3-Chloropropyl and 4-Chlorobutyl Phenyl Ethers as Sources of 1,3-Dilithiopropane and 1,4-Dilithiobutane: Sequential Reaction with Carbonyl Compounds†

Francisco Foubelo,* Sadiq A. Saleh,‡ and Miguel Yus*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain

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The reaction of 3-chloropropyl and 4-chlorobutyl phenyl ethers (**1**) with lithium powder and a catalytic amount of DTBB (5% molar) in THF at −78 °C followed by successive treatment with a carbonyl compound [R^1R^2CO = Bu^tCHO, Me_2CO, $(CH_2)_5CO$, (−)-menthone] at −78 to 20 °C and, after 1.5 h at this temperature, with a second one [R^3R^4CO = Bu^tCHO, PhCHO, Me_2CO, $MeCOPr^n$, $(CH_2)_5CO$, (−)-menthone] at −78 °C leads, after hydrolysis with water, to the corresponding 1,5- and 1,6-diols (**2**). Because of the competition of two different reductive cleavages, 1,4- and 1,5-diols **3** were also obtained as side-reaction products.

Introduction

The problem of introducing two electrophilic fragments in a 1,3- or 1,4-position in a hydrocarbon chain is the need of using 1,3- or 1,4-dianionic synthons. This type of species is normally exemplified by the corresponding organometallic compounds, dilithio derivatives being very representative in this context.[1] 1,3-Dilithioalkanes cannot be generated directly from the corresponding dihalides[2] because the 3-halogenlithioalkane initially formed undergoes spontaneous γ-elimination, even at very low temperatures, giving the corresponding cyclopropane derivatives.[3] Only in special cases [for instance, starting from 3-chloro-2-(chloromethyl)propene] and reaction conditions [combining an arene-catalyzed lithiation[4,5] with carrying out the reaction in the presence of the electrophile (Barbier-type conditions)[6]] was it possible to introduce as many electrophilic fragments as there were chlorine atoms present in the starting materials.[7,8] Except in the mentioned case, a mercury−lithium transmetalation is the only way to generate nonstabilized 1,3-dilithiated intermediates.[9] For 1,4-dilithioalkanes, although they can be prepared by bromine−lithium exchange in moderate yield,[2] the process has been widely used for the generation of cyclobutane derivatives by a δ-elimination using both 1,4-dibromo or 1,4-diiodo compounds.[10] In all cases, when the 1,3- or 1,4-dilithioalkane is generated, the same electrophilic fragment is introduced at the lithiated centers, being impossible to discriminate both carbanionic atoms in order to introduce two different electrophiles in the molecule. In the past few years, we have been using an arene-catalyzed lithiation reaction[4,5] for the preparation of very unstable functionalized organolithium compounds[11] starting from chlorinated materials,[12a] thioethers,[12b] sulfones,[12c] or heterocyclic derivatives.[12d,13,14] Recently, we discovered that this methodology can be applied to the generation of alkyllithiums from alkyl phenyl ethers.[15] In this paper, we report the preparation

* Address correspondence to M.Y. Fax: +34-965-903549. E-mail: yus@ua.es. URL: http://www. ua.es/dept.quimorg/.

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‡ On leave (June−August, 1999) from Yarmouk University, Irbid, Jordan.

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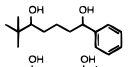
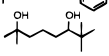
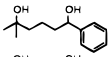
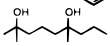
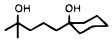
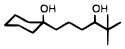
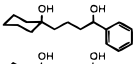
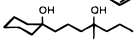
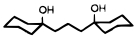
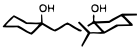
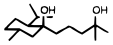
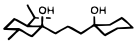
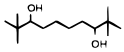
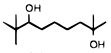
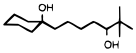
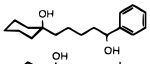
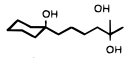
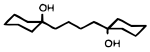
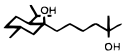
Table 1. Preparation of Diols 2

entry	starting material	R^1R^2CO	R^2R^3CO	Product **2**[a] structure	(no.)	yield (%)[b]
1	**1a**	Bu^{t}CHO	PhCHO		(**2a**)	68[c,d]
2	**1a**	Me_2CO	Bu^{t}CHO		(**2b**)	53
3	**1a**	Me_2CO	PhCHO		(**2c**)	64
4	**1a**	Me_2CO	MeCOPr^n		(**2d**)	45
5	**1a**	Me_2CO	$(CH_2)_5CO$		(**2e**)	48
6	**1a**	$(CH_2)_5CO$	Bu^{t}CHO		(**2f**)	60[e]
7	**1a**	$(CH_2)_5CO$	PhCHO		(**2g**)	52[e]
8	**1a**	$(CH_2)_5CO$	MeCOPr^n		(**2h**)	49[e]
9	**1a**	$(CH_2)_5CO$	$(CH_2)_5CO$		(**2i**)	70[e]
10	**1a**	$(CH_2)_5CO$	(-)-menthone		(**2j**)	43[e,f]
11	**1a**	(-)-menthone	Me_2CO		(**2k**)	46[f,g]
12	**1a**	(-)-menthone	$(CH_2)_5CO$		(**2j**)	50[f,g]
13	**1b**	Bu^{t}CHO	Bu^{t}CHO		(**2l**)	36[c,h]
14	**1b**	Bu^{t}CHO	Me_2CO		(**2m**)	42[h]
15	**1b**	$(CH_2)_5CO$	Bu^{t}CHO		(**2n**)	57[i]
16	**1b**	$(CH_2)_5CO$	PhCHO		(**2o**)	60[i]
17	**1b**	$(CH_2)_5CO$	Me_2CO		(**2p**)	63[i]
18	**1b**	$(CH_2)_5CO$	$(CH_2)_5CO$		(**2q**)	68[i]
19	**1b**	(-)-menthone	Me_2CO		(**2r**)	41[f,j]

