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.

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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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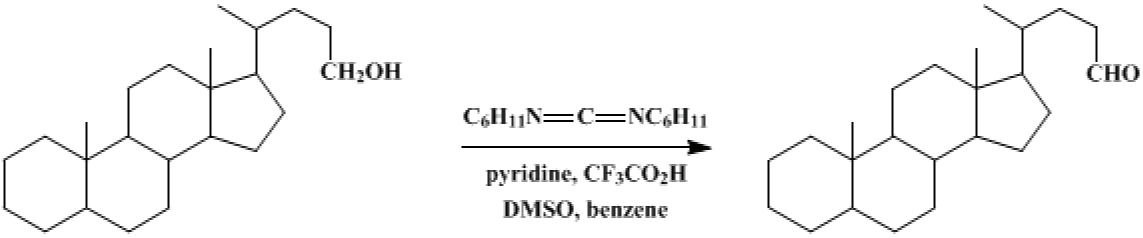
CHOLANE-24-AL



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1. Procedure

Cholane-24-ol (1.033 g., 3 mmoles) (Note 1) is dissolved by gentle warming in 10 ml. of anhydrous benzene (Note 2) in a 50-ml. flask, and 10 ml. of rigorously dried dimethyl sulfoxide (Note 3) is added. To the clear solution are added 0.24 ml. (3.0 mmoles) of anhydrous pyridine (Note 4), 0.12 ml. (1.5 mmoles) of distilled trifluoroacetic acid, and 1.85 g. (9 mmoles) of dicyclohexylcarbodiimide (Note 5), in that order. The flask is tightly stoppered and left at room temperature for 18 hours (Note 6). Benzene (30 ml.) is then added, and the crystalline dicyclohexylurea is removed by filtration (Note 7) and washed with benzene. The combined filtrates and washings are extracted three times with 50-ml. portions of water (Note 8) to remove the dimethyl sulfoxide. The organic layer is dried with sodium sulfate and evaporated to dryness under reduced pressure. There is obtained 2.12 g. of syrup which partially crystallizes. Thin-layer chromatography of this material (Note 9) shows a very intense spot of cholane-24-al, traces of starting material, and two compounds near the solvent front as well as excess carbodiimide (Note 9).

The crude product is dissolved in benzene-hexane (1:1) and applied to a column containing 125 g. of silicic acid (Note 10). Elution with the same solvent gives traces (less than 5 mg. each) of the two fast-moving components in fractions 2 and 4 (125-ml. fractions) and chromatographically pure cholane-24-al in fractions 5–8 (Note 11). Evaporation of the pooled fractions yields 870 mg. (84%) of the pure crystalline aldehyde, m.p. 102–104°. Recrystallization from 5 ml. of acetone raises the melting point to 103–104° (Note 12).

The compound gives a crystalline 2,4-dinitrophenylhydrazone, m.p. 163–164°, from ethanol.

2. Notes

1. Available from Aldrich Chemical Company.
2. Dried by storage over calcium hydride.
3. Dried by distillation under reduced pressure and storage for several days over Linde Molecular Sieves Type 4A.
4. Dried by distillation from, and storage over, calcium hydride.
5. The dry, crystalline material may be obtained from Aldrich Chemical Company. If the reagent is at all oily at room temperature, it should be distilled under reduced pressure, b.p. 140° (5 mm.).
6. Crystalline dicyclohexylurea (m.p. 234°) starts to separate after a short time. The checkers found a decrease in yield if this is allowed to run longer; a yield of 54% was found in a 22-hour reaction time.
7. Roughly 0.6–0.8 g. of the urea is usually obtained, m.p. 232–234°. The excess dicyclohexylcarbodiimide remains in the benzene. The oxidation is generally less satisfactory if less than 2.5 molar equivalents of carbodiimide is used.
8. Some further dicyclohexylurea tends to separate at the interface during the first extraction, and a clean separation of the layers near the interface is aided by mild centrifugation.
9. On Merck Silica G using benzene as the solvent and 5% ammonium molybdate in 10% sulfuric acid followed by brief heating at 150° to develop the spots. Under these conditions cholane-24-al has an R_f of

0.76 while cholane-24-ol has R_f 0.19; dicyclohexylcarbodiimide streaks between 0.3 and 0.5.
10. Merck silica gel with 0.05–0.20 mm. particles obtained from Brinkman Instruments Inc. and packed in a 3-cm. diameter column under benzene-hexane (1:1).
11. The fractions were examined by thin-layer chromatography of 25–50 µl. aliquots as in (Note 9). The checkers found that cholane-24-al is found in fractions 4–7.
12. The compound is very soluble in most organic solvents. In order to get a high recovery, it is necessary to complete the crystallization in the deep freeze. From aqueous ethanol the aldehyde crystallized in high yield as the hemihydrate, m.p. 95°.

3. Discussion

Cholane-24-al has not been previously synthesized by other methods.

4. Merits of the Preparation

The oxidation reaction described is a very general one that may be used for the preparation of both aldehydes and ketones[2] in high yield. The reaction conditions are extremely mild and only slightly acidic, thus allowing the preparation of otherwise very unstable compounds.[2] Of particular merit is the fact that the oxidation of primary alcohols stops selectively at the aldehyde and gives no traces of acidic products. Among the many different acids that have been examined as the proton source for this type of reaction,[2] pyridinium trifluoroacetate consistently gives the best results.

References and Notes

1. Syntex Institute for Molecular Biology, Palo Alto, California.
2. K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5661, 5670 (1965).

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

ethanol (64-17-5)

sulfuric acid (7664-93-9)

Benzene (71-43-2)

sodium sulfate (7757-82-6)

acetone (67-64-1)

pyridine (110-86-1)

benzene-hexane (1077-16-3)

dimethyl sulfoxide (67-68-5)

calcium hydride (7789-78-8)

trifluoroacetic acid (76-05-1)

CHOLANE-24-AL (26606-02-0)

Cholane-24-ol

dicyclohexylcarbodiimide (538-75-0)

dicyclohexylurea (2387-23-7)

ammonium molybdate (13106-76-8)

pyridinium trifluoroacetate (464-05-1)