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Generation of Allylic and Benzylic Organolithium Reagents from the Corresponding Ester, Amide, Carbonate, Carbamate and Urea Derivatives[†]

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Abstract

The reaction of different allylic and benzylic non-enolisable esters or amides (**1**), carbonates (**4**), carbamates (**6**, **7**) and ureas (**8**) with an excess of lithium powder and a catalytic amount of naphthalene (10%) in the presence of an electrophile [*i*PrCHO, *t*BuCHO, PhCHO, Me₂CO, Et₂CO, (CH₂)₅CO, Ph₂CO, Me₃SiCl] in THF at different temperatures (-78, -30 or 0°C) leads, after hydrolysis with water, to the corresponding allylated or benzylated products (**2**). © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: lithiation; catalysis; lithium and compounds; allylation; benzylation

I. Introduction

Typical methods for the preparation of organolithium reagents involve halogenated derivatives as starting materials. However, this general procedure is not useful for the generation of allylic or benzylic lithium intermediates due to the almost exclusive formation of Wurtz-type products [1-3]. Other alternative methodologies have been reported, such as: (a) the direct deprotonation of the corresponding allylic or benzylic hydrocarbons with an alkyllithium, which needs the use of a co-reactant such as an alkoxide (in general potassium

[†] This paper is dedicated to Professor Reinhard W. Hoffmann on occasion of his 65 birthday.

tert-butoxide) [4,5] or an amine [e.g. tetramethylethylenediamine (TMEDA) or 1,4-diazabicyclo[2.2.2]octane (DABCO)] [6] and leads to the corresponding “mixed” carbanions or the complex between the organolithium compound and the amine, respectively; (b) a mercury-lithium or a tin-lithium transmetallation [7], which has been applied to the preparation of benzyl [8] or allyllithium [9], respectively; (c) the reductive cleavage of allyl phenyl ether with lithium, which has been successfully used in the case of allyllithium [10,11].

On the other hand, in recent years we have used an arene-catalysed lithiation [12-14]¹ of different substrates in order to prepare organolithium reagents under very mild reaction conditions. Thus, we could prepare simple organolithium reagents starting from non-halogenated materials [15,16],² functionalised organolithium compounds [17,18] from chlorinated materials [19] or heterocycles [20,21],² and polylithiated synthons [22,23]² using polychlorinated materials as precursors and working under Barbier-type reaction conditions [24,25].³ Concerning allylic derivatives, we have applied the mentioned arene-catalysed lithiation for the *in situ* generation of allylic and benzylic organolithium reagents starting from the corresponding mesylates [26], phosphates [27] and benzyl alcohols or their *O*-silylated derivatives [28,29]. For other allyl or benzyl derivatives such as all type of alcohols, amines or amides, the same reaction has been reported to be useful only for carrying out the corresponding deallylation or debenzylation, after work-up [30]. In this paper we describe the application of the naphthalene-catalysed lithiation for the generation of allylic and benzylic organolithiums starting from different allylic and benzylic esters, amides, carbonates, carbamates and ureas under Barbier-type reaction conditions.

II. Results and discussion

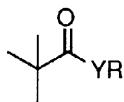
The reaction of benzylic pivalates **1a,b** and allylic or benzylic pivalamides **1c-e** with an excess of lithium powder (*ca.* 1:10 molar ratio) and a catalytic amount of naphthalene (1:0.2 molar ratio, 10 mol %) in the presence of the corresponding electrophile [1:2.4 molar ratio; E = Et₂CO, (CH₂)₅CO, Me₃SiCl] in THF under the conditions shown in Table 1 led, after hydrolysis with water, to the corresponding allylic derivatives **2** (Chart 1 and Table 1). The reaction worked better for benzylic than for allylic compounds: even having two allyl groups, compound **1c** gave only 15% yield using 3-pentanone (compare Table 1, entry 3 with the other entries). When *N*-benzyl-*N*-methylacetamide was used instead of the corresponding pivalamide **1d**, no reaction was observed after 8 h at -78°C; in this case a possible formation of an enolate could prevent the benzylic cleavage. On the other hand, it is necessary to perform the above mentioned process under Barbier conditions (lithiation in the presence of the electrophile): when compounds **1c** or **1d** were lithiated under naphthalene catalysis at -78°C, the starting material disappeared after 1 h, and compounds **3c**

¹ For the first account on this reaction [12], as well as a solid-supported version [13] and a recent review [14], see the included references.

² For the last paper on this topic from our laboratory, as well as a recent review, see the references included in the text in each case.

³ For a monograph [24] and a recent review on the Barbier reaction [25], see the corresponding references.

and **3d** were isolated, after hydrolysis, in 50 and 28%⁴ yield, respectively. These products are formed by *in situ* addition of the organolithium intermediate (allyl or benzyllithium) to the starting amide.



1a : Y = O, R = PhCH₂
1b : Y = O, R = PhCHMe
1c : Y = CH₂=CHCH₂N, R = CH₂=CHCH₂
1d : Y = MeN, R = PhCH₂
1e : Y = MeN, R = PhCHMe

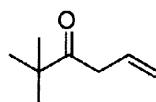
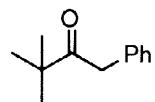
**3c****3d**

Table 1
 Preparation of compounds **2** (RX) from pivalates or pivalamides **1**

Entry	Starting material	Electrophile E	Reaction conditions		Product ^a			Yield (%) ^b
			T (°C) / t (h)	No.	R	X		
1	1a	(CH ₂) ₅ CO	-78 / 5	2m	PhCH ₂	(CH ₂) ₅ COH	65	
2	1b	Et ₂ CO	0 / 2	2q	PhCHMe	Et ₂ COH	22	
3	1c	Et ₂ CO	-78 / 5 ^c	2b	CH ₂ =CHCH ₂	Et ₂ COH	15 ^{c,d}	
4	1d	(CH ₂) ₅ CO	-78 / 5	2m	PhCH ₂	(CH ₂) ₅ COH	36	
5	1e	Et ₂ CO	0 / 2	2q	PhCHMe	Et ₂ COH	92	
6	1e	Me ₃ SiCl	0 / 2	2s	PhCHMe	Me ₃ Si	75	

^a All products **2** were >95% pure (300 MHz ¹H NMR and/or GLC).

