**, and **3h** introduced two chiral centers, forming the corresponding products **2** (and subsequently dithiaetherdithiols **1c**, **1d**, **1g** and **1h**) as roughly 1 : 1 mixtures of diastereomers.

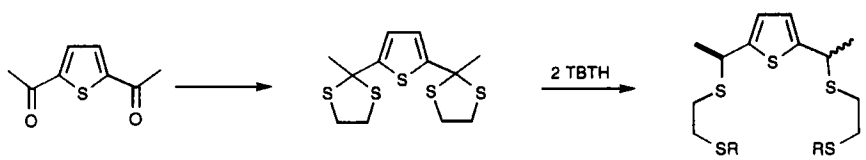
The present procedure offers certain advantages over other available methods for the preparation of polythioetherdithiols: the conditions are mild (refluxing benzene, neutral pH);[12] tolerant of a range of functionality;[4c,e] and the method avoids the use of the strongly vesicant sulfur mustards as reagents or intermediates.[13]

The procedure also allows for the incorporation of more complex structural features into the dithiaether dithiols **1** by using diketones of greater structural diversity as starting materials. For example, the bis(ethylene thioketal) of 5,5-dimethyl-1,3-cyclohexanedione (**5**) was reduced with two equivalents of TBTH, and the resulting bis(tributyltin sulfides) **6a** and **6b** were destannylated on silica gel to give a 62% yield of a 3:2 diastereomeric mixture of dithiols **7a** and **7b**. The composition was estimated from the ^1H NMR spectrum of the product mixture: the axial protons at C-1 or C-3 appear as a broad peak at δ 3.20 ppm (width at half-height = 18 Hz); equatorial protons on these carbons appear at δ 3.01 ppm (width at half-height = 7.5 Hz).



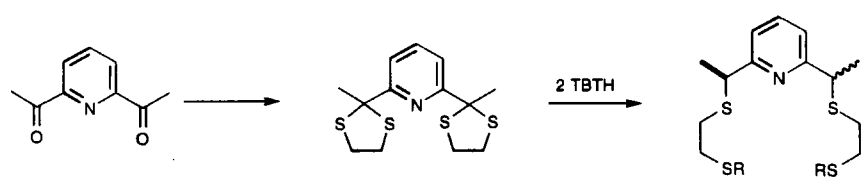
5 **6a** R= $SnBu_3$ **7a** R= H **6b** R= $SnBu_3$ **7b** R= H

The acid catalyzed reaction of 2,5-diacetylthiophene with ethanedithiol produced the bis(thioketal) **8**, whose reduction with two equivalents of TBTH followed by silica gel destannylation gave a diastereomeric mixture of ligands **9** (R = H) in an overall yield of 55% (based on diacetylthiophene).



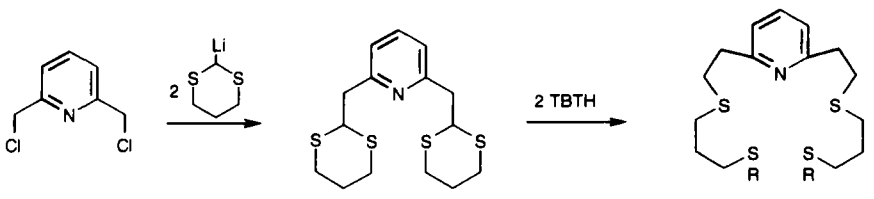
8 **9**

In a similar manner, compound **11** which incorporates pyridine nitrogen and four sulfur donor atoms was synthesized from 2,6-diacetylpyridine [64% yield for the conversion of **10** to **11** (R = H)].



10 **11**

Reduction of 2,6-bis(1,3-dithianylmethyl)pyridine (**12**) with two equivalents of TBTH in refluxing benzene resulted in an 82% yield of **13** (R = H) after passing the crude reaction product through a column of silica gel to effect destannylation and purification. The bisthiane **12** was prepared from 2,6-bis(chloromethyl)pyridine and two equivalents of 2-lithio-1,3-dithiane at −78 °C. The modest yield (56%) may be a consequence of additional reaction pathways available to the pyridine nucleus with organolithium reagents.[14]



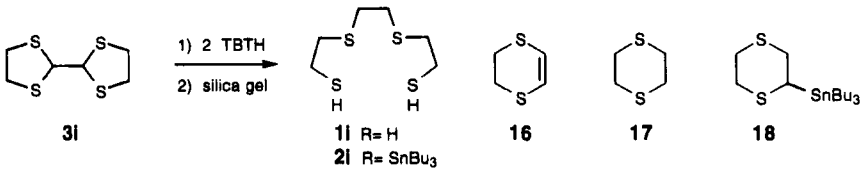
12 **13**

The net result of the above reactions is the controlled monoalkylation of 1,2-ethanedithiol or 1,3-propanedithiol with bifunctional alkylating agents, a transformation achieved otherwise only with some difficulty. Direct alkylation of dithiols with dihaloalkanes has frequently resulted in complex product mixtures.[15,16]

