Pergamon

Tetrahedron 54 (1998) 1853–1866

TETRAHEDRON

DTBB-Catalysed Lithiation of Chlorinated Benzylic Chlorides, Alcohols, Thiols or Amines†

Cecilia Gómez, Fernando F. Huerta and Miguel Yus*

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

Received 2 September 1997; revised 1 December 1997; accepted 4 December 1997

Abstract: The reaction of chlorinated benzyl chlorides (**1**) with an excess of lithium powder and a catalytic amount of DTBB (4 mol %) in the presence of different electrophiles [Pr^iCHO, Bu^tCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, Me_3SiCl] in THF at -50°C followed by hydrolysis with water leads to the corresponding compounds **2**. When the same DTBB-catalysed lithiation is applied to several chlorinated benzylic alcohols or mercaptans (**4** or **5**) it is necessary to deprotonate the starting material with Bu^nLi; treatment of the resulting anions or amine **6** as above, but at -78°C, leads to the expected reaction products **8**, after reaction with different electrophiles [Pr^iCHO, Bu^tCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, Me_3SiCl] and final hydrolysis with water.

INTRODUCTION

Taking advantage of the reactivity at the benzylic position is, in principle, possible to introduce a nucleophile or electrophile at this position, starting from the corresponding benzyl halide, by a S_N or a tandem lithiation-S_E reaction, respectively. However, whilst the first process (S_N) works, in general, nicely the lithiation at the benzylic position does not present synthetic interest because the main process is the formation of the corresponding Wurtz-type coupling products.[1] Some alternatives, such as the direct deprotonation,[2a] mercury-lithium trasmetallation,[2b] or the lithiation of benzyl mesylates[2c] give "mixed" carbanions or are not of general application. Another possibility of using benzyl halogenides would be to perform the lithiation reaction in the presence of the electrophile (Barbier-type conditions[3]), so the benzylic lithium intermediate could react with the electrophile instead of coupling with the halogenated precursor. However, this reaction give large amounts of the coupling product except when an excess of lithium-naphtalenide and benzyl bromides are used.[4] On the other hand, we have recently applied an arene-catalysed lithiation[5] for the preparation of very reactive organolithium intermediates under very mild conditions. The combination of this methodology with

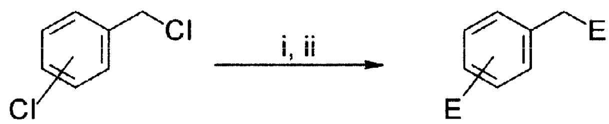
† This paper is warmly dedicated to Professor Antonio González on occasion of his 80 birthday

0040-4020/98/$19.00
PII: S0040-4020(97)10402-1

the Barbier-type reaction conditions allowed us to prepare, for instance, polylithiated synthons starting from the corresponding polychlorinated materials.[6] Continuing with this research, we describe here the lithiation of chlorinated chlorobenzyl chlorides under Barbier-type reaction conditions[7] as well as the two-step lithiation/reaction with electrophiles of chlorinates benzylic alcohols, mercaptans or amines, in both cases the lithiation process being catalysed by 4,4'-di-*tert*-butylbiphenyl (DTBB).[8]

RESULTS AND DISCUSSION

The reaction of chlorobenzyl chlorides **1** with an excess of lithium powder (1:14 molar ratio) and a catalytic amount of DTBB (1:0.17 molar ratio; 4 mol %) in the presence of different electrophiles [Pr^iCHO, Bu^tCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, Me_3SiCl] in THF at -50°C gave, after *ca.* 1h stirring and final hydrolysis with water, the corresponding products **2a-l** (Scheme 1 and Table 1). In order to compare the effect of the arene catalyst, the reactions with isobutyraldehyde and cyclohexanone were carried out in the absence of DTBB giving in both cases lower yields (see Table 1, entries 1 and 4, respectively). On the other hand, when prochiral carbonyl compounds were used as electrophiles, a *ca.* 1:1 diastereomeric mixture was obtained (GLC and/or 300 MHz ^1H NMR; see Table 1 entries 2, 5, 7 and 10 as well as footnote d). In addition, it is necessary to work under Barbier-type conditions: for instance, the two-step reaction (DTBB-catalysed lithiation followed by reaction with the electrophile) of 2-chlorobenzyl chloride and cyclohexanone yielded almost quantitatively 1,2-diphenylethane, resulting from the corresponding Wurtz-coupling process followed by chlorine/hydrogen exchange during the final hydrolysis in the presence of the excess of lithium.[9]



1 **2a-l**

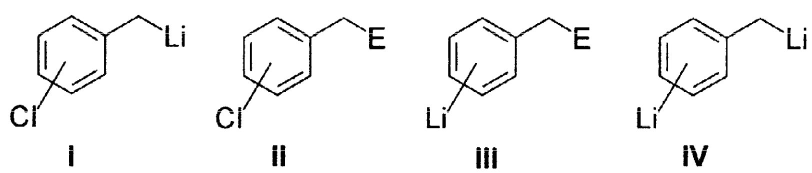
Scheme 1. *Reagents and conditions*: i, Li, DTBB cat. (4 mol %), E^+ = Pr^iCHO, Bu^tCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, Me_3SiCl, THF, -50°C; ii, H_2O, -50 to 20°C.

From a mechanistic point of view, we think that the reaction shown in the Scheme 1 takes part following a lithiation-S_E reaction sequence, involving intermediates of type **I-III**, though the formation of dilithiated species of type **IV** can not be excluded. As the catalyst acts as an electron-carrier from the metal to the organic substrate, the reaction could also involved radical ions or radicals, before the formation of the corresponding "anions" of type **I**, **III** or perhaps **IV**.

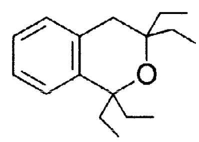
Table 1. Preparation of Compounds **2**

Entry	Starting material **1**	Electrophile E^+	Product[a] No.	E	Yield (%)[b]	R_f or mp (°C)[c]
1	**2-Cl**	Pr^iCHO	**2a**	2-(Pr^iCHOH)	38 (15)	0.62[d]
2	**2-Cl**	Bu^tCHO	**2b**	2-(Bu^tCHOH)	57	0.70[d]
3	**2-Cl**	Et_2CO	**2c**	2-(Et_2COH)	83	106
4	**2-Cl**	$(CH_2)_5CO$	**2d**	2-[$(CH_2)_5COH$]	64 (43)	116
5	**2-Cl**	PhCOMe	**2e**	2-[PhC(OH)Me]	48	0.29[d]
6	**2-Cl**	Me_3SiCl	**2f**	2-Me_3Si	53	0.67[e]
7	**3-Cl**	Bu^tCHO	**2g**	3-(Bu^tCHOH)	40	0.49[f]
8	**3-Cl**	$(CH_2)_5CO$	**2h**	3-[$(CH_2)_5COH$]	60	132
9	**3-Cl**	Me_3SiCl	**2i**	3-Me_3Si	78	0.63[e]
10	**4-Cl**	Bu^tCHO	**2j**	4-(Bu^tCHOH)	58	0.49[d]
11	**4-Cl**	$(CH_2)_5CO$	**2k**	4-[$(CH_2)_5COH$]	74	102
12	**4-Cl**	Me_3SiCl	**2l**	4-Me_3Si	83	0.43[e]

[a] All products **2** were >94% pure (GLC and/or 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) or/and recrystallisation based on the starting material **2-4**. [c] From hexane/ethyl acetate. [d] A *ca.* 1:1 diastereomeric mixture (GLC and/or 300 MHz ^{1}H NMR) was obtained, which could not be separated by TLC; silica gel, hexane/ethyl acetate: 7/3. [e] Silica gel, hexane. [f] Silica gel, hexane/ethyl acetate: 8/2.

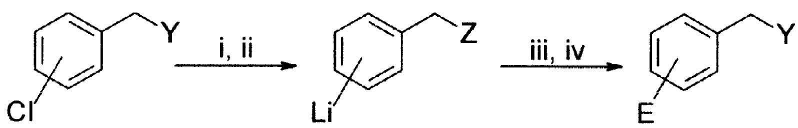


Considering products **2**, we found specially interesting the corresponding diol 1,2-derivatives in order to get cyclic compounds. As an example, the diol **2c** was treated with concentrated hydrochloric acid in diethyl ether giving the expected isochroman **3c** in almost quantitative yield.



3c

In the second part of this study we considered the preparation of aryllithium intermediates bearing an oxygen-, sulphur- or nitrogen-containing functionality at the benzylic position. Thus, the reaction of chlorinated precursors **4** and **5** with *n*-butyllithium, in THF at -78°C, followed by lithiation with an excess of lithium powder (1:10 molar ratio) and a catalytic amount of DTBB (1:0.05 molar ratio; 2.5 mol %) at the same temperature led to a solution of the corresponding dianion intermediate **7** (Z = YLi), which by treatment with different electrophiles [Pr^{i}CHO, Bu^{t}CHO, PhCHO, $(CH_2)_5CO$, Me_3SiCl] and final hydrolysis with water, both at -78°C, afforded the expected products **8** (Scheme 2 and Table 2). In the case of amines **6** it was not necessary to perform the first deprotonation step, so they were directly submitted to the lithiation process, involving the organolithium intermediate **7** with Z = NR_2.



