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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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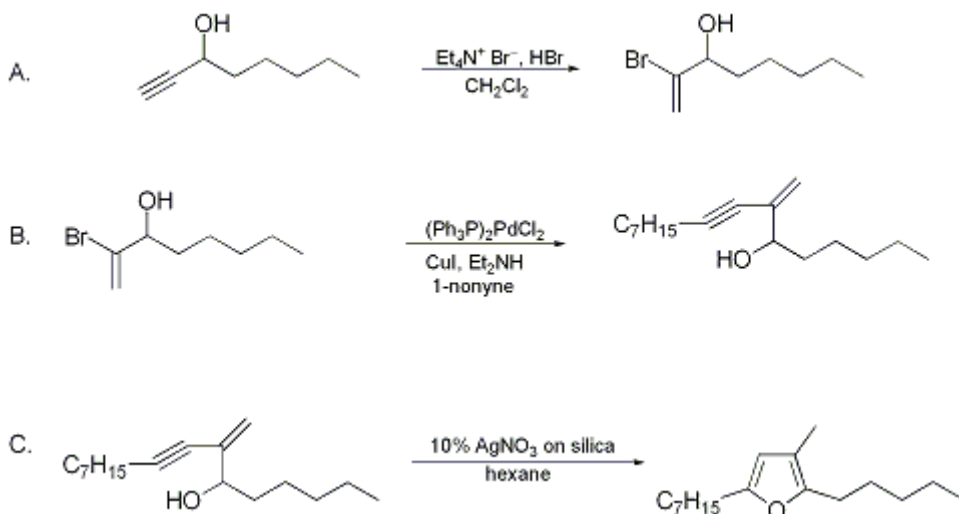
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ISOMERIZATION OF β -ALKYNYL ALLYLIC ALCOHOLS TO FURANS CATALYZED BY SILVER NITRATE ON SILICA GEL: 2-PENTYL-3-METHYL-5-HEPTYLFURAN

[Furan, 5-heptyl-3-methyl-2-pentyl-]



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1. Procedure

Caution! Because of the corrosive and toxic nature of the reagents, steps A and B should be conducted in an efficient fume hood. Eye protection and protective clothing should be worn while performing these experiments.

A. 2-Bromo-1-octen-3-ol² A one-necked, 250-mL, round-bottomed flask equipped with a magnetic stirring bar and a rubber septum is charged with 70 mL of **methylene chloride** (CH_2Cl_2) and 14.71 g (69.7 mmol) of anhydrous **tetraethylammonium bromide** (Et_4NBr) (Note 1). The flask and contents are cooled to 0°C , weighed, and 7.05 g (87.1 mmol) of gaseous **hydrogen bromide** (HBr) is introduced by needle through the septum into the stirred suspension (Note 2). The solid dissolves during the addition of HBr . To this solution is added 10.2 mL (69.7 mmol) of freshly distilled **1-octyn-3-ol** (Note 3), and the reaction is allowed to warm to room temperature. The reaction is closely monitored by thin-layer chromatography (Note 4) until starting material is consumed. The reaction mixture is cooled to 0°C , and 26 mL of **triethylamine** (Et_3N) is carefully added to the solution. The mixture is diluted with 200 mL of water and 200 mL of **ether**, and the layers are separated. The organic layer is washed with saturated **sodium bicarbonate** and brine, dried over **magnesium sulfate**, and concentrated under reduced pressure. Purification of the crude product by flash chromatography (Note 5) followed by bulb to bulb distillation (95°C , 0.5 mm) affords 8.91 g (62%) of **2-bromo-1-octen-3-ol** as a clear colorless oil (Note 6).

B. 7-Methylene-8-hexadecyn-6-ol³ A one-necked, 500-mL, round-bottomed flask equipped with a magnetic stirring bar and a rubber septum is charged with 8.65 g (41.8 mmol) of **2-bromo-1-octen-3-ol** in 210 mL of **diethylamine** (Note 7). A stream of **argon** is bubbled through the stirred solution for 10 min at room temperature. To this solution is added 1.47 g (2.09 mmol) of **dichlorobis(triphenylphosphine)palladium(II)** [$(\text{Ph}_3\text{P})_2\text{PdCl}_2$] (Note 8), 0.80 g (4.18 mmol) of **copper(I) iodide** (CuI) (Note 9), and 6.91 mL (42.1 mmol) of **1-nonyne** (Note 10). The reaction is closely monitored by thin-layer chromatography until all the **vinyl bromide** is consumed (Note 11), (Note 12). The reaction

mixture is poured into a 2-L Erlenmeyer flask and diluted with 500 mL of ether. Saturated ammonium chloride is added to the stirred solution until the evolution of gas ceases. The organic layer is washed with two portions of aqueous 10% hydrochloric acid, and the combined aqueous layers are extracted with 200 mL of ether. The organic extracts are dried over magnesium sulfate and concentrated under reduced pressure. Purification of the crude product by flash chromatography (Note 13) on silica gel (5% ethyl acetate-hexane) yields 9.94 g (95%) of 7-methylene-8-hexadecyn-6-ol as a light yellow oil (Note 14), (Note 15).

