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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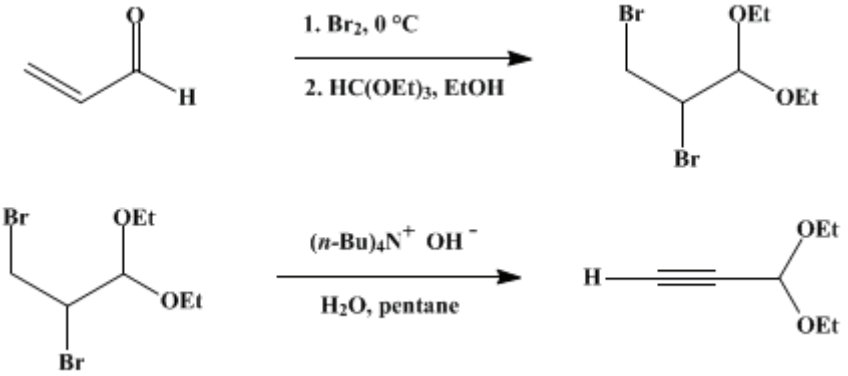
ALKYNES *via* PHASE TRANSFER–CATALYZED DEHYDROHALOGENATION: PROPIOLALDEHYDE DIETHYL ACETAL

[1-Propyne, 3,3-diethoxy-]



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Checked by G. Saucy and P. S. Manchand.

1. Procedure

A. 2,3-*Dibromopropionaldehyde diethyl acetal*. A 500-ml., three-necked, round-bottomed flask is equipped with a mechanical stirrer, a pressure-equalizing dropping funnel fitted with a calcium chloride drying tube, and a thermometer. The flask and dropping funnel are charged with 28.0 g. (0.500 mole) of freshly distilled acrolein and 80.0 g. (0.500 mole) of bromine, respectively. The acrolein is stirred rapidly and cooled to 0° in an ice–salt bath, then bromine is added at a rate such that the temperature is kept at 0–5°, until a permanent red color indicates a slight excess of bromine in the flask. A total of 78–79 g. of bromine is added over a 1-hour period. The crude 2,3-dibromopropionaldehyde is stirred while a solution of 80 g. (0.54 mole) of freshly distilled triethyl orthoformate in 65 ml. of absolute ethanol (Note 1) is added over 15 minutes. The solution warms to 45° and is stirred for 3 hours, after which ethyl formate, ethanol, and triethyl orthoformate are removed on a rotary evaporator. Distillation of the residual liquid through a 15-cm. Vigreux column affords 107–112 g. (74–77%) of 2,3-dibromopropionaldehyde diethyl acetal, b.p. 113–115° (11 mm.), as a pale-yellow liquid (Note 2).

B. *Propiolaldehyde diethyl acetal*. A 500-ml., three-necked, round-bottomed flask equipped with a mechanical stirrer (Note 3), a double-walled condenser, and a pressure-equalizing dropping funnel is charged with 100 g. (0.295 mole) (Note 4) of tetrabutylammonium hydrogen sulfate (Note 5) and 20 ml. of water. The mixture is stirred, forming a thick paste to which a solution of 29 g. (0.10 mole) of 2,3-dibromopropionaldehyde diethyl acetal in 75 ml. of pentane is added. The resulting mixture is stirred rapidly and cooled to 10–15° as a cold (10–15°) solution of 60 g. (1.5 moles) of sodium hydroxide in 60 ml. of water is added over 10 minutes. About 5 minutes later the pentane begins to boil and continues to reflux for another 10–20 minutes. The mixture is stirred for 2 hours at room temperature, cooled to 5°, and made slightly acidic (Note 6) by adding *ca.* 120 ml. of cold (*ca.* 5°) 25% sulfuric acid. Stirring is stopped, the layers are allowed to separate for 30 minutes, and the upper organic layer is carefully decanted (Note 7). The lower, aqueous layer is filtered, removing sodium sulfate, extracted with three 50-ml. portions of pentane, and, if desired, processed to recover the tetrabutylammonium salt (Note 8). The pentane solutions are combined, dried over anhydrous sodium sulfate, and evaporated. The colorless concentrate is distilled, giving 7.8–8.6 g. (61–67%) of propiolaldehyde diethyl acetal as a colorless liquid, b.p. 138–139° (760 mm.), 95–96° (170 mm.) (Note 9).

