Palladium Catalyzed Cyclizative Cross Coupling of Ynone Oximes with 2-Haloaryl N-Acrylamides for Isoxazolyl Indoline Bis-heterocyclics

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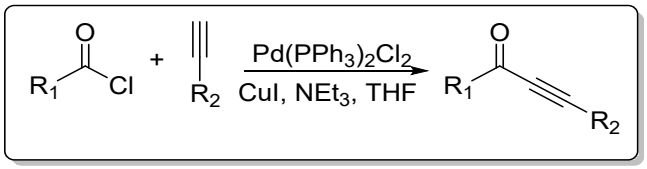
I. General Information and methods.

All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300, 400 or 500 MHz spectrometer for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$ for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using Q-TOF mass spectrometer. Column chromatography was performed with silica gel (100–200 mesh) as the stationary phase. All reactions were monitored by using TLC.

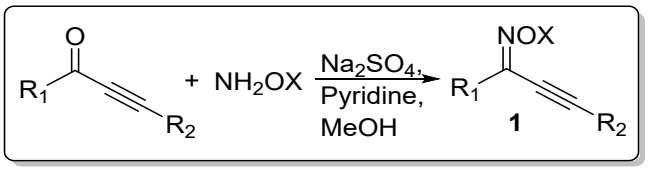
II. General Procedure for the Preparation of starting materials:

General procedure-A for the synthesis of Alkynyl Oxime Ethers 1:

Alkynyl oxime ethers were prepared according to the previously reported procedure[1].



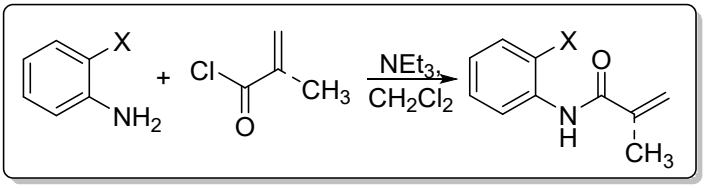
Step 1: To a 100 mL round-bottom flask, $Pd(PPh_3)_2Cl_2$ (2 mol %), CuI (2 mol %), and triethylamine (5 mL) were added. The flask was flushed with nitrogen for 3 min, and the terminal acetylene (6 mmol) was introduced into the reaction mixture, followed by drop-wise addition of acyl chloride (5 mmol). The mixture was stirred at room temperature for overnight. After the fully consumption of starting material by TLC detection, 30 mL of water was added and the resulting solution was extracted with ethyl acetate (3 × 20 mL). The solvent was removed under vacuum, and the residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to obtain alkynone B (85-90% yields).



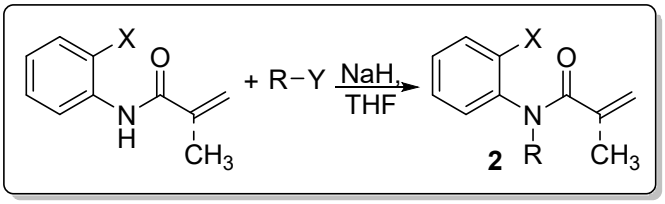
Step 2: Alkynone B (3.5 mmol), methoxylamine hydrochloride (7.0 mmol) anhydrous Na_2SO_4 (7.0 mmol), pyridine (1 mL), and methanol (10 mL) were added to a 50 mL round-bottom flask. The reaction mixture was stirred at room temperature for overnight. Reaction solvent was removed under vacuum and the mixture was diluted with saturated NH_4Cl solution (25 mL) and extracted with EtOAc (3 × 25 mL). The solvent was removed under vacuum, and the residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to give the desired products **1a-1y** in (45-85% yields).

General Procedure-B for the Preparation of N-(2-halo phenyl)-N-acrylamides:

acrylamides were prepared according to the previously reported procedure[2].

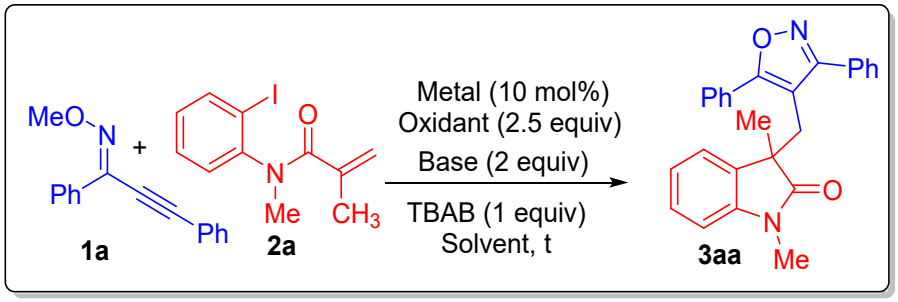


In a flame-dried round bottom was added the corresponding 2-haloaniline in dichloro methane (10 mL), and the solution was cooled to 0 °C. Triethylamine (2 equiv) was added followed by drop-wise addition of acryloyl chloride (1.2 equiv), allowing to warm up to room temperature overnight. The solution was concentrated and then poured into water and extracted with EtOAc , and the extracts were concentrated in vacuum. The crude mixture was taken to the next step without further purification.



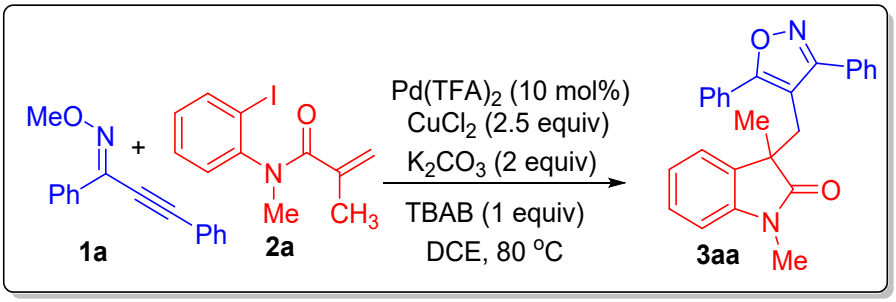
The corresponding acrylamide (1 equiv) was dissolved in THF (0.25 M), and cooled to 0 °C. A 60% dispersion of NaH in mineral oil (1.5 equiv) was added portion-wise and the solution stirred at 0 °C for 5 minutes. The solution was added the corresponding alkyl halide (1.2 equiv) dropwise, and the reaction was warmed to room temperature and stirred for 12 hours. A saturated NH_4Cl solution was added, followed by water and EtOAc and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and concentrated in vacuum. The crude product was purified by flash column silica gel chromatography to get the desired products **2a-2k** in 75-50% yield.

III. Optimisation studies:



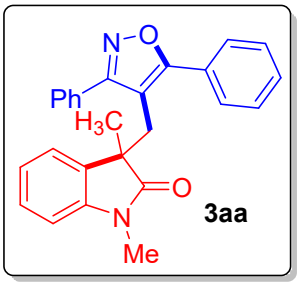
entry	metal	additive	base	solvent	temperature	yield of **3aa**
1	$Pd(PPh_3)_4$	$CuCl_2$	K_2CO_3	THF	60 °C	--
2	$PdCl2(PPh_3)_2$	$CuCl_2$	K_2CO_3	THF	60 °C	62%
3	---	$CuCl_2$	K_2CO_3	THF	60 °C	--
4	$Pd(TFA)_2$	CuI	K_2CO_3	THF	60 °C	traces
5	$Pd(TFA)_2$	Ag_2CO_3	K_2CO_3	THF	60 °C	--
6	$Pd(TFA)_2$	PIDA	K_2CO_3	THF	60 °C	--
7	$Pd(TFA)_2$	$CuCl_2.H_2O$	K_2CO_3	THF	60 °C	58%
8	$Pd(TFA)_2$	$CuCl_2$	Na_2CO_3	THF	60 °C	35%
9	$Pd(TFA)_2$	$CuCl_2$	Li_2CO_3	THF	60 °C	33%
10	$Pd(TFA)_2$	$CuCl_2$	Cs_2CO_3	THF	60 °C	15%
11	$Pd(TFA)_2$	$CuCl_2$	---	THF	60 °C	8%
12	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	DMF	100 °C	traces
13	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	NMP	120 °C	--
14	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	DCE	60 °C	65%
15	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	EtOH	80 °C	--
16	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	HFIP	60 °C	--
17	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	TCE	80 °C	12%
18	$Pd(TFA)_2$	$CuCl_2$	K_2CO_3	DCE	80 °C	78 %

IV. General Procedure-A for the Synthesis of final Products taking 3aa as an example and characteristic data:



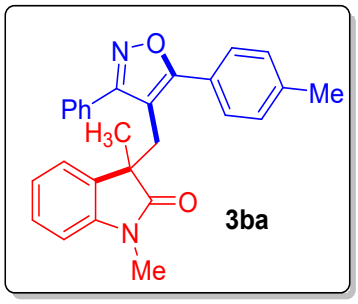
To a 25 mL dried reaction tube was added the mixture of $Pd(TFA)_2$ (10 mol %), $CuCl_2$ (2.5 equiv), TBAB (1.0 equiv), K_2CO_3 (2.0 equiv), alkynyl oxime ethers **1a** (0.45 mmol) and acrylamide **2a** (0.3 mmol) in DCE (3 mL) successively. The mixture was stirred at 80 °C for 10 hours under nitrogen atmosphere. After the reaction was completed, solvent was removed via rotary evaporator and diluted with H_2O (15 mL), and extracted with EtOAc (3 × 10 mL). Collected organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuum. The resulting crude was purified by flash column chromatography on silica gel with petroleum ether/ethyl acetate to give the desired products **3aa**.

3-((3,5-diphenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3aa):



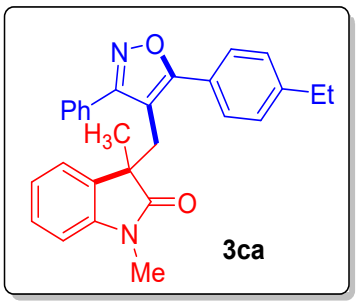
The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (92 mg, 78% yield), mp 210-212 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 – 7.49 (m, 2H), 7.46 – 7.39 (m, 8H), 7.05 (td, *J* = 7.7, 1.2 Hz, 1H), 6.63 – 6.54 (m, 2H), 6.37 (dd, *J* = 7.4, 0.7 Hz, 1H), 3.34 (s, 2H), 2.81 (s, 3H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.1, 167.8, 164.1, 142.6, 131.6, 129.7, 129.5, 129.2, 128.6, 128.6, 128.5, 128.4, 127.7, 127.6, 123.5, 122.1, 108.9, 107.4, 48.6, 30.1, 25.8, 22.8. **HRMS (Q-TOF)** calcd for $C_{26}H_{23}N_2O_2$ $[M+H]^+$ 395.1760, found 395.1765.

1,3-dimethyl-3-((3-phenyl-5-(p-tolyl)isoxazol-4-yl)methyl)indolin-2-one (3ba):



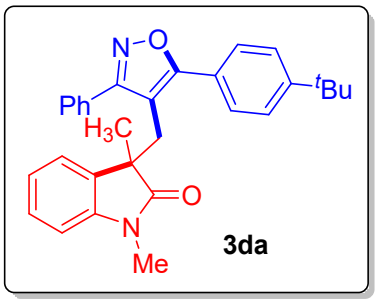
The title compound was prepared from **1b** (112 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.53 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (91 mg, 74% yield), mp 200-203 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 – 7.36 (m, 7H), 7.23 (d, J = 8.0 Hz, 2H), 7.05 (td, J = 7.7, 1.1 Hz, 1H), 6.66 – 6.55 (m, 2H), 6.38 (d, J = 7.2 Hz, 1H), 3.38 – 3.26 (m, 2H), 2.82 (s, 3H), 2.41 (s, 3H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.2, 168.1, 164.1, 142.7, 139.9, 131.7, 129.7, 129.3, 129.2, 128.6, 128.5, 127.7, 127.5, 125.6, 123.6, 122.1, 108.5, 107.4, 48.7, 30.1, 25.9, 22.9, 21.4. **HRMS (Q-TOF)** calcd for $C_{27}H_{25}N_2O_2$ $[M+H]^+$ 409.1916, found 409.1922.

3-((5-(4-ethylphenyl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3ca):



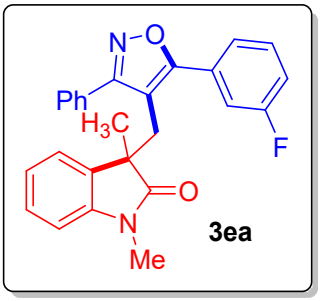
The title compound was prepared from **1c** (118 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.6 SiO_2, EtOAc:Hexane, 1:3) gave pure product as a sticky solid (90 mg, 71% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.45 (dd, J = 12.0, 8.6 Hz, 7H), 7.28 (s, 2H), 7.06 (t, J = 7.5 Hz, 1H), 6.65 – 6.57 (m, 2H), 6.40 (d, J = 7.3 Hz, 1H), 3.39 – 3.29 (m, 2H), 2.84 (s, 3H), 2.72 (q, J = 7.6 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H), 1.11 (s, 3H).**^{13}C NMR (125 MHz, $CDCl_3$)** δ 179.2, 168.1, 164.0, 146.1, 142.6, 131.7, 129.7, 129.2, 128.6, 128.5, 128.1, 127.7, 127.5, 125.8, 123.6, 122.1, 108.5, 107.4, 48.6, 30.1, 28.7, 25.8, 22.9, 15.3. **HRMS (ESI)** calcd for $C_{28}H_{27}N_2O_2$ $[M+H]^+$ 423.2073, found 423.2068.

3-((5-(4-(tert-butyl)phenyl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3da):



The title compound was prepared from **1d** (131 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.52 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a grey solid (97 mg, 72% yield), mp 215-218°C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43 (s, 9H), 7.04 (td, *J* = 7.7, 1.2 Hz, 1H), 6.63 – 6.55 (m, 2H), 6.39 (d, *J* = 6.7 Hz, 1H), 3.40 – 3.24 (m, 2H), 2.82 (s, 3H), 1.36 (s, 9H), 1.09 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.2, 167.9, 167.7, 164.1, 152.9, 142.6, 131.8, 129.7, 129.2, 128.6, 128.5, 127.7, 127.2, 125.5, 123.6, 122.1, 108.6, 107.4, 48.6, 34.8, 31.1, 30.1, 25.8, 22.8. **HRMS (ESI)** calcd for $C_{30}H_{31}N_2O_2$ $[M+H]^+$ 451.2386, found 451.2380.

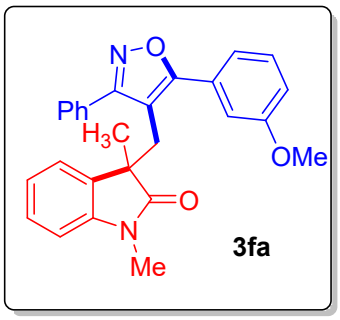
3-((5-(3-fluorophenyl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3ea):



The title compound was prepared from **1e** (114 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55 SiO_2, EtOAc:Hexane, 22:78) gave pure product as a sticky gel (84 mg, 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 – 7.36 (m, 6H), 7.33 – 7.29 (m, 1H), 7.17 – 7.09 (m, 2H), 7.06 (td, *J* = 7.7, 1.2 Hz, 1H), 6.61 (dd, *J* = 11.2, 4.3 Hz, 2H), 6.40 – 6.36 (m, 1H), 3.31 (s, 2H), 2.86 (s, 3H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.9, 166.4, 164.2, 163.7, 161.3, 142.7, 131.5, 130.2,

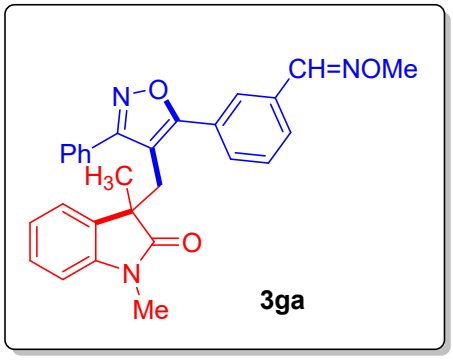
130.2, 129.4, 128.6, 127.9, 123.5, 123.2, 123.2, 122.1, 116.8, 116.6, 114.7, 114.5, 109.6, 107.5, 48.6, 30.1, 25.9, 22.7. **HRMS (ESI)** calcd for $C_{26}H_{22}FN_2O_2$ $[M+H]^+$ 413.1665, found 413.1663.

3-((5-(3-methoxyphenyl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3fa):



The title compound was prepared from **1f** (119 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 1:3) gave pure product as a sticky solid (94 mg, 74% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44 (s, 5H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.12 – 7.01 (m, 3H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.64 – 6.54 (m, 2H), 6.39 (d, *J* = 7.2 Hz, 1H), 3.85 (s, 3H), 3.33 (s, 2H), 2.82 (s, 3H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.1, 167.7, 164.1, 159.6, 142.7, 134.8, 131.7, 129.6, 129.5, 129.5, 129.2, 128.6, 128.5, 127.7, 123.6, 122.1, 119.9, 115.8, 112.9, 109.1, 107.4, 55.3, 48.6, 30.1, 25.9, 23.0. **HRMS (ESI)** calcd for $C_{27}H_{25}N_2O_3$ $[M+H]^+$ 425.1865, found 425.1867.

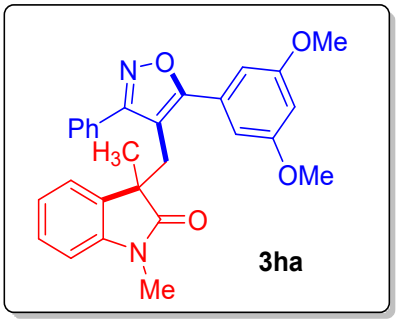
3-(4-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)-3-phenylisoxazol-5-yl)benzaldehyde O-methyl oxime (3ga):



The title compound was prepared from **1g** (131 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.53 SiO_2, EtOAc:Hexane, 18:82) gave pure product as a colourless oil (74 mg, 55% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.06 (s, 1H), 7.68 – 7.63 (m, 2H), 7.53 – 7.49 (m, 1H), 7.48 – 7.40 (m, 6H), 7.05

(td, *J* = 7.7, 1.1 Hz, 1H), 6.59 (t, *J* = 7.5 Hz, 2H), 6.39 (d, *J* = 7.1 Hz, 1H), 4.01 (s, 3H), 3.33 (s, 2H), 2.83 (s, 3H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.0, 167.1, 164.1, 147.5, 142.6, 132.6, 131.5, 129.4, 129.3, 128.9, 128.8, 128.6, 128.6, 127.9, 127.8, 126.2, 123.5, 122.1, 109.3, 107.5, 62.2, 48.6, 30.1, 25.9, 22.8, 14.1. **HRMS (ESI)** calcd for $C_{28}H_{26}N_3O_3$ $[M+H]^+$ 452.1974, found 452.1972.

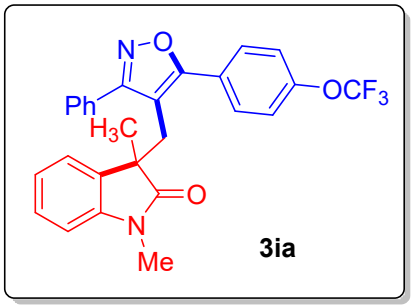
3-((5-(3,5-dimethoxyphenyl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3ha):



3ha

The title compound was prepared from **1h** (133 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.45 SiO_2, EtOAc:Hexane, 3:7) gave pure product as a pale brown solid (95 mg, 70% yield), mp 220-223 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44 (t, *J* = 4.6 Hz, 5H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.66 – 6.62 (m, 3H), 6.57 (d, *J* = 7.8 Hz, 1H), 6.52 (t, *J* = 2.2 Hz, 1H), 6.43 (d, *J* = 7.3 Hz, 1H), 3.82 (s, 6H), 3.33 (s, 2H), 2.84 (s, 3H), 1.11 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.1, 167.6, 164.0, 160.7, 142.6, 134.9, 131.7, 129.8, 129.5, 129.2, 128.6, 128.5, 127.7, 123.6, 122.1, 109.2, 107.4, 105.6, 102.1, 55.4, 48.5, 30.1, 25.8, 23.1. **HRMS (ESI)** calcd for $C_{28}H_{27}N_2O_4$ $[M+H]^+$ 455.1971, found 455.1971.

1,3-dimethyl-3-((3-phenyl-5-(4-(trifluoromethoxy)phenyl)isoxazol-4-yl)methyl)indolin-2-one (3ia):

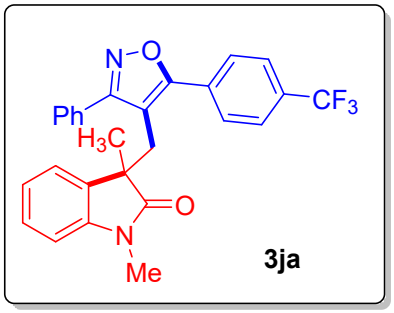


3ia

The title compound was prepared from **1i** (144 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.53 SiO_2, EtOAc:Hexane, 1:3) gave pure product as a pale yellow solid (90 mg, 63% yield), mp 190-195 °C.**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 6.2 Hz, 5H), 7.27 (d, *J* = 7.1 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.60 (t, *J* = 7.2 Hz, 2H), 6.39 (d, *J* = 7.1 Hz, 1H), 3.33 (s, 2H), 2.85 (s, 3H), 1.11 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.9, 166.3, 164.2, 149.9, 142.6,

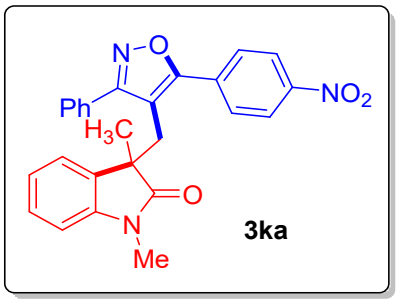
131.5, 129.4, 129.1, 128.7, 128.6, 127.9, 127.0, 123.5, 122.1, 120.9, 109.3, 107.5, 48.6, 30.1, 25.8, 22.7. **HRMS (ESI)** calcd for $C_{27}H_{22}F_3N_2O_3$ $[M+H]^+$ 479.1583, found 479.1579.

1,3-dimethyl-3-((3-phenyl-5-(4-(trifluoromethyl)phenyl)isoxazol-4-yl)methyl)indolin-2-one (3ja):



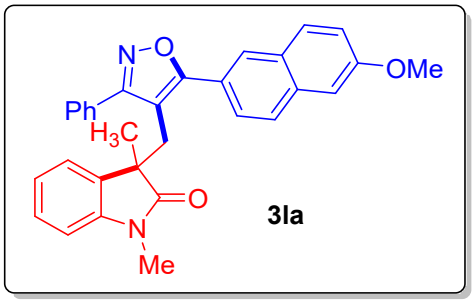
The title compound was prepared from **1j** (136 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a pale yellow sticky solid (80 mg, 58% yield). **^{1}H NMR(500 MHz, $CDCl_3$)** δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.49 – 7.46 (m, 3H), 7.45 – 7.42 (m, 2H), 7.05 (td, *J* = 7.7, 1.2 Hz, 1H), 6.62 – 6.52 (m, 2H), 6.42 – 6.33 (m, 1H), 3.34 (s, 2H), 2.83 (s, 3H), 1.11 (s, 3H).**^{13}C NMR (125 MHz, $CDCl_3$)** δ 178.9, 166.1, 164.4, 142.7, 131.7, 131.5, 129.5, 129.2, 128.7, 128.1, 127.8, 125.6, 125.5, 123.5, 122.2, 110.2, 107.6, 48.6, 30.2, 25.9, 22.8. **HRMS (ESI)** calcd for $C_{27}H_{22}F_3N_2O_2$ $[M+H]^+$ 463.1633, found 463.1632.

1,3-dimethyl-3-((5-(4-nitrophenyl)-3-phenylisoxazol-4-yl)methyl)indolin-2-one (3ka):



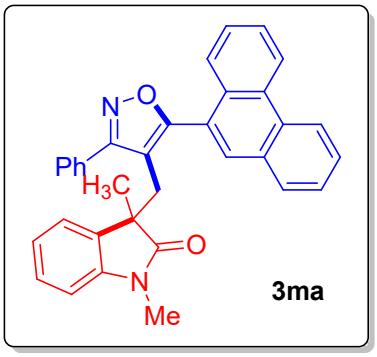
The title compound was prepared from **1k** (126 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (79 mg, 60 % yield), mp 185-190 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.27 (d, *J* = 8.7 Hz, 2H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 4.9 Hz, 3H), 7.43 – 7.39 (m, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.62 – 6.53 (m, 2H), 6.36 (d, *J* = 7.3 Hz, 1H), 3.36 (s, 2H), 2.85 (s, 3H), 1.12 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.7, 165.1, 164.5, 148.1, 142.6, 134.2, 131.2, 129.6, 129.0, 128.7, 128.6, 128.2, 128.1, 123.7, 123.4, 122.3, 111.1, 107.6, 48.6, 30.2, 25.9, 22.7. **HRMS (ESI)** calcd for $C_{26}H_{22}N_3O_4$ $[M+H]^+$ 440.1610, found 440.1606.

3-((5-(6-methoxynaphthalen-2-yl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3la):



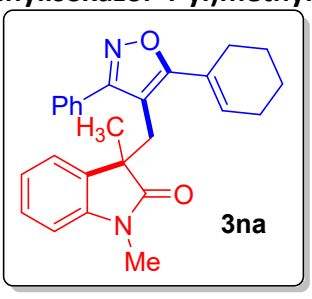
The title compound was prepared from **1l** (142 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 1:3) gave pure product as a pale brown solid (90 mg, 63% yield), mp 215-218 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (s, 1H), 7.75 (dd, *J* = 17.2, 8.8 Hz, 2H), 7.58 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.46 (s, 5H), 7.20 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.15 (d, *J* = 2.3 Hz, 1H), 7.03 (td, *J* = 7.7, 1.2 Hz, 1H), 6.57 (ddd, *J* = 8.3, 6.5, 2.7 Hz, 2H), 6.40 (d, *J* = 6.8 Hz, 1H), 3.96 (s, 3H), 3.39 (q, *J* = 14.9 Hz, 2H), 2.79 (s, 3H), 1.09 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.2, 168.1, 164.1, 158.7, 142.6, 134.9, 131.8, 130.1, 129.7, 129.2, 128.6, 128.5, 128.2, 127.8, 127.2, 127.1, 125.0, 123.7, 123.4, 122.1, 119.5, 108.8, 107.4, 105.6, 55.3, 48.6, 30.2, 25.8, 22.9. **HRMS (ESI)** calcd for $C_{31}H_{27}N_2O_3$ $[M+H]^+$ 475.2022, found 475.2017.

1,3-dimethyl-3-((5-(phenanthren-9-yl)-3-phenylisoxazol-4-yl)methyl)indolin-2-one (3ma):



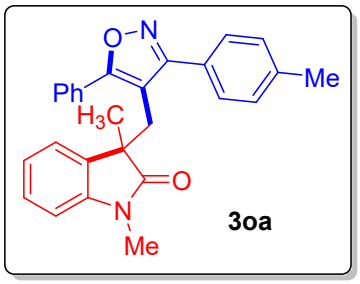
The title compound was prepared from **1m** (151 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (87 mg, 59% yield), mp 200-203 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.83 – 8.69 (m, 2H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.79 – 7.55 (m, 8H), 7.52 (d, *J* = 3.5 Hz, 3H), 6.92 (t, *J* = 7.4 Hz, 1H), 6.41 (dd, *J* = 15.8, 7.7 Hz, 2H), 6.30 (d, *J* = 7.1 Hz, 1H), 3.39 (d, *J* = 14.9 Hz, 1H), 3.25 (d, *J* = 14.8 Hz, 1H), 2.49 (s, 3H), 1.03 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.7, 167.9, 163.8, 142.6, 131.7, 131.1, 130.7, 130.5, 130.1, 129.7, 129.6, 129.3, 129.3, 128.8, 128.6, 128.1, 127.5, 127.1, 127.0, 126.3, 124.2, 123.2, 122.8, 122.6, 121.9, 111.9, 107.4, 48.4, 30.1, 25.5, 24.2. **HRMS (ESI)** calcd for $C_{34}H_{27}N_2O_2$ $[M+H]^+$ 495.2073, found 495.2067.

