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Nitrogen-Containing Remote Functionalised Organolithium Compounds by Reductive Opening of Five- and Six-Membered Heterocycles†

Juan Almena, Francisco Foubelo and Miguel Yus*

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

Abstract: The reaction of different five- or six-membered nitrogen-containing heterocycles such as *N*-isopropyl-2-phenylpyrrolidine (**1**), *N*-phenyl-3-pyrroline (**6**), *N*-phenylisoindoline (**10**), *N*-phenyltetrahydroisoquinoline (**13**) and *N*-methyltetrahydroisoquinoline (**19**) with an excess of lithium powder and a catalytic amount of DTBB (4.5 mol %), followed by treatment with electrophiles [H_2O, D_2O, MeI, $CH_2{=}CHCH_2Br$, Pr^iCHO, Bu^tCHO, PhCHO, Me_2CO, Pr^nCOMe, PhCOMe, $(CH_2)_4CO$, $(CH_2)_5CO$, CO_2] and final hydrolysis gives a wide series of functionalised amines **3**, **8**, **9**, **12** and **19**, the key step in the process, being the reductive opening of the starting material giving a dianionic remote functionalised organolithium compound. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Since nitrogen-containing five- and six-membered rings are very common structures in organic chemistry, their use as starting materials for synthesis is of interest.[1] Concerning saturated heterocycles, their reactivity is limited because they behave almost as the corresponding open-chain amines. On the other hand, five years ago we discovered that the use of an arene as catalyst [naphthalene or 4,4'-di-*tert*-butylbiphenyl (DTBB)] in the lithiation of chlorinated molecules using metallic lithium is a powerful methodology, which allows the preparation of organolithium compounds under very mild reaction conditions.[2] Applying this procedure, it is possible to develop new methods to prepare alkyllithium from non-halogenated materials,[3] polylithium synthons[4] and very reactive functionalised organolithium compounds[5] by chlorine- or bromine-lithium exchange,[6] or reductive opening of saturated heterocycles.[7] Thus three-,[8a] four-,[8b] five-[9] or six-membered[7,9] oxygen-[7,8] or sulfur-containing[9] saturated heterocycles were opened by an arene-catalysed lithiation. In the case of the corresponding nitrogen-containing systems the mentioned reductive opening reaction was applied to the corresponding three-[10a,b] and four-membered[10c] rings. In this paper we extend this process to five- and six-membered saturated nitrogenated heterocycles in order to explore the synthetic possibilities of this reaction.

RESULTS AND DISCUSSION

Since the reductive opening of aziridines or azetidines with an arene-catalysed lithiation works only if a phenyl group is present somewhere at the ring, we first studied the reaction with *N*-phenylpyrrolidine, but after three days at room temperature the starting material remained unchanged. However, the treatment of *N*-isopropyl-2-phenylpyrrolidine (**1**) with lithium powder (1:9 molar ratio) in the presence of a catalytic

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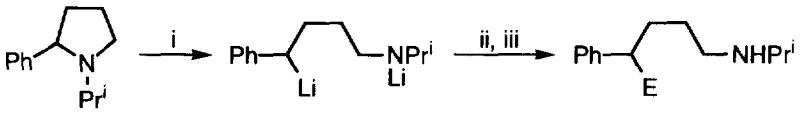
† This paper is dedicated to Professor Rafael Usón on occasion of his 70th birthday.

amount of 4,4'-di-*tert*-butylbiphenyl (DTBB; 1:0.09 molar ratio, 4.5 mol %) in THF at room temperature afforded the corresponding "dianion" **2**, the more stable benzylic carbanion, which by reaction with electrophiles [H_2O, D_2O, MeI, Bu^tCHO, PhCHO, Me_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, CO_2] at -78°C yielded, after hydrolysis, the expected amines (**3**) (Scheme 1 and Table 1). In the case of using methyl iodide (2 eq) the corresponding *C*- and *N*-methylated product **3c'** was isolated. When carbon dioxide was used as electrophile, the carbonation was performed at -50°C, the corresponding amino acid being isolated as the corresponding ethyl ester (**3i'**) by succesive benzoylation (2 eq of PhCOCl, 2.5 M NaOH), treatment with methyllithium (3 eq,-78°C) and final esterification with ethanol in 4 M hydrochloric acid (Table 1, entry 9). The apparently tortuous way to purified the carbonation product is the simplest one in order to separate this compound from the other by-products, specially compound **3a**, obtained by abstraction of a proton from the reaction medium by "dianion" **2**.



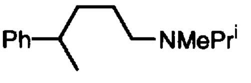
1 **2** **3a-i**

Scheme 1. *Reagents and conditions*: i, Li, DTBB cat. (4.5 mol %), THF, 20°C; ii, E^+ = H_2O, D_2O, MeI, Bu^tCHO, PhCHO, Me_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, CO_2, -78°C; iii, H_2O, -78 to 20°C.

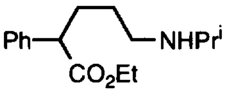
Table 1. Preparation of compounds **3**

Entry	Electrophile E^+	Product[a]			
		No.	E	Yield (%)[b]	R_f[c] or mp (°C)[d]
1	H_2O	**3a**	H	95	0.18
2	D_2O	**3b**	D	91[e]	0.18
3	MeI	**3c'**	-[f]	61	0.16
4	Bu^tCHO	**3d**	Bu^tCHOH	42[g]	0.12[g]
5	PhCHO	**3e**	PhCHOH	35[g]	0.09[g]
6	Me_2CO	**3f**	Me_2COH	43	108-109
7	$(CH_2)_4CO$	**3g**	$(CH_2)_4COH$	41	0.15
8	$(CH_2)_5CO$	**3h**	$(CH_2)_5COH$	45	0.19
9	CO_2	**3i'**	-[f]	28	0.16

[a] All products **3** were >96% pure (GLC and/or 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**. [c] Methanol was used as eluant. [d] From dichloromethane/pentane. [e] >90% Deuterium incorporation (mass spectrum). [f] See text. [g] A 1:1 diastereoisomers mixture was obtained (GLC and/or 300 MHz ^{1}H NMR), which could not be separated by TLC under these conditions.

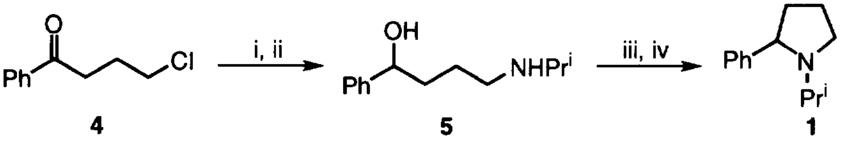


3c'



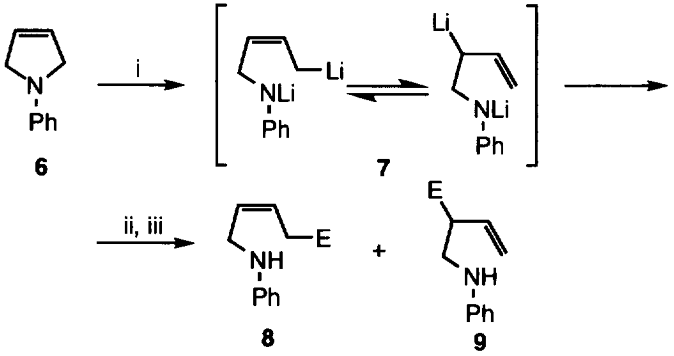
3i'

Starting material **1** was prepared from the corresponding aminoalcohol **5** (succesive treatment with thionyl chloride and 2.5 M sodium hydroxide; 38% overall yield), which was obtained from 4-chlorobutyrophenone (**4**) by reduction with sodium borohydride followed by treatment with isopropylamine (51% overall yield; Scheme 2).



Scheme 2. *Reagents and conditions*: i, $NaHCO_3$, $NaBH_4$, $EtOH$-H_2O, 20°C; ii, Pr^iNH_2, 80°C; iii, $SOCl_2$, $CHCl_3$, 60°C; iv, 2.5 M NaOH.

Whereas *N*-phenylpyrrolidine does not react with lithium in the presence of DTBB as the catalyst (see above), the corresponding 3-pyrroline **6** reacted under the reaction conditions shown in Scheme 1 to give the corresponding allylic delocalised dianion **7**, which by condensation with several electrophiles and final hydrolysis yielded the expected mixture of both possible isomers **8** and **9**, their being dependent on the electrophile used. For instance, the use of water or deuterium oxide afforded exclusively compounds **8** (Table 2, entries 1 and 2). However, in all other cases the mixture of products **8** and **9** was obtained, the latter being always the most abundant. The use of pivalaldehyde as electrophile yielded a *ca.* 1:1 diastereoisomers mixture, for products **9c** (Table 1, entry 4). Finally, when CO_2 was employed as electrophile, under the reaction conditions mentioned for compounds **8g/9g**, it was necessary to esterify the crude aminoacids initially obtained with ethanol under acidic conditions in order to isolate the amino esters **8g'** and **9g'** (Table 2, entries 11 and 12 and footnote i).

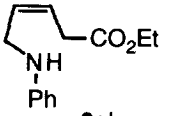


Scheme 3. *Reagents and conditions*: i, Li, DTBB cat. (4.5 mol %), THF, 20°C; ii, E^+ = H_2O, D_2O, Bu^tCHO, Me_2CO, $(CH_2)_4CO$, $(CH_2)_5CO$, CO_2, -78°C; iii, H_2O, -78 to 20°C.

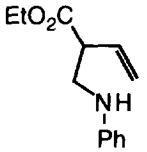
Table 2. Preparation of compounds **8** and **9**

Entry	Electrophile E+	Product[a]				
		No.	E	Yield (%)[b]	R_f or mp (°C)[c]	Global yield (%)[d]
1	H_2O	**8a**	H	85	0.30[e]	85
2	D_2O	**8b**	D	80[f]	0.30[e]	80
3	Bu^tCHO	**8c**	Bu^tCHOH	31	0.33[g]	72
4		**9c**	Bu^tCHOH	19/22[h]	0.48/0.43[g]	
5	Me_2CO	**8d**	Me_2COH	18	0.16[g]	60
6		**9d**	Me_2COH	42	0.28[g]	
7	$(CH_2)_4CO$	**8e**	$(CH_2)_4COH$	11	0.24[g]	58
8		**9e**	$(CH_2)_4COH$	47	0.31[g]	
9	$(CH_2)_5CO$	**8f**	$(CH_2)_5COH$	25	0.26[g]	75
10		**9f**	$(CH_2)_5COH$	50	80-81	
11	CO_2	**8g'**	-[i]	9	0.46[g]	34
12		**9g'**	-[i]	25	0.49[g]	

[a] All isolated products **8** and **9** were >95% pure (GLC and/or 300 MHz ^1H NMR). [b] Isolated yield after chromatographic separation by column (silica gel, hexane/ethyl acetate). [c] From dichloromethane/pentane. [d] **8**+**9** Isolated yield. [e] Silica gel, hexane/ethyl acetate: 20/1. [f] >90% Deuterium incorporation (mass spectrum). [g] Silica gel, hexane/ethyl acetate: 3/1. [h] Diastereoisomers ratio determined after chromatographic separation. [i] The corresponding aminoacids were isolated as their corresponding ethyl esters **8g'** and **9g'** (see text).



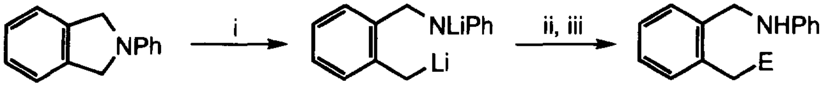
8g'



9g'

Starting material **6** was prepared by reaction of aniline with commercially available (*Z*)-1,4-dichloro-2-butene in the presence of *n*-butyllithium in 38% overall yield.

We then considered the reductive opening of isoindoline finding that *N*-isopropylisoindoline does not react with lithium powder under DTBB catalysis after three days at room temperature. However, when the corresponding *N*-phenyl derivative **10** was submitted to the reaction conditions shown in Scheme 1 it gave in a two-step process the expected products **12**, after hydrolysis, via the corresponding dianion **11** (Scheme 4 and Table 3).