^b Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the allylic or benzylic starting material.

^c No improvement in the yield was observed after allowing the temperature to rise to 0°C.

^d This yield refers to the formation of only one mol of allyllithium per mol of compound **1c** (see text).

Starting materials **1a-d** were easily prepared by acylation of the corresponding alcohol or amine in the presence of triethylamine [31]. Methylation of *N*-benzylpivalamide with methyl iodide afforded compound **1e** [32].

In the second part of this study we considered allylic or benzylic carbonates as starting materials for the *in situ* generation of the corresponding organolithium reagents. Thus, applying the protocol shown above to the carbonates **4a-f** and different electrophiles [E = iPrCHO, tBuCHO, PhCHO, Me₂CO, Et₂CO, (CH₂)₅CO, Ph₂CO, Me₃SiCl] under Barbier-type reaction conditions, the expected products **2** were obtained (Chart 1 and Table 2). Some remarks about this process are: (a) Although in some cases the reaction worked nicely in a

⁴ A 32% isolated yield was obtained performing the same reaction at temperatures ranging between -78 and 0°C.

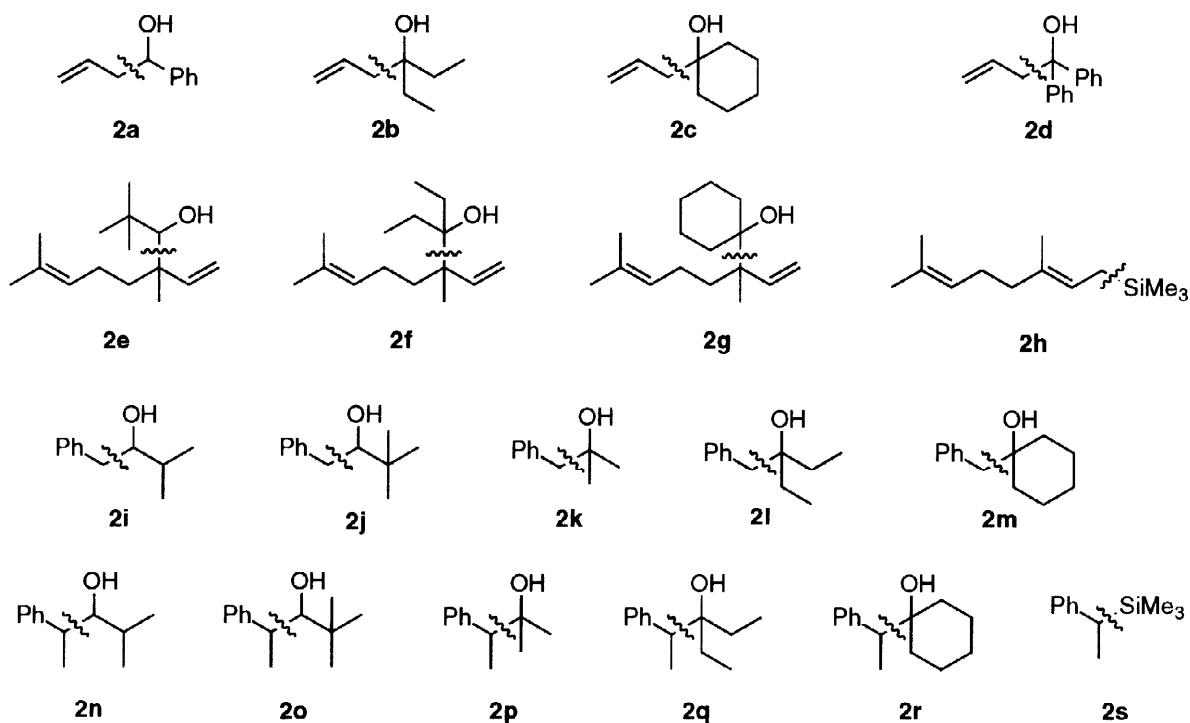


Chart 1. Products 2 ($R-\ddot{\sigma}-X$) prepared.

two-step fashion (Table 2, entry 3 and footnote d), in general the reaction gave better yields under Barbier conditions: for instance, the preparation of compound **2l** from the carbonate **4d** gave 25% yield in the sequential version, the yield being 50% under Barbier conditions (Table 2, entry 14). (b) In some cases the reaction conditions were optimised: the naphthalene-catalysed lithiation of starting materials **4c** and **4d** was performed at different temperatures (-78, -30 and 0°C) in order to find the best conditions, these being 0 and -30°C, respectively (Table 2, entries 8 and 14, and footnotes f-h). (c) In the case of the starting material **4f**, and with aldehydes as electrophiles, the corresponding 1:1 mixture of diastereoisomers was obtained (Table 2, entries 19 and 20). (d) The use of a different arene, such as 4,4'-di-*tert*-butylbiphenyl (DTBB) [33],⁵ under different reaction temperatures did not improve the yields obtained using naphthalene (Table 2, entry 14 and footnotes g and h). (e) In the case of the geranyl carbonate **4c**, the structure of the final product **2** depends on the type of electrophile used: whereas with carbonyl compounds products **2e-g** were the only ones isolated, resulting from a S_E' -type reaction, in the case of chlorotrimethylsilane compound **2h** was obtained, coming from a S_E reaction at the C1 carbon atom. (f) Finally, it is worthy to note that the presence of two allyl or benzyl groups in the starting carbonate (see compounds **4a** and **4e**) did not help for the preparation of two equivalents of the corresponding organolithium: a probable explanation for that is that after the first lithiation, a lithium carbonate of type **5** is formed, which decomposes by loss of carbon dioxide

⁵ For a comparative study on the use of different arenes as electron carrier, see reference [33].

giving an alcoholate which is resistant to further reductive cleavage under the reaction conditions used.