3-((5-(cyclohex-1-en-1-yl)-3-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3na):



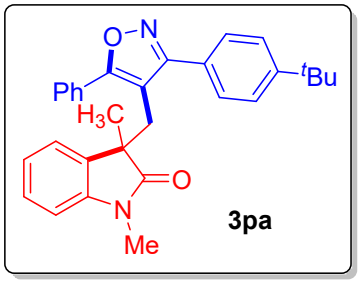
The title compound was prepared from **1n** (108 mg, 0.45 mmol) and **2a** (90 mg, 0.5 mmol) according to general procedure **A**. Purification using column chromatography (R_f= 0.50 SiO_2, EtOAc:Hexane, 18:82) gave pure product as a sticky solid (62 mg, 52% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44 – 7.39 (m, 3H), 7.37 – 7.34 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 6.51 (d, *J* = 7.3 Hz, 1H), 6.16 (s, 1H), 3.30 – 3.07 (m, 2H), 3.01 (s, 3H), 2.24 – 2.12 (m, 5H), 1.67 (d, *J* = 6.2 Hz, 3H), 1.12 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.4, 169.8, 163.7, 142.7, 131.9, 129.9, 129.1, 128.6, 128.5, 127.7, 127.1, 123.7, 122.1, 107.4, 107.3, 48.8, 29.9, 26.1, 25.5, 22.5, 22.1, 21.4. **HRMS (ESI)** calcd for $C_{26}H_{27}N_2O_2$ $[M+H]^+$ 399.2073, found 399.2063.

1,3-dimethyl-3-((5-phenyl-3-(p-tolyl)isoxazol-4-yl)methyl)indolin-2-one (3oa):



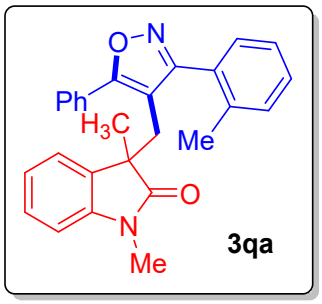
The title compound was prepared from **1o** (112 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.52 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a sticky solid (88 mg, 72% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.51 (d, *J* = 3.4 Hz, 2H), 7.44 (d, *J* = 3.0 Hz, 3H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 1.8 Hz, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.65 – 6.57 (m, 2H), 6.40 (d, *J* = 7.2 Hz, 1H), 3.34 (s, 2H), 2.84 (s, 3H), 2.44 (s, 3H), 1.11 (s, 3H).**^{13}C NMR (125 MHz, $CDCl_3$)** δ 179.1, 167.6, 164.1, 142.6, 139.2, 131.7, 129.6, 129.2, 128.5, 127.7, 127.5, 126.6, 123.6, 122.1, 108.9, 107.4, 48.6, 30.1, 25.8, 22.9, 21.4. **HRMS (ESI**) calcd for $C_{27}H_{25}N_2O_2$ $[M+H]^+$ 409.1916, found 409.1913.

3-((3-(4-(tert-butyl)phenyl)-5-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3pa):



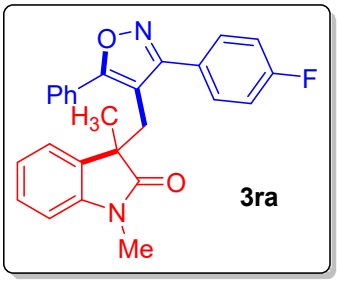
The title compound was prepared from **1p** (131 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.54 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a grey solid (95 mg, 70% yield), mp 210-212°C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.57 – 7.51 (m, 2H), 7.47 – 7.40 (m, 5H), 7.33 (d, J = 8.4 Hz, 2H), 7.08 – 7.01 (m, 1H), 6.59 (ddd, J = 21.6, 10.8, 4.3 Hz, 2H), 6.40 – 6.35 (m, 1H), 3.38 – 3.30 (m, 2H), 2.81 (s, 3H), 1.37 (s, 9H), 1.10 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 179.2, 167.7, 164.0, 152.3, 142.6, 131.8, 129.7, 128.6, 128.5, 128.3, 127.7, 127.6, 126.6, 125.5, 123.6, 122.1, 109.1, 107.4, 48.6, 34.7, 31.3, 30.1, 25.9, 22.9. **HRMS (ESI)** calcd for $C_{30}H_{31}N_2O_2$ $[M+H]^+$ 451.2386, found 451.2380.

1,3-dimethyl-3-((5-phenyl-3-(o-tolyl)isoxazol-4-yl)methyl)indolin-2-one (3qa):



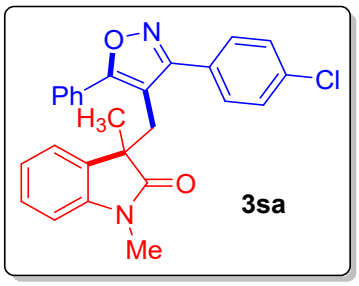
The title compound was prepared from **1q** (112 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.6 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a colourless gel (73 mg, 60% yield). **^{1}H NMR (500 MHz, $CDCl_3$)**δ 7.52 (dd, J = 6.6, 2.9 Hz, 2H), 7.44 – 7.40 (m, 3H), 7.38 – 7.32 (m, 1H), 7.31 – 7.23 (m, 2H), 7.14 (d, J = 7.4 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 6.67 (t, J = 7.5 Hz, 1H), 6.61 (d, J = 7.7 Hz, 1H), 6.43 (d, J = 7.3 Hz, 1H), 3.17 (dd, J = 33.2, 14.8 Hz, 2H), 2.85 (s, 3H), 2.20 (s, 3H), 1.07 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 179.1, 167.3, 164.0, 142.8, 137.2, 131.9, 130.6, 130.1, 129.7, 129.3, 128.5, 128.5, 127.8, 127.5, 125.6, 123.5, 122.3, 109.9, 107.5,48.4, 30.1, 29.7, 26.0, 23.5, 20.1. **HRMS (ESI)** calcd for $C_{27}H_{25}N_2O_2$ $[M+H]^+$ 409.1916, found 409.1907.

3-((3-(4-fluorophenyl)-5-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3ra):



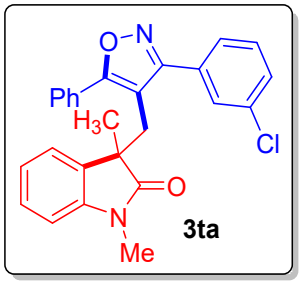
The title compound was prepared from **1r** (114 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 18:82) gave pure product as a white solid (84 mg, 68% yield), mp 220-223 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56 – 7.35 (m, 7H), 7.12 (t, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.60 (dd, *J* = 16.0, 7.7 Hz, 2H), 6.38 (d, *J* = 7.1 Hz, 1H), 3.31 (s, 2H), 2.83 (s, 3H), 1.11 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.9, 168.1, 164.5, 163.2, 162.1, 142.7, 131.6, 130.5, 130.4, 129.8, 128.6, 128.3, 127.8, 127.6, 125.7, 123.5, 122.1, 115.7, 115.5, 108.8, 107.4, 48.6, 30.1, 25.9, 22.9. **HRMS (ESI)** calcd for $C_{26}H_{22}FN_2O_2$ $[M+H]^+$ 413.1665, found 413.1658.

3-((3-(4-chlorophenyl)-5-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3sa):



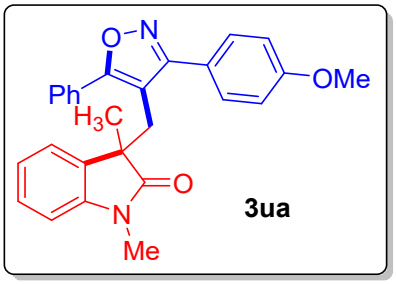
The title compound was prepared from **1s** (108 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.60 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (85 mg, 66% yield), mp 182-185 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.56 – 7.50 (m, 2H), 7.48 – 7.43 (m, 3H), 7.42 – 7.39 (m, 2H), 7.36 – 7.31 (m, 2H), 7.06 (td, *J* = 7.7, 1.2 Hz, 1H), 6.60 (ddd, *J* = 12.7, 9.7, 4.3 Hz, 2H), 6.39 (dd, *J* = 7.4, 0.7 Hz, 1H), 3.35 – 3.27 (m, 2H), 2.83 (s, 3H), 1.12 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 178.9, 168.2, 163.1, 142.7, 135.4, 131.5, 129.9, 128.8, 128.6, 128.2, 128.1, 127.9, 127.6, 123.4, 122.1, 108.8, 107.5, 48.6, 30.1, 25.9, 23.0. **HRMS (ESI)** calcd for $C_{26}H_{22}ClN_2O_2$ $[M+H]^+$ 429.1370, found 429.1351.

3-((3-(3-chlorophenyl)-5-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3ta):



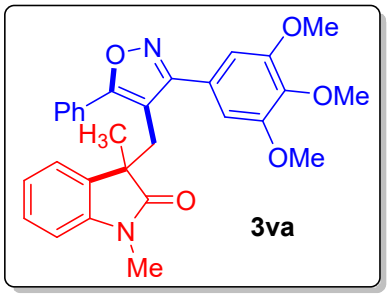
The title compound was prepared from **1t** (108 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.60 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (86 mg, 67% yield), mp 179-182 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.58 – 7.54 (m, 2H), 7.50 – 7.45 (m, 3H), 7.42 – 7.39 (m, 1H), 7.38 – 7.34 (m, 1H), 7.29 – 7.27 (m, 2H), 7.08 (td, *J* = 7.7, 1.2 Hz, 1H), 6.70 – 6.53 (m, 2H), 6.37 (dd, *J* = 7.4, 0.8 Hz, 1H), 3.37 – 3.24 (m, 2H), 2.84 (s, 3H), 1.14 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 178.9, 168.3, 162.9, 142.8, 134.5, 131.4, 131.3, 130.1, 129.7, 129.4, 128.8, 128.7, 128.3, 127.9, 127.7, 126.7, 123.5, 122.1, 108.9, 107.6, 48.7, 30.2, 25.9, 23.1. **HRMS (ESI)** calcd for $C_{26}H_{22}ClN_2O_2$ $[M+H]^+$ 429.1370, found 429.1375.

3-((3-(4-methoxyphenyl)-5-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3ua):



The title compound was prepared from **1u** (119 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 1:3) gave pure product as a white solid (93 mg, 73% yield), mp 215-218 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40 (dd, *J* = 39.4, 19.7 Hz, 7H), 7.08 – 6.93 (m, 3H), 6.66 – 6.55 (m, 2H), 6.39 (d, *J* = 7.1 Hz, 1H), 3.87 (s, 3H), 3.33 (s, 2H), 2.83 (s, 3H), 1.11 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.2, 167.6, 163.7, 160.3, 142.6, 133.4, 131.7, 130.1, 129.9, 129.6, 128.5, 128.4, 128.3, 127.7, 127.5, 123.6, 122.1, 121.9, 114.0, 113.6, 108.9, 107.4, 55.3, 48.6, 30.1, 25.9, 22.9. **HRMS (ESI)** calcd for $C_{27}H_{25}N_2O_3$ $[M+H]^+$ 425.1865, found 425.1858.

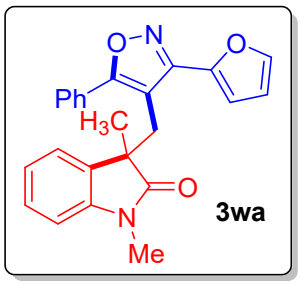
1,3-dimethyl-3-((5-phenyl-3-(3,4,5-trimethoxyphenyl)isoxazol-4-yl)methyl)indolin-2-one (3va):



The title compound was prepared from **1v** (146 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.45 SiO_2, EtOAc:Hexane, 2:3) gave pure product as a brown solid (100 mg, 69% yield), mp 225-227°C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.67 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 6.1 Hz, 3H), 6.45 (d, *J* = 7.3 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 6H), 3.41 – 3.31 (m, 2H), 2.84 (s, 3H), 1.15 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.2, 167.9, 163.8, 153.2, 142.7, 138.8, 131.8, 129.9, 128.7, 128.3, 127.7, 127.6, 124.8,

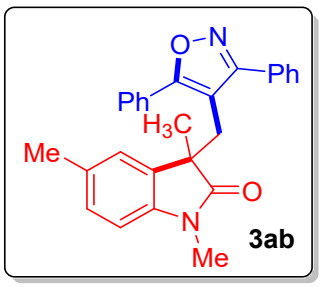
123.6, 122.1, 109.1, 107.5, 105.8, 60.9, 56.2, 48.5, 30.1, 25.8, 23.6. **HRMS (ESI)** calcd for $C_{29}H_{29}N_2O_5$ $[M+H]^+$ 485.2076, found 485.2081.

3-((3-(furan-2-yl)-5-phenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3wa):



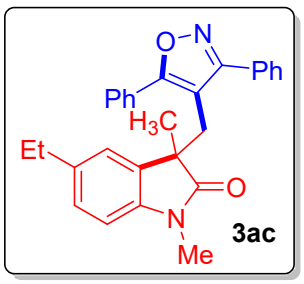
The title compound was prepared from **1w** (101 mg, 0.45 mmol) and **2a** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f= 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a pale yellow gel (61 mg, 53% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.53 (dd, *J* = 6.5, 2.8 Hz, 2H), 7.49 (d, *J* = 0.8 Hz, 1H), 7.44 – 7.42 (m, 3H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.75 (d, *J* = 3.4 Hz, 1H), 6.61 (dd, *J* = 13.7, 7.4 Hz, 2H), 6.53 (d, *J* = 7.3 Hz, 1H), 6.48 – 6.45 (m, 1H), 3.53 (d, *J* = 14.7 Hz, 1H), 3.38 (d, *J* = 14.7 Hz, 1H), 2.94 (s, 3H), 1.19 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.4, 167.9, 155.6, 144.4, 143.3, 142.6, 132.1, 130.8, 129.8, 128.7, 128.6, 128.1, 127.7, 127.5, 123.3, 122.1, 111.4, 110.5, 108.5, 107.4, 68.1, 48.6, 38.7, 30.1, 25.9, 21.7. **HRMS (ESI)** calcd for $C_{24}H_{21}N_2O_3$ $[M+H]^+$ 385.1552, found 385.1549.

3-((3,5-diphenylisoxazol-4-yl)methyl)-1,3,5-trimethylindolin-2-one (3ab):



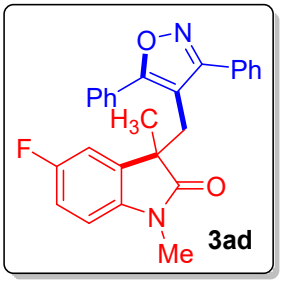
The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2b** (95 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.53 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (83 mg, 68% yield), mp 207-209 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59 – 7.52 (m, 2H), 7.49 – 7.41 (m, 8H), 6.83 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.45 (d, *J* = 7.9 Hz, 1H), 6.17 (s, 1H), 3.35 (q, *J* = 14.8 Hz, 2H), 2.77 (s, 3H), 2.01 (s, 3H), 1.09 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.9, 167.8, 164.1, 140.4, 131.7, 131.3, 129.7, 129.7, 129.2, 128.6, 128.1, 127.5, 124.6, 108.9, 107.2, 48.8, 30.2, 25.9, 22.9, 21.1. **HRMS (ESI)** calcd for $C_{27}H_{25}N_2O_2$ $[M+H]^+$ 409.1916, found 409.1916.

3-((3,5-diphenylisoxazol-4-yl)methyl)-5-ethyl-1,3-dimethylindolin-2-one (3ac):



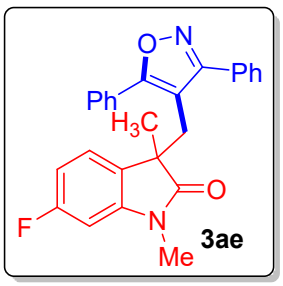
The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2c** (99 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a pale yellow solid (84 mg, 66% yield), mp 202-205 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51 (dt, *J* = 4.9, 2.9 Hz, 2H), 7.42 (dd, *J* = 8.8, 5.3 Hz, 8H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 7.9 Hz, 1H), 6.24 (s, 1H), 3.43 – 3.24 (m, 2H), 2.81 (s, 3H), 2.31 (dt, *J* = 15.0, 7.3 Hz, 2H), 1.08 (s, 3H), 1.01 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.2, 167.7, 164.1, 140.6, 138.0, 134.8, 131.8, 129.7, 129.3, 128.6, 128.4, 127.9, 127.4, 126.9, 123.5, 109.1, 107.3, 48.8, 30.1, 28.3, 25.9, 22.9, 15.5. **HRMS (ESI)** calcd for $C_{28}H_{27}N_2O_2$ $[M+H]^+$ 423.2073, found 423.2065.

3-((3,5-diphenylisoxazol-4-yl)methyl)-5-fluoro-1,3-dimethylindolin-2-one (3ad):



The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2d** (95 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.50 SiO_2, EtOAc:Hexane, 18:82) gave pure product as a brown solid (80 mg, 65% yield), mp 172-175 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 – 7.53 (m, 2H), 7.50 – 7.44 (m, 6H), 7.42 (dd, *J* = 6.8, 3.0 Hz, 2H), 6.76 – 6.69 (m, 1H), 6.46 (dd, *J* = 8.5, 4.1 Hz, 1H), 6.04 (dd, *J* = 7.9, 2.6 Hz, 1H), 3.40 (d, *J* = 14.8 Hz, 2H), 3.32 (d, *J* = 14.8 Hz, 2H), 2.78 (s, 3H), 1.11 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.6, 168.1, 164.0, 159.5, 157.6, 138.7, 133.2, 129.9, 129.4, 129.4, 128.7, 128.7, 128.5, 128.3, 127.6, 114.1, 114.0, 112.1, 111.9, 108.4, 107.8, 107.7, 49.2, 30.1, 26.1, 22.7. **HRMS (ESI)** calcd for $C_{26}H_{22}FN_2O_2$ $[M+H]^+$ 413.1665, found 413.1658.

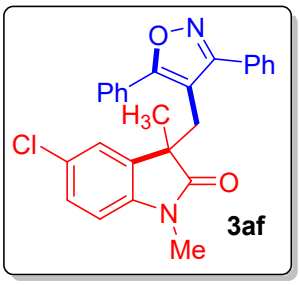
3-((3,5-diphenylisoxazol-4-yl)methyl)-6-fluoro-1,3-dimethylindolin-2-one (3ae):



The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2e** (95 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f= 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a pale yellow solid (79 mg, 64% yield), mp 178-181 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (s, 1H), 7.54 (d, J = 3.5 Hz, 2H), 7.44 (d, J = 7.9 Hz, 7H),

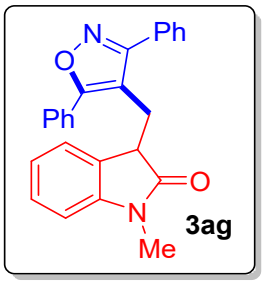
6.32 – 6.17 (m, 3H), 3.39 – 3.29 (m, 2H), 2.79 (s, 3H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 179.3, 167.9, 164.0, 163.7, 161.7, 144.2, 144.1, 134.9, 129.9, 129.5, 129.4, 128.7, 128.6, 128.6, 128.3, 127.6, 126.8, 124.5, 124.4, 108.7, 108.1, 107.9, 96.4, 96.1, 48.3, 30.2, 26.0, 22.9. **HRMS (ESI)** calcd for $C_{26}H_{22}FN_2O_2$ $[M+H]^+$ 413.1665, found 413.1657.

5-chloro-3-((3,5-diphenylisoxazol-4-yl)methyl)-1,3-dimethylindolin-2-one (3af):



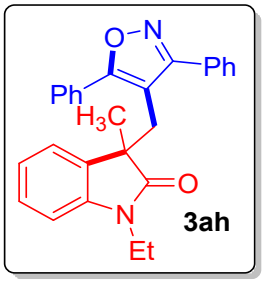
The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2f** (100 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a brown solid (80 mg, 62% yield), mp 182-185 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.58 – 7.55 (m, 2H), 7.51 – 7.42 (m, 8H), 7.00 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.46 (d, *J* = 8.2 Hz, 1H), 6.30 (d, *J* = 2.1 Hz, 1H), 3.41 (d, *J* = 14.8 Hz, 1H), 3.31 (d, *J* = 14.8 Hz, 1H), 2.75 (s, 3H), 1.11 (s, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 178.4, 168.1, 163.9, 141.3, 133.2, 129.9, 129.4, 129.3, 128.7, 128.7, 128.5, 128.2, 127.8, 127.5, 127.3, 124.2, 108.3, 108.3, 49.1, 30.1, 25.9, 22.7. **HRMS (ESI)** calcd for $C_{26}H_{22}ClN_2O_2$ $[M+H]^+$ 429.1370, found 429.1370.

3-((3,5-diphenylisoxazol-4-yl)methyl)-1-methylindolin-2-one (3ag):



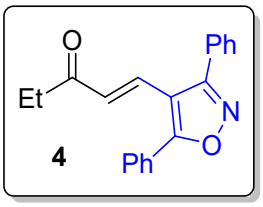
The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2g** (86 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.55 SiO_2, EtOAc:Hexane, 18:82) gave pure product as a pale brown gel (64 mg, 56% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73 – 7.58 (m, 4H), 7.46 (d, J = 19.2 Hz, 6H), 7.16 (t, J = 7.6 Hz, 1H), 6.80 (t, J = 7.5 Hz, 1H), 6.72 (d, J = 7.7 Hz, 1H), 6.58 (d, J = 7.3 Hz, 1H), 3.66 (dd, J = 15.0, 4.9 Hz, 1H), 3.48 (dd, J = 11.1, 4.8 Hz, 1H), 3.10 (s, 3H), 2.91 (dd, J = 14.8, 11.4 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 176.4, 167.2, 163.7, 143.9, 130.0, 129.6, 129.2, 129.1, 128.9, 128.9, 128.7, 128.4, 128.1, 128.0, 127.6, 127.4, 124.2, 122.3, 110.4, 108.0, 43.4, 26.1, 24.5. **HRMS (ESI)** calcd for $C_{25}H_{21}N_2O_2$ $[M+H]^+$ 381.1603, found 381.1594.

3-((3,5-diphenylisoxazol-4-yl)methyl)-1-ethyl-3-methylindolin-2-one (3ah):



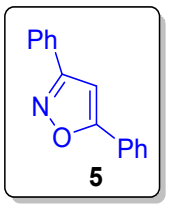
The title compound was prepared from **1a** (106 mg, 0.45 mmol) and **2h** (90 mg, 0.3 mmol) according to general procedure **A**. Purification using column chromatography (R_f= 0.55 SiO_2, EtOAc:Hexane, 1:4) gave pure product as a white solid (80 mg, 65% yield), mp 151-154 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 – 7.51 (m, 2H), 7.45 – 7.37 (m, 8H), 7.03 (td, J = 7.7, 1.2 Hz, 1H), 6.64 – 6.55 (m, 2H), 6.41 (d, J = 6.7 Hz, 1H), 3.48 – 3.35 (m, 2H), 3.33 (d, J = 5.4 Hz, 1H), 3.28 (d, J = 14.8 Hz, 1H), 1.08 (s, 3H), 1.02 (t, J = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.7, 167.9, 164.2, 141.7, 131.9, 129.7, 129.2, 128.6, 127.7, 127.5, 123.8, 122.1, 108.9, 107.6, 48.6, 34.2, 30.0, 22.8, 12.4. **HRMS (ESI)** calcd for $C_{27}H_{25}N_2O_2$ $[M+H]^+$ 409.1916, found 409.1915.

1-(3,5-diphenylisoxazol-4-yl)pent-1-en-3-one (4):



The title compound was prepared from **1a** (118 mg, 0.5 mmol) and **2m** (63 mg, 0.75 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.5 SiO_2, EtOAc:Hexane, 5:95) gave pure product as a off white solid (95 mg, 63% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.77 – 7.72 (m, 2H), 7.62 – 7.57 (m, 2H), 7.53 (ddd, J = 9.0, 6.1, 3.8 Hz, 7H), 6.29 (d, J = 16.3 Hz, 1H), 2.43 (q, J = 7.3 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 200.1, 169.5, 162.4, 130.9, 130.1, 129.6, 129.2, 128.9, 128.8, 128.7, 128.1, 127.2, 110.6, 34.9, 7.9. **Mass (ESI)** calcd for $[M+H]^+$, found 304.

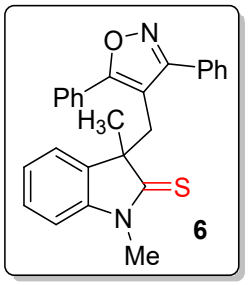
3,5-diphenylisoxazole (5):



The title compound was prepared from **1a** (118 mg, 0.5 mmol) according to general procedure **A**. Purification using column chromatography (R_f = 0.52 SiO_2, EtOAc:Hexane, 5:95) gave pure product as a pale yellow solid (46 mg, 42% yield). **^{1}H NMR (400 MHz, $CDCl_3$)** 1H NMR (400 MHz, CDCl3) δ 7.91 – 7.82 (m, 4H), 7.53 – 7.43 (m, 6H), 6.84 (s, 1H). **Mass (ESI)** calcd for $[M+H]^+$, found 222. Matched with previous literature data[3].

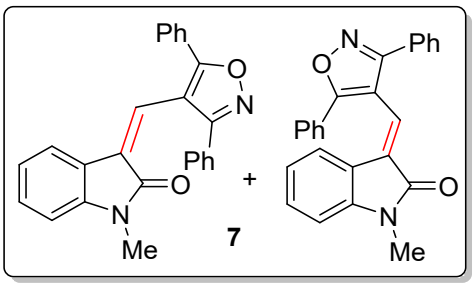
V. General Procedure and Characteristic data of derivatives:

3-((3,5-diphenylisoxazol-4-yl)methyl)-1,3-dimethylindoline-2-thione (6):



6 (98 mg) was synthesized using the following procedure: a mixture of **3aa** (118 mg, 0.3 mmol) and Lawesson's reagent (145 mg, 0.36 mmol) in toluene (10 mL) was refluxed at 100 °C (oil bath temperature) in a round-bottom flask. After completion of reaction (monitored by TLC) (4 h), it was cooled to room temperature, and the volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography: yield 80%; pale yellow solid; mp 201−203 °C; R_f = 0.50 (SiO2, EtOAc:Hexane, 18:82). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50 – 7.46 (m, 2H), 7.43 – 7.36 (m, 8H), 7.10 (td, J = 7.8, 1.2 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 6.73 (td, J = 7.5, 0.8 Hz, 1H), 6.54 – 6.50 (m, 1H), 3.60 (d, J = 14.9 Hz, 1H), 3.39 (s, 3H), 3.15 (d, J = 14.9 Hz, 1H), 1.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 209.7, 168.0, 164.3, 144.0, 136.3, 129.8, 129.7, 129.3, 128.7, 128.6, 128.6, 128.5, 127.9, 127.6, 124.3, 123.8, 109.3, 108.9, 59.1, 33.4, 31.3, 26.1. **HRMS (ESI)** calcd for $C_{26}H_{23}N_2OS$ $[M+H]^+$ 411.1531, found 411.1524.

