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Deallyloxy- and debenzyloxycarbonylation of protected alcohols, amines and thiols via a naphthalene-catalysed lithiation reaction

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Abstract—The naphthalene-catalysed lithiation of Alloc- and Cbz-protected alcohols, amines and thiols in THF at 0 °C led, after quenching with methanol, to the recovery of the free alcohols, amines and thiols in short reaction times and with very good yields. The selectivity for the removal of the Alloc- or the Cbz- group in a polyfunctionalised substrate has been studied. The selective reductive cleavage of a benzylic carbon–oxygen bond was achieved in the presence of an allylic carbon–oxygen or carbon–nitrogen bond. This method represents a great improvement in comparison with the previously reported deprotection procedures by dissolving metals, since it avoids the use of the toxic liquid ammonia and, therefore, the need to perform the reaction at low temperatures.

1. Introduction

The allyloxycarbonyl (Alloc) and the benzyloxycarbonyl (Cbz) are among the most useful protecting groups for alcohols, amines and, to a lesser extent, thiols.[1] They have shown a wide application in organic synthesis, especially in the fields of peptides,[2] nucleotides,[3] and carbohydrates.[4] These blocking groups present the advantages that are easily introduced (generally by acylation with allyl[5a] or benzyl chloroformate[5b] in the presence of a base), deactivate the nucleophilic properties of the protected heteroatom and can readily be removed when needed. The Alloc group can be cleaved by sodium in liquid ammonia,[6] nickel tetracarbonyl or several palladium complexes in the presence of an external nucleophile in order to prevent the liberated functional group from adding to the intermediate π-allyl complex.[7] Concerning the Cbz group, several methods have been reported for its removal: palladium-catalysed hydrogenolysis, reduction by electrolysis, dissolving metals or alkali metal borohydrides, basic hydrolysis, treatment with strong acids, boron trihalides or trimethylsilyl halides.[8] A mild deprotection of allylic and benzylic carbamates using tetrabutylammonium fluoride has recently been reported.[9] However, some of these methods require the use of toxic reagents or expensive transition metal complexes and, in some cases, side reactions have been observed with other functional groups present in the molecule to be deprotected.[8b]

Our research group has extensively been studying an arene-catalysed lithiation methodology.[10,11] The use of an excess of lithium powder and a catalytic amount of an arene [mainly naphthalene or 4,4′-di-*tert*-butylbiphenyl (DTBB)] has allowed us to generate simple organolithium compounds starting from non-halogenated materials,[12] and functionalised organolithium compounds[13] by chlorine–lithium exchange or by ring opening of heterocycles.[14] The application of this lithiation process to the reductive cleavage of several allylic and benzylic carbon-heteroatom bonds has led to methods for removal of some blocking groups from protected alcohols, amines and thiols.[15] In a previous study, we were able to generate allylic and benzylic organolithium reagents by reductive cleavage of carbon–oxygen and carbon–nitrogen bonds in carbonates and carbamates.[16] These results prompted us to test the application of our lithiation methodology to the removal of the Alloc and Cbz groups. In this paper we report the lithium-mediated naphthalene-catalysed reductive cleavage of these two groups from several protected alcohols, amines and thiols in short reaction times under very mild reaction conditions, avoiding the use of the toxic liquid ammonia.

2. Results and discussion

All protected substrates **1–3** (Scheme 1, Table 1) were prepared from commercially available alcohols (for **1**),

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Keywords: Lithium; Naphthalene; Allyloxycarbonyl; Benzyloxycarbonyl; Deprotection; Alcohols; Amines; Thiols.

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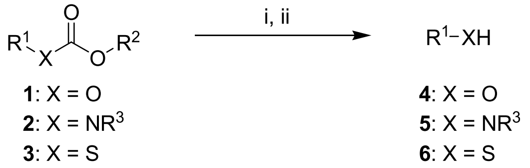

Scheme 1. Reagents and conditions: (i) Li, $C_{10}H_8$ (8 mol%), THF, 0 °C; (ii) H_2O.

amines (for **2**) or thiols (for **3**) and the corresponding allyl or benzyl chloroformate under basic reaction conditions.

Benzyl 1-decyl carbonate **1ab** (Scheme 1 and Table 1, entry 2) was chosen as a model substrate. The reaction of compound **1ab** with an excess of lithium powder (1:9 molar ratio) and a catalytic amount of naphthalene (1:0.16 molar ratio; 8 mol%) in THF at 0 °C for 2 h gave, after quenching the excess of lithium with methanol, the expected 1-decanol **4a** in 86% yield (Table 1, entry 2). The reaction was repeated at −30 and −78 °C, but yields did not improve. Therefore, the temperature of 0 °C was chosen because of the simpler experimental set-up (reaction cooled in an ice-bath).

Next, the process was extended to some other Cbz-protected alcohols. Benzylic carbonates derived from 2-octanol (**1b**) and 3,7-dimethyl-3-octanol (**1d**) were submitted to the naphthalene-catalysed lithiation reaction under the same experimental conditions and gave the corresponding free alcohols **4b** and **4d** in excellent yields (Table 1, entries 3 and 5). However, the lithiation of benzyl geranyl carbonate **1e** under the same conditions only led to a 12% yield of geraniol, probably due to a competitive cleavage of the allylic geranyl-oxygen bond leading to the corresponding hydrocarbon.[17] The selective removal of the Cbz group was achieved when the lithiation of **1e** was performed at −78 °C, which led to a 71% yield of geraniol (Table 1, entry 6). The Alloc group of carbonates **1aa**, **1c** and **1f** could also be effectively cleaved under the typical lithiation conditions, affording the deprotected alcohols **4a** and **4c** and phenol **4f**, respectively, in yields ranging from 58 to 80% (Table 1, entries 1, 4 and 7).