Table 2
Preparation of compounds **2** (RX) from carbonates **4**

Entry	Starting material	Electrophile E	Reaction conditions		Product ^a		
			T (°C) / t (h)	No.	R	X	Yield (%) ^b
1	4a	PhCHO	-78→20 / 4	2a	CH ₂ =CHCH ₂	PhCHOH	22 ^c
2	4a	(CH ₂) ₅ CO	-78→20 / 4	2c	CH ₂ =CHCH ₂	(CH ₂) ₅ COH	20 ^c
3	4a	Ph ₂ CO	-78→20 / 4	2d	CH ₂ =CHCH ₂	Ph ₂ COH	65 ^{c,d}
4	4b	PhCHO	0 / 2	2a	CH ₂ =CHCH ₂	PhCHOH	38
5	4b	Et ₂ CO	0 / 2	2b	CH ₂ =CHCH ₂	Et ₂ COH	37
6	4b	(CH ₂) ₅ CO	0 / 2	2c	CH ₂ =CHCH ₂	(CH ₂) ₅ COH	20
7	4c	^t BuCHO	0 / 2	2e	- ^e	^t BuCHOH	56
8	4c	Et ₂ CO	0 / 2	2f	- ^e	Et ₂ COH	46 (38, ^f 22 ^g)
9	4c	(CH ₂) ₅ CO	0 / 2	2g	- ^e	(CH ₂) ₅ COH	22
10	4c	Me ₃ SiCl	0 / 2	2h	- ^e	Me ₃ Si	64
11	4d	ⁱ PrCHO	-30 / 2	2i	PhCH ₂	ⁱ PrCHOH	50
12	4d	^t BuCHO	-30 / 2	2j	PhCH ₂	^t BuCHOH	62
13	4d	Me ₂ CO	-30 / 2	2k	PhCH ₂	Me ₂ COH	30
14	4d	Et ₂ CO	-30 / 2	2l	PhCH ₂	Et ₂ COH	50 (44, ^g 30 ^h)
15	4d	(CH ₂) ₅ CO	-30 / 2	2m	PhCH ₂	(CH ₂) ₅ COH	48
16	4e	^t BuCHO	-30 / 2	2j	PhCH ₂	^t BuCHOH	79 ^c
17	4e	Me ₂ CO	-30 / 2	2k	PhCH ₂	Me ₂ COH	30 ^c
18	4e	Et ₂ CO	-30 / 2	2l	PhCH ₂	Et ₂ COH	76 ^c
19	4f	ⁱ PrCHO	-30 / 2	2n	PhCHMe	ⁱ PrCHOH	36 ⁱ
20	4f	^t BuCHO	-30 / 2	2o	PhCHMe	^t BuCHOH	66 ⁱ
21	4f	Me ₂ CO	-30 / 2	2p	PhCHMe	Me ₂ COH	40
22	4f	Et ₂ CO	-30 / 2	2q	PhCHMe	Et ₂ COH	83 (66 ^f)
23	4f	(CH ₂) ₅ CO	-30 / 2	2r	PhCHMe	(CH ₂) ₅ COH	32
24	4f	Me ₃ SiCl	-30 / 2	2s	PhCHMe	Me ₃ Si	40

^{a,b} See footnotes a and b in Table 1, respectively.

^c Yield corresponding to the formation of one mol of allyllithium per mol of the starting material **4a**.

^d Yield corresponding to the two-step reaction.

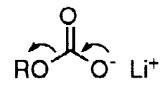
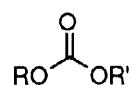
^e For the structure of the group R, see Chart 1.

^f Yield corresponding to the reaction at -30°C.

^g Yield corresponding to the reaction at -78°C.

^h Yield corresponding to the reaction at 0°C.

ⁱ A ca. 1:1 diastereoisomeric mixture was obtained (300 MHz ¹H NMR).

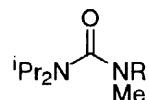
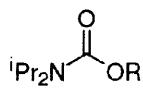
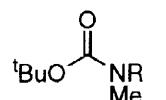


4a : R = R' = $\text{CH}_2=\text{CHCH}_2$
4b : R = $\text{CH}_2=\text{CHCH}_2$, R' = ^tBu
4c : R = geranyl, R' = ^tBu
4d : R = PhCH_2 , R' = ^tBu
4e : R = R' = PhCH_2
4f : R = PhCHMe , R' = ^tBu

5[R = $\text{CH}_2=\text{CHCH}_2$, PhCH_2]

Starting carbonate **4a** was commercially available, whereas **4b-d** and **4f** were prepared from the corresponding alcohols and di-*tert*-butyl dicarbonate in the presence of a base [*n*-butyllithium or 4-(*N,N*-dimethylamino)pyridine (DMAP)] [34]. Finally, carbonate **4e** was obtained from benzyl alcohol and benzyl chloroformate using *n*-butyllithium as the corresponding base.

