Ruthenium-Catalysed Enantioselective Hydrogenation of Trisubstituted Enamides Derived from 2-Tetralone and 3-Chromanone: Influence of Substitution on the Amide Arm and the Aromatic Ring

J. L. Renaud, P. Dupau, A.-E. Hay, M. Guingouain, P. H. Dixneuf, C. Bruneau*

Institut de Chimie, UMR 6509, Organométalliques et Catalyse, Université de Rennes 1, Campus de Beaulieu-35042 Rennes Cedex, France
Fax: [+33]-2-23-23-69-39, e-mail: christian.bruneau@univ-rennes1.fr

Received: July 5, 2002; Accepted: September 20, 2002

Abstract: Cyclic enamides were prepared in one step from tetralone and chromanone derivatives and primary amides under acidic conditions. The enantioselective hydrogenation of these enamides bearing an endocyclic trisubstituted carbon-carbon double bond was performed at room temperature in the presence of ruthenium catalysts. On the one hand, the nature of the amide group had little influence on the enantioselectivity of the hydrogenation when mononuclear precatalysts were used. On the other hand, the presence of a coordinating atom at some specific position on the tetralone and chromanone skeleton led to a dramatic decrease of the enantiomeric excesses.

Keywords: asymmetric catalysis; chiral ligand; hydrogenation; optically active amides; ruthenium

Introduction

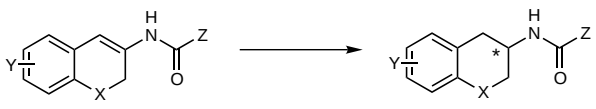
Since the pioneering work on cyclopropanation,[1] and on hydrogenation,[2,3] enantioselective catalysis has undergone an explosive growth,[4] especially during the last decade, due to the synthesis of new chiral ligands and progress in organometallic chemistry.[5] Today, the increasing number of industrial applications clearly demonstrates its efficiency and its practicability.[6]

One of the still challenging enantioselective processes is the preparation of optically active amine derivatives, which constitute a class of key intermediates for human and plant health and are efficient ligands in asymmetric catalysis.[7] Among the methods allowing the synthesis of such enantiopure compounds,[8] the hydrogenation of enamines, ene-amides, ene-carbamates, imines... represents one of the most direct routes.[9]

Precursors of amines can be classified in two major groups: those arising from dehydroamino acids and those from protected enamines. Since Knowles'[2] and Kagan's[3] works, the hydrogenation of dehydroamino acids has been extensively and successfully studied.[10] These intensive efforts have led to the synthesis of variety of new diphosphine ligands: phospholane,[10a] neutral polyhydroxyphospholane,[10a, b] phosphine,[10c, d] phosphite,[10d] and supported phosphine.[10e, f] However, due to the formation of a chelated complex between the dehydroamino acid [an electron-deficient olefin] and rhodium which encourages a high degree of spatial definition on coordination, this is a model reaction that cannot be directly transferred to any type of enamide derivatives. By contrast, electron-rich olefins, such as simple enolates or enamines, are generally poor substrates for asymmetric hydrogenation with most known systems.[9b,11] Recently, some groups have reported that rhodium complexes bearing electron-rich phosphine ligands,[12] a spirocyclic phosphite,[13] or a conformationally rigid cyclic backbone [14] were efficient catalysts for the hydrogenation of enamides.

We focused our interest on the preparation of optically active 3-aminochromanes and 2-aminotetralines which are present in biologically active compounds such as (+)-S20499,[15] MK-0499,[16] and SR-58611A.[17] Our strategy was based on the hydrogenation of the enamides of 2-tetralone and 3-chromanone catalysed by chiral ruthenium complexes.

In this paper, we wish to report the synthesis of trisubstituted enamides bearing different functionalities linked to the aromatic ring in order to understand the influence of the nature of the amide moiety and the



Scheme 1.

  1615-4150/03/3451+2-230–238 $ 17.50-.50/0

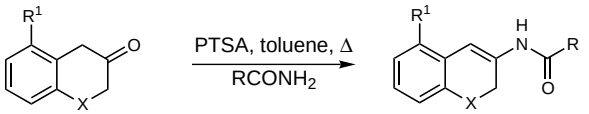
substitution pattern on the aromatic ring during the catalytic hydrogenation process (Scheme 1).

Results and Discussion

Preparation of the Enamides

Recently, the preparation of acetamide derivatives from ketones has been carried out in a two-step procedure which involved transformation of the ketone into an oxime followed by treatment with iron metal in the presence of acetic anhydride and acetic acid.[12e, f] However, this method based on the use of acetic derivatives allows only the preparation of *N*-acetylenamides. A more direct and general transformation of a ketone into an enamide based on the condensation with a primary amide has been performed in the presence of Amberlyst 15 as dehydrating agent to prepare trisubstituted enamides.[16,17]

Recently, we have also reported an easy and direct route to enamides[18] and ene-carbamates[19] based on the condensation of primary enamides and carbamates with cyclic ketones in the presence of *para*-toluenesulfonic acid as catalyst and by using a Dean – Stark apparatus to remove water (Scheme 2).



1a-h: R^1 = H, X = CH_2
2a-b: R^1 = Br, X = CH_2
3a-b: R^1 = H, X = O
4a-b: R^1 = OMe, X = O

Scheme 2.

Table 1. Preparation of the enamides **1a – h, 2a, b, 3a, b, 4a, b**.

Entry	X	R^1	R	Compound	Yield [%]
1	CH_2	H	Me	**1a**	80
2	CH_2	H	Et	**1b**	98
3	CH_2	H	Pr	**1c**	98
4	CH_2	H	Ph	**1d**	80
5	CH_2	H	CH_2Cl	**1e**	75
6	CH_2	H	CH_2OMe	**1f**	80
7	CH_2	H	CH_2OBn	**1g**	80
8	CH_2	H	CH_2SBn	**1h**	90
9	CH_2	Br	Me	**2a**	63
10	CH_2	Br	Ph	**2b**	79
11	O	H	Me	**3a**	55
12	O	H	Ph	**3b**	63
13	O	OMe	Me	**4a**	80
14	O	OMe	CH_2OMe	**4b**	50

Table 2. Enantioselective hydrogenation with catalyst **A**.[a]

Entry	R	Compound	Yield [%]	ee [%9
1	Me	**5a**	94	80 (+)
2	Et	**5b**	94	76 (+)
3	Pr	**5c**	95	80 (+)
4	Ph	**5d**	94	87 (+)
5[b]	CH_2Cl	**5e**	94	47 (+)
6	CH_2OMe	**5f**	95	56 (+)
7	CH_2OBn	**5g**	98	27 (+)

[a] General conditions : substrate **1a – g** (0.5 mmol), catalyst (0.2 mol %), MeOH (5 mL), hydrogen pressure (10 MPa), r.t., isolated yields.
[b] At 60 °C.

Under similar conditions the enamides of 2-tetralone, 3-chromanone and their methoxy- and bromo-substituted derivatives were obtained in good yields (55 – 98%, Table 1). It is noteworthy that this method makes possible the preparation of the enamides **1e – h** and **4b** bearing an additional chelating group on their amide arm, and offer the possibility of studying its influence on the subsequent enantioselective hydrogenation.

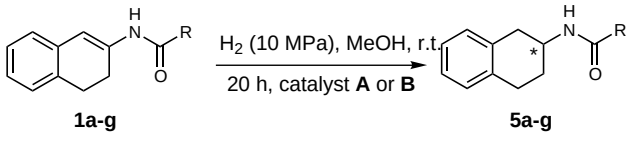
All the enamides were obtained by using 2.5 equivalents of primary amides, except for the compound **1e** which required 5 equivalents of the chloroacetamide. The necessity of increasing the amount of amide might be due to an electron-attracting effect, which leads to the deactivation of the amide moiety. The same effect probably explains that, under similar conditions, no conversion into the desired product was obtained with trichloroacetamide.

This new method opens a general and direct route to enamides from non-activated cyclic ketones and makes possible the preparation of a variety of enamides.

Hydrogenation of Enamides 1a – g

When the enamides **1a – g** were hydrogenated in the presence of 2 mol % of the dimeric catalyst $[NH_2Et_2][\{(S)\text{-BinapRuCl}\}_2(\mu\text{-Cl})_3]$[20] in methanol at room temperature, their conversion was completed within 20 h and the amides **5a – g** were obtained in good yields (94 – 98%, Scheme 3).

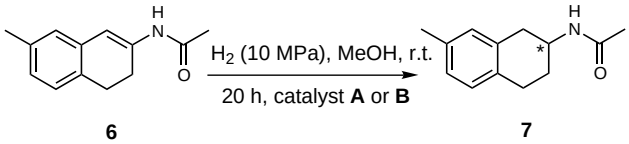
With this catalyst, ees are located in the range 27 – 87%. The nature of the amide moiety plays a role in the enantioselective process. The introduction of a chelating heteroatom at the β-position of the amide dramatically decreased the ees (entries 5 – 7). These results might be explained by a competing chelation between the carbonyl group and the heteroatom of the amide chain with the metal during the hydrogenation reaction.



