



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.

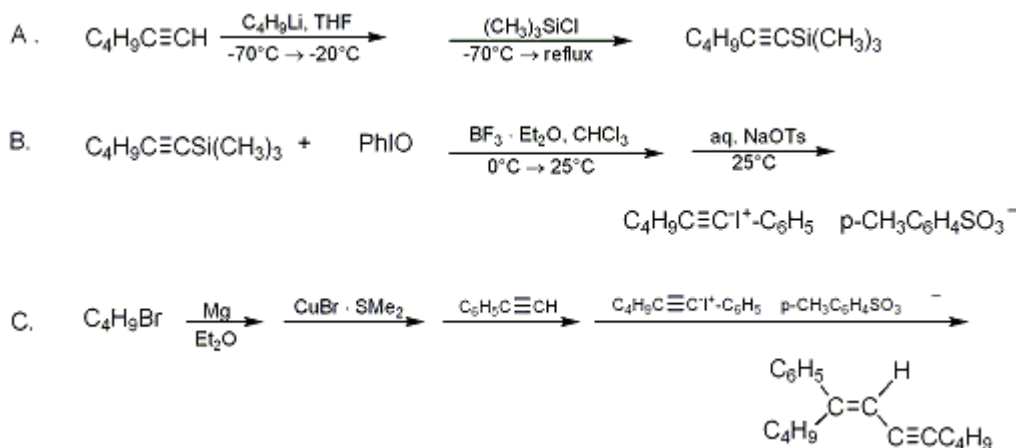
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries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

Organic Syntheses, Coll. Vol. 9, p.477 (1998); Vol. 70, p.215 (1992).

ALKYNYL(PHENYL)IODONIUM TOSYLATES: PREPARATION AND STEREOSPECIFIC COUPLING WITH VINYL COPPER REAGENTS. FORMATION OF CONJUGATED ENYNES. 1-HEXYNYL(PHENYL)IODONIUM TOSYLATE AND (E)-5-PHENYLDODEC-5-EN-7-YNE

[Iodine, 1-hexynyl(4-methylbenzenesulfonato-O)phenyl- and Benzene, (1-butyl-1-octen-3-ynyl)-, (E)-]



Submitted by Peter J. Stang and Tsugio Kitamura¹.

Checked by Kazuaki Ishihara and Hisashi Yamamoto.

1. Procedure

A. *1-Trimethylsilyl-1-hexyne* (Note 1). A dry, 500-mL, three-necked, round-bottomed flask (equipped with a magnetic stirrer system) is fitted with one 50-mL and one 125-mL pressure-equalizing addition funnel and a reflux condenser. The top of the condenser is mounted with a T-piece connected at one end to an argon outlet and at the other end to an oil bubbler. The apparatus is purged with dry argon and the reaction is carried out under an argon atmosphere. The flask is charged with 16.4 g (0.20 mol) of 1-hexyne (Note 2) and 200 mL of tetrahydrofuran (THF, (Note 3)), and the mixture is cooled to approximately -70°C with a dry ice-2-propanol slush bath. The 125-mL dropping funnel is filled with 80 mL (0.20 mol) of 1.63 M butyllithium in hexane (Note 4) which is added over a period of 30 min to the stirred, cold (-70°C) 1-hexyne in THF. After addition is complete the flask is gradually warmed over a 3-hr period to -20°C , then recooled to -70°C with the dry ice-2-propanol slush bath. Chlorotrimethylsilane (Note 5), 25.3 mL (0.20 mol), is placed in the 50-mL dropping funnel and added over a period of 15 min to the stirred, cooled reaction mixture. After the addition is complete the slush bath is removed and the mixture is first stirred at room temperature for 16 hr, then heated under reflux for 1 hr (Note 6). The mixture is cooled to 0°C with an ice-water bath and then 50 mL of water is carefully added. The entire reaction mixture is transferred to a 1-L separatory funnel and extracted with 200 mL of pentane. The organic phase is separated, washed successively with three 100-mL portions of water followed by 100 mL of saturated sodium chloride solution and then dried over anhydrous magnesium sulfate. After filtration the solvent is distilled off through a 15-cm Vigreux column. The pale yellow residue is transferred to a 100-mL round-bottomed flask and distilled through a 15-cm Vigreux column to give 25.0–27.5 g (81–89%) of 1-trimethylsilyl-1-hexyne as a clear, colorless liquid, bp $149\text{--}156^\circ\text{C}$, that can be used as is in the subsequent step.

