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New preparation of benzylic zinc reagents via a fragmentation reaction

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Dedicated to Professor Jean Normant for his 65th birthday

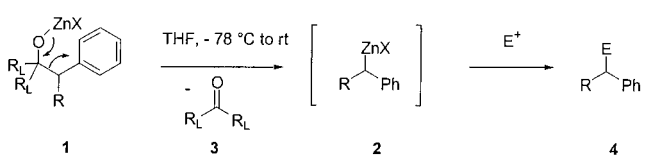
Abstract

The fragmentation of sterically hindered homobenzylic zinc alcoholates proceeds readily leading to benzylic zinc reagents free from any Wurtz-coupling product. Reaction of these organometallic intermediates with various aldehydes produces new homobenzylic alcohols in moderate to good yields. A 1,4-addition of these newly prepared benzylic organometallics to an alkylidenemalonate is also reported. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Zinc; Benzylic organometallics; Fragmentation; Addition to aldehydes

1. Introduction

Benzylic organometallics are important intermediates for preparing polyfunctional molecules of pharmaceutical interest [1]. Although several methods are available for the preparation of benzylic lithium and magnesium compounds [1b,2], these reactions are all complicated by the formation of homocoupling products. Benzylic zinc reagents prepared by the direct insertion of zinc dust are obtained in a more straightforward fashion and the formation of Wurtz-coupling products is minimized in many cases [3]. However, even for the preparation of benzylic zinc reagents starting from electron-rich benzylic halides, the formation of Wurtz-coupling is a serious side-reaction [4]. This is due to the radical nature of the reaction of a metal like magnesium or zinc with a benzylic halide. Recently, we have shown that sterically hindered homoallylic zinc alcoholates undergo a smooth fragmentation reaction providing highly substituted allylic zinc compounds with the absence of formation of any homocoupling product formation [5]. Herein, we wish to report a new preparation of benzylic zinc reagents, based on a similar fragmentation reaction of homobenzylic zinc alcoholates of type **1**. Because of the steric hindrance of the large substituent ($R_L = t$-Bu) a fragmentation reaction occurs leading to the benzylic zinc reagent **2** and to the unreactive sterically hindered ketone **3**. By generating the benzylic organometallic **2** in the presence of an electrophile, products of type **4** are obtained (Scheme 1).



Scheme 1.

2. Results and discussion

The required homobenzylic alcohols **5** were prepared easily starting from commercially available phenylacetyl chloride (**6**). First, reaction of the acid chloride **6** with t-BuCu·MgX_2 [6] provides the ketone **7** in 68% yield. Treatment of the ketone **7** with sodium hydride (room temperature (r.t.), 1 h) followed by the addition of an electrophile (methyl iodide, allyl bromide or 4-methoxybenzyl chloride) furnishes after a reaction time between 3 and 24 h the expected alkylated products **8a–c** in 61–91% yield (Scheme 2). The ketones **8a–c** were treated with t-BuLi at −78°C for 1 h in ether leading

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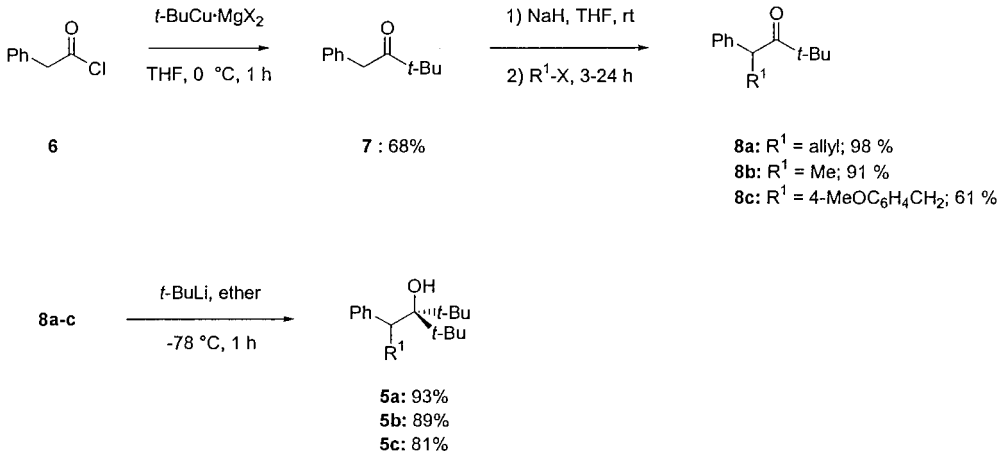