10 **11** **12**

Scheme 4. *Reagents and conditions*: i, Li, DTBB cat. (4.5 mol %), THF, 20°C; ii, E^+ = H_2O, D_2O, Pr^iCHO, Bu^tCHO, PhCHO, Me_2CO, PhCOMe, -78°C; iii, H_2O, -78 to 20°C.

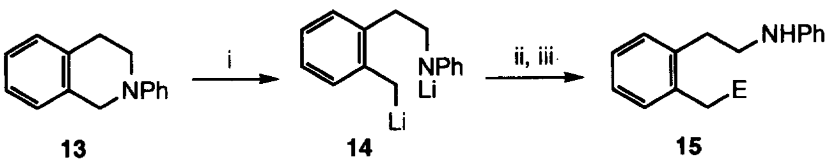
Table 3. Preparation of compounds **12**

Entry	Electrophile E^+	Product 3[a]			
		No.	E	Yield (%)[b]	R_f[c] or mp (°C)[d]
1	H_2O	**12a**	H	70	0.48
2	D_2O	**12b**	D	65[e]	0.48
3	Pr^iCHO	**12c**	Pr^iCHOH	32	0.29
4	Bu^tCHO	**12d**	Bu^tCHOH	40	81-82
5	PhCHO	**12e**	PhCHOH	35	87-88
6	Me_2CO	**12f**	Me_2COH	49	0.15
7	PhCOMe	**12g**	PhC(OH)Me	37	0.25

[a] All products **12** were >94% pure (GLC and/or 300 MHz ^1H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **10**. [c] Silica gel, hexane/ethyl acetate: 5/1. [d] From dichloromethane/pentane. [e] >90% Deuterium incorporation (mass spectrum).

Starting material **10** was easily prepared from commercially available 1,2-bis(bromomethyl)benzene and aniline in the presence of *n*-butyllithium (72% yield).

In the last part of this study we considered nitrogen containing six-membered rings as substrates. *N*-Phenyltetrahydroisoquinoline (**13**) was lithiated in the presence of DTBB as the electron transfer carrier catalyst at room temperature and after reaction with different electrophiles and final hydrolysis, yielded the expected reaction products **15** through the corresponding dianion **14**. In the case of using carbon dioxide as electrophile, the reaction was performed as it was above described for the carbonation of intermediates **2** (Scheme 1), the corresponding final aminoacid being isolated as its ethyl ester **15h'** (Scheme 5 and Table 4).

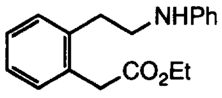


Scheme 5. *Reagents and conditions*: i, Li, DTBB cat. (4.5 mol %), THF, 20°C; ii, $E^+ = H_2O$, D_2O, Bu^{t}CHO, PhCHO, Me_2CO, Pr^{n}COMe, $(CH_2)_4CO$, CO_2, -78°C; iii, H_2O, -78 to 20°C.

Table 4. Preparation of compounds **15**

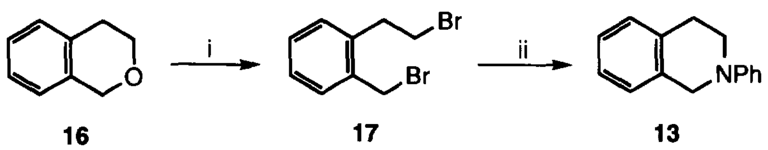
Entry	Electrophile E^+	Product[a] No.	E	Yield (%)[b]	R_f
1	H_2O	**15a**	H	89	0.45[c]
2	D_2O	**15b**	D	84[d]	0.45[c]
3	Bu^{t}CHO	**15c**	Bu^{t}CHOH	40	0.46[e]
4	PhCHO	**15d**	PhCHOH	49	0.23[e]
5	Me_2CO	**15e**	Me_2COH	47	0.23[e]
6	Pr^{n}COMe	**15f**	Pr^{n}C(OH)Me	53	0.22[f]
7	$(CH_2)_4CO$	**15g**	$(CH_2)_4COH$	53	0.25[e]
8	CO_2	**15h'**	-[g]	34	0.26[f]

[a] All products **15** were >97% pure (GLC and/or 300 MHz ^1H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **13**. [c] Silica gel, hexane/ethyl acetate: 10/1. [d] >90% Deuterium incorporation (mass spectrum). [e] Silica gel, hexane/ethyl acetate: 3/1. [f] Silica gel, hexane/ethyl acetate: 5/1. [g] See text.



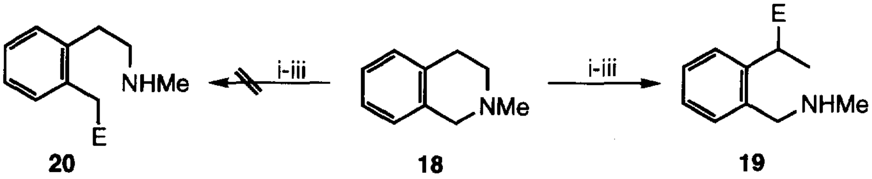
15h'

Starting material **13** was prepared by reaction of aniline with 2-(2-bromoethyl)benzyl bromide **17** [obtained by hydrogen bromide opening of isochromane **16** (56% yield)] under basic reaction conditions (69% yield) (Scheme 6).

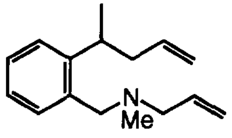


Scheme 6. *Reagents and conditions*: i, 45% HBr, 96% H_2SO_4, Adogen®, 115°C; ii, $PhNH_2$, K_2CO_3, EtOH, reflux.

Finally we applied the DTBB-catalysed lithiation to *N*-methyltetrahydroisoquinoline **18**. In this case we obtained a surprising result: compounds **19** were obtained instead of the expected ones of type **20** (Scheme 7 and Table 5). When allyl bromide was used as electrophile (1:2.5 molar ratio) the corresponding *C*- and *N*-allylation product **19c'** was isolated (Table 5, entry 3).



Scheme 7. *Reagents and conditions*: i, Li, DTBB cat. (4.5 mol %), THF, 20°C; ii, $E^+ = H_2O$, D_2O, $CH_2{=}CHCH_2Br$, $(CH_2)_4CO$, -78°C; iii, H_2O, -78 to 20°C.



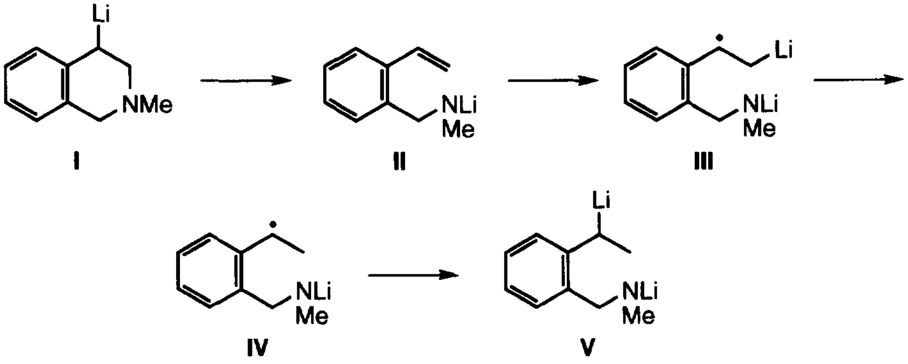
19c'

Table 5. Preparation of compounds **19**

Entry	Electrophile E^+	Product[a] No.	E	Yield (%)[b]	R_f[c] or mp (°C)[d]
1	H_2O	**19a**	H	76	134-136
2	D_2O	**19b**	D	69[e]	135-137
3	$CH_2{=}CHCH_2Br$	**19c'**	-[f]	47	0.10
4	$(CH_2)_4CO$	**19d**	$(CH_2)_4COH$	39	0.51

[a] All products **19** were >96% pure (GLC and/or 300 MHz ^1H NMR) except **19a** (92%). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **18**. [c] Silica gel, methanol. [d] From dichloromethane/pentane. [e] >90% Deuterium incorporation (mass spectrum). [f] See text.

A possible explanation of this strange behaviour can be as follows: a benzylic lithiation takes initially place[11] to give a β-nitrogenated organolithium compound **I**, which undergoes spontaneous β-elimination[12] giving the vinylic derivative **II**. The styrene derivative can add an electron from the strong reductive medium to form an unstable radical-anion of type **III**:[13] this intermediate can take a proton from the reaction medium giving a benzylic radical **IV** (stabilysed by delocalisation through the phenyl group), which by taking a new electron from the activated lithium affords the dianion intermediate **V**. The final trapping of the organolithium species by the electrophile gives the obtained products **19** (Scheme 8).



Scheme 8

Starting material **18** was prepared from commercially available tetrahydroisoquinoline hydrochloride by succesive treatment with *n*-butyllithium (2.1 eq) and methyl iodide (92% yield).

As a conclusion, we have shown that the tandem DTBB-catalysed lithiation of some five- and six-membered nitrogenated heterocycles-reaction with electrophiles is an adequate way to prepare a wide series of functionalised amines (the key step of the process is the regioselective opening of the heterocycle).

EXPERIMENTAL PART

General.- For general information see, for instance, reference 10b.

Preparation of 4-Isopropylamino-1-phenylbutanol (**5**). To a suspension of sodium hydrogencarbonate (1 g, 1.20 mmol) and 4-chlorobutyrophenone (**4**) (1.6 ml, 10 mmol) in ethanol (10 ml) was dropwise added a water solution (5 ml) of sodium borohydryde (0.189 gr, 5 mmol) at room temperature, and the resulting mixture was stirred at the same temperature for 1 h. Ethanol was evaporated (15 Torr) and the residue was hydrolysed with water (25 ml), acidified with 3 M hydrochloric acid (15 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting brown oil was added to isopropyl amine (2.6 ml, 30 mmol) in a sealed tube and was heated to 75°C for 15 h. The reaction mixture was then basified with 2.5 M sodium hydroxide (15 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then recrystallised from pentane/dichloromethane to yield pure product **5**. Yield is given in the text; mp 63-64°C (pentane/dichloromethane); ν_{max} (KBr) 3600-3080 cm^{-1} (OH, NH); δ_H 1.03 [6H, d, *J*=6.3, $(C\mathit{H}_3)_2CH$], 1.47-1.86 (4H, m, $HOCHC\mathit{H}_2C\mathit{H}_2$), 2.49-2.53 (1H, m, *H*CHNH), 2.64-2.67 (1H, m, HC*H*NH), 2.74 (1H, heptet, *J*=6.3, C*H*NH), 3.90 (2H, br s, OH, NH), 4.57 (1H, dd, *J*=8.5, 3.0, HOC*H*), 7.12-7.31 (5H, m, ArH); δ_C 22.4, 22.6 [$(\mathit{C}H_3)_2CH$], 27.5 ($\mathit{C}H_2CH_2N$), 39.5 ($HOCH\mathit{C}H_2$), 46.9 (CH_2N), 48.6 (CHN), 73.4 (CHOH), 125.7, 126.5, 128.0, 145.8 (ArC); *m/z* 207 (M$^+$, 14%), 174 (22), 131 (38), 91 (14), 79 (12), 77 (20), 72 (100), 58 (12), 44 (11) (Found : C, 75.17; H, 10.63; N, 6.40. $C_{13}H_{21}NO$ requires: C, 75.32; H, 10.21; N, 6.76).