B. *1-Hexynyl(phenyl)iodonium tosylate*. The center neck of a dry, 500-mL, three-necked, round-bottomed flask (equipped with a magnetic stirrer system) is fitted with a 50-mL pressure-equalizing

addition funnel One side neck is fitted with a glass stopper and the other with a gas inlet to which is attached a T-piece connected to an [argon](#) supply and an oil bubbler. After the flask is purged with dry [argon](#), it is charged with 22.0 g (0.10 mol) of finely ground [iodosobenzene](#) (Note 7), 200 mL of [chloroform](#) (Note 8) and 17.0 g (0.11 mol) of [1-trimethylsilyl-1-hexyne](#), and the entire mixture is cooled to 0°C with an ice-water bath. [Boron trifluoride etherate](#) (Note 9), 13.0 mL (0.11 mol), is added dropwise over a period of about 5 min to the stirred, cooled reaction mixture (Note 10). After the addition is complete the mixture is stirred at room temperature for about 16 hr (Note 11).

To a 1-L beaker are added 76.1 g (0.4 mol) of [p-toluenesulfonic acid monohydrate](#) (Note 12) and 400 mL of water. To this solution is carefully added 21.2 g (0.2 mol) of anhydrous [sodium carbonate](#) and then the entire solution is purged with [argon](#) for about 15 min to replace all air. This solution of [sodium toluenesulfonate](#) (NaOTs), along with the contents of the reaction flask, are placed in a 1-L separatory funnel and the mixture is vigorously shaken for a period of about 10 min (Note 13). The organic phase is separated and the aqueous phase is extracted with 50 mL of [methylene chloride](#). The combined organic phases are dried over anhydrous [magnesium sulfate](#), filtered and the solvent evaporated on a rotary evaporator. To the residual yellow-brown oil is added a mixture of 75 mL of [diethyl ether](#) and 75 mL of [pentane](#) resulting, after stirring, in fine white crystals. The powdery white crystals are filtered, washed with two 50-mL portions of a [diethyl ether/pentane](#) (1:1 v/v) mixture, air dried, then dried under reduced pressure. The resulting white crystalline solid, 27–34 g (60–75%), mp 77–80°C, (dec) is essentially pure and ready for most uses (Note 14).

C. *(E)-5-Phenyldodec-5-en-7-yne*. **CAUTION:** *Dimethyl sulfide is a volatile, very smelly irritant. This reaction must be conducted in a hood!*

A dry, 100-mL, three-necked, round-bottomed flask (equipped with a magnetic stirrer system) is fitted with a 25-cm Liebig condenser, a 25-mL pressure-equalizing dropping funnel topped off with a gas-inlet, and a glass stopper. After the flask is purged with [argon](#), it is charged with 0.90 g (37.5 mmol) of [magnesium turnings](#) and 15 mL of anhydrous [ether](#). To the dropping funnel is added a solution of 4.0 mL (37.5 mmol) of [1-bromobutane](#) (Note 15) in 20 mL of anhydrous [ether](#). This solution is added to the reaction flask at such a rate (approximately 1 hr) that after the Grignard reaction is initiated a gentle reflux is maintained. After the addition is complete the mixture is stirred for an additional 30 min.