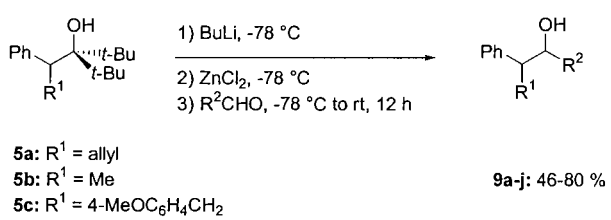
Scheme 2.

to the desired alcohols **5a**–**c** in 81–93% yield. These alcohols were treated at −78°C with *n*-BuLi (1.1 equiv) followed by the addition of a THF solution of zinc chloride (1.1 equiv) and subsequent addition of an aldehyde (1.1 equiv). The reaction mixture was allowed to reach r.t. within 12 h leading to the expected homobenzylic alcohols **9a**–**j** in 46–80% yield (Scheme 3 and Table 1). Aromatic aldehydes like benzaldehyde (entries 1, 7 and 10), 1-naphthaldehyde (entries 2 and 8) and furfural (entries 3 and 9) react rapidly leading to the alcohol **9** as a mixture of diastereoisomers.

The reaction proceeds also with α,β-unsaturated aldehydes such as *trans*-cinnamaldehyde (entry 4) and perillaldehyde (entry 5). Finally, an aliphatic aldehyde such as cyclohexanecarboxaldehyde gives also the expected alcohol **9f** in 60% yield (entry 6). The reaction can be extended to other electrophiles like alkylidenemalonates. Thus, by using diethyl benzylidenemalonate **10** and the alcohol **5a**, the Michael-adduct **11** is obtained as a mixture of diastereoisomers (*syn*/*anti* 40:60) in 60% yield (Scheme 4).

3. Conclusion

We have developed a new preparation of benzylic zinc reagents via the fragmentation of sterically hindered homobenzylic zinc alcoholates. This method completely avoids the formation of Wurtz-byproducts. The starting homobenzylic alcohols **5** required for the fragmentation are readily prepared making our method complementary to other known procedures.



Scheme 3.

4. Experimental

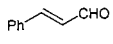
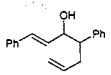
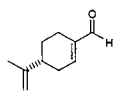
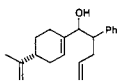
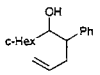
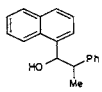
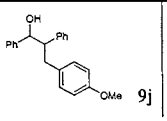
4.1. General considerations

All reactions were carried out under an argon atmosphere. THF was distilled from sodium/benzophenone. Zinc chloride was freshly dried before use for 2 h at 150°C and less than 0.1 mmHg. Reactions were monitored by gas chromatography (GC) analysis of reaction aliquots. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel 60 (70–230 mesh). NMR spectra were recorded on a 300 MHz NMR spectrometer. The ionization method used was electron impact ionization (EI, 70 eV). Elemental analyses were performed by the Microanalytical Service Laboratory of Universität München.

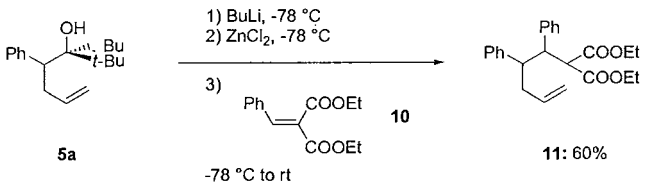
4.2. Preparation of 3,3-dimethyl-1-phenyl-butan-2-one (7) [7]

A solution of *tert*-butylmagnesium chloride (0.11 mol) in THF (1.7 M, 65 ml) was added dropwise over 1 h at 0°C to a stirred suspension of copper(I) bromide (14.3 g, 0.10 mol) in THF (30 ml) containing phenylacetyl chloride (15.5 g, 0.10 mol). After complete addition the black reaction mixture was stirred at r.t. for 1 h and poured into ice (200 ml). The mixture was then filtered over celite and acidified with HCl 1 N. The yellow solution was extracted with ether (3 ×), and the combined organic layer was washed with water (2 ×)

