HETEROCYCLES, Vol. 60, No. 1, 2003, pp. 47 - 56
Received, 16th August, 2002, Accepted, 28th October, 2002, Published online, 28th October, 2002

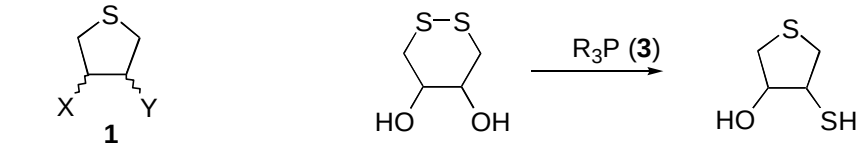
PHOSPHINE-ASSISTED REARRANGEMENT OF 4,5-DIHYDROXY-1,2-DITHIANES TO 4-HYDROXY-3-MERCAPTOTETRAHYDROTHIOPHENES

Sang Hyup Lee and Harold Kohn*

Division of Medicinal Chemistry and Natural Products,
School of Pharmacy, University of North Carolina,
Chapel Hill, NC 27599-7360, USA

Abstract-Treatment of 4,5-dihydroxy-1,2-dithianes with trialkylphosphines and triphenylphosphine under neutral and moderately basic conditions led to the efficient and stereospecific production of 4-hydroxy-3-mercaptotetrahydrothiophenes. The reaction is projected to proceed through three successive intramolecular rearrangements.

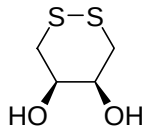
Tetrahydrothiophenes (thiolanes) are heterocycles of interest[1] and recently 3,4-disubstituted tetrahydrothiophenes (**1**)[2-4] have gained importance for the construction of novel nucleosides and glycosides.[2] Few synthetic methodologies exist for the preparation of **1**.[2-4] In this paper, we report an efficient phosphine (**3**)-mediated procedure for the conversion of 4,5-dihydroxy-1,2-dithianes[5] (**2**) to 4-hydroxy-3-mercaptotetrahydrothiophenes (**4**) that proceeds with stereospecificity.



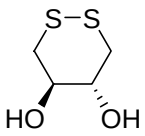
1 X, Y= OH, NH_2, SH **2** **4**

RESULTS AND DISCUSSION

Our starting cyclic disulfides were *cis*-4,5-dihydroxy-1,2-dithiane (DTE^{ox}, **5**)[6] and *trans*-4,5-dihydroxy-1,2-dithiane (DTT^{ox}, **6**)[7] and we employed the three phosphines, triethylphosphine (**7**), tris(2-carboxyethyl)phosphine hydrochloride[8] (TCEP, **8**), and triphenylphosphine (**9**). Dithiane (**6a**) is commercially available while **5**[6] and **6b**[5,7] were prepared by oxidation of dithioerythritol (DTE, **10**) and L-dithiothreitol (L-DTT, **11b**), in basic methanol, respectively (Scheme 1).