4: Y = OH
5: Y = SH
6a: Y = NMe_2
6b: Y = $N(CH_2CH{=}CH_2)_2$

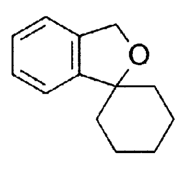
7(Z=YLi, NR_2)

8a-v

Scheme 2. *Reagents and conditions*: i, (only for compounds **4** and **5**) Bu^{n}Li, THF, -78°C; ii, Li, DTBB cat. (2.5 mol %), -78°C; iii, E^+= Pr^{i}CHO, Bu^{t}CHO, PhCHO, Et_2CO, $(CH_2)_5CO$, PhCOMe, Me_3SiCl, -78°C; iv, H_2O, -78 to 20°C.

Starting materials **4** and **5** were commercially available. Starting amine **6a** was *in situ* generated from the corresponding 3-chlorobenzylamine by two successive deprotonations with *n*-butyllithium and reaction with methyl iodide. Once compound **6a** was generated, it was directly lithiated following the general procedure described above. Amines **6b** were easily prepared by double allylation of the corresponding 2- or 4-chlorobenzylamine with allyl bromide under basic conditions.

Also in the case of 2-substituted derivatives **8** is possible to obtain cyclic products. This possibility was materialised by treating compound **8c** under the same reaction conditions as for **3c**, so the corresponding phthalan derivative **9c** was almost quantitatively obtained.



9c

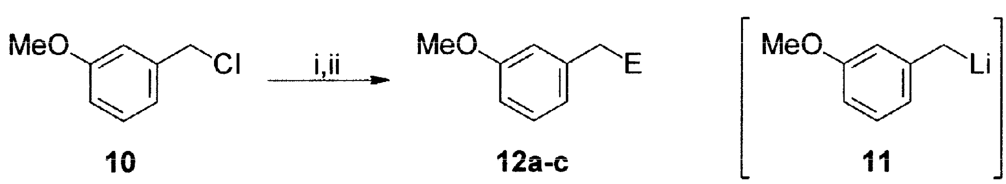
In the last part of this study we considered the preparation of functionalised benzyllithium intermediates. As it happened for compounds **2**, and in order to avoid the formation of Wurtz-type products, was necessary to work under Barbier-type reaction conditions. Commercially available 3-methoxybenzylchloride (**10**) was chosen as starting material and submitted to a DTBB-catalysed lithiation in the presence of different electrophiles [Pr^{i}CHO, Bu^{t}CHO, $(CH_2)_5CO$] following the protocol described above for compounds **2** but

Table 2. Preparation of Compounds **8**.

Entry	Starting material	Electrophile E^+	Product[a] No	Y	E	Yield(%)[b]	R_f or mp (°C)[c]
1	**4** (2-Cl)	Bu^tCHO	**8a**	O	2-(Bu^tCHOH)	43	126
2	**4** (2-Cl)	PhCHO	**8b**	O	2-(PhCHOH)	53	0.42[d]
3	**4** (2-Cl)	$(CH_2)_5CO$	**8c**	O	2-[$(CH_2)_5COH$]	39	0.35[d]
4	**4** (2-Cl)	Me_3SiCl	**8d**	O	2-Me_3Si	62	0.34[d]
5	**4** (3-Cl)	Bu^tCHO	**8e**	O	3-(Bu^tCHOH)	58	0.24[e]
6	**4** (3-Cl)	PhCHO	**8f**	O	3-(PhCHOH)	60	0.28[e]
7	**4** (3-Cl)	$(CH_2)_5CO$	**8g**	O	3-[$(CH_2)_5COH$]	51	0.48[e]
8	**4** (3-Cl)	Me_3SiCl	**8h**	O	3-Me_3Si	56	0.30[f]
9	**4** (4-Cl)	Bu^tCHO	**8i**	O	4-(Bu^tCHOH)	59	0.39[e]
10	**4** (4-Cl)	PhCHO	**8j**	O	4-(PhCHOH)	50	0.30[e]
11	**4** (4-Cl)	$(CH_2)_5CO$	**8k**	O	4-[$(CH_2)_5COH$]	62	0.35[e]
12	**4** (4-Cl)	Me_3SiCl	**8l**	O	4-Me_3Si	56	0.33[e]
13	**5** (4-Cl)	Bu^tCHO	**8m**	S	4-(Bu^tCHOH)	45	0.56[d]
14	**5** (4-Cl)	PhCHO	**8n**	S	4-(PhCHOH)	40	0.76[e]
15	**5** (4-Cl)	$(CH_2)_5CO$	**8o**	S	4-[$(CH_2)_5COH$]	47	0.44[d]
16	**6a** (3-Cl)	Bu^tCHO	**8p**	NMe_2	3-(Bu^tCHOH)	44[g]	0.39[d]
17	**6a** (3-Cl)	$(CH_2)_5CO$	**8q**	NMe_2	3-[$(CH_2)_5COH$]	69[g]	0.37[d]
18	**6b** (2-Cl)	Pr^iCHO	**8r**	$N(CH_2CH{=}CH_2)_2$	2-(Pr^iCHOH)	39	0.52[d]
19	**6b** (2-Cl)	Bu^tCHO	**8s**	$N(CH_2CH{=}CH_2)_2$	2-(Bu^tCHOH)	48	0.57[d]
20	**6b** (2-Cl)	$(CH_2)_5CO$	**8t**	$N(CH_2CH{=}CH_2)_2$	2-[$(CH_2)_5COH$]	70	0.55[d]
21	**6b** (4-Cl)	Bu^tCHO	**8u**	$N(CH_2CH{=}CH_2)_2$	4-(Bu^tCHOH)	43	0.50[d]
22	**6b** (4-Cl)	$(CH_2)_5CO$	**8v**	$N(CH_2CH{=}CH_2)_2$	4-[$(CH_2)_5COH$]	51	0.37[d]

[a] All isolated products **8** were >95% pure (GLC and/or 300 MHz ^1H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) and/or recrystallisation based on the starting material **3-6**. [c] From hexane/ethyl acetate. [d] Silica gel, hexane/ethyl acetate: 8/2. [e] Silica gel, hexane/ethyl acetate: 1/1. [f] Silica gel, hexane/ethyl acetate: 9/1. [g] This yield is based on 3-chlorobenzylamine, precursor of the *in situ* generated material **6a**.

working at -78°C, so products **12** were isolated, the intermediate **11** being probably involved in the process (Scheme 3 and Table 3). The corresponding two-step process gave only Wurtz-type reaction products.



Scheme 3. *Reagents and conditions*: i, Li, DTBB cat. (2.5 mol %), E^+ = Pr^iCHO, Bu^tCHO, $(CH_2)_5CO$, THF, -78°C; ii, H_2O, -78 to 20°C.

Table 3. Preparation of Compounds **12**

	Electrophile	Product[a]			
Entry	E^+	No.	E	Yield (%)[b]	R_f[c]
1	Pr^iCHO	**12a**	Pr^iCHOH	51	0.57
2	Bu^tCHO	**12b**	Bu^tCHOH	80	0.49
3	$(CH_2)_5CO$	**12c**	$(CH_2)_5COH$	72	0.40

[a] All isolated products **12** were >95% pure from GLC and/or 300 MHz ^1H NMR. [b] Isolated yields after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **10**. [c] Silica gel, hexane/ethyl acetate, 8:2.

As a final conclusion, we have described here an easy way to transform chlorinated benzylic derivatives into the corresponding lithiated intermediates, which by reaction with electrophiles allows the preparation of polyfunctionalised aromatic molecules in a one-pot process.

EXPERIMENTAL PART

General.- Mp's are uncorrected and were measured on a Reichert thermovar apparatus. FTIR spectra were determined with a Nicolet Impact 400D instrument. Mass spectra were measured with a Shimadzu QP-5000 mass spectrometer equipped with a GC-17A Gas Chromatograph. ^1H and ^{13}C NMR spectra were recorded in a Bruker AC-300 using $CDCl_3$ as solvent and $SiMe_4$ as internal standard; chemical shifts are given in δ (ppm) and the coupling constants (J) are measured in Hz. ^{13}C NMR assignments were made on the basis of DEPT experiments. MS (EI) were recorded with a Hewlett Packard EM/CG HP-5988A spectrometer. The purity of volatile distilled products and the chromatographic analyses (GLC) were determined with a Hewlett Packard HP-5890 instrument equipped with a flame ionisation detector and a 12 m HP-1 capillary column (0.2 mm diam, 0.33 μm film thickness), using nitrogen (2 ml/min) as the carrier gas, $T_{injector}$=275°C, T_{column}=60°C (3 min) and 60-270°C (15°C/min). Thin layer chromatography (TLC) was carried out on Scheleicher & Schuell F1500/LS 254 plates coated with a 0.2 mm layer of silica gel, using a mixture of hexane/ethyl acetate as eluant; R_f values are given under these conditions. Microanalysis was performed by the corresponding service at the University of Alicante. High resolution mass spectra were performed by the corresponding service at the Universities of Zaragoza and Murcia. Solvents were dried by standard procedures.[10] Lithium powder (Strem), starting materials as well as DTBB and the corresponding electrophiles used were commercially available (Aldrich, Acros, Fluka).