Preparation of N-*Isopropyl-2-phenylpyrrolidine* (**1**).- To a stirred chloroform (20 ml) solution of aminoalcohol **5** (1.04 gr, 5 mmol) was added thionyl chloride (1 ml, 13.7 mmol) at 0°C. The reaction mixture was heated to 60°C for 3 h. The reaction mixture was then carefully hydrolysed with water (20 ml), basified with 2.5 M sodium hydroxide (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was evaporated (15 Torr) and the residue was treated with 2.5 M sodium hydroxide (20 ml) overnight. Then it was extracted with ethyl acetate (3x25 ml) and the organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) to yield pure product **1**. Yield is given in the text; R_f=0.48 (ethyl acetate); ν_{max} (film) 3040, 1590, 750, 690 cm^{-1} (ArH); δ_H 0.80, 0.91 [6H, 2d, *J*=6.5, $(C\mathit{H}_3)_2CH$], 1.52-1.67 (2H, m, $NCH_2C\mathit{H}_2CH_2CHPh$), 1.73-1.83, 1.96-2.05 (2H, 2 m, $C\mathit{H}_2CHPh$), 2.48 (1H, q, *J*=8.4, NC*H*H), 2.69 (1H, heptet, *J*=6.5, CHN), 2.95-3.01 (1H, m, NCH*H*), 3.53 (1H, t, *J*=7.5, NC*H*Ph), 7.06-7.28 (5H, m, ArH); δ_C 14.8 ($NCH_2CH_2CH_2CHPh$), 22.4, 22.8 [$(\mathit{C}H_3)_2CH$], 35.7 ($\mathit{C}H_2CHPh$), 46.1 (CH_2N), 48.5 (CHN), 65.0 (*C*HPh), 126.4, 127.2, 128.1, 145.6 (ArC); *m/z* 189 (M$^+$, 9%), 175 (10), 174 (100), 131 (44), 112 (14), 91 (26), 70 (13) (Found: M$^+$, 189.1514. $C_{13}H_{19}N$ requires M, 189.1518).

Preparation of Compounds **3**. *General Procedure*.- To a blue suspension of lithium powder (0.125g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added pyrrolidine **1** (0.380 ml, 2.0 mmol) under argon and the mixture was stirred for 0.5 h at the same temperature. Then, the mixture was cooled down at -78°C and the corresponding electrophile (3.0 mmol; 0.5 ml in the case of water or deuterium oxide; CO_2 was bubbled for 1.5 h) was added. The mixture was stirred at the same temperature for 0.5 h and hydrolysed with water (25 ml). The resulting mixture was extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) and/or recrystallised to yield pure products **3**. When the electrophile was CO_2, after having hydrolysed the mixture with water at -78°C it was basified with 2.5 M sodium hydroxide (10 ml) and benzoyl chloride was added dropwise (1.15 ml, 10.0 mmol) at 0°C. The reaction mixture was acidified with 3 M hydrochloric acid (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was treated with 1.6 M hexane solution of MeLi (3.1 ml, 5 mmol) in 5 ml of THF at -50°C for 2 h. After that, the organic solvent was removed (15 Torr) and then was hydrolysed with a 4 M ethanol solution of hydrogen chloride overnight. After having evaporated the solvent the residue was hydrolysed with water (20 ml), basified with 2.5 M sodium hydroxyde (20 ml), and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr) to yield pure compound **3i'** [>95% pure (GLC and 300 MHz ^{1}H NMR)]. Yields and physical data (R_f or mp) are included in Table 1; analytical and spectroscopic data follow.

Isopropyl 4-Phenylbutyl Amine (**3a**): ν_{max} (film) 3280 cm^{-1} (NH); δ_H 0.95 [6H, d, J=6.2, $(CH_3)_2CH$], 1.15 (1H, br s, NH), 1.38-1.48 (2H, m, CH_2CH_2Ph), 1.52-1.62 (2H, m, NCH_2CH_2), 2.49-2.56 (4H, m, CH_2Ph, NCH_2), 2.68 (1H, heptet, J=6.2, CHN), 7.05-7.21 (5H, m, ArH); δ_C 22.9 [$(CH_3)_2CH$], 29.2, 30.0 (2xCH_2), 35.7 (CH_2Ph), 47.3 (CH_2N), 48.6 (CHN), 125.5, 128.1, 128.3, 142.3 (ArC); m/z 191 (M$^+$, 16%), 176 (41), 91 (63), 72 (100), 44 (14) (Found: M$^+$, 191.1673. $C_{13}H_{21}N$ requires M, 191.1674).

4-Deuterio-4-phenylbutyl Isopropyl Amine (**3b**): ν_{max} (film) 3280 cm^{-1} (NH); δ_H 0.94 [6H, d, J=6.2, $(CH_3)_2CH$], 1.00 (1H, br s, NH), 1.39-1.47 (2H, m, CH_2CHDPh), 1.51-1.59 (2H, m, NCH_2CH_2), 2.48-2.55 (3H, m, CHPh, NCH_2), 2.66 (1H, heptet, J=6.2, CHN), 7.04-7.19 (5H, m, ArH); δ_C 22.8 [$(CH_3)_2CH$], 29.0, 29.9 (2xCH_2), 35.3 (t, J_{CD}=19.3), 47.2 (CH_2N), 48.5 (CHN), 125.4, 128.0, 128.1, 142.2 (ArC); m/z 192 (M$^+$, 16%), 177 (44), 92 (44), 91 (28), 73 (13), 72 (100), 44 (13) (Found: M$^+$, 192.1737. $C_{13}H_{20}DN$ requires M, 192.1737).

Isopropyl Methyl 4-Methyl-4-phenylbutyl Amine (**3c'**): ν_{max} (film) 3082, 3061, 3026, 761, 700 cm^{-1} (Ar); δ_H 0.97 [6H, d, J=6.7, $(CH_3)_2CH$], 1.24 (3H, d, J=6.7, CH_3CHPh), 1.35-1.61 (4H, m, $NCH_2CH_2CH_2$), 2.15 (3H, s, CH_3N), 2.30-2.36 (2H, m, NCH_2), 2.60-2.72 (1H, m, CHPh), 2.81 (1H, heptet, J=6.7, CHN), 7.13-7.30 (5H, m, ArH); δ_C 17.6 [$(CH_3)_2CH$], 22.2 (CH_3CH), 25.8 (NCH_2CH_2), 36.2 ($PhCHCH_2$), 36.6 (CH_3N), 39.8 (PhCH), 53.1 (CHN), 53.2 (CH_2N), 125.7, 126.9, 128.2, 147.5 (ArC); m/z 219 (M$^+$, 9%), 204 (32), 105 (16), 91 (33), 87 (14), 86 (100), 58 (34), 56 (11), 44 (73) 43 (18), 42 (19), 41 (19) (Found: M$^+$, 219.1997. $C_{15}H_{25}N$ requires M, 219.1987).

7-Isopropylamino-2,2-dimethyl-4-phenyl-3-heptanol (**3d**):[14] ν_{max} (film) 3700-3115 cm^{-1} (NH, OH); δ_H 0.76, 0.86 [9H, 2s, $(CH_3)_3C$], 0.99, 1.00 [6H, 2d, J=6.1, $(CH_3)_2CH$], 1.17-2.03 (6H, m, CH_2CH_2CHPh, OH, NH), 2.46-2.84 (4H, m, CHN, CH_2N, PhCH), 3.44-3.46 (1H, m, CHOH), 7.14-7.32 (5H, m, ArH); δ_C 22.7, 22.8 [$(CH_3)_2CH$], 26.6 [$(CH_3)_3C$], 28.1, 28.5, 29.1, 34.0 (2xCH_2CH_2CHPh), 35.8, 36.3 [$(CH_3)_3C$], 47.2 (1xCH_2N), 47.4 (2xCHN), 47.5 (1xCH_2N), 48.5 (2xPhCH), 81.9, 82.7 (2xCHOH), 125.9, 126.2, 128.0, 128.1, 128.3, 129.5, 142.3, 146.1 (2xArC); tandem GLC/MS (first diastereoisomer): m/z 277 (M$^+$, 0.8%), 220 (37), 202 (11), 131 (18), 91 (22), 85 (17), 72 (100), 70 (11), 58 (25), 57 (27), 56 (13), 44 (22), 43 (29), 42 (15), 41 (38); (second diastereoisomer): m/z 277 (M$^+$, 0.5%), 220 (21), 131 (12), 91 (12), 85 (10), 72 (100), 58 (10), 57 (14), 44 (16), 43 (18), 41 (22).

5-Isopropylamino-1,2-diphenyl-1-pentanol (**3e**): ν_{max} (film) 3600-3100 cm^{-1} (OH, NH); δ_H 0.87, 0.91 [6H, 2d, J=6.2, $(CH_3)_2CH$], 0.94-1.39 (5H, m, CH_2CH_2CHPh, OH or NH), 2.25-2.50 (3H, m, CH_2NH or CH_2NH, OH), 2.54, 2.60 (1H, 2 heptet, J=6.2, CHN), 2.75-2.81 (1H, m, $PhCHCH_2$), 4.61, 4.64 (1H, 2d, J=7.7, 9.5, PhCHOH), 6.97-7.30 (10H, m, 2xArH); δ_C 22.4, 22.5, 27.6, 27.7 [2x$(CH_3)_2CH$], 29.3, 30.7 (2xCH_2CH_2CHPh), 46.8 (2xCH_2N), 48.2 (2xCHN), 53.6, 53.8 ($PhCHCH_2$), 77.7, 77.9 (2xPhCHOH), 125.9, 126.4, 126.5, 126.6, 126.8, 127.3, 127.5, 127.8, 127.9, 128.2, 128.6, 128.7, 141.3, 141.8, 143.0, 143.7 (4xArC); m/z 297 (M$^+$, 2%), 264 (12), 191 (10), 190 (15), 176 (12), 131 (22), 107 (40), 105 (18), 98 (12), 91 (26), 85 (19), 79 (80), 78 (16), 77 (68), 72 (100), 70 (14), 58 (15), 56 (19), 51 (12), 44 (10), 43 (22), 42 (18), 41 (19) (Found: M$^+$, 297.2100. $C_{20}H_{27}NO$ requires M, 297.2093).

6-Isopropylamino-2-methyl-3-phenyl-2-hexanol (**3f**): ν_{max} (KBr) 3600-3100 cm^{-1} (OH, NH); δ_H 0.99 [6H, d, J=6.3, $(CH_3)_2CH$], 1.16 [6H, s, $(CH_3)_2COH$], 1.22-1.96 (6H, m, $PhCHCH_2CH_2$, NH, OH), 2.45-2.74 (4H, m, $PhCHCH_2$, CHN, CH_2N), 7.19-7.32 (5H, m, ArH); δ_C 22.8, 22.9 [$(CH_3)_2CH$], 27.1 ($PhCHCH_2$), 27.6, 28.0 [$(CH_3)_2COH$], 28.9 ($PhCHCH_2CH_2$), 47.4 (CH_2N), 48.5 (CHN), 57.1 (PhCH), 72.6 (COH), 126.5, 128.0, 129.4, 141.2 (ArC); m/z 249 (M$^+$, 0.1%), 98 (18), 91 (17), 85 (10), 72 (100), 59 (36), 58 (14), 44 (12), 43 (31), 42(11), 41 (17) (Found : C, 76.75; H, 10.32; N, 5.13. $C_{16}H_{27}NO$ requires: C, 77.06; H, 10.91; N, 5.62).

1-(4-Isopropylamino-1-phenylbutyl)-1-cyclopentanol (**3g**):[14] ν_{max} (film) 3715-3115 cm^{-1} (OH, NH); δ_H 0.98, 0.99 [6H, 2d, *J*=6.4, 6.1, $(CH_3)_2CH$], 1.09-1.98 (14H, m, 4xringCH$_2$, OH, *H*NCH$_2$C*H*$_2$C*H*$_2$), 2.44-2.60 (3H, m, PhC*H*, CH_2N), 2.63-2.75 [1H, m, $(CH_3)_2CH$], 7.17-7.30 (5H, m, ArH); δ_C 22.7, 22.8 [$(CH_3)_2CH$], 23.1, 23.5 ($HNCH_2CH_2CH_2$), 27.9, 28.7, 38.3, 39.3 (4xringCH$_2$), 47.4 (CH_2N), 48.4 (CHN), 55.3 (PhCH), 84.4 (COH), 126.2, 128.0, 128.9, 142.0 (ArC); *m/z* 271 (M^+-H_2O, 7%), 98 (38), 91 (15), 85 (29), 72 (100), 58 (34), 56 (14), 44 (29), 43 (24), 42 (14), 41 (23).

