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of Reliable Methods
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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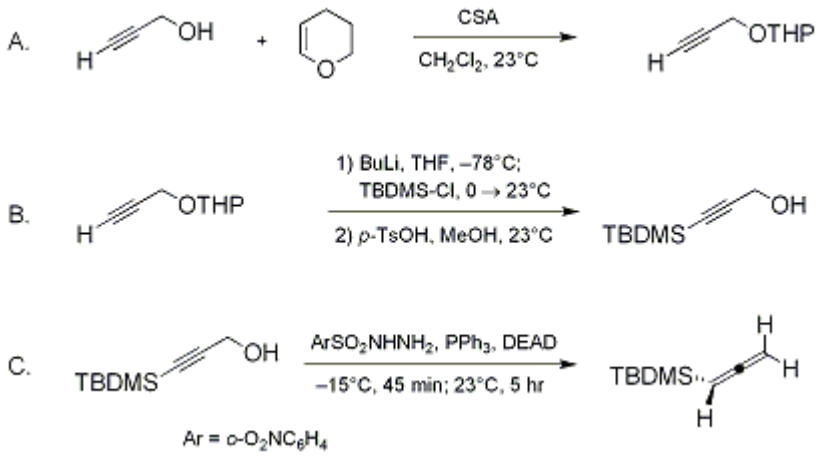
(tert-BUTYLDIMETHYLSILYL)ALLENE

[Silane, (1,1-dimethylethyl)dimethyl-1,2-propadienyl-]



Submitted by Andrew G. Myers and Bin Zheng[1] .
Checked by Kazuya Matsunaga and Rick L. Danheiser.

1. Procedure

A. 2-Propargyloxytetrahydropyran . An oven-dried, 2-L, three-necked, round-bottomed flask is equipped with a large football-shaped Teflon-coated magnetic stirring bar, a rubber septum, an argon inlet adapter, and an oven-dried, 200-mL, pressure-equalizing addition funnel sealed with a rubber septum. The flask is charged sequentially with 0.116 g (0.500 mmol) of (±)-camphorsulfonic acid (Note 1), 750 mL of dichloromethane (Note 2), and 29.4 mL (0.500 mol) of propargyl alcohol (Note 1) under an argon atmosphere. The flask is cooled to 0°C in an ice-water bath, and a solution of 50.2 mL (0.550 mol) of 3,4-dihydro-2H-pyran (Note 1) in 75 mL of dichloromethane is added dropwise to the reaction mixture over 2 hr. Upon completion of the addition, the ice-water bath is removed, and the reaction mixture is allowed to warm to 23°C. After 2 hr at 23°C, the reaction mixture is transferred to a 2-L separatory funnel and extracted with 100 mL of saturated sodium bicarbonate solution (Note 3). The organic phase is separated and washed with 100 mL of saturated sodium chloride solution, dried over anhydrous sodium sulfate , filtered, and concentrated under reduced pressure (Note 4). The residue is purified by distillation through a 15-cm Vigreux column at reduced pressure (13 mm) to afford 67.0 g (96%) of 2-propargyloxytetrahydropyran as a colorless liquid (Note 5).

B. 3-(tert-Butyldimethylsilyl)-2-propyn-1-ol. An oven-dried, 250-mL, three-necked, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar is sealed under argon with three rubber septa, one of which contains a needle adapter to an argon-filled balloon. The flask is charged with 19.5 g (139 mmol) of 2-propargyloxytetrahydropyran and 140 mL of tetrahydrofuran (THF) (Note 6) and cooled to −78°C in a dry ice-acetone bath. To the well-stirred solution, 13.9 mL (139 mmol) of a 10.0 M solution of butyllithium in hexanes (Note 7) is added slowly via syringe over 15 min. The resulting yellow solution is stirred for 5 min at −78°C, after which time the dry ice-acetone bath is removed and replaced with an ice-water bath, and the reaction mixture is stirred for 15 min at 0°C. One of the septa is removed, 22.0 g (146 mmol) of solid tert-butyldimethylsilyl chloride (Note 8) is added to the reaction mixture in one portion, and the reaction flask is sealed again with a rubber septum. After an additional 2 min at 0°C, the ice-water bath is removed. Within 15 min an exotherm is observed (up to 40°C), followed by a slow return to room temperature (Note 9). The orange-red reaction mixture is poured into a 1-L separatory funnel containing 250 mL of aqueous 10% sodium chloride solution and 250 mL of hexanes . The layers are mixed vigorously and separated. The aqueous layer is extracted with two 125-mL portions of hexanes , and the combined organic extracts are dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue is transferred to a 1-L round-bottomed

