(2 mL) was added drop-by-drop. The mixture was stirred for 30 min, and then saturated aqueous NH_4Cl was added. The mixture was filtered, and the two liquid phases of the filtrate were separated. The solid that was collected by filtration was washed with Et_2O (3 × 15 mL). The washings were added to the organic phase of the filtrate. The combined organic phases were washed with saturated aqueous NH_4Cl (2 × 20 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel; (EtOAc/hexane = 10:90) to give 104 mg (70%) of **14**: an oil; TLC (EtOAc/hexane, 10:90) R_f = 0.15; $[\alpha]^{25}_D$ = −85.2° (*c* 2.9, $CHCl_3$); IR (neat) 1767, 1727, 1257 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.74–1.68 (3 H, m), 0.86 (3 H, d, *J* = 6.4 Hz, Me), 1.20–1.58 (3 H, m), 1.52 (3 H, s, Me), 1.88–1.99 (2 H, m), 2.06 (3 H, d, *J* = 1.4 Hz, Me), 4.87 (1 H, ddd, *J* = 10.4, 10.4, 4.5 Hz), 5.81 (1 H, d, *J* = 1.4 Hz), 7.12–7.32 (5 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.2 (q), 20.8 (q), 21.6 (q), 24.8 (q), 27.1 (q), 29.1 (t), 31.3 (t), 34.2 (t), 40.1 (s), 41.4 (d), 49.9 (d), 78.0 (d), 88.1 (s), 117.5 (d), 125.5 (two CH), 128.1 (two CH), 150.0 (s), 167.1 (s), 167.4 (s), 171.5 (s); MS *m/z* (rel intensity) 370 (49, M^+), 347 (11), 311 (5), 252 (3), 214 (20), 157 (30), 119 (100), 112 (44).

Ethyl 5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2-Hydroxy-3-methoxy-2-methyl-3-pentenedioate (15) and 5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2,5-Dihydro-3-methoxy-2-methyl-5-oxofuran-2-carboxylate (16). Under an atmosphere of N_2, but without attempting to rigorously exclude O_2, MeLi (2 mmol, 1.25 mL of a 1.6 M solution in Et_2O) was added drop-by-drop to a cold (−20 °C) stirred suspension of CuI (1 mmol, 190 mg) in Et_2O (5 mL). After 20 min, the mixture was cooled to −30 °C, and a solution of the furanone **11a** (80 mg, 0.2 mmol) in Et_2O (1 mL) was added drop-by-drop. The mixture was allowed to warm to rt and was kept there for 3 h. Then saturated aqueous NH_4Cl was added, and the whole was extracted with EtOAc. The extract was washed with brine, dried (Na_2SO_4), and concentrated. The residue was passed through a column of silica gel (EtOAc:hexane = 10:90) to give compounds **15** (23.3 mg, 27%) and **16** (27.6 mg, 32%). **15**: an oil; HPLC (EtOAc/hexane, 10:90) t_R = 12.5 min; IR (neat) 3450, 2954, 1725, 1710, 1599, 1420 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.77–1.09 (3 H, m), 0.89 (3 H, d, *J* = 6.4 Hz), 1.24 (3 H, s), 1.30 (3 H, t, *J* = 6.7 Hz), 1.31 (3 H, s), 1.35 (3 H, s), 1.36–1.65 (3 H, m), 1.93 (1 H, m), 2.09 (1 H, ddd, *J* = 10.5, 10.5, 4.0 Hz), 3.12 (1 H, s, OH), 3.99 (3 H, s, OMe), 4.18 (1 H, q, *J* = 6.7 Hz), 4.94 (1 H, ddd, *J* = 10.6, 10.6, 4.1 Hz), 5.46 (1 H, s), 7.12–7.22 (1 H, m), 7.25–7.36 (4 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.8 (q), 19.0 (q), 19.2 (q), 21.7 (q), 22.3 (q), 26.0 (q), 27.0 (t), 27.8 (t), 30.7 (t), 32.0 (d), 34.4 (t), 40.0 (s), 41.1 (t), 49.9 (d), 63.9 (t), 76.4 (d), 95.2 (d), 125.4 (d), 125.5 (two CH), 128.2 (two CH), 150.8 (s), 165.5 (s), 169.3 (s), 172.5 (s); MS *m/z* (rel intensity) 432 (1, M^+), 389 (7), 313 (11), 269 (12), 243 (44), 218 (19), 173 (100), 105 (32); HRMS calcd for $C_{25}H_{36}O_6$ 432.2510, found 432.2522. **16**: an oil; HPLC (EtOAc:hexane = 10:90) t_R = 14.3 min; IR (neat) 1735, 1600 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.79–1.10 (3 H, m), 0.88 (3 H, d, *J* = 6.4 Hz), 1.22 (3 H, s), 1.32 (3 H, s), 1.36 (3 H, s), 1.40–1.67 (3 H, m), 1.95 (1 H, m), 2.06 (1 H, ddd, *J* = 10.4, 10.4, 3.9 Hz), 3.85 (3 H, s, OMe), 4.91 (1 H, ddd, *J* = 10.5, 10.5, 4.0 Hz), 5.11 (1 H, s), 7.13–7.25 (1 H, m), 7.28–7.42 (4 H, m); MS *m/z* (rel intensity) 374 (1, M^+), 343 (2), 328 (1), 214 (6), 199 (15), 142 (19), 119 (100), 105 (86).