In the last part of this study we applied the here described naphthalene-catalysed lithiation to *N*- and *O*-benzyl carbamates and ureas. Thus, starting from compounds **6-8** and using pivalaldehyde and 3-pentanone as electrophiles the corresponding products **2** were obtained (Chart 1 and Table 3).



6a : R = PhCH_2
6b : R = PhCHMe

7a : R = PhCH_2
7b : R = PhCHMe

8a : R = PhCH_2
8b : R = PhCHMe

Table 3
Preparation of compounds **2** (RX) from carbamates **6**, **7** and ureas **8**

Entry	Starting material	Electrophile E	Reaction conditions		Product ^a			Yield (%) ^b
			T (°C)	t (h)	No.	R	X	
1	6a	Et_2CO	-78	5	2l	PhCH_2	Et_2COH	67
2	6b	$^t\text{BuCHO}$	-30	2	2o	PhCHMe	$^t\text{BuCHOH}$	47 ^c
3	6b	Et_2CO	-30	2	2q	PhCHMe	Et_2COH	31
4	7a	$^t\text{BuCHO}$	-30	2	2j	PhCH_2	$^t\text{BuCHOH}$	65
5	7a	Et_2CO	-30	2	2l	PhCH_2	Et_2COH	62
6	7b	$^t\text{BuCHO}$	-30	2	2o	PhCHMe	$^t\text{BuCHOH}$	67 ^c
7	7b	Et_2CO	-30	2	2q	PhCHMe	Et_2COH	79
8	8a	Et_2CO	-78	5	2l	PhCH_2	Et_2COH	30
9	8a	$^t\text{BuCHO}$	-30	2	2o	PhCH_2	$^t\text{BuCHOH}$	52 ^c
10	8b	Et_2CO	-30	2	2q	PhCHMe	Et_2COH	39

^{a,b,c} See footnotes a, b and c in Table 1, respectively.

Starting carbamates **6** were prepared from the corresponding amines and di-*tert*-butyl dicarbonate using DMAP as the base [34]. Compounds **7** and **8** were obtained from the corresponding alcohols and amines, respectively, and commercially available diisopropylcarbamoyl chloride using triethylamine as the base [31].

III. Conclusion

From the results reported here, we conclude that allylic and benzylic non-enolisable esters, amides as well as carbonates, carbamates or ureas can be used as starting materials for the *in situ* generation of allylic or benzylic organolithium intermediates, which in the presence of several electrophiles (mainly carbonyl compounds), under Barbier-type reaction conditions, can be trapped to give the corresponding allylated or benzylated products. We think that even working in general with moderate yields this methodology can be useful from a synthetic point of view.

IV. Experimental section

IV.1. General

For general information see reference [35]. 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 mm film thickness, OV-1 stationary phase), using nitrogen (2 ml/min) as carrier gas, $T_{\text{injector}} = 275^{\circ}\text{C}$, $T_{\text{detector}} = 300^{\circ}\text{C}$, $T_{\text{column}} = 60^{\circ}\text{C}$ (3 min) and 60–270°C (15°C/min), $P = 40$ kPa; t_r values are given in min under these conditions.

IV.2. Preparation of starting esters and amides 1.– Esters and amides **1** were prepared from the corresponding amine or alcohol by reaction with pivaloyl chloride in the presence of triethylamine, following the same procedure previously described by us [30]. Compound **1e** was described by us [30] and was characterised by comparison of its physical and spectroscopic data with those reported in the literature. For other compounds **1**, yields, physical and spectroscopic data, as well as literature references for known compounds, follow.

Benzyl 2,2-Dimethylpropanoate (1a) [36]: Yield 65%; Pale yellow oil, R_f 0.54 (hexane/ethyl acetate: 4/1); t_r 9.27; ν (film) 3020, 1480 (C=CH), 1735 cm⁻¹ (C=O); δ_{H} 1.21 (9H, s, 3xMe), 5.08 (2H, s, CH₂), 7.30 (5H, s, Ph); δ_{C} 27.2 (2C), 38.8, 66.0, 127.6 (2C), 128.4 (3C), 136.4, 178.2; m/z 192 (M⁺, 5%), 91 (98), 65 (24), 57 (100), 51 (11).

1-Phenylethyl 2,2-dimethylpropanoate (1b) [37]: Yield 80%; Pale yellow oil, R_f 0.73 (hexane/ethyl acetate: 4/1); t_r 9.56; ν (film) 1730 cm⁻¹ (C=O); δ_{H} 1.21 (9H, s, Me₃C), 1.50 (3H, d, $J=6.6$, MeCH), 5.85 (1H, q, $J=6.6$, CH), 7.25–7.35 (5H, m, Ph); δ_{C} 22.3, 27.0 (3C), 38.6, 71.0, 125.65 (3C), 127.5 (2C), 128.3, 177.45; m/z 206 (M⁺, 9%), 105 (100), 104 (17), 77 (14), 57 (59), 41 (19).

N,N-Diallyl-2,2-dimethylpropanamide (1c) [38]: Yield 89%; Oil, R_f 0.13 (hexane/ethyl acetate: 4/1); t_r 8.49; ν (film) 3035 (C=CH), 1690 cm⁻¹ (C=O); δ_{H} 1.29 (9H, s, Me₃C), 3.95–4.05 (4H, m, 2xCH₂N), 5.00–5.25 (4H, m, 2xCH₂=CH), 5.60–5.85 (2H, m, 2xCH); δ_{C} 28.35 (3C), 38.7, 48.9 (2C), 116.75 (2C), 133.3 (2C), 177.05; m/z 181 (M⁺, 6%), 166 (28), 140 (46), 124 (70), 96 (24), 85 (15), 84 (19), 82 (32), 81 (43), 80 (15), 79 (20), 70 (25), 68 (20), 57 (76), 56 (50), 55 (31), 42 (27), 41 (100).

