Synthesis of diversely substituted bis-pyrrolizidino/thiopyrrolizidino oxindolo/acenaphthyleno curcuminoids via sequential azomethine ylide cycloaddition

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Supplymentary information and Documents:

General Experimental Information: 2-3
Spectral data of compounds 4Aa-4Fd: 3-18
Spectral data of compounds 5Aa-5Bb: 18-20
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Spectral data of compounds 7A-7D: 26-29
Spectral copy of compounds 4Aa-4Fd: 30-101
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2D NMR spectra, 6Aa, 6Ab, 7B and 7D: 157-173
Experimental Section:

General Information:

Chemistry:

All the compounds evaluated in this work were synthesized in two step sequences. Melting points were determined in capillaries and are uncorrected. IR spectra were recorded as KBr pellets using a JASCO 410 FTIR spectrometer. The NMR spectra were recorded using a Bruker 600 DPX spectrometer operating at 600 MHz for $^1$H and 150 MHz for $^{13}$C in Pyridine-$d_5$ with TMS as internal standard and the chemical shifts are reported in $\delta$ units. Mass spectra (positive mode) were obtained on a LC-ESI-Q-TOF micro mass spectrometer in the electrospray ionization mode. Curcumin was isolated from Curcuma longa in the usual way. Isatins, acenaphthoquinone and $\alpha$-amino acids were purchased from Alfa-Aesar Company. All other solvents and chromatographic absorbents were procured from E. Merck (Germany) and SRL (India) Ltd. unless otherwise indicated. Thin layer chromatography was performed on pre-coated silica gel 60 F$_{254}$ aluminum sheets (E. Merck, Germany) using the solvent system 5% MeOH in CHCl$_3$ and spots were developed using UV irradiation, Iodine and Liebermann-Burchard reagent. Compounds were separated using AKROS –“Automatic TLC Smart Flash” of Yamazen Corporation.

Typical experimental procedure for synthesis of mono cycloaddition products 3Aa (±):

A mixture of 1 (13.6 mmol, 5 g), isatin (13.6 mmol, 2.00 g) and proline (13.6 mmol, 1.56 g) was taken in a round bottom flask, dissolved in 50 mL methanol, and heated to reflux for 8 h. After completion of the reaction as evident from TLC, the solvent was removed and the crude product was subjected to column chromatography using gradual increasing methanol in chloroform as eluant using flash chromatography. The product was crystallized from chloroform-methanol mixture (85%, 6.56 g).

Typical experimental procedure for synthesis of mixed cycloaddition products:

A mixture of 3Aa (±) (1.76 mmol, 1 g), 5-iodoisatin (1.76 mmol, 481 mg) and proline (1.76 mmol, 205 mg) or thioproline (1.76 mmol, 235 mg) was taken in a round bottom flask, dissolved in 50 mL methanol, and heated to reflux for 8 h. The solvent was removed after completion of the reaction, evident from TLC, and the crude product was subjected to column chromatography using gradual increasing methanol in chloroform as eluant using flash chromatography to isolate diastereomeric mixed pyrrolizidino/pyrrilizidino-thiopyrrolizidino...
dispiro oxindolo curcuminoids. The product was crystallized from chloroform-methanol mixture.

**Compound 4Aa (±):**

**Color:** Obtained as white solid; **Yield:** 20% (314 mg); **Mp:** 219-221 °C; **Rf** 0.49 (6 % MeOH in CHCl₃);

**IR (KBr, ν_max Cm⁻¹):** 3376, 2960, 2869, 1722, 1612;

**¹H NMR (Py-d₅):** δ 11.51 (1H, s, -NH), 11.19 (1H, s, -NH), 7.97 (1H, s), 7.75 (1H, d, J=7.8 Hz), 7.38 (2H, m), 7.29 (2H, m), 7.22 (2H, m), 7.13 (1H, d, J=1.2 Hz), 6.99 (1H, t, J=7.8 Hz), 6.96 (1H, d, J=6.6 Hz), 6.87 (1H, d, J=8.4 Hz), 6.75 (1H, dd, J=1.8, 8.4 Hz), 5.80 (1H, s), 4.59 (1H, d, J=12.6 Hz), 4.43 (1H, d, J=12.6 Hz), 4.21 (2H, m), 3.82 (3H, s), 3.75 (1H, m), 3.66 (3H, s), 3.64 (1H, m), 2.74 (2H, m), 2.62 (2H, m), 1.87 (3H, m), 1.82 (2H, m), 1.70 (3H, m).

**¹³C NMR (Py-d₅):** δ 191.8 (-C=O), 190.8 (-C=O), 181.1 (-C=O), 180.2 (-C=O), 149.6 (-C), 149.2 (-C), 147.7 (-C), 147.6 (-C), 143.9 (-C), 143.6 (-C), 138.9 (-CH), 135.8 (-CH), 131.9 (-C), 130.9 (-C), 129.7 (-CH), 129.5 (-C), 127.1 (-C), 126.9 (-CH), 121.7 (2x-CH), 121.0 (-CH), 117.4 (-CH), 117.1 (-CH), 113.2 (-CH), 111.7 (-CH), 111.4 (-CH), 110.6 (-CH), 101.4 (-CH), 84.7 (-C), 74.49 (-C), 74.46 (-C), 74.42 (-CH), 73.5 (-CH), 65.2 (-CH), 63.6 (-CH), 56.3 (-OMe), 56.1 (-OMe), 52.8 (-CH), 52.6 (-CH), 48.6 (-CH₂), 48.3 (-CH₂), 31.13 (-CH₂), 31.06 (-CH₂), 28.1 (-CH₂), 27.8 (-CH₂).

**MS [ESI-MS, positive mode]:** found m/z 895 [M+H]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₅H₄₃N₄O₈I; found m/z 917.2042 [M+Na]⁺ [calcd. 917.2023].

**Compound 4Ab (±):**

**Color:** Obtained as white solid; **Yield:** 23% (362 mg); **Mp:** 192-194 °C; **Rf** 0.43 (6 % MeOH in CHCl₃);

**IR (KBr, ν_max Cm⁻¹):** 3383, 2960, 2872, 1718, 1611.

**¹H NMR (Py-d₅):** δ 12.18 (1H, s, -NH), 11.81 (1H, s, -NH), 7.91 (1H, d, J=1.8 Hz), 7.63 (1H, dd, J=1.8, 8.4 Hz), 7.25 (2H, m), 7.19 (1H, m), 7.17 (2H, d, J=7.8 Hz), 7.07 (1H, d, J=1.8 Hz), 7.00 (2H, m), 6.92 (1H, d, J=7.2 Hz), 6.85 (2H, m), 5.94 (1H, s), 4.42 (2H, t, J=12.0 Hz), 4.20 (1H, m), 4.10 (1H, m), 3.85 (1H, m), 3.79 (3H, s), 3.70 (1H, m), 3.67 (3H, s), 2.69 (2H, m), 2.61 (2H, m), 1.86 (2H, m), 1.79 (1H, m), 1.69 (5H, m).
$^{13}$C NMR (Py-d$_5$): δ 191.6 (-C=O), 189.7 (-C=O), 181.2 (-C=O), 180.5 (-C=O), 149.2 (-C), 149.1 (-C), 147.52 (-C), 147.50 (-C), 143.9 (-C), 143.5 (-C), 138.8 (-CH), 135.8 (-CH), 131.4 (-C), 131.2 (-C), 129.8 (-CH), 129.5 (-C), 127.1 (-CH), 126.6 (-C), 121.8 (-CH), 120.7 (2x-CH), 117.2 (-CH), 117.0 (-CH), 113.0 (-CH), 112.2 (-CH), 112.1 (-CH), 110.6 (-CH), 101.3 (-CH), 84.7 (-C), 74.9 (2x-C), 73.7 (-CH), 73.6 (-CH), 65.1 (-CH), 64.3 (-CH), 56.2 (-OMe), 56.1 (-OMe), 52.5 (-CH), 51.8 (-CH), 48.5 (-CH$_2$), 48.2 (-CH$_2$), 31.4 (-CH$_2$), 31.3 (-CH$_2$), 28.4 (-CH$_2$), 28.0 (-CH$_2$).

**MS [ESI-MS, positive mode]:** found m/z 895 [M+H]$^+$$^\dagger$, 917 [M+Na]$^+$. 
**HRMS [ESI-MS, positive mode]:** MF: C$_{45}$H$_{43}$N$_4$O$_8$I; found m/z 917.2034 [M+Na]$^+$ [calcd. 917.2023].

**Compound 4Ac (±):**

**Color:** Obtained as white solid; **Yield:** 21% (330 mg); **Mp:** 175-177 °C; **R$_f$** 0.39 (6 % MeOH in CHCl$_3$); 

$^1$H NMR (Py-d$_5$): δ 11.93 (1H, s, -NH), 11.54 (1H, s, -NH), 8.26 (1H, s), 7.60 (1H, m), 7.35 (1H, s), 7.28 (1H, t, $J$=7.8 Hz), 7.23 (2H, m), 7.16 (1H, m), 7.05 (2H, m), 6.93 (1H, d, $J$=8.4 Hz), 6.89 (2H, m), 6.54 (1H, d, $J$=7.8 Hz), 6.05 (1H, s), 4.71 (1H, m), 4.62 (1H, d, $J$=12 Hz), 4.33 (1H, m), 4.11 (1H, d, $J$=12 Hz), 3.95 (1H, m), 3.71 (3H, s), 3.55 (3H, s), 3.23 (1H, m), 2.83 (2H, m), 1.96 (1H, m), 1.90 (2H, m), 1.74 (2H, m), 1.64 (2H, m), 1.40 (2H, m).

$^{13}$C NMR (Py-d$_5$): δ 196.3 (-C=O), 194.5 (-C=O), 181.2 (-C=O), 179.4 (-C=O), 149.3 (-C), 148.3 (-C), 147.7 (-C), 147.5 (-C), 144.6 (-C), 144.1 (-C), 138.7 (-CH), 136.2 (-CH), 131.4 (-C), 131.0 (-C), 129.9 (-CH), 127.7 (-CH), 126.9 (-C), 126.8 (-C), 124.1 (-CH), 121.7 (-CH), 121.4 (-CH), 117.1 (-CH), 116.5 (-CH), 113.0 (-CH), 112.6 (-CH), 112.3 (-CH), 110.7 (-CH), 102.9 (-CH), 84.3 (-C), 76.5 (-C), 75.1 (-C), 73.8 (-CH), 65.7 (-CH), 64.6 (-CH), 56.1 (-OMe), 55.7 (-OMe), 53.3 (-CH), 52.7 (-CH), 52.0 (-CH), 51.5 (-CH$_2$), 48.5 (-CH$_2$), 31.3 (-CH$_2$), 29.9 (-CH$_2$), 28.2 (-CH$_2$), 26.8 (-CH$_2$).

**MS [ESI-MS, positive mode]:** found m/z 895 [M+H]$^+$$^\dagger$, 917 [M+Na]$^+$. 
**HRMS [ESI-MS, positive mode]:** MF: C$_{45}$H$_{43}$N$_4$O$_8$I; found m/z 917.2034 [M+Na]$^+$ [calcd. 917.2023].

**Compound 4Ad (±):**

**Color:** Obtained as white solid; **Yield:** 24% (378 mg); **Mp:** 218-220 °C; **R$_f$** 0.38 (6 % MeOH in CHCl$_3$);
IR (KBr, ν\text{max} Cm^{-1}): 3391, 2960, 1720, 1613;

$^1$H NMR (Py-d$_5$): δ 11.77 (1H, s, -NH), 11.51 (1H, s, -NH), 8.33 (1H, s), 7.67 (1H, d, J=7.2 Hz), 7.60 (1H, d, J=8.4 Hz), 7.36 (1H, s), 7.30 (1H, t, J=7.8 Hz), 7.20 (1H, m), 7.15 (2H, m), 7.01 (1H, d, J=7.8 Hz), 6.97 (1H, m), 6.92 (1H, m), 6.89 (1H, s), 6.54 (1H, d, J=8.4 Hz), 5.97 (1H, s), 4.96 (1H, m), 4.67 (1H, q, J=8.4 Hz), 4.59 (1H, d, J=12.6 Hz), 4.37 (1H, m), 4.23 (1H, d, J=12.0 Hz), 3.98 (1H, m), 3.70 (3H, s), 3.56 (3H, s), 3.15 (1H, m), 2.88 (1H, m), 2.74 (2H, m), 1.96 (1H, m), 1.89 (2H, m), 1.77 (1H, m), 1.67 (1H, m), 1.61 (1H, m), 1.51 (1H, m), 1.23 (1H, m).

$^{13}$C NMR (Py-d$_5$): δ 197.7 (-C=O), 186.0 (-C=O), 181.2 (-C=O), 179.5 (-C=O), 149.3 (-C), 148.3 (-C), 147.7 (-C), 147.5 (-C), 144.6 (-C), 144.0 (-C), 138.7 (-CH), 136.0 (-CH), 131.5 (-C), 131.0 (-C), 129.9 (-CH), 128.0 (-CH), 127.2 (-C), 126.9 (-C), 121.7 (-CH), 121.4 (-CH), 121.3 (-CH), 117.1 (-CH), 116.5 (-CH), 113.3 (-CH), 112.6 (-CH), 112.4 (-CH), 110.8 (-CH), 102.9 (-CH), 84.3 (-C), 76.4 (-C), 75.4 (-C), 73.7 (-CH), 65.6 (-CH), 64.5 (-CH), 56.1 (-OMe), 55.8 (-OMe), 53.8 (-CH), 52.6 (-CH), 51.5 (-CH$_2$), 51.1 (-CH), 48.6 (-CH$_2$), 31.3 (-CH$_2$), 29.4 (-CH$_2$), 28.2 (-CH$_2$), 26.8 (-CH$_2$).

MS [ESI-MS, positive mode]: found m/z 895 [M+H]$^+$, 917 [M+Na]$^+$.

HRMS [ESI-MS, positive mode]: MF: C$_{45}$H$_{43}$N$_4$O$_8$I; found m/z 895.2209 [M+H]$^+$ [calcd. 895.2204].

**Compound 4Ba (±):**

**Color:** Obtained as white solid; **Yield:** 19% (266 mg); **Mp:** 172-174 ºC; **R$_f$** 0.50 (6 % MeOH in CHCl$_3$);

$^1$H NMR (Py-d$_3$): δ 10.94 (1H, s, -NH), 10.91 (1H, s, -NH), 7.31 (1H, d, J=7.8 Hz), 7.27 (3H, m), 7.21 (1H, s), 7.18 (2H, m), 7.12 (1H, d, J=7.8 Hz), 6.92 (2H, m), 6.88 (1H, d, J=7.8 Hz), 6.77 (1H, s), 5.77 (1H, s), 4.50 (1H, d, J=12.8 Hz), 4.40 (1H, d, J=12.8 Hz), 4.31 (1H, m), 4.21 (1H, m), 3.82 (1H, m), 3.77 (3H, s), 3.74 (1H, m), 3.71 (3H, s), 2.80 (2H, m), 2.65 (1H, m), 2.60 (1H, m), 2.26 (3H, s), 2.22 (3H, s), 1.86 (4H, m), 1.78 (2H, m), 1.68 (2H, m).