DTBB-Catalysed Lithiation of Chlorobenzyl Chlorides **1** *in the Presence of Electrophiles. Isolation of Compounds* **2**. *General Procedure*.- To a green suspension of lithium (200 mg, 28 mmol), and DTBB (80 mg, 0.30 mmol), in THF (5 ml) cooled at -50°C was slowly added (*ca.* 1 h) a solution of the starting chlorinated material **1** (2 mmol) and the corresponding electrophile (4 mmol) in THF (5 ml). After 10 min stirring at the same temperature the reaction mixture was hydrolysed with water (5 ml) and extracted with ethyl acetate (3x10 ml). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo* (15 Torr) to give a residue, which was purified by column chromatography (silica gel, hexane/ethyl acetate) or recrystallised (hexane/ethyl acetate) to yield the pure title compounds. Yields and physical data are included in Table 1. Spectroscopy and analytical data follow.

1-[2-(1-Hydroxy-2-methylpropyl)phenyl]-3-methyl-2-butanol (**2a**):[11] ν (film) 3382 (OH), 3060, 3023, 1595 cm^{-1} (C=C-H); δ_H 0.74, 0.93, 1.01, 1.14 (24H, 4d, *J* = 6.6, 8xCH_3), 1.79, 2.12 [4H, 2m, 4x*C*H(CH_3)$_2$], 2.68 (2H, dd, *J* = 13.8, 2.6, 2xArC*H*HCH), 2.88 (2H, dd, *J* = 13.8, 10.2, 2xArCH*H*CH), 3.46, 3.54 (2H, 2m, 2xArCH_2C*H*OH), 4.44 (1H, d, *J* = 7.9, ArC*H*OH), 4.54 (1H, d, *J* = 8.9, ArC*H*OH), 7.13-7.44 (8H, m, ArH); δ_C 25.7, 25.8, 26.2, 26.4 (8C, 8xCH_3), 34.3, 34.8, 35.1, 35.7, 36.4, 36.8 [6C, 4x*C*(CH_3)$_2$ and 2xArCH_2], 75.8, 82.0 (4C, 4xCHOH), 125.4, 125.5, 126.9, 127.0, 129.1, 131.1, 137.95, 140.2, 142.2 (12C, 2xArC); *m/z* (*minor diastereoisomer*, t_r = 12.80 min) 237 (M$^+$+1, 4%), 236 (M$^+$, 20), 211 (26), 194 (16), 193 (100), 178 (15), 145 (37), 119 (11), 117 (17), 115 (49), 105 (35), 91 (71), 79 (10), 77 (15), 65 (21), 44 (10), 43 (18); *m/z* (*major diastereoisomer*, t_r = 12.87 min) 237 (M$^+$+1, 0.7%), 236 (M$^+$, 5), 193 (17),160 (69), 146 (12), 145 (100), 117 (15), 115 (14), 105 (11), 91 (22), 57 (30).

1-[2-(1-Hydroxy-2,2-dimethylpropyl)phenyl]-3,3-dimethyl-2-butanol (**2b**):[12] ν (film) 3421 (OH), 1653 cm^{-1} (C=C); δ_H 0.89, 0.91, 0.92, 0.97 (36H, 4s, 12xCH_3), 2.54 (2H, dd, *J* = 13.7, 2.1, 2xArC*H*H), 2.84 (2H, dd, *J* = 13.7, 10.8, 2xArCH*H*), 2.91, 2.95 (2H, 2br s, 2xOH), 3.22 (1H, dd, *J* = 10.8, 2.1, ArCH_2C*H*OH), 3.30 (1H, def. d, *J* = 12.8, ArCH_2C*H*OH), 4.57, 4.81 (2H, 2s, 2xC*H*OH), 7.04-7.44 (8H, m, ArH); δ_C 25.7, 25.8, 26.2, 26.4 (12C, 12xCH_3), 34.3, 34.8, 35.1, 35.7, 36.4, 36.8 [6C, 4x*C*(CH_3)$_3$ and 2xAr*C*H_2], 75.8, 82.0 (4C, 4xCHOH), 125.4, 125.5, 126.9, 127.0, 129.1, 131.1, 137.95, 140.2, 142.2 (12C, 2xArC); *m/z* 246 (M$^+$-18, 0.6%), 207 (22), 190 (10), 189 (69), 172 (12), 171 (76), 160 (11), 156 (10), 145 (51), 143 (41), 133 (36), 131 (100), 129 (41), 120 (11), 119 (27), 117 (17), 115 (13), 105 (14), 104 (10), 103 (10), 91 (51), 77 (16), 65 (10), 59 (65), 57 (65), 43 (42).

3-[2-(2-Ethyl-2-hydroxybutyl)phenyl]-3-pentanol (**2c**):[12] ν (film) 3392 (OH), 3018, 1634, 1622, 1614 cm^{-1} (C=C-H); δ_H 0.79, 0.95 (12H, 2t, *J* = 7.3, 4xC*H*$_3$$CH_2$), 1.90, 1.77, 1.57 (8H, 3m, 4xCH_3C*H*$_2$), 3.26 (2H, s, ArC*H*$_2$), 7.09 (4H, m, ArH); δ_C 8.0, 8.15 (4C, 4xCH_3), 30.5, 36.7, 41.5 (5C, 5xCH_2), 75.1, 79.8 (2C, 2xCOH), 125.4, 126.1, 128.0, 134.3, 135.9, 145.0 (6C, ArC); *m/z* 236 (M$^+$-28, 1.7%), 235 (M$^+$-29, 10), 218 (14), 217 (85), 199 (57), 171 (22), 161 (16), 160 (89), 159 (13), 157 (38), 149 (17), 147 (10), 145 (75), 144 (10), 143 (61), 142 (10), 132 (13), 131 (100), 129 (32), 128 (19), 119 (23), 117 (26), 115 (20), 105 (11), 102 (14), 91 (52), 87 (30), 77 (10), 73 (35), 69 (16), 65 (10), 57 (69), 55 (18), 45 (51), 44 (10), 43 (55).

1-[2-(1-Hydroxycyclohexyl)benzyl]-1-cyclohexanol (**2d**): ν (film) 3404 (OH), 1601 cm^{-1} (C=C); δ_H 1.20-1.88 (20H, m, 10xring CH_2), 3.29 (2H, s, ArC*H*$_2$), 7.04-7.38 (4H, m, ArH); δ_C 22.1, 22.2, 25.6, 25.7, 38.1, 40.2 (11C, 10xring CH_2 and ArCH_2), 75.6, 74.95 (2C, 2xCOH), 125.7, 126.3, 126.9, 134.2, 134.3, 148.7 (6C, ArC); *m/z* 288 (M$^+$, 0.8%), 270 (42), 252 (32), 227 (58), 213 (18), 209 (16), 200 (10), 199 (61), 196 (14), 195 (39), 183 (11), 181 (22), 173 (16), 172 (100), 171 (24), 170 (28), 169 (17), 167 (16), 165 (13), 158 (13), 157 (50), 155 (12), 153 (12), 145 (51), 144 (25), 143 (28), 142 (27), 141 (55), 132 (11), 131 (20), 130 (18), 129 (72), 128 (41), 127 (13), 119 (13), 117 (19), 116 (12), 115 (41), 105 (14), 99 (29), 91 (45), 83 (18), 81 (51), 80 (19), 79 (24), 77 (21), 69 (10), 67 (21), 65 (15), 57 (11), 55 (87), 53 (19), 43 (46), 42 (15) (Found: M$^+$, 288.2117. $C_{19}H_{28}O_2$ requires M, 288.2089).

1-[2-(1-Hydroxy-1-phenylethyl)phenyl]-2-phenyl-2-propanol (**2e**): ν (film) 3344 (OH), 3059, 3025, 1666, 1600 cm^{-1} (C=C-H); δ_H 1.59, 1.60, 1.61 (12H, 3s, 4xCH_3), 1.89, 1.90 (4H, 2s, 2xArC*H*$_2$), 7.02-7.34 (14H, m, 3xArH); δ_C 32.1, 33.8, 33.9 (4C, 4xCH_3), 46.4, 46.6 (2C, 2xAr*C*H_2), 74.7, 75.2, 76.7, 76.8 (4C, 4xCOH),124.7, 125.1, 125.3, 126.0, 126.2, 126.5, 126.6, 126.9, 127.5, 127.9, 128.0, 128.1, 135.4, 145.5, 150.8 (28C, 6xArC) ; *m/z* (*minor diastereoisomer*, t_r = 16.28 min) 299 (M$^+$-33, 24%), 296 (20), 281 (27), 219 (14), 205 (20), 203 (21), 195 (10), 194 (44), 193 (11), 192 (11), 191 (34), 180 (15), 179 (100), 178 (34), 165

(10), 132 (15), 115 (12), 105 (75), 91 (15), 77 (25), 51 (13), 44 (10), 43 (55) (Found: M^+, 332.1763. $C_{23}H_{24}O_2$ requires M, 332.1776); *m/z* (*major diastereoisomer*, t_r = 16.37 min) 299 (M^+-33, 19%), 296 (19), 281 (25), 219 (11), 205 (21), 204 (11), 203 (21), 202 (15), 195 (10), 194 (48), 193 (11), 192 (12), 191 (36), 180 (16), 179 (100), 178 (35), 165 (10), 132 (16), 121 (11), 115 (13), 105 (85), 103 (10), 91 (16), 77 (27), 51 (13), 44 (10), 43 (61).

