Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

L-Proline Catalyzed Stereoselective Synthesis of (*E*)-Methyl *α*-Indol-2-yl-*β*-Aryl/Alkyl Acrylates: Easy Access of Substituted Carbazoles, γ-Carbolines and Prenostodione

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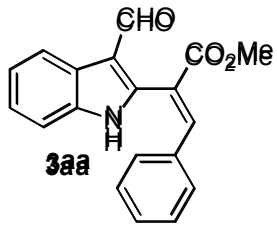
General Information:

All reactions were carried out either under inert atmosphere or air and monitored by TLC using Merck 60 F_{254} pre coated silica gel plates (0.25 mm thickness) and the products were visualized by UV detection. Flash chromatography was carried out with silica gel (200-300 mesh). FT-IR spectra were recorded on a BrukerTensor-27 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance (III) 400 MHz spectrometer. Data for ^{1}H NMR are reported as a chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constant *J* (Hz), integration, and assignment, data for ^{13}C are reported as a chemical shift. High resolutions mass spectral analyses (HRMS) were carried out using ESI-TOF-MS. Single crystal X-ray structural studies were performed on a CCD Agilent Technologies (Oxford Diffraction) SUPER NOVA diffractometer. Data were collected at 293(2) K using graphite-monochromoated Mo Kα radiation (λ_α = 0.71073 Å). The strategy for the Data collection was evaluated by using the CrysAlisPro CCD software. The data were collected by the standard 'phi-omega scan techniques, and were scaled and reduced using CrysAlisPro RED software. The structures were solved by direct methods using SHELXS-97 and refined by full matrix least-squares with SHELXL-97, refining on F^2.[1]

The positions of all the atoms were obtained by direct methods. All non-hydrogen atoms were refined anisotropically. The remaining hydrogen atoms were placed in geometrically constrained positions and refined with isotropic temperature factors, generally 1.2U_{eq} of their parent atoms.

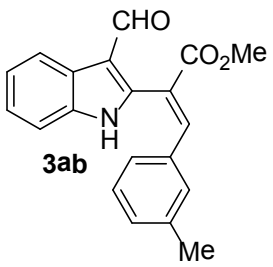
Materials: All these starting materials and catalysts were either purchased from commercial sources or synthesized by literature known procedures.[2] All the solvents dried and distilled under reduced pressure before prior used.

General procedure for the synthesis of (*E*)-methyl α-(3-formyl-1*H*-indol-2-yl)-β-aryl/heteroaryl-substituted acrylates: To a stirred solution of methyl 2-(3-formyl-1*H*-indol-2-yl)acetate (0.2 mmol), aldehydes (0.3 mmol) and L-proline (0.05 mmol) in dry DMSO (1.0 mL) at room temperature under argon atmosphere. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3 × 10 mL), washed with water and brine respectively and dried with Na_2SO_4. The organic phase was evaporated by rotary evaporator under reduced pressure to give the crude product. The crude product was purified by column chromatography over silica gel to furnish the pure product. The product was characterized by corresponding spectroscopic data (^{1}H and ^{13}C NMR, HRMS).

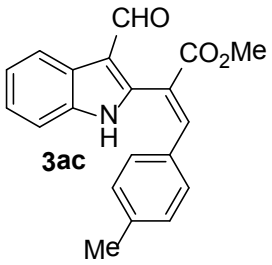


(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-phenylacrylate (3aa): Yield 83%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.86 (s, 1H), 8.70 (br s, 1H), 8.32-8.35 (m, 1H), 8.21 (s, 1H), 7.40-7.42 (m, 1H), 7.30-7.35 (m, 3H), 7.18-7.22 (m, 2H), 7.09-7.11 (m, 2H), 3.84 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.5, 166.5, 147.3, 141.7, 136.0, 132.8, 130.8, 130.4, 129.0, 125.4, 124.3, 123.1, 122.1, 120.1, 115.5, 111.5, 52.9; **HRMS** (ESI) m/z calcd. For $C_{19}H_{15}NO_3$ $[M+Na]^+$: 328.0950; Found 328.0944.

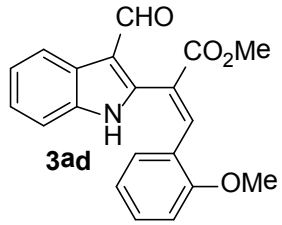
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(3-methylphenyl)acrylate (3ab): Yield 75%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.85 (s, 1H), 8.81 (br s, 1H), 8.31-8.34 (m, 1H), 8.17 (s, 1H), 7.38-7.41 (m, 1H), 7.30-7.34 (m, 2H), 7.01-7.09 (m, 2H), 6.95 (s, 1H), 6.81 (d, *J* = 7.56 Hz, 1H), 3.82 (s, 3H), 2.17 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.5, 166.5, 147.6, 141.7, 138.6, 135.9, 132.8, 131.7, 131.6, 128.8, 127.0, 125.3, 124.3, 123.1, 122.2, 119.9, 115.6, 111.4, 52.9, 21.2; **HRMS** (ESI) m/z calcd. For $C_{20}H_{17}NO_3$ $[M+Na]^+$: 342.1106; Found 342.1101.



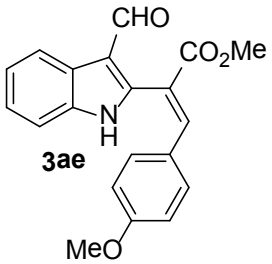
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-methylphenyl)acrylate (3ac): Yield 78%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.84 (s, 1H), 8.86 (br s, 1H), 8.32-8.35 (m, 1H), 8.18 (s, 1H), 7.39-7.41 (m, 1H), 7.31-7.34 (m, 2H), 6.98 (s, 4H), 3.81 (s, 3H), 2.26 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.6, 166.6, 147.5, 142.0, 141.6, 135.9, 130.5, 130.0, 129.7, 125.4, 124.3, 123.1, 122.2, 118.9, 115.5, 111.4, 52.8, 21.4; **HRMS** (ESI) m/z calcd. For $C_{20}H_{17}NO_3$ $[M+Na]^+$: 342.1106; Found 342.1101.



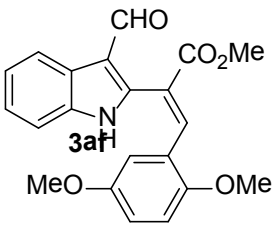
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-methoxyphenyl)acrylate (3ad): Yield 71%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.81 (s, 1H), 8.84 (br s, 1H), 8.55 (s, 1H), 8.28-8.30 (m, 1H), 7.37-7.39 (m, 1H), 7.28-7.31 (m, 2H), 7.22-7.24 (m, 1H), 6.86 (d, *J* = 8.28 Hz, 1H), 6.76 (d, *J* =7.8 Hz, 1H), 6.61(t, *J* = 8.0 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.7, 166.7, 158.5, 142.7, 142.0, 135.8, 132.2, 129.7, 125.4, 124.2, 122.9, 122.2, 122.1, 120.7, 119.9, 115.3, 111.3, 111.0, 55.6, 52.8; **HRMS** (ESI) m/z calcd. For $C_{20}H_{17}NO_4$ $[M+Na]^+$: 358.1055; Found 358.1050.



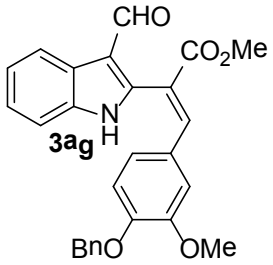
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-methoxyphenyl)acrylate (3ae): Yield 74%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.88 (s, 1H), 8.63 (br s, 1H), 8.35-8.37 (m, 1H), 8.17 (s, 1H), 7.41-7.43 (m, 1H), 7.33-7.35 (m, 2H), 7.05 (d, *J* = 8.76 Hz, 2H), 6.70 (d, *J* = 8.56 Hz, 2H), 3.82 (s, 3H), 3.74 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.7, 166.8, 161.7, 147.2, 142.6, 136.0, 132.6, 125.3 (2C), 124.2, 123.0, 122.2, 117.0, 115.4, 114.5, 111.5, 55.3, 52.7; **HRMS** (ESI) m/z calcd. For $C_{20}H_{17}NO_4$ $[M+Na]^+$: 358.1055; Found 358.1050.



(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2,5-dimethoxyphenyl)acrylate (3af): Yield 72%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.84 (s, 1H), 9.05 (br s, 1H), 8.51 (s, 1H), 8.27-8.29 (m, 1H), 7.32-7.35 (m, 1H), 7.25-7.28 (m, 2H), 6.75-6.78 (m, 2H), 6.16 (s, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.03 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.7, 166.7, 153.1, 153.0, 142.3, 142.2, 135.8, 125.3, 124.3, 123.0, 122.1, 122.0, 119.8, 119.4, 115.6, 112.8, 112.3, 111.3, 56.1, 55.0, 52.8; **HRMS** (ESI) m/z calcd. For $C_{21}H_{19}NO_5$ $[M+Na]^+$: 388.1161; Found 388.1155.

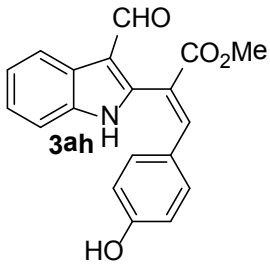


(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-benzyloxy-3-methoxyphenyl)acrylate (3ag): Yield



70%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.91 (s, 1H), 8.68 (br s, 1H), 8.33-8.36 (m, 1H), 8.11(s, 1H), 7.38-7.41 (m, 2H), 7.30-7.35 (m, 6H), 6.72-6.82 (m, 2H), 6.31 (s, 1H), 5.10 (s, 2H), 3.82 (s, 3H), 3.15 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.6, 166.7, 150.6, 149.3, 147.3, 142.5, 136.1, 135.8, 128.6, 128.1, 127.1, 126.1, 125.8, 125.3, 124.4, 123.2, 122.1, 117.2, 115.8, 112.9, 111.8, 111.4, 70.6, 55.0, 52.8; **HRMS** (ESI) m/z calcd. For $C_{27}H_{23}NO_5$ $[M+Na]^+$: 464.1474; Found 464.1468.

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-benzyloxy-3-methoxyphenyl)acrylate (3ah): Yield



76%; **^{1}H NMR (400 MHz, Acetone-d_6)** δ 11.17 (br s, 1H), 9.86 (s, 1H) 9.13 (br s 1H), 8.25-8.27 (m, 1H), 8.15 (s, 1H), 7.52-7.54 (m,1H), 7.26-732 (m, 2H), 7.04 (d, *J* = 8.56 Hz , 2H), 6.69 (d, *J* = 8.76 Hz, 2H), 3.75 (s, 3H); **^{13}C NMR (100 MHz, Acetone-d_6)** δ 185.3, 167.2, 160.8,147.3, 144.5, 137.5, 133.6, 126.4, 125.7, 124.5, 123.2, 122.3, 118.1, 116.6, 115.8, 112.8, 52.7 **HRMS** (ESI) m/z calcd. For $C_{19}H_{15}NO_4$ $[M-H]^-$: 320.0923; Found 320.0917.

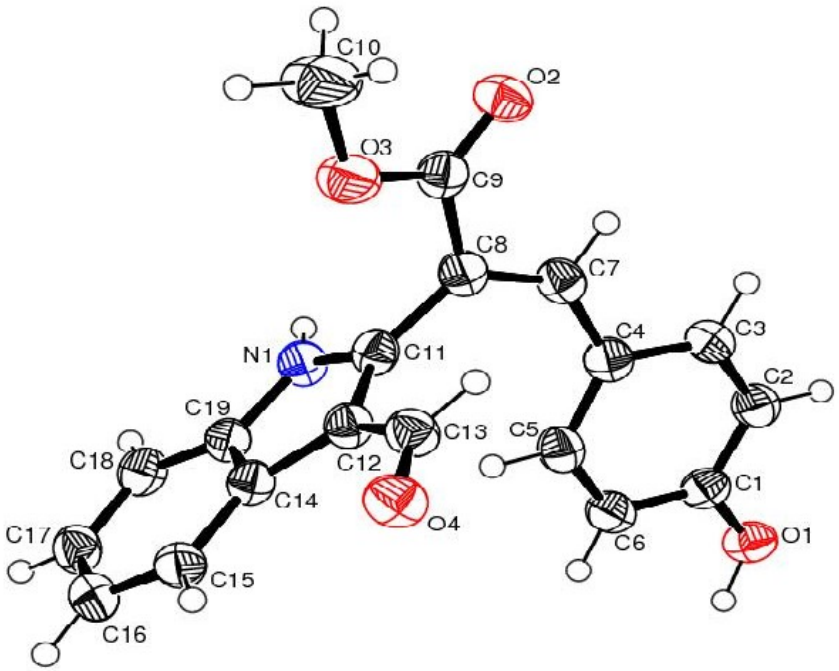
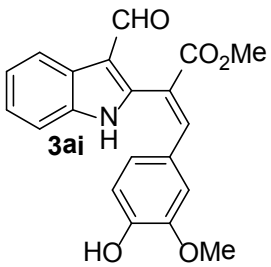


Figure 1. The molecular structure of compound **3ah (CCDC 952076)**

Table 1. Crystal data and structure refinement for **3ah**

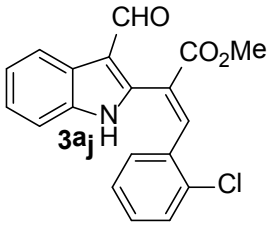
Compound	**Compound 3ah**
Empirical formula	$C_{19}H_{15}NO_4$
Molecular weight	321.32
Temperature	150(2) K
Wavelength (Å)	0.71073 A
Crystal system, space group	orthorhombic, p b c a
a (Å)	a = 9.3019(5) A
b (Å)	b = 16.7028(18) A
c (Å)	c = 20.7326(14) A
α (°)	alpha = 90 deg.
β (°)	beta = 90 deg.
γ (°)	gamma = 90 deg.
Volume ($Å^3$)	3221.2(4) A^3
Z, Calculated density (mg/m^3)	8, 1.325 Mg/m^3
Absorption coefficient (mm^{-1})	0.094 mm^-1
F(000)	1344
Crystal size (mm)	0.23 x 0.18 x 0.14 mm
θ range (deg)	2.94 to 25.00 deg
Limiting indices	-11<=h<=11, -19<=k<=19, -24<=l<=24
Reflections collected / unique	23304 / 2829 [R(int) = 0.0988]
Completeness to θ = 25.00	99.9 %
Max. and min. transmission	0.9870 and 0.9788
Data / restraints / parameters	2829 / 0 / 222
Goodness-of-fit on F^2	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0594, wR2 = 0.1613
R indices (all data)	R1 = 0.0743, wR2 = 0.1796
Absolute structure parameter	0.43 (3)
Largest diff. peak and hole ($e.A^{-3}$)	0.244 and -0.242 e.A^-3
CCDC	**952076**

(*E*)-methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-hydorxy-3-methoxyphenyl)acrylate (3ai): Yield 77%;

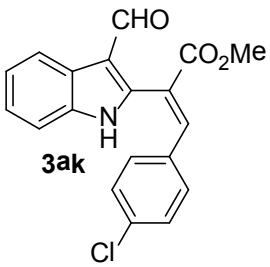


^{1}H NMR (400 MHz, Acetone-d_6) δ 11.21 (br s, 1H), 9.89 (s, 1H), 8.34 (s, 1H), 8.26 (d, *J* = 7.04 Hz, 1H), 8.13 (s, 1H), 7.54 (d, *J* = 7.28 Hz, 1H), 7.26-7.32 (m, 2H), 6.88 (d, *J* = 7.04 Hz, 1H), 6.74 (d, *J* = 8.28 Hz, 1H), 6.38 (s, 1H), 3.77 (s, 3H), 3.13 (s, 3H); **^{13}C NMR (100 MHz, Acetone-d_6)** δ 185.3, 167.1, 150.4, 148.2, 147.6, 144.5, 137.4, 127.4, 126.4, 126.0, 124.6, 123.3, 122.2, 118.2, 116.1, 116.0, 112.9, 112.7, 55.2, 52.7; **HRMS** (ESI) m/z calcd. For $C_{20}H_{17}NO_5$ $[M-H]^-$: 350.1029; Found 350.1023.

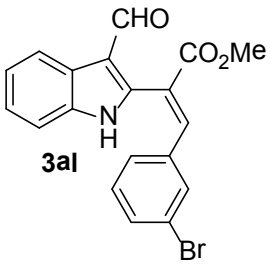
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-chlorophenyl)acrylate (3aj): Yield 82%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.81 (s, 1H), 8.93 (br s, 1H), 8.43 (s, 1H), 8.25-8.27 (m, 1H), 7.39-7.41(m, 2H), 7.28-7.33 (m, 2H), 7.19 (t, *J* = 8.28 Hz, 1H), 6.91 (t, *J* = 7.52 Hz, 1H), 6.81-6.83 (m, 1H), 3.90 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.3, 166.2, 143.5, 140.1, 135.8, 135.4, 132.0, 131.3, 130.1, 127.0, 125.3, 124.5, 123.1, 122.8, 122.1, 115.7, 111.4, 53.1; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}ClNO_3$ $[M+Na]^+$: 362.0560; Found 362.0554.



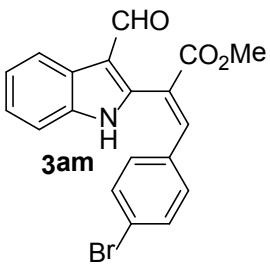
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-chlorophenyl)acrylate (3ak): Yield 85%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.85 (s, 1H), 8.78 (br s, 1H), 8.31-8.33 (m, 1H), 8.14 (s, 1H), 7.41-7.43 (m, 1H), 7.33-7.36 (m, 2H), 7.17 (d, *J* = 8.52Hz, 2H), 7.02 (d, *J* = 8.52Hz, 2H), 3.84 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.3, 166.2, 145.7, 140.8, 137.0, 135.9, 131.5, 131.3, 129.3, 125.3, 124.6, 123.3, 122.2, 120.7, 115.6, 111.5, 53.0; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}ClNO_3$ $[M+Na]^+$: 362.0560; Found 362.0554.



(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(3-bromophenyl)acrylate (3al): Yield 78%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.87 (s, 1H), 8.72 (br s, 1H), 8.31-8.33 (m,1H), 8.10 (s, 1H), 7.39-7.44 (m, 2H), 7.31-7.36 (m, 3H), 7.01 (t, *J* = 8.04 Hz, 1H), 6.90-6.92 (m, 1H), 3.85 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.2, 166.1, 145.2, 140.6, 135.9, 134.9, 133.8, 133.5, 130.4, 127.8, 125.3, 124.6, 123.2, 122.9, 122.1, 121.9, 115.6, 111.5, 53.1; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}NO_3Br$ $[M+Na]^+$: 406.0055; Found 406.0049, 408.0030.



(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(4-bromophenyl)acrylate (3am): Yield 81%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.84 (s, 1H), 8.92 (br s, 1H), 8.30-8.32 (m, 1H), 8.11 (s, 1H), 7.40-7.42 (m, 1H), 7.31-7.34 (m, 4H), 6.94 (d, *J* = 8.52 Hz, 2H), 3.83(s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.3, 166.3, 145.8, 140.9, 135.9, 132.3, 131.7, 131.7, 125.4, 125.3, 124.6, 123.3, 122.2, 120.9, 115.6, 111.5, 53.0; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}NO_3Br$ $[M+Na]^+$: 406.0055; Found 406.0049, 408.0030.



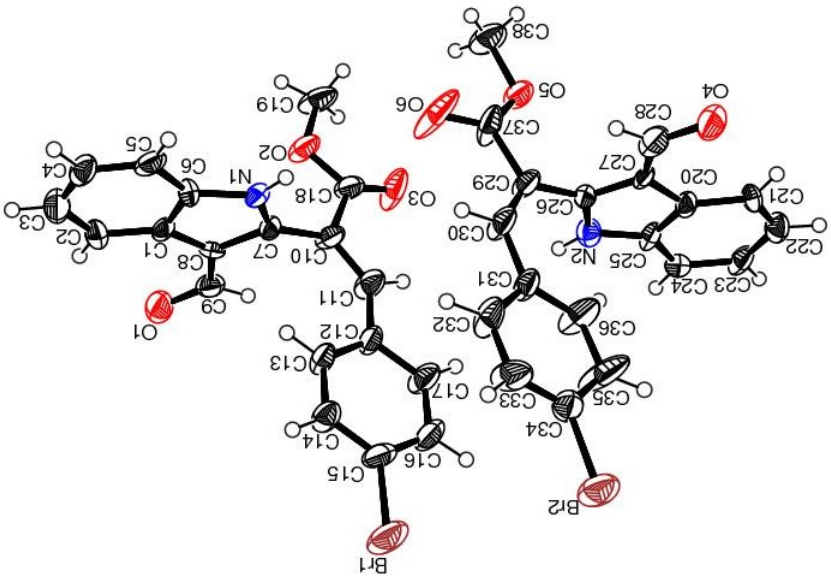
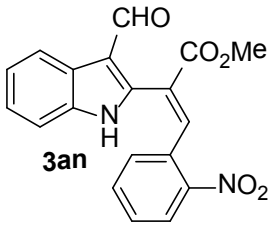


Figure 2. The molecular structure of compound **3am (CCDC 952075)**

Table 2. Crystal data and structure refinement for **3am**

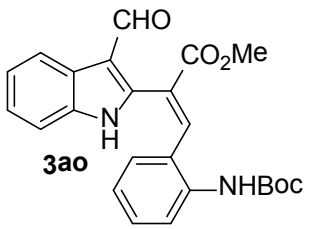
Compound	**Compound 3am**
Empirical formula	C_{19} H_{14} N O_3 Br
Molecular weight	384.22
Temperature	150(2) K
Wavelength (Å)	0.71073 A
Crystal system, space group	Monoclinic, P 21
a (Å)	a = 11.3964(9) A
b (Å)	b = 7.3357 (6) A
c (Å)	c = 20.4793(7) A
α (°)	alpha = 90 deg.
β (°)	beta = 103.585 (5) deg.
γ (°)	gamma = 90 deg.
Volume (Å^3)	1664.2 (2) A^3
Z, Calculated density (mg/m^3)	4, 1.534 Mg/m^3
Absorption coefficient (mm^{-1})	2.486 mm^-1
F(000)	776
Crystal size (mm)	0.16 × 0.08 × 0.06 mm
θ range (deg)	2.96 to 27.50 deg
Limiting indices	-13<=h<=14, -9<=k<=8, -26<=l<=25
Reflections collected / unique	15880 / 7267 [R(int) = 0.0589]
Completeness to θ = 25.00	99.8 %
Max. and min. transmission	0.8651 and 0.6918
Data / restraints / parameters	7267 / 1/ 436
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0574, wR2 = 0.01295
R indices (all data)	R1 = 0.0988, wR2 = 0.01596
Absolute structure parameter	0.43 (3)
Largest diff. peak and hole (e.A^{-3})	0.469 and -0.679 e.A^-3
CCDC	**952075**

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-nitrophenyl)acrylate (3an): Yield 68%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.84 (s, 1H), 9.06 (br s, 1H), 8.43 (s, 1H), 8.19 (d, *J* = 7.52 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H) 7.38-7.44 (m, 2H), 7.28-7.35 (m, 3H), 6.99 (d, *J* = 7.52 Hz, 1H), 3.93 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.4, 165.9, 148.1, 143.8, 139.3, 135.9, 133.9, 130.9, 130.4, 130.3, 125.3, 125.2, 124.6, 123.3, 123.1, 121.9, 116.5, 111.4, 53.2; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}N_2O_5$ $[M+Na]^+$: 373.0800; Found 373.0795.



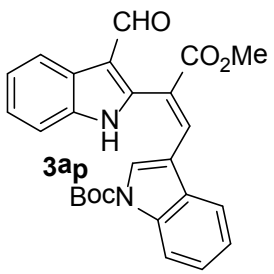
3an

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-[2-(tert-butoxycarbonyl)aminophenyl]acrylate (3ao): Yield 72%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.11 (s, 1H), 10.02 (br s, 1H), 8.24 (d, *J* = 7.52 Hz, 1H), 8.13 (s, 1H), 7.20-7.24 (m, 5H), 6.90-6.94 (m, 1H), 6.83-6.85 (m, 1H), 6.66 (s, 1H), 3.81 (s, 3H), 1.51 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.3, 166.2, 154.5, 144.2, 140.8, 135.6, 135.6, 131.8, 130.1, 129.2, 126.8, 125.8, 125.2, 124.7, 123.8, 122.7, 121.1, 116.8, 111.8, 81.7, 52.8, 28.1; **HRMS** (ESI) m/z calcd. For $C_{24}H_{24}N_2O_5$ $[M+H]^+$: 421.1764; Found 421.1758.



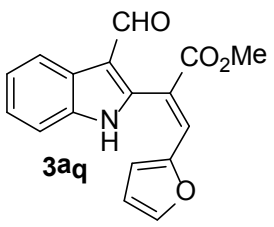
3ao

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(N-(tert-butoxycarbonyl-indol-3-yl)acrylate (3ap): Yield 75%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.96 (s, 1H), 8.66 (br s, 1H), 8.46 (s, 1H), 8.36-8.39 (m, 1H), 8.14 (d, *J* = 7.96 Hz, 1H), 7.66 (d, *J* = 7.76 Hz, 1H), 7.43-7.45 (m, 1H), 7.27-7.37 (m, 4H), 6.73 (s, 1H), 3.85 (s, 3H), 1.24 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.4, 166.4, 148.3, 142.7, 137.8, 136.0, 135.1, 129.1, 127.9, 125.5, 125.3, 124.5, 123.7, 123.2, 122.3, 118.3, 118.2, 115.4, 115.3, 113.7, 111.4, 84.6, 52.8, 27.5; **HRMS** (ESI) m/z calcd. For $C_{26}H_{24}N_2O_5$ $[M+H]^+$: 445.1764; Found 445.1758.



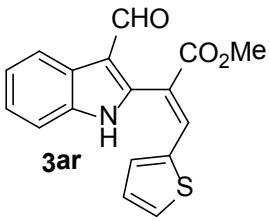
3ap

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-furyl)acrylate (3aq): Yield 76%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.89 (s, 1H), 8.83 (br s, 1H), 8.36-8.38 (m, 1H), 8.00 (s, 1H), 7.42-7.44 (m, 1H), 7.32-7.35 (m, 3H), 6.34-6.38 (m, 2H), 3.81 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 185.5, 166.4, 149.3, 146.5, 141.8, 135.8, 133.2, 125.3, 124.3, 123.0, 122.2, 118.5, 116.2, 115.7, 112.9, 111.3, 52.9; **HRMS** (ESI) m/z calcd. For $C_{17}H_{13}NO_4$ $[M+Na]^+$: 318.0742; Found 318.0737.



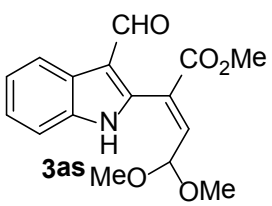
3aq

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-thiophenyl)acrylate (3ar): Yield 78%; **^{1}H NMR (400 MHz, DMSO-d$_6$)** δ 12.30 (br s, 1H), 9.78 (s, 1H), 8.47 (s, 1H), 8.17 (d, *J* = 7.28 Hz, 1H), 7.66 (s, 2H), 7.52 (d, *J* = 7.52 Hz, 1H), 7.26-7.33 (m, 2H), 7.08-7.10 (m, 1H), 3.74 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d$_6$)** δ 184.5, 165.8, 142.0, 139.9, 136.7, 136.6, 134.0, 127.5, 125.2, 123.7, 122.4, 121.0, 116.6, 115.1, 112.3, 52.5; **HRMS** (ESI) m/z calcd. For $C_{17}H_{13}NO_3S$ $[M+Na]^+$: 334.0514; Found 334. 0508.

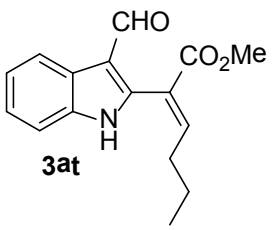


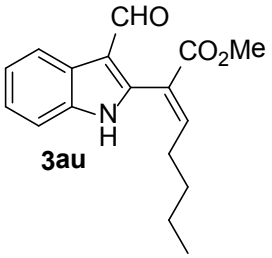
General procedure for the synthesis of (*E*)-methyl α-(3-formyl-1*H*-indol-2-yl)-β-alkyl-substituted acrylates: To a stirred solution of methyl 2-(3-formyl-1*H*-indol-2-yl)acetate (0.2 mmol), aldehydes (0.6 mmol) and L-proline (0.05 mmol) in dry DMSO (1.0 mL) at room temperature under argon atmosphere. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3 × 10 mL), washed with water and brine respectively and dried with Na_2SO_4. The organic phase was evaporated by rotary evaporator under reduced pressure to give the crude product. The crude product was purified by column chromatography over silica gel to furnish the pure product. The product was characterized by corresponding spectroscopic data (^{1}H NMR, ^{13}C NMR and HRMS).

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-dimethoxymethylacrylate (3as): Yield 86%; dr (82:18); **^{1}H NMR (400 MHz, CDCl$_3$)** δ (major isomer) 9.97 (s, 1H), 9.51 (br s, 1H), 8.31-8.34 (m, 1H), 7.42-7.45 (m, 1H), 7.30-7.34 (m, 2H), 7.25 (d, *J* = 7.28 Hz, 1H), 4.84 (d, *J* = 7.56 Hz, 1H), 3.81 (s, 3H), 3.34 (s, 6H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ (major isomer) 185.5, 165.5, 143.6, 138.6, 135.6, 126.5, 125.4, 124.6, 123.2, 121.6, 117.1, 111.5, 99.6, 53.1, 53.0; **HRMS** (ESI) m/z calcd. For $C_{16}H_{17}NO_5$ $[M+Na]^+$: 326.1004; Found 326.0999.



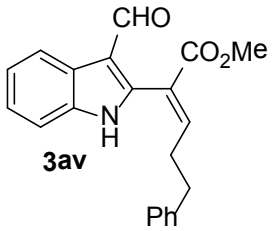
(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-propylacrylate (3at): Yield 81%; dr (4:1) **^{1}H NMR (400 MHz, CDCl$_3$)** δ 9.86 (s, 1H), 9.11 (br s, 1H), 8.34-8.36 (m, 1H), 7.46 (t, *J* = 7.80 Hz, 1H), 7.39-7.42 (m, 1H), 7.29-7.33 (m, 2H), 3.79 (s, 3H), 2.18-2.24 (m, 2H), 1.43-1.52 (m, 2H), 0.86 (t, *J* = 7.28 Hz, 3H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ (major isomer) 185.6, 166.0, 153.1, 141.8, 135.8, 125.0, 124.3, 123.0, 122.8, 121.9, 116.4, 111.3, 52.6, 32.4, 21.7, 13.7; **HRMS** (ESI) m/z calcd. For $C_{16}H_{17}NO_3$ $[M+Na]^+$: 294.1106; Found 294.1101.



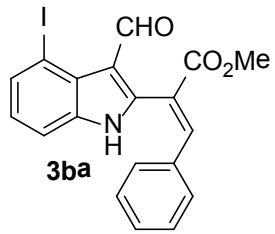


(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-butylacrylate (3au): Yield 85%; dr (4:1); **^{1}H NMR (400 MHz, $CDCl_3$)** δ (major isomer) 9.86 (s, 1H), 9.21 (br s, 1H), 8.34-8.36 (m, 1H), 7.46 (t, *J* = 7.52 Hz, 1H), 7.39-7.41 (m, 1H), 7.29-7.31 (m, 2H), 3.78 (s, 3H), 2.20-2.24 (m, 2H), 1.38-1.46 (m, 2H), 1.22-1.29 (m, 2H), 0.81 (t, *J* = 7.24 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (major isomer) 185.6, 166.0, 153.3, 141.9, 135.8, 125.0, 124.3, 123.0, 122.6, 121.9, 116.4, 111.3, 52.6, 30.5, 30.2, 22.3, 13.7; **HRMS** (ESI) m/z calcd. For $C_{17}H_{19}NO_3$ $[M+Na]^+$: 308.1263; Found 308.1257.

(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-phenylethyl)acrylate (3av): Yield 83%; dr 4:1; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (major isomer) 9.71 (s, 1H), 8.19-8.21 (m, 1H), 7.54 (br s, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.25-7.27 (m, 3H), 7.17-7.22 (m, 2H), 7.11-7.13 (m, 1H), 6.98-7.00 (m, 2H), 3.67(s, 1H), 2.73 (t, *J* = 6.76 Hz, 2H), 2.37-2.43(m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (major isomer) 185.4, 165.6, 151.1, 141.3, 140.2, 135.5, 128.8, 128.7, 126.5, 125.0, 124.1, 124.1, 122.9, 121.6, 116.3, 111.4, 52.6, 34.2, 32.4; **HRMS** (ESI) m/z calcd. For $C_{21}H_{19}NO_3$ $[M+H]^+$: 334.1443; Found 334.1438.

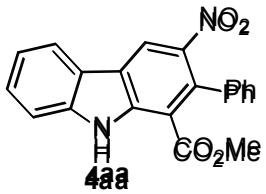


(*E*)-Methyl α-(3-formyl-1*H*-indol-2-yl)-β-(2-phenylethyl)acrylate (3ba): Yield 55%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.30 (s, 1H), 8.50 (br s, 1H), 7.99 (s, 1H), 7.82-7.84 (m, 1H), 7.31-7.35 (m, 2H), 7.18-7.21 (m, 2H), 6.97-6.99 (m, 3H), 3.79 (s, 3H); **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}INO_3$ $[M+Na]^+$: 453.9916; Found 453.9911.



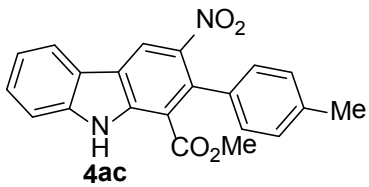
General procedure for the synthesis of carabazole derivatives: To a stirred solution of (*E*)-methyl α-(3-formyl-1*H*-indol-2-yl)-β-aryl/alky substituted acrylate (0.15 mmol), nitromethane (0.45 mmol) and DBU (35 mol%) in dry THF (0.4 mL) at room temperature under air or oxygen. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3 × 10 mL), washed with dilute HCl (1N), brine and dried with Na_2SO_4. The organic phase was evaporated by rotary evaporator under reduced pressure to give the crude product. The crude product was purified by column chromatography over silica gel to furnish the pure product. The product was fully characterized by their corresponding spectroscopic data (^{1}H NMR, ^{13}C NMR and HRMS).

1-Methoxycarbonyl-2-phenyl-3-nitro-9*H*-carbazole (4aa): Yield 81%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.94 (s, 1H), 8.65 (s, 1H), 8.05 (d, *J* = 7.76 Hz, 1H), 7.50-7.48 (m, 2H), 7.35-7.28 (m, 4H), 7.22-7.19 (m, 2H), 3.48 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.6, 143.7, 141.4, 140.6, 137.0, 135.4, 128.5, 128.2, 128.0, 127.8, 123.3, 122.2, 121.4, 121.0, 120.1, 112.7, 111.8, 52.2; HRMS (ESI) m/z calcd For $C_{20}H_{14}N_2O_4[M+Na]^+$ 369.0851; Found 369.0846.



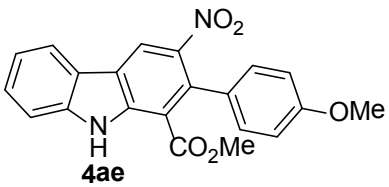
4aa

1-Methoxycarbonyl-2-(4-methylphenyl)-3-nitro-9*H*-carbazole (4ac): Yield 78%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.95 (s, 1H), 8.68 (s, 1H), 8.13-8.11 (m, 1H), 7.57-7.54 (m, 2H), 7.39-7.35 (m, 1H), 7.23-7.16 (m, 4H), 3.59 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.6, 144.0, 141.3, 140.6, 137.5, 135.4, 133.9, 128.6, 128.4, 128.1, 123.1, 122.2, 121.3, 121.0, 119.9, 112.8, 111.7, 52.2, 21.4; HRMS (ESI) m/z calcd For $C_{21}H_{16}N_2O_4[M+Na]^+$ 383.1008; Found 383.1002.



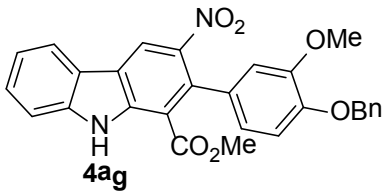
4ac

1-Methoxycarbonyl-2-(4-methoxyphenyl)-3-nitro-9*H*-carbazole (4ae): Yield 76%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.97 (s, 1H), 8.67 (s, 1H), 8.12 (d, *J* = 8.04 Hz, 1H), 7.59-7.56 (m, 2H), 7.39-7.35 (m, 1H), 7.20 (d, *J* = 8.52 Hz, 2H), 6.94 (d, *J* = 8.52 Hz, 2H), 3.87 (s, 3H), 3.61 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.7, 159.3, 144.2, 141.3, 140.6, 135.0, 129.7, 129.0, 128.1, 123.1, 122.2, 121.3, 120.1, 119.9, 113.4, 112.9, 111.7, 55.3, 52.3; **HRMS** (ESI) m/z calcd For $C_{21}H_{16}N_2O_5[M+Na]^+$ 399.0957; Found 399.0951.



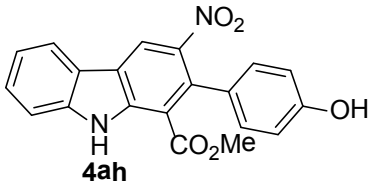
4ae

1-Methoxycarbonyl-2-(4-benzyloxy-3-methoxyphenyl)-3-nitro-9*H*-carbazole (4ag): Yield 74%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.94 (s, 1H), 8.66 (s, 1H), 8.11 (dd, *J* = 0.8, 8.0 Hz, 1H), 7.53-7.58 (m, 2H), 7.47-7.49 (m, 2H), 7.29-7.40 (m, 4H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.84-6.85 (m, 1H), 6.74-6.76 (m, 1H), 5.20-5.22 (m, 2H), 3.87 (s, 3H), 3.54 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.8, 149.2, 147.9, 144.0, 141.3, 140.6, 137.1, 134.7, 129.9, 128.6, 128.1, 127.9, 127.4, 123.1, 122.2, 121.4, 121.1, 121.0, 119.7, 113.5, 113.0, 112.7, 111.7, 71.1, 56.2, 52.2; HRMS (ESI) m/z calcd For $C_{28}H_{22}N_2O_6[M+Na]^+$ 505.1376; Found 505.1370.



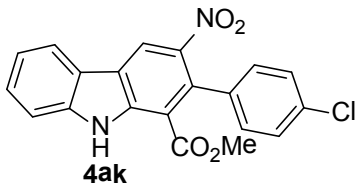
4ag

1-Methoxycarbonyl-2-(4-hydroxyphenyl)-3-nitro-9*H*-carbazole (4ah) : Yield 71%; **^{1}H NMR (400 MHz, DMSO-d$_6$)** δ 11.83 (br s, 1H), 9.60 (br s, 1H), 9.01 (s, 1H), 8.34 (d, *J* = 7.76 Hz, 1H), 7.68 (d, *J* = 8.04 Hz, 1H), 7.53-7.57 (m, 1H), 7.30-7.34 (m, 1H), 7.05 (d, *J* = 8.28 Hz, 2H), 6.79 (d, *J* = 8.52 Hz, 2H), 3.66 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d$_6$)** δ 166.1, 157.1, 142.7, 141.4, 138.6, 132.3, 129.6, 127.7, 126.5, 122.0, 121.7, 121.3, 120.6, 119.1, 116.0, 115.0, 112.3, 52.4; **HRMS** (ESI) m/z calcd. For $C_{20}H_{14}N_2O_5$ $[M+Na]^+$: 385.0800; Found 385.0795.



