Tetrahedron Vol. 46, No. 24, pp. 8187-8198, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00

Ring-Opening SN2' Reactions of 7-Oxanorbornenes by Organolithium Reagents. Regio- and Stereospecific Synthesis of Substituted Cyclohexenediols[1]

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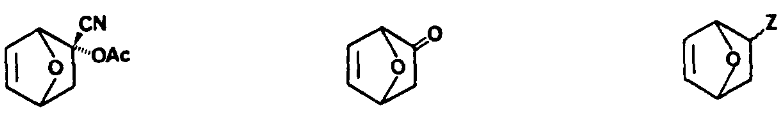
(*Received in UK* 7 *September* 1990)

Abstract: The nucleophilic SN2' bridge opening of 7-oxabicyclo[2.2.1] hept-5-en-2-ols with organolithium reagents occurs in a regio- and stereospecific fashion to produce 6-substituted-cyclohex-4-en-1,3-diols, regardless of the stereochemistry at C-2. A free alcohol functionality is necessary to attain complete regiocontrol of the process. The methodology is utilized to prepare an optically pure cyclohexene derivative, (+)-(1S,3S,6R)-6-*n*-butyl-3-methyl-cyclohex-4-en-1,3-diol (**5b**), as a model system.

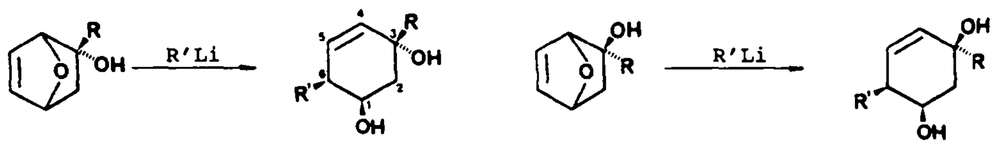
In recent years, derivatives of 7-oxabicyclo[2.2.1]heptane have become important starting materials for a number of synthetic endeavors[2]. Oxanorbornenic substrates 1 and 2 ("naked sugars") (Scheme I) are particularly versatile synthetic intermediates[3] since they are now readily available optically pure[4]; however, the reactivity of these systems remains unexplored.



1 **2** **3**

Scheme I

Within this field, the question of effecting the regioselective opening of the oxygen bridge without concomitant aromatization, to produce functionalized cyclohexenols is a problem of current interest. A relatively general solution proceeds by a base induced β-elimination of the heteroatom bridge in derivatives of 2[5], or in derivatives of **3** (Z = CO_2Me[6], Z = SO_2Ph[7]). Strong acidic conditions have also been used successfully in some cases[8]. Another approach involves the reductive elimination of an *endo* functionality (Cl, SO_2Ph)[9]; this method has been utilized with limited success[10,11]. In this report, we describe the scope and limitations of a new regio- and stereospecific *syn* S_N2' alkylative cleavage of the oxygen bridge of 7-oxanorbornenic substrates to produce highly substituted cyclohexenediols (Scheme II).



4 5 6 7

Scheme II

The reaction between 7-oxanorbornenone 2 and organolithium or Grignard reagents yields the expected *endo* alcohols **4**, with high selectivity[12]. However, when the reaction was carried out with 2 to 3 equivalents of *n*-BuLi (Et_2O, 0°C), low yields of the expected *endo* alcohol **4c** (R = *n*-Bu) were obtained. A detailed study of this reaction allowed the isolation of the unexpected cyclohexenediol **5c** (R = R′ = *n*-Bu) in good yield. Its structure was established by ^{13}C and ^{1}H NMR spectroscopy using selective decoupling. The regio- and stereochemistry of this adduct is supported by the observed coupling constants values for the carbinol proton (11.5 and 4.2 Hz with the adjacent methylene, and 5.3 Hz with the adjacent methine). Although there are two isolated reports in the literature involving the addition of alkyllithiums to 1,4-dihydronaphthalene-1,4-*endo*-oxide with concurrent bridge opening[13], to the best of our knowledge, the reaction of organolithiums with simple oxanorbornenic systems and especially, the complete regioselectivity observed by us are unprecedented in the literature. While this research was in progress, Lautens and coworkers showed that protected oxanorbornene-methanol derivatives reacted with secondary and tertiary higher order cyanocuprates to produce *syn* S_N2' derived cyclohexenols[14]. However, unsymmetrical cases did not display a significant regioselectivity.

The serendipitous observation described above prompted us to further investigate this unexpected process and the results obtained are summarized in Table I.

In order to verify that alcohols **4** are the intermediates of the bridge opening, pure **4c** was treated with 3 equivalents of *n*-BuLi and a good yield of **5c** was obtained. Several *endo* carbinols were then subjected to the reaction conditions (entries 1-6) and good yields of the corresponding adducts were realized. The use of different organolithium reagents was also examined (entries 7-15) and the process was found to proceed even with MeLi, albeit in considerably longer reaction times.

The high regio- and stereoselectivity of the process were found to be independent of the stereochemistry at the carbinol center (entries 16-19). However, the reactions between *exo* alcohols **6** (prepared from **2** and R_2CuLi[12]) and the corresponding organolithium reagent required slightly harsher conditions (5 equivalents R'Li, Et_2O, 25°C).

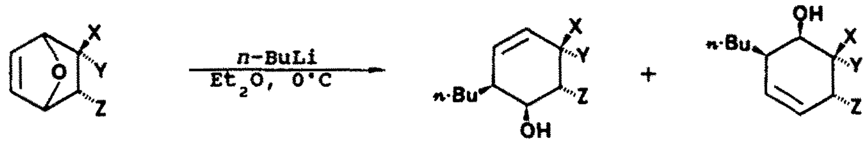
The preparation of enantiomerically pure cyclohexenediols **5** was also addressed. For this purpose, optically active 7-oxanorbornenone (+)-**2**[4b] was treated with MeMgBr to produce (+)-**4b**[12] [ee ≥ 99%[15], $[\alpha]^{28}_{578}$ + 91 (c 6.85 mg/mL, $CHCl_3$)] which in turn provided enantiomerically pure (+)-**5b** [ee ≥ 99%[15], $[\alpha]^{28}_{578}$ + 161 (c 5.72 mg/mL, $CHCl_3$)], upon reaction with *n*-BuLi. (Table I, entry 2).

Table I. Ring Opening Reactions of 7-Oxanorbornenic Alcohols 4 and 6 with Organolithium Reagents.

