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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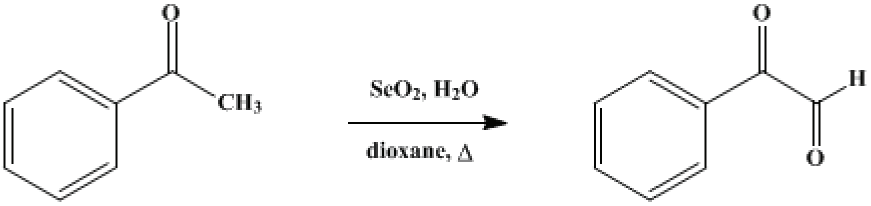
PHENYLGLYOXAL

[Glyoxal, phenyl-]



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1. Procedure

In a 1-l. three-necked, round-bottomed flask, fitted with a liquid-sealed stirrer and a reflux condenser, are placed 600 cc. of dioxane(Note 1), 111 g. (1 mole) of selenium dioxide (Note 2), and 20 cc. of water (Note 3). The mixture is heated to 50–55° and stirred until the solid has gone into solution, 120 g. (1 mole) of acetophenone is added in one lot, and the resulting mixture is refluxed with continued stirring for four hours (Note 4). The hot solution is decanted from the precipitated selenium, and the dioxane and water are removed by distillation through a short column. The phenylglyoxal is distilled at diminished pressure from a 250-cc. Claisen flask (Note 5), and the fraction boiling at 95–97°/25 mm. collected (Note 6). The yield is 93–96 g. (69–72 per cent of the theoretical amount) (Note 7).

The aldehyde sets to a stiff gel on standing, probably as the result of polymerization. It may be recovered without appreciable loss by distillation. Phenylglyoxal may be preserved also in the form of the hydrate, which is conveniently prepared by dissolving the yellow liquid in 3.5–4 volumes of hot water and allowing crystallization to take place (Note 8).

2. Notes

1. Ethyl alcohol (95 per cent) can also be used as solvent. The reaction can be carried out with an excess of acetophenone (2 moles) as solvent, but the results are less satisfactory. The dioxane can be recovered and used in later runs.
2. For the preparation of selenium dioxide, 200 g. (141 cc.) of concentrated nitric acid is heated in a 3-l. beaker on a hot plate under a good hood and 100 g. of selenium is added in portions of 5–10 g. A glass mechanical stirrer to break the foam hastens the process of oxidation. The resulting solution is transferred under the hood to a large evaporating dish and heated on a hot plate at a temperature not exceeding 200° until the selenious acid is completely dehydrated. The crude product is purified by sublimation. A 50-g. portion of the oxide is transferred to a 7-cm. porcelain crucible upon which is placed a 250-cc. filter flask through which a stream of cold water is run from the tap. The crucible is protected with asbestos and heated with a low flame until sublimation is complete (20–30 minutes). When the crucible has cooled, the sublimed selenium dioxide will be found wedged against the condenser. Extreme care should be used when working with selenium dioxide because of its poisonous properties.
An alternative procedure for the oxidation of selenium to the dioxide has been described by Hahn and Schales.[1]
3. Commercial selenious acid (129 g., 1 mole) may be used in place of the mixture of selenium dioxide and water.
4. After about two hours the solution becomes clear and little further precipitation of selenium is observable.
5. Several grams of the hydrate may be obtained by adding the fore-run to an equal volume of warm water and allowing the product to crystallize.
6. Boiling points reported in the literature are 120°/50 mm. and 142°/125 mm.

7. Phenylacetaldehyde may be used in place of acetophenone. Phenylmethylgloxal is obtained in a similar manner from propiophenone, and many other compounds containing a methylene group adjacent to a carbonyl group may be oxidized by means of selenium dioxide to the corresponding α-ketoaldehyde or α-diketone.[2]

For the oxidation of lepidine and quinaldine to the corresponding quinoline aldehydes, the selenium dioxide should be freshly prepared.[3]

8. The solubility of the hydrate at 20° is given in the literature as one part in about thirty-five parts of water. The melting points recorded range from 73° to 91°; the difference is said to be due to varying degrees of dryness of the samples.[4] The hydrate crystallizes well from water; chloroform, carbon disulfide, alcohol, or ether-ligroin also may be used for the purpose. Phenylglyoxal can be recovered from the hydrate by distillation in vacuum.

3. Discussion

Phenylglyoxal has been prepared from isonitrosoacetophenone through the bisulfite compound[4], [5] or by treatment with nitrosylsulfuric acid[6] or with nitrous acid.[7] It also has been prepared by the oxidation of benzoylcarbinol with copper acetate,[8] by heating bromophenacyl acetate,[9] and by the oxidation of acetophenone with selenium dioxide.[2]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 438
- Org. Syn. Coll. Vol. 5, 937

References and Notes

1. Hahn and Schales, Ber. **67**, 1823 (1934).
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3. Kaplan, J. Am. Chem. Soc. **63**, 2654 (1941).
4. Pinner, Ber. **35**, 4132 (1902); ibid. **38**, 1532 (1905).
5. v. Pechmann, ibid. **20**, 2904 (1887); Müller and v. Pechmann, ibid. **22**, 2556 (1889); Smedley, J. Chem. Soc. **95**, 218 (1909).
6. Neuberg and Hofmann, Biochem. Z. **229**, 443 (1930).
7. Neuberg and Hofmann, ibid. **239**, 495 (1931); Cusmano, Gazz. chim. ital. **68**, 130 (1938).
8. Nef, Ann. **335**, 271 (1904); Henze, Z. physiol. Chem. **198**, 83 (1931); ibid. **200**, 232 (1931).
9. Madelung and Oberwegner, Ber. **65**, 935 (1932).

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

ligroin

ethyl alcohol (64-17-5)

ether (60-29-7)

chloroform (67-66-3)

nitric acid (7697-37-2)

nitrous acid (7782-77-6)

Acetophenone (98-86-2)

selenium dioxide (7446-08-4)

Phenylglyoxal,
Glyoxal, phenyl- (1074-12-0)

carbon disulfide (75-15-0)

copper acetate (142-71-2)

Propiophenone (93-55-0)

nitrosylsulfuric acid (7782-78-7)

dioxane (5703-46-8)

selenium

phenylacetaldehyde (122-78-1)

selenious acid (7783-00-8)

Lepidine (491-35-0)

quinaldine (91-63-4)

isonitrosoacetophenone

benzoylcarbinol (582-24-1)

bromophenacyl acetate