3-((3,5-diphenylisoxazol-4-yl)methylene)-1-methylindolin-2-one (Z & E isomers (1:4)) (7):



To a solution of **3ag** (0.3 mmol) in 1,4 dioxane (3.0 mL), DDQ (0.45 mmol, 102 mg) was added into the reaction mixture at room temperature and it was stirred at 80 °C for overnight. After completion of the reaction (detected by TLC), the reaction mixture was quenched with 10% NaOH (15.0 mL), the mixture was extracted with ethyl acetate, solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to provide the desired product in 75% yield (85 mg). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.83 – 7.76 (m, 3H), 7.75 (s, 1H), 7.73 – 7.66 (m, 2.6H), 7.56 (d, J = 7.4 Hz, 0.4H), 7.46 – 7.30 (m, 9H), 7.14 (td, J = 7.8, 0.8 Hz, 1H), 7.08 (t, J = 7.6 Hz, 0.3H), 6.86 (d, J = 7.5 Hz, 1H), 6.77 (d, J = 7.8 Hz, 0.3H), 6.73 – 6.64 (m, 2H), 3.26 (s, 3H), 3.01 (s, 0.75H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.3, 166.8, 162.3, 144.0, 131.8, 130.6, 130.2, 130.0, 129.7, 129.4, 129.0, 128.8, 128.8, 128.6, 128.4, 127.9, 127.5, 126.9, 126.7, 123.7, 123.4, 122.4, 122.1, 121.8,

120.4, 119.9, 108.6, 108.1, 107.9, 77.3, 77.1, 76.7, 26.2, 25.7. **HRMS (ESI)** calcd for $C_{25}H_{19}N_2O_2$ $[M+H]^+$ 379.1447, found 379.1435.

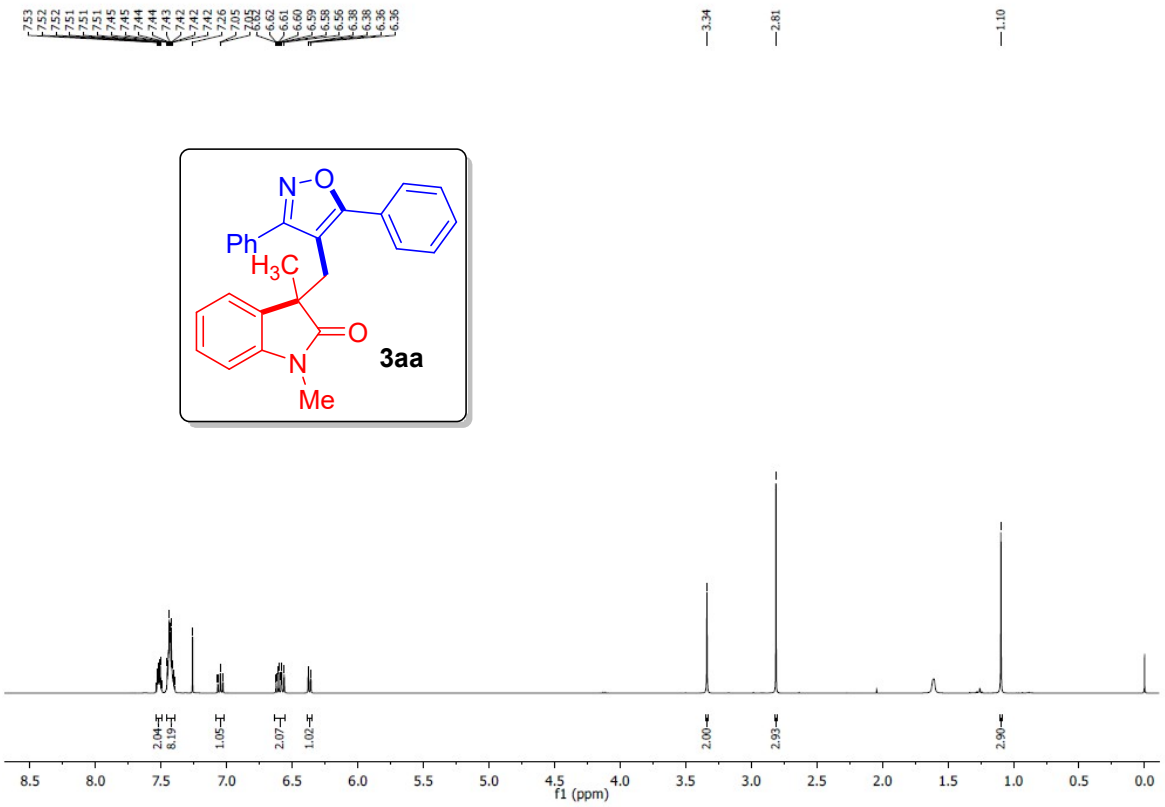
VI. References:

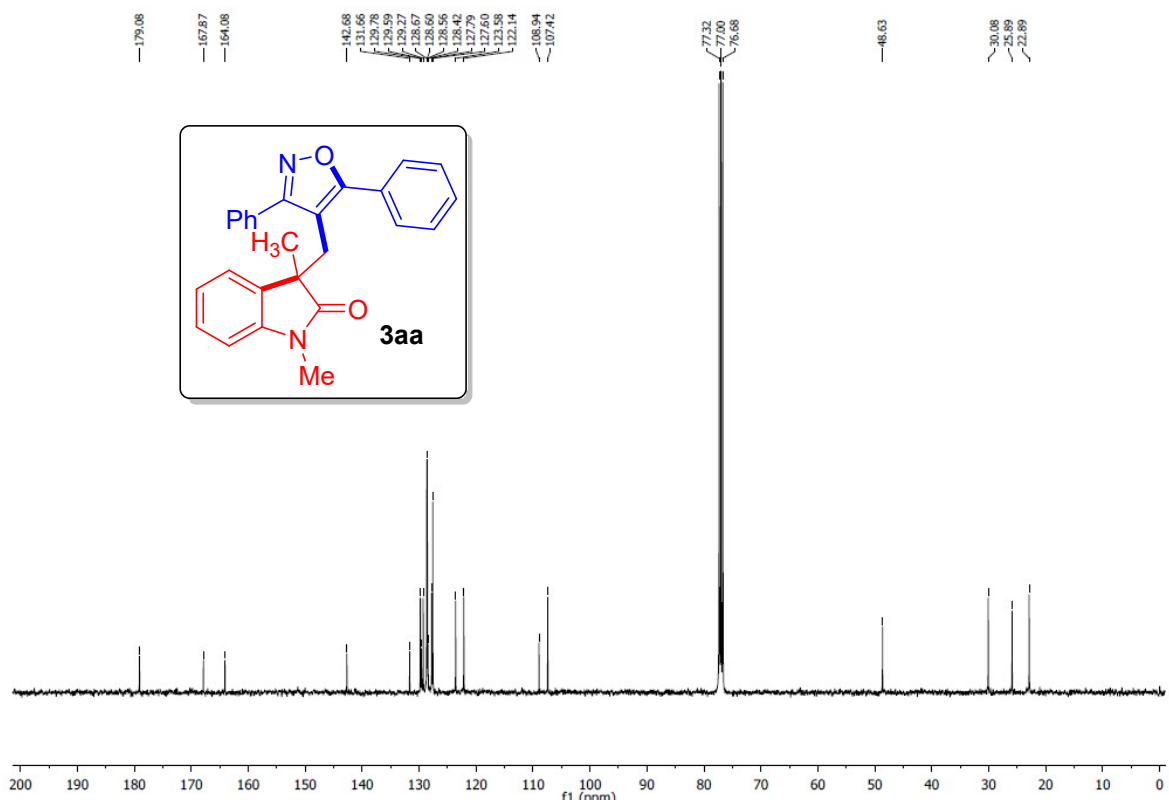
1. (a) W. Wu, C. Li, F. Zhou, J. Li, X. Xu and H. Jiang, *Adv. Synth. Catal.,* 2019, **361**, 3813–3823. (b) A. Sperança, B. Godoi and G. Zeni, *J. Org. Chem.*, 2013, **78**, 1630−1637. (c) F. Zhou, C. Li, M. Li, Y. Jin, H. Jiang, Y. Zhang and W. Wu, *Chem. Commun.,* 2021, **57**, 4799-4802.

2. (a) X.-X. Wu, W.-L. Chen, Y. Shen, S. Chen, P.-F. Xu, Y.-M. Liang, *Org. Lett*., 2016, **18**, 1784−1787. (b) N. Saha, H. Wang, S. Zhang, Y. Du, D. Zhu, Y. Hu, P. Huang, S. Wen, *Org. Lett.,* 2018, **20**, 712−715.

3. M. Ueda, Y. Ikeda, A. Sato, Y. Ito, M. Kakiuchi, H. Shono, T. Miyoshi, T. Naito, O. Miyata, *Tetrahedron*, 2011, **67**, 4612-4615.

VII. Copies of ^{1}H and ^{13}C NMR spectra:






7.44
7.43
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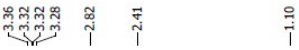
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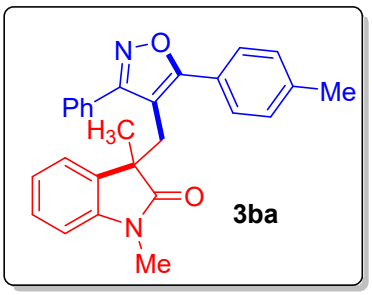
2.41
1.10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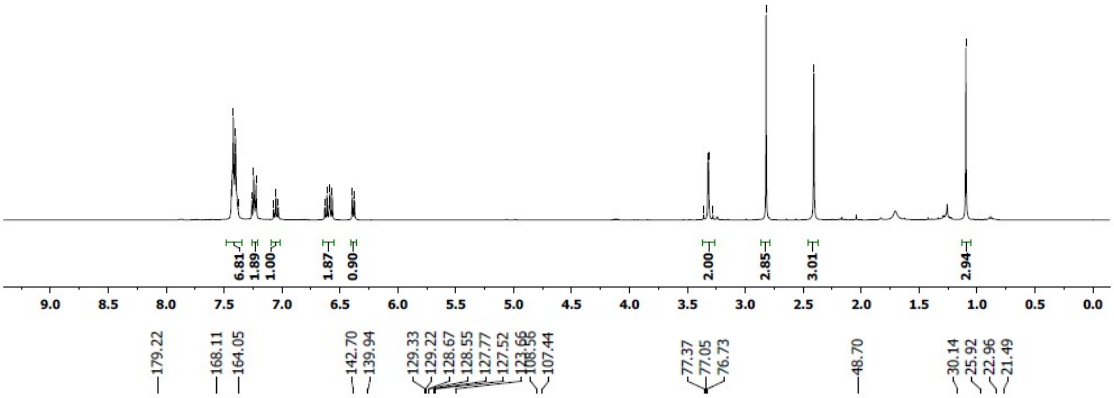
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1.5
1.0
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127.77
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123.66
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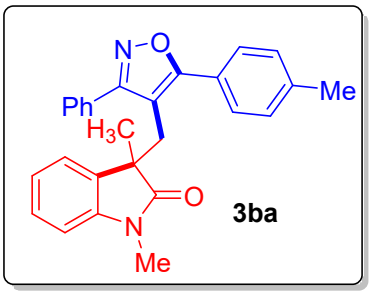
77.05
76.73
48.70
30.14
25.92
22.96
21.49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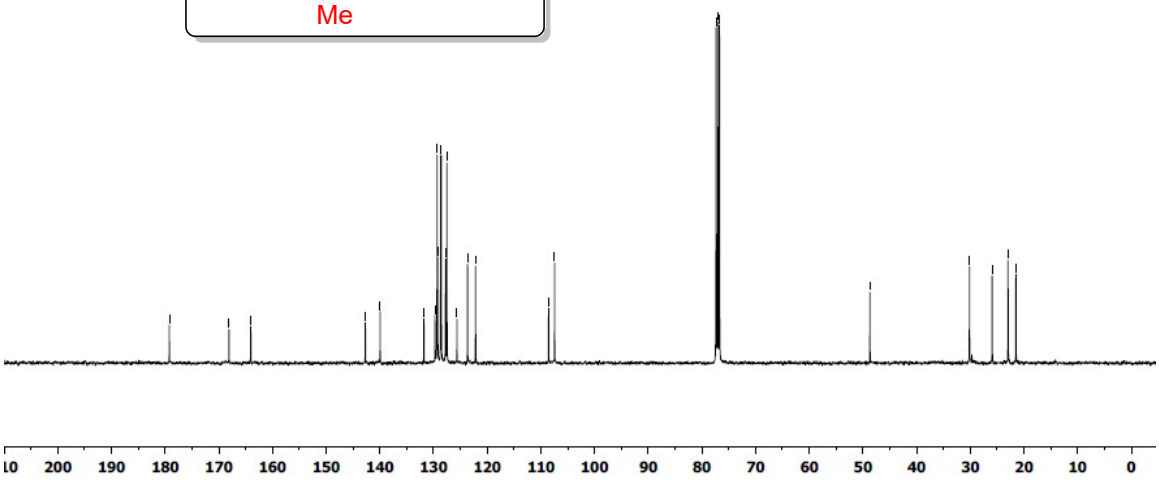
H3C
Me
O
N
Me
3ba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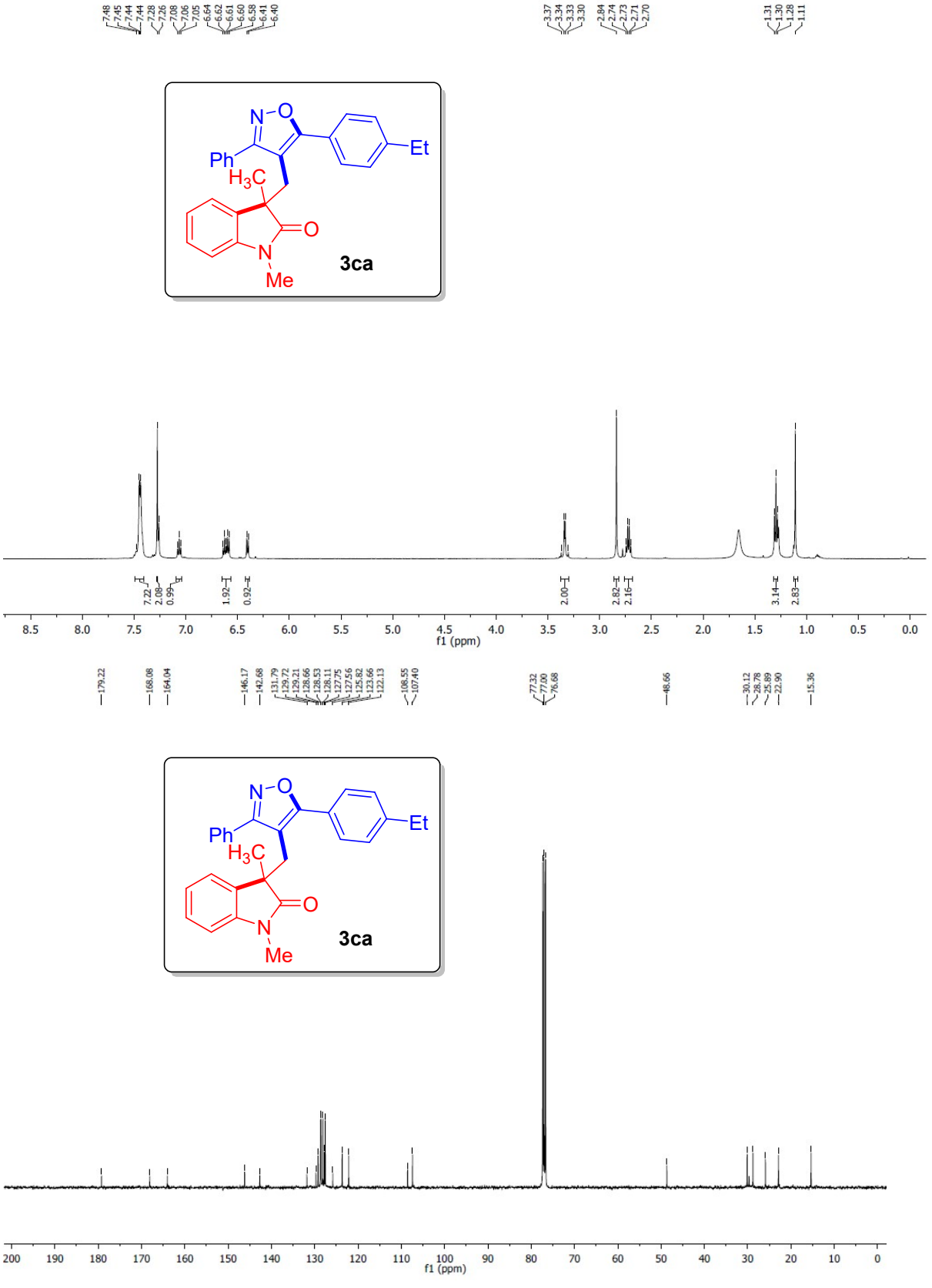
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7.06
7.05
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6.62
6.61
6.60
6.58
6.41
6.40
3.37
3.34
3.33
3.30
2.84
2.74
2.73
2.71
2.70
1.31
1.30
1.28
1.11
N
O
Ph
H3C
Et
O
N
Me
3ca
7.22
2.08
0.99
1.92
0.92
2.00
2.82
2.16
3.14
2.83
8.5
8.0
7.5
7.0
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
0.0
f1 (ppm)
179.22
168.08
164.04
146.17
142.68
131.79
129.72
129.21
128.66
128.53
128.11
127.75
127.56
125.82
123.66
122.13
108.55
107.40
77.32
77.00
76.68
48.66
30.12
28.78
25.89
22.90
15.36
N
O
Ph
H3C
Et
O
N
Me
3ca
200
190
180
170
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130
120
110
100
90
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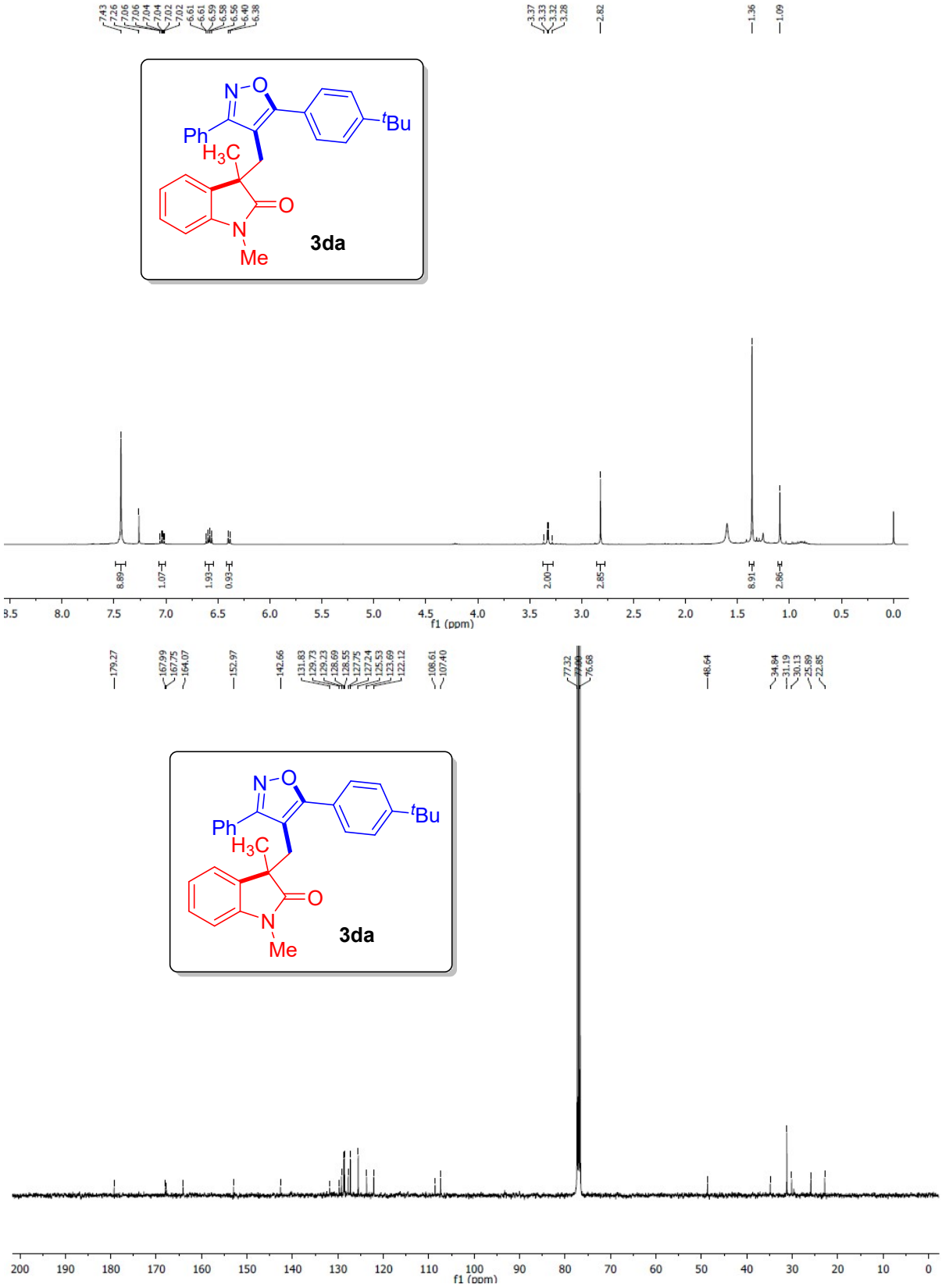
f1 (ppm)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7.06
7.04
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7.02
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6.61
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6.56
6.40
6.38
3.37
3.33
3.32
3.28
2.82
1.36
1.09
N
O
Ph
H3C
tBu
O
N
Me
3da
8.89
1.07
1.93
0.93
2.00
2.85
8.91
2.86
f1 (ppm)
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167.99
167.75
164.07
152.97
142.66
131.83
129.73
129.23
128.69
128.55
127.75
127.24
125.53
123.69
122.12
108.61
107.40
77.32
77.00
76.68
48.64
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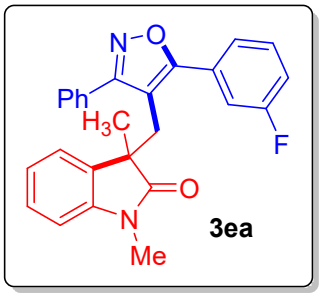
22.85
N
O
Ph
H3C
tBu
O
N
Me
3da
f1 (ppm)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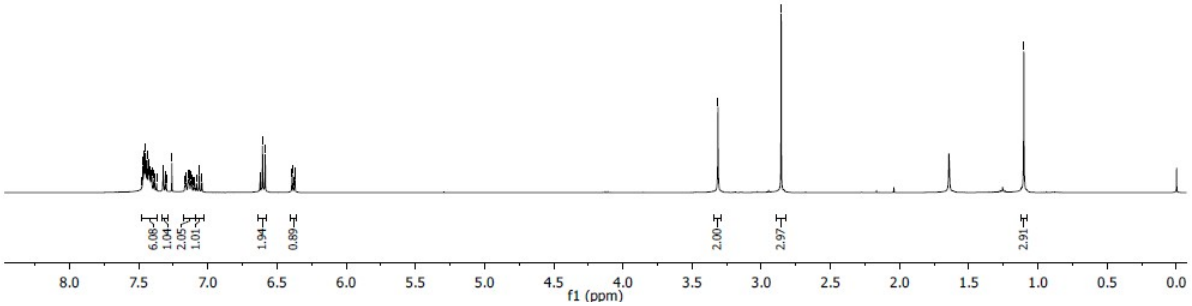
Ph
H3C
F
O
N
Me
3ea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1.01
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0.89
2.00
2.97
2.91
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
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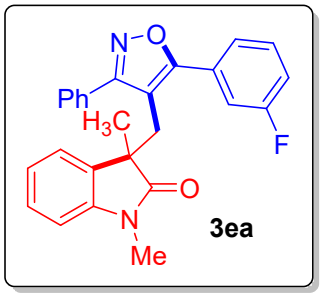
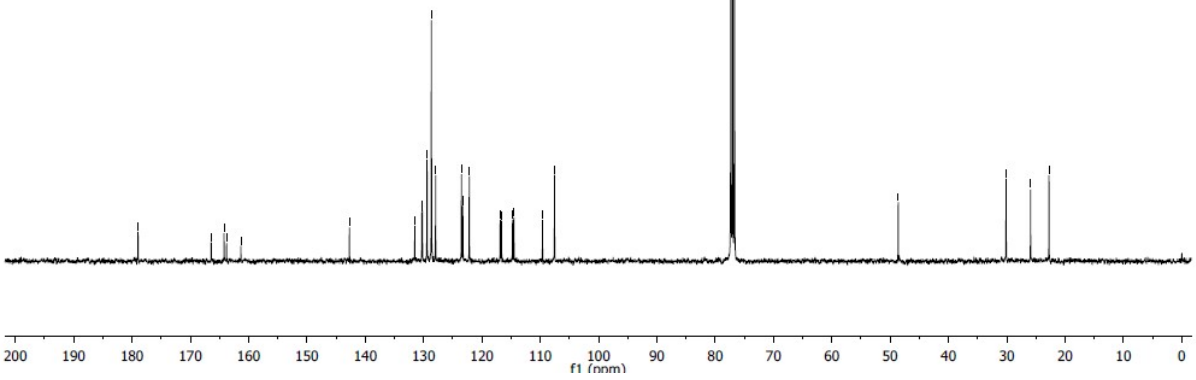
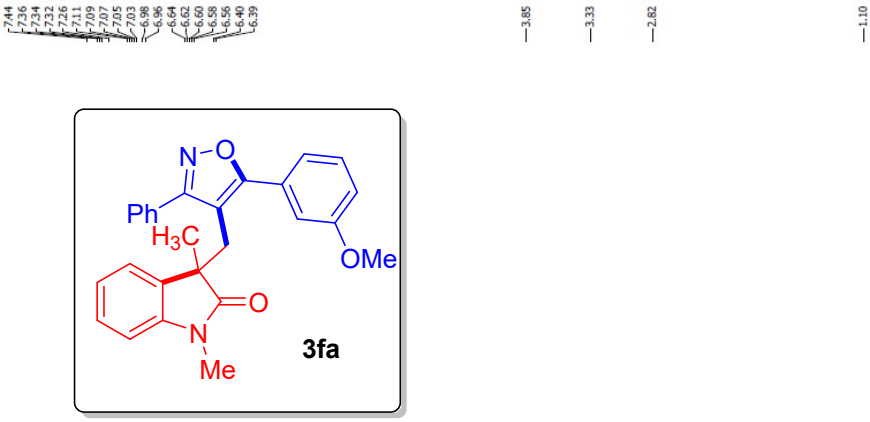
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