Entry	Substrate	R	R'	Product	Yield[a] (%)
1	**4a**	H	*n*-Bu	**5a**	75
2	(+)-**4b**	Me	*n*-Bu	(+)-**5b**	80
3	**4c**	*n*-Bu	*n*-Bu	**5c**	85
4	**4d**	Ph	*n*-Bu	**5d**	80
5	**4e**	Naphthyl	*n*-Bu	**5e**	75
6	**4f**	$-CH=CH_2$	*n*-Bu	**5f**	75
7	**4b**	Me	*t*-Bu	**5g**	75
8	**4d**	Ph	*t*-Bu	**5h**	80
9	**4b**	Me	*s*-Bu	**5i**	75
10[b]	**4b**	Me	Ph	**5j**	75
11[b]	**4c**	*n*-Bu	Ph	**5k**	75
12[b,c]	**4b**	Me	Me	**5l**	65
13[b,c]	**4c**	*n*-Bu	Me	**5m**	65
14[b,d]	**4b**	Me	$-CH=CH_2$	**5n**	75
15	**4g**	$-C(CH_3)=CH_2$	$-C(CH_3)=CH_2$	**5o**	75
16	**6b**	Me	*n*-Bu	**7b**	80
17	**6c**	*n*-Bu	*n*-Bu	**7c**	75
18	**6d**	Ph	*n*-Bu	**7d**	80
19	**6e**	Naphthyl	*n*-Bu	**7e**	75

[a]Isolated yields of pure products. These yields have not been optimized. [b]A large excess of organolithium reagent was employed (5-10 equiv.) at room temperature. [c]Reaction time: 4 days. [d]Reaction time: 10 hours.

In order to extend the methology to related substrates as well as to ascertain the influence of a free hydroxyl group on the regioselectivity of the process, the behavior of benzyl ethers **8** and **9** (Scheme III), hydroxymethyl derivatives 10 and 11[16] and dihydroxymethyl oxanorbornene 12[17] with n-BuLi was examined and the results obtained are shown in Table II.



8 X=Me, Y=OCH_2Ph, Z=H
9 X=OCH_2Ph, Y=Me, Z=H
10 X=Z=H, Y=CH_2OH
11 X=CH_2OH, Y=Z=H
12 X=Z=CH_2OH, Y=H

A B

Scheme III

Table II. Ring Opening Reactions of Oxanorbornenic Benzyl Ethers and Hydroxymethyl Derivatives with *n*-BuLi.

Entry	Substrate	A	B	A/B Ratio	Yield[a] (%)
1	**8**	**13**	**14**	2:1	90
2	**9**	**15**	**16**	2.5:1	90
3	**10**	**17**	**18**	3.5:1	80
4	**11**	**19**	**20**	1:1	80
5	**12**	**21**	**22**	1:1	90

[a]Isolated yields of pure products.

All of the above cases displayed a dramatic decrease in regioselectivity which in some cases disappeared completely. Thus, it appears that a free alcohol functionality on C-2 was instrumental in determining the outcome of the process. Nevertheless, the 3.5:1 ratio encountered for *endo* hydroxymethyl oxanorbornene 10 is noteworthy[18].

In conclusion, this methodology allows for the preparation of highly functionalized cyclohexenediols in a regio- and stereospecific fashion and by means of a straightforward experimental procedure. Furthermore, a large variety of R and R′ groups may be utilized successfully. We are currently pursuing the clarification of the precise origin of this unusual regioselectivity[19] and the possible subsequent transformations to apply this methodology to the synthesis of natural products.

Acknowledgment. This research was supported by D.G.I.C.Y.T. (Grant No. PB87-0064) and by the C.S.I.C. One of us (A. M.-D.) gratefully acknowledges the Universidad Complutense for a doctoral felloship.

Experimental.

General Methods. All reactions were carried out under a positive pressure of dry argon, using freshly distilled solvents under anhydrous conditions. Reagents and solvents were handled by using standard syringe techniques. Melting points were determined on a Büchi 512 apparatus and are uncorrected. Infrared spectra were recorded on either a Perkin-Elmer 781 or 257 grating spectrophotometers. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-200 or a Varian VXR-300 instrument. In both, ^{1}H NMR and ^{13}C NMR chemical shifts are reported in δ units downfield from tetramethylsilane.

General Procedure. To a solution of organolithium reagent in anhydrous ether (10 mL/mmol of alcohol) at the adequate temperature, was added 1 equiv. of alcohol dissolved in anhydrous ether (5 mL/mmol of alcohol). The mixture was stirred for 15 min (except in the cases of **5l** and **5m** in which 4 days were necessary to complete the reaction and 10 hours for **5n**) and then quenched with a saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×10 mL/mmol of alcohol). The combined organic extracts were washed with a saturated NaCl solution and dried over anhydrous $MgSO_4$. Concentration under reduced pressure gave a crude product, which was purified by column chromatography on silica gel, using the appropriate eluent.

2-*exo*-Isopropenyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol (4g). From **2** (110 mg, 1 mmol) and 1.2 equiv. of isopropenyllithium (generated from 1.2 equiv. of 2-bromopropene and 2.4 equiv. of *t*-butyllithium at -78°C for 30 min and at 0°C for 30 min) at 0°C, was isolated **4g** (137 mg, 90%) as a light yellow oil after chromatography (hexane:ethyl acetate, 2:1; R_f 0.31). IR ($CHCl_3$) 720, 810, 880, 920, 950, 1020, 1060, 1100, 1190, 1340, 1400, 1460, 1650, 2880, 2980, 3100, 3440 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (d, 1H, J = 12.0 Hz, H-3endo), 1.68 (br, 1H, OH), 1.87 (s, 3H, CH_3), 2.25 (dd, 1H, J = 12.0, 4.9 Hz, H-3exo), 4.73 (d, 1H, J = 1.8 Hz, H-1), 4.91 (s, 1H), 4.98 (d, 1H, J = 4.9 Hz, H-4), 5.10 (s, 1H), 6.50 (dd, 1H, J = 5.7, 1.8 Hz, H-6), 6.64 (dd, 1H, J = 5.7, 1.8 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 19.9, 41.9, 79.3, 79.6, 83.1, 110.1, 134.3, 138.7, 148.3; Anal. Calcd. for $C_9H_{12}O_2$: C, 71.03; H, 7.94. Found: C, 70.95; H, 8.00.

(1S*,3S*,6R*)-6-*n*-Butyl-cyclohex-4-en-1,3-diol (5a). From **4a** (112 mg, 1 mmol) and 3 equiv. of *n*-butyllitium (1.6 M in ether) at 0°C, was isolated **5a** (127 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 1:1; R_f 0.18) and recrystallization from hexane:ether, mp 66-67°C. IR (KBr) 790, 830, 960, 1010, 1040, 1080, 1110, 1310, 1340, 1460, 2840-2960, 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 6.9 Hz, CH_3), 1.25-1.40 (m, 5H), 1.51-1.54 (m, 1H), 1.64 (ddd, 1H, J = 13.0, 7.8, 2.3 Hz, H-2α), 1.75-1.78 (m, 2H, 2 OH), 2.20-2.32 (m, 1H, H-6), 2.29 (dtd, 1H, J = 13.0, 6.7, 1.0 Hz, H-2β), 4.14-4.18 (m, 1H, H-1), 4.44-4.48 (m, 1H, H-3), 5.63 (dm, 1H, J = 10.2 Hz, H-4), 5.76 (dm, 1H, J = 10.2 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.9, 29.3, 29.8, 38.5, 40.2, 65.0, 67.7, 129.2, 131.2; Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.32; H, 10.51.

