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Diacetone Glucose Architecture as a Chirality Template I. Crucial Effects of the Intramolecular Oxygens upon the $LiAlH_4$ Reduction of the Propargyl Alcohol of 3-*C*-Ethynyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose Derivatives

Katsumi Kakinuma,* Toshihiro Matsuzawa and Tadashi Eguchi

Department of Chemistry, Tokyo Institute of Technology
O-okayama, Meguro-ku, Tokyo 152, Japan

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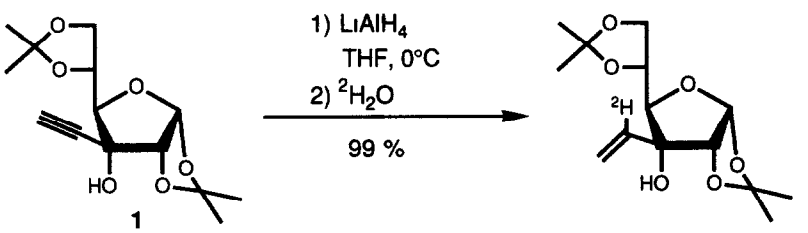
Keywords $LiAlH_4$ reduction of propargyl alcohol, regiochemistry, reactivity, semi-empirical MO calculation, diacetone glucose

Abstract *The facile as well as regio- and stereoselective reactivity of 3-C-ethynyl-1,2 5,6-di-O-isopropylidene-α-D-allofuranose derivatives for $LiAlH_4$ reduction into the corresponding ethenyl derivatives were investigated The effect of oxygen atoms on the reduction is discussed by means of semi-empirical MO calculation*

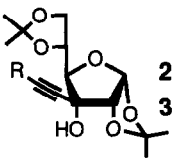
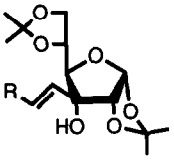
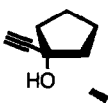
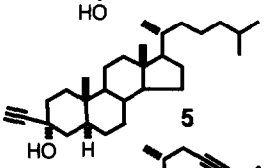
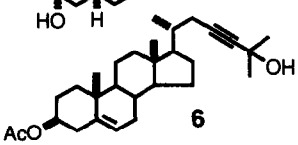
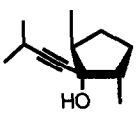
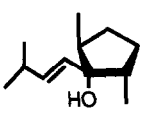
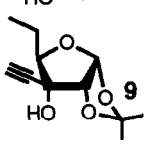
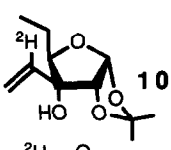
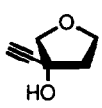
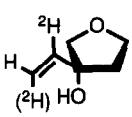
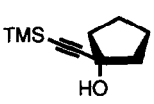
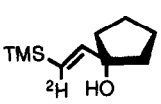
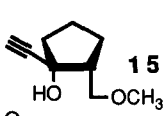
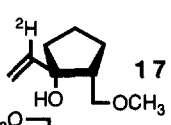
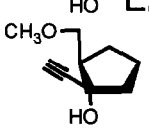
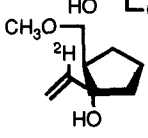
$LiAlH_4$ reduction of propargyl alcohol systems is among simple and convenient entries to allyl alcohols and has been widely used in a number of natural product syntheses [1] One of the drawbacks of this transformation is that regiochemical outcome of the reaction usually varies depending upon either the substrate or the reaction conditions [2] Interestingly enough, however, we found that 3-*C*-ethynyl-1,2 5,6-di-*O*-isopropylidene-α-D-allofuranose **1** and its alkylated derivatives were so reactive toward the $LiAlH_4$ reduction that the corresponding ethenyl derivatives were prepared under mild conditions (at 0 °C or even below) through stereo- and regioselective introduction of the hydride as shown in the Scheme 1 [3,4] This facile and selective reactivity prompted us to investigate the intrinsic natures, especially of the effects of oxygen atoms, in **1**



