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.

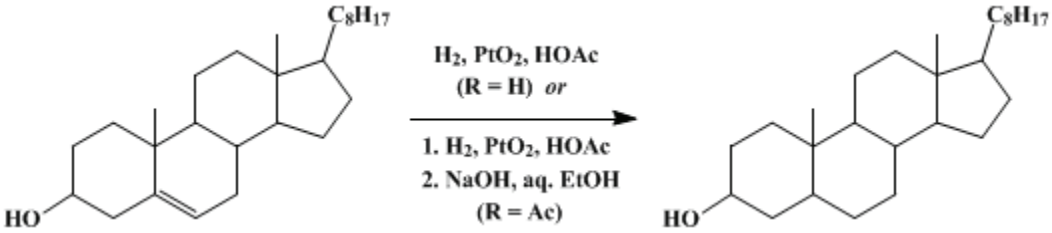
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.017.0045

Organic Syntheses, Coll. Vol. 2, p.191 (1943); Vol. 17, p.45 (1937).

DIHYDROCHOLESTEROL

[β-Cholestanol]



Submitted by W. F. Bruce
Checked by Louis F. Fieser, R. P. Jacobsen, and M. S. Newman.

1. Procedure

(*A*) *From Cholesterol*.—One hundred grams (0.26 mole) of commercial cholesterol is crystallized from 250 cc. of glacial acetic acid, using 1 g. of Norite if required, and the purified material (Note 1) is transferred, conveniently without being dried, to a hydrogenation vessel equipped with a thermometer and a heating device (Note 2). Three hundred cubic centimeters of purified glacial acetic acid (Note 3) and 0.5 g. of platinum oxide are added, and the hydrogenation is conducted at 65–75° at a slight positive pressure. The total amount of hydrogen usually is absorbed in two to four hours (Note 4). After the hydrogen has been replaced by air the solution is filtered hot and the product is obtained by crystallization and concentration. The total yield of air-dried, partially acetylated dihydrocholesterol, m.p. 130–135°, is 85–90 g.

Unless a specially purified product (see below) is desired, the crude material is heated for three hours on the steam bath with 400 cc. of alcohol and a solution of 25 g. of sodium hydroxide in 100 cc. of water. After cooling, the product is collected, washed, and crystallized from 500 cc. of alcohol. The yield is 75–80 g. (75–80 per cent of the theoretical amount), and a well-dried sample (Note 5) melts at 140–141°.

Submitted by J. O. Ralls
Checked by Louis F. Fieser, R. P. Jacobsen, and M. S. Newman.

1. Procedure

(*B*) *From Cholesteryl Acetate* (Note 6).—Five grams of cholesteryl acetate (Note 7) and 0.1 g. of platinum oxide are suspended in 25 cc. of absolute ether and 50 cc. of purified glacial acetic acid (Note 3), and the hydrogenation is conducted at room temperature at a slight positive pressure. The reaction is complete in ten to fifty minutes. The solution is filtered, using ether to dissolve any crystallized material, and, after removing the solvent by distillation at reduced pressure, the residue is either saponified as above or purified in the following manner.

Purification by the Method of Anderson and Nabenhauer.[1]—A solution of 20 g. of crude, partially or completely acetylated dihydrocholesterol in 200 cc. of carbon tetrachloride is placed in a separatory funnel and treated with 100 cc. of acetic anhydride. About 5 cc. of concentrated sulfuric acid is added dropwise through the stem of the inverted funnel with cooling and shaking until there is no further increase in color. A blue or green color develops, the intensity depending on the amount of cholesterol present in the sample. After fifteen to twenty minutes about 10 cc. of water is added, by drops and with cooling and gentle shaking until two distinct layers form. The carbon tetrachloride solution (upper layer) is separated and washed free of acid with sodium chloride or sodium carbonate solution (pure water gives emulsions). After drying with sodium sulfate, the solvent is removed by distillation at diminished pressure and the residue is saponified as above with alcoholic alkali and crystallized from alcohol. The

purified dihydrocholesterol weighs 12–14 g. and melts, after thorough drying (Note 5), at 142–143°. It gives a faint Liebermann-Burchard reaction (Note 8) only after ten to fifteen minutes.