2. Notes

1. Absolute ethanol from a commercial supplier was used without further treatment.
2. The submitters report a yield of 113–122 g. (78–84%), b.p. 113–115° (11 mm.) (lit.,[2] b.p. 108–110°, 10 mm.). The product obtained by the checkers was analyzed. Analysis calculated for $C_7H_{14}Br_2O_2$: C, 28.99; H, 4.87; Br, 55.11. Found: C, 28.81; H, 4.88; Br, 55.37. The ^{1}H NMR spectrum ($CDCl_3$), δ (multiplicity, coupling constant *J* in Hz., number of protons, assignment): 1.27 (t, *J* = 7, 6H, 2 OCH_2CH_3), 3.6–3.9 (m, 6H, 2 OCH_2CH_3 and CH_2Br), 4.22 (apparent d of t, *J* = 4 and 7, 1H, C*H*Br), 4.72 (d, *J* = 4, 1H, C*H*).
3. The submitters used a 1-l. Erlenmeyer flask and a magnetic stirrer. The Erlenmeyer flask was recommended to minimize splattering of the pasty mixture into the condenser. The checkers preferred a 500-ml., round-bottomed flask equipped as described above.
4. The submitters found that the yield of product was reduced to *ca.* 50% when only 1 equivalent (0.2 mole) of tetrabutylammonium hydrogen sulfate was used.
5. The submitters purchased tetrabutylammonium hydrogen sulfate (97% pure) from Fluka AG, Buchs, Switzerland; it was obtained by the checkers from Aldrich Chemical Company, Inc.
6. Care must be exercised during acidification, since excess sulfuric acid lowers the yield, presumably through hydrolysis of the acetal.
7. The checkers often obtained a thick emulsion which separated into three layers after standing for *ca.* 2 hours. When this occurred, the mixture was poured into 500 ml. of water, and the product was extracted with three 150-ml. portions of pentane.
8. The following unchecked procedure has been provided by the submitters for the purpose of recovering the tetrabutylammonium salt. The aqueous layer, which contains 12 g. of sodium bromide, is extracted with two 100-ml. portions of dichloromethane. The solution is dried and evaporated, giving 91–93 g. (96–98%) of crude tetrabutylammonium bromide which can be recrystallized from ethyl acetate or employed directly for regenerating the hydrogen sulfate salt. The submitters recommend that the bromide be accumulated from several runs and then converted to the hydrogen sulfate by the procedure of Brandström.[3] A two-necked, round-bottomed flask fitted with a short distillation column and a dropping funnel is charged with 196 g. (0.609 mole) of recovered tetrabutylammonium bromide and 300 ml. of chlorobenzene. The contents of the flask are heated, and 92 g. (0.73 mole) of dimethyl sulfate is then added dropwise to the hot solution. The methyl bromide formed distills from the flask and is collected in a trap cooled with acetone–dry ice. As the rate of production of methyl bromide decreases, the heating is increased until the temperature at the top of the distillation column starts to rise rapidly. A solution of 1.5 ml. of concentrated sulfuric acid in 600 ml. of water is then cautiously added. The mixture is heated at reflux for 48 hours and evaporated to dryness under reduced pressure. After the residue has been dissolved in 500 ml. of dichloromethane, the resulting solution is washed with two 50-ml. portions of water and dried with anhydrous sodium sulfate. Evaporation of the solvent provides 202.5 g. of almost pure tetrabutylammonium hydrogen sulfate which can be recrystallized from isobutyl methyl ketone.
9. The submitters report a yield of 8.6–9.5 g. (67–74%), b.p. 95–96° (170 mm.) (lit.,[2] b.p. 138–139.5°, 760 mm.). The submitters recommend that the product be distilled under reduced pressure. The spectral characteristics of the product are as follows: IR (liquid film) cm.$^{-1}$: 3260 (≡CH), 2125 (C≡C); ^{1}H NMR ($CDCl_3$), δ (multiplicity, coupling constant *J* in Hz., number of protons, assignment): 1.24 (t, *J* = 7, 6H, $2CH_3$), 2.58 (d, *J* = 2, 1H, ≡C*H*), 3.71 (apparent q of d, *J* = 7 and 2, 4H, $2CH_AH_BCH_3$), 5.21 (d, *J* = 2, 1H, $CH(OC_2H_5)_2$).

