Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Ruthenium(II)-Catalyzed Selective C−H Bond Activation of Imidamides and Coupling with Sulfoxonium Ylides: A Security Approarch for the Synthesis of Highly Functional 3-Ketoindoles

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I. General Information

The reagents were purchased from commercial suppliers and used without further purification. Analytical thin-layer chromatography (TLC) was performed on HSGF 254 (0.15-0.2 mm thickness), visualized by irradiation with UV light (254 nm). Column chromatography was performed using silica gel FCP 200-300. Melting points were measured with a micro melting point apparatus. Nuclear magnetic resonance spectra were recorded on a Brucker AMX-400 MHz and Brucker AMX-500 MHz instrument (TMS as IS). Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd) and broad (br). High-resolution mass spectra (HRMS) were measured on a Micromass Ultra Q-TOF spectrometer.

II. Experimental Information

Preparation of the materials starting materials (1a-1u) were prepared according to literature procedures. [1-2]

To a screw-cap reaction tube was added benzamidine hydrochloride (1 mmol), aryl iodide (1 mmol), CuI (0.1 mmol), and Cs_2CO_3 (2mmol). The reaction tube was placed under high vacuum, backfilled with argon and repeated three times. Dimethylformamide (2 mL) was added using a syringe and the mixture was heated to the desired temperature under oil bath. After the resulting solution was stirred for 12 hours, the product was extracted using ethyl acetate, washed with water 3 times, and the organic layer was dried over anhydrous Na_2SO_4. Following concentration under reduced pressure, the residue was purified by silica gel chromatography to afford the desired product.

[1] J. Huang, Y. He, Y. Wang, Q. Zhu, *Chem. Eur. J.*, 2012, **18**, 13964.

[2] M. Cortes-Salva, C. Garvin, J. C. Antilla, *J. Org. Chem.*, 2011, **76**, 1456.

Preparation of the materials starting materials (2a-2m) were prepared according to literature procedures. [3-4]

To a stirred solution of potassium tert-butoxide (27.2 mmol) in THF (40 mL) was added trimethylsulfoxonium iodide (20.4 mmol) at room temperature. The resulting mixture is refluxed for 3 h. Then reaction mixture is cooled to 0 ^oC, followed by addition of acyl chlorides (6.87 mmol) in THF (5 mL). The reaction was allowed to room temperature and stirred for 3 h. Next, the solvent was evaporated, and water (50 mL) and ethyl acetate (80 mL) were added to the resulting slurry. The layers were separated and the aqueous layer was washed with ethyl acetate and the organic layers were combined. The organic solution was dried over anhydrous sodium sulphate (Na_2SO_4), filtered over a sintered funnel, and evaporated to dryness. The residue was purified by silica gel chromatography to afford the desired product.

[3] M. Barday, Janot. C, R. Nathan, James Muir. H, Aissa C, *Angew. Chem. Int. Ed.*, 2017, **56**, 13117.

[4] Rafael D. C. Gallo, AneesAhmad, GustavoMetzker, Antonio C. B. Burtoloso, *Chem. Eur. J.*, 2017, **23**, 16980.

Preparation of the materials starting materials (2a1 and 2a2) were prepared according to literature procedures. [5-6]

Triethylamine (15 mmol) was added to a solution of 2-bromoacetophenone (10 mmol) in dry THF (20 mL) and the solution was stirred for 12 h at rt. The precipitate was separated, washed with Et_2O, and dried in a vacuum to give triethyl-(2-oxo-2-phenylethyl)-ammonium bromide (**2a1**).

A solution of α-bromoacetophenone (20 mmol) in CH_2Cl_2 (50 mL) was added dropwise over 15 min to a solution of triphenylphosphine (20 mmol) in CH_2Cl_2 (80 mL). The reaction mixture was stirred at room temperature for 24 h, and the resulting mixture was concentrated under reduced pressure. The resulting precipitate was washed with Et_2O. The phosphonium bromide was obtained in quantitative yield, and was used without further purification. A solution of KOTf (4 equiv) in acetone (10 mL) was added to a solution of phosphonium bromide (20 mmol) in acetone (50 mL) and the mixture was stirred at rt for 24 h. All the solvent was removed under reduced pressure and the residue was washed with DCM. The solution was concentrated to give product **2a2**.

[5] S. Yu, S. Liu,; Y. Lan, B. Wan, X. Li, *J. Am. Chem. Soc.*, 2015, **137**, 1623.

[6] Y. Li, Q. Wang, X. Yang, F. Xie, X. Li, *Org. Lett.*, 2017, **19**, 3410.

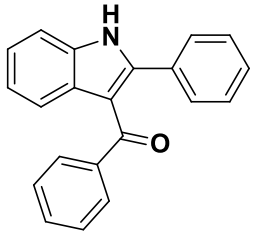
General procedure for the synthesis of product 3aa-3ta, 3ab-3am, and 3uc (compound 3aa as the example).

N-phenylacetimidamide (**1a**, 0.2 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), $Zn(OAc)_2$ (0.04 mmol) were dissolved in EtOH (3 mL) in a pressure tube. The resulting mixture was stirred for seconds under N_2 atmosphere, to which was added sulfur ylide (**2a**, 0.24 mmol). The mixture was stirred at 90 ^oC for 8 hours. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (1:8) to afford product.

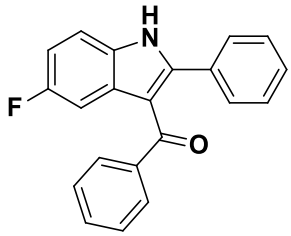
General procedure for the synthesis of 4aa

N-phenylacetimidamide (**1a**, 0.2 mmol), $[Cp^*RhCl_2]_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), $Zn(OAc)_2$ (0.04 mmol) were dissolved in DCE (3 mL) in a pressure tube. The resulting mixture was stirred for seconds under N_2 atmosphere, to which was added sulfur ylide (**2a**, 0.24 mmol). The mixture was stirred at 90 ^oC for 8 hours. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (1:16) to afford product **4aa** as a oily matter (45.0 mg, 76%).^{1}H NMR (400 MHz, DMSO-d_6) δ 9.27 (s, 1H), 8.56 (d, J = 8.3 Hz, 1H), 8.19 – 8.12 (m, 2H), 7.99 (dd, J = 8.6, 1.0 Hz, 2H), 7.90 (d, J = 7.8 Hz, 1H), 7.82 (s, 1H), 7.77 – 7.69 (m, 1H), 7.61 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 7.49 (dd, J = 10.4, 4.7 Hz, 2H), 7.38 (dd, J = 11.4, 4.5 Hz, 3H), 7.03 (t, J = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.16, 147.47, 141.21, 139.34, 137.99, 130.32, 128.67, 128.35, 128.32, 127.50, 126.23, 126.20, 123.34, 121.75, 120.42, 117.89, 108.28; EI-MS (m/z): 297 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{17}N_2^+$ $[M+H]^+$, 297.1386, found: 297.1383.

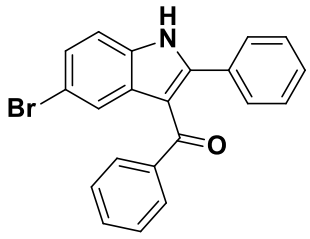
III. Characterization data of compounds 3



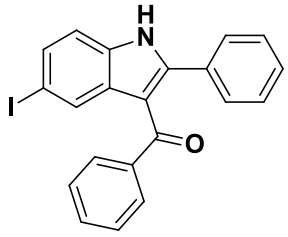
Phenyl(2-phenyl-1*H*-indol-3-yl)methanone (**3aa**): white solid (49.4 mg, yield 83%), m.p. 222–225 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.18 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.55 – 7.48 (m, 3H), 7.42 – 7.32 (m, 3H), 7.29 – 7.18 (m, 6H), 7.17 – 7.12 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.11, 144.04, 139.80, 135.80, 131.55, 131.31, 129.51, 129.02, 128.44, 128.15, 128.00, 127.75, 122.83, 121.37, 120.55, 112.12, 111.83; EI-MS (*m/z*): 298 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{16}NO^+$ $[M+H]^+$ 298.1226, found: 298.1231.



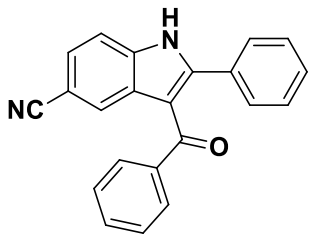
(5-Fluoro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ba**): gray solid (44.8 mg, yield 71%), m.p. 254–256 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.31 (s, 1H), 7.54 – 7.45 (m, 4H), 7.39 – 7.31 (m, 3H), 7.28 – 7.15 (m, 5H), 7.11 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.83, 158.32 (d, $J_{C\text{-}F}$ = 234.2 Hz), 145.94, 139.59, 132.47, 131.28, 129.56, 128.94, 128.78, 128.69, 128.65, 127.99, 127.72, 113.09 (d, $J_{C\text{-}F}$ = 9.9 Hz), 112.21 (d, $J_{C\text{-}F}$ = 4.4 Hz), 111.09 (d, $J_{C\text{-}F}$ = 26.2 Hz), 105.43 (d, $J_{C\text{-}F}$ = 24.6 Hz); ^{19}F NMR (471 MHz, DMSO-d_6) δ -121.61. EI-MS (m/z): 316 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{15}FNO^+$ $[M+H]^+$ 316.1132, found: 316.1133.



(5-Bromo-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ca**): white solid (59.4 mg, yield 79%), m.p. 294–296 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.40 (s, 1H), 7.93 (d, J = 1.9 Hz, 1H), 7.52 – 7.46 (m, 3H), 7.41 – 7.32 (m, 4H), 7.28 – 7.16 (m, 5H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.83, 145.42, 139.42, 134.58, 131.41, 131.02, 129.90, 129.59, 128.98, 128.76, 128.03, 127.75, 125.47, 122.72, 114.09, 113.90, 111.56; EI-MS (*m/z*): 378 ($(M+H)^+$, (Br^{81})), 376 ($(M+H)^+$, (Br^{79})); HRMS (ESI) calculated for $C_{21}H_{15}NOBr^+$ $[M+H]^+$ 376.0332, found:376.0322(Br^{79}), 378.0409(Br^{81}).

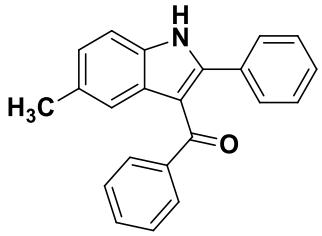


(5-Iodo-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3da**): white solid (64.3 mg, yield 76%), m.p. 202–205 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.13 (d, J = 1.3 Hz, 1H), 7.52 (dd, J = 8.5, 1.6 Hz, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.40 – 7.30 (m, 4H), 7.28 – 7.12 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.35, 145.32, 139.62, 135.22, 131.77, 131.25, 131.19, 130.88, 129.83, 129.28, 129.17, 129.07, 128.37, 128.06, 114.62, 111.47, 85.98; EI-MS (m/z): 424 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{14}NOI^+$ $[M+H]^+$ 424.0193, found: 424.0194.

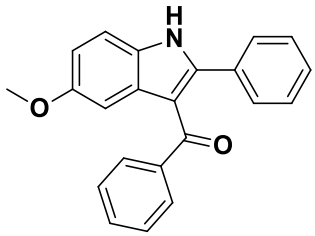


3-Benzoyl-2-phenyl-1*H*-indole-5-carbonitrile (**3ea**): white solid (51.6 mg, yield 80%),

m.p. 256–259 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.75 (s, 1H), 8.17 (s, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.63 (dd, J = 8.4, 1.5 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.43 – 7.35 (m, 3H), 7.32 – 7.25 (m, 3H), 7.25 – 7.17 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.75, 146.23, 139.02, 137.71, 131.70, 130.60, 129.63, 129.06, 128.13, 127.91, 127.84, 125.76, 125.66, 120.15, 113.27, 112.24, 103.59; EI-MS (m/z): 323 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{15}N_2O^+$ $[M+H]^+$ 323.1184, found: 323.1182.

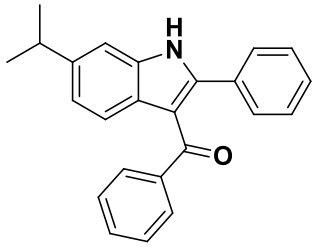


(5-Methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3fa**): pale yellow solid (45.5 mg, yield 73%), m.p. 186–188 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.08 (s, 1H), 7.58 (s, 1H), 7.50 (dd, J = 8.1, 1.2 Hz, 2H), 7.39 (d, J = 8.2 Hz, 1H), 7.37 – 7.32 (m, 3H), 7.26 – 7.17 (m, 5H), 7.08 (dd, J = 8.3, 1.4 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.12, 144.01, 139.86, 134.17, 131.65, 131.21, 130.11, 129.45, 129.00, 128.45, 128.31, 127.95, 127.69, 124.36, 120.21, 111.77, 111.49, 21.36; EI-MS (m/z): 312 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{18}NO^+$ $[M+H]^+$ 312.1383, found: 312.1384.

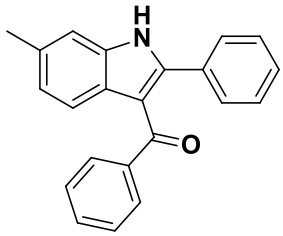


(5-Methoxy-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ga**): white solid (44.5 mg, yield 68%), m.p. 182–186 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.49 (dd, J = 8.1, 1.2 Hz, 2H), 7.40 (d, J = 8.8 Hz, 1H), 7.37 – 7.29 (m, 4H), 7.26 – 7.15 (m, 5H), 6.89 (dd, J = 8.8, 2.5 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.01, 155.10, 144.60, 139.95, 131.67, 131.07, 130.81, 129.47, 128.94, 128.31, 127.92, 127.65, 112.81, 112.58, 111.98, 102.42, 55.18; EI-MS (m/z): 328 $[M+H]^+$;

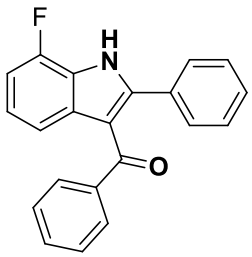
HRMS (ESI) calculated for $C_{22}H_{18}NO_2^+$ $[M+H]^+$ 328.1332, found: 328.1334.



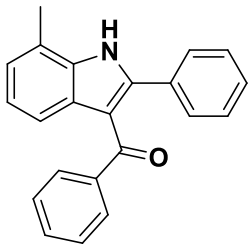
(6-Isopropyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ha**): white solid (50.9 mg, yield 75%), m.p. 171–173 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.03 (s, 1H), 7.61 (d, J = 8.3 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.39 – 7.30 (m, 4H), 7.27 – 7.16 (m, 5H), 7.06 (dd, J = 8.3, 1.3 Hz, 1H), 3.01 (m, 1H), 1.27 (d, J = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.05, 143.71, 143.52, 139.90, 136.10, 131.72, 131.24, 129.44, 128.99, 128.31, 127.98, 127.73, 126.40, 120.60, 120.41, 112.05, 108.72, 33.58, 24.30; EI-MS (m/z): 340 $[M+H]^+$; HRMS (ESI) calculated for $C_{24}H_{22}NO^+$ $[M+H]^+$, 340.1696, found:340.1695.



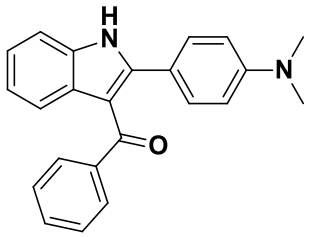
(6-Methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ia**): white solid (43.6 mg, yield 70%), m.p.198–200 ºC. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.60 (d, J = 8.2 Hz, 1H), 7.50 (dd, J = 8.2, 1.2 Hz, 2H), 7.40 – 7.32 (m, 3H), 7.29 (s, 1H), 7.27 – 7.16 (m, 5H), 6.98 (dd, J = 8.2, 1.0 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.09, 143.63, 139.90, 136.24, 132.16, 131.70, 131.29, 129.51, 129.06, 128.35, 128.00, 127.76, 126.10, 123.12, 120.35, 112.06, 111.56, 21.36; EI-MS (m/z): 312 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{18}NO^+$ $[M+H]^+$, 312.1383, found: 312.1384.



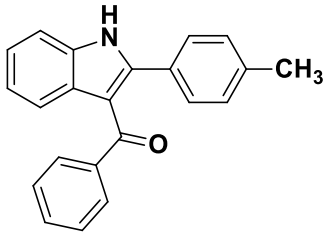
(7-Fluoro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ja**): white solid (38.5 mg, yield 61%), m.p. 174–176 ºC. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.63 (s, 1H), 7.57 – 7.54 (m, 1H), 7.54 – 7.46 (m, 2H), 7.44 – 7.31 (m, 3H), 7.30 – 7.17 (m, 5H), 7.11 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.10, 149.03 (d, J = 244.9 Hz), 145.16, 139.35, 131.74 (d, J = 5.1 Hz), 131.59, 130.96, 129.91, 129.09, 128.74, 127.96, 127.84, 123.85 (d, J = 13.5 Hz), 121.89 (d, J = 6.2 Hz), 116.61 (d, J = 3.3 Hz), 112.96 (d, J = 1.7 Hz), 107.82 (d, J = 15.8 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -131.84; EI-MS (m/z): 314 $[M-H]^-$; HRMS (ESI) calculated for $C_{21}H_{13}FNO^-$ $[M-H]^-$, 314.0987, found: 314.0988.



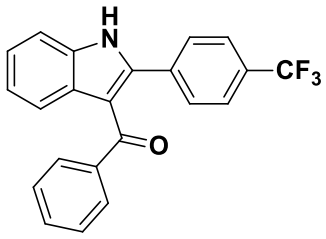
(7-Methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ka**): yellow solid (37.3 mg, yield 60%), m.p. 187–189 ºC. ^{1}H NMR (400 MHz, DMSO) δ 11.96 (s, 1H), 7.60 (d, J = 7.1 Hz, 1H), 7.50 (d, J = 7.2 Hz, 2H), 7.39 (dd, J = 6.9, 2.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.28 – 7.21 (m, 3H), 7.18 (t, J = 7.6 Hz, 2H), 7.12 – 7.01 (m, 2H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.23, 144.39, 139.85, 135.35, 131.68, 131.25, 129.99, 129.04, 128.39, 127.93, 127.85, 127.72, 123.48, 121.64, 121.47, 118.12, 112.72, 16.98; EI-MS (m/z): 310 $[M-H]^-$; HRMS (ESI) calculated for $C_{22}H_{16}FNO^-$ $[M-H]^-$, 310.1237, found: 310.1239.



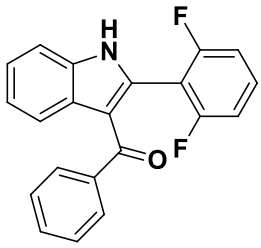
(2-(4-(Dimethylamino)phenyl)-1*H*-indol-3-yl)(phenyl)methanone (**3la**): yellow solid (55.1 mg, yield 81%), m.p. 204–206 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.89 (s, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 7.4 Hz, 1H), 7.26 – 7.23 (m, 4H), 7.17 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.56 (d, J = 8.9 Hz, 2H), 2.87 (s, 6H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.11, 150.21, 145.01, 140.01, 135.70, 131.19, 130.26, 129.05, 128.60, 127.82, 122.17, 120.96, 120.09, 118.55, 111.41, 111.34, 110.60, 39.75; EI-MS (m/z): 341 $[M+H]^+$; HRMS (ESI) calculated for $C_{23}H_{21}N_2O^+$ $[M+H]^+$, 341.1648, found:341.1649.



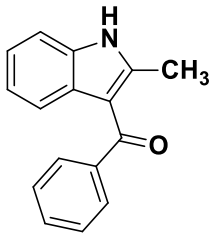
Phenyl(2-(*p*-tolyl)-1*H*-indol-3-yl)methanone (**3ma**): white solid (48.6 mg, yield 78%), m.p. 188–189 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.49 (d, J = 8.0 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.32 – 7.18 (m, 5H), 7.13 (t, J = 7.5 Hz, 1H), 7.06 (dd, J = 4.2, 3.7 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.17, 144.07, 139.84, 138.01, 135.78, 131.39, 129.38, 129.09, 128.70, 128.66, 128.54, 128.25, 127.86, 122.73, 121.30, 120.45, 111.80, 20.82; EI-MS (m/z): 312 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{18}NO^+$ $[M+H]^+$, 312.1383, found: 312.1384.



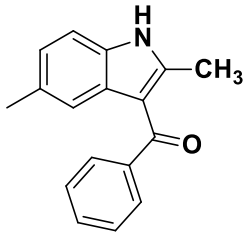
Phenyl(2-(4-(trifluoromethyl)phenyl)-1H-indol-3-yl)methanone (**3na**): white solid (46.8 mg, yield 64%), m.p. 195–197 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.43 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.59 (s, 4H), 7.56 (d, J = 8.1 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.41 – 7.33 (m, 1H), 7.31 – 7.25 (m, 1H), 7.22 (t, J = 7.7 Hz, 2H), 7.19 – 7.14 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.20, 142.33, 139.79, 136.10, 135.73, 131.62, 130.39, 129.21, 128.63 (q, J_{C-F} = 32.1 Hz), 128.00, 125.50, 124.92 (q, J_{C-F} = 3.6 Hz), 123.48, 122.80, 121.83, 120.87, 113.29, 112.23; ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.2; EI-MS (m/z): 366 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{15}F_3NO^+$ $[M+H]^+$, 366.1100, found: 366.1102.



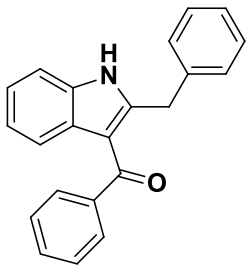
(2-(2,6-Difluorophenyl)-1*H*-indol-3-yl)(phenyl)methanone (**3oa**): white solid (41.9 mg, yield 63%), m.p. 218–220 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.40 (s, 2H), 7.54 (d, J_{C-F} = 8.1 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.37 (m, 2H), 7.33 – 7.27 (m, 1H), 7.27 – 7.19 (m, 3H), 7.01 (t, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.51, 160.23 (d, J_{C-F} = 6.3 Hz), 158.25 (d, J_{C-F} = 6.3 Hz), 139.65, 136.12, 131.98 (t, J_{C-F} = 10.4 Hz), 131.25, 130.63, 128.15, 127.64, 126.92, 123.36, 121.68, 120.83, 114.93, 111.97, 111.60 (d, J_{C-F} = 4.4 Hz), 111.44 (d, J_{C-F} = 4.2 Hz), 110.02 (d, J_{C-F} = 19.4 Hz); ^{19}F NMR (471 MHz, DMSO-d_6) δ -111.24; EI-MS (m/z): 334 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{14}F_2NO^+$ $[M+H]^+$, 334.1038, found: 334.1040.



(2-Methyl-1*H*-indol-3-yl)(phenyl)methanone (**3pa**): white solid (31.5 mg, yield 67%), m.p. 198–199 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.93 (s, 1H), 7.64 – 7.55 (m, 3H), 7.51 (m, 2H), 7.38 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.15 – 7.07 (m, 1H), 7.04 – 6.96 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.69, 144.42, 141.67, 134.94, 131.00, 128.33, 127.98, 127.26, 121.79, 120.91, 119.98, 112.45, 111.23, 14.17; EI-MS (m/z): 236 $[M+H]^+$; HRMS (ESI) calculated for $C_{16}H_{14}NO^+$ $[M+H]^+$, 236.1070, found: 236.1070.

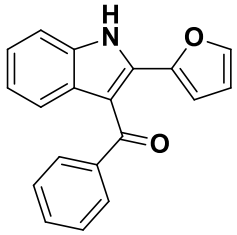


(2,5-Dimethyl-1*H*-indol-3-yl)(phenyl)methanone (**3qa**): white solid (31.9 mg, yield 64%), m.p. 232–234 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.80 (s, 1H), 7.60 – 7.57 (m, 3H), 7.52 – 7.49 (m, 2H), 7.26 (d, J = 8.2 Hz, 1H), 7.20 (s, 1H), 6.94 (dd, J = 8.2, 1.1 Hz, 1H), 2.32 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.67, 144.31, 141.77, 133.28, 130.90, 129.56, 128.30, 127.95, 127.58, 123.22, 119.94, 112.20, 110.85, 21.35, 14.24; EI-MS (m/z): 250 $[M+H]^+$; HRMS (ESI) calculated for $C_{17}H_{16}NO^+$ $[M+H]^+$, 250.1226, found: 250.1227.

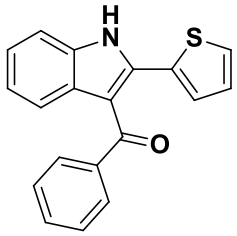


(2-Benzyl-1*H*-indol-3-yl)(phenyl)methanone (**3ra**): white solid (52.3 mg, yield 84%),

m.p. 161–162 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.01 (s, 1H), 7.67 – 7.58 (m, 3H), 7.50 (t, J = 7.6 Hz, 2H), 7.41 (d, J = 8.1 Hz, 1H), 7.27 – 7.16 (m, 5H), 7.15 – 7.10 (m, 1H), 7.08 (d, J = 8.0 Hz, 1H), 7.01 – 6.93 (m, 1H), 4.27 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.79, 145.98, 141.26, 138.73, 135.21, 131.38, 128.40, 128.36, 128.26, 126.92, 126.31, 121.99, 120.85, 120.08, 112.49, 111.66, 32.75; EI-MS (m/z): 334 $[M+Na]^+$; HRMS (ESI) calculated for $C_{22}H_{17}NONa^+$ $[M+Na]^+$, 334.1208, found: 334.1200.

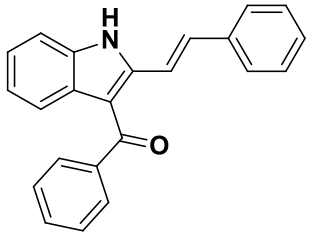


(2-(Furan-2-yl)-1*H*-indol-3-yl)(phenyl)methanone (**3sa**): yellow solid (50.6 mg, yield 88%), m.p. 130-132 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.34 (s, 1H), 7.76 – 7.70 (m, 1H), 7.68 – 7.61 (m, 2H), 7.60 – 7.54 (m, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.43 (dd, J = 10.7, 4.7 Hz, 2H), 7.27 – 7.17 (m, 2H), 7.07 – 6.99 (m, 2H), 6.57 (dd, J = 3.5, 1.8 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.31, 145.41, 144.14, 140.26, 135.68, 132.50, 131.79, 128.67, 128.26, 127.47, 123.02, 121.22, 120.35, 112.11, 112.08, 111.98, 111.34; EI-MS (m/z): 288 $[M+H]^+$; HRMS (ESI) calculated for $C_{19}H_{14}NO_2^+$ $[M+H]^+$, 288.1019, found: 288.1021.

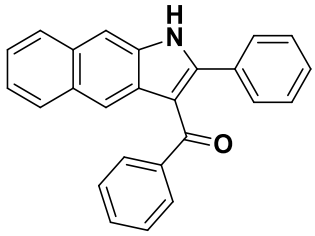


Phenyl(2-(thiophen-2-yl)-1*H*-indol-3-yl)methanone (**3ta**): yellow solid (51.6 mg, yield 85%), m.p. 183–185 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.23 (s, 1H), 7.66 – 7.58 (m, 3H), 7.54 – 7.47 (m, 2H), 7.44 (dd, J = 3.7, 1.2 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.25 – 7.17 (m, 1H), 7.11 – 7.00 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.58, 139.77, 136.31, 135.65, 132.36, 131.86, 129.04, 128.95, 128.79, 128.13, 127.77,

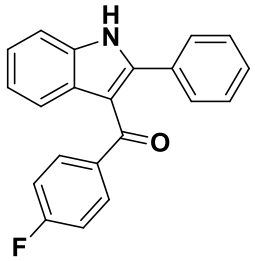
127.31, 123.05, 121.25, 120.32, 112.44, 111.74; EI-MS (m/z): 304 $[M+H]^+$; HRMS (ESI) calculated for $C_{19}H_{14}ONS^+$ $[M+H]^+$, 304.0796, found: 304.0790.



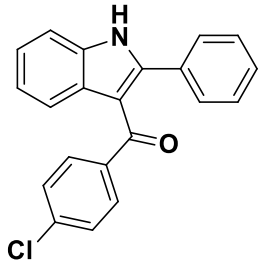
(*E*)-Phenyl(2-styryl-1*H*-indol-3-yl)methanone (**3ua**): yellow solid (52.4 mg, yield 81%), m.p. 134-136 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.33 (s, 1H), 7.66 (m, 3H), 7.54 (t, J = 7.4 Hz, 2H), 7.49 (d, J = 3.0 Hz, 1H), 7.45 (d, J = 11.7 Hz, 1H), 7.42 – 7.28 (m, 6H), 7.22 (m, 2H), 7.11 – 7.00 (m, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.78, 141.41, 141.38, 136.27, 136.11, 131.80, 131.54, 128.99, 128.57, 128.52, 128.42, 127.33, 126.46, 123.46, 121.23, 120.61, 117.74, 114.06, 111.52; EI-MS (m/z): 324 $[M+H]^+$; HRMS (ESI) calculated for $C_{23}H_{17}NO^+$ $[M+H]^+$, 324.1388, found: 324.1385.



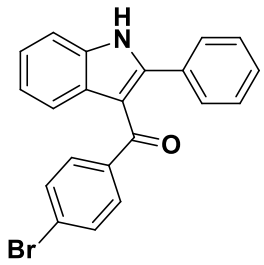
Phenyl(2-phenyl-1*H*-benzo[f]indol-3-yl)methanone (**3va**): yellow solid (56.9 mg, yield 82%), m.p. 260–262 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.29 (s, 1H), 8.47 (s, 1H), 8.09 – 7.91 (m, 3H), 7.56 – 7.50 (m, 2H), 7.45 – 7.31 (m, 5H), 7.26 (m, 3H), 7.18 (t, J = 7.7 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.80, 149.15, 139.92, 136.22, 131.33, 131.09, 130.25, 129.82, 129.49, 129.43, 129.00, 128.97, 128.16, 127.99, 127.66, 127.45, 124.04, 123.22, 118.34, 110.98, 107.14; EI-MS (m/z): 348 $[M+H]^+$; HRMS (ESI) calculated for $C_{25}H_{18}NO^+$ $[M+H]^+$, 348.1383, found: 348.1380.



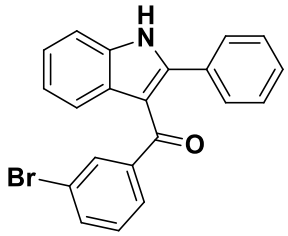
(4-Fluorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ab**): white solid (44.8 mg, yield 71%), m.p. 236–237 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.21 (s, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.51 (d, J = 8.1 Hz, 1H), 7.37 (m, 2H), 7.30 – 7.23 (m, 4H), 7.20 – 7.15 (m, 1H), 7.07 – 6.97 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.62, 163.71 (d, $J_{C\text{-}F}$ = 249.4 Hz), 144.22, 136.42 (d, $J_{C\text{-}F}$ = 2.6 Hz), 135.82, 131.75, 131.68, 131.46, 129.63, 128.51, 128.09, 128.04, 122.93, 121.48, 120.55, 114.74, 114.57, 112.00, 111.85; ^{19}F NMR (471 MHz, DMSO-d_6) δ -108.68; EI-MS (m/z): 316 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{15}FNO^+$ $[M+H]^+$, 316.1132, found: 316.1133.



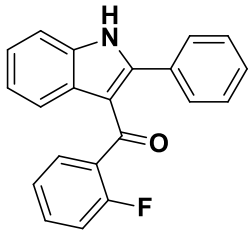
(4-Chlorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ac**): white solid (49.1 mg, yield 74%), m.p. 234–235 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.24 (s, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.56 – 7.45 (m, 3H), 7.40 – 7.35 (m, 2H), 7.30 – 7.22 (m, 6H), 7.21 – 7.15 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.74, 144.53, 138.59, 135.90, 135.83, 131.41, 130.82, 129.68, 128.56, 128.04, 127.77, 122.99, 121.58, 120.58, 111.87; EI-MS (m/z): 332 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{15}ClNO^+$ $[M+H]^+$, 332.0837, found: 332.0840.



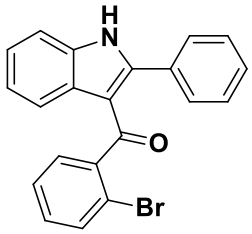
(4-Bromophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ad**): white solid (56.4 mg, yield 75%), m.p. 233–235 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.24 (s, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.40 – 7.34 (m, 4H), 7.32 – 7.23 (m, 4H), 7.21 – 7.15 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.89, 144.55, 138.93, 135.83, 131.40, 130.98, 130.72, 129.68, 128.55, 128.05, 128.02, 124.91, 122.99, 121.59, 120.58, 111.88; EI-MS (*m/z*): 378 ($(M+H)^+$, (Br^{81})), 376 ($(M+H)^+$, (Br^{79})); HRMS (ESI) calculated for $C_{21}H_{15}NOBr^+$ $[M+H]^+$ 376.0332, found:376.0335(Br^{79}), 378.0420(Br^{81}).



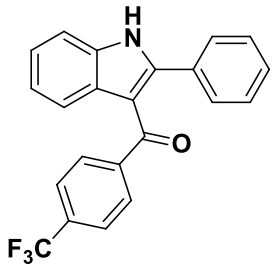
(3-Bromophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ae**): white solid (58.7 mg, yield 78%), m.p. 214–216 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.28 (s, 1H), 7.89 (d, J = 7.9 Hz, 1H), 7.57 – 7.43 (m, 4H), 7.36 (dd, J = 7.7, 1.5 Hz, 2H), 7.30 – 7.23 (m, 4H), 7.20 (m, 1H), 7.14 (t, J = 7.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.20, 145.16, 141.93, 135.85, 133.58, 131.68, 131.41, 129.90, 129.68, 128.68, 128.02, 128.00, 127.79, 123.10, 121.74, 120.98, 120.69, 111.91, 111.74; EI-MS (*m/z*): 400 ($(M+Na)^+$, (Br^{81})), 398 ($(M+Na)^+$, (Br^{79})); HRMS (ESI) calculated for $C_{21}H_{14}NOBrNa^+$ $[M+Na]^+$ 398.0156, found: 398.0146 and 400.0125.



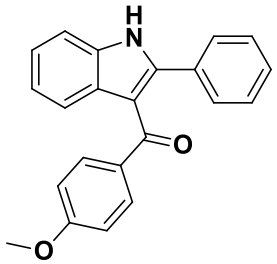
(2-Fluorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3af**): yellow solid (39.7 mg, yield 63%), m.p. 217–219 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.30 (s, 1H), 8.01 (d, J = 7.7 Hz, 1H), 7.49 (d, J = 7.7 Hz, 1H), 7.37 – 7.29 (m, 3H), 7.28 – 7.16 (m, 6H), 7.00 (td, J = 7.5, 0.9 Hz, 1H), 6.84 (dd, J = 14.0, 4.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.41, 158.69 (d, J = 247.6 Hz), 146.69, 135.68, 131.97 (d, J = 8.3 Hz), 131.01, 130.15 (d, J = 3.2 Hz), 129.82, 129.70, 128.67, 127.64, 127.52, 123.95 (d, J = 3.2 Hz), 123.23, 122.16, 120.95, 115.25 (d, J = 21.8 Hz), 113.18, 111.94; ^{19}F NMR (376 MHz, DMSO-d_6) δ -115.39; EI-MS (m/z): 314 $[M-H]^-$; HRMS (ESI) calculated for $C_{21}H_{13}FNO^-$ $[M-H]^-$, 314.0987, found: 314.0988.



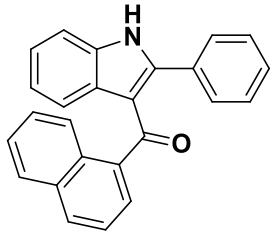
(2-Bromophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ag**): yellow solid (50.4 mg, yield 67%), m.p. 249–251 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.33 (s, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.37 (ddd, J = 12.1, 5.5, 1.6 Hz, 3H), 7.29 – 7.17 (m, 6H), 7.13 (qd, J = 7.8, 3.9 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.04, 147.01, 142.61, 135.78, 132.32, 131.19, 130.56, 129.57, 129.47, 128.67, 127.53, 127.47, 127.07, 123.22, 122.21, 121.11, 119.21, 112.23, 111.94; EI-MS (m/z): 374 ($(M-H)^-$, (Br^{79})),; HRMS (ESI) calculated for $C_{21}H_{13}BrNO^-$ $[M-H]^-$, 314.0987, found: found: 374.0181(Br^{79}), 376.0163(Br^{81}).



