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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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.

DOI:10.15227/orgsyn.072.0112

Organic Syntheses, Coll. Vol. 9, p.415 (1998); Vol. 72, p.112 (1995).

STEREOSPECIFIC SYNTHESIS OF ETHYL (Z)-3-BROMO-2-PROPENOATE

[2-Propenoic acid, 3-bromo-, ethyl ester, (Z)-]

Submitted by Shengming Ma and Xiyan Lu[1].
Checked by Qingzhi Gao and Hisashi Yamamoto.

1. Procedure

Ethyl (2Z)-3-bromopropenoate. To a three-necked, round-bottomed flask are added lithium bromide (10.0 g, 0.115 mol, (Note 1)), acetonitrile (100 mL, (Note 2)), acetic acid (7.0 g, 0.116 mol, (Note 3)), and ethyl 2-propynoate (9.0 g, 0.092 mol, (Note 4), (Note 5)) under nitrogen. The reaction is carried out with magnetic stirring under reflux and monitored by GLC (Note 6). The reaction is complete after 24 hr. The reaction is cooled, water (20 mL) is added to the flask, and the mixture is cautiously neutralized with solid potassium carbonate, added in portions (Note 3). The organic layer is separated, and the aqueous layer is extracted with ether (3 × 20 mL) (Note 3). The combined organic layers are dried with magnesium sulfate and filtered. After removal of the solvent, ethyl (2Z)-3-bromopropenoate is obtained by vacuum distillation (14.0 g, yield, 85%, (Note 7)).

2. Notes

1. Lithium bromide (reagent grade) was dried over phosphorus pentoxide (P_2O_5) with heating at 100°C under vacuum.
2. Acetonitrile was distilled from P_2O_5 before use.
3. Acetic acid, potassium carbonate and ether are reagent grade.
4. The optimum ratio of starting materials for this reaction is LiBr : CH_3CO_2H : 2-propynoate = 1.25 : 1.25 : 1.
5. Ethyl 2-propynoate is available from Aldrich Chemical Company, Inc.
6. GLC was performed on a 2-m column (10% OV-1 supported on 102 silanized white support, 60–80 mesh) at 90°C.
7. Ethyl (2Z)-bromopropenoate boils at 92–93°C/40 mm. Isomerization was not detected during careful distillation (bath temperature: <115°C). The spectral data are as follows: IR (neat) cm^{-1}: 1730, 1605, 1200, 1185; MS m/e: 181 [$M^+(^{81}Br)+1$]/179 [$M^+(^{79}Br)+1$]: ^1H NMR (200 MHz, $CDCl_3$) δ: 1.31 (t, 3 H, J = 7.0), 4.24 (q, 2 H, J = 6.2), 6.61 (d, 1 H, J = 8.4), 6.99 (d, 1 H, J = 8.4). No E isomer was detected by ^1H NMR, GLC (Note 6), or TLC on silica gel (eluent: petroleum ether : CH_3CO_2Et = 10:1).

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

3-Halopropenoic acids and their derivatives are valuable intermediates in organic synthesis because three functional groups are present: the C-X bond, the conjugated C=C bond, and the carbonyl group. These compounds can be used to react with nucleophiles,[2] and, as vinyl halides, to introduce a cis olefinic moiety into an organic molecule using organometallic methods, for the synthesis of (2Z)-en-4-ynoic and (2Z,4Z)- and (2Z,4E)-dienoic acid derivatives.[3] Usually such compounds are prepared as a Z and E isomeric mixture. Only a few stereoselective synthetic methods have been reported, most of which are for E isomers. For example, the title compound was reported to be prepared as a Z and E

isomeric mixture via the reaction of ethyl 2-propynoate with hydrogen bromide in acetic acid.[4] The only possible route for its synthesis is by esterification of (2Z)-3-bromopropenoic acid[5] according to the method for methyl (2Z)-3-chloropropenoate, but isomerization may occur during the prolonged heating of esterification.[6] No one-step method for the synthesis of the pure Z isomer is available. The stereospecific method described here can also be applied to the synthesis of (2Z)-3-halopropenoic acids,[7,8] (2Z)-3-halopropenoates,[7,8,9] (2Z)-3-halo-propenamides,[8] and (2Z)-3-halopropenenitriles[8] (X=I, Br, Cl). In the case of the iodide, sodium iodide and lithium iodide gave similar results, but it is necessary to carry out the reaction under N_2.[9] With the bromide and chloride, lithium salts gave higher yields than sodium salts. The mechanism of this reaction is believed to involve nucleophilic addition of halide anion to the electron-deficient, carbon-carbon triple bond. The stability of a termolecular transition state or stereoelectronic stabilization of the anion intermediate formed in situ by the nucleophilic addition might be responsible for the high stereospecificity.[8]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 9, 510

References and Notes

1. Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai 200032, China.
2. Miyaura, N.; Sasaki, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* **1977**, 3369; Smith, III, A. B.; Kilényi, S. N. *Tetrahedron Lett.* **1985**, *26*, 4419; Dodd, D.; Johnson, M. D.; Meeks, B. S.; Titchmarsh, D. M.; Duong, K. N. V.; Gaudemer, A. *J. Chem. Soc., Perkin Trans. II* **1976**, 1261.
3. Yanagi, T.; Ohe, T.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3892; Lu, X.; Huang, X.; Ma, S. *Tetrahedron Lett.* **1992**, *33*, 2535.
4. Maclnnes, I.; Schorstein, D. E.; Suckling, C. J.; Wrigglesworth, R. *J. Chem. Soc., Perkin Trans. I* **1981**, 1103.
5. Just, G.; Ouelett, R. *Can. J. Chem.* **1976**, *54*, 2925.
6. Bowden, K. *Can. J. Chem.* **1966**, *44*, 661.
7. Ma, S.; Lu, X. *J. Chem. Soc., Chem. Commun.* **1990**, 1643.
8. Ma, S.; Lu, X.; Li, Z. *J. Org. Chem.* **1992**, *57*, 709.
9. Ma, S.; Lu, X. *Tetrahedron Lett.* **1990**, *31*, 7653.

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

silica gel

petroleum ether

P_2O_5

LiBr

CH_3CO_2H

CH_3CO_2Et

potassium carbonate (584-08-7)

acetic acid (64-19-7)

ether (60-29-7)

acetonitrile (75-05-8)

hydrogen bromide (10035-10-6)

nitrogen (7727-37-9)

sodium iodide (7681-82-5)

magnesium sulfate (7487-88-9)

ethyl 2-propynoate (623-47-2)

lithium iodide (10377-51-2)

lithium bromide (7550-35-8)

phosphorus pentoxide (1314-56-3)

2-propynoate

Ethyl (2Z)-3-bromopropenoate,
ETHYL (Z)-3-BROMO-2-PROPENOATE,
2-Propenoic acid, 3-bromo-, ethyl ester, (Z)- (31930-34-4)

Ethyl (2Z)-bromopropenoate

(2Z)-3-bromopropenoic acid (1609-92-3)

methyl (2Z)-3-chloropropenoate