



Supporting Information

for

Synthesis of 9-O-arylated berberines via copper-catalyzed $C_{Ar}-O$ coupling reactions

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Experimental details and characterization data

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General considerations

All operations were performed without taking precautions to exclude air or moisture unless otherwise stated. All solvents and chemicals were used as received. ^1H and ^{13}C NMR spectra were recorded at 298 K on a Bruker AVANCE spectrometer, and the chemical shifts (δ) were internally referenced to the residual solvent signals relative to tetramethylsilane. FTIR spectra were recorded on a Thermo Fischer Scientific Nicolet IS50 infrared spectrometer using KBr pellets. HRMS analyses were performed on an Agilent Technologies 6230 TOF spectrometer. Tetrahydroberberrubine (**1**) was prepared according to the literature procedure and its formation was confirmed by ^1H NMR spectroscopy.¹

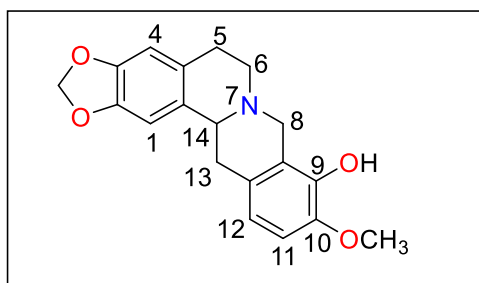
General procedure for the cross-coupling

A Schlenk tube was charged with a mixture of tetrahydroberberrubine (**1**, 228 mg, 0.70 mmol), potassium carbonate (97 mg, 0.70 mmol), copper(I) iodide (13 mg, 0.07 mmol), picolinic acid (17 mg, 0.14 mmol), aryl iodide (1.40 mmol, 2 equiv) and DMSO (6 mL) before it was evacuated and backfilled with N_2 for three times. The reaction mixture was stirred for 24 h at 100 °C and the resulting mixture was subjected to column chromatography (SiO_2 , $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 200:1–150:1) to give the respective product **2a–o** as pale-yellow solids and **4** as yellow solid. Characterization data and the original spectra are presented below.

General procedure for the oxidation

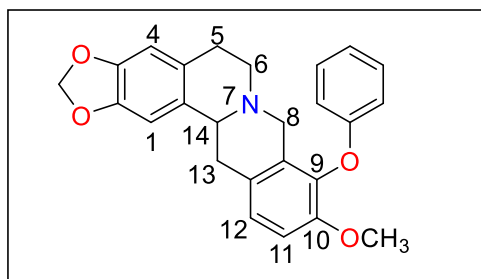
A reaction tube was charged with **2** or **4** (0.20 mmol) and I_2 (152 mg, 0.6 mmol, double amount for **4**) in DMSO (2 mL). The reaction mixture was stirred at 60 °C until

consumption of **2,4** (TLC). Then, the solvent was removed by vacuum distillation before the residue was dissolved in CH₂Cl₂, extracted three times with saturated NaHSO₃, and twice with H₂O. The organic phase was dried over anhydrous Na₂SO₄, filtered, and dried in vacuo to give the respective products **3a–o** as yellow solids. As for **5**, it was purified by direct H₂O wash owing to its low solubility. Characterization data and the original spectra are presented below.



1, off-white solid, yield 62%. ¹H NMR (300 MHz, CDCl₃): δ 6.74 (s, 1 H, H-1), 6.73 (d, *J*=7.1 Hz, 1 H, H-11), 6.66 (d, *J*=7.1 Hz, 1 H, H-12), 6.59 (s, 1 H, H-4), 5.92 (s, 2 H, OCH₂O),

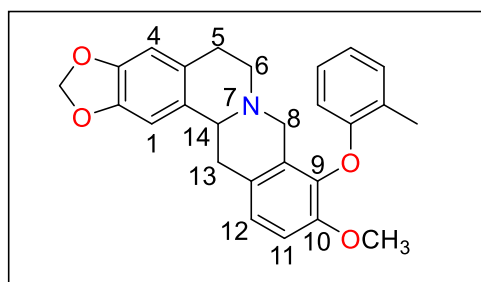
5.71 (s, 1 H, OH), 4.23 (d, 1 H, *J*=15.6 Hz, H-14), 3.86 (s, 3 H, OCH₃), 3.57-3.48 (m, 2 H, H-8), 3.25-3.06 (m, 3 H, H-5 & H-6 & H-13), 2.86-2.77 (m, 1 H, H-5), 2.67-2.60 (m, 2 H, H-6 & H-13).



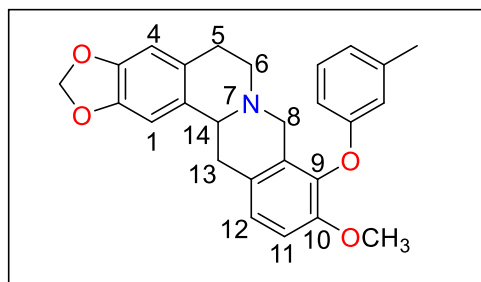
2a, pale yellow solid, m.p.: 144-146 °C, yield 72%. ¹H NMR (300 MHz, CDCl₃): δ 7.28-7.23 (m, 2 H, Ar-H), 7.04-6.96 (m, 2 H, Ar-H), 6.88-6.84 (m, 3 H, Ar-H), 6.74 (s, 1 H, H-1), 6.57 (s,

1 H, H-4), 5.91 (q, 2 H, *J*=1.4 Hz, OCH₂O), 4.07 (d, 1 H, *J*=15.9 Hz, H-8), 3.74 (s, 3 H, OCH₃), 3.56-3.51 (m, 1 H, H-14), 3.43 (d, 1 H, *J*=15.9 Hz, H-8), 3.31-3.24 (m, 1 H, H-13), 3.11-2.98 (m, 2 H, H-6 & H-5), 2.91-2.82 (m, 1 H, H-5), 2.63-2.48 (m, 2 H, H-

6 & H-13); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 158.1, 150.4, 146.3, 146.1, 139.2, 130.8, 129.7, 129.6, 128.2, 127.9, 125.8, 121.7, 114.8, 111.2, 108.5, 105.6 (Ar-C), 100.9 (OCH_2O), 59.7 (C-14), 56.2 (OCH_3), 53.8 (C-8), 51.3 (C-6), 36.5 (C-13), 29.6 (C-5); HRMS (ESI): m/z for $\text{C}_{25}\text{H}_{24}\text{NO}_4^+$ $[\text{M} + \text{H}]^+$ calcd. 402.1705, found 402.1709.

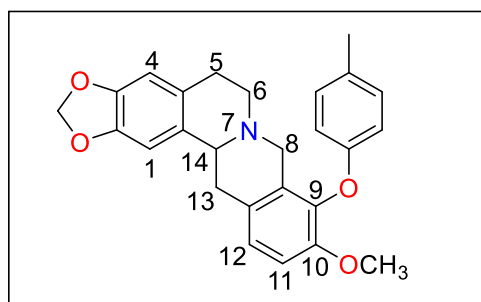


2b, pale yellow solid, m.p. 153-155 °C, yield 69%. ^1H NMR (300 MHz, CDCl_3): δ 7.20 (dd, 1 H, $J=0.8$ Hz, $J=7.3$ Hz, Ar-H), 7.03-6.96 (m, 2 H, Ar-H), 6.91-6.85 (m, 2 H, Ar-H), 6.74 (s, 1 H, H-1), 6.57 (s, 1 H, H-4), 6.44-6.41 (m, 1 H, Ar-H), 5.92 (q, 2 H, $J=1.4$ Hz, OCH_2O), 4.05 (d, 1 H, $J=15.8$ Hz, H-8), 3.72 (s, 3 H, OCH_3), 3.56-3.52 (m, 1 H, H-14), 3.43 (d, 1 H, $J=15.8$ Hz, H-8), 3.30-3.24 (m, 1 H, H-13), 3.12-3.03 (m, 2 H, H-6 & H-5), 2.91-2.82 (m, 1 H, H-5), 2.64-2.48 (m, 2 H, H-6 & H-13), 2.44 (s, 3 H, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 156.1, 150.5, 146.3, 146.1, 139.9, 131.0, 130.8, 129.4, 128.2, 127.9, 126.8, 126.3, 125.6, 121.4, 112.4, 111.4, 108.5, 105.6 (Ar-C), 100.9 (OCH_2O), 59.7 (C-14), 56.3 (OCH_3), 53.7 (C-8), 51.3 (C-6), 36.5 (C-13), 29.6 (C-5), 16.4 (CH_3); HRMS (ESI): m/z for $\text{C}_{26}\text{H}_{26}\text{NO}_4^+$ $[\text{M} + \text{H}]^+$ calcd. 416.1862, found 416.1861.



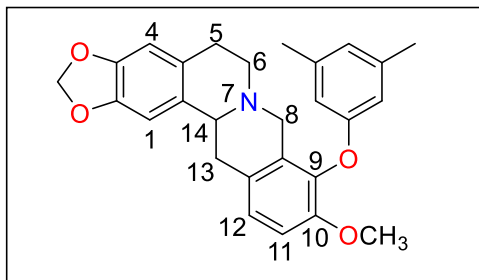
2c, pale yellow solid, m.p. 158-160 °C, yield 90%. ^1H NMR (300 MHz, CDCl_3): δ 7.12 (t, 1 H, $J=7.8$ Hz, Ar-H), 7.02 (d, 1 H, $J=8.4$ Hz, H-11), 6.87 (d, 1 H, $J=8.4$ Hz, H-12), 6.80 (d, 1

H, $J=7.5$ Hz, Ar-H), 6.73 (s, 1 H, H-1), 6.70-6.69 (m, 1 H, Ar-H), 6.62 (dd, 1 H, $J=2.4$ Hz, $J=8.2$ Hz, Ar-H), 6.57 (s, 1 H, H-4), 5.92 (q, 2 H, $J=1.4$ Hz, OCH₂O), 4.06 (d, 1 H, $J=15.9$ Hz, H-8), 3.74 (s, 3 H, OCH₃), 3.56-3.51 (m, 1 H, H-14), 3.43 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.24 (m, 1 H, H-13), 3.11-2.99 (m, 2 H, H-6 & H-5), 2.91-2.81 (m, 1 H, H-5), 2.62-2.49 (m, 2 H, H-6 & H-13), 2.30 (s, 3 H, CH₃); ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 158.1, 150.5, 146.3, 146.1, 139.7, 139.4, 130.8, 129.8, 129.3, 128.2, 127.9, 125.7, 122.6, 115.5, 111.7, 111.3, 108.6, 105.6 (Ar-C), 100.9 (OCH₂O), 59.7 (C-14), 56.3 (OCH₃), 53.8 (C-8), 51.4 (C-6), 36.6 (C-13), 29.6 (C-5), 21.6 (CH₃); HRMS (ESI): m/z for C₂₆H₂₆NO₄⁺ [M + H]⁺ calcd. 416.1862, found 416.1837.



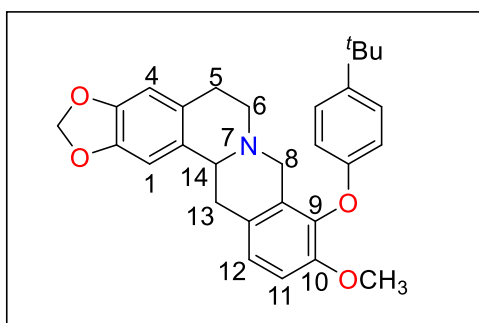
2d, pale yellow solid, m.p. 142-144 °C, yield 88%. ¹H NMR (300 MHz, CDCl₃): δ 7.06-7.00 (m, 3 H, H-11 & Ar-H), 6.86 (d, 1 H, $J=8.4$, H-12), 6.75-6.73 (m, 3 H, H-1 & Ar-H), 6.57 (s,

1 H, H-4), 5.91 (q, 2 H, $J=1.4$ Hz, OCH₂O), 4.07 (d, 1 H, $J=15.9$ Hz, H-8), 3.73 (s, 3 H, OCH₃), 3.55-3.50 (m, 1 H, H-14), 3.42 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.23 (m, 1 H, H-13), 3.12-3.02 (m, 2 H, H-6 & H-5), 2.90-2.81 (m, 1 H, H-5), 2.63-2.48 (m, 2 H, H-13 & H-6), 2.28 (s, 3 H, CH₃); ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 156.0, 150.5, 146.3, 146.1, 139.5, 130.9, 130.8, 130.1, 129.8, 128.2, 127.9, 125.7, 114.5, 111.3, 108.6, 105.6 (Ar-C), 100.9 (OCH₂O), 59.7 (C-14), 56.3 (OCH₃), 53.8 (C-8), 51.4 (C-6), 36.5 (C-13), 29.6 (C-5), 20.7 (CH₃); HRMS (ESI): m/z for C₂₆H₂₆NO₄⁺ [M + H]⁺ calcd. 416.1862, found 416.1859.



2e, pale yellow solid, m.p. 193-195 °C, yield 87%. ^1H NMR (300 MHz, CDCl_3): δ 7.02 (d, 1 H, $J=8.4$ Hz, H-11), 6.87 (d, 1 H, $J=8.4$ Hz, H-12), 6.74 (s, 1 H, H-1), 6.63 (s, 1 H, Ar-H),

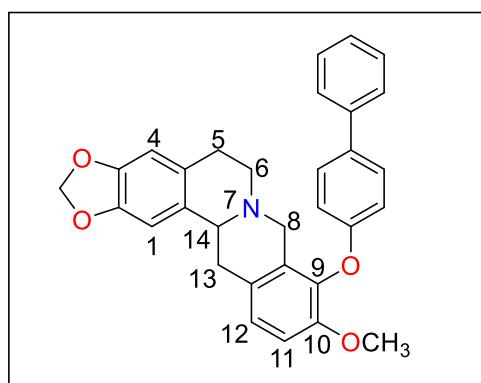
6.57 (s, 1 H, H-4), 6.47 (s, 2 H, Ar-H), 5.92 (q, 2 H, $J=1.4$ Hz, OCH_2O), 4.07 (d, 1 H, $J=15.9$ Hz, H-8), 3.74 (s, 3 H, OCH_3), 3.57-3.52 (m, 1 H, H-14), 3.45 (d, 1 H, $J=15.9$ Hz, H-8), 3.31-3.25 (m, 1 H, H-13), 3.12-2.98 (m, 2 H, H-6 & H-5), 2.92-2.83 (m, 1 H, H-5), 2.64-2.49 (m, 2 H, H-13 & H-6), 2.25 (s, 6 H, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 158.1, 150.5, 146.3, 146.1, 139.4, 139.3, 130.8, 129.7, 128.1, 127.9, 125.6, 123.6, 112.4, 111.3, 108.5, 105.6 (Ar-C), 100.9 (OCH_2O), 59.6 (C-14), 56.3 (OCH_3), 53.8 (C-8), 51.3 (C-6), 36.5 (C-13), 29.5 (C-5), 21.5 (CH_3); HRMS (ESI): m/z for $\text{C}_{27}\text{H}_{28}\text{NO}_4^+ [\text{M} + \text{H}]^+$ calcd. 430.2018, found 430.2014.



2f, pale yellow solid, m.p. 144-146 °C, yield 86%. ^1H NMR (300 MHz, CDCl_3): δ 7.24-7.22 (m, 2 H, Ar-H), 7.01 (d, 1 H, $J=8.4$ Hz, H-11), 6.86 (d, 1 H, $J=8.4$ Hz, H-12), 6.79-6.75 (m, 2 H, Ar-H), 6.73 (s, 1 H, H-1), 6.57 (s, 1 H, H-4),

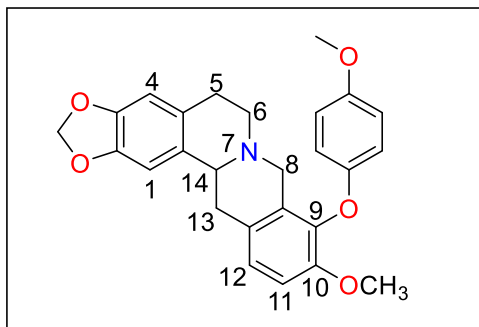
5.91 (q, 2 H, $J=1.4$ Hz, OCH_2O), 4.07 (d, 1 H, $J=15.9$ Hz, H-8), 3.74 (s, 3 H, OCH_3), 3.56-3.51 (m, 1 H, H-14), 3.43 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.23 (m, 1 H, H-13), 3.11-3.03 (m, 2 H, H-6 & H-5), 2.90-2.81 (m, 1 H, H-5), 2.63-2.47 (m, 2 H, H-13 & H-6), 1.29 (s, 9 H, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 155.8, 150.5, 146.3, 146.1,

144.3, 139.6, 130.8, 129.7, 128.2, 127.9, 126.4, 125.7, 114.1, 111.3, 108.5, 105.6 (Ar-C), 100.9 (OCH₂O), 59.7 (C-14), 56.3 (OCH₃), 53.8 (C-8), 51.3 (C-6), 36.5 (C-13), 34.2 (C(CH₃)₃), 31.7 (CH₃), 29.6 (C-5); HRMS (ESI): m/z for C₂₉H₃₂NO₄⁺ [M + H]⁺ calcd. 458.2331, found 458.2333.



2g, pale yellow solid, m.p. 169-171 °C, yield 58%. ¹H NMR (300 MHz, CDCl₃): δ 7.56-7.53 (m, 2 H, Ar-H), 7.50-7.47 (m, 2 H, Ar-H), 7.40-7.38 (m, 2 H, Ar-H), 7.32-7.29 (m, 1 H, Ar-H), 7.05 (d, 1 H, J =8.4 Hz, H-11), 6.93-6.88 (m, 3

H, H-12 & Ar-H), 6.74 (s, 1 H, H-1), 6.57 (s, 1 H, H-4), 5.92 (q, 2 H, J =1.4 Hz, OCH₂O), 4.10 (d, 1 H, J =15.9 Hz, H-8), 3.76 (s, 3 H, OCH₃), 3.57-3.53 (m, 1 H, H-14), 3.47 (d, 1 H, J =15.9 Hz, H-8), 3.32-3.26 (m, 1 H, H-13), 3.12-3.00 (m, 2 H, H-6 & H-5), 2.92-2.83 (m, 1 H, H-5), 2.65-2.50 (m, 2 H, H-13 & H-6); ¹³C {¹H} NMR (75 MHz, CDCl₃): δ 157.7, 150.4, 146.3, 146.1, 140.8, 139.2, 134.8, 130.8, 129.7, 128.8, 128.32, 128.26, 127.9, 126.89, 126.85, 125.9, 115.1, 111.3, 108.5, 105.6 (Ar-C), 100.9 (OCH₂O), 59.7 (C-14), 56.2 (OCH₃), 53.8 (C-8), 51.4 (C-6), 36.5 (C-13), 29.6 (C-5); HRMS (ESI): m/z for C₃₁H₂₈NO₄⁺ [M + H]⁺ calcd. 478.2018, found 478.2015.



2h, pale yellow solid, m.p. 136-138 °C, yield

86%. ^1H NMR (300 MHz, CDCl_3): δ 7.01 (d, 1 H, $J=8.4$ Hz, H-11), 6.86 (d, 1 H, $J=8.4$ Hz, H-12), 6.78 (s, 4 H, Ar-H), 6.73 (s, 1 H, H-1),

6.57 (s, 1 H, H-4), 5.91 (q, 2 H, $J=1.4$ Hz,

OCH_2O), 4.08 (d, 1 H, $J=15.9$ Hz, H-8), 3.76 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.56-

3.51 (m, 1 H, H-14), 3.42 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.23 (m, 1 H, H-13), 3.12-

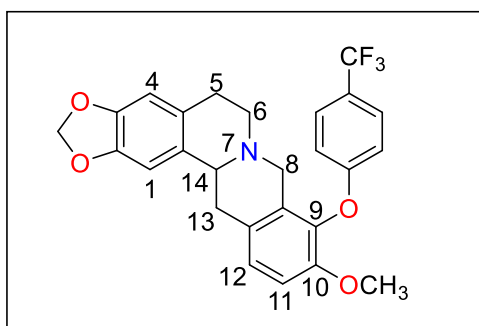
2.98 (m, 2 H, H-6 & H-5), 2.90-2.81 (m, 1 H, H-5), 2.63-2.48 (m, 2 H, H-13 & H-6);

$^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 154.4, 152.2, 150.5, 146.3, 146.1, 139.9, 130.8,

129.7, 128.2, 127.9, 125.6, 115.5, 114.7, 111.4, 108.6, 105.6 (Ar-C), 100.9 (OCH_2O),

59.7 (C-14), 56.3 (OCH_3), 55.8 (OCH_3), 53.9 (C-8), 51.3 (C-6), 36.5 (C-13), 29.6 (C-

5); HRMS (ESI): m/z for $\text{C}_{26}\text{H}_{26}\text{NO}_5^+$ $[\text{M} + \text{H}]^+$ calcd. 432.1811, found 432.1812.



2i, pale yellow solid, m.p. 161-163 °C, yield

92%. ^1H NMR (300 MHz, CDCl_3): δ 7.51 (d, 2 H, $J=8.5$ Hz, Ar-H), 7.06 (d, 1 H, $J=8.4$ Hz,

H-11), 6.93-6.87 (m, 3 H, H-12 & Ar-H), 6.73

(s, 1 H, H-1), 6.57 (s, 1 H, H-4), 5.91 (q, 2 H,

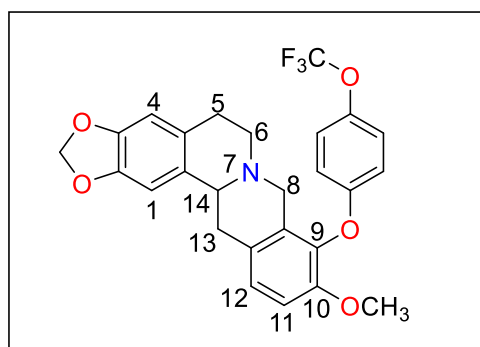
$J=1.4$ Hz, OCH_2O), 4.02 (d, 1 H, $J=15.9$ Hz, H-8), 3.73 (s, 3 H, OCH_3), 3.56-3.51 (m,

1 H, H-14), 3.42 (d, 1 H, $J=15.9$ Hz, H-8), 3.31-3.24 (m, 1 H, H-13), 3.12-3.02 (m, 2

H, H-6 & H-5), 2.90-2.82 (m, 1 H, H-5), 2.64-2.50 (m, 2 H, H-13 & H-6); $^{13}\text{C}\{^1\text{H}\}$

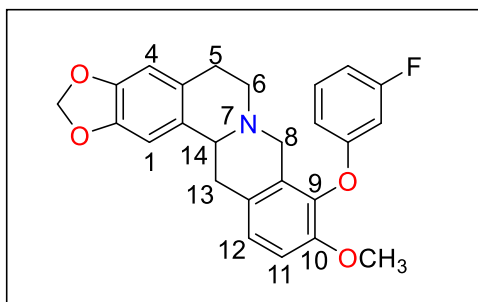
NMR (75 MHz, CDCl_3): δ 160.5, 150.0, 146.3, 146.1, 138.5, 130.6, 129.4, 128.4, 127.8,

127.1 (q, $J=3.7$ Hz), 126.4, 124.5 (q, $J=269.6$ Hz), 124.0 (q, $J=32.5$ Hz), 114.9, 111.2, 108.5, 105.6 (Ar-C & CF₃), 100.9 (OCH₂O), 59.6 (C-14), 56.1 (OCH₃), 53.7 (C-8), 51.3 (C-6), 36.5 (C-13), 29.5 (C-5); ¹⁹F NMR (282 MHz, CDCl₃): δ -61.5; HRMS (ESI): m/z for C₂₆H₂₃F₃NO₄⁺ [M + H]⁺ calcd. 470.1579, found 470.1592.



