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Chemoselective Lithiation of 1-Bromo-*n*-chloroalkanes

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Dedicated to the memory of Professor Julio Rodríguez

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Reactions between different 1-bromo-*n*-chloroalkanes (**1**–**3**), lithium/naphthalene (1:2 molar ratio) and a carbonyl compound R^1R^2CO in THF at –78 °C provide, after hydrolysis with water, the corresponding chlorinated alcohols **4** through selective lithiation of the carbon–bromine bond. When an excess of lithium (1:7 molar ratio) is added to the reaction mixture before the hydrolysis, lithiation of the remaining carbon–chlorine bond takes place. The addition of a second carbonyl compound R^3R^4CO, followed by hydrolysis, affords the corresponding diols **7**.

Introduction

Organolithium compounds are probably the most useful carbanionic intermediates in synthetic organic chemistry, due to their high reactivities even under mild reaction conditions.[1] One special type of organolithium compounds includes species in which – as well as the carbon–lithium bond – some further functional group is present in the molecule: these functionalized organolithium compounds are of interest because the functionality is transferred to the electrophilic reagent in their reaction with an electrophile, so polyfunctionalized molecules are accessible in only one synthetic operation.[2] One such functionality not particularly compatible with the presence of a carbon–lithium bond, especially in aliphatic molecules, is a halogen (chlorine, bromine or iodine).[3] Two problems are inherent in the existence of these halogenated organolithium compounds: namely, (1) it is difficult to generate carbon–lithium bonds in the presence of a halogen in the same molecule, because the other carbon–halogen bond can obviously be lithiated too, and (2) the elimination of lithium halide from the initially generated halogenated organolithium intermediate, especially in intramolecular fashion, would self-destroy it, giving a new, undesirable carbon–carbon bond. The literature offers a few examples of selective monolithiation of *n*-chloro-1-iodoalkanes by use of *t*BuLi in diethyl ether as the lithiating reagent: 1-chloro-4-lithiobutane (**I**, $n = 2$)[4] and 1-chloro-6-lithiohexane (**I**, $n = 4$)[5] have been prepared by this methodology. In the case of the corresponding bromo compounds, *t*BuLi (as well as other organolithium compounds) is not effective for performing the desired bromine–lithium exchange with simple 1-bromo-*n*-chloroalkanes at low temperature. The selective metallation of 1-bromo-*n*-chloroalkanes **1**–**3**[6] with magnesium in diethyl ether to give the corresponding chloroalkylmagnesium bromides is known, but no methodologies for the selective lithiation of 1-bromo-*n*-chloroalkanes **1**–**3** have yet been reported.

In this paper we describe the chemoselective lithiation of a carbon–bromine bond in the presence of a carbon–chlorine one by use of an arene-promoted lithiation. Advantage of the differences in reactivities is taken in two versions of this reaction: the stoichiometric (with a lithium arene reagent[7]) and the catalytic version (with a substoichiometric amount of the arene and an excess of lithium metal[8]).

Results and Discussion

We first studied the monolithiation of bromo chloro compounds **1**–**3**.[9] Treatment of these starting materials with lithium/naphthalene[7,10] in the presence of an excess of a carbonyl compound [R^1R^2CO = *t*BuCHO, PhCHO, Me_2CO, $(n\text{-}C_5H_{11})_2CO$, $(CH_2)_7CO$, adamantanone] in THF at –78 °C yielded, after hydrolysis with water at temperatures ranging between –78 °C and room temperature, the corresponding chlorinated alcohols **4** in moderate yields (Scheme 1 and Table 1).

To provide compounds **4**, the reaction shown in Scheme 1 has to be performed under the indicated reaction conditions. Most importantly, the only way to discriminate between the two carbon–halogen bonds to be lithiated is

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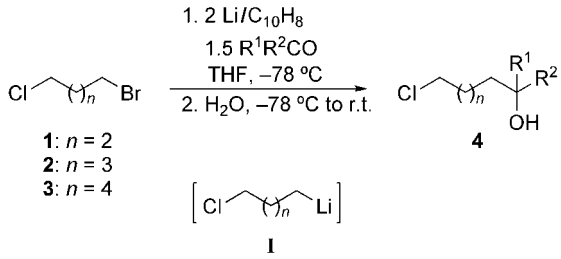


Scheme 1.