1a-g **5a-g**

catalyst **A**: $[NH_2Et_2][\{(S)\text{-BinapRuCl}\}_2(\mu\text{-Cl})_3]$ 0.2 mol %
catalyst **B**: $((R)\text{-Binap})Ru(O_2CCF_3)_2$ 0.5 mol %

Scheme 3.



6 **7**

(+)-**7**: 64% ee with catalyst **A**
(–)-**7**: 94% ee with catalyst **B**

Scheme 4.

Table 3. Enantioselective hydrogenation with catalyst **B**.[a]

Entry	R	Compound	Yield [%]	ee [%]
1	Me	**5a**	95	90 (–)
2[b]	Me	**5a**	95	90 (–)
3	Et	**5b**	95	90 (–)
4	Pr	**5c**	95	92 (–)
5	Ph	**5d**	95	96 (–)
6[c]	CH_2Cl	**5e**	95	71 (–)
7	CH_2OMe	**5f**	95	89 (–)
8[d]	CH_2OBn	**5g**	98	89 (–)
9	CH_2SBn	**5h**	no reaction	

[a] General conditions: substrate **1a – g** (0.5 mmol), catalyst (0.5 mol %), MeOH (5 mL), hydrogen pressure (10 MPa), r.t., isolated yields.
[b] 0.1 mol % of ruthenium complex.
[c] 1 mol % of ruthenium complex.
[d] 0.2 mol % of ruthenium complex.

Better results in terms of enantioselectivity were obtained when $[(R)\text{-Binap}]Ru(O_2CCF_3)_2$ **B** was used as catalyst precursor (Scheme 3, Table 3).

Starting from the enamides **1a – c** where R is an alkyl group or **1f, g** where R is an ether group, ees around 90% were obtained which indicated that the amide chain in these examples had no significant influence on the enantioselectivity of the hydrogenation, even with only 0.1 mol % of catalyst loading (entries 1 and 2). The best enantiomeric excess was obtained from the benzoyl enamide **1d** which led to **5d** in 96% ee. This is in agreement with previous results[17] and might be explained by the rigidity of the enebenzamide system.

The chloromethylacetamide **1e** led to the hydrogenated derivative **5e** in 95% yield but in only 71% ee. This lower enantiomeric excess might arise either from a competing chelation of the chloride atom, or a weaker interaction between the amide moiety and the ruthenium centre, due to the electron-attracting effect of the chloride atom. Nevertheless, this result is still better than that obtained with the dimeric ruthenium precatalyst (47% ee).

By contrast with the good results obtained for the hydrogenation of aliphatic sulfides[21] and sulfones,[22] no reaction occurred with our substrate **1h** in these conditions. This suggests that the sulfide derivative poisons the catalyst and thus inhibits its reactivity. Going from the sulfide to the sulfone **1i** by oxidation with an excess of H_2O_2 did not improve the reaction as no hydrogenation was observed. Further experiments proved that those sulfur-containing enamides could interact with the catalyst. Indeed the hydrogenation of **1a** which furnished the tetrahydronaphthylacetamide **5a** in 95% yield and 90% ee in the presence of 0.5 mol % of $[(R)\text{-Binap}]Ru(O_2CCF_3)_2$, was inhibited by addition of 10 mol % of **1h** to the starting compound. Only the starting material **1a** was totally recovered. When we carried out the hydrogenation of **1h** in the presence of 0.5 mol % of $[Ru(COD)Cl_2]_n$ and (*S*)-MeO-Biphep as a chiral ligand,[23] the same result was observed.

The better efficiency of the precatalyst **B** for the enantioselective hydrogenation of enamides derived from tetralone has been confirmed by the hydrogenation of the 7-methyltetralone-eneacetamide **6**, obtained in 63% yield from the corresponding ketone under the conditions described in Table 1 and Scheme 2. Thus, hydrogenation of **6** in the presence of 0.5 mol % of the catalyst precursor **A** or **B** in methanol at room temperature under 10 MPa of hydrogen pressure and after 20 h afforded quantitative yields of the corresponding amide **7** in 64 and 94% ee, respectively (Scheme 4).

Hydrogenation of Enamides 2, 3 and 4

From the preceding results, it appeared that the right choice of the catalyst precursor was essential to achieve high enantioselectivity. The catalytic activity of the dimeric complex was more sensitive to the presence of an heteroatom on the amide moiety than the monomeric ruthenium complex and the best results for the hydrogenation of this type of enamides were obtained with $[(R)\text{-Binap}]Ru(O_2CCF_3)_2$ as precatalyst.

To study the influence of a coordinating heteroatom on the enantioselectivity of the hydrogenation, the eneacetamides **2a** (63%), **3a** (55%) and enebenzamides **2b** (79%), **3b** (63%) were prepared starting from the corresponding 8-bromo-2-tetralone **9**[24] and the unsubstituted 3-chromanone **10**[25] according to our method (Figure 1).

This influence of an heteroatom was noticed during the hydrogenation of the chromanone derivatives **4a, b** (Scheme 5, Table 4, entries 1 – 4), where the highest enantiomeric excesses were obtained with [(*R*)-Binap]-

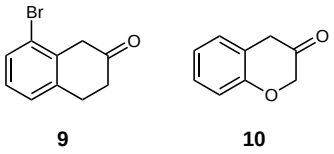
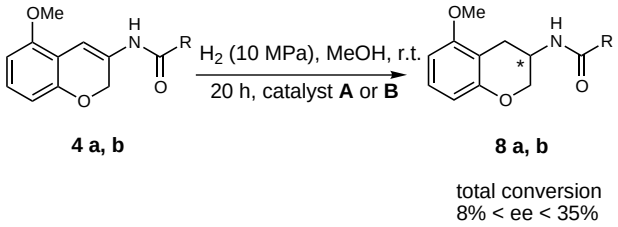


Figure 1.



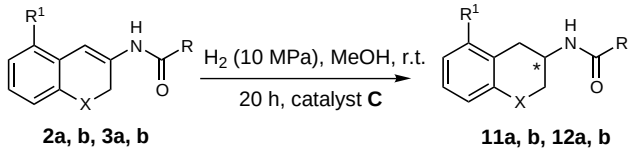
Scheme 5.

$Ru(O_2CCF_3)_2$ **B**. However, these ees were much lower than those obtained from the enamides **1a** and **1f** (Table 3, entries 1 and 7), which suggests that the oxygen atom in the ring or the methoxy group of the chromanone plays a crucial role in the discriminating step of the hydrogenation.

The direct hydrogenation of the enamides **2a, b** and **3a, b** was attempted in the presence of a catalytic amount of [(*S*)-Biphemp]$Ru(O_2CCF_3)_2$ (**C**) (Schema 6).[26] The results are reported in Table 4.

Compounds **2a** and **2b** were hydrogenated at room temperature under our classical conditions without cleavage of the C-Br bond and led to the amides **11a** and **11b** in good yields (90 and 95%, respectively) but the enantiomeric excesses were very low (16% and 22%, respectively). By contrast, the hydrogenation of the enamides **3a** and **3b** was also very efficient and afforded the amides **12a** and **12b** with good enantioselectivities (72 and 92% ee, respectively). Here again, the enebenzamide appeared to be the most appropriate substrate to reach the best enantioselection.

These results clearly indicate that the oxygen atom of the cyclic ether functionality has little influence on the enantioselectivity of the hydrogenation of the unsubstituted chromanone derivative (92% ee for **12b** as compared to 96% ee for the corresponding benzamide **5d** derived from 2-tetralone).



Scheme 6.

The presence of the coordinating bromide atom in **2a** and **2b** has a dramatic negative influence on the enantioselectivity of this reaction. Whereas the presence of a neighbouring bromide atom might bring the greatest benefit in some cases such as in the hydrogenation of 2′-bromoacetophenone,[27] in this special case, the competition with the amide group probably induces a mismatch situation which leads to a poor enantiomeric excess.

Conclusion

We have shown that the transformation of unsubstituted 2-tetralone and 3-chromanone into optically active amine derivatives could be performed efficiently at room temperature *via* the enantioselective hydrogenation of enamides in the presence of a mononuclear ruthenium catalyst such as [(*S*)-Biphemp]$Ru(O_2CCF_3)_2$ or [(*R*)-Binap]$Ru(O_2CCF_3)_2$. A detailed study on the nature of the substructure of the enamide derivative indicates that in the presence of these mononuclear ruthenium precursors, the transient coordination to the metal centre essentially involves the carbonyl group of the amide and is not affected by the presence of a heteroatom such as an oxygen on the amide arm, which is not the case with the binuclear ruthenium catalyst $[NH_2Et_2][\{(S)\text{-BinapRuCl}\}_2(\mu\text{-Cl})_3]$. On the other hand, the presence of a chloroacetyl group on the amide group had a negative effect on the enantioselectivity with both catalytic systems.