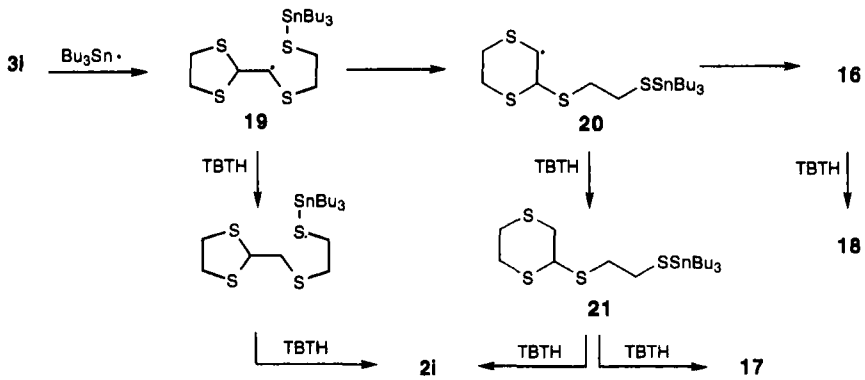
Reductions of Glyoxal Ethylene Mercaptal and Glyoxal Trimethylene Mercaptal

The use of glyoxal as the parent dicarbonyl can allow for the introduction of an additional ethylene bridge into the S_2X_2 ligands **1**. Glyoxal bis(dithioacetals) **3i** and **3j** have been reported from the reaction of 2,3-dichloro-1,4-dioxane with either 1,2-ethanedithiol or 1,3-propanedithiol.[17–19]

The reaction of **3i** with two equivalents of TBTH in refluxing benzene solvent resulted in a mixture of products. Passage through a column of silica gel resulted in destannylation and partial separation of the components, which included: dihydro-1,4-dithiin (**16**)[20] (11%); *p*-dithiane (**17**) (4%); relatively large amounts (53%) of a white solid to which we assigned structure **18** [(mp 58–59°C): NMR (CCl_4) δ 2.8–3.0 (multiplet with singlet at 2.9, 7H), 0.9–1.8 (m, 27H); the infrared spectrum indicated the absence of a Sn-S (consistent with the survival of the tributyltin group on the molecule after chromatography on silica gel)]; and a small amount (17%) of the target 3,6-dithia-1,8-octanedithiol (**1i**).[21]

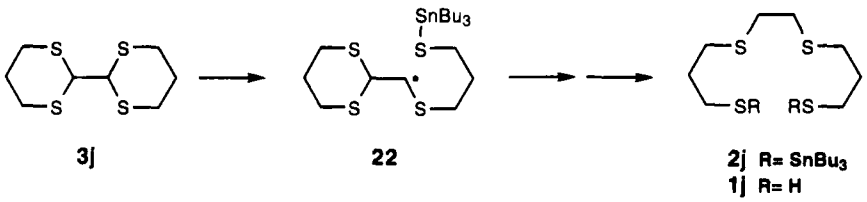


The formation of 1,4-dithiane derivatives **16–18** can be rationalized as arising from the rearrangement of initial radical **19** to 1,4-dithianyl radical **20** (Scheme I). ß-Elimination from **20** would result in the formation of dithiin **16** (and in turn **18** from **16** by hydrostannation with TBTH). Hydrogen atom transfer to **20** from TBTH would produce **21**. Cleavage of the exocyclic C-S bond in dithioacetal **21** by TBTH would produce dithiane (**17**). The bis(stannylthioether) **2i** precursor to S_4 ligand 1,8-dimercapto-3,6-dithiaoctane (**1i**) can be formed from the sequential reduction of one S-C bond in each dithiolane ring in **3i** by two equivalents TBTH, or by the TBTH reduction of the endocyclic thioacetal C-S bond in **21**.



SCHEME 1

The reaction of glyoxal bis(trimethylene dithioacetal) (**3j**) with TBTH was considerably more productive, yielding after destannylation on silica gel, a small amount (5%) of alkenes (indicated by absorptions δ ~ 6 ppm in the ^{1}H NMR spectrum) which were not further characterized; and the desired tetradentate ligand **1j** in 78% yield.[22] In this case the initially formed carbon radical **22** could also rearrange or abstract a hydrogen atom from TBTH. However, rearrangement of the relatively unstrained dithiane **22** to a less stable seven-membered heterocycle is less likely, and the major pathway is hydrogen atom transfer from TBTH. Subsequent reaction with the second equivalent of TBTH produces to 1,10-di(tributylstannylthio)-4,7-dithiadecane (**2j**), and to the corresponding dithiol **1j** after destannylation on silica gel.

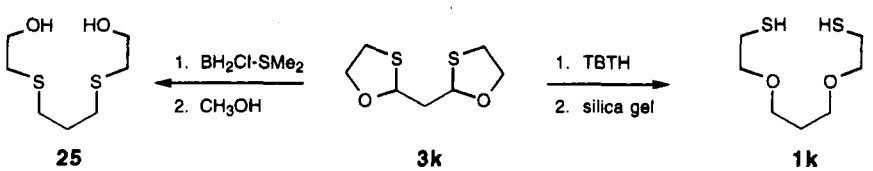


SCHEME 2

S_2O_2 Ligands[5b,23]