3. Discussion

The preparation of 2,3-dibromopropionaldehyde diethyl acetal described here is based on the procedure of Grard.[2,4] The dehydrobromination of the dibromide to propiolaldehyde diethyl acetal has previously been carried out with potassium hydroxide in ethanol.[2,4] and with sodium amide in liquid ammonia.[5] In the present procedure the elimination is effected with aqueous sodium hydroxide in the presence of the phase-transfer agent, tetrabutylammonium hydrogen sulfate.[6,7] The principal advantage of the phase-transfer procedure is its operational simplicity. The method has been used to prepare diphenylacetylene (75%), phenylacetylene (87%), *p*-tolylacetylene (77%), and 3-chloropropiolaldehyde diethyl acetal (70%).[8] The halide reactants were the corresponding 1,2-dibromides in the first two examples and vinyl chlorides in the second two cases. The yields obtained with this method are better than those from traditional procedures, and the conditions are generally milder. In addition, the extent of

substitution and dehalogenation, side reactions that frequently complicate the synthesis of acetylenes by elimination with alkoxide or amide bases, is diminished.[9] The ability to recover efficiently the tetrabutylammonium salt enhances the practicality of this procedure.[3]

Propiolaldehyde diethyl acetal has found numerous synthetic applications in the literature. The compound has been utilized in the synthesis of unsaturated and polyunsaturated acetals and aldehydes by alkylation of metallated derivatives,[5,10,11,12,13] by Cadiot-Chodkiewicz coupling with halo acetylenes,[13,14] and by reaction with organocuprates.[15] Syntheses of heterocyclic compounds including pyrazoles,[16] isoxazoles,[16] triazoles,[2] and pyrimidines[17,18] have employed this three-carbon building block. Propiolaldehyde diethyl acetal has also been utilized in the synthesis of naturally occurring polyacetylenes[19,20,21,22,23] and steroids.[24]