Table 1
Homobenzylic alcohols **9a–j** prepared by the fragmentation of zinc alcoholates obtained from the corresponding homobenzylic alcohols **5a–c** in the presence of an aldehyde[a]

Entry	Alcohol of type **5**	Aldehyde	Product of type **9**	Diastereomeric ratio syn:anti	Yield (%)[a]
1	**5a**	PhCHO	 **9a**	48:52	74
2	**5a**		 **9b**	48:52	63
3	**5a**		 **9c**	32:68	73
4	**5a**		 **9d**	45:55	46
5	**5a**		 **9e**	40:60	70
6	**5a**	c-HexCHO	 **9f**	45:55	60
7	**5b**	PhCHO	 **9g**	43:57	73
8	**5b**		 **9h**	36:64	80
9	**5b**		 **9i**	40:60	66
10	**5c**	PhCHO	 **9j**	42:58	73

[a] Isolated yields of analytically pure products.



Scheme 4.

and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was distilled under vacuum to give the ketone **7** (11.9 g, 68% yield) as a light yellow oil (bp: 115°C, 1 mmHg).

IR (film, cm^{-1}): *v* 2967, 1711, 1477, 1060, 724, 696. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.24–7.08 (m, 5H), 3.71 (s, 2H), 1.11 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 212.8, 135.1, 129.7, 128.5. *m/z* (EI) 176.1199 ([M^+], 12%, $C_{12}H_{16}O$ requires 176.1197), 91 (48), 85 (62), 57 (100).

*4.3. Preparation of 2,2-dimethyl-4-phenylhept-6-en-3-one (**8a**) [8]*

A solution of *tert*-butyl benzyl ketone (6.3g, 35.7 mmol) and allyl bromide (3.7 ml, 42.7 mmol) in THF (10 ml) was added at r.t. to a suspension of sodium

hydride (2.68 g, 67 mmol, 60% in oil) in THF (40 ml). The reaction mixture was stirred for 3 h and a saturated aqueous solution of NH_4Cl was added carefully at 0°C. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with water and brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 9:1) to afford the desired product **8a** as a colourless oil (7.55 g, 98% yield).

IR (film, cm^{-1}): *v* 2967, 1702, 1477, 1073, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.24–7.10 (m, 5H), 5.61–5.47 (m, 1H), 4.96–4.84 (m, 2H), 4.08–4.04 (m, 1H), 2.68–2.58 (m, 1H), 2.38–2.28 (m, 1H), 0.99 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 214.9, 139.6, 136.4, 129.0, 128.6, 127.3, 117.1, 53.3, 45.4, 40.2, 26.9. *m*/*z* (EI) 216 (1), 159 (17), 131 (84), 115 (19), 103 (8), 91 (52), 85 (45), 77 (11), 57 (100). Anal. Calc. for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.16; H, 9.43.

4.4. Preparation of 2,2-dimethyl-4-phenylpentan-3-one (**8b**) [9]

A solution of *tert*-butyl benzyl ketone (1 g, 5.7 mmol) and methyl iodide (0.78 ml, 12 mmol) in THF (5 ml) was added at r.t. to a suspension of sodium hydride (0.48 g, 12 mmol, 60% in oil) in THF (5 ml). The reaction mixture was stirred for 3 h and a saturated aqueous solution of NH_4Cl was carefully added at 0°C. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with water and brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 125:1) to afford the desired product **8b** as a light yellow oil (0.98 g, 91% yield).

IR (film, cm^{-1}): *v* 2969, 1703, 1477, 1367, 1063, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.21–7.17 (m, 5H), 4.18 (q, 1H, $J = 6.9$ Hz), 1.02 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 216.1, 141.6, 128.7, 128.0, 126.9, 46.5, 45.3, 26.7, 21.2. *m*/*z* (EI) 190 (14), 105 (93), 85 (69), 77 (35), 57 (100). Anal. Calc. for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.76; H, 9.63.

