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DTBB-Catalysed Lithiation of 3-Functionalised 1-Chloropropenes†

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Abstract: The reaction of different 3-chlorinated allyl amines **1a,b** or phenylether **1c** with an excess of lithium powder, a catalytic amount of DTBB (5 mol %) and an electrophile [Pr^iCHO, Bu^tCHO, Et_2CO, $(CH_2)_5CO$] in THF at -78°C gives, after hydrolysis with water, the expected *Z/E* mixture of the corresponding products **2**. The corresponding two-step process at temperatures ranging between -30 and -40°C [electrophiles: Pr^iCHO, Bu^tCHO, $(CH_2)_5CO$] yields propargylic derivatives **3**. A mechanistic explanation for this behaviour is given. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

In spite of the interest of using functionalised organolithium compounds[1] in the synthesis of polyfunctionalised molecules by reaction with electrophiles, in some cases their instability can be a significant handicap. In the case of *sp*[2]-hybridised derivatives of the type **I/II**, one question concerning the possible carbanion inversion (stereochemical stability) has to do with the fact that the *trans*-diastereoisomer (**II**) is thermodynamically more stable than the *cis*-one (**I**)[2] for steric reasons; however, in the *cis*-diastereoisomer the intramolecular coordination between the heteroatom and the lithium atom (CIPE effect)[3] can contribute a lot to stabilise the thermodynamically less stable *cis* structure **I**. Other problems to be overcome concerning the chemical stability of this type of species results from a possible intra (γ-elimination; see **III**) or intermolecular S_N reaction, Y acting as a leaving group, and the hydrogen transfer giving a new α-substituted carbanion (see **IV**). α-Deprotonation in the starting material under the basic reaction conditions which could also give a carbenoid the type **V**; this species can suffer α-elimination to give a carbene **VI**, which in general gives uncontrolled reactions, among them acetylene formation. The same result, formation of an acetylene, would occur by a β-elimination from the starting material. In order to clarify all these possible situations we decided to study the lithiation of 3-substituted-1-chloropropenes under very mild reaction conditions using arene-catalysed lithiation.[4] This methodology has been widely used in our group to prepare very unstable functionalised organolithium compounds (starting from chlorinated[5] or non-halogenated materials[6], as well as heterocyclic compounds[7]) and polylithium synthons.[8]

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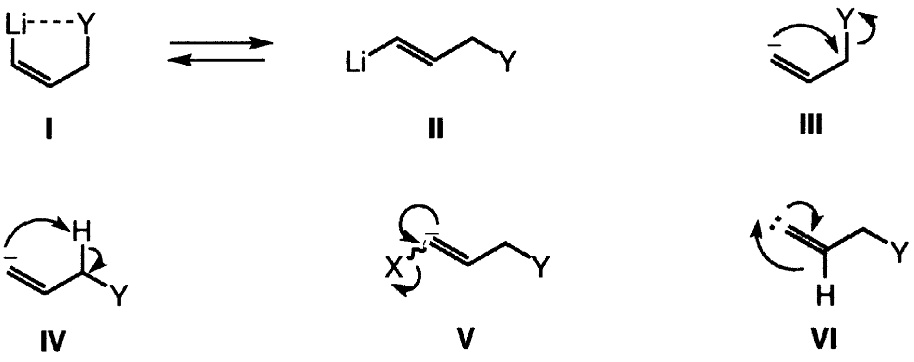


[X = Hal; Y = OR, NR_2, SR]

RESULTS AND DISCUSSION

The reaction of chlorinated allyl amines **1a,b** or the allyl ether **1c** (in all cases as a *ca.* 3/2 *Z/E* mixture) with an excess of lithium powder (1:10 molar ratio) and a catalytic amount of 4,4'-di-*tert*-butyl-biphenyl (DTBB; 1:0.1 molar ratio; 5 mol %) in the presence of different electrophiles [Pr^{i}CHO, Bu^{t}CHO, Et_2CO, $(CH_2)_5CO$] in THF at -78°C led, after hydrolysis with water at the same temperature, to the formation of the expected reaction products **2** with moderate yields (Scheme 1 and Table 1).

1a : Y = $N(CH_2CH_2)_2O$
1b : Y = $N(CH_2CH{=}CH_2)_2$
1c : Y = OPh

2aa-cd

Scheme 1. *Reagents and conditions*: i, Li, DTBB cat. (5 mol %), E^+ = Pr^{i}CHO, Bu^{t}CHO, Et_2CO, $(CH_2)_5CO$, THF, -78°C; ii, H_2O.

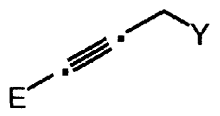
The diastereoisomers ratio of the starting materials **1** were not transferred to the reaction products, so very different *Z/E* ratios were obtained for products **2**, ranging from only the *E*-diastereoisomer (Table 1, entry 4) to only the Z-one (Table 1, entry 10). An explanation for this behaviour is found in the sp^2-carbanion equilibration of intermediates of type **I/II**. One experiment to demonstrate this hypothesis was carried out using pure *E*-**1a** [isolated as the only diastereoisomer by column chromatography (silica gel, hexane/ethyl acetate) from the reaction crude containing a 3/2 *Z/E*-mixture].[9] Thus, performing the reaction as above and using pivalaldehyde as electrophile, a 40% isolated yield of compound **2ab** *as a 2/1* Z/E *diastereoisomers mixture* was obtained, this ratio being the same as when **1a** was used as a *Z/E*-mixture (compare to Table 1, entry 2).