Having proved that our procedure was efficient for the removal of both Alloc and Cbz groups from carbonates, a competition experiment was performed in order to check if any of these groups could be selectively cleaved in the presence of the other one. 1,9-Nonanediol was mono-protected with the Cbz group on one hydroxyl and the Alloc group was introduced on the remaining hydroxyl. The naphthalene-catalysed lithiation of the obtained dicarbonate **1g** led to the recovery of the free diol **4g** in almost quantitative yield (Table 1, entry 8), showing that there was no chemoselectivity in the process. Attempts to get some selectivity at −78 °C did not change the result, the diol **4g** being obtained again.

Our methodology was successfully applied to the deallyloxy- and debenzyloxycarbonylation of protected secondary amines and thiols (Scheme 1 and Table 1, entries 9–16). Both the Alloc and the Cbz groups could easily be removed from the protected dioctylamines **2aa** and **2ab**, respectively, in very good yields (Table 1, entries 9 and 10). The Cbz group could selectively be eliminated in the protected diallylamine **2b**, which contains two allylic carbon–nitrogen bonds that could also be cleaved under the lithiation reaction conditions (Table 1, entry 11).[18] *N*-Methylaniline **5c** was obtained in an excellent yield in the lithiation of substrate **2c** (Table 1, entry 12). We also tried the debenzyloxycarbonylation of a protected primary amine, but it failed. Octylamine was protected with the Cbz group and the removal of the latter was attempted following the same procedure previously used by us in the deprotection of tritylated primary amines,[15c] consisting in deprotonation with *n*-butyllithium and treatment with trimethylsilyl chloride before performing the lithiation step. Although the starting material disappeared, neither octylamine nor *N*-(trimethylsilyl)octylamine were detected in the crude reaction mixture (GC–MS). Concerning sulfur-containing substrates, the lithiation of the allylic and benzylic

Table 1. Deallyloxy- or debenzyloxycarbonylation of compounds **1**–**3** via a naphthalene-catalysed lithiation. Preparation of compounds **4**–**6**

Entry	Substrate				Time (h)	Product	
	No.	X	R^1	R^2		No.	Yield (%)[a]
1	**1aa**	O	$Me(CH_2)_9$	$CH_2{=}CHCH_2$	2.0	**4a**	80
2	**1ab**	O	$Me(CH_2)_9$	$PhCH_2$	2.0	**4a**	86
3	**1b**	O	$Me(CH_2)_5CH(Me)$	$PhCH_2$	5.0	**4b**	>99
4	**1c**	O	$c\text{-}C_6H_{11}$	$CH_2{=}CHCH_2$	1.5	**4c**	74
5	**1d**	O	$Pr^i(CH_2)_3C(Me)(Et)$	$PhCH_2$	5.0	**4d**	81
6	**1e**	O	Geranyl	$PhCH_2$	2.5	**4e**	71[b]
7	**1f**	O	$2,4,6\text{-}Me_3C_6H_2$	$CH_2{=}CHCH_2$	1.0	**4f**	58
8	**1g**	O	$CbzO(CH_2)_9$	$CH_2{=}CHCH_2$	2.0	**4g**[c]	>99
9	**2aa**	$Me(CH_2)_7N$	$Me(CH_2)_7$	$CH_2{=}CHCH_2$	2.0	**5a**	86
10	**2ab**	$Me(CH_2)_7N$	$Me(CH_2)_7$	$PhCH_2$	5.0	**5a**	71
11	**2b**	$CH_2{=}CHCH_2N$	$CH_2{=}CHCH_2$	$PhCH_2$	1.0	**5b**	62
12	**2c**	MeN	Ph	$PhCH_2$	1.0	**5c**	98
13	**3aa**	S	$Me(CH_2)_9$	$CH_2{=}CHCH_2$	2.0	**6a**	78
14	**3ab**	S	$Me(CH_2)_9$	$PhCH_2$	1.0	**6a**	82
15	**3b**	S	$c\text{-}C_6H_{11}$	$PhCH_2$	1.0	**6b**	62
16	**3c**	S	Ph	$CH_2{=}CHCH_2$	1.0	**6c**	96

[a] Yield determined by quantitative GLC, using commercially available compound **4**–**6** and *n*-dodecane (internal standard) in the determination of response factors.

[b] The reaction was performed at −78 °C.

[c] Compound **4g**=1,9-nonanediol.

thiocarbonates **3a**–**3c**, derived from primary, secondary and aromatic thiols, led to the formation of the parent thiols in moderate to excellent yields (Table 1, entries 13–16). The moderate yield obtained with benzyl cyclohexyl thiocarbonate **3b** could be attributed to some oxidation of the obtained cyclohexanethiol to the corresponding disulfide during the work-up, since the latter was detected in the crude reaction mixture (GC–MS).

Concerning a possible reaction mechanism, we assume that the reductive cleavage of the allylic (for Alloc) or benzylic (for Cbz) carbon–oxygen bond takes place first, leading to allyl- or benzyllithium and the corresponding alkyl lithium carbonate (from **1**), carbamate (from **2**) or thiocarbonate (from **3**). Then, the latter carbonic acid derivatives decarboxylate to give the corresponding lithium alkoxide (from **1**), amide (from **2**) or sulfide (from **3**). The final quench with excess of methanol renders the expected alcohols **4**, amines **5** or thiols **6**, respectively, and the hydrocarbons propene (by protonolysis of allyllithium) or toluene (by protonolysis of benzyllithium). The latter was always detected (GC–MS) in all the reactions with Cbz-protected substrates, which is in favour of the proposed reaction mechanism.

