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Enantioselective synthesis of 1-substituted tetrahydro-β-carboline derivatives via the asymmetric transfer hydrogenation

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Abstract

Several 1-substituted-3,4-dihydro-β-carboline derivatives were subjected to asymmetric transfer hydrogenation catalysed by chiral ruthenium complexes to give both enantiomers of 1,2,3,4-tetrahydro-β-carbolines of high optical purity and in good yields. The absolute stereochemistry of **4c** was established on the basis of X-ray analysis of its Mosher amide.

Keywords: Enantioselective reduction; Tryptamine derivatives; Alkaloids; Chirality transfer

1. Introduction

Compounds that possess the tetrahydro-β-carboline skeleton form a class of tryptamine derivatives, which have been studied extensively [1,2]. This skeleton is a common structural feature of numerous secondary metabolites, including *Vinca*-, *Rauvolfia*-, and *Harman*-type alkaloids. Many of these bases have a tremendous value to pharmacology and are attractive synthetic targets to both academic and industrial research groups. Recently, it was shown that several tetrahydro-β-carbolines have the ability to bind with high affinity to serotonin receptors in the central nervous system. This is probably responsible for their observed neuroactivity [3]. Interestingly, some other tetrahydro-β-carbolines formed in vivo from tryptamine and various carbonyl compounds disclosed a significant neurotoxic activity by promoting neuronal death comparable with the most potent endogenous toxins [4].

On the other hand, the derivatives of biologically important amines (e.g. catecholamines) and long-chain fatty acids have gained considerable interest in recent years as a new family of lipids [5].

Recently, we have developed a general method for the construction of a novel class of fatty acids-derived tetrahydroisoquinolines [6]. During our collaboration with biochemical investigators [7] the need arose for the synthesis of an analogous series of tetrahydro-β-carbolines, possibly in a stereoselective way. In this respect, the Bischler–Napieralski-based methodology appeared quite attractive since it provided the prochiral environment for enantioselective reductions of the imine moiety.

2. Experimental

The NMR spectra were recorded on a Varian Unity Plus spectrometer operating at 500 MHz for ^{1}H NMR and at 125 MHz for ^{13}C NMR. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ and are given as δ values (in ppm) relative

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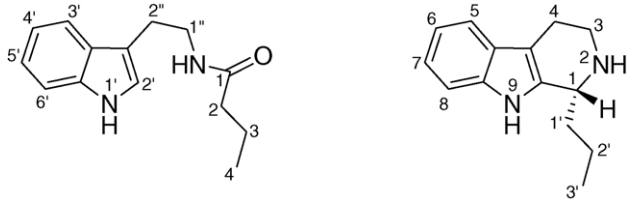


Fig. 1. Atom numbering for spectral data listing.

to TMS. Mass spectra were collected on AMD 604 apparatus. Optical rotation was measured on a Perkin-Elmer 247 MC polarimeter. TLC analyses were performed on silica gel plates (Merck Kiesegel GF_{254}) and visualized using UV light or iodine vapour. Column chromatography was carried out at atmospheric pressure using Silica Gel 60 (230–400 mesh, Merck) using mixtures of chloroform/methanol as eluents. Melting points were determined on a Boetius hot-plate microscope and were uncorrected. All solvents used in the reactions were anhydrous.

Fig. 1 shows the numbering convention for presentation of the NMR data in the experimental part.

The single crystal X-ray measurements were done on a KUMA KM4 CCD κ-axis diffractometer. After initial corrections and data reduction intensities of reflections were used to solve and consecutively refine structures. The direct methods from SHELXS-97 [8] and procedures from SHELXL-97 [9] served for these purposes.

2.1. Synthesis of tryptamides

2.1.1. N-[2-(indol-3-yl)ethyl]acetamide (3a)

To a stirred suspension of tryptamine **1** (3.0 g, 18.7 mmol) in dry CH_2Cl_2 (45 mL) a solution of acetic anhydride **2a** (3.0 mL, 3.18 mmol) and triethylamine (5.2 mL, 37.4 mmol) in CH_2Cl_2 (10 mL) was added dropwise. After 10 min stirring at room temperature the reaction mixture was treated with saturated aqueous $NaHCO_3$ solution, organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. Purification by column chromatography using $CHCl_3$:CH_3OH (95:5) afforded compound **3a** as a colourless solid (3.7 g, 98%), mp 78–79 °C (Ref. [10] mp 76–77 °C). The spectroscopic data were in agreement with those reported in the literature [11].

2.1.2. N-[2-(indol-3-yl)ethyl]butyramide (3b)

Tryptamine **1** (3.0 g, 18.7 mmol) and butyric acid **2b** (5.17 mL, 56.2 mmol) in xylene (60 mL) were heated at reflux using a Dean-Stark apparatus for 4 h. The resulting mixture was cooled to room temperature, basified with 10% aqueous NaOH solution and extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column with $CHCl_3$:CH_3OH (95:5) to give **3b** (4.0 g, 93%) as light beige solid, mp 84–86 °C (Ref. [12] mp 85–86 °C). The spectroscopic data were in agreement with those reported in the literature [12].

2.1.3. N-[2-(indol-3-yl)ethyl]nonanamide (3c)

This compound was synthesised according to the procedure described for amide **3b**. Amide **3c** (4.9 g, 87%) was obtained as a light beige solid, mp 95–97 °C. ^{1}H NMR: δ 8.18 (s, 1H-N1′), 7.61 (d, J = 7.5 Hz, 1H-6′), 7.38 (d, J = 8.0 Hz, 1H-3′), 7.21 (t, J = 7.0 Hz, 1H-5′), 7.123 (t, J = 7.0 Hz, 1H-4′), 7.02 (d, J = 2.0 Hz, 1H-2′), 5.54 (s, 1H-NH), 3.60 (q, J = 6.0 Hz, 2H-1″), 2.97 (t, J = 6.5 Hz, 2H-2″), 2.09 (t, J = 7.5 Hz, 2H-2), 1.57 (m, 2H-3), 1.25 (m, 10H-4,5,6,7,8), 0.87 (t, J = 7.0, 3H-9). ^{13}C NMR: δ 173.21, 136.43, 127.36, 122.19, 122.04, 119.46, 118.73, 113.03, 111.29, 39.67, 36.93, 31.83, 29.32, 29.31, 29.15, 25.76, 25.38, 22.65, 14.11. LRMS (ESI): m/z = 323.3 $[M + Na]^+$.

2.1.4. N-[2-(indol-3-yl)ethyl]octadecanoylamide (3d)

This compound was synthesised according to the procedure described for amide **3b**. Amide **3d** (6.8 g, 85%) was obtained as a colourless solid, mp 111–113 °C (Ref. [13] mp 103 °C).