N
O
Ph
H3C
F
O
N
Me
3ea


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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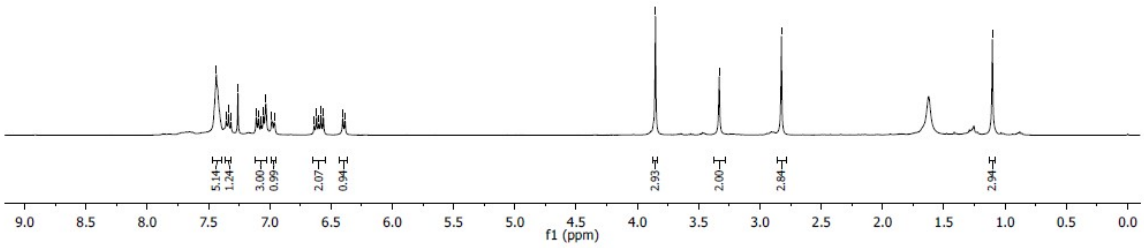
7.36
7.34
7.32
7.26
7.11
7.09
7.07
7.05
7.03
6.98
6.96
6.64
6.62
6.60
6.58
6.56
6.40
6.39
3.85
3.33
2.82
1.10
N
O
Ph
H3C
OMe
O
N
Me
3fa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1.24
3.00
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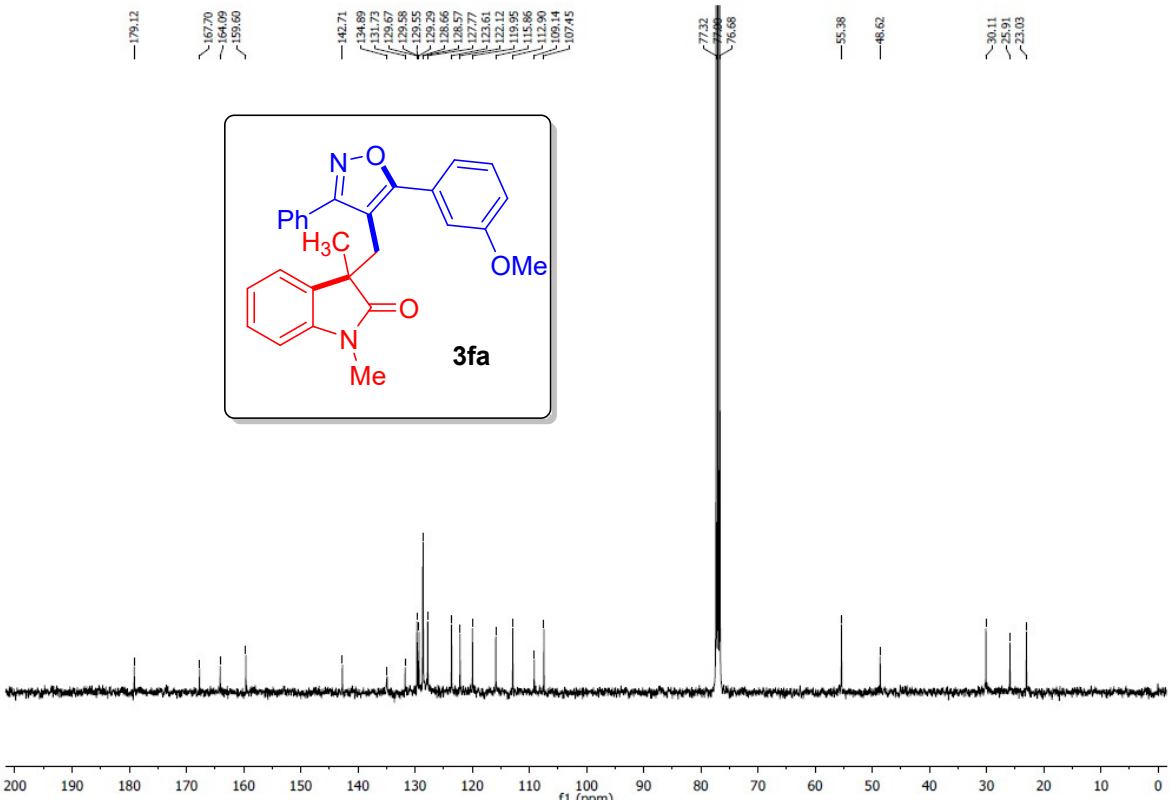
2.07
0.94
2.93
2.00
2.84
2.94
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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159.60
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131.73
129.67
129.58
129.55
129.29
128.66
128.57
127.77
123.61
122.12
119.95
115.86
112.90
109.14
107.45
77.32
77.00
76.68
55.38
48.62
30.11
25.91
23.03
N
O
Ph
H3C
OMe
O
N
Me
3fa
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.06
7.65
7.65
7.64
7.50
7.47
7.46
7.45
7.45
7.44
7.43
6.59
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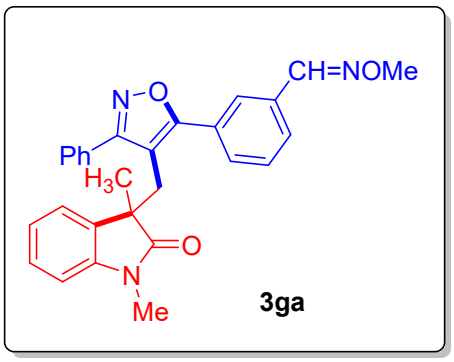
6.39
6.38
4.01
3.33
2.83
1.10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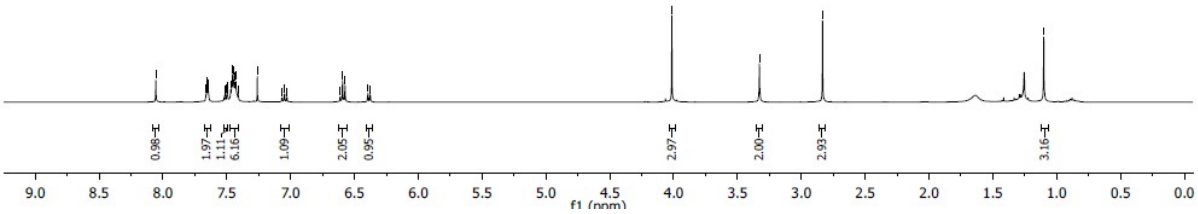
O
Ph
H3C
O
N
Me
3ga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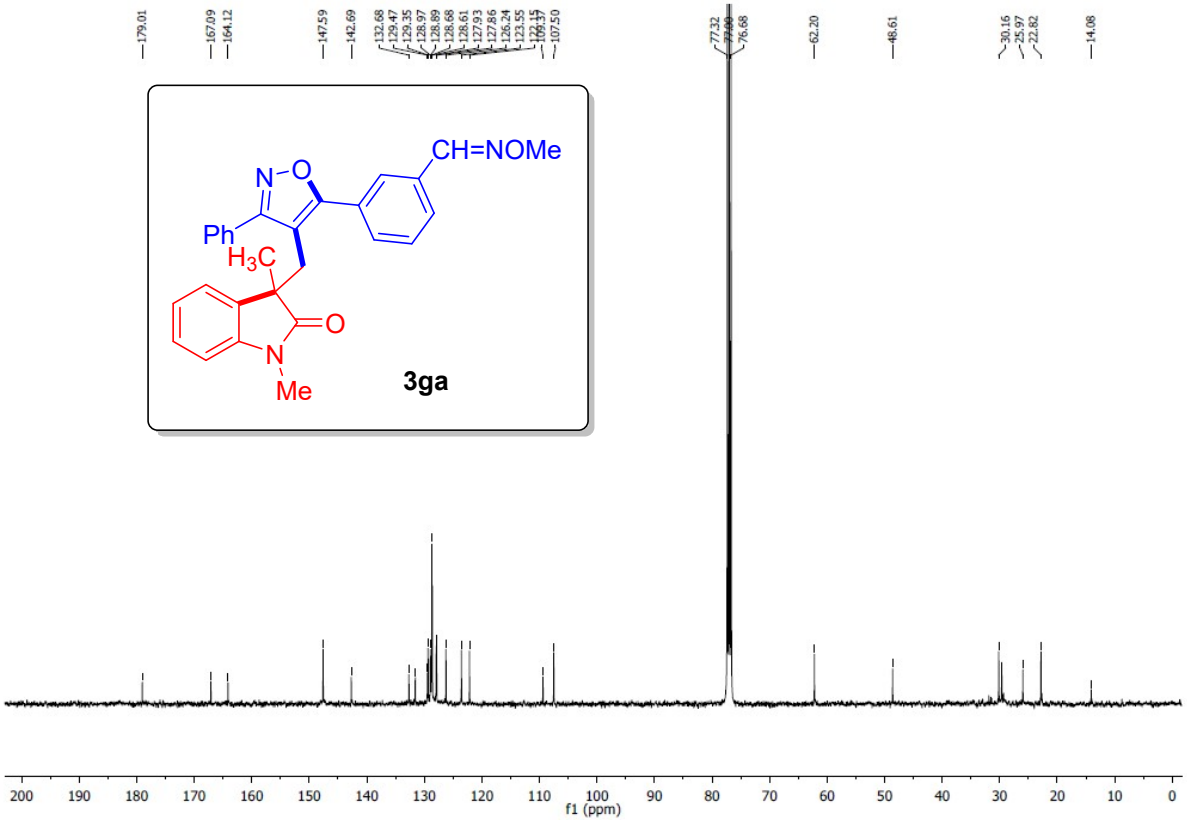
1.97
1.11
6.16
1.09
2.05
0.95
2.97
2.00
2.93
3.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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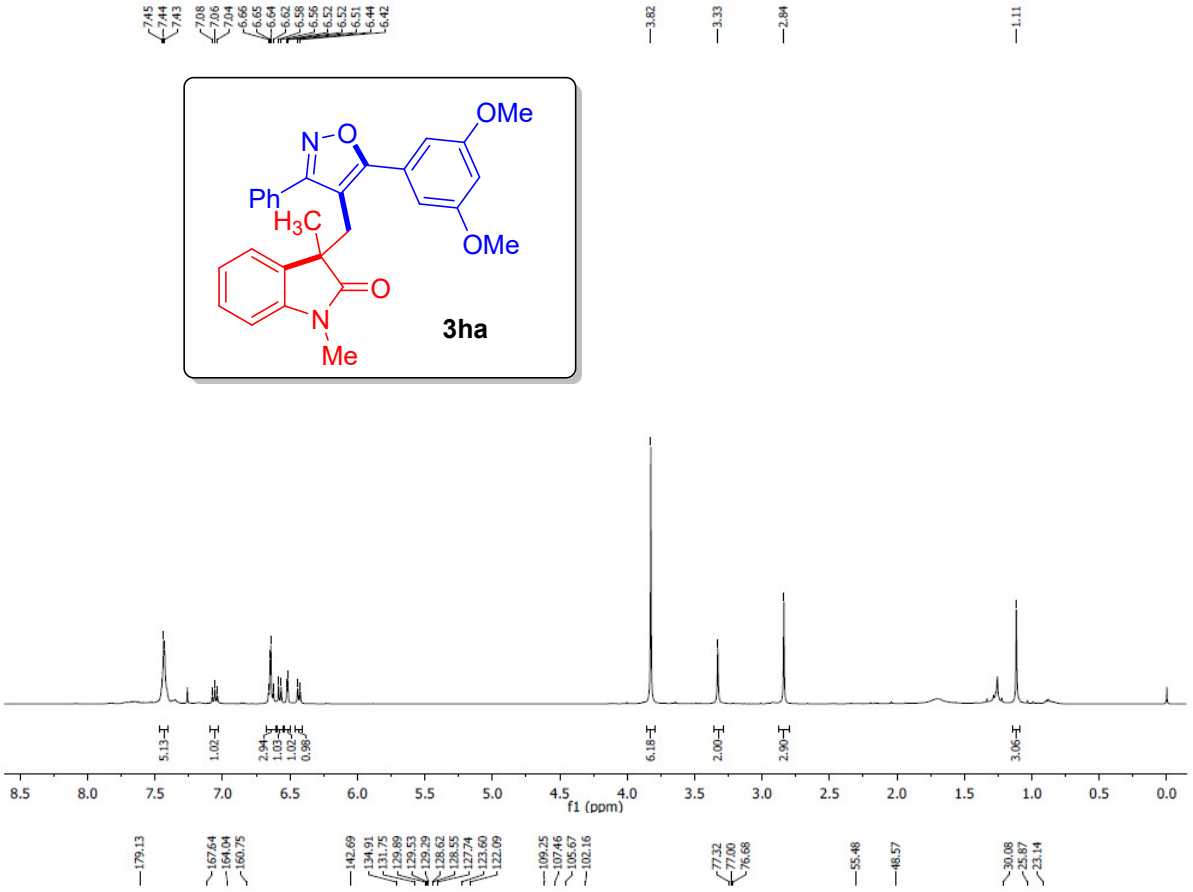
164.12
147.59
142.69
132.68
129.47
129.35
128.97
128.89
128.68
128.61
127.93
127.86
126.24
123.55
107.50
77.32
77.00
76.68
62.20
48.61
30.16
25.97
22.82
14.08
CH=NOMe
N
O
Ph
H3C
O
N
Me
3ga
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.44
7.43
7.08
7.06
7.04
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6.65
6.64
6.62
6.58
6.56
6.52
6.52
6.51
6.44
6.42
3.82
3.33
2.84
1.11
OMe
OMe
Ph
H3C
O
N
Me
3ha
5.13
1.02
2.94
1.03
1.02
0.98
6.18
2.00
2.90
3.06
f1 (ppm)
179.13
167.64
164.04
160.75
142.69
134.91
131.75
129.89
129.53
129.29
128.62
128.55
127.74
123.60
122.09
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55.48
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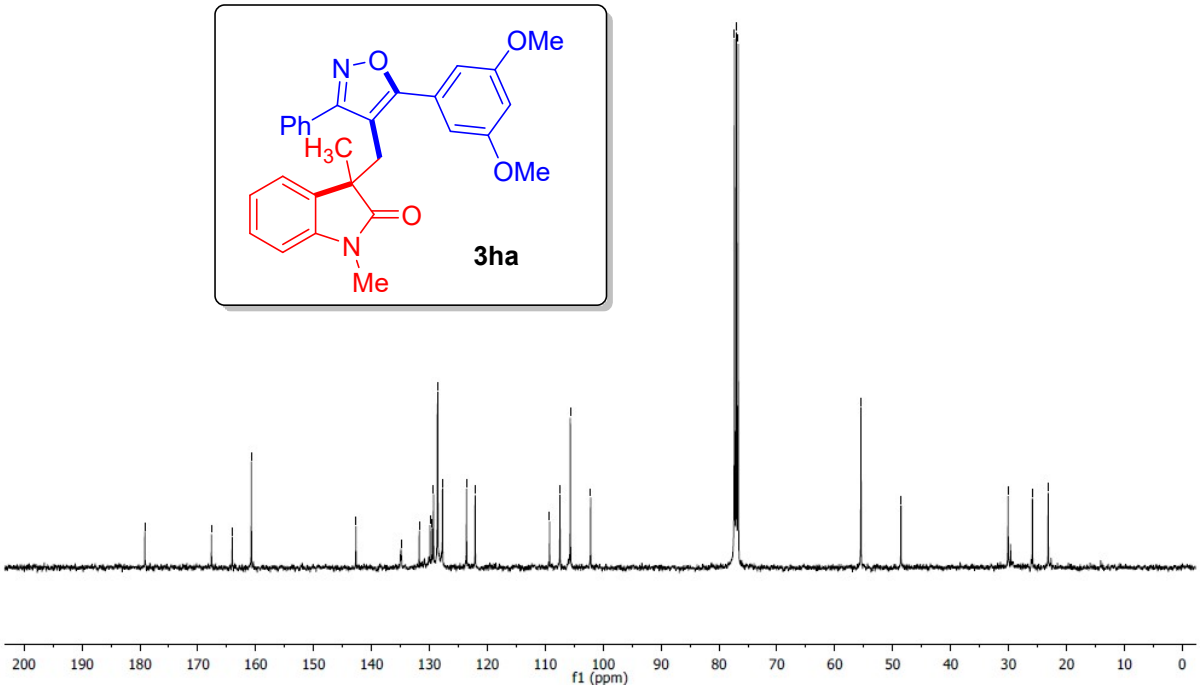
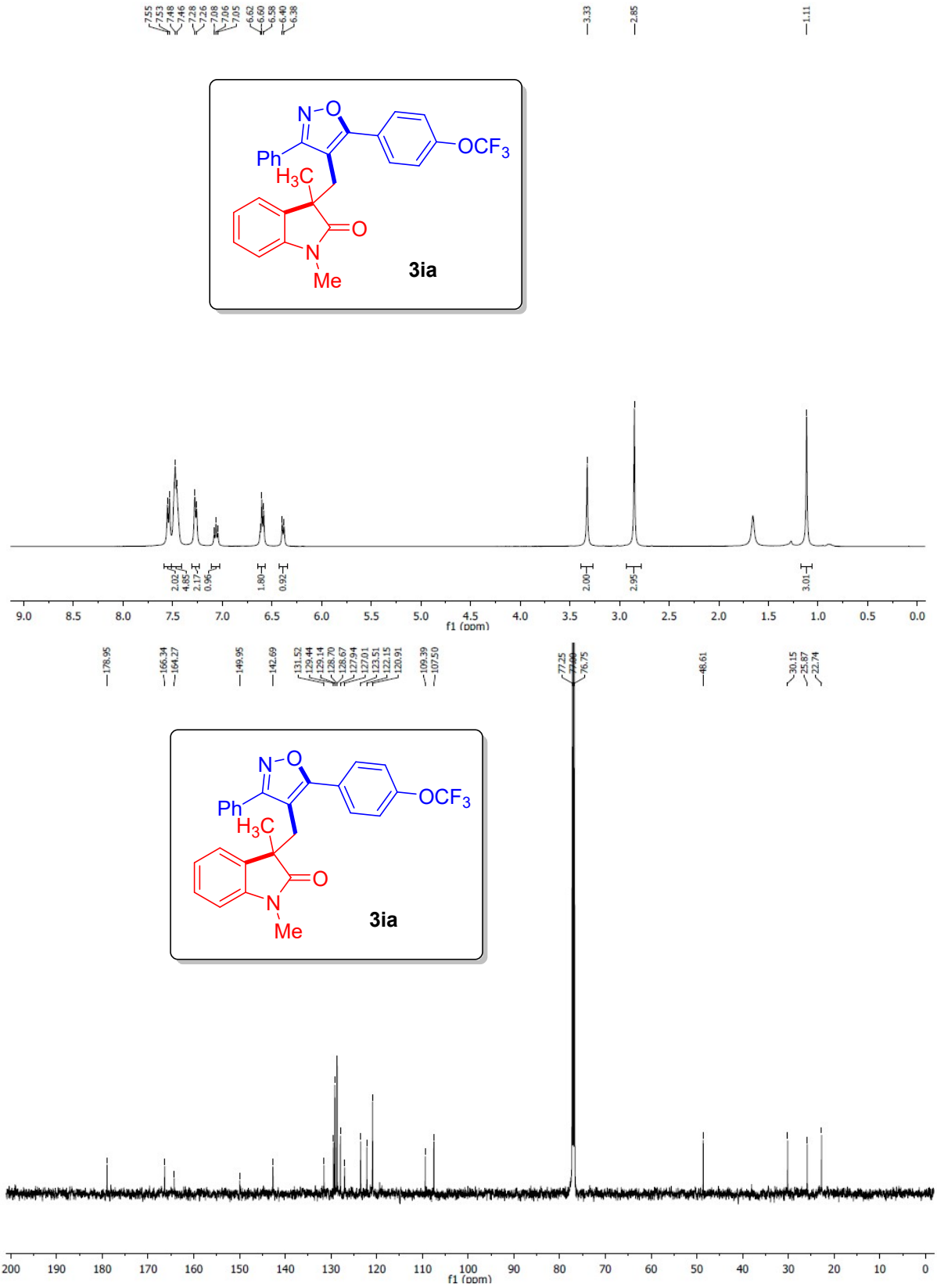
23.14


OMe
OMe
Ph
H3C
O
N
Me
3ha
f1 (ppm)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7.05
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6.60
6.58
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6.38
3.33
2.85
1.11
N
O
Ph
H3C
OCF3
O
N
Me
3ia
2.02
4.85
2.17
0.96
1.80
0.92
2.00
2.95
3.01
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
0.0
f1 (ppm)
178.95
166.34
164.27
149.95
142.69
131.52
129.44
129.14
128.70
128.67
127.94
127.01
123.51
122.15
120.91
109.39
107.50
77.25
77.00
76.75
46.61
30.15
25.87
22.74
N
O
Ph
H3C
OCF3
O
N
Me
3ia
200
190
180
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150
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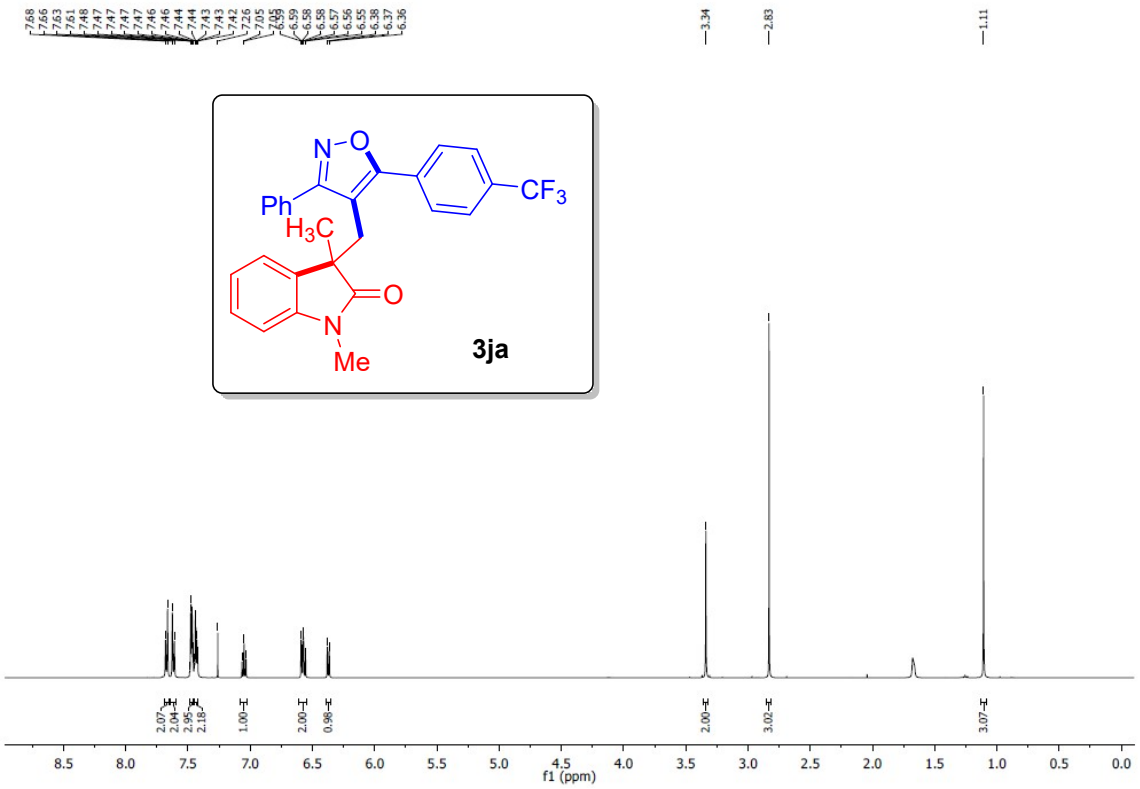
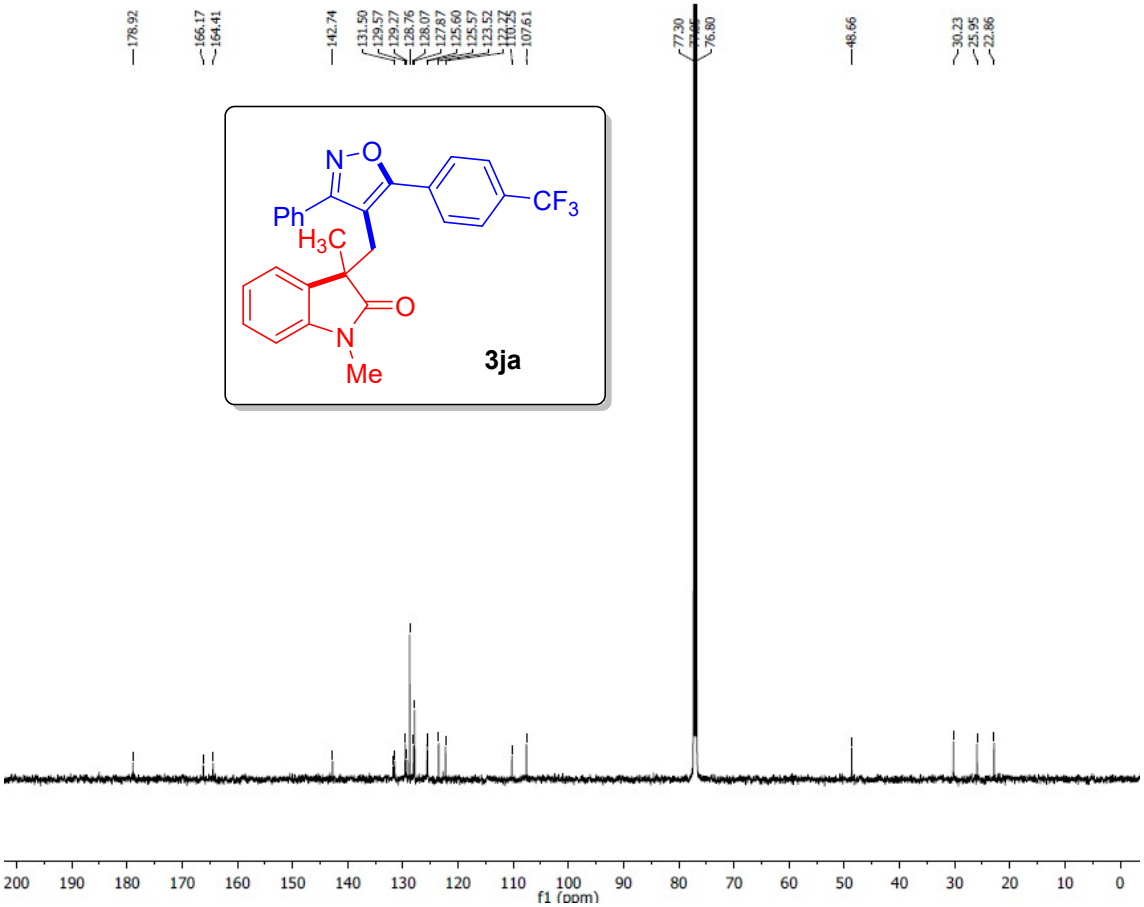
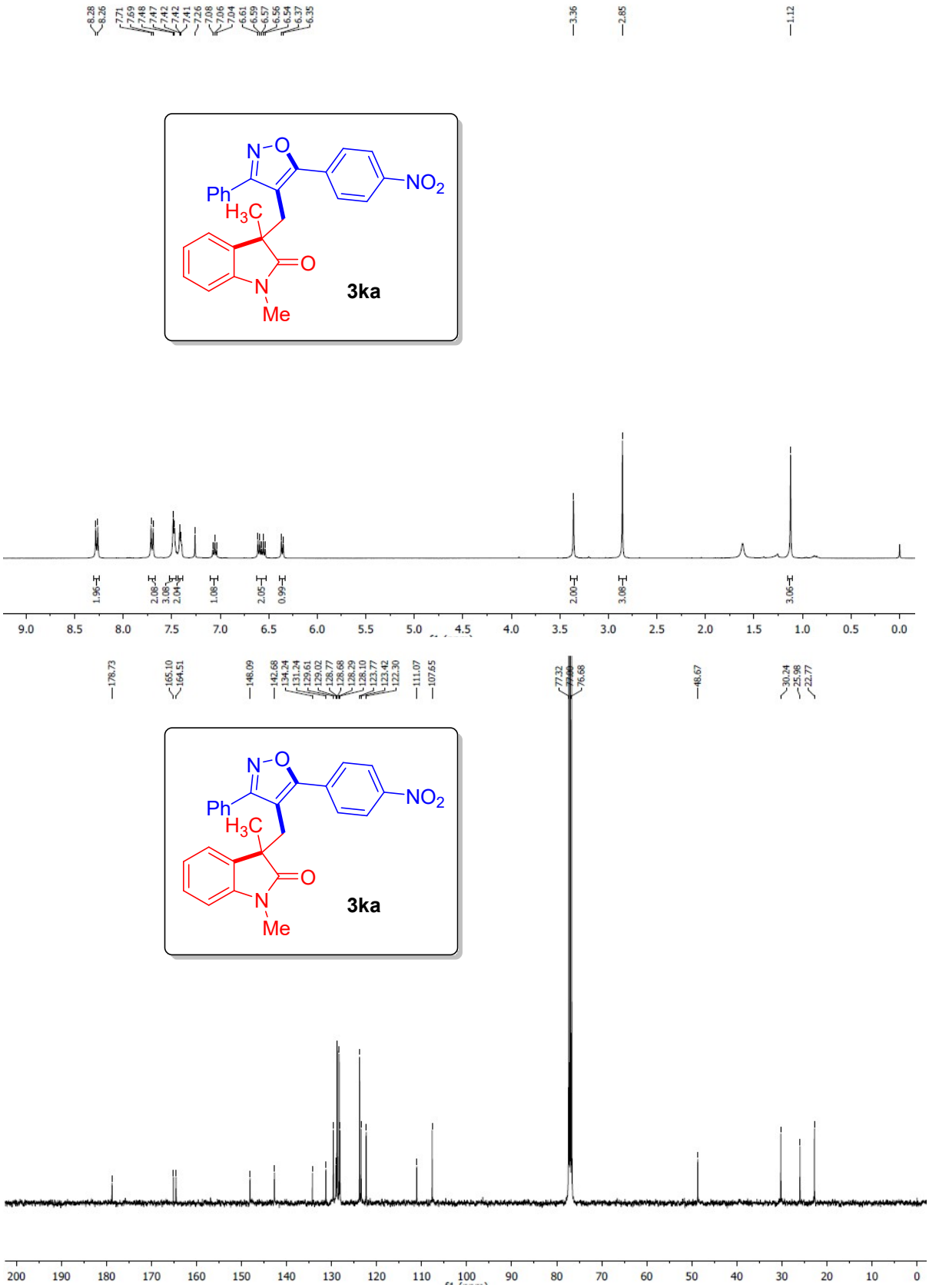
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


