A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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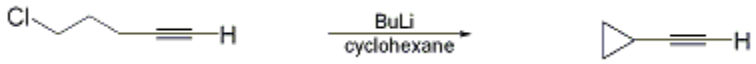
CYCLOPROPYLACETYLENE

[Cyclopropane, ethynyl-]



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Checked by Paul J. Hergenrother and Stephen F. Martin.

1. Procedure

Caution! Butane gas is evolved during the course of the reaction. This preparation should be conducted in a well-ventilated hood.

A 3-L, three-necked, round-bottomed flask is equipped with a mechanical stirrer, a 1-L pressure-equalizing addition funnel, and a reflux condenser that is topped with a nitrogen inlet. The flask is charged with 102 g (1.0 mol) of 5-chloro-1-pentyne and 250 mL of cyclohexane (Note 1), and the mixture is cooled to 0°C. The cooled solution is reacted with 1.05 L of butyllithium (2.0 M in cyclohexane, 2.1 mol , 2.1 equiv) (Note 2) that is added dropwise via the addition funnel over 1.5 hr maintaining the temperature < 20°C (Note 3). After the addition is complete, the mixture is heated to reflux (78°C) and maintained at reflux for 3 hr (Note 4), (Note 5). The reaction is cooled to 0° to −10°C and then quenched carefully by the *dropwise* addition of aqueous saturated ammonium chloride (750 mL) (*Caution*: the quench is very exothermic; (Note 6).) After the quench is complete, the lower (aqueous) layer is separated and the organic layer is fractionally distilled through a 40-cm × 2.3-cm Hempel column containing Pro-Pak® Monel distillation packing, 0.24" × 0.24" (from Ace Glass). A total of 80-110 mL in the boiling range of 35-78°C is collected. This fraction typically contains 60-80 wt% of cyclopropylacetylene with the remainder being cyclohexane and butane (Note 7), (Note 8). The fraction is then distilled a second time through a 30-cm × 2.3-cm packed column and 39-41 g of cyclopropylacetylene, bp 52°-55°C, is collected (58% yield, corrected for purity) (Note 9), (Note 10).

2. Notes

1. 5-Chloro-1-pentyne was purchased from Farchan Laboratories. It is also available from Aldrich Chemical Company, Inc. A freshly opened bottle of cyclohexane contained 16 μg/mL of water (Karl Fisher). If needed, the cyclohexane can be dried over 3Å or 4Å molecular sieves.
2. The use of butyllithium in cyclohexane rather than hexanes was essential to facilitate product purification. Separation of cyclopropylacetylene (bp 52°C) from hexanes (bp 69°C) was more difficult than from cyclohexane (bp 81°C).
3. A thick precipitate was formed as the butyllithium was added. Care should be taken to avoid excessive splashing of the solid onto the walls of the flask, which can result in decreased yield.
4. The reaction was kept under a slight positive pressure of nitrogen that was vented through an oil bubbler. The butane gas escapes through the bubbler during the reflux. An efficient condenser cooled with water from an ice/water bath is necessary.
5. The reaction was monitored by GLC using an HP-5 column: 25-m × 0.32-mm × 0.52-mm fused silica capillary column with a flow rate of 0.5 mL/min of helium.
6. The temperature of the reaction mixture in this highly exothermic manipulation should be kept below 20°C to avoid loss of the low-boiling product. An addition funnel can be used for the dropwise delivery of the aqueous saturated ammonium chloride solution, while leaving the reflux condenser in place.
7. The receiving flask should be cooled in an ice bath to minimize loss of product.
8. If the distillation was terminated sooner, e.g. at 60°C, a significant amount of cyclopropylacetylene was left in the pot. The pot residue should be assayed to ensure that a significant amount of product was not left behind.
9. This fraction typically contains 5-7 mol% of cyclohexane as measured by NMR. Collection of a

narrower boiling range can yield product with less cyclohexane but at lower recovery.
10. The product showed the following NMR data: ^{1}H (300 MHz, $CDCl_3$) δ: 0.65-0.78 (m, 4 H), 1.17-1.27 (m, 1 H), 1.73 (d, 1 H, J = 2.2) . The sample also exhibited a singlet at δ 1.4 corresponding to 7.6 mol% of cyclohexane ; ^{13}C (75 MHz, $CDCl_3$) δ: −0.8, 8.1, 63.4, 87.6 and cyclohexane at 26.9 .

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

Cyclopropylacetylene has been prepared in a two-step procedure by dichlorination of cyclopropyl methyl ketone with phosphorus pentachloride (PCl_5) followed by double dehydrohalogenation with strong base.[2,3,4,5,6,7] This sequence presented significant scale-up problems and the overall yields were low (20-25%). Results in our hands have been unreliable, especially for the chlorination step that employs solid PCl_5 followed by quenching over ice. The reaction must be kept cold to prevent opening of the cyclopropyl ring by hydrogen chloride (HCl) to give 2,5-dichloro-2-pentene , which was a major by-product and often the only product of the reaction. Hanack and Bässler[5] report quantitative cyclopropane ring opening unless highly purified PCl_5 was employed. Hanack[6] was able to improve the chlorination step by using carbon tetrachloride (CCl_4) as the reaction solvent, but his overall yield to cyclopropylacetylene was only 21%. Salaun[7] improved the elimination step by use of potassium t-butoxide in dimethyl sulfoxide (DMSO). In a similar manner cyclopropylacetylene has been prepared by base-induced dehydrohalogenation of bromovinylcyclopropane .[2] Cyclopropylacetylene has also been prepared from the 1-trimethylsilyl derivative of cyclopropylacetylene, which was prepared by treatment of 5-chloro-1-trimethylsilyl-1-pentyne with lithium diisopropylamide at −78°C followed by warming to room temperature, although no details for the desilylation reaction and product isolation are given.[8]

The method presented here offers the advantage of being a one-pot procedure from a commercially available starting material. The initially formed acetylide anion of 5-chloro-1-pentyne undergoes a second deprotonation to the dianion that then cyclizes to cyclopropylacetylide anion. Cyclopropylacetylene itself is a useful building block, but this method can be extended as an in situ source of cyclopropylacetylide anion that can be trapped with a variety of electrophiles to give other useful building blocks. For example, we have used this method to synthesize trifluoromethyl cyclopropylethynyl ketone in 60% isolated yield by quenching the acetylide anion with ethyl trifluoroacetate.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);

(Registry Number)

Cyclopropylacetylene:
Cyclopropane, ethynyl- (8,9); (6746-94-7)

5-Chloro-1-pentyne:
1-Pentyne, 5-chloro- (8,9); (14267-92-6)

Butyllithium:
Lithium, butyl- (8); (109-72-8)