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NITROGEN-CONTAINING COMPOUNDS FROM THE MOSS *FONTINALIS SQUAMOSA*†¶

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Key Word Index—*Fontinalis squamosa*; Musci; Fontinalin; harmol, harmol propionic acid.

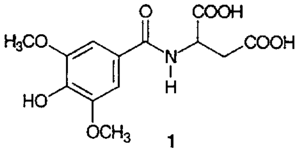
Abstract—The alkaloid harmol and its hitherto unknown propionic acid derivative as well as a new amino acid derivative fontinalin were isolated from the watermoss *Fontinalis squamosa*. The structures have been elucidated spectroscopically and by independent chemical synthesis. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Nitrogen-containing secondary metabolites in bryophytes are fairly rare. Thus the hornwort *Anthoceros agrestis* produces in sterile cultures some glutamic acid amides of hydroxybenzoic-, protocatechuic-, vanillic-, isoferulic- and coumarylic acid [1]. Furthermore, the new alkaloid anthocerodiazonin with a 9-membered ring system was isolated from the same species [1]. Two prenylated indole derivatives occur in the liverwort genus *Riccardia* [2]. The liverwort *Metzgeria rufula* synthesizes rufulamide, an oligopeptide analogue combined with malonic and anthranilic acid [3].

The presence of a cyanogenic glycoside has been shown for the moss *Dicranum scoparium* [4].

In the present paper, we report on the occurrence of nitrogen-containing secondary compounds in a moss species.



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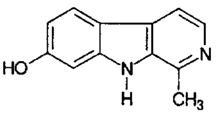

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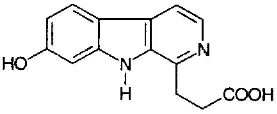

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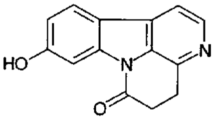

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RESULTS AND DISCUSSION

The work-up of an aqueous methanol extract yielded the two new compounds fontinalin (**1**) and harmol propionic acid ester (**3**) as well as the harmane alkaloid 7-hydroxyharmane(=harmol) (**2**) which is found in different families of angiosperms [5]. The Mr of **1** is 312 (FABMS, *m/z* 312 $[M-H]^+$). The NMR data are presented in Tables 1 (^1H) and 2 (^{13}C). From the ^1H NMR data the symmetry of a 1, 3, 4, 5 tetra substituted benzene ring is apparent, since a singlet (δ 7.20) in the aromatic region integrates to two protons. The downfield shifted doublet at δ 8.59 belongs to a proton of a carbonic acid amide. The singlet at δ 3.8 (6H) is due to two methoxy groups directly bound to the aromatic system. The spectrum is completed by the resonance of an ABX-spin system. The X-part causes a multiplet at δ 4.74, since the couplings of the A- and B-unit, respectively, are superimposed by further coupling of the methine unit with the proton of the amide.

The A-unit shows the corresponding doublet of doublet at δ 2.76 with coupling constants of 16.3 and 7.8 Hz. the B-unit gives rise to a doublet of doublet at δ 2.86 with coupling constants of 16.3 and 6.0 Hz. The correlation peaks in the ^1H, ^1H-Cosy spectrum prove the additional coupling of the X-unit of the ABX-spin system with the proton of the amide. The symmetry of the molecule is obvious from the ^{13}C

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¶ Dedicated to Prof. H. Geiger on the occasion of his 70th birthday.

Table 1. ^1H NMR data of compounds **1** and **3** (measured in DMSO-d_6)

H	1	H	3
NH	8.59 *d* (7, 8)*	NH	11.38 *s*
Aryl-H	7.20 *s*	H-3	8.12 *d* (5, 2)
CH-CH_2	4.77-4.71 *m*	H-5	7.92 *d* (8, 5)
2 × OCH_3	3.80 *s*	H-4	7.73 *d* (5, 2)
CH-CH_2	2.86 *dd* (16.3/6.0)	H-6	6.68 *dd* (8.5/2.0)
CH-CH_2	2.67 *dd* (16.3/7.8)	H-8	6.70 *d* (2.0)
		CH_2-COOH	3.25 *t* (7, 4)
		Ar-CH_2	2.76 *t* (7, 4)