C. *2-Pentyl-3-methyl-5-heptylfuran*.⁴ A one-necked, 500-mL, round-bottomed flask equipped with a magnetic stirring bar and a rubber septum is charged with 9.64 g (38.5 mmol) of 7-methylene-8-hexadecyn-6-ol in 200 mL of hexane. To this solution is added 6.53 g (3.85 mmol) of 10% silver nitrate on silica gel (Note 16); the reaction is protected from light (Note 17) and stirred for 40 min at room temperature. Then 50 mL of ether is added, the mixture is filtered, and the filtrate is concentrated under reduced pressure. The recovered silver catalyst can be used for another reaction if desired, in which case a more extended reaction time (2-2.5 hr) may be required. The product is purified by flash chromatography (Note 18) on deactivated silica gel (Note 19) to afford 9.24 g (96%) of 2-pentyl-3-methyl-5-heptylfuran as a clear light yellow oil (Note 20). In the case at hand, when the above reaction was repeated with the recycled catalyst, a 91% yield of the furan product was obtained after chromatography.

2. Notes

1. The salt is crushed and then azeotropically dried with benzene three times, filtered, dried under vacuum for 2 days, and stored under argon over phosphorus pentoxide.
2. The flask is removed from the ice bath, wiped dry, and weighed every 3-5 min until the desired weight is achieved. Also, to relieve pressure, the flask is vented with an exit needle connected to tygon tubing placed in the back of the hood.
3. 1-Octyn-3-ol (96%) was purchased from Aldrich Chemical Company, Inc. It can be fractionally distilled to remove minor impurities.
4. TLC analysis is performed on E. Merck silica gel 60F-254 glass plates of 0.25-mm thickness purchased from EM Reagents. The eluting solvent was 15% ethyl acetate-hexane.
5. The checkers found that the addition of HBr to the starting propargyl alcohol provided an ca. 20 : 1 mixture of 2-bromo-1-octen-3-ol and the isomeric (Z)-1-bromo-1-octen-3-ol in 86-90% yield (isolated by distillation of the crude product). It proved necessary to purify 2-bromo-1-octen-3-ol by chromatography since products deriving from (Z)-1-bromo-1-octen-3-ol were completely inseparable at all subsequent stages of this procedure. The purification was performed by using a 90 × 500-mm column packed with 350 g of silica gel wetted with 1 L of hexane. The crude compound was charged as a solution in 75 mL of CH₂Cl₂. The column was eluted with 500 mL of hexane, followed by 1 L of 5% ethyl acetate/hexane, and then 2 L of 10% ethyl acetate/hexane. 2-Bromo-1-octen-3-ol eluted first [R_f = 0.64 (25% ethyl acetate-hexane)] followed by (Z)-1-bromo-1-octen-3-ol [R_f = 0.53 (25% ethyl acetate-hexane)].
6. Spectral analysis for 2-bromo-1-octen-3-ol is as follows: IR (film) cm⁻¹: 3358, 2930, 1626, 1465, 896; ¹H NMR (400 MHz, CDCl₃) δ: 0.87 (t, 3 H, J = 6.8), 1.24-1.37 (m, 6 H), 1.57-1.69 (m, 2 H), 1.86 (d, 1 H, J = 6.0), 4.06 (q, 1 H, J = 6.3), 5.54 (d, 1 H, J = 1.9), 5.85 (dd, 1 H, J = 0.74, J = 1.9); ¹³C NMR (100 MHz, CDCl₃) δ: 14.0, 22.5, 24.8, 31.5, 35.5, 76.1, 116.9, 137.6.
7. Diethylamine was purified by distillation from calcium hydride (CaH₂).
8. (Ph₃P)₂PdCl₂ was purchased from the Aldrich Chemical Company, Inc.
9. CuI purchased from the Aldrich Chemical Company, Inc. was washed with tetrahydrofuran in a Soxhlet extractor overnight, dried under vacuum overnight, and stored under argon over calcium sulfate.
10. The reaction mixture turned bright yellow after addition of the palladium catalyst. The color changed to greenish brown after the CuI was added and became yellow upon addition of the 1-nonyne.
11. Extended reaction times cause colored by-products to form, that are difficult to separate. TLC analysis was performed on E. Merck silica gel 60F-254 glass plates of 0.25-mm thickness purchased from EM Reagents. The eluting solvent was 20% ethyl acetate-hexane; in this solvent system, the R_f's of 7-methylene-8-hexadecyn-6-ol and 2-bromo-1-octen-3-ol are 0.68 and 0.55, respectively.
12. If the reaction was not complete within 2 hr, the checkers added an additional 0.25 equiv of 1-nonyne. The reaction was typically complete within 30-45 min following this addition.

