A 1,3-sp^2,sp^3-hybridized dilithio intermediate by direct lithiation of cyclopropylidene diphenylmethane

Victor J. Lillo, Cecília Gómez and Miguel Yus*

Departamento de Química Orgánica, Facultad de Ciencias and Instituto de Síntesis Orgánica (ISO), Universidad de Alicante, Apartado 99, E-03080 Alicante, Spain
E-mail: yus@ua.es

This paper is dedicated to Professor Benito Alcaide on occasion of his 60th birthday

Abstract

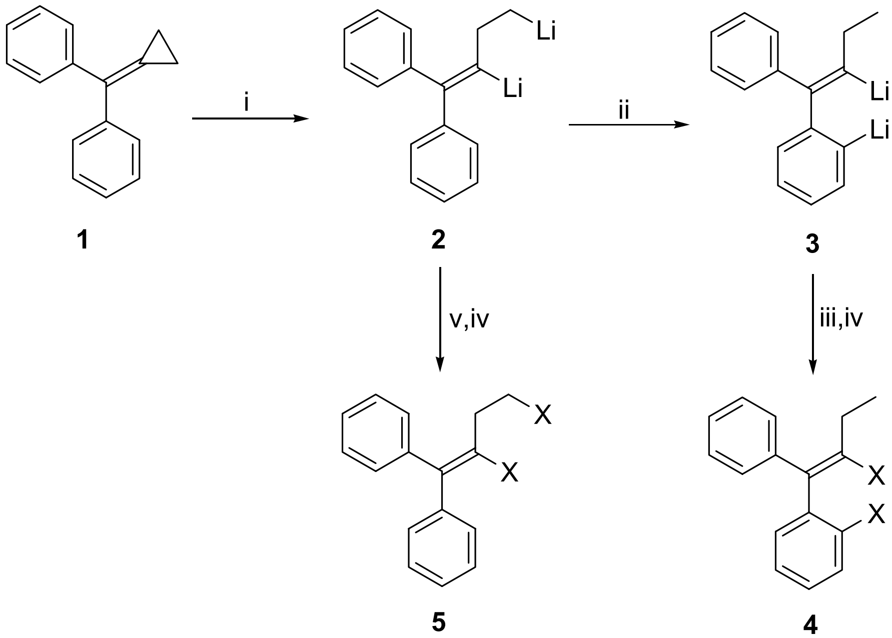
The reaction of cyclopropylidene diphenylmethane **1** with an excess of lithium and a catalytic amount of naphthalene (5 mol %) at -20 ºC, followed by addition of an electrophile [E = H_2O, D_2O, *t*-BuCHO, Me_2CO, Et_2CO, *n*-Pr_2CO, *i*-Pr_2CO, (*c*-$C_3H_5)_2CO$, $(CH_2)_5CO$] at -78 ºC and final hydrolysis with water at -78 ºC to rt gives the corresponding products **5**, which in some case are contaminated with the corresponding by-products **6**, resulting from the incorporation of only one electrophilic moiety at the intermediate dianion of type **2**. The separation of both reaction products is easy by simple column chromatography.

Keywords: Lithium, naphthalene, alkylidene cyclopropane, ring opening, electrophilic substitution, diols

Introduction

Dilithium synthons are interesting intermediates in synthetic organic chemistry because by reaction with electrophiles they are able to introduce two electrophilic fragments in only one synthetic step, thus giving directly polyfunctionalized molecules.[1] The main problem when one wants to generate these intermediates by standard methods (including deprotonation, halogen-lithium exchange or transmetallation methodologies)[2] is that they are usually very unstable and tend to decompose through (a) elimination reactions, (b) hydrogen abstractions from the reaction medium, and (c) rearrangement processes.[1] In the last few years we have been applying the arene-catalyzed lithiation technology[3-5] for the addition of activated lithium to carbon-carbon double bond containing compounds[6] or cyclopropyl derivatives[7] in order to generate directly dilithium species that react with electrophiles to afford polyfunctionalized molecules, this procedure being of great interest from an atom-economy point of view.[8] Namely, the lithiation of cyclopropylidene diphenylmethane (**1**) with lithium in ether was studied years ago by

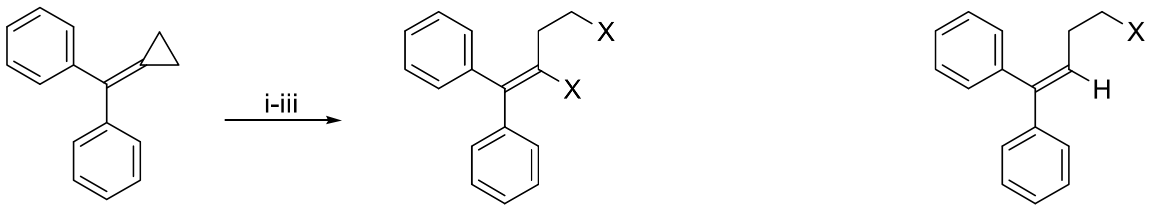
Maercker et al[9] who found that after obtaining of the expected dilithium intermediate **2** at -20 ºC it is converted at room temperature into the undesired new *ortho*-lithiated species **3**, which reacted with different electrophiles to give the final products **4**. Actually, only the hydrolysis and the reaction of intermediate **2** with dimethyl sulphate were described to give compounds **5**. In this paper we report the application of the above mentioned methodology (the arene-catalyzed lithiation) to lithiate the starting material **1** under very mild reaction conditions for the generation of the sp^2,sp^3-hybridized dilithium synthon **2**[10-12] as the only intermediate and its reaction with different electrophiles to give different functionalized products of type **5** (Scheme 1).



Scheme 1. Reagents and conditions: (i) Li, ether, -20 ºC; (ii) rt; (iii) E = H_2O, D_2O, Me_2SO_4, $RMeSiCl_2$, CO_2; (iv) H_2O; (v) E = H_2O, Me_2SO_4.

Results and Discussion

The reaction of cyclopropane **1** [prepared from benzophenone and 3-(bromopropyl)triphenylphosphonium bromide through a Wittig reaction][13] with an excess of lithium powder (1:7 molar ratio) and a catalytic amount of naphthalene (5 mol %) in ether at -20 ºC for 5 h, followed by addition of different electrophiles [E = H_2O, D_2O, *t*-BuCHO, Me_2CO, Et_2CO, *n*-Pr_2CO, *i*-Pr_2CO, (*c*-C_3H_5)$_2$CO, $(CH_2)_5CO$] at -78 ºC and final hydrolysis with water, allowing the reaction to reach the ambient temperature, gave the corresponding products **5** as the main compounds (Scheme 2 and Table 1). In the case of using enolizable ketones (except for dicyclopropyl ketone), variable amounts (<31%; Table 1, entries 4-7 and 9, and footnote b) of the corresponding mono-reduced compounds of type **6** were also obtained, the separation of both products being easy by column chromatography. This product **6** is produced by partial proton abstraction of intermediate **2** from the reaction medium.[14]



1 **5** **6**

a = H
b = D
c = *t*-BuCHOH
d = Me_2COH
e = Et_2COH
f = *n*-Pr_2COH
g = *i*-Pr_2COH
h = (*c*-$C_3H_5)_2COH$
i = $(CH_2)_5COH$

Scheme 2. Reagents and conditions: (i) Li, $C_{10}H_8$ cat. (5 mol %), ether, -20 ºC; (ii) E = H_2O, D_2O, *t*-BuCHO, Me_2CO, Et_2CO, *n*-Pr_2CO, *i*-Pr_2CO, (*c*-$C_3H_5)_2CO$, $(CH_2)_5CO$, -78 ºC; (iii) H_2O, -78 to 20 ºC.

Table 1. Lithiation of compound **1** and reaction with electrophiles. Preparation of products **5**

	Electrophile	Product[a]		
Entry	E	No.	X	Yield (%)[b]
1	H_2O	**5a**	H	70
2	D_2O	**5b**	D	68[c]
3	*t*-BuCHO	**5c**	*t*-BuCHOH	56[d,e]
4	Me_2CO	**5d**	Me_2COH	41 [20]
5	Et_2CO	**5e**	Et_2COH	33 [30]
6	*n*-Pr_2CO	**5f**	*n*-Pr_2COH	39 [29]
7	*i*-Pr_2CO	**5g**	*i*-Pr_2COH	26 [31][f]
8	(*c*-$C_3H_5)_2CO$	**5h**	(*c*-$C_3H_5)_2COH$	55[d]
9	$(CH_2)_5CO$	**5i**	$(CH_2)_5COH$	39 [27]

[a] All products **5** (and **6**) were >95% pure by 300 MHz ^1H NMR and/or GLC.