1-(4-Isopropylamino-1-phenylbutyl)-1-cyclohexanol (**3h**):[14] ν_{max} (film) 3700-3115 cm^{-1} (OH, NH); δ_H 0.98, 0.99 [6H, 2d, *J*=6.4, 6.1, $(CH_3)_2CH$], 1.02-1.96 (16H, m, 5xringCH$_2$, OH, *H*NCH$_2$C*H*$_2$C*H*$_2$), 2.43-2.59 (3H, m, PhC*H*, CH_2N), 2.63-2.75 [1H, m, $(CH_3)_2CH$], 7.16-7.30 (5H, m, ArH); δ_C 21.6, 21.7 (2xringCH$_2$), 22.6, 22.7 [$(CH_3)_2CH$], 25.5, 26.1, 28.8, 35.4, 35.5 (3xringCH$_2$, $HNCH_2CH_2CH_2$), 47.3 (CH_2N), 48.4 (CHN), 56.4 (PhCH), 72.7 (COH), 126.1, 127.8, 129.4, 141.1 (ArC); *m/z* 271 (M^+-H_2O, 5%), 176 (15), 99 (12), 98 (40), 91 (13), 85 (17), 81 (16), 72 (100), 58 (27), 56 (13), 55 (11), 44 (27), 43 (27), 42 (16), 41 (21).

Ethyl 5-Isopropylamino-2-phenylpentanoate (**3i'**): ν_{max} (film) 3313 (NH), 1732 cm^{-1} (C=O); δ_H 1.02 [6H, d, *J*=6.1, $(CH_3)_2CH$], 1.17-1.22 (3H, m, CH_3CH_2O), 1.37-2.16 (5H, m, CH_2CH_2CHPh, NH), 2.75 (1H, heptet, *J*=6.1, CHN), 4.04-4.17 (2H, m, OCH_2CH_3), 7.23-7.31 (5H, m, ArH); δ_C 14.0 (CH_3CH_2O), 22.8 [$(CH_3)_2CH$], 28.3, 31.3 (CH_2CH_2CHPh), 47.0 (CH_2N), 48.5 (CHN), 51.6 (PhCH), 60.6 (OCH_2CH_3), 127.1, 127.8, 128.5, 139.1 (ArC), 173.8 (C=O); *m/z* 263 (M^+, 8%), 248 (14), 174 (10), 131 (15), 87 (11), 72 (100), 58 (13), 56 (13), 44 (22), 43 (17), 42 (12), 41 (12) (Found: M^+, 263.1892. $C_{16}H_{25}NO_2$ requires M, 263.1885).

Preparation of 1-Phenyl-3-pyrroline (**6**).-[15] To a cooled (-50°C) stirred THF solution (10 ml) of aniline (2.7 ml, 30 mmol) was added a 1.6 M hexane solution of Bu^nLi (20.6 ml, 33.0 mmol). After 0.5 h this solution was transfered *via cannula* to a precooled (-78°C) THF solution (40 ml) of *cis*-1,4-dichloro-2-butene and stirring was continued for 3 h at the same temperature. Then, another 1.6 M hexane solution of Bu^nLi (20.6 ml, 33.0 mmol) was added and the mixture was allowed to warm up to room temperature during 5 h. Then, it was hydrolysed with water (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel; hexane) and recrystallised to yield pure product **5**. Yield is given in the text; mp 82-83°C (pentane/dichloromethane) [lit.[15] 101-102°C]; ν_{max} (KBr) 3058, 3028, 1630, 1601, 1567, 1510, 746, 668 cm^{-1} (Ar); δ_H 4.06 (4H, s, 2xCH$_2$N), 5.90 (2H, s, CH=CH), 6.50 (2H, dd, *J*=8.5, 1.0, *o*-ArN), 6.67 (1H, tt, *J*=7.3, 1.0, *p*-ArN), 7.23 (2H, dd, *J*=8.5, 7.3, *m*-ArN); δ_C 54.3 (2xCH$_2$N), 111.1, 115.5, 126.3, 129.2, 147.0 (ArC, CH=CH); *m/z* 146 (M^++1, 10%), 145 (M^+, 100), 144 (68), 143 (20), 117 (13), 104 (70), 91 (13), 77 (77), 51 (41), 50 (18), 41 (19).

Preparation of Compounds **8** *and* **9**. *General Procedure*.- To a blue suspension of lithium powder (0.125g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added pyrroline **6** (0.308 gr, 2 mmol) under argon and the mixture was stirred for 15 h at the same temperature. Then, the mixture was cooled down at -78°C and the corresponding electrophile (3 mmol; 0.5 ml in the case of water or deuterium oxide; CO_2 was bubbled for 1.5 h) was added. The mixture was stirred at the same temperature for 0.5 h and hydrolysed with water (20 ml) at -78°C to room temperature. The resulting mixture was extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) and/or recrystallised to yield pure products **8** and **9**. When the electrophile was CO_2, after having hydrolysed the mixture with ethanol (10 ml) at -78°C it was treated overnight with a 4 M ethanol solution of hydrogen chloride (15 ml). The solvent was evaporated (15 Torr) and the resulting residue was hydrolysed with water (15 ml), acidified with 3 M hydrochloric acid (10 ml) and extracted with ethyl acetate (3x25 ml). The aqueous layer was then basified with 2.5 M sodium hydroxide (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr) to yield compounds **8g'** and **9g'**, which were separated by column chromatography (silica gel; hexane/ethyl acetate). Yields and physical data (R_f or mp) are included in Table 2; analytical and spectroscopic data follow.

(Z)-1-Anilino-2-butene (**8a**): ν_{max} (film) 3407 cm^{-1} (NH); δ_H 1.70 (3H, d, J=5.8, CH$_3$), 3.52 (1H, br s, NH), 3.74 (2H, d, J=6.1, CH_2NH), 5.50-5.67 (2H, m, CH=CH), 6.60 (2H, dd, J=8.5, 0.9, *o*-ArN), 6.70 (1H, tt, J=7.3, 0.9, *p*-ArN), 7.16 (2H, dd, J=8.5, 7.3, *m*-ArN); δ_C 13.1 (CH$_3$), 40.8 (CH$_2$NH), 112.9, 117.4, 127.0, 127.6, 129.1, 148.2 (ArC, CH=CH); *m/z* 147 (M$^+$, 100%), 146 (13), 132 (78), 131 (12), 130 (20), 118 (15), 117 (17), 106 (45), 104 (13), 93 (87), 77 (36), 65 (15), 51 (14) (Found: M$^+$, 147.0996. $C_{10}H_{13}N$ requires M, 147.1048).

*(Z)-*N*-(4-Deuterio-2-butenyl)aniline* (**8b**): ν_{max} (film) 3406 cm^{-1} (NH); δ_H 1.25 (1H, br s, NH), 1.67-1.73 (2H, m, CH$_2$D), 3.76 (2H, d, J=6.7, CH_2NH), 5.51-5.71 (2H, m, CH=CH), 6.62 (2H, dd, J=8.7, 1.0, *o*-ArN), 6.71 (1H, tt, J=7.3, 1.0, *p*-ArN), 7.18 (2H, dd, J=8.7, 7.3, *m*-ArN); δ_C 12.9 (t, J_{CD}=19.5, CH$_2$D), 40.8 (CH$_2$NH), 112.9, 117.4, 127.1, 127.6, 129.2, 148.3 (ArC, CH=CH); *m/z* 148 (M$^+$, 47%), 147 (28), 132 (61), 130 (24), 119 (13), 118 (26), 117 (20), 106 (57), 104 (25), 94 (19), 93 (86), 92 (27), 91 (19), 79 (14), 78 (19), 77 (80), 75 (11), 74 (10), 66 (19), 65 (67), 64 (18), 63 (27), 62 (12), 56 (66), 55 (39), 54 (24), 53 (19), 52 (42), 51 (100), 50 (55), 43 (10), 42 (76), 41 (64) (Found: M$^+$, 148.1109. $C_{10}H_{12}DN$ requires M, 148.1111).

(Z)-7-Anilino-2,2-dimethyl-5-hepten-3-ol (**8c**): ν_{max} (film) 3690-3130 cm^{-1} (OH, NH); δ_H 0.93 [9H, s, (CH$_3$)$_3$C], 2.14-2.32 (2H, m, CH_2CHOH), 2.77 (2H, br s, OH, NH), 3.26 (1H, dd, J=10.0, 2.7, CHOH), 3.73-3.77 (2H, m, CH_2NH), 5.59-5.80 (2H, m, CH=CH), 6.63 (2H, dd, J=8.5, 0.9, *o*-ArN), 6.72 (1H, tt, J=7.3, 0.9, *p*-ArN), 7.17 (2H, dd, J=8.5, 7.3, *m*-ArN); δ_C 25.7 [(CH$_3$)$_3$C], 30.0 (CH$_2$CHOH), 34.8 [(CH$_3$)$_3$$C$], 41.0 (CH$_2$NH), 78.9 (CHOH), 113.2, 117.7, 129.1, 129.2, 130.8, 148.1 (ArC, CH=CH); *m/z* 233 (M$^+$, 19%), 158 (10), 132 (17), 106 (48), 104 (16), 94 (24), 93 (100), 87 (16), 77 (37), 69 (17), 65 (24), 57 (91), 55 (21), 53 (10), 51 (12), 45 (13), 43 (26), 41 (83) (Found: M$^+$, 233.1786. $C_{15}H_{23}NO$ requires M, 233.1780).

4-Anilinomethyl-2,2-dimethyl-5-hexen-3-ol (**9c**): (first diastereoisomer) ν_{max} (film) 3720-3125 cm^{-1} (OH, NH); δ_H 0.95 [9H, s, (CH$_3$)$_3$C], 1.31 (2H, br s, OH, NH), 2.55-2.64 (1H, m, CHCHOH), 3.11-3.15 (1H, m, HCHNH), 3.42 (1H, d, J=6.4, CHOH), 3.48-3.54 (1H, m, HCHNH), 5.09-5.15 (2H, m, CH=CH_2), 5.76-5.88 (1H, m, CH=CH$_2$), 6.73-6.80 (3H, m, *o*-, *p*-ArN), 7.19 (2H, dd, J=8.5, 7.3, *m*-ArN); δ_C 26.5 [(CH$_3$)$_3$C], 36.3 [(CH$_3$)$_3$$C$], 45.3 ($C$HCHOH), 46.8 (CH$_2$NH), 81.2 (CHOH), 114.6 (ArC), 116.4 (CH=CH$_2$), 118.9, 129.3, 140.3, 147.1 (ArC, CH=CH$_2$); *m/z* 233 (M$^+$, 6%), 106 (100), 77 (35), 69 (14), 65 (11), 57 (74), 51 (12), 45 (11), 43 (13), 41 (72) (Found: M$^+$, 233.1764. $C_{15}H_{23}NO$ requires M, 233.1780). (second diastereoisomer) ν_{max} (film) 3740-3130 cm^{-1} (OH, NH); δ_H 0.92 [9H, s, (CH$_3$)$_3$C], 1.31 (2H, br s, OH, NH), 2.66-2.74 (1H, m, CHCHOH), 3.13 (1H, dd, J=12.2, 7.9, HCHNH), 3.29 (1H, dd, J=12.2, 6.1, HCHNH), 3.41 (1H, d, J=1.5, CHOH), 5.14 (1H, dd, J=17.4, 1.8, CH=CHH), 5.22 (1H, dd, J=10.4, 1.8, CH=CH*H*), 5.98 (1H, ddd, *J*=17.4, 10.4, 9.4, C*H*=CH$_2$), 6.64 (2H, d, *J*=7.6, *o*-ArN), 6.72 (1H, t, *J*=7.3, *p*-ArN), 7.17 (2H, dd, *J*=7.6, 7.3, *m*-ArN); δ_C 26.6 [(*C*H$_3$)$_3$C], 35.9 [(CH$_3$)$_3$*C*], 44.4 (*C*HCHOH), 48.3 (CH$_2$NH), 80.0 (CHOH), 113.6, 117.9 (ArC), 118.0 (CH=*C*H$_2$), 129.2, 136.8, 147.6 (ArC, *C*H=CH$_2$); *m/z* 233 (M$^+$, 5%), 106 (100), 77 (31), 57 (61), 41 (47) (Found: M$^+$, 233.1778. $C_{15}H_{23}NO$ requires M, 233.1780).

