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.

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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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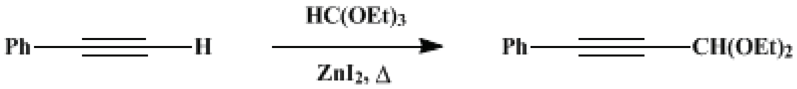
PHENYLPROPARGYLALDEHYDE DIETHYL ACETAL

[Propiolaldehyde, phenyl-, diethyl acetal]



Submitted by B. W. Howk and J. C. Sauer[1].
Checked by N. J. Leonard and S. W. Blum.

1. Procedure

Into a 300-ml. three-necked flask equipped with a nitrogen inlet, a thermometer, and a short fractionating column (Note 1) are charged 74.1 g. (0.50 mole) of triethyl orthoformate, 51.0 g. (0.50 mole) of phenylacetylene (Note 2), and 3.0 g. of zinc iodide (Note 3). Ethanol is slowly distilled from the reaction mixture, which must be heated to about 135° before refluxing in the still-head begins. A total of 29–35 ml. of distillate, b p. 65–88° (mostly 78°), is collected over a period of about 1 hour as the temperature of the reaction mixture gradually rises to 200° to 210° (Note 4). The reaction mixture is cooled to room temperature and filtered with suction. The flask and the small amount of precipitate on the filter paper are washed with 5 ml. of ether. The filtrate and ether washings are combined and distilled. After a small fore-run, phenylpropargylaldehyde diethyl acetal is collected at 99–100°/2 mm. The yield is 73–80 g. (72–78%), n_D^{25} 1.5153–1.5158. The synthesis is applicable to the preparation of other propargyl aldehyde acetals (Note 5).

2. Notes

1. The checkers found a 12-inch Vigreux column satisfactory.
2. The checkers purchased phenylacetylene (p. 763) from Gesellschaft für Teerverwertung mbH., Duisburg-Meiderich, Germany.
3. The submitters report that zinc nitrate appears to be equivalent to zinc iodide as a catalyst and that zinc chloride (commercial anhydrous grade) is satisfactory but requires 2–3 hours of heating and gives 64–70% yield.
4. Yields are lower under forcing conditions of prolonged heating.
5. The method has been applied by the submitters[2] to the preparation of cyclohexylmethylpropiolaldehyde diethyl acetal (54% yield) from cyclohexylmethylacetylene and triethyl orthoformate; of phenylethynyl *n*-butyl dimethyl ketal (40% yield) from phenylacetylene and trimethyl *n*-orthovalerate; and of phenylethynyl methyl diethyl ketal (34% yield) from phenylacetylene and triethyl orthoacetate. *n*-Butylpropiolaldehyde diethyl acetal was isolated in 32% yield by heating an equimolar mixture of 1-hexyne and triethyl orthoformate containing catalytic amounts of a zinc chloride-zinc iodide catalyst under autogenous pressure at 190° for 3 hours.

3. Discussion

The described method of preparing phenylpropargylaldehyde diethyl acetal is that of Howk and Sauer.[2] The method for synthesizing phenylpropargylaldehyde diethyl acetal previously published in *Organic Syntheses*[3] involves three steps beginning with cinnamaldehyde; over-all yields are 49–62%. Other methods of preparative value are the interaction of the Grignard reagent of phenylacetylene with triethyl orthoformate, or the sodium derivative of phenylacetylene with either triethyl orthoformate or ethyl formate. These reactions are discussed critically by Raphael.[4] Phenylpropargylaldehyde diethyl acetal has also been made by the action of the phenyl Grignard reagent with the diethyl acetal of chloropropiolaldehyde.[5]

The acetylenic acetals are easily hydrolyzed to the corresponding aldehydes in high yields in the presence of dilute acids.[3,4] Acetylenic acetals have also been of value in the synthesis of α,β-unsaturated ethylenic acetals or aldehydes by partial catalytic hydrogenation of the triple bond.[4]

References and Notes

1. Contribution No. 474 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours & Co. (Inc.), Wilmington, Delaware.
2. Howk and Sauer, *J. Am. Chem. Soc.*, **80**, 4607 (1958).
3. *Org. Syntheses Coll. Vol.* **3**, 732 (1955).
4. Raphael, *Acetylenic Compounds in Organic Synthesis*, pp. 68–75, Academic Press, New York, 1955.
5. Zakharkin, *Doklady Akad. Nauk S.S.S.R.*, **105**, 985 (1955) [*C. A.*, **50**, 11237a (1956)].

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

phenylethynyl n-butyl dimethyl ketal

phenylethynyl methyl diethyl ketal

zinc chloride-zinc iodide

sodium derivative of phenylacetylene

diethyl acetal of chloropropiolaldehyde

ethanol (64-17-5)

ether (60-29-7)

zinc chloride (7646-85-7)

cyclohexylmethylacetylene (17715-00-3)

triethyl orthoformate (122-51-0)

ethyl formate (109-94-4)

cinnamaldehyde

Phenylacetylene (536-74-3)

1-Hexyne (693-02-7)

Phenylpropargylaldehyde diethyl acetal (6142-95-6)

Propiolaldehyde, phenyl-, diethyl acetal

zinc iodide

zinc nitrate (13778-30-8)

cyclohexylmethylpropiolaldehyde diethyl acetal

triethyl orthoacetate (78-39-7)

trimethyl n-orthovalerate (13820-09-2)

n-Butylpropiolaldehyde diethyl acetal (18232-30-9)