Synthesis of Optically Active Amides from β-Furyl and β-Phenyl Esters by way of Enzymatic Aminolysis

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Candida antarctica lipase efficiently catalyses the aminolysis of non-activated esters with a β-furyl or β-phenyl group; use of racemic amines gives the corresponding optically active amides with high enantiomeric excess.

The synthesis of optically active amides is an area of growing interest in synthetic organic chemistry,[1] since naturally occurring compounds containing an amide bond frequently show biological activity. Since the discovery that enzymes can be active in organic solvents, lipases have been widely used for the synthesis of chiral organic compounds.[2] We have reported that this methodology is of a great synthetic utility for the preparation of chiral amides, a variety of optically active amides being accessible by way of enzymatic aminolysis.[3]

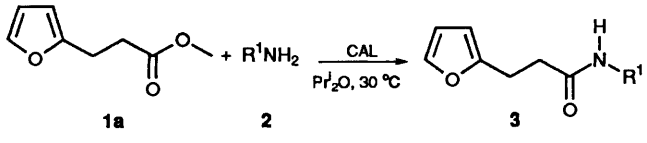
As a part of our program for the preparation of chiral nitrogen organic compounds using lipases, we have considered of interest the synthesis of amides from furfural esters derivatives. Furfural is a product that is isolated from the biomass and can easily be transformed into α,β ethylenic esters by way of a Wittig–Horner reaction.[4] The reduction with magnesium–methanol yields the corresponding saturated esters.[5]

We report here the results of a study of the enzymatic aminolysis of such furfural derived esters together with those for the corresponding cinnamic and 3-phenylpropionic esters with several racemic amines in the presence of a lipase catalyst.

Results and discussion

Initially, we investigated several lipases, porcine pancreatic lipase, *Candida cylindracea* lipase, *Pseudomonas cepacia* lipase, *Candida antarctica* lipase (CAL, SP 435 L) and the protease subtilisin for their effectiveness in the preparation of amides from esters **1** and **6** with butylamine and α-methylbenzylamine. Only CAL showed efficient catalytic activity in this aminolysis. The effect of the solvent was also considered and diisopropyl ether was found to be the most efficient, giving high enantiomeric excesses and good conversions.

The ester **1a** reacted with non-racemic amines **2** at room temperature in the presence of CAL to give the amides **3** in high yield (Scheme 1). Although enzymatic aminolysis with aromatic amines and non-activated esters is known to be a difficult reaction,[6] compound **1a** reacted with aromatic amines and CAL to yield the amides **3** in excellent yield; a summary of the results obtained is given in Table 1.

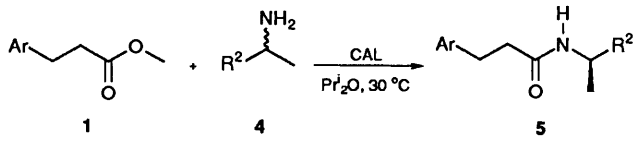


a R^1 = Allyl
b R^1 = Bu
c R^1 = $PhCH_2$
d R^1 = Ph
e R^1 = *p*-MeC_6H_4
f R^1 = *p*-$MeOC_6H_4$

Scheme 1

Conventional preparation of the amides **3**, *e.g.* with aluminium trichloride,[7] gave much lower yields than those obtained through enzymatic aminolysis, *e.g.* the reaction of **1a** with benzylamine in the presence of $AlCl_3$ gives **3c** in a yield < 20% together with side products. Thus, we believe that our enzymatic procedure could be the method of choice for preparing amides of the kind described here.

From the results shown in Table 2 for the reaction of **1a** with racemic amines it can be seen that high enantiomeric excesses were achieved, in all cases, *R* amides being obtained. Similar results were achieved with 3-phenylpropionic ester **1b**, few differences being noted for the two esters (Scheme 2).

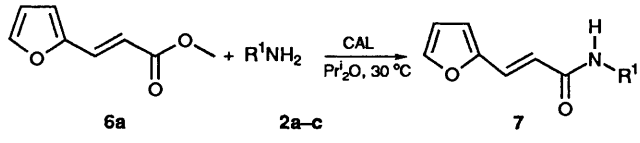


a Ar = 2-Furyl
b Ar = Ph

Scheme 2

The enantioselectivity achieved with CAL in the present work is similar to that observed in the aminolysis of acrylic esters,[8] where high selectivity towards the *R* amide was observed; this contrasts with the selectivity shown by subtilisin in the reaction of 2,2,2-trifluoroethyl butyrate with racemic amines.[9]

The generality of the process with CAL was assessed by studying the reaction of α,β-ethylenic esters from furfural with the non-racemic amines **2a–c** (Scheme 3). The influence of the unsaturation in the ester **6a**, is noteworthy, since its effect was to increase the reaction time to 5 days (*cf.* Table 1: 4 h for **1a–3a**). Further, Michael adduct formation was observed.



