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EPC-Synthesis of Functionalised Amides via Chiral β-Nitrogenated Organolithium Compounds

Francisco Foubelo and Miguel Yus*

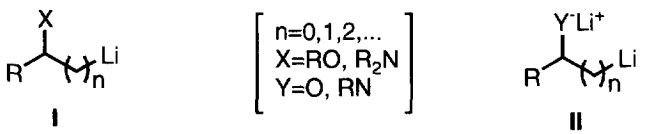
Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain

Abstract: The deprotonation of chiral chloroamides or carbamates **1**, **4**, **7**, **10**, **13** and **16** with *n*-butyllithium followed by *in situ* lithiation with lithium naphthalenide, both at -78°C in THF, leads to the formation of the corresponding chiral dianionic intermediates, which by reaction with different electrophiles [H_2O, D_2O, Me_2S_2, $(CH_2)_5CO$, Bu^tCHO, PhCHO, CO_2, $CO(OEt)_2$, $BrCH_2CO_2Et$ and DCC] at -78 to 20°C affords, after hydrolysis with water, the expected enantiopure compounds.

INTRODUCTION

The preparation of enantiomerically pure compounds (EPC synthesis[1]) is currently of great interest, not only for a theoretical[2] but also and mainly from a practical[3] point of view: very frequently the biological activity of both enantiomers is very different and in some cases even contrary.[4] Among the methodologies to obtain enantiopure compounds one of choice is based on the chiral pool of natural products, such as amino acids, carbohydrates, terpenes, ...: the procedure consists in using readily available (commercially if possible) and cheap chiral starting materials in order to prepare the desirable target molecule. On the other hand, recently we have been interested in the preparation and synthetic applications of functionalised organolithium compounds of the general type **I**:[5,6] these intermediates have the ability to transfer the functionality to an electrophilic reagent, so in one only step it is possible to generate polyfunctionalised molecules, which are widely represented in Nature. The preparation of this type of organolithium species has the inconvenience (inherent to the relative position between the lithium atom and the functionality) of elimination reactions, which decompose the corresponding intermediates. The most dramatic situation appears in the corresponding β-functionalised compounds (**I**, with n=1), which decompose even at very low temperature (<-100°C) giving olefins.[7] Some years ago we could overcome this problem locating a negative charge on the β-heteroatom, preparing dianionic species of the type **II**, which at low temperature (-78°C) are stable and react with electrophiles as typical organolithium compounds.[8] These methods have been used for the generation of nitrogen-containing dianions of the type **II** in racemic form by: (a) mercury/lithium transmetallation;[9] (b) chlorine/lithium exchange in the case of amide derivatives;[10] and (c) arene-catalysed[11] opening of aziridines.[12] To our best knowledge, only the last route (c) has been used for the preparation of chiral nitrogenated intermediates of the type **II**[13] (Y=RN) starting from a chiral aziridine derived from (-)-ephedrine.[12b] In this paper, we take advantage of the

methodology (b) described previously by us[10] for the general preparation of chiral β-nitrogenated intermediates of the type **II** (n=1) using the EPC-strategy[1] and starting from the corresponding chlorinated precursors easily available from commercial β-aminoalcohols, related to natural amino acids.[14]

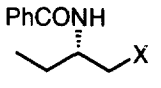


RESULTS AND DISCUSSION

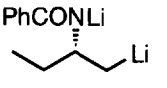
The reaction of (*S*)-*N*-(1-chloromethylpropyl)benzamide [(*S*)-**1**] with *n*-butyllithium at -78°C followed by lithiation with lithium naphthalenide[10,15,16] at the same temperature for 1 h[17] led to the corresponding chiral dianion (*R*)-**2**, which by reaction with different electrophiles [H_2O, D_2O, Me_2S_2, $(CH_2)_5CO$, Bu^tCHO, PhCHO] at temperatures ranging between -78 and 20°C yielded, after hydrolysis with water, the correponding enantiomerically pure compounds **3a-3f** with the same configuration at the stereogenic centre as the starting material (Chart 1 and Table 1, entries 1-6).[18] In the case of using pivalaldehyde or benzaldehyde as electrophilic reagents a 2:1 or 1:1 mixture of diastereomers **3e** or **3f** was, respectively, obtained, showing a poor asymmetric induction[19] (Table 1, entries 5 and 6). Although compounds **3e** and **3f** were obtained as a mixture of the corresponding diastereoisomers, they could be easily separated by flash chromatography (silica gel, hexane/ethyl acetate), so it was possible to isolate all diastereoisomers in enantiomeriacally pure form. The stereochemistry of compounds **3e** and **3f** was assigned according to their 300 MHz ^1H NMR data[12] and n.O.e. experiments. Thus, for instance, whilst in compound (1*S*,3*S*)-**3f** a positive n.O.e. was found at the 1H proton by irradiation at the 3H one, in compound (1*R*,3*S*)-**3f** no enhancement was observed in the same experiment (Chart 2).

When the enantiomeric starting material (*R*)-**1** was used instead (*S*)-**1**, and using the same procedure as above, the expected products **3a-3e** were isolated *via* the corresponding intermediate (*S*)-**2** (Chart 1 and Table 1, entries 9-11). In this case we studied also the reaction with diethyl carbonate and ethyl bromoacetate, so compounds (*R*)-**3i** and (*R*)-**3j** were, respectively obtained (Chart 1 and Table1, entries 12 and 13): using this simple methodology, protected non-proteinogenic β- or γ-amino acids derivatives can be prepared. As it was commented above for the couple **3f**, in the case of compounds (3*R*,5*R*)- and (3*S*,5*R*)-**3e** the stereochemistry was unequivocally assigned also by n.O.e. experiments (Chart 3).

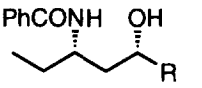
Since the direct carbonation with carbon dioxide of intermediates **2** presented problems,[20] we studied the same reaction using *N*-Boc chlorinated starting materials **4**. Applying the same methodology described above, but with reaction time of about 3 h for the lithiation step, the corresponding protected amino acids **6g** were isolated through the dianions **5** (Chart 1 and Table 1, entries 7 and 14). In both cases the reaction of intermediates **5** with dicyclohexylcarbodiimide (DCC) yielded the heterocycles **6h** in enantiomeric pure form (Chart 1 and Table 1, entries 8 and 15). The last alternative was also applied to starting compounds (*S*)-**7** and (*R*)-**16**, which *via* the corresponding intermediate (*R*)-**8** and (*S*)-**17**, respectively, gave the expected products (*R*)-**9g,h** and (*S*)-**18g,h**, respectively (Chart 1 and Table 1, entries 16, 17, 20 and 21).



