

Supporting information

Ultrasound-assisted ionic liquid-mediated green method for synthesis of 1,3-diphenylpyrazole-based spirooxindolopyrrolizidines, their anti-tubercular activity, molecular docking study and ADME predictions

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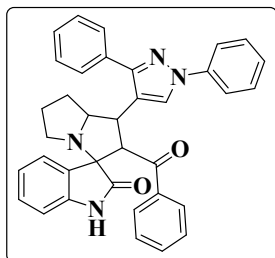
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1. General information

The chemicals isatin with purity 98% was purchased from Spectrochem, Mumbai and L-proline with purity 99% was purchased from Sisco Research Laboratories (SRL) Pvt. Ltd., Mumbai. The ionic liquid [Bmim]BF₄ with purity >98.0% was purchased from Tokyo Chemical Industry (TCI), Tokyo, Japan. All the acetophenones with purity 99% were purchased from Finar chemicals Ltd., Ahmedabad, India. Phenylhydrazine with purity 98% was purchased from AVRA synthesis Pvt. Ltd., Hyderabad, India. All the solvents were purchased from Merck chemicals, Mumbai. The compounds were used without further purification. All the melting points were determined by using Stuart SMP30 melting point apparatus (Bibby Scientific Ltd. United Kingdom) and were uncorrected. Ultrasonication irradiation was performed on PCi-Analytics-6.5L200H1DTC ultrasonic cleaner, the frequency of ultrasonic cleaner is 25 kHz, input voltage range of 170–270VAC at 50 Hz and output power is 250 W (Mumbai, India). The reaction progress was checked with TLC plates (E. Merck, Mumbai, India). IR spectra were recorded on KBr disc by using Perkin-Elmer 100S spectrophotometer (Perkin-Elmer Ltd. United Kingdom) from 400–4000 cm⁻¹ and Bruker spectrometer. ¹H and ¹³C NMR spectra were recorded on Avance-III Bruker-400 MHz spectrometer (Bruker Corporation Ltd., Germany) using DMSO-*d*₆ and CDCl₃ as solvents and TMS as an internal standard, chemical shifts were expressed in ppm. Mass spectra were recorded on a Jeol JMSD-300 spectrometer (Jeol Ltd., Tokyo, Japan) in acetonitrile solvent. The single crystal X-ray diffraction data of the compound **4b** was collected and solved by using Bruker Kappa Apex II CCD diffractometer and ShelXT software. Molecular docking studies were performed by using AutoDock Tools-1.5.6 software and visualized by Discovery studio.

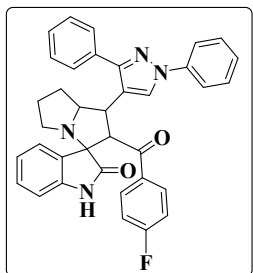
2. Spectral data for compounds

(dl)-2'-(benzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4a). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3248, 1731, 1674, 1598.



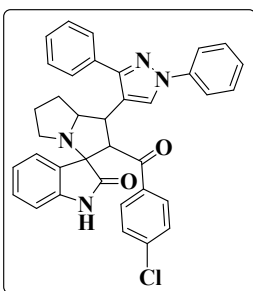
¹H NMR (400 MHz, CDCl₃) δ: 8.11 (s, 1H), 7.92 (d, *J* = 6.8 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.49 – 7.46 (m, 1H), 7.42 (t, *J* = 7.2 Hz, 4H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.31 (s, 1H), 7.25 (s, 1H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.12 (dd, *J* = 14.4, 7.6 Hz, 2H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 7.6 Hz, 1H), 4.98 (d, *J* = 11.6 Hz, 1H), 4.23 (t, *J* = 11.6 Hz, 1H), 4.04 (q, *J* = 6.4 Hz, 1H), 2.56 (dd, *J* = 12.8, 7.2 Hz, 2H), 1.85 (dd, *J* = 12.4, 6.4 Hz, 1H), 1.74 (dd, *J* = 9.6, 7.2 Hz, 2H), 1.45 (dd, *J* = 12.4, 7.2 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ: 197.19, 180.74, 153.15, 140.49, 139.97, 137.12, 133.75, 132.99, 129.47, 129.36, 129.10, 128.59, 128.21, 128.10, 127.93, 127.45, 126.29, 125.04, 124.98, 122.42, 120.61, 118.95, 110.08, 73.61, 64.11, 48.11, 42.73, 30.26, 27.07. HRMS (ESI, *m/z*): [M+H]⁺ calcd. For C₃₆H₃₀N₄O₂: 551.2442; Found: 535.2126.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-fluorobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4b). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3221, 1725, 1676, 1597.



¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.11 (s, 1H), 8.97 (s, 1H), 7.90 (d, *J* = 7.6 Hz, 4H), 7.62 (t, *J* = 7.2 Hz, 2H), 7.56 – 7.46 (m, 5H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 8.8 Hz, 3H), 7.00 (dd, *J* = 13.6, 7.2 Hz, 2H), 6.52 (d, *J* = 8.0 Hz, 1H), 5.14 (d, *J* = 12.0 Hz, 1H), 4.07 (t, *J* = 11.2 Hz, 1H), 3.75 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.38 (dd, *J* = 16.4, 7.2 Hz, 1H), 2.29 (dd, *J* = 11.2, 6.0 Hz, 1H), 1.62 (dt, *J* = 12.4, 6.4 Hz, 3H), 1.21 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 196.90, 179.41, 166.58, 164.08, 152.41, 142.36, 139.98, 134.15, 131.33, 131.23, 129.91, 129.39, 129.11, 128.87, 128.53, 126.96, 126.49, 125.05, 121.65, 120.75, 118.46, 115.69, 115.48, 110.17, 73.41, 73.11, 63.55, 47.71, 42.42, 30.03, 27.12. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₉FN₄O₂: 569.2347; Found: 569.2347.

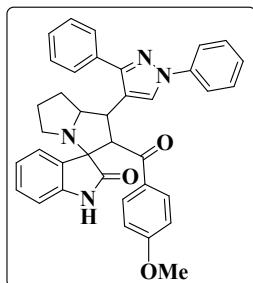
(dl)-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4c). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹):



¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.14 (s, 1H), 8.97 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 3H), 7.69 (t, *J* = 5.2 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.44 (s, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.00 (dd, *J* = 11.2, 6.4 Hz, 2H), 6.53 (d, *J* = 7.6 Hz, 1H), 5.14 (d, *J* = 11.2 Hz, 1H), 4.06 (t, *J* = 10.8 Hz, 1H), 3.75 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.37 (t, *J* = 8.0 Hz, 1H), 2.29 (dd, *J* = 10.8, 4.0 Hz, 1H), 1.66 (dd, *J* = 11.2, 5.2 Hz, 1H), 1.61 – 1.54 (m, 2H), 1.21 (dd, *J* = 12.0, 5.2 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.39, 179.34, 152.41, 142.35, 139.97, 138.46, 136.14, 134.13, 130.59, 130.24, 130.15, 129.91, 129.43, 129.40, 129.12, 128.95, 128.87, 128.68, 128.54, 126.97, 126.51, 124.99, 121.70, 121.55, 120.70, 119.22, 118.46, 110.21, 73.42, 73.07, 63.61, 47.69, 42.38, 30.04, 27.13. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₉ClN₄O₂: 585.2052; Found: 585.2059.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydrospiro

[indoline-3,3'-pyrrolizin]-2-one (4d). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3391, 1721,

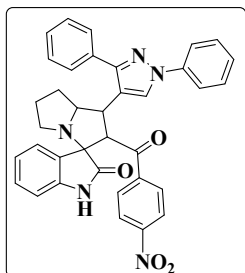


1668, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.13 (s, 1H), 8.93 (s, 1H), 7.90 (t, *J* = 7.6 Hz, 4H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.50 (dd, *J* = 10.8, 8.8 Hz, 5H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 6.8 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 7.6 Hz, 1H), 5.10 (d, *J* = 11.8 Hz, 1H), 4.14 – 4.07 (m, 1H), 3.77 (s, 3H), 3.75 – 3.70 (m, 1H), 2.37 (t, *J* = 8.4 Hz, 1H), 2.29 (dd, *J* = 10.4, 5.2 Hz, 1H), 1.66 (dd, *J* = 12.1, 5.5 Hz, 1H), 1.61 – 1.55 (m, 2H), 1.21 (dd, *J* = 12.4, 5.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 195.97, 179.54, 163.51, 152.42,

142.32, 139.95, 134.13, 130.85, 130.30, 129.90, 129.65, 129.08, 128.87, 128.52, 127.14, 126.89, 126.47, 125.26, 121.52, 120.86, 118.44, 113.83, 110.09, 73.34, 62.73, 55.92, 47.73, 42.70, 30.03, 27.12. HRMS (ESI, *m/z*): [M+H]⁺calcd. for C₃₇H₃₂N₄O₃: 581.2547; Found: 581.2556.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-

hexahydrospiroindolin e-3,3'-pyrrolizin]-2-one (4e). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹):

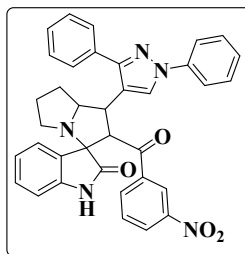


¹): 3383, 1719, 1661, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.02 (s, 1H), 9.00 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 2H), 7.90 (s, 4H), 7.64 (t, *J* = 11.6 Hz, 4H), 7.51 (d, *J* = 4.8 Hz, 4H), 7.33 (t, *J* = 13.2 Hz, 1H), 7.16 (s, 1H), 7.02 (s, 1H), 6.48 (d, *J* = 7.2 Hz, 1H), 5.22 (d, *J* = 10.8 Hz, 1H), 4.04 (t, *J* = 10.0 Hz, 1H), 3.76 (d, *J* = 6.4 Hz, 1H), 2.37 (dd, *J* = 15.6, 8.0 Hz, 1H), 2.29 (d, *J* = 5.2 Hz, 1H), 1.67 (dd, *J* = 11.2, 5.2 Hz, 1H), 1.60 (d, *J* = 5.6 Hz, 2H), 1.23 (dd, *J* = 11.2, 6.0 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 198.09, 198.09, 179.18, 179.18, 152.41, 152.41, 150.11, 142.33, 139.98, 134.12, 130.14,

129.93, 129.56, 129.15, 128.88, 128.58, 127.05, 126.80, 126.54, 124.80, 123.54, 121.91, 120.58, 118.47, 110.42, 73.51, 72.95, 64.62, 47.65, 42.20, 30.12, 27.20. HRMS (ESI, *m/z*): [M+H]⁺calcd. for C₃₆H₂₉N₅O₄: 596.2292; Found: 596.2297.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(3-nitrobenzoyl)-1',2',5',6',7',7a'-

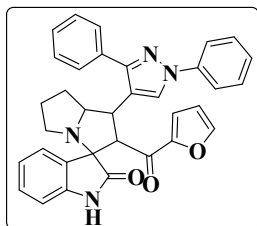
hexahydrospiroindolin e-3,3'-pyrrolizin]-2-one (4f). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹):



¹): 3382, 1719, 1669, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.09 (s, 1H), 9.01 (s, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 8.08 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 4H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.60 (dt, *J* = 12.4, 7.2 Hz, 3H), 7.53 – 7.47 (m, 3H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.14 – 7.07 (m, 1H), 7.04 – 6.97 (m, 2H), 6.42 (d, *J* = 8.0 Hz, 1H), 5.20 (d, *J* = 11.2 Hz, 1H), 4.11 – 4.00 (m, 1H), 3.77 (dd, *J* = 14.4, 6.8 Hz, 1H), 2.39 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.30 (dd, *J* = 10.0, 5.6 Hz, 1H), 1.66 (dd, *J* = 12.4, 5.6 Hz, 1H), 1.62 – 1.53 (m, 2H), 1.23 (dd, *J* = 12.4, 5.6 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.32, 179.29, 152.42,

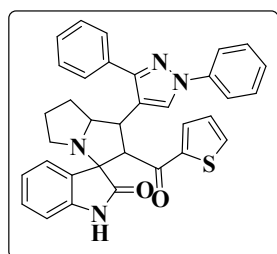
147.75, 142.36, 140.00, 138.53, 134.28, 134.17, 130.33, 130.05, 129.92, 129.13, 128.90, 128.56, 127.66, 127.14, 126.76, 126.52, 124.85, 122.81, 121.88, 120.52, 118.50, 110.21, 73.37, 72.87, 64.39, 47.75, 42.28, 29.94, 27.04. HRMS (ESI, *m/z*): [M+H]⁺calcd. for C₃₆H₂₉N₅O₄: 596.2292; Found: 596.2290.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(furan-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indo line-3,3'-pyrrolizin]-2-one (4g). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3214, 1719, 1669, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.36 (s, 1H), 8.85 (s, 1H), 7.86 (dd, *J* = 11.6, 8.0 Hz, 4H), 7.80 (s, 1H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.51 (dd, *J* = 13.6, 7.6 Hz, 3H), 7.29 (dd, *J* = 15.2, 7.2 Hz, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.97 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.08 (t, *J* = 11.2 Hz, 1H), 3.78 (dd, *J* = 16.4, 7.6 Hz, 1H), 2.45 (dd, *J* = 12.0, 7.6 Hz, 1H), 2.35 (dd, *J* = 12.0, 5.6 Hz, 1H), 1.74 (dd, 11.6, 5.2 Hz, 1H), 1.65 – 1.55



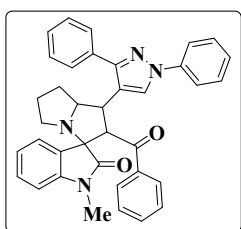
(m, 2H), 1.24 (dd, 12.0, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 184.07, 179.64, 152.41, 152.07, 148.98, 142.31, 139.90, 133.93, 129.93, 129.80, 129.06, 128.84, 128.55, 128.19, 127.29, 127.01, 126.57, 125.13, 121.65, 120.68, 120.43, 118.50, 112.85, 110.31, 73.60, 73.18, 63.32, 47.65, 42.29, 29.93, 27.10. HRMS (ESI, m/z): [M+H]⁺calcd. for C₃₄H₂₈N₄O₃: 541.2234; Found: 541.2232.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(thiophene-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4h). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3203, 1719, 1657, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.30 (s, 1H), 8.90 (s, 1H), 7.86 (dd, *J* = 13.6, 7.2 Hz, 4H), 7.81 (d, *J* = 3.6 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.49 (dd, *J* = 15.2, 8.0 Hz, 4H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.13 (dd, *J* = 8.8, 5.2 Hz, 2H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.61 (d, *J* = 7.6 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.16 (t, *J* = 11.6 Hz, 1H), 3.77 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.41 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.32 (dd, *J* = 10.4, 5.2 Hz, 1H), 1.68 (dd, *J* = 12.0, 5.4 Hz, 1H), 1.60 (dd, *J* = 13.6, 6.4 Hz, 2H), 1.22 (dd, *J* = 12.0, 6.4 Hz, 1H). ¹³C NMR



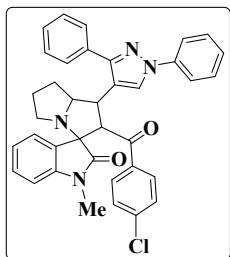
(101 MHz, DMSO-*d*₆) δ: 189.54, 179.69, 152.43, 144.14, 142.22, 139.89, 136.29, 134.37, 133.95, 129.93, 129.79, 129.09, 128.84, 128.57, 127.24, 127.01, 126.56, 125.13, 121.74, 120.41, 118.47, 110.26, 79.62, 73.74, 73.30, 63.89, 47.75, 42.62, 29.97, 27.11. HRMS (ESI, m/z): [M+H]⁺calcd. for C₃₄H₂₈N₄O₂S: 557.2006; Found: 557.2010.

(dl)-2'-benzoyl-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-1',2',5',6',7',7a'-hexahydrospiro[indo line-3,3'-pyrrolizin]-2-one (4i). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1713, 1682, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.97 (s, 1H), 7.93 – 7.90 (m, 4H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 8.0 Hz, 4H), 7.27 (dd, *J* = 5.6, 2.8 Hz, 4H), 7.21 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.05 (dd, *J* = 9.6, 7.6 Hz, 2H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.14 (d, *J* = 11.6 Hz, 1H), 4.08 (t, 1H), 3.80 – 3.73 (m, 1H), 2.59 (s, 3H), 2.38 (dd, *J* = 16.8, 7.2 Hz, 1H), 2.27 (dd, *J* = 11.6, 6.0 Hz, 1H), 1.65 (dd, *J* = 12.4, 5.6 Hz, 1H) 1.63

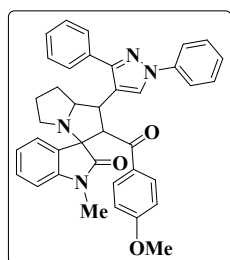


(dd, *J* = 15.2, 7.2 Hz, 2H), 1.24 (dd, *J* = 12.4, 6.8 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 198.26, 177.67, 152.40, 143.56, 140.00, 137.43, 134.22, 133.22, 129.90, 129.11, 128.91, 128.52, 128.29, 128.05, 126.94, 126.47, 126.35, 124.50, 122.33, 120.79, 118.46, 108.98, 73.55, 72.95, 64.52, 47.79, 42.11, 30.17, 27.29, 26.14. HRMS (ESI, m/z): [M+H]⁺calcd. for C₃₇H₃₂N₄O₂: 565.2598; Found: 565.2605.

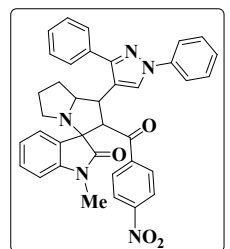
(dl)-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-1',2',5',6',7',7a'-hexahydro spiro[indoline-3,3'-pyrrolizin]-2-one (4j). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1714, 1682, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.96 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 4H), 7.61 (t, *J* = 7.6 Hz, 2H), 7.50 (dd, *J* = 16.0, 8.4 Hz, 3H), 7.37 (d, *J* = 8.8 Hz, 2H), 7.29 (t, *J* = 8.8 Hz, 3H), 7.23 (dd, *J* = 7.6, 4.0 Hz, 1H), 7.09 – 7.02 (m, 2H), 6.67 (d, *J* = 7.6 Hz, 1H), 5.12 (d, *J* = 11.6 Hz, 1H), 4.03 (t, *J* = 11.6, Hz, 1H), 3.76 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.66 (s, 3H), 2.37 (dd, *J* = 13.2, 6.4 Hz, 1H), 2.27 (dd, *J* = 15.2, 5.6 Hz, 1H) 1.72 – 1.54 (m, 3H), 1.23 (dd, *J* = 11.6, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.27, 177.61, 152.38, 143.48, 139.98, 138.28, 136.03, 134.17, 130.10, 129.91, 129.12, 128.88, 128.54, 128.44, 127.02, 126.51, 126.37, 124.36, 122.46, 120.62, 118.46, 109.11, 73.53, 72.88, 64.56, 47.78, 42.06, 30.14, 27.27, 26.20. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₇H₃₁ClN₄O₂: 599.2208; Found: 599.2221.



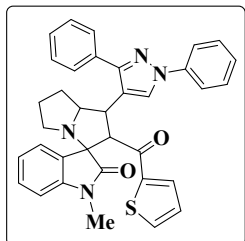
(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1-methyl-1',2',5',6',7',7a'-hexahydro spiro[indoline-3,3'-pyrrolizin]-2-one (4k). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1712, 1671, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.93 (s, 1H), 7.91 (t, *J* = 8.0 Hz, 4H), 7.61 (t, *J* = 7.6 Hz, 2H), 7.52 – 7.46 (m, 3H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.20 (dd, *J* = 7.6, 4.0 Hz, 1H), 7.05 (d, *J* = 4.4 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 7.6 Hz, 1H), 5.07 (d, *J* = 11.2 Hz, 1H), 4.10 – 4.00 (m, 1H), 3.77 (s, 3H), 3.64 – 3.50 (m, 1H), 2.70 (s, 3H), 2.39 (dd, *J* = 15.2, 8.0 Hz, 1H), 2.27 (dd, *J* = 15.4, 5.6 Hz, 1H), 1.67 (dd, *J* = 12.0, 5.2 Hz, 1H), 1.60 (dd, *J* = 14.0, 8.8 Hz, 2H), 1.23 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 195.98, 177.91, 163.39, 152.40, 143.51, 139.98, 134.21, 130.53, 130.20, 129.99, 129.89, 129.82, 129.08, 128.90, 128.50, 128.19, 126.93, 126.46, 124.61, 122.25, 120.84, 118.85, 118.44, 113.58, 108.93, 73.48, 73.16, 63.95, 55.98, 47.82, 42.26, 30.13, 27.27, 26.33. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₈H₃₄N₄O₃: 595.2704; Found: 595.2720.



(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydro spiro[indoline-3,3'-pyrrolizin]-2-one (4l). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1715, 1610, 1531. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.00 (s, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.90 (dd, *J* = 8.8, 3.2 Hz, 5H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.61 (q, *J* = 8.0 Hz, 3H), 7.53-7.48 (m, 3H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.12 – 7.03 (m, 2H), 6.59 (d, *J* = 7.8 Hz, 1H), 5.21 (d, *J* = 11.6 Hz, 1H), 4.04 (t, *J* = 11.2 Hz, 1H), 3.78 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.60 (s, 3H), 2.39 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.27 (dd, *J* = 15.2, 5.6 Hz, 1H), 1.67 (dd, *J* = 12.4, 5.6 Hz, 1H), 1.60 (dd, *J* = 13.2, 6.4 Hz, 2H), 1.24 (dd, *J* = 12.0, 5.6 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ: 195.68, 178.51, 153.06, 147.91, 143.28, 139.92, 138.46, 133.64, 133.20, 129.88, 129.38, 129.12, 129.08, 128.61, 128.17, 126.97, 126.69, 126.37, 125.28, 124.27, 122.68, 122.66, 120.34, 118.92, 108.19, 73.41, 72.90, 65.56, 48.39, 42.52, 29.71, 26.62, 26.16. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₇H₃₁N₅O₄: 610.2449; Found: 610.2455.

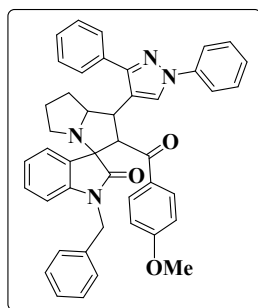


(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-2'-(thiophene-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4m). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1712, 1655, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.91 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 4H), 7.82 (d, *J* = 4.4 Hz, 1H), 7.65 (d, *J* = 3.2 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 14.8, 7.2 Hz, 4H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 7.08 (t, *J* = 5.6 Hz, 2H), 6.75 (d, *J* = 7.8 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.10 (t, *J* = 12.0 Hz, 1H), 3.79 (dd, *J* = 16.4, 6.4 Hz, 1H), 2.84 (s, 3H), 2.42 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.31 (dd, *J* = 11.2, 6.0 Hz, 1H), 1.71 – 1.58 (m, 3H), 1.24 (dd, *J* = 12.4, 6.8 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 189.32, 178.03, 152.42, 143.72, 143.45, 139.91, 136.09, 134.01, 133.87, 129.92, 129.09, 128.86, 128.56, 128.45, 127.04, 126.63, 126.54, 124.46, 122.49, 120.33, 118.47, 109.08, 79.62, 73.64, 73.42, 64.88, 47.85, 42.20, 30.08, 27.27, 26.40. HRMS (ESI, m/z): [M+H]⁺calcd. For C₃₅H₃₀N₄O₂S: 571.2162; Found: 571.2173.



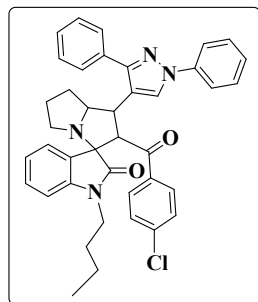
HRMS (ESI, m/z): [M+H]⁺calcd. For C₃₅H₃₀N₄O₂S: 571.2162; Found: 571.2173.

(dl)-1-benzyl-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydro spiroindoline-3,3'-pyrrolizin]-2-one (4n). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1714, 1668, 1600. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.98 (s, 1H), 7.91 (t, *J* = 7.6 Hz, 4H), 7.61 (t, *J* = 7.6 Hz, 2H), 7.54 – 7.46 (m, 6H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.18 (d, *J* = 6.4 Hz, 2H), 7.12 (t, *J* = 9.6 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 7.6 Hz, 1H), 5.24 (d, *J* = 11.6 Hz, 1H), 4.71 (d, *J* = 16.0 Hz, 1H), 4.45 (d, *J* = 16.0 Hz, 1H), 4.17 (t, *J* = 10.8 Hz, 1H), 3.83 (t, *J* = 9.2 Hz, 1H), 3.79 (s, 3H), 2.37 – 2.27 (m, 2H), 1.69 (dd, *J* = 11.6, 5.6 Hz, 1H), 1.64 – 1.56 (m, 2H), 1.23 (dd, *J* = 11.6, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 195.61, 178.08, 163.75, 152.44, 142.73, 139.96, 136.33, 134.11, 130.92, 130.07, 129.91, 129.74, 129.10, 128.94, 128.89, 128.54, 127.65, 127.16, 127.00, 126.50, 124.74, 122.39, 120.68, 118.46, 113.97, 109.70, 73.33, 72.98, 62.56, 56.00, 47.61, 43.18, 42.85, 30.10, 27.27. HRMS (ESI, m/z): [M+H]⁺ calcd. for C₄₄H₃₈N₄O₃: 671.3017; Found: 671.3022.



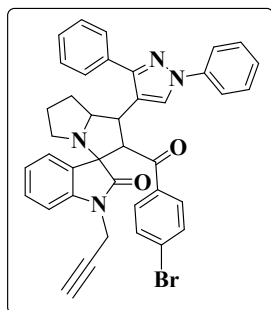
HRMS (ESI, m/z): [M+H]⁺ calcd. for C₄₄H₃₈N₄O₃: 671.3017; Found: 671.3022.

(dl)-1-butyl-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydro spiroindoline-3,3'-pyrrolizin]-2-one (4o). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1710, 1681, 1600. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.99 (s, 1H), 7.89 (t, *J* = 6.8 Hz, 4H), 7.62 (t, *J* = 8.0 Hz, 2H), 7.50 (dd, *J* = 16.0, 8.8 Hz, 4H), 7.37 (d, *J* = 1.2 Hz, 3H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.24 (dd, *J* = 8.8, 4.0 Hz, 1H), 7.07 (d, *J* = 4.0 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 5.20 (d, *J* = 12.0 Hz, 1H), 4.08 (t, *J* = 11.2 Hz, 1H), 3.76 (dd, *J* = 16.0, 6.4 Hz, 1H), 3.22 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.28 (dd, *J* = 13.6, 6.4 Hz, 2H), 1.67 (dd, *J* = 12.0, 5.6 Hz, 1H), 1.59 (t, *J* = 6.8 Hz, 2H), 1.25-1.19 (m, 2H), 1.07 (dd, *J* = 16.0, 6.4 Hz, 3H), 0.92 (dd, *J* = 13.6, 6.4 Hz, 1H), 0.81 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.25, 177.27, 152.41, 142.99, 139.95, 138.58, 136.13, 134.10, 130.10, 129.92, 129.13, 128.88, 128.73, 128.57, 127.03, 126.77, 126.53, 124.45, 122.23, 120.49, 118.45, 109.29, 73.41, 72.65, 63.52, 47.56, 42.39, 30.16, 28.99, 27.30, 19.84, 14.12. HRMS (ESI, m/z): [M+H]⁺calcd. for C₄₀H₃₇ClN₄O₂: 641.2678; Found: 641. 2693.

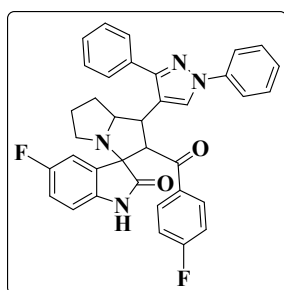


HRMS (ESI, m/z): [M+H]⁺calcd. for C₄₀H₃₇ClN₄O₂: 641.2678; Found: 641. 2693.

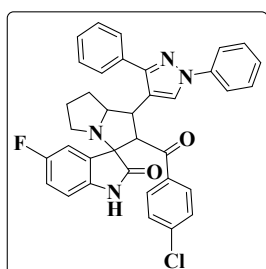
(dl)-2'-(4-bromobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-(prop-2-yn-1-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4p). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1721, 1680, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.96 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 4H), 7.60 (t, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 5H), 7.28 (d, *J* = 8.4 Hz, 4H), 7.09 (d, *J* = 6.4 Hz, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 5.16 (d, *J* = 12.0 Hz, 1H), 4.29 (dd, *J* = 17.6, 2.4 Hz, 1H), 4.10 – 3.99 (m, 3H), 3.79 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.37 (d, *J* = 6.4 Hz, 1H), 2.27 (dd, *J* = 10.8, 5.6 Hz, 1H), 1.68 (dd, *J* = 12.4, 5.6 Hz, 1H), 1.60 (dd, *J* = 12.0, 6.4 Hz, 2H), 1.24 (dd, *J* = 12.4, 5.6 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ: 196.13, 177.81, 153.10, 141.40, 139.93, 135.76, 133.73, 131.65, 129.58, 129.37, 129.31, 129.11, 128.60, 128.13, 127.09, 126.34, 125.06, 124.28, 122.82, 120.28, 118.95, 109.37, 73.47, 73.05, 72.33, 64.22, 48.24, 42.62, 30.04, 29.71, 29.37, 26.88. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₉H₃₁BrN₄O₂: 667.1703; Found: 667.1718.



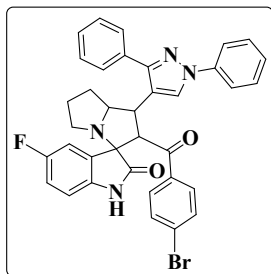
(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(4-fluorobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4q). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3210, 1723, 1681, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.18 (s, 1H), 8.97 (s, 1H), 7.88 (dd, *J* = 7.6, 5.6 Hz, 4H), 7.60 (t, *J* = 7.6 Hz, 4H), 7.50 (dd, *J* = 15.2, 7.6 Hz, 3H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 8.8 Hz, 2H), 7.00 (t, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.53 (dd, *J* = 8.4, 4.4 Hz, 1H), 5.17 (d, *J* = 12.0 Hz, 1H), 4.01 (t, *J* = 11.2 Hz, 1H), 3.83 – 3.70 (m, 1H), 2.42 – 2.36 (m, 1H), 2.34 (d, *J* = 4.8 Hz, 1H), 1.87 – 1.67 (m, 1H), 1.64 (dd, *J* = 12.0, 5.6 Hz, 2H), 1.24 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 196.67, 179.22, 166.75, 164.24, 158.92, 156.56, 152.43, 139.94, 138.59, 134.05, 133.94, 131.46, 131.37, 129.93, 129.07, 128.90, 128.61, 127.09, 126.54, 120.36, 118.45, 116.56, 116.33, 115.86, 115.64, 114.50, 114.25, 111.07, 110.99, 73.45, 73.33, 63.53, 47.57, 42.42, 30.10, 27.44. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈F₂N₄O₂: 587.2253; Found: 587.2266.



(dl)-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4r). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3210, 1722, 1681, 1597. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.23 (s, 1H), 8.98 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.95 (t, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 3H), 7.68 (dd, *J* = 8.4, 4.4 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.51 (dd, *J* = 8.4, 6.4 Hz, 3H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.8 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.55 (dd, *J* = 8.4, 4.4 Hz, 1H), 5.17 (d, *J* = 11.2 Hz, 1H), 4.02 (t, *J* = 10.4 Hz, 1H), 3.80 (d, *J* = 8.0 Hz, 1H), 2.41 (d, *J* = 7.6 Hz, 1H), 2.35 (d, *J* = 6.4 Hz, 1H), 1.79 – 1.68 (m, 1H), 1.65 (dd, *J* = 12.0, 6.4 Hz, 2H), 1.26 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.12, 188.08, 179.05, 158.94, 156.58, 152.42, 139.94, 138.78, 136.80, 135.86, 135.21, 134.03, 130.60, 130.24, 129.93, 129.43, 129.40, 129.08, 128.94, 128.90, 128.83, 128.62, 127.12, 126.55, 121.53, 120.25, 119.21, 118.46, 118.24, 116.67, 116.44, 114.52, 114.27, 111.15, 111.07, 73.41, 73.35, 63.54, 47.63, 42.35, 30.07, 27.42. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈ClFN₄O₂: 603.1958; Found: 603.1968.

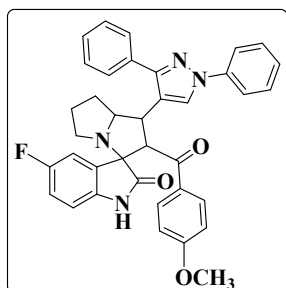


(dl)-2'-(4-bromobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4s). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3213, 1719, 1682, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.20 (s, 1H), 8.97 (s, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 3H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.56 – 7.51 (m, 4H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 10.4 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.54 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.16 (d, *J* = 11.6 Hz, 1H), 4.04 – 3.97 (m, 1H), 3.77 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.39 (dd, *J* = 10.4, 7.6 Hz, 1H), 2.33 (dd, *J* = 10.4, 5.2 Hz, 1H), 1.69 (dd, *J* = 11.6, 5.2 Hz, 1H), 1.66 – 1.60 (m, 2H), 1.24 (dd, *J* = 11.6, 6.2 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.35, 188.34, 179.22, 158.95, 156.58, 153.59, 153.57, 152.44, 139.92, 138.56, 136.17, 134.02, 132.37, 131.77, 130.70, 130.31, 130.24, 129.93, 129.40, 129.07, 128.94, 128.90, 128.63, 128.02, 127.07, 126.77, 126.70, 126.57, 120.31, 119.23, 118.47, 116.62, 116.38, 114.47, 114.22, 111.14, 111.07, 105.53, 73.43, 73.31, 63.56, 47.53, 42.40, 30.11, 27.44. HRMS (ESI, m/z): [M+H]⁺ calcd. for C₃₆H₂₈BrFN₄O₂: 647.1452; Found: 647.1458.



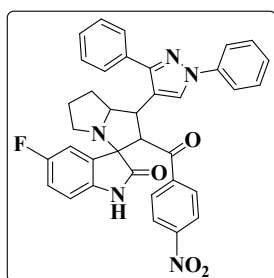
(101 MHz, DMSO-*d*₆) δ: 197.35, 188.34, 179.22, 158.95, 156.58, 153.59, 153.57, 152.44, 139.92, 138.56, 136.17, 134.02, 132.37, 131.77, 130.70, 130.31, 130.24, 129.93, 129.40, 129.07, 128.94, 128.90, 128.63, 128.02, 127.07, 126.77, 126.70, 126.57, 120.31, 119.23, 118.47, 116.62, 116.38, 114.47, 114.22, 111.14, 111.07, 105.53, 73.43, 73.31, 63.56, 47.53, 42.40, 30.11, 27.44. HRMS (ESI, m/z): [M+H]⁺ calcd. for C₃₆H₂₈BrFN₄O₂: 647.1452; Found: 647.1458.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydro spiro[indoline-3,3'-pyrrolizin]-2-one (4t). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3209, 1722, 1669, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.19 (s, 1H), 8.94 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 4H), 7.59 (t, *J* = 8.8 Hz, 4H), 7.49 (dd, *J* = 15.6, 8.0 Hz, 3H), 7.28 (t, *J* = 7.2 Hz, 1H), 6.99 (t, *J* = 10.8 Hz, 1H), 6.83 (t, *J* = 9.2 Hz, 3H), 6.55 (dd, *J* = 8.4, 4.4 Hz, 1H), 5.13 (d, *J* = 11.6 Hz, 1H), 4.04 (t, *J* = 11.2 Hz, 1H), 3.88 (s, 1H), 3.78 (s, 3H), 2.40 (dd, *J* = 10.8, 7.6 Hz, 1H), 2.34 (dd, *J* = 10.4, 5.2 Hz, 1H), 1.73 – 1.67 (m, 1H), 1.63 (dd, *J* = 12.4, 6.2 Hz, 2H), 1.23 (dd, *J* = 11.6, 6.2 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 195.77, 179.38, 163.71, 158.84, 156.49, 152.45, 139.94, 138.59, 134.06, 130.94, 130.11, 129.91, 129.03, 128.90, 128.59, 127.00, 126.51, 120.49, 118.45, 116.33, 116.09, 114.68, 114.44, 113.96, 110.93, 110.85, 73.67, 73.27, 62.78, 55.96, 47.57, 42.72, 30.11, 27.43. HRMS (ESI, m/z): [M+H]⁺ calcd. for C₃₇H₃₁FN₄O₃: 599.2453; Found: 599.2464.



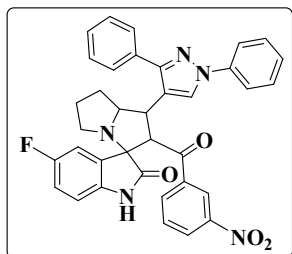
(101 MHz, DMSO-*d*₆) δ: 195.77, 179.38, 163.71, 158.84, 156.49, 152.45, 139.94, 138.59, 134.06, 130.94, 130.11, 129.91, 129.03, 128.90, 128.59, 127.00, 126.51, 120.49, 118.45, 116.33, 116.09, 114.68, 114.44, 113.96, 110.93, 110.85, 73.67, 73.27, 62.78, 55.96, 47.57, 42.72, 30.11, 27.43. HRMS (ESI, m/z): [M+H]⁺ calcd. for C₃₇H₃₁FN₄O₃: 599.2453; Found: 599.2464.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4u). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3124, 1736, 1693, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.09 (s, 1H), 9.01 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 2H), 7.89 (t, *J* = 8.4 Hz, 4H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.51 (dd, *J* = 15.6, 8.0 Hz, 3H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 9.2 Hz, 1H), 6.82 (d, *J* = 10.0 Hz, 1H), 6.50 (dd, *J* = 8.4, 4.4 Hz, 1H), 5.25 (d, *J* = 11.6 Hz, 1H), 3.99 (t, *J* = 11.2 Hz, 1H), 3.79 (dd, *J* = 16.0, 9.2 Hz, 1H), 2.37 (dd, *J* = 12.4, 6.2 Hz, 2H), 1.65 (dd, *J* = 13.2, 6.2 Hz, 3H), 1.26 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.87, 179.04, 159.05, 156.69, 152.43, 150.27, 142.00, 139.95, 138.60, 138.58, 134.04, 132.25, 130.25, 130.01, 129.94, 129.70, 129.42, 127.16, 126.57, 124.42, 123.68, 120.22, 120.18, 119.26, 118.47, 116.87, 116.64, 114.34, 114.12, 111.35, 111.27, 73.41, 73.32, 64.62, 47.48, 42.21, 30.22, 27.55. HRMS (ESI, m/z): [M+H]⁺ calcd. For C₃₆H₂₈FN₅O₄: 614.2198; Found: 614.2206.



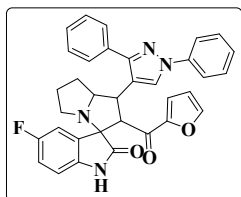
(101 MHz, DMSO-*d*₆) δ: 197.87, 179.04, 159.05, 156.69, 152.43, 150.27, 142.00, 139.95, 138.60, 138.58, 134.04, 132.25, 130.25, 130.01, 129.94, 129.70, 129.42, 127.16, 126.57, 124.42, 123.68, 120.22, 120.18, 119.26, 118.47, 116.87, 116.64, 114.34, 114.12, 111.35, 111.27, 73.41, 73.32, 64.62, 47.48, 42.21, 30.22, 27.55. HRMS (ESI, m/z): [M+H]⁺ calcd. For C₃₆H₂₈FN₅O₄: 614.2198; Found: 614.2206.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(3-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4v). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3179, 1717, 1689, 1600. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.15 (s, 1H), 9.01 (s, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.17 (t, *J* = 7.6 Hz, 1H), 7.88 (dd, *J* = 7.6, 5.6 Hz, 4H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.61 (dd, *J* = 14.0, 8.0 Hz, 3H), 7.53 – 7.47 (m, 3H), 7.29 (t, *J* = 7.6 Hz, 1H), 6.99 (td, *J* = 9.2, 2.4 Hz, 1H), 6.81 (dd, *J* = 8.8, 4.4 Hz, 1H), 6.44 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.23 (d, *J* = 11.6 Hz, 1H), 4.05 – 3.96 (m, 1H), 3.84 – 3.76 (m, 1H), 2.40 (dt, *J* = 12.4, 6.4 Hz, 1H), 2.34 (dd, *J* = 12.0, 5.6 Hz, 1H), 1.73 – 1.67 (m, 1H), 1.64 (dd, *J* = 12.4, 6.4 Hz, 2H), 1.26 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C



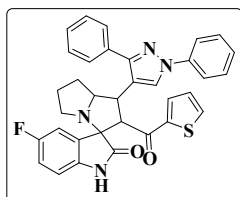
NMR (101 MHz, DMSO-*d*₆) δ: 197.04, 179.15, 159.05, 156.68, 152.45, 147.85, 139.97, 138.60, 138.24, 134.36, 134.09, 130.52, 129.93, 129.08, 128.94, 128.62, 127.95, 127.25, 126.61, 126.55, 122.92, 120.17, 118.50, 116.76, 116.53, 114.32, 114.07, 111.17, 111.09, 73.27, 73.25, 64.38, 47.56, 42.30, 30.03, 27.39. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈FN₅O₄: 614.2198; Found: 614.2194.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(furan-2-carbonyl)-1',2',5',6',7',7a'-hexahydro spiro[indoline-3,3'-pyrrolizin]-2-one (4w). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3222, 1723, 1669, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.40 (s, 1H), 8.86 (s, 1H), 7.87 (dd, *J* = 20.4, 8.0 Hz, 4H), 7.57 (t, *J* = 7.2 Hz, 2H), 7.49 (dd, *J* = 13.2, 7.6 Hz, 4H), 7.34 (d, *J* = 3.2 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.02 (t, *J* = 9.6 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.68 (dd, *J* = 8.4, 4.4 Hz, 1H), 6.61 (s, 1H), 4.80 (d, *J* = 11.6 Hz, 1H), 4.02 (t, *J* = 11.2 Hz, 1H), 3.80 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.40 (dd, *J* = 24.4, 8.4 Hz, 2H), 1.66 (dd, *J*



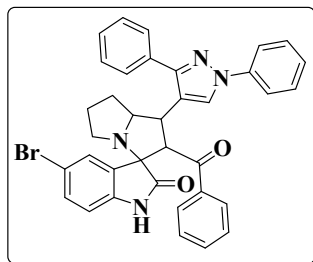
= 13.2, 7.6 Hz, 2H), 1.26 (dd, *J* = 11.2, 6.4 Hz, 1H), 1.13 (t, *J* = 7.2 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 183.89, 179.44, 158.88, 156.52, 152.42, 151.99, 149.27, 139.88, 138.55, 133.86, 129.94, 129.22, 129.02, 128.87, 128.62, 128.19, 127.13, 126.96, 126.89, 126.60, 125.93, 121.04, 120.05, 118.49, 114.86, 114.61, 112.95, 111.15, 111.07, 73.90, 73.13, 63.40, 47.50, 42.30, 30.01, 27.41. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₄H₂₇FN₄O₃: 559.2140; Found: 559.2142.

(dl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(thiophene-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4x). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 1722, 1656, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.36 (s, 1H), 8.92 (s, 1H), 7.90 – 7.85 (m, 4H), 7.83 (s, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.49 (dd, *J* = 15.2, 7.6 Hz, 4H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 4.8 Hz, 1H), 7.01 (td, *J* = 10.4, 4.0 Hz, 1H), 6.85 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.63 (dd, *J* = 8.8, 4.4 Hz, 1H), 5.01 (d, *J* = 11.2 Hz, 1H), 4.07 – 3.98 (m, 1H), 3.80 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.43 (dd, *J* = 11.6, 4.4 Hz, 1H), 2.36



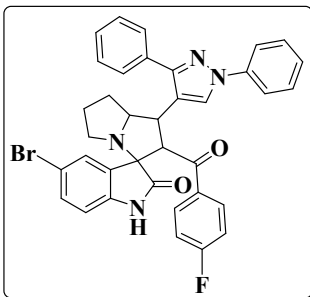
(dd, *J* = 10.4, 5.2 Hz, 1H), 1.74 – 1.69 (m, 1H), 1.65 (dd, *J* = 13.2, 5.6 Hz, 2H), 1.25 (dd, *J* = 11.2, 6.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 189.43, 179.48, 156.58, 152.45, 144.02, 139.90, 138.52, 136.63, 134.63, 133.91, 129.92, 129.03, 128.95, 128.87, 128.62, 127.14, 126.99, 126.92, 126.57, 120.06, 118.48, 116.48, 116.24, 114.81, 114.57, 111.09, 111.02, 74.04, 73.25, 64.01, 47.59, 42.62, 30.05, 27.43. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₄H₂₇FN₄O₂S: 575.1912; Found: 575.1917.