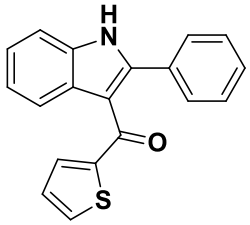
(2-Phenyl-1*H*-indol-3-yl)(4-(trifluoromethyl)phenyl)methanone (**3ah**): white solid (53.3 mg, yield 73%), m.p. 276–278 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.32 (s, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.2 Hz, 2H), 7.35 – 7.29 (m, 2H), 7.29 – 7.24 (m, 1H), 7.24 – 7.15 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.85, 145.65, 143.65, 135.85, 131.29, 130.45 (q, J_{C-F} = 63.6 Hz), 129.83, 129.47, 128.53, 127.94, 127.88, 124.88 (d, J_{C-F} = 272.5 Hz), 124.50, 124.47, 123.19, 121.90, 120.79, 111.93; ^{19}F NMR (471 MHz, DMSO-d_6) δ -61.51; EI-MS (m/z): 366 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{15}F_3NO$ $[M+H]^+$, 366.1106, found: 366.1102.



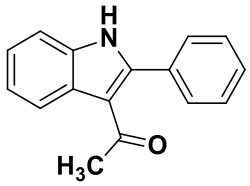
(4-Methoxyphenyl)(2-phenyl-1H-indol-3-yl)methanone (**3ai**): white solid (52.4 mg, yield 80%), m.p. 152–153 ºC. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.65 – 7.56 (m, 3H), 7.50 (d, J = 8.1 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.35 – 7.25 (m, 3H), 7.21 (dd, J = 8.1, 1.0 Hz, 1H), 7.16 – 7.08 (m, 1H), 6.87 – 6.74 (m, 2H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.90, 162.06, 142.50, 135.75, 132.09, 131.64, 131.44, 129.22, 128.34, 128.17, 122.62, 121.02, 120.30, 113.19, 112.37, 111.77, 55.32; EI-MS (m/z): 328 $[M+H]^+$; HRMS (ESI) calculated for $C_{22}H_{18}NO_2$ $[M+H]^+$, 328.1332, found: 328.1334.



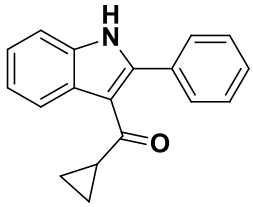
Naphthalen-1-yl(2-phenyl-1*H*-indol-3-yl)methanone (**3aj**): pale yellow solid (43.8 mg, yield 63%), m.p. 200–201 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.23 (s, 1H), 8.08 (m, 1H), 7.88 – 7.84 (m, 1H), 7.80 (dd, J = 18.5, 8.1 Hz, 2H), 7.51 (m, 3H), 7.35 (dd, J = 7.0, 1.1 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.21 – 7.13 (m, 4H), 7.13 – 7.01 (m, 1H), 6.96 (t, J = 7.7 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.53, 146.18, 138.85, 135.73, 132.88, 131.46, 130.29, 129.80, 129.12, 128.31, 128.07, 127.75, 127.26, 126.88, 126.72, 125.88, 124.99, 124.41, 123.01, 121.86, 121.03, 113.90, 111.87; EI-MS (m/z): 348 $[M+H]^+$; HRMS (ESI) calculated for $C_{25}H_{18}NO^+$ $[M+H]^+$, 348.1388, found: 348.1390.



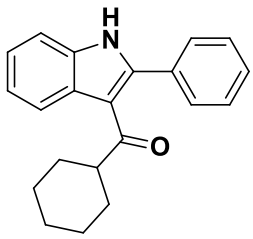
(2-Phenyl-1*H*-indol-3-yl)(thiophen-2-yl)methanone (**3ak**): pale yellow solid (47.3 mg, yield 78%), m.p. 180–181 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.16 (s, 1H), 7.80 (dd, J = 4.9, 1.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.53 – 7.48 (m, 3H), 7.40 – 7.30 (m, 3H), 7.27 – 7.22 (m, 1H), 7.20 (dd, J = 3.7, 1.1 Hz, 1H), 7.17 – 7.12 (m, 1H), 6.87 (dd, J = 4.9, 3.8 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 183.85, 145.03, 142.23, 135.77, 133.84, 133.46, 131.68, 129.16, 128.56, 128.38, 127.86, 127.69, 122.86, 121.16, 120.06, 112.37, 111.87; EI-MS (m/z): 326 $[M+Na]^+$; HRMS (ESI) calculated for $C_{19}H_{13}NOSNa^+$ $[M+Na]^+$, 326.0610, found: 326.0606.



1-(2-Phenyl-1*H*-indol-3-yl)ethanone (**3al**): white solid (32.5 mg, yield 69%), m.p. 191–193 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.19 (d, J = 7.3 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.60 – 7.52 (m, 3H), 7.42 (d, J = 7.4 Hz, 1H), 7.27 – 7.17 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.55, 144.87, 135.37, 132.70, 130.00, 129.33, 128.40, 126.97, 122.81, 121.74, 121.54, 114.25, 111.55, 30.06; EI-MS (m/z): 236 $[M+H]^+$; HRMS (ESI) calculated for $C_{16}H_{14}NO^+$ $[M+H]^+$, 236.1075, found: 236.1070.



Cyclopropyl(2-phenyl-1H-indol-3-yl)methanone (**3am**): white solid (38.2 mg, yield 73%), m.p. 193–195 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.70 (dd, J = 8.0, 1.4 Hz, 2H), 7.60 – 7.48 (m, 3H), 7.44 (d, J = 7.9 Hz, 1H), 7.30 – 7.12 (m, 2H), 1.99 – 1.85 (m, 1H), 1.04 – 0.96 (m, 2H), 0.67 (td, J = 6.8, 3.2 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 196.16, 143.98, 135.49, 132.32, 130.03, 129.29, 128.41, 127.04, 122.82, 121.57, 121.24, 114.35, 111.59, 20.50, 10.74; EI-MS (m/z): 284 $[M+Na]^+$; HRMS (ESI) calculated for $C_{18}H_{15}NONa$ $[M+Na]^+$, 284.1046, found: 284.1044.

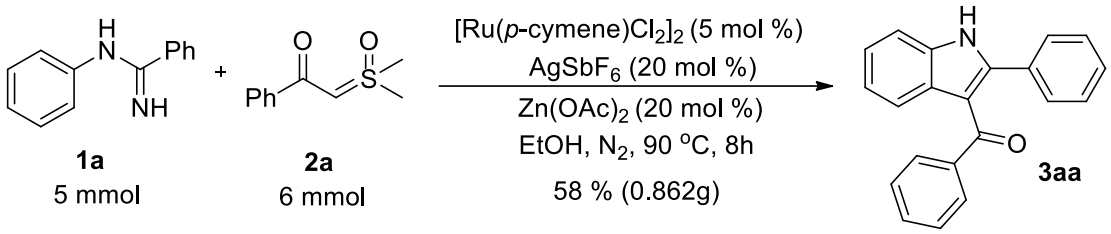


Cyclohexyl(2-phenyl-1*H*-indol-3-yl)methanone (**3an**): white solid (40.4 mg, yield

66%), m.p. 194–198 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.05 (s, 1H), 8.14 (d, J = 7.5 Hz, 1H), 7.65 – 7.53 (m, 5H), 7.41 (d, J = 7.5 Hz, 1H), 7.20 (m, 2H), 1.63 – 1.53 (m, 4H), 1.46 (d, J = 12.8 Hz, 1H), 1.33 – 1.17 (m, 3H), 1.12 – 0.89 (m, 1H), 0.82 – 0.66 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 200.25, 143.96, 135.44, 132.99, 129.61, 129.21, 128.29, 127.24, 122.73, 121.59, 121.42, 112.95, 111.51, 47.22, 29.06, 25.34; EI-MS (m/z): 304 $[M+H]^+$; HRMS (ESI) calculated for $C_{21}H_{21}NO$ $[M+H]^+$, 304.0796, found: 304.1694.

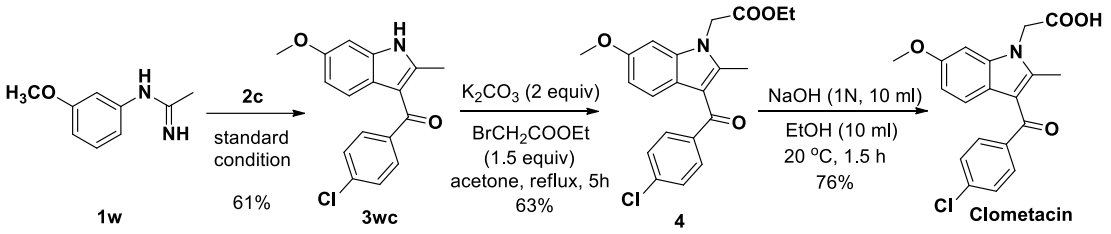
IV. 5 mmol-scale synthesis and synthetic applications

(a) 5 mmol-scale synthesis



N-phenylacetimidamide (**1a**, 5 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.25 mmol), $AgSbF_6$ (1 mmol), $Zn(OAc)_2$ (1 mmol) were dissolved in EtOH (10 mL) in a pressure tube. The resulting mixture was stirred for seconds under N_2 atmosphere, to which was added sulfur ylide (**2a**, 6 mmol). The mixture was stirred at 90 °C for 8 hours. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (1:8) to afford product **3aa** as a white solid (862 mg, 58%).

(b) Synthetic application



N-(3-methoxyphenyl)acetimidamide (**1w**, 0.8 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.04 mmol), $AgSbF_6$ (0.16 mmol), $Zn(OAc)_2$ (0.16 mmol) were dissolved in EtOH (3 mL) in a pressure tube. The resulting mixture was stirred for seconds under N_2 atmosphere, to which was added sulfur ylide (**2c**, 0.96 mmol). The mixture was stirred at 90 °C for 8 hours. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using ethyl acetate/petroleum ether (1:8) to afford product **3wc** as a pale yellow solid (146 mg, 61%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (s, 1H), 7.64 – 7.59 (m, 2H), 7.59 – 7.53 (m, 2H), 7.23 (d, J = 8.7 Hz, 1H), 6.88 (d, J = 2.3 Hz, 1H), 6.70 (dd, J = 8.7, 2.4 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.18, 155.80, 143.74, 140.32, 135.83,

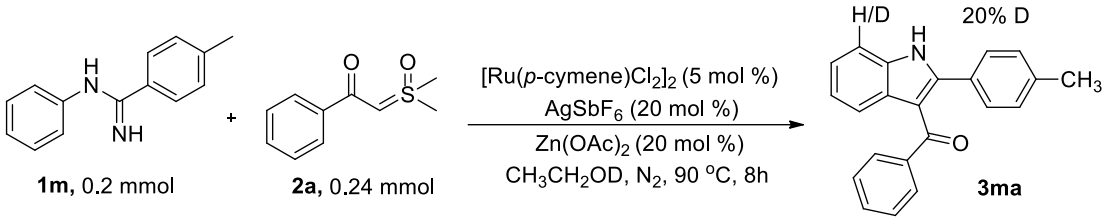
135.70, 130.03, 128.51, 121.13, 120.67, 112.16, 110.53, 94.80, 55.26, 14.29; EI-MS (m/z): 300 $[M+H]^+$.

To a solution of (4-chlorophenyl)(6-methoxy-2-methyl-1*H*-indol-3-yl)methanone (**3wc**) (120 mg, 0.4 mmol) and ethyl 3-bromopropanoate ($BrCH_2COOEt$) (109 mg, 0.6 mmol) in acetone (10 mL) was added potassium carbonate (K_2CO_3) (110 mg, 0.8 mmol), and the resulting mixture was heated to reflux for 5 h. Water (50 mL) was added to the residue, the mixture was extracted with ethyl acetate, the organic extracts were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography to give **4** (97 mg, 63%) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.67 – 7.61 (m, 2H), 7.61 – 7.55 (m, 2H), 7.32 – 7.05 (m, 2H), 6.74 (dd, J = 8.8, 2.2 Hz, 1H), 5.22 (s, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 2.33 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.27, 168.34, 156.21, 144.11, 139.76, 137.41, 136.28, 130.32, 128.61, 120.58, 120.17, 112.75, 110.90, 94.26, 61.33, 55.50, 44.48, 14.06, 12.21; EI-MS (m/z): 386 $[M+H]^+$.

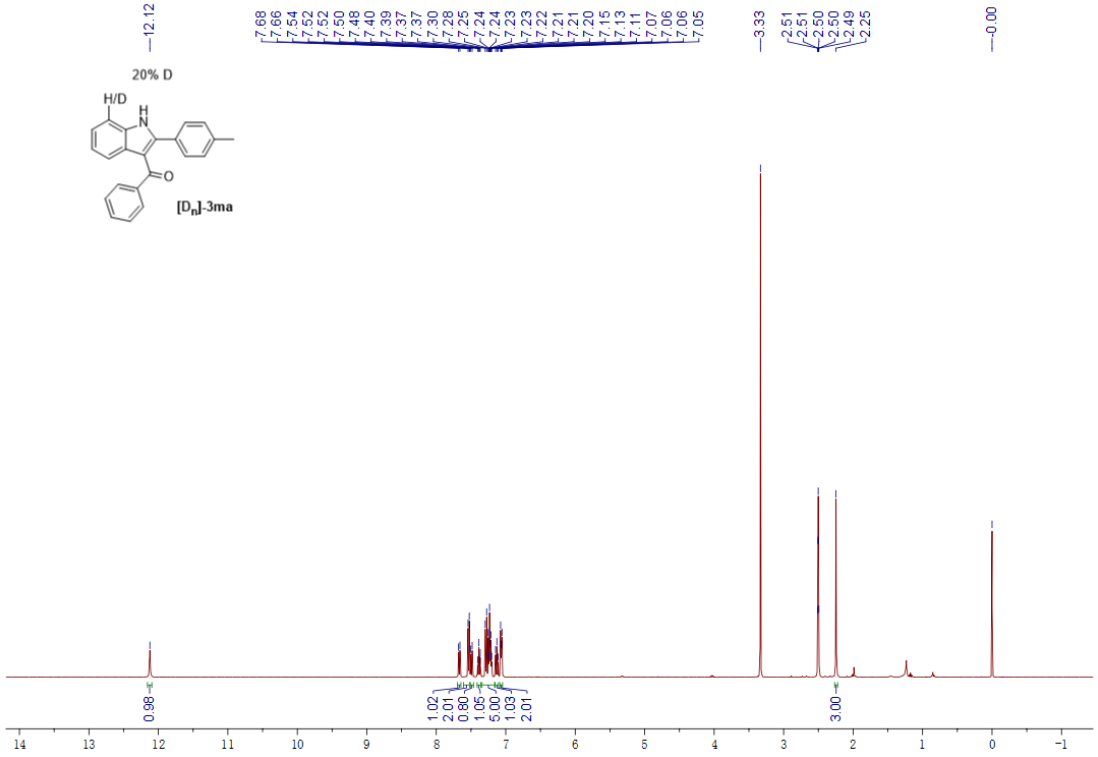
To a solution of ethyl 2-(3-(4-chlorobenzoyl)-6-methoxy-2-methyl-1*H*-indol-1-yl) acetate (**4**) (77 mg, 0.2 mmol) in EtOH (10 mL) was added 1N sodium hydroxide (10 ml), and the resulting mixture was heated to reflux for 1.5 h. Water (100 mL) was added and the mixture was washed with diethyl ether (150 mL). The aqueous phase was acidified with 3N hydrochloric acid to afford drug clometacin as a white solid (54 mg, 76%). 2-(3-(4-chlorobenzoyl)-6-methoxy-2-methyl-1H-indol-1-yl)acetic acid (clometacin): ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.26 (s, 1H), 7.61 (dd, J = 19.5, 8.1 Hz, 4H), 7.14 (d, J = 8.1 Hz, 2H), 6.73 (d, J = 8.5 Hz, 1H), 5.11 (s, 2H), 3.78 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.24, 169.73, 156.17, 144.28, 139.86, 137.45, 136.21, 130.31, 128.60, 120.55, 120.19, 112.58, 110.85, 94.22, 55.51, 44.55, 12.25; EI-MS (m/z): 357 $[M+H]^+$.

V. Mechanistic Studies

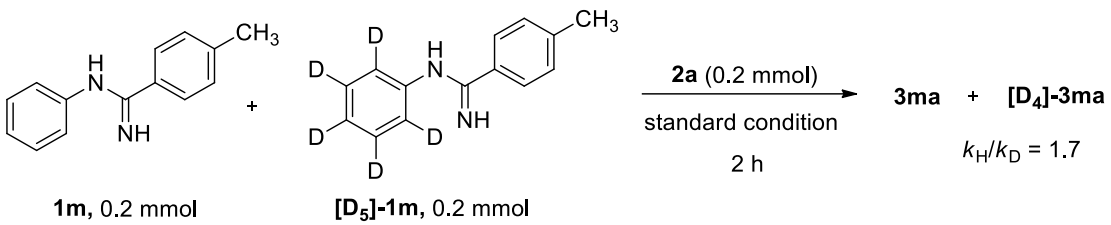
(a) H/D exchange studies



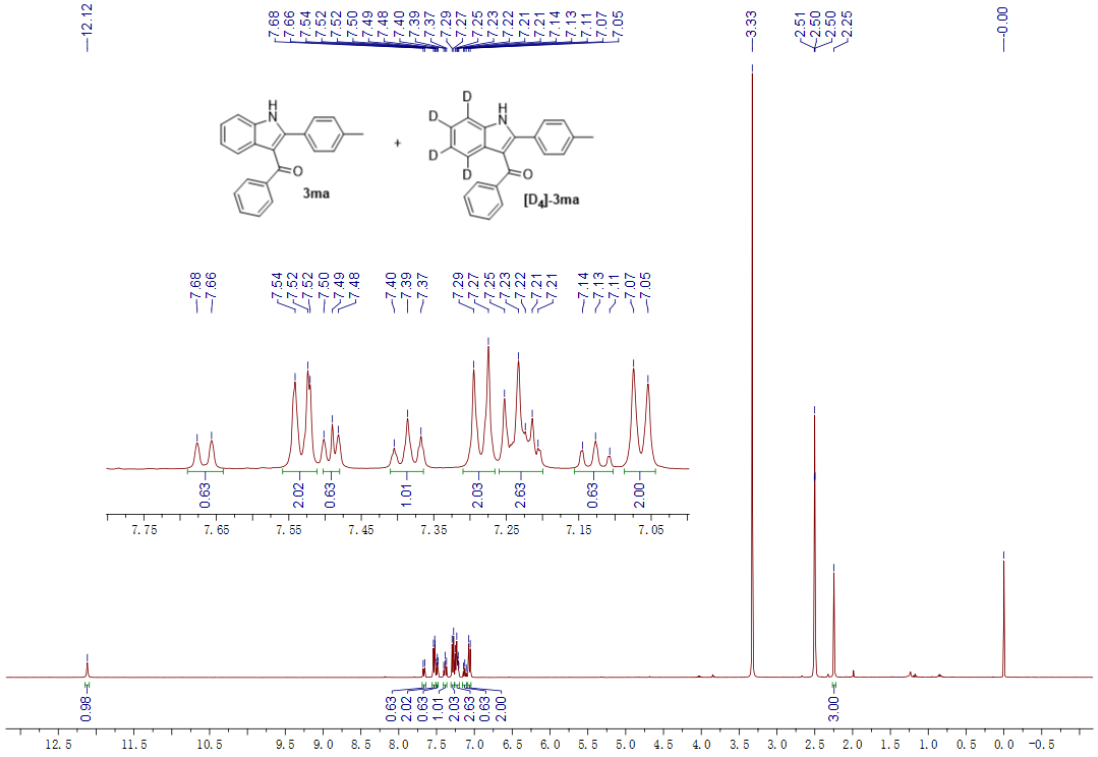
A mixture of **1m** (0.2 mmol), **2a** (0.24 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), $Zn(OAc)_2$ (0.04 mmol) were added in CH_3CH_2OD (3 mL) in a pressure tube under N_2 atmosphere that the mixture was stirred for 8 hours. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) to afford white solid, which was characterized by ^{1}H NMR spectroscopy. ^{1}H NMR analysis of the coupled product **3ma** revealed 20% deuteration at the *ortho* position (7-position of the indole).



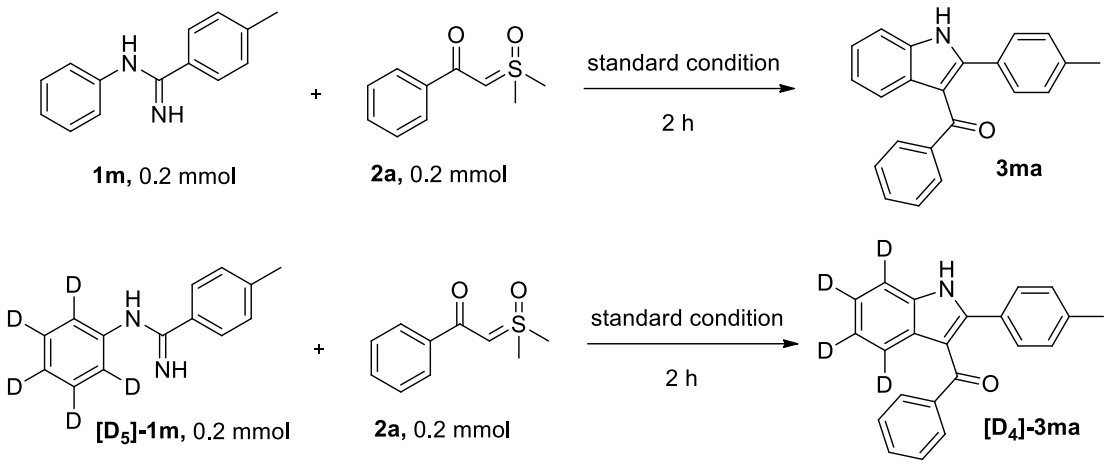
(b) Kinetic Isotope Effect (the competition experiment)



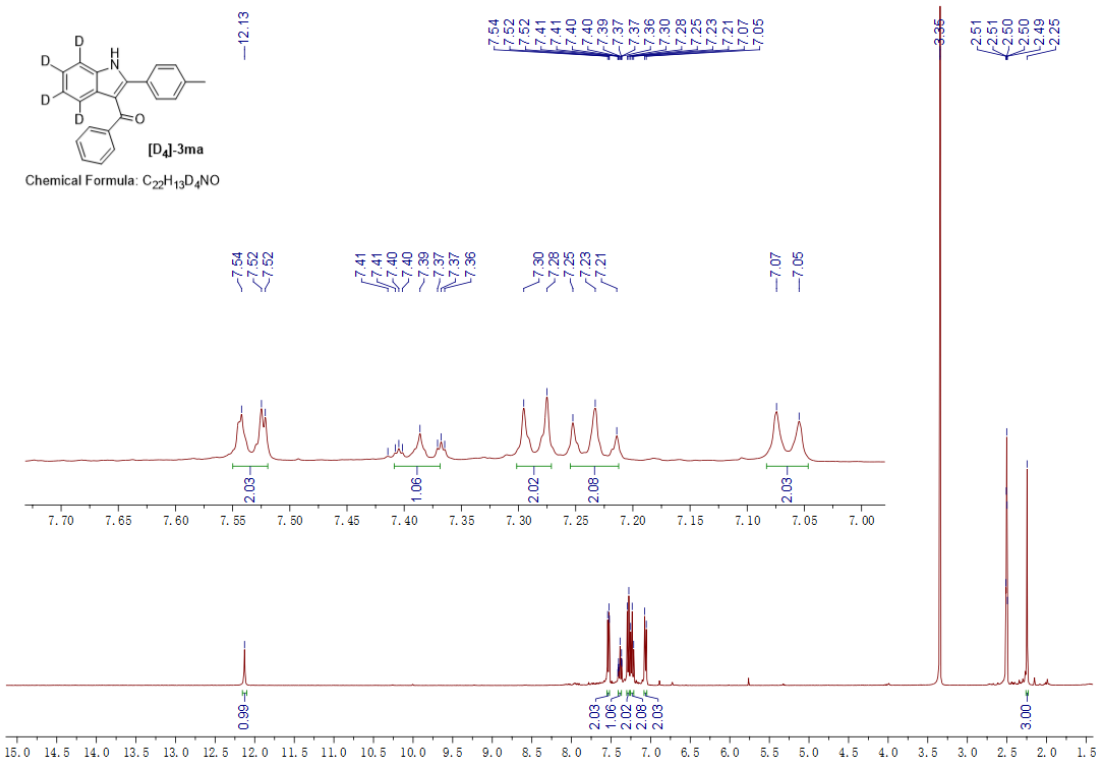
A mixture of **1m** (0.2 mmol), [D_5]-**1m** (0.2 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), $Zn(OAc)_2$ (0.04 mmol) were added in EtOH (3 mL) in a pressure tube under N_2 atmosphere that the mixture was stirred for a few minutes, subsequently, sulfur ylide (**2a**, 0.2 mmol) was added into foregoing mixture, the new mixture was stirred at 90 ^oC for 2 hours. Then, the reaction was cooled to 0 ^oC rapidly and was quenched with pentane. And the solvent was removed under vacuum and the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) to afford product **3ma** and **3ma**-d_4 as white solid. The KIE value was determined to be k_H/k_D = 0.63/0.37 = 1.7 on the basis of ^{1}H NMR analysis.



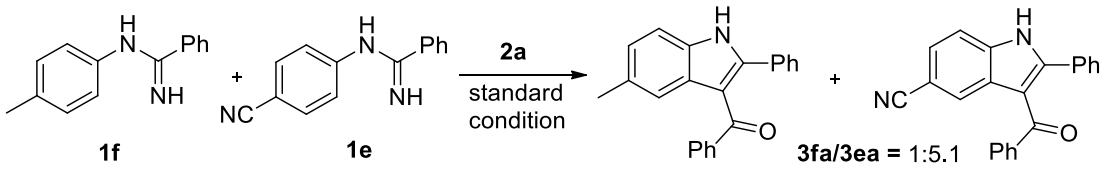
(c) Kinetic Isotope Effect (the parallel experiment)



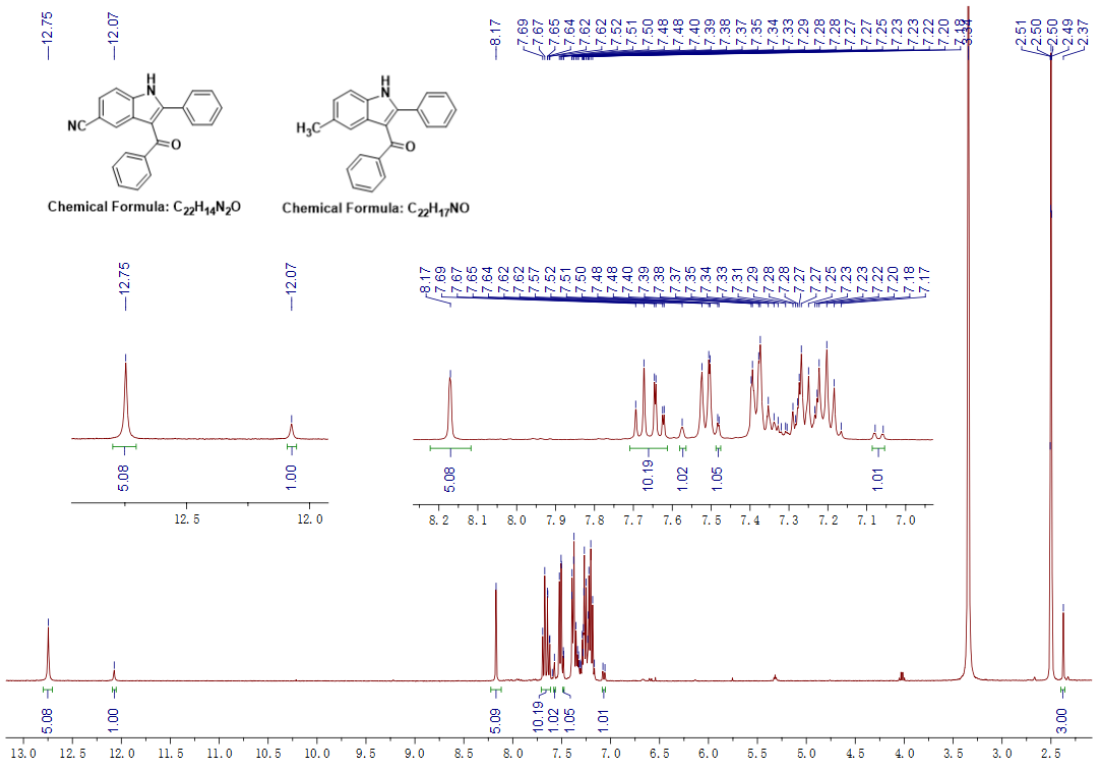
Two pressure tubes each was charged with [Ru(*p*-cymene)Cl_2]$_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), $Zn(OAc)_2$ (0.04 mmol), sulfoxonium ylide (**2a**, 0.2 mmol) and EtOH. To the parallel tubes was then separately introduced **1m** (0.2 mmol), [D_5]-**1m** (0.2 mmol). The reaction mixtures were stirred side-by-side at 90 °C for 2 h. Then, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA(8/1) to afford the product **3ma** and **[D_4]-3ma**, respectively. The KIE value was calculated according to the isolated yields of **3ma** and **[D_4]-3ma** from the two reactions.



(d) Competition Experiment

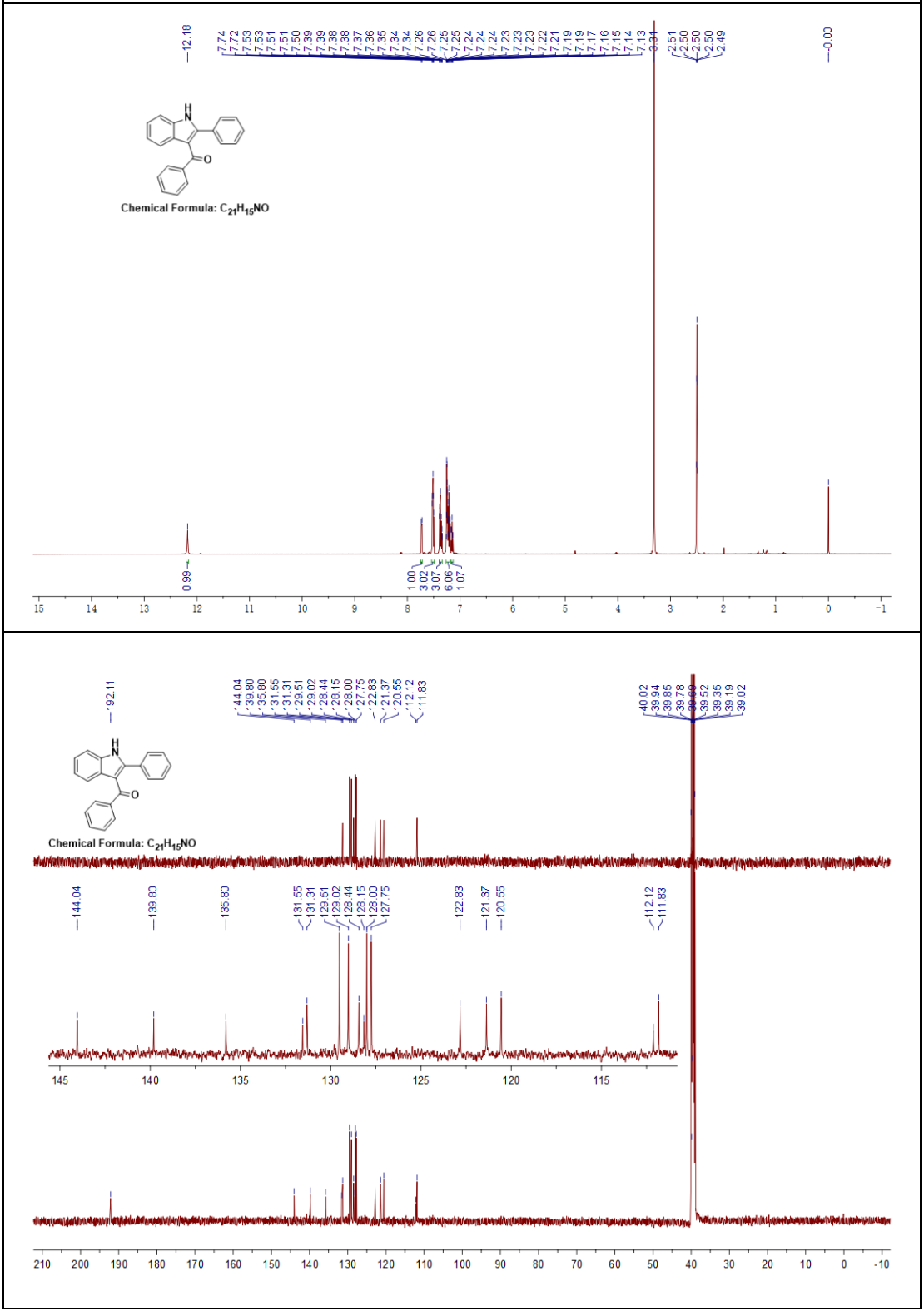


A mixture of **1f** (0.2 mmol), **1e** (0.2 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), $Zn(OAc)_2$ (0.04 mmol) were dissolved in EtOH (3 mL) in a pressure tube under N_2 atmosphere that the mixture was stirred for a few minutes, subsequently, sulfur ylide (**2a**, 0.2 mmol) was added into foregoing mixture, the new mixture was stirred at 90 ^oC for 8 hours. After that, the solvent was removed under vacuum and the residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1) to afford product **3fa** and **3ea** as white solid. The ratio of **3ba**: **3ea** = 1:5.1 was determined on the basis of ^1H NMR analysis.