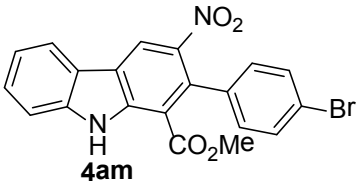
4ah

1-Methoxycarbonyl-2-(4-chlorophenyl)-3-nitro-9*H*-carbazole (4ak): Yield 82%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.07 (s, 1H), 8.75 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.56-7.61 (m, 2H), 7.37-7.41 (m, 3H), 7.21-7.24 (m, 2H), 3.61 (s, 3H); **^{13}C NMR (100 MHz, CDCl$_3$) δ** 167.3, 143.5, 141.5, 140.7, 135.6, 134.1, 133.9, 129.9, 128.4, 128.0, 123.6, 122.1, 121.5, 121.1, 120.3, 112.4, 111.8, 52.3; HRMS (ESI) m/z calcd For $C_{20}H_{13}ClN_2O_4[M+Na]^+$ 403.0462; Found 403.0456.



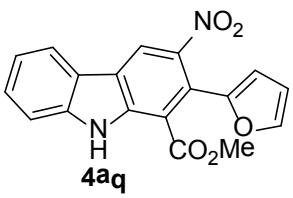
4ak

1-Methoxycarbonyl-2-(4-bromophenyl)-3-nitro-9*H*-carbazole (4am): Yield 79%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.07 (s, 1H), 8.74 (d, *J* = 0.76 Hz, 1H), 8.13 (dd, *J* = 0.8, 7.76 Hz, 1H), 7.59-7.53 (m, 4H), 7.41-7.37 (m, 1H), 7.17-7.15 (m, 2H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 143.4, 141.5, 140.7, 136.1, 134. 1, 130.9, 130.2, 128.4, 123.6, 122.1, 122.0, 121.5, 121.0, 120.3, 112.3, 111.8, 52.3; HRMS (ESI) m/z calcd For $C_{20}H_{13}BrN_2O_4[M+Na]^+$ 446.9956; Found 446.9951 and [M+Na+2] 448.9931.



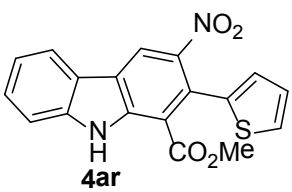
4am

1-Methoxycarbonyl-2-(2-furyl)-3-nitro-9*H*-carbazole (4aq): Yield 82%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 9.99 (s, 1H), 8.70 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.53-7.61 (m, 3H), 7.35-7.38 (m, 1H), 6.52-6.53 (m, 1H), 6.42-6.44 (m, 1H), 3.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 146.9, 143.4, 143.0, 141.1, 140.8, 128.6, 124.3, 123.8, 122.0, 121.5, 121.1, 120.1, 113.4, 111.8, 111.4, 110.1, 52.9; HRMS (ESI) m/z calcd For $C_{18}H_{12}N_2O_5[M+Na]^+$ 359.0644; Found 359.0638.



4aq

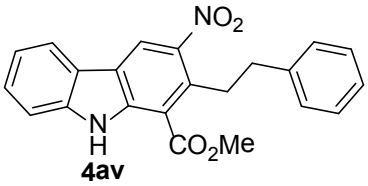
1-Methoxycarbonyl-2-(2-thiophenyl)-3-nitro-9*H*-carbazole (4ar): Yield 84%; **^{1}H NMR (400 MHz, CDCl$_3$)** δ 9.96 (s, 1H), 8.65 (s, 1H), 8.11 (d, *J* =7.2 Hz, 1H), 7.62-7.52 (m, 2H), 7.46 (dd, *J* = 0.16 Hz, 5.2 Hz, 1H), 7.39-7.35 (m, 1H), 7.09-7.07 (m, 1H), 7.02-7.01 (m, 1H), 3.69 (s, 3H); **^{13}C NMR (100 MHz, CDCl$_3$)** δ 167.3, 144.6, 141.0, 140.7, 136.4, 128.5, 128.1, 127.1, 127.0, 126.7, 124.0, 122.1, 121.5,



4ar

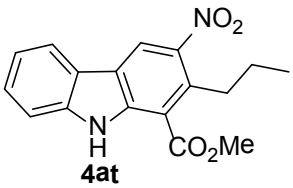
121.1, 119.6, 114.1, 111.8, 52.6 ; **HRMS** (ESI) m/z calcd For $C_{18}H_{12}N_2O_4S[M+Na]^+$ 375.0415; Found 375.0410.

1-Methoxycarbonyl-2-(2-ethylphenyl)-3-nitro-9*H*-carbazole (4av): Yield 92%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.03 (s, 1H), 8.70 (d, *J* = 0.48 Hz, 1H), 8.08 (dd, *J* = 0.80 Hz, 7.6 Hz, 1H), 7.53-7.55 (m, 2H), 7.31-7.37 (m, 5H), 7.22-7.27 (m, 1H), 4.11 (s, 3H), 3.54-3.59 (m, 2H), 3.06-3.11 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.5, 144.7, 142.3, 141.7, 140.3, 136.1, 128.5 (2C), 127.9, 126.2, 122.5, 122.2, 121.3, 121.2, 120.8, 112.2, 111.6, 52.7, 37.7, 32.7; **HRMS** (ESI) m/z calcd For $C_{22}H_{18}N_2O_4[M+Na]^+$ 397.1164; Found 397.1159.



4av

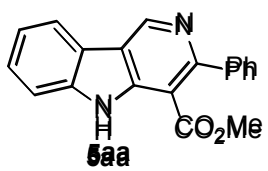
1-Methoxycarbonyl-2-propyl-3-nitro-9*H*-carbazole (4at) : Yield 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.96 (s, 1H), 8.61 (s, 1H), 8.05 (d, *J* = 7.78 Hz, 1H), 7.48-7.53 (m, 2H), 7.30-7.34 (m, 1H), 4.09 (s, 3H), 3.20-3.24 (m, 2H), 1.70-1.80 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.7, 144.8, 142.2, 140.2, 137.2, 127.8, 122.2 (2C), 121.2, 120.9, 120.7, 112.1, 111.5, 52.6, 32.2, 25.3, 14.5; HRMS (ESI) m/z calcd For $C_{17}H_{16}N_2O_4[M+Na]^+$ 335.1002; Found 335.1021.



4at

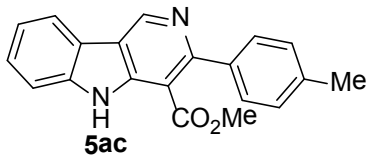
General procedure for the synthesis of substituted γ-carboline derivatives: A homogeneous solution of (*E*)-methyl α-(3-formyl-1*H*-indol-2-yl)-β-aryl/alky substituted acrylates (0.15 mmol) and ammonium acetate (0.225 mmol) in DMSO (1.0 mL) was stirred at room temperature under air or oxygen. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was extracted with ethyl acetate (3 × 10 mL), washed with brine and dried with Na_2SO_4. The organic phase was evaporated by rotary evaporator under reduced pressure to give the crude product. The crude product was purified by column chromatography over silica gel to furnish the pure product. The products were characterized by their corresponding spectroscopic data (^{1}H NMR, ^{13}C NMR and HRMS).

Methyl 3-phenyl-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.89 (br s, 1H), 9.38 (s, 1H), 8.17 (d, *J* = 7.76 Hz, 1H), 7.52-7.58 (m, 4H), 7.42-7.48 (m, 3H), 7.35-7.39 (m, 1H), 3.70 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.4, 156.9, 145.2, 143.6, 141.7, 139.9, 129.1, 128.1, 127.8, 127.5, 121.5, 121.1, 120.9, 119.8, 111.5, 107.6, 51.9; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}N_2O_2$ $[M+H]^+$: 303.1134; Found 303.1128.



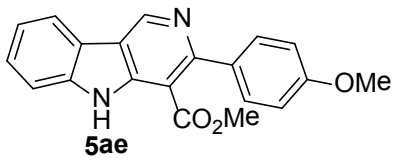
5aa

Methyl 3-(4-methylphenyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 93%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.84 (br s, 1H), 9.36 (s, 1H), 8.15(d, *J* = 7.76 Hz, 1H), 7.51-7.53 (m, 2H), 7.47(d, *J* = 8.0 Hz, 2H), 7.34-7.38 (m, 1H), 7.25 (d, *J* = 7.76 Hz, 2H), 3.73 (s, 3H), 2.43 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.6, 159.9, 145.2, 143.6, 139.9, 138.7, 137.9, 129.1, 128.5, 127.4, 121.4, 121.1, 120.8, 119.6, 111.4, 107.5, 51.9, 21.3; **HRMS** (ESI) m/z calcd. For $C_{20}H_{16}N_2O_2$ $[M+H]^+$: 317.1290; Found 317.1285.



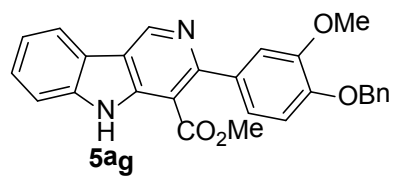
5ac

Methyl 3-(4-methoxyphenyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 89%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.83 (br s, 1H), 9.34 (s, 1H), 8.15 (d, *J* = 7.80 Hz, 1H), 7.50-7.55 (m, 4H), 7.34-7.38 (m, 1H), 6.98 (d, *J* = 8.76 Hz, 2H), 3.88 (s, 3H), 3.75 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.8, 159.8, 156.5, 145.3, 143.6, 139.9, 134.1, 130.6, 127.4, 121.4, 121.2, 120.8, 119.4, 113.3, 111.4, 107.2, 55.3, 51.9; **HRMS** (ESI) m/z calcd. For $C_{20}H_{16}N_2O_3$ $[M+H]^+$: 333.1239; Found 333.1234.



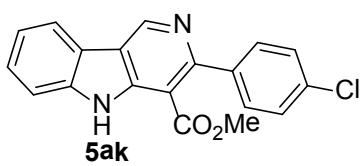
5ae

Methyl 3-(4-benzyloxy-3-methoxyphenyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 86%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.82 (br s, 1H), 9.33 (s, 1H), 8.15 (d, *J* = 7.76 Hz, 1H), 7.52-7.54 (m, 2H), 7.46-7.48 (m, 2H), 7.34-7.39 (m, 3H), 7.28-7.32(m, 1H), 722-7.23(m, 1H), 7.00-7.03(m, 1H), 6.94-6.96 (m, 1H), 5.24 (s, 2H), 3.96 (s, 3H), 3.70 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.5, 156.1, 149.2, 148.3, 145.1, 143.3, 139.9, 137.0, 134.7, 128.4, 127.8, 127.4, 127.3, 122.0, 121.4, 121.0, 120.7, 119.5, 113.3, 112.8, 111.4, 107.5, 70.9, 56.0, 51.9; **HRMS** (ESI) m/z calcd. For $C_{27}H_{22}N_2O_4$ $[M+H]^+$: 439.1657; Found 439.1652.



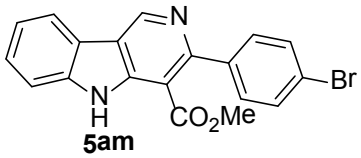
5ag

Methyl 3-(4-chlorophenyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.92 (br s, 1H), 9.36 (s, 1H), 8.16 (d, *J* = 7.76 Hz, 1H), 7.54-7.55 (m, 2H), 7.50 (d, *J* = 8.56 Hz, 2H), 7.42 (d, *J* = 8.28, 2H), 7.36-7.40 (m, 1H), 3.74 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.1, 155.6, 145.2, 143.7, 140.2, 140.0, 134.2, 130.5, 128.0, 127.7, 121.6, 121.0, 120.9,120.0, 111.5, 107.5, 52.0; **HRMS** (ESI) m/z calcd. For $C_{19}H_{13}N_2O_2Cl$ $[M+H]^+$: 337.0744; Found 337.0738.



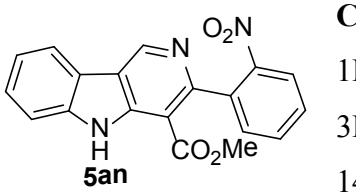
5ak

Methyl 3-(4-bromophenyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 96%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.92 (br s, 1H), 9.36 (s, 1H), 8.16 (d, *J* = 7.76 Hz, 1H), 7.54-7.59 (m, 4H), 7.43-7.45 (m, 2H), 7.36-7.40 (m, 1H), 3.74 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.1, 155.6, 145.2, 143.7, 140.7, 140.0, 130.9, 130.8, 127.7, 122.5, 121.6, 121.0, 120.9, 120.1, 111.5, 107.5, 52.0; **HRMS** (ESI) m/z calcd. For $C_{19}H_{14}N_2O_2Br$ $[M]^+$: 381.0238; Found 381.0233, 383.0214.



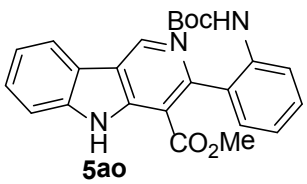
5am

Methyl 3-(2-nitrophenyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 93%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.08 (br s, 1H), 9.34 (s, 1H), 8.16-8.21 (m, 2H), 7.69-7.72 (m, 1H), 7.56-7.60 (m, 3H), 7.44 (d, *J* = 7.52 Hz, 1H), 7.37-7.41 (m, 1H), 3.70(s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.7, 154.1, 147.8, 144.9, 144.2, 140.0, 138.1, 133.0, 131.3, 128.6, 127.9, 124.0, 121.7, 120.0, 120.9, 120.7, 111.6, 107.0, 52.2; **HRMS** (ESI) m/z calcd. For $C_{19}H_{13}N_3O_4$ $[M+H]^+$: 348.0948; Found 348.0979.



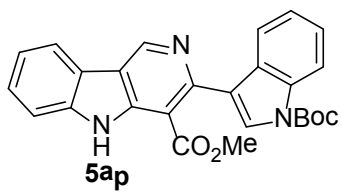
5an

Methyl 3-[2-(*tert*-butoxycarbonyl)aminophenyl]-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 86%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.98 (br s, 1H), 9.37 (s, 1H), 8.16-8.20 (m, 3H), 7.55-7.58 (m, 2H), 7.36-7.41 (m, 2H), 7.15-7.17 (m, 1H), 7.05-7.08 (m, 1H), 3.66 (s, 3H), 1.46 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.0, 154.3, 153.0, 145.4, 143.2, 139.9, 136.0, 130.8, 129.9, 129.1, 127.8, 122.1, 121.6, 120.9, 120.9, 120.5, 119.9, 111.6, 109.0, 80.1, 52.0, 28.3; **HRMS** (ESI) m/z calcd. For $C_{24}H_{23}N_3O_4$ $[M+H]^+$: 418.1767; Found 418.1761.



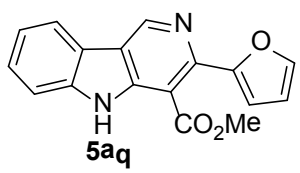
5ao

Methyl 3-[N-*tert*-butoxycarbonyl-3-indolyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 94%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.00 (br s, 1H), 9.40 (s, 1H), 8.28 (d, *J* = 7.04 Hz, 1H), 8.17 (d, *J* = 7.52Hz, 1H), 8.00 (s, 1H), 7.52-7.55 (m, 2H), 7.45-7.47 (m, 1H), 7.32-7.39 (m, 2H), 7.22-7.26 (m, 1H), 3.53 (s, 3H), 1.69 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.3, 149.6, 145.2, 144.4, 139.9, 135.3, 129.7, 127.5, 125.5, 124.3, 123.0,122.9, 121.5, 121.1, 120.8, 120.8, 119.8, 119.2, 115.4, 111.5, 108.4, 83.8, 52.0, 28.1 **HRMS** (ESI) m/z calcd. For $C_{26}H_{23}N_3O_4$ $[M+H]^+$: 442.1767; Found 331.1761.



5ap

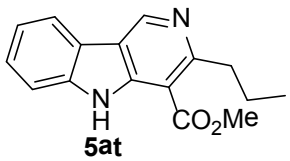
Methyl 3-(2-furyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 90%; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 12.80 (br s, 1H), 9.66 (s, 1H), 8.45(d, *J* = 7.76 Hz, 1H), 8.03 (s, 1H), 7.76(d, *J* = 8.28 Hz, 1H), 7.64 (t, *J* = 7.52 Hz, 1H), 7.43-7.48 (m, 2H), 6.80 (s, 1H), 4.01 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 164.9,



5aq

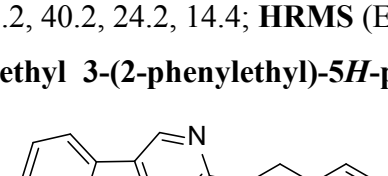
147.3, 146.3, 143.3, 141.5, 139.1, 136.6, 128.8, 122.3, 121.9, 120.4, 119.4, 113.9, 112.8, 112.7, 108.9, 53.2; **HRMS** (ESI) m/z calcd. For $C_{17}H_{12}N_2O_3$ $[M+H]^+$: 293.0926; Found 293.0921.

Methyl 3-(2-propyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 91%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.98 (br s, 1H), 9.26 (s, 1H), 8.11 (d, *J* = 7.76 Hz; 1H), 7.47-7.53 (m, 2H), 7.31-7.35 (m, 1H), 4.08 (s,3H), 3.30-3.34 (m, 2H), 1.18-1.83 (m, 2H), 1.05 (t, *J* = 7.28 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.1, 161.0, 145.6, 144.1, 139.5, 127.1, 121.3, 121.2, 120.6, 119.3, 111.3, 107.1, 52.2, 40.2, 24.2, 14.4; **HRMS** (ESI) m/z calcd. For $C_{16}H_{16}N_2O_2$ $[M+H]^+$: 269.1290; Found 269.1285.



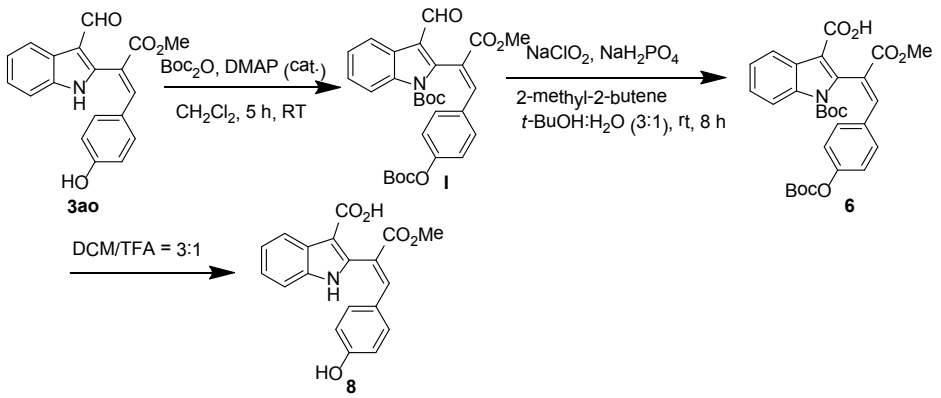
5at

Methyl 3-(2-phenylethyl)-5*H*-pyrido[4,3-*b*]indole-4-carboxylate: Yield 95%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.01 (br s, 1H), 9.30 (s, 1H), 8.13 (d, *J* = 7.76 Hz, 1H), 7.49-7.54 (m, 2H), 7.33-7.37 (m, 1H), 7.29-7.31 (m, 4H), 7.20-7.23 (m, 1H), 4.07 (s, 3H), 3.63-3.67 (m, 2H), 3.07-3.11 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.8, 159.6, 145.5, 144.1, 142.1, 139.5, 128.5, 128.3, 127.2, 125.9, 121.3, 121.0, 120.6, 119.5, 111.4, 107.3, 52.3, 40.2, 37.0 **HRMS** (ESI) m/z calcd. For $C_{21}H_{18}N_2O_2$ $[M+H]^+$: 331.1446; Found 331.1441.



5av

Synthesis of prenostodione (8) from 3ao:

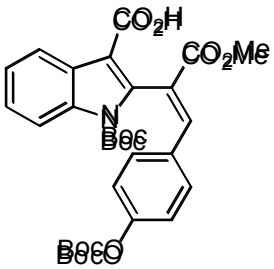


To a stirred solution of compound **3ao** (321 mg, 1.0 mmol) and DMAP (12.2 mg, 0.1 mmol) at 0 ºC in DCM was added Boc_2O (545 mg, 2.5 mmol). The stirring was continued for 5 h at room temperature, and then the reaction mixture was extracted with DCM before being quenched with dilute HCl. Evaporation of the solvent left the crude product which was sufficiently pure and used directly for the next step.

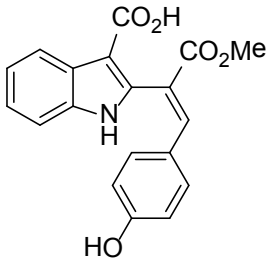
A heterogeneous mixture of aldehyde **I** (1.0 mmol) and 2-methyl-2-butene (280 mg, 4.0 mmol) in *t*-BuOH:H_2O (3:1 = 20 mL) were added $NaH_2PO_4.H_2O$ (414 mg, 3.0 mmol) and $NaClO_2$ (273 mg, 3.0 mmol) respectively at room temperature. The stirring was continued for 8 h (monitored by TLC). After

completion of the reaction, the mixture was extracted with EtOAc (3 × 20 mL), washed with water, brine and dried over Na_2SO_4. The combined organic phase was concentrated by rotary evaporator under reduced pressure to leave the crude product. The white solid was purified by column chromatography over silica gel to furnish the pure product **6** (484 mg, 90% two steps).

A homogeneous solution of compound **6** (268.5 mg, 0.5 mmol) in CH_2Cl_2 (9.0 mL) was added TFA (3.0 mL) at 0 ºC. After that, reaction mixture was stirred for another 8 h (monitored by TLC). After completion of the reaction mixture was concentrated by rotary evaporator to give the crude product. The purification was done by column chromatography over silica-gel to furnish the pure product **8** (154.0 mg, 91%).



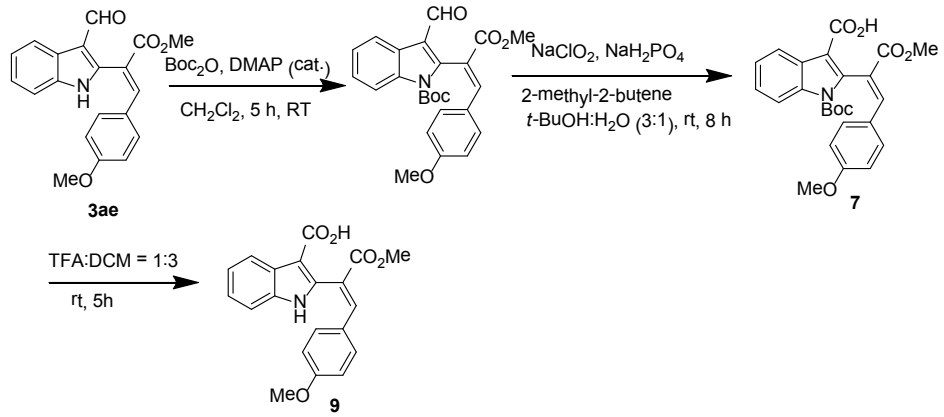
Compound 6: Yield 90%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.26 (t, *J* = 9.02 Hz, 2H), 7.96 (s, 1H), 7.37-7.44 (m, 2H), 6.97-7.02 (m, 4H), 3.77 (s, 3H), 1.49 (s, 9H), 1.48 (s, 9H) ; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.9, 166.5, 151.9, 151.1, 148.9, 141.4, 139.7, 136.0, 131.4, 130.7, 127.1, 125.4, 124.2, 124.0, 122.2, 121.5, 115.4, 111.2, 85.7, 83.8, 52.4, 27.7, 27.6 **HRMS** (ESI) m/z calcd. For $C_{29}H_{31}NO_9$ $[M+H]^+$: 538.2077. Found 538.2072.



Prenostodione 8: Yield 91%;

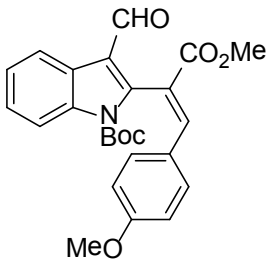
The product was characterized by spectroscopic data (^{1}H and ^{13}C NMR, HRMS) which is good agreement with literature data.

Synthesis of methylated prenostodione 9:

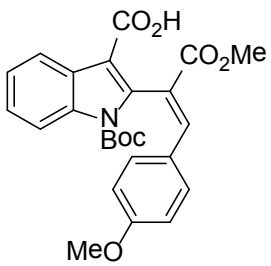


Similar synthetic methods were followed for the synthesis of compound 9.

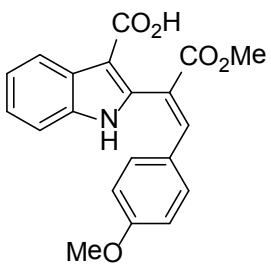
Methyl α-(1-tert-butoxycarbonyl-3-formyl-1H-indol-2yl)-β-(4-methoxyphenyl)acrylate: Yield 97%; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.82 (s, 1H), 8.28-8.34 (m, 2H), 8.13 (s, 1H), 7.37-7.47 (m, 2H), 7.06 (d, *J* = 9.09 Hz, 2H), 6.71 (d, *J* = 8.80 Hz, 2H), 3.77 (s, 3H), 3.73 (s, 3H), 1.56 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 187.0, 166.4, 161.3, 149.1, 144.3, 144.3, 136.4, 132.0, 125.9, 125.7, 124.7, 122.2, 119.0, 117.8, 115.4, 114.5, 86.0, 55.2, 52.4, 27.7 **HRMS** (ESI) m/z calcd. For $C_{25}H_{25}NO_6$ $[M+Na]^+$: 458.1579. Found 458.1574.



Compound 7: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.25-8.28 (m, 2H), 7.92 (s, 1H), 7.37-7.44 (m, 2H), 6.91(d, *J* = 8.67 Hz, 2H), 6.67 (d, *J* = 9.0 Hz, 2H), 3.76(s, 3H), 3.70 (s, 3H), 1.46(s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.0, 166.8, 160.8, 149.0, 142.3, 140.5, 136.1, 131.4, 127.3, 126.6, 125.3, 124.1, 122.2, 121.4, 115.4, 114.3, 110.9, 85.5, 55.2, 52.3, 27.7 **HRMS** (ESI) m/z calcd. For $C_{25}H_{25}NO_7$ $[M+Na]^+$: 474.1529. Found 474.1523.



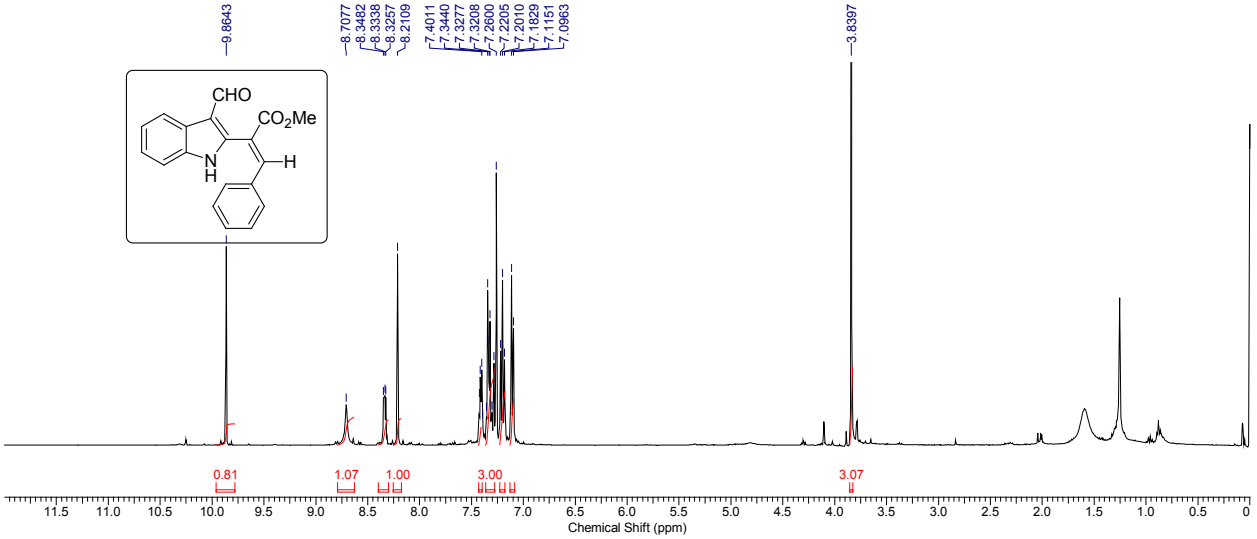
Compound 9: Yield 93%; **^{1}H NMR (400 MHz, DMSO-d_6)** δ 11.87 (br s, 2H), 8.05-8.07 (m, 1H), 7.85 (s, 1H), 7.38-7.40 (m, 1H), 7.17-7.22 (m, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.69 (s, 3H), 3.66 (s, 3H); **^{13}C NMR (100 MHz, DMSO-d_6)** δ 166.6, 165.7, 160.6, 141.7, 138.9, 135.7, 131.9, 126.9, 126.2,



122.4, 121.3, 121.1, 121.1, 114.3, 112.0, 105.7, 55.3, 52.0. **HRMS** (ESI) m/z calcd. For $C_{20}H_{17}NO_5$ $[M-H]^+$: 350.1029. Found 350.1023.

References:

1. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *A64,* 112-122. *Program for Crystal Structure Solution and Refinement;* University of Goettingen: Goettingen, Germany, 1997.
2. (a) Somei, M.; Ohnishi, H.; Shoken, Y. *Chem. Pharm. Bull.* **1986**, *34*, 677. (b) Somei, M.; Kawasaki, T.; Shimizu, K.; Fukui, Y.; Ohta, T. *Chem. Pharm. Bull*. **1991**, *39***,** 1905; (c) Kawasaki, T.; Kodama, A.;, Nishida,T.; Shimizu, K.; Somei, M. *Heterocycles* **1991**, *32*, 221.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7.1829
7.1151
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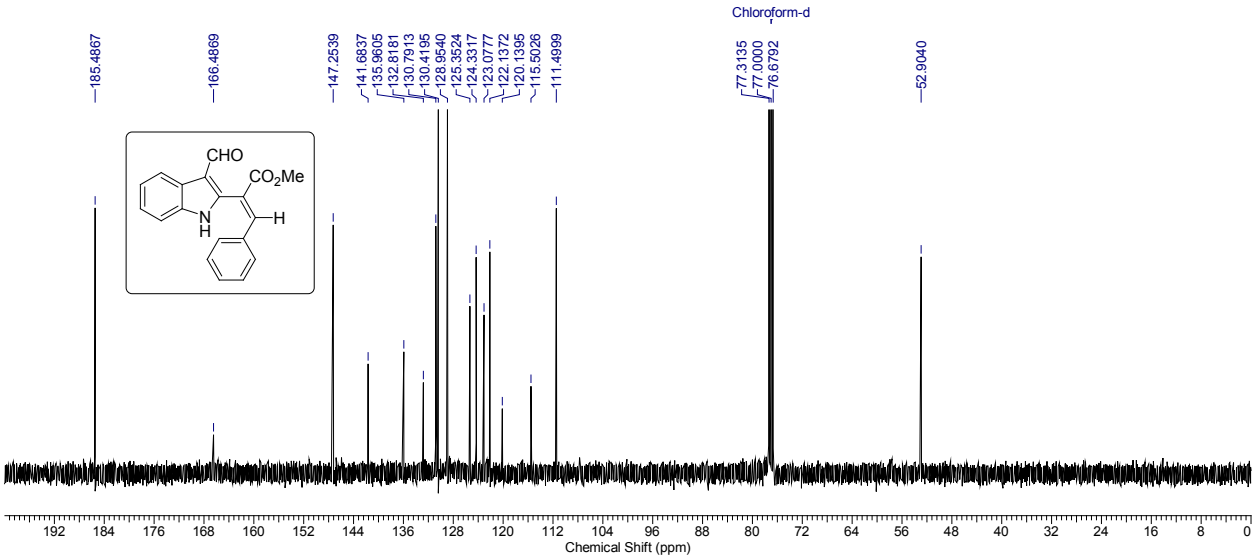
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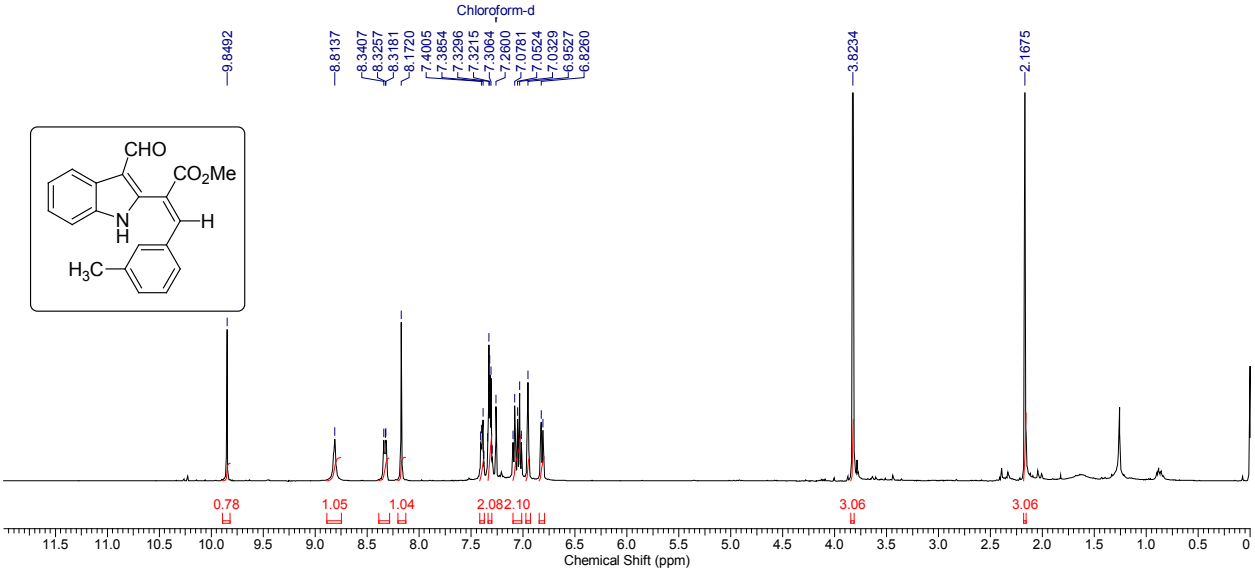
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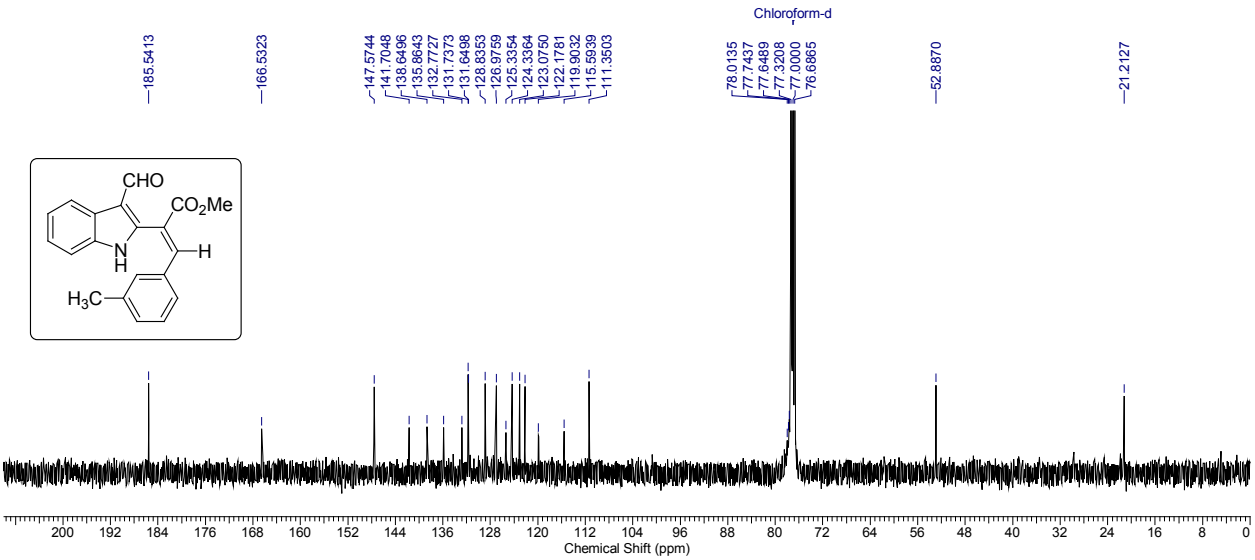
Chemical Shift (ppm)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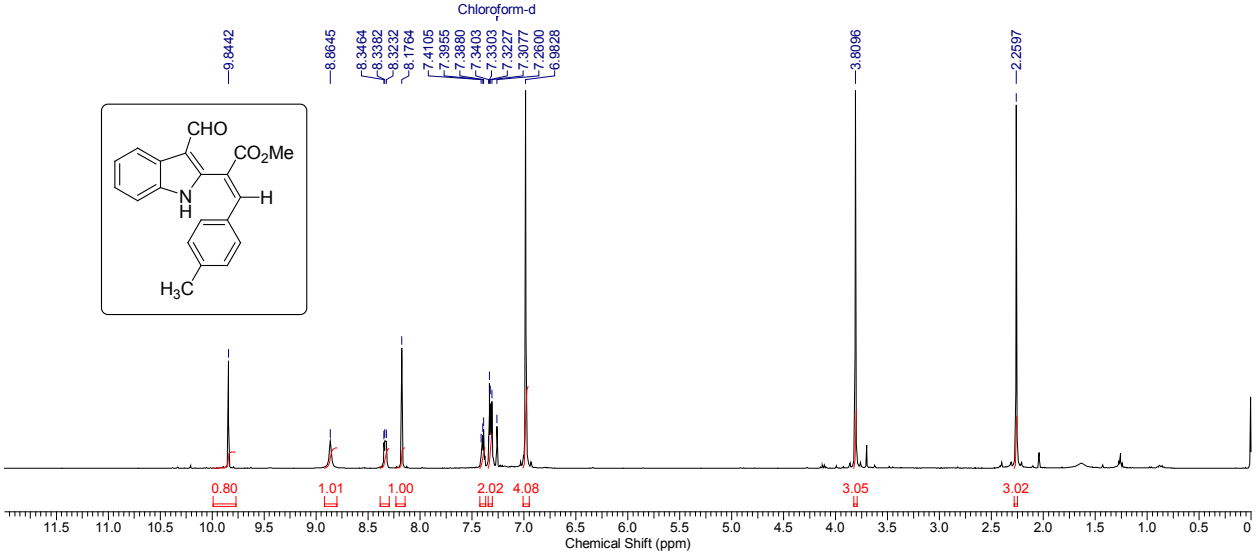
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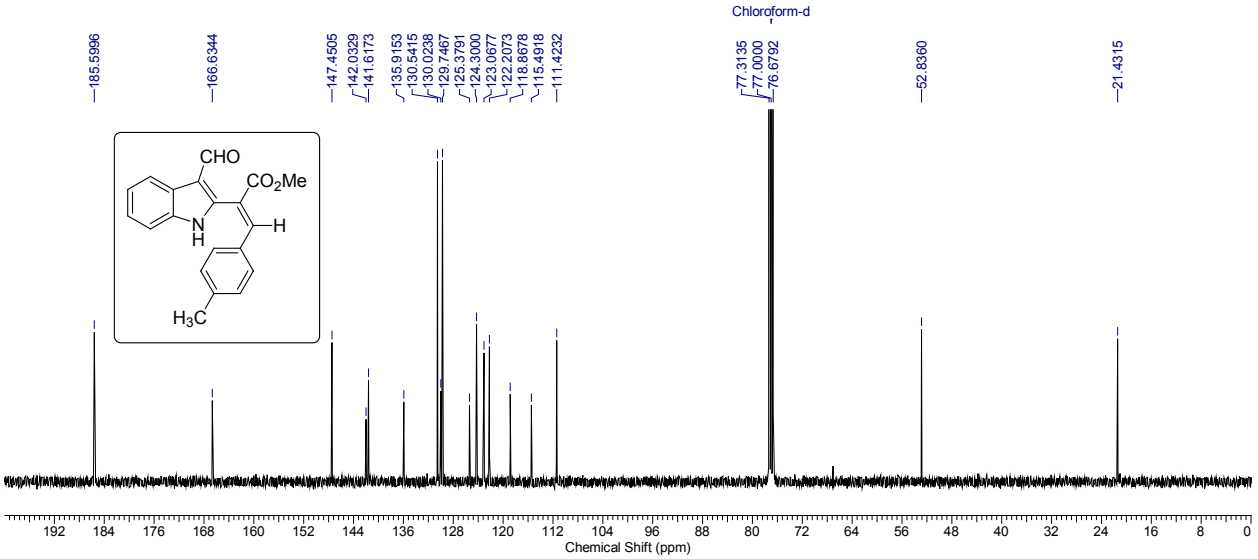
Chemical Shift (ppm)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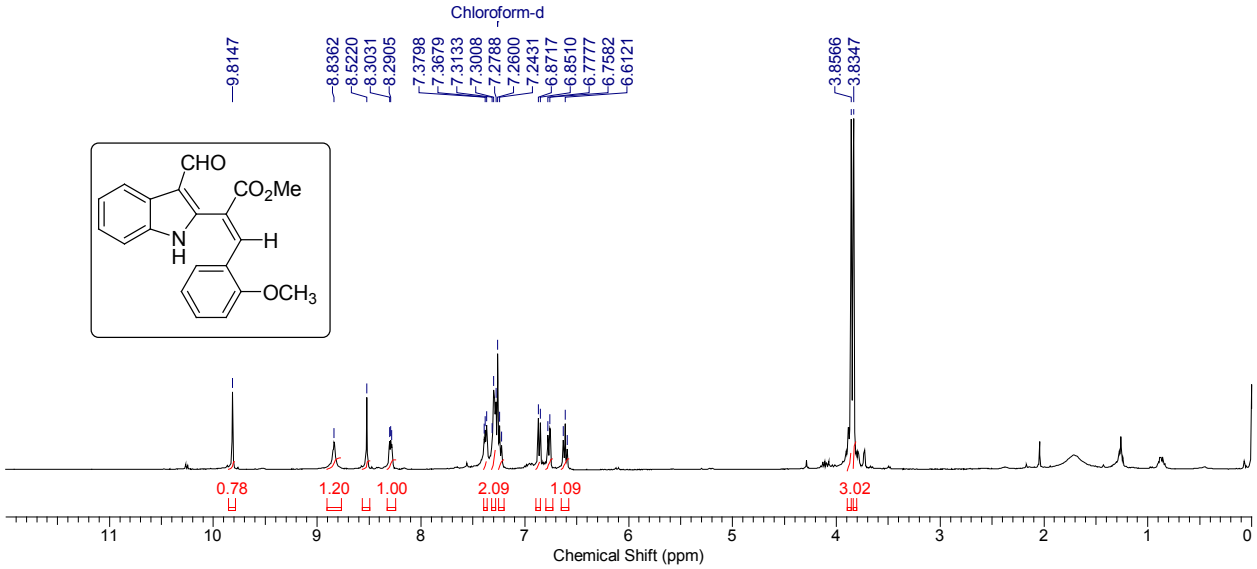
Chemical Shift (ppm)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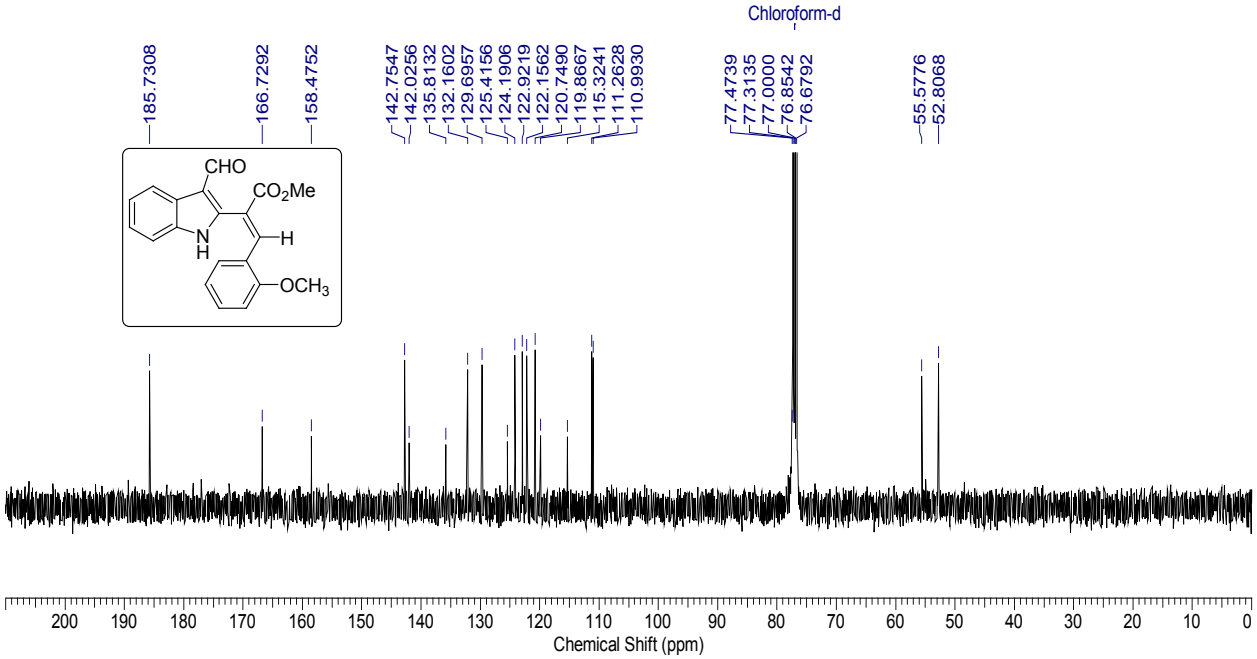
Chemical Shift (ppm)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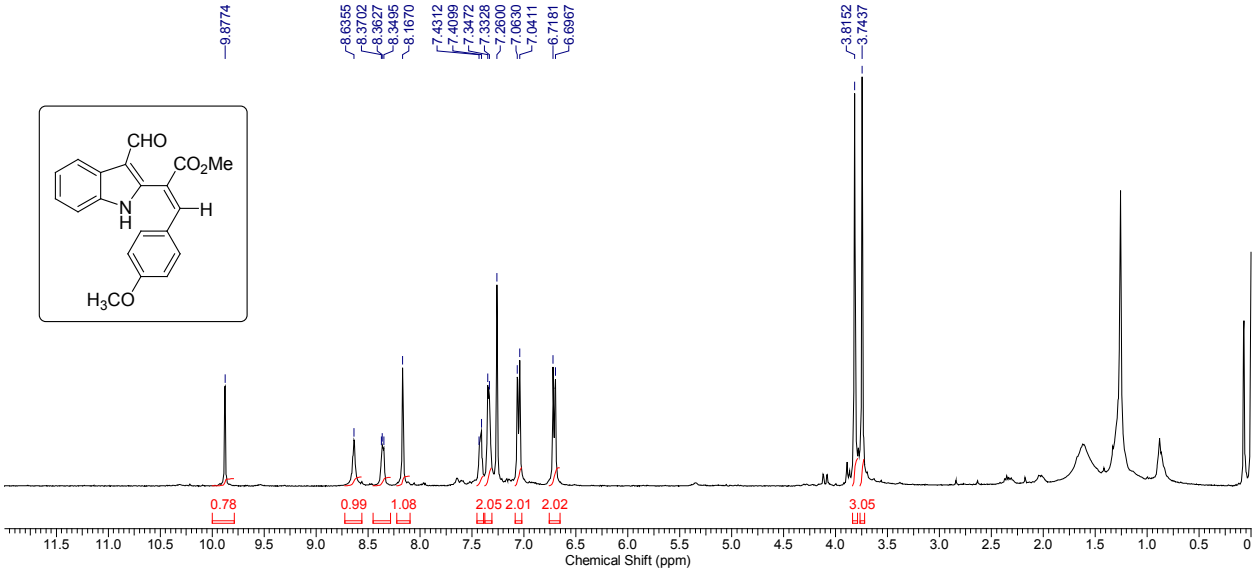
Chemical Shift (ppm)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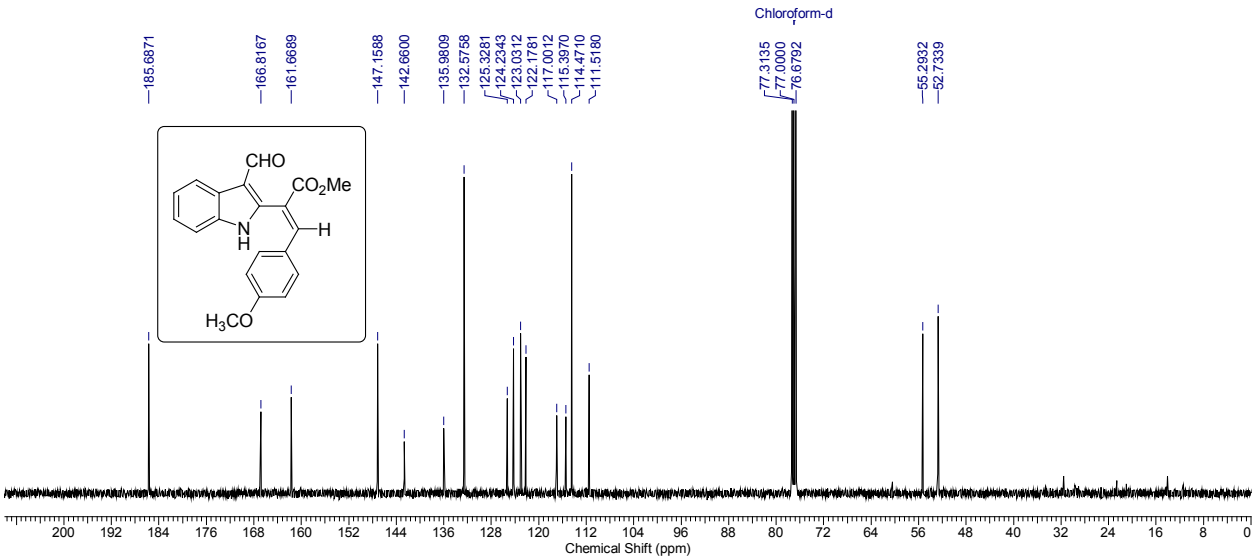
3.05
Chemical Shift (ppm)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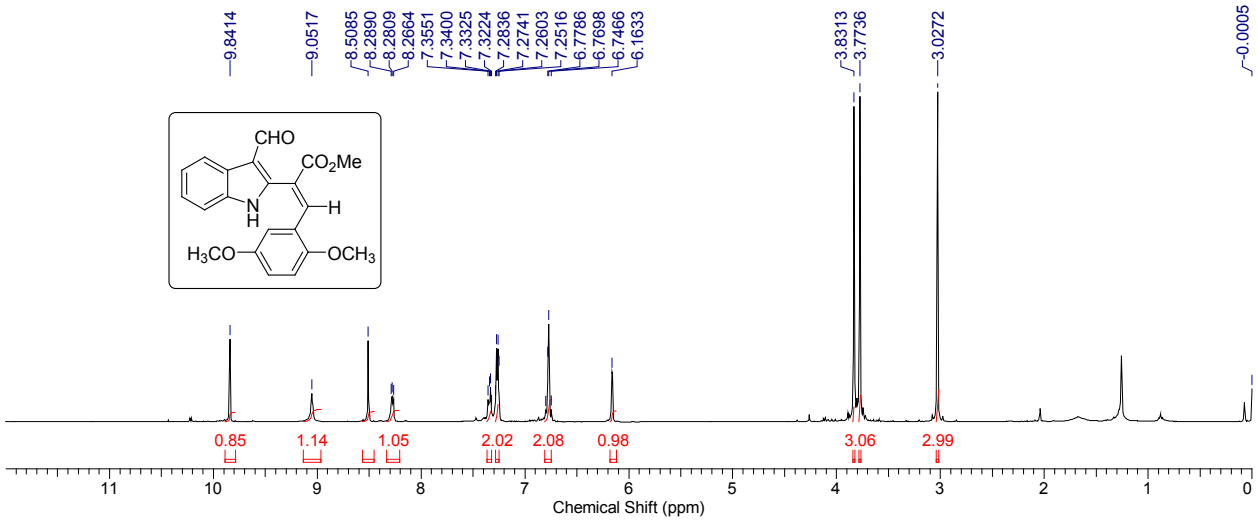
Chemical Shift (ppm)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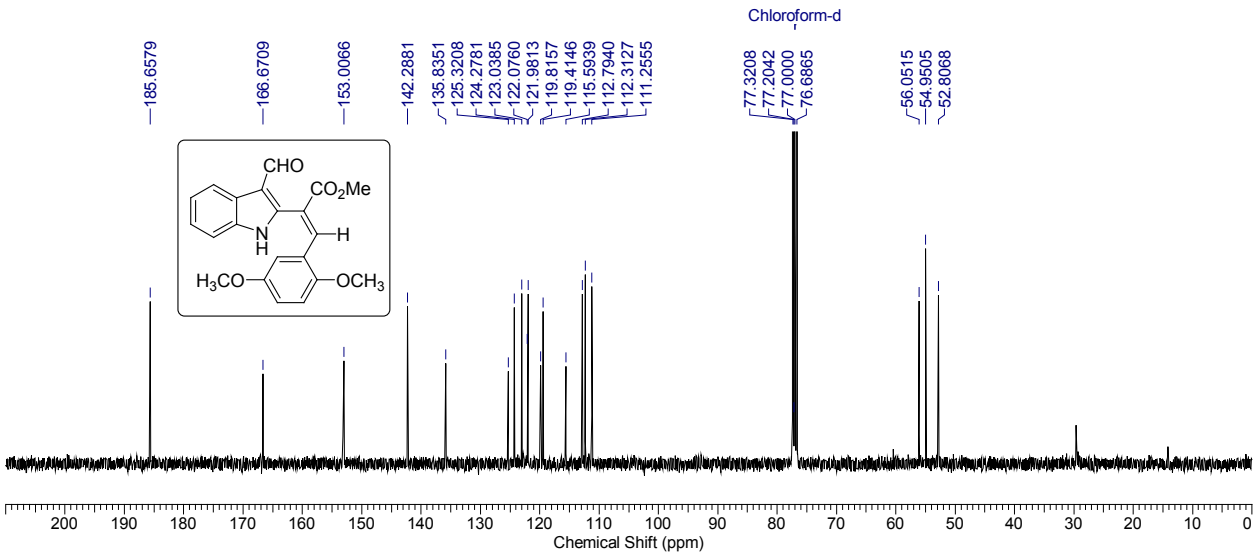
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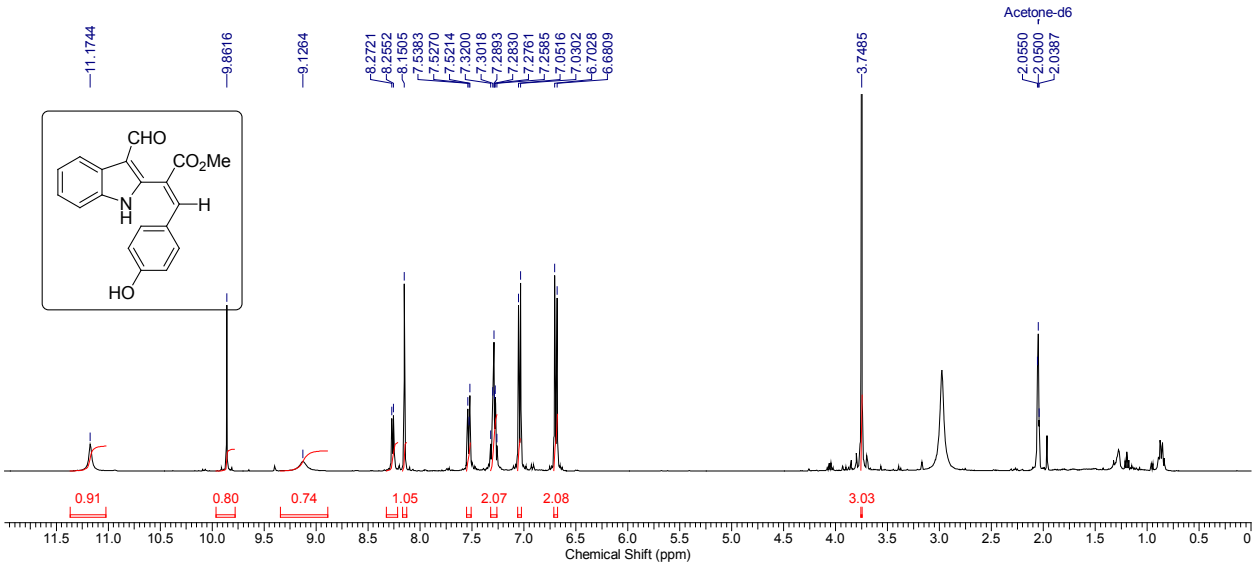
Chemical Shift (ppm)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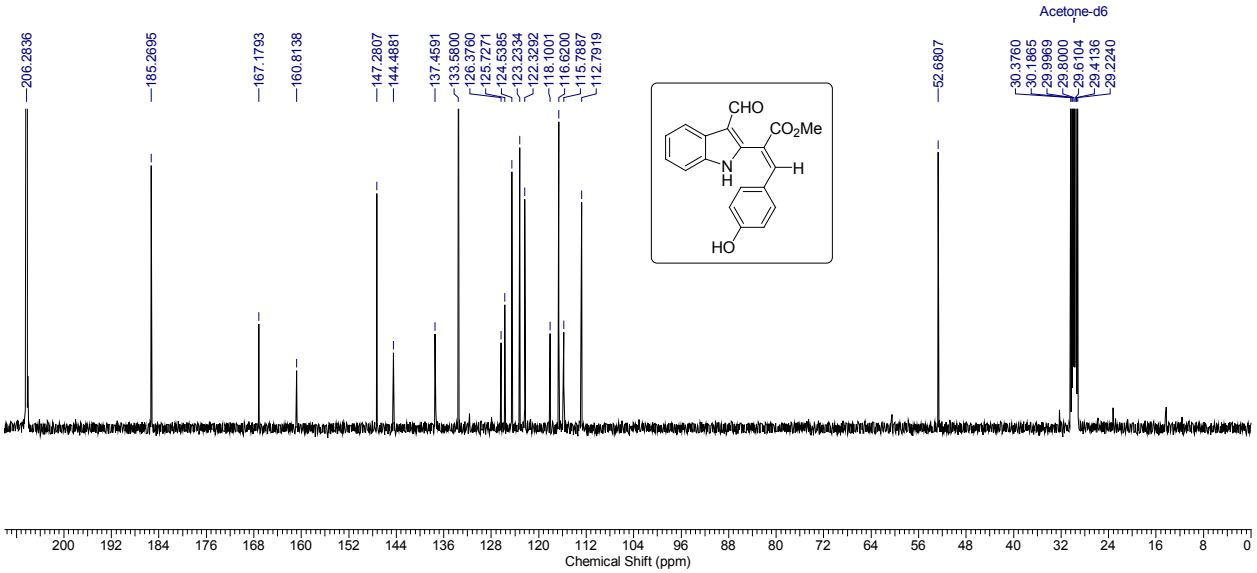
Chemical Shift (ppm)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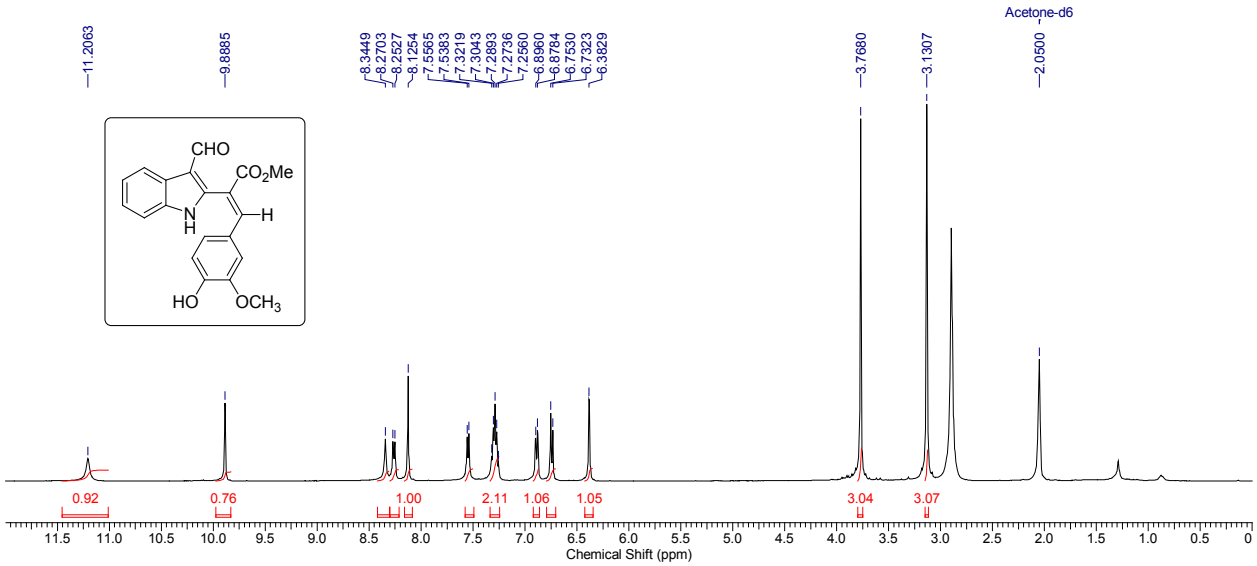
Chemical Shift (ppm)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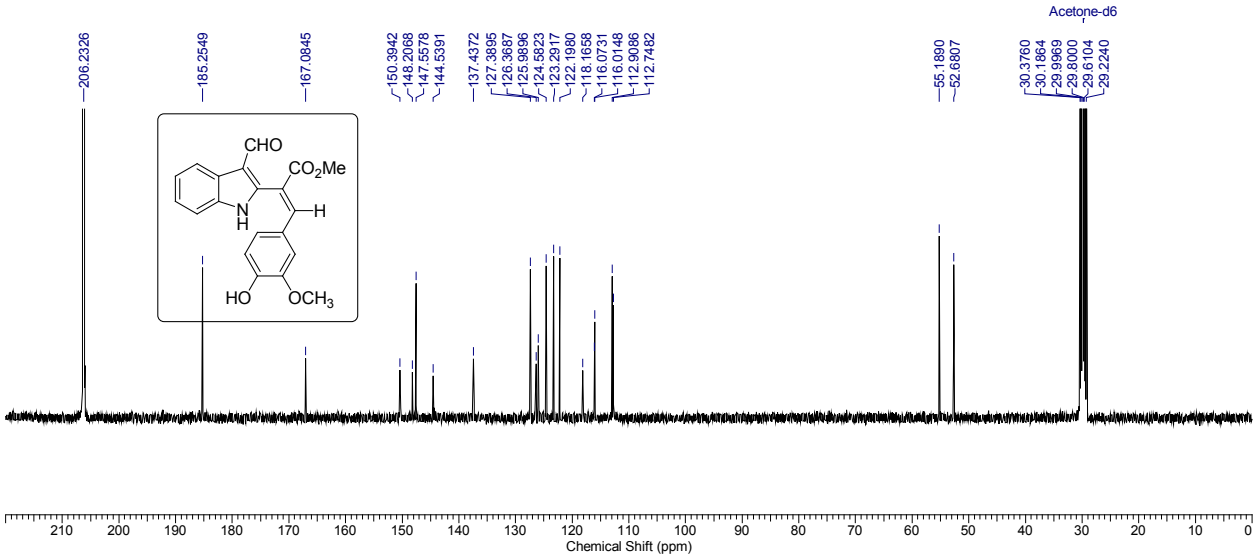
Chemical Shift (ppm)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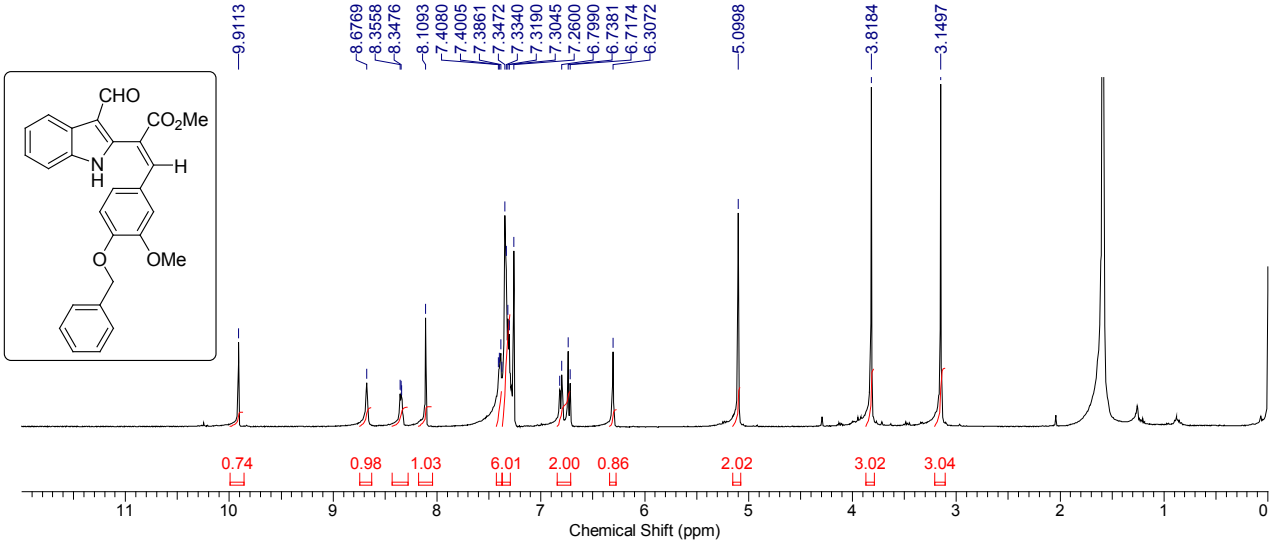
Chemical Shift (ppm)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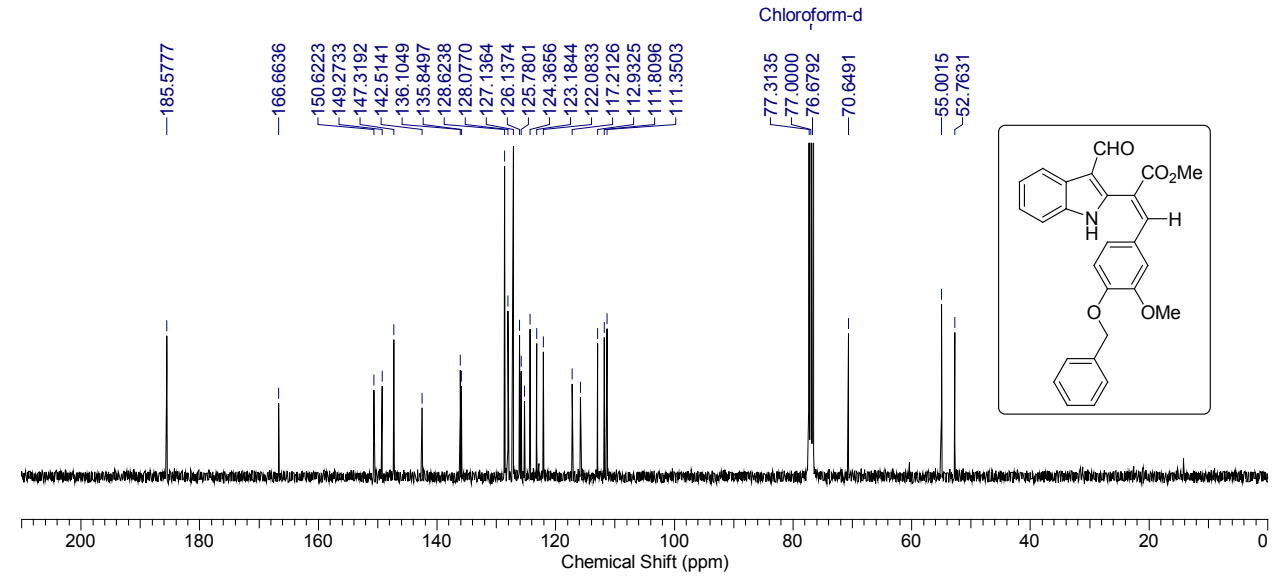
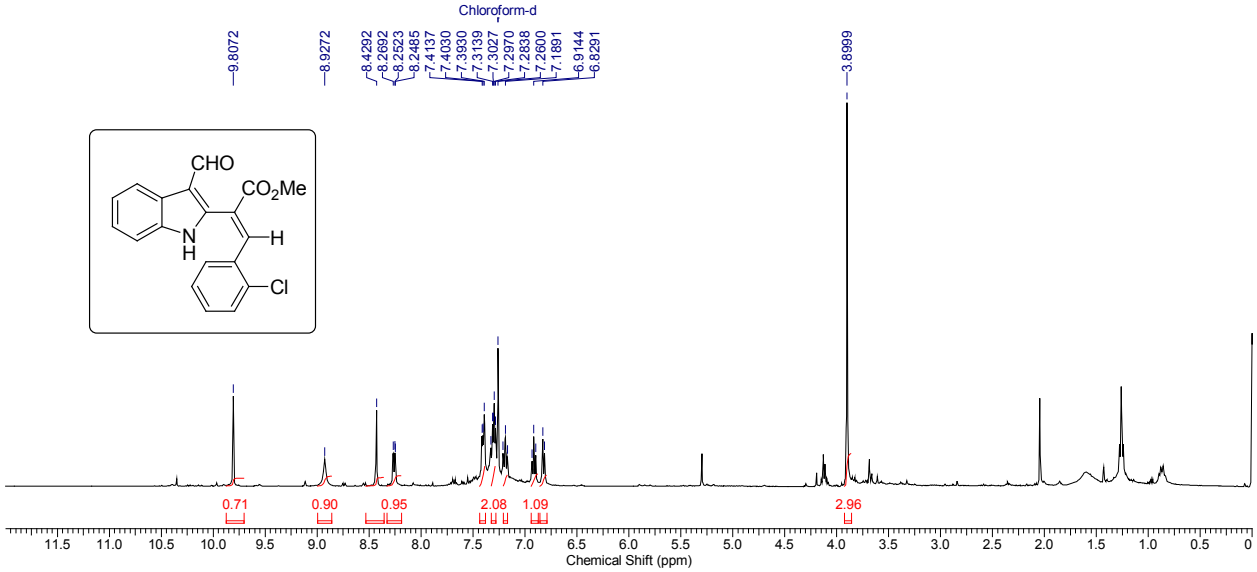
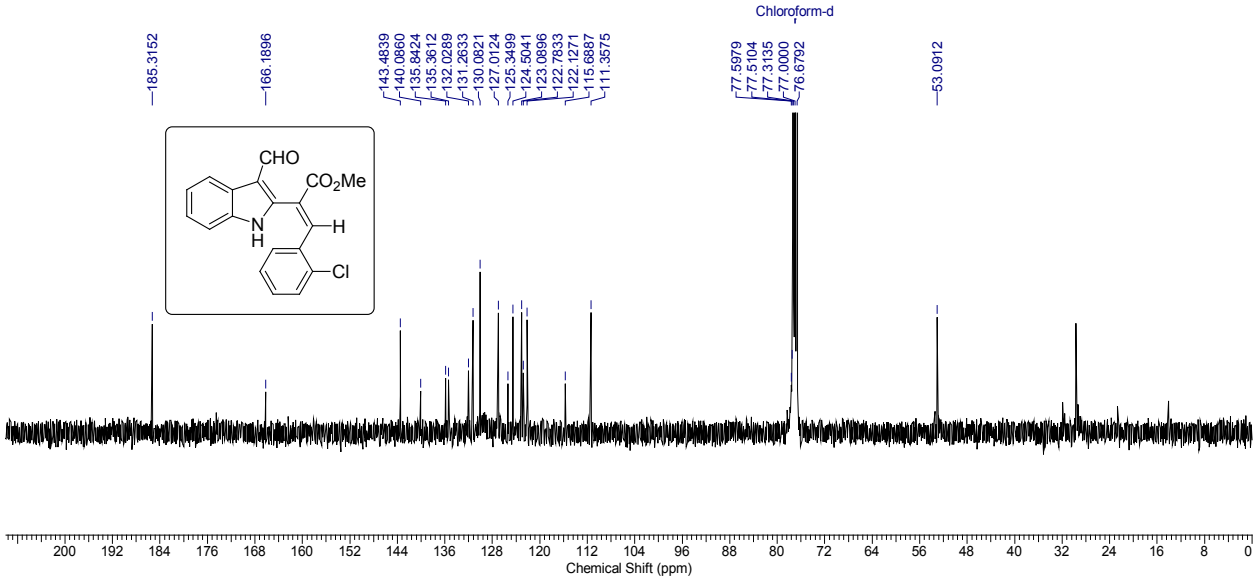
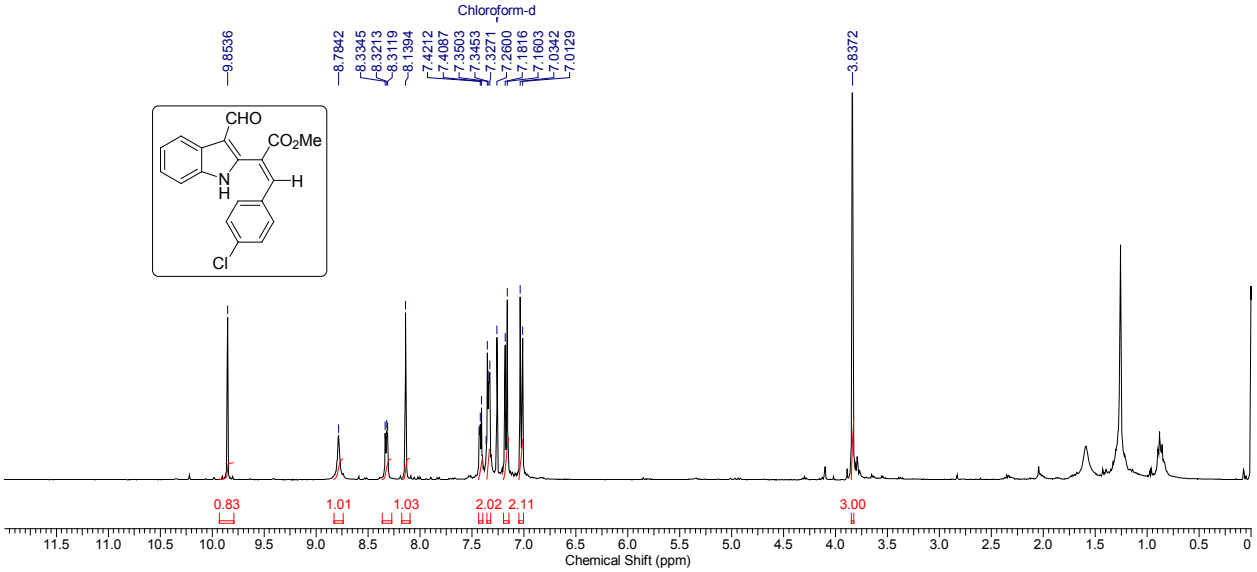
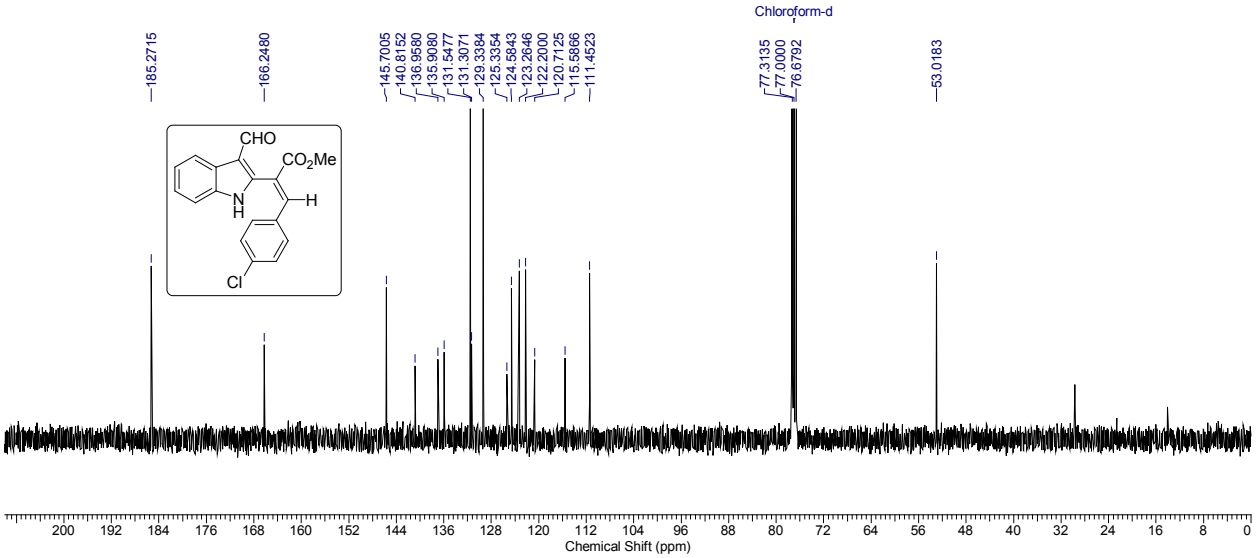
8.3476
8.1093
7.4080
7.4005
7.3861
7.3472
7.3340
7.3190
7.3045
7.2600
6.7990
6.7381
6.7174
6.3072
5.0998
3.8184
3.1497
CHO
CO2Me
N
H
H
O
OMe
0.74
0.98
1.03
6.01
2.00
0.86
2.02
3.02
3.04
Chemical Shift (ppm)

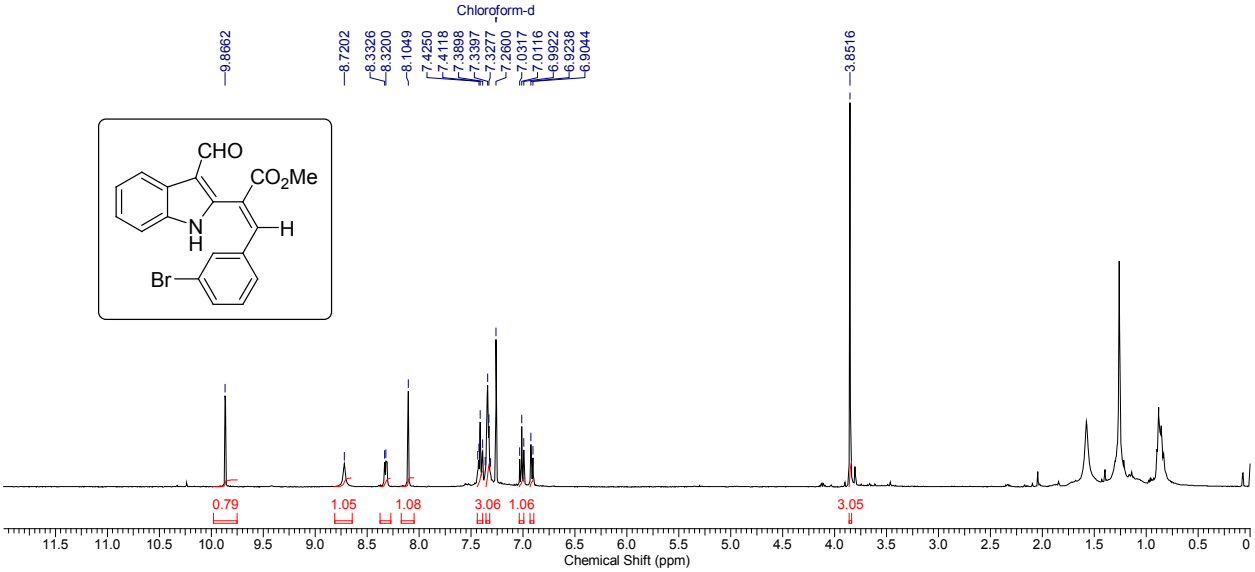

Chloroform-d
185.5777
166.6636
150.6223
149.2733
147.3192
142.5141
136.1049
135.8497
128.6238
128.0770
127.1364
126.1374
125.7801
124.3656
123.1844
122.0833
117.2126
112.9325
111.8096
111.3503
77.3135
77.0000
76.6792
70.6491
55.0015
52.7631
CHO
CO2Me
N
H
H
O
OMe
Chemical Shift (ppm)