4.5. Preparation of 1-(4-methoxyphenyl)-4,4-dimethyl-2-phenylpentan-3-one (**8c**)

A solution of *tert*-butyl benzyl ketone (2 g, 11.4 mmol) and 4-methoxybenzyl chloride (1.7 ml, 12.5 mmol) in THF (10 ml) was added at r.t. to a suspension of sodium hydride (0.5 g, 12.5 mmol, 60% in oil) in THF (10 ml). The reaction mixture was stirred for 24 h and a saturated aqueous solution of NH_4Cl was added carefully at 0°C. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 98.5:1.5) to afford the desired product **8c** (2.03 g, 61% yield) as an orange solid (mp: 63°C).

IR (film, cm^{-1}): *v* 2970, 1694, 1454, 1176, 1036, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.39 (d, 2H, $J = 8.0$ Hz), 7.25–7.05 (m, 3H), 6.96 (d, 2H, $J = 8.4$ Hz), 3.91 (m, 1H), 3.67 (s, 3H), 3.59 (m, 2H), 1.35 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 212.8, 156.2, 137.6, 130.1, 128.3, 126.7, 126.4, 125.0, 111.7, 53.7, 53.3, 43.2, 39.2, 24.3. *m*/*z* (EI) 296.1771 ([M^+], 9%, $C_{20}H_{24}O_2$ requires 296.1776), 211 (27), 121 (100).

4.6. Preparation of 3-tert-butyl-2,2-dimethyl-4-phenylhept-6-en-3-ol (**5a**)

A solution of *tert*-butyllithium (30 ml, 18.3 mmol, 1.64 M in pentane) was added at −78°C to a solution of the ketone **8a** (5 g, 23.1 mmol) in ether (35 ml). The reaction mixture was stirred at this temperature for 1 h and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 9:1) to afford a colourless oil (5.9 g, 93% yield).

IR (film, cm^{-1}): *v* 3592, 2963, 1491, 1393, 994, 911, 705. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.33–7.08 (m, 5H), 5.49–5.37 (m, 1H), 4.90 (d, 1H, $J = 17.0$ Hz), 4.83 (d, 1H, $J = 14$ Hz), 3.42 (d, 1H, $J = 7.4$ Hz), 3.10–2.87 (m,2H), 1.21 (s, 9H), 1.07 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 140.0, 138.4, 132.5, 127.8, 126.7, 115.6, 81.9, 52.4, 44.2, 44.0, 35.6, 31.1, 30.0. *m*/*z* (EI) 217 (5), 161 (2), 143 (21), 131 (39), 87 (54), 57 (100). Anal. Calc. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.28; H, 11.21.

4.7. Preparation of 2,2,4,4-tetramethyl-3-(1-phenylethyl)-pentan-3-ol (**5b**)

A solution of *tert*-butyllithium (2.7 ml, 3.3 mmol, 1.2 M in pentane) was added at −78°C to a solution of the ketone **8b** (0.3 g, 1.6 mmol) in ether (2.5 ml). The reaction mixture was stirred at this temperature for 45 min and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 99:1) to afford a colourless oil (0.34 g, 89% yield).

IR (film, cm^{-1}): *v* 3595, 2963, 1393, 988. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.37–7.33 (m, 2H), 7.20–7.10 (m, 3H), 3.55 (q, 1H, $J = 7.4$ Hz), 1.65 (d, 3H, $J = 7.4$ Hz), 1.20 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 144.0,

131.6, 127.8, 126.5, 81.9, 45.7, 44.3, 43.8, 30.8, 30.4, 27.0, 19.6. *m/z* (EI) 191 (2), 143 (13), 105 (72), 87 (49), 57 (100). Anal. Calc. for $C_{17}H_{28}O$: C, 82.20; H, 11.36. Found: C, 81.94; H, 11.42.

4.8. Preparation of 1-(4-methoxyphenyl)-4,4-dimethyl-3-(2-methyl-2-propyl)-2-phenylpentan-3-one (**5c**)

A solution of *tert*-butyllithium (8.4 ml, 12.3 mmol, 1.46 M in pentane) was added at −78°C to a suspension of **8c** (1.82 g, 6.15 mmol) in ether (40 ml). The reaction mixture was slowly warmed to r.t. over 4 h and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 98:2) to afford a colourless oil (1.75 g, 81% yield).