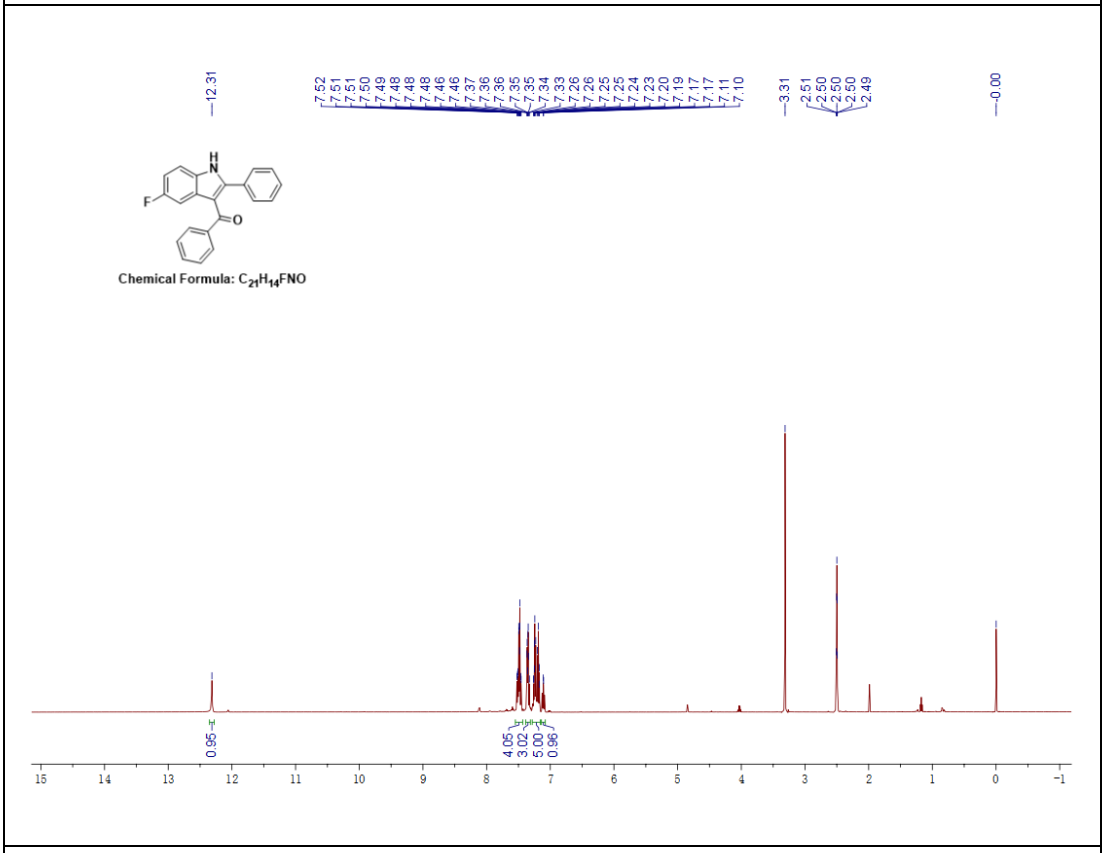


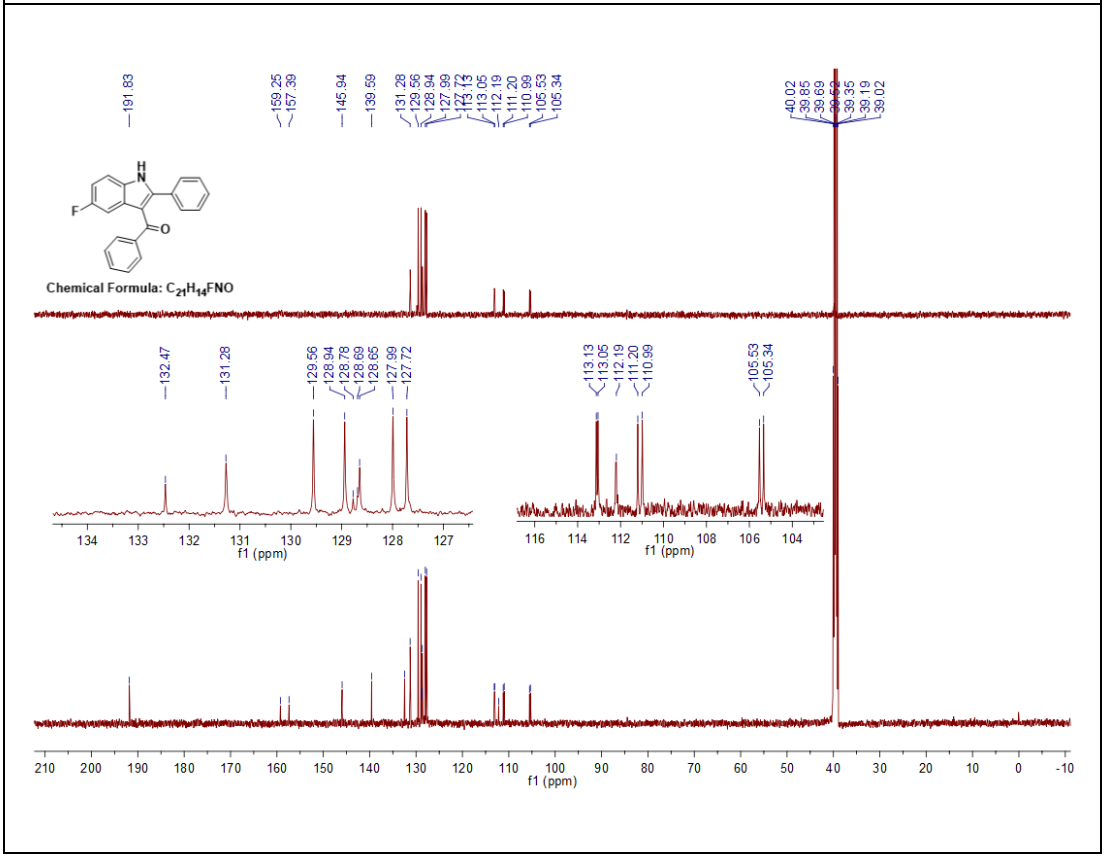
VI. ^{1}H and ^{13}C NMR Spectra

phenyl(2-phenyl-1*H*-indol-3-yl)methanone (**3aa**)

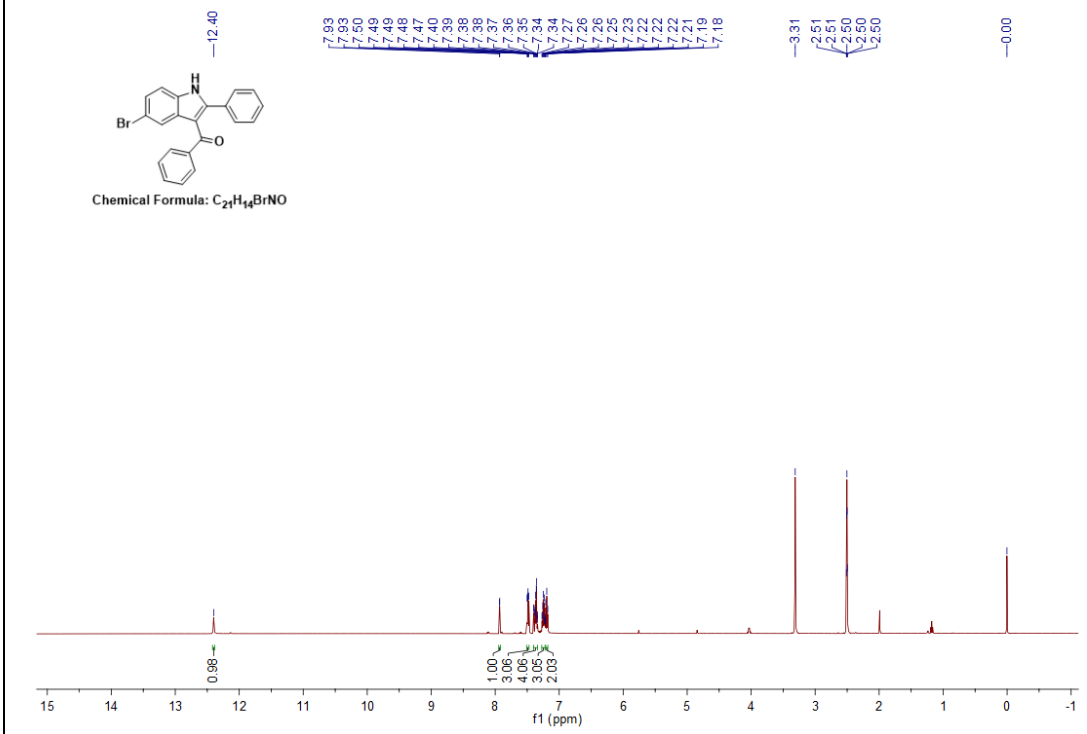


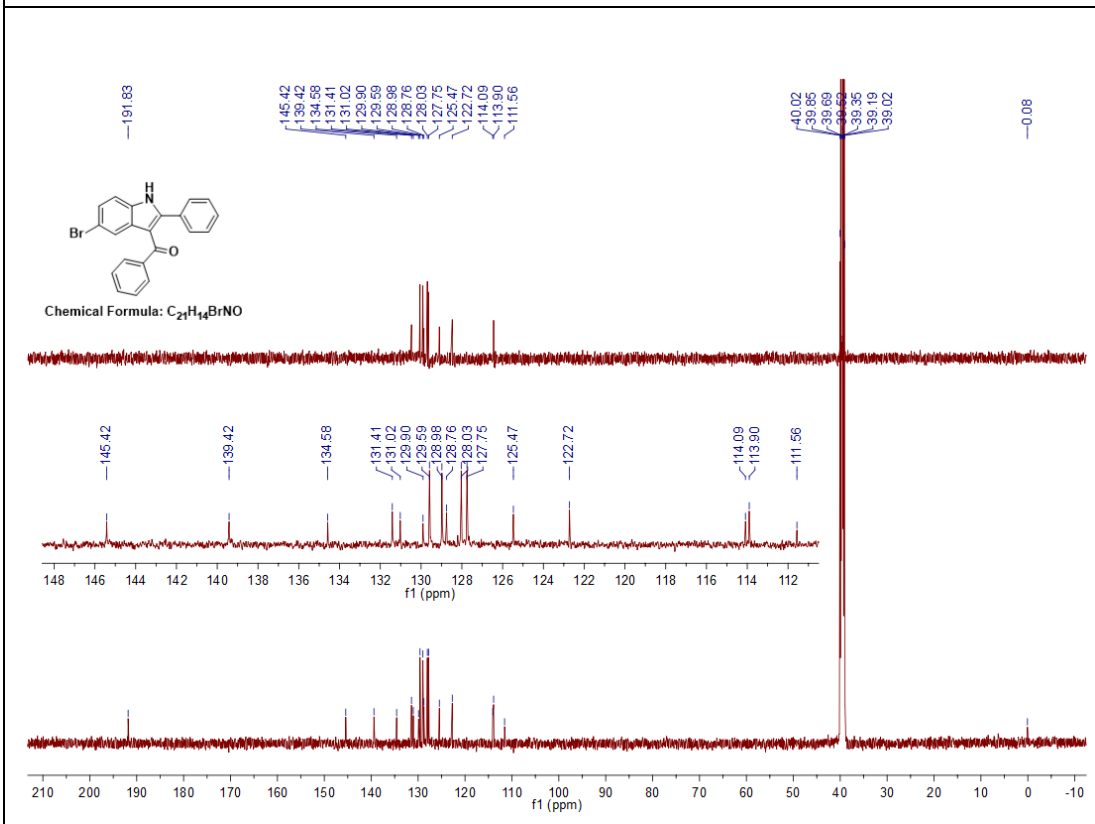
(5-fluoro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ba**)



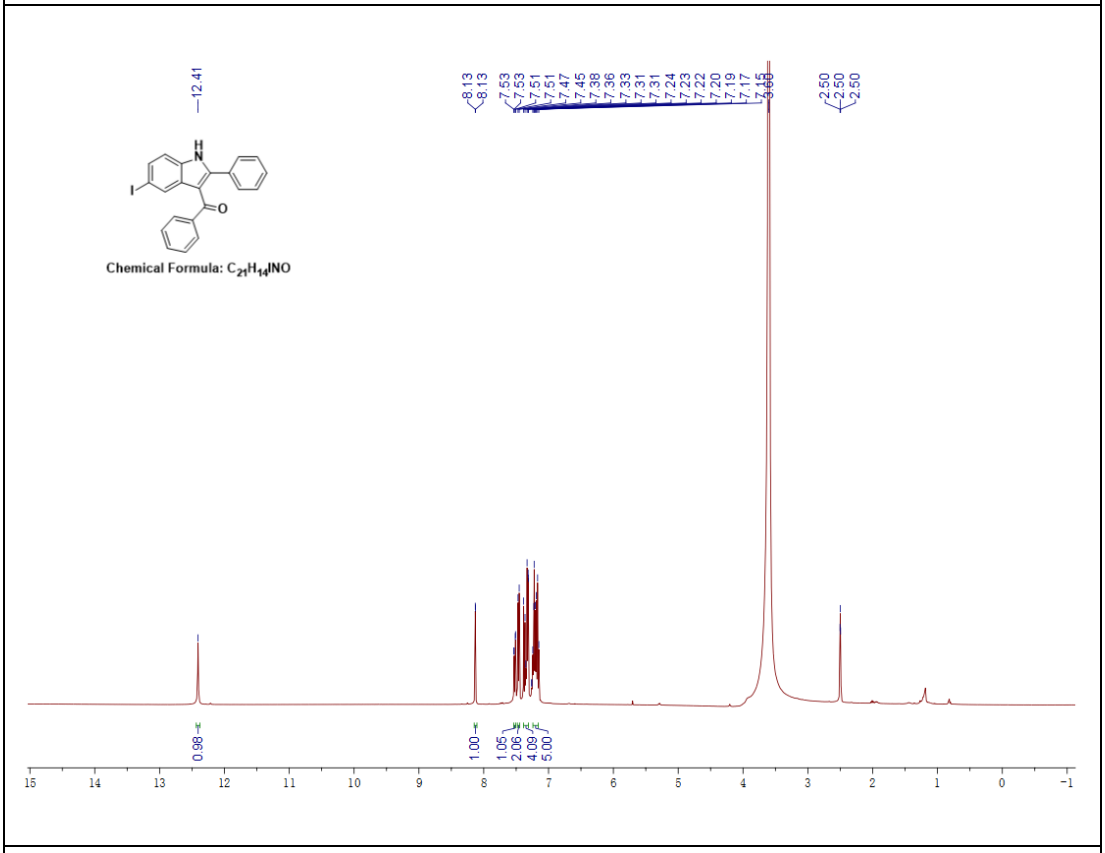


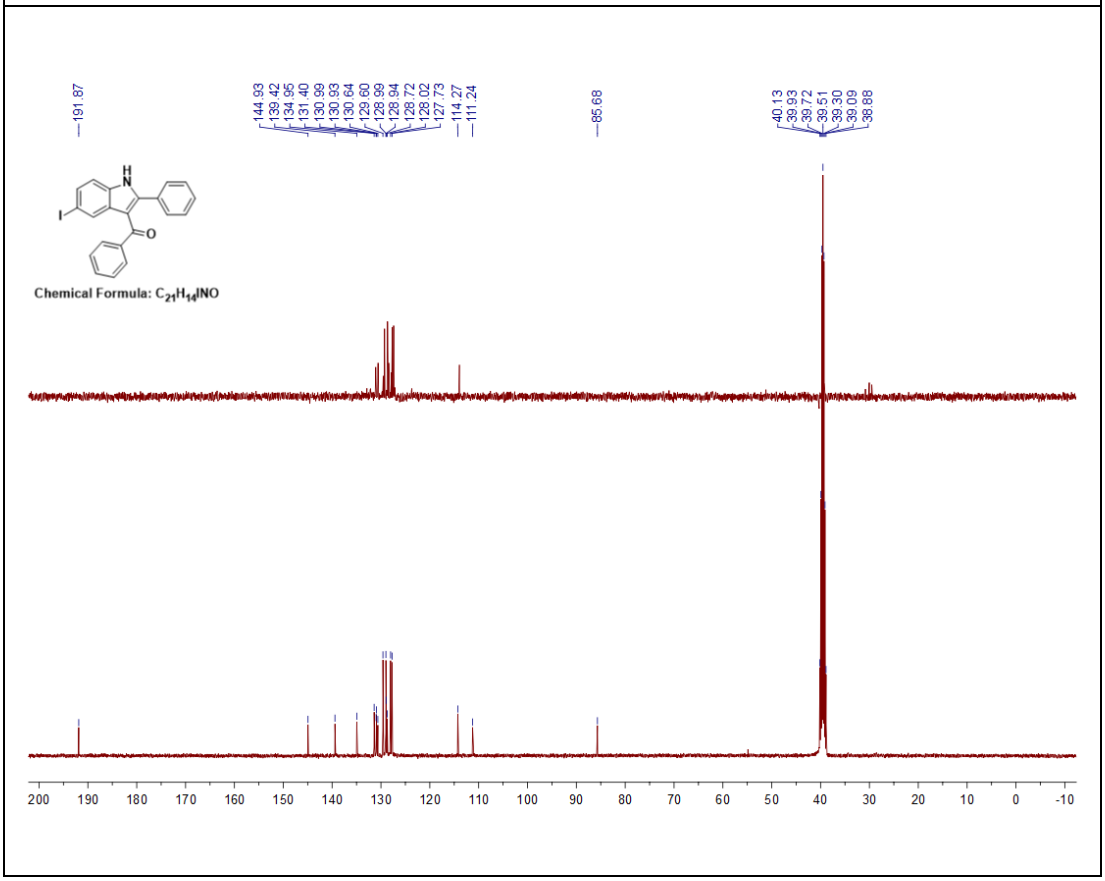
(5-bromo-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ca**)



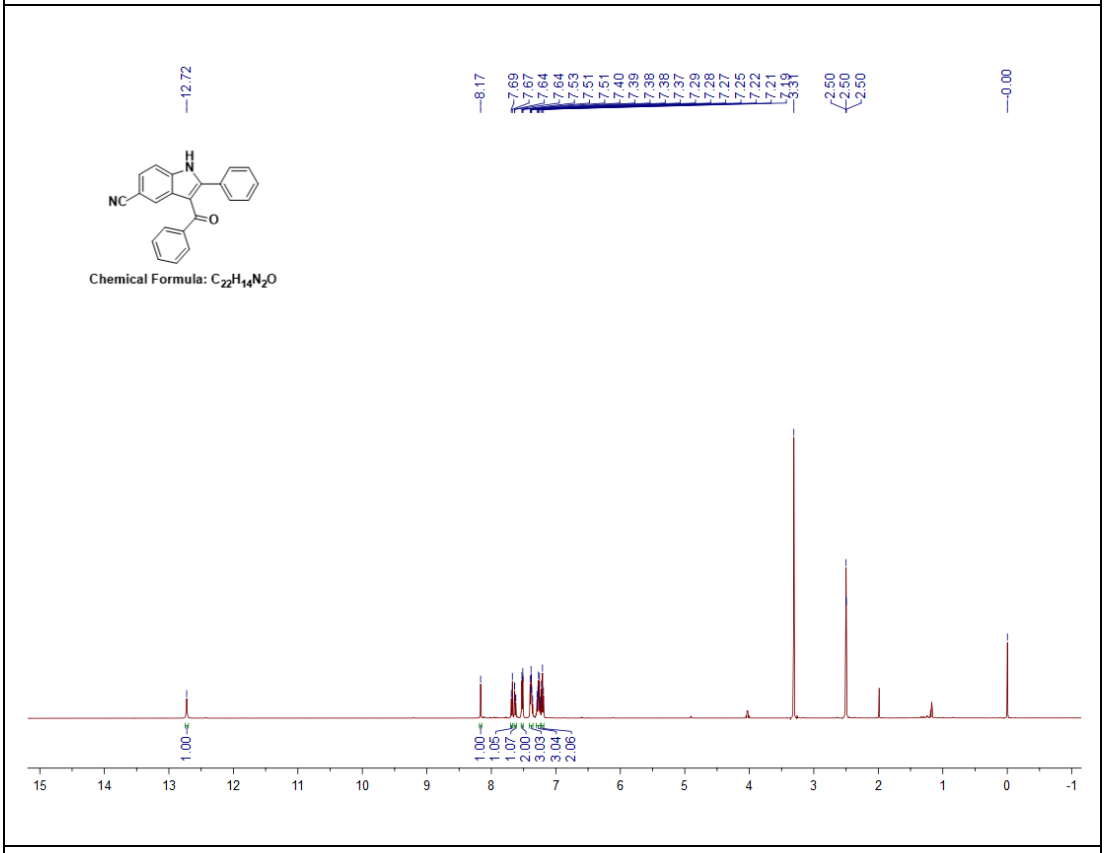


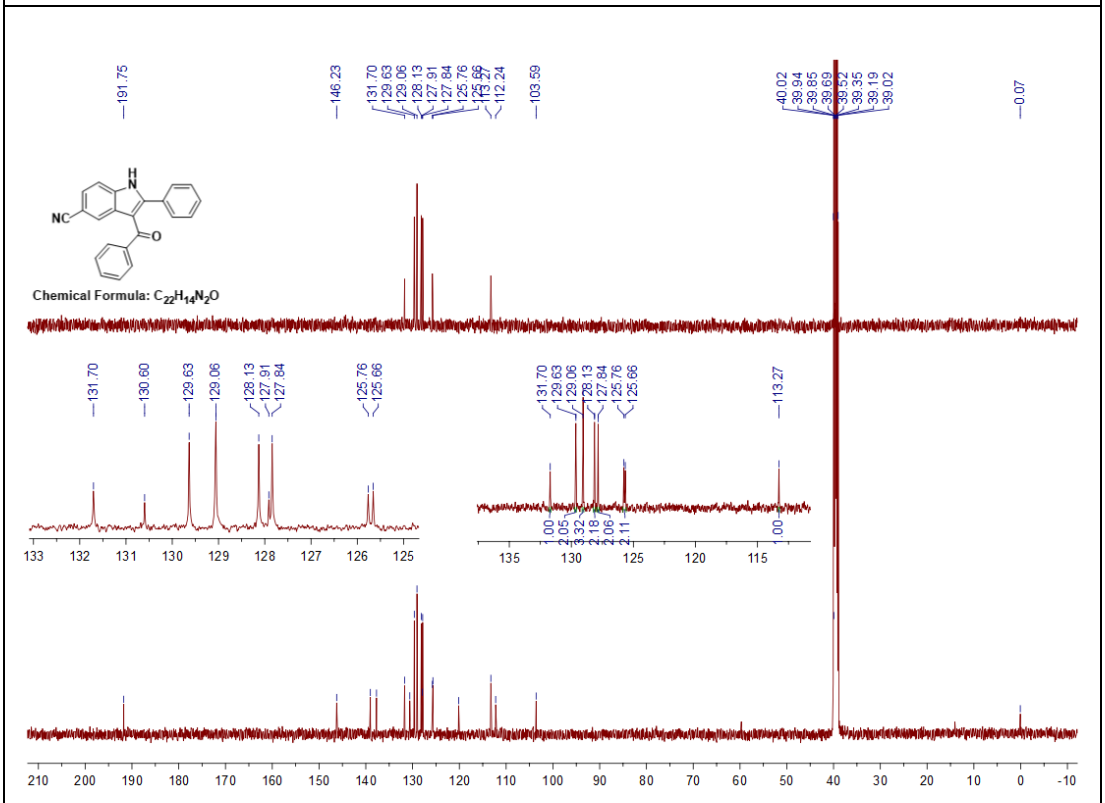
(5-iodo-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3da**)



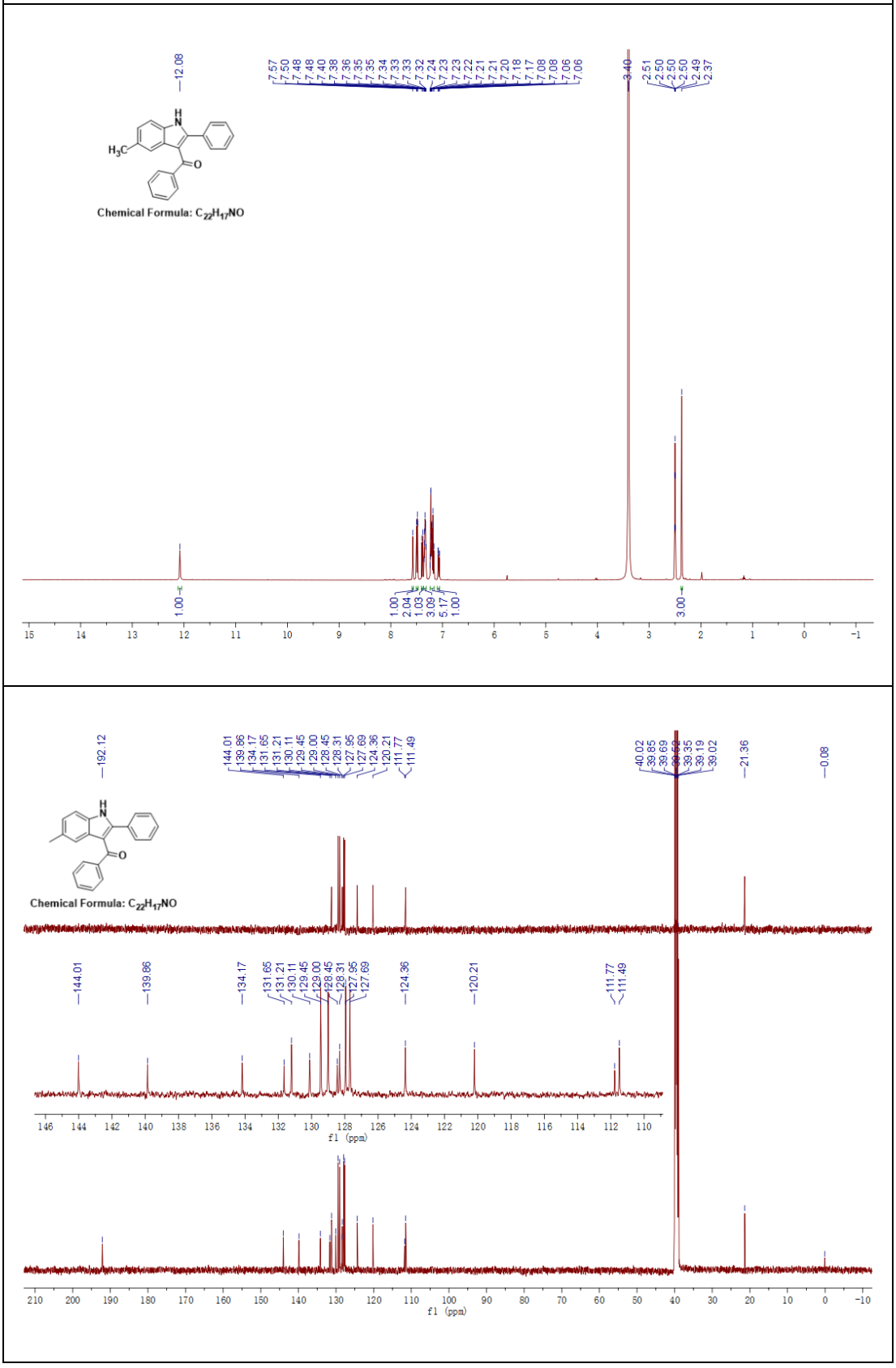


3-benzoyl-2-phenyl-1*H*-indole-5-carbonitrile (**3ea**)

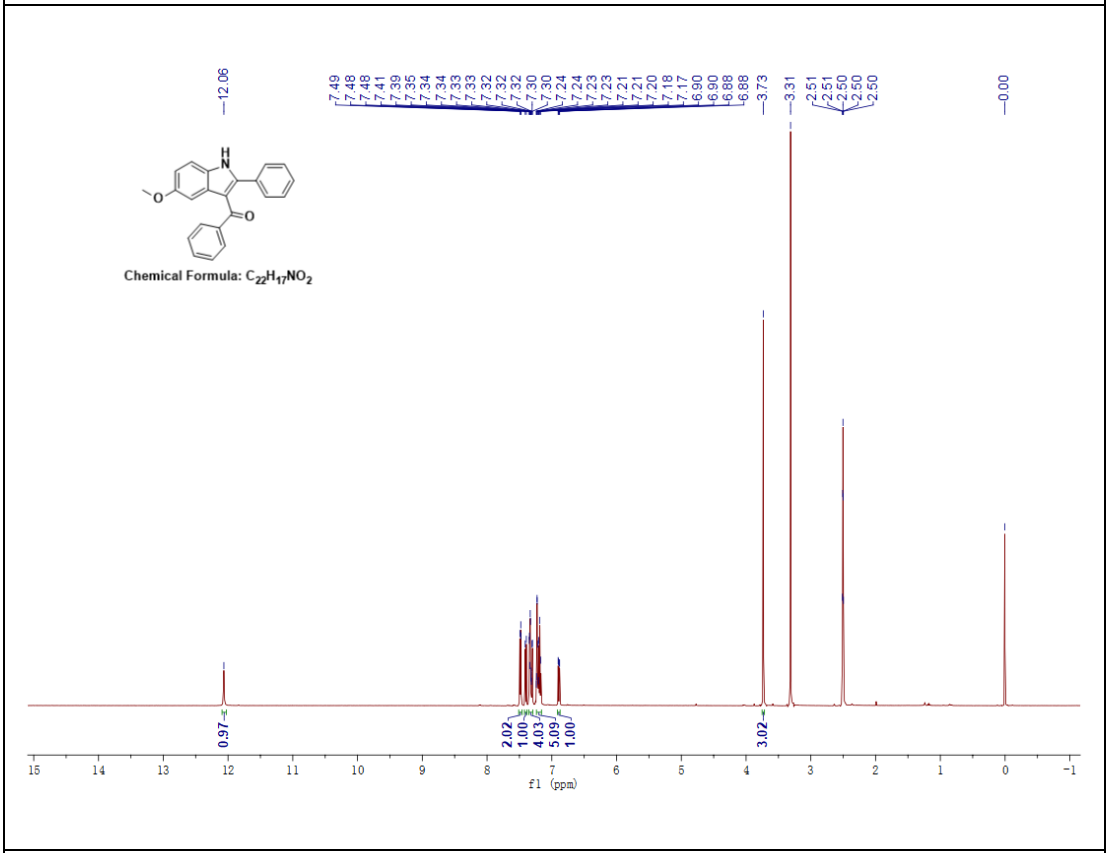


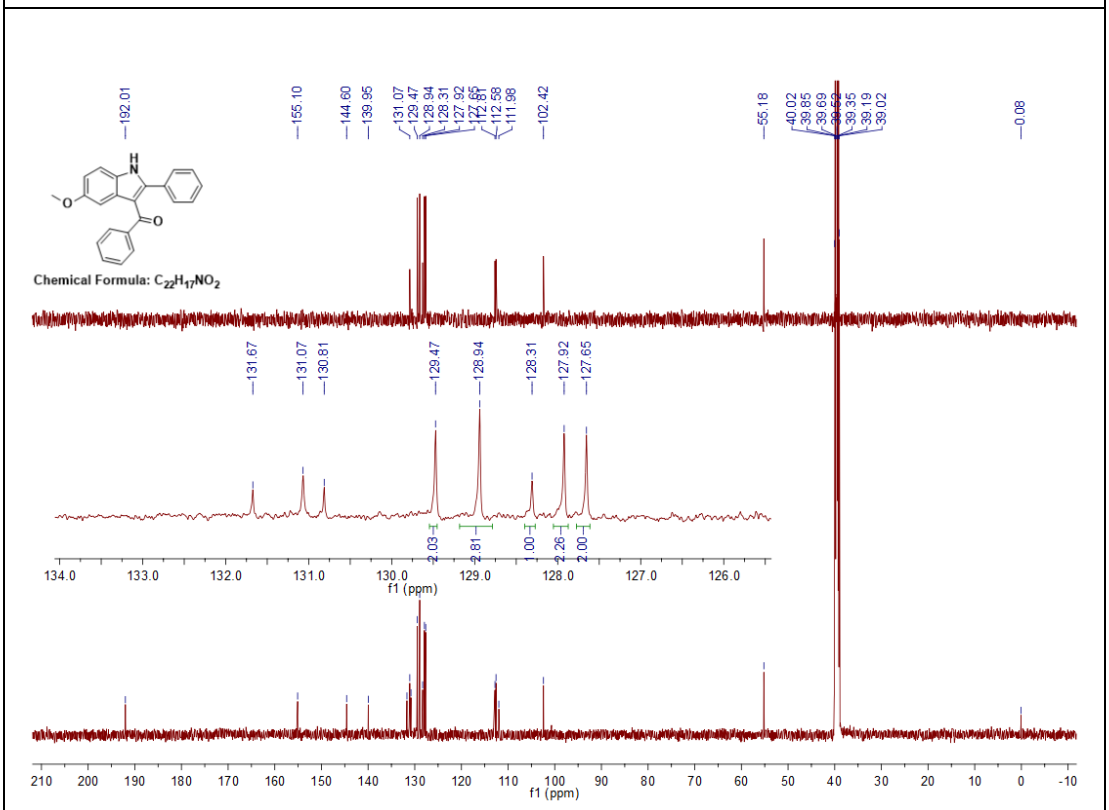


(5-methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3fa**)

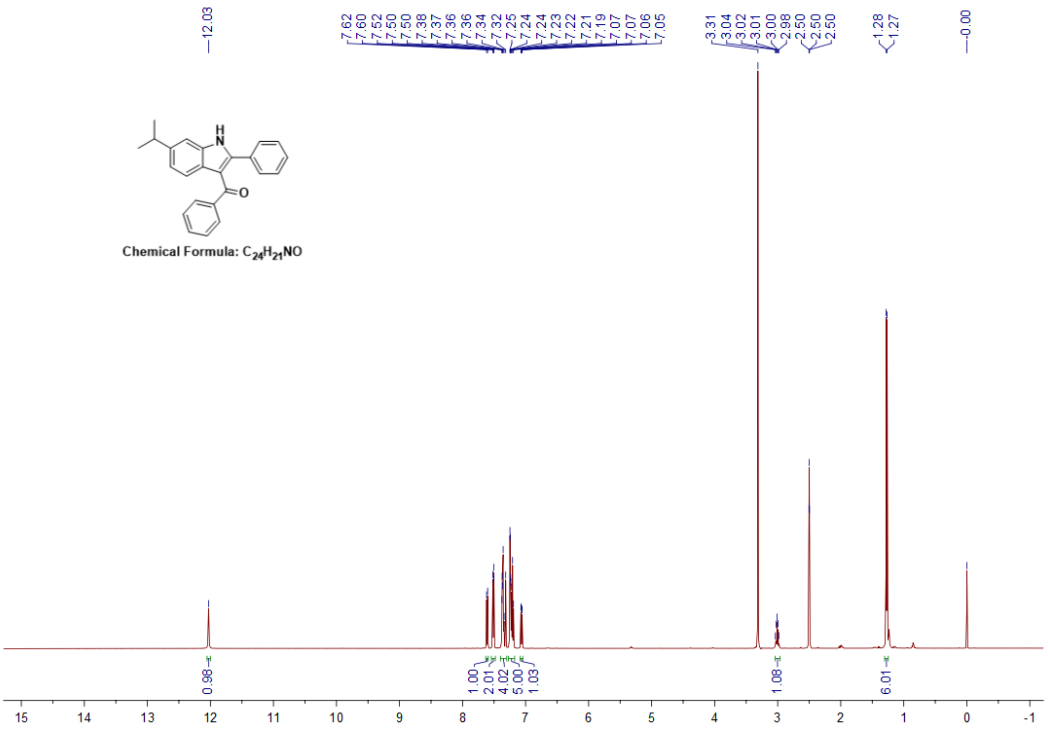


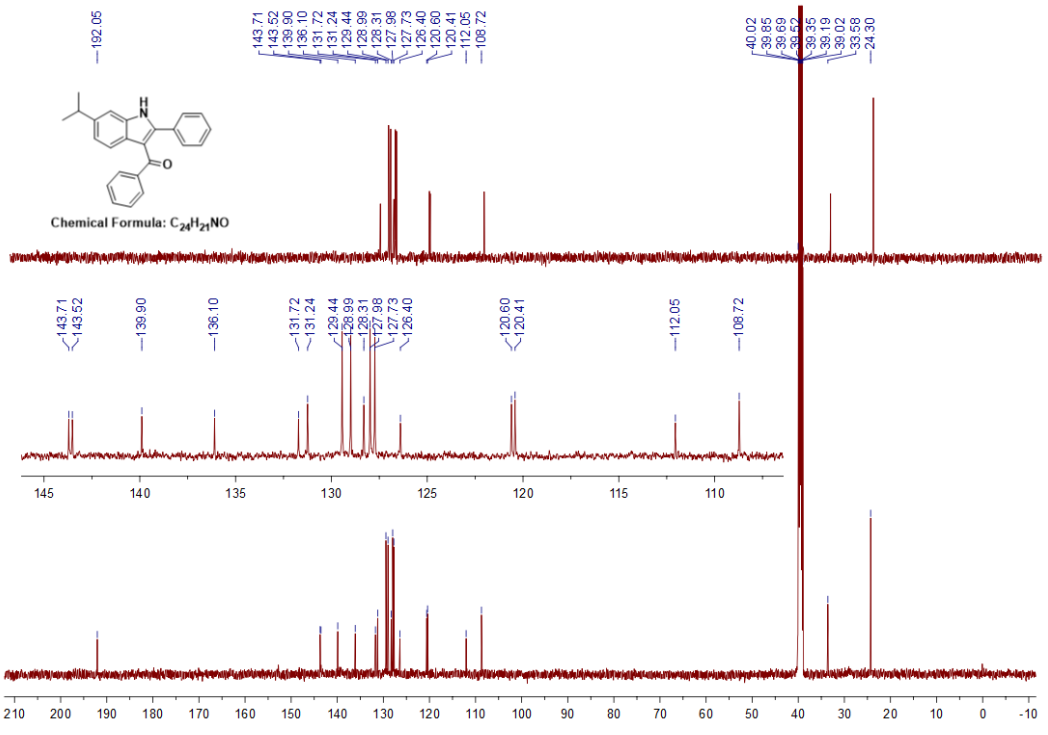
(5-methoxy-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ga**)