$^{13}$C NMR (Py-d$_3$): δ 192.1 (-C=O), 190.3 (-C=O), 181.3 (-C=O), 181.1 (-C=O), 149.24 (-C), 149.18 (-C), 147.5 (-C), 147.4 (-C), 143.5 (-C), 139.9 (-C), 131.9 (-CH), 131.8 (-C), 131.5 (-C), 130.6 (-C), 129.7 (-CH), 127.3 (-CH), 126.6 (-C), 126.2 (-C), 125.5 (-CH), 121.6 (-CH), 121.13 (-CH), 121.07 (-CH), 119.4 (-C), 117.2 (-CH), 117.1 (-CH), 112.2 (-CH), 111.8 (-CH), 110.6 (-CH), 101.6 (-CH), 74.9 (-C), 74.5 (-C), 73.7 (-CH), 73.5 (-CH), 65.1 (-CH), 56.1 (-CH), 48.6 (-CH$_2$), 31.3 (-CH$_2$), 29.4 (-CH$_2$), 28.2 (-CH$_2$), 26.8 (-CH$_2$).
64.2 (-CH), 56.2 (-OMe), 56.1 (-OMe), 52.53 (-CH), 52.50 (-CH), 48.6 (-CH$_2$), 48.4 (-CH$_2$), 31.2 (-CH$_2$), 30.9 (-CH$_2$), 28.1 (-CH$_2$), 27.6 (-CH$_2$), 21.2 (-CH$_3$), 17.2 (-CH$_3$).

MS [ESI-MS, positive mode]: found m/z 797 [M+H]$^+$.  
HRMS [ESI-MS, positive mode]: MF: C$_{47}$H$_{48}$N$_4$O$_8$; found m/z 819.3361 [M+Na]$^+$ [calcd. 819.3370].

**Compound 4Bb (±):**

**Color:** Obtained as white solid; **Yield:** 22% (308 mg); **Mp:** 188-190 ºC; **R$_f$** 0.44 (6 % MeOH in CHCl$_3$);

$^1$H NMR (Py-d$_5$): $\delta$ 11.85 (1H, s, -NH), 11.73 (1H, s, -NH), 7.25 (2H, m), 7.21 (1H, m), 7.18 (2H, d, $J$=7.8 Hz), 7.11 (2H, m), 7.03 (1H, d, $J$=7.8 Hz), 6.97 (1H, d, $J$=7.8 Hz), 6.91 (2H, m), 6.75 (1H, s), 6.00 (1H, s), 4.48 (1H, d, $J$=12.0 Hz), 4.41 (1H, d, $J$=12.0 Hz), 4.18 (2H, m), 3.87 (1H, m), 3.74 (3H, s), 3.71 (3H, s), 3.66 (1H, m), 2.80 (1H, m), 2.73 (1H, m), 2.66 (1H, m), 2.61 (1H, m), 2.31 (3H, s), 2.16 (3H, s), 1.90 (1H, m), 1.83 (3H, m), 1.71 (3H, m), 1.63 (1H, m).

$^{13}$C NMR (Py-d$_5$): $\delta$ 191.7 (-C=O), 190.1 (-C=O), 181.6 (-C=O), 181.2 (-C=O), 149.3 (-C), 149.2 (-C), 147.63 (-C), 147.57 (-C), 143.9 (-C), 140.0 (-C), 131.9 (-CH), 131.7 (-C), 131.5 (-C), 130.7 (-C), 129.8 (-CH), 127.1 (-CH), 126.7 (-C), 126.4 (-C), 125.3 (-CH), 121.6 (-CH), 120.9 (-CH), 120.8 (-CH), 119.4 (-C), 117.1 (2x-CH), 112.2 (-CH), 112.0 (-CH), 110.5 (-CH), 101.0 (-CH), 75.1 (-C), 74.8 (-C), 73.8 (-CH), 73.7 (-CH), 64.7 (-CH), 64.2 (-CH), 56.12 (-OMe), 56.09 (-OMe), 52.4 (-CH), 52.2 (-CH), 48.6 (-CH$_2$), 48.3 (-CH$_2$), 31.5 (-CH$_2$), 31.2 (-CH$_2$), 28.3 (-CH$_2$), 27.9 (-CH$_2$), 21.4 (-CH$_3$), 17.3 (-CH$_3$).

MS [ESI-MS, positive mode]: found m/z 797 [M+H]$^+$.  
HRMS [ESI-MS, positive mode]: MF: C$_{47}$H$_{48}$N$_4$O$_8$; found m/z 819.3351 [M+Na]$^+$ [calcd. 819.3370].

**Compound 4Bc (±):**

**Color:** Obtained as white solid; **Yield:** 21% (294 mg); **Mp:** 169-171 ºC; **R$_f$** 0.40 (6 % MeOH in CHCl$_3$);

$^1$H NMR (DMSO-d$_6$): $\delta$ 10.36 (1H, s, -NH), 9.93 (1H, s, -NH), 8.84 (1H, d, $J$=4.2 Hz), 7.46 (1H, d, $J$= 7.2 Hz), 7.17 (1H, m), 7.02 (1H, s), 6.95 (1H, m), 6.74 (4H, m), 6.41 (1H, m), 6.26 (1H, s), 6.18 (1H, d, $J$= 6.6 Hz), 5.62 (1H, s), 4.24 (1H, m), 4.02 (1H, m), 3.78 (3H, s), 3.72
(2H, m), 3.56 (2H, m), 2.97 (1H, m), 2.42 (2H, m), 2.36 (1H, m), 2.25 (3H, s), 2.07 (3H, m), 1.96 (3H, s), 1.82 (2H, m), 1.68 (3H, m), 1.40 (1H, m), 1.15 (1H, m), 0.86 (1H, m).

\(^{13}\)C NMR (DMSO-\textit{d}_6): \(\delta\) 197.2 (-C=O), 183.6 (-C=O), 179.2 (-C=O), 178.7 (-C=O), 147.6 (-C), 146.6 (-C), 145.4 (-C), 145.1 (-C), 142.3 (-C), 139.3 (-C), 130.8 (-CH), 130.3 (-C), 129.9 (-C), 129.1 (-CH), 127.0 (-CH), 126.5 (-C), 126.3 (-C), 125.2 (-C), 124.6 (-CH), 120.7 (-CH), 119.9 (-CH), 119.7 (-CH), 118.2 (-C), 115.6 (-CH), 114.9 (-CH), 111.8 (2x-CH), 109.8 (-CH), 101.6 (-CH), 74.8 (-C), 73.6 (-C), 72.5 (-CH), 64.1 (-CH), 62.3 (-CH), 55.6 (-OMe), 54.9 (-OMe), 52.6 (-CH), 50.4 (-CH), 50.3 (-CH\(_2\)), 48.9 (-CH), 47.4 (-CH\(_2\)), 30.1 (-CH\(_2\)), 28.0 (-CH\(_2\)), 27.2 (-CH\(_2\)), 25.6 (-CH\(_2\)), 20.7 (-CH\(_3\)), 16.2 (-CH\(_3\)).

MS [ESI-MS, positive mode]: found m/z 797 [M+H] +.

HRMS [ESI-MS, positive mode]: MF: C\(_{47}\)H\(_{48}\)N\(_4\)O\(_8\); found m/z 819.3395 [M+Na] + [calcd. 819.3370].

**Compound 4Bd (±):**

**Color:** Obtained as white solid; **Yield:** 23% (322 mg); **Mp:** 170-172 ºC; **R\(_f\):** 0.39 (6 % MeOH in CHCl\(_3\));

**IR (KBr, \(\nu_{\max}\) Cm\(^{-1}\)):** 3390, 2960, 1713, 1618;

\(^1\)H NMR (Py-d\(_5\)): \(\delta\) 11.84 (1H, s, -NH), 11.17 (1H, s, -NH), 7.69 (1H, d, \(J=7.2\) Hz), 7.43 (1H, s), 7.38 (1H, s), 7.31 (1H, t, \(J=7.2\) Hz), 7.22 (1H, d, \(J=7.2\) Hz), 7.18 (1H, d, \(J=1.2\) Hz), 7.16 (1H, t, \(J=7.8\) Hz), 7.06 (1H, d, \(J=7.8\) Hz), 6.93 (3H, m), 6.81 (1H, s), 6.04 (1H, s), 4.99 (1H, m), 4.73 (1H, q, \(J=7.8\) Hz), 4.64 (1H, d, \(J=6.6\) Hz), 4.39 (1H, m), 4.25 (1H, d, \(J=12\) Hz), 3.99 (1H, dd, \(J=9.6, 12\) Hz), 3.75 (3H, s), 3.56 (3H, s), 3.23 (1H, m), 2.86 (1H, m), 2.79 (1H, t, \(J=7.2\) Hz), 2.73 (1H, m), 2.38 (3H, s), 2.01 (3H, s), 1.97 (1H, m), 1.90 (2H, m), 1.76 (2H, m), 1.65 (1H, m), 1.59 (1H, m), 1.30 (1H, m).

\(^{13}\)C NMR (Py-d\(_5\)): \(\delta\) 198.0 (-C=O), 186.2 (-C=O), 181.4 (-C=O), 180.6 (-C=O), 149.3 (-C), 148.3 (-C), 147.6 (-C), 147.3 (-C), 143.9 (-C), 141.0 (-C), 131.8 (-CH), 131.6 (2x-C), 130.9 (-C), 130.0 (-CH), 128.0 (-CH), 127.9 (-C), 126.9 (-C), 125.4 (-CH), 121.8 (-CH), 121.7 (-CH), 121.5 (-CH), 119.4 (-C), 117.1 (-CH), 116.4 (-CH), 113.2 (-CH), 112.4 (-CH), 110.9 (-CH), 102.9 (-CH), 76.5 (-C), 75.4 (-C), 73.8 (-CH), 65.5 (-CH), 64.4 (-CH), 56.2 (-OMe), 55.7 (-OMe), 54.3 (-CH), 52.6 (-CH), 51.5 (-CH\(_2\)), 50.9 (-CH), 48.6 (-CH\(_2\)), 31.3 (-CH\(_2\)), 29.4 (-CH\(_2\)), 28.2 (-CH\(_2\)), 26.8 (-CH\(_2\)), 21.4 (-CH\(_3\)), 17.1 (-CH\(_3\)).

MS [ESI-MS, positive mode]: found m/z 797 [M+H] +.
HRMS [ESI-MS, positive mode]: MF: C_{47}H_{48}N_{4}O_{8}; found m/z 819.3378 [M+Na] + [calcd. 819.3370].

**Compound 4Ca (±):**

**Color:** Obtained as white solid; **Yield:** 17% (230 mg); **Mp:** 183-185 ºC; **R_F** 0.48 (6 % MeOH in CHCl_3);

**IR (KBr, v_{max} Cm^{-1}):** 3391, 2961, 2868, 1722, 1615;

**^{1}H NMR (Py-d_5):** δ 11.28 (1H, s, -NH), 10.88 (1H, s, -NH), 7.59 (1H, dd, J=4.8, 6.6 Hz), 7.34 (1H, s), 7.24 (2H, m), 7.22 (1H, m), 7.18 (2H, m), 7.00 (3H, m), 6.85 (2H, m), 5.70 (1H, s), 4.52 (1H, d, J=12.0 Hz), 4.37 (1H, d, J=12.0 Hz), 4.29 (1H, m), 4.20 (1H, m), 3.81 (2H, m), 3.73 (3H, s), 3.70 (3H, s), 2.83 (1H, m), 2.77 (1H, m), 2.62 (2H, m), 2.16 (3H, s), 1.85 (4H, m), 1.78 (2H, m), 1.69 (2H, m).

**^{13}C NMR (Py-d_5):** δ 191.2 (-C=O), 190.9 (-C=O), 181.0 (-C=O), 180.8 (-C=O), 149.22 (-C), 149.16 (-C), 147.5 (-C), 147.4 (-C), 142.4 (-C), 141.2 (-C), 131.6 (-C), 131.5 (-C), 130.8 (-C), 130.2 (-CH), 129.7 (-CH), 128.6 (-C), 128.0 (-CH), 127.5 (-CH), 126.7 (-C), 126.6 (-C), 120.8 (2x-CH), 117.1 (2x-CH), 112.2 (-CH), 111.8 (-CH), 111.7 (-CH), 110.4 (-CH), 101.7 (-CH), 74.7 (-C), 74.5 (-C), 73.7 (-CH), 73.2 (-CH), 65.1 (-CH), 64.0 (-CH), 56.1 (-OMe), 56.0 (-OMe), 52.2 (2x-CH), 48.54 (-CH_2), 48.51 (-CH_2), 31.0 (-CH_2), 30.6 (-CH_2), 27.9 (-CH_2), 27.7 (-CH_3), 21.2 (-CH_3).

**MS [ESI-MS, positive mode]:** found m/z 817 [M+H] +.

**HRMS [ESI-MS, positive mode]:** MF: C_{46}H_{46}N_{4}O_{8}Cl; found m/z 839.2817 [M+Na] + [calcd. 839.2824].

**Compound 4Cb (±):**

**Color:** Obtained as white solid; **Yield:** 20% (271 mg); **Mp:** 208-210 ºC; **R_F** 0.43 (6 % MeOH in CHCl_3);

**IR (KBr, v_{max} Cm^{-1}):** 3382, 1711, 1613, 1516;

**^{1}H NMR (Py-d_5):** δ 12.14 (1H, s, -NH), 11.77 (1H, s, -NH), 7.59 (1H, m), 7.35 (1H, s), 7.20 (1H, m), 7.15 (2H, d, J=8.4 Hz), 7.10 (1H, d, J=1.8 Hz), 7.05 (1H, d, J=1.2 Hz), 6.94 (1H, d, J=7.8 Hz), 6.86 (1H, d, J=7.8 Hz), 6.84 (1H, d, J=1.2 Hz), 6.82 (1H, d, J=7.8 Hz), 6.80 (1H, dd, J=1.2, 8.4 Hz), 5.92 (1H, s), 4.39 (2H, d, J=12.0 Hz), 4.20 (1H, m), 4.12 (1H, m), 3.92 (1H, m), 3.82 (1H, m), 3.66 (3H, s), 3.65 (3H, s), 2.82 (1H, m), 2.65 (3H, m), 2.11 (3H, s), 1.85 (5H, m), 1.71 (3H, m).
\( ^{13} \text{C NMR (Py-d}_5 \): \delta 191.2 (-C=O), 189.8 (-C=O), 181.2 (-C=O), 180.9 (-C=O), 149.0 (2\times-\text{C}), 147.42 (-\text{C}), 147.36 (-\text{C}), 142.6 (-\text{C}), 141.2 (-\text{C}), 131.6 (-\text{C}), 131.2 (-\text{C}), 130.7 (-\text{C}), 130.3 (-\text{CH}), 129.9 (-\text{CH}), 128.7 (-\text{C}), 128.2 (-\text{CH}), 127.5 (-\text{CH}), 126.7 (-\text{C}), 126.6 (-\text{C}), 120.35 (-\text{CH}), 120.31 (-\text{CH}), 116.99 (-\text{CH}), 116.97 (-\text{CH}), 112.5 (-\text{CH}), 112.3 (-\text{CH}), 111.7 (-\text{CH}), 110.3 (-\text{CH}), 101.5 (-\text{CH}), 75.25 (-\text{C}), 75.22 (-\text{C}), 73.7 (-\text{CH}), 73.4 (-\text{CH}), 65.3 (-\text{CH}), 64.9 (-\text{CH}), 56.0 (2\times-\text{OMe}), 51.8 (-\text{CH}), 51.6 (-\text{CH}), 48.3 (-\text{CH}_2), 48.2 (-\text{CH}_2), 31.4 (2\times-\text{CH}_2), 28.4 (-\text{CH}_2), 28.3 (-\text{CH}_2), 21.3 (-\text{CH}_3).}

\text{MS [ESI-MS, positive mode]:} \text{ found } m/z 817 [\text{M+H}]^+, 839 [\text{M+Na}]^+.