2-Trimethylsilylbenzyl(trimethyl)silane (**2f**): ν (film) 1587, 1559 (C=C), 839 cm^{-1} (C-Si); δ_H 0.03, 0.32 [18H, 2s, 2x$(CH_3)_3$Si], 2.29 (2H, s, ArCH_2), 7.04, 7.23, (4H, 2m, ArH); δ_C 0.8 [6C, 2x$(CH_3)_3$Si], 26.6 (ArCH_2), 123.4, 128.1, 128.8, 134.8, 146.6 (6C, ArC); *m/z* 238 (M^++2, 2.8%), 237 (M^++1, 8), 236 (M^+, 32), 221 (17), 150 (10), 149 (37), 148 (100), 145 (13), 134 (23), 133 (88), 131 (13), 105 (15), 75 (16), 74 (33), 73 (63), 59 (18), 45 (43), 44 (15), 43 (32) (Found: M^+, 236.1428. $C_{13}H_{24}Si_2$ requires M, 236.1417).

1-[3-(1-Hydroxy-2,2-dimethylpropyl)phenyl]-3,3-dimethyl-2-butanol (**2g**):[12] ν (film) 3440 (OH), 3054, 3027, 1607, 1589 cm^{-1} (C=C-H); δ_H 0.92, 0.93, 0.99, 1.00 (36H, 4s, 12xCH_3), 1.43, 1.57, 1.86 (4H, 4xbr s, 4xOH), 2.47 (2H, dd, *J* = 13.3, 10.9, 2xArCH_2C*H*OH), 2.92 (2H, d, *J* = 13.3, 2xArC*H*HCH), 3.42 (2H, d, *J* = 10.9, 2xArCH*H*CH), 4.39 (2H, br s, 2xArC*H*OH), 7.20 (8H, m, ArH); δ_C 25.9, 26.0 (12C, 12xCH_3), 34.8, 35.6 [4C, 4x*C*$(CH_3)_3$], 38.4, 38.45 (2C, 2xArCH_2), 80.6, 82.3, 82.4 (4C, 4xCHOH), 125.7, 127.8, 128.2, 128.3, 128.6, 139.1, 142.5 (12C, 2xArC); *m/z* 246 (M^+-18, 4%), 207 (17), 189 (14), 161 (23), 160 (25), 145 (27), 134 (11), 133 (100), 121 (16), 120 (16), 119 (43), 105 (73), 92 (11), 91 (54), 87 (10), 77 (12), 69 (29), 57 (65), 45 (16), 43 (33).

1-[3-(1-Hydroxycyclohexyl)benzyl]-1-cyclohexanol (**2h**): ν (film) 3395 (OH), 1605 cm^{-1} (C=C); δ_H 1.23-1.82 (20H, m, 10xring CH_2), 2.74 (2H, s, ArCH_2), 7.07, 7.26, 7.36 (4H, 3m, ArH); δ_C 22.0, 22.1, 25.5, 25.7, 37.3, 38.8 (11C, 10xring CH_2 and ArCH_2), 71.1, 72.9 (2C, 2xCOH), 122.6, 127.0, 127.8, 128.8, 136.9, 149.3 (6C, ArC); *m/z* 270 (M^+-18, 2.3%), 253 (14), 252 (68), 172 (100), 171 (40), 170 (10), 157 (32), 144 (12), 143 (26), 142 (13), 141 (22), 130 (15), 129 (45), 128 (27), 115 (20), 105 (11), 104 (19), 99 (34), 91 (32), 81 (68), 80 (17), 79 (31), 77 (15), 67 (15), 65 (15), 55 (31), 53 (17), 44 (10), 43 (19) (Found: C, 79.42; H, 9.66. $C_{19}H_{28}O_2$ requires C, 79.12; H, 9.78).

3-Trimethylsilylbenzyl(trimethyl)silane (**2i**): ν (film) 3055, 3020, 1589 cm^{-1} (C=C-H); δ_H 0.01, 0.27 [18H, 2s, 2x$(CH_3)_3$Si], 2.10 (2H, s, ArCH_2), 7.00-7.27 (4H, 2m, ArH); δ_C -2.0, -1.1 [6C, 2x$(CH_3)_3$Si], 27.0 (ArCH_2), 123.9, 127.5, 128.1, 128.5, 133.1, 139.9 (6C, ArC); *m/z* 238 (M^++2, 3.3%), 237 (M^++1, 8), 236 (M^+, 32), 221 (19), 150 (11), 149 (38), 148 (100), 133 (28), 75 (12), 74 (27), 73 (57), 59 (11), 45 (37), 43 (18) (Found: M^+, 236.1407. $C_{13}H_{24}Si_2$ requires M, 236.1417).

1-[4-(1-Hydroxy-2,2-dimethylpropyl)phenyl]-3,3-dimethyl-2-butanol (**2j**):[12] ν (film) 3548, 3471 (OH), 1650, 1643 cm^{-1} (C=C); δ_H 0.91, 1.00 (36H, 4s, 12xCH_3), 1.51, 1.52, 1.80 (4H, 3xbr s, 4xOH), 2.46 (2H, dd, *J* = 13.4, 10.7, 2xArCH_2C*H*OH), 2.90 (2H, d, *J* = 13.4, 2xArC*H*HCH), 3.42 (2H, def. d, *J* = 10.7, 2xArCH*H*CH), 4.36 (2H, br s, 2xArC*H*OH), 7.18 (4H, d, *J* = 7.9, ArH), 7.25 (4H, d, *J* = 8.3, ArH); δ_C 25.8, 25.9 (12C, 12xCH_3), 34.8, 35.6 [4C, 4x*C*$(CH_3)_3$], 38.0 (2C, 2xArCH_2), 80.5, 82.2 (4C, 4xCHOH), 127.8, 128.5, 138.9, 140.2, 140.3 (12C, 2xArC); *m/z* 246 (M^+-18, 3%), 208 (14), 207 (93), 160 (33), 159 (13), 145 (53), 121 (100), 120 (12), 93 (25), 91 (34), 87 (25), 77 (12), 69 (36), 57 (41), 45 (21), 43 (26).

1-[4-(1-Hydroxycyclohexyl)benzyl]-1-cyclohexanol (**2k**): ν (film) 3423 (OH), 3051, 3025, 1605 cm^{-1} (C=C-H); δ_H 1.23-1.81 (20H, m, 10xring CH_2), 2.71 (2H, s, ArCH_2), 7.17, 7.41 (4H, 2d, *J* = 7.9, ArH); δ_C 22.0, 22.1, 25.5, 25.7, 37.2, 38.7 (11C, 10xring CH_2 and ArCH_2), 71.1, 72.8 (2C, 2xCOH), 124.3, 130.4, 135.4, 147.5 (6C, ArC); *m/z* 270 (M^+-18, 2.7%), 253 (12), 252 (53), 173 (14), 172 (100), 171 (32), 157 (40), 144 (10), 143

(14), 141 (14), 129 (34), 128 (20), 115 (16), 104 (35), 99 (27), 91 (27), 81 (42), 79 (21), 77 (10), 55 (26), 53 (12), 43 (18) (Found: M^+, 270.1962. $C_{19}H_{26}O$ requires M, 270.1984).

4-Trimethylsilylbenzyl(trimethyl)silane (**21**): ν (film) 3059, 3005, 1598 cm^{-1} (C=C-H); δ_H -0.03, 0.22 [18H, 2s, $2x(CH_3)_3Si$], 2.01 (2H, s, ArCH_2), 6.96, 7.33 (4H, 2d, J = 7.6, ArH); δ_C -1.9, -1.0 [6C, $2x(CH_3)_3Si$], 27.1 (ArCH_2), 127.6, 128.0, 133.2, 141.2 (6C, ArC); *m/z* 238 (M^++2, 2.6%), 237 (M^++1, 7), 236 (M^+, 26), 222 (11), 221 (46), 149 (32), 148 (100), 133 (15), 75 (11), 74 (23), 73 (58), 45 (40), 43 (27) (Found: M^+, 236.1567. $C_{13}H_{24}Si_2$ requires M, 236.1417).

Preparation of Starting Amines **6b**. *General Procedure*.- A mixture of the corresponding chlorobenzylamine (2 mmol), allyl bromide (0.35 ml, 4 mmol) and a solution of 4M NaOH (10 ml) was stirred for *ca.* 12 h. Then the resulting mixture was extracted with ethyl acetate (3x10 ml), the organic layer dried over anhydrous Na_2SO_4 and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to give the pure title compounds. Yields, physical and spectroscopy data follow.

N-*Allyl*-N-*(2-chlorobenzyl)-2-propen-1-amine* [**6b**(2-Cl)]:[11] (81%); R_f 0.56 (hexane/ethyl acetate: 8/2); ν (film) 3072, 1643, 1558 cm^{-1} (C=C-H); δ_H 3.12 (4H, d, J = 6.1, $2xCH_2N$), 3.67 (2H, s, CH_2N), 5.18 (4H, m, 2xHC=CH_2), 5.83 (2H, m, 2x*H*C=CH_2), 7.14-7.25 (2H, m, ArH), 7.31 (1H, d, J = 7.9, ArH), 7.55 (1H, d, J = 7.6, ArH); δ_C 54.3, 56.8 (3C, $3xCH_2$), 117.3, 126.5, 127.7, 129.2, 130.3, 133.9, 135.7, 137.3 (10C, $2xHC=CH_2$ and ArC); *m/z* 223 (M^++2, 4.9%), 221 (M^+, 15), 196 (14), 194 (48), 192 (10), 180 (11), 127 (40), 126 (11), 125 (100), 110 (20), 96 (21), 89 (21), 56 (16), 42 (25).

