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for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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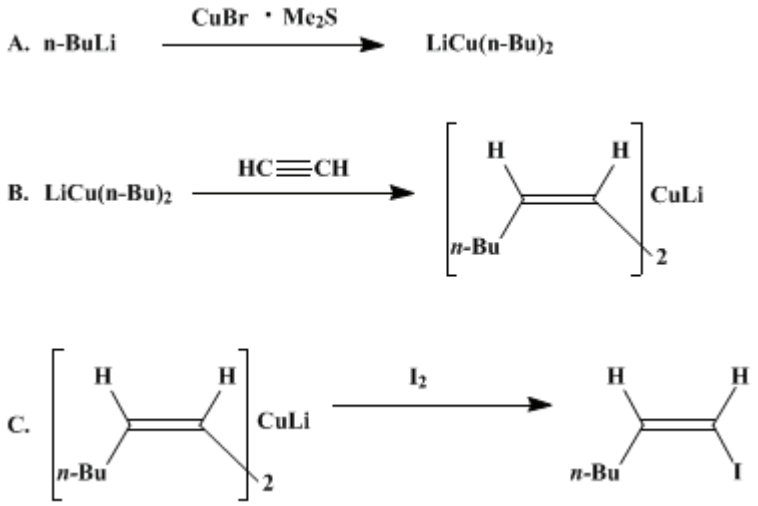
Organic Syntheses, Coll. Vol. 7, p.290 (1990); Vol. 62, p.1 (1984).

Z-1-IODOHEXENE

[1-Hexene, 1-iodo-, (Z)-]

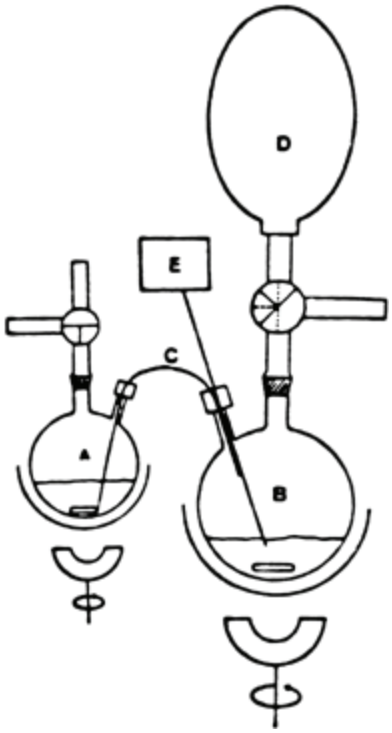


Submitted by A. Alexakis, G. Cahiez, and J. F. Normant[1].
Checked by J. Gabriel, P. Knochel, and Dieter Seebach.

1. Procedure

A. *Preparation of an ether solution of lithium dibutylcuprate*. A 500-mL flask (Figure 1) with a side arm is equipped with a magnetic stirring bar, rubber septum, and three-way stopcock, on top of which is attached a rubber balloon, D. A Pt-100-thermometer, E, is inserted into the flask through the septum (Note 1). The air in the flask is replaced by dry nitrogen (Note 2). The flask is charged with 10.8 g (0.0525 mol) of cuprous bromide–dimethyl sulfide complex (Note 3) and 100 mL of ether, then immersed in a bath at −50°C; 0.10 mol of butyllithium, ca. 1.6 *M* solution in hexane (Note 4), is added dropwise, with stirring, via a syringe inserted through the rubber septum, at such a rate that the temperature of the reaction mixture does not exceed −20°C.

Figure 1



After the addition is complete, stirring is continued at −30°C for 10 min to produce a gray–blue or dark-blue solution of the cuprate (Note 5).

B. *Preparation of a solution of lithium di(Z-hexenyl)cuprate*. A needle connected to an acetylene supply (Note 6) is introduced through the rubber septum of the flask, with its end at least 1 cm below the surface of the cuprate solution. The stopcock is fully opened toward the balloon, the solution is cooled to −50°C, and 2.64 L (0.11 mol) of acetylene (Note 6) is bubbled into the stirred cuprate solution, the temperature of which should not rise above −25°C. The gas inlet is removed and the greenish solution is stirred at −25°C for 30 min.

