Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

$Cu(OTf)_2$ catalysed [6+2] cycloaddition reaction for the synthesis of highly substituted pyrrolo[1,2-a]indoles: rapid construction of yuremamine core.

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Table of Contents:

General Information

All reactions were carried out under nitrogen or argon atmosphere with dry solvents under anhydrous conditions, unless otherwise mentioned. Anhydrous THF and diethyl ether were distilled from sodium-benzophenone and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically pure material, unless otherwise stated.

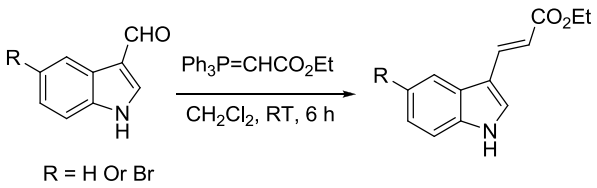
Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and an p-anisaldehyde or ninhydrin stain, and heat as developing agents. Merck silica gel (particle size 100-200 and 230-400 mesh) was used for flash column chromatography.

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. NMR spectra were recorded on either a Bruker Avance 200 (^{1}H: 200 MHz, ^{13}C: 50MHz), Bruker Avance 400 (^{1}H: 400 MHz, ^{13}C: 100MHz), Bruker Avance 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz), JEOL ECX 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) Mass spectrometric data were obtained using WATERS-Q-Tof Premier-ESI-MS.

Diastereomeric ratios (dr) were determined by crude ^{1}H NMR.

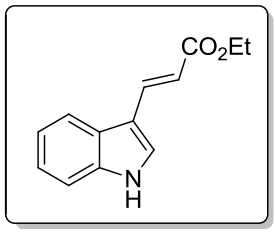
The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of a doublet of a doublet, dm = doublet of a multiplet, m = multiplet, br = broad.

Procedure A: Wittig reaction



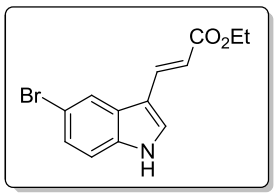
To a solution of aldehyde (1 equiv) in anhydrous CH_2Cl_2, was added dry $Ph_3P{=}CHCO_2Et$ (1.5 equiv) and stirred magnetically for 6 h at RT. Solvent was evaporated and residue was purified by flash chromatography over silica gel column.

Synthesis of compound 13a



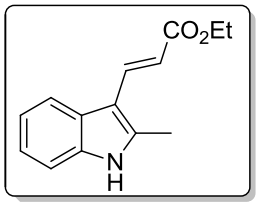
According to the procedure A, 1H-indole-3-carbaldehyde (10 g, 68.9 mmol) and $Ph_3P{=}CHCO_2Et$ (36 g, 103.4 mmol) were used to furnish the product **13a** (14.5 g, 98%) as yellow solid; *Rf* = 0.4 (EtOAc-hexane 1:4); **IR** (KBr): ν_{max}/cm^{-1} 3285, 2983, 1672, 1621, 1435, 1259, 1245, 832, 749, 727; **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 9.13 (s, 1H), 7.94 (d, *J* = 16.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.27-7.21 (m, 2H), 6.48 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 8.0 Hz, 2H), 1.35 (t, *J* = 8.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$,100 MHz): δ 168.7, 138.6, 137.2, 129.3, 125.2, 123.7, 121.4, 120.3, 113.2, 112.9, 111.9, 60.2, 14.4; **HRMS-ESI**: m/z calcd for $C_{13}H_{14}NO_2$ [M+H]:216.1025; found: 216.1025.

Synthesis of compound 13b



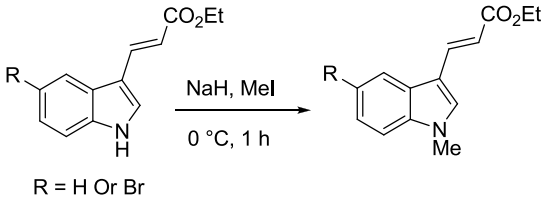
According to the procedure A, 5-bromo-1H-indole-3-carbaldehyde (10 g, 45.0 mmol) and $Ph_3P{=}CHCO_2Et$ (23.5 g, 67.6 mmol) were used to furnish the product **13b** (12.6 g, 97%) as yellow solid; *Rf* = 0.4 (EtOAc-hexane 1:4); **IR** (KBr): ν_{max}/cm^{-1} 3275, 2982, 1687, 1625, 1614, 1475, 1273, 1226, 1179, 1125, 1035, 790, 608; **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.76 (s, 1H), 8.04 (s, 1H), 7.85 (d, *J* = 16.0 Hz, 1H), 7.45(s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 6.40 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 8.0 Hz, 2H), 1.36 (t, *J* = 8.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 168.3, 137.7, 135.7, 129.8, 126.8, 126.1, 123.0, 114.8, 113.7, 113.2, 112.9, 60.4, 14.4; **HRMS-ESI**: m/z calcd for $C_{13}H_{13}BrNO_2$ [M+H]: 294.0130; found: 294.0131.

Synthesis of compound 13c



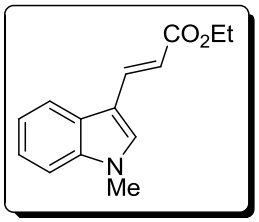
According to the procedure A, 2-methyl-1H-indole-3-carbaldehyde (10 g, 62.9 mmol) and $Ph_3P{=}CHCO_2Et$ (32.8 g, 94.3 mmol) were used to furnish the product **13c** (14 g, 97%) as a white solid; *Rf* = 0.4 (EtOAc-hexane 1:4); **IR** (KBr): ν_{max}/cm^{-1} 3293, 2981, 2898, 1687, 1608, 1454, 1280, 1176, 1149, 777; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 8.41 (s, 1H), 7.96 (d, *J* = 16.0 Hz, 1H), 7.86 (t, *J* = 4.5 Hz, 1H), 7.33-7.30 (m, 1H), 7.21-7.19 (m, 2H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 2.54 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 168.9, 140.1, 137.6, 135.8, 126.5, 122.6, 121.5, 120.1, 112.2, 111.0, 109.7, 60.2, 14.6, 12.4; **HRMS-ESI**: m/z calcd for $C_{14}H_{16}NO_2$ [M+H]:230.1181; found: 230.1181.

Procedure B: Methylation



A solution of NaH (3 equiv, 60% suspension in mineral oil) in THF was cooled to 0 °C and added dropwise a solution of compound **13** (1 equiv) in THF. After 15 min MeI (2 equiv) was added slowly, the reaction mixture was allowed to stir at RT for 1 h. The reaction mixture was cooled to 0 °C, water was added to the reaction mixture and extracted with EtOAc. Solvent was evaporated and residue was purified by flash chromatography over silica gel column.

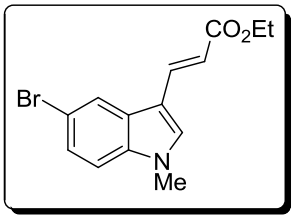
Synthesis of compound 13d



According to the procedure B, compound **13a** (5 g, 23.2 mmol), NaH (1.7 g, 69.7 mmol, 60% suspension in mineral oil) and MeI (3 ml, 46.5 mmol) were used to furnish the product **13d** (5.2 g, 97%) as a yellow solid; *Rf* = 0.4 (EtOAc-hexane 1:4); **IR** (KBr): ν_{max}/cm^{-1} 3105, 2974, 2924, 1695, 1615, 1378, 1285, 1190, 1074, 739; **^{1}H NMR** ($CDCl_3$, 200 MHz): δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 16.0 Hz, 1H), 7.29-7.21 (m, 4H), 6.40 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 8.0 Hz, 2H), 3.71 (s, 3H), 1.34 (t, *J* = 8.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 50 MHz): δ 168.2, 137.9, 133.1, 125.9,

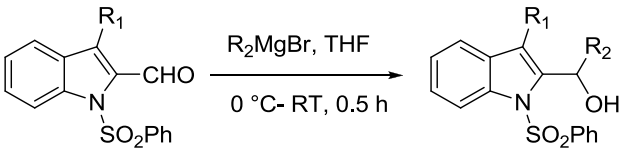
122.8, 121.1, 120.4, 112.3, 111.8, 109.8, 59.9, 32.9, 14.4; **HRMS-ESI**: m/z calcd for $C_{14}H_{16}NO_2$ [M+H]: 230.1181; found: 230.1188.

Synthesis of compound 13e



According to the procedure B, compound **13b** (5 g, 17.0 mmol), NaH (1.2 g, 51.2 mmol, 60% suspension in mineral oil) and MeI (2.1 ml, 34.1 mmol) were used to furnish the product **13e** (5.2 g, 96%) as a white solid; *Rf* = 0.4 (EtOAc-hexane 1:4); **IR** (KBr): ν_{max}/cm^{-1} 3106, 2973, 2931, 1696, 1623, 1301, 1170, 1078, 795; **^{1}H NMR** ($CDCl_3$, 200 MHz): δ 7.98 (s, 1H), 7.78 (d, *J* = 16.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.31(d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 6.0 Hz, 1H), 3.74 (s, 3H), 1.35 (t, *J* = 6.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 50 MHz): δ 167.9, 137.1, 136.5, 133.7, 127.3, 125.6, 122.9, 114.6, 112.9, 111.3, 60.0, 33.2, 14.4; **HRMS-ESI**: m/z calcd for $C_{14}H_{15}BrNO_2$ [M+H]: 308.0286; found: 308.0284.

Procedure C: Grignard reaction

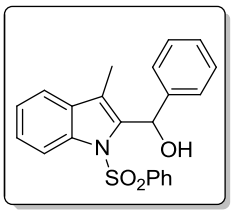


R_1 = CH_3 Or CH_2CH_2OTBS

R_2 = Phenyl Or 2, 4-dimethoxyphenyl

To a cold (0 °C), magnetically stirred solution of the phenyl magnesium bromide [prepared from magnesium turnings (1.5 equiv), bromobenzene (1.5 equiv) and few crystals of iodine in dry THF] was added aldehyde **9** (1 equiv) in dry THF drop wise through dropping funnel and stirred for 0.5 h at RT. The reaction mixture was then quenched with aq NH_4Cl solution and extracted with EtOAc. Organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure. The crude was purified by flash chromatography over silica gel column.

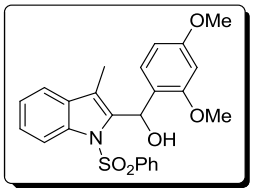
Synthesis of compound 10a



According to the procedure C, aldehyde **9a** (2 g, 6.7 mmol), magnesium turnings (240 mg, 10.0 mmol) and bromobenzene (1.1 ml, 10.0 mmol) were used to furnish the product **10a** (2.4 g, 94%) as a yellowish solid; *Rf* = 0.6

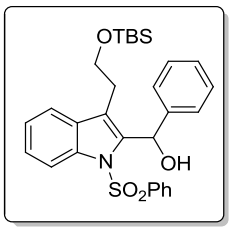
(EtOAc-hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 3526, 3065, 2918, 1444, 1351, 1168, 1149, 1120, 749, 599 ; **^{1}H NMR** ($CDCl_3$, 500MHz): δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.44-7.10 (m, 13H), 6.52 (d, *J* = 8.0 Hz, 1H), 4.35 (t, *J* = 10.0 Hz, 1H), 2.13 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 141.7, 138.0, 136.7, 136.2, 133.4, 130.7, 128.8, 128.1, 126.8, 126.2, 125.5, 125.3, 123.6, 120.3, 119.2, 114.7, 67.7, 9.4; **HRMS-ESI**: m/z calcd for $C_{22}H_{18}NO_2S$ [M-OH]: 360.1053; found: 360.1052.

Synthesis of compound 10b



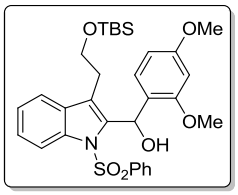
According to the procedure C, aldehyde **9a** (2 g, 6.7 mmol), magnesium turnings (240 mg, 10.0 mmol) and 2, 4- dimethoxy bromobenzene (0.5 ml, 10 mmol) were used to furnish the product **10b** (2.6 g, 90%) as a colorless liquid. *Rf* = 0.4 (EtOAc–hexane 1:3); **IR** (neat): ν_{max}/cm^{-1} 3427, 2925, 2855, 1613, 1587, 1504, 1453, 1367, 1208, 1168, 745, 592, 575; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 8.18 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.45-7.10 (m, 7H), 6.78 (s, 1H), 6.42-6.34 (m, 2H), 3.87 (brs, 1H), 3.72 (s, 3H), 3.47 (s, 3H), 1.90 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 160.2, 157.3, 138.4, 136.0, 135.9, 133.2, 131.3, 128.7, 128.0, 126.2, 124.7, 123.2, 121.5, 119.3, 118.8, 114.7, 103.6, 98.1, 64.1, 55.0, 9.3; **HRMS-ESI**: m/z calcd for $C_{24}H_{23}NNaO_5S$ [M+Na]: 460.1195; found: 460.1199.

Synthesis of compound 10c



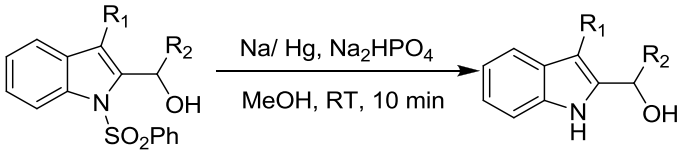
According to the procedure C, aldehyde **9b** (2 g, 4.5 mmol), magnesium turnings (164 mg, 6.7 mmol) and bromobenzene (0.7 ml, 6.7 mmol) were used to furnish the product **10c** (2.3 g, 91%) as a colorless liquid. *Rf* = 0.3 (EtOAc–hexane 1:9); **IR** (neat): ν_{max}/cm^{-1} 3382, 2925, 2854, 1599, 1449, 1372, 1169, 1088, 1032, 837, 782, 596; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 8.23 (d, *J* = 8.5 Hz, 1H), 7.67 (d, *J* = 7.0 Hz, 2H), 7.46-7.40 (m, 2H), 7.36-7.18 (m, 8H), 6.76 (d, *J* = 8.5 Hz, 1H), 4.70 (d, *J* = 8.5 Hz, 1H), 3.84-3.78 (m, 1H), 3.72-3.65 (m, 1H), 2.93-2.85 (m, 1H), 2.76-2.70 (m, 1H), 0.75 (s, 9H), -0.15 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 142.9, 140.1, 138.7, 136.4, 133.5, 130.0, 129.0, 128.1, 126.9, 126.6, 126.1, 125.2, 123.5, 120.1, 118.9, 115.2, 67.6, 62.3, 27.3, 25.9, 18.3, -5.8; **HRMS-ESI**: m/z calcd for $C_{29}H_{35}NNaO_4SSi$ [M+Na]: 544.1954; found: 544.1952.

Synthesis of compound 10d



According to the procedure C, aldehyde **9b** (2 g, 4.5 mmol), magnesium turnings (164 mg, 6.7 mmol) and 2, 4- dimethoxy bromobenzene (1 ml, 6.7 mmol) were used to furnish the product **10d** (2.3 g, 87%) as a colorless liquid. *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 3399, 3066, 2953, 2928, 2855, 1611, 1587, 1503, 1452, 1417, 1371, 1293, 1255, 1230, 1208, 1168, 1089, 1033, 835, 777, 747, 585, 571; **^{1}H NMR** (CD_3CN, 500 MHz): δ 7.92 (dt, *J* = 0.8 Hz, 8.4 Hz, 1H), 7.60-7.55 (m, 2H), 7.36-7.28 (m, 2H), 7.23-7.17 (m, 2H), 7.13-7.07 (m, 1H), 7.06-7.00 (m, 1H), 6.95 (dd, *J* = 0.4 Hz, 8.5 Hz, 1H), 6.70 (d, *J* = 5.5 Hz, 1H), 6.29 (d, *J* = 2.4 Hz, 1H), 6.21 (dd, *J* = 2.4 Hz, 8.5 Hz, 1H), 3.94 (d, *J* = 5.6 Hz, 1H), 3.56 (s, 3H), 3.45 (s, 3H), 3.43-3.34 (m, 2H), 2.65-2.59 (m, 2H), 0.56 (s, 9H), -0.33 (s, 6H); **^{13}C NMR** (CD_3CN, 125 MHz): δ 161.6, 158.8, 140.1, 139.3, 136.9, 134.9, 131.9, 130.2, 128.9, 127.4, 125.8, 124.4, 123.9, 121.3, 120.4, 115.8, 104.9, 99.4, 64.8, 63.6, 56.2, 55.9, 28.2, 26.2, 18.8, -5.3; **HRMS-ESI**: m/z calcd for $C_{31}H_{39}NNaO_6SSi$ [M+Na]: 604.2165; found: 604.2162.

Procedure D: Desulfonylation.

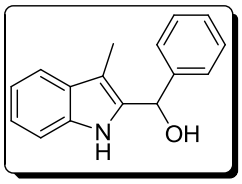


R_1 = CH_3 Or CH_2CH_2OTBS

R_2 = Phenyl Or 2, 4-dimethoxyphenyl

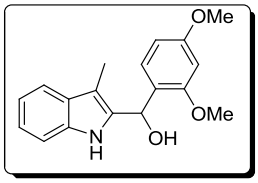
To a solution of compound **10** (1equiv) in anhydrous methanol, were added Na_2HPO_4 (4 equiv) and Na-Hg (2 equiv). The reaction mixture was stirred for 10 min at RT. Progress of the reaction was monitored by TLC. The reaction mixture was then quenched with water, extracted with ether and dried over Na_2SO_4. Solvent was evaporated and residue was purified by flash chromatography over silica gel column.

Synthesis of compound 11a



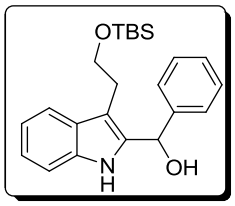
According to the procedure D, compound **10a** (2 g, 5.3 mmol), Na_2HPO_4 (3.0 g, 21.2 mmol) and Na-Hg (244 mg, 10.6 mmol) were used to furnish the product **11a** (1.2 g, 96%) as a colorless liquid; *Rf* = 0.6 (EtOAc - hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 3418, 3057, 2917, 1452, 1332, 1002, 742, 701; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 8.06 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.42-7.29 (m, 5H), 7.27-7.25 (m, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.14 (s, 1H), 2.29 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 141.7, 135.3, 134.9, 128.9, 128.6, 127.9, 126.2, 122.1, 119.2, 118.7, 110.9, 108.3, 68.59, 8.84; **HRMS-ESI**: m/z calcd for $C_{16}H_{14}N$ [M-OH]: 220.1127; found: 220.1121.

Synthesis of compound 11b



According to the procedure D, compound **10b** (2 g, 4.6 mmol), Na_2HPO_4 (2.6 g, 18.3 mmol) and Na-Hg (211 mg, 9.2 mmol) were used to furnish the product **11b** (1.2 g, 87%) as a colorless liquid; *Rf* = 0.3 (EtOAc-hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 3417, 2935, 2837, 1612, 1587, 1504, 1461, 1291, 1157, 1208, 1119, 1036, 744; **^{1}H NMR** (CD_3CN, 500 MHz): δ 8.93 (brs, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.28-7.21 (m, 2H), 7.02-6.97 (m, 1H), 6.95-6.91 (m, 1H), 6.46-6.43 (m, 2H), 6.17 (d, *J* = 3.9 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.65 (d, *J* = 3.9 Hz, 1H), 2.15 (s, 3H); **^{13}C NMR** (CD_3CN, 125 MHz): δ 161.3, 158.3, 137.3, 136.3, 129.9, 128.5, 124.5, 122.0, 119.4, 119.0, 111.6, 107.0, 105.4, 99.1, 63.8, 56.1, 55.9, 8.5; **HRMS-ESI**: m/z calcd for $C_{18}H_{18}NO_2$ [M-OH]: 280.1338; found: 280.1337.

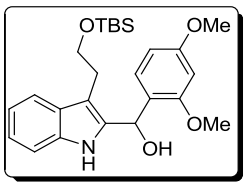
Synthesis of compound 11c



According to the procedure D, compound **10c** (2 g, 3.8 mmol), Na_2HPO_4 (2.2 g, 15.3 mmol) and Na-Hg (174 mg, 7.6 mmol) were used to furnish the product **11c** (1.3 g, 88%) as a yellow liquid. *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 3407, 3060, 2956, 2928, 1460, 1255, 1089, 1008, 835, 778, 741, 700; **^{1}H NMR** (CD_3CN, 500 MHz): δ 9.01 (brs, 1H), 7.50 (d, *J* = 7.7 Hz, 1H), 7.45-7.41 (m, 2H), 7.36-7.32 (m, 2H), 7.30-7.24 (m, 2H), 7.07 (dt, *J* = 1.1 Hz, 7.2 Hz, 1H), 7.01-6.97 (m ,1H), 6.06 (brd, 1 H), 4.10 (brd, 1H), 3.78-3.70 (m, 2H), 3.02-2.94 (m, 2H), 0.84 (s, 9H), -0.03 (s, 6H); **^{13}C NMR** (CD_3CN, 125 MHz): δ 144.1, 138.8, 136.5, 129.4, 129.3, 128.3, 127.3,

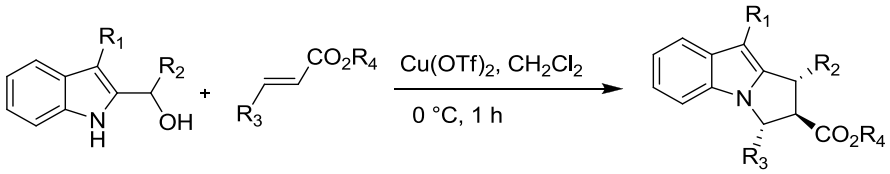
122.4, 119.8, 119.4, 111.9, 109.1, 68.9, 64.5, 28.4, 26.3, 19.0, -5.1; **HRMS-ESI**: m/z calcd for $C_{23}H_{30}NOSi$ [M-OH]: 364.2097; found: 364.2092.

Synthesis of compound 11d



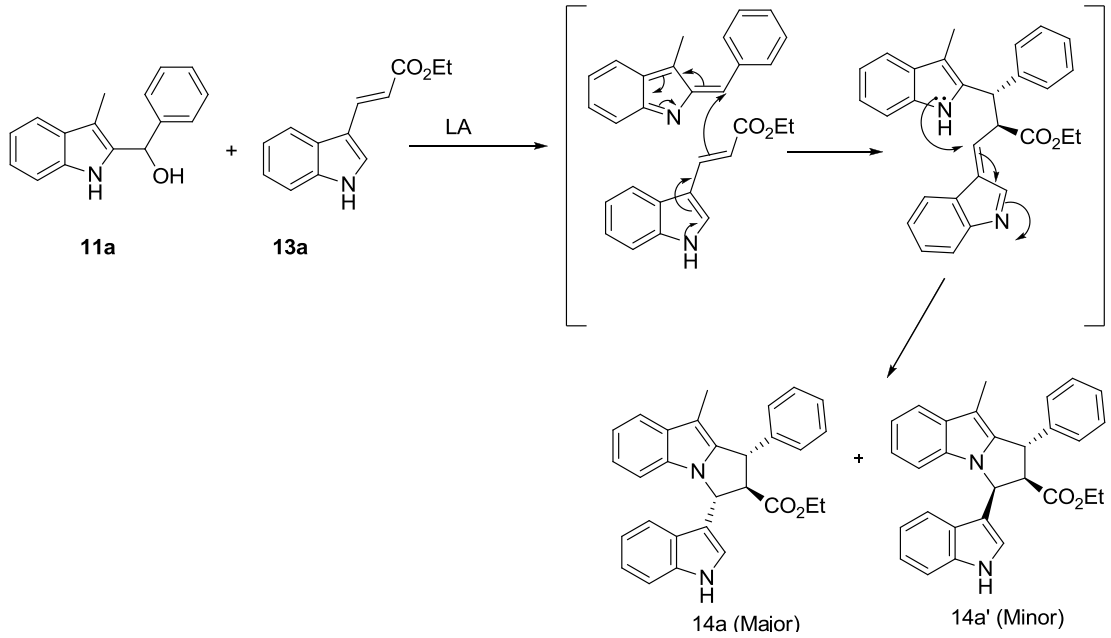
According to the procedure D, compound **10d** (2 g, 3.4 mmol), Na_2HPO_4 (2.0 g, 13.8 mmol) and Na-Hg (156 mg, 6.8 mmol) were used to furnish the product **11d** (1.5 g, 82%) as a colorless liquid; *Rf* = 0.3 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 3412, 3000, 2953, 2928, 2855, 1612, 1587, 1505, 1460, 1291, 1256, 1208, 1157, 1089, 1036, 936, 835, 777, 741; **^{1}H NMR** (CD_3CN, 500 MHz): δ 8.81 (s, 1H), 7.32-7.28 (m, 1H), 7.14-7.07 (m, 2H), 6.90-6.83 (m, 1H), 6.82-6.77 (m, 1H), 6.35-6.29 (m, 2H), 6.06 (d, *J* = 3.6 Hz, 1H), 3.67 (d, *J* = 3.7 Hz, 1H), 3.59 (s, 3H), 3.57 (s, 3H), 3.56-3.46 (m, 2H), 2.77-2.71 (m, 2H), 0.65 (s, 9H), -0.22 (s, 6H); **^{13}C NMR** (CD_3CN, 125 MHz): δ 161.5, 158.4, 138.8, 136.2, 129.5, 129.0, 124.3, 122.0, 119.6, 119.2, 111.9, 108.4, 105.6, 99.1, 64.4, 63.8, 56.2, 55.9, 28.4, 26.3, 19.0, -5.2; **HRMS-ESI**: m/z calcd for $C_{25}H_{35}NNaO_4Si$ [M+Na]: 464.2233; found: 464.2237.

Procedure E: [6+2] cycloaddition reaction.

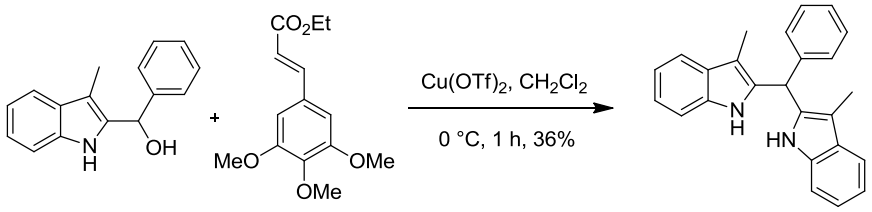


To a cold (0 °C), magnetically stirred solution of secondary alcohol **11** (1 equiv) and ester **13** (1 equiv) in dry DCM, was added catalytic amount of $Cu(OTf)_2$ and stirred for 1 h. Progress of the reaction was monitored by TLC till the starting alcohol was consumed completely. The reaction mixture was then quenched with aq $NaHCO_3$ solution, extracted with CH_2Cl_2. Dried over Na_2SO_4 and solvent was evaporated. To determine the diastereoselectivity of compound, the residue was first dissolved in $CDCl_3$, and took some samples for NMR analysis. Then the sample for analysis and the rest of the product were recombined for column chromatographic purification using the indicated solvent mixtures to afford the desired product.

Mechnism for [6+2] cycloaddition reaction.

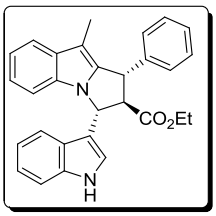


Synthesis of compound 12

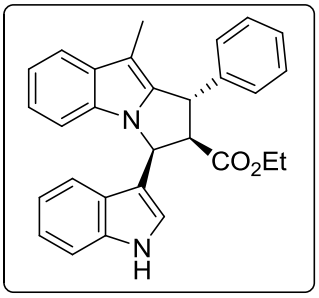


According to the procedure E, secondary alcohol **11a** (200 mg, 0.8 mmol), ester (224 mg, 0.8 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **12** (106 mg, 72%) *Rf* = 0.4 (EtOAc–hexane 1:32); **IR** (neat): ν_{max}/cm^{-1} 3441, 3058, 2920, 2855, 1579, 1459, 1309, 743, 701; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.60 (brs, 2H), 7.56 (d, *J* = 7.0 Hz, 2H), 7.37-7.29 (m, 3H), 7.25-7.23 (m, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.17-7.12 (m, 4H), 6.00 (s, 1H), 2.17 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 140.0, 135.2, 133.4, 129.5, 129.0, 128.5, 127.3, 121.6, 119.4, 118.5, 110.8, 108.9, 40.8, 8.5.

Synthesis of compound 14a & 14a'

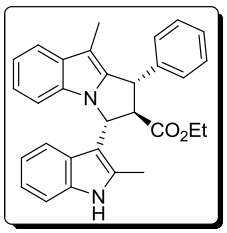


According to the procedure E, secondary alcohol **11a** (200 mg, 0.8 mmol), ester **13a** (181 mg, 0.8 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14a (major)**(328 mg, 90%) as a colorless liquid; *Rf* = 0.5 (EtOAc-hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 3402, 2923, 1729, 1456, 1181, 742; **^{1}H NMR** ($CDCl_3$, 200 MHz): δ 8.17 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.48-7.30 (m, 7H), 7.24-7.16 (m, 2H), 7.04 (t, *J* = 8.0 Hz, 2H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.99 (d, *J* = 8.4 Hz, 1H), 4.89 (d, *J* = 8.4 Hz, 1H), 4.29-4.04 (m, 2H), 3.87 (t, *J* = 8.4 Hz, 1H), 1.97 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 50 MHz): δ 172.0, 140.7, 140.5, 136.6, 133.6, 132.6, 128.7, 128.0, 127.2, 125.4, 122.9, 122.5, 120.5, 120.1, 119.2, 118.8, 118.5, 113.9, 111.4, 110.3, 102.6, 65.6, 61.1, 57.3, 47.4, 14.1, 8.3; **HRMS-ESI**: m/z calcd for $C_{29}H_{26}N_2O_2$ [M+H]: 435.2067; found: 435.2077;



Product 14a'(minor); **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.0 (brs, 1H), 7.56-7.49 (m, 2H), 7.43-7.27 (m, 6H), 7.20-7.03 (m, 3H), 7.02-6.98 (m, 2H), 6.52 (brs, 1H), 6.32 (d, *J* = 8.3 Hz, 1H), 5.16 (d, *J* = 9.5 Hz, 1H), 4.12 (dd, *J* = 8.3 Hz, 9.5 Hz, 1H), 3.76-3.67 (m, 1H), 3.50-3.41 (m, 1H), 1.96 (s, 3H), 0.84 (td, *J* = 1.3, 7.1 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 169.7, 140.7, 140.4, 136.0, 133.5, 131.6, 128.7, 128.4, 127.1, 126.0, 122.6, 120.7, 119.7, 118.9, 118.6, 112.7, 111.2, 110.0, 102.5, 63.6, 60.8, 54.2, 44.1, 13.4, 8.4.

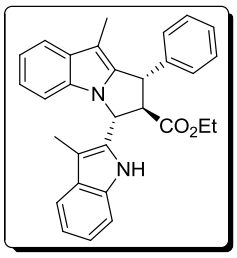
Synthesis of compound 14b



According to the procedure E, secondary alcohol **11a** (200 mg, 0.8 mmol), ester **13c** (193 mg, 0.8 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14b** (321 mg, 85%) as a white solid; *Rf* = 0.5 (EtOAc-hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 3399, 2919, 1729, 1458, 1180, 741; **^{1}H NMR** ($CDCl_3$, 200 MHz): δ 7.95 (s, 1H), 7.58-7.37 (m, 6H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 3H), 6.90-6.82 (m, 2H), 6.68 (d, *J* = 8.0 Hz, 1H), 5.94 (d, *J* = 9.1 Hz, 1H), 4.91 (d, *J* = 9.3 Hz, 1H), 4.30-4.03, (m, 2H), 2.56 (s, 3H), 2.03 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 50 MHz): δ 171.9, 140.4, 140.2, 135.6, 133.4, 132.8, 128.7, 128.2,

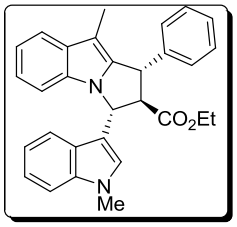
127.3, 126.1, 121.4, 120.5, 119.8, 118.7, 118.3, 110.4, 109.8, 107.8, 102.7, 63.7, 60.9, 56.8, 47.7, 14.1, 11.7, 8.3; **HRMS-ESI**: m/z calcd for $C_{30}H_{28}N_2O_2$ [M+H]: 449.2224; found: 449.2220.

Synthesis of compound 14c



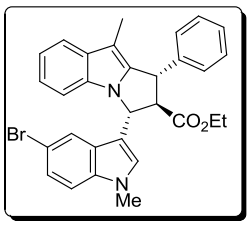
According to the procedure E, secondary alcohol **11a** (200 mg, 0.8 mmol), ester (193 mg, 0.8 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14c** (317 mg, 84%) as a solid; *Rf* = 0.6 (EtOAc-hexane 1:9); **IR** (neat): ν_{max}/cm^{-1} 3386, 2919, 1730, 1457, 1181, 742; **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.91 (s, 1H), 7.56 (d, *J* = 6.7 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.38-7.25 (m, 5H), 7.09-7.03 (m, 3H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.81 (t, *J* = 8.0 Hz, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 5.85 (d, *J* = 8.5 Hz, 1H), 4.78 (d, *J* = 8.5 Hz, 1H), 4.16-4.00 (m, 2H), 3.70 (t, *J* = 8.5 Hz, 1H), 2.34 (s, 3H), 1.93 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.2, 140.3, 140.1, 136.0, 133.7, 132.5, 130.2, 129.2, 128.8, 127.9, 127.5, 122.4, 121.2, 119.4, 118.9, 118.6, 111.0, 110.7, 109.9, 103.4, 64.8, 61.4, 55.8, 47.3, 14.0, 8.5, 8.2; **HRMS-ESI**: m/z calcd for $C_{30}H_{28}N_2O_2$ [M+H]: 449.2224; found: 449.2226.

Synthesis of compound 14d



According to the procedure E, secondary alcohol **11a** (200 mg, 0.8 mmol), ester **13d** (193 mg, 0.8 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14d** (336 mg, 89%) as a colorless liquid; *Rf* = 0.5 (EtOAc-hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 2919, 1730, 1457, 1179, 740; **^{1}H NMR** ($CDCl_3$, 200MHz): δ 7.49 (d, *J* = 8.0 Hz, 1H), 7.44-7.27 (m, 7H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 7.01 (t, *J* = 8.0 Hz, 2H), 6.85 (t, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 5.94 (d, *J* = 8.0 Hz, 1H), 4.84 (d, *J* = 8.0 Hz, 1H), 4.26-4.00 (m, 2H), 3.82 (t, *J* = 8.0 Hz, 1H), 3.76 (s, 3H), 1.96 (s, 3H), 1.13 (t, *J* = 8.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 50 MHz): δ 172.0, 140.7, 140.4, 137.4, 133.6, 132.6, 128.7, 128.1, 127.5, 127.2, 126.0, 122.0, 120.4, 119.6, 119.3, 118.7, 118.4, 112.2, 110.3, 109.5, 102.6, 65.9, 61.0, 57.2, 47.5, 32.9, 14.1, 8.3; **HRMS-ESI**: m/z calcd for $C_{30}H_{28}N_2O_2$ [M+H$^+$]: 449.2224; found: 449.2233.

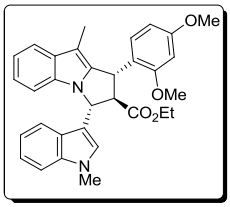
Synthesis of compound 14e



According to the procedure E, secondary alcohol **11a** (200 mg, 0.8 mmol), ester **13e** (260 mg, 0.8 mmol) and catalytic amount of $Cu(OTf)_2$ were used

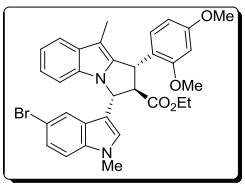
to furnish the product **14e** (383 mg, 86%) as a solid; *Rf* = 0.5 (EtOAc-hexane 1:4); **IR** (neat): ν_{max}/cm^{-1} 2918, 1730, 1476, 1456, 1179, 790; **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.59 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.41-7.33 (m, 4H), 7.28-7.26 (m, 2H), 7.15 (d, *J* = 8.3 Hz, 1H), 7.03 (s, 2H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 5.87 (d, *J* = 8.0 Hz, 1H), 4.86 (d, *J* = 8.0 Hz, 1H), 4.28-4.11 (m, 2H), 3.74 (t, *J* = 8.0 Hz, 3H), 3.69 (s, 3H), 1.98 (s, 3H), 1.17 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 171.9, 140.7, 140.4, 136.0, 133.7, 132.5, 128.7, 128.5, 127.9, 127.6, 127.2, 124.9, 121.7, 120.5, 118.9, 118.6, 113.0, 112.3, 111.1, 110.2, 102.8, 65.9, 61.3, 56.7, 47.1, 33.0, 14.1, 8.3; **HRMS-ESI**: : m/z calcd for $C_{30}H_{27}N_2O_2Br$ [M+H]: 527.1329; found: 527.1332.

Synthesis of compound 14f



According to the procedure E, secondary alcohol **11b** (200 mg, 0.7 mmol), ester **13d** (154 mg, 0.7 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14f** (311 mg, 91%) as a white solid; *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 2917, 1730, 1613, 1506, 1458, 1178, 1208, 1157, 1034, 740; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.54 (d, *J* = 7.9 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.21-7.25 (m, 1H), 7.08 (s, 1H), 7.06-7.01 (m, 2H), 6.88 (t, *J* = 7.0 Hz, 1H), 6.78 (d, *J* = 7.9 Hz, 1H), 6.54-6.50 (m, 2H), 5.94 (d, *J* = 7.9 Hz, 1H), 5.15 (d, *J* = 7.9 Hz, 1H), 4.22-4.13 (m, 2H), 3.85-3.76 (m, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H), 2.06 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.7, 159.9, 158.3, 140.7, 137.4, 133.7, 132.7, 129.2, 127.4, 126.0, 121.9, 120.9, 120.0, 119.5, 119.4, 118.5, 118.2, 112.5, 110.2, 109.4, 104.2, 101.9, 98.4, 64.3, 60.8, 57.6, 55.3, 55.2, 41.3, 32.8, 14.1, 8.4; **HRMS-ESI**: m/z calcd for $C_{32}H_{33}N_2O_4$ [M+H]: 509.2440; found: 509.2440.