^{1}H NMR: δ 8.26 (s, 1H-N1′), 7.61 (d, J = 8.0 Hz, 1H-6′), 7.38 (d, J = 8.0 Hz, 1H-3′), 7.21 (m, 1H-5′), 7.12 (t, 1H-4′), 7.03 (d, J = 2.0 Hz, 1H-2′), 5.51 (s, 1H–NH), 3.61 (q, J = 6.0 Hz, 2H-1″), 2.97 (t, J = 6.5 Hz, 2H-2″), 2.09 (t, J = 7.5 Hz, 2H-2), 1.57 (m, 2H-3), 1.25 (m, 28H-4–17), 0.88 (t, J = 7.0, 3H-18). ^{13}C NMR: δ 173.18, 136.42, 127.37, 122.18, 122.01, 119.49, 118.75, 113.10, 111.27, 39.65, 36.94, 31.94, 29.71, 29.67, 29.64, 29.51, 29.38, 29.31, 25.77, 25.38, 22.71, 14.14. LRMS (ESI): m/z = 449.5 $[M + Na]^+$.

2.1.5. (9Z)-N-[2-(indol-3-yl)ethyl]octadec-9-enamide (3e)

Amide **3e** was synthesised according to the procedure described by us [14] by reacting tryptamine **1** with oleic acid **2e** in the presence of BOP. Compound **3e** was obtained as a colourless solid (1.97 g, 89%), mp 69–71 °C.

^{1}H NMR: δ 8.38 (s, 1H-N1′), 7.60 (d, J = 8.5 Hz, 1H-6′), 7.37 (d, J = 8.0 Hz, 1H-3′), 7.19 (t, J = 7.5 Hz, 1H-5′), 7.11 (t, J = 7.5 Hz, 1H-4′), 7.00 (s, 1H-2′), 5.84 (s, 1H–NH), 5.34 (m, 2H-9,10), 3.60 (q, J = 6.0 Hz, 2H-1″), 2.97 (t, J = 6.5 Hz, 2H-2″), 2.11 (t, J = 7.5 Hz, 2H-2), 2.00 (m, 4H-8,11), 1.57 (m, 2H-3), 1.26 (m, 22H-4–7,12–17), 0.88 (t, J = 7.5, 3H-18).

^{13}C NMR: δ 173.62, 136.44, 130.02, 129.77, 127.33, 122.14, 122.10, 119.42, 118.66, 111.79, 111.35, 39.89, 36.67, 31.92, 29.78, 29.73, 29.63, 29.54, 29.34, 29.27, 29.25, 29.15, 27.24, 27.19, 25.81, 25.28, 22.69, 14.14.

2.1.6. (5Z,8Z,11Z,14Z)-N-[2-(indol-3-yl)ethyl]icosa-5,8,11,14-tetraenamide (3f)

Amide **3f** was synthesised according to the procedure described by us [14] by reacting tryptamine **1** with arachidonic acid **2e** in the presence of BOP. Compound **3f** (0.21 g, 86%) was obtained as a yellow oil.

^{1}H NMR: δ 8.26 (s, 1H-N1′), 7.60 (d, J = 8.0 Hz, 1H-6′), 7.38 (d, J = 8.0 Hz, 1H-3′), 7.20 (t, J = 7.5 Hz, 1H-5′), 7.12 (t, J = 7.5 Hz, 1H-4′), 7.02 (s, 1H-2′), 5.75 (s, 1H–NH), 5.30–5.42 (m, 8H-5,6,8,9,11,12,14,15), 3.60 (q, J = 6.0 Hz, 2H-1″), 2.97 (t, J = 6.5 Hz, 2H-2″), 2.81 (m, 6H-7,10,13), 2.13 (t, J = 8.0 Hz, 2H-2), 2.05 (m, 4H-4,16), 1.67 (m, 2H-3), 1.25–1.38 (m, 6H-17,18,19), 0.88 (t, J = 7.0, 3H-18). ^{13}C NMR: δ 173.18, 136.41, 130.554, 129.07, 128.74, 128.62, 128.23, 128.17, 127.75, 127.51, 127.32, 122.19, 122.06, 119.47, 118.67, 112.87, 111.31, 39.84, 36.03, 31.51, 29.32, 27.22, 26.65, 25.64, 25.63, 25.62, 25.56, 25.29, 22.57, 14.08. HR MS (ESI): m/z = 469.3190 $[M + Na]^+$; calcd. mass for $C_{30}H_{42}N_2ONa$ 469.3195.

2.2. Synthesis of 1-substituted-3,4-dihydro-β-carbolines (4a–f)

Imines **4a** and **4b** were synthesised as described in the literature [15] by reacting tryptamides with P_2O_5 in boiling xylene. Compound **4a** was obtained in a form of colourless crystals (92%), mp 176–179 °C (Ref. [16] mp 175–178 °C) and **4b** as yellow crystals (90%), mp 165–167 °C (Ref. [17] mp 162–165 °C). The spectroscopic data were in agreement with those reported in the literature [18] – for imine **4a**, and [12] – for imine **4b**.

Typical procedure for the synthesis of imine **4c**: $POCl_3$ (2.19 mL, 23.3 mmol) was added to a solution of amide **4c** (1.0 g, 3.3 mmol) in CH_2Cl_2 (30 mL). The solution was heated at reflux for **4h** and then cooled to room temperature. The volatiles were evaporated under reduced pressure and the residue was dissolved in 30 mL of $CHCl_3$, made alkaline with 10% NaOH, extracted with $CHCl_3$, dried over $MgSO_4$. The residue after evaporation of the solvent was chromatographed on a silica column with $CHCl_3$:CH_3OH (95:5) to give compound (**4c**) as a yellow oil (0.49 g, 52%). The imines **4d–f** were obtained accordingly.

^{1}H NMR: δ 12.16 (s, 1H-N9), 7.68 (d, J = 8.5 Hz, 1H-5), 7.59 (d, J = 8.5 Hz, 1H-8), 7.34 (t, J = 7.5 Hz, 1H-6), 7.15 (t, J = 7.5 Hz, 1H-7), 3.91 (t, J = 8.5 Hz, 2H-3), 3.28 (t, J = 8.0 Hz, 2H-4), 3.11 (t, J = 8.5 Hz, 2H-1′), 1.82 (q, J = 7.5 Hz, 2H-2′), 1.37 (m, 2H-3′), 1.08–1.19 (m, 8H-4′–7′), 0.77 (t, J = 7.0 Hz, 3H-8′). ^{13}C NMR: δ 169.06, 141.00, 128.03, 126.17, 124.41, 122.35, 121.53, 120.90, 113.94, 43.12, 33.45, 31.80, 29.41, 29.34, 29.13, 28.47, 22.58, 19.52, 14.04.