2j, pale yellow solid, m.p. 119-121 °C, yield 82%. ¹H NMR (300 MHz, CDCl₃): δ 7.11-7.02 (m, 3 H, H-11 & Ar-H), 6.88-6.82 (m, 3 H, H-12 & Ar-H), 6.73 (s, 1 H, H-1), 6.57 (s, 1 H, H-4), 5.91 (q, 2 H, $J=1.4$ Hz, OCH₂O), 4.03 (d, 1

H, $J=15.9$ Hz, H-8), 3.74 (s, 3 H, OCH₃), 3.56-3.51 (m, 1 H, H-14), 3.43 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.24 (m, 1 H, H-13), 3.10-2.99 (m, 2 H, H-6 & H-5), 2.90-2.81 (m, 1 H, H-5), 2.64-2.49 (m, 2 H, H-13 & H-6); ¹³C {¹H} NMR (75 MHz, CDCl₃): δ 156.4, 150.1, 146.3, 146.1, 143.5 (br-s, CF₃-O-C), 139.0, 130.6, 129.4, 128.3, 127.8, 126.1, 122.5 (br-s, CF₃-O-C-CH), 115.6, 111.2, 108.5, 105.5 (Ar-C, the CF₃ quartet was not resolved), 100.9 (OCH₂O), 59.6 (C-14), 56.0 (OCH₃), 53.7 (C-8), 51.3 (C-6), 36.4 (C-13), 29.5 (C-5); ¹⁹F NMR (282 MHz, CDCl₃): δ -58.2; HRMS (ESI): m/z for C₂₆H₂₃F₃NO₅⁺ [M + H]⁺ calcd. 486.1528, found 486.1531.



2k, pale yellow solid, m.p. 106-108 °C, yield

84%. ^1H NMR (300 MHz, CDCl_3): δ 7.23-7.16

(m, 1 H, Ar-H), 7.04 (d, 1 H, $J=8.4$ Hz, H-11),

6.87 (d, 1 H, $J=8.4$ Hz, H-12), 6.73-6.64 (m, 3

H, H-1 & Ar-H), 6.58-6.53 (m, 2 H, H-4 & Ar-H), 5.92 (q, 2 H, $J=1.4$ Hz, OCH_2O),

4.04 (d, 1 H, $J=15.9$ Hz, H-8), 3.75 (s, 3 H, OCH_3), 3.56-3.51 (m, 1 H, H-14), 3.42 (d,

1 H, $J=15.9$ Hz, H-8), 3.30-3.24 (m, 1 H, H-13), 3.12-2.99 (m, 2 H, H-6 & H-5), 2.90-

2.81 (m, 1 H, H-5), 2.64-2.48 (m, 2 H, H-13 & H-6); ^{13}C $\{^1\text{H}\}$ NMR (75 MHz, CDCl_3):

δ 163.7 (d, $J=243.9$ Hz), 159.3 (d, $J=10.7$ Hz), 150.1, 146.3, 146.1, 138.8, 130.6, 130.3

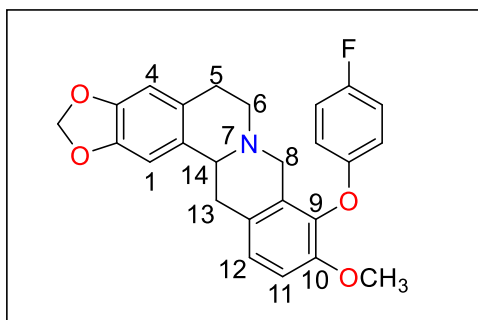
(d, $J=9.8$ Hz), 129.5, 128.3, 127.8, 126.1, 111.2, 110.6 (d, $J=2.8$ Hz), 108.6 (d, $J=21.2$

Hz), 108.5, 105.6, 102.7 (d, $J=25.2$ Hz) (Ar-C), 100.9 (OCH_2O), 59.6 (C-14), 56.1

(OCH_3), 53.7 (C-8), 51.3 (C-6), 36.4 (C-13), 29.5 (C-5); ^{19}F NMR (282 MHz, CDCl_3):

δ -111.7; HRMS (ESI): m/z for $\text{C}_{25}\text{H}_{23}\text{FNO}_4^+$ $[\text{M} + \text{H}]^+$ calcd. 420.1611, found

420.1608.



2l, pale yellow solid, m.p. 129-131 °C, yield

84%. ^1H NMR (300 MHz, CDCl_3): δ 7.02 (d,

1 H, $J=8.4$ Hz, H-11), 6.96-6.90 (m, 2 H, Ar-

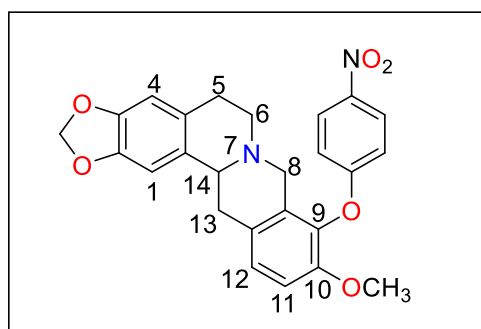
H), 6.86 (d, 1 H, $J=8.4$ Hz, H-12), 6.81 (m, 2

H, Ar-H), 6.73 (s, 1 H, H-1), 6.57 (s, 1 H, H-4),

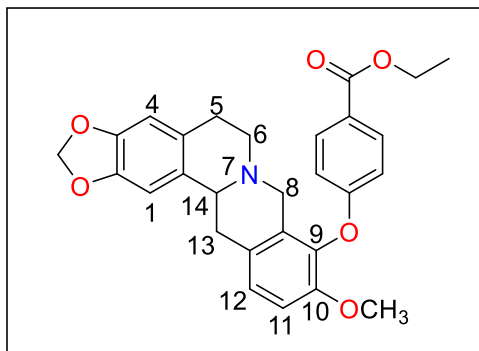
5.92 (q, 2 H, $J=1.4$ Hz, OCH_2O), 4.05 (d, 1 H, $J=15.9$ Hz, H-8), 3.73 (s, 3 H, OCH_3),

3.56-3.51 (m, 1 H, H-14), 3.42 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.23 (m, 1 H, H-13),

3.12-2.98 (m, 2 H, H-6 & H-5), 2.90-2.81 (m, 1 H, H-6), 2.64-2.48 (m, 2 H, H-13 & H-6); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 157.8 (d, $J=237.3$ Hz), 154.1 (d, $J=1.8$ Hz), 150.2, 146.3, 146.1, 139.4, 130.6, 129.5, 128.3, 127.8, 125.9, 115.9 (d, $J=31.3$ Hz), 115.7 (d, $J=8.0$ Hz), 111.3, 108.5, 105.6 (Ar-C), 100.9 (OCH_2O), 59.6 (C-14), 56.1 (OCH_3), 53.8 (C-8), 51.3 (C-6), 36.4 (C-13), 29.5 (C-5); ^{19}F NMR (282 MHz, CDCl_3): δ -123.1; HRMS (ESI): m/z for $\text{C}_{25}\text{H}_{23}\text{FNO}_4^+$ $[\text{M} + \text{H}]^+$ calcd. 420.1611, found 420.1615.

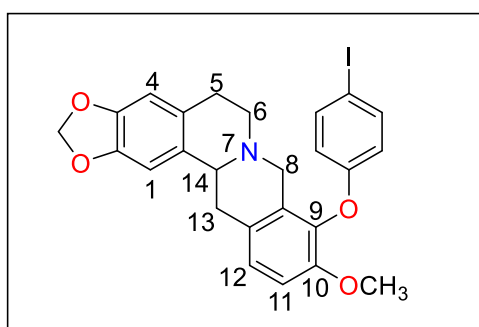


2m, brownish yellow solid, m.p. 182-184 °C, yield 80%. ^1H NMR (300 MHz, CDCl_3): δ 8.20-8.14 (m, 2 H, Ar-H), 7.08 (d, 1 H, $J=8.4$ Hz, H-11), 6.94-6.88 (m, 3 H, H-12 & Ar-H), 6.73 (s, 1 H, H-1), 6.57 (s, 1 H, H-4), 5.92 (q, 2 H, $J=1.4$ Hz, OCH_2O), 3.99 (d, 1 H, $J=15.8$ Hz, H-8), 3.73 (s, 3 H, OCH_3), 3.57-3.52 (m, 1 H, H-14), 3.43 (d, 1 H, $J=15.8$ Hz, H-8), 3.32-3.25 (m, 1 H, H-13), 3.12-2.98 (m, 2 H, H-6 & H-5), 2.91-2.82 (m, 1 H, H-5), 2.64-2.50 (m, 2 H, H-13 & H-6); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 163.0, 149.7, 146.4, 146.2, 142.5, 138.2, 130.5, 129.1, 128.5, 127.8, 126.8, 126.1, 115.1, 111.2, 108.6, 105.6 (Ar-C), 101.0 (OCH_2O), 59.6 (C-14), 56.1 (OCH_3), 53.6 (C-8), 51.4 (C-6), 36.4 (C-13), 29.5 (C-5); HRMS (ESI): m/z for $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_6^+$ $[\text{M} + \text{H}]^+$ calcd. 447.1556, found 447.1553.



2n, pale yellow solid, m.p. 124-126 °C, yield 87%. ^1H NMR (300 MHz, CDCl_3): δ 7.99-7.94 (m, 2 H, Ar-H), 7.05 (d, 1 H, $J=8.4$ Hz, H-11), 6.89-6.86 (m, 3 H, H-12 & Ar-H), 6.73 (s, 1 H, H-1), 6.56 (s, 1 H, H-4), 5.91 (q, 2 H, $J=1.4$ Hz,

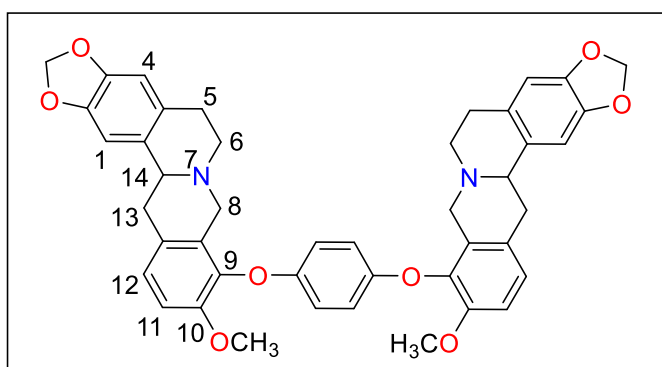
OCH_2O), 4.33 (q, 2 H, $J=7.1$ Hz, CH_2), 4.02 (d, 1 H, $J=15.9$ Hz, H-8), 3.72 (s, 3 H, OCH_3), 3.55-3.50 (m, 1 H, H-14), 3.41 (d, 1 H, $J=15.9$ Hz, H-8), 3.30-3.24 (m, 1 H, H-13), 3.11-2.98 (m, 2 H, H-6 & H-5), 2.90-2.81 (m, 1 H, H-5), 2.63-2.48 (m, 2 H, H-13 & H-6), 1.36 (t, 3 H, $J=7.1$ Hz, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 166.4 (CO), 161.7, 150.0, 146.3, 146.1, 138.6, 131.7, 130.6, 129.3, 128.3, 127.8, 126.2, 124.1, 114.6, 111.2, 108.5, 105.6 (Ar-C), 100.9 (OCH_2O), 60.8 (CH_2), 59.6 (C-14), 56.1 (OCH_3), 53.7 (C-8), 51.3 (C-6), 36.4 (C-13), 29.5 (C-5), 14.5 (CH_3); HRMS (ESI): m/z for $\text{C}_{28}\text{H}_{28}\text{NO}_6^+ [\text{M} + \text{H}]^+$ calcd. 474.1917, found 474.1919.



2o, pale yellow solid, m.p. 124-126 °C, yield 87%. ^1H NMR (500 MHz, CDCl_3): δ 7.53-7.50 (m, 2 H, Ar-H), 7.03 (d, 1 H, $J=8.4$ Hz, H-11), 6.86 (d, 1 H, $J=8.4$ Hz, H-12), 6.73 (s, 1 H, H-1), 6.64-6.61 (m, 2 H, Ar-H), 6.57 (s, 1 H, H-

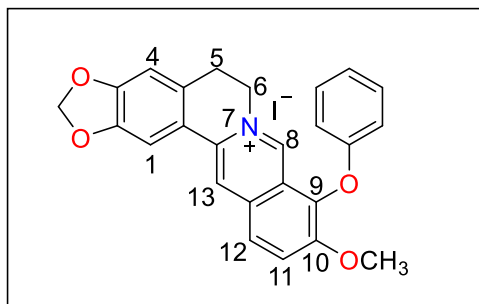
4), 5.92 (q, 2 H, $J=1.4$ Hz, OCH_2O), 4.02 (d, 1 H, $J=15.9$ Hz, H-8), 3.73 (s, 3 H, OCH_3), 3.55-3.52 (m, 1 H, H-14), 3.41 (d, 1 H, $J=15.9$ Hz, H-8), 3.29-3.25 (m, 1 H, H-13), 3.10-3.03 (m, 2 H, H-6 & H-5), 2.89-2.83 (m, 1 H, H-5), 2.63-2.51 (m, 2 H, H-13 & H-

6); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 158.0, 150.1, 146.3, 146.1, 138.8, 138.4, 130.6, 129.4, 128.3, 127.9, 126.1, 117.2, 111.2, 108.6, 105.6 (Ar-C), 100.9 (OCH_2O), 84.0 (Ar-C), 59.6 (C-14), 56.2 (OCH_3), 53.7 (C-8), 51.3 (C-6), 36.4 (C-13), 29.5 (C-5); HRMS (ESI): m/z for $\text{C}_{28}\text{H}_{28}\text{NO}_6^+ [\text{M} + \text{H}]^+$ calcd. 528.0672, found 528.0683.



4, brownish yellow solid, m.p.: 293-295 °C, yield 60%. ^1H NMR (300 MHz, CDCl_3): δ 6.99 (d, 2 H, $J=8.4$ Hz, H-11), 6.88-6.77 (m, 3 H, H-12 & Ar-

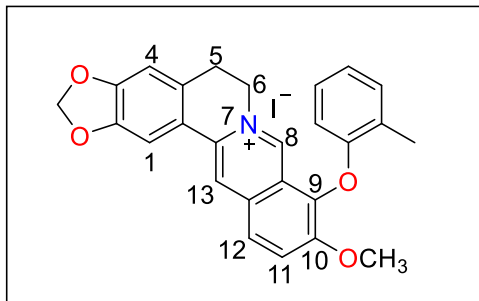
H), 6.73-6.72 (m, 5 H, Ar-H), 6.58 (d, 2 H, $J=6.5$ Hz, Ar-H), 5.91 (br-s, 4 H, OCH_2O), 4.24, 4.07 (m, 2 H, 1:3, H-8), 3.85, 3.74 (s, 6 H, 1:3, OCH_3), 3.55-3.51 (m, 2 H, H-14), 3.45-3.39 (m, 2 H, H-8), 3.28-3.17 (m, 2 H, H-13), 3.12-3.03 (m, 4 H, H-6 & H-5), 2.88-2.77 (m, 2 H, H-5), 2.68-2.49 (m, 4 H, H-13 & H-6); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 152.73, 152.70, 150.5, 146.3, 146.1, 139.9, 139.8, 130.8, 129.6, 128.2, 127.9, 125.7, 115.6, 111.3, 108.5, 105.6 (Ar-C), 100.9 (OCH_2O), 59.6 (C-14), 56.2 (OCH_3), 53.9 (C-8), 51.4 (C-6), 36.5 (C-13), 29.6 (C-5); HRMS (ESI): m/z for $\text{C}_{44}\text{H}_{41}\text{N}_2\text{O}_8^+ [\text{M} + \text{H}]^+$ calcd. 725.2863, found 725.2861.



3a, yellow solid, m.p.: 242-244 °C, yield 97%.

^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 9.81 (s, 1 H, H-8), 9.06 (s, 1 H, H-13), 8.31 (d, 1 H, $J=9.2$ Hz, H-12), 8.20 (d, 1 H, $J=9.2$ Hz, H-11), 7.83

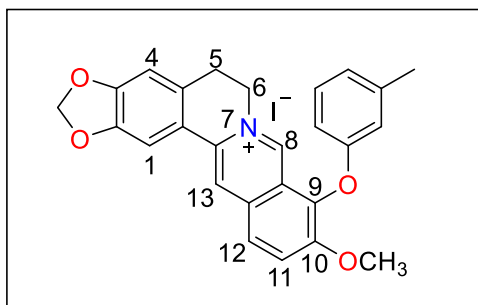
(s, 1 H, H-1), 7.38-7.33 (m, 2 H, Ar-H), 7.13-7.08 (m, 2 H, H-4 & Ar-H), 6.97-6.94 (m, 2 H, Ar-H), 6.18 (s, 2 H, OCH_2O), 4.91 (t, 2 H, $J=6.0$ Hz, H-6), 3.92 (s, 3 H, OCH_3), 3.18 (t, 2 H, $J=6.0$ Hz, H-5); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $\text{DMSO-}d_6$): δ 157.7, 150.8, 150.0, 147.7, 144.6, 138.1, 137.0, 133.4, 130.9, 129.7, 126.7, 125.8, 122.8, 122.0, 120.6, 120.4, 115.5, 108.4, 105.5 (Ar-C), 102.1 (OCH_2O), 57.0 (OCH_3), 55.3 (C-6), 26.2 (C-5); HRMS (ESI): m/z for $\text{C}_{25}\text{H}_{20}\text{NO}_4^+$ [$\text{M} - \text{I}$] $^+$ calcd. 398.1387, found 398.1392.



3b, yellow solid, m.p. 252-254 °C, yield 84%.

^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 9.78 (s, 1 H, H-8), 9.07 (s, 1 H, H-13), 8.30 (d, 1 H, $J=9.2$ Hz, H-12), 8.20 (d, 1 H, $J=9.2$ Hz, H-11), 7.82

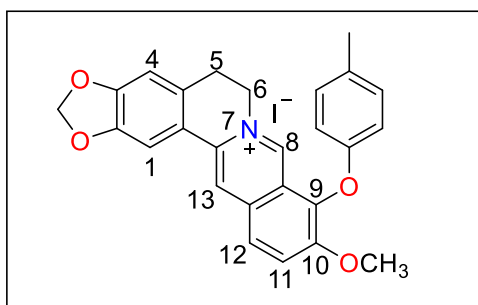
(s, 1 H, H-1), 7.35-7.32 (m, 1 H, Ar-H), 7.08 (s, 1 H, H-4), 7.07-6.97 (m, 2 H, Ar-H), 6.44-6.41 (m, 1 H, Ar-H), 6.18 (s, 2 H, OCH_2O), 4.93 (t, 2 H, $J=6.0$ Hz, H-6), 3.89 (s, 3 H, OCH_3), 3.20 (t, 2 H, $J=6.0$ Hz, H-5), 2.50 (s, 3 H, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $\text{DMSO-}d_6$): δ 156.0, 150.6, 149.9, 147.7, 144.6, 138.0, 137.6, 133.3, 131.1, 130.8, 126.9, 126.7, 126.3, 125.5, 122.6, 122.0, 120.6, 120.4, 113.2, 108.4, 105.5 (Ar-C), 102.1 (OCH_2O), 57.1 (OCH_3), 55.3 (C-6), 26.2 (C-5), 16.2 (CH_3); HRMS (ESI): m/z for $\text{C}_{26}\text{H}_{22}\text{NO}_4^+$ [$\text{M} - \text{I}$] $^+$ calcd. 412.1543, found 412.1550.



3c, yellow solid, m.p. 239-241 °C, yield 93%.

^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 9.77 (s, 1 H, H-8), 9.07 (s, 1 H, H-13), 8.31 (d, 1 H, $J=9.2$ Hz, H-12), 8.21 (d, 1 H, $J=9.2$ Hz, H-11), 7.82

(s, 1 H, H-1), 7.21 (t, 1 H, $J=15.8$ Hz, Ar-H), 7.08 (s, 1 H, H-4), 6.91 (d, 1 H, $J=7.5$ Hz, Ar-H), 6.80 (s, 1 H, Ar-H), 6.70 (dd, 1 H, $J=2.5$ Hz, $J=8.2$ Hz, Ar-H), 6.18 (s, 2 H, OCH_2O), 4.92 (t, 2 H, $J=6.0$ Hz, H-6), 3.92 (s, 3 H, OCH_3), 3.19 (t, 2 H, $J=6.0$ Hz, H-5), 2.27 (s, 3 H, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $\text{DMSO}-d_6$): δ 157.7, 150.9, 149.9, 147.7, 144.6, 139.4, 138.1, 137.0, 133.4, 130.9, 129.4, 126.7, 125.8, 123.5, 122.0, 120.7, 120.4, 116.0, 112.4, 108.4, 105.5 (Ar-C), 102.2 (OCH_2O), 57.0 (OCH_3), 55.3 (C-6), 26.2 (C-5), 21.0 (CH_3); HRMS (ESI): m/z for $\text{C}_{26}\text{H}_{22}\text{NO}_4^+ [\text{M} - \text{I}]^+$ calcd. 412.1543, found 412.1548.



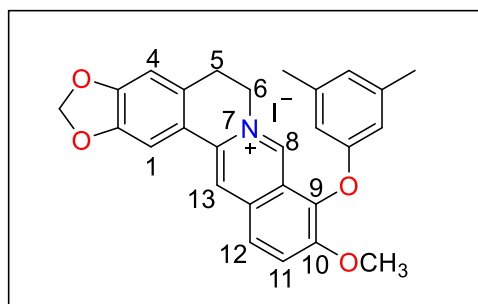
3d, yellow solid, m.p. 257-259 °C, yield 98%.

^1H NMR (500 MHz, $\text{DMSO}-d_6$): δ 9.77 (s, 1 H, H-8), 9.05 (s, 1 H, H-13), 8.30 (d, 1 H, $J=9.2$ Hz, H-12), 8.19 (d, 1 H, $J=9.2$ Hz, H-11), 7.83 (s, 1 H, H-1), 7.14 (d, 2 H, $J=8.4$ Hz, Ar-H),

7.08 (s, 1 H, H-4), 6.84 (d, 2 H, $J=8.6$ Hz, Ar-H), 6.18 (s, 2 H, OCH_2O), 4.91 (t, 2 H, $J=6.0$ Hz, H-6), 3.92 (s, 3 H, OCH_3), 3.18 (t, 2 H, $J=6.0$ Hz, H-5), 2.27 (s, 3 H, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, $\text{DMSO}-d_6$): δ 155.7, 150.9, 149.9, 147.7, 144.6, 138.1, 137.3, 133.4, 131.7, 130.9, 130.0, 126.7, 125.7, 122.0, 120.6, 120.4, 115.3, 108.4, 105.5 (Ar-

C), 102.1 (OCH₂O), 57.0 (OCH₃), 55.3 (C-6), 26.2 (C-5), 20.1 (CH₃); HRMS (ESI):

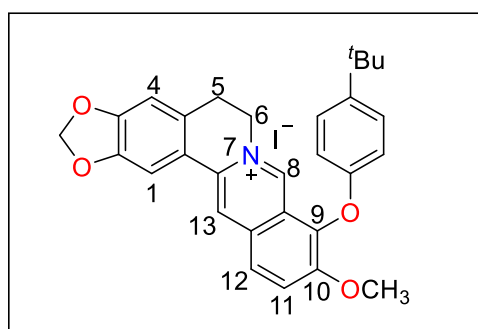
m/z for C₂₆H₂₂NO₄⁺ [M - I]⁺ calcd. 412.1543, found 412.1550.



