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Synthesis and Biological Evaluation of a Indomethacin-Library Reveals a New Class of Angiogenesis-Related Kinase Inhibitors**

Claudia Rosenbaum[a], Patrick Baumhof[b], Ralf Mazitschek[c], Oliver Müller[d], Athanassios Giannis[b]* and Herbert Waldmann[a]*

[a*] Prof. Dr. H. Waldmann, Dr. C. Rosenbaum
Max-Planck-Institut für molekulare Physiologie,
Abteilung Chemische Biologie
Otto-Hahn-Strasse 11, 44227 Dortmund (Deutschland) und
Universität Dortmund, Fachbereich 3, Organische Chemie
Fax.: (+49)231-133-2499
E-mail: herbert.waldmann@mpi-dortmund.mpg.de

[b*] Prof. Dr. A. Giannis, Dipl.-Chem. Patrick Baumhof
Universität Leipzig
Institut für Organische Chemie
Johannisallee 29, 04103 Leipzig (Deutschland)
Fax.: (+49)341-9736-599
E-mail: giannis@chemie.uni-leipzig.de

[c] Dr. R. Mazitschek
Universität Karlsruhe
Institut für Organische Chemie
Richard-Willstätter-Allee 2
76128 Karlsruhe (Deutschland)

[d] PD Dr. O. Müller
Max-Planck-Institut für molekulare Physiologie,
Abteilung Strukturelle Biologie

General Methods for Chemical Synthesis

Materials: Unless otherwise noted, reagents were purchased from Acros Chimica, Fluka, Sigma, Aldrich and used without further purification. LC-MS was performed on the 1100 series from Hewlett-Packard with a VP 50/10 Nucleosil C18PPN-column (Macherey-Nagel) and a Finnigan LCQ ESI-Spectrometer with a gradient: 90/10 (v/v) H_2O/acetonitrile (0.1% trifluoroacetic acid) to 10/90 (v/v) in 30 min, flow 1 ml/min. Preparative HPLC was conducted by using Pro Star 215/Varian HPLC with a VP 250/21 Nucleosil C18PPN-column (Macherey-Nagel) and a gradient: 90/10 (v/v) H_2O/acetonitrile (0.1% trifluoroacetic acid) to 10/90 (v/v) in 30 min, flow 20 ml/min. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Mercury 400 (400 MHz ^{1}H-, 100,6 MHz ^{13}C-NMR). ^{1}H NMR spectra are tabulated in the following order: chemical shifts calculated with reference to solvent standards based on tetramethylsilane, multiplicity (s, singulet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constants in Hz, and number of protons. 70 eV- electron ionisation (EI) high-resolution mass spectra (HR-MS) were recorded on Finnigan MAT MS 70 spectrometer.

General procedure for hydrazone formation

The aldehyde resin (0.5 g; 0.55 mmol) was dried in high vacuum overnight and suspended in 5 ml of dichloroethane (DCE). To the mixture 2.75 mmol (5 equiv.) hydrazine hydrochloride and 194 µl (6 equiv.) triethylamine (NEt_3) were added under argon

atmosphere. The mixture was shaken at 45°C overnight. After cooling the resin was filtered and washed three times with each 5 ml *N*,*N*-dimethylformamide (DMF), 90/10 (v/v) DMF/H_2O, DMF, dichloromethane, ethyl acetate and methanol.

General procedure for hydrazone acylation

The hydrazone resin (0.5 g; 0.45 mmol) was dried in high vacuum overnight and suspended in 5 ml of pyridine. To the mixture 1.35 mmol (3 equiv.) acid chloride was added under argon. The mixture was shaken at 80°C over night. After cooling the resin was filtered and washed three times with *N*,*N* dimethylformamide (DMF), 90/10 (v/v) DMF/H_2O, DMF, dichloromethane, ethyl acetate and methanol.

General procedure for cleavage and indole rearrangement

The acylated hydrazone resin (150 mg; 0.11 mmol) was suspended in 6 ml DCE/TFA (1/1). The corresponding ketone (10 equiv.) was added and the mixture was heated for 15 min to 2 h at 70°C. After cooling the mixture was quenched with methanol and the resin was filtered and washed with 5 ml dichloromethane, methanol, ethyl acetate and methanol. The filtrate was evaporated to dryness and the crude product was purified by preparative HPLC.