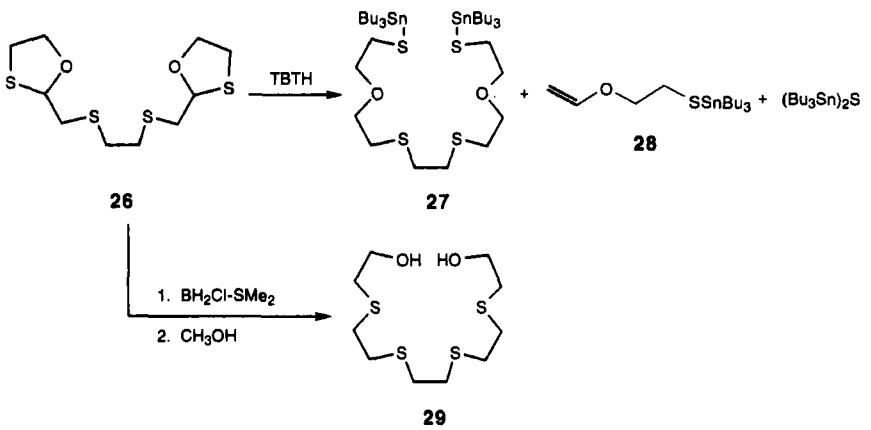
The bis-1,3-oxathiolanes **3k–3n** were prepared from the reaction of dialdehydes (as the bisacetal derivatives), or diketones, and mercaptoethanol and a catalytic amount of *p*-toluenesulfonic acid in toluene with azeotropic removal of water (or methanol). These bis(1,3-oxathiolanes) were formed as diastereomeric mixtures [separation of the diastereomers of **3k** and also **3m** was achieved using medium pressure chromatography. In the case of **3m**, one diastereomer was a white solid (mp 52–53 °C) while the other was a colorless liquid]. The most salient features of the ^{1}H NMR spectra of the bis(1,3-oxathiolanes) were the splitting patterns which C-4 and C-5 hydrogens exhibit, ranging from AMXY to ABXY to AA′XX′ depending on the substituents at C-2.[22] The diastereomeric mixtures **3k–n** were reduced with two equivalents of the TBTH to the corresponding bis(tributylstannyl) sulfides **2k–n**. Reaction times for the reduction of bis(oxathiolanes) (28–40 h) were two or more times greater than for the reduction of bis(dithiolanes and dithianes) (6–20 h). The ^{1}H NMR spectra of the bis(oxathiolanes) simplified considerably on reduction: the complex splitting among the protons on C-4 and C-5 in the bis(oxathiolanes) simplified to two A_2X_2 triplets in the product (although the triplet from the CH_2O generally overlaps other ether methylene signals). These reduced products were then destannylated on silica gel to dioxadimercaptans **1k–n**.

The TBTH reduction of malonaldehyde bis(ethylene hemithioacetal) (**3k**) to the dioxadithiol **1k** is complementary to other work in this laboratory using borane reagents wherein reduction leads to the production of isomeric dithiadiol **25**.[25] In no case have we observed cleavage of a C-O bond by TBTH, nor of a C-S bond by borane or monochloroborane.



In contrast to the clean reduction of **3k**, the reaction of bis(oxathiolane) **26** and two equivalents of TBTH was complicated. TBTH was consumed at a much faster rate (under one h) than **26**: indeed, after the disappearance of TBTH the reaction mixture consisted largely of unreacted **26** (70%), and a complex mixture of compounds including enol ether **28**, and bis(dibutylstannyl) sulfide, yet none corresponding to **27**, or its corresponding dithiol after destannylation. It appears that the initial radical intermediate formed from attack of tributyltin radical on an oxathiolane sulfur[26] of **26** β-eliminates to produce enol ether **28** and other fragments which react faster with TBTH than does **26**, and result in the cleavage of C-S bonds and the formation of bistributyltin sulfide.

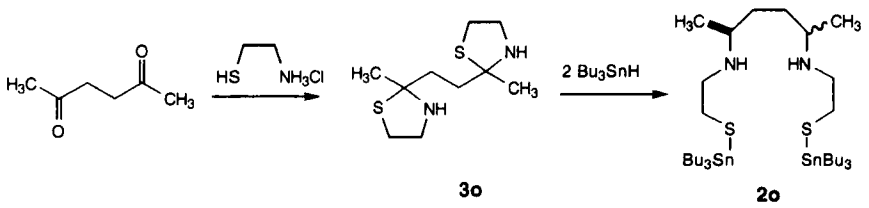
The complementary reduction of **26** by monochloroborane-dimethyl sulfide produced the 3,6,9,12-tetrathiatetraundecane-1,14-diol (**29**) in 69% yield. Bis-(ethylene hemithioacetal) **26** was prepared by the dialkylation of ethanedithiol with 2-chloroacetaldehyde dimethyl acetal; followed by reaction of that intermediate with mercaptoethanol.



26 **27** **28** **29**

S_2N_2 Compound[5b,27]

Diastereomeric bis(thiazolidine) **3o** was synthesized in 40% yield from acetonylacetone and ß-aminoethanethiol. The reduction with two equivalents of TBTH was again conveniently monitored by ^{1}H NMR: as the carbon to sulfur bond was cleaved, the methyl protons began to appear as a doublet at δ 1.8 ppm, while the amine protons shifted from 5.3 to 5.8 ppm (in benzene) in product **2o**. However, attempts at destannylation on silica gel were unsuccessful.



3o **2o**

CONCLUSION

The selective reduction of bis(1,3-dithianes, -dithiolanes, -oxathiolanes, and thiazolidines) by two equivalents of tributyltin hydride represents a mild and experimentally simple method for the preparation of S_2X_2 ligands (X = S,O,N). This is a very versatile procedure as many dialdehydes and diketones (or their synthetic equivalents) are available for elaboration into bis(thioheterocycles) **3**, and their varied structural features can be incorporated into S_2X_2 ligands **1**. The net result of the procedure is the controlled formal monoalkylation of 1,2-ethane- and 1,3-propanedithiols to form compounds **1** (X = S); and the alkylation of the less nucleophilic heteroatom (O or N) of mercaptoethanol or mercaptoethylamine to form **1** (X = O,N). In those cases where there is a sulfur atom ß to the initially formed carbon radical (cf. reduction of compounds **3i** and **26**), the reduction is complicated by rearrangement and/or elimination.