Table 4. Hydrogenation of compounds **2**, **3** and **4**.[a]

Entry	X	R	R^1	Enamide	Product	Catalyst	Yield [%]	ee [%]
1	O	Me	OMe	**4a**	**8a**	**B**	97	35 (+)
2	O	CH_2OMe	OMe	**4b**	**8b**	**B**	94	22 (+)
3	O	Me	OMe	**4a**	**8a**	**A**	95	8 (−)
4	O	CH_2OMe	OMe	**4b**	**8b**	**A**	95	20 (−)
5	CH_2	Me	Br	**2a**	**11a**	**C**	90	16 (+)
6	CH_2	Ph	Br	**2b**	**11b**	**C**	95	22 (+)
7	O	Me	H	**3a**	**12a**	**C**	95	72 (+)
8	O	Ph	H	**3b**	**12b**	**C**	95	92 (+)

[a] General conditions: substrate **1a – g** (0.5 mmol), catalyst (0.5 mol %), MeOH (5 mL), hydrogen pressure (10 MPa), isolated yields.

Whereas the presence of a bromide at C-6[16] or a methoxy group at C-7[17] has no effect on the enantioselectivity during the hydrogenation of enamides derived from tetralone, we demonstrated that the enantioselectivity is much lower when a coordinating group is introduced at the C-8 position on the aromatic ring of this type of substrates.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were taken on 200 MHz Bruker AC 200 spectrometers. Chemical shifts are reported in ppm referenced to the residual proton resonances of the solvents. Mass spectra (MS) were obtained on GC-MS Hewlett-Packard HP 5971 apparatus. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F 254. Silica gel Merck Geduran SI (40 – 63 μm) was used for column chromatography.

General Procedure for the Preparation of the Enamides 1a – h, 2a, b, 3a, b, 4a, b

In a 250 mL round-bottom flask equipped with a Dean – Stark apparatus were introduced the ketone (10 mmol, 1 equiv.), the primary amide (25 mmol, 2.5 equiv.) and *para*-toluene sulfonic acid (1 mmol, 0.1 equiv.) in 60 mL of toluene. The mixture was refluxed for 20 h under an inert atmosphere. After cooling down to room temperature, 150 mL of a saturated solution of hydrogen carbonate were added and the mixture was warmed to 60 °C for 30 min. After cooling down to room temperature, the organic layer was extracted, washed with water (3 × 100 mL), dried over magnesium sulfate and concentrated. The enamide was purified by chromatography on silica gel.

***N*-(3,4-Dihydronaphthalen-2-yl)-acetamide (1a):** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 2.09 (s, 3H, CH_3 amide), 2.42 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 2.85 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 6.87 (broad s, 1H, NH), 6.90 – 7.10 (m, 5H, 4 CH ar.+ CH=C); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.6 (CH_3 amide), 27.2 (CH_2 ring), 28.1 (CH_2 ring), 111.6 (CH=), 125.9 (CH ar.), 126.0 (CH ar.), 126.8 (CH ar.), 127.20 (CH ar.), 132.9 (C quat. =CN), 134.9 (C quat. ar.), 135.7 (C quat. ar.), 169.7 (CO amide).

***N*-(3,4-Dihydronaphthalen-2-yl)-propionamide (1b):** Isolated as a white solid in 98% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, CD_3OD): δ = 1.11 (t, *J* = 7.0 Hz, 3H, CH_3 amide), 2.27 (q, *J* = 7.0 Hz, 2H, CH_2 amide), 2.38 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 2.78 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 6.80-7.20 (m, 5H, 4CH ar. + CH=C); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 9.8 (CH_3 amide), 27.5 (CH_2 ring), 28.0 (CH_2 ring), 30.8 (CH_2 amide), 111.4 (CH=), 125.8 (CH ar.), 126.0 (CH ar.), 126.7 (CH ar.), 127.1 (CH ar.), 132.7 (C quat. =CN), 134.9 (C quat. ar.), 135.3 (C quat. ar.), 172.9 (CO amide).

***N*-(3,4-Dihydronaphthalen-2-yl)-butyramide (1c):** Isolated as a beige solid in 98% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, CD_3OD): δ = 0.97 (t, *J* = 7.4 Hz, 3H, CH_3 amide), 1.70 (sextuplet, *J* =7.4 Hz, 2H, CH_2 amide), 2.25 (t, *J* = 7.4 Hz, 2H, CH_2 amide), 2.42 (t, *J* = 8.2 Hz, 2H, CH_2 ring), 2.86 (t, *J* = 8.2 Hz, 2H, CH_2 ring), 6.58 (broad s, 1H, NH), 6.80 – 7.20 (m, 5H, 4CH ar. + CH=C); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.9 (CH_3 amide), 19.2 (CH_2 amide), 27.5 (CH_2 ring), 28.0 (CH_2 ring), 39.6 (CH_2 amide), 111.4 (CH=), 125.8 (CH ar.), 126.0 (CH ar.), 126.7 (CH ar.), 127.1 (CH ar.), 132.8 (C quat. =CN), 134.9 (C quat. ar.), 135.4 (C quat. ar.), 172.2 (CO amide); HRMS: calcd. for $C_{14}H_{17}NO$: 215.13101; found : 215.13260.

***N*-(3,4-Dihydronaphthalen-2-yl)-benzamide (1d):** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, CD_3OD): δ = 2.55 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 2.84 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 6.80 – 7.20 (m, 5H, 4 H ar.+ CH=C), 7.30 – 7.60 (m, 3H ar.), 7.70 – 7.90 (2H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.5 (CH_2 ring), 28.1 (CH_2 ring), 112.4 (CH=), 126.0 (CH ar.), 126.3 (CH ar.), 126.8 (CH ar.), 127.2 (3 CH ar.), 128.7 (2 CH ar.), 131.8 (CH ar.), 133.0 (C quat. =CN), 134.8 (C quat. ar.), 134.9 (C quat. ar.), 135.6 (C quat. ar.), 166.4 (CO amide); HRMS: calcd. for $C_{17}H_{15}NO$: 249.11536; found : 249.11644.

***N*-(3′,4′-Dihydronaphthalen-2′-yl)-(2-chloroacetamide) (1e):** For compound **1e**, 5 equivalents of chloroacetamide were used and the reflux was maintained for 48 hours. This enamide was isolated as a beige solid in 75% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 2.48 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 2.90 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 4.10 (s, 2H, CH_2Cl), 6.90 – 7.20 (m, 5H, 4 H ar.+ CH=C), 7.61 (broad s, 1H, NH); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.2 (CH_2 ring), 27.9 (CH_2 ring), 43.0 (CH_2Cl), 112.9 (CH=), 126.4 (CH ar.), 126.4 (CH ar.), 126.8 (CH ar.), 127.2 (CH ar.), 132.9 (C quat. =CN), 133.98 (C quat. ar.), 134.2 (C quat. ar.), 164.0 (CO amide); HRMS: calcd. for $C_{12}H_{12}ClNO$: 221.06074; found : 221.06002.

***N*-(3′,4′-Dihydronaphthalen-2′-yl)-(2-methoxyacetamide) (1f):** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 2.46 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 2.87 (t, *J* = 8.0 Hz, 2H, CH_2 ring), 3.44 (s, 3H, OCH_3), 3.93 (s, 2H, CH_2O), 6.90 – 7.12 (m, 4H ar.), 7.13 (s, 1H, CH), 7.62 (broad s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 27.36 (CH_2 ring), 27.96 (CH_2 ring), 59.26 (OCH_3), 72.10 (CH_2O), 111.75 (CH=), 125.92 (CH ar.), 126.17 (CH ar.), 126.73 (CH ar.), 127.11 (CH ar.), 132.80 (C quat. =CN), 134.33 (C quat. ar.), 134.70 (C quat. ar.), 167.71 (CO amide).

***N*-(3′,4′-Dihydronaphthalen-2′-yl)-(2-benzyloxyacetamide) (1g):** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$); δ = 2.44 (t, *J* = 8.2 Hz, 2H, CH_2 ring), 2.87 (t, *J* = 8.2 Hz, 2H, CH_2 ring), 4.01 (s, 2H, CH_2O), 4.61 (s, 2H, OCH_2Ph), 6.90 – 7.11 (m, 4H ar.), 7.13 (s, 1H, CH=), 7.25 – 7.50 (m, 5H ar.), 7.70 (broad s, 1H, NH); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.4 (CH_2 ring), 28.0 (CH_2 ring), 69.7 (OCH_2Ph), 73.8 (OCH_2), 111.9 (CH=), 126.0 (CH ar.), 126.2 (CH ar.), 126.8 (CH ar.), 127.1 (CH ar.), 128.1 (2 CH ar.), 128.5 (CH ar.), 128.8 (2 CH ar.), 132.8 (C quat. =CN), 134.2 (C quat. ar.), 134.7 (C quat. ar.), 136.6 (C quat. ar.), 167.7 (CO amide).

