Synthesis of 2-aminopropyle-3-indole–acetic(propionic) acid derivatives

Sophie-Isabelle Bascop, Jean-Yves Laronze, Janos Sapi*

Laboratoire de Chimie Thérapeutique, UMR 6013 du CNRS ‘Isolement, Structure, Transformations et Synthèse de Produits Naturels’, IFR 53 ‘Biomolécules’, Faculté de Pharmacie, Université de Reims-Champagne-Ardenne, F-51096 Reims, Cedex, France
E-mail: janos.sapi@univ-reims.fr

Dedicated to Professor Gábor Bernáth on his 70th birthday
(received 24 Jan 03; accepted 03 Mar 03; published on the web 14 Mar 03)

Abstract
2-Aminopropyl-3-indole acetic(propionic) acid derivatives have been prepared and characterised starting from 3-[(3-methoxycarbonylmethyl)-indol-2-yl] propionic acid methyl ester by means of chemoselective functional group manipulations.

Keywords: Chemoselective transformation, 2-aminopropyl-indole-3-acetic acid, 2-aminopropyl-3-indole-propionic acid, aminolysis, reduction

Introduction
Indole nucleus is a common structural feature of a wide variety of biologically active compounds. 2(3)-Carboxy(alkyl) 2,3-disubstituted indole derivatives were reported to be efficient glycine/NMDA, 2 non-peptide endothelin 3 antagonists, cyclooxygenase-2, 4 thromboxane synthase, 5 steroid 5α-reductase, 6 phospholipase-A2 7 inhibitors. Indole-3-acetic acid is a well-known plant growth hormone 8 and some of its derivatives have recently been found to be active against a number of human cancer cell lines. 9

The corresponding 2(3)-aminoalkyl counterparts (tryptamine, homotryptamine, isotryptamine derivatives) have attracted considerable interest as potent and selective serotonin, 10 or melatonin 11 receptor ligands.
Apart from possible biological activities 2(3)-carboxy and aminoalkyl substituted indoles may be considered as valuable synthetic intermediates for more complex indole heterocycles or linkers in solid-phase synthesis or supramolecular chemistry.\textsuperscript{12}

As part of a biological program we were interested in preparing 2-aminopropyl-3-indole carboxylic acid homologues 1,2, starting from diester 3, by simple functional group manipulations.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure1.png}
\caption{Figure 1}
\end{figure}

### Results and Discussion

Since selective hydrolysis of the C-2 located ester function in 3 had already been accomplished,\textsuperscript{13} we firstly tried a selective aminolysis using the non-volatile benzylamine (Scheme 1). From technical point of view introduction of benzyl group seemed to be advantageous and the formation of the required primary (eventually secondary) amine function by hydrogenolysis could be ensured. Unfortunately, selective amidification of diester 3 failed only a small part of the starting material was converted to the corresponding ester amide 4b.
Scheme 1

Then we turned our attention to ester acid 5, prepared from 3 by chemoselective hydrolysis. Activated by i-butylchloroformate the carboxylic acid function smoothly reacted with ammonia and some representative primary and secondary amines (1.15-1.25 eq) to give ester amides 4a-e in good yield (Scheme 2).
For the chemoselective reduction of the amide function diborane dimethylsulfide complex was chosen. Using a slight excess of diborane complex reduction of tertiary or benzyl amides afforded amino esters 6b,d,e, along with some over-reduced compounds 7b,d,e. On the contrary, reduction of primary 4a and methyl amide 4c even at lower temperature showed no selectivity.
However, this problem was circumvented by debenzylation of \textbf{6b} and \textbf{6d} leading to amino esters \textbf{6a}, and \textbf{6c} in 70 and 95 \% yield, respectively.

Hydrolysis of the ester function was achieved by means of aqueous barium or potassium hydroxide allowing the isolation of the required amino acids \textbf{1a-e} (Scheme 3). In the case of primary amine \textbf{6a}, indolazocinone \textbf{9} side product (5 \%) was also isolated. When \textbf{6a} was treated with potassium hydroxide in boiling aqueous methanol 2-azocinone \textbf{9} was obtained exclusively.

![Scheme 3](image)

**Scheme 3**

In accordance with our objective to prepare 2-aminopropyl-3-indole carboxylic acid derivatives we selected cyanide anion assisted homologation. By this simple method reiteration of the process may also be envisaged. To this end benzyl amide \textbf{4b} as model compound was selected enabling selective \textit{O}-activation followed by debenzylation by hydrogenolysis. Treatment of \textbf{4b} with lithium aluminium hydride in THF at room temperature chemoselectively afforded alcohol \textbf{10b} in 92 \% yield. Mesylation of \textbf{10b} with mesyl chloride in the presence of triethylamine and subsequent heating of the intermediate mesylate with potassium cyanide led to nitrile \textbf{11b} in 48 \% overall yield. Transformation of cyano amide \textbf{11b} into the aimed amino acid \textbf{2b} was achieved by selective amide function reduction to \textbf{12b} and subsequent two-step hydrolysis \textit{via} \textbf{13b}, as depicted in Scheme 4.

In conclusion, we have developed a simple method for the preparation of 2-aminopropyl-3-indole carboxylic acid homologues \textbf{1,2} based on selective functional group transformations. Extension of the procedure to higher homologues and synthetic applications of the resulting derivatives are under investigation.
Experimental Section

General Procedures. Melting points were determined on a Reichert Thermovar hot-stage apparatus and are not corrected. IR spectra were measured with a Bomem FTIR instrument. $^1$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) spectra were acquired on a Bruker AC 300 spectrometer using TMS as internal standard. Mass spectra were recorded with a VG Autospec apparatus. Reactions were monitored using Merck TLC aluminium sheets (Kieselgel 60 F$_{254}$).

Attempted direct amidification of 3
A solution of 3 (200 mg, 0.73 mmol) and benzylamine (0.1 mL, 0.92 mmol) in toluene (4 mL) was heated at 90°C under nitrogen for 6 days. After evaporation of the solvent the residue was purified by chromatography (eluent: CH$_2$Cl$_2$:MeOH 99:1) to obtain 4b (36 mg, 14 %), along with recovered starting material 3 (123 mg).