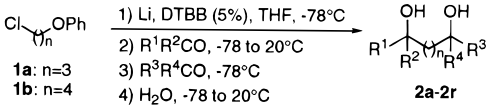
[a] All compounds **2** were >95% pure (GLC and/or 300 MHz ^{1}H NMR). [b] Isolated overall yield of pure compounds after column chromatography (silica gel, hexane/ethyl acetate) based on the starting chloroether **1**. [c] Ca. 1/1 diastereomeric mixture (75 MHz ^{13}C NMR). [d] Compounds **3a** was isolated as a side reaction product in less than 15% yield. [e] Compound **3b** was isolated as a side reaction product in less than 15% yield. [f] 4-5/1 diastereomeric mixture (75 MHz ^{13}C NMR). [g] Compound **3c** was isolated as a side reaction product in less than 15% yield. [h] Compound **3d** was isolated as a side reaction product in less than 15% yield. [i] Compound **3e** was isolated as a side reaction product in less than 15% yield. [j] Compound **3f** was isolated as a side reaction product in less than 15% yield.

of new 1,3- and 1,4-dilithioalkane synthons, taking advantage of the different reactivity of both carbon−chlorine and carbon−oxygen bonds toward an arene-catalyzed lithiation, making it possible to introduce two different electrophilic fragments in the 1,3- or 1,4-positions of the saturated hydrocarbon skeleton.[16]

Results and Discussion

The reaction of 3-chloropropyl phenyl ether (**1a**, easily prepared by treatment of 1-bromo-3-chloropropane with potassium phenolate in methanol in 90% yield) with a dark green suspension of an excess of lithium powder (1:10 molar ratio; theoretical amount, 1:4) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB; 1:0.1 molar ratio; 5 mol %) in THF at −78 °C for 30 min gave a solution of an intermediate of type **I**, which reacted with

Scheme 1



a carbonyl compound [R^1R^2CO = Bu^{t}CHO, Me_2CO, $(CH_2)_5CO$, (−)-menthone] at the same temperature to form an alcoholate of type **II**. After 1.5 h of stirring at 20 °C, a second lithiation took place, leading to a intermediate of type **III**, which reacted with a second carbonyl compound [R^3R^4CO = Bu^{t}CHO, PhCHO, Me_2CO, MeCOPr^n, $(CH_2)_5CO$, (−)-menthone] at −78 °C to yield a dialcoholate of type **IV** which, after hydrolysis with water at −78 to 20 °C, gave the expected 1,5-diols **2** (Scheme 1, Chart 1 and Table 1, entries 1−12). When 4-chlorobutyl phenyl ether (**1b**, prepared by treatment of 1-bromo-4-chlorobutane with potassium phenolate in methanol in 95% yield) was submitted to the same protocol as **1a**, 1,6-diols **2** were obtained, the same intermediates **I**−**IV** being involved (Scheme 1, Chart 1, and Table 1, entries 13−19). In the case of using (−)-menthone as electrophile, a

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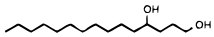
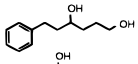
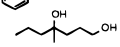
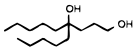
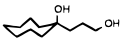
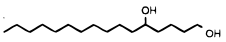
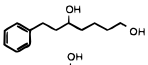
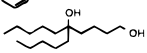
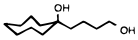
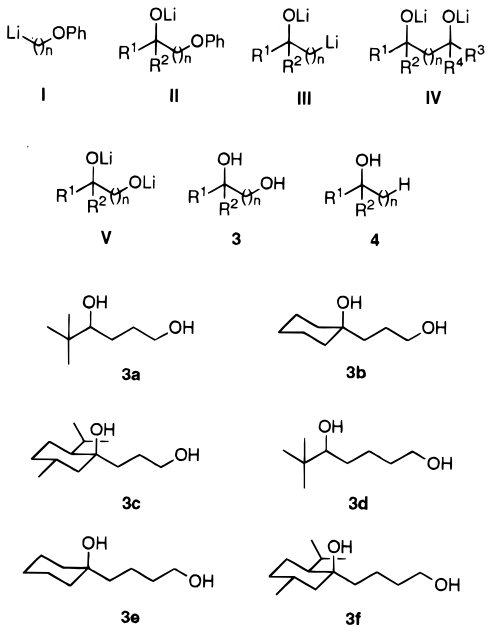
Table 2. Isolation of Diols 3

entry	starting material	R^1R^2CO	product **3**[a] structure	(no.)	yield (%)[b]
1	**1a**	n-$C_{11}H_{23}CHO$		(**3g**)	20
2	**1a**	$Ph(CH_2)_2CHO$		(**3h**)	23
3	**1a**	$MeCOPr^n$		(**3i**)	21
4	**1a**	$(n$-$C_5H_{11})_2CO$		(**3j**)	24
5	**1a**	$(CH_2)_7CO$		(**3k**)	23
6	**1b**	n-$C_{11}H_{23}CHO$		(**3l**)	20
7	**1b**	$Ph(CH_2)_2CHO$		(**3m**)	21
8	**1b**	$MeCOPr^n$		(**3n**)	21
9	**1b**	$(CH_2)_7CO$		(**3o**)	20

[a] All compounds **3** were >95% pure (GLC and/or 300 MHz ^1H NMR). [b] Isolated overall yield of pure compounds after column chromatography (silica gel, hexane/ethyl acetate) based on the starting chloroether **1**.

