Electronic Supplementary Material (ESI) for ChemComm.
This journal is © The Royal Society of Chemistry 2019

**Supporting Information**

# Rhodium(III)-Catalysed Carboxylate-Directed C-H Functionalizations of Isoxazoles with Alkynes

Somaraju Yugandar [a] and Hiroyuki Nakamura *

Laboratory for Chemistry and Life Sciece, Institute of Innovative Research, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8503, Japan

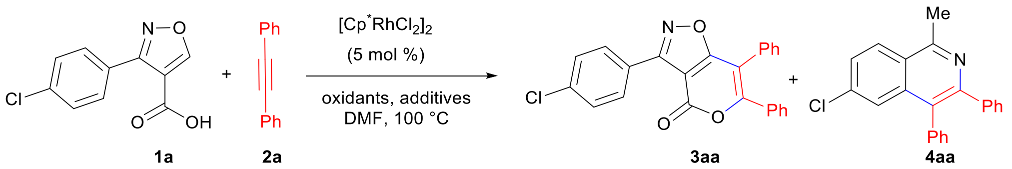
Corresponding E-mail: hiro@res.titech.ac.jp

## Contents

## General Information

NMR spectra were recorded on a Bruker biospin AVANCE Ⅱ (400 MHz for $^1$H, 100 MHz for $^{13}$C) or a Bruker biospin AVANCE Ⅲ (500 MHz for $^1$H, 125 MHz for $^{13}$C) instrument in the indicated solvent. Chemical shifts are reported in parts per million (ppm) relative to the signal (0.00 ppm) for internal tetramethylsilane for solutions in $CDCl_3$ (7.26 ppm for $^1$H, 77.16 ppm for $^{13}$C) or DMSO–$d_6$ (2.50 ppm for $^1$H, 39.52 ppm for $^{13}$C). Multiplicities are reported using the following abbreviations: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), quin (quintet), sex (sextet), m (multiplet), br (broad) *J*; coupling constants in Hertz. IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. Only the strongest and/or structurally important peaks are reported as IR data given in cm$^{-1}$. Mass spectra were measured using a JMS-700 Mstation and Bruker microTOF II. HRMS (EI, 70 eV) was calibrated as perfluorokerosene and HRMS (ESI-TOF) was calibrated as sodium formate. All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light (254 nm) and were visualized using an aqueous alkaline $KMnO_4$ solution. Column chromatography was performed on Silica Gel 60 N, purchased from Kanto Co. All the reagents were purchased from commercial suppliers and used without further purification. The required 3-substituted-isoxazolyl-4-carboxylic acids **1a**,[1] **1b-d**[2] and **6**[3] are prepared according to reported literature, alkynes **2a**, **2f-m** are purchased from Aldrich and TCI and **2b-e**[4] are prepared according to the reported procedures.

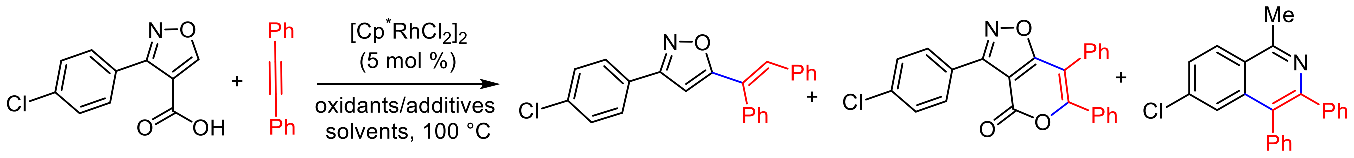
**Table S1**. Optimization of reaction conditions for the formation of **3aa** and **4aa**[a]



| Entry | Oxidant | Additive | Time (h) | **3aa** (%)[b] | **4aa** (%)[b] |
|---|---|---|---|---|---|
| 1[c] | $Ag_2CO_3$ | - | 16 | 27 | - |
| 2 | $Ag_2CO_3$ | - | 2 | 72 | - |
| 3 | $K_2S_2O_8$ | - | 12 | N.R |  |
| 4 | $AgNTf_2$ | - | 12 | N.R |  |
| 5 | AgOAc | - | 4 | 53 |  |
| 6[d] | $Ag_2CO_3$ | - | 15 | 6 | - |
| 7[e] | $Ag_2CO_3$ | - | 15 | 9 | - |
| 8 | $Ag_2CO_3$ | $AgSbF_6$ | 20 | 25 | - |
| 9 | $Ag_2CO_3$ | NaOPiv | 2 | 60 | - |
| 10 | $Ag_2CO_3$ | NaOAc | 2 | 32 | - |
| 11 | $Ag_2CO_3$ | $K_2CO_3$ | 8 | 38 | - |
| 12[f] | $Ag_2CO_3$ | - | 2 | 76 | - |
| 13 | - | - | 24 | 8 | - |
| 14 | $Cu(OAc)_2 \cdot H_2O$ | - | 2 | - | 60 |
| 15[e] | $Cu(OAc)_2 \cdot H_2O$ | - | 2 | - | 52 |
| 16 | $Cu(OAc)_2 \cdot H_2O$ | - | 4 | - | 55 |
| 17 | CuO | - | 14 | - | - |
| 18[g] | $Cu(OAc)_2 \cdot H_2O$ | - | 20 | - | - |

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), $[Cp^*RhCl_2]_2$ (5 mol %), oxidant (1 equiv.), additive (20 mol %), solvent (1 mL) under Ar atmosphere at 100 °C. [b] Isolated yield. [c] $Ag_2CO_3$ (0.5 equiv.). [d] In dichloroethane. [e] In *o*-xylene [f] Under open air. [g] Absence of Rh-catalyst. N.R = no reaction.

**Table S2.** [Cp*RhCl$_2$]$_2$ catalyst (acidic conditions) [a]

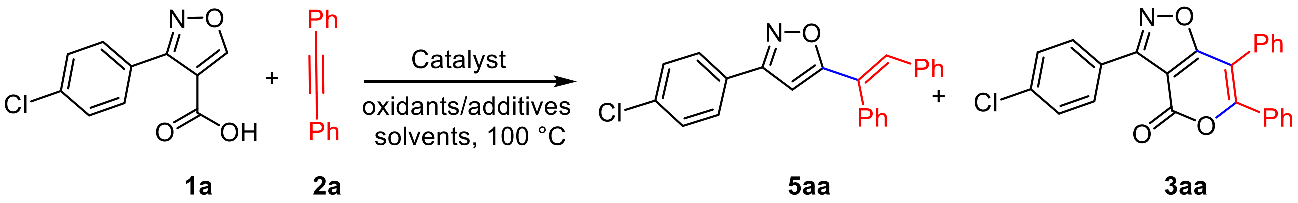


**1a** **2a** **5aa** **3aa** **4aa**

| entry | oxidant/additive<br>(1.0 equiv) | solvent | time h | yield (%)[b] | | |
|---|---|---|---|---|---|---|
| | | | | **5aa** | **3aa** | **4aa** |
| 1 | AcOH | PhCF$_3$ | 20 h | 6 | 0 | 47 |
| 2 | Ag$_2$CO$_3$ | MeOH | 6 h | 8 | 52 | 0 |
| 3 | TFA | DCE | 30 h | trace | 32 | 0 |
| 4 | AcOH | DCE | 14 h | 15 | trace | 32 |
| 5 | AcOH (3.0) | DCE | 10 h | 21 | trace | 24 |
| 6 | AcOH<br>AgSbF$_6$ (0.1) | DCE | 8h | trace | 0 | 30 |
| 7 | AcOH | MeCN | 20 h | 11 | 0 | 24 |
| 8 | AcOH | DMF | 20 h | 34 | 0 | 12 |

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), catslyst (5 mol %), oxidant (1 equiv.), additive (10 mol %), solvent (0.5 mL) at 100 °C. [b] Isolated yield.

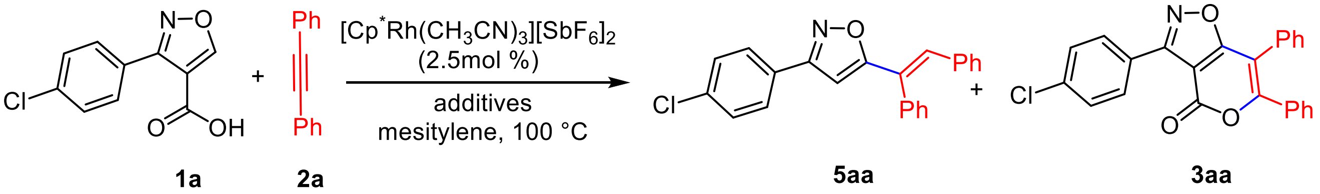
**Table S3.** *Ru, Co, Ir* catalysts[a]



| entry | Catalyst (2.5 mol %) | oxidant/additive (1.0 equiv) | solvent | time h | yield (%) [b] **5aa** | yield (%) [b] **3aa** |
|---|---|---|---|---|---|---|
| 1 | [Ru(*p*-cymene)$Cl_2$]$_2$ | NaOAc | Dioxane | 16 h | trace | 12 |
| 2 | [Ru(*p*-cymene)$Cl_2$]$_2$ | NaOAc | MeOH:$H_2O$ | 16 h | trace | 0 |
| 3 | [Ru(*p*-cymene)$Cl_2$]$_2$ | AcOH | toluene | 20 h | 8 | 0 |
| 4 | [Ru(*p*-cymene)$Cl_2$]$_2$ | $K_2CO_3$ | DMF | 8 h | decomposed | |
| 5 | [Ru(*p*-cymene)$Cl_2$]$_2$ | PivOH | $CH_3CN$ | 12 h | 16 | trace |
| 6 | [Ru(*p*-cymene)$Cl_2$]$_2$ | $AgSbF_6$ | DCM | 12 h | N.R | |
| 7 | [Ru(*p*-cymene)$Cl_2$]$_2$ | $K_2CO_3$ | DMSO | 8 h | decomposed | |
| 8 | [Ru(*p*-cymene)$Cl_2$]$_2$ | KOAc | THF | 8 h | N.R | |
| 9 | Cp*Co(CO)$I_2$ | AcOH | DMF | 24 h | N.R | |
| 10 | Cp*Co(CO)$I_2$ | TFA | DMF | 24 h | decomposed | |
| 11 | Cp*Co(CO)$I_2$ | $Ag_2CO_3$ | DMF | 12 h | decomposed | |
| 12 | Cp*Co(CO)$I_2$ | $AdCO_2H$/$AgSbF_6$ (0.2) | DCE | 20 h | N.R | |
| 13 | Cp*Co(CO)$I_2$ | $AdCO_2H$/NaOPiv (0.2) | DCE | 15 h | N.R | |
| 14 | Cp*Co(CO)$I_2$ | AcOH/KOAc (0.2) | DCE | 15 h | N.R | |
| 15 | [Cp*Ir$Cl_2$]$_2$ | $Ag_2CO_3$ | DMF | 8 h | N.R | |

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), catalyst (2,5 mol %), oxidant (1 equiv.), additive (20 mol %), solvent (0.5 mL) at 100 °C. [b] Isolated yield. N.R = no reaction.

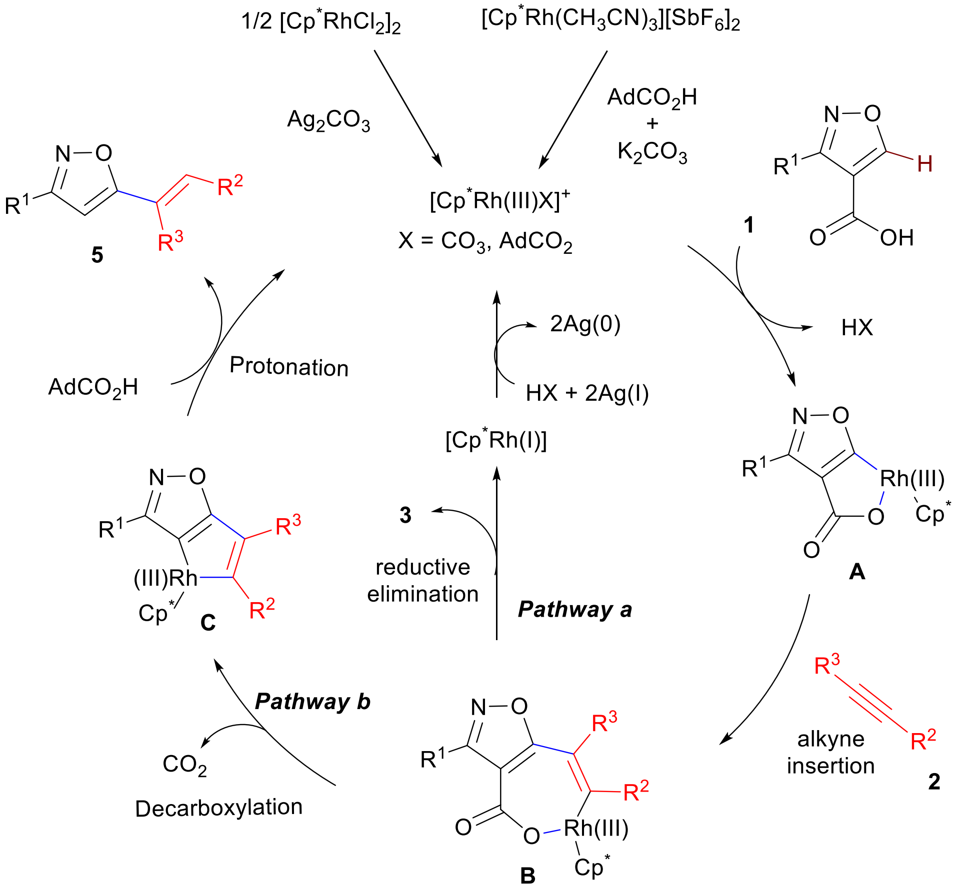
**Table S4.** [Cp*Rh(CH3CN)3][SbF6]2 catalyst[a]



| entry | additive (1.0 equiv) | base (1.0 equiv) | time h | yield (%)[b] | |
|---|---|---|---|---|---|
| | | | | **5aa** | **3aa** |
| 1 | AcOH | - | 20 h | 22 | 39 |
| 2 | PivOH | - | 20 h | 18 | 31 |
| 3 | $AdCO_2H$ | - | 20 h | 30 | 22 |
| 4 | - | $K_2CO_3$ | 20 h | 38 | 16 |
| 5 | - | KOAc | 20 h | 14 | 36 |
| 6 | - | NaOAc | 20 h | 19 | 25 |
| 7 | - | NaOPiv | 20 h | 24 | 21 |
| 8 | - | $K_3PO_4$ | 20 h | 10 | 32 |
| 9 | - | $K_2HPO_4$ | 20 h | 15 | 10 |
| 10 | - | $Et_3N$ | 20 h | 12 | 14 |
| 11 | - | DABCO | 20 h | 7 | 18 |
| 12 | AcOH | $K_2CO_3$ | 18 h | 52 | 18 |
| 13 | PivOH | $K_2CO_3$ | 18 h | 49 | 23 |
| 14 | $AdCO_2H$ | $K_2CO_3$ | 16 h | 68 | 12 |
| 15[c] | $AdCO_2H$ | $K_2CO_3$ | 8 h | 73 | 8 |
| 16[c] | $AdCO_2H$ | $K_2CO_3$(0.5) | 8 h | 75 | 10 |
| **17[c]** | **$AdCO_2H$** | **$K_2CO_3$(0.3)** | **8 h** | **78** | **6** |
| 18[c] | $AdCO_2H$ | $K_2CO_3$(0.2) | 8 h | 67 | 14 |

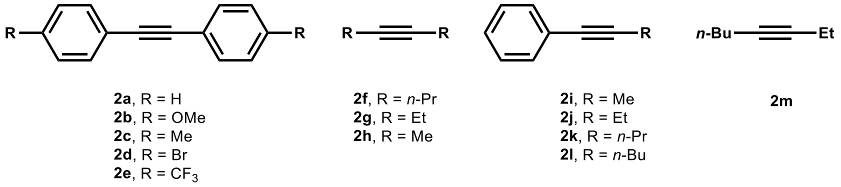
[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), catalyst (2,5 mol %), additive (1 equiv.), base (1 equiv.), solvent (0.5 mL) at 100 °C. [b] Isolated yield. [c] Reaction at 120 °C.

**Scheme S1** Plausible mechanism for the formation of **3** and **5**



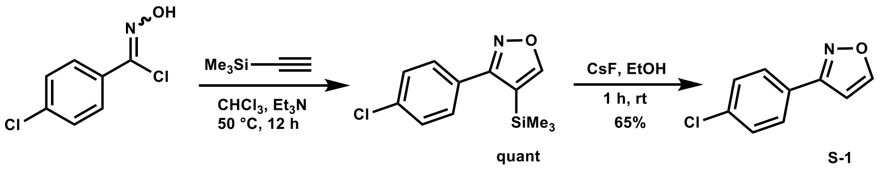
At first, isoxazolyl-4-carboxylic acid **1** coordinates with active Rh(III) catalyst to provide five-membered rhodacyle **A** through C-H activation at C-5 position. Subsequently, rhodacycle **A** coordinates with alkyne **2** followed by insertion gives the seven-membered rhodacycle **B**. In *pathway a*, rhodacyle **B** undergoes reductive elimination to give pyranoisoxazolone **3** and Rh(I) complex, which is reoxdized by Ag(I) to regenerates the Rh(III) catalyst.[5] At high temperatures and in non-polar solvents, *pathway b* favours the decarboxylation to give rhodacycle **C**, which on protonation/protodemetalation provides hydroarylation product **5** with regeneratin of Rh(III) catalyst.[6,7]

## Structures of alkynes

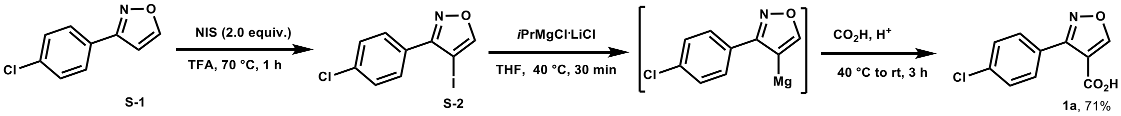


## Preparation of 3-substituted-isoxazolyl-4-carboxylic acids 1a-d

### 3-(4-Chlorophenyl)isoxazole-4-carboxylic acid (1a)



To a stirred solution of 4-chloro-*N*-hydroxybenzimidoyl chloride[8] (1.89 g, 0.01 mol) and trimethylsilylacetylene (1.56 mL, 0.011 mol) in $CHCl_3$ (20.0 mL), $Et_3N$ (3.48 mL, 0.025 mol, 2.50 eq.) was added at 0 °C under an argon atmosphere. After being stirred for 1 h at 50 °C, the reaction mixture was diluted with $CH_2Cl_2$. The organic phase was washed with water and brine and dried over $MgSO_4$ and concentrated *in vacuo*. The residue was dissolved in ethanol (25.0 ml) and CsF (3.03 g, 0.02 mol, 2.00 eq.) was added under an argon atmosphere. After being stirred for 1 h at room temperature, the reaction mixture was poured into water. The aqueous layer was extracted with two portions of $CH_2Cl_2$. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with hexane : ethyl acetate = 95 : 5 to afford 3-(4-chlorophenyl)isoxazole (**S-1**) as a white solid (1.16 g, 65%). Spectral properties were identical to those previously reported:[9] mp 74-76 °C; $R_f$ 0.6 (1:19 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 3151, 3128, 1546, 1504, 1429, 1274, 1121, 781; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.47 (d, $J$ = 1.2 Hz, 1H), 7.77 (d, $J$ = 8.4 Hz, 2H), 7.44 (d, $J = 8.4$ Hz, 2H), 6.64 (d, $J = 1.6$ Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 160.6, 159.2, 136.2, 129.3, 128.2, 127.4, 102.4.

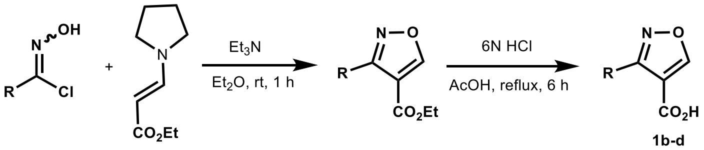


To a stirred solution of 3-(4-chlorophenyl)isoxazole **S-1** (1.00 eq.) in TFA (1.00 mL), *N*-iodosuccinimide (2.0 eq.) was added under an argon atmosphere. After being stirred at 70 °C for 1 h, saturated aq. $NaHCO_3$ was added. The mixture was poured into diethyl ether, the aqueous layer was extracted with two portions of $Et_2O$. The combined extract was washed with 10% aq. $Na_2S_2O_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo* to get 3-(4-chlorophenyl)-4-iodo-isoxazole (**S-2**)[1] in 74% yield. Now, to this 3-(4-chlorophenyl)-4-iodo-isoxazole (3.75 gm, 0.012 mol) in THF (20 mL), 0.8 M solution of *i*PrMgCl·LiCl[10] in THF (16.25 mL, 0.013 mol, 1.10 e.) was added dropwise at -40 °C under an argon atmosphere. After being stirred at the same temperature for 30 min, the vessel was filled with $CO_2$ gas that was collected in a balloon by sublimation of dry ice. After being stirred at room temperature for 3 h, the reaction mixture was acidified with 1 M aq. HCl. The aqueous layer was extracted with two portions of chloroform. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give crude **1a,** which was purified by column chromatography using EtOAc/hexane (1:1) as eluent.