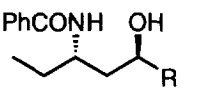
(*S*)-**1** : X=Cl
(*R*)-**3a** : X=H
(*R*)-**3b** : X=D
(*S*)-**3c** : X=MeS
(*S*)-**3d** : X=$(CH_2)_5COH$



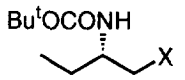
(*R*)-**2**



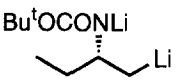
(3*S*,5*S*)-**3e** : R=Bu^t
(1*S*,3*S*)-**3f** : R=Ph



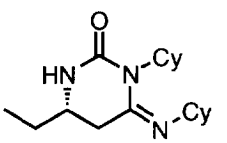
(3*R*,5*S*)-**3e** : R=Bu^t
(1*R*,3*S*)-**3f** : R=Ph



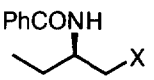
(*S*)-**4** : X=Cl
(*S*)-**6g** : X=CO_2H



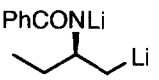
(*R*)-**5**



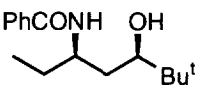
(*S*)-**6h**



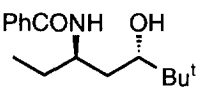
(*R*)-**1** : X=Cl
(*S*)-**3a** : X=H
(*S*)-**3b** : X=D
(*R*)-**3i** : X=CO_2Et
(*R*)-**3j** : X=CH_2CO_2Et



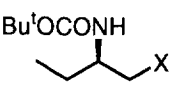
(*S*)-**2**



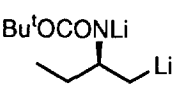
(3*R*,5*R*)-**3e**



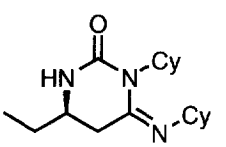
(3*S*,5*R*)-**3e**



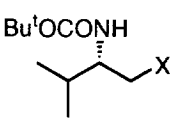
(*R*)-**4** : X=Cl
(*R*)-**6g** : X=CO_2H



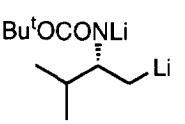
(*S*)-**5**



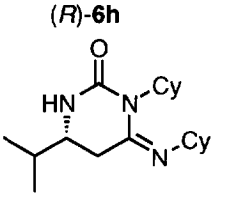
(*R*)-**6h**



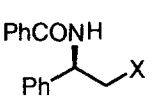
(*S*)-**7** : X=Cl
(*R*)-**9g** : X=CO_2H



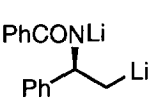
(*R*)-**8**



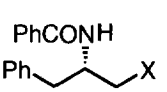
(*R*)-**9h**



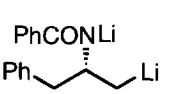
(*R*)-**10** : X=Cl
(*S*)-**12a** : X=H



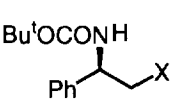
(*S*)-**11**



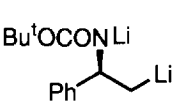
(*S*)-**13** : X=Cl
(*R*)-**15a** : X=H



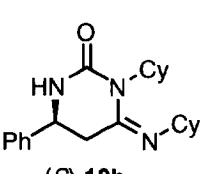
(*R*)-**14**



(*R*)-**16** : X=Cl
(*S*)-**18g** : X=CO_2H



(*S*)-**17**



(*S*)-**18h**

Chart 1.

Table 1. Preparation of Enantiomerically Pure Compounds **3**, **6**, **9**, **12**, **15** and **18**

Entry	Starting material	Intermediate	Electrophile	Product[a]			
				No.	Yield (%)[b]	mp (°C)[c]	$[\alpha]_D^{25}$[d]
1	(*S*)-**1**	(*R*)-**2**	H_2O	(*R*)-**3a**	91	85-86	-21.5 (1.15)
2	(*S*)-**1**	(*R*)-**2**	D_2O	(*R*)-**3b**	89	85-86	-22.9 (1.15)
3	(*S*)-**1**	(*R*)-**2**	Me_2S_2	(*S*)-**3c**	88	96-97	+32.3 (1.15)
4	(*S*)-**1**	(*R*)-**2**	$(CH_2)_5CO$	(*S*)-**3d**	69	117-118	+7.5 (1.00)
5	(*S*)-**1**	(*R*)-**2**	Bu^tCHO	(3*S*,5*S*)-**3e**	78[e]	101-102	-19.2 (1.05)
				(3*R*,5*S*)-**3e**		103-104	+8.8 (0.95)
6	(*S*)-**1**	(*R*)-**2**	PhCHO	(1*S*,3*S*)-**3f**	72[h]	-[f,g]	-28.2 (1.35)
				(1*R*,3*S*)-**3f**		117-118	+24.4 (0.75)
7	(*S*)-**4**	(*R*)-**5**	CO_2	(*S*)-**6g**	81	86-87	-20.0 (1.15)
8	(*S*)-**4**	(*R*)-**5**	DCC[i]	(*S*)-**6h**	68	149-150	-8.15 (1.05)
9	(*R*)-**1**	(*S*)-**2**	H_2O	(*S*)-**3a**	85	85-86	+22.7 (1.05)
10	(*R*)-**1**	(*S*)-**2**	D_2O	(*S*)-**3b**	85	85-86	+23.5 (0.85)
11	(*R*)-**1**	(*S*)-**2**	Bu^tCHO	(3*R*,5*R*)-**3e**	69[e]	101-102	+18.4 (0.85)
				(3*S*,5*R*)-**3e**		103-104	-8.5 (0.80)
12	(*R*)-**1**	(*S*)-**2**	$CO(OEt)_2$	(*R*)-**3i**	64	72-73	+44.9 (1.00)
13	(*R*)-**1**	(*S*)-**2**	$BrCH_2CO_2Et$	(*R*)-**3j**	25	85-86	+4.6 (0.60)
14	(*R*)-**4**	(*S*)-**5**	CO_2	(*R*)-**6g**	84	86-87	+17.9 (0.95)
15	(*R*)-**4**	(*S*)-**5**	DCC[i]	(*R*)-**6h**	68	149-150	+7.2 (1.05)
16	(*S*)-**7**	(*R*)-**8**	CO_2	(*R*)-**9g**	90	71-72	-16.6 (0.75)
17	(*S*)-**7**	(*R*)-**8**	DCC[i]	(*R*)-**9h**	67	148-149	-8.2 (1.05)
18	(*R*)-**10**	(*S*)-**11**	H_2O	(*S*)-**12a**	84	130-132	-5.1 (1.00)
19	(*S*)-**13**	(*R*)-**14**	H_2O	(*R*)-**15a**	85	123-124	+2.2 (1.50)
20	(*R*)-**16**	(*S*)-**17**	CO_2	(*S*)-**18g**	71	116-117	-30.0 (0.75)
21	(*R*)-**16**	(*S*)-**17**	DCC[i]	(*S*)-**18h**	42	104-105	-8.2 (0.80)