Table 1. Preparation of Compounds **2**

Entry	Starting material	Electrophile E^+	Product[a] No.	Y	E	Yield (%)[b]	*Z/E*-ratio[c]
1	**1a**	Pr^iCHO	**2aa**	$N(CH_2CH_2)_2O$	Pr^iCHOH	54	2/1
2	**1a**	Bu^tCHO	**2ab**	$N(CH_2CH_2)_2O$	Bu^tCHOH	51	2/1
3	**1a**	$(CH_2)_5CO$	**2ad**	$N(CH_2CH_2)_2O$	$(CH_2)_5COH$	64	2/1
4	**1b**	Pr^iCHO	**2ba**	$N(CH_2CHCH_2)_2$	Pr^iCHOH	14[d]	-/1
5	**1b**	Bu^tCHO	**2bb**	$N(CH_2CHCH_2)_2$	Bu^tCHOH	60	1/1
6	**1b**	$(CH_2)_5CO$	**2bd**	$N(CH_2CHCH_2)_2$	$(CH_2)_5COH$	42[e]	2/1
7	**1c**	Pr^iCHO	**2ca**	PhO	Pr^iCHOH	34	1.5/1
8	**1c**	Bu^tCHO	**2cb**	PhO	Bu^tCHOH	35	1.5/1
9	**1c**	Et_2CO	**2cc**	PhO	Et_2COH	38	10/1
10	**1c**	$(CH_2)_5CO$	**2cd**	PhO	$(CH_2)_5COH$	24[f]	1/-

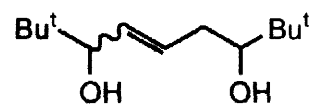
[a] All products **2** were ≥92% pure (GLC and/or 300MHz ^1H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate), based on the starting material **1**. [c] Determined by tandem GLC-MS. [d] A 53% of compound **3ba** was also isolated. [e] A 28% of compound **3bd** was also isolated. [f] A 5% of compound **3cd** was also isolated.

As shown in Scheme 1, the **1** → **2** transformation has to be carried out in the presence of the electrophile (Barbier-type reaction conditions)[10] in order to avoid not only decomposition of the organolithium intermediate of the type **I/II** involved in the process (only 5-10% of compound **2** was isolated in the two-step reaction either at -78 or at -30°C), but also and mainly to avoid the formation of acetylenic derivatives of type **3**. These compounds resulted either from an α-deprotonation of the starting material, giving a carbenoid of type **V** or from a β-elimination from the same starting material; the final formation of the corresponding lithium acetylide and reaction with the electrophile would give products **3**. Taking advantage of this behaviour we performed the two-step reaction with the starting materials **1a** and **1b** at temperatures ranging between -30 and -40°C, so compounds **3** were isolated as the main products [using Pr^iCHO, Bu^tCHO, $(CH_2)_5CO$ as electrophiles], after hydrolysis with water, also in moderate yields (Table 2).



3aa-bb

1d



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Finally, we studied the reaction shown in Scheme 1 using the starting thioether **1d** (also as a *ca.* 3/2 *Z/E*-mixture): in this case, and working under the same reaction conditions as for compounds **3** using pivalaldehyde as electrophile, only <15% of compound **4** as a complex mixture of four diastereoisomers was detected. This reaction is not interesting not only because of the very poor yield but also because compound **4** can be directly obtained starting from 1,3-dichloropropene.[11] In the case of the lithiation of compound **1d**, together with the chlorine/lithium exchange, a carbon-sulphur reductive cleavage takes place[12] giving mainly decomposition products.

Table 2. Preparation of Compounds **3**

Entry	Starting material	Electrophile E$^+$	Product[a]			
			No.	Y	E	Yield (%)[b]
1	**1a**	Pr^{i}CHO	**3aa**	$N(CH_2CH_2)_2O$	Pr^{i}CHOH	45
2	**1a**	Bu^{t}CHO	**3ab**	$N(CH_2CH_2)_2O$	Bu^{t}CHOH	40
3	**1a**	$(CH_2)_5CO$	**3ad**	$N(CH_2CH_2)_2O$	$(CH_2)_5COH$	48
4	**1b**	Bu^{t}CHO	**3bb**	$N(CH_2CHCH_2)_2$	Bu^{t}CHOH	38

[a] All products **3** were ≥95% pure (GLC and 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate), based on the starting material **1**.

Starting materials **1** could be easily prepared from commercially available 1,3-dichloropropene (as *ca.* 1.3:1 *Z/E*-diastereoisomers ratio) by selective allylic nucleophilic substitution (see experimental part).

From the results described in this study we can conclude that γ-substituted *sp*^{2}-hybridised organolithium intermediates of type **I/II** are very unstable species due to the different ways that they can decompose even at low temperature. However, even considering the limited synthetic utility of this chemistry, due to the moderate yields obtained, we think that some light on the structure/stability/reactivity of intermediates of type **I/II** has been given.