3ja
f1 (ppm)


3ja
f1 (ppm)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7.06
7.04
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6.59
6.57
6.56
6.54
6.37
6.35
3.36
2.85
1.12
N
O
Ph
H3C
NO2
O
N
Me
3ka
1.96
2.08
3.08
2.04
1.08
2.05
0.99
2.00
3.08
3.06
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
0.0
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128.10
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123.42
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77.00
76.68
48.67
30.24
25.98
22.77
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10
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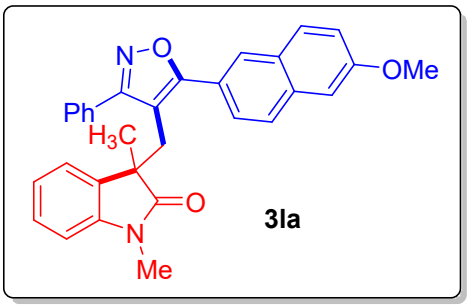
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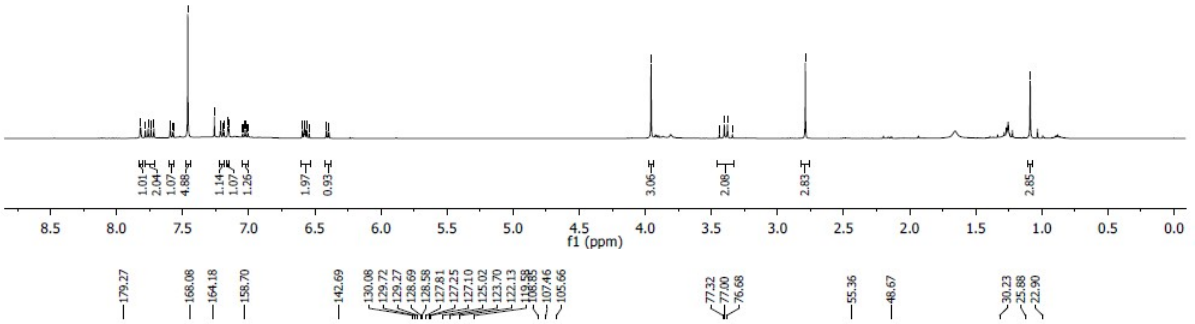
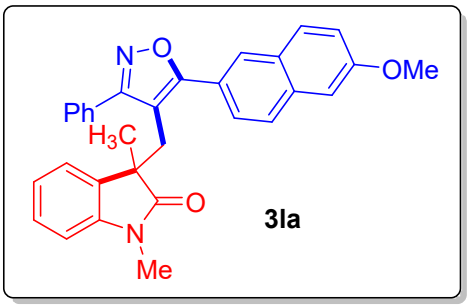
Ph
H3C
O
N
Me
3la


f1 (ppm)


N
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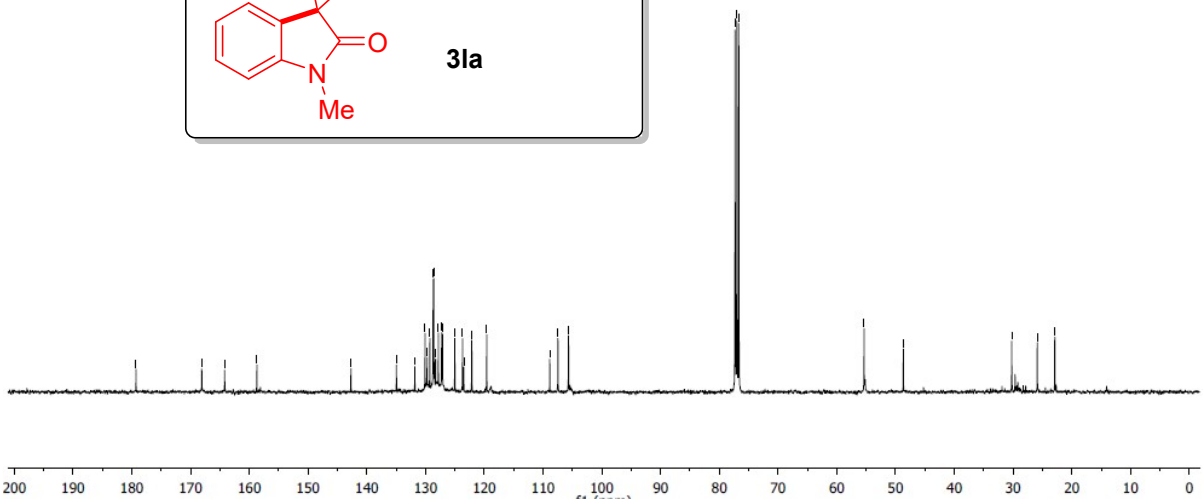
OMe
Ph
H3C
O
N
Me
3la

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7.72
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7.63
7.61
7.59
7.57
7.52
7.51
7.26
6.93
6.92
6.90
6.44
6.42
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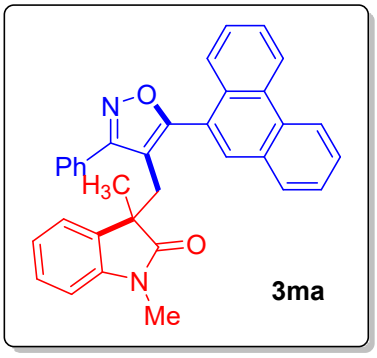
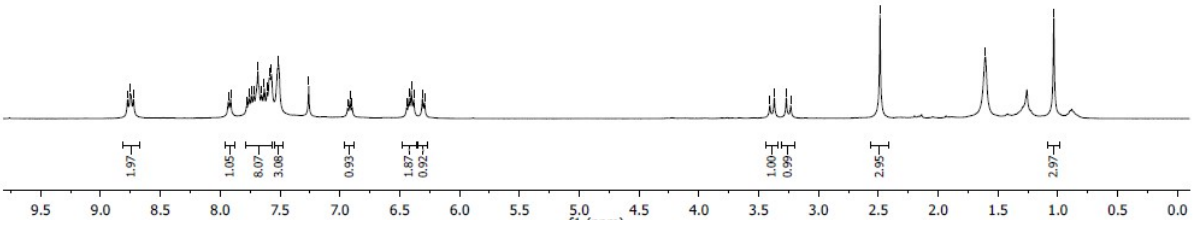
6.29
3.41
3.37
3.27
3.23
2.49
1.61
1.03


N
O
Ph
H3C
O
N
Me
3ma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8.5
8.0
7.5
7.0
6.5
6.0
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3.0
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2.0
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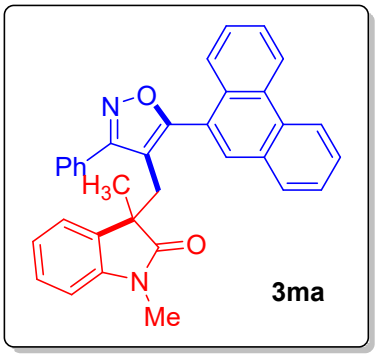
1.0
0.5
0.0


N
O
Ph
H3C
O
N
Me
3ma

178.79
167.92
163.83
142.68
130.11
129.39
129.33
128.85
128.62
127.59
127.07
127.01
123.25
122.87
122.64
121.95
107.44
77.32
77.00
76.68
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30.18
25.58
24.22
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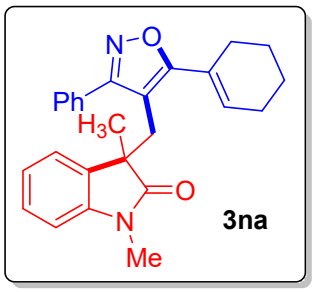
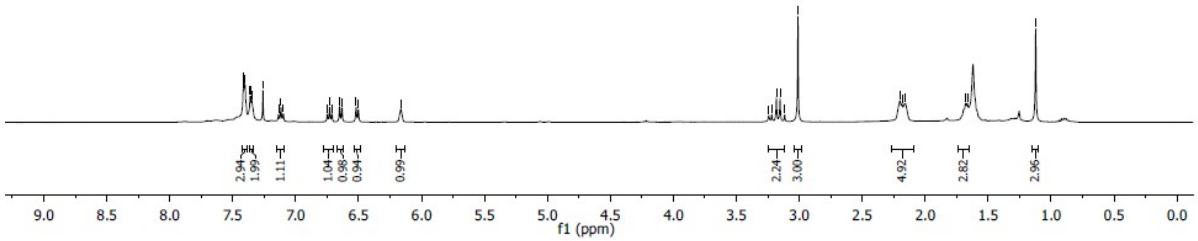
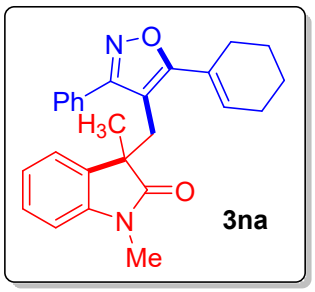
0


N
O
Ph
H3C
O
N
Me
3na


f1 (ppm)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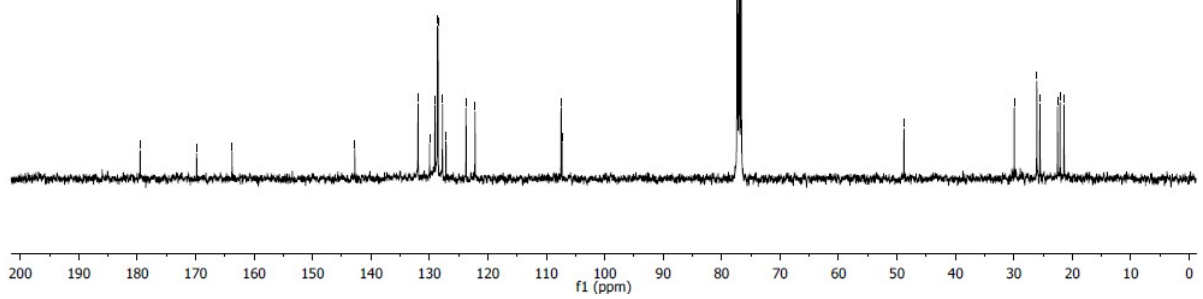
Ph
H3C
O
N
Me
3na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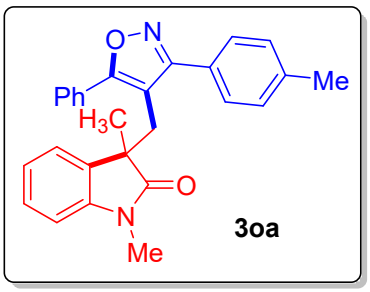
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Me
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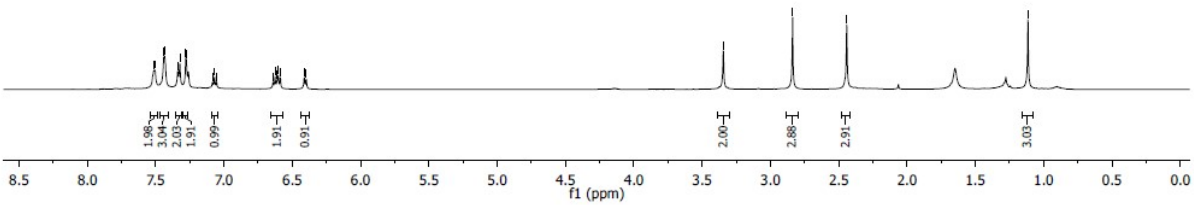
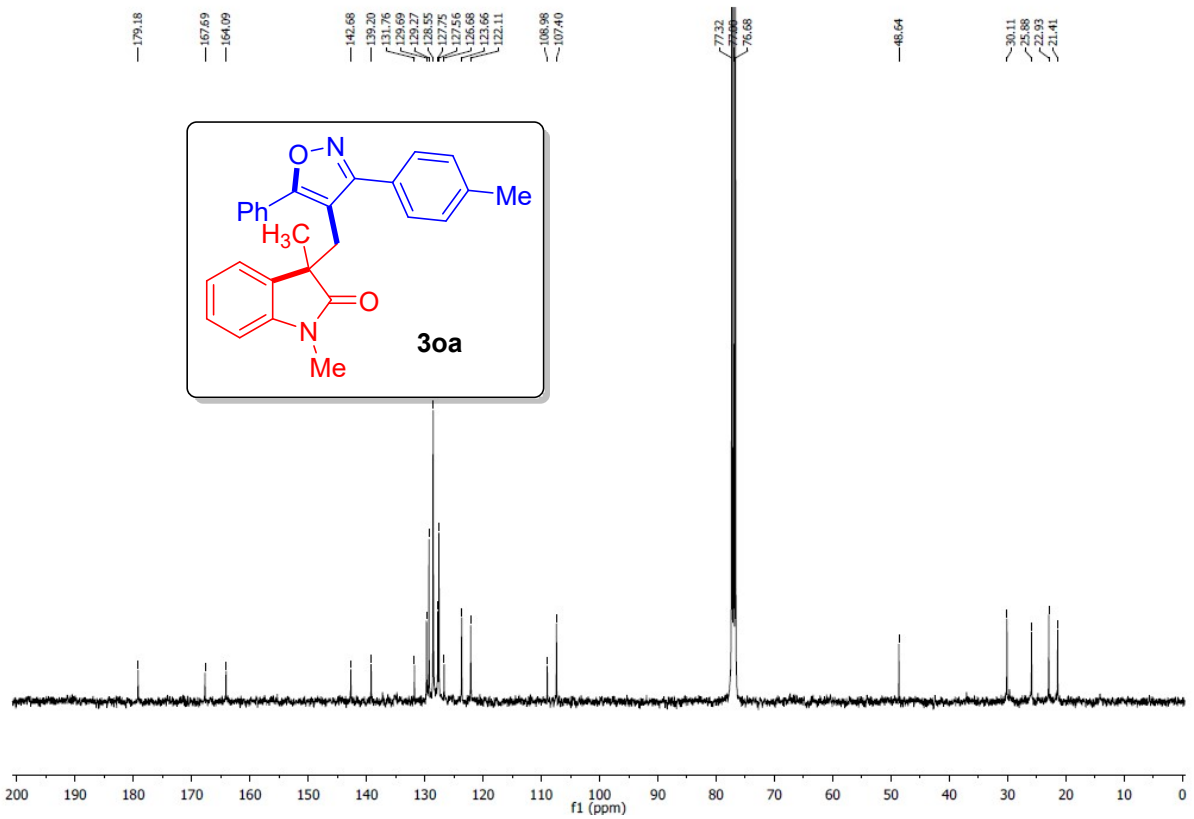

f1 (ppm)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O
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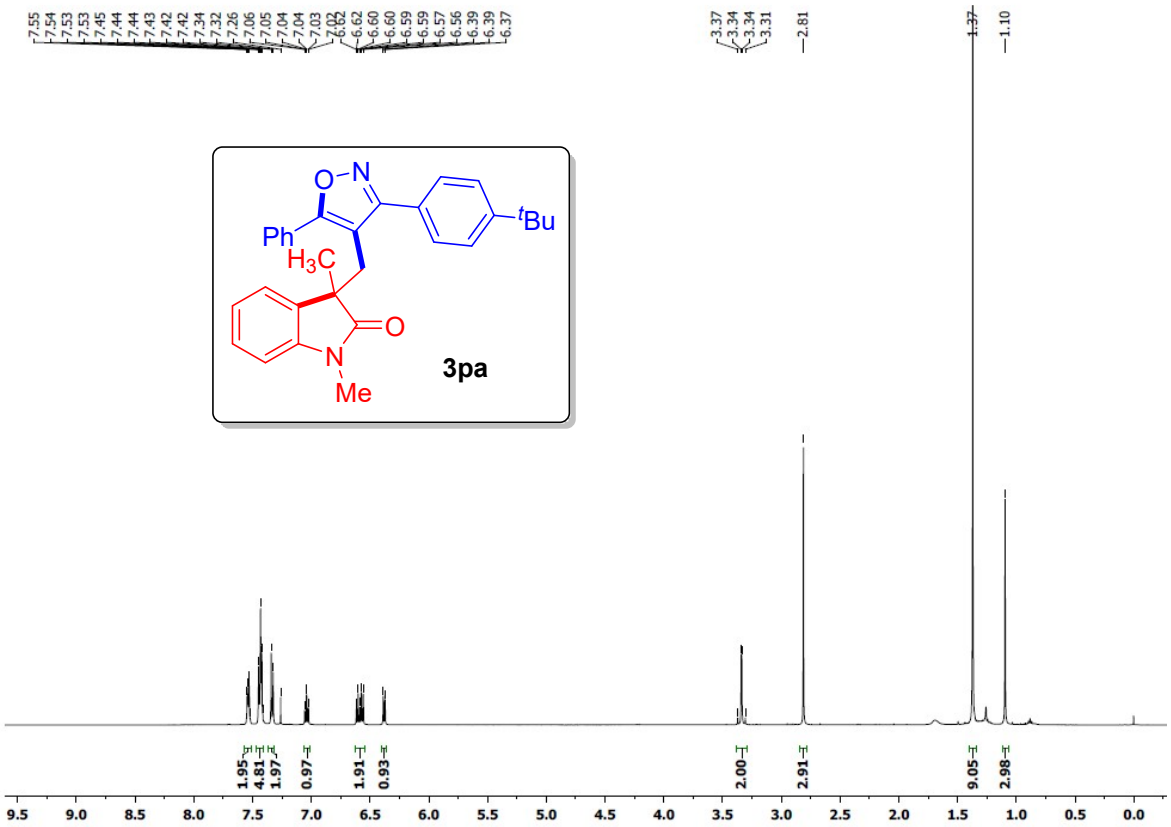
f1 (ppm)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7.05
7.04
7.04
7.03
7.02
7.02
6.62
6.60
6.60
6.59
6.59
6.57
6.56
6.39
6.39
6.37
3.37
3.34
3.34
3.31
2.81
1.37
1.10
O
N
Ph
H3C
tBu
O
N
Me
3pa
1.95
4.81
1.97
0.97
1.91
0.93
2.00
2.91
9.05
2.98
9.5
9.0
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8.0
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7.0
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6.0
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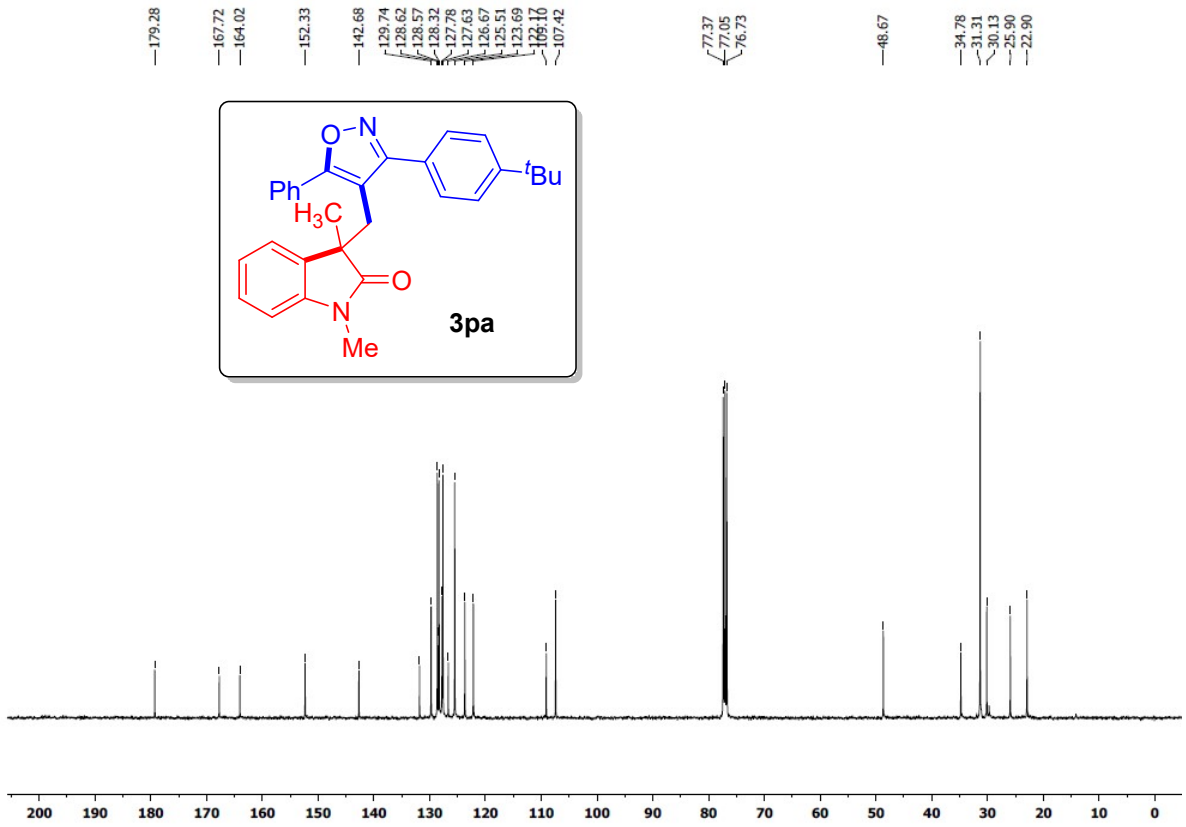
1.0
0.5
0.0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127.63
126.67
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123.69
122.17
109.10
107.42
77.37
77.05
76.73
48.67
34.78
31.31
30.13
25.90
22.90
O
N
Ph
H3C
tBu
O
N
Me
3pa
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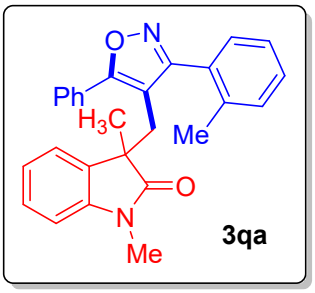
10
0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Me
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N
Me
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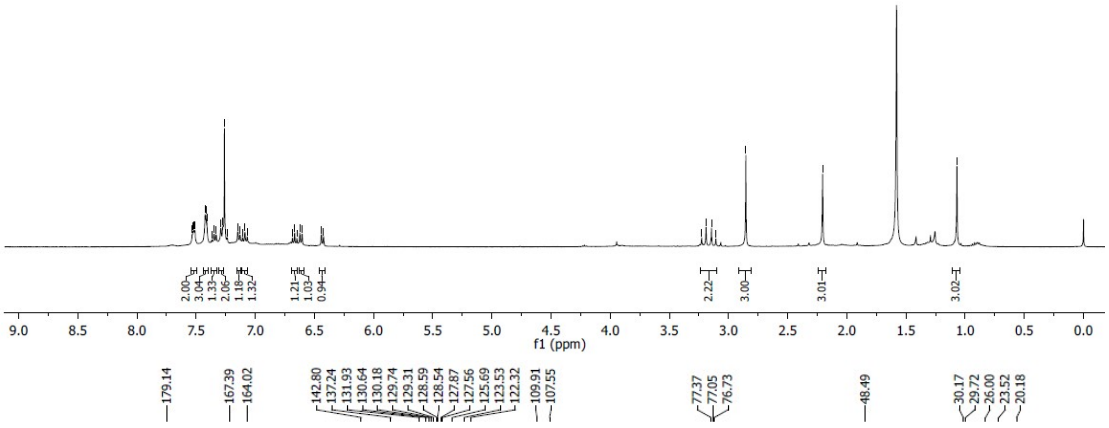
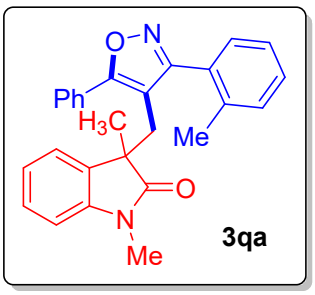
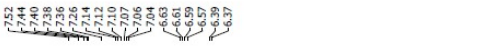
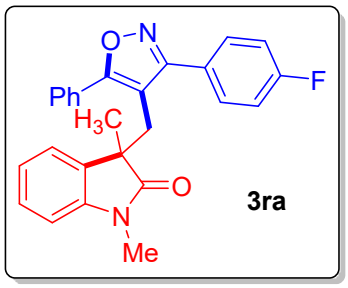

f1 (ppm)


O
N
Ph
H3C
Me
O
N
Me
3qa

f1 (ppm)