3. Conclusion

In conclusion, we have reported here a very efficient procedure to remove the Alloc and the Cbz groups from protected alcohols, amines and thiols under mild reaction conditions. The methodology is applicable to aliphatic and aromatic substrates. This deprotection procedure works very efficiently even for branched alcohols and thiols. Concerning amines, this reductive cleavage is only applicable to carbamates bearing two substituents at the nitrogen atom. This method has shown to be a very good alternative to the reported methods to remove this two popular protecting groups, since it uses safer reagents and simpler experimental set-up conditions.

4. Experimental

4.1. General

All moisture sensitive reactions were carried out under argon atmosphere. Commercially available anhydrous THF (99.9%, water content $\leq 0.006\%$, Acros) was used as solvent in all the reactions. All reagents used for the synthesis of protected substrates **1**–**3** and naphthalene were commercially available (Acros, Aldrich) and were used without further purification. Lithium powder was prepared according to the procedure described in Ref. 19. Commercially available *n*-butyllithium was titrated with a 1 M solution of *sec*-butanol in xylene using 1,10-phenanthroline as indicator.[20] All glassware was dried in an oven at 100 °C and cooled to room temperature under Ar before use. Column chromatography was performed with Merck silica gel 60 (0.040–0.063 μm, 240–400 mesh). Thin-layer chromatography (TLC) was performed on precoated silica gel plates (Merck 60, F254, 0.25 mm). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker ARX-300 spectrophotometer using $CDCl_3$ (unless otherwise stated) as solvent and tetramethylsilane (TMS) as internal reference. Mass spectra (EI) were obtained at 70 eV on a Hewlett Packard HP-5890 GC/MS instrument equipped with a HP-5972 selective mass detector. Infrared (FT-IR) spectra were obtained on a Nicolet-Nexus spectrophotometer. The purity of volatile compounds and the chromatographic analyses (GC) were determined with a Shimadzu GC-9A instrument equipped with a flame-ionization detector and a 2 m column (1.5% OV17 9_A SUS Chrom 103 80/1000), using nitrogen as carrier gas.

4.2. Synthesis of the carbonates 1a–1f, carbamates 2 and thiocarbonates 3. General procedure

n-BuLi (6.3 mL of a 1.6 M solution of *n*-BuLi in hexane, 10.0 mmol) was dropwise added to a stirred solution of the corresponding alcohol (for **1a**–**1f**), amine (for **2**) or thiols (for **3**) (10.0 mmol) in anhydrous THF (10 mL) under Ar at 0 °C. Ten minutes after the addition had been completed, allyl or benzyl chloroformate (10.0 mmol) was added during ca. 5 min. After stirring for 2 h at the same temperature, the crude reaction mixture was adsorbed on basic aluminium oxide, transferred to a short column of basic aluminium oxide and eluted with hexane. Evaporation of the solvent (15 Torr) afforded the expected Alloc- and Cbz-protected compounds **1a**–**1f**, **2** and **3** in pure form. Their corresponding physical, spectroscopic and analytical data follow.

4.2.1. Allyl 1-decyl carbonate (1aa).[21] Colourless oil; yield: 22%; R_f 0.88 (hexane/ethyl acetate: 9/1); ν (film) 1747 (C=O), 1256 cm^{-1} (CO); δ_H 0.88 (3H, t, $J=6.8$ Hz, Me), 1.00–1.51 [14H, m, $Me(CH_2)_7$], 1.53–1.82 (2H, m, CH_2CO), 4.12 (2H, t, $J=6.6$ Hz, CH_2CH_2O), 4.63 (2H, d, $J=6.9$ Hz, $CHCH_2O$), 5.21–5.44 (2H, m, CH_2=C), 5.84–6.03 (1H, m, CH=CH_2); δ_C 14.1 (Me), 22.6, 28.6, 29.2, 29.3, 29.5, 30.9 (2C), 31.8 [$Me(CH_2)_8$], 68.0, 68.2 ($2\times$CO), 118.8 (CH_2=C), 131.5 (CH=C), 155.1 (C=O); *m/z* (DIP) 242 (M^+, <1%), 203 (10), 141 (80), 140 (47), 112 (25), 111 (25), 99 (27), 98 (16), 97 (39), 85 (100), 84 (25), 83 (49), 82 (17), 71 (84), 70 (37), 69 (43), 68 (12), 57 (90), 56 (31), 55 (48), 43 (54), 42 (11), 41 (30).

4.2.2. Benzyl 1-decyl carbonate (1ab).[22] Colourless oil; yield: 61%; R_f 0.38 (hexane); ν (film) 3071, 3034, 1587 (HC=C), 1746 (C=O), 1261 cm^{-1} (CO); δ_H 0.88 (3H, t, $J=6.9$ Hz, Me), 1.18–1.44 [14H, m, $Me(CH_2)_7$], 1.58–1.73 (2H, m, CH_2CO), 4.13 (2H, t, $J=6.8$ Hz, CH_2CH_2O), 5.15 (2H, s, $PhCH_2$), 7.26–7.43 (5H, m, ArH); δ_C 14.1 (Me), 22.6, 25.6, 28.6, 29.15, 29.2, 29.5 (2C), 31.8 [$Me(CH_2)_8$], 68.3 (CH_2CO), 69.4 ($PhCH_2$), 128.3 (2C), 128.4, 128.5 (2C), 135.3 (ArC), 155.2 (C=O); *m/z* (DIP) 292 (M^+, <1%), 286 (14), 273 (11), 272 (27), 271 (100), 257 (47), 239 (26), 195 (12), 194 (14), 193 (64), 149 (66), 135 (16), 129 (20), 128 (11), 116 (10), 111 (11), 97 (18), 89 (17), 85 (16), 83 (19), 73 (19), 71 (22), 69 (19), 61 (10), 60 (13), 57 (46), 56 (61), 55 (27), 43 (38), 41 (24).