3e, yellow solid, m.p. 251-253 °C, yield 99%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.74 (s, 1 H, H-8), 9.06 (s, 1 H, H-13), 8.31 (d, 1 H, *J*=9.2 Hz, H-12), 8.20 (d, 1 H, *J*=9.2 Hz, H-11), 7.82

(s, 1 H, H-1), 7.08 (s, 1 H, H-4), 6.73 (s, 1 H, Ar-H), 6.54 (s, 2 H, Ar-H), 6.18 (s, 2 H, OCH₂O), 4.91 (t, 2 H, *J*=6.0 Hz, H-6), 3.93 (s, 3 H, OCH₃), 3.18 (t, 2 H, *J*=6.0 Hz, H-5), 2.21 (s, 6 H, CH₃); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆): δ 157.8, 150.9, 149.9, 147.7, 144.6, 139.0, 138.1, 137.0, 133.4, 130.9, 126.8, 125.7, 124.4, 122.1, 120.7, 120.4, 112.9, 108.4, 105.5 (Ar-C), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5), 20.9 (CH₃); HRMS (ESI): m/z for C₂₇H₂₄NO₄⁺ [M - I]⁺ calcd. 426.1700, found 426.1708.

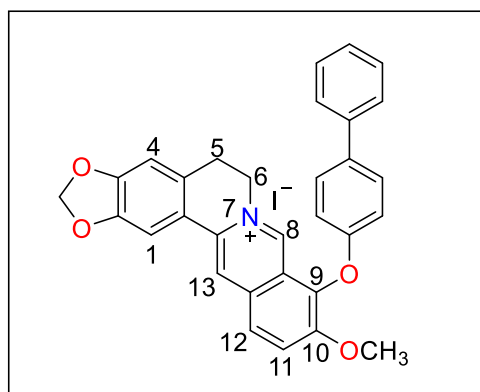


3f, yellow solid, m.p. 236-238 °C, yield 98%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.77 (s, 1 H, H-8), 9.06 (s, 1 H, H-13), 8.31 (d, 1 H, *J*=9.2 Hz, H-12), 8.21 (d, 1 H, *J*=9.2 Hz, H-11), 7.82 (s, 1 H, H-1), 7.35 (d, 2 H, *J*=8.7 Hz, Ar-H),

7.07 (s, 1 H, H-4), 6.86 (d, 2 H, *J*=8.7 Hz, Ar-H), 6.18 (s, 2 H, OCH₂O), 4.91 (t, 2 H, *J*=6.0 Hz, H-6), 3.94 (s, 3 H, OCH₃), 3.18 (t, 2 H, *J*=6.0 Hz, H-5), 1.26 (s, 9 H, CH₃); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆): δ 155.5, 151.0, 149.9, 147.7, 145.0, 144.6, 138.1,

137.0, 133.4, 130.9, 126.6, 126.4, 125.8, 122.1, 120.7, 120.4, 114.8, 108.4, 105.5 (Ar-C), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 34.0 (C(CH₃)₃), 31.3 (CH₃), 26.2 (C-5); HRMS (ESI): m/z for C₂₉H₂₈NO₄⁺ [M - I]⁺ calcd. 454.2013, found 454.2020.

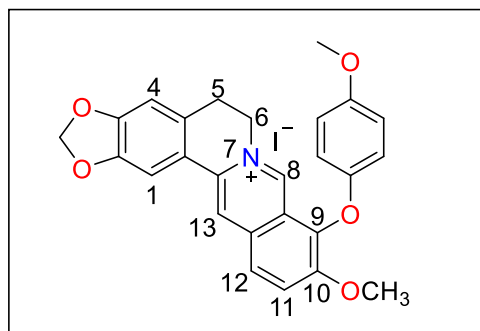


3g, yellow solid, m.p. 222-224 °C, yield 95%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.83 (s, 1 H, H-8), 9.08 (s, 1 H, H-13), 8.34 (d, 1 H, *J*=9.2 Hz, H-12), 8.23 (d, 1 H, *J*=9.2 Hz, H-11), 7.83 (s, 1 H, H-1), 7.63 (t, 4 H, *J*=14.7 Hz, Ar-H),

7.45 (t, 2 H, *J*=7.5 Hz, Ar-H), 7.34 (t, 1 H,

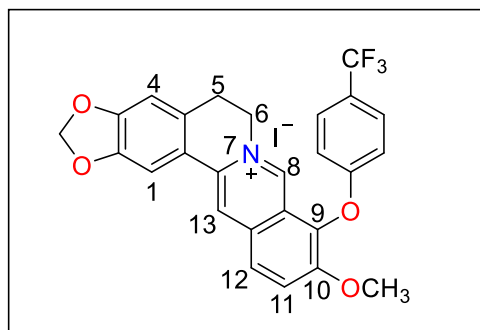
J=7.3 Hz, Ar-H), 7.05 (t, 3 H, *J*=8.7 Hz, H-4 & Ar-H), 6.18 (s, 2 H, OCH₂O), 4.93 (t, 2 H, *J*=6.0 Hz, H-6), 3.96 (s, 3 H, OCH₃), 3.19 (t, 2 H, *J*=6.0 Hz, H-5); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆): δ 157.3, 150.9, 150.0, 147.7, 144.6, 139.5, 138.2, 136.8, 134.9, 133.4, 130.9, 129.0, 128.0, 127.1, 126.6, 126.4, 126.0, 122.0, 120.7, 120.4, 115.9, 108.4, 105.5 (Ar-C), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5); HRMS (ESI): m/z for C₃₁H₂₄NO₄⁺ [M - I]⁺ calcd. 474.1700, found 474.1708.



3h, yellow solid, m.p. 226-228 °C, yield 95%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.80 (s, 1 H, H-8), 9.05 (s, 1 H, H-13), 8.30 (d, 1 H, *J*=9.2 Hz, H-12), 8.18 (d, 1 H, *J*=9.2 Hz, H-11), 7.82 (s, 1 H, H-1), 7.08 (s, 1 H, H-4), 6.90 (s, 4 H,

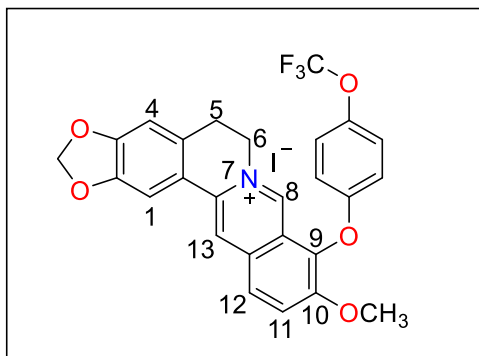
Ar-H), 6.18 (s, 2 H, OCH₂O), 4.92 (t, 2 H, *J*=6.0 Hz, H-6), 3.91 (s, 3 H, OCH₃), 3.72 (s, 3 H, OCH₃), 3.19 (t, 2 H, *J*=6.0 Hz, H-5); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆): δ 154.9, 151.8, 150.9, 149.9, 147.7, 144.7, 138.1, 137.8, 133.3, 130.9, 126.8, 125.5, 122.1, 120.6, 120.4, 116.5, 114.6, 108.4, 105.5 (Ar-C), 102.2 (OCH₂O), 57.0 (OCH₃), 55.5 (OCH₃), 55.3 (C-6), 26.2 (C-5); HRMS (ESI): *m/z* for C₂₆H₂₂NO₅⁺ [M - I]⁺ calcd. 428.1492, found 428.1495.



3i, yellow solid, m.p. 273-275 °C, yield 96%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.83 (s, 1 H, H-8), 9.09 (s, 1 H, H-13), 8.35 (d, 1 H, *J*=9.2 Hz, H-12), 8.25 (d, 1 H, *J*=9.2 Hz, H-11), 7.82 (s, 1 H, H-1), 7.73 (d, 2 H, *J*=8.6 Hz, Ar-H),

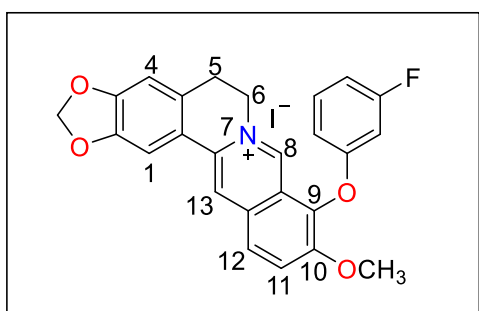
7.16 (d, 2 H, *J*=8.46 Hz, Ar-H), 7.08 (s, 1 H, H-4), 6.18 (s, 2 H, OCH₂O), 4.91 (t, 2 H, *J*=6.0 Hz, H-6), 3.95 (s, 3 H, OCH₃), 3.19 (t, 2 H, *J*=6.0 Hz, H-5); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆): δ 160.1, 150.7, 150.0, 147.7, 144.6, 138.2, 135.8, 133.4, 130.9, 127.2 (q, *J*=3.5 Hz), 126.5, 126.4, 124.3 (q, *J*=269.9 Hz), 123.4 (q, *J*=31.8 Hz), 121.6, 120.7, 120.3, 116.2, 108.4, 105.5 (Ar-C & CF₃), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5); ¹⁹F NMR (282 MHz, CDCl₃): δ -60.1; HRMS (ESI): *m/z* for C₂₆H₁₉F₃NO₄⁺ [M - I]⁺ calcd. 466.1261, found 466.1273.



3j, yellow solid, m.p. 246-248 °C, yield 98%.

^1H NMR (300 MHz, DMSO- d_6): δ 9.84 (s, 1 H, H-8), 9.07 (s, 1 H, H-13), 8.33 (d, 1 H, $J=9.2$ Hz, H-12), 8.23 (d, 1 H, $J=9.2$ Hz, H-11), 7.83 (s, 1 H, H-1), 7.37 (d, 2 H, $J=8.0$ Hz, Ar-H),

7.07 (d, 3 H, $J=8.0$ Hz, Ar-H), 6.18 (s, 2 H, OCH₂O), 4.91 (t, 2 H, $J=6.0$ Hz, H-6), 3.94 (s, 3 H, OCH₃), 3.19 (t, 2 H, $J=6.0$ Hz, H-5); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, DMSO- d_6): δ 156.2, 150.7, 150.0, 147.7, 144.6, 143.3 (d, $J=1.4$ Hz), 138.2, 136.5, 133.4, 130.8, 126.6, 126.2, 122.7 (br-s, CF₃-O-C-CH), 121.8, 120.6, 120.3, 120.1 (q, $J=254.0$ Hz), 117.0, 108.4, 105.5 (Ar-C & CF₃), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5); ^{19}F NMR (282 MHz, CDCl₃): δ -57.2; HRMS (ESI): m/z for C₂₆H₁₉F₃NO₅⁺ [M - I]⁺ calcd. 482.1210, found 482.1224.

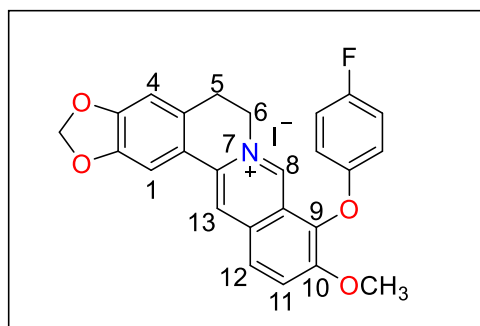


3k, yellow solid, m.p. 221-223 °C, yield 99%.

^1H NMR (300 MHz, DMSO- d_6): δ 9.81 (s, 1 H, H-8), 9.07 (s, 1 H, H-13), 8.32 (d, 1 H, $J=9.2$ Hz, H-12), 8.23 (d, 1 H, $J=9.2$ Hz, H-11), 7.83

(s, 1 H, H-1), 7.43-7.35 (m, 1 H, Ar-H), 7.09 (s, 1 H, H-4), 7.00-6.92 (m, 1 H, Ar-H), 6.87-6.80 (m, 2 H, Ar-H), 6.18 (s, 2 H, OCH₂O), 4.91 (t, 2 H, $J=6.0$ Hz, H-6), 3.95 (s, 3 H, OCH₃), 3.19 (t, 2 H, $J=6.0$ Hz, H-5); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, DMSO- d_6): δ 162.8 (d, $J=242.7$ Hz), 158.8 (d, $J=10.8$ Hz), 150.7, 150.0, 147.7, 144.4, 138.1, 136.3, 133.4, 131.0 (d, $J=9.9$ Hz), 130.8, 126.6, 126.2, 121.8, 120.6, 120.3, 111.8 (d, $J=2.1$ Hz), 109.7

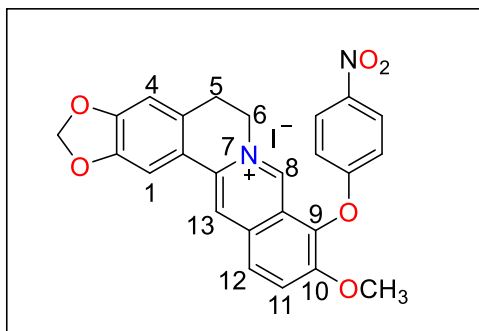
(d, $J=21.2$ Hz), 108.4, 105.5, 103.6 (d, $J=25.4$ Hz) (Ar-C), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5); ¹⁹F NMR (282 MHz, CDCl₃): δ -111.4; HRMS (ESI): m/z for C₂₅H₁₉FNO₄⁺ [M - I]⁺ calcd. 416.1293, found 416.1296.



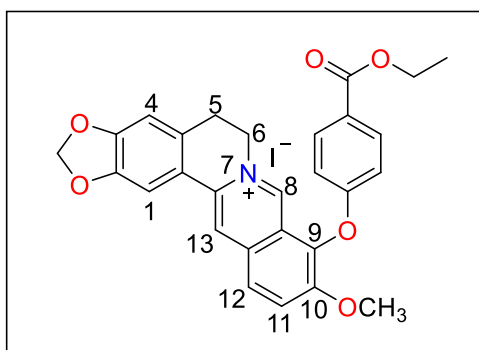
3l, yellow solid, m.p. 232-234 °C, yield 97%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.83 (s, 1 H, H-8), 9.06 (s, 1 H, H-13), 8.31 (d, 1 H, $J=9.2$ Hz, H-12), 8.20 (d, 1 H, $J=9.2$ Hz, H-11), 7.83 (s, 1 H, H-1), 7.19 (t, 2 H, $J=8.9$ Hz, Ar-H),

7.09 (s, 1 H, H-4), 7.02-6.98 (m, 2 H, Ar-H), 6.18 (s, 2 H, OCH₂O), 4.92 (br-s, 2 H, H-6), 3.92 (s, 3 H, OCH₃), 3.19 (br-s, 2 H, H-5); ¹³C{¹H} NMR (75 MHz, DMSO-*d*₆): δ 157.7 (d, $J=237.5$ Hz), 153.9 (d, $J=1.8$ Hz), 150.7, 150.0, 147.7, 144.6, 138.1, 137.2, 133.4, 130.8, 126.7, 125.9, 121.9, 120.6, 120.4, 117.1 (d, $J=8.3$ Hz), 116.1 (d, $J=23.5$ Hz), 108.4, 105.5 (Ar-C), 102.2 (OCH₂O), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5); ¹⁹F NMR (282 MHz, CDCl₃): δ -121.2; HRMS (ESI): m/z for C₂₅H₁₉FNO₄⁺ [M - I]⁺ calcd. 416.1293, found 416.1298.

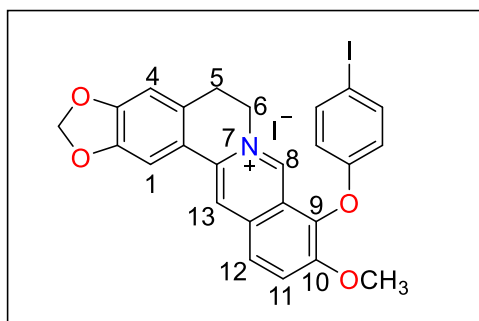


3m, brownish yellow solid, m.p. 245-247 °C, yield 80%. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 9.87 (s, 1 H, H-8), 9.10 (s, 1 H, H-13), 8.37 (d, 1 H, $J=9.2$ Hz, H-12), 8.29-8.24 (m, 3 H, H-11 & Ar-H), 7.83 (s, 1 H, H-1), 7.23-7.17 (m, 2 H, Ar-H), 7.09 (s, 1 H, H-4), 6.18 (s, 2 H, OCH_2O), 4.90 (t, 2 H, $J=6.0$ Hz, H-6), 3.96 (s, 3 H, OCH_3), 3.19 (t, 2 H, $J=6.0$ Hz, H-5); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $\text{DMSO}-d_6$): δ 162.1, 150.5, 150.0, 147.7, 144.4, 142.6, 138.3, 135.4, 133.4, 130.9, 126.7, 126.5, 125.9, 121.4, 120.7, 120.3, 116.4, 108.4, 105.5 (Ar-C), 102.2 (OCH_2O), 57.2 (OCH_3), 55.3 (C-6), 26.2 (C-5); HRMS (ESI): m/z for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}_6^+ [\text{M} - \text{I}]^+$ calcd. 443.1238, found 443.1247.



3n, yellow solid, m.p. 258-260 °C, yield 75%. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 9.84 (s, 1 H, H-8), 9.08 (s, 1 H, H-13), 8.34 (d, 1 H, $J=9.2$ Hz, H-12), 8.24 (d, 1 H, $J=9.2$ Hz, H-11), 7.96 (d, 2 H, $J=8.7$ Hz, Ar-H), 7.83 (s, 1 H, H-1), 7.08 (s, 2 H, Ar-H), 7.06 (s, 1 H, H-4), 6.18 (s, 2 H, OCH_2O), 4.90 (br-s, 2 H, H-6), 4.30 (q, 2 H, $J=6.9$ Hz, CH_2), 3.93 (s, 3 H, OCH_3), 3.19 (br-s, 2 H, H-5), 1.30 (t, 3 H, $J=6.9$ Hz, CH_3); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $\text{DMSO}-d_6$): δ 165.1 (CO), 161.0, 150.6, 150.0, 147.7, 144.5, 138.3, 136.1, 133.4, 131.3, 130.9, 126.6, 126.3, 124.5, 121.6, 120.7, 120.3, 115.7, 108.4, 105.5 (Ar-C), 102.2 (OCH_2O), 60.6 (CH_2), 57.1 (OCH_3), 55.3 (C-6), 26.2

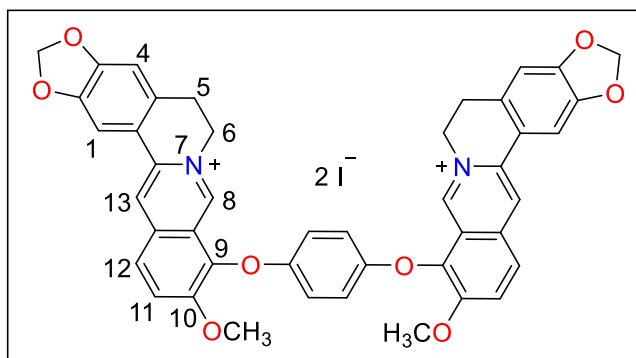
(C-5), 14.2 (CH₃); HRMS (ESI): m/z for C₂₈H₂₄NO₆⁺ [M - I]⁺ calcd. 470.1598, found 470.1605.



30, yellow solid, m.p. 251-253 °C, yield 81%.

¹H NMR (300 MHz, DMSO-*d*₆): δ 9.79 (s, 1 H, H-8), 9.06 (s, 1 H, H-13), 8.31 (d, 1 H, *J*=9.2 Hz, H-12), 8.21 (d, 1 H, *J*=9.2 Hz, H-11), 7.82 (s, 1 H, H-1), 7.66 (d, 2 H, *J*=8.9 Hz, Ar-H),

7.08 (s, 1 H, H-4), 6.80 (d, 2 H, *J*=8.9 Hz, Ar-H), 6.18 (s, 2 H, OCH₂O), 4.90 (br-s, 2 H, Hz, H-6), 3.93 (s, 3 H, OCH₃), 3.18 (br-s, 2 H, *J*=6.0 Hz, H-5); ¹³C {¹H} NMR (75 MHz, DMSO-*d*₆): δ 157.6, 150.7, 150.0, 147.7, 144.6, 138.23, 138.18, 136.4, 133.4, 130.9, 126.6, 126.1, 121.8, 120.7, 120.4, 118.2, 108.5, 105.5 (Ar-C), 102.2 (OCH₂O), 86.2 (Ar-C), 57.1 (OCH₃), 55.3 (C-6), 26.2 (C-5); HRMS (ESI): m/z for C₂₅H₁₉INO₄⁺ [M - I]⁺ calcd. 524.0353, found 524.0361.