IR (film, cm^{-1}): *v* 3586, 2922, 1512, 1246, 1179, 1038, 704. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.39 (d, 2H, $J = 8.0$ Hz), 7.25–7.05 (m, 3H), 6.96 (d, 2H, $J = 8.4$ Hz), 3.91 (m, 1H), 3.67 (s, 3H), 3.59 (m, 2H), 1.35 (s, 9H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 157.9, 140.1, 133.8, 132,8, 129.6, 127.8, 126.7, 113.9, 82.3, 55.4, 53.8, 44.4, 44.3, 36.1, 31.4, 30.5. *m/z* (EI) 331 (3), 301 (5), 211 (15), 143 (21), 121 (100), 87 (46), 57 (50). Anal. Calc. for $C_{24}H_{34}O_2$: C, 81.31; H, 9.66. Found: C, 81.25; H, 9.64.

4.9. Preparation of 1,2-diphenylpent-4-en-1-ol (**9a**)

A solution of *n*-butyllithium (0.53 ml, 0.84 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5a** (0.27 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (115 mg, 0.84 mmol) in THF (2 ml) was added, followed by benzaldehyde (68 μl, 672 μmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 92:8) to afford a colourless oil (118 mg, 74% yield).

IR (film, cm^{-1}): *v* 3436, 1680, 1494, 698. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.33–7.05 (m, 10H), 5.72–5.41 (m, 1H), 4.99–4.77 (m, 3H), 3.13–2.95 (m, 1H), 2.75–2.58 (m, 1H), 2.35–2.18 (m, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 143.0, 142.9, 141.3, 140.8, 137.3, 136.6, 130.6, 129.4, 129.3, 128.9, 128.7, 128.5, 128.4, 128.2, 127.7, 127.4, 127.3, 126.9, 126.2, 116.7, 116.5, 78.5, 78.3, 54.4, 53.7, 36.8, 34.8. *m/z* (EI) 220.1247 ([M–H_2O], 3%, $C_{17}H_{16}$ requires 220.1252), 178 (5), 132 (62), 107 (100), 91 (55).

4.10. Preparation of 1-(2-naphthyl)-2-phenylpent-4-en-1-ol (**9b**)

A solution of *n*-butyllithium (0.57 ml, 0.84 mmol, 1.47 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5a** (0.3 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (115 mg, 0.84 mmol) in THF (2 ml) was added, followed by 1-naphthaldehyde (0.118 ml, 0.87 mmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 9:1) to afford a light yellow oil (158 mg, 63% yield).

IR (film, cm^{-1}): *v* 3436, 1678, 1494, 699. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.95–6.97 (m, 12H), 5.44–5.36 (m, 2H), 4.78–4.64 (m, 2H), 3.34–3.31 (m, 1H), 3.19-3.16 (m, 2H), 2.70–2.25 (m, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 141.2, 137.3, 135.9, 132.7, 129.3, 128.1, 127.9, 127.5, 127.3, 127.1, 127.0, 126.8, 125.8, 125.5, 124.9, 124.4, 124.3, 124.0, 123.8, 123.4, 123.3, 122.2, 122.1, 115.5, 114.9, 73.9, 72.7, 52.7, 51.6, 35.7, 31.8. *m/z* (EI) 288 (5), 270 (7), 229 (8), 158 (29), 129 (100). Anal. Calc. for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.35; H, 6.68.

4.11. Preparation of 1-(2-furyl)-2-phenylpent-4-en-1-ol (**9c**)

A solution of *n*-butyllithium (2.5 ml, 4.3 mmol, 1.7 M in pentane) was added at −78°C to a solution of the tertiary alcohol **5a** (1.3 g, 4.7 mmol) in THF (5 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (600 mg, 4.4 mmol) in THF (5 ml) was added, followed by furfural (0.3 ml, 3.6 mmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 9:1) to afford a colourless oil (600 mg, 73% yield).