N-Benzyl-N,2,2-trimethylpropanamide (1d) [39]: Yield 75%; Pale yellow oil, R_f 0.29 (hexane/ethyl acetate: 4/1); t_r 11.85; ν (film) 3050, 3020, 1480 (C=CH), 1670 cm⁻¹ (C=O); δ_H 1.26 (9H, s, Me₃C), 2.91 (3H, s, MeN), 4.57 (2H, s, CH₂), 7.15-7.25 (5H, m, Ph); δ_C 28.3 (3C), 36.0, 38.8, 53.1, 127.1 (3C), 128.5 (2C), 137.5, 177.7; m/z 205 (M⁺, 13%), 120 (12), 92 (15), 91 (100), 57 (63), 42 (13), 41 (25).

IV.3. Preparation of starting carbonates 4.

IV.3.1. Preparation of carbonates 4b, 4c and 4e. *Method A. General Procedure.* - *n*-BuLi (11 mmol, 6.9 ml 1.6 M solution in hexane) was added dropwise to a solution of the corresponding alcohol (10 mmol) in THF (40 ml), under Ar, at 0°C. After 15 min, a solution of di-*tert*-butyl dicarbonate (for compounds 4b and 4c) or benzyl chloroformate (for compound 4e) (10 mmol) in THF (10 ml) was slowly added and the mixture was stirred at room temperature for 2 h. The reaction was hydrolysed with water (10 ml), acidified with 2M HCl (10 ml) and extracted with ethyl acetate (3x15 ml). The organic layer was washed with saturated NaHCO₃ (5 ml), water (5 ml) and brine (5 ml), and dried over anhydrous Na₂SO₄. Carbonate 4b was isolated pure by distillation of the solvent at atmospheric pressure. For compounds 4c and 4e, the residue obtained after evaporation of the solvent at reduced pressure was purified by column chromatography (silica gel, hexane/ethyl acetate), affording the expected carbonates. Yields, physical, analytical and spectroscopic data, as well as literature references for known compounds, follow.

Allyl tert-butyl carbonate (4b) [40]: Yield 87%; Oil, t_r 4.0; ν (film) 3087, 1650 (C=CH), 1742 (C=O), 1276 cm⁻¹ (CO); δ_H 1.49 (9H, s, Me₃C), 4.55-4.60 (2H, m, CH₂O), 5.20-5.40 (2H, m, CH₂=C), 5.90-6.00 (1H, m, CH=C); δ_C 27.7 (3C), 67.5, 82.1, 118.45, 131.95, 153.25; m/z 102 (M⁺-56, 5%), 57 (66), 43 (33), 41 (100).

tert-Butyl geranyl carbonate (4c): Yield 87%; Oil, R_f 0.49 (hexane/ethyl acetate: 9/1); t_r 11.9; ν (film) 1740 (C=O), 1664 (C=CH), 1277, 1254 cm⁻¹ (CO); δ_H 1.49 (9H, s, Me₃C), 1.60 (3H, s, MeC=CHCH₂O), 1.67, 1.68 (3 and 3H, respectively, 2s, Me₂C=C), 2.00-2.10 (4H, m, CH₂CH₂), 4.59 (2H, d, *J*=7.0, CH₂O), 5.10-5.40 (1 and 1H, respectively, 2m, 2xCH=C); δ_C 16.45, 17.6, 25.6, 26.2, 39.5, 27.75 (3C), 63.7, 81.75, 118.0, 123.7, 131.75, 142.45, 153.6; m/z 198 (M⁺-56, < 1%), 120 (12), 93 (29), 81 (24), 80 (20), 69 (100), 67 (29), 59 (11), 57 (55), 55 (12), 53 (15), 44 (20), 43 (17), 41 (72) (Found: M⁺-C₄H₁₀, 196.1073. C₁₁H₁₆O₃ requires 196.1099).

Dibenzyl carbonate (4e) [41]: Yield 61%; Oil, R_f 0.50 (hexane/ethyl acetate: 4/1); t_r 14.0; ν (film) 3091, 3066, 3035, 1587, 1498 (C=CH), 1746 (C=O), 1264 cm⁻¹ (CO); δ_H 5.16 (4H, s, 2xCH₂), 7.30-7.40 (10H, m, Ph); δ_C 69.65 (2C), 128.25 (4C), 128.5 (6C) 135.15 (2C), 155.0; m/z 180 (M⁺-62, 29%), 107 (63), 92 (37), 91 (100), 79 (60), 77 (32), 65 (39), 51 (22).

IV.3.2. Synthesis of carbonates 4d and 4f. *Method B.* - Carbonates 4d and 4f were prepared from the corresponding alcohol by reaction with di-*tert*-butyl dicarbonate in the presence of 4-(*N,N*-dimethylamino)pyridine, following the same procedure previously described by us for the synthesis of *N*-Boc protected amides [30]. Yields, physical, analytical and spectroscopic data, as well as literature reference for known compound, follow.

