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Reaction of a Polymerization-Resistant 1,2-Dithiolane with Lithiated Nitrogen Heterocycles

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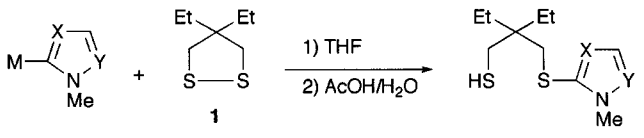
ABSTRACT: *Nitrogen-containing five-membered heterocycles, N-methylpyrrole* **2,** *N-methylpyrazole* **4,** *N-methylimidazole* **6,** *4-methylthiazole* **11,** *N-methylindole* **14,** *benzothiazole* **16,** *N-methylbenzimidazole* **18,** *and benzoxazole* **20** *were lithiated with BuLi and LDA in THF and reacted with the polymerization-resistant 1,2-dithiolane* **1.** *All of the corresponding lithioheterocycles cleaved the S–S bond of the 1,2-dithiolane* **1** *to give the ring-opened products in line with the carbanion mechanism proposed for the enzyme-reductive acylations of lipoic acid. The ring-opened products* **8, 9, 13, 22,** *and* **23** *were isolated in good yields and high purity. The ring-opened products from benzothiazole and N-methylbenzimidazole were decomposed by the action of excess lithioheterocycles. The lithiobenzoxazole was less reactive than the other lithioheterocycles.* © 1998 John Wiley & Sons, Inc. Heteroatom Chem 9:289–294, 1998

INTRODUCTION

The S–S bond cleavage of 1,2-dithiolane by a carbon nucleophile as described in a preceding article is of interest since this kind of reaction was proposed for the carbanion mechanism [1] in the enzyme-reductive acylations of lipoic acid. The polymerization-resistant 1,2-dithiolane, 4,4-diethyl-1,2-dithiolane **1** is a suitable model to elucidate the chemical behavior of the enzyme-bound lipoic acids toward carbon nucleophiles [2]. We have now examined the reaction with lithium reagents [3] derived from some nitrogen-containing five-membered heterocycles.

RESULTS AND DISCUSSION

N-methylpyrrole **2** (3.2 mmol) was lithiated with BuLi (2.0 mmol) in THF (5 mL) at room temperature for 0.5 hour, and 4,4-diethyl-1,2-dithiolane **1** (1.6 mmol) was added dropwise to the solution containing the lithiated *N*-methylpyrrole **3** (see Scheme 1).



	M	X	Y
2	H	CH	CH
3	Li	CH	CH
4	H	CH	N
5	Li	CH	N
6	H	N	CH
7	Li	N	CH

	X	Y
8	CH	CH
9	CH	N
10	N	CH

SCHEME 1

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After the usual workup, the product **8** was separated by kugelrohr distillation in good yield (Table 1, entry 1) and high purity (97%). The structure of **8** was confirmed by the following evidence. (1) The characteristic triplet at δ 1.066 and doublet at δ 2.542 with a coupling constant 8.8 Hz in its ^{1}H NMR spectrum show the presence of the CH_2SH group. (2) Each resonance from the three protons on the pyrrole ring was separate and showed the coupling patterns and coupling constants consistent with 1,2-disubstituted pyrroles. (3) The parent peak in MS and the number of carbons from ^{13}C NMR spectroscopy agree well with the proposed structure **8.**

Since the lithiation of *N*-methylpyrrole **2** (*p*K*a* 39.5 [4]) is known to occur preferentially at C-2 under similar conditions, this result shows that the reaction was the simple ring opening by the initially produced lithio-derivative **3,** and no isomerization of **3** occurred during the reaction. The exclusive formation of the mono-*S*-substituted 1,3-propanedithiol **8** was confirmed by gc and GC-MS analyses; i.e., neither the unsubstituted 2,2-diethyl-1,3-propanedithiol **26** nor the *S,S′*-bis-substituted 1,3-propanedithiol was found in the mixture. The simple distillation is sufficient to isolate **8** in high purity.