EXPERIMENTAL PART

General.- For general information see reference 13.

Preparation of Starting Amines **1a** *and* **1b**. *General Procedure.-* To a solution of 1,3-dichloropropene (0.46 ml, 5 mmol) in THF (10 ml) was added the corresponding amine (10 mmol) at room temperature and the resulting mixture was stirred for 12 h (overnight). Then, ethyl acetate (10 ml) was added and it was extracted with 1 M hydrochloric acid (3 x 10 ml). The aqueous layer was basified with 4 M sodium hydroxide and extracted with ethyl acetate (3 x 10 ml), the organic layer dried over sodium sulfate and evaporated (15 Torr) to give the title compounds in essentially pure (>94% from GLC) as a *ca.* 3/2 *Z/E*-diastereoisomers mixture).

(Z/E)-*1-Chloro-3-morpholinopropene* (**1a**):[14,15] 77% yield; R_f 0.41 (hexane/ethyl acetate: 8/2); ν (film) 1612, 1453 cm^{-1} (C=CH); δ_H 2.49, 3.19 (10H, 2m, 5xCH_2N), 3.22 (2H, d, J = 1.8, CH_2N), 3.70 (8H, m, 4xCH_2O), 5.85-6.19 (4H, 2m, CH=CH); δ_C 53.15, 53.3, 54.7, 58.4 (6C, 6xCH_2N), 66.6, 66.7 (4C, 4xCH_2O), 120.5, 120.7, 127.6, 129.7 (2xCH=CH); *m/z* (mixture) 163 (M^++2, 22%), 162 (M^++1, 12), 161 (M^+, 65), 160 (19), 127 (11), 126 (100), 115 (11), 100 (37), 97 (11), 94 (15), 88 (12), 86 (53), 77 (68), 69 (26), 68 (66), 56 (43), 55 (25), 54 (17), 51 (12), 49 (29), 44 (10), 43 (27), 42 (54).

(Z/E)-*3-(Diallylamino)-1-chloropropene* (**1b**):[14] 63% yield; R_f 0.64 (hexane/ethyl acetate: 9/1); ν (film) 3079, 3008, 1643, 1634, 1447 cm^{-1} (C=CH); δ_H 3.08, 3.27 (12H, 2m, 6xCH_2N), 5.16 (8H, m, 4xCH=CH_2), 5.75-5.99, 6.08, 6.15 (8H, 3m, 8xCH=C); δ_C 49.6, 51.5, 52.7, 56.2, 56.6 (6C, 6xCH_2N), 115.9, 117.6, 119.9, 128.9, 130.4, 135.2, 136.4 (12xC, 6xC=C); *m/z* (first isomer, t_r 5.83 min) 173 (M^++2, 3.9%), 171 (M^+, 11), 146 (21), 144 (64), 136 (34), 110 (20), 96 (10), 94 (15), 81 (10), 79 (14), 77 (33), 75 (100), 68 (33), 67 (16), 56 (30), 55 (13), 54 (20), 49 (17), 44 (11), 42 (91); (second isomer, t_r 5.87 min) 173 (M^++2, 4%), 172 (M^++1, 4), 171 (M^+, 12), 146 (20), 144 (68), 136 (39), 110 (21), 96 (75).

Preparation of Starting Ether **1c**.-[16] To a solution of a 60% mineral oil suspension of lithium hydride (0.4 g, 10 mmol) in THF (10 ml) was added phenol (0.89 ml, 10 mmol) and the mixture was refluxed for 1 h. Then, 1,3-dichloropropene (1.0 ml, 11 mmol) was added to the resulting mixture maintaining the reflux for 2 additional h. After cooling it to ambient temperature it was hydrolysed with water (10 ml), extracted with ethyl acetate (3 x 10 ml), the organic layer dried over sodium sulfate and evaporated (15 Torr) giving an oily residue, which was purified by column chromatography (silica gel, hexane/ethyl acetate) to give (Z/E)-*1-chloro-3-phenoxypropene* (**1c**): 77 % yield; R_f 0.69 (hexane); ν (film) 3064, 1639, 1633, 1599 (C=CH), 1240 cm^{-1} (C-O); δ_H 4.51, 4.77 (4H, 2dd, *J* = 5.8, 1.7, 2xCH_2O), 6.03-6.25, 6.36, 6.40 (4H, 3m, 2xCH=CH), 6.93, 7.27 (10H, 2m, 2xArH); δ_C 63.5, 66.0 (2xCH_2O), 114.6, 114.7, 121.1, 121.2, 122.0, 128.0, 129.5, 158.1, 158.15 (16C, 2xCH=CH and 2xArC); *m/z* (mixture) 170 (M$^+$+2, 2%), 168 (M$^+$, 6), 133 (21), 94 (28), 77 (33), 75 (100), 66 (11), 5 (19), 51 (20), 49 (10), 45 (10), 44 (31), 43 (68).