[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**. In brackets isolated yield of the corresponding product **6**.

[c] 85% deuterium content from 300 MHz ^1H NMR.

[d] <10% of the alcohol resulting from the reduction of the carbonyl compound used as electrophile was detected by GLC/MS and not isolated.

[e] A *ca.* 1:1 mixture of diastereomers (GLC) were obtained and separated by column chromatography (silica gel, hexane/ethyl acetate).

[f] Compounds **5g** and **6g** could not be separated by column chromatography.

The structure of compounds **5** was unequivocally assigned not only through their analytical and spectroscopic data but also thanks to the X-ray structure determination for compound **5d** (see Experimental Part and Figure 1).

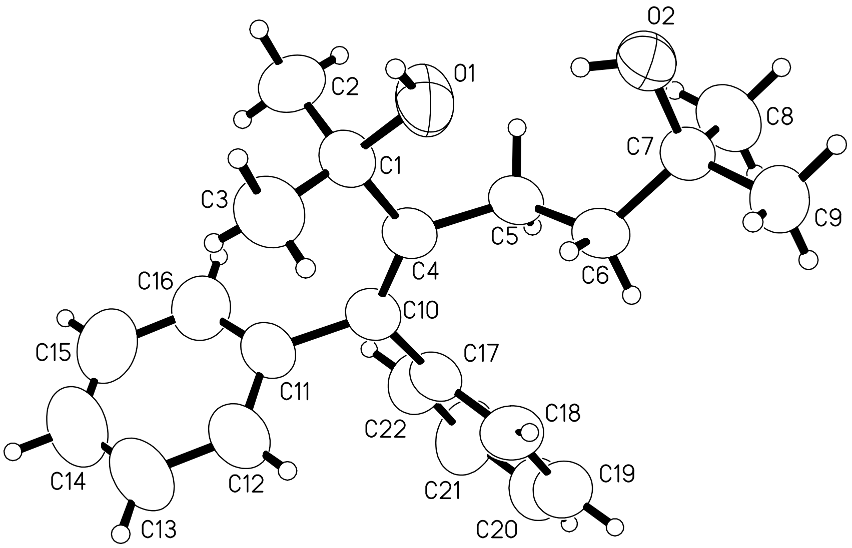
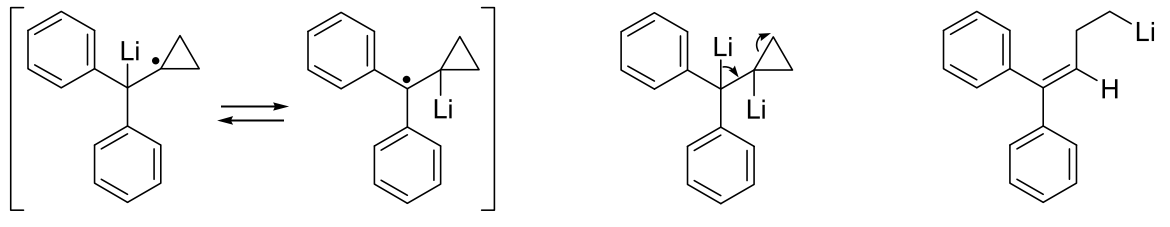


Figure 1. X-ray structure of compound **5d**.

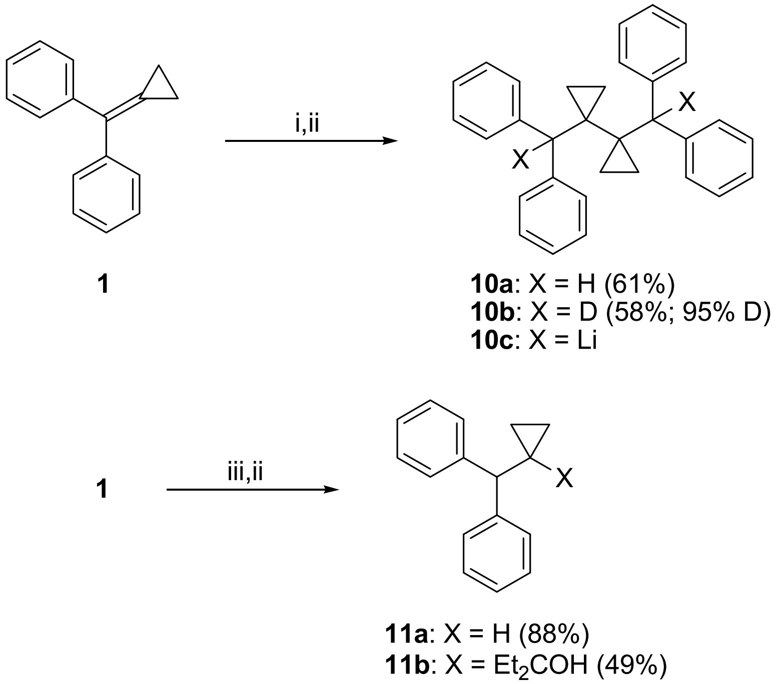
Concerning the possible mechanism for the reaction shown in Scheme 2, after one electron transfer from the lithiating mixture[4] a lithium radical-anion of type **7** is generated that can get a second electron to give the dilithium dianion **8**, which upon rearrangement suffers ring opening to yield the more stable dilithium intermediate **2** able to react with two molecules of the electrophile to yield, after final hydrolysis, compounds **5**. Depending on its stability it can abstract a proton from the reaction medium to yield the monolithiated species **9**, precursor of by-products **6** (Chart 1).



7a **7b** **8** **9**

Chart 1. Intermediates **7-9**.

Some light to the proposed mechanism was brought in the 4,4'-di-*tert*-butylbiphenyl (DTBB)-catalyzed lithiation of the starting material **1** in THF at -78 ºC for 1 h: after hydrolysis with water or deuterium oxide, the dimeric products **10a,b** were isolated, the saturated cyclopropyl derivative **11a** being the other detected (<10%; GLC-MS) by-product (Scheme 3). On the other hand, performing the same reaction but under Barbier type conditions (in the presence of the electrophile: E = $PhNH_2$, Et_2CO),[15] the monosubstituted species **11** were isolated (Scheme 3). It seems that the initially formed radical anion of type **7a** can dimerize to give a dilithioderivative of type **10c**, the precursor of compounds **10a,b**, after final quenching with the electrophile. Under Barbier conditions either the intermediate **7b** reacts with the electrophile present in the reaction medium (before being converted in the anion and final abstraction of a proton) or probably via a sequential process takes two protons (through intermediates **7** or **8**) to yield compound **11a**.



1

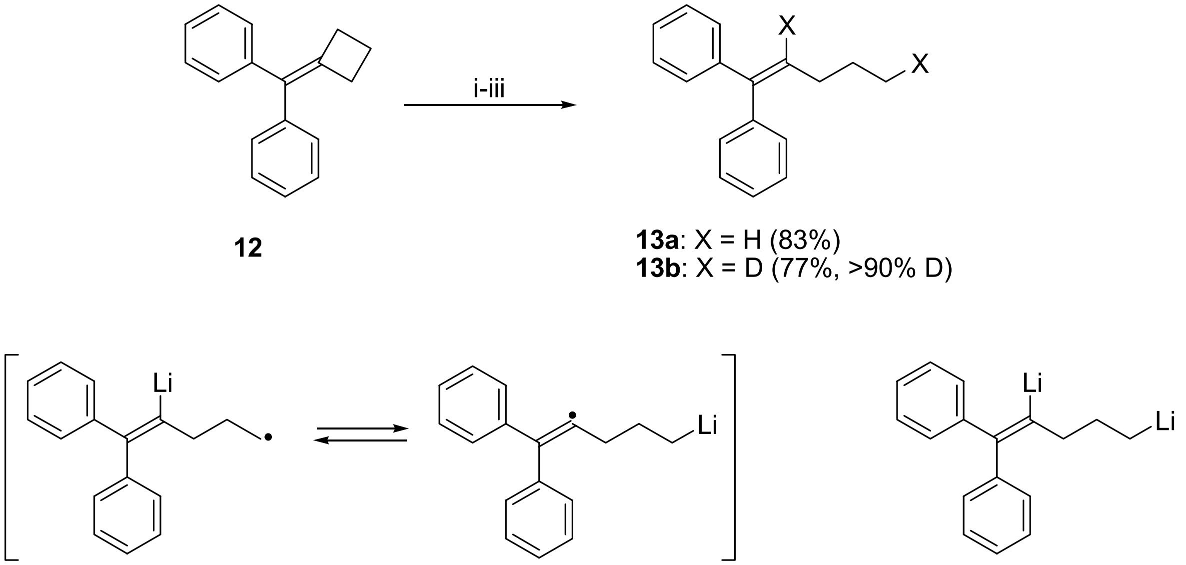
10a: X = H (61%)
10b: X = D (58%; 95% D)
10c: X = Li

1

11a: X = H (88%)
11b: X = Et_2COH (49%)

Scheme 3. Reagents and conditions: (i) Li, DTBB cat. (5 mol %), THF, -78 ºC, 2 h; (ii) H_2O, -78 ºC to rt, 1 h; (iii) Li, DTBB cat. (5 mol %), Electrophile [E = $PhNH_2$ (for **11a**), Et_2CO (for **11b**)], -78 to -50 ºC, 2 h (slow addition).