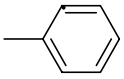


5

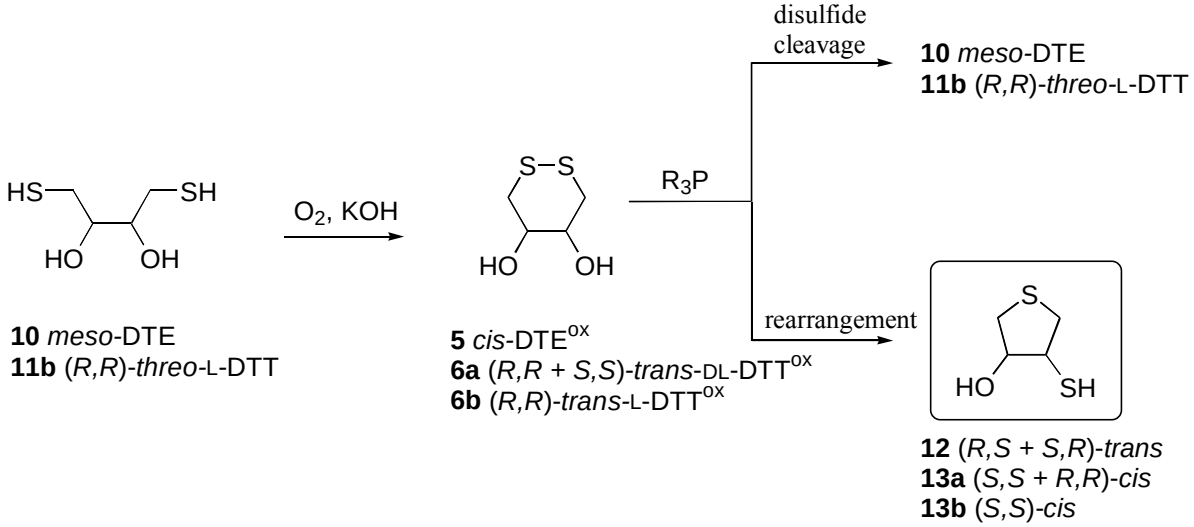


6
a (*R,R* + *S,S*)
b (*R,R*)

R_3P

7 R = CH_2CH_3
8 R = $CH_2CH_2CO_2H{\cdot}HCl$
9 R = 

Scheme 1. Phosphine-mediated Transformations

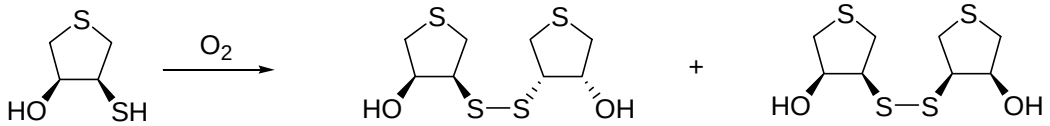


The reactions of 4,5-dihydroxy-1,2-dithianes (**5** and **6**) with phosphines (**7**-**9**) were pH-dependent (Table 1). Under mildly acidic conditions, TCEP (**8**) efficiently reduced **5** (Table 1, Entries a,b) and **6b** (Table 1, Entries h-j) to the corresponding dithiols (**10**) and (**11b**), respectively, at room temperature. These findings mirrored the earlier report of Whitesides and coworkers.[8] Correspondingly, when the reactions with **5**, **6a** and **6b** were conducted under neutral or moderately basic conditions (Table 1, Entries c-g,k,l) we did not obtain the corresponding dithiols, but rather, we observed the efficient production of 4-hydroxy-3-mercaptotetrahydrothiophenes (**12, 13a** and **13b**), respectively. For **5** and **6a**, we obtained racemic **12** and **13a**, respectively, while for **6b**, we isolated the stereospecific product (**13b**). Air oxidation of **13a** gave a 1.1:1 diastereomeric mixture of disulfide (**14**) (NMR spectral analysis). We found that the reaction rate for Et_3P (**7**) was comparable to TCEP (**8**) (< 0.2 h) but that the Ph_3P (**9**) transformation was significantly slower (~ 24 h) (Table 1, Entries c,d,e). This finding was consistent with the nucleophilicity of alkyl- and aryl- phosphines[9-11] and likely reflects, in part, the rate of the disulfide cleavage reaction.

Table 1. Reaction of **5**, **6a** and **6b** with Phosphine Reagents (**7-9**)

Entry	Compound	R_3P[a] (2 equiv.)	Base (equiv.)	Reaction time (h)	Product (% yield)[b]
a	**5**	**8**	-	6	**10** (70)
b	**5**	**8**	pyridine (10)	0.2	**10** (65)
c	**5**	**8**	K_2CO_3 (10)	0.2	**12** (45)
d	**5**	**7**	-	0.2	**12** (79)
e	**5**	**9**	-	24	**12** (45)
f	**6a**	**7**	-	0.2	**13a** (51)
g	**6a**	**9**	-	48	**13a** (68)
h	**6b**	**8**	-	6	**11b** (80)
i	**6b**	**8**	pyridine (2)	0.5	**11b** (70)
j	**6b**	**8**	pyridine (8)	0.2	**11b** (55)
k	**6b**	**7**	pH 7.0[c]	0.2	**13b** (66)
l	**6b**	**8**	K_2CO_3 (10)	0.2	**13b** (73)

[a]Two equiv. of R_3P was used. [b]Isolated yield. [c]Buffered methanolic solution (0.5 M bis-Tris·HCl).