\text{HRMS [ESI-MS, positive mode]:} \text{ MF: } C_{46}H_{45}N_4O_8Cl; \text{ found } m/z 839.2820 [\text{M+Na}]^+ [\text{calcd. } 839.2824].

\text{Compound 4Cc (±):}

\text{Color:} \text{ Obtained as white solid; Yield:} 20\% (271 mg); \text{ Mp:} 174-176 \degree\text{C}; R_f 0.36 (6 \% \text{MeOH in CHCl}_3);

\( ^1\text{H NMR (Py-d}_5 \): \delta 12.14 (1H, s, -\text{NH}), 11.20 (1H, s, -\text{NH}), 7.90 (1H, d, J=1.8 \text{ Hz}), 7.53 (1H, s), 7.39 (1H, dd, J=1.8, 7.8 \text{ Hz}), 7.30 (1H, m), 7.17 (1H, d, J=7.8 \text{ Hz}), 7.07 (1H, d, J=8.4 \text{ Hz}), 7.04 (1H, d, J=8.4 \text{ Hz}), 7.01 (1H, d, J=8.4 \text{ Hz}), 6.91 (1H, m), 6.86 (2H, m), 6.67 (1H, d, J=7.8 \text{ Hz}), 6.21 (1H, s), 5.04 (1H, m), 4.86 (1H, m), 4.66 (1H, d, J=12.6 \text{ Hz}), 4.31 (1H, m), 4.25 (1H, d, J=12.0 \text{ Hz}), 4.01 (1H, m), 3.68 (3H, s), 3.51 (3H, s), 3.34 (1H, m), 2.88 (1H, m), 2.82 (1H, m), 2.74 (1H, m), 2.34 (3H, s), 1.94 (3H, m), 1.88 (1H, m), 1.78 (4H, m).

\( ^{13} \text{C NMR (Py-d}_5 \): \delta 197.5 (-\text{C=O}), 187.4 (-\text{C=O}), 181.0 (-\text{C=O}), 180.2 (-\text{C=O}), 149.3 (-\text{C}), 148.2 (-\text{C}), 147.7 (-\text{C}), 147.4 (-\text{C}), 143.0 (-\text{C}), 142.4 (-\text{C}), 131.1 (-\text{C}), 131.0 (-\text{C}), 130.2 (-\text{CH}), 130.0 (-\text{CH}), 129.2 (-\text{C}), 128.4 (-\text{C}), 128.1 (-\text{CH}), 127.7 (-\text{CH}), 127.3 (-\text{C}), 127.0 (-\text{C}), 121.6 (-\text{CH}), 121.2 (-\text{CH}), 117.2 (-\text{CH}), 116.4 (-\text{CH}), 112.9 (-\text{CH}), 112.4 (-\text{CH}), 112.0 (-\text{CH}), 110.2 (-\text{CH}), 103.0 (-\text{CH}), 76.6 (-\text{C}), 75.2 (-\text{C}), 74.0 (-\text{CH}), 65.9 (-\text{CH}), 64.6 (-\text{CH}), 56.1 (-\text{OMe}), 55.7 (-\text{OMe}), 53.9 (-\text{CH}), 52.4 (-\text{CH}), 52.1 (-\text{CH}), 51.5 (-\text{CH}_2), 48.5 (-\text{CH}_2), 31.3 (-\text{CH}_2), 29.1 (-\text{CH}_2), 28.4 (-\text{CH}_2), 27.0 (-\text{CH}_2), 21.5 (-\text{CH}_3).

\text{MS [ESI-MS, positive mode]:} \text{ found } m/z 817 [\text{M+H}]^+, 839 [\text{M+Na}]^+.

\text{HRMS [ESI-MS, positive mode]:} \text{ MF: } C_{46}H_{45}N_4O_8Cl; \text{ found } m/z 839.2839 [\text{M+Na}]^+ [\text{calcd. } 839.2824].

\text{Compound 4Cd (±):}
**Compound 4Da (±):**

**Color:** Obtained as white solid; **Yield:** 18% (246 mg); **Mp:** 238-240 °C; **Rf** 0.47 (6 % MeOH in CHCl₃);

**1H NMR (Py-d₅):** δ 11.19 (1H, s, -NH), 10.89 (1H, s, -NH), 7.30 (1H, dd, J=2.4 Hz), 7.28 (1H, d, J=8.4 Hz), 7.25 (1H, d, J=7.8 Hz), 7.22 (1H, d, J=1.8 Hz), 7.20 (1H, d, J=1.2 Hz), 7.14 (1H, d, J=1.8 Hz), 7.08 (1H, dd, J=1.8, 8.4 Hz), 7.00 (1H, td, J=2.4, 8.4 Hz), 6.89 (3H, m), 6.85 (1H, q, J=4.2), 5.75 (1H, s), 4.49 (2H, m), 4.20 (2H, m), 3.75 (3H, s), 3.72 (1H, m), 3.70 (3H, s), 3.69 (3H, m), 3.68 (1H, m), 2.82 (1H, m), 2.73 (1H, m), 2.63 (2H, m), 1.88 (2H, m), 1.78 (4H, m), 1.69 (2H, m).

**13C NMR (Py-d₅):** δ 191.15 (-C=O), 191.11 (-C=O), 180.9 (-C=O), 180.8 (-C=O), 158.7 (-C, J_C,F=-237.0 Hz), 155.4 (-C), 149.3 (-C), 149.2 (-C), 147.6 (-C), 147.5 (-C), 139.8 (-C), 137.1 (-C), 131.5 (-C), 131.3 (-C), 128.6 (-C), 127.9 (-C), 121.2 (-CH), 121.0 (-CH), 117.2 (-CH), 117.1 (-CH), 116.1 (-CH, J_C,F=24.0 Hz), 115.3 (-CH), 114.8 (-CH, J_C,F=24.0 Hz), 114.3 (-CH), 114.2 (-CH), 114.1 (-CH), 113.2 (-CH), 113.1 (-CH), 112.6 (-CH), 112.5 (-CH), 112.4 (-CH), 112.3 (-CH), 111.9 (-CH), 111.8 (-CH), 111.7 (-CH), 111.6 (-CH), 111.5 (-CH), 111.4 (-CH), 111.3 (-CH), 111.2 (-CH), 111.1 (-CH), 111.0 (-CH), 103.0 (-CH), 76.5 (-CH), 75.3 (-CH), 73.3 (-CH), 65.5 (-CH), 64.7 (-CH), 56.0 (-CH), 55.7 (-CH), 54.0 (-CH), 52.4 (-CH), 51.5 (-CH), 50.9 (-CH), 48.7 (-CH), 31.0 (-CH), 28.1 (-CH), 23.2 (-CH), 21.5 (-CH), 20.1 (-CH).
CH), 111.9 (-CH), 111.5 (-CH), 111.1 (-CH, \(^3J_{C,F}=9.0\) Hz), 110.9 (-CH), 101.6 (-CH), 74.9 (-C), 74.8 (-C), 73.8 (-CH), 73.5 (-CH), 64.6 (-CH), 64.5 (-CH), 56.2 (-OMe), 56.1 (-OMe), 56.0 (-OMe), 52.6 (-CH), 52.4 (-CH), 48.4 (2\(\times\)-CH\(_2\)), 31.1 (-CH\(_2\)), 30.9 (-CH\(_2\)), 28.0 (-CH\(_2\)), 27.9 (-CH\(_2\)).

**MS [ESI-MS, positive mode]:** found \(m/z\) 817 [M+H]⁺, 839 [M+Na]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C\(_{46}\)H\(_{45}\)N\(_4\)O\(_9\)F; found \(m/z\) 839.3084 [M+Na]⁺ [calcd. 839.3068].

**Compound 4Db (±):**

**Color:** Obtained as white solid; **Yield:** 22% (300 mg); **Mp:** 178-180 °C; **R\(_f\)** 0.43 (6 % MeOH in CHCl\(_3\));

**IR (KBr, \(\nu_{\text{max}}\) Cm\(^{-1}\)):** 3385, 2961, 2870, 1721, 1605;

**\(^1\)H NMR (Py-d\(_5\)):** \(\delta\) 11.91 (1H, s, -NH), 11.74 (1H, s, -NH), 7.33 (1H, dd, \(J=2.4, 8.4\) Hz), 7.18 (2H, m), 7.14 (1H, d, \(J=7.8\) Hz), 7.11 (2H, dd, \(J=1.8, 7.8\) Hz), 7.01 (1H, td, \(J=2.4, 9.0\) Hz), 6.96 (1H, d, \(J=8.4\) Hz), 6.87 (3H, m), 6.83 (1H, dd, \(J=2.4, 8.4\) Hz), 5.96 (1H, s), 4.44 (2H, m), 4.13 (2H, m), 3.84 (1H, m), 3.76 (1H, m), 3.73 (3H, s), 3.71 (3H, s), 3.63 (3H, s), 2.76 (1H, m), 2.65 (3H, m), 1.86 (2H, m), 1.78 (2H, m), 1.69 (4H, m).

**\(^{13}\)C NMR (Py-d\(_5\)):** \(\delta\) 191.4 (-C=O), 189.5 (-C=O), 181.14 (-C=O), 181.08 (-C=O), 158.7 (-C, \(^1J_{C,F}=237\) Hz), 155.4 (-C), 149.1 (2\(\times\)-C), 147.42 (-C), 147.40 (-C), 139.9 (-C), 137.1 (-C), 131.5 (-C), 131.2 (-C), 128.4 (-C, \(^1J_{C,F}=7.5\) Hz), 128.0 (-C), 120.7 (-CH), 120.6 (-CH), 117.1 (-CH), 117.0 (-CH), 116.2 (-CH, \(^2J_{C,F}=24.0\) Hz), 115.4 (-CH), 114.9 (-CH, \(^2J_{C,F}=25.5\) Hz), 114.0 (-CH), 112.2 (-CH), 112.1 (-CH), 111.2 (-CH, \(^3J_{C,F}=9\) Hz), 110.9 (-CH), 101.5 (-CH), 75.4 (-C), 75.3 (-C), 73.9 (-CH), 73.6 (-CH), 65.0 (-CH), 64.5 (-CH), 56.08 (-OMe), 56.06 (-OMe), 55.9 (-OMe), 51.9 (-CH), 51.8 (-CH), 48.2 (2\(\times\)-CH\(_2\)), 31.6 (-CH\(_2\)), 31.5 (-CH\(_2\)), 28.41 (-CH\(_2\)), 28.40 (-CH\(_2\)).

**MS [ESI-MS, positive mode]:** found \(m/z\) 817 [M+H]⁺, 839 [M+Na]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C\(_{46}\)H\(_{45}\)N\(_4\)O\(_9\)F; found \(m/z\) 839.3062 [M+Na]⁺ [calcd. 839.3068].

**Compound 4Dc (±):**

**Color:** Obtained as white solid; **Yield:** 21% (286 mg); **Mp:** 196-198 °C; **R\(_f\)** 0.37 (6 % MeOH in CHCl\(_3\));
$^1$H NMR ($\text{Py-d}_5$): $\delta$ 11.81 (1H, s, -NH), 11.39 (1H, s, -NH), 7.66 (1H, dd, $J=2.4$, 8.4 Hz), 7.40 (1H, d, $J=1.8$ Hz), 7.34 (1H, s), 7.15 (1H, d, $J=7.8$ Hz), 7.09 (1H, d, $J=9.0$ Hz), 7.03 (1H, m), 7.00 (1H, dd, $J=2.4$, 8.4 Hz), 6.92 (3H, m), 6.86 (1H, d, $J=7.8$ Hz), 6.64 (1H, q, $J=4.2$ Hz), 6.11 (1H, s), 4.97 (1H, m), 4.77 (1H, m), 4.66 (1H, d, $J=12.6$ Hz), 4.31 (1H, m), 4.19 (1H, d, $J=12.0$ Hz), 3.97 (1H, m), 3.71 (3H, s), 3.68 (3H, s), 3.53 (3H, s), 3.25 (1H, m), 2.90 (1H, m), 2.83 (1H, m), 2.74 (1H, m), 1.93 (1H, m), 1.86 (3H, m), 1.72 (4H, m).

$^{13}$C NMR ($\text{Py-d}_5$): $\delta$ 195.7 (-C=O), 189.0 (-C=O), 181.2 (-C=O), 180.1 (-C=O), 158.9 (-C, $^1J_{C,F}=235.5$ Hz), 155.6 (-C), 149.2 (-C), 148.3 (-C), 147.64 (-C), 147.56 (-C), 140.9 (-C), 137.5 (-C), 131.5 (-C), 129.9 (-C, $^3J_{C,F}=9.4$ Hz), 128.4 (-C), 126.9 (-C), 121.8 (-CH), 121.2 (-CH), 117.1 (-CH), 116.5 (-CH), 116.1 (-CH, $^2J_{C,F}=22.5$ Hz), 115.7 (-CH), 115.2 (-CH, $^2J_{C,F}=24.0$ Hz), 113.8 (-CH), 112.7 (-CH), 112.4 (-CH), 110.9 (-CH, $^3J_{C,F}=7.5$ Hz), 110.8 (-CH), 102.7 (-CH), 76.8 (-C), 75.4 (-C), 73.9 (-CH), 65.8 (-CH), 64.7 (-CH), 56.1 (-OMe), 56.0 (-OMe), 55.7 (-OMe), 53.4 (-CH), 52.5 (-CH), 52.1 (-CH), 51.5 (-CH), 48.5 (-CH), 31.4 (-CH), 28.9 (-CH), 28.3 (-CH), 26.9 (-CH).

MS [ESI-MS, positive mode]: found m/z 817 [M+H]$^+$, 839 [M+Na]$^+$.

HRMS [ESI-MS, positive mode]: MF: C$_{46}$H$_{45}$N$_4$O$_9$F; found m/z 839.3059 [M+Na]$^+$ [calcd. 839.3068].

**Compound 4Dd (±):**

**Color:** Obtained as white solid; **Yield:** 24% (327 mg); **Mp:** 189-191 °C; **$R_f$** 0.36 (6 % MeOH in CHCl$_3$);

$^1$H NMR ($\text{Py-d}_5$): $\delta$ 11.66 (1H, s, -NH), 11.37 (1H, s, -NH), 7.72 (1H, d, $J=8.4$ Hz), 7.45 (1H, s), 7.37 (1H, s), 7.18 (1H, d, $J=8.4$ Hz), 7.10 (1H, d, $J=7.8$ Hz), 7.02 (2H, m), 6.95 (3H, m), 6.92 (1H, m), 6.66 (1H, q, $J=3.6$ Hz), 5.97 (1H, s), 4.93 (1H, t, $J=10.2$ Hz), 4.71 (1H, m), 4.60 (1H, d, $J=11.4$ Hz), 4.41 (1H, m), 4.25 (1H, d, $J=12.0$ Hz), 4.01 (1H, m), 3.80 (3H, s), 3.69 (3H, s), 3.52 (3H, s), 3.20 (1H, m), 2.97 (1H, m), 2.78 (2H, m), 1.91 (4H, m), 1.77 (2H, m), 1.65 (1H, m), 1.60 (1H, m).