Methyl [2-(2-benzylcarbamoyl-ethyl)-1H-indol-3-yl]-acetate (4b). White crystals; mp 107-107.5°C (diethyl ether). IR (KBr): 3297, 3086, 3030, 2930, 1728, 1650 cm$^{-1}$. MS (EI) m/z (%): 350 (M$^+$, 92), 318 (41), 291 (31), 184 (100). $^1$H NMR (CDCl$_3$) $\delta$: 2.55 (2H, t, J = 6 Hz), 3.03
(2H, t, J = 6 Hz), 3.51 (3H, s), 3.66 (2H, s), 4.26 (2H, d, J = 5 Hz), 6.41 (1H, d, J = 5 Hz), 6.85 (2H, d, J = 7.7 Hz), 7.03 (2H, t, J = 7.7 Hz), 7.09 (2H, dt, J = 8, 1.5 Hz), 7.21 (1H, m), 7.22 (1H, dd, J = 8, 1.5 Hz), 7.50 (1H, dd, J = 8, 1.5 Hz), 9.22 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 21.8, 30.0, 36.0, 43.4, 51.8, 103.7, 110.9, 117.9, 119.3, 121.3, 127.1, 128.1, 128.4, 135.1, 135.9, 137.7, 172.7, 173.1. Anal. Calcd. for C$_{21}$H$_{22}$N$_2$O$_3$ (350.41): C, 71.98; H, 6.33; N, 7.99; Found: C, 71.68; H, 6.33; N, 8.26.

**Amidification of acid 5**

**General procedure.** To a cooled (-10°C) solution of acid 5 and triethylamine in anhydrous CH$_2$Cl$_2$ was added i-butylchloroformate. After 45 min stirring at –10°C amine (R$_1$R$_2$NH) was added dropwise and the reaction mixture was allowed to stand at rt for 1.5-2 h. After dilution with water (30-60 mL) the separated organic phase was washed with 10% HCl, water and 10% NaHCO$_3$, dried (Na$_2$SO$_4$), and evaporated to dryness. The residue was purified by crystallisation or flash chromatography to obtain the corresponding amides.

**Methyl [2-(2-carbamoyl-ethyl)-1H-indol-3-yl]-acetate (4a).** Acid 5: 1.50 g (5.74 mmol); Et$_3$N: 1.00 mL (0.73 g, 7.18 mmol); CH$_2$Cl$_2$: 80 mL; ClCO$_2$i-Bu: 0.93 mL (0.98 g, 7.17 mmol); 32% NH$_4$OH: 0.44 mL (7.36 mmol); Flash chromatography: eluent CH$_2$Cl$_2$:MeOH 98:2. Yield: 1.38 g (92%). Viscous oil. IR (film): 3363, 3060, 3013, 2950, 1726, 1665 cm$^{-1}$. MS (EI) m/z (%): 260 (M$^+$+, 92), 228 (24), 201 (68), 184 (98). $^1$H NMR (CDCl$_3$) δ: 2.46 (2H, t, J = 7 Hz), 5.92 (2H, s), 3.63 (3H, s), 3.67 (2H, s), 7.07 (1H, dt, J = 8, 1.7 Hz), 7.08 (1H, d, J = 8, 1.7 Hz), 7.21 (1H, dd, J = 8, 1.7 Hz), 7.48 (1H, dd, J = 11, 1.7 Hz), 9.18 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 21.3, 29.9, 35.1, 51.9, 103.7, 110.8, 117.8, 119.3, 121.3, 127.9, 135.1, 136.0, 173.2, 175.6. HREIMS: calcd: 260.1160, found: 260.1158.

**Methyl [2-(2-benzylcarbamoyl-ethyl)-1H-indol-3-yl]-acetate (4b).** Acid 5: 2.73 g (10.45 mmol); Et$_3$N: 1.67 mL (1.21 g, 12.00 mmol); CH$_2$Cl$_2$: 150 mL; ClCO$_2$i-Bu: 1.56 mL (1.64 g, 12.03 mmol); BnNH$_2$: 1.31 mL (1.29 g, 12.00 mmol); Crystallisation from diethyl ether. Yield: 3.47 g (95%).

**Methyl [2-(2-methylcarbamoyl-ethyl)-1H-indol-3-yl]-acetate (4c).** Acid 5: 2.00 g (7.65 mmol); Et$_3$N: 1.33 mL (0.97 g, 9.56 mmol); CH$_2$Cl$_2$: 120 mL; ClCO$_2$i-Bu: 1.24 mL (1.31 g, 9.56 mmol); 40% MeNH$_2$: 0.85 mL (9.87 mmol); Crystallisation from diethyl ether. Yield: 1.85 g (88%); White crystals; mp 117.5-119°C (diethyl ether). IR (KBr): 3397, 3300, 3061, 2950, 1730, 1650 cm$^{-1}$. MS (EI) m/z (%): 274 (M$^+$+, 83), 256 (11), 242 (37), 215 (63), 184 (99). $^1$H NMR (CDCl$_3$) δ: 2.41 (2H, t, J = 7.5 Hz), 2.48 (2H, d, J = 5.2 Hz), 3.63 (3H, s), 6.03 (1H, q, J = 5.2 Hz), 7.04 (1H, dt, J = 8.1, 1.6 Hz), 7.08 (1H, dt, J = 8.1, 1.6 Hz), 7.22 (1H, dd, J = 8.1, 1.6 Hz), 7.48 (1H, dd, J = 9.1, 1.6 Hz), 4.95 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 21.4, 26.1, 29.8, 35.4, 51.8, 103.5, 110.7, 117.7, 119.1, 121.1, 127.8, 135.1, 136.1, 173.1, 173.4. Anal. Calcd. for C$_{13}$H$_{18}$N$_2$O$_3$ (274.31): C, 65.68; H, 6.61; N, 10.21; Found: C, 65.45; H, 6.76; N, 10.16.
Methyl \{2-[2-(benzyl-methyl-carbamoyl)-ethyl]-1H-indol-3-yl\}-acetate (4d). Acid 5: 1.96 g (7.50 mmol); Et3N: 1.20 mL (0.87 g, 8.62 mmol); CH2Cl2: 120 mL; ClCO2t-Bu: 1.12 mL (1.18 g, 8.63 mmol); BnMeNH: 1.12 mL (1.05 g, 8.68 mmol); Crystallisation from diethyl ether. Yield: 2.33 g (85 %). White crystals; mp 87-89 °C (diethyl ether). IR (KBr): 3285, 3060, 2975, 1738, 1615 cm⁻¹. MS (EI) m/z (%): 364 (M⁺, 100), 332 (31), 305 (21), 243 (22), 216 (14), 184 (90). ¹H NMR (CDCl3) δ: 2.74 (2H, t, J = 7.1 Hz), 2.82 (3H, s), 3.12 (2H, t, J = 7.1 Hz), 3.51 (2H, s), 3.63 (3H, s), 4.41 (2H, s), 6.96-7.18 (5H, m), 7.04 (1H, dt, J = 7.7, 2 Hz), 7.11 (1H, dt, J = 7.7, 2 Hz), 7.24 (1H, dd, J = 7.7, 2 Hz), 7.54 (1H, dd, J = 7.7, 2 Hz), 9.33 (1H, brs).