(dl)-2'-benzoyl-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indolin-e-3,3'-pyrrolizin]-2-one (4y). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 33209, 1726, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.16 (s, 1H), 8.96 (s, 1H), 7.89 (dd, *J* = 7.6, 4.0 Hz, 4H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.54 – 7.48 (m, 6H), 7.31 (dd, 15.6, 8.0 Hz, 3H), 6.99 (t, *J* = 11.6 Hz, 1H), 6.80 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.50 (dd, *J* = 8.4, 4.4 Hz, 1H), 5.18 (d, *J* = 11.6 Hz, 1H), 4.03 (t, *J* = 11.6 Hz, 1H), 3.79 (dd, *J* = 16.0, 6.4 Hz, 1H), 2.41 (dd, *J* = 9.2, 7.6 Hz, 1H), 2.33 (dd, *J* = 11.2, 6.0 Hz, 1H), 1.70 (dd, *J* = 12.4, 5.6 Hz, 1H), 1.63 (dd, *J* = 13.6, 7.2 Hz, 2H), 1.24 (dd, *J* = 12.0, 6.8 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ:

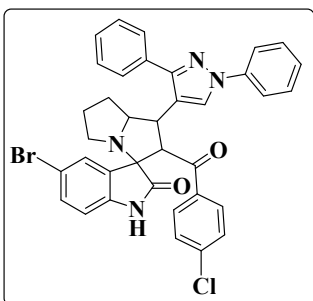


198.09, 178.73, 152.50, 141.72, 139.94, 137.19, 134.03, 133.83, 132.55, 129.92, 129.62, 129.01, 128.95, 128.72, 128.64, 128.40, 127.72, 127.04, 126.53, 120.21, 118.45, 113.28, 112.14, 73.26, 73.15, 63.18, 47.65, 42.66, 29.91, 27.31. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₉BrN₄O₂: 629.1547; Found: 629.1516.

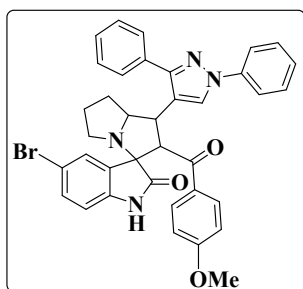
(dl)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-fluorobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4z). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3198, 1740, 1683, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.29 (s, 1H), 8.99 (s, 1H), 7.89 (dd, *J* = 11.6, 8.0 Hz, 4H), 7.60 (s, 4H), 7.49 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 6.0 Hz, 1H), 7.18 (t, *J* = 8.4 Hz, 2H), 7.13 (s, 1H), 6.52 (d, *J* = 7.6 Hz, 1H), 5.18 (d, *J* = 11.2 Hz, 1H), 4.01 (t, *J* = 12.0 Hz, 1H), 3.81 – 3.70 (m, 1H), 2.38 – 2.30 (m, 2H), 1.69 – 1.53 (m, 3H), 1.16 (dd, *J* = 10.4, 3.2 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 196.72, 178.67, 168.34, 166.79, 152.49, 141.66, 139.94, 134.03, 133.95, 133.93, 132.64, 131.48, 131.38, 129.94, 129.56, 129.02, 128.94, 128.65, 127.63, 127.10, 126.54, 120.13, 118.43, 115.91, 115.69, 113.35, 112.21, 73.35, 73.20, 63.35, 47.63, 42.52, 30.00, 27.41. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈BrFN₄O₂: 647.1452; Found: 647.1459.



(dl)-5-bromo-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4aa). White Solid. mp: 179-180 °C. IR (KBr, cm⁻¹): 3208, 1724, 1679, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.30 (s, 1H), 8.99 (s, 1H), 7.89 (dd, 10.4, 7.2 Hz, 4H), 7.60 (t, *J* = 6.8 Hz, 3H), 7.50 – 7.47 (m, 4H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.12 (s, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 5.17 (d, *J* = 11.6 Hz, 1H), 4.00 (t, *J* = 11.2 Hz, 1H), 3.77 (d, *J* = 7.6 Hz, 1H), 2.34 (s, 2H), 1.62 (dd, *J* = 10.4, 6.4 Hz, 3H), 1.17 (dd, *J* = 10.4, 4.8 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.24, 178.60, 153.24, 152.48, 141.65, 139.93, 139.42, 138.85, 136.79, 135.87, 134.01, 132.70, 132.33, 130.60, 130.25, 129.95, 129.40, 129.03, 128.94, 128.87, 128.67, 127.56, 127.11, 126.56, 121.54, 120.07, 119.21, 118.43, 113.38, 112.26, 73.32, 73.21, 63.41, 47.64, 42.48, 30.00, 27.42. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈BrClN₄O₂: 663.1157; Found: 663.1165.



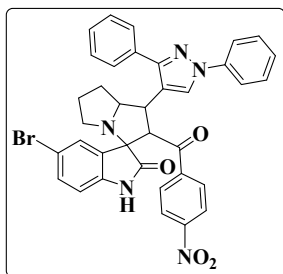
(dl)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydro spiro[indoline-3,3'-pyrrolizin]-2-one (4ab). White Solid. mp: 179-180 °C. IR (KBr,



cm⁻¹): 3118, 1721, 1668, 1598. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.31 (s, 1H), 8.96 (s, 1H), 7.90 (dd, *J* = 22.4, 7.2 Hz, 4H), 7.59 (d, *J* = 6.4 Hz, 4H), 7.49 (d, *J* = 8.4 Hz, 3H), 7.31 (dd, 16.4, 7.2 Hz, 2H), 7.17 (s, 1H), 6.86 (d, *J* = 7.6 Hz, 2H), 6.54 (d, *J* = 7.6 Hz, 1H), 5.14 (d, *J* = 11.6 Hz, 1H), 4.04 (t, *J* = 104 Hz, 1H), 3.88 (s, 1H), 3.78 (s, 3H), 2.34 (s, 2H), 1.61 (s, 3H), 1.16 (dd, *J* = 11.2, 10.4 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 195.77, 178.80, 163.77, 152.50, 141.64, 139.93, 134.02, 132.44, 130.97, 130.09, 129.92, 129.78, 128.98, 128.94, 128.63, 127.85, 127.02, 126.51, 120.24, 118.42, 113.99, 113.25, 112.11, 73.59, 73.16,

62.56, 55.97, 47.65, 42.79, 30.01, 27.41. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₇H₃₁BrN₄O₃: 659.1652; Found: 659.1658.

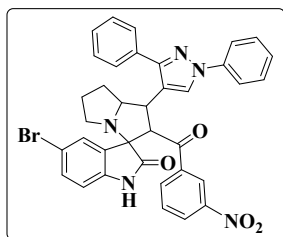
(dl)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (4ac). White Solid. mp: 179-180 °C. IR (KBr,



cm⁻¹): 3379, 1719, 1615, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.20 (s, 1H), 9.03 (s, 1H), 8.15 (d, *J* = 4.8 Hz, 2H), 7.89 (s, 4H), 7.63 (dd, *J* = 22.8, 7.6 Hz, 4H), 7.51 (d, *J* = 6.4 Hz, 3H), 7.38 (d, *J* = 6.8 Hz, 1H), 7.30 (t, *J* = 6.4 Hz, 1H), 7.12 (s, 1H), 6.49 (d, *J* = 6.4 Hz, 1H), 5.27 (d, *J* = 9.2 Hz, 1H), 4.03 – 3.92 (m, 1H), 3.81 – 3.72 (m, 1H), 2.34 (d, *J* = 4.0 Hz, 2H), 1.62 (dd, *J* = 3.6, 2.4 Hz, 3H), 1.19 (dd, *J* = 6.4, 4.0 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.92, 178.46, 152.51, 150.33, 141.96, 141.65, 139.94, 134.00, 132.94, 129.96, 129.69, 129.36, 129.06, 128.95,

128.70, 127.36, 127.17, 126.60, 123.74, 119.95, 118.46, 113.56, 112.48, 73.27, 73.21, 64.40, 47.59, 42.33, 30.07, 27.48. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈BrN₅O₄: 674.1397; Found: 674.1409.

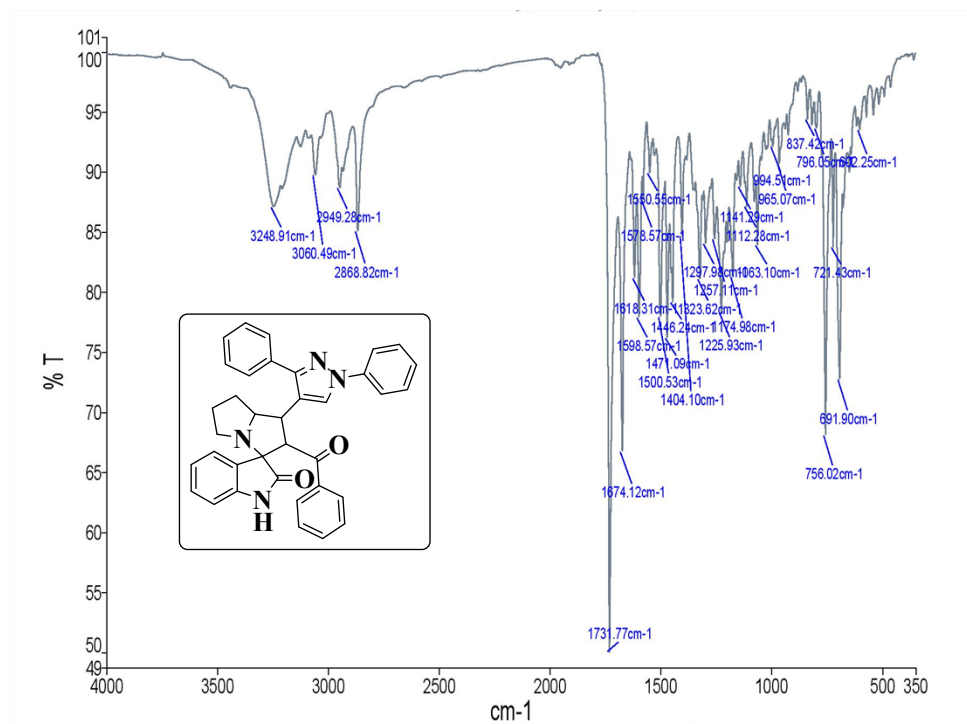
(dl)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(3-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospir -ofindoline-3,3'-pyrrolizin]-2-one (4ad): White Solid. mp: 179-180 °C. IR (KBr,



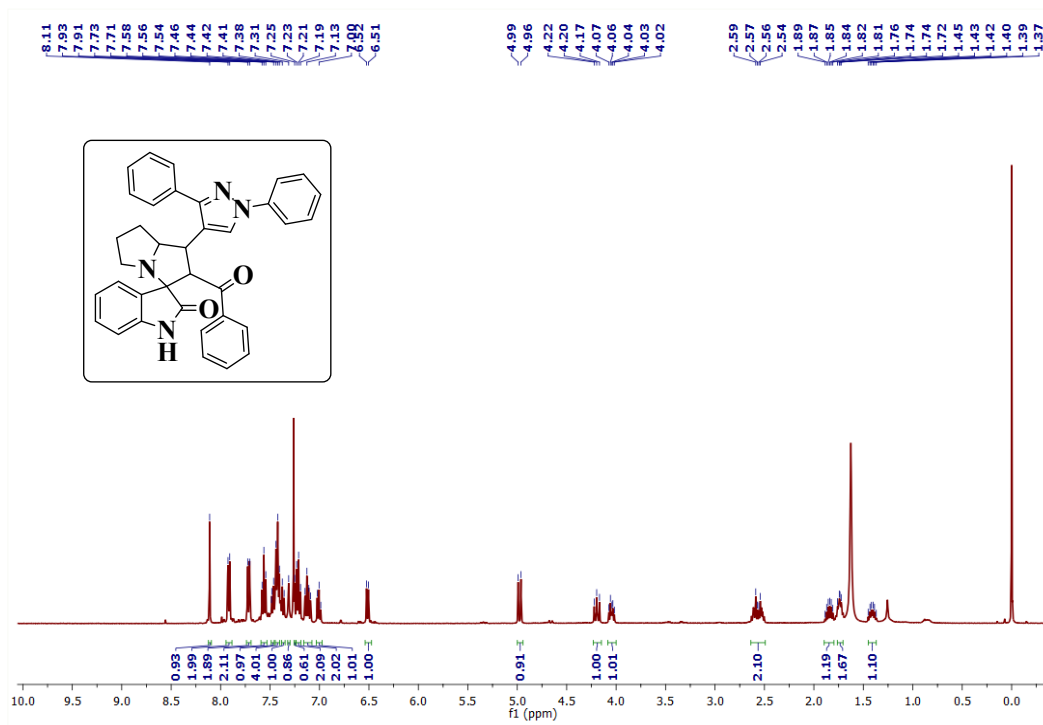
cm⁻¹): 3168, 1719, 1689, 1599. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 10.28 (s, 1H), 9.02 (s, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.18 (s, 1H), 7.89 (t, *J* = 8.8 Hz, 4H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.5–7.58 (m, 3H), 7.51 (dd, *J* = 15.6, 8.0 Hz, 3H), 7.31 (dd, *J* = 15.6, 8.8 Hz, 2H), 7.12 (s, 1H), 6.44 (d, *J* = 8.4 Hz, 1H), 5.24 (d, *J* = 11.6 Hz, 1H), 4.00 (t, *J* = 11.2 Hz, 1H), 3.80 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.35 (d, *J* = 3.2 Hz, 2H), 1.72 – 1.57 (m, 3H), 1.19 (dd, *J* = 11.6, 8.0 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 197.11,

178.57, 152.51, 147.88, 141.65, 139.97, 138.23, 134.33, 134.06, 132.84, 130.58, 129.94, 129.34, 129.04, 128.97, 128.67, 128.02, 127.42, 127.28, 126.57, 122.94, 119.92, 118.49, 113.53, 112.28, 73.14, 73.10, 64.17, 47.66, 42.38, 29.87, 27.33. HRMS (ESI, *m/z*): [M+H]⁺ calcd. for C₃₆H₂₈BrN₅O₄: 674.1397; Found: 674.1409.

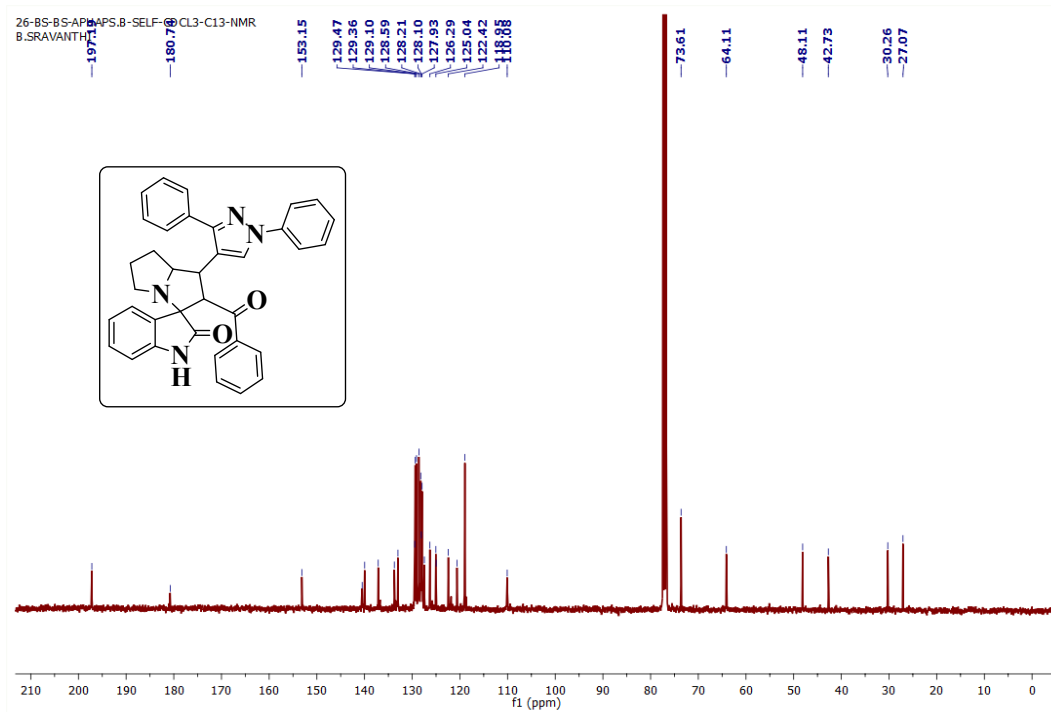
3. FT-IR, ¹H-NMR, ¹³C-NMR and Mass Spectra of the Compounds