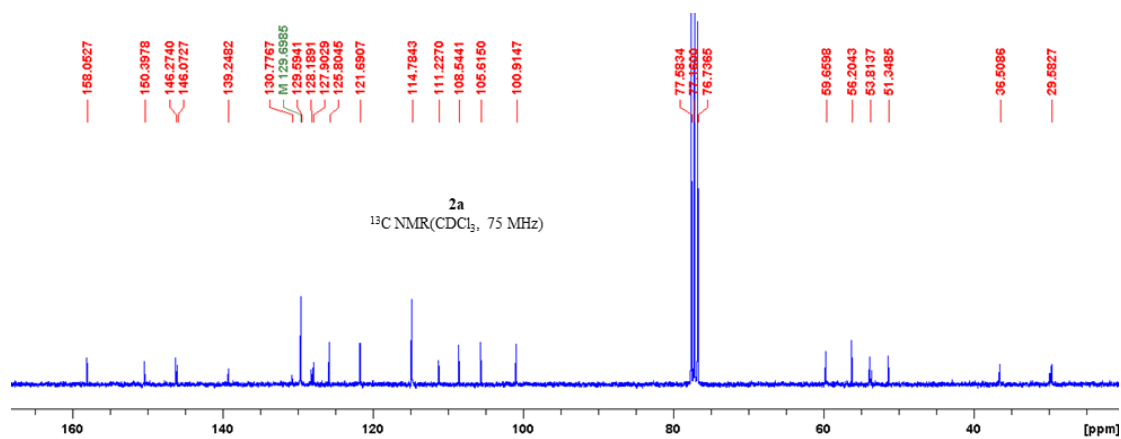
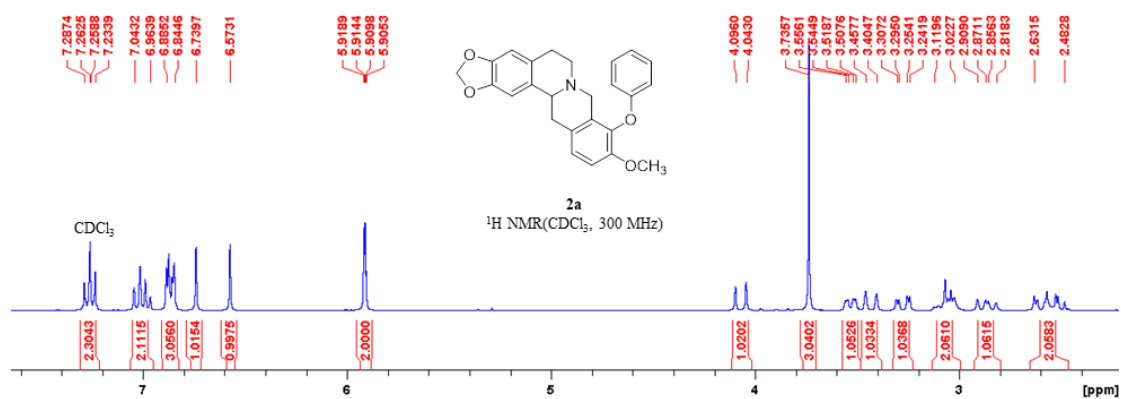


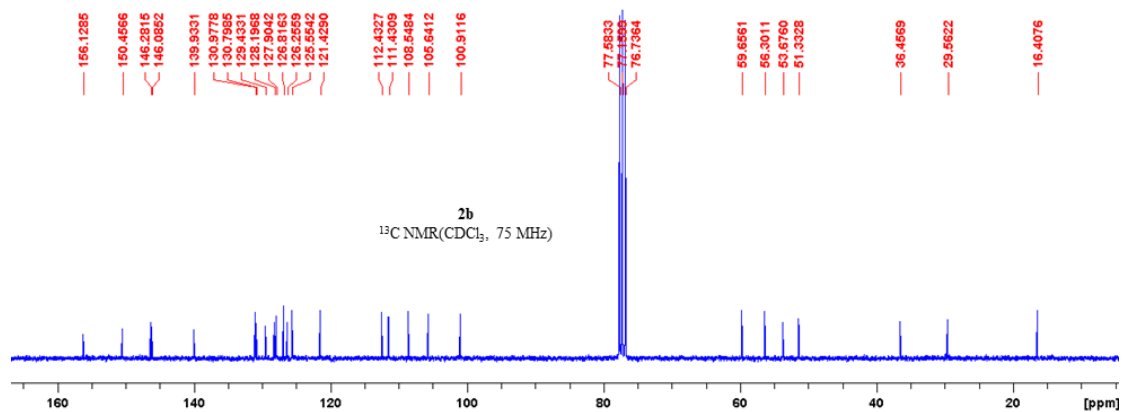
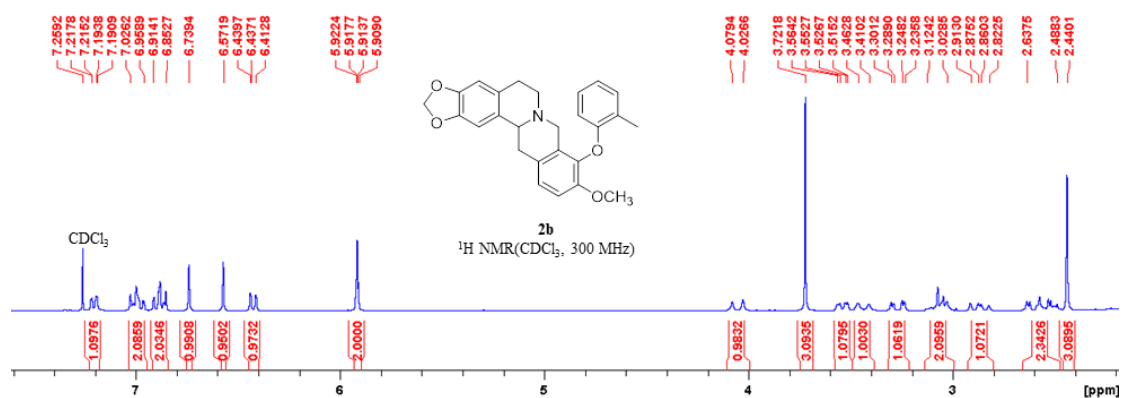
5, yellow solid, m.p. > 300 °C, yield 68%. ¹H NMR (300 MHz, DMSO-*d*₆): δ 9.85 (s, 2 H, H-8), 9.06 (s, 2 H, H-13), 8.31 (d, 2 H, *J*=9.2 Hz, H-12), 8.22 (d, 2 H,

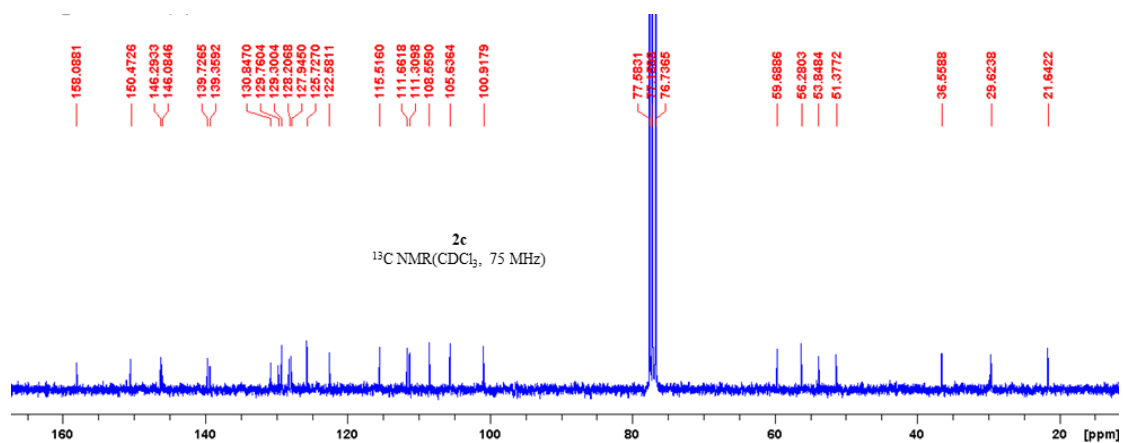
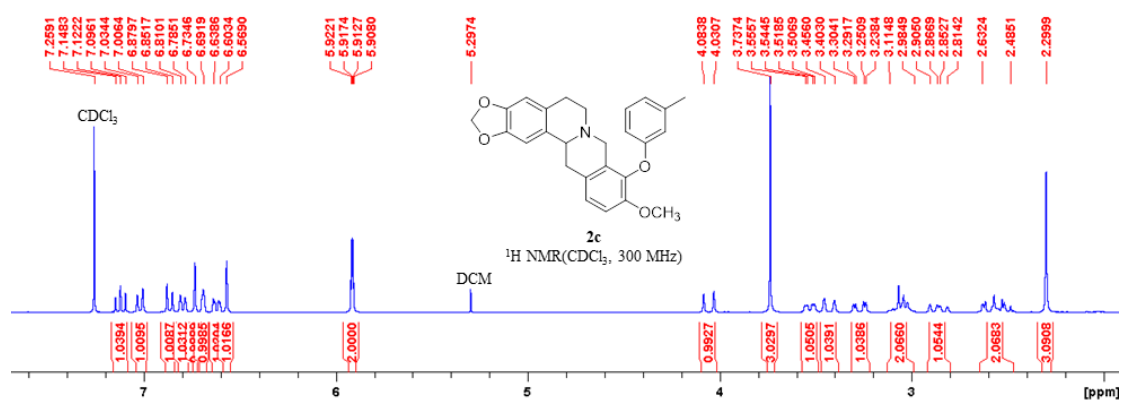
J=9.2 Hz, H-11), 7.83 (s, 2 H, H-1), 7.10 (s, 2 H, H-4), 6.95 (s, 4 H, Ar-H), 6.18 (s, 4 H, OCH₂O), 4.92 (br-s, 4 H, H-6), 3.93 (s, 6 H, OCH₃), 3.19 (br-s, 4 H, H-5); Due to

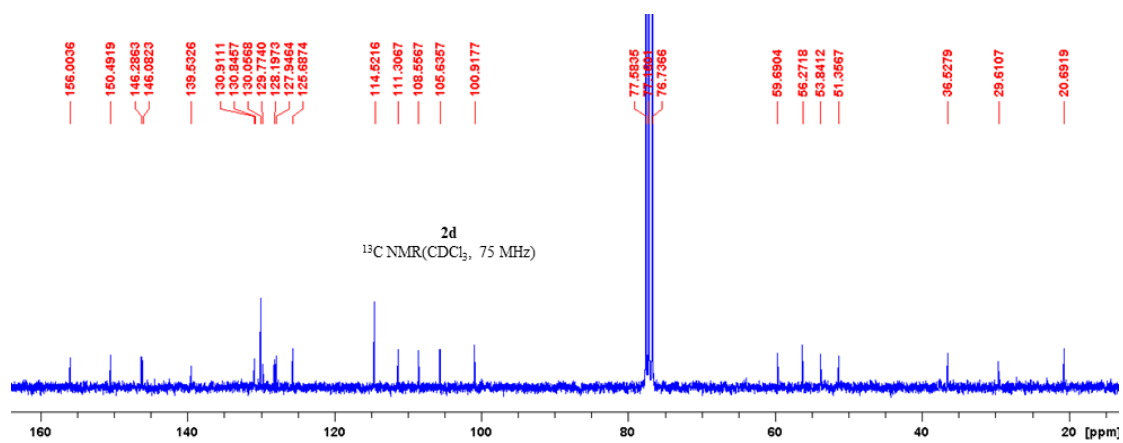
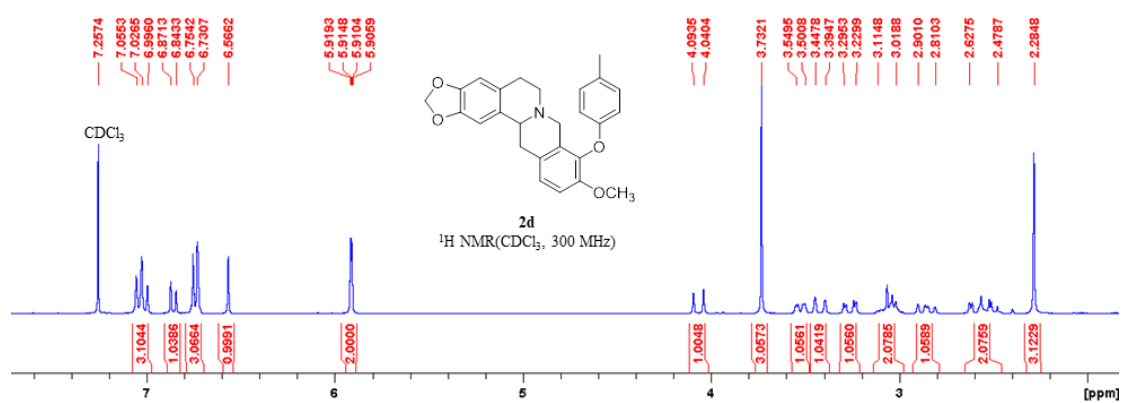
the poor solubility, the ^{13}C spectrum only showed few signals even with long acquisition time. HRMS (ESI): m/z for $\text{C}_{44}\text{H}_{34}\text{N}_2\text{O}_8^{2+} [\text{M} - 2\text{I}]^{2+}$ calcd. 359.1152, found 359.1159.

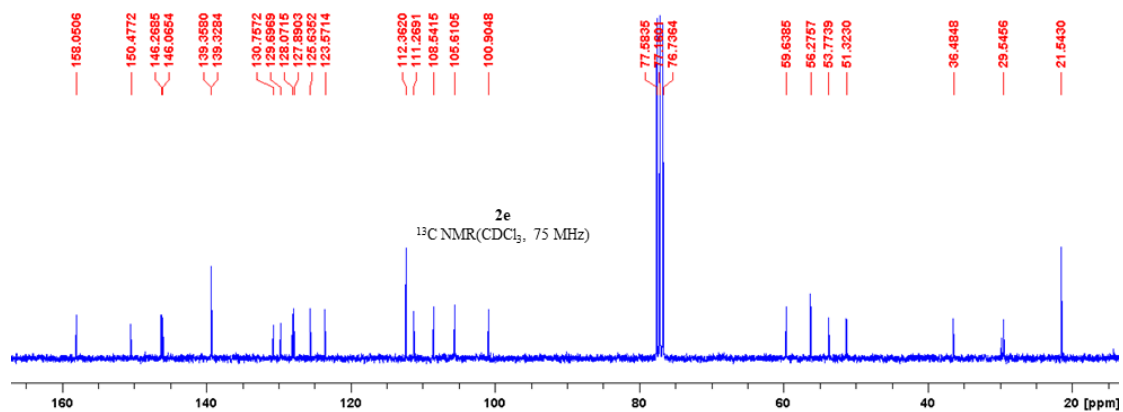
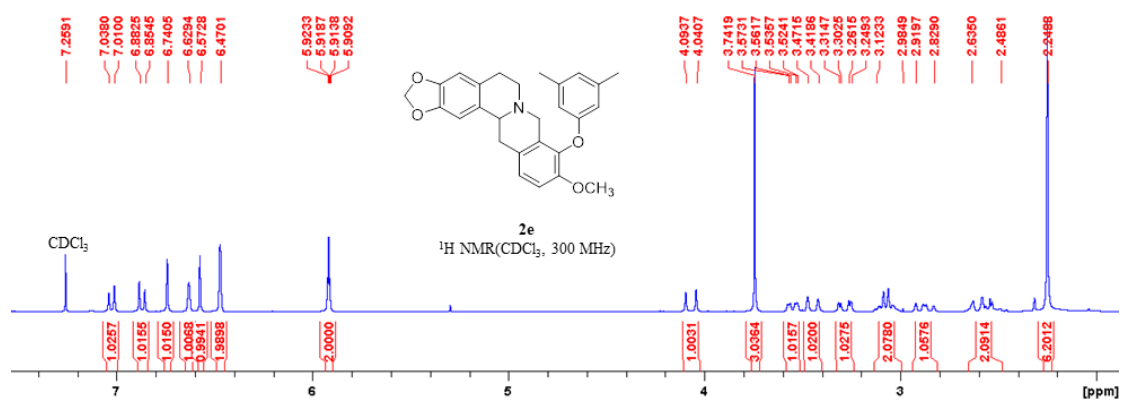
NMR spectra

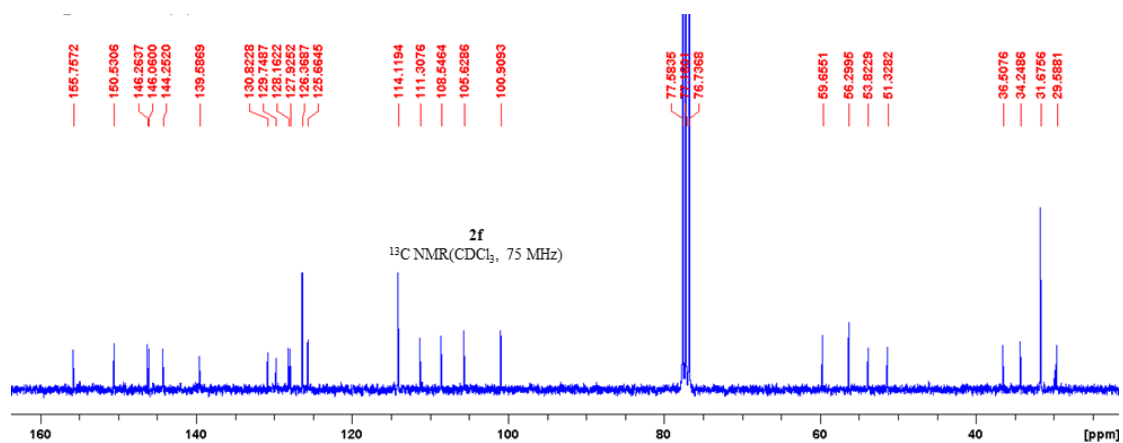
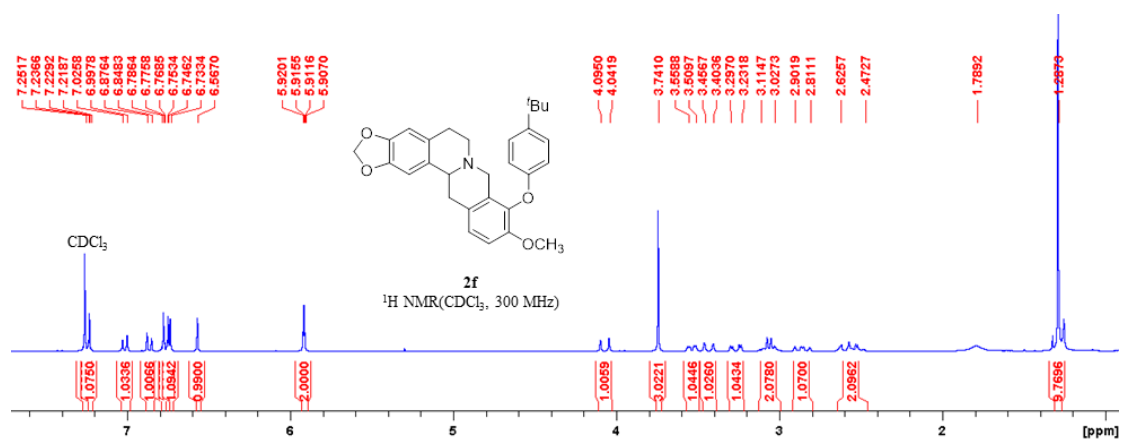


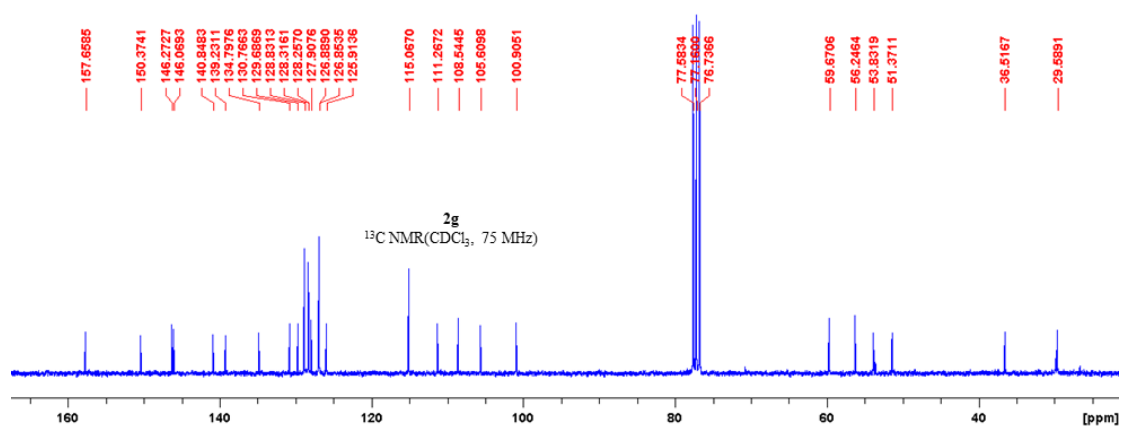
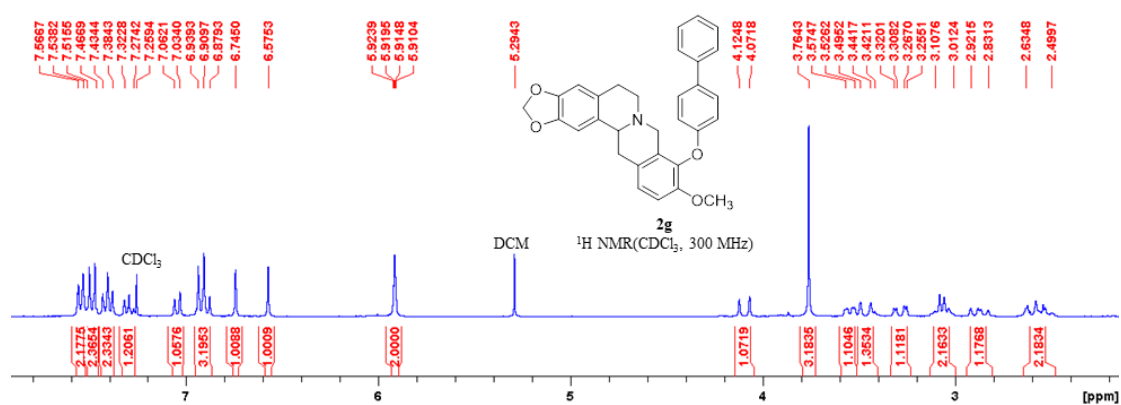


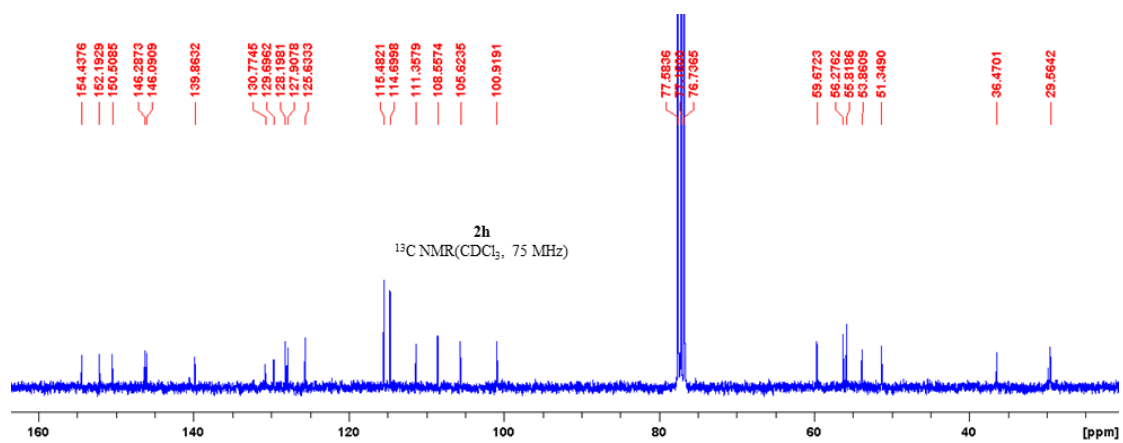
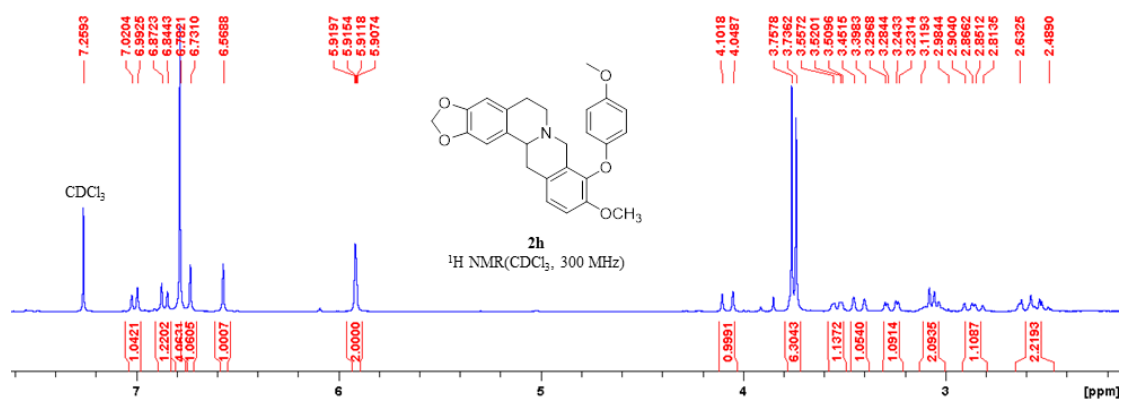


