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.

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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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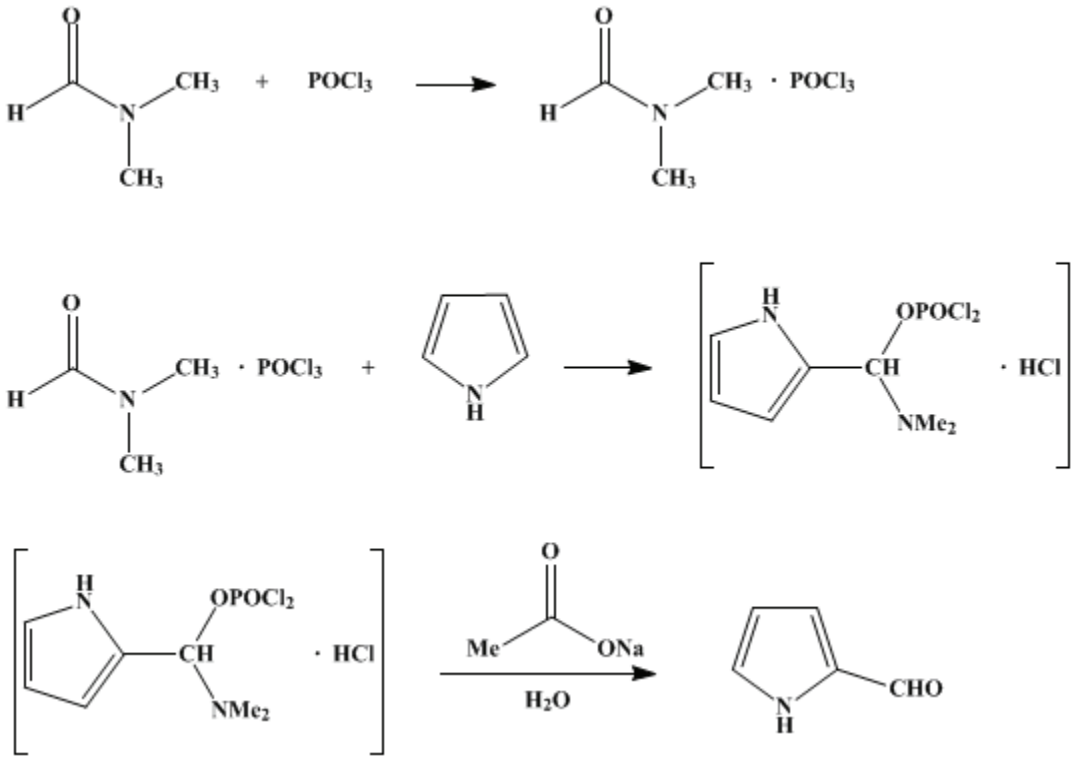
2-PYRROLEALDEHYDE

[Pyrrole-2-carboxaldehyde]



Submitted by Robert M. Silverstein, Edward E. Ryskiewicz, and Constance Willard[1].
Checked by Max Tishler and George Purdue.

1. Procedure

In a 3-l. three-necked round-bottomed flask, fitted with a sealed stirrer, a dropping funnel, and a reflux condenser, is placed 80 g. (1.1 moles) of dimethylformamide (Note 1). The flask is immersed in an ice bath, and the internal temperature is maintained at 10–20°, while 169 g. (1.1 moles) of phosphorus oxychloride is added through the dropping funnel over a period of 15 minutes. An exothermic reaction occurs with the formation of the phosphorus oxychloride-dimethylformamide complex. The ice bath is removed, and the mixture is stirred for 15 minutes (Note 2).

The ice bath is replaced, and 250 ml. of ethylene dichloride is added to the mixture. When the internal temperature has been lowered to 5°, a solution of 67 g. (1.0 mole) of freshly distilled pyrrole in 250 ml. of ethylene dichloride is added through a clean dropping funnel to the stirred, cooled mixture over a period of 1 hour. After the addition is complete, the ice bath is replaced with a heating mantle, and the mixture is stirred at the reflux temperature for 15 minutes, during which time there is copious evolution of hydrogen chloride.

The mixture is then cooled to 25–30°, and to it is added through the dropping funnel a solution of 750 g. (5.5 moles) of sodium acetate trihydrate (Note 3) in about 1 l. of water, cautiously at first, then as rapidly as possible. The reaction mixture is again refluxed for 15 minutes, vigorous stirring being maintained all the while (Note 4).