**J* (H_2) in parenthesis

Table 2. ^{13}C NMR data of compounds **1** and **3** (measured in DMSO-d_6)

C	1	C	3
COOH	172.73	COOH	177.26
COOH	171.89	C-1	143.29
CONHR	165.71	C-3	137.34
2 × C_{AR}-OCH_3.	147.51	C-4	112.00
C_{AR}-OH	139.01	C-4a	127.74
C_{AR}-$CONH_3$	123.68	C-4b	113.76
2 × C_{AR}-H	105.53	C-5	122.40
2 × OCH_3	56.20	C-6	109.64
CH-CH_2	49.48	C-7	158.30
CH-CH_2	36.23	C-8	96.65
		C-8a	133.89
		C-8b	134.00
		Ar-CH_2	32.25
		CH_2COOH	28.43

NMR spectrum (Table 2). An additional DEPT-spectrum allowed the exact assignment of the corresponding signals. Thus for fontinalin (**1**) the structure of N-(4-hydroxy-3,5-dimethoxybenzoyl)aspartic acid with the substitution pattern 1,3,4,5 in the aromatic nucleus can be assigned from the spectroscopic data. However, the NMR data do not rigorously exclude the possibility of an alternative 1,2,4,6 tetrasubstitution at the benzene ring. Therefore, an independent structure proof was achieved by chemical synthesis of **1** according to Scheme 1.

Synthesis of fontinalin

O-Benzyl syringa acid (**5**) [6] and the hydrogen tosylate of dibenzyl aspartate (**6**) [7, 8] were reacted with DCC in the presence of triethyl amine to give tribenzyl fontinalin (**7**). Catalytic debenzylation of **7** by means of H_2/Pd-C yielded fontinalin **1** identical in all spectroscopic data with the natural product.

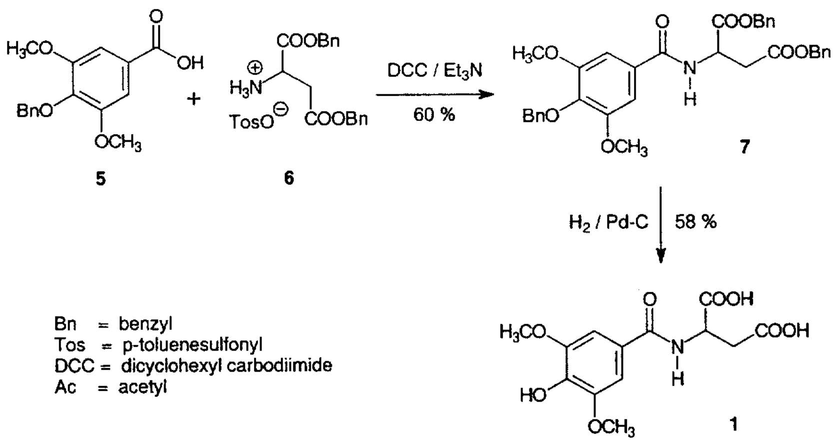
Compound **2** was identified as harmol by its spectral data (UV, MS, ^1H NMR, ^{13}C NMR) in comparison with an authentic sample [9–11].

The Mr of **3** is 256. A comparison between the NMR spectra of **3** (Tables 1 and 2) and the known harmol (**2**) shows the identity of the aromatic protons and the indole-NH-proton. There is, however, a difference in the aliphatic region of **2** which contains instead of a methyl group at CH_2-CH_2 unit giving rise to an A_2B_2 spin system with triplets at δ_H 2.76 and 3.25 and signals δ_C 28.43 and 32.25 in addition the signals of a carboxylic group are found (see Experimental). Thus, for **3**, the structure of 3-(7-hydroxy-β-carbolin-l-yl) propionic acid can be assigned. Accordingly, the EI- and CI-mass of **3** spectrum is dominated by the dehydration product 4,5-dihydro-9-hydroxycanthinone (**4**).