4.2.3. Benzyl 2-octyl carbonate (1b).[23] Colourless oil; yield: 70%; R_f 0.58 (hexane/ethyl acetate: 9:1); ν (film) 3093, 3055, 3034, 1498 (HC=C), 1734 (C=O), 1263 cm^{-1} (CO); δ_H 0.87 (3H, t, $J=6.5$ Hz, $MeCH_2$), 1.17–1.75 [10H, m, $(CH_2)_5$], 1.27 (3H, d, $J=6.1$ Hz, *Me*CH), 4.68–4.85 (1H, m, CHO), 5.14 (2H, s, PhC*H*$_2$), 7.24–7.47 (5H, m, ArH); δ_C 14.0 (*Me*CH$_2$), 19.8 (*Me*CO), 22.5, 25.15, 25.2, 29.0, 31.6 [$(CH_2)_5$], 69.2 (Ph*C*H$_2$), 75.6 (Me*C*O), 128.2 (2C), 128.3, 128.5 (2C), 135.4 (ArH), 154.8 (C=O); *m/z* (DIP) 264 (M^+, 2%), 180 (14), 152 (56), 151 (26), 112 (13), 111 (11), 110 (10), 108 (58), 107 (70), 92 (19), 91 (100), 90 (13), 79 (26), 77 (11), 71 (30), 69 (10), 65 (14), 57 (30), 55 (10), 43 (19), 41 (13).

4.2.4. Allyl cyclohexyl carbonate (1c). Colourless oil; yield: 44%; R_f 0.40 (hexane/ethyl acetate: 9:1); ν (film) 1742 (C=O), 1651 (HC=C), 1254 cm^{-1} (CO); δ_H 1.06–2.11 (10H, m, 5×CH$_2$ ring), 4.47–4.73 (1H, m, CHO), 4.62 (2H, d, $J=4.5$ Hz, CH$_2$O), 5.15–5.42 (2H, m, CH$_2$=C), 5.80–6.04 (1H, m, CH=C); δ_C=23.0, 25.2 (2C), 31.6 (2C) (5×CH$_2$ ring), 68.1 (CH$_2$O), 89.2 (CHO), 118.7 (*C*H$_2$=C), 131.8 (*C*H=C), 154.5 (C=O); *m/z* (DIP) 184 (M^+, 5%), 183 (30), 149 (15), 143 (12), 141 (15), 137 (12), 135 (18), 127 (18), 125 (21), 123 (15), 113 (17), 112 (12), 111 (39), 109 (21), 99 (26), 98 (16), 97 (48), 96 (14), 95 (28), 91 (12), 85 (78), 84 (21), 83 (83), 82 (28), 81 (32), 71 (75), 70 (25), 69 (55), 67 (29), 57 (100), 56 (21), 55 (72), 43 (55), 41 (64); HRMS: $M^+-C_4H_5O_2$, found 99.0813. $C_6H_{11}O$ requires 99.0810.

4.2.5. Benzyl 3,7-dimethyl-3-octyl carbonate (1d). Colourless oil; yield: 87%; R_f 0.68 (hexane/ethyl acetate: 9:1); ν (film) 3088, 3066, 3034, 1580, 1498 (HC=C), 1740 (C=O), 1263 cm^{-1} (CO); δ_H 0.75–0.99 (9H, m, 2×*Me*CH and *Me*CH$_2$), 1.07–1.61 [7H, m, C*H*Me and $(CH_2)_3$], 1.41 (3H, s, MeC), 1.63–1.96 (2H, m, C*H*$_2$Me), 5.09 (2H, s, PhC*H*$_2$), 7.24–7.50 (5H, m, ArH); δ_C 8.0, 22.5, 23.0, 27.8 (4×Me), 21.2, 30.6, 37.6, 39.1 [$(CH_2)_3$ and *C*H$_2$Me], 68.6 (Ph*C*H$_2$), 87.1 (CO), 128.1 (2C), 128.2, 128.5 (2C), 135.8 (ArC), 153.3 (C=O); *m/z* (DIP) 292 (M^+, <1%), 181 (16), 180 (11), 140 (29), 91 (100), 85 (12), 71 (13), 70 (17), 57 (13), 43 (11); HRMS: M^+, found 292.2064. $C_{18}H_{28}O_3$ requires 292.2038.

4.2.6. Benzyl geranyl carbonate (1e).[24] Colourless oil; yield: 26%; R_f 0.50 (hexane/ethyl acetate: 9:1); ν (film) 3082, 3055, 3033, 1596, 1498 (HC=C), 1744 (C=O), 1255 cm^{-1} (CO); δ_H 1.60, 1.68, 1.71 (3H each, 3s, 3×Me), 1.99–2.12 [4H, m, $(CH_2)_2$], 4.54–4.74 (2H, m, CHC*H*$_2$O), 4.99–5.20 (3H, m, C*H*=CMe$_2$ and PhC*H*$_2$), 5.33–5.46 (1H, m, C*H*CH$_2$O), 7.29–7.42 (5H, m, ArH); δ_C 16.5, 17.7, 25.7 (3×Me), 26.2, 39.5 [$(CH_2)_2$], 66.5 (CH*C*O), 69.6 (Ph*C*H$_2$), 117.8, 123.6 (2×*C*H=CMe), 131.7, 135.3 (2×*C*=CH), 128.2 (2C), 128.25, 128.5 (2C), 142.8 (ArC), 155.1 (C=O); *m/z* 288 (M^+, <1%), 136 (29), 135 (12), 121 (26), 108 (12), 107 (18), 93 (41), 92 (20), 91 (100), 80 (15), 79 (15), 77 (15), 69 (81), 68 (50), 67 (16), 65 (10).

