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DTBB-Catalysed dilithiation of styrene and its methyl-derivatives: introduction of two electrophilic reagents

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This paper is dedicated to Professor David Evans on the occasion of his 60th birthday

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Abstract—The reaction of styrene and some methyl-substituted styrenes **1** with lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB) in the presence of several electrophiles [Me_3SiCl, Me_2CO, Et_2CO, $(CH_2)_5CO$, Pr_2CO], in THF, at temperatures ranging from −78 to 0°C, gave, after hydrolysis, products **2** resulting from addition of lithium to the olefinic double bond and successive trapping with the electrophilic reagent. When a carbonyl compound was used as electrophile, mixtures of the monoaddition–reduction compounds **3** and **4** were obtained as by-products, which could be easily separated from the diaddition products **2**. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Simple olefins cannot be reduced by alkali metals, including lithium, in alcohols or liquid ammonia.[1] In the case of substituted styrenes, the reaction works or not depending on the substitution; as an example, styrene itself readily polymerises in the presence of lithium using an aprotic solvent such as diethyl ether. The polymerisation can be avoided using a proton source (i.e. *N*-methylaniline), giving then ethylbenzene as reduction product.[1] 1,1-Diphenylethylene is probably the best studied system in lithiation processes. In its reaction with lithium metal, the corresponding dianion dimer (1,1,4,4-tetraphenyl-1,4-butadiyl) is formed through the initially generated radical-anion.[2–4] For β-substituted styrenes, the corresponding dianion dimers have been chemically characterised by hydrolysis, giving the expected products resulting from a lithium–hydrogen exchange.[5] Concerning the reactivity of the intermediates generated by lithiation of styrene derivatives, to the best of our knowledge, only two reports have appeared: (a) styrene and α-methylstyrene react with lithium in the presence of chlorotrimethylsilane to give a mixture of the corresponding disilylated monomers and dimers in different proportions depending on the stoichiometry used;[6] (b) stilbene reacts with lithium to give the corresponding dianion, which is stable enough to react with alkyl halides yielding a complex mixture of alkylated products.[7] On the other hand, in the last few years we have been using a lithiation methodology consisting in employing an excess of lithium powder and a catalytic amount of an arene,[8–11] naphthalene and 4,4′-di-*tert*-butylbiphenyl (DTBB) being the most commonly used.[12] This procedure allows the preparation of highly reactive functionalised organolithium compounds[13] (using halogenated or non-halogenated compounds as starting materials[14,15]) and polylithium synthons[16] under very mild reaction conditions. In the last case, we always used a hydrogen– or heteroatom–lithium exchange for the generation of the dianionic intermediates, being in all cases necessary to work under Barbier conditions (i.e. performing the lithiation in the presence of the electrophile)[17] in order to avoid decomposition of the very reactive anionic intermediates. In this paper, we report for the first time on the application of the above mentioned arene-catalysed lithiation to carry out the electron addition to substituted styrenes in order to introduce one electrophilic fragment in each olefinic carbon atom of the styrene skeleton.

2. Results and discussion

The reaction of styrene **1a** with an excess of lithium (1:10 molar ratio) and a catalytic amount of DTBB (1:0.1 molar ratio; 5 mol%) in the presence of chlorotrimethylsilane (1:3 molar ratio) in THF at temperatures ranging between −78 and 0°C led, after hydrolysis with water, to the corresponding disilylated compound **2aa** (Scheme 1 and Table 1, entry 1). In order to get a good yield, it is important to perform the lithiation reaction by slow addition of a THF solution of styrene to the mixture of the lithiating agent and chlorotrimethylsilane in the same solvent. Under these reaction conditions, the corresponding monosilylated products **3aa** and **4aa** (Chart 1) were not detected by GLC (Table 1, entry

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Keywords: lithium; lithiation; styrene derivatives; electron transfer; 1,4-diols.

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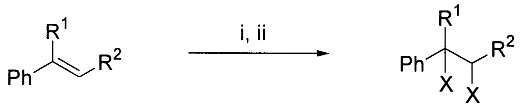

1a: $R^1 = R^2 = H$
1b: $R^1 = Me, R^2 = H$
1c: $R^1 = H, R^2 = Me$

2aa-2ce

Scheme 1. *Reagents and conditions*: (i) Li, DTBB (5 mol%), E=Me_3SiCl, Me_2CO, Et_2CO, $(CH_2)_5CO$, Pr_2CO (1:3 molar ratio), THF, −78–0°C; (ii) H_2O.