Synthesis of harmol propionic acid

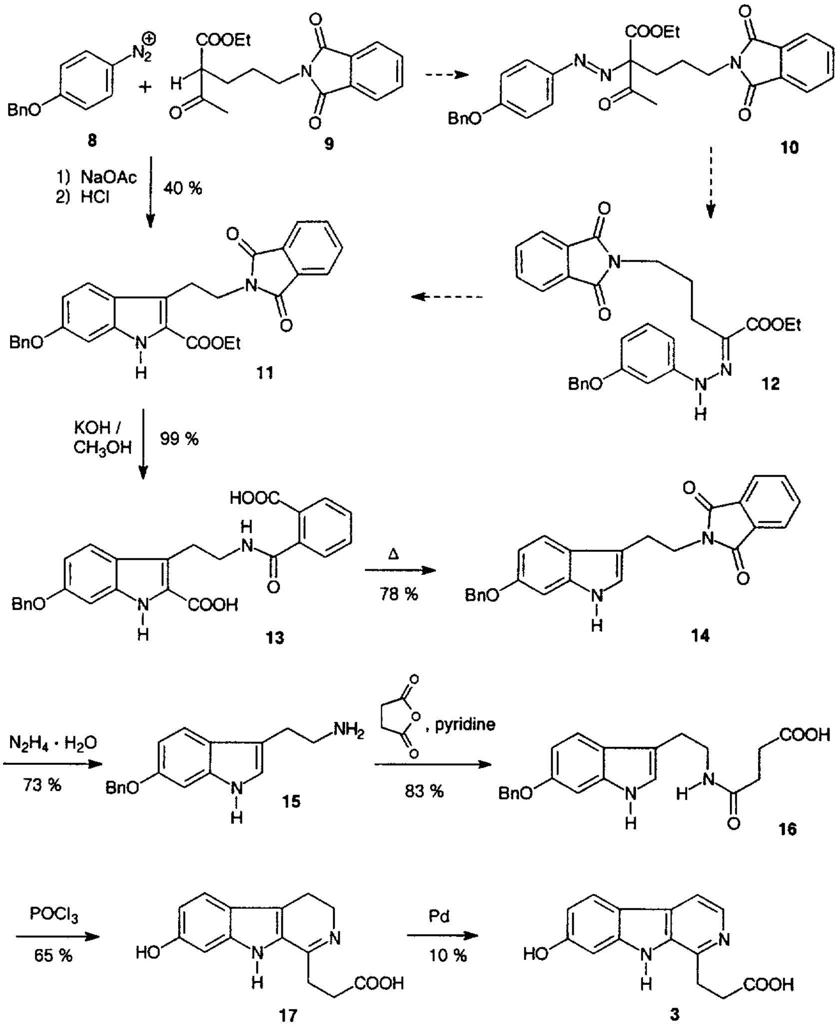
The structure of this new natural product was also proven by independent synthesis according to scheme 2.

Ethyl 2-(3-phthalimidopropyl) acetoacetate (**9**) [12] was coupled with the diazonium salt of 3-benzyloxy aniline (**8**) [13] in the presence of sodium acetate followed by treatment with HCl in anhydrous toluene. This one-pot procedure proceeded via a multi-step sequence including JAPP-KLINGEMANN reaction of the primarily formed azo compound **10** to give the hydrazone **12** after acid cleavage of **10** and tautomerization of the resulting azo system; finally FISCHER indole synthesis occurred, giving rise to **11**. Saponification of the ester function in **11** (KOH/methanol) was accompanied by opening of the phthalimide moiety to give the dicarboxylic acid **13**, whose thermolysis led to decarboxylation at the indole α-position and to recyclization forming **14** [14]. Cleavage of the phthalimide was achieved by hydrazinolysis to yield 6-benzyloxy tryptamine (**15**), which was acylated by succinic anhydride in pyridine to give **16**. Treatment of **16** with $POCl_3$ effected ring closure of the 3,4-dihydro-β-carboline system and concomitant debenzylation at the phenolic OH-group (**17**). Subsequently, **17** was dehydrogenated with palladium to give (7-hydroxy-β-carbolin-l-yl)propionic acid (**3**) identical in all spectroscopic respects with the natural product.