[a] All isolated products **3**, **6**, **9**, **12**, **15** and **18** were >95% pure (from GLC and 300 MHz ^1H NMR). [b] Isolated yield after flash chromatography (silica gel, hexane/ethyl acetate) based on the starting chloroamide. [c] From hexane/ chloroform. [d] In dichloromethane; concentration is given in g/100 ml. [e] 2:1 Diastereoisomers ratio (GLC). [f] Oil. [g] R_f 0.18 (hexane/ethyl acetate: 2/1). [h] 1:1 Diastereomers ratio (300 MHz ^1H NMR). [i] Dicyclohexyl-carbodiimide.

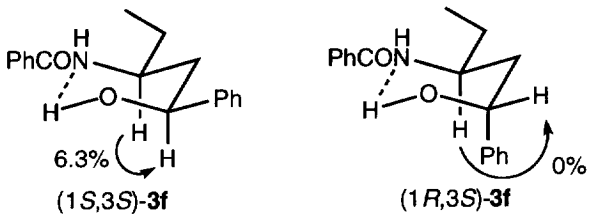


Chart 2.

Finally, the use of chloro amides (*R*)-**10** and (*S*)-**13** as starting materials led to the "reduced" products (*S*)-**12a** and (*R*)-**15a**, respectively, by trapping of the corresponding intermediate (*S*)-**11** and (*R*)-**14**, respectively, with water (Chart 1 and Table 1, entries 18 and 19).

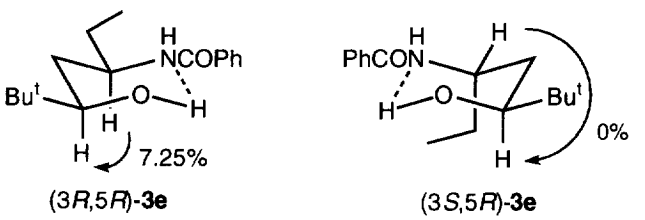


Chart 3.

All benzoylated chiral starting materials **1** , **10** and **13** were easily prepared in a tandem chlorination/benzoylation one-pot procedure from the corresponding commercially available aminoalcohols by successive *in situ* treatment with thionyl chloride and benzoyl chloride under basic conditions. In the case of *N*-Boc chiral chlorinated starting materials **4**, **7** and **16** two different methods were used for their preparation. Compounds **4** and **7** were prepared from the corresponding commercially available aminoalcohols by successive chlorination with thionyl chloride followed by treatment with di-*tert*-butyl dicarbonate. On the contrary, compound **16** was isolated after succesive *N*-Boc protection and chlorination with the triphenylphosphine/carbon tetrachloride combination.

From the results described in this paper, we conclude that it is easy to prepare enantiomerically pure β-nitrogenated organolithium intermediates **2**, **5**, **8**, **11**, **14** and **17** (of the general type **II**) from commercially available chiral aminoalcohols, through the corresponding chlorinated derivatives. The reaction of these dianions with different electrophiles affords enantiomerically pure compounds, so being this methodology a typical example of EPC-synthesis.

EXPERIMENTAL PART

General.- For general information see reference 12b.

Preparation of Starting Chloroamides **1**, **10** and **13**. *General Procedure.*- To a stirred solution of the corresponding aminoalcohol (10.0 mmol) in chloroform (20 ml) at 0°C, was added dropwise thionyl chloride (2.40 g, 20.0 mmol). The reaction mixture was heated at 65°C for 4 h and after that, the reaction was allowed to

cool down to 20°C, hydrolysed carefully with a saturated aqueous solution of sodium bicarbonate and extrated with dichloromethane. The organic layer was evaporated (15 mmHg) and the resulting 2-chloroamine, without purification, was treated with a 2.0 M sodium hydroxide aqueous solution (20 ml) and benzoyl chloride (1.60 g, 12.0 mmol) was added dropwise at 0°C to the resulting suspension. After stirring 2 h at the same temperature, the reaction mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) and recrystallised to yield the title compounds. Yields, physical, spectroscopic and analytical data follow.

(S)-N-(1-Chloromethylpropyl)benzamide [(*S*)-**1**]: (51% yield) mp 100-101°C (hexane/chloroform); ν 3025, 3010, 1650 cm^{-1}; δ_H 0.99 (3H, d, *J* = 7.5, CH_3), 1.67-1.80 (2H, m, CH_2CH_3), 3.71 (1H, dd, *J* = 11.3, 3.4, CHHCl), 3.80 (1H, dd, *J* = 11.3, 3.8, CHHCl), 4.30-4.38 (1H, m, CHN), 6.46 (1H, d, *J* = 7.1, NH), 7.39-7.80 (3H, m, ArH), 8.09 (2H, d, *J* = 7.5, ArH); δ_C 10.3 (CH_3), 24.8 (CH_2CH_3), 47.7 (CH_2Cl), 51.1 (CHN), 126.9, 128.5, 131.5, 134.2 (ArC), 167.3 (C=O); m/z 213 [M^+ (Cl^{37}), 2%], 211 [M^+ (Cl^{35}), 5%), 162 (13), 105 (100), 77 (49), 51 (20). Anal. Calcd. for $C_{11}H_{14}ClNO$: C, 62.40; H, 6.66; N, 6.62. Found: C, 62.55; H, 6.72; N, 6.44. $[\alpha]_D^{25}$= -58.9 [c= 1.35 (CH_2Cl_2)].

(R)-N-(1-Chloromethylpropyl)benzamide [(*R*)-**1**]: (76% yield) physical and spectroscopic data were found to be the same than for (*S*)-**1a**. Anal. Calcd. for $C_{11}H_{14}ClNO$: C, 62.40; H, 6.66; N, 6.62. Found: C, 62.50; H, 6.71; N, 6.32. $[\alpha]_D^{25}$= +60.3 [c= 1.45 (CH_2Cl_2)].