(+)-(1S, 3S, 6R)-6-*n*-Butyl-3-methyl-cyclohex-4-en-1,3-diol (5b). From (+)-**4b** (126 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated (+)-**5b** (147 mg, 80%) as a white solid after chromatography (hexane:ethyl acetate, 1:2; R_f 0.22) and recrystallization from hexane:ether, mp 56-57°C. [ee ≥ 99%, $[\alpha]^{28}_{578}$ +161 (c 5.72 mg/mL, $CHCl_3$)]. IR (KBr) 740, 1050, 1150, 1210, 1370, 2860, 2960, 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7.3 Hz, CH_3), 1.15-1.42 (m, 5H), 1.32 (s, 3H, CH_3), 1.65-1.70 (m, 1H), 1.83 (d_{ap}, 2H, H-2β, H-2α), 2.07-2.30 (m, 3H, H-6, 2 OH), 4.17 (m, 1H, H-1), 5.56 (dd, 1H, J = 10.0, 1.2 Hz, H-4), 5.75 (dd, 1H, J = 10.0, 4.7 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 13.9, 23.0, 28.0, 29.6, 30.1, 40.1, 42.4, 67.0, 70.0, 131.1, 132.2; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.58; H, 10.71.

(1S*, 3S*, 6R*)-3,6-Di-*n*-butyl-cyclohex-4-en-1,3-diol (5c). From **4c** (168 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated **5c** (192 mg, 85%) as a white solid after chromatography (hexane:ethyl acetate, 1:2; R_f 0.24) and recrystallization from hexane:ether, mp 55-56°C. IR (KBr) 760, 800, 890, 950, 990, 1010, 1050, 1130, 1160, 1280, 1370, 1460, 2840-3000, 3300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 6H, J = 6.5 Hz, 2 CH_3), 1.08-1.17 (m, 1H), 1.28-1.57 (m, 11H), 1.73 (dd, 1H, J = 13.2, 4.2 Hz, H-2α), 1.80 (dd, 1H, J = 13.2, 11.5 Hz, H-2β), 1.94 (br, 2H, 2 OH), 2.25-2.29 (m, 1H, H-6), 4.20 (ddd, 1H, J = 11.5, 5.3, 4.2 Hz, H-1), 5.54 (dt_{ap}, 1H, J = 10.0 Hz, H-4), 5.84 (dd, 1H, J = 10.0, 5.3 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.9, 25.7, 27.4, 29.7, 39.2, 40.3, 42.4, 66.4, 72.5, 131.1, 132.2; Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.28; H, 11.57. Found: C, 74.00; H, 11.62.

(1S*,3S*,6R*)-6-*n*-Butyl-3-phenyl-cyclohex-4-en-1,3-diol (5d). From **4d** (188 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated **5d** (197 mg, 80%) as a white solid after chromatography (hexane:ethyl acetate, 1:2; R_f 0.38) and recrystallization from hexane:ether, mp 118-119°C. IR (KBr) 700, 760, 960, 1010, 1030, 1070, 1080, 1220, 1360, 1380, 1450, 1490, 2920, 2960, 3360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.0 Hz, CH_3), 1.20-1.50 (m, 5H), 1.71-1.79 (m, 1H; br, 1H, OH), 2.01 (d, 2H, J = 7.9 Hz, H-2α, H-2β), 2.23 (br, 1H, OH), 2.37 (m, 1H, H-6), 4.30 (m, 1H, H-1), 5.71 (d, 1H, J = 10.0 Hz, H-4), 6.04 (dd, 1H, J = 10.0, 5.3 Hz, H-5), 7.22-7.45 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 13.9, 23.0, 27.6, 29.7, 40.1, 43.5, 66.8, 74.1, 124.7, 126.8, 128.1, 130.6, 133.2, 147.4; Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.82; H, 8.98.

(1S*, 3S*, 6R*)-6-*n*-Butyl-3-naphthyl-cyclohex-4-en-1,3-diol (5e). From **4e** (238 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated **5e** (222 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 1:1; R_f 0.31) and recrystallization from hexane:ether, mp 104-105°C. IR (KBr) 750, 770, 800, 900, 950, 1010, 1060, 1220, 1280, 1370, 1390, 1440, 1450, 1460, 1500, 1590, 1630, 2860-2950, 3350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (t, 3H, J = 7.0 Hz, CH_3), 1.25-1.52 (m, 7H), 1.73 (m, 1H), 2.27 (dd, 1H, J = 13.7, 3.5 Hz, H-2α), 2.43 (m, 1H, H-6), 2.50 (dd, 1H, J = 13.7, 10.2 Hz, H-2β), 4.37 (m, 1H, H-1), 5.98 (d, 1H, J = 10.0 Hz, H-4), 6.06 (dd, 1H, J = 10.0, 4.4 Hz, H-5), 7.25-7.46 (m, 3H, H-Ar), 7.69-7.86 (m, 3H, H-Ar), 8.66 (m, 1H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.9, 27.1, 29.5, 39.9, 41.8, 67.0, 74.7, 123.3, 124.8, 125.0, 126.1, 128.4, 128.9, 130.2, 131.8, 132.2, 134.5, 141.9; Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.26; H, 8.36.

(1S*, 3S*, 6R*)-6-*n*-Butyl-3-vinyl-cyclohex-4-en-1,3-diol (5f). From **4f** (138 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated **5f** (147 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 1:1; R_f 0.18) and recrystallization from hexane:ether, mp 50-51°C. IR (KBr) 670, 760, 780, 850, 960, 990, 1640, 1700, 2850-3000, 3300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 6.7 Hz, CH_3), 1.16-1.46 (m, 6H), 1.56-1.78 (m, 1H), 1.84 (br, 1H, OH; dd, 1H, J = 13.4, 3.5 Hz, H-2α), 2.02 (dd, 1H, J = 13.4, 9.6 Hz, H-2β), 2.28 (m, 1H, H-6), 4.21 (ddd, 1H, J = 9.6, 5.0, 3.5 Hz, H-1), 5.08 (dd, 1H, J = 10.6, 1.16 Hz, H-2′c), 5.28 (dd, 1H, J = 17.4, 1.16 Hz, H-2′t), 5.55 (ddd, 1H, J = 10.0, 1.0, 0.7 Hz, H-4), 5.85 (dd, 1H, J = 10.0, 4.4 Hz, H-5), 6.01 (dd, 1H, J = 17.4, 10.6 Hz, H-1′); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.9, 28.4, 29.5, 40.2, 41.1, 67.1, 71.9, 112.4, 129.6, 132.6, 144.5; Anal. Calcd. for $C_{12}H_{21}O_2$: C, 73.42; H, 10.27. Found: C, 73.60; H, 10.15.

