4.45 (d, J = 16 Hz, 2 H), 6.40 (s, 4 H). The crude product (100 mg) was purified by preparative TLC (silica gel, 2 × 200 μM thickness) using 50% CH_2Cl_2 in hexane to give 80 mg (80% recovery) of the desired calix[4]arene as white solid (R_f 0.55): mp 335–365 °C (CH_2Cl_2); ^1H NMR ($CDCl_3$, 60 MHz) identical with the above data; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.12 (s, 3 H), 1.17 (s, 3 H), 1.18 (s, 3 H), 1.23 (s, 3 H), 2.36 (s, 6 H), 2.37 (s, 3 H), 3.52 (d, 1 H, J = 16.63 Hz), 3.58 (d, 1 H, J = 16.66 Hz), 3.78 (s, 3 H), 3.78 (s, 3 H), 3.79 (s, 3 H), 3.80 (s, 3 H), 3.81 (s, 2 H), 4.06 (s, 2 H), 4.34 (d, 1 H, J = 16.66 Hz), 4.36 (d, 1 H, J = 16.63 Hz,), 6.48 (s, 3 H), 6.49 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.39 (10%, CH_3), 16.90 (30%, 2 × CH_3), 17.25 (12%, CH_3), 21.89 (47%, 4 × CH_3), 26.25 (19%, $ArCH_2Ar$), 30.77 (9%, $ArCH_2Ar$), 55.58 (34%, OCH_3), 55.75 (20%, OCH_3), 109.95 (21%, Ar), 110.06 (15%, Ar), 110.14 (17%, Ar), 127.53 (16%, Ar), 127.66 (17%, Ar), 127.77 (13%, Ar), 132.16 (28%, Ar), 133.40 (6%, Ar), 133.46 (9%, Ar), 133.54 (9%, Ar), 133.62 (11%, Ar), 133.68 (12%, Ar), 133.81 (15%, Ar), 133.92 (9%, Ar), 137.36 (10%, Ar), 137.49 (22%, Ar), 137.68 (10%, Ar), 154.40 (13%, Ar), 154.51 (12%, Ar), 154.59 (11%, Ar), 154.70 (14%, Ar), 154.78 (8%, Ar); high-resolution mass spectrum calcd for $C_{40}H_{48}O_4$ 592.3552, found 592.3554. Anal. (dried in vacuo at 100 °C for 30 min prior to analysis). Calcd for $C_{40}H_{48}O_4 \cdot {}^1/_2H_2O$: C, 79.83; H, 8.21; O, 11.96. Found: C, 79.64; H, 8.29; O, 11.72.

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A Convenient Procedure for the Preparation of Ethoxyacetylene and Ethoxyethynyl Carbinols

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The use of ethoxyacetylene in organic synthesis is well-known.[2a,b] The condensation of ketones or aldehydes with the anion of ethoxyacetylene yields carbinols, which may be converted to α,β-unsaturated esters, aldehydes, or carboxylic acids.[2c-f] Ethoxyacetylene undergoes cycloaddition reactions with ketenes to form cyclobutenone ethers.[2g-i] It has also been used as a coupling reagent in the synthesis of peptides[2j] and acid anhydrides.[2b]

Although ethoxyacetylene is commercially available, it is expensive and generally requires distillation prior to use. The standard methods for the preparation of ethoxyacetylene involve the reaction of chloroacetaldehyde diethyl acetal[3,4] or β-bromovinyl ethers[5] with either sodium amide or lithium amide in liquid ammonia. These methods are time consuming and inconvenient, and the isolated ethoxyacetylene often contains significant amounts of ethanol.[6] Furthermore, it is not practical to synthesize carbinols by the direct reaction of ketones or aldehydes with sodium ethoxyacetylide prepared by these methods.[7]

Scheme I

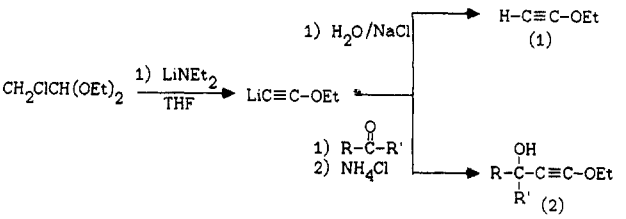

Table I

entry	carbonyl compd	2 isolated yield, %	2 lit. yield, % (ref)
a	acetone	95	60 (10)
b	propionaldehyde	91	47 (11)
c	methyl vinyl ketone	72	30 (10)
d	benzaldehyde	71	72 (11)
e	cyclohexanone	81	67 (7)
f	cholestan-3-one	75	~90[a] (12)

[a] Crude yield.