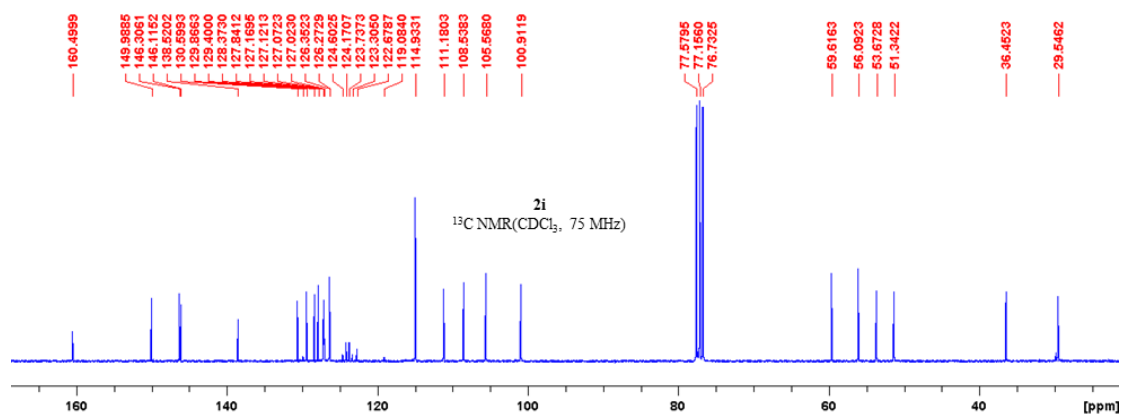
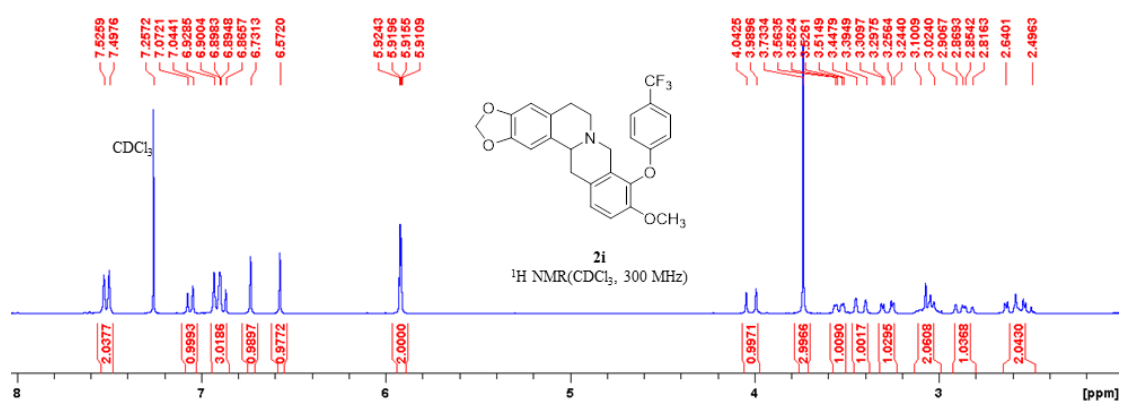


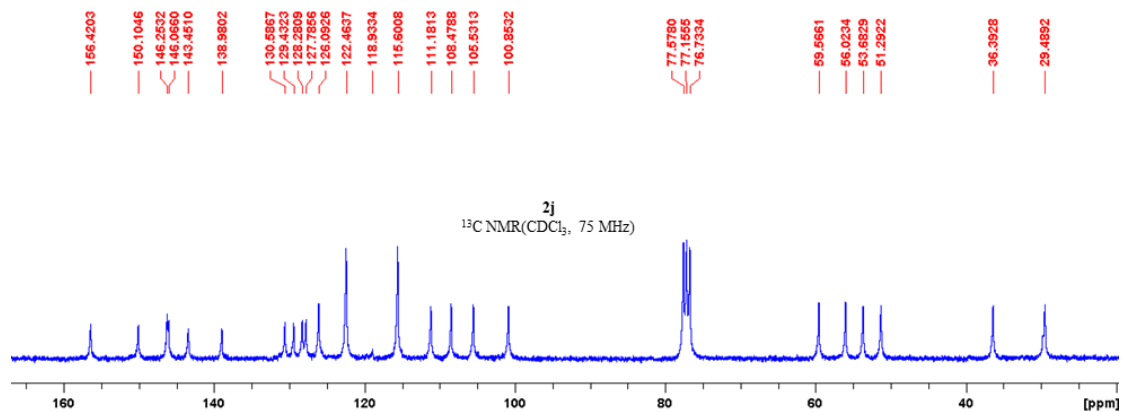
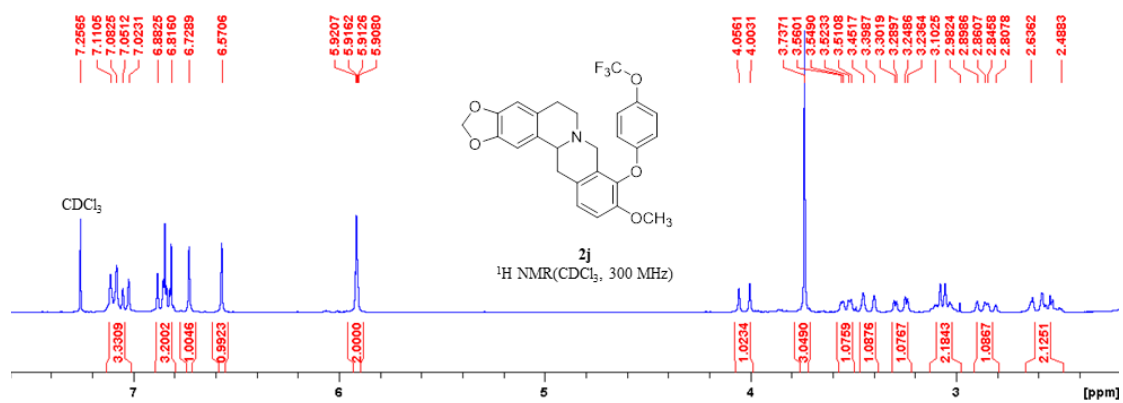


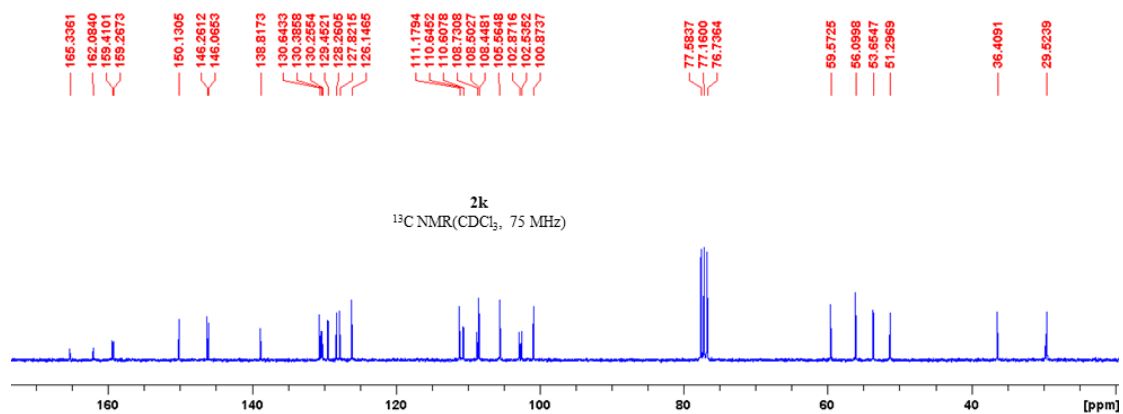
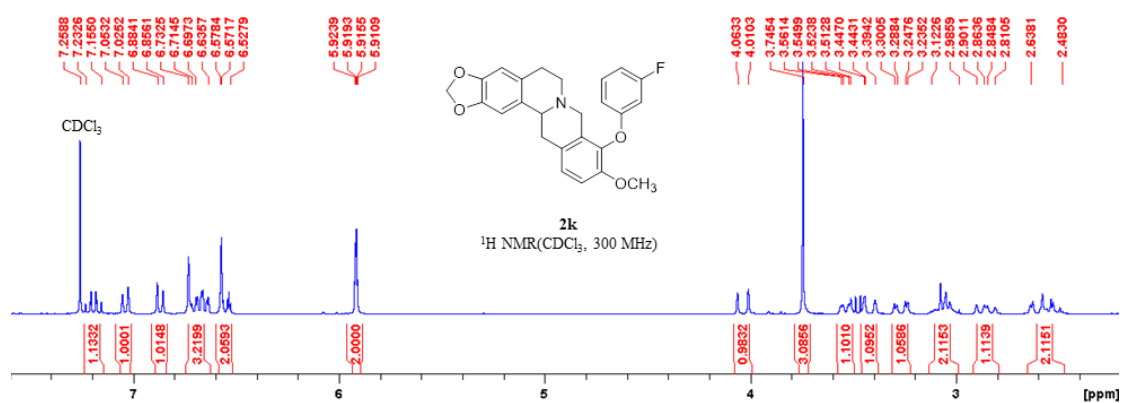


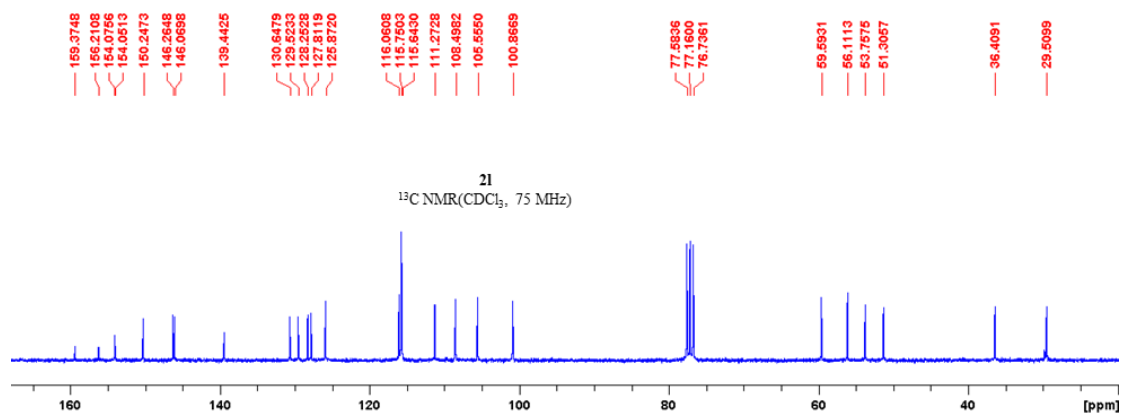
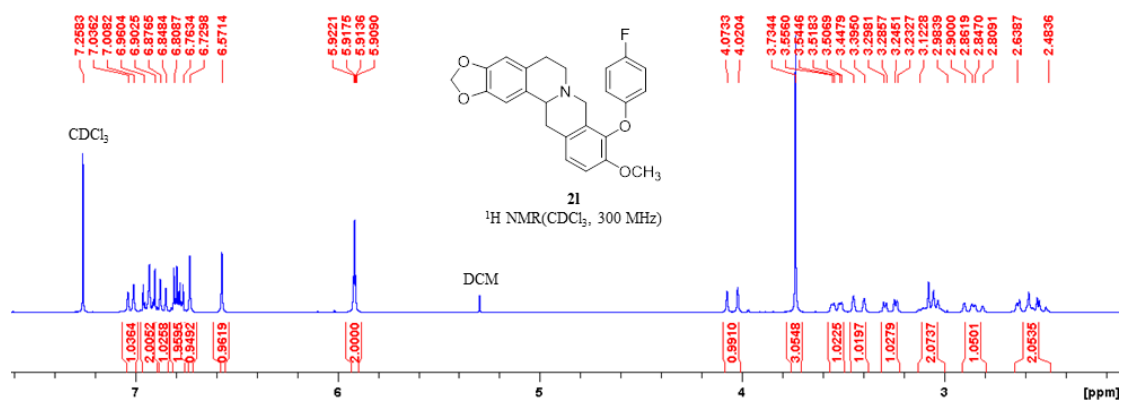


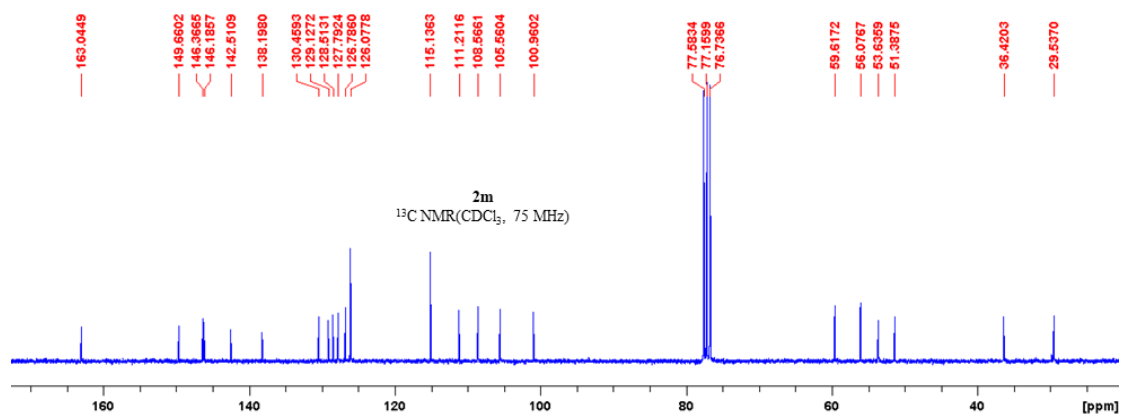
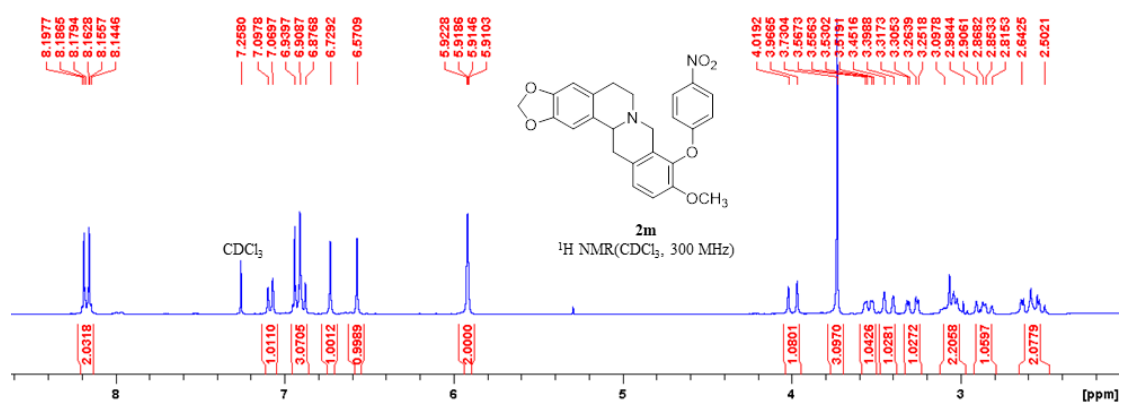


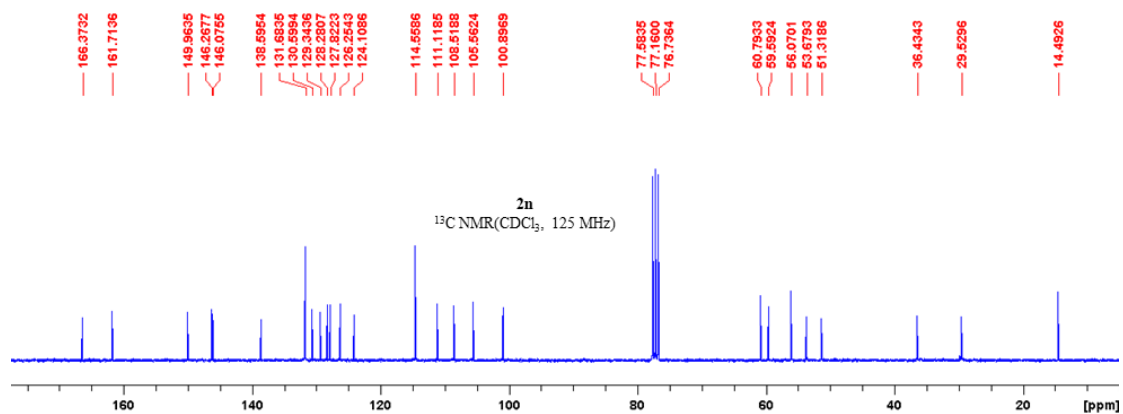
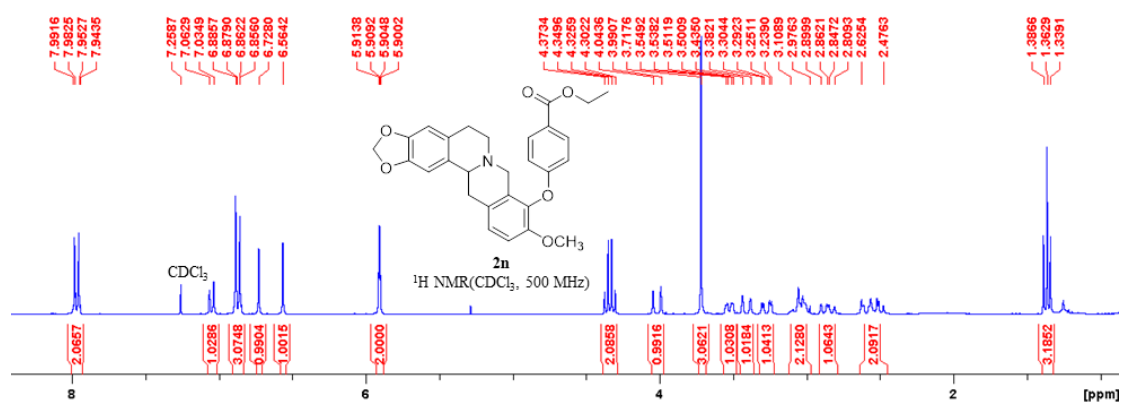


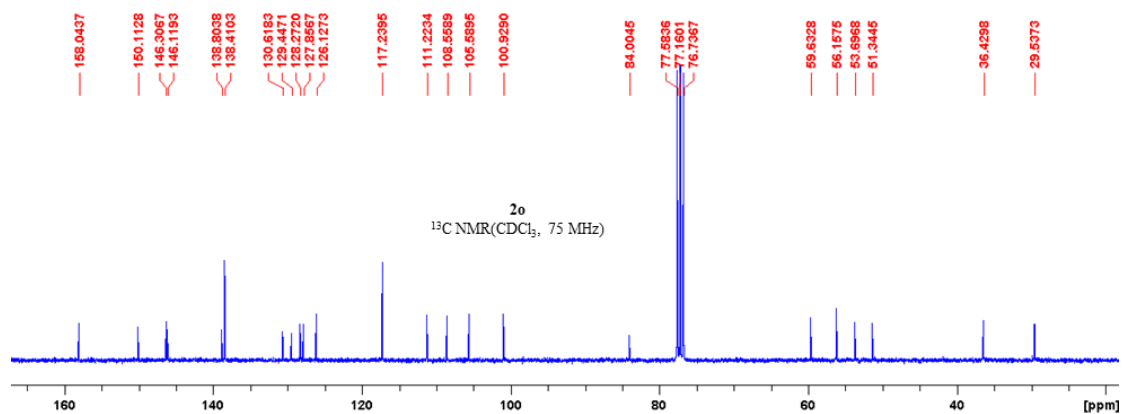
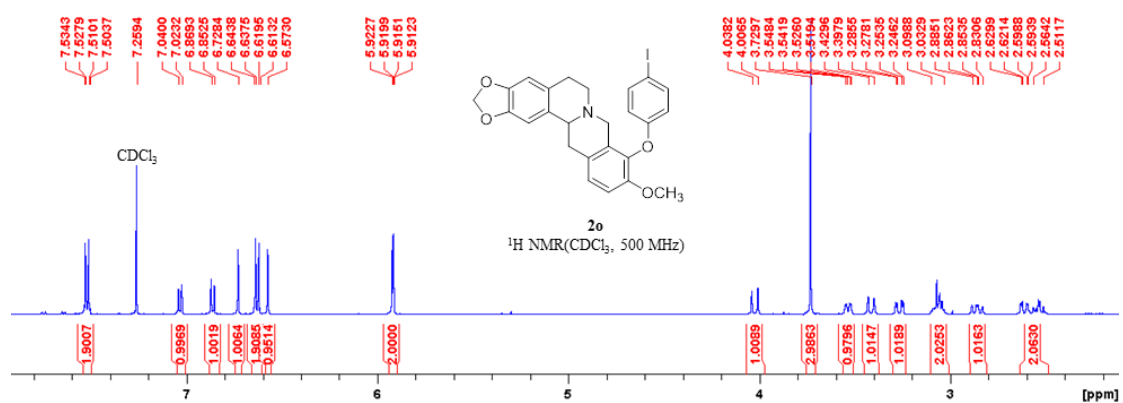


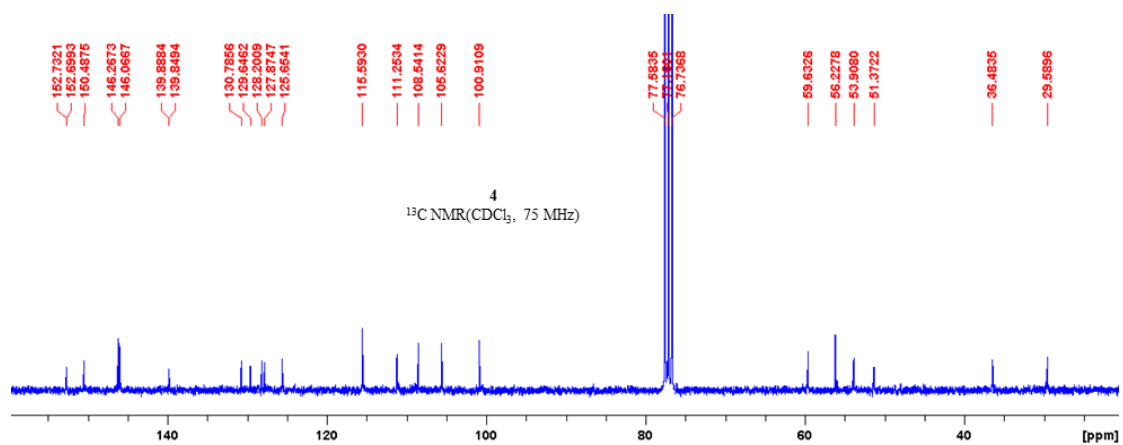
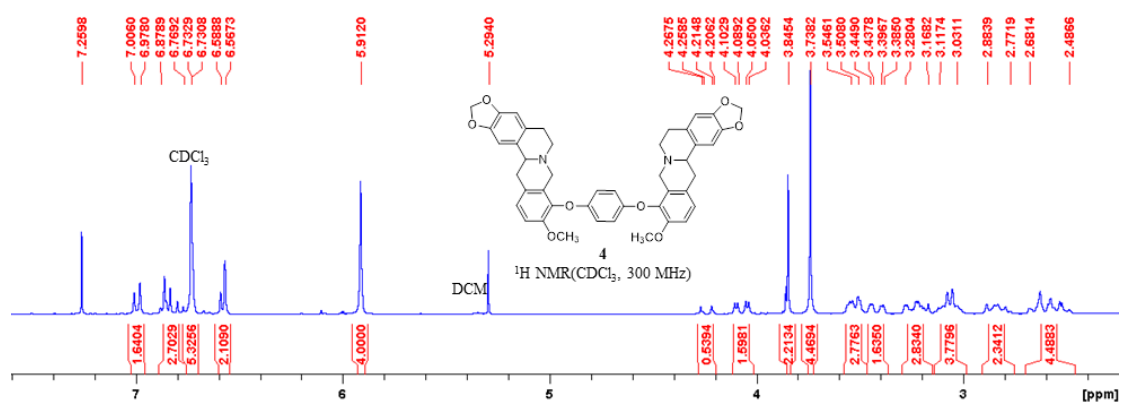