**3-(4-Chlorophenyl)isoxazole-4-carboxylic acid (1a)**. Obtained as a white solid (1.94 g, 71%): mp 180-182 °C; $R_f$ 0.2 (7:3 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 3094, 1714, 1602, 1557, 1464, 1309, 778; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 9.11 (s, 1H), 7.73 (d, $J = 8.8$ Hz, 2H), 7.46 (d, $J = 8.4$ Hz, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 165.9, 165.4, 160.5, 136.9, 130.9, 128.8, 125.4, 112.1; HRMS (ESI) *m/z* calcd for $C_{10}H_5ClNO_3$ $[M-H]^+$ 221.9958 and 223.9928, found 221.9963 and 223.9937.

**3-Substituted-isoxazolyl-4-carboxylic acids (1b-d)**

To a solution of *N*-hydroxybenzimidoyl chloride (0.01 mol) and (*E*) ethyl-3-(pyrrolidin-1-yl)acrylate (1.69 g, 0.01 mol) in diethyl ether, triethylamine (3.48 mL, 0.025 mol) was added at room temperature. The reaction mixture was stirred at room temperature for 1h, and then reaction mixture was poured into saturated $NH_4Cl$ solution, extracted with EtOAc, washed with brine, dried over $Na_2SO_4$ and the solvent was evaporated under reduced pressure to give crude 3-substituted-isoxazolyl-4-carboxylates. Now, these crude isoxazolyl-4-carboxylates were treated with 6N HCl and AcOH (3:2) and the reaction mixture was refluxed for 6 h (monitored by TLC). The reaction mixture cooled to room temperature, quenched with saturated aq. $NaHCO_3$, extracted with EtOAc, washed with brine, dried over $Na_2SO_4$ and the solvent was evaporated under reduced pressure to give crude **1b-d** which were purified by column chromatography using EtOAc/hexane as eluent.



**3-(4-Methoxyphenyl)isoxazole-4-carboxylic acid (1b)**. Obtained as a white solid (0.29 g, 67%): mp 195-197 °C; R*f* 0.2 (7:3 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2954, 2916, 1712, 1613, 1466, 1253, 827; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 9.07 (s, 1H), 7.75 (d, $J$ = 8.4 Hz, 2H), 7.00 (d, $J$ = 8.8 Hz, 2H), 3.86 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 165.6, 164.8, 161.4, 161.0, 131.0, 119.1, 113.9, 111.9, 55.4; HRMS (ESI) *m/z* calcd for $C_{11}H_8NO_4$ $[M-H]^+$ 218.0453 found 218.0447

**3-(4-Nitrophenyl)isoxazole-4-carboxylic acid (1c)**. Obtained as a white solid (0.32 g, 73%): mp 218-220 °C; R*f* 0.2 (7:3 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 3108, 1714, 1529, 1348, 1162, 851; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.72 (s, 1H), 8.33 (d, $J$ = 8.8 Hz, 2H), 8.01 (d, $J$ = 8.8 Hz, 2H); $^{13}C$ NMR (125 MHz, DMSO-$d_6$) $\delta$ 166.3, 161.6, 159.5, 148.4, 133.7, 130.8, 123.3, 113.4; HRMS (ESI) *m/z* calcd for $C_{10}H_5N_2O_5$ $[M-H]^+$ 233.0198, found 233.0206.

**3-Propylisoxazole-4-carboxylic acid (1d)**. Obtained as a white solid (0.29 g, 70%): mp 83-85 °C; R*f* 0.3 (7:3 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 3120, 2963, 1730, 1579, 1427, 1242, 1109; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 8.95 (s, 1H), 2.91 (t, *J* = 7.6 Hz, 2H), 1.77 (sextet, *J* = 7.2 Hz, 2H), 1.01 (s, *J* = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 166.8, 164.5, 162.5, 112.4, 27.1, 21.1, 13.9; HRMS (FAB) *m/z* calcd for $C_7H_{10}NO_3$ $[M + H]^+$ 156.0661, found 156.0659.

**General procedure for the synthesis of pyranoisoxazolones 3 from isoxazolyl-4-carboxylic acids 1 and alkynes 2:** In an oven dried vial tube, isoxazolyl-4-carboxylic acid **1** (0.2 mmol), alkyne **2** (0.24 mmol), silver carbonate (0.2 mmol) and $[Cp^*RhCl_2]_2$ (5 mol %) were taken in DMF (1 mL). This vial tube was placed in a pre-heated metal block at 100 °C for 2 h in open air (monitored by TLC). After completion of the reaction, the residue was filtered through a pad of celite using EtOAc (3 x 25 mL). To the filtrate saturated $NH_4Cl$ (25 mL) solution added, organic layer was separated, washed with brine (20 mL), dried over $Na_2SO_4$ and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent to give **3**.

**3-(4-Chlorophenyl)-6,7-diphenyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3aa)**. Obtained as a white solid (60.6 mg, 76%): mp 194-196 °C; R*f* 0.4 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2957, 2923, 1752, 1545, 1446, 962; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 8.25 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.46-7.41 (m, 5H), 7.38-7.26 (m, 5H); $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 174.4, 159.9, 159.3, 156.6, 137.5, 131.0, 130.9, 130.5, 130.4, 129.8, 129.4, 129.2, 129.1, 128.4, 125.0, 108.8, 102.2; HRMS (EI, 70 eV) *m/z* calcd for $C_{24}H_{14}ClNO_3$ $[M]^+$ 399.0662, found 399.0662.

**3-(4-Chlorophenyl)-6,7-bis(4-methoxyphenyl)-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ab)**. Obtained as a white solid (74.3 mg, 81%): mp 213-215 °C; R*f* 0.3 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2925, 1747, 1604, 1504, 1256, 835; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 8.24 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 3.85 (s, 3H), 3.80 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.8, 161.5, 160.0, 159.6, 159.2, 156.8, 137.4, 131.6, 131.5, 130.5, 129.2, 125.2, 123.3, 121.7, 114.8, 113.9, 107.2, 101.6, 55.49, 55.45; HRMS (EI, 70 eV) *m/z* calcd for $C_{26}H_{18}ClNO_5$ [M]$^+$ 459.0874, found 459.0875.

**6,7-Bis(4-bromophenyl)-3-(4-chlorophenyl)-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ad)**. Obtained as a pale yellow solid (68.6 mg, 62%): mp 230-232 °C; R$_f$ 0.3 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2956, 1753, 1543, 1487, 1008, 833; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.22 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.8, 159.4, 158.8, 156.1, 137.7, 132.8, 131.9, 131.2, 130.5, 129.6, 129.3, 128.0, 126.0, 124.7, 123.8, 108.1, 102.5; HRMS (EI, 70 eV) *m/z* calcd for $C_{24}H_{12}Br_2ClNO_3$ [M]$^+$ 554.8872, found 554.8876.

**3-(4-chlorophenyl)-6,7-bis(4-(trifluoromethyl)phenyl)-4H-pyrano[3,4-d]isoxazol-4-one (3ae)**. Obtained as a white solid (8.56 mg, 8%): mp 211-212 °C; R$_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2917, 1752, 1551, 1322, 1066, 851;$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.23 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.61-7.55 (m, 4H), 7.53-7.49 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.5, 159.5, 158.6, 155.8, 137.9, 133.9, 133.0 (q, $J_{C\text{-}F}$ = 32.7 Hz), 132.7, 131.7 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.9, 130.5, 130.2, 129.4, 126.5 (q, $J_{C\text{-}F}$ = 3.5 Hz), 125.8 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.6, 123.7 (q, $J_{C\text{-}F}$ = 270.5 Hz), 108.8, 102.9; HRMS (EI, 70 eV) *m/z* calcd for $C_{26}H_{12}ClF_6NO_3$ [M]$^+$ 535.0410, found 535.0408.

**3-(4-Chlorophenyl)-6,7-dipropyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3af)**. Obtained as a pale yellow solid (46.3 mg, 70%): mp 68-70 °C; R$_f$ 0.5 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2963, 1748, 1565, 1445, 966, 835; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.21 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 2.65-2.60 (m, 4H), 1.77 (sextet, *J* = 7.2 Hz, 2H), 1.65 (sextet, *J* = 7.6 Hz, 2H), 1.01 (triplet, *J* = 7.2 Hz, 6H);

$^{13}$C NMR (125 MHz, CDCl$_3$) *δ* 175.1, 164.5, 159.1, 157.6, 137.3, 130.5, 129.1, 125.2, 106.8, 101.7, 32.4, 26.4, 22.7, 21.2, 13.9, 13.8; HRMS (EI, 70 eV) *m/z* calcd for $C_{18}H_{18}ClNO_3$ [M]$^+$ 331.0975, found 331.0968.

**3-(4-Chlorophenyl)-6,7-diethyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ag)**. Obtained as a pale yellow solid (44.2 mg, 73%): mp 107-109 °C; R$_f$ 0.4 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2957, 2923, 1747, 1566, 1459, 1377, 837; $^1$H NMR (400 MHz, CDCl$_3$) *δ* 8.22 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 2.72-2.65 (m, 4H), 1.33-1.25 (m, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) *δ* 175.0, 165.3, 159.2, 157.6, 137.3, 130.5, 129.1, 125.2, 107.7, 101.8, 23.9, 17.9, 14.3, 12.4; HRMS (EI, 70 eV) *m/z* calcd for $C_{16}H_{14}ClNO_3$ [M]$^+$ 303.0662, found 303.0656.

**3-(4-Chlorophenyl)-6,7-dimethyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ah)**. Obtained as a pale yellow solid (36.3 mg, 66%): mp 154-156 °C; R$_f$ 0.4 (1:4 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2920, 1753, 1566, 1438, 843, 776; $^1$H NMR (400 MHz, CDCl$_3$) *δ* 8.21 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 2.36 (s, 3H), 2.24 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) *δ* 175.1, 161.0, 159.2, 157.4, 137.4, 130.5, 129.1, 125.1, 102.1, 101.3, 17.1, 9.4; HRMS (EI, 70 eV) *m/z* calcd for $C_{14}H_{10}ClNO_3$ [M]$^+$ 275.0349, found 275.0350.

**3-(4-Chlorophenyl)-7-methyl-6-phenyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ai)**. Obtained as a white solid (45.8 mg, 68%): mp 206-208 °C; R$_f$ 0.4 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2923, 1751, 1564, 1094, 776; $^1$H NMR (400 MHz, CDCl$_3$) *δ* 8.26 (d, *J* = 8.4 Hz, 2H), 7.68-7.64 (m, 2H), 7.53-7.48 (m, 5H), 2.43 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) *δ* 175.5, 160.0, 159.4, 157.1, 137.5, 131.1, 130.9, 130.5, 129.24, 129.21, 128.7, 125.1, 102.6, 102.1, 10.8; HRMS (EI, 70 eV) *m/z* calcd for $C_{19}H_{12}ClNO_3$ [M]$^+$ 337.0506, found 337.0501.

**3-(4-Chlorophenyl)-7-ethyl-6-phenyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3aj)**. Obtained as a white solid (45.6 mg, 65%): mp 150-152 °C; R$_f$ 0.5 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2959, 1747, 1562, 1495, 1093, 770; $^1$H NMR (400 MHz, CDCl$_3$) *δ* 8.26 (d, *J* = 8.4 Hz, 2H), 7.63-7.61 (m, 2H), 7.52-7.49 (m, 5H),

2. 81 (q, $J$ = 7.6 Hz, 2H), 1.38 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.3, 160.0, 159.2, 157.1, 137.4, 131.3, 130.9, 130.5, 129.2, 128.9, 128.8, 125.1, 109.0, 102.6, 19.0, 14.1; HRMS (EI, 70 eV) *m/z* calcd for $C_{20}H_{14}ClNO_3$ [M]$^+$ 351.0662, found 351.0668.

**3-(4-Chlorophenyl)-6-phenyl-7-propyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ak)**. Obtained as a white solid (40.8 mg, 56%): mp 134-136 °C; R$_f$ 0.4 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2960, 1751, 1561, 1495, 990, 777; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.26 (d, $J$ = 8.5 Hz, 2H), 7.61-7.60 (m, 2H), 7.52-7.49 (m, 5H), 2.74 (t, $J$ = 7.5 Hz, 2H), 1.77 (sextet, $J$ = 7.5 Hz, 2H), 0.99 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.4, 160.3, 159.2, 157.1, 137.4, 131.4, 130.8, 130.5, 129.2, 128.9, 128.8, 125.1, 107.7, 102.5, 27.3, 22.8, 14.1; HRMS (EI, 70 eV) *m/z* calcd for $C_{21}H_{16}ClNO_3$ [M]$^+$ 365.0819, found 365.0819.

**7-Butyl-3-(4-chlorophenyl)-6-phenyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3al)**. Obtained as a white solid (45.4 mg, 60%): mp 135-137 °C; R$_f$ 0.5 (1:19 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2955, 2923, 1746, 1560, 1468, 843, 774; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.26 (d, $J$ = 8.4 Hz, 2H), 7.62-7.60 (m, 2H), 7.52-7.49 (m, 5H), 2.76 (t, $J$ = 7.6 Hz, 2H), 1.72 (quintet, $J$ = 7.2 Hz, 2H), 1.40 (sextet, $J$ = 7.2 Hz, 2H), 0.92 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.4,160.2, 159.2, 157.1, 137.4, 131.4, 130.8, 130.5, 129.2, 128.9, 128.8, 125.1, 107.9, 102.5, 31.5, 25.1, 22.6, 13.7; HRMS (EI, 70 eV) *m/z* calcd for $C_{22}H_{18}ClNO_3$ [M]$^+$ 379.0975, found 379.0975.

**7-Butyl-3-(4-chlorophenyl)-6-ethyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3am) and 6-Butyl-3-(4-chlorophenyl)-7-ethyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3a'm')**. Obtained as a mixture of regio-isomers: Semi solid (41.0 mg, 62%): R$_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2959, 1748, 1565, 1445, 1094, 835; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.21 (d, $J$ = 8.4 Hz, 4H), 7.48 (d, $J$ = 8.4 Hz, 4H), 2.71-2.63 (m, 8H), 1.75-1.67 (m, 2H), 1.65-1.58 (m, 2H), 1.42 (sextet, $J$ = 7.2 Hz, 4H), 1.33-1.25 (m, 6H), 0.99-0.94 (m, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 175.1, 175.0, 165.5, 164.4, 159.1, 157.68, 157.67, 137.3, 130.5, 129.1, 125.2, 108.1, 106.4, 101.8, 101.7, 31.7, 30.2, 30.0, 24.2, 24.0, 22.5, 18.0, 14.2, 13.9, 13.8, 12.3; HRMS (EI, 70 eV) *m/z* calcd for $C_{18}H_{18}ClNO_3$ $[M]^+$ 331.0975, found 331.0981.

**3-(4-Methoxyphenyl)-6,7-diphenyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ba)**. Obtained as a pale yellow solid (63.2 mg, 80%): mp 188-190 °C; $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2958, 2923, 1741, 1546, 1251, 782; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.26 (d, $J$ = 8.8 Hz, 2H), 7.46-7.44 (m, 2H), 7.41-7.35 (m, 6H), 7.29-7.25 (m, 2H), 7.04 (d, $J$ = 8.8 Hz, 2H), 3.88 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 174.1, 161.9, 159.8, 159.6, 156.9, 131.1, 130.88, 130.8, 129.8, 129.6, 129.2, 129.0, 128.4, 118.9, 114.3, 108.9, 102.3, 55.5; HRMS (EI, 70 eV) *m/z* calcd for $C_{25}H_{17}NO_4$ $[M]^+$ 395.1158, found 395.1159.

**6,7-Diethyl-3-(4-methoxyphenyl)-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3bg)**. Colourless liquid (50.2 mg, 84%): $R_f$ 0.3 (1:4 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2972, 1745, 1610, 1567, 1437, 1254, 837; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.21 (d, $J$ = 8.8 Hz, 2H), 7.00 (d, $J$ = 8.8 Hz, 2H), 3.86 (s, 3H), 2.69-2.63 (m, 4H), 1.32-1.23 (m, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 174.7, 164.9, 161.8, 159.6, 157.8, 130.7, 119.0, 114.2, 107.6, 101.8, 55.4, 23.9, 17.9, 14.2, 12.4; HRMS (EI, 70 eV) *m/z* calcd for $C_{17}H_{17}NO_4$ $[M]^+$ 299.1158, found 299.1159.

**3-(4-Nitrophenyl)-6,7-diphenyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3ca)**. Obtained as a white solid (52.4 mg, 64%): mp 215-217 °C; $R_f$ 0.3 (1: 9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2948, 1751, 1523, 1445, 1015, 753; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.53 (d, $J$ = 8.8 Hz, 2H), 8.38 (d, $J$ = 8.8 Hz, 2H), 7.47-7.42 (m, 5H), 7.40-7.35 (m, 3H), 7.32-7.28 (m, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 174.7, 160.3, 158.5, 156.5, 149.4, 132.6, 131.1, 130.8, 130.4, 130.3, 129.8, 129.37, 129.32, 129.1, 128.5, 124.0, 108.8, 102.3; HRMS (EI, 70 eV) *m/z* calcd for $C_{24}H_{14}N_2O_5$ $[M]^+$ 410.0903, found 410.0909.

**7-Methyl-3-(4-nitrophenyl)-6-phenyl-4*H*-pyrano[3,4-d]isoxazol-4-one (3ci)**. Obtained as a white solid (41.7 mg, 60%): mp 229-231 °C; $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2965, 1730, 1516, 1294, 1068, 753; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.54 (d, $J$ = 9.2 Hz, 2H), 8.38 (d, $J$ = 9.2 Hz, 2H), 7.69-7.67 (m, 2H), 7.54-7.53 (m, 3H), 2.45 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 175.9, 160.4, 158.6, 156.9, 149.4, 132.7, 131.1, 131.0, 130.3, 129.2, 128.8, 124.0, 102.6, 102.1, 10.9; HRMS (EI, 70 eV) *m/z* calcd for $C_{19}H_{12}N_2O_5$ $[M]^+$ 348.0746, found 348.0747.

**6,7-Diphenyl-3-propyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3da)**. Obtained as a white solid (51.6 mg, 78%): mp 114-116 °C; $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2960, 2926, 1758, 1546, 1201, 1056, 779; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43-7.41 (m, 2H), 7.39-7.36 (m, 3H), 7.34-7.25 (m, 5H), 2.99 (t, $J$ = 7.6 Hz, 2H), 1.90 (sextet, $J$ = 7.2 Hz, 2H), 1.05 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 173.2, 161.9, 159.7, 156.9, 131.3, 130.7, 130.4, 129.8, 129.7, 129.1, 128.9, 128.4, 109.0, 103.4, 27.2, 20.9, 13.8; HRMS (EI, 70 eV) *m/z* calcd for $C_{21}H_{17}NO_3$ $[M]^+$ 331.1208, found 331.1208.

**6,7-Dimethyl-3-propyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (3dh)**. Obtained as a semi-solid (23.5 mg, 57%): $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2965, 1752, 1578, 1256, 1006, 775; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.89 (t, $J$ = 7.2 Hz, 2H), 2.31 (s, 3H), 2.17 (s, 3H), 1.81 (sextet, $J$ = 7.6 Hz, 2H), 0.98 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 173.9, 161.7, 160.6, 157.7, 102.4, 102.2, 27.1, 20.8, 17.1, 13.7, 9.4; HRMS (EI, 70 eV) *m/z* calcd for $C_{11}H_{13}NO_3$ $[M]^+$ 207.0895, found 207.0890.

**General procedure for the synthesis of isoquinolines 4 from isoxazolyl-4-carboxylic acids 1 and alkynes 2**. In an oven dried vial tube, isoxazolyl-4-carboxylic acid **1** (0.2 mmol), alkyne **2** (0.24 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.2 mmol) and $[Cp^*RhCl_2]_2$ (5 mol %) were taken under argon atmosphere. To this reaction mixture DMF (1 mL) was added and then it was placed in a pre-heated metal block at 100 °C for 2 h (monitored by TLC). After completion of the reaction, the residue was filtered through a pad of celite using EtOAc (3 x 25 mL). To the filtrate saturated $NH_4Cl$ (25 mL) solution was added, organic layer was separated, washed with brine (20 mL), dried over $Na_2SO_4$ and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

**6-Chloro-1-methyl-3,4-diphenylisoquinoline (4aa)**.[11a] Obtained as a yellow solid (39.4 mg, 60%): mp 173-175 °C; R*f* 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2921, 1604, 1568, 1097, 819; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.13 (d, *J* = 9.2 Hz, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 7.53 (dd, *J* = 9.2 Hz, 2.0 Hz, 1H), 7.38-7.31 (m, 5H), 7.21-7.17 (m, 5H), 3.05 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 157.8, 150.7, 140.7, 137.2, 137.0, 136.5, 131.4, 130.3, 128.6, 128.5, 127.8, 127.5, 127.4, 127.3, 125.2, 124.5, 22.8; HRMS (ESI) *m/z* calcd for $C_{22}H_{17}ClN$ (M+H) 330.1050 and 332.1020, found 330.1042 and 332.1017.