(R)-N-(2-Chloro-1-phenylethyl)benzamide [(*R*)-**10**]: (58% yield) mp 121-122°C (hexane/chloroform); ν 3030, 3005, 1660 cm^{-1}; δ_H 3.96 (2H, d, *J* = 5.2, CH_2Cl), 5.54 (1H, dt, *J* = 7.9, 5.2, CHN), 6.89 (1H, d, *J* = 7.9, NH), 7.28-7.53 (8H, m, ArH), 7.81 (2H, dd, *J* = 8.6, 1.5, ArH); δ_C 47.6 (CH_2Cl), 53.9 (CHN), 126.7, 127.05, 128.1, 128.6, 128.8, 131.8, 133.9, 138.4 (ArC), 167.0 (C=O); m/z 223 [M+-HCl, 62%], 193 (100), 165 (26), 105 (39), 89 (79), 77 (71), 63 (24), 51 (57). $[\alpha]_D^{25}$= -38.9 [c= 1.25 (CH_2Cl_2)].

(S)-N-(1-Benzyl-2-chloroethyl)benzamide [(*S*)-**13**]: (61% yield) mp 131-132°C (hexane/chloroform); ν 3035, 3015, 1655 cm^{-1}; δ_H 2.96-3.15 (2H, m, CH_2Ar), 3.64 (1H, dd, *J* = 11.2, 3.1, CHHCl), 3.76 (1H, dd, *J* = 11.2, 4.1, CHHCl), 4.67-4.81 (1H, m, CHN), 6.35 (1H, d, *J* = 7.6, NH), 7.28-7.51 (8H, m, ArH), 7.73 (2H, dd, *J* = 8.3, 1.3, ArH); δ_C 37.3 (CH_2Ar), 46.6 (CH_2Cl), 51.0 (CHN), 126.8, 126.9, 128.4, 128.6, 129.1, 131.5, 134.0, 136.8 (ArC), 166.9 (C=O); m/z 237 [M+-HCl, 2%], 147 (10), 146 (100), 118 (24), 91 (88), 77 (36), 65 (15), 51 (24). $[\alpha]_D^{25}$= +10.7 [c= 1.20 (CH_2Cl_2)].

Preparation of Chlorocarbamates **4** and **7**. *General Procedure.*- To a stirred solution of the corresponding aminoalcohol (10.0 mmol) in chloroform (20 ml) at 0°C, was added dropwise thionyl chloride (2.40 g, 20.0 mmol). The reaction mixture was heated at 65°C for 4 h and after that, the reaction was allowed to cool down to 20°C and the solvents were evaporated (15 mmHg). Methanol (30 ml), triethylamine (4 ml), sodium carbonate (2 g) and di-*tert*-butyl dicarbonate (3.00 g, 15.0 mmol) were added to the resulting residue.[21] The reaction mixture was heated at 65°C for 1 h. After that, the reaction was cooled down to 20°C and the solvents were evaporated (15 mmHg). The resulting residue was treated with ethyl acetate and water. The aqueous layer was extracted with ethyl acetate and the organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) and recrystallised to yield the title compounds. Yields, physical, spectroscopic and analytical data follow.

(S)-tert-*Butyl N-(1-Chloromethylpropyl) Carbamate* [(*S*)-**4**]: (73% yield) mp 43-44°C (hexane); ν 3200, 1695 cm^{-1}; δ_H 0.95 (3H, d, *J* = 7.6, CH_3CH_2), 1.45 [9H, s, $(CH_3)_3C$], 1.48-1.69 (2H, m, CH_2CH_3), 3.61 (1H,

dd, J = 10.1, 3.3, C*H*HCl), 3.68 (1H, dd, J = 10.1, 3.6, CH*H*Cl), 3.69-3.86 (1H, m, CHN), 4.69 (1H, br s, NH); δ_C 10.3 (CH_3CH_2), 25.0 (CH_2CH_3), 28.3 [$(CH_3)_3C$], 47.8 (CH_2Cl), 52.2 (CHN), 79.5 [$C(CH_3)_3$], 155.3 (C=O); m/z 178 (M^+-CH_3CH_2, 1%), 158 (10), 102 (19), 78 (17), 59 (66), 58 (65), 57 (100). Anal. Calcd. for $C_9H_{18}ClNO_2$: C, 52.05; H, 8.74; N, 6.74. Found: C, 51.97; H, 8.80; N, 6.55. $[\alpha]_D^{25}$= -40.9 [c= 1.20 (CH_2Cl_2)].

(R)-tert-*Butyl* N-*(1-Chloromethylpropyl) Carbamate* [(*R*)-**4**]: (68% yield) physical and spectroscopic data were found to be the same than for (*S*)-**4**. Anal. Calcd. for $C_9H_{18}ClNO_2$:C, 52.05; H, 8.74; N, 6.74. Found: C, 51.53; H, 8.66; N, 6.26. $[\alpha]_D^{25}$= +38.4 [c= 1.00 (CH_2Cl_2)].

(S)-tert-*Butyl* N-*(1-Chloromethyl-2-methylpropyl) Carbamate* [(*S*)-**7**]: (55% yield) mp 64-65°C (hexane); ν 3320, 1695 cm^{-1}; δ_H 0.88 (3H, d, J = 6.7, C*H*$_3$CHCH$_3$), 0.89 (3H, d, J = 6.7, CH$_3$CCHC*H*$_3$), 1.38 [9H, s, $(CH_3)_3C$], 1.83 [1H, octet, J = 6.7, $(CH_3)_2CH$], 3.50-3.61 (3H, m, CH_2Cl, CHN), 4.72 (1H, d, J = 6.9, NH); δ_C 18.4, 19.3 [$(CH_3)_2CH$], 28.2 [$(CH_3)_3C$], 29.3 [$CH(CH_3)_2$], 46.8 (CH_2Cl), 56.3 (CHN), 79.3 [$C(CH_3)_3$], 155.5 (C=O); m/z 178 [M^+-$CH(CH_3)_2$, 6%], 80 (20), 78 (60), 72 (24), 59 (55), 57 (100), 56 (21), 55 (17). Anal. Calcd. for $C_{10}H_{20}ClNO_2$: C, 54.12; H, 9.09; N, 6.32. Found: C, 53.71; H, 9.04; N, 5.95. $[\alpha]_D^{25}$= -37.6 [c= 1.00 (CH_2Cl_2)].

