Organic Syntheses

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.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 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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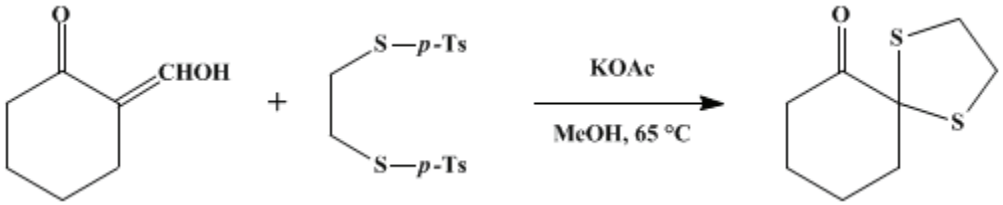
Organic Syntheses, Coll. Vol. 6, p.590 (1988); Vol. 54, p.37 (1974).

2,2-(ETHYLENEDITHIO)CYCLOHEXANONE

[1,4-Dithiaspiro[4,5]decan-6-one]



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1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A 300-ml., one-necked flask equipped with a reflux condenser, the top of which is attached to a nitrogen inlet tube, is charged with 3.85 g. (0.0338 mole) of 2-hydroxymethylenecyclohexanone (Note 1), 10 g. (0.025 mole) of ethylene dithiotosylate (Note 2), and 10 g. of potassium acetate in 150 ml. of methanol. The mixture is refluxed under nitrogen for 3 hours with stirring, the solvent is removed from the reaction mixture on a rotary evaporator, and the residue is extracted with three 50-ml. portions of diethyl ether. The combined ethereal extracts are washed with cold, aqueous 2 *N* sodium hydroxide (Note 3) until the aqueous layer is basic to litmus, then with 50 ml. of saturated aqueous sodium chloride. The ethereal layer is dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator. The oily residue is diluted with 1 ml. of benzene and 3 ml. of cyclohexane and transferred to a chromatographic column (14 × 2 cm.) prepared with 50 g. of alumina (Note 4) and a 3:1 mixture of cyclohexane and benzene. With this solvent system the desired product moves with the solvent front, and the first 100 ml. of eluent contains 85% of the total product. Further elution with approximately 100 ml. of the same solvent mixture removes the rest of the material before a second component begins to come off. Evaporation of the solvent from the combined 200 ml. of eluent leaves an oily residue which crystallizes on standing, yielding 2.76–3.04 g. (57–64%) of crude 2,2-(ethylenedithio)cyclohexanone. Recrystallization from approximately 50 ml. of pentane affords 2.1–2.6 g. (45–55%) of needles, m.p. 56–57° (Note 5).

2. Notes

1. 2-Hydroxymethylenecyclohexanone was prepared by both the submitters and checkers by a procedure similar to, but slightly modified from, that described in *Org. Synth.*, **Coll. Vol. 4**, 536 (1963). To a cooled (ice bath), stirred suspension of 10.2 g. (0.189 mole) of commercial sodium methoxide in 75 ml. of anhydrous benzene under nitrogen was added dropwise, but rapidly (*ca.* 2 minutes), a mixture of 9.8 g. (0.10 mole) of distilled cyclohexanone and 14.8 g. (0.200 mole) of distilled ethyl formate. After addition, the reaction was allowed to warm to room temperature and left overnight. Ice water (100 ml.) was added to the resulting suspension. The aqueous layer was separated, and the benzene layer was washed three times with 50 ml. of cold, aqueous 0.1 *N* sodium hydroxide. The aqueous layers were combined, and the product was isolated according to the procedure referenced above. This modified version provided slightly higher yields of the product than that recorded in *Org. Synth.*, and the ease of handling sodium methoxide, compared with sodium metal, is advantageous.
2. Ethylene dithiotosylate, m.p. 73–73.5°, as described in *Org. Synth.*, **Coll. Vol. 6**, 1016 (1988), is employed.

3. Treatment with alkali removes the various acidic by-products and their salts (acetate, sulfinate, and formate) and also serves to hydrolyze and remove unreacted starting materials.
4. The checkers used "Aluminum Oxide" purchased from J. T. Baker Chemical Company.
5. The ^{1}H NMR spectrum of the product ($CDCl_3$): δ 1.83 (m, 4H), 2.42 (m, 2H), 2.73 (m, 2H), 3.30 (s, 4H).

3. Discussion

The procedure for the preparation of a dithiolane from a hydroxymethylene derivative of a ketone and ethylene dithiotosylate (ethane-1,2-dithiol di-*p*-toluenesulfonate) can be varied to produce dithianes, when the latter reagent is replaced with trimethylene dithiotosylate.[4,5] Dithiotosylates also react with enamine derivatives, producing dithiaspiro compounds.[5,6]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 1014
- Org. Syn. Coll. Vol. 6, 1016
- Org. Syn. Coll. Vol. 9, 180

References and Notes

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4. R. B. Woodward, I. J. Pachter, and M. L. Scheinbaum, *Org. Synth.*, **Coll. Vol. 6**, 1016 (1988).
5. R. B. Woodward, I. J. Pachter, and M. L. Scheinbaum, *J. Org. Chem.*, **36**, 1137 (1971).
6. R. B. Woodward, I. J. Pachter, and M. L. Scheinbaum, *Org. Synth.*, **Coll. Vol. 6**, 1014 (1988).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

Benzene (71-43-2)

methanol (67-56-1)

diethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

Cyclohexanone (108-94-1)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

cyclohexane (110-82-7)

sodium methoxide (124-41-4)

sodium (13966-32-0)

ethyl formate (109-94-4)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

potassium acetate (127-08-2)

aluminum oxide (1344-28-1)

2-Hydroxymethylenecyclohexanone (823-45-0)

2,2-(Ethylenedithio)cyclohexanone,
1,4-Dithiaspiro[4,5]decan-6-one (27694-08-2)

ethylene dithiotosylate

trimethylene dithiotosylate (3866-79-3)

ethane-1,2-dithiol di-p-toluenesulfonate