Analytical data of selected compounds

[1-(4-Bromo-benzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-acetic acid (C-III-*9*): white solid; yield 57%; mp 151 °C; 1H-NMR (400

MHz, CD3OD): δ = 7.73 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.60 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7,00 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.91 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.67 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.80 (s, 3 H, OCH_3), 3.69 (s, 2 H, CH_2), 2.31 (s, 3 H, CH_3); MS (ESI): 400,0 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{19}H_{15}BrNO_4$ $[M-H]^-$ 400,0185, found 400,0181.

3-[1-(4-Bromo-benzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-propionic acid (C-III-*10*): white solid; yield 25%; mp 210 °C; ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.73 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.60 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7,00 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.91 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.67 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.80 (s, 3 H, OCH_3), 2.81 (t, ^3J = 7.6 Hz, 2 H, CH_2), 2.49 (t, ^3J = 7.6 Hz, 2 H, CH_2), 2.29 (s, 3 H, CH_3); MS (ESI): 414.39; 416.36 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{20}H_{17}BrNO_4$ $[M-H]^-$ 414,0341, found 414,0346.

4-[1-(4-Bromo-benzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-butyric acid (C-III-*14*): green solid; yield 71%; mp 210 °C; ^{1}H-NMR (400 MHz, CD3OD): δ = 7.70 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.57 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7,08 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.23 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.65 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.81 (s, 3 H, OCH_3), 2.73 (t, ^3J = 7,00 Hz, 2 H, CH_2), 2.37 (t, ^3J = 7,00 Hz, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 1.91 (q, ^3J = 7,00 Hz, 2 H, CH_2).

MS(ESI): 430.23; 428.23 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{21}H_{19}BrNO_4$ $[M-H]^-$ 428,0497, found. 428,0505

4-[1-(4-Chloro-benzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-butyric acid (C-I-*14*): white solid; yield 46%; mp 105 °C; ^{1}H-NMR (400 MHz, CD3OD): δ = 7.64 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.54 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7,03 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.2 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.65 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.81 (s, 3 H, OCH_3), 2.73 (t, ^3J = 7,00 Hz, 2 H, CH_2), 2.37 (t, ^3J = 7,00 Hz, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 1.91 (q, ^3J = 7,00 Hz, 2 H, CH_2); MS (ESI): 384.18 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{21}H_{19}ClNO_4$ $[M-H]^-$ 384.1002, found 384.1013.

9-(4-Chloro-benzoyl)-6,7,8,9-tetrahydro-5H-carbazole-3-carboxylic acid (G-I-*1*): white solid; yield 26%; mp 254-255 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, ^4J = 2,0 Hz, 1 H, arom. CH), 7.78 (dd, ^3J = 9 Hz, ^4J = 2,0 Hz, 1 H, arom. CH), 7.66 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 7.54 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 7.24 (d, ^3J = 9 Hz, 1 H, arom. CH), 2.73 (t, ^3J = 6 Hz, 2 H, CH_2), 2.57 (t, ^3J = 6 Hz, 2 H, CH_2), 2,03-1.82 (m, 4 H, CH_2); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 210.19 (C=O), 179.37 (C=O).139.26 (C_q), 137.59 (C_q), 137.29 (C_q), 139.97 (C_q), 131,02 (arom. CH), 129.15 (arom. CH), 127.35 (C_q), 125.12 (C_q), 124.83 (arom. CH), 120.20 (arom. CH).118.28 (C_q), 114,00 (arom. CH), 25.77 (CH_2), 23.58 (CH_2), 22.33 (CH_2), 21,05 (CH_2); MS (ESI): 352.16 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{20}H_{15}ClNO_3$ $[M-H]^-$ 352,0741, found 352,0767.