Preparation of (R)-tert-*Butyl* N-*(2-Chloro-1-phenylethyl) Carbamate* (**16**).- To a stirred solution of (*R*)-2-phenylglycinol (0.79 g, 5.0 mmol) in methanol (20 ml) was added triethylamine (4.0 ml), sodium carbonate (2.00 g) and di-*tert*-butyl dicarbonate (1.50 g, 7.5 mmol). The reaction mixture was heated at 65°C for 1 h. After that, the reaction was cooled down to 20°C and the solvents were evaporated (15 mmHg). The resulting residue was treated with ethyl acetate and water. The aqueous layer was extracted with ethyl acetate and the organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). Triphenylphosphine (1.50 g, 6.0 mmol) and carbon tetrachloride (20 ml) were added to the resulting residue and the reaction mixture was heated at 80°C for 4 h then, the reaction mixture was hydrolysed with water and extracted with ethyl acetate.[22] The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) and recrystallised to yield the title compounds **16**: (59% overall yield) mp 104-105°C (hexane); ν 3300, 1690 cm^{-1}; δ_H 1.43 [9H, s, $(CH_3)_3C$], 3.68-3.86 (2H, m, CH_2), 4.92-5.11 (1H, m, CHN), 5.22 (1H, d, J = 6.7, NH), 7.26-7.38 (5H, m, ArH); δ_C 28.3 [$(CH_3)_3C$], 48.0 (CH_2), 55.2 (CHN), 80.0 [$C(CH_3)_3$], 126.5, 127.9, 128.6, 139.1 (ArC), 155.0 (C=O); m/z 206 (M^+-CH_2Cl, 7%), 163 (15), 150 (35), 106 (69), 104 (12), 79 (19), 77 (21), 59 (31), 57 (100), 56 (23), 55 (10), 51 (20). Anal. Calcd. for $C_{13}H_{18}ClNO_2$: C, 61.05; H, 7.09; N, 5.48. Found: C, 60.67; H, 7.05; N, 5.20. $[\alpha]_D^{25}$= -35.8 [c= 1.15 (CH_2Cl_2)].

Lithiation of Compounds **1**, **4**, **7**, **10**, **13** *and* **16** *and Reaction with Electrophiles. Isolation of Products* **3**, **6**, **9**, **12**, **15** and **18**. *General Procedure.*- To a cooled (-78°C) solution of the corresponding chiral chloroamide or carbamate (1.0 mmol) was added succesively a 1.6 M hexane solution (1.1 mmol) of Bu^{n}Li and a 0.8 M THF solution (2.4 mmol) of lithium naphthalenide and the mixture was stirred at the same temperature for 1 h in the case of amides **1**, **10** and **13** or 3 h in the case of carbamates **4**, **7** and **16**. Then the corresponding electrophile (1.3 mmol; 0.5 ml in the case of water or deuterium oxide; CO_2 was bubbled for 30 min) was added at -78°C and the reaction was allowed to rise to 20°C overnight. The resulting mixture was hydrolysed with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) and recrystallised to yield pure compounds **3**, **6**, **9**, **12**, **15** and **18**. Yields and physical data (mp's or

R_f values and especific rotations) are included in Table1; analytical and spectroscopic data, as well as literature references for known compounds, follow.

(R)-N-(1-Methylpropyl)benzamide [(*R*)-**3a**]:[23] ν 3290, 1635 cm^{-1}; δ_H 0.95 (3H, d, J = 7.3, CH_3CH_2), 1.21 (3H, d, J = 6.3, CH_3CH), 1.56 (2H, quintet, J = 7.3, CH_2CH_3), 4.11 (1H, tq, J = 7.3, 6.3, CHN), 6.14 (1H, br s, NH), 7.33-7.49 (3H, m, ArH), 7.76 (2H, dd, J = 6.8, 1.6, ArH); δ_C 10.35 (CH_3CH_2), 20.4 (CH_3CH), 29.6 (CH_2), 47.7 (CHN), 126.8, 128.4, 131.1, 135.0 (ArC), 166.9 (C=O); m/z 177 [M$^+$, 7%], 148 (15), 105 (100), 77 (54), 51 (18). Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.68; H, 8.48; N, 7.74.

(R)-N-(1-Deuteriomethylpropyl)benzamide [(*R*)-**3b**]: ν 3295, 1635 cm^{-1}; δ_H 0.96 (3H, t, J = 7.3, CH_3), 1.22 (2H, d, J = 6.3, CH_2D), 1.52-1.62 (2H, m, CH_2CH_3), 4.08-4.20 (1H, m, CHN), 6.09 (1H, br s, NH), 7.38-7.50 (3H, m, ArH), 7.75 (2H, dd, J = 6.7, 1.6, ArH); δ_C 10.4 (CH_3), 20.2 (t, J = 19.6, CH_2D), 29.7 (CH_2CH_3), 47.0 (CHN), 126.8, 128.5, 131.2, 135.0 (ArC), 166.9 (C=O); m/z 178 [M$^+$, 6%], 149 (12), 105 (100), 77 (54), 51 (28), 50 (19). Anal. Calcd. for $C_{11}H_{14}DNO$: C, 74.12; H, 9.05; N, 7.86. Found: C, 74.01; H, 8.93; N, 7.46.

(S)-N-[1-(Methylthiomethyl)propyl]benzamide [(*S*)-**3c**]: ν 3300, 1630 cm^{-1}; δ_H 0.97 (3H, t, J = 7.3, CH_3CH_2), 1.53-1.65, 1.66-1.81 (2H, 2 m, CH_2CH_3), 2.12 (2H, s, CH_3S), 2.69-2.79 (2H, m, CH_2S), 4.17-4.29 (1H, m, CHN), 6.52 (1H, br s, NH), 7.36-7.49 (3H, m, ArH), 7.78 (2H, dd, J = 6.9, 1.0, ArH); δ_C 10.4 (CH_3CH_2), 16.3 (CH_3S), 26.2 (CH_2CH_3), 38.8 (CH_2S), 50.15 (CHN), 126.8, 128.35, 131.2, 134.5 (ArC), 167.2 (C=O); m/z 223 [M$^+$, 2%], 162 (10), 122 (12), 105 (100), 102 (44), 77 (44), 61 (21), 51 (14). Anal. Calcd. for $C_{12}H_{17}NOS$: C, 64.54; H, 7.67; N, 6.27; S, 14.36. Found: C, 64.60; H, 7.70; N, 6.01; S, 12.87.

(S)-1-[2-(N-Benzoylamino)butyl]cyclohexanol [(*S*)-**3d**]: ν 3410, 1630 cm^{-1}; δ_H 0.87 (3H, t, J = 7.3, CH_3), 1.30-1.71 (14H, m, 7XCH_2), 2.75 (1H, br s, OH), 4.04-4.10 (1H, m, CHN), 6.82 (1H, br s, NH), 7.28-7.41 (3H, m, ArH), 7.70 (2H, dd, J = 7.0, 1.6, ArH); δ_C 10.1 (CH_3), 22.2, 25.6, 29.2, 30.8, 36.4, 39.3, 45.3 (CH_2), 48.0 (CHN), 71.2 (COH), 126.9, 128.4, 131.2, 134.7 (ArC), 167.45 (C=O); m/z 275 [M$^+$, 3%], 162 (14), 148 (37), 122 (27), 106 (12), 105 (100), 99 (10), 77 (48), 55 (17). Anal. Calcd. for $C_{17}H_{25}NO_2$: C, 71.14; H, 9.15; N, 5.09. Found: C, 71.50; H, 9.04; N, 5.42.