1 and footnote c). However, when a carbonyl compound [Me_2CO, Et_2CO, $(CH_2)_5CO$, Pr_2CO] was used as electrophile, the best results were obtained when a THF solution of styrene and the electrophile was slowly added to the cooled lithiating mixture. In these cases, together with the expected compounds **2**, resulting from the double addition to the olefinic double bond, variable amounts of the corresponding monoaddition–reduction products **3** and **4** were also obtained, the β-substituted ones (**4**) being the most abundant in all cases (Chart 1 and Table 1, entries 2–5). The separation and purification of all products **2** was very easy by column chromatography. On the contrary, byproducts **3** and **4** could not be separated from each other due to their similar behaviour in column chromatography. Pivalaldehyde was also tested as electrophilic reagent in the lithiation reaction of styrene, giving a mixture of three diastereoisomers (GLC ratio 1.5:8:6) due to the generation of three stereogenic centers during the process. The mixture of diaddition products was obtained in low overall yield and could not be separated.

Some methyl substituted styrenes were also used as substrates in this reaction. When α- and *E*-β-methylstyrene (**1b** and **1c**, respectively) were used as starting olefins, the expected products **2ba–ce** were isolated using the above mentioned reaction conditions (Scheme 1, Chart 1 and Table 1, entries 6–9). An excellent yield of the diaddition product **2ba** was obtained in the lithiation of α-methylstyrene **1b** in the presence of chlorotrimethylsilane (Table 1, entry 6). A small amount of the β-product **4ca** (Chart 1) was found as a by-product in the reaction between olefin **1c** and chlorotrimethylsilane (Table 1, entry 8 and footnote d). In the reaction of **1c** with 4-heptanone, a very low yield of the diaddition product **2ce** was obtained as a mixture of the corresponding diastereoisomers (Table 1, entry 9 and footnote e), compound **4ce** being the major product of the reaction and the only monoaddition derivative detected (GLC, 300 MHz ^{1}H NMR). In all the cases studied, the reaction conditions are crucial to get the diaddition products

Table 1. Preparation of compounds **2**

Entry	Starting material	Electrophile E	Compound 2[a]				
			No.	R^1	R^2	X	Yield (%)[b]
1	**1a**	Me_3SiCl	**2aa**	H	H	Me_3Si	70 [–[c]]
2	**1a**	Me_2CO	**2ab**	H	H	Me_2COH	33 [33 (1:2.3)]
3	**1a**	Et_2CO	**2ac**	H	H	Et_2COH	51 [19 (1:2.7)]
4	**1a**	$(CH_2)_5CO$	**2ad**	H	H	$(CH_2)_5COH$	50 [47 (1:3.3)]
5	**1a**	Pr_2CO	**2ae**	H	H	Pr_2COH	55 [40 (1:5)]
6	**1b**	Me_3SiCl	**2ba**	Me	H	Me_3Si	90 [–[c]]
7	**1b**	Pr_2CO	**2be**	Me	H	Pr_2COH	38 [32 (1:1.7)]
8	**1c**	Me_3SiCl	**2ca**	H	Me	Me_3Si	3 [5[d]]
9	**1c**	Pr_2CO	**2ce**	H	Me	Pr_2COH	10[e] [47[f]]

[a] All compounds **2** were ≥95% pure (GLC and/or 300 MHz ^{1}H NMR).

[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**. In square brackets, GLC overall yield of the monosubstituted compounds **3**+**4**, the corresponding ratio given in parentheses (ratio 3:4 from GLC).

[c] The corresponding compound **3** or **4** could not be detected by GC-MS and ^{1}H NMR.

[d] Yield corresponding to **4ca**. The α-monoaddition product was not detected by GC-MS and ^{1}H NMR.

[e] A 2.3:1 mixture of diastereoisomers was obtained (GLC).

[f] Yield corresponding to **4ce**. The α-monoaddition product was not detected by GC-MS and ^{1}H NMR.

3aa: $R^1 = H, X = Me_3Si$
3ab: $R^1 = H, X = Me_2COH$
3ac: $R^1 = H, X = Et_2COH$
3ad: $R^1 = H, X = (CH_2)_5COH$
3ae: $R^1 = H, X = Pr_2COH$
3be: $R^1 = Me, X = Pr_2COH$

4aa: $R^1 = R^2 = H, X = Me_3Si$
4ab: $R^1 = R^2 = H, X = Me_2COH$
4ac: $R^1 = R^2 = H, X = Et_2COH$
4ad: $R^1 = R^2 = H, X = (CH_2)_5COH$
4ae: $R^1 = R^2 = H, X = Pr_2COH$
4be: $R^1 = Me, R^2 = H, X = Pr_2COH$
4ca: $R^1 = H, R^2 = Me, X = Me_3Si$
4ce: $R^1 = H, R^2 = Me, X = Pr_2COH$

Chart 1. Compounds **3** and **4** detected.