Bn = benzyl
Tos = p-toluenesulfonyl
DCC = dicyclohexyl carbodiimide
Ac = acetyl

Scheme 1. Chemical synthesis of compound **1**.



Scheme 2. Chemical synthesis of compound **3**.

EXPERIMENTAL

Plant material

Fontinalis squamosa (Hedw.) was collected in July 1992 in a brook near Grimburger Hof, Wadrill, Saarland, (Germany). A voucher specimen is deposited in the herbarium SAAR, no. 2411, Saarbrücken.

Extraction and isolation

Cleaned, air dried gametophytic material (700 g) was ground and digested with $CHCl_2$. The residue was extracted then with 80% MeOH (containing 1% HOAc). The crude extracts were submitted to VLC on RP 18 with 75% aq. MeOH. Further fractionation was performed by MPLC on RP-18 using a gradient between 5% aq. MeOH and 100% MeOH containing 5% HOAc. The final purification of compounds **1**–**3** was achieved as follows: **1**, Sephadex LH 20 with 10% aq. MeOH; **2**, Sephadex LH 20 using a gradient between 5% and 20% aq. MeOH; **3**, Sephadex LH 20 using a gradient between 5% and 40% aq. MeOH and RP 18 with 5% HOAc/25% aq. MeOH. The yields were 86 mg **1**, 6 mg **2** and 2 mg **3**.

Chromatography

TLC: Cellulose Avicel, TLC-Ready-Foils (Schleicher & Schuell) F 1440, Polygram pre-coated plastic sheets, polyamide 6 (Macherey-Nagel); CC: Sephadex LH 20, (Pharmacia) and silica gel, particle size 63–200 μm (J. T. Baker); HPLC: Nucleosil 5 C_{18}(ET-250/8/4, Macherey-Nagel), flow rate 1 ml min^{-1}; MPLC: LiChroprep RP-18, particle size 40–63 μm (Merck).

Spectroscopic data

NMR: 400 MHz (1D) and 500 MHz (2D; 1H, 1H-COSY-correlation); FABMS: Xenon, glycerol as matrix, 5-6KeV; CIMS:CH_4, 120 eV.

Compound 1. NMR: Tables 1 and 2; λ_{max}^{MeOH} nm: 240–271; FABMS *m/z* 312 $[M-H]^-$.

Synthesis of fontinalin (*Scheme* 1)

(*a*) *Dibenzyl N-*(4*-benzyloxy-*3,5*-dimethoxybenzoyl*) *aspartate* (**7**). 4-Benzyloxy-3,5-dimethoxy benzoic acid (**5**) [6] (10.0 g, 34.8 mM) and dibenzyl aspartate hydrogen tosylate (**6**) [7, 8] (17.0 g, 35.0 mM) were suspended in dry CH_2Cl_2 (35 ml) at 0°. Triethyl amine (4.8 ml, 35.0 mM) was added dropwise followed by DCC (8.00 g, 38.8 mM) in CH_2Cl_2 (6 ml). The reaction mixture was stirred for 1 h at 0° and 12 h at room temp. The ppd DCU was filtered off and washed with CH_2Cl_2. The filtration was washed successively with 2 M HCl, H_2O, a satd soln of $NaHCO_3$ and H_2O (each 60 ml) and dried over anhydr. $MgSO_4$. After removal of the solvent the residue was crystallized from EtOAc–petrol (40–60°) (1:1). Yield: 12.1 g (60%) **7**, colourless crystals, mp 110°. IR (KBr) ν cm^{-1}: 3295, 1710, 1640, 1585; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.95 (1H, *d J* = 7.8 Hz), 7.46-7.24 (15H, *m*), 7.17 (2H, *s*), 5.14, 5.10 (2H, *s*), 4.98-4.92 (3H, *m*), 3.81 (6H, *s*), 3.08 (1H, *dd*, *J* = 16.3/6.3 Hz), 2.93 (1H, *dd*, *J* = 16.3/7.9 Hz); ^{13}C NMR (400 MHz, DMSO-d_6): δ 170.49, 169.83, 165.75, 152.77, 139.27, 137.53, 135.87, 135.75, 128.60, 128.27, 128.15, 128.00, 127.93, 127.81, 127.70, 127.60, 116.58, 105.25, 73.92, 49.52, 35.66; EIMS *m/z* (rel. int.): 583 $[M]^+$ (4), 492 (10), 181 (36), 91 (100), 65 (15).