Scheme 3

Optically active amides **8** from **6a** were obtained with racemic amines, the *R* isomer of the amine being preferentially formed. Similar results were also achieved with methyl cinnamic ester (see Table 3).

In conclusion, CAL catalysed amidation of furfural and

Table 1 Reaction of methyl-3-furylpropanoate **1a** and methyl 3-furylpropenoate **6a**, with amines **2**

	Entry	R^1	*t*/h	Yield (%)	Entry	R^1	*t*/days	Yield (%)
	3a	Allyl	4	91	**7a**	Allyl	5	87
	3b	Bu	4.5	83	**7b**	Bu	5	86
	3c	$PhCH_2$	5	87	**7c**	$PhCH_2$	6	79
	3d	Ph	38	77				
	3e	*p*-MeC_6H_4	24	83				
	3f	*p*-$MeOC_6H_4$	72	74				

Table 2 Amidation of methyl 3-arylpropanoates **1** with racemic amines **4**

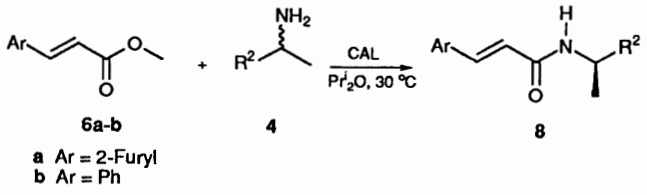
Entry	Ar	R^2	*t*/h	Yield (%)	e.e. (%)*
5a	2-Furyl	Et	7.5	81	63
5b	2-Furyl	Pentyl	10	79	79
5c	2-Furyl	Ph	8	83	>95
5d	Ph	Et	9	77	68
5e	Ph	Pentyl	13	79	>95
5f	Ph	Ph	10	84	>95

* In all cases the configuration of the amide was *R*.

Table 3 Amidation of methyl 3-arylpropenoates **6** with racemic amines **4**

Entry	Ar	R^2	*t*/days	Yield (%)	e.e. (%)*
8a	2-Furyl	Et	8	72	63
8b	2-Furyl	Pentyl	10	78	84
8c	2-Furyl	Et	8	79	>95
8d	Ph	Et	9	71	70
8e	Ph	Pentyl	12	75	83
8f	Ph	Ph	10	78	>95

* In all cases the configuration of the amide was *R*.



Scheme 4

cinnamic esters derivatives allows the preparation of optically active amides in high enantiomeric excess.

Experimental

Porcine pancreatic (Type II crude) and *Candida cylindracea* (Type VII crude) lipases were purchased from Sigma Chemical Co. and *Pseudomonas cepacia* from Amano Pharmaceutical Co. *Candida antarctica* lipase, SP 435 L, was a gift from Novo Nordisk Co. All reagents were of commercial quality and purchased from Aldrich Chemie. Solvents were distilled over an adequate desiccant and stored under argon. For column chromatography, Merck silica gel 60/230–400 mesh was used. Melting points were taken using a Gallenkamp apparatus and are uncorrected. Optical rotations were measured using a Perkin-Elmer 241 polarimeter and are quoted in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded on a Perkin-Elmer 1720-X FT Infrared spectrophotometer. ^1H and ^{13}C NMR were obtained with TMS (tetramethylsilane) as internal standard; using a Bruker AC-300 (^1H- 300 MHz and ^{13}C- 75.5 MHz) spectrometer. Mass spectra were recorded on a Hewlett-Packard 5987 A spectrometer. Microanalyses were performed on a Perkin-Elmer 240B elemental analyzer. Compound yields have been calculated on the basis of percentage conversion.

Configurations of the amides **5** and **8** were assigned by comparison of the optical rotations of the latter with those of authentic amides obtained from esters and the corresponding e.e.s were calculated by ^1H NMR spectroscopy using the chiral shift reagent tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate]europium(III).

Reaction of the Esters **1** *and* **6** *with the Amines in Diisopropyl Ether catalysed by CAL: General Procedure.*—CAL (0.25 g) was added to a solution of the ester (2.5 mmol) and amine (5 mmol) in diisopropyl ether. The suspension was stirred at 30 °C. When the reaction was complete, the enzyme was filtered off and washed with chloroform. The combined organic filtrate and workings were evaporated and flash chromatography on silica of the residue, yielded the corresponding amide.