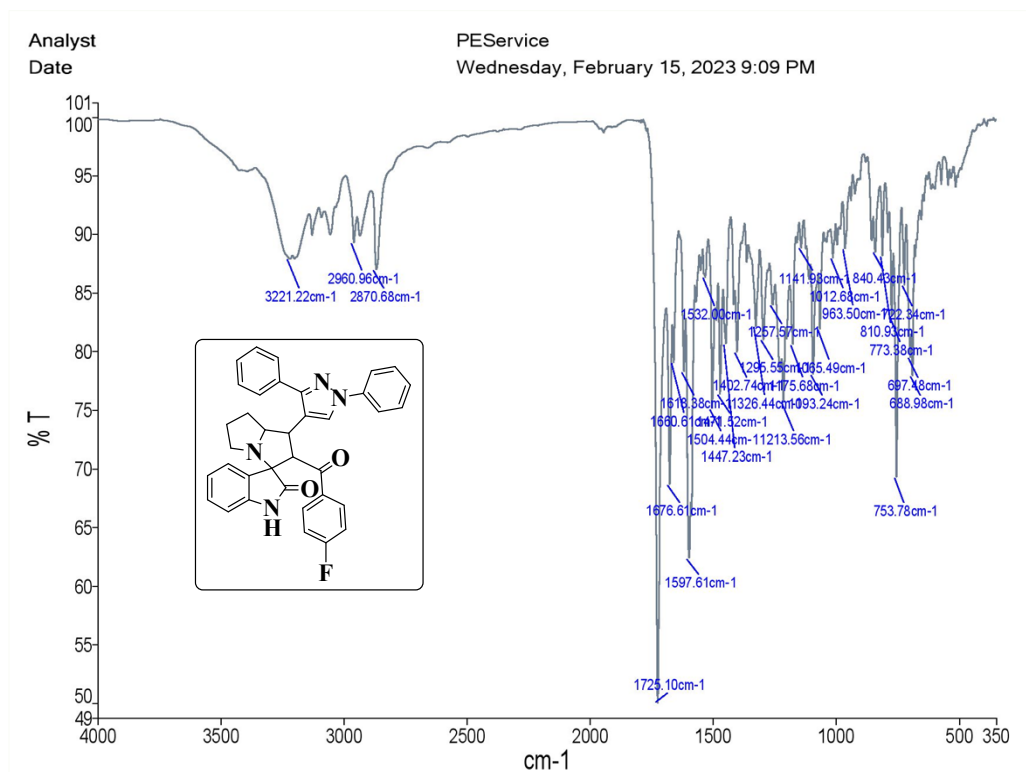
FT-IR Spectrum of the compound 4a



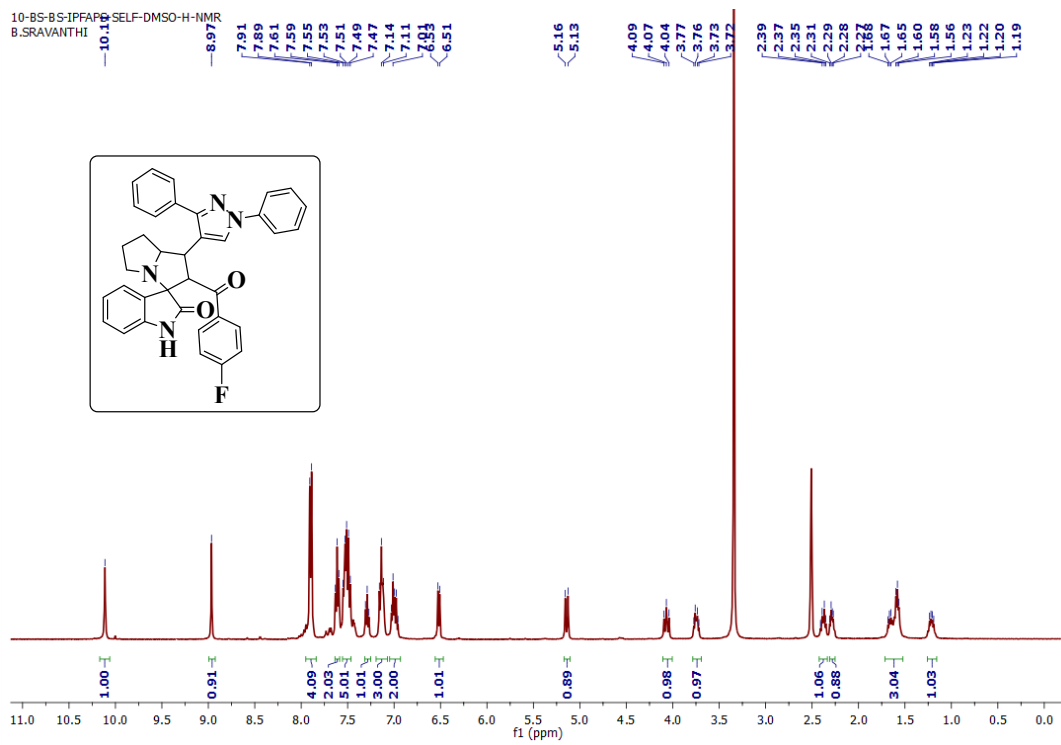
¹H NMR Spectrum of the compound 4a



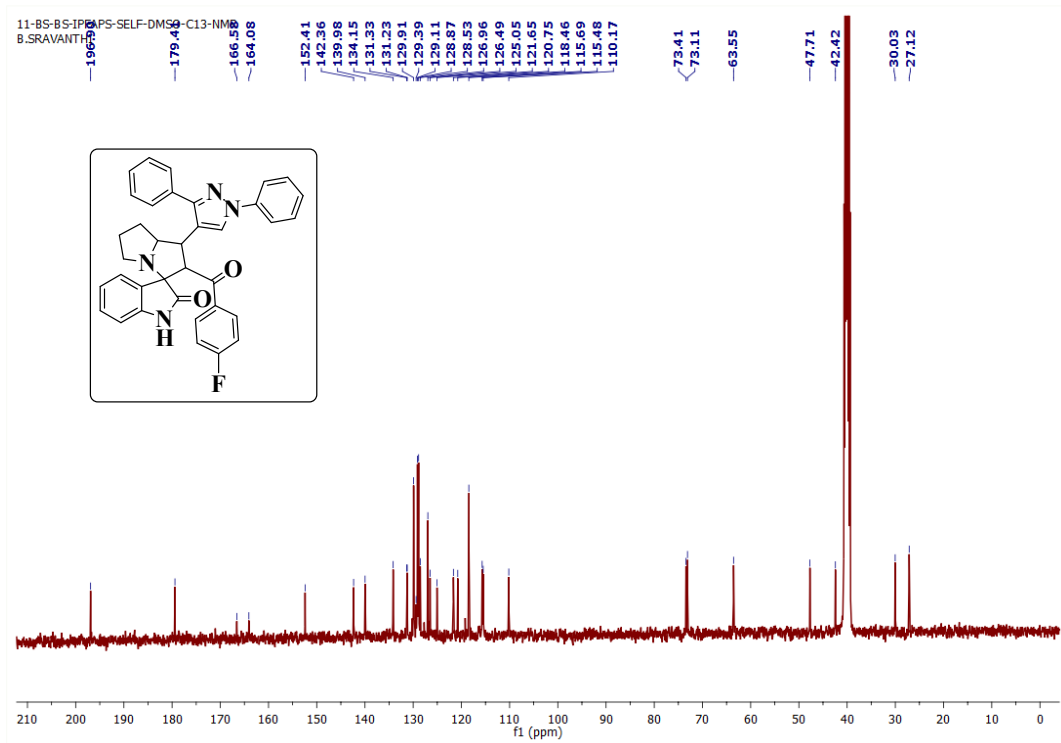
¹³C NMR Spectrum of the compound 4a



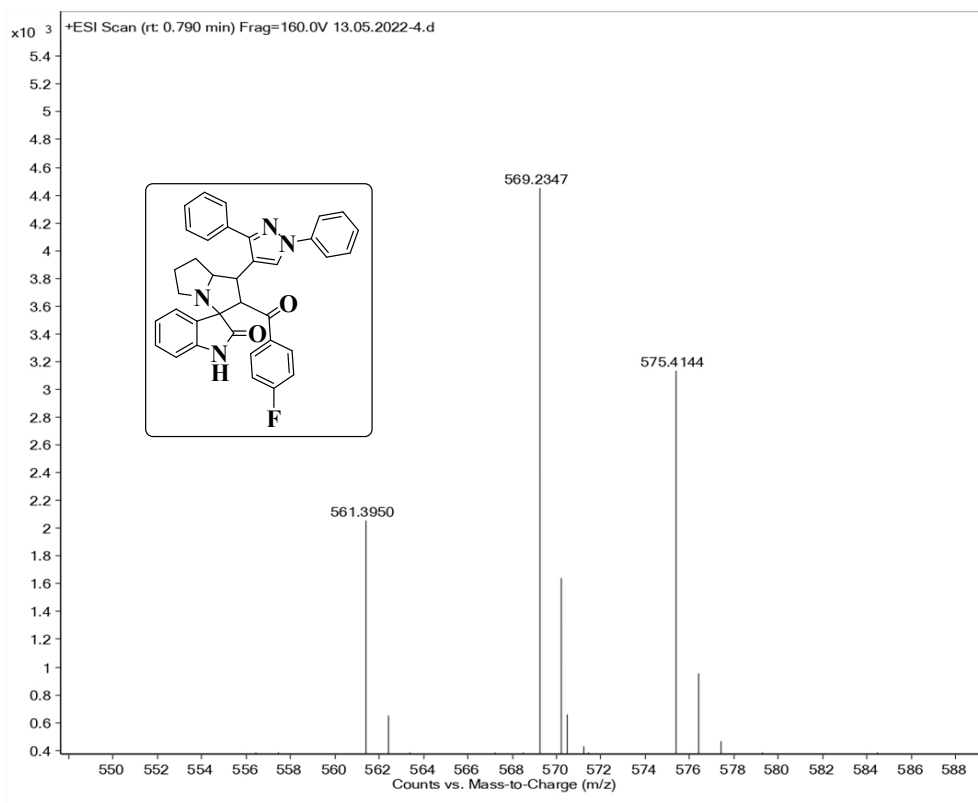
FT-IR Spectrum of the compound 4b



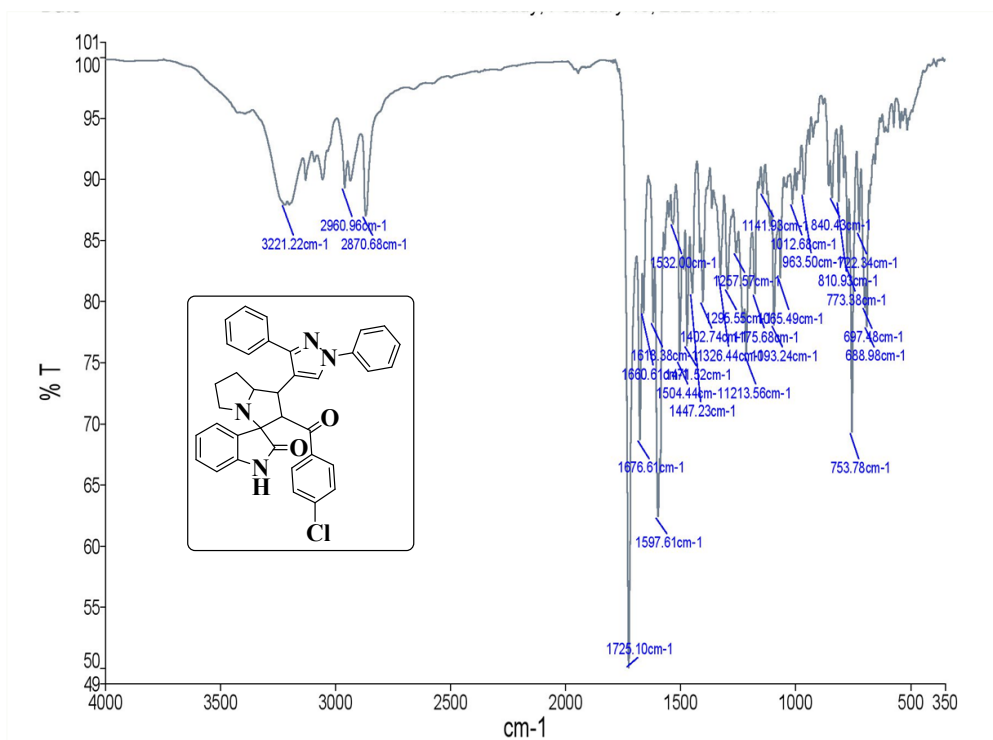
¹H NMR Spectrum of the compound 4b



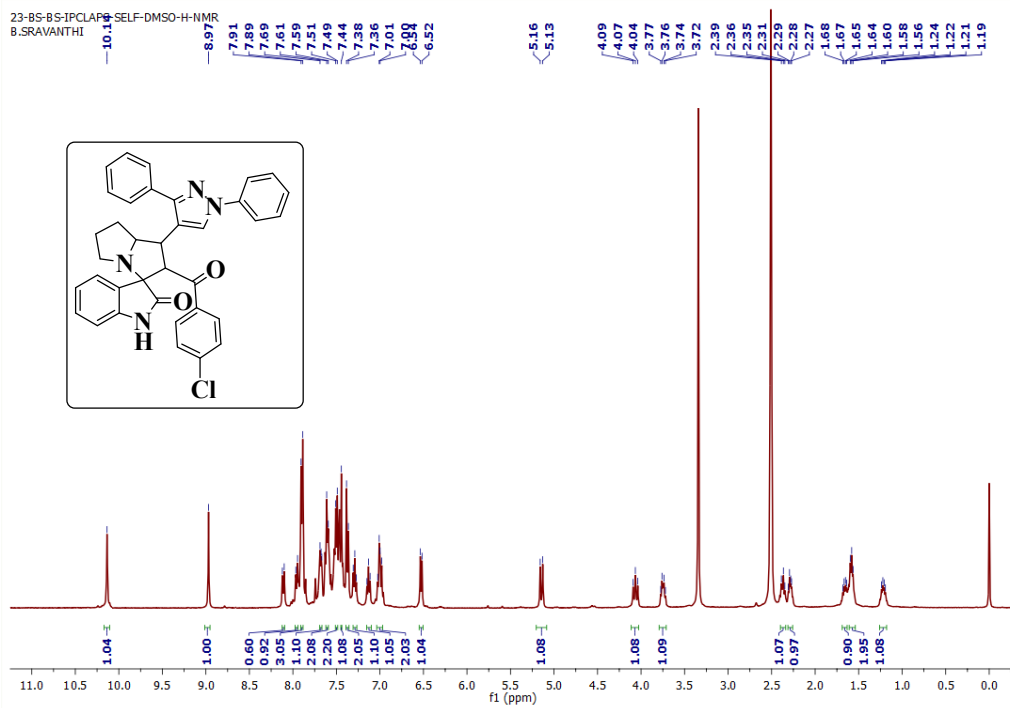
¹³C NMR Spectrum of the compound 4b



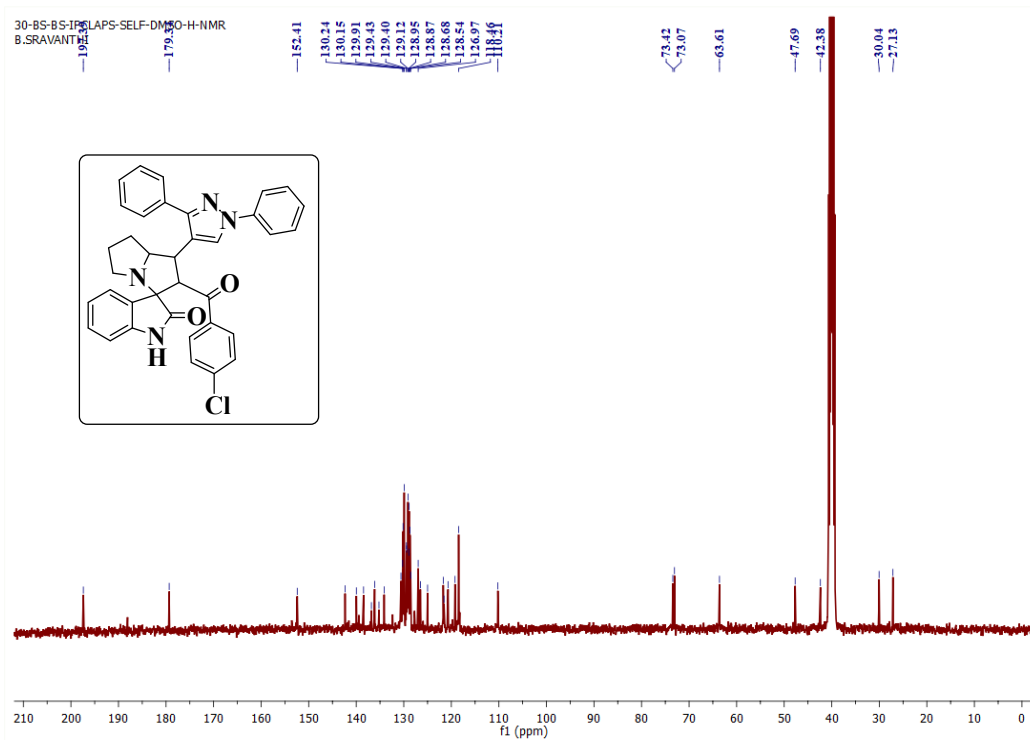
Mass spectrum of the compound 4b



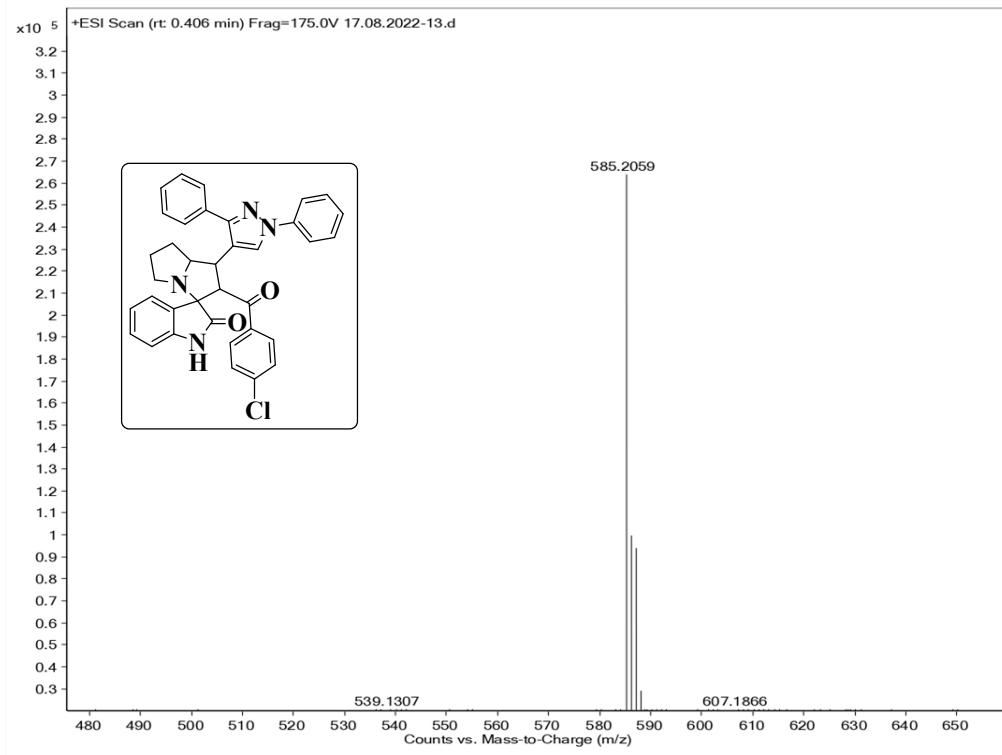
FT-IR Spectrum of the compound 4c



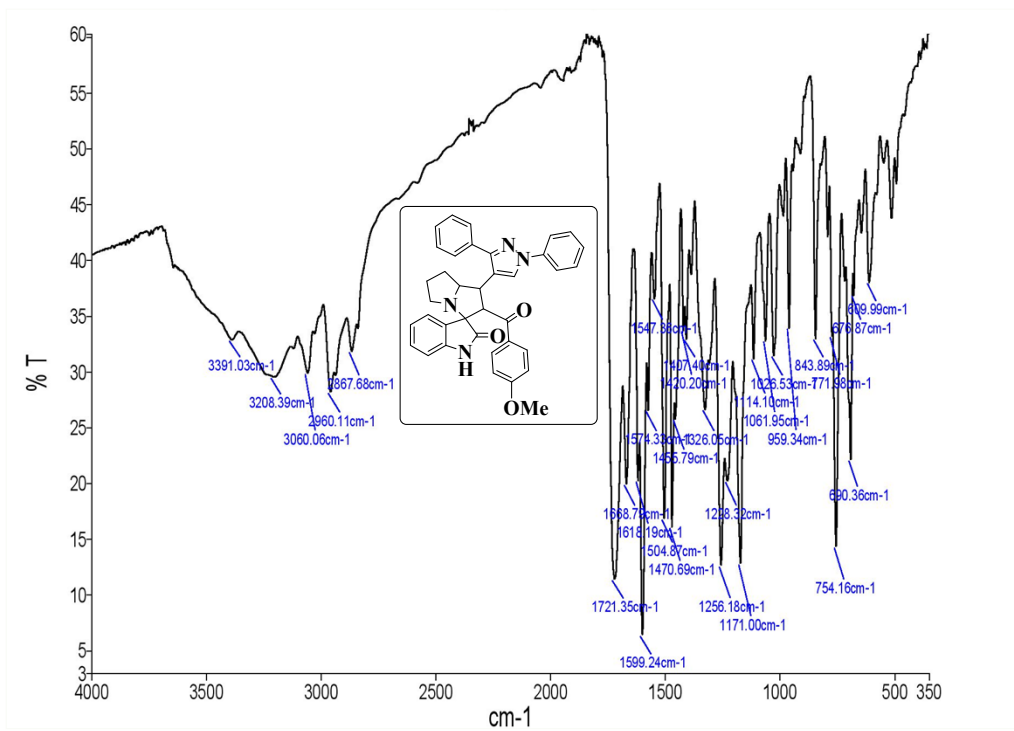
¹H NMR Spectrum of the compound 4c



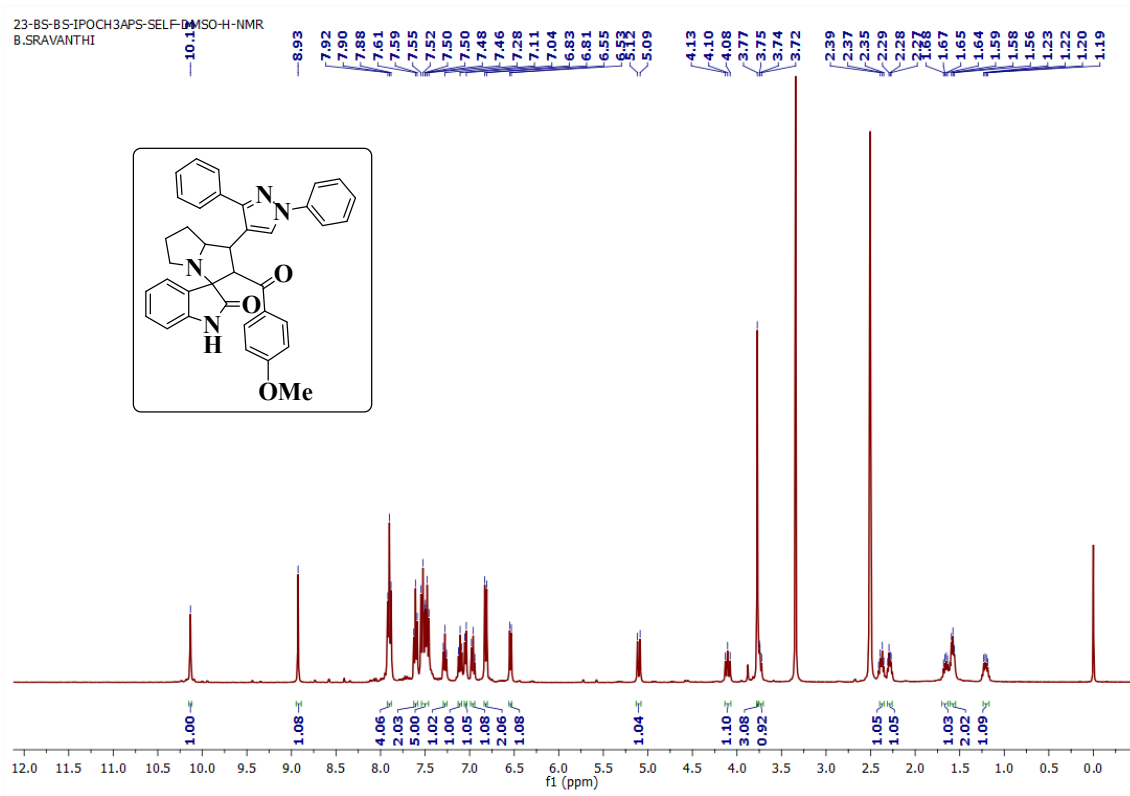
¹³C NMR Spectrum of the compound 4c



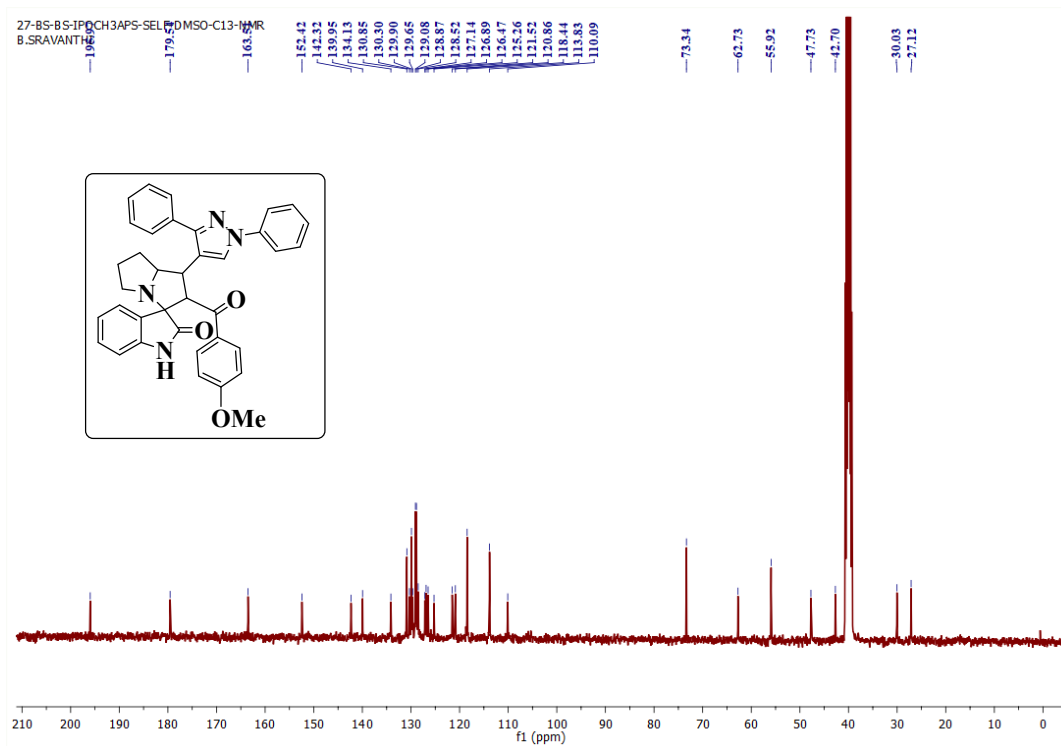
Mass spectrum of the compound 4c



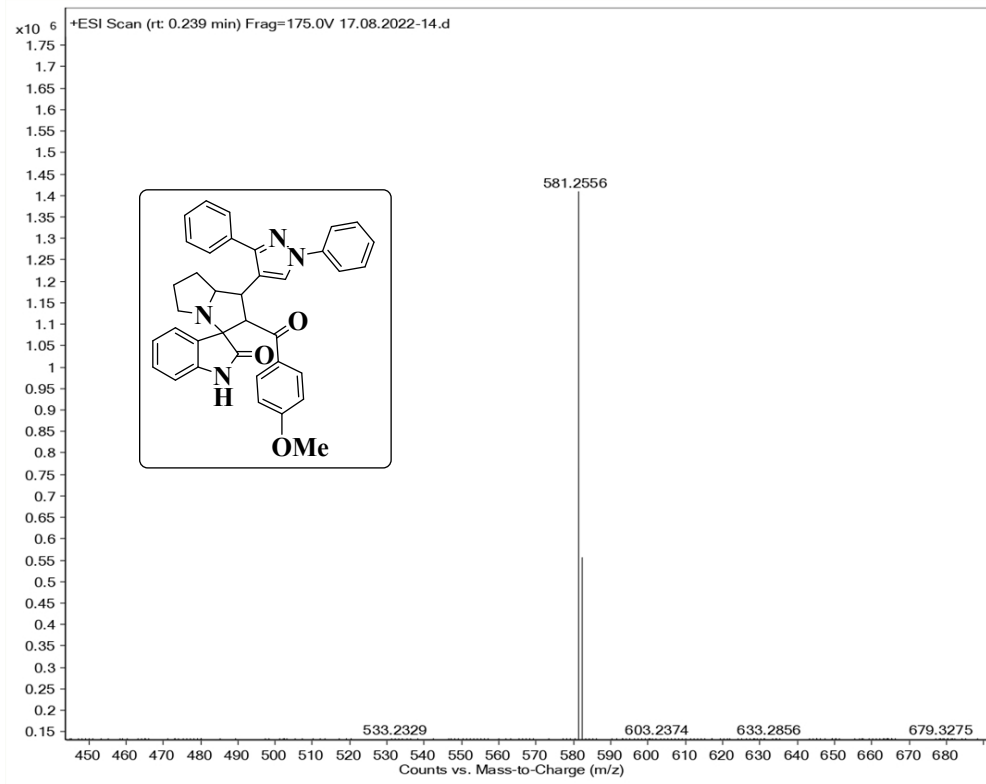
FT-IR Spectrum of the compound 4d



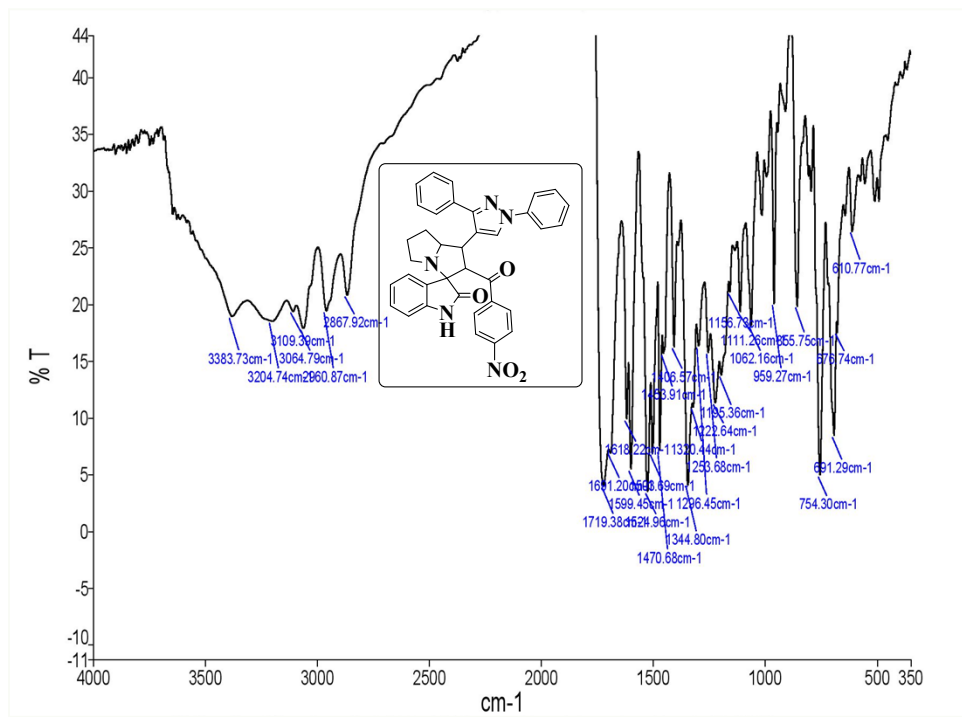
¹H NMR Spectrum of the compound 4d



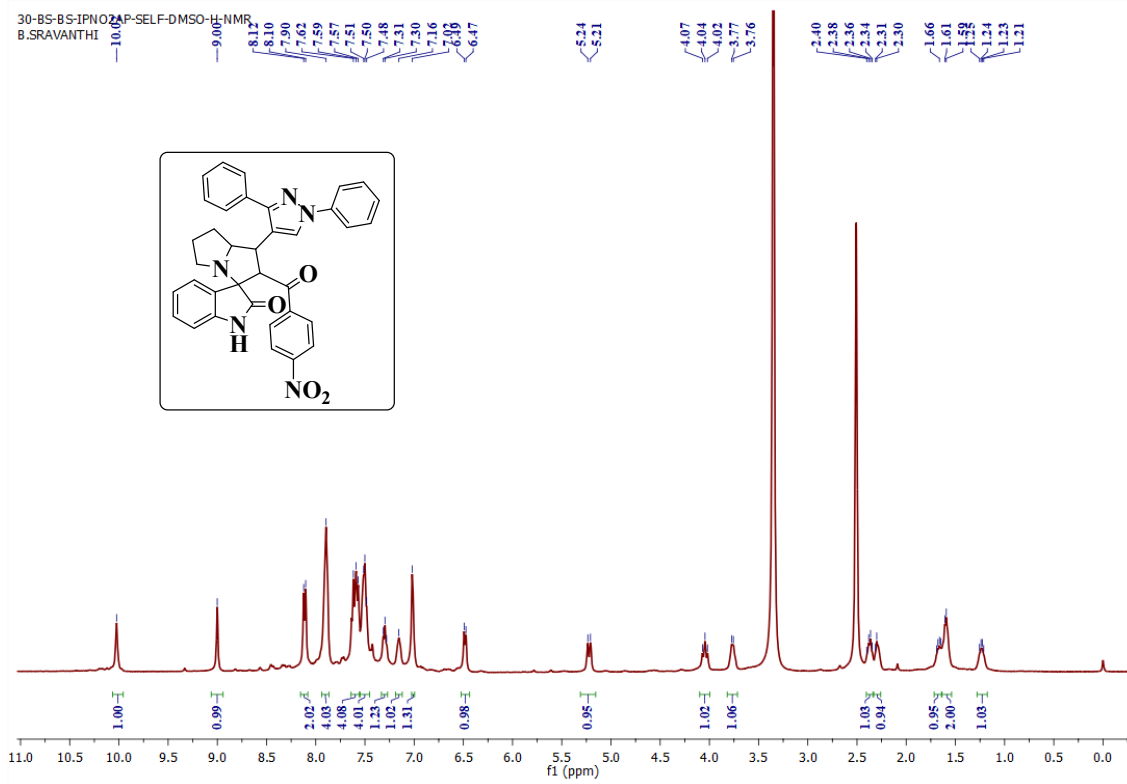
¹³C NMR Spectrum of the compound 4d



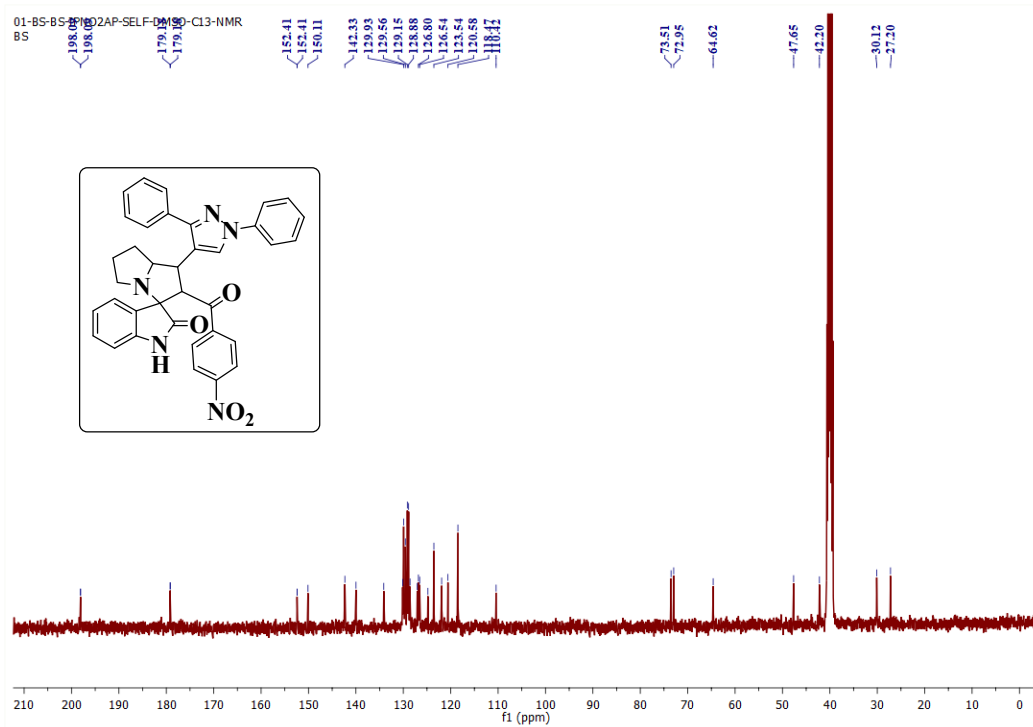
Mass spectrum of the compound 4d



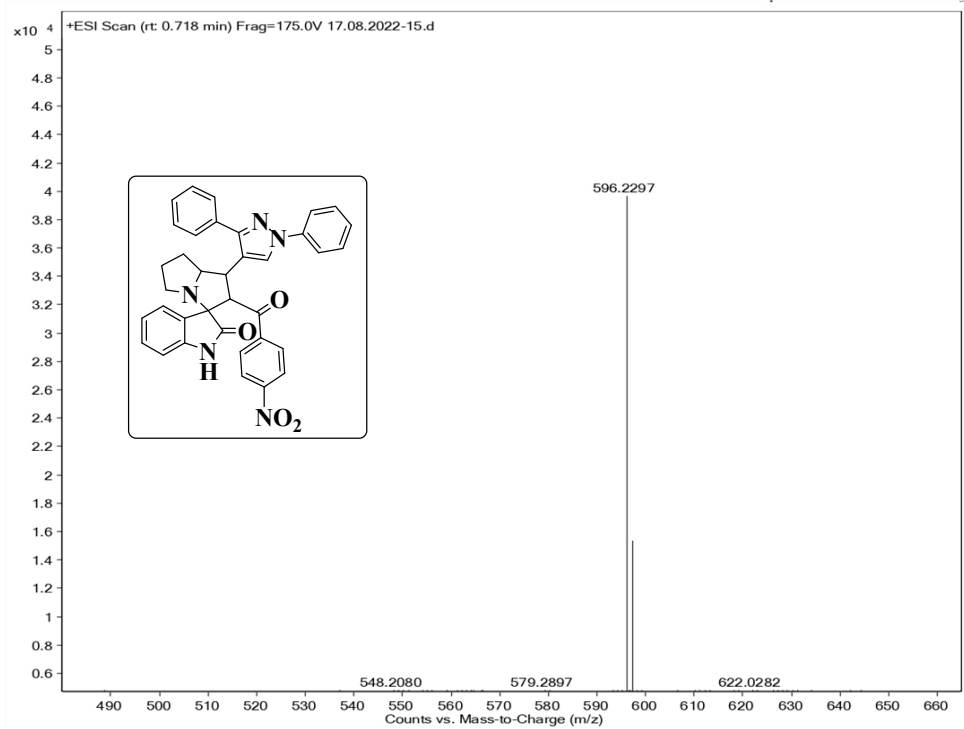
FT-IR Spectrum of the compound 4e



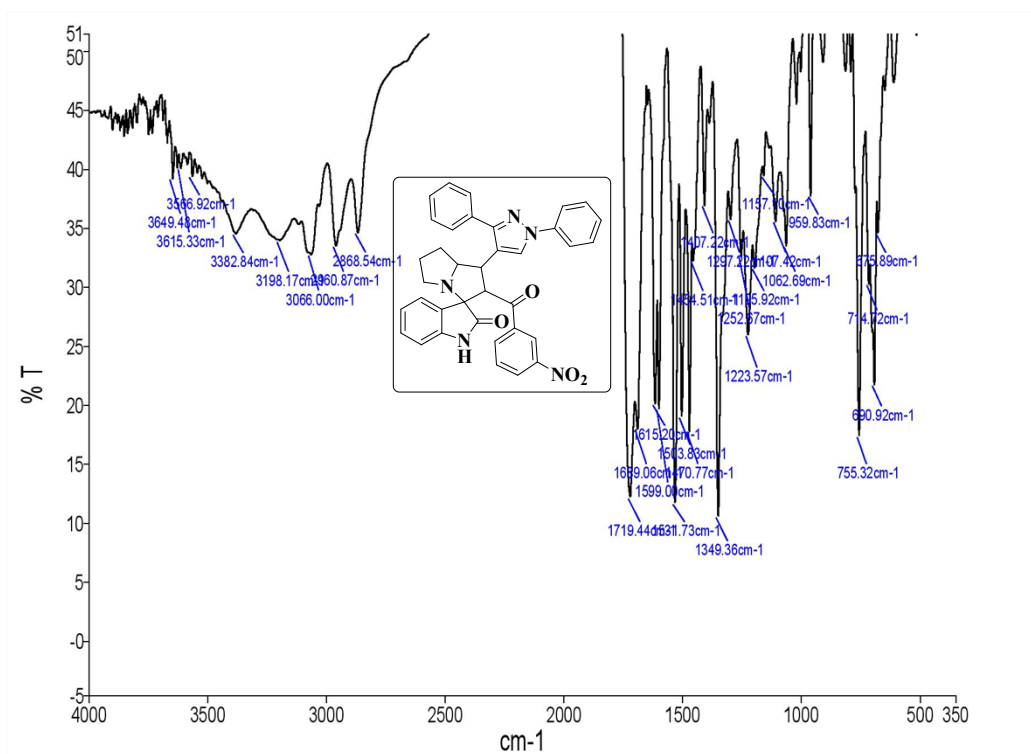
¹H NMR Spectrum of the compound 4e



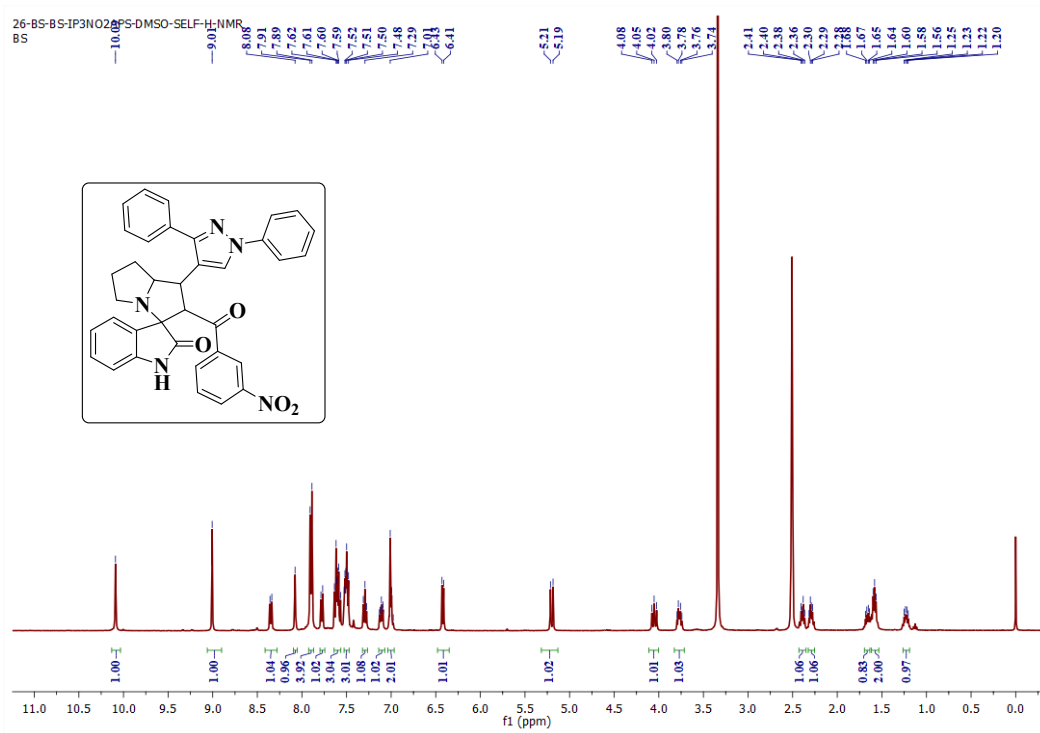
¹³C NMR Spectrum of the compound 4e



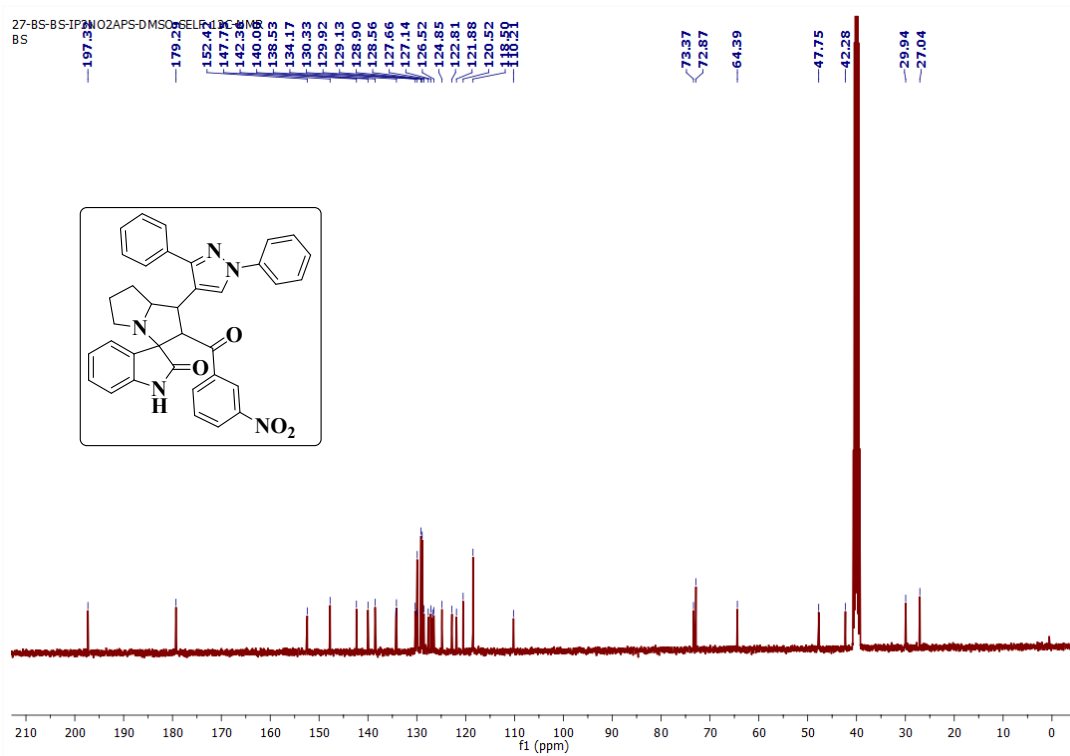
Mass spectrum of the compound 4e



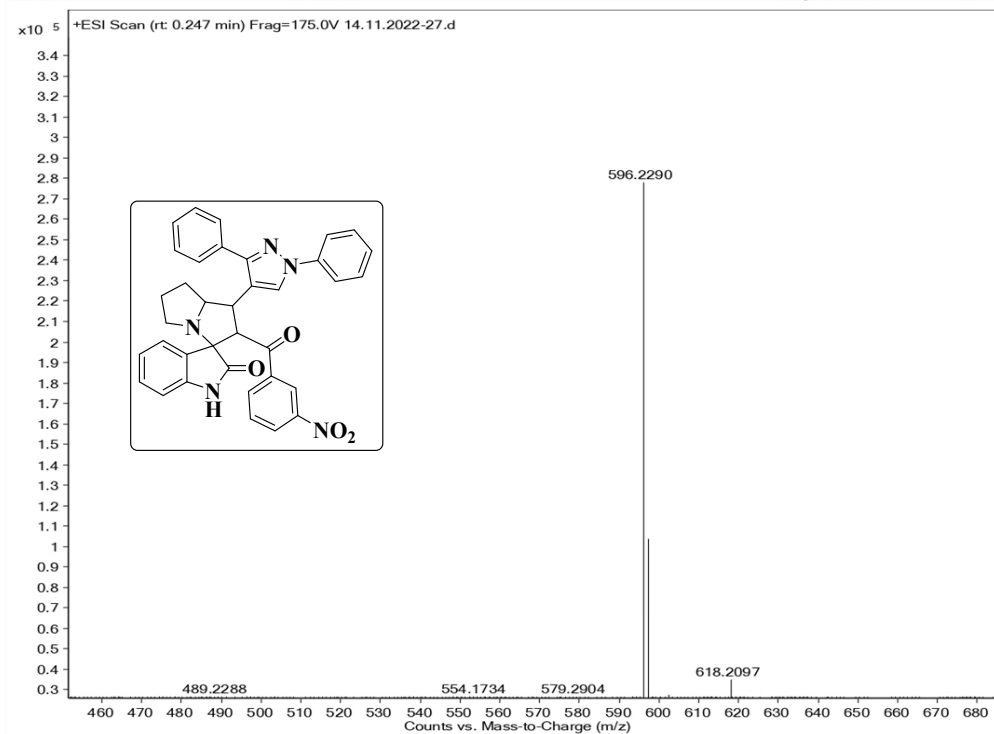
FT-IR Spectrum of the compound 4f



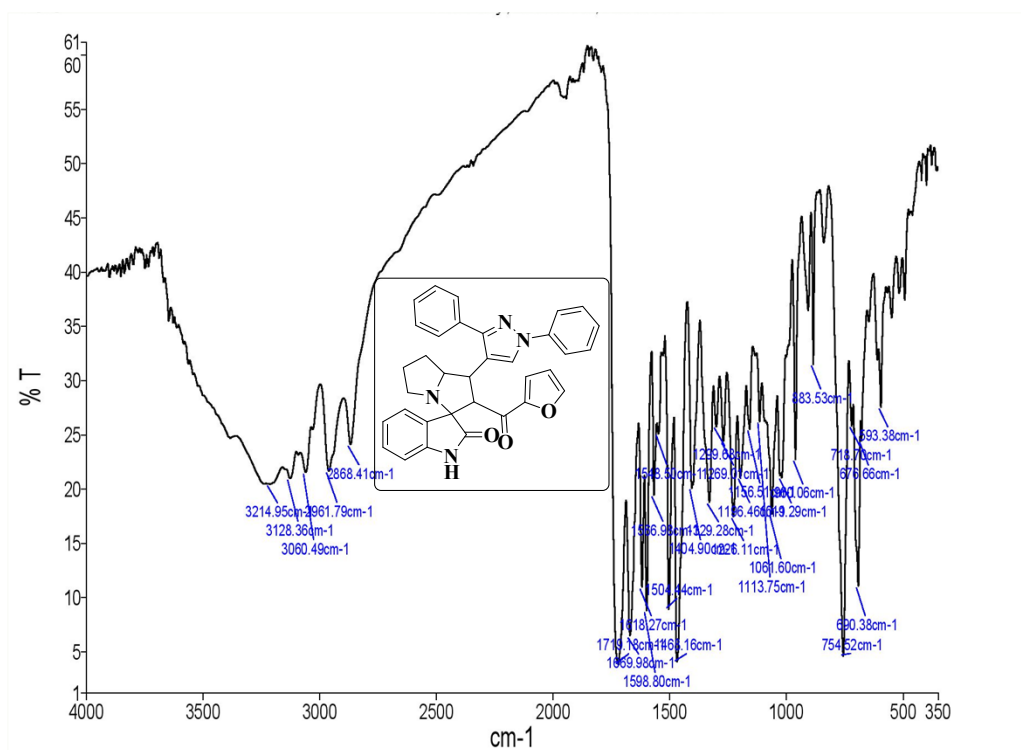
¹H NMR Spectrum of the compound 4f



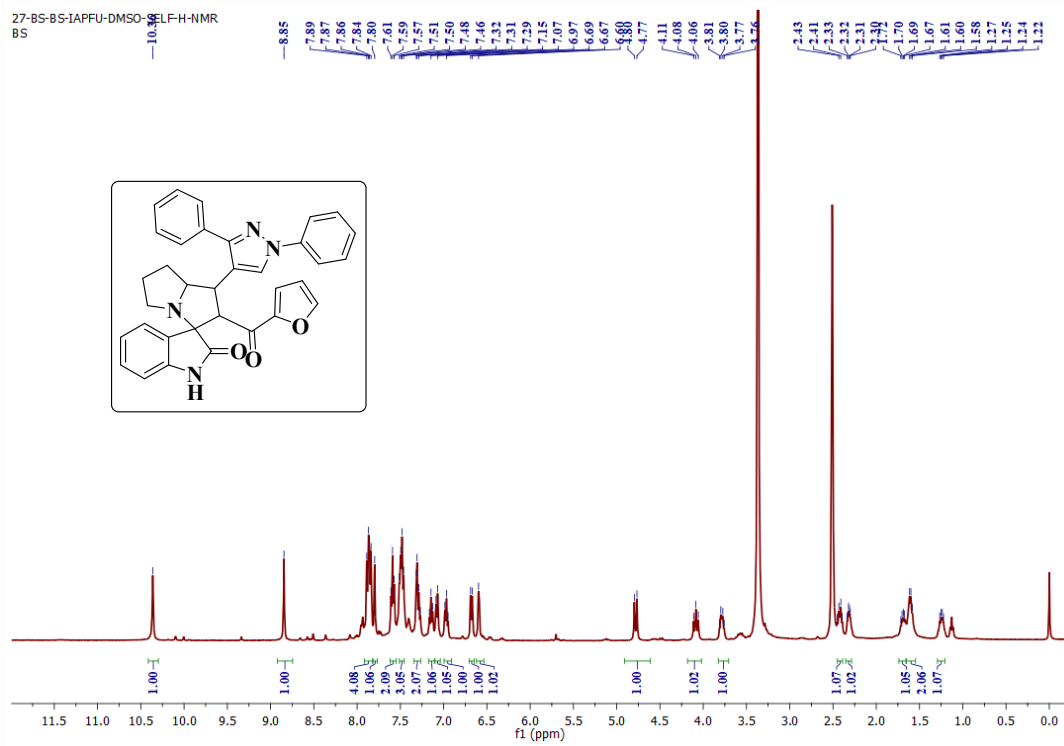
¹³C NMR Spectrum of the compound 4f



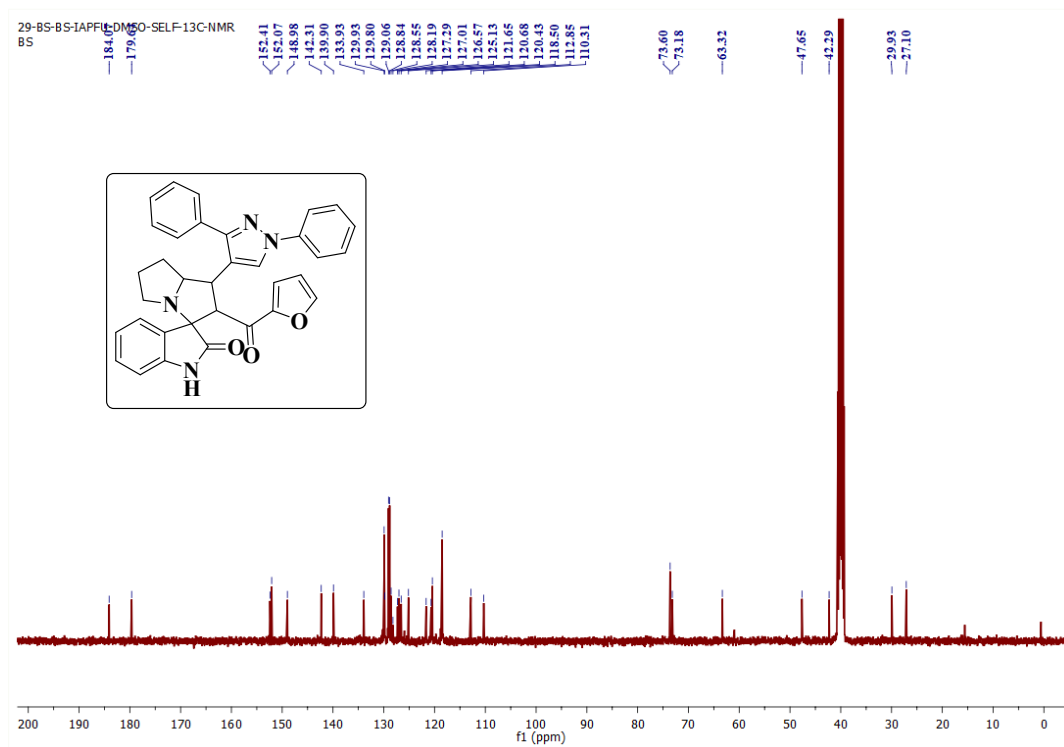
Mass spectrum of the compound 4f



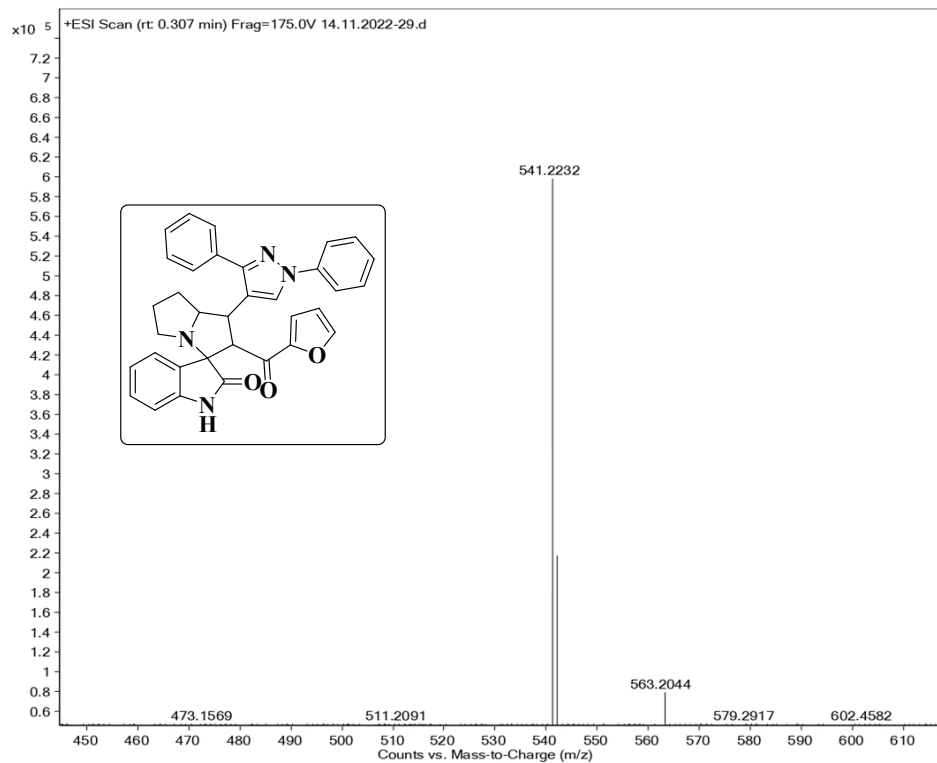
FT-IR Spectrum of the compound 4g



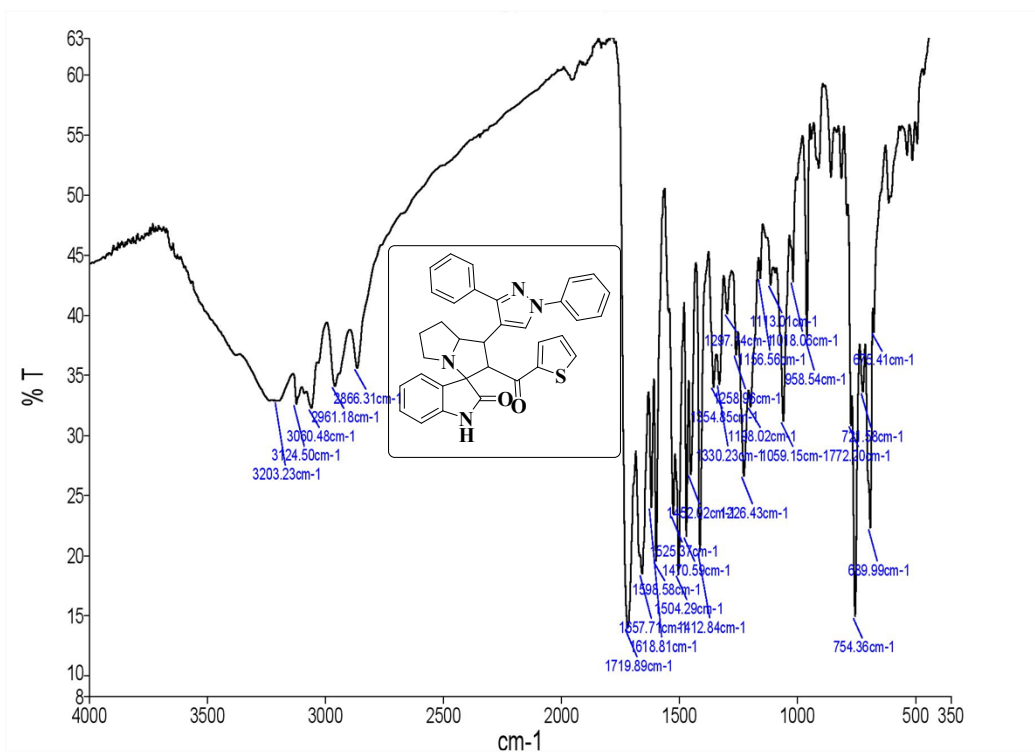
¹H NMR Spectrum of the compound 4g



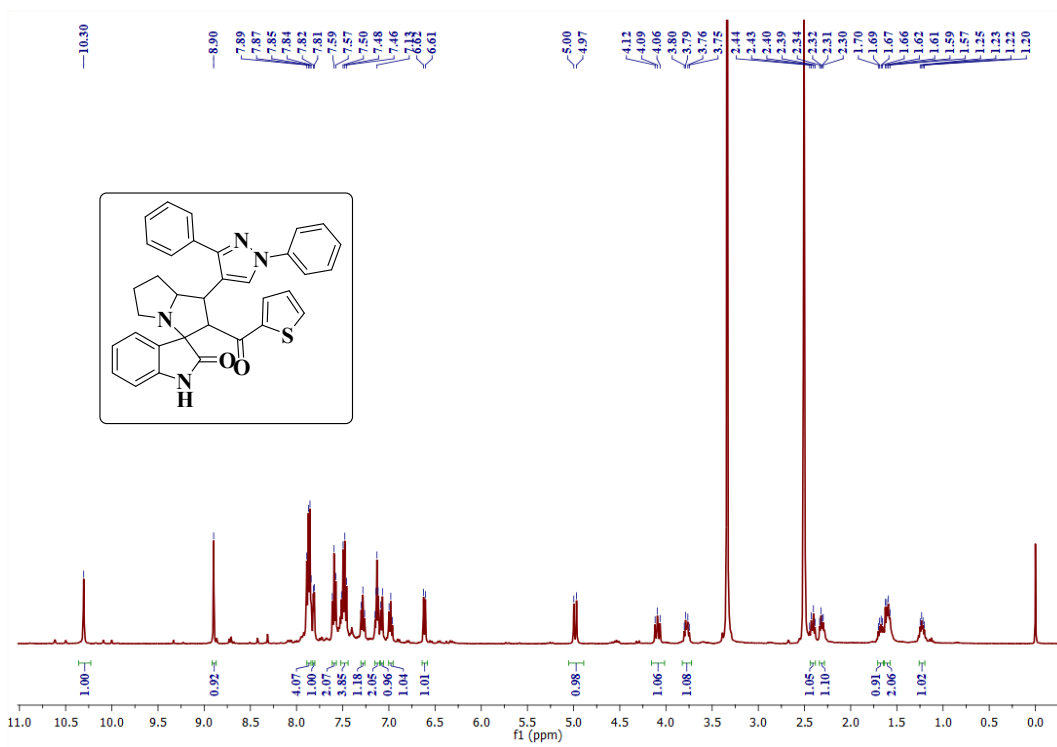
¹³C NMR Spectrum of the compound 4g



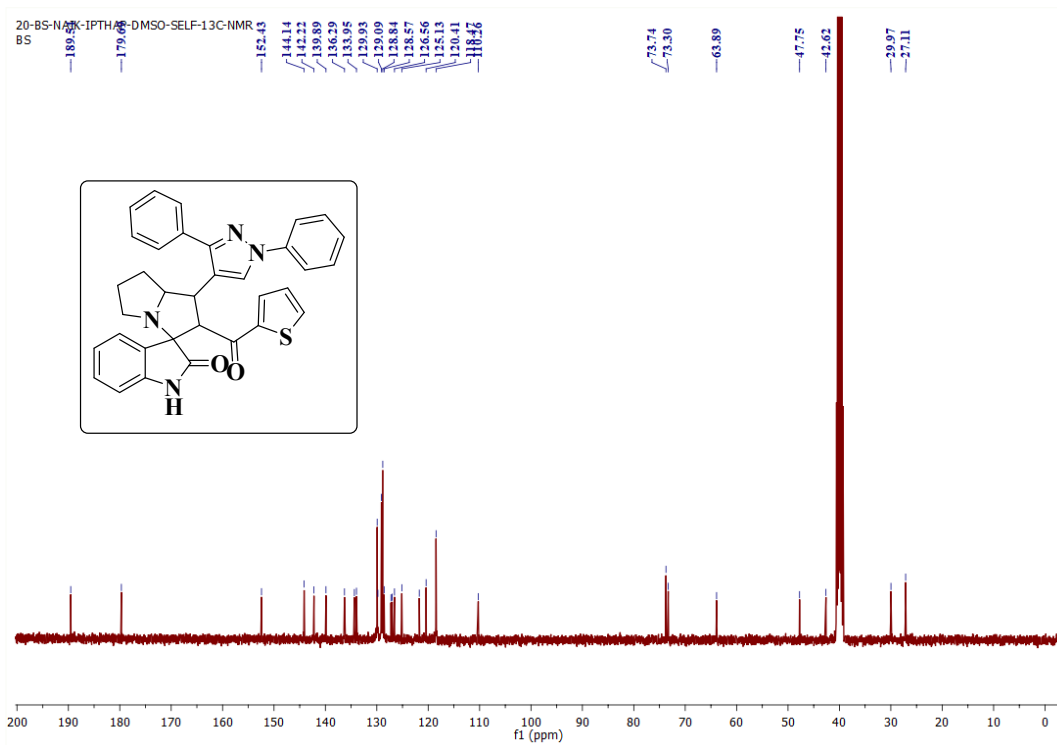
Mass spectrum of the compound 4g



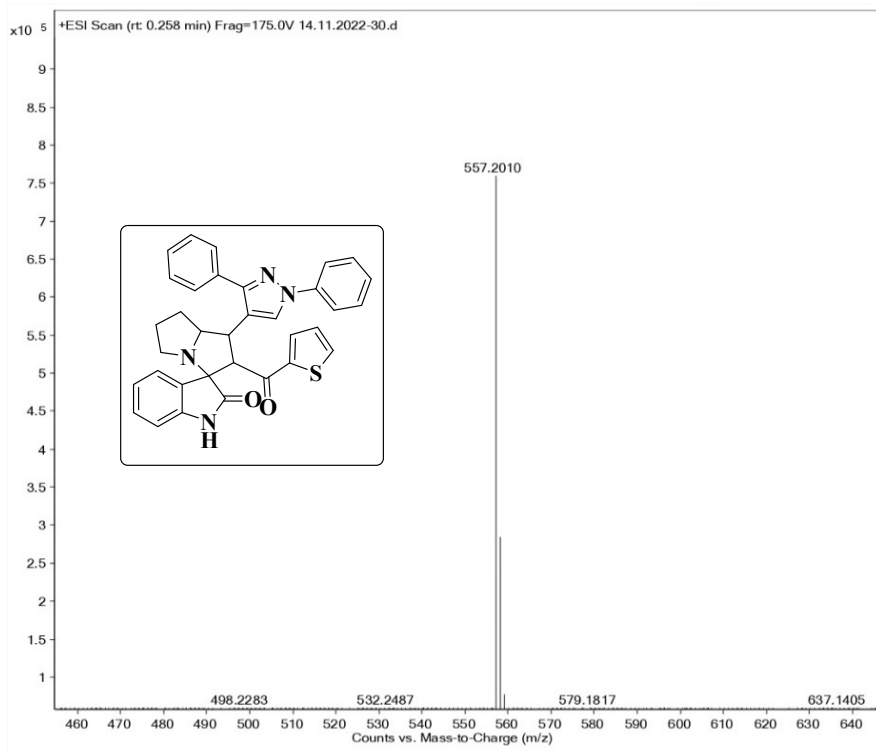
FT-IR Spectrum of the compound 4h



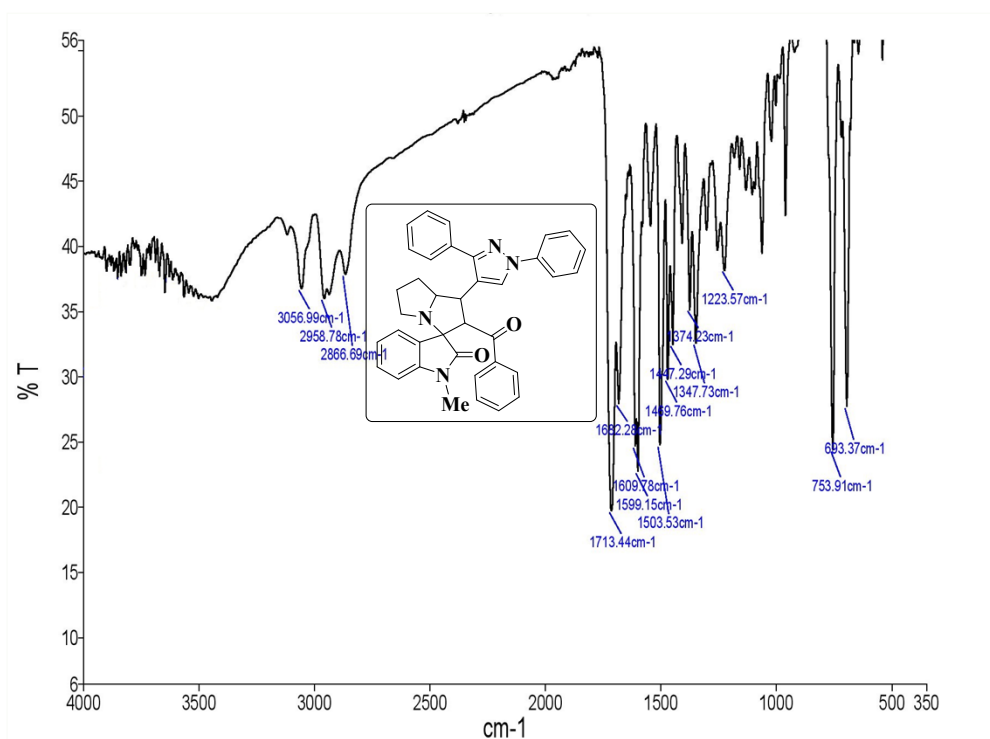
¹H NMR Spectrum of the compound 4h



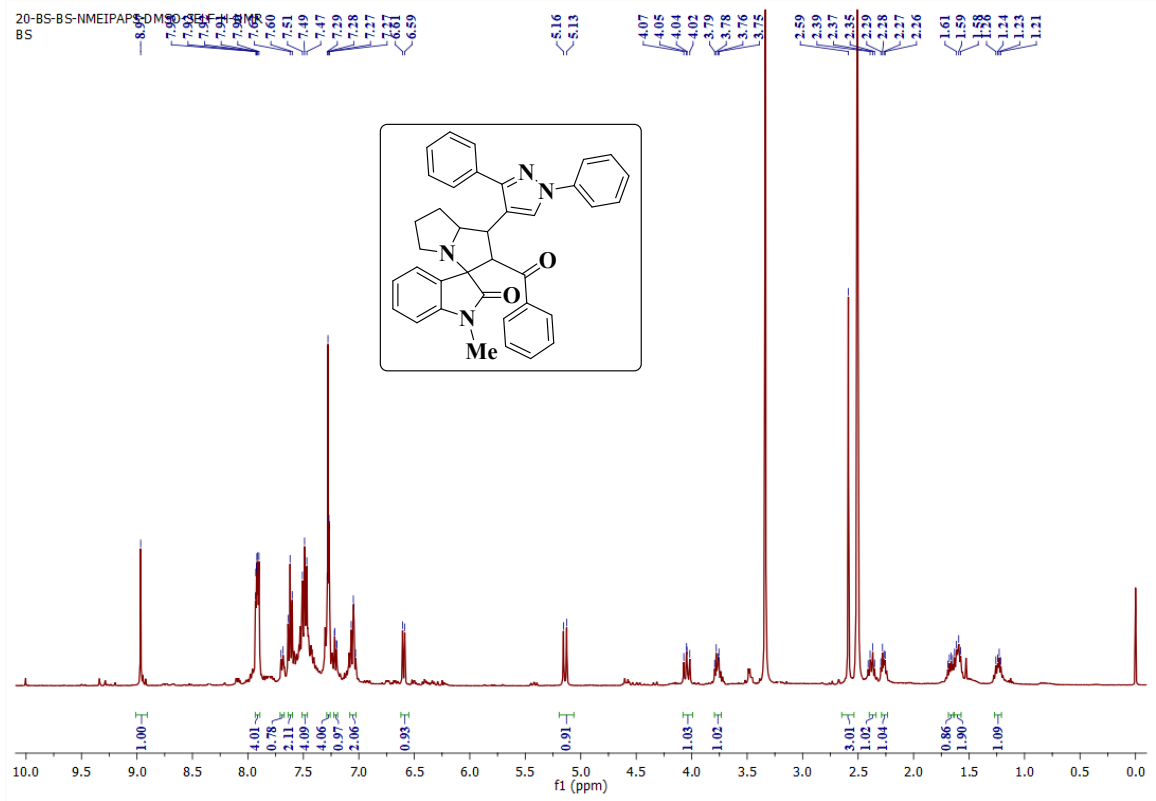
¹³C NMR Spectrum of the compound 4h



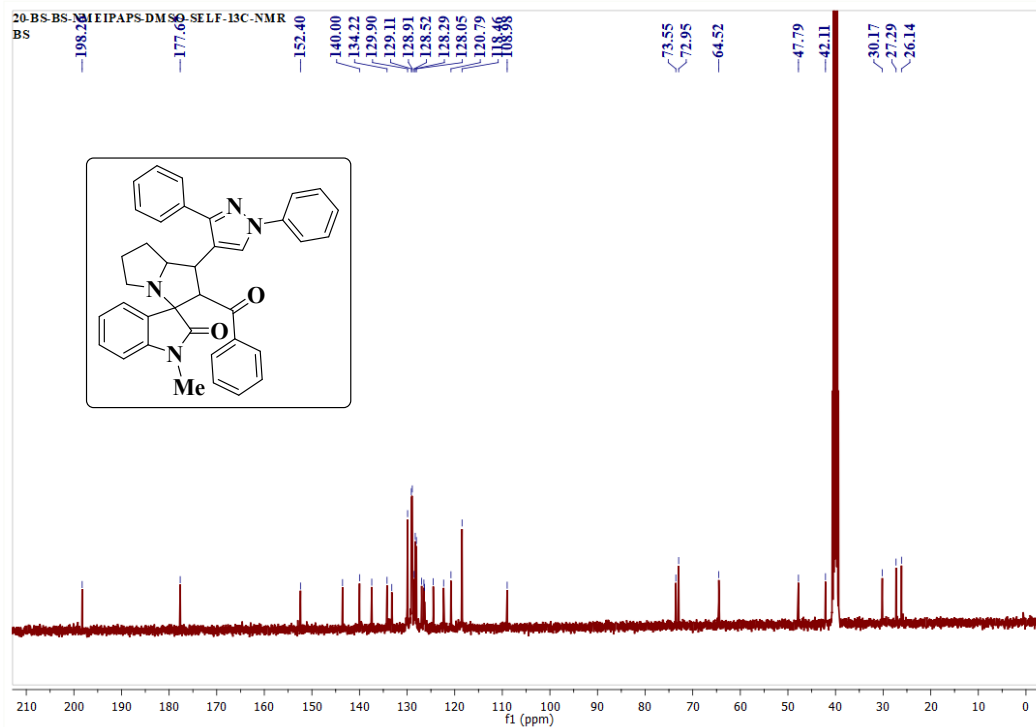
Mass spectrum of the compound 4h



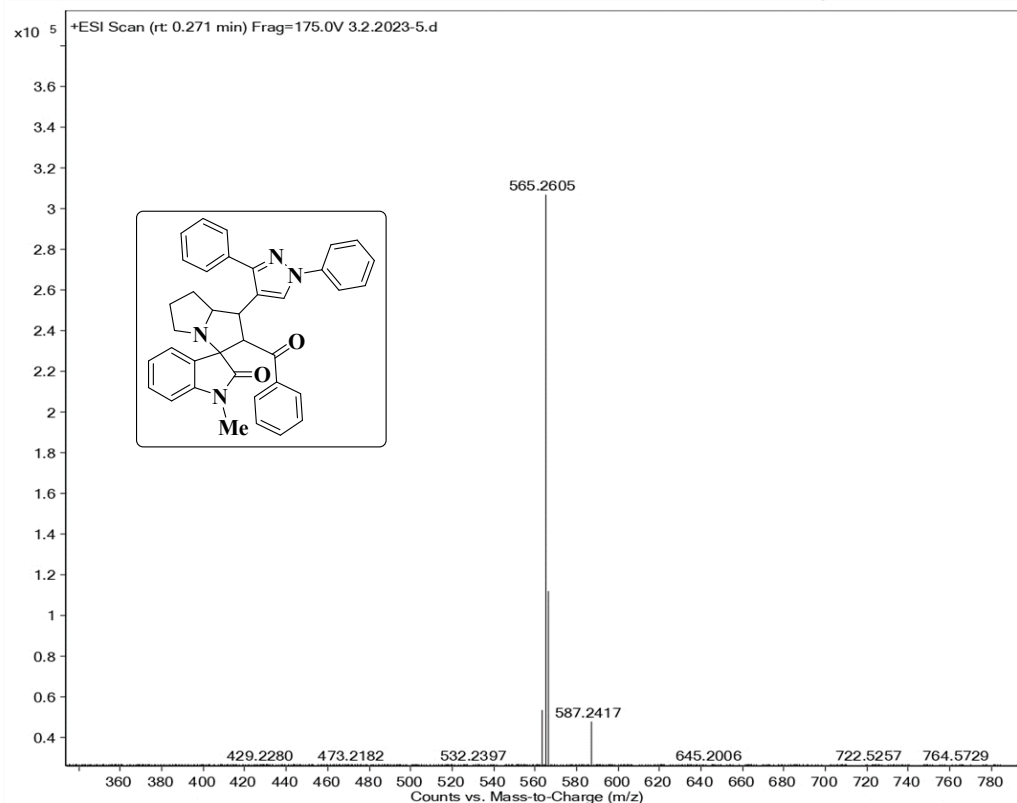
FT-IR Spectrum of the compound 4i



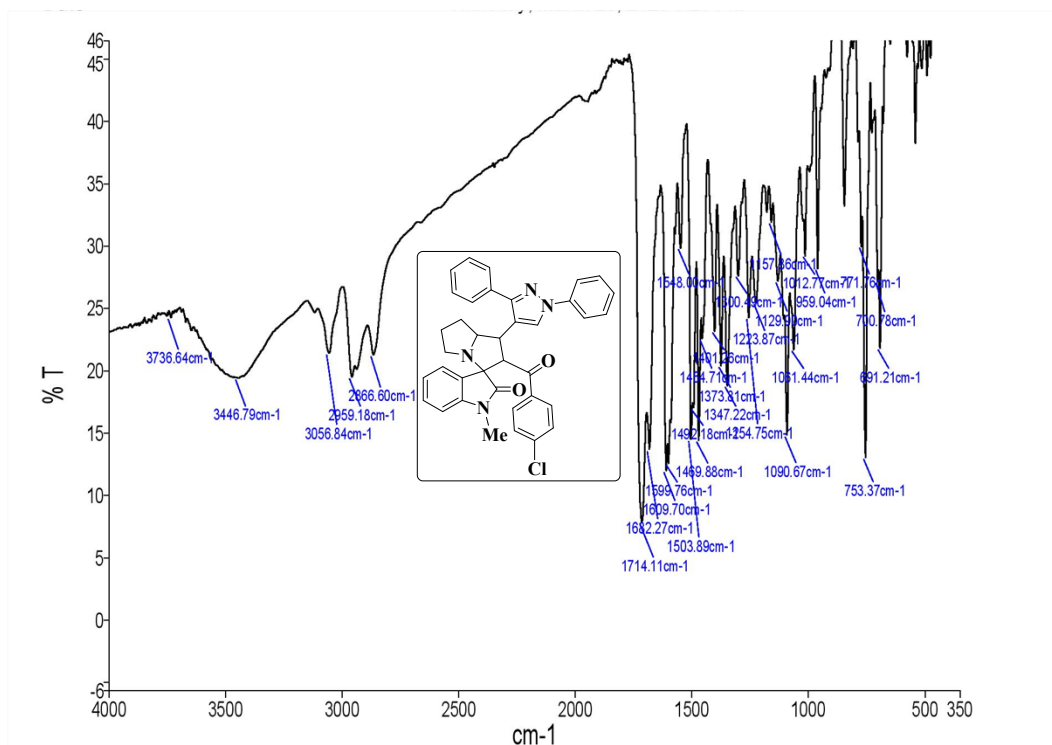
¹H NMR Spectrum of the compound 4i



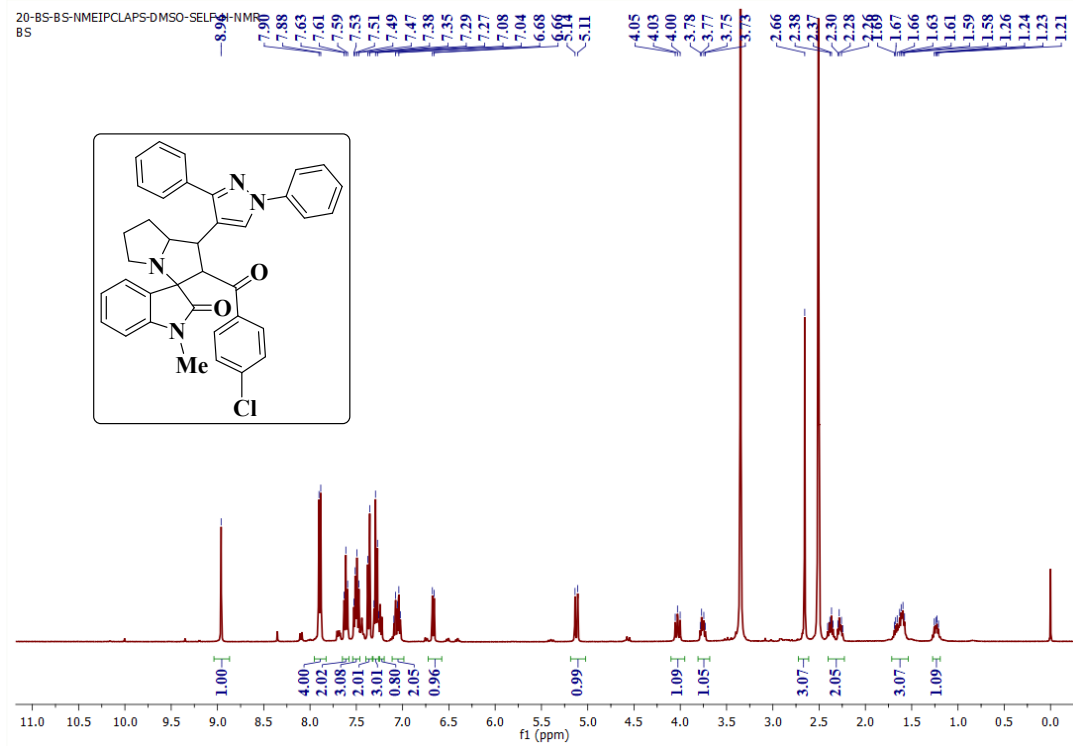
¹³C NMR Spectrum of the compound 4i



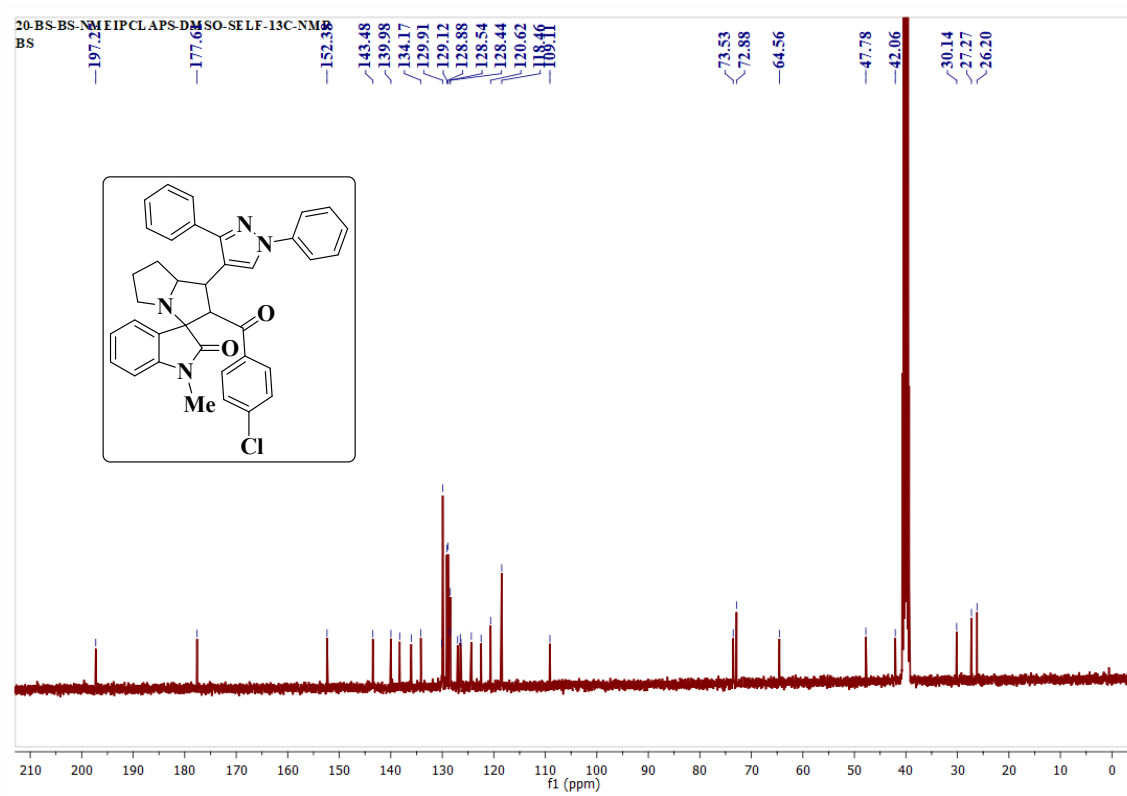