The lithiation of 1-methylpyrazole **4** occurs at C-5 (*p*K*a* about 36 [4]). The reaction of the corresponding lithium reagent **5** with the dithiolane **1** gave a simple product **9** that was isolated in excellent yield by kugelrohr distillation (Table 1, entry 2).

The lithiation of 1-methylimidazole **6** (*p*K*a* 33.7 [4]) occurs preferentially at the C-2 position. The reaction of the lithiated methylimidazole **7** was also a simple ring-opening reaction. The product **10** was rather unstable thermally, and a considerable amount of product **10** decomposed during kugelrohr distillation to reproduce the starting 1,2-dithiolane **1** (Table 1, entry 3). The crude product obtained before the distillation, however, contained only 2% of an unidentifiable by-product; thus, the product may be used without further purification for ordinary purposes.

This type of thermal decomposition was not observed in the ring-opened products, mono-*S*-substituted 1,3-propanedithiols, obtained in our studies. The enhanced instability of **10** is probably due to the fact that the N-3 in the imidazole ring is sufficiently basic to deprotonate partially the free SH group in **10,** and the protonated imidazole ring can act as an effective leaving group at a higher temperature (Scheme 2).

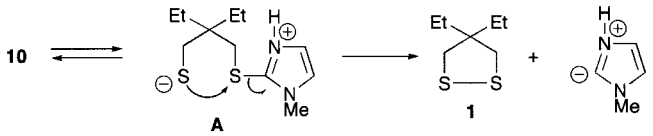
Lithiation of 4-methylthiazole **11** is known to occur at the C-2 position [6]. An attempt to react the 1,2-dithiolane **1** with excess 2-lithio-4-methylthiazole **12** at room temperature resulted in the recovery of **1** (81%). The ring opening may be an entropically unfavored condensation between the dithiolane and the lithium reagent; thus, it could be favored at a lower temperature. The polymerization of the 1,2-dithiolane initiated by a thiolate during the reaction would also be favored, since it is a multistep condensation, and it is affected by the ceiling temperature of the monomer 1,2-dithiolane. The lithium reagent (1.5 equiv) was prepared by lithiating **11** with LDA at room temperature, and then reaction with **1** (1.0 equiv) was carried out at the temperature of a Dry Ice–acetone bath (about −70°C). In this manner, the ring-opened product **13** was produced in a quantitative yield (Scheme 3 and Table 1, entry 4). This result shows that the dithiolane has a high reactivity even at the low temperature, and its polymerization does not compete with the ring opening.

The lithiation of 1-methylindole **14** (*p*K*a* 38.1 [4]) occurs preferentially at the C-2 position under

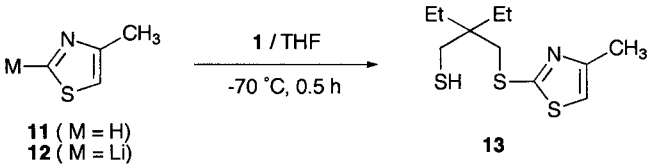
TABLE 1 Reaction of Lithiated Heterocycles with 4,4-Diethyl-1,2-dithiolane **1**

Entry	*Li-Het*[a]	*[Li-Het]$_o$/[1]$_o$*	*Conditions*	*Products (yield/%)*[b]
1	**3**	1.2	rt, 40 min	**8** (94)
2	**5**	1.3	rt, 30 min	**9** (93)
3	**7**	2.0	rt, 30 min	**10** (81)
4	**12**	1.5	−70°C, 30 min	**13** (99)
5	**15**	1.0	rt, 30 min	**22** (84)
6	**17**	1.0	−70°C, 30 min	**23** (97)
7	**17**	2.5	rt, 30 min	**27** (84), **26** (92)
8	**19**	2.5	rt, 30 min	**28** (107)
9	**19**	1.0	−70°C, 30 min	**24** (77), **28** (20)
10	**21**	1.7	rt, 12 h	**25** (63)

[a]Lithiated heterocycles.
[b]Yields after isolation.