2.3. Synthesis of (1S)- and (1R)-1-substituted-1,2,3,4-tetrahdro-β-carbolines (6a–f)

2.3.1. (1S)-1-methyl-2,3,4,9-tetrahydro-1H-β-carboline

Representative procedure for the enantioselective hydrogenation of imine **4a**–**f**: the catalyst (*R*,*R*)-5 was pre-formed from $[RuCl_2(C_6H_6)]_2$ (6 mg, 24 μmol) and (1*R*,2*R*)-1,2-diphenyl-*N*-(*p*-toluoylsulfonyl)ethylenediamine (7.3 mg, 20 μmol) in 4 mL CH_3CN.

To a solution of imine **4a** (0.84 g, 4.58 mmol) in CH_3CN (5 mL) a 5:2 formic acid/triethylamine azeotropic mixture (2.5 mL) was introduced, and then the pre-formed catalyst (*R*,*R*)-5 was added. The mixture was stirred at room temperature for 12 h and afforded, after column chromatography with $CHCl_3$:CH_3OH:NH_{3aq} (95:5:1), (1*S*)-**6a** (0.71 g, 84%) as colourless crystals mp 179–181 °C (Ref. [15] mp 176–177 °C), $[\alpha]_D^{23} = -56.8$ (*c* 2.0, EtOH) (Ref. [19] $[\alpha]_D^{23} = -52.0$ (*c* 2.0, EtOH)). The spectroscopic data were in agreement with those reported in the literature [20].

Melting point of (1*S*)-**6a** and (1*R*)-**6a** were identical. For compound (1*R*)-**6a** $[\alpha]_D^{23} = +55.6$ (*c* 2.0, EtOH).

2.3.2. (1S)- and (1R)-1-propyl-2,3,4,9-tetrahydro-1H-β-carboline (6b)

(1*S*)-**6b**: a yellow oil (79%), $[\alpha]_D^{23} = -73.5$ (*c* 1.0, EtOH) (Ref. [21] $[\alpha]_D^{23} = -30.0$); (1*R*)-**6b**: (88%), $[\alpha]_D^{23} = +72.7$ (*c* 1.0, EtOH).

^{1}H NMR: δ 7.87 (s, 1H-N9), 7.49 (d, J = 8.5 Hz, 1H-5), 7.29 (d, J = 8.0 Hz, 1H-8), 7.15–7.07 (m, 2H-6,7), 4.05 (m, 1H-1), 3.35 (m, 1H-3), 3.02 (m, 1H-3), 2.73 (m, 2H-4), 1.86–1.79 (m, 2H-1′), 1.69–1.62 (m, 1H-N2), 1.59–1.45 (m, 2H-2′), 0.98 (t, J = 7.0 Hz, 3H-3′).

^{13}C NMR: δ 136.37, 135.59, 127.54, 121.42, 119.31, 118.03, 110.66, 108.90, 52.43, 42.60, 37.23, 22.71, 19.12, 14.26. LR MS (ESI): m/z = 215.2 $[M + H]^+$.

2.3.3. (1S)- and (1R)-1-octyl-2,3,4,9-tetrahydro-1H-β-carboline (6c)

(1*S*)-**6c**: a yellow oil (81%), $[\alpha]_D^{23} = -54.0$ (*c* 1.0, EtOH); (1*R*)-**6c**: (85%), $[\alpha]_D^{23} = +54.7$ (*c* 1.0, EtOH).

^{1}H NMR: δ 7.79 (s, 1H-N9), 7.49 (d, J = 7.0 Hz, 1H-5), 7.32 (d, J = 7.0 Hz, 1H-8), 7.16–7.08 (m, 2H-6,7), 4.05 (m, 1H-1), 3.36 (m, 1H-3), 3.02 (m, 1H-3), 2.75 (m, 2H-4), 1.91–1.82 (m, 2H-N2,1′), 1.69–1.62 (m, 1H-1′), 1.59–1.42 (m, 2H-2′), 1.41–1.27(m, 10H-3′–7′), 0.88 (t, J = 7.0 Hz, 3H-8′). ^{13}C NMR: δ 136.32, 135.58, 127.55, 121.47, 119.36, 118.05, 110.67, 108.95, 52.72, 42.64, 35.09, 31.87, 29.89, 29.54, 29.29, 25.93, 22.69, 22.67, 14.12.

2.3.4. (1S)- and (1R)-1-heptadecyl-2,3,4,9-tetrahydro-1H-β-carboline (6d)

(1*S*)-**6d**: a yellow solid (77%), mp 87–89 °C, $[\alpha]_D^{23} = -34.0$ (*c* 1.0, $CHCl_3$); (1*R*)-**6d**: (79%), mp 86–88 °C, $[\alpha]_D^{23} = +33.7$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 7.78 (s, 1H-N9), 7.49 (d, J = 7.5 Hz, 1H-5), 7.29 (d, J = 8.0 Hz, 1H-8), 7.15–7.07 (m, 2H-6,7), 4.08 (m, 1H-1), 3.36 (m, 1H-3), 3.03 (m, 1H-3), 2.75 (m, 2H-4), 2.12–1.83 (m, 2H-N2,1′), 1.72–1.64 (m, 1H-1′), 1.59–1.42 (m, 2H-2′), 1.39–1.22 (m, 28H-3′–16′), 0.88 (t, J = 7.0 Hz, 3H-3′). ^{13}C NMR: δ 136.09, 135.60, 127.52, 121.53, 119.40, 118.06, 110.69, 108.92, 52.70, 42.55, 35.02, 31.94, 29.89, 29.71, 29.67, 29.63, 29.58, 29.38, 25.93, 22.71, 22.56, 14.14. LR MS (ESI): m/z = 411.4 $[M + H]^+$.

*2.3.5. (1S)- and (1R)-1-[(8′Z)-heptadec-8′-enyl]-2,3,4,9-tetrahydro-1H-β-carboline (**6e**)*

(1*S*)-**6e**: a yellow oil (77%), $[\alpha]_D^{23} = -26.5$ (*c* 1.0, $CHCl_3$); (1*R*)-**6e**: (84%), $[\alpha]_D^{23} = +25.8$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 7.87 (s, 1H-N9), 7.48 (d, *J* = 8.0 Hz, 1H-5), 7.32 (d, *J* = 8.0 Hz, 1H-8), 7.16–7.08 (m, 2H-6,7), 5.39–5.30 (narrow m, 2H-8′,9′), 4.09 (m, 1H-1), 3.36 (m, 1H-3), 3.05 (m, 1H-3), 2.76 (m, 2H-4), 2.03–1.92 (m, 5H-N2,7′,10′), 1.91–1.82 (m, 1H-1′), 1.74–1.66 (m, 1H-1′), 1.59–1.41 (m, 2H-2′), 1.42–1.21 (m, 20H-6′,11′-16′), 0.88 (t, *J* = 7.0 Hz, 3H, H-17′).