**6-Chloro-3,4-bis(4-methoxyphenyl)-1-methylisoquinoline (4ab)**. Obtained as a yellow solid (27.2 mg, 35%): mp 136-138 °C; R*f* 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2930, 1602, 1509, 1246, 1032, 833; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 7.49 (dd, *J* = 8.8 Hz, 1.6 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 3.85 (s, 3H), 3.76 (s, 3H), 3.02 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 158.9, 158.8, 157.4, 150.4, 137.7, 136.3, 133.4, 132.4, 131.6, 129.3, 127.6, 127.4, 127.2, 125.2, 124.3, 114.1, 113.3, 55.4, 55.3, 22.8; HRMS (ESI) *m/z* calcd for $C_{24}H_{21}ClNO_2$ $[M + H]^+$ 390.1261 and 392.1231, found 390.1259 and 392.1236.

**6-Chloro-1-methyl-3,4-dipropylisoquinoline (4af)**. Obtained as a semi solid (21.9 mg, 42%): R*f* 0.5 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2959, 2871, 1607, 1393, 1103, 812; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.01 (d, *J* = 8.8 Hz, 1H), 7.906-7.903 (m, 1H), 7.41 (dd, *J* = 8.8 Hz, 1.2 Hz, 1H), 2.94-2.86 (m, 7H), 1.77 (sextet, *J* = 7.2 Hz, 2H), 1.65 (sextet, *J* = 7.2 Hz, 2H), 1.09 (t, *J* = 7.6 Hz, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.7, 153.1, 136.6, 135.9, 128.0, 126.2, 125.6, 124.3, 122.8, 37.6, 29.8, 24.2, 23.8, 22.4, 14.6, 14.5; HRMS (ESI) *m/z* calcd for $C_{16}H_{21}ClN$ $[M + H]^+$ 262.1363 and 264.1333, found 262.1357 and 264.1325.

**6-Chloro-3,4-diethyl-1-methylisoquinoline (4ag).**[11b] Obtained as a yellow semi solid (17.7 mg, 38%): R*f* 0.5 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2965, 2932, 1607, 1567, 1391, 1099, 816; $^{1}$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.01 (d, *J* = 9.0 Hz, 1H), 7.93 (s, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 3.01-2.92 (m, 4H), 2.88 (s, 3H), 1.33 (t, *J* = 7.5 Hz, 3H), 1.27 (t, *J* = 7.5 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.8, 154.0, 136.3, 136.0, 128.0, 126.6, 126.2, 124.4, 122.6, 28.6, 22.4, 15.3, 14.9; HRMS (ESI) *m/z* calcd for $C_{14}H_{17}ClN$ $[M + H]^+$ 234.1050 and 236.1020, found 234.1047 and 236.1018.

**6-Chloro-1,4-dimethyl-3-phenylisoquinoline (4ai)**. Obtained as a yellow solid (27.7 mg, 52%): mp 90-92 °C; R*f* 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2922, 1606, 1392, 1097, 815, 700; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 (d, *J* = 9.2 Hz, 1H), 8.02 (d, *J* = 1.6 Hz, 1H), 7.56-7.53 (m, 3H), 7.49-7.45 (m, 2H), 7.41-7.37 (m, 1H), 2.96 (s, 3H), 2.56 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 156.0, 151.9, 141.3, 137.5, 136.3, 129.9, 128.3, 128.0, 127.8, 127.2, 124.6, 123.5, 121.6, 22.6, 15.5; HRMS (ESI) *m/z* calcd for $C_{17}H_{15}ClN$ $[M + H]^+$ 268.0893 and 270.0864, found 268.0880 and 270.0855.

**6-Chloro-4-ethyl-1-methyl-3-phenylisoquinoline (4aj)**. Obtained as a pale yellow solid (25.8 mg, 46%): mp 108-110 °C; R*f* 0.5 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2967, 2929, 1606, 1493, 1391, 1099, 700; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.11 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 2.0 Hz, 1H), 7.54 (dd, *J* = 8.8 Hz, 2.0 Hz, 1H), 7.51-7.38 (m, 5H), 2.97-2.92 (m, 5H), 1.25 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 155.9, 152.0, 141.6, 136.44, 136.40, 129.2, 128.3, 128.2, 128.0, 127.7, 127.2, 125.1, 123.4, 22.6, 21.7, 15.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{17}ClN$ $[M + H]^+$ 282.1050 and 284.1020, found 282.1037 and 284.1009.

**4-Butyl-6-chloro-1-methyl-3-phenylisoquinoline (4al)**. Obtained as a yellow solid (30.3 mg, 49%): mp 58-60 °C; R*f* 0.4 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2956, 2926, 1606, 1443, 1391, 1094, 700; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 (d, *J* = 8.8 Hz, 1H), 8.00 (d, *J* = 1.2 Hz, 1H), 7.53 (dd, *J* = 9.2 Hz, 7.6 Hz, 1H), 7.49-7.38 (m, 5H), 2.97-2.88 (m, 5H), 1.59 (quintet, *J* = 7.6 Hz, 2H), 1.32 (sextet, *J* = 7.2 Hz, 2H), 0.84 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 155.8, 152.3, 141.6, 136.6, 136.3, 129.3, 128.3, 128.1, 127.7, 127.1, 126.8, 125.0, 123.5, 33.4, 28.2, 22.9, 22.6, 13.8; HRMS (ESI) *m/z* calcd for $C_{20}H_{21}ClN$ $[M + H]^+$ 310.1363 and 312.1333, found 310.1358 and 312.1333.

**3,4-Bis(4-bromophenyl)-6-methoxy-1-methylisoquinoline (4bd)**. Obtained as a yellow solid (60.6 mg, 63%): mp 171-173 °C; $R_f$ 0.5 (1:4 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2923, 1616, 1575, 1489, 1232, 1011, 833; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 8.10 (d, *J* = 9.2 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.23 (dd, *J* = 9.2 Hz, 6.4 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 2.4 Hz, 1H), 3.75 (s, 3H), 2.99 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 161.0, 157.7, 149.0, 139.6, 137.8, 136.7, 133.0, 131.98, 131.91, 131.0, 127.7, 127.4, 122.0, 121.7, 121.6, 119.1, 104.2, 55.4, 22.7; HRMS (ESI) *m/z* calcd for $C_{23}H_{18}Br_2NO$ $[M + H]^+$ 481.9755 and 483.9735, found 481.9740 and 483.9728.

**6-Methoxy-1-methyl-3-phenyl-4-propylisoquinoline (4bk)**. Obtained as a pale yellow solid (32.0 mg, 55%): mp 125-127 °C; $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2950, 2849, 1618, 1565, 1223, 1019, 825; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 8.07 (d, *J* = 8.8 Hz, 1H), 7.49-7.42 (m, 4H), 7.39-7.35 (m, 1H), 7.27 (d, *J* = 2.4 Hz, 1H), 7.22 (dd, *J* = 9.2 Hz, 6.8 Hz, 1H), 3.97 (s, 3H), 2.91 (s, 3H), 2.90-2.86 (m, 2H), 1.72-1.62 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 160.5, 155.3, 151.8, 142.2, 137.5, 129.3, 128.29, 128.23, 127.4, 126.5, 122.4, 118.2, 103.0, 55.4, 30.9, 24.0, 22.5, 14.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{22}NO$ $[M + H]^+$ 292.1701 found 292.1696.

**3,4-Bis(4-methoxyphenyl)-1-methyl-6-nitroisoquinoline (4cb)**. Obtained as a yellow solid (32.0 mg, 40%): mp 67-69 °C; $R_f$ 0.4 (1:4 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2930, 2836, 1606, 1531, 1344, 1248, 841; $^1$H NMR (400 MHz, $CDCl_3$) *δ* 8.60 (d, *J* = 1.6 Hz, 1H), 8.32-8.26 (m, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 3.78 (s, 3H), 3.10 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 159.3, 159.1, 157.7, 151.4, 148.3, 136.4, 132.7, 132.4, 131.6, 129.6, 128.4, 127.7, 127.6, 122.8, 119.6, 114.4, 113.4, 55.4, 55.3, 23.0; HRMS (ESI) *m/z* calcd for $C_{24}H_{21}N_2O_4$ [M + H]$^+$ 401.1501 found 401.1496.

**General procedure for the synthesis of hydroarylation of alkynes 5**. In an oven dried vial tube 4-isoxazolyl carboxylic acid **1** (0.1 mmol), diphenyl acetylene **2** (0.15 mmol), $AdCO_2H$ (0.1 mmol), base (0.03 mmol) and Rh catalyst (0.025 mmol) were taken in mesitylene (0.5 mL). The vial was sealed with a screw cap and then placed in a pre-heated metal block at 120 °C for 8 h (monitored by TLC). After completion of the reaction, the residue was filtered through a pad of celite using EtOAc (3 x 25 mL). The solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

**(*E*)-3-(4-Chlorophenyl)-5-(1,2-diphenylvinyl)isoxazole (5aa)**. Obtained as a white solid (27.84 mg, 78%): mp 147-148 °C; $R_f$ 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 3156, 1602, 1559, 1426, 1092; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.70 (d, $J$ = 8.4 Hz, 2H), 7.55 (s, 1H), 7.46-7.444 (m, 3H), 7.39 (d, $J$ = 8.4 Hz, 2H), 7.36-7.33(m, 2H), 7.20-7.14 (m, 3H), 7.08-7.06 (m, 2H), 6.07 (s, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 172.2, 161.8, 136.9, 136.0, 135.3, 131.5, 130.1, 129.7, 129.3, 129.2, 128.5, 128.43, 128.40, 128.3, 128.1, 127.6, 100.9; HRMS (ESI) *m/z* calcd for $C_{23}H_{16}ClNONa$ [M+Na]$^+$ 380.0818 and 382.0789, found 380.0804 and 382.0780.

**(*E*)-3-(4-chlorophenyl)-5-(1,2-di-p-tolylvinyl)isoxazole (5ac)**. Obtained as a white solid (20.02 mg, 52%): mp 155-156 °C; $R_f$ 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2919, 1602, 1509, 1427, 1375, 1092; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 7.69 (d, $J$ = 8.5 Hz, 2H), 7.47 (s, 1H), 7.38 (d, $J$ = 8.5 Hz, 2H), 7.23-7.20 (m, 4H), 6.97 (br s, 4H), 6.04 (s, 1H), 2.43 (s, 3H), 2.27 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 172.6, 161.8, 138.4, 138.2, 135.9, 134.1, 132.6, 131.3, 130.1, 130.0, 129.6, 129.19, 129.10, 128.1, 127.8, 127.5, 100.5, 21.5, 21.4; HRMS (ESI) *m/z* calcd for $C_{25}H_{20}ClNONa$ [M+Na]$^+$ 408.1131 and 410.1102, found 408.1126 and 410.1091.

**(*E*)-5-(1,2-bis(4-bromophenyl)vinyl)-3-(4-chlorophenyl)isoxazole (5ad)**. Obtained as a pale yellow solid (40.52 mg, 79%): mp 174-175 °C; $R_f$ 0.7 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2921, 1557, 1487, 1427, 1092, 817; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.69 (d, $J$ = 8.4 Hz, 2H), 7.58 (d, $J$ = 8.0 Hz, 2H), 7.46 (s, 1H), 7.40 (d, $J$ = 8.4 Hz, 2H), 7.32 (d, $J$ = 8.4 Hz, 2H), 7.20 (d, $J$ = 8.0 Hz, 2H), 6.92 (d, $J$ = 8.4 Hz, 2H), 6.08 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 171.3, 161.9, 136.2, 135.4, 133.8, 132.7, 131.7, 131.49, 131.43, 130.7, 129.3, 128.1, 127.9, 127.4, 123.1, 122.8, 101.2; HRMS (ESI) *m/z* calcd for $C_{23}H_{14}Br_2ClNONa$ [M+Na]$^+$ 535.9028 and 537.9008, found 535.9049 and 537.9025.

**(*E*)-5-(1,2-bis(4-(trifluoromethyl)phenyl)vinyl)-3-(4-chlorophenyl)isoxazole (5ae)**. Obtained as a white solid (33.03 mg, 67%): mp 197-198 °C; $R_f$ 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2922, 1613, 1562, 1428, 1323, 1116, 825;$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74-7.69 (m, 4H), 7.61 (s, 1H), 7.48-7.44 (m, 4H), 7.40 (d, $J$ = 6.4 Hz, 2H), 7.14 (d, $J$ = 6.4 Hz, 2H), 6.11 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.7, 162.0, 140.0, 138.2, 136.4, 131.2 (q, $J_{C\text{-}F}$ = 32.6 Hz), 130.7, 130.3 (q, $J_{C\text{-}F}$ = 32.7 Hz), 130.2, 130.1, 129.3, 129.2, 128.1, 127.2, 126.5 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125.5 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.9 (q, $J_{C\text{-}F}$ = 270.7 Hz), 123.8 (q, $J_{C\text{-}F}$ = 270.6 Hz), 101.7; HRMS (EI, 70 eV) *m/z* calcd for $C_{25}H_{14}ClF_6NO$ [M]$^+$ 493.0668, found 493.0672.

**(*E*)-3-(4-Chlorophenyl)-5-(1-phenylprop-1-en-2-yl)isoxazole (5ai)**. Obtained as a mixture of isomers (62:1), White solid (20.06 mg, 68%): mp 139-140 °C; $R_f$ 0.5 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 3099, 1453, 1103, 919, 808; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78 (d, $J$ = 8.4 Hz, 2H), 7.45 (d, $J$ = 8.8 Hz, 2H), 7.42-7.38 (m, 5H), 7.35-7.29 (m, 1H), 6.55 (s, 1H), 2.29 (d, $J$ = 1.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 172.8, 161.9, 136.2, 136.0, 131.3, 129.5, 129.3, 128.5, 128.1, 127.9, 127.8, 123.7, 98.2, 15.4; HRMS (ESI) *m/z* calcd for $C_{18}H_{14}ClNONa$ [M+Na]$^+$ 318.0662 and 320.0632, found 318.0655 and 320.0630.

**(*E*)-3-(4-Chlorophenyl)-5-(1-phenylbut-1-en-2-yl)isoxazole (5aj)**. Obtained as a mixture of isomers (72:1), white solid (24.54 mg, 71%): mp 114-115 °C; $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2908, 1600, 1557, 1427, 1090, 813; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78 (d, $J$ = 8.8 Hz, 2H), 7.44 (d, $J$ = 8.4 Hz, 2H), 7.41-7.38 (m, 4H), 7.35 (s, 1H), 7.34-7.30 (m, 1H), 6.56 (s, 1H), 2.70 (q, $J$ = 7.6 Hz, 2H), 1.29 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 172.3, 161.9, 136.1, 136.0, 131.1, 130.3, 129.3, 129.1, 128.6, 128.1, 128.0, 127.8, 98.1, 22.2, 14.0; HRMS (ESI) *m/z* calcd for $C_{19}H_{16}ClNONa$ [M+Na]$^+$ 332.0818 and 334.0789, found 332.0811 and 334.0787.

**(*E*)-3-(4-chlorophenyl)-5-(1-phenylpent-1-en-2-yl)isoxazole (5ak)**. Obtained as a mixture of isomers (99:1), white solid (24.54 mg, 76%): mp 76-77 °C; R$_f$ 0.5 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2960, 1602, 1559, 1427, 1092, 788; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78 (d, $J$ = 8.8 Hz, 2H), 7.44 (d, $J$ = 8.4 Hz, 2H), 7.41-7.36 (m, 5H), 7.34-7.30 (m, 1H), 6.54 (s, 1H), 2.64 (quintate, $J$ = 5.6 Hz, 2H), 1.69 (septet, $J$ = 7.2 Hz, 2H), 1.02 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 172.6, 161.8, 136.2, 136.0, 131.5, 129.3, 129.2, 129.1, 128.6, 128.1, 127.98, 127.90, 98.0, 31.0, 22.7, 14.3; HRMS (ESI) *m/z* calcd for $C_{20}H_{19}ClNO$ [M+H]$^+$ 324.1155 and 326.1126, found 324.1150 and 326.1116.

**(*E*)-5-(1,2-Diphenylvinyl)-3-(4-methoxyphenyl)isoxazole (5ba)**. Obtained as a white solid (25.76 mg, 73%); mp 155-156 °C; R$_f$ 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 3055, 2933, 1612, 1524, 1429, 1251, 1028; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.69 (d, $J$ = 8.8 Hz, 2H), 7.52 (s, 1H), 7.45-7.41 (m, 3H), 7.36-7.32 (m, 2H), 7.19-7.13 (m, 3H), 7.07-7.05 (m, 2H), 6.93 (d, $J$ = 9.2 Hz, 2H), 6.04 (s, 1H), 3.83 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 171.6, 162.4, 161.0, 137.1, 135.4, 131.1, 130.1, 129.8, 129.2, 128.6, 128.5, 128.3, 128.2, 121.7, 114.3, 101.0, 55.4; HRMS (ESI) *m/z* calcd for $C_{24}H_{19}NO_2Na$ [M+Na]$^+$ 376.1313, found 376.1296.

**(*E*)-5-(1,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(4-methoxyphenyl)isoxazole (5be)**. Obtained as a pale yellow solid (40.09 mg, 82%); mp 164-165 °C; R$_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2919, 1613, 1430, 1324, 1018; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73-7.69 (m, 4H), 7.59 (s, 1H), 7.48-7.43 (m, 4H), 7.13 (d, $J$ = 8.0 Hz, 2H), 6.94 (d, $J$ = 8.8 Hz, 2H), 6.08 (s, 1H), 3.84 (s, 3H); $^{13}$C NMR (125 MHz,

$CDCl_3$) $\delta$ 170.1, 162.6, 161.2, 140.1, 138.3, 131.0 (q, $J_{C\text{-}F}$ = 32.4 Hz), 130.4, 130.3, 130.2 (q, $J_{C\text{-}F}$ = 32.2 Hz), 130.1, 129.4, 128.3, 126.4 (q, $J_{C\text{-}F}$ = 3.6 Hz), 125.4 (q, $J_{C\text{-}F}$ = 4.0 Hz), 124.0 (q, $J_{C\text{-}F}$ = 270.8 Hz), 123.9 (q, $J_{C\text{-}F}$ = 270.3 Hz), 114.4, 101.8; HRMS (ESI) *m/z* calcd for $C_{26}H_{17}F_6NO_2Na$ $[M+Na]^+$ 512.1061, found 512.1066.

**(*E*)-5-(1,2-Diphenylvinyl)-3-(4-nitrophenyl)isoxazole (5ca)**. Obtained as a white solid (25.76 mg, 70%): mp 175-176 °C; $R_f$ 0.5 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2916, 1561, 1519, 1429, 1340, 851; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.28 (d, *J* = 8.8 Hz, 2H), 7.94 (d, *J* = 9.2 Hz, 2H), 7.57 (s, 1H), 7.47-7.44 (m, 3H), 7.37-7.33 (m, 2H), 7.22-7.15 (m, 3H), 7.08-7.06 (m, 2H), 6.15 (s, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 173.0, 161.0, 148.7, 136.7, 135.3, 135.1, 132.0, 130.2, 129.7, 129.4, 128.7, 128.6, 128.4, 128.1, 127.7, 124.2, 100.9; HRMS (ESI) *m/z* calcd for $C_{23}H_{16}N_2O_3Na$ $[M+Na]^+$ 391.1059, found 391.1041.

**(*E*)-5-(1,2-Bis(4-bromophenyl)vinyl)-3-(4-nitrophenyl)isoxazole (5cd)**. Obtained as a pale yellow solid (33.99 mg, 65%); mp 199-200 °C; $R_f$ 0.4 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2922, 1607, 1519, 1455, 1344, 1071; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (d, *J* = 8.8 Hz, 2H), 7.94 (d, *J* = 9.2 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.18 (s, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 172.0, 161.1, 148.8, 135.1, 135.0, 133.6, 132.8, 131.8, 131.5, 131.3, 131.2, 127.7, 127.6, 124.3, 123.2, 123.1, 101.2; HRMS (ESI) *m/z* calcd for $C_{23}H_{14}Br_2N_2O_3Na$ $[M+Na]^+$ 546.9269 and 548.9248, found 546.9282 and 548.9264.

**(*E*)-3-(4-Nitrophenyl)-5-(1-phenylhex-1-en-2-yl)isoxazole (5cl)**. Obtained as mixer of isomers (99:1), red solid (25.05 mg, 72%): mp 98-99 °C; $R_f$ 0.6 (1:9 EtOAc/hexane); FT-IR (neat, $cm^{-1}$) 2956, 2869, 1606, 1562, 1518, 1348, 857; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.34 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.41-7.31 (m, 6H), 6.64 (s, 1H), 2.69 (t, *J* = 7.6 Hz, 2H), 1.65 (sextet, *J* = 7.2 Hz, 2H), 1.45 (sextet, *J* = 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H) ; $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 173.5, 161.0, 148.7, 136.0, 135.5, 131.9, 129.1, 128.7, 128.1, 127.7, 124.3, 98.1, 31.5, 28.7, 23.0, 13.9; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}N_2O_3Na$ [M+Na]$^+$ 371.1372, found 371.1360.

