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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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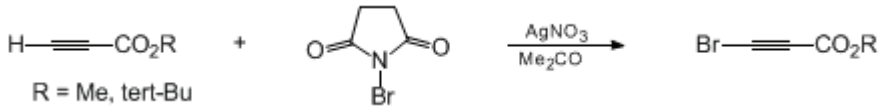
PREPARATION OF 3-BROMOPROPIOLIC ESTERS:METHYL AND tert-BUTYL 3-BROMOPROPIOLATES

[2-Propynoic acid, 3-bromo-, methyl and 1,1-dimethylethyl esters]



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1. Procedure

CAUTION! Propiolates and their bromo derivatives are lachrymators and must be handled under an efficient hood. Distillation of bromopropiolates should be carried out behind a safety shield (Note 1).

Methyl 3-bromopropiolate. A 250-mL, one-necked, round-bottomed flask equipped with a magnetic stirring bar is charged with 100 mL of acetone (Note 2) and 4.0 g (47.6 mmol) of methyl propiolate (Note 3). To the stirred solution at room temperature is added 0.8 g (4.7 mmol) of silver nitrate. After 5 min, 9.8 g of N-bromosuccinimide (55 mmol) is added at once. The homogeneous mixture becomes cloudy and a grayish precipitate develops. Stirring is continued for 2 hr (Note 4). The solids are filtered through a pad of Celite, which is rinsed with acetone (30–50 mL). After careful rotary evaporation of the acetone at ≈20°C under 20 mm, the oily residue is bulb-to-bulb distilled at room temperature under reduced pressure (≈0.1 mm), affording methyl 3-bromopropiolate as a colorless liquid (7.0–7.5 g, 42.9–46.0 mmol, 90–97%) solidifying in the refrigerator (mp ≈20°C) (Note 5).

tert-Butyl 3-bromopropiolate. tert-Butyl propiolate (Note 6) (5.42 g, 42.8 mmol) dissolved in 150 mL of acetone is treated as above with 0.8 g of silver nitrate (4.7 mmol) and, after 5 min of stirring at room temperature, with 9.8 g (55 mmol) of N-bromosuccinimide introduced at once into the suspension. Stirring is continued for 90 min. The solids are filtered through a pad of Celite, rinsed with acetone (30–50 mL) and the filtrate is concentrated at 20–25°C (20 mm) to give a white pasty solid. Water (80 mL) is added and the mixture is extracted with ether (3 × 80 mL). The ethereal layer is dried over anhydrous magnesium sulfate and the solvent is evaporated, leaving a semi-solid residue which is bulb-to-bulb distilled in an oil-bath at 45–50°C (≈0.1 mm) to give tert-butyl 3-bromopropiolate as a white semi-solid (8.51 g, 41.5 mmol, 97%) (Note 7).

2. Notes

1. Explosions during distillation of certain bromoalkynes have been reported.[2] Although methyl 3-bromopropiolate was not specifically cited, precautionary measures are recommended. The tert-butyl ester is a new compound[3] and must be handled like the methyl ester.
2. Acetone may be redistilled before use to remove the eventual autocondensation product, 4-hydroxy-4-methyl-2-pentanone (diacetone alcohol, bp 166°C). The submitter used, as received, fresh 99% pure acetone from Prolabo.
3. Methyl propiolate 99%, N-bromosuccinimide 99%, and silver nitrate were obtained from Janssen Chimica and used as received.
4. One hour of stirring is usually sufficient for completion of the reaction, but this time can be exceeded; longer reaction times improve the succinimide particle size, which aids the subsequent filtration. The product seems to adhere to the succinimide.
5. Depending on the conditions of the preliminary evaporation this product is contaminated with up to 5% of residual acetone. Nevertheless, it can be considered as pure enough for certain uses. Complete

removal of acetone may be obtained by distillation in a small Vigreux column, although a yellowing of the distillate is observed: bp 86–88°C/100 mm (lit.[2] 88°C/100 mm and lit.[4] 40–45°C/5 mm). The spectral and analytical properties of methyl 3-bromopropiolate are as follows: ^{1}H NMR (200 MHz, $CDCl_3$) d: 3.73 (s, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 52.8 (C-3), 52.9 (CH_3), 72.4 (C-2), 152.8 (C-1). Anal. Calcd for $C_4H_3BrO_2$ (undistilled sample): C, 29.48; H, 1.86; Br, 49.03. Found: C, 29.11; H, 1.92; Br 48.79.