(3S,5S)-5-(N-Benzoylamino)-2,2-dimethyl-3-heptanol [(3*S*,5*S*)-**3e**]: ν 3400, 1640 cm^{-1}; δ_H 0.89 [9H, s, $(CH_3)_3C$], 0.96 (3H, t, J = 7.4, CH_3CH_2), 1.43-1.85 (4H, m, 2XCH_2), 2.84 (1H, br s, OH), 3.35 (1H, dd, J = 9.8, 1.2, CHO), 3.98-4.09 (1H, m, CHN), 6.67 (1H, d, J = 6.6, NH), 7.34-7.48 (3H, m, ArH), 7.77 (2H, dd, J = 7.5, 1.5, ArH); δ_C 10.0 (CH_3CH_2), 25.45 [$(CH_3)_3C$], 28.0 (CH_2CH_3), 35.1 (CH_2CHOH), 36.3 [$C(CH_3)_3$], 51.4 (CHN), 78.6 (CHOH), 126.8, 128.4, 131.2, 134.7 (ArC), 167.4 (C=O); m/z 234 [M$^+$-CH_3CH_2, 1%], 206 (13), 162 (12), 148 (10), 122 (21), 105 (100), 77 (42), 57 (29), 51 (10), 43 (12). Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 72.88; H, 9.61; N, 5.07.

(3R,5S)-5-(N-Benzoylamino)-2,2-dimethyl-3-heptanol [(3*R*,5*S*)-**3e**]: ν 3400, 1635 cm^{-1}; δ_H 0.89 [9H, s, $(CH_3)_3C$], 0.97 (3H, t, J = 7.5, CH_3CH_2), 1.52-1.67 (4H, m, 2XCH_2), 3.30 (1H, dd, J = 10.8, 2.4, CHO), 4.10 (1H, br s, OH), 4.16-4.23 (1H, m, CHN), 6.79 (1H, d, J = 8.8, NH), 7.34-7.49 (3H, m, ArH), 7.78 (2H, dd, J = 8.4, 1.5, ArH); δ_C 10.9 (CH_3CH_2), 25.9 [$(CH_3)_3C$], 28.0 (CH_2CH_3), 34.3 (CH_2CHOH), 36.5 [$C(CH_3)_3$], 49.2 (CHN), 75.0 (CHOH), 126.9, 128.4, 131.4, 134.15 (ArC), 168.3 (C=O); m/z 263 [M$^+$, 0.5%], 206 (28), 162 (17), 148 (14), 122 (27), 105 (100), 77 (43), 57 (21). Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 71.71; H, 9.42; N, 4.97.

(1S,3S)-3-(N-Benzoylamino)-1-phenyl-1-pentanol [(1*S*,3*S*)-**3f**]:[24] ν 3330, 1635 cm^{-1}; δ_H 0.90 (3H, t, *J* = 7.4, CH_3), 1.52-1.68 (2H, m, CH_2CH_3), 1.96 (2H, t, *J* = 6.2, CH_2CHOH), 2.80 (1H, br s, OH), 4.09 (1H, sextet, *J* = 6.2, CHN), 4.80 (1H, t, *J* = 6.2, CHOH), 6.21 (1H, d, *J* = 8.0, NH), 7.15-7.44 (8H, m, ArH), 7.65 (2H, dd, *J* = 7.9, 1.3, ArH); δ_C 10.2 (CH_3), 28.3 (CH_2CH_3), 44.1 (CH_2CHOH), 50.4 (CHN), 73.1 (CHOH), 125.7, 127.2, 127.6, 128.4, 128.5, 131.6, 134.5, 144.9 (ArC), 167.7 (C=O); m/z 177 [M$^+$-PhCHO, 9%], 162 (11), 148 (16), 105 (100), 79 (16), 77 (79), 51 (18).

(1R,3S)-3-(N-Benzoylamino)-1-phenyl-1-pentanol [(1*R*,3*S*)-**3f**]: ν 3320 , 1640 cm^{-1}; δ_H 0.96 (3H, t, *J* = 7.5, CH_3), 1.52-1.67 (3H, m, CH_2CH_3, CHHCHOH), 1.90 (1H, ddd, *J* = 14.1, 11.0, 2.9, CHHCHOH), 3.92 (1H, br s, OH), 4.23-4.30 (1H, m, CHN), 4.66 (1H, dd, *J* = 11.0, 2.4, CHOH), 6.27 (1H, d, *J* = 8.5, NH), 7.13-7.35 (5H, m, ArH), 7.36-7.49 (3H, m, ArH), 7.74 (2H, dd, *J* = 7.6, 1.5, ArH); δ_C 10.8 (CH_3), 28.2 (CH_2CH_3), 45.4 (CH_2CHOH), 49.1 (CHN), 70.1 (CHOH), 125.5, 127.0, 127.1, 128.3, 128.6, 131.7, 134.0, 144.0 (ArC), 168.6 (C=O); m/z 265 [M$^+$-H_2O, 3%], 148 (13), 122 (15), 105 (100), 104 (19), 77 (44), 51 (13). Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 75.03; H, 7.35; N, 4.70.

(S)-3-(N-tert-Butoxycarbonylamino)pentanoic Acid [(*S*)-**6g**]: ν 3500-2600, 1710, 1650 cm^{-1}; δ_H 0.93 (3H, d, *J* = 7.6, CH_3CH_2), 1.44 [9H, s, $(CH_3)_3C$], 1.52-1.64 (2H, m, CH_2CH_3), 2.48-2.58 (2H, m, CH_2CO_2), 3.76-3.88 (1H, m, CHN), 5.12 (1H, d, *J* = 8.2, NH), 10.81 (1H, br s, OH); δ_C 10.4 (CH_3CH_2), 27.3 (CH_2CH_3), 28.2 [$(CH_3)_3C$], 38.6 (CH_2CO_2), 48.8 (CHN), 79.3 [$C(CH_3)_3$], 155.6 (NC=O), 176.5 (CO_2H); m/z 188 (M$^+$-CH_3CH_2, 5%), 88 (34), 59 (35), 58 (20), 57 (100), 56 (15), 44 (17). Anal. Calcd. for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.28; H, 8.76; N, 5.27.