Preparation of Starting Thioether **1d**.- To a solution of *tert*-butyl mercaptane (0.65 ml, 5 mmol) in THF was added a hexane solution of *n*-butyllithium (3.1 ml, 5 mmol) at -78°C and after 5 min was added 1,3-dichloropropene (0.47 ml, 5 mmol) allowing the temperature to rise to 20°C for 12 h (overnight). The resulting mixture was worked-up as for compound **1c**, except that it was not necessary to purify the crude product, which was pure enough to be used in the lithiation step (>90% from GLC), so *3-*tert*-butylmercapto-1-chloropropene* (**1d**) was isolated: 85% yield; R_f 0.72 (hexane/ethyl acetate: 9/1); ν (film) 1618, 1468 cm^{-1} (C=CH); δ_H 1.33, 1.35 (18H, 2s, 6xMe), 3.21, 3.37 (4H, 2dt, *J* = 7.6, 1.2, 2xCH_2), 5.85-6.16 (4H, m, 2xCH=CH); δ_C 25.2, 28.9 (2xCH_2), 30.8, 30.85 (6C, 6xMe), 42.7, 42.75 (2x*C*Me_3), 119.2, 119.3, 129.4, 130.6 (2xCH=CH); *m/z* (first isomer, t_r 5.28 min) 166 (M$^+$+2, 2.6%), 164 (M$^+$, 6), 75 (13), 57 (100), 56 (12), 45 (12); (second isomer, t_r 5.55 min) 166 (M$^+$+2, 2.7%), 164 (M$^+$, 8.6), 75 (12), 57 (100), 56 (12), 45 (15), 44 (19), 43 (21).

DTBB-Catalysed Lithiation of Compounds **1** *Under Barbier Conditions. Isolation of Compounds* **2**. *General Procedure*.- To a green suspension of lithium powder (150 mg, 21 mmol) and DTBB (52 mg, 0.2 mmol) in THF (3 ml) was slowly added (*ca.* 1 h) a solution of the corresponding substrate **1** (2 mmol) and the electrophile (2 mmol) in THF (3 ml) at -78°C, stirring being continued for 10 additional min at the same temperature. After that, the resulting mixture was hydrolysed with water (10 ml),[17] extracted with ethyl acetate (3x10 ml), the organic layer dried over sodium sulfate and evaporated (15 Torr) giving a residue which was purified by column chromatography (silica gel, hexane/ethyl acetate) to afford the title compounds. *Z/E*-Diastereoisomers could be in many cases separated chromatographycally. In the case of using the starting material **1d** the crude reaction mixture was analysed by tandem GLC-MS and the corresponding four diastereoisomers **4** (see text) identified by comparison with authentic samples.[11] Yields and *Z/E* ratios are included in Table 1; physical, analytical and spectroscopic data follow.

(Z)*-2-Methyl-6-morpholino-4-hexen-3-ol* [(Z)-**2aa**]:[18] δ_H 0.92 0.96 (6H, 2d, *J* = 6.7, 2xMe), 1.75 (1H, m, C*H*Me_2), 2.53 (4H, m, 2xCH_2N), 2.90, 3.14 (2H, 2dd, *J* = 13.2, 6.4, CH_2N), 3.74 (4H, m, 2xCH_2O), 4.06 (1H, t, *J* = 6.1, C*H*OH), 5.68 (1H, m, C*H*=CH), 5.79 (1H, dd, *J* = 11.6, 6.1, CH=C*H*); δ_C 18.0, 18.3 (2xMe), 33.9 (*C*HMe_2), 53.3, 55.2 (3C, 3xCH_2N), 66.8 (2C, 2CH_2O), 73.1 (CHOH), 126.9, 137.6 (CH=CH); *m/z* 181 (M$^+$-18, 4%), 156 (40), 126 (12), 112 (39), 100 (23), 88 (100), 87 (12), 86 (23), 70 (21), 69 (79), 68 (16), 57 (32), 56 (26), 55 (19), 44 (24), 43 (46), 42 (32).

(E)*-2-Methyl-6-morpholino4-hexen-3-ol* [(*E*)-**2aa**]: *m/z* 199 (M$^+$, 0.9%), 181 (M$^+$-18, 3), 156 (17), 126 (38), 112 (34), 100 (32), 96 (14), 88 (100), 86 (31), 70 (19), 69 (63), 68 (21), 57 (26), 56 (33), 55 (24), 44 (29), 443 (69), 42 (42).