**(*E*)-5-(1,2-diphenylvinyl)-3-(4-propylphenyl)isoxazole (5da)**. Obtained as a white solid (24.09 mg, 66%): mp 79-80 °C; R*f* 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2962, 1566, 1496, 1420, 1006; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45 (s, 1H), 7.42-7.39 (m, 3H), 7.30-7.28 (m, 2H), 7.15-7.13 (m, 3H), 7.04-7.01 (m, 2H), 5.64 (s, 1H), 2.58 (t, *J* = 7.6 Hz, 2H), 1.65 (sextet, *J* = 7.6 Hz, 3H), 0.95 (t, *J* = 7.6 Hz, 3H) ; $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 171.0, 164.5, 137.2, 135.5, 130.8, 130.0, 129.7, 129.1, 128.8, 128.3, 128.2, 128.1, 102.8, 28.1, 21.7, 13.9; HRMS (ESI) *m/z* calcd for $C_{20}H_{19}NONa$ [M+Na]$^+$ 312.1364, found 312.1350.

**(*E*)-5-(1,2-Bis(4-bromophenyl)vinyl)-3-(4-propylphenyl)isoxazole (5dd)**. Obtained as a white solid (31.20 mg, 60%): mp 120-121°C; R*f* 0.6 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2960, 1571, 1487, 1421, 1071, 817; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.55 (d, *J* = 8.4 Hz, 2H), 7.37 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H) 5.66 (s, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.65 (sextet, *J* = 7.6 Hz, 3H), 0.95 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 170.1, 164.5, 135.6, 134.1, 132.6, 131.6, 131.43, 131.41, 130.0, 128.2, 122.8, 122.5, 103.1, 28.1, 21.7, 13.8; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}Br_2NONa$ [M+Na]$^+$ 467.9575 and 469.9554, found 467.9576 and 469.9553.

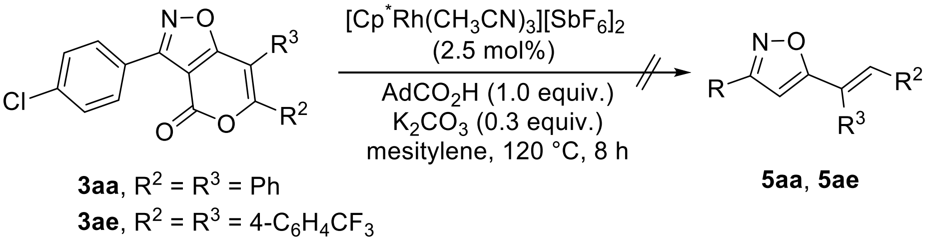
**(*E*)-5-(1,2-Bis(4-(trifluoromethyl)phenyl)vinyl)-3-(4-propylphenyl)isoxazole (5de)**. Obtained as a white solid (26.05 mg, 52%): mp 84-85°C; R*f* 0.5 (1:9 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2964, 1616, 1408, 1323, 1067, 835; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.69 (d, *J* = 8.0 Hz, 2H), 7.52 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 4H), 7.11 (d, *J* = 8.0 Hz, 2H), 5.69 (s, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.66 (sextet, *J* = 7.6 Hz, 2H), 0.96 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 169.5, 164.6, 140.2, 138.4, 131.1 (q, $J_{C\text{-}F}$ = 32.5 Hz), 130.2, 130.1, 130.0, 129.8 (q, $J_{C\text{-}F}$ = 32.3 Hz), 126.3 (q, $J_{C\text{-}F}$ = 3.5 Hz), 125.4 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.0

(q, $J_{C-F}$ = 270.7 Hz), 123.8 (q, $J_{C-F}$ = 270.3 Hz), 103.7, 28.1, 21.7, 13.8; HRMS (ESI) *m/z* calcd for $C_{22}H_{17}F_6NONa$ $[M+Na]^+$ 448.1112 found 448.1110.

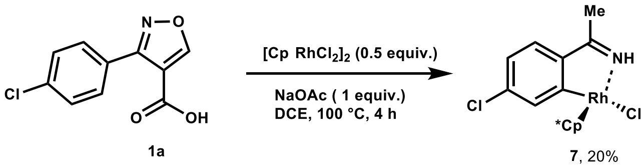
## Mechanistic studies

We treated **3aa** and **3ae** under decarboxylative hydroarylation conditions (Rh(III)/acidic conditions), but, we did not observe the formation of **5aa** and **5ae** respectively. These results suggest that reaction did not proceed via/through annulated product formation to give hydroarylation product **5** (Scheme S1).

**Scheme S1.** Decarboxylative experiment/reaction from **3ae** and **3ae** under optimized reaction conditions



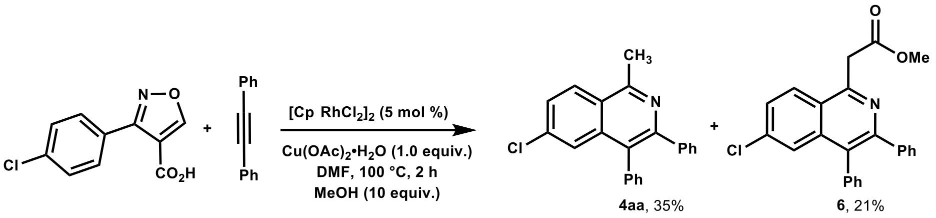
## Synthesis of rhodacyle 7



In an oven dried vial tube isoxazolyl-4-carboxylic acid **1a** (0.1 mmol), $[Cp^*RhCl_2]_2$ (0.05 mmol) and NaOAc (0.1 mmol) were added in DCE (1 mL) under argon atmosphere, and then the reaction mixture was heated at 100 °C for 4 h (monitored by TLC). After completion of the reaction, the solvent was evaporated, and the crude residue was purified by column chromatography using EtOAc/hexane (4:1) as eluent to give rhodacyle **7** as a brown solid **(**7.8 mg, 20%). mp 147-149 °C; $R_f$ 0.2 (4:1 EtOAc/hexane);

FT-IR (neat, cm$^{-1}$) 3202, 2914, 1567, 1536, 1455, 1380, 1083, 753; $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.80 (br s, 1H), 7.75 (d, *J* = 1.6 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.00 (dd, *J* = 8.0 Hz, 6.0 Hz, 1H), 2.50 (s, 3H), 1.68 (s, 15H); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 185.8, 185.5, 184.0, 144.2, 137.1, 136.0, 128.6, 122.8, 95.9, 95.8, 22.8, 9.4; HRMS (ESI) *m/z* calcd for $C_{18}H_{22}NCl_2RhNa$ [M + Na]$^{+}$ 448.0082 and 450.0053 found 448.0077 and 450.0035.

## Trapping of ketene intermediate with methanol for the formation of 6



In an oven dried vial tube, isoxazolyl-4-carboxylic acid **1a** (0.1 mmol), alkyne **2a** (0.12 mmol), $Cu(OAc)_2$•$H_2O$ (0.1 mmol) and [Cp*$RhCl_2$]$_2$ (5 mol%) were taken under argon atmosphere. To this reaction mixture methanol (10 equiv.) and DMF (0.5 mL) were added and then it was placed in a pre-heated metal block at 100 °C for 2 h (monitored by TLC). After completion of the reaction, the residue was filtered through a pad of celite using EtOAc (3 x 25 mL). To the filtrate saturated $NH_4Cl$ (25 mL) solution was added, organic layer was separated, washed with brine (20 mL), dried over $Na_2SO_4$ and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent to give products **4aa** and **6**.

**Methyl 2-(6-chloro-3,4-diphenylisoquinolin-1-yl)acetate (6)**. Obtained as a yellow solid (8.12 mg, 21%): mp 126-127 °C; $R_f$ 0.4 (1:4 EtOAc/hexane); FT-IR (neat, cm$^{-1}$) 2955, 2921, 1738, 1606, 1456, 769; $^{1}$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.06 (dd, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.53 (dd, *J* = 7.2 Hz, 1.6 Hz, 1H), 7.38-7.33 (m, 5H), 7.22-7.18 (m, 5H), 4.47 (s, 2H), 3.75 (s, 3H) ; $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 171.0, 153.6, 150.8, 140.3, 137.7, 136.7, 131.3, 130.4, 129.7, 128.6, 128.1, 127.7, 127.4, 127.0, 125.4, 124.5, 52.4, 42.4; HRMS (ESI) *m/z* calcd for $C_{24}H_{18}ClNNaO_2$ $[M+Na]^+$ 410.0924 and 412.0894 found 410.0922 and 412.0904.

## Crystal data and ORTEP diagram of compounds 3aa, 3ai, 4aa, 5aa, 5ae and 7

**3aa**: $C_{24}H_{14}ClNO_3$, M = 399.81, space group = P21, a = 11.1094(16), b = 5.7150(8), c = 15.077 (2) Å, V = 893.6(2) Å$^3$, α = 90, β = 111.014(2), γ = 90, Z = 2, T = 90 K, F(000) = 412, Reflections collected = 3890, unique = 3743, R1 = 0.0290, wR2 = 0.0746.

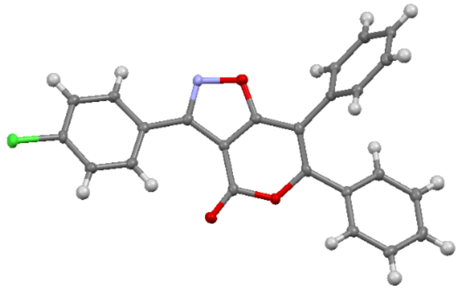


**Figure S1.** ORTEP diagram of **3aa** (CCDC 1870838)

### Crystal data and ORTEP diagram of compound 3ai

**3ai**: $C_{19}H_{12}ClNO_3$, M = 337.75, space group = Pbca, a = 7.1186(6), b = 19.2065(17), c = 21.5744 (17) Å, V = 2949.7(4) Å$^3$, α = 90, β = 90, γ = 90, Z = 8, T = 90 K, F(000) = 1392, Reflections collected = 3722, unique = 3299, R1 = 0.0294, wR2 = 0.0829.

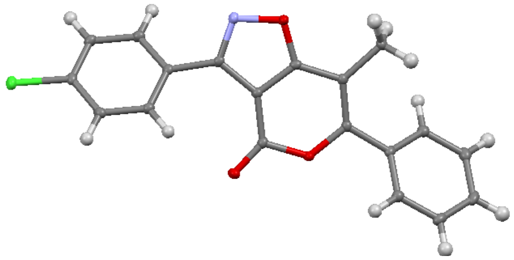


**Figure S2.** ORTEP diagram of **3ai** (CCDC 1870840)

## Crystal data and ORTEP diagram of compound 4aa

**4aa**: $C_{22}H_{16}ClN$, M = 329.81, space group = P21/n, a = 10.8409(15), b = 10.0705(14), c = 15.263 (2) Å, V = 1665.5(4) Å$^3$, α = 90, β = 91.756(2), γ = 90, Z = 4, T = 90 K, F(000) = 688, Reflections collected = 4080, unique = 3653, R1 = 0.0328, wR2 = 0.0988.

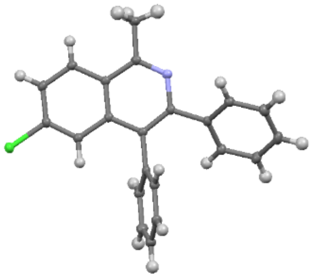


**Figure S3.** ORTEP diagram of **4aa** (CCDC 1870841)

## Crystal data and ORTEP diagram of compound 5aa

**5aa**: $C_{23}H_{16}ClNO$, M = 357.82, space group = P21/c, a = 11.027 (3), b = 8.159 (2), c = 19.126 (5) Å, V = 1718.5 (7) Å$^3$, α = 90, β = 92.913 (2), γ = 90, Z = 4, T = 90 K, F(000) = 744, Reflections collected = 4233, unique = 3088, R1 = 0.0328, wR2 = 0.1134.

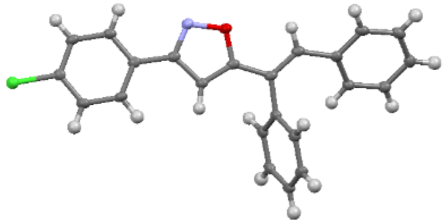


**Figure S4.** ORTEP diagram of **5aa** (CCDC 1899700)

## Crystal data and ORTEP diagram of compound 5ae

**5ae**: $C_{25}H_{14}ClF_6NO$, M = 493.82, space group = P21/c, a = 14.7536(19), b = 6.9198(9), c = 22.084 (3) Å, V = 2133.5(5) Å$^3$, α = 90, β = 108.867(2), γ = 90, Z = 4, T = 90 K, F(000) = 1000, Reflections collected = 5256, unique = 4226, R1 = 0.0402, wR2 = 0.1151.

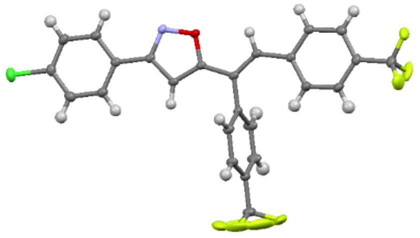


**Figure S5.** ORTEP diagram of **5ae** (CCDC 1899699)

## Crystal data and ORTEP diagram of Rodacycle 7

**7**: $C_{18}H_{22}Cl_2NRh$, M = 425.01, space group = P 21, a = 8.4219(12), b = 35.714(5), c = 13.5618 (19) Å, V = 3991.8(10) Å$^3$, α = 90, β = 101.876(2), γ = 90, Z = 8, T = 90 K, F(000) = 1828, Reflections collected = 14947, unique = 13719, R1 = 0.0487, wR2 = 0.1058.

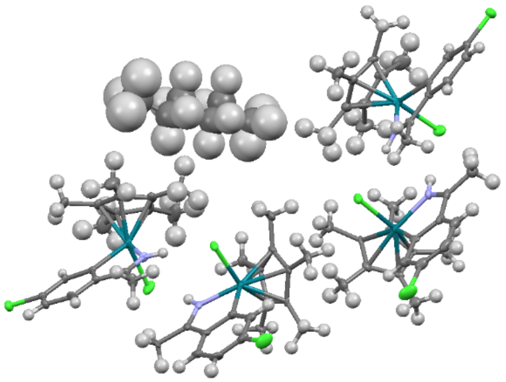
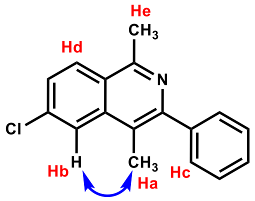


**Figure S6.** ORTEP diagram of **7** (CCDC 1870842)

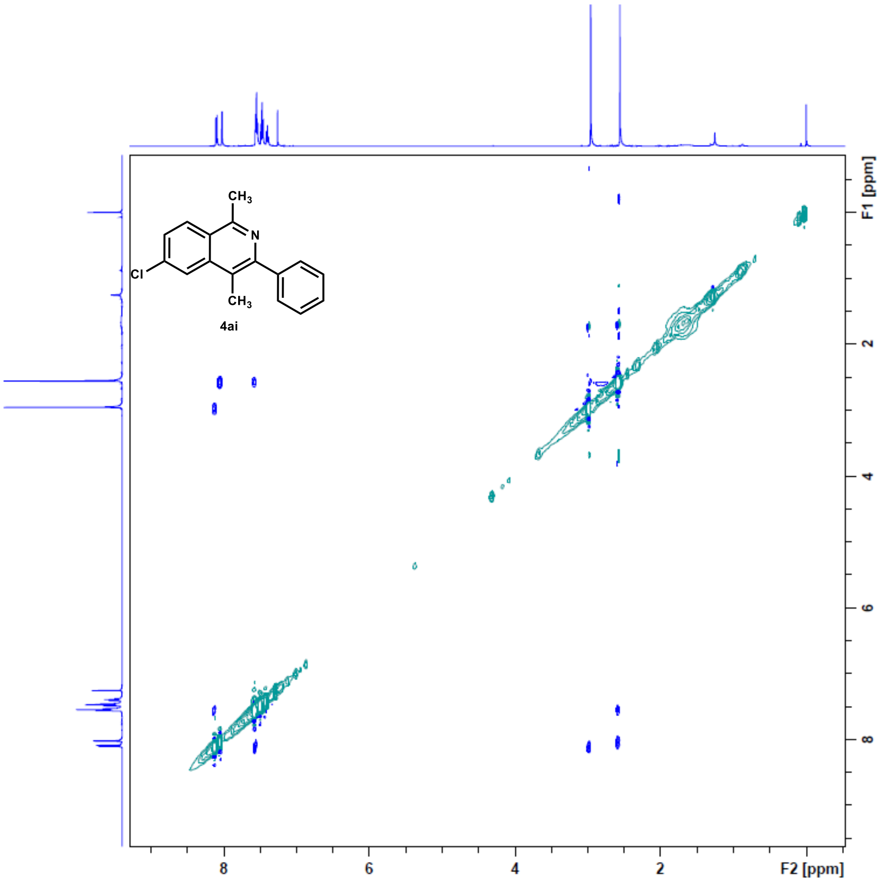
## NOESY of compounds 4ai, 4aj and 4al.

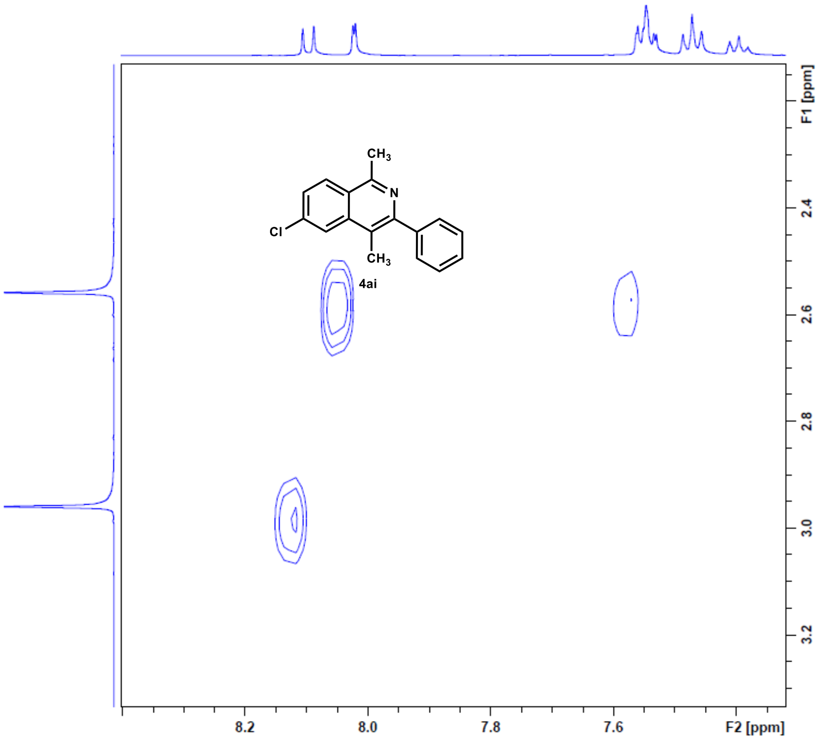
NOESY of compound **4ai**.