(*b*) *N-*(3,5*-Dimethoxy-*4*-hydroxy benzoyl*) *aspartic acid* (*fontinalin*) (**1**). The benzyl protected fontinalin (**7**) (5.00 g, 9.00 mM) was dissolved in HOAc (150 ml) and EtOAc (60 ml). Pd on charcoal (5%, 0.50 g) was added and the soln was hydrogenated at a H_2 pressure of 5 bar for 12 h. The catalyst was filtered off and washed with EtOAc, the solvents are removed *in vacuo* and the residue is recrystallized from MeOH. Yield: 1.60 g (58%) **1**, colourless crystals, mp 160°. IR (KBr) ν cm^{-1}: 3565, 3495, 3240, 1705, 1640, 1605, 1545; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.58 (1H, *d J* = 7.8 Hz), 7.20 (2H, *s*), 4.76-4.71 (1H, *m*), 3.82 (6H, *s*), 2.87 (1H, *dd*, *J* = 16.3/6.0 Hz), 2.69 (1H, *dd*, *J* = 16.3/7.8 Hz); ^{13}C NMR (400 MHz, DMSO-d_6): δ 172.58, 171.75, 165.64, 147.43, 138.93, 123.57, 105.44, 56.13, 49.40, 36.07; CIMS *m/z* (rel. int.): 313 $[M]^+$ (20), 312 (100), 298 (5), 275 (3), 222 (4).

Synthesis of (7*-hydroxy-β-carbolin -l-yl*) *propionic acid* (**3**) (Scheme 2)

(*a*) *Ethyl* 6*-benzyloxy-*3*-*(2*-*N*-phthalimidoethyl*) *indole* 2*-carboxylate* (**11**). To a soln of 3-benzyloxy aniline (**8**) [13] (15.7 g, 79.0 mM) in hot EtOH (50 ml) a mixture of conc. HCl (32 ml) and H_2O (50 ml) followed by crushed ice (75 g) was added with stirring. To the resulting suspension a soln of $NaNO_2$ (7.10 g, 0.12 M) in H_2O (25 ml) was added dropwise, while the temp was maintained below 5°. When the addition was complete, stirring was continued for 40 min at 8–10°. Excess HNO_2 was destroyed by addition of urea, then charcoal was added, the mixture filtered and the filtrate cooled to 0° (soln A).

Ethyl 2-(3-N*-phthalimidopropyl*) *acetoacetate* (**9**) [12] (25.0 g, 79.0 mM) was dissolved in hot EtOH (125 ml) and NaOAc (65.0 g, 0.80 M) followed by crushed ice (50 g) was added. With vigorous stirring, soln A was added rapidly at ca 5°, and stirring was continued until the temp. of the reaction mixture reached 20°. Then the dark suspension was extracted (× 3) with toluene (100 ml), the combined extracts were dried over unhydr. Na_2SO_4 and the solvent was removed *in vacuo*. The crude phenylhydrazone **12** was dissolved in EtOH (175 ml), the soln was heated under reflux and saturated with gaseous HCl. After 3 h the reaction mixture was cooled to 0°, the precipitate formed was filtered, washed with EtOH and ice-cold water, dried and recrystallized from toluene.

Yield: 22.2 g (40%) **11**, brownish needles, mp 199°.