4.2.7. Allyl 2,4,6-trimethylphenyl carbonate (1f). Colourless oil; yield: 64%; R_f 0.55 (hexane/ethyl acetate: 9:1); ν (film) 3088, 3068, 1650, 1607, 1486 (HC=C), 1759 (C=O), 1245 cm^{-1} (CO); δ_H 2.59, 2.69 (6H and 3H, respectively, 2s, 3×Me), 5.18 (2H, d, $J=5.8$ Hz, CHC*H*$_2$O), 5.67–5.92, (2H, m, CH$_2$=C), 6.32–6.52 (1H, m, C*H*=CH$_2$), 7.29 (2H, s, 2×ArH); δ_C 16.0 (2C), 20.7 (3×Me), 69.0 (CH$_2$O), 119.2 (*C*H$_2$=C), 131.3 (*C*H=CH$_2$), 129.3 (2C), 129.6 (2C), 135.6, 146.2 (ArC), 153.0 (C=O); *m/z* (DIP) 220 (M^+, 8%), 136 (23), 135 (100), 97 (17), 91 (33), 85 (28), 83 (15), 71 (35), 70 (12), 69 (16), 57 (44), 56 (12), 55 (18), 43 (26), 41 (37); HRMS: M^+, found 220.1098. $C_{13}H_{16}O_3$ requires 220.1099.

4.2.8. *N*-(Allyloxycarbonyl)dioctylamine (2aa).[25] Colourless oil; yield: 41%; R_f 0.60 (hexane/ethyl acetate: 9:1); ν (film) 3082, 1649 (HC=C), 1705 (C=O), 1237 cm^{-1} (CO); δ_H 0.88 (6H, t, $J=6.6$ Hz, 2×Me), 1.14–1.38, 1.41–1.61 [20H and 4H, respectively, 2m, 2×Me(C*H*$_2$)$_6$], 3.06–3.30 (4H, m, 2×CH$_2$N), 4.59 (2H, d, $J=5.3$ Hz, CH$_2$O), 5.20, 5.31 (1H each, 2d, $J=10.1$, 17.2 Hz, respectively, CH$_2$=C), 5.81–6.02 (1H, m, CH=C); δ_C 14.1 (2C, 2×Me), 22.6 (2C), 26.8 (2C), 29.2 (2C), 29.3 (2C), 29.4 (2C), 31.8 (2C) [2×Me(*C*H$_2$)$_6$], 46.9 (2C, 2×CN), 65.6 (CO), 118.8 (*C*H$_2$=C), 133.4 (*C*H=C), 155.1 (C=O); *m/z* (DIP) 325 (M^+, <1%), 269 (27), 268 (100), 241 (16), 240 (86), 142 (26), 71 (28), 57 (28), 43 (13).

4.2.9. *N*-(Benzyloxycarbonyl)dioctylamine (2ab).[26] Colourless oil; yield: 68%; R_f 0.56 (hexane/ethyl acetate: 9:1); ν (film) 3065, 3032, 1498 (HC=C), 1704, 1643 (C=O), 1237 cm^{-1} (CO); δ_H 0.88 (6H, t, $J=7.0$ Hz, 2×Me), 1.07–1.38, 1.40–1.66 [20H and 4H, respectively, 2m, 2×Me(C*H*$_2$)$_6$], 3.13–3.32 (4H, m, 2×CH$_2$N), 5.12 (2H, s, PhC*H*$_2$), 7.07–7.46 (5H, m, ArH); δ_C 14.1 (2C, 2×Me), 22.6 (2C), 26.8 (2C), 29.2 (2C), 29.3 (2C), 29.4 (2C), 31.8 (2C) [2×Me(*C*H$_2$)$_6$], 46.9, 47.5 (2×CN), 66.7 (CO), 127.65 (2C), 127.7, 128.3 (2C), 137.1 (ArC), 156.1 (C=O); *m/z* (DIP) 375 (M^+, 5%), 269 (24), 268 (100), 240 (35), 232 (42), 170 (25), 142 (20), 91 (74), 71 (33), 57 (31), 43 (14).

4.2.10. *N*-(Benzyloxycarbonyl)diallylamine (2b).[27] Colourless oil; yield: 65%; R_f 0.23 (hexane/ethyl acetate: 9:1); ν (film) 3082, 3060, 3028, 1651, 1591, 1503 (HC=C), 1744, 1702 (C=O), 1241 cm^{-1} (CO); δ_H 3.77–3.99 (4H, m, 2×CH$_2$N), 5.15 (2H, s, PhC*H*$_2$), 5.01–5.25 (4H, m, 2×CH$_2$=C), 5.67–5.86 (2H, m, 2×C*H*=CH$_2$), 7.26–7.50 (5H, m, ArH); δ_C 46.2, 49.1 (2×CN), 67.1 (Ph*C*H$_2$), 116.7, 117.1 (2×*C*H$_2$=C), 127.7 (2C), 128.4 (2C), 128.5, 136.8 (ArC), 133.4 (2C, 2×*C*H=CH$_2$), 156.0 (C=O); *m/z* (DIP) 231 (M^+, 3%), 181 (12), 180 (37), 151 (33), 107 (57), 92 (31), 91 (100), 79 (36), 77 (17), 65 (17).