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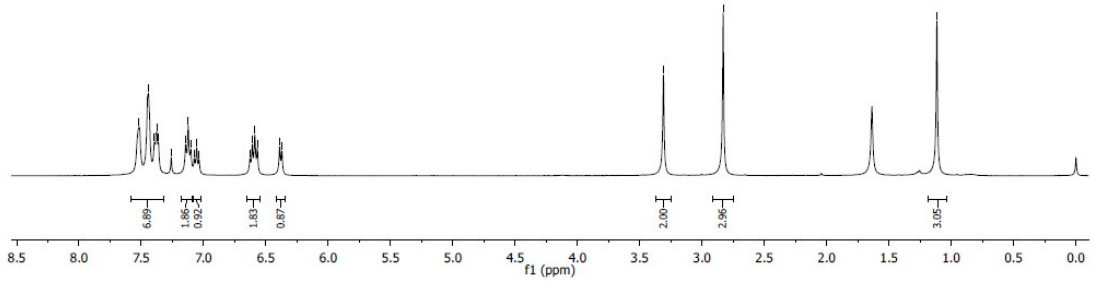
Ph
H3C
F
O
N
Me
3ra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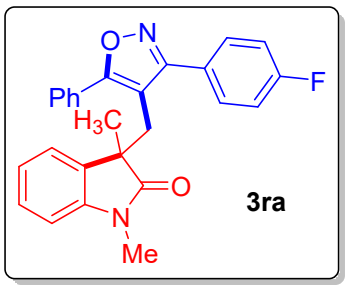
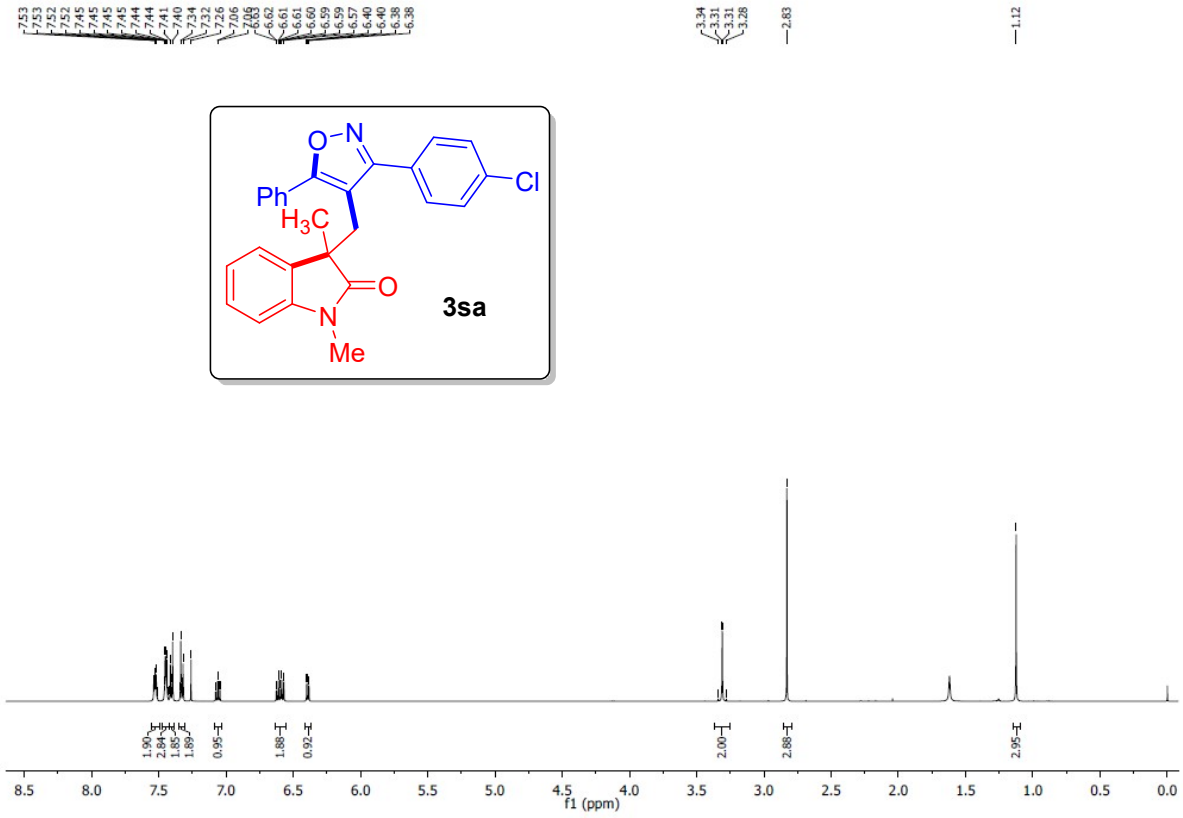
0.92
1.83
0.87
2.00
2.96
3.05
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


O
N
Ph
H3C
F
O
N
Me
3ra

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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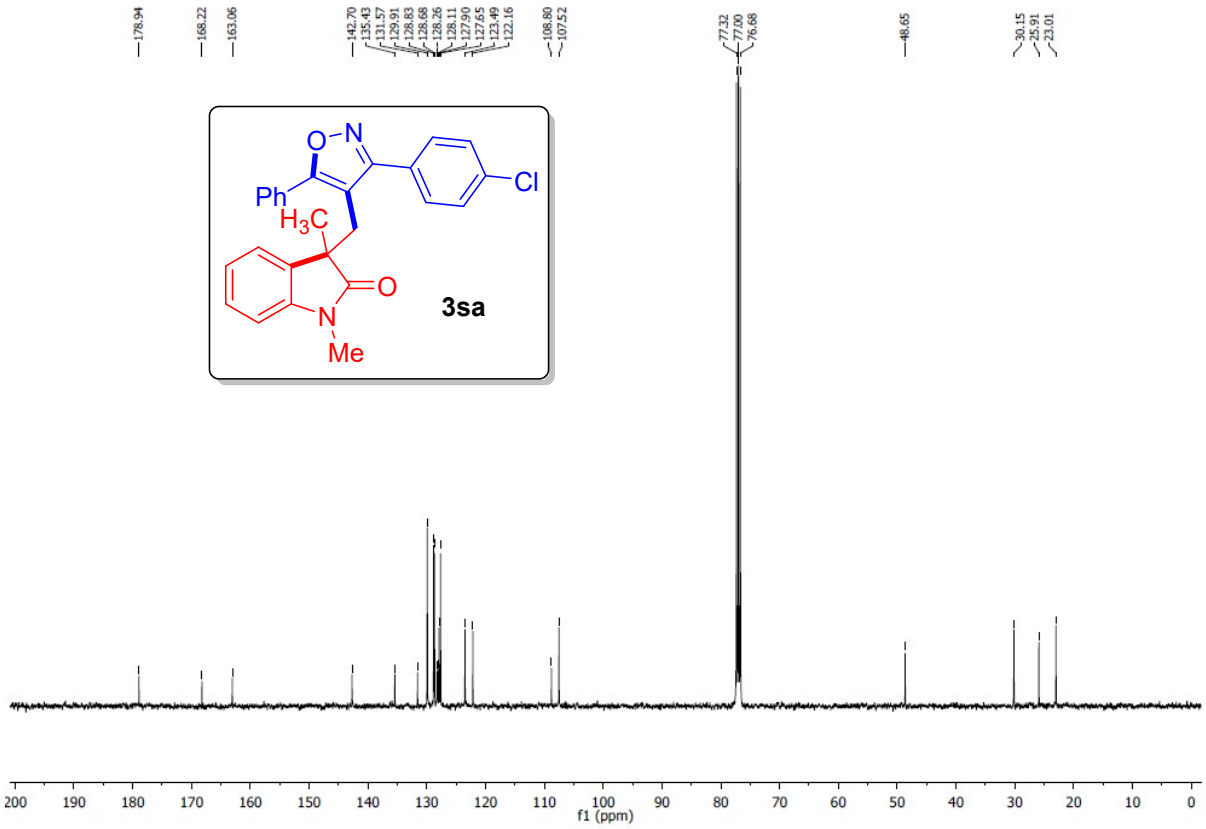
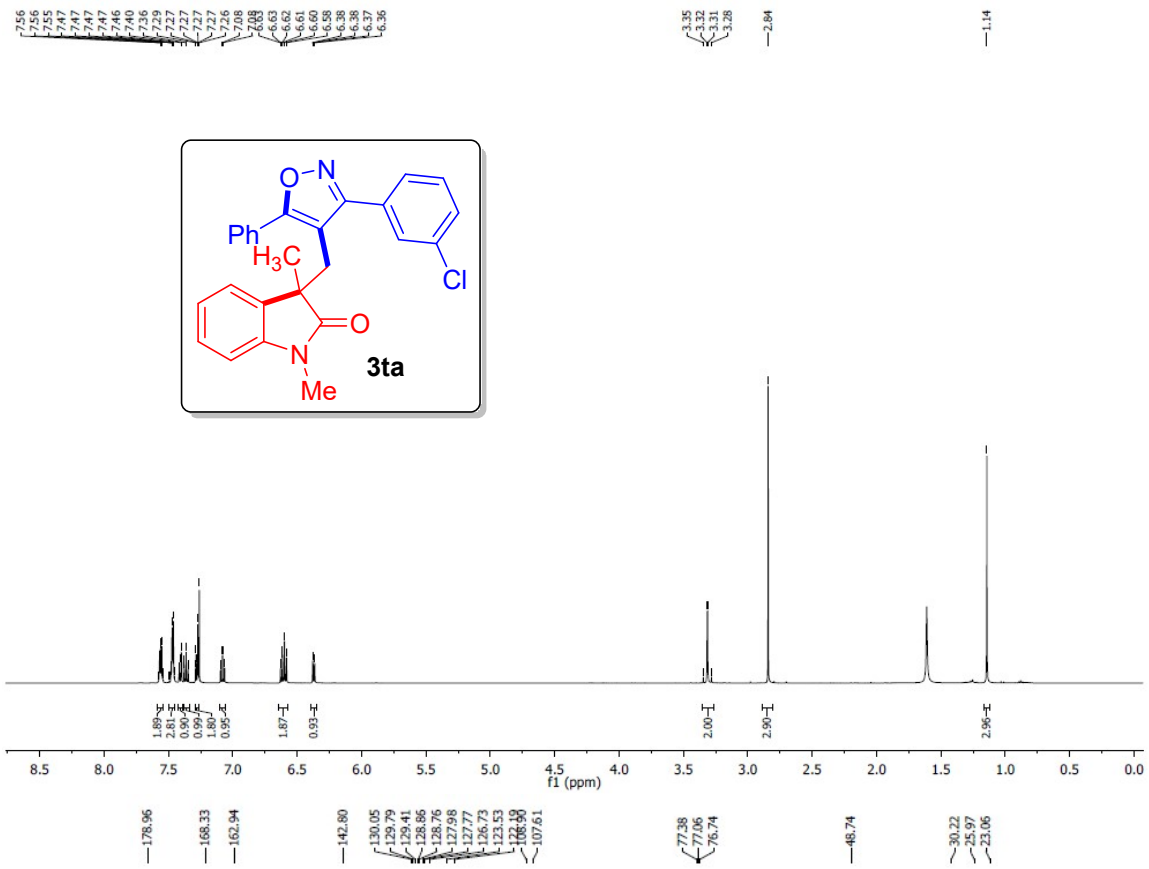
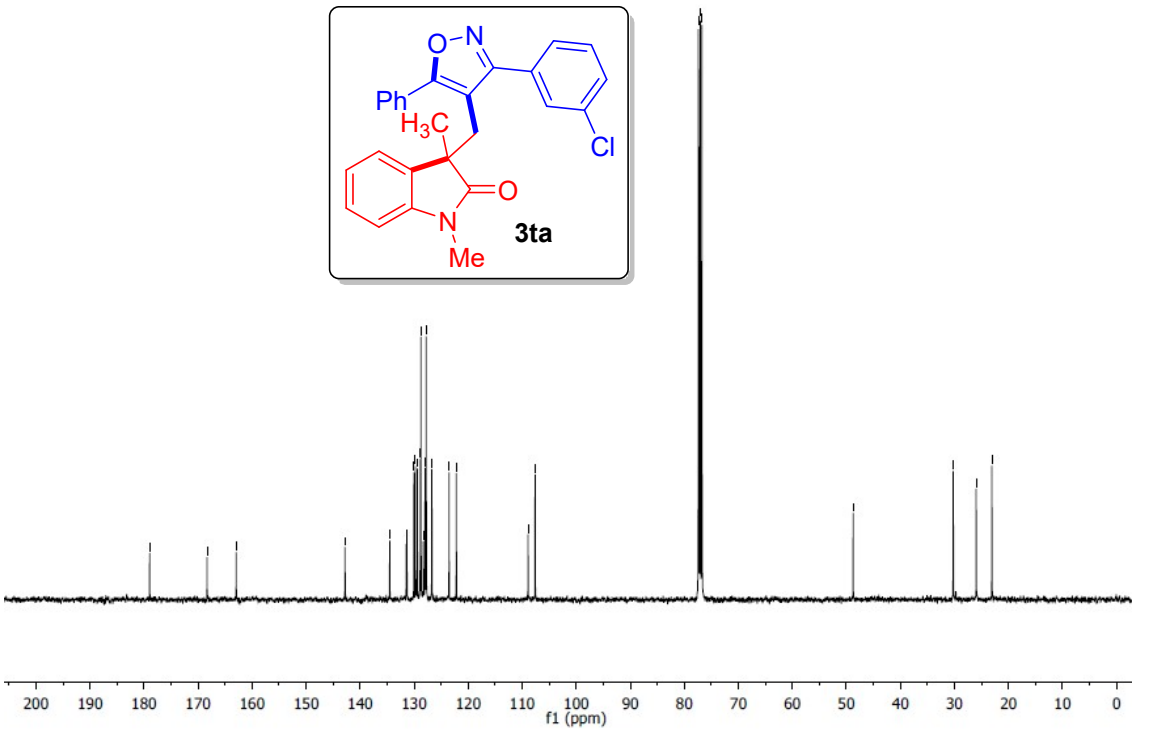
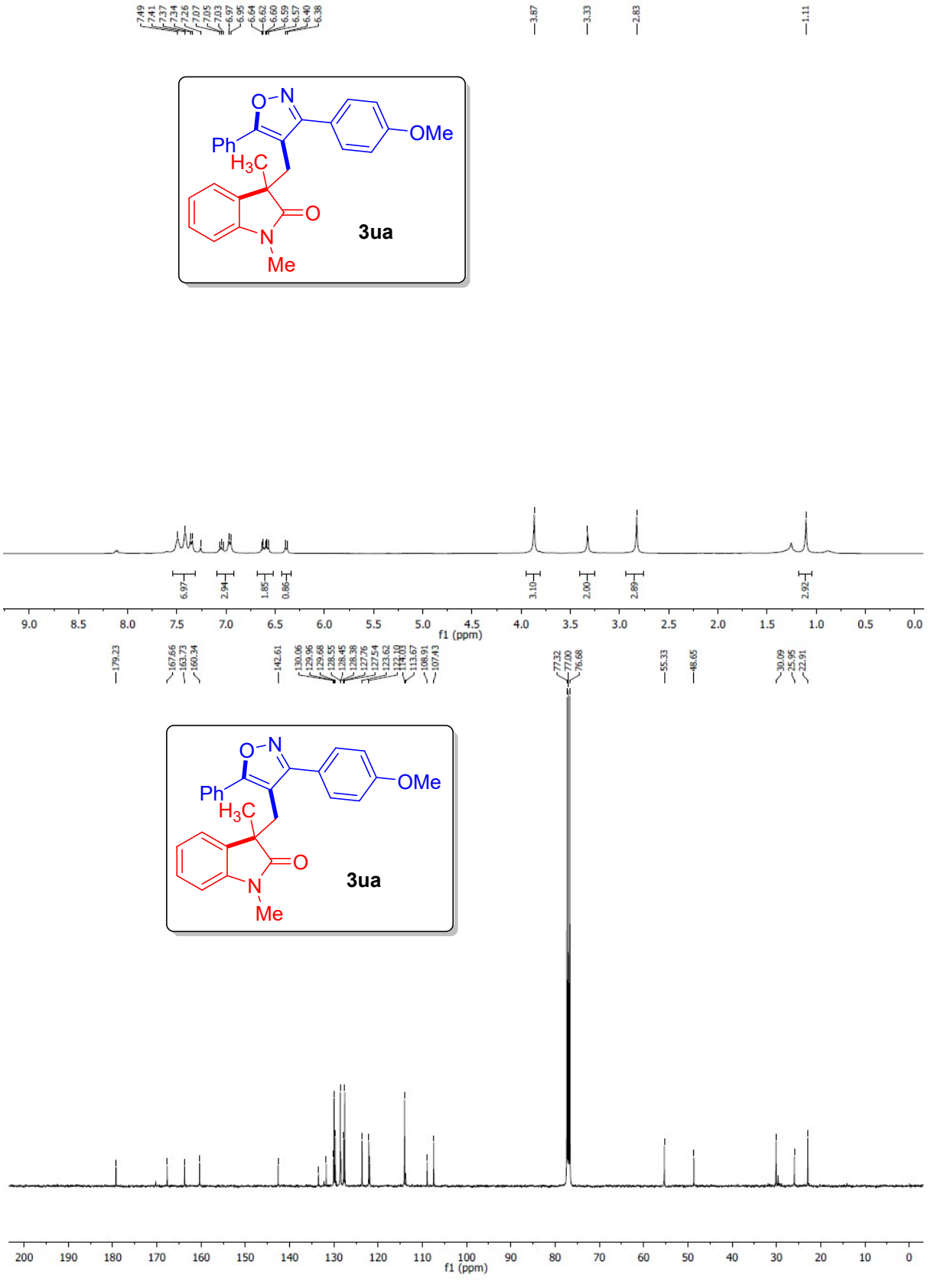
Cl
O
N
Me
3sa
f1 (ppm)


Ph
H3C
Cl
O
N
Me
3sa
f1 (ppm)


Ph
H3C
Cl
O
N
Me
3ta
f1 (ppm)


Ph
H3C
Cl
O
N
Me
3ta
f1 (ppm)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6.97
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6.64
6.62
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6.59
6.57
6.40
6.38
3.87
3.33
2.83
1.11
O
N
Ph
H3C
OMe
O
N
Me
3ua
6.97
2.94
1.85
0.86
3.10
2.00
2.89
2.92
f1 (ppm)
179.23
167.66
163.73
160.34
142.61
130.06
129.96
129.68
128.55
128.45
128.38
127.76
127.54
123.62
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76.68
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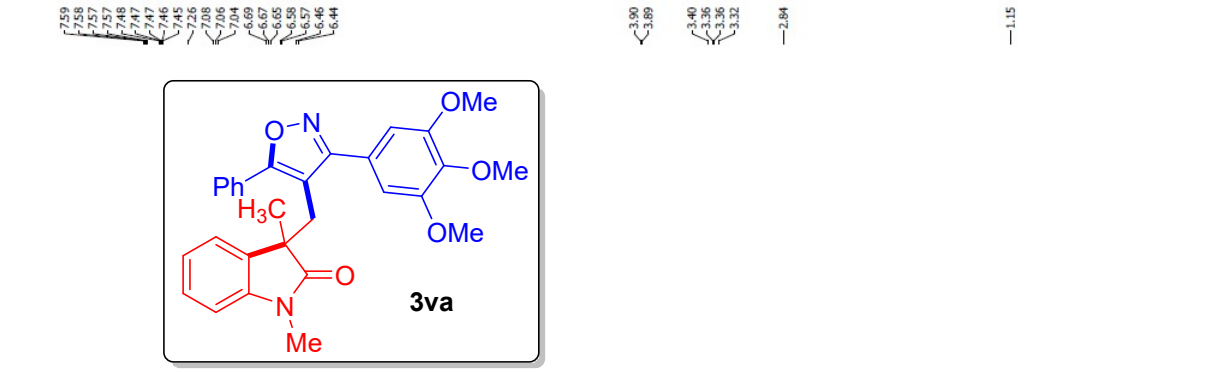
30.09
25.95
22.91
f1 (ppm)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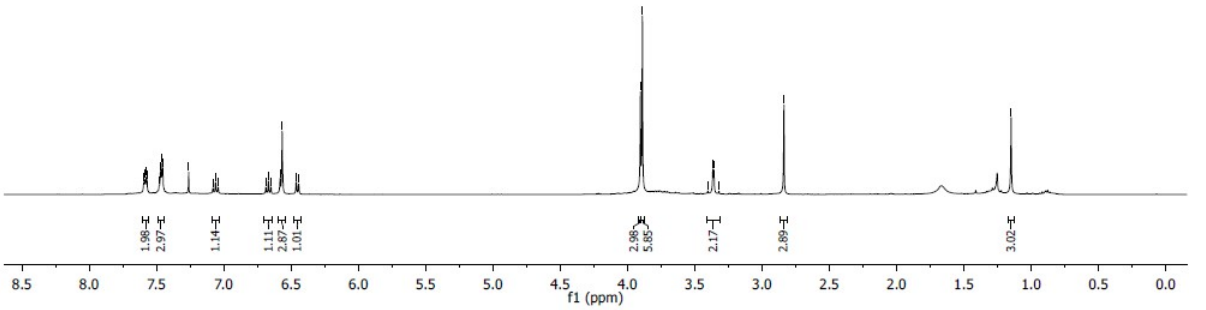
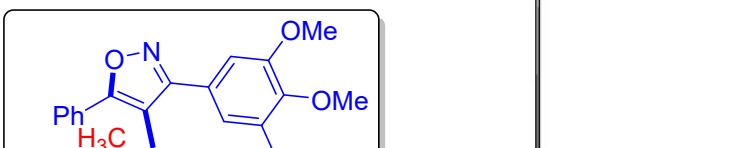
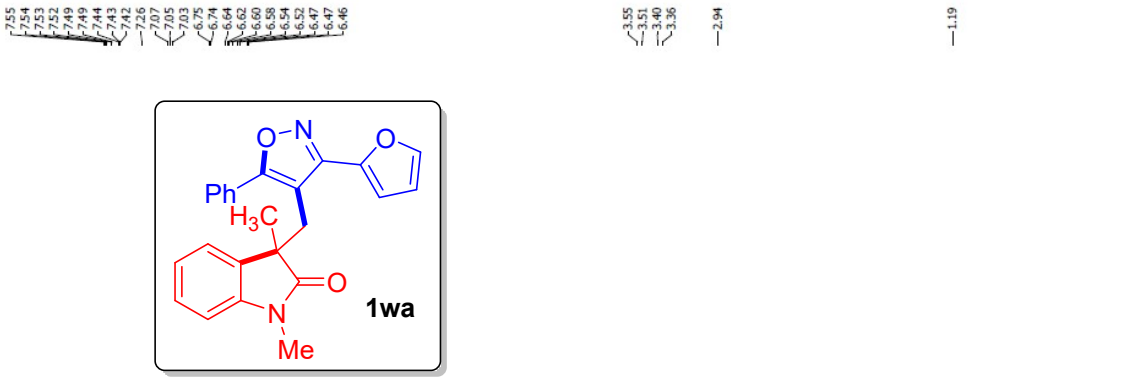
OMe
OMe
O
N
Ph
H3C
O
N
Me
3va


f1 (ppm)


OMe
OMe
OMe
O
N
Ph
H3C
O
N
Me
3va

f1 (ppm)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7.03
6.75
6.74
6.64
6.62
6.60
6.58
6.54
6.52
6.47
6.47
6.46
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3.36
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1.19
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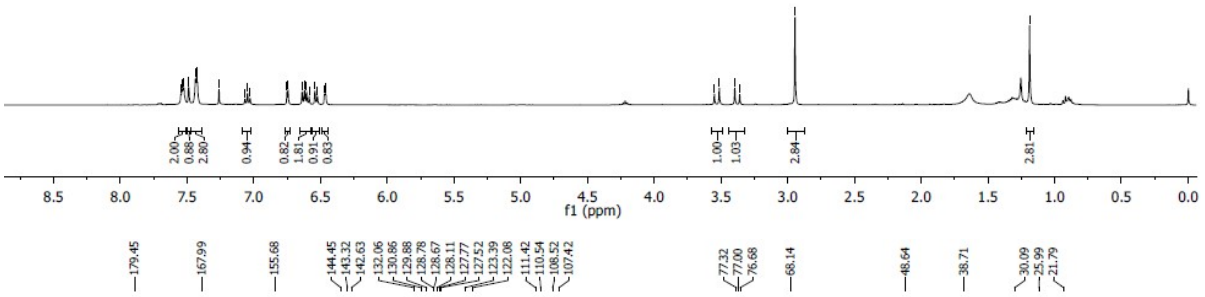
O
Ph
H3C
O
N
Me
1wa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0.91
0.83
1.00
1.03
2.84
2.81
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

179.45
167.99
155.68
144.45
143.32
142.63
132.06
130.86
129.88
128.78
128.67
128.11
127.77
127.52
123.39
122.08
111.42
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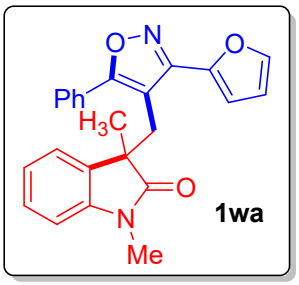
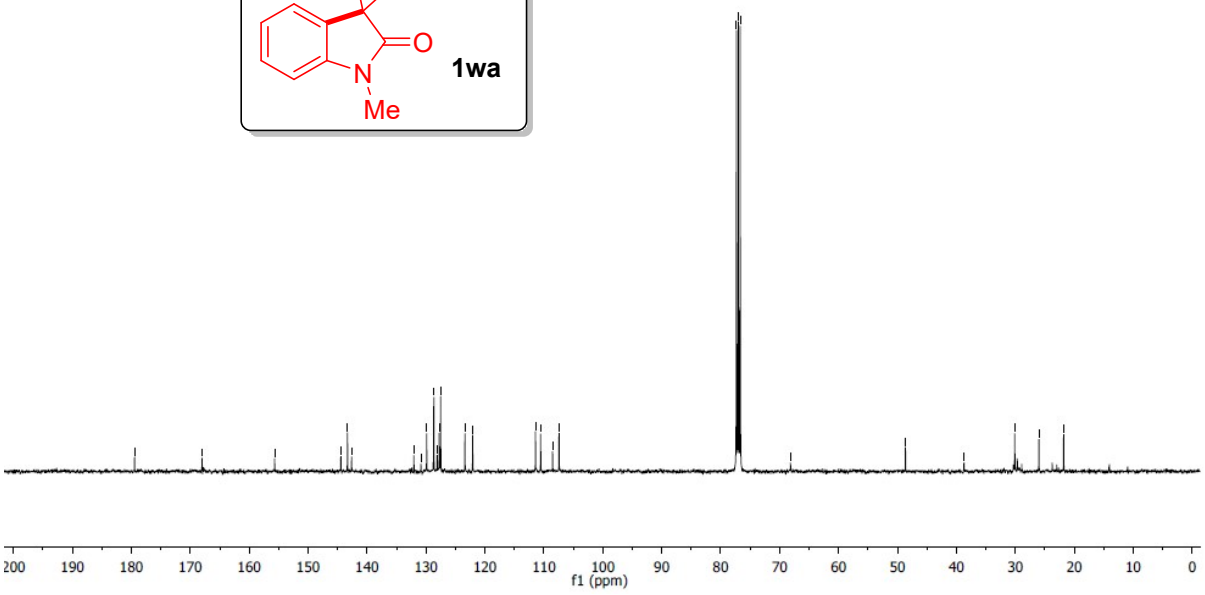
25.99
21.79