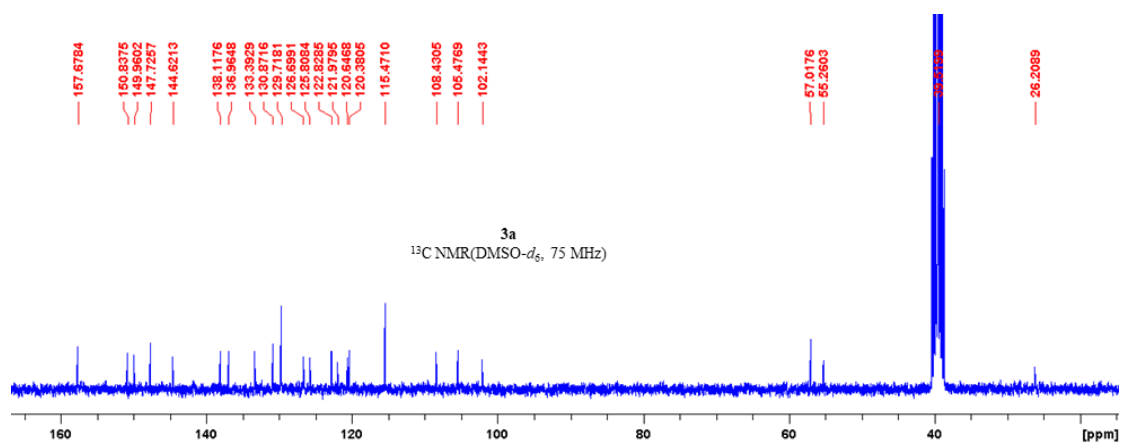
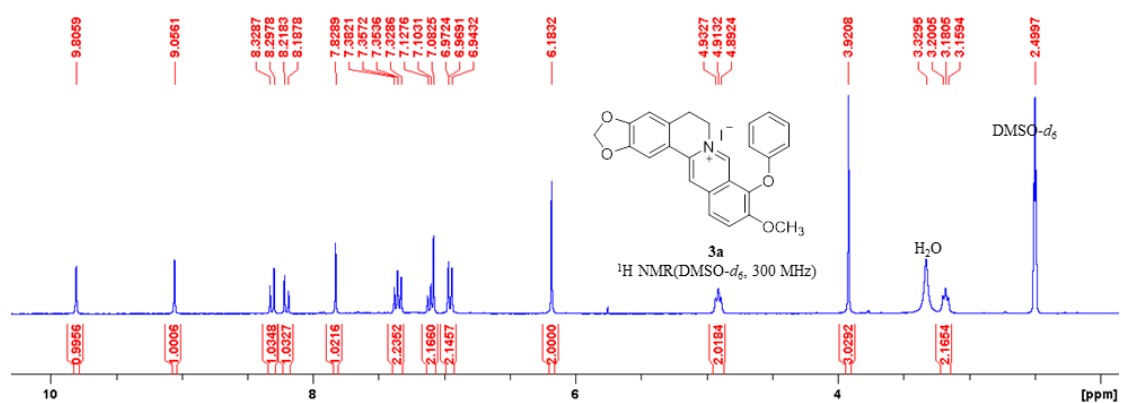


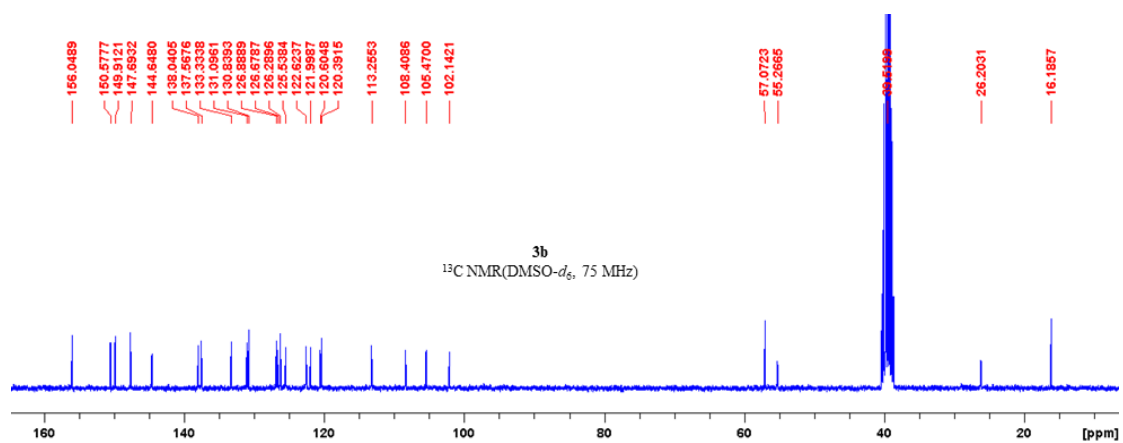
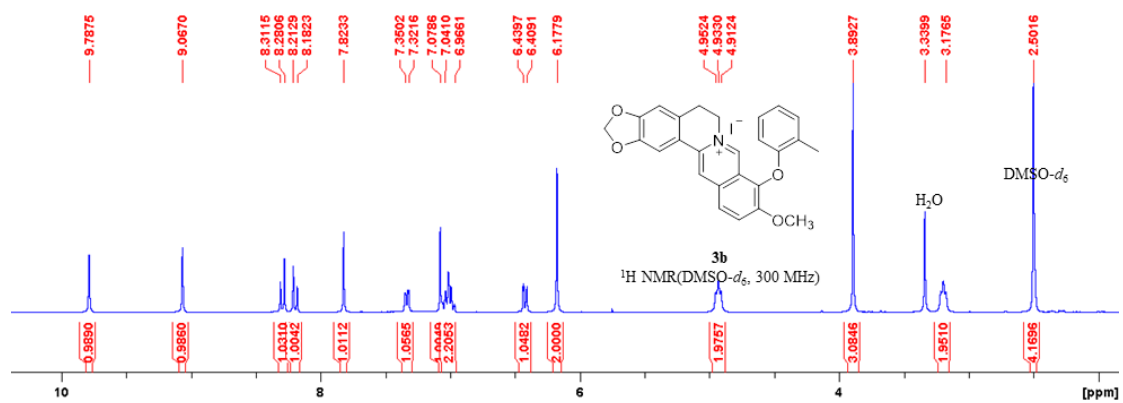


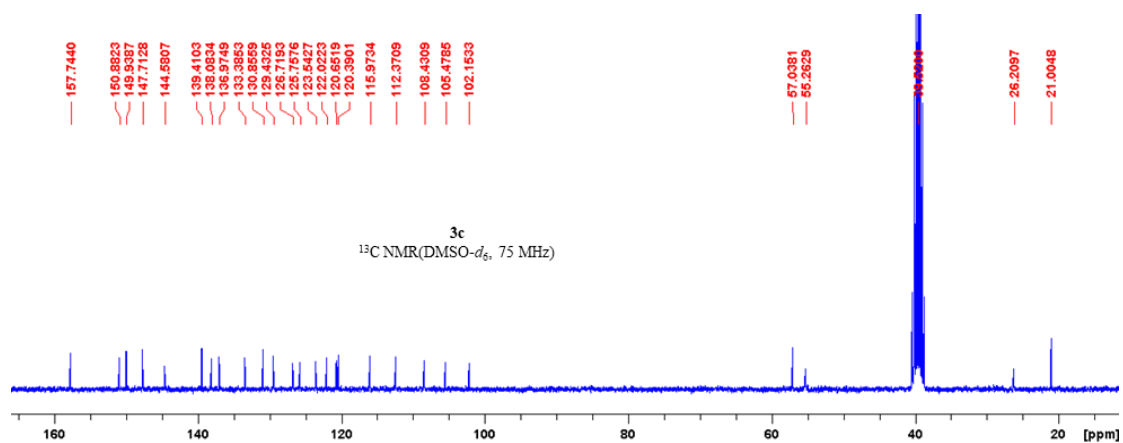
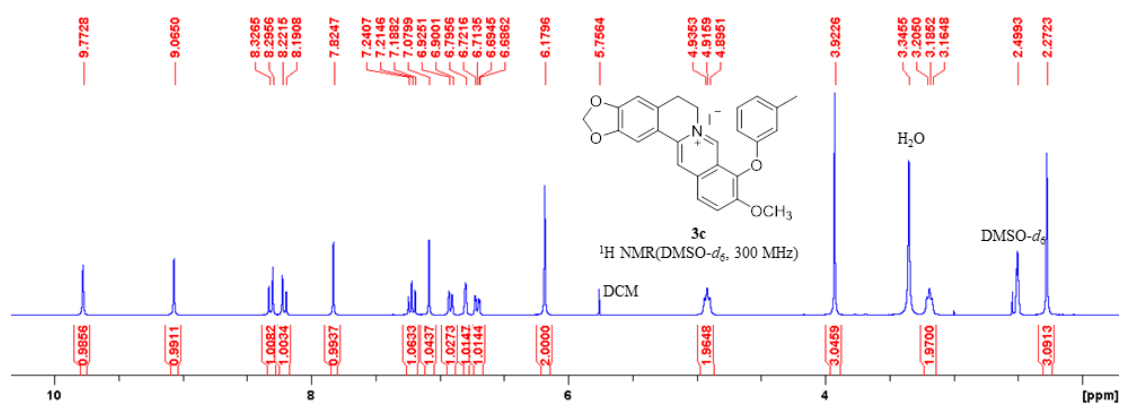


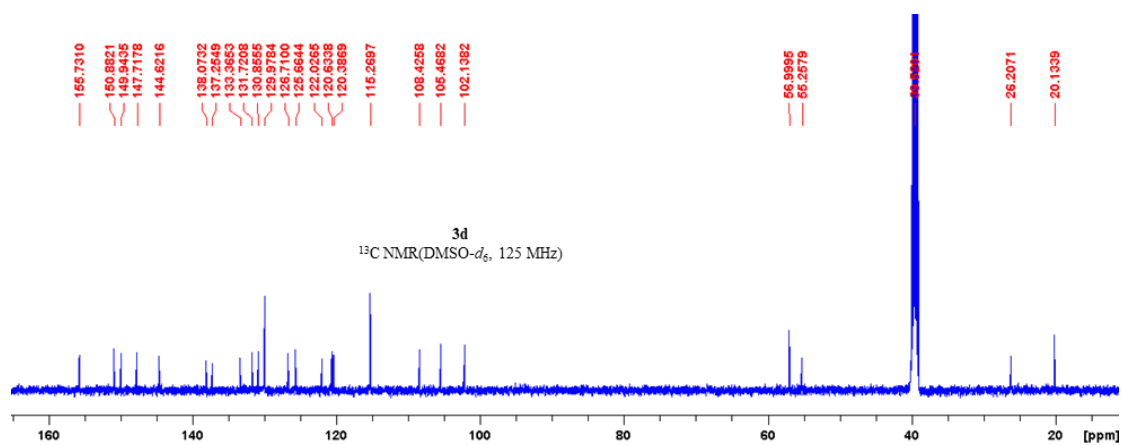
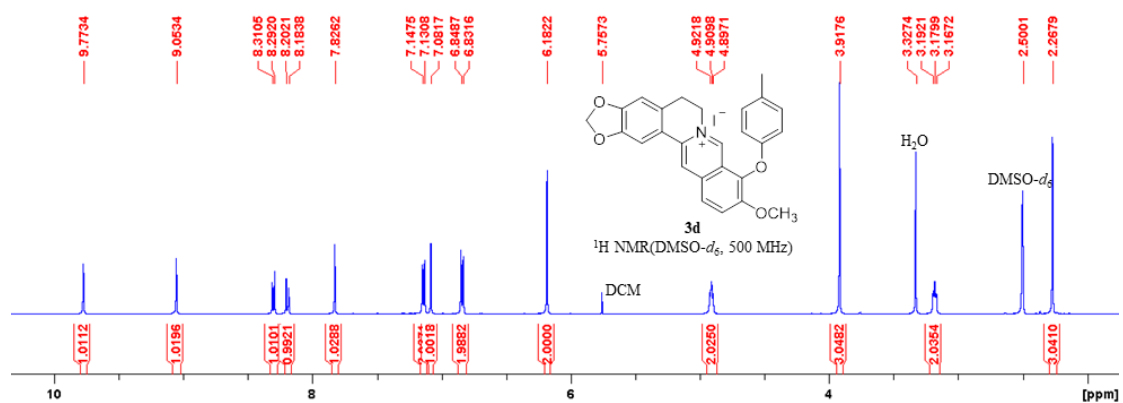


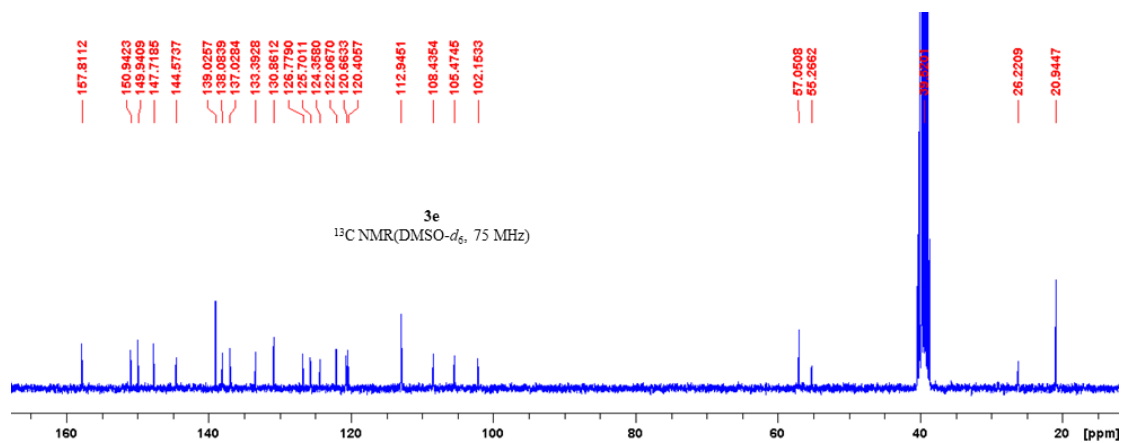
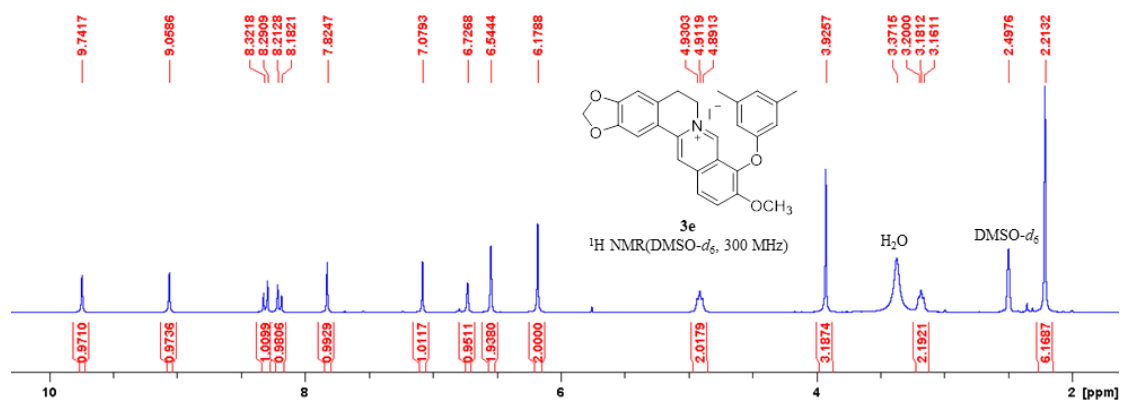


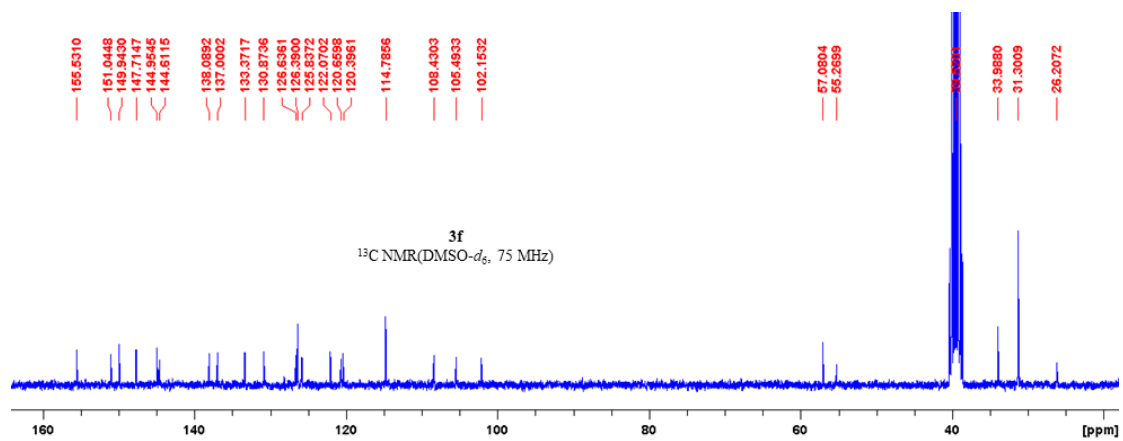
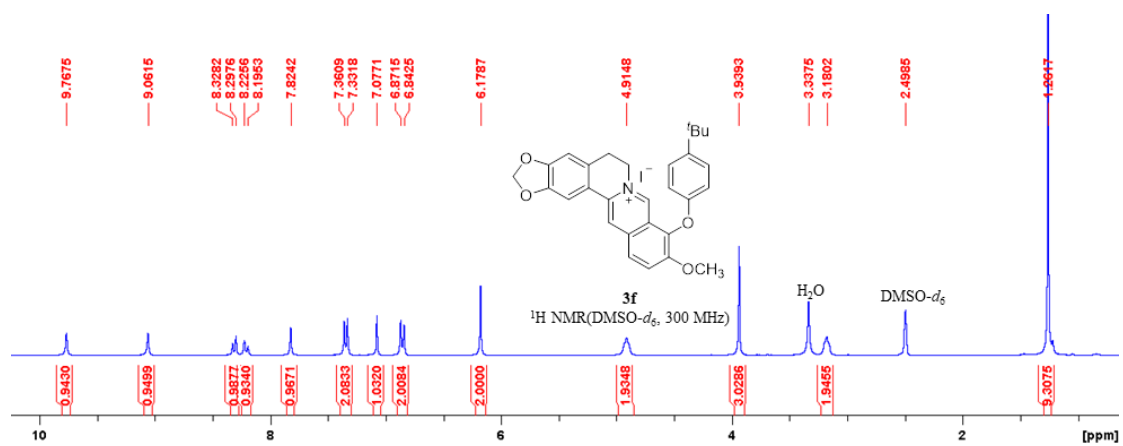


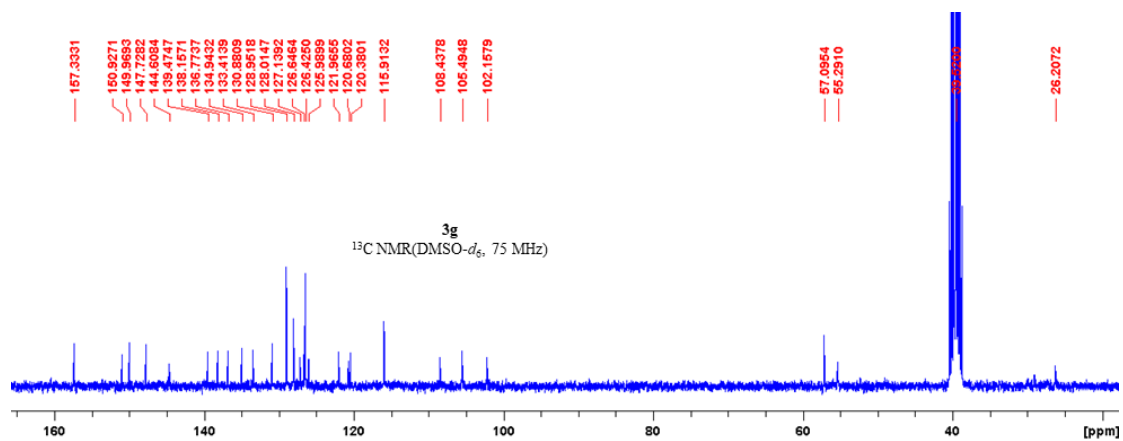
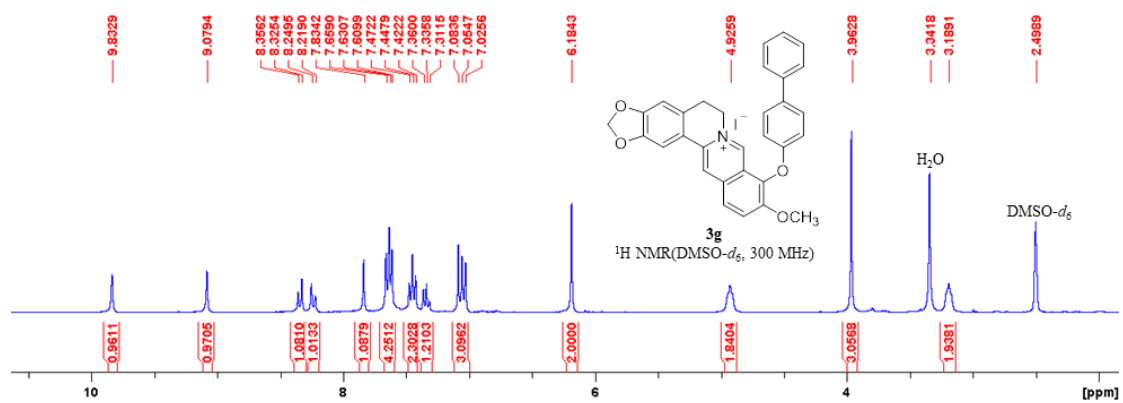