(S)-3-Cyclohexyl-4-(N-cyclohexylimino)-6-ethyltetrahydropyrimidin-2-one [(*S*)-**6h**]: ν 3300, 1685, 1640 cm^{-1}; δ_H 0.96 (3H, d, *J* = 7.3, CH_3), 1.12-1.84 (22H, m, 10xringCH_2, CH_2CH_3), 2.18 (1H, dd, *J* = 15.0, 9.4, CHHC=N), 2.42 (2H, dquintet, *J* = 15.0, 3.1), 2.71 (1H, dd, *J* = 15.0, 3.3, CHHC=N), 3.15-3.26 (2H, m, 2xCHN), 4.58-4.71 (1H, m, CHNH), 5.68 (1H, br s, NH); δ_C 9.8 (CH_3CH_2), 24.2, 25.7, 25.8, 26.7, 26.75, 27.95, 28.7, 29.1, 29.35, 34.1, 34.2 (CH_2), 48.3, 53.6, 56.65 (CHN), 149.5 (C=N), 156.0 (C=O); m/z 305 (M$^+$, 4%), 225 (15), 224 (100), 209 (23), 127 (12), 98 (11), 82 (16), 69 (11), 67 (10), 58 (21), 56 (21), 55 (53). Anal. Calcd. for $C_{18}H_{31}N_3O$: C, 70.78; H, 10.23; N, 13.76. Found: C, 70.01; H, 10.23; N, 12.98.

(S)-N-(1-Methylpropyl)benzamide [(*S*)-**3a**]: physical and spectroscopic data were found to be the same than for (*R*)-**3a**. Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.59; H, 8.40; N, 7.73.

(S)-N-(1-Deuteriomethylpropyl)benzamide [(*S*)-**3b**]: physical and spectroscopic data were found to be the same than for (*R*)-**3b**. Anal. Calcd. for $C_{11}H_{14}DNO$: C, 74.12; H, 9.05; N, 7.86. Found: C, 74.28; H, 8.93; N, 7.58.

(3R,5R)-5-(N-Benzoylamino)-2,2-dimethyl-3-heptanol [(3*R*,5*R*)-**3e**]: physical and spectroscopic data were found to be the same than for [(3*S*,5*S*)-**3e**]. Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 72.84; H, 9.60; N, 5.16.

(3S,5R)-5-(N-Benzoylamino)-2,2-dimethyl-3-heptanol [(3*S*,5*R*)-**3e**]: physical and spectroscopic data were found to be the same than for [(3*R*,5*S*)-**3e**]. Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 73.05; H, 9.71; N, 5.16.

(R)-Ethyl 3-(N-Benzoylamino)pentanoate [(*R*)-**3i**]: ν 3325, 1730, 1640 cm^{-1}; δ_H 0.97 (3H, t, *J* = 7.3, CH_3CH_2CH), 1.25 (3H, t, *J* = 7.0, CH_3CH_2O), 1.61-1.71 (2H, m, CH_3CH_2CH), 2.61, (1H, dd, *J* = 12.4, 5.1, $CHHCO_2$), 2.65 (1H, dd, *J* = 12.4, 5.3, $CHHCO_2$), 4.15 (2H, q, *J* = 7.0, CH_3CH_2O), 4.33-4.40 (1H,

m, CHN), 7.20 (1H, d, J = 8.1, NH), 7.37-7.50 (3H, m, ArH), 7.78 (2H, dd, J = 7.7, 1.3, ArH); δ_C 10.6 (CH_3CH_2CH), 14.1 (CH_3CH_2O), 27.15 (CH_3CH_2CH), 37.9 (CH_2CO_2), 47.8 (CHN), 60.6 (CH_2O), 126.8, 128.4, 131.25, 134.55 (ArC), 166.7 (NC=O), 172.1 (CO_2); m/z 249 [M+, 1%], 162 (12), 144 (10), 122 (24), 106 (12), 105 (100), 77 (51), 51 (20). Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 68.05; H, 7.64; N, 4.98.

(R)-Ethyl 4-(N-Benzoylamino)hexanoate [(*R*)-**3j**]: ν 3330, 1730, 1635 cm^{-1}; δ_H 0.96 (3H, t, J = 7.4, CH_3CH_2CH), 1.17 (3H, t, J = 7.0, CH_3CH_2O), 1.56-1.65 (2H, m, CH_3CH_2CH), 1.78-2.01 (2H, m, CH_2CH_2CH), 2.37-2.50 (2H, m, CH_2CO_2), 4.04 (2H, q, J = 7.0, CH_3CH_2O), 4.08-4.16 (1H, m, CHN), 6.13 (1H, d, J = 8.0, NH), 7.31-7.49 (3H, m, ArH), 7.76 (2H, dd, J = 7.2, 1.8, ArH); δ_C 10.2 (CH_3CH_2CH), 14.1 (CH_3CH_2O), 28.3 (CH_3CH_2CH), 29.2 ($CH_2CH_2CO_2$), 31.15 (CH_2CO_2), 51.2 (CHN), 60.6 (CH_2O), 126.8, 128.5, 131.4, 134.5 (ArC), 167.2 (NC=O), 174.2 (CO_2); m/z 234 [M+-CH_3CH_2, 5%], 122 (10), 112 (15), 105 (100), 77 (39), 51 (12). Anal. Calcd. for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.03; N, 5.32. Found: C, 68.51; H, 8.06; N, 5.22.

(R)-3-(N-tert-Butoxycarbonylamino)pentanoic Acid [(*R*)-**6g**]: physical and spectroscopic data were found to be the same than for [(*S*)-**6g**]. Anal. Calcd. for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.81; N, 6.45. Found: C, 55.19; H, 8.76; N, 6.02.

(R)-3-Cyclohexyl-4-(N-cyclohexylimino)-6-ethyltetrahydropyrimidin-2-one [(*R*)-**6h**]: physical and spectroscopic data were found to be the same than for [(*S*)-**6h**]. Anal. Calcd. for $C_{18}H_{31}N_3O$: C, 70.78; H, 10.23; N, 13.76. Found: C, 70.44; H, 10.29; N, 13.33.