^{13}C NMR: δ 135.70, 135.62, 130.01, 129.78, 127.41, 121.59, 119.42, 118.08, 110.75, 108.76, 52.67, 42.37, 34.87, 31.92, 29.84, 29.78, 29.67, 29.54, 29.48, 29.33, 29.28, 29.21, 27.24, 27.20, 25.91, 22.70, 22.30, 14.14. LR MS (ESI): *m*/*z* = 409.4 $[M + H]^+$.

*2.3.6. (1R)-1-[(4′Z,7′Z,10′Z,13′Z)-nonadeca-4′,7′,10′,13′-tetraenyl]-2,3,4,9-tetrahydro-1H-β-carboline (**6f**)*

A yellow oil (70%), $[\alpha]_D^{23} = +10.2$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 7.89 (s, 1H-N9), 7.48 (d, *J* = 8.0 Hz, 1H-5), 7.32 (d, *J* = 8.0 Hz, 1H-8), 7.17–7.08 (m, 2H-6,7), 5.41–5.32 (m, 8H-4′,5′,7′,8′10′,11′,13′,14′), 4.17 (s, 1H-1), 3.38 (m, 1H-3), 3.09 (m, 1H-3), 2.81 (m, 8H-4,6′,9′,12′), 2.19–2.02 (m, 5H-N2,3′,15′), 1.94–1.86 (m, 1H-1′), 1.80–1.72 (m, 1H-1′), 1.70–1.52 (m, 2H-2′), 1.38–1.25 (m, 6H-6′,16′–17′,18′), 0.88 (t, *J* = 7.0 Hz, 3H, H-19′). ^{13}C NMR: δ 136.06, 135.75, 130.57, 129.49, 128.63, 128.56, 128.25, 128.23, 127.86, 127.53, 127.27, 121.81, 119.55, 118.16, 110.83, 108.67, 52.54, 42.03, 34.05, 31.52, 29.33, 27.23, 27.13, 25.73, 25.71, 25.67, 25.66, 22.59, 21.84, 14.09. HR MS (ESI): *m*/*z* = 431.3436 $[M + H]^+$; calcd. mass for $C_{30}H_{43}N_2$ 431.3426.

*2.4. Synthesis of Mosher acid derivatives (**7a**–**e**)*

*2.4.1. (1S)-1-methyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1S,2″R)-**7a**]*

Representative procedure for the synthesis of Mosher acid amides. The Mosher acid chloride was prepared without isolation: *R*-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (0.12 g, 0.53 mmol) with $SOCl_2$ (0.058 mL, 0.79 mmol) in toluene (12 mL) was heated at reflux for 3 h. To a stirred solution of amine (1*S*)-**6a** (78 mg, 0.42 mmol) and triethylamine (0.14 mL, 1.01 mmol) in hexane (15 mL) a pre-formed Mosher acid chloride (0.13 g, 0.50 mmol) in CH_2Cl_2 (10 mL) was added dropwise and heated at reflux for 1 h. The reaction mixture was then treated with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2, washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by chromatography with $CHCl_3$:CH_3OH (98:2) to give (1*S*,2″*R*)-**7a** (140 mg, 83%) as a colourless solid, mp 307–309 °C, $[\alpha]_D^{23} = +162.8$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.93 (s, 1H-N9), 7.55–7.24 (m, 7H-5,8, Ph), 7.11–6.99 (m, 2H-6,7), 6.1 (q, *J* = 7.0 Hz, 1H-1), 4.33 (dd, J_1 = 4.5 Hz, J_2 = 5.0 Hz, 1H-3), 3.82 (d, *J* = 1.0 Hz, 3H–OCH_3), 3.30 (m, 1H-4), 2.17 (dd, J_1 = 3.0 Hz, J_2 = 3.0 Hz, 1H-3), 1.67 (d, *J* = 7.0 Hz, 3H-1′), 1.45 (m, 1H-4). ^{13}C NMR: δ 164.89, 136.22, 134.13, 133.96, 129.44, 128.38, 126.76, 126.28, 123.94 (q, $^1J_{CF}$ = 289.5 Hz), 121.88, 119.35, 117.91, 111.20, 106.79, 84.88 (q, $^2J_{CF}$ = 25.2 Hz), 55.50, 46.32, 38.87, 19.90, 19.41. LR MS (ESI): *m*/*z* = 425.2 $[M + Na]^+$.

*2.4.2. (1R)-1-methyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1R,2″R)-**7a**]*

A colourless solid (77%), mp 136–138 °C, $[\alpha]_D^{23} = -54.0$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.23 (s, 1H-N9), 7.62–7.45 (m, 7H-5,8, Ph), 7.42–7.36 (m, 2H-6,7), 5.96 (q, *J* = 7.0 Hz, 1H-1), 4.10 (dd, J_1 = 5.0 Hz, J_2 = 4.5 Hz, 1H-3), 3.22 (d, *J* = 1.5 Hz, 3H–OCH_3), 2.91–2.73 (m, 2H-4), 2.65 (dd, J_1 = 3.0 Hz, J_2 = 3.0 Hz, 1H-3), 1.65 (d, *J* = 6.5 Hz, 3H-1′). ^{13}C NMR: δ 164.99, 136.25, 134.59, 134.15, 129.50, 128.61, 126.43, 126.37, 123.77 (q, $^1J_{CF}$ = 289.5 Hz), 121.98, 119.50, 117.93, 111.28, 106.47, 85.04 (q, $^2J_{CF}$ = 25.2 Hz), 56.44, 46.85, 39.97, 21.68, 18.31. LR MS (ESI): *m*/*z* = 425.2 $[M + Na]^+$.

*2.4.3. (1S)-1-propyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1S,2″R)-**7b**]*

A colourless solid (74%), mp 198–201 °C, $[\alpha]_D^{23} = +127.0$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.26 (s, 1H-N9), 7.53–7.23 (m, 7H-5,8, Ph), 7.11 (t, *J* = 7.0 Hz, 1H-6), 7.02 (t, *J* = 7.0 Hz, 1H-7), 5.95 (t, *J* = 7.0 Hz, 1H-1), 4.43 (dd, J_1 = 5.0 Hz, J_2 = 5.5 Hz, 1H-3), 3.83 (d, *J* = 1.0 Hz, 3H–OCH_3), 3.32 (m, 1H-4), 2.10 (dd, J_1 = 4.0 Hz, J_2 = 4.5 Hz, 1H-3), 1.98–1.87 (m, 2H-1′), 1.63–1.57 (m, 2H-2′), 1.28 (m, 1H-4), 1.01 (t, *J* = 7.0 Hz, 3H-3′).