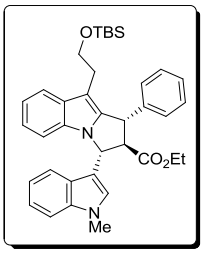
Synthesis of compound 14g



According to the procedure E, secondary alcohol **11b** (200 mg, 0.7 mmol), ester **13e** (206 mg, 0.7 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14g** (334 mg, 85%) as a colorless liquid; *Rf* = 0.4 (EtOAc–hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 2921, 2851, 1730, 1612, 1586, 1506, 1475, 1457, 1208, 1178,1157, 1034, 794, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.58 (d, *J* = 1.7 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.28 (dd, *J* = 1.7 Hz, 8.6 Hz, 1H), 7.23(d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 1H), 7.05-7.00 (m, 2H), 6.88 (t, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H),

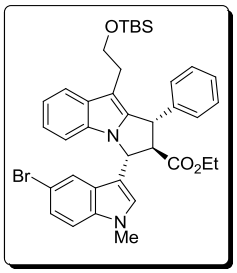
6.50-6.46 (m,2H), 5.80 (d, *J* = 8.0 Hz, 1H), 5.07 (d, *J* = 8.0 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.83-3.72 (m, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.73 (s,3H), 2.03 (s,3H), 1.21 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.7, 160.1, 158.3, 140.7, 136.1, 133.9, 132.7, 128.4, 127.6, 124.9, 122.0, 120.1, 118.7, 118.4, 112.9, 112.6, 111.0,110.1, 104.2, 102.2, 98.6, 61.0, 57.3, 55.4, 55.3, 33.0, 22.7, 14.2, 8.4; **HRMS-ESI**: m/z calcd for $C_{32}H_{32}BrN_2O_4$ [M+H]: 587.1545; found: 587.1545.

Synthesis of compound 14h



According to the procedure E, secondary alcohol **11c** (200 mg, 0.5 mmol), ester **13d** (120 mg, 0.5 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14h** (310 mg, 89%) as a colorless liquid; *Rf* = 0.4 (EtOAc–hexane 1:9); **IR** (neat): ν_{max}/cm^{-1} 2953, 2928, 2855, 1731, 1471, 1456, 1255, 1177, 1095, 835, 776, 739, 699; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.59 (d, *J* = 7.9 Hz, 1H), 7.41-7.46 (m, 3H), 7.40-7.34 (m, 3H). 7.33-7.29 (m, 1H), 7.28-7.23 (m, 1H), 7.13 (s, 1H), 7.09-7.01 (m, 2H), 6.89 (t, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 5.98 (d, *J* = 8.2 Hz, 1H), 4.85 (d, *J* = 8.9 Hz, 1H), 4.24-4.17 (m, 1H), 4.16-4.09 (m, 1H), 3.85 (dd, *J* = 8.2 Hz, 8.9 Hz, 1H), 3.80 (s, 3H), 3.71-3.58 (m, 2H), 2.82-2.74 (m, 1H), 2.64-2.56 (m, 1H), 1.17 (t, *J* = 7.3 Hz, 3H) , 0.86 (s, 9H), -0.06 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.0, 141.5, 140.9, 137.4, 133.2, 132.7, 128.8, 128.0, 127.5, 127.4, 126.0, 122.0, 120.5, 119.6, 119.3, 118.9, 118.8, 112.2, 110.5, 109.5, 103.8, 65.8, 63.3, 61.1, 57.2, 47.7, 32.9, 27.8, 26.0, 18.4, 14.1, -5.3; **HRMS-ESI**: m/z calcd for $C_{37}H_{45}N_2O_3Si$ [M+H]: 593.3199; found: 593.3196.

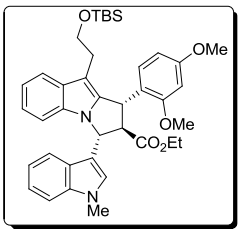
Synthesis of compound 14i



According to the procedure E, secondary alcohol **11c** (200 mg, 0.5 mmol), ester **13e** (161 mg, 0.5 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14i** (316 mg, 90%) as a white solid; *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 2952, 2927, 2854, 1731, 1474, 1456, 1255, 1177, 1094, 1028, 835, 776, 741, 700; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.64 (brs, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.44-7.40 (m, 2H), 7.39-7.35 (m, 2H), 7.34-7.29 (m, 2H), 7.20 (d, *J* = 8.5 Hz, 1H), 7.07-7.09 (m, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.90-6.95 (m, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 5.90 (dd, *J* = 2.1 Hz, 7.9 Hz, 1H), 4.88 (dd, *J* = 2.1 Hz, 8.2 Hz, 1H), 4.25-4.13

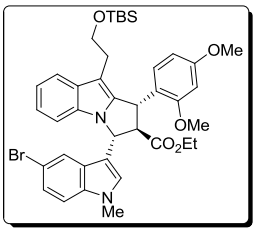
(m, 2H), 3.76-3.79 (m, 1H), 3.75 (s, 3H), 3.68-3.59 (m, 2H), 2.81-2.74 (m, 1H), 2.65-2.58 (m, 1H), 1.21 (dt, *J* = 1.5 Hz, 7.0 Hz, 3H), 0.84 (s, 9H), -0.07 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 171.9, 141.5, 141.0, 136.0, 133.4, 132.6, 128.8, 128.4, 127.9, 127.6, 127.4, 125.0, 121.8, 120.5, 119.1, 119.0, 113.1, 112.4, 111.0, 110.4, 104.1, 65.8, 63.2, 61.3, 56.8, 47.4, 33.1, 27.8, 26.0, 18.4, 14.1, -5.3 **HRMS-ESI**: m/z calcd for $C_{37}H_{44}BrN_2O_3Si$ [M+H]: 671.2305; found: 671.2303.

Synthesis of compound 14j



According to the procedure E, secondary alcohol **11d** (200 mg, 0.5 mmol), ester **13d** (104 mg, 0.5 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14j** (269 mg, 91%) as a yellow color gel type compound; *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 2953, 2929, 2855, 1731, 1613, 1507, 1458, 1178, 1260, 1208, 1095, 835, 740; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.55 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 9.2 Hz, 1H), 7.22 (dd, *J* = 0.9 Hz , 7.0 Hz, 1H), 7.06 (s, 1H), 7.00 (dd, *J* = 7.0 Hz , 15.0 Hz, 2H), 6.84 (t, *J* = 7.3 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.48-6.45 (m, 2H), 5.89 (d, *J* = 8.2 Hz, 1H), 5.10 (d, *J* = 7.9 Hz, 1H), 4.18-4.07 (m, 2H), 3.75-3.83 (m, 1H), 3.81 (s, 3H), 3.77 (brs, 6H), 3.68-3.57 (m, 2H), 2.83-2.75 (m, 1H), 2.67-2.59 (m, 1H), 1.15 (t, *J* = 7.02, 3H), 0.85 (brs, 9H), -0.06 (brs, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.6, 160.1, 158.2, 141.7, 137.4, 133.4, 132.8, 127.4, 126.1, 121.9, 120.1, 119.6, 119.5, 118.7, 118.5, 112.4, 110.4, 109.4, 104.3, 102.9 , 98.5, 63.4, 60.8, 57.6, 55.3, 55.2, 32.9, 29.7, 27.9, 26.0, 18.4, 14.1, -5.4; **HRMS-ESI**: m/z calcd for $C_{39}H_{49}N_2O_5Si$ [M+H]: 653.3411; found: 653.3410.

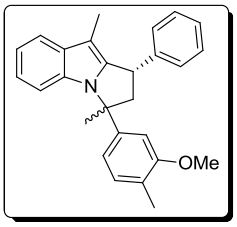
Synthesis of compound 14k



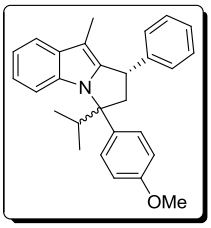
According to the procedure E, secondary alcohol **11d** (200 mg, 0.5 mmol), ester **13e** (139 mg, 0.5 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14k** (304 mg, 92%) as a colorless liquid; *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 2953, 2928, 2855, 1731, 1613, 1475, 1458, 1208, 1158,1095, 836, 778, 740; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.60 (brs, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.30 (dd, *J* = 1.8 Hz, 8.5 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 7.05-7.03 (m, 2H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.49-6.44 (m, 2H), 5.80 (d, *J* = 7.9 Hz, 1H), 4.98-5.12 (m, 1H), 4.21-4.11 (m, 2H), 3.82-

3.73 (m, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H), 3.70-3.58 (m, 2H), 2.83-2.75 (m, 1H), 2.68-2.60 (m, 1H), 1.19 (t, *J* = 7.3 Hz, 3H), 0.84 (brs, 9H), -0.07 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.5, 160.2, 158.2, 141.7, 136.1, 133.5, 132.8, 128.5, 127.6, 124.9, 121.9, 120.1, 118.9,118.7, 113.0, 112.4, 111.0,110.2, 104.3, 103.2, 98.7, 63.3, 61.0, 57.3, 55.3, 33.1, 27.9, 26.0, 18.4, 14.2, -5.4; **HRMS-ESI**: m/z calcd for $C_{39}H_{48}BrN_2O_5Si$ [M+H]: 731.2516; found: 731.2513.

Synthesis of compound 14l



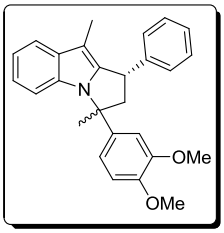
According to the procedure E, secondary alcohol **11a** (100 mg, 0.4 mmol), 2-methoxy-1-methyl-4-(prop-1-en-2-yl)benzene (68 mg, 0.4 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14l** (139 mg, 87%) as a red solid with 10:7 diastereomeric mixture; *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (neat): ν_{max}/cm^{-1} 2966, 2922, 1453, 1259, 1244, 1136, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz); δ 7.59 (d, *J* = 7.9 Hz, 1H), 7.40-7.24 (m, 5H), 7.16-7.06 (m, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 7.01-6.95 (m, 1H), 6.38-6.34 (m, 1H), 6.33 (brs, 1H), 4.39 (t, *J* = 8.5 Hz, 1H), 4.39 (t, *J* = 8.5 Hz, 1H), 3.62 (s, 3H), 3.20-3.09 (m, 1H), 2.76-2.67 (m, 1H), 2.21 (s, 3H), 2.19 (s, 3H), 1.97 (s, 3H); **HRMS-ESI**: m/z calcd for $C_{27}H_{26}NO$ [M-H]: 380.2015; found: 380.2019.



Synthesis of compound 14m

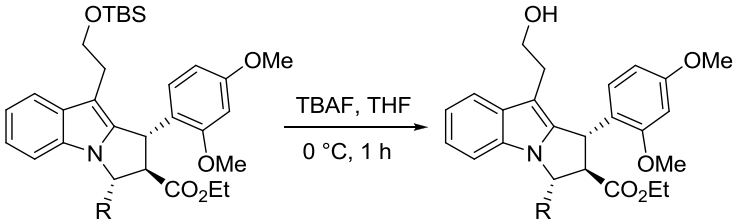
According to the procedure E, secondary alcohol **11a** (100 mg, 0.4 mmol), 1-methoxy-4-(3-methylbut-1-en-2-yl)benzene (74 mg, 0.4 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14m** (143 mg, 86%) as a colorless liquid with 5:3 diastereomeric mixture; *Rf* = 0.4 (EtOAc-hexane 1:9); **IR** (thin film): ν_{max}/cm^{-1} 2930, 2961, 1512, 1452, 1253, 1184, 1037, 828, 756, 739, 699; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.58-7.45 (m, 2H), 7.39-7.23 (m, 5H), 7.21-7.14 (m, 2H), 7.12-6.95 (m, 2H), 6.83-6.78 (m, 2H), 4.38-4.32 (m, 1H), 3.76 (s, 3H), 3.20-3.15 (m, 1H), 3.14-3.01 (m, 1H), 2.72-2.60 (m, 1H), 1.79 (s, 3H), 1.06 (d, *J* = 6.6 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H); **HRMS-ESI**: m/z calcd for $C_{28}H_{30}NO$ [M+H]: 396.2327; found: 396.2327.

Synthesis of compound 14n



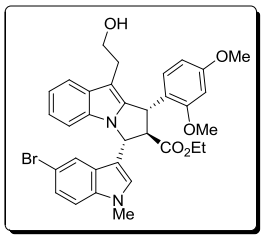
According to the procedure E, secondary alcohol **11a** (100 mg, 0.4 mmol), 1, 2-dimethoxy-4-(prop-1-en-2-yl) benzene (75 mg, 0.4 mmol) and catalytic amount of $Cu(OTf)_2$ were used to furnish the product **14n** (139 mg, 83%) as a colorless liquid with 5:2 diastereomeric mixture; *Rf* = 0.4 (EtOAc-hexane 1:6); **IR** (thin film): ν_{max}/cm^{-1} 3025, 2973, 2933, 1454, 1515, 1262, 1144, 1027, 742, 700; **^{1}H NMR** ($CDCl_3$, 500 MHz); δ 7.56 (d, *J* = 7.7 Hz, 1 H), 7.36-7.30 (m, 3H), 7.29-7.23 (m, 2H), 7.22-7.19 (m, 1H), 7.12-6.98 (m, 2H), 6.74-6.69 (m, 1H), 6.44 (brs, 1H), 6.31-6.26 (m, 1H), 4.35 (t, *J* = 8.6 Hz, 1H), 3.83 (s, 3H), 3.69 (s, 3H), 3.13-3.05 (m, 1H), 2.70-2.63 (m, 1H), 2.14 (s, 3H), 1.93 (s, 3H); **HRMS-ESI**: m/z calcd for $C_{27}H_{28}NO_2$ [M+H]: 398.2120; found: 398.2127.

Procedure F: TBS deprotection.



Tetrabutylammoniumfluoride (1.3 equiv) was added dropwise to a cold (0 °C) solution of compound **14** (1 equiv) in THF under Ar and stirred for 1 h at the same temperature. The reaction mixture was then quenched with water, extracted with EtOAc and dried over Na_2SO_4. Solvent was evaporated and residue was purified by flash chromatography over silica gel column.

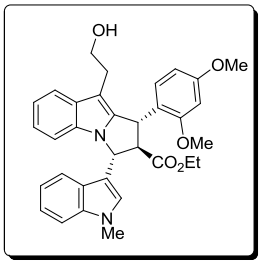
Synthesis of compound 15a



According to the procedure F, Tetrabutylammoniumfluoride (0.33 ml, 0.3 mmol, 1M solution in THF) and compound **14k** (200 mg, 0.3 mmol) were used to furnish the alcohol **15a** (158 mg, 94 %) as a liquid; *Rf* = 0.5 (EtOAc-hexane 1:1); **IR** (neat): ν_{max}/cm^{-1} 3443, 2925, 2853, 1729, 1612, 1507, 1476, 1208,1035, 795, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz):δ 7.59 (s, 1H), 7.56 (d, *J* =7.9 Hz, 1H), 7.30 (dd, *J* = 1.5 Hz , 8.5 Hz, 1H), 7.20 (t, *J* = 8.5 Hz, 2H), 7.04 (t,

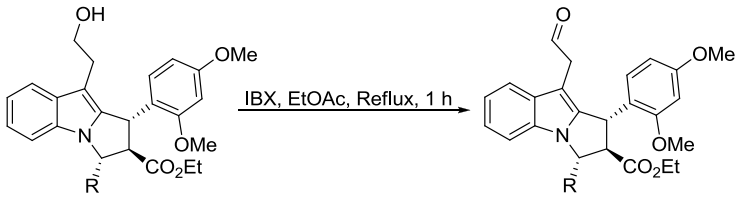
J = 7.6 Hz, 2H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.51-6.45 (m, 2H), 5.82 (d, *J* = 7.6 Hz, 1H), 5.06 (brd, 1H), 4.21-4.10 (m, 2H), 3.85-3.72 (m, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.74 (s, 3H), 3.68 (t, *J* = 6.7 Hz, 2H), 2.88-2.77 (m, 1H), 2.73-2.61 (m, 1H), 1.19 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.5, 160.3, 158.2, 142.3, 136.1, 133.3, 132.8, 128.5, 127.5, 125.0, 121.9, 120.4, 119.1, 118.6, 113.0, 111.0, 110.3, 104.3, 102.5, 98.8, 62.6, 61.1, 57.3, 55.5, 55.3, 33.1, 27.5, 14.2; **HRMS-ESI**: m/z calcd for $C_{33}H_{34}BrN_2O_5$ [M+H]: 617.1651; found: 617.1654.

Synthesis of compound 15b



According to the procedure F, Tetrabutylammoniumfluoride (0.4 ml, 0.4 mmol, 1M solution in THF) and compound **14j** (200 mg, 0.3 mmol) were used to furnish the alcohol **15b** (156 mg, 95 %) as a liquid; *Rf* = 0.4 (EtOAc–hexane 1:1); **IR** (neat): ν_{max}/cm^{-1} 3443, 2927, 2853, 1729, 1613, 1507, 1458, 1180, 1208, 1035, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.60 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.31 (s, 1H), 7.30-7.27 (m, 1H), 7.12 (s, 1H), 7.09-7.04 (m, 2H), 6.91 (t, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.55-6.50 (m, 2H), 5.97 (d, *J* = 8.2 Hz, 1H), 5.15 (brd, 1H), 4.24-4.13 (m, 2H), 4.00-3.91 (m, 1H), 3.89-3.77 (m, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 3.82 (s, 3H), 3.75-3.70 (m, 2H), 2.91-2.83 (m, 1H), 2.73-2.65 (m, 1H), 1.20 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.5, 160.1, 158.2, 142.2, 137.4, 133.2, 132.8, 129.5, 127.4, 126.0, 121.9, 120.3, 119.5, 119.0, 118.4, 112.3, 110.5, 109.4, 104.3, 102.3, 98.6, 62.7, 60.9, 57.5, 55.3, 32.9, 29.7, 29.6, 27.4, 14.1; **HRMS-ESI**: m/z calcd for $C_{33}H_{35}N_2O_5$ [M+H]: 539.2546; found: 539.2540.

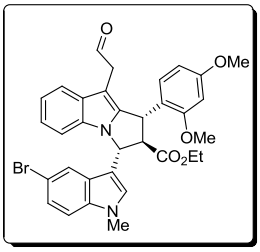
Procedure G: IBX oxidation.



To a solution of alcohol **15** (1 equiv) in ethyl acetate, was added IBX (3 equiv) and refluxed for 1 h. The reaction mixture was cooled to RT and filtered through sintered funnel. The

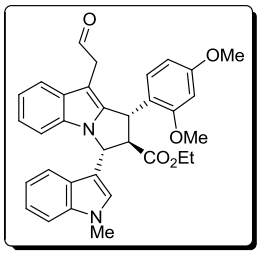
filter cake was washed with ethyl acetate for 2 to 3 times. Combined filtrates were concentrated and the residue was purified by flash chromatography over silica gel column.

Synthesis of compound 15a'



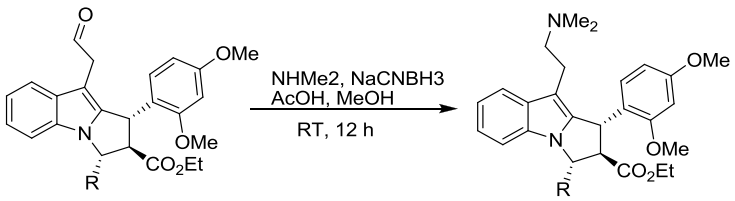
According to the procedure G, alcohol **15a** (120 mg, 0.2 mmol) and IBX (164 mg, 0.6 mmol) were used to furnish the aldehyde **15a'** (89 mg, 74%) as a liquid; *Rf* = 0.4 (EtOAc-hexane 3:7); **IR** (neat): ν_{max}/cm^{-1} 2924, 2875, 1725, 1612, 1507, 1457, 1208, 1178, 1030, 795, 742; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 9.51 (brs, 1H), 7.55 (s, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.32-7.29 (m, 1H), 7.23-7.19 (m, 2H), 7.09 (s, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.90 (t, *J* = 7.2 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.50-6.45 (m, 2H), 5.89 (d, *J* = 8.3 Hz, 1H), 5.07 (brd, 1H), 4.21-4.10 (m, 2H), 4.00-3.85 (m, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.50 (dd, *J* = 1.7 Hz, 16.6 Hz, 1H), 3.36 (dd, *J* = 1.7 Hz, 16.6 Hz, 1H), 1.18 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 199.7, 172.2, 160.5, 158.3, 143.1, 136.1, 133.0, 132.7, 128.7, 127.5, 125.0, 121.9, 120.8, 119.5, 118.2, 113.1, 111.9, 111.1, 110.4, 104.4, 98.9, 96.5, 61.1, 57.5, 55.5, 55.3, 39.1, 33.1, 14.2; **HRMS-ESI**: m/z calcd for $C_{33}H_{32}BrN_2O_5$ [M+H]: 615.1495; found: 615.1498.

Synthesis of compound 15b'



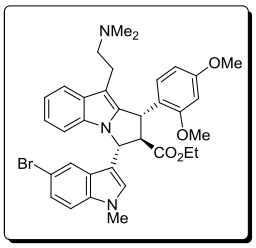
According to the procedure G, alcohol **15b** (120 mg, 0.2 mmol) and IBX (187 mg, 0.6 mmol) were used to furnish the aldehyde **15b'** (86 mg, 72%) as a liquid; *Rf* = 0.4 (EtOAc-hexane 3:7); **IR** (neat): ν_{max}/cm^{-1} 2934, 2885, 1726, 1613, 1507, 1457, 1208, 1179, 1158, 1031, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 9.51 (t, *J* = 2.6 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.39-7.32 (m, 2H), 7.28-7.20 (m, 2H), 7.12 (s, 1H), 7.04-6.98 (m, 2H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.50-6.46 (m, 2H), 5.99 (d, *J* = 8.6 Hz, 1H), 5.13 (brd, 1H), 4.19-4.07 (m, 2H), 4.01-3.89 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.77 (s, 3H), 3.54-3.47 (m, 1H), 3.35 (dd, *J* = 2.6 Hz, 16.6 Hz, 1H), 1.14 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 199.8, 172.2, 160.4, 158.3, 143.1, 137.4, 132.9, 132.8, 127.5, 126.0, 122.0, 120.7, 119.6, 119.4, 118.0, 111.9, 110.6, 109.5, 104.5, 98.7, 96.2, 60.9, 57.8, 55.4, 55.3, 39.1, 32.9, 14.1; **HRMS-ESI**: m/z calcd for $C_{33}H_{33}N_2O_5$ [M+H]: 537.2389; found: 537.2382.

Procedure H: Reductive amination.



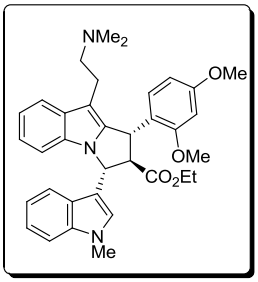
To a magnetically stirred solution of aldehyde **15a' or 15b'** (1 equiv) in MeOH, were added $NHMe_2$ (8 equiv) and one drop of acetic acid. After five minutes $NaCNBH_3$ (4 equiv) was added and stirred for 12 h at RT. The reaction mixture was then quenched with a saturated solution of $NaHCO_3$, extracted with EtOAc and washed with brine. The combined organic layers were dried over Na_2SO_4. Solvent was evaporated and residue was purified by flash chromatography over silica gel column.

Synthesis of compound 16a

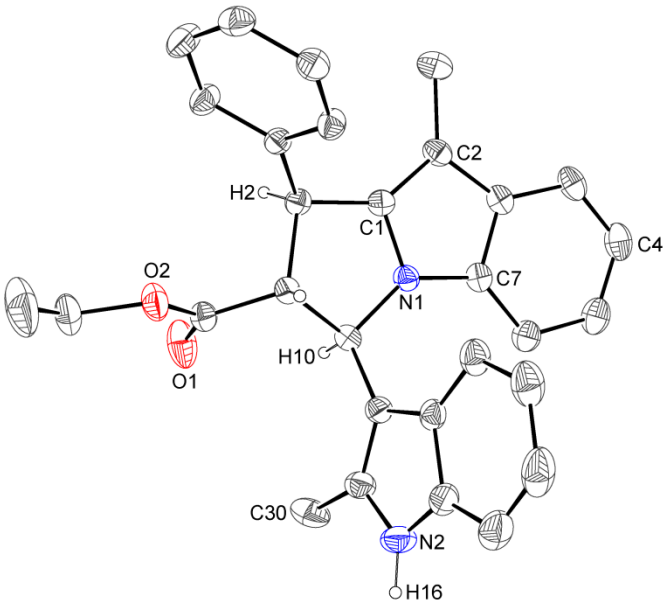


According to the procedure H, aldehyde **15a'** (50 mg, 0.1 mmol), $NHMe_2$ (0.3 ml, 0.6 mmol, 2.0 *M* solution), one drop of acetic acid and $NaCNBH_3$ (20 mg, 0.3 mmol) were used to furnish the compound **16a** (42 mg, 80%) as a solid; *Rf* = 0.4 (MeOH-CH_2Cl_2 1:99); **IR** (neat): ν_{max}/cm^{-1} 2932, 2851, 1730, 1612, 1475, 1458, 1158, 1179, 1031, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.56 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 1.5 Hz, 8.5 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 7.07 (s, 1H), 7.02 (t, *J* = 7.9 Hz, 1H), 6.87 (t, *J* = 7.9 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.55-6.45 (m, 2H), 5.82 (d, *J* = 7.9 Hz, 1H), 5.03 (brd, 1H), 4.20-4.10 (m, 2H), 3.86-3.79 (m, 1H), 3.81(s, 3H), 3.80 (s, 3H), 3.76 (s, 3H), 2.84-2.69 (m, 2H), 2.68-2.58 (m, 2H), 2.22 (s, 3H), 1.17 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.3, 160.4, 158.4, 141.5, 136.1, 132.9, 132.7, 128.6, 127.6, 125.0, 121.9, 120.3, 119.0, 118.4, 113.0, 111.1, 110.3, 104.4, 98.8, 61.0, 58.9, 57.3, 55.5, 55.4, 44.3, 33.1, 29.7, 21.0, 14.2; **HRMS-ESI**: m/z calcd for $C_{35}H_{39}BrN_3O_4$ [M+H]: 644.2124; found: 644.2120.

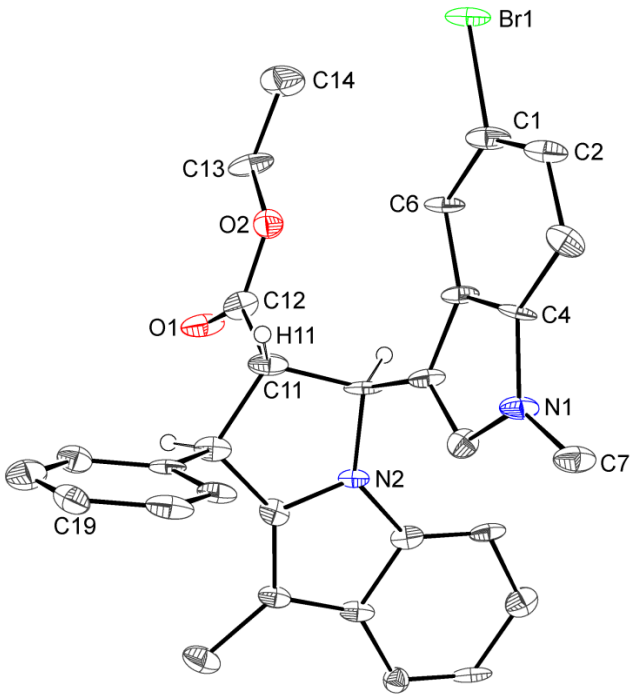
Synthesis of compound 16b



According to the procedure H, aldehyde **15b'** (50 mg, 0.1 mmol), $NHMe_2$ (0.4 ml, 0.7 mmol, 2.0 *M* solution), one drop of acetic acid and $NaCNBH_3$ (23 mg, 0.4 mmol) were used to furnish the compound **16b** (45 mg, 87%) as red color solid; *Rf* = 0.4 (MeOH-CH_2Cl_2 1:99); **IR** (neat): ν_{max}/cm^{-1} 2930, 2850, 1730, 1612, 1507, 1458, 1208, 1178, 1158, 1032, 741; **^{1}H NMR** ($CDCl_3$, 500 MHz): δ 7.52 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.29-7.25 (m, 1H), 7.24-7.20 (m, 1H), 7.10 (s, 1H), 7.03-6.97 (m, 2H), 6.83 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.51-6.46 (m, 2H), 5.92 (d, *J* = 8.2 Hz, 1H), 5.08 (brd, 1H), 4.16-4.06 (m, 2H), 3.97-3.87 (m, 1H), 3.81 (s, 3H), 3.78 (s, 6H), 2.79-2.71 (m, 1H), 2.67-2.58 (m, 2H), 2.44-2.36 (m, 1H), 2.23 (s, 6H), 1.13 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz): δ 172.4, 160.2, 158.3, 141.5, 137.4, 132.70, 132.68, 127.5, 126.0, 121.9, 120.2, 119.5, 118.9, 118.2 , 112.1, 110.5, 109.5, 109.4, 104.5, 102.8, 98.6, 60.8, 58.9, 57.5, 55.4, 55.3, 44.1, 32.9, 29.6, 20.8, 14.1; **HRMS-ESI**: m/z calcd for $C_{35}H_{40}N_3O_4$ [M+H]: 566.3019; found: 566.3019.



X-ray crystal structure for compound **14b**

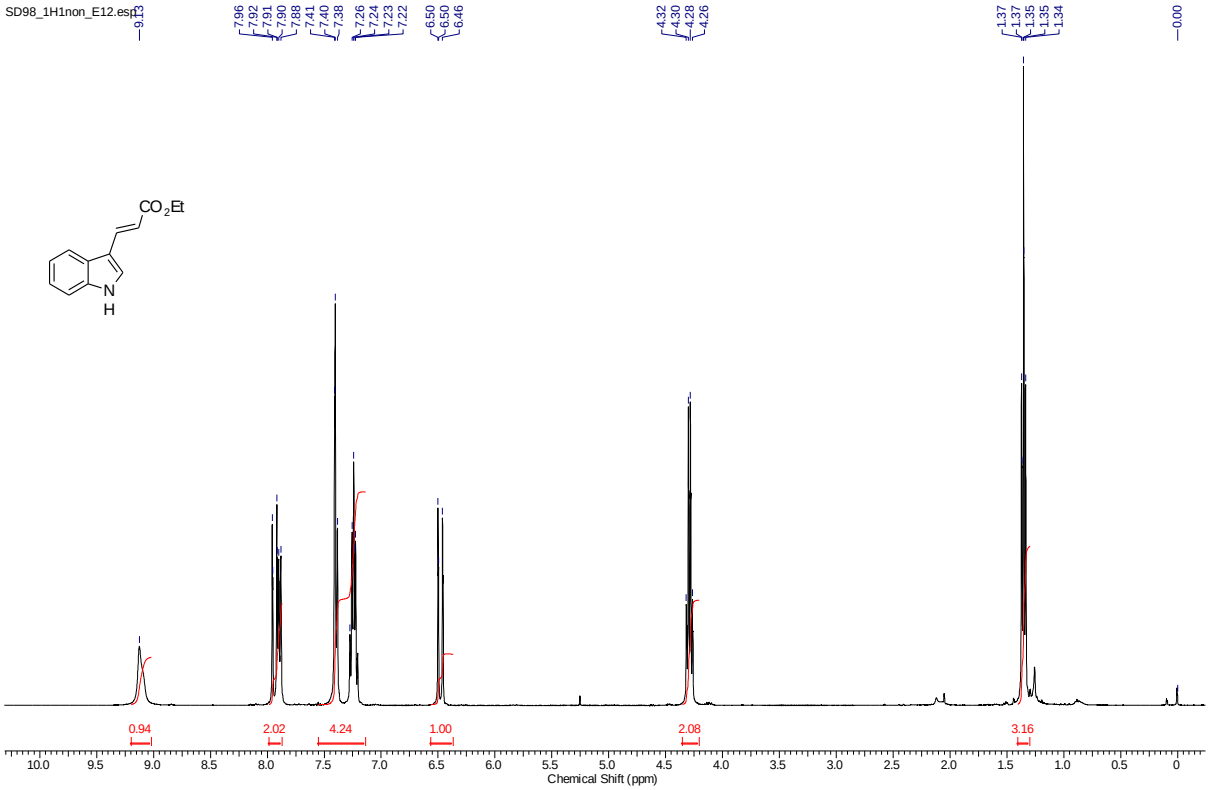


X-ray crystal structure for compound **14e**

X-ray crystallographic data and structure refinement

compounds	**14e.CH_2Cl_2**	**14b**
Empirical formula	$C_{31}H_{29}BrCl_2N_2O_2$	$C_{30}H_{28}N_2O_2$
Formula Weight	612.37	872.51
Crystal System	Orthorhombic	Monoclinic
Space Group	Pn21a	P 21/n
a (Å)	11.149(5)	11.4304(7)
b (Å)	19.600(5)	12.7197(7)
c (Å)	25.468(5)	16.8479(8)
α (deg)	90	90
β (deg)		96.853(5)
γ (deg)		90.00
V (Å3)	5565(3)	2432.0(2)
Z	8	4
ρcalcd (g cm-3)	1.462	1.225
μ (mm-1)	1.701	0.077
F(000)	2512	952
Reflections		
Collected	29575	12200
Independent	8083	5599
Observed [I >2σ (I)]	5359	3360
No. of variables	691	311
GooF	1.061	1.049
Rint	0.1094	0.0369
Final R indices [I > 2σ(I)]a	R1 = 0.0747	R1 = 0.0592
	wR2 = 0.1845	wR2 = 0.1429
R indices (all data)a	R1 = 0.1280	R1 = 0.1019
	wR2 = 0.2300	wR2 = 0.1745