N-*Allyl*-3-(2-*furyl*)*propanamide* **3a**. Yield, 91%; m.p. 42–44 °C (Found: C, 67.1; H, 7.3; N, 7.8; O, 17.9. $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.32; N, 7.82; O, 17.86%); ν_{max}(KBr)/cm^{-1} 1641 (C=O); δ_H($CDCl_3$) 2.54 (t, 2 H, CH_2), 2.97 (t, 2 H, CH_2), 3.85 (m. 2 H, CH_2NH), 5.03–5.19 (m, 2 H, CH_2=CH), 5.79 (m, 1 H, CH_2=CH), 6.01 (d, 1 H, CH_{furyl}), 6.27 (m, 1 H, CH_{furyl}), 6.54 (br s, 1 H, NH) and 7.29 (d, 1 H, CH_{furyl}); δ_C($CDCl_3$) 23.8 (CH_2), 34.5 (CH_2), 41.7 (CH_2), 105.1 (CH_{furyl}), 110.0 (CH_{furyl}), 115.8 (CH_{2olef}), 134.0 (CH_{olef}), 140.9 (CH_{furyl}), 154.3 (C_{furyl}) and 171.7 (C=O); *m*/*z* 171 (M^+, 47%) and 81 (100).

N-*Butyl*-3-(2-*furyl*)*propanamide* **3b**. Yield, 83%; m.p. 35–37 °C (Found: C, 68.4; H, 7.8; N, 7.3; O, 16.6. $C_{11}H_{17}NO_2$ requires C, 68.35; H, 7.83; H, 7.25; O, 16.57%); ν_{max}(KBr)/cm^{-1} 1643 (C=O); δ_H($CDCl_3$) 0.91 (t, 3 H, CH_3), 1.18–1.53 (m, 4 H, $2CH_2$), 2.51 (t, 2 H, CH_2), 2.97 (t, 2 H, CH_2), 3.21 (q, 2H, CH_2NH), 6.01 (d, 1 H, CH_{furyl}), 6.26 (m, 1 H, CH_{furyl}), 6.37 (br s, 1 H, NH) and 7.29 (d, 1 H, CH_{furyl}); δ_C($CDCl_3$) 13.6 (CH_3), 19.8 (CH_2), 24.0 (CH_2), 31.4 (CH_2), 34.8 (CH_2), 39.1 (CH_2), 105.2 (CH_{furyl}), 110.1 (CH_{furyl}), 140.9 (CH_{furyl}), 154.3 (C_{furyl}) and 171.7 (C=O); *m*/*z* 195 (M^+, 47.3%) and 81 (100).

N-*Benzyl*-3-(2-*furyl*)*propanamide* **3c**. Yield, 87%; m.p. 71–73 °C (Found: C, 73.3; H, 6.6; N, 6.2; O, 14.0. $C_{14}H_{15}NO_2$ requires C, 73.33; H, 6.6; N, 6.11; O, 13.96%); ν_{max}(KBr)/cm^{-1} 1639 (C=O); δ_H($CDCl_3$) 2.54 (t, 2 H, CH_2), 2.99 (t, 2 H, CH_2), 4.38 (d, 2 H, CH_2NH), 5.87 (br s, 1 H, NH), 6.01 (d, 1 H, CH_{furyl}), 6.26 (m, 1 H, CH_{furyl}) and 7.11–7.39 (m, 6 H, CH_{furyl}, $5CH_{arom}$); δ_C($CDCl_3$) 24.0 (CH_2), 34.9 (CH_2) 43.5 (CH_2), 105.5 (CH_{furyl}), 110.2 (CH_{furyl}), 127.4 (CH_{arom}), 127.7 (CH_{arom}), 128.6 (CH_{arom}), 138.1 (C_{arom}), 141.1 (CH_{furyl}), 154.3 (C_{furyl}) and 171.6 (C=O); *m*/*z* 229 (M^+, 73%) and 91 (100).

N-*Phenyl*-3-(2-*furyl*)*propanamide* **3d**. Yield, 77%; m.p. 91–93 °C (Found: C, 73.0; H, 6.1; N, 6.1; O, 14.9. $C_{13}H_{13}NO_2$ requires C, 72.53; H, 6.09; N, 6.51; O, 14.87%); ν_{max}(KBr)/cm^{-1} 1662 (C=O); δ_H($CDCl_3$) 2.66 (t, 2 H, CH_2), 3.03 (t, 2 H, CH_2), 6.01 (d, 1 H, CH_{furyl}), 6.27 (m, 1 H, CH_{furyl}), 7.07 (t, 1 H, CH_{arom}), 7.18–7.32 (m, 3 H, $2CH_{arom}$, CH_{furyl}), 7.47 (d, 2 H, $2CH_{arom}$), 7.78 (br s, 1 H, NH); δ_C($CDCl_3$) 23.8 (CH_2), 35.8 (CH_2), 105.6 (CH_{furyl}), 110.3 (CH_{furyl}), 120.1 (CH_{arom}), 124.3 (CH_{arom}), 128.8

(CH_{arom}), 137.8 (C_{arom}), 141.2 (CH_{furyl}), 154.1 (C_{furyl}) and 170.3 (C=O); *m/z* 215 (M^+, 26%) and 93 (100).