Benzyl tert-butyl carbonate (4d) [42]: Yield 50%; Oil, R_f 0.53 (hexane/ethyl acetate: 4/1); t_r 10.0; ν (film) 3066, 3034, 1498 (C=CH), 1740 (C=O), 1277, 1255 cm⁻¹ (CO); δ_H 1.49 (9H, s, Me₃C), 5.09 (2H, s, CH₂), 7.25-7.45 (5H, m, Ph); δ_C 27.7 (3C), 68.65, 82.15, 128.2 (2C), 128.25, 128.45 (2C), 135.6, 153.4; m/z 208 (M⁺, < 1%), 108 (15), 107 (17), 91 (85), 90

(12), 79 (14), 77 (10), 57 (100), 56 (16), 51 (11), 41 (38).

tert-Butyl 1-phenylethyl carbonate (4f): Yield 82%; Oil, R_f 0.47 (hexane/ethyl acetate); t_r 10.0; ν (film) 3065, 3034, 1610, 1493 (C=CH), 1740 (C=O), 1275, 1255 cm^{-1} (CO); δ_H 1.45 (9H, s, Me_3C), 1.56 (3H, d, $J=6.4$, MeCH), 5.66 (1H, q, $J=6.4$, CHMe), 7.25-7.40 (5H, m, Ph); δ_C 22.35, 27.7 (3C), 75.2, 81.9, 125.85 (2C), 127.8, 128.4 (2C), 141.55, 152.85; m/z 165 (M^+-57 , 12%), 122 (17), 121 (23), 107 (23), 105 (84), 104 (78), 103 (13), 79 (42), 78 (25), 77 (56), 57 (100), 56 (36), 55 (10), 52 (10), 51 (39), 50 (15), 44 (45), 43 (90), 41 (72), 40 (11) (Found: $\text{M}^+-\text{C}_4\text{H}_9$, 165.0553. $\text{C}_9\text{H}_9\text{O}_3$ requires 165.0552).

IV.4. Preparation of starting carbamates **6**, **7** and ureas **8**.

IV.4.1. Preparation of carbamates **6.**– Carbamates **6** were prepared from the corresponding amines and di-*tert*-butyl dicarbonate, following the same procedure as for the synthesis of compounds **1** (see section IV.2) [30]. Compound **6a** was described by us [30] and was characterised by comparison of its physical and spectroscopic data with those reported in the literature. For carbamate **6b**, yield, physical and spectroscopic data, as well as literature reference, follow.

tert-Butyl N-methyl-N-(1-phenylethyl)carbamate (6b) [43]: Yield 72%; Oil R_f 0.53 (hexane/ethyl acetate: 7/3); t_r 11.2; ν (film) 3062, 3030, 1603, 1495 (C=CH), 1689 cm^{-1} (C=O); δ_H 1.49 (9H, br. s, Me_3C), 1.49 (3H, d, $J=11.0$, MeCH), 2.58 (3H, s, MeN), 5.47 (1H, br. s, CHN), 7.20-7.35 (5H, m, Ph); δ_C 16.4, 27.85, 28.45 (3C), 52.45, 79.45, 126.85, 126.95 (2C), 128.25 (2C), 141.45, 155.9; m/z 220 (M^+-15 , < 1%), 179 (42), 164 (32), 120 (48), 105 (48), 77 (14), 58 (21), 57 (100), 44 (13), 42 (30), 41 (53).

IV.4.2. Preparation of carbamates **7 and ureas **8**. General Procedure.**– To a solution of diisopropylcarbamoyl chloride (5 mmol) and triethylamine (5 mmol) in CH_2Cl_2 (5 ml), under Ar, was added dropwise the corresponding alcohol (for carbamates **7**) or amine (for ureas **8**) at room temperature, and the mixture was stirred for 4 days (for compounds **7**), 2h (for compound **8a**) or 1 day (for compound **8b**). Ethyl acetate (30 ml) was added and the mixture was washed with 2M HCl (5 ml) and 2M NaOH (5 ml), and dried over anhydrous Na_2SO_4 . Removing of the solvent and column chromatography (silica gel, hexane/ethyl acetate) yielded the expected products **7** and **8**. Compound **8a** was described by us [30] and was characterised by comparison of its physical and spectroscopic data with those reported in the literature. For compounds **7** and **8b**, yields, physical, analytical and spectroscopic data, as well as literature references for known compounds, follow.

Benzyl N,N-diisopropylcarbamate (7a) [44]: Yield 69% Oil, R_f 0.51 (hexane/ethyl acetate: 7/3); t_r 11.7; ν (film) 3065, 3033, 1586, 1497 (C=CH), 1692 cm^{-1} (C=O); δ_H 1.20 (12H, d, $J=6.7$, 4xMe), 3.88 (2H, br. s, 2xCHN), 7.25-7.40 (5H, m, Ph); δ_C 20.9 (4C), 45.85 (2C), 66.4, 127.65, 127.8 (2C), 128.3 (2C), 137.05, 155.4; m/z 235 (M^+ , 2%), 91 (100), 43 (14), 41 (10).

1-Phenylethyl N,N-diisopropylcarbamate (7b) [45]: Yield 60%; Oil, R_f 0.49 (hexane/ethyl acetate: 7/3); t_r 11.8; ν (film) 3064, 3033, 1586, 1495 (C=CH), 1689 cm^{-1} (C=O); δ_H 1.20-1.25 (12H, m, 2x Me_2CH), 1.55 (3H, d, $J=6.7$, MeCH), 3.88 (2H, br. s, 2xCHN), 5.85 (1H, q, $J=6.7$, CHO), 7.25-7.40 (5H, m, Ph); δ_C 21.0 (4C), 22.8, 45.75 (2C), 72.65, 125.95 (2C), 127.35, 128.3 (2C), 142.8, 155.0; m/z 249 (M^+ , 2%), 106 (12), 105 (100), 86 (28), 79 (11), 77 (15), 44 (16), 43 (22), 41 (11).