In the final part of this study we tried to extend the chemistry described above to the corresponding four-membered ring starting material **12**.[12b,13] When this compound was submitted to the lithiation under the same reaction conditions shown in Scheme 2, only the expected reaction products **13** coming from the use of water and deuterium oxide were obtained (Scheme 4).[16] The use of other electrophiles, such as *t*-BuCHO, Et_2CO or Me_3SiCl, even under Barbier-type reaction conditions (or using DTBB as the arene catalyst) failed, the main reaction product being the corresponding reduced material **13a**. This result could indicate us that the real cyclobutane opening (in the formation of compounds **13**) takes place during the work-up between H_2O or D_2O and the lithium present in the reaction mixture. Anyhow, for the formation of compounds **13**, intermediates **14** and/or **15** could be involved in the process.



12

13a: X = H (83%)
13b: X = D (77%, >90% D)

14

15

Scheme 4. Reagents and conditions: (i)-(iii) as in Scheme 2.

In conclusion, we report here the selective naphthalene-catalyzed lithiation of cyclopropylidene diphenylmethane (**1**), which by a ring opening allowed the generation of a dilithium intermediate **2** with both lithium atoms attached to a two differently hybridized (sp^2, sp^3) carbon atom. This species react with two molecules of several electrophiles to give, after final hydrolysis, the expected polyfunctionalized products in one only synthetic operation, this procedure being very productive from an atom-economy point of view.

Experimental Section

General Procedures. All lithiation reactions were carried out under argon atmosphere in oven-dried glassware. All commercially available reagents (Acros, Aldrich, Fluka) were used without further purification. Commercially available anhydrous THF (99.5%, water content ≤0.005%, Fluka) and ether (99.8%, water content ≤0.005%, Fluka) were used as solvents in all the lithiation reactions. Elemental analyses were performed by the Microanalyses Service at the University of Alicante. The IR spectra were measured (film) with a Nicolet Impact 400 D-FT Spectrometer. NMR spectra were recorded in the Technical Services of the University of

Alicante with a Bruker AC-300 or Bruker AC-400 spectrometer using $CDCl_3$ as solvent and TMS as internal standard; chemical shifts are given in parts per million and coupling constants (*J*) are given in hertz. ^{13}C NMR assignments were made on the basis of DEPT experiments. LRMS were measured with a Hewlett–Packard EM/CG-5973N spectrometers, and HRMS were measured in the Technical Services of the University of Alicante with a Finnigan MAT95 S spectrometer, fragment ions in *m*/*z* with relative intensities (%) in parentheses. The purity of volatile products and the chromatographic analyses (GLC) were determined with a Hewlett–Packard HP-6890 instrument equipped with a flame ionisation detector and a 30 m HP-5 capillary column (0.32 mm diam., 0.25 µm film thickness), using nitrogen (2 mL/min) as carrier gas, $T_{injector}$=275 °C, $T_{detector}$=300 °C, T_{column}=60 °C (3 min) and 60–270 °C (15 °C/min), *P*=40 kPa; retention times (t_R) are given under these conditions. Thin layer chromatography (TLC) was carried out on Merck plastic sheets coated with silica gel 60 F_{254}. Melting points were obtained with a *Reichert Thermovar* apparatus. Lithium powder, which can be prepared from commercially available lithium granules (99%, high sodium content, Aldrich) as it was already reported by us,[17] was supplied by Medalchemy S.L. and Chemetall GmbH.

Naphthalene-catalyzed lithiation of cyclopropylidene diphenylmethane (1) and reaction with electrophiles. Isolation of compounds 5 and byproducts 6. General procedure

To a purple suspension of lithium (49 mg, 7 mmol) and naphthalene (13 mg, 0.10 mmol) in ether (1 mL) cooled at –20 ºC was added dropwise a solution of cyclopropylidene diphenylmethane (206 mg, 1 mmol) in ether (2 mL). The resulting mixture was stirred for 5 h at the same temperature then the suspension was cooled at -78 ºC and the corresponding electrophile (2.2 mmol) was added dropwise. The resulting mixture was stirred for 0.5 h at the same temperature and then it was hydrolyzed with water (5 mL), allowing the temperature to rise to rt. The resulting mixture was extracted with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvents were evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to afford the corresponding product(s). Isolated yields for compounds **5** are given in Table 1. Yields for compounds not included in Table 1, physical and spectroscopic data, as well as literature references for known compounds, follow.

1,1-Diphenyl-1-butene (5a).[9] Colourless liquid; t_R = 13.1 min; R_f (hexane) = 0.53; ν (film) 3078, 3054 (=CH) cm^{-1}; δ_H (300 MHz) 1.03 (3H, t, *J* = 7.3, CH_3), 2.12 (2H, dq, *J* = 7.3, CH_2), 6.07 (1H, t, *J* = 7.3, CH), 7.03-7.46 (10H, m, 10×ArH); *m/z* 208 (M^+, 87), 207 (22), 194 (11), 193 (67), 191 (13), 189 (11), 179 (32), 178 (49), 165 (46), 152 (16), 131 (11), 130 (49), 129 (32), 128 (19), 116 (12), 115 (100), 91 (33), 89 (13), 78 (15), 77 (17), 63 (10), 51 (17).

2,4-Dideutero-1,1-diphenyl-1-butene (5b). Colourless liquid; t_R = 13.1 min; R_f (hexane) = 0.53; ν (film) 3077, 3054 (=CH) cm^{-1}; δ_H (300 MHz) 1.01 (2H, t, *J* = 7.3, CH_2D), 2.11 (2H, t, *J* = 7.3, CH_2CH_2D), 7.16-7.38 (10H, m, 10×ArH); δ_C (75 MHz) 14.2 (t, *J* = 19, CH_2D), 23.0 (CH_2CH_2D), 126.7, 126.8, 127.2, 128.0, 128.1, 129.9 (ArCH), 131.3 (t, *J* = 23, C=*C*D), 140.2, 140.8, 142.8 (ArC, *C*=CD); *m/z* 210 (M^+, 100%), 209 (48), 208 (23), 207 (10), 195 (16), 194 (83), 193 (29), 192 (18), 191 (13), 190 (13), 180 (28), 179 (58), 178 (34), 167 (12), 166 (24), 165 (39), 152 (13), 133 (11), 132 (38), 131 (36), 130 (25), 129 (15), 117 (13), 116 (72), 115 (47), 92 (23), 91 (23), 89 (11), 77 (13), 51 (11); HRMS: M$^+$, found 210.1339. $C_{16}H_{14}D_2$ requires 210.1378.

4-Diphenylmethylene-2,2,8,8-tetramethyl-3,7-nonanediol (5c'). White solid, 29% yield; mp 114 ºC (diethyl ether); t_R = 19.9 min; R_f (hexane/ethyl acetate 8/2) = 0.44; ν (KBr) 3354 (OH), 3077, 3056 (=CH) cm^{-1}; δ_H (300 MHz) 0.76 (9H, s, 3×CH_3), 0.87 (9H, s, 3×CH_3), 0.91-1.26 (2H, m, C*H*$_2$CHOH), 1.60 (1H, br, OH), 2.37-2.49 (1H, m, C*H*HCH_2CH), 2.62-2.71 (1H, m, CH*H*CH_2CH), 2.92 (1H, br, OH), 3.32-3.37 (1H, m, CH_2C*H*OH), 4.49 (1H, s, C=CC*H*OH), 7.09-7.30 (10H, m, 10×ArH); δ_C (75 MHz) 23.2 (*C*H_2CH_2CH), 26.0, 27.0 (CH_3), 29.7 (*C*H_2CHOH), 34.4, 37.8 [*C*(CH_3)$_3$], 76.4, 79.9 (*C*HOH), 126.4, 126.8, 128.2, 128.3, 128.9, 129.7 (ArCH), 137.6, 143.2, 143.6, 143.9 (ArC, C=C); *m/z* 344 (M$^+$-2×H_2O, 2%), 324 (14), 323 (50), 306 (14), 305 (60), 287 (18), 261 (29), 247 (49), 245 (17), 232 (11), 231 (53), 221 (28), 219 (19), 218 (28), 217 (37), 216 (18), 215 (30), 207 (10), 206 (17), 205 (100), 204 (48), 203 (67), 202 (52), 193 (26), 192 (27), 191 (40), 190 (16), 189 (19), 179 (15), 178 (38), 169 (18), 167 (25), 165 (33), 143 (16), 129 (15), 128 (12), 115 (58), 105 (20), 91 (41), 77 (10), 69 (14), 57 (99), 56 (10), 55 (23); HRMS: M$^+$-H_2O, found 362.2573. $C_{26}H_{34}O$ requires 362.2610.