(1S*, 3S*, 6R*)-6-*t*-Butyl-3-methyl-cyclohex-4-en-1,3-diol (5g). From **4b** (126 mg, 1 mmol) and 3 equiv. of *t*-butyllithium (1.7 M in pentane) at 0°C, was isolated **5g** (138 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 1:1; R_f 0.22) and recrystallization from hexane:ether, mp 69-70°C. IR (KBr) 800, 840, 860, 910, 1070, 1110, 1130, 1300, 1330, 1370, 1470, 1490, 2980, 3300 cm^{-1}; ^1H NMR (C_6D_6) δ 0.98 (s, 10H, 3 CH_3, OH), 1.37 (s, 4H, CH_3, OH), 1.64 (dd, 1H, J = 13.8, 2.5 Hz, H-2α), 1.71 (ddd, 1H, J = 5.3, 2.8, 1.8 Hz, H-6), 1.90 (ddd, 1H, J = 13.8, 4.7, 1.5 Hz, H-2β), 3.98 (m, 1H, H-1), 5.49 (ddd, 1H, J = 10.4, 1.6, 1.6 Hz, H-5), 5.60 (ddd, 1H, J = 10.4, 2.8, 1.5 Hz, H-4); ^{13}C NMR (C_6D_6) δ 28.5, 31.0, 32.7, 46.6, 48.5, 68.5, 68.9, 125.9, 135.0; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.78; H, 10.88.

(1S*, 3S*, 6R*)-6-*t*-Butyl-3-phenyl-cyclohex-4-en-1,3-diol (5h). From **4d** (188 mg, 1 mmol) and 3 equiv. of *t*-butyllithium (1.7 M in pentane) at 0°C, was isolated **5h** (197 mg, 80%) as a white solid after chromatography (hexane:ethyl acetate, 2:1; R_f 0.28) and recrystallization from hexane:ether, mp 123-124°C. IR (KBr) 700, 770, 840, 1030, 1060, 1090, 1190, 1220, 1360, 1450, 2960, 3320, 3380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 9H, 3 CH_3), 1.57 (br, 1H, OH), 1.91 (br, 1H, OH), 2.03 (ddd, 1H, J = 3.9, 2.6, 1.9 Hz, H-6), 2.15 (dd, 1H, J = 13.8, 2.5 Hz, H-2α), 2.63 (ddd, 1H, J = 13.8, 4.9, 1.6 Hz, H-2β), 4.32 (m, 1H, H-1), 5.96 (ddd, 1H, J = 10.5, 2.6, 1.6 Hz, H-5), 6.06 (ddd, 1H, J = 10.5, 1.6, 1.6 Hz, H-4), 7.20-7.39 (m, 3H, H-Ar), 7.53-7.59 (m, 2H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 28.4, 33.1, 46.6, 49.4, 69.1, 71.7, 125.8, 127.7, 128.7, 129.7, 131.7, 147.6; Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.90; H, 9.06.

(1S*, 3S*, 6R*)-6-*s*-Butyl-3-methyl-cyclohex-4-en-1,3-diol (5i). From **4b** (126 mg, 1 mmol) and 3 equiv. of *s*-butyllithium (1.4 M in cyclohexane) at 0°C, was isolated **5i** (138 mg, 75%) as a light yellow oil after chromatography (hexane:ethyl acetate, 1:1; R_f 0.18). The product was isolated as an inseparable mixture of two diastereomers due to the presence of the *s*-butyl radical. IR ($CHCl_3$) 830, 860, 920, 990, 1020, 1050, 1060, 1120, 1140, 1390, 1460, 2880, 2940, 2980, 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (m, 9H, 3 CH_3), 1.02 (d, 3H, J = 6.6 Hz, CH_3), 1.25 (m, 2H, CH_2), 1.37 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.57 (m, 3H, CH_2, CH), 1.69 (m, 1H, CH), 1.85 (m, 1H, H-2α), 1.89 (m, 4H, H-2α, 3 OH), 1.98-2.07 (m, 3H, H-2β, H-6, OH), 2.13 (dd, 1H, J = 13.8, 7.2 Hz, H-2β), 2.28 (m, 1H, H-6), 4.27 (ddd, 1H, J = 8.8, 5.4, 3.7 Hz, H-1), 5.63-5.73 (m, 4H, H-4, H-5); ^{13}C NMR ($CDCl_3$) δ 11.1, 11.5, 16.8, 17.2, 28.2, 30.2, 32.9, 33.8, 43.7, 44.3, 44.4, 67.0, 67.4, 69.1, 69.4, 127.7, 133.6; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.75; H, 10.87.

(1S*, 3S*, 6R*)-6-Phenyl-3-methyl-cyclohex-4-en-1,3-diol (5j). From **4b** (126 mg, 1 mmol) and 9 equiv. of phenyllithium (2M in benzene:ether, 70-30%) at 25°C, was isolated **5j** (153 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 1:3; R_f 0.18) and recrystallization from hexane:ether, mp 88-89°C. IR (KBr) 700, 750, 770, 800, 830, 900, 1050, 1060, 1080, 1120, 1150, 1260, 1280, 1420, 1450, 1490, 2920, 2960, 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40-1.43 (br, 1H, OH), 1.42 (s, 3H, CH_3), 1.66 (dd, 1H, J = 13.4, 11.3 Hz, H-2β), 1.80-1.95 (br, 1H, OH), 1.83 (ddd, 1H, J = 13.4, 3.8, 1.2 Hz, H-2α), 3.70 (dd, 1H, J = 5.3, 4.6 Hz, H-6), 4.29 (ddd, 1H, J = 11.3, 5.3, 3.8 Hz, H-1), 5.78 (dd, 1H, J = 9.8, 4.6 Hz, H-5), 5.88 (ddd, 1H, J = 9.8, 1.2, 1.2 Hz, H-4), 7.15-7.39 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 30.1, 42.0, 46.9, 66.7, 70.3, 127.3, 128.4, 128.6, 130.3, 134.5, 136.6; Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.61; H, 7.63.

(1S*, 3S*, 6R*)-3-*n*-Butyl-6-phenyl-cyclohex-4-en-1,3-diol (5k). From **4c** (168 mg, 1 mmol) and 9 equiv. of phenyllithium (2M in benzene:ether, 70-30%) at 25°C, was isolated **5k** (184 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 1:3; R_f 0.31) and recrystallization from hexane:ether, mp 89-90°C. IR (KBr) 710, 770, 800, 950, 990, 1020, 1040, 1080, 1400, 1450, 1460, 1490, 2850, 2930, 2960, 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.98 (t, 3H, J = 7.0 Hz, CH_3), 1.17 (d, 1H, J = 8.7 Hz, OH), 1.37-1.52 (m, 5H), 1.65 (dd, 1H, J = 13.2, 12.0 Hz, H-2β), 1.68 (br, 1H, OH), 1.62-1.75 (m, 1H), 1.79 (dd, 1H, J = 13.2, 3.7 Hz, H-2α), 3.77 (dd, 1H, J = 5.4, 5.0 Hz, H-6), 4.38 (m, 1H, H-1), 5.87 (dd, 1H, J = 9.8, 5.0 Hz, H-5), 5.93 (ddd, 1H, J = 9.8, 1.2, 1.2 Hz, H-4), 7.23-7.42 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 14.0, 23.1, 25.7, 39.8, 42.7, 47.1, 66.5, 72.6, 127.3, 128.3, 129.5, 130.3, 133.8, 136.3; Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.00; H, 9.00. Found: C, 78.15; H, 8.97.