¹³C NMR (CDCl3) δ: 20.8, 30.0, 33.5, 34.6, 51.7, 53.1, 103.7, 110.7, 117.9, 119.1, 121.2, 127.6, 127.8, 128.8, 134.9, 136.6, 136.9, 172.6, 173.3. Anal. Calcd. for C22H24N2O3 (364.43): C, 72.50; H, 6.64; N, 7.69; Found: C, 72.35; H, 6.39; N, 7.82.

Methyl \{2-(2-dimethylcarbamoyl-ethyl)-1H-indol-3-yl\}-acetate (4e). Acid 5: 1.99 g (7.62 mmol); Et3N: 1.11 mL (0.81 g, 7.97 mmol); CH2Cl2: 120 mL; ClCO2t-Bu: 1.04 mL (1.10 g, 8.02 mmol); 40% Me₂NH: 1.00 mL (7.97 mmol); Crystallisation from diethyl ether. Yield: 1.92 g (87 %). White needles; mp 140-140.5 °C (diethyl ether). IR (KBr): 3252, 3115, 3036, 2934, 1738, 1625 cm⁻¹. MS (EI) m/z (%): 288 (M⁺, 75), 256 (17), 243 (12), 229 (34), 216 (12), 184 (100). ¹H NMR (CDCl3) δ: 2.66 (2H, t, J = 6 Hz), 2.98 (3H, s), 3.03 (3H, s), 3.09 (2H, t, J = 6 Hz), 3.62 (3H, s), 3.70 (2H, s), 7.04 (1H, dt, J = 8, 1.8 Hz), 7.09 (1H, dt, J = 8, 1.8 Hz), 7.27 (1H, dd, J = 8, 1.8 Hz), 7.51 (1H, dd, J = 8, 1.8 Hz), 9.40 (1H, brs).

¹³C NMR (CDCl3) δ: 20.4, 30.0, 33.4, 35.5, 36.9, 51.7, 103.3, 110.7, 117.9, 119.0, 121.1, 127.9, 134.9, 137.0, 172.6, 172.8. Anal. Calcd. for C16H20N2O3 (288.34): C, 66.65; H, 6.99; N, 9.71; Found: C, 66.91; H, 6.85; N, 9.62.

Reduction of amido esters 4a-e by diborane-dimethylsulfide complex

**General procedure.** To a 6°C cooled solution of a mido ester in anhydrous THF was added B2H6/DMS 2M solution in toluene. The reaction mixture was stirred at 10-12 °C for 20-24 h. After evaporation of the solvent the amine-borane complex was destroyed in refluxing ethanol in the presence of Na2CO3 or CsF. After filtration on celite, the filtrate was evaporated to dryness, and the residue was purified by flash chromatography to afford reduced products.

**Reduction of 4a.** Amido ester 4a: 0.55 g (2.11 mmol); THF: 20 mL; B2H6/DMS (2M solution in toluene): 2.85 mL (5.70 mmol); Flash chromatography, eluent: CHCl3:MeOH:NH4OH 95:5:0.5 - > 80:20:2. Isolated products: 7a and 8a.

2-[2-(3-Aminopropyl)-1H-indol-3-yl]-ethanol (7a). Yield: 0.24 g (52 %). Viscous yellowish oil. IR (film): 3395, 3354, 3290, 2935, 1590 cm⁻¹. MS (EI) m/z (%): 218 (M⁺, 17), 200 (10), 188 (7), 170 (35), 162 (17), 158 (25), 144 (100). ¹H NMR (CDCl3+DMSO-d6) δ: 1.81 (2H, quint., J = 7.1 Hz), 2.60 (2H, t, J = 7.1 Hz), 2.78 (2H, t, J = 7.1 Hz), 2.86 (2H, brs), 2.90 (1H, brs), 2.94 (2H, t, J = 6.6 Hz), 3.73 (2H, t, J = 6.6 Hz), 6.95 (1H, dt, J = 8, 2 Hz), 7.09 (1H, dt, J = 8, 2 Hz), 7.36 (1H, dd, J = 8, 2 Hz), 7.46 (1H, dd, J = 8, 2 Hz), 10.1 (1H, brs). ¹³C NMR
(CDCl₃+DMSO-d₆) δ: 22.4, 27.2, 31.5, 40.1, 61.6, 106.6, 109.8, 117.0, 117.6, 119.6, 127.8, 134.8, 135.6. HREIMS: calcld: 218.1419, found: 218.1399.

3-[3-(2-Hydroxy-ethyl)-1H-indol-2-yl]-propionamide (8a). Yield: 0.16 g (32 %). Viscous yellowish oil. IR (film): 3395, 3060, 2940, 1670 cm⁻¹. MS (EI) m/z (%): 232 (M⁺, 68), 214 (58), 201 (100), 184 (97), 170 (10), 156 (72), 144 (28). ¹H NMR (CDCl₃+DMSO-d₆) δ: 2.55 (2H, t, J = 7 Hz), 2.89 (2H, t, J = 7 Hz), 3.00 (2H, t, J = 7.2 Hz), 3.66 (2H, t, J = 7.2 Hz), 4.40 (1H, brs), 6.21 (2H, brs), 6.92 (1H, dt, J = 8.1, 1.8 Hz), 6.98 (1H, dt, J = 8.1, 1.8 Hz), 7.24 (1H, dd, J = 8.1, 1.8 Hz), 7.43 (1H, dd, J = 8.1, 1.8 Hz). ¹³C NMR (CDCl₃+DMSO-d₆) δ: 20.3, 26.5, 34.1, 60.8, 106.1, 109.2, 116.4, 116.8, 118.9, 127.0, 134.1, 134.4, 173.4. Anal. Calcd. for C₁₃H₁₆N₂O₂ (232.28): C, 67.22; H, 6.94; N, 12.06; Found: C, 66.95; H, 6.75; N, 11.62.