Scheme 1

Corey *et al* [2] reported some uncertainty of the regiochemical outcome that reduction of a long-chain propargyl alcohol with $LiAlH_4$ in THF, followed by hydrolysis with ^2H_2O, resulted in giving a mixture of allyl alcohols substituted with a deuterium either at the γ-position or at the β-position to the OH group in varying ratio of regioisomers from one experiments to another Dependency of the regiochemistry upon the basicity of the solvent was described by Djerassi *et al* ,[5] who suggested a possible reaction mechanism Denmark *et al* [6] also described participation of oxygen atoms in the reduction of propargyl alcohol systems with Red-Al™ ($[(CH_3OCH_2CH_2O)_2AlH_2]Na$) Borden[7] suggested a five-membered ate-complex for the intermediate in such reactions where the γ-deuterated olefins are formed by ^2H_2O quench However, under such conditions that β-deuterated olefins are formed by ^2H_2O quench, it seems less likely to form a four-membered ate-complex The mechanism suggested by Djerassi *et al* seems plausible in these cases [5]

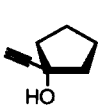
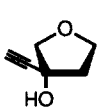
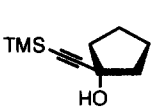
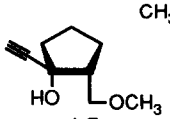
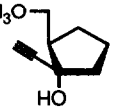
Table 1 $LiAlH_4$ Reduction of Propargyl Alcohols

Propargyl Alcohol	Product[a]	Conditions[b]	Yield[c]
 **2** R=^{i}Pr **3** R=Me		rt, 3 h	94 %[d]
 **4**	—	rt, 3 h	No Reaction
 **5**	—	rt, 3 h	No Reaction
 **6**	—	rt, 2 h	No Reaction[e]
 **7**	 **8**	reflux, 7 hr	28 %
 **9**	 **10**	rt, 3 hr	93 %
 **11**	 **12**[f]	rt, 1 hr	68 %
 **13**	 **14**	rt, 1 hr	76 %
 **15**	 **17**	rt, 2 hr	65 %[g]
 **16**	 **18**	rt, 3 hr	65 %[g]

[a]Structures are shown in the case of quenching the reactions with ^2H_2O [b]All reactions were carried out in THF See experimental [c]Yields are indicated in the case of quenching the reactions with H_2O [d]See ref 8
[e]Deacetylated product was obtained [f]The deuterated position was varied depending on the source of the reducing agent in this case [g]Yields were determined by NMR spectra

Since our particular compound **1** reacts with $LiAlH_4$ quite readily with high regioselectivity, we first compared reactivities of various tertiary acetylene carbinols under standard conditions (room temp, 5 mol eq $LiAlH_4$ in THF solvent) First, the homologs of **1**, 3-*C*-(3-methylbut-1-ynyl)-1,2 5,6-di-*O*-isopropylidene-α-D-allofuranose **2** and 3-*C*-(propyn-1-yl) analog **3** were proved to be reduced readily under these conditions or at 0 °C in the presence of 1 5 eq of $LiAlH_4$ [8] In contrast, two ethynyl carbinols, *i e* 1-ethynylcyclopentanol **4** and 3β-ethynylcholestanol **5**[9], and an internal acetylene, cholest-5-en-23-yne-3,25-diol 3-*O*-acetate **6**[9,10] were unreactive and no olefinic products were obtained under the same reaction conditions As an exception, 1-(3-methylbut-1-ynyl)-2,5-dimethylcyclohexanol **7** afforded an allyl alcohol **8** in 28 % yield only under reflux with large excess of $LiAlH_4$ These results apparently suggest that the stereochemical bulkiness of the neighboring groups around the acetylenic bond is not a major cause of these unreactiveness, but rather, some specific features of **1** and **2** may facilitate susceptibility of the acetylenic bond toward the reduction As might be anticipated, ethereal oxygens at the C-5 and C-6 positions could play a crucial role through a chelation with metal in the case of **1** and **2** as suggested by Denmark [6] Interestingly however, the reduction of a 5,6-dideoxy analog **9** underwent quite smoothly to afford a β-deuterated olefin **10** after quenching with ^2H_2O What this meant was that there must be still other major factor(s) controlling the reactivity, *i e* , either the 1,2-*O*-isopropylidene oxygens or the furanose oxygen, or both To test this, we further prepared 1-ethynyl-3-oxacyclopentanol **11** To our surprise, this simple oxygen analog of **4** was easily reduced *per se* to the corresponding olefin **12** in good yield This result strongly suggests an intrinsic higher reactivity of **11** toward $LiAlH_4$ compared with **4** This reactivity might well be due to the electron-withdrawing effect of the C-O bond in the ring resulting in the lowering the energy levels of the corresponding frontier orbitals To get some insight into these reactivity differences, we attempted rather simple theoretical calculation of the energy levels involved in the acetylenic carbons of these compounds, since the most crucial step of this reduction would be the transfer of a hydride into the acetylenic bond In other words, it was anticipated that the reactivity of individual compounds might reflect the electron-accepting capability of the LUMOs Calculations were carried out at the semi-empirical level with the MOPAC AM-1 program[11] and the results are summarized in Table 2