(4-Chloro-phenyl)-(2-methoxy-6,7,8,9,10,11-hexahydro-cycloocta[β]indol-5-yl)-methanone (C-I-7): white solid; yield 6%; mp 127°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, ^{3}J = 8.6 Hz, 2 H, arom. CH), 7.62 (d, ^{3}J = 8.6 Hz, 2 H, arom. CH), 6.92 (d, ^{4}J = 2.5 Hz, 1 H, arom. CH), 6.71 (d, ^{3}J = 8.6 Hz, 1 H, arom. CH), 6.62 (dd, ^{3}J = 8.6 Hz, ^{4}J = 2.5 Hz, 1 H, arom. CH), 3.85 (s, 3 H, OCH_3), 2.97 (t, ^{3}J = 6.24 Hz, 2 H, CCH_2CH_2), 2.81 (t, ^{3}J = 6.24 Hz, 2 H, CCH_2CH_2), 1.74 (m, 4 H, $CH_2CH_2CH_2$), 4.51 (m, 2 H, $CH_2CH_2CH_2$), 1.38 (m, 2 H, $CH_2CH_2CH_2$).; ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 155.96 (C=O), 148.80 (C_q), 146.10 (C_q), 139.17 (NC_q), 138.82 (C_q), 134.40 (C_q), 131.32 (2 C, arom. CH), 130.94 (C_q), 129.26 (2 C, arom. CH), 120.98 (C_qCH_2), 115.26 (arom. CH), 111.15 (arom. CH), 101.21 (arom. CH), 56.09 (CH_3O), 30.38 (CH_2), 30.14 (CH_2), 27.06 (CH_2), 26, 11 (CH_2), 24.71 (CH_2), 23.44 (CH_2); GC-MS, m/z (rel. int. %): 367 (54) [M^+], 339 (13), 228 (23), 200 (15), 139 (100), 111 (25), 75 (5); HR-MS (FAB, m/z): calcd for $C_{22}H_{22}ClNO_2$ $[M+H]^+$ 368.1417, found 368.1445.

(4-Chloro-phenyl)-(10-methoxy-5,6-dihydro-benzo[c]carbazol-7-yl)-methanone (C-I-*13*): white solid; yield 31%; mp 76°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, ^{3}J = 7.6 Hz, 1 H, arom. CH), 7.67 (d, ^{3}J = 8.4 Hz, 2 H, arom. CH), 7.52 (d, ^{4}J = 2.4 Hz, 1 H, arom. CH), 7.49 (d, ^{3}J = 8.4 Hz, 2 H, arom. CH), 7.47 (d, ^{3}J = 8.6 Hz, 1 H, arom. CH), 7.36 (t, ^{3}J = 7.6 Hz, 1 H, arom. CH), 7.26 (d, ^{3}J = 7.6 Hz, 1 H, arom. CH), 7.20 (t, ^{3}J = 7.6 Hz, 1 H, arom. CH), 6.85 (dd, ^{3}J = 8.4 Hz, ^{4}J = 2.4 Hz, 1 H, arom. CH), 3.93 (s, 3 H, OCH_3), 2.94 (t, ^{3}J = 7.4 Hz, 2 H, CH_2) 2.74

(t, ^3J = 7.4 Hz, 2 H, CH_2).; ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 189.96 (C=O), 156.66 (C_q), 139.49 (C_q), 138.58 (C_q), 132.19 (C_q), 132.17 (C_q), 131.19 (2 C, arom. CH), 129.32 (2 C, arom. CH), 128.14 (arom. CH), 128.04 (C_q), 127.80 (C_q), 127.14 (arom. CH), 126.35 (arom. CH), 123.31 (2 C, arom. CH), 115.86 (arom. CH), 113.02 (C_q), 111.15 (arom. CH), 103.50 (arom. CH), 56.26 (CH_3O), 30.12 (CH_2), 24.45 (CH_2); GC-MS, m/z (rel. int. %): 387 (57) [M^+], 248 (7), 232 (5), 204 (10), 139 (100), 111 (19), 75 (4); HR-MS (FAB, m/z): calcd for $C_{20}H_{19}ClNO_4$ $[M+H]^+$ 388.1104, found 388.1084.

[1-(4-Fluoro-benzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]-acetic acid (C-II-*9*): white solid; yield 35%; mp 129-131°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (dd, ^3J (H,H) = 8.6 Hz, ^4J (H,F) = 5.5 Hz, 2 H, arom. CH), 7.16 (t, ^3J (H,H), (H,F) = 8.6 Hz, 2 H, arom. CH), 6.94 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.85 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.66 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.83 (s, 3 H, OCH_3), 3.70 (s, 2 H, CH_2), 2.39 (s, 3 H, CH_3); MS (ESI): 340.1 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{19}H_{15}FNO_4$ $[M-H]^-$ 340,0985, found 340,0974.