[a] $R_1 = \Sigma ||F_o| - |F_c||/\Sigma|F_o|$ with $F_o^2 > 2\sigma(F_o^2)$. $wR_2 = [\Sigma w(|F_o^2| - |F_c^2|)^2/\Sigma|F_o^2|^2]^{1/2}$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7.92
7.91
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7.41
7.40
7.38
7.26
7.24
7.23
7.22
6.50
6.50
6.46
4.32
4.30
4.28
4.26
1.37
1.37
1.35
1.35
1.34
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CO2Et
N
H
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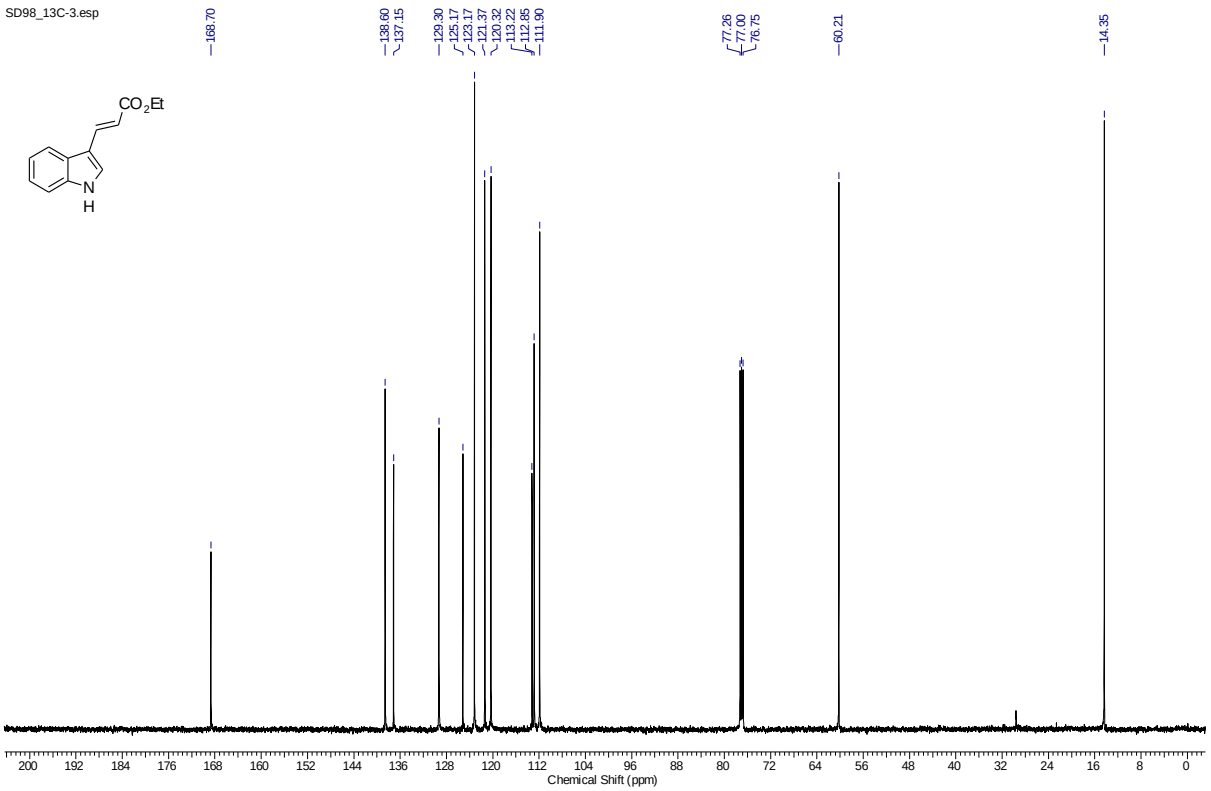
4.24
1.00
2.08
3.16
Chemical Shift (ppm)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125.17
123.17
121.37
120.32
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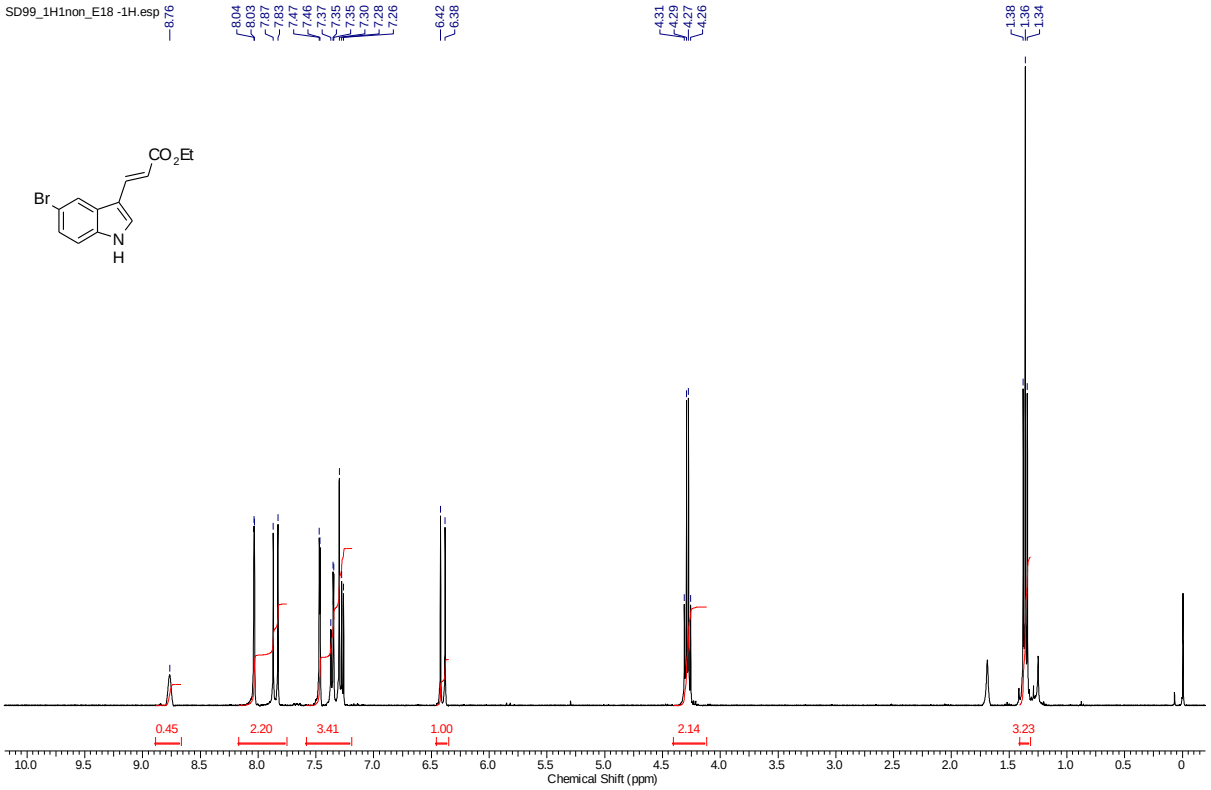
111.90
77.26
77.00
76.75
60.21
14.35
CO2Et
N
H
Chemical Shift (ppm)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8.03
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7.83
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7.46
7.37
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7.30
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7.26
6.42
6.38
4.31
4.29
4.27
4.26
1.38
1.36
1.34
CO2Et
Br
N
H
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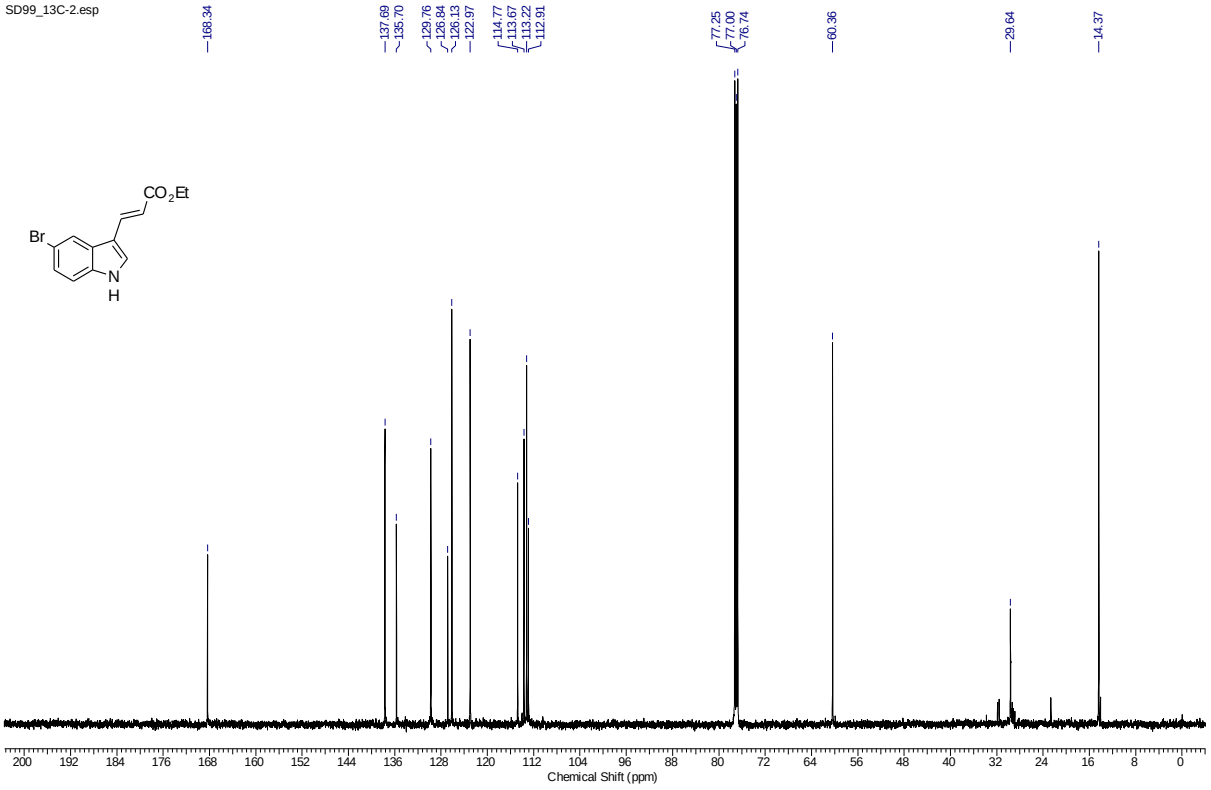
2.20
3.41
1.00
2.14
3.23
Chemical Shift (ppm)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77.00
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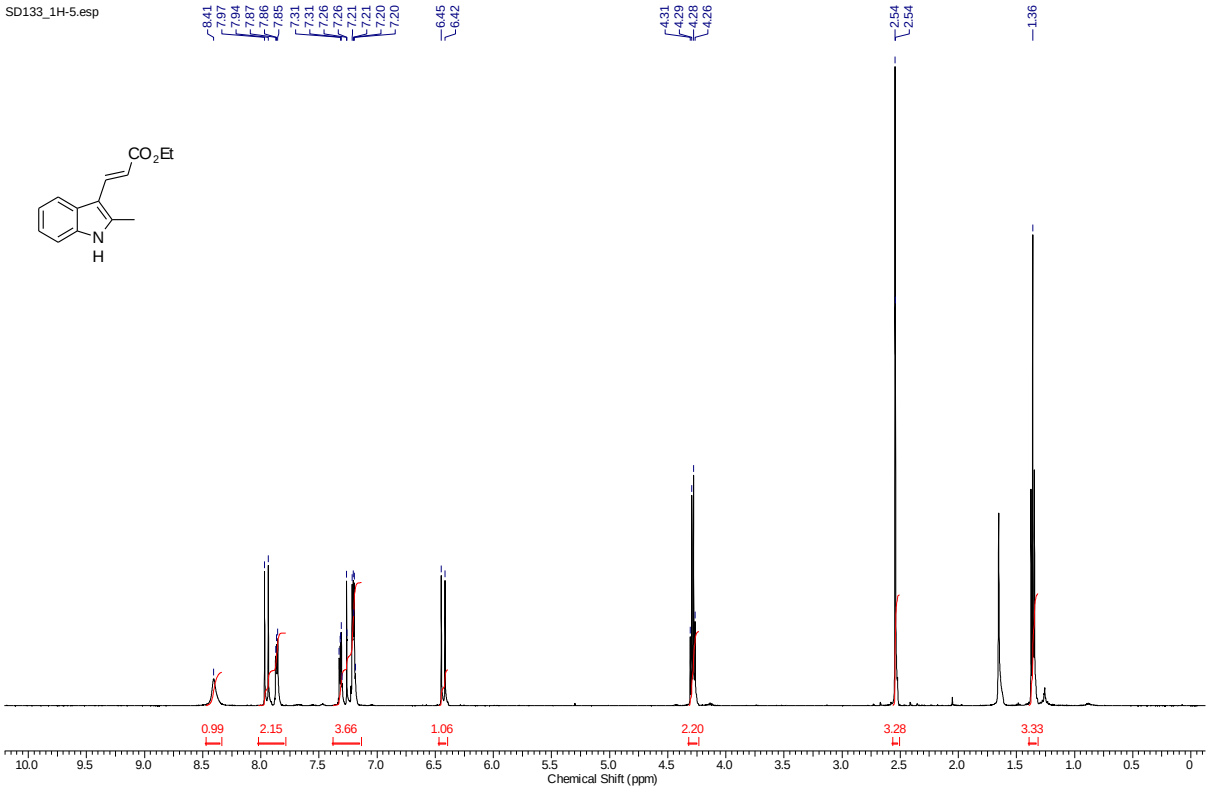
60.36
29.64
14.37
CO2Et
Br
N
H
Chemical Shift (ppm)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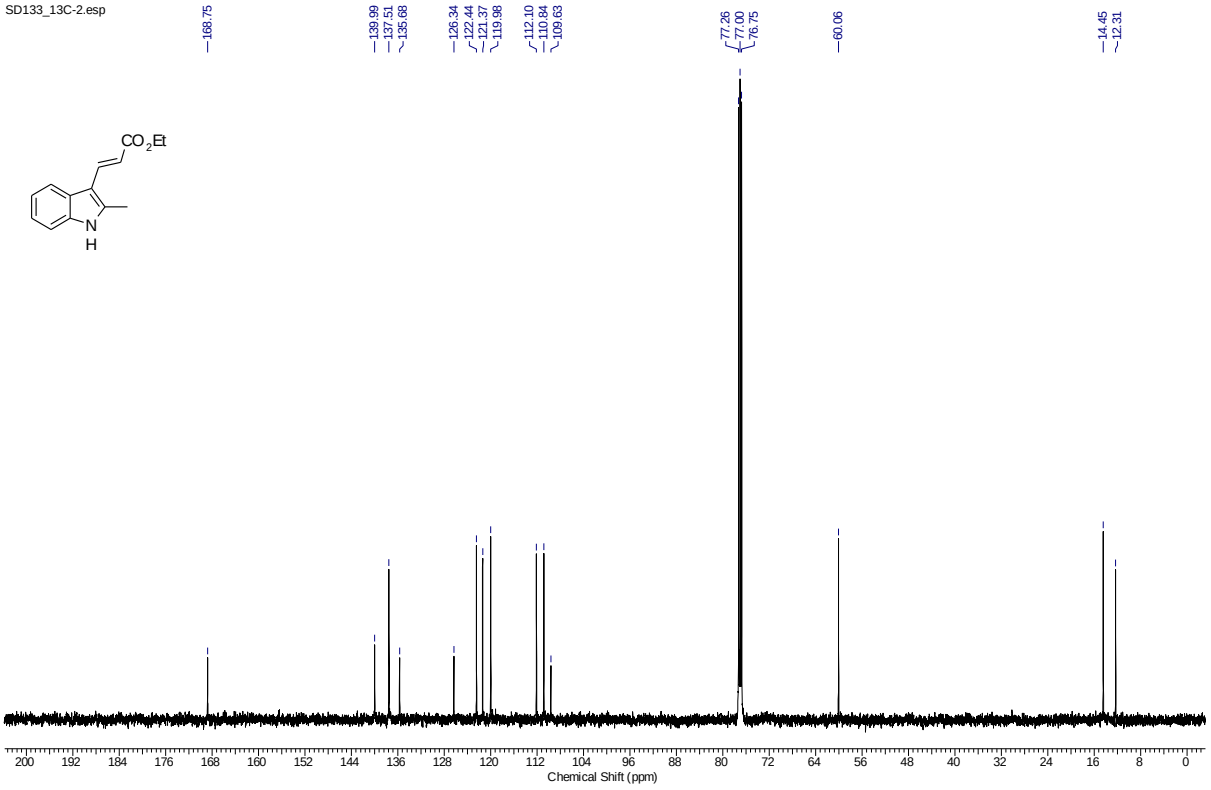
7.94
7.87
7.86
7.85
7.31
7.31
7.26
7.26
7.21
7.21
7.20
7.20
6.45
6.42
4.31
4.29
4.28
4.26
2.54
2.54
1.36
CO2Et
N
H
0.99
2.15
3.66
1.06
2.20
3.28
3.33
Chemical Shift (ppm)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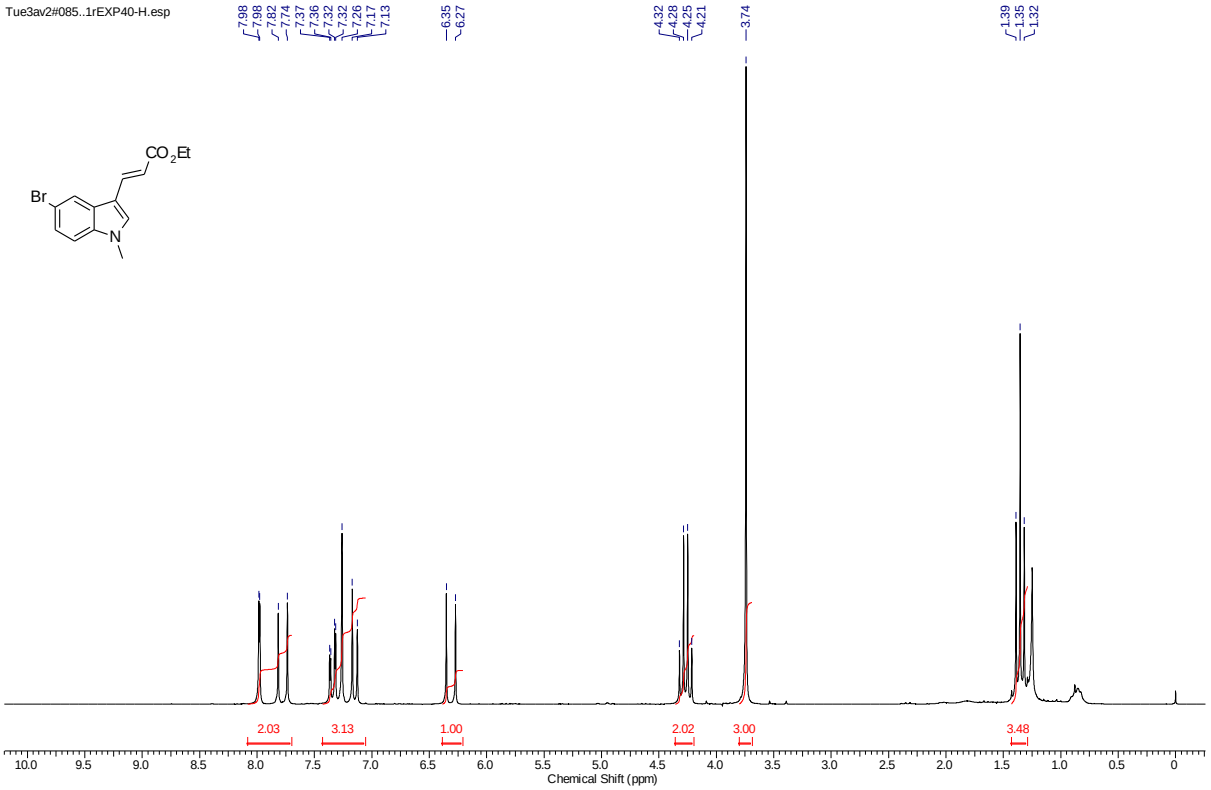
60.06
14.45
12.31
CO2Et
N
H
Chemical Shift (ppm)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7.32
7.26
7.17
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6.35
6.27
4.32
4.28
4.25
4.21
3.74
1.39
1.35
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CO2Et
Br
N
2.03
3.13
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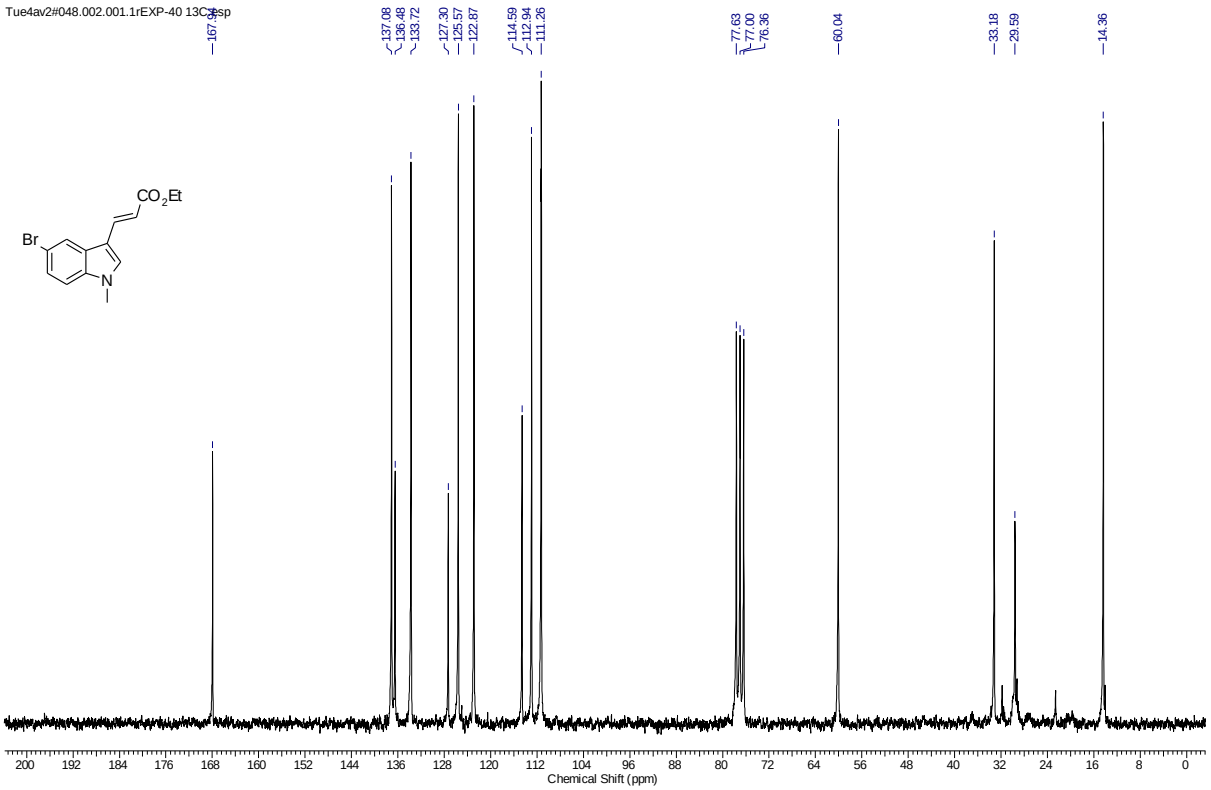
2.02
3.00
3.48
Chemical Shift (ppm)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125.57
122.87
114.59
112.94
111.26
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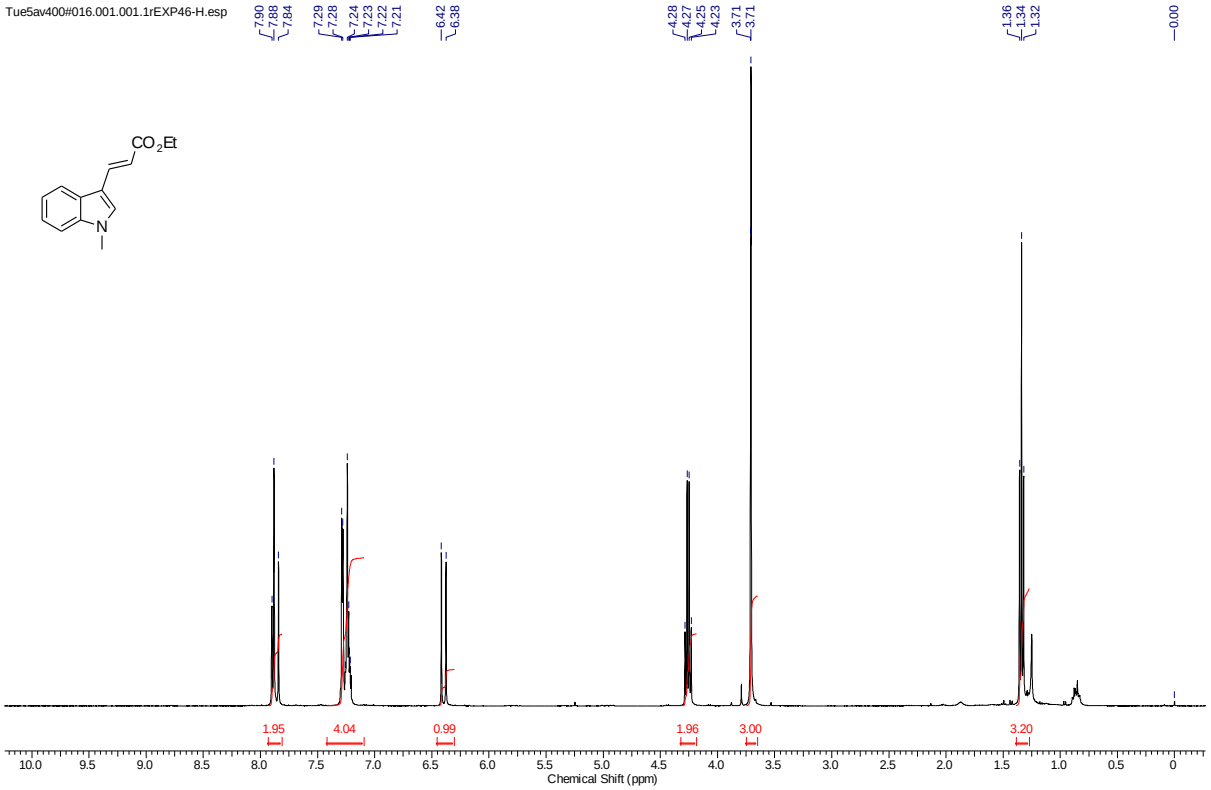
77.00
76.36
60.04
33.18
29.59
14.36
CO2Et
Br
N
Chemical Shift (ppm)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7.24
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7.22
7.21
6.42
6.38
4.28
4.27
4.25
4.23
3.71
3.71
1.36
1.34
1.32
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CO2Et
N
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4.04
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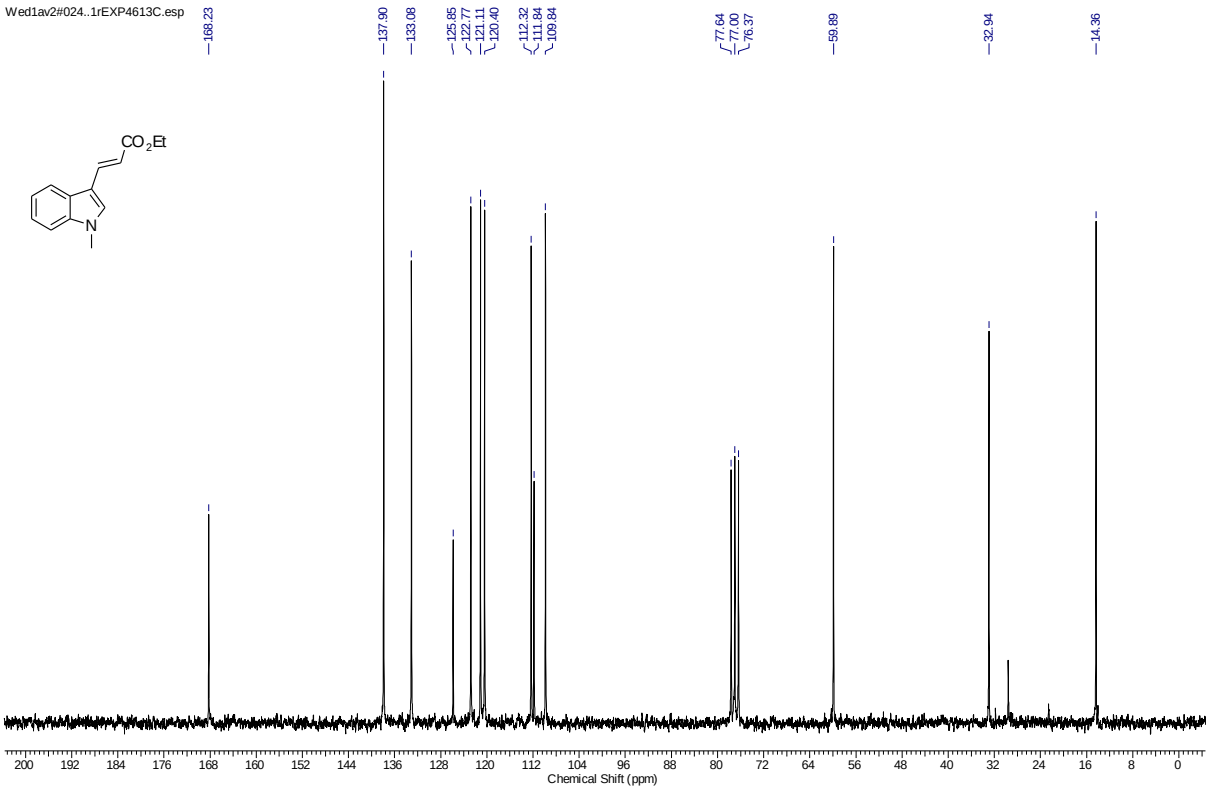
1.96
3.00
3.20
Chemical Shift (ppm)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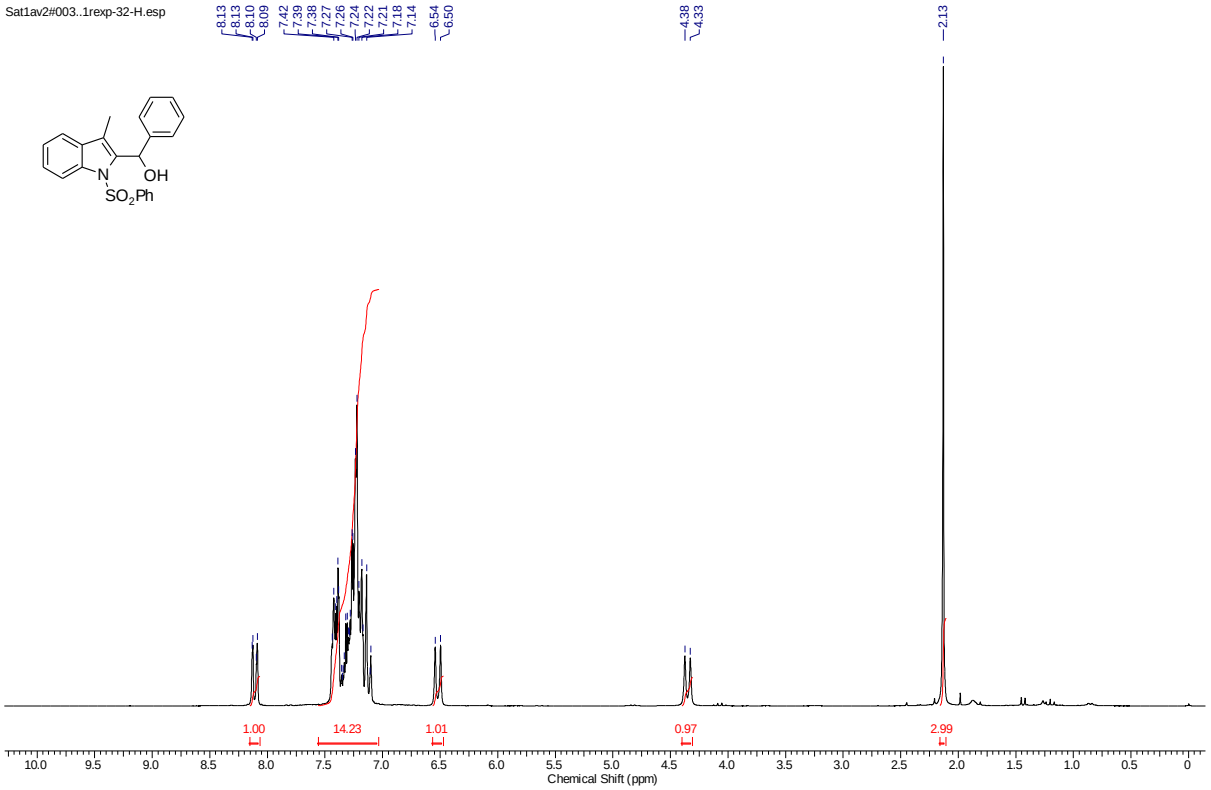
32.94
14.36
CO2Et
N
Chemical Shift (ppm)