4-Diphenylmethylene-2,2,8,8-tetramethyl-3,7-nonanediol (5c''). Colourless crystals, 27% yield; mp 147 ºC (diethyl ether); t_R = 19.9 min; R_f (hexane/ethyl acetate 8/2) = 0.15; ν (KBr) 3386 (OH), 3077, 3054 (=CH) cm^{-1}; δ_H (300 MHz) 0.73 (9H, s, 3×CH_3), 0.87 (9H, s, 3×CH_3), 1.15-1.25 (1H, m, C*H*HCHOH), 1.34-1.42 (1H, m, CH*H*CHOH), 1.60 (2H, br, 2×OH), 2.35-2.46 (1H, m, C*H*HCH_2CH), 2.52-2.63 (1H, m, CH*H*CH_2CH), 3.00-3.06 (1H, m, CH_2C*H*OH), 4.49 (1H, s, C=CC*H*OH), 7.10-7.31 (10H, m, 10×ArH); δ_C (75 MHz) 25.5 (CH_3), 26.0 (CH_2), 27.2 (CH_3), 31.2 (CH_2), 34.8, 37.4 [*C*(CH_3)$_3$], 79.3, 81.7 (CHOH), 126.2, 126.5, 128.2, 128.3, 129.1, 129.5 (ArCH), 140.5, 142.2, 143.6, 143.9 (ArC, C=C); *m/z* 362 (M$^+$-H_2O, 1%), 323 (18), 305 (32), 287 (14), 261 (40), 247 (22), 245 (13), 231 (30), 229 (11), 221 (10), 219 (12), 218 (29), 217 (26), 216 (15), 215 (29), 206 (20), 205 (100), 204 (45), 203 (63), 202 (50), 193 (14), 192 (17), 191 (26), 178 (16), 167 (11), 165 (16), 15 (20), 91 (16), 57 (50), 55 (13); HRMS: M$^+$-H_2O, found 362.2587. $C_{26}H_{34}O$ requires 362.2610.

3-Diphenylmethylene-2,6-dimethyl-2,6-heptanediol (5d).[18] Colourless crystals; mp 106 ºC (diethyl ether); t_R = 17.8 min; R_f (hexane/ethyl acetate 6/4) = 0.16; ν (KBr) 3410 (OH), 3053 (=CH) cm^{-1}; δ_H (400 MHz) 0.92 [6H, s, CH_2COH(C*H*$_3$)$_2$], 1.20 (1H, s, OH), 1.36 [6H, s, C=CCOH(C*H*$_3$)$_2$], 1.56-1.61 (2H, m, CH_2C*H*$_2$COH), 1.84 (1H, br, OH), 2.15-2.21 (2H, m, C*H*$_2$CH_2COH), 7.12-7.13 (10H, m, 10×ArH); δ_C (100 MHz) 26.2 (*C*H_2CH_2COH), 28.5, 31.5 (CH_3), 44.0 (CH_2*C*H_2COH), 70.8, 75.3 (COH), 126.2, 126.5, 128.2, 128.3, 128.4 (ArCH), 138.4, 143.9, 144.4, 145.0 (ArC, C=C); *m/z* 306 (M$^+$-H_2O, 1%), 288 (34), 273 (11), 245 (13), 233 (38), 220 (23), 219 (100), 218 (15), 217 (23), 216 (11), 215 (28), 205 (12), 204 (21), 203 (29), 202 (30), 91 (14); Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70. Found: C, 81.27; H, 8.65; HRMS: M$^+$-H_2O, found 306.1981. $C_{22}H_{26}O$ requires 306.1984.

2-Methyl-6,6-diphenyl-5-hexen-2-ol (6d). Colourless oil, 20% yield; t_R = 16.3 min; R_f (hexane/ethyl acetate 6/4) = 0.53; ν (film) 3399 (OH), 3078, 3055 (=CH) cm^{-1}; δ_H (400 MHz)

1.14 (6H, s, CH_3), 1.60-1.68 (2H, m, CH_2*C*H_2COH), 2.16-2.23 (2H, m, *C*H_2CH_2COH), 6.09 (1H, t, *J* = 7.5, C=CH), 7.17-7.36 (10H, m, 10×ArH); δ_C (100 MHz) 24.9 (*C*H_2CH_2COH), 29.1 (CH_3), 43.7 (CH_2*C*H_2COH), 70.9 (COH), 125.2, 126.8, 127.0, 127.2, 127.2, 128.1, 128.2 (ArCH, C=*C*H), 140.0, 141.7, 144.2 (ArC, *C*=CH); *m/z* 266 (M^+, 1%), 249 (11), 248 (53), 233 (42), 219 (13), 206 (20), 205 (93), 204 (19), 203 (17), 202 (13), 193 (100), 192 (23) 191 (36), 190 (13), 189 (20), 180 (12), 179 (17), 178 (52), 167 (10), 165 (42), 157 (14), 155 (15), 152 (15), 129 (14), 128 (15), 116 (11), 115 (89), 91 (63); HRMS: M^+, found 266.1692. $C_{19}H_{22}O$ requires 266.1671.

4-Diphenylmethylene-3,7-diethyl-3,7-nonanediol (5e). White solid; mp 72 ºC (diethyl ether); t_R = 20.7 min; R_f (hexane/ethyl acetate 8/2) = 0.23; ν (KBr) 3437 (OH), 3076, 3052 (=CH) cm^{-1}; δ_H (400 MHz) 0.59 (6H, t, *J* = 7.4, 2×CH_3), 1.00 (6H, t, *J* = 7.4, 2×CH_3), 0.97-1.25 (4H, m, 2×*C*H_2CH_3), 1.39-1.50 (4H, m, 2×*C*H_2CH_3), 1.64-1.78 (2H, m, CH_2*C*H_2COH), 2.03-2.10 (2H, m, *C*H_2CH_2COH), 7.10-7.31 (10, m, 10×ArH); δ_C (100 MHz) 7.5, 8.5 (CH_3), 24.8, 30.3, 33.9, 37.2 (*C*H_2CH_3, *C*H_2CH_2COH, CH_2*C*H_2COH), 74.3, 81.1 (COH), 126.2, 126.4, 127.7, 128.2, 128.5, 128.5 (ArCH), 139.7, 141.2, 143.9, 145.0 (ArC, C=C); *m/z* 362 (M^+-H_2O, 1%), 344 (13), 334 (25), 333 (99), 315 (22), 266 (12), 265 (47), 262 (24), 261 (100), 249 (37), 248 (10), 247 (32), 245 (10), 233 (10), 232 (20), 231 (35), 230 (10), 229 (18), 228 (18), 226 (11), 219 (34), 218 (17), 217 (49), 216 (41), 215 (83), 205 (25), 204 (26), 203 (74), 202 (70), 193 (18), 191 (22), 189 (18), 179 (11), 178 (20), 167 (26), 165 (26), 152 (13), 131 (11), 129 (11), 128 (11), 117 (11), 115 (25), 105 (24), 91 (53), 69 (10), 67 (11), 57 (50), 55 (67); HRMS: M^+-2×H_2O, found 344.2502. $C_{26}H_{32}$ requires 344.2504.