(Z)-6-Anilino-2-methyl-4-hexen-2-ol (**8d**): ν_{max} (film) 3700-3125 cm^{-1} (OH, NH); δ_H 1.25 (6H, s, 2xCH$_3$), 2.30 (2H, d, *J*=6.7, C*H*$_2$COH), 3.70 (2H, br s, OH, NH), 3.78 (2H, d, *J*=5.2, C*H*$_2$NH), 5.68-5.82 (2H, m, CH=CH), 6.75-6.82 (3H, m, *o*-, *p*-ArN), 7.18-7.23 (2H, m, *m*-ArN); δ_C 29.2 (2xCH$_3$), 41.2, 42.1 (2xCH$_2$), 70.9 (COH), 114.5, 119.2, 128.7, 129.2, 129.3, 146.3 (ArC, CH=CH); *m/z* 205 (M$^+$, 65%), 106 (16), 93 (35), 77 (23), 65 (17), 59 (100), 43 (87), 41 (26) (Found: M$^+$, 205.1329. $C_{13}H_{19}NO$ requires M, 205.1467).

3-Anilinomethyl-2-methyl-4-penten-2-ol (**9d**): ν_{max} (film) 3710-3130 cm^{-1} (OH, NH); δ_H 1.23 (6H, s, 2xCH$_3$), 2.29-2.36 (1H, m, C*H*CH=CH$_2$), 2.97 (1H, dd, *J*=11.9, 9.1, *H*CHNH), 3.03 (2H, br s, OH, NH), 3.47 (1H, dd, *J*=11.9, 4.6, HC*H*NH), 5.17 (1H, dd, *J*=16.8, 1.8, CH=C*H*H), 5.24 (1H, dd, *J*=10.3, 1.8, CH=CH*H*), 5.70 (1H, ddd, *J*=16.8, 10.3, 9.4, C*H*=CH$_2$), 6.63 (2H, d, *J*=7.9, *o*-ArN), 6.71 (1H, t, *J*=7.3, *p*-ArN), 7.15-7.20 (2H, m, *m*-ArN); δ_C 26.4, 28.7 (2xCH$_3$), 43.8 (CH$_2$NH), 54.7 (*C*HCH=CH$_2$), 71.8 (COH), 113.4, 117.6 (ArC), 119.3 (CH=*C*H$_2$), 129.1, 137.1, 148.1 (ArC, *C*H=CH$_2$); *m/z* 206 (M$^+$+1, 15%), 205 (M$^+$, 65), 146 (14), 132 (10), 130 (15), 118 (12), 107 (66), 106 (100), 105 (61), 104 (47), 94 (10), 93 (70), 92 (17), 91 (15), 82 (40), 79 (44), 78 (34), 77 (72), 69 (17), 67 (27), 66 (25), 65 (53), 59 (64), 55 (10), 54 (17), 53 (17), 52 (13), 51 (49), 50 (10), 43 (56), 41 (43) (Found: M$^+$, 205.1424. $C_{13}H_{19}NO$ requires M, 205.1467).

(Z)-1-(4-Anilino-2-butenyl)cyclopentanol (**8e**): ν_{max} (film) 3660-3130 cm^{-1} (OH, NH); δ_H 1.58-1.84 (8H, m, 4xringCH$_2$), 2.42 (2H, d, *J*=6.1, CH=CHC*H*$_2$COH), 2.63 (2H, br s, OH, NH), 3.76 (2H, d, *J*=5.2, C*H*$_2$NH), 5.67-5.82 (2H, m, CH=CH), 6.62 (2H, dd, *J*=8.6, 0.9, *o*-ArN), 6.72 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.17 (2H, dd, *J*=8.6, 7.3, *m*-ArN); δ_C 23.7, 39.1, 39.5, 41.1 (6xCH$_2$), 81.8 (COH), 113.1, 117.6, 128.7, 129.2, 129.8, 148.1 (ArC, CH=CH); *m/z* 231 (M$^+$, 8%), 132 (10), 118 (11), 106 (22), 104 (15), 94 (10), 93 (90), 92 (14), 91 (12), 85 (39), 79 (12), 78 (13), 77 (54), 67 (42), 66 (13), 65 (36), 57 (28), 55 (68), 53 (17), 52 (10), 51 (21), 43 (41), 42 (39), 41 (100) (Found: M$^+$, 231.1633. $C_{15}H_{21}NO$ requires M, 231.1623).

1-[(2-Anilino-1-vinylethyl)]cyclopentanol (**9e**): ν_{max} (film) 3660-3135 cm^{-1} (OH, NH); δ_H 1.26-1.81 (8H, m, 4xringCH$_2$), 2.33-2.40 (1H, m, C*H*CH=CH$_2$), 2.90 (2H, br s, OH, NH), 3.09 (1H, dd, *J*=12.0, 8.8, *H*CHNH), 3.43 (1H, dd, *J*=12.0, 4.3, HC*H*NH), 5.15 (1H, dd, *J*=17.1, 1.7, CH=C*H*H), 5.21 (1H, dd, *J*=10.3, 1.7, CH=CH*H*), 5.80 (1H, ddd, *J*=17.1, 10.3, 9.4, C*H*=CH$_2$), 6.61 (2H, d, *J*=8.2, *o*-ArN), 6.67-6.72 (1H, m, *p*-ArN), 7.18-7.21 (2H, m, *m*-ArN); δ_C 23.3, 23.5, 38.2, 38.6, 44.2 (4xringCH$_2$, CH$_2$NH), 52.7 (*C*HCH=CH$_2$), 83.5 (COH), 113.3, 117.5 (ArC), 118.6 (CH=*C*H$_2$), 129.1, 137.3, 148.1 (ArC, *C*H=CH$_2$); *m/z* 231 (M$^+$, 5%), 106 (100), 93 (13), 77 (17), 41 (11) (Found: M$^+$, 231.1627. $C_{15}H_{21}NO$ requires M, 231.1623).

(Z)-1-(4-Anilino-2-butenyl)cyclohexanol (**8f**): ν_{max} (film) 3700-3130 cm^{-1} (OH, NH); δ_H 1.19-1.65 (10H, m, 5xringCH$_2$), 2.27 (2H, d, *J*=6.7, CH=CHC*H*$_2$COH), 2.74 (2H, br s, OH, NH), 3.74 (2H, d, *J*=5.5, C*H*$_2$NH), 5.66-5.80 (2H, m, CH=CH), 6.62 (2H, dd, *J*=8.5, 0.9, *o*-ArN), 6.71 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.16 (2H, dd, *J*=8.5, 7.3, *m*-ArN); δ_C 22.1, 25.6, 37.3, 40.1, 41.1 (7xCH$_2$), 71.5 (COH), 113.1, 117.6, 127.8, 129.1, 129.7, 148.0 (ArC, CH=CH$_2$); *m/z* 245 (M$^+$, 22%), 146 (10), 132 (17), 119 (25), 106 (27),

104 (13), 99 (12), 94 (10), 93 (100), 81 (25), 77 (22), 65 (12), 55 (11) (Found: M$^+$, 245.1763. $C_{16}H_{23}NO$ requires M, 245.1780).

1-[(2-Anilino-1-vinylethyl)]cyclohexanol (**9f**): ν_{max} (KBr) 3715-3130 cm^{-1} (OH, NH); δ_H 1.15-1.67 (11H, m, 5xringCH$_2$, NH or OH), 2.24-2.32 (1H, m, C*H*CH$_2$NH), 2.89 (1H, br s, OH or NH), 2.99 (1H, dd, *J*=11.8, 8.9, *H*CHNH), 3.46 (1H, dd, *J*=11.8, 4.3, HC*H*NH), 5.12 (1H, dd, *J*=17.0, 2.1, CH=C*H*H), 5.22 (1H, dd, *J*=10.0, 2.1, CH=CH*H*), 5.75 (1H, ddd, *J*=17.0, 10.0, 9.7, C*H*=CH$_2$), 6.61 (2H, dd, *J*=8.5, 0.9, *o*-ArN), 6.69 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.15 (2H, dd, *J*=8.5, 7.3, *m*-ArN); δ_C 21.5, 21.6, 25.6, 34.6, 35.9, 42.8 (7xCH$_2$), 53.8 (*C*HCH$_2$NH), 72.3 (COH), 113.3, 117.5 (ArC), 119.0 (CH=*C*H$_2$), 129.1, 137.0, 148.1 (ArC); *m/z* 245 (M$^+$, 18%), 122 (28), 107 (35), 106 (100), 105 (12), 104 (14), 93 (35), 81 (14), 79 (13), 77 (24) (Found : C, 77.65; H, 9.44; N, 5.41. $C_{16}H_{23}NO$ requires: C, 78.32; H, 9.45; N, 5.71).

Ethyl (Z)-5-Anilino-3-pentenoate (**8g'**): ν_{max} (film) 3396 (NH), 1734 cm^{-1} (C=O); δ_H 1.27 (3H, t, *J*=7.3, CH$_3$), 1.33 (1H, br s, NH), 3.18 (2H, d, *J*=5.8, CH$_2$C=O), 3.77 (2H, d, *J*=4.9, C*H*$_2$NH), 4.16 (2H, q, *J*=7.3, OC*H*$_2$CH$_3$), 5.76-5.79 (2H, m, CH=CH), 6.62 (2H, dd, *J*=8.7, 1.0, *o*-ArN), 6.73 (1H, tt, *J*=7.3, 1.0, *p*-ArN), 7.18 (2H, dd, *J*=8.7, 7.3, *m*-ArN); δ_C 14.2 (CH$_3$), 33.2 (*C*HC=O), 41.2 (CH$_2$NH), 60.9 (OCH$_2$), 113.0, 117.7, 124.1, 129.2, 130.4, 147.9 (ArC, CH=CH), 171.4 (C=O); *m/z* 219 (M$^+$, 22%), 133 (10), 132 (100), 130 (12), 117 (10), 106 (15), 104 (14), 93 (26), 81 (37), 77 (30), 66 (14), 65 (31), 53 (17), 51 (16), 44 (12), 43 (10), 41 (12), 40 (16) (Found: M$^+$, 219.1261. $C_{13}H_{17}NO_2$ requires M, 219.1259).

Ethyl 2-Anilinomethyl-3-butenoate (**9g'**): ν_{max} (film) 3408 (NH), 1730 cm^{-1} (C=O); δ_H 1.25 (3H, t, *J*=7.0, CH$_3$), 3.28 (1H, dd, *J*=12.2, 6.7, *H*CHNH), 3.34-3.41 (1H, m, CHC=O), 3.56 (1H, dd, *J*=12.2, 6.7, HC*H*NH), 3.91 (1H, br s, NH), 4.16 (2H, q, *J*=7.0, OC*H*$_2$CH$_3$), 5.22 (1H, dd, *J*=17.1, 1.2, CH=C*H*H), 5.25 (1H, dd, *J*=10.4, 1.2, CH=CH*H*), 5.87 (1H, ddd, *J*=17.1, 10.4, 8.2, C*H*=CH$_2$), 6.61 (2H, dd, *J*=8.5, 0.9, *o*-ArN), 6.72 (1H, t, *J*=7.3, *p*-ArN), 7.17 (2H, dd, *J*=8.5, 7.3, *m*-ArN); δ_C 14.1 (CH$_3$), 45.2 (CH$_2$NH), 49.5 (*C*HC=O), 60.9 (OCH$_2$), 113.1, 117.7 (ArC), 118.9 (CH=*C*H$_2$), 129.3, 133.5, 147.4 (ArC, *C*H=CH$_2$), 172.6 (C=O); *m/z* 219 (M$^+$, 28%), 146 (13), 107 (27), 106 (100), 104 (17), 79 (11), 77 (39), 65 (12) (Found: M$^+$, 219.1261. $C_{13}H_{17}NO_2$ requires M, 219.1259).