Chart 1



4−5/1 mixture of diastereoisomers was obtained, due to the two possible approaches of the organolithium especies to the carbonyl group, the major isomers being those shown in Table 1 (entries 10−12 and 19), which result from the attack to the less sterically hindered face. On the other hand, when two prostereogenic carbonyl compounds were used as electrophiles, a ca. 1/1 diastereomeric mixture was obtained (Table 1, entries 1 and 13). Benzaldehyde cannot be used as electrophile after the first lithiation step because the corresponding formed alcoholate of type **II** undergoes a benzylic cleavage together with the expected ether cleavage, leading finally to a complex mixture of products. In all cases, diols **3a**−**f** were obtained as side reaction products in less than 15% yield, based on the starting material **1**. An explanation for this result comes from the fact that two reductive cleavages in intermediates **II** can occur under the reaction conditions during the second lithiation step (20 °C, 1.5 h): the major one leads to species of type **III**, after cleavage of carbon−oxygen bond of the alkyl group, and the minor one, giving dialcoholates **V**, by cleavage of the oxygen-phenyl bond. Trying to take advantage of this undesired process, we attempted to improve the yield for the preparation of diols **3** starting from the chloroalkyl phenyl ethers **1a**,**b**. Thus, after chlorine−lithium exchange and addition of the first carbonyl compound [R^1R^2CO = n-$C_{11}H_{23}CHO$, $Ph(CH_2)_2CHO$, $MeCOPr^n$, $(n$-$C_5H_{11})_2CO$, $(CH_2)_7CO$], water was used as electrophile after the second lithiation instead of a new carbonyl compound. Isolated yields of compouds **3** were always lower than 25% in all cases, compounds **4** being the major reaction products, which were characterized by tandem MS−GC. All attempts to improve the yield in diols **3** by changing the reaction temperatures during the second lithiation step and the lithium-DTBB ratio failed (Table 2). Even though the process for compounds **3** produces low yields, the reaction can be interesting from a synthetic point of view due to the easy separation of the diols **3** from the corresponding "reduced" compound **4**.

As a conclusion, we describe here a new way to generate the equivalents of the 1,3-dianion of propane and the 1,4-dianion of butane and the introduction of two different electrophiles in a sequential manner. This is possible due to the different reactivities of the carbon−chlorine and carbon−oxygen bond toward an arene-catalyzed lithiation: carbon/chlorine exchange takes place at −78 °C and carbon/oxygen reductive cleavage needs temperatures above −40 °C to occur. When carbonyl compounds were used as electrophiles, 1,5- and 1,6-diols were obtained. Compounds of this type have proven to be appropriate starting materials for cyclic ethers by intramolecular dehydration.[17]

Experimental Section

General Methods. Melting points are uncorrected. IR spectra were recorded using NaCl plates for liquids or KBr pellets for solid samples. ^1H and ^{13}C NMR spectra were

(17) See, for instance: (a) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 3351- 3364. (b) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 3365−3374.

recorded at 300 and 75 MHz, respectively, using $CDCl_3$ as solvent and TMS (0.00 ppm, ^1H) and $CDCl_3$ (77.00 ppm, ^{13}C) as internal standards; chemical shifts are given in δ (ppm) and coupling constants (J) are given in Hz. ^{13}C NMR assignments were made on the basis of DEPT experiments. Mass spectra (EI) were obtained at 70 eV, fragment ions given in *m/z* with relative intensities in parentheses. Elemental analyses were performed by the Microanalyses Service at the University of Alicante. High-resolution mass spectra were performed by the corresponding service at the University of Alicante. The purity of volatile products and the chromatographic analyses (GLC) were determinated with a flame ionization detector and a 12 m capillary column (0.2 mm diam, 0.33 mm film thickness), using nitrogen (2 mL/min) as carrier gas, $T_{injector}$= 275 °C, T_{column}= 80 °C (3 min) and 80−270 °C (15 °C/min). Thin-layer chromatography (TLC) was carried out on Schleicher & Schuell F1500/LS 254 plates coated with a 0.2 mm layer of silica gel; R_f values are given under these condtions. Column chromatography was performed using silica gel 60 of 35−70 mesh. All starting materials were commercially available (Acros, Aldrich, Fluka) of the best grade and were used without further purification. THF was dried over benzophenone ketyl under an argon atmosphere and distilled before use.