N-*Allyl*-N-*(4-chlorobenzyl)-2-propen-1-amine*[**6b**(4-Cl)]:[11] (90%); R_f 0.77 (hexane/ethyl acetate: 8/2); ν (film) 3078, 1643, 1605 cm^{-1} (C=C-H); δ_H 3.05 (4H, d, J = 6.4, $2xCH_2N$), 3.52 (2H, s, CH_2N), 5.15 (4H, m, 2xHC=CH_2), 5.85 (2H, m, 2x*H*C=CH_2), 7.27 (4H, s, ArH); δ_C 56.3, 56.7 (3C, $3xCH_2$), 117.5, 128.2, 128.5, 129.4, 130.1, 132.4, 135.6, 138.0 (10C, $2xHC=CH_2$ and ArC); *m/z* 223 (M^++2, 4.4%), 221 (M^+, 14), 194 (28), 127 (41), 126 (12), 125 (100), 110 (19), 96 (20), 89 (21), 56 (13), 42 (18).

DTBB-Catalysed Lithiation of Compounds **4-6** *and Reaction with Electrophiles. Preparation of Compounds* **8**. *General Procedure*.- To a solution of starting materials **4** and **5** (2 mmol) in THF (3 ml) was added a solution of *n*-butyllithium in hexane (2 mmol) at -78°C for 10 min The resulting mixture was transferred *via* cannula to a suspension of lithium powder (0.15 g, 20 mmol) and DTBB (0.026 g, 0.1 mmol) in THF (5 ml) at -78°C, the resulting mixture being stirred for *ca.* 45 min. at the same temperature. Then, the corresponding electrophile (2 mmol) was added and the mixture was stirred at -78°C until the green colour was recovered. The resulting mixture was then hydrolysed with water (5 ml) at -78°C allowing the temperature to rise to 20°C, extracted with ethyl acetate (3x10 ml), the organic layer was dried over anhydrous Na_2SO_4 and the solvent removed *in vacuo* (15 Torr). The obtained residue was purified by column chromatography (silica gel, hexane/ethyl acetate) or recrystallised (hexane/ethyl acetate) to give pure compounds **8**.

In the case of the starting material **6a**, which was prepared *in situ*, to a solution of 3-chloro benzylamine (0.25 ml, 2 mmol) in THF (3 ml) was added a solution of *n*-butyllithium in hexane (2 mmol) at -78°C. After 10 min methyl iodide (0.13 ml, 2 mmol) was added at the same temperature and after 5 min stirring these two operations were repeated again. Then, the *in situ* generated 3-chloro-*N,N*-dimethylbenzylamine (**6a**) or starting amines **6b** were submitted to the same lithiation-S_E tandem reactions as above.[13]

Yields and physical data for compounds **8** are included in Table 2. Spectroscopic and analytical data follow.

***2-(2,2-Dimethyl-1-hydroxypropyl)benzyl Alcohol* (8a)**: ν (film) 3353 (OH), 3066, 3030, 1635, **1603 cm^{-1} (C=C-H); δ_H 0.89 [9H, s, C(CH$_3$)$_3$], 3.20, 3.28,** (2H, 2 br s, 2xOH), 4.40 (1H, d, *J* = 12.2, CHO), **4.61 (2H, m, CH$_2$O), 7.24, and 7.41 (4H, 2m, ArH); δ_C 26.2** [3C, C(CH$_3$)$_3$], 36.4 [*C*(CH$_3$)$_3$], 63.0 (CH$_2$O), 77.2 (CHO), 127.25, 127.3, 128.5, 138.1, 140.3 (6C, ArC); *m/z* 161 (M$^+$-33, 3.6%), 137 (26), 120 (24), 119 (100), 91 (66), 77 (11), 65 (21), 57 (21), 43 (11) (Found: M$^+$, 176.1210. $C_{12}H_{16}O$ requires M, 176.1201).

2-(1-Hydroxy-1-phenylmethyl)benzyl Alcohol (**8b**): ν (film) 3357 (OH), 3060, 3027, 1601 (C=C-H), 1018 cm^{-1} (C-O); δ_H 4.33, 4.48 (2H, 2d, *J* = 12.0, CH$_2$O), 4.55 (1H, s, OH), 5.90 (1H, s, CHO), 7.13-7.32 (9H, m, 2xArH); δ_C 63.45 (CH$_2$O), 73.9 (CHO), 126.3, 127.2, 128.1, 128.2, 128.25, 128.4, 128.8, 130.1, 138.3, 142.2, 142.5 (12C, 2xArC); *m/z* 198 (M$^+$-H$_2$O+2, 1%), 197 (M$^+$-H$_2$O+1, 11), 196 (M$^+$-H$_2$O, 73), 195 (100), 194 (11), 178 (15), 177 (16), 165 (33), 152 (14), 119 (29), 105 (87), 91 (42), 90 (21), 89 (28), 82 (28), 79 (10), 77 (44), 65 (23), 63 (18), 51 (28) (Found: M$^+$, 196.0884. $C_{14}H_{12}O$ requires M, 196.0888).

2-(1-Hydroxycyclohexyl)benzyl Alcohol (**8c**):[11] ν (film) 3356 (OH), 3063, 3029, 1598, 1449 cm^{-1} (C=C-H); δ_H 1.28, 1.59-2.06 (10H, 2m, 5x ring CH$_2$), 3.54 (2H, br s, 2xOH), 4.82 (2H, s, ArC*H*$_2$), 7.21-7.38 (4H, m, ArH); δ_C 21.9, 25.3, 38.8 (5C, 5xring CH$_2$) 65.7 (COH), 75.6 (CH$_2$OH), 126.1, 127.1, 127.9, 132.3, 138.5, 48.9 (6C, ArC); *m/z* 207 (M$^+$+1, 1.3%), 206 (M$^+$, 7), 188 (12), 146 (12), 145(100), 142 (13), 141 (11), 132 (11),117 (17), 115 (12), 91 (17), 77 (15).

2-Trimethylsilylbenzyl Alcohol (**8d**): ν (film) 3327 (OH), 3057, 1435 (C=C-H), 1017 (C-O), 839 cm^{-1} (Si-CH$_3$); δ_H 0.48 (9H, s, 3xCH$_3$), 4.89 (2H, br s, CH$_2$O), 7.40-7.68 (4H, m, ArH); δ_C 0.3 (3C, 3xCH$_3$), 65.3 (CH$_2$OH), 126.9, 127.6, 129.4, 134.6, 138.0, 146.1 (6C, ArC); *m/z* 165 (M$^+$-15, 73%), 149 (12), 148 (17), 147 (100), 146 (14), 145 (78), 105 (13), 91 (15), 77 (11), 75 (33), 74 (10), 73 (49), 61 (23), 53 (10), 47 (17), 45 (49), 43 (27) (Found: M$^+$, 180.0936. $C_{10}H_{16}OSi$ requires M, 180.0970).

3-(2,2-Dimethyl-1-hydroxypropyl)benzyl Alcohol (**8e**): ν (film) 3369 (OH), 3055, 3024, 1601 (C=C-H), 1017 cm^{-1} (C-O); δ_H 0.91 (9H, s, 3xCH$_3$), 2.24 (1H, br s, OH), 4.37 (1H, s, C*H*OH), 4.64 (2H, s, C*H*$_2$OH), 7.19-7.34 (4H, m, ArH); δ_C 25.9 (3C, 3xCH$_3$), 35.6 [*C*(CH$_3$)$_3$], 65.2 (CH$_2$OH), 82.3 (CHOH), 125.9, 126.1, 127.0, 127.7, 140.1, 142.51 (6C, ArC); *m/z* 176 (M$^+$-18, 3.2%), 138 (11), 137 (100), 120 (14), 107 (31), 91 (23), 79 (49), 77 (18), 57 (24), 43 (12) (Found: M$^+$, 176.1143. $C_{12}H_{16}O$ requires M, 176.1201).

3-(1-Hydroxy-1-phenylmethyl)benzyl Alcohol (**8f**): ν (film) 3371 (OH), 3062, 3029, 1666, 1603 (C=C-H), 1024 cm^{-1} (C-O); δ_H 2.72, 3.20 (2H, 2xbr s, 2xOH), 4.48 (2H, s, CH$_2$O), 5.69 (1H, s, CHO), 7.13-7.29 (9H, m, 2xArH); δ_C 64.9 (CH$_2$O), 76.0 (CHO), 125.0, 125.8, 126.1, 126.5, 127.5, 128.4, 128.5, 141.0, 143.6, 144.1 (12C, 2xArC); *m/z* 215 (M$^+$+1, 1%), 214 (M$^+$, 6), 183 (10), 165 (10), 135 (34), 107 (18), 106 (13), 105 (100), 91 (12), 89 (12), 79 (45), 78 (16), 77 (54), 51 (24) (Found: M$^+$, 214.0988. $C_{14}H_{14}O_2$ requires M, 214.0994).