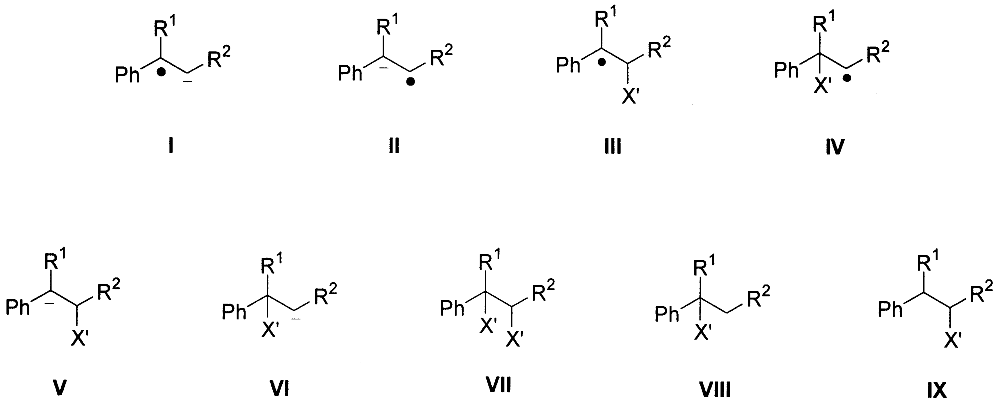

Chart 2. Possible intermediates in the preparation of compounds **2**, **3** or **4** [X′=Me_3Si or RR′C(OLi)].

2 and to avoid either polymerisation products or decomposition of the intermediate species.

Concerning a possible reaction pathway, radical-anions **I** and **II** (Chart 2) are probably generated after the first electron transfer to the starting olefin. In the presence of the electrophile (Barbier-type reaction conditions), **I** and **II** give the new radicals **III** and **IV**, respectively, the benzylic one being more stable. A second electron transfer to these species would produce the corresponding anions **V** and **VI**, respectively, which can evolve by either a second reaction with the electrophile (giving intermediates **VII**, precursors of compounds **2**) or a proton abstraction from the reaction medium (affording in some extent the corresponding monoaddition–reduction intermediates **VIII** and **IX**, precursors of by-products **3** and **4**, respectively). The higher stability of intermediates **III** and **V** (compared to **IV** and **VI**, respectively) could explain why by-products **4** are always favored with respect to **3**.

Finally, the reaction shown in Scheme 1 failed when *E*-stilbene or 1,1-diphenylethylene were used as starting olefins. In these cases, either 1,2-diphenylethane or an intractable mixture of products was, respectively, obtained.

3. Conclusion

In conclusion, we have reported here an efficient procedure to lithiate styrene derivatives using lithium and a catalytic amount of DTBB and performing the metallation in the presence of the electrophile (Barbier-type reaction conditions). Together with the expected products **2**, resulting from a double addition of the electrophile to the olefinic carbon atoms, some by-products, **3** and **4**, resulting from a monoaddition of the electrophile followed by a lithium-proton exchange, were isolated in variable amounts. The method represents a simple way to prepare 1,2 and 1,4-difunctionalised compounds from olefins in a one-pot process.

4. Experimental

4.1. General

FT-IR spectra were obtained on a Nicolet Impact 400D spectrophotometer using NaCl plates. NMR spectra were recorded on a Bruker AC-300 (300 MHz for ^1H and 75 MHz for ^{13}C) using $CDCl_3$ as solvent and TMS (0.00 ppm, ^1H) and $CDCl_3$ (77.0 ppm, ^{13}C) as internal standards; chemical shifts are given in δ (ppm) and coupling constants (J) in Hz. ^{13}C NMR assignments were made on the basis of DEPT experiments. Mass spectra (EI) were obtained at 70 eV on a Shimadzu QP-5000 spectrometer, giving fragment ions in *m*/*z* with relative intensities (%) in parentheses. High resolution mass spectra were measured by the Mass Spectrometry Service at the University of Alicante. Chromatographic analyses (GLC) were determined with a Hewlett Packard HP-5890 instrument equipped with a flame ionization detector and a 12 m HP-1 capillary column (0.2 mm diam, 0.33 μm film thickness, OV-1 stationary phase), using nitrogen (2 mL min^{-1}) as carrier gas, $T_{injector}$=275°C, $T_{detector}$=300°C, T_{column}=80°C (3 min) and 80–270°C (15°C min^{-1}), P=40 kPa; t_r values are given in min under these conditions, unless otherwise stated. Thin layer chromatography (TLC) was carried out on Schleicher and Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection was done by UV_{254} light and staining with phosphomolybdic acid (5 g of phosphomolybdic acid in 120 mL of absolute ethanol); R_f values are given under these conditions. Column chromatography was performed using silica gel 60 of 35–70 mesh. Starting olefins, DTBB and the electrophiles were commercially available (Acros, Aldrich, Fluka) and were used without further purification. THF was dried over sodium benzophenone ketyl under a nitrogen atmosphere and distilled before use.

