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.

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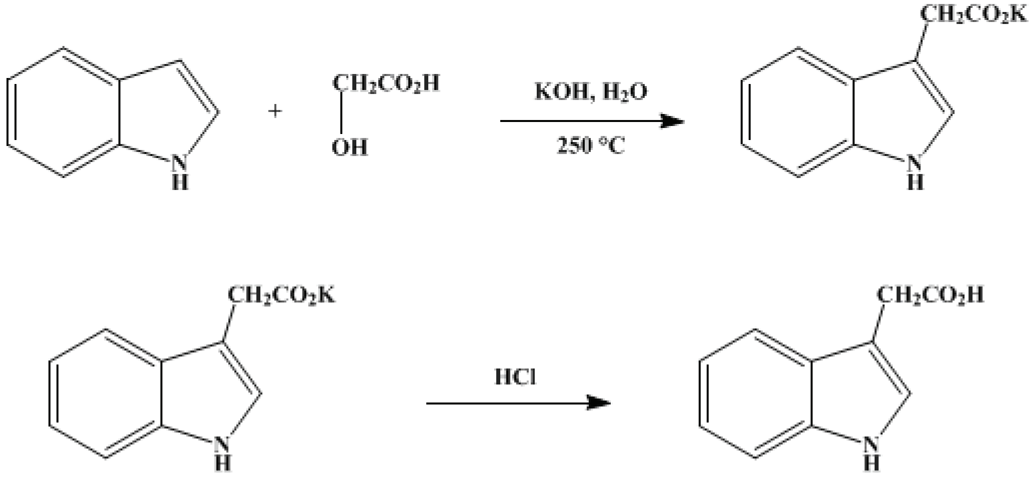
INDOLE-3-ACETIC ACID



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1. Procedure

A 3-l. stainless steel, rocking autoclave (Note 1) is charged with 270 g. (4.1 moles) of 85% potassium hydroxide and 351 g. (3.00 moles) of indole (Note 2), and then 360 g. (3.3 moles) of 70% aqueous glycolic acid is added gradually (Note 3). The autoclave is closed and rocked at 250° for about 18 hours (Note 4). The reaction mixture is cooled to below 50°, 500 ml. of water is added, and the autoclave is rocked at 100° for 30 minutes to dissolve the potassium indole-3-acetate. The aqueous solution is cooled to 25° and removed from the autoclave, the autoclave is rinsed out well with water, and water is added until the total volume of solution is 3 l. The solution is extracted with 500 ml. of ether (Note 5). The aqueous phase is acidified at 20–30° with 12*N* hydrochloric acid and then is cooled to 10° (Note 6). The indole-3-acetic acid that precipitates is collected on a Büchner funnel, washed with copious amounts of cold water, and dried in air or a vacuum desiccator out of direct light (Note 7); weight 455–490 g. (87–93%); m.p. 163–165° (dec.).

The indole-3-acetic acid, which is cream-colored, is of high purity. If further purification is desired, it may be done conveniently by recrystallization from water. One liter of water is used for 30 g. of acid, with 10 g. of decolorizing carbon added. Recovery is about 22 g. of a nearly colorless product, m.p. 164–166° (dec.).

2. Notes

1. A stirred autoclave is just as satisfactory. The scale is not critical, for the checkers got equally good results on one-third the scale; they used a 1-l. rocking autoclave.
2. Indole from the Union Carbide Olefins Company, Institute, West Virginia, is satisfactory.
3. If the reactants are added in this order, with the glycolic acid being introduced over a 5–10 minute period, there is no violent heating because the heat of neutralization is used to melt the indole. An equivalent amount of anhydrous glycolic acid may be used, but this offers no special advantage.
4. These limits are not critical, but they are probably optimum. Reaction times of 24–30 hours are not particularly detrimental, and high yields of product can be obtained within 12 hours. The temperature can range from 230° to 270° with but slight effect on the yield of product.
5. This extraction may be omitted. It does, however, remove traces of neutral material and consequently gives a product with greater color stability.
6. This operation is most conveniently conducted in a flask equipped with a stirrer.
7. The product dries slowly, and several days in air or 24 hours in a vacuum desiccator is usually

required. Considerable coloration will result if this is done in direct light. Drying in a heated oven or removing the water as a benzene azeotrope is not satisfactory because of some decarboxylation to skatole. The product should be stored in a dark bottle away from direct sunlight.

3. Discussion

Indole-3-acetic acid has been prepared by the Fischer indole synthesis,[2] by hydrolysis of indoleacetonitrile,[3] from the reaction of gramine-type compounds with cyanide ion under conditions which hydrolyze the nitrile,[4] by the reaction of indole with ethyl diazoacetate followed by hydrolysis,[5] through oxidation of indolepyruvic acid,[6] and by ultraviolet irradiation of tryptophan.[7]

4. Merits of the Preparation

This is the most convenient method of preparing indole-3-acetic acid if an agitated autoclave is available. The method can be used to prepare other indole-3-acetic acids from α-hydroxy acids. For example, α-methylindole-3-acetic acid has been prepared by condensing indole with lactic acid.

Indole-3-acetic acid is a natural plant auxin and is used as a control in research on plant growth.

References and Notes

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

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

decolorizing carbon (7782-42-5)

potassium hydroxide (1310-58-3)

lactic acid (50-21-5)

ethyl diazoacetate (623-73-4)

glycolic acid (79-14-1)

tryptophan (73-22-3)

Indole (120-72-9)

Indole-3-acetic acid (87-51-4)

potassium indole-3-acetate (2338-19-4)

indoleacetonitrile

indolepyruvic acid

α-methylindole-3-acetic acid