Preparation of Chloroalkyl Phenyl Ethers 1. General Procedure. Phenol (1.98 g, 21.0 mmol) was added to a solution of KOH (1.25 g, 22.5 mmol) in methanol (40 mL) at 20 °C. After 10 min, the corresponding 1-bromo-*n*-chloroalkane (20.0 mmol) was added, and stirring was continued at 60 °C for 2 h. Then, the solvent was removed in a rotary evaporator, and the residue was hydrolyzed with water and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and evaporated (15 mmHg). The residue was purified by column chromatography (silica gel; hexane) to yield pure products **1**. Yields and physical and spectroscopic data as well as literature references follow.

3-Chloropropyl phenyl ether (1a):[18] 98% yield; R_f 0.21 (silica gel; hexane); IR (film) 3064, 3042, 2965, 2942, 1603, 1245 cm^{-1}; ^1H NMR δ 2.21 (quintet, J = 6.1 Hz, 2H), 3.72 (t, J = 6.1 Hz, 2H), 4.09 (t, J = 6.1, 2H), 6.88−6.96 (m, 3H), 7.24−7.30 (m, 2H); ^{13}C NMR δ 32.3, 41.5, 64.1, 114.5, 120.9, 129.45, 158.7; MS *m/z* 172 (M^+, 13), 94 (100).

4-Chlorobutyl phenyl ether (1b):[19] 95% yield; R_f 0.27 (silica gel; hexane); IR (film) 3062, 3036, 2968, 2944, 1602, 1240 cm^{-1}; ^1H NMR δ 1.90−1.99 (m, 4H), 3.60 (t, J = 6.1 Hz, 2H), 3.98 (t, J = 6.1, 2H), 6.86−6.95 (m, 3H), 7.22−7.29 (m, 2H); ^{13}C NMR δ 26.6, 29.3, 44.7, 66.8, 114.4, 120.6, 129.4, 158.8; MS *m/z* 186 (M^+, 4), 94 (100).

Preparation of Compounds 2 and 3 from Chloroalkyl Phenyl Ethers (1). General Procedure. To a blue suspension of lithium powder (0.105 g, 15.0 g atoms) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (0.040 g, 0.15 mmol) in THF (5 mL) at −78 °C was added the corresponding chloroalkyl phenyl ether **1** (1.5 mmol) under nitrogen, and the mixture was stirred for 30 min at the same temperature. The corresponding carbonyl compound (1.6 mmol) was added, and the cold bath was removed. Stirring was continued at 20 °C for 1.5 h. Then, the reaction mixture was cooled −78 °C, and a second electrophile (1.6 mmol in the case of carbonyl compounds, 0.5 mL in the case of H_2O) was added. After 5 min of stirring, the reaction mixture was hydrolyzed with water and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and evaporated (15 mmHg). The residue was purified by column chromatography (silica gel; hexane/ethyl acetate) and recrystallized to yield pure products **2** and **3**. Yields and structures are included in Tables 1 and 2; physical, analytical, and spectroscopic data as well as literature references follow.

6,6-Dimethyl-1-phenyl-1,5-heptanediol (2a): R_f 0.20 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3550−3120, 3023, 2928, 1640 cm^{-1}; ^1H NMR δ 0.86 (s, 9H), 1.25−1.84 (m, 8H), 3.11−3.17 (m, 1H), 4.63−4.68 (m, 1H), 7.19−7.34 (m, 5H); ^{13}C NMR δ 23.2, 25.6, 30.85, 31.2, 34.8, 38.9, 74.3, 74.6, 79.6, 79.7, 125.8, 127.4, 128.3, 144.9; MS *m/z* 218 (M^+-H_2O, 2), 57 (100); HRMS calcd for $C_{15}H_{22}O$ 218.1670, found 218.1684.

2,7,7-Trimethyl-2,6-octanediol (2b): R_f 0.16 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3500−3100, 2934, 1440 cm^{-1}; ^1H NMR δ 0.89 (s, 9H), 1.22 (s, 6H), 1.26−1.69 (m, 8H), 3.21 (dd, J = 8.6, 1.8 Hz, 1H); ^{13}C NMR δ 21.7, 25.7, 27.6, 29.1, 29.3, 34.9, 43.6, 49.55, 71.0, 79.8; MS *m/z* 152 (M^+ − $2H_2O$, 2), 43 (100); HRMS calcd for $C_{11}H_{20}$ 152.1565, found 152.1591.

5-Methyl-1-phenyl-1,5-hexanediol (2c): R_f 0.15 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3600−3180, 3019, 2932, 1643 cm^{-1}; ^1H NMR δ 1.24 (s, 3H), 1.33 (s, 3H), 1.36−1.74 (m, 6H), 2.85 (br s, 2H), 4.67 (dd, J = 8.0, 5.5 Hz, 1H); ^{13}C NMR δ 29.25, 31.9, 39.45, 43.4, 48.45, 71.7, 74.3, 125.8, 127.4, 128.4, 144.85; MS *m/z* 190 (M^+ − H_2O, 5), 56 (100); HRMS calcd for $C_{13}H_{18}O$ 190.1357, found 190.1362.

2,6-Dimethyl-2,6-nonanediol (2d): R_f 0.10 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3450−3080, 2932, 1443 cm^{-1}; ^1H NMR δ 0.92 (t, J = 6.7 Hz, 3H), 1.16 (s, 3H), 1.22 (s, 6H), 1.20−1.42 (m, 10H), 1.98 (br s, 2H); ^{13}C NMR δ 14.6, 18.5, 26.8, 27.7, 29.2, 31.85, 42.2, 44.3, 71.0, 72.8; MS *m/z* 152 (M^+ − $2H_2O$, 3), 43 (100); HRMS calcd for $C_{11}H_{20}$ 152.1565, found 152.1550.