Table 2 LUMO Level of Propargyl Alcohols by AM-1 Calculation

	 **4**	 **11**	 **13**	 **15**	 **16**
LUMO (eV)	1 677	1 416	1 179	1 752	1 672

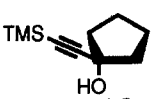
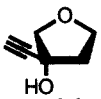
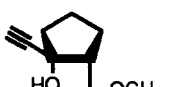
Based on a preliminary calculation of the most stable conformation of 1-ethynylcyclopentanol, the dihedral angle between the O-H group being coordinated with the aluminum atom of $LiAlH_4$ during the reduction and the acetylenic bond was determined to be fixed to 60° throughout the present calculation Since the carbohydrate derivative **1** was not suitable for calculation, rather simple model structures were used

The energy levels of the acetylenic LUMO of 1-ethynyl-3-oxacyclopentanol **11** was lower by 0 26 eV than that of 1-ethynylcyclopentanol **4** This difference of the LUMO level seemed to be significant and might well be attributed to the major factor for the higher reactivity of the former compound In this context, we anticipated that, in contrast to 1-ethynylcyclopentanol **4**, 1-(2-trimethylsilylethynyl)cyclopentanol **13** would be susceptible to the $LiAlH_4$ reduction, since the vacant 3*d* orbitals of the attached silicon would lower the LUMO energy level of an acetylenic bond The silylated compound **13** was subjected to the reduction and this prediction turned out to be the case Thus, **13** was readily reduced under the standard conditions to give an olefin **14** in 77 % yield Thus, although the present study deals only with tertiary carbinols, all the results apparently suggest that the reactivity of the propargyl alcohol systems toward the $LiAlH_4$ reduction well corresponds to the energy

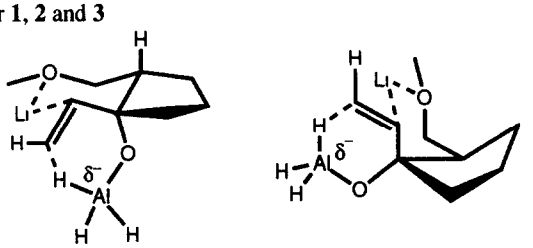
level of the LUMO of the acetylenic bond Theoretical reasoning for the lower LUMO energy level of **11** is not clear at present

Quite interestingly, the product **14**, after quenching the reaction with ^2H_2O, turned out to be deuterated at the γ-position rather than at the β-position, which was rigorously assigned by the ^1H-^{13}C COSY and INADEQUATE experiments The regiochemistry of this particular case was completely opposite to the all reactions described above Based on the frontier orbital theory, the regiochemistry may reflect the LUMO coefficients of the relevant atoms This seemed to be the case, since in every case, except the silylated acetylene **13**, the absolute values of LUMO coefficients of the γ-carbons are larger than those of the β-carbons as shown in the Table 3 The coefficients of **13** are actually reversed However, care must be taken to predict the regiochemistry of the hydride introduction based on the difference of the LUMO coefficients, because it seems difficult to assign the border between the significant difference of the LUMO coefficients and the insignificant level, and because we experienced in one experiment that the regiochemical outcomes of the reduction of **11** reversed This might be due to unknown impurities or the freshness of the reducing agent