Mass spectrum of the compound 4i



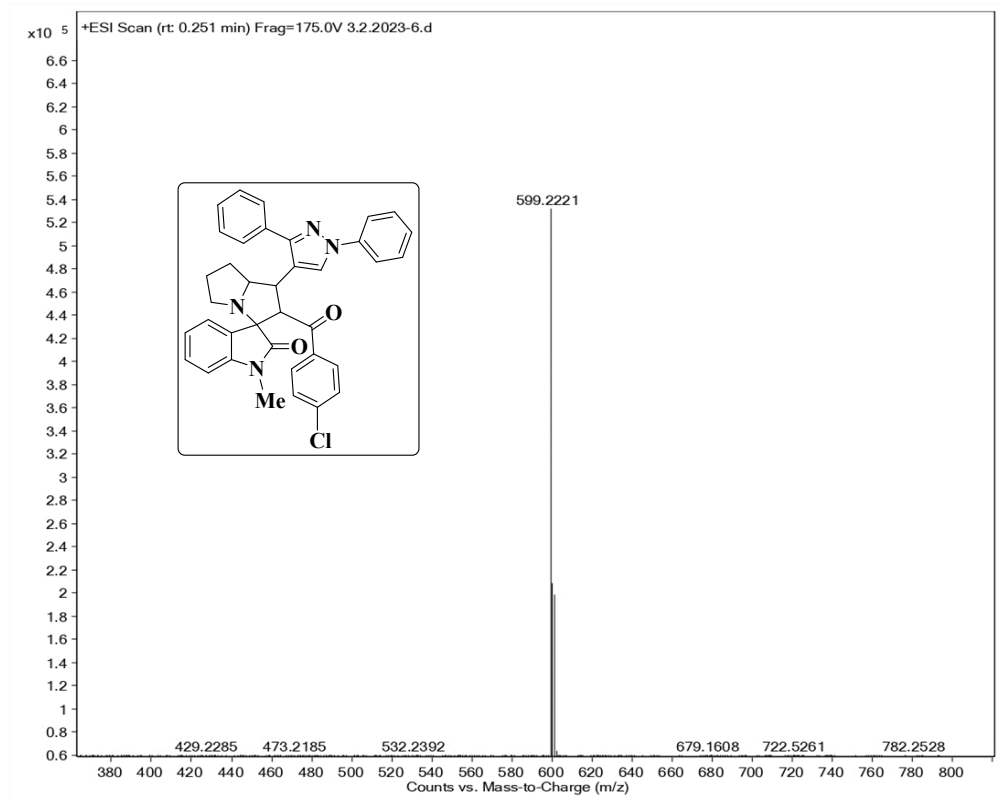
FT-IR Spectrum of the compound 4j



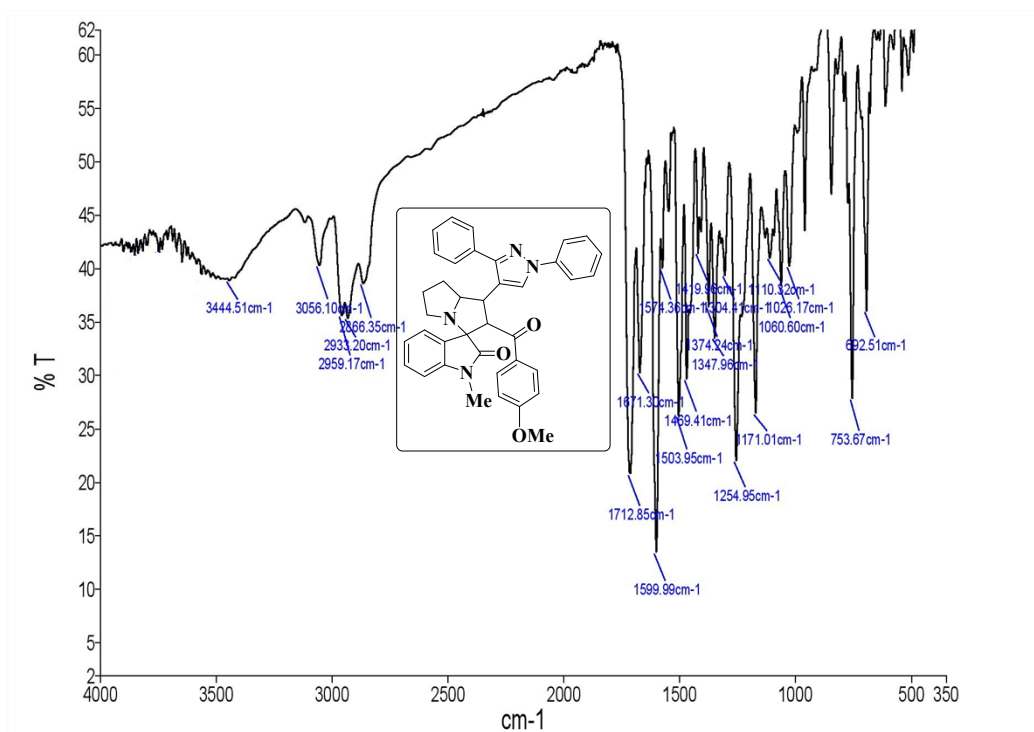
¹H NMR Spectrum of the compound 4j



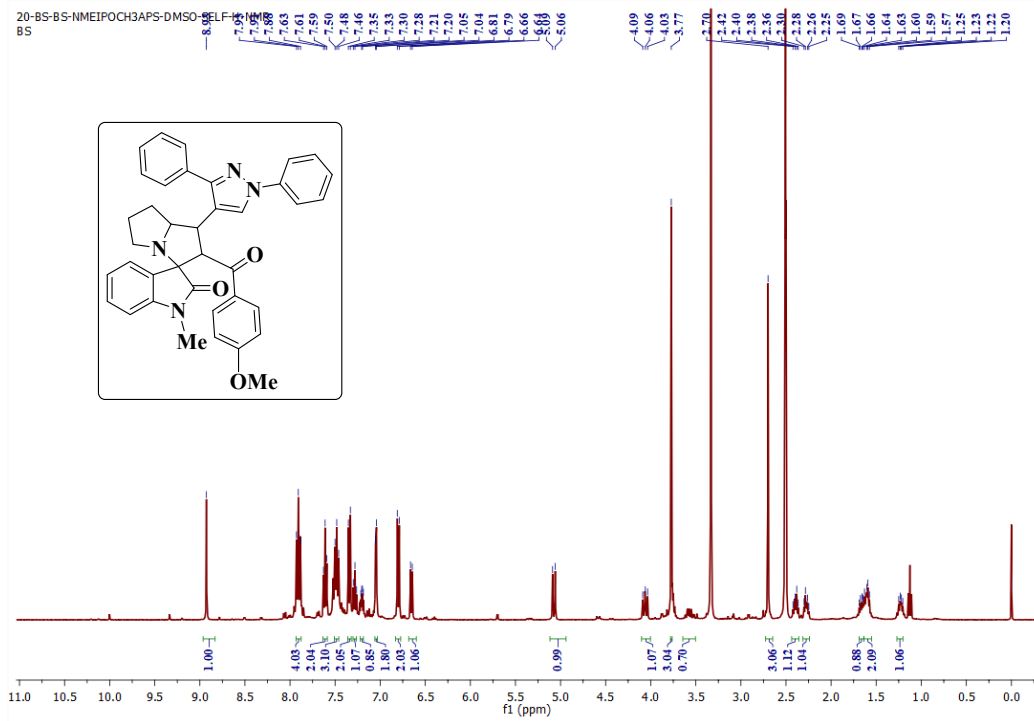
¹³C NMR Spectrum of the compound 4j



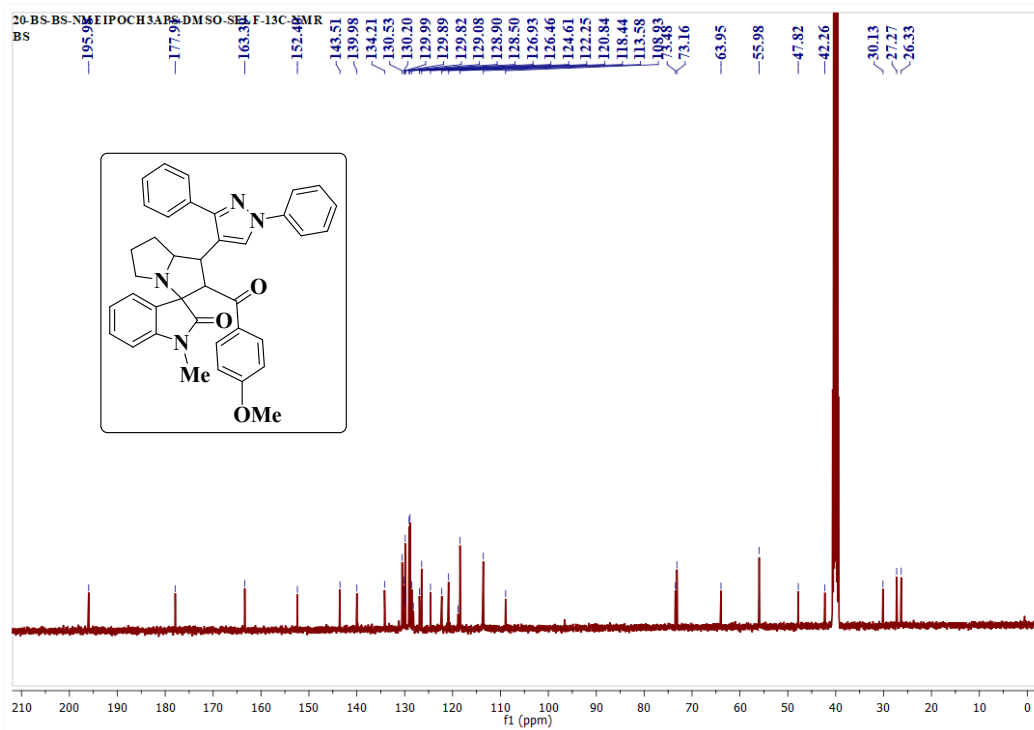
Mass spectrum of the compound 4j



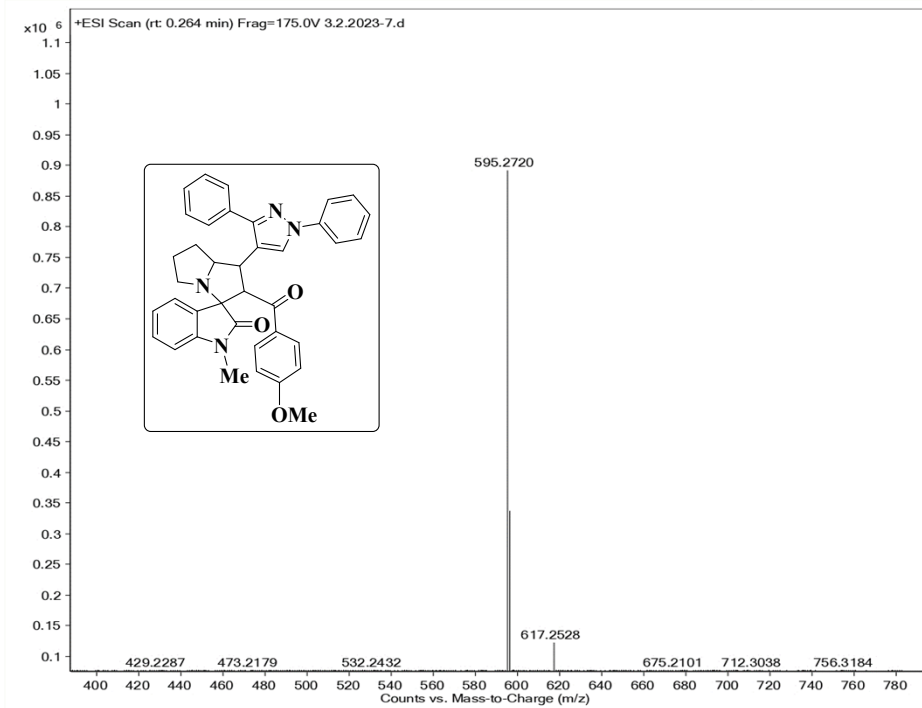
FT-IR Spectrum of the compound 4k



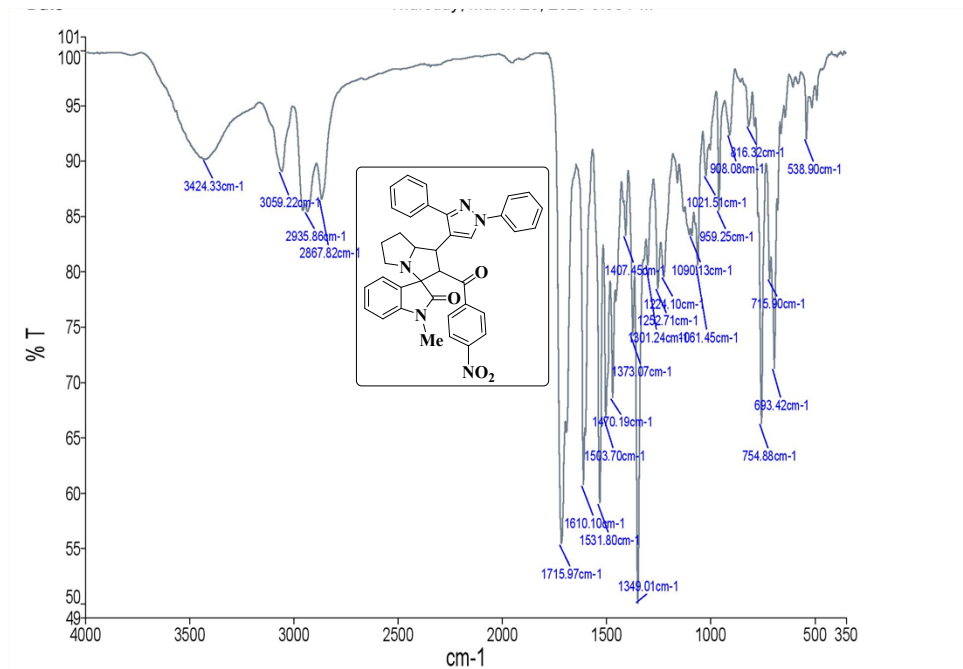
¹H NMR Spectrum of the compound 4k



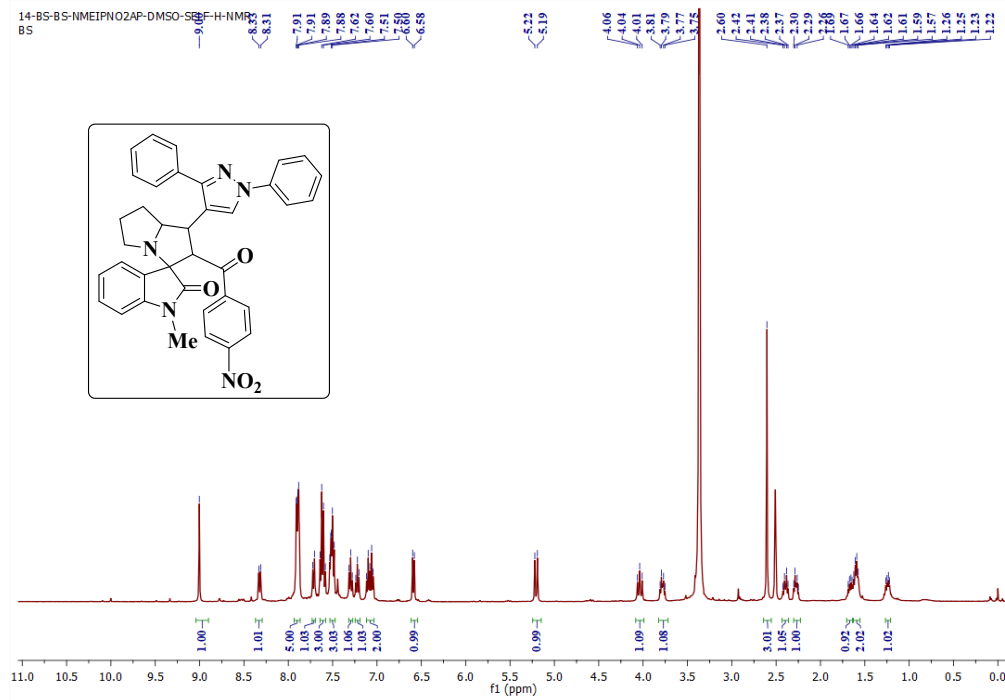
¹³C NMR Spectrum of the compound 4k



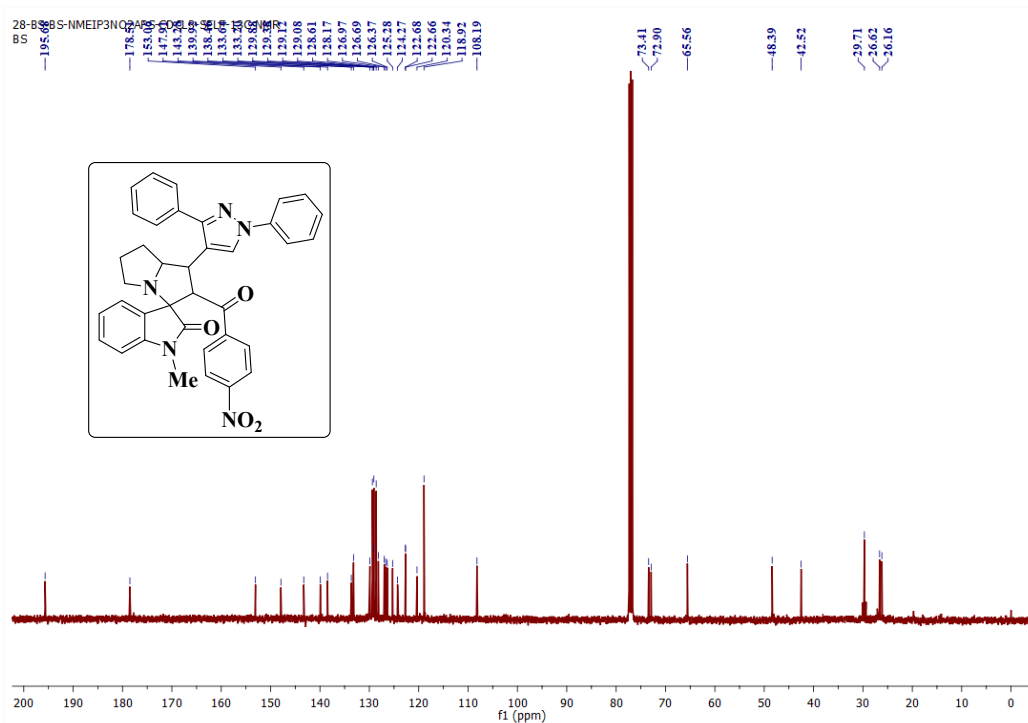
Mass spectrum of the compound 4k



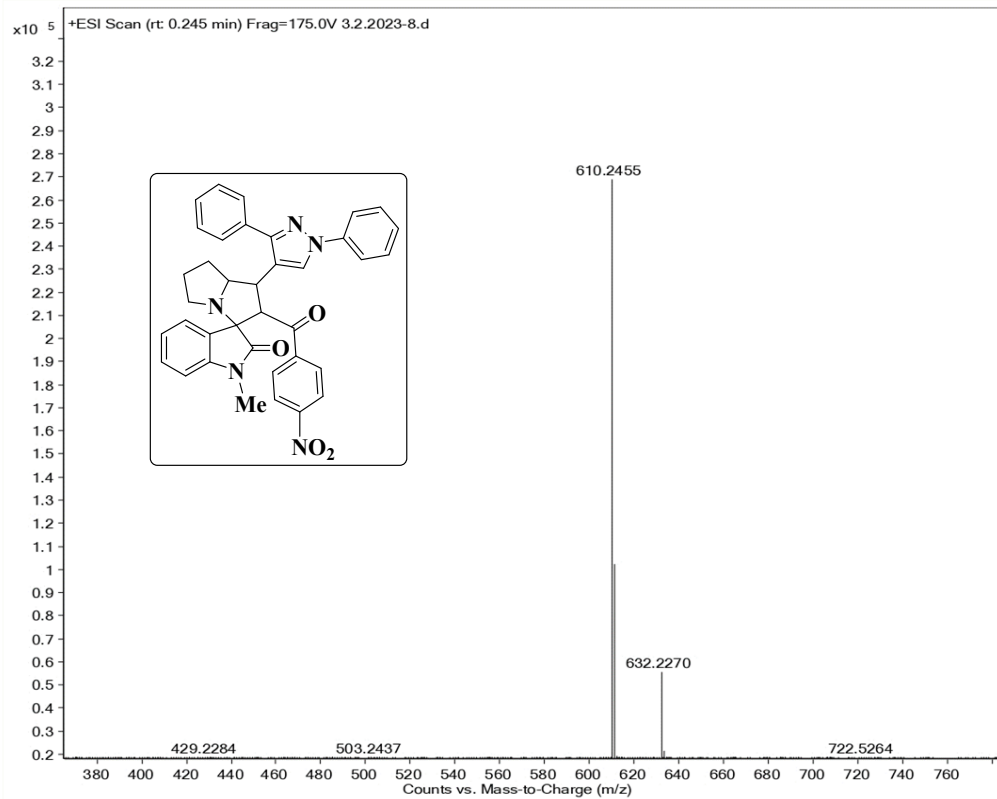
FT-IR Spectrum of the compound 4l



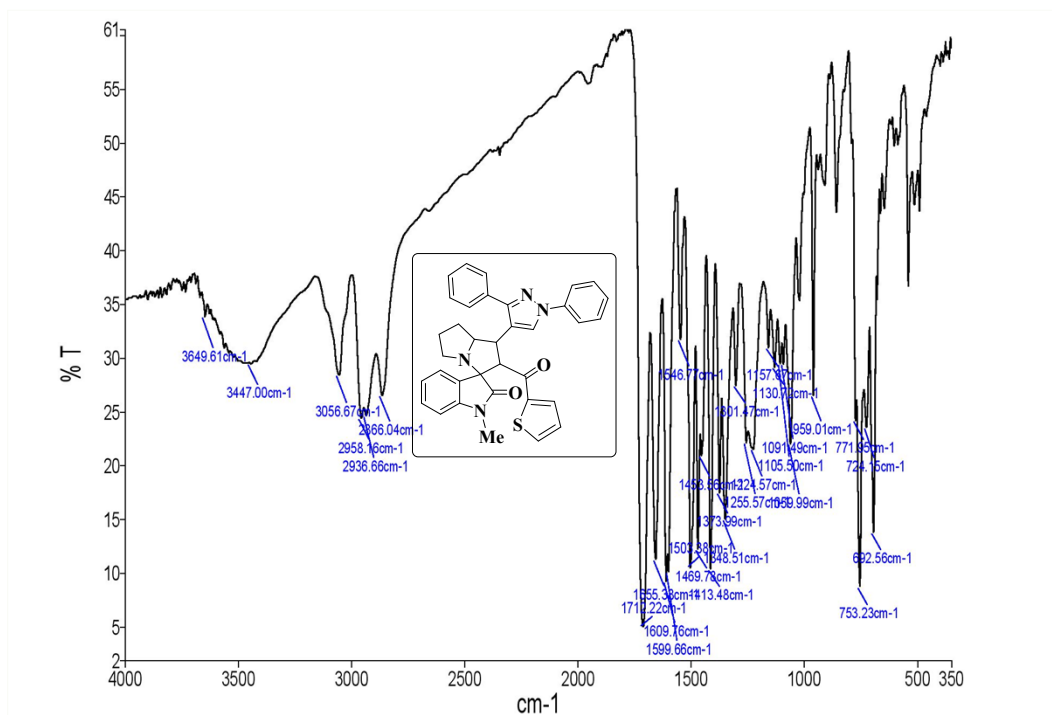
¹H NMR Spectrum of the compound 4I



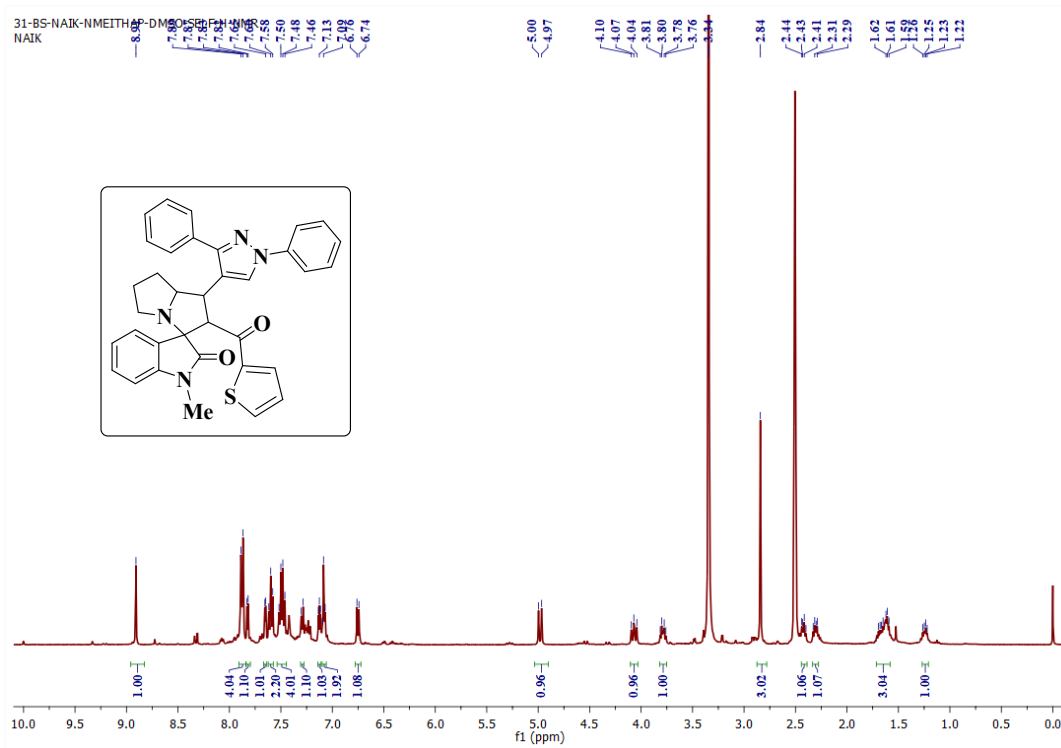
¹³C NMR Spectrum of the compound 4I



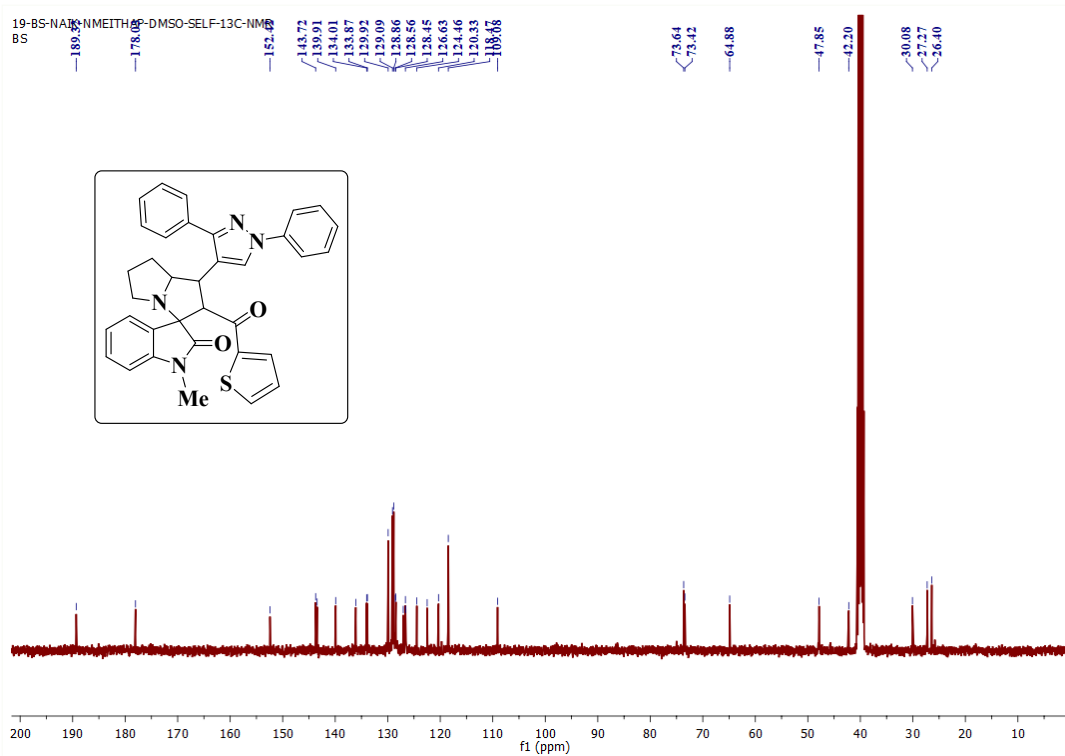
Mass spectrum of the compound 4l



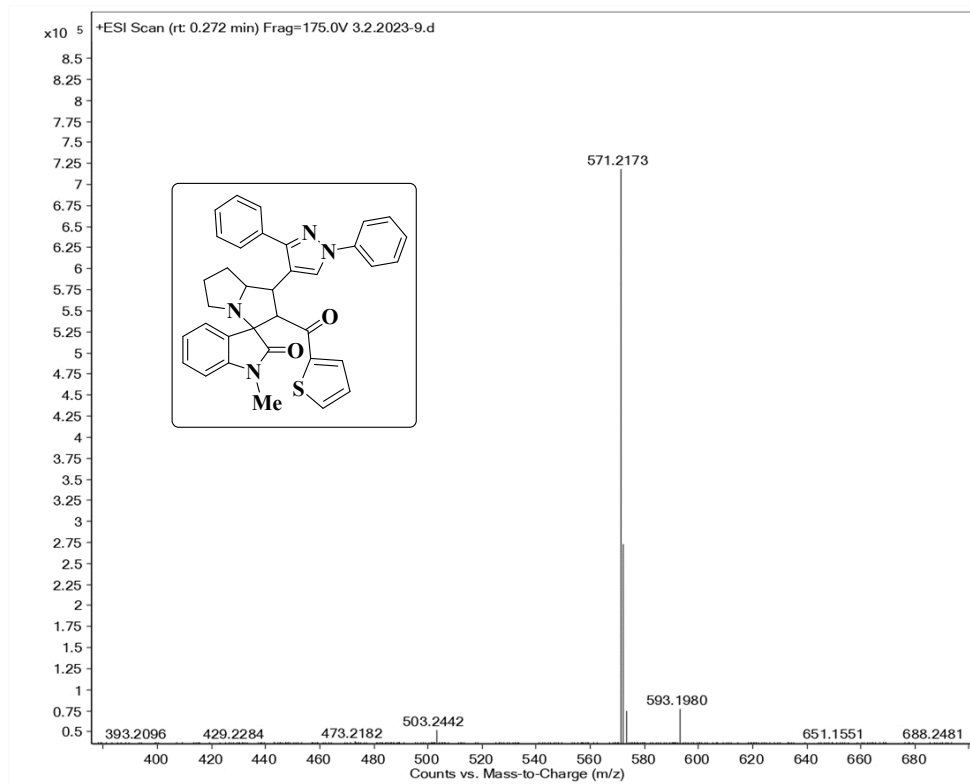
FT-IR Spectrum of the compound 4m



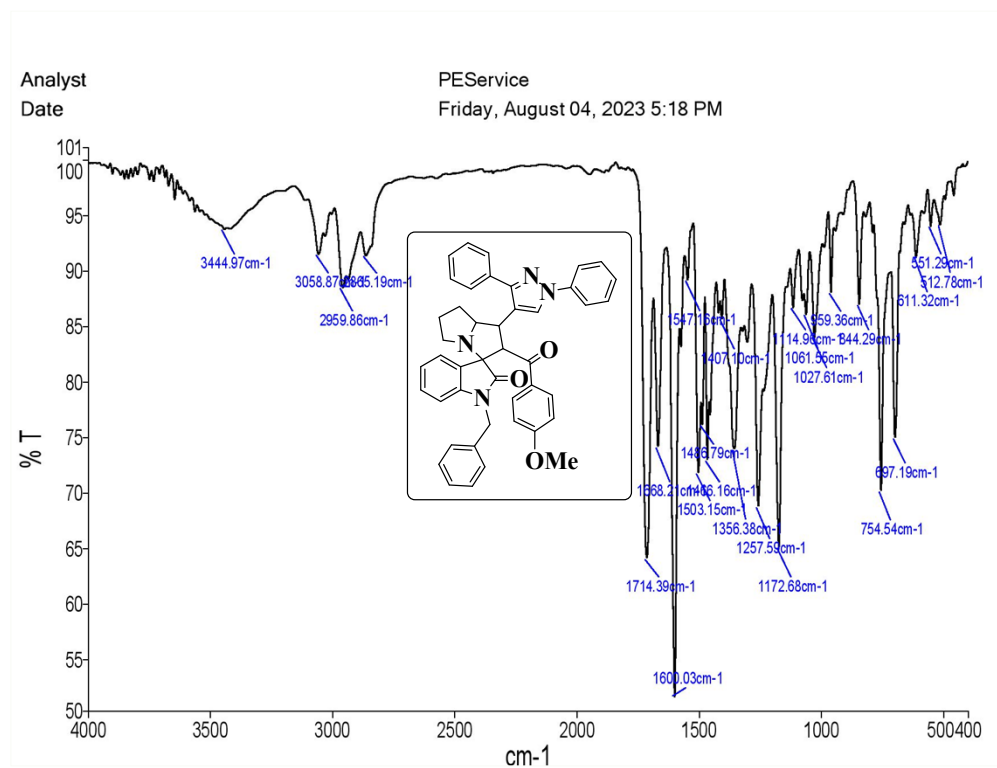
¹H NMR Spectrum of the compound 4m

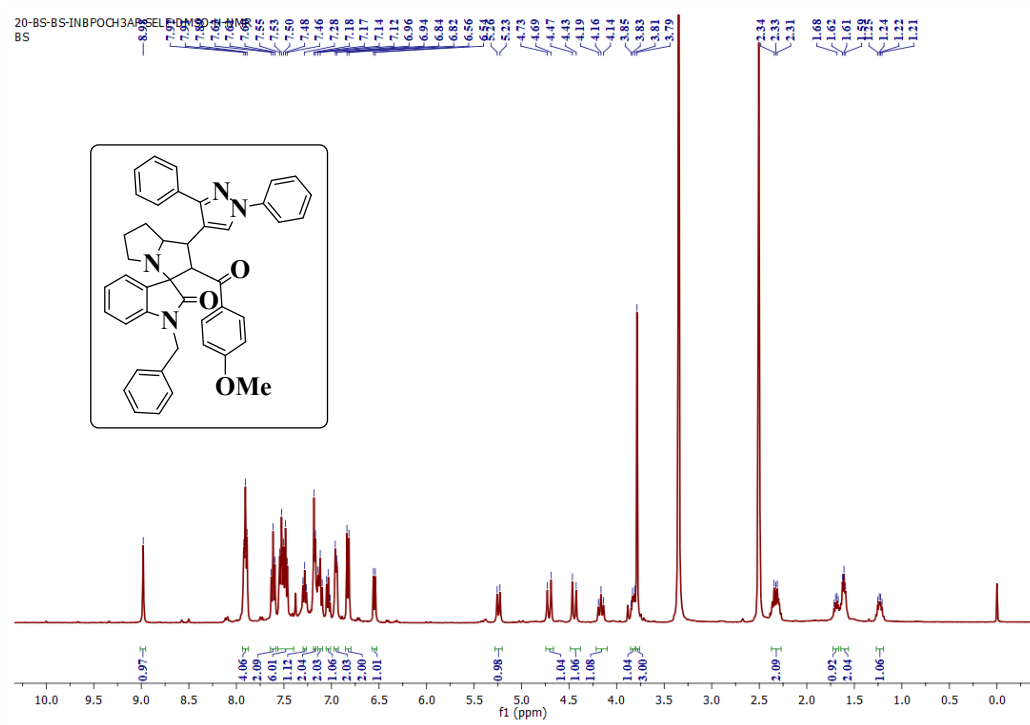


¹³C NMR Spectrum of the compound 4m

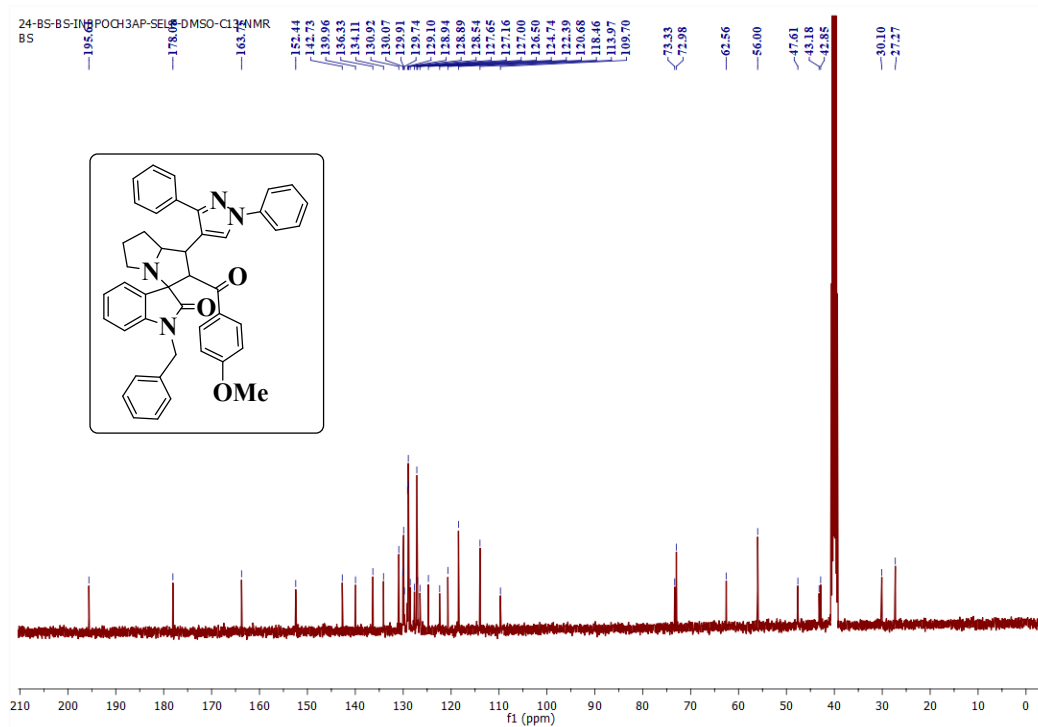


Mass spectrum of the compound 4m

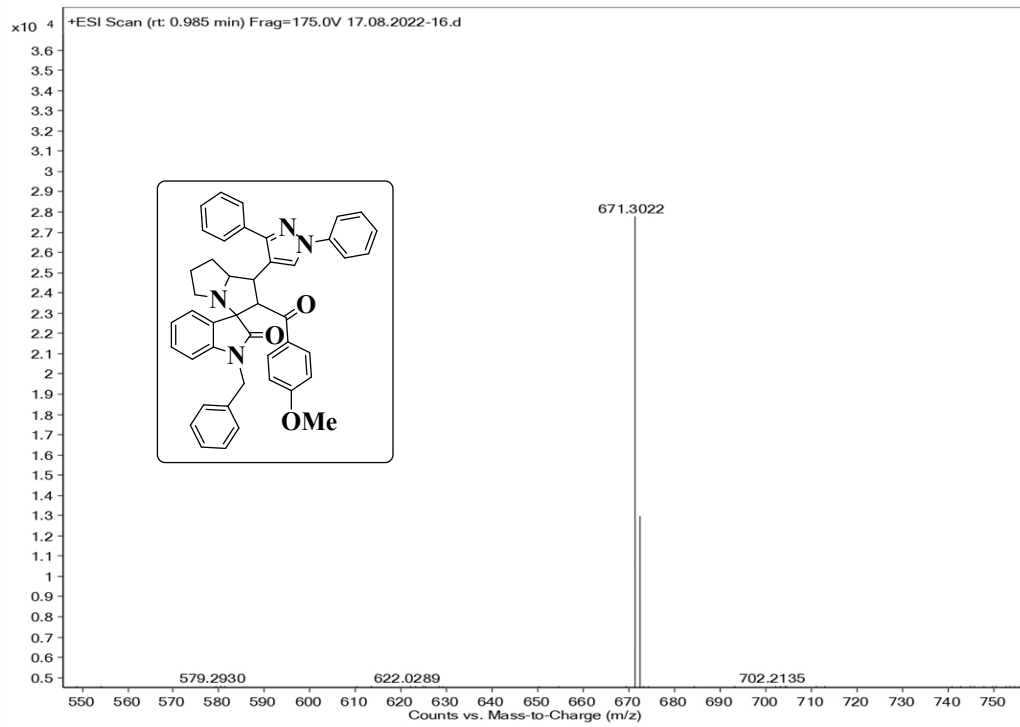




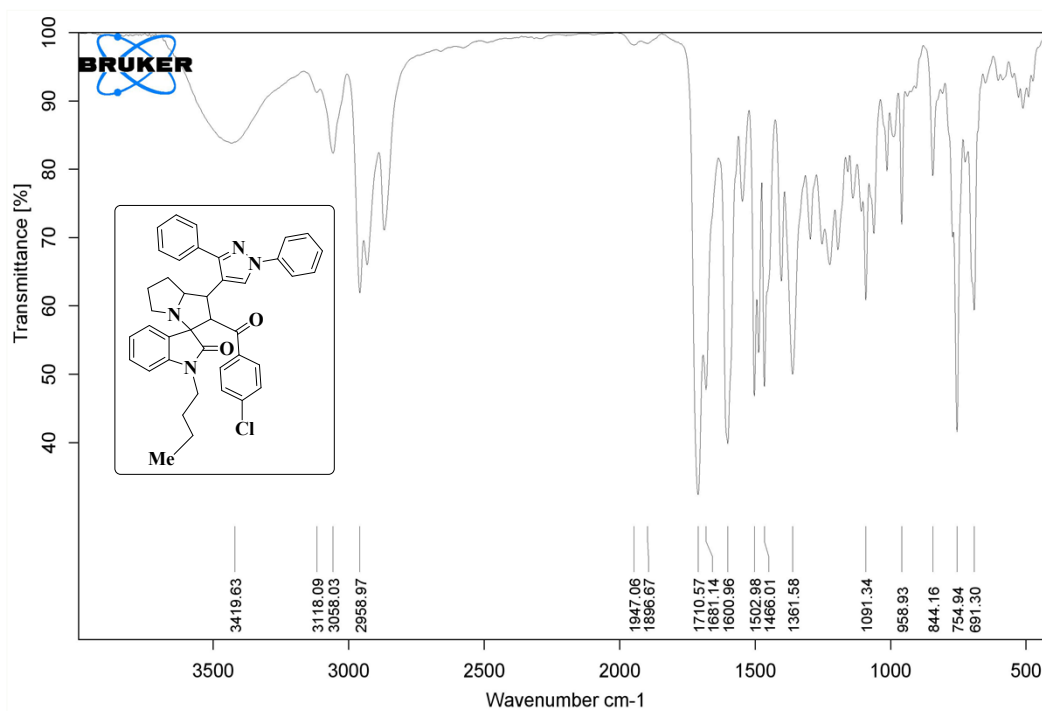
¹H NMR Spectrum of the compound 4n



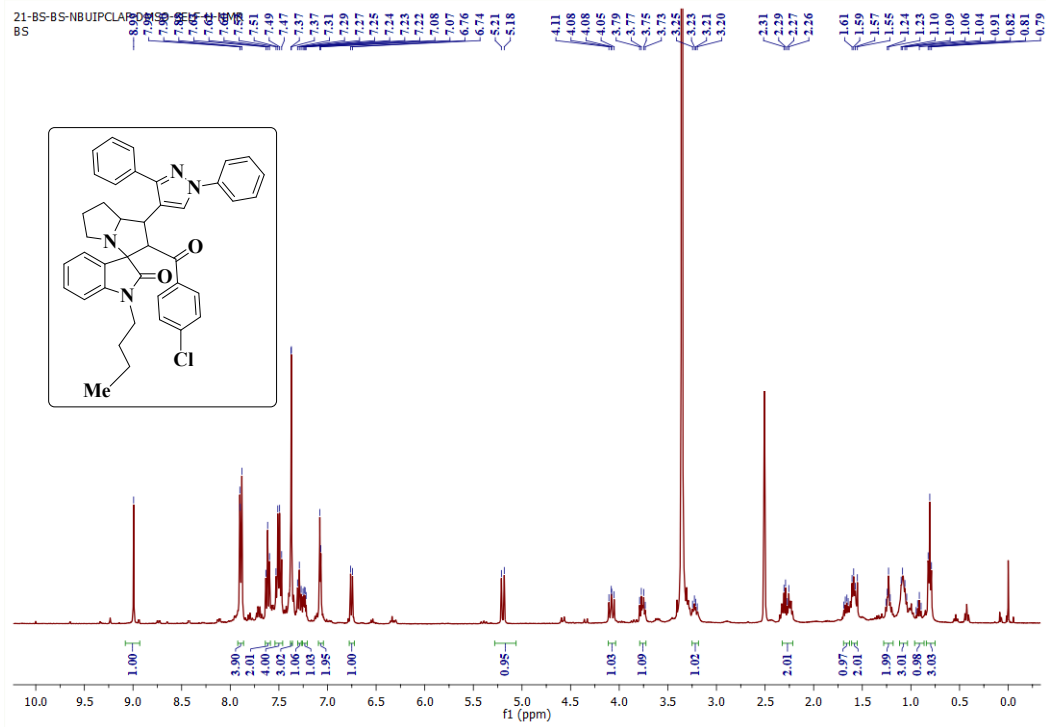
¹³C NMR Spectrum of the compound 4n



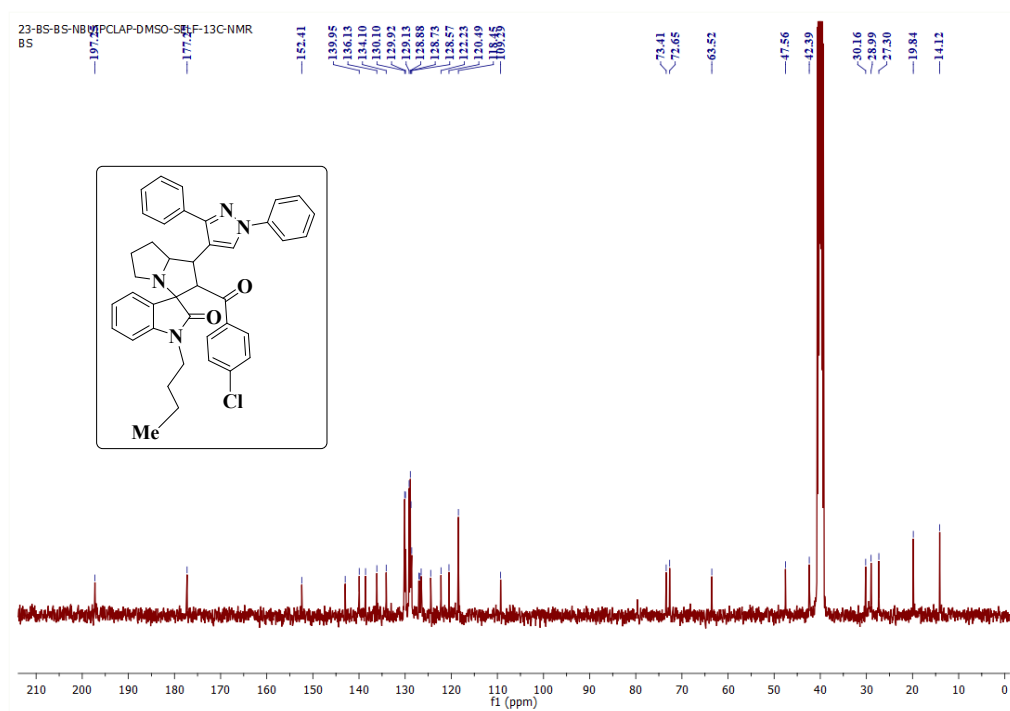
Mass spectrum of the compound 4n



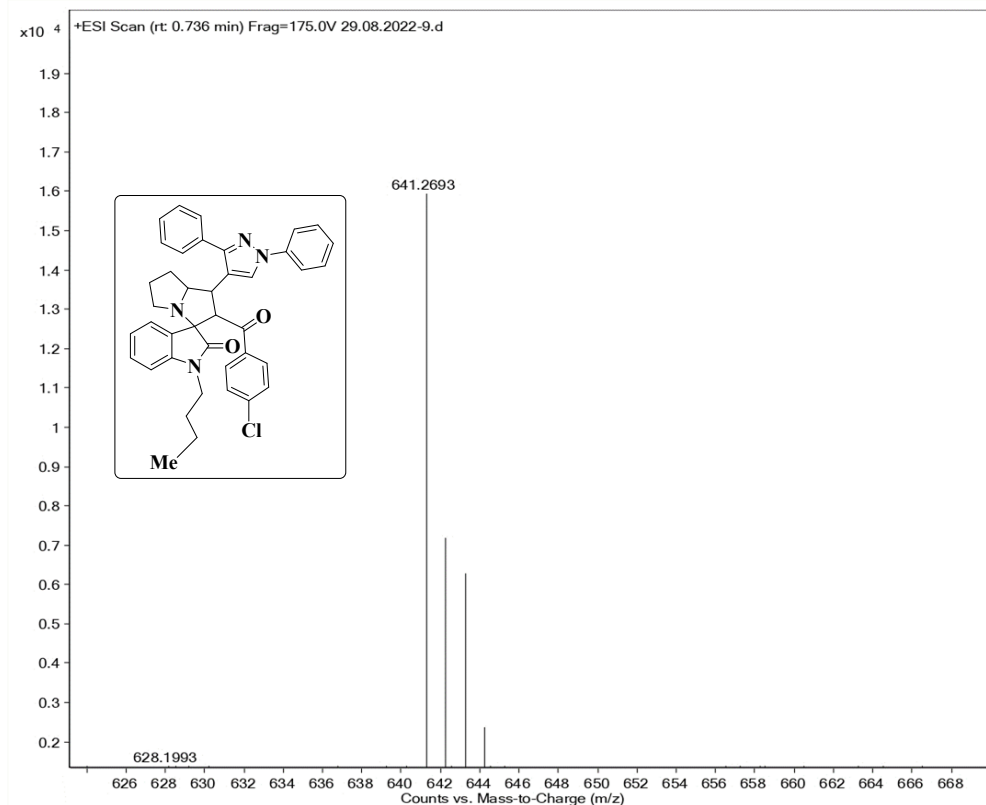
FT-IR Spectrum of the compound 4o



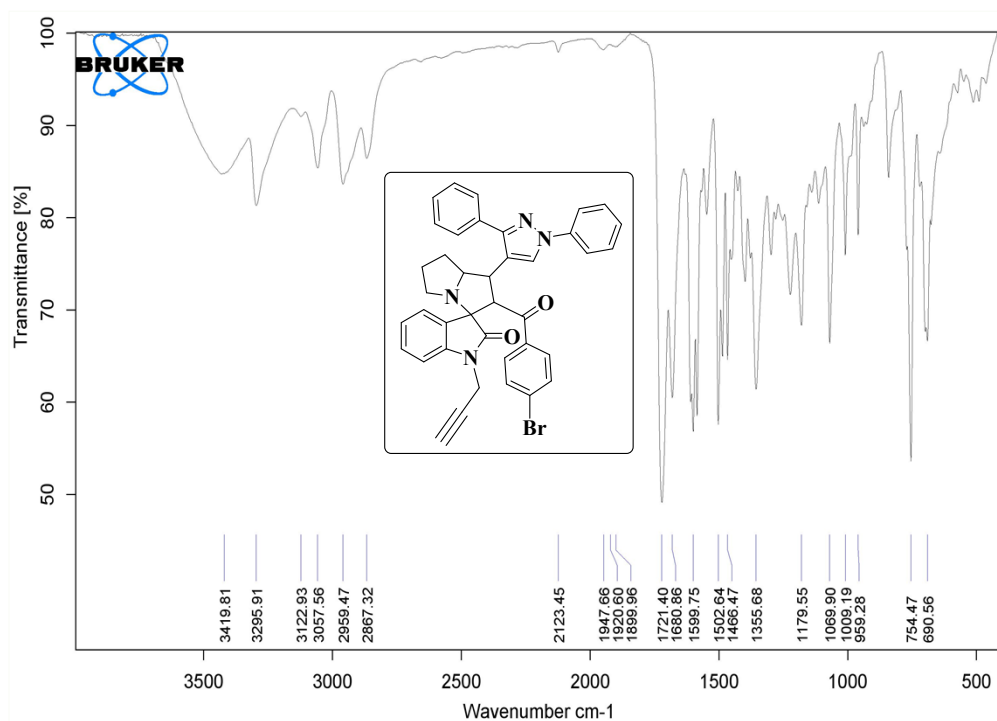
¹H NMR Spectrum of the compound 4o



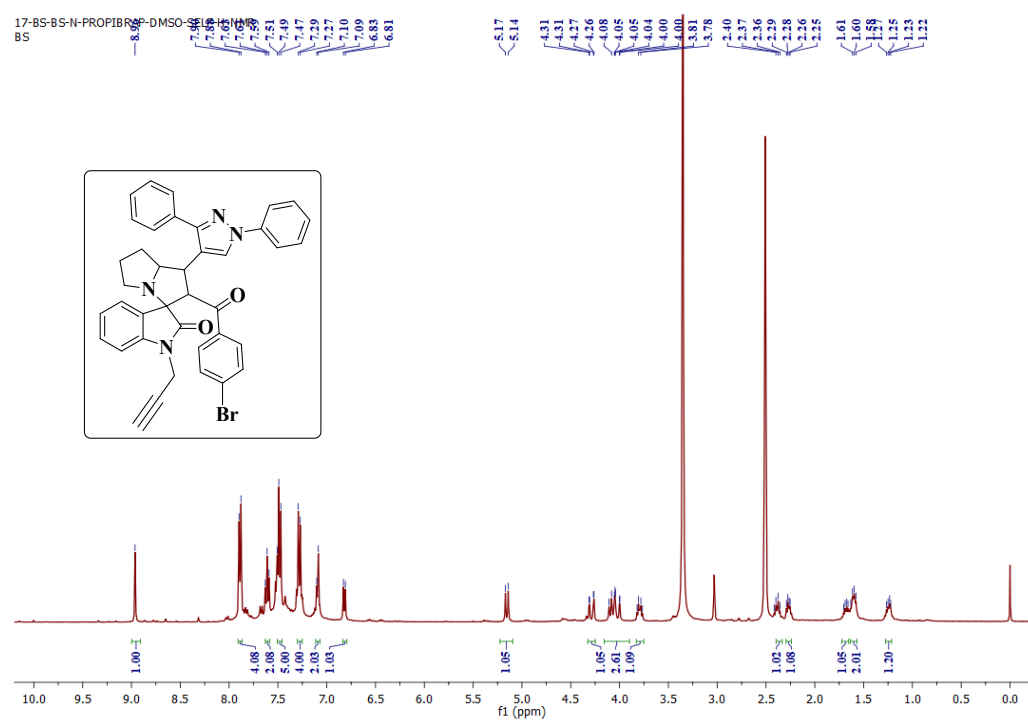
¹³C NMR Spectrum of the compound 4o



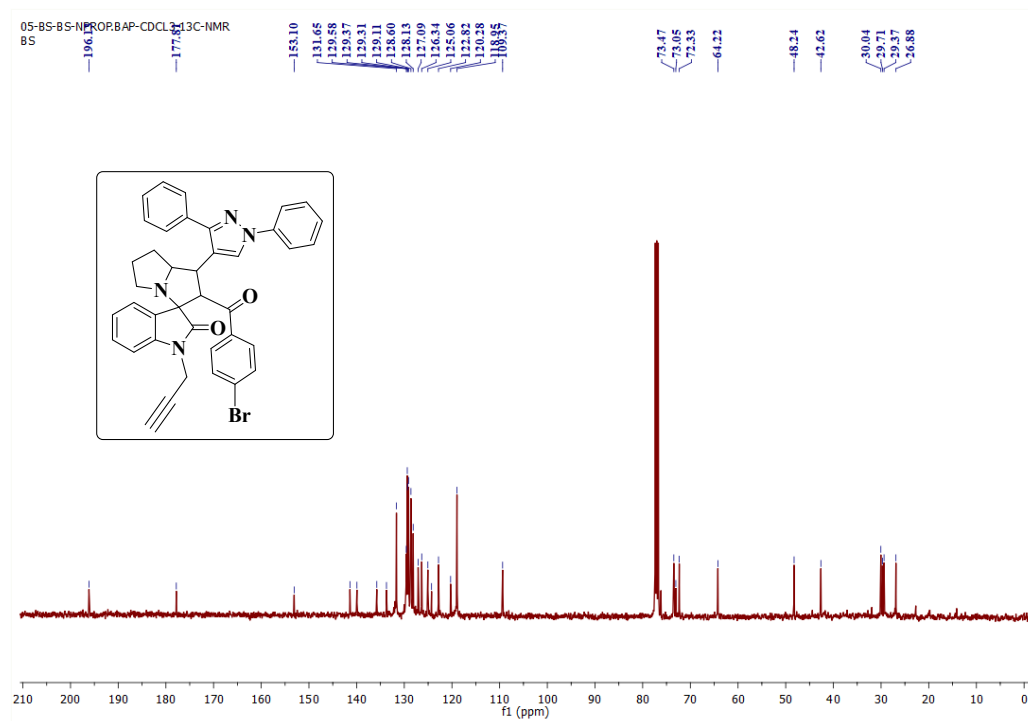
Mass spectrum of the compound 4o



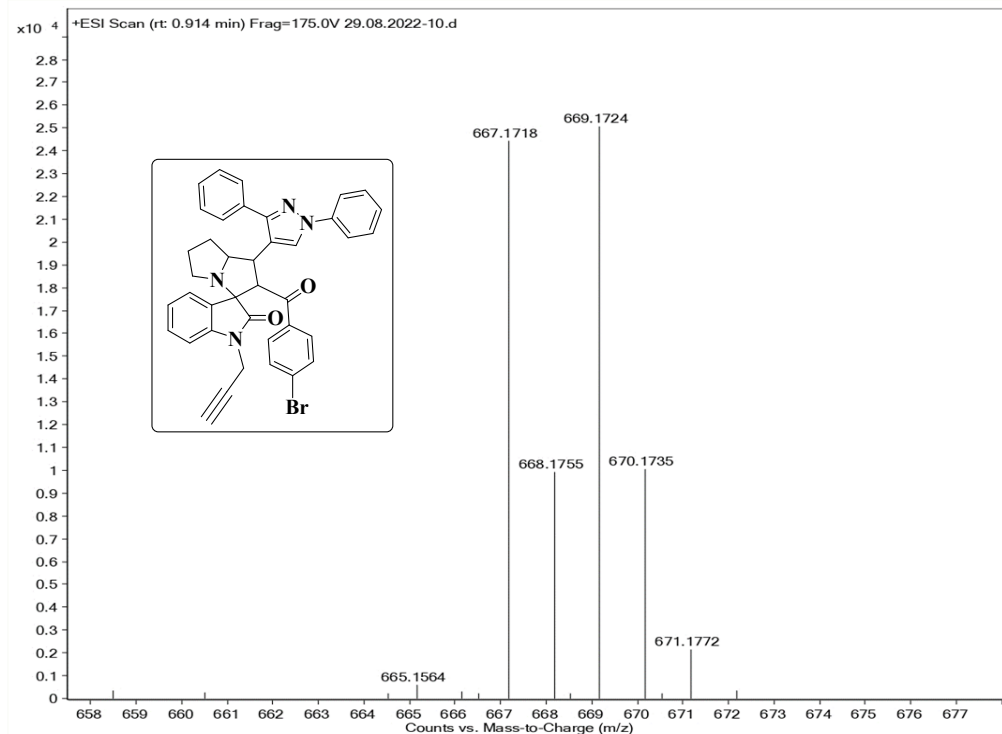
FT-IR Spectrum of the compound 4p



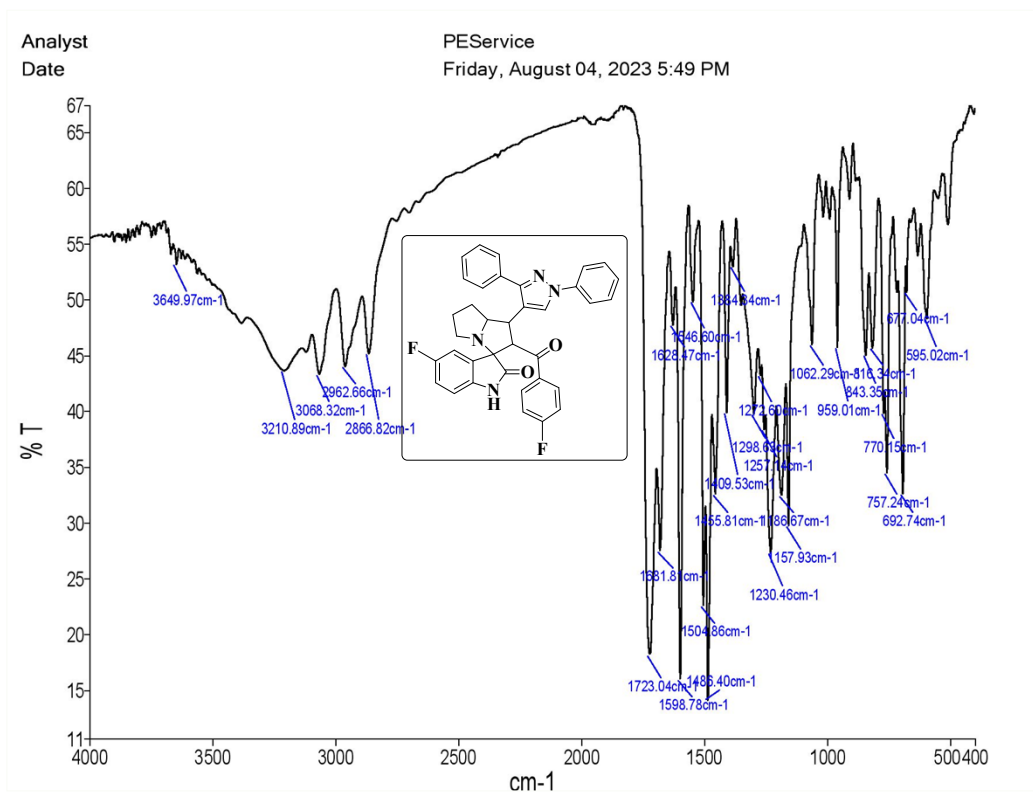
¹H NMR Spectrum of the compound 4p



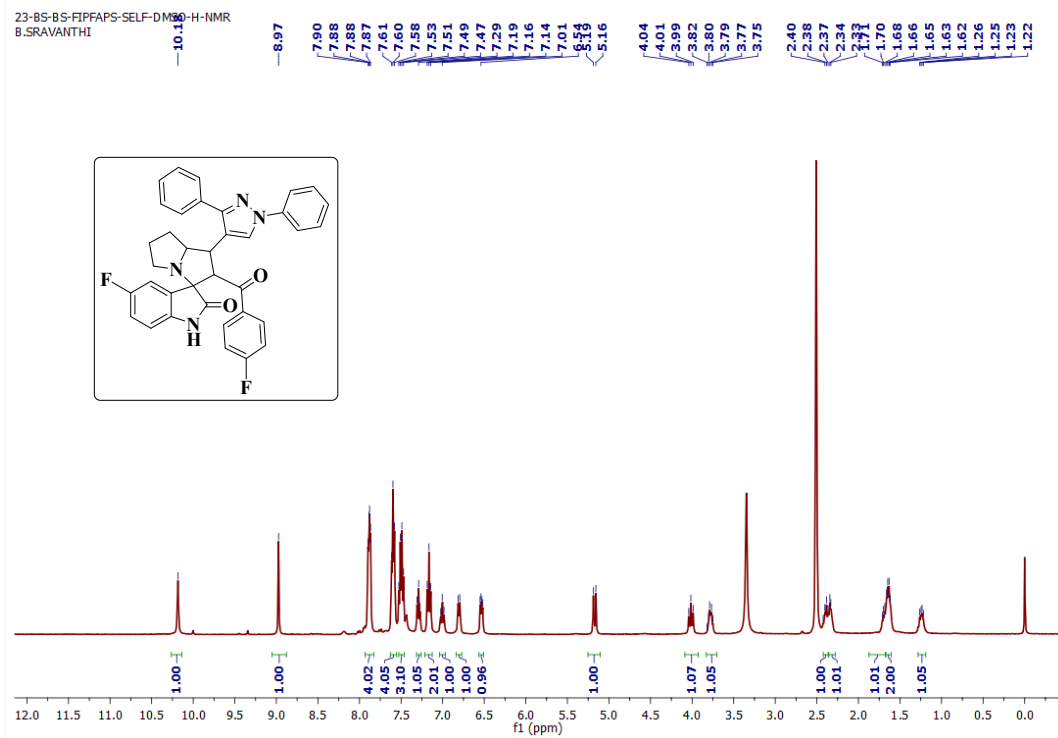
¹³C NMR Spectrum of the compound 4p



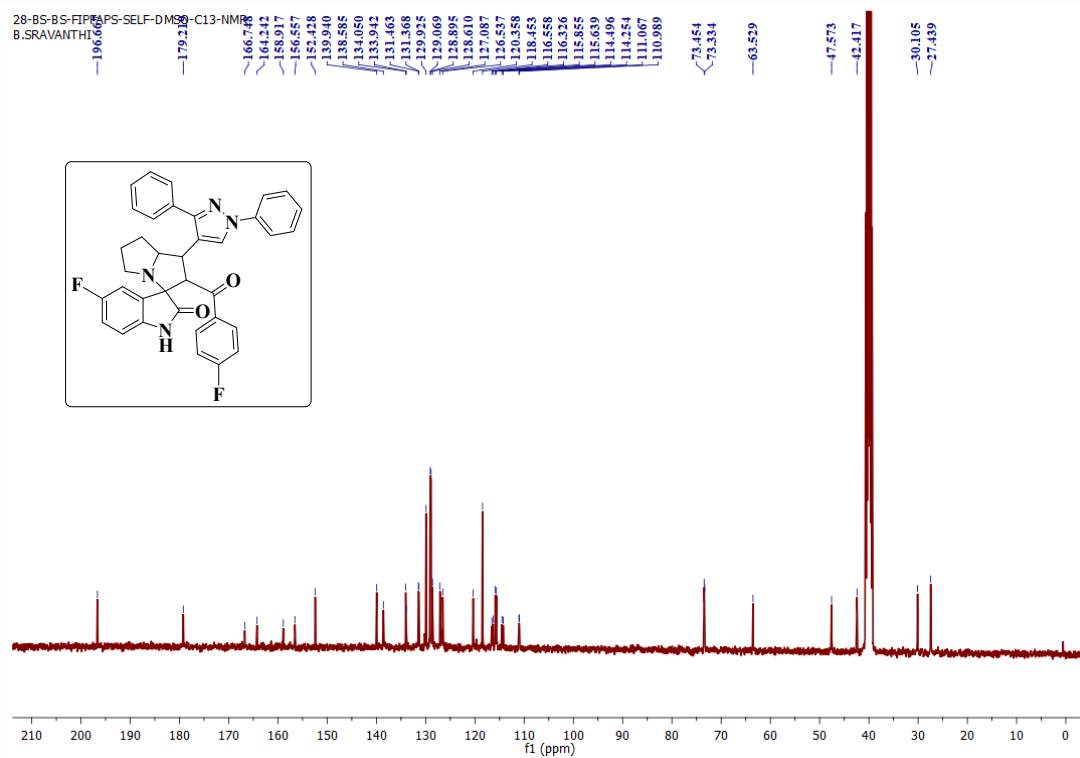
Mass spectrum of the compound 4p



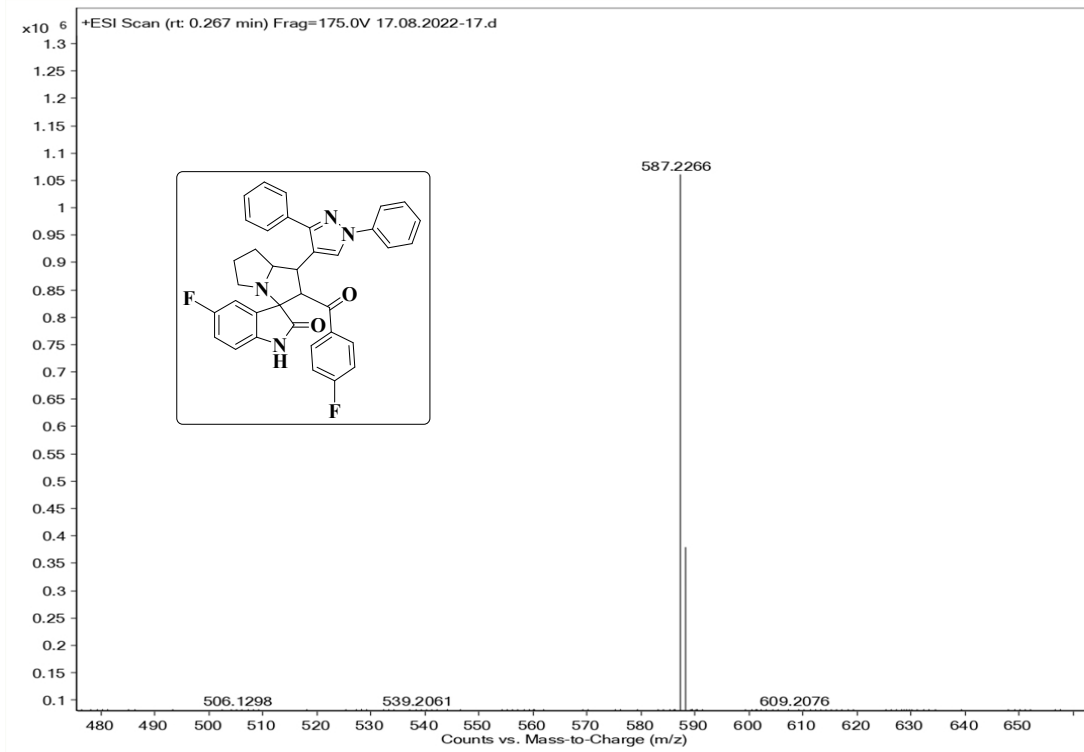
FT-IR Spectrum of the compound 4q



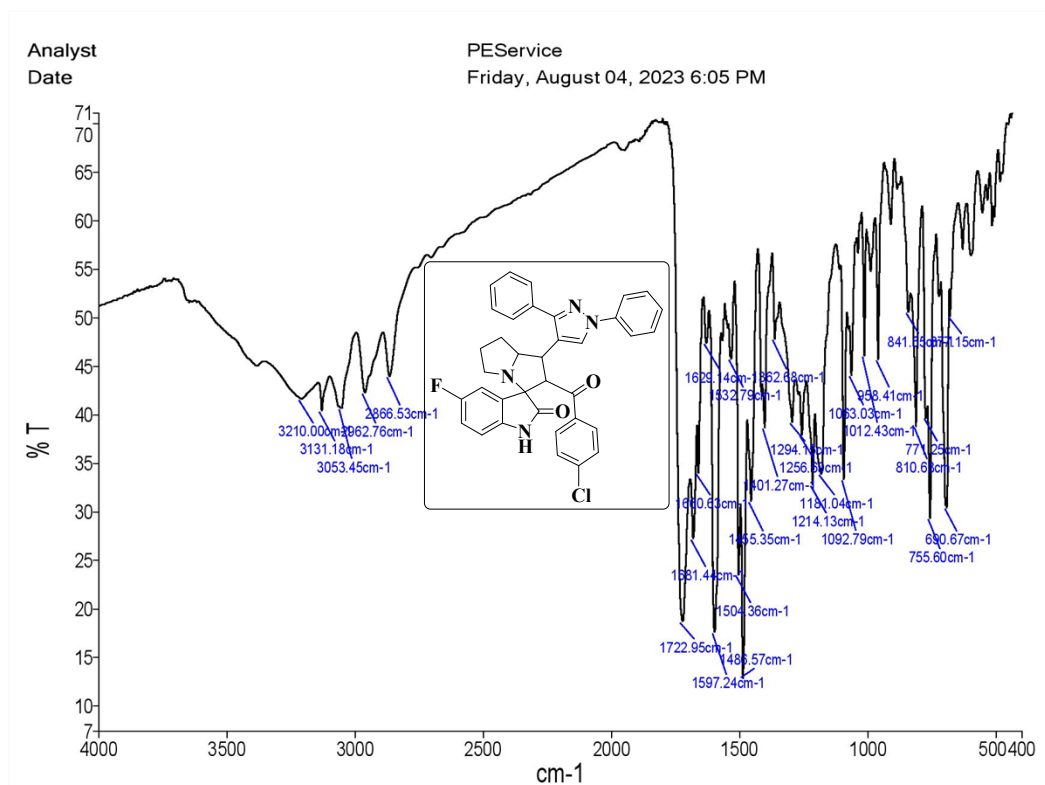
¹H NMR Spectrum of the compound 4q



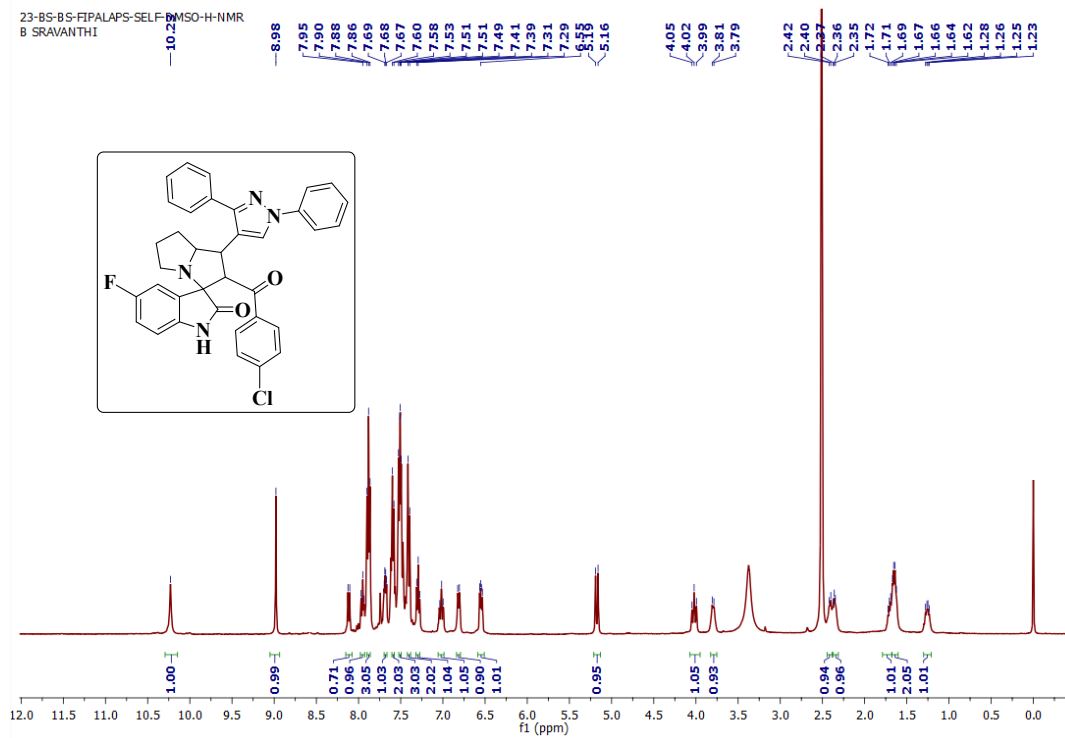
¹³C NMR Spectrum of the compound 4q



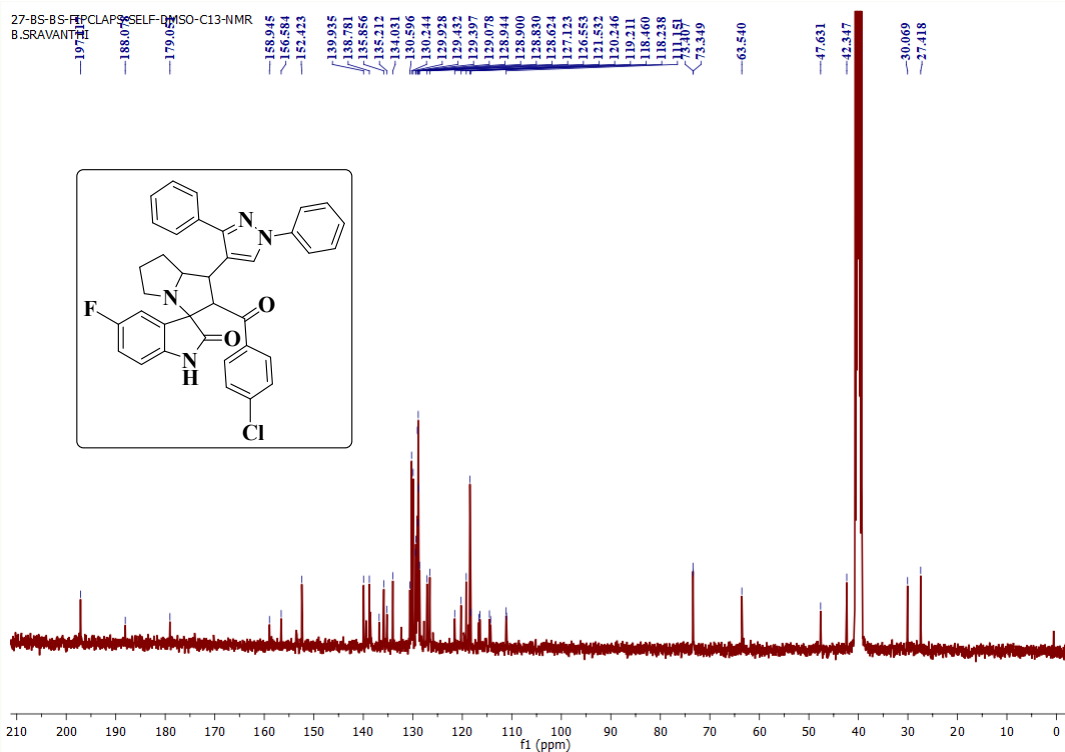
Mass spectrum of the compound 4q



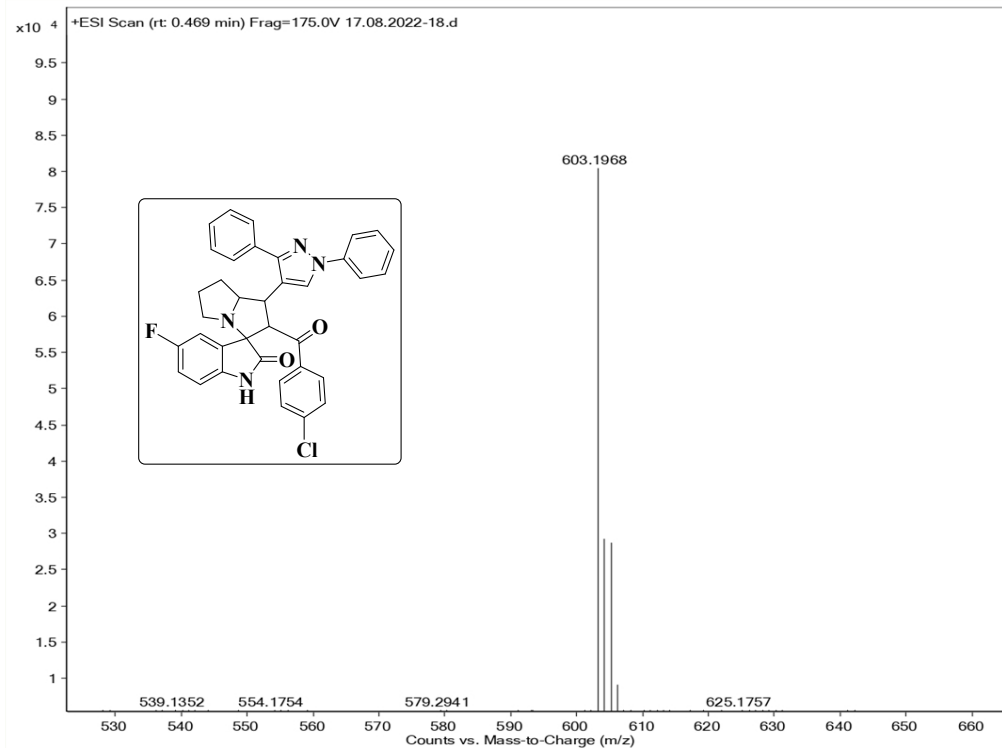
FT-IR Spectrum of the compound 4r



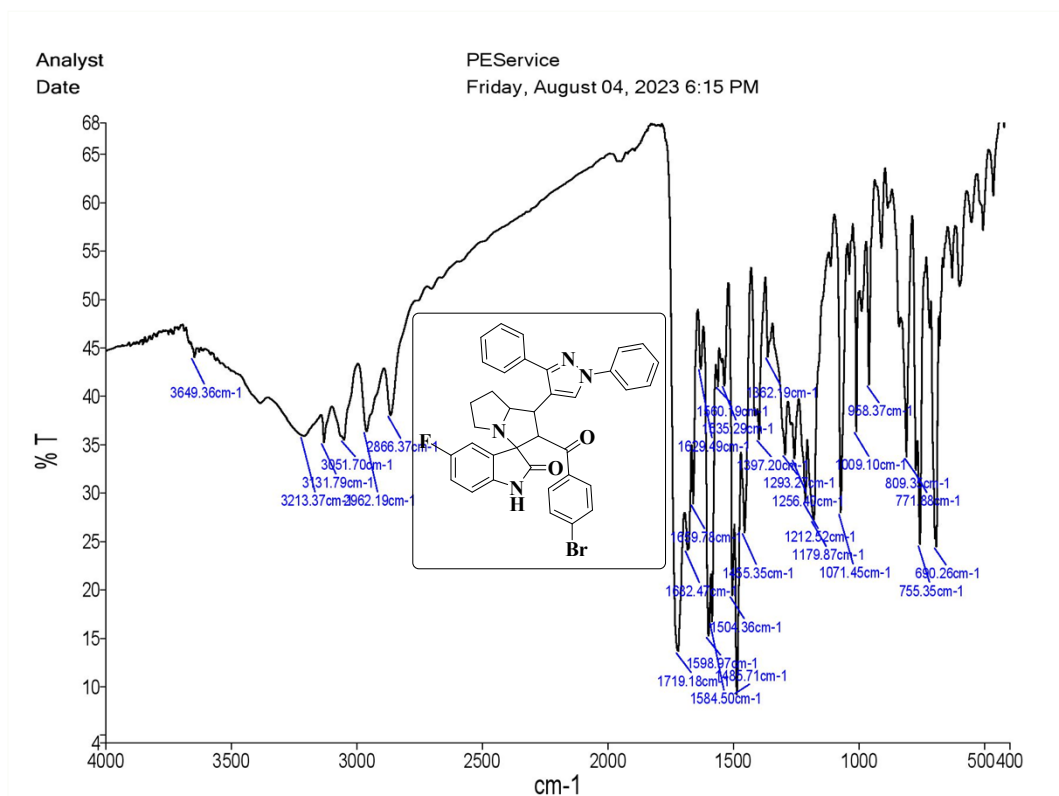
¹H NMR Spectrum of the compound 4r