4.2. Preparation of lithium powder

Lithium powder was prepared from commercially available lithium granules (99%, high sodium content, Aldrich) using an impact grinding mill (brand: IKA MF 10) with a 2.0 mm thin sieve having 1.5 mm diameter holes. The lithium granules in silicon oil were passed through the mill under nitrogen atmosphere. The addition was carried out very slowly in order to avoid agregation of the metal granules. Silicon oil should be added constantly to the system to avoid dryness. The lithium powder suspension was collected in a flask under nitrogen and silicon oil was separated by successive washings with dry hexane. The obtained lithium powder was then dried under vacuum (0.1 Torr) and stored under nitrogen. Silicon oil was heated to 200°C at reduced pressure (0.1 Torr) for 2 h before use. Hexane was refluxed over sodium under nitrogen and distilled before use.

4.3. Lithiation of styrene derivatives 1 under Barbier-type reaction conditions. Isolation of compounds 2 and by-products 3 and 4

Lithiation of olefins **1** *in the presence of chlorotrimethylsilane. General procedure*. To a green suspension of lithium powder (70 mg, 10.0 mmol), DTBB (27 mg, 0.1 mmol) and TMSCl (0.39 mL, 3.0 mmol) in THF (5 mL), under N_2, at −78°C, was added dropwise a solution of olefin **1** (1.0 mmol) in THF (2 mL) during ca. 2 h using a syringe pump. After the addition was complete, the reaction mixture was stirred for ca. 5 h allowing the temperature to rise to 0°C. The reaction was then hydrolysed with water (10 mL), acidified with 2 M HCl and extracted with ethyl acetate (3×20 mL). The combined organic layers were successively washed with a saturated solution of $NaHCO_3$ (5 mL), water (5 mL) and brine (5 mL), being then dried (Na_2SO_4). After evaporation of the solvents (15 Torr), the resulting residue was purified by column chromatography (silica gel, hexane) to yield products **2aa**, **2ba** and **2ca**. The corresponding physical and spectroscopic data for these compounds follow. A small amount of the monoaddition product **4ca** was detected (GC–MS and ^1H NMR spectra of the crude mixture) in the reaction with olefin **2ca**. The structure of compound **4ca** was confirmed by comparison with the reported data.[18]

4.3.1. 1-Phenyl-1,2-bis(trimethylsilyl)ethane (2aa).[6] Colourless oil; R_f 0.37 (hexane); t_r 9.5 [T_{column}=60°C (3 min) and 60–270°C (15°C min^{-1})]; ν (film) 3080, 3060, 3022, 1599, 1493 (HC═C), 836 cm^{-1} (SiMe); δ_H −0.21, −0.08 (9H each, 2s, 2×Me_3Si), 0.84 (1H, dd, J=14.6, 2.4 Hz, C*H*H), 1.06 (1H, dd, J=14.6, 13.4 Hz, C*H*H), 2.06 (1H, dd, J=13.4, 2.4 Hz, CH), 7.02–7.24 (5H, m, ArH); δ_C −3.3, −1.1 (3C each, 2×Me_3Si), 15.95 (CH_2), 31.55 (CH), 124.15, 127.75 (2C), 127.8 (2C), 145.1 (ArC); m/z 250 (M^+, 4%), 162 (18), 147 (13), 73 (100), 45 (27).

4.3.2. 2-Phenyl-1,2-bis(trimethylsilyl)propane (2ba).[6] Colourless oil; R_f 0.57 (hexane); t_r 9.6; ν (film) 3086, 3056, 3031, 3017, 1598, 1494 (HC═C), 836 cm^{-1} (SiMe); δ_H −0.21, −0.12 (9H each, 2s, 2×Me_3Si), 0.86 (1H, d, J=15.3 Hz, C*H*H), 1.41 (3H, s, MeC), 1.51 (1H, d, J=15.3 Hz, C*H*H), 7.04–7.23 (5H, m, ArH); δ_C −4.25, 1.23 (3C each, 2×Me_3Si), 22.5 (*Me*C), 23.9 (CH_2), 29.3 (C), 123.7, 126.45 (2C), 127.45 (2C), 147.85 (ArC); m/z 264 (M^+, 7%), 191 (20), 161 (15), 135 (17), 74 (15), 73 (100), 45 (37), 43 (13).

4.3.3. 1-Phenyl-1,2-bis(trimethylsilyl)propane (2ca).[19] Colourless oil; R_f 0.58 (hexane); t_r 9.7; ν (film) 3080, 3061, 3021, 1601, 1495 (HC═C), 834 cm^{-1} (SiMe); δ_H −0.31, −0.04 (9H each, 2s, 2×Me_3Si), 1.16 (3H, d, J=7.9 Hz, *Me*CH), 1.41–1.48 (1H, m, C*H*Me), 2.02 (1H, d, J=12.2 Hz, C*H*Ph), 7.01–7.57 (5H, m, ArH); δ_C −2.2, −0.6 (3C each, 2×Me_3Si), 16.5 (*Me*CH), 23.1 (*C*HMe), 39.95 (*C*HPh), 124.45 (2C), 128.0 (2C), 132.95, 146.0 (ArC); m/z 264 (M^+, 5%), 161 (18), 135 (12), 74 (12), 73 (100), 45 (29), 43 (10).

