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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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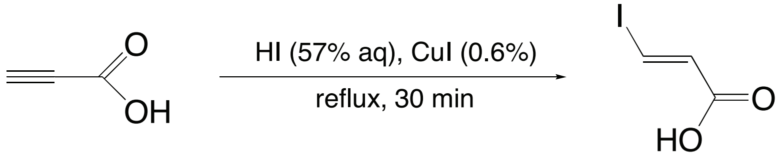
# COPPER(I)-CATALYZED PREPARATION OF (*E*)-3-IODOPROP-2-ENOIC ACID

## [(2-Propenoic acid, 3-iodo-, (2*E*)-)]



Submitted by Darren J. Dixon, Steven V. Ley, and Deborah A. Longbottom.[1]
Checked by Michelle DeRitter and Steven Wolff.

## 1. Procedure

A 250-mL, three-necked, round-bottomed flask, equipped with a magnetic stirring bar, thermometer and water condenser, is charged with copper(I) iodide (200 mg, 1.1 mmol) (Note 1) and hydriodic acid (57% aq, 40 mL) (Notes 2, 3). Propiolic acid (10 ml, 162 mmol) (Note 4) is added over 1 min via syringe (Note 5), during which time the reaction temperature rises to ~100 °C. The reaction mixture is immediately immersed in an oil bath, preheated with a thermostatically controlled stirrer-hotplate to 130 °C (Note 6) and a gentle reflux (110 °C) is reached after ~4 min. The mixture is heated to reflux for a further 30 min, then the oil bath is removed and replaced with a room temperature water bath. The vigorously stirred reaction mixture is allowed to cool to 28 °C over 15 min (Note 7), during which time a large quantity of white needles crystallizes from the reaction mixture (Note 8). The solution is stirred for a further 15 min at room temperature, then filtered through a sintered glass funnel. The crystals are washed with 3 × 70 mL of distilled water and dried with suction for ~1 hr, then over phosphorus pentoxide in a vacuum desiccator to constant weight. Analytically and isomerically pure (*E*)-3-iodoprop-2-enoic acid [25.3 g (79%)] is obtained as white needles (Note 9).

## 2. Notes

1. Copper(I) iodide (99%) was purchased from Aldrich Chemical Company, Inc. (Cat. No. 20,554-0) and used as received.

2. Hydriodic acid was purchased from Aldrich Chemical Company, Inc. (Cat. No. 21,002-1) and used as received.

3. Propiolic acid was purchased from Lancaster Synthesis Ltd. (Cat. No. 0669) and used as received.

4. Commercially available HI must be colorless to straw-yellow colored (not brown or darker) for a successful reaction.

5. On larger scales (up to 50 grams of propiolic acid) the addition should still be complete within 1 min to allow the internal reaction temperature to rise to ~100 °C.

6. The temperature of the reaction mixture must be raised to the reflux temperature (110 °C) immediately after the addition of propiolic acid.

7. On larger scales the water bath may be replaced with an ice bath to reduce the temperature of the reaction mixture to 25-30 °C over 15 min.

8. The exact ratio of reagents for this procedure is important for successful formation of pure product in this reaction.

9. Full characterization of the product is as follows: mp 146-149 °C; $\nu_{max}$ ($CH_2Cl_2$) $cm^{-1}$: 3500-2500 (OH, CH), 1701 (C=O); $^1H$ NMR (400 MHz, $CD_3OD$) δ: 6.90 (1H, d, *J* =14.9, ICH=C$\underline{H}$), 8.07 (1H, d, *J* =14.9, ICH); $^{13}C$ NMR (100 MHz, $CD_3OD$) δ: 103.0 (I$\underline{C}$H), 135.7 (ICH=$\underline{C}$H), 169.2 (C=O); *m/z* (EI) 198 (100, $[M]^+$), 181 (11), 153 (12), 127 (53), 71 (15). Anal. Calcd for $C_3H_3IO_2$: C, 18.20; H, 1.52%. Found: C, 18.13; H, 1.49%.

## Waste Disposal Information

Aqueous washings from the filtration and isolation of desired product were extracted with ether and disposed of as halogenated waste.

## 3. Discussion

Pure (*E*)-3-iodoprop-2-enoic acid can be obtained in one step by heating propiolic acid and HI at 130 °C in a sealed tube for extended periods. It can also be formed by thermal isomerization of the pure (*Z*)-isomer under similar conditions.[2] In a recent improvement to this protocol, (*Z*)-3-iodoacrylic acid was isomerized by extended periods of heating in hydriodic acid, thus obviating the use of a sealed tube.[3,4,5]

However, in order to obtain isomerically pure (*E*)-3-iodoprop-2-enoic acid, a two-step protocol is still required and reactions must be heated for 24 hr in both steps; work-up and purification of the reaction mixture is also necessary in each case. We were hopeful that we could improve upon these procedures by the use of copper(I) salts to catalyze the reaction.

Copper(I) halides have been shown previously to accelerate the formation of (*Z*)-3-iodoprop-2-enoic acid.[6,7,8,9,10] The formation of the (E)-isomer during these low temperature investigations indicated that, at higher temperature, copper catalysis could accelerate the formation of the thermodynamically favored (E)-isomer. Therefore, we decided to investigate the effect of temperature on the copper-catalyzed addition of HI to propiolic acid, with a view to creating a copper-catalyzed, one-step synthesis of the (E)-isomer.

Following optimization studies, we have now found that our method is a dramatic improvement of existing methods and relies on the copper(I)-catalyzed (0.6%) addition-isomerization of hydriodic acid to propiolic acid. The reaction time is short (30 min) and the analytically pure crystalline product is filtered directly from the reaction mixture, providing the desired material in excellent yield (79%). No further purification is necessary, all of which make this procedure the most attractive yet for the synthesis of (*E*)-3-iodoprop-2-enoic acid.

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

(*E*)-3-Iodoprop-2-enoic acid: 2-Propenoic acid, 3-iodo-, (2*E*)- (9); (6372-02-7)
Copper(I) Iodide: Copper iodide (CuI) (8, 9); (7681-65-4)
Hydriodic acid (8, 9); (10034-85-2)
Propiolic acid: 2-Propynoic acid (9); (471-25-0