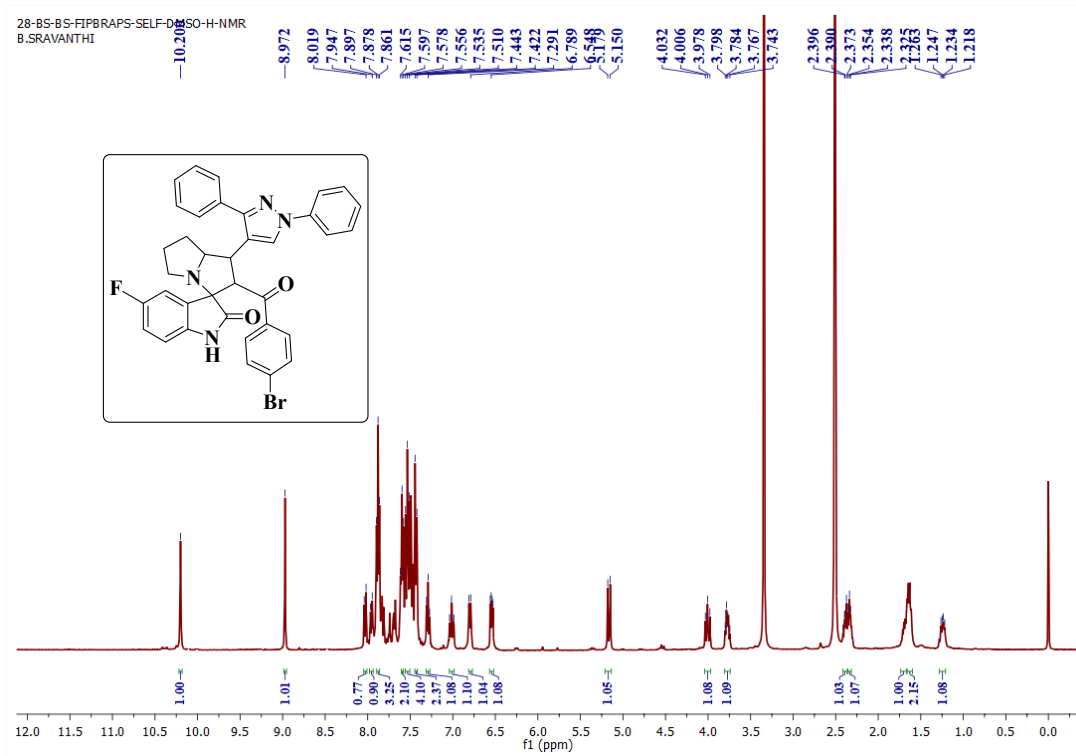
¹³C NMR Spectrum of the compound 4r



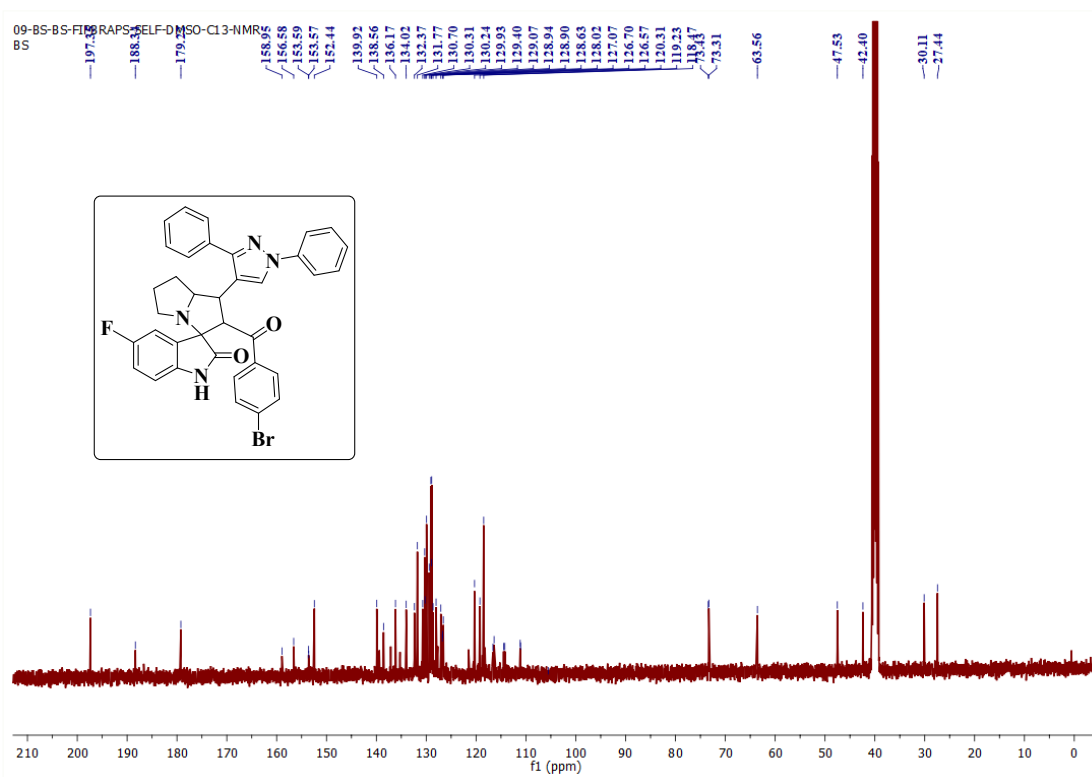
Mass spectrum of the compound 4r



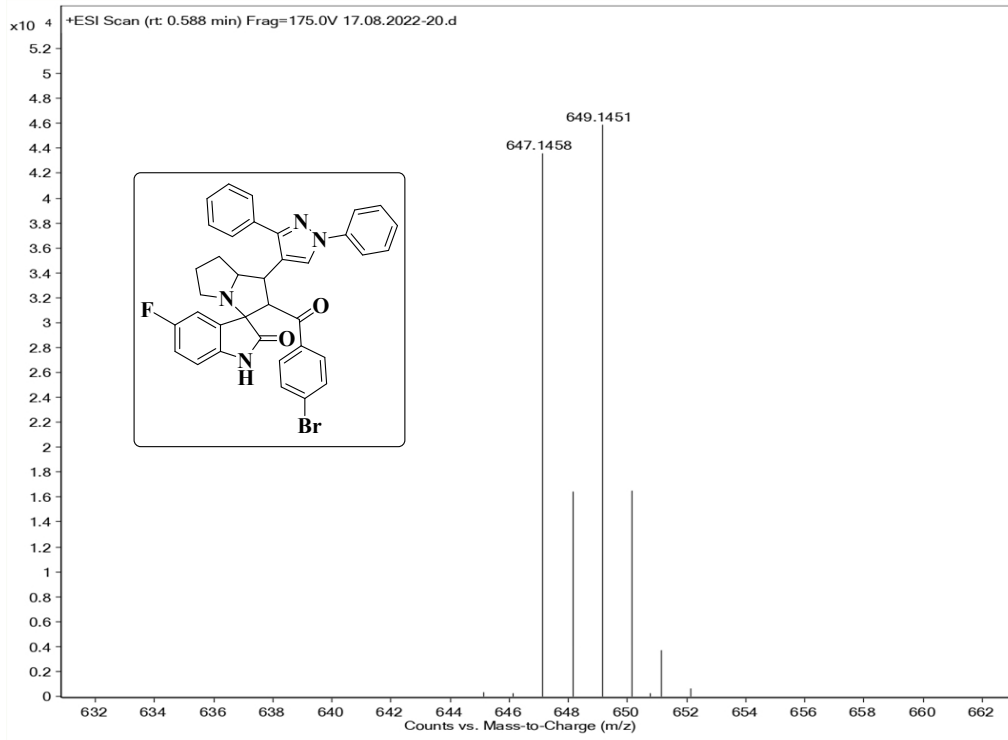
FT-IR Spectrum of the compound 4s



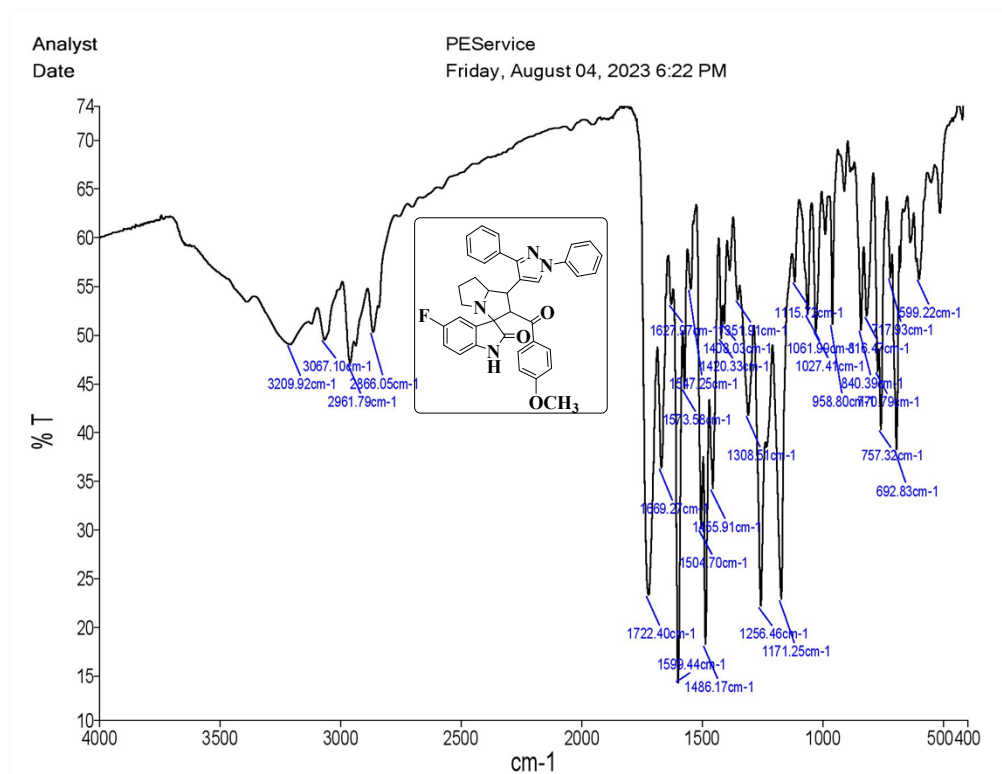
¹H NMR Spectrum of the compound 4s



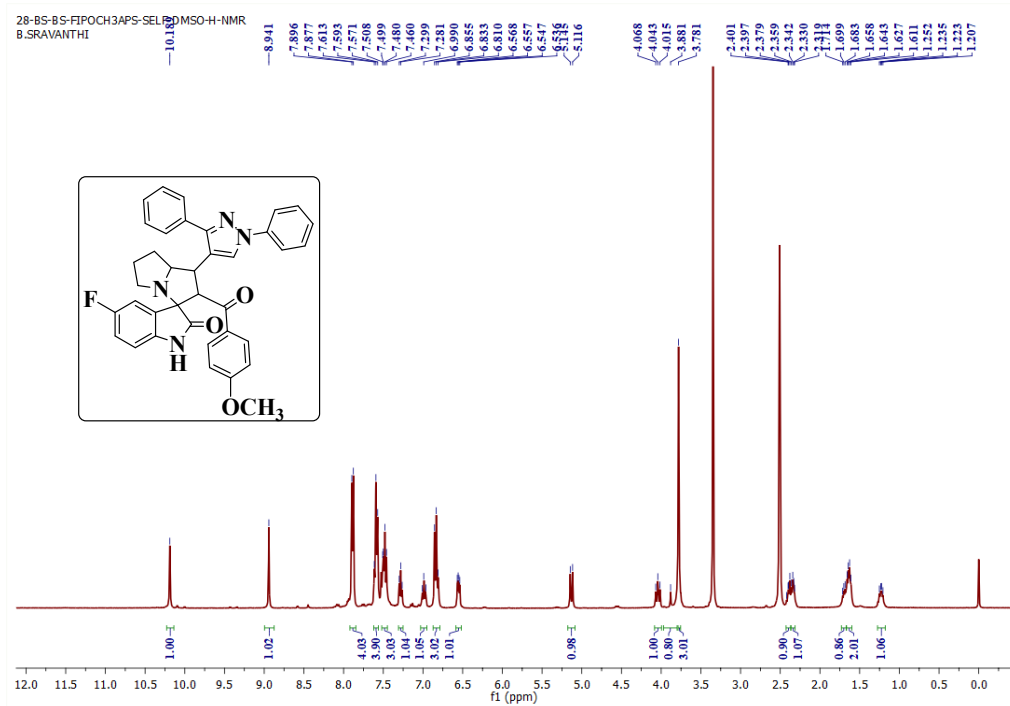
¹³C NMR Spectrum of the compound 4s



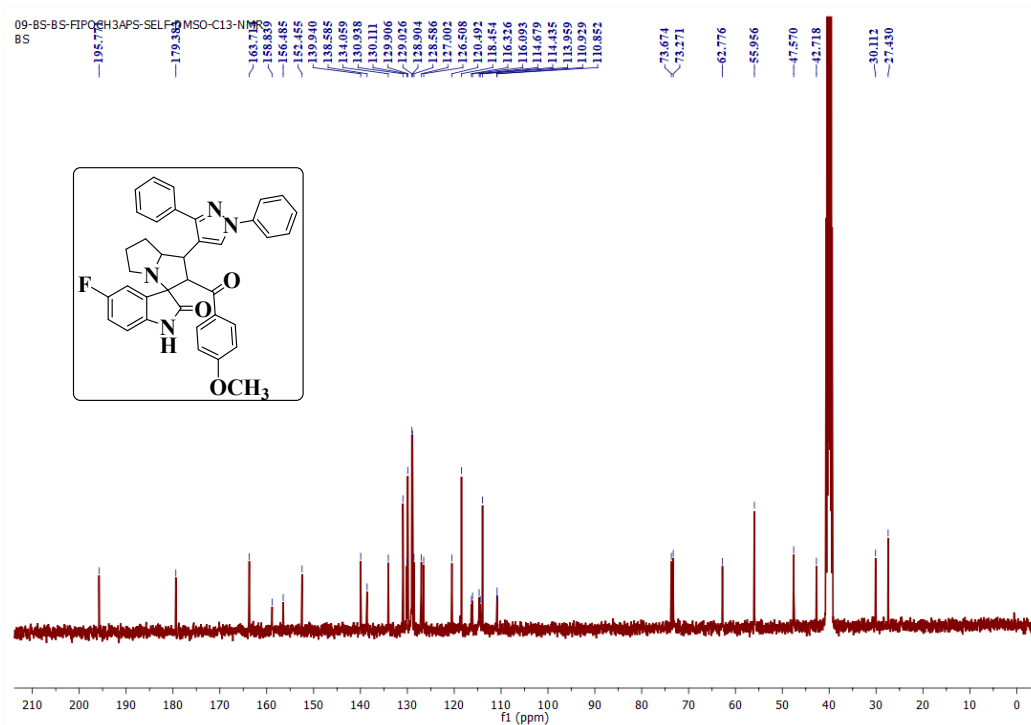
Mass spectrum of the compound 4s



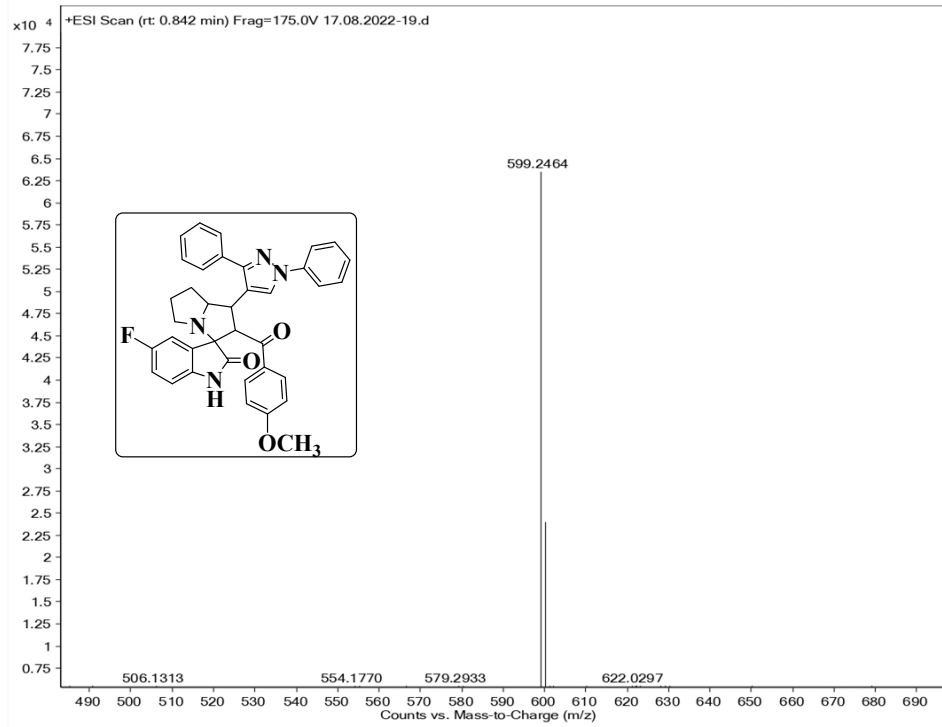
FT-IR Spectrum of the compound 4t



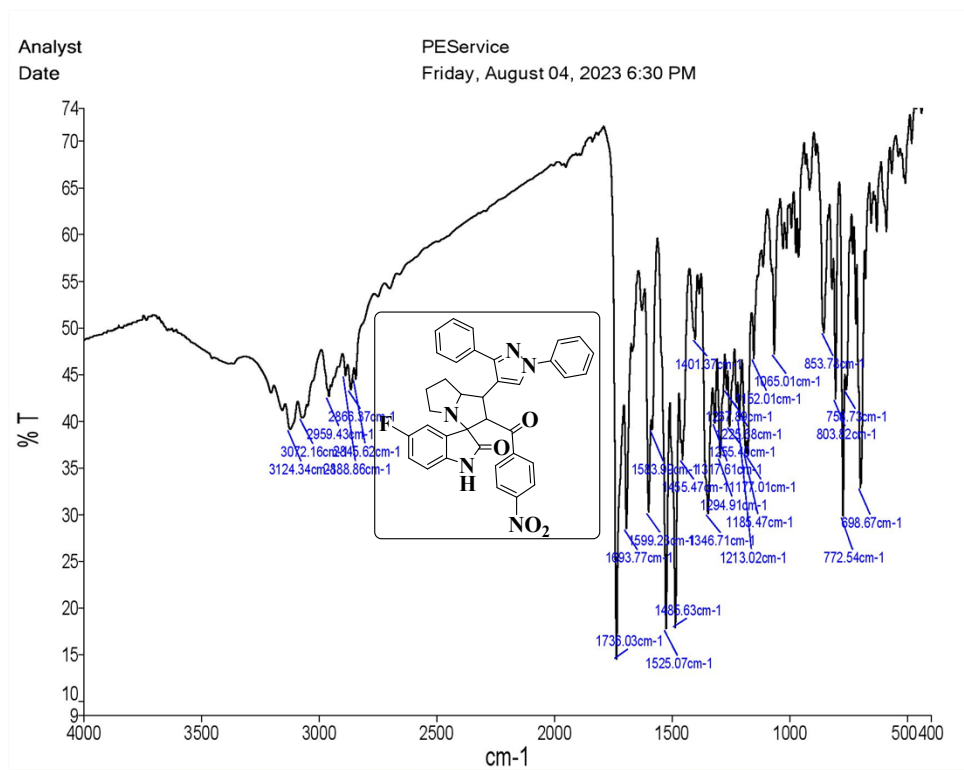
¹H NMR Spectrum of the compound 4t



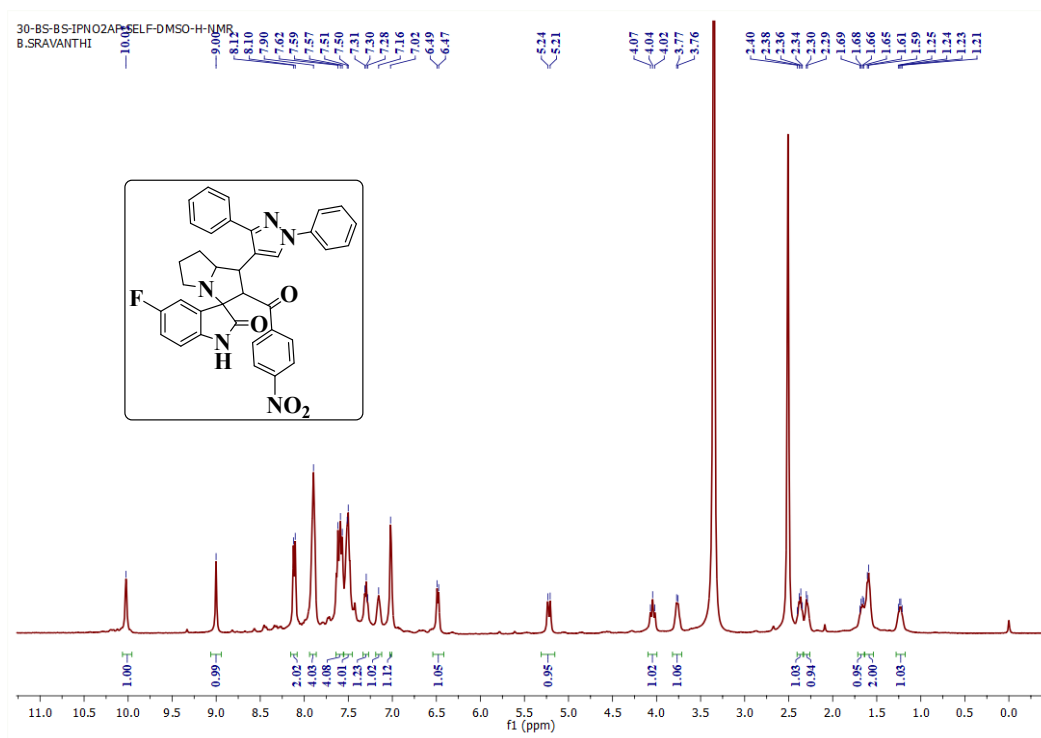
¹³C NMR Spectrum of the compound 4t



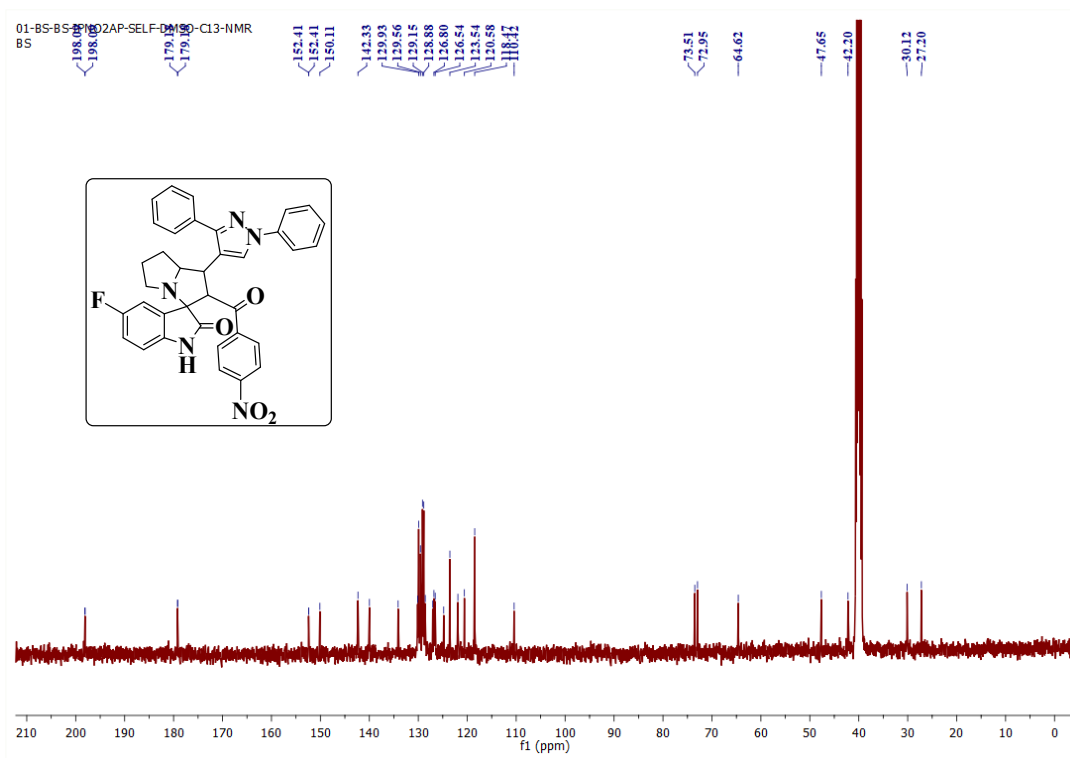
Mass spectrum of the compound 4t



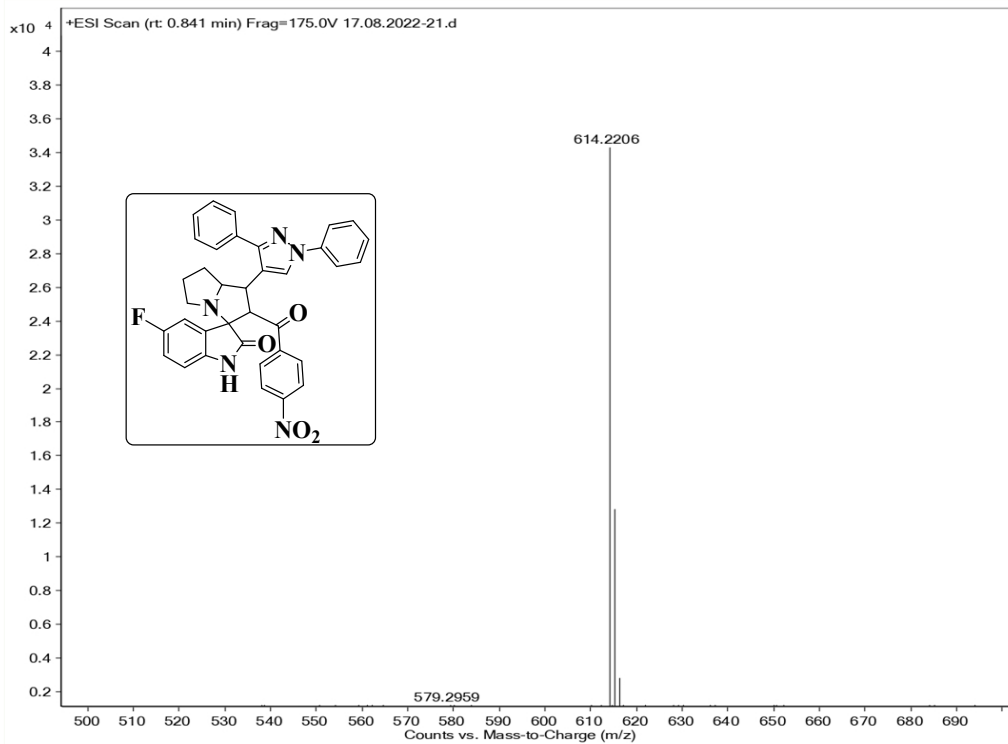
FT-IR Spectrum of the compound 4u



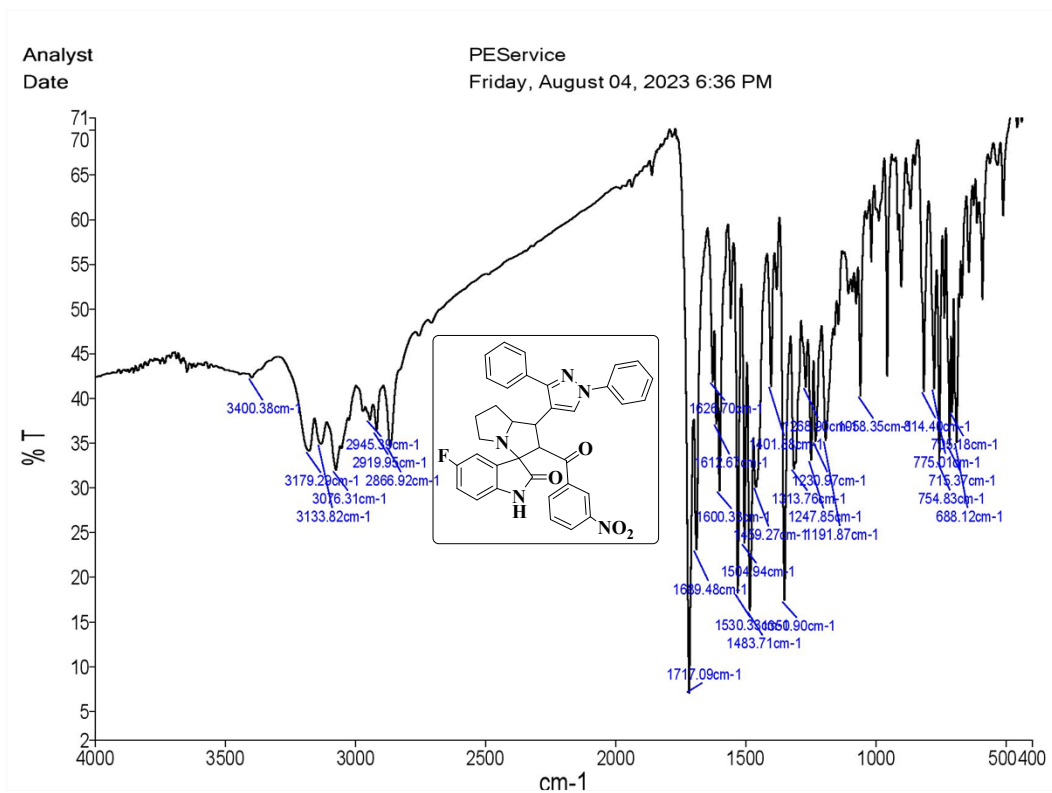
¹H NMR Spectrum of the compound 4u



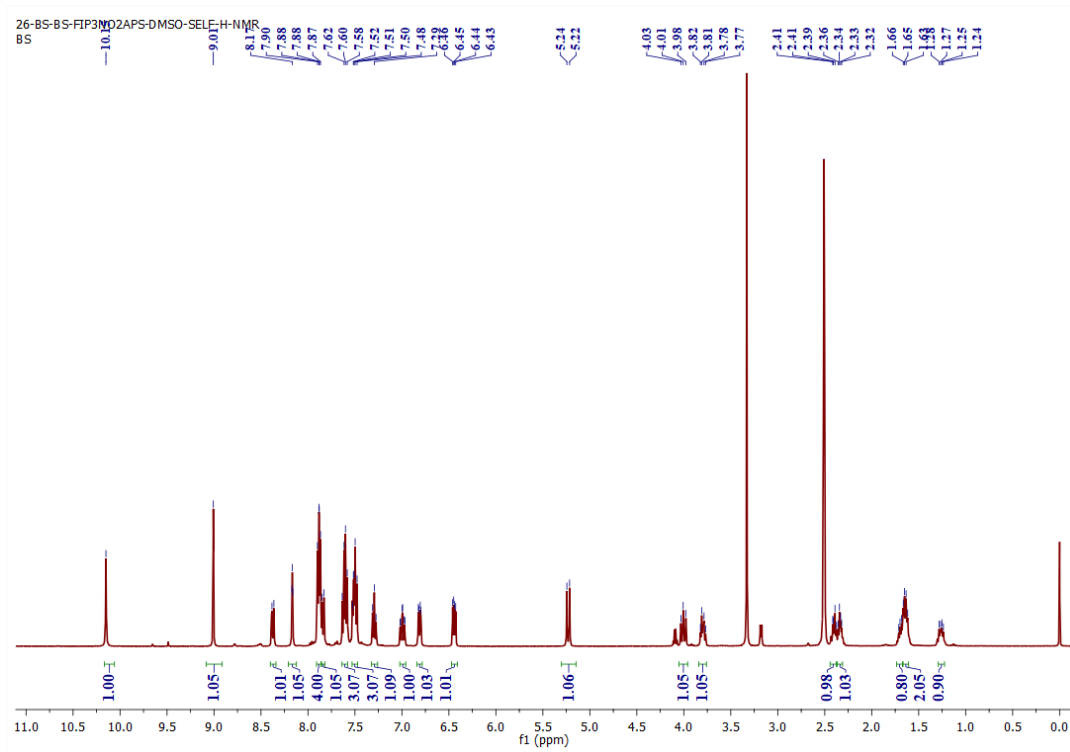
¹³C NMR Spectrum of the compound 4u



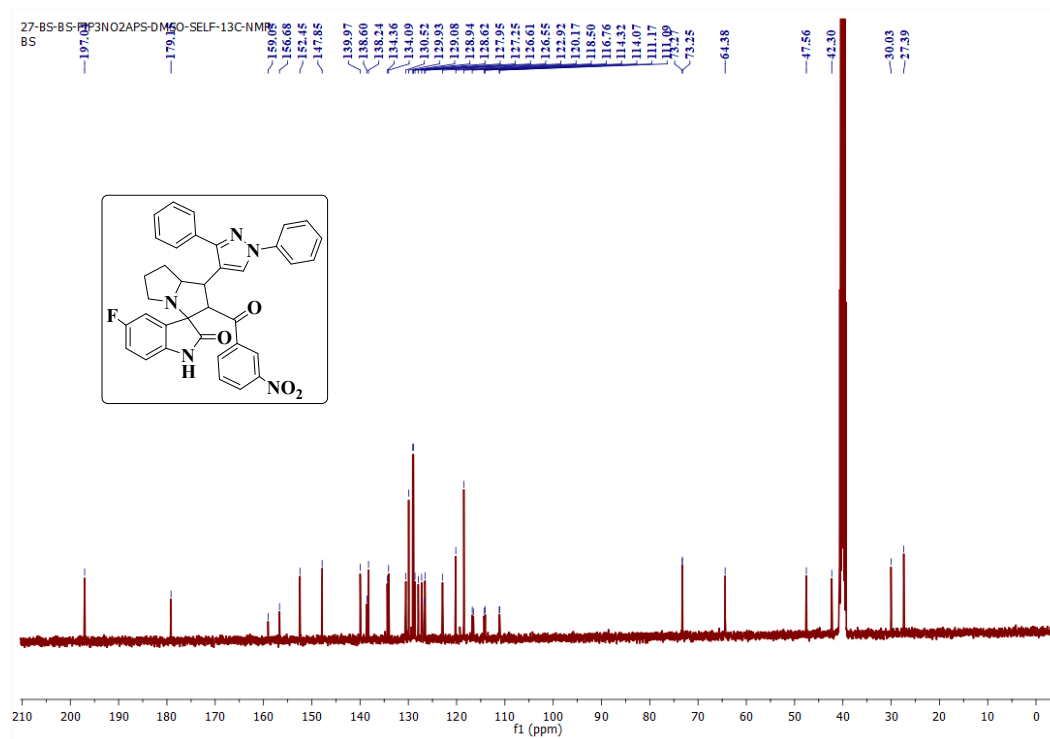
Mass spectrum of the compound 4u



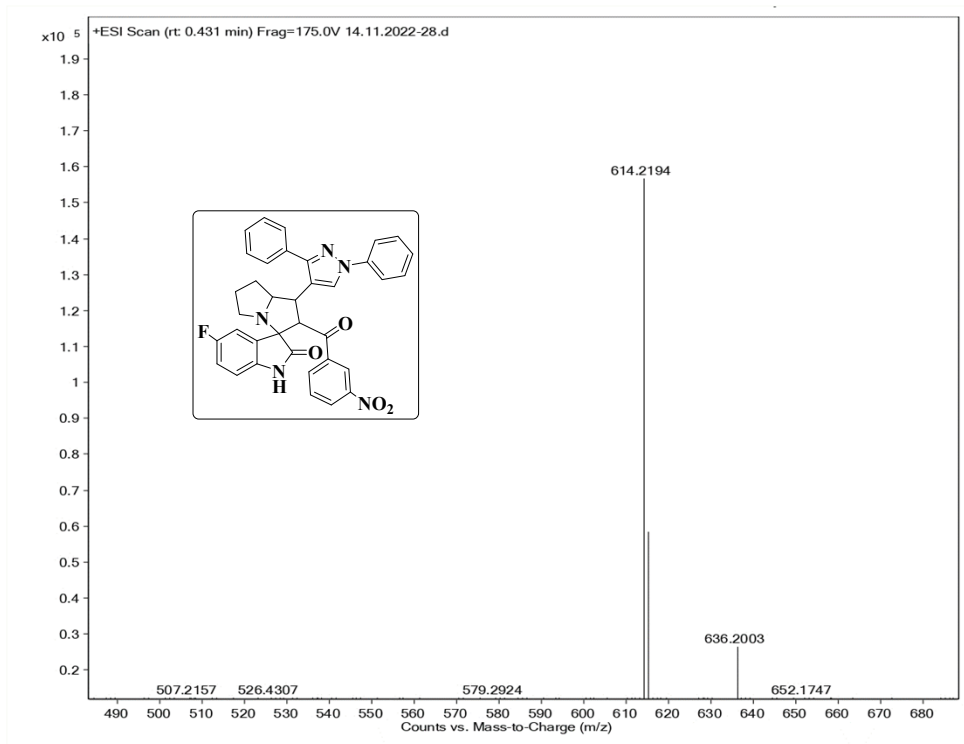
FT-IR Spectrum of the compound 4v



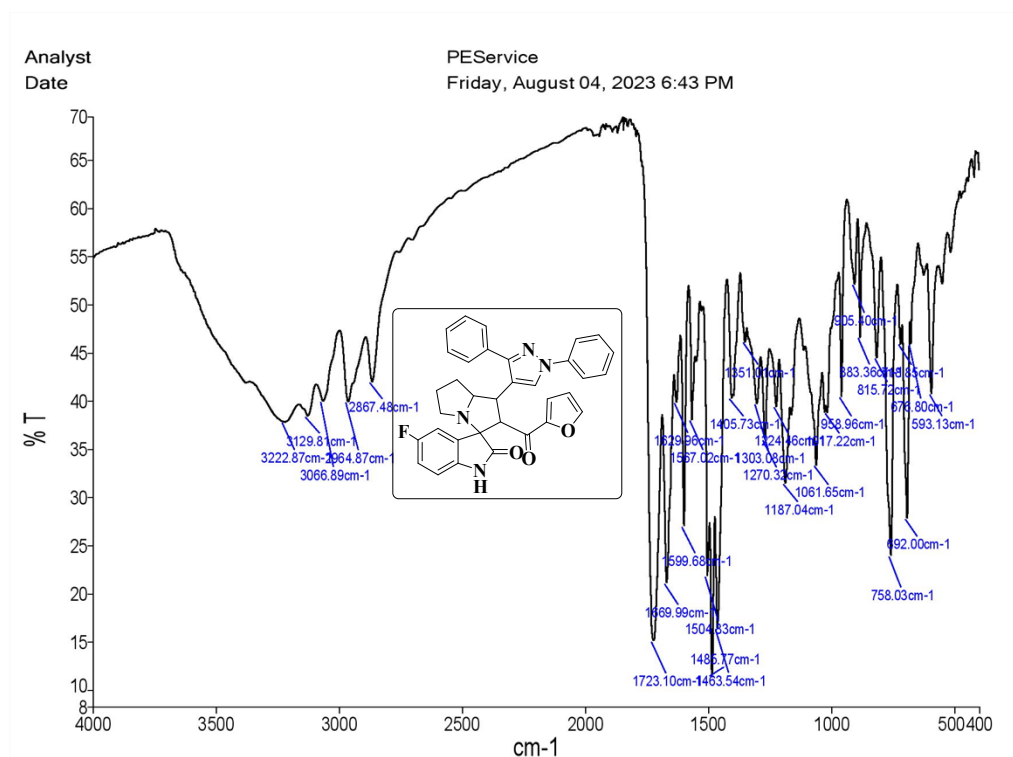
¹H NMR Spectrum of the compound 4v



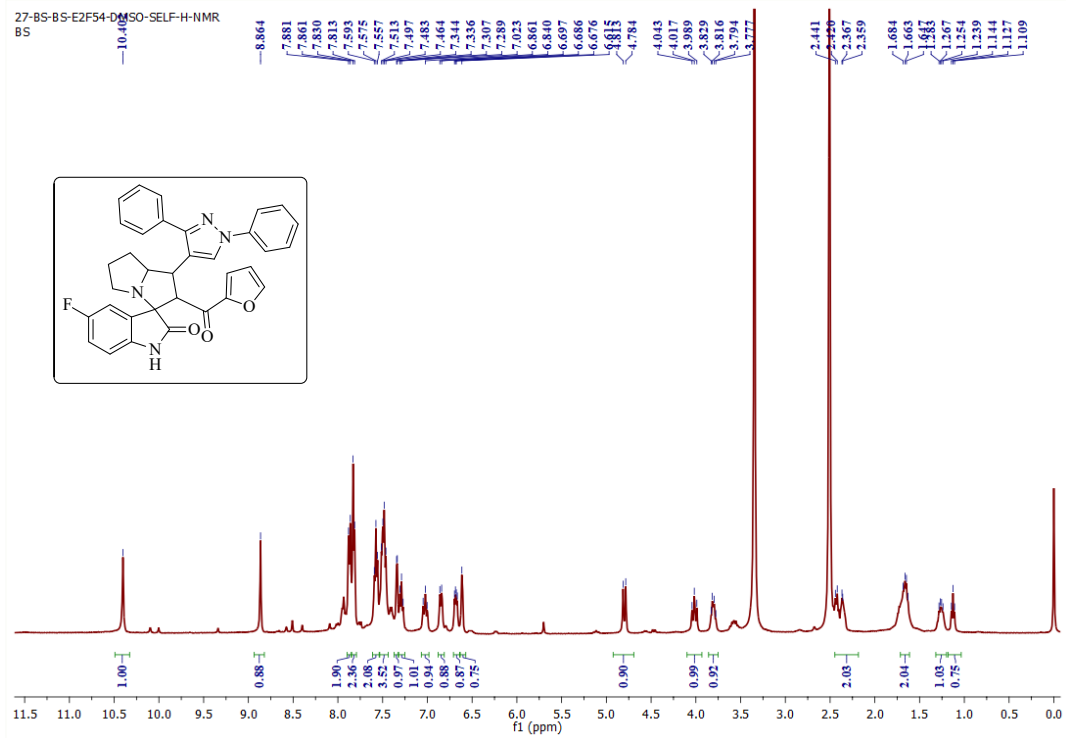
¹³C NMR Spectrum of the compound 4v



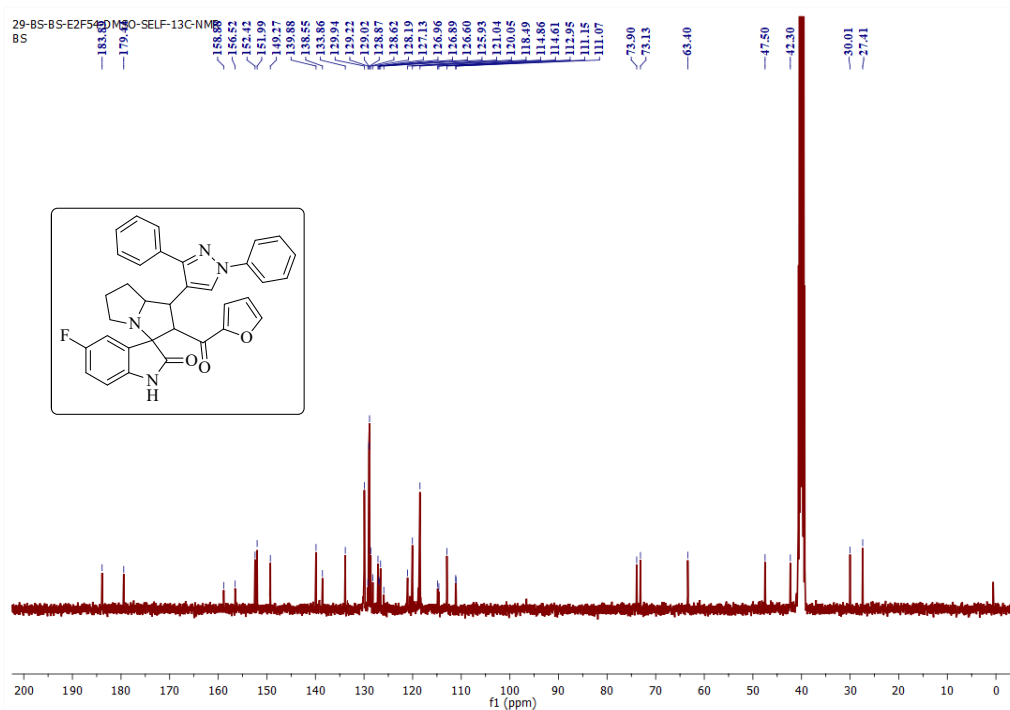
Mass spectrum of the compound 4v



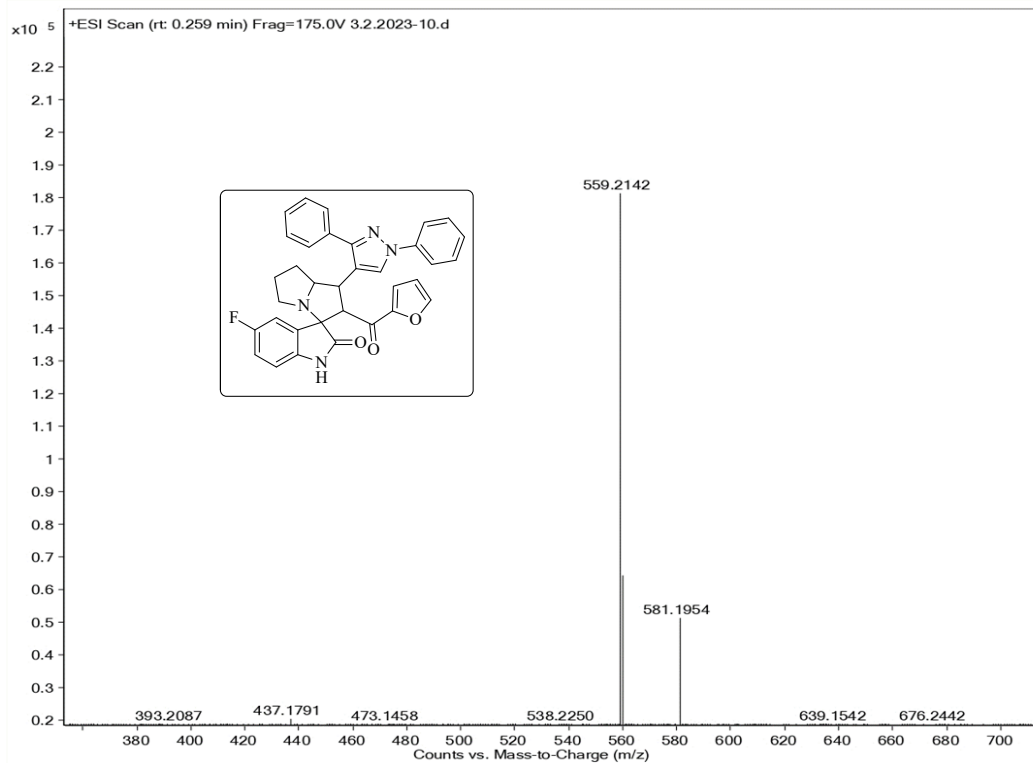
FT-IR Spectrum of the compound 4w



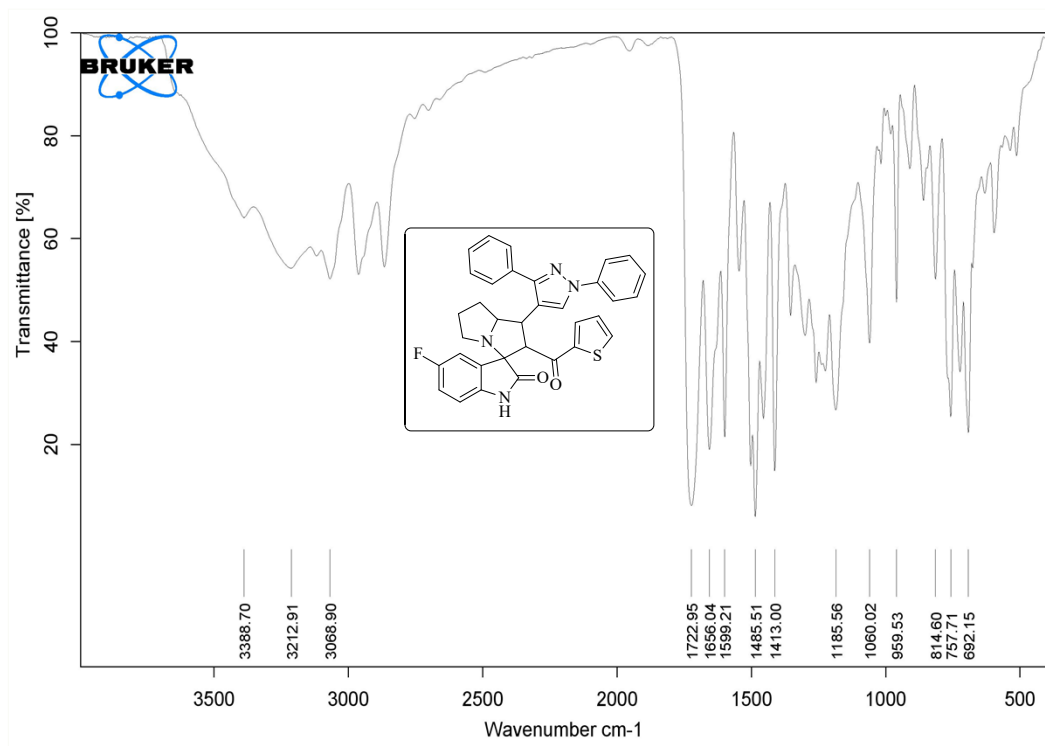
¹H NMR Spectrum of the compound 4w



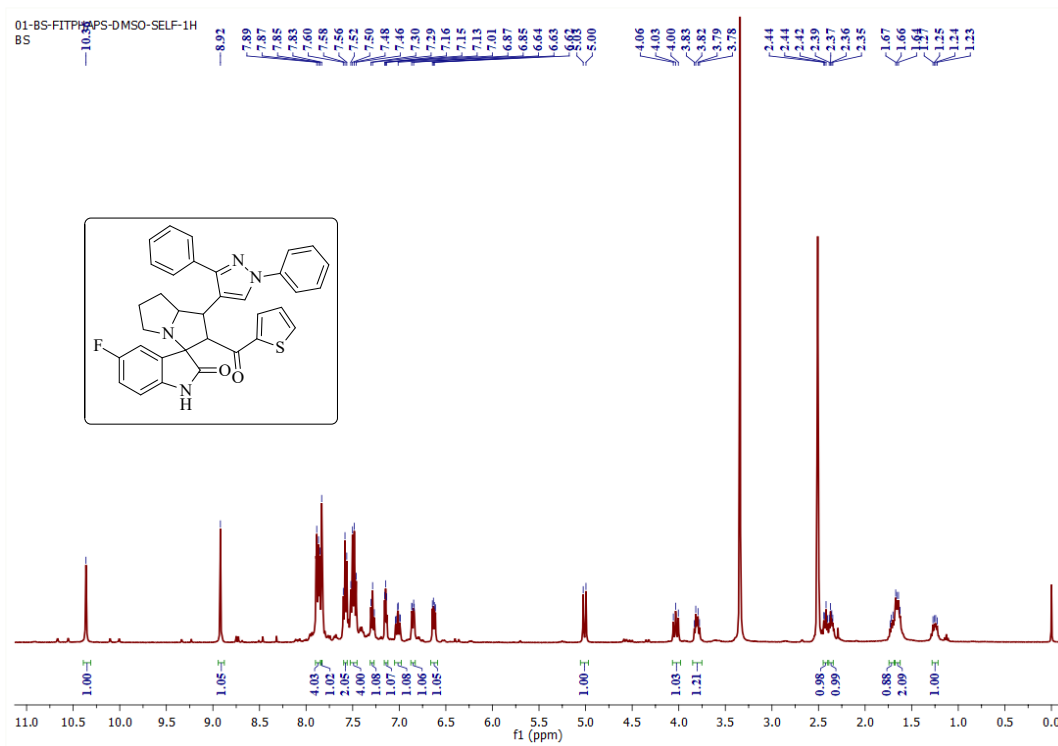
¹³C NMR Spectrum of the compound 4w



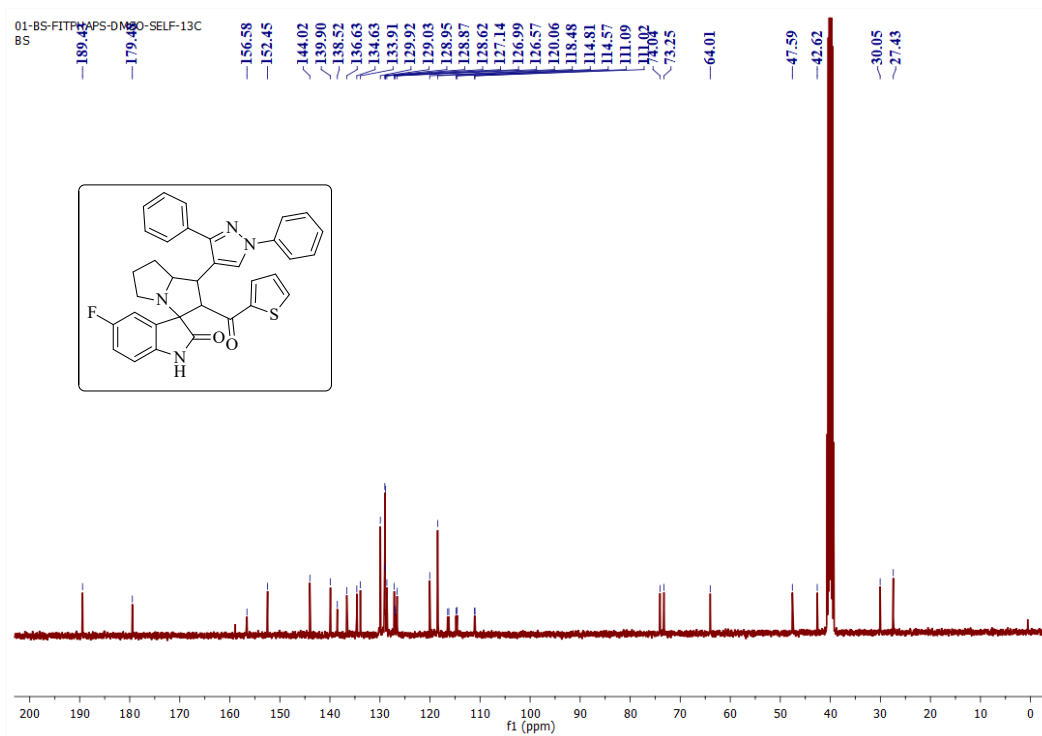
Mass spectrum of the compound 4w



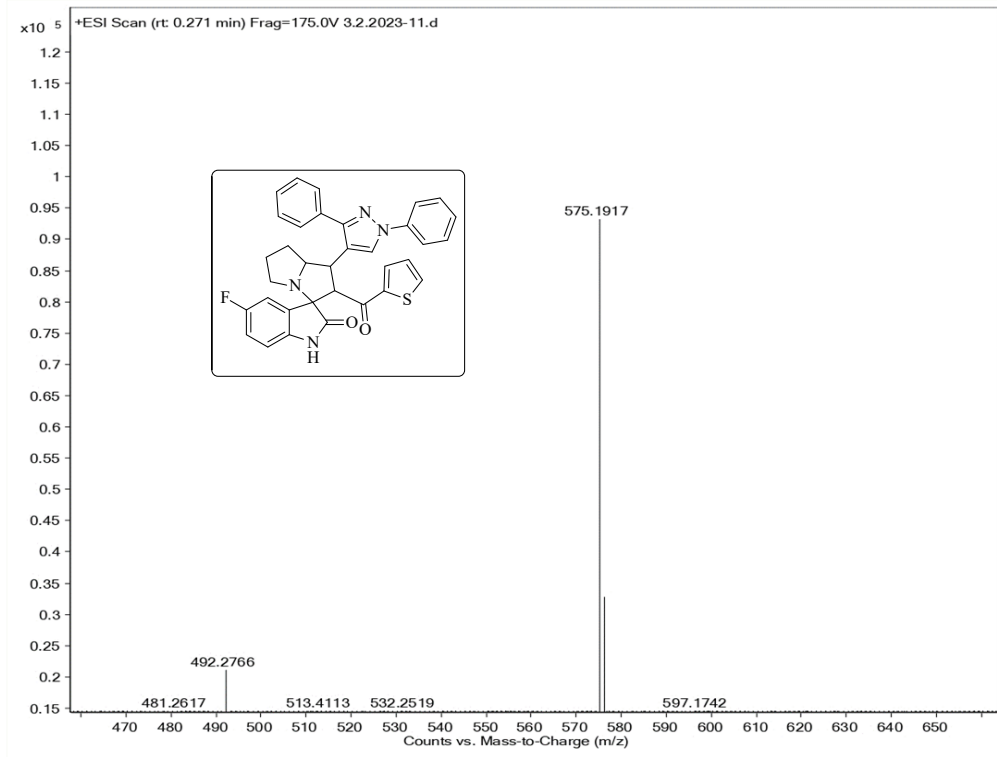
FT-IR Spectrum of the compound 4x



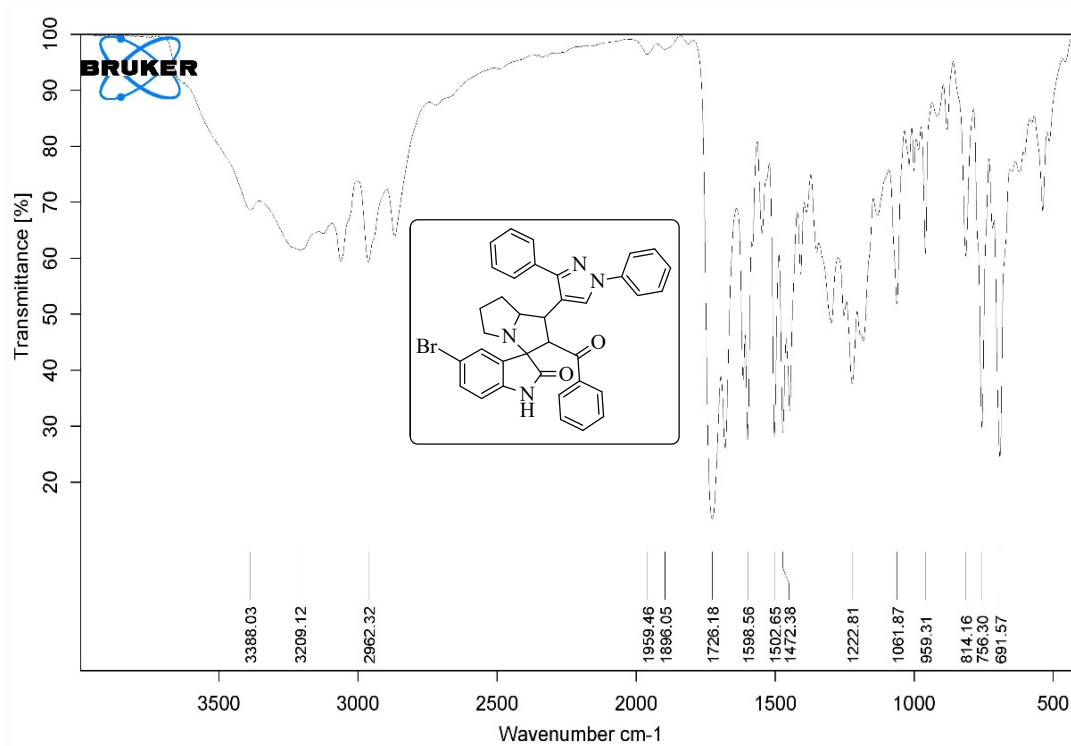
¹H NMR Spectrum of the compound 4x



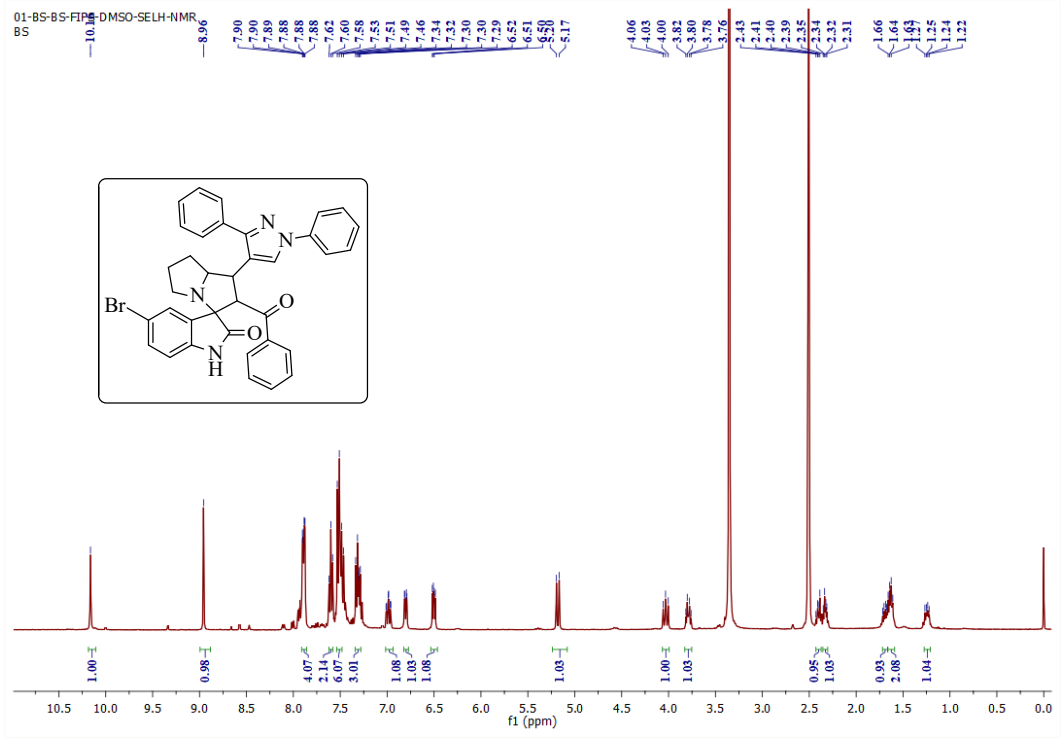
¹³C NMR Spectrum of the compound 4x



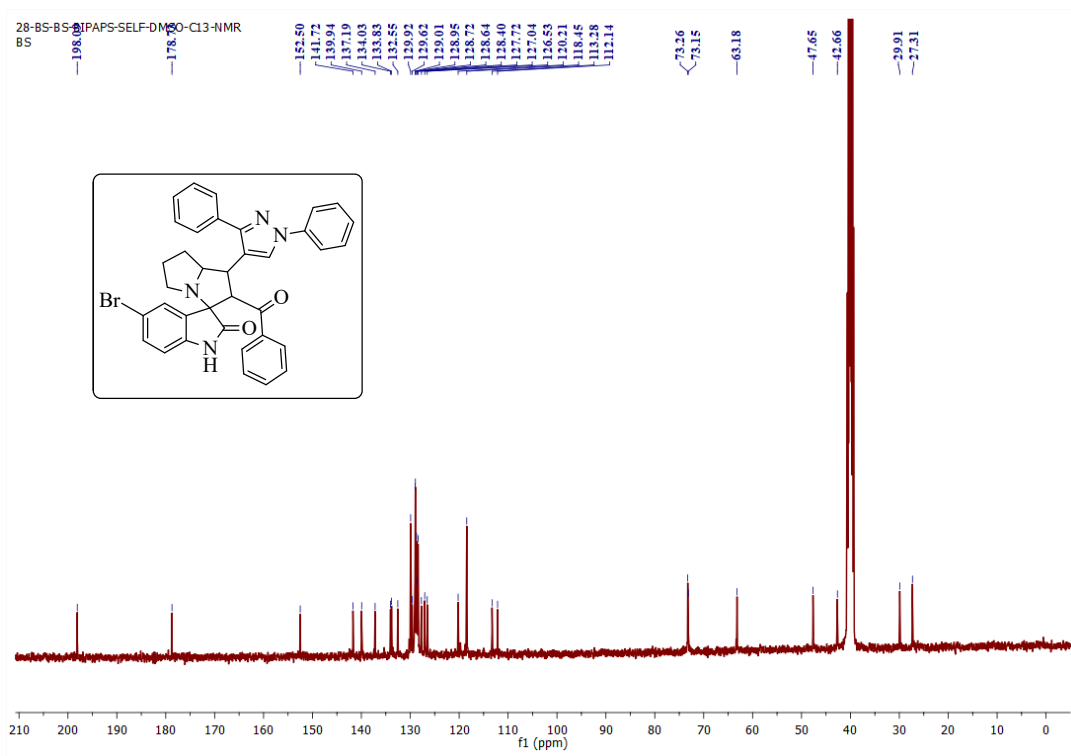
Mass spectrum of the compound 4x



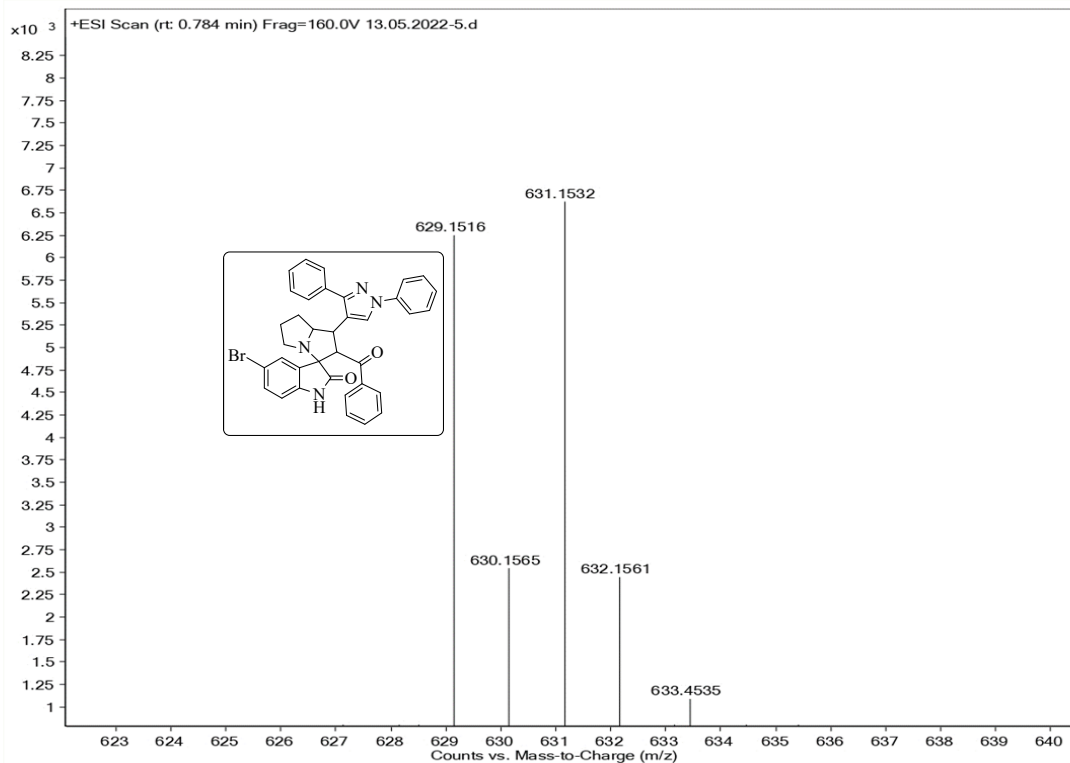
FT-IR Spectrum of the compound 4y



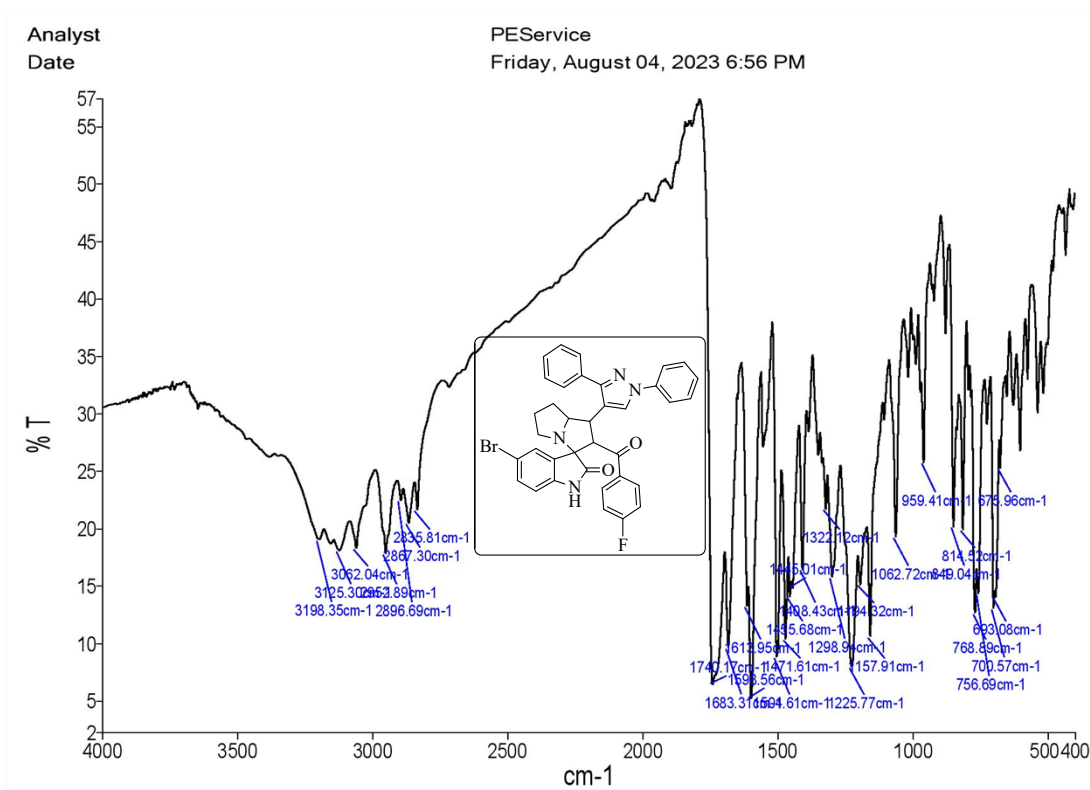
¹H NMR Spectrum of the compound 4y



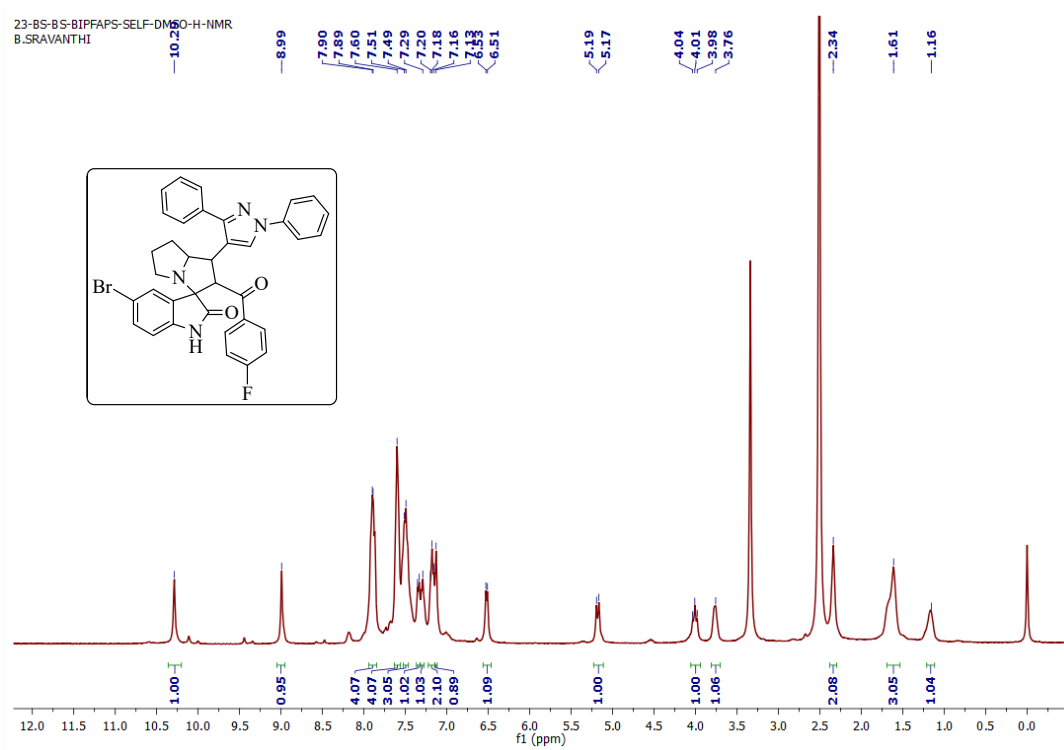
¹³C NMR Spectrum of the compound 4y



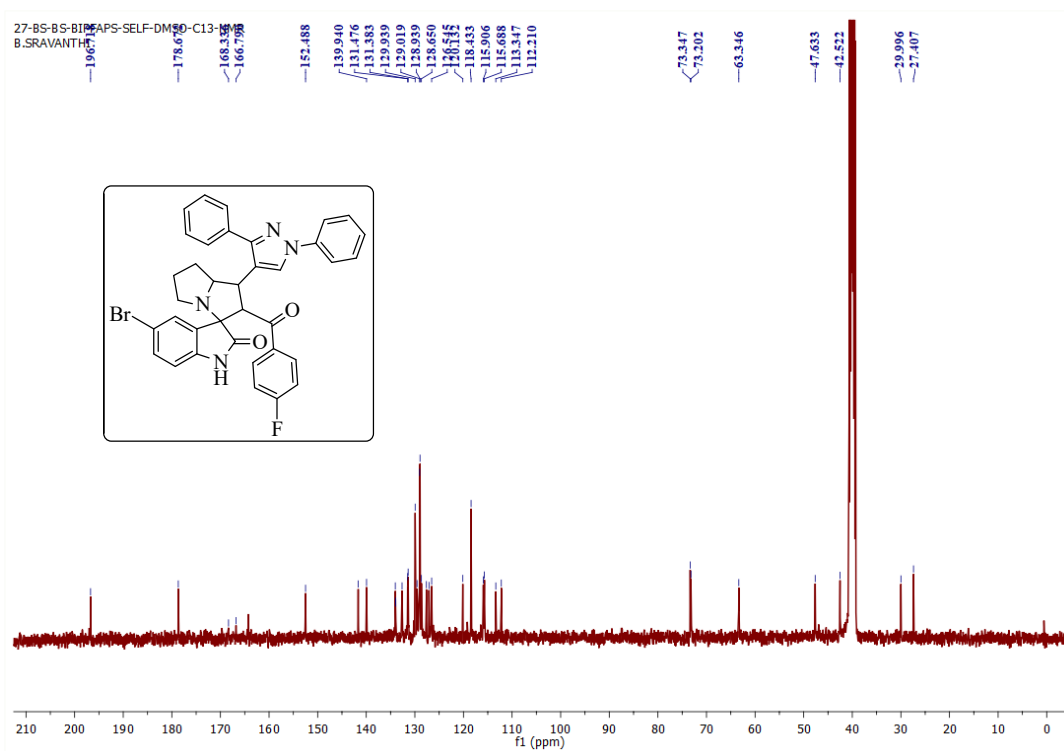
Mass spectrum of the compound 4y



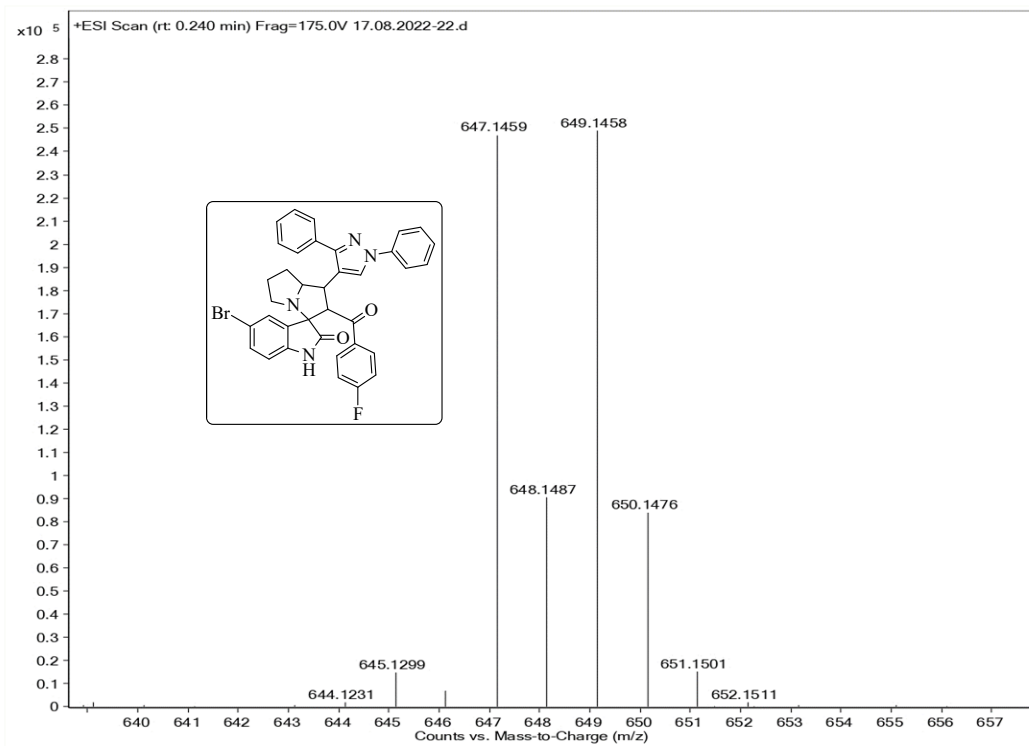
FT-IR Spectrum of the compound 4z



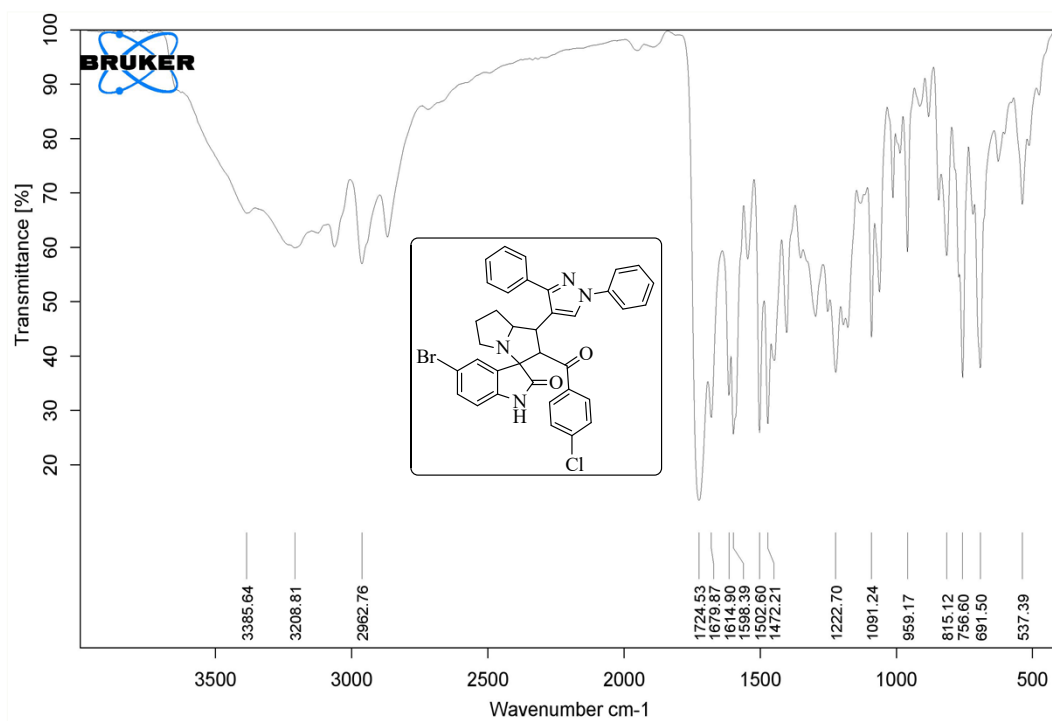
¹H NMR Spectrum of the compound 4z



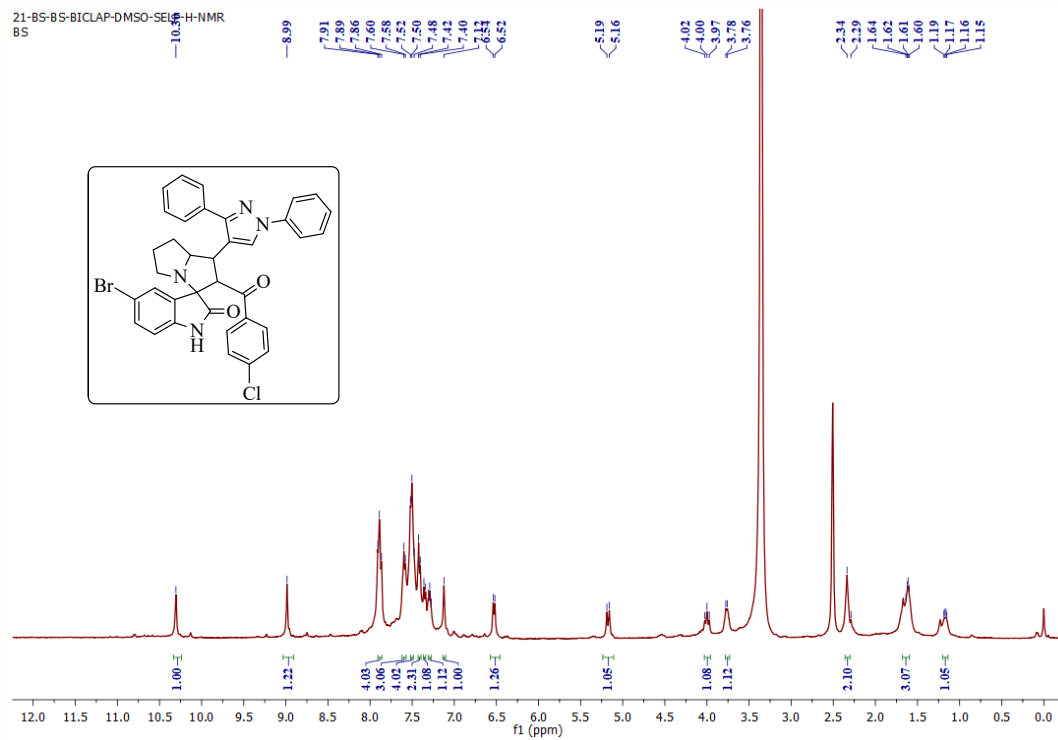
¹³C NMR Spectrum of the compound 4z



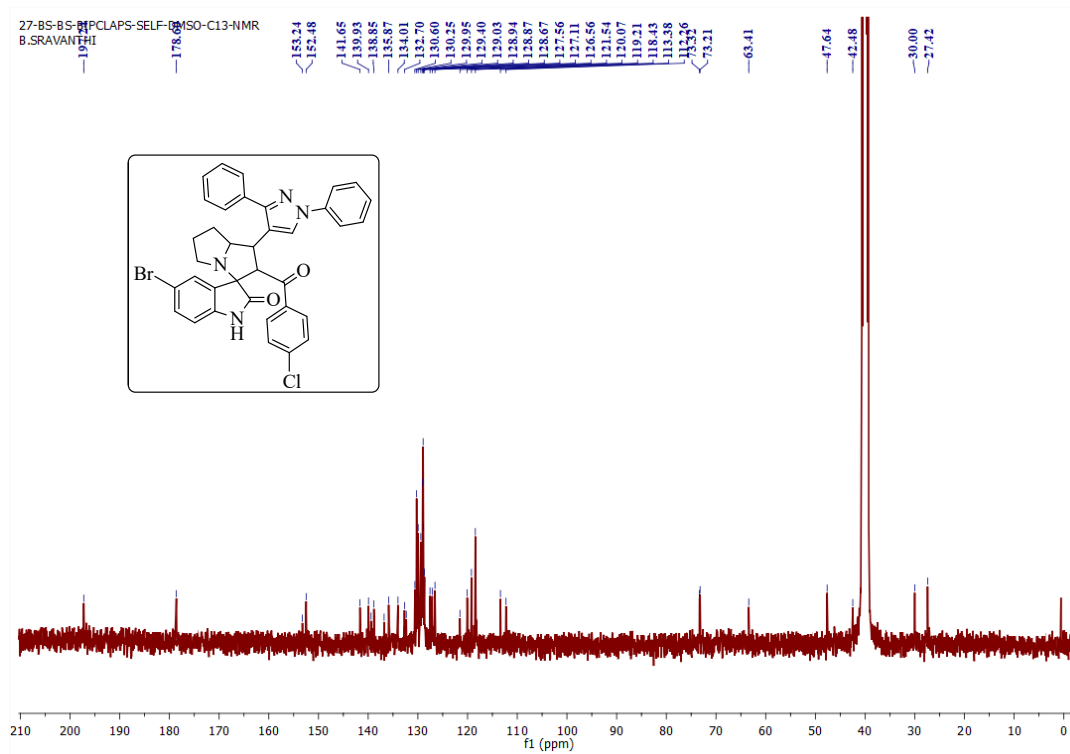
Mass spectrum of the compound 4z



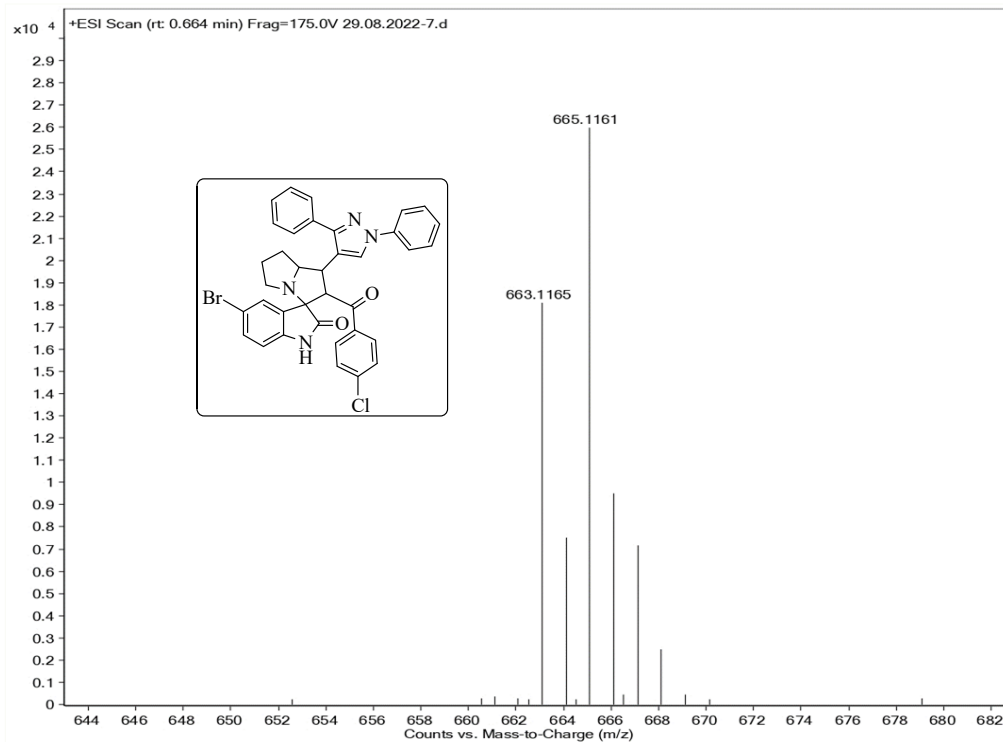