^{13}C NMR: δ 164.99, 135.95, 133.95, 133.45, 129.38, 128.38, 126.71, 126.39, 123.83 (q, $^1J_{CF}$ = 289.5 Hz), 121.88, 119.39, 117.97, 110.95, 107.29, 85.91 (q, $^2J_{CF}$ = 25.2 Hz), 55.69, 49.89, 39.08, 37.18, 19.98, 19.75, 14.29. LR MS (ESI): *m*/*z* = 453.2 $[M + Na]^+$.

*2.4.4. (1R)-1-propyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1R,2″R)-**7b**]*

A colourless solid (68%), mp 239–241 °C, $[\alpha]_D^{23} = -12.0$ (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.29 (s, 1H-N9), 7.64–7.34 (m, 7H-5,8, Ph), 7.16 (t, *J* = 7.0 Hz,1H-6), 7.08 (t, *J* = 7.0 Hz, 1H-7), 5.82 (t, *J* = 7.0 Hz, 1H-1), 4.08 (dd, J_1 = 5.5 Hz, J_2 = 4.0 Hz, 1H-3), 3.67 (d, *J* = 1.5 Hz, 3H–OCH_3), 2.94–2.80 (m, 2H-4), 2.64–2.61 (dd, J_1 = 2.5 Hz, J_2 = 3.5 Hz, 1H-3), 1.96–1.87 (m, 2H-1′), 1.62–1.57 (m, 2H-2′), 1.02 (t, *J* = 7.0 Hz, 3H-3′). ^{13}C

NMR: δ 165.12, 136.05, 134.36, 133.96, 129.44, 128.49, 126.58, 126.46, 123.69 (q, $^1J_{CF}$ = 289.5 Hz), 122.02, 119.58, 117.97, 111.12, 106.88, 85.08 (q, $^2J_{CF}$ = 25.2 Hz), 56.45, 50.29, 40.31, 36.35, 21.51, 19.68, 14.32. LR MS (ESI): *m/z* = 453.2 $[M + Na]^+$.

*2.4.5. (1S)-1-octyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1S,2″R)-**7c**]*

A colourless solid (67%), mp 197–199 °C, $[\alpha]_D^{23}$ = +105.4 (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.23 (s, 1H-N9), 7.53–7.23 (m, 7H-5,8, Ph), 7.11 (t, *J* = 7.0 Hz, 1H-6), 7.02 (t, *J* = 7.5 Hz, 1H-7), 5.95 (t, *J* = 7.0 Hz, 1H-1), 4.38 (dd, J_1 = 5.5 Hz, J_2 = 5.5 Hz, 1H-3), 3.83 (d, *J* = 1.0 Hz, 3H–OCH_3), 3.35–3.29 (m, 1H-4), 2.11 (dd, J_1 = 3.5 Hz, J_2 = 3.5 Hz, 1H-3), 2.02–1.84 (m, 2H-1′), 1.61–1.54 (m, 3H-4,2′), 1.28 (m, 10H-3′-7′), 0.88 (t, *J* = 7.0, 3H-8′). ^{13}C NMR: δ 164.94, 135.93, 133.95, 133.49, 129.38, 128.39, 126.71, 126.38, 123.82 (q, $^1J_{CF}$ = 289.5 Hz), 121.87, 119.38, 117.97, 110.96, 107.25, 85.00 (q, $^2J_{CF}$ = 25.2 Hz), 55.67, 50.03, 39.13, 35.07, 31.83, 29.86, 29.49, 29.24, 26.63, 22.65, 19.78, 14.10. LR MS (ESI): *m/z* = 523.3 $[M + Na]^+$.

*2.4.6. (1R)-1-octyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1R,2″R)-**7c**]*

Colourless crystals (74%), mp 187–188 °C, $[\alpha]_D^{23}$ = −3.2*c* (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.38 (s, 1H-N9), 7.64–7.35 (m, 7H-5,8, Ph), 7.16 (t, *J* = 6.5 Hz,1H-6), 7.08 (t, *J* = 6.5 Hz, 1H-7), 5.83 (t, *J* = 6.5 Hz, 1H-1), 4.09 (dd, J_1 = 5.0 Hz, J_2 = 4.5 Hz, 1H-3), 3.68 (d, *J* = 1.5 Hz, 3H–OCH_3), 2.94–2.80 (m, 2H-4), 2.63 (dd, J_1 = 3.0 Hz, J_2 = 3.0 Hz, 1H-3), 2.01–1.84 (m, 2H-1′), 1.54–1.48 (m, 2H-2′), 1.29 (m, 10H-3′-7′), 0.89 (t, *J* = 7.0 Hz, 3H-8′). ^{13}C NMR: δ 165.09, 136.04, 134.35, 134.00, 129.42, 128.45, 126.60, 126.46, 123.69 (q, $^1J_{CF}$ = 289.5 Hz), 121.97, 119.53, 117.93, 111.13, 106.78, 85.07 (q, $^2J_{CF}$ = 25.2 Hz), 56.46, 50.41, 40.32, 34.32, 31.89, 29.99, 29.61, 29.30, 26.31, 22.67, 21.51, 14.12. LR MS (ESI): *m/z* = 523.3 $[M + Na]^+$.

Crystal structure: plate-like, colourless orthorhombic crystals from the $P2_12_12_1$ space group; *a* = 9.124(3), *b* = 11.974(3), *c* = 24.397(5) Å, *V* = 2665.4(12) Å^3, *Z* = 4, ρ = 1.247 g cm^{-3}, *F*(0 0 0) = 1064, μ(Mo Kα) = 0.092 mm^{-1}. A 20,580 reflections measured, 5994 of them independent (R_{int} = 0.0446). Final *R* and *wR* of 0.0357 and 0.0772, respectively, for 5075 observed independent reflections with $I > 2\sigma(I)$. The absolute structure was determined basing on the configuration of the Mosher acid residue and confirmed by the Flack parameter determination [−0.4(5)] [22].

