

References

- van Loon, J. D.; Arduini, A.; Verboom, W.; Ungaro, R.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *Tetrahedron Lett.* **1989**, 30, 2681.
- van Loon, J. D.; Arduini, A.; Coppi, L.; Verboom, W.; Pochini, A.; Ungaro, R.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1990**, 55, 5639.
- Groenen, L. C.; Ruel, B. H. M.; Casnati, A.; Timmerman, P.; Verboom, W.; Harkema, S.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. *Tetrahedron Lett.* **1991**, 32, 2675.
- Iwamoto, K.; Araki, K.; Fujishima, H.; Shinkai, S. *J. Chem. Soc. Perkin Trans. 1*, **1992**, 1885.
- Iwamoto, K.; Shimizu, H.; Araki, K.; Shinkai, S. *J. Am. Chem. Soc.* **1993**, 115, 3997.
- Gutsche, C. D.; Lin, L. G. *Tetrahedron* **1986**, 42, 1640.
- Casnati, A.; Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R. *Tetrahedron* **1991**, 47, 2221.
- Groenen, L. C.; Ruel, B. H. M.; Casnati, A.; Verboom, W.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. *Tetrahedron* **1991**, 47, 8379.
- See, K. A.; Fronczek, F. R.; Watson, W. H.; Kashyap, R. P.; Gutsche, C. D. *J. Org. Chem.* **1991**, 56, 7256.

Convenient Synthesis of Symmetrical Sulfides from Alkyl Halides and Epoxides

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Sometime ago symmetrical sulfides were reported to be prepared in excellent yields from alkyl halides and sodium sulfide in water in the presence of a phase-transfer catalyst (PTC)¹ or polymer supported phase-transfer catalyst.² Primary alkyl chlorides and secondary alkyl bromides reacted a little slower than primary bromides, but not with much difference. Bis(tributyltin) sulfide was also reported to give excellent yields of symmetrical sulfides, but require longer reaction time (12 h) at elevated temperature (110 °C).³ Recently we have observed the synthesis of phenyl sulfides is facilitated by the presence of an anion exchange resin,⁴ and also showed good chemoselectivity: primary bromides reacted selectively in the presence of primary chlorides and secondary bromides. We anticipated the presence of a catalytic amount of a commercial anion exchange resin⁵ in the synthesis of symmetrical sulfides from alkyl halides and sodium sulfide might also show a good chemoselectivity, rate acceleration and simplification of work-up procedure as we observed in the synthesis of phenyl sulfides.⁴ We tested the possibility, and have found a convenient synthetic procedure for symmetrical sulfides.

As shown in Table 1, octyl bromide, iodide and tosylate

Table 1. Synthesis of Symmetrical Sulfides from Alkyl Halides and Epoxides using Sodium Sulfide in the Presence of Amberlite IRA-400 in Methanol^a

Entry	Substrate	Time (h)	Product	Yield ^b
1	octyl chloride	12	dioctyl sulfide	95 ^c
2	octyl bromide	1	dioctyl sulfide	95
3	octyl iodide	1	dioctyl sulfide	96
4	octyl tosylate	1	dioctyl sulfide	94
5	neopentyl bromide	6	dineopentyl sulfide	0
6	benzyl chloride	1	dibenzyl sulfide	96
7	benzyl bromide	1	dibenzyl sulfide	95
8	cinnamyl chloride	1	dicinnamyl sulfide	90
9	2-hexyl bromide	6	di-2-hexyl sulfide	(65) ^d
10	2-octyl tosylate	6	di-2-octyl sulfide	(72)
11	cyclohexyl bromide	6	dicyclohexyl sulfide	0
12	1-bromo-4-chloro-butane	1	tetrahydrothiophene	(97)
13	1,2-dibromooctane	1	1,2-octene episulfide	95 ^e
14	1,2-decene oxide	1	di-β-hydroxydecyl sulfide	92
15	cyclohexene oxide	1	di-β-hydroxycyclohexyl sulfide	96

^aReactions were carried out with 0.55 eq of Na₂S in the presence of 0.1 eq of Amberlite IRA-400 under reflux in methanol. ^bIsolated yields. GC yields were in parenthesis. ^cWith 1 eq of Amberlite. ^dWith 0.7 eq of Na₂S. ^eWith 1.1 eq of Na₂S and 0.2 eq of Amberlite.