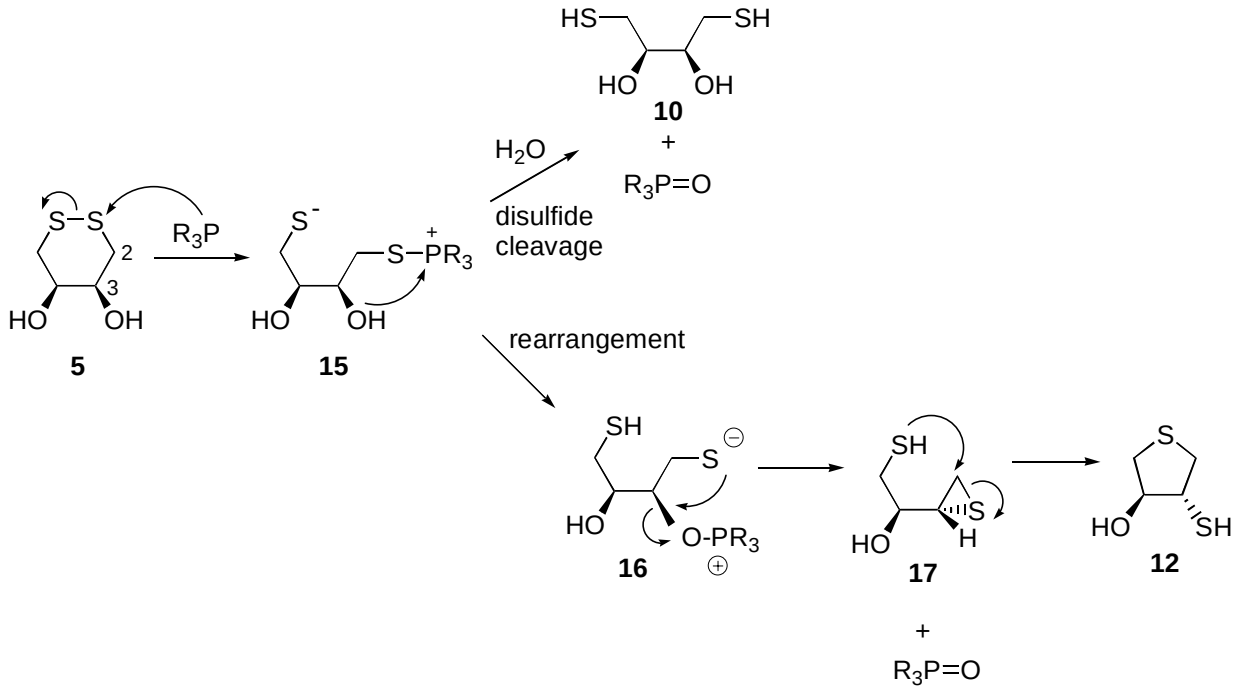
13a (*dl*) **14** (*dl*) **14** (*meso*)

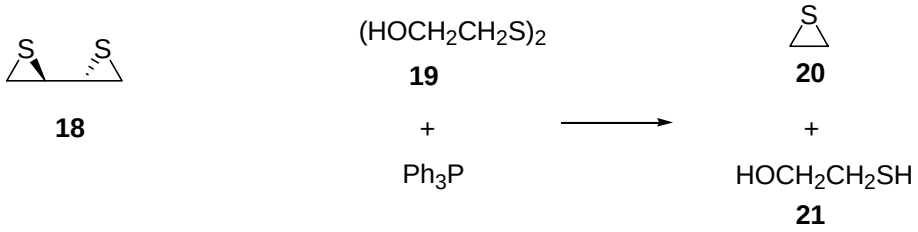
We documented the identity of 4-hydroxy-3-mercaptotetrahydrothiophenes (**12**) and (**13**). Characteristic signals in the ^1H and ^{13}C NMR spectra[12,13] in related structures permitted the identity of the C(3) and C(4) methine hydrogen and carbon signals, respectively. Furthermore, we were able to assign the relative orientation of the C(3) and C(4) substituents by inspection of the ^{13}C and ^1H NMR resonances for these signals. We observed that in the ^{13}C NMR, the C(3) and C(4) signals for *cis*-tetrahydrothiophene (**13a**) appeared upfield (0.5-4.8 ppm) compared to the *trans*-isomer (**12**) while the corresponding ^1H NMR signals for the methine hydrogens appeared downfield (0.03-0.2 ppm). This inverse relationship of ^{13}C and ^1H NMR signals is diagnostic of a γ-effect[14,15] and has been observed in structurally related systems.[16] Our assignment for the *cis*-adduct (**13a**) was bolstered by the NOESY spectrum where we observed a strong interaction for the C(3)H_α and C(4)H_α methine hydrogens, a strong interaction for