Reduction of 4b. Amido ester 4b: 4.00 g (11.41 mmol); THF: 100 mL; B₂H₆.DMS (2M solution in toluene): 14.30 mL (28.6 mmol); Flash chromatography, eluent: CHCl₃:MeOH:NH₄OH 95:5:0.5. Isolated products: 6b and 7b.

Methyl [2-(3-benzylamino-propyl)-1H-indol-3-yl]-acetate (6b). Yield: 2.64 g (69 %). Viscous yellowish oil. IR (film): 3390, 3295, 3060, 2950, 1730 cm⁻¹. MS (EI) m/z (%): 336 (M⁺+, 39), 277 (6), 229 (9), 216 (19), 203 (66), 170 (50), 156 (33), 144 (68). ¹H NMR (CDCl₃) δ: 1.87 (2H, quint., J = 6.3 Hz), 2.73 (2H, t, J = 6.3 Hz), 2.85 (2H, t, J = 6.3 Hz), 3.62 (3H, s), 3.68 (2H, s), 3.78 (2H, s), 7.07 (2H, m), 7.19-7.31 (5H, m), 7.35 (1H, dd, J = 8.1, 2 Hz), 7.52 (1H, dd, J = 8.1, 2 Hz), 9.53 (1H, brs). ¹³C NMR (CDCl₃) δ: 24.0, 28.4, 30.1, 48.6, 51.8, 53.7, 103.7, 110.6, 118.0, 119.2, 121.1, 127.4, 128.3, 128.4, 128.6, 135.1, 136.7, 139.0, 172.7. Anal. Calcd. for C₂₁H₂₄N₂O₂ (336.42): C, 74.97; H, 7.19; N, 8.33; Found: C, 75.41; H, 6.95; N, 8.42.

2-[2-(3-Benzylamino-propyl)-1H-indol-3-yl]-ethanol (7b). Yield: 0.65 g (18 %). White crystals; mp 162-164 °C [(diethyl ether + ethyl acetate (1:1)]. IR (KBr): 3395, 3280, 3060, 1462 cm⁻¹. MS (EI) m/z (%): 232 (M⁺+, 73), 214 (45), 202 (34), 188 (41), 183 (27), 175 (27), 170 (92). ¹H NMR (CDCl₃+DMSO-d₆) δ: 1.81 (2H, quint., J = 7 Hz), 2.34 (3H, s), 2.53 (2H, t, J = 7 Hz), 2.74 (2H, t, J = 7 Hz), 2.83 (2H, t, J = 6.8 Hz), 3.26 (1H, brs), 3.58 (2H, t, J = 6.8 Hz), 6.90
(1H, dt, J = 8.1, 2 Hz), 7.03 (1H, dt, J = 8.1, 2 Hz), 7.22 (1H, dd, J = 8.1, 2 Hz), 7.40 (1H, dd, J = 8.1, 2 Hz), 10.61 (1H, brs). $^{13}$C NMR (CDCl$_3$+DMSO-d$_6$) δ: 23.5, 28.1, 29.6, 36.1, 51.1, 62.0, 107.0, 110.4, 117.6, 118.0, 119.8, 128.5, 135.4, 136.5. Anal. Calcd. for C$_{14}$H$_{20}$N$_2$O (232.32): C, 72.37; H, 8.67; N, 12.06; Found: C, 71.92; H, 8.68; N, 11.83.

**Reduction of 4d.** Amido ester 4d: 1.78 g (4.88 mmol); THF: 40 mL; B$_2$H$_6$/DMS (2M solution in toluene): 6.10 mL (12.2 mmol); Flash chromatography, eluent: CHCl$_3$:MeOH:NH$_4$OH 95:5:0.3->90:10:1. Isolated products: 6d and 7d.

**Methyl [2-[3-(benzyl-methyl-amino)-propyl]-1H-indol-3-yl]-acetate (6d).** Yield: 1.60 g (93%). Viscous yellow oil. IR (film): 3400, 3060, 2950, 1735, 1462 cm$^{-1}$. MS (El) m/z (%): 350 (M$^+$, 49), 291 (4), 203 (28), 170 (24), 160 (11). $^1$H NMR (CDCl$_3$) δ: 1.87 (2H, quint., J = 6 Hz), 2.20 (3H, s), 2.50 (2H, t, J = 6 Hz), 2.87 (2H, t, J = 6 Hz), 3.55 (2H, s), 3.62 (3H, s), 3.69 (2H, s), 7.10 (2H, m), 7.10-7.35 (5H, m), 7.35 (1H, dd, J = 7.8, 1.5 Hz), 7.53 (1H, dd, J = 7.8, 1.5 Hz), 9.66 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 24.2, 26.2, 30.2, 41.5, 51.8, 57.3, 62.6, 103.5, 110.6, 118.0, 119.1, 120.9, 127.3, 128.5, 128.6, 129.3, 135.1, 137.1, 138.4, 172.6. Anal. Calcd. for C$_{22}$H$_{28}$N$_2$O (350.45): C, 75.39; H, 7.48; N, 7.99; Found: C, 75.51; H, 7.85; N, 7.62.

**2-[2-[3-(Benzyl-amino)-propyl]-1H-indol-3-yl]-ethanol (7d).** Yield: 0.07 g (5%). White crystals; mp 128-130 °C (diethyl ether). IR (KBr): 3312, 3065, 2926, 2880, 1460 cm$^{-1}$. MS (El) m/z (%): 322 (M$^+$, 19), 304 (4), 292 (9), 175 (9), 170 (35), 148 (32). $^1$H NMR (CDCl$_3$) δ: 1.89 (2H, quint., J = 6.9 Hz), 2.19 (3H, s), 2.47 (2H, t, J = 6.9 Hz), 2.80 (2H, t, J = 6.9 Hz), 2.96 (2H, t, J = 7.1 Hz), 3.01 (1H, brs), 3.52 (2H, s), 3.79 (2H, t, J = 7.1 Hz), 7.04 (1H, dt, J = 8, 1.5 Hz), 7.10 (1H, dt, J = 8, 1.5 Hz), 7.23 (1H, dd, J = 8, 1.5 Hz), 7.30-7.36 (5H, m), 7.51 (1H, dd, J = 8, 1.5 Hz), 9.66 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 23.8, 26.6, 27.6, 41.5, 56.9, 62.3, 62.6, 106.6, 110.5, 117.8, 118.7, 120.7, 127.3, 128.2, 128.3, 129.4, 135.3, 136.4, 137.5. HREIMS: calcd: 322.2045, found: 322.2030.