N-p-*Tolyl*-3-(2-*furyl*)*propanamide* **3e**. Yield, 83%; m.p. 117–119 °C (Found: 73.4; H, 6.7; N, 6.1; O, 14.0. $C_{14}H_{15}NO_2$ requires C, 73.33; H, 6.6; N, 6.11; O, 13.96%); ν_{max}(KBr)/cm^{-1} 1656 (C=O); δ_H($CDCl_3$) 2.30 (s, 3 H, CH_3) 2.65 (t, 2 H, CH_2), 3.04 (t, 2 H, CH_2), 6.05 (d, 1 H, CH_{furyl}), 6.27 (m, 1 H, CH_{furyl}), 7.09 (d, 2 H, $2CH_{arom}$), 7.28–7.47 (m, 3 H, $2CH_{arom}$, CH_{furyl}) and 7.46 (br s, 1 H, NH); δ_C($CDCl_3$) 20.8 (CH_3), 23.9 (CH_2), 35.8 (CH_2), 105.6 (CH_{furyl}), 110.3 (CH_{furyl}), 120.1 (CH_{arom}), 129.4 (CH_{arom}), 133.9 (C_{arom}), 135.2 (C_{arom}), 141.2 (CH_{furyl}), 154.2 (C_{furyl}) and 169.9 (C=O); *m/z* 229 (M^+, 16%) and 107 (100).

N-p-*Methoxyphenyl*-3-(2-*furyl*)*propanamide* **3f**. Yield, 74%; m.p. 121–123 °C (Found: C, 69.0; H, 6.2; N, 5.8; O, 19.7. $C_{14}H_{15}NO_3$ requires C, 68.54; H, 6.17; N, 5.71; O, 19.58%); ν_{max}(KBr)/cm^{-1} 1645 (C=O); δ_H($CDCl_3$) 2.64 (t, 2 H, CH_2), 3.03 (t, 2 H, CH_2), 3.76 (s, 3 H, CH_3), 6.05 (d, 1 H, CH_{furyl}), 6.28 (m, 1 H, CH_{furyl}), 6.81 (d, 2 H, $2CH_{arom}$), 7.27–7.48 (m, 3 H, $2CH_{arom}$, CH_{furyl}) and 7.57 (br s, 1 H, NH); δ_C($CDCl_3$) 23.8 (CH_2), 35.4 (CH_2), 55.3 (CH_3), 105.5 (CH_{furyl}), 110.2 (CH_{furyl}), 113.9 (CH_{arom}), 122.0 (CH_{arom}), 130.8 (C_{arom}), 141.1 (C_{furyl}), 154.1 (C_{furyl}), 156.2 (C_{arom}) and 170.2 (C=O); *m/z* 245 (M^+, 17%) and 122 (100).

N-*Allyl*-3-(2-*furyl*)*propenamide* **7a**. Yield, 87%; m.p. 67–69 °C (Found: C, 67.8; H, 6.3; N, 8.0; O, 18.1. $C_{10}H_{11}NO_2$ requires C, 67.77; H, 6.26; N, 7.91; O, 18.07%); ν_{max}(KBr)/cm^{-1} 1614 (C=O); δ_H($CDCl_3$) 3.99 (m, 2 H, CH_2NH), 5.06–5.26 (m, 2 H, CH_2=CH), 5.88 (m, CH, CH_2=CH), 6.13 (br s, 1 H, NH), 6.41 (d, 1 H, CH_{olef}), 6.44 (m, 1 H, CH_{furyl}), 6.49 (d, 1 H, CH_{furyl}), 7.40 (d, 1 H, CH_{furyl}) and 7.42 (d, 1 H, CH_{olef}); δ_C($CDCl_3$) 42.1 (CH_2), 112.0 (CH_{olef}), 113.6 (CH_{furyl}), 116.3 (CH_{2olef}), 118.3 (CH_{furyl}) 127.8 (CH_{olef}), 134.1 (CH_{furyl}), 143.8 (CH_{furyl}), 151.2 (C_{furyl}) and 165.9 (C=O); *m/z* 177 (M^+, 14%) and 121 (100).

N-*Butyl*-3-(2-*furyl*)*propenamide* **7b**. Yield, 86%; m.p. 51–53 °C (Found: C, 68.4; H, 7.8; N, 7.3; O, 16.6. $C_{11}H_{15}NO_2$ requires C, 68.35; H, 7.83; H, 7.25; O, 16.57%); ν_{max}(KBr)/cm^{-1} 1614 (C=O); δ_H($CDCl_3$) 0.91 (t, 3 H, CH_3), 1.20–1.66 (m, 4 H, $2CH_2$), 3.37 (q, 2 H, CH_2NH), 6.02 (br s, 1 H, NH), 6.36 (d, 1 H, CH_{olef}), 6.44 (m, 1 H, CH_{furyl}), 6.52 (d, 1 H, CH_{furyl}), 7.40 (d, 1 H, CH_{furyl}), 7.42 (d, 1 H, CH_{olef}); δ_C($CDCl_3$) 13.7 (CH_3), 20.1 (CH_2), 31.7 (CH_2), 39.4 (CH_2), 112.0 (CH_{olef}), 113.5 (CH_{furyl}), 118.6 (CH_{furyl}), 127.6 (CH_{olef}), 143.8 (CH_{furyl}) 151.3 (C_{furyl}) and 165.9 (C=O); *m/z* 193 (M^+, 16.4) and 121 (100).