$^{13}$C NMR ($\text{Py-d}_5$): $\delta$ 194.0 (-C=O), 187.2 (-C=O), 181.3 (-C=O), 180.1 (-C=O), 158.9 (-C, $^1J_{C,F}=235.5$ Hz), 155.6 (-C), 149.3 (-C), 148.3 (-C), 147.6 (-C), 147.5 (-C), 140.9 (-C), 137.5 (-C), 131.7 (-C), 130.0 (-C), 128.5 (-C), 127.4 (-C), 121.8 (-CH), 121.6 (-CH), 117.0 (-CH), 116.4 (-CH), 116.0 (-CH, $^2J_{C,F}=24.0$ Hz), 115.8 (-CH), 115.3 (-CH, $^2J_{C,F}=24.0$ Hz), 114.3 (-CH), 113.1 (-CH), 112.3 (-CH), 110.9 (-CH), 110.8 (-CH), 102.8 (-CH), 76.8 (-C), 75.7 (-C), 73.6 (-CH), 65.8 (-CH), 65.0 (-CH), 56.3 (-OMe), 56.1 (-OMe), 55.8 (-OMe), 53.9 (-CH),
52.7 (-CH), 51.45 (-CH), 51.41 (-CH₂), 48.6 (-CH₂), 31.2 (-CH₂), 29.3 (-CH₂), 28.1 (-CH₂), 26.8 (-CH₂).

**MS [ESI-MS, positive mode]:** found m/z 817 [M+H]⁺, 839 [M+Na]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₆H₄₅N₄O₉F; found m/z 839.3059 [M+Na]⁺ [calcd. 839.3068].

**Compound 4Ea (±):**

Color: Obtained as white solid; Yield: 18% (250 mg); Mp: 180-182 ºC; Rf 0.47 (6 % MeOH in CHCl₃);

IR (KBr, νmax Cm⁻¹): 3397, 2959, 2868, 1720, 1615;

**¹H NMR (Py-d₅):** δ 11.02 (1H, s, -NH), 10.96 (1H, s, -NH), 7.32 (1H, dd, J=2.4, 8.4 Hz), 7.28 (2H, m), 7.23 (1H, d, J=1.8 Hz), 7.21 (1H, m), 7.17 (1H, d, J=1.2 Hz), 7.09 (1H, dd, J=1.2, 7.8 Hz), 6.97 (2H, m), 6.81 (1H, m), 6.77 (1H, s), 5.74 (1H, s), 4.52 (1H, d, J=12.6 Hz), 4.38 (1H, d, J=12.0 Hz), 4.33 (1H, m), 4.17 (1H, m), 3.79 (2H, m), 3.75 (3H, s), 3.70 (3H, s), 2.82 (1H, m), 2.76 (1H, m), 2.63 (2H, m), 2.24 (3H, s), 2.20 (3H, s), 1.82 (6H, m), 1.69 (2H, m).

**¹³C NMR (Py-d₅):** δ 192.4 (-C=O), 190.2 (-C=O), 181.2 (-C=O), 181.0 (-C=O), 158.7 (-C, J_C_F=235.5 Hz), 149.22 (-C), 149.17 (-C), 147.5 (-C), 147.4 (-C), 139.8 (-C), 139.6 (-C), 131.9 (-CH), 131.7 (-C), 131.5 (-C), 130.6 (-C), 128.3 (-C), 126.1 (-C), 125.4 (-CH), 120.91 (-CH), 120.87 (-CH), 119.3 (-C), 117.2 (-CH), 117.1 (-CH), 116.1 (-CH, ²J_C_F=22.5 Hz), 115.1 (-CH, ²J_C_F=24.0 Hz), 112.4 (-CH), 111.6 (-CH), 111.1 (-CH), 101.6 (-CH), 74.9 (-C), 74.8 (-C), 73.8 (-CH), 73.3 (-CH), 65.6 (-CH), 63.6 (-CH), 56.1 (-OMe), 56.0 (-OMe), 52.4 (-CH), 52.3 (-CH), 48.5 (-CH₂), 48.4 (-CH₂), 31.1 (-CH₂), 30.7 (-CH₂), 28.0 (-CH₂), 27.7 (-CH₂), 21.2 (-CH₃), 17.1 (-CH₃).

**MS [ESI-MS, positive mode]:** found m/z 815 [M+H]⁺, 837 [M+Na]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₇H₄₇N₄O₉F; found m/z 837.3240 [M+Na]⁺ [calcd. 837.3276].

**Compound 4Eb (±):**

Color: Obtained as white solid; Yield: 22% (305 mg); Mp: 182-184 ºC; Rf 0.43 (6 % MeOH in CHCl₃);

IR (KBr, νmax Cm⁻¹): 3403, 3208, 2964, 2871, 1713, 1605;
\(^1\)H NMR (Py-d5): δ 12.03 (1H, s, -NH), 11.73 (1H, s, -NH), 7.28 (1H, d, \(J=7.8\) Hz), 7.17 (2H, m), 7.13 (2H, m), 7.08 (1H, s), 6.98 (1H, m), 6.82 (3H, m), 6.69 (1H, s), 5.93 (1H, s), 4.38 (2H, m), 4.20 (1H, m), 4.13 (1H, m), 3.92 (1H, m), 3.78 (1H, m), 3.67 (3H, s), 3.64 (3H, s), 2.84 (1H, m), 2.68 (3H, m), 2.28 (3H, s), 2.12 (3H, s), 1.92 (1H, m), 1.84 (4H, m), 1.72 (3H, m).

\(^{13}\)C NMR (Py-d5): δ 190.7 (-C=O), 190.3 (-C=O), 181.5 (-C=O), 181.3 (-C=O), 158.6 (-C, \(^1\)J\(_{C,F}=237.0\) Hz), 149.0 (2xC=O), 147.44 (-C), 147.38 (-C), 139.9 (2xC=O), 131.9 (-CH), 131.6 (-C), 131.3 (-C), 130.6 (-C), 128.3 (-C), 126.2 (-C), 125.5 (-CH), 120.3 (-CH), 120.2 (-CH), 119.4 (-C), 117.0 (-CH), 116.9 (-CH), 116.2 (-CH, \(^2\)J\(_{C,F}=24.0\) Hz), 115.1 (-CH, \(^2\)J\(_{C,F}=24.0\) Hz), 112.6 (-CH), 112.3 (-CH), 111.0 (-CH, \(^3\)J\(_{C,F}=7.5\) Hz), 101.4 (-CH), 75.4 (2xC=O), 73.6 (-CH), 73.4 (-CH), 65.2 (-CH), 64.9 (-CH), 56.04 (-OMe), 55.98 (-OMe), 51.8 (-CH), 51.5 (-CH), 48.33 (-CH\(_2\)), 48.29 (-CH\(_2\)), 31.5 (-CH\(_2\)), 31.3 (-CH\(_2\)), 28.4 (-CH\(_2\)), 28.2 (-CH\(_2\)), 21.3 (-CH\(_3\)), 17.2 (-CH\(_3\)).

MS [ESI-MS, positive mode]: found m/z 815 [M+H]^+, 837 [M+Na]^+.
HRMS [ESI-MS, positive mode]: MF: C\(_{47}\)H\(_{47}\)N\(_4\)O\(_8\)F; found m/z 837.3305 [M+Na]^+ [calcd. 837.3276].

**Compound 4Ec (+):**

**Color:** Obtained as white solid; **Yield:** 21% (292 mg); **Mp:** 172-174 °C; **R\(_f\)** 0.38 (6 % MeOH in CHCl\(_3\));

\(^1\)H NMR (Py-d5): δ 12.01 (1H, s, -NH), 11.15 (1H, s, -NH), 7.66 (1H, dd, \(J=2.4, 8.4\) Hz), 7.37 (1H, s), 7.31 (1H, d, \(J=1.8\) Hz), 7.17 (1H, m), 7.13 (2H, m), 7.01 (1H, m), 6.92 (2H, m), 6.85 (1H, m), 6.79 (1H, s), 6.15 (1H, s), 4.99 (1H, dd, \(J=9.6, 12.0\) Hz), 4.80 (1H, q, \(J=8.4\) Hz), 4.66 (1H, d, \(J=12.0\) Hz), 4.31 (1H, m), 4.23 (1H, d, \(J=12.0\) Hz), 4.00 (1H, dd, \(J=9.6, 12.0\) Hz), 3.70 (3H, s), 3.52 (3H, s), 3.21 (1H, m), 2.83 (2H, m), 2.74 (1H, m), 2.33 (3H, s), 1.99 (3H, s), 1.91 (3H, m), 1.83 (2H, m), 1.76 (2H, m), 1.69 (1H, m).

\(^{13}\)C NMR (Py-d5): δ 196.8 (-C=O), 188.2 (-C=O), 181.3 (-C=O), 180.4 (-C=O), 158.9 (-C, \(^1\)J\(_{C,F}=237.0\) Hz), 149.3 (-C), 148.2 (-C), 147.7 (-C), 147.4 (-C), 141.0 (-C), 140.2 (-C), 131.8 (-CH), 131.2 (-C), 130.8 (-C), 128.8 (-C, \(^3\)J\(_{C,F}=7.5\) Hz), 127.8 (-C), 127.5 (-C), 125.3 (-CH), 121.7 (-CH), 121.2 (-CH), 119.3 (-C), 117.1 (-CH), 116.4 (-CH), 116.3 (-CH, \(^2\)J\(_{C,F}=24.0\) Hz), 115.4 (-CH, \(^2\)J\(_{C,F}=24.0\) Hz), 113.0 (-CH), 112.3 (-CH), 111.2 (-CH, \(^3\)J\(_{C,F}=7.5\) Hz), 102.8 (-CH), 76.6 (-C), 75.4 (-C), 73.9 (-CH), 65.6 (-CH), 64.7 (-CH), 56.1 (-OMe), 55.6 (-OMe),
54.0 (-CH), 52.3 (-CH), 51.7 (-CH), 51.5 (-CH$_2$), 48.4 (-CH$_2$), 31.3 (-CH$_2$), 29.0 (-CH$_2$), 28.3 (-CH$_2$), 26.9 (-CH$_2$), 21.4 (-CH$_3$), 17.0 (-CH$_3$).

**MS [ESI-MS, positive mode]:** found m/z 815 [M+H]$^+$, 837 [M+Na]$^+$.

**HRMS [ESI-MS, positive mode]:** MF: C$_{47}$H$_{47}$N$_4$O$_8$F; found m/z 837.3284 [M+Na]$^+$ [calcd. 837.3276].

### Compound 4Ed (±):

**Color:** Obtained as white solid; **Yield:** 23% (319 mg); **Mp:** 170-172 °C; **R$_f$** 0.37 (6 % MeOH in CHCl$_3$);

**$^1$H NMR (Py-d$_5$):** $\delta$ 11.87 (1H, s, -NH), 11.14 (1H, s, -NH), 7.74 (1H, dd, $J$=2.4, 8.4 Hz), 7.40 (1H, s), 7.31 (1H, d, $J$=1.8 Hz), 7.27 (1H, m), 7.18 (1H, m), 7.12 (2H, m), 6.95 (2H, m), 6.91 (1H, d, $J$=8.4 Hz), 6.80 (1H, s), 6.04 (1H, s), 5.05 (1H, dd, $J$=9.6, 12.0 Hz), 4.68 (1H, m), 4.61 (1H, d, $J$=12.0 Hz), 4.37 (1H, m), 4.25 (1H, d, $J$=12.0 Hz), 4.00 (1H, m), 3.66 (3H, s), 3.54 (3H, s), 3.29 (1H, m), 2.77 (2H, m), 2.38 (3H, s), 1.99 (3H, s), 1.93 (2H, m), 1.76 (3H, m), 1.64 (2H, m), 1.55 (2H, m).

**$^{13}$C NMR (Py-d$_5$):** $\delta$ 198.0 (-C=O), 186.2 (-C=O), 181.2 (-C=O), 180.4 (-C=O), 158.9 (-C, $^1J_{C\cdot F}$=237.0 Hz), 149.3 (-C), 148.3 (-C), 147.7 (-C), 147.4 (-C), 141.0 (-C), 140.1 (-C), 131.8 (-CH), 131.2 (-C), 130.8 (-C), 128.8 (-C, $^2J_{C\cdot F}$=7.5 Hz), 127.8 (-C), 127.3 (-C), 125.4 (-CH), 121.7 (-CH), 121.3 (-CH), 119.3 (-C), 117.14 (-CH), 117.08 (-CH), 116.3 (-CH, $^2J_{C\cdot F}$=24.0 Hz), 115.6 (-CH, $^2J_{C\cdot F}$=24.0 Hz), 113.1 (-CH), 112.3 (-CH), 111.3 (-CH, $^2J_{C\cdot F}$=7.5 Hz), 102.9 (-CH), 76.5 (-C), 75.7 (-C), 73.7 (-CH), 65.5 (-CH), 64.7 (-CH), 56.1 (-OMe), 55.7 (-OMe), 54.2 (-CH), 52.4 (-CH), 51.5 (-CH$_2$), 50.8 (-CH), 48.5 (-CH$_2$), 31.2 (-CH$_2$), 29.9 (-CH$_2$), 28.3 (-CH$_2$), 26.8 (-CH$_2$), 21.4 (-CH$_3$), 17.0 (-CH$_3$).

**MS [ESI-MS, positive mode]:** found m/z 815 [M+H]$^+$, 837 [M+Na]$^+$.

**HRMS [ESI-MS, positive mode]:** MF: C$_{47}$H$_{47}$N$_4$O$_8$F; found m/z 837.3264 [M+Na]$^+$ [calcd. 837.3276].

### Compound 4Fa (±):

**Color:** Obtained as white solid; **Yield:** 17% (232 mg); **Mp:** 170-172 °C; **R$_f$** 0.37 (6 % MeOH in CHCl$_3$);

**IR (KBr, $v_{\text{max}}$ Cm$^{-1}$):** 3385, 2959, 2868, 1719, 1607;

**$^1$H NMR (Py-d$_5$):** $\delta$ 10.96 (2H, s, -NH), 7.32 (1H, dd, $J$=2.4, 8.4 Hz), 7.27 (2H, m), 7.23 (1H, d, $J$=1.8 Hz), 7.22 (1H, m), 7.16 (1H, d, $J$=1.8 Hz), 7.09 (1H, dd, $J$=1.8, 7.8 Hz), 6.96 (2H,
m), 6.80 (1H, m), 6.77 (1H, s), 5.74 (1H, s), 4.52 (1H, d, J=12.6 Hz), 4.38 (1H, d, J=12.0 Hz), 4.33 (1H, m), 4.16 (1H, m), 3.79 (2H, m), 3.75 (3H, s), 3.70 (3H, s), 2.80 (1H, m), 2.76 (1H, m), 2.62 (2H, m), 2.24 (3H, s), 2.20 (3H, s), 1.82 (6H, m), 1.69 (2H, m).