6. tert-Butyl propiolate was prepared from propiolic acid and isobutene in the presence of sulfuric acid.[5] It is now commercially available from Fluka Chemical Corp. and Aldrich Chemical Company, Inc.

7. Although pure enough to be used as obtained, tert-butyl 3-bromopropiolate may be distilled in a Vigreux column at 75–77°C (15 mm) to give a colorless oil crystallizing as plates: mp 25–27°C. The spectral and analytical properties of tert-butyl 3-bromopropiolate are as follows: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.46 (s, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 27.8 (CH_3), 50.0 (C-3), 73.9 (C-2), 84.0 (CMe_3), 151.3 (C-1). Anal. Calcd for $C_7H_9BrO_2$ (undistilled sample): C, 41.00; H, 4.42; Br, 38.48. Found: C, 40.48, H, 4.40; Br, 38.10.

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

Methyl 3-bromopropiolate has been prepared by esterification of 3-bromopropiolic acid with methanol and sulfuric acid for 6 days (75% yield),[4] the starting bromo acid being prepared by bromination of propiolic acid with aqueous potassium hypobromite.[6] This reaction is particularly delicate to control, giving erratic results. Moreover, direct bromination of methyl propiolate with sodium hypobromite[2] could not be reproduced.

Bromination of 1-alkynes with N-bromosuccinimide in the presence of catalytic amounts of silver nitrate, was used first for the bromination of 17-ethynyl steroids.[7] Similarly, N-iodosuccinimide led to 17-iodoethynyl steroids. Iodination of propiolates in this way has not been studied. A recent method of preparation of 1-iodoalk-1-ynes under phase-transfer conditions involves molecular iodine and copper (I) iodide as catalyst, in the presence of potassium or sodium carbonate as a base. Ethyl 3-iodopropiolate was prepared by this route in 80% yield.[8]

The present procedure provides ready access to 3-bromopropiolic esters, the methyl ester requiring adapted work up, because of its low boiling point. Less volatile esters, like tert-butyl, can be conveniently isolated by a standard aqueous-extraction work up.

Methyl 3-bromopropiolate has been used in Diels-Alder reactions either as a methoxycarbonyl ketene equivalent[9] [10] or for the synthesis of functionalized naphthalenes.[11]

References and Notes

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

METHYL AND tert-BUTYL 3-BROMOPROPIOLATES

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

methanol (67-56-1)

ether (60-29-7)

silver nitrate (7761-88-8)

sodium carbonate (497-19-8)

iodine (7553-56-2)

acetone (67-64-1)

4-hydroxy-4-methyl-2-pentanone (123-42-2)

sodium hypobromite

copper(I) iodide (7681-65-4)

magnesium sulfate (7487-88-9)

isobutene (9003-27-4)

potassium hypobromite

N-bromosuccinimide (128-08-5)

methyl propiolate (922-67-8)

N-Iodosuccinimide (516-12-1)

propiolic acid (471-25-0)

Methyl 3-bromopropiolate,
2-Propynoic acid, 3-bromo-, methyl ester (23680-40-2)

tert-Butyl propiolate (13831-03-3)

tert-Butyl 3-bromopropiolate,
2-Propynoic acid, 3-bromo-, 1,1-dimethylethyl ester

3-bromopropiolic acid

Ethyl 3-iodopropiolate