N-*Benzyl*-3-(2-*furyl*)*propenamide* **7c**. Yield, 79%; m.p. 141–143 °C (Found: C, 74.0; H, 5.8; N, 6.8; O, 14.1. $C_{14}H_{13}NO_2$ requires C, 73.98; H, 5.77; N, 6.17; O, 14.09%); ν_{max}(KBr)/cm^{-1} 1614 (C=O); δ_H($CDCl_3$) 4.49 (d, 2 H, CH_2NH), 6.29–6.62 (m, 4 H, CH_{olef}, $2CH_{furyl}$, NH), 7.13–7.48 (m, 7 H, CH_{furyl}, $5CH_{arom}$, CH_{olef}); δ_C($CDCl_3$) 43.5 (CH_2), 111.8 (CH_{olef}), 113.5 (CH_{furyl}), 118.1 (CH_{furyl}), 127.2 (CH_{olef}), 127.5 (CH_{arom}), 127.8 (CH_{arom}), 128.4 (CH_{arom}), 138.0 (C_{arom}), 143.7 (CH_{furyl}), 151.0 (C_{furyl}) and 165.7 (C=O); *m/z* 227 (M^+, 30%) and 121 (100).

(R)-(−)-N-(1-*Methylpropyl*)-3-(2-*furyl*)*propanamide* (*R*)-(−)-**5a**. Yield, 81%; m.p. 44–46 °C; $[\alpha]_D^{22}$ −6.7 (*c*, 0.92), e.e. 63% (Found: C, 67.6; H, 8.8; N, 7.2; O, 16.4. $C_{11}H_{17}NO_2$ requires C, 67.65; H, 8.78; N, 7.18; O, 16.39%); ν_{max}(KBr)/cm^{-1} 1643 (C=O); δ_H($CDCl_3$) 0.86 (t, 3 H, CH_3), 1.07 (d, 3 H, CH_3), 1.41 (m, 2 H, CH_2), 2.48 (t, 2 H, CH_2), 2.97 (t, 2 H, CH_2), 3.88 (m, 1 H, CHNH), 5.62 (d, 1 H, NH), 6.01 (d, 1 H, CH_{furyl}), 6.25 (m, 1 H, CH_{furyl}) and 7.28 (d, 1 H, CH_{furyl}); δ_C($CDCl_3$) 10.1 (CH_3), 20.1 (CH_3), 24.0 (CH_2), 29.3 (CH_2), 34.8 (CH_2), 46.2 (CH), 105.1 (CH_{furyl}), 109.9 (CH_{furyl}), 140.8 (CH_{furyl}), 154.3 (C_{furyl}) and 170.9 (C=O); *m/z* 195 (M^+, 49.8%) and 81 (100).

(R)-(−)-N-(1-*Methylhexyl*)-3-(2-*furyl*)*propanamide* (*R*)-(−)-**5b**. Yield, 79%; m.p. 69–71 °C; $[\alpha]_D^{22}$ −1.5 (*c*. 0.90), e.e. 79% (Found: C, 67.6; H, 9.8; N, 6.0; O, 13.5. $C_{14}H_{23}NO_2$ requires C, 70.83; H, 9.77; N, 5.9; O, 13.49); ν_{max}(KBr)/cm^{-1} 1639 (C=O); δ_H($CDCl_3$) 0.86 (t, 3 H, CH_3), 1.07 (d, 3 H, CH_3), 1.17–1.45 (m, 8 H, 4 CH_2), 2.47 (t, 2 H, CH_2), 2.97 (t, 2 H, CH_2), 3.94 (m, 1 H, CHNH), 5.54 (d, 1 H, NH), 6.01 (d, 1 H, CH_{furyl}), 6.26 (m, 1 H, CH_{furyl}) and 7.29 (d, 1 H, CH_{furyl}); δ_C($CDCl_3$) 13.8 (CH_3), 20.7 (CH_3), 22.4 (CH_2), 24.1 (CH_2), 25.5 (CH_2), 31.5 (CH_2), 35.0 (CH_2), 36.6 (CH_2), 45.0 (CH), 105.3 (CH_{furyl}), 110.1 (CH_{furyl}), 140.9 (CH_{furyl}), 154.3 (C_{furyl}) and 170.8 (C=O); *m/z* 237 (M^+, 66.5%) and 81 (100).