1-(4-Hydroxy-4-methylpentyl)cyclohexanol (2e): R_f 0.12 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3650−3120, 2921, 1640 cm^{-1}; ^1H NMR δ 1.14 (s, 6H), 1.17−1.54 (m, 16H), 2.08 (br s, 2H); ^{13}C NMR δ 17.55, 22.2, 25.75, 29.2, 37.4, 42.6, 44.3, 70.95, 71.4; MS *m/z* 182 (M^+ − H_2O, 1), 43 (100); HRMS calcd for $C_{12}H_{22}O$ 182.1670, found 182.1668.

1-(4-Hydroxy-5,5-dimethylhexyl)cyclohexanol (2f): R_f 0.18 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3700−3120, 2940, 1446 cm^{-1}; ^1H NMR δ 0.89 (s, 9H), 1.23−1.66 (m, 18H), 3.21 (dd, J = 10.4, 1.8 Hz, 1H); ^{13}C NMR δ 20.3, 22.3, 25.7, 25.8, 31.6, 31.9, 37.3, 37.6, 71.5, 79.9; MS *m/z* 210 (M^+ − H_2O, 2), 55 (100); HRMS calcd for $C_{14}H_{28}O_2$ 228.2089, found 228.2090.

1-(4-Hydroxy-4-phenylbutyl)cyclohexanol (2g): R_f 0.19 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3650−3130, 3030, 2925, 1436 cm^{-1}; ^1H NMR δ 1.21−1.78 (m, 16H), 2.25 (br s, 2H), 4.64 (dd, J = 7.9, 5.5 Hz, 1H); ^{13}C NMR δ 19.1, 22.15, 25.7, 37.2, 37.4, 39.5, 71.5, 74.3, 125.8, 127.3, 128.3, 144.9; MS *m/z* 230 (M^+ − H_2O, 4), 79 (100); HRMS calcd for $C_{16}H_{22}O$ 230.1670, found 230.1695.

1-(4-Hydroxy-4-methylheptyl)cyclohexanol (2h): R_f 0.16 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3720−3080, 2953, 1446 cm^{-1}; ^1H NMR δ 0.92 (t, J = 6.7 Hz, 3H), 1.16 (s, 3H), 1.17−1.92 (m, 22H); ^{13}C NMR δ 14.6, 17.1, 17.2, 22.2, 25.8, 26.85, 37.4, 42.4, 48.5, 44.3, 71.5, 72.85; MS *m/z* 210 (M^+ − H_2O, 1), 55 (100); HRMS calcd for $C_{14}H_{26}O$ 210.1983, found 210.1955.

1-[3-(1-Hydroxycyclohexyl)propyl]cyclohexanol (2i):[20] R_f 0.17 (silica gel; hexane/ethyl acetate 2/1); mp 122−123 °C (pentane/dichloromethane); IR (KBr) 3450−3220, 2934, 1445 cm^{-1}; ^1H NMR δ 1.24−1.64 (m, 26H), 2.05 (br s, 2H); ^{13}C NMR δ 22.2, 25.8, 34, 37.5, 42.8, 71.5; MS *m/z* 222 (M^+ − H_2O, 2), 67 (100). Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.32; H, 11.71.

(1*S*,2*S*,5*R*)-1-[3-(1-Hydroxycyclohexyl)propyl]-2-isopropyl-5-methylcyclohexanol (2j): R_f 0.51 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3560−3130, 2940, 1440 cm^{-1}; ^1H NMR δ 0.79 (d, J = 6.7 Hz, 3H), 0.81 (d, J = 6.7 Hz, 3H), 0.82 (d, J = 7.3 Hz, 3H), 0.86−2.04 (m, 27H); ^{13}C NMR δ 17.1, 18.0, 20.4, 21.6, 22.1, 23.5, 25.3, 25.7, 27.8, 35.0, 37.1, 37.4, 41.6, 42.8, 46.6, 47.7, 71.2, 75.0; MS *m/z* 278 (M^+ − H_2O, 2), 55 (100); HRMS calcd for $C_{19}H_{34}O$ 278.2610, found 278.2614; $[\alpha]^{25}_D$ = +6.2° [c = 1.0 (CH_2Cl_2)].

(1*S*,2*S*,5*R*)-1-(4-Hydroxy-4-methylpentyl)-2-isopropyl-5-methylcyclohexanol (2k): R_f 0.36 (silica gel; hexane/ethyl

(18) Yakabe, S.; Hirano, M.; Morimoto, T. *Org. Prep. Proced. Int.* **1998**, *30*, 218−222.

(19) Ogawa, A.; Sumino, Y.; Nanke, T.; Ohya, S.; Sonoda, N.; Hirao, T. *J. Am. Chem. Soc.* **1997**, *119*, 2745−2746.