Biphenyl-4-yl-(6-methoxy-1,2,3,4-tetrahydro-carbazol-9-yl)-methanone (C-IV-*1*): white solid; 31%; mp 84-85°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.70-7.59 (m, 6 H, arom. CH), 7.44-7.36 (m, 3 H, arom. CH), 7.11 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.81 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.63 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.78 (s, 3 H, OCH_3), 2.58 (m, 4 H, CH_2), 1.79-1.77 (m, 4 H, CH_2); GC-MS, m/z (rel. int. %): 381 (31) [M^+],

207 (3), 193 (2), 181 (100), 152 (30), 127 (2), 75 (2); HR-MS (FAB, m/z): calcd for $C_{26}H_{23}NO_2$ $[M]^+$ 381.1729, found 381.1754.

[5-Methoxy-2-methyl-1-(pyridine-2-carbonyl)-1H-indol-3-yl]-acetic acid (C-VI-*9*): white solid; yield 37%; mp 150-153°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.89-8.84 (m, 2 H, arom. CH), 8.24 (d, ^3J = 8.0 Hz, 1 H, arom. CH), 7.71 (dd, ^3J = 8.0 Hz, ^4J = 5.0 Hz, 1 H, arom. CH), 7.00 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.96 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.68 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.81 (s, 3 H, OCH_3), 3.71 (s, 2 H, CH_2), 2.32 (s, 3 H, CH_3); MS (ESI): 323.30 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{18}H_{15}N_2O_4$ $[M-H]^-$ 323.1032, found 323.1055.

[5-Methoxy-2-methyl-1-(thiophene-2-carbonyl)-1H-indol-3-yl]-acetic acid methyl ester (C-VIII-*9Me*): oil; yield 26%; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.73 (dd, ^3J = 5.0 Hz, ^4J = 1.2 Hz, 1 H, arom. CH), 7.55 (dd, ^3J = 5.0 Hz, ^4J = 1.2 Hz, 1 H, arom. CH), 7.13-7.10 (m, 2 H, arom. CH), 6.96 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.69 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.84 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.68 (s, 2 H, CH_2), 2.44 (s, 3 H, CH_3); GC-MS, m/z (rel Int. %): 343 (69) $[M^+]$, 284 (23), 190 (5), 173 (9), 158 (13), 130 (5), 111 (100), 83 (8); HR-MS (FAB, m/z): calcd for $C_{18}H_{18}NO_4S$ $[M+H]^+$ 344.0956, found 344.0959.

(3-Benzyl-5-bromo-2-methyl-indol-1-yl)-(4-chloro-phenyl)-methanone (A-I-*12*): white solid; yield 45%; mp 110-112°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 7.41-7.39 (m, 3 H, arom. CH), 7.25-7.20 (m, 2 H, arom. CH),

7.12-7.10 (m, 3 H, arom. CH), 7.04 (dd, ^3J = 9 Hz, ^4J = 2.0 Hz, 1 H, arom. CH), 6.80 (d, ^3J = 9.0 Hz, 1 H, arom. CH), 3.95 (s, 3 H, CH_2), 2.31 (s, 3 H, CH_3); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 168.42 (C=O), 139.50 (C_q), 135.69 (C_q), 135.29 (C_q), 133.73 (C_q), 132.13 (C_q), 131.40 (2 C, arom. CH), 129.42 (2 C, arom. CH), 129.00 (arom. CH), 128.80 (2 C, arom. CH), 128.28 (arom. CH), 126.52 (arom. CH), 126.02 (arom. CH), 121.56 (2 C, arom. CH), 117.72 (C_q), 116.21 (C_q), 115.60 (arom. CH), 30.19 (CH_2), 13.73 (CH_3); GC-MS, m/z (rel Int. %): 439 (32); 437 (24) [M^+], 218 (8), 176 (7), 139 (100), 111 (24), 75 (6); HR-MS (FAB, m/z): calcd for $C_{23}H_{17}Br(79)Cl(35)NO$ $[M]^+$ 437.0182, found 437.0156.