IR (KBr) ν cm^{-1}: 3330, 1780, 1720, 1680, 1630, 1585; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 11.30 (1H, *s*), 7.79 (4H, *s*), 7.49 (1H, *d*, $J = 8.8$ Hz), 7.47-7.32 (5H, *m*), 6.91 (1H, *d*, $J = 2.1$ Hz), 6.74 (1H, *dd*, $J = 8.8/2.1$ Hz), 5.10 (2H, *s*), 4.18 (2H, *q*, $J = 7.1$ Hz), 3.84, 3.33 (2H, *t*, $J = 6.8$ Hz), 1.28 (3H, *t*, $J = 7.1$ Hz); ^{13}C NMR (400 MHz, DMSO-d$_6$): δ 167.58, 161.44, 157.09, 137.15, 134.18, 131.52, 128.35, 127.70, 127.68, 127.51, 127.48, 122.79, 121.96, 120.57, 119.45, 111.56, 95.47, 69.39, 59.91, 37.91, 23.36, 14.07; CIMS *m/z* (rel. int.): 470 $[M]^+$ (8), 469 (27), 468 (100), 378 (18), 377 (61), 160 (17), 91 (24).

(*b*) 6-*Benzyloxy*-3-[2-(2-*carboxybenzoylamino*)*ethyl*] *indole* 2-*carboxylic acid* (**13**). A suspension of the ester **11** (20.0 g, 42.8 mM) in EtOH (80 ml) and aq. KOH [23.4 g (0.40 M) KOH in H_2O (320 ml) was heated under reflux for 1.75 h. Then the major amount of EtOH was distilled off, the soln cooled to 10° and acidified by the slow addition of 4 M HCl. The resulting precipitate was filtered by suction, washed with ice water (150 ml) and dried *in vacuo* at 120°.

Yield: 19.4 g (99%) **13**, colourless crystals, mp 248° (dec.). IR (KBr) ν cm^{-1}: 3395, 1705, 1690, 1655, 1630, 1580; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 11.27 (1H, *s*), 8.51 (1H, *s*), 7.75-7.72 (1H, *m*), 7.66 (1H, *d*, $J = 8.8$ Hz), 7.51-7.28 (8H, *m*), 6.94 (1H, *d*, $J = 2.2$ Hz), 6.82 (1H, *dd*, $J = 8.8/2.2$ Hz), 5.13 (2H, *s*), 3.42, 2.50 (2H, *t*, $J = 6.8$ Hz); ^{13}C NMR (400 MHz, DMSO-d$_6$): δ 168.29, 168.15, 163.22, 138.19, 137.18, 136.89, 131.26, 130.68, 128.92, 128.30, 128.08, 128.00, 127.62, 127.48, 123.41, 122.34, 121.18, 120.26, 111.07, 95.48, 69.38, 40.28, 24.29; CIMS *m/z* (rel. int.): 458 $[M]^+$ (1), 397 (24), 396 (77), 305 (85), 292 (30), 266 (67), 237 (42), 236 (41), 214 (15), 201 (27), 175 (23), 160 (15), 158 (18), 146 (57), 117 (16), 104 (29), 91 (100), 76 (20).

(*c*) 6-*Benzyloxy*-3-(2-N-*phthalimidoethyl*) *indole* (**14**). The acid **13** (20.0 g, 43.6 mM) was fused under a N_2 atmosphere at 250° and kept for 1 h at this temp. When the evolution of CO_2 ceased, the melt was cooled to room temp and dissolved in ethyl methyl ketone (80 ml). The soln was filtered, the filtrate concentrated to a vol of ca 20 ml and EtOH (80 ml) added. The precipitate was cooled to 0°, filtered by suction and washed with cold EtOH. After trituration with 0.1 M NaOH (50 ml) at 20° for 30 min and filtration the product was recrystallized from toluene.