**Reduction of 4e.** Amido ester 4e: 5.19 g (18.00 mmol); THF: 140 mL; B$_2$H$_6$/DMS (2M solution in toluene): 22.50 mL (45.0 mmol); Flash chromatography, eluent: CHCl$_3$:MeOH:NH$_4$OH 95:5:0.5->90:10:1. Isolated products: 6e and 7e.

**Methyl [2-(3-dimethylamino-propyl)-1H-indol-3-yl]-acetate (6e).** Yield: 3.26 g (66%). For spectral data, see ref. 14.

**2-[2-(3-Dimethylamino-propyl)-1H-indol-3-yl]-ethanol (7e).** Yield: 0.87 g (20%). White crystals; mp 108-110 °C (diethyl ether). IR (KBr): 3403, 3262, 3057, 2944, 2864, 1465 cm$^{-1}$. MS (El) m/z (%): 246 (M$^+$, 67), 228 (18), 216 (24), 201 (8), 188 (19), 170 (78), 157 (58), 144 (73). $^1$H NMR (CDCl$_3$) δ: 1.75 (2H, quint., J = 7.1 Hz), 2.14 (6H, s), 2.23 (2H, t, J = 7.1 Hz), 2.73 (2H, t, J = 7.1 Hz), 2.95 (2H, t, J = 6.8 Hz), 3.75 (1H, brs), 3.79 (2H, t, J = 6.8 Hz), 7.02 (1H, dt, J = 8.2, 2 Hz), 7.08 (1H, dt, J = 8.2, 2 Hz), 7.21 (1H, dd, J = 8.2, 2 Hz), 7.50 (1H, dd, J = 8.2, 2 Hz), 9.42 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 23.6, 26.8, 27.8, 44.8, 58.5, 62.6, 107.2, 110.5, 117.8, 118.7, 120.6, 128.5, 135.4, 136.2. Anal. Calcd. for C$_{15}$H$_{22}$N$_2$O (246.35): C, 73.13; H, 9.00; N, 11.37; Found: C, 72.83; H, 9.23; N, 11.18.
Debenzylation of amines 6b and 6d

**General procedure.** A mixture of amine, 10 % Pd-C catalyst was stirred in MeOH at rt under H₂ atmosphere until the disappearance of the starting material. After filtration of the catalyst, the filtrate was evaporated to dryness and the residue was purified by chromatography to obtain 6a or 6c.

**Debenzylation of 6b.** Amine 6b: 2.00 g (5.94 mmol); MeOH: 30 mL; 10% Pd-C catalyst: 0.2 g; Flash chromatography, eluent CHCl₃:MeOH:NH₄OH 95:5:0.5.

**Methyl [2-(3-amino-propyl)-1H-indol-3-yl]-acetate (6a).** Yield: 1.03 g (70 %). Viscous yellow oil. IR (film): 3366, 3295, 3180, 3060, 2944, 1730, 1462 cm⁻¹. MS (EI) m/z (%): 246 (M⁺, 65), 229 (9), 216 (23), 203 (33), 187 (10), 170 (67), 156 (38), 144 (100). ¹H NMR (CDCl₃) δ: 1.68 (2H, brs), 1.78 (2H, quint., J = 7.1 Hz), 2.74 (2H, t, J = 7.1 Hz), 2.81 (2H, t, J = 7.1 Hz), 3.64 (3H, s), 3.69 (2H, s), 7.09 (2H, m), 7.25 (1H, dd, J = 8.2, 2 Hz), 7.53 (1H, dd, J = 8.2, 2 Hz), 9.18 (1H, brs).


**Debenzylation of 6d.** Amine 6d: 2.80 g (7.99 mmol); MeOH: 30 mL; 10% Pd-C catalyst: 0.3 g.

**Methyl [2-(3-methylamino-propyl)-1H-indol-3-yl]-acetate (6c).** Yield: 1.97 g (95 %). Viscous colourless oil. IR (film): 3590, 3293, 3320, 3160, 3050, 2940, 1730, 1564 cm⁻¹. MS (EI) m/z (%): 260 (M⁺, 61), 229 (16), 217 (38), 203 (52), 170 (74), 156 (62), 144 (100). ¹H NMR (CDCl₃) δ: 1.79 (2H, quint., J = 7.1 Hz), 1.98 (1H, brs), 2.39 (3H, s), 2.59 (2H, t, J = 7.1 Hz), 2.78 (2H, t, J = 7.1 Hz), 3.53 (3H, s), 3.69 (2H, s), 7.06 (1H, dt, J = 8, 2 Hz), 7.09 (1H, dt, J = 8, 2 Hz), 7.21 (1H, dd, J = 8, 2 Hz), 7.52 (1H, dd, J = 8, 2 Hz), 9.59 (1H, brs). ¹³C NMR (CDCl₃) δ: 23.5, 30.2, 32.1, 41.2, 51.8, 103.8, 110.5, 118.1, 119.3, 121.1, 128.3, 135.1, 136.8, 172.6. Anal. Calcd. for C₁₅H₂₀N₂O₂ (260.33): C, 69.20; H, 7.74; N, 10.76; Found: C, 68.91; H, 7.95; N, 10.32.

**Hydrolysis of amino esters 6a-e**

**General procedure for Ba(OH)₂ assisted reaction.** A mixture of amino ester and Ba(OH)₂·8H₂O in MeOH-water was stirred at rt until the disappearance of the starting material. After evaporation of the MeOH the remaining aqueous solution was acidified to pH=6 with 10% H₂SO₄ under cooling. The precipitate was filtered off, and the filtrate was extracted with CHCl₃. After separation, the aqueous phase was evaporated to afford amino acids 1a,c,e.

**Hydrolysis of 6a.** Amino ester 6a: 0.96 g (3.90 mmol); Ba(OH)₂·8H₂O: 3.46 g (10.97 mmol); MeOH: 10 mL; Water: 10 mL; From the organic layer azocinone 9 was isolated.

