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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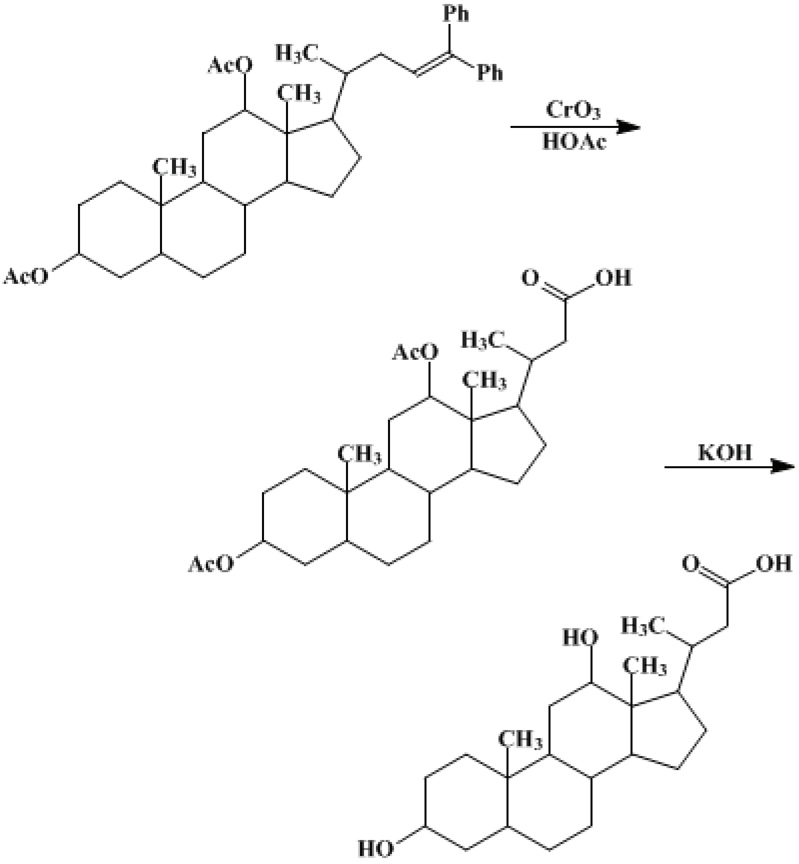
nor-DESOXYCHOLIC ACID

[3,12-Dihydroxy-*nor*-cholanic acid]



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1. Procedure

A solution of 59.6 g. (0.1 mole) of 3,12-diacetoxy-*bisnor*-cholanyldiphenylethylene (p. 237) in 60 ml. of chloroform is prepared by warming and poured into a 1-l. round-bottomed flask containing 300 ml. of glacial acetic acid at about 40°. The flask is provided with a stirrer, a thermometer dipping below the surface of the solution, and a dropping funnel, and is surrounded by a water bath through which cold water can be circulated. A solution of 37 g. of chromium trioxide in 30 ml. of water and 200 ml. of acetic acid is added from the dropping funnel at such a rate that the temperature is kept at about 50°; the mixture is stirred and cooled. This operation should require about 10 minutes. When the temperature starts to drop, the water bath is warmed and the temperature is maintained at about 50° for an additional 20 minutes. The solution is then cooled, and the excess chromic acid is destroyed by adding carefully about 30 ml. of methanol, the temperature being kept below 50° (Note 1).

The reaction mixture is concentrated by distillation under reduced pressure. At first the solvent may be distilled rapidly, but, after the mixture becomes syrupy, the distillation should be carried out below 30° until the residue is almost solid. At a pressure of 10 mm. the concentration requires about 2 hours. The residue is diluted with 500 ml. of cold water, which should be added in several portions with thorough shaking to break up all the lumps. The product is collected on a filter and washed with dilute hydrochloric acid until the filtrate comes through colorless.

The solid crystalline cake (Note 2) is dissolved in about 400 ml. of ether and extracted with 500 ml. of 2.5% potassium hydroxide solution (Note 3). The alkaline solution is immediately acidified with 200 ml. of 10% hydrochloric acid, and the crude 3,12-diacetoxy-*nor*-cholanic acid (Note 4) is collected on a filter.

The crude diacetate is hydrolyzed by dissolving it in 350 ml. of 10% aqueous potassium hydroxide and refluxing the solution for 2 hours. The alkaline solution is diluted to about 700 ml., cooled, and filtered. The filtrate is poured into 300 ml. of 10% hydrochloric acid, and the *nor*-desoxycholic acid is separated by filtration and dried. The crude product is dissolved in about 600 ml. of acetone and filtered, while hot, to remove small amounts of salt. On cooling, 25–30 g. (57–68%) of white crystals which melt at 209–211° is obtained in two crops (Note 5). This material contains 1 molecule of acetone of crystallization. The fully purified substance softens at about 160° (loss of acetone) and melts at 213.5–214.5°.

2. Notes

1. Solid chromic acid and methanol will ignite spontaneously; care should be taken that the methanol does not come in contact with any of the chromic acid solution that may have dried around the edges of the dropping funnel.
2. If the cake is not nearly colorless it should be stirred with 250 ml. of 10% hydrochloric acid and the mixture extracted with 400 ml. of ether. The ether solution is then extracted with the 2.5%potassium hydroxide as described.
3. Vigorous mixing should be avoided in order to prevent the formation of an emulsion.
4. The 3,12-diacetoxy-*nor*-cholanic acid may be purified by crystallization from acetone. It melts at 207–208°.
5. This procedure, coupled with the procedure described on p. 237, illustrates the Barbier-Wieland method for systematically degrading carboxylic acids. *bisnor*-Desoxycholic acid may be prepared from *nor*-desoxycholic acid by repetition of this procedure. If the chromic acid oxidation product is not sufficiently solid to filter after dilution with water, the mixture must be extracted with ether and washed with dilute hydrochloric acid before the alkaline extraction. *bisnor*-Desoxycholic acid may be crystallized from ethyl alcohol. It melts at 239–241.°

3. Discussion

nor-Desoxycholic acid has been prepared from desoxycholic acid by modification of the Barbier-Wieland degradation.[1]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 237

References and Notes

1. Hoehn and Mason, *J. Am. Chem. Soc.*, **60**, 1493 (1938); Sawlewicz, *Roczniki Chem.*, **18**, 250, 755 (1938); Kazuno and Simizu, *J. Biochem. Japan*, **29**, 421 (1939); Reichstein and Arx, *Helv. Chim. Acta*, **23**, 747 (1940).

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

nor-Desoxycholic acid

3,12-Dihydroxy-nor-cholanic acid

3,12-Diacetoxy-bisnor-cholanyldiphenylethylene

3,12-Diacetoxy-nor-cholanic acid

bisnor-Desoxycholic acid

ethyl alcohol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

methanol (67-56-1)

ether (60-29-7)

chloroform (67-66-3)

acetone (67-64-1)

potassium hydroxide (1310-58-3)

chromic acid (7738-94-5)

chromium trioxide (1333-82-0)