***N*-(3′,4′-Dihydronaphthalen-2′-yl)-[2-(benzyl sulfide)acetamide] (1h):** Isolated as a yellow solid in 90% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 2.32 (t, *J* = 8.1 Hz, 2H, CH_2 ring), 2.84 (t, *J* = 8.1 Hz, 2H, CH_2 ring), 3.21 (s, 2H, CH_2S), 3.74 (s, 2H, CH_2S), 6.90 – 7.15 (m, 5H, 4H ar. + CH=), 7.17 – 7.45 (m, 5H ar.), 7.77 (broad s, 1H, NH); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ =

27.2 (CH_2 cycle), 28.0 (CH_2 ring), 36.5 (CH_2S), 37.5 (CH_2S), 111.6 (CH=), 126.0 (CH ar.), 126.2 (CH ar.), 126.8 (CH ar.), 127.1 (CH ar.), 127.7 (CH ar.), 128.9 (3 CH ar.), 129.0 (2 CH ar.), 132.8 (C quat. =CN), 134.6 (C quat. ar.), 134.6 (C quat. ar.), 137.2 (C quat. ar.), 166.9 (CO amide).

***N*-(3′,4′-Dihydronaphthalen-2′-yl)-[2-(benzylsulfonyl)acetamide] (1i):** Sulfide **1h** was dissolved in methanol before adding an aqueous solution of H_2O_2 (10 equiv.) at room temperature. A white precipitate appeared quickly. The mixture was stirred at room temperature for one hour. The solid was filtered, washed with water and dried under vacuum. The sulfone derivative was obtained as white solid in 95% yield. ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 2.40$ (t, $J = 8.2$ Hz, 2H, CH_2 ring), 2.84 (t, $J = 8.4$ Hz, 2H, CH_2 ring), 3.26 (d, $J = 14.2$ Hz, 1H, CH_2SO_2), 3.64 (d, $J = 14.2$ Hz, 1H, CH_2SO_2), 4.14 (d, $J = 13.0$ Hz, 1H, CH_2SO_2), 4.23 (d, $J = 13.0$ Hz, 1H, CH_2SO_2), 6.90 – 7.12 (m, 4H ar.), 7.15 (s, 1H, CH=), 7.28 – 7.50 (m, 5H ar.), 8.51 (broad s, 1H, NH); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 27.0$ (CH_2 ring), 27.9 (CH_2 ring), 53.5 (CH_2SO_2), 57.3 (CH_2SO_2), 112.5 (CH=), 126.0 (CH ar.), 126.3 (CH ar.), 126.7 (CH ar .), 127.1 (CH ar.), 128.8 (C quat. ar.), 128.9 (CH ar.), 129.2 (2 CH ar.), 130.7 (2 CH ar.), 132.9 (C quat. =CN), 134.5 (C quat. ar.), 135.0 (C quat. ar.), 162.1 (CO amide); HRMS: calcd. for $C_{19}H_{19}NO_2S$: 325.11365; found: 325.11420.

***N*-(8′-Bromo-3′,4′-dihydronaphthalen-2′-yl)-acetamide (2a):** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 2.09$ (s, 3H, CH_3 amide), 2.42 (t, $J = 8.0$ Hz, 2H, CH_2 ring), 2.85 (t, $J = 8.0$ Hz, 2H, CH_2 ring), 6.87 (broad s, 1H, NH), 6.90 – 7.10 (m, 5H, 4 CH ar. + CH=C); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 24.6$ (CH_3 amide), 27.2 (CH_2 ring), 28.1 (CH_2 ring), 111.6 (CH=), 125.9 (CH ar.), 126.0 (CH ar.), 126.8 (CH ar.), 127.20 (CH ar.), 132.9 (C quat. =CN), 134.9 (C quat. ar.), 135.7 (C quat. ar.), 169.7 (CO amide); HRMS: calcd. for $C_{12}H_{12}NOBr$: 265.01023; found: 265.01254.

***N*-(8′-Bromo-3′,4′-dihydronaphthalen-2′-yl)-benzamide (2b):** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 2.09$ (s, 3H, CH_3 amide), 2.42 (t, $J = 8.0$ Hz, 2H, CH_2 ring), 2.85 (t, $J = 8.0$ Hz, 2H, CH_2 ring), 6.87 (broad s, 1H, NH), 6.90 – 7.10 (m, 5H, 4 CH ar. + CH=C); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 24.6$ (CH_3 amide), 27.2 (CH_2 ring), 28.1 (CH_2 ring), 111.6 (CH=), 125.9 (CH ar.), 126.0 (CH ar.), 126.8 (CH ar.), 127.20 (CH ar.), 132.9 (C quat. =CN), 134.9 (C quat. ar.), 135.7 (C quat. ar.), 169.7 (CO amide); HRMS: calcd. for $C_{17}H_{14}BrNO$: 327.02588; Found: 327.02374.

***N*-(Benzo[*b*]pyran-3-yl)-acetamide (3a):** Isolated as an oil in 55% yield after flash chromatography on silica gel (ether/pentane: 1/1). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 4.86$ (d, $J = 1.2$ Hz, 2H , CH_2), 6.54 (broad s, 1H, NH), 6.78 (d, $J = 7.9$ Hz, 1H ar.), 6.87 (dd, $J = 7.4, 1.2$ Hz, 1H ar.), 6.93 – 7.05 (m, 3H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 24.1$ (CH_3 amide), 65.6 (OCH_2 ring), 107.8 (CH ar.), 115.4 (CH ar.), 122.0 (CH=), 122.8 (C quat. ar.), 126.4 (CH ar.), 127.8 (CH ar.), 129.6 (C quat., =CN), 152.0 (C quat. ar.), 169.0 (CO amide); HRMS: calcd. for $C_{11}H_{11}NO_2$: 189.07898; found: 189.07902.

***N*-(Benzo[*b*]pyran-3-yl)-benzamide (3b):** Isolated as an oil in 63% yield after flash chromatography on silica gel (ether/pentane: 1/1). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 5.01$ (d, $J = 1.0$ Hz, 2H, CH_2), 6.68 (broad s, 1H, NH), 6.82 (d, $J = 8.6$ Hz, 1H), 6.87 (dd, $J = 7.2$, 1.3 Hz, 1H), 6.98 – 7.14 (m, 3H), 7.40 – 7.55 (m, 3H), 7.68 – 7.81 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 30.8$ (CH_2 ring), 42.8 (CH ring), 68.3 (OCH_2 ring), 117.0 (CH=), 119.4 (CH ar.), 121.5 (CH ar.), 127.0 (2 CH ar.), 127.9 (CH ar.), 128.6 (2 CH ar.), 130.6 (CH ar.), 131.7 (C quat. =CN), 134.2 (C quat. ar.), 153.9 (C quat. ar.), 167.3 (CO amide); HRMS: calcd. for $C_{16}H_{13}NO_2$: 251.09463; found: 251.09367.

***N*-(5-Methoxybenzo[*b*]pyran-3-yl)-acetamide (4a);** Isolated as a white solid in 80% yield after flash chromatography on silica gel (ether/pentane: 1/1). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 2.06$ (s, 3H, CH_3 amide), 3.78 (s, 3H, OCH_3), 4.90 (s, 2H, OCH_2 cycle), 6.43 (d, $J = 8.2$ Hz, 1H ar.), 6.45 (d, $J = 8.2$ Hz, 1H ar.), 6.60 (s, 1H, CH=), 6.98 (t, $J = 8.2$ Hz, 1H ar.), 7.07 (s large, 1H, NH); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 23.9$ (CH_3 amide), 55.7 (OCH_3), 65.3 (OCH_2 ring), 102.9 (CH ar.), 104.0 (CH ar.), 108.5 (CH=), 108.8 (C quat. ar.), 127.6 (CH ar.), 133.9 (C quat., =CN), 152.9 (C quat. ar.), 155.1 (C quat. ar.), 169.1 (CO amide).