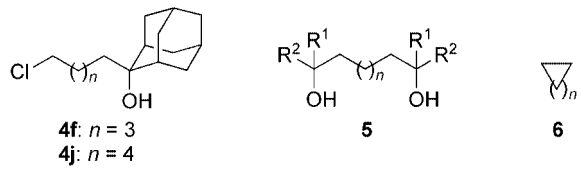
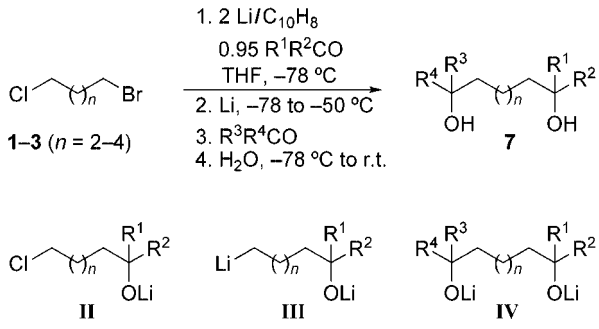


Figure 1. Structures of compounds **4f**, **4j**, **5** and **6**.



Scheme 2.

through the use of two equivalents of lithium/naphthalene, because with the most active catalytic version of the reaction both the bromine–carbon and the chlorine–carbon bonds are cleaved. Thus, under the reaction conditions shown in Scheme 1, but with use of excess lithium and a catalytic amount of naphthalene (ca. 5 mol%) a mixture of compound **4** and the corresponding diol **5** (Figure 1) was obtained. On the other hand, the initially formed intermediate **I** is a very unstable species, which decomposes very easily even at low temperatures, probably through lithium chloride intramolecular elimination to give the corresponding carbocycle **6** (Figure 1) or through intermolecular reactions: these are the processes that occurred when the lithiation was carried out in the absence of the electrophile (Grignard conditions), so the two-step reaction (tandem lithiation/reaction with the electrophile) never gave products **4**. Even in the presence of the electrophile (Barbier conditions[11]) such elimination takes place to some extent, this probably being one of the reasons for the moderate yields generally obtained (Table 1), along with the possible formation of a cyclic ether from the alkoxide **II** (Scheme 2), the scale of the processes (1 mmol)[12] and the difficulty of chromatographic purification of chlorohydrins **4**.

Another control reaction, demonstrating the impossibility of discriminating between the same halogens, was carried out with the use of 1,6-dibromohexane as starting material: in this case, both the stoichiometric and the catalytic versions of the arene-promoted lithiation (benzaldehyde, Barbier conditions, THF, –78 °C) gave compound **5** with R^1 = H, R^2 = Ph in 40–60% yields and as a ca. 1:1 mixture of diastereomers. In the second part of this study we examined the introduction of two different electrophiles in a one-pot reaction. Thus, when compounds **1**–**3** were treated under the same reaction conditions as shown in Scheme 1, but with use of a slightly smaller amount of the first electrophile [R^1R^2CO = *t*BuCHO, PhCHO; 1:0.95 molar ratio], the corresponding alkoxide **II** (precursor of the product **4** by hydrolysis) was again lithiated by addition of an excess of lithium powder (1:7 molar ratio) to the reaction mixture. By this approach, the naphthalene-catalysed lithiation conditions[8,13,14] produced a new organolithium intermediate **III** at temperatures between –78 and –50 °C. Subsequent addition of a second carbonyl compound [R^3R^4CO = $(CH_2)_4CO$, $(CH_2)_5CO$] at –78 °C first gave dialkoxide **IV** and, after final hydrolysis with water at temperatures ranging between –78 °C and room temperature, the differently substituted diols **7** (Scheme 2 and Table 2).

It is worth noting that the yields of compounds **7** were even higher than those of compounds **4**, which is probably due to the chromatographic purification of the latter compounds in the isolation process (see above).

Table 1. Preparation of compounds **4**.