4.2.11. *N*-(Benzyloxycarbonyl)-*N*-methylaniline (2c).[28] Colourless oil; yield: 62%; R_f 0.28 (hexane/ethyl acetate: 9:1); ν (film) 3088, 3063, 3032, 1598, 1497 (HC=C), 1749, 1708 (C=O), 1298 cm^{-1} (CO); δ_H 3.31 (3H, s, Me), 5.15 (2H, s, PhC*H*$_2$), 6.99–7.51 (10H, m, ArH); δ_C 38.4 (Me), 67.2 (Ph*C*H$_2$), 126.6 (2C), 126.8, 127.6, 127.8 (2C), 128.3 (2C), 128.8 (2C), 136.6, 138.9 (ArC), 155.4 (C=O); *m/z* (DIP) 241 (M^+, 58%), 197 (65), 196 (17), 181 (11), 120 (28), 106 (14), 92 (28), 91 (100), 77 (28), 65 (24).

4.2.12. *O*-Allyl *S*-(1-decyl) thiocarbonate (3aa). Colourless oil; yield: 81%; R_f 0.33 (hexane); ν (film) 3082, 1648 (HC=C), 1744, 1713 (C=O), 1138 cm^{-1} (CO); δ_H 0.88 (3H, t, $J=6.6$ Hz, Me), 1.15–1.46, 1.55–1.71 [14H and 2H, respectively, 2m, Me(C*H*$_2$)$_8$], 2.86 (2H, t, $J=7.3$ Hz, CH$_2$S), 4.71 (2H, d, $J=5.8$ Hz, CH$_2$O), 5.28, 5.37 (1H each, 2d, $J=10.5$, 17.2 Hz, respectively, CH$_2$=C), 5.83–6.03, (1H, m, CH=C); δ_C 14.1 (Me), 22.6, 28.7, 29.1, 29.3, 29.4, 29.5, 29.7, 31.0, 31.9 [$(CH_2)_9$], 67.6 (CO), 118.9 ($H_2C{=}C$), 131.6 ($CH{=}C$), 171.1 (C═O); *m*/*z* (DIP) 258 (M^+, <1%), 201 (49), 174 (10), 173 (68), 172 (29), 140 (16), 99 (17), 97 (18), 85 (92), 83 (20), 71 (79), 69 (23), 57 (100), 55 (37), 43 (61), 42 (14), 41 (32); HRMS: M^+, found 258.1654. $C_{14}H_{26}O_2S$ requires 258.1654.

4.2.13. *O*-Benzyl *S*-(1-decyl) thiocarbonate (3ab). Colourless oil; yield: 62%; R_f 0.33 (hexane); ν (film) 3099, 3065, 3033, 1498 (HC═C), 1744, 1710 (C═O), 1134 cm^{-1} (CO); δ_H 0.88 (3H, t, $J=6.6$ Hz, Me), 1.14–1.45, 1.50–1.71 [14H and 2H, respectively, 2m, $Me(CH_2)_8$], 2.86 (2H, t, $J=7.5$ Hz, CH_2S), 5.22 (2H, s, $PhCH_2$), 7.18–7.44, (5H, m, ArH); δ_C 14.1 (Me), 22.7, 28.7, 29.1, 29.3, 29.4, 29.5, 29.7, 31.1, 31.9 [$(CH_2)_9$], 68.7 (CO), 128.3 (2C), 128.4, 128.6 (2C), 135.3 (ArC), 171.3 (C═O); *m*/*z* (DIP) 264 (M^+, 7%), 201 (16), 181 (49), 180 (30), 179 (16), 174 (11), 173 (88), 172 (12), 165 (12), 97 (21), 92 (59), 91 (100), 85 (26), 83 (15), 77 (11), 71 (23), 69 (17), 65 (20), 57 (32), 55 (28), 43 (34), 41 (30); HRMS: M^+, found 308.1809. $C_{18}H_{28}O_2S$ requires 308.1810.

4.2.14. *O*-Benzyl *S*-cyclohexyl thiocarbonate (3b). Colourless oil; yield: 74%; R_f 0.25 (hexane); ν (film) 3099, 3064, 3032, 1591, 1503 (HC═C), 1705 (C═O), 1132 cm^{-1} (CO); δ_H 1.10–2.10 (10H, m, 5×CH_2 ring), 3.28–3.43 (1H, m, CHS), 5.21 (2H, s, $PhCH_2$), 7.15–7.43 (5H, m, ArH); δ_C 25.4, 25.8 (2C), 33.1 (2C) (5×CH_2 ring), 44.4 (CS), 68.4 (CO), 128.2 (2C), 128.3, 128.5 (2C), 135.3 (ArC), 170.8 (C═O); *m*/*z* (DIP) 250 (M^+, 9%), 181 (28), 180 (17), 92 (70), 91 (100), 83 (17), 81 (18), 79 (13), 77 (24), 65 (34), 55 (28), 41 (22); HRMS: M^+, found 250.1024. $C_{14}H_{18}O_2S$ requires 250.1028.

4.2.15. *O*-Allyl *S*-phenyl thiocarbonate (3c). Colourless oil; yield: 57%; R_f 0.70 (hexane/ethyl acetate: 9:1); ν (film) 3078, 3055, 1636, 1583, 1479 (HC═C), 1726 (C═O), 1135 cm^{-1} (CO); δ_H 4.72 (2H, d, $J=5.8$ Hz, CH_2O), 5.28, 5.31 (1H each, 2d, $J=10.5$, 17.2 Hz, respectively, $CH_2{=}C$), 5.78–6.01 (1H, m, $CH{=}CH_2$), 6.93–7.74 (5H, m, ArH); δ_C 68.2 (CO), 117.6 ($CH_2{=}C$), 129.6, 129.8 (2C), 134.8 (2C), 135.9 (ArC), 133.5 ($C{=}CH_2$), 169.4 (C═O); *m*/*z* (DIP) 194 (M^+, 2%), 165 (15), 150 (15), 149 (77), 137 (10), 135 (64), 125 (15), 124 (69), 123 (100), 111 (13), 110 (39), 109 (50), 97 (14), 91 (17), 85 (13), 83 (12), 79 (11), 77 (22), 71 (14), 69 (17), 65 (16), 57 (22), 55 (13), 51 (13), 45 (26), 43 (12), 41 (21); HRMS: M^+, found 194.0415. $C_{10}H_{10}O_2S$ requires 194.0402.