FT-IR Spectrum of the compound 4aa



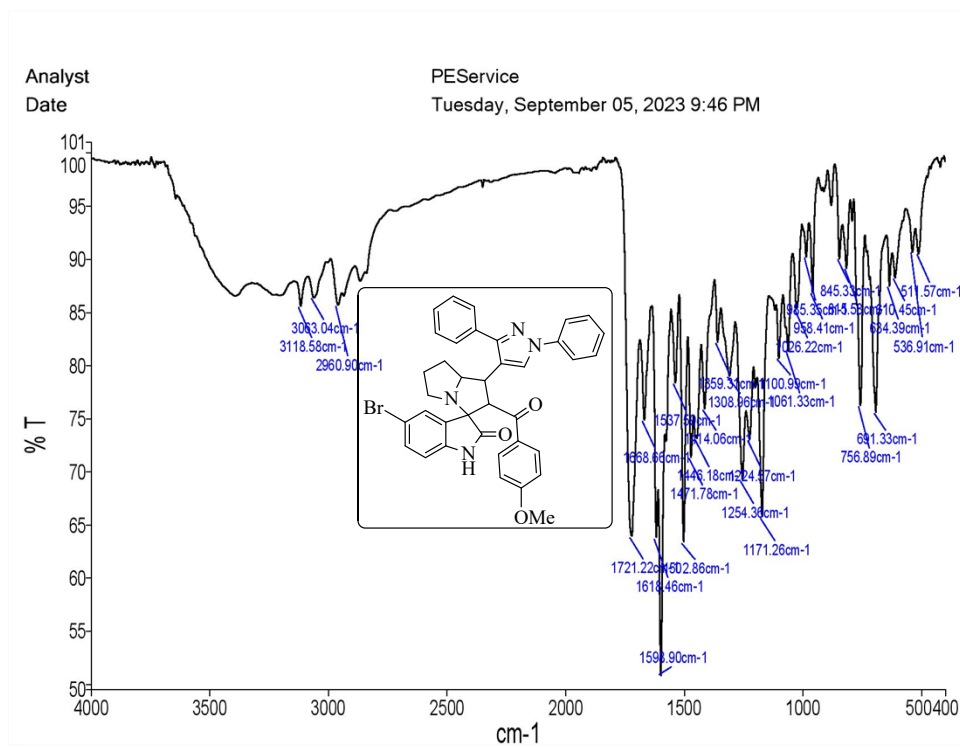
¹H NMR Spectrum of the compound 4aa



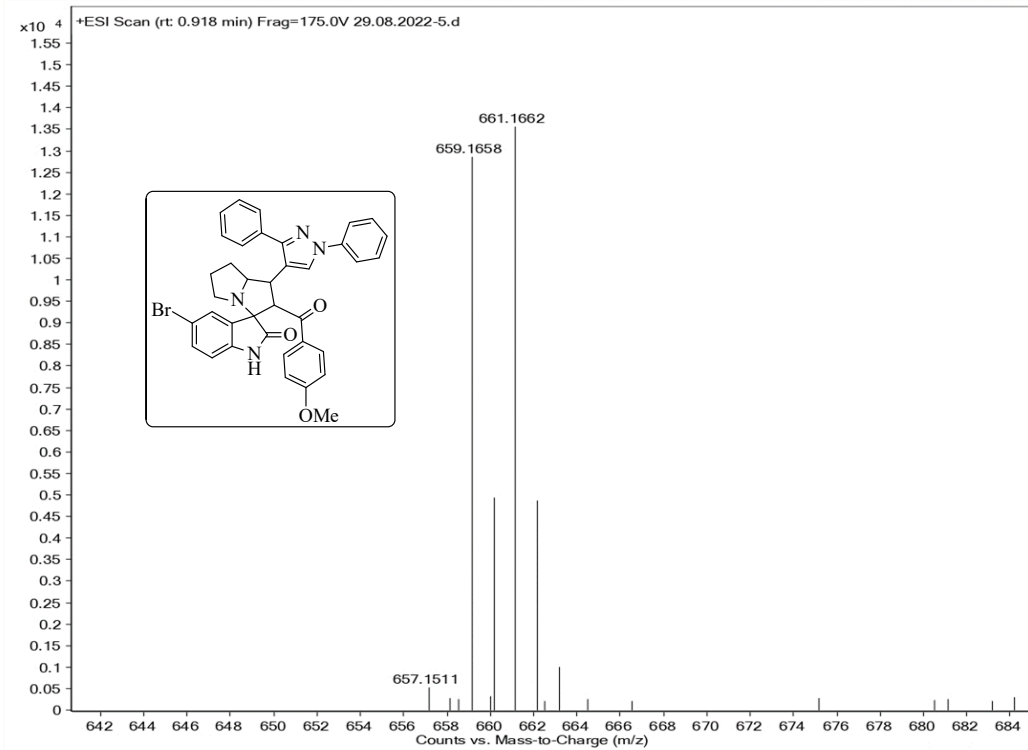
¹³C NMR Spectrum of the compound 4aa



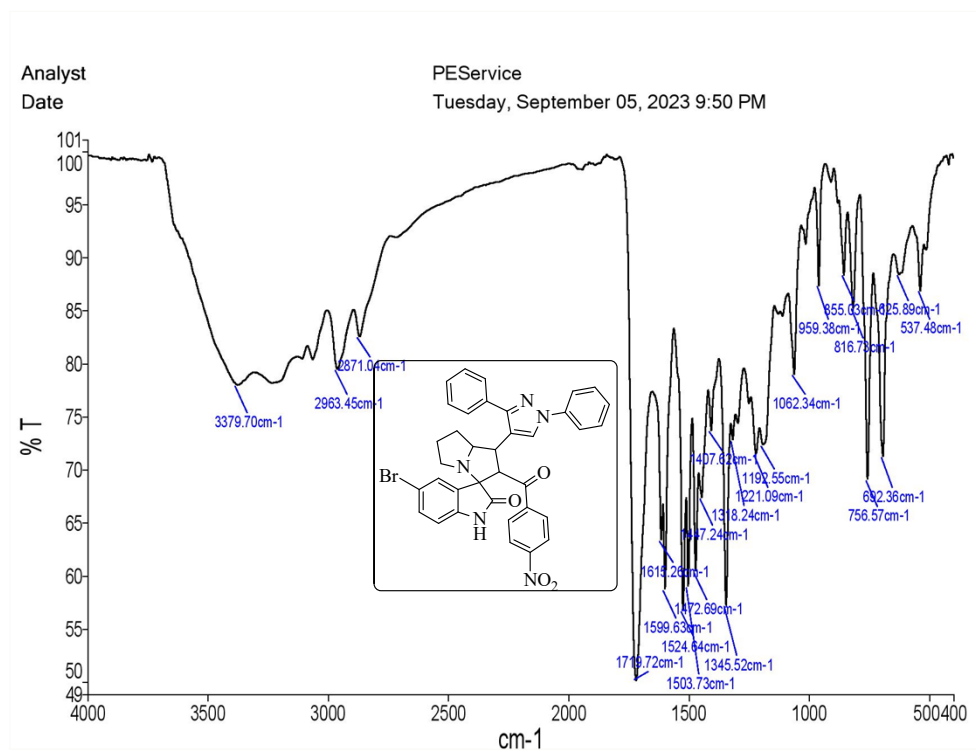
Mass spectrum of the compound 4aa



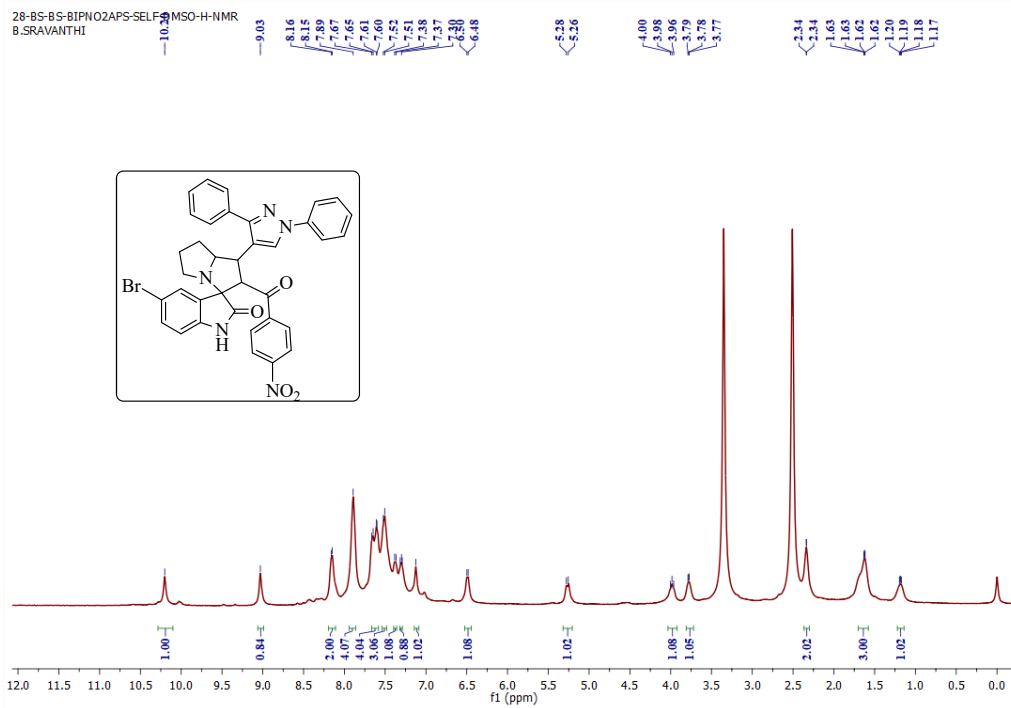
FT-IR Spectrum of the compound 4ab



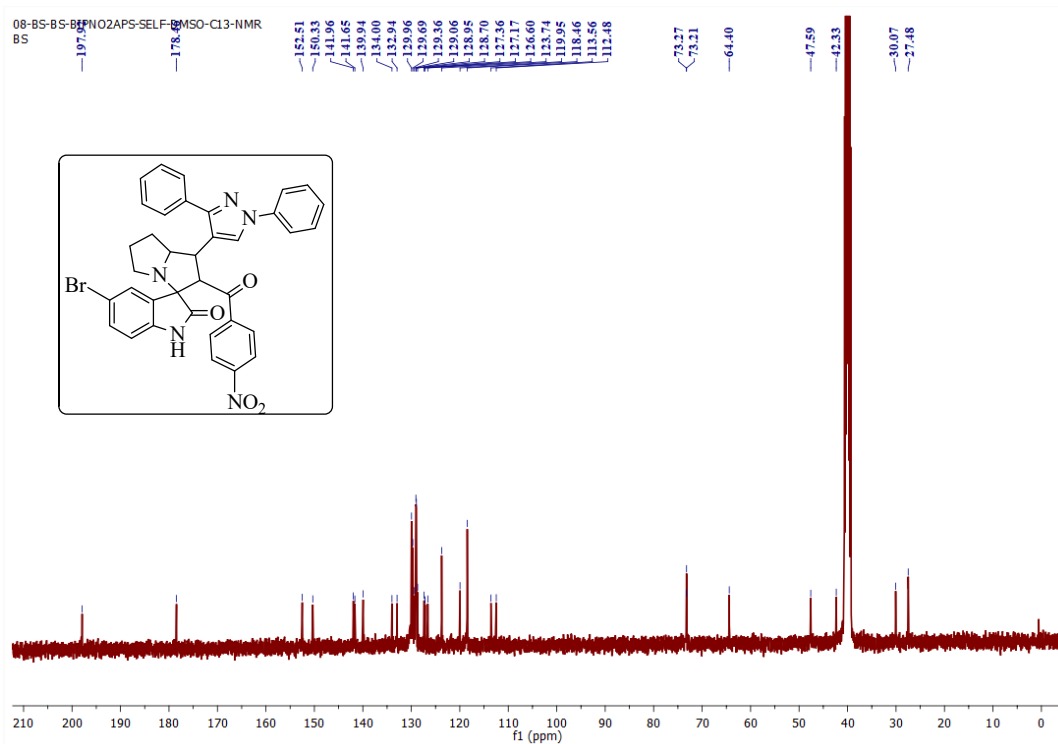
Mass spectrum of the compound 4ab



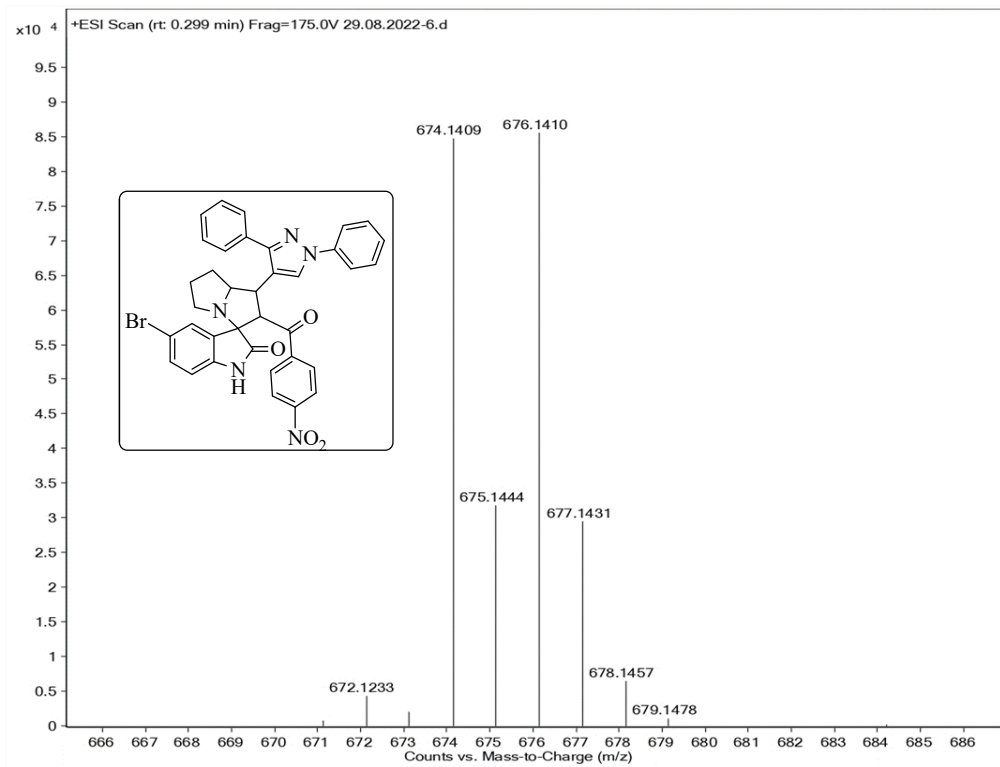
FT-IR Spectrum of the compound 4ac



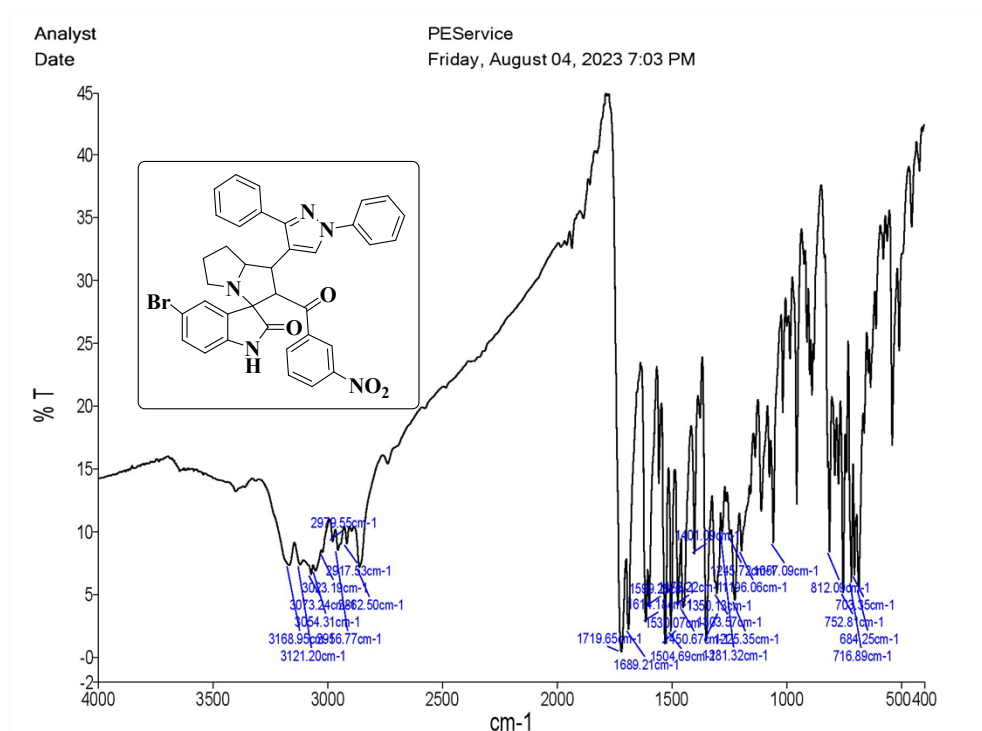
¹H NMR Spectrum of the compound 4aC



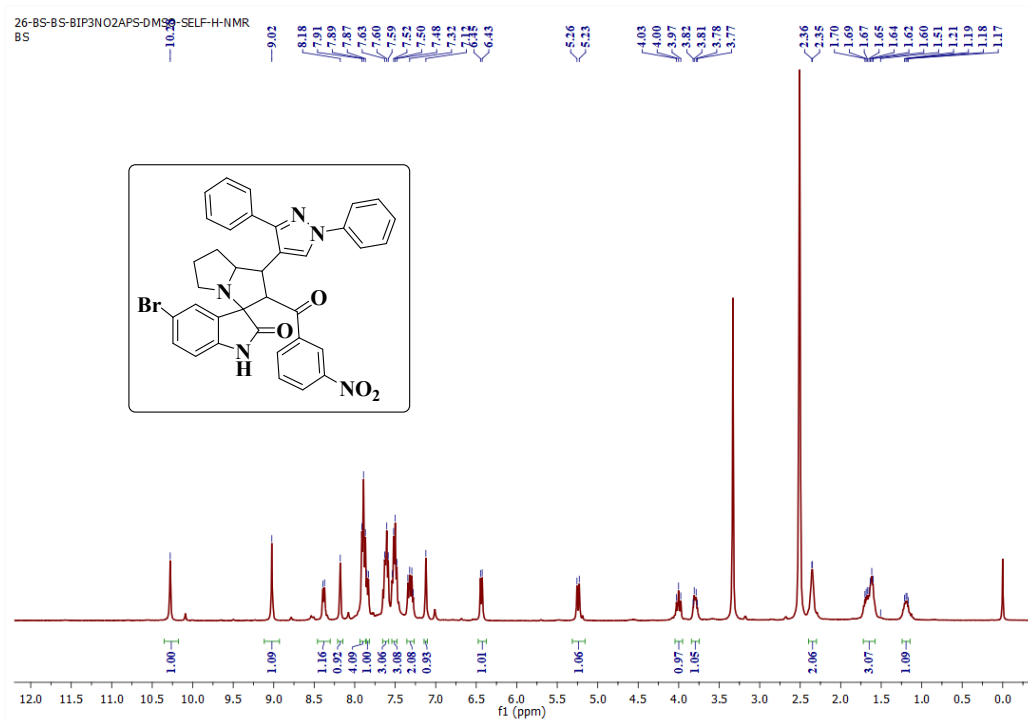
¹³C NMR Spectrum of the compound 4aC



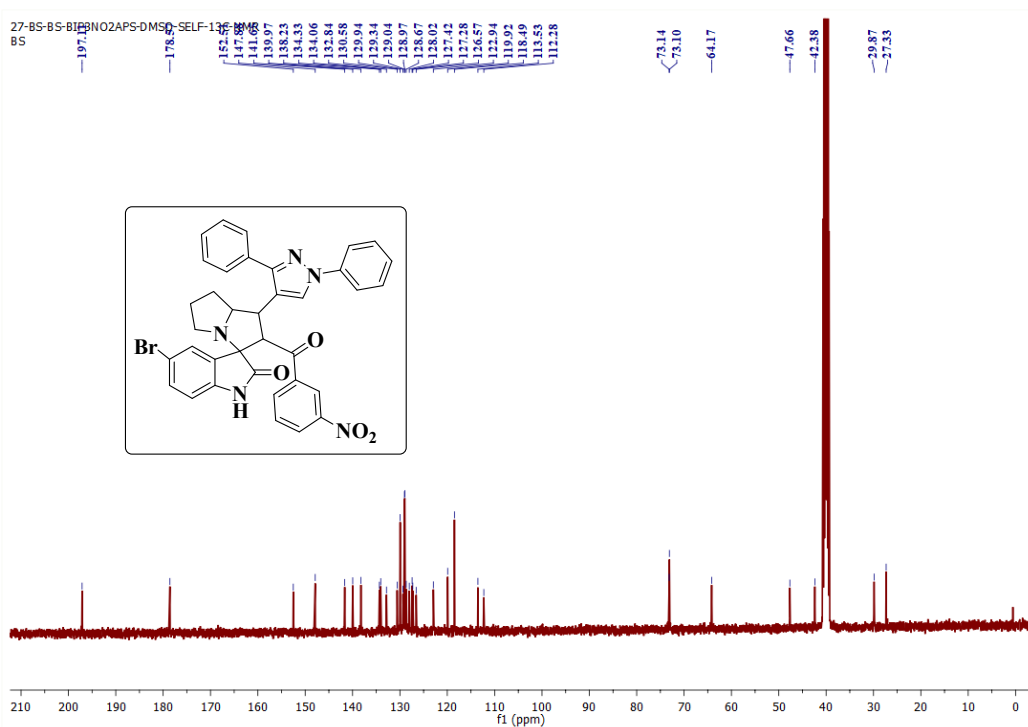
Mass spectrum of the compound 4ac



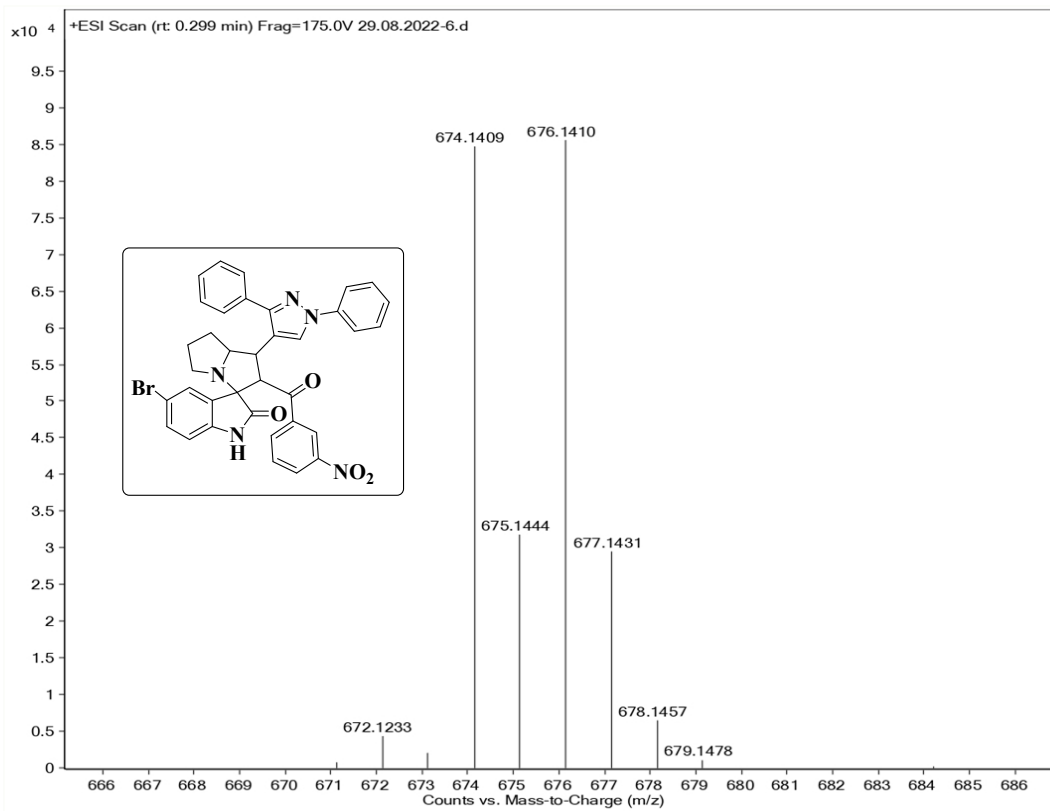
FT-IR Spectrum of the compound 4ad



¹H NMR Spectrum of the compound 4ad



¹³C NMR Spectrum of the compound 4ad



Mass spectrum of the compound 4ad

4. Salient features of crystallographic data of compound 4b

Identification code	4b
Empirical formula	C ₃₆ H ₂₉ FN ₄ O ₂
Formula weight	568.65
Crystal system	Monoclinic
Space group	P 21/n
<i>T</i> (K)	293 K
<i>a</i> (Å)	11.1333(10)
<i>b</i> (Å)	11.4934(10)
<i>c</i> (Å)	22.104(2)
α (°)	90
β (°)	91.270(4)
γ (°)	90
<i>Z</i>	4
<i>V</i> (Å ³)	2827.7 (4)
<i>D</i> _{calc} (g/cm ³)	1.336
<i>F</i> (000)	1192.0
μ (mm ⁻¹)	0.089
θ (°)	26.998
Index ranges	-14 ≤ <i>h</i> ≤ 14 -14 ≤ <i>k</i> ≤ 14 -28 ≤ <i>l</i> ≤ 28
<i>N</i> -total	6177
Parameters	389
<i>R</i> ₁ [<i>I</i> > 2 σ (<i>I</i>)]	0.0414
<i>wR</i> ₂ (all data)	0.1027
GOF	1.066
CCDC	2330349

5. In-vitro *MTB* MABA assay

Briefly, the inoculum was prepared from fresh LJ medium re-suspended in 7H9-S medium (7H9 broth, 0.1% casitone, 0.5% glycerol, supplemented oleic acid, albumin, dextrose, and catalase [OADC]), adjusted to a OD₅₉₀ 1.0, and diluted 1:20; 100 µl was used as inoculum. Each drug stock solution was thawed and diluted in 7H9-S at four-fold the final highest concentration tested. Serial two-fold dilutions of each drug were prepared directly in a sterile 96-well microtiter plate using 100 µl 7H9-S. A growth control containing no antibiotic and a sterile control were also prepared on each plate. Sterile water was added to all perimeter wells to avoid evaporation during the incubation. The plate was covered, sealed in plastic bags and incubated at 37°C in normal atmosphere. After 7 days incubation, 30 µl of alamar blue solution was added to each well, and the plate was re-incubated overnight. A change in colour from blue (oxidised state) to pink (reduced) indicated the growth of bacteria, and the MIC was defined as the lowest concentration of drug that prevented this change in colour.