Entry	Starting material	Electrophile	Product[a]				
			No.	*n*	R^1	R^2	Yield (%)[b]
1	**1**	PhCHO	**4a**	2	H	Ph	33
2	**1**	$(n\text{-}C_5H_{11})_2CO$	**4b**	2	$n\text{-}C_5H_{11}$	$n\text{-}C_5H_{11}$	24
3	**1**	$(CH_2)_7CO$	**4c**	2	$(CH_2)_7$		27
4	**2**	*t*BuCHO	**4d**	3	H	*t*Bu	37
5	**2**	PhCHO	**4e**	3	H	Ph	39
6	**2**	adamantanone	**4f**	3	—[c]		41
7	**3**	*t*BuCHO	**4g**	4	H	*t*Bu	48
8	**3**	Me_2CO	**4h**	4	Me	Me	37
9	**3**	$(CH_2)_4CO$	**4i**	4	$(CH_2)_4$		42
10	**3**	adamantanone	**4j**	4	—[c]		51

[a] All products **4** were ≥95% pure (GLC and/or 300 MHz ^{1}H NMR) and were fully characterised spectroscopically and spectrometrically [IR, ^{1}H and ^{13}C NMR, MS (LR and HR)]. [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting materials **1**–**3**. [c] For structures **4f** and **4j** see Figure 1.

Table 2. Preparation of compounds **7**.

Entry	Starting material	First electrophile	Second electrophile	Product[a] No.	*n*	R^1	R^2	R^3-R^4	Yield (%)[b]
1	**1**	*t*BuCHO	$(CH_2)_5CO$	**7a**	2	H	*t*Bu	$(CH_2)_5$	45
2	**1**	PhCHO	$(CH_2)_5CO$	**7b**	2	H	Ph	$(CH_2)_5$	35
3	**2**	*t*BuCHO	$(CH_2)_5CO$	**7c**	3	H	*t*Bu	$(CH_2)_5$	43
4	**2**	PhCHO	$(CH_2)_4CO$	**7d**	3	H	Ph	$(CH_2)_4$	38
5	**3**	*t*BuCHO	$(CH_2)_5CO$	**7e**	4	H	*t*Bu	$(CH_2)_5$	41
6	**3**	PhCHO	$(CH_2)_5CO$	**7f**	4	H	Ph	$(CH_2)_5$	64

[a] All products **4** were ≥95% pure (GLC and/or 300 MHz ^{1}H NMR) and were fully characterised spectroscopically and spectrometrically [IR, ^{1}H and ^{13}C NMR, MS (LR and HR)]. [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the first electrophile (R^1R^2CO).

Conclusions

In conclusion, in this paper we report discrimination between bromine and chlorine in the lithiation of aliphatic bromo chloro compounds for the first time, thus making possible either the monolithiation (by cleavage only of the carbon–bromine bond) and the introduction of only one electrophile or, more interestingly, the one-pot tandem introduction of two electrophilic fragments in the molecule through careful choice of lithiation conditions: at –78 °C the use of lithium/naphthalene (stoichiometric conditions) allowed selective lithiation of the carbon–bromine bond, so that, after treatment of the corresponding chlorinated organolithium intermediate with a carbonyl compound, a second lithiation by use of an excess of lithium (catalytic conditions) allowed a secondary metallation of the remaining carbon–chlorine bond, so that a second carbonyl compound could be used as electrophile. It is remarkable that the tandem double lithiation–S_E reaction worked with better yields (from the point of view of isolated yields) than the monolithiation–S_E reaction to give the corresponding chloro alcohols.

Experimental Section

General Methods: All reactions were carried out under nitrogen in oven-dried glassware. All reagents were commercially available (Acros, Aldrich) and were used without further purification. Commercially available anhydrous THF (99.9%, water content ≤0.006%, Acros) was used as solvent in all the lithiation reactions. IR spectra were measured (film) with a Nicolet Impact 400 D-FT spectrometer. NMR spectra were recorded with a Bruker AC 300, in $CDCl_3$ as solvent. LRMS and HRMS were measured with Shimadzu GC/HS QP-5000 and Finnigan MAT95 S spectrometers, respectively. The purities of volatile products and the chromatographic analyses (GLC) were determined with a flame ionisation detector and a 12-m capillary column (0.2 mm diam., 0.33 μm film thickness), with nitrogen (2 mL min^{-1}) as carrier gas, $T_{injector}$ = 275 °C, $T_{detector}$ = 300 °C, T_{column} = 60 °C (3 min) and 60–270 °C (15 °C min^{-1}), P = 40 kPa.

General Procedure for Compounds 4: A THF solution of lithium/naphthalene (0.7 M, 3.0 mL, 2.1 mmol) was added dropwise at –78 °C over 45 min to a stirred THF solution (3 mL) of the corresponding 1-bromo-*n*-chloroalkane **1**–**3** (1.0 mmol) and a carbonyl compound (R^1R^2CO, 1.5 mmol). Stirring was continued for 10 additional min, the reaction mixture was carefully hydrolysed with water (5 mL), and the system was allowed to reach room temperature. The reaction mixture was extracted with ethyl acetate (2 × 20 mL), dried with anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 40:1) to yield pure products **4**. Yields are given in Table 1; spectroscopic data and literature references follow.