$^{13}$C NMR (Py-d$_5$): $\delta$ 192.3 (-C=O), 190.2 (-C=O), 181.2 (-C=O), 181.0 (-C=O), 158.7 (-C, $^1J_{C,F}=240.0$ Hz), 149.21 (-C), 149.16 (-C), 147.5 (-C), 147.4 (-C), 139.8 (-C), 139.6 (-C), 131.9 (-CH), 131.6 (-C), 131.5 (-C), 130.6 (-C), 128.3 (-C, $^3J_{C,F}=7.5$ Hz), 126.1 (-C), 125.4 (-CH), 120.91 (-CH), 120.87 (-CH), 119.3 (-C), 117.2 (-CH), 117.1 (-CH), 116.1 (-CH, $^2J_{C,F}=22.5$ Hz), 115.1 (-CH, $^2J_{C,F}=24.0$ Hz), 112.4 (-CH), 111.6 (-CH), 111.1 (-CH), 101.7 (-CH), 74.9 (-C), 74.8 (-C), 73.8 (-CH), 73.3 (-CH), 65.6 (-CH), 63.8 (-CH), 56.1 (-OMe), 56.0 (-OMe), 52.4 (-CH), 52.3 (-CH), 48.5 (-CH$_2$), 48.4 (-CH$_2$), 31.1 (-CH$_2$), 30.7 (-CH$_2$), 28.0 (-CH$_2$), 27.7 (-CH$_2$), 21.2 (-CH$_3$), 17.1 (-CH$_3$).

MS [ESI-MS, positive mode]: found $m/z$ 815 [M+H]$^+$, 837 [M+Na]$^+$.

HRMS [ESI-MS, positive mode]: MF: C$_{47}$H$_{47}$N$_4$O$_8$F; found $m/z$ 815.3458 [M+H]$^+$ [calcd. 815.3456].

**Compound 4Fb (±):**

**Color:** Obtained as white solid; **Yield:** 20% (273 mg); **Mp:** 184-186 ºC; **R$_f$** 0.43 (6 % MeOH in CHCl$_3$);

**IR (KBr, $\nu_{max}$ Cm$^{-1}$):** 3402, 2958, 2869, 1714, 1613, 1518;

$^1$H NMR (Py-d$_5$): $\delta$ 12.03 (1H, s, -NH), 11.73 (1H, s, -NH), 7.28 (1H, dd, J=2.4, 7.8 Hz), 7.19 (1H, s), 7.16 (1H, d, J=8.4 Hz), 7.13 (2H, m), 7.08 (1H, d, J=1.8 Hz), 6.98 (1H, td, J=2.4, 9.0 Hz), 6.82 (3H, m), 6.69 (1H, s), 5.92 (1H, s), 4.38 (2H, m), 4.20 (1H, m), 4.13 (1H, m), 3.92 (1H, m), 3.78 (1H, m), 3.67 (3H, s), 3.64 (3H, s), 2.85 (1H, m), 2.67 (3H, m), 2.28 (3H, s), 2.12 (3H, s), 1.92 (1H, m), 1.85 (2H, m), 1.81 (2H, m), 1.71 (3H, m).

$^{13}$C NMR (Py-d$_5$): $\delta$ 190.6 (-C=O), 190.3 (-C=O), 181.5 (-C=O), 181.3 (-C=O), 158.6 (-C, $^1J_{C,F}=237.0$ Hz), 149.0 (2x-C), 147.44 (-C), 147.38 (-C), 139.9 (2x-C), 131.9 (-CH), 131.6 (-C), 131.3 (-C), 130.6 (-C), 128.4 (-C, $^3J_{C,F}=7.5$ Hz), 126.2 (-C), 125.5 (-CH), 120.3 (-CH), 120.2 (-CH), 119.4 (-C), 117.0 (-CH), 116.9 (-CH), 116.2 (-CH, $^3J_{C,F}=24.0$ Hz), 115.1 (-CH, $^2J_{C,F}=24.0$ Hz), 112.6 (-CH), 112.3 (-CH), 111.0 (-CH, $^3J_{C,F}=7.5$ Hz), 101.4 (-CH), 75.44 (-C), 75.41 (-C), 73.6 (-CH), 73.4 (-CH), 65.3 (-CH), 64.9 (-CH), 56.03 (-OMe), 55.98 (-OMe), 51.8 (-CH), 51.5 (-CH), 48.33 (-CH$_2$), 48.29 (-CH$_2$), 31.5 (-CH$_2$), 31.3 (-CH$_2$), 28.4 (-CH$_2$), 28.2 (-CH$_2$), 21.3 (-CH$_3$), 17.2 (-CH$_3$).
MS [ESI-MS, positive mode]: found \(m/z\) 815 [M+H]⁺, 837 [M+Na]⁺.

HRMS [ESI-MS, positive mode]: MF: C\(_{47}H_{47}N_4O_8\)F; found \(m/z\) 815.3456 [M+H]⁺ [calcd. 815.3456].

**Compound 4Fc (±):**

**Color:** Obtained as white solid; **Yield:** 20% (273 mg); **Mp:** 173-175 °C; **R\(_f\) 0.37** (6 \% MeOH in CHCl\(_3\));

\(^1\)H NMR (Py-d\(_5\)): \(\delta 11.77 (1\text{H, s, }-\text{NH}), 11.38 (1\text{H, s, }-\text{NH}), 7.63 (1\text{H, m}), 7.44 (1\text{H, s}), 7.34 (1\text{H, s}), 7.16 (1\text{H, d, }J=8.4\text{ Hz}), 7.12 (1\text{H, m}), 7.00 (1\text{H, td, }J=2.4, 9.0\text{ Hz}), 6.91 (2\text{H, m}), 6.86 (2\text{H, m}), 6.64 (1\text{H, q, }J=4.2\text{ Hz}), 6.10 (1\text{H, s}), 4.99 (1\text{H, m}), 4.74 (1\text{H, m}), 4.65 (1\text{H, d, }J=12.0\text{ Hz}), 4.33 (1\text{H, m}), 4.14 (1\text{H, d, }J=12.0\text{ Hz}), 4.05 (1\text{H, m}), 3.67 (3\text{H, s}), 3.51 (3\text{H, s}), 3.22 (1\text{H, m}), 2.95 (1\text{H, m}), 2.83 (1\text{H, m}), 2.75 (1\text{H, m}), 2.39 (3\text{H, s}), 2.28 (3\text{H, s}), 1.95 (3\text{H, m}), 1.78 (3\text{H, m}), 1.69 (2\text{H, m}).

\(^{13}\)C NMR (Py-d\(_5\)): \(\delta 195.7 (-\text{C}=\text{O}), 189.0 (-\text{C}=\text{O}), 181.6 (-\text{C}=\text{O}), 180.1 (-\text{C}=\text{O}), 158.9 (-\text{C}, ^1J_{C,F}=235.5\text{ Hz}), 149.2 (-\text{C}), 148.3 (-\text{C}), 147.61 (-\text{C}), 147.58 (-\text{C}), 140.9 (-\text{C}), 140.3 (-\text{C}), 131.9 (-\text{CH}), 131.6 (-\text{C}), 130.8 (-\text{C}), 129.8 (-\text{C}, ^3J_{C,F}=7.4\text{ Hz}), 126.8 (-\text{C}), 126.7 (-\text{C}), 125.7 (-\text{CH}), 121.7 (-\text{CH}), 121.2 (-\text{CH}), 119.5 (-\text{C}), 117.1 (-\text{CH}), 116.4 (-\text{CH}), 116.1 (-\text{CH}, ^2J_{C,F}=22.5\text{ Hz}), 115.2 (-\text{CH}, ^2J_{C,F}=24.0\text{ Hz}), 112.7 (-\text{CH}), 112.4 (-\text{CH}), 110.9 (-\text{CH}, ^3J_{C,F}=7.5\text{ Hz}), 102.8 (-\text{CH}), 76.8 (-\text{C}), 75.2 (-\text{C}), 73.8 (-\text{CH}), 65.9 (-\text{CH}), 64.6 (-\text{CH}), 56.1 (-\text{OMe}), 55.7 (-\text{OMe}), 53.2 (-\text{CH}), 52.6 (-\text{CH}), 52.0 (-\text{CH}), 51.5 (-\text{CH}_2), 48.6 (-\text{CH}_2), 31.3 (-\text{CH}_2), 29.0 (-\text{CH}_2), 28.2 (-\text{CH}_2), 26.9 (-\text{CH}_2), 21.3 (-\text{CH}_3), 17.4 (-\text{CH}_3).

MS [ESI-MS, positive mode]: found \(m/z\) 815 [M+H]⁺, 837 [M+Na]⁺.

HRMS [ESI-MS, positive mode]: MF: C\(_{47}H_{47}N_4O_8\)F; found \(m/z\) 815.3462 [M+H]⁺ [calcd. 815.3456].

**Compound 4Fd (±):**

**Color:** Obtained as white solid; **Yield:** 22% (300 mg); **Mp:** 186-188 °C; **R\(_f\) 0.36** (6 \% MeOH in CHCl\(_3\));

\(^1\)H NMR (Py-d\(_5\)): \(\delta 11.73 (1\text{H, s, }-\text{NH}), 11.37 (1\text{H, s, }-\text{NH}), 7.66 (1\text{H, d, }J=7.8\text{ Hz}), 7.54 (1\text{H, s}), 7.41 (1\text{H, s}), 7.18 (2\text{H, s}), 7.01 (1\text{H, td, }J=3.0, 9.0\text{ Hz}), 6.95 (1\text{H, dd, }J=1.8, 8.4\text{ Hz}), 6.90 (3\text{H, m}), 6.68 (1\text{H, q, }J=4.2\text{ Hz}), 6.00 (1\text{H, s}), 4.91 (1\text{H, m}), 4.71 (1\text{H, m}), 4.64 (1\text{H, d, }J=12.0\text{ Hz}), 4.40 (1\text{H, m}), 4.29 (1\text{H, d, }J=12.0\text{ Hz}), 4.12 (1\text{H, m}), 3.70 (3\text{H, s}), 3.49 (3\text{H, s}), 3.18 (1\text{H, m}), 2.97 (1\text{H, m}), 2.76 (2\text{H, m}), 2.37 (3\text{H, s}), 2.34 (3\text{H, s}), 2.25 (1\text{H, m}), 1.96 (3\text{H, m}), 1.79 (1\text{H, m}), 1.73 (1\text{H, m}), 1.63 (1\text{H, m}), 1.58 (1\text{H, m}).
$^{13}$C NMR (Py-d$_5$): $\delta$ 195.2 (-C=O), 190.8 (-C=O), 185.8 (-C=O), 180.3 (-C=O), 158.9 (-C, $^1J_{C,F}=235.5$ Hz), 149.2 (-C), 148.2 (-C), 147.45 (-C), 147.37 (-C), 140.9 (-C), 140.2 (-C), 131.9 (-CH), 130.7 (-C), 130.2 (-C), 129.6 (-C), 127.75 (-C), 127.0 (-C), 126.1 (-CH), 121.6 (-CH), 121.4 (-CH), 119.5 (-C), 117.0 (-CH), 116.3 (-CH), 116.0 (-CH, $^2J_{C,F}=24.0$ Hz), 115.9 (-CH, $^2J_{C,F}=25.5$ Hz), 113.3 (-CH), 112.5 (-CH), 110.8 (-CH, $^3J_{C,F}=7.5$ Hz), 102.85 (-CH), 76.8 (-C), 75.7 (-C), 73.7 (-CH), 65.1 (-CH), 64.7 (-CH), 56.1 (-OMe), 55.7 (-OMe), 54.4 (-CH), 52.6 (-CH), 51.3 (-CH, CH$_2$), 48.7 (-CH$_2$), 31.3 (-CH$_2$), 29.2 (-CH$_2$), 28.2 (-CH$_2$), 26.8 (-CH$_2$), 21.4 (-CH$_3$), 17.4 (-CH$_3$).

**MS [ESI-MS, positive mode]:** found m/z 815 [M+H]$^+$, 837 [M+Na]$^+$.

**HRMS [ESI-MS, positive mode]:** MF: C$_{47}$H$_{47}$N$_4$O$_8$F; found m/z 815.3452 [M+H]$^+$ [calcd. 815.3456].

**Compound 5Aa (±):**

**Color:** Obtained as white solid; **Yield:** 30% (655 mg); **Mp:** 230-232 ºC; **R$_f$** 0.65 (5 % MeOH in CHCl$_3$);

**IR (KBr, $\nu_{\text{max}}$ Cm$^{-1}$):** 3336, 2927, 1725, 1615, 1517;

$^1$H NMR (Py-d$_5$): $\delta$ 11.26 (2H, s, -NH), 7.64 (2H, d, $J=7.8$ Hz), 7.31 (2H, m), 7.25 (2H, dd, $J=0.6$, 7.8 Hz), 7.22 (2H, m), 6.99 (4H, m), 6.93 (2H, d, $J=7.8$ Hz), 5.74 (1H, s), 4.36 (2H, d, $J=12.6$ Hz), 4.33 (2H, m), 3.92 (2H, d, $J=10.2$ Hz), 3.76 (6H, s), 3.65 (4H, m), 3.11 (2H, dd, $J=2.4$, 11.4 Hz), 3.00 (2H, m).

$^{13}$C NMR (Py-d$_5$): $\delta$ 190.5 (-C=O), 180.0 (-C=O), 149.5 (-C), 148.0 (-C), 143.8 (-C), 130.5 (-C), 130.3 (-CH), 128.5 (-CH), 124.5 (-C), 121.7 (-CH), 121.5 (-CH), 117.3 (-CH), 111.7 (-CH), 110.5 (-CH), 101.4 (-CH), 76.7 (-CH), 75.1 (-C), 62.6 (-CH), 56.2 (-OMe), 54.9 (-CH$_2$), 51.5 (-CH), 36.7 (-CH$_2$).

**MS [ESI-MS, positive mode]:** found m/z 827 [M+Na]$^+$.

**HRMS [ESI-MS, positive mode]:** MF: C$_{43}$H$_{40}$N$_4$O$_8$S$_2$; found m/z 827.2180 [M+Na]$^+$ [calcd. 827.2185].

**Compound 5Ab (±):**

**Color:** Obtained as white solid; **Yield:** 35% (765 mg); **Mp:** 242-244 ºC; **R$_f$** 0.55 (5 % MeOH in CHCl$_3$);

**IR (KBr, $\nu_{\text{max}}$ Cm$^{-1}$):** 3407, 2928, 1718, 1617, 1518;
\[ ^1H \text{NMR (Py-d5):} \delta 11.94 (2H, s, -NH), 7.43 (4H, m), 7.30 (2H, d, J=1.8 Hz), 7.20 (1H, d, J=1.8 Hz), 7.18 (3H, t, J=7.8 Hz), 6.94 (4H, m), 5.98 (1H, s), 4.36 (2H, d, J=13.2 Hz), 4.32 (2H, t, J=10.8 Hz), 3.86 (6H, s), 3.63 (4H, m), 3.15 (2H, d, J=11.4 Hz), 3.00 (2H, dd, J=6.6, 11.4 Hz). \]

\[ ^13C \text{NMR (Py-d5):} \delta 190.5 (-C=O), 180.3 (-C=O), 148.2 (2x-C), 144.0 (-C), 130.3 (-CH), 130.2 (-C), 128.4 (-CH), 123.5 (-C), 121.8 (-CH), 121.6 (-CH), 117.5 (-CH), 111.7 (-CH), 110.5 (-CH), 101.1 (-CH), 76.9 (-CH), 75.5 (-C), 61.6 (-CH), 56.3 (-OMe), 55.9 (-CH2), 51.9 (-CH), 36.9 (-CH2). \]

MS [ESI-MS, positive mode]: found \( m/z \) 827 [M+Na] +.

