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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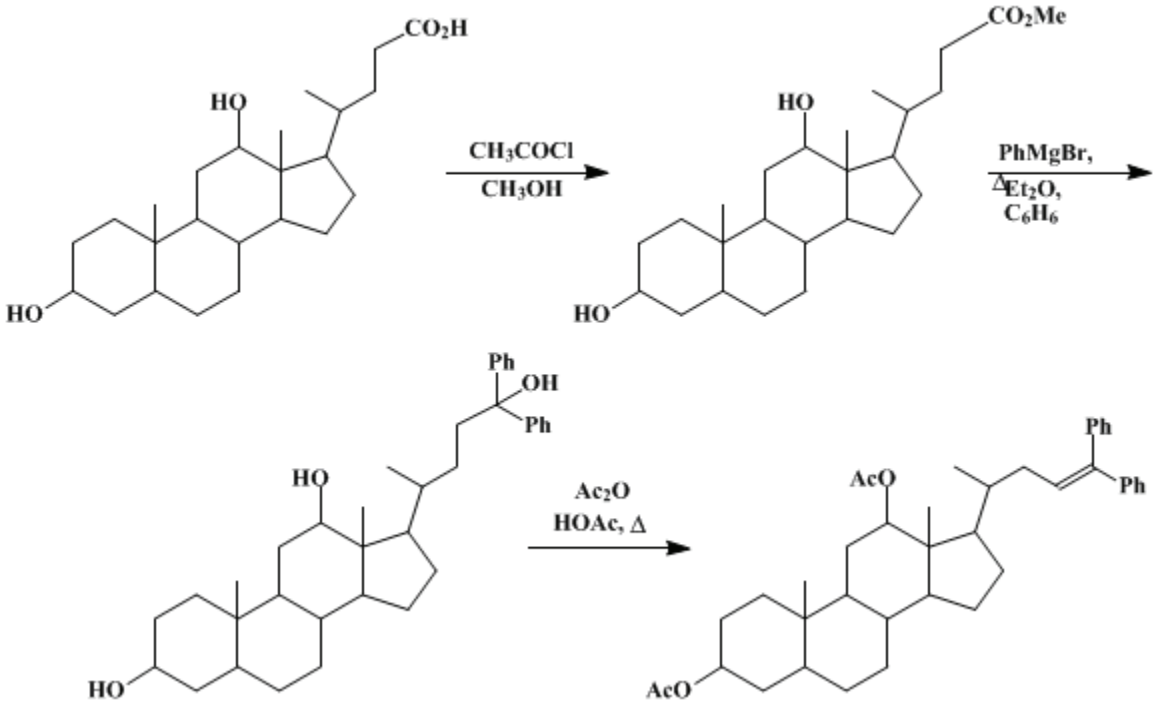
3,12-DIACETOXY-*bisnor*-CHOLANYLDIPHENYLETHYLENE

[Bisnorcholanyldiphenylethylene, 3,12-diacetoxy-]



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1. Procedure

A. *Methyl desoxycholate*. To a cooled solution of 100 g. (0.255 mole) of desoxycholic acid (Note 1) in 1 l. of methanol is added carefully 50 ml. of acetyl chloride. The solution is allowed to stand overnight at room temperature (Note 2) and is then diluted with cold water until just turbid. Crystallization is induced by scratching and seeding, if necessary. When much of the ester has crystallized, the mixture is further diluted to about 2.5 l. and allowed to stand for 30 minutes until crystallization is complete. The ester is collected on a filter, washed with water, and dried. The yield is 100–103 g. (97–100%) of material which melts at 95–100° (Note 3).

B. 3,12-*Diacetoxy-bisnor-cholanyldiphenylethylene*. A solution of phenylmagnesium bromide is prepared in a 5-l. three-necked flask, fitted with a dropping funnel, an efficient reflux condenser, and a mechanical stirrer, from 97.2 g. (4 gram atoms) of magnesium, 675 g. (450 ml., 4.3 moles) of bromobenzene, and 1250 ml. of dry ether.

To the solution of the Grignard reagent is added a solution of 102 g. (0.25 mole) of methyl desoxycholate in 700 ml. of dry benzene (Note 4). The desoxycholate is washed into the flask with 500 ml. of dry benzene, and the mixture is refluxed with stirring for 3 hours. After cooling, the complex is decomposed by pouring its benzene solution into a mixture of about 4 l. of ice and 700 ml. of concentrated hydrochloric acid. After thorough shaking, the layers are separated, and the aqueous layer is extracted twice with ether. The combined ether solution is washed with dilute hydrochloric acid, water, 5% sodium hydroxide solution, and finally with water. The solvent and some biphenyl are removed by steam distillation; approximately 5 hours is required to remove the biphenyl formed during the preparation of the Grignard reagent. The lumps should be broken up from time to time, if necessary. After cooling, the residue of crude 3,12-dihydroxy-*nor*-cholanyldiphenylcarbinol is collected and dried.

The crude carbinol is acetylated and dehydrated by refluxing its solution in 1 l. of glacial acetic acid and 500 ml. of acetic anhydride for 1 hour. The solution is then concentrated to about 500 ml. by distillation. After cooling overnight, the crystalline 3,12-diacetoxy-*bisnor*-cholanyldiphenylethylene is collected on a filter and washed with acetic acid. The yield is 95–105 g. (63.5–70.0%) of material melting at 154–157° (Note 5). This product is sufficiently pure to be used for the preparation of *nor*-desoxycholic acid (p. 234); one crystallization from acetone gives white crystals which melt at 156–157.5°; fully purified material melts at 159.5–160.5°.

2. Notes

1. A good grade of desoxycholic acid should be used. The product from Wilson Laboratories has been found to be satisfactory.
2. At this point the solution should be filtered if any insoluble material is present.
3. This methyl desoxycholate is pure enough for most purposes, but if desired it may be recrystallized from methanol or from a mixture of ether and petroleum ether.
4. The solution of methyl desoxycholate in dry benzene is conveniently prepared by dissolving the ester in 900 ml. of ordinary benzene and distilling the excess solvent.
5. An additional 5–7 g. of product may be obtained by concentrating the filtrate and recrystallizing the product from acetone. If the material is to be used for the preparation of *nor*-desoxycholic acid (p. 234), it is more convenient to oxidize the filtrate directly with chromic acid and isolate the product as the acid.

3. Discussion

The literature on methods of preparation is the same as that given for *nor*-desoxycholic acid (p. 234).

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 234

References and Notes

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

petroleum ether

nor-Desoxycholic acid

3,12-Diacetoxy-bisnor-cholanyldiphenylethylene

Bisnorcholanyldiphenylethylene, 3,12-diacetoxy-

Methyl desoxycholate

desoxycholic acid

3,12-dihydroxy-nor-cholanyldiphenylcarbinol

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

methanol (67-56-1)

ether (60-29-7)

acetic anhydride (108-24-7)

sodium hydroxide (1310-73-2)

acetyl chloride (75-36-5)

magnesium (7439-95-4)

acetone (67-64-1)

chromic acid (7738-94-5)

bromobenzene (108-86-1)

Phenylmagnesium bromide (100-58-3)