Sat1av2#003..1rexp-32-H.esp
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7.26
7.24
7.22
7.21
7.18
7.14
6.54
6.50
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4.33
2.13
OH
N
SO2Ph
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1.01
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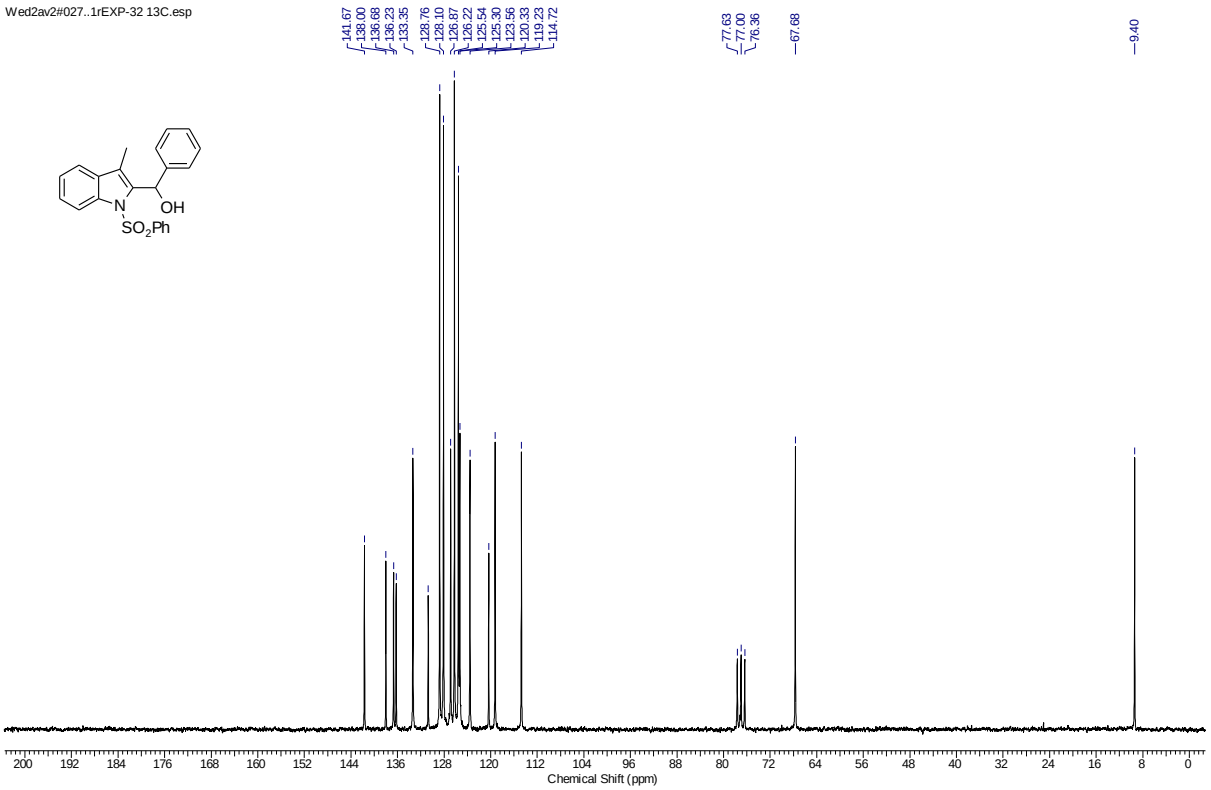
2.99
Chemical Shift (ppm)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9.40
OH
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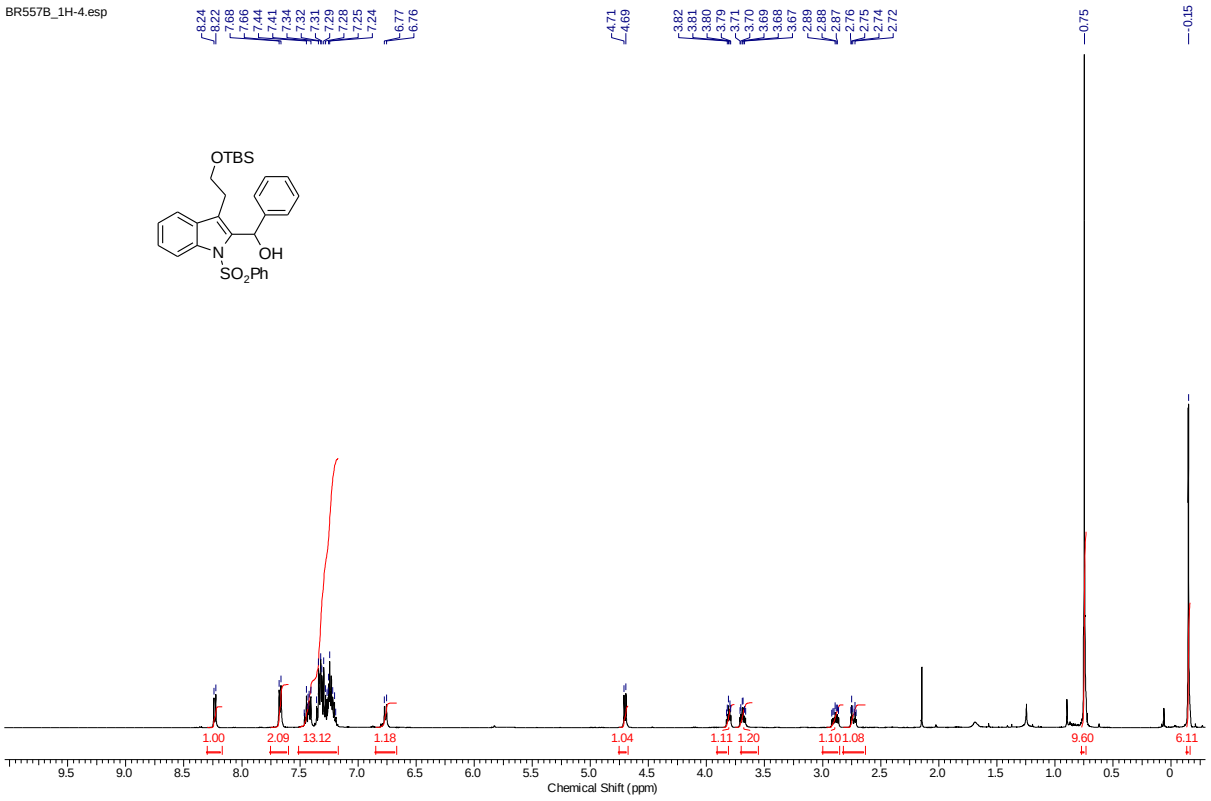
SO2Ph
Chemical Shift (ppm)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3.70
3.69
3.68
3.67
2.89
2.88
2.87
2.76
2.75
2.74
2.72
0.75
0.15
OTBS
N
OH
SO2Ph
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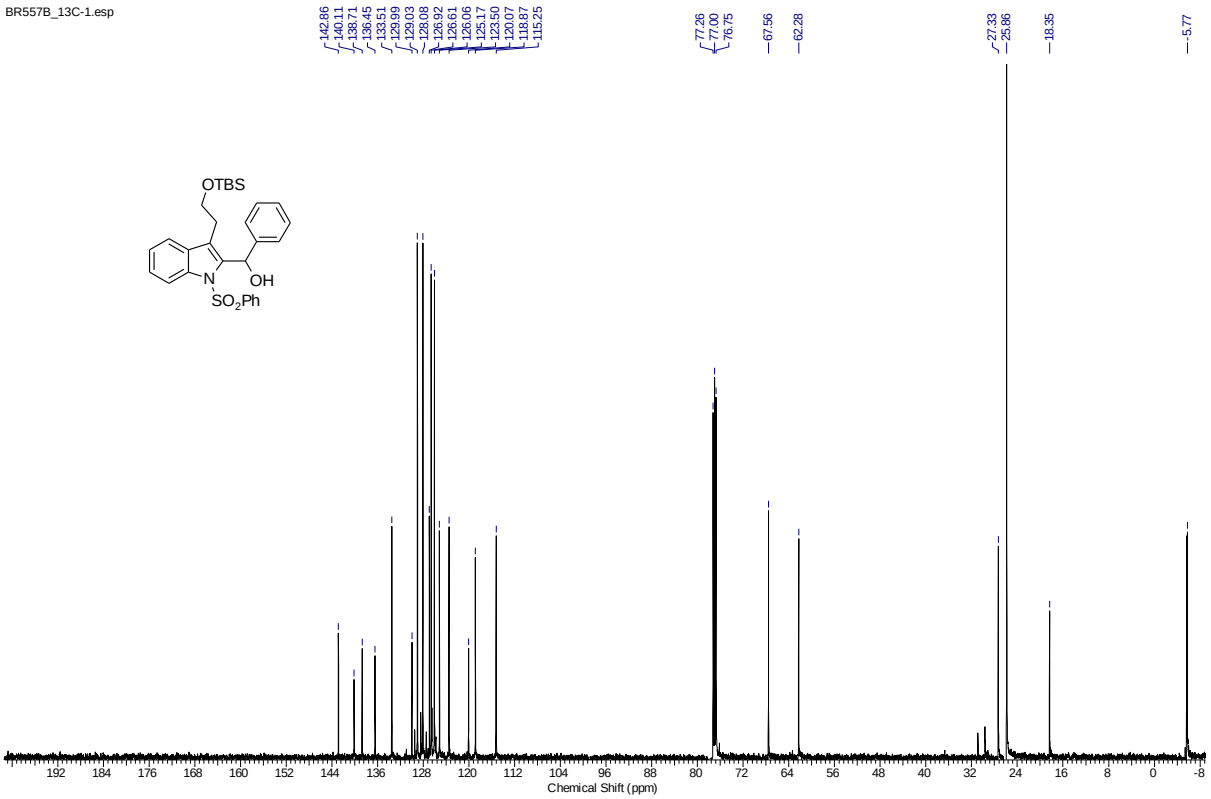
1.04
1.11
1.20
1.10
1.08
9.60
6.11
Chemical Shift (ppm)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125.17
123.50
120.07
118.87
115.25
77.26
77.00
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62.28
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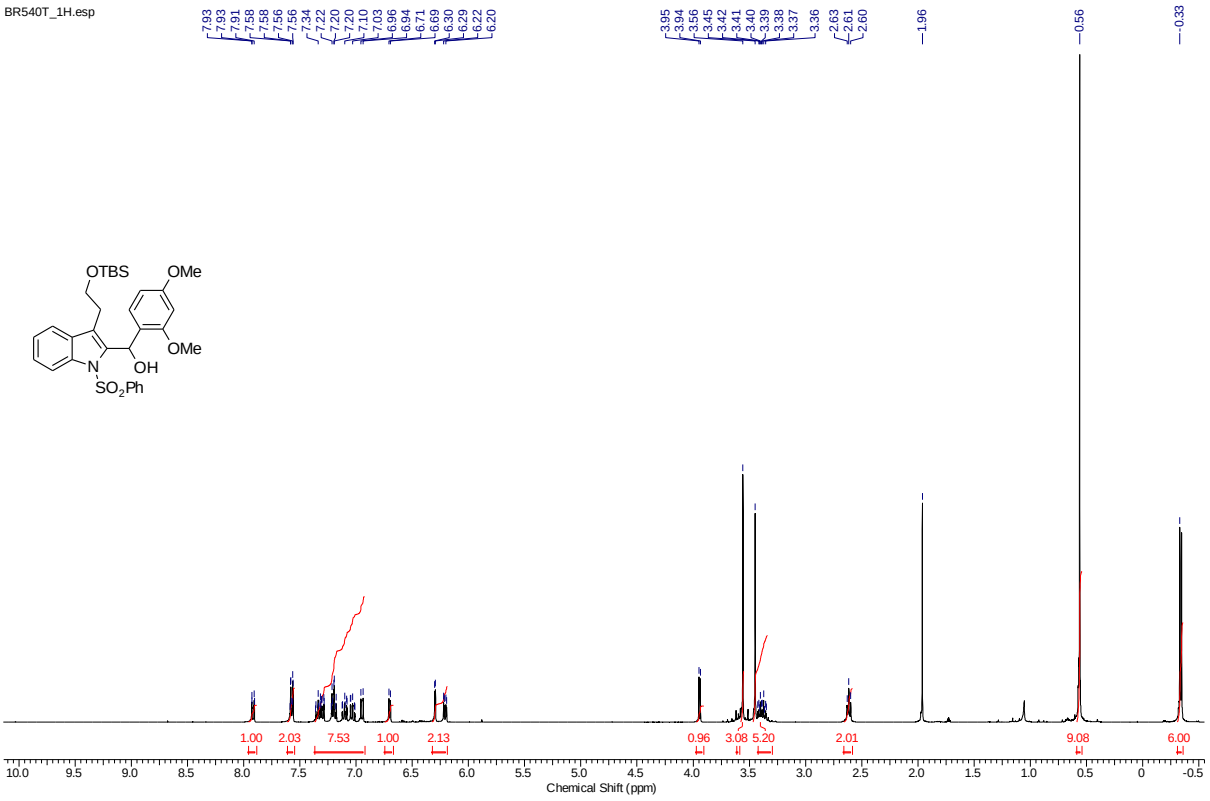
-5.77
OTBS
N
OH
SO2Ph
Chemical Shift (ppm)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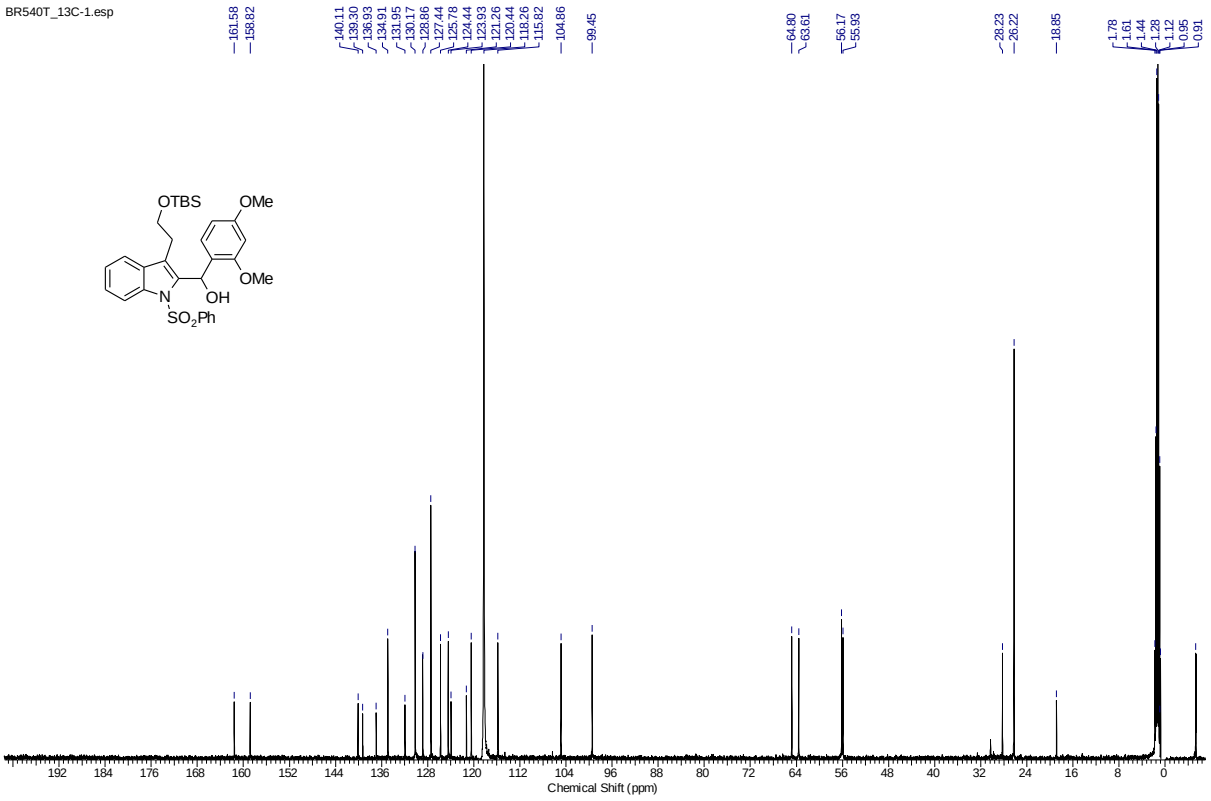
7.20
7.10
7.03
6.96
6.94
6.71
6.69
6.30
6.29
6.22
6.20
3.95
3.94
3.56
3.45
3.42
3.41
3.40
3.39
3.38
3.37
3.36
2.63
2.61
2.60
1.96
0.56
0.33
OTBS
OMe
OMe
N
OH
SO2Ph
1.00
2.03
7.53
1.00
2.13
0.96
3.08
5.20
2.01
9.08
6.00
Chemical Shift (ppm)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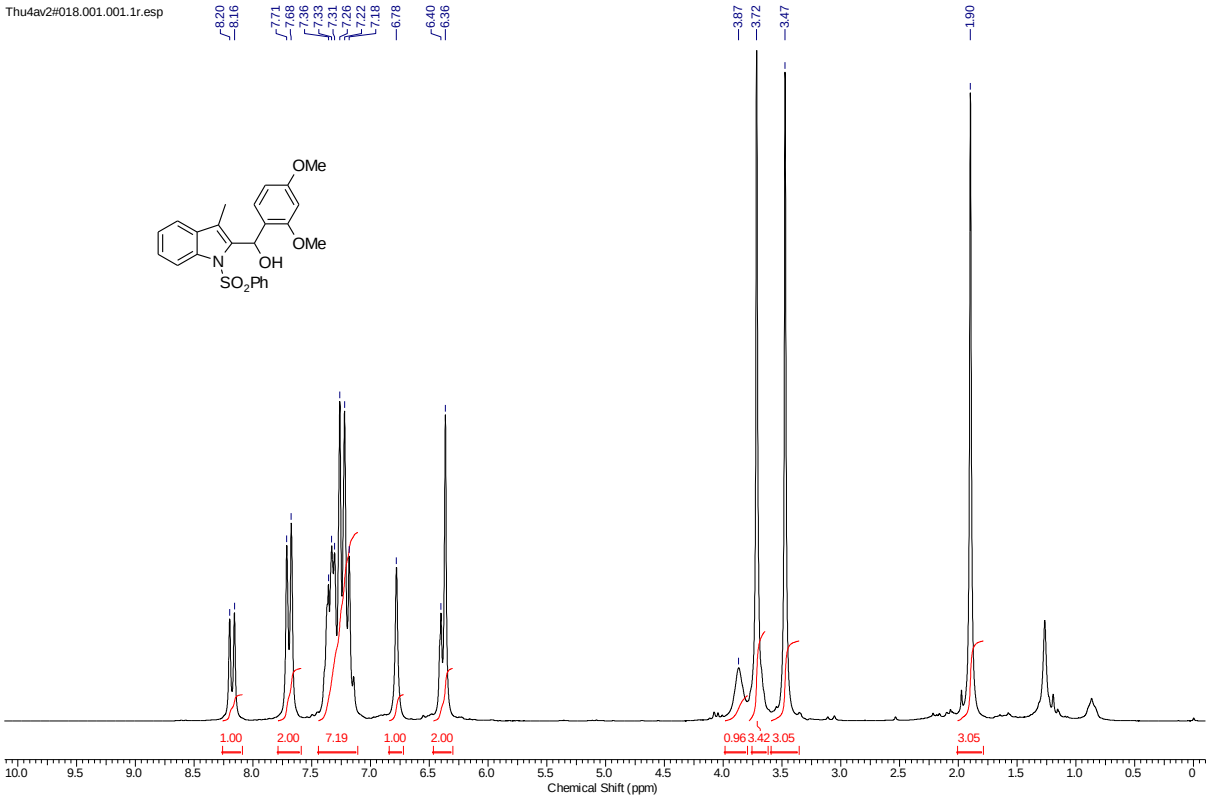
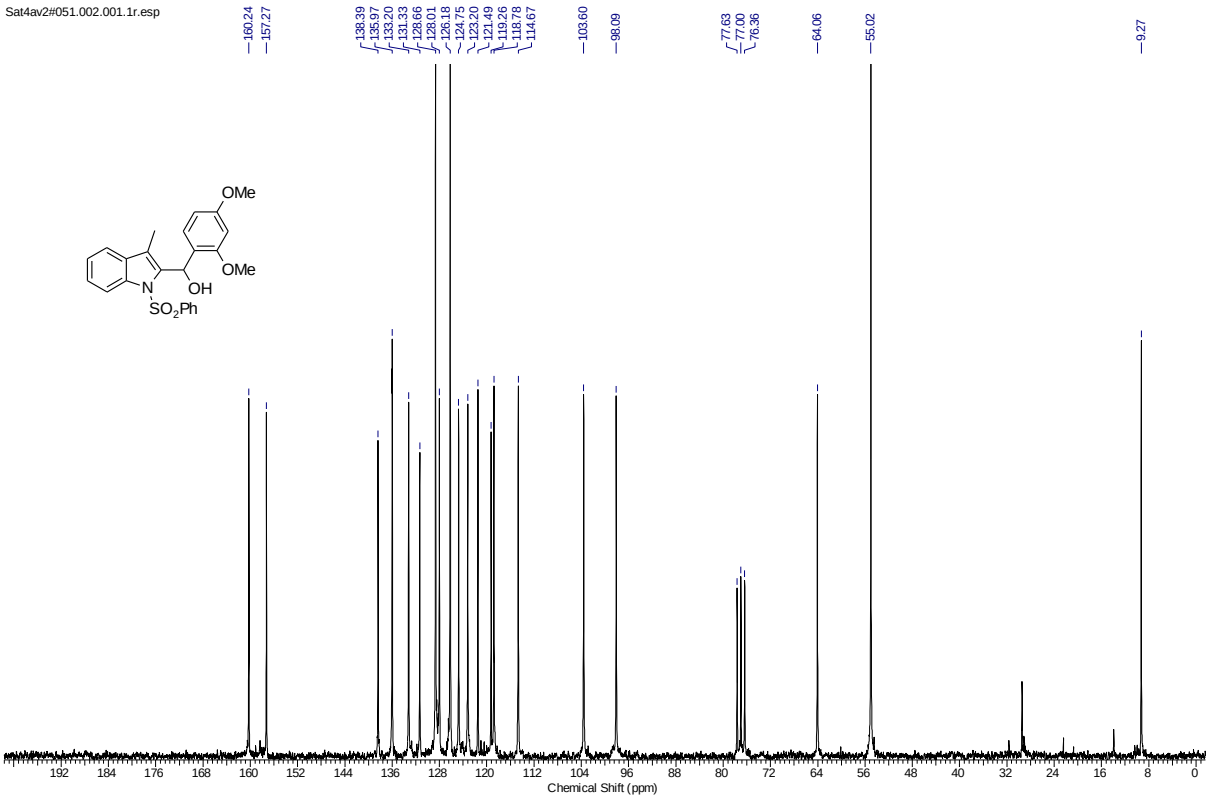
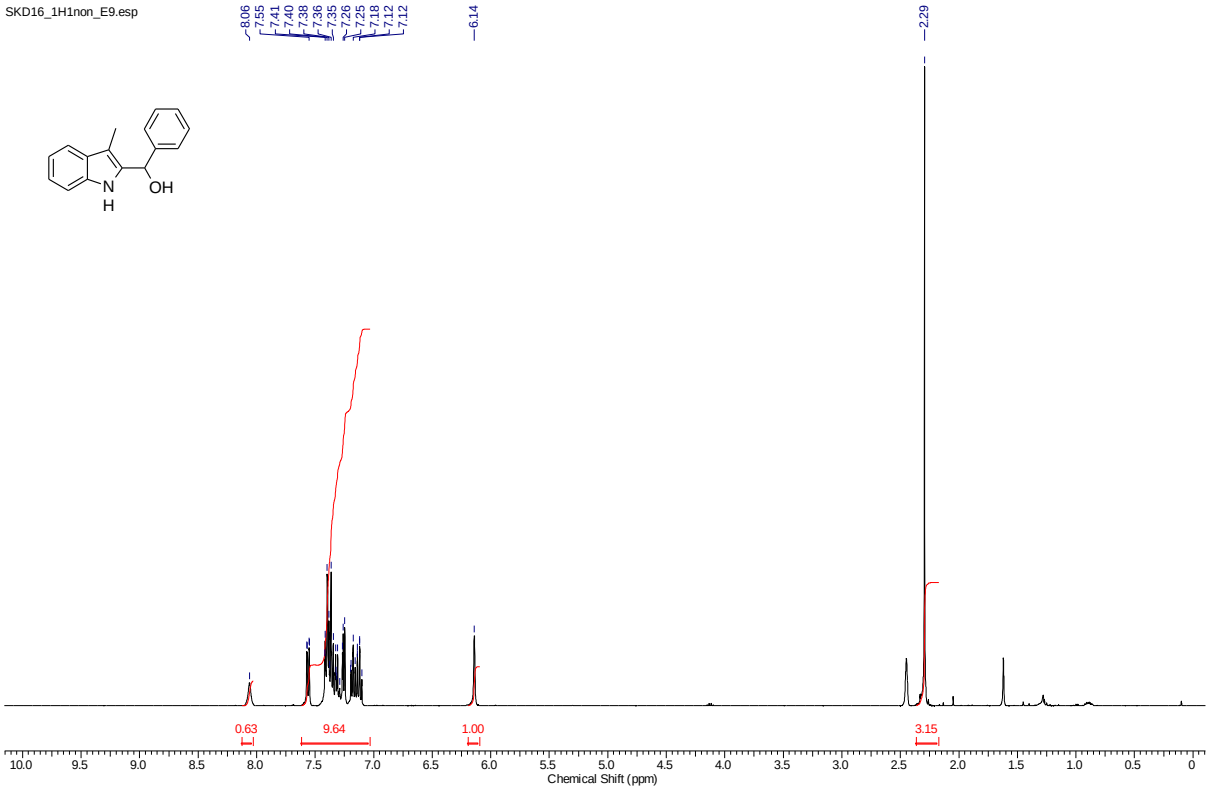
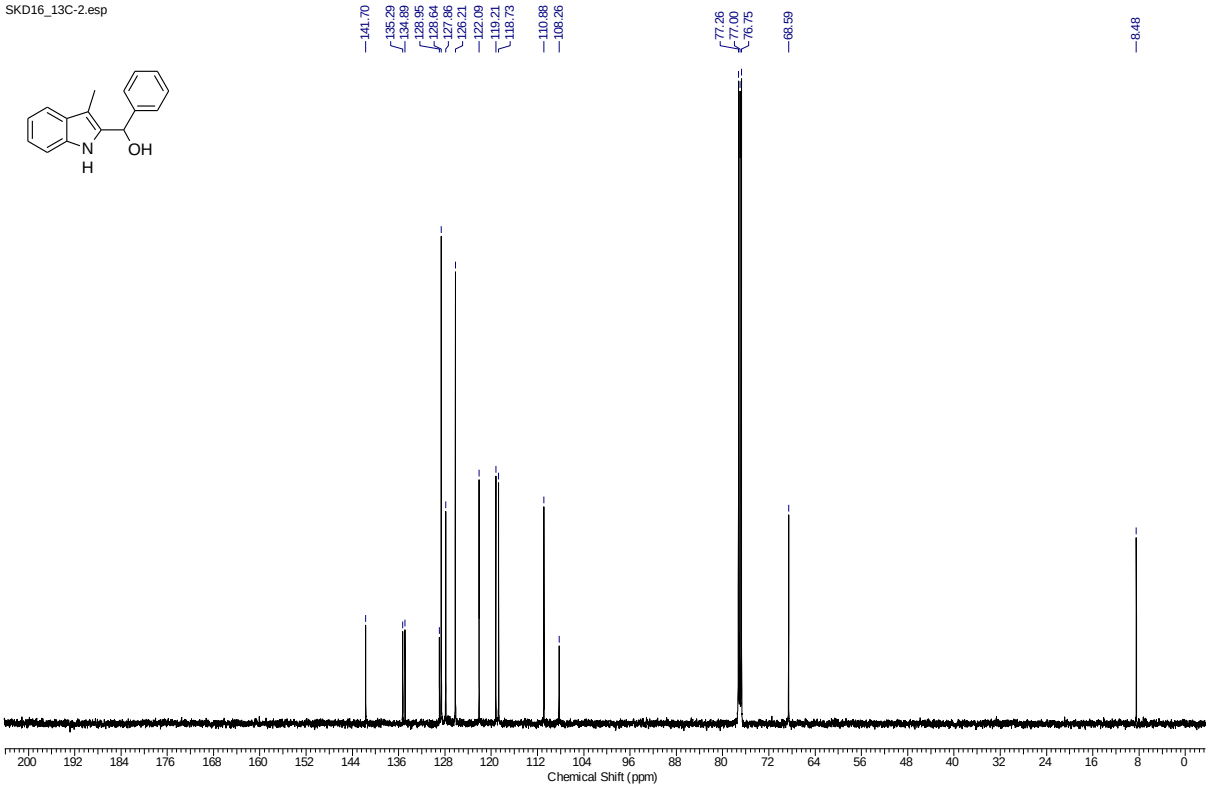
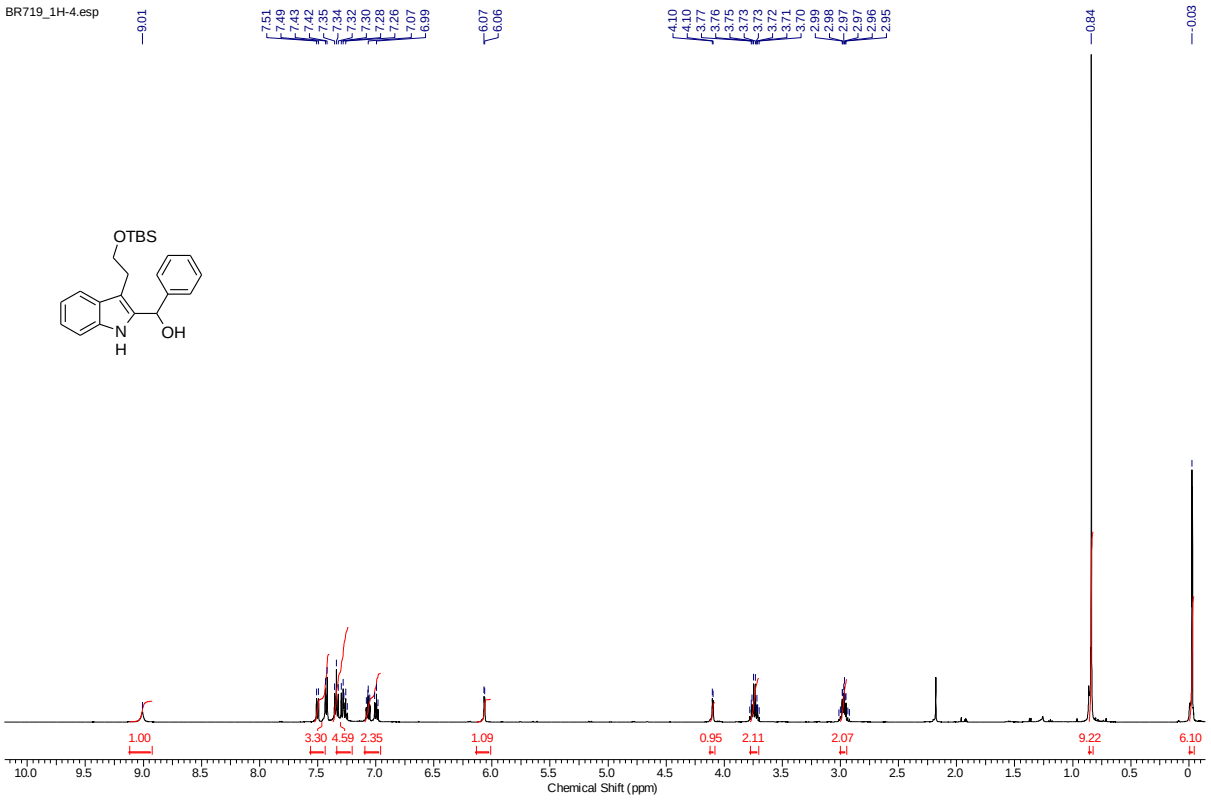
118.26
115.82
104.86
99.45
64.80
63.61
56.17
55.93
28.23
26.22
18.85
1.78
1.61
1.44
1.28
1.12
0.95
0.91
OTBS
OMe
OMe
N
OH
SO2Ph
Chemical Shift (ppm)

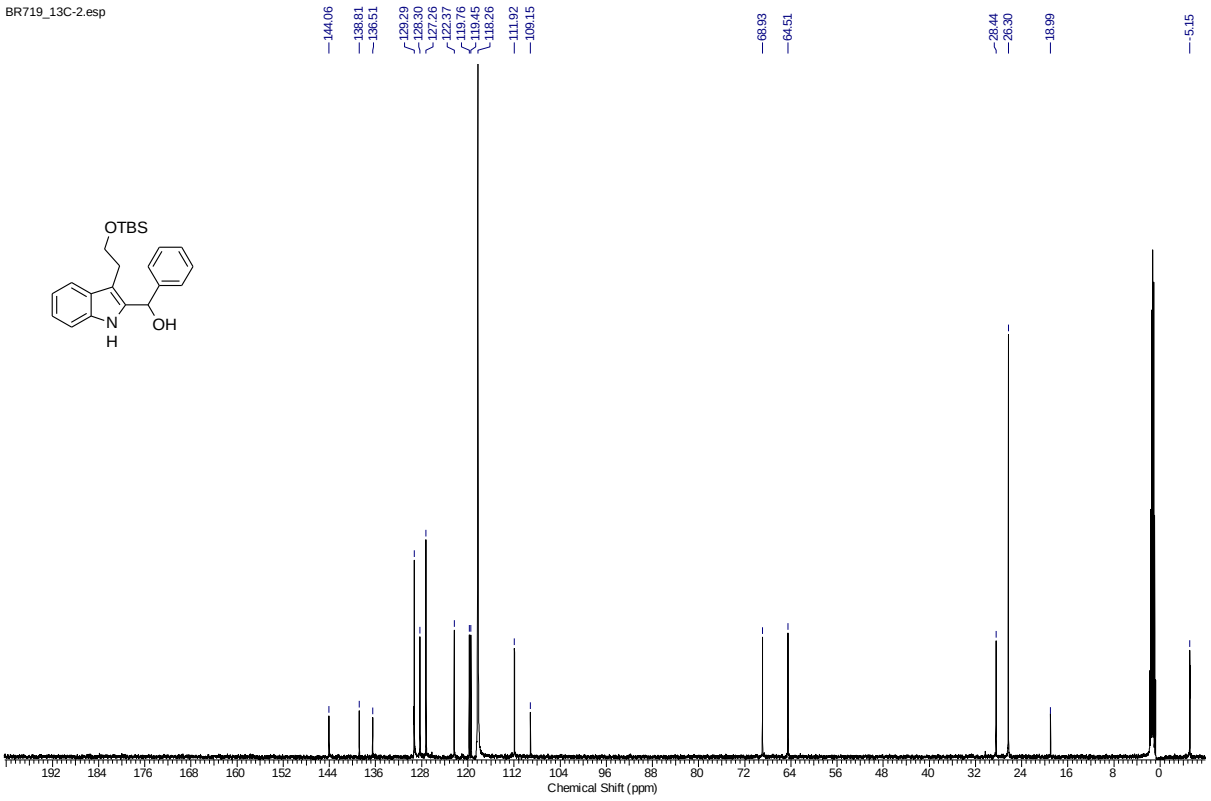

Thu4av2#018.001.001.1r.esp
8.20
8.16
7.71
7.68
7.36
7.33
7.31
7.26
7.22
7.18
6.78
6.40
6.36
3.87
3.72
3.47
1.90
OMe
OMe
OH
N
SO2Ph
1.00
2.00
7.19
1.00
2.00
0.96
3.42
3.05
3.05
Chemical Shift (ppm)

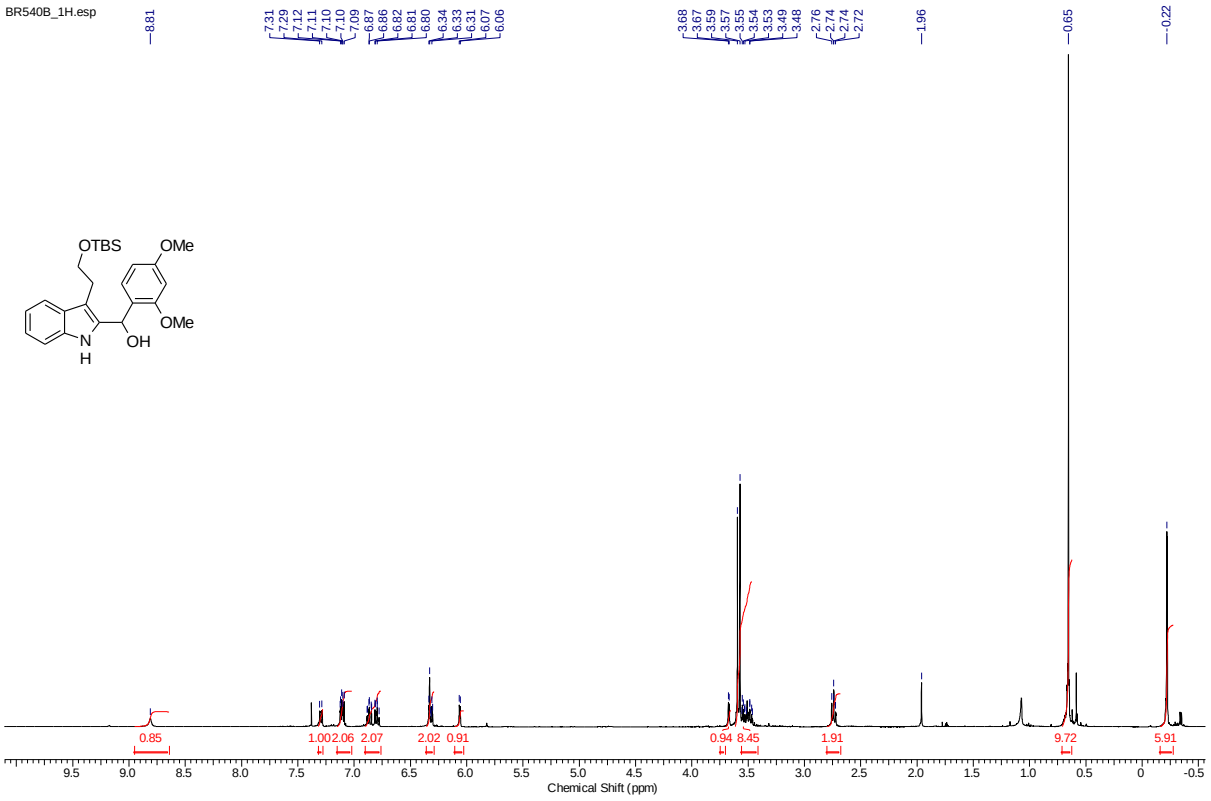

Sat4av2#051.002.001.1r.esp
160.24
157.27
138.39
135.97
133.20
131.33
128.66
128.01
126.18
124.75
123.20
121.49
119.26
118.78
114.67
103.60
98.09
77.63
77.00
76.36
64.06
55.02
9.27
OMe
OMe
OH
N
SO2Ph
Chemical Shift (ppm)

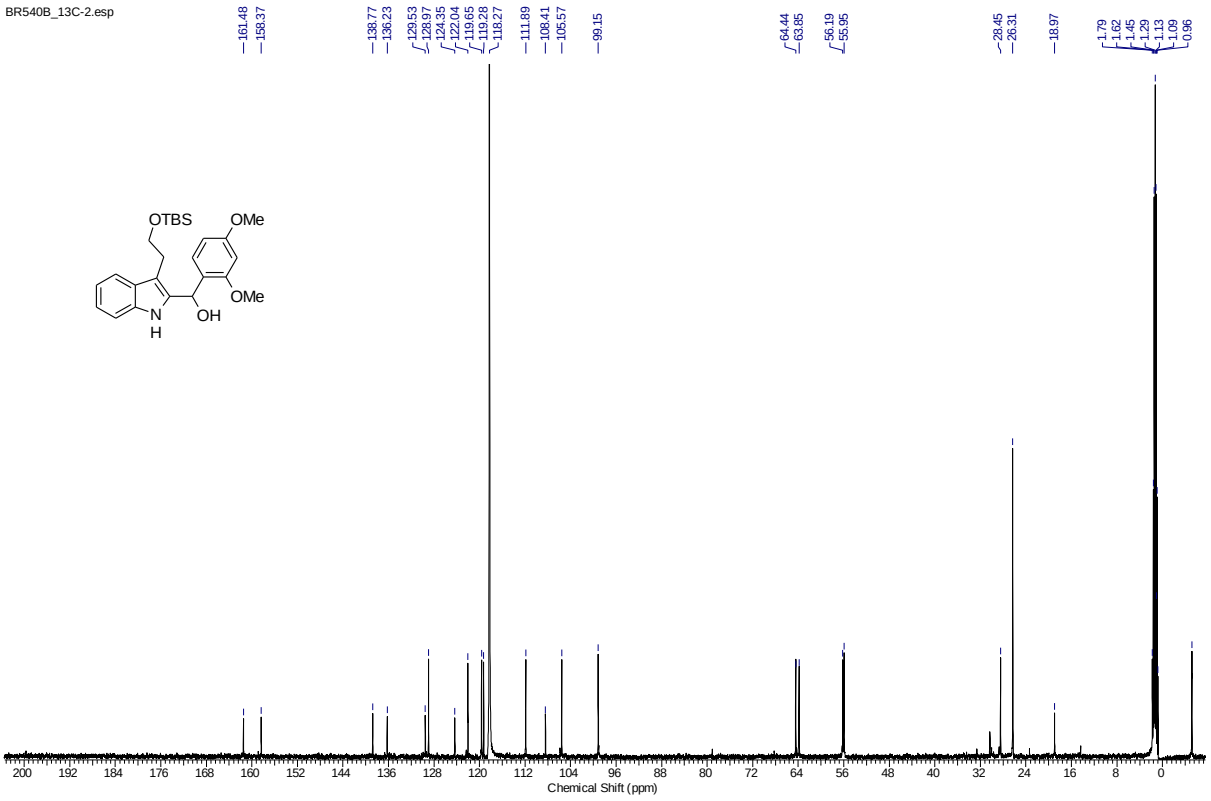

SKD16_1H1non_E9.esp
8.06
7.55
7.41
7.40
7.38
7.36
7.35
7.26
7.25
7.18
7.12
7.12
6.14
2.29
N
H
OH
0.63
9.64
1.00
3.15
Chemical Shift (ppm)

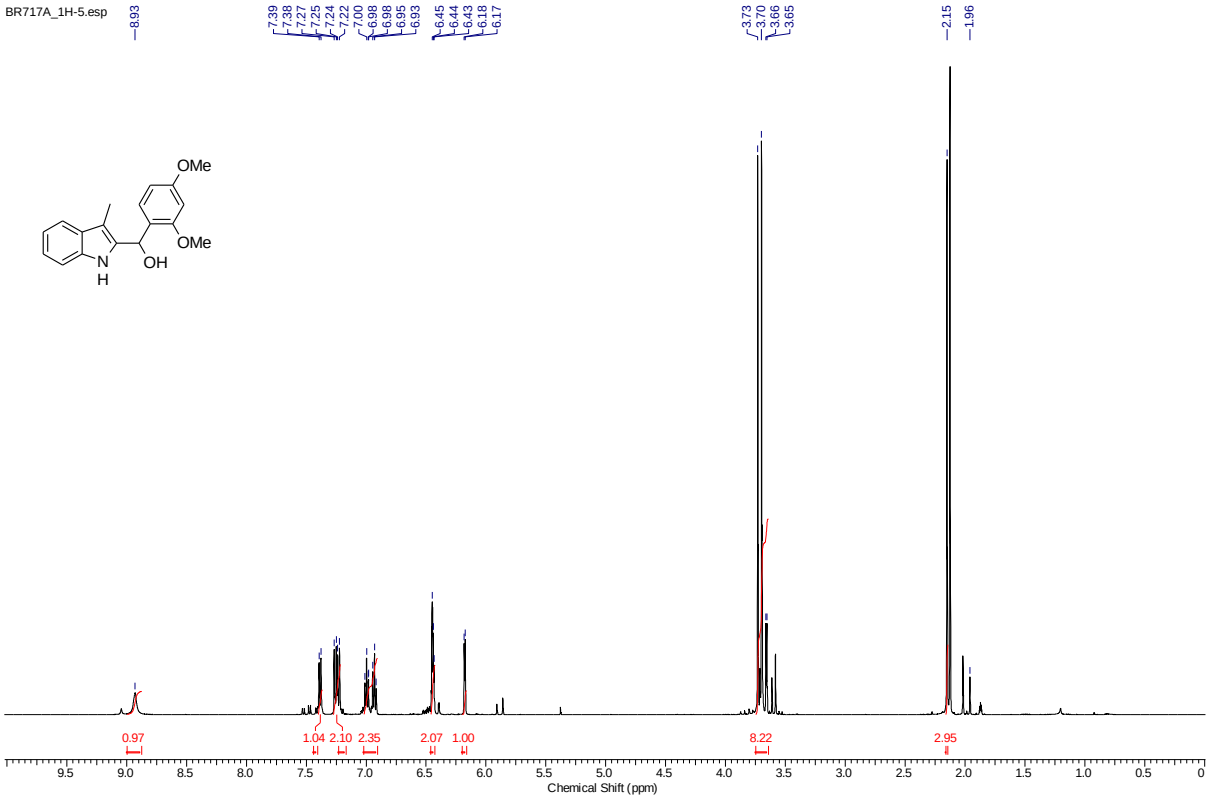

SKD16_13C-2.esp
141.70
135.29
134.89
128.95
128.64
127.86
126.21
122.09
119.21
118.73
110.88
108.26
77.26
77.00
76.75
68.59
8.48
N
H
OH
Chemical Shift (ppm)