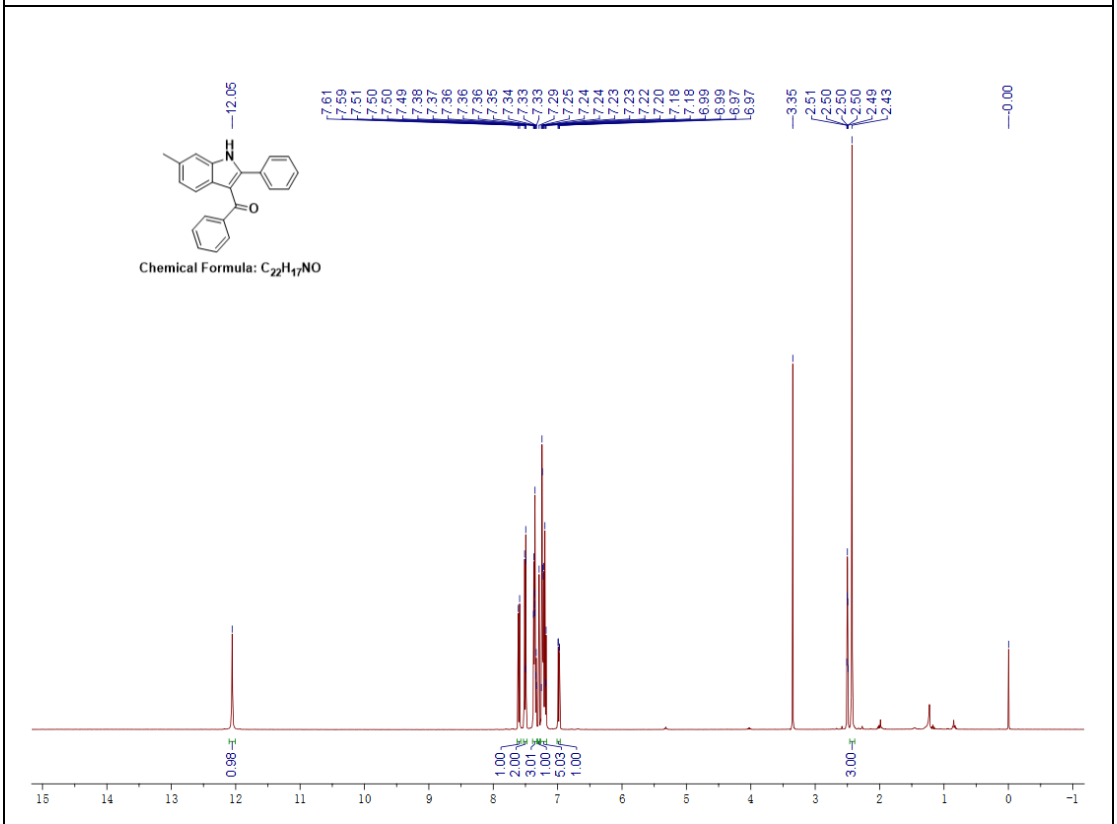


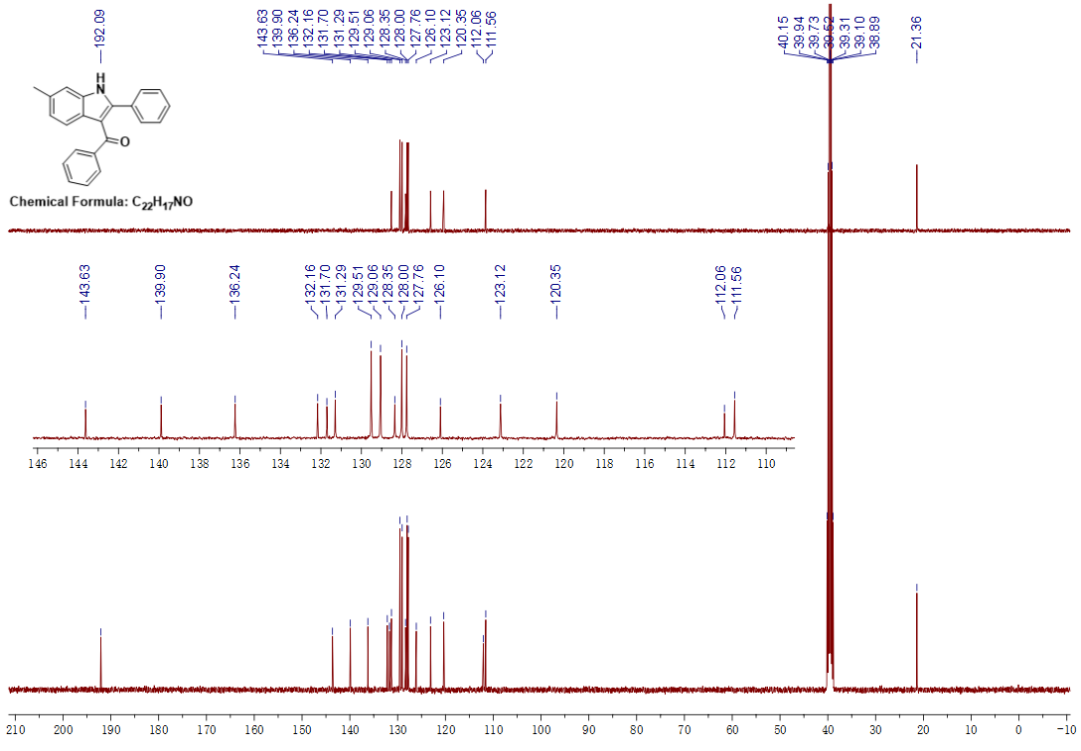
(6-isopropyl-2-phenyl-1H-indol-3-yl)(phenyl)methanone (**3ha**)



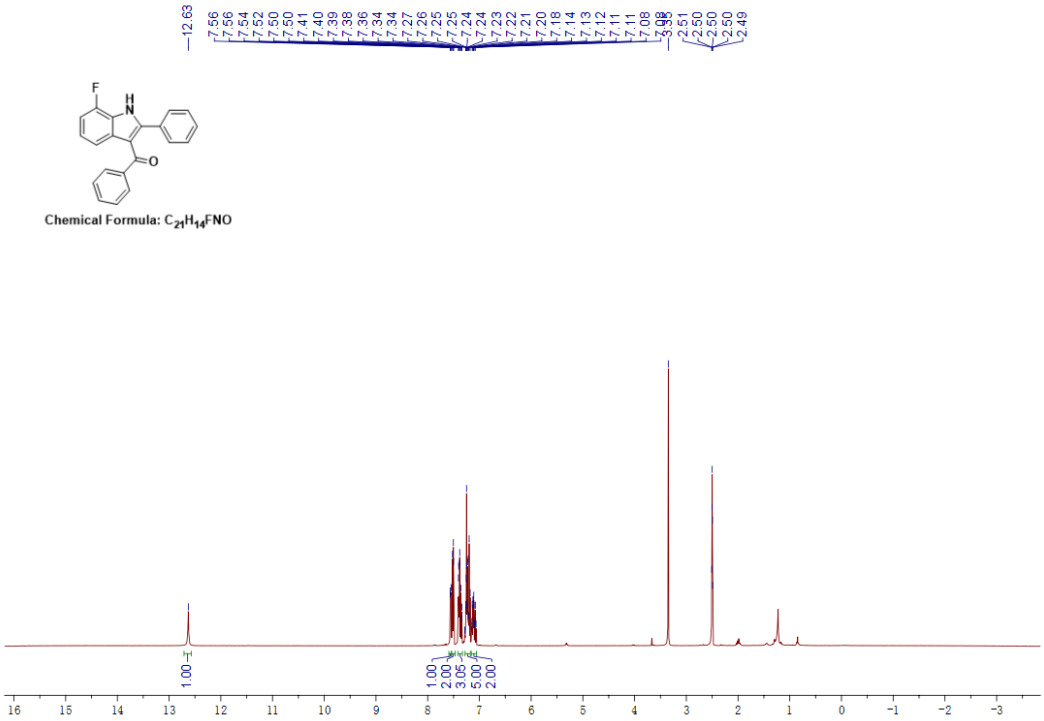


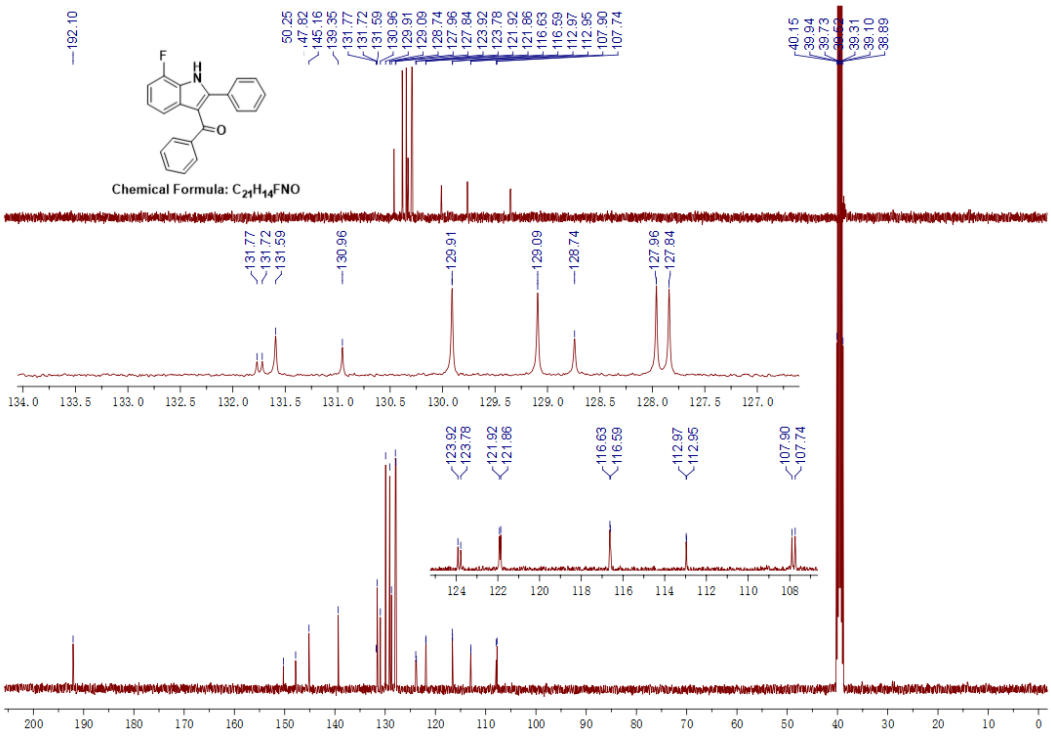
(6-methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ia**)



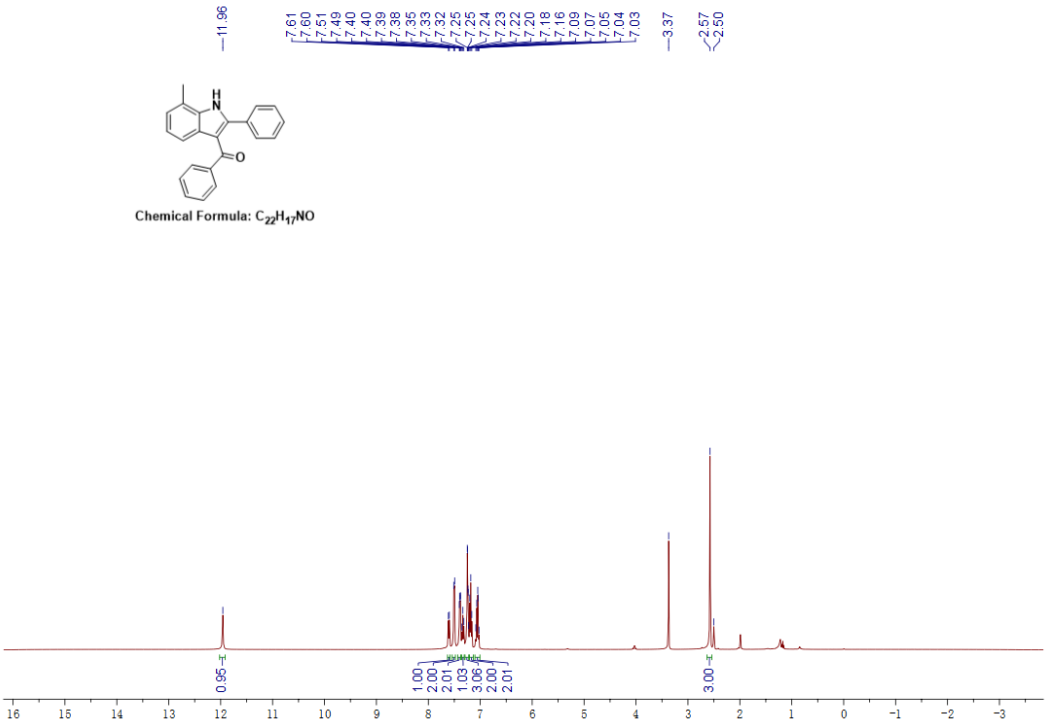


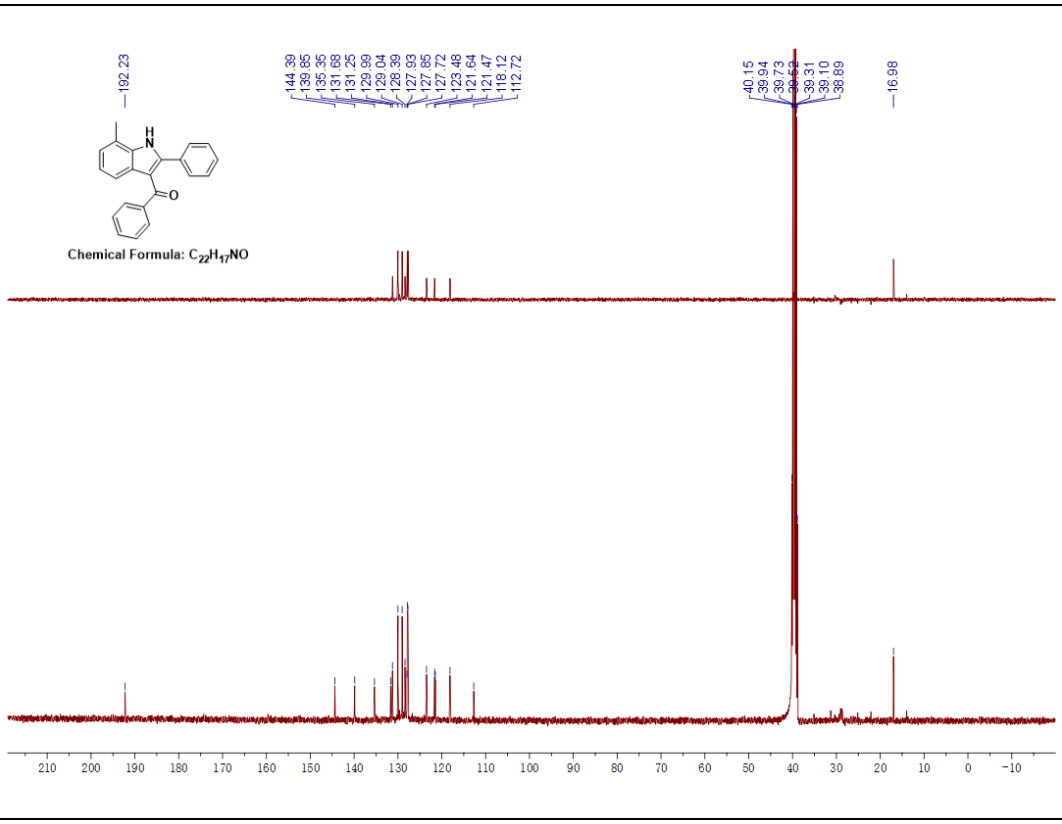
(7-Fluoro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ja**)



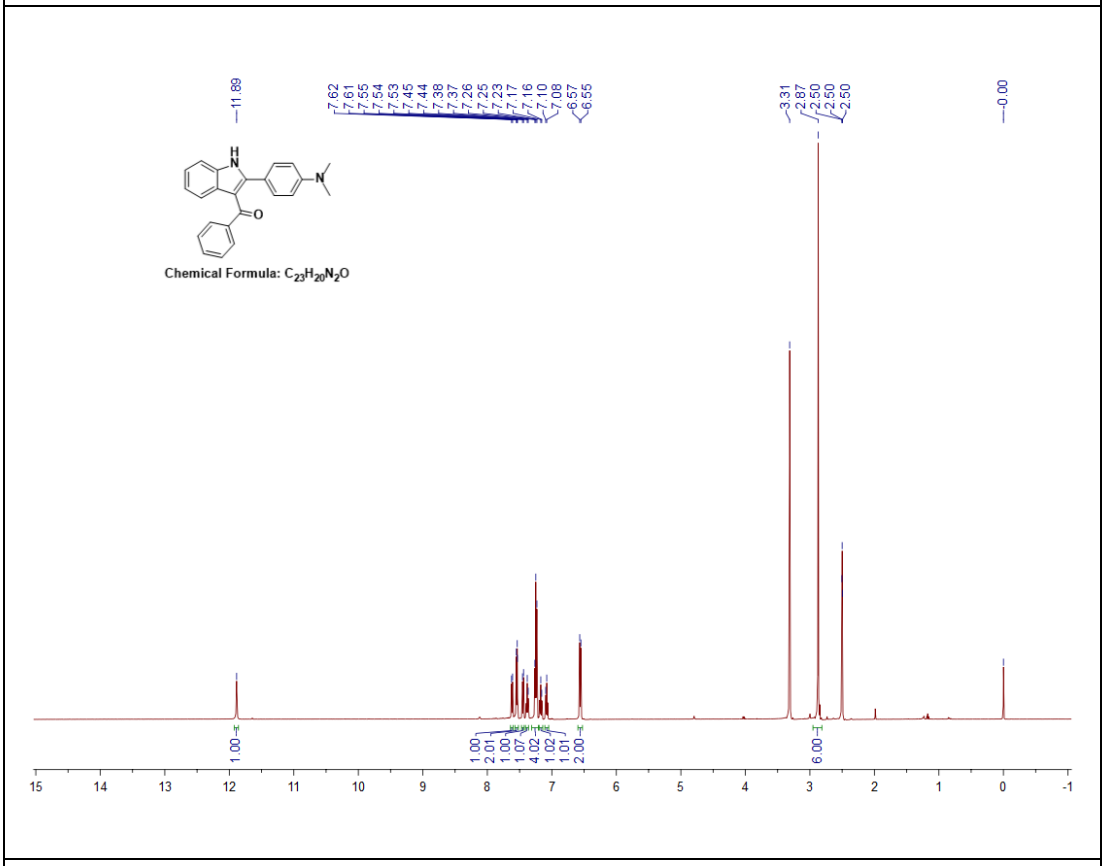


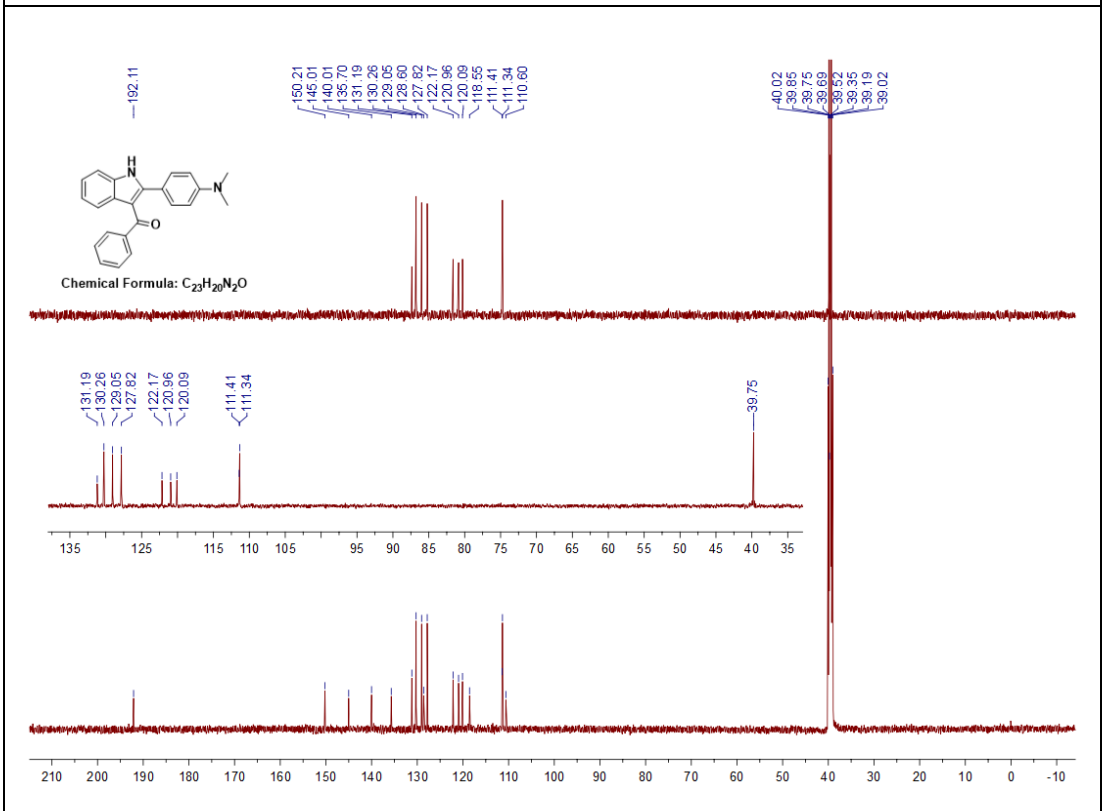
(7-Methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ka**)



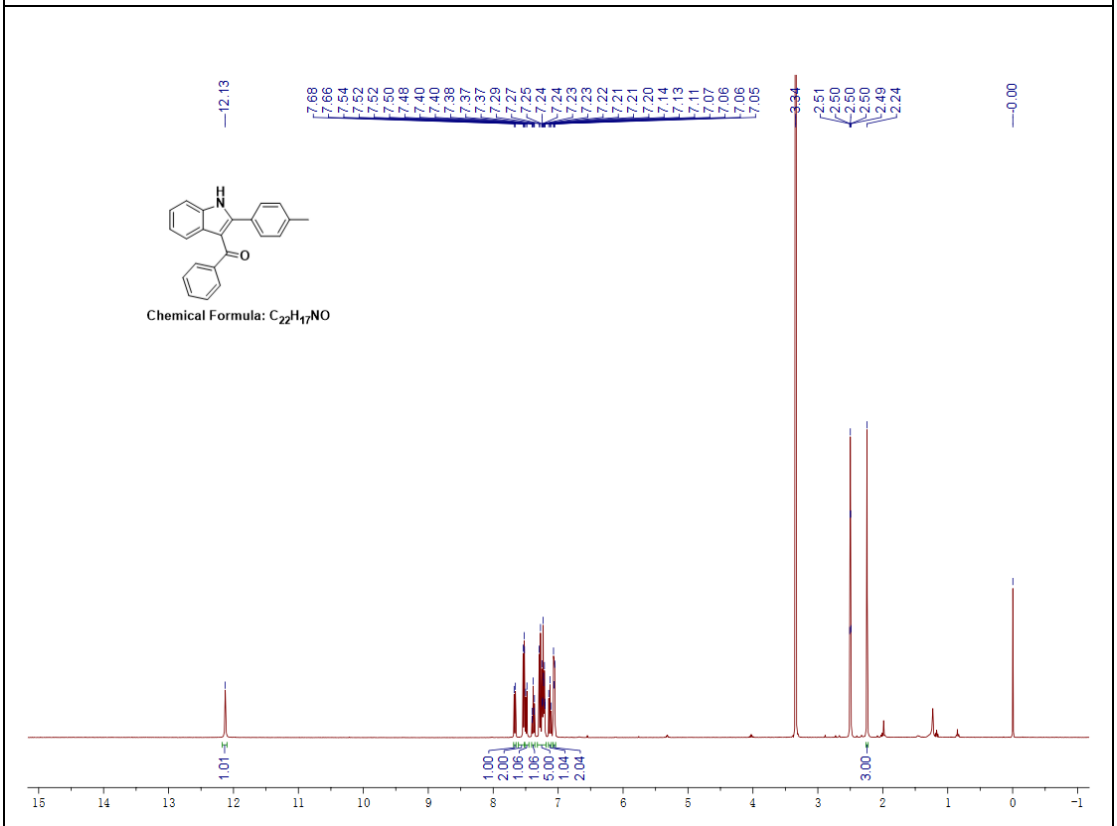


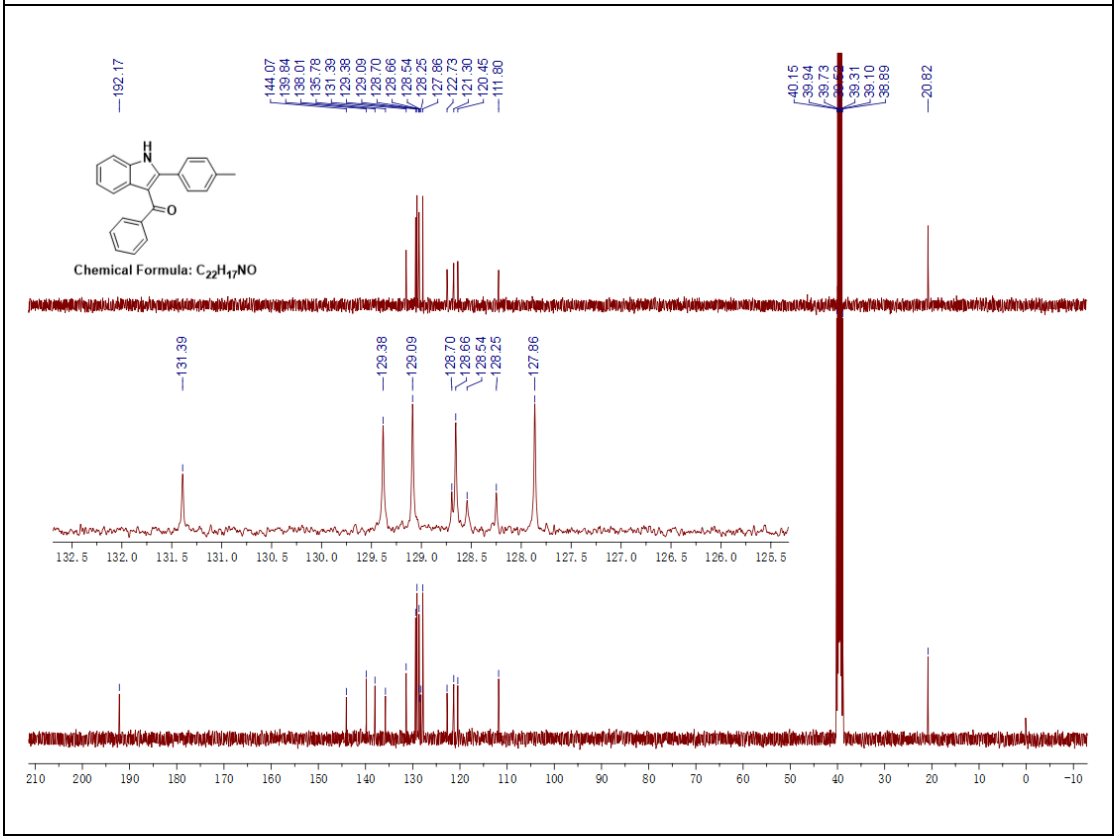
(2-(4-(dimethylamino)phenyl)-1*H*-indol-3-yl)(phenyl)methanone (**3la**)



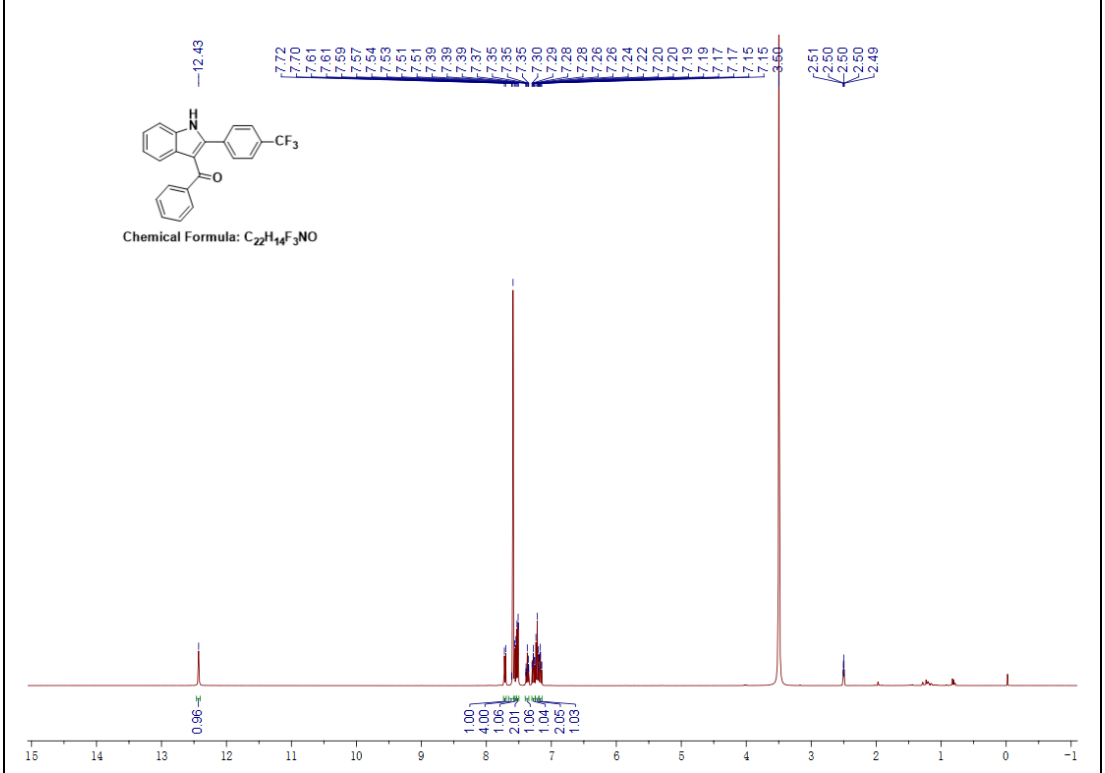


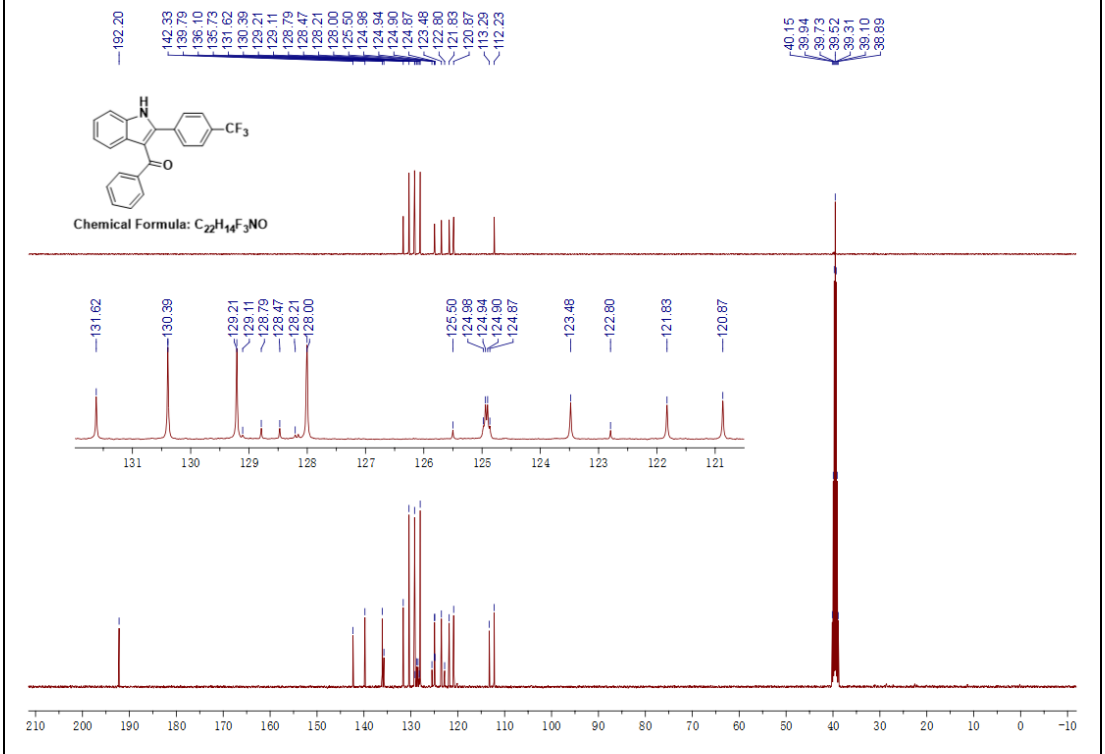
phenyl(2-(p-tolyl)-1*H*-indol-3-yl)methanone (**3ma**)



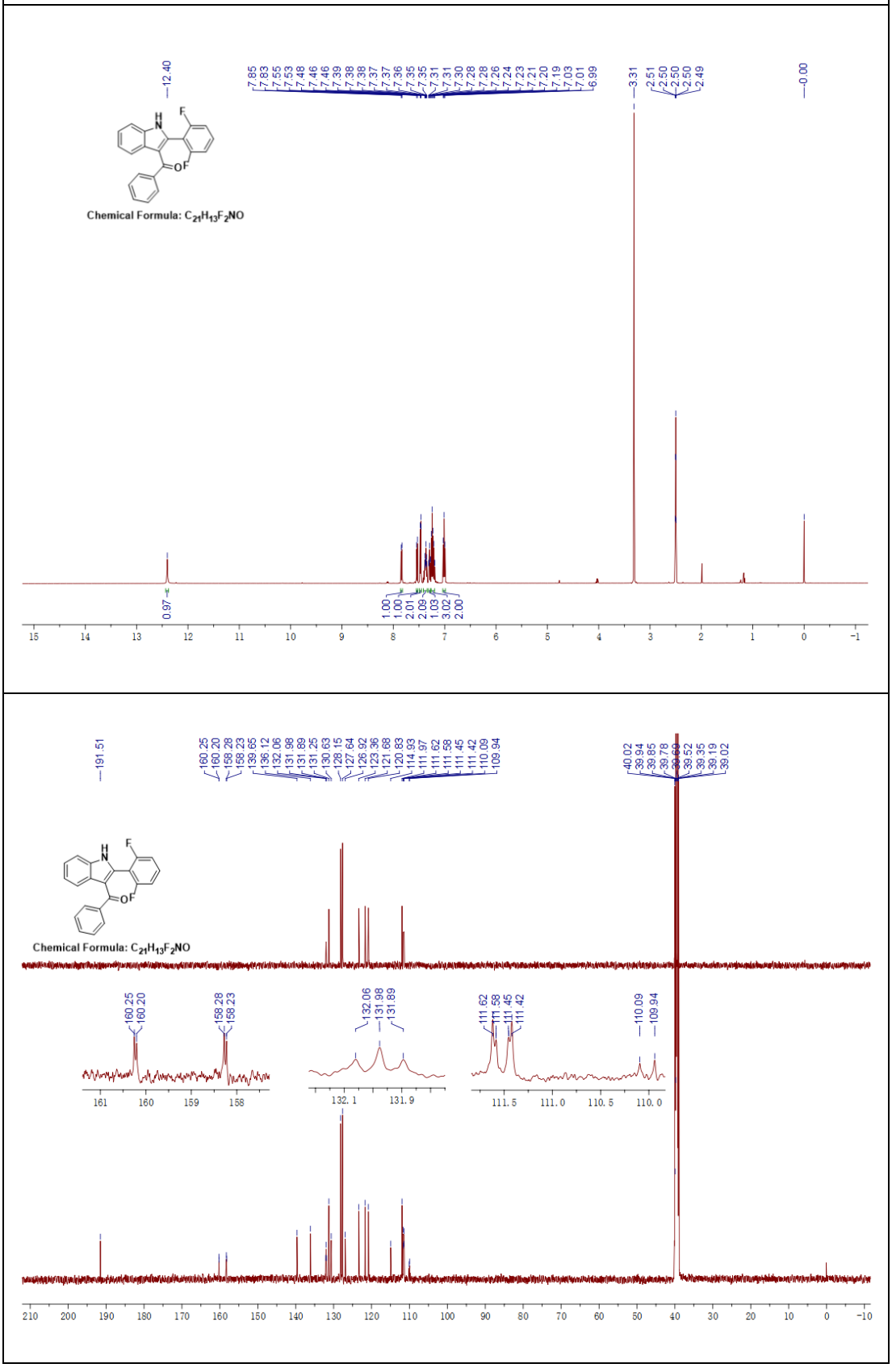


phenyl(2-(4-(trifluoromethyl)phenyl)-1*H*-indol-3-yl)methanone (**3na**)