(6-Bromo-3-tert-butyl-1,2,3,4-tetrahydro-carbazol-9-yl)-furan-2-yl-methanone (A-VII-*8*): yellow solid; yield 89%; mp 110°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.63 (dd, ^3J = 1.8 Hz, ^4J = 0.8 Hz, 1 H, arom. CH), 7.55 (d, ^4J = 1.8 Hz, 1 H, arom. CH), 7.23-7.20 (m, 2 H, arom. CH), 7.12 (d, ^3J = 9.0 Hz, 1 H, arom. CH), 6.63 (dd, ^3J = 3.6 Hz, ^4J = 1.8 Hz, 1 H, arom. CH), 2.7 (m, 2 H, CH_2), 2.34 (m, H, CH), 2.00 (m, 2 H, CH_2), 1.55 (m, 2 H, CH_2), 0.98 (m, 9 H, -*t*Bu); GC-MS, m/z (rel Int. %): 401 (61); 399 (62) [M^+], 315 (9), 287 (13), 260 (8), 208 (7), 167 (11), 140 (3), 95 (100), 57 (5); HR-MS (FAB, m/z): calcd for $C_{21}H_{22}Br(79)NO_2$ $[M]^+$ 399.0834, found 399.0811.

(4-Chloro-phenyl)-(6,8-difluoro-1,4-dihydro-2H-3-thia-9-aza-fluoren-9-yl)-methanone (B-I-*6*): white solid; yield 60%; mp 107-108°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, ^3J = 8.6 Hz, 2

H, arom. CH), 7.44 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 6.95 (dd, ^3J (HF) = 9 Hz, ^4J (HH) = 2.0 Hz, 1 H, arom. CH), 6.63 (ddd, ^3J (HF) = 9 Hz, ^4J (HH) = 2.0 Hz, 1 H, arom. CH), 3.79 (s, 2 H, CH_2S), 3.05 (t, ^3J = 5.5 Hz, 2 H, CH_2CH$_2$S), 2.97 (t, ^3J = 5.5 Hz, 2 H, CH$_2$CH_2S); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 166.79 (C=O), 157.13 (C_q), 145.48 (C_q), 138.93 (C_q), 131.70 (C_q), 131.17 (2 C, arom. CH), 129.98 (C_q), 129.83 (2 C, arom. CH), 126.09 (C_q), 119.70 (C_q), 117.81 (C_q), 108.46 (arom. CH), 99.80 (arom. CH), 26.89 (CH_2), 26.18 (CH_2), 23.02 (CH_3); GC-MS, m/z (rel Int. %): 363 (37) [M^+], 224 (7), 190 (5), 152 (5), 139 (100), 111 (33), 75 (12); HR-MS (FAB, m/z): calcd for $C_{18}H_{12}(35)ClF_2NOS$ $[M]^+$ 363.0296, found 363.0268.

(4-Bromo-phenyl)-(3-ethyl-5-methoxy-2-methyl-indol-1-yl)-methanone (C-III-*4*): green oil; 73%; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, ^3J = 8.5 Hz, 2 H, arom. CH), 7.49 (d, ^3J = 8.5 Hz, 2 H, arom. CH), 6.85 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.83 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.58 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.77 (s, 3 H, OCH_3), 2.59 (q, ^3J = 7.6 Hz, 2 H, CH_2), 2.24 (s, 3 H, CH_3), 1.14 (t, ^3J = 7.6 Hz, 3 H, CH$_2$CH_3); GC-MS, m/z (rel Int. %): 373 (53); 371 (55) [M^+], 356 (7), 249 (7), 183 (100), 173 (5), 157 (28), 145 (9), 130 (7), 115 (3), 104 (8), 76 (9); HR-MS (FAB, m/z): calcd for $C_{19}H_{18}(79)BrNO_2$ $[M]^+$ 371.0521, found 371.0542.

Biphenyl-4-yl-(6-methoxy-2-methyl-1,2,3,4-tetrahydro-b-carbolin-9-yl)-methanone (C-IV-*5*): white solid; yield 81%; mp 197-199°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.79-7.73 (m, 3 H,