Lithiation of olefins **1** *in the presence of a carbonyl compound. General procedure*. To a green suspension of lithium powder (70 mg, 10.0 mmol) and DTBB (27 mg, 0.1 mmol) in THF (5 mL), under N_2, at −78°C, was added dropwise a solution of olefin **1** (1.0 mmol) and the corresponding ketone (3 mmol) in THF (2 mL) during ca. 2 h using a syringe pump. After the addition was complete, the reaction mixture was stirred for ca. 5 h allowing the temperature to rise to 0°C. The reaction was then hydrolysed with water (10 mL), acidified with 2 M HCl and extracted with ethyl acetate (3×20 mL). The combined organic layers were successively washed with a saturated solution of $NaHCO_3$ (5 mL), water (5 mL) and brine (5 mL), being then dried (Na_2SO_4). After evaporation of the solvents (15 Torr) the resulting residue was purified by column chromatography (silica gel, hexane) to yield products **2ab–ae**, **2be** and **2ce**, together with variable amounts of the corresponding monoaddition products **3** and **4**. Compounds **3aa**,[20] **3ab**,[21] **3ac**[20] and **3ad**,[22] previously prepared in our laboratory, and commercially available (Aldrich) **4ab** were identified by comparison of their spectroscopic data with authentic samples. For diaddition products **2ab–ae**, **2be** and **2ce**, the corresponding physical, spectroscopic and analytical data follow, together with some physical and spectroscopic data for by-products **3ae**, **3be**, **4ac–ae,** **4be** and **4ce**.

4.3.4. 2,5-Dimethyl-3-phenyl-2,5-hexanediol (2ab).[23] Colourless oil; R_f 0.24 (hexane/ethyl acetate: 1/1); t_r 11.1; ν (film) 3354 (OH), 3084, 3061, 3027, 1601, 1493 (HC═C), 1152 cm^{-1} (CO); δ_H 1.09, 1.11, 1.18, 1.19 (3H each, 4s, 4×Me), 1.95 (1H, dd, J=14.3, 7.6 Hz, C*H*H), 2.25 (1H, dd, J=14.3, 3.7 Hz, C*H*H), 2.94 (1H, dd, J=7.6, 3.7 Hz, CH), 7.17–7.37 (5H, m, ArH); δ_C 25.45, 28.6, 29.4, 31.15 (4×Me), 43.75 (CH_2), 52.6 (CH), 71.0, 73.1 (2×CO), 126.4, 128.1 (2C), 129.4 (2C), 143.6 (ArC); m/z 186 (M^+-2H_2O, <1%), 146 (40), 131 (94), 91 (36), 59 (100), 43 (68), 41 (20).

4.3.5. 3,6-Diethyl-4-phenyl-3,6-octanediol (2ac). Colourless oil; R_f 0.44 (hexane/ethyl acetate: 1/1); t_r 13.5; ν (film) 3405 (OH), 3083, 3060, 3027, 1599, 1493 (HC═C), 1128 cm^{-1} (CO); δ_H 0.62 (3H, t, J=7.5 Hz, Me), 0.80–0.93 (9H, m, 3×Me), 1.22–1.65 (8H, m, 4×C*H*$_2$Me), 1.95 (1H, dd, J=14.8, 8.7 Hz, C*H*HCH), 2.09 (1H, dd, J=14.8, 2.9 Hz, C*H*HCH), 3.03 (1H, dd, J=8.7, 2.9 Hz, CH), 7.13–7.33 (5H, m, ArH); δ_C 7.55, 7.8 (2C), 7.85 (4×Me), 28.4, 28.45, 30.55, 31.4, 38.5 (5×CH_2), 46.85 (CH), 75.1, 76.55 (2×CO), 126.3, 128.1 (2C), 129.7 (2C), 143.45 (ArC); m/z 242 (M^+-2H_2O, <1%), 174 (30), 159 (27), 145 (71), 131 (11), 129 (16), 128 (12), 117 (55), 115 (14), 105 (17), 104 (18), 91 (52), 87 (72), 83 (11), 77 (16), 69 (27), 67 (10), 65 (13), 57 (100), 53 (13), 45 (95), 43 (55), 41 (72); HRMS: M^+-2H_2O, found 242.2025. $C_{18}H_{26}$ requires 242.2035.