(20) Kostas, I. D.; Screttas, C. G. *J. Org. Chem.* **1997**, *62*, 5575−5577.

acetate 2/1); IR (film) 3600−3100, 2945, 1442 cm^{-1}; ^1H NMR δ 0.87 (d, J = 6.7 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H), 1.22 (s, 6H), 0.94−2.06 (m, 17H); ^{13}C NMR δ 18.6, 20.5, 22.4, 23.6, 25.5, 29.0, 35.1, 41.7, 44.5, 46.7, 47.9, 70.95, 75.1; MS m/z 220 ($M^+ - 2H_2O$, 4), 69 (100); HRMS calcd for $C_{16}H_{28}$ 220.2191, found 220.2195; $[\alpha]^{25}_D = +9.1°$ [c = 0.8 (CH_2Cl_2)].

2,2,9,9-Tetramethyl-3,8-decanediol (2l): R_f 0.46 (silica gel; hexane/ ethyl acetate 2/1); IR (film) 3450−3150, 2944, 1430 cm^{-1}; ^1H NMR δ 0.89 (s, 18H), 0.92−1.62 (m, 10H), 3.18−3.21 (m, 2H); ^{13}C NMR δ 25.6, 26.9, 27.1, 31.4, 34.9, 79.7, 79.9; MS m/z 194 ($M^+ - 2H_2O$, 1), 67 (100); HRMS calcd for $C_{14}H_{26}$ 194.2034, found 194.2038.

2,8,8-Trimethyl-2,7-nonanediol (2m): R_f 0.28 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3600−3150, 2945, 1430 cm^{-1}; ^1H NMR δ 0.89 (s, 9H), 1.21 (s, 3H), 1.23 (s, 3H), 1.18−1.64 (m, 8H), 2.22 (br s, 2H), 3.18 (dd, J = 10.5, 1.2 Hz, 1H); ^{13}C NMR δ 25.7, 27.6, 29.1, 29.25, 31.4, 32.0, 43.9, 49.5, 71.0, 79.8; MS m/z 184 ($M^+ - H_2O$, 1), 43 (100); HRMS calcd for $C_{12}H_{24}O$ 184.1827, found 184.1806.

1-(5-Hydroxy-6,6-dimethylheptyl)cyclohexanol (2n): R_f 0.39 (silica gel; hexane/ ethyl acetate 2/1); IR (film) 3620−3160, 2932, 1431 cm^{-1}; ^1H NMR δ 0.88 (s, 9H), 1.27−1.64 (m, 20H), 3.17 (dd, J = 9.7, 4.2 Hz, 1H); ^{13}C NMR δ 22.2, 22.8, 25.7, 27.6, 31.4, 34.9, 37.2, 37.5, 42.3, 71.4, 79.8; MS m/z 224 ($M^+ - H_2O$, 2), 41 (100); HRMS calcd for $C_{15}H_{28}O$ 224.2140, found 224.2154.

1-(5-Hydroxy-5-phenylpentyl)cyclohexanol (2o): R_f 0.25 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3520−3100, 2931, 1442 cm^{-1}; ^1H NMR δ 1.21−1.82 (m, 18H), 2.23 (br s, 2H), 4.62 (dd, J = 7.3, 5.5 Hz, 1H), 7.23−7.33 (m, 5H); ^{13}C NMR δ 22.1, 22.6, 25.7, 26.3, 37.2, 37.3, 38.95, 71.4, 74.3, 125.8, 127.3, 128.3, 144.9; MS m/z 244 ($M^+ - H_2O$, 3), 130 (100); HRMS calcd for $C_{17}H_{24}O$ 244.1827, found 244.1831.

1-(5-Hydroxy-5-methylhexyl)cyclohexanol (2p): R_f 0.18 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3500−3110, 2942, 1432 cm^{-1}; ^1H NMR δ 1.20 (s, 6H), 1.23−1.61 (m, 20H); ^{13}C NMR δ 22.2, 23.3, 24.9, 25.8, 29.15, 37.35, 43.85, 48.50, 70.95, 71.4; MS m/z 178 ($M^+ - 2H_2O$, 6), 82 (100); HRMS calcd for $C_{13}H_{22}$ 178.1721, found 178.1719.

1-[4-(1-Hydroxycyclohexyl)butyl]cyclohexanol (2q): R_f 0.29 (silica gel; hexane/ethyl acetate 2/1); mp 99−100 °C (pentane/dichloromethane); IR (KBr) 3420−3180, 2941, 1438 cm^{-1}; ^1H NMR δ 1.22−1.68 (m, 30H); ^{13}C NMR δ 22.2, 23.4, 25.7, 37.3, 42.2, 71.35; MS m/z 218 ($M^+ - 2H_2O$, 3), 122 (100). Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.53; H, 11.88. Found: C, 75.21; H, 11.62.

(1*S*,2*S*,5*R*)-1-(5-Hydroxy-5-methylhexyl)-2-isopropyl-5-methylcyclohexanol (2r): R_f 0.42 (silica gel; hexane/ethyl acetate 2/1); IR (film) 3620−3130, 2932, 1443 cm^{-1}; ^1H NMR δ 0.88 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.7 Hz, 3H), 0.91 (d, J = 7.3 Hz, 3H), 1.23 (s, 6H), 0.95−2.21 (m, 19H); ^{13}C NMR δ 18.2, 18.6, 20.5, 22.4, 23.6, 25.5, 28.0, 29.25, 35.1, 41.6, 44.5, 46.7, 47.9, 70.95, 75.15; MS m/z 252 ($M^+ - H_2O$, 1), 69 (100); HRMS calcd for $C_{17}H_{32}O$ 252.2453, found 252.2464; $[\alpha]^{25}_D$= +4.6° [c = 1.1 (CH_2Cl_2)].