HRMS [ESI-MS, positive mode]: MF: C_{43}H_{40}N_{4}O_{8}S_{2}; found \( m/z \) 827.2167 [M+Na] + [calcd. 827.2185].

**Compound 5Ba (±):**

*Color:* Obtained as white solid; *Yield:* 31% (700 mg); *Mp:* 216-218 ºC; \( R_f \) 0.60 (5 % MeOH in CHCl3);

**IR (KBr, \( \nu_{\text{max}} \text{ Cm}^{-1} \):** 3379, 2923, 1718, 1602, 1521;

\[ ^1H \text{NMR (Py-d5):} \delta 10.96 (2H, s, -NH), 7.52 (2H, s), 7.27 (2H, d, J=8.4 Hz), 7.22 (2H, m), 7.00 (2H, dd, J=1.8, 8.4 Hz), 6.94 (2H, d, J=8.4 Hz), 6.84 (2H, d, J=7.8 Hz), 5.66 (1H, s), 4.36 (2H, m), 4.30 (2H, d, J=12.0 Hz), 3.88 (2H, d, J=10.2 Hz), 3.78 (2H, m), 3.73 (6H, s), 3.60 (2H, d, J=9.6 Hz), 3.10 (2H, dd, J=2.4, 10.8 Hz), 2.98 (2H, m), 2.12 (6H, s). \]

\[ ^13C \text{NMR (Py-d5):} \delta 190.2 (-C=O), 180.2 (-C=O), 149.3 (-C), 147.7 (-C), 141.1 (-C), 130.9 (-C), 130.724 (-C), 130.716 (-CH), 129.1 (-CH), 124.6 (-C), 121.2 (-CH), 117.3 (-CH), 112.2 (-CH), 110.3 (-CH), 101.6 (-CH), 76.4 (-CH), 75.2 (-C), 62.9 (-CH), 56.2 (-OMe), 54.6 (-CH2), 50.9 (-CH), 36.7 (-CH2), 21.3 (-CH3). \]

MS [ESI-MS, positive mode]: found \( m/z \) 855 [M+Na] +.

HRMS [ESI-MS, positive mode]: MF: C_{45}H_{44}N_{4}O_{8}S_{2}; found \( m/z \) 855.2495 [M+Na] + [calcd. 855.2498].

**Compound 5Bb (±):**

*Color:* Obtained as white solid; *Yield:* 35% (791 mg); *Mp:* 260-262 ºC; \( R_f \) 0.53 (5 % MeOH in CHCl3);

**IR (KBr, \( \nu_{\text{max}} \text{ Cm}^{-1} \):** 3388, 2921, 1708, 1617, 1516;
1H NMR (Py-d$_5$): $\delta$ 11.93 (2H, s, -NH), 7.55 (2H, s), 7.17 (2H, d, $J$=7.8 Hz), 7.11 (2H, d, $J$=1.8 Hz), 6.93 (2H, d, $J$=7.8 Hz), 6.88 (2H, dd, $J$=1.2, 7.8 Hz), 6.79 (2H, d, $J$=7.8 Hz), 5.88 (1H, s), 4.30 (2H, m), 4.27 (2H, d, $J$=12.0 Hz), 3.95 (2H, d, $J$=10.2 Hz), 3.86 (2H, m), 3.70 (2H, d, $J$=10.2 Hz), 3.67 (6H, s), 3.15 (2H, dd, $J$=1.8, 11.4 Hz), 3.02 (2H, m), 2.08 (6H, s).

13C NMR (Py-d$_5$): $\delta$ 189.9 (-C=O), 181.0 (-C=O), 149.2 (-C), 147.8 (-C), 141.4 (-C), 130.8 (-CH), 130.7 (-C), 130.5 (-C), 129.2 (-CH), 124.6 (-C), 120.8 (-CH), 117.2 (-CH), 112.4 (-CH), 110.0 (-CH), 101.3 (-CH), 76.7 (-CH), 75.9 (-C), 63.0 (-CH), 56.0 (-OMe), 55.1 (-CH$_2$), 50.8 (-CH), 37.0 (-CH$_2$), 21.3 (-CH$_3$).

MS [ESI-MS, positive mode]: found m/z 855 [M+Na]$^+$. 

HRMS [ESI-MS, positive mode]: MF: C$_{45}$H$_{44}$N$_4$O$_8$S$_2$; found m/z 855.2498 [M+Na]$^+$. [calcd. 855.2498].

Compound 6Aa (±):

Color: Obtained as white solid; Yield: 30% (431 mg); Mp: 172-174 ºC; $R_f$ 0.60 (5 % MeOH in CHCl$_3$);

IR (KBr, $\nu_{max}$ cm$^{-1}$): 3290, 2926, 1720, 1608, 1520;

1H NMR (Py-d$_5$): $\delta$ 11.13 (2H, s, -NH), 7.61 (1H, s), 7.32 (2H, d, $J$=8.4 Hz), 7.26 (1H, d, $J$=8.4 Hz), 7.18 (2H, m), 7.15 (1H, m), 7.13 (1H, s), 6.94 (4H, m), 6.81 (1H, m), 5.77 (1H, s), 4.49 (1H, d, $J$=12.0 Hz), 4.36 (1H, d, $J$=12.6 Hz), 4.32 (1H, m), 4.23 (1H, m), 3.96 (1H, d, $J$=9.6 Hz), 3.81 (3H, s), 3.73 (3H, s), 3.70 (1H, m), 3.68 (3H, s), 3.63 (2H, m), 3.08 (1H, d, $J$=10.2 Hz), 2.98 (1H, m), 2.76 (1H, m), 2.61 (1H, m), 1.89 (1H, m), 1.79 (2H, m), 1.67 (1H, m).

13C NMR (Py-d$_5$): $\delta$ 191.8 (-C=O), 189.9 (-C=O), 181.0 (-C=O), 179.9 (-C=O), 155.2 (-C), 149.4 (-C), 149.3 (-C), 147.9 (-C), 147.6 (-C), 143.8 (-C), 137.2 (-C), 131.8 (-C), 130.2 (-C), 129.7 (-CH), 126.94 (-C), 126.89 (-CH), 125.9 (-C), 121.8 (-CH), 121.6 (-CH), 121.1 (-CH), 117.3 (-CH), 117.2 (-CH), 116.4 (-CH), 115.0 (-CH), 111.8 (-CH), 111.5 (-CH), 110.8 (-CH), 110.6 (-CH), 101.6 (-CH), 76.5 (-CH), 75.7 (-C), 74.4 (-C), 73.9 (-CH), 64.0 (-CH), 63.0 (-CH), 56.19 (-OMe), 56.16 (-OMe), 56.12 (-OMe), 55.1 (-CH$_2$), 52.7 (-CH), 51.6 (-CH), 48.6 (-CH$_2$), 36.7 (-CH$_2$), 30.9 (-CH$_2$), 27.6 (-CH$_2$).

MS [ESI-MS, positive mode]: found m/z 817 [M+H]$^+$, 839 [M+Na]$^+$. 

HRMS [ESI-MS, positive mode]: MF: C$_{45}$H$_{44}$N$_4$O$_9$S; found m/z 839.2722 [M+Na]$^+$. [calcd. 839.2727].
**Compound 6Ab (±):**

**Color:** Obtained as white solid; **Yield:** 35% (503 mg); **Mp:** 176-178 °C; **Rf** 0.55 (5 % MeOH in CHCl₃);

**¹H NMR** *(Py-d₅)*: δ 11.91 (1H, s, -NH), 11.78 (1H, s, -NH), 7.49 (1H, d, J=2.4 Hz), 7.22 (2H, m), 7.19 (1H, m), 7.16 (2H, dd, J=1.8, 7.8 Hz), 7.13 (1H, d, J=7.2 Hz), 7.01 (1H, dd, J=1.8, 7.8 Hz), 6.94 (4H, m), 6.87 (1H, dd, J=2.4, 8.4 Hz), 5.95 (1H, s), 4.38 (2H, m), 4.28 (1H, m), 4.16 (1H, m), 3.97 (1H, d, J=10.8 Hz), 3.79 (1H, m), 3.76 (3H, s), 3.72 (3H, s), 3.68 (1H, m), 3.63 (3H, s, 1H, m), 3.13 (1H, dd, J=1.8, 11.4 Hz), 3.00 (1H, m), 2.69 (1H, m), 2.60 (1H, m), 1.85 (1H, m), 1.68 (3H, m).

**¹³C NMR** *(Py-d₅)*: δ 191.2 (-C=O), 189.6 (-C=O), 181.1 (-C=O), 180.3 (-C=O), 155.1 (-C), 149.3 (-C), 149.2 (-C), 147.9 (-C), 147.6 (-C), 143.8 (-C), 137.3 (-C), 131.3 (-C), 130.6 (-C), 129.7 (-CH), 127.1 (-CH), 126.6 (-C), 125.8 (-C), 121.7 (-CH), 121.3 (-CH), 120.9 (-CH), 117.2 (-CH), 117.1 (-CH), 115.8 (-CH), 115.3 (-CH), 112.1 (-CH), 111.9 (-CH), 110.7 (-CH), 110.6 (-CH), 101.2 (-CH), 76.7 (-CH), 76.1 (-C), 74.9 (-C), 73.8 (-CH), 64.1 (-CH), 62.7 (-CH), 56.15 (-OMe), 56.11 (-OMe), 55.90 (-OMe), 55.6 (-CH₂), 52.3 (-CH), 51.2 (-CH), 48.5 (-CH₂), 37.0 (-CH₂), 31.3 (-CH₂), 28.0 (-CH₂).

**MS [ESI-MS, positive mode]:** found m/z 817 [M+H]⁺, 839 [M+Na]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₅H₄₄N₄O₉S; found m/z 839.2728 [M+Na]⁺ [calcd. 839.2727].

**Compound 6Ba (±):**

**Color:** Obtained as white solid; **Yield:** 32% (508 mg); **Mp:** 212-214 °C; **Rf** 0.56 (5 % MeOH in CHCl₃);

**IR (KBr, νmax cm⁻¹):** 3511, 3209, 2924, 1713, 1606, 1515;

**¹H NMR** *(Py-d₃)*: δ 11.73 (1H, s, -NH), 11.29 (1H, s, -NH), 8.38 (1H, d, J=1.2 Hz), 7.84 (1H, d, J=7.8 Hz), 7.42 (1H, d, J=1.2 Hz), 7.37 (1H, d, J=7.8 Hz), 7.28 (3H, m), 7.08 (1H, d, J=1.8 Hz), 7.01 (1H, m), 6.85 (2H, m), 6.60 (1H, dd, J=1.8, 7.8 Hz), 5.79 (1H, s), 4.64 (1H, d, J=12.0 Hz), 4.32 (1H, d, J=12.6 Hz), 4.26 (1H, m), 4.17 (1H, m), 3.94 (1H, d, J=10.8 Hz), 3.88 (3H, s), 3.80 (1H, m), 3.69 (1H, m), 3.62 (3H, s), 3.48 (1H, m), 3.04 (1H, m), 2.95 (1H, m), 2.66 (2H, m), 1.86 (3H, m), 1.66 (1H, m).

**¹³C NMR** *(Py-d₃)*: δ 193.3 (-C=O), 188.9 (-C=O), 180.8 (-C=O), 179.3 (-C=O), 158.7 (-C, J_C-F=239.1 Hz), 149.6 (-C), 149.5 (-C), 148.1 (-C), 147.8 (-C), 143.8 (-C), 140.1 (-C), 139.6
(-CH), 137.1 (-CH), 132.0 (-C), 129.6 (-C), 129.4 (-C), 127.1 (-C), 122.4 (-CH), 120.8 (-CH), 117.7 (-CH), 117.2 (-CH), 115.9 (-CH, \(^2J_{C,F}=22.5\) Hz), 114.3 (-CH, \(^2J_{C,F}=24\) Hz), 112.9 (-CH), 112.0 (-CH), 111.0 (-CH, \(^3J_{C,F}=6.45\) Hz), 110.7 (-CH), 101.0 (-CH), 84.4 (-C), 76.6 (-CH), 75.5 (-C), 74.9 (-CH), 74.6 (-C), 64.1 (-CH), 62.6 (-CH), 56.5 (-OMe), 56.0 (-OMe), 55.7 (-CH), 52.5 (-CH), 51.7 (-CH), 48.2 (-CH\(_2\)), 36.9 (-CH\(_2\)), 31.1 (-CH\(_2\)), 28.0 (-CH\(_2\)).

**MS [ESI-MS, positive mode]:** found m/z 953 [M+Na] \(^+\).

**HRMS [ESI-MS, positive mode]:** MF: C\(_{44}\)H\(_{40}\)N\(_4\)O\(_8\)IFS; found m/z 953.1488 [M+Na] \(^+\) [calc. 953.1493].

**Compound 6Bb (±):**

**Color:** Obtained as white solid; **Yield:** 37% (587 mg); **Mp:** 220-222 °C; **Rf:** 0.48 (5 % MeOH in CHCl\(_3\));

\(^1\)H NMR (Py-d\(_5\)): \(\delta\) 12.25 (1H, s, -NH), 11.88 (1H, s, -NH), 8.31 (1H, s), 7.59 (1H, d, \(J=7.8\) Hz), 7.30 (1H, d, \(J=7.8\) Hz), 7.14 (1H, d, \(J=7.8\) Hz), 7.09 (1H, d, \(J=8.4\) Hz), 7.06 (1H, s), 7.02 (1H, s), 6.96 (1H, m), 6.81 (2H, m), 6.76 (2H, d, \(J=7.8\) Hz), 5.82 (1H, s), 4.32 (1H, d, \(J=12.0\) Hz), 4.25 (1H, m), 4.21 (1H, d, \(J=12.0\) Hz), 4.14 (1H, m), 3.93 (1H, d, \(J=10.8\) Hz), 3.83 (1H, m), 3.73 (3H, s), 3.71 (1H, m), 3.65 (1H, m), 3.63 (3H, s), 3.12 (1H, d, \(J=12.0\) Hz), 2.99 (1H, m), 2.63 (2H, m), 1.84 (1H, m), 1.76 (1H, m), 1.67 (2H, m).

\(^{13}\)C NMR (Py-d\(_5\)): \(\delta\) 190.4 (-C=O), 189.2 (-C=O), 181.0 (-C=O), 179.6 (-C=O), 158.6 (-C, \(^1J_{C,F}=237.0\) Hz), 149.1 (-C), 149.0 (-C), 147.8 (-C), 147.4 (-C), 143.5 (-C), 139.8 (-C), 139.1 (-CH), 137.4 (-CH), 131.1 (-C), 130.1 (-C), 128.3 (-C), 127.0 (-C), 120.7 (-CH), 120.3 (-CH), 117.2 (-CH), 117.1 (-CH), 116.2 (-CH, \(^2J_{C,F}=24.0\) Hz), 115.0 (-CH, \(^2J_{C,F}=24\) Hz), 112.6 (-CH), 112.5 (2x-CH), 111.2 (-CH, \(^3J_{C,F}=7.5\) Hz), 101.7 (-CH), 84.5 (-C), 76.4 (-CH), 76.0 (-C), 75.3 (-C), 73.6 (-CH), 64.8 (-CH), 63.5 (-CH), 56.1 (-OMe), 56.0 (-OMe), 55.5 (-CH\(_2\)), 51.9 (-CH), 51.0 (-CH), 48.2 (-CH\(_2\)), 37.1 (-CH\(_2\)), 31.4 (-CH\(_2\)), 28.3 (-CH\(_2\)).