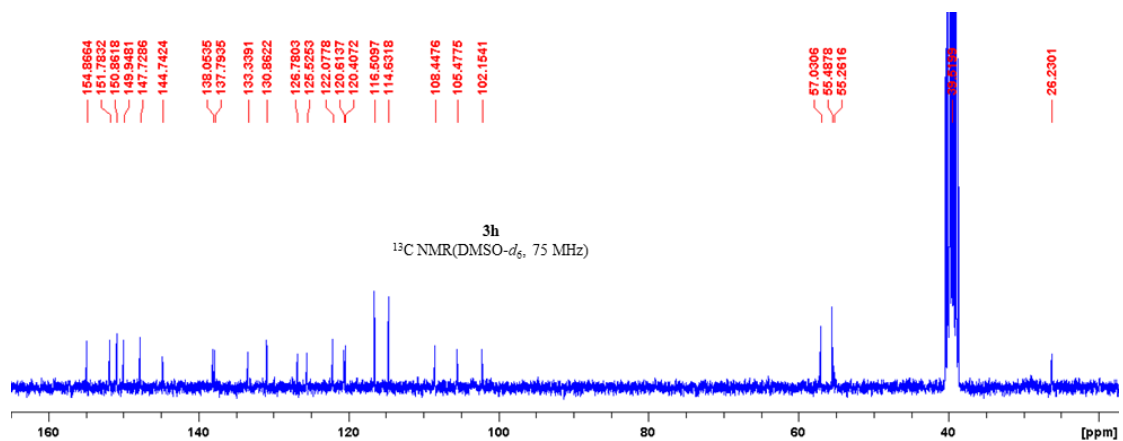
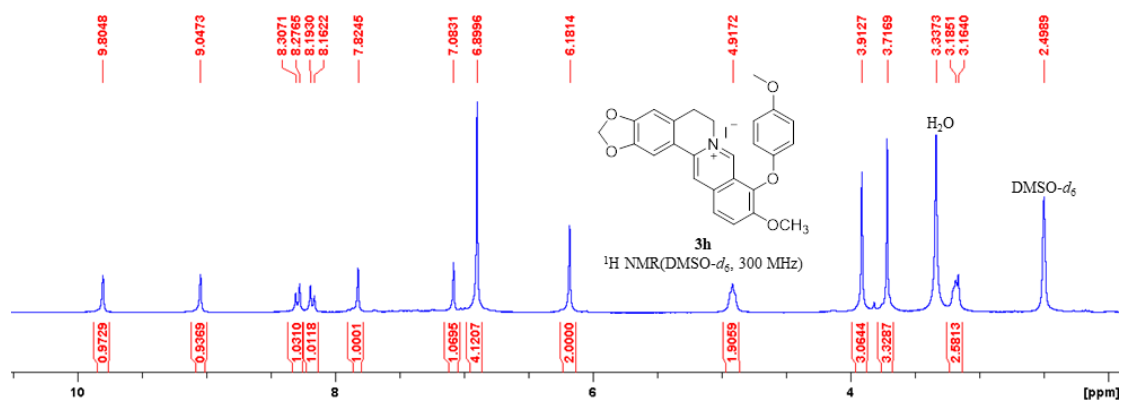


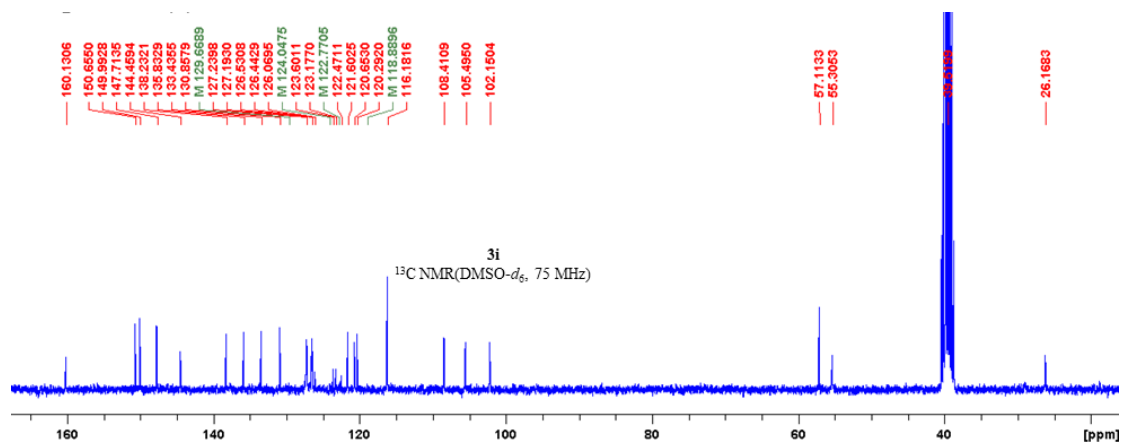
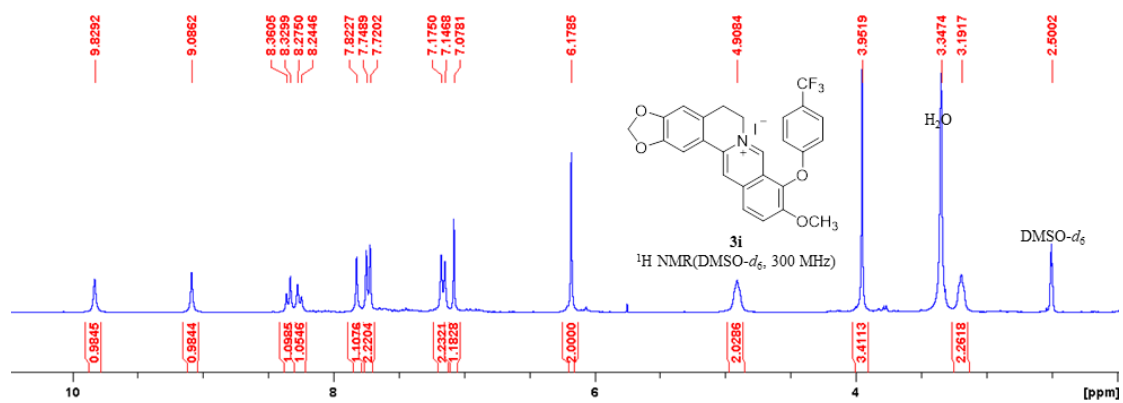


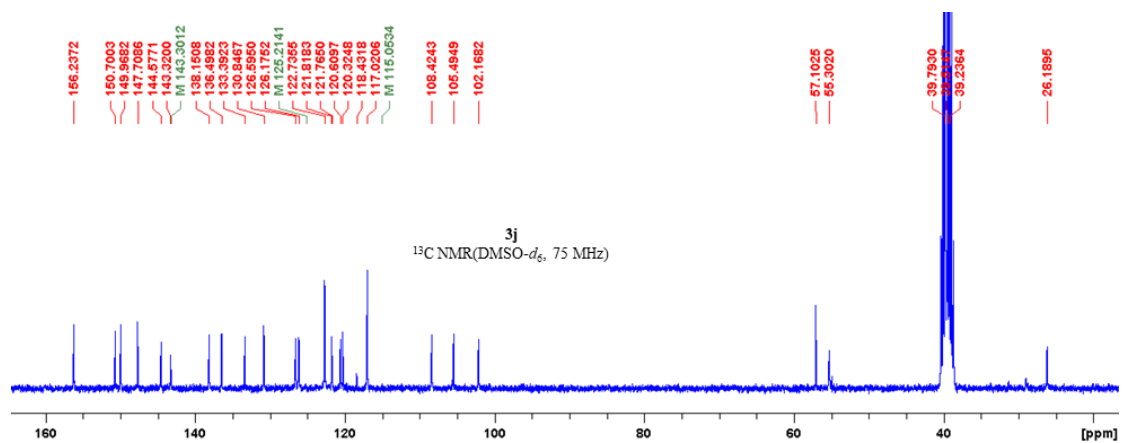
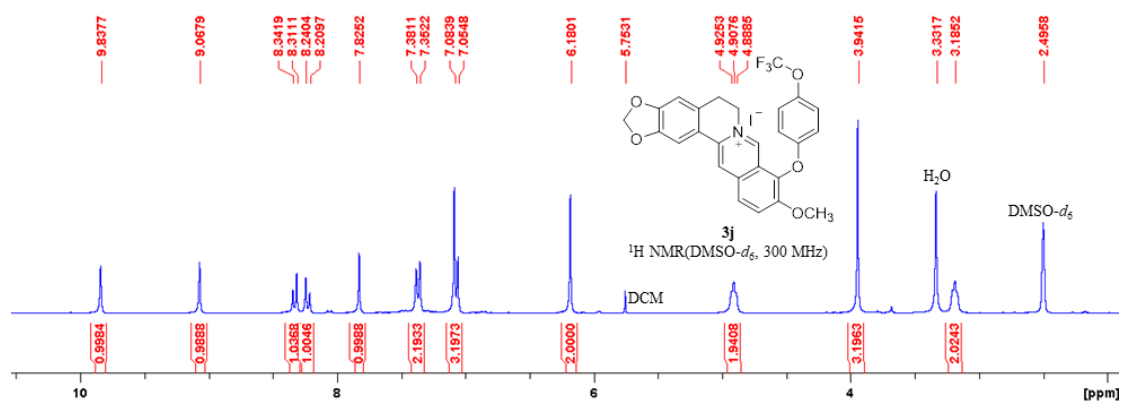


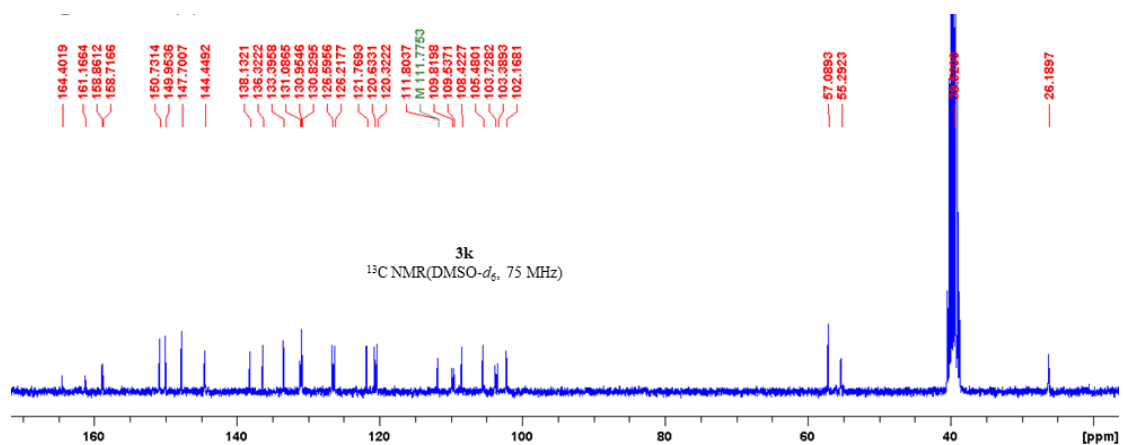
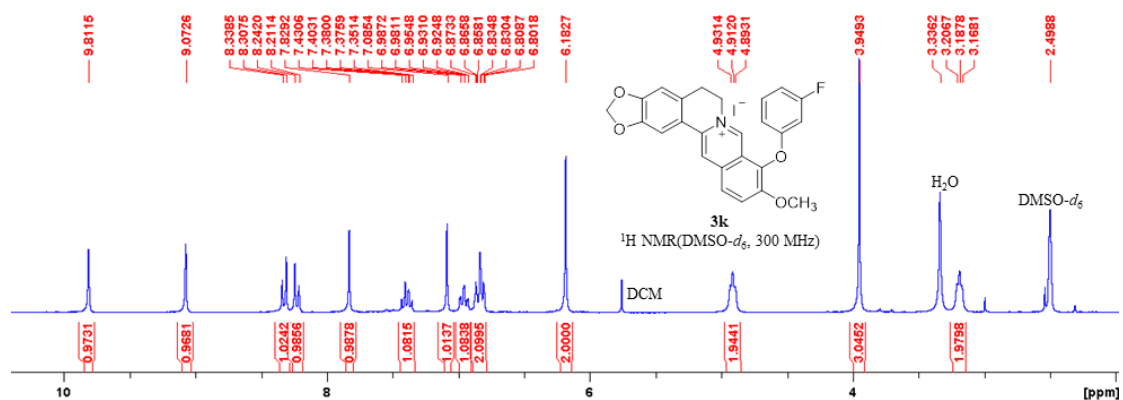


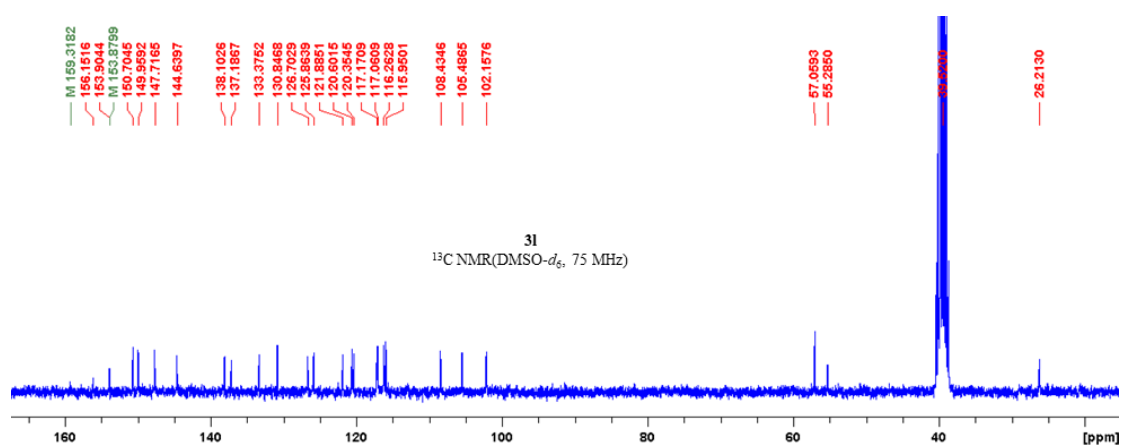
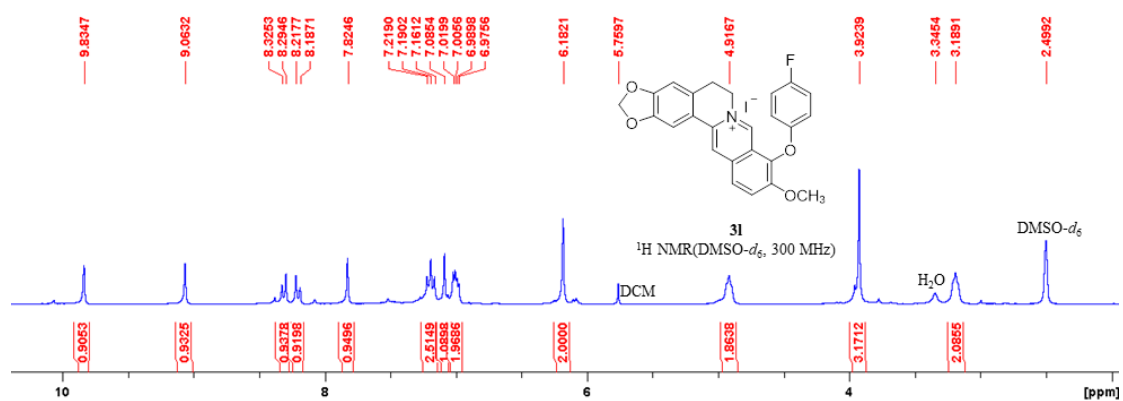


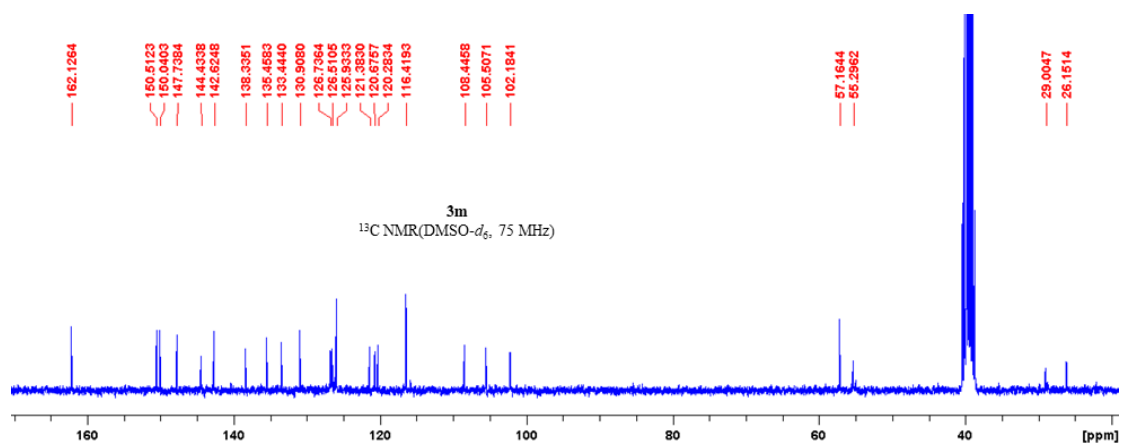
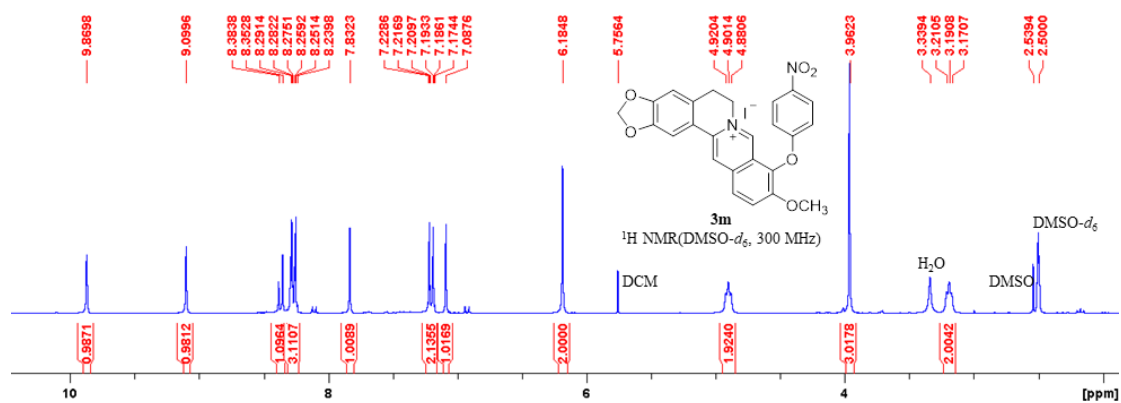


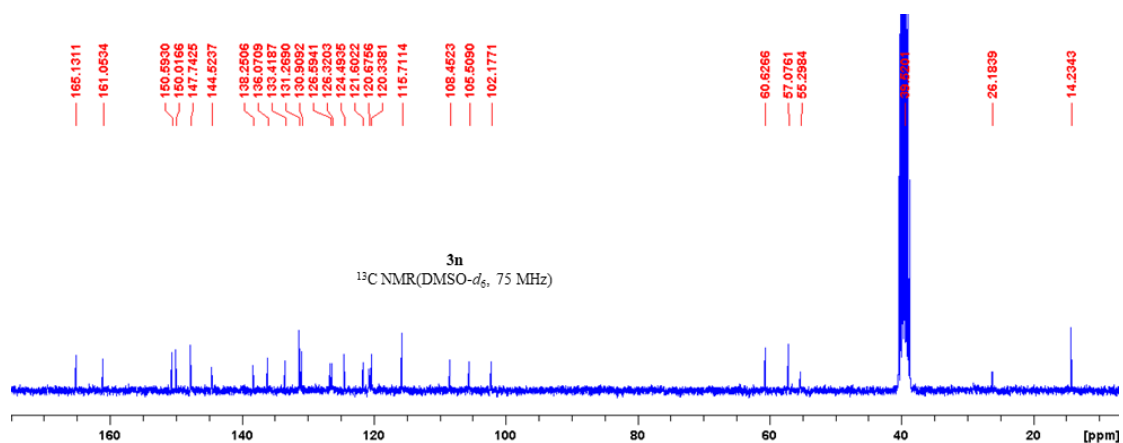
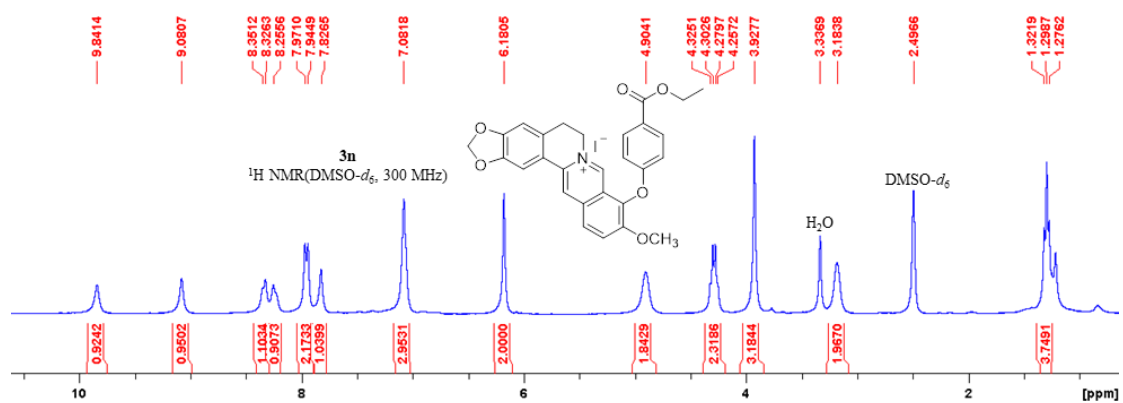


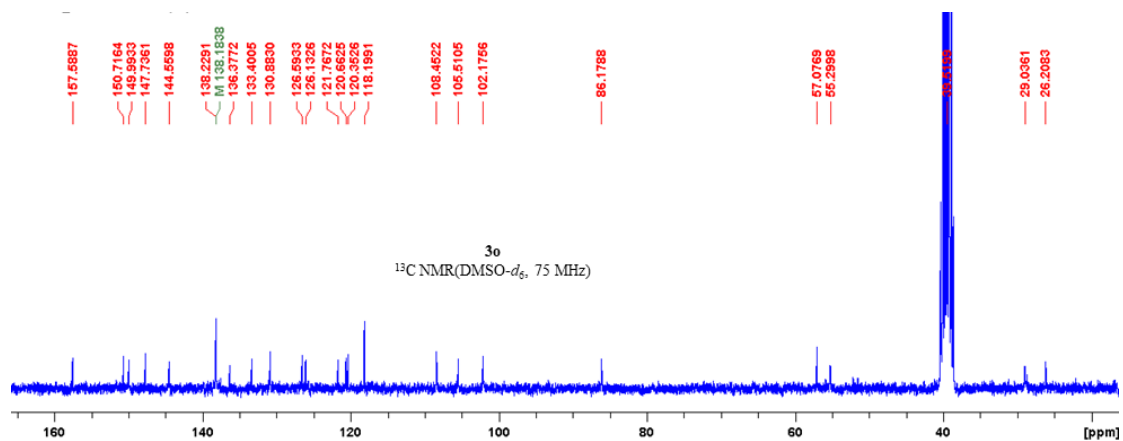
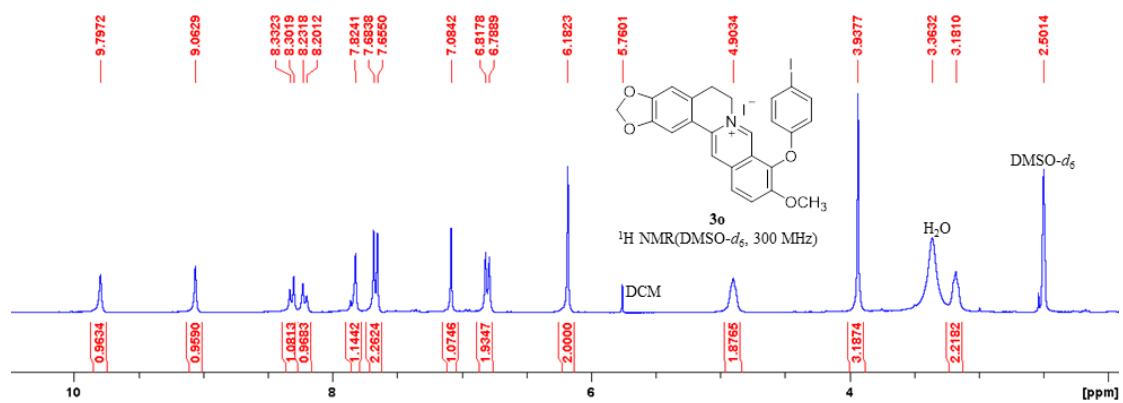