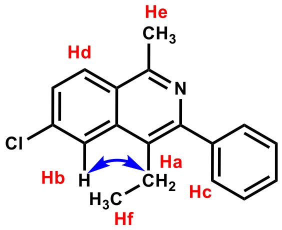
Ha = 2.60; Hb = 8.01; Hc = 7.59;
Hd = 8.09; He = 2.90;

There is a NOE correlation between Ha ($\delta$ 2.60, s) and Hb ($\delta$ 8.01, d). NOE is also observed between Ha ($\delta$ 2.6 s) and Hc ($\delta$ 7.49). There is no correlation between Hb and Hc. This suggests that regiochemistry of compound **4ai** is correct. Similar type of regiochemistry was observed in rhodium catalyzed reactions.[12]


CH3
N
Cl
CH3
4ai
F1 [ppm]
2
4
6
8
8
6
4
2
F2 [ppm]

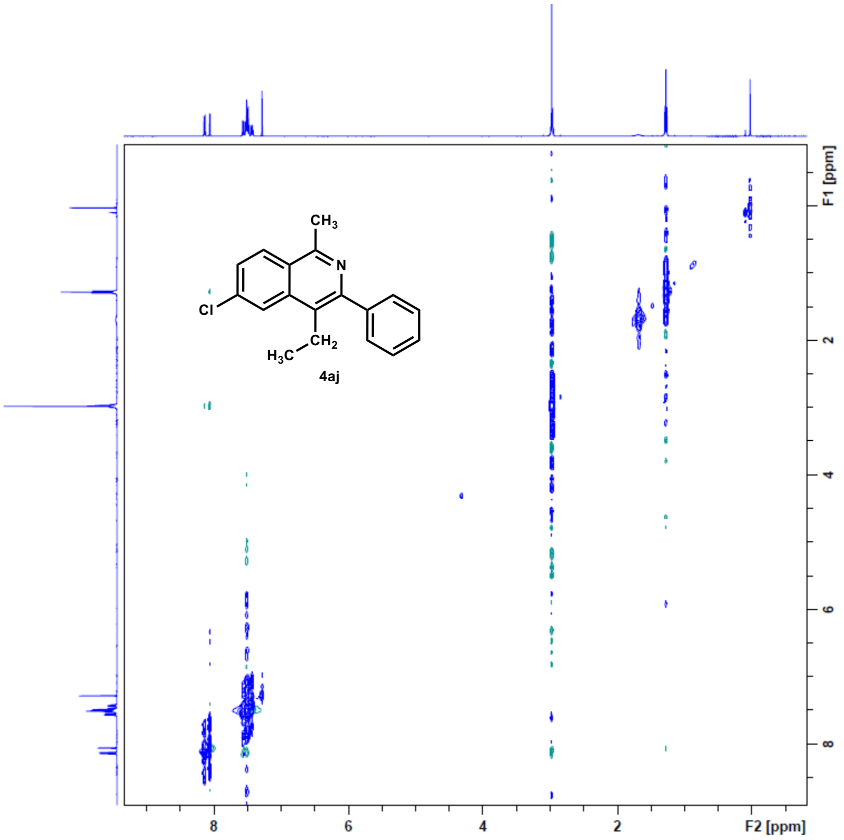

CH3
N
Cl
CH3
4ai
F1 [ppm]
2.4
2.6
2.8
3.0
3.2
8.2
8.0
7.8
7.6
F2 [ppm]

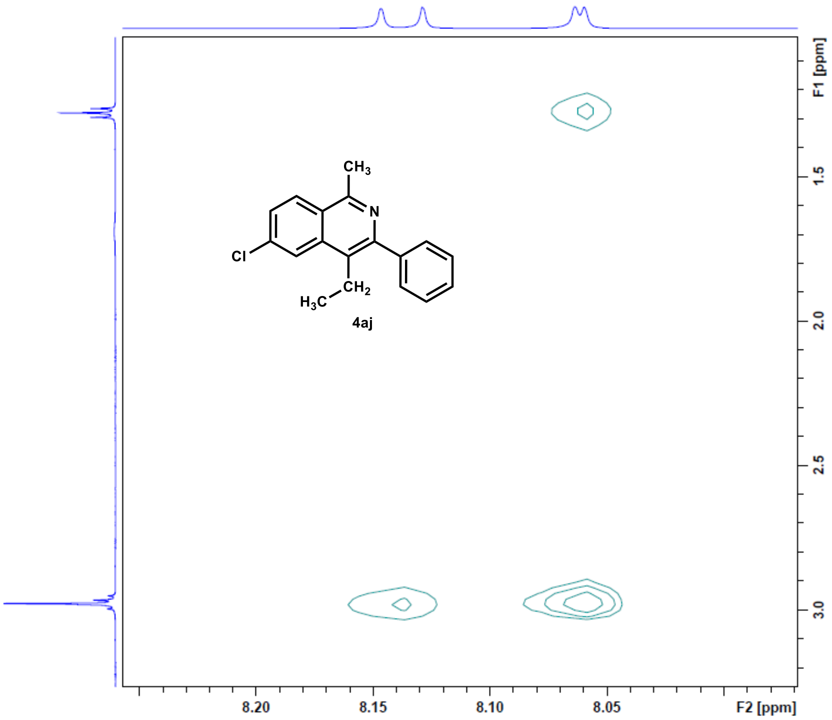
NOESY of compound **4aj**.



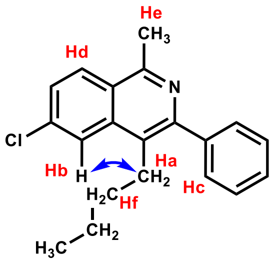
Ha = 2.95; Hb = 8.05; Hc = 7.50;
Hd = 8.13; He = 3.00; Hf = 1.38;

There is a NOE correlation between Ha (δ 2.95, q) and Hb (δ 8.05, d). NOE is also observed between Hf (δ 1.38, t) and Hb (δ 8.05, d). There is no correlation between Hb and Hc. This suggests that regiochemistry of compound **4aj** is correct.



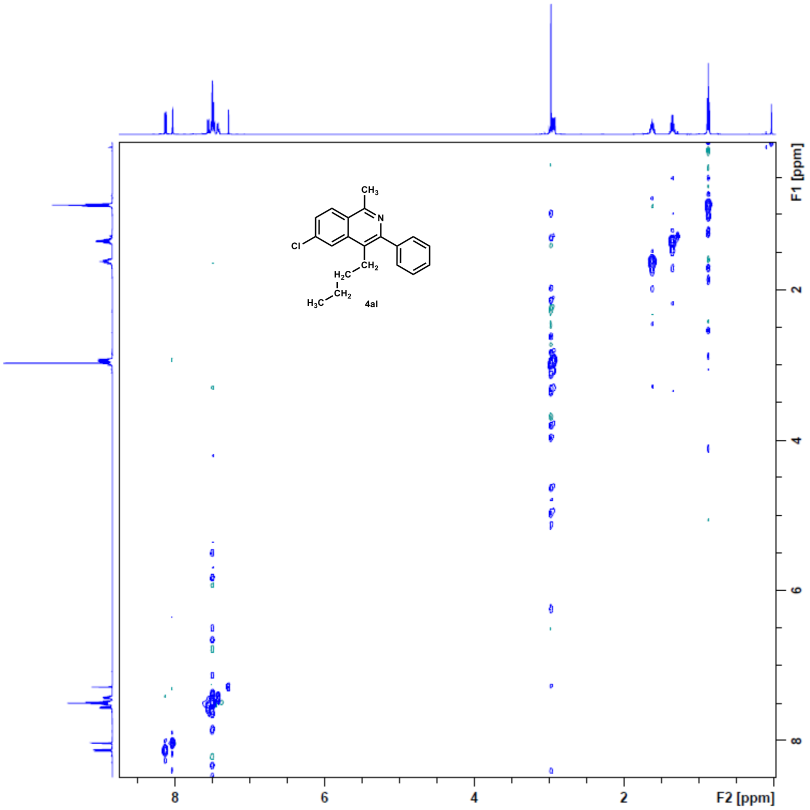


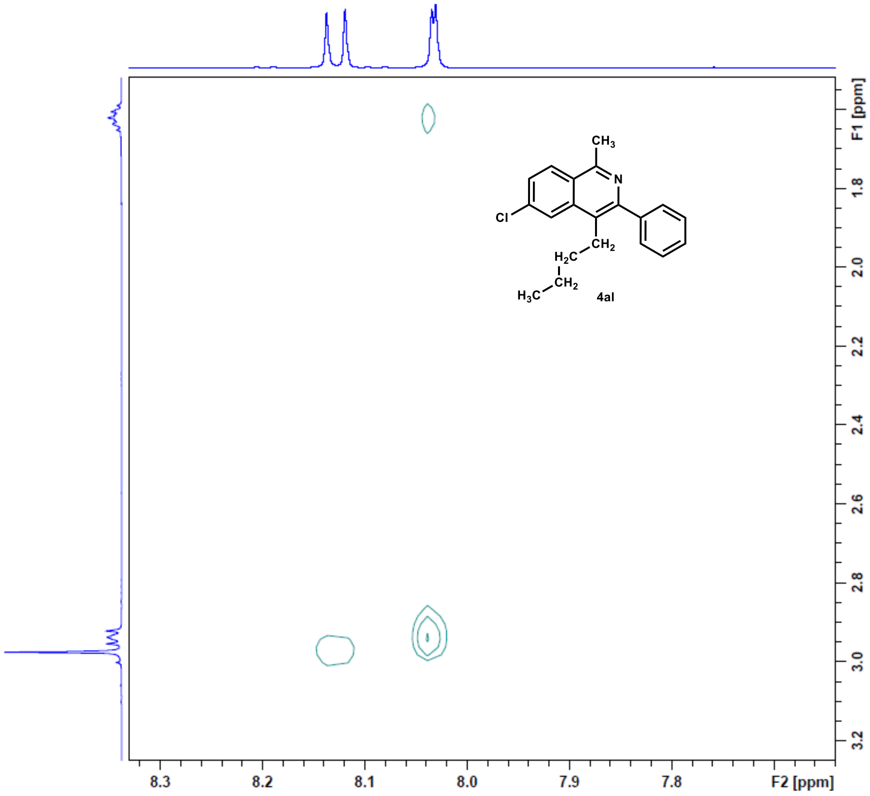
NOESY of compound **4al**.



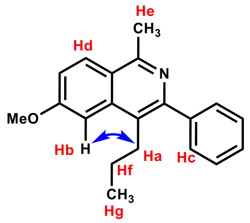
**Ha = 2.95; Hb = 8.04; Hc = 7.45;**
**Hd = 8.15; He = 2.98; Hf = 1.65;**

There is a NOE correlation between Ha (*δ* 2.95, q) and Hb (*δ* 8.04, d). NOE is also observed between Hf (*δ* 1.65, quintet) and Hb (*δ* 8.04, d). There is no correlation between Hb and Hc. This suggests that regiochemistry of compound **4al** is correct.


CH3
N
Cl
CH2
H2C
CH2
H3C
4al
8
6
4
2
F2 [ppm]
2
4
6
8
F1 [ppm]

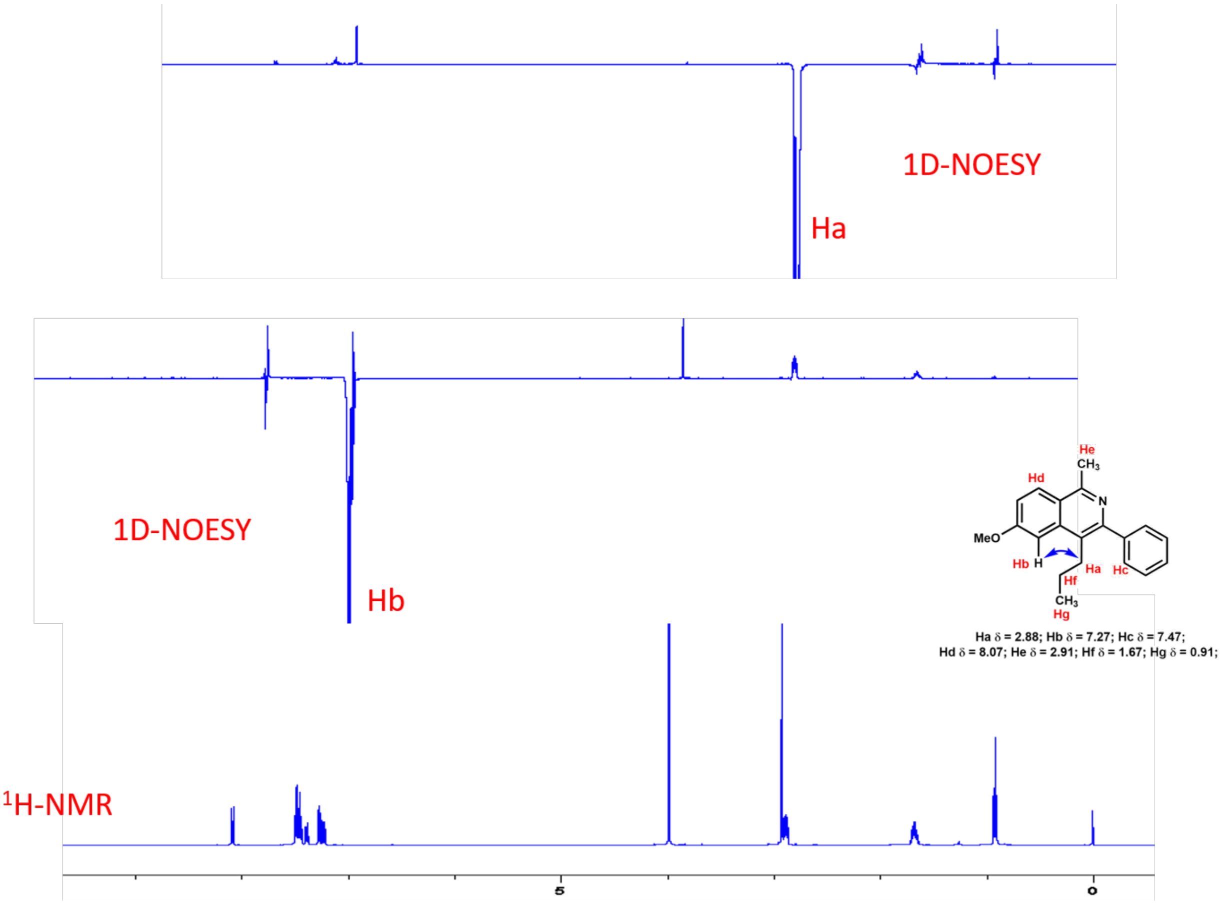

CH3
N
Cl
CH2
H2C
CH2
H3C
4al
8.3
8.2
8.1
8.0
7.9
7.8
F2 [ppm]
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
F1 [ppm]

1D-NOESY of compound **4bk**.



Ha = 2.88; Hb = 7.27; Hc = 7.47;
Hd = 8.07; He = 2.91; Hf = 1.67; Hg = 0.91;

First, we selectively irradiated Hb ($\delta$ 7.27, d) protons and the NOE was observed on Ha ($\delta$ 2.88, s) protons. Similarly, Ha ($\delta$ 2.88, s) protons irradiated and the NOE was observed at Hb ($\delta$ 7.27, d). There is no NOE in between Hb and Hc protons. This suggests that regiochemistry of compound **4bk** is correct.



**References:**

1. T. Morita, S. Fuse and H. Nakamura, *Angew. Chem. Int. Ed.* 2016, **55**, 13580.
2. B. C. Hamper, K. L. Leschinsky, S. S. Massey, C. L. Bell, L. H. Brannigan and S. D. Prosch, *J. Agric. Food Chem* 1995, ***43***, 219.
3. M. T. Herrero, I. Tellitu, E. Dominguez, S. Hernandez, I. Moreno and R. SanMartin, *Tetrahedron*, 2002, **58**, 8581.
4. M. J. Mio, L. C. Kopel, J. B. Barun, T. L. Gadzikawa, K. L. Hull, R. G. Brisbois, C. J. Markworth and P. A. Grieco, *Org. Lett.* 2002, **4**, 3199.
5. (a) E. Kudo, Y. Shibata, M. Yamazaki, K. Masutomi, Y. Miyauchi, M. Fukui, H. Sugiyama, H. Uekusa, T. Satoh, M. Miura and K. Tanaka, *Chem. Eur. J.,* 2016, **22**, 14190; (b) S. Warratz, C. Kornhaab, A. Cajaraville, B. Niepotter, D. Stalke and L. Ackermann, *Angew. Chem. Int. Ed.,* 2015, **54**, 5513; (c) X. Xu, H. Zhao, J. Xu, C. Chen, Y. Pan, Z. Luo, Z. Zhang, H. Li and L. Xu, *Org. Lett*., 2018, **20**, 3843; (d) Z. Long, Y. Yang and J. You, *Org. Lett*., 2017, **19**, 2781; (e) R. Mandal and B. Sundararaju, *Org. Lett*., 2017, **19**, 2544.
6. J. Zhang, R. Shrestha, J. F. Hartwig and P. Zhao, *Nat. Chem.,* 2016, **8**, 1144.
7. (a) L. Huang, A. Biafora, G. Zhang, V. Bragoni and L. J. Goossen, *Angew. Chem. Int. Ed*., 2016, **55**, 6933; (b) N. Y. Phani Kumar, A. Bechtoldt, K. Raghuvanshi and L. Ackermann, *Angew. Chem. Int. Ed*., 2016, **55**, 6929; (c) A. Biafora, B. A. Khan, J. Bahri, J. M. Hewer and L. J. Goossen, *Org. Lett.,* 2017, **19**, 1232. (d) X.-Q. Hu, Z. Hu, A. S. Trita, G. Zhang and L. J. Goossen, *Chem. Sci.,* 2018, **9**, 5289; (e) M. Simonetti and I. Larossa, *Nat. Chem.,* 2016, **8**, 1086.
8. A. V. Dubrovskiy and R. C. Larock, *Org. Lett.* 2010, **12**, 1180.
9. M. Shigenobu, K. Takenaka and H. Sasai, *Angew. Chem. Int. Ed.* 2015, **54**, 9572.
10. (a) A. Krasovskiy and P. Knochel, *Angew. Chem. Int. Ed.* 2004, **43**, 3333. (b) A. Krasovskiy and P. Knochel, *Synthesis* **2006**, 890.
11. (a) S.-C. Chuang, P. Gandeepan, C.-H. Cheng, *Org. Lett.* 2013, **15**, 5750. (b) H. Wang, J. Koeller, W. Liu, L. Ackermann, *Chem. Eur. J.,* 2015, **21**, 15525.
12. (a) P. C. Too, Y.-F. Wang, S. Chiba, *Org. Lett.* **2010**, **12**, 5688. (b) T. K. Hyster, T. Rovis, *Chem. Commun*. 2011, **47**, 11846.