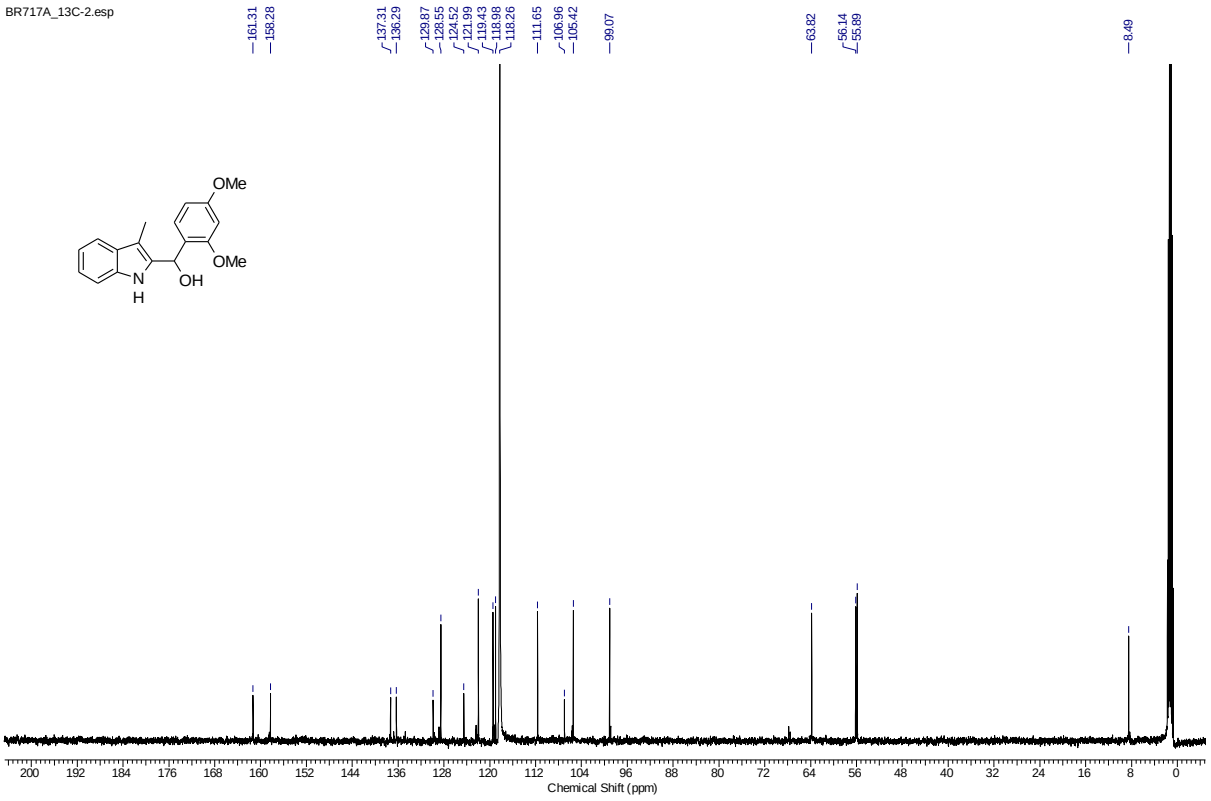

BR719_1H-4.esp
9.01
7.51
7.49
7.43
7.42
7.35
7.34
7.32
7.30
7.28
7.26
7.07
6.99
6.07
6.06
4.10
4.10
3.77
3.76
3.75
3.73
3.73
3.72
3.71
3.70
2.99
2.98
2.97
2.97
2.96
2.95
0.84
-0.03
OTBS
N
H
OH
1.00
3.30
4.59
2.35
1.09
0.95
2.11
2.07
9.22
6.10
Chemical Shift (ppm)

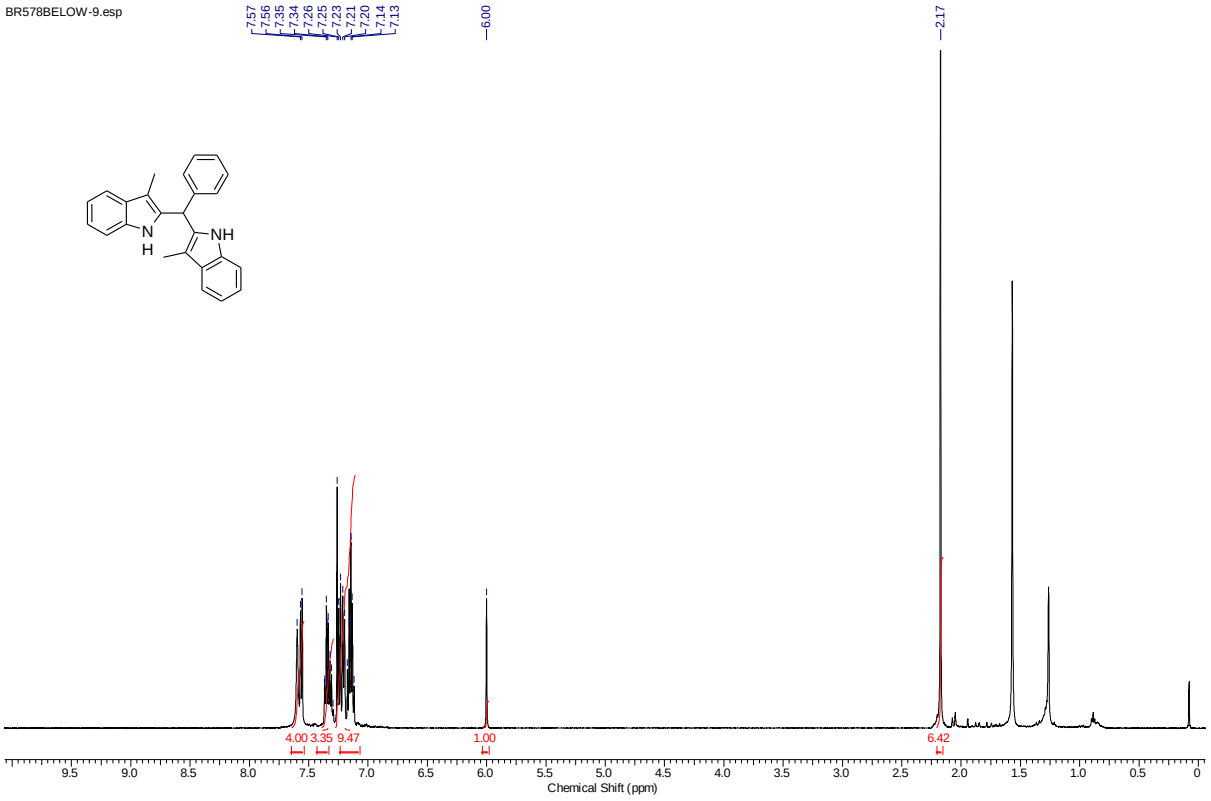

BR719_13C-2.esp
144.06
138.81
136.51
129.29
128.30
127.26
122.37
119.76
119.45
118.26
111.92
109.15
68.93
64.51
28.44
26.30
18.99
-5.15
OTBS
N
H
OH
Chemical Shift (ppm)

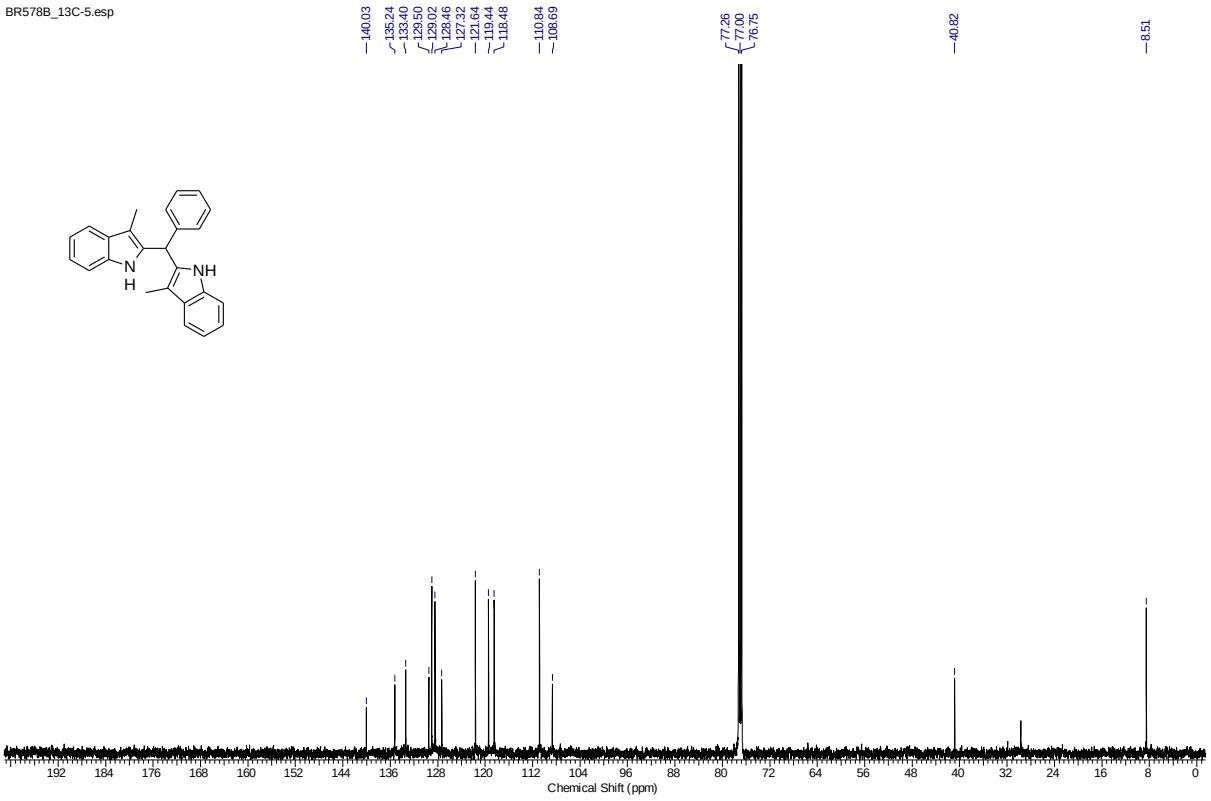

BR540B_1H.esp
OTBS
OMe
OMe
N
H
OH
Chemical Shift (ppm)

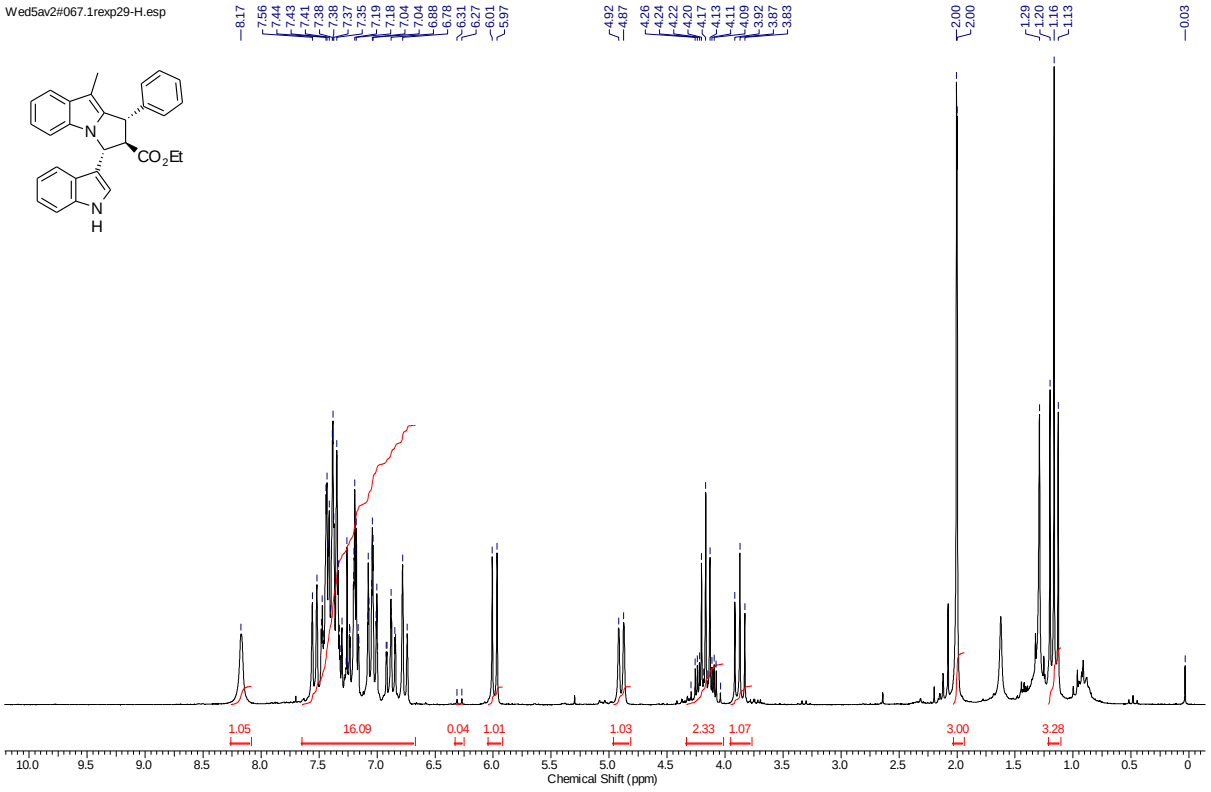

BR540B_13C-2.esp
OTBS
OMe
OMe
N
H
OH
Chemical Shift (ppm)

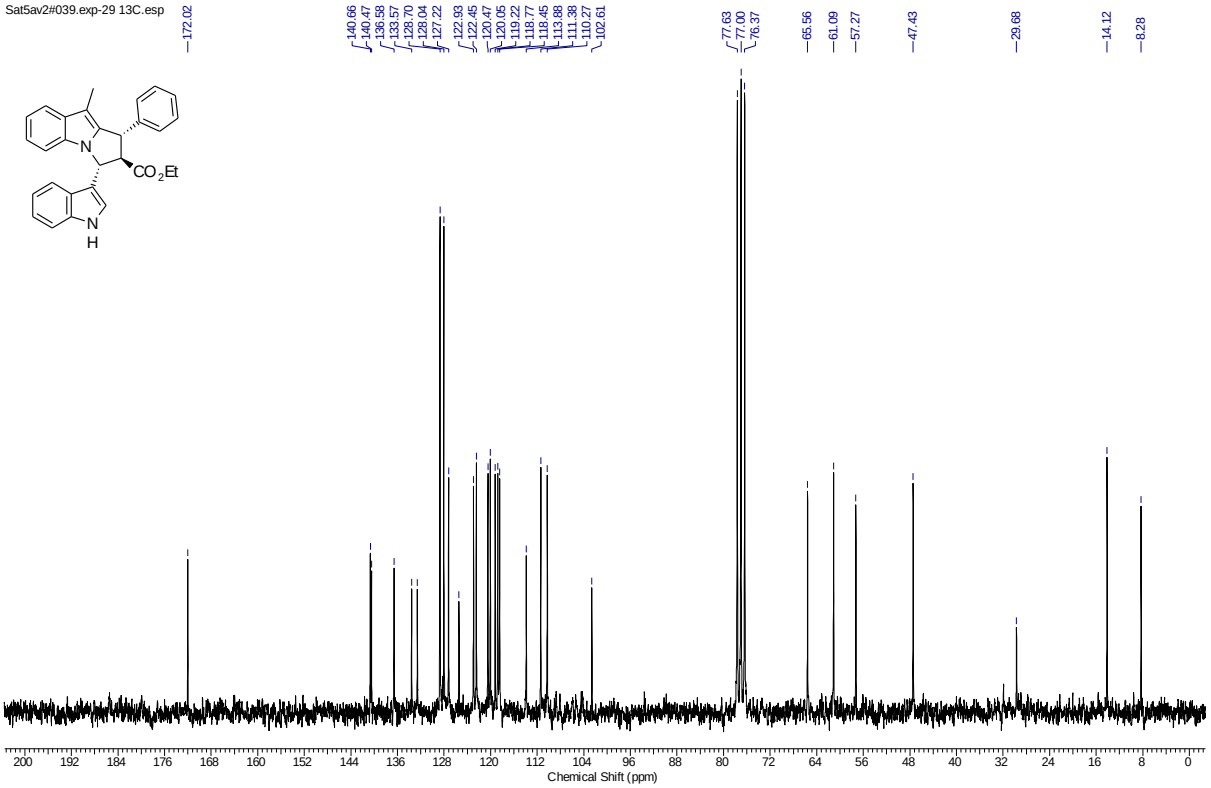


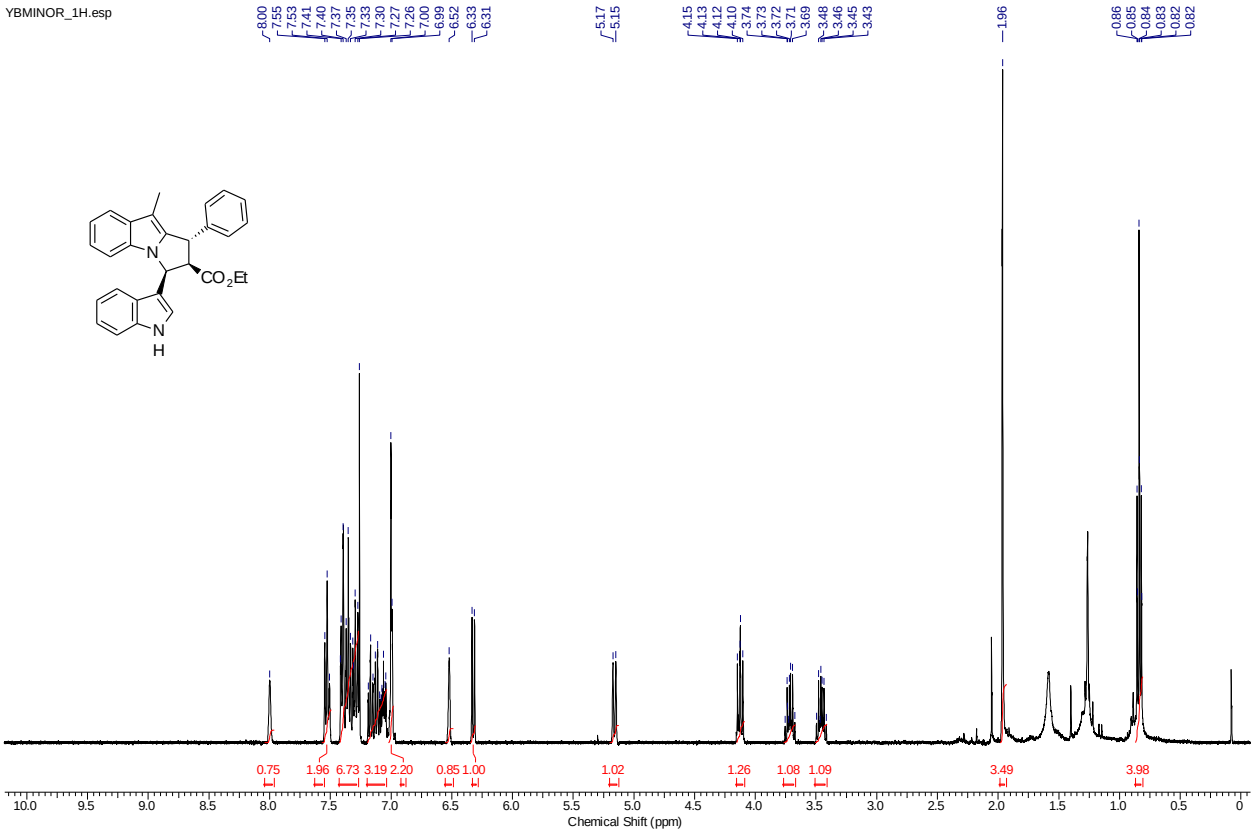


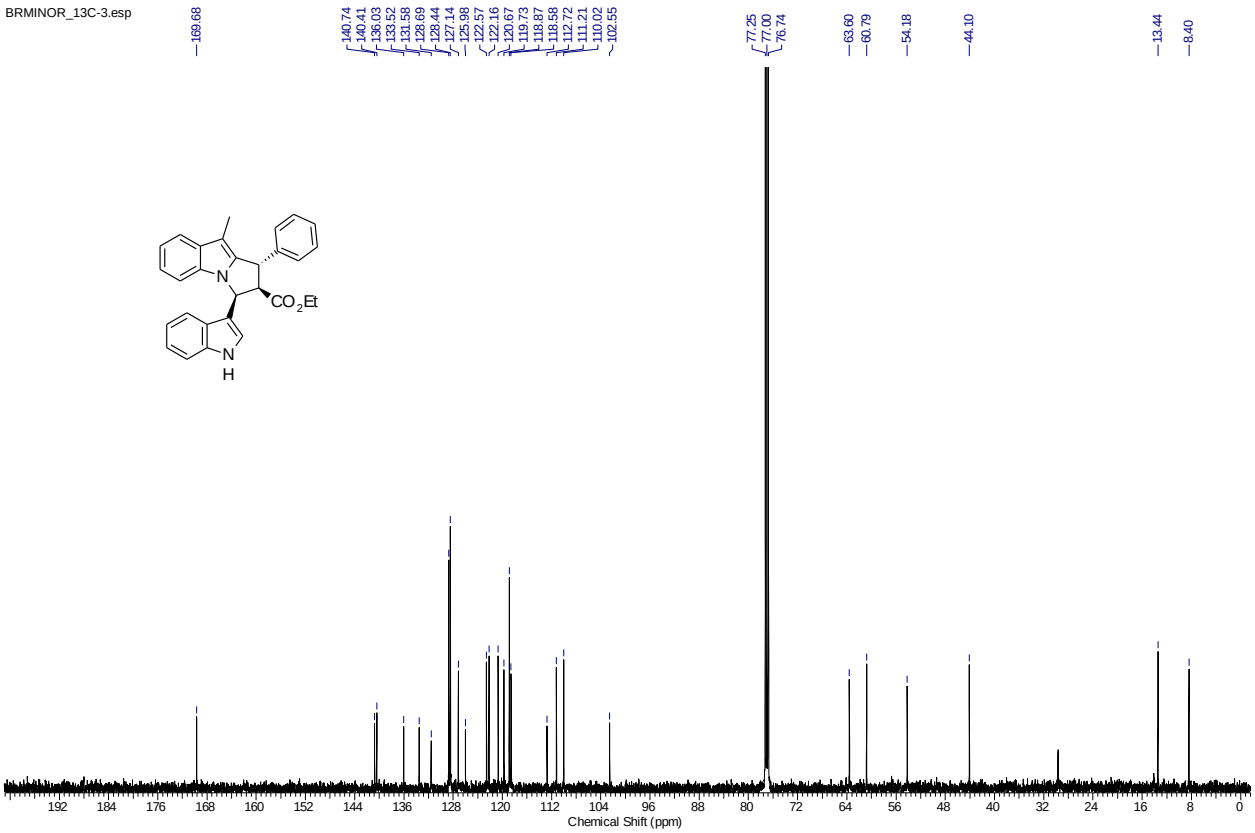

BR578BELOW-9.esp
7.57
7.56
7.35
7.34
7.26
7.25
7.23
7.21
7.20
7.14
7.13
6.00
2.17
N
H
NH
4.00
3.35
9.47
1.00
6.42
Chemical Shift (ppm)

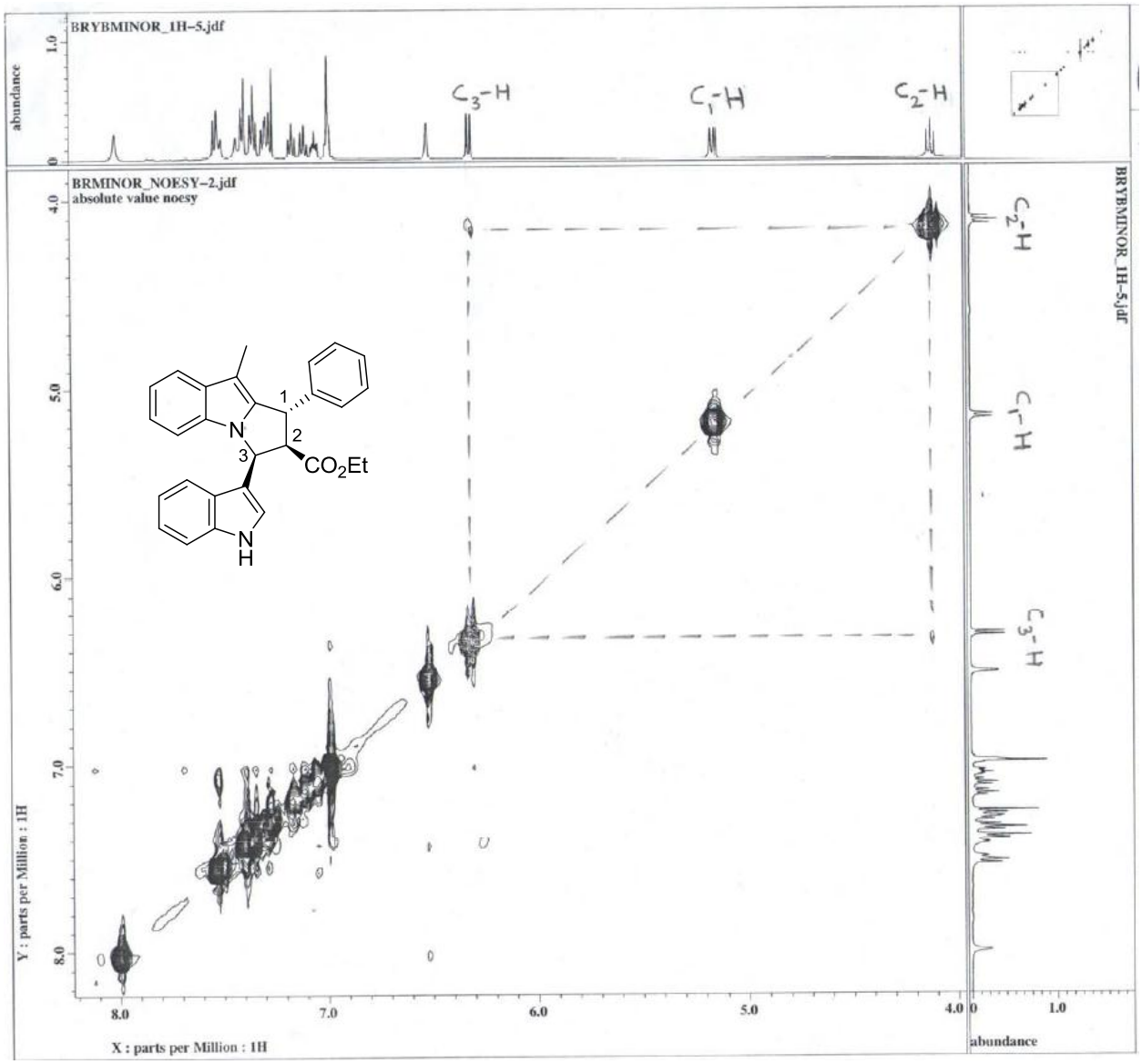

BR578B_13C-5.esp
140.03
135.24
133.40
129.50
129.02
128.46
127.32
121.64
119.44
118.48
110.84
106.69
77.26
77.00
76.75
40.82
8.51
N
H
NH
Chemical Shift (ppm)


Wed5av2#067.1rexp29-H.esp
8.17
7.56
7.44
7.43
7.41
7.38
7.38
7.37
7.35
7.19
7.18
7.04
7.04
6.88
6.78
6.31
6.27
6.01
5.97
4.92
4.87
4.26
4.24
4.22
4.20
4.17
4.13
4.11
4.09
3.92
3.87
3.83
2.00
2.00
1.29
1.20
1.16
1.13
0.03
CO2Et
N
H
1.05
16.09
0.04
1.01
1.03
2.33
1.07
3.00
3.28
Chemical Shift (ppm)

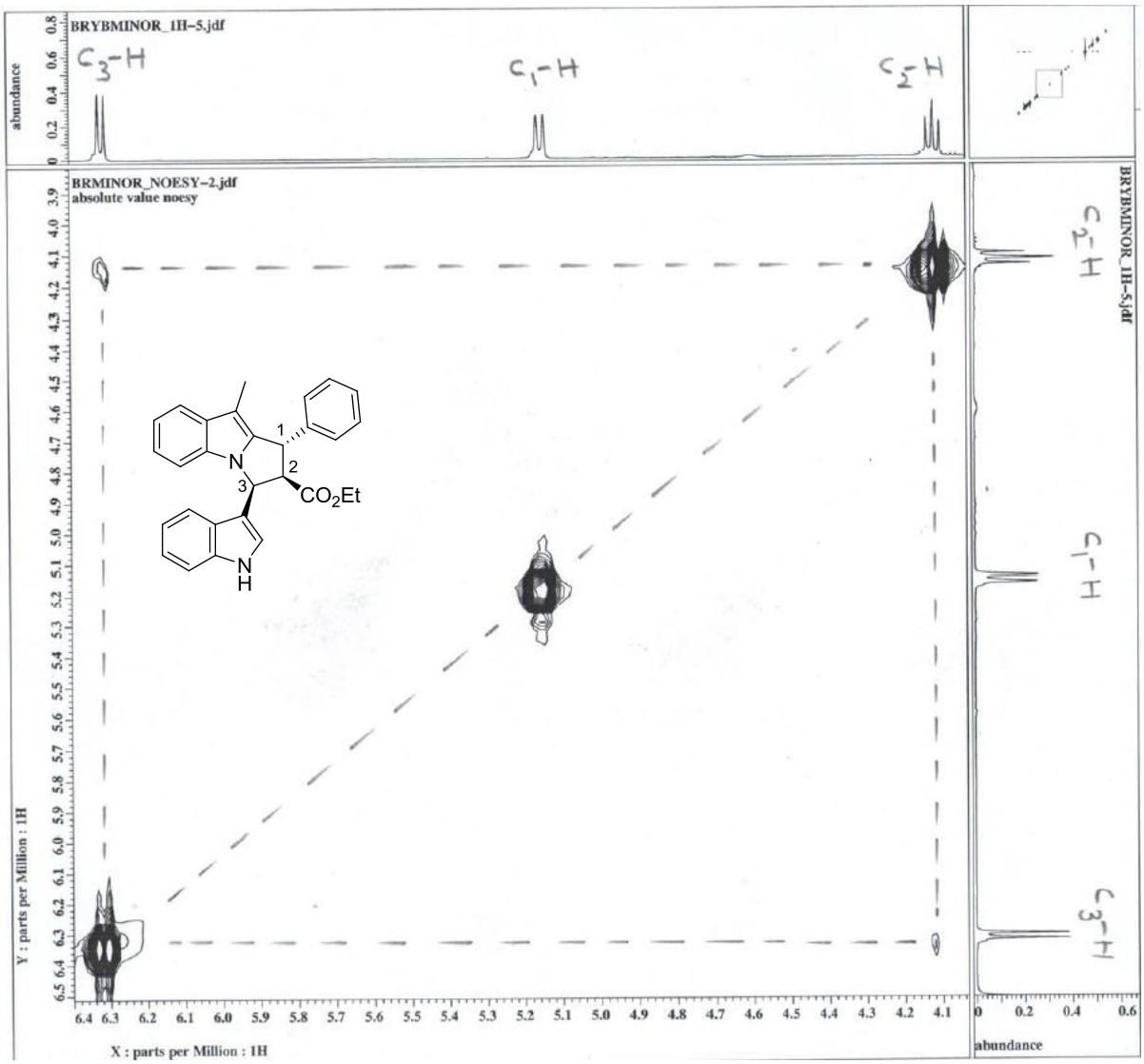

Sat5av2#039.exp-29 13C.esp
172.02
140.66
140.47
136.58
133.57
128.70
128.04
127.22
122.93
122.45
120.47
120.05
119.22
118.77
118.45
113.88
111.38
110.27
102.61
77.63
77.00
76.37
65.56
61.09
57.27
47.43
29.68
14.12
8.28
CO2Et
N
H
Chemical Shift (ppm)


YBMINOR_1H.esp
8.00
7.55
7.53
7.41
7.40
7.37
7.35
7.33
7.30
7.27
7.26
7.00
6.99
6.52
6.33
6.31
5.17
5.15
4.15
4.13
4.12
4.10
3.74
3.73
3.72
3.71
3.69
3.48
3.46
3.45
3.43
1.96
0.86
0.85
0.84
0.83
0.82
0.82
CO2Et
N
H
0.75
1.96
6.73
3.19
2.20
0.85
1.00
1.02
1.26
1.08
1.09
3.49
3.98
Chemical Shift (ppm)

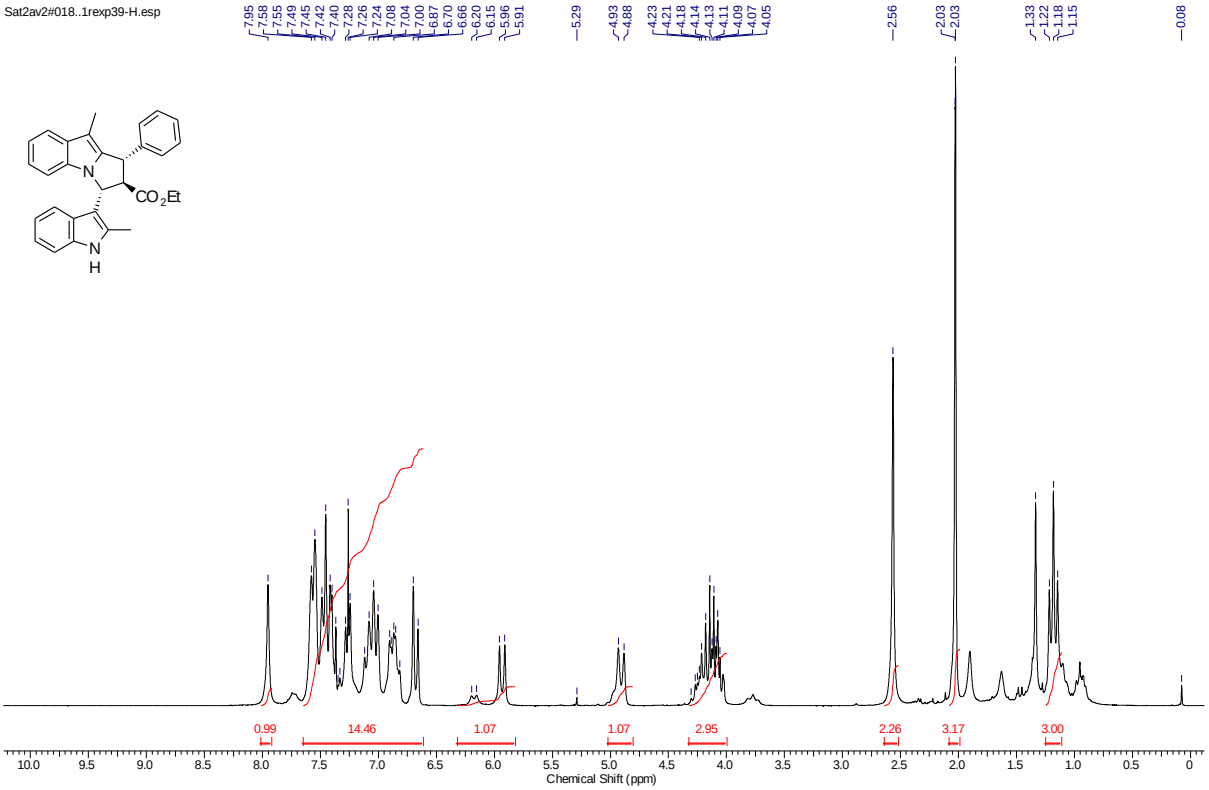

BRMINOR_13C-3.esp
169.68
140.74
140.41
136.03
133.52
131.58
128.69
128.44
127.14
125.98
122.57
122.16
120.67
119.73
118.87
118.58
112.72
111.21
110.02
102.55
77.25
77.00
76.74
63.60
60.79
54.18
44.10
13.44
8.40
CO2Et
N
H
Chemical Shift (ppm)