**[2-(3-Amino-propyl)-1H-indol-3-yl]-acetic acid (1a).** Yield: 0.51 g (56 %). Yellowish powder; mp 239-244 °C (water). IR (KBr): 3405, 3185, 2945, 2900, 1640 cm⁻¹. MS (EI) m/z (%): 232
1H NMR (DMSO-d$_6$+D$_2$O) $\delta$: 1.95 (2H, quint., $J$ = 7.2 Hz), 2.70-2.81 (4H, m), 3.37 (2H, s), 6.92 (1H, dt, $J$ = 8, 2 Hz), 6.99 (1H, dt, $J$ = 8, 2 Hz), 7.24 (1H, dd, $J$ = 8, 2 Hz), 7.42 (1H, dd, $J$ = 8, 2 Hz). $^{13}$C NMR (DMSO-d$_6$+D$_2$O) $\delta$: 23.5, 27.6, 34.6, 40.0, 109.2, 112.1, 119.8, 120.2, 122.3, 129.8, 135.7, 136.7, 175.8. Anal. Calcd. for C$_{13}$H$_{16}$N$_2$O$_2$ (232.28): C, 67.22; H, 6.94; N, 12.06; Found: C, 67.51; H, 6.88; N, 11.72.

1,3,4,5,6,7-Hexahydro-azocino[5,4-b]indol-2-one (9). Yield: 0.04 g (5 %). Yellow ish crystals; mp 196-199 °C (diethyl ether). IR (KBr): 3397, 3280, 3060, 2930, 2855, 1650 cm$^{-1}$. MS (EI) m/z (%): 214 (M$^+$, 100), 185 (43), 174 (25), 156 (68).

$^{1}$H NMR (DMSO-d$_6$) $\delta$: 1.72 (2H, quint., $J$ = 6.2 Hz), 2.87 (2H, t, $J$ = 6.2 Hz), 3.32 (2H, dt, $J$ = 7, 6.2 Hz), 3.64 (2H, s), 6.98 (1H, dt, $J$ = 8, 1.8 Hz), 7.04 (1H, dt, $J$ = 8, 1.8 Hz), 7.22 (1H, t, $J$ = 7 Hz), 7.28 (1H, dd, $J$ = 8, 1.8 Hz), 7.41 (1H, dd, $J$ = 8, 1.8 Hz), 10.81 (1H, brs). $^{13}$C NMR (DMSO-d$_6$) $\delta$: 23.9, 29.5, 32.0, 41.3, 105.3, 110.8, 117.5, 118.6, 120.6, 128.6, 134.3, 134.5, 174.1. HREIMS: calcd: 214.1106, found: 214.1126.

Hydrolysis of 6c. Amino ester 6c: 1.12 g (4.30 mmol); Ba(OH)$_2$.8H$_2$O: 3.76 g (11.92 mmol); MeOH: 12 mL; Water: 12 mL.

[2-(3-Methylamino-propyl)-1H-indol-3-yl]-acetic acid (1c). Yield: 0.39 g (37 %). Yellowish powder; mp 240-245 °C (water). IR (KBr): 3405, 3312, 3185, 3044, 2945, 2900, 1613 cm$^{-1}$. MS (EI) m/z (%): 246 (M$^+$, 3), 202 (41), 189 (49), 170 (52), 158 (84).

$^{1}$H NMR (DMSO-d$_6$) $\delta$: 2.00 (2H, quint., $J$ = 7.1 Hz), 2.32 (3H, s), 2.62 (2H, t, $J$ = 7.1 Hz), 2.81 (2H, m), 3.42 (2H, s), 4.10 (1H, m), 6.94 (1H, dt, $J$ = 8, 2 Hz), 6.99 (1H, dt, $J$ = 8, 2 Hz), 7.25 (1H, dd, $J$ = 8, 2 Hz), 7.42 (1H, dd, $J$ = 8, 2 Hz). $^{13}$C NMR (DMSO-d$_6$) $\delta$: 22.5, 25.3, 32.8, 33.8, 47.5, 107.7, 110.6, 118.1, 118.5, 120.3, 128.8, 134.9, 135.6, 178.2. Anal. Calcd. for C$_{14}$H$_{18}$N$_2$O$_2$ (246.30): C, 68.26; H, 7.37; N, 11.38; Found: C, 68.41; H, 7.08; N, 11.82.

Hydrolysis of 6e. Amino ester 6e: 0.74 g (2.70 mmol); Ba(OH)$_2$.8H$_2$O: 2.46 g (7.80 mmol); MeOH: 8 mL; Water: 8 mL.

[2-(3-Dimethylamino-propyl)-1H-indol-3-yl]-acetic acid (1e). Yield: 0.68 g (97 %). For spectral data, see ref. 14.

General procedure for KOH assisted reaction. A mixture of amino ester and KOH in MeOH-water was heated under reflux for 2-2.5 h. After evaporation of the MeOH, the residue was dissolved in water (8-10 mL), acidified to pH=6 with 10% HCl under cooling, the precipitate was filtered off, washed with ice-water, and dried to yield amino acids 1b and 1d.

Hydrolysis of 6b. Amino ester 6b: 0.55 g (1.63 mmol); KOH: 0.33 g (5.88 mmol); MeOH: 6 mL; Water: 1 mL.

[2-(3-Benzylamino-propyl)-1H-indol-3-yl]-acetic acid (1b). Yield: 0.50 g (95 %). White-grey powder; mp 172-176 °C (water). IR (KBr): 3420, 3170, 3100, 3030, 2980, 1632 cm$^{-1}$. MS (EI) m/z (%): 322 (M$^+$, 2), 308 (14), 290 (14), 278 (26), 188 (12), 170 (39), 157 (26). $^{1}$H NMR
(DMSO-d$_6$) δ: 1.91 (2H, quint., $J = 7.1$ Hz), 2.60 (2H, t, $J = 7.1$ Hz), 2.78 (2H, t, $J = 7.1$ Hz), 3.53 (2H, s), 3.73 (2H, s), 5.90 (1H, brs), 6.94 (1H, dt, $J = 8.1$, 2 Hz), 7.00 (1H, dt, $J = 8.1$, 2 Hz), 10.87 (1H, brs). $^{13}$C NMR (DMSO-d$_6$) δ: 23.2, 27.7, 31.8, 46.9, 51.6, 106.0, 110.6, 118.2, 118.3, 120.3, 127.4, 128.4, 128.7, 128.9, 135.5, 136.3, 137.7, 174.9. HREIMS: calcd: 322.1681, found: 322.1703.

Hydrolysis of 6d. Amino ester 6d: 0.88 g (2.51 mmol); KOH: 0.55 g (9.80 mmol); MeOH: 10 mL; Water: 2 mL.