5-Chloro-1-phenylpentan-1-ol (4a):[15] R_f = 0.28 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.27–1.76 (m, 6 H), 1.88 (br s, 1 H), 3.42 (t, J = 6.7 Hz, 2 H), 4.57 (dd, J = 7.4, 5.8 Hz, 1 H), 7.20–7.27 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 23.2, 32.4, 38.1, 44.8, 74.3, 125.8, 127.6, 128.4, 144.5 ppm. IR (film): $\tilde{\nu}$ = 3550–3245, 3060, 3033 cm^{-1}. MS (EI): *m*/*z* (%) = 198 [M]$^+$ (3), 107 (100), 79 (49), 77 (23).

6-(4-Chlorobutyl)undecan-6-ol (4b): R_f = 0.47 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, J = 6.9 Hz, 6 H), 1.23–1.35 (m, 14 H), 1.39–1.45 (m, 9 H), 3.55 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.0, 20.8, 22.6, 23.1, 32.4, 33.0, 38.3, 39.1, 44.9, 74.3 ppm. IR (film): $\tilde{\nu}$ = 3610–3320 cm^{-1}. MS (EI): *m*/*z* (%) = 244 [M – H_2O]$^+$ (1), 193 (27), 191 (80), 83 (22), 71 (23), 69 (37), 57 (27), 55 (89), 43 (100), 41 (74). HMRS (EI): calcd. for $C_{15}H_{29}Cl$ 244.1958; found 244.1956.

1-(4-Chlorobutyl)cyclooctanol (4c): R_f = 0.31 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.32–1.80 (m, 23 H), 3.55 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.5, 22.3, 24.9, 28.2, 33.1, 36.2, 40.5, 45.0, 74.7 ppm. IR (film): $\tilde{\nu}$ = 3590–3295 cm^{-1}. MS (EI): *m*/*z* (%) = 200 [M – H_2O]$^+$ (4), 127 (46), 81 (27), 67 (43), 57 (26), 55 (100), 43 (34), 41 (69). HMRS (EI): calcd. for $C_{12}H_{23}ClO$ 218.1437; found 218.1416.

8-Chloro-2,2-dimethyloctan-3-ol (4d): R_f = 0.44 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.89 (s, 9 H), 1.25–1.59 (m, 6 H), 1.79 (quintet, J = 6.9 Hz, 2 H), 3.15–3.19 (m, 1 H), 3.54 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 25.2, 25.9, 26.5, 30.8, 32.1, 34.4, 44.6, 79.4 ppm. IR (film): $\tilde{\nu}$ = 3580–3275 cm^{-1}. MS (EI): *m*/*z* (%) = 135 [M – *t*Bu]$^+$ (38), 117 (26), 87 (34), 81 (65), 57 (86), 55 (57), 43 (57), 41 (100). HMRS (EI): calcd. for $C_{10}H_{19}Cl$ 174.1175; found 174.1157.

6-Chloro-1-phenylhexan-1-ol (4e):[16] R_f = 0.34 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.25–1.47 (m, 4 H), 1.67–1.78 (m, 4 H), 2.12 (br s, 1 H), 3.49 (t, J = 6.7 Hz, 2 H), 4.63 (dd, J = 7.2, 5.9 Hz, 1 H), 7.23–7.34 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 25.0, 26.7, 32.4, 38.7, 44.9, 74.4, 125.8, 127.5, 128.4, 144.6 ppm. IR (film): $\tilde{\nu}$ = 3570–3285, 3060, 3035 cm^{-1}. MS (EI): *m*/*z* (%) = 212 [M]$^+$ (2), 107 (100), 79 (42), 77 (18).

2-(5-Chloropentyl)adamantan-2-ol (4f): R_f = 0.49 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.39–1.80 (m, 21 H), 2.13 (br s, 1 H), 2.17 (br s, 1 H), 3.54 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.3, 27.2, 27.3, 27.5, 32.6, 32.8, 34.5, 36.8, 38.0, 38.2, 45.0, 74.9 ppm. IR (film): $\tilde{\nu}$ = 3555–3260 cm^{-1}. MS (EI): m/z (%) = 238 [M – H_2O]$^+$ (2), 151 (100), 55 (16), 41 (30) ppm. HMRS (EI): calcd. for $C_{15}H_{23}Cl$ 238.1488; found 238.1475.