*2.4.7. (1S)-1-heptadecyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1S,2″R)-**7d**]*

A colourless solid (58%), mp 90–92 °C, $[\alpha]_D^{23}$ = +73.2 (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.12 (s, 1H-N9), 7.53–7.23 (m, 7H-5,8, Ph), 7.11 (t, *J* = 7.0 Hz, 1H-6), 7.02 (t, *J* = 7.0 Hz, 1H-7), 5.93 (t, *J* = 7.0 Hz, 1H-1), 4.37 (dd, J_1 = 5.0 Hz, J_2 = 4.5 Hz, 1H-3), 3.82 (s, 3H–OCH_3), 3.34–3.28 (m, 1H-4), 2.11 (dd, J_1 = 3.5 Hz, J_2 = 3.5 Hz, 1H-3), 2.01–1.83 (m, 2H-1′), 1.61–1.54 (m, 3H-4,2′), 1.25 (m, 28H-3′-16′), 0.88 (t, *J* = 7.0, 3H-17′).

^{13}C NMR: δ 163.90, 134.90, 132.94, 132.45, 128.36, 127.36, 125.69, 125.38, 122.81 (q, $^1J_{CF}$ = 289.5 Hz), 120.87, 118.39, 116.97, 109.92, 106.31, 83.97 (q, $^2J_{CF}$ = 25.2 Hz), 54.65, 49.00, 38.12, 34.04, 30.92, 28.84, 28.70, 28.67, 28.65, 28.63, 28.57, 28.52, 28.35, 28.30, 25.63, 21.68, 18.75, 13.11. LR MS (ESI): *m/z* = 649.5 $[M + Na]^+$.

*2.4.8. (1R)-1-heptadecyl-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1R,2″R)-**7d**]*

A colourless solid (64%), mp 114–116 °C, $[\alpha]_D^{23}$ = −3.2 (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.42 (s, 1H-N9), 7.64–7.35 (m, 7H-5,8, Ph), 7.16 (t, *J* = 7.0 Hz, 1H-6), 7.08 (t, *J* = 6.5 Hz, 1H-7), 5.85 (t, *J* = 6.5 Hz, 1H-1), 4.09 (dd, J_1 = 5.0 Hz, J_2 = 4.5 Hz, 1H-3), 3.68 (s, 3H–OCH_3), 2.94–2.80 (m, 2H-4), 2.63 (dd, J_1 = 3.0 Hz, J_2 = 3.5 Hz, 1H-3), 2.02–1.85 (m, 2H-1′), 1.56–1.48 (m, 2H-2′), 1.26 (m, 28H-3′-16′), 0.88 (t, *J* = 7.0 Hz, 3H-8′).

^{13}C NMR: δ 165.10, 136.04, 134.35, 134.01, 129.41, 128.45, 126.60, 126.45, 123.69 (q, $^1J_{CF}$ = 289.5 Hz), 121.95, 119.51, 117.91, 111.13, 106.73, 85.07 (q, $^2J_{CF}$ = 25.2 Hz), 56.46, 50.39, 40.31, 34.32, 31.92, 30.00, 29.71, 29.66, 29.65, 29.59, 29.56, 29.36, 26.28, 22.69, 21.50, 14.12. LR MS (ESI): *m/z* = 649.5 $[M + Na]^+$.

*2.4.9. (1S)-1-[(8′Z)-heptadec-8′-enyl]-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1S,2″R)-**7e**]*

An oil (62%), $[\alpha]_D^{23}$ = +65.8 (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.17 (s, 1H-N9), 7.53–7.23 (m, 7H-5,8, Ph), 7.12 (t, *J* = 7.5 Hz, 1H-6), 7.02 (t, *J* = 7.5 Hz, 1H-7), 5.91 (t, *J* = 7.0 Hz, 1H-1), 5.36 (m, 2H-8′,9′), 4.37 (dd, J_1 = 5.5 Hz, J_2 = 5.5 Hz, 1H-3), 3.82 (s, 3H–OCH_3), 3.34–3.27 (m, 1H-4), 2.10 (dd, J_1 = 3.5 Hz, J_2 = 3.0 Hz, 1H-3), 2.01–1.83 (m, 6H-1′,7′,10′), 1.63–1.52 (m, 3H-4,2′), 1.26 (m, 20H-3′–6′,11′–16′), 0.88 (t, *J* = 7.0, 3H-17′). ^{13}C NMR: δ 164.92, 135.92, 133.96, 133.44, 130.03, 129.67, 129.38, 128.37, 126.70, 126.39, 123.81 (q, $^1J_{CF}$ = 289.5 Hz), 121.90, 119.42, 117.99, 110.94, 107.35, 84.98 (q, $^2J_{CF}$ = 25.2 Hz), 55.65, 50.01, 39.12, 35.04, 32.62, 31.91, 29.77, 29.70, 29.66, 29.61, 29.53, 29.49, 29.32, 29.20, 27.23,26.66, 22.69, 19.76, 14.12. LR MS (ESI): *m/z* = 647.4 $[M + Na]^+$.

*2.4.10. (1R)-1-[(8′Z)-heptadec-8′-enyl]-2-[(2″R)-3″,3″,3″-trifluoro-2″-methoxy-2″-phenylpropanoyl]-3,4,9-trihydro-1H-β-carboline [(1R,2″R)-**7e**]*

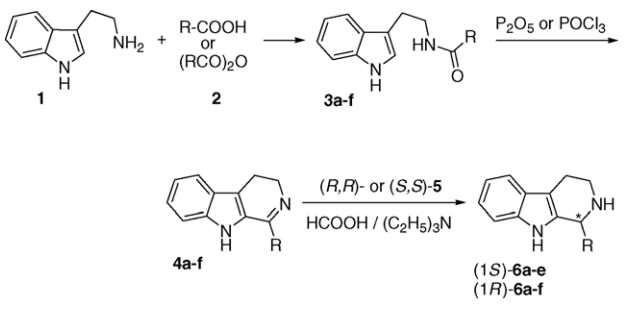
An oil (58%), $[\alpha]_D^{23}$ = +4.9 (*c* 1.0, $CHCl_3$).

^{1}H NMR: δ 8.41 (s, 1H-N9), 7.64–7.35 (m, 7H-5,8, Ph), 7.16 (t, J = 7.5 Hz, 1H-6), 7.08 (t, J = 7.5 Hz, 1H-7), 5.84 (t, J = 6.5 Hz, 1H-1), 5.37 (m, 2H-8′,9′), 4.09 (dd, J_1 = 5.0 Hz, J_2 = 4.5 Hz, 1H-3), 3.68 (s, 3H–OCH_3), 2.94–2.80 (m, 2H-4), 2.63 (dd, J_1 = 3.0 Hz, J_2 = 3.5 Hz, 1H-3), 2.03–1.86 (m, 2H-1′,7′,10′), 1.56–1.48 (m, 2H-2′), 1.26 (m, 20H-3′–6′,11′–16′), 0.87 (t, J = 7.0 Hz, 3H-8′). ^{13}C NMR: δ 165.12, 136.05, 134.34, 133.98, 130.05, 129.72, 129.43, 128.46, 126.60, 126.44, 123.69 (q, $^1J_{CF}$ = 289.5 Hz), 121.97, 119.53, 117.92, 111.15, 106.75, 85.08 (q, $^2J_{CF}$ = 25.2 Hz), 56.48, 50.42, 40.33, 34.24, 32.63, 31.90, 29.98, 29.78, 29.67, 29.59, 29.54, 29.34, 29.32, 29.20, 27.22, 26.31, 22.69, 21.51, 14.12. LR MS (ESI): m/z = 647.5 $[M + Na]^+$.