4.3.6. 1-[2-(1-Hydroxycyclohexyl)-1-phenylethyl]cyclohexanol (2ad). Colourless oil; R_f 0.50 (hexane/ethyl acetate: 1/1); t_r 16.3; ν (film) 3371 (OH), 3083, 3059, 3026, 1600, 1493 (HC═C), 1150 cm^{-1} (CO); δ_H 1.29–1.80 (22H, m, 10×CH_2 ring and 2×OH), 1.97 (1H, dd,

J=14.7, 8.6 Hz, C*H*HCH), 2.14 (1H, dd, J=14.7, 3.1 Hz, C*H*HCH), 2.87 (1H, dd, J=8.6, 3.1 Hz, CH), 6.79–7.30 (5H, m, ArH); δ_C 18.8, 21.65, 21.8, 22.0, 22.3, 25.55, 25.7, 33.55, 36.25, 37.25, 38.85 (11×CH_2), 51.45 (CH), 71.7, 73.45 (2×CO), 126.35 (2C), 128.1 (2C), 129.75, 143.45 (ArC); m/z 284 (M^+-H_2O, <1%), 186 (46), 129 (12), 105 (15), 104 (100), 99 (32), 91 (19), 81 (29), 55 (25), 43 (17), 41 (24); HRMS: M^+-H_2O, found 284.2119. $C_{20}H_{28}O$ requires 284.2140.

4.3.7. 5-Phenyl-4,7-dipropyl-4,7-decanediol (2ae). Colourless oil; R_f 0.65 (hexane/ethyl acetate: 1/1); t_r 14.8; ν (film) 3420 (OH), 3087, 3061, 3027, 1601, 1494 (HC=C), 1131 cm^{-1} (CO); δ_H 0.66 (3H, t, J=7.0 Hz, Me), 0.82–0.94 (9H, m, 3×Me), 1.07–1.53 (16H, m, 4×C*H*$_2$C*H*$_2$Me), 1.75 (2H, s, 2×OH), 1.94 (1H, dd, J=15.0, 8.5 Hz, C*H*HCH), 2.09 (1H, dd, J=15.0, 2.4 Hz, C*H*HCH), 3.01 (1H, dd, J=8.5, 2.4 Hz, CH), 7.19–7.29 (5H, m, ArH); δ_C 14.3, 14.6 (3C) (4×Me), 16.6, 16.75, 16.8, 16.95, (4×*C*H$_2$Me), 38.9, 39.25, 39.4, 41.25, 42.3 (5×*C*H$_2$CO), 47.8 (CH), 74.8, 76.5 (2×CO), 126.35, 128.1 (2C), 129.7 (2C), 143.4 (ArC); m/z 298 (M^+-2H_2O, 2%), 202 (27), 187 (22), 160 (12), 159 (75), 145 (23), 131 (39), 129 (15), 128 (16), 117 (42), 115 (71), 105 (12), 104 (24), 91 (53), 79 (12), 77 (11), 73 (16), 71 (42), 69 (23), 57 (15), 55 (77), 44 (31), 43 (100), 41 (66), 40 (45); HRMS: M^+-2H_2O, found 298.2660. $C_{22}H_{34}$ requires 298.2661.

4.3.8. 5-Methyl-5-phenyl-4,7-dipropyl-4,7-decanediol (2be). Colourless oil; R_f 0.23 (hexane/ethyl acetate: 4/1); t_r 15.4; ν (film) 3404 (OH), 3090, 3056, 1600, 1495 (HC=C), 1131 cm^{-1} (CO); δ_H 0.70–0.94 (12H, m, 4× *Me*CH$_2$), 1.20–1.55 (18H, m, 4×C*H*$_2$C*H*$_2$Me and 2×OH), 1.59 (3H, s, MeC), 1.98, 2.51 (1H each, 2d, J=15.0 Hz each, C*H*$_2$CPh), 7.20–7.53 (5H, m, ArH); δ_C 14.45, 14.6, 14.9, 15.0 (4×Me), 16.8, 17.25, 18.0, 18.05, (4×*C*H$_2$Me), 21.2 (*Me*C), 38.3, 38.35, 42.3, 44.0, 44.2 (5×*C*H$_2$CO), 49.5 (*C*Ph), 75.5, 78.35 (2×CO), 126.01, 127.8 (2C), 128.15 (2C), 145.85 (ArC); m/z 312 (M^+-2H_2O, <1%), 216 (25), 201 (14), 174 (11), 173 (72), 131 (30), 120 (20), 118 (31), 115 (99), 105 (35), 91 (25), 73 (24), 71 (34), 59 (20), 57 (14), 55 (89), 45 (11), 43 (100), 41 (50); HRMS: M^+-2H_2O, found 312.2792. $C_{23}H_{36}$ requires 312.2817.