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Registry No. **7**, 88292-41-5; **8a**, 139944-71-1; **8b**, 140147-00-8; **8c**, 140147-01-9; **8d**, 140147-02-0; **9a**, 139944-72-2; **9b**, 140147-03-1; **9c**, 140147-04-2; **9d**, 140147-05-3; **11a**, 139944-73-3; **11b**, 139944-79-9; **12**, 139944-74-4; **13**, 139944-75-5; **14**, 139944-76-6; **15**, 139944-77-7; **16**, 139944-78-8; 2-propenyl-1,3-dithiane, 51102-63-7; ethyl propiolate, 623-47-2.

Supplementary Material Available: X-ray crystallographic data for compound **9a** (ORTEP drawing, atomic coordinates, bond distances, and bond angles) and physical properties of compounds **8–9** and **11–16**, including ^1H and ^{13}C NMR spectra (35 pages). Ordering information is given on any current masthead page.

B-[2-(Trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane. A New Organoboron Reagent for the Preparation of Propargylic Alcohols†

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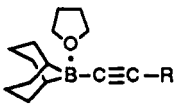
Introduction

Propargylic alcohols are key intermediates in the synthesis of many natural products including the prostaglandins,[1] steroids,[2] carotenoids,[3] and leukotrienes.[4] Researchers in this area have focused their attention mainly on the addition of alkynylmetals (Li, Na, K, Mg, Zn, and Al) to aldehydes as a means of preparing propargylic alcohols,[5] but these alkynylmetal reagents are not without limitations.

As an alternative to the alkynylmetals, Brown et al.[6,7] prepared a series of *B*-1-alkynyl-9-borabicyclo[3.3.1]nonanes as 1:1 complexes with THF (*B*-1-alkynyl-9-BBN, 1)



1; R= C_4H_9, $-CH(CH_3)_2$, $-C(CH_3)_3$, Ph
2; R= $Si(CH_3)_3$

and demonstrated their reaction with aldehydes and ketones to give the corresponding propargylic alcohols. These reagents were very mild, showing no reactivity toward a variety of functional groups[8] such as esters, nitriles, acetals, ketals, acid chlorides, alkyl halides, and amides, and perferentially react with aldehydes in the presence of ketones. Unfortunately, *B*-ethynyl-9-borabicyclo[3.3.1]nonane, the simplest member of this series, decomposed upon warming from −78 °C to room temperature and could not be isolated or studied.

We now wish to report the preparation of *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (**2**) and its reaction with aldehydes and ketones to give the corresponding trimethylsilyl-protected propargylic alcohols.[9]

Results and Discussion

B-[2-(Trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (**2**) was prepared from (trimethylsilyl)acetylene and *B*-methoxy-9-borabicyclo[3.3.1]nonane, using a modification of a literature procedure[7] (Scheme I), and isolated under a nitrogen atmosphere as a solid 1:1 complex with THF in 90% yield. Similar to the reagents reported by Brown et al.,[6-8] *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (**2**) reacted with a variety of aldehydes and ketones to afford the corresponding 2-(trimethylsilyl)ethynyl alcohols in excellent yields (Table I).