C(4)H_α and C(5)H_α, and a weak interaction for C(4)H_α and C(5) H_β. We ran the corresponding NOESY spectrum on the *trans*-tetrahydrothiophene (**12**) but overlapping signals did not permit structural assignment. The ^{13}C NMR data for **12** and **13a** documented the stereospecific conversion of dithiane (**2**) to tetrahydrothiophene (**4**). For each reaction we observed a unique set of four signals in the ^{13}C NMR spectrum. Racemization at either C(3) or C(4) would have led to diastereomeric mixtures and the observation of a pair of four signals in the ^{13}C NMR spectrum.

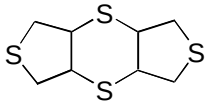
Why are dithiols (**10, 11**) produced from dithianes (**5, 6**) under acidic conditions while the ring-contracted tetrahydrothiophenes (**12, 13**) are the sole adducts under neutral and moderately basic conditions? We suggest that both reactions proceed by initial phosphine-assisted disulfide cleavage[8,9,17-19] (Scheme 2 for **5**). Under acidic conditions, the ring-cleaved product (**15**) is hydrolyzed to give dithiol (**10**) and phosphine oxide. Under neutral and basic conditions, rearrangement of **15** to **16** competes with solvolysis. Subsequent cyclization of **16** leads to thiirane (**17**) and the release of the corresponding phosphine oxide. Intramolecular nucleophilic substitution at the methylene site in thiirane (**17**) by the terminal thiol gives the stable tetrahydrothiophene (**12**). We have evidence for the overall pathway depicted in Scheme 2. We monitored the conversion of **6a** to **13a** in CD_3OD-$CDCl_3$-D_2O using ^{1}H and ^{13}C NMR spectrometry (data not shown). We observed the appearance of diagnostic signals in the ^{1}H NMR (δ 2.23 (dd), 2.51 (dd)) and the ^{13}C NMR (δ 24.0, 31.5) in the early stages of the reaction that have been tentatively assigned to **17** and which disappeared with time. These signals are similar to those reported for **18**.[20]

Scheme 2. Proposed Pathway for Phosphine-mediated Disulfide Transformations

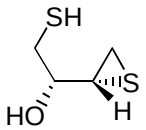




The proposed pathway of **5** with phosphines to **17** and the conversion of **17** to **12** gains support from previous studies. First, Grayson[21] and Overman[10] have reported that treatment of 2-hydroxyethyl disulfide (**19**) with triphenylphosphine gave thiirane (**20**) and 2-mercaptoethanol (**21**). We have repeated this reaction with **7** (1.3 equiv) under the conditions employed in our study and observed the rapid production (< 0.2 h) of **20** and **21** (NMR spectral analysis, data not shown).[22] Second, Sanchez showed that heating **6a** with concentrated aqueous HCl led to a moderate yield (32%) of **13a**.[4] Attempts to convert **5** to **12** were unsuccessful and gave **22**.[4] Sanchez proposed that **13a** formation proceeded through intermediate (**23**).[23]



22



23

CONCLUSIONS

In summary, we report a mild and efficient procedure for the stereospecific rearrangement of 4,5-dihydroxy-1,2-dithianes (**2**) to 4-hydroxy-3-mercaptotetrahydrothiophenes (**4**). We attribute the ease of this transformation to the phosphine (**3**), which initiates disulfide cleavage and assists in the removal of the C(3) hydroxyl group permitting tetrahydrothiophene formation. Stereospecific conversion of **2** to **4** is projected to proceed through three successive intramolecular rearrangements. The importance of this novel transformation is underscored by recent reports for the introduction of nucleic bases at the C(2) site in 3,4-dihydroxytetrahydrothiophenes.[2]

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on Varian VXR-300 and Bruker DRX-500 MHz spectrometer. MS spectral data were obtained by Dr. Mehdi Moini at the University of Texas at Austin. The low-resolution MS spectral studies were run on a Finnegan TSQ-70 triple quadrupole mass spectrometer, and the high-resolution MS spectral studies were conducted on a Micromass ZAB-E mass spectrometer. FT-IR spectra were run on a Mattson Galaxy Series FT-IR 5000 spectrophotometer. Melting points were determined in open capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. Microanalyses were provided by Atlantic Microlab, Inc. (Norcross, GA).