IR (film, cm^{-1}): *v* 3398, 1668, 1475, 703. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.30–7.01 (m, 6H), 6.22 (d, $J = 3.1$ Hz, 1H), 6.11 (d, $J = 3.4$ Hz, 1H), 5.70–5.30 (m, 1H), 4.85–4.72 (m, 3H), 3.15–3.08 (m, 1H), 2.60–2.40 (m, 1H), 2.97–2.24 (m, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 155.5, 142.3, 141.9, 141.1, 140.6, 137.0, 136.3, 129.2, 129, 128.9, 128.5, 127.5, 127.0, 126.2, 116.8, 116.7, 110.5, 107.9, 107.3, 72.3, 71.6, 66.2, 51.6, 51.4, 36.8, 35.5, 15.6. *m/z* (EI) 228 (6), 210 (6), 170 (4),

141 (8), 132 (100), 115 (32), 104 (12). Anal. Calc. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.82; H, 6.99.

4.12. Preparation of (1E)-1,4-diphenylhepta-1,6-dien-3-ol (9d)

A solution of *n*-butyllithium (0.53 ml, 0.84 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5a** (0.30 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (115 mg, 0.84 mmol) in THF (2 ml) was added, followed by 3-phenyl-2-propenal (85 μl, 672 μmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 88:12) to afford a colourless oil (80 mg, 46% yield).

IR (film, cm^{-1}): *v* 3027, 1640, 1494, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): *δ* 7.36–7.20 (m, 10H), 6.51 and 6.57 (2d, *J* = 21.0 Hz, 1H), 6.15 and 6.08 (2dd, *J* = 21.0, 6.6 Hz, 1H), 5.78–5.55 (m, 1H), 5.06–4.85 (m, 2H), 4.52–4.40 (m, 1H), 3.02–2.83 (m, 1H), 2.73–2.38 (m, 2H). ^{13}C-NMR ($CDCl_3$, 75 MHz): *δ* 141.0, 140.8, 137.2, 137.1, 136.8, 134.9, 132.4, 131.4, 130.8, 130.5, 129.4, 129.0, 128.8, 128.7, 128.2, 128.0, 127.4, 127.2, 127.0, 126.9, 126.2, 125.9, 116.8, 116.7, 76.5, 76.3, 52.8, 52.4, 36.6, 35.6. *m/z* (EI) 246.1402 ([M − H_2O], 0.7%, $C_{19}H_{18}$ requires 246.1409), 205 (2), 133 (100), 115 (23), 91 (32), 77 (14).

4.13. Preparation of 1-(4-isopropenylcyclohex-1-en-1-yl)-2-phenylpent-4-en-1-ol (9e)

A solution of *n*-butyllithium (3.5 ml, 4.9 mmol, 1.4 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5a** (1.3 g, 4.6 mmol) in THF (5 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (690 mg, 5 mmol) in THF (5 ml) was added, followed by L-perillaldehyde (0.26 ml, 1.7 mmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 95:5) to afford an oil (340 mg, 70% yield).

IR (film, cm^{-1}): *v* 3435, 2921, 1642, 1453, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): *δ* 7.26–7.06 (m, 5H), 5.70–5.46 (m, 2H), 4.87–4.56 (m, 4H), 4.06–4.02 (m, 1H), 2.80–1.97 (m, 7H), 1.68 (s, 3H), 1.60 (s, 3H), 1.44 (s, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): *δ* 150.2, 149.9, 142.3, 141.3, 138.5, 138.0, 137.6, 136.9, 136.8, 129.2, 128.5, 127.3, 126.2, 116.4, 109.1, 80.5, 50.2, 41.4, 37.3, 31.1, 27.9, 25.4, 24.8, 23.9, 21.3, 21.1. *m/z* (EI) 282 (1), 241 (37), 223 (12), 157 (16), 131 (45), 117 (19), 91 (100). Anal. Calc. for $C_{20}H_{26}O$: C, 85.09; H, 9.28. Found: C, 84.84; H, 9.82.

4.14. Preparation of 1-cyclohexyl-2-phenylpent-4-en-1-ol (9f)

A solution of *n*-butyllithium (3.2 ml, 5.1 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5a** (1.5 g, 5.4 mmol) in THF (5 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (700 mg, 5.1 mmol) in THF (5 ml) was added, followed by cyclohexanecarboxaldehyde (0.49 ml, 4.1 mmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 95:5) to afford a light yellow oil (600 mg, 60% yield).