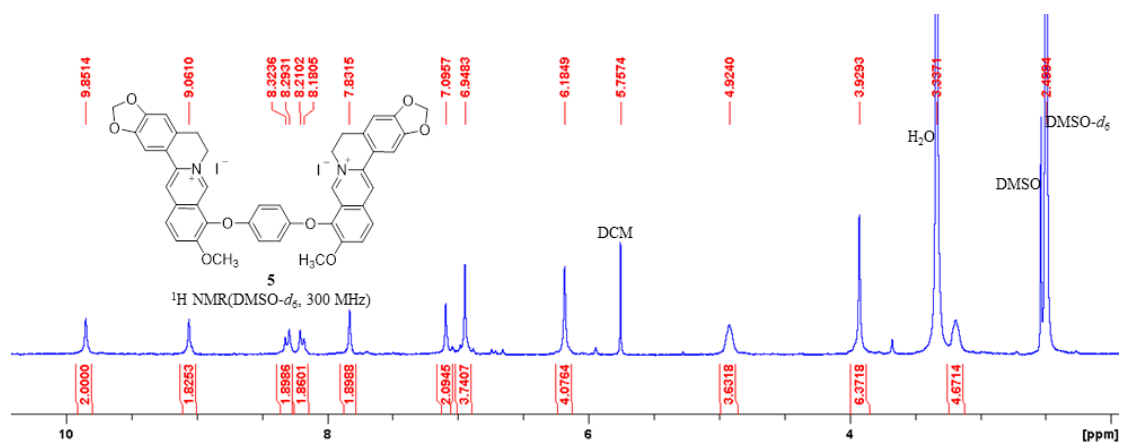












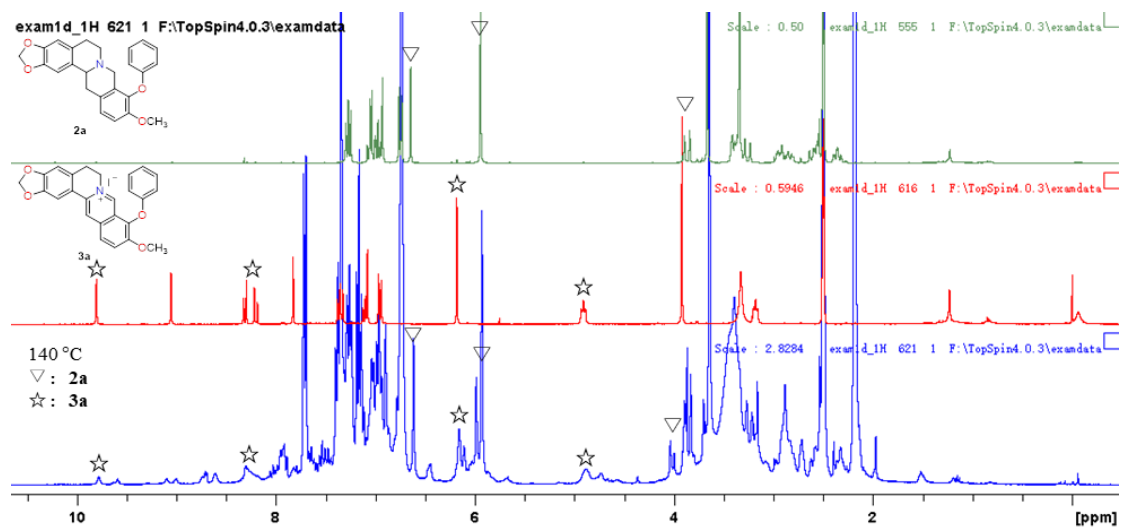


Figure S1: NMR analysis of reaction mixture at 140 °C.

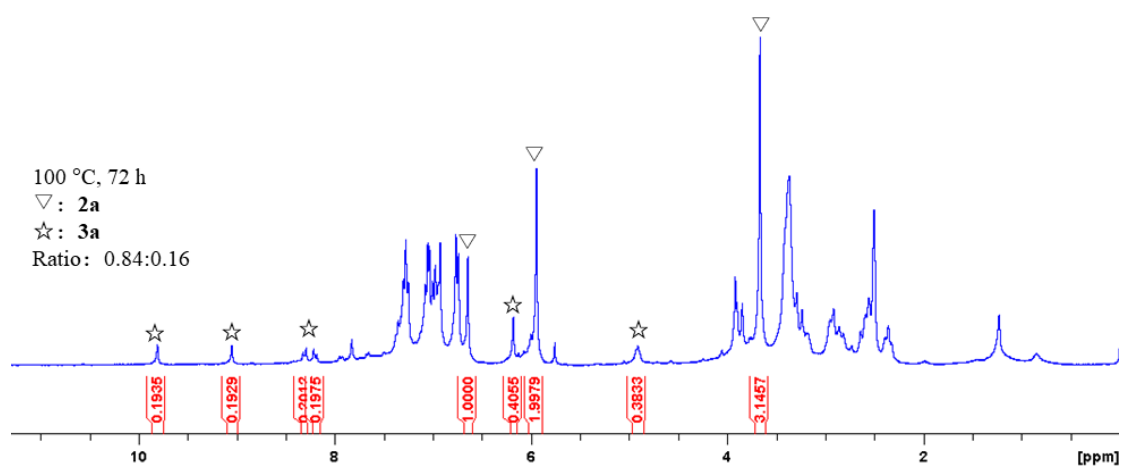
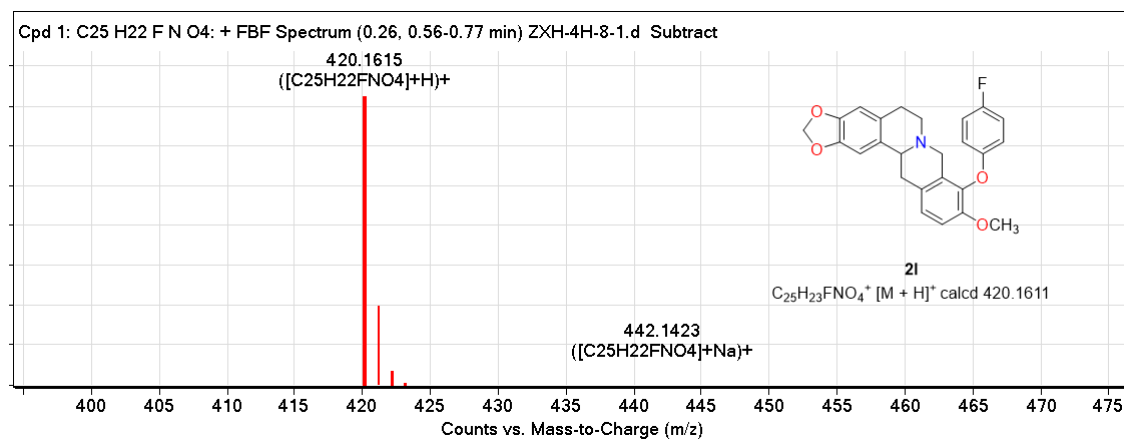
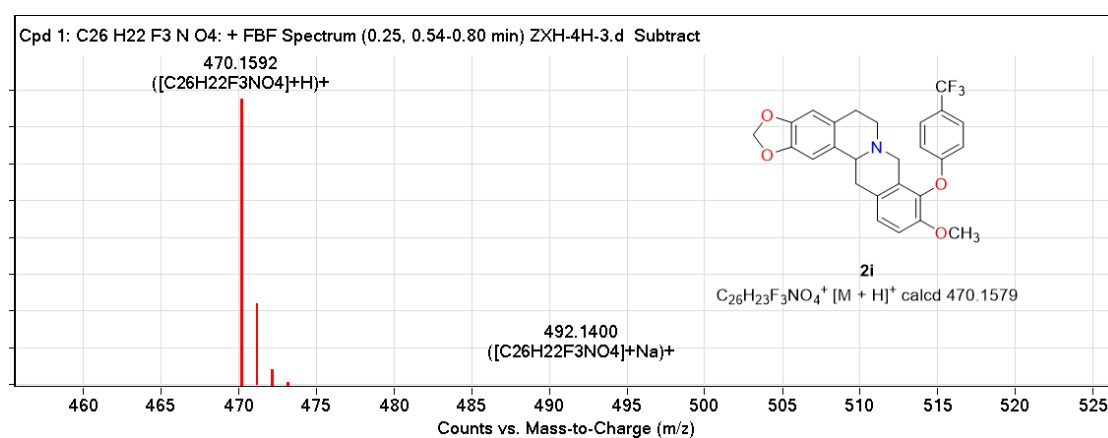
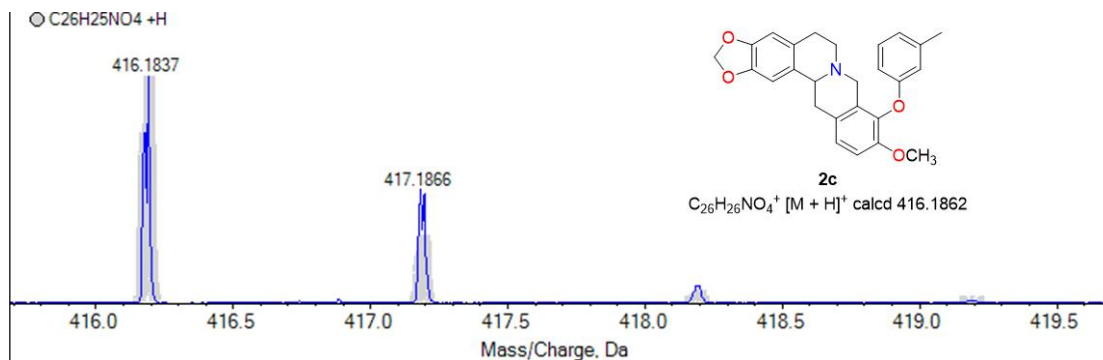
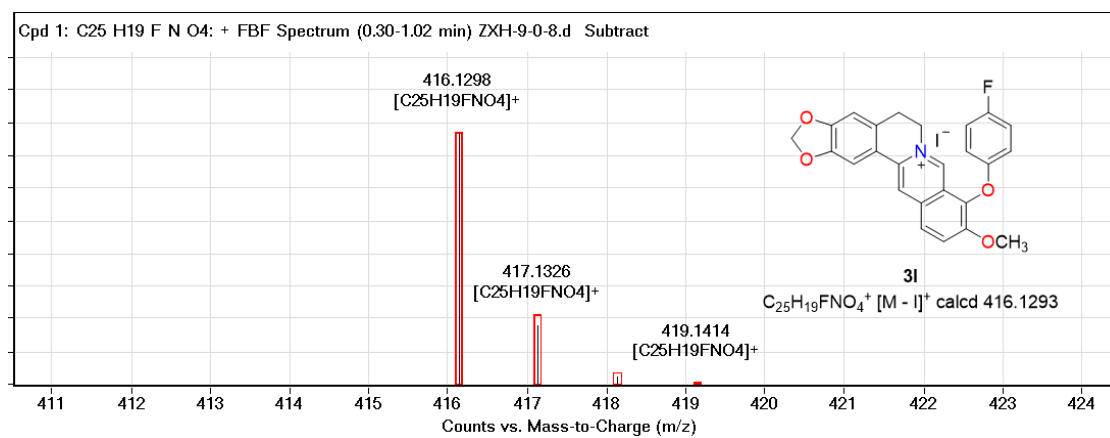
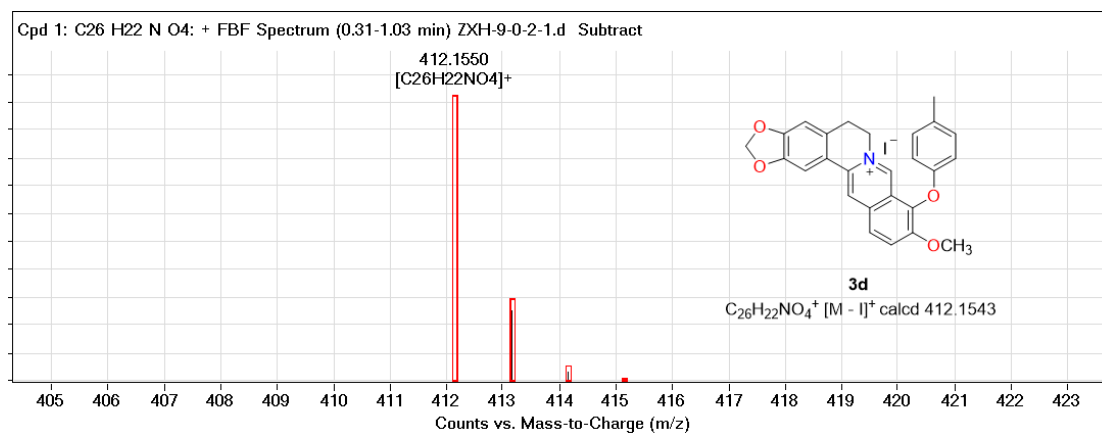


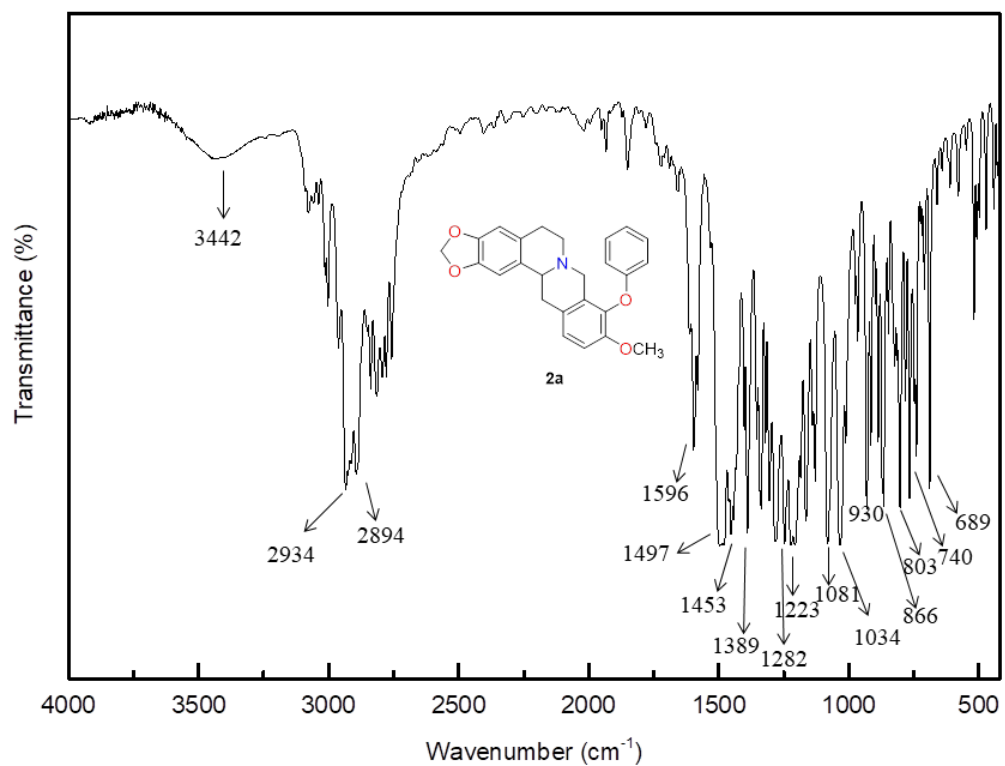
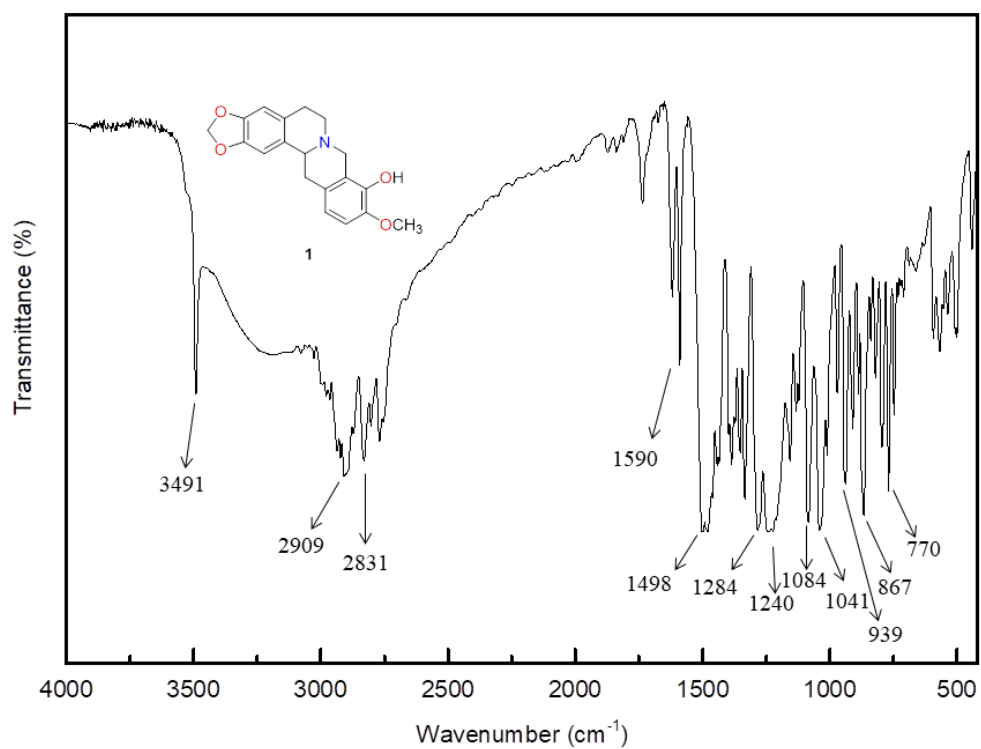
Figure S2: Oxidation of 2a with DMSO.

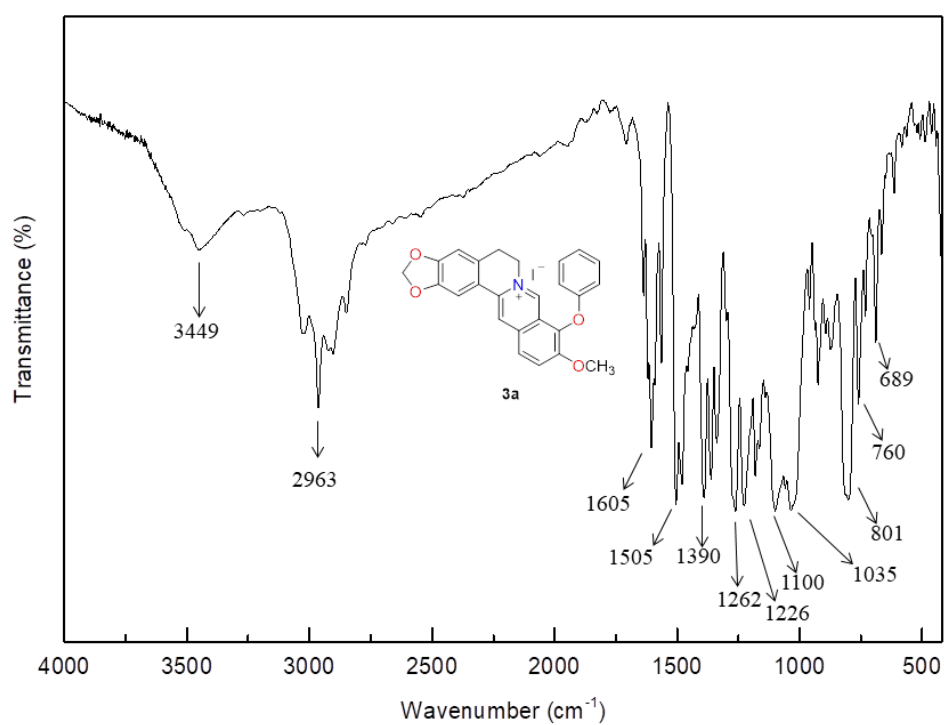
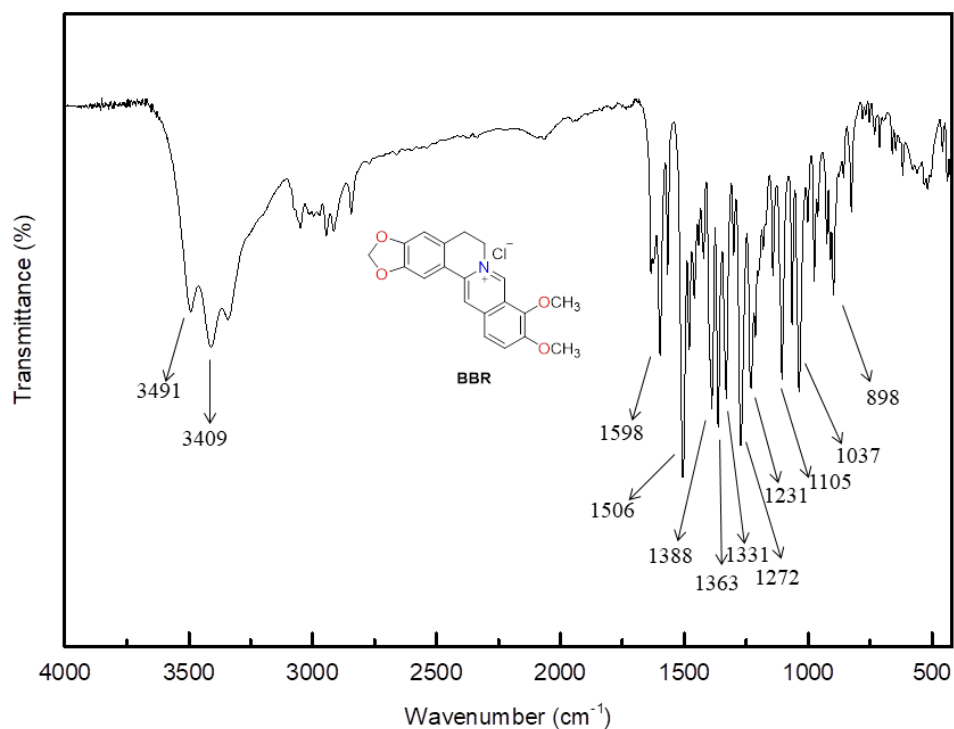
Selected examples of HRMS spectra





Representative IR spectra





IR spectra discussion: The strong absorption bands in the range of 1200-1000 cm^{-1} are due to the C-O stretching vibrations. The absorptions at 740, 689 and 760, 689 cm^{-1} for

2a and **3a**, respectively, are assignable to the bending vibrations of the C-H bonds in mono-substituted phenyl ring.

References

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- 1 Ge, H.-X.; Zhang, J.; Chen, L.; Kou, J.-P.; Yu, B.-Y. *Bioorg. Med. Chem.* **2013**, *21*, 62-69.