This procedure is very good for X = S and O, but less so for X = N. The TBTH reduction of the bis(thiazolides) to the acyclic diazabis(tributyltin sulfides) is certainly effective, but we have yet to develop a useful procedure for the destannylation of these to the diazadithiols.

EXPERIMENTAL

Melting points were recorded on an electrothermal capillary melting point apparatus and are reported uncorrected. Only selected infrared absorptions are reported. Nuclear magnetic resonance spectra were recorded at 90 MHz. Chemical shifts are reported in δ values (ppm) relative to tetramethylsilane internal standard. The observed multiplicity of the absorptions are abbreviated as s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Solvents were dried by standard methods and stored over 4 Å molecular sieves. Separations were done by medium pressure chromatography, or by centrifugally accelerated radial thin layer chromatography. Glassware was dried at 140°C for a minimum

of four hours. All reactions were run under a dry nitrogen atmosphere, and were stirred magnetically. Since several reactions are similar, only representative examples of each type are presented.

Bis(1,3-Dithiolanes, -Dithianes, Oxathiolanes, and -Thiazolidine)

Compounds **3a–d**,[28] **3f**,[29] **3g–h**,[30] and **3i–j**,[17] are known and were prepared by literature procedures. The synthesis of new bis(thioheterocycles) is described below.

5,5-Dimethyl-1,3-cyclohexanedione bis(ethylene dithioketal) (5).

A solution of 5.0 g (35 mmol) of 5,5-dimethyl-1,3-cyclohexanedione, 6.4 g (72 mmol) of 1,2-ethanedithiol, and .05 g of *p*-toluenesulfonic acid in 80 mL toluene was refluxed until the theoretical amount of water was collected in a Dean Stark trap. The reaction mixture was cooled to room temperature, diluted with 50 mL diethyl ether, and stirred with 0.5 g solid $NaHCO_3$. The solution was filtered and the solvent evaporated to a yellow solid, which was recrystallized from ethanol/chloroform to yield 5.5 g of colorless product **5**. Column chromatography on the residue from the mother liquor provided an additional 2.8 g of product **5** (combined yield 80%): mp 180–182°C; ^{1}H NMR (CCl_4) δ 3.22 (s, 8H), 2.56 (s, 2H), 1.90 (s, 4H), 1.12 ppm (s, 6H); mass spectrum, parent peak m/z = 292. Anal. Calcd for $C_{12}H_{20}S_4$: C 49.27, H 6.89. Found C 49.35, H 6.73.

2,5-Diacetylthiophene bis(ethylene dithioketal) (8) was prepared as above from 2,5-diacetylthiophene and 1,2-ethanedithiol and isolated isolated as white crystals: mp. 70–72°C; ^{1}H NMR (CCl_4) δ 6.80 (s, 2H), 3.38 (s, 8H), 2.12 ppm (s, 6H); mass spectrum, parent peak m/z = 320. Anal. Calcd for $C_{12}H_{16}S_5$: C 44.96, H 5.03. Found C 44.82, H 5.12.

2,6-Diacetylpyridine bis(ethylene dithioketal) (10) was produced as above from 2,6-diacetylpyridine and 1,2-ethanedithiol as white crystals: mp. 101–102.5°C; ^{1}H NMR δ 7.50–7.80 (m, 3H), 3.45 (s, 8H), 2.20 ppm (s, 6H); mass spectrum, parent peak m/z = 315. Anal. Calcd for $C_{13}H_{17}NS_4$: C 49.48, H 5.43, N 4.44. Found C 49.53, H 5.40, N 4.63.

Hemithioketals **3l**, **3n**, and thiazolidine **3o** were produced in an analogous manner by replacement of the dithiol with mercaptoethanol or mercaptoethylamine.

2,4-Pentanedione bis(ethylene hemithioketal) (3l) was isolated as a colorless oil: IR (neat) 1070 cm^{-1} (C-O-C); ^{1}H NMR (CCl_4) δ 4.19 (t, 4H), 2.06 (t, 4H), 2.55 (s, 2H), 1.70 (s, 6H). Anal. Calcd for $C_9H_{16}O_2S_2$: C 49.06, H 7.32. Found: C 49.28, H 7.49.

2,5-Hexanedione bis(ethylene hemithioketal) (3n) was produced as a colorless oil: IR (neat) 1080 cm^{-1} (C-O-C); ^1H NMR (CCl_4) δ 4.03 (t, 4H), 2.97 (t, 4H), 1.90 (s, 4H), 1.52 ppm (s, 6H). Anal. Calcd for $C_{10}H_{18}O_2S_2$: C 51.25, H 7.74. Found: C 51.53, H 7.60.

Bis(thiazolidine) of 2,5-hexanedione (3o) was produced as white needles (from methanol): mp. 97–99°C; IR ($CHCl_3$) 3400cm^{-1} (N-H); ^1H NMR (CCl_4) δ 5.31 (broad s, 4H), 3.72 (t, 4H), 2.42 (t, 4H), 2.03 ppm (s, 10H). The crystals analyzed for the monohydrate: the amine absorption at 5.31 ppm integrated for four hydrogens instead of two. Anal. Calcd for $C_{10}H_{20}S_2N_2 \cdot H_2O$: C 47.96, H 8.86, N 11.19. Found C 47.72, H 8.97, N 11.34.