Table 3 LUMO Coefficients of β and γ-Carbons of Propargyl Alcohols

		 **13**	 **11**	 **15**
LUMO Coefficient	β	-0 5410	0 4745	0 5953
	γ	0 4894	-0 5134	-0 6408

To study the effects of the side-chain for the reduction of **1**, **2** and **3**, we prepared model compounds, *cis*- and *trans*-1-ethynyl-2-methoxymethylcyclopentanol **15** and **16**, which were separately subjected to the standard reduction conditions In either case, reduction underwent slowly to give β-deuterated olefins and starting material remained even after 18 hr of stirring However, the reduction did take place, which implied some participation of the side chain oxygen to the reaction The AM-1 calculation as above showed no significant lowering of the acetylene LUMO compared with that of 1-ethynylcyclopentanol **5**. Therefore, the effect of the side-chain oxygen is presently attributed, as suggested by Djerassi *et al* [5] and Denmark *et al* ,[6] to the coordination for the counter metal of the transition state as shown in the Scheme 2 to gain entropically favorable forces A similar effect can be extrapolated for **1**, **2** and **3**



Scheme 2

In conclusion, the high reactivity and regioselectivity of a series of 3-*C*-alkynyl-1,2 5,6-di-*O*-isopropylidene-α-D-allofuranoses toward the $LiAlH_4$ reduction can be attributed to its intrinsic architecture In addition, although the results described above deal only with $LiAlH_4$ reduction of substituted tertiary propargyl carbinols, this approach may aid to estimate chemical reactivities of other propargyl alcohols by rather simple calculation

Experimental

Melting points were measured with a Yanagimoto BY-1 micromelting point apparatus and are uncorrected IR spectra were taken on a JASCO IR-810 or a Hitachi 285 infrared spectrometer ^1H and ^{13}C NMR spectra were recorded on JEOL FX-200, JEOL GSX-270, and/or JEOL GSX-500 spectrometers. Deuteriochloroform (99 75 % atom enriched, Merck) was used for the NMR solvent throughout ^1H NMR chemical shifts were reported in ppm relative to the signal of internal tetramethylsilane ^{13}C NMR chemical shifts were calculated from the resonance frequency of the center peak (77 0 ppm) of the solvent signal Column chromatography was carried out with a Kieselgel 60 (70-230 mesh, Merck) All reactions, except for coupling reactions of magnesium acetylide with ketone, were carried out in an inert (Ar or N_2) atmosphere

General procedure for $LiAlH_4$ reduction of propargyl alcohols

A solution of propargyl alcohol (1 mmol) in THF (5 ml) was added to a suspension of $LiAlH_4$ (5 eq) in THF (10 ml) at 0°C The mixture was stirred at room temperature and the reaction was monitored by TLC analysis After the reaction was completed (ca 1-5 hr), water (or ^2H_2O) was added, followed by anhydrous Na_2SO_4 The insoluble materials were filtered and washed with ether The filtrate and washings were combined and concentrated to dryness The product was analyzed by ^1H NMR spectroscopy without further purification Analytical samples were obtained after purification by column chromatography

(2*R**,5*R**)-2,5-dimethyl-1-(3-methylbut-1-ynyl)cyclopentanol (7)