C. *Preparation of Z-iodohexene*. A dry, 100-mL flask with a sidearm is charged with 26.7 g (0.105 mol) of iodine, equipped with a stirring bar, three-way stopcock, and rubber septum, and flushed with argon as described above (Section A). The iodine is dissolved by introducing, with stirring, 30 mL of tetrahydrofuran through the septum with a syringe. Flask A, which contains the iodine solution, is connected to flask B, which contains the vinyl cuprate solution as shown in Figure 1. The cuprate solution is kept between −60° and −50°C while the iodine solution is pushed through the Teflon tubing, C. Then the cooling bath is removed and the temperature is allowed to rise to −10°C, whereupon a precipitate of copper(I) iodide is formed and the mixture turns yellow. After 10 min at −10°C, a mixture of 100 mL of saturated aqueous ammonium chloride and 10 mL of saturated sodium bisulfite is added with vigorous stirring. The mixture is filtered by suction through 10 g of Celite on a sintered-glass funnel (No. 3), the contents of the funnel are washed twice with 50 mL of ether, and the filtrate is separated into two layers (Note 7). The inorganic layer is washed twice with 50 mL of pentane, and the combined organic layers are washed with aqueous sodium bisulfite (Note 8) and saturated ammonium chloride solution and dried over anhydrous $MgSO_4$. The solvents are removed by distillation through a 20-cm Vigreux column at atmospheric pressure. A spatula of copper powder is added to the residue, and the stirred mixture is distilled under reduced pressure through a 10-cm Vigreux colum to give 13.5–15.5 g (65–75%) of *Z*-1-iodohexene, bp 47°C/(15 mm) (Note 9) and (Note 10).

2. Notes

1. The technique used here has been described previously by the checkers.[2] Instead, the submitters used a dry 500-mL, three-necked flask equipped with a variable-speed mechanical stirrer, a 100-mL pressure-

equalizing dropping funnel topped by a gas inlet and a Claisen head containing a low-temperature thermometer (−70°C to +35°C), and a bubbler. A stream of nitrogen followed from the gas inlet.

2. This manipulation is described in detail in *Org. Synth., Coll. Vol. VI* **1988**, 869.

3. This complex[3] should be used when the organolithium is in solution in a hydrocarbon solvent. For organolithium reagents prepared in ether (see (Note 4)), the same complex may be used or, more conveniently, copper iodide (CuI) can be used. The CuI purchased from Prolabo or Merck & Company, Inc. may be used directly. Other commercial sources of CuI (Fluka, Aldrich Chemical Company, Inc., Alfa Products, Morton Thiokol, Inc.) furnish a salt that affords better results when purified. First 1 mol of CuI is stirred for 12 hr with 500 mL of anhydrous tetrahydrofuran, then filtered on a sintered-glass funnel (No. 3), washed twice with 50 mL of anhydrous tetrahydrofuran, once with 50 mL of anhydrous ether, and finally dried under reduced pressure (0.1 mm) for 4 hr.

4. Butyllithium was used as purchased from Aldrich Chemical Company, Inc., Fluka, or Metallgesellschaft (Frankfurt). Ethereal solutions of butyllithium may also be used. Other organolithium compounds are easily prepared in ether; the following is representative.

Under an atmosphere of argon, a solution of butyl bromide (137 g, 1 mol) in anhydrous ether (500 mL) is added with stirring to small chips of lithium containing 1–2% of sodium (15.5 g, 2.2 g-atom) in ether (150 mL). The reaction starts after the addition of about 40 mL of butyl bromide solution at room temperature. The temperature rises and the lithium metal becomes bright. If the reaction does not start, the addition of a small amount of 1,2-dibromoethane (1 mL) is often effective. Then the reaction mixture is cooled (−5°C to −10°C) and addition of the butyl bromide solution is continued slowly (about 4 hr). At the end of the addition, the solution is stirred for 2 hr at −5 to −10°C; then the reaction mixture is allowed to warm to room temperature. After 2 hr, excess lithium metal is removed. For many purposes, the use of a clear solution, obtained after the reaction mixture has stood overnight at 0 to −5° C, is preferable. Butyllithium in ether can be stored under an argon atmosphere without decomposition for 15 days at 0°C or for 2 months at −15°C.

5. During all of the operations, the rate of stirring is adjusted to avoid splashing the wall of the flask; above −10°C, thermal decomposition of the cuprate occurs. This is indicated by the presence of a black suspension, which is also formed if a copper(I) salt of insufficient purity is used, or when oxygen gets into the reaction flask.