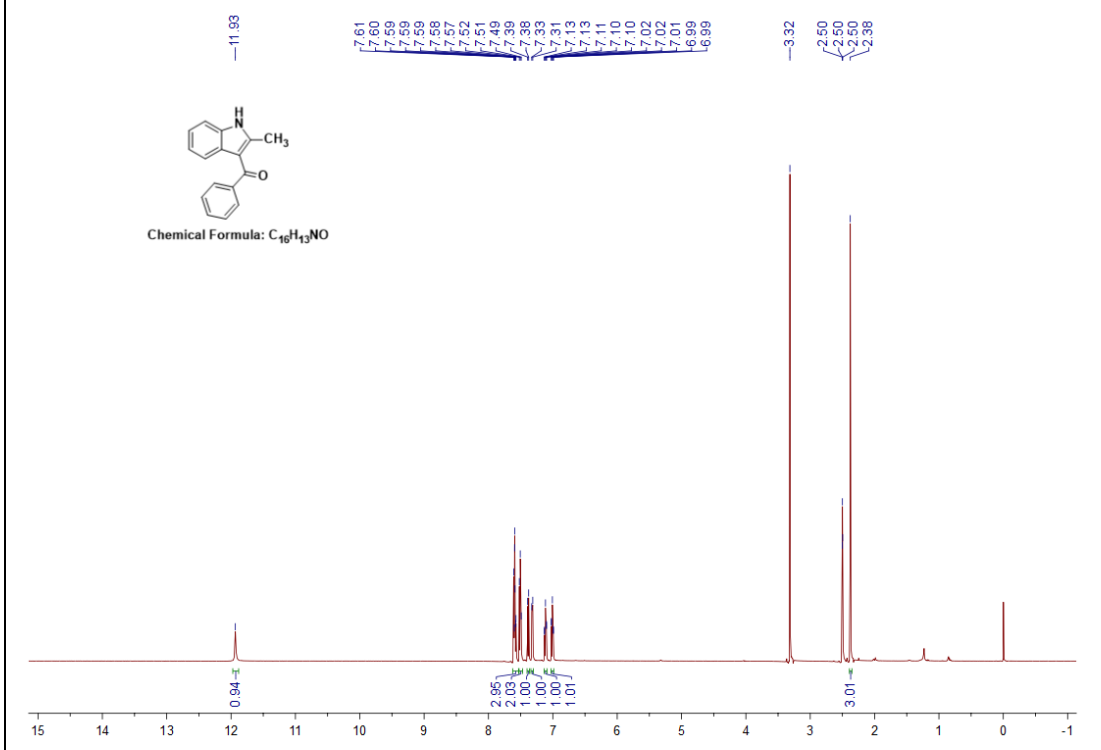


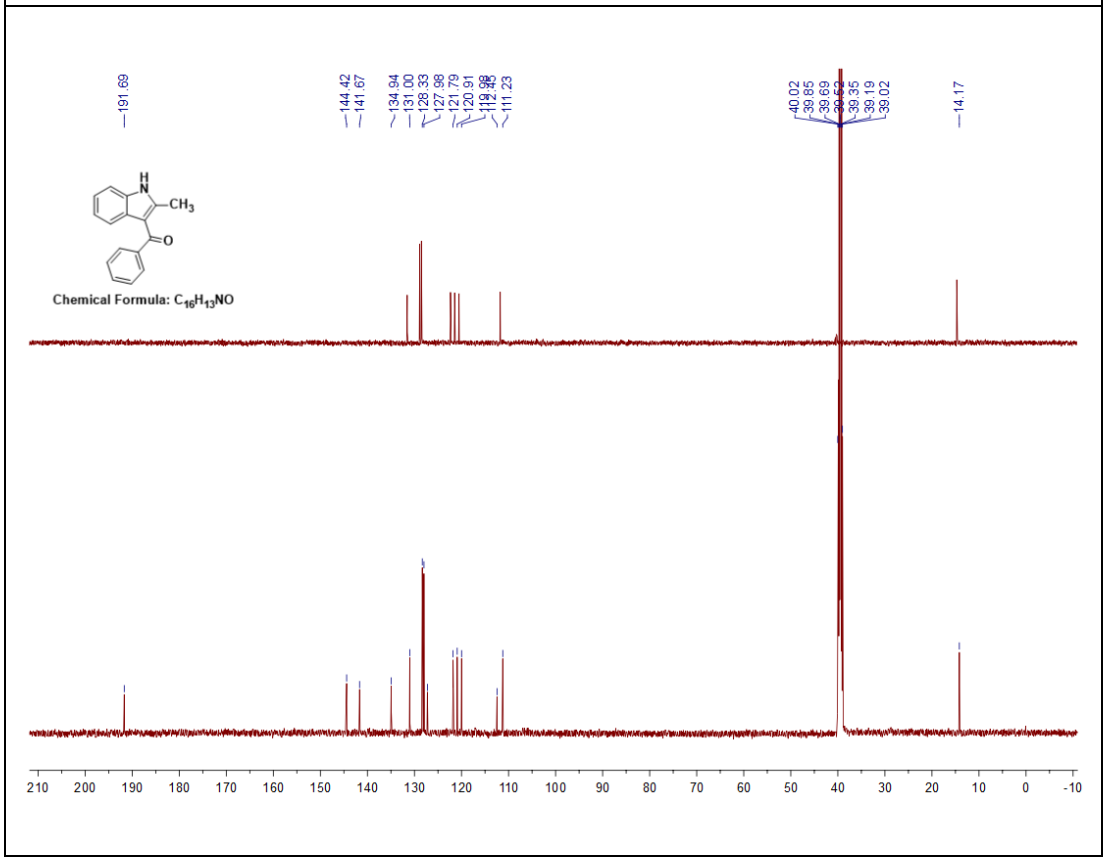


(2-(2,6-difluorophenyl)-1*H*-indol-3-yl)(phenyl)methanone (**3oa**)

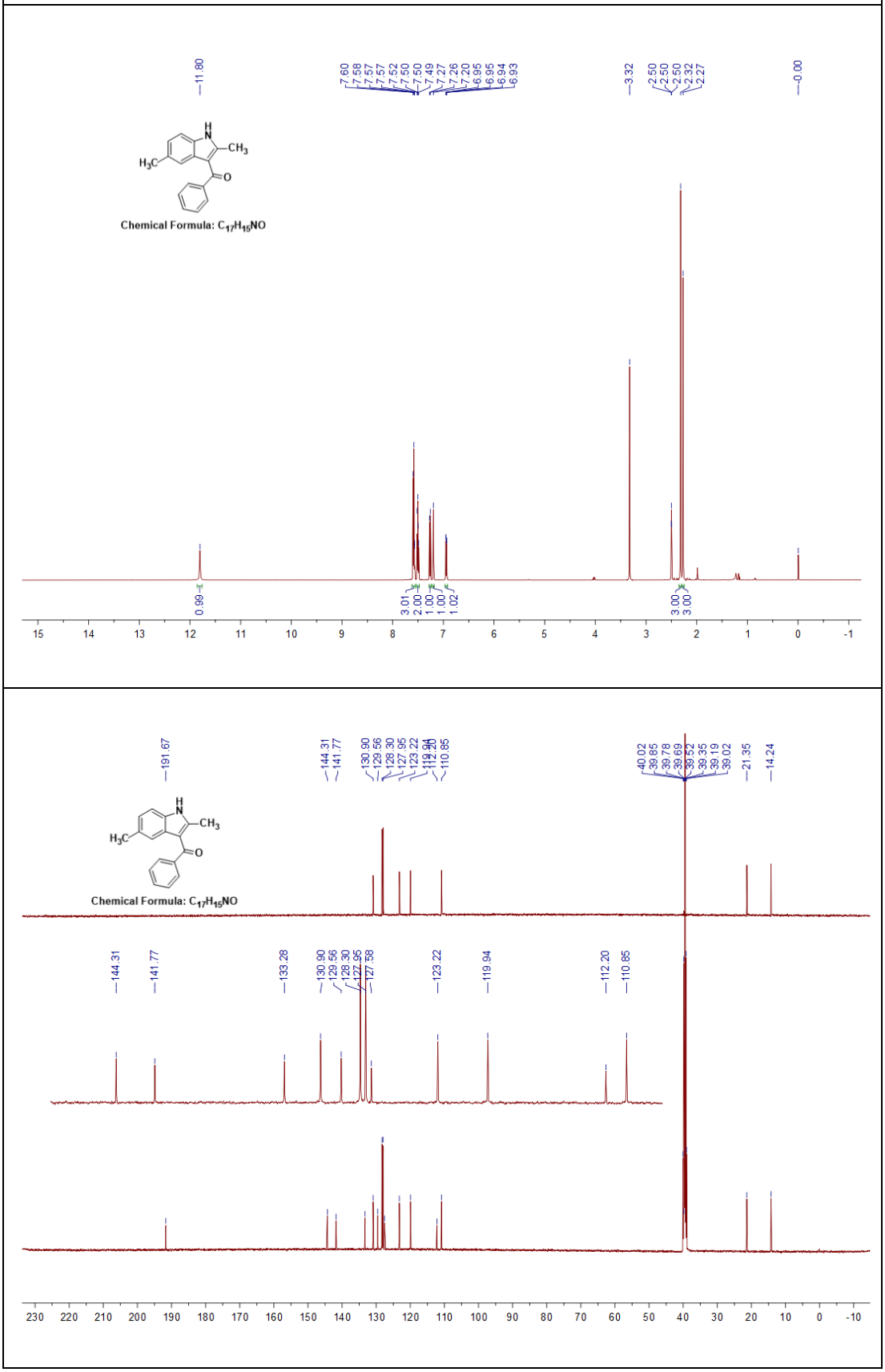


(2-methyl-1*H*-indol-3-yl)(phenyl)methanone (**3pa**)

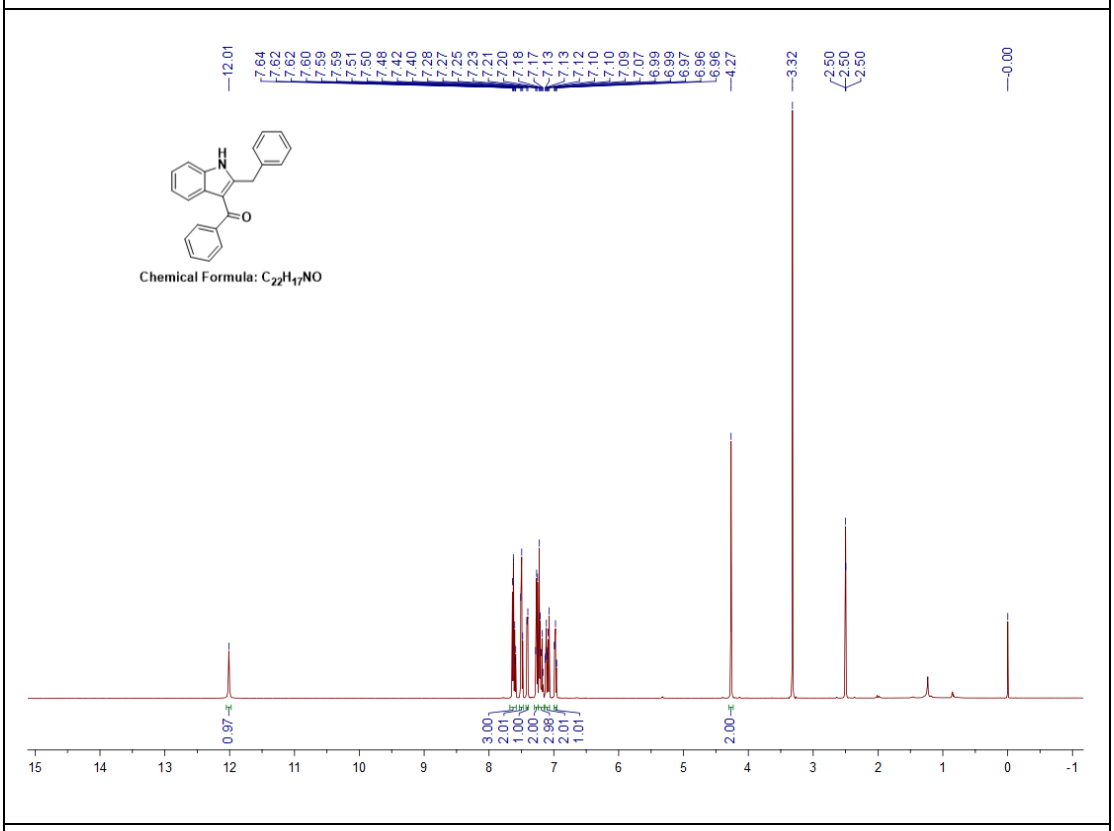


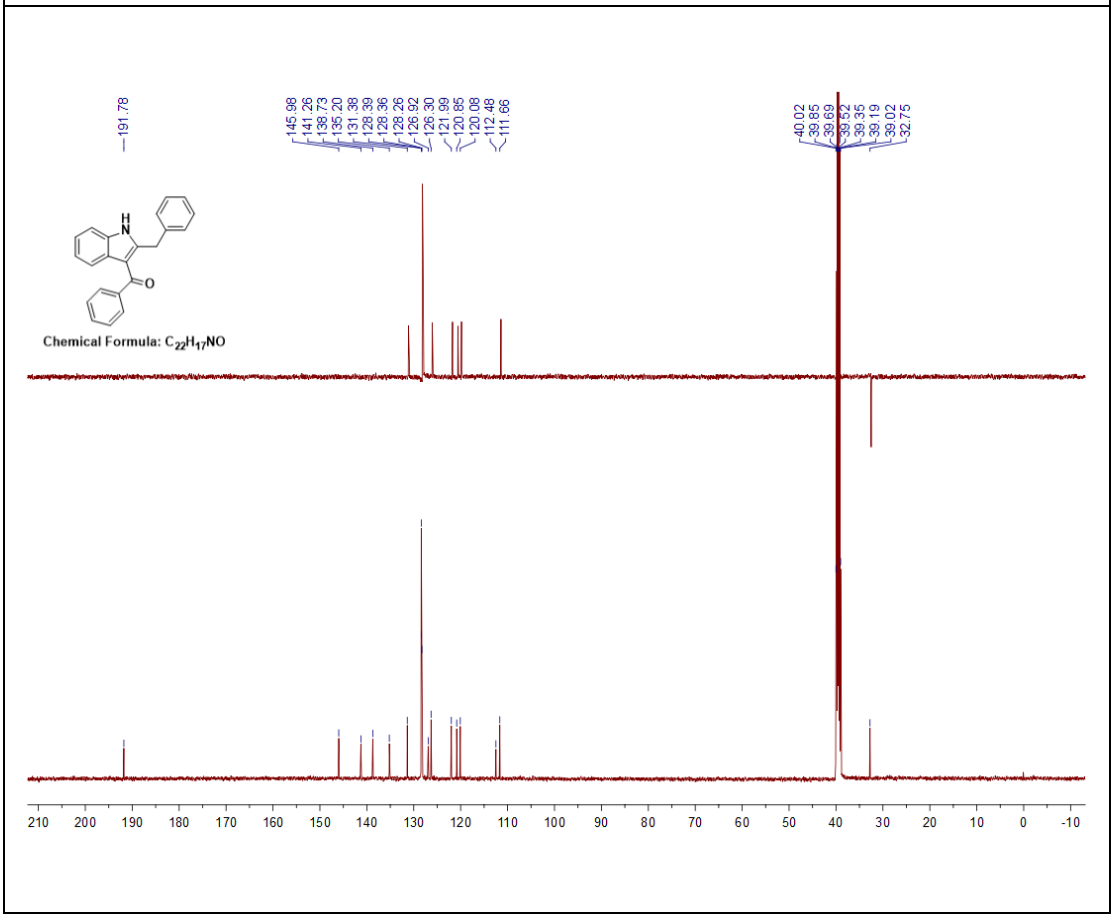


(2,5-dimethyl-1*H*-indol-3-yl)(phenyl)methanone (**3qa**)

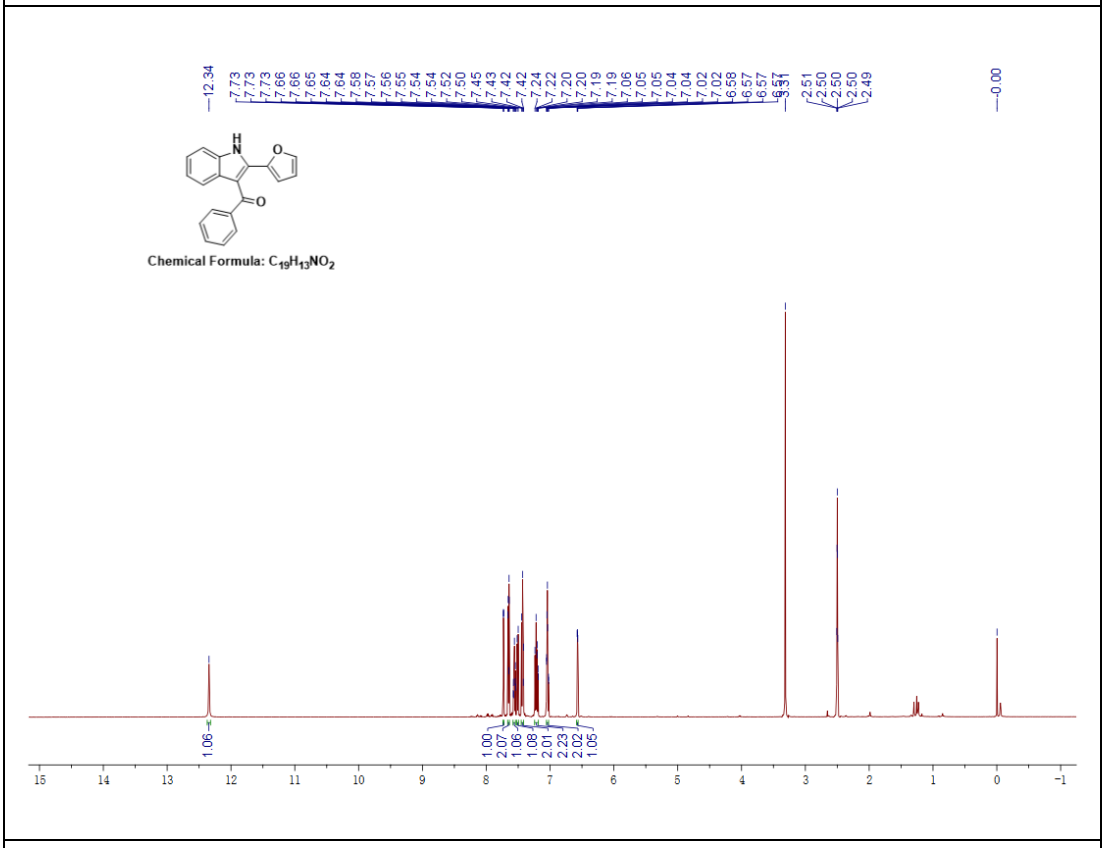


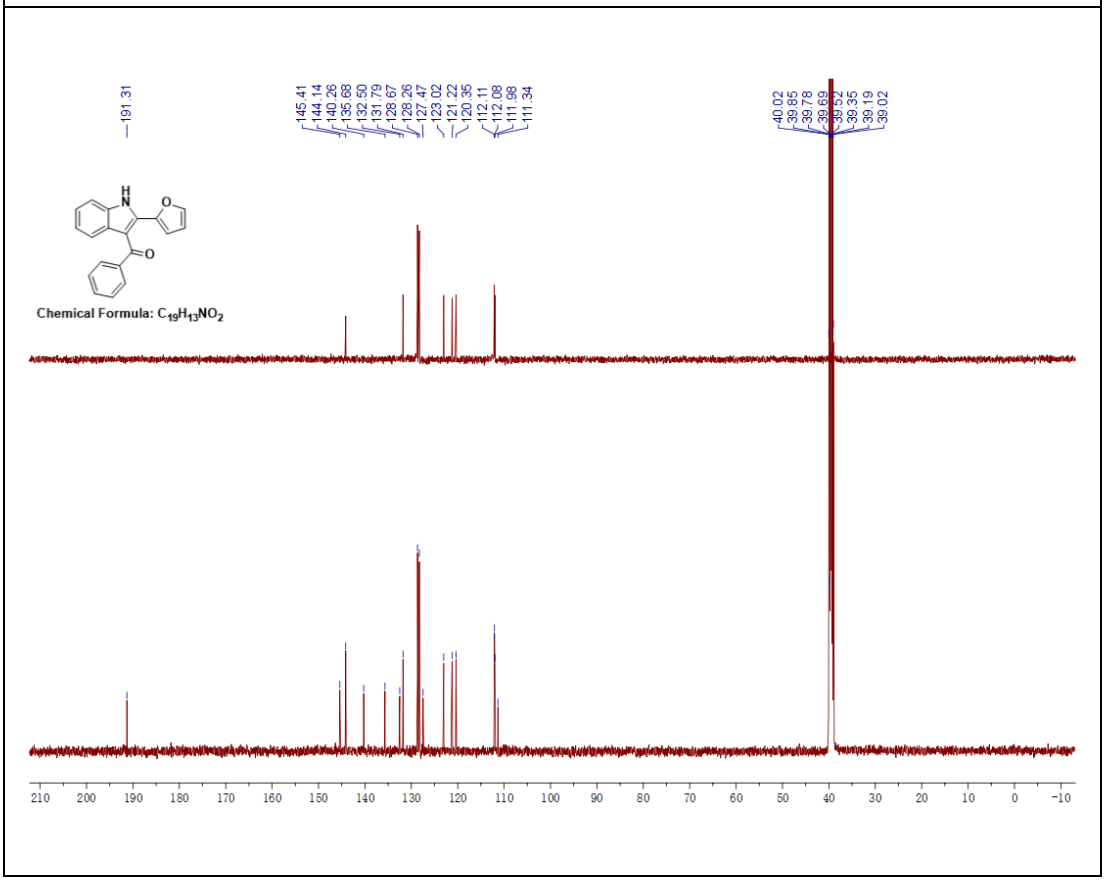
(2-benzyl-1*H*-indol-3-yl)(phenyl)methanone (**3ra**)



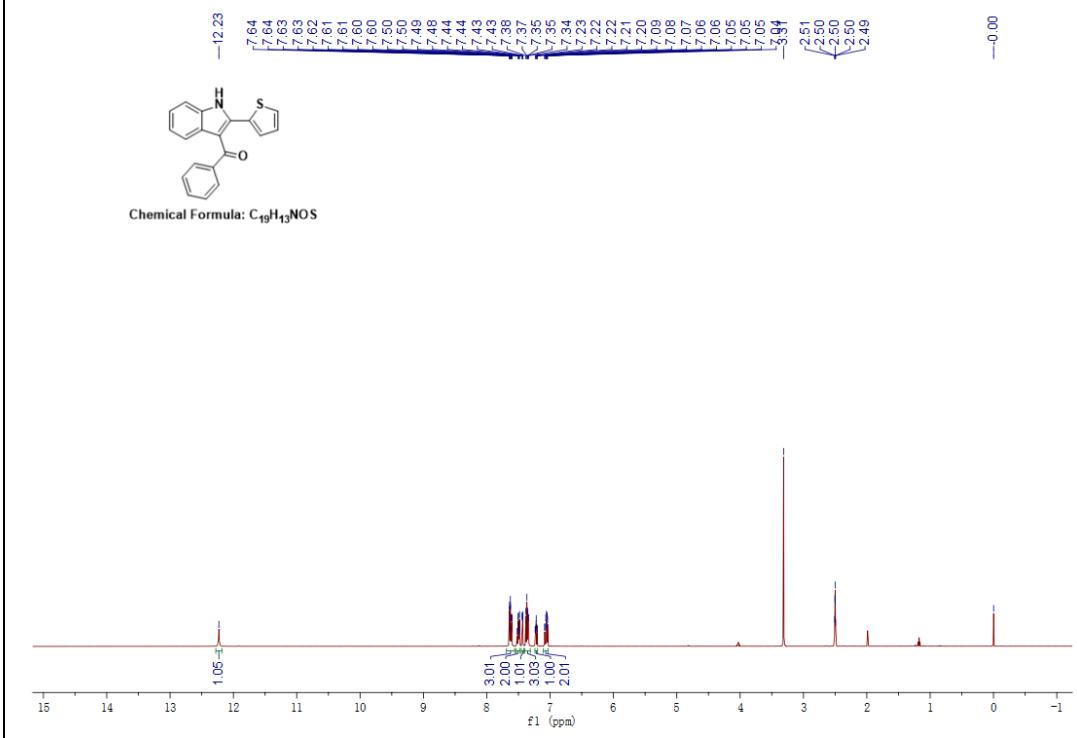


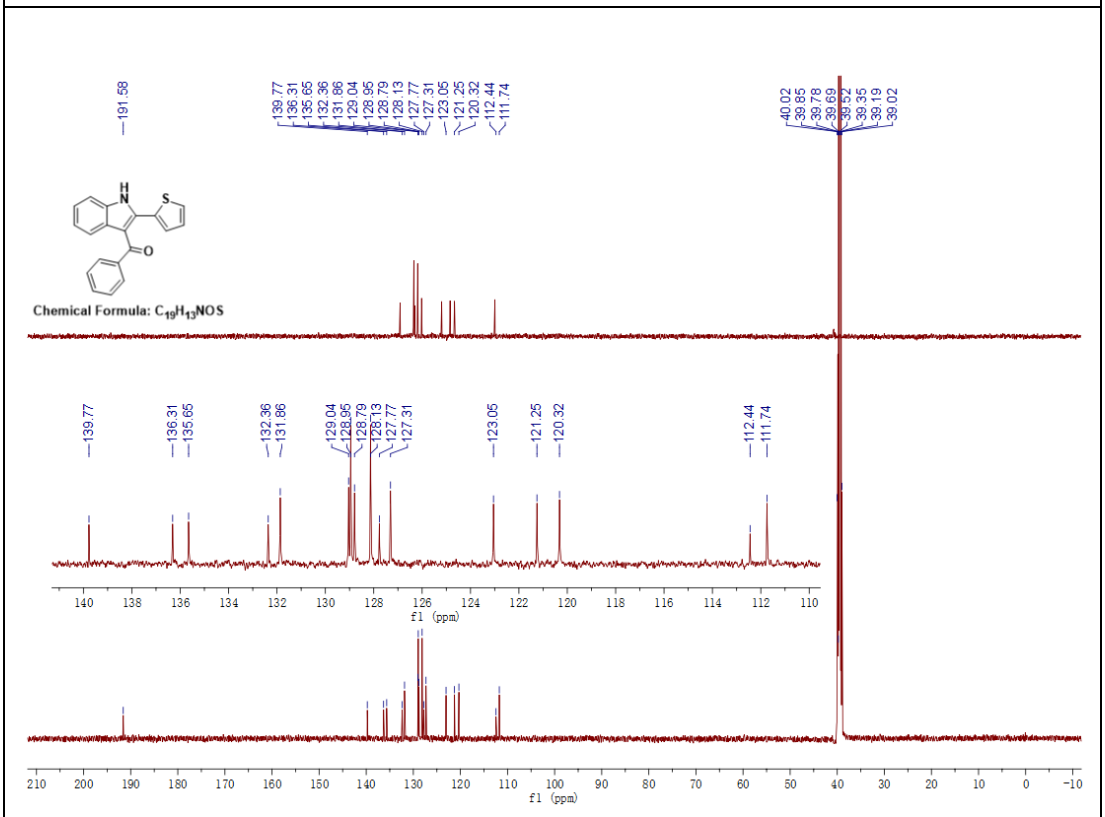
(2-(furan-2-yl)-1*H*-indol-3-yl)(phenyl)methanone (**3sa**)



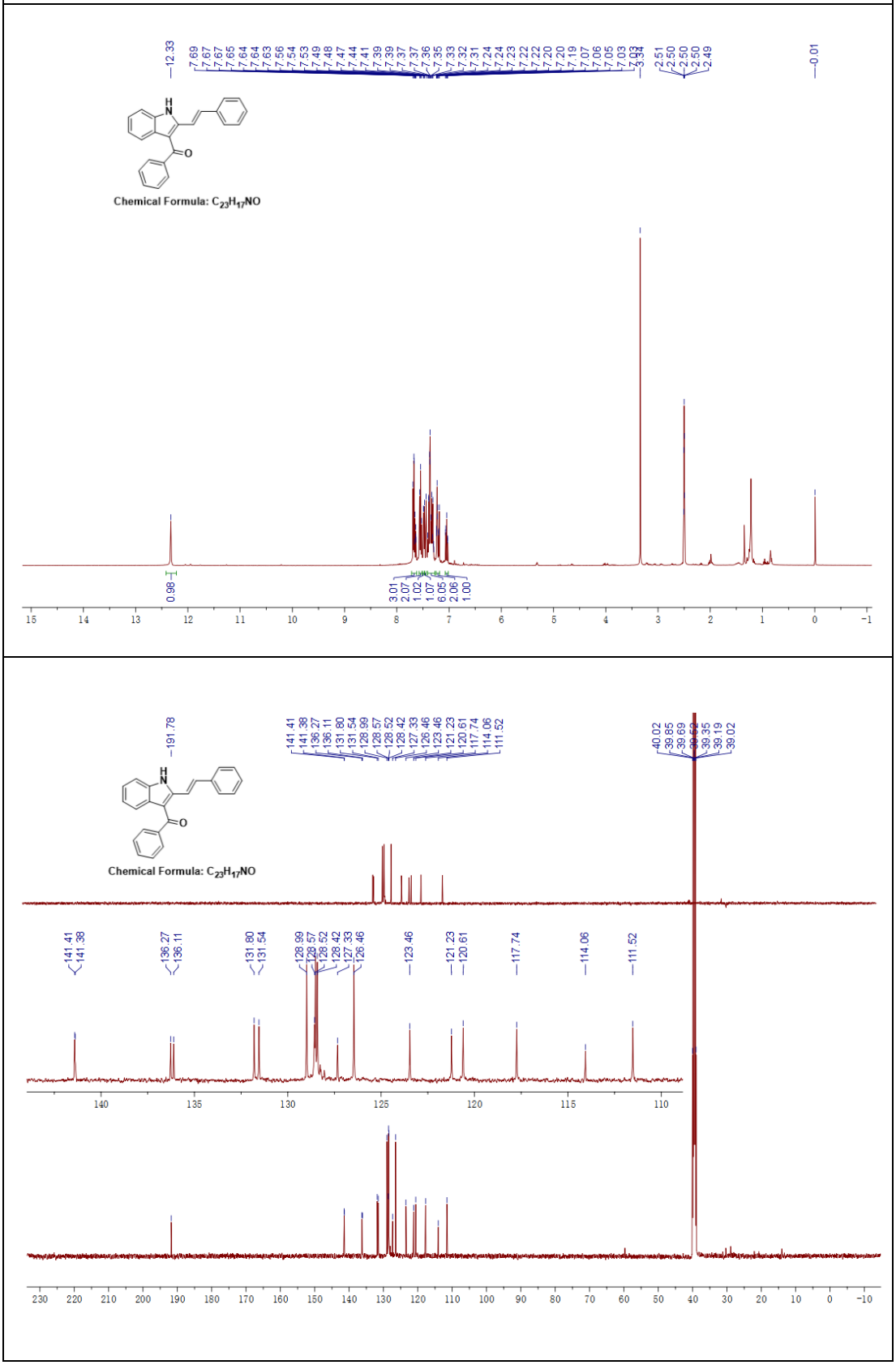


phenyl(2-(thiophen-2-yl)-1*H*-indol-3-yl)methanone (**3ta**)

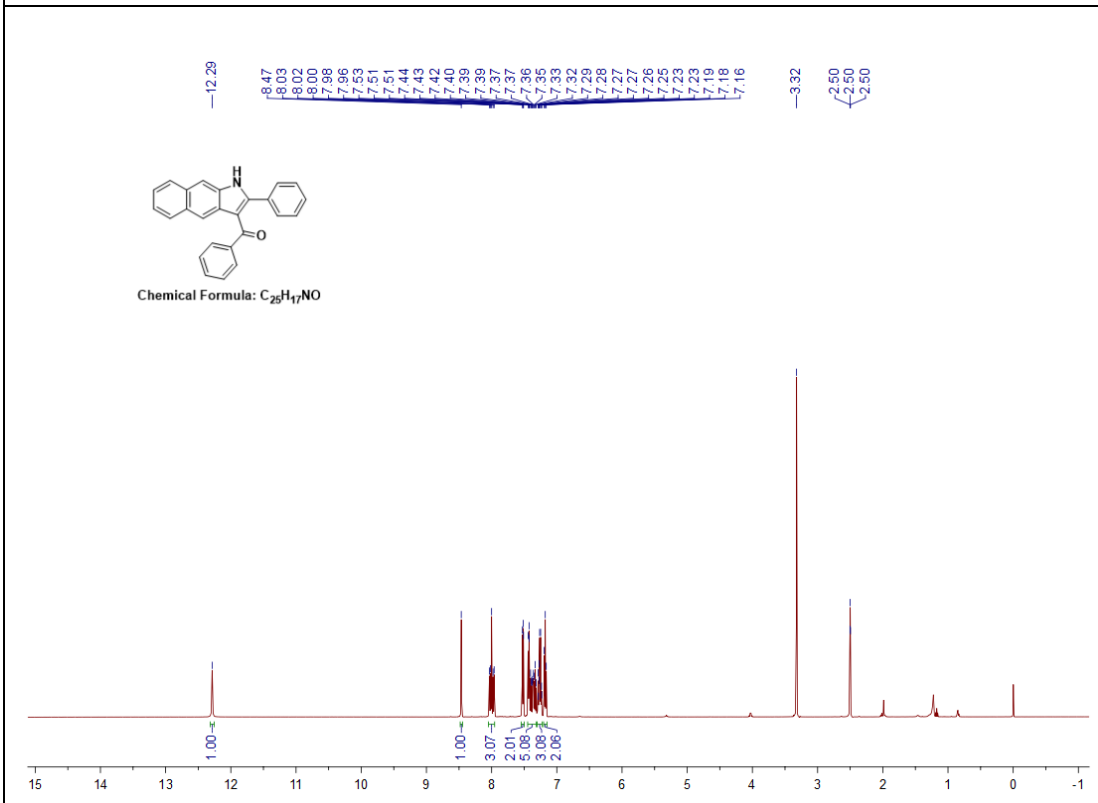


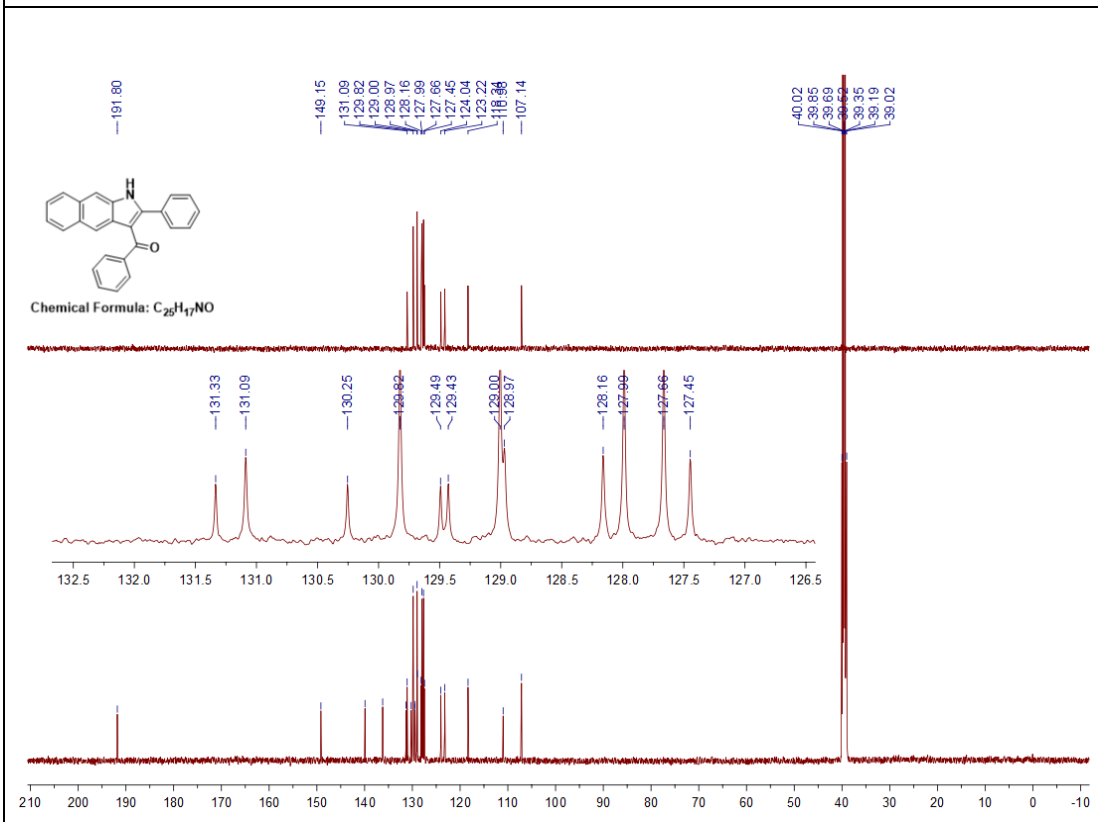


(*E*)-phenyl(2-styryl-1*H*-indol-3-yl)methanone (**3ua**)