**MS [ESI-MS, positive mode]:** found m/z 953 [M+Na] \(^+\).

**HRMS [ESI-MS, positive mode]:** MF: C\(_{44}\)H\(_{40}\)N\(_4\)O\(_8\)IFS; found m/z 953.1487 [M+Na] \(^+\) [calc. 953.1493].

**Compound 6Ca (±):**

**Color:** Obtained as white solid; **Yield:** 31% (455 mg); **Mp:** 220-222 °C; **Rf:** 0.48 (5 % MeOH in CHCl\(_3\));

IR (KBr, \(\nu_{max} Cm^{-1}\)): 3514, 3200, 1713, 1610, 1515;
$^1$H NMR ($\text{Py-d}_5$): $\delta$ 11.61 (1H, s, -NH), 11.39 (1H, s, -NH), 8.29 (1H, s), 7.76 (1H, d, $J$=7.8 Hz), 7.57 (1H, m), 7.34 (2H, m), 7.28 (2H, m), 7.18 (1H, d, $J$=7.8 Hz), 7.13 (1H, s), 6.88 (1H, d, $J$=7.8 Hz), 6.80 (1H, d, $J$=7.8 Hz), 6.77 (1H, d, $J$=8.4 Hz), 5.74 (1H, s), 4.57 (1H, d, $J$=12.0 Hz), 4.38 (1H, m), 4.27 (1H, m), 4.20 (1H, m), 3.92 (1H, d, $J$=7.8 Hz), 3.18 (3H, s), 3.67 (3H, s), 3.64 (1H, m), 3.57 (1H, m), 3.08 (1H, d, $J$=11.4 Hz), 2.96 (1H, m), 2.71 (1H, m), 2.61 (1H, m), 1.82 (3H, m), 1.66 (1H, m).

$^{13}$C NMR ($\text{Py-d}_5$): $\delta$ 192.8 (-C=O), 189.0 (-C=O), 180.5 (-C=O), 179.3 (-C=O), 149.9 (-C), 149.5 (-C), 148.0 (-C), 147.7 (-C), 143.7 (-C), 142.6 (-C), 139.4 (-CH), 137.0 (-CH), 131.9 (-C), 130.0 (-CH), 129.8 (-C), 129.3 (-C), 127.2 (-C), 126.9 (-CH), 126.6 (-C), 121.9 (-CH), 120.9 (-CH), 117.5 (-CH), 117.3 (-CH), 112.8 (-CH), 112.0 (-CH), 111.8 (-CH), 111.2 (-CH), 101.1 (-CH), 84.5 (-C), 76.7 (-CH), 75.2 (2×-C), 74.4 (-CH), 64.6 (-CH), 62.4 (-CH), 56.3 (-OMe), 56.1 (-OMe), 55.3 (-CH$_2$), 52.4 (-CH), 51.4 (-CH), 48.2 (-CH$_2$), 36.9 (-CH$_2$), 31.0 (-CH$_2$), 27.9 (-CH$_2$).

MS [ESI-MS, positive mode]: found m/z 947 [M+H]$^+$.  
HRMS [ESI-MS, positive mode]: MF: C$_{44}$H$_{40}$ClIN$_4$O$_8$S; found m/z 947.1375 [M+H]$^+$ [calcd. 947.1378].

Compound 6Cb (±):  
**Color:** Obtained as white solid; **Yield:** 35% (549 mg); **Mp:** 230-232 ºC; **R$_f$** 0.46 (5 % MeOH in CHCl$_3$);

$^1$H NMR ($\text{Py-d}_3$): $\delta$ 12.23 (1H, s, -NH), 12.06 (1H, s, -NH), 8.30 (1H, s), 7.59 (1H, m), 7.55 (1H, d, $J$=1.8, 8.4 Hz), 7.17 (1H, d, $J$=1.8, 8.4 Hz), 7.10 (2H, d, $J$=3.0, 8.4 Hz), 7.02 (2H, m), 6.79 (1H, d, $J$=8.4 Hz), 6.75 (2H, m), 6.68 (1H, d, $J$=7.8 Hz), 5.80 (1H, s), 4.28 (2H, d, $J$=12.0 Hz), 4.18 (1H, m), 4.14 (1H, m), 3.92 (1H, d, $J$=10.8 Hz), 3.82 (2H, t, $J$=10.8 Hz), 3.68 (3H, s), 3.64 (3H, s), 3.62 (1H, m), 3.10 (1H, m), 2.99 (1H, m), 2.67 (1H, m), 2.60 (1H, m), 1.85 (1H, m), 1.79 (1H, m), 1.70 (2H, m).

$^{13}$C NMR ($\text{Py-d}_3$): $\delta$ 189.8 (2×-C=O), 180.8 (-C=O), 179.5 (-C=O), 149.0 (-C), 148.9 (-C), 147.7 (-C), 147.3 (-C), 143.5 (-C), 142.4 (-C), 139.1 (-CH), 137.4 (-CH), 131.1 (-C), 130.1 (-C), 129.9 (-CH), 128.5 (-C), 127.6 (-CH), 127.0 (-C), 126.7 (-C), 120.5 (-CH), 120.1 (-CH), 117.1 (-CH), 117.0 (-CH), 112.8 (-CH), 112.6 (-CH), 112.5 (-CH), 111.8 (-CH), 101.7 (-CH), 84.5 (-C), 76.3 (-CH), 76.1 (-C), 75.3 (-C), 73.3 (-CH), 65.5 (-CH), 63.6 (-CH), 56.13 (-OMe), 56.06 (-OMe), 55.5 (-CH$_2$), 51.7 (-CH), 50.9 (-CH), 48.2 (-CH$_2$), 37.1 (-CH$_2$), 31.3 (-CH$_2$), 28.4 (-CH$_2$).
MS [ESI-MS, positive mode]: found m/z 947 [M+H]⁺.

HRMS [ESI-MS, positive mode]: MF: C_{44}H_{40}ClIN_{4}O_{8}S; found m/z 969.1193 [M+Na]⁺ [calcd. 969.1198].

**Compound 6Da (+):**

**Color:** Obtained as white solid; **Yield:** 32% (452 mg); **Mp:** 202-204 °C; **Rf:** 0.55 (5 % MeOH in CHCl₃);

**IR (KBr, v_max Cm⁻¹):** 3411, 2930, 1721, 1604, 1518;

**¹H NMR (Py-d₅):** δ 11.26 (1H, s, -NH), 10.63 (1H, s, -NH), 7.43 (1H, s), 7.28 (2H, t, J=8.4 Hz), 7.23 (2H, m), 7.10 (1H, d, J=2.4 Hz), 7.06 (1H, dd, J=1.2, 7.8 Hz), 7.01 (1H, dd, J=1.2, 7.8 Hz), 6.86 (1H, d, J=7.8 Hz), 6.81 (1H, dd, J=2.4, 8.4 Hz), 6.75 (1H, s), 5.72 (1H, s), 4.38 (3H, m), 4.28 (1H, m), 3.95 (1H, m), 3.81 (1H, m), 3.75 (3H, s), 3.74 (3H, s), 3.71 (2H, m), 3.64 (3H, s), 3.17 (1H, m), 3.00 (1H, m), 2.88 (1H, m), 2.62 (1H, m), 2.23 (3H, s), 2.15 (3H, s), 1.88 (1H, m), 1.79 (1H, m), 1.70 (2H, m).

**¹³C NMR (Py-d₅):** δ 194.0 (-C=O), 187.9 (-C=O), 180.9 (-C=O), 180.4 (-C=O), 155.4 (-C), 149.4 (-C), 149.1 (-C), 147.7 (-C), 147.5 (-C), 140.0 (-C), 136.8 (-C), 132.3 (-CH), 132.0 (-C), 130.6 (-C), 130.5 (-C), 127.8 (-C), 126.5 (-CH), 124.2 (-C), 121.3 (-CH), 121.0 (-CH), 119.0 (-C), 117.3 (-CH), 117.1 (-CH), 115.0 (-CH), 114.5 (-CH), 112.4 (-CH), 111.7 (-CH), 110.8 (-CH), 101.9 (-CH), 77.1 (-CH), 75.5 (-C), 74.8 (-C), 72.9 (-CH), 66.1 (-CH), 61.5 (-CH), 56.13 (2×-OMe), 56.09 (-OMe), 55.2 (-CH₂), 52.5 (-CH), 51.1 (-CH), 48.5 (-CH₂), 36.7 (-CH₂), 30.6 (-CH₂), 27.5 (-CH₂), 21.1 (-CH₃), 17.2 (-CH₃).

MS [ESI-MS, positive mode]: found m/z 845 [M+H]⁺.

HRMS [ESI-MS, positive mode]: MF: C_{47}H_{48}N_{4}O_{9}S; found m/z 845.3238 [M+H]⁺ [calcd. 845.3220].

**Compound 6Db (+):**

**Color:** Obtained as white solid; **Yield:** 36% (508 mg); **Mp:** 182-184 °C; **Rf:** 0.47 (5 % MeOH in CHCl₃);

**¹H NMR (Py-d₃):** δ 11.83 (1H, s, -NH), 11.79 (1H, s, -NH), 7.47 (1H, s), 7.18 (1H, dd, J=1.2, 7.8 Hz), 7.12 (2H, m), 7.07 (2H, m), 6.84 (3H, m), 6.77 (1H, dd, J=2.4, 8.4 Hz), 6.69 (1H, s), 5.87 (1H, d, J=1.2 Hz), 4.33 (2H, m), 4.27 (1H, d, J=12.6 Hz), 4.19 (1H, m), 3.98 (1H, d, J=10.2 Hz), 3.90 (1H, m), 3.80 (1H, t, J=10.2 Hz), 3.75 (1H, d, J=10.2 Hz), 3.68 (3H,
1H NMR (Py-d$_5$):  $\delta$ 11.16 (1H, s, -NH), 10.69 (1H, s, -NH), 7.46 (1H, s), 7.30 (2H, m), 7.28 (1H, s), 7.25 (2H, d, $J= 9.6$ Hz), 7.08 (1H, d, $J= 7.8$ Hz), 7.03 (1H, d, $J=7.8$ Hz), 6.95 (1H, d, $J=7.8$ Hz), 6.83 (1H, d, $J=7.8$ Hz), 6.73 (1H, s), 5.73 (1H, s), 4.37 (3H, m), 3.95 (1H, d, $J=10.2$ Hz), 3.87 (1H, m), 3.81 (1H, m), 3.76 (3H, s), 3.73 (3H, s), 3.71 (1H, m), 3.16 (1H, m), 3.01 (1H, m), 2.86 (1H, m), 2.63 (1H, m), 2.24 (3H, s), 2.15 (6H, s), 2.01 (1H, m), 1.90 (1H, m), 1.82 (2H, m), 1.69 (1H, m).

13C NMR (Py-d$_5$):  $\delta$ 192.6 (-C=O), 187.8 (-C=O), 180.5 (-C=O), 179.9 (-C=O), 148.7 (-C), 148.5 (-C), 147.1 (-C), 146.8 (-C), 140.4 (-C), 139.3 (-C), 131.7 (-CH), 131.4 (-C), 130.2 (3x-C), 129.9 (-C), 129.6 (-CH), 127.5 (-CH), 126.0 (-C), 125.9 (-CH), 120.5 (-CH), 120.3 (-CH), 118.4 (-C), 116.7 (-CH), 116.5 (-CH), 111.8 (-CH), 111.4 (-CH), 109.7 (-CH), 101.2 (-CH), 76.2 (-CH), 75.0 (-C), 74.1 (-C), 72.6 (-CH), 65.0 (-CH), 61.4 (-CH), 55.5 (2x-OMe), 54.4 (-CH$_2$), 51.7 (-CH), 50.5 (-CH), 48.0 (-CH$_2$), 36.1 (-CH$_2$), 30.2 (-CH$_2$), 27.0 (-CH$_2$), 20.7 (-CH$_3$), 20.6 (-CH$_3$), 16.6 (-CH$_3$).

MS [ESI-MS, positive mode]: found m/z 829 [M+H]$^+$.

HRMS [ESI-MS, positive mode]: MF: C$_{47}$H$_{58}$N$_4$O$_8$S; found m/z 829.3268 [M+H]$^+$ [calcd. 829.3271].

Compound 6Ea (±):
Color: Obtained as white solid; Yield: 31% (441 mg); Mp: 172-174 ºC; $R_f$ 0.51 (5 % MeOH in CHCl$_3$);

1H NMR (Py-d$_5$):  $\delta$ 11.16 (1H, s, -NH), 10.69 (1H, s, -NH), 7.46 (1H, s), 7.30 (2H, m), 7.28 (1H, s), 7.25 (2H, d, $J= 9.6$ Hz), 7.08 (1H, d, $J= 7.8$ Hz), 7.03 (1H, d, $J=7.8$ Hz), 6.95 (1H, d, $J=7.8$ Hz), 6.83 (1H, d, $J=7.8$ Hz), 6.73 (1H, s), 5.73 (1H, s), 4.37 (3H, m), 3.95 (1H, d, $J=10.2$ Hz), 3.87 (1H, m), 3.81 (1H, m), 3.76 (3H, s), 3.73 (3H, s), 3.71 (1H, m), 3.16 (1H, m), 3.01 (1H, m), 2.86 (1H, m), 2.63 (1H, m), 2.24 (3H, s), 2.15 (6H, s), 2.01 (1H, m), 1.90 (1H, m), 1.82 (2H, m), 1.69 (1H, m).

13C NMR (Py-d$_5$):  $\delta$ 192.6 (-C=O), 187.8 (-C=O), 180.5 (-C=O), 179.9 (-C=O), 148.7 (-C), 148.5 (-C), 147.1 (-C), 146.8 (-C), 140.4 (-C), 139.3 (-C), 131.7 (-CH), 131.4 (-C), 130.2 (3x-C), 129.9 (-C), 129.6 (-CH), 127.5 (-CH), 126.0 (-C), 125.9 (-CH), 120.5 (-CH), 120.3 (-CH), 118.4 (-C), 116.7 (-CH), 116.5 (-CH), 111.8 (-CH), 111.4 (-CH), 109.7 (-CH), 101.2 (-CH), 76.2 (-CH), 75.0 (-C), 74.1 (-C), 72.6 (-CH), 65.0 (-CH), 61.4 (-CH), 55.5 (2x-OMe), 54.4 (-CH$_2$), 51.7 (-CH), 50.5 (-CH), 48.0 (-CH$_2$), 36.1 (-CH$_2$), 30.2 (-CH$_2$), 27.0 (-CH$_2$), 20.7 (-CH$_3$), 20.6 (-CH$_3$), 16.6 (-CH$_3$).

MS [ESI-MS, positive mode]: found m/z 829 [M+H]$^+$.