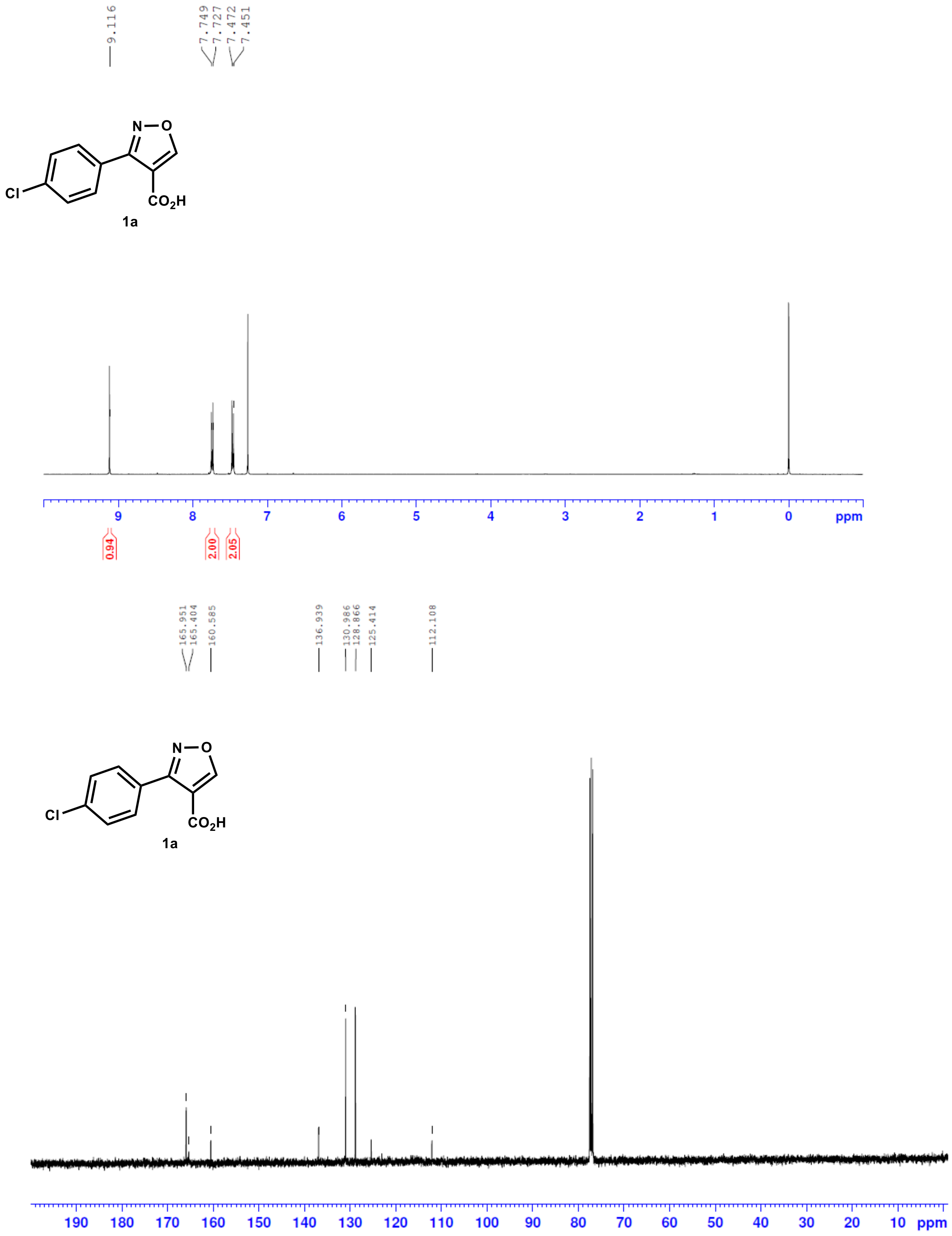


**Figure S7.** $^1$H and $^{13}$C NMR Spectra of compound **1a**

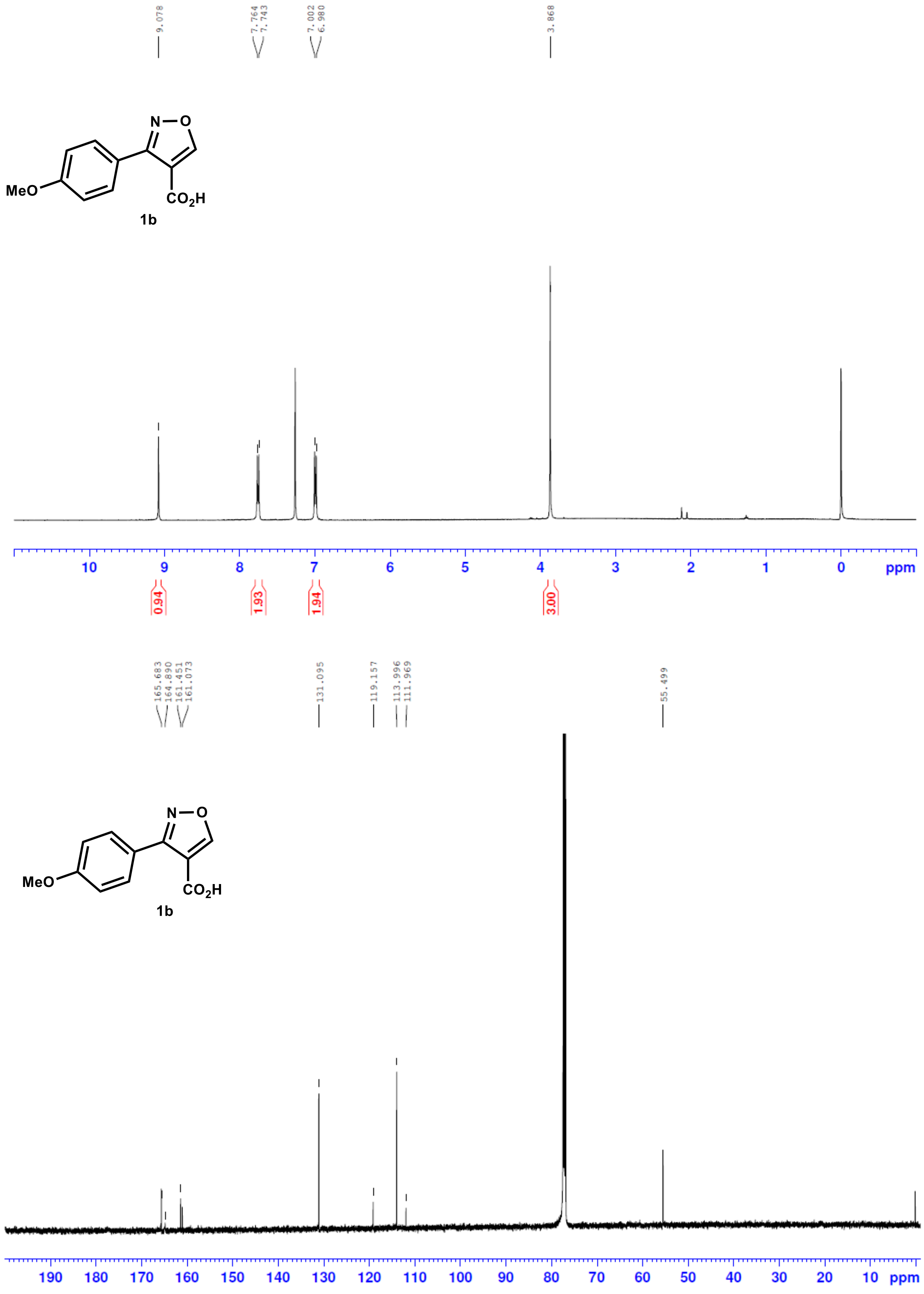


**Figure S8.** $^1$H and $^{13}$C NMR Spectra of compound **1b**

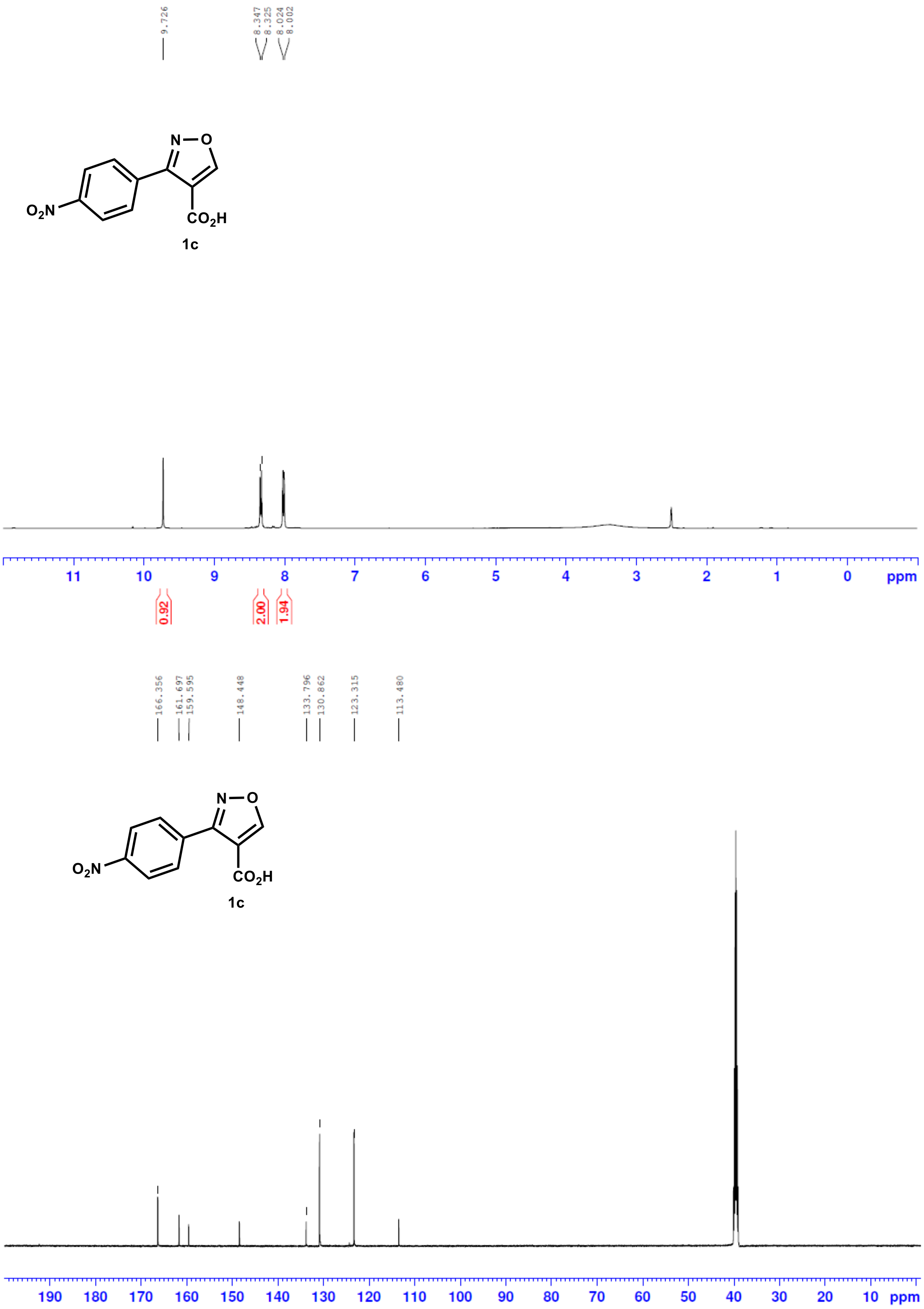


**Figure S9.** $^{1}$H and $^{13}$C NMR Spectra of compound **1c**

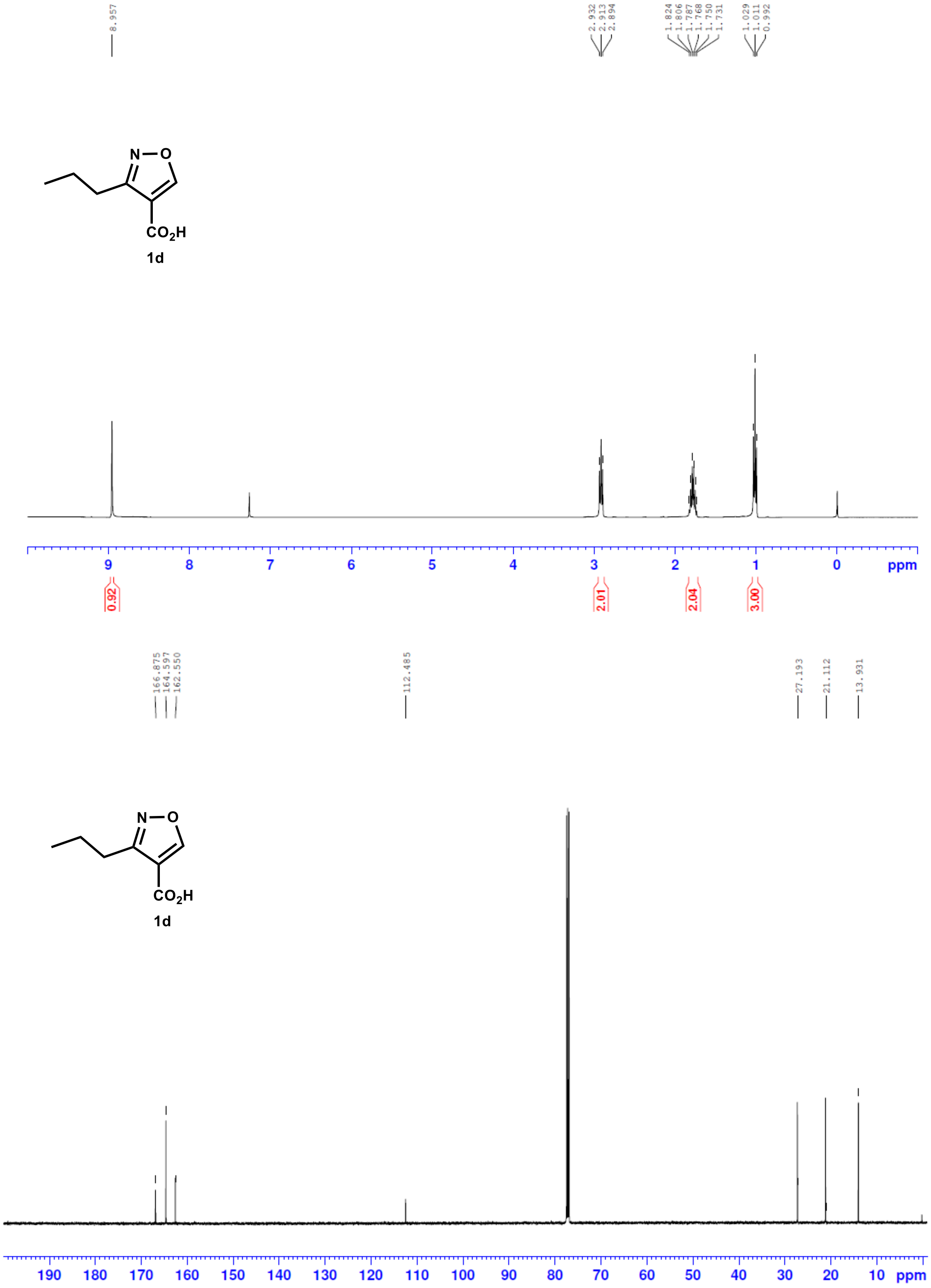


**Figure S10.** $^1$H and $^{13}$C NMR Spectra of compound **1d**

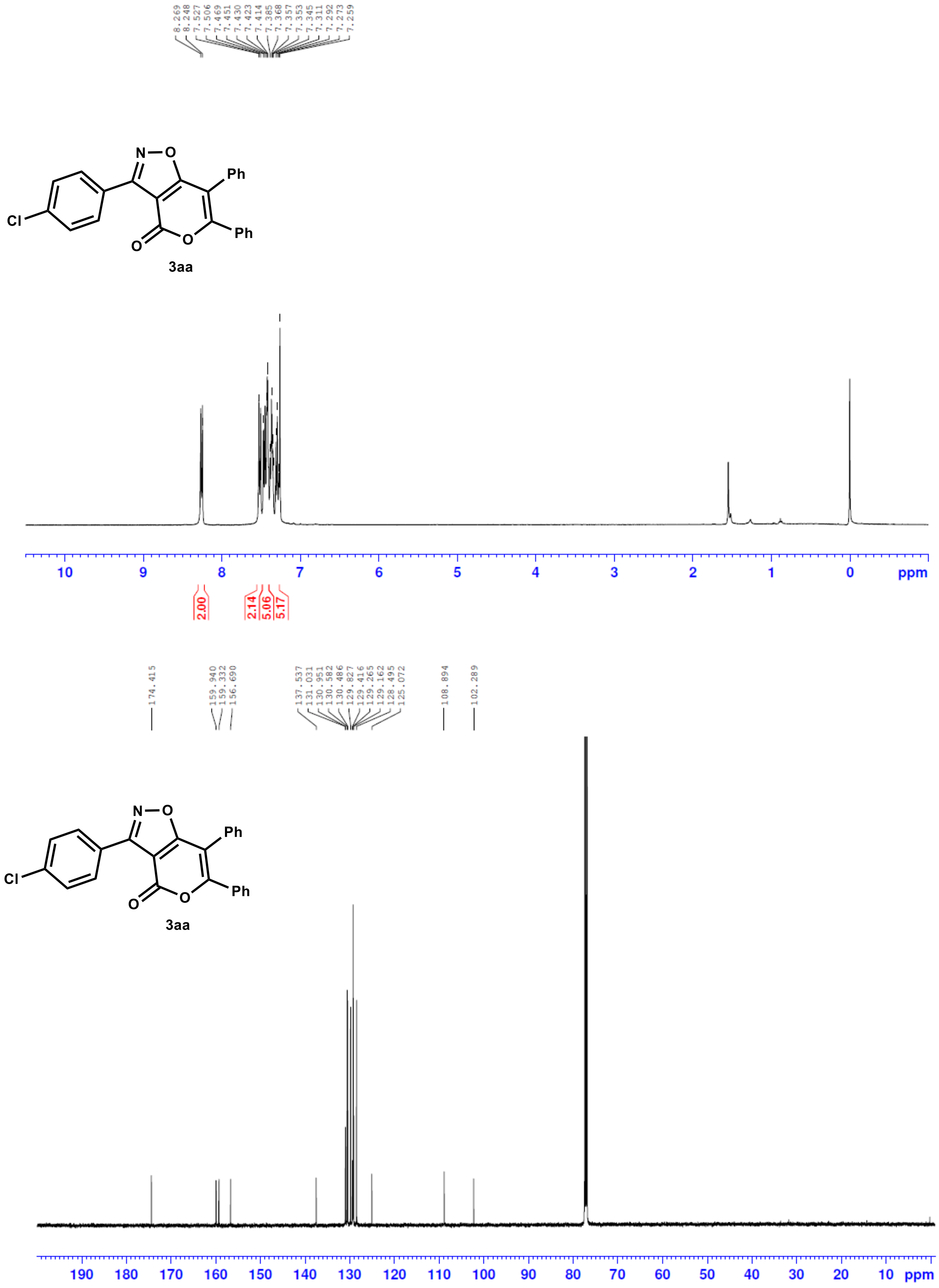


**Figure S12.** $^1$H and $^{13}$C NMR Spectra of compound **3aa**

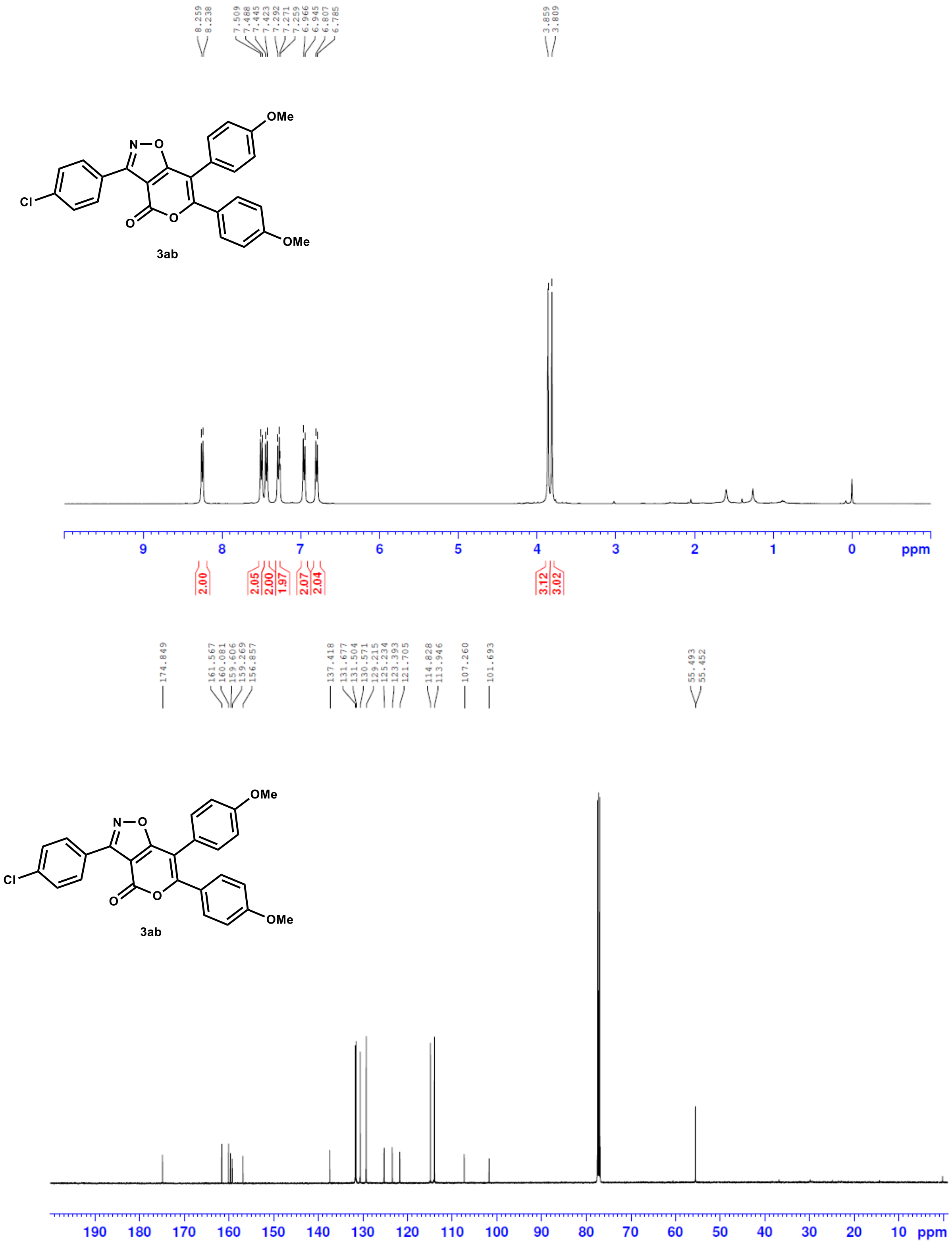