SCHEME 2



SCHEME 3

various conditions. The reaction of the corresponding lithio-derivative **15** with 1,2-dithiolane **1** was also simple, giving the ring-opened product **22,** which was isolated in good yield and high purity by simple distillation when an equimolar amount of the lithium reagent was employed (Scheme 4 and Table 1, entry 5).

In the case of the analogous 2-lithiobenzo[*b*]furan, the excess reagents caused a decomposition of the ring-opened product, and the reaction did not give the simple product unless equimolar amounts of the lithium reagent and dithiolane were employed [5]. On the other hand, an excess of the lithium reagent from *N*-methylindole could be used without any decomposition of the ring-opened products. The difference may be attributed to the greater stability of the ring-opened product in this case.

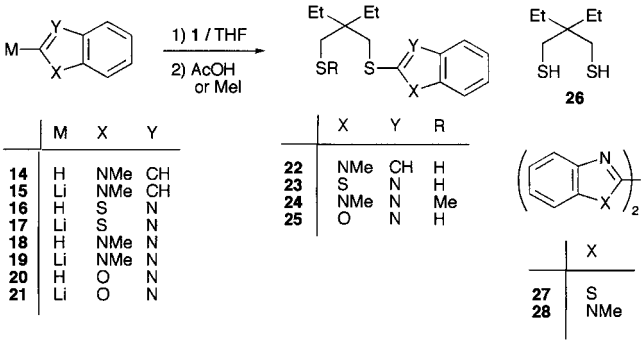
The lithium reagent **17** (1.0 equiv) of benzothiazole **16** reacted similarly at a lower temperature to produce the corresponding ring-opened product **23** in good yield (Scheme 4 and Table 1, entry 6). However, the reaction with excess lithium reagent **17** (2.5 equiv) did not give **23** but gave 2,2′-bisbenzothiazolyl **27** and the propanedithiol **26** in a molar ratio of 1:1 (Table 1, entry 7).

The formation of **27** is considered to occur as shown in Scheme 5. The reaction of **1** with **17** gives the ring-opened product **B,** which is further attacked by the excess **17** at C-2 to produce the intermediate **C.** This decomposes to produce **27** and **26.**

The reaction of the 1,2-dithiolane **1** (1.0 equiv) with an excess of 2-lithio-1-methylbenzimidazole **19** (2.5 equiv) gave 1,1′-dimethyl-2,2′-bisbenzimidazolyl **28** and the 1,3-propane dithiol **26** in a molar ratio of 1:1 via a pathway similar to that operation for benzothiazole (Table 1, entry 8). The equimolar reaction of **1** with **19** at the Dry Ice–acetone bath temperature for 0.5 hour gave the corresponding ring-opened product **24** (77%), but the by-product **28** (20%) could not be excluded (entry 9). These products were separated by column chromatography after methylation of the crude product mixture.

Finally, the reaction with lithiated benzoxazole was examined. The lithiation of benzoxazole **20** occurs at the C-2 position, and the corresponding reagent **21** is considered to isomerize preferentially to the *o*-isocyanophenolate **29** on the basis of the equilibrium acidity of **20** ($pKa < 15.7$) [4]. The reaction of **21** with the 1,2-dithiolane **1** at room temperature was sluggish but gave the corresponding ring-opened product **25** in moderate yield (63%) after 12 hours of reaction. This suggests that the reaction occurs between the dithiolane **1** and 2-lithiobenzoxazole **21** present in equilibrium with the isocyanophenolate **29.** But the possibility of a direct reaction of **1** with **29** has not been excluded (Scheme 6).