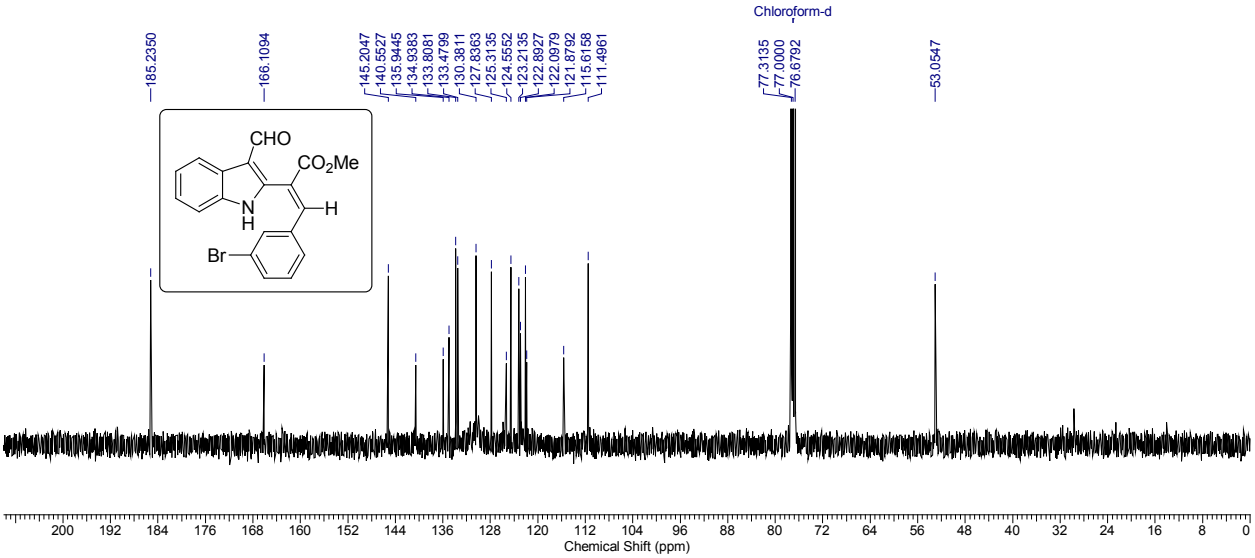

Chloroform-d
9.8072
8.9272
8.4292
8.2692
8.2523
8.2485
7.4137
7.4030
7.3930
7.3139
7.3027
7.2970
7.2838
7.2600
7.1891
6.9144
6.8291
3.8999
CHO
CO2Me
N
H
H
Cl
0.71
0.90
0.95
2.08
1.09
2.96
Chemical Shift (ppm)

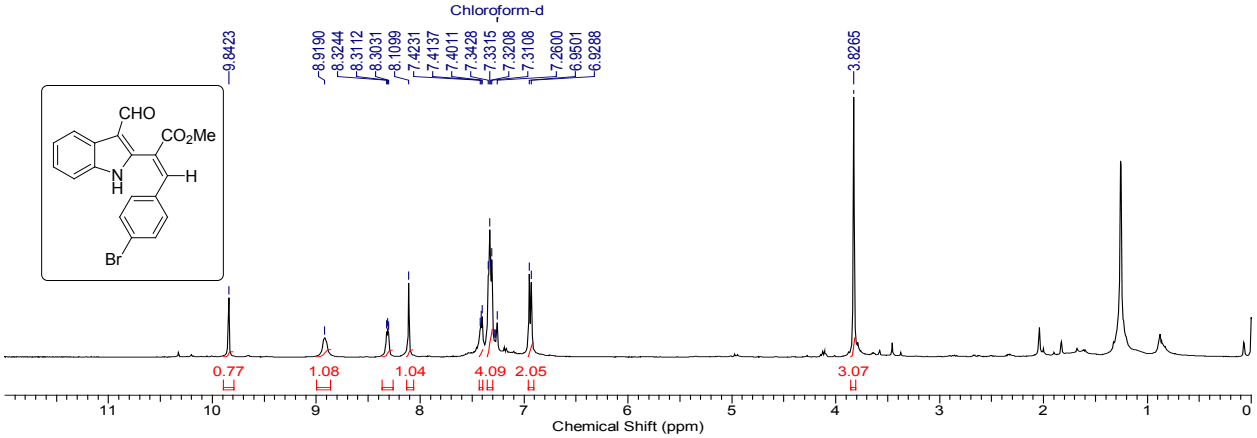

Chloroform-d
185.3152
166.1896
143.4839
140.0860
135.8424
135.3612
132.0289
131.2633
130.0821
127.0124
125.3499
124.5041
123.0896
122.7833
122.1271
115.6687
111.3575
77.5979
77.5104
77.3135
77.0000
76.6792
53.0912
CHO
CO2Me
N
H
H
Cl
Chemical Shift (ppm)

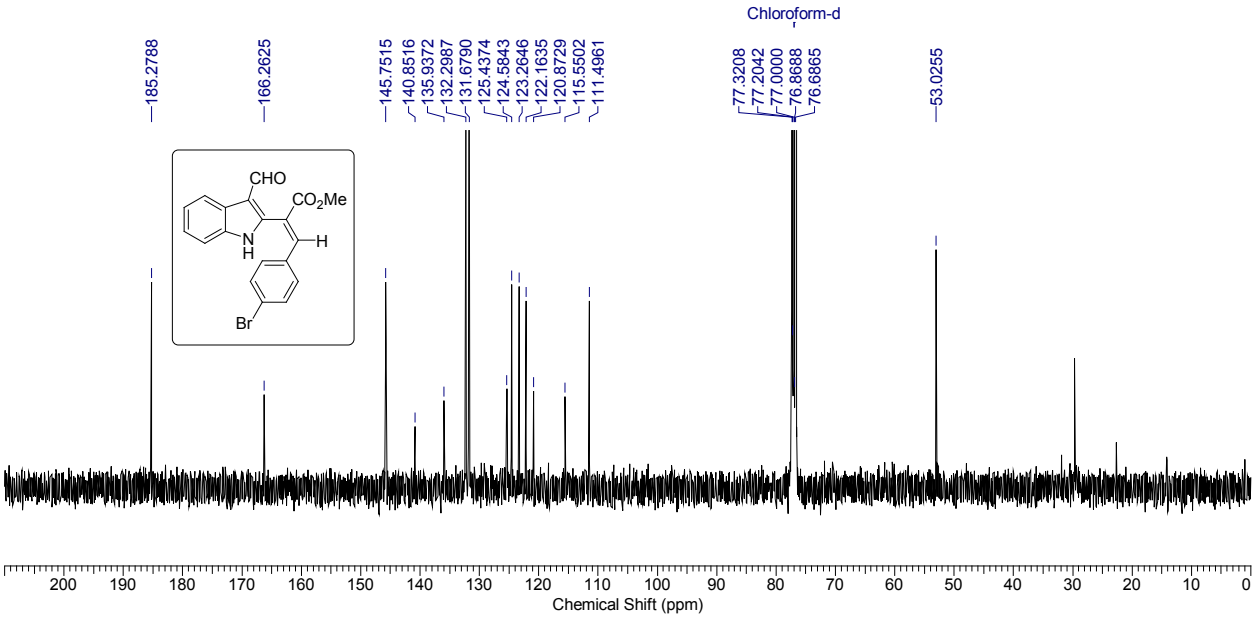

Chloroform-d
9.8536
8.7842
8.3345
8.3213
8.3119
8.1394
7.4212
7.4087
7.3503
7.3453
7.3271
7.2600
7.1816
7.1603
7.0342
7.0129
3.8372
CHO
CO2Me
N
H
H
Cl
0.83
1.01
1.03
2.02
2.11
3.00
Chemical Shift (ppm)

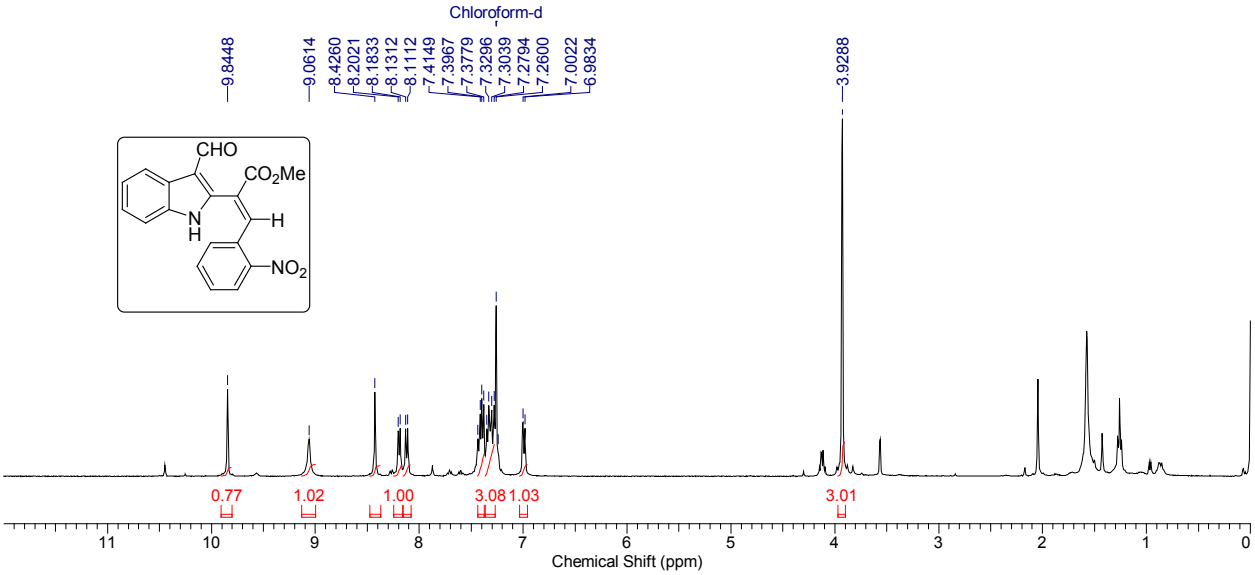

Chloroform-d
185.2715
166.2480
145.7005
140.8152
136.9580
135.9080
131.5477
131.3071
129.3384
125.3354
124.5843
123.2646
122.2000
120.7125
115.5866
111.4523
77.3135
77.0000
76.6792
53.0183
CHO
CO2Me
N
H
H
Cl
Chemical Shift (ppm)

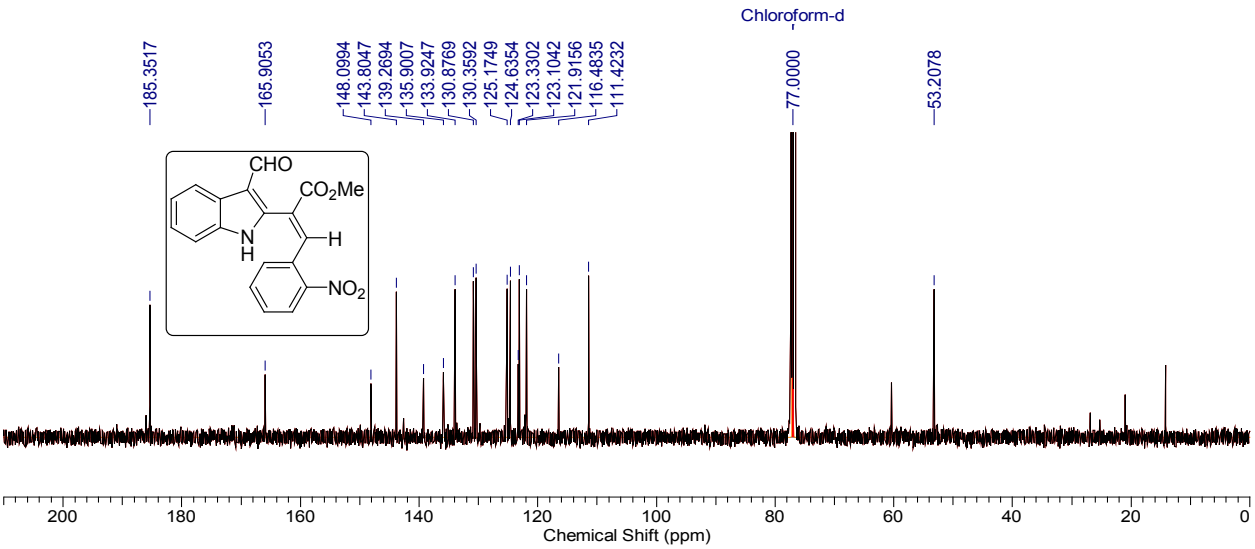


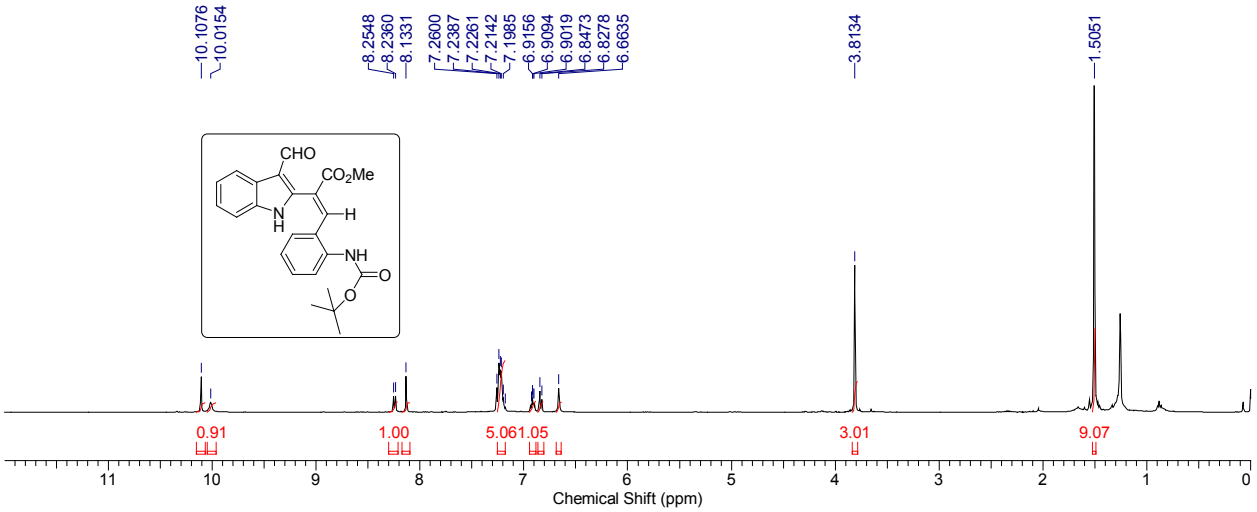


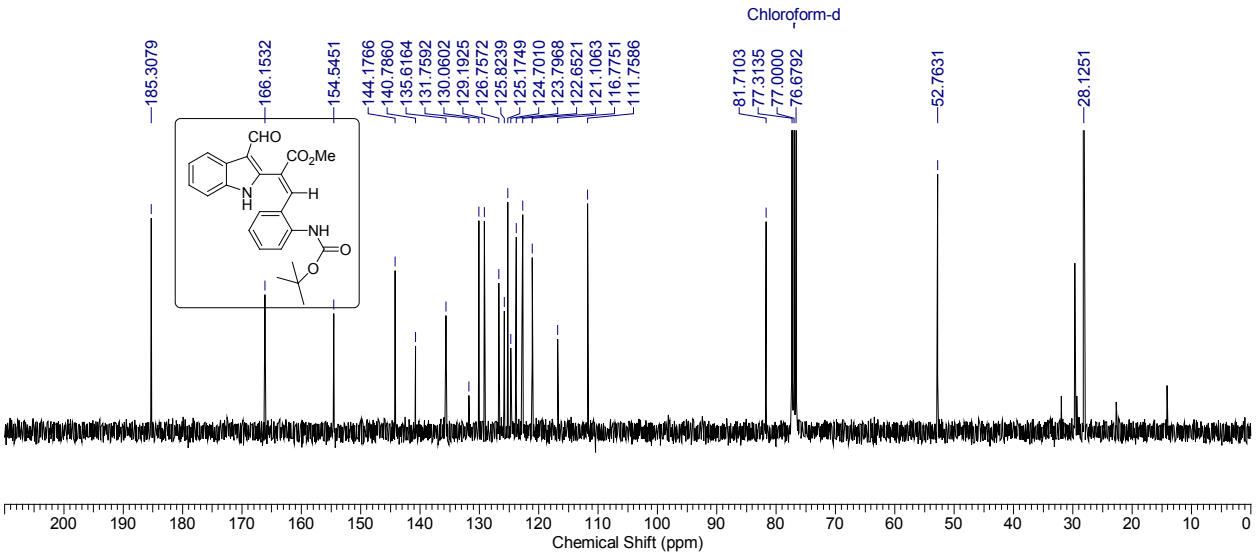

Chloroform-d
9.8423
8.9190
8.3244
8.3112
8.3031
8.1099
7.4231
7.4137
7.4011
7.3428
7.3315
7.3208
7.3108
7.2600
6.9501
6.9288
3.8265
CHO
CO2Me
H
N
H
Br
0.77
1.08
1.04
4.09
2.05
3.07
Chemical Shift (ppm)

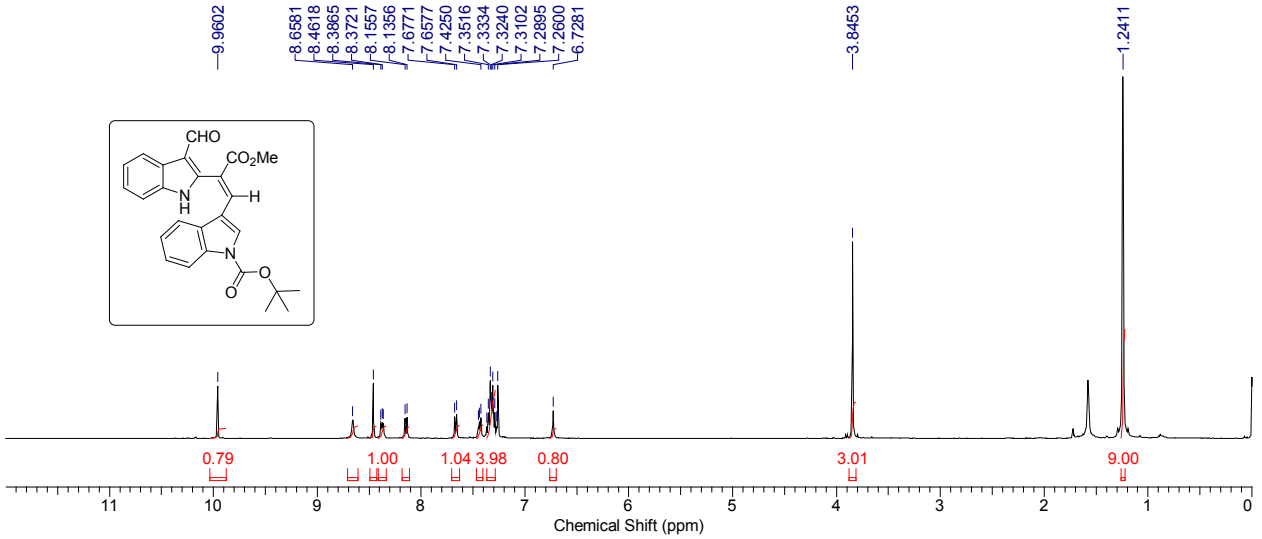

Chloroform-d
185.2788
166.2625
145.7515
140.8516
135.9372
132.2987
131.6790
125.4374
124.5843
123.2646
122.1635
120.8729
115.5502
111.4961
77.3208
77.2042
77.0000
76.8688
76.6865
53.0255
CHO
CO2Me
H
N
H
Br
Chemical Shift (ppm)

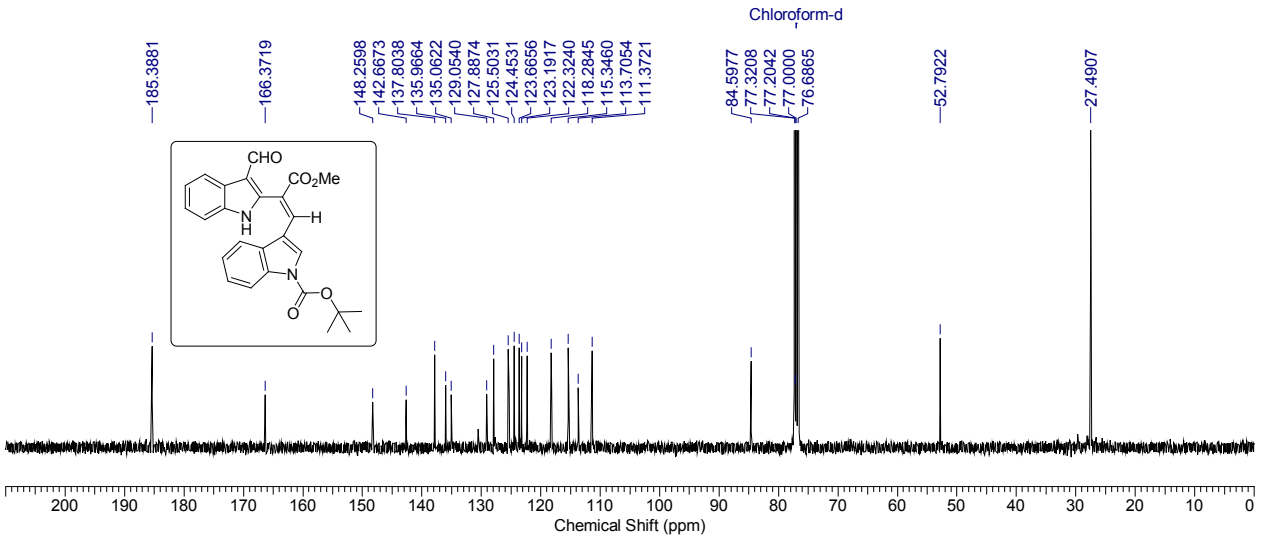

Chloroform-d
9.8448
9.0614
8.4260
8.2021
8.1833
8.1312
8.1112
7.4149
7.3967
7.3779
7.3296
7.3039
7.2794
7.2600
7.0022
6.9834
3.9288
CHO
CO2Me
N
H
H
NO2
0.77
1.02
1.00
3.08
1.03
3.01
Chemical Shift (ppm)

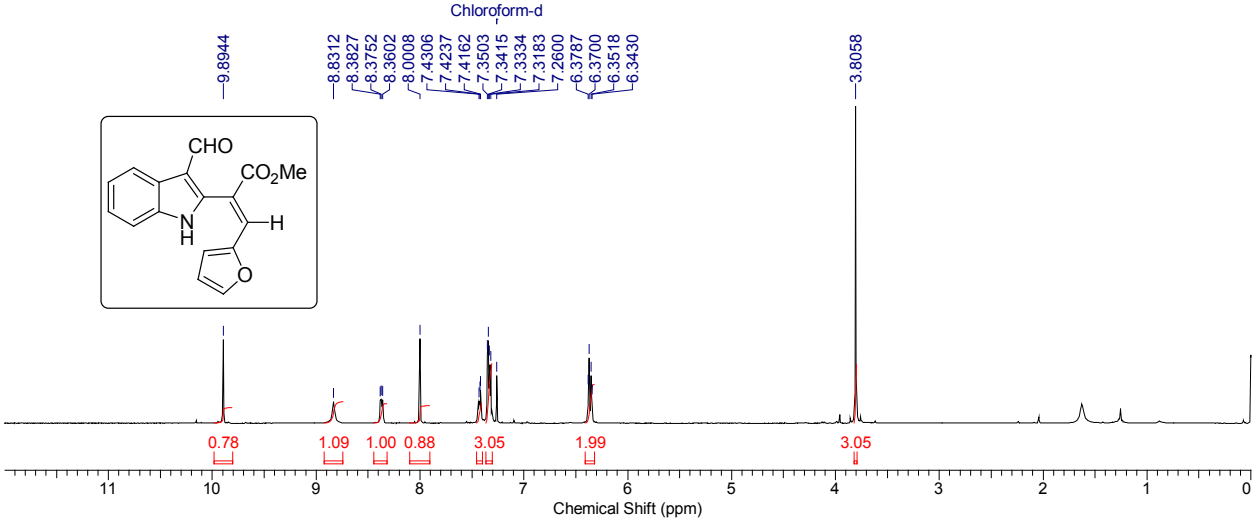

Chloroform-d
185.3517
165.9053
148.0994
143.8047
139.2694
135.9007
133.9247
130.8769
130.3592
125.1749
124.6354
123.3302
123.1042
121.9156
116.4835
111.4232
77.0000
53.2078
CHO
CO2Me
N
H
H
NO2
Chemical Shift (ppm)

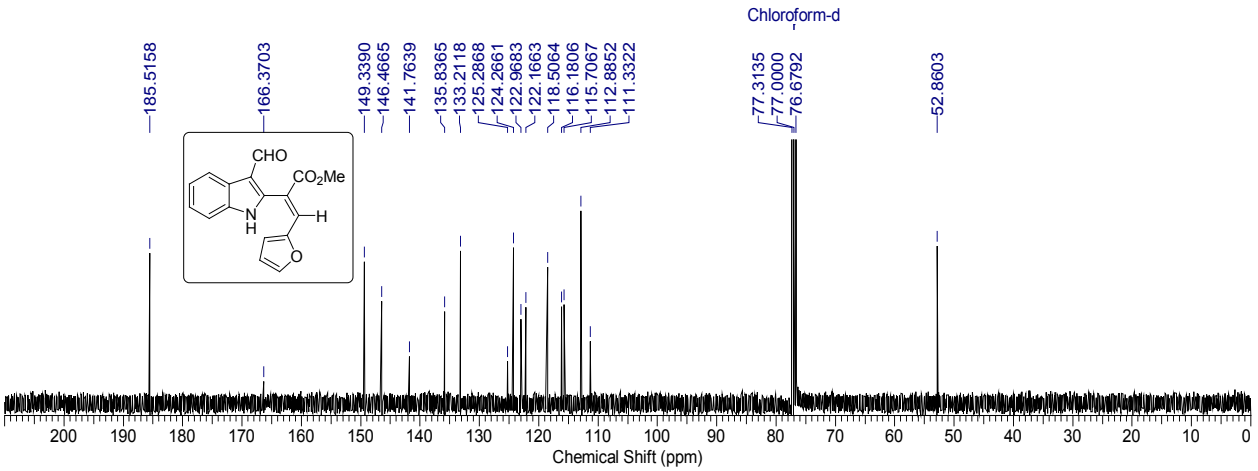

10.1076
10.0154
8.2548
8.2360
8.1331
7.2600
7.2387
7.2261
7.2142
7.1985
6.9156
6.9094
6.9019
6.8473
6.8278
6.6635
3.8134
1.5051
CHO
CO2Me
N
H
H
NH
O
O
0.91
1.00
5.06
1.05
3.01
9.07
Chemical Shift (ppm)

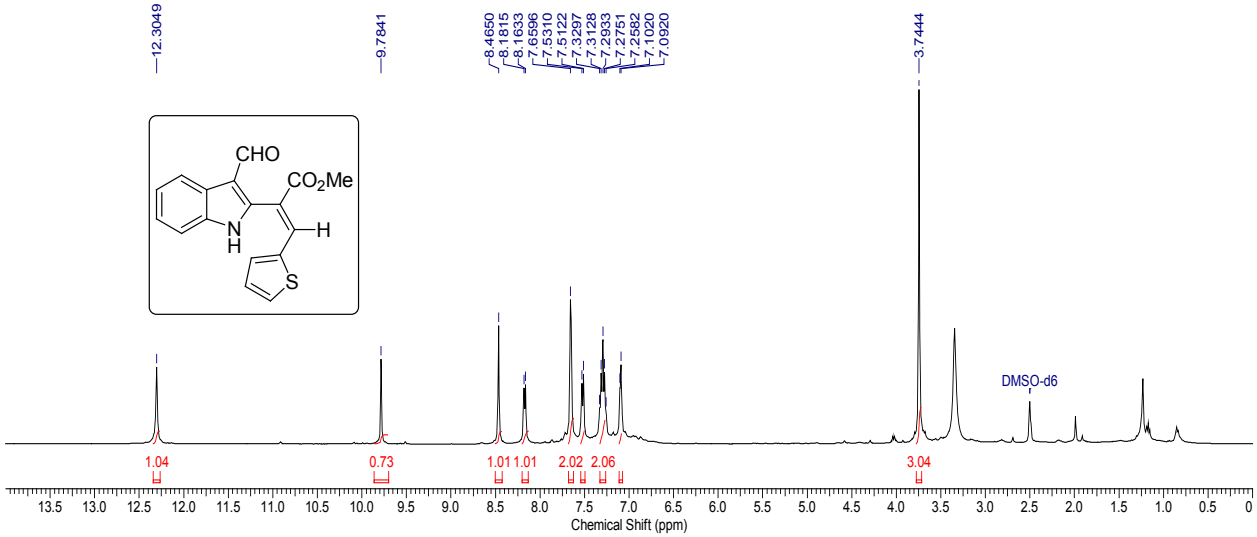

Chloroform-d
185.3079
166.1532
154.5451
144.1766
140.7860
135.6164
131.7592
130.0602
129.1925
126.7572
125.8239
125.1749
124.7010
123.7968
122.6521
121.1063
116.7751
111.7586
81.7103
77.3135
77.0000
76.6792
52.7631
28.1251
CHO
CO2Me
N
H
H
NH
O
O
Chemical Shift (ppm)

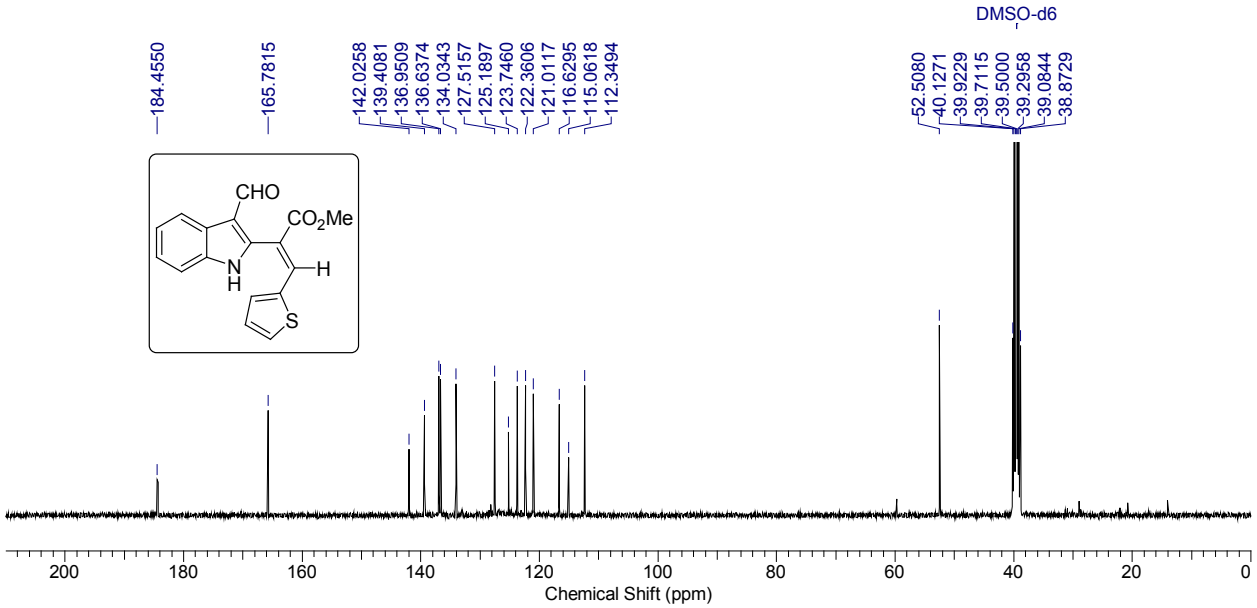

9.9602
8.6581
8.4618
8.3865
8.3721
8.1557
8.1356
7.6771
7.6577
7.4250
7.3516
7.3334
7.3240
7.3102
7.2895
7.2600
6.7281
3.8453
1.2411
CHO
CO2Me
N
H
H
N
O
O
0.79
1.00
1.04
3.98
0.80
3.01
9.00
Chemical Shift (ppm)

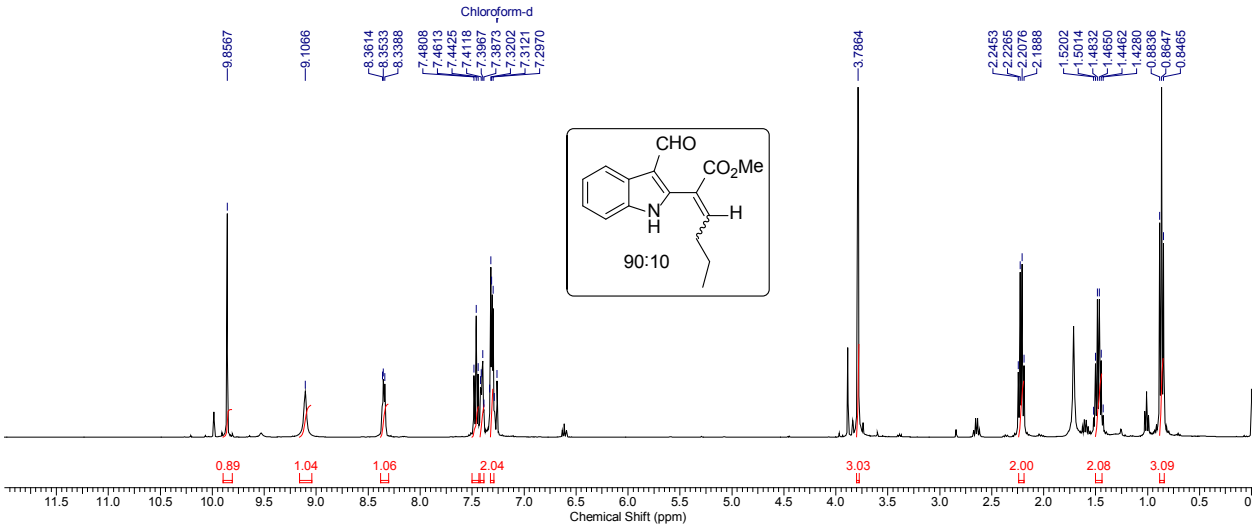

Chloroform-d
185.3881
166.3719
148.2598
142.6673
137.8038
135.9664
135.0622
129.0540
127.8874
125.5031
124.4531
123.6656
123.1917
122.3240
118.2845
115.3460
113.7054
111.3721
84.5977
77.3208
77.2042
77.0000
76.6865
52.7922
27.4907
CHO
CO2Me
N
H
H
N
O
O
Chemical Shift (ppm)

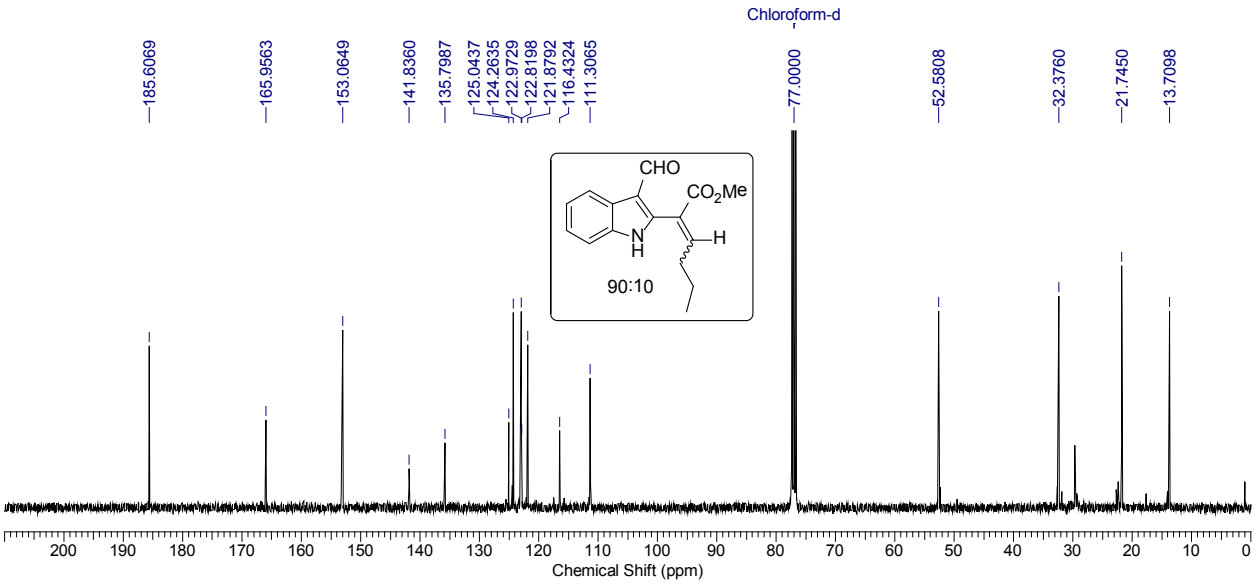

Chloroform-d
9.8944
8.8312
8.3827
8.3752
8.3602
8.0008
7.4306
7.4237
7.4162
7.3503
7.3415
7.3334
7.3183
7.2600
6.3787
6.3700
6.3518
6.3430
3.8058
CHO
CO2Me
N
H
H
O
0.78
1.09
1.00
0.88
3.05
1.99
3.05
Chemical Shift (ppm)

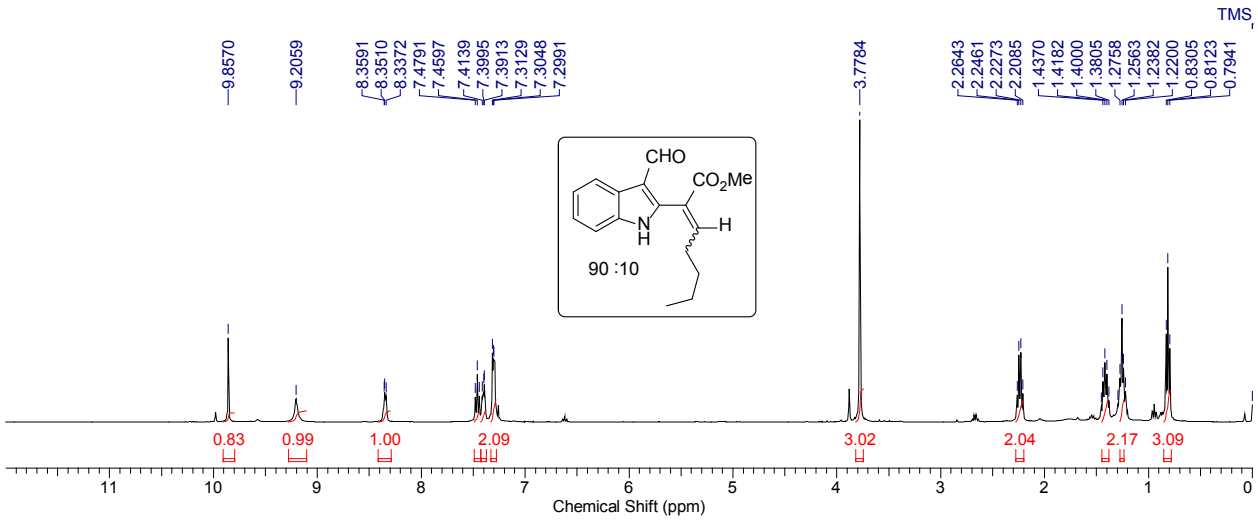

Chloroform-d
185.5158
166.3703
149.3390
146.4665
141.7639
135.8365
133.2118
125.2868
124.2661
122.9683
122.1663
118.5064
116.1806
115.7067
112.8852
111.3322
77.3135
77.0000
76.6792
52.8603
CHO
CO2Me
N
H
H
O
Chemical Shift (ppm)