arom. CH), 7.68-7.63 (m, 3 H, arom. CH), 7.52-7.74 (m, 3 H, arom. CH), 7.05 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.81 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.76 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 4.83 (m, 1 H, $CH_2N(CH_3)$), 4.12 (m, 1 H, $CH_2N(CH_3)$), 3.83 (s, 3 H, OCH_3), 3.74 (m, 1 H, $N(CH_3)CH_2$), 2.58 (m, 2 H, CH_2CH_2), 3.22 (m, 1 H, $N(CH_3)CH_2$), 3.06 (s, 3 H, NCH_3); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 168.53 (C=O), 156.53 (C_q), 146.22 (C_q), 139.53 (C_q), 133.11 (C_q), 131.62 (C_q), 131.42 (C_q), 130.36 (2 C, arom. CH), 129.27 (2 C, arom. CH), 128.80 (2 C, arom. CH), 128.43 (C_q), 127.69 (arom. CH), 127.50 (2 C, arom. CH), 116.19 (arom. CH), 113.65 (arom. CH), 109.55 (C_q), 110.68 (arom. CH), 56.10 (CH_3O), 51.18 (CH_2), 50.20 (CH_2), 41.95 (CH_3), 22.39 (CH_2); GC-MS, m/z (rel Int. %): 396 (10) [M^+], 353 (32), 325 (7), 281 (13), 215 (6), 207 (33), 181 (100), 152 (32), 73 (5); HR-MS (FAB, m/z): calcd for $C_{26}H_{24}N_2O_2$ $[M]^+$ 396.1838, found 396.1829.

(2-Benzoyl-8-methoxy-1,2,3,4-tetrahydro-pyrido[4,3-b]indol-5-yl)-pyridin-2-yl-methanone (C-VI-*15*): white solid; yield 49%; mp 107°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.89-8.84 (m, 2 H, arom. CH), 8.16 (d, ^3J = 8.0 Hz, 1 H, arom. CH), 7.63 (dd, ^3J = 8.0 Hz, ^4J = 5.0 Hz, 1 H, arom. CH), 7.47-7.57(m, 6 H, arom. CH), 6.92-6.87 (m, 1 H, arom. CH), 6.74 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 4.91 (m, 1 H, CH_2N), 4.28 (m, 2 H, CH_2), 3.84 (s, 3 H, OCH_3), 3.70 (m, 1 H, CH_2), 2.87 (m, 2 H, CH_2); MS (ESI): 412.18 $[M+H]^+$; HR-MS (FAB, m/z): calcd for $C_{25}H_{22}N_3O_3$ $[M+H]^+$ 412.1661, found 412.1673.

[3-(4-Hydroxy-benzyl)-5-methoxy-2-methyl-indol-1-yl]-pyridin-2-yl-methanone (C-VI-*16*): colorless oil; yield 48%; mp °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.96-8.92 (m, 2 H, arom. CH), 8.33 (d, ^3J = 8.0 Hz, 1 H, arom. CH), 7.75 (dd, ^3J = 8.0 Hz, ^4J = 5.0 Hz, 1 H, arom. CH), 7.06 (d, ^3J = 8.4 Hz, 2 H, arom. CH), 6.88 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 6.81 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.75-6.73 (m, 2 H, arom. CH), 6.65 (dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.95 (s, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 2.35 (s, 3 H, CH_3); MS (ESI): 373.26 $[M+H]^+$; HR-MS (FAB, m/z): calcd for $C_{23}H_{21}N_2O_3$ $[M+H]^+$ 373.1552, found 373.1524.

9-(4-Chloro-benzoyl)-1,2,4,9-tetrahydro-3-thia-9-aza-fluorene-6-sulfonic acid (17; F-I-*6*): yellow solid; yield 53%; mp 153-155°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, ^4J = 1.8 Hz, 1 H, arom. CH), 7.69 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 7.57 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 7.47 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 1 H, arom. CH), 7.09 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 3.87 (s, 2 H, CH_2S), 2.94-2.89 (m, 4 H, CH_2CH_2S); MS (ESI): 406.15 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{18}H_{13}ClNO_4S_2$ $[M-H]^-$ 405.9974, found 405.9972.