The cooled mixture is transferred to a 3-l. separatory funnel, and the ethylene dichloride layer is removed. The aqueous phase is extracted three times with a total of about 500 ml. of ether. The ether and ethylene chloride solutions are combined and washed with three 100-ml. portions of saturated

aqueous sodium carbonate solution, which is added cautiously at first to avoid too rapid evolution of carbon dioxide. The non-aqueous solution is then dried over anhydrous sodium carbonate, the solvents are distilled, and the remaining liquid is transferred to a Claisen flask and distilled from an oil bath under reduced pressure (Note 5). The aldehyde boils at 78° at 2 mm.; there is very little fore-run and very little residue. The yield of crude 2-pyrrolealdehyde is 85–90 g. (89–95%), as an almost water-white liquid which soon crystallizes. A sample dried on a clay plate melts at 35–40°. The crude product is purified by dissolving in boiling petroleum ether (b.p. 40–60°), in the ratio of 1 g. of crude 2-pyrrolealdehyde to 25 ml. of solvent, and cooling the solution slowly to room temperature, followed by refrigeration for a few hours. The pure aldehyde is obtained from the crude in approximately 85% recovery. The over-all yield from pyrrole is 78–79% of pure 2-pyrrolealdehyde, m.p. 44–45°.

2. Notes

1. The dimethylformamide is available as technical grade DMF from the Grasselli Chemicals Department of E. I. duPont de Nemours and Company, Wilmington, Delaware.
2. If the ice bath is not removed, the mixture may solidify and must be dissolved by adding solvent and heating slightly. Mixing of the reactants at ice-bath temperature prevents discoloration. Practical grades of materials were used.
3. The use of sufficient sodium acetate is essential. If the acidic reaction products are not neutralized, the yield drops to as low as 15–20% of badly discolored product which cannot be readily purified.
4. Efficient stirring must be maintained to keep the two phases in close contact. Hydrolysis is not complete if the mixture is not heated.
5. The use of a wide-bore condenser and a simple receiver, without a stopcock, is preferable. Usually the product does not solidify at once, but occasionally it crystallizes during distillation. The use of a fraction cutter is not necessary or advisable.

3. Discussion

2-Pyrrolealdehyde has been prepared from pyrrole, chloroform, and potassium hydroxide;[2] from pyrrolemagnesium iodide and ethyl, propyl, or isoamyl formate;[3] from 2-furaldehyde dimethyl acetal and ammonium acetate;[4] and, by the method here described, from pyrrole, phosphorus oxychloride, and dimethylformamide.[5] Smith[5] has suggested a possible intermediate in this process. The method has also been applied to substituted pyrroles[6] and is similar to that described on p. 331 for the preparation of *p*-dimethylaminobenzaldehyde from dimethylaniline.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 539

References and Notes

1. Stanford Research Institute, Stanford, California.
2. Bamberger and Djierdjian, *Ber.*, **33**, 536 (1900); Fischer, Beller, and Stern, *Ber.*, **61B**, 1074 (1928).
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4. Elming and Clauson-Kaas, *Acta Chem. Scand.*, **6**, 867 (1952).
5. Silverstein, Ryskiewicz, and Chaikin, *J. Am. Chem. Soc.*, **76**, 4485 (1954); Smith, *J. Chem. Soc.*, **1954**, 3842.
6. Ryskiewicz and Silverstein, *J. Am. Chem. Soc.*, **76**, 5802 (1954); Chu and Chu, *J. Org. Chem.*, **19**, 266 (1954); Silverstein, Ryskiewicz, Willard, and Koehler, *J. Org. Chem.*, **20**, 668 (1955).

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

petroleum ether

phosphorus oxychloride-dimethylformamide complex

ethyl, propyl, or isoamyl formate

hydrogen chloride (7647-01-0)

ether (60-29-7)

ammonium acetate (631-61-8)

sodium acetate (127-09-3)

chloroform (67-66-3)

sodium carbonate (497-19-8)

ethylene chloride,
ethylene dichloride (107-06-2)

carbon dioxide (124-38-9)

Phosphorus Oxychloride (21295-50-1)

potassium hydroxide (1310-58-3)

dimethylaniline (121-69-7)

Pyrrole (109-97-7)

dimethylformamide (68-12-2)

sodium acetate trihydrate (6131-90-4)

2-furaldehyde dimethyl acetal

2-Pyrrolealdehyde,
Pyrrole-2-carboxaldehyde (1003-29-8)

pyrrolemagnesium iodide

p-Dimethylaminobenzaldehyde (100-10-7)