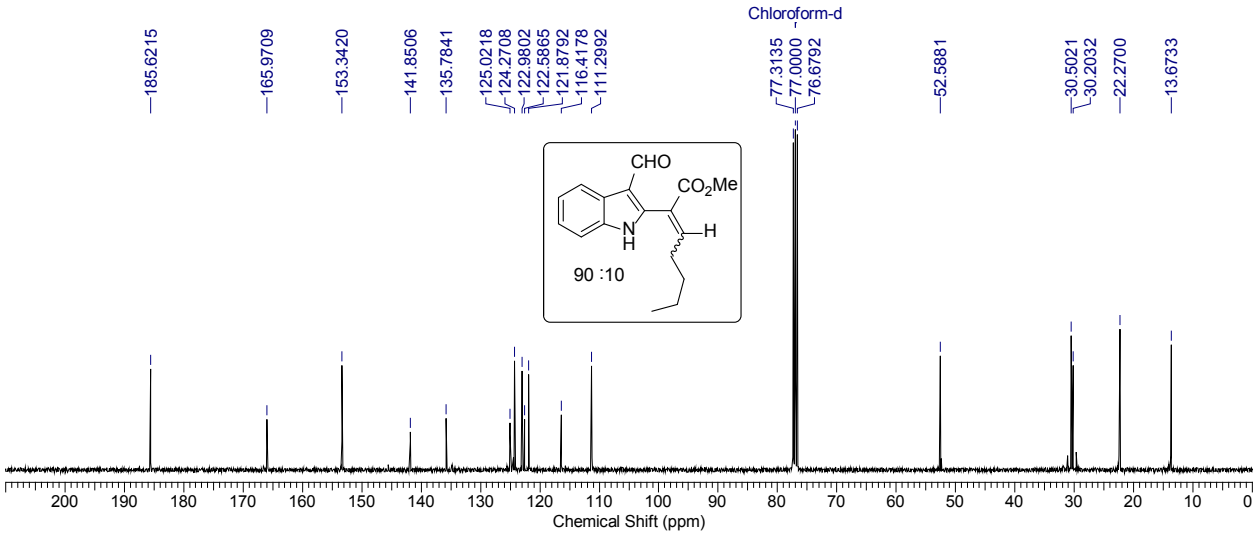

12.3049
9.7841
8.4650
8.1815
8.1633
7.6596
7.5510
7.5122
7.3297
7.3128
7.2933
7.2751
7.2582
7.1020
7.0920
3.7444
CHO
CO2Me
N
H
H
S
DMSO-d6
1.04
0.73
1.01
1.01
2.02
2.06
3.04
Chemical Shift (ppm)

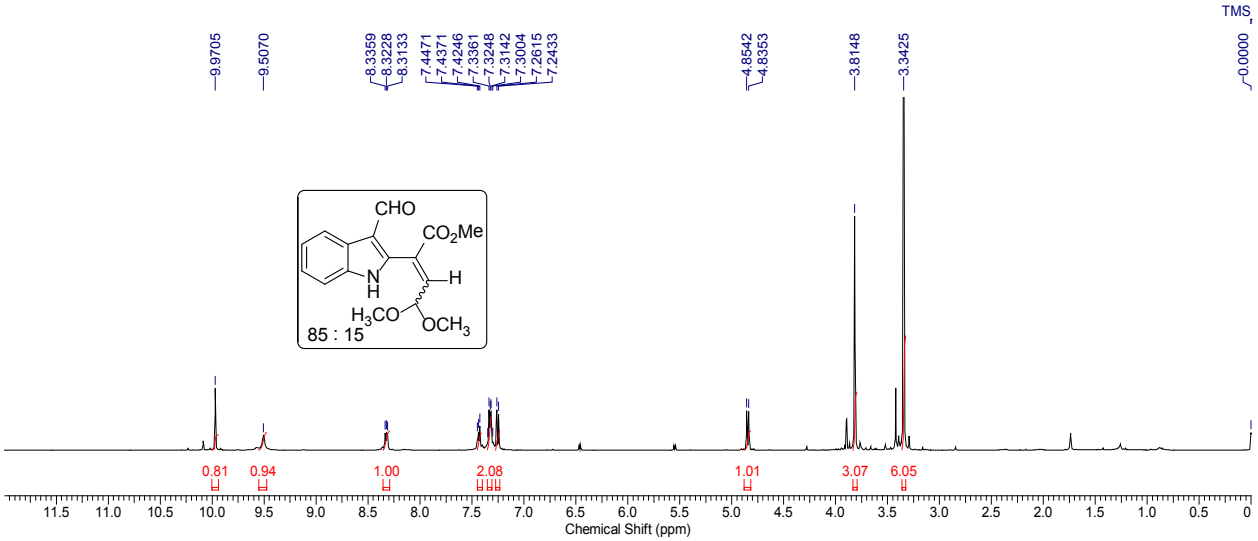

184.4550
165.7815
142.0258
139.4081
136.9509
136.6374
134.0343
127.5157
125.1897
123.7460
122.3606
121.0117
116.6295
115.0618
112.3494
52.5080
40.1271
39.9229
39.7115
39.5000
39.2958
39.0844
38.8729
DMSO-d6
CHO
CO2Me
N
H
H
S
Chemical Shift (ppm)

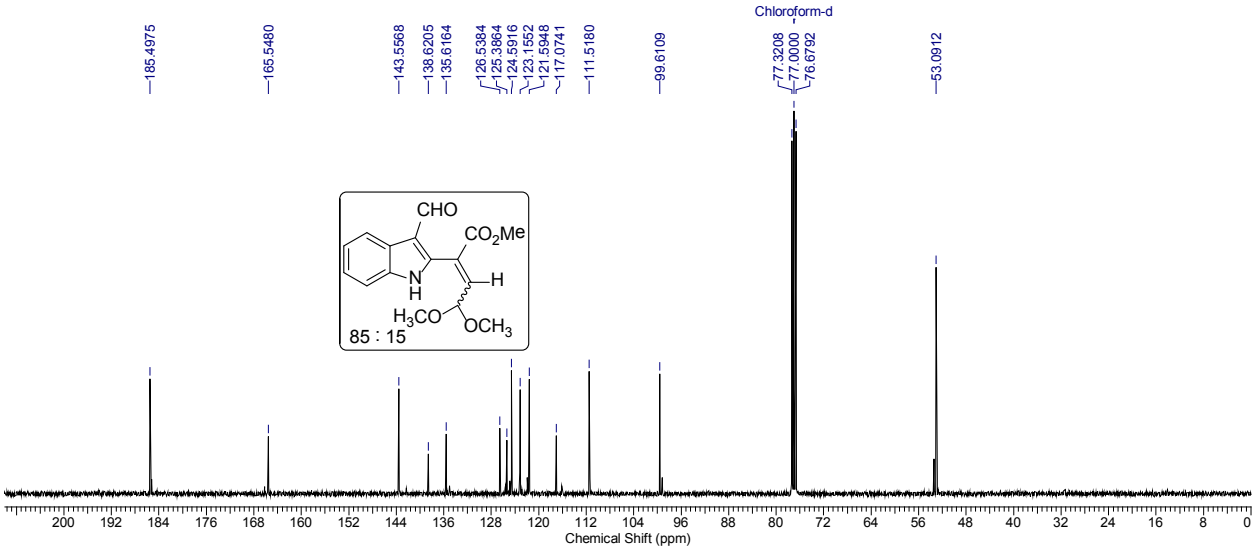

Chloroform-d
9.8567
9.1066
8.3614
8.3533
8.3388
7.4808
7.4613
7.4425
7.4118
7.3967
7.3873
7.3202
7.3121
7.2970
3.7864
2.2453
2.2265
2.2076
2.1888
1.5202
1.5014
1.4832
1.4650
1.4462
1.4280
0.8836
0.8647
0.8465
CHO
CO2Me
N
H
H
90:10
0.89
1.04
1.06
2.04
3.03
2.00
2.08
3.09
Chemical Shift (ppm)

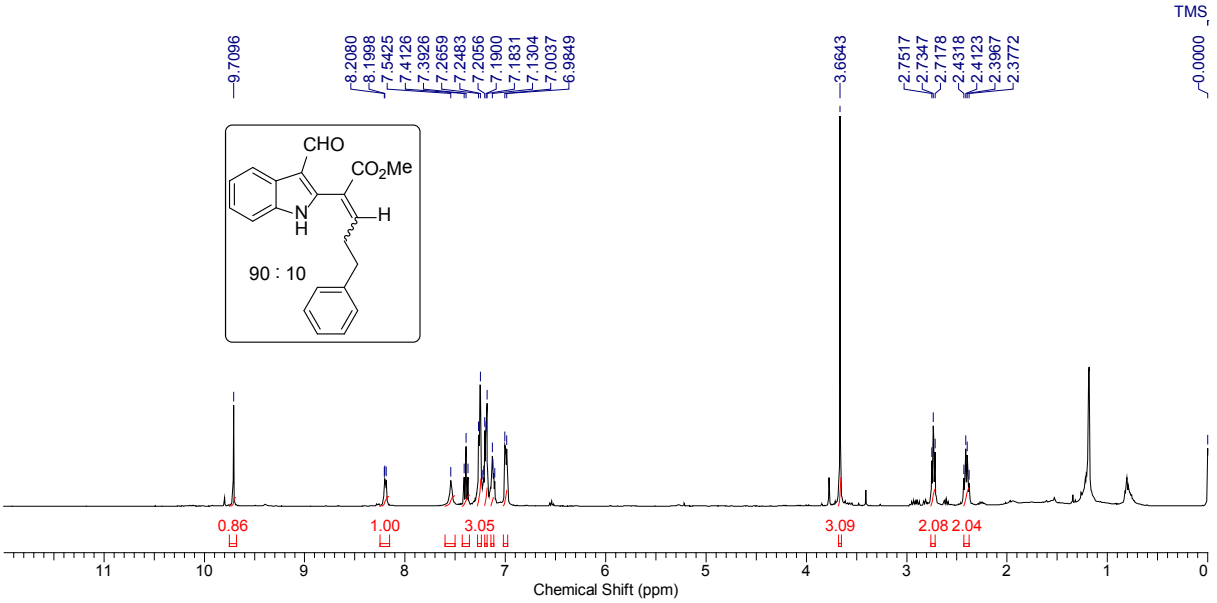

Chloroform-d
185.6069
165.9563
153.0649
141.8360
135.7987
125.0437
124.2635
122.9729
122.8198
121.8792
116.4324
111.3065
77.0000
52.5808
32.3760
21.7450
13.7098
CHO
CO2Me
N
H
H
90:10
Chemical Shift (ppm)

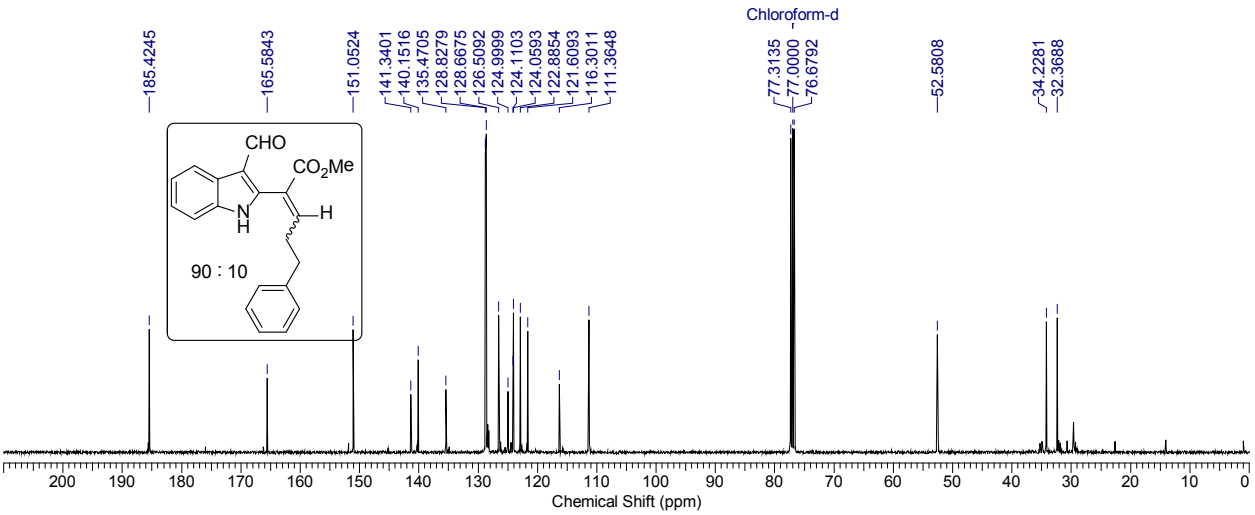

TMS
9.8570
9.2059
8.3591
8.3510
8.3372
7.4791
7.4597
7.4139
7.3995
7.3913
7.3129
7.3048
7.2991
3.7784
2.2643
2.2461
2.2273
2.2085
1.4370
1.4182
1.4000
1.3805
1.2758
1.2563
1.2382
1.2200
0.8305
0.8123
0.7941
CHO
CO2Me
N
H
H
90 :10
0.83
0.99
1.00
2.09
3.02
2.04
2.17
3.09
Chemical Shift (ppm)

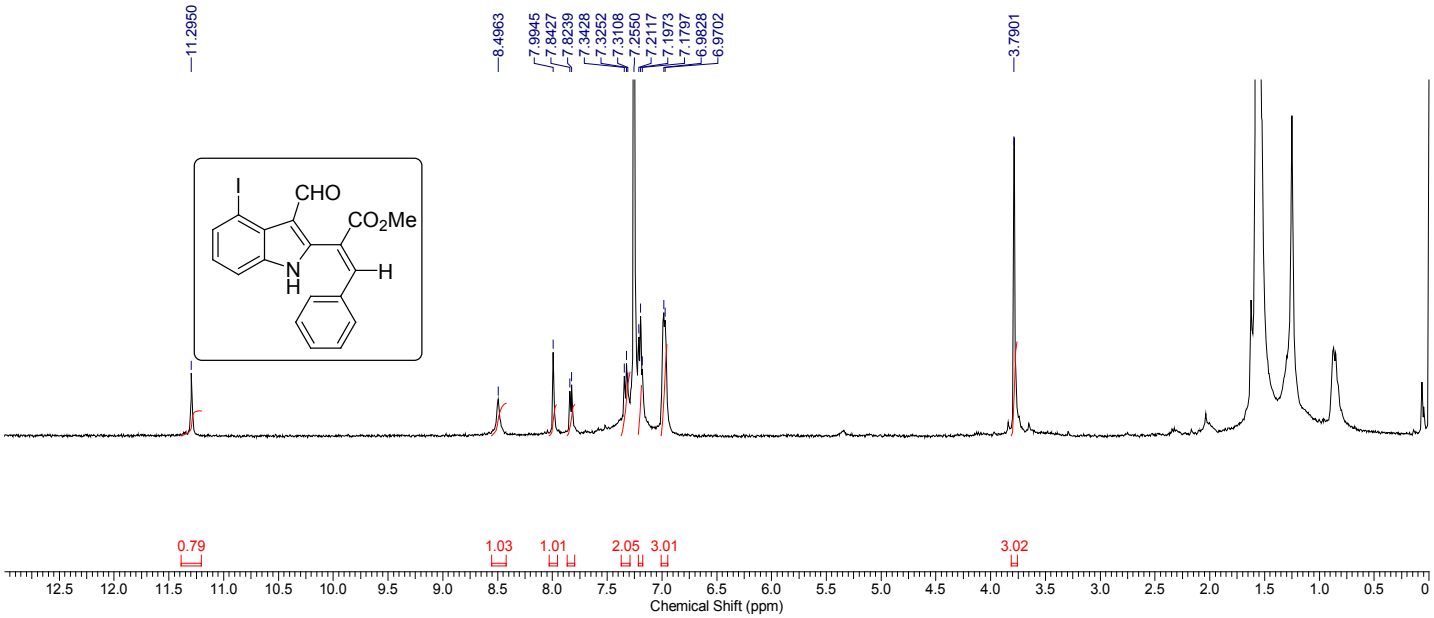

Chloroform-d
185.6215
165.9709
153.3420
141.8506
135.7841
125.0218
124.2708
122.9802
122.5865
121.8792
116.4178
111.2992
77.3135
77.0000
76.6792
52.5881
30.5021
30.2032
22.2700
13.6733
CHO
CO2Me
N
H
H
90 :10
Chemical Shift (ppm)

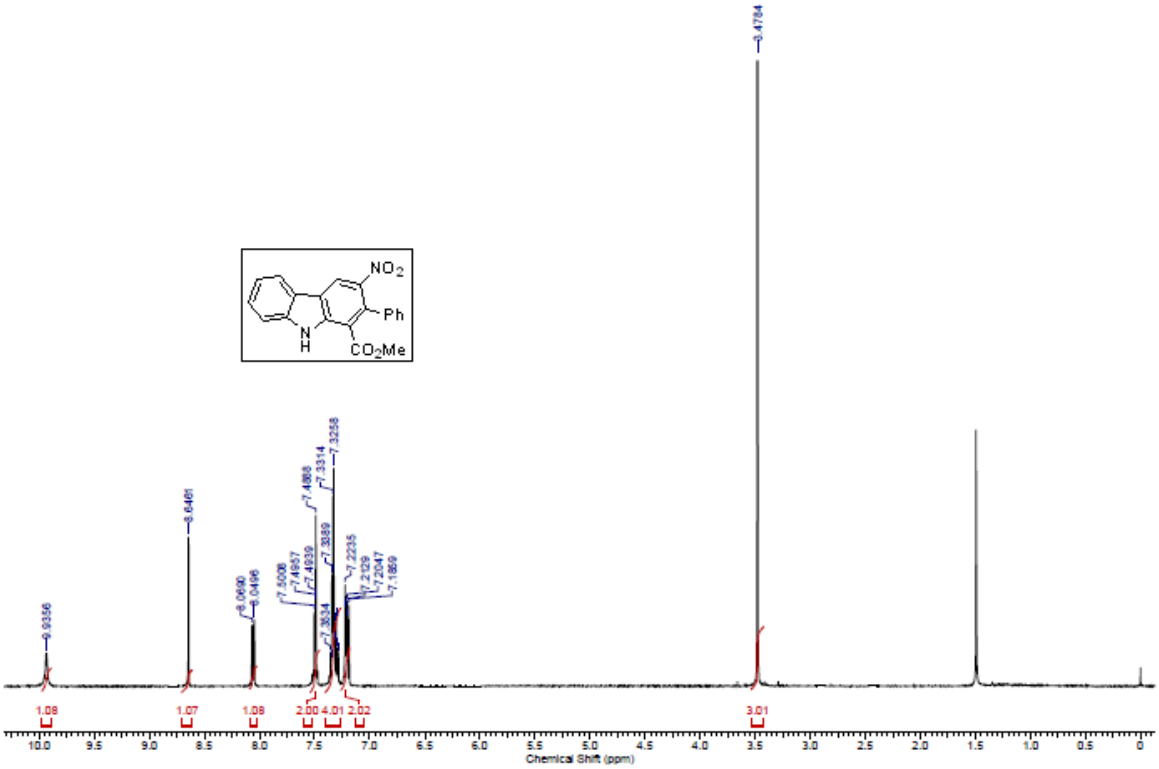

TMS
9.9705
9.5070
8.3359
8.3228
8.3133
7.4471
7.4371
7.4246
7.3361
7.3248
7.3142
7.3004
7.2615
7.2433
4.8542
4.8353
3.8148
3.3425
0.0000
CHO
CO2Me
N
H
H
H3CO
OCH3
85 : 15
0.81
0.94
1.00
2.08
1.01
3.07
6.05
Chemical Shift (ppm)

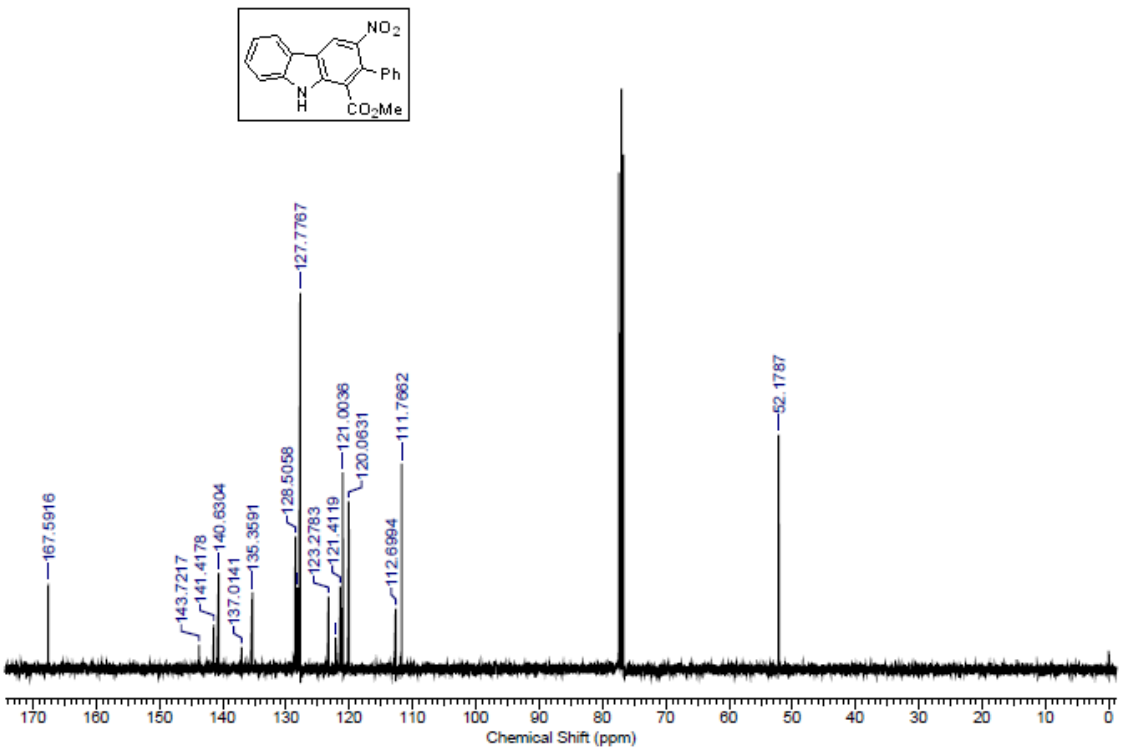

Chloroform-d
185.4975
165.5480
143.5568
138.6205
135.6164
126.5384
125.3864
124.5916
123.1552
121.5948
117.0741
111.5180
99.6109
77.3208
77.0000
76.6792
53.0912
CHO
CO2Me
N
H
H
H3CO
OCH3
85 : 15
Chemical Shift (ppm)

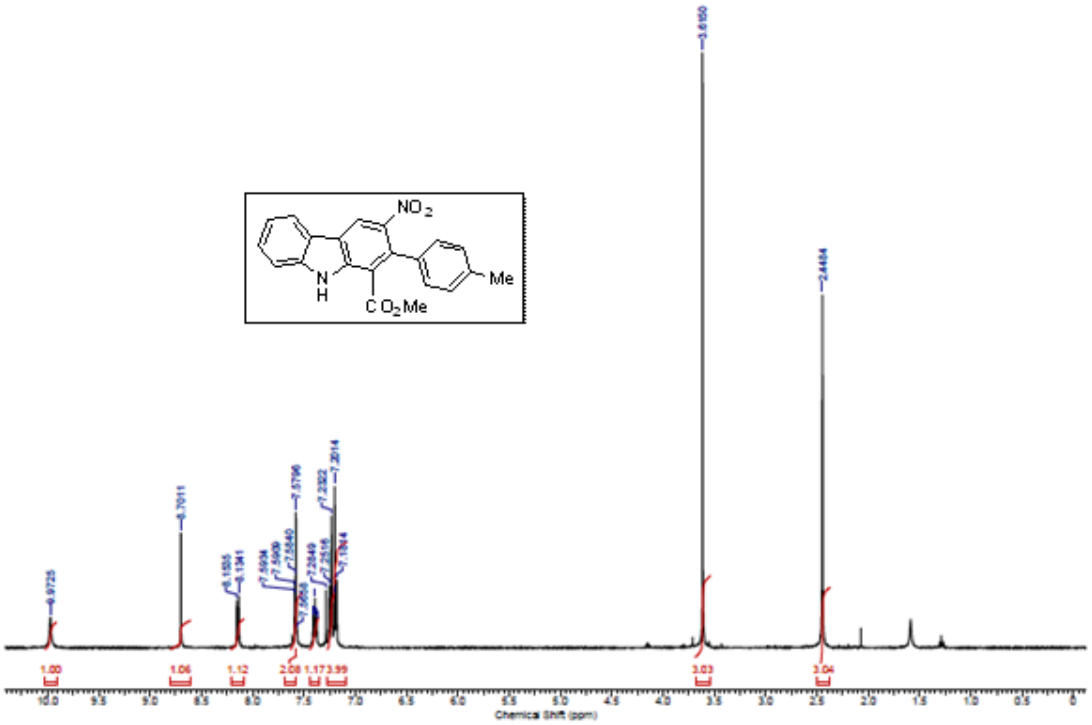

TMS
9.7096
8.2080
8.1998
7.5425
7.4126
7.3926
7.2659
7.2483
7.2056
7.1900
7.1831
7.1304
7.0037
6.9849
3.6643
2.7517
2.7347
2.7178
2.4318
2.4123
2.3967
2.3772
0.0000
CHO
CO2Me
N
H
H
90 : 10
0.86
1.00
3.05
3.09
2.08
2.04
Chemical Shift (ppm)

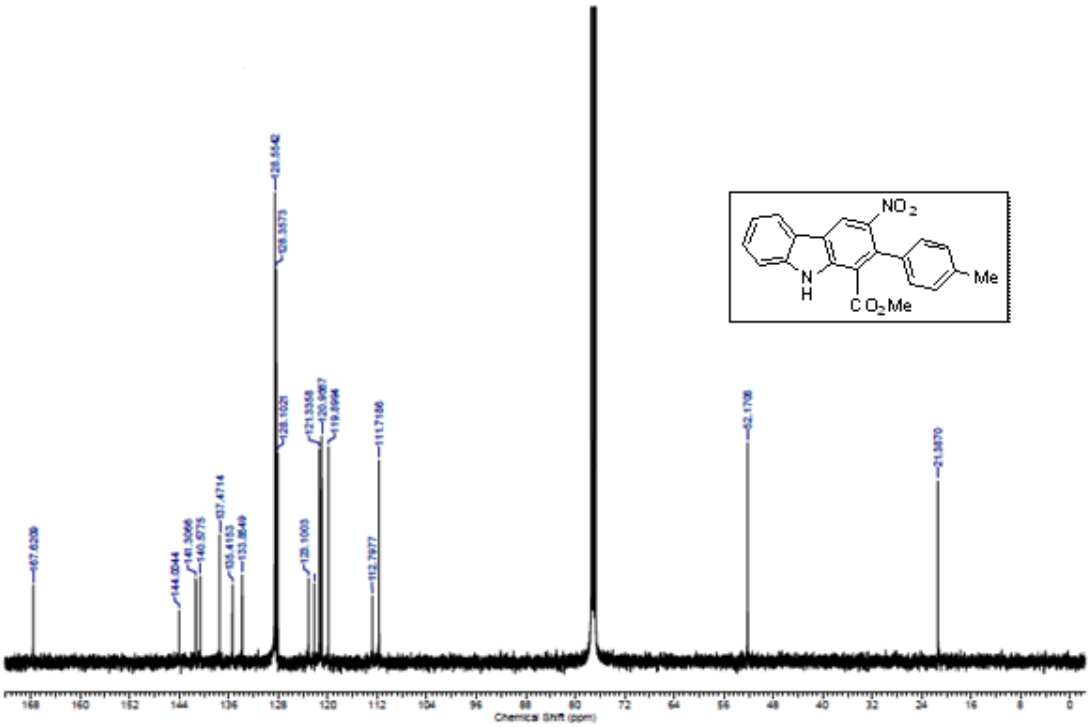

Chloroform-d
185.4245
165.5843
151.0524
141.3401
140.1516
135.4705
128.8279
128.6675
126.5092
124.9999
124.1103
124.0593
122.8854
121.6093
116.3011
111.3648
77.3135
77.0000
76.6792
52.5808
34.2281
32.3688
CHO
CO2Me
N
H
H
90 : 10
Chemical Shift (ppm)

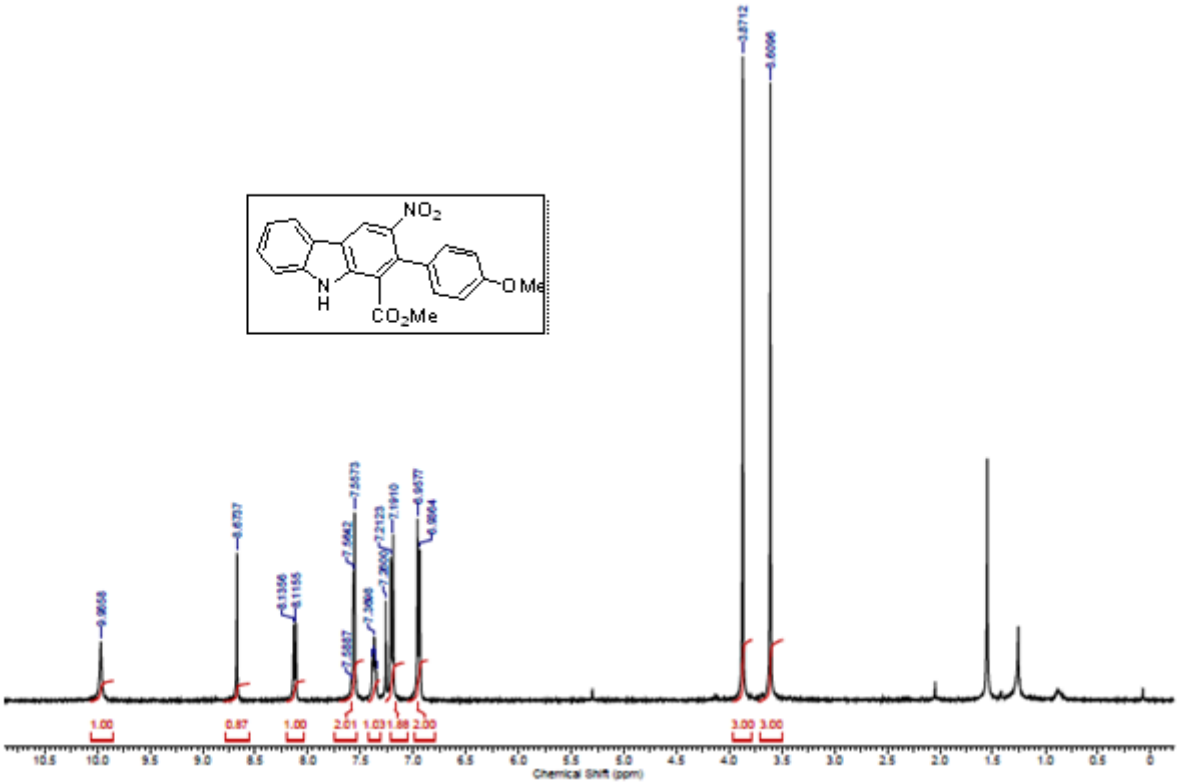


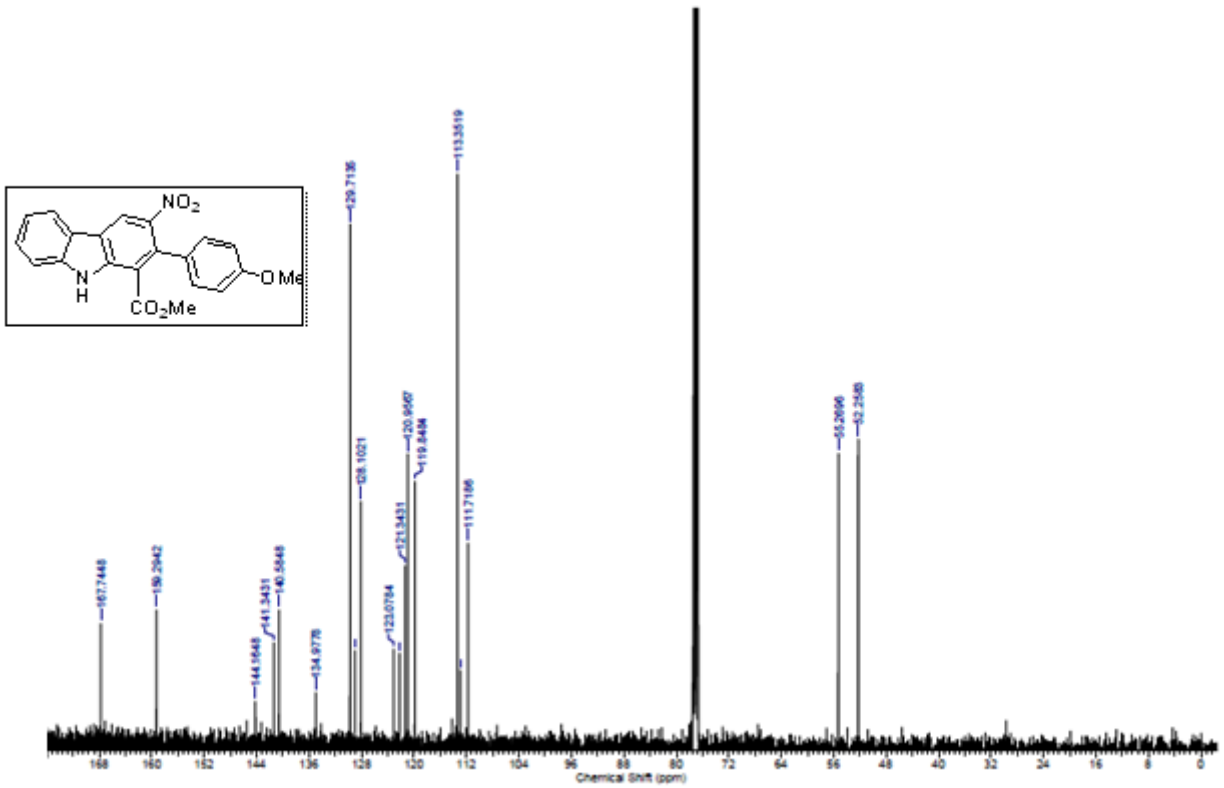

NO2
Ph
N
H
CO2Me
9.9356
8.6461
8.0690
8.0496
7.5006
7.4957
7.4939
7.4868
7.3834
7.3314
7.3258
7.3089
7.2235
7.2129
7.2047
7.1889
3.4784
1.08
1.07
1.08
2.00
4.01
2.02
3.01
Chemical Shift (ppm)

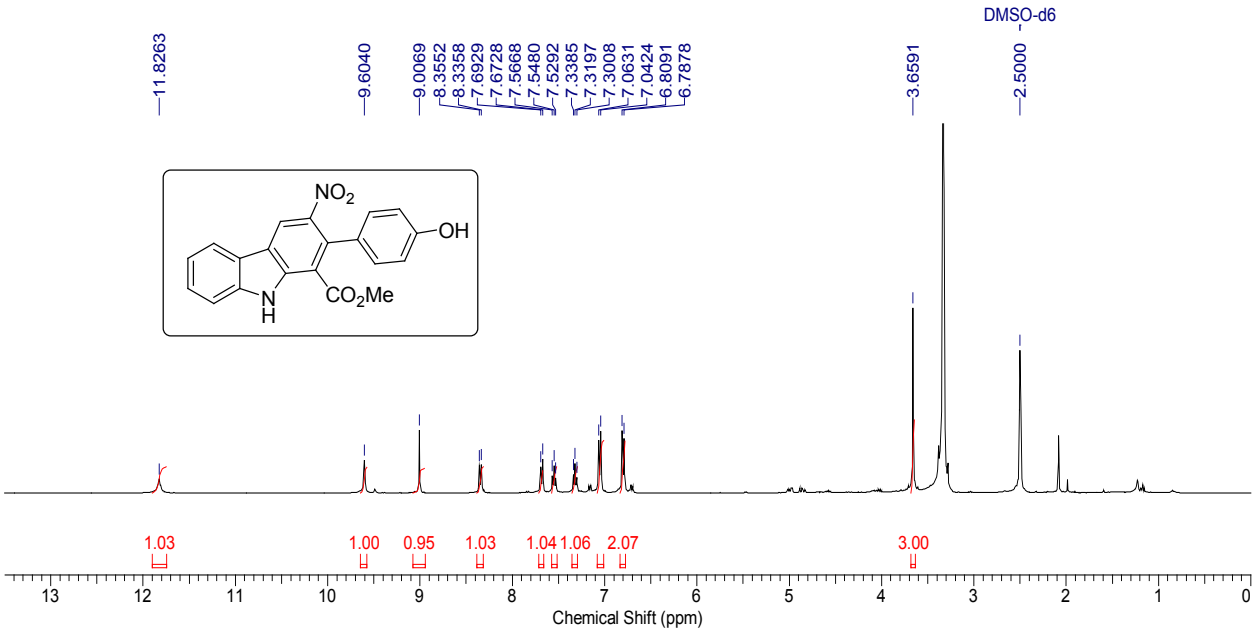

NO2
Ph
N
H
CO2Me
167.5916
143.7217
141.4178
140.6304
137.0141
135.3591
128.5058
127.7767
123.2783
121.4119
121.0036
120.0631
112.6994
111.7662
52.1787
Chemical Shift (ppm)