(1S*, 3S*, 6R*)-3,6-Dimethyl-cyclohex-4-en-1,3-diol (5l). From **4b** (126 mg, 1mmol) and 9 equiv. of methyllithium (1.6 M in ether) at 25°C, was isolated **5l** (92 mg, 65%) as a light yellow oil after chromatography (hexane:ethyl acetate, 1:4; R_f 0.17). IR (neat) 1010, 1040, 1100, 1210, 1260, 1450, 1540, 2840, 2920-2960, 3360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (d, 3H, J = 7.1 Hz, CH_3), 1.30 (s, 3H, CH_3), 1.74 (dd, 1H, J = 13.2, 11.1 Hz, H-2β), 1.82 (ddd, 1H, J = 13.2, 4.3, 1.1 Hz, H-2α), 2.10 (br, 2H, 2 OH), 2.43 (m, 1H, H-6), 4.18 (m, 1H, H-1), 5.53 (dt$_{ap}$, 1H, J = 9.8 Hz, H-4), 5.67 (dd, 1H, J = 9.8, 5.0 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 12.4, 30.0, 34.7, 41.1, 66.6, 70.3, 131.4, 132.9; Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.33; H, 9.90.

(1S*, 3S*, 6R*)-3-n-Butyl-6-methyl-cyclohex-4-en-1,3-diol (5m). From 4c (168 mg, 1 mmol) and 9 equiv. of methyllithium (1.6 M in ether) at 25°C, was isolated 5m (120 mg, 65%), as a light yellow oil after chromatography (hexane:ethyl acetate, 1:3; R_f 0.21). IR ($CHCl_3$) 910, 940, 1020, 1060, 1100, 1180, 1390, 1470, 1660, 1720, 2880, 2960, 2980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3H, J = 7.0 Hz, CH_3), 0.95 (d, 3H, J = 7.1 Hz, CH_3), 1.24-1.35 (m, 5H), 1.52 (br, 1H, OH), 1.51-1.56 (m, 1H), 1.66 (br, 1H, OH), 1.70 (m, 1H, H-2α), 1.76 (dd, 1H, J = 13.2, 10.7 Hz, H-2β), 2.43 (m, 1H, H-6), 4.21 (m, 1H, H-1), 5.49 (dt$_{ap}$, 1H, J = 9.8, 1.2 Hz, H-4), 5.74 (dd, 1H, J = 9.8, 5.4 Hz, H-5); ^{13}C NMR ($CDCl_3$) δ 12.3, 14.0, 23.1, 25.9, 35.1, 38.7, 42.5, 66.8, 72.8, 130.8, 133.9; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.62; H, 10.97.

(1S*, 3S*, 6R*)-3-Methyl-6-vinyl-cyclohex-4-en-1,3-diol (5n). From 4b (126 mg, 1 mmol) and 10 equiv. of vinyllithium (generated from methyllithium and tetravinyltin)[20] at 25°C, was isolated 5n (115 mg, 75%) as a light yellow oil after chromatography (hexane:ethyl acetate, 1:1; R_f 0.11). IR ($CHCl_3$) 820, 920, 940, 970, 1010, 1020, 1060, 1090, 1120, 1150, 1180, 1390, 1520, 2940, 2980, 3380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 3H, CH_3), 1.65 (dd, 1H, J = 13.2, 12.0 Hz, H-2β), 1.80 (dd, 1H, J = 13.2, 3.6 Hz, H-2α), 2.30 (br, 1H, OH), 2.36 (br, 1H, OH), 3.02 (m, 1H, H-6), 4.12 (ddd, 1H, J = 12.0, 5.5, 3.6 Hz, H-1), 5.08 (d, 1H, J = 17.4 Hz, H-2't), 5.18 (dd, 1H, J = 10.3, 1.6 Hz, H-2'c), 5.56 (dd, 1H, J = 10.0, 4.8 Hz, H-5), 5.62 (d, 1H, J = 10.0 Hz, H-4), 5.72 (ddd, 1H, J = 17.4, 10.3, 7.8 Hz, H-1'); ^{13}C NMR ($CDCl_3$) δ 30.0, 41.9, 44.9, 66.0, 70.3, 119.1, 128.6, 133.4, 134.6; Anal. Calcd. for $C_9H_{14}O_2$: C, 70.09; H, 9.15. Found: C, 70.13; H, 9.21.

(1S*, 3S*, 6R*)-3,6-di-Isopropenyl-cyclohex-4-en-1,3-diol (5o). From 4g (152 mg, 1 mmol) and 2 equiv. of isopropenyllithium (generated from 2 equiv. of 2-bromopropene and 4 equiv. of t-butyllithium at -78°C for 30 min and at 0°C for 30 min) at 0°C, was isolated 5o (145 mg, 75%) as a white solid after chromatography (hexane:ethyl acetate, 2:1; R_f 0.21) and recrystallization from hexane:ether, mp 103-104°C. IR (KBr) 760, 810, 910, 1000, 1030, 1080, 1100, 1360, 1380, 1410, 1460, 1650, 3300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.81 (br, 2H, 2 OH), 1.81-1.86 (m, 1H, H-2α), 1.83 (s, 3H, CH_3), 1.86 (s, 3H, CH_3), 2.06 (dd, 1H, J = 13.2, 11.1 Hz, H-2β), 3.13 (d, 1H, J = 6.0 Hz, H-6), 4.31 (m, 1H, H-1), 4.84 (m, 2H, H-4, H-5), 5.08 (s, 2H), 5.76 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 18.7, 24.2, 39.4, 47.7, 66.4, 74.3, 110.4, 115.4, 130.8, 131.6, 143.1, 150.1; Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.31; H, 9.37.

(1S*, 3R*, 6R*)-6-n-Butyl-3-methyl-cyclohex-4-en-1,3-diol (7b). From 6b (126 mg, 1mmol) and 5 equiv. of n-butyllithium (1.6 M in ether) at 25°C, was isolated 7b (148 mg, 80%) as a light yellow oil after chromatography (hexane:ethyl acetate, 5:1; R_f 0.14). IR (neat) 710, 850, 910, 950, 970, 990, 1110, 1130, 1140, 1180, 1380, 1440, 1460, 2890-2980, 3380 cm^{-1}; ^1H NMR (C_6D_6) δ 0.92 (t, 3H, J = 7.0 Hz, CH_3), 1.25 (s, 3H, CH_3), 1.20-1.37 (m, 5H), 1.44 (dd, 1H, J = 14.0, 1.8 Hz, H-2α), 1.49-1.58 (m, 1H), 1.74-1.79 (m, 1H, H-6), 2.13 (ddd, 1H, J = 14.0, 4.5, 1.8 Hz, H-2β), 3.30 (br, 1H, OH), 3.70 (br, 1H, OH), 3.86-3.91 (m, 1H, H-1), 5.37 (ddd, 1H, J = 10.0, 1.7, 1.7 Hz, H-5), 5.72 (ddd, 1H, J = 10.0, 2.7, 1.8 Hz, H-4); ^{13}C NMR (C_6D_6) δ 14.3, 23.2, 29.5, 29.9, 31.2, 41.0, 42.5, 67.8, 67.9, 129.0, 133.4; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.52; H, 10.90.