The center neck of a dry, 250-mL, three-necked, round-bottomed flask (equipped with a magnetic stirrer system) is fitted with a 50-mL pressure-equalizing dropping funnel topped off with a rubber septum and an [argon](#) inlet. The side necks are fitted with a glass stopper and a rubber septum, respectively. The apparatus is purged with [argon](#) and to the flask are added 7.7 g (37.5 mmol) of [copper \(I\) bromide-dimethyl sulfide complex](#) (Note 16), 60 mL of anhydrous [ether](#), and 38 mL of [dimethyl sulfide](#) (Note 17). The mixture is cooled to –70°C with a dry ice-2-propanol slush bath. The previously prepared butyl Grignard reagent is transferred to the addition funnel via a double-ended needle with a positive [argon](#) pressure. The Grignard reagent is added dropwise, over a 30-min period, to the cooled reaction mixture (Note 18). After the addition is complete the reaction is maintained between –40°C to –50°C for 2 hr, then re-cooled to –70°C. [Phenylacetylene](#) (Note 19), 4.1 mL (37.1 mmol), is slowly added via a syringe through the rubber septum. After addition, the reaction mixture is maintained at –30°C to –25°C for 2 hr (Note 20), then re-cooled to –70°C and 6.8 g (15 mmol) of the previously prepared [iodonium tosylate](#) is added, in the solid form, through the side neck, over a positive [argon](#) pressure. The stirring reaction mixture is gradually warmed to room temperature and stirred for an additional 12 hr at room temperature. The mixture is poured into a 1-L beaker containing 200 mL of saturated [ammonium chloride](#) solution and stirred vigorously. The undissolved materials are filtered off and the organic phase is separated. The aqueous phase is extracted with three 50-mL portions of [ether](#). The combined organic phase are washed with 100 mL of water followed by 100 mL of saturated [sodium chloride](#) solution, and dried over anhydrous [magnesium sulfate](#) and filtered. The solvent is removed on a rotary evaporator in the hood and the residual oil chromatographed (4 × 50 cm column) on alumina (600 g, (Note 21)). The column is successively eluted with 1 L of [hexane](#), 750 mL of 10% [dichloromethane-hexane](#), 500 mL of 20% [dichloromethane-hexane](#) and 250 mL of 30% [dichloromethane-hexane](#). The fractions are analyzed by TLC on silica gel (Note 22) using 10% [dichloromethane-hexane](#) as eluent and the product-containing fractions (Note 23) are combined. The solvent is evaporated on a rotary evaporator and the residual yellow-brown oil (5.8 g) (Note 24) is distilled under reduced pressure, bp

135–143°C (3–4 mm), to give 2.3 g of crude product. Redistillation under reduced pressure affords 1.9–2.1 g (53–58%) of product as a pale yellow liquid, bp 143–144°C (1 mm) (Note 25).