reacted rapidly with stoichiometric amount of sodium sulfide (0.55 eq) in methanol giving the corresponding symmetrical sulfides quantitatively in 1 h at 65 °C in the presence of 0.1 eq of Amberlite (entries 2, 3 and 4). However octyl bromide required 9 h in the absence of the resin showing the catalytic activity of anion exchange resin. Octyl chloride reacted even more slowly showing only 20% progress of the reaction in 1 h and 60% in 24 h, however quantitative yield of dioctyl sulfide could be obtained in 12 h using 1 eq of Amberlite (entry 1). Benzyl and cinnamyl halides also gave the corresponding sulfides quantitatively even at room temperature (entries 6, 7 and 8). On the other hand, the reaction with 2-hexyl bromide and 2-octyl tosylate proceeded slowly accompanying elimination and gave only moderate yields of di-2-hexyl sulfide (65%) and di-2-octyl sulfide (72%) (entries 9 and 10). However neopentyl bromide and cyclohexyl bromide, more hindered halides, did not react at all in 6 h (entries 5 and 11). 1-Bromo-4-chlorobutane reacted readily but gave tetrahydrothiophene instead of expected di-4-chlorobutyl sulfide (entry 12). Presumably 4-chlorobutyl sulfide anion, the initially formed intermediate, reacted intramolecularly rather than intermolecularly. Similarly 1,2-dibromooctane gave 1,2-octene episulfide quantitatively instead of di-2-bromooctyl sulfide (entry 13). Since vicinal dibromo compounds are readily prepared from the corresponding alkenes, this could be a convenient alternative synthetic method of thiiranes, valuable intermediates in organic synthesis.⁶ Finally both 1,2-decene oxide and cyclohexene oxide gave the corresponding di-β-hydroxy sulfides in excellent yields (ent-

Table 2. Competitive Reaction of Halides with Sodium Sulfide in the Presence of Amberlite IRA-400 in Methanol and Triphase System^a

Entry	Substrate	Temp. (°C)	Time (h)	Product	Yields ^b
1	octyl chloride	65	1.0	octyl chloride	97 (77)
	octyl bromide			3 (23)	
	diocetyl sulfide			100 (100)	
2	octyl bromide	65	1.0	octyl bromide	5 (25)
	2-hexyl bromide			95 (73)	
	diocetyl sulfide			90 (63)	
	2-hexyl octyl sulfide			5 (12)	
3	octyl bromide	25	1.0	octyl bromide	95 (89)
	benzyl bromide			5 (11)	
	diocetyl sulfide			3 (2)	
	benzyl octyl sulfide			2 (9)	
	dibenzyl sulfide			93 (80)	

^aMixtures of one mmol each of two halides were reacted with 0.5 eq of Na₂S in the presence of 0.1 eq of Amberlite IRA-400 in methanol. In triphase system, alkyl halides (organic phase) were reacted with aqueous solution of Na₂S (0.5 eq) in the presence of 0.1 eq of Amberlite. ^bGC yields, number in parenthesis are for triphase system.

ries 14 and 15). And as shown in general procedure, work up procedure is very simple giving essentially pure product by filtering the resin and evaporating the solvent methanol.

In order to confirm the unique chemoselectivity of this system, competitive experiments were performed between halides and compared with those of triphase system.^{25a} The results are summarized in Table 2. As shown in Table 2, this system shows much better selectivity than the triphase system. Since the less chemoselectivity was also observed in the PTC condition which utilizes aqueous solution of sodium sulfide, the good chemoselectivity exhibited in the present system might be due to the absence of water.

In conclusion this method which involves two phase system is an excellent synthetic method for symmetrical sulfides since it utilizes commercially available resin, exhibits good chemoselectivity, and has advantage of simple work up.

Experimental Section

General Procedure for Preparation of Symmetrical Sulfides. The reaction of octyl bromide is representative. To the dried anion exchange resin (Amberlite IRA-400, 0.26 g, 1 mmol Cl⁻), the methanol solution (50 mL) of Na₂S (0.429 g, 5.5 mmol) and octyl bromide (1.93 g, 10 mmol) was added, and the mixture was stirred under reflux for 1 h. Complete

reaction was confirmed by GLPC. Then the resin was removed by filtration and the filtrate was evaporated under reduced pressure to give the pure dioctyl sulfide (1.23 g, 95%); ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J*=6.4), 1.27-1.40 (m, 16H), 1.51-1.62 (m, 4H), 2.50 (t, 4H, *J*=7.0); IR (neat) 2957 2926 2854 1464 cm⁻¹; MS *m/z* (relative intensity) (EI, 70 eV) 258 (M⁺, 7) 145 (21) 84 (29) 83 (39) 70 (55) 69 (49) 61 (14) 57 (31) 56 (86) 55 (73) 47 (35) 43 (80) 42 (58) 41 (100).