**Figure S13.** $^1$H and $^{13}$C NMR Spectra of compound **3ab**

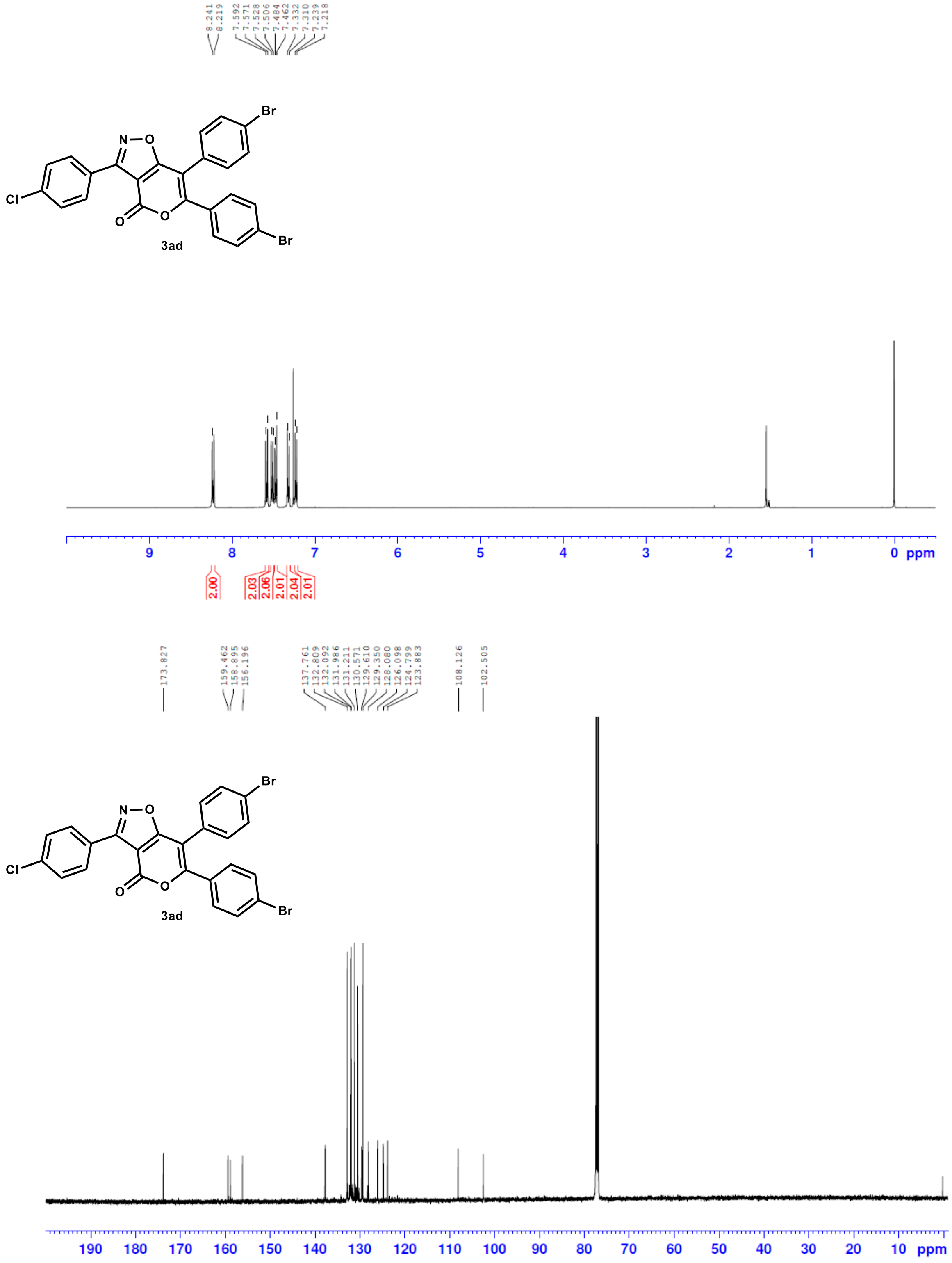


**Figure S14.** $^{1}$H and $^{13}$C NMR Spectra of compound **3ad**

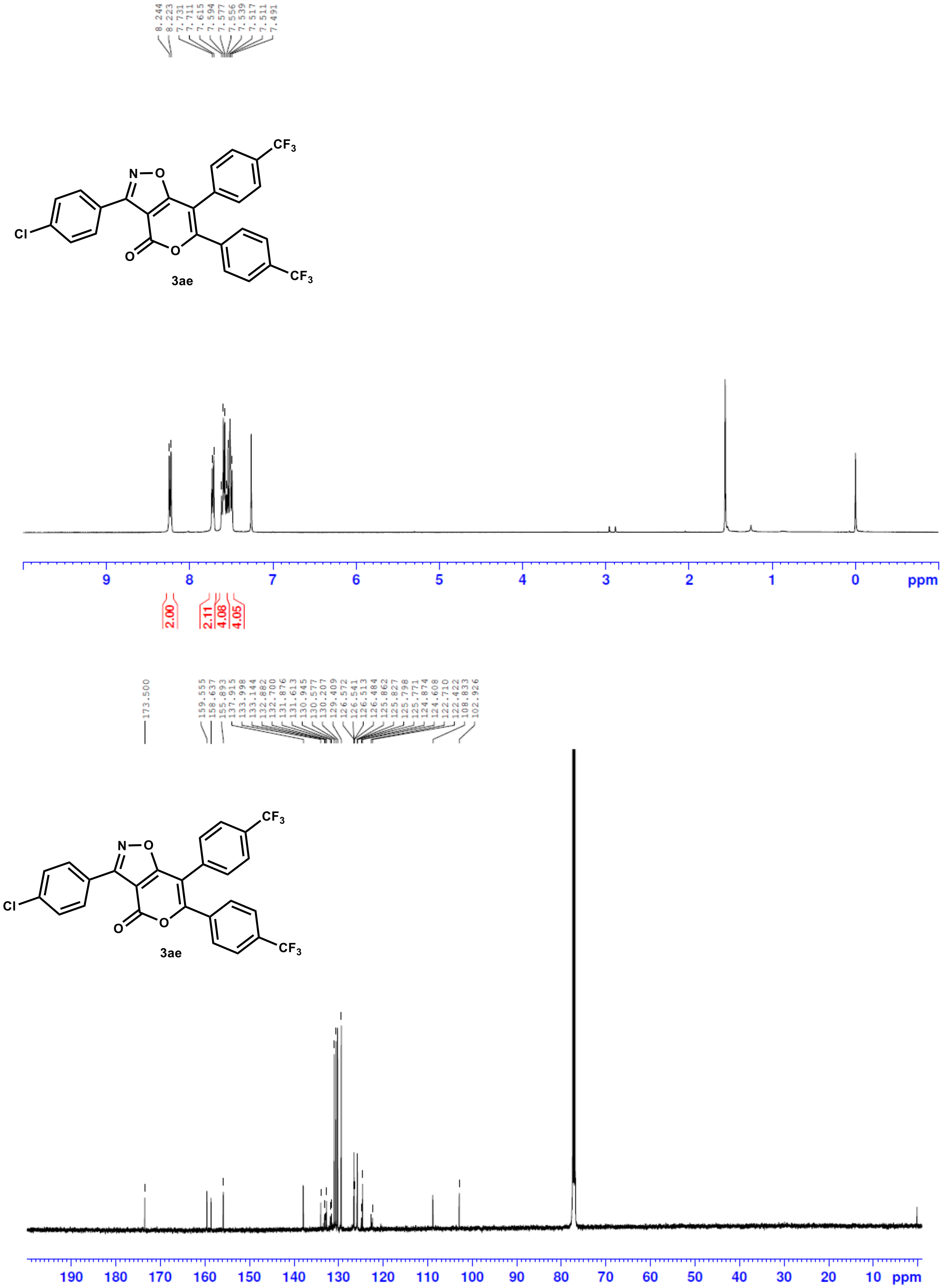


**Figure S15.** $^{1}H$ and $^{13}C$ NMR Spectra of compound **3ae**

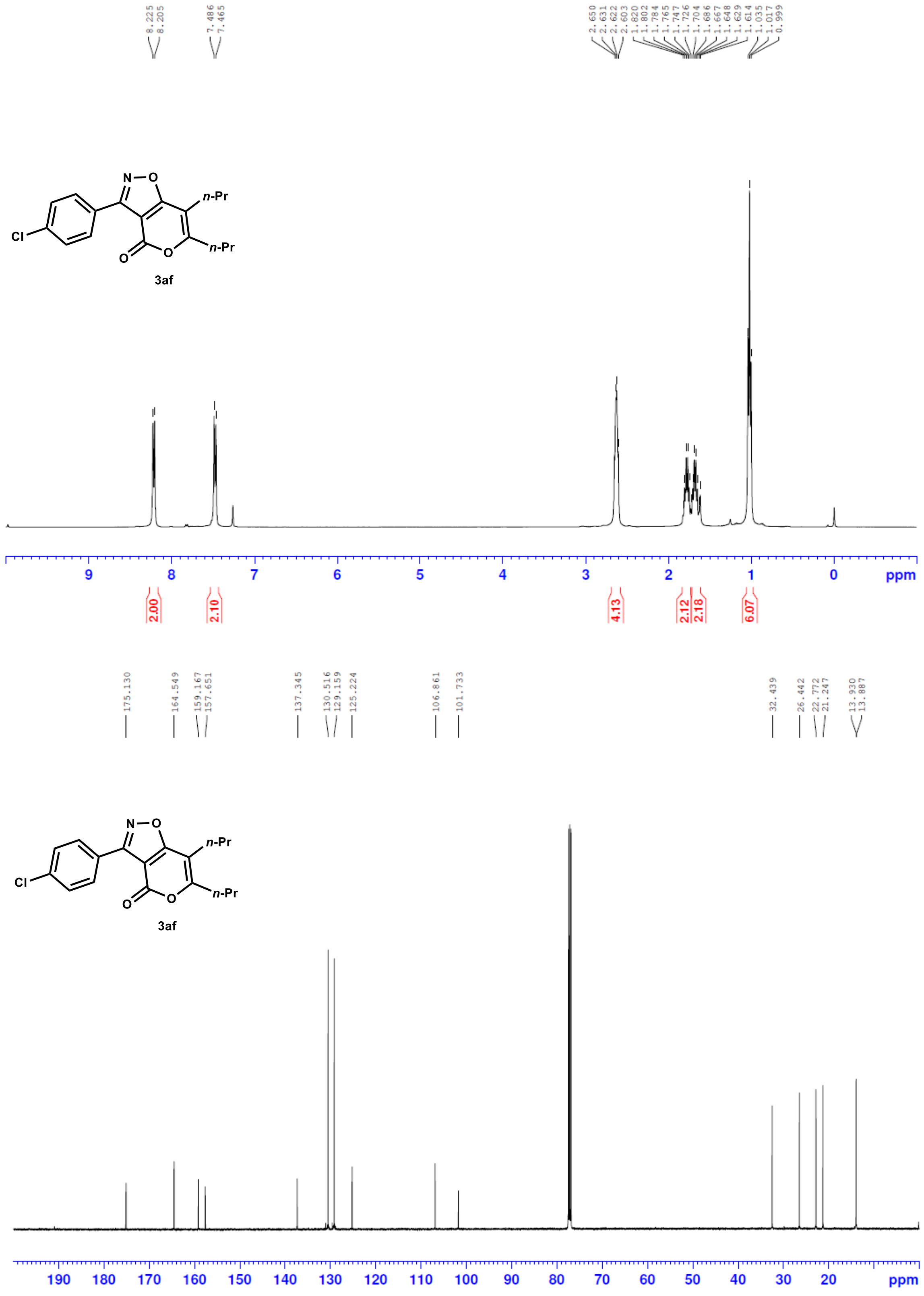


**Figure S16.** ${}^{1}$H and ${}^{13}$C NMR Spectra of compound **3af**

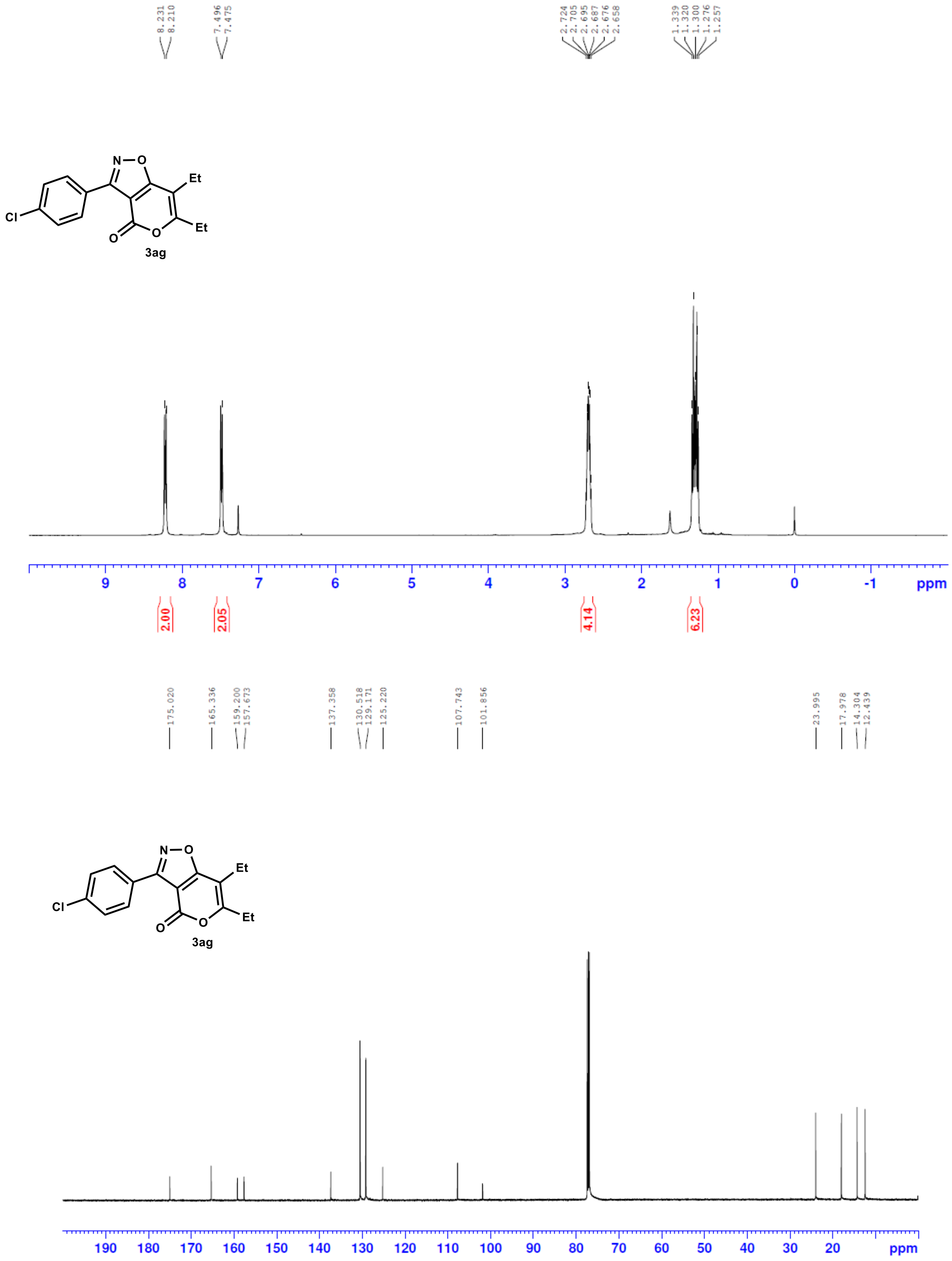


**Figure S17.** $^{1}$H and $^{13}$C NMR Spectra of compound **3ag**

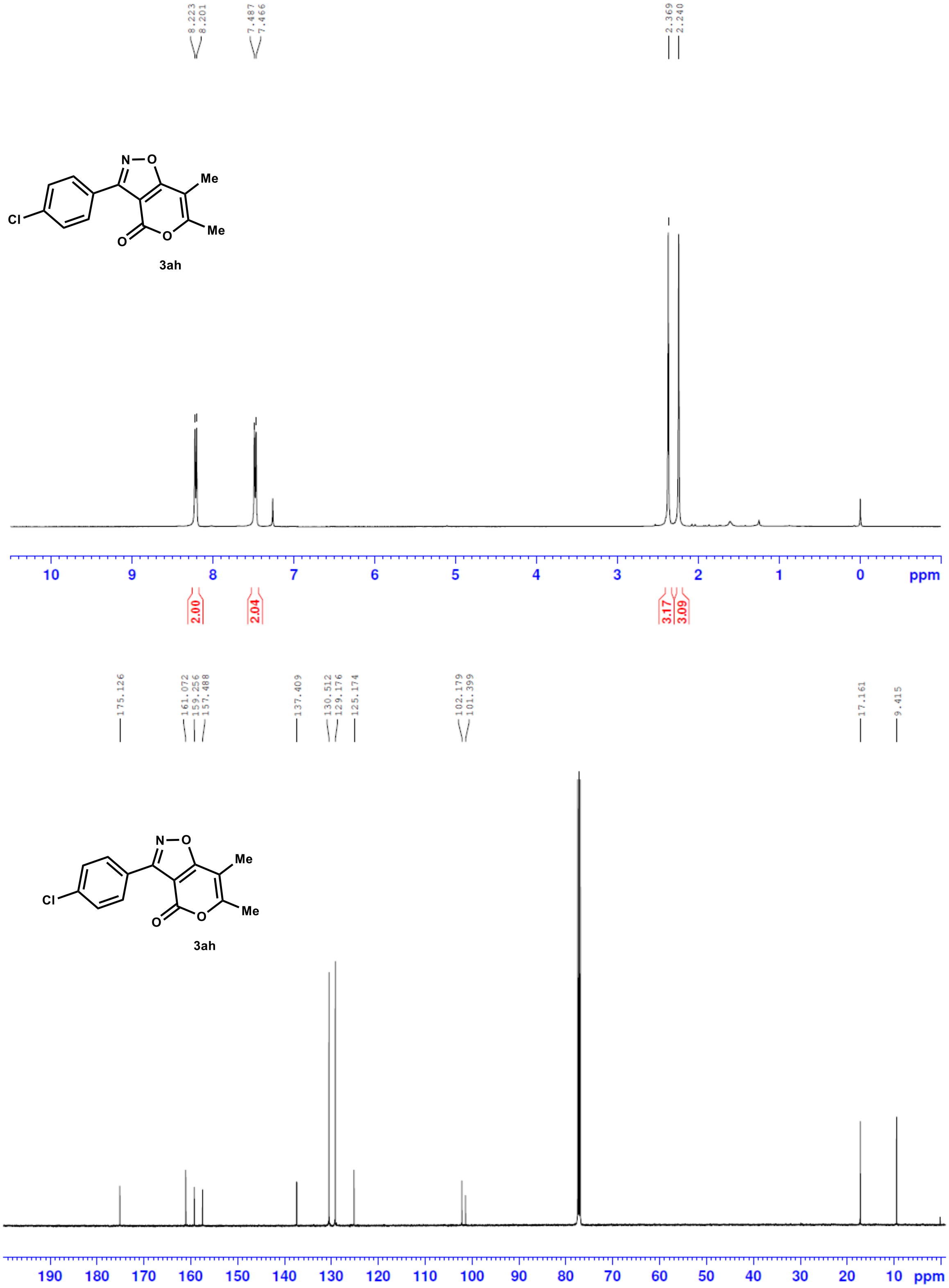


**Figure S18.** $^1$H and $^{13}$C NMR Spectra of compound **3ah**

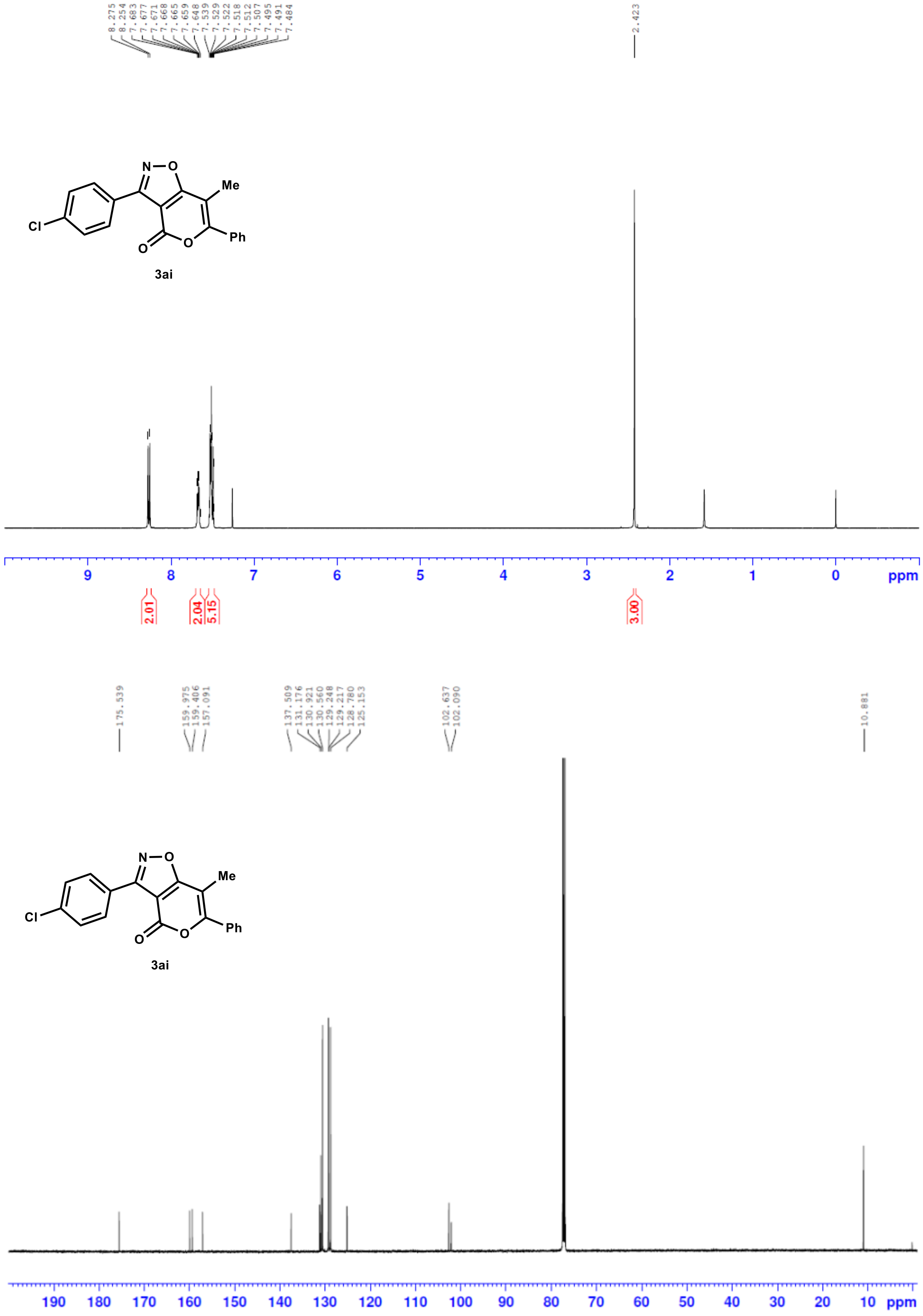