4.3. Preparation of diprotected nonane-1,9-diol 1g

n-BuLi (6.3 mL of a 1.6 M solution of *n*-BuLi in hexane, 10.0 mmol) was dropwise added to a stirred solution of nonane-1,9-diol (1.635 g, 10.0 mmol) in anhydrous THF (10 mL) at 0 °C. Five minutes after the addition had been completed, benzyl chloroformate (1.5 mL, 10.0 mmol) was added during ca. 5 min. After stirring for 10 min at the same temperature, the same amount of *n*-BuLi as above was dropwise added, the reaction mixture was stirred for 5 min and allyl chloroformate (1.1 mL, 10.0 mmol) was added during ca. 5 min. The reaction was then stirred for 5 min, the cooling bath was removed and stirring was continued at room temperature for 2 h. The crude reaction mixture was adsorbed on basic aluminium oxide, transferred to a short column of basic aluminium oxide and eluted with hexane. Evaporation of the solvent (15 Torr) gave the pure diprotected diol **1g** in 26% yield. The corresponding physical, spectroscopic and analytical data follow.

4.3.1. Benzyl 9-(allyloxycarbonyloxy)-1-nonyl carbonate (1g). Colourless oil; yield: 26%; R_f 0.50 (hexane/ethyl acetate: 9:1); ν (film) 3060, 3028, 1645, 1497 (HC═C), 1747 (C═O), 1259 cm^{-1} (CO); δ_H 1.13–1.74 [14H, m, $(CH_2)_7CO$], 4.13 (2H, t, $J=6.6$ Hz, 1×CH_2CH_2O), 4.57–4.68 (4H, m, CH_2CH and 1×CH_2CH_2O), 5.17 (2H, s, $PhCH_2$), 5.28, 5.39 (1H each, 2d, $J=10.3$, 17.7 Hz, respectively, $CH_2{=}C$), 5.85–6.01 (1H, m, $H_2C{=}CH$), 7.31–7.42 (5H, m, ArH); δ_C 14.1 (2C), 23.3 (2C), 25.7 (2C), 39.0 [$(CH_2)_7CO$], 68.3 (2C), 69.6, 74.3 (4×CO), 118.8 ($CH_2{=}C$), 128.3 (2C), 128.5, 128.6 (2C), 131.7 (ArC), 131.5 ($CH{=}CH_2$), 155.2 (2C, 2×C═O); *m*/*z* (DIP) 378 (M^+, 1%), 125 (14), 108 (16), 107 (79), 92 (11), 91 (100), 83 (31), 81 (15), 69 (56), 57 (15), 55 (27), 41 (27); HRMS: M^+, found 378.2050. $C_{21}H_{30}O_6$ requires 378.2042.

4.4. Naphthalene-catalysed lithiation of compounds 1–3. Preparation of products 4–6. General procedure

A solution of the protected substrate **1**–**3** (1.0 mmol) in THF (2 mL) was dropwise added to a green suspension of lithium powder (63 mg, 9.0 mmol) and naphthalene (20 mg, 0.16 mmol) in THF (5 mL), under Ar, at 0 °C. After stirring at the same temperature for the time indicated in Table 1, methanol (5 mL) was carefully added, the cooling bath was removed and the reaction was stirred till it reached room temperature. The yields of the deprotected products were determined by quantitative GLC. Commercially available alcohols **4**, amines **5**, thiols **6**, *n*-dodecane (internal standard) and *n*-hexadecane (internal standard for **4f**) were used in the determination of response factors. Compounds **4**–**6** (commercially available) were characterised by comparison of their physical and spectroscopic data with authentic samples.

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References and notes

1. (a) Kunz, H.; Waldman, H. In Trost, B. M., Fleming, I., Eds.; *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 6; Chapter 3.1, pp 631–701. (b) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1999. (c) Kocienski, P. J. *Protecting Groups*, Thieme: Stuttgart, 2004.
2. See, for instance: (a) Bodanszky, M. *Peptide Chemistry. A Practical Text Book*; Springer: Berlin, 1988. (b) Bailey, P. D.

An Introduction to Peptide Chemistry; Wiley: Chichester, 1990. (c) Bergeron, R. J.; Ludin, C.; Muller, R.; Smith, R. E.; Phanstiel, O. *J. Org. Chem.* **1997**, *62*, 3285–3290.