9-Chloro-2,2-dimethylnonan-3-ol (4g): R_f = 0.47 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.88 (s, 9 H), 1.25–1.53 (m, 8 H), 1.67 (br s, 1 H), 1.77 (quintet, J = 7.5 Hz, 2 H), 3.14–3.19 (m, 1 H), 3.53 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 25.2, 26.3, 26.4, 28.4, 30.8, 32.1, 34.4, 44.6, 79.4 ppm. IR (film): $\tilde{\nu}$ = 3565–3280 cm^{-1}. MS (EI): m/z (%) = 188 [M – H_2O]$^+$ (1), 149 (23), 95 (56), 87 (23), 69 (35), 57 (64), 43 (44), 41 (100) ppm. HMRS (EI): calcd. for $C_{11}H_{21}Cl$ 188.1332; found 188.1354.

8-Chloro-2-methyloctan-2-ol (4h):[17] R_f = 0.23 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.14 (s, 6 H), 1.18–1.40 (m, 8 H), 1.71 (quintet, J = 6.9 Hz, 2 H), 1.94 (br s, 1 H), 3.46 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 24.1, 26.8, 29.2, 29.7, 32.5, 43.7, 45.1, 71.0 ppm. IR (film): $\tilde{\nu}$ = 3595–3260 cm^{-1}. MS (EI): m/z (%) = 163 [M – Me]$^+$ (7), 59 (100), 43 (43), 41 (25).

1-(6-Chlorohexyl)cyclopentanol (4i): R_f = 0.45 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.25–1.80 (m, 19 H), 3.53 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 23.7, 24.5, 26.8, 29.4, 32.5, 39.6, 41.3, 45.0, 82.4 ppm. IR (film): $\tilde{\nu}$ = 3550–3265 cm^{-1}. MS (EI): m/z (%) = 204 [M]$^+$ (0.5), 175 (18), 113 (18), 85 (100), 67 (20), 58 (17), 57 (16), 55 (21). HMRS (EI): calcd. for $C_{11}H_{21}ClO$ 204.1281; found 204.1277.

2-(6-Chlorohexyl)adamantan-2-ol (4j): R_f = 0.50 (silica gel; hexane/ethyl acetate, 5:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.25–1.85 (m, 23 H), 2.14 (br s, 1 H), 2.18 (br s, 1 H), 3.53 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.8, 26.8, 27.1, 27.3, 29.4, 32.5, 32.8, 34.5, 36.8, 38.0, 38.2, 45.0, 74.8 ppm. IR (film): $\tilde{\nu}$ = 3570–3265 cm^{-1}. MS (EI): m/z (%): 252 [M – H_2O]$^+$ (0.5), 151 (100), 55 (20), 41 (30). HMRS (EI): calcd. for $C_{16}H_{25}Cl$ 252.1645; found 252.1639.

General Procedure for Compounds 7: A THF solution of lithium/naphthalene (0.7 M, 3.0 mL, 2.1 mmol) was added dropwise at –78 °C over 45 min to a stirred THF (3 mL) solution of the corresponding 1-bromo-*n*-chloroalkane **1**–**3** (1.0 mmol) and a carbonyl compound (R^1R^2CO, 0.95 mmol). After 10 min, lithium metal (35 mg, 5.0 mmol) was added to the reaction mixture and stirring was continued for 30 min at temperatures ranging from –78 to –50 °C. The system was then cooled down to –78 °C and a second carbonyl compound (R^3R^4CO, 1.4 mmol) was added. After 10 min, the system was hydrolysed with water (5 mL) and allowed to reach room temperature. The reaction mixture was extracted with ethyl acetate (2 × 20 mL), dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 5:1) to yield pure products **7**. Yields are given in Table 2; spectroscopic data and literature references follow.

1-(5-Hydroxy-6,6-dimethylheptyl)cyclohexanol (7a):[18] R_f = 0.39 (silica gel; hexane/ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.88 (s, 9 H), 1.27–1.64 (m, 20 H), 3.17 (dd, J = 9.7, 4.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 22.2, 22.8, 25.7, 27.6, 31.4, 34.9, 37.2, 37.5, 42.3, 71.4, 79.8 ppm. IR (film): $\tilde{\nu}$ = 3620–3160 cm^{-1}. MS (EI): m/z (%) = 224 [M – H_2O]$^+$ (2), 41 (100). HMRS (EI): calcd. for $C_{11}H_{28}O$ 224.2140; found 224.2154.