***N*-(5′-Methoxybenzo[*b*]pyran-3′-yl)-2-methoxyacetamide (4b):** Isolated as a colourless oil in 50% yield after flash chromatography on silica gel (ether/pentane: 1/1). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 3.44$ (s, 3H, OCH_3 amide), 3.79 (s, 3H, OCH_3), 3.91 (s, 2H, OCH_2 amide), 4.99 (d, $J = 1.0$ Hz, 2H, CH_2 ring), 6.43 (d, $J = 8.2$ Hz, 1H ar.), 6.46 (d, $J = 8.2$ Hz, 1H ar.), 6.75 (s, 1H, CH=), 6.98 (t, $J = 8.2$ Hz, 1H ar.), 7,85 (broad s, 1H, NH); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 55.7$ (OCH_3), 59.26 (OCH_3), 65.3 (OCH_2 ring), 72.10 (CH_2O), 102.9 (CH ar.), 104.0 (CH ar.), 108.5 (CH=), 108.8 (C quat. ar.), 127.6 (CH ar.), 133.9 (C quat., =CN), 152.9 (C quat. ar.), 155.1 (C quat. ar.), 169.1 (CO amide).

***N*-(7-Methyl-3,4-dihydronaphthalen-2-yl)-acetamide (6a):** Isolated as a beige solid in 63% yield after flash chromatography on silica gel (ether/pentane: 1/2). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 2.09$ (s, 3H, CH_3 amide), 2.25 (s, 3H, CH_3), 2.40 (t, $J = 8.1$ Hz , 2H, CH_2 ring), 2.81 (t, $J = 8.1$ Hz , 2H, CH_2 ring), 6.75 (broad s, 1H, NH), 6.80 – 7.15 (m, 4H, 3H ar. + CH=); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 21.1$ (CH_3), 24.7 (CH_3 amide), 27.5 (CH_2 ring), 27.6 (CH_2 ring), 111.7 (CH=), 126.5 (CH ar.), 126.9 (CH ar.), 126.9 (CH ar.), 129.8 (C quat, =CN), 134.7 (C quat, ar.), 135.4 (C quat, ar.), 136.2 (C quat, ar.), 169.2 (CO amide).

***N*-(7-Methyl-3,4-dihydronaphthalen-2-yl)-propionamide (6b):** Isolated as a beige solid in 98% yield after flash chromatography on silica gel (ether/pentane: 1/1). ^{1}H NMR (200.13 MHz, $CDCl_3$): $\delta = 1.19$ (t, $J = 7.5$ Hz, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.26 (q, $J = 7.5$ Hz , 2H, CH_2), 2.40 (t, $J = 8.0$ Hz, 2H, CH_2 ring), 2.82 (t, $J = 8.0$ Hz , 2H, CH_2 ring), 6.56 (broad s, 1H, NH), 6.75 – 7.15 (m, 4H, 3H ar. + CH=); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 9.8$ (CH_3 amide), 21.2 (CH_3), 27.5 (CH_2 cycle), 27.6 (CH_2 ring), 30.7 (CH_2 amide), 111.7 (CH=), 126.5 (CH ar.), 126.9 (CH ar.), 126.9 (CH ar.), 129.8 (C quat, =CN), 134.7 (C quat, ar.), 135.4 (C quat, ar.), 136.2 (C quat, ar.), 172.8 (CO amide).

Catalysts for Enantioselective Hydrogenation

Chiral catalysts [(*R*)-Binap]Ru(O_2CCF_3)$_2$,[28] [NH_2Et_2][{((*S*)-Binap)RuCl}$_2$(μ-Cl)$_3$],[20] and [(*S*)-Biphemp]Ru(O_2CCF_3)$_2$[28] were prepared using previously described procedures.

General Procedure for the Hydrogenation of Enamides

In a 125 mL stainless steel autoclave were placed under an argon atmosphere the enamide (1 mmol, 1 equiv.), the chiral precatalyst (0.005 mmol, 0.5% mol.). The mixture was degassed by three vacuum-filling with argon cycles before adding 8 mL of degassed and distilled methanol. Air present in the gas inlet tube was removed by flushing with a stream of hydrogen. Then the autoclave was purged three times by hydrogen and the vessel was pressurised to 100 bar. After 20 h under mechanical stirring at 20 °C, the autoclave was carefully opened, the solvent was removed under reduced pressure. Conversion was determined by ^{1}H NMR analysis of the crude mixture. Subsequently, the residue was purified by chromatography on silica gel, eluted with a 1:1 mixture of heptane and ether. Enantiomeric excesses was determined by HPLC on Chiracel OD column (eluent: hexane/*i*-PrOH: 95/5; flow: 1 mL/min; temperature: 25 °C; detection : 210 nm).

***N*-(1,2,3,4-Retrahydronaphthalen-2-yl)-acetamide (5a):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.60 – 1.86 (m, 1H, CH_2 ring), 1.95 (s, 3H, CH_3 amide), 1.96 – 2.10 (m, 1H, CH_2 ring), 2.62 (dd, *J* = 16.0, 7.8 Hz, 1H, CH_2 ring), 2.75 – 2.95 (m, 2H, CH_2 ring), 3.10 (dd, *J* = 16.0, 4.8 Hz, 1H, CH_2 ring), 4.10 – 4.50 (m, 1H, CHN), 5.50 (broad s, 1H, NH), 7.09 (broad s, 4H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.5 (CH_3 amide), 27.2 (CH_2 ring), 28.6 (CH_2 ring), 35.7 (CH_2 ring), 45.2 (CHN), 126.0 (CH ar.), 126.2 (CH ar.), 128.9 (CH ar.), 129.5 (CH ar.), 134.1 (C quat, ar.), 135.5 (C quat, ar.), 169.8 (CO amide); HRMS: calcd. for $C_{12}H_{15}NO$: 189.11536; found: 189.11573; HPLC retention time: (−) enantiomer: 22 min; (+) enantiomer: 27 min.

***N*-(1,2,3,4-Tetrahydronaphthalen-2-yl)-propionamide (5b):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.6 Hz, 3H, CH_3 amide), 1.50 – 1.80 (m, 1H, CH_2 ring), 1.85 – 2.13 (m, 1H, CH_2 ring), 2.15 (q, *J* = 7.6 Hz, 2H, CH_2 amide), 2.59 (dd, *J* = 16.2, 9.8 Hz, 1H, CH_2 ring), 2.70 – 2.85 (m, 2H, CH_2 ring), 2.96 (dd, *J* = 16.2, 4.9 Hz, 1H, CH_2 ring), 3.85 – 4.15 (m, 1H, CHN), 4.84 (broad s, 1H, NH), 7.00 (broad s, 4H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.1 (CH_3 amide), 27.4 (CH_2 ring), 28.8 (CH_2 ring), 29.8 (CH_2 amide), 35.7 (CH_2 ring), 45.1 (CHN), 125.9 (CH ar.), 126.2 (CH ar.), 128.9 (CH ar.), 129.5 (CH ar.), 134.3 (C quat, ar.), 135.6 (C quat, ar.), 173.5 (CO amide); HRMS: calcd. for $C_{13}H_{17}NO$: 203.13101; found: 203.13123; HPLC retention time: (−) enantiomer: 21 min; (+) enantiomer: 24 min.

***N*-(1,2,3,4-Tetrahydronaphthalen-2-yl)-butyramide (5c):** Beige solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.6 Hz, 3H, CH_3 amide), 1.64 (sext., *J* = 7.6 Hz, 2H, CH_2 amide), 1.71 – 1.87 (m, 1H, CH_2 ring), 1.92 – 2.06 (m, 1H, CH_2 ring), 2.11 (t, *J* = 7.6 Hz, 2H, CH_2 amide), 2.61 (dd, *J* = 16.5, 7.9 Hz, 1H, CH_2 ring), 2.70 – 3.00 (m, 2H, CH_2 ring), 3.11 (dd, *J* = 16.3, 5.2 Hz, 1H, CH_2 cycle), 4.10 – 4.50 (m, 1H, CHN), 5.43 (broad s, 1H, NH), 6.90 – 7.20 (m, 4H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.8 (CH_3 amide), 19.4 (CH_2 amide), 27.5 (CH_2 ring), 28.9 (CH_2 ring), 35.8 (CH_2 ring), 38.8 (CH_2 amide), 45.2 (CHN), 125.9 (CH ar.), 126.1 (CH ar.), 128.9 (CH ar.), 129.44 (CH ar.), 134.4 (C quat, ar.), 135.6 (C quat, ar.), 172.7 (CO amide); anal. calcd. for $C_{14}H_{19}NO$: C 77.10, H 9.18, N 6.27%; found: C 77.38, H 8.82, N 6.44; HPLC retention time: (−) enantiomer: 16 min; (+) enantiomer: 13 min.

