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Convenient Generation of 1-Propynyllithium. One-Pot Synthesis of Acetylenic Carbinols from 1,2-Dibromopropane and Aldehydes and Ketones

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SYNTHETIC COMMUNICATIONS, 22(20), 2997-3002 (1992)

CONVENIENT GENERATION OF 1-PROPYNYLLITHIUM. ONE-POT SYNTHESIS OF ACETYLENIC CARBINOLS FROM 1,2-DIBROMOPROPANE AND ALDEHYDES AND KETONES

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Abstract: Treatment of 1,2-dibromopropane (**1**) with 3 equiv of lithium diisopropylamide (–60° to 0 °C, THF) generates 1-propynyllithium (**2**), which with aldehydes or ketones affords acetylenic carbinols **3** in 82-96% yields.

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Although the synthesis of terminal alkynes by base treatment of either 1,2- or 1,1-dihaloalkanes is well established[1-4] and the C-1 metalation and quenching of terminal alkynes is an important tactic in synthesis (e.g., chain elongation), the combination of these two reactions into a one-pot operation does not appear to have been reported. We now report that treatment of 1,2-dibromopropane (**1**) with lithium diisopropylamide (LDA) (3 equiv, THF, –60° to 0 °C) followed by quenching the presumed intermediate 1-propynyllithium (**2**) with aldehydes or ketones (–60 °C) furnishes the acetylenic carbinols **3** ($R^1 = CH_3$, Ph; R^2 = H, CH_3, Ph) in excellent yields. Our results are summarized in the Table.

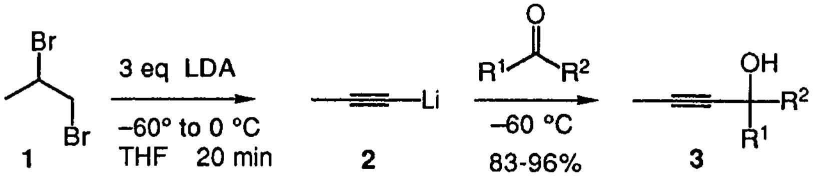

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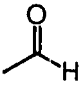
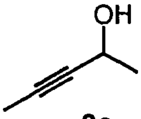
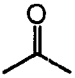
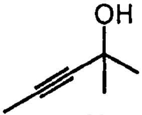
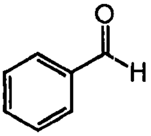
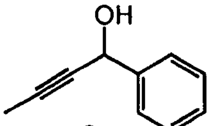
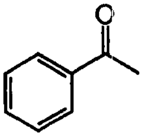
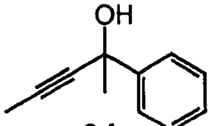
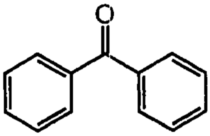
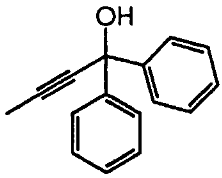
Table. Syntheses of Acetylenic Carbinols **3a-e** by the Reaction of 1,2-Dibromopropane (**1**) with Lithium Diisopropylamide and Aldehydes or Ketones.

Substrate	Product	Yield, %
	 **3a**	83
	 **3b**	84
	 **3c**	96
	 **3d**	89
	 **3e**	82

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The method is operationally simple and avoids the need for gaseous propyne. Moreover, our yields are substantially higher than those reported for preparations of the same compounds starting from propyne (83% vs. 64% for **3a**[5], 84% vs. 47% for **3b**[6] and 96% vs. 68% for **3c**[7]). It remains to be seen if this reaction can be extended to other 1,2-dibromoalkanes as well as other electrophiles.

In related chemistry, Corey and Fuchs have described the generation of terminal acetylenides by *n*-BuLi treatment of 1,1-dibromoalkenes and subsequent trapping with water or CO_2.[8] Anthony and Diederich have used the reaction between (*E*)-1,2-dichloroethylene and MeLi to generate 2-chloroethynyllithium followed by quenching with biphenyldimethylsilyl chloride.[9] And, in what is perhaps the closest analogy to the present work, Normant and coworkers have generated lithium acetylenides from the reaction between 1,1-dichloroalkanes and excess *n*-BuLi.[10] In the latter study, only chloromethyl ethyl ether was employed as the electrophile.

In summary, the reaction of 1,2-dibromopropane (**1**) with 3 equivalents of lithium diisopropylamide followed by treatment of the presumed 1-propynyllithium (**2**) intermediate with aldehydes or ketones provides acetylenic carbinols **3a-e** in excellent yields.