A solution of n-BuLi in hexane (57 ml, 1 5 mol/l) was added dropwise to a solution of 1,1-dibromo-3-methyl-1-butene (10 0 g, 44 mmol) in THF (20 ml) at -70°C The mixture was stirred for 1 hr at -70°C, and then for 1 hr at room temperature The mixture was re-cooled to -70°C and a solution of 2,5-dimethylcyclopentanone (4 8 g, 43 mmol) in THF (10 ml) was added dropwise After addition was completed, the reaction mixture was poured into aqueous NH_4Cl solution The mixture was extracted with ether The extract was washed with 1*M* HCl, aqueous $NaHCO_3$ solution, and brine, successively, dried over Na_2SO_4, filtered, and concentrated to dryness The obtained residue was chromatographed over silica gel (400 g) with hexane-CH_2Cl_2 (3 1-1 2) to give **7** (1 91 g, 25 %) as an oil, IR (neat) 3420, 2950, 2860, 2210, 1445, 1375, 1315, 945 cm^{-1}, ^1H NMR (200MHz) δ 1 03 (3H, d, *J*=7 1 Hz, CH_3), 1 04 (3H, d, *J*=6 8 Hz, CH_3), 1 16 (6H, d, *J*=6 8 Hz, $CH(CH_3)_2$), 2 04 (2H, m), 2 59 (1H, septet, *J*=6 8 Hz, $CH(CH_3)_2$), ^{13}C NMR (50 MHz) δ 13 1, 19 2, 20 5, 23 2, 29 8, 30 5, 43 7, 45 0, 80 0, 88 9, 91 7

(2*R**,5*R**)-2,5-dimethyl-1-[(*E*)-3-methylbuten-1-yl]cyclopentanol (8)

A solution of **7** (249 mg, 1 38 mmol) and $LiAlH_4$ (145 mg, 3 0 mmol) in THF (18 ml) was refluxed for 7 hr After cooling to room temperature, water was added The mixture was dried over anhydrous Na_2SO_4 The insoluble materials were filtered and washed with ether The filtrate and washings were combined and concentrated to dryness The residue was chromatographed over silica gel (18 g) with hexane-ethyl acetate (20 1) to give **8** (70 mg, 28 %) as an oil, ^1H NMR (200MHz) δ 0 86 (3H, d, *J*=7 8 Hz, CH_3), 0 87 (3H, d, *J*=6.6 Hz, CH_3), 1 00 (6H, d, *J*=6 6 Hz, $CH(CH_3)_2$), 1 91 (2H, m, 2-H and 5-H), 2 34 (1H, m, $CH(CH_3)_2$), 5 40 (1H, dd, *J*=15 6, 1 0 Hz, 1'-H), 5 59 (1H, dd, *J*=15 6, 6 6 Hz, 2'-H), ^{13}C NMR (50 MHz) δ 12 7, 18 8, 22 8, 30 6, 31 1, 31 2, 40 7, 45 8, 83 9, 130 5, 136 2

5,6-Dideoxy-3-*C*-ethynyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose (9)

A three-necked flask was equipped with a drying tube, a gas inlet, and a dropping funnel. Dry THF (20 ml) was placed in the flask and acetylene gas was introduced through the gas inlet Acetylene gas was continuously introduced until the coupling reaction was completed A solution of ethylmagnesium bromide in THF (8 ml, 0 9 mol/l) was added dropwise during 1 hr with stirring The mixture was cooled in an ice-water bath and a solution of 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*erythro*-hexofuranos-3-ulose[12] (1 12 g, 6 0 mmol) in THF (10 ml) was added dropwise over a period of 50 min The mixture was stirred for additional 4 hr at room

temperature, and then poured into aqueous NH_4Cl solution The mixture was extracted with ether The extract was washed with brine, dried over Na_2SO_4, filtered, and concentrated to dryness The residue was chromatographed over silica gel (100 g) with hexane-ether (3 1-1 1) to give **9** (336 mg, 26 %) as colorless oil, IR (neat) 3470, 3275, 2980, 2950, 2890, 2120, 1460, 1380, 1220, 1145, 1105, 1070, 1020, 1000, 875 cm^{-1}, ^1H NMR (270 MHz) δ 1 06 (3H, t, *J*=7 3 Hz, 6-H), 1 38 (3H, s, C-CH_3), 1 58 (3H, s, C-CH_3), 1 80 (2H, dq, J=6 8, 7 3 Hz, 5-H), 2 59 (1H, s, acetylene), 2 86 (1H, s, OH), 3 69 (1H, t, *J*=6 8 Hz, 4-H), 4 54 (1H, d, *J*=3.9 Hz, 2-H), 5 86 (1H, d, *J*=3 9 Hz, 1-H), ^{13}C NMR (67 9 MHz) δ 10 3, 22 7, 26 3, 26 7, 76 1, 76.4, 80 4, 83 1, 83 8, 103 6, 112 9 *Anal* Calcd for $C_{11}H_{16}O_4$ C, 62 25, H, 7 60 Found C, 62 53, H, 7 88