2. Notes

1. Many 1-trimethylsilylalkynes are commercially available from Aldrich, Petrarch and other vendors of silicon compounds. Alternatively they are readily made from 1-alkynes and [chlorotrimethylsilane](#) as described in part A.
2. [1-Hexyne](#) was obtained from Tokyo Kasei Kogyo Co., Ltd. or Aldrich Chemical Company, Inc. and used without purification.
3. [Tetrahydrofuran](#) was obtained from Wako Pure Chemical Industries, Ltd., and distilled from potassium benzophenone ketyl immediately before use.
4. [Butyllithium](#) in [hexane](#) (2.6 M) was obtained from Mitsuwas Pure Chemical or Aldrich Chemical Company, Inc. and a freshly opened sample was used without assay or purification.
5. [Chlorotrimethylsilane](#) was obtained from Shin-ETSU Silicon Chemicals or PCR Research Chemicals, Inc., and distilled prior to use.
6. During this period copious amounts of a white precipitate (LiCl) is formed.
7. [Iodosobenzene](#) was purchased by the checkers from Tokyo Kasei Kogyo Co., Ltd. and dried under reduced pressure prior to use.
8. [Chloroform](#) was distilled from [phosphorus oxide](#) (P_2O_5) and passed through an alumina column prior to use.
9. [Boron trifluoride etherate](#) (98%) was obtained from Wako Pure Chemical Industries, Ltd., or MC and B Manufacturing Chemists, and distilled from granular [calcium hydride](#) prior to use.
10. The pale yellow suspension turns to a deeper yellow suspension during addition.
11. [Iodosobenzene](#) is a polymer and depolymerizes as it reacts, forming a clear, yellow-light brown, homogeneous solution during the course of the reaction. It is not ready for work-up until a clear homogeneous solution is obtained.
12. [p-Toluenesulfonic acid monohydrate](#) was obtained from Wako Pure Chemical Industries, Ltd., or MC and B Manufacturing Chemists, and used without further purification.
13. Care must be taken to release periodically the pressure formed. It is advisable to chill both solutions prior to mixing and shaking.
14. The spectral properties of [1-hexynyl\(phenyl\)iodonium tosylate](#) are as follows: IR (nujol) cm^{-1} : 2185 (m, $C\equiv C$), 1225 (s), 1175 (m), 1145 (vs), 1115 (m), 1025 (m), 1000 (s), 985 (m, sh), 807 (m), 730 (m), 675 (s); FAB-MS m/z 285 (n, $BuC\equiv CIPh^+$); 1H NMR ($CDCl_3$) δ 0.73–0.92 (m, CH_3), 1.12–1.58 (m, CH_2CH_2), 2.30 (s, $ArCH_3$), 2.30–2.50 (m, CH_2), 6.98–7.60 (m, ArH), 7.92–8.05 (m, ArH).
15. [1-Bromobutane](#) was obtained from Wako Pure Chemical Industries, Ltd., or Eastman Kodak Company, and distilled through a 10-cm Vigreux column prior to use.
16. [Copper\(I\) bromide-dimethyl sulfide complex](#), ($CuBr\cdot SMe_2$), 99%, was obtained from Aldrich Chemical Company, Inc. and purified prior to use as follows: 10 g of $CuBr\cdot SMe_2$ was dissolved in 20 mL of [dimethyl sulfide](#) and triturated with 30 mL of [pentane](#). The resulting white crystals were filtered, washed with three 20-mL portions of [pentane](#) and dried under reduced pressure.
17. [Dimethyl sulfide](#), 99+%, anhydrous, was obtained from Tokyo Kasei Kogyo Co., Ltd., or Aldrich Chemical Company, Inc.
18. The white suspension turned to an orange suspension during the course of the addition.
19. [Phenylacetylene](#) was obtained from Tokyo Kasei Kogyo Co., Ltd., or Farchan Laboratories and distilled through a 15-cm Vigreux column prior to use.
20. During this period the color changed from orange through brown to black.
21. Unactivated alumina from J. T. Baker Chemical Company was used.
22. TLC silica gel 60F₂₅₄ sheets were obtained from Merck & Company, Inc.
23. The desired product appears as the second spot on TLC with an $R_f = 0.42$ – 0.45 with 10% [dichloromethane-hexane](#).
24. The major by-product is [5,8-diphenyldodeca-5,7-diene](#), which can be separated by distillation.
25. GC analysis of the product on a 10% UCW-982 Chromosorb W column (0.25 in \times 6 ft) at 200°C showed a single isomer with a purity of 99%. The spectral properties of the product are as follows: IR (neat) cm^{-1} : 3070 (m, sh), 3050 (m), 3015 (m), 2950 (vs), 2925 (vs), 2855 (s), 2200 (w), 1595 (m), 1570 (w), 1490 (m), 1465 (s), 1442 (s), 1375 (m), 1325 (m), 847 (m), 752 (vs), 690 (vs), MS (EI) m/z : 240

M⁺, 57%, 141 (100%), 105 (53%); ¹H NMR (CDCl₃) δ 0.81–1.00 (m, CH₃), 1.21–1.59 (m, CH₂CH₂), 2.30–2.46 (m, CH₂), 2.67–2.84 (m, CH₂), 5.74 (t, J = 2, C=CH), 7.14–7.51 (m, ArH); ¹³C NMR (300 MHz, CDCl₃) δ 13.52 (CH₃), 13.81 (CH₃), 19.35 (CH₂), 21.91 (CH₂), 22.50 (CH₂), 30.50 (CH₂), 30.96 (CH₂), 31.70 (CH₂), 78.93 (C≡C), 95.47 (C≡C), 107.42 (C=CH), 125.78, 127.44, 128.24, 140.52 (aromatic), 151.88 (C=CH).