We now wish to report that treatment of chloroacetaldehyde diethyl acetal with 3 equiv of lithium diethylamide in THF at 0 °C affords lithium ethoxyacetylide, which may be conveniently converted to either ethoxyacetylene or ethoxyethynyl carbinols (Scheme I). Ethoxyacetylene is obtained by evaporation of the volatiles (THF, diethylamine, and hexanes) at reduced pressure, quenching the resulting lithium salts with saturated aqueous sodium chloride, and extraction of the aqueous solution with xylenes. Ethoxyacetylene (bp 48–50 °C) is distilled from the xylenes as a colorless liquid free of ethanol in 70% yield. If the presence of small amounts of ethanol and water in the ethoxyacetylene is acceptable, an alternate workup may be employed. The ethoxyacetylene is distilled directly from the aqueous solution through a short Vigreux column (bp 40–50 °C) into a −78 °C trap, and the ethoxyacetylene is decanted from the water that freezes at the bottom of the trap.

Ethoxyethynyl carbinols may be prepared directly from the lithium ethoxyacetylide generated in THF at 0 °C by reaction with aldehydes or ketones (Table I). If necessary, the ethoxyethynyl carbinol may be purified by Kugelrohr distillation or flash chromatography. Valuable or high-boiling carbonyl compounds may be used as the limiting reagent.[8]

The application of this modified procedure in the synthesis of ethoxyacetylene or ethoxyethynyl carbinols involves considerably less time than the previously reported procedures and does not require liquid ammonia solvent, and the reactions proceed cleanly and efficiently.

Experimental Section

Boiling points are uncorrected. ^1H NMR spectra were obtained on a Varian EM-360 (60 MHz), a Varian CFT-20 (80 MHz), or a Varian VXR-300 (300 MHz) instrument. Chemical shifts are reported in ppm (δ) downfield from tetramethylsilane, and cou-

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(6) NMR integration shows that ethoxyacetylene thus obtained contains 15–20 mol % ethanol.

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pling constants (J) are reported in hertz. Mass spectra were obtained by GC or direct insertion probe on a Hewlett-Packard 5985 GC/MS and the associated 7906 data system. IR spectra were obtained on a Beckman Acculab 4 and are reported in cm^{-1}. Gas chromatography was conducted on a Hewlett-Packard 5790A instrument fitted with a 12-m DB-5 fused-quartz capillary column. THF was distilled from sodium/benzophenone. The aldehydes and ketones were passed through a short column of silica gel 60 (40–63 μm, E. Merck) prior to use. All reactions were conducted in flame-dried glassware and under a slight positive pressure of argon.

Ethoxyacetylene. To a solution of diethylamine (16.6 mL, 160 mmol) in THF (300 mL) at 0 °C was added a 2.30 M solution of *n*-BuLi (61.7 mL, 142 mmol) in hexanes. The solution was stirred for 10 min, and chloroacetaldehyde diethyl acetal (7.00 mL, 45.9 mmol) was added over 5 min. The solution was stirred for 30 min at 0 °C, and the volatiles (THF, diethylamine, and hexanes) were removed at reduced pressure (30 °C, 15 mm). The lithium salts were further dried to an off-white powder at reduced pressure (0.15 mmHg, several hours). *CAUTION: exposure of the dried lithium salts to air results in an exothermic reaction and the evolution of a noxious yellow gas.*[9] The flask containing the dried lithium salts (still under vacuum) was then cooled to −78 °C in an acetone/dry ice bath and purged with argon. As rapidly as possible, an ice cooled, saturated aqueous sodium chloride solution (125 mL) was added while the flask was manually swirled to prevent the water from freezing. The aqueous quenching of the lithium salts is exothermic. If this procedure is not followed, the yield of ethoxyacetylene decreases, primarily due to evaporation from the warm aqueous solution. Ethoxyacetylene was extracted from the cold solution with xylenes at 0 °C (3 × 30 mL); the combined xylene extracts were dried ($MgSO_4$) and filtered. The ethoxyacetylene was distilled from the xylenes through a short Vigreux column and collected in a 0 °C flask as a colorless liquid (2.25 g, 32.14 mmol) in 70% yield: bp 48–50 °C (lit.[3] 49–51 °C); IR (neat, cm^{-1}) 3300, 2145; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.37 (t, J = 7.5, 3 H), 1.53 (s, 1 H), 4.23 (q, J = 7.5, 2 H).

1-Ethoxy-3-methylbut-1-yn-3-ol (2a). General Procedure. To a solution of diethylamine (2.37 mL, 22.9 mmol) in THF (150 mL) at 0 °C was added 2.4 M *n*-BuLi (8.50 mL, 20.4 mmol) in hexane. The solution was stirred for 10 min, chloroacetaldehyde diethyl acetal (1.00 mL, 6.55 mmol) was slowly added, and the solution was stirred at 0 °C for 2 h. Acetone (0.96 mL, 13.1 mmol) was added rapidly, the solution was stirred at 0 °C for 30 min, the volatiles were evaporated under reduced pressure, and saturated aqueous ammonium chloride (100 mL) was added. The aqueous layer was extracted with ether (3 × 25 mL), the combined ether extracts were dried ($MgSO_4$) and filtered, and the ether was evaporated under reduced pressure to yield **2a** as a liquid (0.796 g, 95%) with no impurities detected by NMR, TLC, or IR: ^1H NMR ($CDCl_3$, 60 MHz) δ 1.33 (t, J = 7, 3 H), 1.48 (s, 6 H), 2.67 (s, 1 H), 4.08 (q, J = 7, 2 H); IR (neat, cm^{-1}) 3380, 3000–2900, 2280; direct insertion probe MS, m/e 128 (M^+), 99, 97, 83, 69, 53.