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*C*-ethenyl-α-D-*ribo*-hexofuranose (10)

Compound **9** (99 mg, 0 47 mmol) was treated under the general conditions for $LiAlH_4$ reduction to give **10** (94 mg, 93 %) ^1H NMR (200 MHz) δ 0 98 (3H, t, *J*=7 3 Hz, 6-H), 1 36 (3H, s, C-CH_3), 1 50 (2H, dq, *J*=7 3, 6 8 Hz, 5-H), 1 60 (3H, s, C-CH_3), 2 66 (1H, d, *J*=1 0 Hz, OH), 3 71 (1H, t, *J*=6 8 Hz, 4-H), 4 21 (1H, d, *J*=4 4 Hz, 2-H), 5 30 (1H, dd, *J*=10 7, 2 0 Hz, 2'*E*-H), 5 50 (1H, dd, *J*=17 1, 2 0 Hz, 2'Z-H), 5 75 (1H, ddd, *J*=17 1, 10 7, 1 0 Hz, 1'-H), 5.82 (1H, d, *J*=4 4 Hz, 1-H) *Anal* Cacld for $C_{11}H_{18}O_4$ C, 61.66, H, 8 47 Found C, 61 64, H, 8 75 The corresponding deuterated product obtained by quenching with ^2H_2O showed the following olefinic ^1H NMR signals (200 MHz) δ 5 29 (1H, brs), 5 48 (1H, brs).

1-Ethynyl-3-oxacyclopentanol (11)

A mixture of 3-hydroxytetrahydrofuran (900 mg, 10 4 mmol), molecular sieves 3A (10 g), and pyridinium chlorochromate (8 7 g) in CH_2Cl_2 (10 ml) was stirred for 1 hr at room temperature The mixture was diluted with ether and passed through a column of Florisil The eluent was concentrated to give an oily residue (594 mg) ^1H NMR (200 MHz) δ 2 50 (2H, t, *J*=7 4 Hz, 4-H), 3 88 (2H, s, 2-H), 4 23 (2H, t, *J*=7 4 Hz, 5-H) This was subjected to the next step without further purification A three-necked flask was equipped with a drying tube, a gas inlet, and a dropping funnel Dry THF (20 ml) was placed in the flask and acetylene gas was introduced through the gas inlet Acetylene gas was continuously introduced until the coupling reaction was completed A solution of ethylmagnesium bromide in THF (8 ml, 1 01 mol/l) was added dropwise during 10 min with stirring After 1 hr of stirring at room temperature, a solution of the residue (594 mg) in THF (6 ml) was added dropwise during 10 min The mixture was stirred for 1 hr at room temperature and then poured into aqueous NH_4Cl solution The mixture was extracted three times with ether and four times with ethyl acetate The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated to dryness The residue was chromatographed over silica gel (50 g) with hexane-ethyl acetate (2 1-1 2) to give **11** (154 mg, 2 steps 13 %) as an oil, IR (neat) 3370, 3250, 2940, 2860, 2100, 1240, 1035, 650 cm^{-1}, ^1H NMR (200 MHz) δ 2 30 (2H, m, 4-H), 2 59 (1H, s, acetylene), 2 99 (1H, s, OH), 3 87 (1H, d, *J*=9 5 Hz, 2-H), 3 91 (1H, d, *J*=9 5 Hz, 2-H), 4 03 (2H, m, 5-H), ^{13}C NMR (50 MHz) δ 41 8, 67 3, 72 1, 73 0, 79 4, 83 6 *Anal* Calcd for $C_6H_8O_2$ C, 64 27, H, 7 19 Found C, 64 13, H, 7 40