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

The only known alternative procedure for the preparation of alkynyl(phenyl)iodonium arylsulfonates, the latest member of the family² of polyvalent iodine compounds, involves the reaction of [hydroxy(tosyloxy)iodo]benzene, PhIOH·OTs, with terminal alkynes as first reported by Koser³ and elaborated by us.⁴ This procedure has a number of shortcomings. Formation of the desired alkynyliodonium salt is usually accompanied by a related vinyl species, R(TsO)C=CHIPh·OTs, that both decreases the yields and causes purification problems. Furthermore, when the alkyl substituent of the starting alkyne is small, such as CH₃, n-Pr, n-Bu, etc., this procedure gives either no product³ or low yields⁴ at best.

The present procedure, similar to that of Fujita⁵ for the preparation of alkynyl(phenyl)iodonium tetrafluoroborates, RC≡CIPh·BF₄, is simpler, much more general and in most cases gives significantly better yields.⁶ Table I gives yields of alkynyl(phenyl)iodonium sulfonates prepared by this procedure.

TABLE I
ALKYNYL(PHENYL)IODONIUM SULFONATES

Starting Alkyne	Product	Yields (%)	M.P. (dec.) °C
CH ₃ C≡CH	CH ₃ C≡CIPh·OTs	62	123–125
EtC≡CH	EtC≡CIPh·OTs	81	108–110
n-PrC≡CH	n-PrC≡CIPh·OTs	89	93–95
Me ₃ SiC≡CSiMe ₃	Me ₃ SiC≡CIPh·OTs	70	107–109
PhC≡CH	PhC≡CIPh·OTs	61	128–133 ⁴
t-BuC≡CH	t-BuC≡CIPh·OTs	67	118–124 ⁴

Alkynyl(phenyl)iodonium sulfonates are stable, microcrystalline substances that can be stored and used indefinitely with little or no decomposition. They have been employed in the formation of aryl (2-furyl)iodonium tosylates,⁷ alkynyl sulfonate,⁴ carboxylate⁸ and phosphate⁹ esters, tricoordinate vinyliodinane species,¹⁰ and alkylidenecarbene-iodonium ylides.¹¹

The stereoselective formation of conjugated enynes has been reported¹² via the coupling of vinylcopper reagents with alkynyl(phenyl)iodonium tosylates. A representative example of this process is described in part C of the present procedure. This method¹² affords stereoisomerically pure 1,1-disubstituted conjugated 1,3-enynes with a trisubstituted olefin component with complete control of olefin geometry. The simplicity of the procedure, mild reaction conditions, reasonable yields (46–94%) and total stereocontrol¹² should make this an attractive alternative and complement to the known^{13,14} Pd-catalyzed olefin-alkyne couplings for the synthesis of this important class of aliphatic compounds.

References and Notes

1. Department of Chemistry, The University of Utah, Salt Lake City, UT 84112. Financial support

from the Cancer Institute of NIH (2ROCA16903) is gratefully acknowledged.