1-(4-Chloro-benzoyl)-3-decyl-2-methyl-1H-indole-5-sulfonic acid (19; F-I-*11*): yellow solid; yield 12%; mp 126-128°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, ^4J = 1.8 Hz, 1 H, arom. CH), 7.67 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.57 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.53 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 1 H, arom. CH), 7.03 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 2.74 (t, ^3J = 7.4 Hz, 2 H, CH_2), 2.35 (s, 3 H, CH_3), 1.66 (q, ^3J = 7.4 Hz, 2 H,

$CH_2CH_2CH_2$), 1.41 – 1.29 (m, 14 H, CH_2), 0.89 (t, ^3J = 7.0 Hz, 3 H, CH_3); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 168.65 (C=O), 139.27 (C_q), 137.25 (C_q), 134.31 (C_q), 134.18 (C_q), 131.25 (2 C, arom. CH), 129.71 (C_q), 129.12 (2 C, arom. CH), 127.57 (C_q), 120.64 (arom. CH), 120.25 (C_q), 116.25 (arom. CH), 113.43 (arom. CH), 32.09 (CH_2), 30.10-29.48 (6C, CH_2), 23.79 (CH_2), 22.77 (CH_2), 13.51 (CH_3), 12.31 (CH_3); MS (ESI): 488.33 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{26}H_{32}ClNO_4S$ $[M-H]^-$ 488.1663, found 488.1671.

3-Benzyl-1-(4-chloro-benzoyl)-2-methyl-1H-indole-5-sulfonic acid (18; F-I-*12*): yellow solid; yield 6%; mp 107-108°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, ^4J = 1.8 Hz, 1 H, arom. CH), 7.71 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.58 (d, ^3J = 8.2 Hz, 2 H, arom. CH), 7.54 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 1 H, arom. CH), 7.24-7.23 (m, 4 H, arom. CH), 7.16-7.13 (m, 1 H, arom. CH), 7.03 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 4.12 (s, 2 H, CH_2), 2.39 (s, 3 H, CH_3); MS (ESI): 438.22 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{23}H_{17}ClNO_4S$ $[M-H]^-$ 438.0567, found 438.0594.

(6-Bromo-1,2,3,4-tetrahydro-carbazol-9-yl)-pyridin-2-yl-methanone (A-VI-*1*): white solid; yield 99%; mp 113-114°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.95 (m, 2 H, arom. CH), 8.28 (d, ^3J = 8.0 Hz, 1 H, arom. CH), 7.75 (dd, ^3J = 8.0 Hz, ^4J = 5.0 Hz, 1 H, arom. CH), 7.56 (s, 1 H, arom. CH), 7.20-7.25 (m, 2 H, arom. CH), 2.64 (m, 2 H, CH_2), 2.43 (m, 2 H, CH_2), 1.85-1.77 (m, 4 H, CH_2); HR-MS (FAB, m/z): calcd for $C_{18}H_{16}(79)BrN_2O$ $[M+H]^+$ 355.0446, found 355.0427.

(4-Chloro-phenyl)-(6-methyl-1,2,3,4-tetrahydro-carbazol-9-yl)-methanone (E-I-*1*): white solid; yield 90%; mp 134-136°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, ^{3}J = 8.2 Hz, 2 H, arom. CH), 7.64 (d, ^{3}J = 8.2 Hz, 2 H, arom. CH), 7.21 (s, 1 H, arom. CH), 7.05 (d, ^{3}J = 8.4 Hz, 1 H, arom. CH), 6.91 (d, ^{3}J = 8.4 Hz, 1 H, arom. CH), 2.67 (m, 2 H, CH_2), 2.62 (m, 2 H, CH_2), 2.43 (s, 3 H, CH_3), 1.86-1.80 (m, 4 H, CH_2); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 168.20 (C=O), 138.75 (C_q), 136.22 (C_q), 134.78 (C_q), 132.63 (C_q), 131.79 (C_q), 130.99 (2 C, arom. CH), 130.58 (C_q), 129.14 (2 C, arom. CH), 124.68 (arom. CH), 118.27 (arom. CH), 115.35 (C_q), 114.56 (arom. CH), 26.19 (CH_2), 23.98 (CH_2), 21.3 (CH_3), 22.68 (CH_2), 21.55 (CH_2); GC-MS, m/z (rel Int. %): 323 (60) [M^+], 184 (8), 167 (5), 139 (100), 111 (24), 75 (6).; HR-MS (FAB, m/z): calcd for $C_{20}H_{18}ClNO$ $[M]^+$ 323.1077, found 323.1083.