6. The proper volume of acetylene is measured with a water gasometer as described in *Org. Synth., Coll. Vol. I* **1941**, 230, with two modifications: (a) Two traps immersed in an acetone–dry ice bath at −65°C are placed between the acetylene tank and the gasometer in order to remove acetone; (b) the washing bottles between the gasometer and the reaction flask are replaced by a drying tube (2-cm × 30-cm column packed with anhydrous $CaCl_2$). The apparatus must be flushed with acetylene in order to remove all traces of oxygen. Acetylene dissolved in acetone is most appropriate. Acetylene obtained from tanks that contain solvents such as dimethylformamide (or other solvents) gave lower yields of carbocupration.

7. If a precipitate appears in the filtrate, filtration is repeated until two layers can be clearly distinguished.

8. A mixture of 10 mL of saturated sodium bisulfite and 50 mL of water is used. One or more washings with sodium bisulfite solution are necessary if iodine is present.

9. The sample thus obtained is >99% pure by GC analysis (3% OV 101 in a 2-m × 4-mm glass column, on Chromosorb G, with an injection temperature of 175°C, raised 100°C in 5 min, then 5°C/min).

10. The ^1H NMR spectrum of *Z*-1-iodohexene (in CCl_4) is as follows: δ: 0.94 (m, 3 H), 1.42 (m, 4 H, $-CH_2-$), 2.12 (m, 2 H, $-CH_2-C=$), 6.12 (m, 2 H).

3. Discussion

1-Iodoalkenes of the *Z* configuration are usually prepared by hydroboration of 1-iodoalkynes. The present method affords a product of higher configurational purity and constitutes an easier way to obtain such compounds in high yield, starting from less expensive reagents. In addition, the reaction can be performed easily on a larger scale (the submitters have prepared up to 1.8 mol of dialkenyl cuprate). The *Z*-1-iodo-1-alkenes shown in Table I have been prepared by the submitters.

TABLE I

EXAMPLES OF ALKENYL IODIDE PREPARATION FROM

CARBOCUPRATION

Entry	Organolithium	Product[a]	Yield (%)
1	EtLi	EtCH=CHI	72
2	*n*-$C_5H_{11}Li$	(*n*-C_5H_{11})CH=CHI	89
3	*n*-$C_7H_{15}Li$	(*n*-C_7H_{15})CH=CHI	90
4	$EtCH=CHCH_2CH_2Li$	$EtCH=CHCH_2CH_2CH=CHI$	79
5	$RO(CH_2)_3Li$[b]	$HO(CH_2)_3CH=CHI$[c]	58
6	$RO(CH_2)_8Li$[b]	$HO(CH_2)_8CH=CHI$[c]	70

[a]All alkenes, reactants and products, are *Z*.
[b]*R* = CHMeOEt.
[c]After acid hydrolysis.

This reaction illustrates a stereoselective preparation of (*Z*)-vinylic cuprates,[4,5] which are very useful synthetic intermediates. They react with a variety of electrophiles such as carbon dioxide.[5,6] epoxides,[5,6] aldehydes,[6] allylic halides,[7] alkyl halides,[7] and acetylenic halides;[7] they undergo conjugate addition to α,β-unsaturated esters,[5,6] ketones,[6] aldehydes,[6] and sulfones.[8] Finally, they add smoothly to activated triple bonds[6] such as HC≡C-OEt, HC≡C-SEt, and $HC≡C-CH(OEt)_2$. In most cases these cuprates transfer both alkenyl groups. The uses and applications of the carbocupration reaction have been reviewed recently.[9] The configurational purity in the final product is at least 99.9% *Z* in the preceding transformations.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 8, 295

References and Notes

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

vinyl cuprate

CuI

acetylene (74-86-2)

ether (60-29-7)

ammonium chloride (12125-02-9)

Butyl bromide (109-65-9)

oxygen (7782-44-7)

nitrogen (7727-37-9)

sodium bisulfite (7631-90-5)

carbon dioxide (124-38-9)

copper powder (7440-50-8)

iodine (7553-56-2)

acetone (67-64-1)

sodium (13966-32-0)

1,2-dibromoethane (106-93-4)

cuprous bromide (7787-70-4)

Pentane (109-66-0)

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

lithium (7439-93-2)

$MgSO_4$ (7487-88-9)

dimethyl sulfide (75-18-3)

butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

dimethylformamide (68-12-2)

hexane (110-54-3)

argon (7440-37-1)

Z-1-IODOHEXENE,
1-Hexene, 1-iodo-, (Z)- (16538-47-9)

lithium dibutylcuprate

lithium di(Z-hexenyl)cuprate

Z-iodohexene (18922-04-8)