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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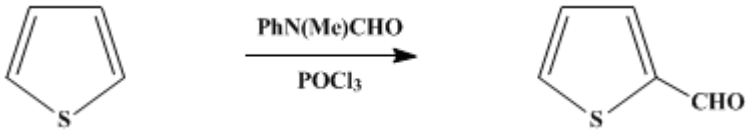
2-THENALDEHYDE

[2-Thiophenecarboxaldehyde]



Submitted by Arthur W. Weston and R. J. Michaels, Jr.[1].
Checked by Cliff S. Hamilton and Joe R. Willard.

1. Procedure

The reaction is carried out in a 500-ml. three-necked round-bottomed flask fitted with ground-glass joints and equipped with a thermometer, a mechanical stirrer, a dropping funnel, and a calcium chloride tube. In the flask are placed 135 g. (1.0 mole) of N-methylformanilide (Note 1) and 153 g. (91 ml., 1.0 mole) of phosphorus oxychloride, and the mixture is allowed to stand for 30 minutes (Note 2). Mechanical stirring is then begun, and the flask is immersed in a cold-water bath while 92.4 g. (1.1 moles) of thiophene is added at such a rate that the temperature is maintained at 25–35° (Note 3). After the addition is complete, the reaction mixture is stirred 2 hours longer at the same temperature and is then allowed to stand at room temperature for 15 hours. The dark, viscous solution is poured into a vigorously stirred mixture of 400 g. of cracked ice and 250 ml. of water. The aqueous layer is separated and extracted with three 300-ml. portions of ether. The ether extracts are combined with the organic layer and washed twice with 200-ml. portions of dilute hydrochloric acid (Note 4) to remove all traces of N-methylaniline (Note 5). These aqueous washings are in turn extracted with 200 ml. of ether, and the ether extract is added to the ether solution of the product. The combined ether extracts are washed twice with 200-ml. portions of saturated sodium bicarbonate solution (Note 6), then with 100 ml. of water, and finally are dried over anhydrous sodium sulfate. The yellow oil obtained by concentrating the ether solution is distilled from a 100-ml. flask fitted with a satisfactory column (Note 7). The yield of 2-thiophenecarboxaldehyde boiling at 97–100°/27 mm., n_D^{23} 1.5893, is 80–83 g. (71–74%). The product darkens on standing.

2. Notes

1. Directions for preparing this intermediate have been published.[2]
2. The temperature of the mixture rises slowly to 40–45°, and a color change from yellow to red also occurs.
3. If the temperature is allowed to exceed 35°, a lower yield of aldehyde results.
4. This solution is prepared by mixing 50 g. of concentrated hydrochloric acid and 400 ml. of water. The aldehyde has appreciable solubility in strongly acidic solutions.
5. The original aqueous layer and the acidic extracts are combined, cooled, and made strongly alkaline with 450 ml. of 40% sodium hydroxide solution. The liberated N-methylaniline is extracted with three 200-ml. portions of ether. The ether extracts are combined, washed with 100 ml. of water, dried over anhydrous sodium sulfate, and concentrated. Distillation of the residue from a 200-ml. flask equipped with an 11-cm. Vigreux column gives 95.6 g. (89%) of N-methylaniline boiling at 96–100°/27 mm.; n_D^{23} 1.5717.
6. Care must be taken in adding the bicarbonate solution, as vigorous foaming occurs until neutralization is complete.
7. The submitters used an 11-cm. Vigreux column; the checkers employed a 10-in. column of the same type.

3. Discussion

In addition to the methods given earlier,[3] 2-thenaldehyde has been prepared by the decarboxylation

of 2-thienylglyoxylic acid;[4] by the hydrolysis of the acetal obtained by the action of 2thienylmagnesium iodide on ethyl orthoformate;[4] by the oxidation of 2-thenyl alcohol;[5] by treatment of N-2-thenylformaldimine with ammonium chloride and formaldehyde;[6] by the action of 2thienylmagnesium bromide on ethyl formate;[7] by the reaction of thiophene with dimethylformamide in the presence of phosphorus oxychloride;[8] by the condensation of thiophene with 1,4-diformylpiperazine in the presence of phosphorus oxychloride;[9] and by the reaction of thiophene with dichloromethyl methyl ether in the presence of stannic chloride.[10]

The present procedure is a modification of a previously described method.[11,12]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 811

References and Notes

1. The Abbott Laboratories, North Chicago, Illinois.
2. *Org. Syntheses Coll. Vol.* **3**, 590 (1955).
3. *Org. Syntheses Coll. Vol.* **3**, 811 (1955).
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6. Hartough, Meisel, Koft, and Schick, *J. Am. Chem. Soc.*, **70**, 4013 (1948).
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10. Rieche, Gross, and Höft, *Chem. Ber.*, **93**, 88 (1960).
11. King and Nord, *J. Org. Chem.*, **13**, 635 (1948).
12. Weston and Michaels, *J. Am. Chem. Soc.*, **72**, 1422 (1950).

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

hydrochloric acid (7647-01-0)

ether (60-29-7)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

formaldehyde (50-00-0)

sodium bicarbonate (144-55-8)

sodium sulfate (7757-82-6)

Phosphorus Oxychloride (21295-50-1)

Ethyl orthoformate

ethyl formate (109-94-4)

Thiophene (110-02-1)

stannic chloride (7646-78-8)

N-Methylaniline (100-61-8)

2-thienylmagnesium iodide

N-methylformanilide (93-61-8)

dimethylformamide (68-12-2)

2-thenyl alcohol (636-72-6)

2-Thenaldehyde,
2-Thiophenecarboxaldehyde (98-03-3)

2-thienylglyoxylic acid (4075-59-6)

Dichloromethyl methyl ether (4885-02-3)

N-2-thenylformaldimine

2-thienylmagnesium bromide

1,4-diformylpiperazine (4164-39-0)