(Z)*-2,2-Dimethyl-6-morpholino-4-hexen-3-ol* [(*Z*)-**2ab**]: R_f 0.80 (hexane/ethyl acetate: 1/1); ν (film) 3441 (OH), 1653, 1456 (C=C), 1118 cm^{-1} (C-O); δ_H 0.93 (9H,s, 3xMe), 2.53 (4H, m, 2xCH_2N), 2.93 (1H, dd, *J* = 13.1, 5.7, C*H*HN), 3.15 (1H, ddd, *J* = 13.1, 6.7, 1.3, CH*H*N), 3.72 (4H, t, *J* = 4.7, 2xCH_2O), 4.00 (1H, dd, *J* = 6.7, 1.3, C*H*OH), 5.70 (1H, dddd, *J* = 11.9, 6.7, 5.7, 1.3, C*H*=CH), 5.85 (1H, ddt, *J* = 11.9, 6.7, 1.3, CH=C*H*); δ_C 25.6 (3xMe), 35.1 (*C*Me_3), 53.3, 55.2 (3C, 3xCH_2N), 66.7 (2C, 2CH_2O), 75.8 (CHOH), 127.3, 135.8 (CH=CH); *m/z* 214 (M$^+$+1, 1%), 195 (M$^+$-18, 2), 180 (17), 157 (10), 156 (93), 126 (69), 111 (26), 100 (35), 98 (14), 95 (11), 89 (13), 88 (100), 86 (45), 83 (19), 71 (17), 70 (43), 69 (54), 68 (39), 67 (15), 58 (13), 57 (50), 56 (37), 55 (35), 44 (29), 43 (44), 42 (40) (Found: M$^+$, 195.1619.$C_{12}H_{21}NO$ requires M, 195.1623).

(E)*-2,2-Dimethyl-6-morpholino-4-hexen-3-ol* [(*E*)-**2ab**]: R_f 0.40 (hexane/ethyl acetate: 1/1); ν (film) 3423 (OH), 1637, 1456 (C=C), 1117 cm^{-1} (C-O); δ_H 0.90 (9H, s, 3xMe), 2.47 (4H, m, 2xCH_2N), 3.03 (2H, m, 2xCH$_2$N), 3.71-3.75 (5H, m, 2xCH$_2$O and C*H*OH), 5.71 (1H, m, C*H*=CH), 5.75 (1H, def dd, *J* = 15.6, CH=C*H*); δ_C 25.5 (3xMe), 34.8 (*C*Me$_3$), 53.3, 60.7 (3C, 3xCH$_2$N), 66.7 (2C, 2CH$_2$O), 80.2 (CHOH), 128.0, 134.2 (CH=CH); *m/z* 213 (M$^+$, 2%), 195 (M$^+$-18, 4), 180 (10), 156 (80), 127 (10), 126 (100), 100 (63), 98 (12), 96 (13), 89 (10), 88 (94), 87 (29), 86 (61), 83 (10), 71 (16), 70 (44), 69 (62), 68 (33), 67 (13), 58 (14), 57 (64), 56 (43), 55 (32), 44 (30), 43 (49), 42 (47) (Found: M$^+$, 198.1499.$C_{11}H_{20}NO_2$ requires M, 198.1494).

*(*Z*)-1-Morpholino-1-propenyl-1-cyclohexanol* [(*Z*)-**2ad**]: R_f 0.67 (hexane/ethyl acetate: 1/1); ν (film) 3416 (OH), 3013, 1652, 1646, 1449 (C=CH), 1118 cm^{-1} (C-O); δ_H 1.24-1.77 (10H, m, 5xring CH$_2$), 2.55 (4H, br s, 2xCH$_2$N), 3.06 (2H, dd, *J* = 6.1, 1.2, CH$_2$N), 3.72 (4H, t, *J* = 4.8, 2xCH$_2$O), 5.38 (1H, dt, *J* = 12.2, 6.1, C*H*=CH), 5.71 (1H, d, *J* = 12.2, CH=C*H*); δ_C 21.9, 25.55, 38.5 (5C, 5xring CH$_2$), 52.9, 55.0 (3C, 3xCH$_2$N), 66.6 (2C, 2xCH$_2$O), 71.7 (COH), 120.9, 143.4 (CH=CH); *m/z* 226 (M$^+$+1, 1%), 225 (M$^+$, 7), 208 (12), 207 (67), 178 (16), 138 (12), 127 (10), 126 (87), 124 (25), 122 (11), 121 (13), 120 (10), 112 (29), 109 (11), 100 (82), 98 (10), 97 (12), 96 (58), 95 (27), 94 (22), 93 (21), 92 (10), 91 (23), 88 (74), 87 (43), 86 (100), 83 (20), 82 (30), 81 (28), 80 (16), 79 (42), 77 (21), 70 (14), 69 (32), 68 (29), 67 (35), 65 (11), 58 (11), 57 (42), 56 (76), 55 (92), 53 (24), 44 (53), 43 (55), 42 (66) (Found: M$^+$, 225.1727.$C_{13}H_{23}NO_2$ requires M, 225.1729).

*(*E*)-1-Morpholino-1-propenyl-1-cyclohexanol* [(*E*)-**2ad**]: R_f 0.54 (hexane/ethyl acetate: 1/1); ν (film) 3440 (OH), 1653, 1454 (C=C), 1117 cm^{-1} (C-O); δ_H 1.26-1.73 (10H, m, 5xring CH$_2$), 2.44 (4H, m, 2xCH$_2$N), 3.06 (2H, d, *J* = 5.5, CH$_2$N), 3.72 (4H, m, 2xCH$_2$O), 5.70 (1H, m, C*H*=CH), 5.77 (1H, d, *J* = 15.6, CH=C*H*); δ_C 22.0, 25.4, 37.8 (5C, 5xring CH$_2$), 53.4, 60.9 (3C, 3xCH$_2$N), 66.8 (2C, 2xCH$_2$O), 71.1 (COH), 123.3, 142.0 (CH=CH); *m/z* 226 (M$^+$+1, 0.7%), 225 (M$^+$, 4), 207 (39), 182 (25),138 (11), 126 (32), 124 (21), 112 (21), 109 (11), 100 (35), 96 (21), 95 (38), 94 (22), 93 (13), 91 (15), 88 (85), 87 (100), 86 (77), 83 (10), 82 (20), 81 (20), 80 (12), 79 (27), 77 (12), 70 (10), 69 (17), 68 (21), 67 (25), 57 (62), 56 (44), 55 (55), 54 (14), 53 (15), 44 (27), 43 (34), 42 (38) (Found: M$^+$, 225.1727.$C_{13}H_{23}NO_2$ requires M, 225.1729).