Experimental

General: Melting points were determined with a Mel-Temp Laboratory Devices apparatus, and are uncorrected. Infrared spectra were recorded on a Bio-Rad FT-IR Infrared Spectrophotometer, mass spectra were measured at 70 eV on a Hewlett Packard gas chromatograph-mass spectrometer, and ^{13}C and ^{1}H NMR spectra were recorded on a Varian XL-300 Fourier-transform NMR spectrometer operating at 75 and 300 MHz, respectively. Flash chromatography was performed using 230-400 mesh silica gel 60 from EM Science. Thin layer chromatography

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(TLC) was performed on 0.2 mm silica gel 60 F_{254} aluminum backed plates from E. Merck. Tetrahydrofuran (THF) was distilled from sodium/benzophenone, and diisopropylamine was distilled from calcium hydride. Reactions were performed in oven-dried glassware, with magnetic stirring, and under dry argon. Alkyllithium reagents were titrated with diphenylacetic acid, 1,3-diphenyl-2-propanone tosylhydrazone,[11] or *sec*-butyl alcohol and 2,2'-bipyridine[12] prior to use.

3-Pentyn-2-ol (3a) (General Procedure). To a solution of lithium diisopropylamide (31 mmol) in dry THF (30 mL) at –60 °C was added dropwise 2.02 g (10 mmol, 1.04 mL) of 1,2-dibromopropane. The resulting mixture was allowed to warm to 0 °C for 20 min and then recooled to –60 °C. To the reaction mixture was added 0.528 g (12 mmol, 0.67 mL) of acetaldehyde in one portion. The reaction was stirred at –60 °C for 25 min and then poured into a solution of saturated NH_4Cl. The aqueous layer was extracted with ether (3 x 50 mL) and the combined ether layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was distilled to give 0.70 g (83%) of 3-pentyn-2-ol (3a): bp 80 °C/ 20 Torr (Kugelrohr, pot temp; lit.[5] bp 50-55 °C/16 Torr); IR (neat) 3361, 2983, 2923, 2259, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.46 (m, 1 H), 2.18 (br s, 1 H), 1.81 (s, 3 H), 1.40 (dd, 3 H, J=3.9 Hz, J= 2.7 Hz); ^{13}C NMR ($CDCl_3$) δ 81.4, 80.0, 58.4, 24.6, 3.39.

2-Methyl-3-pentyn-2-ol (3b). The crude product was distilled under reduced pressure (Kugelrohr, pot temp; 100 °C/2.5 Torr) (lit.[6] bp 133.5-134.5 °C/750 Torr) to give 0.820 g (84%) of 2-methyl-3-pentyn-2-ol (3b); IR (neat) 3420, 2238, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.81 (s, 1 H), 1.48 (s, 3 H), 1.25 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 84.3, 77.3, 65.0, 31.6, 3.32.

1-Phenyl-2-butyn-1-ol (3c). The crude product was distilled under reduced pressure (Kugelrohr, pot temp; 150 °C/3.0 Torr) (lit.[7] bp 99.5-103 °C/1.3 Torr) to give 1.40 g (96%) of 1-phenyl-2-butyn-1-ol (3c); IR (neat) 3364, 3060, 2921, 2230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53 (d, 2 H, J = 7.0 Hz), 7.36 (m, 3 H), 5.40 (s, 1 H), 2.35 (br s, 1 H), 1.88 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 141.2, 128.5, 128.2, 126.5, 83.0, 79.1, 64.7, 3.66.

2-Phenyl-3-pentyn-2-ol (3d). The crude product was distilled under reduced pressure (Kugelrohr, pot temp; 170 °C/0.75 Torr) to give 1.42 g (89%) of 2-phenyl-3-pentyn-2-ol (3d) as a crystalline solid. Recrystallization from petroleum ether gave material having mp 41-42 °C (lit.[13] mp 41-42.5 °C); IR (neat) 3468, 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.63 (d, 2 H, J = 7.0 Hz), 7.30 (m, 3 H), 3.18 (br s, 1 H), 1.90 (s, 3 H), 1.73 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.0, 127.9, 127.1, 124.8, 83.0, 80.6, 69.6, 33.2, 3.31.

1,1-Diphenyl-2-butyn-1-ol (3e). The crude product was chromatographed on silica gel (eluent; 8:1 hexane/ethyl acetate, Rf 0.23) to give 1.83 g (82%) of 1,1-diphenyl-2-pentyn-1-ol (3e) as an oil (lit.[13] bp 136-138 °C/0.003 Torr) ; IR (neat) 3438, 2234 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.57-7.60 (m, 4 H), 7.23-7.34 (m, 6 H), 2.72 (br s, 1 H), 1.96 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 145.4, 128.1, 127.5, 126.0, 83.7, 76.5, 74.4, 3.83.

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