{2-[3-(Benzyl-methyl-amino)-propyl]-1H-indol-3-yl}-acetic acid (1d). Yield: 0.74 g (88 %). White crystals; mp 163-165 °C (water). IR (KBr): 3391, 3270, 3060, 2944, 1640 cm$^{-1}$. MS (EI) m/z (%): 336 (M$^+$, 1), 292 (16), 191 (5), 170 (16). $^1$H NMR (DMSO-d$_6$) δ: 1.87 (2H, quint., $J = 7.2$ Hz), 2.11 (3H, s), 2.41 (2H, t, $J = 7.2$ Hz), 2.74 (2H, t, $J = 7.2$ Hz), 3.40 (2H, s), 3.46 (2H, s), 5.18 (1H, brs), 6.87 (1H, dt, $J = 8.1$, 2 Hz), 6.95 (1H, dt, $J = 8.1$, 2 Hz), 7.22 (1H, dd, $J = 8.1$, 2 Hz), 7.25-7.32 (5H, m), 7.48 (1H, dd, $J = 8.1$, 2 Hz), 10.80 (1H, brs). $^{13}$C NMR (DMSO-d$_6$) δ: 23.9, 27.3, 33.4, 41.8, 56.9, 61.7, 107.5, 110.3, 117.7, 118.7, 119.6, 126.9, 128.3, 128.9, 135.4, 136.4, 139.4, 174.9. HREIMS: calcd: 336.1838, found: 336.1818.

Reduction of ester amide 4b by LiAlH$_4$. To a solution of 4b (3.47 g, 9.90 mmol) in anhydrous THF (120 mL) LiAlH$_4$ (1.34 g, 35.3 mmol) was added in portions and the reaction mixture was stirred at rt for 30 min. The excess of LiAlH$_4$ was destroyed with sat. aq. solution of Na$_2$SO$_4$ at 0°C, filtered, and washed with THF (5x20 mL). The combined filtrates were concentrated under reduced pressure, the residue was acidified to pH=6 with 10% HCl and extracted with CHCl$_3$ (5x20 mL). The combined organic layers were dried (Na$_2$SO$_4$), filtered, evaporated to dryness, and crystallised in diethyl ether to obtain N-benzyl-3-[3-(2-hydroxy-ethyl)-1H-indol-2-yl]propionamide (10b) (2.95 g, 92 %), as white crystals. Mp 126-128 °C (diethyl ether). IR (KBr): 3393, 3347, 3246, 3052, 2936, 1650 cm$^{-1}$. MS (EI) m/z (%): 322 (M$^+$, 3), 304 (2), 291 (3), 231 (16), 200 (37), 184 (4), 168 (12), 160 (68). $^1$H NMR (CDCl$_3$) δ: 2.28 (1H, brs), 2.49 (2H, t, $J = 7.3$ Hz), 2.90 (2H, t, $J = 7.3$ Hz), 3.01 (2H, t, $J = 7.3$ Hz), 3.75 (2H, t, $J = 7.3$ Hz), 4.27 (2H, d, $J = 5.1$ Hz), 6.38 (1H, t, $J = 5.1$ Hz), 7.01 (1H, dt, $J = 8$, 1.7 Hz), 7.11 (1H, dt, $J = 8$, 1.7 Hz), 7.05-7.18 (5H, m), 7.22 (1H, dd, $J = 8$, 1.7 Hz), 7.46 (1H, dd, $J = 8$, 1.7 Hz), 9.02 (1H, brs). $^{13}$C NMR (CDCl$_3$) δ: 20.8, 27.0, 35.6, 43.0, 62.0, 106.9, 110.3, 117.5, 118.5, 120.7, 126.8, 126.9, 127.6, 128.0, 135.0, 135.1, 137.2, 174.2. Anal. Calcd. for C$_{20}$H$_{22}$N$_2$O$_2$ (322.40): C, 74.50; H, 9.23; N, 11.66; Found: C, 74.77; H, 9.11; N, 11.23.

Homologation. To a solution of alcohol 10b (0.69 g, 2.14 mmol) triethylamine (0.60 mL, 4.31 mmol) in anhydrous CH$_2$Cl$_2$ (30 mL) mesyl chloride (0.33 mL, 4.26 mmol) was added, and the reaction mixture was stirred at 0°C for 30 min. under N$_2$. After dilution with glacial 5 % NaOH solution (40 mL) the mixture was extracted with CH$_2$Cl$_2$ (3x40 mL). The combined organic layers were washed with water (10 mL), dried (Na$_2$SO$_4$), and evaporated to dryness under reduced pressure.
The residue (1.04 g) was dissolved in anhydrous DMSO (40 mL), KCN (0.42 g, 6.45 mmol) was added, and the reaction mixture was heated at 100 °C for 1 h. After dilution with ice-water (40 mL), the mixture was extracted with CHCl₃ (4x30 mL), the combined organic layers were washed with water (2x10 mL), dried (Na₂SO₄), and evaporated to dryness under reduced pressure. The residue was purified by flash chromatography (eluent: CHCl₃:MeOH 200:1), and crystallised to give N-benzyl-3-[3-(2-cyano-ethyl)-1H-indol-2-yl]propionamide (11b) (0.34 g, 48 %), as a white powder. Mp 158-160 °C (diethyl ether). IR (KBr): 3366, 3280, 3065, 2960, 2245, 1650 cm⁻¹. MS (EI) m/z (%): 331 (M⁺, 98), 291 (71), 224 (11), 197 (11), 184 (100).

1H NMR (DMSO-d₆) δ: 2.62 (2H, t, J = 7.7 Hz), 2.72 (2H, t, J = 7.1 Hz), 3.02 (2H, t, J = 7.1 Hz), 3.07 (2H, t, J = 7.7 Hz), 4.31 (2H, d, J = 5.1 Hz), 7.00 (1H, dt, J = 8.1, 2 Hz), 7.08 (1H, dt, J = 8.1, 2 Hz), 7.10-7.17 (5H, m), 7.21 (1H, dd, J = 8.1, 2 Hz), 7.54 (1H, dd, J = 8.1, 2 Hz), 8.38 (1H, t, J = 5.1 Hz), 10.84 (1H, brs).

13C NMR (DMSO-d₆) δ: 18.4, 20.1, 21.9, 35.9, 42.2, 107.7, 110.9, 117.9, 118.5, 120.6, 120.9, 126.8, 127.2, 127.6, 128.3, 135.6, 136.2, 139.6, 171.4. Anal. Calcd. for C₂₁H₂₁N₃O (331.41): C, 76.10; H, 6.39; N, 12.68; Found: C, 76.51; H, 6.78; N, 12.72.