***cis*-4,5-Dihydroxy-1,2-dithiane (DTE^{ox}, 5).**[6] To a stirred solution of **10** (Aldrich Co., 500 mg, 3.24 mmol) in MeOH (150 mL) was added KOH (381 mg, 6.8 mmol) at rt and then O_2 was bubbled through

the solution (2.5 d). The reaction solution was evaporated to one-fourth of its volume and H_2O (100 mL) was added. The mixture was extracted with EtOAc (2 X 150 mL). The combined organic layers were washed with H_2O (100 mL), dried ($MgSO_4$), and concentrated to one-tenth of its volume leading to formation of a precipitate. The solid was collected and washed with Et_2O to give **5** without further purification: yield, 320 mg (65%); mp 129-131 °C (lit.,[6] mp 132 °C); R_f 0.42 (2:1 EtOAc/hexanes); IR (KBr) 3404, 3314, 2896, 1399, 1269, 1212, 1047, 916, 743, 591 cm^{-1}; ^1H NMR (CD_3OD, -20 °C) δ 2.52 (dd, 1 H, J = 12.5, 3.5 Hz), 3.02 (dd, 1 H, J = 13.8, 4.5 Hz), 3.20 (app t, 1 H, J = 11.8 Hz), 3.28-3.37 (m, 1 H), 3.66 (br d, 1 H, J = 11.0 Hz), 4.10 (s, 1 H); ^{13}C NMR (CD_3OD, -20 °C) δ 32.4, 42.4, 67.3, 70.8, the ^1H and ^{13}C NMR spectral data were in agreement with the COSY and HMQC spectra.

(*4R,5R*)-*trans*-4,5-Dihydroxy-1,2-dithiane (L-DTT^{ox}, 6b).[7] Employing the preceding procedure and using **11b** (Aldrich Co., 500 mg, 3.24 mmol), MeOH (60 mL), and KOH (381 mg, 6.8 mmol) gave **6b** without further purification: yield, 315 mg (64%); mp 113-115 °C (lit.,[7] mp 113-115 °C); R_f 0.47 (2:1 EtOAc/hexanes); IR (KBr) 3368, 2903, 1403, 1278, 1177, 1031, 874, 738, 581, 540 cm^{-1}; ^1H NMR (CD_3OD, -60 °C) δ 2.91 (dd, 2 H, J = 13.5, 10.5 Hz), 3.04 (dd, 2 H, J = 13.5, 3.0 Hz), 3.45-3.52 (m, 2 H); ^{13}C NMR (CD_3OD, -60 °C) δ 42.1, 75.7, the ^1H and ^{13}C NMR spectral data were in agreement with the COSY and HMQC spectra.

General Procedure for Disulfide Cleavage to Dithiols. To a stirred solution of 4,5-dihydroxy-1,2-dithiane (**5**, **6b**) (20 mg, 0.13 mmol) in the appropriate solvent mixture either in the absence or presence of a base was added the phosphine reagent (0.26 mmol) at rt. Stirring was continued for 10 min - 6 h. After the reaction was completed H_2O (20 mL) was added and the mixture was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with H_2O (20 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by PTLC using EtOAc/hexanes (1:2) as the eluent.

Dithioerythritol (DTE, 10).[5]

(A) *Using TCEP*: Using **5** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), and **8** (75 mg, 0.26 mmol) and the general procedure gave **10** as a white solid (6 h) without further purification: yield, 14 mg (70%); mp 79-81 °C (lit.,[5] mp 83 °C).

(B) *Using TCEP and pyridine*: Using **5** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), **8** (75 mg, 0.26 mmol), and pyridine (105 μL, 1.3 mmol) and the general procedure gave **10** as a white solid (0.2 h): yield, 13 mg (65%).

L-Dithiothreitol (L-DTT, 11b).[5]

(A) *Using TCEP*: Using **6b** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), and **8** (75 mg, 0.26 mmol) and the general procedure gave **11b** as a white solid (6 h) without further purification: yield, 16 mg (80%) mp 44-47 °C (lit.,[5] mp 48-50 °C).

(B) *Using TCEP and pyridine (2 equiv)*: Using **6b** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), **8** (75 mg, 0.26 mmol), and pyridine (21 μL, 0.26 mmol) and the general procedure gave **11b** as a white solid (0.5 h): yield, 14 mg (70%).