6. Cytotoxicity, % of inhibition assay

Cytotoxicity was carried out in mouse macrophage cell line (RAW 264.7) at 25 µg/mL concentration. After 48 h of exposure, viability was assessed on the basis of cellular conversion of MTT into a formazan product using the cell proliferation assay. Cells were grown in RPMI medium supplemented with 10% fetal bovine serum (FBS), 10,000 units penicillin and 10 mg streptomycin per mL in T25 flasks to attain 80-90% confluency. Cells were scraped and seeded into wells approx 5,000 cells per well in poly-L-lysine coated plates. The microtiter plates were incubated at 37 °C, 5% CO₂ and 100% relative humidity for 24 h prior to addition of experimental drugs. The test compounds at 50 µg/mL concentrations were then added to cells and incubated at 37 °C for 48 h; later 10 µL of 0.5 mg/mL concentration of MTT was added and incubated for 3 h at 37 °C and the final product formazan crystals were measured at 595nm and 625nm.

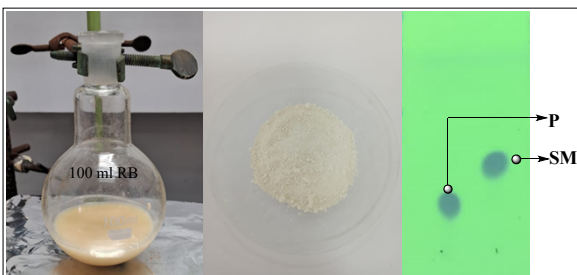
7. Molecules 4a-4ad with their stereochemical configurations used in silico studies

S. No.	Compound	Name
1	4a	(1'S,2'R,3R,7a'R)-2'-benzoyl-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
2	4b	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-fluorobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
3	4c	(1'S,2'R,3R,7a'R)-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
4	4d	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
5	4e	(1'S,2'R,3S,7a'R)-1'-(1,3-dicyclohexyl-1H-pyrazol-4-yl)-2'-(4-nitrobenzoyl)dodecahydrospiro[indole-3,3'-pyrrolizin]-2(1H)-one
6	4f	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(3-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
7	4g	(1'R,2'S,3R,7a'R)-1'-(3-(cyclohexa-2,5-dien-1-ylidene)-1-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2'-(tetrahydrofuran-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
8	4h	(1'R,2'S,3R,7a'R)-1'-(3-(cyclohexa-2,5-dien-1-ylidene)-1-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2'-(thiophene-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
9	4i	(1'S,2'R,3R,7a'R)-2'-benzoyl-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
10	4j	(1'S,2'R,3R,7a'R)-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
11	4k	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1-methyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
12	4l	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
13	4m	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-methyl-2'-(tetrahydrothiophene-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
14	4n	(1'S,2'R,3R,7a'R)-1-benzyl-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-

		pyrrolizin]-2-one