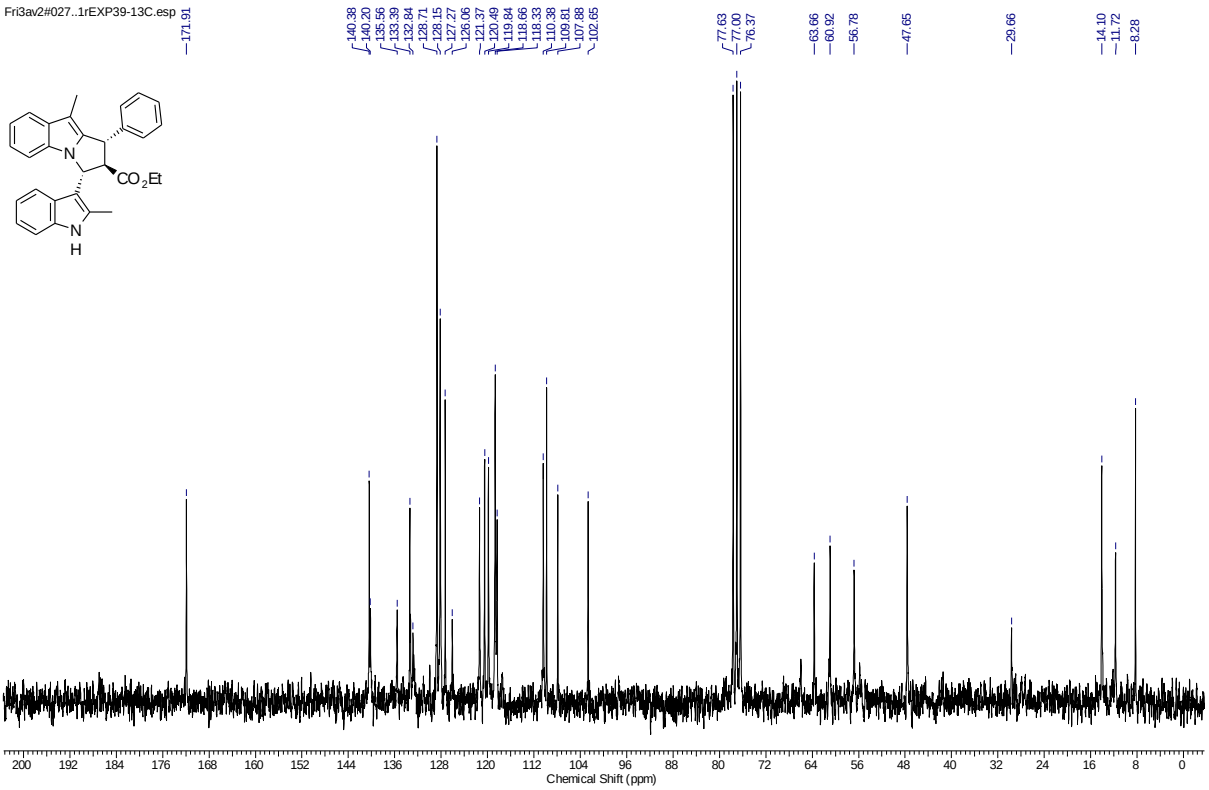


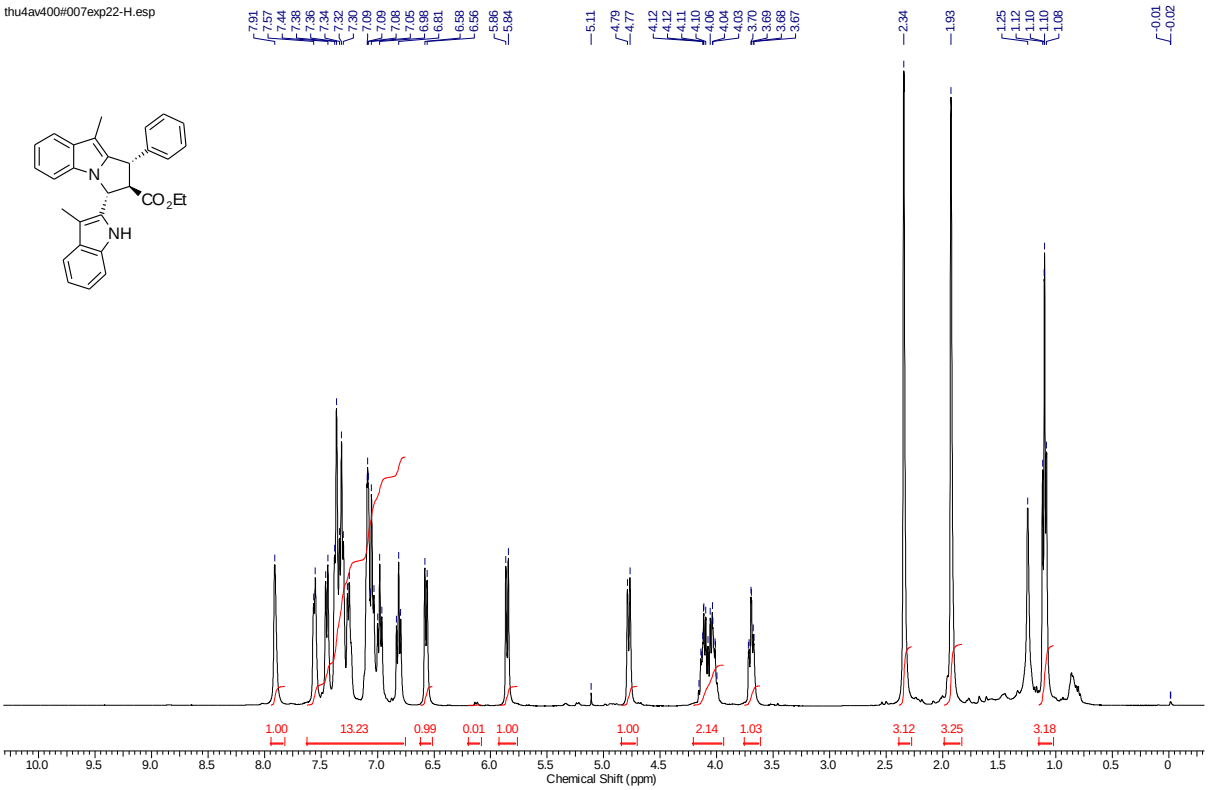
Compound 14a' NOESY

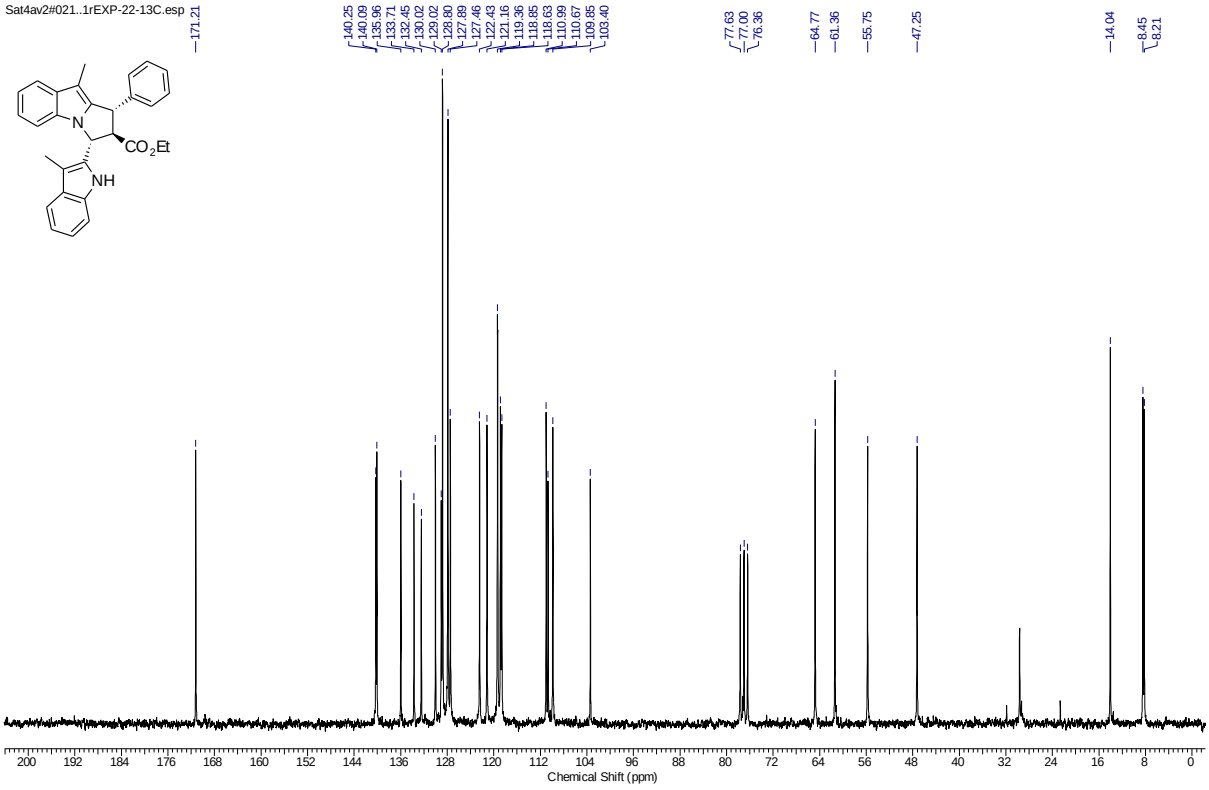


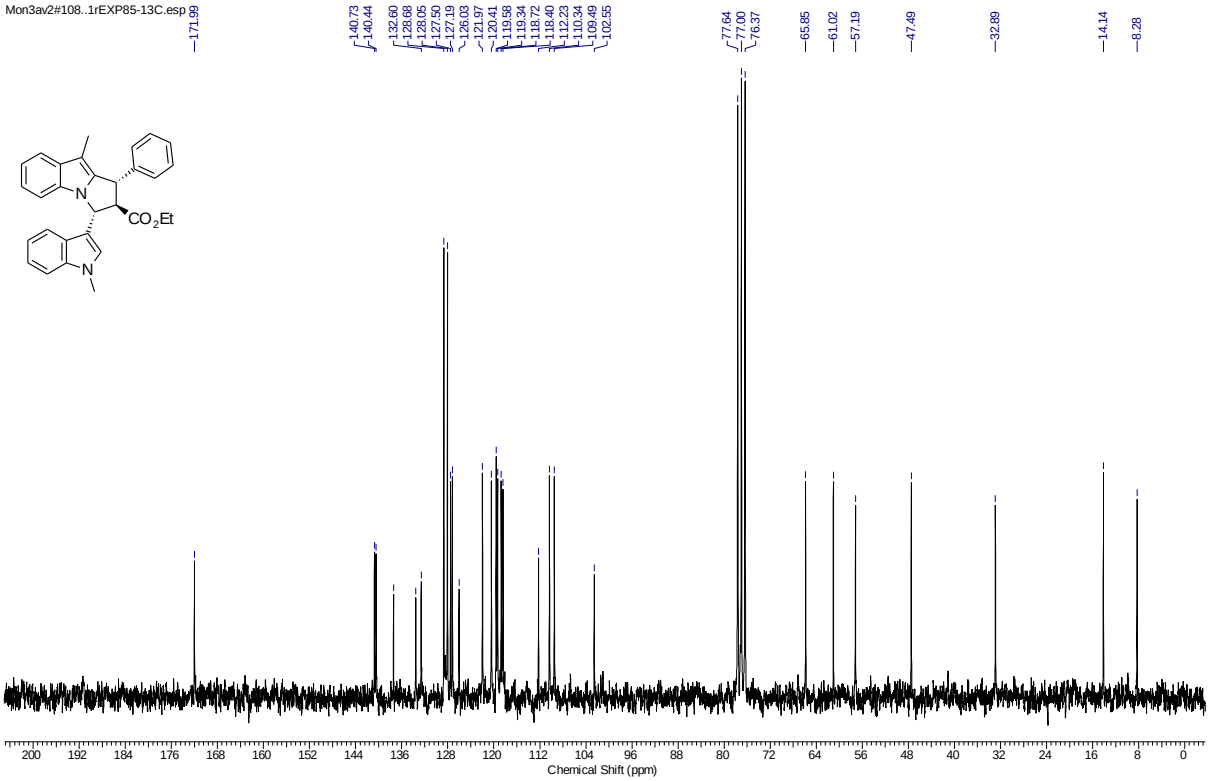
Compound 14a' NOESY

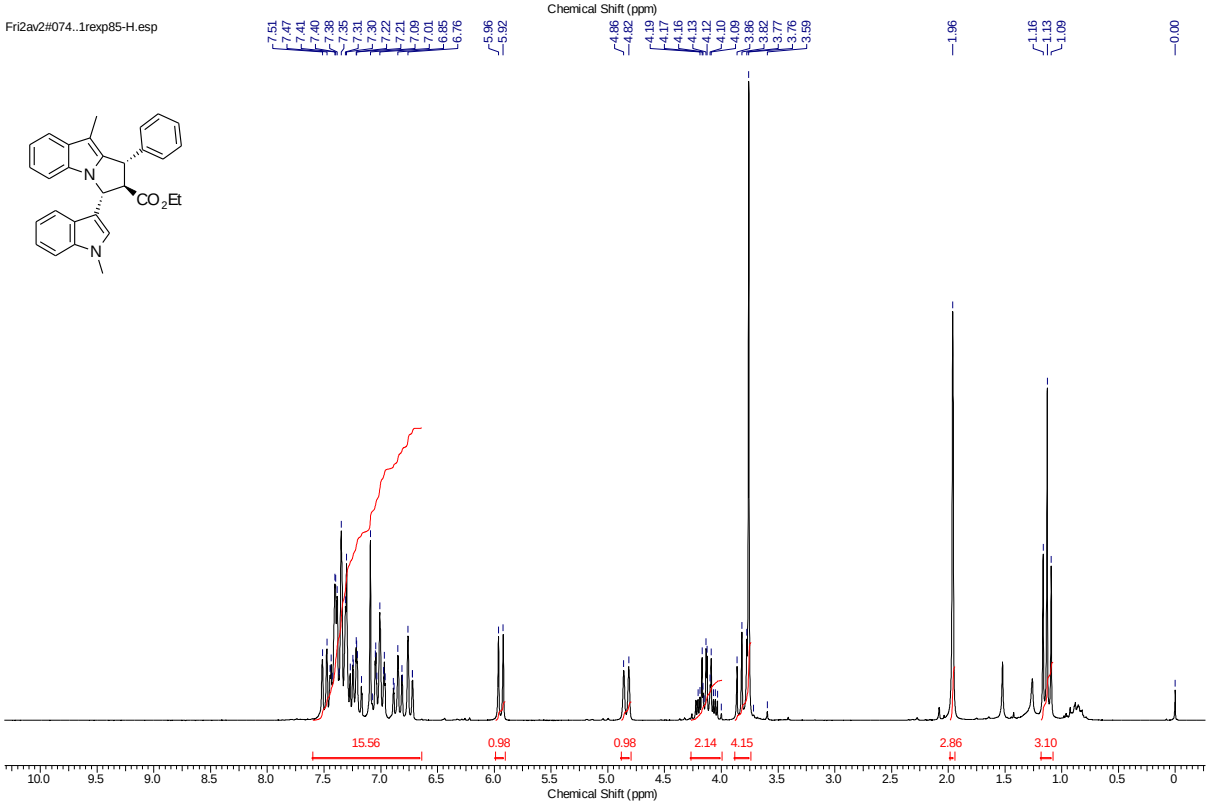

Sat2av2#018..1rexp39-H.esp
7.95
7.58
7.55
7.49
7.45
7.42
7.40
7.28
7.26
7.24
7.08
7.04
7.00
6.87
6.70
6.66
6.20
6.15
5.96
5.91
5.29
4.93
4.88
4.23
4.21
4.18
4.14
4.13
4.11
4.09
4.07
4.05
2.56
2.03
2.03
1.33
1.22
1.18
1.15
0.08
CO2Et
N
H
0.99
14.46
1.07
1.07
2.95
2.26
3.17
3.00
Chemical Shift (ppm)

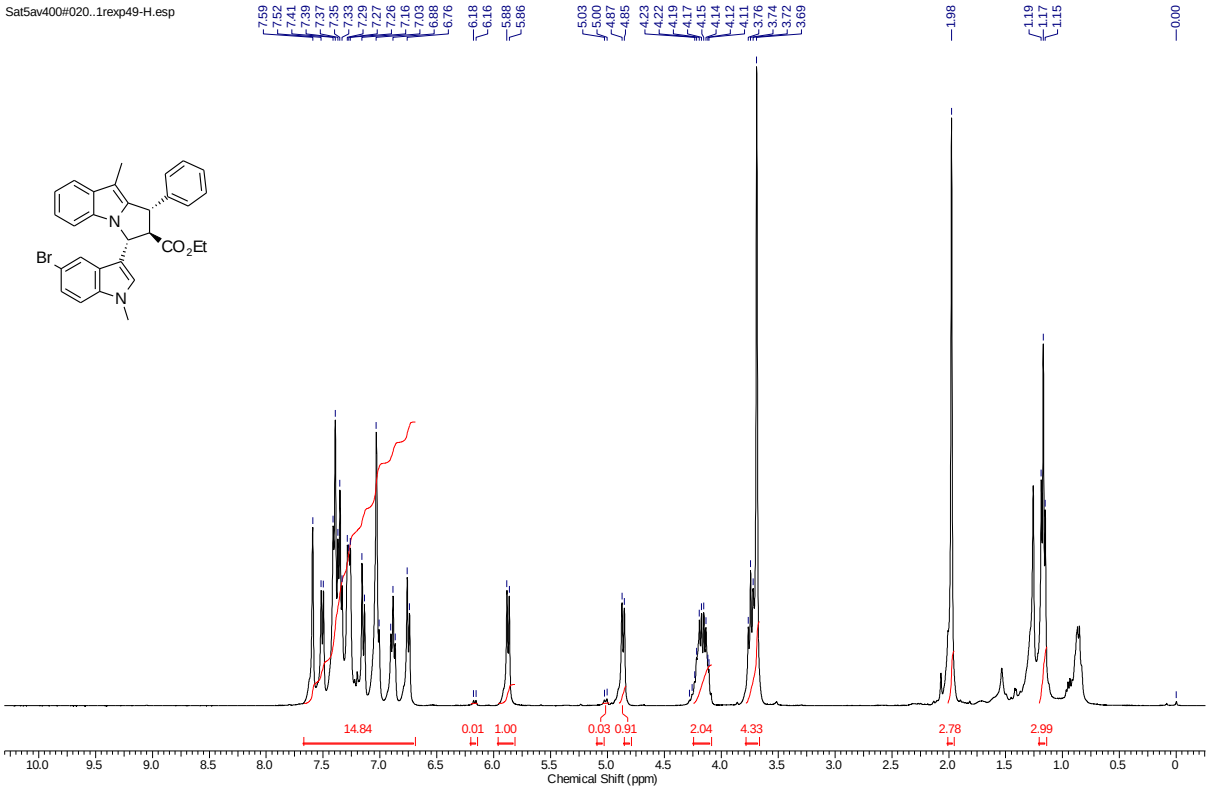

Fri3av2#027..1rEXP39-13C.esp
171.91
140.38
140.20
135.56
133.39
132.84
128.71
128.15
127.27
126.06
121.37
120.49
119.84
118.66
118.33
110.38
109.81
107.88
102.65
77.63
77.00
76.37
63.66
60.92
56.78
47.65
29.66
14.10
11.72
8.28
CO2Et
N
H
Chemical Shift (ppm)

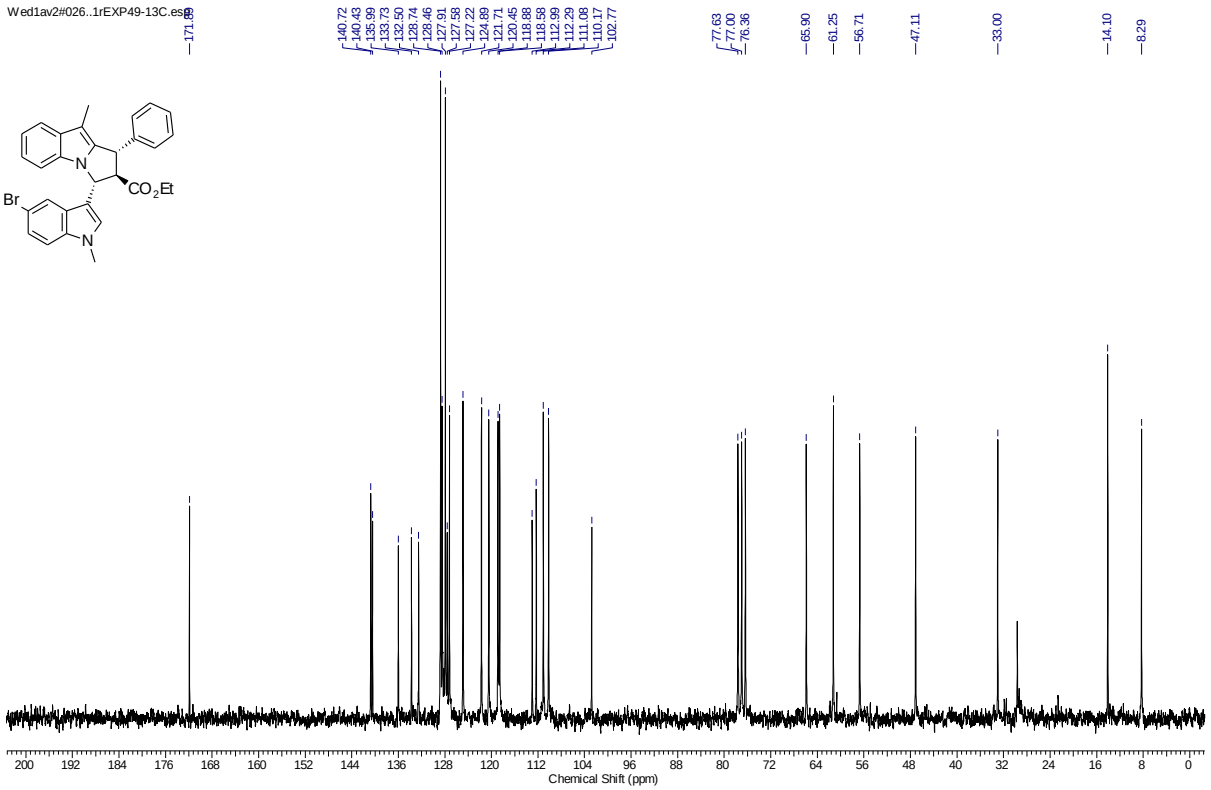

thu4av400#007exp22-H.esp
7.91
7.57
7.44
7.38
7.36
7.34
7.32
7.30
7.09
7.09
7.08
7.05
6.98
6.81
6.58
6.56
5.86
5.84
5.11
4.79
4.77
4.12
4.12
4.11
4.10
4.06
4.04
4.03
3.70
3.69
3.68
3.67
2.34
1.93
1.25
1.12
1.10
1.10
1.08
-0.01
-0.02
CO2Et
NH
1.00
13.23
0.99
0.01
1.00
1.00
2.14
1.03
3.12
3.25
3.18
Chemical Shift (ppm)

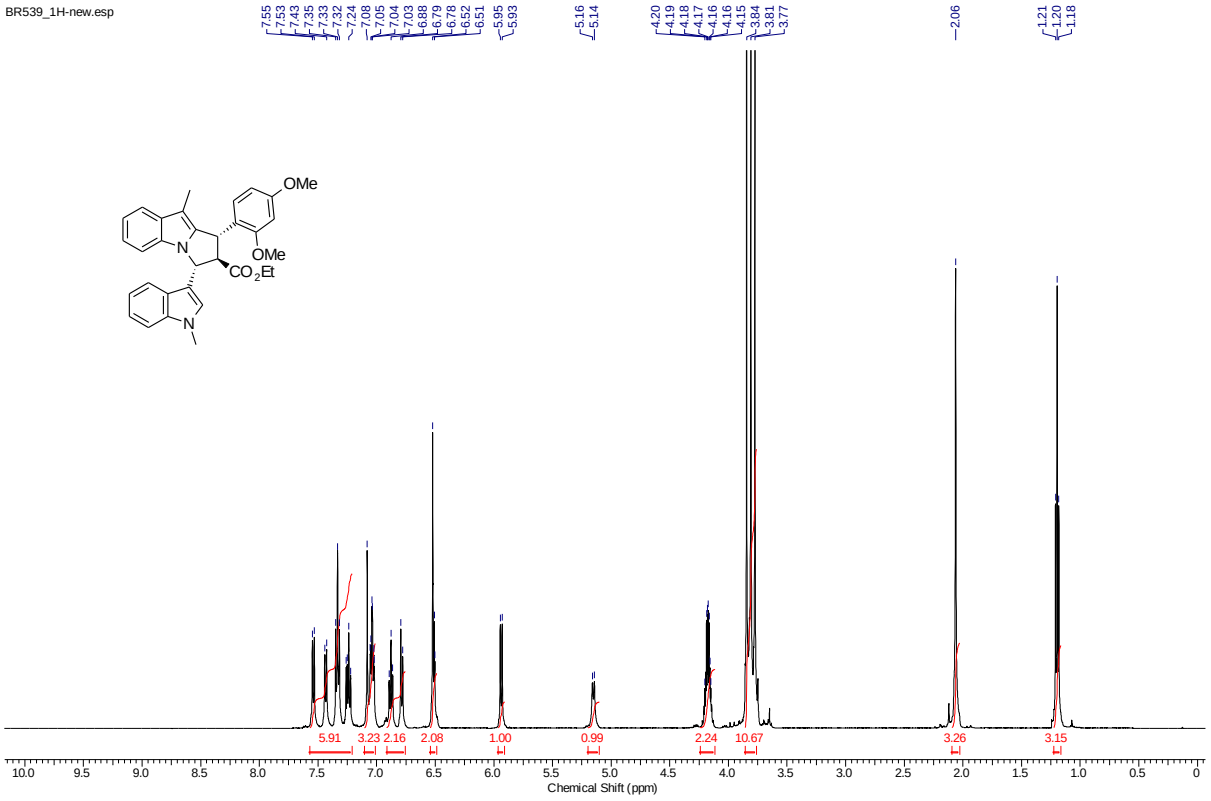

Sat4av2#021..1rEXP-22-13C.esp
171.21
140.25
140.09
135.96
133.71
132.45
130.02
129.02
128.80
127.89
127.46
122.43
121.16
119.36
118.85
118.63
110.99
110.67
109.85
103.40
77.63
77.00
76.36
64.77
61.36
55.75
47.25
14.04
8.45
8.21
CO2Et
NH
Chemical Shift (ppm)

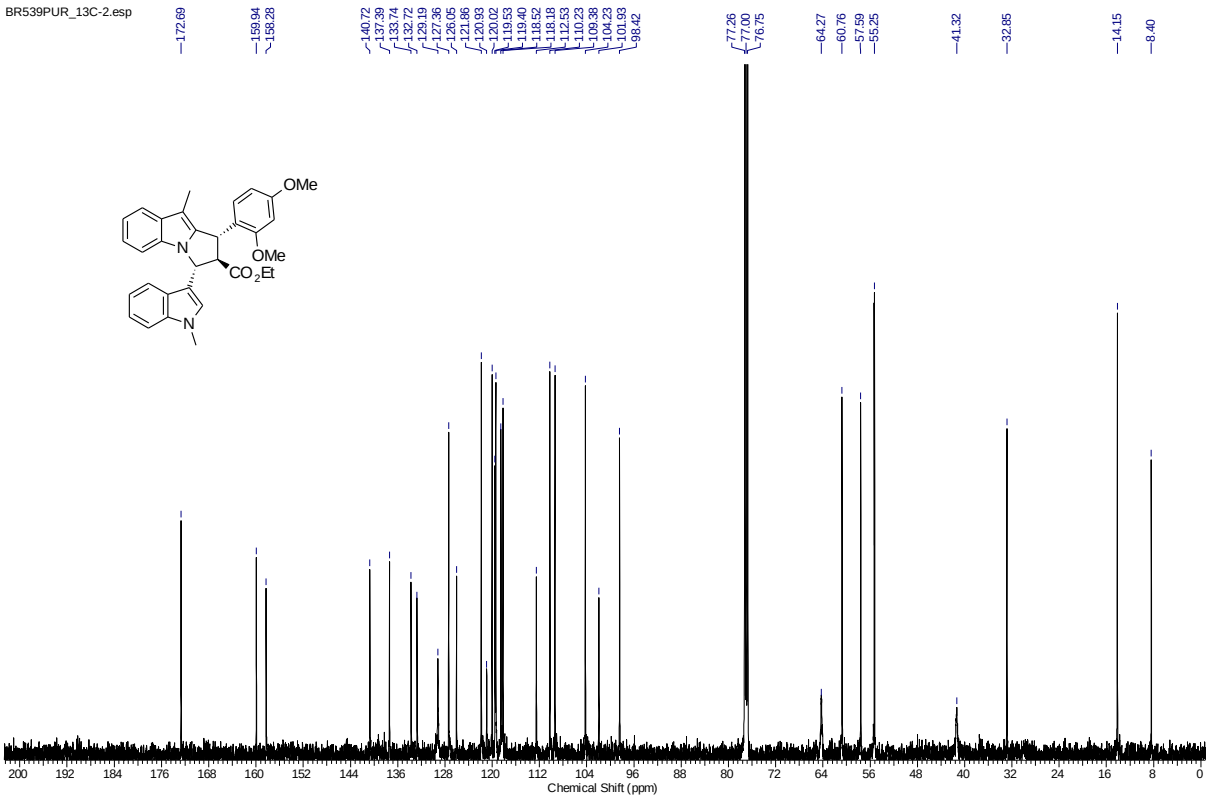

Mon3av2#108..1rEXP85-13C.esp
171.99
140.73
140.44
132.60
128.68
128.05
127.50
127.19
126.03
121.97
120.41
119.58
119.34
118.72
118.40
112.23
110.34
109.49
102.55
77.64
77.00
76.37
65.85
61.02
57.19
47.49
32.89
14.14
8.28
CO2Et
Chemical Shift (ppm)


Fri2av2#074..1rexp85-H.esp
7.51
7.47
7.41
7.40
7.38
7.35
7.31
7.30
7.22
7.21
7.09
7.01
6.85
6.76
5.96
5.92
4.86
4.82
4.19
4.17
4.16
4.13
4.12
4.10
4.09
3.86
3.82
3.77
3.76
3.59
1.96
1.16
1.13
1.09
0.00
CO2Et
15.56
0.98
0.98
2.14
4.15
2.86
3.10
Chemical Shift (ppm)


Sat5av400#020..1rexp49-H.esp
7.59
7.52
7.41
7.39
7.37
7.35
7.33
7.29
7.27
7.26
7.16
7.03
6.88
6.76
6.18
6.16
5.88
5.86
5.03
5.00
4.87
4.85
4.23
4.22
4.19
4.17
4.15
4.14
4.12
4.11
3.76
3.74
3.72
3.69
1.98
1.19
1.17
1.15
0.00
Br
N
CO2Et
N
14.84
0.01
1.00
0.03
0.91
2.04
4.33
2.78
2.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Wed1av2#026..1rEXP49-13C.esp
171.89
140.72
140.43
135.99
133.73
132.50
128.74
128.46
127.91
127.58
127.22
124.89
121.71
120.45
118.88
118.58
112.99
112.29
111.08
110.17
102.77
77.63
77.00
76.36
65.90
61.25
56.71
47.11
33.00
14.10
8.29
Br
N
CO2Et
N
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


BR539_1H-new.esp
7.55
7.53
7.43
7.35
7.33
7.32
7.24
7.08
7.05
7.04
7.03
6.88
6.79
6.78
6.52
6.51
5.95
5.93
5.16
5.14
4.20
4.19
4.18
4.17
4.16
4.16
4.15
3.84
3.81
3.77
2.06
1.21
1.20
1.18
OMe
OMe
CO2Et
N
N
5.91
3.23
2.16
2.08
1.00
0.99
2.24
10.67
3.26
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


BR539PUR_13C-2.esp
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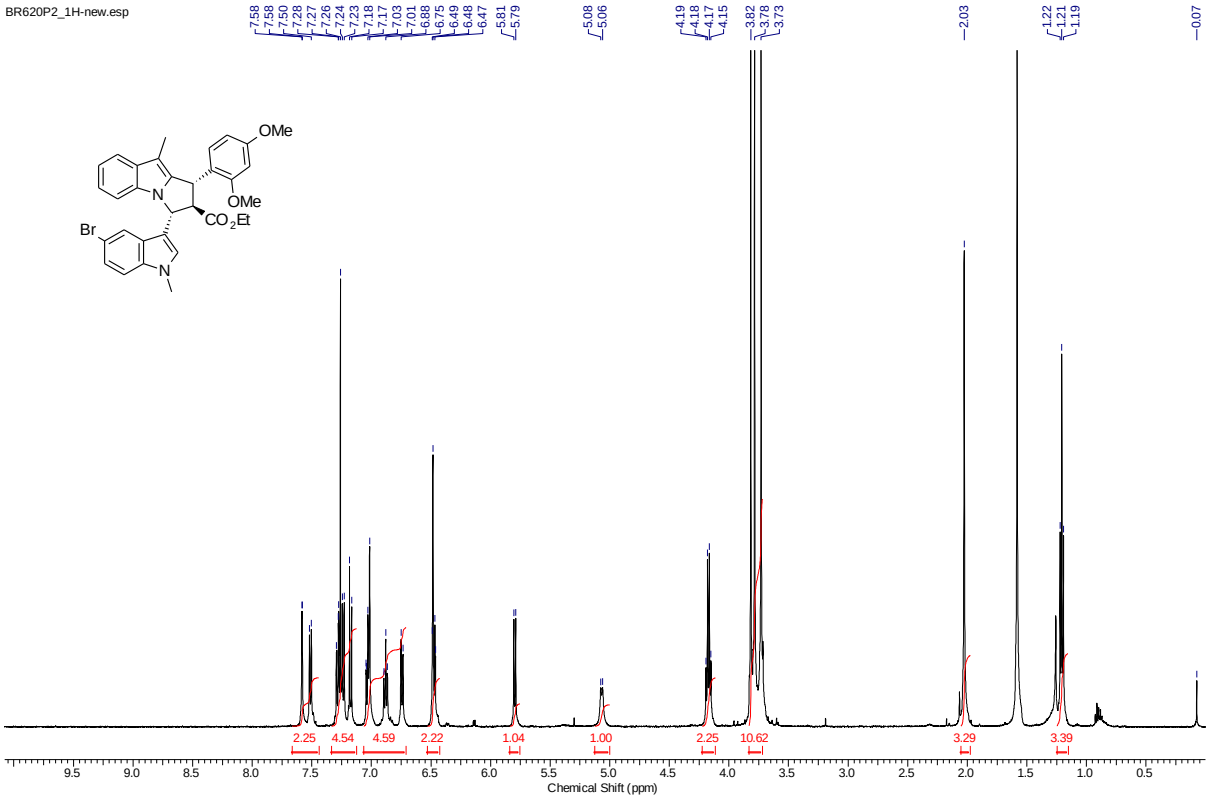
158.28
140.72
137.39
133.74
132.72
129.19
127.36
126.05
121.86
120.93
120.02
119.53
119.40
118.52
118.18
112.53
110.23
109.38
104.23
101.93
98.42
77.26
77.00
76.75
64.27
60.76
57.59
55.25
41.32
32.85
14.15
8.40
OMe
OMe
CO2Et
N
N
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


BR620P2_1H-new.esp
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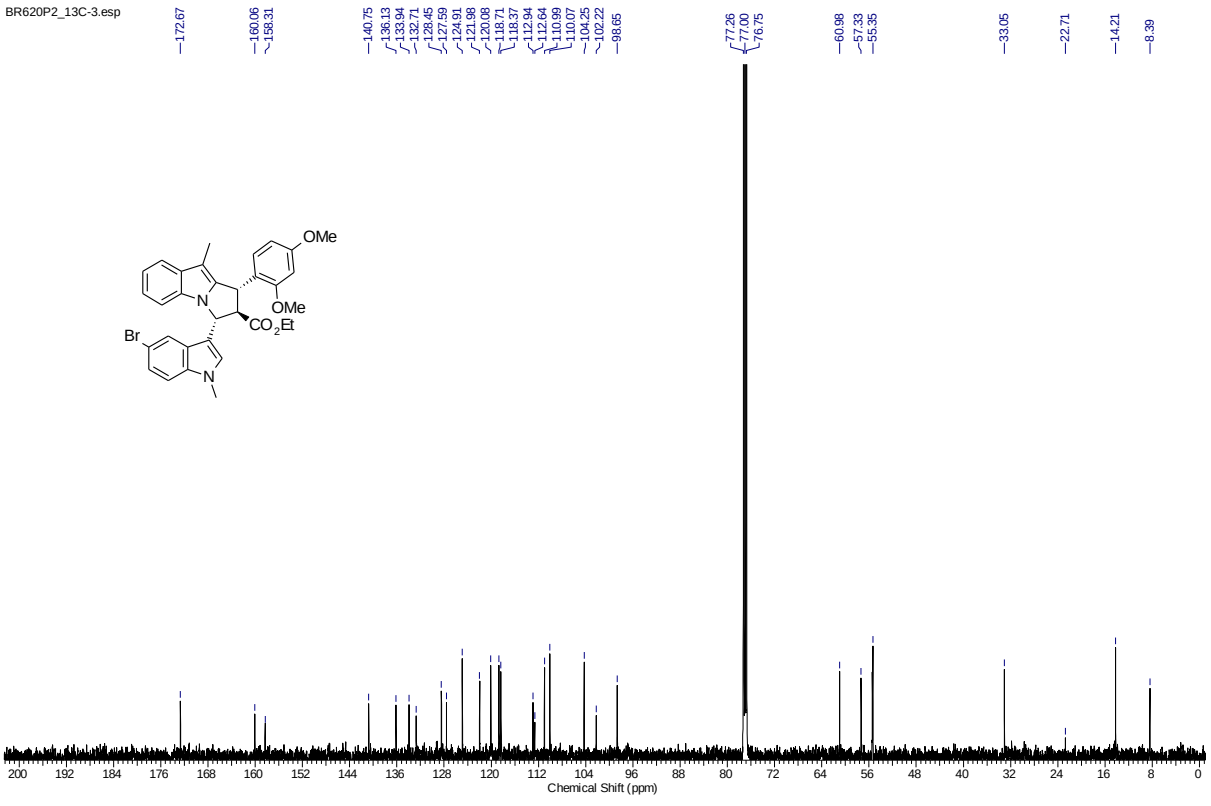
7.58
7.50
7.28
7.27
7.26
7.24
7.23
7.18
7.17
7.03
7.01
6.88
6.75
6.49
6.48
6.47
5.81
5.79
5.08
5.06
4.19
4.18
4.17
4.15
3.82
3.78
3.73
2.03
1.22
1.21
1.19
0.07
OMe
OMe
CO2Et
Br
N
N
2.25
4.54
4.59
2.22
1.04
1.00
2.25
10.62
3.29
3.39
Chemical Shift (ppm)


BR620P2_13C-3.esp
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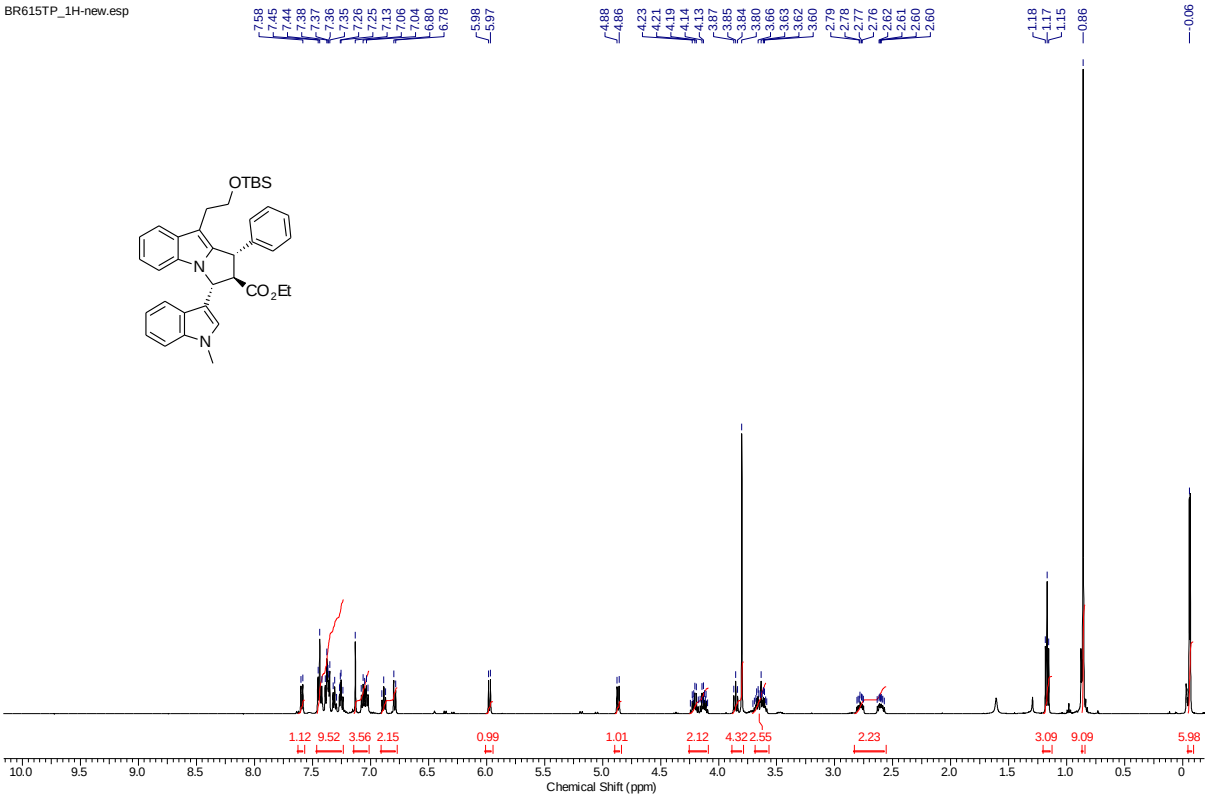
133.94
132.71
128.45
127.59
124.91
121.98
120.08
118.71
118.37
112.94
112.64
110.99
110.07
104.25
102.22
98.65
77.26
77.00
76.75
60.98
57.33
55.35
33.05
22.71
14.21
8.39
OMe
OMe
CO2Et
Br
N
N
Chemical Shift (ppm)