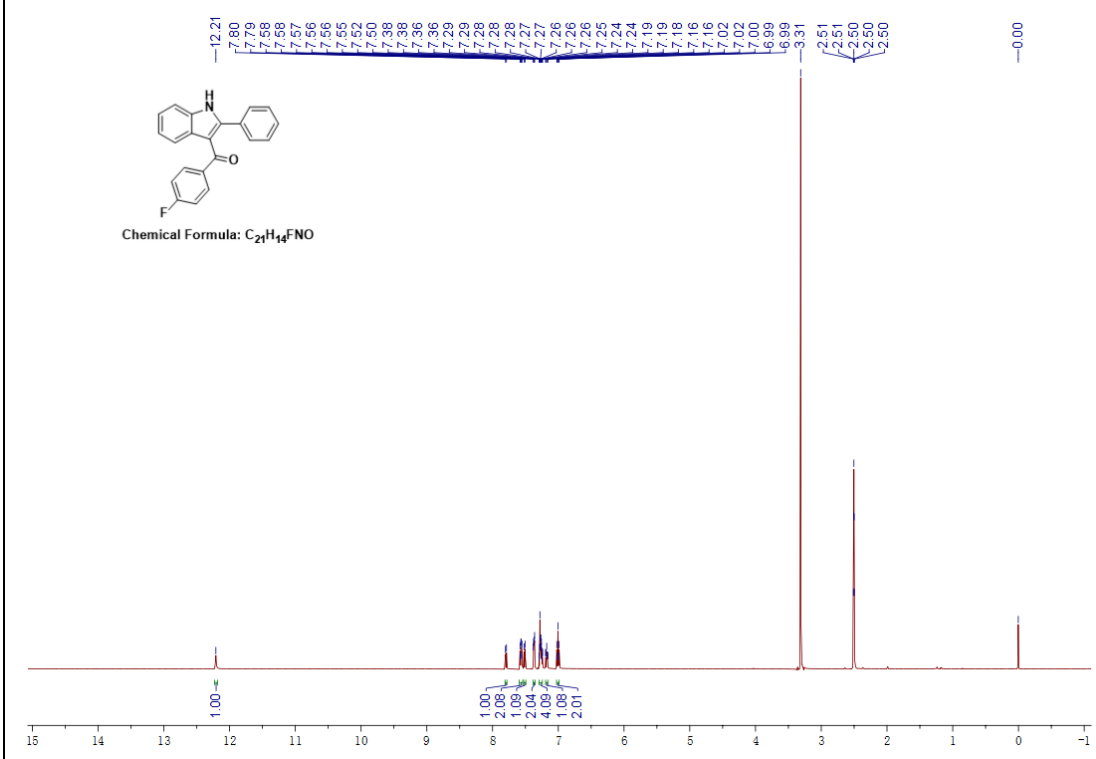


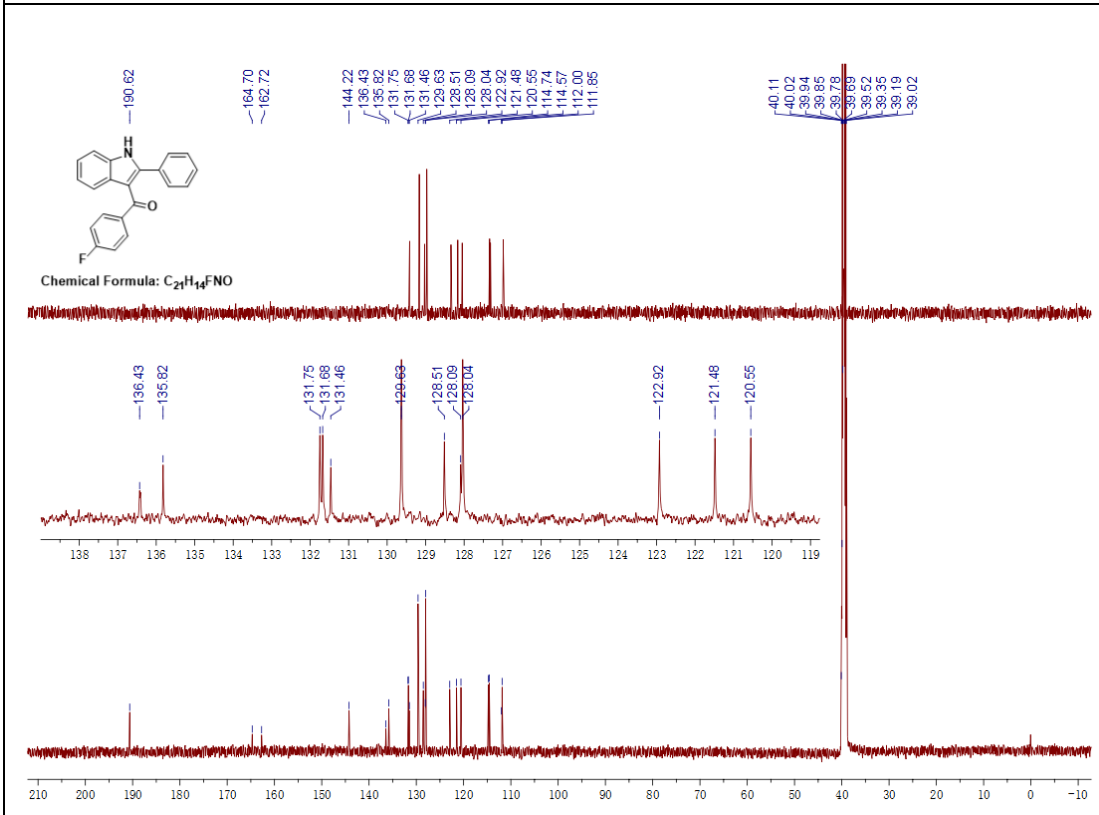
phenyl(2-phenyl-1*H*-benzo[f]indol-3-yl)methanone (**3va**)



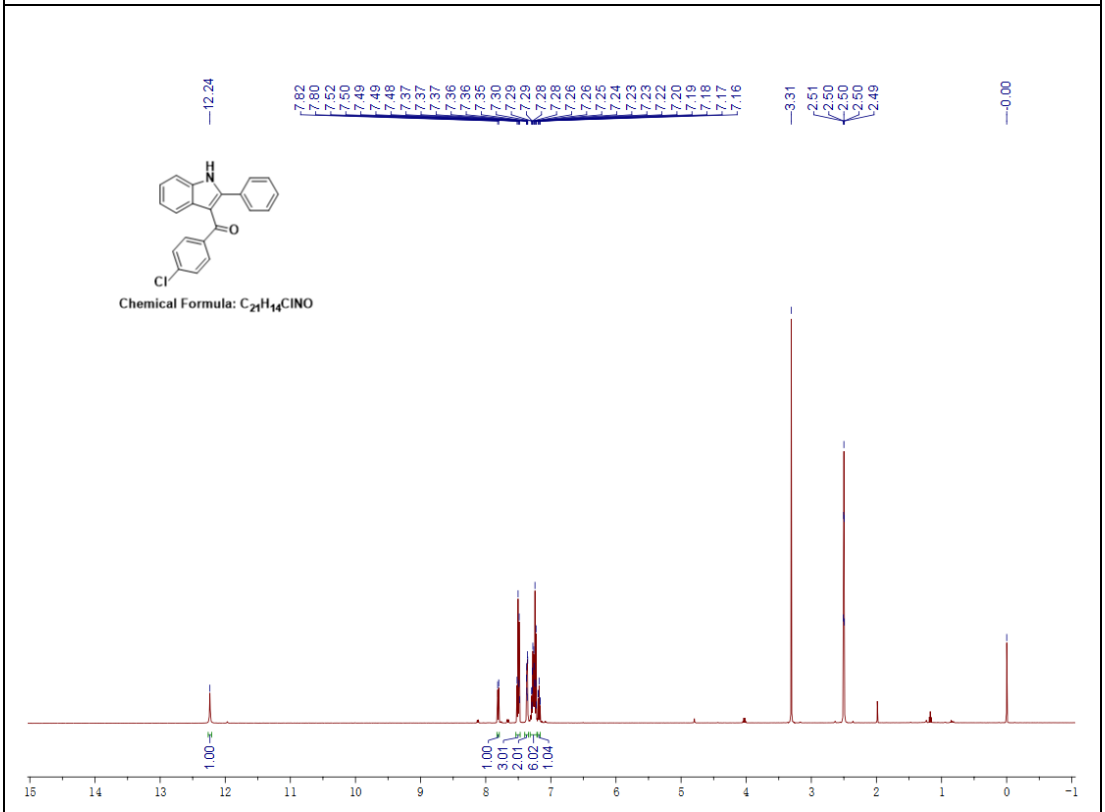


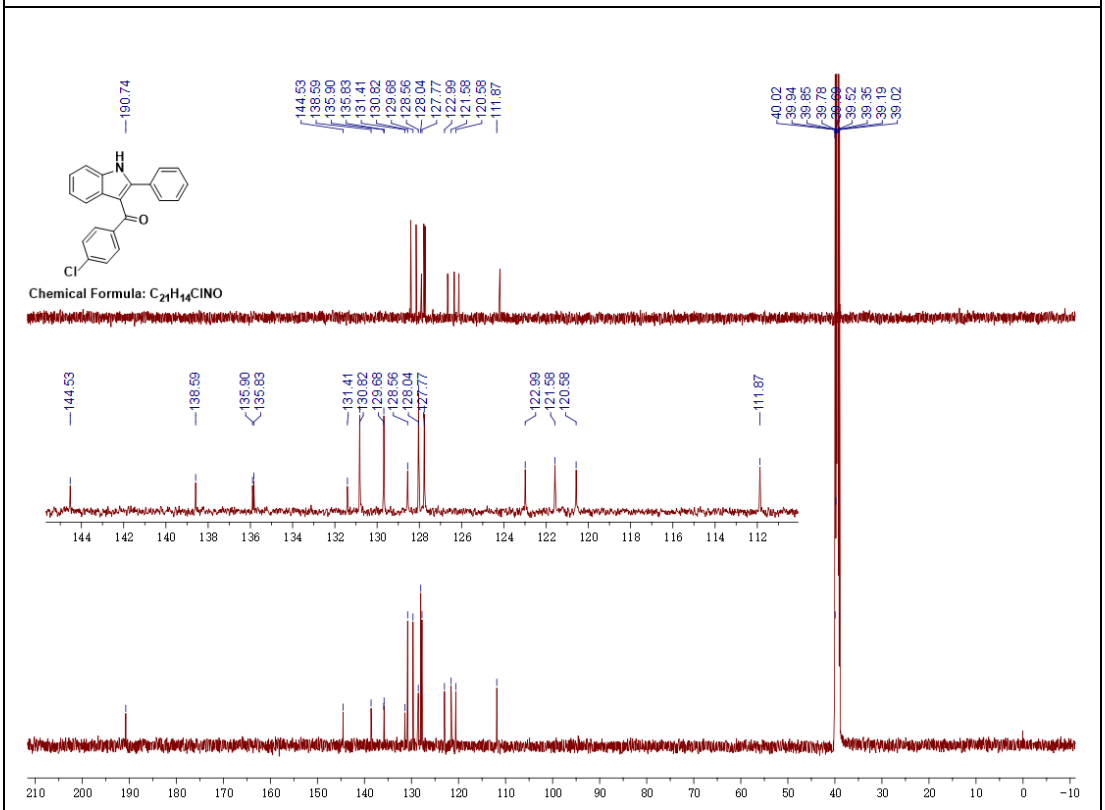
(4-fluorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ab**)



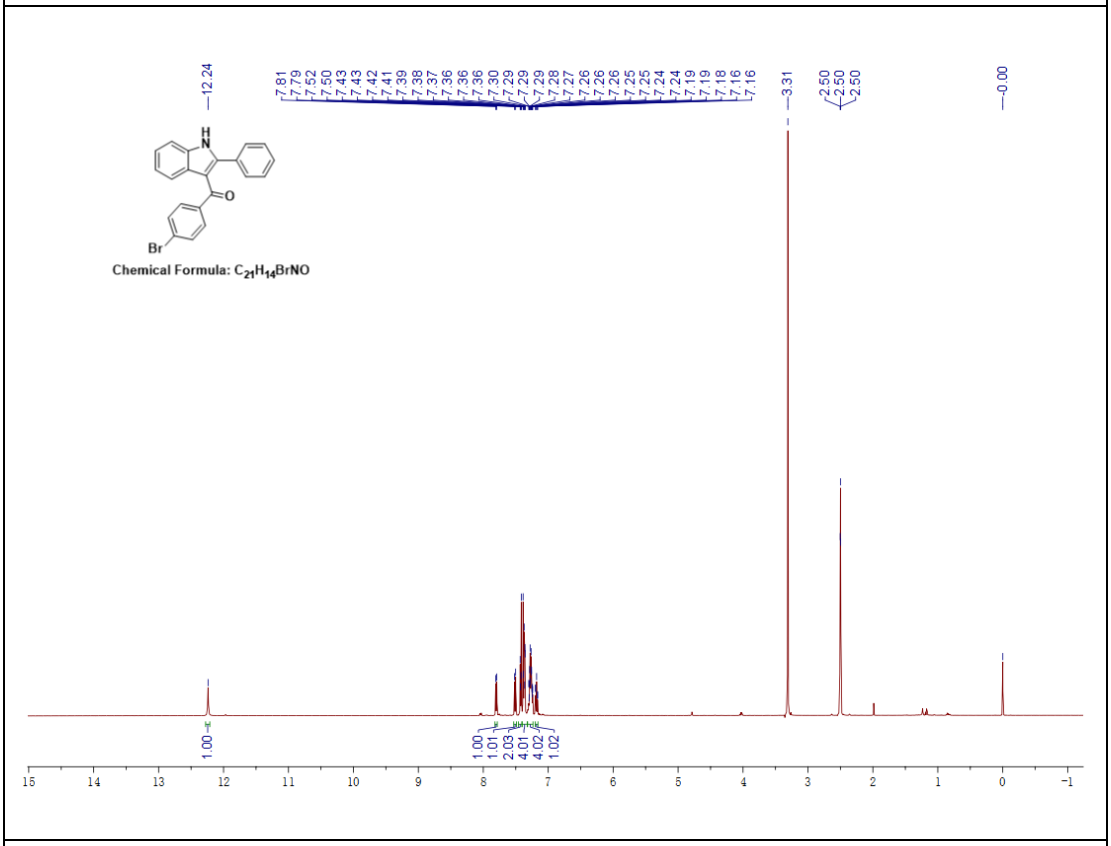


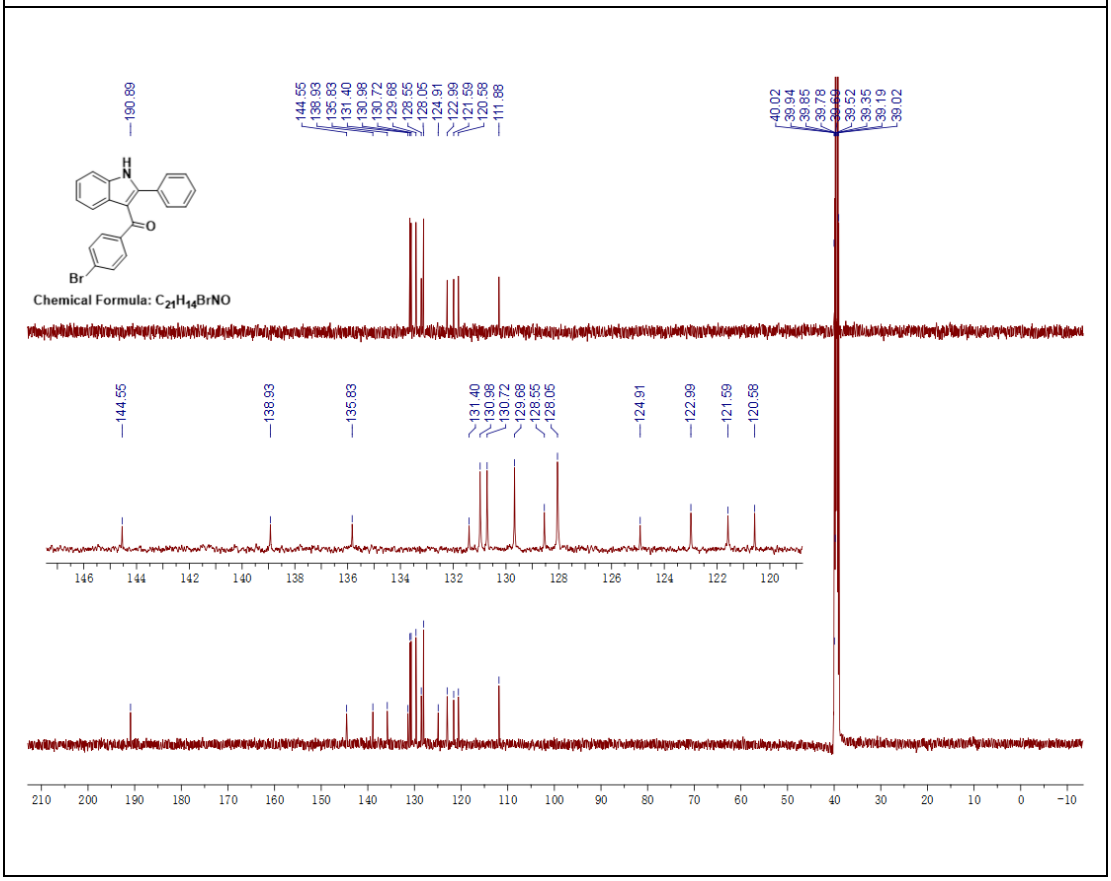
(4-chlorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ac**)



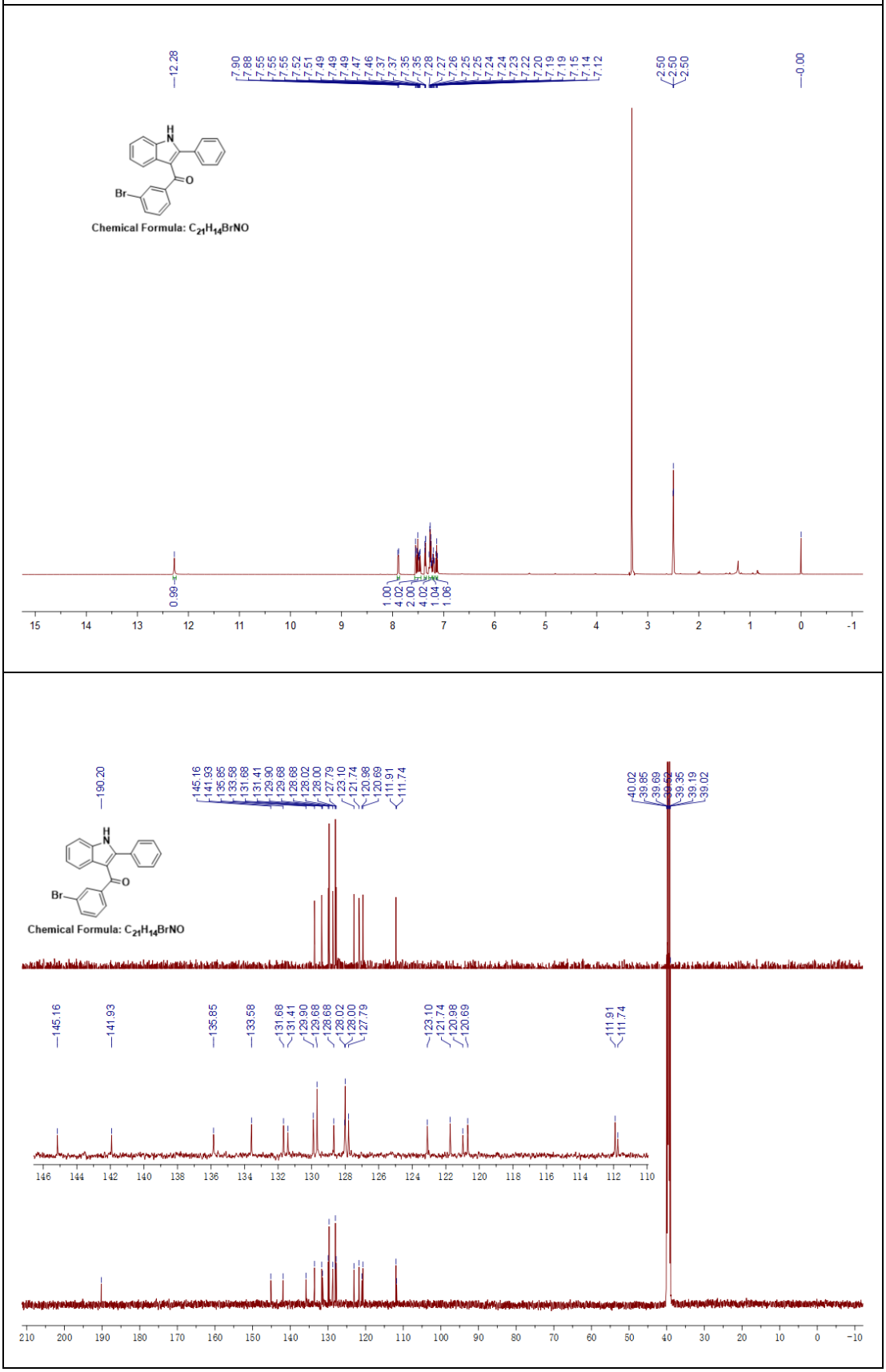


(4-bromophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ad**)

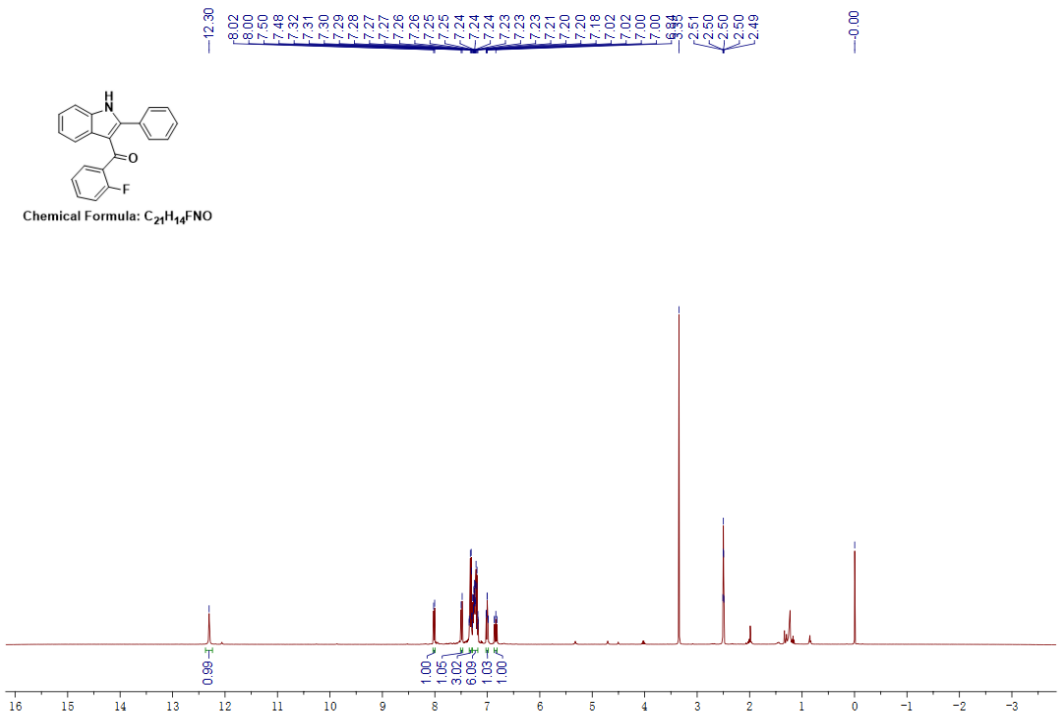


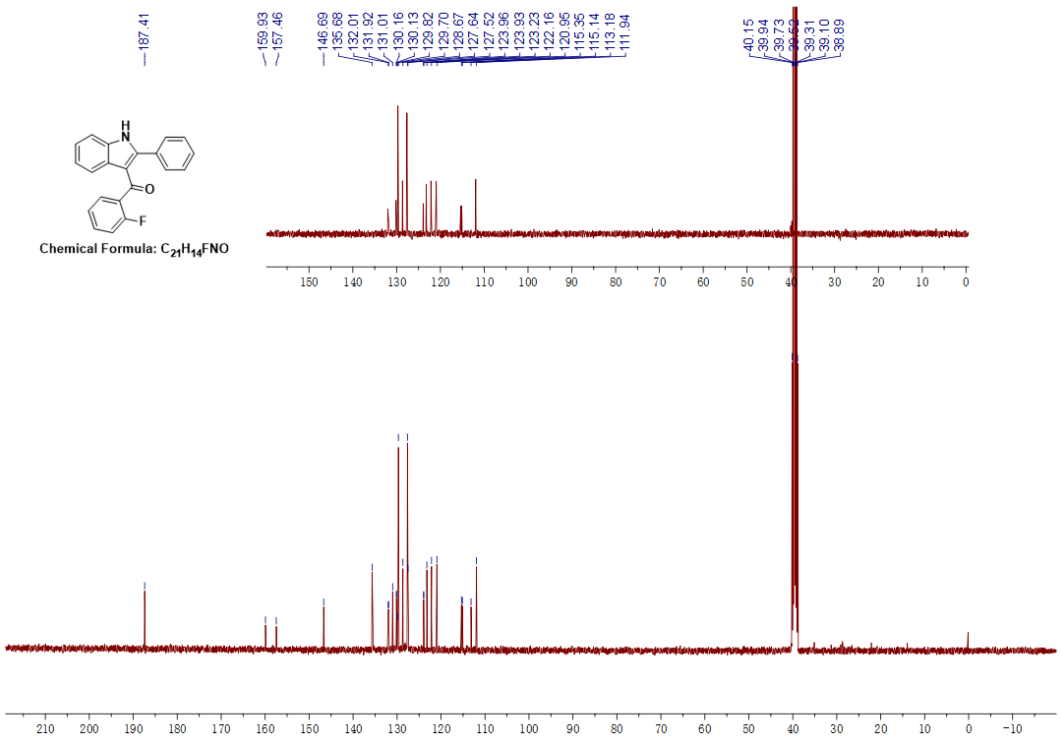


(3-bromophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ae**)

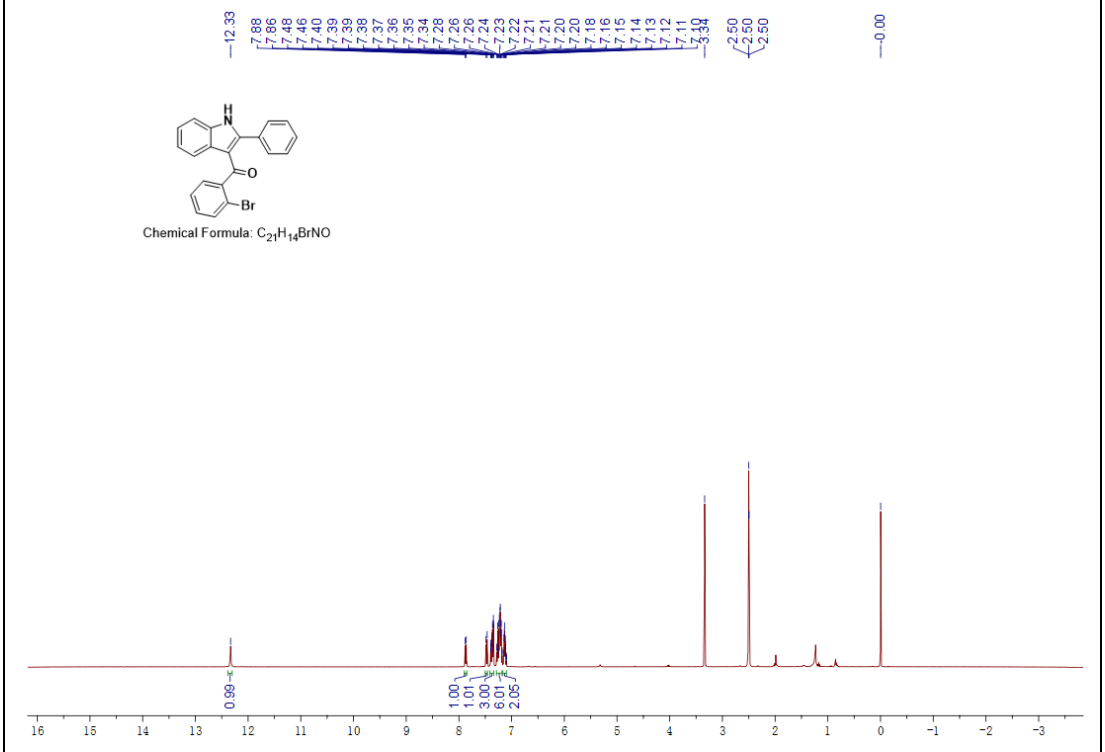


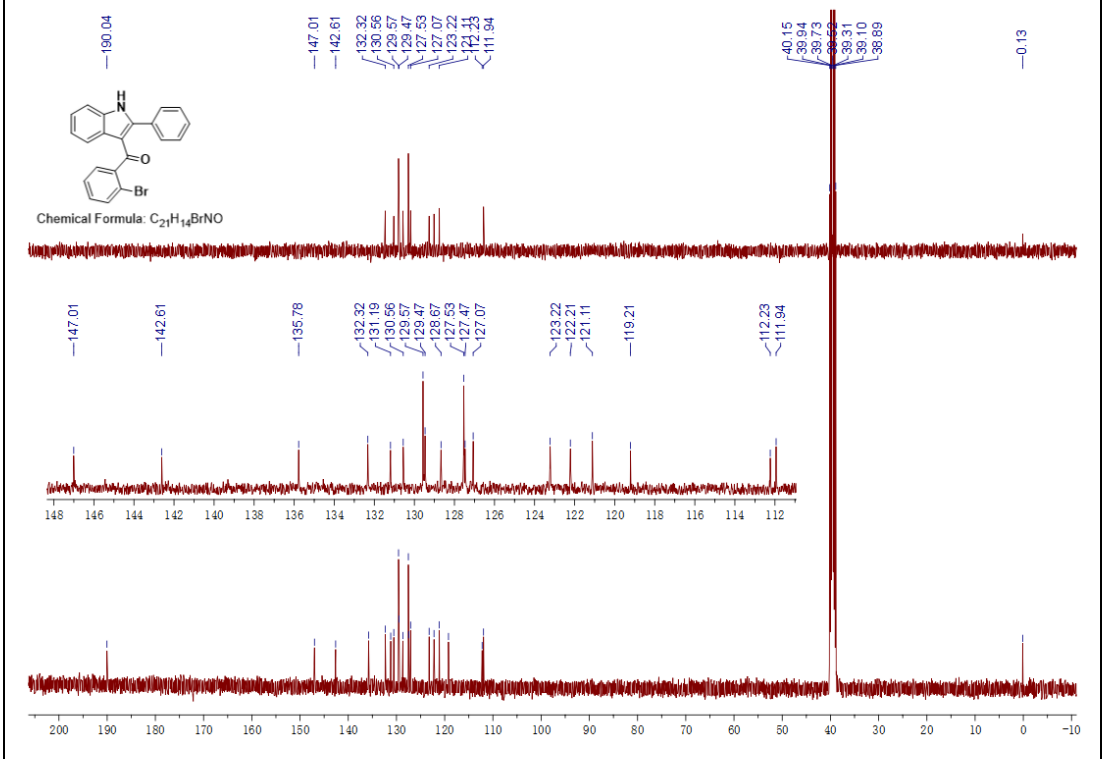
(2-Fluorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3af**)