***N*-(1,2,3,4-Tetrahydronaphthalen-2-yl)-benzamide (5d):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.70 – 2.00 (m, 1H, CH_2 ring), 2.05 – 2.30 (m, 1H, CH_2 ring), 2.74 (dd, *J* = 16.2, 8.2 Hz, 1H, CH_2 ring), 2.82 – 3.05 (m, 2H, CH_2 ring), 3.23 (dd, *J* = 16.2, 5.1 Hz, 1H, CH_2 ring), 4.30 – 4.65 (m, 1H, CHN), 6.08 (broad s, 1H, NH), 7.11 (broad s, 4H ar.), 7.25 – 7.50 (m, 3H ar.), 7.60 – 7.80 (m, 2H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.5 (CH_2 ring), 28.9 (CH_2 ring), 35.7 (CH_2 ring), 45.9 (CHN), 126.00 (CH ar.), 126.2 (CH ar.), 127.1 (2 CH ar.), 128.6 (2 CH ar.), 128. 9 (CH ar.), 129.5 (CH ar.), 131.4 (CH ar.), 134.2 (C quat, ar.), 134.8 (C quat, ar.), 135.6 (C quat, ar.), 167.3 (CO amide); anal. calcd. for $C_{17}H_{17}NO$: C 81.11, H 6.77, N 5.50%; found: C 81.24, H 6.82, N 5.57%; HPLC retention time: (−) enantiomer: 47 min; (+) enantiomer: 35 min.

***N*-(1′,2′,3′,4′-Tetrahydronaphthalen-2′-yl)-(2-chloroacetamide) (5e):** Beige solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.65 – 1.90 (m, 1H, CH_2 ring), 1.95 – 2.20 (m, 1H, CH_2 ring), 2.69 (dd, *J* = 16.2, 8.5 Hz, 1H, CH_2 cycle), 2.80 – 3.00 (m, 2H, CH_2 ring), 3.13 (dd, *J* = 16.2, 5.5 Hz, 1H, CH_2 ring), 4.03 (s, 2H, $ClCH_2$), 4.15 – 4.40 (m, 1H, CHN), 6.54 (broad s, 1H, NH), 6.95 – 7.20 (m, 4H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.5 (CH_2), 28.9 (CH_2), 35.7 (CH_2), 44.7 (CHN), 59.1 (OCH_3), 72.1 (OCH_2), 125.9 (CH ar.), 126.2 (CH ar.), 128.8 (CH ar.), 129.4 (CH ar.), 134.1 (C quat, ar.), 135.4 (C quat, ar.), 169.0 (CO amide); HRMS (FAB): calcd. for $C_{12}H_{15}ClNO$ (MH^+): 224.0842; found: 224.0844; HPLC retention time: (−) enantiomer: 17 min; (+) enantiomer: 14 min.

***N*-(1′,2′,3′,4′-Tetrahydronaphthalen-2′-yl)-(2-methoxyacetamide) (5f):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.68 – 1.88 (m, 1H, CH_2 ring), 1.95 – 2.18 (m, 1H, CH_2 ring), 2.66 (dd, *J* = 16.3, 8.6 Hz, 1H, CH_2 ring), 2.80 – 2.96 (m, 2H, CH_2 ring), 3.11 (dd, *J* = 16.3, 5.4 Hz, 1H, CH_2 ring), 3.37 (s, 3H, OCH_3), 3.87 (s, 2H, OCH_2), 4.15 – 4.45 (m, 1H, CHN), 6.51 (broad s, 1H, NH), 6.98 – 7.16 (m, 4H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.5 (CH_2 ring), 28.9 (CH_2 ring), 35.7 (CH_2 ring), 44.7 (CHN), 59.1 (OCH_3), 72.1 (OCH_2), 125.9 (CH ar.), 126.2 (CH ar.), 128.8 (CH ar.), 129.4 (CH ar.), 134.1 (C quat, ar.), 135.4 (C quat, ar.), 169.0 (CO amide); HRMS: calcd. for $C_{13}H_{17}NO_2$: 219.12593; found: 219.12577; HPLC retention time: (−) enantiomer: 16 min; (+) enantiomer: 14 min.

***N*-(1′,2′,3′,4′-tetrahydronaphthalen-2′-yl)-(2-benzyloxyacetamide) (5g):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.60 – 1.90 (m, 1H, CH_2 ring), 1.95 – 2.20 (m, 1H, CH_2 ring), 2.65 (dd, *J* = 16.3, 8.5 Hz, 1H, CH_2 ring), 2.75 – 2.95 (m, 2H, CH_2 ring), 3.10 (dd, *J* = 16.3, 5.2 Hz, 1H, CH_2 cycle), 3.97 (s, 2H, OCH_2), 4.15 – 4.40 (m, 1H, CHN), 4.52 (s, 2H, OCH_2), 6.60 (d large, *J* = 7.3 Hz, 1H, NH), 6.95 – 7.15 (m, 4H ar.), 7.16-7.40 (m, 5H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 27.3 (CH_2 ring), 28.8 (CH_2 ring), 35.7 (CH_2 ring), 44.7 (CHN), 69.7 (OCH_2), 73.7 (OCH_2), 126.0 (CH ar.), 126.2 (CH ar.), 128.04 (2 CH ar.), 128.3 (CH ar.), 128.7 (2 CH ar.), 128.9 (CH ar.), 129.5 (CH ar.), 134.1 (C quat, ar.), 135.5 (C quat, ar.), 136.8 (C quat, ar.), 169.1 (CO amide); anal. calcd. for $C_{19}H_{21}NO_2$: C 76.89, H 7.13, N 4.76%; found: C 77.26, H 7.17, N 4.74%; HPLC retention time: (−) enantiomer: 12 min; (+) enantiomer: 10 min.

***N*-(7-Methyl-1,2,3,4-tetrahydronaphthalen-2-yl)-acetamide (7a):** Beige solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.60 – 1.86 (m, 1H, CH_2 ring), 1.96 (s, 3H, CH_3 amide), 1.90 – 2.10 (m, 1H, CH_2 ring), 2.27 (s, 3H, CH_3), 2.58 (dd, *J* = 16.2, 7.8 Hz, 1H, CH_2 ring), 2.70 – 2.90 (m, 2H, CH_2 ring), 3.10 (dd, *J* = 16.2, 4.9 Hz, 1H, CH_2 cycle), 4.10 – 4.40 (m, 1H, CHN), 5.50 (broad s, 1H, NH), 6.75 – 7.05 (m, 3H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$):

δ = 21.0 (CH_3), 23.5 (CH_3 amide), 26.7 (CH_2 ring), 28.7 (CH_2 ring), 35.7 (CH_2 ring), 45.1 (CHN), 127.1 (CH ar.), 128.8 (CH ar.), 130.0 (CH ar.), 132.5 (C quat, ar.), 133.9 (C quat, ar.), 135.4 (C quat, ar.), 169.9 (CO amide); HPLC retention time: (−) enantiomer: 19 min; (+) enantiomer: 13 min.

***N*-(7-Methyl-1,2,3,4-tetrahydronaphthalen-2-yl)-propionamide (7b):** Beige solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.7 Hz, 3H, CH_3 amide), 1.60 – 1.85 (m, 1H, CH_2 ring), 1.87 – 2.08 (m, 1H, CH_2 ring), 2.16 (q, *J* = 7.7 Hz, 2H, CH_2 amide), 2.26 (s, 3H, CH_3), 2.7 (dd, *J* = 16.2, 8.0 Hz, 1H, CH_2 cycle), 2.70 – 2.90 (m, 2H, CH_2 cycle), 3.06 (dd, *J* = 16.2, 5.3 Hz, 1H, CH_2 ring), 4.10 – 4.40 (m, 1H, CHN), 5.47 (broad s, 1H, NH), 6.75 – 7.05 (m, 3H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 10.0 (CH_3 amide), 21.0 (CH_3), 26.7 (CH_2 ring), 28.8 (CH_2 ring), 29.9 (CH_2 amide), 35.7 (CH_2 ring), 45.0 (CHN), 127.1 (CH ar.), 128.8 (CH ar.), 130.0 (CH ar.), 132.5 (C quat, ar.), 134.0 (C quat, ar.), 135.4 (C quat, ar.), 173.4 (CO amide); HRMS: calcd. for $C_{14}H_{19}NO$: 217.14666; found: 217.14854; HPLC retention time: (−) enantiomer: 19 min ; (+) enantiomer: 11 min.