Preparation of N*-Phenylisoindoline* (**10**).- To a cooled (-80°C) stirred THF solution (30 ml) of aniline (0.46 ml, 5.0 mmol) and α,α'-*ortho*-dibromoxylene was added a 1.6 M hexane solution of Bu^{n}Li (3.4 ml, 6.5 mmol). After 0.75 h another 1.6 M hexane solution of Bu^{n}Li (3.4 ml, 6.5 mmol) was added and the mixture was allowed to reach room temperature for 2 h. Then it was hydrolysed with water (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then purified by column chromatography (silica gel; hexane) and recrystallised to yield pure product **10**. Yield is given in the text; mp 152°C (pentane/dichloromethane); ν_{max} (KBr) 3060, 3040, 1602, 1505, 744, 690 cm^{-1} (Ar); δ_H 4.60 (4H, s, 2xCH$_2$N), 6.65 (2H, dd, *J*=8.8, 0.9, *o*-ArN), 6.73 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.25-7.32 (6H, m, *m*-ArN, ArH); δ_C 53.7 (2xCH$_2$N), 111.5, 116.1, 122.5, 127.1, 129.3, 137.9, 147.1 (ArC); *m/z* 195 (M$^+$, 52%), 194 (100), 116 (12), 91 (11), 89 (12), 77 (46), 63 (10), 51 (28) (Found: C, 85.96; H, 6.80; N, 5.84. $C_{14}H_{13}N$ requires: C, 86.12; H, 6.71; N, 5.98).

Preparation of Compounds **12**. *General Procedure*.- To a blue suspension of lithium powder (0.125g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added isoindoline **10** (0.390 gr, 2.0 mmol) under argon and the mixture was stirred for 3 h at the same temperature. Then, the mixture was cooled down to -78°C and the corresponding electrophile (3.0 mmol; 0.5 ml in the case of water or deuterium oxide) was added. The reaction mixture was stirred at the same temperature for 0.5 h and was hydrolysed with water (20 ml). The resulting mixture was extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) and/or recrystallised to yield pure products **12**. Yields and physical data (R_f or mp) are included in Table 3; analytical and spectroscopic data follow.

N-*{[2-(Methyl)phenyl]methyl}aniline* (**12a**): ν_{max} (film) 3417 cm^{-1} (NH); δ_H 2.34 (3H, s, CH$_3$), 3.77 (1H, br s, NH), 4.22 (2H, s, CH$_2$N), 6.59 (2H, dd, *J*=8.5, 1.0, *o*-ArN), 6.70 (1H, tt, *J*=7.3, 1.0, *p*-ArN), 7.13-7.31 (6H, m, *m*-ArN, ArH); δ_C 18.9 (CH$_3$), 46.3 (CH$_2$N), 112.6, 117.4, 126.1, 127.3, 128.2, 129.2, 130.3, 136.3, 137.0, 148.2 (ArC); *m/z* 197 (M$^+$, 43%), 106 (14), 105 (100), 104 (51), 103 (12), 93 (17), 79 (16), 78 (11), 77 (40), 65 (17), 51 (14) (Found: M$^+$, 197.1214. $C_{14}H_{15}N$ requires M, 197.1205).

N-*{[2-(Deuteriomethyl)phenyl]methyl}aniline* (**12b**): ν_{max} (film) 3416 cm^{-1} (NH); δ_H 2.34 (2H, t, *J*=2.1, CH$_2$D), 3.74 (1H, br s, NH), 4.24 (2H, s, CH$_2$N), 6.61 (2H, dd, *J*=8.7, 0.9, *o*-ArN), 6.71 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.15-7.32 (6H, m, *m*-ArN, ArH); δ_C 18.6 (t, J_{CD}=19.5, CH$_2$D), 46.3 (CH$_2$N), 112.6, 117.4, 126.1, 127.4, 128.2, 129.2, 130.4, 136.2, 137.0, 148.3 (ArC); *m/z* 198 (M$^+$, 39%), 106 (100), 105 (45), 104 (29), 93 (12), 79 (10), 78 (16), 77 (29), 65 (10), 51 (12) (Found: M$^+$, 198.1276. $C_{14}H_{14}DN$ requires M, 198.1267).

1-(2-Anilinomethylphenyl)-3-methyl-2-butanol (**12c**): ν_{max} (film) 3570-3140 cm^{-1} (OH, NH); δ_H 0.97 [6H, d, *J*=6.7, (C*H*$_3$)$_2$CHOH], 1.75 [1H, heptet, *J*=6.7, 5.2, (CH$_3$)$_2$C*H*OH], 2.70 (1H, dd, *J*=14.0, 10.0, *H*CHCHOH), 2.86 (1H, dd, *J*=14.0, 3.0, HC*H*CHOH), 3.16 (2H, br s, OH, NH), 3.59 (1H, ddd, *J*=10.0, 5.2, 3.0, C*H*OH), 4.20 (1H, d, *J*=12.8, *H*CHNH), 4.32 (1H, d, *J*=12.8, HC*H*NH), 6.67 (2H, d, *J*=7.6, *o*-ArN), 6.74 (1H, t, *J*=7.3, *p*-ArN), 7.15-7.35 (6H, m, *m*-ArN, ArH); δ_C 17.6, 18.6 [(*C*H$_3$)$_2$CH], 34.0 [(CH$_3$)$_2$*C*H], 36.6 (*C*H$_2$CHOH), 46.7 (CH$_2$NH), 77.6 (CHOH), 113.6, 118.0, 126.6, 127.9, 129.2, 129.6, 130.3, 137.3, 138.5, 148.1 (ArC); *m/z* 269 (M$^+$, 60%), 197 (15),), 196 (21), 194 (14), 182 (13), 159 (19), 143 (41), 133 (43), 118 (11), 117 (44), 116 (10), 115 (20), 106 (39), 105 (62), 104 (98), 103 (45), 94 (40), 93 (100), 92 (10), 91 (50), 89 (11), 79 (25), 78 (43), 77 (89), 73 (57), 71 (89), 65 (30), 63 (10), 57 (16), 55 (74), 51 (18), 45 (25), 43 (94), 41 (63) (Found: M$^+$, 270.1839. $C_{18}H_{24}NO$ requires M, 270.1858).

1-(2-Anilinomethylphenyl)-3,3-dimethyl-2-butanol (**12d**): ν_{max} (KBr) 3640-3130 cm^{-1} (OH, NH); δ_H 0.95 [9H, s, (CH$_3$)$_3$C], 2.63 (1H, dd, *J*=13.7, 10.9, *H*CHCHOH), 2.90 (1H, dd, *J*=13.7, 2.1, HC*H*CHOH), 3.18 (2H, br s, OH, NH), 3.43 (1H, dd, *J*=10.9, 2.1, CH$_2$C*H*OH), 4.17 (1H, d, *J*=12.5, *H*CHNH), 4.33 (1H, d, *J*=12.5, HC*H*NH), 6.68 (2H, dd, *J*=8.1, 0.9, *o*-ArN), 6.74 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.15-7.33 (6H, m, *m*-ArN, ArH); δ_C 25.7 [(*C*H$_3$)$_3$C], 34.2 (*C*H$_2$CHOH), 35.1 [(CH$_3$)$_3$*C*], 46.8 (CH$_2$NH), 80.8 (CHOH), 113.4, 118.0, 126.6, 127.9, 129.2, 129.6, 130.3, 137.3, 139.1, 148.1 (ArC); *m/z* 283 [M$^+$, 31%], 208 (12), 157 (10), 134 (33), 133 (18), 132 (11), 106 (18), 105 (40), 104 (44), 103 (16), 94 (24), 93 (58), 91 (19), 79 (12), 78 (16), 77 (42), 57 (100), 41 (26) (Found: C, 80.58; H, 8.88; N, 4.62. $C_{14}H_{13}N$ requires: C, 80.52; H, 8.89; N, 4.94).

2-(2-Anilinomethylphenyl)-1-phenylethanol (**12e**): ν_{max} (KBr) 3680-3100 cm^{-1} (OH, NH); δ_H 3.03-3.05 (2H, m, C*H*$_2$CHOH), 3.42 (2H, br s, OH, NH), 4.12 (1H, d, *J*=12.8, *H*CHNH), 4.23 (1H, d, *J*=12.8, HC*H*NH), 4.88 (1H, dd, *J*=7.3, 5.8, C*H*OH), 6.64 (2H, dd, *J*=8.7, 1.0, *o*-ArN), 6.75 (1H, tt, *J*=7.3, 1.0, *p*-ArN), 7.15-7.32 (6H, m, *m*-ArN, ArH); δ_C 42.3 (*C*H$_2$CHOH), 46.5 (CH$_2$NH), 75.3 (CHOH), 113.3, 118.1, 125.7, 126.9, 127.5, 127.8, 128.4, 129.2, 129.5, 130.6, 137.1, 137.4, 144.2, 148.0 (ArC); *m/z* 303 (M$^+$, 7%), 107 (34), 106 (11), 105 (84), 104 (43), 103 (14), 93 (18), 91 (13), 79 (75), 78 (22), 77 (100), 65

(12), 51 (22) (Found: C, 81.98; H, 6.92; N, 4.11. $C_{21}H_{21}NO$ requires: C, 83.13; H, 6.98; N, 4.62).

1-(2-Anilinomethylphenyl)-2-methyl-2-propanol (**12f**): ν_{max} (film) 3700-3135 cm^{-1} (OH, NH); δ_H 1.26 [6H, s, $(CH_3)_2COH$], 2.88 (2H, s, CH_2COH), 3.10 (2H, br s, OH, NH), 4.30 (2H, s, CH_2N), 6.68 (2H, dd, *J*=8.5, 0.9, *o*-ArN), 6.74 (1H, tt, *J*=7.3, 0.9, *p*-ArN), 7.16-7.38 (6H, m, *m*-ArN, ArH); δ_C 29.9 [$(CH_3)_2COH$], 45.1 (CH_2COH), 46.8 (CH_2N), 70.9 (COH), 113.4, 118.1, 126.9, 127.2, 129.2, 129.6, 132.1, 136.5, 138.0, 148.0 (ArC); *m/z* 255 (M+, 33%), 147 (12), 145 (100), 129 (25), 119 (48), 117 (11), 106 (17), 105 (29), 104 (82), 103 (18), 93 (56), 91 (18), 78 (20), 77 (47), 65 (11), 59 (45), 51 (10), 43 (20) (Found: M+, 255.1622. $C_{17}H_{21}NO$ requires M, 255.1623).

1-(2-Anilinomethylphenyl)-2-phenyl-2-propanol (**12g**): ν_{max} (film) 3640-3130 cm^{-1} (OH, NH); δ_H 1.60 (3H, s, CH_3), 3.15 (2H, s, CH_2COH), 3.43 (2H, br s, OH, NH), 4.08 (2H, s, CH_2NH), 6.64 (2H, d, *J*=8.1, *o*-ArN), 6.76 (1H, t, *J*=7.3, *p*-ArN), 6.94-7.36 (11H, m, *m*-ArN, 2xArH); δ_C 29.9 (CH_3), 46.4 (CH_2COH), 46.7 (CH_2NH), 74.5 (COH), 113.6, 118.3, 124.9, 126.6, 126.9, 127.1, 128.0, 129.2, 129.4, 132.0, 135.7, 138.2, 147.9, 148.1 (ArC); *m/z* 317 (M+, 15%), 207 (14), 197 (25), 121 (32), 105 (23), 104 (67), 103 (15), 93 (21), 91 (11), 78 (19), 77 (46), 65 (10), 51 (10), 43 (100) (Found: M+, 317.1790. $C_{22}H_{23}NO$ requires M, 317.1780).