flask equipped with a Teflon-coated magnetic stirring bar. To this flask, 500 mL of anhydrous methanol (Note 10) is added, followed by 0.530 g (2.79 mmol) of p-toluenesulfonic acid monohydrate (Note 11). The flask is sealed with a rubber septum containing a needle adapter to an argon-filled balloon. The reaction mixture is stirred at 23°C for 2 hr and then quenched by the addition of 100 mL of an aqueous saturated sodium bicarbonate solution. The resulting suspension is stirred for an additional 10 min, after which time the mixture is concentrated under reduced pressure to remove most of the methanol. The residue is transferred to a 1-L separatory funnel containing 250 mL of an aqueous 10% sodium chloride solution, and the mixture is extracted with three 200-mL portions of 1:1 hexanes-ethyl acetate . The combined organic extracts are dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue is purified by distillation at reduced pressure (1.5 mm) using a 15-cm Vigreux column to afford 22.0 g (93%) of 3-(tert-butyldimethylsilyl)-2-propyn-1-ol as a colorless oil that solidifies on standing at 23 °C (Note 12).

C. (tert-Butyldimethylsilyl)allene . An oven-dried, 500-mL, round-bottomed flask equipped with a large football-shaped Teflon-coated magnetic stirring bar is charged with 15.7 g (60.0 mmol) of triphenylphosphine (Note 13) under an argon atmosphere. The flask is sealed with a rubber septum containing a needle adapter to an argon-filled balloon, and 120 mL of THF (Note 6) is added via cannula. The solution is cooled in a −15°C bath (Note 14), and 9.02 mL (57.5 mmol) of diethyl azodicarboxylate (Note 13) is added via syringe over 2 min (Note 15), followed immediately by the addition of a solution of 8.52 g (50.0 mmol) of 3-(tert-butyldimethylsilyl)-2-propyn-1-ol in 18 mL of THF (Note 6) via cannula over 2 min. After an additional 5 min, a solution of 13.0 g (60.0 mmol) of o-nitrobenzenesulfonyl hydrazide (Note 16) in 65 mL of THF (Note 6) is added to the reaction mixture over 5 min via cannula. The resulting orange-red solution is stirred at −15°C for 45 min, after which time the cold mixture is allowed to warm to 23°C and is held at that temperature for 5 hr. During this time, the evolution of dinitrogen is observed. The reaction mixture is poured into a 2-L separatory funnel containing 400 mL of pentane , and the resulting mixture is washed with four 500-mL portions of ice-cold water (Note 17). The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated by rotary evaporation at 0°C. The residue is purified (Note 18) by flash chromatography using a short column of 230-400 mesh silica gel (60 g, packed dry and eluted with pentane). The fractions containing the product (Note 19) are concentrated by rotary evaporation at 0°C to afford 5.38-5.39 g (70%) of (tert-butyldimethylsilyl)allene as a colorless liquid (Note 20).

2. Notes

1. (±)-10-Camphorsulfonic acid, propargyl alcohol and 3,4-dihydro-2H-pyran were obtained from Aldrich Chemical Company, Inc. ; (±)-10-camphorsulfonic acid was used without further purification; propargyl alcohol was dried over potassium carbonate and then was distilled at reduced pressure (18 mm) prior to use; 3,4-dihydro-2H-pyran was dried over sodium carbonate and then distilled under argon (atmospheric pressure).
2. Dichloromethane was obtained from EM Science and was distilled from calcium hydride under an atmosphere of nitrogen.
3. Extraction with bicarbonate removes residual acid and ensures that no hydrolysis of the acetal product takes place during concentration and distillation.
4. Rotary evaporation (at 22 mm) was conducted at or below 23°C to prevent evaporative loss of the product.
5. The product exhibits the following properties: bp 69-70°C/13 mm (lit.[2] 63-65°C/9 mm); TLC R_f = 0.53 (25% ethyl acetate-hexanes); IR (neat, cm^{-1}): 3290, 2943, 1442, 1220, 1120, 1029, 901, 870 ; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.50-1.88 (m, 6 H), 2.41 (t, 1 H, J = 2.4), 3.51-3.58 (m, 1 H), 3.80-3.88 (m, 1 H), 4.22 (dd, 1 H, J = 15.6, 2.4), 4.28 (dd, 1 H, J = 15.6, 2.4), 4.82 (t, 1 H, J = 3.0) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.8, 25.2, 30.0, 53.8, 61.8, 74.0, 79.6, 96.6 .
6. Tetrahydrofuran was obtained from EM Science and distilled from sodium benzophenone ketyl under an atmosphere of argon.
7. Butyllithium was purchased from Aldrich Chemical Company, Inc. , and titrated with N-benzylidenebenzylamine as indicator according to an established procedure.[3] The use of the highly concentrated organolithium reagent is essential because the use of more dilute solutions of butyllithium in hexanes results in precipitation of the lithium acetylide and therefore less efficient coupling with tert-butyldimethylsilyl chloride.