O
N
O
Ph
H3C
O
N
Me
1wa


200
190
180
170
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150
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130
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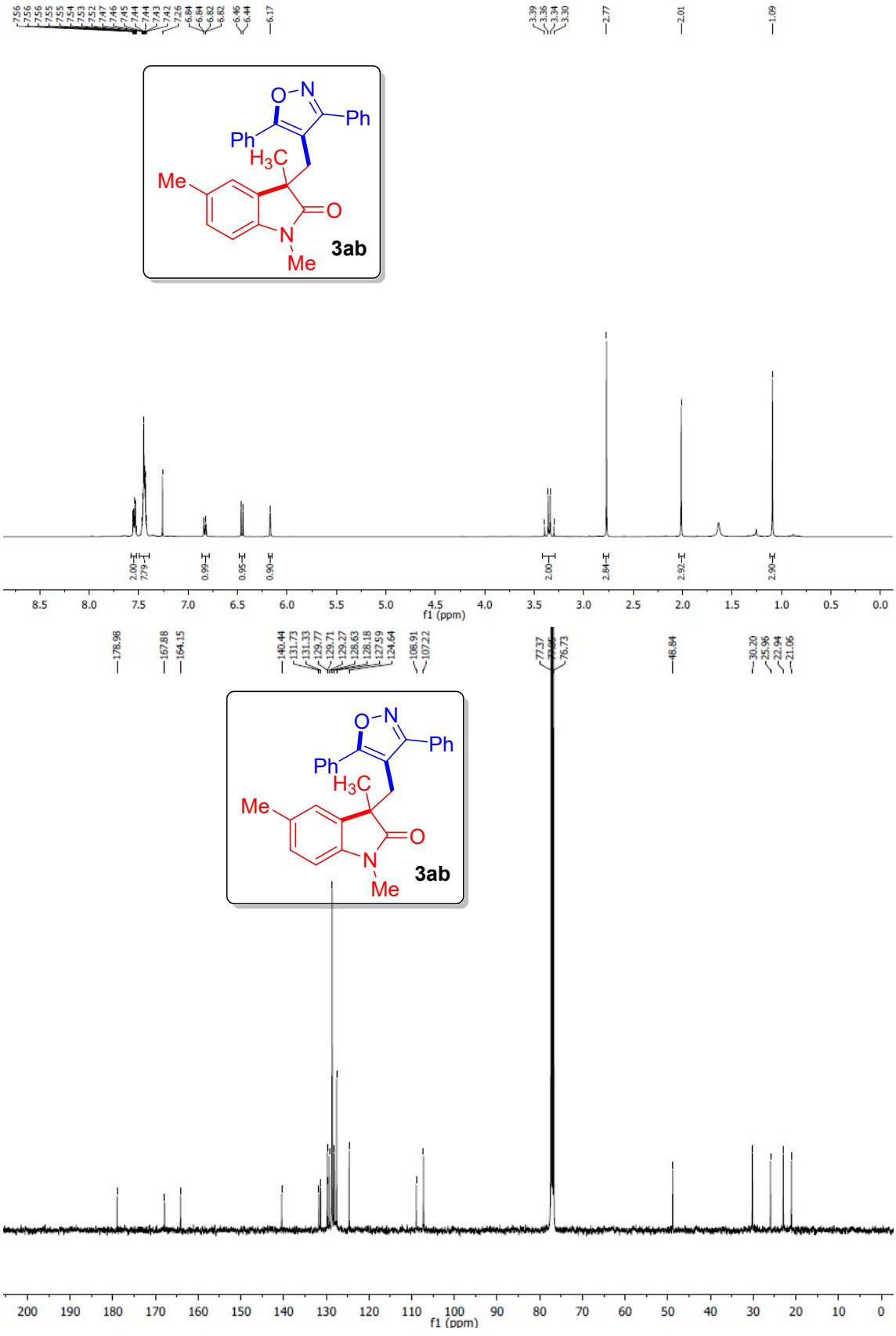
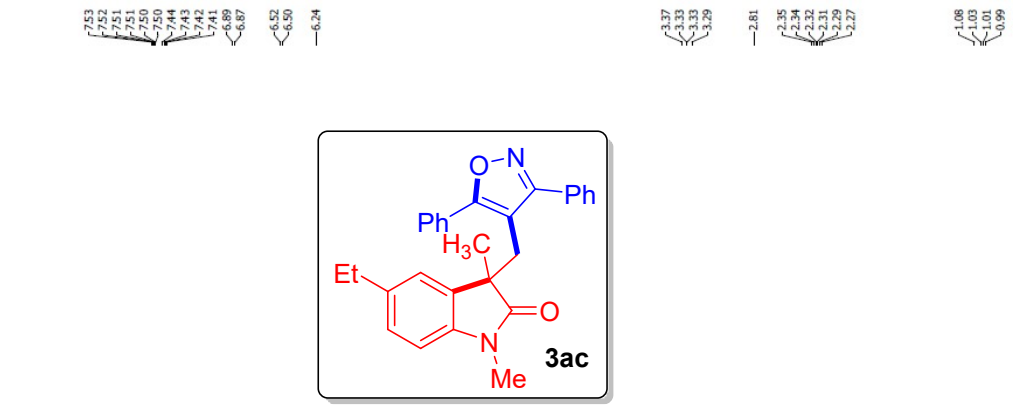
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


3ab
f1 (ppm)
3ab
f1 (ppm)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7.41
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6.50
6.24
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3.33
3.33
3.29
2.81
2.35
2.34
2.32
2.31
2.29
2.27
1.08
1.03
1.01
0.99
O
N
Ph
Ph
H3C
Et
O
N
Me
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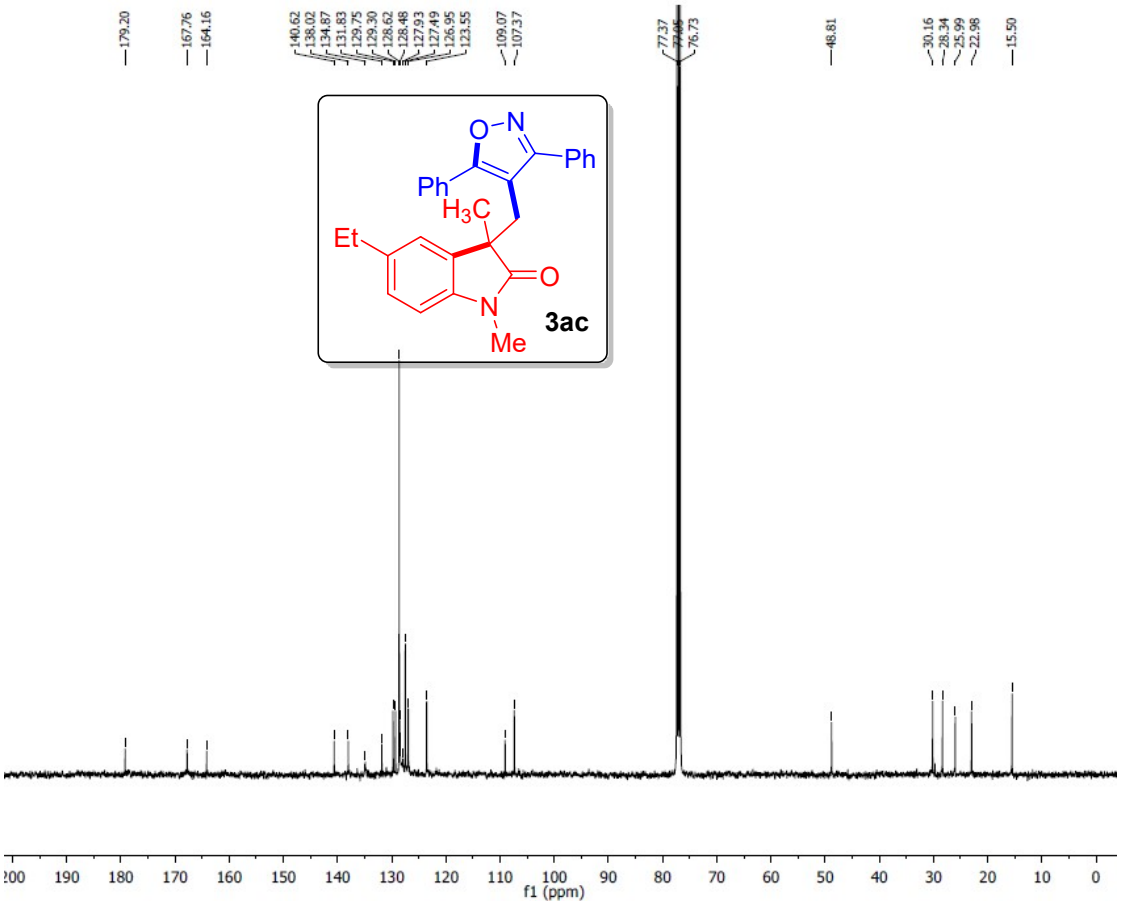
1.00
1.00
0.90
2.00
2.84
2.12
3.07
3.00
f1 (ppm)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127.49
126.95
123.55
109.07
107.37
77.37
76.73
48.81
30.16
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22.98
15.50
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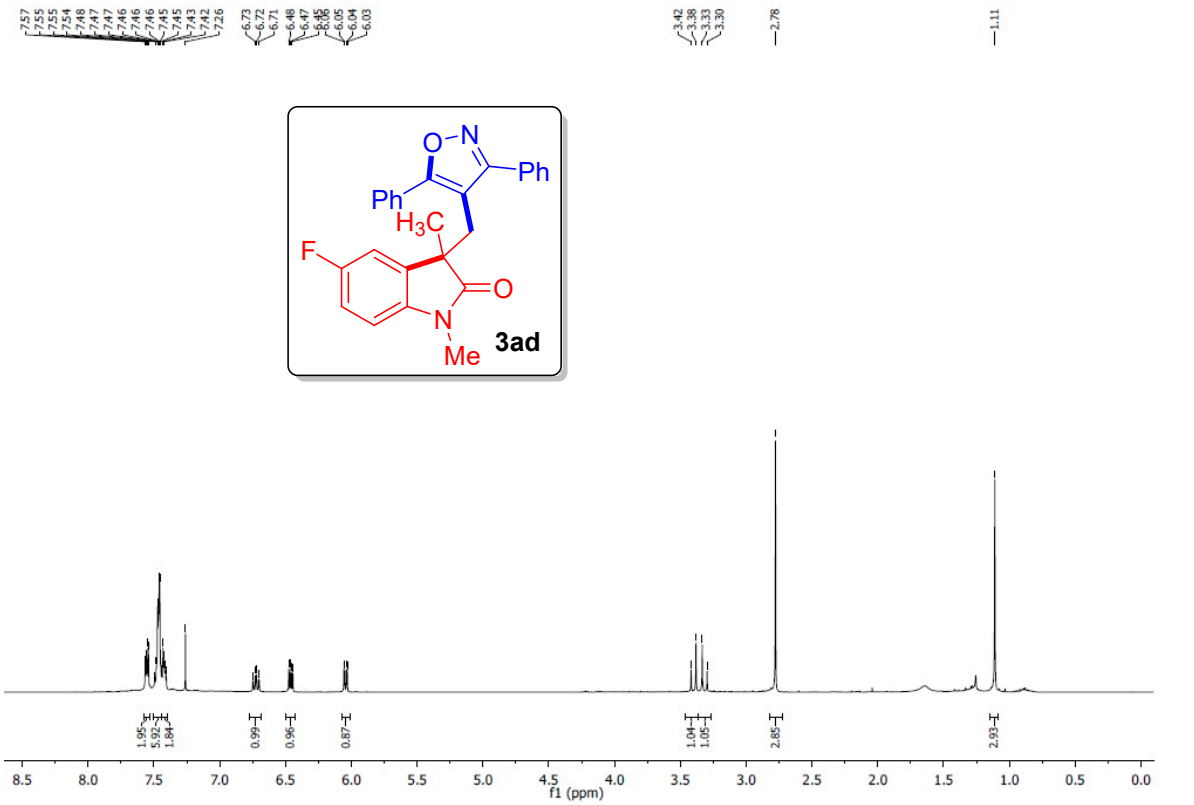
N
Ph
Ph
H3C
Et
O
N
Me
3ac
f1 (ppm)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6.73
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6.71
6.48
6.47
6.05
6.04
6.03
3.42
3.38
3.33
3.30
2.78
1.11
O
N
Ph
Ph
H3C
F
O
N
Me
3ad
1.95
5.92
1.84
0.99
0.96
0.87
1.04
1.05
2.85
2.93
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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3.5
3.0
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2.0
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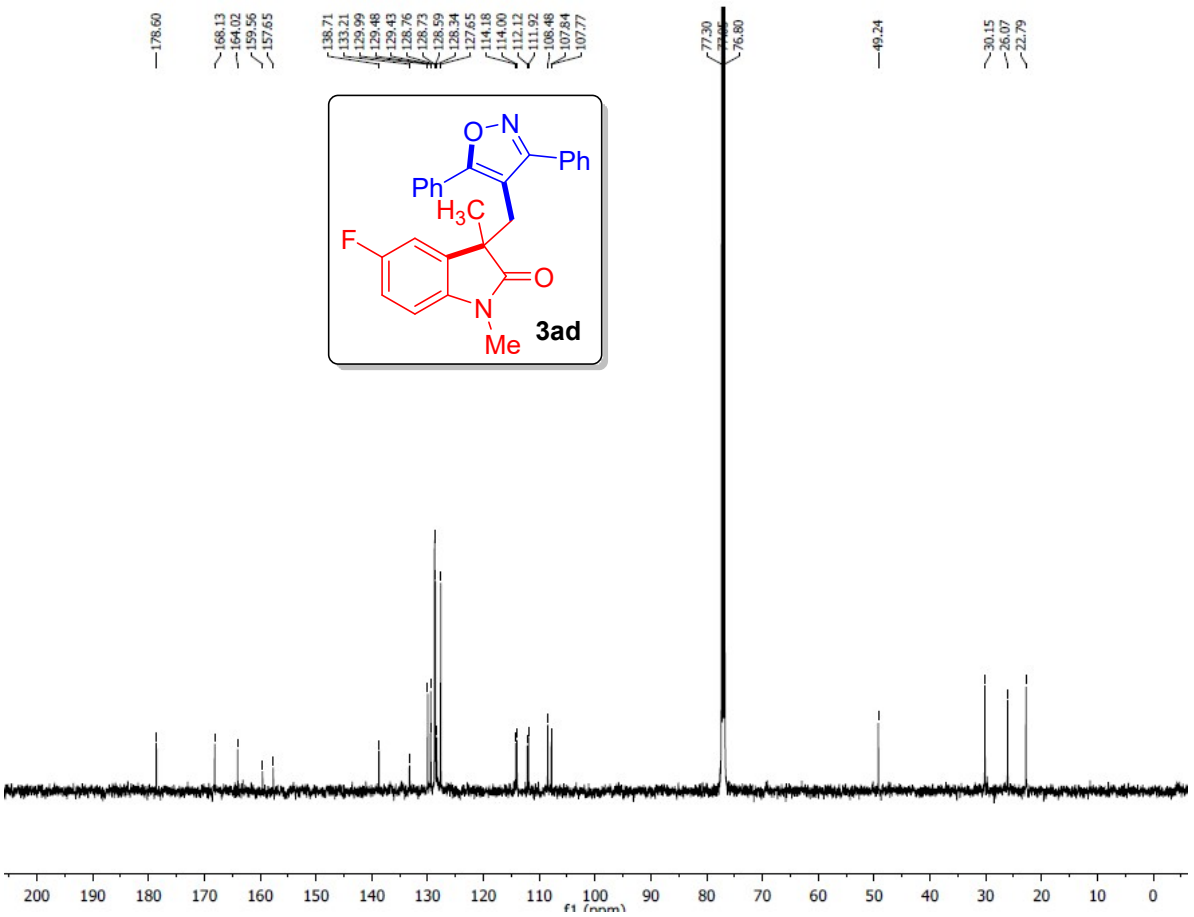
1.0
0.5
0.0
f1 (ppm)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128.73
128.59
128.34
127.65
114.18
114.00
112.12
111.92
106.48
107.84
107.77
77.30
76.80
49.24
30.15
26.07
22.79
O
N
Ph
Ph
H3C
F
O
N
Me
3ad
200
190
180
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90
80
70
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50
40
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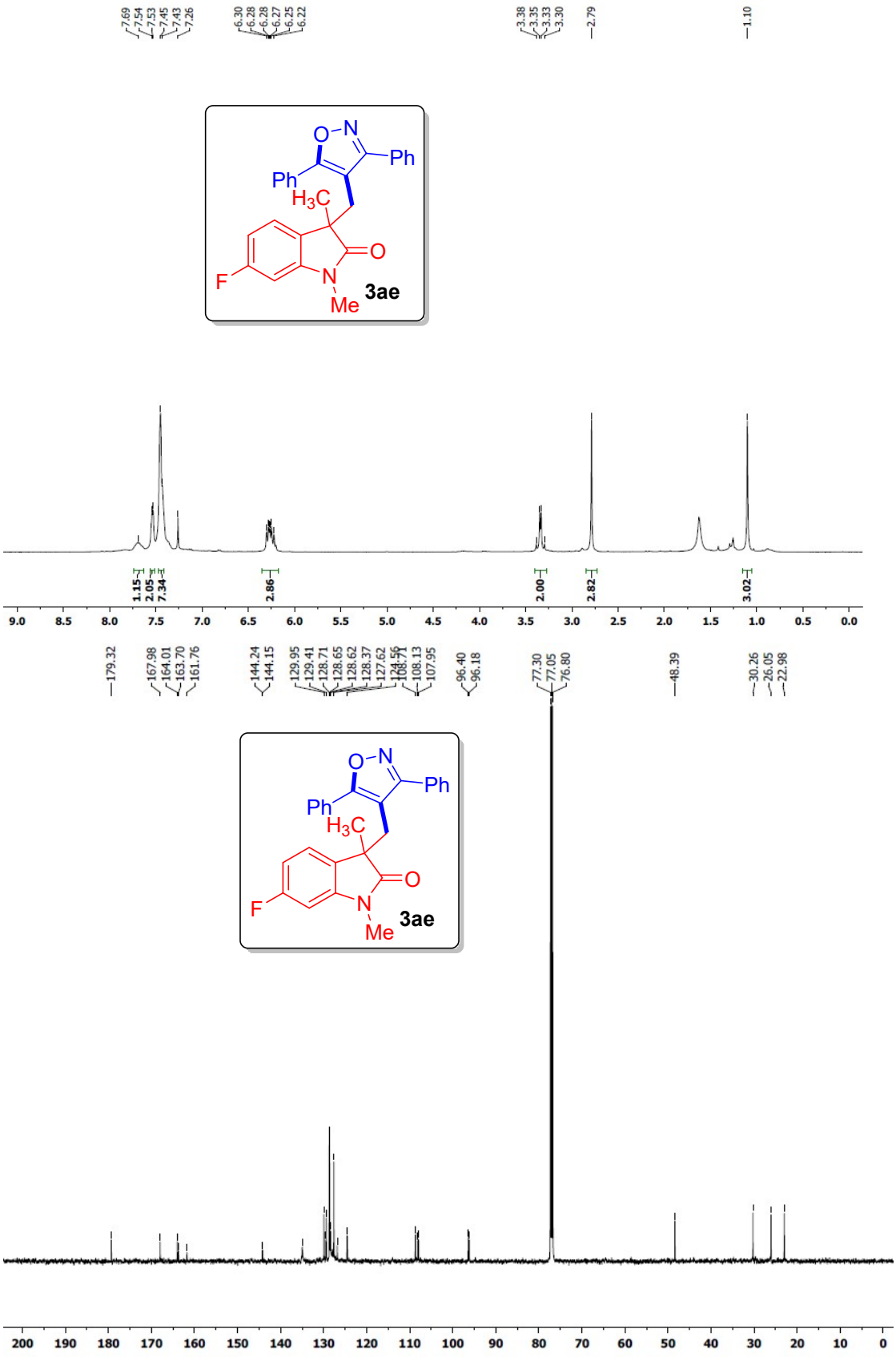
10
0
f1 (ppm)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6.28
6.28
6.27
6.25
6.22
3.38
3.35
3.33
3.30
2.79
1.10
O
N
Ph
Ph
H3C
O
F
N
Me
3ae
1.15
2.05
7.34
2.86
2.00
2.82
3.02
9.0
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8.0
7.5
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6.0
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
179.32
167.98
164.01
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161.76
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144.15
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128.65
128.62
128.37
127.62
124.56
108.71
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107.95
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77.30
77.05
76.80
48.39
30.26
26.05
22.98
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10
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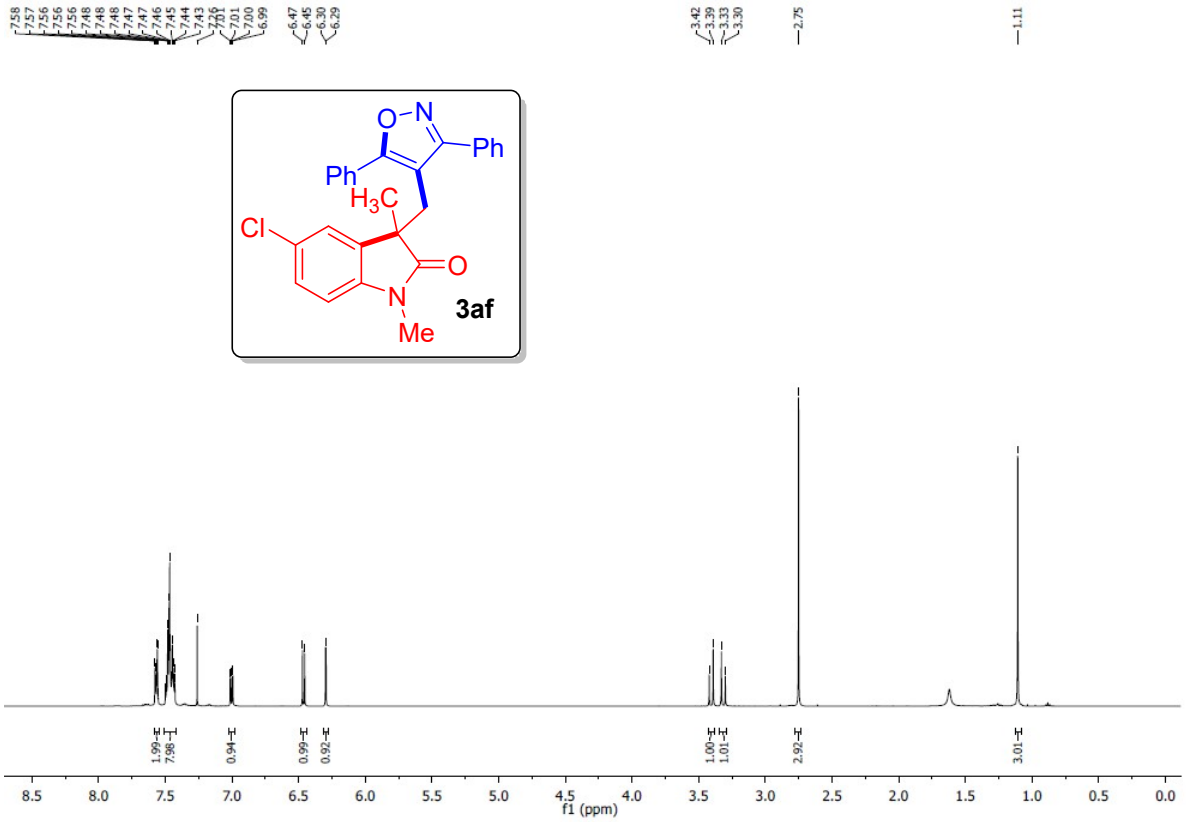
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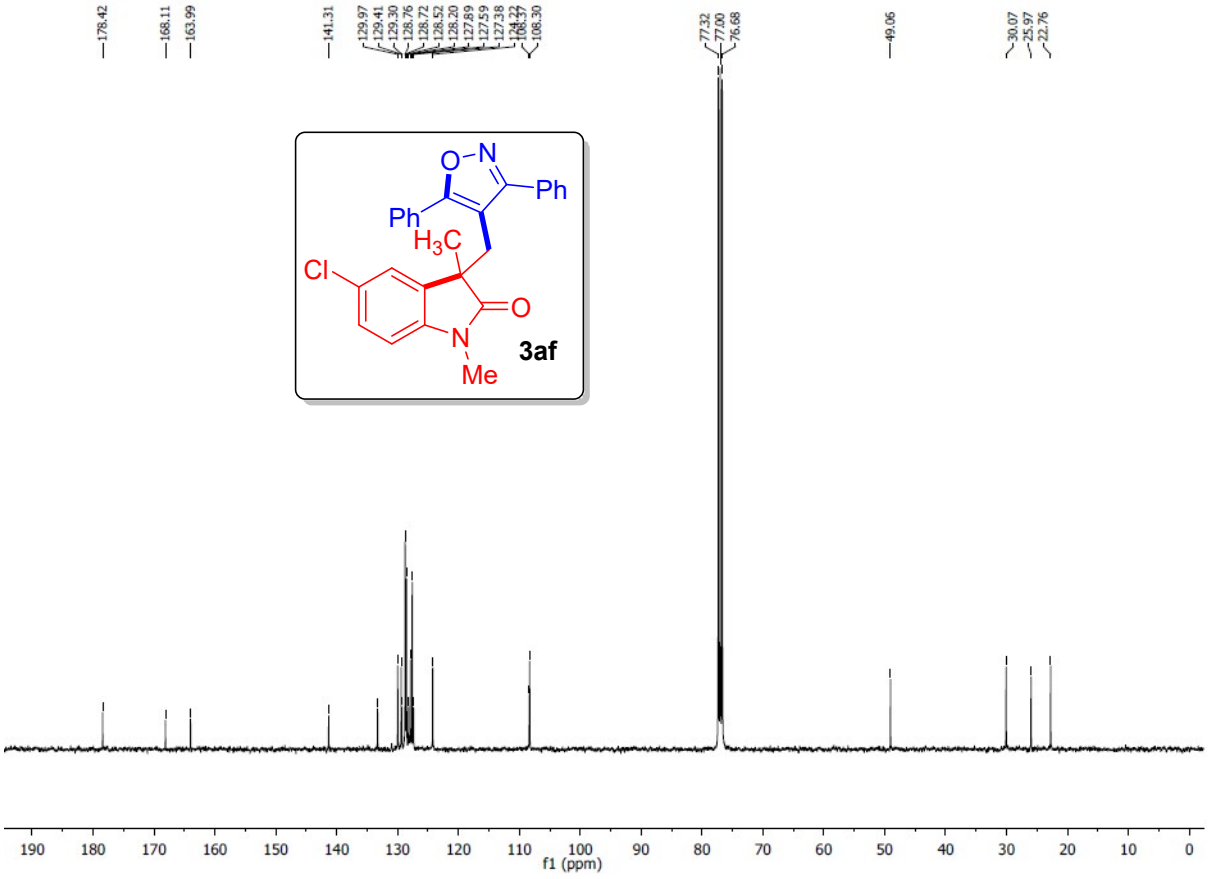
f1 (ppm)


3af
f1 (ppm)