(Z/E)*-6-(*N,N*-Diallylamino)-2-methyl-4-hexen-3-ol* (**2ba**):[18] ν (film) 3399 (OH), 1645, 1464, 1447 cm^{-1} (C=C); δ_H [(*E*)-isomer] 0.90, 0.94 (6H, 2d, *J* = 6.7, 2xMe), 1.55-1.70 (2H, br s and m, C*H*Me$_2$ and OH), 3.10 (6H, m, 3xCH$_2$N), 3.87 (1H, m, C*H*OH), 5.18 (4H, m, 2x CH=C*H*$_2$), 5.68 (2H, m, 2xC*H*=CH$_2$), 5.79-5.93 (2H, m, CH=CH); δ_H [(Z)-isomer] 0.91, 0.96 (6H, 2d, *J* = 6.7, 2xMe), 1.74 (1H, m, CHMe$_2$), 2.94, 3.06, 3.19, 3.24 (6H, (dd, *J* = 14.0, 5.2), (dd, *J* = 13.4, 7.0), (dd, *J* = 14.0, 5.8) and (dd, *J* = 14.0, 6.4), 3xCH$_2$N), 4.05 (1H, t, *J* = 6.1, C*H*OH), 5.19 (4H, m, 2xCH=C*H*$_2$), 5.71 (2H, m, 2xC*H*=CH$_2$), 5.81-5.95 (2H, m, CH=CH); *m/z* [(*E*)-isomer] 209 (M$^+$, 0.8%), 98 (15), 81 (10), 70 (19), 69 (24), 68 (15), 67 (11), 57 (14), 56 (21), 55 (23), 45 (14), 44 (66), 43 (100), 42 (33); *m/z* [(*Z*)-isomer] 209 (M$^+$, 0.9%), 110 (12), 98 (14), 81 (10), 70 (22), 69 (14), 68 (14), 57 (16), 56 (19), 55 (19), 45 (15), 44 (67), 43 (100), 42 (33).

*(*Z*)-6-(*N,N*-Diallylamino)-2,2-dimethyl-4-hexen-3-ol* [(Z)-**2bb**]:[18] R_f 0.41 (hexane/ethyl acetate: 7/3); ν (film) 3415 (OH), 3078, 1643, 1479 cm^{-1} (C=CH); δ_H 0.92 (9H, s, 3xMe), 2.93-3.26 (6H, m, 3xCH$_2$N), 5.18 (5H, m, C*H*=CH and 2xCH=C*H*$_2$), 5.69 (1H, m, CH=C*H*), 5.77-5.94 (2H, m, 2xC*H*=CH$_2$); δ_C 25.6 (3C, 3xMe), 35.0 (*C*Me$_3$), 49.95, 56.3 (3C, 3xCH$_2$N), 75.6 (CHOH), 118.4, 128.6, 134.6, 135.2 (6C, CH=CH and 2xCH=CH$_2$); *m/z* 208 (M$^+$-15, 1.4%), 190 (23), 126 (17), 110 (22), 108 (16), 98 (73), 96 (19), 95 (17), 94 (10), 83 (10), 82 (11), 81 (13), 71 (10), 70 (36), 69 (72), 68 (35), 67 (18), 57 (68), 56 (42), 55 (31), 45 (11), 44 (48), 43 (100), 42 (54).

*(*E*)-6-(*N,N*-Diallylamino)-2,2-dimethyl-4-hexen-3-ol* [(*E*)-**2bb**]:[18] R_f 0.33 (hexanc/ethyl acetate: 7/3); ν (film) 3413 (OH), 3078, 1644, 1643 cm^{-1} (C=CH); δ_H 0.91 (9H, s, 3xMe), 3.10 (6H, m, 3xCH$_2$N), 5.14-5.22 (4H, m, CH=C*H*$_2$), 5.64-5.72 (1H, m, CH=C*H*), 5.79-5.93 (3H, m, C*H*=CH and 2xC*H*=CH$_2$); δ_C 25.7 (3C, 3xMe), 34.8 (*C*Me$_3$), 54.9, 56.3 (3C, 3xCH$_2$N), 80.5 (CHOH), 117.9, 129.2, 133.6, 135.1 (6C, CH=CH and 2xCH=CH$_2$); *m/z* 223 (M$^+$, 0.65%), 194 (16), 166 (24), 126 (14), 110 (38), 108 (15), 98 (48), 96 (25), 95 (11), 94 (13), 82 (14), 81 (14), 80 (10), 79 (13), 70 (60), 69 (34), 68 (39), 67 (16), 57 (100), 56 (36), 55 (27), 54 (12), 53 (10), 44 (33), 43 (77), 42 (54).