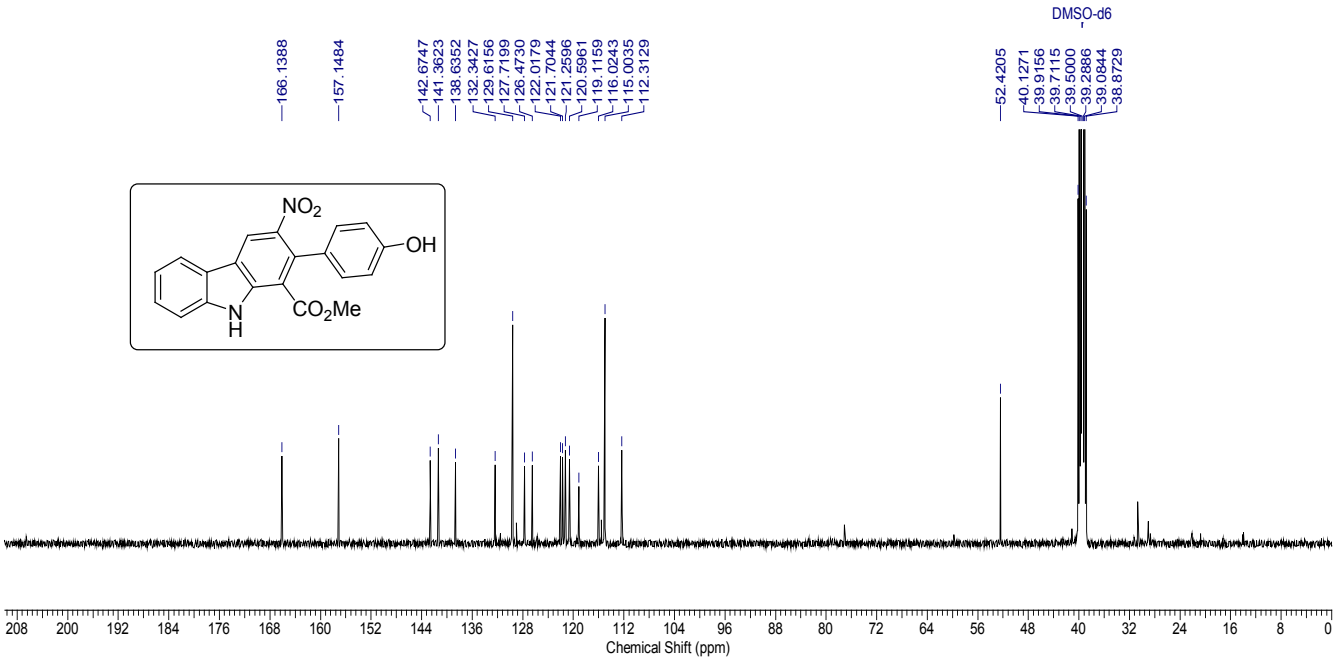


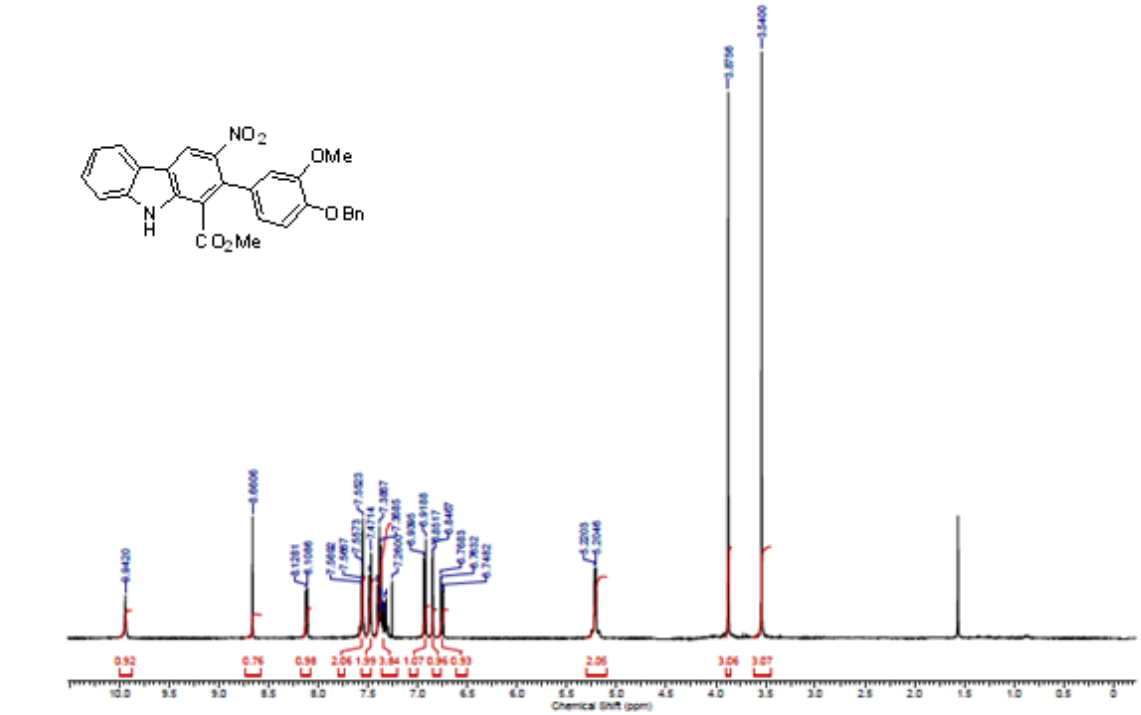


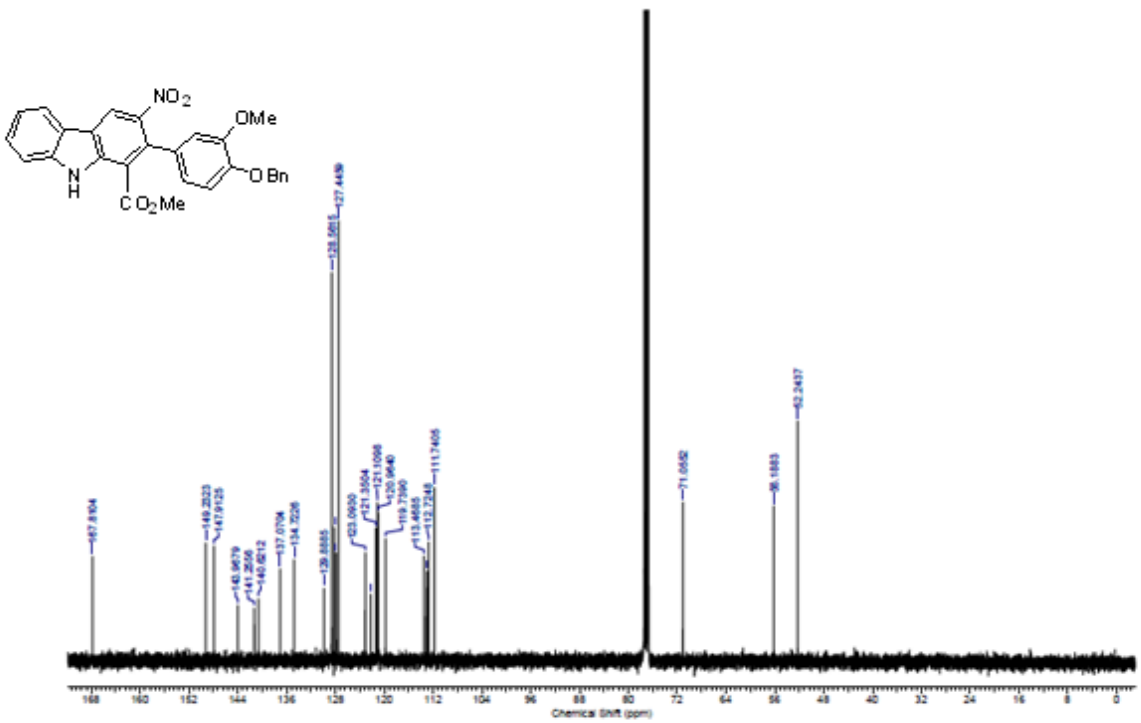


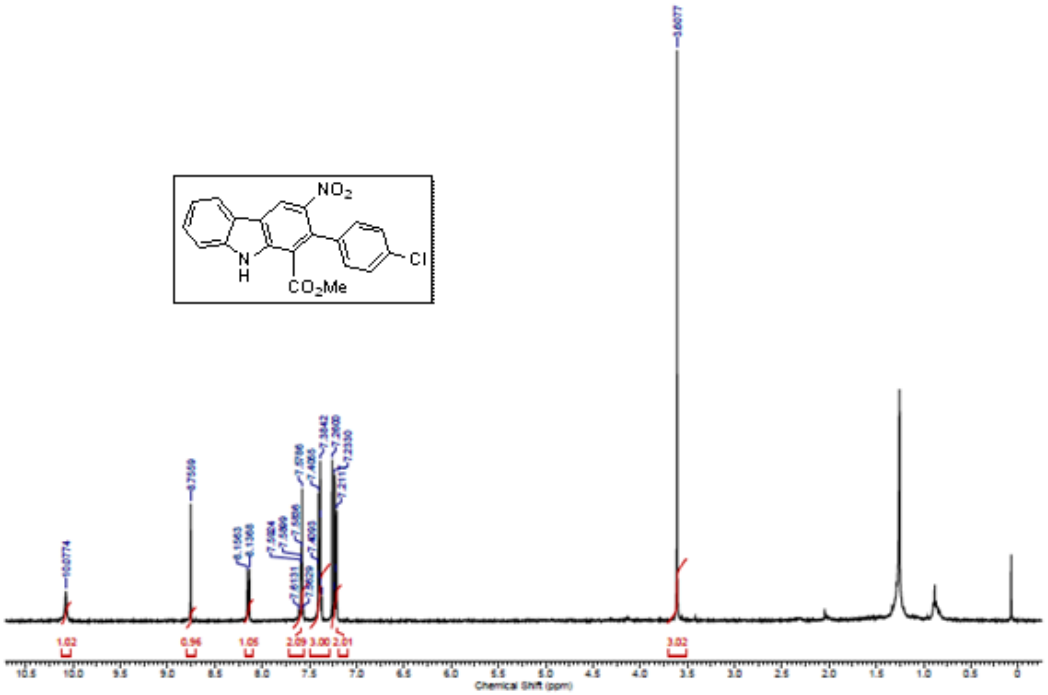


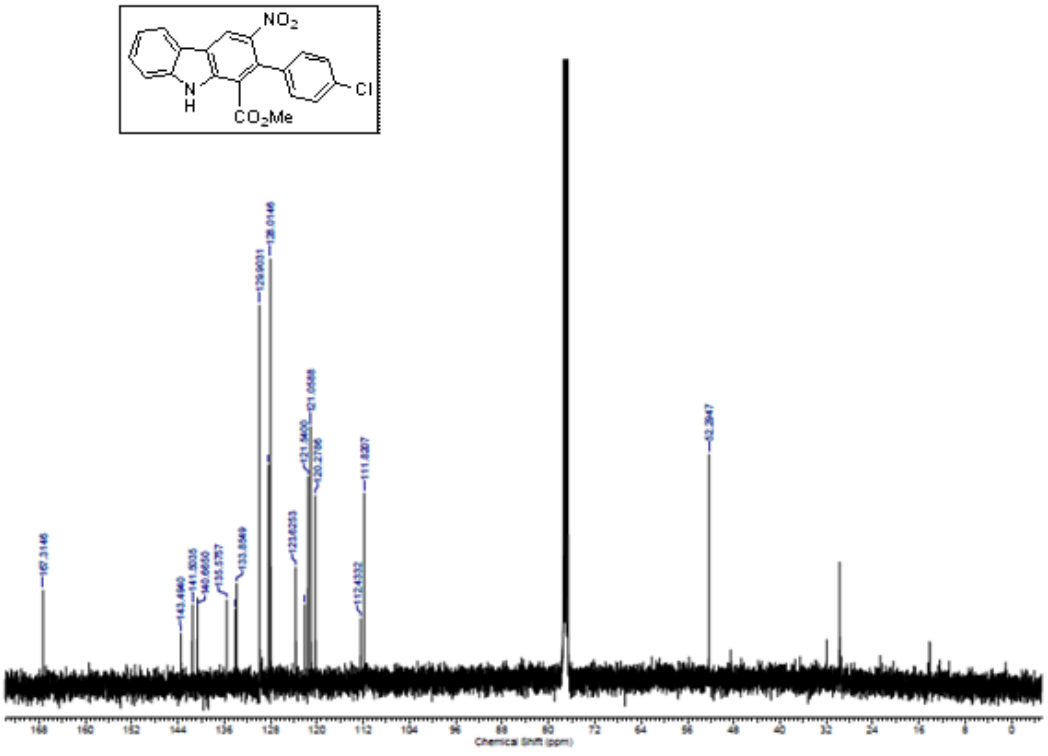

DMSO-d6
11.8263
9.6040
9.0069
8.3552
8.3358
7.6929
7.6728
7.5668
7.5480
7.5292
7.3385
7.3197
7.3008
7.0631
7.0424
6.8091
6.7878
3.6591
2.5000
NO2
OH
N
H
CO2Me
1.03
1.00
0.95
1.03
1.04
1.06
2.07
3.00
Chemical Shift (ppm)

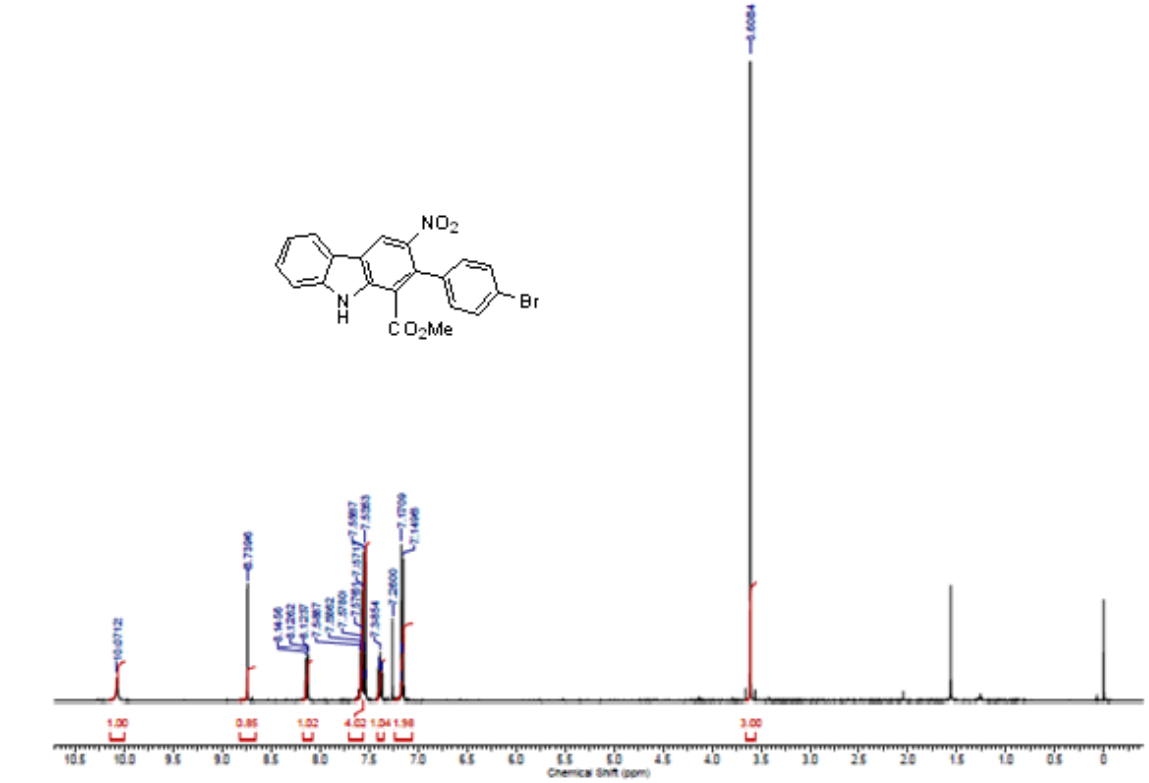

DMSO-d6
166.1388
157.1484
142.6747
141.3623
138.6352
132.3427
129.6156
127.7199
126.4730
122.0179
121.7044
121.2596
120.5961
119.1159
116.0243
115.0035
112.3129
52.4205
40.1271
39.9156
39.7115
39.5000
39.2886
39.0844
38.8729
NO2
OH
N
H
CO2Me
Chemical Shift (ppm)

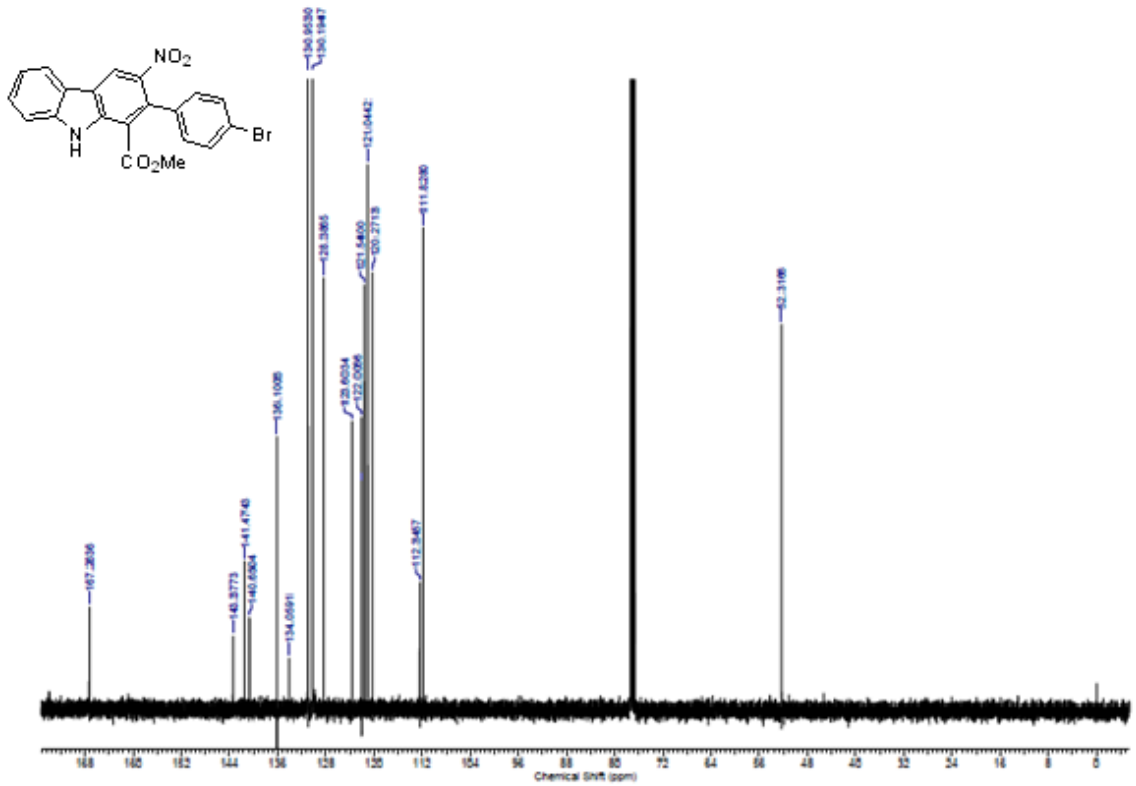

NO2
OMe
O Bn
N
H
C O2Me
Chemical Shift (ppm)

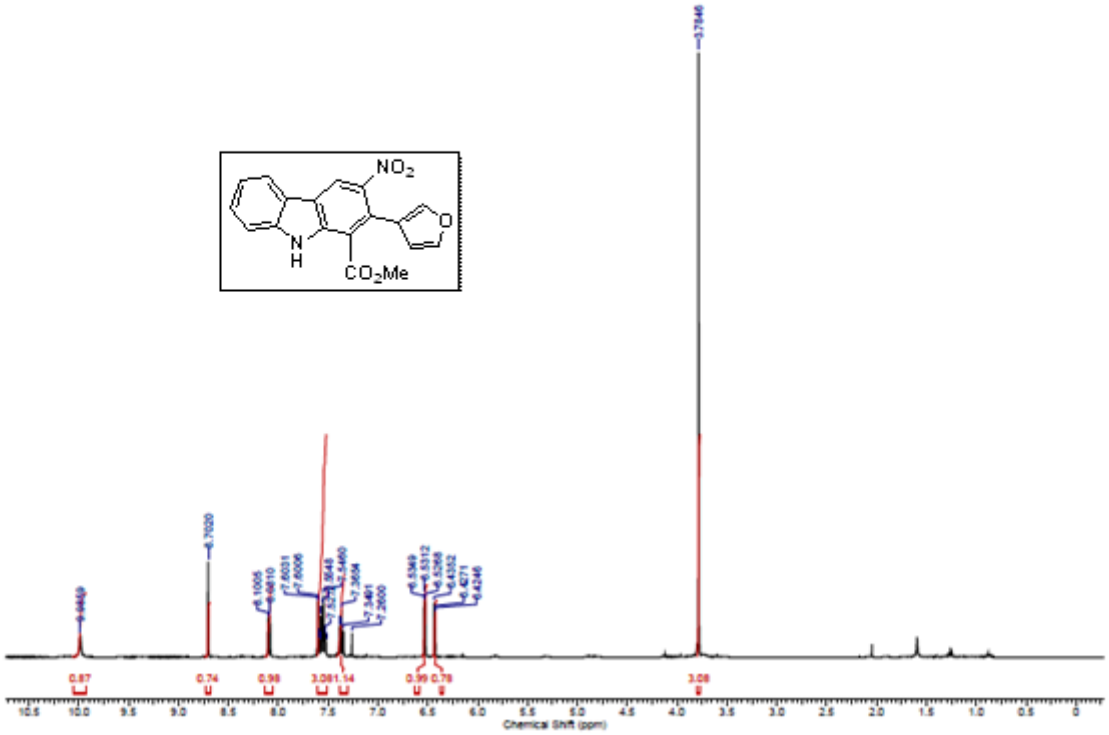

NO2
OMe
O Bn
N
H
C O2Me
Chemical Shift (ppm)

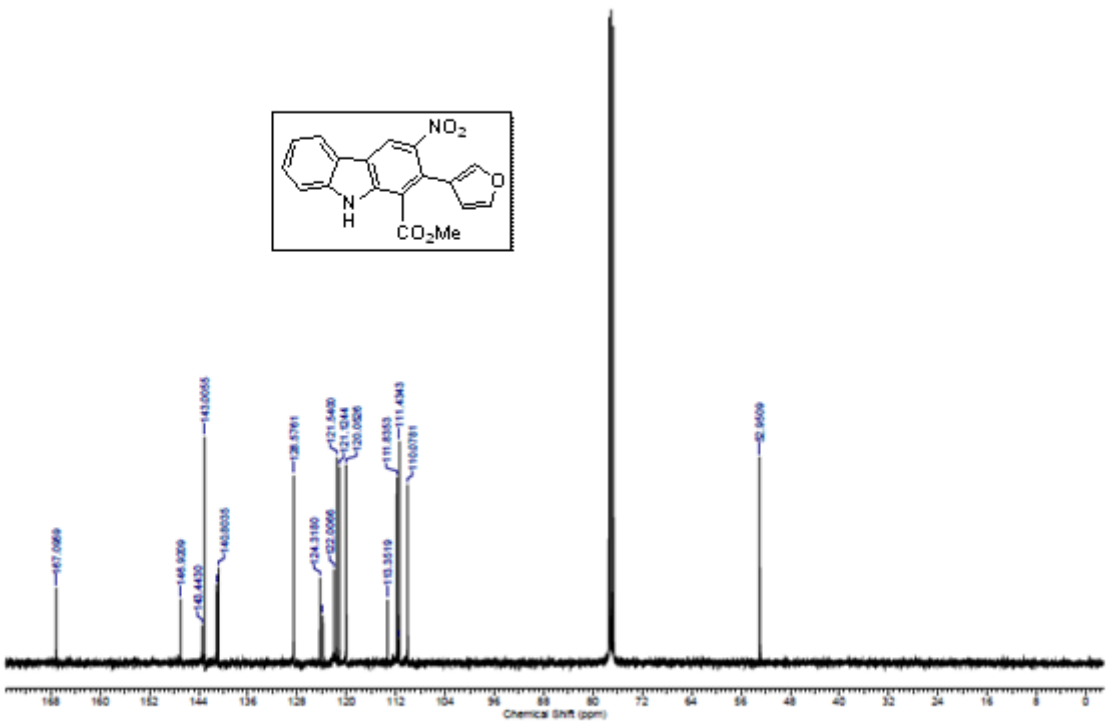


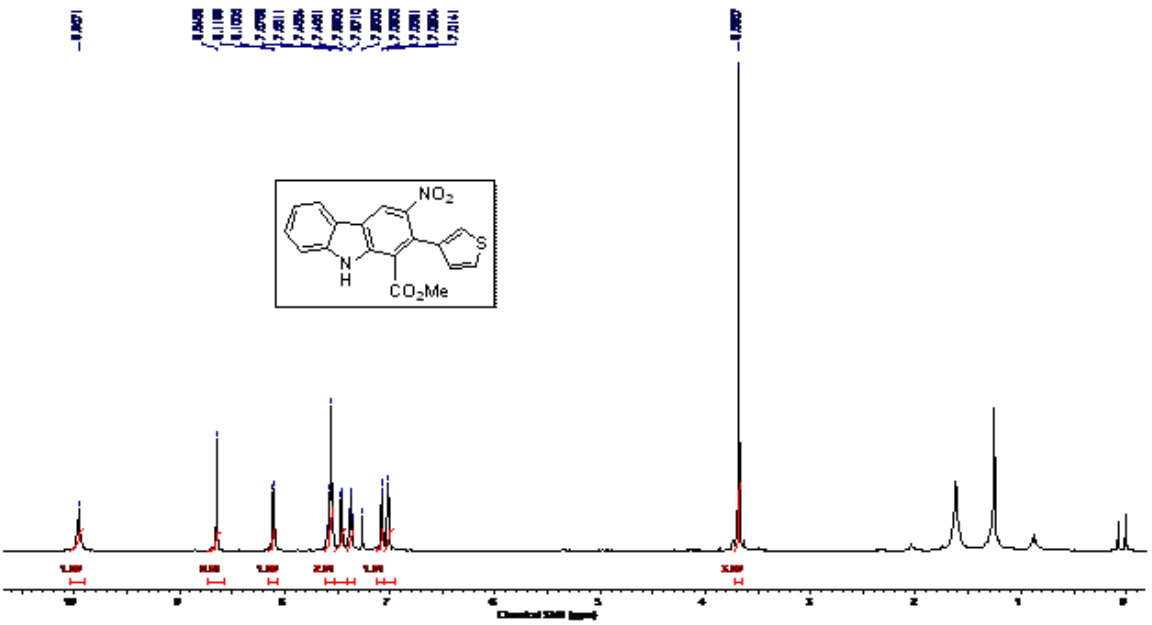


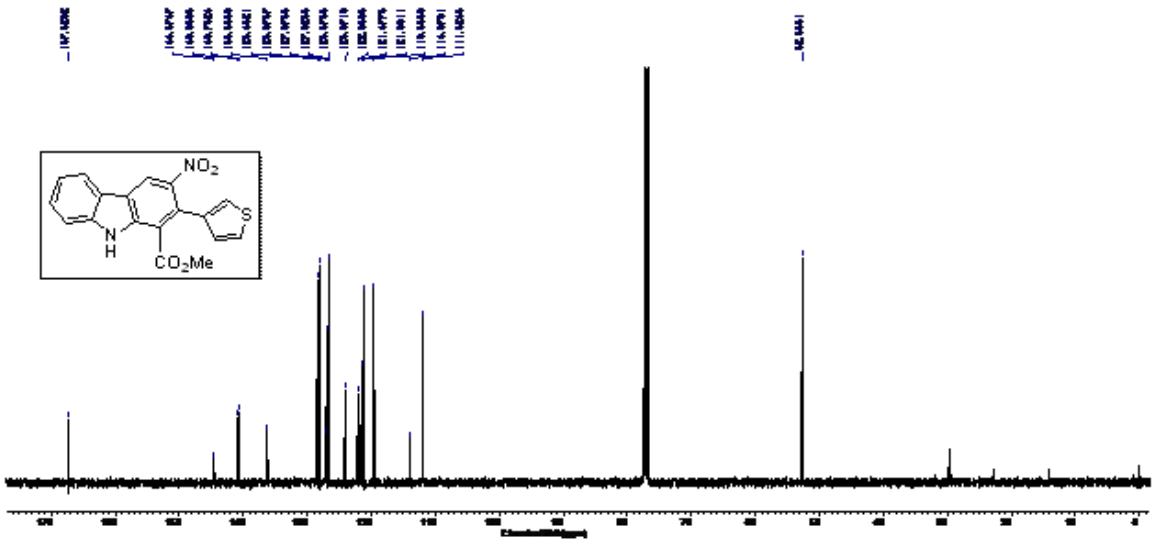

NO2
Br
N
H
CO2Me
Chemical Shift (ppm)

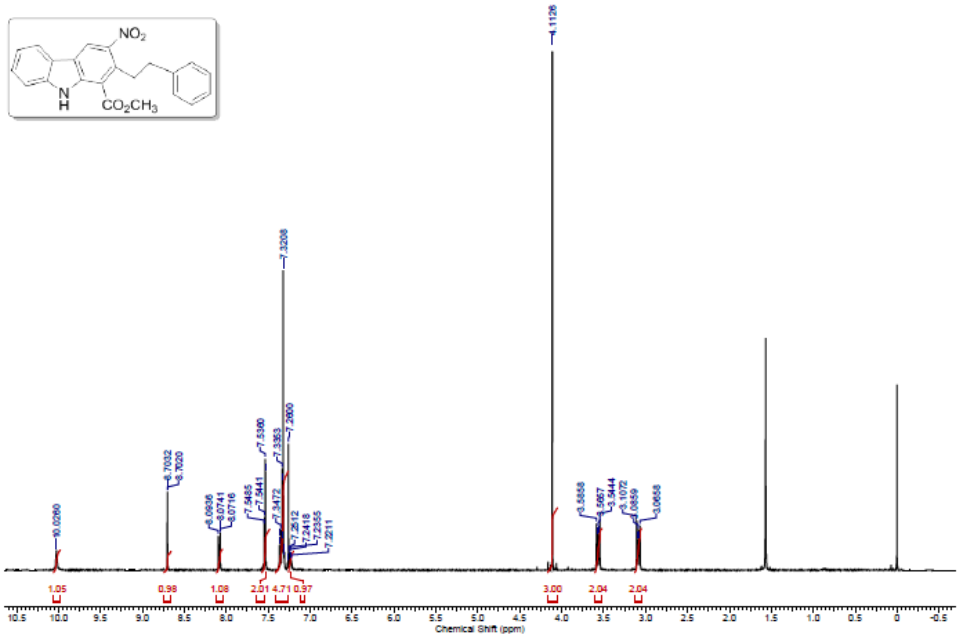

NO2
Br
N
H
CO2Me
Chemical Shift (ppm)

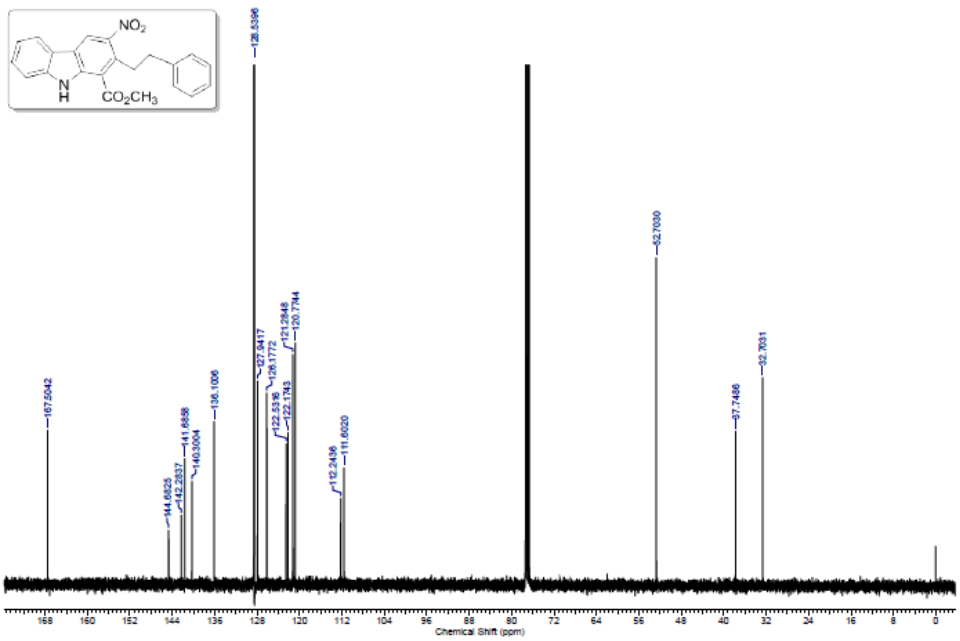

NO2
O
N
H
CO2Me
Chemical Shift (ppm)

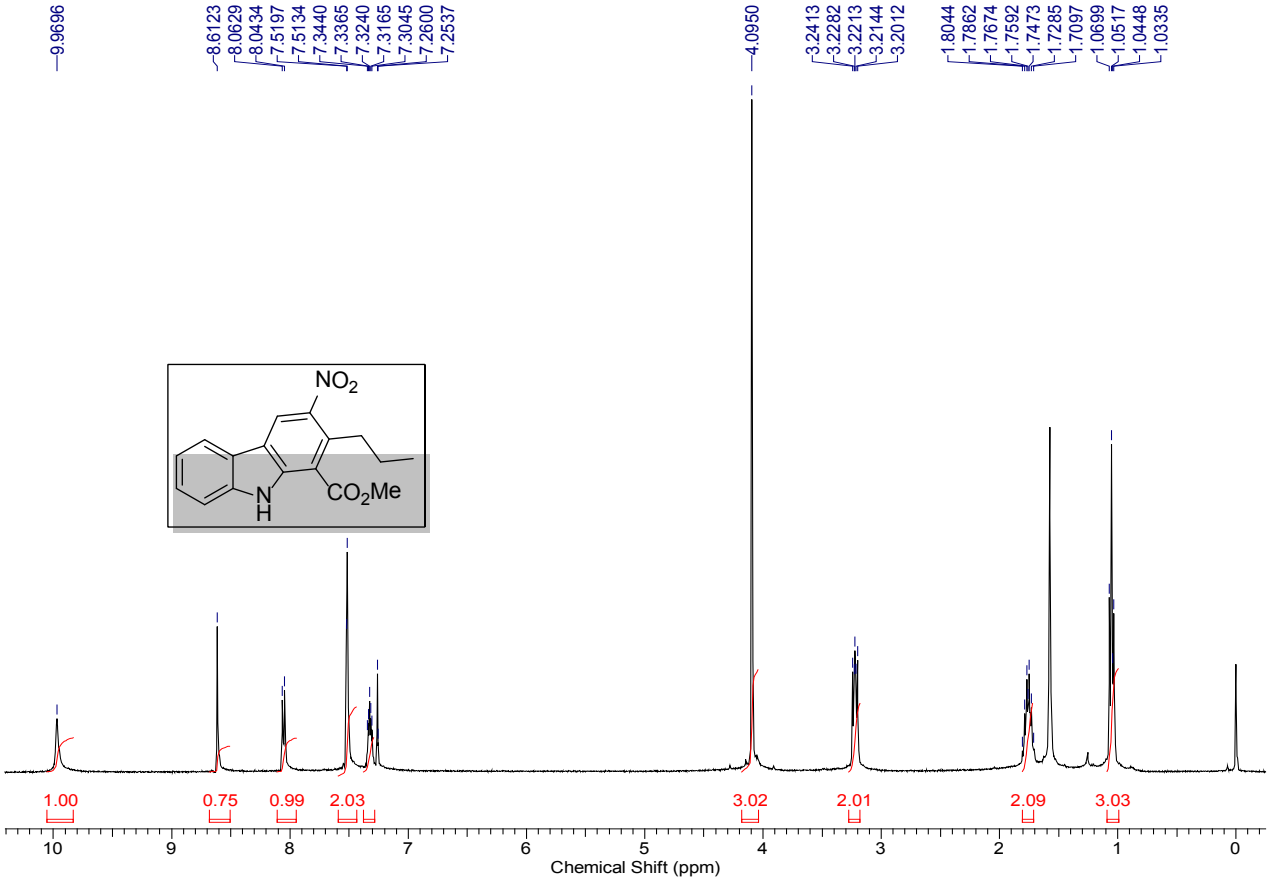

NO2
O
N
H
CO2Me
Chemical Shift (ppm)






NO2
N
H
CO2CH3
Chemical Shift (ppm)


NO2
N
H
CO2CH3
Chemical Shift (ppm)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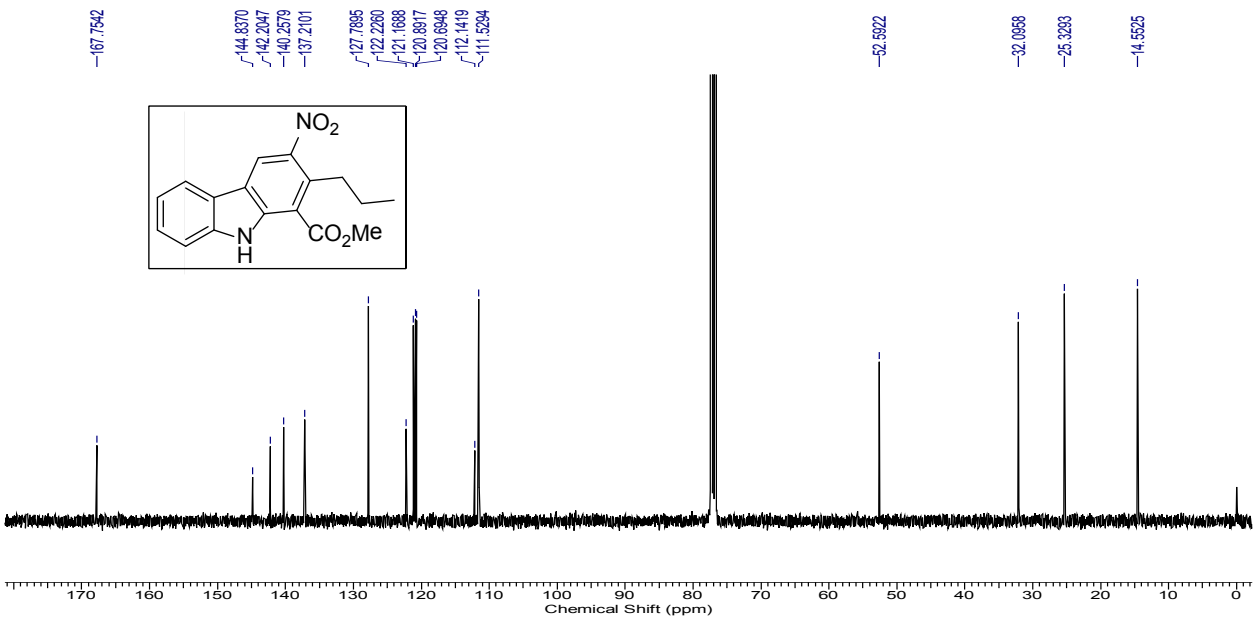
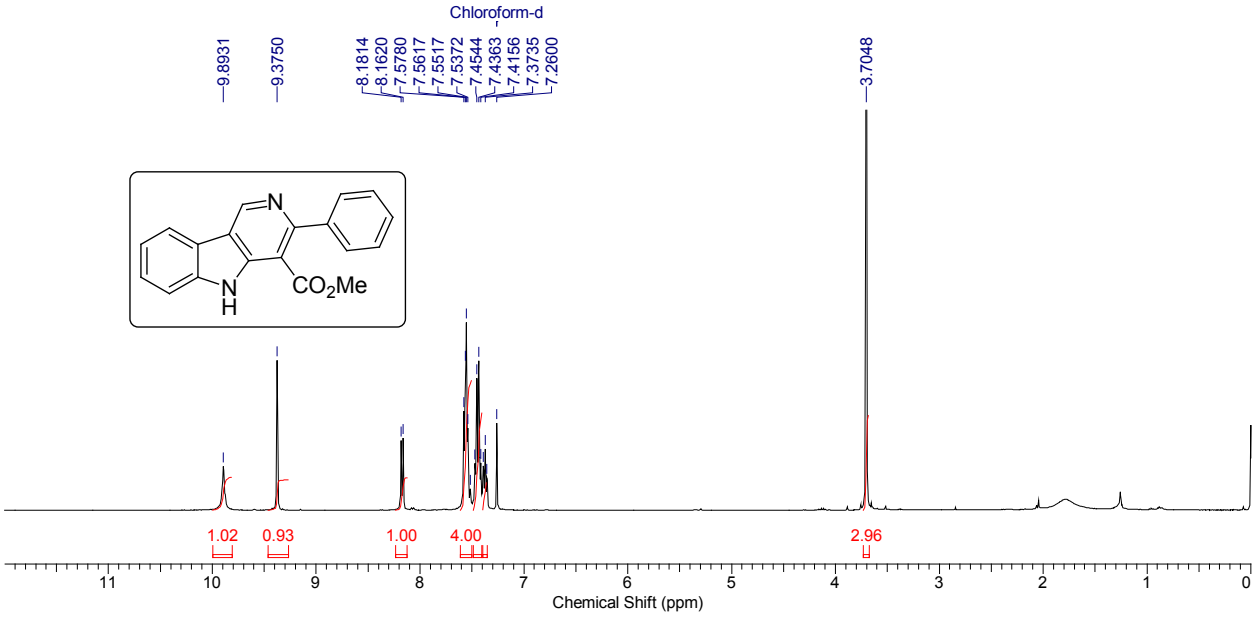
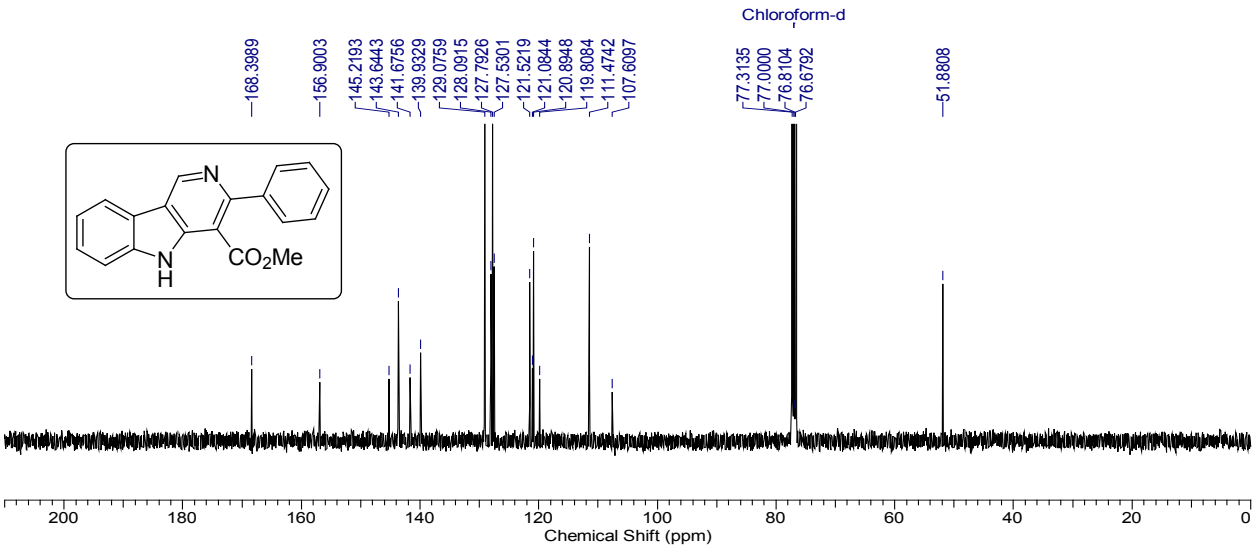
8.0629
8.0434
7.5197
7.5134
7.3440
7.3365
7.3240
7.3165
7.3045
7.2600
7.2537
4.0950
3.2413
3.2282
3.2213
3.2144
3.2012
1.8044
1.7862
1.7674
1.7592
1.7473
1.7285
1.7097
1.0699
1.0517
1.0448
1.0335
NO2
N
H
CO2Me
1.00
0.75
0.99
2.03
3.02
2.01
2.09
3.03
Chemical Shift (ppm)


