



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

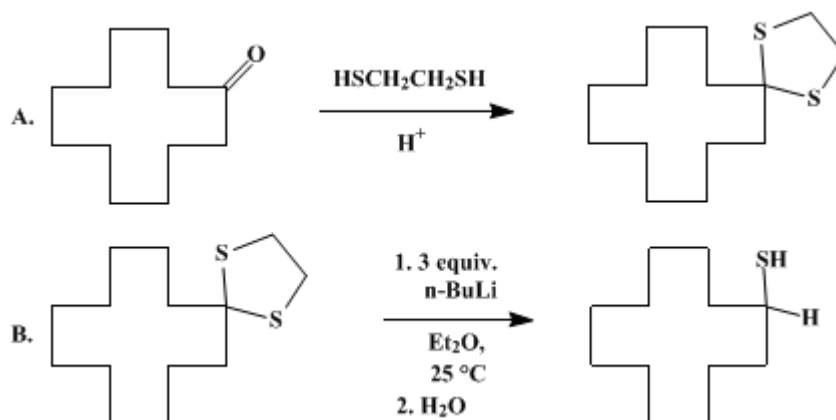
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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MERCAPTANS FROM THIOKETALS: CYCLODODECYL MERCAPTAN



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1. Procedure

Caution! This procedure should be carried out in an efficient hood to prevent exposure to alkane thiols.

A. *1,4-Dithiaspiro[4.11]hexadecane*. A mixture of 46.5 g (0.26 mol) of cyclododecanone (Note 1), 24.1 g (21.5 mL, 0.26 mol) of 1,2-ethanedithiol (Note 1), and 0.75 g (0.004 mol) of *p*-toluenesulfonic acid monohydrate (Note 2), in 200 mL of toluene (Note 3) is placed in a 500-mL, three-necked reaction flask equipped for reflux under a water separator.² The mixture is heated at reflux for several hours until the theoretical amount of water (0.26 mol = 4.6 mL) has collected in the Dean-Stark trap. The reaction mixture is cooled and transferred to a separatory funnel. The mixture is washed with water, the toluene is removed on a rotary evaporator, and the residue is placed under reduced pressure (< 0.1 mm) for several hours to remove traces of solvent. Approximately 66 g (99%) of a white solid is recovered (0.26 mol, mp 84–86°C). The crude material is pure by GLC and TLC, and is used in the next step with no further purification.

B. *Cyclododecyl mercaptan*. In a 1-L, three-necked, round-bottomed flask equipped with a mechanical stirrer and nitrogen inlet and outlet stopcocks are placed 25.8 g (0.10 mol) of 1,4-dithiaspiro[4.11]hexadecane and 300 mL of ether, freshly distilled from sodium. The mixture is purged with nitrogen, cooled to 0°C with an ice bath, and 125 mL (0.30 mol, 2.4 M in hexane) of butyllithium is added by syringe (Note 4), (Note 5) under a slow flow of nitrogen. The light-yellow mixture is then allowed to warm to room temperature and stirred overnight with nitrogen stopcocks closed (Note 6). The reaction mixture is cooled to 0°C and 50 mL of water is added slowly and very carefully (Note 7). The resulting light brown solution is poured into 200 mL of water in a separatory funnel and, after shaking, the organic layer is separated. The solution is dried over MgSO₄, concentrated (aspirator), and distilled through a 10-cm Vigreux column at 103–108°C (1 mm) to give 17.2–17.9 g (86–90%) of pure cyclododecyl mercaptan (Note 8), (Note 9). A small forerun, bp < 95°C, (ca. 2 mL) is discarded.

2. Notes

1. The submitters used cyclododecanone and 1,2-ethanedithiol obtained from Aldrich Chemical Company, Inc.
2. The submitters used *p*-toluenesulfonic acid monohydrate from MCB, Inc.
3. The submitters used benzene in place of toluene.
4. The submitters used butyllithium from Alfa Products, Ventron Corporation.