1-Ethynyl-3-oxacyclopentanol (12)

Compound **11** (56 mg, 0 5 mmol) was treated under the general conditions for $LiAlH_4$ reduction to give **12** (39 mg, 68 %) ^1H NMR (200 MHz) δ 2 0 (2H, m, 4-H), 2 59 (1H, s, OH), 3 65 (1H, d, *J*=9 5 Hz, 2-H), 3 71 (1H, d, *J*=9 5 Hz, 2-H), 4 0 (2H, m, 5-H), 5 19 (1H, dd, *J*=10 7, 1 2 Hz, 2'*E*-H), 5 43 (1H, dd, *J*=17 2, 1 2 Hz, 2'Z-H), 5 97 (1H, dd, *J*=17 2, 10 7 Hz, 1'-H)

1-(2-Trimethylsilylethynyl)cyclopentanol (13)

A solution of n-BuLi in hexane (16 ml, 1 58 mol/l) was added to a solution of 1-ethynylcyclopentanol (1 1 g, 10 mmol) in THF (12 ml) at 0°C and the mixture was stirred for 50 min at the same temperature Chlorotrimethylsilane (3 4 ml, 26 8 mmol) was added and stirring was continued for an additional 20 min Aqueous NH_4Cl solution was added and the mixture was extracted three times with ether The organic layers were combined and successively washed with 1*M* HCl, aqueous $NaHCO_3$ solution, and brine After drying over

Na_2SO_4, the solvent was removed The residue (2 13 g) was dissolved in methanol (15 ml) and 2*M* HCl (25 ml) was added After being stirred for 2 hr at room temperature, the mixture was diluted with water and extracted three times with ether The organic layers were combined and washed with aqueous $NaHCO_3$ solution and brine, successively After drying over Na_2SO_4, the solvent was removed The residue was purified by column chromatography over silica gel (50 g) with hexane-ethyl acetate (20 1-5 1) to give **13** (1 33 g, 73 %) as an oil, which was kept in a refrigerator to give colorless needles m p 31-32 °C , IR (neat) 3580, 2940, 2150, 1245, 985, 840 cm^{-1}, ^1H NMR (200 MHz) δ 0 17 (9H, s, $SiMe_3$), 1 8 (4H, m), 1 9 (4H, m), ^{13}C NMR (67 9 MHz) δ -0 06, 23 5, 42 5, 74 6, 86 9, 109 8 *Anal* Calcd for $C_{10}H_{18}OSi$ C, 65 87, H, 9 95 Found C, 66 16, H, 10 11

1-[(*E*)-2-trimethylsilylethenyl]cyclopentanol (14)

Compound **13** (185 mg, 1 0 mmol) was treated under the general conditions for $LiAlH_4$ reduction to give **14** (141 mg, 76 %) ^1H NMR (200 MHz) δ 0 05 (9H, s, $SiMe_3$), 1 65 (6H, m), 1 85 (2H, m), 5 86 (1H, d, *J*=18 9 Hz, 2'-H), 6 12 (1H, d, *J*=18 9 Hz, 1'-H), ^{13}C NMR (67 9 MHz) δ -1 2, 23 9, 40 3, 83 1, 124 8, 151 8 *Anal* Calcd for $C_{10}H_{20}OSi$ C, 65 15, H, 10 94 Found C, 64 88, H, 11 23 The corresponding deuterated product obtained by quenching with ^2H_2O showed the following olefinic ^1H NMR signals (200 MHz) δ 6 14 (1H, t, *J*=0 9 Hz)