N,N-diisopropyl-N'-methyl-N'-(1-phenylethyl)urea (8b): Yield 60%; Oil, R_f 0.51 (hexane/ethyl acetate: 7/3); t_r 13.1; ν (film) 3060, 3027, 1584, 1497 (C=CH), 1638 cm^{-1}

(C=O); δ_H 1.30 (12H, d, $J=6.7$, 2xMe₂CH), 1.52 (3H, d, $J=7.3$, MeCH), 2.44 (3H, s, MeN), 3.65 (2H, h, $J=6.7$, 2xCH(Me)₂), 4.97 (1H, q, $J=7.3$, CHMe), 7.20-7.35 (5H, m, Ph); δ_C 16.75, 21.6 (2C), 21.9 (2C), 31.65, 47.4 (2C), 55.4, 126.75, 127.15 (2C), 128.25 (2C), 142.05, 164.6; m/z 262 (M⁺, 9%), 134 (24), 105 (99), 100 (46), 86 (65), 79 (14), 77 (19), 58 (57), 56 (12), 44 (34), 43 (100), 42 (35), 41 (31) (Found: M⁺-C₆H₁₅, 175.0864. C₁₀H₁₁N₂O requires 175.0871).

IV.5. Naphthalene-catalysed lithiation of compounds 1, 4 and 6-8. General Procedure. - To a green suspension of lithium powder (70 mg, 10 mmol) and naphthalene (27 mg, 0.2 mmol) in THF (5 ml) was slowly added (ca. 1 h) the solution of the substrate **1**, **4** or **6-8** (1 mmol) and the corresponding electrophile (2.4 mmol) in THF (2 ml), under Ar, at the temperature indicated in Tables 1-3. The reaction temperature was kept constant when the reaction was performed at 0 or -30°C. When the initial temperature was -78°C, the reaction was stirred allowing the temperature to rise to 0°C (ca. 5 h). After hydrolysis with water (5 ml) at 0°C, the mixture was extracted with ethyl acetate (3x20 ml). The organic layers were washed with saturated NaHCO₃ (5 ml), water (5 ml) and brine (5 ml), and dried over anhydrous Na₂SO₄. After evaporation of the solvent, the resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate), giving products **2** in the yields indicated in Tables 1-3. Compounds **2a-2d** [26], **2f** [28], **2h** [28], **2i** [26], **2l-2m** [26], **2n** [28], **2p** [46], **2q** [28] and **2s** [28] were already described by us and were characterised by comparison of their physical and spectroscopic data with those reported in the literature. For the rest of compounds **2**, yields, physical, analytical and spectroscopic data, as well as literature references for known compounds, follow.

2,2,4,8-Tetramethyl-4-vinyl-7-nonen-3-ol (2e): Diastereoisomeric mixture 1:0.8; Pale yellow oil, R_f 0.66 (hexane/ethyl acetate: 7/3); t_r 11.1; v (film) 3516 (OH), 3080, 1674, 1634 (C=CH), 1006 cm⁻¹ (CO); δ_H 0.97 (9H, s, Me₃C major), 1.00 (7.5H, s, Me₃C minor), 1.09 (3H, s, MeCCO major), 1.13 (2.5H, s, MeCCO minor), 1.55-1.65 (7+5.8H, m, Me₂C and OH major and minor), 1.80-1.90 (2+1.6H, m, CH₂CMe major and minor) 2.00-2.15 (2+1.6H, m, CH₂C=C major and minor), 3.08 (1H, s, CHO major) 3.16 (0.8H, s, CHO minor) 5.00-5.10 (3+2.5H, m, CH₂=CH and CH=C major and minor), 5.85-5.95 (1+0.8H, m HC=CH₂ major and minor); δ_C 16.2, 17.6 (1+0.8C), 18.4 (2C), 19.85 (1.6 C), 25.8 (3C), 28.8 (2.4C), 22.6, 23.0 (0.8C), 26.6, 30.5 (0.8C), 37.2 (0.8C), 37.6, 46.5, 46.75 (0.8C), 83.3 (0.8C), 83.7 (1+0.8C), 112.1, 113.2 (0.8C), 124.9 (1+0.8C), 131.2, 138.85 (0.8C), 145.5 (0.8C), 145.65; m/z 206 (M⁺-18, < 1%), 123 (17), 95 (46), 87 (24), 69 (100), 68 (11), 67 (17), 57 (34), 55 (33), 45 (16), 43 (26), 41 (98) (Found: M⁺-C₄H₉, 167.1467. C₁₁H₁₉O requires 167.1436).

1-(1,5-Dimethyl-1-vinyl-4-hexenyl)cyclohexanol (2g) [47]: Pale yellow oil, R_f 0.74 (hexane/ethyl acetate: 7/3); t_r 13.1; v (film) 3488 (OH), 3079, 1634 (C=CH), 1129 cm⁻¹ (CO); δ_H 1.01 (3H, s, MeCCO), 1.20-2.20 [21H, m, (CH₂)₅CO, OH, 2xMeC=C, (CH₂)₂CH], 5.02 (1H, dd, $J=17.5$, 1.5, CHH=C), 5.05-5.15 (1H, m, CH=C), 5.20 (1H, dd, $J=11.0$, 1.5, CHH=C), 5.87 (1H, dd, $J=17.7$, 11.0, CH=CH₂); δ_C 16.05, 17.55, 27.65, 21.85, 22.0, 23.35, 25.85, 30.95, 31.7, 34.7, 47.6, 74.8, 115.3, 125.1, 143.75, 131.05; m/z 218 (M⁺, < 1%), 138 (12), 136 (17), 123 (44), 99 (90), 96 (12), 95 (100), 83 (14), 82 (18), 81 (75), 79 (17), 70 (22), 69 (87), 68 (18), 67 (29), 57 (10), 55 (52), 53 (20), 43 (43), 42 (13), 41 (87).