3-(1-Hydroxycyclohexyl)benzyl Alcohol (**8g**): ν (film) 3309 (OH), 3058, 3026, 1621, 1589 (C=C-H), 979 cm^{-1} (C-O); δ_H 1.25-1.79 (10H, m, 5xring CH$_2$), 2.45 (1H, br s, OH), 4.56 (2H, s, C*H*$_2$OH), 7.14-7.49 (4H, m, ArH); δ_C 22.0, 25.4, 38.7 (5C, 5xring CH$_2$), 65.1 (CH$_2$OH), 73.2 (CHOH), 123.2, 123.8, 125.25, 128.2, 140.75, 149.8 (6C, ArC); *m/z* 207 (M$^+$+1, 3%), 206 (M$^+$, 20), 189 (13), 188 (80), 175 (13), 170 (11), 163 (18), 158 (11), 157 (72), 150 (29), 145 (22), 143(14), 142 (26), 141 (22), 135 (26), 134 (13), 133 (85), 130 (28), 129 (100), 128 (38), 127 (14), 117 (19), 116 (10), 115 (47), 107 (11), 103 (14), 91 (72), 89 (20), 80 (20), 79 (42), 78 (16), 77 (53), 67 (10), 65 (18), 63 (16), 55 (62), 53 (22), 51 (33), 50 (10), 43 (18) (Found: M$^+$, 206.1318. $C_{13}H_{18}O_2$ requires M, 206.1307).

3-Trimethylsilylbenzyl Alcohol (**8h**): ν (film) 3327 (OH), 3047, 3020, 1598 (C=C-H), 837 cm^{-1} (C-Si); δ_H 0.27 (9H, s, 3xCH$_3$), 4.66 (2H, s, CH$_2$O), 7.33-7.50 (4H, m, ArH); δ_C -1.2 (3C, 3xCH$_3$), 65.5 (CH$_2$O), 127.6, 127.9,

131.9, 132.6, 139.9, 140.9 (6C, 6xArC); ***m/z*** **182 (M^++2, 1%)**, 181 (M^++1, 3), 180 (M^+, 20), 166 (23), 165 (100), 147 (29), 75 (36), 73 (16), 53 (11), 45 (30), 43 (26) (Found: M^+, 180.0975. $C_{10}H_{16}OSi$ requires M, 180.0970).

4-(2,2-Dimethyl-1-hydroxypropyl)benzyl Alcohol (**8i**): ν (film) 3438 (OH), 3055, 3025, 1511 cm^{-1} (C=C-H); δ_H 0.89 (9H, s, 3xCH_3), 2.26, 2.41 (2H, 2br s, 2xOH), 4.35 (1H, s, CHO), 4.60 (2H, s, CH_2O), 7.25 (4H, br s, ArH); δ_C 25.8 (3C, 3xCH_3), 35.5 [*C*(CH_3)$_3$], 64.85 (CH_2O), 82.1 (COH), 126.2, 127.7, 139.75, 141.5 (6C, 6xArC); *m/z* 176 (M^+-18, 2.6%), 138 (16), 137 (100), 120 (26), 107 (27), 91 (35), 79 (58), 77 (24), 57 (29), 51 (11), 43 (19) (Found: M^+, 176.1209. $C_{12}H_{16}O$ requires M, 176.1201).

4-(1-Hydroxy-1-phenylmethyl)benzyl Alcohol (**8j**): ν (film) 3275 (OH), 3080, 3060, 3026, 1609, 1522 (C=C-H), 1025, 1010 cm^{-1} (C-O); δ_H 4.59 (2H, s, CH_2O), 5.78 (1H, s, CHO), 7.22-7.36 (9H, m, ArH); δ_C 63.5 (CH_2O), 75.0 (CHO), 126.0, 126.4, 126.6, 127.6, 127.7, 139.6, 142.9, 143.8 (12C, 2xArC); *m/z* 215 (M^++1, 1.9%), 214 (M^+, 5), 183 (10), 165 (10), 135 (28), 107 (13), 106 (12), 105 (100), 91 (12), 89 (10), 79 (35), 78 (15), 77 (48), 51 (21) (Found: M^+, 214.0995. $C_{14}H_{14}O_2$ requires M, 214.0994).

4-(1-Hydroxycyclohexyl)benzyl Alcohol (**8k**): ν (film) 3371 (OH), 3093, 3058, 3027, 1611, 1510 (C=C-H), 1035, 1013 cm^{-1} (C-O); δ_H 1.20-1.76 (10H, m, 5xring CH_2), 2.64, 3.50 (2H, 2br s, 2xOH), 4.51 (2H, s, CH_2O), 7.19-7.39 (4H, m, ArH); δ_C 21.9, 25.3, 38.5 (5C, 5xring CH_2), 64.3 (CH_2OH), 72.9 (COH), 124.6, 126.6, 126.7, 128.2, 139.1, 148.5 (6C, 6xArC); *m/z* 207 (M^+1, 14.5%), 206 (M^+, 20), 189 (11), 188 (69), 175 (13), 163 (19), 158 (12), 157 (86), 150 (20), 145 (10), 143 (10), 142 (16), 141 (15), 135 (19), 133 (56), 130 (29), 129 (100), 128 (35), 127 (12), 117 (16), 116 (10), 115 (44), 107 (11), 105 (11), 103 (11), 91 (78), 89 (13), 80 (14), 79 (43), 78 (13), 77 (48), 65 (16), 63 (14), 55 (45), 53 (22), 51 (29), 43 (12) (Found: M^+, 206.1309. $C_{13}H_{18}O_2$ requires M, 206.1307).

4-Trimethylsilylbenzyl Alcohol (**8l**): ν (film) 3341 (OH), 3070, 3013, 1559, 1509 (CH=C-H), 842 cm^{-1} (C-Si); δ_H 0.29 (9H, s, 3xCH_3), 4.63 (2H, s, CH_2O), 7.33, 7.53 (4H, 2d, *J* = 7.7, ArH); δ_C -1.2 (3C, 3xCH_3), 65.0 (CH_2O), 126.2, 133.5, 139.6, 141.4 (6C, ArC); *m/z* 182 (M^++2, 1%), 181 (M^++1, 3), 180 (M^+, 21), 167 (10), 166 (32), 165 (100), 105 (10), 91 (12), 75 (17), 73 (14), 45 (26), 43 (25) (Found: M^+, 180.0978. $C_{10}H_{16}OSi$ requires M, 180.0970).

4-(2,2-Dimethyl-1-hydroxypropyl)benzyl Mercaptan (**8m**): ν (film) 3456 (OH), 3060, 3026, 1620, 1602 cm^{-1} (C=C-H); δ_H 0.90 (9H, s, 3xCH_3), 1.74 (1H, t, *J* = 7.6, CH_2S*H*), 2.01 (1H, br s, OH), 3.70 (2H, d, *J* = 7.6, C*H_2*SH), 4.33 (1H, s, C*H*OH), 7.23 (4H, br s, ArH); δ_C 25.8 (3C, 3xCH_3), 28.5 (CH_2SH), 35.5 [*C*(CH_3)$_3$], 81.9 (CHOH), 127.1, 127.8, 139.9, 141.0 (6C, ArC); *m/z* 210 (M^+, 3.3%), 155 (10), 154 (19), 153 (100), 120 (47), 119 (27), 107 (14), 92 (10), 91 (59), 79 (11), 65 (10), 57 (37), 47 (28), 43 (14) (Found: M^+, 210.1073. $C_{12}H_{18}OS$ requires M, 210.1078).

4-(1-Hydroxy-1-phenylmethyl)benzyl Mercaptan (**8n**): ν (film) 3403 (OH), 3059, 3027 1679, 1602 (C=C-H), 1035 cm^{-1} (C-O); δ_H 1.73 (1H, t, *J* = 7.6, CH_2S*H*), 2.35 (1H, br s, OH), 3.70 (2H, d, *J* = 7.6, C*H_2*SH), 5.80 (1H, s, CHO), 7.22-7.38 (10H, m, ArH); δ_C 28.6 (CH_2SH), 75.9 (CHO), 126.5, 126.6, 126.8, 127.6, 128.1, 128.5, 136.2, 143.3 (12C, ArC); *m/z* 232 (M^++2, 0.7%), 231 (M^++1, 1.6), 230 (M^+, 10), 151 (11), 105 (100), 91 (19), 89 (10), 79 (10), 77 (27), 51 (10) (Found: M^+, 230.0763. $C_{14}H_{14}OS$ requires M, 230.0765).

4-(1-Hydroxycyclohexyl)benzyl Mercaptan (**8o**): ν (film) 3364 (OH), 1633, 1603 (C=C), 1019 cm^{-1}(C-O); δ_H 1.27-1.81 (10H, m, 5xring CH_2), 3.72 (2H, d, *J* = 7.6, C*H_2*SH), 7.28, 7.44 (4H, 2d, *J* = 8.2, ArH); δ_C 22.1, 25.4, 28.4 (5C, 5xring CH_2), 38.7 (CH_2SH), 72.9 (COH), 124.9, 127.75, 139.3, 148.25 (6C, ArC); *m/z* 224 (M^+, 1%), 222 (20), 204 (38),179 (15), 172 (16), 171 (100), 166 (12), 151 (12), 145(28), 143 (13), 141 (10),

133 (34), 129 (16), 128 (18), 117 (10), 115 (19), 91 (39), 79 (13), 77 (18), 55 (18), 51 (10), 45 (22) (Found: M^+, 222.1086. $C_{13}H_{18}OS$ requires M, 222.1078).