(1S*, 3R*, 6R*)-3,6-di-n-Butyl-cyclohex-4-en-1,3-diol (7c). From 6c (168 mg, 1 mmol) and 5 equiv. of n-butyllithium (1.6 M in ether) at 25°C, was isolated 7c (169 mg, 75%) as a light yellow oil after chromatography (hexane:ethyl acetate, 5:1; Rf 0.17). IR ($CHCl_3$) 910, 1040-1080, 1180, 1390, 1470, 1480, 1670, 1690, 1720, 2890-2980, 3420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7.0 Hz, CH_3), 0.92 (t, 3H, J = 7.0 Hz, CH_3), 1.25-1.56 (m, 14H), 1.73 (dd, 1H, J = 14.3, 2.0 Hz, H-2α), 2.04 (m, 1H, H-6), 2.13 (ddd, 1H, J = 14.3, 4.3, 1.8 Hz, H-2β), 4.13 (m, 1H, H-1), 4.49 (ddd, 1H, J = 10.0, 1.6, 1.6 Hz, H-5), 5.68 (ddd, 1H, J = 10.0, 2.7, 1.8 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.8, 23.2, 25.7, 29.1, 32.8, 39.8, 40.7, 42.3, 68.0, 70.0, 129.4, 132.2; Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.28; H, 11.57. Found: C, 74.13; H, 11.65.

(1S*, 3R*, 6R*)-6-*n*-Butyl-3-phenyl-cyclohex-4-en-1,3-diol (7d). From **6d** (188 mg, 1 mmol) and 5 equiv. of *n*-butyllithium (1.6 M in ether) at 25°C, was isolated **7d** (197 mg, 80%) as a light yellow oil after chromatography (hexane:ethyl acetate, 5:1; Rf 0.30). IR ($CHCl_3$) 770, 810, 850, 940, 1010, 1030, 1100, 1180, 1410, 1460, 1480, 2840, 2860, 2980, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 7.0 Hz, CH_3), 1.20-1.60 (m, 6H), 1.86 (dd, 1H, J = 14.3, 1.6 Hz, H-2α), 2.09 (m, 1H, H-6), 2.32 (ddd, 1H, J = 14.3, 4.2, 1.5 Hz, H-2β), 3.17 (br, 1H, OH), 3.91 (br, 1H, OH), 4.10 (m, 1H, H-1), 5.67 (d, 1H, J = 10.0 Hz, H-5), 5.83 (ddd, 1H, J = 10.0, 1.7, 1.7 Hz, H-4), 7.21-7.42 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.6, 28.9, 30.2, 40.2, 44.1, 66.9, 68.8, 123.7, 125.9, 126.9, 129.0, 132.6, 147.3; Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.93; H, 8.90.

(1S*, 3R*, 6R*)-6-*n*-Butyl-3-naphthyl-cyclohex-4-en-1,3-diol (7e). From **6e** (238 mg, 1 mmol) and 5 equiv. of *n*-butyllithium (1.6 M in ether) at 25°C, was isolated **7e** (222 mg, 75%) as a light yellow oil after chromatography (hexane:ethyl acetate, 5:1; Rf 0.24). IR ($CHCl_3$) 810, 880, 920, 950, 1030, 1050, 1090, 1390, 1410, 1440, 1480, 1520, 1610, 1670, 1720, 2880, 2940, 2980, 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (t, 3H, J = 7.0 Hz, CH_3), 1.43-1.73 (m, 6H), 2.37 (m, 1H, H-6), 2.44 (dd, 1H, J = 14.8, 2.3 Hz, H-2α), 2.54 (ddd, 1H, J = 14.8, 3.9, 1.7 Hz, H-2β), 3.04 (br, 1H, OH), 3.96 (br, 1H, OH), 4.24 (m, 1H, H-1), 5.78 (ddd, 1H, J = 10.1, 1.7, 1.7 Hz, H-5), 6.08 (ddd, 1H, J = 10.1, 2.7, 1.7 Hz, H-4), 7.42-7.50 (m, 3H, H-Ar), 7.77-7.90 (m, 3H, H-Ar), 8.38-8.41 (m, 1H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.9, 29.2, 30.9, 40.5, 42.2, 68.2, 72.6, 123.6, 125.0, 125.2, 125.3, 128.4, 129.1, 129.2, 130.0, 133.6, 134.5, 141.7; Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.97; H, 8.20.

2-*endo*-Benzyloxy-2-*exo*-methyl-7-oxabicyclo[2.2.1]hept-5-ene (8). A solution of **4b** (126 mg, 1 mmol) and 2 equiv. of HNa (50% in mineral oil) in DME was stirred at room temperature, after one hour, 2 equiv. of benzyl bromide were added and the reaction mixture was refluxed for 3 hours and then quenched with a saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×10 mL/mmol of benzyl ether). The combined organic extracts were washed with a saturated NaCl solution and dried over anhydrous $MgSO_4$. Concentration under reduced pressure gave a crude product, which was purified by column chromatography on silica gel, using the appropriate eluent. Was isolated **8** (173 mg, 80%) as a light yellow oil after chromatography (hexane:ethyl acetate, 5:1; Rf 0.41). IR (neat) 700, 730, 1090, 1210, 1460, 2860-3100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (d, 1H, J = 11.4 Hz, H-3endo), 1.62 (s, 3H, CH_3), 1.80 (dd, 1H, J = 11.4, 4.8 Hz, H-3exo), 4.41 (m, 2H, $-OCH_2Ph$), 4.59 (d, 1H, J = 1.2 Hz, H-1), 4.94 (dd, 1H, J = 4.8, 1.2 Hz, H-4), 6.44 (dd, 1H, J = 5.5, 1.5 Hz, H-5), 6.48 (dd, 1H, J = 5.5, 1.5 Hz, H-6), 7.22-7.31 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 23.1, 38.8, 65.2, 78.3, 80.2, 83.2, 126.8, 127.1, 128.2, 133.0, 135.2, 137.9; Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.45. Found: C, 77.60; H, 7.50.

2-*exo*-Benzyloxy-2-*endo*-methyl-7-oxabicyclo[2.2.1]hept-5-ene (9). From **6b** (126 mg, 1 mmol), 2 equiv. of HNa and 2 equiv. of benzyl bromide (the same procedure as for **8**), was isolated **9** (173 mg, 80%), as a light yellow oil after chromatography (hexane:ethyl acetate, 1:1; Rf 0.34). IR (neat) 700, 1020, 1090, 1310, 1450, 1500, 2870, 3000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (d, 1H, J = 11.7 Hz, H-3endo; s, 3H, CH_3), 2.14 (dd, 1H, J = 11.7, 4.8 Hz, H-3exo), 4.56 (m, 2H, $-OCH_2Ph$), 4.79 (d, 1H, J = 1.5 Hz, H-1), 5.04 (d, 1H, J = 4.8 Hz, H-4), 6.38 (dd, 1H, J = 5.7, 1.9 Hz, H-5), 6.44 (dd, 1H, J = 5.7, 1.5 Hz, H-6), 7.24-7.39 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 22.1, 39.3, 65.5, 78.6, 82.3, 84.1, 127.0, 127.1, 128.1, 133.1, 138.1, 140.5; Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.45. Found: C, 77.80; H, 7.40.