For example, when 1-octanal was added to a solution of **2** in pentane at 25 °C, a slight yellow color developed and dissipated within 30 min, indicating that the reaction was nearly complete. The reaction was complete in less than 1 h. Ethanolamine and methanol were added to the reaction at 0 °C, resulting in the precipitation of the 9-BBN-ethanolamine adduct **4**. Upon centrifugation and

† Dedicated to Professor Herbert C. Brown on the occasion of his 80th birthday.
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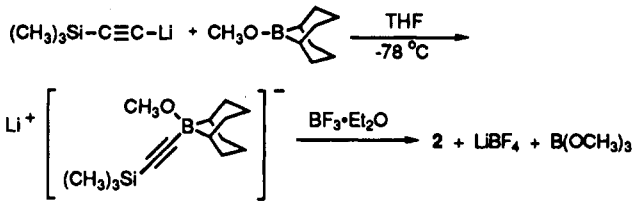
Table I. Reaction of *B*-[2-(Trimethylsilyl)ethynyl]-9-BBN (2) with Aldehydes and Ketones

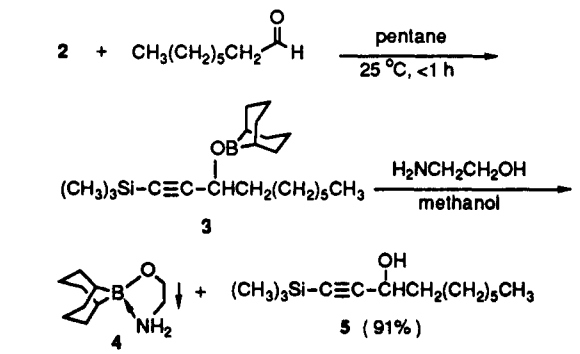
carbonyl compd[a]	reaction time	product(s)	isolated yield, %
1-octanal	<1 h	1-(trimethylsilyl)-1-decyn-3-ol (5)	91
hydrocinnamaldehyde	6 h	5-phenyl-1-(trimethylsilyl)-1-pentyn-3-ol (6)	89
pivaldehyde	5 d	4,4-dimethyl-1-(trimethylsilyl)-1-pentyn-3-ol (7)	93
(2*R*)-2-methoxy-2-methylhexanal	3 d	(3*S*,4*R*)-4-methoxy-4-methyl-1-(trimethylsilyl)-1-octyn-3-ol (8)	51
		(3*R*,4*R*)-4-methoxy-4-methyl-1-(trimethylsilyl)-1-octyn-3-ol (9)	10
cyclohexanone	16 h	1-[2-(trimethylsilyl)ethynyl]cyclohexanol (10)	88
2-octanone	2 d	1-(trimethylsilyl)-3-methyl-1-nonyn-3-ol (11)	71

[a] All reactions were performed at 25 °C in pentane, except the reaction of 2-octanone which was performed at 60 °C in pentane.

Scheme I



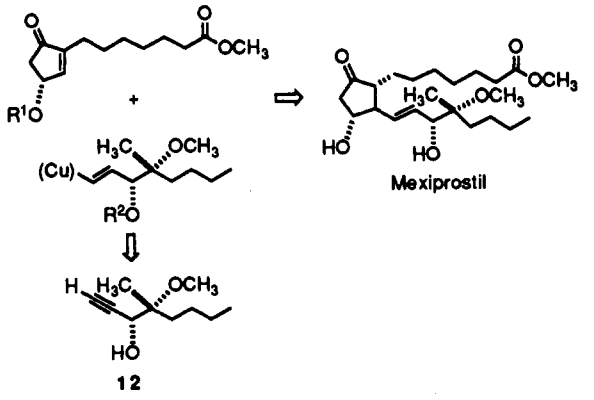
Scheme II



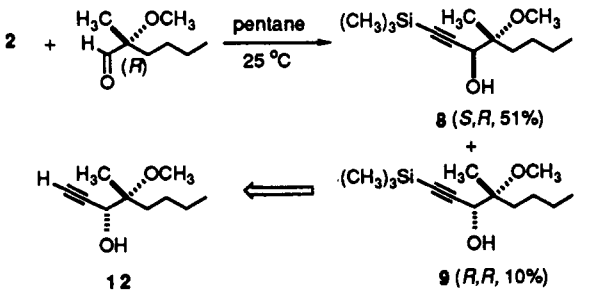
flash chromatography on silica gel, 1-(trimethylsilyl)-1-decyn-3-ol (**5**) was isolated in 91% yield (Scheme II).