(R)-3-(N-tret-Butoxycarbonylamino)-4-methylpentanoic Acid [(*R*)-**9g**]: ν 3450-2500, 1715, 1640 cm^{-1}; δ_H 0.92 [6H, d, J = 6.7, $(CH_3)_2CH$], 1.43 [9H, s, $(CH_3)_3C$], 1.77-1.88 [1H, m, $CHC(H_3)_2$], 2.46-2.57 (2H, m, CH_2), 3.70-3.81 (1H, m, CHN), 5.03 (1H, d, J = 8.0, NH), 10.53 (1H, br s, OH); δ_C 18.4, 19.2 [$(CH_3)_2CH$)], 28.3 [$(CH_3)_3C$], 31.6 [$CH(CH_3)_2$], 37.0 (CH_2), 52.8 (CHN), 79.3 [$C(CH_3)_3$], 155.7 (NC=O), 176.8 (CO_2H); m/z 188 [M+-$(CH_3)_2CH$, 6%], 132 (15), 88 (56), 70 (10), 59 (20), 57 (100), 56 (14), 44 (22). Anal. Calcd. for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.05. Found: C, 57.43; H, 9.64; N, 5.76.

(R)-3-Cyclohexyl-4-(N-cyclohexylimino)-6-isopropyltetrahydropyrimidin-2-one [(*R*)-**9h**]: ν 3320, 1690, 1645 cm^{-1}; δ_H 0.94, 0.96 [6H, 2 d, J = 6.2, $(CH_3)_2CH$], 1.12-1.75 (18H, m, 9xringCH_2), 2.26 (1H, dd, J = 15.0, 9.5, CHHC=N), 2.42 [2H, dquintet, J = 12.2, 3.4, CHHN(CO)CHH], 2.65 (1H, dd, J = 15.0, 4.3, CHHC=N), 3.01-3.09, 3.20-3.28 (2H, 2 m, CHN=C, CHNH), 4.67 (1H, tt, J = 12.0, 3.6, CHNCO), 5.78 (1H, br s, NH); δ_C 17.9, 18.2 [$(CH_3)_2CH$)], 24.2, 25.7, 25.8, 26.1, 26.65, 26.7, 29.1, 29.3, (CH_2), 31.7 [$CH(CH_3)_2$], 34.1, 34.2 (CH_2), 52.4, 53.4, 56.6 (CHN), 149.6 (C=N), 156.1 (C=O); m/z 319 (M+, 3%), 238 (100), 223 (23), 194 (16), 156 (27), 141 (12), 98 (14), 96(11), 81 (15), 72 (15), 69 (29), 55 (62). Anal. Calcd. for $C_{19}H_{33}N_3O$: C, 71.43; H, 10.41; N, 13.15. Found: C, 70.81; H, 10.35; N, 12.93.

(S)-N-(1-Phenylethyl)benzamide [(*S*)-**12a**];[25] ν 3305, 1630 cm^{-1}; δ_H 1.53 (3H, d, J = 6.9, CH_3), 5.28 (1H, quintet, J = 6.9, CHN), 6.93 (1H, br s, NH), 7.21-7.45 (8H, m, ArH), 7.75 (2H, dd, J = 8.3, 1.2, ArH); δ_C 21.6 (CH_3), 49.05 (CHN), 126.1, 126.9, 127.1, 128.2, 128.4, 131.2, 134.4, 143.2 (ArC), 166.6 (C=O); m/z 225 [M+, 29%] 105 (100), 104 (22), 78 (10), 77 (77), 51 (25).

(R)-N-(1-Methyl-2-phenylethyl)benzamide [(*R*)-**15a**]: ν 3310, 1625 cm^{-1}; δ_H 1.20 (3H, d, J = 6.6, CH_3), 2.83 (1H, dd, J = 13.5, 7.0, CHHAr), 2.94 (1H, dd, J = 13, 5.7, CHHAr), 4.46 (1H, quintet, J = 6.6, CHN), 6.07 (1H, d, J = 7.0, NH), 7.19-7.48 (8H, m, ArH), 7.67 (2H, dd, J = 7.8, 1.2, ArH); δ_C 19.9 (CH_3), 42.3 (CH_2Ar), 46.4 (CHN), 126.45, 126.7, 128.3, 128.4, 129.5, 131.2, 134.8, 137.8 (ArC), 166.7 (C=O); m/z

239 [M+, 2%], 149 (10), 148 (30), 105 (100), 91 (15), 77 (39).

*(S)-3-(*N*-tert-Butoxycarbonylamino)-3-phenylpropanoic Acid* [(*S*)-**18g**]: ν 3400-2500, 1720, 1635 cm^{-1}; δ_H 1.40 [9H, s, $(CH_3)_3C$], 2.79-2.83 (2H, m, CH_2), 5.06-5.12 (1H, m, CHN), 5.45 (1H, br s, NH), 7.22-7.35 (5H, m, ArH), 8.36 (1H, br s, OH); δ_C 28.2 [$(CH_3)_3C$], 41.7 (CH_2), 58.3 (CHN), 80.1 [$C(CH_3)_3$], 126.1, 127.5, 128.6, 138.9 (ArC), 155.8 (NC=O), 177.1 (CO_2H); m/z 209 [M^+-CH_2=$C(CH_3)_2$, 13%], 163 (23), 150 (17), 107 (14), 106 (41), 104 (23), 77 (18), 59 (17), 57 (80), 56 (41), 44 (100). Anal. Calcd. for $C_{14}H_{19}NO_4$: C, 62.90; H, 7.91; N, 5.24. Found: C, 63.49; H, 7.44; N, 4.97.

*(S)-3-Cyclohexyl-4-(*N*-cyclohexylimino)-6-phenyltetrahydropyrimidin-2-one* [(*S*)-**18h**]: ν 3300, 1685, 1640 cm^{-1} (C=O); δ_H 1.10-1.81 (18H, m, 9xringCH_2), 2.36-2.54 (3H, m, C*H*HNC*H*H, C*H*HC=N), 2.94 (1H, dd, *J* = 13.4, 4.0, CH*H*C=N), 3.10-3.17 (1H, m, CHN), 4.47 (1H, dd, *J* = 10.2, 4.0, C*H*NH), 4.79 (1H, tt, *J* = 12.2, 3.6, CHNC=N), 5.32 (1H, br s, NH), 7.30-7.48 (5H, m, ArH); δ_C 24.2, 24.3, 25.7, 25.8, 26.75, 26.8, 29.2, 29.4, 32.2, 33.9, 34.25 (CH_2), 51.9, 54.0, 56.8 (CHN), 126.11, 128.4, 129.0, 139.1 (ArC), 148.6 (C=N), 155.9 (C=O); m/z 353 (M^+, 5%), 272 (100), 257 (13), 190 (15), 132 (18), 130 (15), 106 (30), 104 (13), 98 (15), 85 (15), 67 (15), 55 (50), 41 (45). Anal. Calcd. for $C_{22}H_{31}N_3O$: C, 74.75; H, 8.84; N, 11.89. Found: C, 74.60; H, 8.83; N, 11.64.

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