The results described above show that a range of lithiated nitrogen heterocycles can cleave the S–S bond of the polymerization-resistant 1,2-dithiolane in line with the carbanion mechanism proposed for enzymic reductive acylation. The benzene-fused 1,3-azoles give ring-opened products that are susceptible to attack by the excess lithium reagent, and this makes the reaction pathway somewhat complicated. The reaction of simple lithioheterocycles is straightforward to give the ring opening in a quantitative manner. The latter reaction is suitable to the achievement of a chemoselective synthesis of 1,3-propanedithiol derivatives containing one nitrogen hetero-

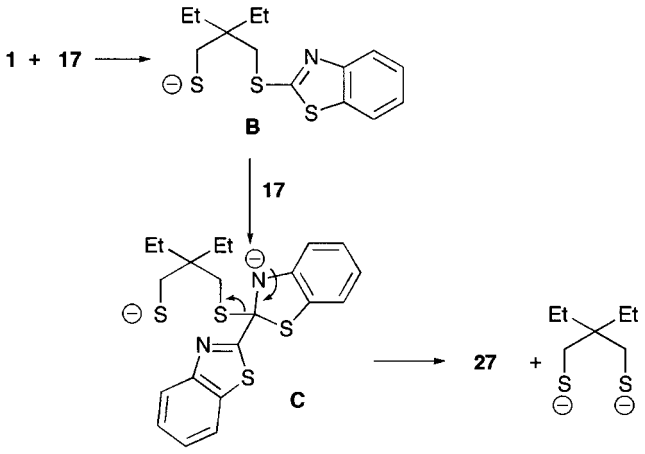


	M	X	Y
14	H	NMe	CH
15	Li	NMe	CH
16	H	S	N
17	Li	S	N
18	H	NMe	N
19	Li	NMe	N
20	H	O	N
21	Li	O	N

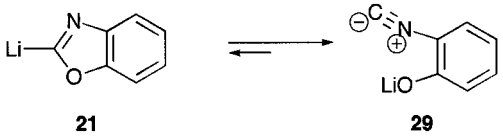
	X	Y	R
22	NMe	CH	H
23	S	N	H
24	NMe	N	Me
25	O	N	H

	X
27	S
28	NMe

SCHEME 4



SCHEME 5



SCHEME 6

cycle on the sulfur as well as to a kinetic study to elucidate the reactivity of 1,2-dithiolane toward carbanions centered on sp^2 carbon atoms of varying basicity.

EXPERIMENTAL

General. The general method was described in the preceding article. Melting points were measured on a Yanaco micromelting-point apparatus and are not corrected.

Reaction of 4,4-Diethyl-1,2-dithiolane **1** *with 2-Lithio-1-methylpyrrole* **3.** A hexane solution of BuLi (2.0 mmol) was added to a THF solution (5 mL) of N-methylpyrrole **2** (261 mg, 3.22 mmol) with stirring under argon at room temperature. After the mixture had been stirred for 0.5 hour, 4,4-diethyl-1,2-dithiolane **1** (267 mg, 1.64 mmol) was added to the mixture by means of a gas-tight syringe, and the new mixture was stirred at room temperature for 40 minutes. The mixture was acidified with acetic acid (3 mL), diluted with water (15 mL), and extracted with dichloromethane (15 mL). The organic layer was concentrated under reduced pressure and distilled by the kugelrohr method to give **8.**

8: Yield 376 mg (94%), pale yellow oil, OT (oven temperature) 163–194°C/20 mmHg, purity 97% (gc). ^{1}H NMR ($CDCl_3$) δ 0.768 (6H, t, J = 7.4 Hz, $2CH_3$), 1.066 (1H, t, J = 8.8 Hz, SH), 1.398 (4H, q, J = 7.4 Hz, $2CH_2$), 2.542 (2H, d, J = 8.8 Hz, $C\underline{H}_2SH$), 2.666 (2H, s, CH_2S), 3.684 (3H, s, NCH_3), 6.086 (1H, dd, J = 3.6, 2.8 Hz, 4-H in pyrrole), 6.334 (1H, dd, J = 3.6, 1.8 Hz, 3-H in pyrrole), and 6.724 ppm (1H, dd, J = 2.8, 1.8 Hz, 5-H in pyrrole). ^{13}C NMR ($CDCl_3$) δ 7.54 ($2CH_3$), 26.14 ($2CH_2$), 30.32 (CH_2), 34.00 (CH_3), 40.82 (C), 43.60 (CH_2), 108.06 (CH), 116.84 (CH), 121.94 (C), and 124.54 ppm (CH). IR (KBr) ν 2968 (s, C-H), 2932 (m), 2880 (w), 2562 (vw, S-H), 1462 (m), 1294 (m), and 717 cm^{-1} (s). MS m/z (%) 243 (18, M^+), 113 (100), 112 (33), 81 (27), 80 (23). Found: C, 59.04; H, 8.41; N, 5.45%. Calcd for $C_{12}H_{21}NS_2$: C, 59.21; H, 8.69; N, 5.75%.