(C) *Using TCEP and pyridine (8 equiv)*: Using **6b** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), **8** (75 mg, 0.26 mmol), and pyridine (84 μL, 1.04 mmol) and the general procedure gave **11b** as a white solid (0.2 h): yield, 11 mg (55%).

General Procedure for 4-Hydroxy-3-mercaptotetrahydrothiophenes. To a stirred solution of 4,5-dihydroxy-1,2-dithiane (**5**, **6a**, **6b**) (20 mg, 0.13 mmol) in the appropriate solvent mixture either in the absence or presence of a base was added the phosphine reagent (0.26 mmol) at rt. Stirring was continued for 10 min- 2 d. After the reaction was completed CH_3CN (2 mL) and H_2O (20 mL) was added and the mixture was extracted with EtOAc (2 X 20 mL). The combined organic layers were washed with H_2O (20 mL), dried ($MgSO_4$), and concentrated *in vacuo* (2 h). The crude product was purified by PTLC using EtOAc/hexanes (1:2) as the eluent.

***trans*-4-Hydroxy-3-mercaptotetrahydrothiophene (12).**

(A) *Using Et_3P*: Using **5** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:5:1, v/v, 2.2 mL), and **7** (39 μL, 0.26 mmol) and the general procedure gave **12** as a viscous liquid (0.2 h): yield, 14 mg (79%); R_f 0.49 (1:2 EtOAc/hexanes); IR (neat) 3384, 2930, 2537, 1434, 1269, 1063, 1014 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.82 (d, 1 H, J = 8.7 Hz), 2.30 (br s, 1 H), 2.76-2.84 (m, 2 H), 3.21-3.38 (m, 3 H), 4.18 (q, 1 H, J = 5.2 Hz); ^{13}C NMR ($CDCl_3$) δ 35.2, 36.1, 47.2, 80.7, the ^1H and ^{13}C NMR data were in agreement with the COSY, HMQC, and DEPT spectra; MS (+CI) m/z 137 $[M+1]^+$; M_r (+CI) 137.00905 $[M+1]^+$ (calcd for $C_4H_9OS_2$ 137.00948). Anal. Calcd for $C_4H_8OS_2 \cdot 0.2\ CH_3CN$: C, 36.59; H, 6.00. Found: C, 36.69; H, 5.66.

(B) *Using Ph_3P*: Using **5** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (3:6:1, v/v, 3.0 mL), and **9** (68 mg, 0.26 mmol) and the general procedure gave **12** as a viscous liquid (24 h): yield, 8 mg (45%).

(C) *Using TCEP*: Using **5** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), **8** (Fluka, 75 mg, 0.26 mmol), and K_2CO_3 (180 mg, 1.3 mmol) and the general procedure gave **12** as a viscous liquid (0.2 h): yield, 8 mg (45%).

***cis*-4-Hydroxy-3-mercaptotetrahydrothiophene (13a).[4]**

(A) *Using Et_3P*: Using **6a** (Aldrich Co., 20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:5:1, v/v, 2.2 mL), and **7** (39 μL, 0.26 mmol) and the general procedure gave **13a** as a viscous liquid (0.2 h): yield, 9 mg (51%); R_f 0.49 (1:2 EtOAc/hexanes); IR (neat) 3422, 2932, 2545, 1436, 1263, 1160, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.86 (d, 1 H, J = 8.7 Hz), 2.45 (br s, 1 H), 2.84 (t, 1 H, J = 10.4 Hz), 2.92 (dd, 1 H, J = 11.4, 3.0 Hz), 3.09 (dd, 1 H, J = 11.4, 4.8 Hz), 3.18 (dd, 1 H, J = 10.4, 6.6 Hz), 3.25-3.38 (m, 1 H), 4.30-4.38 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 35.5, 36.1, 46.8, 76.0, the ^1H and ^{13}C NMR data were in agreement with

the COSY, HMQC, and DEPT spectra; MS (+CI) m/z 137 $[M+1]^+$; M_r (+CI) 137.01017 $[M+1]^+$ (calcd for $C_4H_9OS_2$ 137.00948). Anal. Calcd for $C_4H_8OS_2 \cdot 1.75\ CH_3CN$: C, 43.29; H, 6.42. Found: C, 43.35; H, 6.32.

(B) *Using Ph_3P*: Using **6a** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (3:6:1, v/v, 3.0 mL), and **9** (68 mg, 0.26 mmol) and the general procedure gave **13a** as a viscous liquid (48 h): yield, 12 mg (68%).