8. tert-Butyldimethylsilyl chloride was obtained from Lithium Division, FMC Corp. , and used without further purification.
9. The checkers observed this exotherm to take place immediately following the addition of tert-butyldimethylsilyl chloride.
10. Anhydrous methanol was obtained from J. T. Baker Inc. , and used without further purification.
11. p-Toluenesulfonic acid monohydrate was obtained from Aldrich Chemical Company, Inc. , and used without further purification.
12. The product exhibits the following properties: bp 69-72°C/1.5 mm (lit.[4] 68-70°C/0.3 mm); mp 34-37°C (lit.[4] 36-38°C); TLC R_f = 0.43 (25% ethyl acetate-hexanes); IR ($CHCl_3$) cm^{-1}: 3423, 2960, 1506, 1455, 1348, 1273, 1212, 1138, 1012, 958, 830, 715, 679 ; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.10 (s, 6 H), 0.93 (s, 9 H), 1.91 (bs, 1 H), 4.27 (s, 2 H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8, 16.5, 26.0, 51.6, 88.8, 104.4 .
13. Triphenylphosphine (PPh_3) and diethyl azodicarboxylate (DEAD) were obtained from Aldrich Chemical Company, Inc. , and used without further purification.
14. Comparable results are obtained using either a cryobath (−15°C) or a bath containing a mixture of solid sodium chloride and ice (−12 to −18°C) for cooling.
15. Extended stirring of PPh_3 and DEAD can lead to precipitation of the betaine and inferior results. Similarly, more concentrated solutions of PPh_3 and DEAD, or cooling below −15°C, can induce precipitation. For this reason, the indicated protocol and concentrations are recommended. With other substrates, a modified order of addition, involving the addition of DEAD to a solution of PPh_3 and substrate followed by addition of o-nitrobenzenesulfonylhydrazine, may prove beneficial. In the present case this modified order of addition provided nearly identical results (isolated yield 68%).
16. o-Nitrobenzenesulfonyl hydrazide (NBSH) was prepared as follows:[5] Hydrazine monohydrate (12.1 mL, 0.25 mol, 2.5 equiv) is added dropwise to a solution of o-nitrobenzenesulfonyl chloride (22.2 g, 0.10 mol, 1 equiv) in THF (100 mL) at −30°C under an argon atmosphere. During the addition the reaction mixture becomes brown and a white precipitate of hydrazine hydrochloride is deposited. After stirring at −30°C for 30 min, thin-layer chromatographic (TLC) analysis indicates that the sulfonyl chloride has been consumed (2:1 ethyl acetate-hexanes eluent). Ethyl acetate (200 mL, 23°C) is added to the cold reaction solution, and the mixture is washed repeatedly with ice-cold aqueous 10% sodium chloride solution (5 × 150 mL); each wash involved a contact time of ≤ 1 min. The organic layer is dried over sodium sulfate at 0°C, then added slowly to a stirring solution of hexanes (1.2 L) at 23°C over 5 min. o-Nitrobenzenesulfonyl hydrazide precipitates within 10 min as an off-white solid and is collected by vacuum filtration. The filter cake is washed with hexanes (2 × 50 mL, 23°C), and dried under reduced pressure (< 1.5 mm) at 23°C for 14 hr to afford pure NBSH as an off-white powder (17.6 g, 81%); mp 100-101°C; IR (EtOAc) cm^{-1}: 3100-3400, 1547, 1352, 1165 ; ^1H NMR (300 MHz, CD_3CN) δ: 3.90 (bs, 2 H), 5.97 (bs, 1 H), 7.78-7.91 (m, 3 H), 8.03-8.17 (m, 1 H) ; ^{13}C NMR (75 MHz, CD_3CN) δ: 125.8, 130.8, 133.2, 133.4, 135.5, 149.4 . Anal. Calcd for $C_6H_7N_3O_4S$: C, 33.18; H, 3.25; N, 19.35. Found: C, 33.41; H, 3.27; N, 19.20; R_f = 0.19 (2:1 ethyl acetate-hexanes). Because solutions of NBSH are unstable at room temperature, the solution of NBSH in tetrahydrofuran should be prepared just prior to addition to the reaction mixture.
17. An orange oil composed of tetrahydrofuran and reaction by-products separates during the work-up and is removed.
18. A short silica gel pad approximately 10 cm in length by 5 cm in diameter is recommended. Isolation of the product by distillation (bp 111-120°C, bath temperature 150°C) resulted in significant material loss presumably due to its thermal decomposition.[6]
19. A suitable stain for detection of the allene (TLC analysis) is basic aqueous potassium permanganate solution.
20. On the basis of ^1H NMR analysis, the product contains 6-10% of pentane that can be removed by further rotary evaporation at 23°C, accompanied by evaporative loss of the product. The submitters obtained the product in 72% yield and report that their material contains 3-5% pentane . The allene product exhibits the following properties: TLC R_f = 0.64 (hexanes); IR (neat, cm^{-1}): 2953, 2858, 1933, 1617, 1471, 1250, 1214, 827, 805, 781 ; ^1H NMR (300 MHz, C_6D_6) δ: 0.06 (s, 6 H), 0.89 (s, 9 H), 4.26 (d, 2 H, J = 7.2), 4.86 (dd, 1 H, J = 7.2, 7.2) ; ^{13}C NMR (75 MHz, C_6D_6) δ: −5.8, 17.3, 26.4, 66.9, 78.2, 213.8 ; high resolution mass spectrum (EI) m/z 154.1176 [(M)+ calcd for $C_9H_{18}Si$: 154.1178].