IR (film, cm^{-1}): *v* 3400, 2913, 1640, 701. ^{1}H-NMR ($CDCl_3$, 300 MHz): *δ* 7.23–7.06 (m, 5H), 5.52 (m, 1H), 4.94–4.80 (m, 2H), 3.42–3.38 (m, 1H), 2.3–2.40 (m, 2H), 1.64–0.97 (m, 11H). ^{13}C-NMR ($CDCl_3$, 75 MHz): *δ* 143.1, 141.6, 137.7, 137.3, 129.5, 128.8, 127.0, 126.7, 116.5, 116.2, 80.4, 78.6, 66.2, 49.1, 48.2, 40.9, 40.4, 37.7, 35.5, 30.8, 30.6, 27.9, 27.0, 26.9, 26.7, 26.6, 26.4, 15.7. *m/z* (EI) 226 (4), 185 (4), 132 (100), 117 (37), 91 (74). Anal. Calc. for $C_{17}H_{24}O$: C, 83.55; H, 9.89. Found: C, 83.53; H, 9.99.

4.15. Preparation of 1,2-diphenylpropan-1-ol (9g) [10]

A solution of *n*-butyllithium (0.6 ml, 0.91 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5b** (0.25 g, 1 mmol) in THF (2 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (115 mg, 0.84 mmol) in THF (1 ml) was added, followed by benzaldehyde (68 μL, 670 μmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 88:12) to afford a colourless oil (104 mg, 73% yield).

IR (film, cm^{-1}): *v* 3436, 2259, 1681, 1494, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): *δ* 7.30–7.05 (m, 10H),

4.73 (d, $J = 6.0$ Hz, 1H), 2.97 (m, 1H), 1.22 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 7.0$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 143.7, 143.6, 143.1, 142.7, 128.8, 128.4, 128.2, 128.1, 128.0, 127.4, 127.2, 127.1, 126.6, 126.5, 79.9, 78.9, 48.3, 47.4, 18.5, 15.1. m/z (EI) 107 (100), 106 (81), 105 (38), 91 (45), 79 (54). Anal. Calc. for $C_{15}H_{16}O$: C, 84.87, H, 7.60. Found C, 84.67, H, 7.65.

4.16. Preparation of 1-(2-naphthyl)-2-phenylpropan-1-ol (9h)

A solution of *n*-butyllithium (0.53 ml, 0.84 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5b** (0.30 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (124 mg, 0.91 mmol) in THF (2 ml) was added, followed by 1-naphthaldehyde (90 μl, 670 μmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 92:8) to afford a light yellow oil (140 mg, 80% yield).

IR (film, cm^{-1}): ν 3428, 2919, 1678, 1489, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.03–7.12 (m, 12H), 5.55 (d, $J = 5.7$ Hz, 1H), 5.45 (d, $J = 8.7$ Hz, 1H), 3.30 (m, 2H), 1.85 (s, 2H), 1.16 (d, $J = 7.1$ Hz, 3H), 1.12 (d, $J = 7.1$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 143.7, 137.4, 132.7, 129.2, 128.0, 127.5, 126.7, 125.5, 124.9, 124.3, 124. 2, 123.0, 122.0, 75.6, 73.9, 44.1, 43.8, 12.6, 11.5. m/z (EI) 262 (4), 233 (7), 158 (45), 128 (100), 105 (23). Anal. Calc. for $C_{19}H_{18}O$: C, 86.99; H, 6.91. Found: C, 86.78; H, 7.17.

4.17. Preparation of 1-(2-furyl)-2-phenylpropan-1-ol (9i) [11]

A solution of *n*-butyllithium (0.7 ml, 1.1 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5b** (0.30 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (180 mg, 1.3 mmol) in THF (3 ml) was added, followed by furfural (75 μl, 0.9 mmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 9:1) to afford a red oil (120 mg, 66% yield).