(*S,S*)-*cis*-4-Hydroxy-3-mercaptotetrahydrothiophene (13b). Using **6b** (20 mg, 0.13 mmol), MeOH-$CHCl_3$-H_2O (5:2:5, v/v, 3.6 mL), **8** (75 mg, 0.26 mmol), and K_2CO_3 (180 mg, 1.3 mmol) and the general procedure gave **13b** as a viscous liquid (0.2 h): yield, 13 mg (73%); $[\alpha]_D^{25} = -125^o$ (c = 0.1, $CHCl_3$); IR (neat) 3409, 2926, 2857, 2549, 1437, 1385, 1268, 1198, 1159, 1021 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (d, 1 H, J = 8.7 Hz), 2.34 (d, 1 H, J = 5.4 Hz), 2.84 (dd, 1 H, J = 10.8, 9.3 Hz), 2.92 (dd, 1 H, J = 11.4, 3.0 Hz), 3.09 (dd, 1 H, J = 11.4, 4.8 Hz), 3.18 (dd, 1 H, J = 10.8, 6.6 Hz), 3.28-3.39 (m, 1 H), 4.30-4.37 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 35.6, 36.1, 46.8, 76.1; MS (+CI) m/z 137 $[M+1]^+$; M_r (+CI) 137.009175 $[M+1]^+$ (calcd for $C_4H_9OS_2$ 137.00948). Anal. Calcd for $C_4H_8OS_2 \cdot 0.05$ EtOAc: C, 35.87; H, 6.02. Found: C, 36.00; H, 6.02.

Bis(4-hydroxytetrahydrothiophenyl) 3,3'disulfide (14). To a stirred solution of 4,5-dihydroxy-1,2-dithiane (**6a**, 20 mg, 0.13 mmol) in MeOH-$CHCl_3$-H_2O (3:6:1, v/v, 3.0 mL) was added **9** (68 mg, 0.26 mmol) at rt and then stirring was continued (2 d) followed by bubbling O_2 through the solution (6 d). H_2O (20 mL) was added to the reaction and the mixture was extracted with EtOAc (2 X 20 mL). The combined organic layers were washed with H_2O (20 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by PTLC using EtOAc/hexanes (1:2) as the eluent to give **14** as a mixture of diastereomers (1.1:1, ^{13}C NMR spectral analysis): yield, 8 mg (42%); mp 75-85 ^oC; R_f 0.23 (1:2 EtOAc/hexanes); IR (KBr) 3414, 2931, 1436, 1320, 1153, 1024, 916 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.37 (br s, 2 H), 2.85-3.16 (m, 8 H), 3.38-3.48 (m, 2 H), 4.55-4.63 (m, 2 H), ^{13}C NMR ($CDCl_3$) δ 31.6, 31.7, 37.3, 37.4, 60.0, 60.1, 74.3, 74.4; MS (+CI) m/z 393 $[M+1]^+$; M_r (+CI) 270.99643 $[M+1]^+$ (calcd for $C_8H_{15}O_2S_4$ 270.99549). Anal. Calcd for $C_4H_{14}O_2S_4 \cdot 0.15$ EtOAc: C, 36.41; H, 5.41. Found: C, 36.69; H, 5.33.

ACKNOWLEDGEMENTS

This investigation was supported, in part, by NIH grant CA29756.

REFERENCES AND NOTES

1. H. D. Hartough 'The Chemistry of Heterocyclic Compounds; Thiophene and Its Derivatives' ed. by A. Weissberger, Intersciences, New York, 1952, pp. 76-78; T. Eicher and S. Hauptmann, 'The Chemistry of Heterocycles: Structure, Reactions, Syntheses and Applications' George Thieme Verlag Stuttgart, New York, New York, 1995, pp. 84-85.