4.3.9. 5-Methyl-6-phenyl-4,7-dipropyl-4,7-decanediol (2ce). Colourless oil; R_f 0.63 (minor) and 0.73 (major) (hexane/ethyl acetate: 1/1); t_r 15.1 (major) and 15.2 (minor); ν (film) (major) 3308 (OH), 3080, 3059, 3027, 1599, 1494 (HC=C), 1133 cm^{-1} (CO); δ_H (major) 0.60–2.10 (30H, m, 4×C*H*$_2$C*H*$_2$*Me* and 2×OH), 1.02 (3H, d, J=7.3 Hz, *Me*CH), 2.35–2.42 (1H, m, C*H*Me), 3.25 (1H, d, J=2.4 Hz, C*H*Ph), 7.15–7.60 (5H, m, ArH); δ_H (minor) 0.64, 0.74 (6H each, 2t, J=7.3, 6.7 Hz, respectively, 4×*Me*CH$_2$), 0.76–1.64 (18H, m, 8×CH$_2$ and 2×OH), 1.06 (3H, d, J=7.3 Hz, *Me*CH), 2.53 (1H, qd, J=7.3, 1.8 Hz, C*H*Me), 2.84 (1H, d, J=1.8 Hz, C*H*Ph), 7.21–7.46 (5H, m, ArH); δ_C (major) 13.85, 14.7 (2C), 14.8, 15.1 (5×Me), 16.45, 16.75, 16.95, 17.85 (4×*C*H$_2$Me), 38.0 (*C*HMe), 38.05, 38.2, 40.05, 40.55 (4×*C*H$_2$CO), 50.65 (*C*HPh), 77.5, 78.75 (2×CO), 126.35 (4C), 127.85, 140.85 (ArC); m/z (major and minor) 348 (M^+, <1%), 287 (14), 216 (17), 187 (25), 174 (14), 173 (70), 145 (16), 131 (31), 125 (11), 117 (27), 115 (55), 105 (11), 91 (33), 83 (10), 73 (11), 71 (68), 69 (30), 57 (17), 55 (66), 45 (11), 43 (100), 41 (47); HRMS: M^+-2H_2O, found 312.2817. $C_{23}H_{36}$ requires 312.2817.

4.3.10. 4-(1-Phenylethyl)-4-heptanol (3ae). Colourless oil; R_f 0.39 (hexane/ethyl acetate: 4/1); t_r 10.4; ν (film) 3470 (OH), 3085, 3062, 3026, 1603, 1496 (HC=C), 1132 cm^{-1} (CO); δ_H 0.81 (6H, t, J=6.7 Hz, 2×*Me*CH$_2$), 1.12–1.64 (12H, m, 4×CH$_2$, *Me*CH and OH), 2.84 (1H, q, J=7.3 Hz, CH) 7.18–7.29 (5H, m, ArH); δ_C 14.55 (2C, 2×*Me*CH$_2$), 15.35 (*Me*CH), 16.9 (2C, 2×*C*H$_2$Me), 39.75 (2C, 2× *C*H$_2$CO), 46.15 (CH), 75.6 (CO), 126.25, 128.0 (2C), 129.1 (2C), 143.6 (ArC); m/z 202 (M^+-H_2O, 3%), 177 (14), 115 (100), 106 (25), 105 (21), 91 (28), 77 (12), 73 (25), 71 (15), 59 (20), 55 (86), 43 (66), 41 (27).

4.3.11. 4-(1-Methyl-1-phenylethyl)-4-heptanol (3be). Colourless oil; R_f 0.43 (hexane/ethyl acetate: 4/1); t_r 11.1; ν (film) 3584, 3504 (OH), 3089, 3057, 3021, 1600, 1496 (HC=C), 1129 cm^{-1} (CO); δ_H 0.83 (6H, t, J=7.0 Hz, 2×*Me*CH$_2$), 1.02–1.55 (9H, m, 4×CH$_2$ and OH), 1.41 (6H, s, 2×MeC) 7.08–7.54 (5H, m, ArH); δ_C 15.0 (2C, 2×*Me*CH$_2$), 17.95 (2C, 2×*C*H$_2$Me), 24.65 (2C, 2×*Me*C), 37.9 (2C, 2×*C*H$_2$CO), 46.25 (CH), 77.4 (CO), 125.85, 127.55 (2C), 128.1 (2C), 147.0 (ArC); m/z 216 (M^+-H_2O, 2%), 191 (11), 131 (11), 120 (49), 115 (100), 105 (64), 91 (34), 77 (11), 73 (31), 71 (16), 59 (39), 57 (11), 55 (92), 45 (10), 43 (88), 41 (59).

4.3.12. 3-Ethyl-1-phenyl-3-pentanol (4ac).[24] t_r 9.0; m/z 174 (M^+-H_2O, 19%), 163 (21), 145 (34), 92 (10), 91 (100), 87 (42), 65 (13), 57 (12), 45 (38), 43 (14), 41 (16).