Reaction of **1** *with 5-Lithio-1-methylpyrazole* **5.** 1-Methylpyrazole **4** (162 mg, 1.97 mmol) was lithiated with BuLi (1.60 mmol) in THF (5 mL) and reacted with **1** (206 mg, 1.27 mmol) at room temperature for 30 minutes to give the product **9** after kugelrohr distillation.

9: Yield 289.9 mg (93%), pale yellow oil, OT 113–151°C/0.8 mmHg, purity 98.9% (gc). ^{1}H NMR ($CDCl_3$) δ 0.786 (6H, t, J = 7.4 Hz, $2CH_3$), 1.114 (1H, t, J = 8.6 Hz, SH), 1.406 (4H, q, J = 7.4 Hz, $2CH_2$), 2.542 (2H, d, J = 8.8 Hz, $C\underline{H}_2SH$), 2.826 (2H, s, SCH_2), 3.916 (3H, s, NCH_3), 6.324 (1H, d, J = 2.0 Hz, CH), and 7.456 ppm (1H, d, J = 2.0 Hz, CH). ^{13}C NMR ($CDCl_3$) δ 7.54 ($2CH_3$), 26.24 ($2CH_2$), 30.26 (CH_2), 36.54 (CH_3), 40.76 (C), 42.44 (CH_2), 110.68 (CH), 134.72 (C), and 138.74 ppm (CH). IR (KBr) ν 2968 (s, C-H), 2934 (m), 2880 (w), 2566 (vw, S-H), 1454 (m), 1410 (m), 1381 (m), and 781 cm^{-1} (m). MS m/z (%) 244 (65, M^+), 131 (33), 128 (33), 115 (100), 114 (78), 113 (85), 110 (23), 97 (72), 83 (47), 81 (16), 75 (37), 69 (43), 67 (31), 61 (30). Found: C, 53.90; H, 8.14; N, 11.50%. Calcd for $C_{11}H_{20}N_2S_2$: C, 54.05; H, 8.25; N, 11.46%.

Reaction of **1** *with 2-Lithio-1-methylimidazole* **7.** N-Methylimidazole **6** (215 mg, 2.62 mmol) was lithiated with BuLi (2.0 mmol) in THF (8 mL) and reacted with **1** (164 mg, 1.01 mmol) at room temperature for 0.5 hour. After extraction with dichloromethane, the organic layer gave a residue (324 mg) containing **10** (97% by glc.) This was distilled by kugelrohr, OT 116–128°C/0.7 mmHg, to give a mixture of the ring-opened product **10** and starting dithiolane **1** in a ratio of 85:15. Pale yellow liquid. Yield 234 mg (mixture of **10** and **1,** estimated yield of **10** 81%).

10: ^{1}H NMR (CDCl3) δ 0.796 (6H, t, J = 7.4 Hz, $2CH_3$), 1.360 (1H, t, J = 8.8 Hz, SH), 1.428 (4H, q, J = 7.4 Hz, $2CH_2$), 2.542 (2H, d, J = 8.8 Hz, $C\underline{H}_2SH$), 3.152 (2H, s, SCH_2), 3.626 (3H, s, NCH_3), 6.906 (1H, d, J = 1.4 Hz, CH), and 7.036 ppm (1H, d, J = 1.4 Hz, CH). ^{13}C NMR ($CDCl_3$) δ 7.60 ($2CH_3$), 26.32 ($2CH_2$), 30.42 (CH_2), 33.22 (CH_3), 39.98 (CH_2), 40.70 (C), 122.08 (CH), 129.18 (CH), and 142.08 ppm (C).