Even pivaldehyde, a very hindered aldehyde, gave an excellent yield of the corresponding propargylic alcohol. Recently, Kolb, et al.[10] reported a convergent synthesis (Scheme III) of the gastroprotector mexiprostil[11] utilizing a vinyl cuprate which had been prepared from the corresponding propargylic alcohol **12**. The reaction of **2** with

Scheme III



Scheme IV



(2*R*)-2-methoxy-2-methylhexanal afforded a mixture of diastereomers **8** and **9**, in a 5:1 ratio (Scheme IV). Unfortunately, the desired propargylic alcohol **9**, suitable for the preparation of the lower side chain of mexiprostil,[11] was obtained as the minor product. An authentic sample of **12**, prepared by the method of Kolb et al.,[11] was used to assign the absolute stereochemistry of **8** and **9** by comparison of its high-field ^1H and ^{13}C NMR spectra with those of the products obtained by desilylation of **8** and **9** with tetrabutylammonium fluoride in THF at 25 °C.[12]

Conclusions

B-[2-(Trimethylsilyl)ethynyl]-9-BBN (**2**) has been shown to add to aldehydes and ketones under very mild conditions to provide 2-(trimethylsilyl)ethynyl alcohols in excellent yields. Unlike the alkynylmetals, **2** reacted much faster with aldehydes than ketones (Table I), thus affording the synthetic chemist a chemoselective tool.

Experimental Section

All air-sensitive reactions were performed in oven-dried glassware under a nitrogen atmosphere. Thin-layer chromatography (TLC) analysis was performed on glass plates precoated with 0.25 mm of silica gel (Anspec Co., Inc., silica gel MK6F) and viewed by UV, I_2 staining or heating with a 10% solution of

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phosphomolybdic acid (PMA) in ethanol. Flash chromatography was performed on EM 230–400-mesh silica gel 60.

***B*-[2-(Trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (2).** To a solution of 3.5 mL (25.0 mmol) of (trimethylsilyl)-acetylene in THF (40 mL) at −78 °C was added 10.4 mL (26.0 mmol) of 2.5 N *n*-butyllithium in hexane dropwise over a 10-min period. The solution was stirred at −78 °C for an additional 15 min to ensure complete generation of the acetylenic anion before 25.0 mL (25.0 mmol) of a 1.0 M solution of *B*-methoxy-9-borabicyclo[3.3.1]nonane in hexane was added. The reaction mixture was stirred at −78 °C for 1.5 h. Boron trifluoride etherate (4.0 mL, 33 mmol) was then added, and the reaction mixture was stirred at −78 °C for an additional 15 min before being allowed to warm to room temperature. The volatiles were evaporated under vacuum to afford a white solid and 25 mL of pentane was added. The suspension was stirred for a few minutes and allowed to settle, and the supernatant liquid was carefully decanted via a double-ended needle to a second flask. The remaining solid was then washed with pentane (2 × 10 mL), and the extracts were combined. The pentane solution was then cooled to −78 °C to precipitate the product. The mother liquor was removed, and the crystals were dried (vacuum) to afford 6.52 g (90%) of *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane·THF complex (**2**) as a white crystalline material (extremely hygroscopic): ^{11}B NMR (THF-d_8) δ −9.06 (s); ^{29}Si NMR (THF-d_8) δ −22.67 (s); ^{13}C NMR (THF-d_8) δ 103.5, 31.93, 26.19, 0.787; ^{1}H NMR (THF-d_8) δ 0.60 (s, −Si(CH_3)$_3$, 9 H), 1.29 (br, 2 H), 1.92 (m, 2 H), 2.11 (m, 4 H), 2.29 (m, 10 H), 4.14 (m, 4); IR (CCl_4) 2187 cm^{-1} (C≡C).