(R)-(+)-N-(1-*Methylphenyl*)-3-(2-*furyl*)*propanamide* (*R*)-(+)-**5c**. Yield, 83%; m.p. 62–64; $[\alpha]_D^{22}$ +70.8 (*c*, 1) e.e. >95% (Found: C, 74.0; H, 7.0; N, 5.8; O, 13.2. $C_{15}H_{17}NO_2$ requires C, 74.05; H, 7.04; N, 5.76; O, 13.16%); ν_{max}(KBr)/cm^{-1} 1639 (C=O); δ_H($CDCl_3$) 1.39 (d, 3 H, CH_3) 2.47 (t, 2 H, CH_2), 2.92 (t, 2 H, CH_2), 5.07 (m, 1 H, CHNH), 5.54 (d, 1 H, NH), 5.95 (d, 1 H, CH_{furyl}), 6.24 (m, 1 H, CH_{furyl}) and 7.13–7.35 (m, 6 H, 5 CH_{arom}, CH_{furyl}); δ_C($CDCl_3$) 21.4 (CH_3), 23.7 (CH_2), 34.2 (CH_2), 48.2 (CH), 105.0 (CH_{furyl}), 109.8 (CH_{furyl}), 125.7 (CH_{arom}), 126.6 (CH_{arom}), 128.0 (CH_{arom}), 140.6 (CH_{furyl}), 143.2 (C_{arom}) 154.2 (C_{furyl}) and 170.8 (C=O); *m/z* 243 (M^+, 26.4%) and 105 (100).

(R)-(−)-N-(1-*Methylpropyl*)-3-*phenylpropanamide* (*R*)-(−)-**5d**. Yield, 77%; m.p. 51–53 °C; $[\alpha]_D^{22}$ −7.2 (*c*, 0.98), e.e. 68% (Found: C, 76.1; H, 9.3; N, 6.8; O, 7.8. $C_{13}H_{19}NO$ requires C, 76.04; H, 9.33; N, 6.83; O, 7.8%); ν_{max}(KBr)/cm^{-1} 1641 (C=O); δ_H($CDCl_3$) 0.85 (t, 3 H, CH_3), 1.07 (d, 3 H, CH_3), 1.40 (m, 2 H, CH_2), 2.47 (t, 2 H, CH_2), 2.99 (t, 2 H, CH_2), 3.91 (m, 1 H, CHNH), 5.20 (br, s, 1 H, NH) and 7.15–7.39 (m, 5 H, CH_{arom}); δ_C($CDCl_3$) 10.2 (CH_3), 20.3 (CH_3), 29.5 (CH_2), 31.8 (CH_2), 38.7 (CH_2), 46.4 (CH), 126.1 (CH_{arom}), 128.3 (CH_{arom}), 128.4 (CH_{arom}), 140.8 (C_{arom}) and 171.3 (C=O); *m/z* 205 (M^+, 99.1%) and 91 (100).

(R)-(−)-N-(1-*Methylhexyl*)-3-*phenylpropanamide* (*R*)-(−)-**5e**. Yield, 79%; m.p. 71–73 °C; $[\alpha]_D^{22}$ −7.6 (*c*, 0.94), e.e. >95% (Found: C, 77.7; H, 10.2; N, 5.6; O, 6.5. $C_{16}H_{25}NO$ requires C, 77.67; H, 10.19; N, 5.66; O, 6.47); ν_{max}(KBr)/cm^{-1} 1639 (C=O); δ_H($CDCl_3$) 0.88 (t, 3 H, CH_3), 1.05 (d, 3 H, CH_3), 1.13–1.41 (m, 8 H, 4 CH_2), 2.43 (t, 2 H, CH_2), 2.94 (t, 2 H, CH_2), 3.92 (m, 1 H, CHNH), 5.27 (d, 1 H, NH) and 7.12–7.33 (m, 5 H, CH_{arom}); δ_C($CDCl_3$) 14.0 (CH_3), 20.9 (CH_3), 22.5 (CH_2), 25.5 (CH_2), 31.6 (CH_2), 31.8 (CH_2), 36.7 (CH_2), 38.7 (CH_2), 45.1 (CH), 126.1 (CH_{arom}), 128.3 (CH_{arom}), 128.4 (CH_{arom}), 140.8 (C_{arom}) and 171.2 (C=O); *m/z* 247 (M^+, 59.1%) and 44 (100).

(R)-(+)-N-(1-*Methylphenyl*)-3-*phenylpropanamide* (*R*)-(+)-**5f**. Yield, 84%; m.p. 92–94; $[\alpha]_D^{22}$ +56.5 (*c*, 1), e.e. >95% (Found: C, 80.6; H, 7.6; N, 5.5; O, 6.3. $C_{17}H_{19}NO$ requires C, 80.6; H, 7.56; N, 5.53; O, 6.32); ν_{max}(KBr)/cm^{-1} 1639 (C=O); δ_H($CDCl_3$) 1.40 (d, 3 H, CH_3) 2.47 (t, 2 H, CH_2), 2.97 (t, 2 H, CH_2), 5.10 (m, 1 H, CHNH), 5.66 (d, 1 H, NH) and 7.11–7.39 (m, 10 H, 10 CH_{arom}); δ_C($CDCl_3$) 21.5 (CH_3) 31.5 (CH_2), 38.1 (CH_2), 48.3 (CH), 125.9 (CH_{arom}) 126.9 (CH_{arom}) 128.2 (CH_{arom}),128.3 (CH_{arom}), 140.6 (C_{arom}), 143.1 (C_{arom}) and 171.1 (C=O); *m/z* 253 (M^+, 65.0%) and 105 (100).