Reaction of **1** *with 2-Lithio-4-methylthiazole* **12.** A solution of **12** from **11** (174.7 mg, 1.76 mmol) and BuLi (1.50 mmol) in THF (5 mL) was cooled in a Dry Ice–acetone bath, mixed with the dithiolane **1** 161.9 mg (1.00 mmol), and stirred for 0.5 hour with cooling. The mixture was acidified with acetic acid (2 mL) at the lower temperature, diluted with water at room temperature, and extracted with dichloromethane (15 mL). The organic layer was evaporated and distilled by kugelrohr to give **13.**

13: Yield 262 mg (99%), colorless oil, OT 61–146°C/0.2 mmHg, purity 99% (gc). ^{1}H NMR (CDCl3) δ 0.805 (6H, t, J = 7.2 Hz, $2CH_3$), 1.398 (1H, t, J = 8.8 Hz, SH), 1.404 (4H, q, J = 7.2 Hz, $2CH_2$), 2.390 (3H, d, J = 1.0 Hz, CH_3), 2.534 (2H, d, J = 8.8 Hz, $C\underline{H}_2SH$), 3.274 (2H, s, SCH_2), and 6.728 ppm (1H, q, J = 1.0 Hz, 5-H in thiazole). ^{13}C NMR ($CDCl_3$) δ7.66 ($2CH_3$), 17.14 (CH_3), 26.46 ($2CH_2$), 30.46 (CH_2), 40.36 (CH_2), 40.88 (C), 113.26 (CH), 152.88 (C), and 164.08 ppm (C). IR (KBr) ν 2968 (s, C-H), 2926 (m), 2524

(vw, S-H), 1454 (m), and 1031 cm^{-1} (s). Found: C, 50.72; H, 6.99; N, 5.19%. Calcd for $C_{11}H_{19}NS_3$: C, 50.53; H, 7.32; N, 5.36%.

Reaction of **1** *with 2-Lithio-1-methylindole* **15.** 1-Methylindole **14** (134 mg, 1.02 mmol) was lithiated with BuLi (1.00 mmol) and reacted with dithiolane **1** (162 mg, 1.00 mmol) at room temperature for 30 minutes. The mixture was acidified with acetic acid (1.5 mL) and water (15 mL), and extracted with dichloromethane (10 mL). The organic layer was concentrated and distilled by kugelrohr. When the unreacted **1** was distilled (3.7 mg, OT 68–133°C/20 mmHg), the product **22** was obtained by further distillation as a pale yellow oil.

22: Yield 246.3 mg (84%), OT 154–179°C/0.4 mmHg, purity 95% (gc). ^{1}H NMR ($CDCl_3$) δ 0.756 (6H, t, J = 7.4 Hz, $2CH_3$), 1.080 (1H, t, J = 8.8 Hz, SH), 1.396 (4H, q, J = 7.4 Hz, $2CH_2$), 2.532 (2H, d, J = 8.8 Hz, $C\underline{H}_2SH$), 2.812 (2H, s, CH_2S), 3.740 (3H, s, NCH_3), 6.664 (1H, s, CH), 7.046–7.228 (3H, m, CH), and 7.458–7.568 ppm (1H, m, CH). ^{13}C NMR ($CDCl_3$) δ 7.54 ($2CH_3$), 26.28 ($2CH_2$), 29.86 (CH_3), 30.34 (CH_2), 40.76 (C), 42.84 (CH_2), 107.38 (CH), 109.34 (CH), 119.68 (CH), 120.02 (CH), 121.96 (CH), 127.50 (C), 132.28 (C), and 138.12 ppm (C). IR (KBr) ν 2966 (s, C-H), 2930 (m), 2568 (vw, S-H), 1460 (s), 1325 (m), 783 (m), and 748 cm^{-1} (m). MS *m/z* (%) 293 (26, M^+), 292 (10), 291 (46), 194 (16), 193 (12), 192 (14), 164 (19), 163 (100), 162 (27), 131 (15), 130 (143), 129 (13), 118 (12), 69 (12). Found: C, 65.83; H, 7.77; N, 4.88%. Calcd for $C_{16}H_{23}NS_2$: C, 65.48; H, 7.90; N, 4.77%.

