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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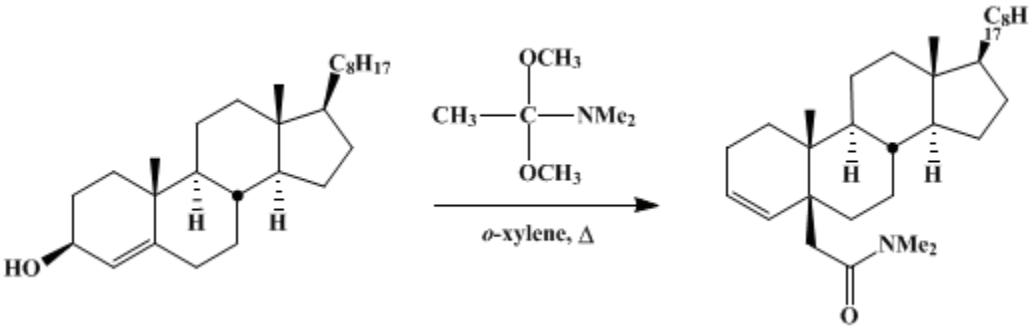
N,N-DIMETHYL-5β-CHOLEST-3-ENE-5-ACETAMIDE

[Cholest-3-ene-5-acetamide, *N,N*-dimethyl-, (5β)-]



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1. Procedure

A 50-ml., round-bottomed flask, equipped with a Teflon®-covered magnetic stirring bar and a reflux condenser connected to a gas-inlet tube, is charged with 970 mg. (2.51 mmoles) of cholest-4-en-3β-ol (Note 1) and 30 ml. of *o*-xylene (Note 2). The mixture is stirred to effect solution before 1.67 g. (0.0125 mole) of *N,N*-dimethylacetamide dimethyl acetal (Note 3) is added. The flask is flushed with argon, then heated (Note 4) at reflux under a positive pressure of argon with vigorous stirring for 65 hours. After cooling, the volatile materials are removed at reduced pressure (Note 5), and the yellow, oily residue (1.2 g.) is chromatographed on 60 g. of silica gel with diethyl ether (Note 6). Elution of the column with 200 ml. of ether gives a mixture of cholestadienes which is discarded; further elution with 500 ml. of ether affords 740 mg. of *N,N*-dimethyl-5β-cholest-3-ene-5-acetamide as a clear, colorless oil, which on trituration with acetone gives 740 mg. (65%) of the amide as white plates, m.p. 128–129.5°.

2. Notes

1. Cholest-4-en-3β-ol can be prepared by the procedure of Burgstahler and Nordin[2]. A melting point below 130° indicates that the material is contaminated with some of the 3α-hydroxy isomer. The material used above melted at 130.5–131° (from ethanol).
2. The Matheson, Coleman and Bell product was used without purification.
3. *N,N*-Dimethylacetamide dimethyl acetal was obtained from Fluka A. G. and used without purification.
4. A sand bath set into an electric heating mantle was found to be satisfactory for the long-term heating process.
5. The volatile materials were removed by rotary evaporation followed by vacuum (0.1 mm.) drying for 1 hour.
6. Merck silica gel (0.05–0.2 mm., 70–325 mesh ASTM) was used in a 2.5 × 25 cm. column. Mallinckrodt anhydrous ether was employed as the eluant.

3. Discussion

The amide–Claisen rearrangement procedure of Eschenmoser and co-workers[3] was modified for use with cholest-4-en-3β-ol.

References and Notes

1. Division of Chemistry and Chemical Engineering, Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109.
2. A. W. Burgstahler and I. C. Nordin, *J. Am. Chem. Soc.*, **83**, 198 (1961).
3. A. E. Wick, D. Felix, K. Steen, and A. Eschenmoser, *Helv. Chim. Acta*, **47**, 2425 (1964).

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

ethanol (64-17-5)

ether,
diethyl ether (60-29-7)

acetone (67-64-1)

argon (7440-37-1)

cholest-4-en-3β-ol

o-Xylene (95-47-6)

N,N-Dimethyl-5β-cholest-3-ene-5-acetamide,
Cholest-3-ene-5-acetamide, N,N-dimethyl-, (5β)- (56255-03-9)

N,N-dimethylacetamide dimethyl acetal (18871-66-4)