5,5-Dimethyl-1,4-hexanediol (3a):[21] R_f 0.19 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3620−3100, 2940, 1444 cm^{-1}; ^1H NMR δ 0.88 (s, 9H), 1.70−1.74 (m, 2H), 1.87 (quintet, J = 6.1 Hz, 2H), 2.39 (br s, 2H), 3.23 (dd, J = 10.4, 1.2 Hz, 1H), 3.69 (t, J = 6.1 Hz, 2H); ^{13}C NMR δ 25.7, 30.4, 31.6, 35.0, 63.0, 80.1; MS m/z 128 ($M^+ - H_2O$, 3), 71 (100); HRMS calcd for $C_8H_{16}O$ 128.1201, found 128.1189.

1-(3-Hydroxypropyl)cyclohexanol (3b):[22] R_f 0.12 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3640−3110, 2938, 1442 cm^{-1}; ^1H NMR δ 1.13−1.59 (m, 14H), 3.47 (br s, 2H), 3.54 (t, J = 6.1 Hz, 2H); ^{13}C NMR δ 22.2, 25.7, 25.9, 37.3, 38.5, 62.8, 71.0; MS m/z 140 ($M^+ - H_2O$, 4), 55 (100).

(1*S*,2*S*,5*R*)-1-(3-Hydroxypropyl)-2-isopropyl-5-methylcyclohexanol (3c): R_f 0.36 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3630−3120, 2945, 1454 cm^{-1}; ^1H NMR δ 0.88 (d, J = 7.3 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H), 0.91 (d, J = 7.3 Hz, 3H), 0.96−2.14 (m, 15H), 3.62−3.67 (m, 2H); ^{13}C NMR δ 18.1, 20.55, 22.4, 23.6, 25.4, 27.0, 28.0, 35.0, 37.4, 46.5, 48.6, 63.4, 74.8; MS m/z 214 (M^+, 1), 111 (100); HRMS calcd for $C_{13}H_{26}O_2$ 214.1933, found 214.1941; $[\alpha]^{25}_D = +19.0°$ [c = 0.6 (CH_2Cl_2)].

6,6-Dimethyl-1,5-heptanediol (3d):[23] R_f 0.20 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3630−3110, 2938, 1435 cm^{-1}; ^1H NMR δ 0.88 (s, 9H), 1.19−1.68 (m, 6H), 2.75 (br s, 2H), 3.18 (dd, J = 9.8, 1.2 Hz, 1H), 3.63 (t, J = 6.1 Hz, 2H); ^{13}C NMR δ 23.1, 25.7, 30.8, 32.4, 34.9, 62.3, 79.7; MS m/z 127 [$M^+ - (CH_3, H_2O)$, 3], 57 (100).

1-(4-Hydroxybutyl)cyclohexanol (3e):[24] R_f 0.15 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3650−3120, 2943, 1436 cm^{-1}; ^1H NMR δ 1.18−1.56 (m, 16H), 2.24 (br s, 2H), 3.57 (t, J = 6.7 Hz, 2H); ^{13}C NMR δ 18.9, 22.2, 25.8, 33.0, 37.35, 41.6, 62.4, 71.5; MS m/z 154 ($M^+ - H_2O$, 3), 55 (100).

(1*S*,2*S*,5*R*)-1-(4-Hydroxybutyl)-2-isopropyl-5-methylcyclohexanol (3f): R_f 0.46 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3600−3130, 2942, 1438 cm^{-1}; ^1H NMR δ 0.80 (d, J = 7.0 Hz, 3H), 0.82 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.7 Hz, 3H), 0.86−1.71 (m, 16H), 1.98−2.04 (m, 1H), 3.59 (t, J = 6.7 Hz, 2H); ^{13}C NMR δ 18.1, 20.1, 20.5, 22.4, 23.6, 25.5, 28.0, 33.3, 35.1, 40.9, 46.7, 47.8, 62.7, 75.1; MS m/z 210 ($M^+ - H_2O$, 6), 69 (100); HRMS calcd for $C_{14}H_{26}O$ 210.1984, found 210.1999; $[\alpha]^{25}_D = +19.0°$ [c = 0.6 (CH_2Cl_2)].

1,4-Pentadecanediol (3g): R_f 0.26 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3600−3110, 2941, 1436 cm^{-1}; ^1H NMR δ 0.88 (t, J = 6.7 Hz, 3H), 1.26−1.72 (m, 26H), 3.63−3.71 (m, 3H); ^{13}C NMR δ 14.1, 22.7, 25.7, 29.1, 29.3, 29.6, 29.65, 29.7, 31.9, 34.3, 37.6, 63.1, 72.0; MS m/z 226 ($M^+ - H_2O$, 3), 71 (100); HRMS calcd for $C_{15}H_{30}O$ 226.2297, found 226.2302.