BR615TP_1H-new.esp
OTBS
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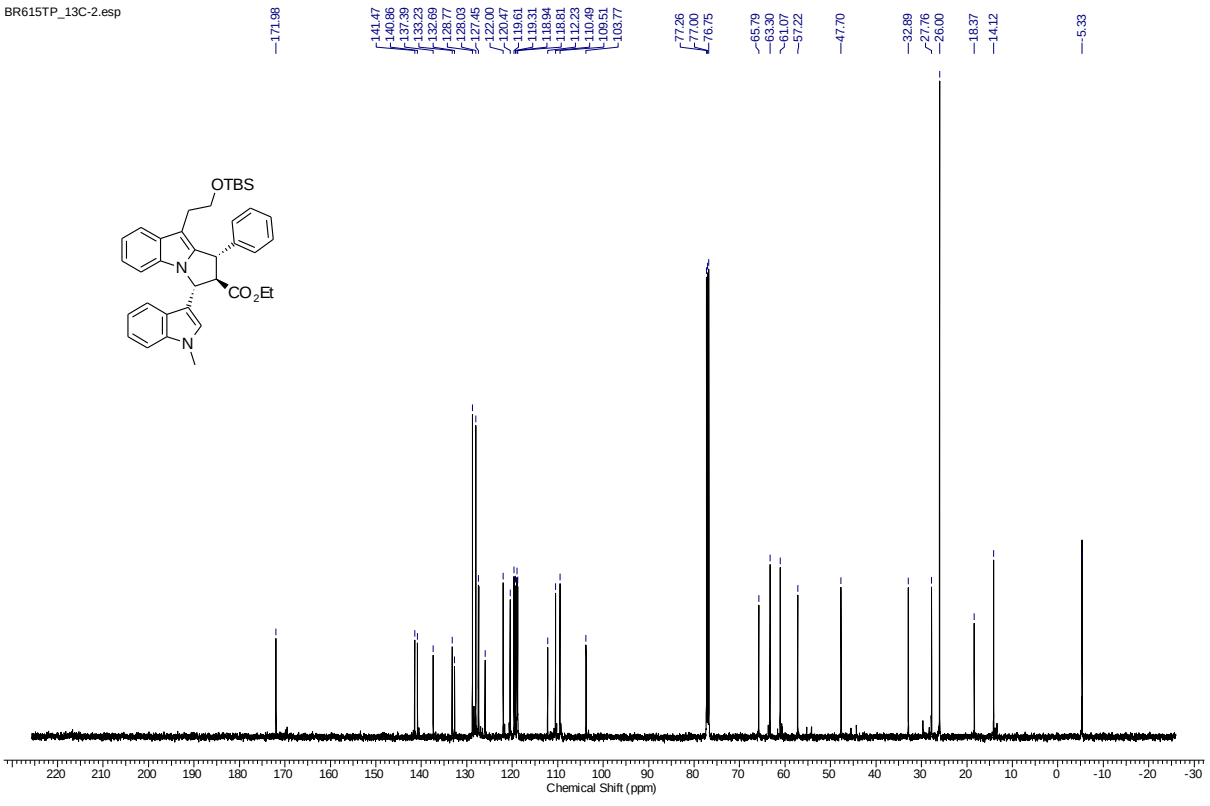
CO2Et
N
Chemical Shift (ppm)


BR615TP_13C-2.esp
OTBS
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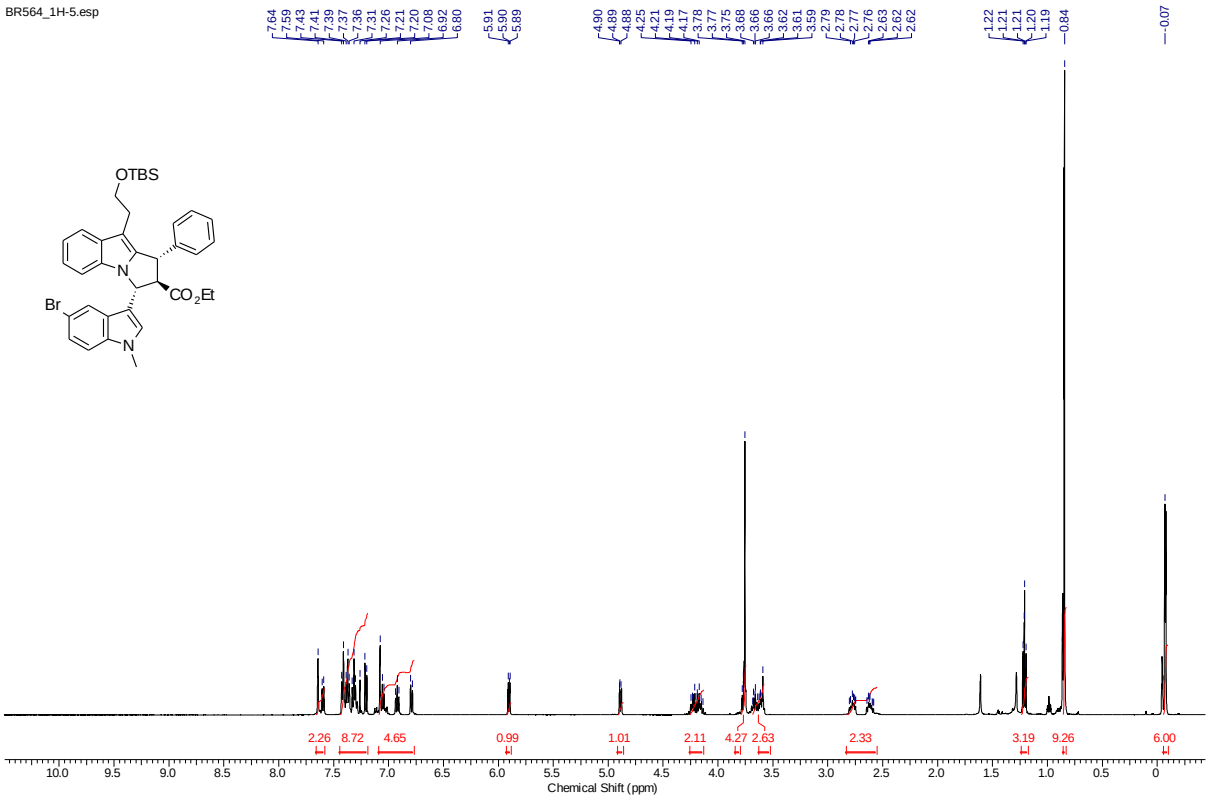
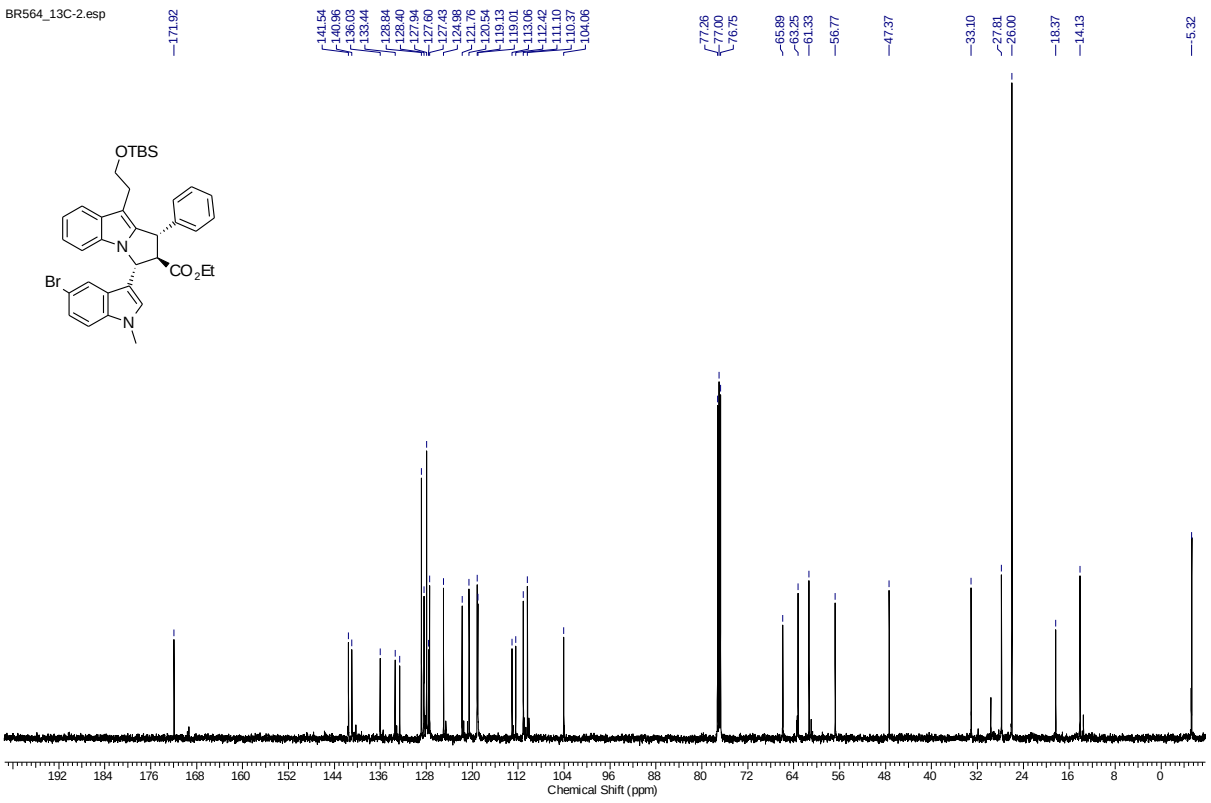
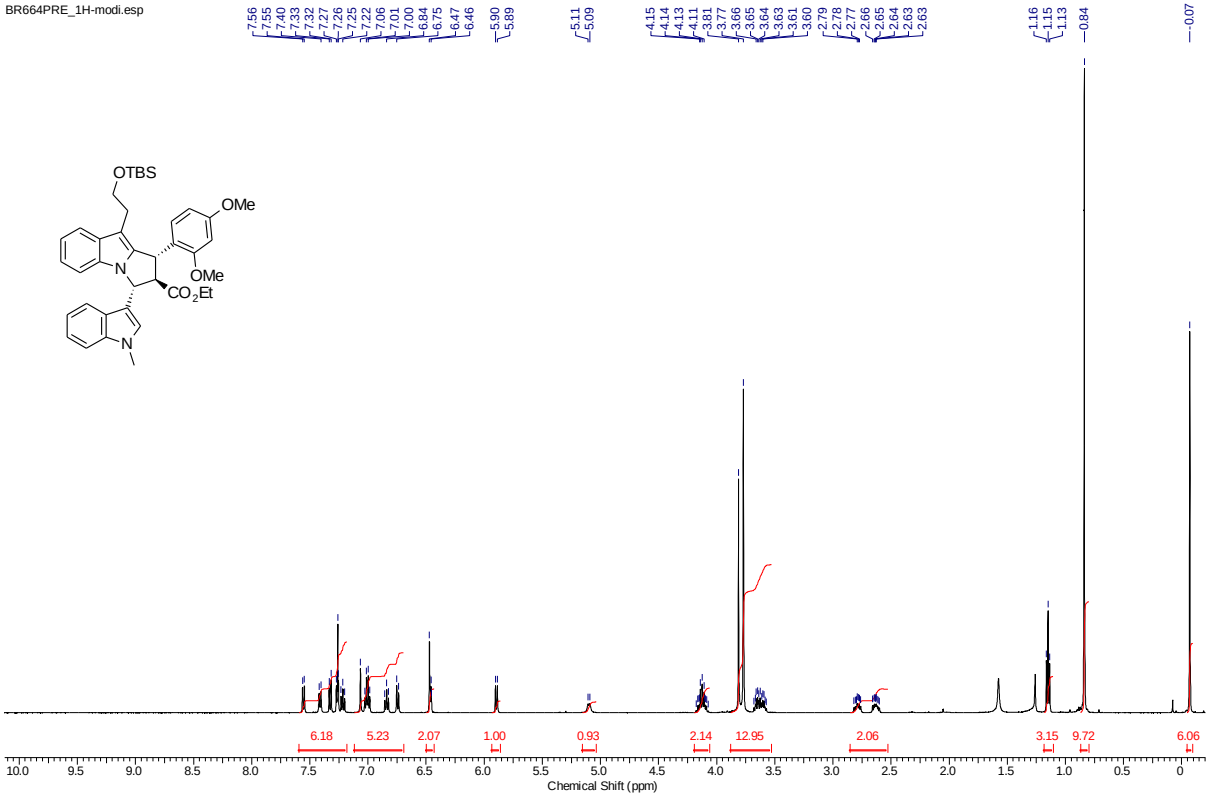
CO2Et
N
Chemical Shift (ppm)


BR564_1H-5.esp
OTBS
Br
N
CO2Et
Chemical Shift (ppm)


BR564_13C-2.esp
OTBS
Br
N
CO2Et
Chemical Shift (ppm)


BR664PRE_1H-modi.esp
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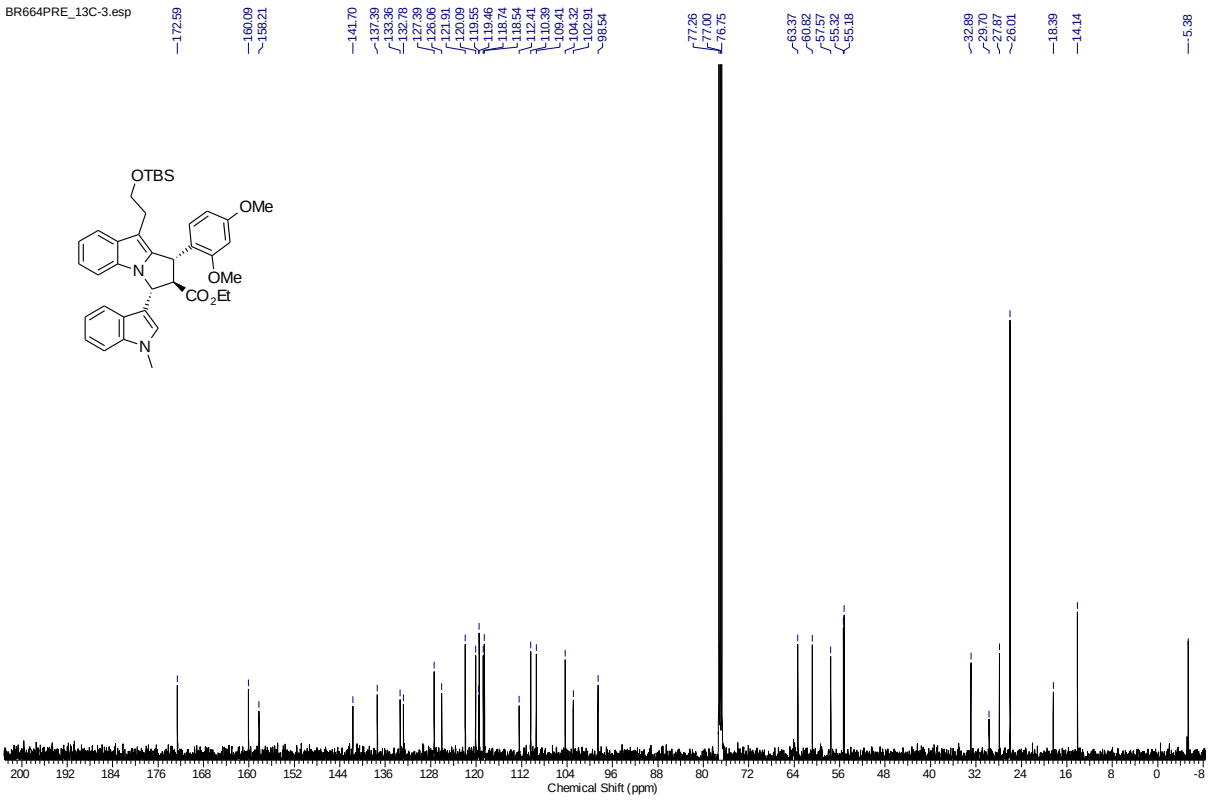
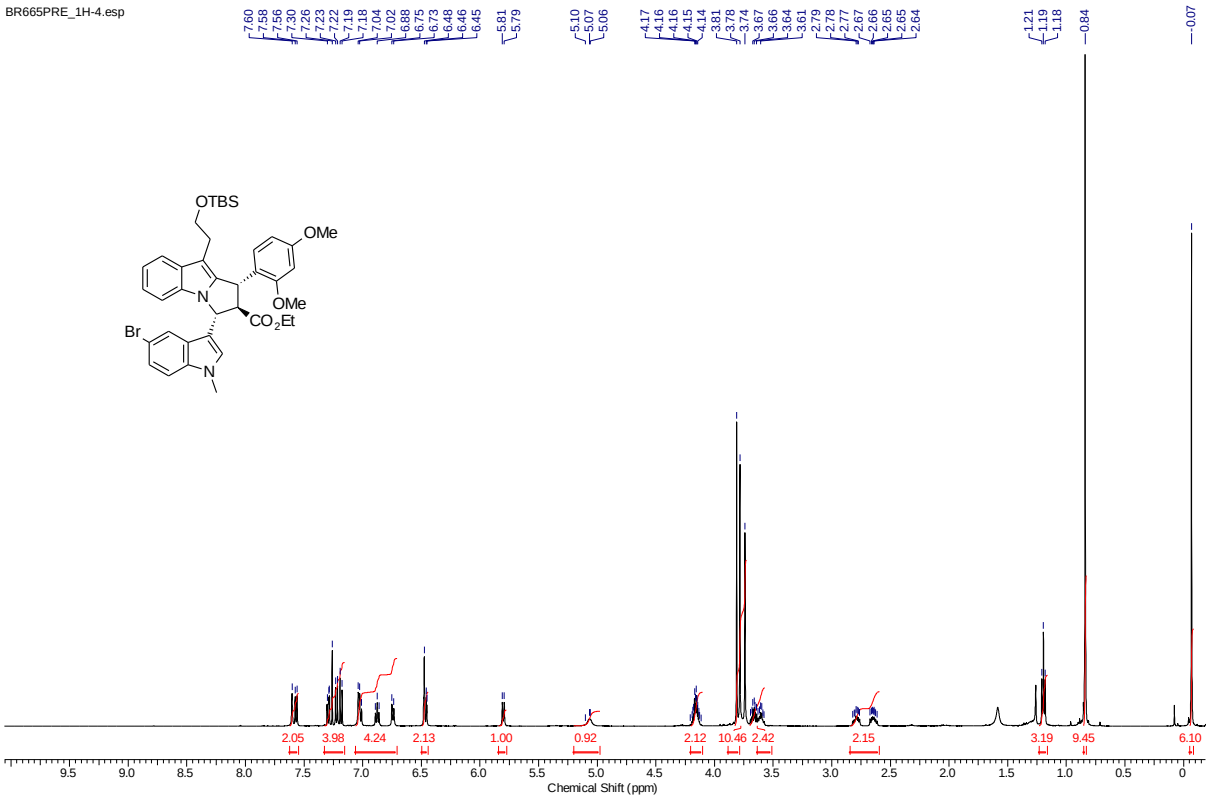
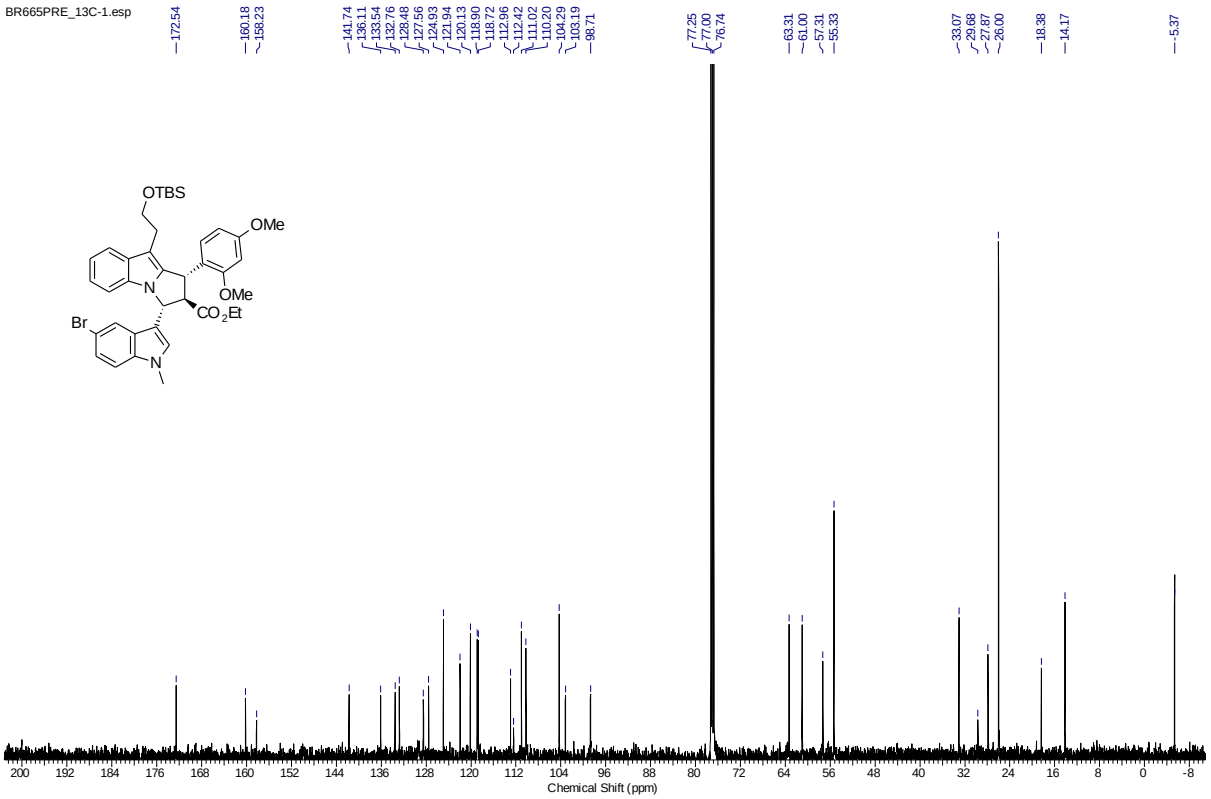
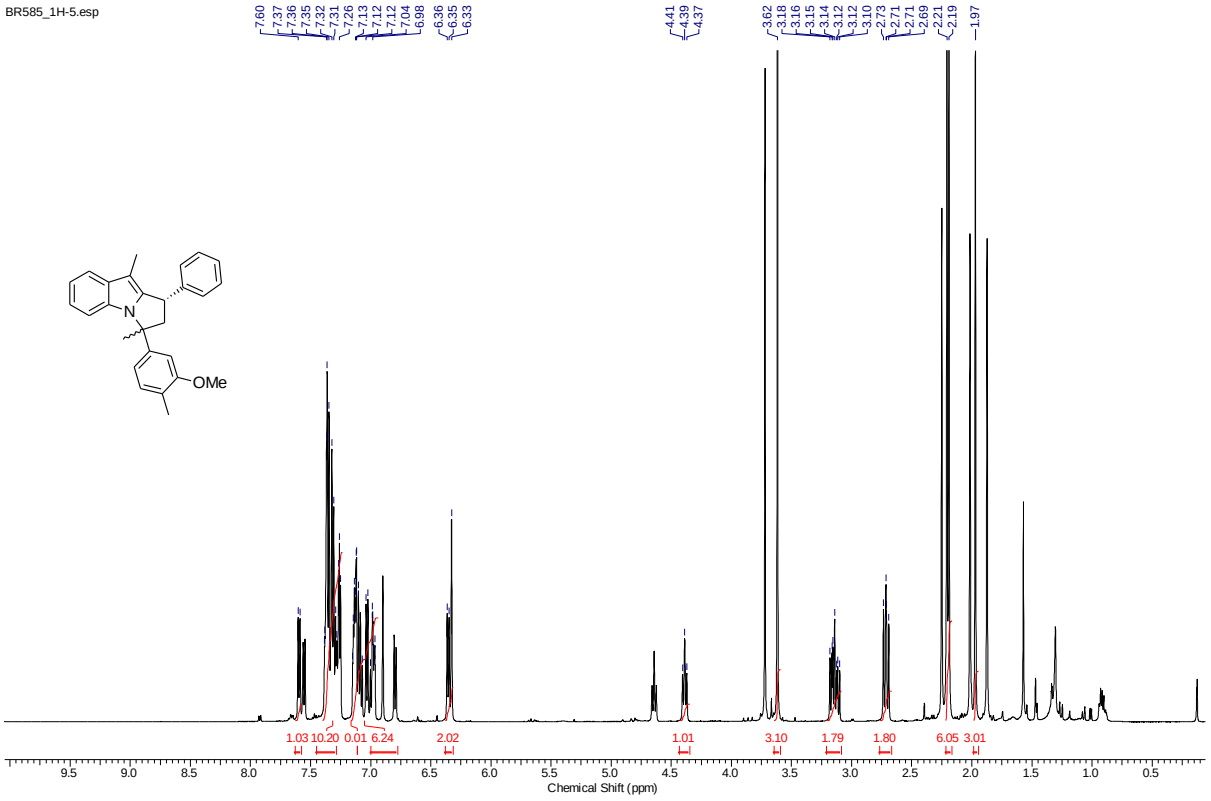
OMe
OMe
CO2Et
N
N
Chemical Shift (ppm)


BR664PRE_13C-3.esp
OTBS
OMe
OMe
CO2Et
N
N
Chemical Shift (ppm)


BR665PRE_1H-4.esp
7.60 7.58 7.56 7.30 7.26 7.23 7.22 7.19 7.18 7.04 7.02 6.88 6.75 6.73 6.48 6.46 6.45 5.81 5.79 5.10 5.07 5.06 4.17 4.16 4.16 4.15 4.14 3.81 3.78 3.74 3.67 3.66 3.64 3.61 2.79 2.78 2.77 2.67 2.66 2.65 2.65 2.64 1.21 1.19 1.18 0.84 0.07
OTBS
OMe
OMe
CO2Et
Br
N
2.05 3.98 4.24 2.13 1.00 0.92 2.12 10.46 2.42 2.15 3.19 9.45 6.10
Chemical Shift (ppm)


BR665PRE_13C-1.esp
172.54 160.18 158.23 141.74 136.11 133.54 132.76 128.48 127.56 124.93 121.94 120.13 118.90 118.72 112.96 112.42 111.02 110.20 104.29 103.19 98.71 77.25 77.00 76.74 63.31 61.00 57.31 55.33 33.07 29.68 27.87 26.00 18.38 14.17 5.37
OTBS
OMe
OMe
CO2Et
Br
N
Chemical Shift (ppm)


BR585_1H-5.esp
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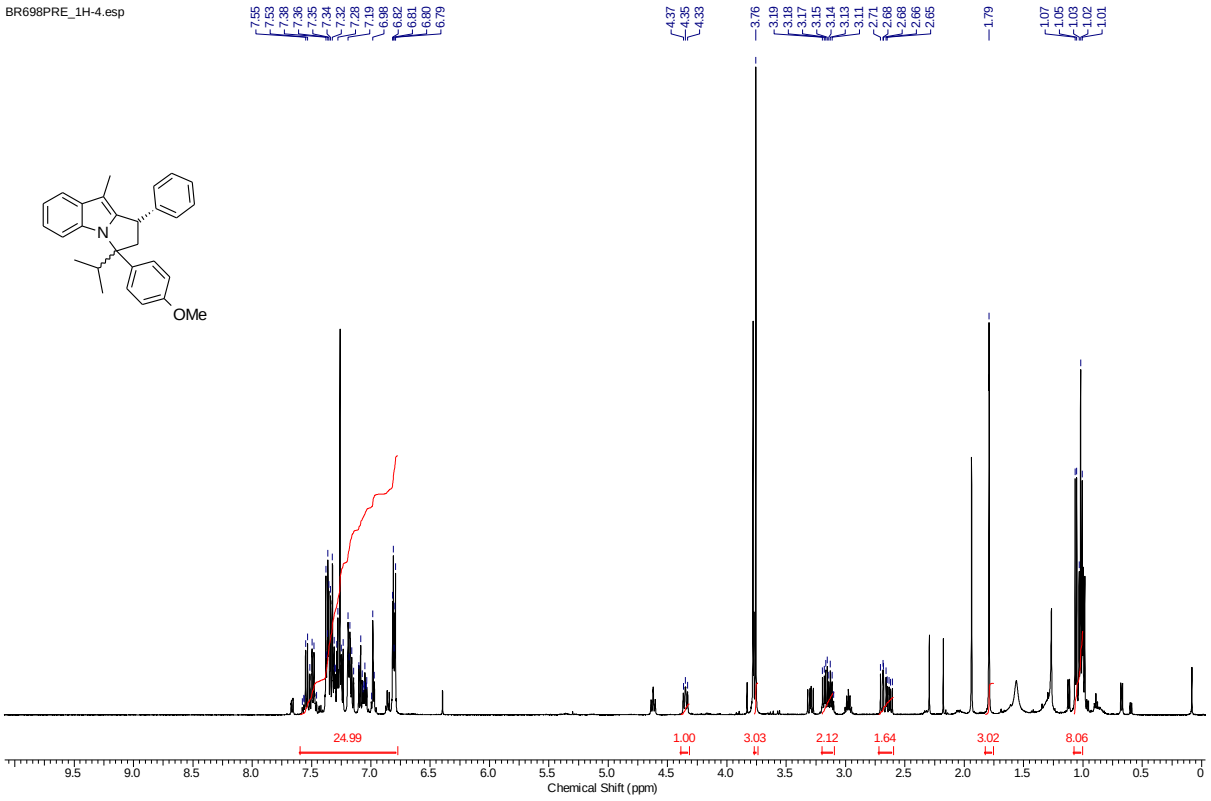
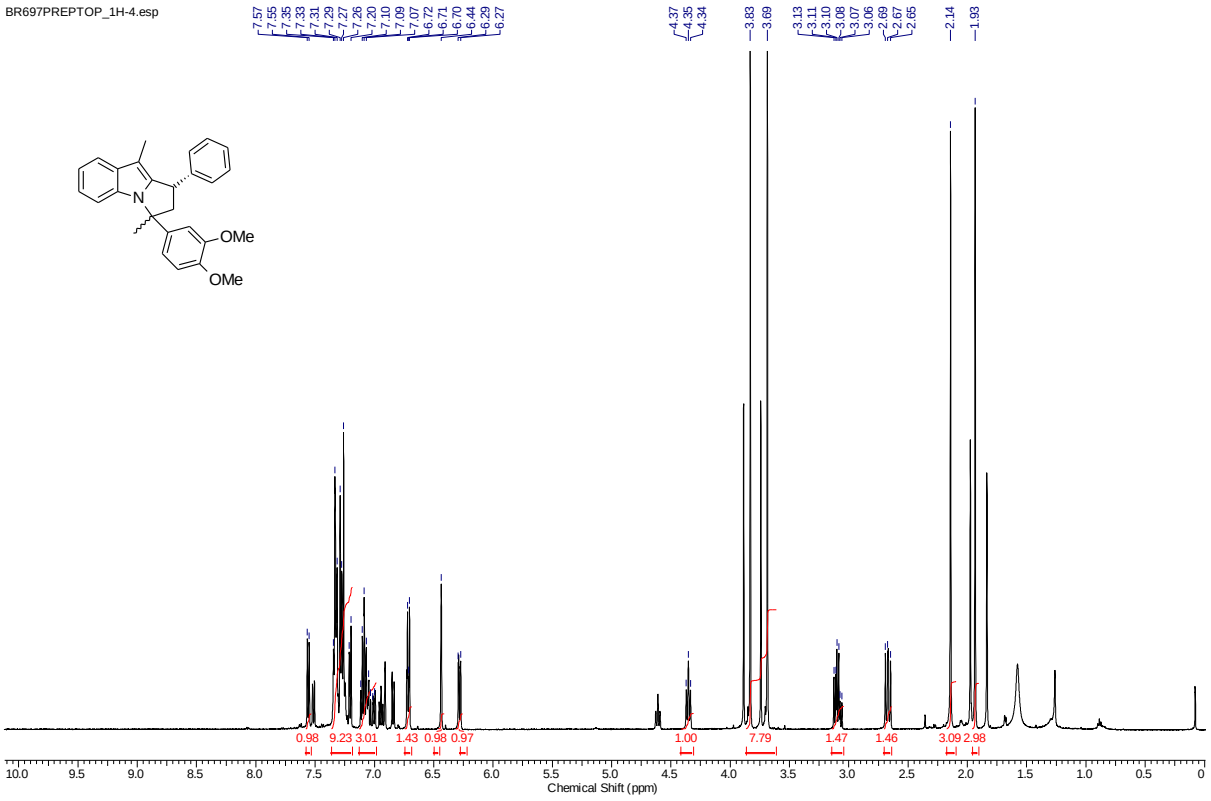
7.37
7.36
7.35
7.32
7.31
7.26
7.13
7.12
7.12
7.04
6.98
6.36
6.35
6.33
4.41
4.39
4.37
3.62
3.18
3.16
3.15
3.14
3.12
3.10
2.73
2.71
2.71
2.69
2.21
2.19
1.97
N
OMe
1.03
10.20
0.01
6.24
2.02
1.01
3.10
1.79
1.80
6.05
3.01
Chemical Shift (ppm)


BR698PRE_1H-4.esp
7.55
7.53
7.38
7.36
7.35
7.34
7.32
7.28
7.19
6.98
6.82
6.81
6.80
6.79
4.37
4.35
4.33
3.76
3.19
3.18
3.17
3.15
3.14
3.13
3.11
2.71
2.68
2.68
2.66
2.65
1.79
1.07
1.05
1.03
1.02
1.01
N
OMe
24.99
1.00
3.03
2.12
1.64
3.02
8.06
Chemical Shift (ppm)


BR697PREPTOP_1H-4.esp
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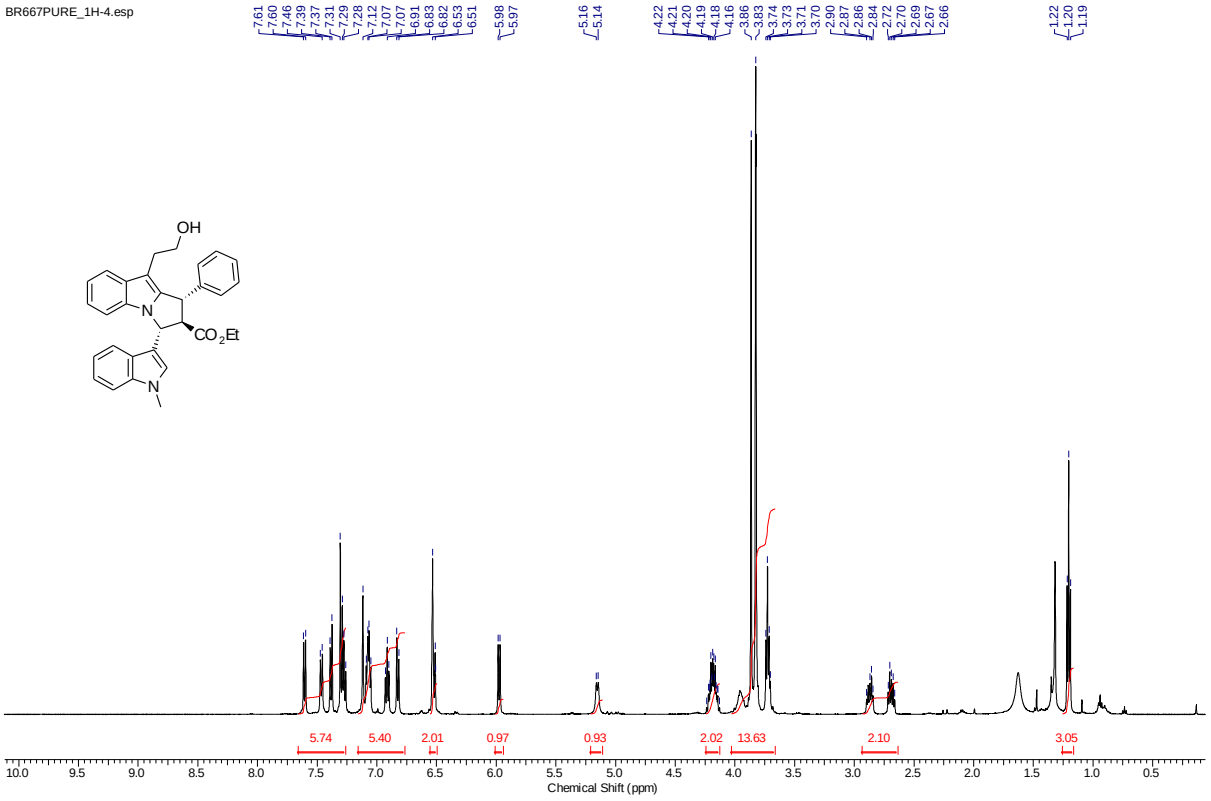
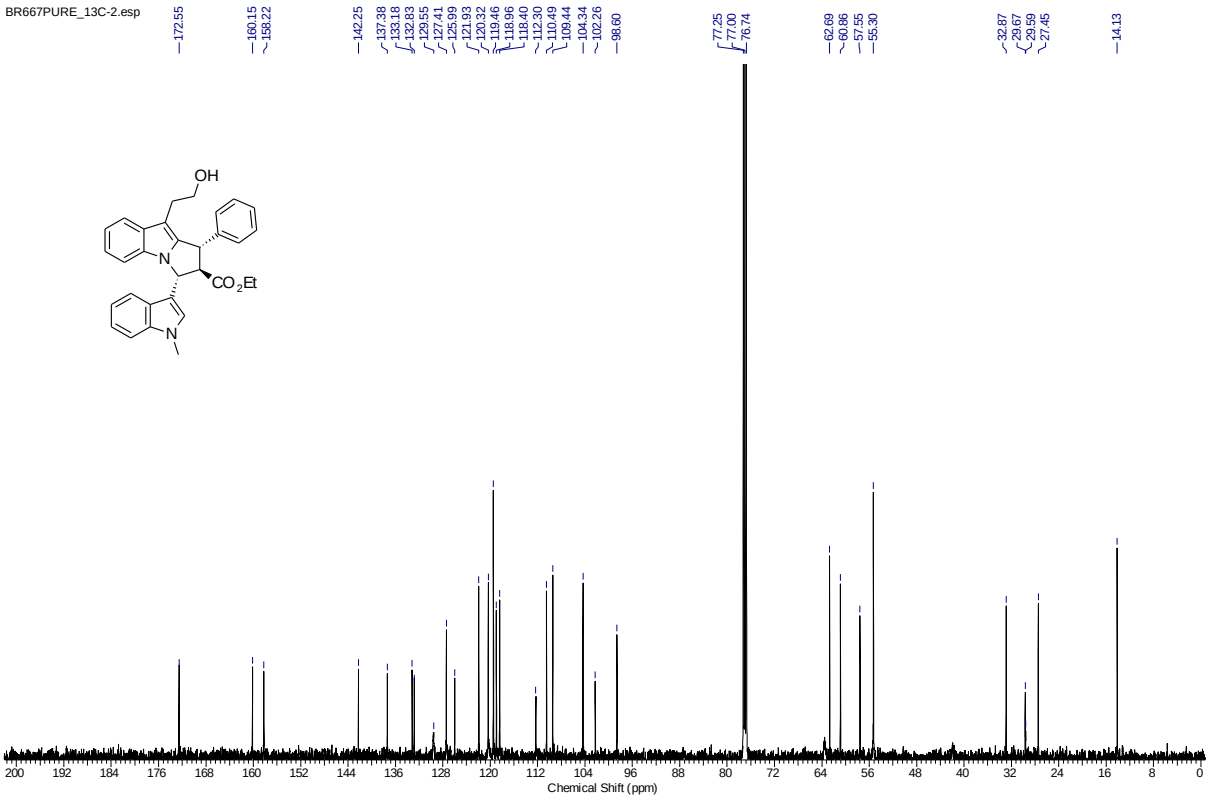
7.55
7.35
7.33
7.31
7.29
7.27
7.26
7.20
7.10
7.09
7.07
6.72
6.71
6.70
6.44
6.29
6.27
4.37
4.35
4.34
3.83
3.69
3.13
3.11
3.10
3.08
3.07
3.06
2.69
2.67
2.65
2.14
1.93
N
OMe
OMe
0.98
9.23
3.01
1.43
0.98
0.97
1.00
7.79
1.47
1.46
3.09
2.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