Reaction of **1** *with 2-Lithiobenzothiazole* **17** *at Low Temperature.* Benzothiazole **16** 140.0 mg (1.04 mmol) was lithiated with LDA (*i*-Pr_2NH, 1.37 mmol plus BuLi, 1.07 mmol) in THF (5 mL) at 0°C, and reacted with **1** 164.4 mg (1.01 mmol) in a Dry Ice–acetone bath for 0.5 hour to give **23** after kugelrohr distillation.

23: 291.3 mg (97%), yellow oil, OT 148–183°C/0.4 mmHg, purity 98% (gc). ^{1}H NMR ($CDCl^3$) δ 0.780 (6H, t, J = 7.2 Hz, $2CH_3$), 1.410 (4H, q, J = 7.0 Hz, $2CH_2$), 1.444 (1H, t, SH), 2.488 (2H, d, $C\underline{H}_2SH$), 3.458 (2H, s, CH_2S), 7.11–7.42 (2H, m, CH), and 7.60–7.89 ppm (2H, m, CH). ^{13}C NMR ($CDCl_3$) δ 7.64 ($2CH_3$), 26.52 ($2CH_2$), 30.46 (CH_2), 38.82 (CH_2), 40.60 (C), 120.78 (CH), 121.28 (CH), 124.06 (CH), 125.86 (CH), 135.10 (C), 152.96 (C), and 166.90 ppm (C).

Reaction of **1** *with Excess 2-Lithiobenzothiazole* **17.** Benzothiazole **16** 331.6 mg (2.5 mmol) was lithiated with LDA (2.5 mmol) in THF (5 mL) and reacted with **1** 161.7 mg (1.00 mmol) at room temperature for 0.5 hour. The mixture was acidified with acetic acid (2 mL) and extracted with dichloromethane (15 mL). The precipitates produced during the extraction were filtered off to give **27,** 224.9 mg (84%).

27: Yield 224.9 mg (84%), yellow powder, mp 301–304°C (lit. 301°C [7]). IR (KBr) ν 1466 (m), 1456 (m), 1429 (m), 1313 (m), 919 (m), and 764 cm^{-1} (s). Found: C, 62.36; H, 3.33; 10.19%. Calcd for $C_{14}H_8N_2S_2$: C, 62.66; H, 3.00; N, 10.44%.

The organic layer of the filtrate was concentrated and distilled to give the impure 1,3-propanedithiol **26** 182.3 mg (purity 83% by gc, estimated yield 92%), pale yellow liquid, OT 79–132°C/20 mm Hg.

Reaction of **1** *with Excess 2-Lithio-1-methylbenzimidazole* **19.** N-methylbenzimidazole **18** 369.3 mg (2.79 mmol) was lithiated with an LDA (2.5 mmol) solution in THF (5 mL) and reacted with **1** 158.1 mg (0.97 mmol) at room temperature for 0.5 hour. The mixture was acidified with acetic acid (2 mL), diluted with water (20 mL), and extracted with dichloromethane (15 mL). The organic layer was evaporated to give a residue, the ^{13}C NMR spectrum of which showed the presence of a 1:1 mixture of **28** and 2,2-diethyl-1,3-propanedithiol **26.** The residue was recrystallized from hexane to give **28** 272.4 mg (107%), white powder, mp 211–212°C (from hexane, lit. 213–214°C [8]).