3-Ethyl-7,7-diphenyl-6-hepten-3-ol (6e). Colourless oil, 30% yield; t_R = 18.0 min; R_f (hexane/ethyl acetate 8/2) = 0.44; ν (film) 3404 (OH), 3079, 3054 (=CH); δ_H (400 MHz) 0.78 (6H, t, *J* = 7.5, 2×CH_3), 0.94 (1H, s, OH), 1.37 (4H, q, *J* = 7.5, 2×*C*H_2CH_3), 1.51-1.63 (2H, m, CH_2*C*H_2COH), 2.03-2.16 (2H, m, *C*H_2CH_2COH), 6.10 (1H, t, *J* = 7.5, C=CH), 7.16-7.39 (10H, m, 10×ArH); δ_C (100 MHz) 7.6 (CH_3), 24.0 (*C*H_2CH_2COH), 30.8 (*C*H_2CH_3), 38.1 (CH_2*C*H_2COH), 74.5 (COH), 126.8, 126.9, 127.1, 128.0, 128.1, 129.7, 129.8 (ArCH, C=*C*H), 140.0, 141.6, 142.6 (ArC, *C*=CH); *m/z* 276 (M^+-H_2O, 41%), 247 (39), 205 (26), 194 (17), 193 (100), 192 (17), 191 (25), 189 (14), 180 (18), 179 (12), 178 (39), 167 (13), 165 (33), 152 (12), 128 (11), 115 (84), 91 (46), 55 (20); HRMS: M^+, found 294.1979. $C_{21}H_{26}O$ requires 294.1984.

5-Diphenylmethylene-4,8-dipropyl-4,8-undecanediol (5f). Colourless oil; t_R = 22.9 min; R_f (hexane/ethyl acetate 8/2) = 0.09; ν (film) 3416 (OH), 3076, 3053 (=CH) cm^{-1}; δ_H (400 MHz) 0.73-1.67 (32H, m, 4×CH_2CH_2*C*H_3, 4×CH_2*C*H_2CH_3, 4×*C*$H_2CH_2CH_3$, CH_2*C*H_2COH, 2×OH), 2.02-2.09 (2H, m, *C*H_2CH_2COH), 7.10-7.35 (10H, m, 10×ArH); δ_C (100 MHz) 14.4, 14.7 (CH_3), 16.4, 17.3 (*C*H_2CH_3), 25.1 (*C*H_2CH_2COH), 38.2, 41.0, 44.2 (CH_2*C*H_2COH, *C*$H_2CH_2CH_3$), 74.1, 80.6 (COH), 126.1, 126.4, 127.8, 128.2, 128.4, 128.5 (ArCH), 139.0, 141.8, 143.9, 145.0 (ArC, C=C); *m/z* 400 (M^+-2×H_2O, 6%), 376 (31), 375 (100), 357 (17), 294 (14), 293 (58), 290 (12), 289 (46), 275 (14), 263 (32), 251 (12), 247 (31), 245 (15), 233 (12), 229 (14), 228 (12), 219 (20), 218 (14), 217 (46), 216 (24), 215 (48), 205 (31), 204 (17), 203 (31), 202 (40), 193 (18), 191 (15), 189 (11), 178 (12), 167 (25), 165 (18), 115 (22), 105 (12), 91 (37), 71 (46), 69 (27), 67 (10), 55 (46); HRMS: M^+-H_2O, found 418.3254. $C_{30}H_{42}O$ requires 418.3236.

8,8-Diphenyl-4-propyl-7-octen-4-ol (6f). Colourless oil, 29% yield; t_R = 18.9 min; R_f (hexane/ethyl acetate 8/2) = 0.37; ν (film) 3412 (OH), 3055 (=CH) cm^{-1}; δ_H (400 MHz) 0.81-0.90 (6H, m, $2\times CH_3$), 1.14-1.41 (9H, m, $2\times CH_2C\mathit{H}_2CH_3$, $2\times C\mathit{H}_2CH_2CH_3$, OH), 1.49-1.68 (2H, m, $CH_2C\mathit{H}_2COH$), 2.03-2.15 (2H, m, $C\mathit{H}_2CH_2COH$), 6.10 (1H, t, *J* = 7.5, C=CH), 7.15-7.40 (10H, m, 10×ArH); δ_C (100 MHz) 14.6 (CH_3), 15.1 ($CH_2\mathit{C}H_2CH_3$), 24.1 ($\mathit{C}H_2CH_2COH$), 39.0, 41.4 ($CH_2\mathit{C}H_2COH$, $\mathit{C}H_2CH_2CH_3$), 74.4 (COH), 126.8, 126.9, 127.1, 128.0, 128.2, 129.6, 128.8 (ArCH, C=*C*H), 140.0, 141.7, 142.5 (ArC, *C*=CH); *m/z* 304 (M^+-H_2O, 28%), 261 (29), 205 (21), 194 (17), 193 (100), 192 (14), 191 (22), 189 (11), 180 (14), 178 (34), 167 (11), 165 (26), 115 (76), 91 (44), 55 (15); HRMS: M^+-H_2O, found 304.2164. $C_{23}H_{28}$ requires 304.2191.

4-Diphenylmethylene-3,7-diisopropyl-2,8-dimethyl-3,7-nonanediol (5g) and 3-isopropyl-2-methyl-7,7-diphenyl-6-hepten-3-ol (6g). Colourless oil, **5g** 26% yield, **6g** 31% yield; t_R (**5g**) = 24.8 min, t_R (**6g**) = 19.3 min; R_f (hexane/ethyl acetate 8/2) = 0.22; δ_H (400 MHz) 0.69, 0.71 (12H, 2d, *J* = 6.9, $4\times CH_3$), 0.82, 0.86 (12H, 2d, *J* = 6.9, $4\times CH_3$), 1.01, 1.11 (12H, 2d, *J* = 6.9, $4\times CH_3$), 1.34-1.64 (4H, 2m, $2\times CH_2$), 1.68, 1.80 (4H, 2h, *J* = 6.9, 4×CH), 2.02-2.27 (6H, 2m, $2\times CH_2$, 2×CH), 6.08 (1H, t, *J* = 7.5, C=CH), 7.09-7.46 (20H, m, 20×ArH); δ_C (100 MHz) 17.2, 17.3, 17.4, 17.5, 17.9, 19.7 (CH_3, CH), 24.7, 29.7, 31.8, 33.7 (CH_2), 33.9, 34.0 (CH), 77.1, 85.3 (COH), 126.2, 126.8, 126.9, 127.0, 127.4, 128.0, 128.1, 128.3, 128.7, 128.9, 129.7, 129.7 (ArCH, C=*C*H), 140.0, 141.6, 141.8, 142.4, 144.5, 145.3 (ArC, *C*=CH, C=C); *m/z* (**5g**) 400 (M^+-$2\times H_2O$, 14%), 375 (19), 357 (32), 302 (23), 301 (15), 290 (25), 289 (100), 260 (12), 259 (46), 247 (23), 246 (16), 245 (39), 233 (32), 232 (11), 231 (30), 230 (14), 229 (17), 219 (14), 218 (13), 217 (31), 216 (24), 215 (42), 205 (32), 204 (12), 203 (26), 202 (17), 193 (10), 191 (13), 167 (30), 165 (13), 115 (11), 105 (15), 91 (34), 71 (14), 69 (28), 55 (19); HRMS (**5g**): M^+-$2\times H_2O$, found 400.3041. $C_{30}H_{40}$ requires 400.3130; *m/z* (**6g**) 304 (M^+-H_2O, 12%), 261 (18), 206 (31), 205 (13), 194 (17), 193 (100), 191 (19), 178 (24), 167 (20), 165 (15), 124 (18), 115 (45), 91 (29); HRMS (**6g**): M^+-H_2O, found 304.2180. $C_{23}H_{28}$ requires 304.2191.

1,1,5,5-Tetracyclopropyl-2-diphenylmethylene-1,5-pentanediol (5h). Colourless oil; t_R = 29.1 min; R_f (hexane/ethyl acetate 8/2) = 0.28; ν (film) 3586, 3488 (OH), 3080 (=CH) cm^{-1}; δ_H (400 MHz) 0.46-1.06 (19H, m, 8×ring CH_2, 2×ring CH, OH), 1.55-1.73 (3H, m, 2×ring CH, OH), 2.16-2.23 (2H, m, $CH_2C\mathit{H}_2COH$), 2.89-2.96 (2H, m, $C\mathit{H}_2CH_2COH$), 7.56-7.77 (10H, m, 10×ArH); δ_C (100 MHz) -1.0, 0.2, 0.5, 2.4 (ring CH_2), 17.9, 19.9 (ring CH), 25.5 ($\mathit{C}H_2CH_2COH$), 42.4 ($CH_2\mathit{C}H_2COH$), 70.5, 75.4 (C=C*C*OH, $CH_2\mathit{C}OH$), 126.0, 126.3, 128.1, 128.3, 128.5, 128.6 (ArCH), 137.6, 143.6, 144.7, 145.0 (ArC, C=C); *m/z* 410 (M^+-H_2O, 1%), 289 (40), 285 (10), 265 (12), 257 (10), 256 (14), 255 (18), 254 (12), 253 (19), 252 (21), 244 (26), 243 (79), 242 (13), 241 (25), 240 (14), 239 (28), 229 (26), 228 (28), 227 (13), 226 (18), 217 (14), 216 (18), 215 (43), 205 (14), 203 (19), 202 (27), 192 (16), 191 (23), 189 (15), 180 (13), 179 (18), 167 (31), 165 (32), 152 (12), 129 (11), 121 (21), 115 (18), 111 (25), 105 (19), 93 (19), 91 (49), 79 (30), 77 (27), 69 (100), 67 (20), 65 (10), 55 (18); HRMS: M^+-$2\times H_2O$, found 392.2520. $C_{30}H_{32}$ requires 392.2504.