Preparation of 1-Bromo-2-[2-(bromomethyl)phenyl]ethane (**17**).[16] A mixture of isochromane (1.26 ml, 10 mmol), 0.5 g of Adogen (Aldrich), 45% hydrobromic acid (17 ml, 140 mmol) and sulfuric acid 96% (10 ml, 180 mmol) was placed in a sealed tube and was stirred at 115°C for 3 h. Then it was hydrolysed with water (40 ml) and extracted with ethyl ether (3x40 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The resulting brown oil was then purified by column chromatography (silica gel; hexane) to yield pure product **17**. Yield is given in the text; R_f=0.21 (hexane); ν_{max} (film) 3063, 3022, 1603, 1578, 762, 648 cm^{-1} (Ar); δ_H 3.28 (2H, t, *J*=7.7, CH_2CH_2Br), 3.62 (2H, t, *J*=7.7, CH_2CH_2Br), 4.53 (2H, s, CH_2Br), 7.20-7.35 (4H, m, ArH); δ_C 31.2, 31.7, 35.6 (3xCH_2), 127.5, 129.2, 130.1, 130.8, 135.8, 137.7 (ArC); *m/z* 278 (M+ , 5%), 199 (58), 197 (61), 118 (33), 117 (100), 116 (12), 115 (45), 104 (16), 91 (20), 78 (11), 77 (11), 65 (11), 63 (14), 58 (38), 51 (17), 50 (10).

Preparation of N-*Phenyltetrahydroisoquinoline* (**13**).-[17] A stirred absolute ethanol solution (50 ml) of compound **17** (1.39 gr, 5.0 mmol), aniline (0.450 ml, 5.0 mmol) and K_2CO_3 (13.6 gr, 100 mmol) was refluxed for 3 h. The solvent was evaporated (15 Torr) and the resulting residue was hydrolysed with water (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then purified by column chromatography (silica gel; hexane) to yield pure product **13**. Yield is given in the text; R_f=0.50 (hexane/ethyl acetate, 10:1); ν_{max} (film) 3061, 3023, 1599, 1577, 752, 692 cm^{-1} (Ar); δ_H 2.93-2.97 (2H, m, $ArCH_2CH_2N$), 3.51-3.54 (2H, m, $ArCH_2CH_2N$), 4.38 (2H, s, $ArCH_2N$), 6.59-7.29 (9H, m, ArH); δ_C 29.1 ($ArCH_2CH_2N$), 46.4 ($ArCH_2CH_2N$), 50.7 ($ArCH_2N$), 115.1, 118.6, 126.0, 126.3, 126.5, 128.4, 129.1, 134.4, 134.8, 150.5 (ArC); *m/z* 210 (M++1, 16%), 209 (M+, 88), 208 (100), 115 (11), 105 (17), 104 (75), 103 (21), 78 (34), 77 (47), 51 (28).

Preparation of Compounds **15**. *General Procedure.*- To a blue suspension of lithium powder (0.125g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added isoquinoline **13** (0.210 ml, 1 mmol) under argon and the mixture was stirred for 0.5 h at the same temperature. Then, the mixture was cooled down to -78°C and the corresponding electrophile (3.0 mmol; 0.5 ml in the case of water or deuterium oxide; CO_2 was bubbled for 1.5 h) was added. The reaction mixture was stirred at the same temperature for 0.5 h and was hydrolysed with water (20 ml). The resulting mixture was extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) to yield pure products **15**. When the electrophile was CO_2, after having hydrolysed the mixture with ethanol (10 ml) at -78°C it was treated overnight with a 4 M ethanol solution of hydrogen chloride (15 ml). The solvent was evaporated (15 Torr) and the resulting residue was hydrolysed with water (15 ml), acidified with 3 M hydrochloric acid (10 ml) and extracted with ethyl acetate (3x25 ml). The aqueous layer was then basified with 2.5 M sodium hydroxide (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr) to yield compound **15h'** [>95% pure (GLC and 300 Mhz ^{1}H NMR)]. Yields and physical data (R_f or mp) are included in Table 4; analytical and spectroscopic data follow.

1-Anilino-2-(2-methylphenyl)ethane (**15a**): ν_{max} (film) 3408 cm^{-1} (NH); δ_H 2.31 (3H, s, CH_3), 2.88 (2H, t, J=7.3, $\mathrm{C}\mathit{H}_2\mathrm{CH_2NH}$), 3.33 (2H, t, J=7.3, $\mathrm{CH_2C}\mathit{H}_2\mathrm{NH}$), 3.54 (1H, br s, NH), 6.59 (2H, dd, J=7.6, 1.2, *o*-ArNH), 6.69 (1H, tt, J=7.3, 1.2, *p*-ArNH), 7.12-7.19 (6H, m, *m*-ArNH, ArH); δ_C 19.3 (CH_3), 32.9 ($\mathit{C}\mathrm{H_2CH_2NH}$), 43.8 ($\mathrm{CH_2}\mathit{C}\mathrm{H_2NH}$), 112.8, 117.3, 126.0, 126.5, 129.1, 129.2, 130.4, 136.2, 137.3, 148.0 (ArC); *m/z* 211 (M$^+$, 32%), 107 (26), 106 (100), 105 (19), 104 (10), 79 (33), 78 (16), 77 (57), 51 (29) (Found: M$^+$, 211.1355. $C_{15}H_{17}N$ requires M, 211.1361).

1-Anilino-2-[2-(deuteriomethyl)phenyl]ethane (**15b**): ν_{max} (film) 3408 cm^{-1} (NH); δ_H 2.29-2.31 (2H, m, CH_2D), 2.89 (2H, t, J=7.3, $\mathrm{C}\mathit{H}_2\mathrm{CH_2NH}$), 3.34 (2H, t, J=7.3, $\mathrm{CH_2C}\mathit{H}_2\mathrm{NH}$), 3.54 (1H, br s, NH), 6.59-6.72 (3H, m, *o*- *p*-ArNH), 7.14-7.19 (6H, m, *m*-ArNH, ArH); δ_C 19.1 (t, J_{CD}=19.5, CH_2D), 32.8 ($\mathit{C}\mathrm{H_2CH_2NH}$), 43.8 ($\mathrm{CH_2}\mathit{C}\mathrm{H_2NH}$), 112.8, 117.3, 126.0, 126.5, 129.1, 129.2, 130.4, 136.2, 137.4, 148.0 (ArC); *m/z* 212 (M$^+$, 31%), 107 (32), 106 (100), 104 (13), 79 (35), 78 (21), 77 (55), 51 (30) (Found: M$^+$, 212.1426. $C_{15}H_{16}DN$ requires M, 212.1424).

1-[2-(Anilinoethyl)phenyl]-3,3-dimethyl-2-butanol (**15c**): ν_{max} (film) 3695-3150 cm^{-1} (OH, NH); δ_H 0.89 [9H, s, $(CH_3)_3C$], 2.49 (1H, dd, J=13.7, 10.6, $\mathit{H}\mathrm{CHCHOH}$), 2.55 (2H, br s, NH, OH), 2.79 (1H, dd, J=13.7, 2.1, $\mathrm{HC}\mathit{H}\mathrm{CHOH}$), 2.84-2.90 (2H, m, $\mathrm{C}\mathit{H}_2\mathrm{CH_2NH}$), 3.28-3.34 (3H, m, $\mathrm{CH_2C}\mathit{H}_2\mathrm{NH}$, $\mathrm{C}\mathit{H}\mathrm{OH}$), 6.53 (2H, dd, J=7.6, 0.9, *o*-ArNH), 6.61 (1H, tt, J=7.3, 0.9, *p*-ArNH), 7.06-7.15 (6H, m, *m*-ArNH, ArH); δ_C 25.7 [$(\mathit{C}\mathrm{H_3})_3\mathrm{C}$], 32.1, 34.5 ($2\mathrm{xArCH_2}$), 35.0 [$(\mathrm{CH_3})_3\mathit{C}$], 44.7 ($CH_2NH$), 80.2 (CHOH), 112.9, 117.4, 126.5, 126.6, 129.2, 129.8, 130.5, 138.0, 138.1, 148.0 (ArC); *m/z* 297 [M$^+$, 20%], 107 (23), 106 (100), 79 (17), 77 (32), 57 (11), 41 (19) (Found: M$^+$, 297.2093. $C_{20}H_{27}NO$ requires M, 297.2093).

2-[2-(2-Anilinoethyl)phenyl]-1-phenylethanol (**15d**): ν_{max} (film) 3710-3130 cm^{-1} (OH, NH); δ_H 2.84-3.08 (6H, m, $\mathrm{C}\mathit{H}_2\mathrm{CH_2N}\mathit{H}$, $\mathrm{C}\mathit{H}_2\mathrm{CHO}\mathit{H}$), 3.30 (2H, t, J=7.3, $\mathrm{CH_2C}\mathit{H}_2\mathrm{NH}$), 4.81 (1H, dd, J=8.0, 5.3, $\mathrm{C}\mathit{H}\mathrm{OH}$), 6.57 (2H, dd, J=8.5, 0.9, *o*-ArNH), 6.69 (1H, tt, J=7.3, 0.9, *p*-ArNH), 7.12-7.33 (11H, m, *m*-ArNH, ArH); δ_C 32.1, 42.4, 44.6 ($\mathrm{CH_2CH_2NH}$, $\mathit{C}\mathrm{H_2CHOH}$), 75.1 (CHOH), 112.9, 117.4, 125.7, 126.5, 126.8, 127.6, 128.4, 129.2, 129.7, 130.6, 136.4, 138.0, 143.9, 147.9 (ArC); *m/z* 317 (M$^+$, 9%), 299 (13), 107 (14), 106 (100), 79 (17), 77 (30) (Found: M$^+$, 317.1790. $C_{22}H_{23}NO$ requires M, 317.1780).

1-[2-(Anilinoethyl)phenyl]-2-methyl-2-propanol (**15e**): ν_{max} (film) 3690-3140 cm^{-1} (OH, NH); δ_H 1.21 [6H, s, $(\mathrm{C}\mathit{H}_3)_2\mathrm{COH}$], 2.60 (2H, br s, OH, NH), 2.81 (2H, s, $\mathrm{C}\mathit{H}_2\mathrm{COH}$), 3.01 (2H, t, J=7.3, $\mathrm{C}\mathit{H}_2\mathrm{CH_2NH}$), 3.32 (2H, t, J=7.3, $\mathrm{CH_2C}\mathit{H}_2\mathrm{NH}$), 6.59 (2H, dd, J=8.5, 0.9, *o*-ArNH), 6.69 (1H, t, J=7.3, *p*-ArN), 7.12-7.22 (6H, m, *m*-ArNH, ArH); δ_C 29.5 [$(\mathit{C}\mathrm{H_3})_2\mathrm{COH}$], 32.6 ($\mathit{C}\mathrm{H_2CH_2NH}$), 44.8, 44.9 ($\mathrm{CH_2}\mathit{C}\mathrm{H_2NH}$, $\mathit{C}\mathrm{H_2COH}$), 71.3 (COH), 112.9, 117.4, 126.1, 126.8, 129.2, 129.7, 131.8, 136.1, 138.6, 147.9 (ArC); *m/z* 269 (M$^+$, 39%), 107 (33), 106 (100), 104 (10), 91 (11), 79 (29), 78 (14), 77 (46), 59 (20), 51 (18), 43 (21) (Found:

M$^+$, 269.1769. $\mathrm{C_{18}H_{23}NO}$ requires M, 269.1780).