Bis(heterocycles) **3e**, **3k**, and **3m** were prepared from the methyl acetals of the parent dialdehydes and the dithiol or mercaptoethanol. They were prepared as described above with the modification that the mixture was refluxed one hour and then the methanol-toluene azeotrope was slowly removed by distillation.

Succinaldehyde bis(ethylene dithioacetal) (3e) was made (from 2,5-dimethoxytetrahydrofuran) as white crystals: mp. 70–71°C; ^1H NMR ($CDCl_3$) δ 4.20–4.52 (m, 2H), 3.15 (s, 8H), 1.80–2.10 ppm (m, 4H); mass spectrum, parent peak m/z = 238. Anal. Calcd for $C_8H_{14}S_4$: C 40.29, H 5.93. Found C 40.67, H 6.21.

Malonaldehyde bis(ethylene hemithioacetal) (3k) was produced (from malonaldehyde tetramethyl acetal) as a mixture of colorless liquid diastereomers: ^1H NMR (CCl_4) δ 5.12 (t, 2H), 4.2–4.6 (m, 2H), 3.52–4.02 (m, 2H), 2.71–3.40 (m, 4H), 1.91–2.42 ppm (m, 2H). Anal. Calcd for $C_7H_{12}O_2S_2$: C 43.72, H 6.29. Found: C 43.82, H 6.51.

Succinaldehyde bis(ethylene hemithioacetal) (3m), a mixture of diastereomers, was made (from 2,5-dimethoxytetrahydrofuran) as a white solid (mp 52–53°C) and a colorless oil. Both exhibited the same spectra: ^1H NMR δ 4.80–5.25 (m, 2H), 4.05–4.48 (m, 2H), 3.47–4.00 (m, 2H), 2.65–3.20 (m, 4H), 1.60–2.24 (m, 4H). Anal. Calcd for $C_8H_{14}O_2S_2$: C 46.57, H 6.84. Found: C 46.74, H 6.63 and C 46.43, H 6.71.

2,6-Di[(1,3-dithianyl)methyl]pyridine (12).

Freshly sublimed 1,3-dithiane (0.25 g, 0.010 mol) in 20 mL dry THF at −15°C was deprotonated by the dropwise addition of 4.6 mL of 2.7 *M* *n*-butyllithium. The mixture was stirred 1 h, and then cooled to −78°C. 2,6-Bis(chloromethyl)pyridine[31] (0.88 g, 0.005 mol) was added, and the reaction mixture stirred 4 h and then quenched with water. The solvent was removed under vacuum and the residue dissolved in dichloromethane, washed sequen-

tially with water and brine, then dried over anhydrous magnesium sulfate. The solvent was evaporated and the product purified by centrifugally accelerated radial thin layer chromatography (with CH_2Cl_2 as eluant) to give 0.56 g (56%) of **12**: ^{1}H NMR δ 7.40 (m, 1H), 6.95 (d, 2H), 4.95 (t, 2H), 3.18 (d, 4H), 2.81 (t, 8H), 2.02 (m, 4H). Anal. Calcd for $C_{15}H_{21}S_4N$: C 52.44, H 6.16, N 4.08. Found 52.27, H 6.50, N 4.25.

Reductions with Tri-*n*-butyltin Hydride[32]

Reductions were performed under a dry nitrogen atmosphere on 3–20 mmol of the organosulfur heterocycles **3** with 2.1 equivalents freshly distilled TBTH and 1 mole percent recrystallized azobis(isobutyronitrile) (AIBN) in 5–20 mL refluxing benzene solvent. Aliquots were periodically withdrawn, analyzed by ^{1}H NMR and returned to the reaction vessel. Progress was monitored by the disappearance of the Bu_3Sn-**H** signal and the $S(CH_2)_nX$ signal (X = S, O, N; n = 2, 3) of the thiaheterocycles **3** and the appearance of product signals. On completion, the solvent was evaporated to give the products **2** as colorless oils. The compounds were not purified further as they decomposed on distillation, and destannylated on attempted column chromatography. The crude yields are given in the **Table**.

1,9-Di(tributylstannylthio)-4,6-dithianonane (2a).

^{1}H NMR (CCl_4) δ 2.32–2.72 (m, 12H), 0.51–1.83 ppm (m, 56H).

1,11-Di(tributystannylthio)-4,8-dithiaundecane (2b).

^{1}H NMR (CCl_4) δ 2.42–2.70 (m, 12H), 0.61–2.09 ppm (m, 60H).

4,6-Dimethyl-1,9-di(tributystannylthio)-3,7-dithianonane (2c).

^{1}H NMR (CCl_4) δ 2.42–2.81 (m, 10H), 0.49–2.21 ppm (m, 62H).

5,7-Dimethyl-1,11-di(tributystannylthio)-4,8-dithiaundecane (2d).

^{1}H NMR (CCl_4) δ 2.39–3.11 (m, 10H), 0.62–2.11 ppm (m, 66H).

1,10-Di(tributystannylthio)-3,8-dithiadecane (2e).

^{1}H NMR (CCl_4) δ 2.31–2.78 (m, 12H), 0.48–2.02 ppm (m, 58H).