2. Notes

1. The dry weight of the crystallized material is 90–95 g. Some samples may require recrystallization.
2. A suitable arrangement for heating the hydrogenation vessel is described in Org. Syn. Coll. Vol. I, **1941**, 61. An alternative arrangement is the following: a round-bottomed long-necked flask is supported at the top by a two-piece clamp with a loosened checknut, connected below to an eccentric, and heated in motion by means of a stationary microburner.
3. glacial acetic acid is purified by boiling for one hour with 5 g. of potassium permanganate per liter and distilling.
4. The catalyst sometimes loses its activity when about half of the theoretical amount of hydrogen has been absorbed, probably because of the poisoning action of impurities not removed from the commercial cholesterol. If this happens the addition of one or two 0.2-g. portions of catalyst usually suffices to bring the reaction practically to completion.
5. The sterol forms a hydrate from which the water is eliminated only after thorough drying, as in vacuum at 100°.
6. The acetyl derivative is more easily reduced than the free sterol.
7. Cholesteryl acetate is prepared by boiling for one hour a solution of 5 g. of cholesterol in 7.5 cc. of acetic anhydride, cooling, filtering, and washing the crystalline product with cold methanol. The yield of material melting at 114–115° is 5 g.
8. This test for cholesterol is made by dissolving about 5 mg. of the material in 2 cc. of carbon tetrachloride, and adding 1 cc. of acetic anhydride and 3–4 drops of concentrated sulfuric acid. Cholesterol gives rise to a succession of color changes.

3. Discussion

Dihydrocholesterol has been prepared by the reduction of cholestenone with sodium and amyl alcohol[2] and by the hydrogenation of cholesterol. In the presence of platinum black or platinum oxide, yields varying from 6.5 per cent to 40 per cent have been obtained in ether,[3] acetone,[4] ethyl acetate,[5] and acetic acid.[6]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 139
- Org. Syn. Coll. Vol. 5, 245

References and Notes

1. Anderson and Nabenhauer, J. Am. Chem. Soc. **46**, 1957 (1924).
2. Diels and Abderhalden, Ber. **39**, 889 (1906); Diels and Stamm, ibid. **45**, 2230 (1912); Neuberg, ibid. **39**, 1155 (1906).
3. Willstätter and Mayer, ibid. **41**, 2200 (1908); Dorée, J. Chem. Soc. **95**, 644 (1909); Boehm, Biochem. Z. **33**, 474 (1911); Windaus and Uibrig, Ber. **47**, 2386 (1914); Ellis and Gardner, Biochem. J. **12**, 72 (1918); Anderson, J. Biol. Chem. **71**, 411 (1926); Vavon and Jakubowicz, Bull. soc. chim. (4) **53**, 584 (1933); Ruzicka, Brüngger, Eichenberger, and Meyer, Helv. Chim. Acta **17**, 1407 (1934).
4. Nord, Biochem. Z. **99**, 265 (1919).
5. Shriner and Ko, J. Biol. Chem. **80**, 6 (1928).
6. v. Fürth and Felsenreich, Biochem. Z. **69**, 420 (1915).

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

platinum black

β-Cholestanol

alcohol (64-17-5)

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

methanol (67-56-1)

ether (60-29-7)

acetic anhydride (108-24-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

potassium permanganate (7722-64-7)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

platinum oxide

acetone (67-64-1)

Norite (7782-42-5)

sodium (13966-32-0)

amyl alcohol (71-41-0)

Dihydrocholesterol (80-97-7)

Cholesterol (57-88-5)

Cholesteryl acetate (604-35-3)

Cholestenone