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

There are few methods for the stereodefined construction of allenes.[7,8,9,10,11,12,13] The procedure described here provides a general and practical method for the synthesis of allenes from propargylic alcohol precursors in a single operation. The transformation involves the Mitsunobu invertive displacement of an alcohol with o-nitrobenzenesulfonyl hydrazide (NBSH), followed by elimination of o-nitrobenzenesulfinic acid to form a propargylic diazene intermediate that undergoes spontaneous sigmatropic elimination of dinitrogen to form an allene. The method is highly efficient and proceeds with complete stereospecificity under mild reaction conditions (neutral pH, reaction temperatures ≤23° C). The method is also well suited for the synthesis of (trialkylsilyl)allenes, including the heretofore difficultly accessible parent (tert-butyldimethylsilyl)allene,[12,13] as illustrated here. In addition, the method is applicable for the preparation of allenes with a wide variety of sensitive functional groups.[14,15]

References and Notes

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15. Generous financial support from the National Science Foundation is gratefully acknowledged.

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

(tert-Butyldimethylsilyl)allene:
Silane, (1,1-dimethylethyl)dimethyl-1,2-propadienyl- (13); (176545-76-9)

2-Propargyloxytetrahydropyran:
2H-Pyran, tetrahydro-2-(2-propynyloxy)- (8,9); (6089-04-9)

(±)-Camphorsulfonic acid:
Bornanesulfonic acid, 2-oxo-, (±)- (8);
Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-, (±)- (9); (5872-08-2)

Propargyl alcohol:
2-Propyn-1-ol (8,9); (107-19-7)

3,4-Dihydro-2H-pyran:
2H-Pyran, 3,4-dihydro- (8,9); (110-87-2)

3-(tert-Butyldimethylsilyl)-2-propyn-1-ol:
2-Propyn-1-ol, 3-[(1,1-dimethylethyl)dimethylsilyl]- (12); (120789-51-7)

Butyllithium:
Lithium, butyl- (8,9); (109-72-8)

tert-Butyldimethylsilyl chloride:
Silane, chloro(1,1-dimethylethyl)dimethyl- (9); (18162-48-6)

p-Toluenesulfonic acid monohydrate (8);
Benzenesulfonic acid, 4-methyl-, monohydrate (9); (6192-52-5)

Triphenylphosphine:
Phosphine, triphenyl- (8,9); (603-35-0)

Diethyl azodicarboxylate:
Formic acid, azodi-, diethyl ester (8);
Diazenedicarboxylic acid, diethyl ester (9); (1972-28-7)

o-Nitrobenzenesulfonyl hydrazide:
Benzenesulfonic acid, 2-nitro-, hydrazide (9); (5906-99-0)

N-Benzylidenebenzylamine:
Benzylamine, N-benzylidene- (8);
Benzenemethanamine, N-(phenylmethylene)- (9); (780-25-6)

Hydrazine HIGHLY TOXIC. CANCER SUSPECT AGENT (8,9); (302-01-2)

o-Nitrobenzenesulfonyl chloride:
Benzenesulfonyl chloride, o-nitro- (8);
Benzenesulfonyl chloride, 2-nitro- (9); (1694-92-4)

Hydrazine hydrochloride CANCER SUSPECT AGENT (8,9); (14011-37-1)