6-Phenyl-1,4-hexanediol (3h): R_f 0.17 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3580−3100, 3025, 2943, 1438 cm^{-1}; ^1H NMR δ 1.40−1.71 (m, 6H), 2.51−2.74 (m, 2H), 3.20 (br s, 2H), 3.49−3.59 (m, 3H), 7.05−7.21 (m, 5H); ^{13}C NMR δ 28.9, 32.05, 34.4, 39.1, 62.65, 71.0, 125.7, 128.3, 142.1; MS m/z 176 ($M^+ - H_2O$, 5), 44 (100); HRMS calcd for $C_{12}H_{16}O$ 176.1201, found 176.1211.

4-Methyl-1,4-heptanediol (3i):[25] R_f 0.19 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3600−3125, 2940, 1441 cm^{-1}; ^1H NMR δ 0.85 (t, J = 7.3 Hz, 3H), 1.09 (s, 3H), 1.28−1.56 (m, 8H), 2.97 (br s, 2H), 3.55 (t, J = 6.0 Hz, 2H); ^{13}C NMR δ 14.6, 17.2, 26.6, 26.85, 38.3, 44.5, 63.0, 72.4; MS m/z 182 ($M^+ - H_2O$, 2), 43 (100).

4-Pentyl-1,4-nonanediol (3j): R_f 0.39 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3630−3130, 2942, 1431 cm^{-1}; ^1H NMR δ 0.82 (t, J = 6.7 Hz, 6H), 1.20−1.57 (m, 20H), 2.37 (br s, 2H), 3.57 (t, J = 6.1 Hz, 2H); ^{13}C NMR δ 14.0, 22.6, 23.2, 26.6, 32.4, 36.05, 39.1, 63.3, 74.3; MS m/z 212 ($M^+ - H_2O$, 2), 43 (100); HRMS calcd for $C_{14}H_{28}O$ 212.2140, found 212.2149.

1-(3-Hydroxypropyl)cyclooctanol (3k): R_f 0.20 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3580−3115, 2936, 1438 cm^{-1}; ^1H NMR δ 1.32−1.72 (m, 18H), 2.49 (br s, 2H), 3.57 (t, J = 6.1 Hz, 2H); ^{13}C NMR δ 22.3, 25.0, 26.45, 28.2, 36.15, 38.0, 63.3, 74.65; MS m/z 212 ($M^+ - H_2O$, 2), 43 (100); HRMS calcd for $C_{11}H_{20}O$ 168.1514, found 168.1505.

1,5-Hexadecanediol (3l): R_f 0.28 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3610−3130, 2938, 1442 cm^{-1}; ^1H NMR δ 0.81 (t, J = 6.6 Hz, 3H), 1.28−1.51 (m, 26H), 2.38 (brs, 2H), 3.55−3.59 (m, 3H); ^{13}C NMR δ 14.1, 21.7, 22.65, 25.7, 29.3, 29.6, 29.65, 29.7, 31.9, 32.45, 36.8, 37.5, 62.5, 71.8; MS m/z 222 ($M^+ - H_2O$, 1), 98 (100); HRMS calcd for $C_{16}H_{32}O$ 240.2453, found 240.2459.

7-Phenyl-1,5-heptanediol (3m): R_f 0.18 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3620−3130, 3030, 2936, 1443 cm^{-1}; ^1H NMR δ 1.38−1.55 (m, 6H), 1.70−1.78 (m, 2H), 2.59−2.82 (m, 4H), 3.58−3.64 (m, 3H), 7.14−7.29 (m, 5H); ^{13}C NMR δ

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21.7, 32.0, 32.3, 36.9, 39.1, 62.3, 71.0, 125.7, 128.3, 142.1; MS *m*/*z* 190 ($M^+ - H_2O$, 3), 91 (100); HRMS calcd for $C_{13}H_{18}O$ 190.1358, found 190.1376.

5-Pentyl-1,5-decanediol (3n): R_f 0.40 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3600−3100, 2936, 1442 cm^{-1}; ^1H NMR δ 0.87 (t, J = 7.0 Hz, 6H), 1.25−1.58 (m, 22H), 1.85 (br s, 2H), 3.64 (t, J = 6.7 Hz, 2H); ^{13}C NMR δ 14.0, 19.5, 22.6, 23.15, 32.4, 33.1, 38.8, 39.1, 62.6, 74.5; MS *m*/*z* 226 ($M^+ - H_2O$, 3), 43 (100); HRMS calcd for $C_{15}H_{30}O$ 226.2297, found 226.2286.

1-(4-Hydroxybutyl)cyclooctanol (3o): R_f 0.18 (silica gel; hexane/ethyl acetate 1/1); IR (film) 3610−3140, 2950, 1446 cm^{-1}; ^1H NMR δ 1.29−1.72 (m, 20H), 2.36 (br s, 2H), 3.56 (t, J = 6.1 Hz, 2H); ^{13}C NMR δ 19.1, 22.3, 25.0, 28.2, 32.95, 36.1, 40.7, 62.3, 74.9; MS *m*/*z* 182 ($M^+ - H_2O$, 5), 55 (100); HRMS calcd for $C_{12}H_{22}O$ 182.1670, found 182.1681.

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Supporting Information Available: Copies of ^1H (300 MHz) and ^{13}C (75 MHz) spectra of new compounds lacking microanalyses (**2a**−**h**,**j**−**p**,**r** and **3c**,**f**−**h**,**j**−**o**). This material is available free of charge via the Internet at http://pubs.acs.org.

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