28: ^{1}H NMR ($CDCl_3$) δ 4.317 (6H, s, $2NCH_3$), 7.296–7.465 (6H, m, CH), and 7.819–7.932 ppm (2H, m, CH). ^{13}C NMR ($CDCl_3$) δ 32.30 (CH_3), 110.20 (CH), 120.24 (CH), 123.10 (CH), 124.14 (CH), 136.10 (C), 142.28 (C), and 142.82 ppm (C). MS *m/z* (%) 262 (72, M^+), 261 (100), 247 (9), 131 (28), 77 (18). Found: C, 73.14; H, 5.54; N, 21.57%. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36%.

Reaction of **1** *with 2-Lithio-1-methylbenzimidazole* **19** *at a Low Temperature.* *N*-methylbenzimidazole **18** 143.7 mg (1.09 mmol) was lithiated with LDA (1.07 mmol) in THF (5 mL) and reacted with **1** 165.7 mg (1.02 mmol) in a Dry-Ice–acetone bath for 0.5 hour. The mixture was treated with methanol (1 mL) and methyl iodide 750.6 mg (5.3 mmol) at the lower temperature, and then stirred at room temperature for 12 hours. The mixture gave **24** 241.0 mg and **28** 54.1 mg (20%) after a chromatographic separation using silica gel and as eluent, hexane-ether (4:1).

24: Yield 241.0 mg (77%), colorless oil, purity 99% (gc). ^{1}H NMR ($CDCl_3$) δ 0.858 (6H, t, J = 7.4 Hz, $2CH_3$), 1.505 (4H, q, J = 7.4 Hz, $2CH_2$), 2.905

(3H, s, SMe), 2.600 (2H, s, CH_2S), 3.516 (2H, s, CH_2S), 3.640 (3H, s, NMe), 7.15–7.20 (3H, m, CH), and 7.60–7.72 ppm (3H, m, CH). ^{13}C NMR ($CDCl_3$) δ 7.74 ($2CH_3$), 17.42 (SCH_3), 27.72 ($2CH_2$), 29.90 (NCH_3), 38.98 (CH_2), 40.95 (C), 41.86 (CH_2), 108.28 (CH), 118.14 (CH), 121.62 (CH), 121.68 (CH), 136.74 (C), 143.36 (C), and 152.46 ppm (C). IR (KBr) ν 2974 (m), 2924 (m), 1464 (m), 1446 (m), 1423 (s), 1361 (m), 1280 (m), and 741 cm^{-1} (s). Found: C, 62.09; H, 7.87; N, 9.09%. Calcd for $C_{16}H_{24}N_2S_2$: C, 62.29; H, 7.84; N, 9.08%.

Reaction of **1** *with 2-Lithiobenzoxazole* **21.** 2-Lithiobenzoxazole **21,** prepared from benzoxazole **20** 268.0 mg (2.25 mmol) and LDA (1.30 mmol) in THF (5 mL), was reacted with **1** 122.2 mg (0.75 mmol) at room temperature for 12 hours. The mixture was acidified with acetic acid and extracted with dichloromethane. The organic layer contained the starting benzoxazole **20** (46%) and the ring-opened product **25** (52%) as shown by gc. The layer was concentrated and distilled by kugelrohr; after benzoxazole **20** (18.6 mg, OT 87–103°C/20 mmHg) had been distilled, **25** was obtained by further distilled as a pale yellow oil, OT 121–168°C/0.4 mmHg.

25: Yield 134.0 mg (63%), purity 88% (gc). ^1H NMR ($CDCl_3$) δ 0.832 (6H, t, J = 7.2 Hz, $2CH_3$), 1.380 (4H, q, J = 7.4 Hz, $2CH_2$), 1.419–1.598 (1H, m, SH), 2.542 (2H, d, J = 8.8 Hz, $C\underline{H}_2SH$), 3.450 (2H, s, CH_2S), and 7.175–7.647 ppm (4H, m, CH). ^{13}C NMR ($CDCl_3$) δ 7.65 ($2CH_3$), 26.60 ($2CH_2$), 30.42 (CH_2), 37.94 (CH_2), 40.46 (C), 109.81 (CH), 118.34 (CH), 123.89 (CH), 124.29 (CH), 141.78 (C), 151.83 (C), and 165.21 ppm (C).

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