HRMS [ESI-MS, positive mode]: MF: C$_{47}$H$_{58}$N$_4$O$_8$S; found m/z 829.3268 [M+H]$^+$ [calcd. 829.3271].
**Compound 6Eb (±):**

**Color:** Obtained as white solid; **Yield:** 36% (512 mg); **Mp:** 169-171 °C; **Rf** 0.45 (5 % MeOH in CHCl₃);

**IR (KBr, ν<sub>max</sub>Cm<sup>-1</sup>):** 3404, 2926, 1712, 1605, 1517, 1485;

**<sup>1</sup>H NMR (Py-d₅):** δ 7.41 (1H, s), 7.17 (2H, m), 7.09 (3H, m), 6.90 (1H, d, J=7.8 Hz), 6.82 (2H, m), 6.78 (1H, d, J=7.8 Hz), 6.64 (1H, s), 5.85 (1H, s), 4.27 (3H, m), 4.16 (1H, m), 3.93 (1H, d, J=9.6 Hz), 3.83 (2H, q, J=9.6, 21 Hz), 3.70 (1H, d, J=9.6 Hz), 3.63 (3H, s), 3.58 (3H, s), 3.13 (1H, m), 2.99 (1H, m), 2.78 (1H, m), 2.59 (1H, m), 2.21 (3H, s), 2.05 (3H, s), 2.00 (3H, s), 1.84 (1H, m), 1.75 (2H, m), 1.64 (1H, m).

**<sup>13</sup>C NMR (Py-d₅):** δ 190.6 (-C=O), 188.8 (-C=O), 180.8 (-C=O), 180.1 (-C=O), 148.6 (-C), 148.4 (-C), 147.2 (-C), 146.8 (-C), 140.7 (-C), 139.5 (-C), 131.8 (-CH), 131.1 (-C), 130.2 (2×-C), 130.1 (-C), 129.8 (-C), 129.7 (-CH), 127.5 (-CH), 126.0 (-C), 125.9 (-CH), 120.1 (-CH), 119.7 (-CH), 118.5 (-C), 116.6 (-CH), 116.4 (-CH), 111.9 (-CH), 111.7 (-CH), 109.7 (-CH), 100.7 (-CH), 76.1 (-CH), 75.5 (-C), 74.7 (-C), 73.0 (-CH), 64.5 (-CH), 62.5 (-CH), 55.5 (-OMe), 55.4 (-OMe), 54.5 (-CH₂), 51.1 (-CH), 50.2 (-CH), 47.9 (-CH₂), 36.3 (-CH₂), 30.7 (-CH₂), 27.5 (-CH₂), 20.8 (-CH₃), 20.7 (-CH₃), 16.7 (-CH₃).

**MS [ESI-MS, positive mode]:** found m/z 829 [M+H]<sup>+</sup>.

**HRMS [ESI-MS, positive mode]:** MF: C₄₇H₄₉N₄O₈S; found m/z 829.3268 [M+H]<sup>+</sup> [calcd. 829.3271].

**Compound 7A (±):**

**Color:** Obtained as white solid; **Yield:** 54% (636 mg); **Mp:** 192-194 °C; **Rf** 0.52 (5 % MeOH in CHCl₃);

**IR (KBr, ν<sub>max</sub>Cm<sup>-1</sup>):** 3511, 2960, 1720, 1607, 1515;

**<sup>1</sup>H NMR (Py-d₅):** δ 11.82 (1H, s, -NH), 7.87 (2H, m), 7.84 (2H, m), 7.76 (1H, t, J= 7.2 Hz ), 7.69 (1H, d, J=7.2 Hz), 7.41 (1H, t, J=7.2 Hz), 7.37 (1H, d, J=1.2 Hz), 7.30 (1H, t, J=7.8 Hz), 7.16 (3H, m), 7.02 (1H, d, J=7.8 Hz), 6.79 (1H, dd, J=1.2, 8.4 Hz), 6.75 (1H, d, J=8.4 Hz), 6.70 (1H, s), 6.03 (1H, s), 4.96 (1H, m), 4.61 (2H, m), 4.45 (1H, d, J=11.4 Hz), 4.38 (1H, m), 4.01 (1H, dd, J=9.6, 12 Hz), 3.71 (3H, s), 3.36 (3H, s), 3.14 (1H, m), 2.90 (1H, m), 2.74 (1H, m), 2.54 (1H, t, J=7.2 Hz), 1.98 (1H, m), 1.90 (2H, m), 1.78 (1H, m), 1.70 (1H, m), 1.64 (1H, m), 1.50 (1H, m), 1.31 (1H, m).
Compound 7B (±):

**Color:** Obtained as yellowish white solid; **Yield:** 56% (629 mg); **Mp:** 163-165 °C; **Rf** 0.50 (5 % MeOH in CHCl₃);

**1H NMR (Py-d₅):** δ 12.17 (1H, s, -NH), 8.06 (2H, d, J = 7.2 Hz), 7.88 (1H, d, J = 8.4 Hz), 7.84 (1H, s), 7.67 (2H, m), 7.62 (1H, t, J=7.2 Hz), 7.47 (1H, d, J=7.2 Hz), 7.34 (1H, d, J=7.8 Hz), 7.30 (1H, s), 7.19 (1H, d, J=8.4 Hz), 7.15 (1H, d, J=8.4 Hz), 7.03 (1H, s), 6.91 (1H, d, J= 8.4 Hz), 6.83 (1H, d, J= 7.8 Hz), 5.81 (1H, s), 4.52 (1H, d, J= 11.4 Hz), 4.30 (1H, d, J= 12.0 Hz), 4.23 (1H, m), 4.09 (1H, m), 3.88 (3H, s), 3.74 (2H, m), 3.66 (3H, s), 2.62 (2H, m), 2.52 (1H, m), 2.35 (1H, m), 1.84 (2H, m), 1.70 (5H, m), 1.58 (1H, m).

**13C NMR (Py-d₅):** δ 204.6 (-C=O), 197.4 (-C=O), 186.5 (-C=O), 181.2 (-C=O), 149.3 (-C), 148.1 (-C), 147.7 (-C), 147.2 (-C), 144.0 (-C), 143.2 (-C), 138.1 (-C), 133.2 (-C), 131.7 (-CH), 131.5 (-C), 131.3 (-C), 129.9 (-CH), 128.83 (-CH), 128.79 (-CH), 128.0 (-CH), 127.5 (-C), 126.9 (-C), 125.9 (-CH), 123.7 (-CH), 121.9 (-CH), 121.8 (-CH), 121.7 (-CH), 121.4 (-CH), 117.1 (-CH), 116.3 (-CH), 113.2 (-CH), 112.3 (-CH), 110.8 (-CH), 103.0 (-CH), 79.3 (-C), 75.3 (-C), 73.7 (-CH), 66.0 (-CH), 64.6 (-CH), 56.1 (-OMe), 55.6 (-OMe), 54.8 (-CH), 52.6 (-CH), 51.8 (-CH₂), 50.7 (-CH), 48.6 (-CH₂), 31.3 (-CH₂), 2.95 (-CH₂), 2.67 (-CH₂).

**MS [ESI-MS, positive mode]:** found m/z 804 [M+H]⁺, 826 [M+Na]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₉H₄₅N₃O₈; found m/z 826.3113 [M+Na]⁺ [calcd. 826.3104].

Compound 7C (±):

**MS [ESI-MS, positive mode]:** found m/z 930 [M+H]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₉H₄₅N₃O₈; found m/z 930.2252 [M+H]⁺ [calcd. 930.2251].
**Color:** Obtained as white solid; **Yield:** 50% (607 mg); **Mp:** 204-206 °C; **R<sub>f</sub>** 0.49 (5 % MeOH in CHCl<sub>3</sub>);

**<sup>1</sup>H NMR (Py-d<sub>5</sub>):** δ 11.78 (1H, s, -NH), 8.08 (1H, dd, J=2.4, 6.6 Hz), 8.05 (1H, dd, J=2.4, 8.4 Hz), 7.83 (1H, dd, J=2.4, 8.4 Hz), 7.74 (1H, m ), 7.62 (2H, m), 7.47 (1H, dd, J=1.8, 7.8 Hz), 7.41 (1H, dd, J=1.8, 7.8 Hz), 7.31 (1H, s), 7.26 (1H, d, J=8.4 Hz), 7.18 (2H, m), 7.12 (1H, d, J=7.8 Hz), 6.96 (1H, d, J=7.8 Hz), 6.91 (2H, m), 5.86 (1H, s), 4.46 (1H, m), 4.32 (2H, m), 4.11 (1H, m), 3.87 (3H, s), 3.82 (3H, s), 3.76 (2H, m), 3.49 (1H, m), 3.24 (1H, d, J=10.8 Hz), 3.20 (1H, d, J=11.4 Hz), 3.02 (1H, m), 2.57 (2H, m), 1.86 (1H, m), 1.71 (2H, m), 1.64 (1H, m).

**<sup>13</sup>C NMR (Py-d<sub>5</sub>):** δ 205.0 (-C=O), 190.9 (-C=O), 190.5 (-C=O), 180.9 (-C=O), 149.8 (-C), 149.6 (-C), 148.3 (-C), 147.9 (-C), 143.9 (-C), 143.4 (-C), 133.2 (-C), 132.51 (-CH), 132.47 (-C), 131.2 (-C), 131.0 (-C), 130.3 (-C), 129.7 (-CH), 128.7 (-CH), 128.6 (-CH), 126.8 (-CH), 126.4 (-C), 126.2 (-CH), 125.1 (-CH), 122.4 (-CH), 121.9 (-CH), 121.7 (-CH), 121.5 (-CH), 117.5 (-CH), 117.3 (-CH), 111.9 (-CH), 111.3 (-CH), 100.9 (-CH), 78.7 (-C), 77.4 (-CH), 74.4 (-C), 73.8 (-CH), 63.8 (-CH), 61.2 (-CH), 56.3 (-OMe), 56.2 (-OMe), 55.9 (-CH<sub>2</sub>), 53.0 (-CH), 52.4 (-CH), 48.4 (-CH<sub>2</sub>), 37.2 (-CH<sub>2</sub>), 31.3 (-CH<sub>2</sub>), 27.9 (-CH<sub>2</sub>).

**MS [ESI-MS, positive mode]:** found m/z 822 [M+H]<sup>+</sup>, 844 [M+Na]<sup>+</sup>.

**HRMS [ESI-MS, positive mode]:** MF: C<sub>48</sub>H<sub>43</sub>N<sub>3</sub>O<sub>8</sub>S; found m/z 844.2670 [M+Na]<sup>+</sup> [calcd. 844.2669].

**Compound 7D (±):**

**Color:** Obtained as yellowish white solid; **Yield:** 49% (588 mg); **Mp:** 160-162 °C; **R<sub>f</sub>** 0.48 (5 % MeOH in CHCl<sub>3</sub>);

**<sup>1</sup>H NMR (Py-d<sub>5</sub>):** δ 8.05 (2H, m), 7.87 (1H, d, J=8.4 Hz), 7.76 (1H, d, J= 8.4 Hz ), 7.65 (1H, t, J= 7.8 Hz), 7.60 (1H, d, J=7.2 Hz), 7.39 (1H, d, J=7.8 Hz), 7.31 (1H, d, J=1.2 Hz), 7.27 (1H, d, J=8.4 Hz), 7.20 (1H, m), 7.15 (1H, s), 7.07 (2H, m), 7.01 (1H, d, J= 7.8 Hz), 6.96 (1H, dd, J= 1.2, 7.8 Hz), 5.88 (1H, s), 4.46 (1H, d, J= 12.6 Hz), 4.33 (2H, m), 4.12 (1H, m), 3.88 (3H, s), 3.76 (2H, m), 3.73 (3H, s), 3.70 (1H, m), 3.24 (1H, d, J=10.8 Hz), 3.12 (1H, d, J=11.4 Hz), 3.00 (1H, m), 2.72 (1H, m), 2.63 (1H, m), 2.13 (3H, s), 1.87 (1H, m), 1.77 (2H, m), 1.68 (1H, m).

**<sup>13</sup>C NMR (Py-d<sub>5</sub>):** δ 204.5 (-C=O), 192.0 (-C=O), 188.1 (-C=O), 180.4 (-C=O), 149.0 (-C), 148.7 (-C), 147.6 (-C), 147.1 (-C), 142.8 (-C), 140.8 (-C), 132.8 (-C), 131.9 (-CH), 131.8 (-C), 149.8 (-C), 149.6 (-C), 148.3 (-C), 147.9 (-C), 143.9 (-C), 143.4 (-C), 133.2 (-C), 132.51 (-CH), 132.47 (-C), 131.2 (-C), 131.0 (-C), 130.3 (-C), 129.7 (-CH), 128.7 (-CH), 128.6 (-CH), 126.8 (-CH), 126.4 (-C), 126.2 (-CH), 125.1 (-CH), 122.4 (-CH), 121.9 (-CH), 121.7 (-CH), 121.5 (-CH), 117.5 (-CH), 117.3 (-CH), 111.9 (-CH), 111.3 (-CH), 100.9 (-CH), 78.7 (-C), 77.4 (-CH), 74.4 (-C), 73.8 (-CH), 63.8 (-CH), 61.2 (-CH), 56.3 (-OMe), 56.2 (-OMe), 55.9 (-CH<sub>2</sub>), 53.0 (-CH), 52.4 (-CH), 48.4 (-CH<sub>2</sub>), 37.2 (-CH<sub>2</sub>), 31.3 (-CH<sub>2</sub>), 27.9 (-CH<sub>2</sub>).
C), 130.8 (-C), 130.5 (-C), 130.3 (-C), 129.8 (-CH, -C), 128.1 (-CH), 128.0 (-CH), 127.3 (-CH), 126.1 (-C), 125.5 (-CH), 124.3 (-CH), 121.8 (-CH), 120.9 (-CH), 120.6 (-CH), 116.8 (-CH), 116.5 (-CH), 111.4 (-CH), 110.8 (-CH), 109.9 (-CH), 100.4 (-CH), 78.2 (-C), 77.1 (-CH), 74.1 (-C), 73.1 (-CH), 64.1 (-CH), 60.5 (-CH), 55.6 (-OMe), 55.5 (-OMe), 55.2 (-CH₂), 51.8 (-CH), 51.6 (-CH), 47.7 (-CH₂), 36.8 (-CH₂), 30.8 (-CH₂), 27.7 (-CH₂), 20.8 (-CH₃).

**MS [ESI-MS, positive mode]:** found m/z 836 [M+H]⁺.

**HRMS [ESI-MS, positive mode]:** MF: C₄₉H₄₆N₃O₈S; found m/z 836.3009 [M+H]⁺ [calcd. 836.3006].
13C-NMR in Py-d5
13C-NMR in Py-d5
$^{1}H$ NMR in Py-d5

4Da (±)

$\text{MeO}$

$\text{HO}$

$\text{F}$

$\text{HO}$

$\text{H}$

$\text{H}$

$\text{H}$

$\text{OMe}$

$\text{OMe}$
13C-NMR in Py-d5
1H NMR in Py-d5

4Dd (±)
1H NMR in Py-d5

4Ec (±)
13C-NMR in Py-d5
1H NMR in Py-d5

![1H NMR Spectrum of 4Fa (±)]
13C-NMR in Py-d5
1H NMR in Py-d5

4Fb (±)
1H NMR in Py-d5

![NMR Spectrogram](image)

![Chemical Structure](image)

4Fc (±)
$^{13}$C-NMR in Py-d5

The spectrum shows chemical shifts ranging from 10 to 200 ppm. The peaks are labeled with their respective chemical shifts. The structure inset illustrates the molecular framework with specific groups marked for chemical identification.
$^1$H NMR in Py-d5

$\text{5Bb} (\pm)$
13C-NMR in Py-d5
1H NMR in Py-d5
$1\text{H NMR in Py-d5}$

$7\text{C (±)}$
1H-NMR in Py-d5
Figure 2. Important correlations of 6Aa and 6Ab [HMBC ( ), COSY ( )]

Figure 3. Important correlations of 7B and 7D [HMBC ( ), COSY ( )]