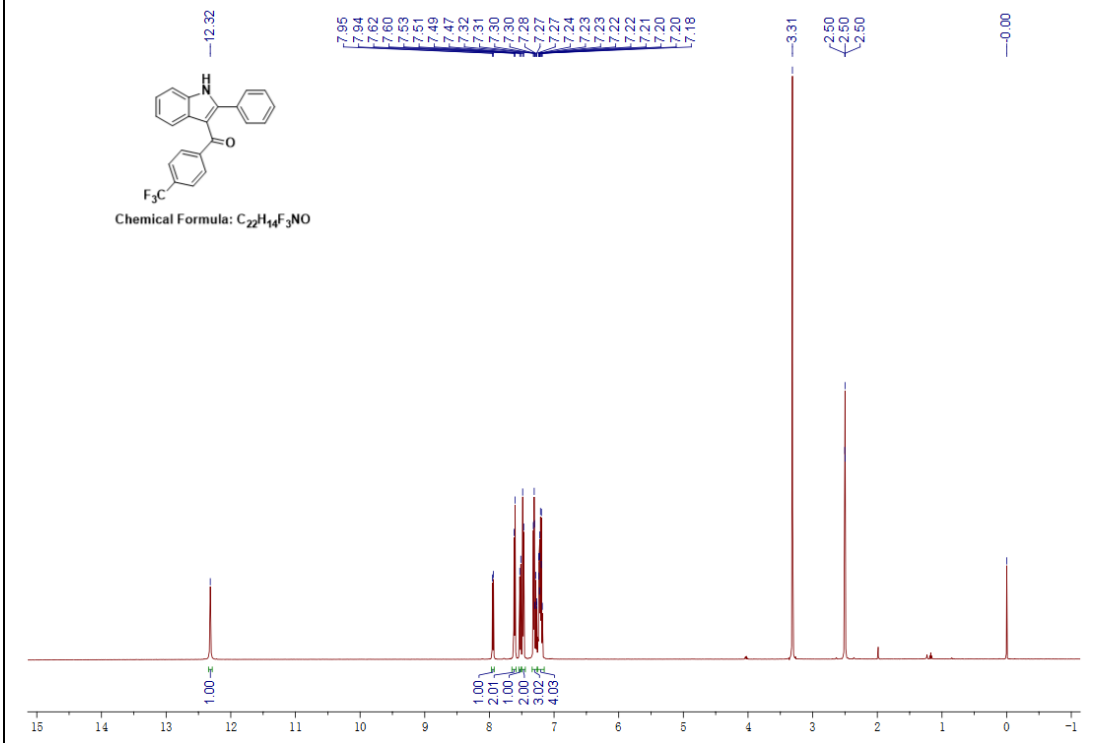


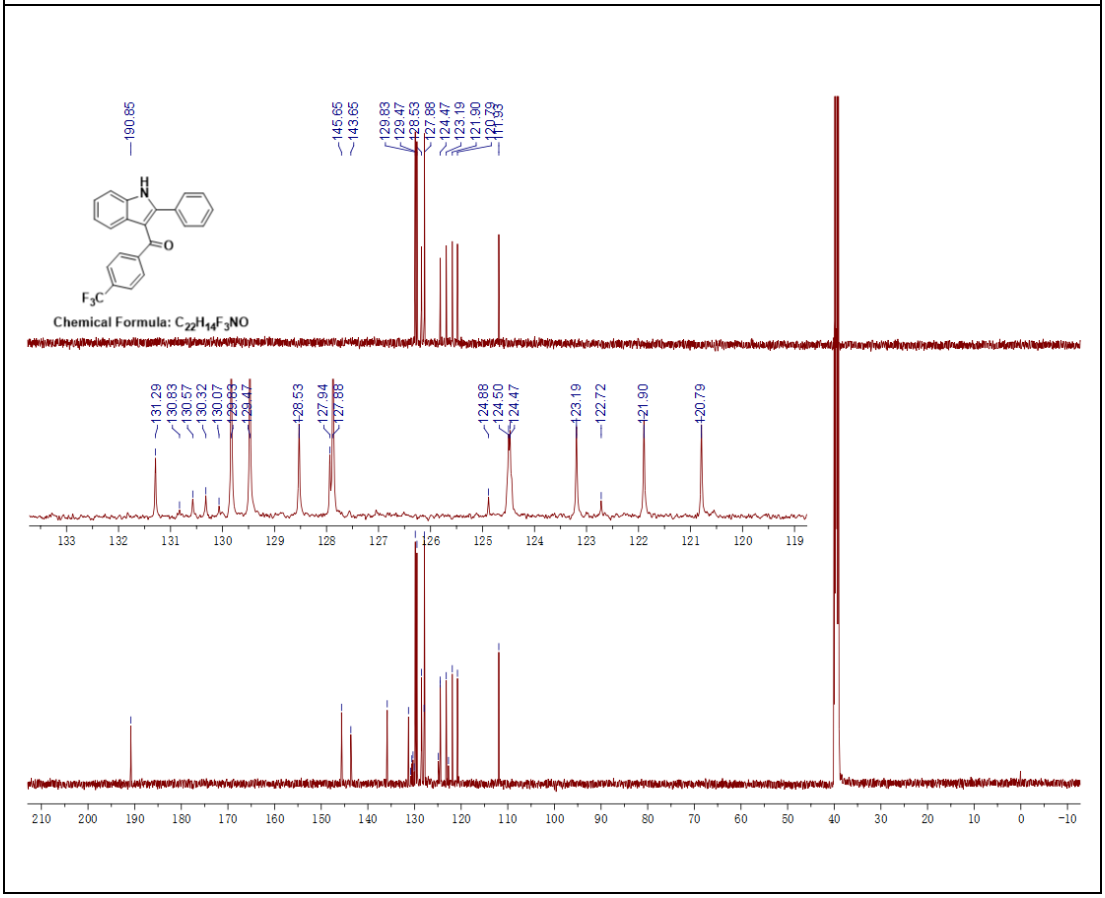
(2-bromophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ag**)



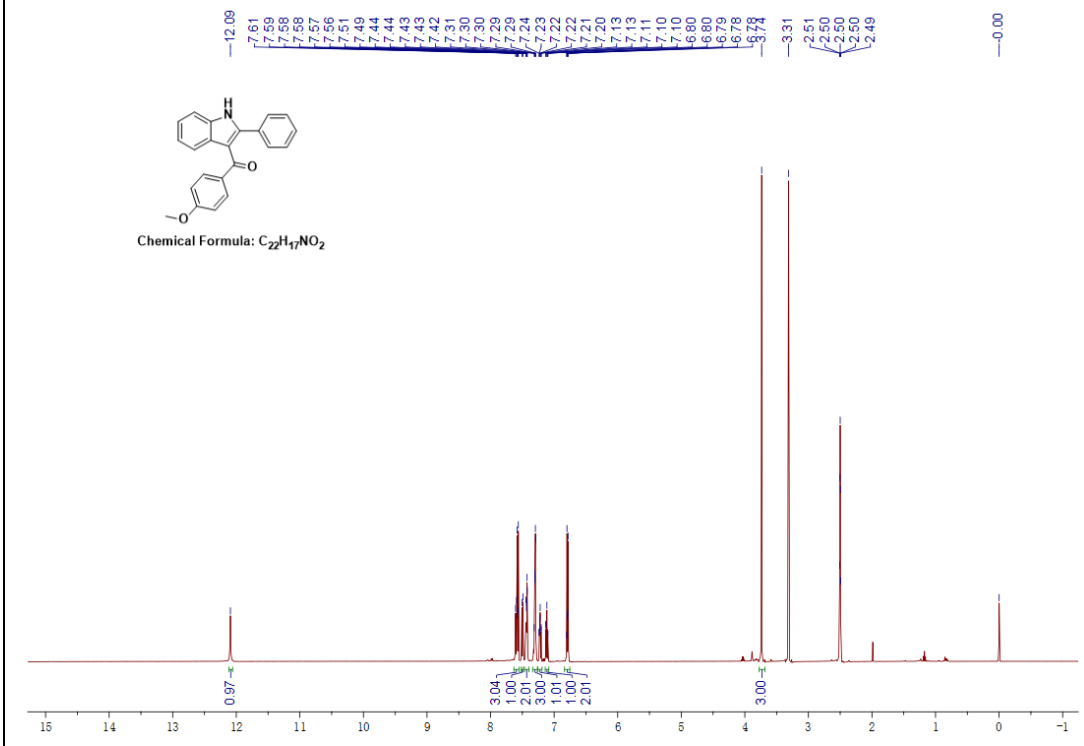


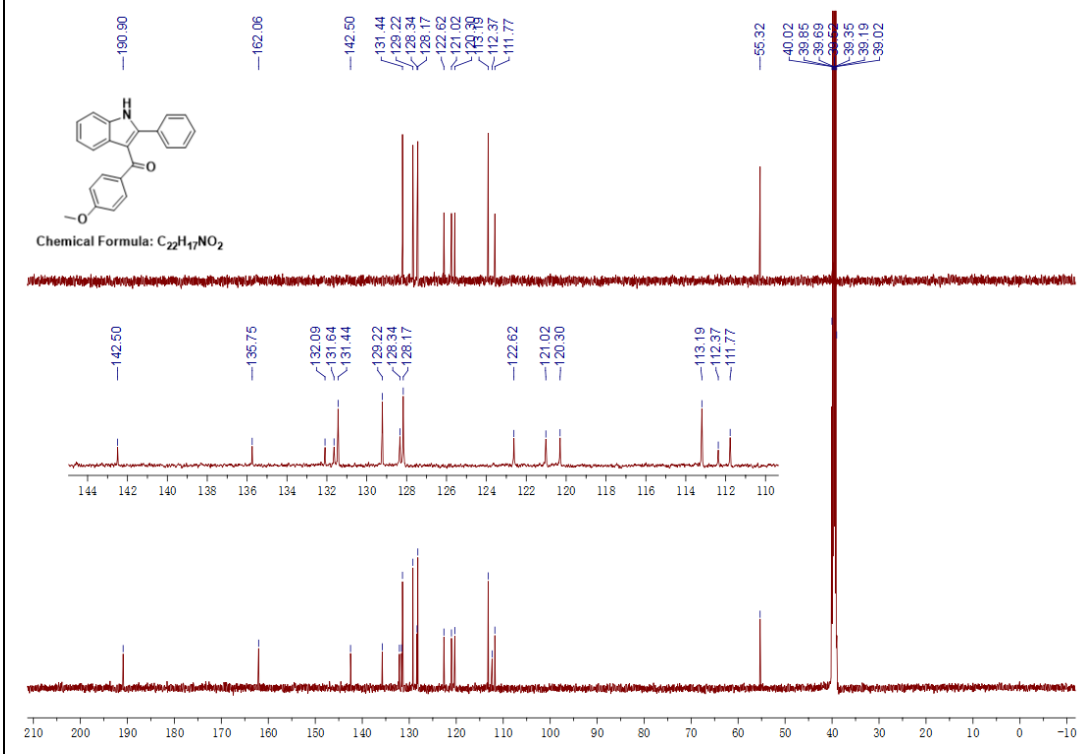
(2-phenyl-1*H*-indol-3-yl)(4-(trifluoromethyl)phenyl)methanone (**3ah**)



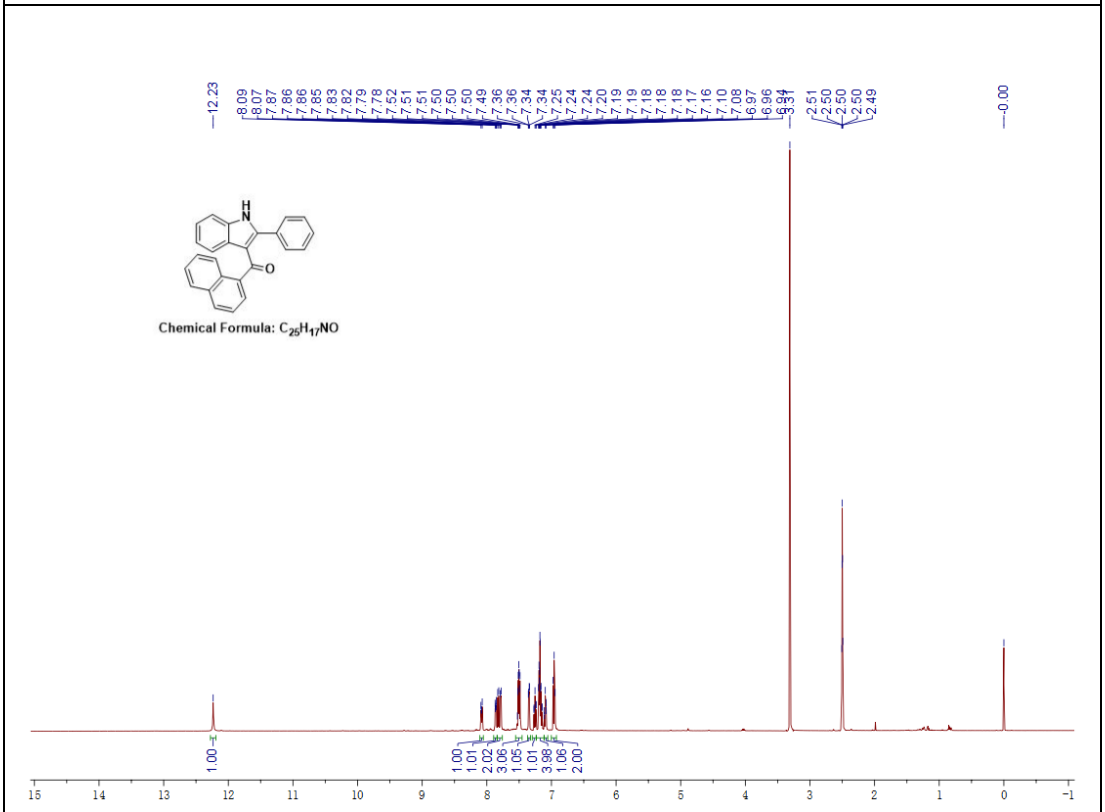


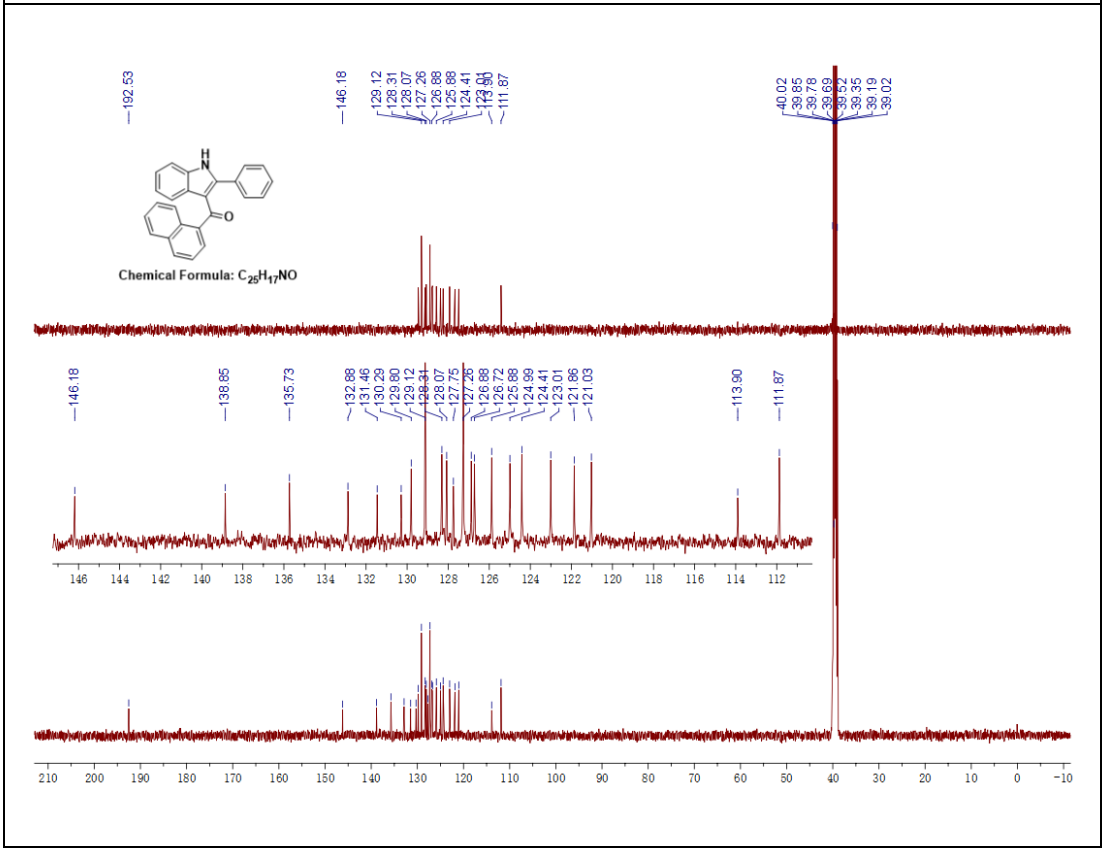
(4-methoxyphenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ai**)



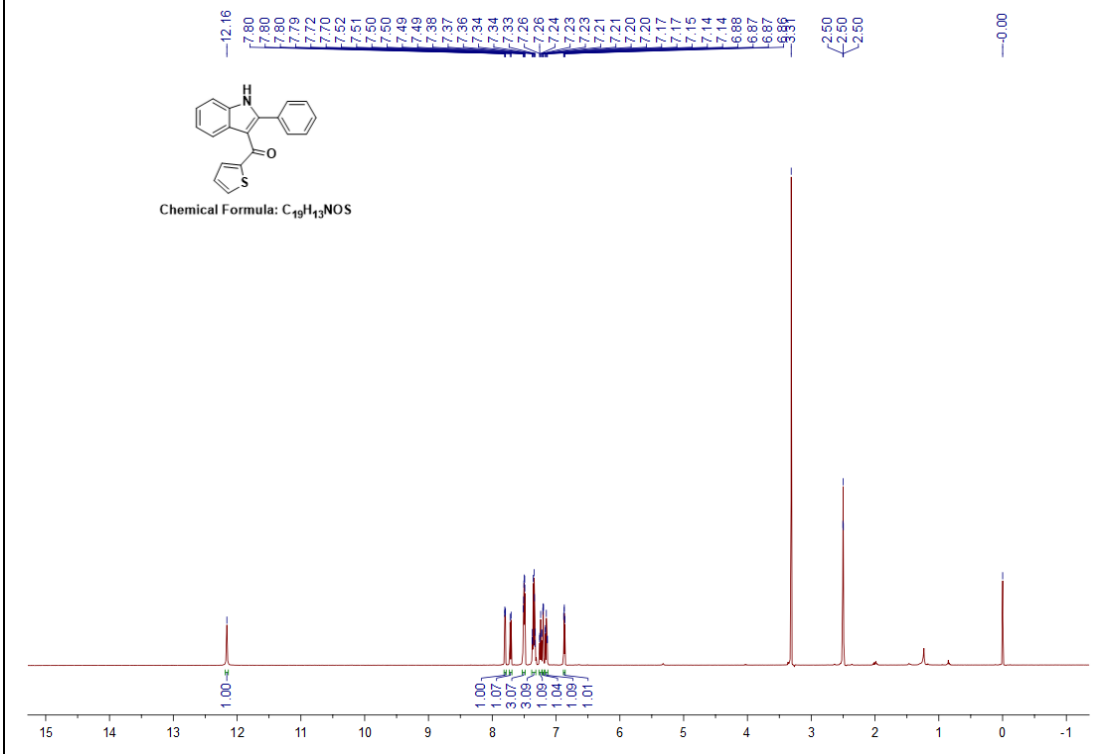


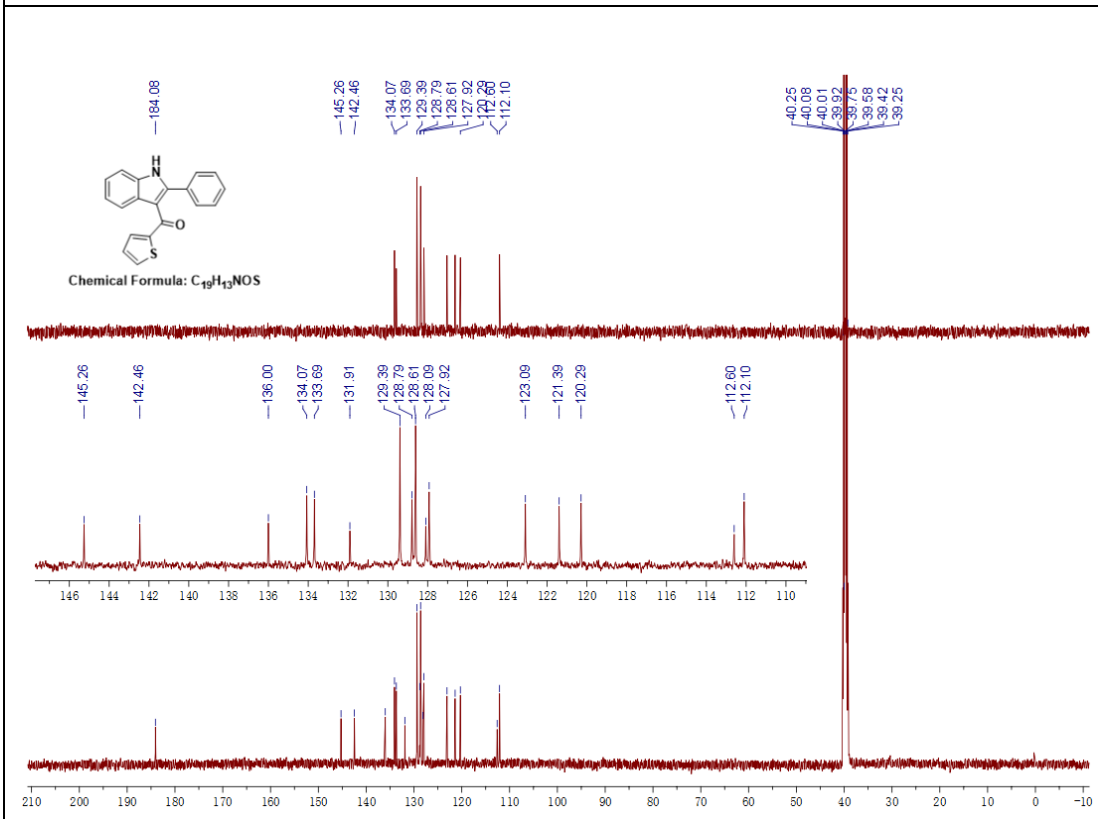
naphthalen-1-yl(2-phenyl-1*H*-indol-3-yl)methanone (**3aj**)



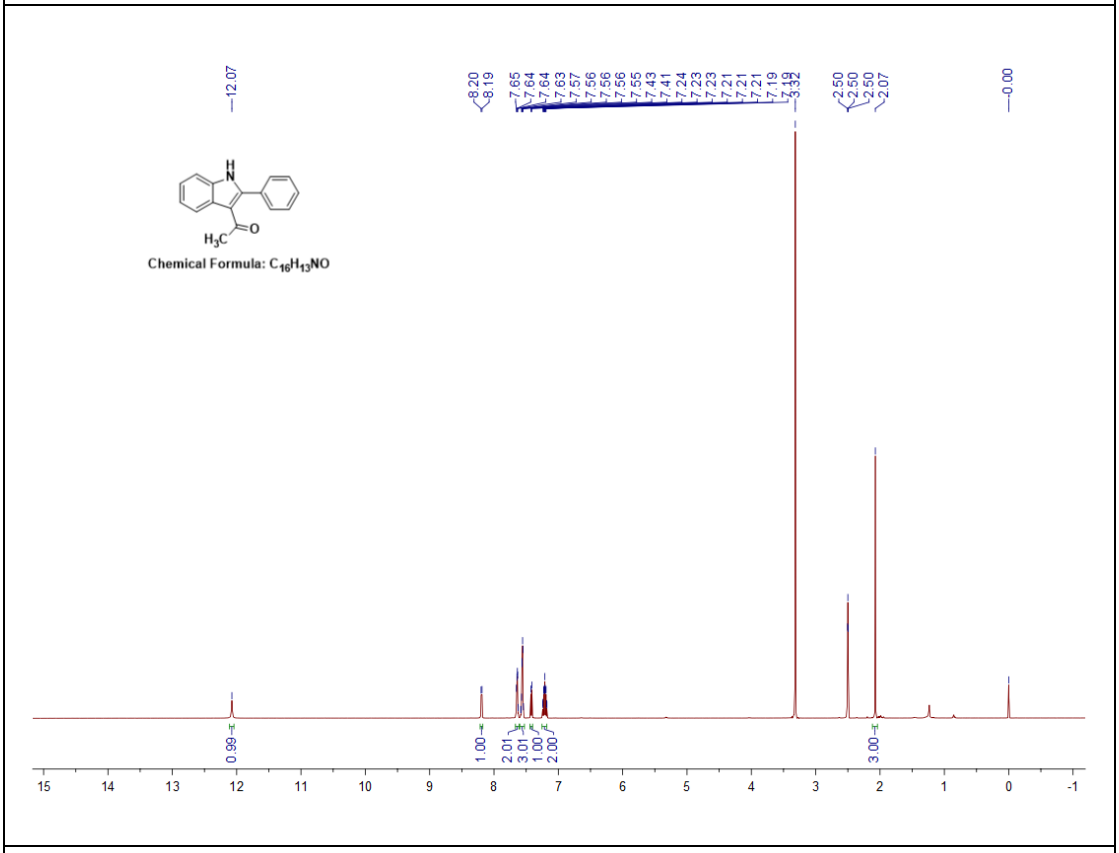


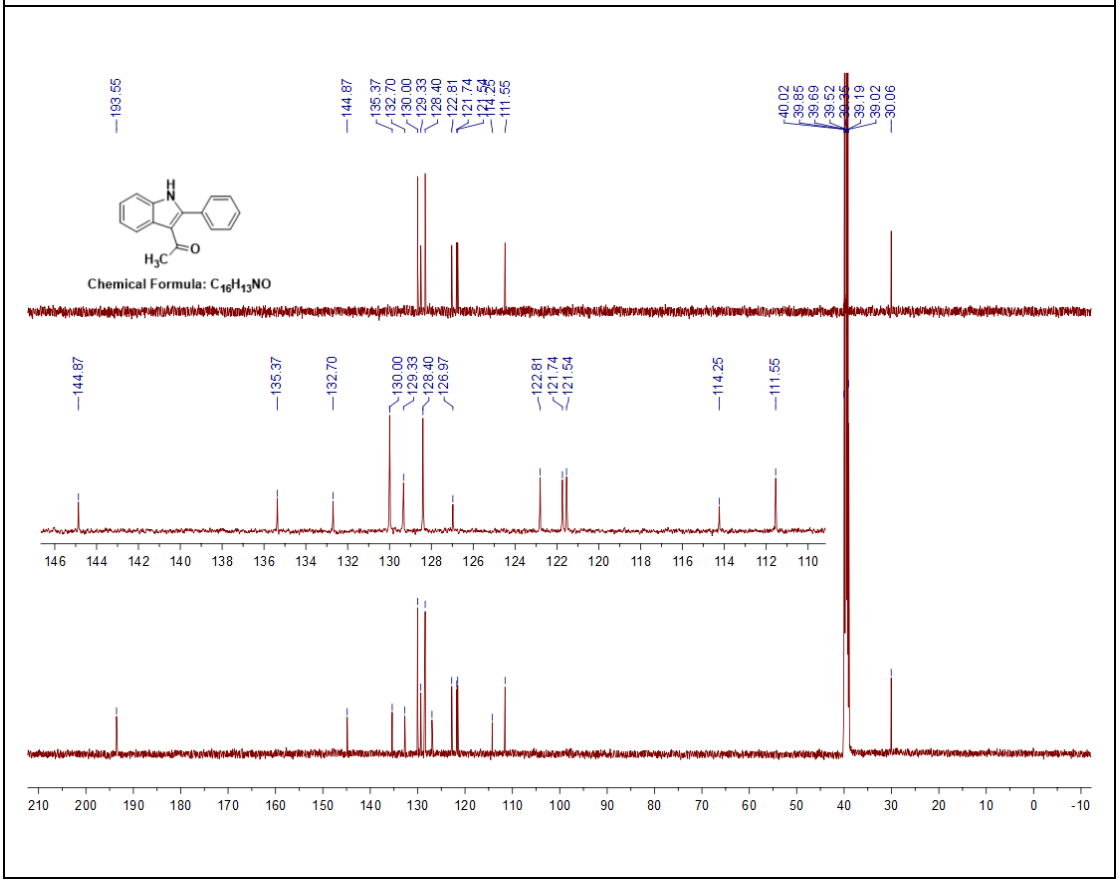
(2-phenyl-1*H*-indol-3-yl)(thiophen-2-yl)methanone (**3ak**)



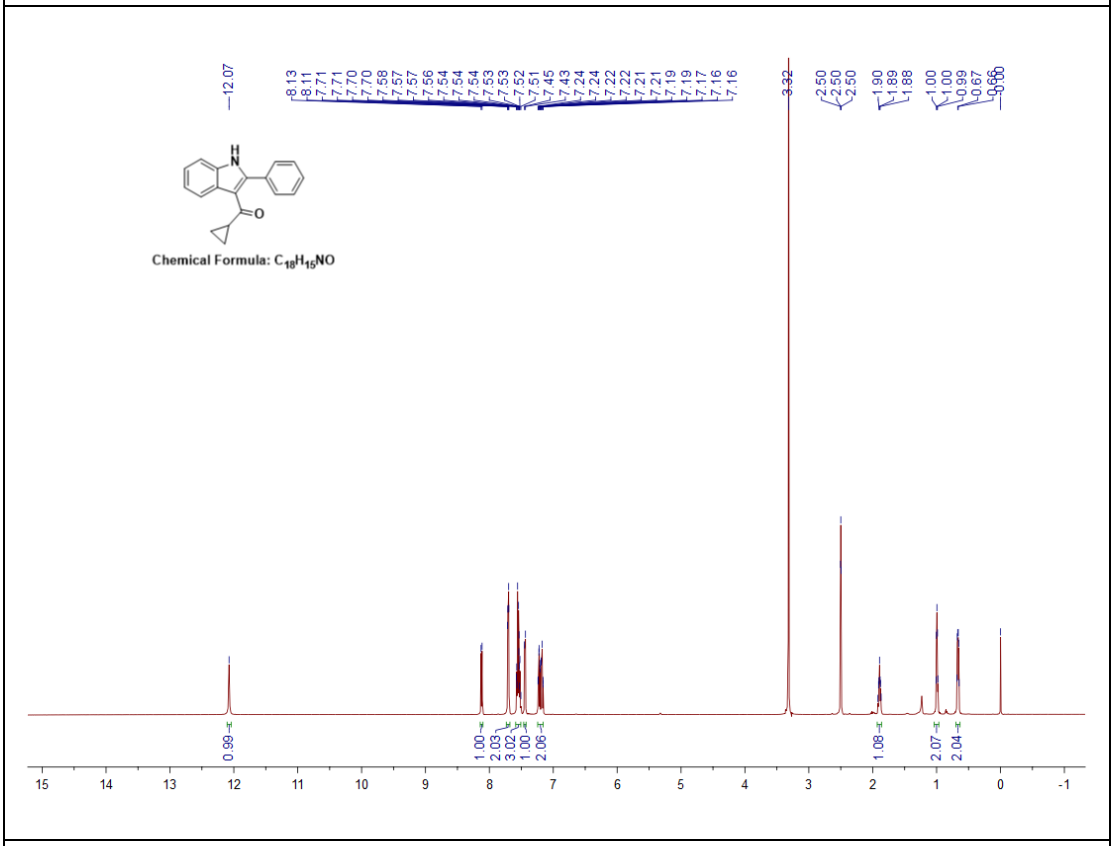


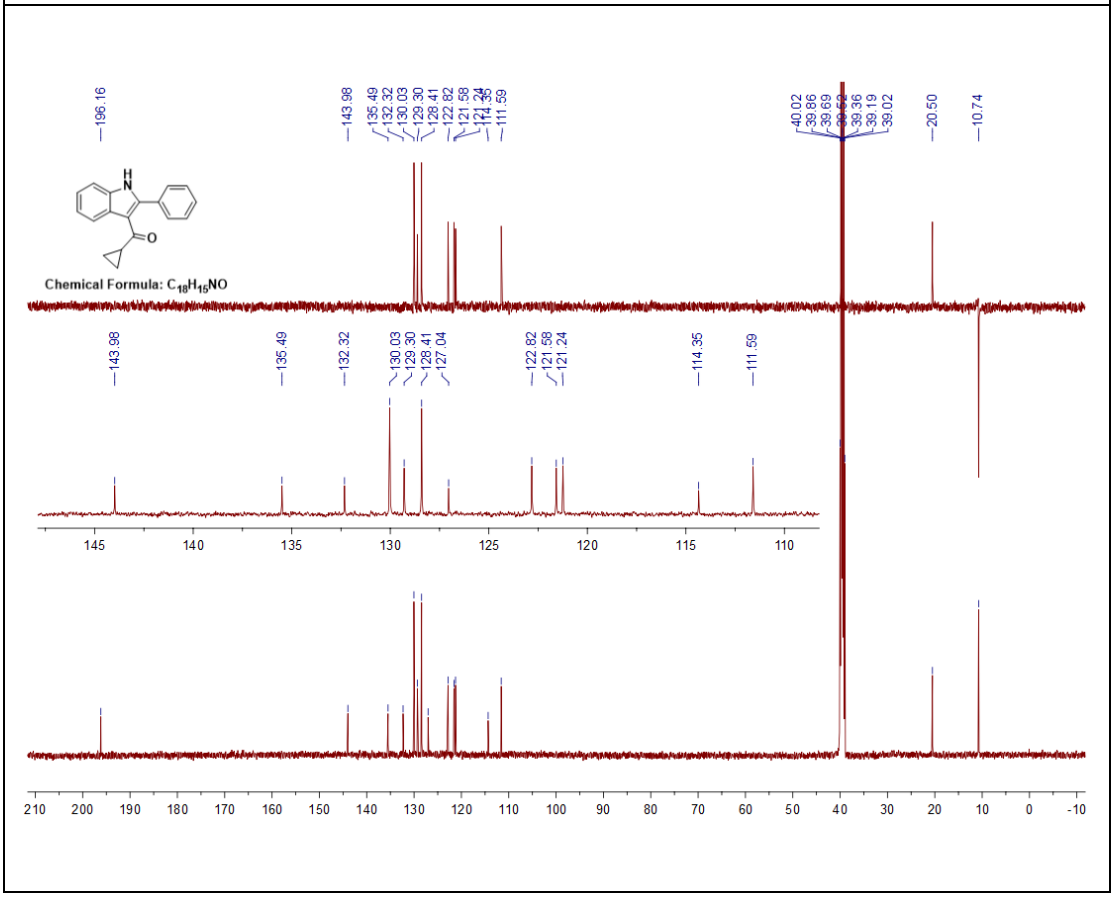
1-(2-phenyl-1*H*-indol-3-yl)ethanone (**3al**)



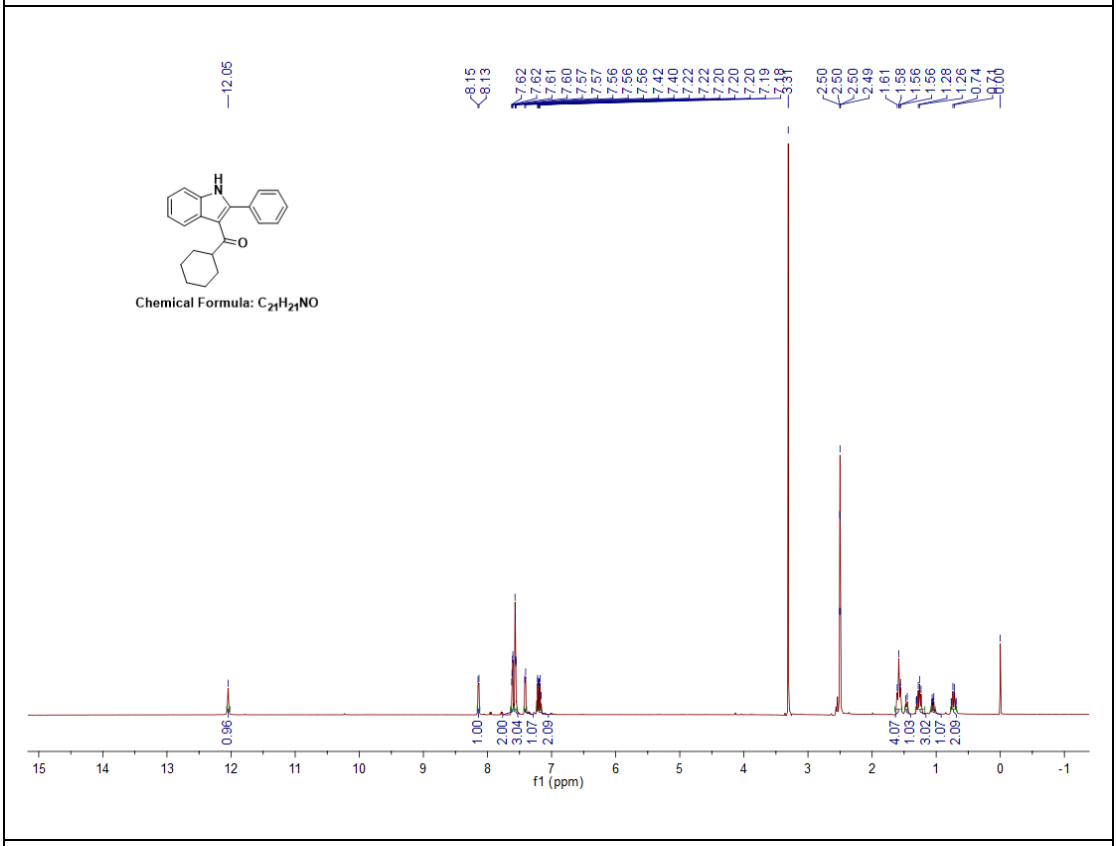


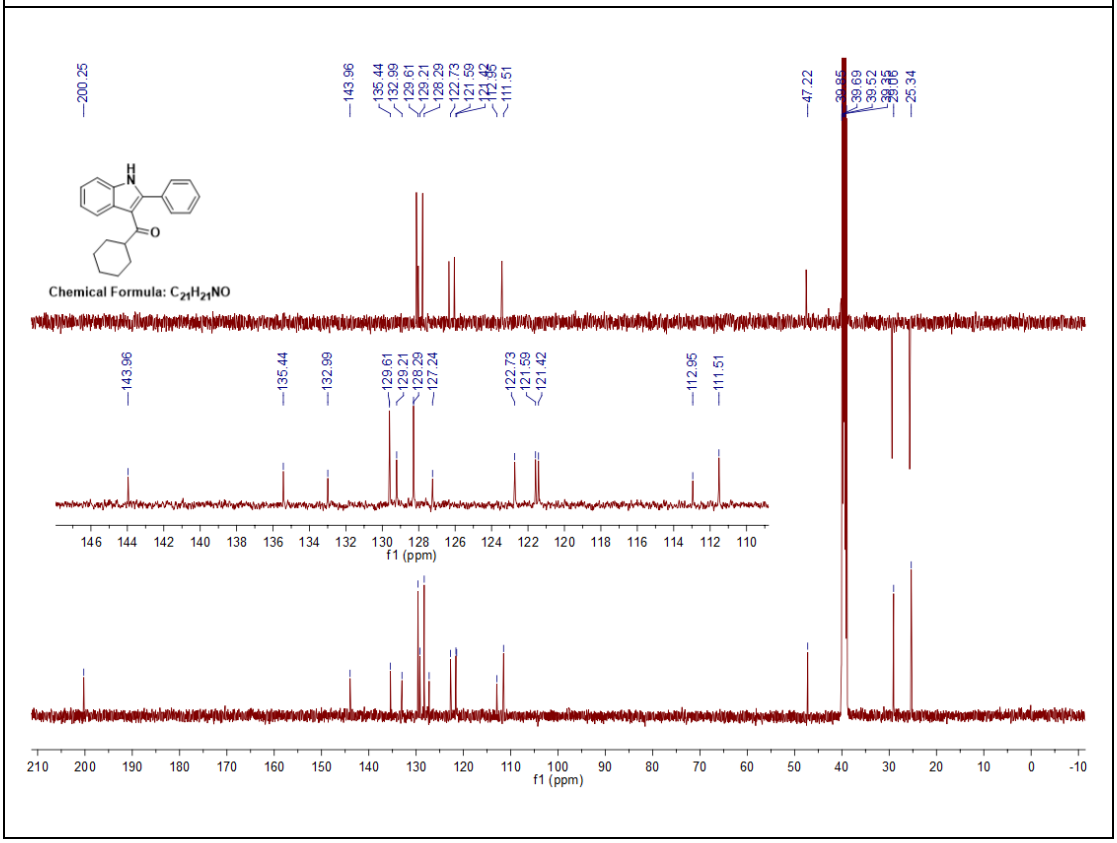
cyclopropyl(2-phenyl-1*H*-indol-3-yl)methanone (**3am**)