2. Koser, G. F. In "The Chemistry of Halides, Pseudo-Halides and Azides" [The Chemistry of Functional Groups, Supplement D]; Patai, S.; Rappoport, Z., Eds.; Wiley: 1983, Part 2, Chapter 25, pp. 1265–1351.
3. Rebrovic, L.; Koser, G. F. *J. Org. Chem.* **1984**, *49*, 4700; Koser, G. F.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1981**, *46*, 4324.
4. Stang, P. J.; Surber, B. W.; Chen, Z.-C.; Roberts, K. A.; Anderson, A. G. *J. Am. Chem. Soc.* **1987**, *109*, 228; Stang, P. J.; Surber, B. W. *J. Am. Chem. Soc.* **1985**, *107*, 1452.
5. Ochiai, M.; Kunishima, M.; Sumi, K.; Nagao, Y.; Fujita, E.; Arimoto, M.; Yamaguchi, H. *Tetrahedron Lett.* **1985**, *26*, 4501.
6. Kitamura, T.; Stang, P. J. *J. Org. Chem.* **1988**, *53*, 4105.
7. Margida, A. J.; Koser, G. F. *J. Org. Chem.* **1984**, *49*, 4703.
8. Stang, P. J.; Boehshar, M.; Wingert, H.; Kitamura, T. *J. Am. Chem. Soc.* **1988**, *110*, 3272.
9. Stang, P. J.; Boehshar, M.; Lin, J. *J. Am. Chem. Soc.* **1986**, *108*, 7832.
10. Stang, P. J.; Wingert, H.; Arif, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 7235.
11. Kitamura, T.; Stang, P. J. *Tetrahedron Lett.* **1988**, *29*, 1887.
12. Stang, P. J.; Kitamura, T. *J. Am. Chem. Soc.* **1987**, *109*, 7561.
13. Stille, J. K.; Simpson, J. H. *J. Am. Chem. Soc.* **1987**, *109*, 2138.
14. Scott, W. J.; McMurry, J. E. *Acc. Chem. Res.* **1988**, *21*, 47; Heck, R. F. "Palladium Reagents in Organic Synthesis"; Academic Press: New York, 1985.

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

potassium benzophenone ketyl

(LiCl)

$\text{CH}_3\text{C}\equiv\text{CH}$

$\text{CH}_3\text{C}\equiv\text{CPh}\cdot\text{OTs}$

$\text{EtC}\equiv\text{CH}$

$n\text{-PrC}\equiv\text{CH}$

$n\text{-PrC}\equiv\text{CPh}\cdot\text{OTs}$

$\text{Me}_3\text{SiC}\equiv\text{CSiMe}_3$

$\text{PhC}\equiv\text{CH}$

$\text{PhC}\equiv\text{CPh}\cdot\text{OTs}$

$t\text{-BuC}\equiv\text{CH}$

$t\text{-BuC}\equiv\text{CPh}\cdot\text{OTs}$

Iodine, 1-hexynyl(4-methylbenzenesulfonato-O)phenyl-

ether,
diethyl ether (60-29-7)

ammonium chloride (12125-02-9)

chloroform (67-66-3)

magnesium turnings (7439-95-4)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

1-bromobutane (109-65-9)

Pentane (109-66-0)

methylene chloride,
dichloromethane (75-09-2)

Phenylacetylene (536-74-3)

magnesium sulfate (7487-88-9)

dimethyl sulfide (75-18-3)

butyllithium (109-72-8)

Tetrahydrofuran,
THF (109-99-9)

Iodosobenzene (536-80-1)

hexane (110-54-3)

1-Hexyne (693-02-7)

argon (7440-37-1)

boron trifluoride etherate (109-63-7)

calcium hydride (7789-78-8)

CHLOROTRIMETHYLSILANE (75-77-4)

phosphorus oxide (1314-56-3)

p-toluenesulfonic acid monohydrate (6192-52-5)

1-Trimethylsilyl-1-hexyne (3844-94-8)

1-Hexynyl(phenyl)iodonium tosylate (94957-42-3)

(E)-5-Phenyldodec-5-en-7-yne,
Benzene, (1-butyl-1-octen-3-ynyl)-, (E)- (111525-79-2)

sodium toluenesulfonate

iodonium tosylate

5,8-diphenyldodeca-5,7-diene

copper(I) bromide-dimethyl sulfide complex (54678-23-8)