1-[3-(1-Hydroxycyclohexyl)-4,4-diphenyl-3-butenyl]-1-cyclohexanol (5i). White solid; mp 82 ºC (diethyl ether); t_R = 29.3 min; R_f (hexane/ethyl acetate 8/2) = 0.13; ν (film) 3384 (OH), 3054 (=CH) cm^{-1}; δ_H (300 MHz) 0.87-2.16 (26H, m, 10×ring CH_2, $CH_2C\mathit{H}_2COH$, $C\mathit{H}_2CH_2COH$, 2×OH), 7.14-7.26 (10H, m, 10×ArH); δ_C (75 MHz) 21.5, 22.1, 24.5, 25.2, 25.6 (ring CH_2, *C*H_2CH_2COH), 37.0, 37.3 (ring CH_2), 42.0 (CH_2*C*H_2COH), 71.4, 76.6 (COH), 126.1, 126.3, 128.3, 128.4 (ArCH), 138.6, 144.2, 144.8, 145.5 (ArC C=C); *m/z* 386 (M^+-H_2O, 48%), 368 (33), 360 (12), 330 (23), 329 (45), 304 (18), 303 (56), 291 (20), 290 (13), 286 (17), 285 (42), 278 (20), 277 (79), 274 (29), 273 (93), 272 (40), 271 (10), 260 (16), 259 (28), 258 (12), 252 (17), 247 (11), 243 (13), 241 (16), 239 (26), 234 (21), 233 (48), 232 (11), 231 (29), 230 (17), 229 (36), 228 (35), 227 (13), 226 (14), 221 (11), 219 (22), 218 (18), 217 (67), 216 (40), 215 (94), 213 (12), 207 (13), 206 (22), 205 (59), 204 (34), 203 (53), 202 (76), 195 (11), 193 (20), 192 (18), 191 (52), 190 (23), 189 (36), 181 (14), 179 (26), 178 (54), 168 (15), 167 (63), 166 (18), 165 (58), 155 (14), 152 (29), 145 (11), 141 (27), 129 (28), 128 (33), 117 (19), 116 (11), 115 (43), 105 (25), 99 (21), 95 (27), 91 (100), 81 (41), 79 (33), 78 (19), 77 (30), 69 (15), 67 (48), 65 (14), 55 (65), 54 (11), 53 (24), 51 (14); HRMS: M^+-2×H_2O, found 368.2536. $C_{28}H_{32}$ requires 368.2504.

1-(4,4-Diphenyl-3-butenyl)-1-cyclohexanol (6i). Colourless oil, 27% yield; t_R = 19.8 min; R_f (hexane/ethyl acetate 8/2) = 0.37; ν (film) 3375 (OH), 3052 (=CH) cm^{-1}; δ_H (300 MHz) 0.82-1.82 (13H, m, 5×ring CH_2, CH_2C*H*$_2COH$, OH), 2.15-2.24 (2H, m, C*H*$_2CH_2COH$), 6.09 (1H, t, *J* = 7.5, C=CH), 7.15-7.40 (10H, m, 10×ArH); δ_C (75 MHz) 22.1, 23.6, 25.7 (ring CH_2, *C*H_2CH_2COH), 37.3 (ring CH_2), 42.3 (CH_2*C*H_2COH), 71.4 (COH), 126.8, 126.9, 127.1, 128.0, 128.1, 129.8, 130.0 (ArCH, C=*C*H), 140.0, 141.6, 142.7 (ArC, *C*=CH); *m/z* 288 (M^+-H_2O, 39%), 206 (27), 205 (72), 204 (16), 203 (12), 202 (13), 194 (15), 193 (95), 192 (17), 191 (32), 189 (17), 180 (12), 179 (16), 178 (51), 167 (21), 165 (42), 152 (15), 128 (14), 116 (13), 115 (100), 91 (53), 81 (11), 79 (14), 77 (19), 67 (12), 65 (11), 55 (12), 51 (11); HRMS: M^+, found 306.1950. $C_{22}H_{26}O$ requires 306.1984.

DTBB-catalyzed lithiation of cyclopropylidene diphenylmethane (1) and reaction with electrophiles. Isolation of compounds 10. General procedure

To a green suspension of lithium (49 mg, 7 mmol) and DTBB (26 mg, 0.10 mmol) in THF (1 mL) cooled at -78 ºC was added dropwise a solution of cyclopropylidene diphenylmethane (206 mg, 1 mmol) in THF (2 mL). The resulting mixture was stirred for 2 h at the same temperature and then the corresponding electrophile was added dropwise. The resulting mixture was stirred for 1 h at the same temperature and then it was hydrolyzed with water (5 mL), allowing the temperature to rise to rt. The resulting mixture was extracted with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvents were evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to afford the corresponding product. Isolated yields are given in Scheme 3. Physical, analytical and spectroscopic data, as well as literature references for known compounds, follow.

1-[1-(1-Benzhydrylcyclopropyl)cyclopropyl(phenyl)methyl]benzene (10a). Colourless crystals; mp 186 ºC (hexane/ethyl acetate); t_R = 31.5 min; R_f (hexane) = 0.29; ν (KBr) 3082, 3058 (=CH) cm^{-1}; δ_H (400 MHz) -0.01-0.03 (4H, m, 2×ring CH_2), 0.14-0.18 (4H, m, 2×ring CH_2), 4.70 (2H, s, 2×CH), 7.12-7.27 (20H, 20×ArH); δ_C (100 MHz) 6.3 (CH_2), 23.9 [*C*$(CH_2)_2$], 52.6 (CH), 126.2, 127.7, 130.3 (ArCH), 142.0 (ArC); *m/z* 414 (M^+, 1%), 247 (29), 219 (39), 217 (14), 215 (19), 206 (12), 205 (14), 204 (12), 203 (17), 202 (20), 193 (15), 191 (15), 189 (10), 179 (11), 178 (18), 168 (19), 167 (100), 166 (25), 165 (75), 153 (11), 152 (42), 143 (10), 141 (16), 129 (14), 128 (21), 117 (11), 115 (35), 105 (16), 91 (73), 77 (16); Anal. Calcd for $C_{32}H_{30}\cdot 0.25C_4H_8O_2$: C, 90.78; H, 7.39. Found: C, 90.91; H, 7.36.

Dideutero-1-[1-(1-benzhydrylcyclopropyl)cyclopropyl(phenyl)methyl]benzene (10b). Colourless crystals; mp 188 ºC (diethyl ether); t_R = 31.5 min; R_f (hexane) = 0.29; ν (KBr) 3080, 3056 (=CH) cm^{-1}; δ_H (300 MHz) -0.01-0.02 (4H, m, 2×ring CH_2), 0.11-0.28 (4H, m, 2×ring CH_2), 7.11-7.27 (20H, 20×ArH); δ_C (75 MHz) 6.3 (CH_2), 23.8 [$C(CH_2)_2$], 52.1 (t, *J* = 19.9, CD), 126.2, 127.7, 130.2 (ArCH), 142.0 (ArC); *m/z* 388 (M^+-2×CH_2, 2%), 248 (34), 221 (14), 220 (42), 219 (10), 207 (10), 206 (11), 194 (17), 179 (10), 169 (18), 168 (100), 167 (17), 166 (38), 165 (14), 153 (23), 116 (12), 115 (11), 105 (12), 92 (26), 91 (43); HRMS: M^+-2×CH_2, found 388.2132. $C_{30}H_{24}D_2$ requires 388.2160.