2. T. Naka, N. Nishizono, N. Minakawa, and A. Matsuda, *Tetrahedron Lett.,* 1999, **40**, 6297; J. E. McCormick and R. S. McElhinney, *J. Chem. Soc., Perkin Trans. I,* 1976, 2533.
3. J. E. McCormick and R. S. McElhinney, *J. Chem. Soc., Perkin Trans. I,* 1972, 2795; V. Glaçon, M. Benazza, D. Beaupère, and G. Demailly, *Tetrahedron Lett.,* 2000, **41**, 5053.
4. R. A. Sanchez, *Synthesis,* 1982, 148.
5. W. W. Cleland, *Biochemistry,* 1964, **3**, 480; M. Carmack and C. J. Kelley, *J. Org. Chem.,* 1968, **33**, 2171.
6. S. Capasso, I. Mazzarella, and A. Zagari, *J. Cryst. & Spectros. Res.,* 1984, **14**, 303.
7. C. A. Evans, L. Bernier, J. Dugas, and T. S. Mansour, *Tetrahedron Lett.,* 1977, **38**, 7657.
8. J. A. Burns, J. C. Butler, J. Moran, and G. M. Whitesides, *J. Org. Chem.,* 1991, **56**, 2648; M. R. Levison, A. S. Josephson, and D. M. Kirschenbaum, *Experientia,* 1968, **25**, 126.
9. L. E. Overman, D. Matzinger, E. M. O'Connor, and J. D. Overman, *J. Am. Chem. Soc.,* 1974, **96**, 6081; L. E. Overman and S. T. Petty, *J. Org. Chem.,* 1975, **40**, 2779.
10. L. E. Overman and E. M. O'Connor, *J. Am. Chem. Soc.,* 1976, **98**, 771.
11. A. J. Parker and N. Kharasch, *J. Am. Chem. Soc.*, 1960, **82**, 3071; J. L. Kice, 'Sulfur in Organic and Inorganic Chemistry' Vol. 1, ed. by A. Senning, Marcel Dekker, New York, NY, 1971, Chapter 6.
12. J. Skarżewski and A. Gupta, *Tetrahedron Asymmetry,* 1997, **8**, 1861; H. Dulphy, J.-L. Gras, and T. Lejon, *Tetrahedron,* 1996, **52**, 8517; A. H. Haines, K. C. Symes, and A. G. Wells, *Carbohydr. Res.,* 1975, **41**, 85.
13. R. G. Ritchie, N. Cyr, B. Korsch, H. J. Koch, and A. S. Perlin, *Can. J. Chem.,* 1975, **53**, 1424.
14. A. S. Perlin and H. J. Koch, *Can. J. Chem.,* 1970, **48**, 2639.
15. D. M. Grant and B. V. Cheney, *J. Am. Chem. Soc.,* 1967, **89**, 5315; D. K. Dalling and D. M. Grant, *J. Am. Chem. Soc.,* 1967, **89**, 6612; D. K. Dalling and D. M. Grant, *J. Am. Chem. Soc.,* 1972, **94**, 5318.
16. S. Cortes and H. Kohn, *J. Org. Chem.,* 1983, **48**, 2246; J. P. Monti, R. Faure, and E. Vincent, *J. Org. Magn. Reson.,* 1976, **8**, 611.
17. A. Schönberg and M. Z. Barakat, *J. Chem. Soc.*, 1949, Part II, 892; J. T. Ayers and S. R. Anderson, *Syn. Commun.,* 1999, **29**, 351.
18. B. J. Sweetman and J. A. Maclaren, *Aust. J. Chem.,* 1966, **19**, 2347; J. A. Maclaren and B. J. Sweetman, *Aust. J. Chem.,* 1966, **19**, 2355.
19. B. Kim, M. Kodomari, and S. L. Regen, *J. Org. Chem.,* 1984, **49**, 3233; R. A. Amos and S. M. Fawcett, *J. Org. Chem.,* 1984, **49**, 2637.
20. J. Brånalt, I. Kvarnström, B. Classon, and B. Samuelsson, *J. Org. Chem.,* 1996, **61**, 3611.

21. M. Grayson and C. E. Farley, *Chem. Commun.,* 1967, 831.
22. Attempts to extend this transformation for the preparation of other heterocycles were unsuccessful. We observed disulfide conversion to the corresponding thiol when **7** was added to 3-hydroxypropyl disulfide, 4-hydroxybutyl disulfide, 2',2'-dithioethanoic acid, 3,3'-dithiopropanoic acid, and *N,N'*-di-Cbz-cystamine.
23. For a related transformation, see: F. P. Doyle, D. O. Holland, K. R. L. Mansford, J. H. C. Nayler, and A. Queen, Antituberculous Sulfur Compounds. II. Some Cyclic Sulfides Derived from Dimercaptoalkanols, *J. Chem. Soc.,* 1960, 2660.