1-(Trimethylsilyl)-1-decyn-3-ol (5). The following procedure is representative. To the *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane·THF complex (2.4 g, 8.3 mmol) in pentane (25 mL) at 25 °C was added 1-octanal (1.3 mL, 8.3 mmol). A slight yellow color immediately developed. After 40 min TLC revealed the disappearance of the starting aldehyde and the appearance of a new spot. The solvent was removed under positive nitrogen pressure, resulting in a yellow solid. To the solid was added ether (30 mL) and 336 μL (8.3 mmol) of methanol. The resulting solution was colled to 0 °C, and 0.5 mL (8.3 mmol) of ethanolamine was added dropwise. A white precipitate was instantly formed. The solution was stirred overnight to ensure complete cleavage of the borinate ester. The reaction mixture was then centrifuged and the clear supernatant liquid separated. The precipitate was washed with pentane (2 × 10 mL), and the phases were combined, washed with water (2 × 25 mL) and dried ($MgSO_4$). Concentration and purification of the resulting oil by flash chromatography on silica gel using hexane/ethyl acetate (19:1) afforded 1.71 g (91%) of **5** as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 0.16 (s, −Si(CH_3)$_3$, 9 H), 1.13 (t, 3 H), 2.23–1.35 (m, 13 H), 4.25 (m, 1 H); IR (neat) 3550–3150 (br), 2967, 2925 (s), 2868, 2190, 1470, 1251 (s), 848 (vs) cm^{-1}.

5-Phenyl-1-(trimethylsilyl)-1-pentyn-3-ol (6). From 1.0 mL (7.6 mmol) of hydrocinnamaldehyde there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 1.57 g (89%) of **6** as a pale yellow liquid: ^{13}C NMR ($CDCl_3$) δ 141.2, 128.4, 128.3, 125.4, 106.6, 89.6, 61.9, 39.1, 31.3, −0.181; ^{1}H NMR ($CDCl_3$) δ 0.16 (s, −Si(CH_3)$_3$, 9 H), 2.00 (m, 2 H), 2.42 (br, −O*H*, 1 H), 2.78 (t, 2 H), 4.34 (t, 1 H), 7.26 (m, 5 H); IR (neat) 3600–3250 (br), 3027, 2960, 2945, 2865, 2188, 1495, 1455, 1253 (s), 1048, 848 (vs), 760, 701 cm^{-1}.

4,4-Dimethyl-1-(trimethylsilyl)-1-pentyn-3-ol (7). From 795 μL (7.3 mmol) of trimethylacetaldehyde there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 1.25 g (93%) of **7** as a clear liquid: ^{13}C NMR ($CDCl_3$) δ 105.6, 90.1, 71.7, 35.7, 25.2, −0.139; ^{1}H NMR ($CDCl_3$) δ 0.102 (s, −Si(CH_3)$_3$, 9 H), 0.919 (s, 9 H), 1.67 (s, −O*H*, 1 H), 3.92 (d, 1 H); IR (neat) 3600–3180 (br), 2975 (s), 2963, 2901, 2875, 2187, 1481, 1460, 1365, 1253 (s), 1065, 1008 (s), 882, 858 (s), 845 (vs), 712 cm^{-1}.

(3*S*,4*R*)-4-Methoxy-4-methyl-1-(trimethylsilyl)-1-octyn-3-ol (8) and (3*R*,4*R*)-4-Methoxy-4-methyl-1-(trimethylsilyl)-1-octyn-3-ol (9). From 1.06 g (7.3 mmol) of (2*R*)-2-methyl-2-methoxyhexanal there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 900 mg (51%) of **8** as a clear liquid: ^{13}C NMR ($CDCl_3$) δ 104.3, 90.7, 78.6, 67.5, 49.7, 33.7, 25.5, 23.3, 19.0, 13.9, −0.307; ^{1}H NMR ($CDCl_3$) δ 0.145 (s, −Si(CH_3)$_3$, 9 H), 0.895 (t, 3 H), 1.19 (s, 3 H), 1.30 (m, 4 H), 1.66 (m, 2 H), 2.48 (d, −O*H*, *J* = 5.0 Hz, 1 H), 3.24 (s, 3 H), 4.28 (d, *J* = 4.9 Hz, 1 H); IR (neat) 3600–3120 (br), 2958 (s), 2940, 2186, 1465, 1375, 1250 (s), 1069 (s), 845 (vs), 760 cm^{-1}.

A second product, **9** (180 mg, 10%), eluted as a clear liquid: ^{13}C NMR ($CDCl_3$) δ 103.6, 90.7, 79.5, 67.2, 49.7, 33.6, 24.9, 23.1, 17.6, 13.9, −0.298; ^{1}H NMR ($CDCl_3$) δ 0.146 (s, −Si(CH_3)$_3$, 9 H), 0.890 (t, 3 H), 1.22 (s, 3 H), 1.26 (m, 4 H), 2.47 (br, −O*H*, 1 H), 3.21 (s, 3 H) 4.33 (s, 1 H); IR (neat) 3600–3120 (br), 2960 (vs), 2941 (vs), 2871, 2186, 1465, 1375, 1251 (s), 1065, 1055, 845 (vs), 760 cm^{-1}.

