



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.

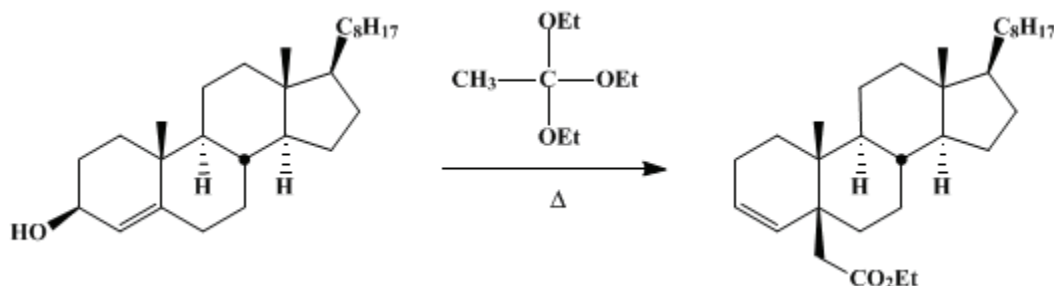
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.584 (1988); Vol. 54, p.74 (1974).

ETHYL 5 β -CHOLEST-3-ENE-5-ACETATE

[Cholest-3-ene-5-acetic acid, ethyl ester, (5 β)-]



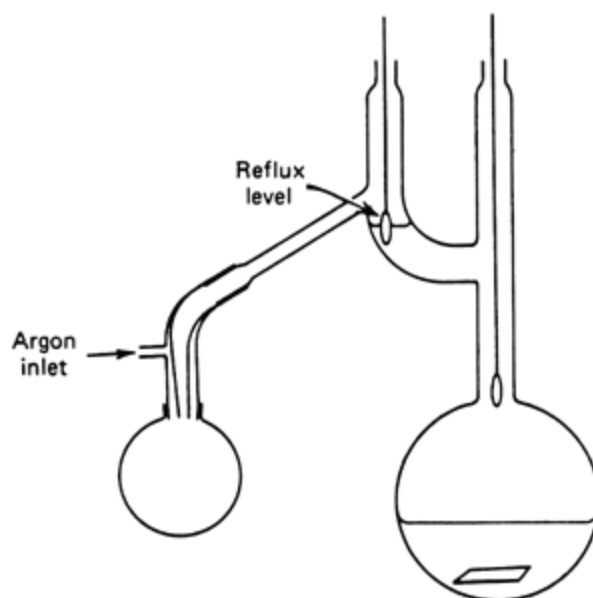
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1. Procedure

A 100-ml., Claisen distillation flask with two 14/20 standard taper joints and a thermometer-inlet is equipped with a gas-inlet adapter, a receiver, a thermometer, and a magnetic stirring bar. A 40-ml. calibration mark is made on the flask, and 970 mg. (2.50 mmoles) of *cholest-4-en-3 β -ol* (Note 1) is introduced. *Triethyl orthoacetate* is then distilled under *argon* into the flask to the 40-ml. mark (Note 2). The mixture is stirred, effecting solution while the flask is purged with *argon*, then the top joint is sealed with a thermometer (Figure 1). The stirred solution is heated under a positive pressure of *argon* so that the vapor reflux level is just below the side arm of the flask; the temperature on the lower thermometer is 142–147°; the upper thermometer temperature is kept between 25 and 70° (Note 3). After 8 days of reflux, during which time a small amount of the volatile material distills into the receiver, the reaction flask is cooled, and all the volatile materials are removed at reduced pressure (Note 4). The residue (1.3 g. of a pale yellow oil) is chromatographed on 120 g. of silica gel with 10% *diethyl ether* in petroleum ether as the eluant (Note 5). The side products eluted with the first 240 ml. of the solvent are discarded; further elution with 120 ml. of the solvent affords 690 mg. of *ethyl 5 β -cholest-3-ene-5-acetate* as a clear, colorless oil. Trituration of this product with *acetone* produces 560–690 mg. (49–60%) of the ester as white plates, m.p. 89–92.5°.

Figure 1.



2. Notes

1. [Cholest-4-en-3 \$\beta\$ -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 3 α -hydroxy isomer. The material used above melted at 130.5–131° (from [ethanol](#)).
2. The Matheson, Coleman and Bell product was used without purification. After a 10-ml. forerun, the [triethyl orthoacetate](#) was distilled (b.p. 142–147°) directly into the reaction flask.
3. A sand bath in an electric heating mantle was found to be satisfactory for the long-term heating process.
4. The volatile materials were removed by rotary evaporation followed by vacuum (0.1 mm.) drying for 1 hour.
5. Merck silica gel (0.05–0.2 mm., 70–325 mesh ASTM) was used in a 3.5 × 26 cm. column. Mallinckrodt anhydrous [ether](#) and Baker petroleum ether (b.p. 30–60°) were employed as eluants.

3. Discussion

The ester–Claisen rearrangement procedure of Johnson and co-workers³ was modified for use with [cholest-4-en-3 \$\beta\$ -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. W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T.-t. Li, D. J. Faulkner, and M. R. Peterson, *J. Am. Chem. Soc.*, **92**, 741 (1970).

Appendix

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

petroleum ether

ethanol (64-17-5)

ether,
diethyl ether (60-29-7)

acetone (67-64-1)

argon (7440-37-1)

triethyl orthoacetate (78-39-7)

cholest-4-en-3 β -ol

Ethyl 5 β -cholest-3-ene-5-acetate,
Cholest-3-ene-5-acetic acid, ethyl ester, (5 β)- (56101-56-5)