1,12-Di(tributystannylthio)-4,9-dithiadodecane (2f).

^{1}H NMR (CCl_4) δ 2.31–2.69 (m, 12 H), 0.5–2.1 ppm (m, 62H).

4,7-Dimethyl-1,10-di(tributystannylthio)-3,8-dithiadecane (2g).

^{1}H NMR (CCl_4) δ 2.39–2.71 (m, 10H), 0.61–1.72 ppm (m, 64H).

5,8-Dimethyl-1,12-di(tributystannylthio)-4,9-dithiadodecane (2h).

^{1}H NMR (CCl_4) δ 2.31–2.89 (t, 10H), 0.53–2.21 ppm (m, 68H).

1,9-Di(tributylstannylthio)-3,7-dioxanonane (2k).

^{1}H NMR (CCl_4) δ 3.20–3.61 (m, 8H), 2.51 (t, 4H), 0.70–1.82 ppm (m, 56H).

4,6-Dimethyl-1,9-di(tributylstannylthio)-3,7-dioxanonane (2l).

^{1}H NMR (CCl_4) δ 3.21–3.59 (m, 6H), 2.51 (t, 4H), 0.62–1.78 ppm (m, 62H).

1,10-Di(tributystannylthio)-3,8-dioxadecane (2m).

^{1}H NMR (CCl_4) δ 3.22–3.61 (m, 8H), 2.61 (t, 4H), 0.62–1.89 ppm (m, 58H).

4,7-Dimethyl-1,10-di(tributystannylthio)-3,8-dioxadecane (2n).

^{1}H NMR (CCl_4) δ 3.10–3.61 (m, 6H), 2.50 (t, 4H), 0.61–1.81 pp, (m, 64H).

4,6-Dimethyl-1,9-di(tributylstannylthio)-3,7-diazanonane (2o).

^{1}H NMR (CCl_4) δ 5.81 (s, 2H), 2.13–2.42 (m, 8H), 0.51–2.79 ppm (m, 66H).

1,3-di[b-(tributylstannylthio)ethylthio]-5,5-dimethylcyclohexanes (6a and 6b) were produced from **5** after 12 h of reflux: ^{1}H NMR (CCl_4) δ 3.01–3.22 (m, 2H), 2.10–2.72 (m, 8H), 0.51–2.09 ppm (m, 66H).

2,5-Di(1-methyl-4-tributylstannylthio-2-thiabutyl)thiophene (9, R=SnBu$_3$) was produced from **8** after 10 h of reflux: ^{1}H NMR (CCl_4) δ 6.71 (s, 2H), 4.12 (q, 2H), 2.50 (broad s, 8H), 0.72–1.89 ppm (m, 60H).

2,6-Di(1-methyl-4-tributylstannylthio-2-thiabutyl)pyridine (11, R=SnBu$_3$) was produced from **10** after 14 h of reflux: ^{1}H NMR (CCl_4) δ 6.91–7.60 (m, 3H), 4.05 (q, 2H), 2.42–2.72 (m, 8H), 0.63–1.81 (m, 60H).

2,6-Di(7-tributylstannylthio-3-thiahexyl)pyridine (13, R=SnBu$_3$) was produced from **12** after 4 h of reflux: ^{1}H NMR δ 6.8–7.5 (m, 3H), 2.3–3.1 (m, 16H), 0.70–1.85 (m, 27H).

Silica Gel Destannylation of Bis(tri-*n*-butyltin) Mercaptides to Dithiols

A long glass column was packed with 90 g of silica gel (60–200 mesh) per g of bis(tributyltin sulfide) **2** to be destannylated. The compounds **2** were dissolved in a small amount of pentane and loaded onto the column, which was then eluted slowly, beginning with pentane (or petroleum ether), then with the CH_2Cl_2/pentane mixtures containing increasing amounts of CH_2Cl_2 (5%, 10%, 20%, etc.). Dithiols **1** are colorless oils which eluted after small amounts of bis(tributyltin) oxide. The yields are given in the **Table** (compounds **1a–o**), or in the text (compounds **9**, **11**, **13**, **26**).

3,7-dithia-1,9-nonanedithiol (1a).[7,12]

IR (neat) 2540 cm^{-1} (S-H); ^{1}H NMR (CCl_4) δ 2.46–2.95 (m, 12H), 1.68–2.01 (m, 2H), 1.45 ppm (t, 2H).

4,8-dithia-1,11-undecanedithiol (1b).[7]

IR (neat) 2540 cm^{-1} (S-H); ^{1}H NMR (CCl_4) δ 2.5–3.0 (m, 12H), 1.5–2.2 (m, 6H), 1.4 ppm (t, 2H).

4,6-dimethyl-3,7-dithia-1,9-nonanedithiol (1c).

IR (neat) 2560 cm^{-1} (S-H); ^{1}H NMR (CCl_4) δ 2.5–3.1 (m, 10H), 1.4–1.8 (m, 4H), 1.15 ppm (d, 6H). Anal. Calcd for $C_9H_{20}S_4$: C 42.14, H 7.86. Found: C 42.31, H 8.01.

5,7-dimethyl-4,8-dithia-1,11-undecanedithiol (1d).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 2.45–3.20 (nm, 10H), 1.50–2.20 (m, 8H), 1.55 ppm (d, SH). Anal. Calcd for $C_{11}H_{24}S_4$: C 46.43, H 8.50. Found: C 46.61, H 8.35.

3,8-dithia-1,10-decanedithiol (1e).