7.70
7.65
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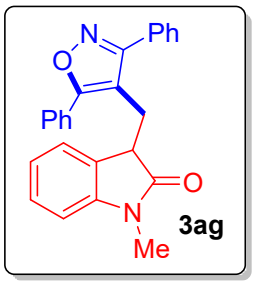
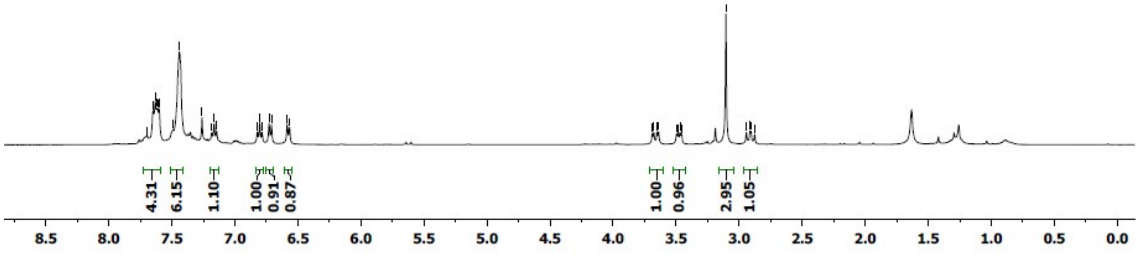
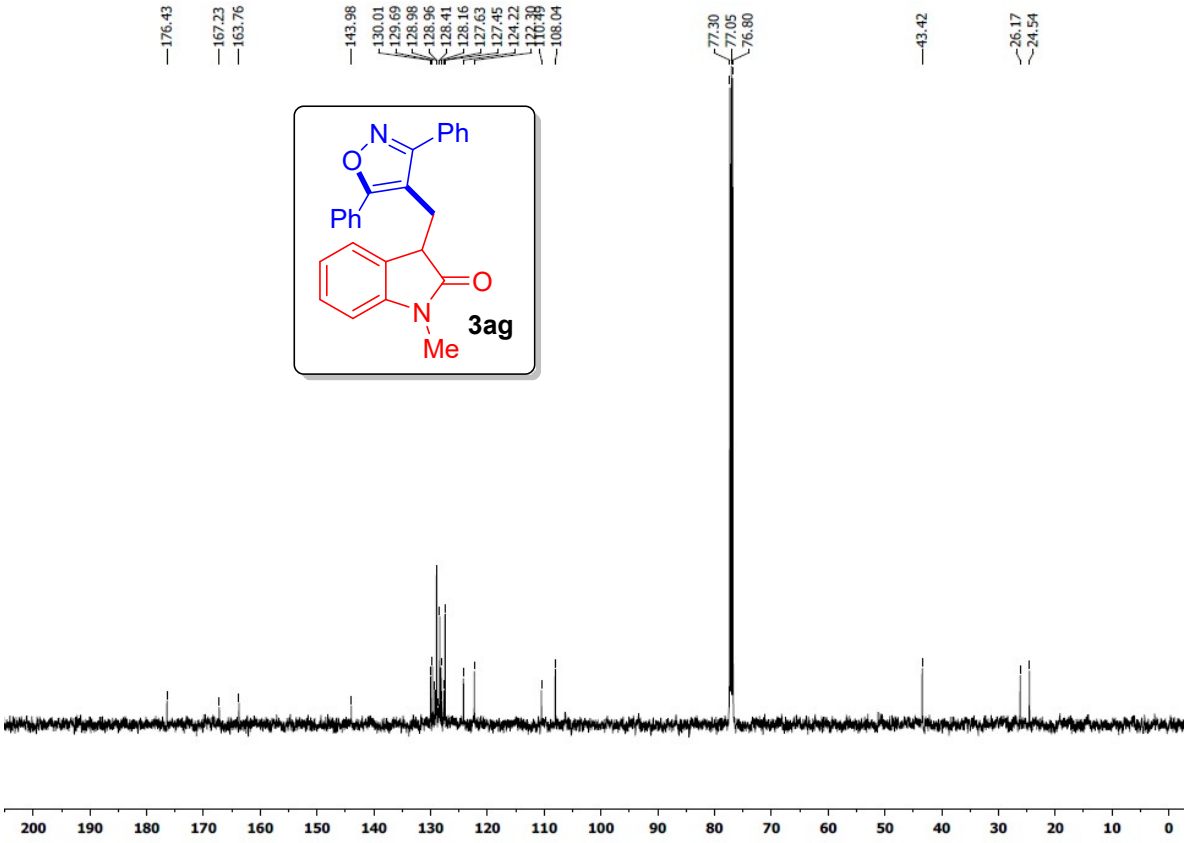
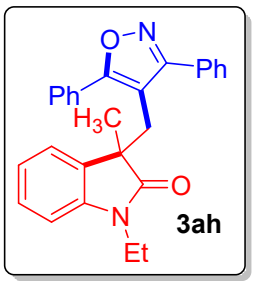
7.60
7.49
7.44
7.26
7.18
7.16
7.14
6.82
6.80
6.78
6.73
6.71
6.58
6.57
3.69
3.68
3.65
3.64
3.50
3.48
3.47
3.46
3.10
2.94
2.91
2.91
2.88

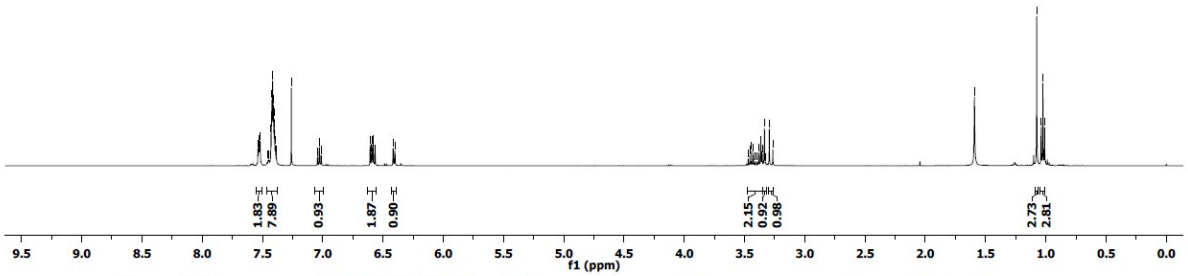

N
Ph
O
Ph
O
N
Me
3ag


4.31
6.15
1.10
1.00
0.91
0.87
1.00
0.96
2.95
1.05
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
0.0


176.43
167.23
163.76
143.98
130.01
129.69
128.98
128.96
128.41
128.16
127.63
127.45
124.22
108.04
77.30
77.05
76.80
43.42
26.17
24.54
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

N
Ph
O
Ph
O
N
Me
3ag


O
N
Ph
Ph
H3C
O
N
Et
3ah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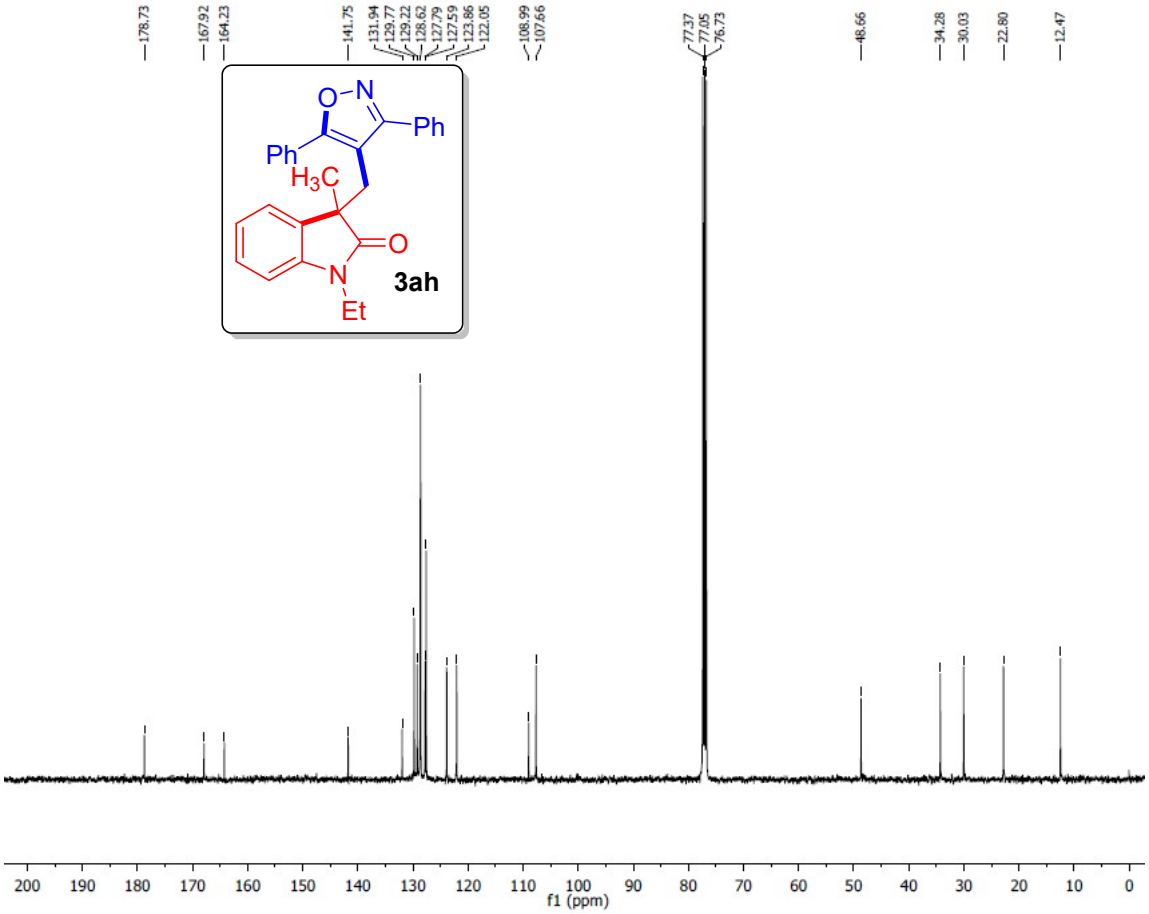
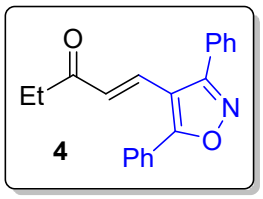
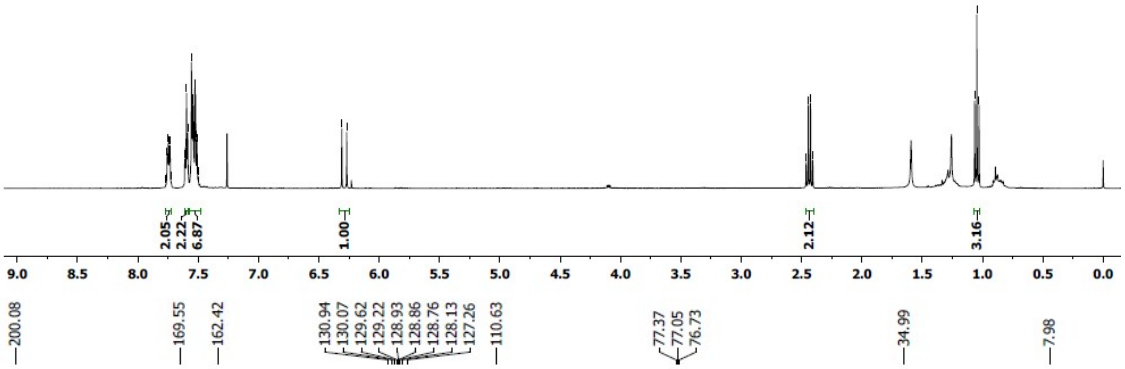
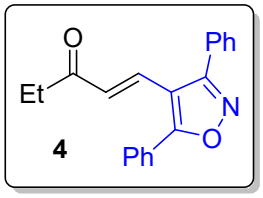
7.89
0.93
1.87
0.90
2.15
0.92
0.98
2.73
2.81
f1 (ppm)

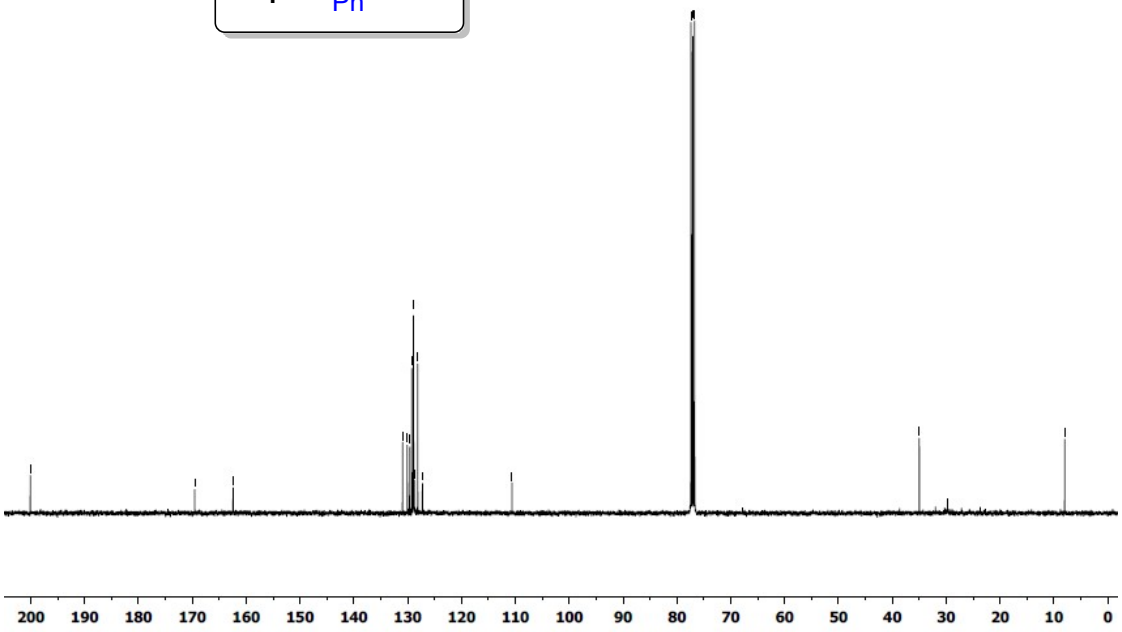

178.73
167.92
164.23
141.75
131.94
129.77
129.22
128.62
127.79
127.59
123.86
122.05
108.99
107.66
77.37
77.05
76.73
48.66
34.28
30.03
22.80
12.47
O
N
Ph
Ph
H3C
O
N
Et
3ah
f1 (ppm)

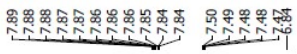

7.76
7.75
7.75
7.74
7.74
7.73
7.73
7.61
7.60
7.60
7.59
7.58
7.56
7.55
7.54
7.53
7.52
7.51
7.51
7.50
6.31
6.27
2.46
2.44
2.42
2.41
1.07
1.05
1.03

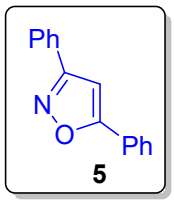

O
Et
Ph
N
O
Ph
4


2.05
2.22
6.87
1.00
2.12
3.16
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
0.0
200.08
169.55
162.42
130.94
130.07
129.62
129.22
128.93
128.86
128.76
128.13
127.26
110.63
77.37
77.05
76.73
34.99
7.98

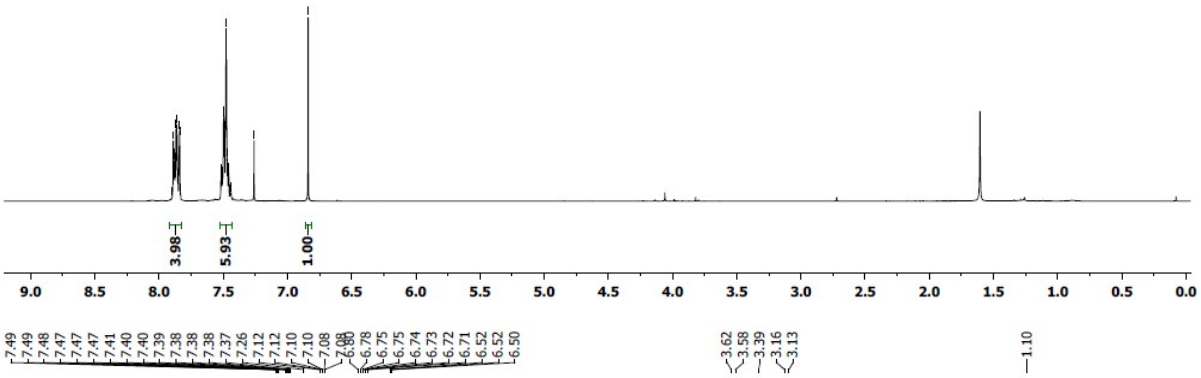

O
Et
Ph
N
O
Ph
4

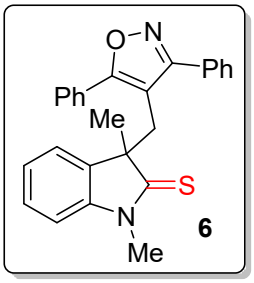

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



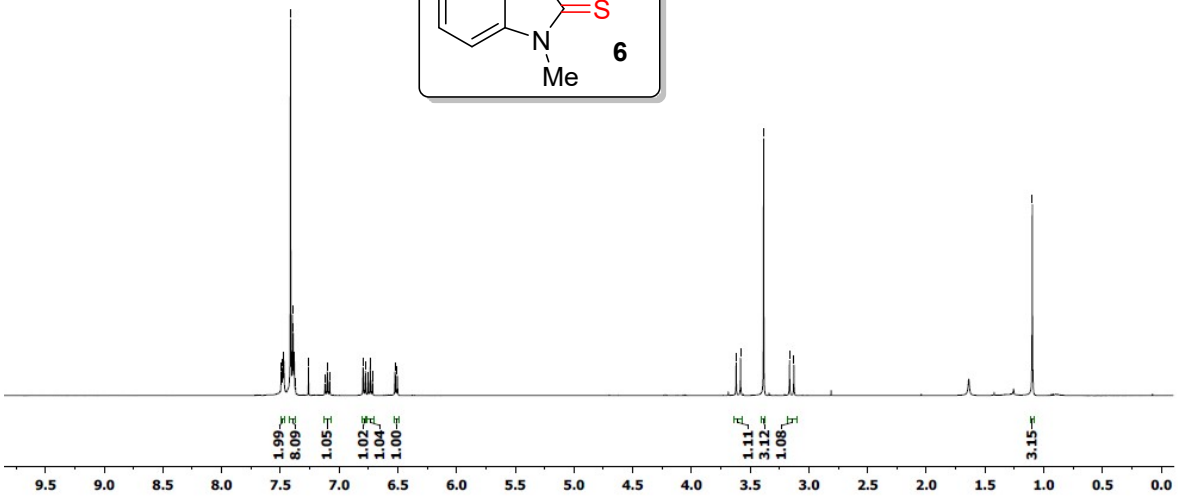

Ph
N
O
Ph

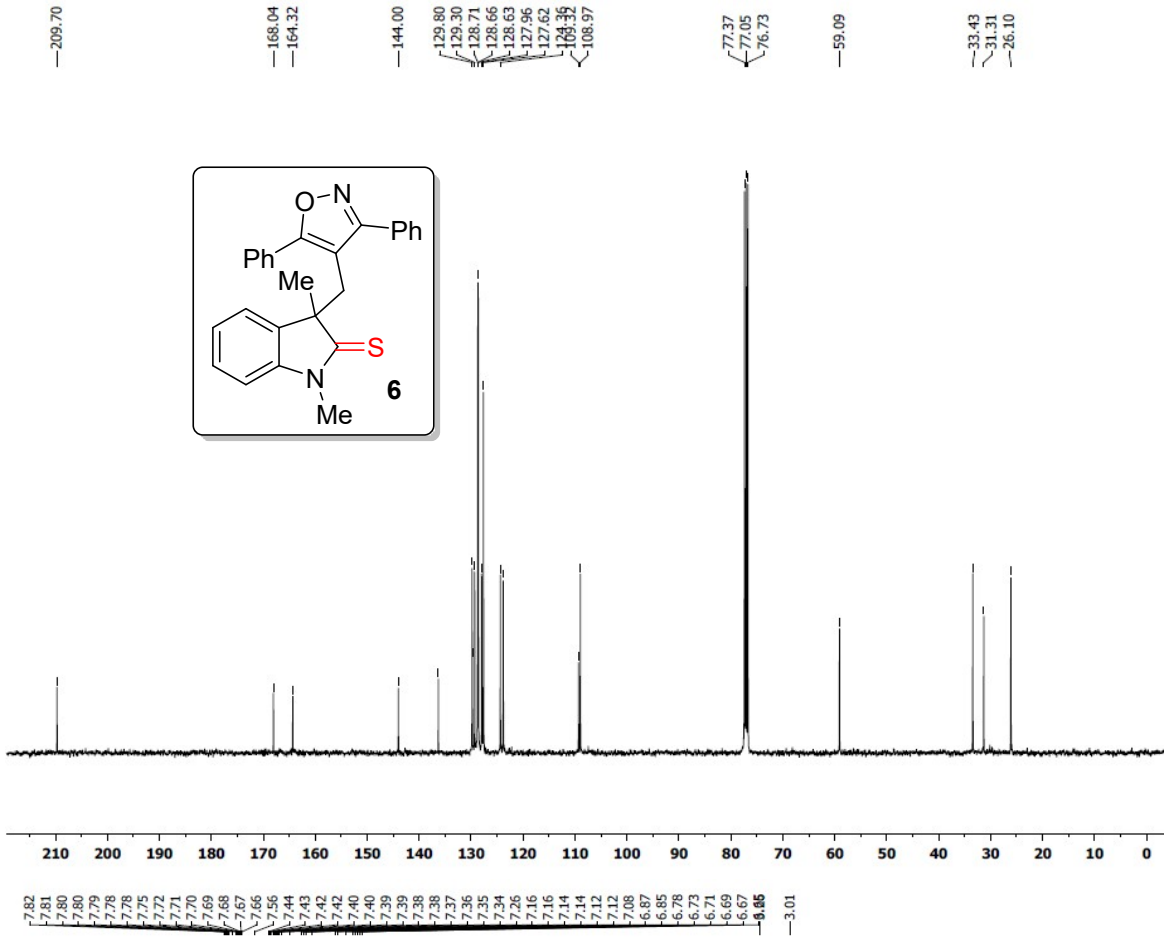
5


3.98
5.93
1.00
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
0.0


O
N
Ph
Ph
Me
S
N
Me

6


1.99
8.09
1.05
1.02
1.04
1.00
1.11
3.12
1.08
3.15
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
0.0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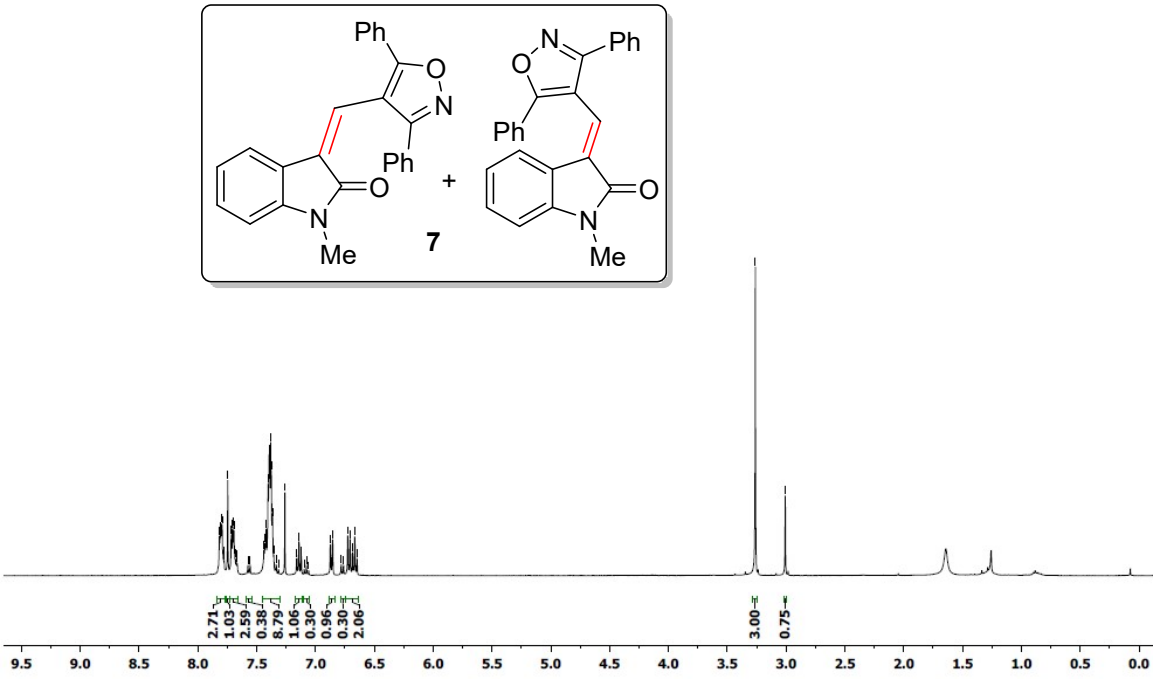
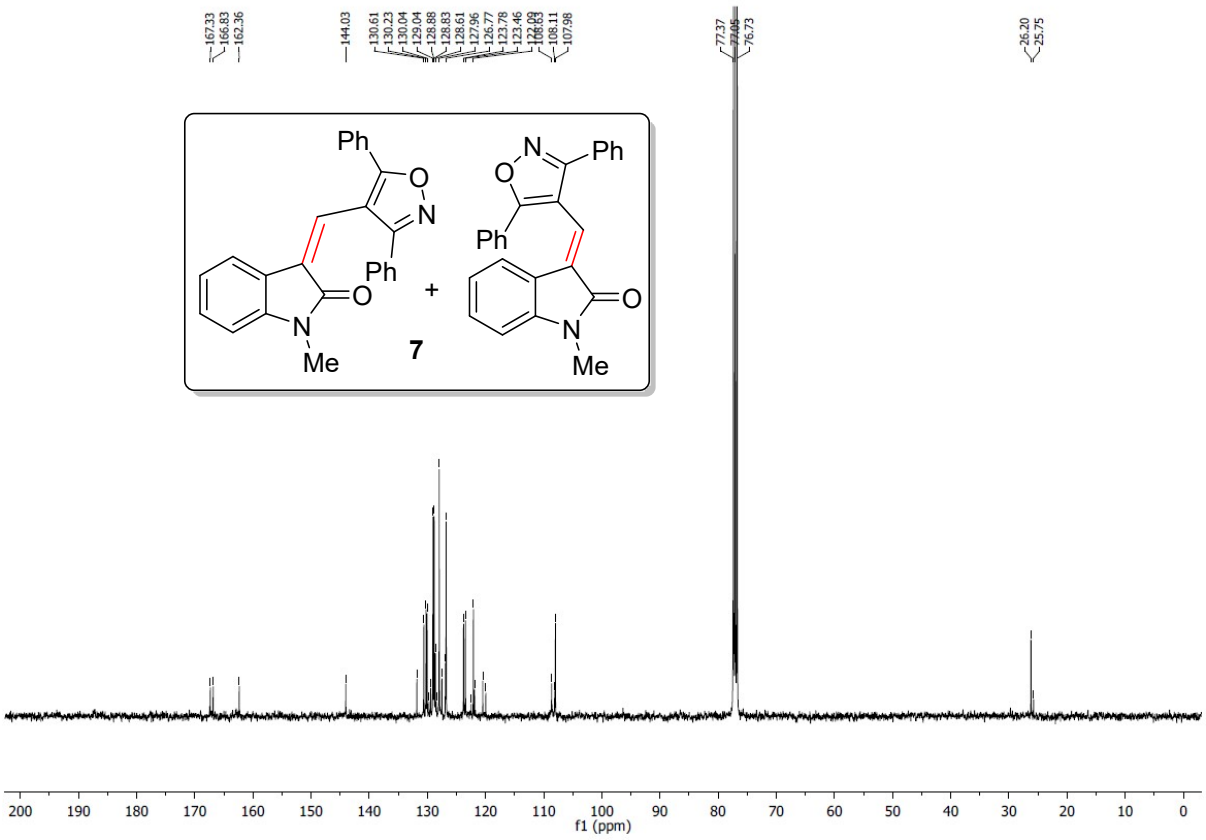
168.04
164.32
144.00
129.80
129.30
128.71
128.66
128.63
127.96
127.62
108.97
77.37
77.05
76.73
59.09
33.43
31.31
26.10
Ph
Ph
Me
S
N
Me
6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
7.82
7.81
7.80
7.80
7.79
7.78
7.78
7.75
7.72
7.71
7.70
7.69
7.68
7.67
7.66
7.56
7.44
7.43
7.42
7.42
7.40
7.40
7.39
7.39
7.38
7.38
7.37
7.36
7.35
7.34
7.26
7.16
7.16
7.14
7.14
7.12
7.12
7.08
6.87
6.85
6.78
6.73
6.71
6.69
6.67
3.01


Ph
Ph
Me
7
+
Ph
Ph
Me
2.71
1.03
2.59
0.38
8.79
1.06
0.30
0.96
0.30
2.06
3.00
0.75
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 0.0


167.33
166.83
162.36
144.03
130.61
130.23
130.04
129.04
128.88
128.83
128.61
127.96
126.77
123.78
123.46
122.03
108.63
108.11
107.98
77.37
77.05
76.73
26.20
25.75
Ph
O
N
Ph
O
N
Me
+
7
N
Ph
O
Ph
O
N
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)