3. Results and discussion

The synthetic sequence started with the preparation of a series of fatty acid-substituted tryptamides **3a**–**f** (Scheme 1).

The amide **3a** was prepared from tryptamine **1** and acetic anhydride **2a** in the presence of triethylamine, whereas amides **3b**–**d** were formed effectively from **1** and butyric, nonanoic or stearic acids **2b**–**d** in xylene at reflux temperature using a Dean-Stark apparatus. In the case of oleic (**2e**) and arachidonic (**2f**) acids, procedures involving acid chlorides or thermal amidation gave a substantial contamination of chlorinated and/or trans-isomerised by-products. Thus, in order to ensure the (stereo)chemical integrity of the amides, we applied the protocol successfully employed by us to the synthesis of sensitive dopamides [14]. Accordingly, amides **3e** and **3f** were prepared by a BOP-mediated coupling of tryptamine **1** with oleic (**2e**) or arachidonic (**2f**) acids in 89 and 86% yield, respectively. No traces of undesired products were detected. All amides **3a**–**f** were then treated in a mild Bischler–Napieralski cyclization [15] yielding relatively unstable imines **4a**–**f**. They were then immediately subjected to the asymmetric transfer hydrogenation protocol under the conditions described by Noyori et al. [23], using both enantiomers of the chiral catalysts (*S*,*S*)-**5** or (*R*,*R*)-**5** [24] (Fig. 2). We observed that stereochemistry of the catalyst determined



a: R= -CH_3; **b:** R= -$(CH_2)_2CH_3$; **c:** R= -$(CH_2)_7CH_3$; **d:** R= -$(CH_2)_{16}CH_3$;

e: R= (*Z*)-$(CH_2)_7(CH{=}CH)(CH_2)_7CH_3$; **f:** R= (*Z*)-$(CH_2)_3[(CH{=}CH)CH_2]_4(CH_2)_3CH_3$

Scheme 1. Synthesis of teterahydro-β-carboline derivatives.

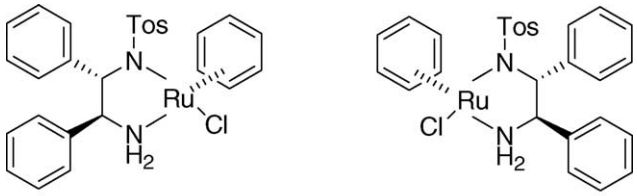


Fig. 2. Catalysts for the enantioselective transfer hydrogenation.

the stereochemistry of the amine. Therefore products with (1*R*) configuration were obtained when (*S*,*S*)-**5** were used, whereas the (1*S*) isomers were obtained under the influence (*R*,*R*)-**5**.

We found the above method superior over the procedure for the enantioselective C=N reduction with sodium borohydride modified by chiral, non-racemic acids [25], which in our case gave only fair stereoselection (ee < 80%).

Much better stereochemical output could be gained by the use of a high pressure homogenous hydrogenation over chiral phosphine–rhodium complexes (the procedure according to Morimoto and Achiwa [26]) of imines **4a**–**d** but this protocol proved inapplicable to the unsaturated imines **4e** and **4f**.

On the other hand, the asymmetric transfer hydrogenation over (*S*,*S*)-**5** or (*R*,*R*)-**5** in the presence of triethylamine-formic acid azeotrope proceeded smoothly affording the desired secondary amines **6a**–**f** in excellent chemical yields (Table 1).

The amines were then transformed into their derivatives (Table 2) with (*R*)-Mosher acid chloride (Scheme 2) in order to determine the diastereomeric ratios in ^{1}H NMR spectra. In all cases we found that virtually no observable contamination with the second diastereomer was present.

The Mosher's amide of (1*R*)-**7c** was also obtained in a form of monocrystal suitable for X-ray crystallography (Fig. 3) that served for an unambiguous stereochemistry assignment [27].

Table 1
Asymmetric transfer hydrogenation of imines **4a**–**f**

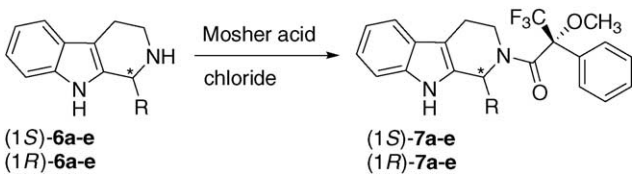
Imine	Catalyst **5**	Amine	Yield %[a]	ee %[b]	Config.[c]	$[\alpha]_D^{23}$
4a	*S*,*S*	(1*R*)-**6a**	84	>98	*R*	+55.6[d]
4a	*R*,*R*	(1*S*)-**6a**	82	>98	*S*	−56.8[d]
4b	*S*,*S*	(1*R*)-**6b**	79	>98	*R*	+72.7[e]
4b	*R*,*R*	(1*S*)-**6a**	88	>98	*S*	−73.5[e]
4c	*S*,*S*	(1*R*)-**6c**	85	>98	*R*	+54.7[e]
4c	*R*,*R*	(1*S*)-**6c**	81	>98	*S*	−54.0[e]
4d	*S*,*S*	(1*R*)-**6d**	79	>98	*R*	+33.7[f]
4d	*R*,*R*	(1*S*)-**6d**	77	>98	*S*	−34.0[f]
4e	*S*,*S*	(1*R*)-**6e**	84	>98	*R*	+25.8[f]
4e	*R*,*R*	(1*S*)-**6e**	77	>98	*S*	−26.5[f]
4f	*S*,*S*	(1*R*)-**6f**	70	>98	*R*	+10.2[f]

[a] Isolated yield of pure compounds.
[b] On the basis of ^{1}H NMR of Mosher's amides.
[c] By comparison of $[\alpha]_D$ sign and X-ray analysis of **7c**.
[d] EtOH, c = 2.
[e] EtOH, c = 1.0.
[f] $CHCl_3$, c = 1.0.