Dibenzyl sulfide. ¹H NMR (CDCl₃) δ 3.62 (s, 4H), δ 7.25-7.34 (m, 10H); IR (neat) 3058 2028 2916 1492 1452 cm⁻¹; MS *m/z* (relative intensity) (EI, 70 eV) 214 (M⁺, 6) 123 (17) 92 (16) 91 (100) 65 (17) 45 (27).

Dicinnamyl sulfide. ¹H NMR (CDCl₃) δ 3.32 (d, 4H, *J*=7.3), δ 6.20 (dt, 2H, *J*=15.8 7.3), δ 6.47 (d, 2H, *J*=15.8), δ 7.21-7.42 (m, 10H); IR (neat) 3059 3026 2908 1676 1492 1446 cm⁻¹; MS *m/z* (relative intensity) (EI, 70 eV) 266 (M⁺, 5) 219 (9) 149 (58) 147 (12) 117 (100) 91 (31)

1,2-Octene episulfide. ¹H NMR (CDCl₃) 0.87 (t, 3H, *J*=6.5), δ 1.27-1.40 (m, 8H), δ 1.51 (dt, 2H, *J*=6.5 7.0), δ 2.13 (d, 1H, *J*=7.2), δ 2.51 (d, 1H, *J*=7.2), δ 2.93 (tt, 1H, *J*=7.0 7.2); IR (neat) 2957 2926 2854 1460 cm⁻¹; MS *m/z* (relative intensity) (EI, 70 eV) 144 (M⁺, 11) 115 (10) 101 (11) 87 (20) 81 (27) 74 (16) 55 (83) 41 (100).

Di-β-hydroxydecyl sulfide. ¹H NMR (CDCl₃) δ 0.88 (t, 6H, *J*=5.6), δ 1.27-1.63 (m, 28H), δ 2.50-2.82 (m, 6H), δ 3.39-3.70 (m, 2H); IR (neat) 3367 2928 2854 1465 cm⁻¹; MS *m/z* (relative intensity) (EI, 70 eV) 346 (M⁺, 1) 215 (1) 138 (14) 83 (25) 69 (35) 62 (100) 55 (27).

Di-β-hydroxycyclohexyl sulfide. ¹H NMR (CDCl₃) δ 1.16-1.53 (m, 8H), δ 1.71-1.77 (m, 4H), δ 2.05-2.12 (m, 4H), 2.37-2.64 (m, 2H), δ 2.76 (br s, 2H), δ 3.24-3.39 (m, 2H); IR (neat) 3373 2933 2856 1448 1068 cm⁻¹; MS *m/z* (relative intensity) (EI, 70 eV) 230 (M⁺, 7) 212 (6) 131 (5) 115 (17) 114 (16) 103 (22) 98 (100) 81 (99) 79 (51) 70 (28) 57 (20).

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References

- Landini, D.; Rolla, F. *Synthesis* 1974, 565.
- Chiles, M. S.; Jackson, D. D.; Reeves, P. C. *J. Org. Chem.* 1980, 45, 2915.
- Harpp, D. N.; Gingras, M.; Aida, T.; Chan, T. H. *Synthesis* 1987, 1122.
- Yoon, N. M.; Choi, J.; Ahn, J. H. *J. Org. Chem.* 1994, 59, 3490.
- (a) Regen, S. L. *J. Org. Chem.* 1977, 42, 875. (b) Arrad, O.; Sasson, Y. *J. Org. Chem.* 1989, 54, 4993.
- Thiiranes may be prepared from alkenes but usually from the corresponding epoxides: (a) Capozzi, F.; Capozzi, G.; Menicetti, S. *Tetrahedron Lett.* 1989, 33, 4177. (b) Bouda, H.; Borredon, M. E.; Gaset, A. *Synth. Commun.* 1989, 491 and references therein.