167.7542
144.8370
142.2047
140.2579
137.2101
127.7895
122.2260
121.1688
120.8917
120.6948
112.1419
111.5294
52.5922
32.0958
25.3293
14.5525
NO2
N
H
CO2Me
Chemical Shift (ppm)


Chloroform-d
9.8931
9.3750
8.1814
8.1620
7.5780
7.5617
7.5517
7.5372
7.4544
7.4363
7.4156
7.3735
7.2600
3.7048
N
N
H
CO2Me
1.02
0.93
1.00
4.00
2.96
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Chloroform-d
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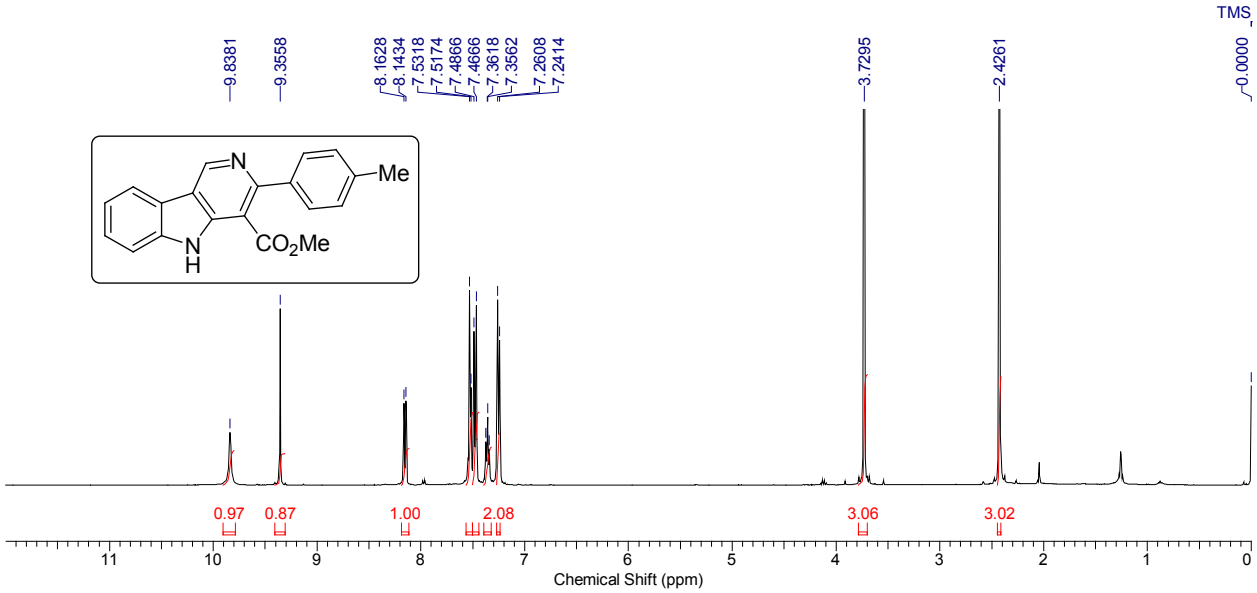
156.9003
145.2193
143.6443
141.6756
139.9329
129.0759
128.0915
127.7926
127.5301
121.5219
121.0844
120.8948
119.8084
111.4742
107.6097
77.3135
77.0000
76.8104
76.6792
51.8808
N
N
H
CO2Me
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


TMS
9.8381
9.3558
8.1628
8.1434
7.5318
7.5174
7.4866
7.4666
7.3618
7.3562
7.2608
7.2414
3.7295
2.4261
0.0000
N
Me
N
H
CO2Me
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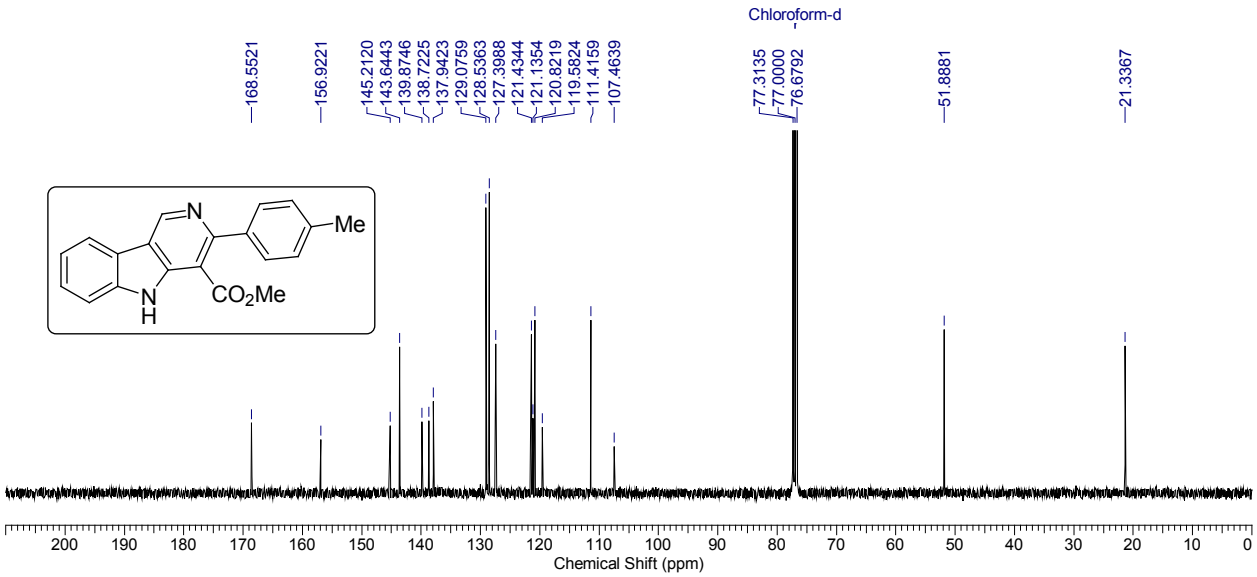
0.87
1.00
2.08
3.06
3.02
Chemical Shift (ppm)


Chloroform-d
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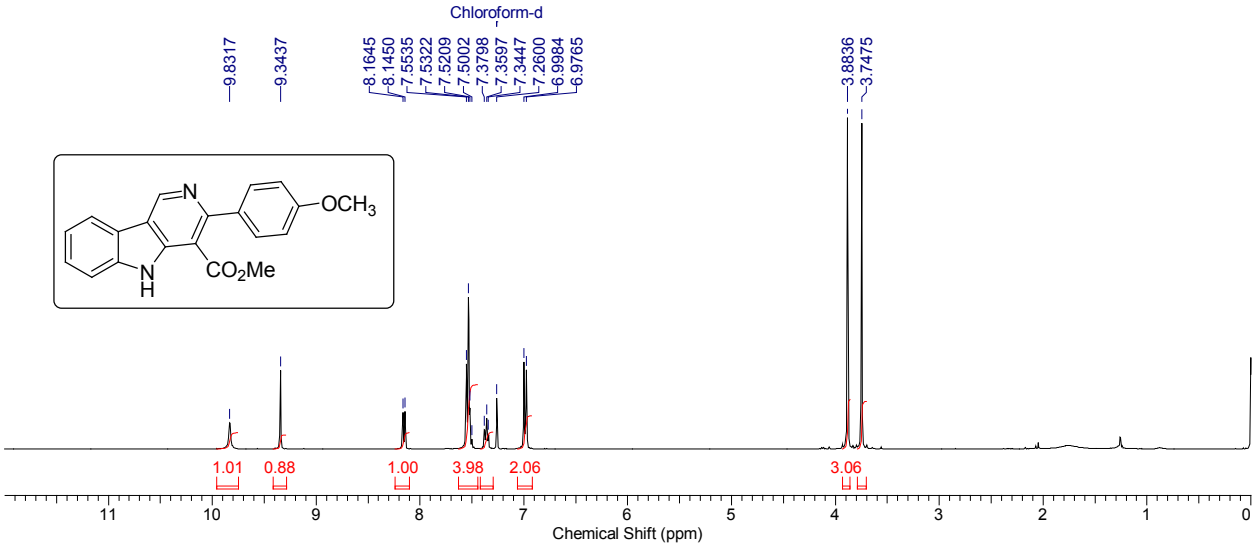
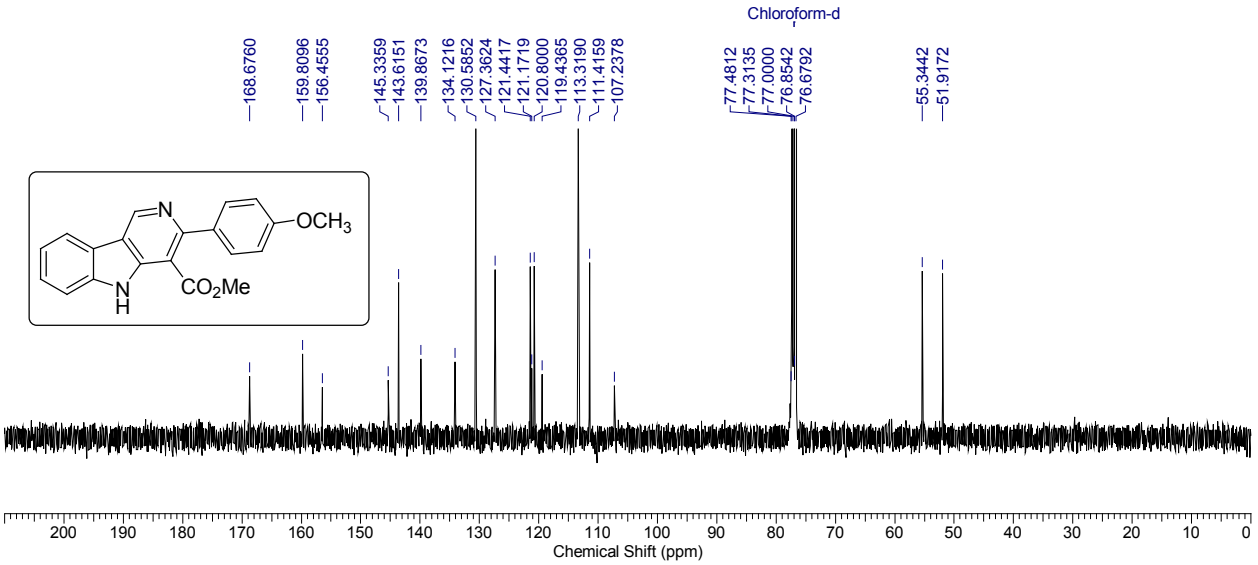
156.9221
145.2120
143.6443
139.8746
138.7225
137.9423
129.0759
128.5363
127.3988
121.4344
121.1354
120.8219
119.5824
111.4159
107.4639
77.3135
77.0000
76.6792
51.8881
21.3367
N
Me
N
H
CO2Me
Chemical Shift (ppm)


Chloroform-d
9.8317
9.3437
8.1645
8.1450
7.5535
7.5322
7.5209
7.5002
7.3798
7.3597
7.3447
7.2600
6.9984
6.9765
3.8836
3.7475
OCH3
N
N
H
CO2Me
1.01
0.88
1.00
3.98
2.06
3.06
Chemical Shift (ppm)


Chloroform-d
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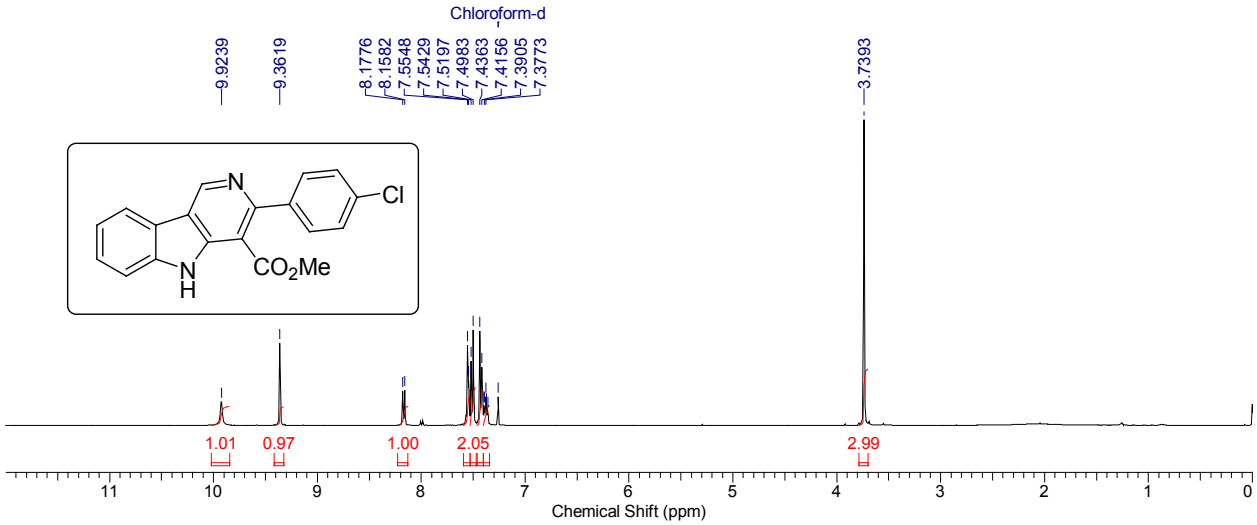
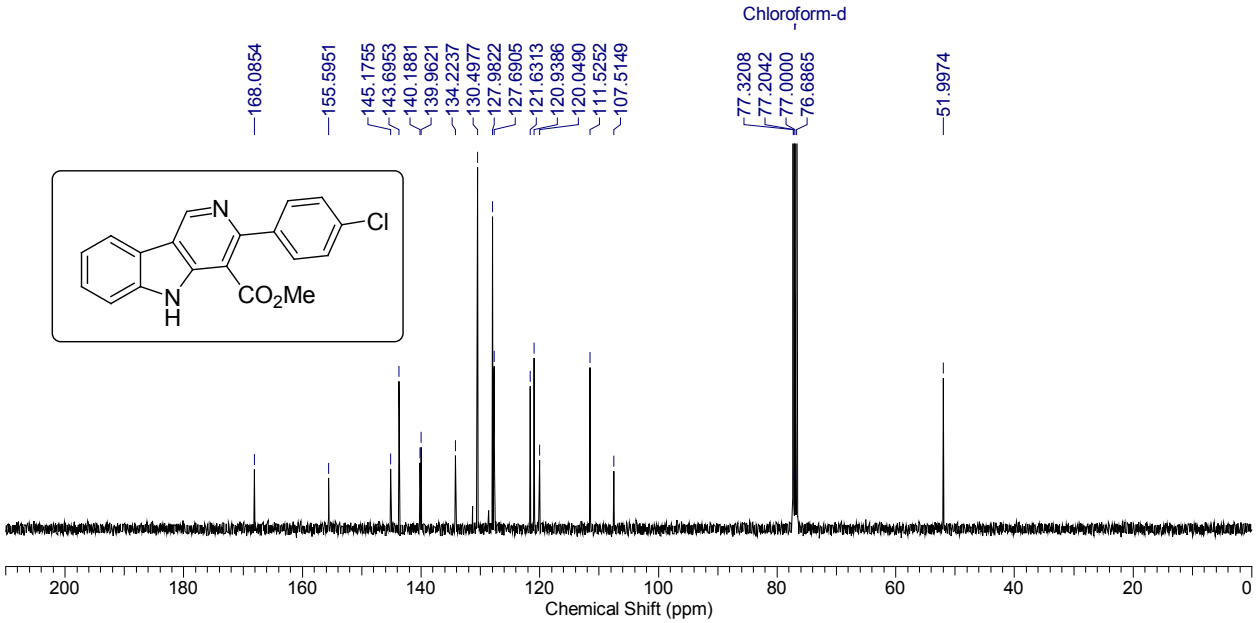
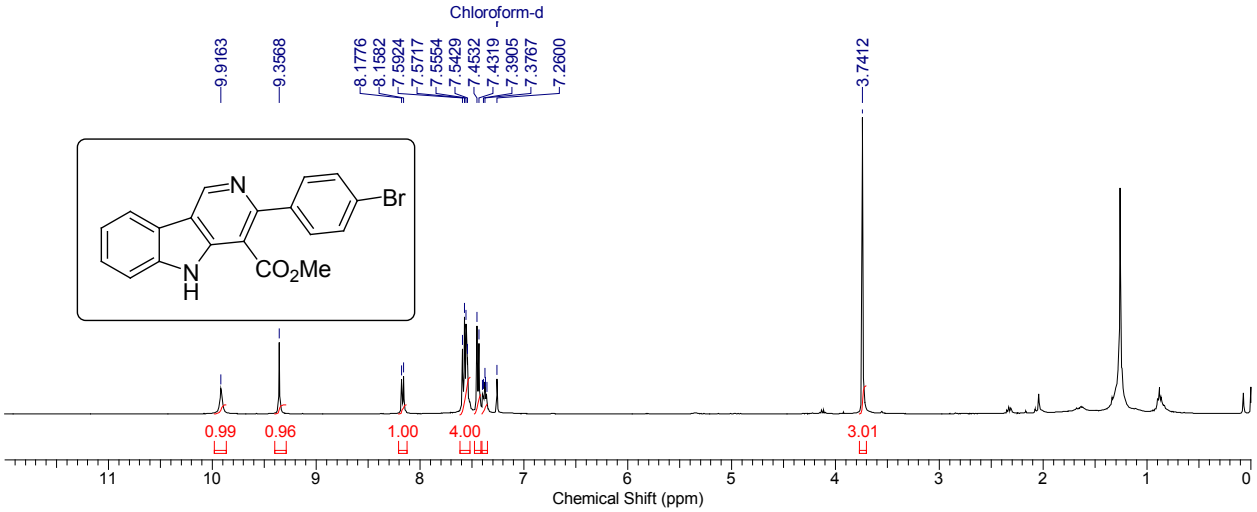
156.4555
145.3359
143.6151
139.8673
134.1216
130.5852
127.3624
121.4417
121.1719
120.8000
119.4365
113.3190
111.4159
107.2378
77.4812
77.3135
77.0000
76.8542
76.6792
55.3442
51.9172
OCH3
N
N
H
CO2Me
Chemical Shift (ppm)






Chloroform-d
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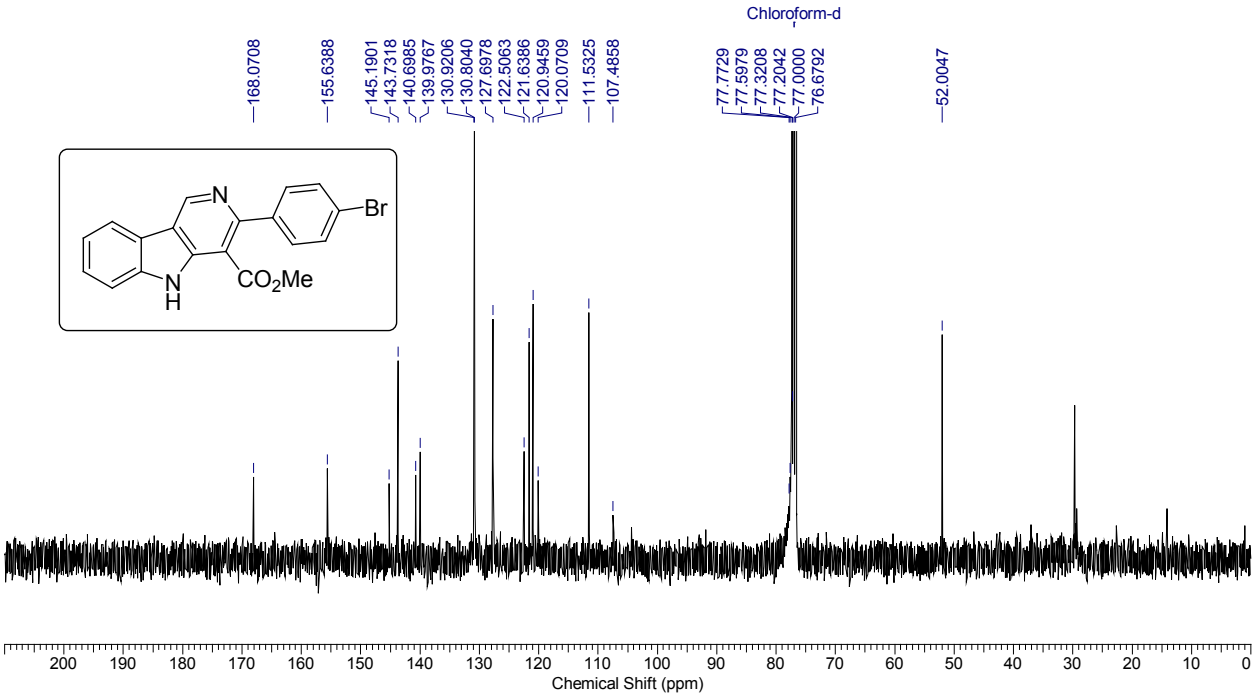
8.1776
8.1582
7.5924
7.5717
7.5554
7.5429
7.4532
7.4319
7.3905
7.3767
7.2600
3.7412
Br
N
H
CO2Me
0.99
0.96
1.00
4.00
3.01
Chemical Shift (ppm)


Chloroform-d
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143.7318
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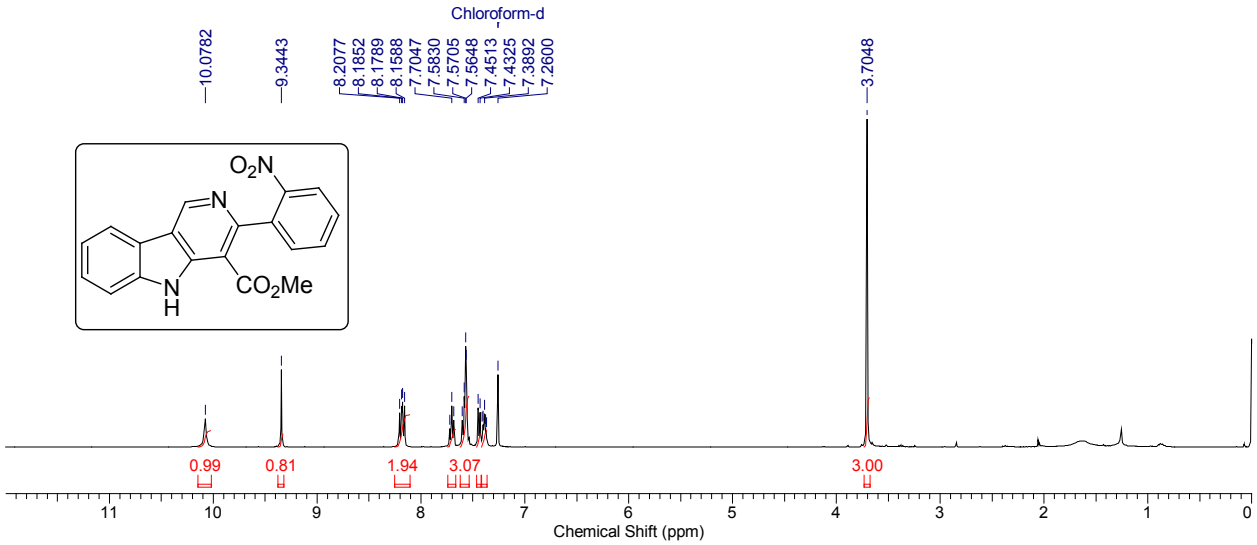
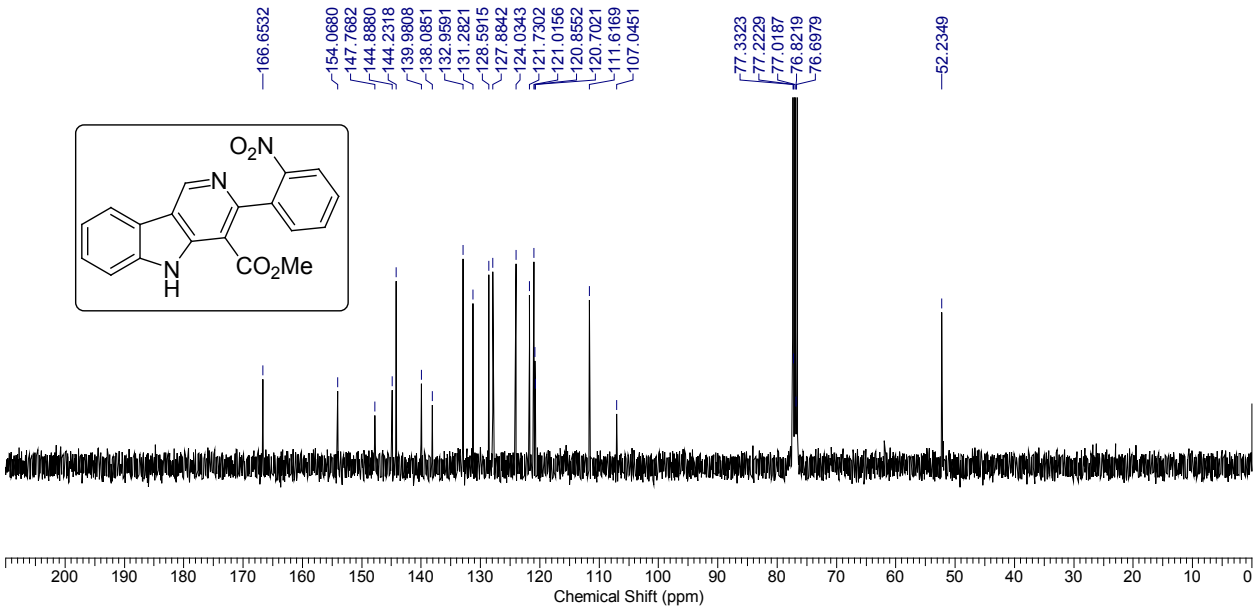
139.9767
130.9206
130.8040
127.6978
122.5063
121.6386
120.9459
120.0709
111.5325
107.4858
77.7729
77.5979
77.3208
77.2042
77.0000
76.6792
52.0047
Br
N
H
CO2Me
Chemical Shift (ppm)


Chloroform-d
10.0782
9.3443
8.2077
8.1852
8.1789
8.1588
7.7047
7.5830
7.5705
7.5648
7.4513
7.4325
7.3892
7.2600
3.7048
O2N
N
N
H
CO2Me
0.99
0.81
1.94
3.07
3.00
Chemical Shift (ppm)


166.6532
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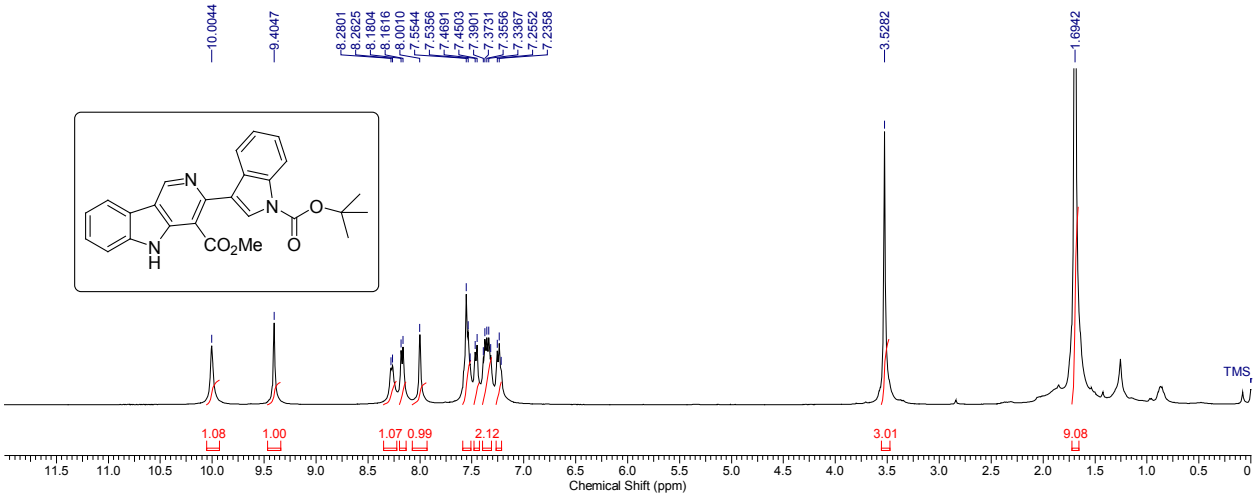
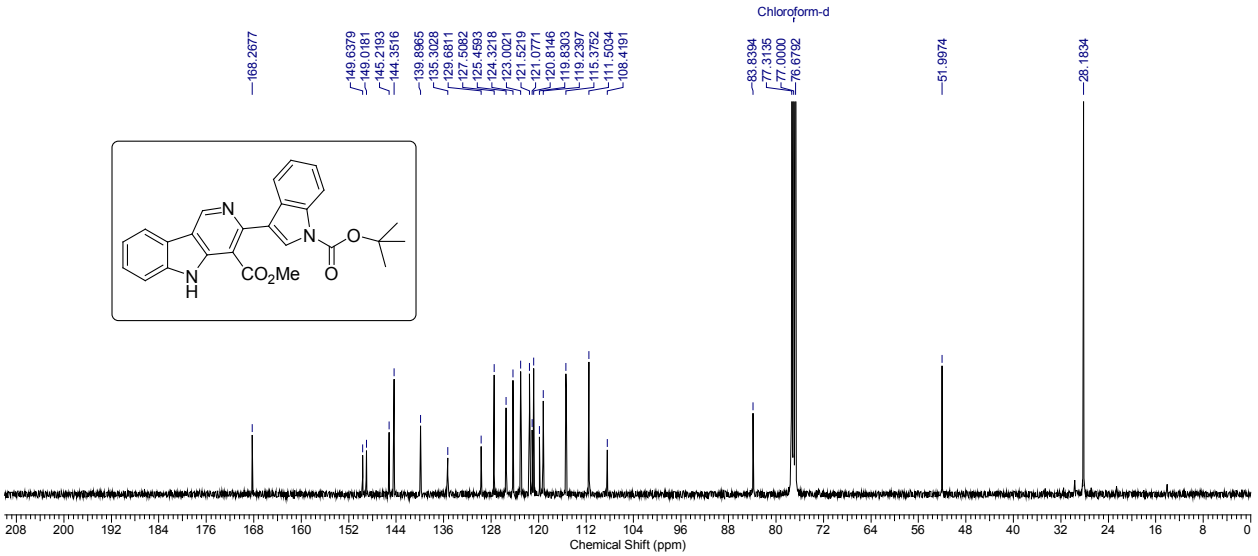
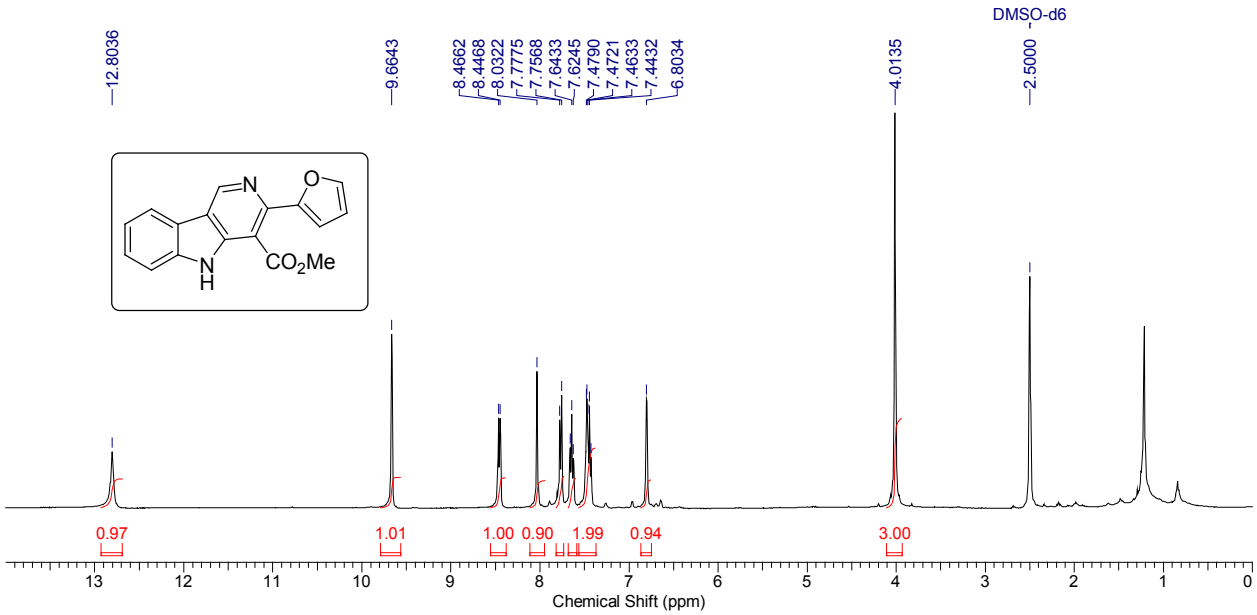
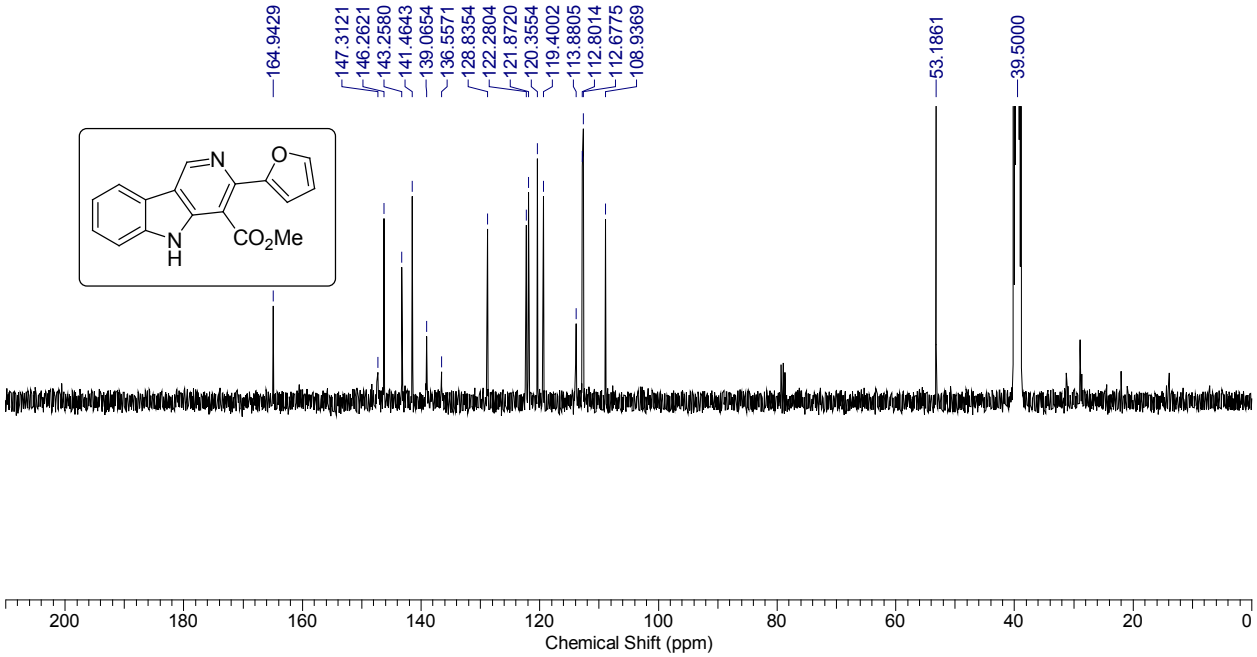
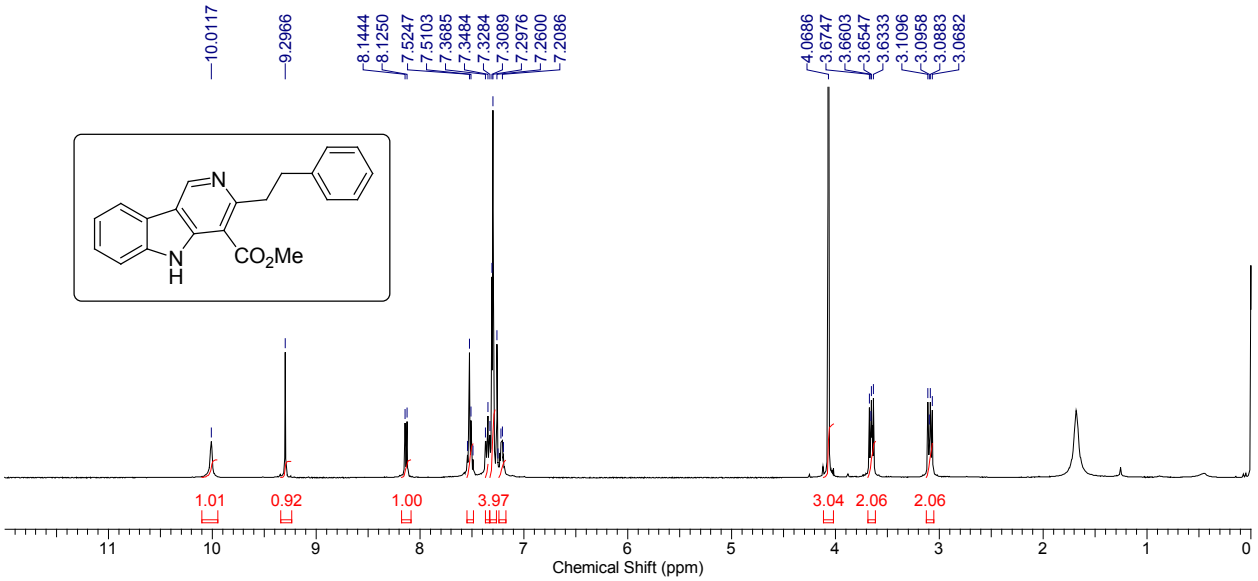
147.7682
144.8880
144.2318
139.9808
138.0851
132.9591
131.2821
128.5915
127.8842
124.0343
121.7302
121.0156
120.8552
120.7021
111.6169
107.0451
77.3323
77.2229
77.0187
76.8219
76.6979
52.2349
O2N
N
N
H
CO2Me
Chemical Shift (ppm)