(4-Chloro-phenyl)-(6-nitro-1,2,3,4-tetrahydro-carbazol-9-yl)-methanone (H-I-*1*): white solid; yield 11%; mp 189°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, ^{4}J = 2.0 Hz, 1 H, arom. CH), 8.01 (dd, ^{3}J = 9 Hz, ^{4}J = 2.0 Hz, 1 H, arom. CH), 7.67 (d, ^{3}J = 8.6 Hz, 2 H, arom. CH), 7.51 (d, ^{3}J = 8.6 Hz, 2 H, arom. CH), 7.32 (d, ^{3}J = 9 Hz, 1 H, arom. CH), 2.75 (t, ^{3}J = 6 Hz, 2 H, CH_2), 2.60 (t, ^{3}J = 6 Hz, 2 H, CH_2), 1.90-1.83 (m, 4 H, CH_2); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 168.00 (C=O), 143.77 (C_q), 139.69 (C_q), 139.34 (C_q), 131.27 (2 C, arom. CH), 130.13 (C_q), 129.52 (2 C, arom. CH), 127.66 (C_q), 118.85 (arom. CH), 118.53 (C_q), 114.95 (C_q), 114.52 (arom. CH), 114.51 (arom. CH), 26.03 (CH_2), 23.61

(CH_2), 22.40 (CH_2), 21.30 (CH_2); HR-MS (FAB, m/z): calcd for $C_{19}H_{16}ClN_2O_3$ $[M+H]^+$ 355.0849, found 355.0862.

9-(4-Dimethylamino-benzoyl)-6,7,8,9-tetrahydro-5H-carbazole-3-sulfonic acid (F-IX-*1*): white solid; yield 24%; mp 215-217°C; MS (ESI): 397.20 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{21}H_{21}N_2O_4S$ $[M-H]^-$ 397.1222, found 397.1195.

9-(Thiophene-2-carbonyl)-6,7,8,9-tetrahydro-5H-carbazole-3-sulfonic acid (F-VIII-*1*): white solid; yield 66%; mp 65°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.95 (m, 2 H, arom. CH), 7.60-7.57 (m, 2 H, arom. CH), 7.32 (d, ^3J = 8.6 Hz, 1 H, arom. CH), 7.22 (m, 1 H, arom. CH), 2.3 (m, 4 H, CH_2), 1.88 (m, 4 H, CH_2); MS (ESI): 360.20 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{17}H_{14}NO_4S_2$ $[M-H]^-$ 360.0364, found 360.0336.

(4-Dimethylamino-phenyl)-(6-methoxy-1,4-dihydro-2H-3-thia-9-aza-fluoren-9-yl)-methanone (C-IX-*6*): white solid; yield 47%; mp 80-82°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 6.99 (d, ^3J = 9.0 Hz, 1 H, arom. CH), 6.90 (d, ^4J = 2.5 Hz, 1 H, arom. CH), 6.73 (d, ^3J = 8.6 Hz, 2 H, arom. CH), 6.66 (dd, ^3J = 9 Hz, ^4J = 2.5 Hz, 1 H, arom. CH), 3.81 (m, 5 H, OCH_3, CH_2S), 3.09 (s, 6 H, NCH_3), 2.97 (t, ^3J = 5.5 Hz, 2 H, CH_2CH_2S), 2.87 (t, ^3J = 5.5 Hz, 2 H, CH_2CH_2S); MS (ESI): 367.20 $[M+H]^+$; HR-MS (FAB, m/z): calcd for $C_{21}H_{22}N_2O_2S$ $[M+H]^+$ 367.4780, found 367.1452.

3-[5-Bromo-1-(furan-2-carbonyl)-2-methyl-1H-indol-3-yl]-propionic acid (A-VII-*10*): white solid; yield 27%; mp 144°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.59 (s, 1 H, arom. CH), 7.52 (d,

^4J = 1.8 Hz, 1 H, arom. CH), 7.11 (d, ^4J = 3.5 Hz, 1 H, arom. CH), 7.09 (d, ^3J = 8.8 Hz, 1 H, arom. CH), 6.89 (d, ^3J = 8.8 Hz, 1 H, arom. CH), 6.56 (s, 1 H, arom. CH), 2.91 (t, ^3J = 7.6 Hz, 2 H, CH_2), 2.49 (t, ^3J = 7.6 Hz, 2 H, CH_2), 2.29 (s, 3 H, CH_3); MS (ESI): 376.10; 374.10 $[M-H]^-$; HR-MS (FAB, m/z): calcd for $C_{17}H_{13}(79)BrNO_4$ $[M-H]^-$ 374.0028, found 373.9996.