IR (neat) 2545 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 2.30–2.95 (m, 12H), 1.4–2.0 ppm (m, 6H). Anal. Calcd for $C_8H_{18}S_4$: C 39.63, H 7.48. Found: C 39.48, H 7.76.

4,7-dimethyl-3,8-dithia-1,10-decanedithiol (1g).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 2.45–2.65 (m, 10H), 1.40–1.70 (m, 10H), 1.20 ppm. Anal. Calcd for $C_{10}H_{20}S_4$: C 44.73, H 7.51. Found: C 44.59, H 7.79.

5,8-dimethyl-4,9-dithia-1,12-dodecanedithiol (1h).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 2.35–2.90 (m, 10H), 1.50–2.15 (m, 8H), 1.15–140 pm (m, 8H). Anal. Calcd for $C_{12}H_{26}S_4$: C 48.27, H 8.78. Found: C 48.39, H 8.59.

3,7-Dioxa-1,9-nonanedithiol (1k).

IR (neat) 2550 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 3.2–3.6 (m, 6H), 2.4–2.7 (m, 4H), 1.75 (t, 2H), 1.65 ppm (t, 2H). Anal. Calcd for $C_7H_{16}O_2S_2$: C 42.83, H 8.21. Found: C 42.64, H 8.52.

4,6-Dimethyl-3,7-dioxa-1,9-nonanedithiol (1l).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 3.4–3.7 (m, 6H), 2.4–2.7 (m, 4H), 1.6 (d, 2H), 1.2 ppm (d, 6H). Anal. Calcd for $C_9H_{20}O_2S_2$: C 48.18, H 8.98. Found: C 48.43, H 9.16.

3,8-Dioxa-1,10-decanedithiol (1m).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 3.2–3.6 (m, 8H), 2.5–2.8 (m, 4H), 1.5–1.8 (m, 4H), 1.2 ppm (t, 2H). Anal. Calcd for $C_8H_{18}O_2S_2$: C 45.68, H 8.63. Found: C 45.79, H 8.42.

5,8-Dimethyl-1,12-dithia-4,9-dioxadodecane (1n).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 3.3–3.8 (m, 6H), 2.4–2.8 (m, 4H), 1.4–1.7 (m, 6H), 1.2 ppm (d, 6H). Anal. Calcd for $C_{10}H_{22}O_2S_2$: C 50.38, H 9.30. Found: C 50.15, H 9.62.

5,5-Dimethyl-1,3-di(β-mercaptoethylthio)cyclohexanes (7a and 7b).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 3.20 (m, 1.6H, $w_{1/2}$ = 18Hz), 3.01 (m, 0.4H, $w_{1/2}$ = 7.5Hz), 2.40–2.89 (m, 8H), 1.2–1.9 (m, 8H), 1.00 ppm (s, 6H). Anal. Calcd for $C_{12}H_{24}S_4$: C 48.60, H 8.16. Found: C 48.96, H 8.37.

2,5-di(1-methyl-4-mercapto-2-thiabutyl) thiophenes (9, R = H).

IR (neat) 2540 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 6.70 (s, 2H), 3.15 (q, 2H), 2.34–2.75 (m, 8H), 1.45–1.80 ppm (m, 8H). Anal. Calcd for $C_{12}H_{20}S_5$: C 44.40, H 6.21. Found: C 44.59, H 6.32.

2,6-Di(1-methyl-4-mercapto-2-thiabutyl)pyridines (11, R = H).

IR (neat) 2550 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 7.02–7.28 (m, 3H), 4.02 (q, 2H), 2.35–2.80 (m, 8H), 1.35–1.80 ppm (m, 8H). Anal. Calcd for $C_{13}H_{21}NS_4$: C 48.86, H 6.62, N 4.38. Found: C 48.61, H 6.78, N 4.21.

2,6-Bis(6-mercapto-3-thiahexyl)pyridine (13, R = H).

IR (neat) 2545 cm^{-1}; ^1H NMR (CCl_4) δ 6.8–7.5 (m, 3H), 2.3–3.1 (m, 16H), 1.90 (t, 4H). Anal. Calcd for $C_{15}H_{25}NS_4$: C 51.83, H 7.25, N 4.03. Found: C 51.61, H 7.48, N 4.23.

Reduction of 1,1'-bi(1,3-dithiolane) (3i).

A solution of **3i** (2.0 g, 9.5 mmol), TBTH (5.5 g, 19.0 mmol), and .1 g of AIBN in 20 mL of dry benzene was refluxed for 20 h. Evaporation of the solvent and subsequent chromatography on silica gel resulted in destannylation and some separation of the components of the mixture, which included: 0.25 g (11%) of dihydro-1,4-dithiin, (**16**):[20] IR (neat) 1640 cm^{-1}; ^1H NMNR (CCl_4) δ 5.91 (s, 2H), 3.10 ppm (s, 4H); 0.02 g (4%) of *p*-dithiane (**17**), which had identical ^1H NMR and IR spectra as an authentic sample; 1.17 g of 2-tributylstannyl-1,4-dithiane as a white solid: mp 57–59°C; ^1H NMR (CCl_4) δ 2.60–3.12 (m, 7H,

including a sharp singlet at 2.92 ppm) 0.92–1.82 ppm (m, 27H) [Anal. Calcd for $C_{16}H_{34}S_2Sn$: C 46.96, H 8.37. Found: C 47.21, H 8.56]; 0.39 g (17%) of 3,6-dithia-1,10-decanedithiol (**1i**)[7,21] as a pale straw-colored oil: IR (neat) 2520 cm^{-1} (S-H); ^1H NMR δ 2.62–3.10 (m, 12H), 1.12 ppm (t, 2H).