Yield: 13.5 g (78%) **14**, faintly yellow crystals, mp 200° (lit [14]: mp 203°). IR (KBr) ν cm^{-1}: 3395, 1710, 1695, 1660, 1635, 1565; ^{1}H NMR (400 MHz, pyridine-d$_5$): δ 11.52 (1H, *s*), 7.86 (1H, *d*, $J = 8.6$), 7.81-7.19 (10H, *m*), 7.17 (1H, *s*), 7.08 (1H, *dd*, $J = 8.6/2.2$ Hz), 5.10 (2H, *s*), 4.14, 3.31 (2H, *t*, $J = 7.8$ Hz); ^{13}C NMR (400 MHz, pyridine-d$_5$): δ 168.38, 156.05, 138.42, 138.34, 134.09, 132.74, 128.78, 127.95, 122.42, 119.71, 112.08, 110.15, 97.11, 70.69, 39.11, 25.14; CIMS *m/z* (rel. int.): 396 $[M]^+$ (37), 305 (50), 292 (21), 266 (100), 237 (55), 201 (17), 199 (11), 175 (28), 147 (63), 146 (66), 117 (11), 104 (31), 91 (89), 76 (25).

(*d*) 2-(6-*benzyloxyindol*-3-*yl*) *Ethylamine-hydrochloride* (6-*benzyloxy tryptamine-hydrochloride*) (**15**). The soln of **14** (13.0 g, 32.8 mM) and hydrazine hydrate (80%, 6.2 ml) in EtOH (350 ml) was heated under reflux for 2.5 h. The solvent was removed *in vacuo* and 2 M NaOH (100 ml) together with Et_2O (160 ml) is added. The mixture is cooled to 0° and the precipitate (impurities) was filtered off, the Et_2O phase was separated and washed with H_2O. Addition of 1M HCl (100 ml) gave the hydrochloride, which was filtered and dried *in vacuo*.

Yield: 7.24 g (73%) **15**, colourless crystals, mp 237°. IR (KBr) ν cm^{-1}: 3395, 3195, 1630, 1595, 1555; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.77 (1H, *s*), 8.12 (3H, *s*), 7.47-7.29 (6H, *m*), 7.08 (1H, *d*, $J = 1.8$ Hz), 6.96 (1H, *s*), 6.76 (1H, *dd*, $J = 8.6/1.8$ Hz), 5.11 (2H, s), 3.03-2.98 (4H, *m*); ^{13}C NMR (400 MHz, DMSO-d$_6$): δ 154.44, 137.58, 136.89, 128.26, 127.50, 127.33, 122.00, 121.46, 118.61, 109.47, 109.28, 96.59, 69.59, 40.12, 23.02; CIMS *m/z* (rel. int.): 266 $[M-HCl]^+$ (100), 252 (22), 237 (32), 175 (21), 146 (39), 91 (15).

(*e*) *Succinic acid* [(6-*benzyloxyindol*-3-*yl*)*ethyl*] *monoamide* (**16**). A soln of the hydrochloride **15** (5.00 g, 17.0 mM) in dry pyridine (100 ml) was heated to reflux, succinic anhydride (1.70 g, 17.0 mM) was added portionwise and heating was continued for 1.5 h. The solvent was removed *in vacuo*, the residue suspended in water (100 ml) and conc. HCl was added until a pH of 1 was reached. The aq. phase was extracted several times with CH_2Cl_2, the extracts combined and concentrated, until the product crystallized. It was then filtered off, washed with H_2O and recrystallized from EtOAc.

Yield: 5.00 g (83%) **16**, colourless needles, mp 174°. IR (KBr) ν cm^{-1}: 3405, 3265, 3075, 1690, 1650, 1640, 1565; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.59 (1H, *s*), 7.94 (1H, *t*, $J = 5.5$), 7.47-7.29 (6H, *m*), 7.00 (1H, *s*), 6.92 (1H, *d*, $J = 2.0$ Hz), 6.73 (1H, *dd*, $J = 8.5/2.0$ Hz), 5.10 (2H, s), 3.30 (2H, *m*), 2.76 (2H, *t*, $J = 7.5$ Hz), 2.44, 2.32 (2H, *t*, $J = 7.0$ Hz); ^{13}C NMR (400 MHz, DMSO-d$_6$): δ 173.73, 170.76, 154.41, 137.69, 136.78, 128.27, 127.49, 127.35, 121.91, 121.28, 118.74, 111.84, 109.03, 96.11, 69.58, 40.11, 30.09, 29.19, 25.20; CIMS *m/z* (rel. int.): 366 $[M]^+$ (2), 348 (100), 266 (94), 257 (76), 237 (45), 175 (11), 158 (19), 146 (51), 117 (11), 91 (35).