*(*E*)-1-[3-(*N,N*-Diallyl)amino-1-propenyl]cyclohexan-1-ol* [(*E*)-**2bd**]: R_f 0.51 (hexane/ethyl acetate: 7/3); ν (film) 3444 (OH), 1660, 1570 cm^{-1} (C=C); δ_H 1.30-1.67 (10H, m, 5xring CH$_2$), 3.08 (6H, m, 3xCH$_2$N), 5.14, 5.20 (6H, 2m, 2xCH=CH$_2$), 5.84, 5.87 (2H, 2 dt, *J* = 17.1, 6.4, CH=CH); δ_C 22.2, 25.5, 37.95 (5C, 5xring CH$_2$), 55.1, 56.3 (3C, 3xCH$_2$N), 71.3 (COH), 117.8, 124.1, 135.3, 141.5 (6C, CH=CH and

2xCH=CH$_2$); *m/z* 235 (M$^+$, 3%), 136 (11), 110 (35), 108 (20), 96 (13), 93 (11), 91 (17), 82 (13), 80 (11), 79 (20), 77 (10), 70 (31), 68 (17), 67 (23), 57 (14), 56 (18), 55 (32), 54 (10), 53 (14), 45 (12), 44 (100), 43 (57), 42 (41) (Found: M$^+$, 235.1934. $C_{15}H_{25}NO$ requires M, 235.1936).

(Z)-4-Ethyl-1-phenoxy-2-hexen-4-ol [(*Z*)-**2cc**]: R_f 0.70 (hexane/ethyl acetate: 8/2); ν (film) 3450 (OH), 1599, 1586, 1496, 1459 (C=C), 1244 cm^{-1} (C-O); δ_H 0.93 (6H, t, *J* = 7.6, 2xMe), 1.58 (4H, q, *J* = 7.6, 2xCH$_2$), 4.90 (2H, dd, *J* = 5.8, 1.5, CH$_2$O), 5.42 (1H, dd, *J* = 12.2, 1.2, C*H*CH$_2$), 5.75 (1H, m, C*H*COH), 6.94, 7.27 (5H, 2m, ArH); δ_C 7.9 (2C, 2xMe), 34.1 (2C, 2xCH$_2$), 64.9 (CHO), 72.1 (CH$_2$O), 114.8, 120.7, 126.8, 129.4, 136.8, 158.5 (8C, CH=CH and ArC); *m/z* 220 (M$^+$, 1%), 109 (17), 97 (26), 94 (64), 79 (12), 77 (13), 69 (13), 67 (25), 65 (14), 57 (100), 55 (19), 43 (32).

1-[(Z)-3-Phenoxy-1-propenyl]-1-cyclohexanol [(*Z*)-**2cd**]: R_f 0.41 (hexane/ethyl acetate: 8/2); ν (film) 3415 (OH), 3062, 3038, 1599, 1587, 1496 (C=CH), 1241 cm^{-1} (CO); δ_H 1.58 (10H, m, 5xring CH$_2$), 4.54 (2H, d, *J* = 4.3, CH$_2$O), 5.92 (1H, dd, *J* = 15.9, 4.3, C*H*CH$_2$), 5.99 (1H, d, *J* = 15.9, C*H*COH), 6.94, 7.28 (5H, 2m, ArH); δ_C 22.0, 25.4, 37.7 (5C, 5xring CH$_2$), 68.3 (COH), 71.3 (CH$_2$O), 114.7, 120.8, 122.5, 129.4, 141.4, 158.6 (8C, CH=CH and ArC); *m/z* 232 (M$^+$, 1%), 214 (10), 139 (10), 121 (34), 120 (32), 105 (15), 95 (14), 94 (100), 93 (31), 92 (21), 91 (43), 79 (66), 78 (13), 77 (36), 69 (21), 67 (34), 66 (19), 65 (34), 57 (13), 55 (55), 53 (16), 51 (21), 44 (15), 43 (24) (Found: M$^+$, 232.1455. $C_{15}H_{20}O_2$ requires M, 232.1463).

Two-step DTBB-Catalysed Lithiation of Compounds **1**. *Isolation of Compounds* **3**. *General Procedure*.- To a green suspension of lithium powder (150 mg, 21 mmol) and DTBB (52 mg, 0.2 mmol) in THF (5 ml) was added the corresponding substrate **1** (2 mmol) at temperatures ranging between -30 and -40°C. After *ca*. 20 min. (the green colour appeared again) the corresponding electrophile was added at the same temperature and the mixture was stirred for 20 additional min under the same reactions conditions. Then, the resulting green mixture was hydrolysed with water (10 ml) at the same temperature, extracted with ethyl acetate (3x10 ml), the organic layer dried over sodium sulfate and evaporated (15 Torr) giving a residue which was purified by column chromatography (silica gel, hexane/ethyl acetate) to afford the title compounds **3**. Yields are given in Table 2; physical, analytical and spectroscopic data follow.