(R)-(−)-N-(1-*Methylpropyl*)-3-(2-*furyl*)*propenamide* (*R*)-(−)-**8a**. Yield, 72%; m.p. 90–92 °C; $[\alpha]_D^{22}$ −19.4 (*c*, 0.80), e.e. 63% (Found: C, 68.4; H, 7.8; N, 7.3; O, 16.6. $C_{11}H_{15}NO_2$ requires C, 68.35; H, 7.83; N, 7.25; O, 16.57%); ν_{max}(KBr)/cm^{-1} 1615 (C=O); δ_H($CDCl_3$) 0.91 (t, 3 H, CH_3), 1.17 (d, 3 H, CH_3), 1.51 (m, 2 H, CH_2), 4.05 (m, 1 H, CHNH), 5.60 (br s, 1 H, NH), 6.31 (d, 1 H, CH_{olef}), 6.35 (m, 1 H, CH_{furyl}), 6.44 (d, 1 H, CH_{furyl}), 7.40 (d, 1 H, CH_{furyl}) and 7.41 (d, 1 H, CH_{olef}); δ_C($CDCl_3$) 10.1 (CH_3), 20.0 (CH_3), 29.2 (CH_2), 46.5 (CH), 111.6 (CH_{furyl}), 112.8 (CH_{olef}), 119.1 (CH_{furyl}), 126.8 (CH_{olef}) 143.4 (CH_{furyl}), 151.0 (C_{furyl}) and 165.5 (C=O); *m/z* 193 (M^+, 15.4%) and 121 (100).

(R)-(−)-N-(1-*Methylhexyl*)-3-(2-*furyl*)*propenamide* (*R*)-(−)-**8b**. Yield, 78%; m.p. 101–103 °C; $[\alpha]_D^{22}$ −32.5 (*c*, 0.70), e.e. 84% (Found: C, 71.4; H, 9.0; N, 6.0; O, 13.6. $C_{14}H_{21}NO_2$ requires C, 71.44; H, 9.0; N, 5.95; O, 13.6); ν_{max}(KBr)/cm^{-1} 1618 (C=O); δ_H($CDCl_3$) 0.87 (t, 3 H, CH_3), 1.17 (d, 3 H, CH_3), 1.21–1.55 (m,

8 H, 4 CH_2), 4.10 (m, 1 H, C*H*NH), 5.72 (d, 1 H, NH), 6.32 (d, 1 H, CH_{olef}), 6.42 (m, 1 H, CH_{furyl}), 6.50 (d, 1 H, CH_{furyl}), 7.39 (d, 1 H, CH_{olef}), 7.40 (d, 1 H, CH_{furyl}); δ_C($CDCl_3$) 13.9 (CH_3), 20.8 (CH_3), 22.4 (CH_2), 25.6 (CH_2), 31.6 (CH_2), 36.8 (CH_2), 45.3 (CH), 111.9 (CH_{olef}), 113.2 (CH_{furyl}), 119.0 (CH_{furyl}), 127.3 (CH_{olef}), 143.6 (CH_{furyl}), 151.3 (C_{furyl}) and 165.1 (C=O); *m*/*z* 235 (M^+, 9.2%) and 121 (100).

(R)-(−)-N-(1-*Methylphenyl*)-3-(2-*furyl*)*propenamide* (*R*)-(−)-**5c**. Yield, 79%; m.p. 153–155 °C; $[\alpha]_D^{22}$ −11.3 (*c*, 1), e.e. >95% (Found: C, 74.7; H, 6.3; N, 5.8; O, 13.3. $C_{15}H_{15}NO_2$ requires C, 74.65; H, 6.27; N, 5.81; O, 13.27%); ν_{max}(KBr)/cm^{-1} 1610 (C=O); δ_H($CDCl_3$) 1.52 (d, 3 H, CH_3), 5.23 (m, 1 H, CHNH), 6.17 (d, 1 H, NH), 6.36 (d, 1 H, CH_{olef}), 6.41 (m, 1 H, CH_{furyl}), 6.50 (d, 1 H, CH_{furyl}) 7.19–7.49 (m, 7 H, 5 CH_{arom}, CH_{olef}, CH_{furyl}); δ_C($CDCl_3$) 21.7 (CH_3), 48.9 (CH), 112.1 (CH_{olef}), 113.7 (CH_{furyl}), 118.3 (CH_{furyl}), 126.2 (CH_{arom}), 127.3 (CH_{olef}), 128.1 (CH_{arom}), 128.6 (CH_{arom}), 143.1 (CH_{furyl}), 143.9 (C_{arom}), 151.2 (C_{furyl}) and 164.9 (C=O); *m*/*z* 241 (M^+, 12.7%) and 121 (100).