15	4o	(1'S,2'R,3R,7a'R)-1-butyl-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
16	4p	(1'S,2'R,3R,7a'R)-2'-(4-bromobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-(prop-2-yn-1-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
17	4q	(1'S,2'R,3R,7a'R)-2'-(4-bromobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1-(prop-2-yn-1-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
18	4r	(1'S,2'R,3R,7a'R)-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
19	4s	(1'S,2'R,3R,7a'R)-2'-(4-bromobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
20	4t	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
21	4u	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
22	4v	(1'S,2'R,3R,7a'R)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-5-fluoro-2'-(3-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
23	4w	(1'R,2'S,3R,7a'R)-1'-(3-(cyclohexa-2,5-dien-1-ylidene)-1-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-5-fluoro-2'-((Z)-furan-2(5H)-ylidene(hydroxy)methyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
24	4x	(1'R,2'S,3R,7a'R)-1'-(3-(cyclohexa-2,5-dien-1-ylidene)-1-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-5-fluoro-2'-(thiophene-2-carbonyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
25	4y	(1'S,2'R,3R,7a'R)-2'-benzoyl-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
26	4z	(1'S,2'R,3R,7a'R)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-fluorobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
27	4aa	(1'S,2'R,3R,7a'R)-5-bromo-2'-(4-chlorobenzoyl)-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one

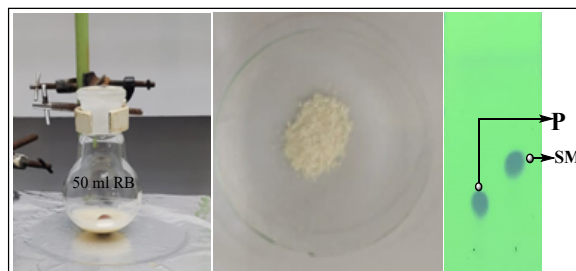
28	4ab	(1'S,2'R,3R,7a'R)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-methoxybenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
29	4ac	(1'S,2'R,3R,7a'R)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(4-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one
30	4ad	(1'S,2'R,3R,7a'R)-5-bromo-1'-(1,3-diphenyl-1H-pyrazol-4-yl)-2'-(3-nitrobenzoyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one

Bulk purity of the synthesized compound 4c; (500 mg and 100 mg scale reactions)



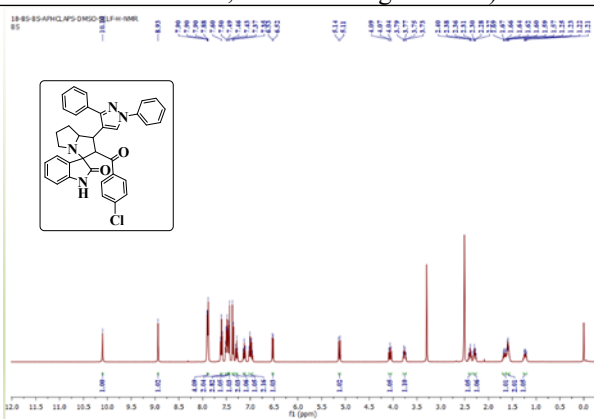
500 mg scale reaction

(TLC: Solvent system: *n*-hexane : EtOAc (7:3)
P = Product, SM = Starting Material)

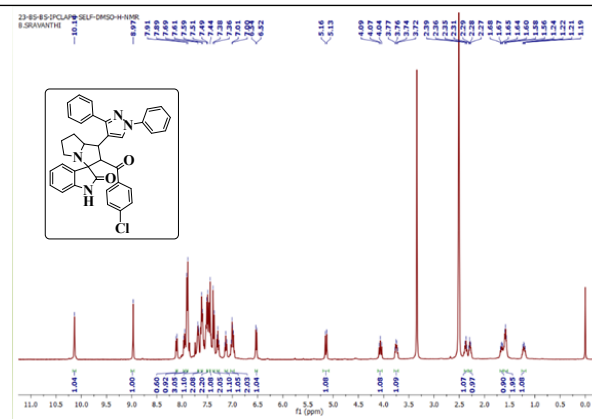


100 mg scale reaction

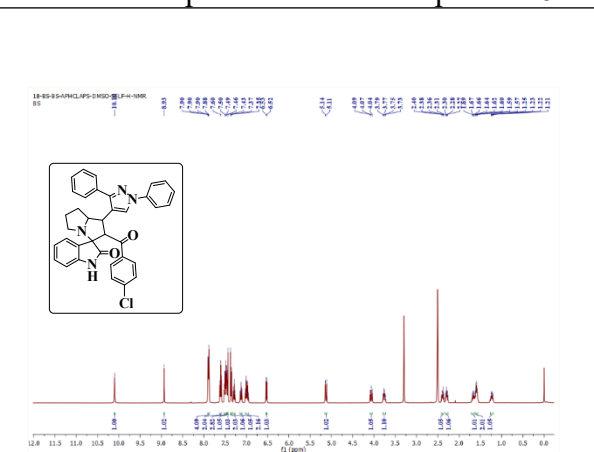
(TLC: Solvent system: *n*-hexane : EtOAc (7:3)
P = Product, SM = Starting Material)



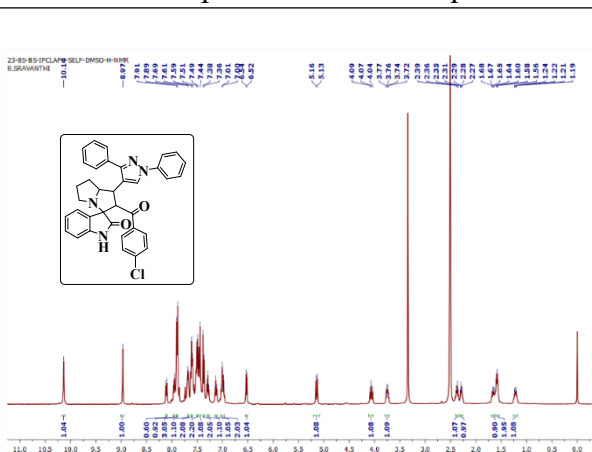
¹H NMR Spectrum of the compound **4c**



¹³C NMR Spectrum of the compound **4c**



¹H NMR Spectrum of the compound **4c**



¹³C NMR Spectrum of the compound **4c**