***N*-(5-Methoxy-3,4-dihydrobenzo[*b*]pyran-3-yl)-acetamide (8a):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.93 (s, 3H, CH_3 amide), 2.69 (d large, *J* = 17.5 Hz, 1H, CH_2 ring), 2.84 (dd, *J* = 17.5, 5.5 Hz, 1H, CH_2 ring), 3.77 (s, 3H, OCH_3), 4.00 (dd, *J* = 10.9, 1.3 Hz, 1H, CH_2 ring), 4.11 (ddd, *J* = 10.9, 3.5, 2 Hz, 1H, CH_2 cycle), 4.35 – 4.60 (m, 1H, CHN), 5.79 (broad s, 1H, NH), 6.43 (d, *J* = 8.2 Hz, 1H ar.), 6.48 (d, *J* = 8.2 Hz, 1H ar.), 7.07 (t, *J* = 8.2 Hz, 1H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.4 (CH_3 amide), 25.6 (CH_2 ring), 41.9 (CHN), 55.5 (OCH_3), 67.7 (OCH_2 ring), 102.5 (CH ar.), 108.7 (C quat, ar.), 109.5 (CH ar.), 127.4 (CH ar.), 154.7 (C quat. ar.), 158.4 (C quat. ar.), 170.0 (CO amide); anal. calcd. for $C_{12}H_{15}NO_3$: C 65.19, H 6.99, N 6.32%; found: C 65.14, H 6.83, N 6.33%; HPLC retention time: (−) enantiomer: 16 min; (+) enantiomer: 19 min.

***N*-(5′-Methoxy-3′,4′-dihydrobenzo[*b*]pyran-3′-yl)-(2-methoxyacetamide) (8b):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 2.68 (dd, *J* = 17.4, 4.1 Hz, 1H, CH_2 ring), 2.91 (dd, *J* = 17.5, 6.0 Hz, 1H, CH_2 ring), 3.33 (s, 3H, OCH_3 amide), 3.77 (s, 3H, OCH_3), 3.85 (s, 2H, OCH_2 amide), 4.06 (dd, *J* = 3.4, 1.1 Hz, 2H, CH_2 ring), 4.35 – 4.60 (m, 1H, CHN), 6.43 (dd, *J* = 8.3, 1.0 Hz, 1H ar), 6.49 (dd, *J* = 8.3, 1.0 Hz, 1H ar.), 6.73 (d large, *J* = 7.3 Hz, 1H, NH), 7.07 (t, *J* = 8.3 Hz, 1H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 25.7 (CH_2 ring), 41.5 (CHN), 55.4 (OCH_3), 59.0 (OCH_3 amide), 67.5 (OCH_2 ring), 71.9 (OCH_2 amide), 102.5 (CH ar.), 108.6 (C quat, ar.), 109.5 (CH ar.), 127.4 (CH ar.), 154.7 (C quat, ar.), 158.4 (C quat., ar.), 169.4 (CO amide); anal. calcd. for $C_{12}H_{15}NO_3$: C 65.19, H 6.99, N 6.32%; found: C 65.14, H 6.83, N 6.33%; HPLC retention time: (−) enantiomer: 14 min; (+) enantiomer: 15 min.

***N*-(8′-Bromo-1,2,3,4-tetrahydronaphthalen-2-yl)-acetamide (11a):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.80 – 1.61 (m, 2H, CH_2 ring), 2.00 (s, 3H, CH_3), 2.53 (dd, *J* = 17.2, 8.4 Hz, 1H, CH_2), 2.93 – 2.80 (m, 2H, CH_2), 3.15 (dd, *J* = 17.2, 5.4 Hz, 1H, CH_2), 4.90 – 4.65 (m, 1H, CHN), 5.62 (br s, 1H, NH), 7.10 – 6.97 (m, 2H, ar), 7.40 (d, *J* = 7.1 Hz, 1H ar); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.6 (CH_3), 28.0 (CH_2 ring), 28.3 (CH_2 ring), 36.6 (CH_2 ring), 45.5 (CH), 127.4 (CH ar.), 128.0 (CH ar.), 130.2 (CH ar.), 133.8 (C quat, ar.), 138.3 (C quat., ar.), 169.6 (CO amide); HPLC retention time: (−) enantiomer: 14 min; (+) enantiomer: 22 min.

***N*-(8′-Bromo-1,2,3,4-tetrahydronaphthalen-2-yl)-benzamide (11b):** White solid. ^{1}H-NMR (200.13 MHz, $CDCl_3$): δ = 2.68 (dd, *J* = 17.4, 4.1 Hz, 1H, CH_2 ring), 2.91 (dd, *J* = 17.5, 6.0 Hz, 1H, CH_2 ring), 3.33 (s, 3H, OCH_3 amide), 3.77 (s, 3H, OCH_3), 3.85 (s, 2H, OCH_2 amide), 4.06 (dd, *J* = 3.4, 1.1 Hz, 2H, CH_2 cycle), 4.35 – 4.60 (m, 1H, CHN), 6.43 (dd, *J* = 8.3, 1.0 Hz, 1H ar.), 6.49 (dd, *J* = 8.3, 1.0 Hz, 1H ar.), 6.73 (d large, *J* = 7.3 Hz, 1H, NH), 7.07 (t, *J* = 8.3 Hz, 1H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.2 (CH_2 ring), 28.5 (CH_2 ring), 36.7 (CH_2 ring), 46.1 (CHN), 125.8 (C quat. ar.), 127.0 (2 CH ar.), 127.4 (CH ar.), 128.1 (2 CH ar.), 128.6 (CH ar.), 130.3 (CH ar.), 131.6 (CH ar.), 133.8 (C quat. ar), 134.7 (C quat. ar), 138.3 (C quat. ar.), 167.1 (CO amide); HRMS: calcd. for $C_{17}H_{16}BrNO$: 392.04153; found: 329.04398; HPLC retention time: (−) enantiomer: 21 min; (+) enantiomer: 24 min.

***N*-(3,4-Dihydrobenzo[*b*]pyran-3-yl)-acetamide (12a):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.93 (s, 3H, CH_3 amide), 2.69 (d large, *J* = 17.5 Hz, 1H, CH_2 ring), 2.84 (dd, *J* = 17.5, 5.5 Hz, 1H, CH_2 ring), 3.77 (s, 3H, OCH_3), 4.00 (dd, *J* = 10.9, 1.3 Hz, 1H, CH_2 ring), 4.11 (ddd, *J* = 10.9, 3.5, 2 Hz, 1H, CH_2 ring), 4.35 – 4.60 (m, 1H, CHN), 5.79 (broad s, 1H, NH), 6.43 (d, *J* = 8.2 Hz, 1H ar.), 6.48 (d, *J* = 8.2 Hz, 1H ar.), 7.07 (t, *J* = 8.2 Hz, 1H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.4 (CH_3 amide), 25.6 (CH_2 cycle), 41.9 (CHN), 55.5 (OCH_3), 67.7 (OCH_2 ring), 102.5 (CH ar.), 108.7 (C quat, ar.), 109.5 (CH ar.), 127.4 (CH ar.), 154.7 (C quat. ar.), 158.4 (C quat. ar.), 170.0 (CO amide); HRMS: calcd. for $C_{11}H_{13}NO_2$: 191.09463; found: 191.09161; HPLC retention time: (−) enantiomer: 16 min; (+) enantiomer: 19 min.

***N*-(3,4-Dihydrobenzo[*b*]pyran-3-yl)-benzamide (12b):** White solid. ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.93 (s, 3H, CH_3 amide), 2.69 (d large, *J* = 17.5 Hz, 1H, CH_2 ring), 2.84 (dd, *J* = 17.5, 5.5 Hz, 1H, CH_2 ring), 3.77 (s, 3H, OCH_3), 4.00 (dd, *J* = 10.9, 1.3 Hz, 1H, CH_2 ring), 4.11 (ddd, *J* = 10.9, 3.5, 2 Hz, 1H, CH_2 ring), 4.35 – 4.60 (m, 1H, CHN), 5.79 (broad s, 1H, NH), 6.43 (d, *J* = 8.2 Hz, 1H ar.), 6.48 (d, *J* = 8.2 Hz, 1H ar.), 7.07 (t, *J* = 8.2 Hz, 1H ar.); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 30.8 (CH_2 ring), 42.8 (CHN), 68.3 (OCH_2 ring), 117.0 (CH ar.), 119.4 (C quat. ar.), 109.5 (CH ar.), 127.4 (CH ar.), 154.7 (C quat. ar.), 158.4 (C quat. ar.), 170.0 (CO amide); HPLC retention time: (−) enantiomer: 14 min ; (+) enantiomer: 19 min.

Acknowledgements

The authors wish to thank Oril Industries and la Région Bretagne for support.

References and Notes

[1] H. Nozaki, S. Moriati, R. Noyori, *Tetrahedron Lett.* **1966**, 5239.

[2] W. S. Knowles, M. J. Sabacky, *J. Chem. Soc. Chem. Commun.* **1968**, 1445.

[3] H. B. Kagan, T. P. Dang, *J. Am. Chem. Soc.* **1972**, *94*, 6429.

[4] a) R. Noyori, in *Asymmetric Catalysis in Organic Synthesis*, John Wiley & Sons, New York, **1994**; b) *Catalytic Asymmetric Synthesis*, (Ed.: I. Ojima), VCH, New York, **1993**.