DTBB-catalyzed lithiation of cyclopropylidene diphenylmethane (1) and reaction with electrophiles under Barbier conditions. Isolation of compounds 11. General procedure

When the reaction was performed under Barbier conditions, a mixture of cyclopropylidene diphenylmethane (206 mg, 1 mmol) and the corresponding electrophile (3 mmol) in THF (2 mL) was added dropwise over 2 h to a green suspension of lithium (49 mg, 7 mmol) and DTBB (26 mg, 0.10 mmol) in THF (1 mL) cooled at -78 ºC. The mixture was stirred for 1 h at the same temperature and then it was hydrolyzed with water (5 mL), allowing the temperature to rise to rt After the workup described above, the resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to afford the corresponding product. Isolated yields are given in Scheme 3. Physical, analytical and spectroscopic data, as well as literature references for known compounds, follow.

1-Cyclopropyl(phenyl)methylbenzene (11a).[19] Colourless liquid; t_R = 13.4 min; R_f (hexane) = 0.35; ν (film) 3059 (=CH) cm^{-1}; δ_H (300 MHz) 0.26-0.32 (2H, m, ring CH_2), 0.61-0.69 (2H, m, ring CH_2), 1.25-1.46 (1H, m, ring CH), 3.20 (1H, d, *J* = 9.5, CH), 7.14-7.31 (10H, m, 10×ArH); δ_C (100 MHz) 5.3 (ring CH_2), 16.7 (ring CH), 55.6 (CH), 126.1, 128.2, 128.2 (ArCH), 145.2 (ArC); *m/z* 208 (M^+, 8%), 181 (15), 180 (100), 179 (66), 178 (30), 167 (11), 166 (13), 165 (62), 152 (17), 115 (23), 104 (55), 91 (15), 77 (12), 51 (12).

3-(1-Benzhydrylcyclopropyl)-3-pentanol (11b). Colourless oil; t_R = 17.4 min; R_f (hexane/ethyl acetate 8/2) = 0.30; ν (film) 3587 (OH), 3084, 3058 (=CH) cm^{-1}; δ_H (300 MHz) 0.19-0.24 (2H, m, ring CH_2), 0.69-0.74 (2H, m, ring CH_2), 0.93 (6H, t, *J* = 7.4, 2×CH_3), 1.44-1.52 (4H, m, 2×CH_2), 4.54 (1H, s, CH), 7.10-7.32 (10H, m, 10×ArH); δ_C (75 MHz) 4.7 (ring CH_2), 8.3 (CH_3), 27.6 [$C(CH_2)_2$], 30.1 (CH_2), 51.6 (CH), 126.2, 128.1, 129.5 (ArCH), 143.5 (ArC); *m/z* 276 (M^+-H_2O, 21%), 248 (14), 247 (64), 219 (23), 215 (15), 206 (10), 205 (24), 204 (15), 203 (20), 202 (21), 193 (39), 192 (13), 191 (20), 189 (14), 179 (10), 178 (21), 168 (15), 167 (100), 166 (24), 165 (74), 153 (12), 152 (38), 143 (12), 141 (15), 129 (19), 128 (23), 115 (45), 105 (18), 91 (56), 79 (10), 78 (10), 77 (20), 67 (11), 55 (11), 51 (11); HRMS: M^+-H_2O, found 276.1906. $C_{21}H_{24}$ requires 276.1878.

Naphthalene-catalyzed lithiation of cyclobutylidene diphenylmethane (12) and reaction with electrophiles. Isolation of compounds 13. General procedure

To a purple suspension of lithium (49 mg, 7 mmol) and naphthalene (13 mg, 0.10 mmol) in ether (1 mL) cooled at -20 ºC was added dropwise a solution of cyclobutylidene diphenylmethane (220 mg, 1 mmol) in ether (2 mL). The resulting mixture was stirred for 6 h at the same temperature then the suspension was cooled at -78 ºC and the corresponding electrophile was added dropwise. The resulting mixture was stirred for 0.5 h at the same temperature and then it was hydrolyzed with water (5 mL), allowing the temperature to rise to rt. The resulting mixture was extracted with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvents were evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to afford the corresponding product. Isolated yields are given at Scheme 4. Physical, analytical and spectroscopic data, as well as literature references for known compounds, follow.

1,1-Diphenyl-1-pentene (13a).[20] Colourless oil; t_R = 13.9 min; ν (film) 3051 (=CH) cm^{-1}; δ_H (300 MHz) 0.90 (3H, t, *J* = 7.4, CH_3), 1.40-1.52 (2H, m, CH_2CH_3), 2.02-2.13 (2H, m, $CHCH_2$), 6.09 (1H, t, *J* = 7.5, CH), 7.13-7.43 (10H, m, 10×ArH); δ_C (75 MHz) 13.8 (CH_3), 23.1 (CH_2CH_3), 31.8 ($CHCH_2$), 126.7, 126.7, 127.2, 128.0, 128.1, 129.9, 130.1 (ArCH, C=*C*H), 140.3, 141.5, 142.9 (ArC); *m/z* 222 (M^+, 50%), 194 (16), 193 (100), 191 (11), 179 (14), 178 (36), 165 (24), 115 (66), 91 (21).

2,4-Dideutero-1,1-diphenyl-1-pentene (13b)[20] **and 2-deutero-1-(2-deuterophenyl)-1-phenyl-1-pentene (13b').**[20] Colourless oil; t_R = 13.9 min; ν (film) 3055 (=CH); δ_H (400 MHz) 0.97-1.06 (5H, m, CH_3, CH_2D), 1.53-1.66 (4H, m, CH_2CH_3, CH_2CH_2D), 2.22 (4H, t, *J* = 7.3, $CDCH_2$), 7.26-7.53 (20H, m, 20×ArH); δ_C (100 MHz) 13.5 (t, *J* = 19.8, CH_2D), 13.8 (CH_3), 23.0, 23.1 (CH_2CH_3, CH_2CH_2D), 31.7 (CH_2D), 126.7, 126.8, 127.2, 128.0, 128.1, 129.9 (ArCH), 140.3, 141.4, 141.5, 142.8, 142.9 (ArC, *C*=CD).

Acknowledgements

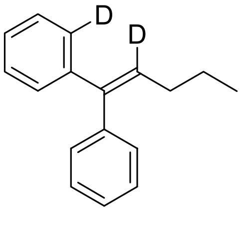
This work was generously supported by the Spanish Ministerio de Educación y Ciencia (MEC; grant no. CTQ2007-65218 and Consolider Ingenio 2010-CSD2007-00006) and the Generalitat Valenciana (GV; grants no. GRUPOS05/052 and GRUPOS05/058). V.J.L. thanks the University of Alicante for a predoctoral fellowship. We also thank MEDALCHEMY S.L. for a gift of chemicals, especially lithium powder.