4.3.13. 1-(2-Phenylethyl)cyclohexanol (4ad).[25] Colourless oil; R_f 0.55 (hexane/ethyl acetate: 1/1); t_r 11.4; ν (film) 3402 (OH), 3083, 3060, 3024, 1603, 1493 (HC=C), 1149 cm^{-1} (CO); δ_H 1.43–1.87 (13H, m, 5×CH$_2$ ring, C*H*$_2$CH$_2$Ph and OH), 2.67–2.73 (2H, m, C*H*$_2$Ph), 7.07–7.29 (5H, m, ArH); δ_C 22.2 (2C), 25.75, 37.45 (2C) (5×CH$_2$ ring), 29.35 (*C*H$_2$Ph), 44.25 (*C*H$_2$CO), 71.3 (CO), 125.2, 125.6 (2C), 128.55 (2C), 142.85 (ArC); m/z 186 (M^+-H_2O, 32%), 105 (18), 104 (66), 99 (66), 95 (11), 91 (100), 81 (43), 79 (11), 77 (10), 65 (17), 55 (24), 43 (29), 41 (28).

4.3.14. 4-(2-Phenylethyl)-4-heptanol (4ae).[26] Colourless oil; R_f 0.38 (hexane/ethyl acetate: 4/1); t_r 11.2; ν (film) 3438 (OH), 3085, 3062, 3026, 1603, 1496 (HC=C), 1129 cm^{-1} (CO); δ_H 0.94 (6H, t, J=7.0 Hz, 2×Me), 1.17–1.59 (9H, m, 2×C*H*$_2$C*H*$_2$Me and OH), 1.70–1.76 (2H, m, C*H*$_2$CH$_2$Ph), 2.60–2.66 (2H, m, C*H*$_2$Ph), 7.14–7.29 (5H, m, ArH); δ_C 14.65 (2C, 2×Me), 16.8 (2C, 2×*C*H$_2$Me), 29.95 (*C*H$_2$Ph), 41.35 (*C*H$_2$CH$_2$Ph), 41.6 (2C, 2×*C*H$_2$CH$_2$Me), 74.35 (CO), 125.65, 128.25 (2C), 128.35 (2C), 142.7 (ArC); m/z 202 (M^+-H_2O, 10%), 177 (22), 159 (13), 115 (29), 91 (100), 69 (14), 55 (35), 43 (21), 41 (22).

4.3.15. 2-Phenyl-4-propyl-4-heptanol (4be). Colourless oil; R_f 0.25 (hexane/ethyl acetate: 4/1); t_r 11.1; ν (film) 3466 (OH), 3083, 3062, 3026, 1602, 1494 (HC=C), 1136 cm^{-1} (CO); δ_H 0.79–1.00 (6H, m, 2×*Me*CH$_2$), 1.13–1.47 (9H, m, 2×C*H*$_2$C*H*$_2$Me and OH), 1.26 (3H, d, J=6.7 Hz, *Me*CH), 1.71 (1H, dd, J=14.7, 4.3 Hz, C*H*HCH), 1.92 (1H, dd, J=14.7, 8.6 Hz, C*H*HCH), 2.86–2.98 (1H, m, CH), 7.15–7.31 (5H, m, ArH); δ_C 14.55, 14.6 (2×*Me*CH$_2$), 16.75, 16.9 (2×*C*H$_2$Me), 25.15 (*Me*CH), 35.7 (CH), 41.8, 42.0, 47.1 (3×*C*H$_2$CO), 75.0 (CO), 125.05, 127.1 (2C), 128.6 (2C), 148.2 (ArC); *m*/*z* 216 (M^+-H_2O, 4%), 191 (11), 115 (27), 105 (100), 55 (17), 43 (15), 41 (13).

4.3.16. 4-(1-Methyl-2-phenylethyl)-4-heptanol (4ce). Colourless oil; R_f 0.39 (hexane/ethyl acetate: 4/1); t_r 11.5; ν (film) 3483 (OH), 3084, 3062, 3026, 1603, 1496 (HC═C), 1132 cm^{-1} (CO); δ_H 0.77 (3H, d, *J*=6.7 Hz, *Me*CH), 0.95 (6H, t, *J*=7.0 Hz, 2×*Me*CH$_2$), 1.34–1.60 (9H, m, 2×C*H*$_2$C*H*$_2$Me and OH), 1.79–1.90 (1H, m, CH), 2.18 (1H, t, *J*=13.1 Hz, C*H*HPh), 3.00 (1H, dd, *J*=13.1, 2.4 Hz, C*H*HPh), 7.15–7.29 (5H, m, ArH); δ_C 13.1 (*Me*CH), 14.75, 14.8 (2×*Me*CH$_2$), 16.4, 16.5 (2×*C*H$_2$Me), 37.15 (*C*H$_2$Ph), 38.75, 38.95, (2×*C*H$_2$CO), 42.35 (*C*HMe), 76.05 (CO), 125.6, 128.15 (2C), 129.1 (2C), 142.1 (ArC); *m*/*z* 216 (M^+-H_2O, 2%), 191 (12), 115 (100), 91 (77), 73 (17), 69 (23), 59 (12), 55 (61), 43 (34), 41 (30).

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