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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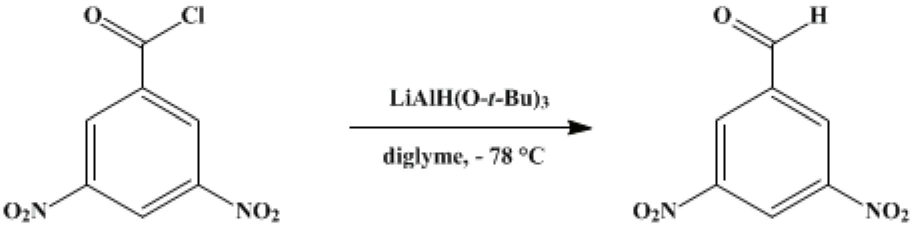
3,5-DINITROBENZALDEHYDE

[Benzaldehyde, 3,5-dinitro-]



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1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A 3-l., three-necked, round-bottomed flask is equipped with an efficient stirrer, a pressure-equalizing dropping funnel with a nitrogen inlet, and a Y-tube fitted with a low temperature thermometer and a nitrogen outlet. The outlet is vented through a bubbler tube, maintaining a slight positive pressure. The flask and dropping funnel are flamed in a stream of dry nitrogen (Note 1). To the flask is added 115.0 g. (0.4989 mole) of 3,5-dinitrobenzoyl chloride (Note 2) followed by 500 ml. of dry diglyme (Note 3). The solution is stirred vigorously, and the flask is immersed in a cooling bath at −78° (Note 4). A diglyme solution of lithium aluminum tri-*tert*-butoxyhydride (Note 5) is prepared in the following manner. Dry diglyme (450 ml.) is added with vigorous stirring to an Erlenmeyer flask containing 140.0 g. (0.5512 mole) of lithium aluminum tri-*tert*-butoxyhydride. After standing overnight, the resulting suspension is filtered under a blanket of dry nitrogen through a thick layer of Celite packed tightly on a Büchner funnel (Note 6). The flask containing the filtrate is kept stoppered until the reducing agent is transferred to the dropping funnel. Dropwise addition of this solution is started when the contents of the reaction flask reach −72°. There is a color change and a temperature rise of a few degrees. The rate of addition is adjusted, maintaining the temperature of the mixture between −78° and −68° (Note 7). After addition is complete the mixture is stirred at −78° for 30 minutes longer.

The cold reaction mixture is poured slowly with stirring into a 3-l. beaker containing 150 ml. of concentrated hydrochloric acid, 300 ml. of saturated aqueous sodium chloride, and 150 g. of ice. A white precipitate starts to separate (Note 8). An additional 150 ml. of saturated aqueous sodium chloride is added to the beaker and, after a minute, an upper layer begins to appear. The contents are transferred to a 2-l. separatory funnel and allowed to stand for 15 to 30 minutes while an upper brown layer separates. The upper layer is reserved while the lower layer is extracted with several portions of benzene, totalling 900 ml. The upper layer and the benzene extracts are combined and washed with seven 1-l. portions of water containing 10 ml. of concentrated hydrochloric acid. The benzene layer is washed successively with 100-ml. portions of aqueous 2% sodium hydrogen carbonate until the washings are basic, dried over 100 g. of anhydrous sodium sulfate, treated with 1 g. of charcoal, and filtered. The filtrate is concentrated at reduced pressure, yielding 59–62 g. (60–63%) of crude 3,5-dinitrobenzaldehyde, as a tan solid, m.p. 76–80°. Trituration in an ice bath with cold dry diethyl ether (*ca.* 0.3 ml./g.) gives a spongy solid, m.p. 85–87° (lit.[3] 85°), with losses of 5–10%, sufficiently pure for most uses. Further purification may be effected by recrystallization from toluene-hexane.

2. Notes

1. These operations are best done the day before the experiment is performed.
2. Since commercial 3,5-dinitrobenzoyl chloride is contaminated with 3,5-dinitrobenzoic acid, it was treated with thionyl chloride in boiling benzene under dry nitrogen. The product obtained after evaporation under vacuum melted at 68–70° and was stored over phosphorus pentoxide and potassium hydroxide in a vacuum desiccator.
3. "Diglyme" is the dimethyl ether of diethylene glycol. Commercial diglyme (Ansul Ether 141, Ansul Chemical Company, Marinette, Wisconsin) was used after drying over lithium aluminum hydride followed by distillation under reduced pressure; b.p. 59–61° (15 mm.).
4. An insulated bucket such as the "Nicer" available from B.F. Goodrich Company contains the mixture of dry ice and 2-propanol. Acetone foams excessively and has a high vapor pressure.
5. This hydride is obtained from Ventron, Inc., Beverly, Massachusetts.
6. Suspended particles will plug the dropping funnel in the subsequent operation. Two funnels may be used if the filtration is too slow.
7. At elevated temperatures reduction to the alcohol takes place. The addition time varies from 75 to 100 minutes.
8. The supernatant liquid is a brilliant yellow. A troublesome blue color may appear in an occasional run.

3. Discussion

3,5-Dinitrobenzaldehyde has been made previously by reducing 4-bromo-3,5-dinitrobenzaldehyde with copper(I) hydride.[3]

The method described is that of Brown.[4] Lithium aluminum tri-*tert*-butoxyhydride reduction of acid chlorides to aldehydes is a synthetic method of wide utility, and the yields of 20 aromatic and 10 aliphatic aldehydes so prepared have been tabulated.[5] This reagent is also used widely to reduce steroid aldehydes and ketones to alcohols, frequently at 0°.[6] Having only one active hydrogen, it has been used for the partial reduction of diketones to hydroxy ketones.[7] With proper temperature control, it does not affect oxido,[8] ester,[6,9] acetal,[10] nitrile, or nitro groups, or lactone rings,[8] all of which react with lithium aluminum hydride. In contrast to some other complex hydrides, this reagent may reduce a ketone stereoselectively, resulting in a high relative yield of the more stable epimeric alcohol[11] and an improved absolute yield.[7,12]

References and Notes

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

lithium aluminum tri-tert-butoxyhydride

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

diethyl ether (60-29-7)

hydrogen (1333-74-0)

thionyl chloride (7719-09-7)

sodium hydrogen carbonate (144-55-8)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

acetone (67-64-1)

potassium hydroxide (1310-58-3)

2-propanol (67-63-0)

lithium aluminum hydride (16853-85-3)

3,5-Dinitrobenzoic acid (99-34-3)

diglyme,
dimethyl ether of diethylene glycol (111-96-6)

3,5-Dinitrobenzaldehyde,
Benzaldehyde, 3,5-dinitro- (14193-18-1)

3,5-dinitrobenzoyl chloride (99-33-2)

toluene-hexane

4-bromo-3,5-dinitrobenzaldehyde

copper(I) hydride

phosphorus pentoxide (1314-56-3)