3,3-Dimethyl-1-phenyl-2-butanol (2j) [48]: Pale yellow oil, R_f 0.47 (hexane/ethyl acetate: 4/1); t_r 9.3; v (film) 3472 (OH), 3084, 3062, 3027, 1604, 1494 (C=CH), 1069 cm⁻¹ (CO); δ_H 0.99 (9H, s, Me₃C), 2.46 (1H, dd, $J=13.4$, 11.0, CHH), 2.90 (1H, dd, $J=13.4$, 1.8, CHH), 3.42 (1H, dd, $J=11.0$, 1.8, CHOH), 7.20-7.35 (5H, m, Ph); δ_C 25.85 (3C), 38.35, 77.0,

80.55, 126.25 (2C), 128.55 (2C), 129.3, 139.9; m/z 178 (M⁺, < 1%), 121 (18), 103 (17), 92 (100), 87 (25), 69 (26), 65 (16), 57 (22), 45 (27), 43 (19), 41 (46).

2-Methyl-1-phenyl-2-propanol (2k) [49]: Pale yellow oil, R_f 0.63 (hexane/ethyl acetate: 4/1); t_r 7.2; ν (film) 3404 (OH), 3062, 3028, 1602, 1493 (C=CH), 1153 cm⁻¹ (CO); δ_H 1.22 (6H, s, 2xMe), 2.76 (2H, s, CH₂), 7.10-7.35 (5H, m, Ph); δ_C 29.1 (2C), 49.7, 70.8, 126.45, 128.15 (2C), 130.4 (2C), 137.7; m/z 150 (M⁺, < 1%), 92 (88), 91 (53), 65 (21), 59 (100), 57 (10), 55 (12), 51 (11), 43 (100), 41 (20), 40 (11).

2,2-Dimethyl-4-phenyl-3-pentanol (2o) [50]: Diastereoisomeric mixture 1:0.45; Pale yellow oil, R_f 0.44 (hexane/ethyl acetate: 4/1); t_r 10.0, 10.3; ν (film) 3492 (OH), 3084, 3061, 3026, 1602, 1494, (C=CH), 1028 cm⁻¹ (CO); δ_H 0.83 (4.05H, s, Me₃C minor), 0.93 (9H, s, Me₃C major), 1.30 (3H, d, J =6.7, CHMe major), 1.37 (1.35H, d, J =6.7, CHMe minor), 3.00-3.05 (1+0.45H, m, CHMe major and minor), 3.35-3.45 (1+0.45H, m, CHO major and minor), 7.15-7.35 (5+2.25H, m, Ph major and minor); δ_C 16.4, 22.4 (0.45C), 26.65 (1.35C), 26.8 (3C), 35.85, 41.7 (0.45C), 36.05 (0.45C), 41.1, 83.0 (0.45C), 83.4, 125.95, 126.35 (0.45C), 127.4 (2C), 128.3 (0.90C), 128.4 (2C), 128.85 (0.90C), 144.15 (0.45 C), 148.0; m/z 192 (M⁺, < 1%), 135 (15), 117 (10), 107 (12), 106 (100), 105 (51), 91 (78), 87 (27), 79 (13), 78 (11), 77 (20), 69 (28), 57 (38), 51 (10), 45 (28), 43 (44), 41 (44).

1-(1-Phenylethyl)cyclohexanol (2r) [51]: Pale yellow oil, R_f 0.50 (hexane/ethyl acetate: 7/3); t_r 11.2; ν (film) 3471 (OH), 3082, 3059, 3025, 1602, 1493 (C=CH), 1154 cm⁻¹ (CO); δ_H 1.10-1.90 (11H, m, 5xCH₂ and OH), 1.31 (3H, d, J =7.2, Me), 2.75 (1H, q, J =7.2, CHMe), 7.20-7.30 (5H, m, Ph); δ_C 14.85, 21.9 (2C), 25.7, 34.65, 36.05, 49.5, 72.65, 126.3, 127.95 (2C), 129.1 (2C), 143.4; m/z 204 (M⁺, < 1%), 106 (65), 105 (44), 103 (10), 99 (100), 91 (52), 81 (66), 79 (25), 78 (10), 77 (23), 57 (13), 55 (32), 51 (11), 43 (48), 41 (33).

2,2-Dimethyl-5-hexen-3-one (3c) [52]: Pale yellow oil, R_f 0.60 (hexane/ethyl acetate: 2/1); t_r 4.00; ν (film) 1710 cm⁻¹ (C=O); δ_H 1.16 (9H, s, 3xMe), 3.29 (2H, d, J =7.2, CH₂CO), 5.10, 5.15 (1 and 1H, respectively, 2d, J =18.0 and 11.0, respectively, CH₂CH), 5.90-5.95 (1H, m, CHCH₂); δ_C 26.6 (3C), 38.3, 45.5, 117.1, 129.3, 213.8; m/z 126 (M⁺, 1%), 85 (25), 57 (100), 41 (41).

3,3-Dimethyl-1-phenyl-2-butanone (3d) [53]: Pale yellow oil, R_f 0.55 (hexane/ethyl acetate: 2/1); t_r 9.69; ν (film) 3030, 1595 (C=CH), 1710 cm⁻¹ (C=O); δ_H 1.20 (9H, s, 3xMe), 3.81 (2H, s, CH₂), 7.10-7.35 (5H, m, Ph); δ_C 26.4 (3C), 43.25, 44.65, 126.6, 128.35 (2C), 129.5 (2C), 134.9, 212.85; m/z 176 (M⁺, 10%), 91 (98), 85 (100).

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VI. References

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