3. See, for instance: (a) Amarnath, V.; Broom, A. D. *Chem. Rev.* **1977**, *77*, 183–217. (b) Watkins, B. E.; Rapoport, H. *J. Org. Chem.* **1982**, *47*, 4471–4477. (c) Myers, A. G.; Gin, D. Y.; Rogers, D. H. *J. Am. Chem. Soc.* **1994**, *116*, 4697–4718.
4. See, for instance: (a) Saito, H.; Nishimura, Y.; Kondo, S.; Umezawa, H. *Chem. Lett.* **1987**, 799–802. (b) Teshima, T.; Nakajima, K.; Takahashi, M.; Shiba, T. *Tetrahedron Lett.* **1992**, *33*, 363–366. (c) Adinolfi, M.; Barone, G.; Guariniello, L.; Iadonisi, A. *Tetrahedron Lett.* **2000**, *41*, 9305–9309.
5. (a) Paquette, L. A. In *Encyclopedia of Reagents for Organic Synthesis*, *Vol. 1*; Wiley: Chichester, 1995; pp 95–96. (b) Paquette, L. A. In *Encyclopedia of Reagents for Organic Synthesis*, *Vol. 1*; Wiley: Chichester, 1995; pp 323–326.
6. Umemura, E.; Tsuchiya, T.; Koyama, Y.; Umezawa, S. *Carbohydr. Res.* **1993**, *238*, 147–162.
7. (a) Ref. 1b, pp 183–185 and 526–528. (b) Ref. 1c, pp 345–347 and 524–528.
8. (a) Ref. 1a, pp 635–636. (b) Ref. 1b, pp 186, 283, 485 and 531–535. (c) Ref. 1c, pp 339–340, 378–380 and 512–524.
9. Jacquemard, U.; Bénéteau, V.; Lefoix, M.; Routier, S.; Mérour, J.-Y.; Coudert, G. *Tetrahedron* **2004**, *60*, 10039–10047.
10. For reviews, see: (a) Yus, M. *Chem. Soc. Rev.* **1996**, *25*, 155–161. (b) Ramón, D. J.; Yus, M. *Eur. J. Org. Chem.* **2000**, 225–237. (c) Yus, M. *Synlett* **2001**, 1197–1205. (d) Yus, M.; Ramón, D. J. *Latv. J. Chem.* **2002**, 79–92. (e) Ramón, D. J.; Yus, M. *Rev. Cubana Quim.* **2002**, *14*, 75–115. (f) Yus, M. In *The Chemistry of Organolithium Compounds*; Rappoport, Z., Mareck, I., Eds.; Wiley: Chichester, 2004; pp 647–747. For a mechanistic study, see: (g) Yus, M.; Herrera, R. P.; Guijarro, A. *Tetrahedron Lett.* **2001**, *42*, 3455–3458. (h) Yus, M.; Herrera, R. P.; Guijarro, A. *Chem. Eur. J.* **2002**, *8*, 2574–2584. (i) Herrera, R. P.; Guijarro, A.; Yus, M. *Tetrahedron Lett.* **2003**, *44*, 1309–1312.
11. For a polymer-supported version of this reaction, see: (a) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 1397–1400. (b) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron* **1999**, *55*, 7017–7026. (c) Yus, M.; Gómez, C.; Candela, P. *Tetrahedron* **2002**, *58*, 6207–6210. (d) Candela, P.; Gómez, C.; Yus, M. *Rus. J. Org. Chem.* **2004**, *40*, 795–801.
12. For a review, see: Guijarro, D.; Yus, M. *Recent Res. Dev. Org. Chem.* **1998**, *2*, 713–744.
13. For reviews, see: (a) Nájera, C.; Yus, M. *Trends Org. Chem.* **1991**, *2*, 155–181. (b) Nájera, C.; Yus, M. *Recent Res. Dev. Org. Chem.* **1997**, *1*, 67–96. (c) Nájera, C.; Yus, M. *Curr. Org. Chem.* **2003**, *7*, 867–926. (d) Nájera, C.; Sansano, J. M.; Yus, M. *Tetrahedron* **2003**, *59*, 9255–9303. (e) Chinchilla, R.; Nájera, C.; Yus, M. *Chem. Rev.* **2004**, *104*, 2667–2722.
14. For reviews, see: (a) Yus, M.; Foubelo, F. *Rev. Heteroat. Chem.* **1997**, *17*, 73–107. (b) Yus, M.; Foubelo, F. *Targets Heterocycl. Syst.* **2002**, *6*, 136–171. (c) Yus, M. *Pure Appl. Chem.* **2003**, *75*, 1453–1475.
15. (a) Alonso, E.; Ramón, D. J.; Yus, M. *Tetrahedron* **1997**, *53*, 14355–14368. (b) Yus, M.; Behloul, C.; Guijarro, D. *Synthesis* **2003**, 2179–2184. (c) Behloul, C.; Guijarro, D.; Yus, M. *Synthesis* **2004**, 1274–1280. (d) Behloul, C.; Guijarro, D.; Yus, M. *Tetrahedron* **2005**, *61*, 6908–6915.
16. Alonso, E.; Guijarro, D.; Martínez, P.; Ramón, D. J.; Yus, M. *Tetrahedron* **1999**, *55*, 11027–11038.
17. We have reported that geranyllithium can be generated from a geranyl carbonate by a naphthalene-catalysed lithiation at 0 °C: see Ref. 16.
18. For one example of this kind of allylic carbon–nitrogen bond cleavage, see Ref. 15a.
19. Yus, M.; Martínez, P.; Guijarro, D. *Tetrahedron* **2001**, *57*, 10119–10124.
20. Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165–168.
21. Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1973**, *38*, 3223–3224.
22. Jung, K. W. *PCT Int. Appl.* **2000**, WO 2000050376; *Chem. Abstr.* **2000**, *133*, 207676.
23. Pozo, M.; Pulido, R.; Gotor, V. *Tetrahedron* **1992**, *48*, 6477–6484.
24. Flemming, S.; Kabbara, J.; Nickisch, K.; Westermann, J.; Mohr, J. *Synlett* **1995**, 183–185.
25. Cabou, J.; Bricout, H.; Hapiot, F.; Monflier, E. *Catal. Commun.* **2004**, *5*, 265–270; *Chem. Abstr.* **2004**, *141*, 71153.
26. Tanaka, H.; Ogasawara, K. *Tetrahedron Lett.* **2002**, *43*, 4417–4420.
27. Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2000**, *56*, 8433–8441.
28. Yasuhara, T.; Nagaoka, Y.; Tomioka, K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2233–2234.