[5] *Catalytic Asymmetric Catalysis*; (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, Vol. 1 – 3.

[6] a) H.-U. Blaser, F. Spindler, M. Studer, *Appl. Catal. A: General* **2001**, *221*, 119; b) S. Akutagawa, *Appl. Catal. A: General* **1995**, *128*, 171.
[7] a) M. J. Burk, J. P. Martinez, J. E. Feaster, N. Cosford, *Tetrahedron* **1994**, *50*, 4399; b) D. Lucet, T. Le Gall, C. Mioskowski, *Angew. Chem. Int. Ed.* **1998**, *37*, 2580; c) H.-U. Blaser, F. Spindler, *Topics in Catal*. **1997**, *4*, 275; d) F. Fache, E. Schulz, M. L. Tommasino, M. Lemaire, *Chem. Rev.* **2000**, *100*, 2159.
[8] S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069.
[9] a) H. Takaya, T. Ohta, R. Noyori, in *Catalytic Asymmetric Synthesis; Asymmetric Hydrogenation*, VCH, Weinheim, **1993**, chapter 1; b) J. M. Brown, in *Catalytic Asymmetric Catalysis*; (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, Vol. 1, 119; c) M. J. Burk, F. Bienewald, in *Transition Metals for Organic Synthesis*, (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, 13; d) M. J. Burk, *Acc. Chem. Res.* **2000**, *33*, 363.
[10] For some recent references of hydrogenation of dehydroamino acids, see: a) T. V. RajanBabu, Y.-Y. Yan, S. Shin, *J. Am. Chem. Soc.* **2001**, *123*, 10207; b) Q.-H. Fan, G.-J. Deng, C.-C. Lin, A. S. C. Chan, *Tetrahedron: Asymmetry* **2001**, *12*, 1241; c) W. Wang, C. Xiong, J. Yang, V. J. Hruby, *Tetrahedron Lett.* **2001**, *42*, 7717; d) A. J. Robinson, C. Y. Lim, L. He, P. Ma, H.-Y. Li, *J. Org. Chem.* **2001**, *66*, 4141; e) A. J. Robinson, P. Stanislawski, D. Mulholland, L. He, H.-Y. Li, *J. Org. Chem.* **2001**, *66*, 4148; f) M. T. Reetz, D. Moulin, A. Gosberg, *Org. Lett.* **2001**, *4*, 4083; g) W. Li, Z. Zhang, D. Xiao, X. Zhang, *J. Org. Chem.* **2000**, *65*, 3489; h) M. L. Tommasino, M. Casalta, J. A. J. Breuzard, M. Lemaire, *Tetrahedron: Asymmetry* **2000**, *11*, 4835; i) K. Yonehara, K. Ohe, S. Uemura, *J. Org. Chem.* **1999**, *64*, 9381; j) S. R. Gilbertson, X. Wang, *Tetrahedron* **1999**, *55*, 11609; k) N. Derrien, C. B. Dousson, S. M. Roberts, U. Berens, M. J. Burk, M. Ohff, *Tetrahedron: Asymmetry* **1999**, *10*, 3341; l) M. J. Burk, K. M. Bedingfield, W. F. Kiesman, J. G. Allen, *Tetrahedron Lett.* **1999**, *40*, 3093; m) J. J. A. Perea, A. Börner, P. Knochel, *Tetrahedron Lett.* **1998**, *39*, 8073; n) T. Imamoto, J. Watanabe, Y. Wada, H. Masuda, H. Yamada, H. Tsuruta, S. Matsukawa, K. Yamaguchi, *J. Am. Chem. Soc.* **1998**, *120*, 1635; o) I. D. Gridnev, Y. Yamanoi, N. Higashi, H. Tsuruta, M. Yasutake, T. Imamoto, *Adv. Synth. Catal.* **2001**, *343*, 118; p) Y. Yamanoi, T. Imamoto, *J. Org. Chem.* **1999**, *64*, 2988; q) I. D. Gridnev, T. Imamoto, *Organometallics* **2001**, *20*, 545; r) F. Y. Zhang, W. H. Kwok, A. S. C. Chan, *Tetrahedron: Asymmetry* **2001**, *12*, 2337; s) M. Van Den Berg, A. J. Minnaard, E. P. Schudde, J. Van Esch, A. H. M. De Vries, J. G. De Vries, B. L. Feringa, *J. Am. Chem. Soc.* **2000**, *122*, 11539.
[11] a) B. R. James, *Catalysis Today* **1997**, *37*, 209; b) N. E. Lee, S. L. Buchwald, *J. Am. Chem. Soc*, **1994**, *116*, 5985; c) N. W. Boaz, *Tetrahedron Lett.*, **1998**, *39*, 5505.
[12] a) M. J. Burk, Y. M. Wang, J. R. Lee, *J. Am. Chem. Soc.* **1996**, *118*, 5142; b) I. D. Gridnev, M. Yasutake, N. Higashi, T. Imamoto, *J. Am. Chem. Soc.* **2001**, *123*, 5268; c) I. D. Gridnev, N. Higashi, T. Imamoto, *J. Am. Chem. Soc.* **2000**, *122*, 10486; d) W. Li, X. Zhang, *J. Org. Chem.* **2000**, *65*, 5871; e) Z. Zhang, G. Zhu, Q. Jiang, D. Xia, X. Zhang, *J. Org. Chem.* **1999**, *64*, 1774; f) M. J. Burk, G. Casy, N. B. Johnson, *J. Org. Chem.* **1998**, *63*, 6084.
[13] W. Hu, M. Yan, C.-P. Lau, S. M. Yang, A. S. C. Chan, Y. Jiang, A. Mi, *Tetrahedron Lett.* **1999**, *40*, 973.
[14] G. Zhu, X. Zhang, *J. Org. Chem.* **1998**, *63*, 9590.
[15] S. Usse, G. Guillaumet, M. C. Viaud, *10th IUPAC Symposium on Organometallic Chemistry directed towards Organic Synthesis*, 18–22 July **1999**, Versailles (France), P-495.
[16] D. M. Tschaen, L. Abramsom, D. Cai, R. Desmond, U. H. Dolling, L. Frey, S. Karady, Y. J. Shi, T. R. Kerhoeven, *J. Org. Chem.* **1995**, *60*, 4324.
[17] M. Devocelle, A. Mortreux, F. Agbossou, J. R. Dormoy, *Tetrahedron Lett.* **1999**, *40*, 4551.
[18] P. Dupau, P. Le Gendre, C. Bruneau, P. H. Dixneuf, *Synlett* **1999**, 1832.
[19] P. Dupau, C. Bruneau, P. H. Dixneuf, *Tetrahedron: Asymmetry* **1999**, *10*, 3467.
[20] a) T. Ikaryia, Y. Ishii, H. Kawano, T. Arai, M. Saburi, S. Yoshikawa, S. Akutagawa, *J. Chem. Soc. Chem. Commun.* **1985**, 922; b) T. Ohta, Y. Tonomura, K. Nozaki, H. Takaya, K. Mashima, *Organometallics* **1996**, *15*, 1521.
[21] J. P. Tranchier, V. Ratovelomanana-Vidal, J. P. Genêt, S. Troy, T. Cohen, *Tetrahedron Lett.* **1997**, *38*, 2951.
[22] P. Berthus, P. Phansavath, V. Ratovelomanana-Vidal, J. P. Genêt, A. R. Touati, T. Homri, B. Ben Hassine, *Tetrahedron: Asymmetry* **1999**, *10*, 1369.
[23] P. Guerreiro, M.-C. Caño de Andrade, J.-C Henry, J.-P. Tranchier, P. Phansavath, V. Ratovelomanana-Vidal, J. P. Genêt, T. Homri, A. R. Touati, B. Ben Hassine, *C. R. Acad .Sci. Paris. Série IIc.* **1999**, 175.
[24] S. Lee, S. P. Frescas, D. E. Nichols, *Synth. Commun.* **1995**, 2781.
[25] R. Verhe, N. Schamp, *Bull. Soc. Belg.* **1973**, *82*, 283.
[26] [(*S*)-Biphemp]Ru(O_2CCF_3)$_2$ or [(*S*)-Binap]Ru(O_2CCF_3)$_2$ gave almost the same results in this study with the eneacetamide of tetralone.
[27] a) R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.* **2001**, *40*, 40; b) M. Kitamura, T. Ohkuma, S. Inoue, N. Sayo, H. Kumobayashi, S. Akutagawa, T. Ohta, H. Takaya, R. Noyori, *J. Am. Chem. Soc.* **1988**, *110*, 629.
[28] H. Doucet, P. Le Gendre, C. Bruneau, P. H. Dixneuf, J.-C. Souvie, *Tetrahedron: Asymmetry* **1996**, *7*, 525.