IR (film, cm^{-1}): ν 3400, 2963, 1675, 1478, 711. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.32–7.06 (m, 6H), 6.18–6.14 (dt, $J = 3.1$ and 0.8 Hz, 1H), 5.96 (dd, $J = 3.1$ and 2.6, 1H), 4.15 (d, $J = 4.8$, 1H), 3.18 (q, $J = 4.8$ Hz, 1H), 1.9 (bs, 1H), 1.29 (d, $J = 13.1$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 155.8, 155.4, 147.7, 143.6, 143.2, 142.4, 141.9, 129.1, 128.7, 128.3, 128.8, 127.4, 126.9, 110.6, 110.5, 107.9, 107.0, 77.9, 77.4, 77.0, 73.3, 73.2, 46.0, 45.3, 18.5, 16.4. m/z (EI) 202 (3), 185 (2), 105 (21), 97 (100), 91 (25), 77 (19). Anal. Calc. for $C_{13}H_{14}O_2$: C, 77.72; H, 6.97. Found: C, 77.67; H, 7.10.

4.18. Preparation of 3-(4-methoxyphenyl)-1,2-diphenylpropan-1-ol (9j)

A solution of *n*-butyllithium (0.54 ml, 0.87 mmol, 1.6 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5c** (0.40 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 15 min and a solution of zinc chloride (120 mg, 0.87 mmol) in THF (2 ml) was added, followed by benzaldehyde (71 μl, 695 μmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chromatography (eluent: pentane/ether 8:2) to afford a light yellow oil (160 mg, 73% yield).

IR (film, cm^{-1}): ν 3446, 3029, 1611, 1512, 1494, 1453, 701. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.29–6.99 (m, 10H), 6.86 (d, $J = 8.7$ Hz, 1H), 6.79 (d, $J = 8.7$ Hz), 6.65 (d, $J = 8.7$ Hz), 4.91–4.82 (m, 1H), 3.67 (s, 3H), 3.28–2.72 (m, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 158.1, 143.2 141.4, 140.7, 132.8, 130.8, 130.4, 130.2, 129.5, 129.4, 128.9, 128.7, 128.4, 128.1, 127.7, 127.2, 127.0, 126.8, 113.9, 78.3, 77.6, 56.8, 55.9, 55.5, 38.2, 36.0. m/z (EI) 318 (1), 212 (50), 121 (100), 107 (46), 91 (10), 77 (26). Anal. Calc. for $C_{22}H_{14}O_2$: C, 77.72; H, 6.97. Found: C, 77.67; H, 7.10.

4.19. Preparation of 2-(1,2-diphenyl)-4-pentenyl]-malonic acid diethyl ester (11)

A solution of *n*-butyllithium (0.54 ml, 0.84 mmol, 1.56 M in hexane) was added at −78°C to a solution of the tertiary alcohol **5a** (0.30 g, 1.1 mmol) in THF (3 ml). The reaction mixture was stirred at this temperature for 30 min and a solution of zinc chloride (115 mg, 0.84 mmol) in THF (2 ml) was added, followed by diethyl benzylidenemalonate **10** (169 mg, 0.672 mmol). The reaction was slowly warmed to r.t. overnight and quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with ether (3 ×). The combined organic layer was washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil was purified by flash chro-

matography (eluent: pentane/ether 85:15) to afford a colourless oil (150 mg, 60% yield).

IR (film, cm^{-1}): ν 2964, 1690, 1462, 736, 698. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.32–6-98 (m, 10H), 5.70–5.51 and 5.42–5.25 (dm, 1H), 5.03–4.85 (m, 1H), 4.77–4.62 (m, 1H), 4.34–4-20 (m, 2H), 3.86–3.60 (m, 5H), 3.19–3.01 (m, 1H), 2.48–2.05 (m, 2H), 1.28, 1.03, 0.85, 0.72 (4t, $J = 7.2$ Hz, 6H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 168.9, 168.2, 168.0, 167.0, 142.5, 141.9, 139.9, 139.2, 137.1, 136.8, 130.6, 130.2, 130.0, 129.8, 129.5, 128.9, 128.6, 128.3, 128.0, 127.6, 127.4, 117.1, 116.4, 62.1, 61.7, 61.5, 61.4, 56.5, 56.2, 51.6, 49.6, 49.2, 47.3, 38.0, 37.2, 15.6, 14.6, 14.4, 14.0, 13.9. m/z (EI) 339 (3), 250 (25), 220 (29), 176 (20), 131 (100), 115 (12), 91 (26), 77 (9). Anal. Calc. for $C_{24}H_{28}O_4$: C, 75.76, H, 7.42. Found C, 75.80, H, 7.39.

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