References and Notes

1. Laboratoire de Synthése Organique, Université de Rennes, Rennes, France.
2. J. C. Sheehan and C. A. Robinson, *J. Am. Chem. Soc.*, **71**, 1436 (1949).
3. A. Brandström, "Preparative Ion Pair Extraction," Apotekarsocieteten/Hässle Läkemedel, Sweden, 1974, pp. 141–142.
4. M. Grard, *Justus Liebigs Ann. Chem.*, **13**, 336 (1930).
5. J. P. Ward and D. A. Van Dorp, *Recl. Trav. Chim. Pays-Bas*, **85**, 117 (1966).
6. For reviews, see E. V. Dehmlow, *Angew. Chem. Int. Ed. Engl.*, **16**, 493 (1977); W. P. Weber and G. W. Gokel, "Phase Transfer Catalysis in Organic Synthesis," Springer-Verlag, Berlin, 1977.
7. For other procedures using phase-transfer catalysis in this series, see M. Makosza and A. Jonczyk, *Org. Synth.*, **Coll. Vol. 6**, 897 (1988); G. W. Gokel, R. P. Widera, and W. P. Weber, *Org. Synth.*, **Coll. Vol. 6**, 232 (1988).
8. A. Gorgues and A. Le Coq, *Tetrahedron Lett.*, 4723 (1976).
9. G. Köbrich and P. Buck, "Synthesis of Acetylenes and Polyacetylenes by Elimination Reactions," in H. G. Viehe, Ed., "Chemistry of Acetylenes," Dekker, New York, 1969, pp. 99–168.
10. Unilever N. V., Neth. Pat. 296,925 (1965) [*Chem. Abstr.*, **65**, 13547c (1966)].
11. E. K. Raunio and H. A. Schroeder, *J. Org. Chem.*, **22**, 570 (1957).
12. P. H. M. Schreurs, W. G. Galesloot, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, **94**, 70 (1975).
13. J. P. Ward and D. A. Van Dorp, *Recl. Trav. Chim. Pays-Bas*, **86**, 545 (1967).
14. A. Gorgues, *Justus Liebigs Am. Chem.*, **7**, 211, 373 (1972).
15. A. Alexakis, A. Commercon, J. Villieras, and J. F. Normant, *Tetrahedron Lett.*, 2313 (1976).
16. L. Claisen, *Ber. Dtsch, Chem. Ges.*, **31**, 1021 (1898); L. Claisen, *Ber. Dtsch. Chem. Ges.* **36**, 3664 (1903).
17. M. L. A. Fluchaire and G. L. A. Bost, U.S. Pat. 2,497,163 (1950) [*Chem. Abstr.*, **44**, 5908a (1950)].
18. G. W. Hearne, T. W. Evans, and H. L. Yale, U.S. Pat., 2,455,172 (1948) [*Chem. Abstr.*, **43**, 1813f (1949)].
19. F. Bohlmann and H. Bornowski, *Chem. Ber.*, **94**, 3189 (1961).
20. S. Prévost, J. Meier, W. Chodkiewicz, P. Cadiot, and A. Willemart, *Bull. Soc. Chim. Fr.*, 2171 (1961).
21. A. G. Fallis, M. T. W. Hearn, E. R. H. Jones, V. Thaller, and J. L. Turner, *J. Chem. Soc., Perkin Trans. 1*, 743 (1973).
22. C. A. Higham, E. R. H. Jones, J. W. Keeping, and V. Thaller, *J. Chem. Soc., Perkin Trans. 1*, 1991 (1974).
23. E. R. H. Jones, V. Thaller, and J. L. Turner, *J. Chem. Soc., Perkin Trans. 1*, 424 (1975).
24. M. Rosenberger, A. J. Duggan, R. Borer, R. Muller, and G. Saucy, *Helv. Chim. Acta*, **55**, 2663 (1972).

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

1,2-dibromides

ACETAL (105-57-7)

ethanol (64-17-5)

sulfuric acid,
hydrogen sulfate (7664-93-9)

ammonia (7664-41-7)

ethyl acetate (141-78-6)

sodium hydroxide (1310-73-2)

Acrolein (107-02-8)

bromide (24959-67-9)

bromine (7726-95-6)

sodium bromide (7647-15-6)

sodium sulfate (7757-82-6)

dimethyl sulfate (77-78-1)

chlorobenzene (108-90-7)

potassium hydroxide (1310-58-3)

methyl bromide (74-83-9)

triethyl orthoformate (122-51-0)

ethyl formate (109-94-4)

Pentane (109-66-0)

isobutyl methyl ketone (108-10-1)

dichloromethane (75-09-2)

Phenylacetylene (536-74-3)

sodium amide (7782-92-5)

Diphenylacetylene (501-65-5)

tetrabutylammonium bromide (1643-19-2)

Propiolaldehyde diethyl acetal,
1-Propyne, 3,3-diethoxy- (10160-87-9)

2,3-dibromopropionaldehyde (5221-17-0)

2,3-Dibromopropionaldehyde diethyl acetal (10160-86-8)

3-chloropropiolaldehyde diethyl acetal

tetrabutylammonium

tetrabutylammonium hydrogen sulfate (32503-27-8)

p-tolylacetylene (766-97-2)