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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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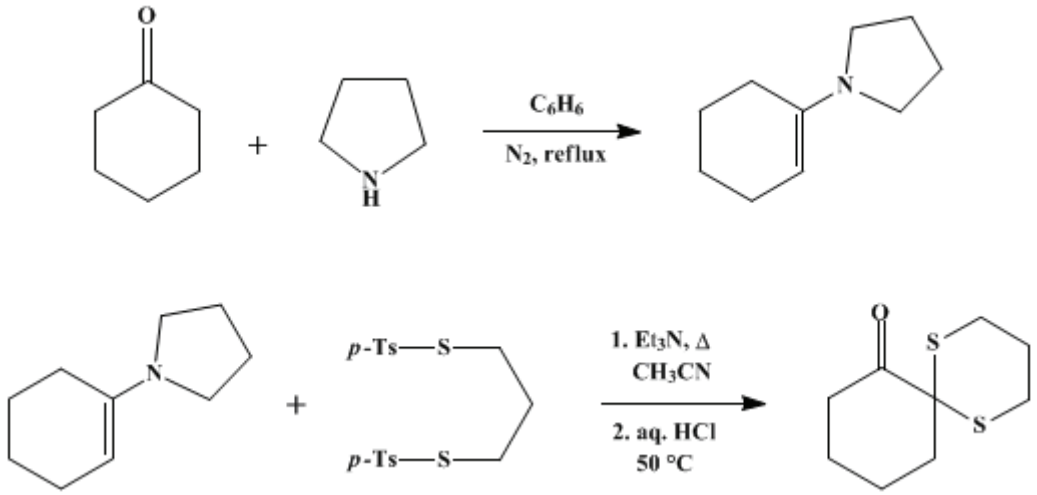
Organic Syntheses, Coll. Vol. 6, p.1014 (1988); Vol. 54, p.39 (1974).

2,2-(TRIMETHYLENEDITHIO)CYCLOHEXANONE

[1,5-Dithiaspiro[5.5]undecan-7-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. *1-Pyrrolidinocyclohexene*.[4] A solution of 29.4 g. (0.300 mole) of cyclohexanone and 28.4 g. (0.394 mole) of pyrrolidine in 150 ml. of benzene is placed in a 500-ml., one-necked flask attached to a Dean-Stark trap. The solution is refluxed under a nitrogen atmosphere until the separation of water ceases (Note 1). The excess pyrrolidine and benzene are removed from the reaction mixture on a rotary evaporator. The resulting residue is stored under refrigeration and distilled just before use in the next step, yielding 44.6 g. (98%) of 1-pyrrolidinocyclohexene, b.p. 76–77° (0.5 mm.), 105–106° (13 mm.).

B. *2,2-(Trimethylenedithio)cyclohexanone*. A solution of 3.02 g. (0.0200 mole) of freshly distilled 1-pyrrolidinocyclohexene, 8.32 g. (0.0200 mole) of trimethylene dithiotosylate[4] (Note 2), and 5 ml. of triethylamine (Note 3) in 40 ml. of anhydrous acetonitrile (Note 4), is refluxed for 12 hours in a 100-ml., round-bottom flask under a nitrogen atmosphere. The solvent is removed with a rotary evaporator, and the residue is treated with 100 ml. of 0.1 *N* hydrochloric acid for 30 minutes at 50° (Note 5). The mixture is cooled to ambient temperature and extracted with three 50-ml. portions of diethyl ether. The combined ether extracts are washed with 10% aqueous potassium hydrogen carbonate solution (Note 6), until the aqueous layer remains basic to litmus, and with saturated sodium chloride solution. The ethereal solution is dried over anhydrous sodium sulfate, filtered, and concentrated on a rotary evaporator. The resulting oily residue is diluted with 1 ml. of benzene then with 3 ml. of cyclohexane. The solution is poured into a chromatographic column (13 × 2.5 cm.), prepared with 50 g. of alumina (Note 7) and 3:1 cyclohexane–benzene. With this solvent system, the desired product moves with the solvent front; the first 250 ml. of eluent contains 95% of the total product. Elution with an additional 175 ml. of solvent removes the remainder. The combined fractions are evaporated, and the pale-yellow, oily residue crystallizes readily on standing. Recrystallization of this material from pentane gives 1.82 g. (45% yield) of white, crystalline 2,2-(trimethylenedithio)cyclohexanone, m.p. 52–55° (Note 8).

2. Notes

1. The time required for this operation generally is 3.5–5 hours.
2. Trimethylene dithiotosylate, m.p. 66–67°,[4] as described in *Org. Synth.*, **Coll. Vol. 6**, 1016 (1988) was employed.
3. Eastman white label triethylamine was distilled from sodium hydroxide.
4. Fisher Reagent acetonitrile was distilled from phosphorus pentoxide.
5. Treatment with the dilute acid effects aqueous extraction of pyrrolidine and hydrolysis of unreacted dithiotosylate and enamine starting materials.
6. Hydrogen carbonate washing ensures removal of the sulfonic and sulfinic acids.
7. The checkers used "Aluminum Oxide" purchased from J. T. Baker Chemical Company.
8. The ^{1}H NMR spectrum of the product ($CDCl_3$) exhibits multiplets in the region 8 1.65–2.45. The IR spectrum ($CHCl_3$) shows peaks at 2980 (m), 2940 (s), 2870 (m), 1690 (s), 1445 (m), 1420 (m), 1120 (m), 1110 (m), and 910 (s) cm^{-1}.

3. Discussion

The preparation of dithianes from enamines by reaction with trimethylene dithiotosylate has been applied with enamines derived from cholestan-3-one, acetoacetic ester, and phenylacetone.[5] Reactions of trimethylene dithiotosylate with hydroxymethylene derivatives of ketones also give rise to dithianes; thus, the hydroxymethylene derivative of cholest-4-en-3-one can be converted to 2,2-_ (trimethylenedithio)cholest-4-en-3-one.[6] 1,3-Dithiolanes are obtained in a similar manner by reaction of ethylene dithiotosylate[7] with the appropriately activated substrate.[5,8]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 590

References and Notes

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2. Present address: Bristol Laboratories, Division of Bristol-Myers Company, Syracuse, New York 13201.
3. Present address: Sterling-Winthrop Research Institute, Rensselaer, New York 12144.
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7. R. B. Woodward, I. J. Pachter, and M. L. Scheinbaum, *Org. Synth.*, **Coll. Vol. 6**, 1016 (1988).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

acetoacetic ester

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether,
diethyl ether (60-29-7)

acetonitrile (75-05-8)

sodium hydroxide (1310-73-2)

Cyclohexanone (108-94-1)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

cyclohexane (110-82-7)

Pentane (109-66-0)

phenylacetone (103-79-7)

cholestan-3-one (566-88-1)

aluminum oxide (1344-28-1)

pyrrolidine (123-75-1)

triethylamine (121-44-8)

potassium hydrogen carbonate (298-14-6)

ethylene dithiotosylate

trimethylene dithiotosylate (3866-79-3)

2,2-(Trimethylenedithio)cyclohexanone,
1,5-Dithiaspiro[5.5]undecan-7-one (51310-03-3)

Laureate

1-Pyrrolidinocyclohexene (1125-99-1)

2,2-(trimethylenedithio)cholest-4-en-3-one

phosphorus pentoxide (1314-56-3)