1-Ethoxypent-1-yn-3-ol (2b). The reaction was carried out by the general procedure using propionaldehyde (0.95 mL, 13.1 mmol) to give a viscous brown liquid (0.836 g), which was purified by Kugelrohr distillation to afford **2b** as a colorless liquid [0.761 g, 91%, bp 55 °C (1 mm) (lit.[11] bp 68–71 °C (3 mm))]: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.03 (t, J = 7, 3 H), 1.41 (t, J = 7.5, 3 H), 1.6–1.8 (m, 3 H), 4.14 (q, J = 7.5, 2 H), 4.39 (q, J = 9, 1 H); IR (neat, cm^{-1}) 3360, 2980–2880, 2270; direct insertion probe MS, m/e 128 (M^+), 99, 71, 57.

1-Ethoxy-3-methylpent-4-en-1-yn-3-ol (2c). The reaction was carried out by the general procedure using methyl vinyl ketone (0.425 mL, 5.24 mmol) to give a heavy brown liquid (0.70 g), which was purified by Kugelrohr distillation to afford **2c** as a clear liquid [0.524 g, 72%, bp 55–60 °C (0.1 mm) (lit.[10] bp 54–55 °C (0.1 mm))]: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.42 (t, J = 7, 3 H), 1.57 (s, 3 H), 2.02 (s, 1 H), 4.15 (q, J = 7, 2 H), 5.12 (dd, J = 10, 1, 1 H), 5.50 (dd, J = 17, 1, 1 H), 6.02 (dd, J = 17, 10, 1 H); IR (neat, cm^{-1}) 3410, 3100–2800, 2285; direct insertion probe MS, m/e 140 (M^+), 128, 125, 111, 97, 85, 71, 69, 55.

1-Ethoxy-3-phenylprop-1-yn-3-ol (2d). The reaction was carried out by the general procedure using benzaldehyde (0.532 mL, 5.24 mmol) to give a heavy brown liquid (1.39 g), which was purified by flash chromatography (95% methylene chloride/ether) to give **2d** as a liquid (0.652 g, 71%): ^1H NMR ($CDCl_3$, 80 MHz) δ 1.34 (t, J = 8, 3 H), 2.53 (d, J = 6, 1 H), 4.07 (q, J = 8, 2 H), 5.44 (d, J = 6, 1 H), 7.2–7.6 (m, 5 H); IR (neat, cm^{-1}) 3400, 3100–2900, 2283; GCMS, m/e 176 (M^+), 161, 158, 147, 131, 99.

1-(2-Ethoxyethynyl)cyclohexanol (2e). The reaction was carried out by the general procedure using cyclohexanone (0.543 mL, 5.24 mmol) to give a heavy brown liquid (1.10 g), which was purified by flash chromatography (95% methylene chloride/ether) to give **2e** as a pale liquid (0.712 g, 81%): ^1H NMR ($CDCl_3$, 80 MHz) δ 1.36 (t, J = 8, 3 H), 1.2–2.0 (m, 10 H), 2.23 (s, 1 H), 4.05 (q, J = 8, 2 H); IR (neat, cm^{-1}) 3400, 3000–2800, 2280; GCMS, m/e 168 (M^+), 153, 139, 97, 69.

3-(Ethoxyethynyl)cholestan-3-ol (2f). The reaction was carried out by the general procedure using cholestan-3-one (0.50 g, 1.29 mmol) to give a brown foam (0.65 g), which was purified by flash chromatography (95% chloroform/ether) to afford **2f** as a white foam (0.43 g, 75%). Crystallization from ethanol/water gave white plates [mp 72–73 °C (lit.[12] (2 mol of carbinol/mol of acetone) mp 85–86 °C)]: ^1H NMR ($CDCl_3$, 60 MHz) δ 0.67–2.20 (m, 50 H), 4.08 (q, J = 7, 2 H); IR (CCl_4, cm^{-1}) 3612, 3650–3250, 3000–2800, 2280; direct insertion probe MS, m/e 456 (M^+), 441, 427, 69. The stereochemistry of addition (at C_3) was not determined.

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(9) Pyrophoric properties have also been reported for the analogous sodium salts (see ref 3). We have not experienced explosions with these lithium salts; however, we would recommend handling them with caution.

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