(*f*) 3-(3,4-*Dihydro*-7-*hydroxy*-β-*carbolin*-1-*yl*) *propionic acid* (**17**). A soln of **16** (4.00 g, 12.0 mM) in $POCl_3$ (100 ml) was heated to 100°. The green soln was cooled to room temp. and poured on crushed ice (300 g). After stirring for 1 h, the yellowish precipitate was filtered off, washed with H_2O, triturated with MeOH (20 ml) and dried *in vacuo*.

Yield: 2.05 g (65%) **17**, yellowish microcrystalline powder, mp 225° (dec.). IR (KBr) ν cm^{-1}: 3325, 1720, 1630, 1550; ^{1}H NMR (400 MHz, DMSO): δ 13.70 (1H, *s*), 12.65 (1H, *s*), 9.70 (1H, *s*), 7.88 (1H, *d*, $J = 8.4$), 7.02 (1H, *d*, $J = 2.0$ Hz), 6.73 (1H, *dd*, $J = 8.4/2.0$ Hz), 3.88, 3.18 (2H, *t*, $J = 8.6$ Hz), 3.25, 2.85 (2H, *t*, $J = 7.3$ Hz); ^{13}C NMR (400 MHz, DMSO): δ 172.29, 158.71, 143.69, 133.93, 133.84, 128.25, 122.74, 113.30, 109.45, 97.02, 41.98, 31.95, 27.87, 18.50; EIMS *m/z* (rel. int.): 258 $[M]^+$ (1), 240 (73), 238 (50), 211 (100), 184 (78), 170 (20), 158 (21), 131 (37).

(*g*) 3-(*7-Hydroxy-β-carbolin-*1*-yl*) *propionic acid* (**3**). The acid **17** (1.05 g, 4.1 mM) was heated with Pd black (2.0 g) to 180° for 30 min. After cooling to room temp. H_2O (50 ml) was added and the suspension was heated to reflux for 10 min. The Pd was removed by filtration and the filtrate was cooled to 0°. The crystallized product was filtered by suction, washed with water and Et_2O and dried *in vacuo*.

Yield: 0.11 g (10%) **3**, colourless microcrystalline powder, mp 245° (dec.). IR (KBr) ν cm^{-1}: 3325, 1715, 1640, 1550; ^{1}H NMR (400 MHz, DMSO): δ 13.75 (1H, *s*), 11.34 (1H, *s*), 9.76 (1H, *s*), 8.13 (1H, *d*, $J = 5.2$ Hz), 7.93 (1H, *d*, $J = 8.4$ Hz), 7.75 (1H, *d*, $J = 5.2$ Hz), 6.78 (1H, *d*, $J = 2.0$ Hz), 6.70 (1H, *dd*, $J = 8.4/2.0$ Hz), 3.25, 2.81 (2H, *t*, $J = 7.3$ Hz); [Remark: the signals assigned to the COOH group (13.75) and to the OH group (9.76) of **3** do not appear in the ^{1}H NMR spectrum of the natural product (Table 1, measured in DMSO-d_6) due to H-D exchange in the deuterated solvent. Concerning all other signals, the spectra of the synthetic and natural product are practically identical.]; ^{13}C NMR (400 MHz, DMSO): δ 172.30, 158.30, 143.29, 137.35, 134.04, 133.85, 127.76, 122.43, 113.75, 112.05, 109.67, 96.65, 32.25, 28.46; EIMS *m/z* (rel. int.): 256 $[M]^+$ (1), 138 (100), 211 (43), 184 (67), 131 (35).

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