1-[2-(Anilinoethyl)phenyl]-2-methyl-2-pentanol (**15f**): ν_{max} (film) 3700-3135 cm^{-1} (OH, NH); δ_H 0.92 (3H, t, *J*=6.9, $\mathrm{C}H_3\mathrm{CH_2}$), 1.10 (3H, s, $\mathrm{C}H_3\mathrm{COH}$), 1.36-1.51 (4H, m, $\mathrm{CH_3C}H_2\mathrm{C}H_2$), 2.46 (2H, br s, OH, NH), 2.73 (1H, d, *J*=13.7, $\mathrm{Ar}H\mathrm{CHCOH}$), 2.83 (1H, d, *J*=13.7, $\mathrm{ArHC}H\mathrm{COH}$), 3.01 (2H, t, *J*=7.3, $\mathrm{C}H_2\mathrm{CH_2NH}$), 3.32 (2H, t, *J*=7.3, $\mathrm{CH_2C}H_2\mathrm{NH}$), 6.58 (2H, dd, *J*=8.5, 0.9, *o*-ArNH), 6.69 (1H, t, *J*=7.3, *p*-ArNH), 7.12-7.22 (6H, m, *m*-ArNH, ArH); δ_C 14.6 ($C\mathrm{H_3CH_2}$), 17.2 ($\mathrm{CH_3}C\mathrm{H_2}$), 26.4 ($C\mathrm{H_3COH}$), 32.6, 43.4, 44.7, 44.8 ($\mathrm{CH_2CH_2NH}$, $\mathrm{ArCH_2COH}C\mathrm{H_2}$), 73.0 (COH), 112.9, 117.4, 126.0, 126.7, 129.2, 129.7, 131.9, 135.9, 138.9, 147.9 (ArC); *m/z* 297 (M$^+$, 24%), 107 (28), 106 (100), 79 (21), 78 (10), 77 (37), 45 (28), 43 (28), 41 (14) (Found: M$^+$, 297.2094. $\mathrm{C_{20}H_{27}NO}$ requires M, 297.2093).

1-{[2-(2-Anilinoethyl)phenyl]methyl}-1-cyclopentanol (**15g**): ν_{max} (film) 3715-3145 cm^{-1} (OH, NH); δ_H 1.54-1.80 (8H, m, 4xringCH$_2$), 2.60 (2H, br s, OH, NH), 2.91 (2H, s, $\mathrm{C}H_2\mathrm{COH}$), 3.00 (2H, t, *J*=7.3, $\mathrm{C}H_2\mathrm{CH_2NH}$), 3.31 (2H, t, *J*=7.3, $\mathrm{CH_2C}H_2\mathrm{NH}$), 6.57 (2H, dd, *J*=8.5, 0.9, *o*-ArNH), 6.68 (1H, tt, *J*=7.3, 0.9, *p*-ArNH), 7.11-7.25 (6H, m, *m*-ArNH, ArH); δ_C 23.1, 32.5, 39.3, 42.3, 44.7 (7xCH$_2$), 82.6 (COH), 112.6, 117.3, 126.1, 126.6, 129.1, 129.6, 131.3, 136.7, 138.5, 147.9 (ArC); *m/z* 295 (M$^+$, 14%), 107 (18), 106 (100), 79 (14), 77 (26) (Found: M$^+$, 295.1938. $\mathrm{C_{20}H_{25}NO}$ requires M, 295.1936).

Ethyl 2-[2-(Anilinoethyl)phenyl]acetate (**15h'**): ν_{max} (film) 3398 (NH), 1727 cm^{-1} (C=O); δ_H 1.22 (3H, t, *J*=7.0, $\mathrm{C}H_3\mathrm{CH_2O}$), 2.94 (2H, t, *J*=7.3, $\mathrm{C}H_2\mathrm{CH_2NH}$), 3.36 (2H, t, *J*=7.3, $\mathrm{CH_2C}H_2\mathrm{NH}$), 3.65 (2H, s, $\mathrm{CH_2C{=}O}$), 3.80 (1H, br s, NH), 4.12 (2H, q, *J*=7.0, OCH$_2$), 6.59 (2H, d, *J*=8.0, *o*-ArNH), 6.68 (1H, t, *J*=7.3, *p*-ArNH), 7.13-7.26 (6H, m, *m*-ArNH, ArH); δ_C 14.1 (CH$_3$), 32.3, 38.6, 44.2 ($\mathrm{CH_2CH_2NH}$, $C\mathrm{H_2C{=}O}$), 60.9 (OCH$_2$), 112.7, 117.3, 126.7, 127.5, 129.2, 129.7, 130.7, 132.8, 137.8, 147.9 (ArC), 171.6 (C=O); *m/z* 283 (M$^+$, 11%), 107 (10), 106 (100), 77 (19) (Found: M$^+$, 283.1570. $\mathrm{C_{18}H_{21}NO_2}$ requires M, 283.1572).

Preparation of N-*Methyltetrahydroisoquinoline* (**18**).-[11] To a cooled (-50°C) stirred THF solution (15 ml) of tetrahydroisoquinoline hydrochloride (0.848 ml, 5.0 mmol) was added a 1.6 M hexane solution of Bu^{n}Li (6.6 ml, 10.5 mmol). After 0.5 h, MeI (0.342 ml, 5.5 mmol) was added at -50°C and the mixture was allowed to reach the room temperature during 3 h. Then it was hydrolysed with water (20 ml), acidified with 3 M hydrochloric acid (10 ml) and extracted with ethyl acetate (3x25 ml). The aqueous layer was basified with 2.5 M sodium hydroxide (20 ml) and extracted with ethyl acetate (3x25 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was pure product **18**. Yield is given in the text; R_f=0.17 (ethyl acetate); ν_{max} (film) 3064, 3044, 3021, 1650, 1608, 1583, 740 cm^{-1} (Ar); δ_H 2.44 (3H, s, CH$_3$N), 2.67 (2H, t, *J*=5.8, $\mathrm{ArC}H_2\mathrm{CH_2N}$), 2.91 (2H, t, *J*=5.8, $\mathrm{ArCH_2C}H_2\mathrm{N}$), 3.56 (2H, s, $\mathrm{ArC}H_2\mathrm{N}$), 6.98-7.13 (4H, m, ArH); δ_C 29.2 ($\mathrm{Ar}C\mathrm{H_2CH_2N}$), 46.1 (CH$_3$), 52.9 ($\mathrm{ArCH_2}C\mathrm{H_2N}$), 57.9 ($\mathrm{Ar}C\mathrm{H_2N}$), 125.5, 126.3, 128.5, 133.7, 134.7 (ArC); *m/z* 147 (M$^+$, 69%), 146 (100), 144 (25), 131 (18), 130 (12), 118 (11), 115 (14), 105 (17), 104 (69), 103 (38), 78 (44), 77 (37), 74 (12), 72 (49), 65 (16), 63 (11), 52 (10), 51 (30), 50 (14), 42 (64) (Found: M$^+$, 147.1046. $\mathrm{C_{10}H_{13}N}$ requires M, 147.1048).

Preparation of Compounds **19**. *General Procedure.*- To a blue suspension of lithium powder (0.125g, 18.0 mmol) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (0.047 g, 0.18 mmol) in THF (10 ml) at 20°C was added isoquinoline **18** (0.200, 1.47 mmol) under argon and the mixture was stirred for 0.5 h at the same temperature. Then, the mixture was cooled down at -78°C and the corresponding electrophile (3.0 mmol; 0.5 ml in the case of water or deuterium oxide) was added. The mixture was stirred at the same temperature for 0.5 h and was hydrolysed with water (20 ml). The resulting mixture was extracted with ethyl acetate (3x25 ml).

The organic layer was dried over anhydrous sodium sulfate and evaporated (15 Torr). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) and/or recrystallised to yield pure products **19**. Yields and physical data (R_f or mp) are included in Table 5; analytical and spectroscopic data follow.

(2-Ethylphenyl)methyl methyl amine (**19a**): ν_{max} (KBr) 3323 cm^{-1} (NH); δ_H 1.21 (3H, t, J=7.6, CH_3CH$_2$), 1.25 (1H, br s, NH), 2.48 (3H, s, CH$_3$N), 2.70 (2H, q, J=7.6, CH$_3$CH_2), 3.74 (2H, s, CH$_2$N), 7.14-7.30 (4H, m, ArH); δ_C 15.3 (CH$_3$CH$_2$), 25.2 (CH$_3$$CH_2$), 36.4 (CH$_3$N), 53.1 (CH$_2$N), 125.8, 127.0, 128.3, 128.6, 137.5, 142.2 (ArC); *m/z* 149 (M$^+$, 8%), 134 (37), 119 (20), 118 (87), 117 (100), 115 (16), 103 (10), 91 (40), 77 (20), 65 (20), 51 (19), 44 (89), 42 (59), 41 (14) (Found : C, 79.81; H, 10.76; N, 9.31. $C_{10}H_{15}N$ requires: C, 80.47; H, 10.14; N, 9.39).

[2-(1-Deuterioethyl)phenyl]methyl methyl amine (**19b**): ν_{max} (KBr) 3323 cm^{-1} (NH); δ_H 1.21 (3H, d, J=7.4, CH_3CHD), 1.32-1.42 (1H, br s, NH), 2.47 (3H, s, CH$_3$N), 2.63-2.73 (1H, m, CHD), 3.73 (2H, s, CH$_2$N), 7.12-7.29 (4H, m, ArH); δ_C 15.1 (CH$_3$CHD), 24.8 (t, J_{CD}=19.2, CHD), 36.3 (CH$_3$N), 53.0 (CH$_2$N), 125.7, 127.0, 128.3, 128.6, 137.4, 142.1 (ArC); *m/z* 150 (M$^+$, 6%), 135 (23), 134 (21), 120 (14), 119 (48), 118 (100), 117 (92), 115 (12), 92 (14), 91 (31), 78 (11), 77 (16), 65 (18), 51 (18), 44 (88), 42 (70) (Found : C, 78.96; H, 11.02; N, 9.24. $C_{10}H_{14}DN$ requires: C, 79.94; H, 10.73; N, 9.32).

Allyl Methyl [2-(1-Methyl-3-butenyl)phenyl]methyl Amine (**19c'**):[14] ν_{max} (film) 1641, 1026, 994, 915 cm^{-1} (CH=CH$_2$); δ_H 1.21 (3H, d, J=7.0, CH_3CH), 2.14 (3H, s, CH$_3$N), 2.26-2.43 (2H, m, CH_2CH), 2.99 (2H, ddd, J=6.4, 3.0, 1.5, NCH_2CH=CH$_2$) 3.25-3.37 (1H, m, CH$_3$CH), 3.44 (1H, d, J=13.1, ArHCHN), 3.50 (1H, d, J=13.1, ArHCHN), 4.91-5.22 (4H, m, 2xCH=CH_2), 5.67-5.94 (2H, m, 2xCH=CH$_2$), 7.09-7.25 (4H, m, ArH); δ_C 21.4 (CH$_3$CH$_2$), 33.5 (CH$_3$$C$H), 42.0 (CH$_3$N), 42.5 (CH$CH_2$), 59.7, 60.7 (2xCH$_2$N), 105.6, 117.1 (2xCH=$CH_2$), 125.2, 125.8, 127.3, 130.4, 136.1 (ArC), 136.3, 137.6 (2xCH=CH$_2$), 146.7 (ArC); *m/z* 229 (M$^+$, 0.6%), 144 (20), 143 (93), 131 (12), 130 (36), 129 (24), 128 (23), 117 (36), 115 (21), 91 (19), 84 (16), 72 (11), 70 (18), 44 (43), 42 (25), 41 (36), 40 (100).

{1-[2-(Methylaminomethyl)phenyl]ethyl}-1-cyclopentanol (**19d**):[14] ν_{max} (film) 3720-3120 cm^{-1} (OH, NH); δ_H 1.31 (3H, d, J=7.0, CH_3CH), 1.38-1.99 (10H, m, 4xringCH$_2$, OH, NH), 2.43 (3H, s, CH$_3$N), 3.43 (2H, q, J=7.0, CH$_3$CH), 3.52 (1H, d, J=12.2, HCHNCH$_3$), 3.95 (1H, d, J=12.2, HCHNCH$_3$), 7.10-7.40 (4H, m, ArH); δ_C 18.0 (CH$_3$CH$_2$), 23.4, 24.2, 33.3 (3xringCH$_2$), 35.3 (CH$_3$$C$H), 40.2 (1xringCH$_2$), 41.2 (CH$_3$N), 54.2 (CH$_2$N), 83.7 (COH), 125.6, 127.7, 127.9, 130.1, 136.8, 144.7 (ArC); *m/z* 215 (M$^+$-H$_2$O, 9%), 184 (39), 170 (16), 169 (100), 156 (12), 155 (25), 143 (15), 142 (12), 141 (43), 132 (14), 129 (13), 128 (13), 118 (48), 117 (39), 115 (20), 91 (18), 67 (10), 55 (13), 44 (48), 43 (12), 42 (19), 41 (19), 40 (31).

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