5. The reaction also occurs well with only 2 mol of **butyllithium**, but traces of starting material remain.
6. The reaction is complete in about 6 hr.
7. **Caution! Quenching of excess butyllithium is exothermic.**
8. By GLC analysis, the distilled **cyclododecyl mercaptan** is >95% pure. Sometimes the product is pale pink.
9. The distilled **cyclododecyl mercaptan** has the following spectral data: ¹H NMR (CCl₄) δ: 1.1 (d, 1 H, *J* = 6, S-H), 1.32 (broad s, 20 H), 1.64–1.82 (m, 2 H), 2.81 (m, 1 H, CHSH); IR (neat, μ) 3.4, 6.82, 6.94. Anal. calcd. for C₁₂H₂₄S: C, 71.93; H, 12.07; S, 16.00. Found: C, 71.83; H, 12.19; S, 16.03.

3. Discussion

Mercaptans are generally prepared by displacement reactions.³ However, secondary or hindered mercaptans are more difficult to obtain. The dithiolane cleavage reaction⁴ is a convenient "in situ" generation of thioketones which are known to be reduced⁵ with **butyllithium** to secondary mercaptans by β-hydrogen transfer. Table I shows a number of mercaptans prepared from *saturated* thioketals in 78–90% yields. The aryl example gives lower yields partly because of ring metalation.

TABLE I
MERCAPTANS FROM ETHYLENE THIOKETAL CLEAVAGE/REDUCTION

Ketone Thioketal	Bp/mp (°C)	Yield (%)
Cyclododecanone	103–108 (1 mm)	90
4- <i>tert</i> -Butylcyclohexanone	~ 100 (0.5 mm)	90 ^a
2-Adamantanone	mp 139–142	79
4-Heptanone	127–135 (760)	81
Acetophenone	70–75 (0.5 mm)	36 ^b
Cyclohexanone	130–140 (760)	78 ^c
Estrone	mp 170–175	90 ^d
Pregnenolone	mp 108–113	65 ^d
Undecan-5-one	110–120 (0.3 mm)	93

^a Axial: equatorial ratio, 2:1.

^b By extraction into KOH (purity = 85–93%).

^c Distillation could not cleanly separate thiol from **octane** (formed from the **butyllithium**).

^d Mixture of isomers.

References and Notes

1. Department of Chemistry, Indiana University, Bloomington, IN 47405. Present address: Department of Chemistry, New York University, New York, NY 10003.
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3. Klayman, D. L.; Shine, R. J.; Bower, J. D. *J. Org. Chem.* **1972**, 37, 1532.
4. Wilson, S. R.; Georgiadis, G. M.; Khatri, H. N.; Bartmess, J. E. *J. Am. Chem. Soc.* **1980**, 102, 3577.
5. Rautenstrauch, V. *Helv. Chim. Acta* **1974**, 57, 496; Ohno, A.; Yamabe, T.; Nagata, S. *Bull. Chem. Soc. Jpn.* **1975**, 48, 3718.

(Registry Number)

Benzene (71-43-2)

ether (60-29-7)

Cyclohexanone (108-94-1)

nitrogen (7727-37-9)

Acetophenone (98-86-2)

toluene (108-88-3)

sodium (13966-32-0)

butyllithium (109-72-8)

octane (111-65-9)

hexane (110-54-3)

1,2-ethanedithiol (540-63-6)

4-Heptanone (123-19-3)

cyclododecanone (830-13-7)

2-adamantanone (700-58-3)

4-tert-Butylcyclohexanone (98-53-3)

Cyclododecyl mercaptan (7447-11-2)

1,4-Dithiaspiro[4.11]hexadecane (16775-67-0)

Ketone Thioketal

Estrone

Pregnenolone

Undecan-5-one (33083-83-9)

p-toluenesulfonic acid monohydrate (6192-52-5)