Reduction of 1,1'-bi(1,3-dithiane) (3j).

A solution of 1.00 g (4.2 mmol) of **3j** and 2.50 g (8.5 mmol) of TBTH and AIBN in dry benzene were reacted as above for 24 h. Evaporation of the solvent gave 3.31 g of products which were chromatographed to give 0.16 g of alkenes (NMR absorptions ~ δ 6 ppm) in the early fractions. In the later fractions 0.79 g (78%) of 4,7-dithia-1,10-decanedithiol (**1j**)[8] was obtained as a colorless oil: IR (neat) 2520 cm^{-1} (S-H); ^1H NMR (CCl_4) δ 2.42–3.03 (m, 12H), 1.60–2.02 (m, 4H), 1.35 ppm (t, 2H).

3,6-Dithiaoctanedicarboxaldexyde tetramethyl acetal.

To a solution of sodium ethoxide [prepared from 50 mL of absolute ethanol and 2.00 g (86.9 mmol) of freshly cleaned sodium metal] was added 3.65 mL (43.5 mmol) of 1,2-ethanedithiol dropwise *via* syringe over 15 min. The reaction was refluxed for 30 min and then 9.9 mL (86.9 mmol) of 2-chloroacetaldehyde dimethyl acetal was slowly added dropwise, followed by an additional 6 h of reflux. The mixture was cooled to room temperature, and then a few drops of water were added. The solvent was evaporated at reduced presure and the residue taken up in 100 mL ether. The organic solution was washed with water until neutral and then with saturated brine. The organic layer was dried over anhydrous magnesium sulfate, filtered, and evaporation of solvent gave 9.92 g of product (93%) as an oil. A sample was chromatographed on silica gel for analysis: ^1H NMR (CCl_4) δ 4.33 (t, 2H), 3.25 (s, 12H), 2,70 (s, 4H), and 2.57 ppm (d, 4H). Anal. Calcd for $C_{10}H_{22}O_4S_2$: C 44.42, H 8.20. Found: C 44.17, H 7.93.

3,6-Dithiaoctanedicarboxaldexyde bis(ethylene hemithioacetal) (26).

A solution of 7.31 g (29.6 mmol) of 3,6-dithiaoctanedicarboxaldexyde tetramethyl acetal, 4.15 mL (59.3 mmol) of 2-mercaptoethanol and .1 g of *p*-toluenesulfonic acid in 40 mL of toluene was refluxed one h. The toluene/methanol azeotrope (bp 74°C) was then removed by distillation, and the reaction judged as complete when the distillate temperature rose to the boiling point of

toluene. The reaction mixture was cooled to room temperature, diluted with anhydrous ethyl ether, and neutralized with solid sodium bicarbonate. The organic solution was washed sequentially with water and brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated and 8.17 g (92%) of **26** was isolated as an oil, which was made analytically pure by chromatography on silica gel: ^{1}H NMR (CCl_4) δ 5.12 (t, 2H), 4.4-3.4 (m, 4H), 3.2-2.3 ppm (multiplet, 12H, including a singlet at 2.78). Anal. Calcd for $C_{10}H_{18}O_2S_2$: C 40.24, H 6.08. Found: C 40.37, H 6.31.

Reduction of 3,6-dithiaoctanedicarboxaldexyde bis(ethylene hemithioacetal) (26).

A solution of 0.138 g (0.46 mmol) of bis(ethylene hemithioacetal) **26**, 0.309 g (1.06 mmol) of TBTH, and 50 mg of 2,2′-azobis(isobutyronitrile) (AIBN), in 10 mL of dry freshly distilled benzene was refluxed one hour. All TBTH had been consumed by this time, as indicated by the disappearance of the Sn-**H** NMR signal at 4.5 ppm in benzene. The solvent was evaporated, and the crude reaction mixture consisted of unreacted starting material (70%); material consistent with enol ether **28**: NMR (CCl_4) δ 6.23 (m, 1H) 4.1 (m, 1H), 3.9–3.5 (m, 3H), 3.8 (m, 2H), 0.6–1.8 ppm (m, 27H); bis(tributyltin)sulfide; and trace amounts of uncharacterized materials.

3,6,9,12-Tetrathia-1,14-tetraundecandiol (29) A solution of 0.360 g (1.21 mmol) of bis(ethylene hemithioacetal) **26** in 20 mL anhydrous ethyl ether was reacted with 0.30 mL (2.69 mmol) of monochloroborane-methyl sulfide complex for 35 h at reflux. The solvent was removed at reduced pressure and 25 mL of methanol was added to the residue and the solution refluxed an additional 6 h. The reaction mixture was evaporated at reduced pressure, and additional methanol was added and evaporated three more times to remove all boron species as trimethylborate. Product **29** was isolated as an oil (0.251 g, 69%): ^{1}H NMR ($CDCl_3$) δ 3.70 (s, 2H), 3.52 (t, 4H, J = 4.5 Hz), 3.05-2.5 ppm (m, 16H). IR: 3417 cm^{-1} (O-H stretch). Anal Calcd for $C_{10}H_{22}S_4O_2$: C 39.70, H 7.33. Found C 42.21, H 7.25.

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