Table 2
The (*R*)-Mosher acid derivatives

Amide	Yield (%)[a]	de (%)[b]	mp (°C)	$[\alpha]_D^{23}$
(1*R*)-**7a**	77	>98	136–138	−54.0
(1*S*)-**7a**	83	>98	307–309	+162.8
(1*R*)-**7b**	68	>98	239–241	−12.0
(1*S*)-**7b**	74	>98	198–201	+127.0
(1*R*)-**7c**	74	>98	187–188	−3.2
(1*S*)-**7c**	67	>98	197–199	+105.4
(1*R*)-**7d**	64	>98	114–116	−3.2
(1*S*)-**7d**	58	>98	90–92	+73.2
(1*R*)-**7e**	58	>98	Oil	+4.9
(1*S*)-**7e**	62	>98	Oil	+65.8

$CHCl_3$, $c = 1.0$.
[a] Isolated yield of pure compounds.
[b] On the basis of ^{1}H NMR.



Scheme 2. Synthesis of the Mosher's amides.

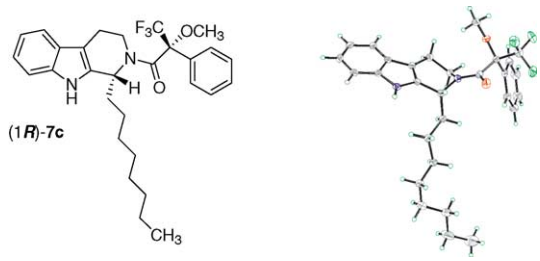


Fig. 3. The rentgenostructural analysis for compound (1*R*)-**7c**.

In the crystal, molecules related by a two-fold screw-axis symmetry in the *a* direction form infinite chains of molecules bonded with the $N–H\cdots O_{carbonyl}$ hydrogen bonds. Distinct hydrophobic and hydrophilic regions could be discerned in the structure.

4. Conclusions

In conclusion, an effective method for highly enantioselective preparation of 1-substituted-1,2,3,4-tetrahydro-β-carboline derivatives is described. The substituent at C-1 position could also contain (*Z*)-double bond(s), which was retained within the whole procedure. Following our interest in biological activity of fatty acids derivatives of biogenic amines [7], the final compounds will be in vivo evaluated for their ability to cross the blood-brain barrier. This ability is of importance in modern pharmacochemistry since there are evidences that dysfunction in brain catecholamine or indolamine pathways contribute to Parkinson's disease [28] together with affective disorders and schizophrenia [29].

References

[1] J.D. Philipson, M.F. Roberts, M.H. Zenk (Eds.), The Chemistry and Biology of Isoquinoline Alkaloids, Springer-Verlag, New York, 1985.
[2] J.D. Philipson, M.H. Zenk (Eds.), Indole and Biogenetically Related Alkaloids, Academic Press, London, 1980.
[3] A. Agarwal, P.P. Rearson, E.W. Taylor, H.B. Li, T. Dahlgren, M. Herslöf, Y. Yang, G. Lambert, D.L. Nelson, J.W. Regan, A.R. Martin, J. Med. Chem. 36 (1993) 4006.
[4] T. Nagatsu, Neurotoxicol. Teratol. 24 (2002) 565.
[5] D.L. Boger, S.J. Henriksen, B.F. Cravat, Curr. Pharm. Design 4 (1998) 303.
[6] I. Matuszewska, A. Leniewski, P. Roszkowski, Z. Czarnocki, Chem. Phys. Lipids, 2005, in press.
[7] M. Pokorski, Z. Matysiak, M. Marczak, R.P. Ostrowski, A. Kapuściński, I. Matuszewska, M. Kańska, Z. Czarnocki, Drug Develop. Res. 60 (2003) 217.
[8] G.M. Sheldrick, Acta Cryst. A 46 (1990) 467.
[9] G.M. Sheldrick, SHELXL-97 Program for X-ray Structure Refinement, University of Göttingen, Germany, 1997.
[10] K.M. Biswas, A.H. Jackson, M.M. Kobaisy, P.V. Shanon, J. Chem. Soc. Perkin Trans. 14 (1992) 461.
[11] S.C. Benson, L. Lee, L. Yang, J.K. Snyder, Tetrahedron 56 (2000) 1165.
[12] A. Cobas, E. Guitian, L. Castedo, J. Org. Chem. 57 (1992) 6765.
[13] G. Hahn, H.F. Gudjons, Ber. Dtsch. Chem. Ges. 71 (1938) 2175.
[14] Z. Czarnocki, M.P. Matuszewska, I. Matuszewska, Org. Prep. Proced. Int. 30 (1998) 699.
[15] H. Hulinska, P. Taufman, H. Frycowa, M. Protiva, Collect. Czech. Chem. Commun. 53 (1988) 373.
[16] S. Misztal, M. Cegła, Synthesis (1985) 1134.
[17] G. Kalaus, P. Györy, L. Szabo, C. Szantay, Acta Chim. Acad. Sci. Hung. 97 (1978) 429.
[18] D.H. Hua, S.N. Bharathi, J.A.K. Panangadan, A. Tsujimoto, J. Org. Chem. 56 (1991) 6998.
[19] H. Akimoto, K. Okamura, M. Yui, T. Shioiri, M. Kuramoto, Y. Kikugawa, S. Yamada, Chem. Pharm. Bull. 22 (1974) 2164.
[20] T. Kawate, M. Nakagawa, H. Yamazaki, M. Hirayama, T. Hino, Chem. Pharm. Bull. 41 (1993) 287.
[21] C. Gremmen, B. Willemse, M.J. Wanner, G.J. Koomen, Org. Lett. 2 (2000) 1955.
[22] H.D. Flack, Acta Cryst. A 39 (1983) 876.
[23] N. Uematsu, A. Fuji, S. Hashigichi, T. Ikariya, R. Noyori, J. Am. Chem. Soc. 118 (1996) 4916.
[24] L.F. Tietze, Y. Zhou, E. Töpken, Eur. J. Org. Chem. (2000) 2247.
[25] A.R. Hajipour, M. Hantehzadeh, J. Org. Chem. 64 (1999) 8475.
[26] T. Morimoto, K. Achiwa, Tetrahedron: Asymm. 6 (1995) 2661.
[27] The crystal structure of (1*R*)-**7c** has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 251663.
[28] C. Martinez, J.A. Agundez, G. Gervasini, R. Martin, J. Benitez, Pharmacogenetics 7 (2) (1997) 85.
[29] P. Moore, H.P. Landolt, E. Seifritz, C. Clark, T. Bhatti, J. Kelsoe, M. Rapaport, J.C. Gillin, Neurophysopharmacology 23 (2000) 601.