BR667PURE_1H-4.esp
7.61
7.60
7.46
7.46
7.39
7.37
7.31
7.29
7.28
7.12
7.07
7.07
6.91
6.83
6.82
6.53
6.51
5.98
5.97
5.16
5.14
4.22
4.21
4.20
4.19
4.18
4.16
3.86
3.83
3.74
3.73
3.71
3.70
2.90
2.87
2.86
2.84
2.72
2.70
2.69
2.67
2.66
1.22
1.20
1.19
OH
CO2Et
N
N
5.74
5.40
2.01
0.97
0.93
2.02
13.63
2.10
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


BR667PURE_13C-2.esp
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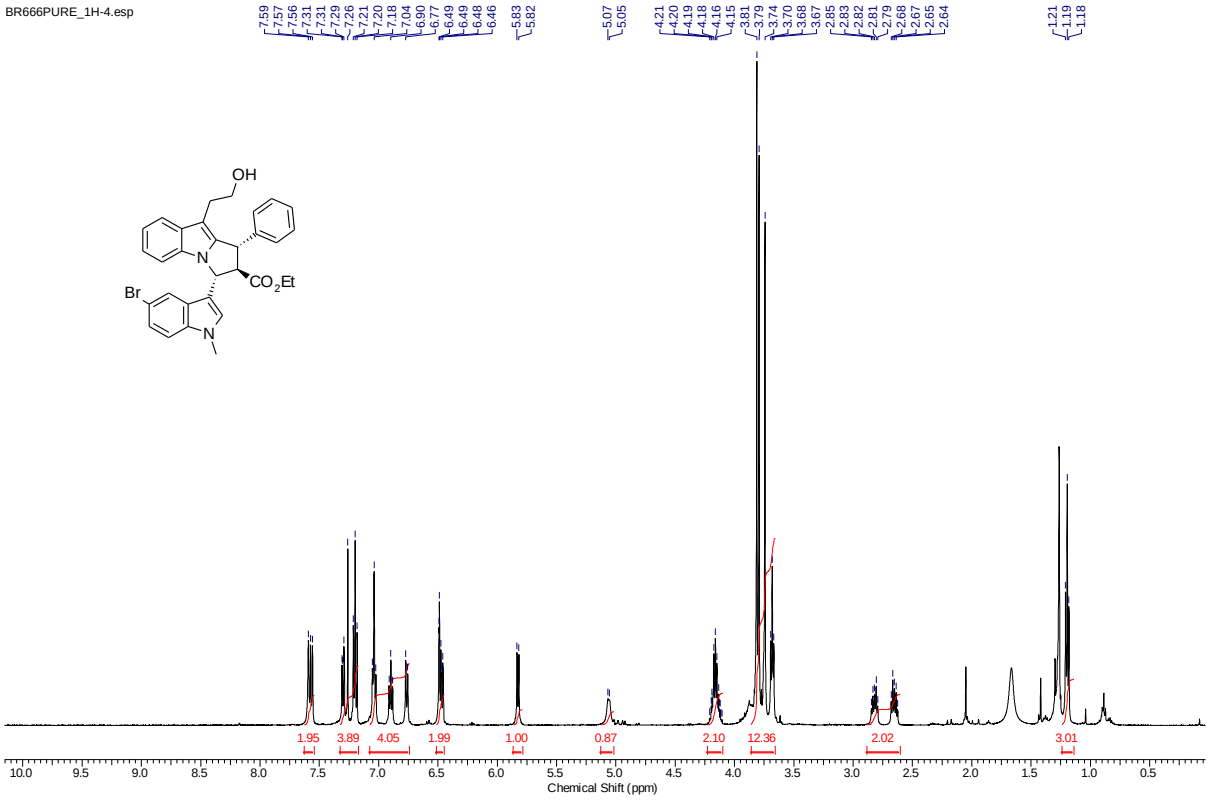
158.22
142.25
137.38
133.18
132.83
129.55
127.41
125.99
121.93
120.32
119.46
118.96
118.40
112.30
110.49
109.44
104.34
102.26
98.60
77.25
77.00
76.74
62.69
60.86
57.55
55.30
32.87
29.67
29.39
27.45
14.13
OH
CO2Et
N
N
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


BR666PURE_1H-4.esp
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7.57
7.56
7.31
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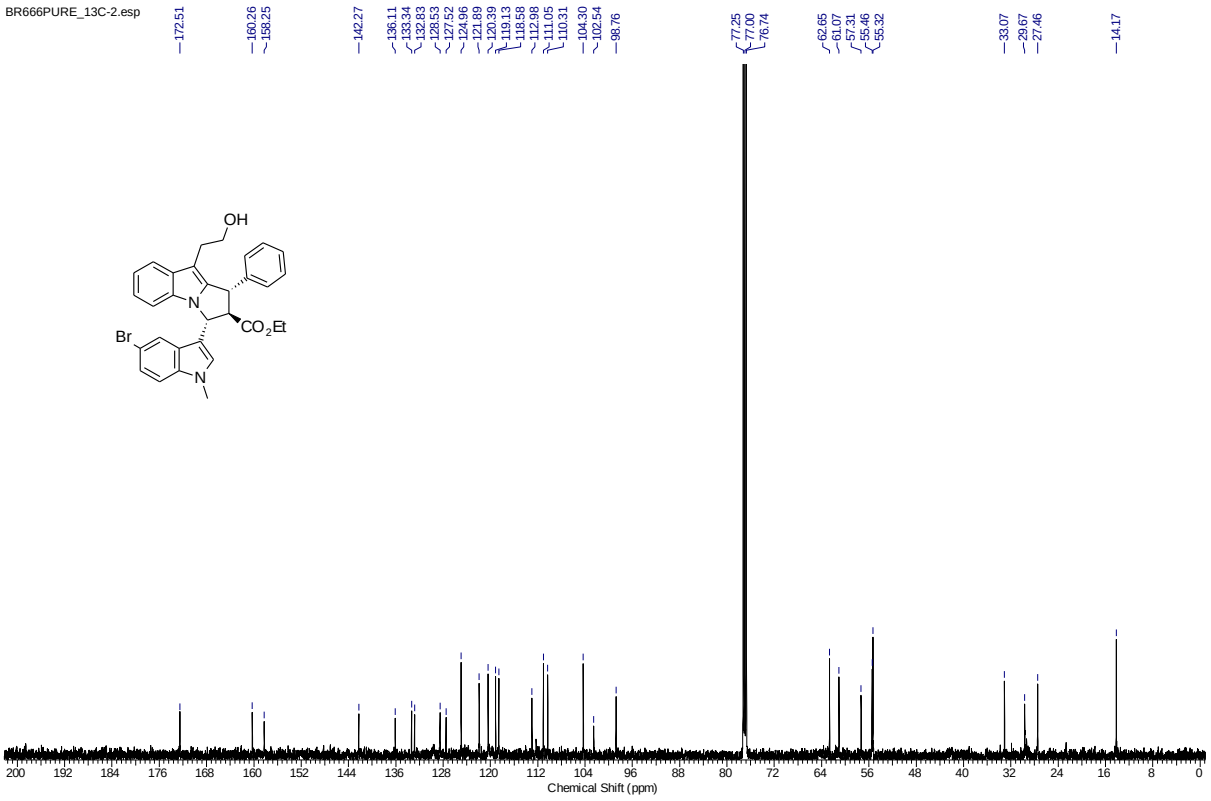
7.26
7.21
7.20
7.18
7.04
6.90
6.77
6.49
6.49
6.48
6.46
5.83
5.82
5.07
5.05
4.21
4.20
4.19
4.18
4.16
4.15
3.81
3.79
3.74
3.70
3.68
3.67
2.85
2.83
2.82
2.81
2.79
2.68
2.67
2.65
2.64
1.21
1.19
1.18
OH
N
CO2Et
Br
N
1.95
3.89
4.05
1.99
1.00
0.87
2.10
12.36
2.02
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


BR666PURE_13C-2.esp
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132.83
128.53
127.52
124.96
121.89
120.39
119.13
118.58
112.98
111.05
110.31
104.30
102.54
98.76
77.25
77.00
76.74
62.65
61.07
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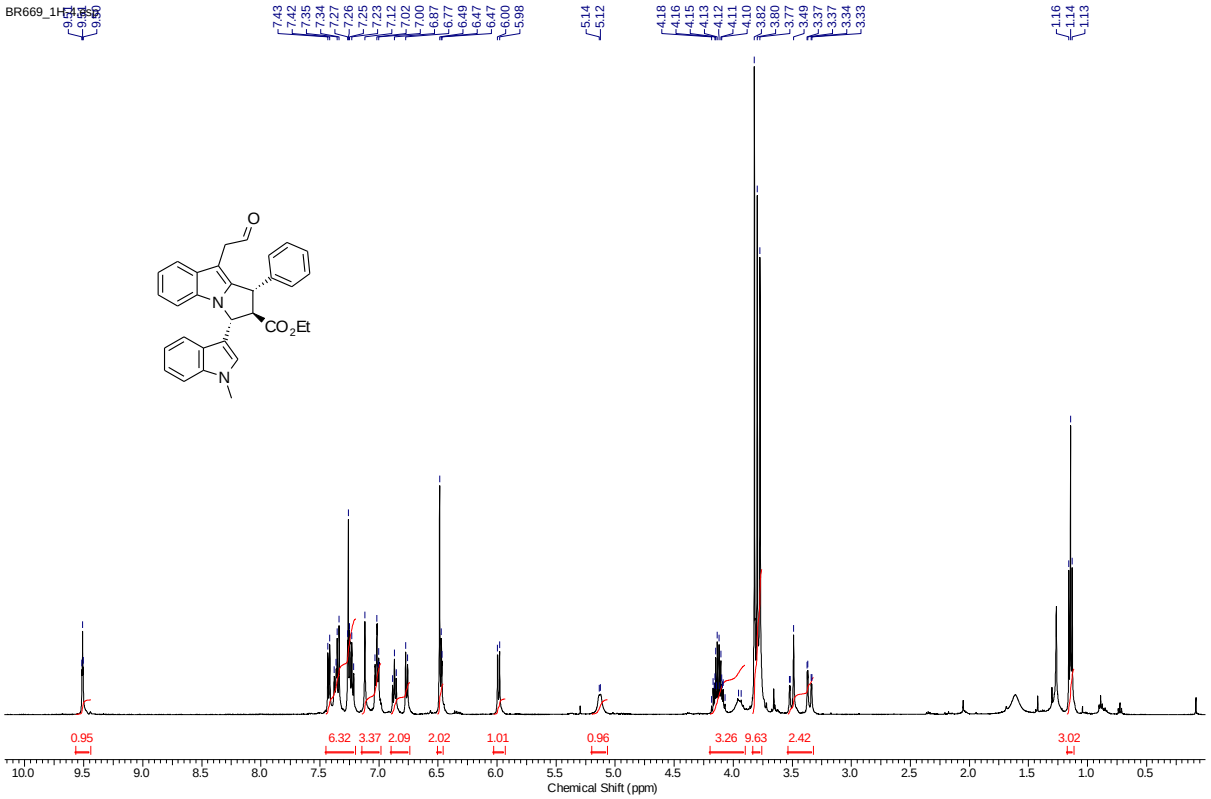
55.46
55.32
33.07
29.67
27.46
14.17
OH
N
CO2Et
Br
N
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


BR669_1H-1.esp
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9.56
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7.42
7.35
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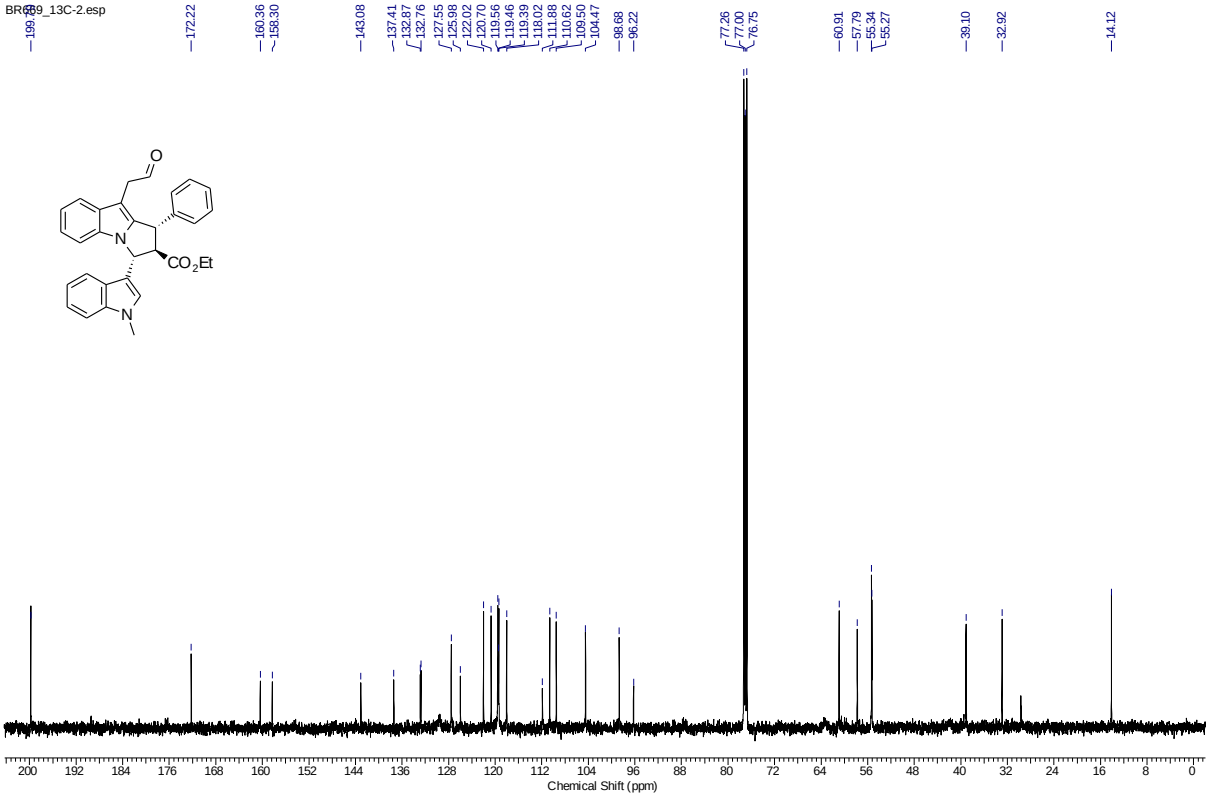
7.27
7.26
7.25
7.23
7.12
7.02
7.00
6.87
6.77
6.49
6.47
6.47
6.00
5.98
5.14
5.12
4.18
4.16
4.15
4.13
4.12
4.11
4.10
3.82
3.80
3.77
3.49
3.37
3.37
3.34
3.33
1.16
1.14
1.13
O
N
CO2Et
N
0.95
6.32
3.37
2.09
2.02
1.01
0.96
3.26
9.63
2.42
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


BR669_13C-2.esp
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132.76
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122.02
120.70
119.56
119.46
119.39
118.02
111.88
110.62
109.50
104.47
98.68
96.22
77.26
77.00
76.75
60.91
57.79
55.34
55.27
39.10
32.92
14.12
O
N
CO2Et
N
200
192
184
176
168
160
152
144
136
128
120
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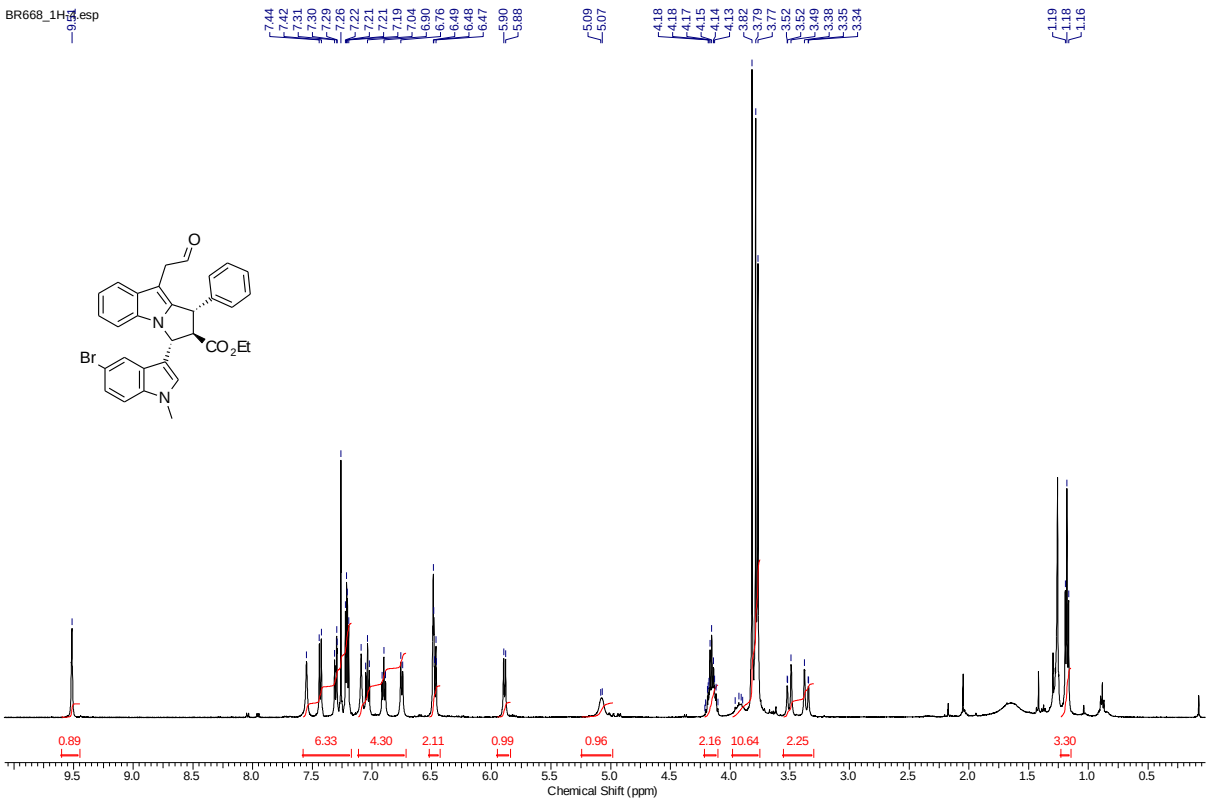
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


BR668_1H-4.esp
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7.22
7.21
7.21
7.19
7.04
6.90
6.76
6.49
6.48
6.47
5.90
5.88
5.09
5.07
4.18
4.18
4.17
4.15
4.14
4.13
3.82
3.79
3.77
3.52
3.52
3.49
3.38
3.35
3.34
1.19
1.18
1.16
O
N
CO2Et
Br
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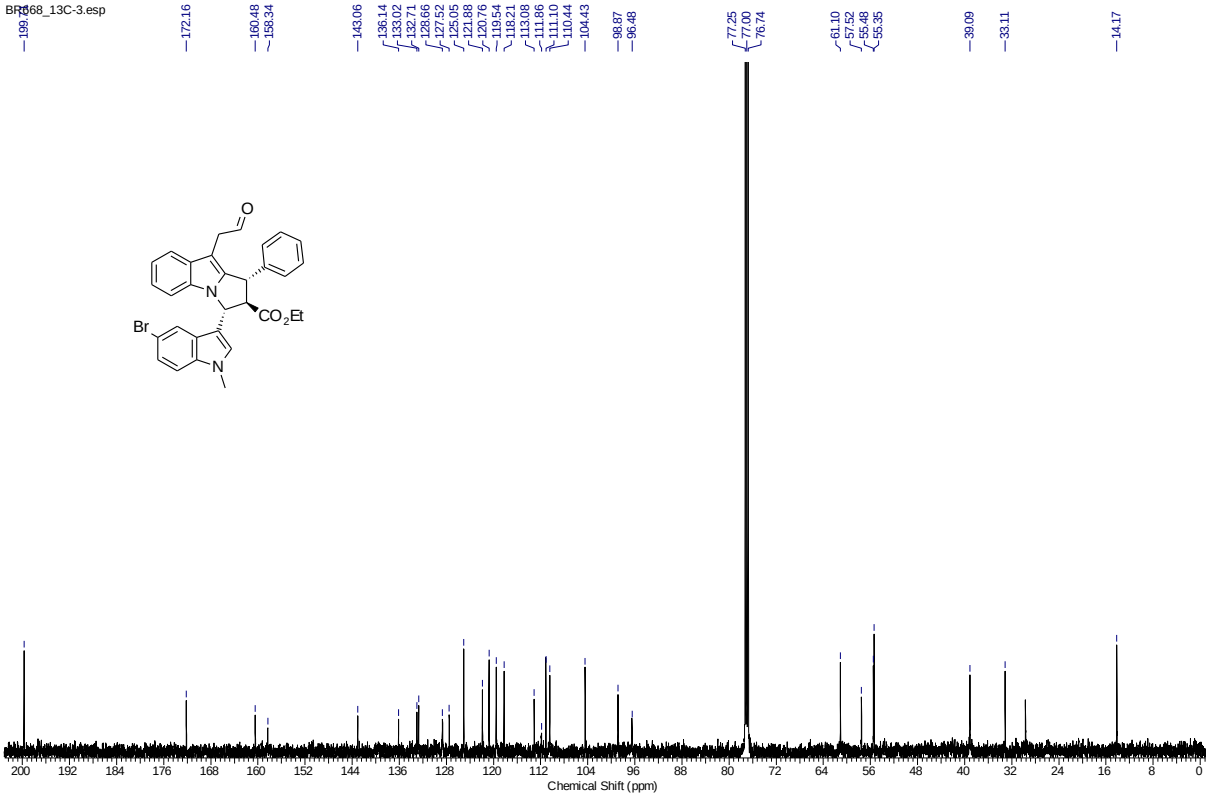
4.30
2.11
0.99
0.96
2.16
10.64
2.25
3.30
Chemical Shift (ppm)


BR668_13C-3.esp
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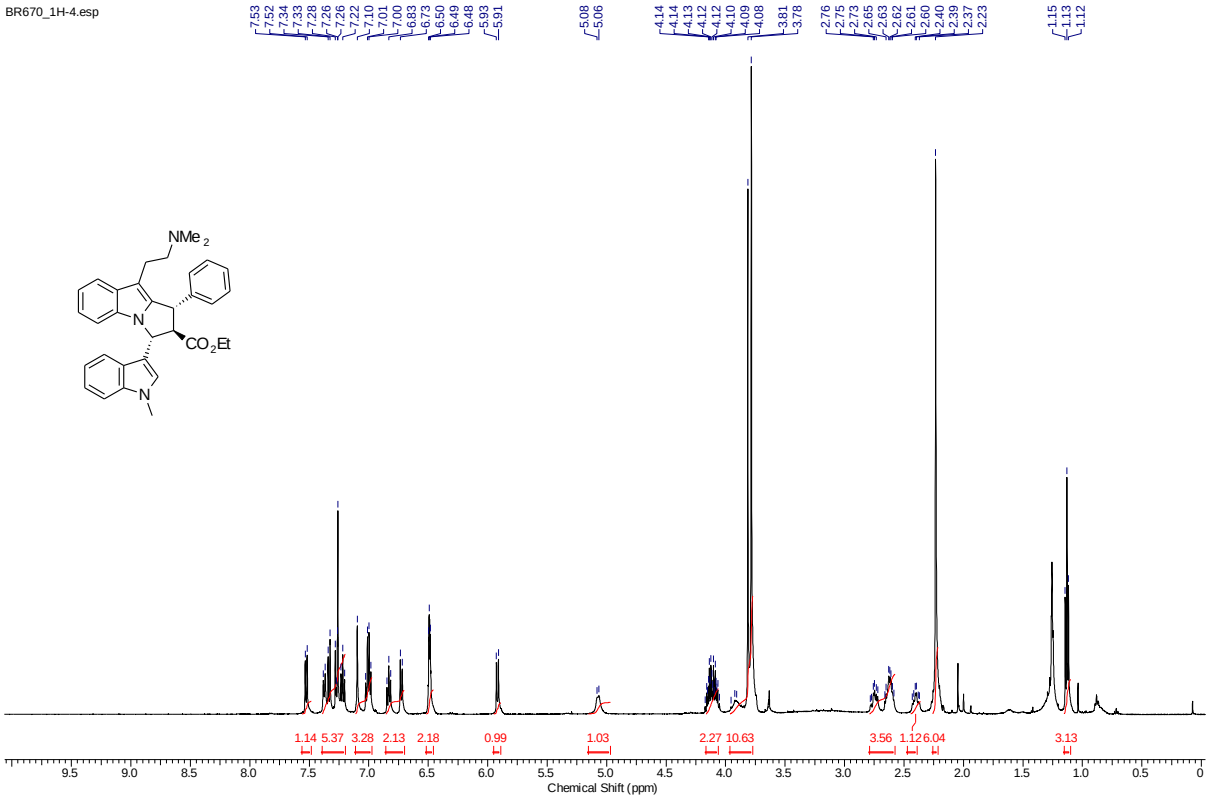
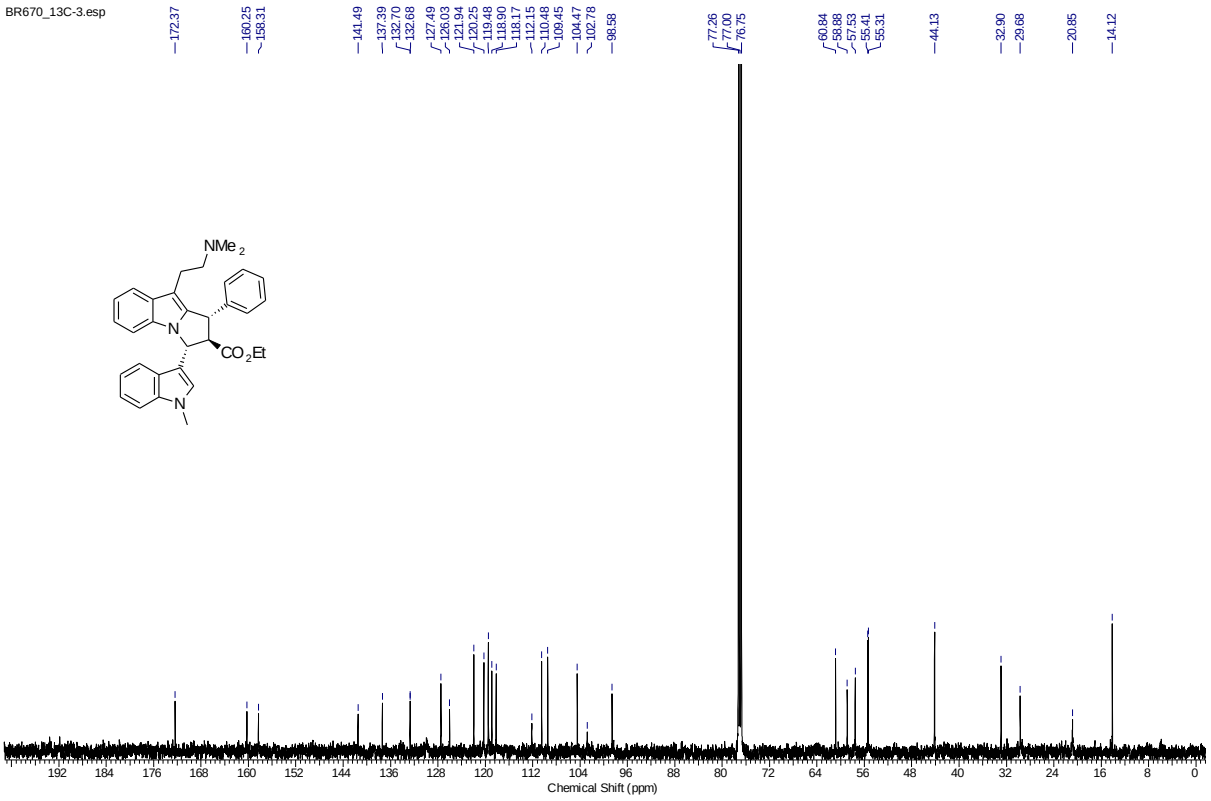
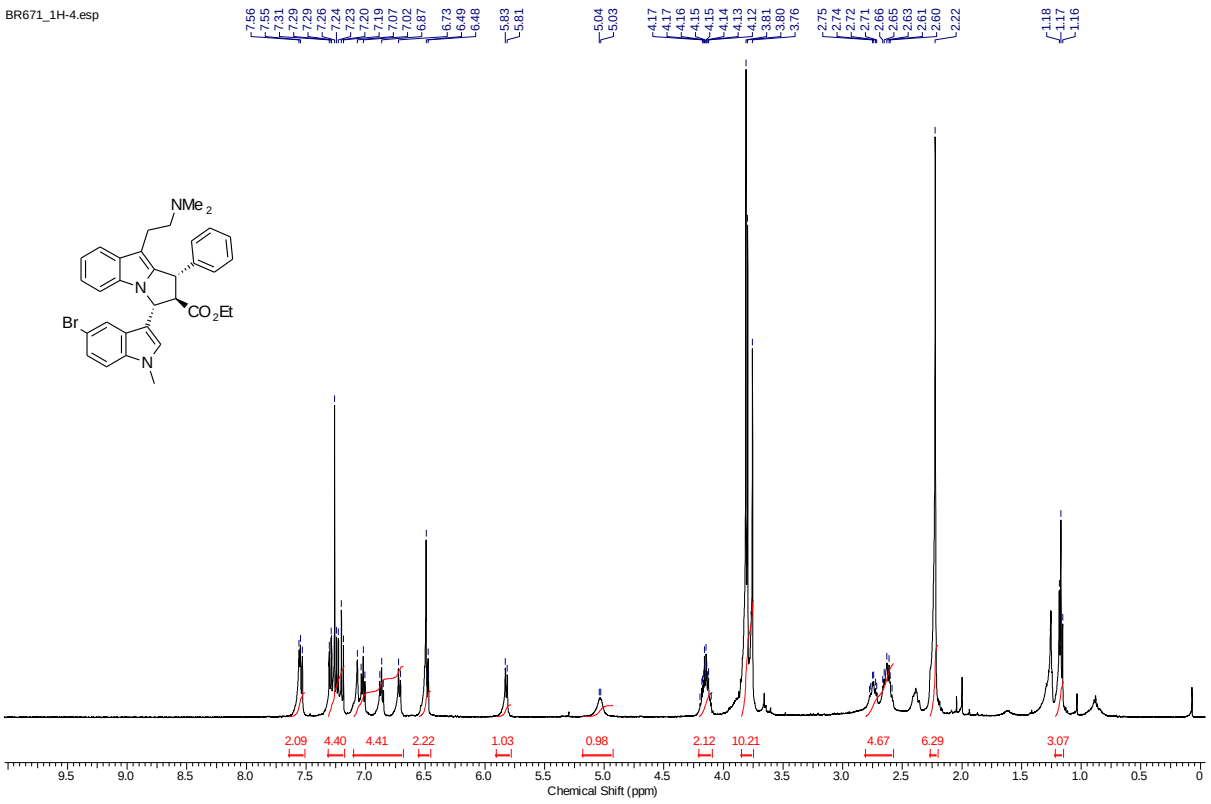
158.34
143.06
136.14
133.02
132.71
128.66
127.52
125.05
121.88
120.76
119.54
118.21
113.08
111.86
111.10
110.44
104.43
98.87
96.48
77.25
77.00
76.74
61.10
57.52
55.48
55.35
39.09
33.11
14.17
O
N
CO2Et
Br
N
Chemical Shift (ppm)


BR670_1H-4.esp
7.53 7.52 7.34 7.33 7.28 7.26 7.26 7.22 7.10 7.01 7.00 6.83 6.73 6.50 6.49 6.48 5.93 5.91
5.08 5.06
4.14 4.14 4.13 4.12 4.12 4.10 4.09 4.08 3.81 3.78
2.76 2.75 2.73 2.65 2.63 2.62 2.61 2.60 2.40 2.39 2.37 2.23
1.15 1.13 1.12
NMe2
CO2Et
N
N
1.14 5.37 3.28 2.13 2.18 0.99 1.03 2.27 10.63 3.56 1.12 6.04 3.13
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


BR670_13C-3.esp
172.37
160.25 158.31
141.49
137.39 132.70 132.68
127.49 126.03 121.94 120.25 119.48 118.90 118.17 112.15 110.48 109.45 104.47 102.78
98.58
77.26 77.00 76.75
60.84 58.88 57.53 55.41 55.31
44.13
32.90 29.68
20.85
14.12
NMe2
CO2Et
N
N
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)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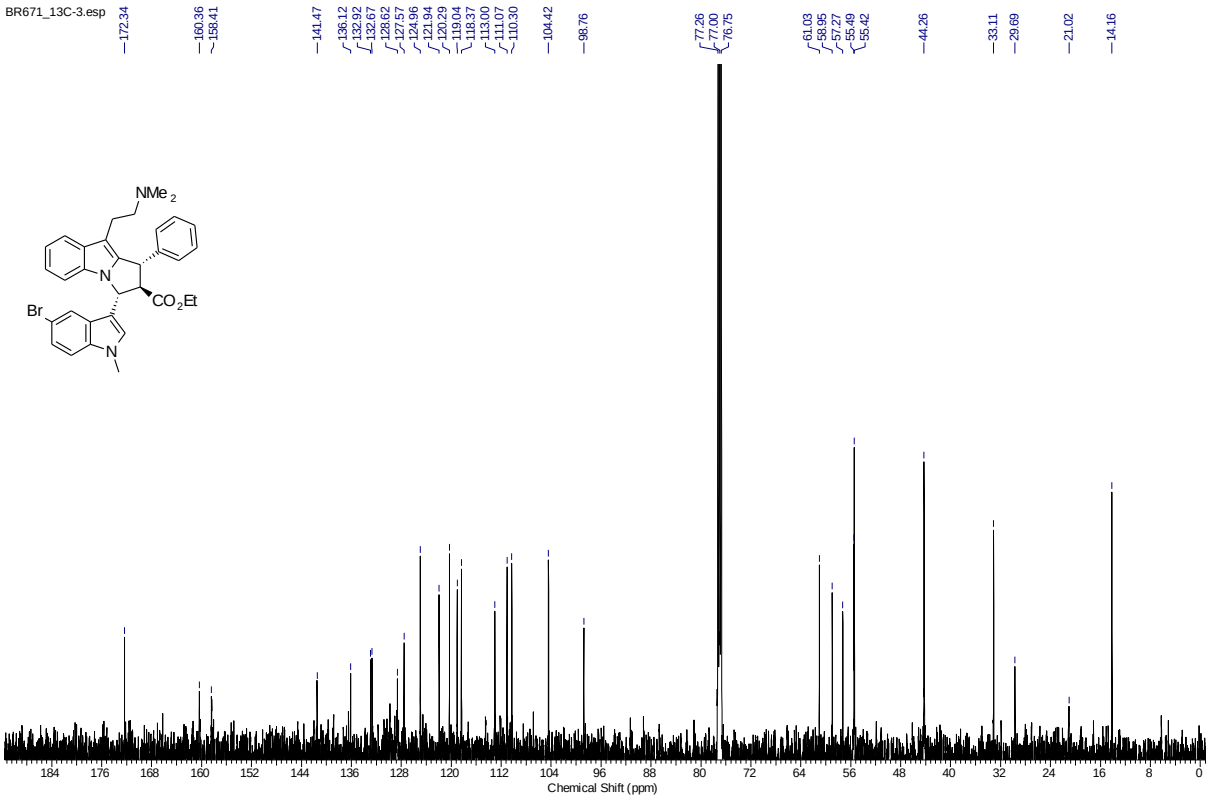
NMe2
CO2Et
Br
N
Chemical Shift (ppm)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CO2Et
Br
N
Chemical Shift (ppm)