(1S*, 2R*, 5S*)-5-Benzyloxy-2-*n*-butyl-5-methyl-cyclohex-3-en-1-ol (13), and (1S*, 2S*, 6S*)-6-benzyloxy-2-*n*-butyl-6-methyl-cyclohex-3-en-1-ol (14). From **8** (216 mg, 1 mmol), and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated a 2:1 mixture of **13** and **14**; **13**(164 mg, 60%) as a light yellow oil and **14** (82 mg, 30%) as a white solid after chromatography (hexane:ethyl acetate, 5:1).

13: R_f 0.27 (hexane:ethyl acetate, 5:1). IR (neat) 1050, 1375, 1450, 1490, 1670, 2920, 2955, 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.0 Hz, CH_3), 1.35-1.38 (m, 6H), 1.39 (s, 3H, CH_3), 1.80 (dd, 1H, J = 13.7, 9.2 Hz, H-6β), 1.92 (br, 1H, OH), 2.05 (dd, 1H, J = 13.7, 3.5 Hz, H-6α), 2.18-2.30 (m, 1H, H-2), 4.23 (ddd, 1H, J = 9.2, 4.9, 3.5 Hz, H-1), 4.42 (m, 2H, $-OCH_2Ph$), 5.65 (dd, 1H, J = 10.1, 1.8 Hz, H-4), 5.83 (dd, 1H, J = 10.1, 3.9 Hz, H-3), 7.27-7.34 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.9, 27.5, 28.7, 29.5, 39.6, 40.0, 64.5, 67.5, 74.5, 127.0, 127.2, 128.1, 130.8, 132.5, 139.4; Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.69; H, 9.63.

14: R_f 0.35 (hexane:ethyl acetate, 5:1); mp 46-47°C. IR (KBr) 1050, 1100, 1380, 1450, 1460, 1490, 1645, 2920, 2950, 3020, 3520 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.86 (t, 3H, J = 7.0 Hz, CH_3), 1.20-1.45 (m, 7H), 1.30 (s, 3H, CH_3), 1.93 (dm, 1H, J = 17.0 Hz, H-5β), 2.11 (dm, 1H, J = 17.0 Hz, H-5α), 2.73-2.76 (m, 1H, H-2), 3.60 (d, 1H, J = 3.5 Hz, H-1), 4.29 (m, 2H, $-OCH_2Ph$), 5.39-5.54 (m, 2H, H-3, H-4), 7.07-7.27 (m, 5H, H-Ar); ^{13}C NMR (C_6D_6) δ 13.9, 21.8, 22.8, 29.1, 30.1, 30.7, 36.9, 63.4, 73.0, 75.8, 123.6, 126.9, 128.0, 128.5, 139.4; Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.78; H, 9.50.

(1S*, 2R*, 5R*)-5-Benzyloxy-2-*n*-butyl-5-methyl-cyclohex-3-en-1-ol (15), and (1S*, 2S*, 6R*)-6-Benzyloxy-2-*n*-butyl-6-methyl-cyclohex-3-en-1-ol (16). From **9** (216 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated a 2.5:1 mixture of **15** and **16**; **15** (175 mg, 64%) as a light yellow oil and **16** (71 mg, 24%) as a light yellow oil after chromatography (hexane:ethyl acetate, 5:1).

15: R_f 0.45 (hexane:ethyl acetate, 5:1). IR ($CHCl_3$) 710, 840, 860, 890, 930, 1000, 1040, 1060, 1110, 1140, 1160, 1190, 1390, 1470, 1510, 1620, 1660, 2880, 2940, 2980, 3460 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.0 Hz, CH_3), 1.29-1.47 (m, 8H), 1.64 (dd, 1H, J = 14.3, 2.3 Hz, H-6α), 1.65 (m, 1H), 2.04 (m, 1H, H-2), 2.44 (ddd, 1H, J = 14.3, 4.7, 1.7 Hz, H-6β), 3.84 (d, 1H, J = 7.8 Hz, OH), 3.99 (m, 1H, H-1), 4.50 (s, 2H, $-OCH_2Ph$), 5.69 (ddd, 1H, J = 10.2, 2.2, 1.3 Hz, H-3), 5.84 (ddd, 1H, J = 10.2, 2.3, 1.7 Hz, H-4), 7.24-7.34 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.9, 25.6, 29.3, 30.6, 39.5, 41.5, 64.2, 67.0, 73.3, 127.2, 127.4, 128.4, 129.1, 132.9, 138.5; Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.60; H, 9.60.

16: R_f 0.37 (hexane:ethyl acetate, 5:1). IR ($CHCl_3$) 670, 710, 760, 1040, 1050, 1090, 1380, 1460, 1500, 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (s, 6H, 2 CH_3), 1.31-1.48 (m, 5H), 1.60 (m, 1H), 1.75 (dd, 1H, J = 14.4, 3.4 Hz, H-5α), 2.13 (m, 1H, H-2), 2.18 (dd, 1H, J = 14.4, 6.1 Hz, H-5β), 3.19 (br, 1H, OH), 4.05 (m, 1H, H-1), 4.49 (s, 2H, $-OCH_2Ph$), 5.56 (dd, 1H, J = 10.4, 2.1 Hz, H-3), 5.65 (dd, 1H, J = 10.4, 2.7 Hz, H-4), 7.29-7.38 (m, 5H, H-Ar); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.9, 27.8, 29.3, 30.5, 39.9, 40.2, 41.8, 66.4, 82.0, 127.4, 127.5, 128.0, 129.9, 141.3; Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.85; H, 9.50.

(1S*, 2R*, 5S*)-2-*n*-Butyl-5-hydroxymethyl-cyclohex-3-en-1-ol (17), and (1S*, 2S*, 6S*)-2-*n*-Butyl-6-hydroxymethyl-cyclohex-3-en-1-ol (18). From **10** (126 mg, 1 mmol), and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated a 3.5:1 mixture of **17** and **18**; **17** (114 mg, 62%) as a light yellow oil and **18** (33 mg, 18%) as a light yellow oil after chromatography (hexane:ethyl acetate, 1:1).