1-(3-Dimethylaminomethylphenyl)-2,2-diethyl-1-propanol (**8p**): ν (film) 3405 (OH), 3062, 3029, 1674, 1605 cm^{-1} (C=C-H); δ_H 0.91 (9H, s, 3xCH_3), 2.16 (6H, s, 2xCH_3N), 3.02 (1H, br s, HO), 3.39 (2H, s, CH_2N), 4.35 (1H, s, CHO), 7.16-7.29 (4H, m, ArH); δ_C 25.95 (3C, 3xCH_3), 35.5 [*C*(CH_3)$_3$], 45.1 (2C, 2xCH_3N), 64.2 (ArCH_2), 82.0 (CHO), 126.4, 127.3, 128.0, 128.5, 137.5, 142.5 (6C, ArC); *m/z* 222 (M^++1, 3.6%), 221 (M^+, 29), 165 (10), 164 (61), 121 (42), 120 (12), 119 (46), 91 (27), 77 (10), 58 (82), 57 (20), 46 (18), 44 (100), 43 (14), 42 (26) (Found: M^+, 221.1779. $C_{14}H_{23}NO$ requires M, 221.1780).

1-(3-Dimethylaminomethylphenyl)-1-cyclohexanol (**8q**): ν (film) 3363 (OH), 3062, 3028, 1605 cm^{-1} (C=C-H); δ_H 1.63-2.02 (10H, m, 5xring CH_2), 2.20 (6H, s, 2xCH_3N), 3.41, 3.82 (2H, 2s, CH_2N), 7.15-7.44 (4H, m, ArH); δ_C 22.1, 25.6, 38.8 (5C, 5xring CH_2), 45.3 (2C, 2xCH_3N), 64.5 (Ar*C*H_2), 72.9 (COH), 123.3, 127.4, 127.9, 128.5, 138.4, 149.6 (6C, ArC); *m/z* 234 (M^++1, 2.1%), 233 (M^+, 13), 172 (12), 58 (100), 44 (64), 42 (18) (Found: M^+, 233.1782. $C_{15}H_{23}NO$ requires M, 233.1780).

1-(2-Diallylaminomethylphenyl)-2-methyl-1-propanol (**8r**): ν (film) 3385 (OH), 3074, 3016, 1642 (C=C-H), 922 cm^{-1} (C-O); δ_H 0.71, 1.19 (6H, d, J = 6.4, 2xCH_3), 2.20 [1H, m, C*H*(CH_3)$_2$], 3.06 (4H, m, 2xNCH_2), 3.62, 3.75 (2H, 2d, J = 13.0, CH_2N), 4.15 (1H, d, J = 9.4, CHO), 5.19 (4H, m, 2xHC=C*H*$_2$), 5.88 (2H, m, 2x*H*C=CH_2), 7.17-7.32 (4H, m, ArH); δ_C 20.1, 20.2 (2C, 2xCH_3), 32.2 [*C*H(CH_3)$_2$], 55.9, 57.4 (3C, 3xCH_2), 80.2 (CHO), 119.1, 126.8, 127.9, 128.9, 132.2, 134.0, 135.8, 143.5 (10C, 2xHC=CH_2 and ArC); *m/z* 259 (M^+, 0.6%), 216 (15), 120 (10), 119 (100), 98 (53), 91 (26), 43 (13) (Found: M^+, 259.1942. $C_{17}H_{25}NO$ requires M, 259.1936).

1-(2-Diallylaminomethylphenyl)-2,2-dimethyl-1-propanol (**8s**): ν (film) 3416 (OH), 3074, 1637 (C=C-H), 1091 cm^{-1} (C-O); δ_H 0.98 (9H, s, 3xCH_3), 2.98 (2H, dd, J = 13.7, 7.2, 2xNCH*H*), 3.11 (2H, dd, J = 13.7, 6.4, 2xNC*H*H), 3.46, 3.92 (2H, 2d, J = 12.8, CH_2N), 4.63 (1H, s, CHO), 5.15 (4H, m, 2xHC=C*H*$_2$), 5.54 (2H, m, 2x*H*C=CH_2), 7.14-7.35 (4H, m, ArH); δ_C 26.8 (3C, 3xCH_3), 37.2 [*C*(CH_3)$_3$], 55.8, 58.0 (3C, 3xCH_2), 81.7 (CHO), 118.6, 126.7, 126.8, 130.4, 132.1, 134.4, 141.9 (10C, 2xHC=CH_2 and ArC); *m/z* 255 (M^+-18, 2.8%), 212 (50), 159 (17), 146 (10), 132 (23), 131 (36), 130 (47), 129 (95), 128 (60), 116 (12), 115 (18), 104 (26), 99 (100), 98 (14), 91 (32), 81 (85), 79 (14), 77 (13), 65 (11), 57 (19), 55 (41), 53 (12), 43 (37), 42 (11) (Found: M^+, 273.2062. $C_{18}H_{27}NO$ requires M, 273.2093).

1-(2-Diallylaminomethylphenyl)-1-cyclohexanol (**8t**): ν (film) 3141 (OH), 3076, 3012, 1643 cm^{-1} (C=C-H); δ_H 1.55-1.99 (10H, m, 5xring CH_2), 3.10 (4H, d, J = 6.7, 2xCH_2N), 3.86 (2H, s, CH_2N), 5.18 (4H, m, 2xHC=C*H*$_2$), 5.90 (2H, m, 2x*H*C=CH_2), 7.12-7.42 (4H, m, ArH); δ_C 22.1, 25.9, 39.3 (5C, 5xring CH_2), 55.1, 59.4 (3C, 3xCH_2), 73.8 (COH), 119.05, 126.1, 127.2, 127.95, 133.5, 133.6, 134.4, 149.3 (10C, 2xHC=CH_2 and ArC); *m/z* 285 (M^+, 0.9%), 266 (14), 244 (36), 242 (24), 227 (12), 226 (57), 224 (11), 187 (13), 186 (40), 184 (20), 172 (16), 171 (25), 170 (16), 169 (18), 167 (10), 157 (13), 146 (10), 145 (34), 144 (19), 143 (23), 142 (32), 141 (32), 131 (18), 130 (21), 129 (84), 128 (31), 127 (11), 119 (10), 117 (26), 116 (12), 115 (33), 110 (24), 105 (18), 98 (11), 96 (59), 94 (11), 92 (13), 91 (100), 79 (17), 77 (21), 70 (19), 68 (17), 67 (12), 65 (19), 56 (38), 55 (50), 54 (10), 53 (11), 44 (38), 43 (23), 42 (40) (Found: M^+, 285.2103. $C_{19}H_{27}NO$ requires M, 285.2093).

1-(4-Diallylaminomethylphenyl)-2,2-dimethyl-1-propanol (**8u**): ν (film) 3443 (OH), 3077, 3009, 1647 (C=C-H), 1055 cm^{-1} (C-O); δ_H 0.92 (9H, s, 3xCH_3), 1.95 (1H, br s, OH), 3.06 (4H, d, J = 6.7, 2xNCH_2), 3.56 (2H, s,CH_2N), 4.37 (1H, s, CHO), 5.15 (4H, m, 2xHC=C*H*$_2$), 5.87 (2H, m, 2x*H*C=CH_2), 7.25 (4H, m, ArH); δ_C 25.9

(3C, 3xCH$_3$), 35.6 [*C*(CH$_3$)$_3$], 56.4, 57.2 (3C, 3xCH$_2$), 82.2 (CHO), 117.4, 127.4, 128.1, 135.8, 138.3, 140.8 (10C, 2xHC=CH$_2$ and ArC); *m/z* 275 (M$^+$+2, 0.6%), 274 (M$^+$+1, 6), 273 (M$^+$, 28), 246 (13), 217 (16), 216 (100), 177 (12), 174 (15), 121 (47), 120 (13), 119 (14), 110 (27), 96 (68), 93 (15), 92 (17), 91 (55), 79 (16), 77 (12), 70 (20), 68 (18), 57 (53), 56 (15), 43 (19), 42 (30) (Found: M$^+$, 273.2120. $C_{18}H_{27}NO$ requires M, 273.2093).

1-(4-Diallylaminomethylphenyl)-1-cyclohexanol (**8v**): ν (film) 3383 (OH), 3079, 3010, 1653 cm^{-1} (C=C-H); δ_H 1.59-1.89 (10H, m, 5xring CH$_2$), 3.07 (4H, d, J = 6.1, 2xCH$_2$N), 3.58 (2H, s, CH$_2$N), 5.16 (4H, m, 2xHC=C*H*$_2$), 5.88 (2H, m, 2x*H*C=CH$_2$), 7.29 (2H, d, J = 8.2, 2xArH), 7.43 (2H, d, J = 10.2, 2xArH); δ_C 22.2, 25.5, 38.8 (5C, 5xring CH$_2$), 56.3, 57.1 (3C, 3xCH$_2$), 73.0 (COH), 117.35, 124.4, 128.7, 135.8, 137.7, 148.0 (10C, 2xHC=CH$_2$ and ArC); *m/z* 286 (M$^+$+1, 3.6%), 285 (M$^+$, 0.9), 267 (20), 258 (13), 189 (37), 172 (19), 171 (77), 133 (12), 129 (16), 115 (17), 110 (37), 107 (15), 105 (18), 104 (12), 99 (17), 96 (100), 91 (31), 81 (12), 79 (13), 77 (10), 68 (15), 56 (13), 55 (19), 43 (10), 42 (26) (Found: M$^+$, 285.2091. $C_{19}H_{27}NO$ requires M, 285.2093).