Reduction of cyano amide 11b by B₂H₆.DMS. To a 6 °C solution of cyano amide 11b (1.26 g, 3.80 mmol) in anhydrous THF (70 mL) was added B₂H₆.DMS 2M solution in toluene (4.80 mL, 9.60 mmol). The reaction mixture was stirred at 10 °C for 20 h. After evaporation of the solvent, the amine-borane complex was destroyed in refluxing ethanol in the presence of Na₂CO₃. After filtration on celite, the solvent was evaporated to dryness and the residue was purified by flash chromatography (eluent: CHCl₃:MeOH 96:4→92:8) to obtain 3-[2-(3-benzylamino-propyl)-1H-indol-3-yl]propionitrile (12b) (0.91 g, 75 %), as a viscous yellow oil. IR (film): 3395, 3330, 3295, 3240, 3100, 3060, 2930, 2245, 1495 cm⁻¹. MS (EI) m/z (%): 317 (M⁺, 66), 277 (28), 210 (15), 198 (25), 184 (35), 170 (58). ¹H NMR (CDCl₃) δ: 1.68 (2H, quint., J = 7.2 Hz), 2.55 (2H, t, J = 8.1 Hz), 2.70 (2H, t, J = 7.2 Hz), 2.75 (1H brs), 2.81 (2H, t, J = 7.2 Hz), 3.01 (2H, t, J = 8.1 Hz), 3.76 (2H, s), 7.05 (1H, dt, J = 8.1, 2 Hz), 7.10 (1H, dt, J = 8.1, 2 Hz), 7.28 (1H, dd, J = 8.1, 2 Hz), 7.22-7.31 (5H, m), 7.40 (1H, dd, J = 8.1, 2 Hz), 9.76 (1H, brs). ¹³C NMR (CDCl₃) δ: 18.7, 20.5, 23.8, 28.7, 48.5, 53.6, 107.2, 110.8, 117.1, 119.9, 121.0, 127.3, 128.3, 128.5, 128.6, 135.3, 136.4, 138.8. Anal. Calcd. for C₂₁H₂₃N₃ (317.42): C, 79.45; H, 7.30; N, 13.24; Found: C, 79.59; H, 7.78; N, 12.92.

Hydrolysis of nitrile. A cold (-15 °C) solution of nitrile 12b (0.65 g, 2.05 mmol) in 30 mL saturated HCl-MeOH was allowed to stand for 16 h. After warming to rt MeOH (25 mL) and water (0.5 mL) were added and the reaction mixture was heated under reflux for 3-5 h. After evaporation of the solvent, the residue was dissolved in water (15 mL), rendered alkaline with 30 % NaOH under cooling, and extracted with CHCl₃ (5x20 mL). The organic layers were dried (Na₂SO₄), filtered, evaporated to dryness, and purified by column chromatography (eluent: CHCl₃:MeOH 98:2) to afford methyl 3-[2-(3-benzylamino-propyl)-1H-indol-3-yl]propionate (13b) (0.545 g, 76 %), as a viscous oil. IR (film): 3395, 3195, 3055, 3030, 2945, 1735 cm⁻¹. MS (EI) m/z (%): 350 (M⁺, 81), 319 (20), 277 (25), 243 (25), 230 (42), 217 (64), 184 (14), 170 (56).
$^1$H NMR (CDCl$_3$) $\delta$: 1.80 (2H, quint., $J = 7.2$ Hz), 2.01 (1H, brs), 2.60 (2H, t, $J = 8.1$ Hz), 2.69 (2H, t, $J = 7.2$ Hz), 2.80 (2H, t, $J = 7.2$ Hz), 3.01 (2H, t, $J = 8.1$ Hz), 3.63 (3H, s), 3.75 (2H, s), 7.03 (1H, dt, $J = 8$, 1.8 Hz), 7.07 (1H, dt, $J = 8$, 1.8 Hz), 7.24 (1H, dd, $J = 8$, 1.8 Hz), 7.14-7.35 (5H, m), 7.48 (1H, dd, $J = 8$, 1.8 Hz), 9.24 (1H, brs). $^{13}$C NMR (CDCl$_3$) $\delta$: 18.9, 23.0, 28.3, 47.9, 50.6, 53.1, 108.6, 109.7, 117.0, 118.0, 120.0, 126.3, 127.2, 127.4, 127.7, 134.5, 134.7, 138.9, 173.0. HREIMS: calcd: 350.1994, found: 350.1964.

Hydrolysis of amino ester 13b. A mixture of amino ester 13b (0.407 g, 1.16 mmol) and KOH (0.22 g, 3.90 mmol) in MeOH (6 mL) water (0.5 mL) was heated under reflux for 3-4 h. The reaction mixture was evaporated to dryness, the residue was dissolved in water (8 mL), and washed with diethyl ether (2x10 mL). The aqueous phase was acidified to pH=6 with 10 % HCl under cooling and the precipitate was filtered off, washed with ice-water and dried to obtain 3-[(2-(3-benzylamino-propyl)-1H-indol-3-yl)propionic acid (2b) (0.334 g, 85 %), as a white-grey powder. Mp 123-126 °C (water). IR (KBr): 3340, 3230, 3195, 3060, 3030, 2950, 1615 cm$^{-1}$. MS (EI) $m/z$ (%): 336 (M$^+$, 42), 277 (5), 264 (7), 257 (8), 239 (10), 236 (14), 229 (13), 216 (18), 203 (36), 156 (32). $^1$H NMR (DMSO-d$_6$ at 353 K) $\delta$: 1.92 (2H, quint., $J = 7.5$ Hz), 2.53 (2H, t, $J = 8$ Hz), 2.71 (2H, t, $J = 7.5$ Hz), 2.83 (2H, t, $J = 7.5$ Hz), 2.98 (2H, t, $J = 8$ Hz), 3.83 (2H, s), 5.85 (1H, brs), 6.99 (2H, m), 7.24-7.48 (7H, m), 10.52 (1H, brs). $^{13}$C NMR (DMSO-d$_6$ at 353 K) $\delta$: 19.6, 23.2, 28.8, 35.6, 47.8, 52.3, 109.0, 110.3, 117.3, 117.8, 119.7, 126.5, 127.8, 127.9, 128.0, 135.4, 135.6, 139.4, 174.2. HREIMS: calcd: 336.1838, found: 336.1817.

Acknowledgements

An Europol Agro doctoral fellowship for S.-I. B. is gratefully acknowledged.

References