



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.

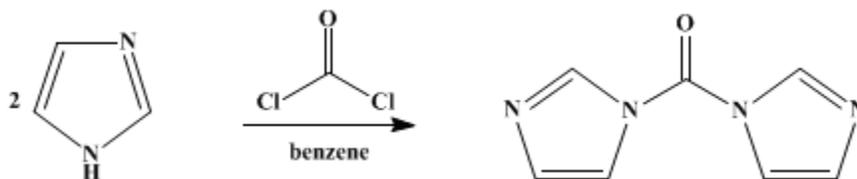
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.201 (1973); Vol. 48, p.44 (1968).

1,1'-CARBONYLDIIMIDAZOLE

[Imidazole, 1,1'-carbonyldi-]



Submitted by Heinz A. Staab and Kurt Wendel¹.

Checked by A. C. Mackay and Peter Yates.

1. Procedure

Caution! This preparation must be carried out in a hood to avoid exposure to phosgene.

Anhydrous benzene (*ca.* 200 ml.) (Note 1) is poured into a calibrated, 500-ml., standard-taper dropping funnel equipped with a gas-inlet tube containing a fritted-glass filter; the dropping funnel is stoppered and weighed accurately. The funnel is protected with a calcium chloride tube, and 15–20 g. of phosgene is introduced at room temperature over a period of *ca.* 1 hour; this quantity corresponds to an increase in volume of 12–16 ml. (Note 2). The calcium chloride tube is removed, and the funnel is immediately restoppered and reweighed (Note 3). The amount of imidazole corresponding to the increase in weight observed (*e.g.*, 16.55 g., 0.167 mole, of phosgene) is calculated on the basis of a phosgene:imidazole molar ratio of 1:4 (Note 4). The funnel is placed on a 1-l., three-necked, round-bottomed flask, that contains a solution of the imidazole (here, 45.60 g., 0.669 mole) in 500 ml. of anhydrous tetrahydrofuran (Note 5) and is equipped with a sealed mechanical stirrer and a calcium chloride tube. The flask is cooled with cold water, and the solution of phosgene in benzene is added with stirring from the dropping funnel over a period of 15–30 minutes. The reaction mixture is stirred for an additional 15 minutes and then allowed to stand for 1 hour at room temperature. The precipitate of imidazolium chloride is removed by suction filtration with exclusion of atmospheric moisture by the use of a standard-taper fritted-glass filter funnel (Note 6). The filtrate is evaporated to dryness under reduced pressure on a water bath at 40–50° (Note 7). The yield of colorless crystalline 1,1'-carbonyldiimidazole is 80–94% (here, 24.8 g.; 91%). The product obtained in this way sinters at 110° and melts between 112° and 117° (here, 114–115°). This material can be used without further purification for most reactions, *e.g.*, ester, peptide, and aldehyde syntheses² (Note 8). The purity of a product of m.p. 113–117° was 98±2%.³ The quality and yield of 1,1'-carbonyldiimidazole are not reduced when the scale is doubled.

1,1'-Carbonyldiimidazole may be kept for a long period of time in either a desiccator over phosphorus pentoxide or in a sealed tube. It is hydrolyzed by water to give carbon dioxide and imidazole.

2. Notes

1. The benzene is heated under reflux over sodium with benzophenone until a permanent blue coloration develops and then is distilled with exclusion of atmospheric moisture.
2. Use of a calibrated dropping funnel permits approximate estimation of the amount of phosgene absorbed; a volume increase of 1 ml. corresponds to about 1.3 g. of phosgene. The stream of phosgene is led through a wash bottle containing concentrated sulfuric acid and should not be too fast in order to avoid loss of solvent by evaporation.
3. The checkers used a fritted-glass inlet tube and drying tube incorporated in a standard-taper adapter that fitted the neck of the dropping funnel. Owing to small losses of solution on withdrawal of the

adapter, the weight of **phosgene** was slightly underestimated.

4. Technical grade **imidazole** (from Badische Anilin- und Soda-Fabrik, Ludwigshafen, Rhein, Germany) was recrystallized from **benzene** containing 1.0–1.5% **ethanol**; m.p. 90°. The checkers used **imidazole** obtained from Aldrich Chemical Co without further purification.

5. Technical grade **tetrahydrofuran** was predried for a few days over **sodium hydroxide**. It was then heated under reflux over **sodium** wire with **benzophenone** until it developed a permanent blue color and distilled with exclusion of atmospheric moisture. [*Caution! See p. 976 of this volume for a warning regarding purification of tetrahydrofuran.*]

6. By working quickly, the **imidazolium chloride** may be removed by suction filtration through a Buchner funnel. However, the precipitate should not be freed of solvent completely because **imidazolium chloride** is extremely hygroscopic. If the moist precipitate is washed with 50–100 ml. of anhydrous **tetrahydrofuran**, the yield of **1,1'-carbonyldiimidazole** may be slightly increased; however, there is some danger of the introduction of too much moisture into the reaction solution.

7. The checkers used an antifoaming head for the solvent evaporation.

8. In order to obtain a purer product the crude material may be recrystallized from hot anhydrous **tetrahydrofuran** with careful exclusion of moisture. After this operation the yield is reduced to 65–75%; the m.p. is then between 114° and 118°; e.g., recrystallization of 24.8 g. (91%) of **1,1'-carbonyldiimidazole** from 60 ml. of anhydrous **tetrahydrofuran** yielded 19.9 g. (73%); m.p. 116–118°.

3. Discussion

1,1'-Carbonyldiimidazole has been prepared by the reaction of **imidazole** and **phosgene** in anhydrous **benzene** and anhydrous **tetrahydrofuran**.^{3,4,5} It has also been obtained by the reaction of **1-(trimethylsilyl)imidazole** and **phosgene** in anhydrous **benzene**,⁶ but that method offers no advantages that justify the more extensive preparative effort required.

4. Merits of the Preparation

1,1'-Carbonyldiimidazole has been used for the preparation of such compounds as esters, anhydrides, amides, peptides, ketones, ethers, and isocyanates.² The present procedure provides a convenient method for its preparation in good yield.

This preparation is referenced from:

- *Org. Syn. Coll. Vol. 6, 560*

References and Notes

1. Department of Chemistry, University of Heidelberg, Heidelberg, Germany.
2. H. A. Staab, *Angew. Chem.*, **74**, 407 (1962); *Angew. Chem. Intern. Ed. Engl.*, **1**, 351 (1962).
3. R. Paul and G. W. Anderson, *J. Am. Chem. Soc.*, **82**, 4596 (1960); G. W. Anderson and R. Paul, *J. Am. Chem. Soc.*, **80**, 4423 (1958).
4. H. A. Staab, *Ann.*, **609**, 75 (1957).
5. H. A. Staab and K. Wendel, *Ber.*, **93**, 2910 (1960).
6. L. Birkofer, P. Richter, and A. Ritter, *Ber.*, **93**, 2804 (1960).

Appendix

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

ethanol (64-17-5)

sulfuric acid (7664-93-9)

Benzene (71-43-2)

sodium hydroxide (1310-73-2)

carbon dioxide (124-38-9)

Benzophenone (119-61-9)

sodium (13966-32-0)

phosgene (75-44-5)

Tetrahydrofuran (109-99-9)

Imidazole (288-32-4)

imidazolium chloride

1-(trimethylsilyl)imidazole (18156-74-6)

phosphorus pentoxide (1314-56-3)

1,1'-Carbonyldiimidazole,
Imidazole, 1,1'-carbonyldi- (530-62-1)