(R)-(−)-N-(1-*Methylpropyl*)-3-*phenylpropenamide* (*R*)-(−)-**8d**. Yield, 71%; m.p. 115–117 °C; $[\alpha]_D^{22}$ −16.7 (*c*, 0.98), e.e. 70% (Found: C, 76.8; H, 8.4; N, 6.9; O, 7.9. $C_{13}H_{17}NO$ requires C, 76.8; H, 8.43; N, 6.89; O, 7.87%); ν_{max}(KBr)/cm^{-1} 1620 (C=O); δ_H($CDCl_3$) 0.92 (t, 3 H, CH_3), 1.18 (d, 3 H, CH_3), 1.53 (m, 2 H, CH_2), 4.07 (m, 1 H, C*H*NH), 5.70 (br s, 1 H, NH), 6.61 (d, 1 H, CH_{olef}), 7.25–7.29 (m, 3 H, CH_{arom}), 7.43–7.48 (m, 2 H, CH_{arom}) and 7.63 (d, CH_{olef}); δ_C($CDCl_3$) 10.4 (CH_3), 20.3 (CH_3), 29.5 (CH_2), 46.6 (CH), 121.4 (CH_{olef}) 127.5 (CH_{arom}), 128.5 (CH_{arom}), 129.3 (CH_{arom}), 134.8 (C_{arom}), 140.2 (CH_{olef}) and 165.4 (C=O); *m*/*z* 203 (M^+, 19.8%) and 131 (100).

(R)-(−)-N-(1-*Methylhexyl*)-3-*phenylpropenamide* (*R*)-(−)-**8e**. Yield, 75%; m.p. 123–125 °C; $[\alpha]_D^{22}$ −21.4 (*c*, 0.84), e.e. 83% (Found: C, 78.3; H, 9.5; N, 5.7; O, 6.5. $C_{16}H_{23}NO$ requires C, 78.31; H, 9.45; N, 5.71; O, 6.58%); ν_{max}(KBr)/cm^{-1} 1622 (C=O); δ_H($CDCl_3$) 0.86 (t, 3 H, CH_3), 1.16 (d, 3 H, CH_3), 1.23–1.61 (m, 8 H, 4 CH_2), 4.13 (m, 1 H, C*H*NH), 5.78 (br s, 1 H, NH), 6.42 (d, 1 H, CH_{olef}), 7.28–7.38 (m, 3 H, CH_{arom}), 7.42–7.54 (m, 3 H, CH_{arom}), 7.62 (d, 1 H, CH_{olef}); δ_C($CDCl_3$) 14.0 (CH_3), 21.0 (CH_3), 22.5 (CH_2), 25.7 (CH_2), 31.7 (CH_2), 36.9 (CH_2), 45.4 (CH), 121.1 (CH_{olef}), 127.6 (CH_{arom}), 128.7 (CH_{arom}), 129.4 (CH_{arom}), 134.9(C_{arom}), 140.5 (CH_{olef}) and 165.2 (C=O); *m*/*z* 245 (M^+, 4.5%) and 131 (100).

(R)-(+)-N-(1-*Methylphenyl*)-3-*phenylpropenamide* (*R*)-(+)-**8f**. Yield, 78%; m.p. 144–146; $[\alpha]_D^{22}$ +20.2 (*c*, 1), e.e. >95% (Found: C, 81.2; H, 6.8; N, 5.5; O, 6.4. $C_{17}H_{17}NO$ requires C, 81.23; H, 6.82; N, 5.58; O, 6.37); ν_{max}(KBr)/cm^{-1} 1622 (C=O); δ_H($CDCl_3$) 1.56 (d, 3 H, CH_3), 5.28 (m, 1 H, C*H*NH), 6.19 (d, 1 H, NH), 6.44 (d, 1 H, CH_{olef}), 7.20–7.41 (m, 8 H, 8 CH_{arom}), 7.41–7.54 (m, 8 H, 8 CH_{arom}), 7.65 (d, 1 H, CH_{olef}); δ_C($CDCl_3$) 21.7 (CH_3), 48.8 (CH), 120.9 (CH_{olef}), 126.1 (CH_{arom}), 127.1 (CH_{arom}), 127.6 (CH_{arom}), 128.4 (CH_{arom}), 128.6 (CH_{arom}), 129.4 (CH_{arom}), 134.7 (C_{arom}), 140.8 (CH_{olef}), 143.2 (C_{arom}) and 165.2 (C=O); *m*/*z* 251 (M^+, 38.9%) and 131 (100).

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