Cyclisation of Diols **2c** *and* **8c**. *Isolation of Compounds* **3c** *and* **9c**. *General Procedure.*- To a solution of the corresponding diol (1 mmol) in ether (5 ml) was added concentrated HCl (0.5 ml) and the mixture was stirred for *ca.* 12 h. Then, water (3 ml) was added to the resulting mixture and it was extracted with ethyl acetate (3x10 ml), the organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo* (15 Torr) to give the crude pure title compounds in almost quantitative yields (>99%). Physical, spectroscopic and analytical data, as well as literature references for known compounds, follow.

3,3-Diethyl-3,4-dihydro-1H-2-benzopyran (**3c**): This compound was characterised by comparation of its chromatographic and spectroscopic data with those described in the literature.[14]

Spiro[cyclohexane-1,1'-(1',3'-dihydroisobenzofuran)] (**9c**): R_f 0.35 (hexane/ethyl acetate: 8/2); ν (film) 3080, 3029, 1621, 1614 (C=C-H), 1046 cm^{-1} (C-O); δ_H 1.61, 1.82 (10H, m, 5xring CH$_2$), 5.06 (2H, s, CH$_2$O), 7.19-7.26 (4H, m, ArH); δ_C 22.6, 25.3, 36.8 (5C, 5xring CH$_2$), 70.6 (CH$_2$O), 86.9 (1C, COH), 120.7, 121.0, 127.1, 127.2, 138.8, 146.9 (6C, ArC); *m/z* 189 (M$^+$+1, 4.8%), 188 (M$^+$, 31), 146 (19), 145 (100), 132 (10), 131 (10), 117 (24), 115 (14), 104 (10), 91 (13) (Found: M$^+$, 188.1194. $C_{13}H_{16}O$ requires M, 188.1201).

DTBB-Catalysed Lithiation of 3-Methoxybenzyl Chloride (**10**) *in the Presence of Electrophiles. Isolation of Compounds* **12**. *General Procedure.*- To a green suspension of lithium (0.15 g, 20 mmol) and DTBB (0.026 g, 0.1 mmol) in THF (5 ml) was slowly added a solution of compound **10** (0.29 ml, 2 mmol) and the corresponding electrophile (2 mmol) in THF (3 ml) for *ca.* 1h at -78°C. The resulting mixture was stirred for 10 additional min at the same temperature, being then hydrolysed with water (10 ml) allowing the temperature to rise to 20°C. Then, it was worked-up as it was described above for compounds **2** and **8**, giving the pure title compounds. Yields and physical data are included in Table 3. Spectroscopic and analytical data follow.

3-Methyl-1-(3'-methoxyphenyl)-2-butanol (**12a**):[11] ν (film) 3453 (OH), 3034, 1601, 1585 (C=C-H), 1258 cm^{-1} (C-O); δ_H 0.99 (6H, d, J = 8.2, 2xCH$_3$), 1.63 (1H, br s, OH), 1.76 [1H, m, C*H*(CH$_3$)$_2$], 2.56 (1H, dd, J = 13.4, 9.5, ArCH*H*), 2.84 (1H, m, ArC*H*H), 3.58 (1H, m, CHO), 3.79 (3H, s, CH$_3$O), 6.73, 7.22 (4H, 2m, ArH); δ_C 17.4, 18.8, (2C, 2xCH$_3$), 33.0 [*C*H(CH$_3$)$_2$], 40.8 (Ar*C*H$_2$), 55.1 (CH$_3$O), 77.4 (CHO), 111.7, 115.0, 121.6, 129.5, 14.7, 159.7 (6C, ArC); *m/z* 194 (M$^+$, 2.1%), 108 (100), 107 (25), 91 (11), 87 (13), 77 (10), 69 (20), 57 (22), 45 (17), 43 (19).

3,3-Dimethyl-1-(3'-methoxyphenyl)-2-butanol (**12b**): ν (film) 3471 (OH), 1601, 1585 (C=C), 1263 cm^{-1} (C-O); δ_H 0.99 (9H, s, 3xCH$_3$), 1.53 (1H, br s, OH), 2.44 (1H, dd, J = 13.4, 10.7, ArCH*H*), 2.88 (1H, dd, J = 13.4, 1.8, ArC*H*H), 3.43 (1H, def. d, J = 10.7, CHO), 3.80 (3H, s, CH_3O), 6.79, 7.22 (4H, 2m, ArH); δ_C 25.8 (3C, 3xCH_3), 34.8 [$C(CH_3)_3$], 38.5 (ArCH_2), 55.1 (CH_3O), 80.45 (CHO), 111.7, 114.9, 121.6, 129.5, 141.5, 159.8 (6C, ArC); *m/z* 209 (M^++1, 2.2%), 208 (M^+, 15), 175 (12), 151 (19), 123 (23), 122 (100), 121 (49), 107 (22), 92 (17), 91 (47), 90 (11), 87 (28), 79 (10), 78 (13), 77 (20), 69 (39), 65 (16), 57 (34), 45 (37), 43 (24) (Found: M^+, 208.1458. $C_{13}H_{20}O_2$ requires M, 208.1463).

3'-Methoxybenzylcyclohexanol (**12c**): ν (film) 3451 (OH), 3052, 3026, 1601, 1583 (C=C-H), 1261 cm^{-1} (C-O); δ_H 1.23-1.60 (10H, m, 5xring CH_2), 2.71 (2H, s, ArCH_2), 3.79 (3H, s, CH_3O), 6.78, 7.22 (4H, 2m, ArH); δ_C 22.1, 25.7, 37.3 (5C, 5xring CH_2), 48.9 (ArCH_2), 55.1 (CH_3O), 71.1 (CO), 111.6, 116.3, 123.0, 129.0, 138.7, 159.3 (6C, ArC); *m/z* 220 (M^+, 1.4%), 202 (44), 159 (13), 123 (16), 122 (100), 121 (49), 107 (10), 99 (47), 92 (10), 91 (35), 81 (70), 80 (10), 79 (31), 78 (15), 77 (22), 65 (17), 55 (29), 53 (13), 51 (11), 43 (26) (Found : M^+, 220.1464. $C_{14}H_{20}O_2$ requires M, 220.1463).

ACKNOWLEDGEMENTS

This work was generously supported by DGICYT from the Spanish MEC (no. PB94-1514). F.F.H. thanks ASAC PHARMACEUTICAL INTERNATIONAL for a grant.

REFERENCES AND NOTES

1. See, for instance: Wakefield, B. J. *Organolithium Methods*, Academic Press: London, 1988.
2. (a) Akiyama, S.; Hooz, J. *Tetrahedron Lett.* **1973**, 4115-4118. (b) Schlenk, W.; Holtz, J. *Ber. Dtsch. Chem. Ger.* **1917**, *50*, 262-274. (c) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron* **1992**, *48*, 4593-4600.
3. (a) For a monograph, see: Blomberg, C. *The Barbier Reaction and Related One-step Processes*; Springer-Verlag: Berlin, 1993. (b) Alonso, F.; Yus, M. *Recent Res. Devel. Org. Chem.*, in press.
4. (a) See reference 3a pp. 79 and 83. (b) For a recent paper on the use of 2-bromobenzyl bromide for benzylic coupling by bromine/lithium exchange, see: Warren, S.; Wyatt, P.; McPartlin, M.; Woodroffe, T. *Tetrahedron Lett.* **1996**, *37*, 5609-5612.
5. (a) For the first account on this reaction, see: Yus, M.; Ramón, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 398-400. For a recent review, see: Yus, M. *Chem. Soc. Rev.* **1996**, 155-161.
6. For the last paper on this topic from our laboratory, see: Guijarro, A.; Yus, M. *Tetrahedron* **1996**, *52*, 1797-1810.
7. For a preliminary communication, see: Gómez, C.; Huerta, F. F.; Yus, M. *Tetrahedron Lett.* **1997**, *38*, 687-690.
8. For the preparation of the equivalent magnesiated *o*-derivative (1-magnesacyclobutabenzene), see: de Boer, H. J. R.; Akkerman, O. S.; Bickelhaupt, F. *Organometal. Synth.* **1988**, *4*, 396-398.
9. Under the reaction condition (-50°C), the nuclear Cl/Li exchange works very slowly, so for short reaction times (*ca.* 20 min), no aromatic lithiation was observed; we never found reaction products in which the electrophile was attached to the aromatic ring for the two-step process. See, also: Guijarro, A.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 469-482.
10. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals,* 3rd edn.; Pergamon Press: Oxford, 1988.
11. For this product was not possible to obtain the corresponding HRMS due to its decomposition.
12. For this compound was not possible to obtain the corresponding HRMS due to the low intensity or the the absence of the M^+ signal.
13. When amines **6** were used as starting materials, an acidic-basic work-up gave essentially pure products **8**.
14. Almena, J. ; Foubelo, F. ; Yus, M. *Tetrahedron* **1995**, *51*, 3351-3364.