1-[2-(Trimethylsilyl)-1-ethynyl]cyclohexanol (10). From 907 μL (9.0 mmol) of cyclohexanone there was obtained, after purification by flash chromatography on silica gel using hexane/ethyl acetate (19:1), 1.56 g (88%) of **10** as a white crystalline material, mp 72–73 °C: ^{13}C NMR ($CDCl_3$) δ 109.6, 88.4, 68.7, 39.9, 25.2, 23.3, −0.010; ^{1}H NMR ($CDCl_3$) δ 0.138 (s, −Si(CH_3)$_3$, 9 H), 1.21 (m, 2 H), 1.53 (m, 4 H), 1.65 (m, 2 H), 1.85 (m, 2 H), 2.05 (s, −O*H*, 1 H); IR (KBr) 3400–3250 (br), 2937 (s), 2902, 2861, 2166, 1450, 1348, 1285, 1251 (s), 1169, 1075 (s), 975 (s), 866 (vs), 840 (vs), 760, 699 cm^{-1}.

1-(Trimethylsilyl)-3-methyl-1-nonyn-3-ol (11). From 1.41 mL (9.0 mmol) of 2-octanone there was obtained, after purification by flash chromatography on silica gel using hexane/chloroform/methanol (20:5:1), 1.56 g (88%) of **11** as a pale yellow liquid: ^{13}C NMR ($CDCl_3$) δ 109.8, 87.2, 68.4, 43.5, 31.6, 29.7, 29.3, 24.5, 22.5, 14.0, −0.059; ^{1}H NMR ($CDCl_3$) δ 0.129 (s, −Si(CH_3)$_3$, 9 H), 0.862 (m, 3 H), 1.29 (m, 6 H), 1.43 (s, 3 H), 1.45 (m, 2 H), 1.60 (m, 2 H), 2.02 (br, −O*H*, 1 H); IR (neat) 3550–3220 (br), 2975 (s), 2941 (s), 2865, 2179, 1470, 1258 (s), 939, 865 (s), 845 (vs), 765 cm^{-1}.

(3*R*,4*R*)-4-Methoxy-4-methyl-1-octyn-3-ol (12). A solution of 40 mg (0.17 mmol) of **9** in 1.4 mL (1.4 mmol) of a 1.0 M solution of tetrabutylammonium fluoride in THF was stirred at rt for 3 h. The reaction was diluted with 5 mL of water and extracted with ethyl acetate (3 × 5 mL), and the organic layer was dried ($MgSO_4$). Concentration and purification of the resulting oil by flash chromatography on silica gel using hexane/ethyl acetate (19:1) afforded 21 mg (75%) of **12** as an oil: ^{13}C NMR ($CDCl_3$) δ 82.2, 79.3, 74.1, 66.9, 49.8, 33.6, 25.2, 23.2, 17.8, 14.0.

Registry No. **2**, 140149-83-3; **5**, 140149-76-4; **6**, 140149-77-5; **7**, 71321-14-7; **8**, 140149-78-6; **9**, 140149-79-7; **10**, 17962-22-0; **11**, 140149-80-0; **12**, 140149-81-1; (trimethylsilyl)acetylene, 1066-54-2; *B*-methoxy-9-borabicyclo[3.3.1]nonane, 38050-71-4; 1-octanal, 124-13-0; hydrocinnamaldehyde, 104-53-0; trimethylacetaldehyde, 630-19-3; (2*R*)-2-methyl-2-methoxyhexanal, 140149-82-2; cyclohexanone, 108-94-1; 2-octanone, 111-13-7.

Supplementary Material Available: IR and ^{1}H and ^{13}C NMR spectra of the (trimethylsilyl)ethynyl alcohols reported in this study (22 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Efficient Chemical Synthesis of GDP-fucose

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Sugar nucleotide-dependent glycosyltransferases are a class of enzymes with great potential for oligosaccharide synthesis. Several preparative-scale syntheses of saccharides have been demonstrated based on glycosyltransferases with in situ regeneration of sugar nucleotides.[1] As part of our interest in the field of enzymatic oligo-

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