1-(5-Hydroxy-5-phenylpentyl)cyclohexanol (7b):[18] R_f = 0.25 (silica gel; hexane/ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.21–1.82 (m, 18 H), 2.23 (br s, 2 H), 4.62 (dd, J = 7.3, 5.5 Hz, 1 H), 7.23–7.33 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): 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 ppm. IR (film): $\tilde{\nu}$ = 3520–3100 cm^{-1}. MS (EI): m/z (%) = 244 [M – H_2O]$^+$ (3), 180 (100). HMRS (EI): calcd. for $C_{17}H_{24}O$ 244.1827; found 244.1831.

1-(6-Hydroxy-7,7-dimethyloctyl)cyclohexanol (7c): R_f = 0.34 (silica gel; hexane/ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.89 (s, 9 H), 1.23–1.57 (m, 22 H), 3.15–3.20 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 22.2, 22.8, 25.7, 25.8, 27.1, 30.3, 31.4, 34.9, 37.4, 42.3, 71.4, 79.9 ppm. MS (EI): m/z (%) = 238 [M – H_2O]$^+$ (3), 181 (22), 163 (78), 99 (100), 95 (57), 83 (41), 81 (92), 67 (30), 55 (45) ppm. IR (film): $\tilde{\nu}$ = 3615–3185 cm^{-1}. HMRS (EI): calcd. for $C_{16}H_{30}O$ 238.2297; found 238.2303.

1-(6-Hydroxy-6-phenylhexyl)cyclopentanol (7d): R_f = 0.20 (silica gel; hexane/ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.25–1.78 (m, 20 H), 4.63 (dd, J = 13.5, 7.4 Hz, 1 H), 7.22–7.34 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 23.7, 24.5, 25.6, 25.7, 39.0, 39.6, 41.3, 74.6, 82.6, 125.8, 127.4, 128.4, 144.8 ppm. IR (film): $\tilde{\nu}$ = 3535–3210 cm^{-1}. MS (EI): m/z (%) = 244 [M – H_2O]$^+$ (3), 138 (59), 122 (55), 117 (30), 107 (100), 95 (31), 91 (47), 79 (64), 77 (34), 67 (33) ppm. HMRS (EI): calcd. for $C_{17}H_{24}O$ 244.1827; found 244.1824.

1-(7-Hydroxy-8,8-dimethylnonanyl)cyclohexanol (7e): R_f = 0.42 (silica gel; hexane/ethyl acetate, 2:1). IR (film): $\tilde{\nu}$ = 3600–3215 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.88 (s, 9 H), 1.21–1.65 (m, 24 H), 3.14–3.19 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 22.2, 22.8, 25.6, 25.8, 27.0, 29.6, 30.2, 31.4, 34.8, 37.3, 42.3, 71.4, 79.9 ppm. MS (EI): m/z (%) = 252 [M – H_2O]$^+$ (2), 195 (20), 177 (40), 135 (20), 121 (18), 109 (25), 99 (100), 95 (79), 81 (63), 69 (25), 57 (31), 55 (32) ppm. HMRS (EI): calcd. for $C_{17}H_{32}O$ 252.2453; found 252.2461.

1-(7-Hydroxy-7-phenylheptyl)cyclohexanol (7f): R_f = 0.29 (silica gel; hexane/ethyl acetate, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.18–1.79 (m, 22 H), 2.21 (br s, 2 H), 4.59 (dd, J = 13.1, 7.2 Hz, 1 H), 7.21–7.34 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 22.1, 22.6, 25.6, 25.7, 29.3, 29.9, 37.2, 38.95, 42.1, 71.5, 74.4, 125.8, 127.2, 128.2, 144.9 ppm. IR (film): $\tilde{\nu}$ = 3545–3220, 3060, 3035 cm^{-1}. MS (EI): m/z (%) = 272 [M – H_2O]$^+$ (2.5), 166 (21), 150 (25), 130 (24), 129 (31), 117 (56), 115 (23), 107 (91), 104 (64), 99 (59), 94 (38), 91 (79), 81 (80), 79 (94), 77 (42), 67 (61), 55 (97), 43 (52), 41 (100). HMRS (EI): calcd. for $C_{19}H_{28}O$ 272.2140; found 272.2133.

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