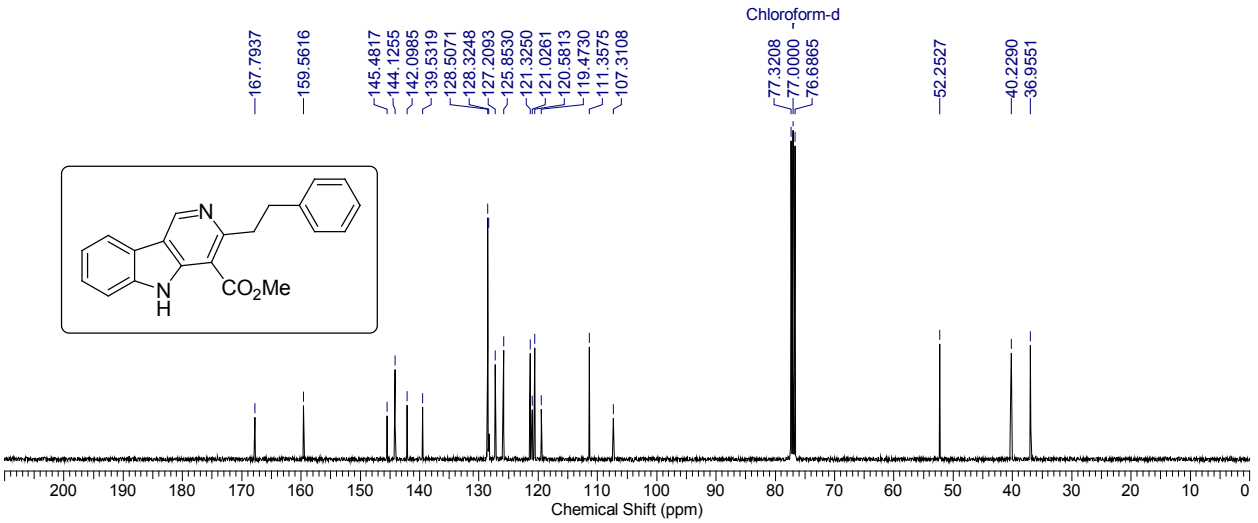

10.0044
9.4047
8.2801
8.2625
8.1804
8.1616
8.0010
7.5544
7.5356
7.4691
7.4503
7.3901
7.3731
7.3556
7.3367
7.2552
7.2358
3.5282
1.6942
TMS
1.08
1.00
1.07
0.99
2.12
3.01
9.08
Chemical Shift (ppm)

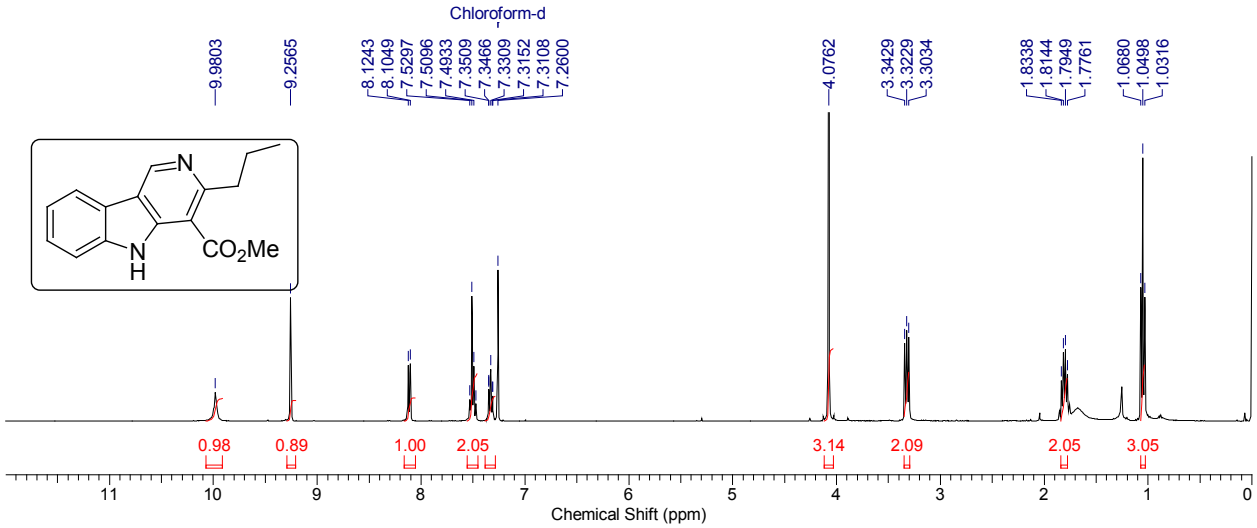

168.2677
149.6379
149.0181
145.2193
144.3516
139.8965
135.3028
129.6811
127.5082
125.4593
124.3218
123.0021
121.5219
121.0771
120.8146
119.8303
119.2397
115.3752
111.5034
108.4191
Chloroform-d
83.8394
77.3135
77.0000
76.6792
51.9974
28.1834
Chemical Shift (ppm)

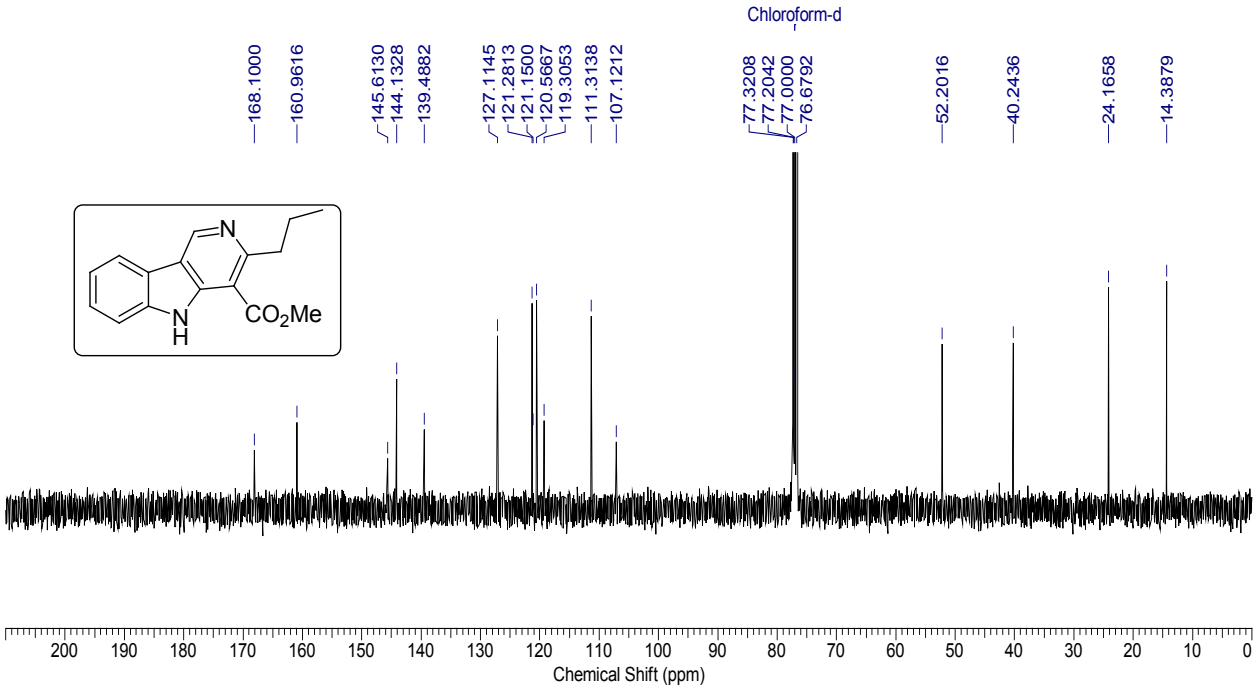

DMSO-d6
12.8036
9.6643
8.4662
8.4468
8.0322
7.7775
7.7568
7.6433
7.6245
7.4790
7.4721
7.4633
7.4432
6.8034
4.0135
2.5000
N
O
N
H
CO2Me
0.97
1.01
1.00
0.90
1.99
0.94
3.00
Chemical Shift (ppm)

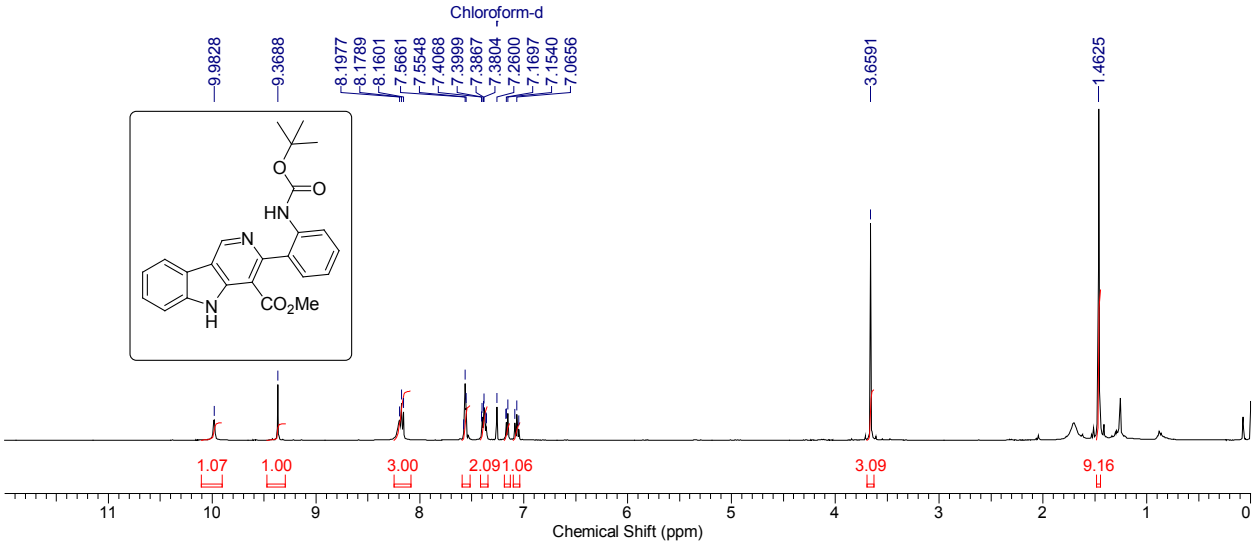

164.9429
147.3121
146.2621
143.2580
141.4643
139.0654
136.5571
128.8354
122.2804
121.8720
120.3554
119.4002
113.8805
112.8014
112.6775
108.9369
53.1861
39.5000
N
O
N
H
CO2Me
Chemical Shift (ppm)

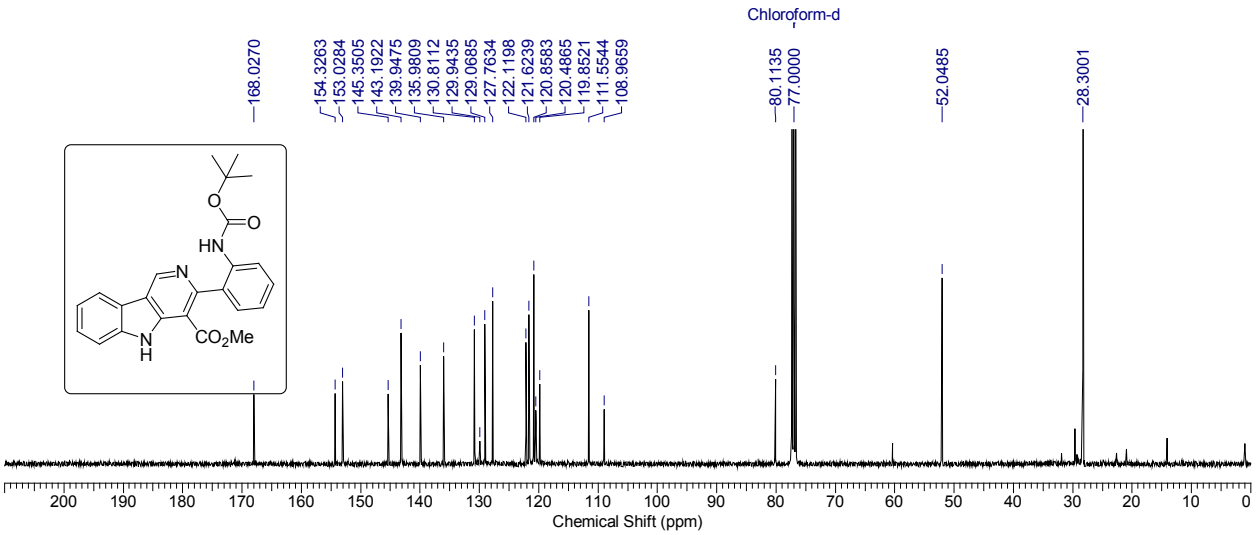

10.0117
9.2966
8.1444
8.1250
7.5247
7.5103
7.3685
7.3484
7.3284
7.3089
7.2976
7.2600
7.2086
4.0686
3.6747
3.6603
3.6547
3.6333
3.1096
3.0958
3.0883
3.0682
N
N
H
CO2Me
1.01
0.92
1.00
3.97
3.04
2.06
2.06
Chemical Shift (ppm)

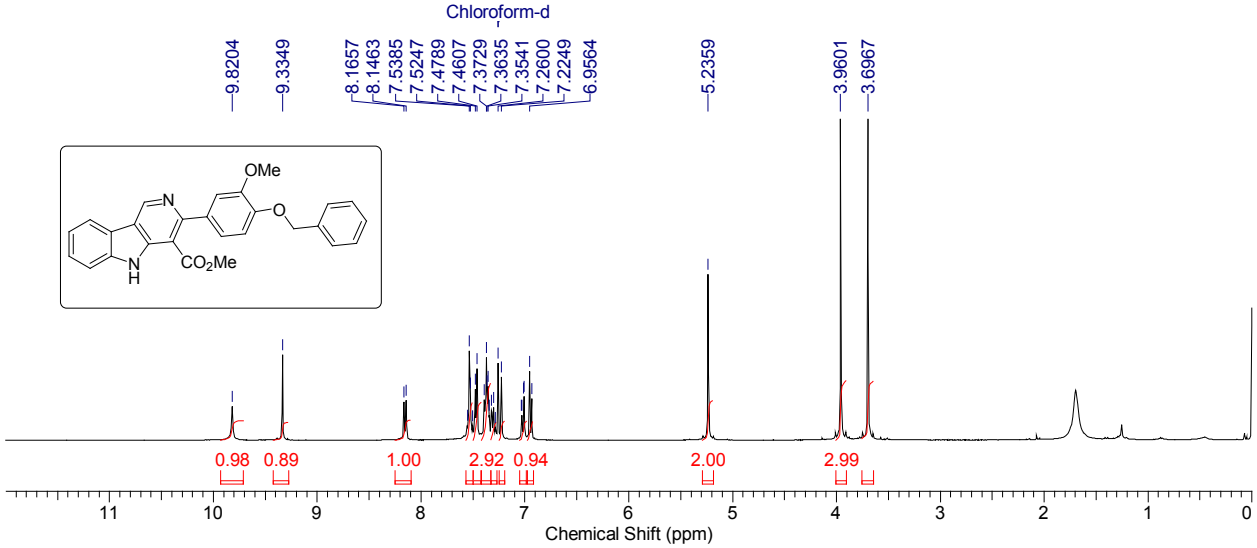

Chloroform-d
167.7937
159.5616
145.4817
144.1255
142.0985
139.5319
128.5071
128.3248
127.2093
125.8530
121.3250
121.0261
120.5813
119.4730
111.3575
107.3108
77.3208
77.0000
76.6865
52.2527
40.2290
36.9551
N
N
H
CO2Me
Chemical Shift (ppm)

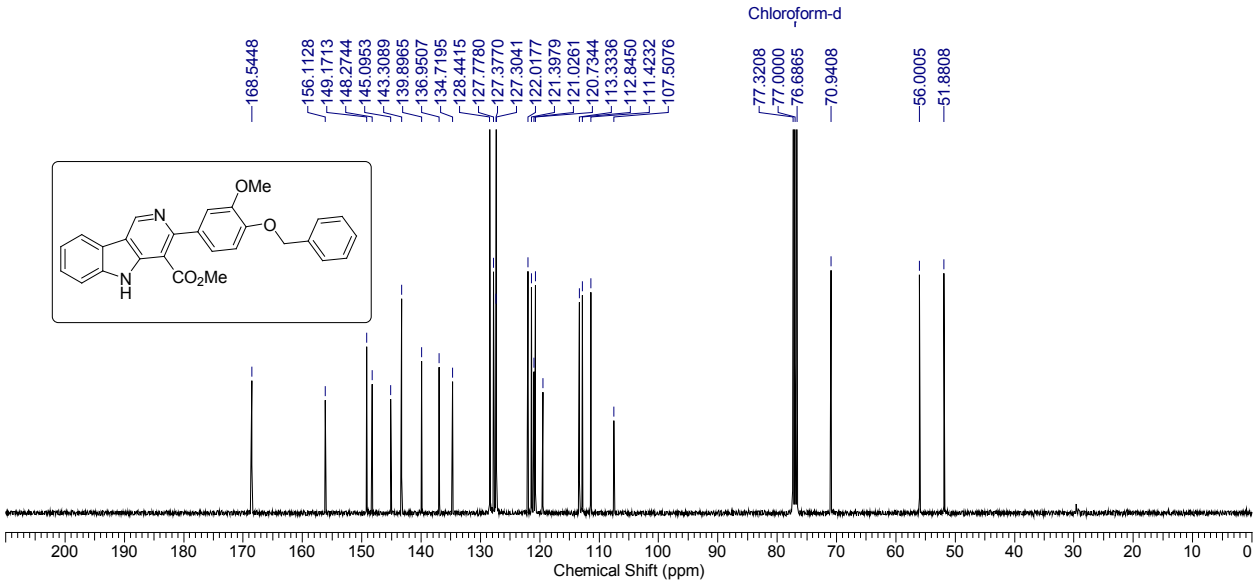

Chloroform-d
9.9803
9.2565
8.1243
8.1049
7.5297
7.5096
7.4933
7.3509
7.3466
7.3309
7.3152
7.3108
7.2600
4.0762
3.3429
3.3229
3.3034
1.8338
1.8144
1.7949
1.7761
1.0680
1.0498
1.0316
N
N
H
CO2Me
0.98
0.89
1.00
2.05
3.14
2.09
2.05
3.05
Chemical Shift (ppm)

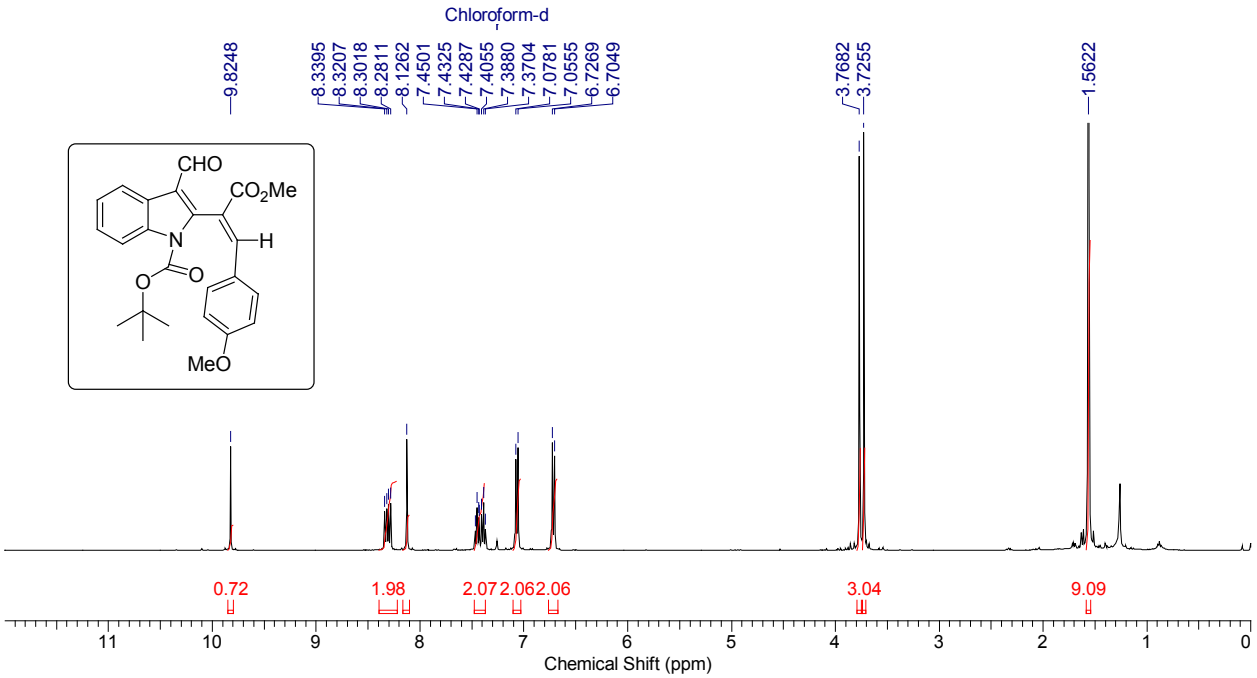

Chloroform-d
168.1000
160.9616
145.6130
144.1328
139.4882
127.1145
121.2813
121.1500
120.5667
119.3053
111.3138
107.1212
77.3208
77.2042
77.0000
76.6792
52.2016
40.2436
24.1658
14.3879
N
N
H
CO2Me
Chemical Shift (ppm)

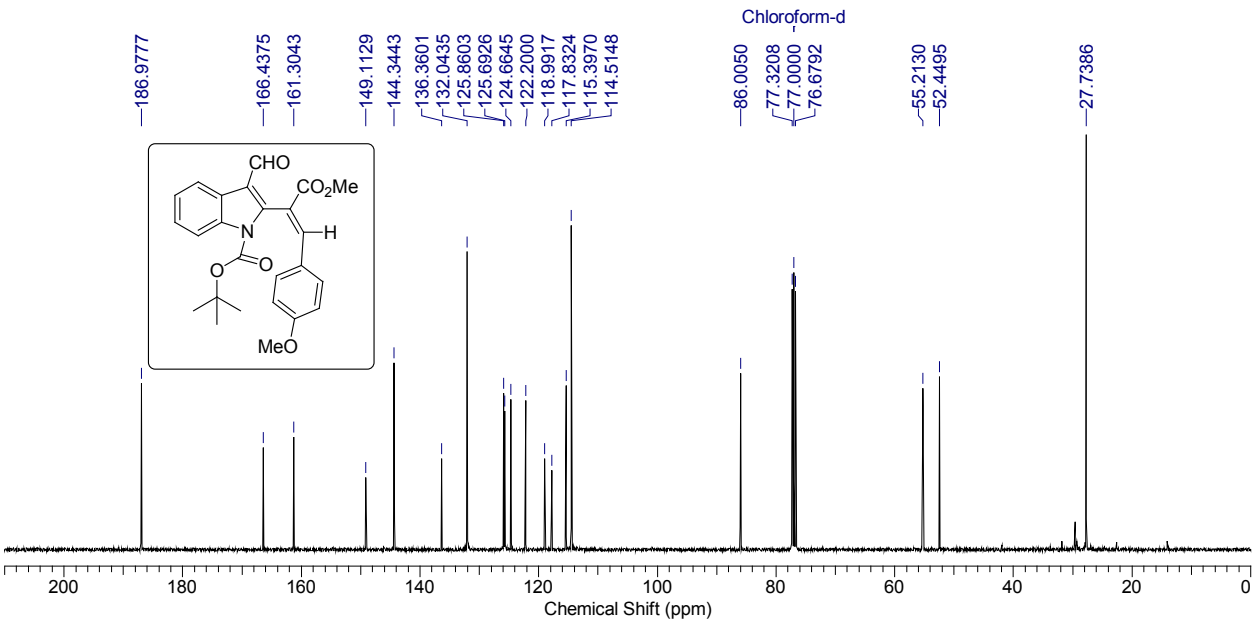

Chloroform-d
9.9828
9.3688
8.1977
8.1789
8.1601
7.5661
7.5548
7.4068
7.3999
7.3867
7.3804
7.2600
7.1697
7.1540
7.0656
3.6591
1.4625
1.07
1.00
3.00
2.09
1.06
3.09
9.16
Chemical Shift (ppm)

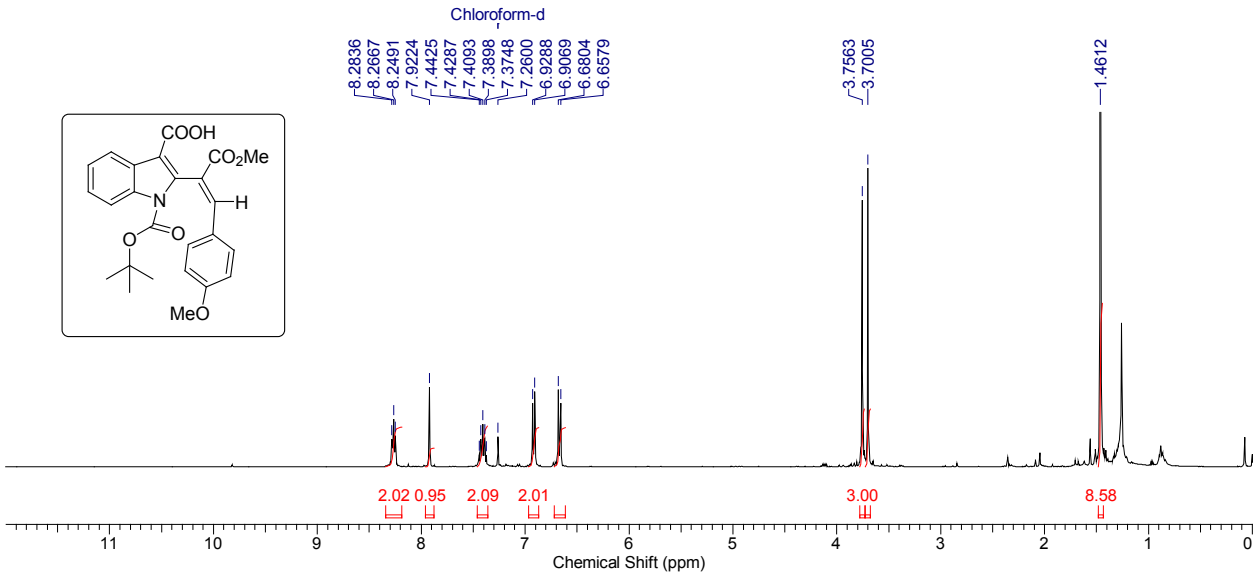

Chloroform-d
168.0270
154.3263
153.0284
145.3505
143.1922
139.9475
135.9809
130.8112
129.9435
129.0685
127.7634
122.1198
121.6239
120.8583
120.4865
119.8521
111.5544
108.9659
80.1135
77.0000
52.0485
28.3001
Chemical Shift (ppm)

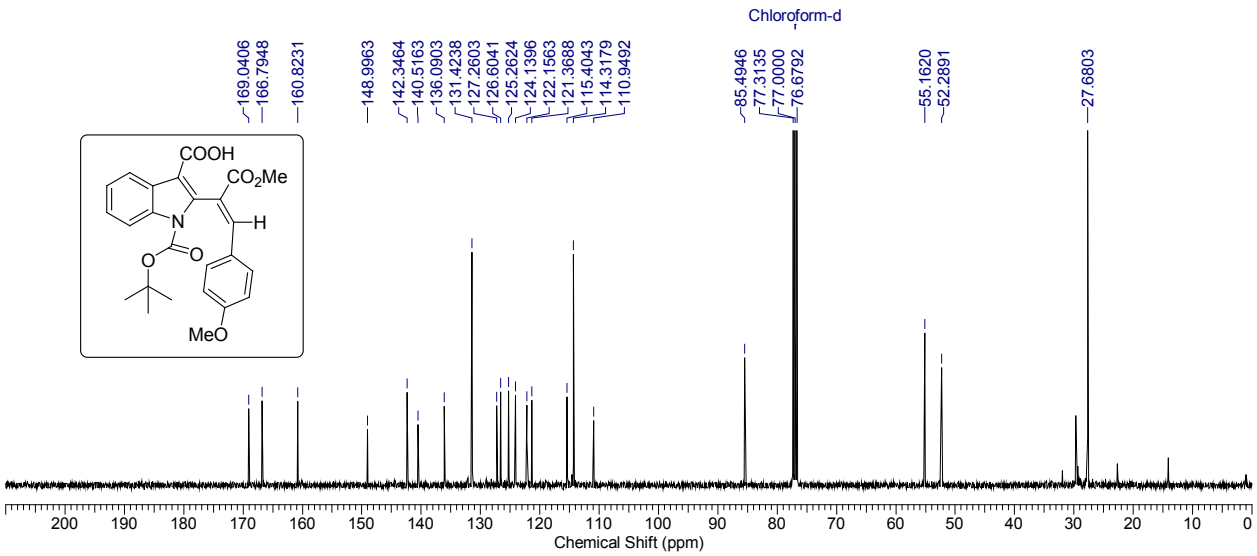

Chloroform-d
9.8204
9.3349
8.1657
8.1463
7.5385
7.5247
7.4789
7.4607
7.3729
7.3635
7.3541
7.2600
7.2249
6.9564
5.2359
3.9601
3.6967
OMe
N
O
N
H
CO2Me
0.98
0.89
1.00
2.92
0.94
2.00
2.99
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

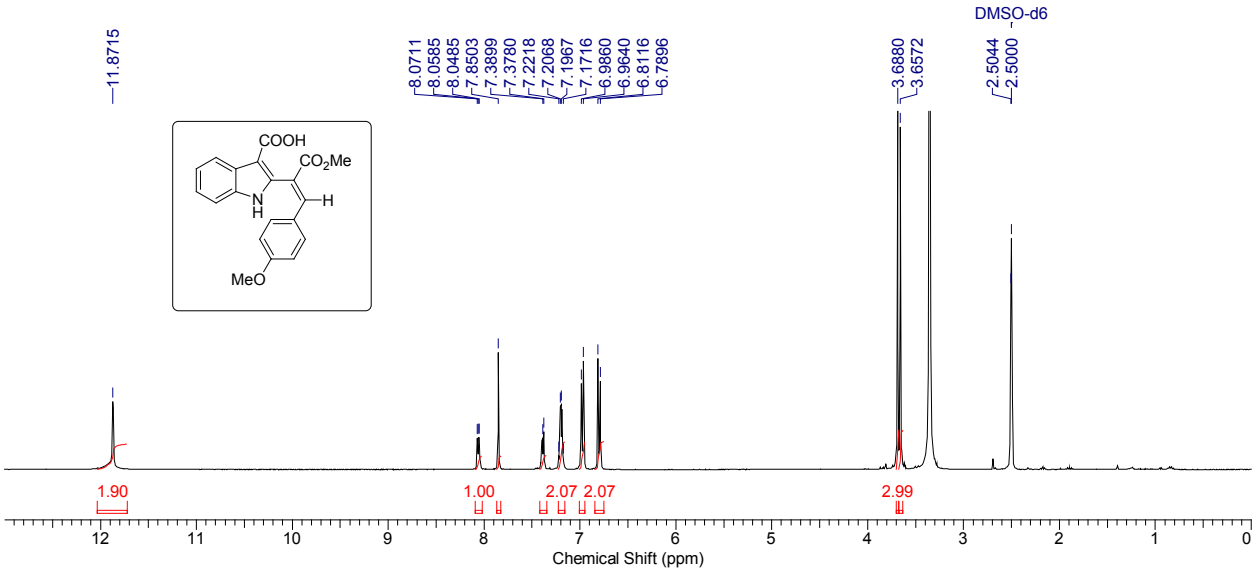

Chloroform-d
168.5448
156.1128
149.1713
148.2744
145.0953
143.3089
139.8965
136.9507
134.7195
128.4415
127.7780
127.3770
127.3041
122.0177
121.3979
121.0261
120.7344
113.3336
112.8450
111.4232
107.5076
77.3208
77.0000
76.6865
70.9408
56.0005
51.8808
OMe
N
O
N
H
CO2Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

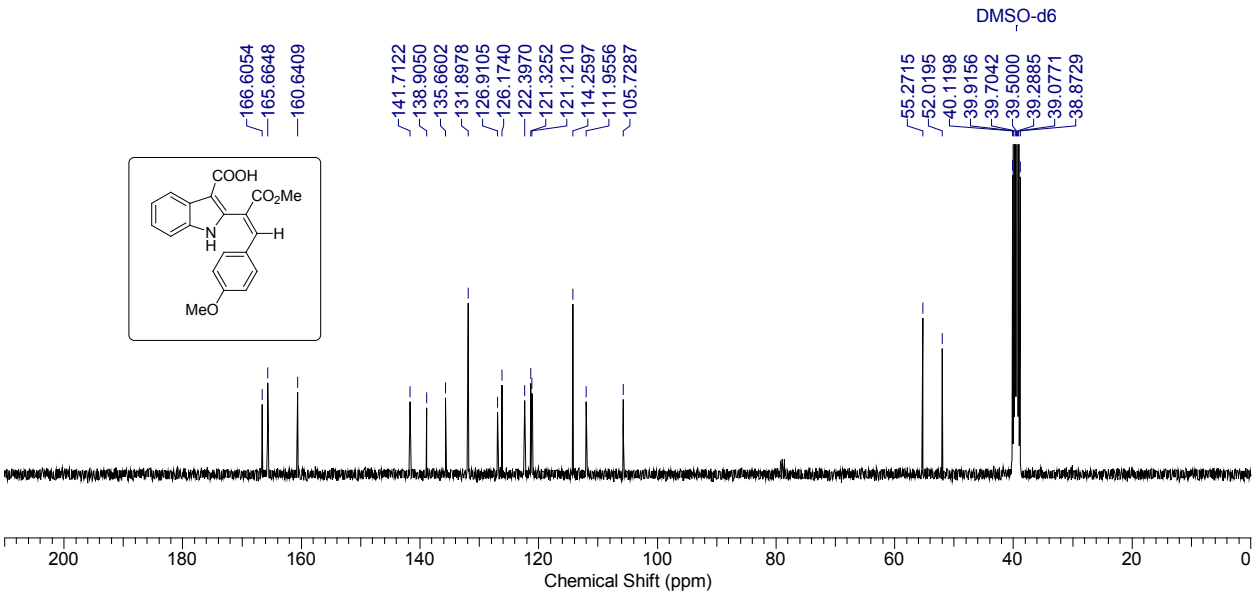


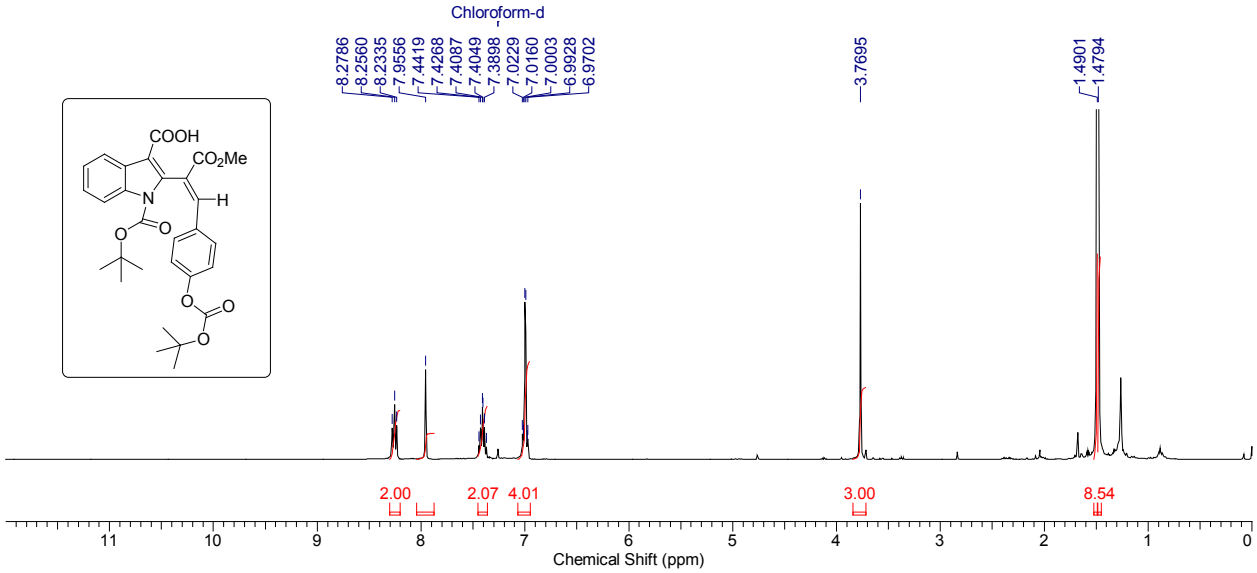


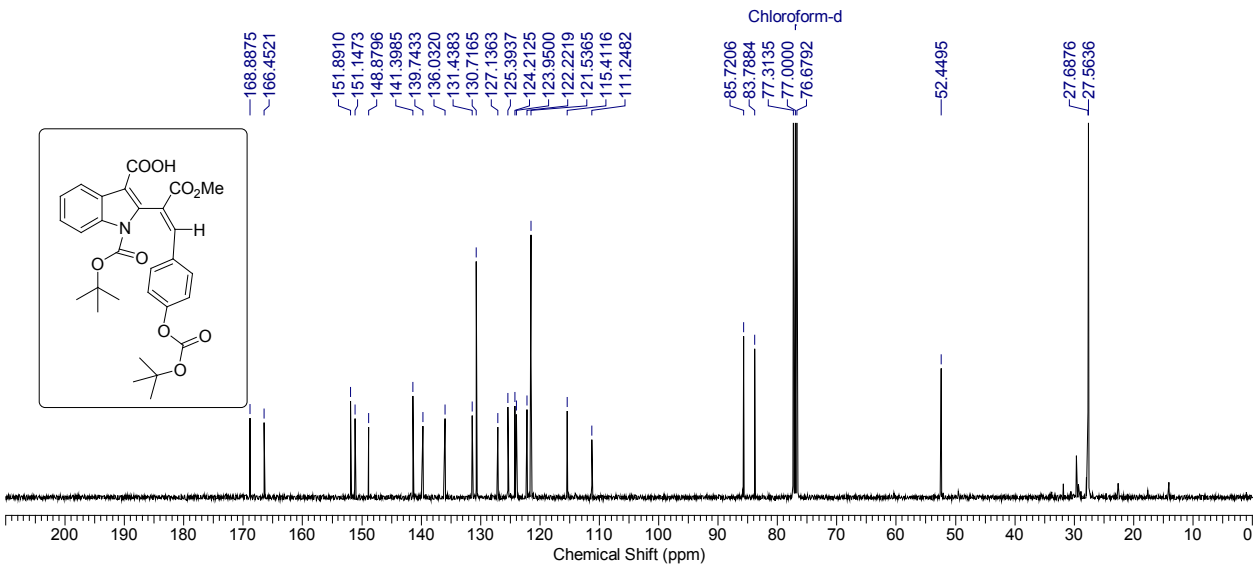

Chloroform-d
8.2836
8.2667
8.2491
7.9224
7.4425
7.4287
7.4093
7.3898
7.3748
7.2600
6.9288
6.9069
6.6804
6.6579
3.7563
3.7005
1.4612
COOH
CO2Me
N
H
O
O
MeO
2.02 0.95 2.09 2.01 3.00 8.58
Chemical Shift (ppm)


Chloroform-d
169.0406
166.7948
160.8231
148.9963
142.3464
140.5163
136.0903
131.4238
127.2603
126.6041
125.2624
124.1396
122.1563
121.3688
115.4043
114.3179
110.9492
85.4946
77.3135
77.0000
76.6792
55.1620
52.2891
27.6803
COOH
CO2Me
N
H
O
O
MeO
Chemical Shift (ppm)






Chloroform-d
8.2786
8.2560
8.2335
7.9556
7.4419
7.4268
7.4087
7.4049
7.3898
7.0229
7.0160
7.0003
6.9928
6.9702
3.7695
1.4901
1.4794
COOH
CO2Me
H
N
O
O
O
O
O
O
2.00
2.07
4.01
3.00
8.54
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Chloroform-d
168.8875
166.4521
151.8910
151.1473
148.8796
141.3985
139.7433
136.0320
131.4383
130.7165
127.1363
125.3937
124.2125
123.9500
122.2219
121.5365
115.4116
111.2482
85.7206
83.7884
77.3135
77.0000
76.6792
52.4495
27.6876
27.5636
COOH
CO2Me
H
N
O
O
O
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)