13. A 70 × 370-mm column packed with 500 g of silica gel was used.
14. Spectral analysis for **7-methylene-8-hexadecyn-6-ol** is as follows: IR (film) cm^{-1} : 3363, 2929, 2858, 2225, 1614, 1465, 902 ; ^1H NMR (400 MHz, CDCl_3) δ : 0.75-0.98 (m, 6 H), 1.09-1.40 (m, 14 H), 1.41-1.66 (m, 5 H), 2.31 (t, 2 H, $J = 6.9$), 4.03 (q, 1 H, $J = 6.3$ Hz), 5.33 (d, 2 H, $J = 7.5$) ; ^{13}C NMR (100 MHz, CDCl_3) δ : 14.0, 14.0, 19.2, 22.5, 22.6, 25.0, 28.6, 28.7, 28.8, 31.6, 31.7, 35.9, 74.8, 77.7, 92.7, 119.2, 135.2 .
15. The checkers obtained a 92% yield for this reaction.
16. The 10% **silver nitrate** on silica gel (200 mesh) was purchased from the Aldrich Chemical Company, Inc.
17. The flask was wrapped with aluminum foil.
18. A 70 × 370-mm column packed with 300 g of silica gel was eluted with **hexane**; in this solvent system, the product has $R_f = 0.65$.
19. The silica gel was deactivated by flushing with 1 L of 5% **triethylamine-hexane** solution followed by 2 L of **hexane** to remove excess **triethylamine**.
20. Spectral analysis for **2-pentyl-3-methyl-5-heptylfuran** is as follows: IR (film) cm^{-1} : 2927, 2856, 1577, 1467, 792 ; ^1H NMR (300 MHz, CDCl_3) δ : 0.93 (t, 3 H, $J = 6.8$), 0.94 (t, 3 H, $J = 6.8$), 1.23-1.45 (m, 12 H), 1.57-1.67 (m, 4 H), 1.94 (s, 3 H), 2.54 (t, 2 H, $J = 7.3$), 2.57 (t, 2 H, $J = 7.3$), 5.77 (s, 1 H) ; ^{13}C NMR (100 MHz, CDCl_3) δ : 9.8, 14.0, 14.0, 22.4, 22.6, 25.9, 28.0, 28.2, 28.4, 29.1, 29.6, 31.4, 31.8, 107.6, 113.7, 149.3, 153.4 . Anal. Calcd for $\text{C}_{17}\text{H}_{30}\text{O}$: C, 81.53; H, 12.07. Found: C, 81.42; H, 11.99.

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 present procedure evolved from our previous work on the conversion of allenals, allenones, and allenylcarbinols to furans and 2,5-dihydrofurans with catalytic **silver nitrate** (AgNO_3) in **acetone**.^{5,6,7,8,9,10} It has also been shown that allenylcarbinols can be converted to **2,5-dihydrofuran** under these conditions.¹¹ β - and γ -Alkynyl **allylic alcohols** can also be isomerized to furans under strongly basic conditions with **potassium tert-butoxide** in tetrahydrofuran-tert-butyl alcohol-18-crown-6 or **hexamethylphosphoramide** (KO-t-Bu in THF-t-BuOH-18-crown-6 or HMPA).¹² The AgNO_3 /silica gel method is milder, faster, and more efficient than the previously reported procedures.¹³ Moreover, it offers the potential advantage of catalyst recovery and possible applicability to a flow system in which a packed column, protected from light, could serve as the reactor.⁴

References and Notes

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

2-Pentyl-3-methyl-5-heptylfuran:
Furan, 5-heptyl-3-methyl-2-pentyl- (13); (170233-67-7)

2-Bromo-1-octen-3-ol:
1-Octen-3-ol, 1-bromo-, (E)- (9); (52418-90-3)

Tetraethylammonium bromide:
Ammonium, tetraethyl-, bromide (8);
Ethaniminium, N,N,N-triethyl-, bromide (9); (71-91-0)

Hydrogen bromide:
Hydrobromic acid (8,9); (10035-10-6)

1-Octyn-3-ol (8,9); (818-72-4)

7-Methylene-8-hexadecyn-6-ol:
8-Hexadecyn-6-ol, 7-methylene- (13); (170233-66-6)

Dichlorobis(triphenylphosphine)palladium(II);
Palladium, dichlorobis(triphenylphosphine)- (8,9); (13965-03-2)

Copper(I) iodide:
Copper iodide (8,9); (7681-65-4)

1-Nonyne (8,9); (3452-09-3)

Silver nitrate ~ 10 wt, % on silica gel:
Nitric acid silver(+) salt (9); (7761-88-8)

Phosphorus pentoxide:
Phosphorus oxide (8,9); (1314-56-3)

(Z)-1-Bromo-1-octen-3-ol:
1-Octen-3-ol, 1-bromo-, (Z)- (11); (87937-09-5)