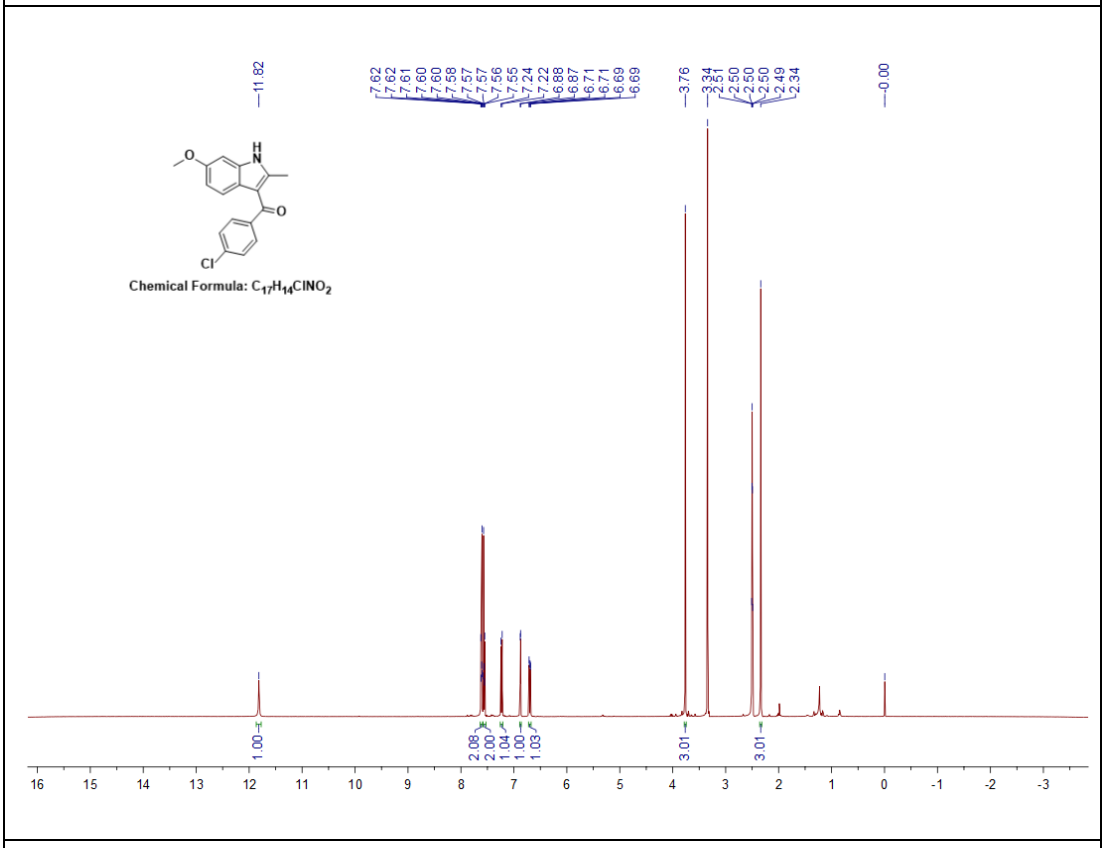


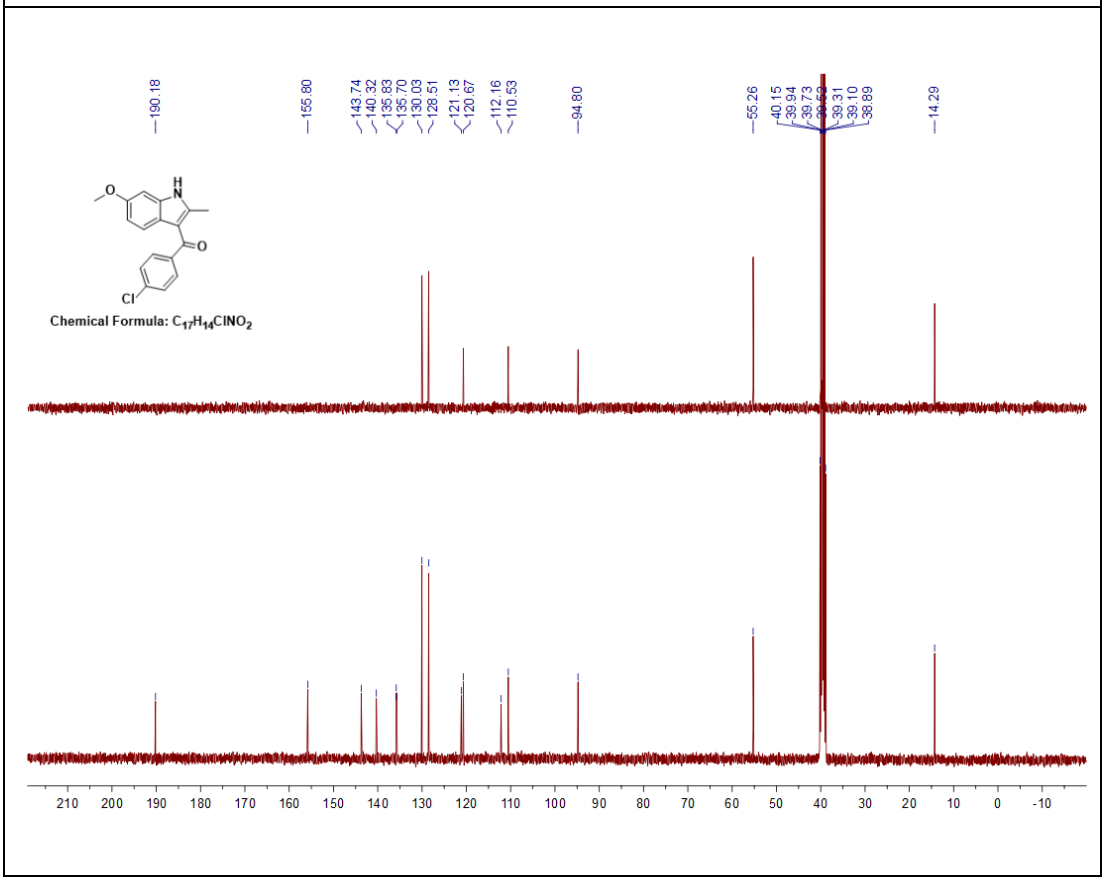
cyclohexyl(2-phenyl-1*H*-indol-3-yl)methanone (**3an**)



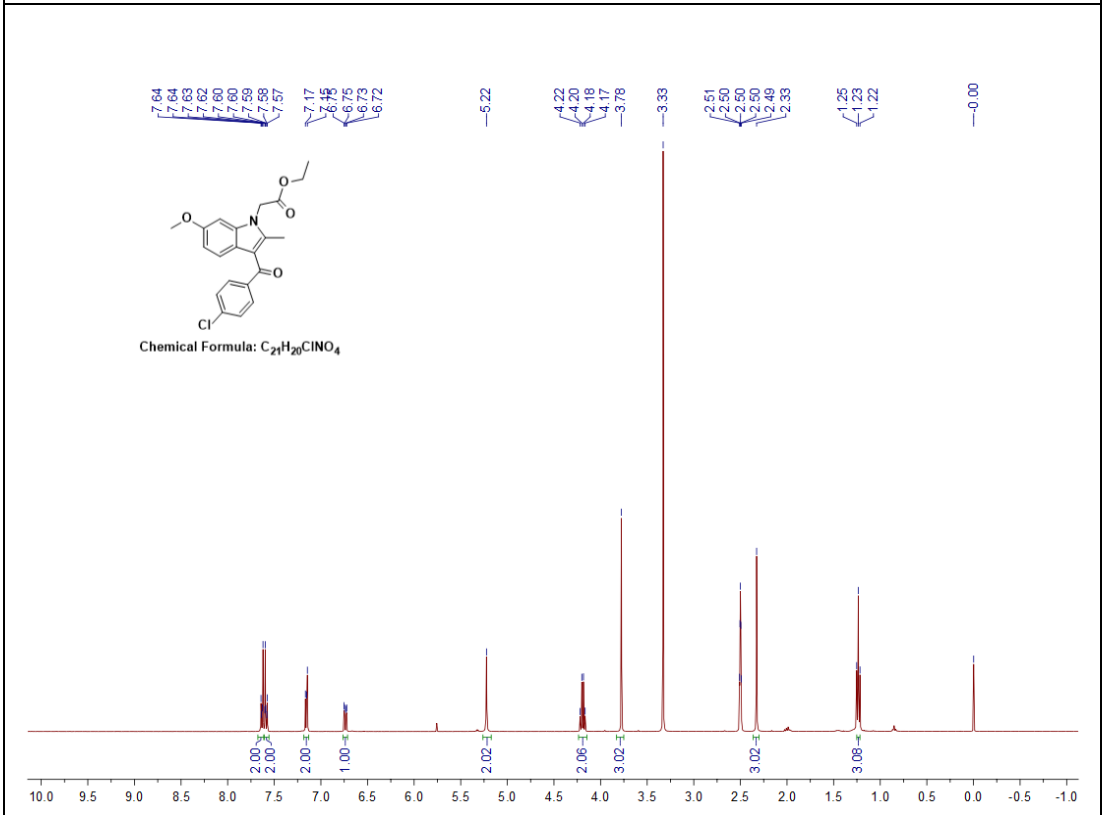


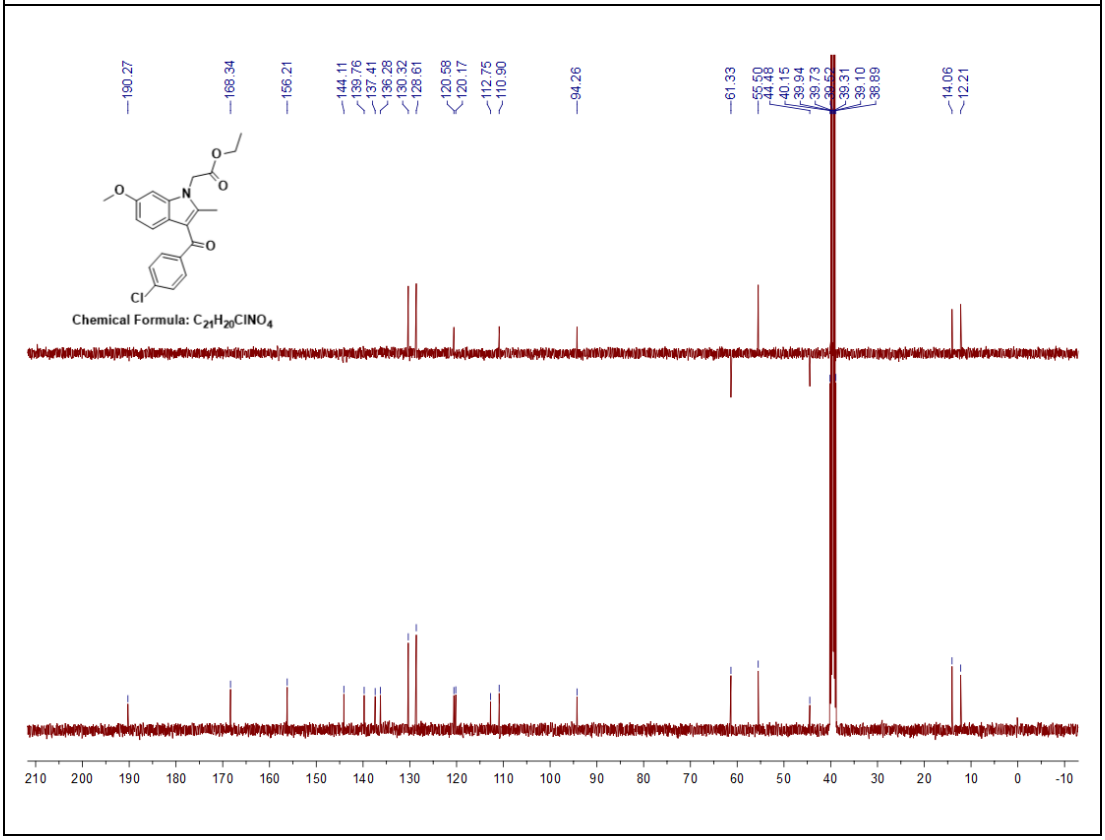
(4-chlorophenyl)(6-methoxy-2-methyl-1*H*-indol-3-yl)methanone (**3wa**)



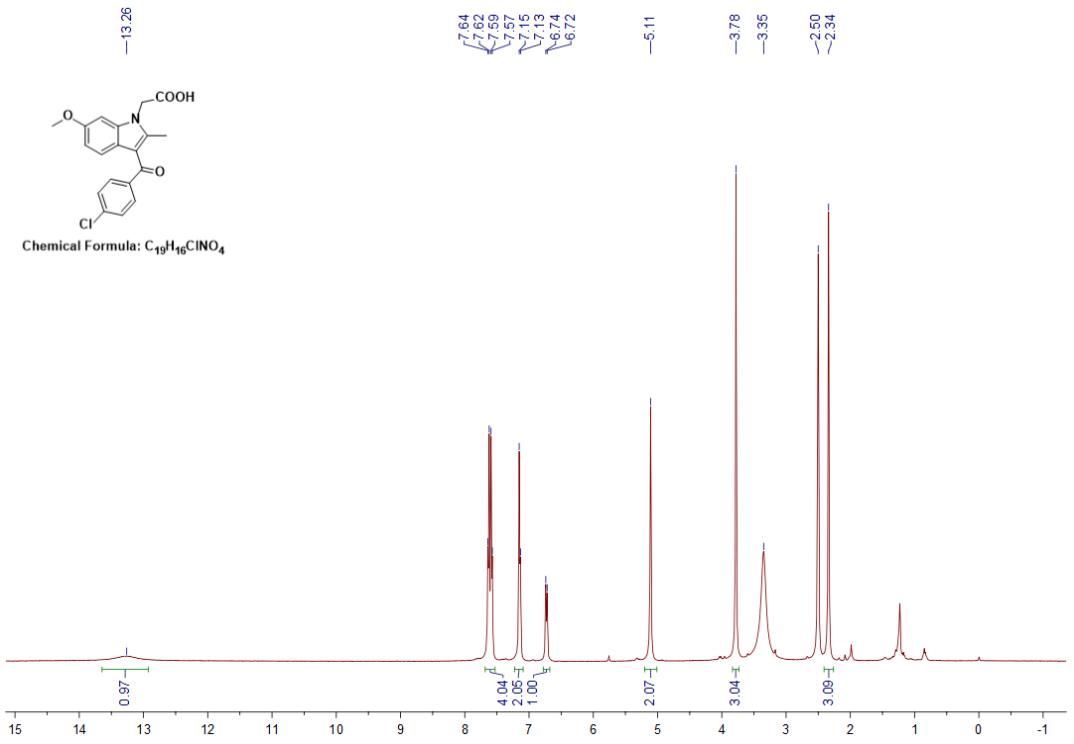


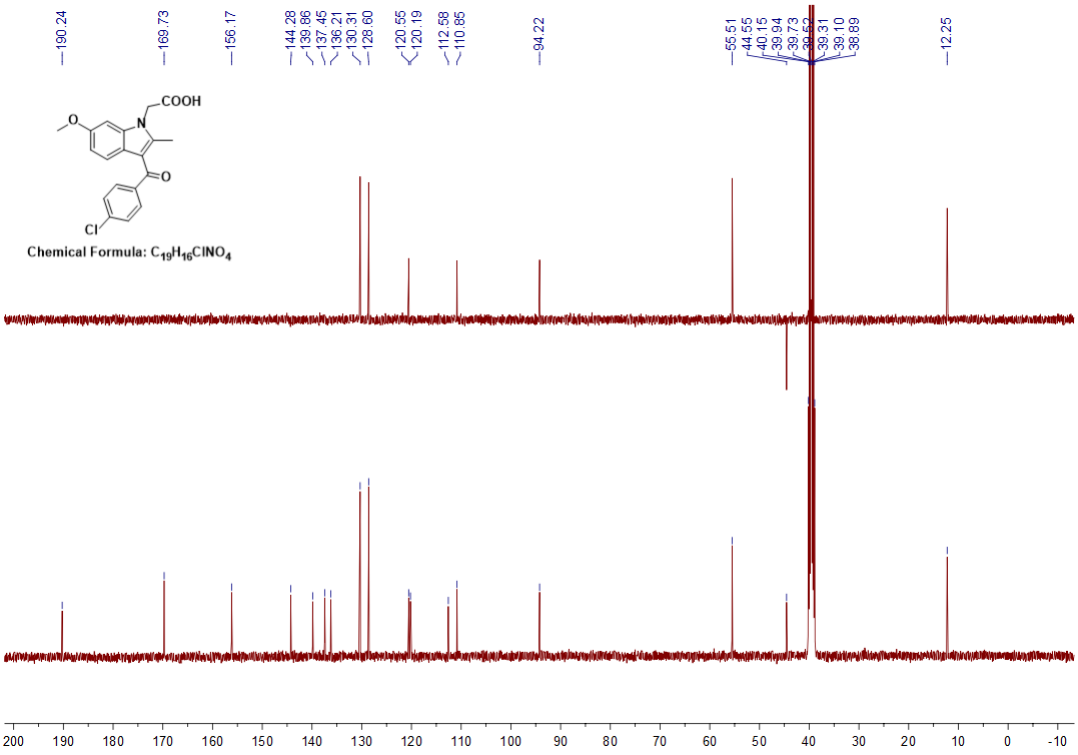
ethyl 2-(3-(4-chlorobenzoyl)-6-methoxy-2-methyl-1*H*-indol-1-yl)acetate (**4**)



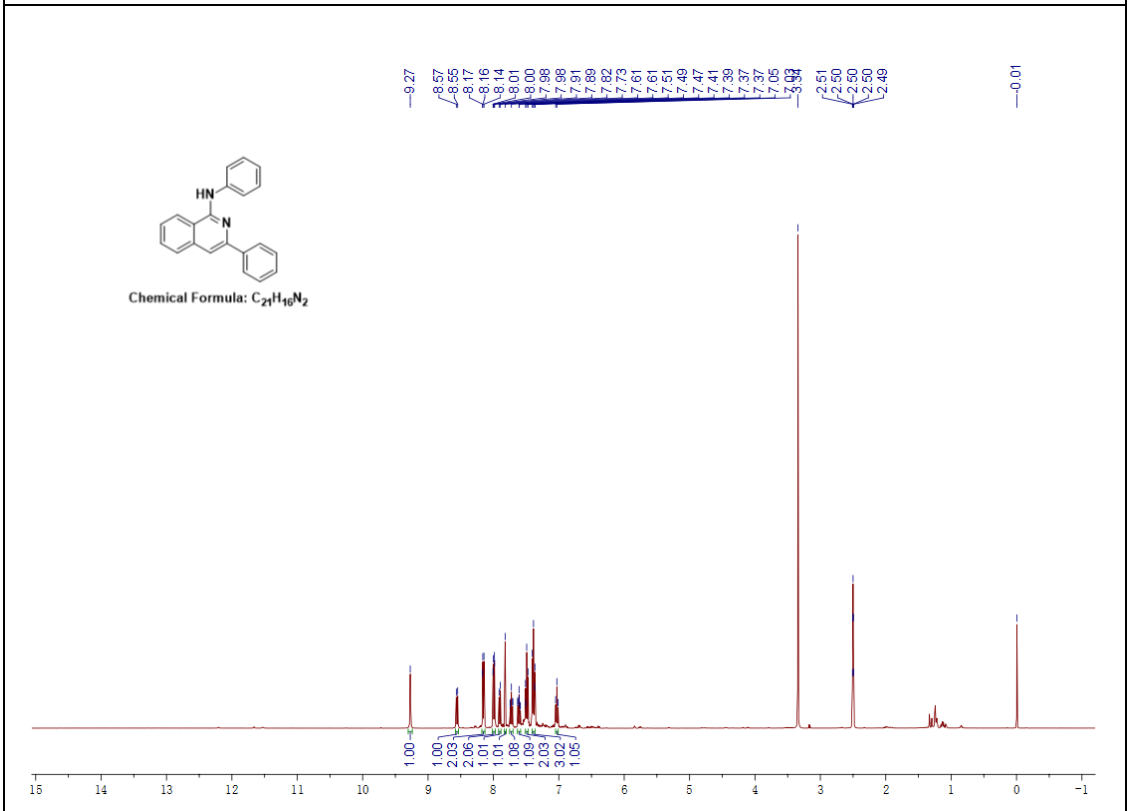


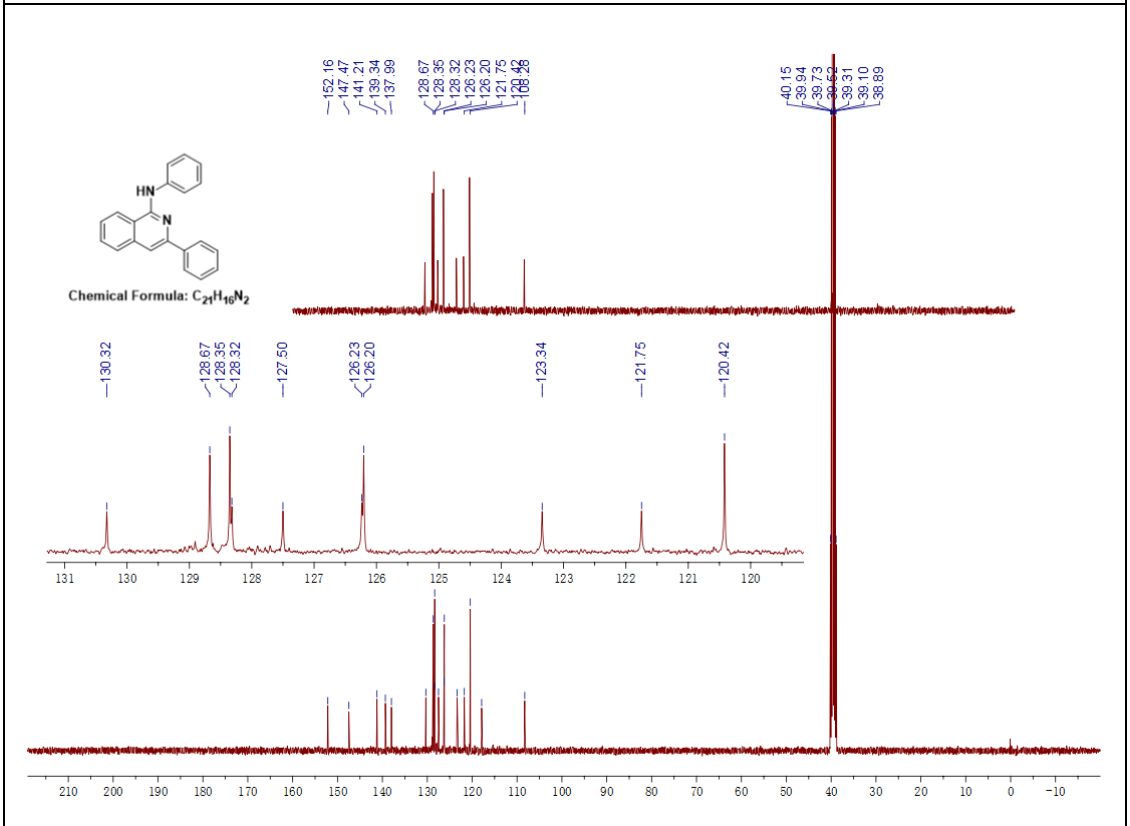
2-(3-(4-chlorobenzoyl)-6-methoxy-2-methyl-1*H*-indol-1-yl)acetic acid (**clometacin**)





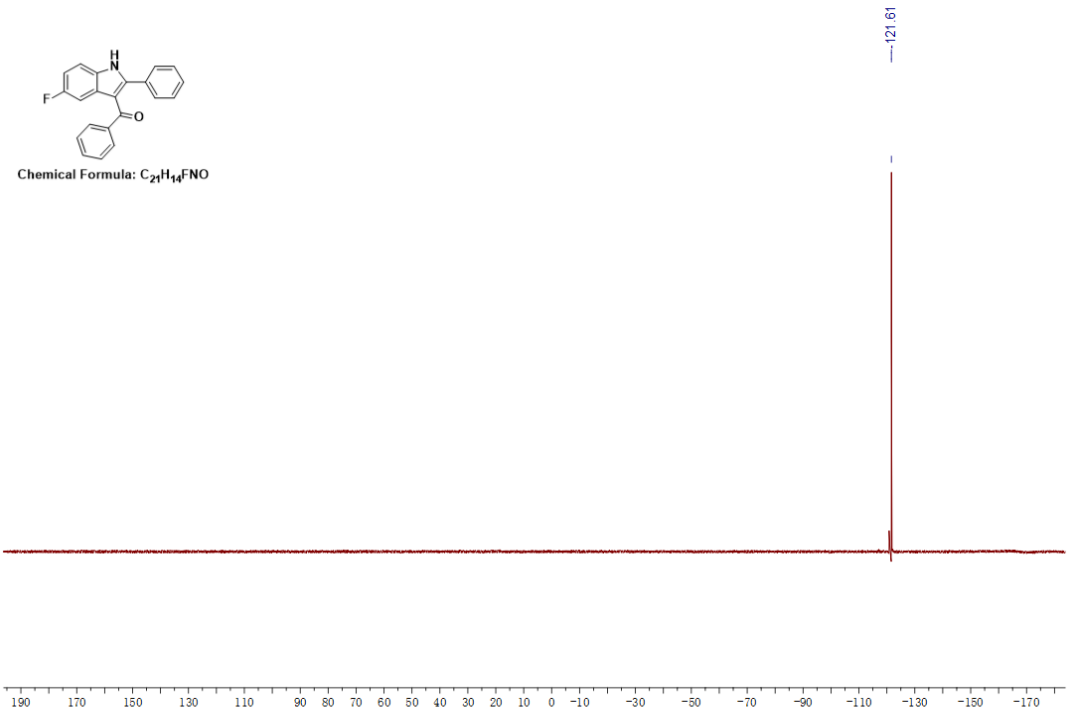
N,3-diphenylisoquinolin-1-amine (**4aa**)



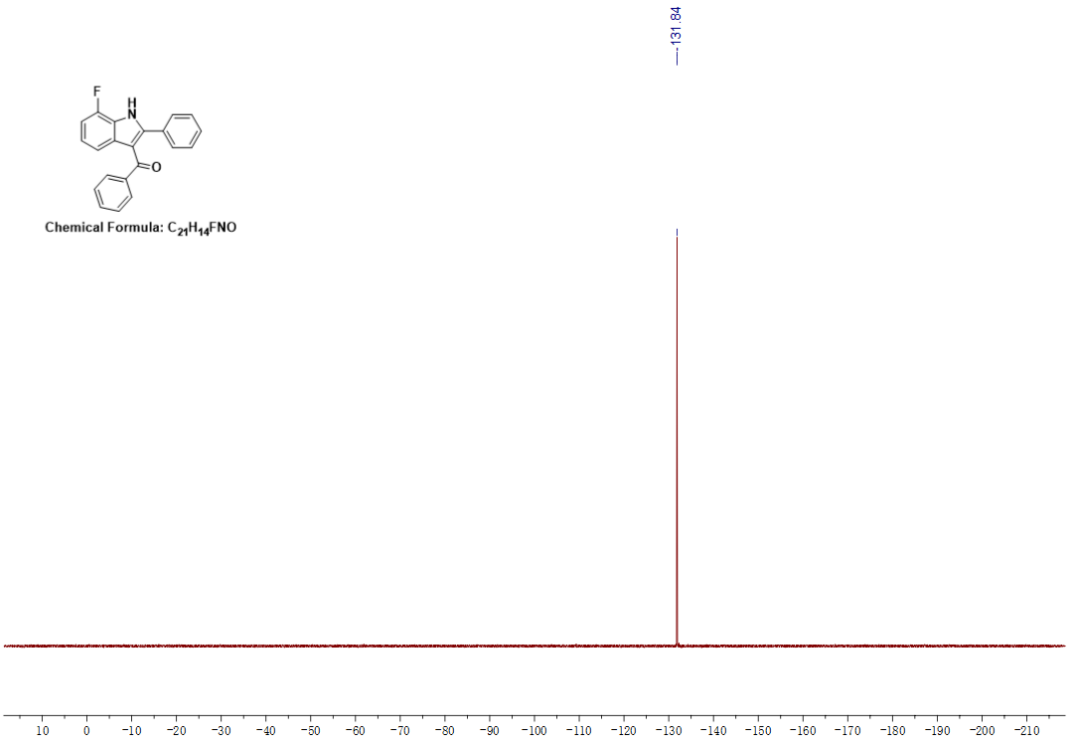


VII. ^{19}F NMR Spectra

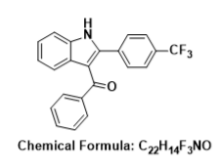
(5-Fluoro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ba**)



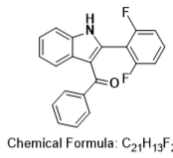
(7-Fluoro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (**3ja**)



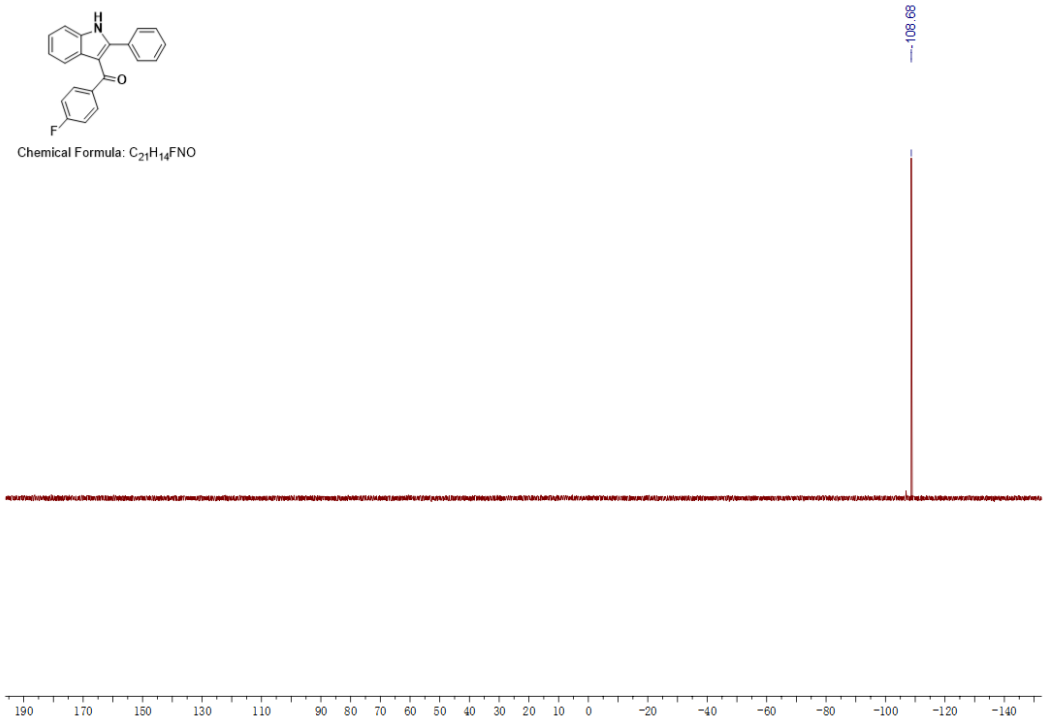
Phenyl(2-(4-(trifluoromethyl)phenyl)-1*H*-indol-3-yl)methanone (**3na**)



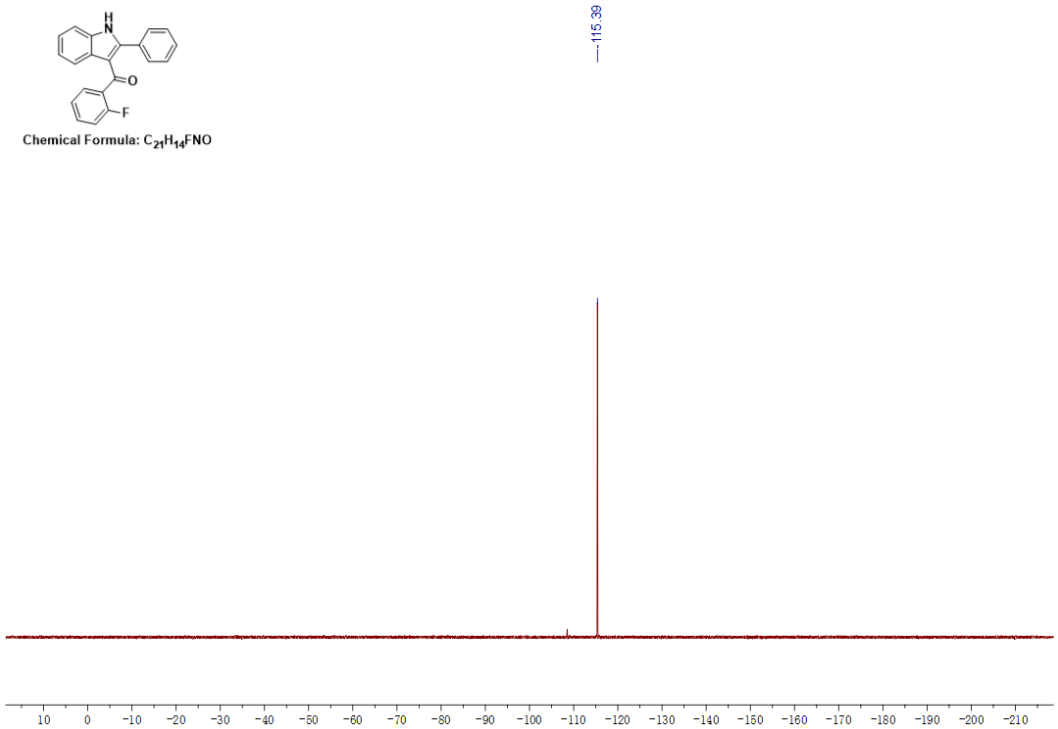
(2-(2,6-Difluorophenyl)-1*H*-indol-3-yl)(phenyl)methanone (**3oa**)



(4-Fluorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3ab**)



(2-Fluorophenyl)(2-phenyl-1*H*-indol-3-yl)methanone (**3af**)



(2-Phenyl-1*H*-indol-3-yl)(4-(trifluoromethyl)phenyl)methanone (**3ah**)