References

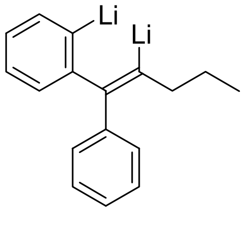
1. For reviews, see: (a) Foubelo, F.; Yus, M. *Trends Org. Chem.* **1998**, *7*, 1. (b) Foubelo, F.; Yus, M. *Curr. Org. Chem.* **2005**, *9*, 459.
2. For monographs, see: (a) Wakefield, B. J. *Organolithium Methods*; Academic Press: London, 1988. (b) Sapse, A. M.; von Ragué Schleyer, P., Eds. *Lithium Chemistry: A Theoretical and Experimental Overview*; J. Wiley & Sons: New York, 1995. (c) Gray, M.; Tinkel, M.; Snieckus, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G.; McKillop, A., Eds.; Pergamon: Oxford, 1995; Vol. 11, pp. 1-92. (d) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon: Oxford, 2002. (e) *The Chemistry of Organolithium Compounds*; Rappoport, Z.; Marek, I., Eds.; Wiley: Chichester, 2004.
3. For reviews, see: (a) Yus, M. *Chem. Soc. Rev.* **1996**, *25*, 155. (b) Ramón, D. J.; Yus, M. *Eur. J. Org. Chem.* **2000**, 225. (c) Yus, M. *Synlett* **2001**, 1197. (d) Yus, M.; Ramón, D. J. *Lat. J. Chem.* **2002**, 79. (e) Ramón, D. J.; Yus, M. *Rev. Cubana Quim.* **2002**, *14*, 75. (f) Yus, M. In *The Chemistry of Organolithium Compounds*; Rappoport, Z.; Marek, I., Eds.; J. Wiley & Sons: Chichester, 2004; Vol. 1, Part 2, Chapter 11.
4. For mechanistic studies, see: (a) Yus, M.; Herrera, R. P.; Guijarro, A. *Tetrahedron Lett.* **2001**, *42*, 3455. (b) Yus, M.; Herrera, R. P.; Guijarro, A. *Chem. Eur. J.* **2002**, *8*, 2574. (c) Yus, M.; Herrera, R. P.; Guijarro, A. *Tetrahedron Lett.* **2003**, *44*, 1309. (d) Herrera, R. P.; Guijarro, A.; Yus, M. *Tetrahedron Lett.* **2003**, *44*, 1313. (e) Yus, M.; Herrera, R. P.; Guijarro, A. *Tetrahedron Lett.* **2006**, *47*, 6267. (f) Melero, C.; Pérez, H.; Guijarro, A.; Yus, M. *Tetrahedron Lett.* **2007**, *48*, 4105. (h) Melero, C.; Guijarro, A.; Baumann, V.; Pérez-Jiménez, A. J.; Yus, M. *Eur. J. Org. Chem.* **2007**, 5514. (i) Melero, C.; Herrera, R. P.; Guijarro, A.; Yus, M. *Chem. Eur. J.* **2007**, *13*, 10096.
5. For a polymer supported version of this process, see: (a) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 1397. (b) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron* **1999**, *55*, 7017. (c) Yus, M.; Candela, P.; Gómez, C. *Tetrahedron* **2002**, *58*, 6207. (d) Alonso, F.; Gómez, C.; Candela, P.; Yus, M. *Adv. Synth. Catal.* **2003**, *345*, 275. (e) Candela, P.; Gómez, C.; Yus, M. *Russ. J. Org. Chem.* **2004**, *40*, 795.
6. (a) Lillo, V. J.; Gómez, C.; Yus, M. *Synthesis* **2008**, 1241. (b) Lillo, V. J.; Gómez, C.; Yus, M. *Tetrahedron Lett.* **2008**, *49*, 5182.
7. (a) Gómez, C.; Lillo, V. J.; Yus, M. *Tetrahedron* **2007**, *63*, 4655. (b) See also reference 6b.
8. (a) Trost**,** B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259. (c) Sheldon R. A. *Pure Appl. Chem.* **2000**, *72*, 1233.
9. Maercker, A.; Daub, E. E. *Tetrahedron* **1994**, *50*, 2439.
10. Dilithium intermediates belong to a special type of functionalized organolithium compounds, in which the functionality is the second carbon-lithium bond. For general reviews on functionalized organolithium compounds, see: (a) Nájera, C.; Yus, M. *Trends Org. Chem.* **1991**, *2*, 155. (b) Nájera, C.; Yus, M. *Org. Prep. Proced. Int.* **1995**, *27*, 383. (c) Nájera, C.; Yus, M. *Recent Res. Devel. Org. Chem.* **1997**, *1*, 67. (d) Yus, M.; Foubelo, F. *Rev.*

Heteroatom Chem. **1997**, *17*, 73. (e) Yus, M. Foubelo, F. In *Targets in Heterocyclic Systems*; Attanasi, O. A., Spinelli, D., Eds.; Italian Society of Chemistry: Rome, 2002; pp 136-171. (f) Nájera, C.; Yus, M. *Curr. Org. Chem.* **2003**, *7*, 867. (g) Yus, M. *Pure Appl. Chem.* **2003**, *75*, 1453. (h) Nájera, C.; Sansano, J. M.; Yus, M. *Tetrahedron* **2003**, *59*, 9255. (i) Chinchilla, R.; Nájera, C.; Yus, M. *Chem. Rev.* **2004**, *104*, 2667. (j) Chinchilla, R.; Nájera, C.; Yus, M. *Tetrahedron* **2005**, *61*, 3139. (k) Yus, M.; Foubelo, F. In *Functionalized Organometallics*; Knochel, P., Ed.; Wiley-VCH: Weinheim, 2005; Vol 1, Chapter 2; (l) Nájera, C.; Yus, M. In *The Chemistry Of Organolithium Compounds*; Rappoport, Z.; Marek, I., Eds.; J. Wiley & Sons: Chichester, 2006; Vol 2, Chapter 3. (m) Yus, M.; Foubelo, F. *Adv. Heterocycl. Chem.* **2006**, *91*, 135 (n) Chinchilla, R.; Nájera, C.; Yus, M. *Arkivoc* **2007**, *x*, 152. (o) See also the especial issue of Tetrahedron Symposium in Print (Eds.: Nájera, C.; Yus, M.) devoted to "Functionalised Organolithium Compounds" *Tetrahedron* **2005**, *61*, no. 13.

11. For the cyclopropane deprotonation on compounds of type **1** with *n*-BuLi, see: Huang, J.-W.; Shi, M. *Org. Biomol. Chem.* **2005**, *3*, 399.
12. For some ring opening of compounds of type **1** promoted by metallic reagents see, for instance: (a) Xu, B.; Shi, M. *Org. Lett.* **2003**, *5*, 1415. (b) Siriwardana, A. I.; Nakamura, I.; Yamamoto, Y. *Tetrahedron Lett.* **2003**, *44*, 4547. (c) Huang, J.-W.; Shi, M. *Tetrahedron* **2004**, *60*, 2057. (d) Liu, L.-P.; Shi, M. *J. Org. Chem.* **2004**, *69*, 2805.
13. (a) We generate the ylide in situ from the corresponding phosphonium salt: Stafford, J. A.; McMurry, J. E. *Tetrahedron Lett.* **1988**, *29*, 2531. For related papers, see: (b) Utimoto, K.; Tamura, M.; Sisido, K. *Tetrahedron* **1973**, *29*, 1169. (c) Zhou, H.; Huang, X.; Chen, W. *Synlett* **2003**, 2080.
14. See, for instance: Clayden, J.; Yasin, S. A. *New J. Chem.* **2002**, *26*, 191.
15. For a review on Barbier-type reactions, see: Alonso, F.; Yus, M. *Recent Devel. Org. Chem.* **1997**, *1*, 397.
16. In the case of using D_2O as electrophile, together with compound **13b**, the corresponding *ortho*-deuteriated regioisomer **13b'** obtained (*ca.* 1:1 mixture by NMR) with the same D content. It would mean that intermediate **15** suffered lithium rearrangement to form partially the new *ortho*-lithiated dianion **16**. See references 9 and 11 for related processes. See also: Dunkelblum, E.; Brenner, S. *Tetrahedron Lett.* **1973**, 669.



13b'



16

17. Yus, M.; Martínez, P.; Guijarro, D. *Tetrahedron* **2001**, *57*, 10119.

18. (a) Crystal data, excluding structure factors, deposited at the Cambridge Crystallographic Data Centre as supplementary publication numbers follow: (**5d**), CCDC 717711: $C_{22}H_{28}O_2$, M = 324.44; triclinic, a = 10.3773(14) Å, b = 12.0151(17) Å, c = 16.262(2) Å, α = 101.782(3)º, β = 97.158(3)º, γ = 92.683(4)º; V = 1964.0(5) Å^3; space group P-1; Z = 4; D_c = 1.097 Mg m^{-3}; λ = 0.71073 Å; μ = 0.068 mm^{-1}; F(000) = 704; T = 24±1ºC. Data collection was performed on a Bruker Smart CCD diffractometer, based on three ω-scan runs (starting = -34º) at values ϕ =0º, 120º, 240º with the detector at 2θ=-32º. For each of these runs, 606 frames were collected at 0.3º intervals and 20 s per frame. An additional run at ϕ =0º of 100 frames was collected to improve redundancy. The diffraction frames were integrated using the program SAINT[18b] and the integrated intensities were corrected for Lorentz-polarisation effects with SADABS.[18c] The structure was solved by direct methods[4d] and refined to all 2463 unique F_o^2 by full matrix least squares.[18d] All the hydrogen atoms were placed at idealised positions and refined as rigid atoms. Final wR_2 = 0.1300 for all data and 246 parameters; R_1 = 0.0424 for 2051 $F_o > 4\sigma(F_o)$; (b) *SAINT Version 6.02A: Area-Detector Integration Software*; Siemens Industrial Automation, Inc.: Madison, WI, **1995**; (c) Sheldrick, G. M. *SADABS: Area-Detector Absorption Correction*, Göttingen University, **1996**; (d) *SHELX97 (Includes SHELXS97, SHELXL97 and CIFTAB)-Programs for Crystal Structure Analysis (Release 97-2)*. Sheldrick, G.M., Institüt für Anorganische Chemie der Universität, Tammanstrasse 4, D-3400 Göttingen, Germany, **1998.**
19. Hall, S. S.; Sha, C.; Jordan, F. *J. Org. Chem.* **1976**, *41*, 1494.
20. Maercker, A.; Klein, K. D. *J. Organomet. Chem.* **1991**, *401*, C1.