***cis*- and *trans*-1-Ethynyl-2-methoxymethylcyclopentanol (15 and 16)**

A three-necked flask was equipped with a drying tube, a gas inlet, and a dropping funnel Dry THF (30 ml) was placed in the flask and acetylene gas was introduced through the gas inlet Acetylene gas was continuously introduced until the coupling reaction was completed A solution of ethylmagnesium bromide in THF (21 ml, 1 01 mol/l) was added dropwise during 30 min with stirring The mixture was stirred for 1 5 hr and a solution of 2-methoxymethylcyclopentanone[13] (2 43 g) in THF (5 ml) was added dropwise during 30 min The mixture was stirred for 30 min at room temperature, and then poured into aqueous NH_4Cl solution The mixture was extracted three times with ether The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated to dryness The residue was chromatographed over silica gel (50 g) with hexane-ethyl acetate (2 1-1 2) to give oily products **15** (1 72 g, 59 %) and **16** (26 3 mg, 1%) **15**, IR (neat) 3400, 3280, 2940, 2860, 2090, 1445, 1385, 1295, 1195, 1095, 610 cm^{-1}, ^1H NMR (500 MHz) δ 1 22 (1H, m, 3-H), 1 62 (2H, m), 1 69 (1H, m), 1 79 (1H, m, 5-H), 1 98 (1H, m, 5-H), 2 11 (1H, m, 2-H), 2 44 (1H, s, acetylene), 3 25 (3H, s, OCH_3), 3 39 (1H, m, CH_2O), 3 51 (1H, m, CH_2O), 3 61 (1H, br, OH), ^{13}C NMR (67 9 MHz) δ 20 3, 25 3, 40 7, 49 6, 58 8, 73 3, 74 4, 77 2, 85 0 *Anal* Calcd for $C_9H_{14}O_2$ C, 70 10, H, 9 15 Found C, 69 91, H, 9 44 **16**, ^1H NMR (270 MHz) δ 1 69 (1H, m,), 1 8 (3H, m), 2 0 (2H, m), 2 18 (1H, m, 2-H), 2 49 (1H, s, acetylene), 3 39 (3H, s, OCH_3), 3 64 (1H, m, CH_2O), 3 85 (1H, m, CH_2O), 3 91 (s, 1H, OH), ^{13}C NMR (67 9 MHz) δ 21 6, 25 6, 42 1, 50 0, 59 2, 71 0, 71 9, 75 5, 87 4

***cis*-1-Ethenyl-2-methoxymethylcyclopentanol (17)**

Compound **15** (130 mg, 1 0 mmol) was treated under the general conditions for $LiAlH_4$ reduction The crude product (119 mg) was analyzed by ^1H NMR without purification The ^1H NMR spectrum exhibited signals due to **17** (65 %) and the starting material **15** (35 %) ^1H NMR (270 MHz) δ 3,30 (3H, s, OCH_3), 3 6 (2H, m, CH_2O), 5 15 (1H, dd, *J*=17 1, 10 7 Hz, 2'*E*-H), 5 32 (1H, dd, *J*=17 1, 1 7 Hz, 2'Z-H), 5 99 (1H, dd, *J*=10 7, 1 7 Hz, 1'-H) The corresponding product obtained by quenching with ^2H_2O showed the following olefinic ^1H NMR signals (200 MHz) δ 5 14 (1H, m), 5 30 (1H, m)

***trans*-1-Ethenyl-2-methoxymethylcyclopentanol (18)**

Compound **16** (15 mg, 0 11 mmol) was treated under the general conditions for $LiAlH_4$ reduction The crude product was analyzed by ^1H NMR without purification The ^1H NMR spectrum exhibited signals due to **18** (65 %) and the starting material **16** (35 %) ^1H NMR (270 MHz) δ 3 33 (3H, s, OCH_3), 3 54 (2H, m, CH_2O), 5 10 (1H, dd, *J*=17 1, 10 7 Hz, 2'*E*-H), 5 36 (1H, dd, *J*=17 1, 1 7 Hz, 2'Z-H), 5 91 (1H, dd,

J=10.7, 1 7 Hz, 1'-H) The corresponding product obtained by quenching the reaction with ^2H_2O showed the following olefinic ^1H NMR signals (200 MHz) δ 5 10 (1H, m), 5 35 (1H, m)

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