17: R_f 0.11 (hexane:ethyl acetate, 1:1). IR ($CHCl_3$) 830, 940, 1040, 1070, 1080, 1100, 1140, 1370, 1390, 1420, 1450, 1480, 1720, 2880, 2940, 2980, 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (t, 3H, J = 6.6 Hz, CH_3), 1.19-1.35 (m, 6H), 1.43

(m, 1H, H-6α), 1.93 (m, 1H, H-6β), 2.07 (m, 1H, H-2), 2.44 (m, 1H, H-5), 2.81 (br, 2H, 2 OH), 3.47 (d, 2H, J = 6.0 Hz, $-CH_2OH$), 3.99 (m, 1H, H-1), 5.48 (d, 1H, J = 10.2 Hz, H-4), 5.59 (d, 1H, J = 10.2, Hz, H-3); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.7, 29.0, 30.4, 32.2, 34.6, 40.1, 66.4, 66.8, 127.2, 130.2; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.50; H, 11.00.

18: R_f 0.18 (hexane:ethyl acetate, 1:1). IR ($CHCl_3$) 880, 990, 1020, 1040, 1080, 1110, 1160, 1190, 1270, 1310, 1380, 1460, 1480, 1720, 2900, 2980, 3450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 6.8 Hz, CH_3), 1.18-1.45 (m, 5H), 1.74 (m, 1H, H-5α; m, 1H), 2.05 (m, 2H, H-2, H-5β), 2.18 (m, 1H, H-6), 3.41 (br, 2H, 2 OH), 3.64 (m, 2H, $-CH_2OH$), 3.90 (dd, 1H, J = 9.5, 1.0 Hz, H-1), 5.57 (dd, 1H, J = 10.2, 3.0 Hz, H-3), 5.68 (dd, 1H, J = 10.2, 4.5 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.9, 26.9, 29.5, 29.6, 37.0, 39.9, 66.3, 73.8, 124.5, 129.3; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.75; H, 10.90.

(1S*, 2R*, 5R*)-2-*n*-Butyl-5-hydroxymethyl-cyclohex-3-en-1-ol (19), and (1S*, 2S*, 6R*)-2-*n*-Butyl-6-hydroxymethyl-cyclohex-3-en-1-ol (20). From **11** (126 mg, 1 mmol), and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated a 1:1 mixture of **19** and **20**; **19** (73.6 mg, 40%) as a light yellow oil and **20** (73.6 mg, 40%) as a light yellow oil after chromatography (hexane:ethyl acetate, 1:1).

19: R_f 0.16 (hexane:ethyl acetate, 1:1). IR ($CHCl_3$) 770, 940, 1060, 1110, 1230, 1390, 1480, 1650, 3340 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7.0 Hz, CH_3), 1.20-1.40 (m, 5H), 1.32 (br, 1H, OH), 1.50 (m, 1H), 1.83 (ddd, 1H, J = 13.9, 8.5, 3.1 Hz, H-6β), 2.04 (ddd, 1H, J = 13.9, 5.8, 3.4 Hz, H-6α), 2.11 (m, 1H, H-2), 2.47 (m, 1H, H-5), 3.18 (br, 1H, OH), 3.62 (m, 2H, $-CH_2OH$), 3.95 (m, 1H, H-1), 5.58 (ddd, 1H, J = 10.2, 2.4, 2.4 Hz, H-3), 5.65 (ddd, 1H, J = 10.2, 2.7, 1.8 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.8, 29.2, 30.6, 32.9, 36.3, 39.7, 65.7, 66.2, 126.9, 131.2; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.50; H, 11.00.

20: R_f 0.21 (hexane:ethyl acetate, 1:1). IR ($CHCl_3$) 940, 980, 1040, 1060, 1090, 1170, 1390, 1450, 1480, 2860, 2940, 2960, 3380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7.0 Hz, CH_3), 1.24-1.39 (m, 5H), 1.45 (m, 1H), 1.82 (m, 1H, H-5α), 1.95 (m, 1H, H-2), 2.01 (m, 1H, H-5β), 2.13 (br, 1H, OH), 2.17 (m, 1H, H-6), 2.60 (br, 1H, OH), 3.75 (m, 2H, $-CH_2OH$), 4.07 (m, 1H, H-1), 5.39 (ddd, 1H, J = 10.1, 3.8, 1.8 Hz, H-3), 5.74 (ddd, 1H, J = 10.1, 4.9, 2.5 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.7, 23.1, 29.0, 30.7, 39.9, 41.2, 65.5, 69.2, 126.1, 128.2; Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.93. Found: C, 71.73; H, 10.82.

(1R*, 2R*, 5S*, 6S*)-2-*n*-Butyl-5,6-dihydroxymethyl-cyclohex-3-en-1-ol (21), and (1S*, 2S*, 5S*, 6S*)-2-*n*-Butyl-5,6-dihydroxymethyl-cyclohex-3-en-1-ol (22). From **12** (156 mg, 1 mmol) and 3 equiv. of *n*-butyllithium (1.6 M in ether) at 0°C, was isolated a 1:1 mixture of **21** and **22**; **21** (96 mg, 45%) as a light yellow oil and **22** (96 mg, 45%) as a light yellow oil after chromatography (ethyl acetate: ethanol, 10:1).

21: R_f 0.40 (ethyl acetate: ethanol, 10:1). IR ($CHCl_3$) 740, 760, 840, 950, 960, 1020, 1040, 1070, 1120, 1180, 1330, 1380, 1470, 2880, 2960, 3300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.24-1-51 (m, 6H), 1.60-1.75 (m, 2H), 1.98-2.20 (m, 3H, H-2, H-5 or H-6, OH), 2.50 (m, 1H, H-5 or H-6), 3.64-3.70 (m, 4H, 2 CH_2OH), 4.08 (m, 1H, H-1), 5.30 (d, 1H, J = 10.0 Hz, H-3 or H-4), 5.70 (d, 1H, J = 10.0 Hz, H-3 or H-4); ^{13}C NMR ($CDCl_3$) δ 14.0, 23.0, 29.5, 30.4, 38.1, 40.0, 43.1, 62.5, 65.5, 126.2, 130.9; Anal. Calcd. for $C_{12}H_{22}O_3$: C, 67.25; H, 10.34. Found: C, 67.35; H, 10.30.

22: R_f 0.32 (ethyl acetate: ethanol, 10:1). IR ($CHCl_3$) 740, 750, 850, 940, 960, 1000, 1020, 1040, 1060, 1080, 1120, 1170, 1330, 1360, 1480, 2880, 2960, 3300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3H, J = 6.8 Hz, CH_3), 1.27-1.43 (m, 4H), 1.65-1.78 (m, 3H), 2.12-2.42 (m, 4H, H-2, H-5 or H-6, 2 OH), 2.50 (m, 1H, H-5 or H-6), 3.65-3.73 (m, 3H, 2 CH_2OH), 3.88 (m, 1H, CH_2OH), 4.08 (br, 1H, H-1), 5.54 (d, 1H, J = 10.0 Hz, H-3 or H-4), 5.65 (ddd, 1H, J = 10.0, 2.6, 2.6 Hz, H-3 or H-4); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.8, 29.1, 30.6, 37.1, 41.0, 43.4, 64.7, 65.1, 71.2, 127.9, 130.1; Anal. Calcd. for $C_{12}H_{22}O_3$: C, 67.25; H, 10.34. Found: C, 67.13; H, 10.40.

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