2-Methyl-6-morpholino-4-hexyn-3-ol (**3aa**): R_f 0.38 (hexane/ethyl acetate: 8/2); ν (film) 3416 (OH), 2356 cm^{-1} (C≡C); δ_H 1.01 (6H, 2d, *J* = 5.8, 2xMe), 2.57 (4H, t, *J* = 4.7, 2xCH$_2$C*H*$_2$N), 3.35 (2H, d, *J* = 1.8, CCH$_2$N), 3.75 (4H, t, *J* = 4.7, 2xCH$_2$O), 4.21 (1H, dt, *J* = 5.8, 1.8, C*H*OH); *m/z* 197 (M$^+$, 4.7%), 86 (27), 68 (13), 57 (13), 56 (22), 55 (19), 45 (16), 44 (73), 43 (100), 42 (44) (Found: M$^+$, 197.1410. $C_{11}H_{19}NO_2$ requires M, 197.1416).

2,2-Dimethyl-6-morpholino-4-hexyn-3-ol (**3ab**): R_f 0.42 (hexane/ethyl acetate: 8/2); ν (film) 3441 cm^{-1} (OH); δ_H 1.00 (9H, s, 3xMe), 2.57 (4H, t, *J* = 4.7, 2xCH$_2$C*H*$_2$N), 3.35 (2H, d, *J* = 1.8, CCH$_2$N), 3.75 (4H, t, *J* = 4.7, 2xCH$_2$O), 4.04 (1H, t, *J* = 1.8, C*H*OH); δ_C 25.3 (3C, 3xMe), 35.7 (*C*Me$_3$), 47.4, 52.2 (3C, 3xCH$_2$N), 66.7 (2C, 2xCH$_2$), 71.2 (CHOH), 79.9, 85.5 (C≡C); *m/z* 212 (M$^+$+1, 3.3%), 211 (M$^+$, 23), 178 (40), 154 (34), 124 (30), 109 (13), 108 (13), 100 (53), 96 (16), 95 (11), 94 (13), 88 (47), 87 (57), 86 (100), 82 (11), 81 (10), 70 (11), 69 (16), 68 (35), 67 (17), 58 (16), 57 (96), 56 (60), 55 (28), 54 (13), 53 (15), 45 (12), 44 (35), 43 (60), 42 (68) (Found: M$^+$, 211.1571. $C_{12}H_{21}NO_2$ requires M, 211.1572).

1-(3-Morpholino-1-propenyl)-1-cyclohexanol (**3ad**): R_f 0.50 (hexane/ethyl acetate: 8/2); ν (film) 3405 (OH), 2241 cm^{-1} (C≡C); δ_H 1.23-1.67 (10H, 2m, 5xring CH$_2$), 2.57 (4H, t, *J* = 4.6, 2xCH$_2$C*H*$_2$N), 3.34 (2H, s, CCH$_2$N), 3.75 (4H, t, *J* = 4.6, 2xCH$_2$O); δ_C 23.2, 25.05, 39.9 (5C, 5xring CH$_2$), 47.3, 52.0 (3C, 3xCH$_2$N), 66.5 (2C, 2xCH$_2$O), 68.2 (COH), 78.7, 89.7 (C≡C); *m/z* 224 (M$^+$+1, 1.7%), 223 (M$^+$, 14), 205 (26), 124 (15), 122 (12), 108 (10), 100 (30), 96 (23), 95 (17), 94 (17), 91 (25), 86 (100), 82 (15), 81 (22), 80 (14), 79 (21), 77 (14), 69 (17), 68 (11), 67 (24), 66 (12), 65 (16), 57 (20), 56 (57), 55 (64), 54 (17), 53 (24), 52 (10), 44 (49), 43 (59), 42 (78) (Found: M$^+$, 223.1569. $C_{13}H_{21}NO_2$ requires M, 223.1572).

6-(Diallylamino)-2-methyl-4-hexyn-3-ol (**3bb**): R_f 0.53 (hexane/ethyl acetate: 8/2); ν (film) 3462 (OH), 1637, 1517 cm^{-1} (C=C); δ_H 1.01 (9H, s, 3xMe), 3.13 (4H, d, *J* = 6.4, 2xCHC*H*$_2$N), 3.43 (2H, d, *J* = 1.5, CCH$_2$N), 4.05 (1H, t, *J* = 1.5, C*H*OH), 5.18, 5.82 (6H, 2m, 2xCH=CH$_2$); δ_C 25.4 (3C, 3xMe), 31.35 (*C*Me$_3$), 41.5, 56.5 (3C, 3xCH$_2$N), 71.5 (CHOH), 80.3, 85.0 (C≡C), 118.1, 135.25 (4C, 2xCH=CH$_2$); *m/z* 222 (M$^+$+1, 0.8%), 221 (M$^+$, 5), 194 (37), 164 (12), 149 (13), 110 (22), 108 (13), 96 (20), 94 (17), 82 (12), 81 (12), 79 (11), 70 (49), 69 (14), 68 (40), 67 (17), 58 (10), 57 (100), 56 (26), 55 (19), 54 (13), 53 (10), 44 (38), 43 (42).

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