**Figure S19.** $^{1}H$ and $^{13}C$ NMR Spectra of compound **3ai**

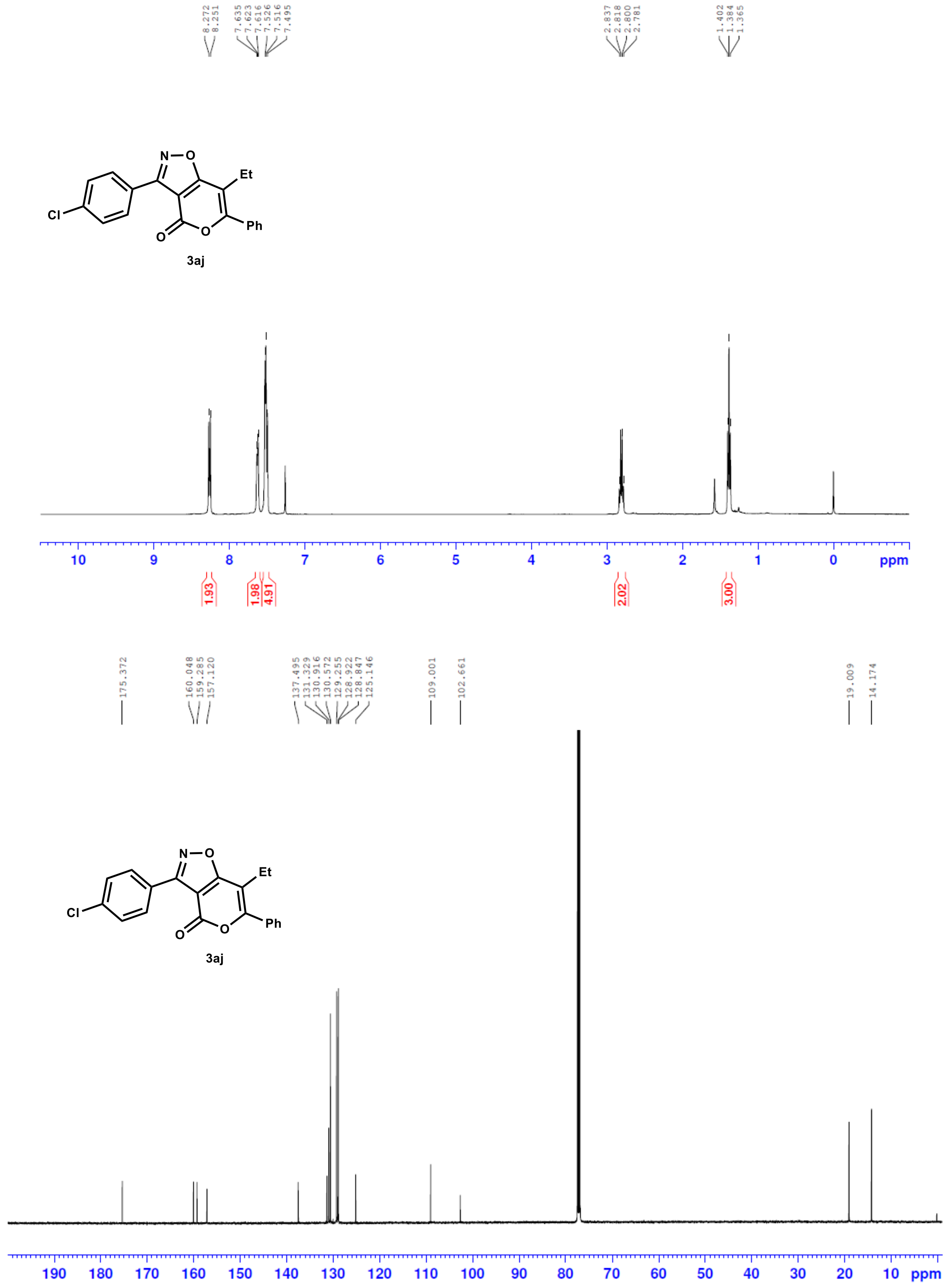
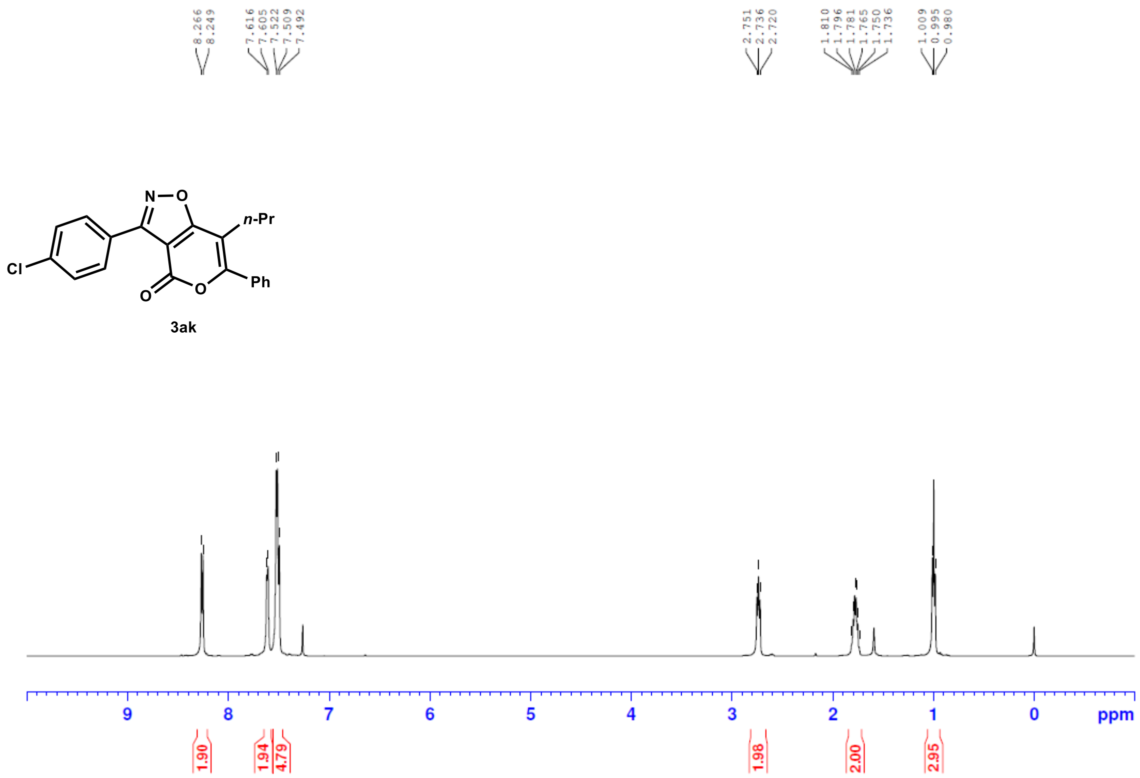


**Figure S20.** $^1$H and $^{13}$C NMR Spectra of compound **3aj**



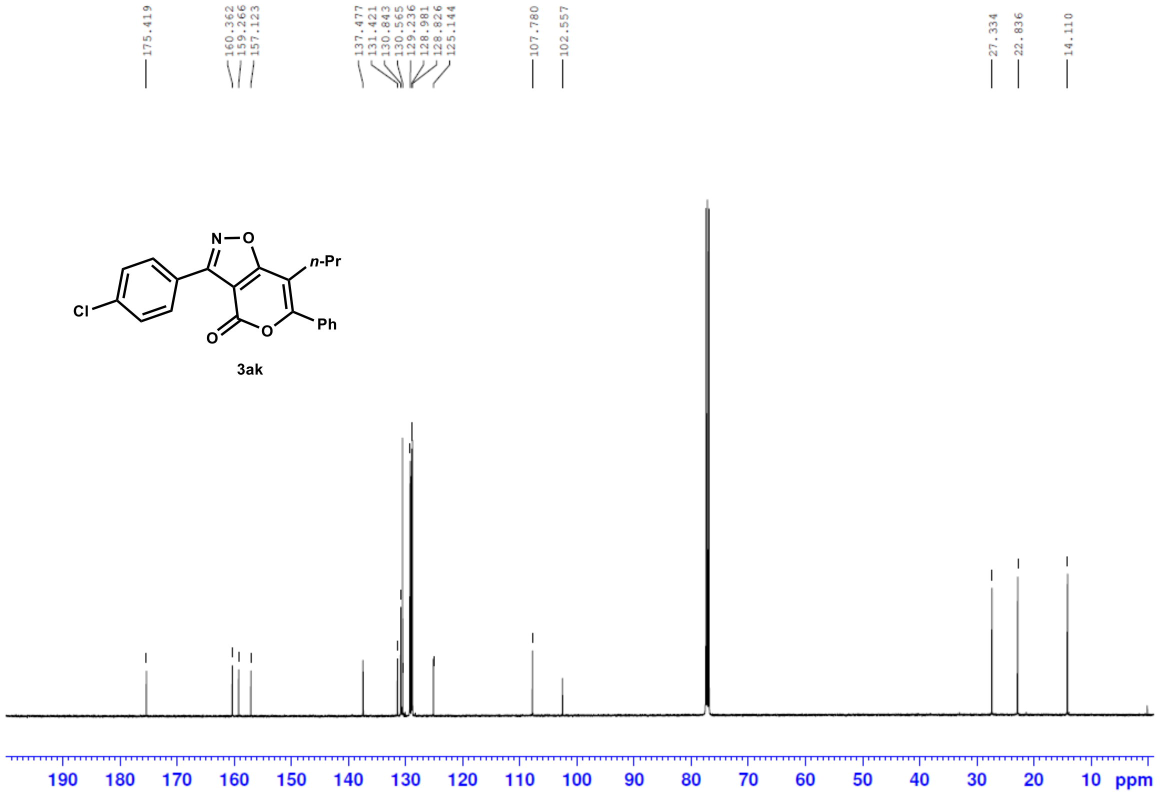


**Figure S21.**

$^1$H and $^{13}$C NMR Spectra of compound **3ak**

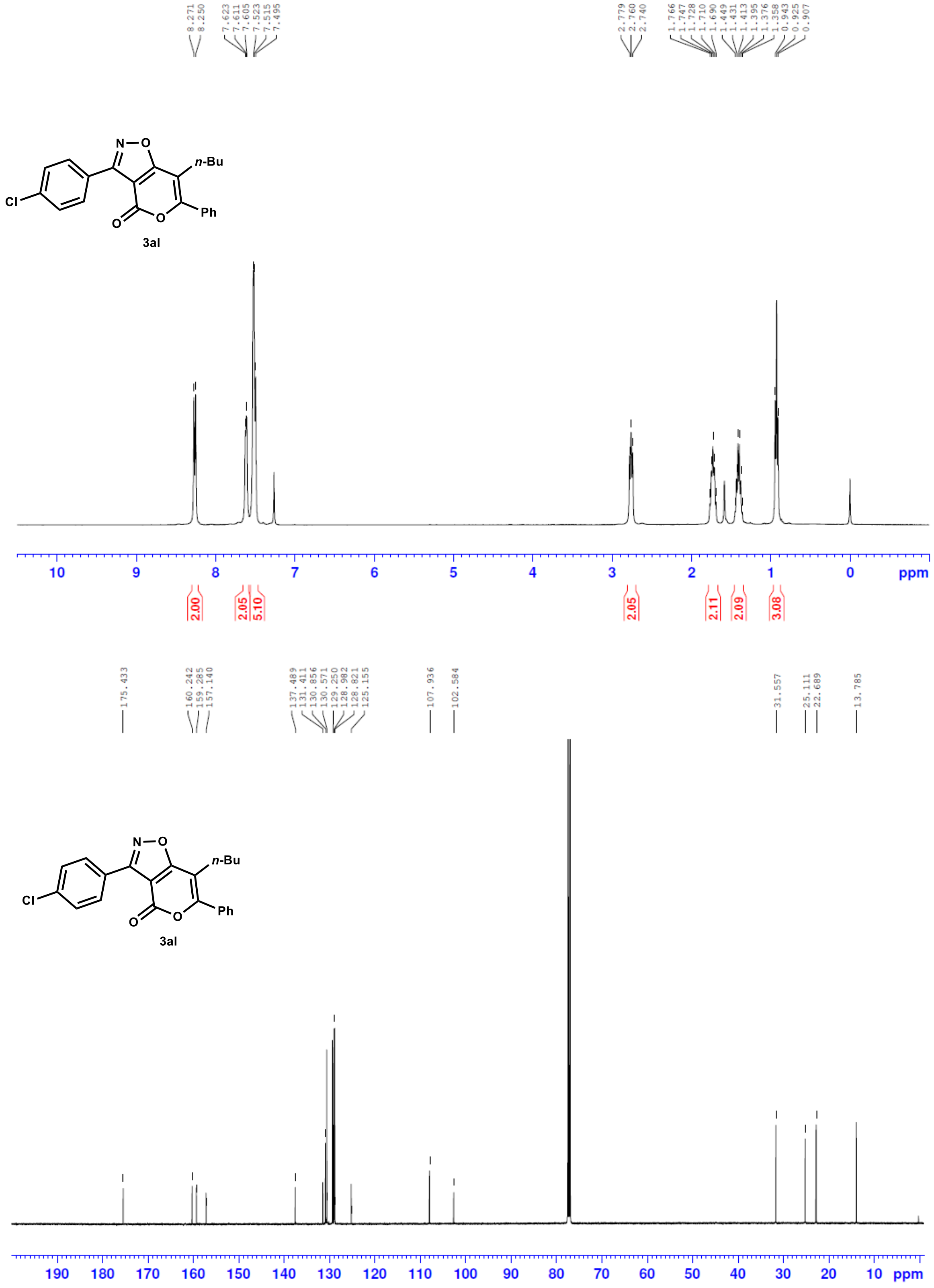


**Figure S22.** $^1$H and $^{13}$C NMR Spectra of compound **3al**

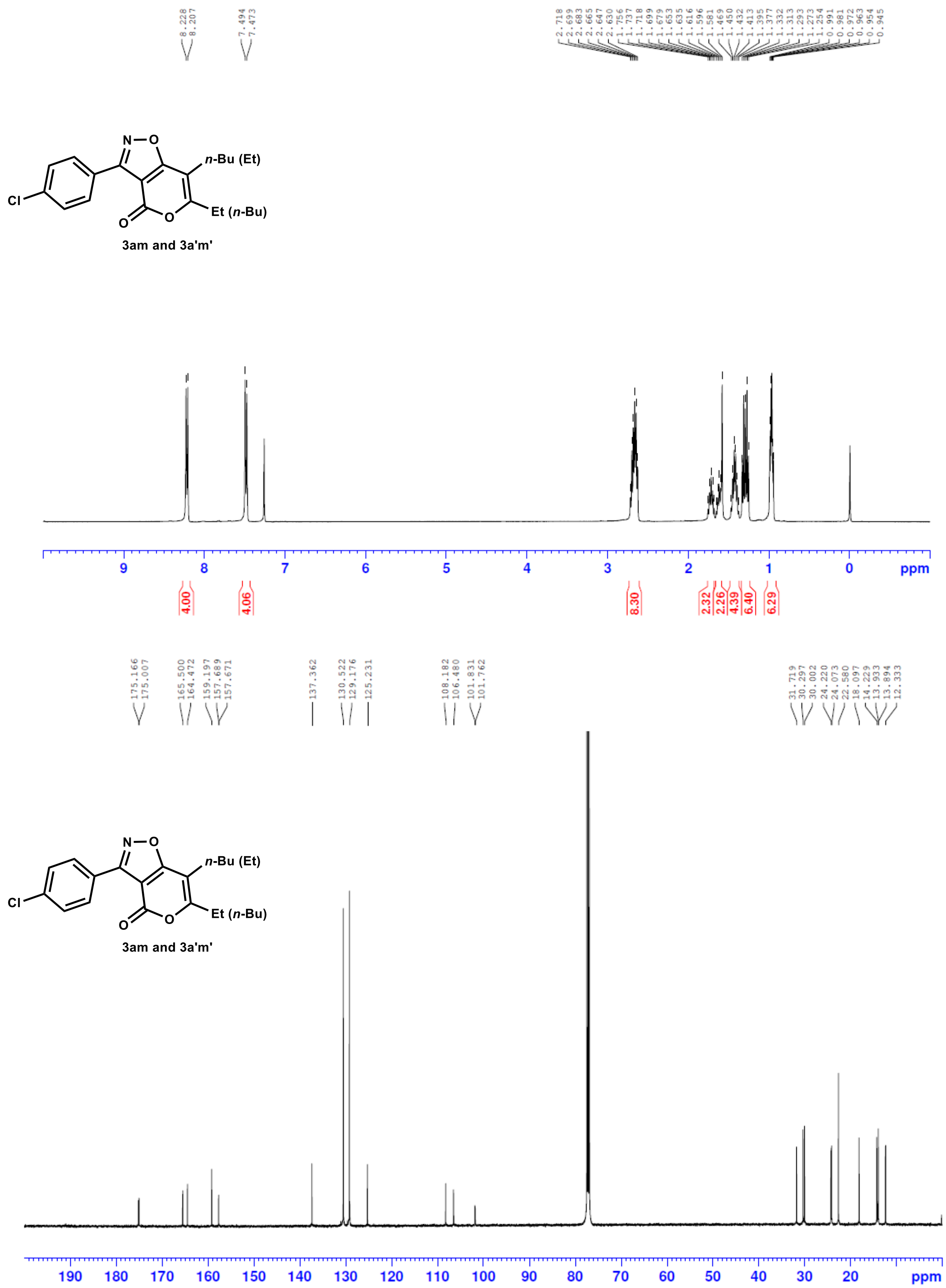


**Figure S23.** $^1$H and $^{13}$C NMR Spectra of compound **3ak**

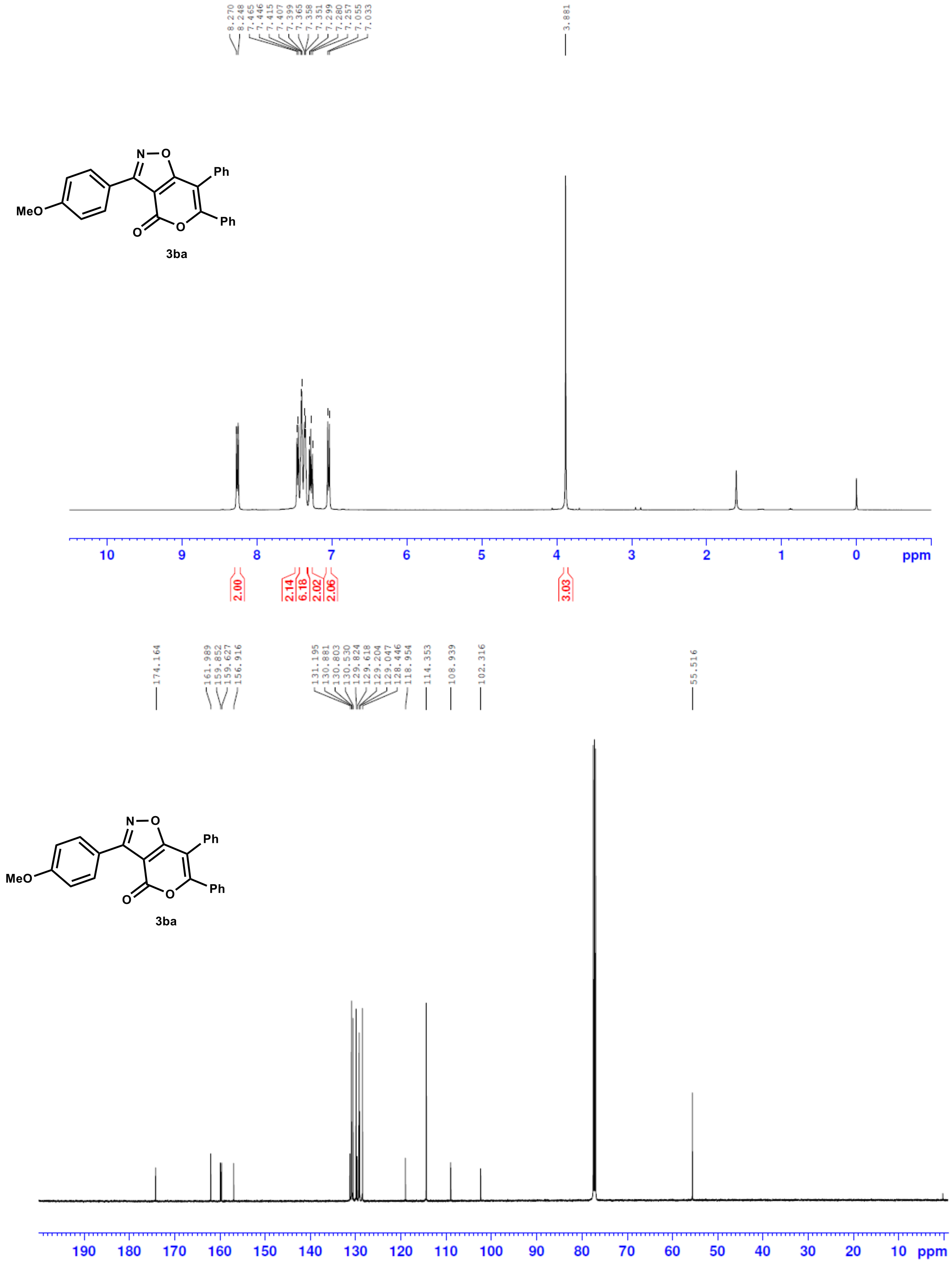


**Figure S24.** $^1$H and $^{13}$C NMR Spectra of compound **3ba**

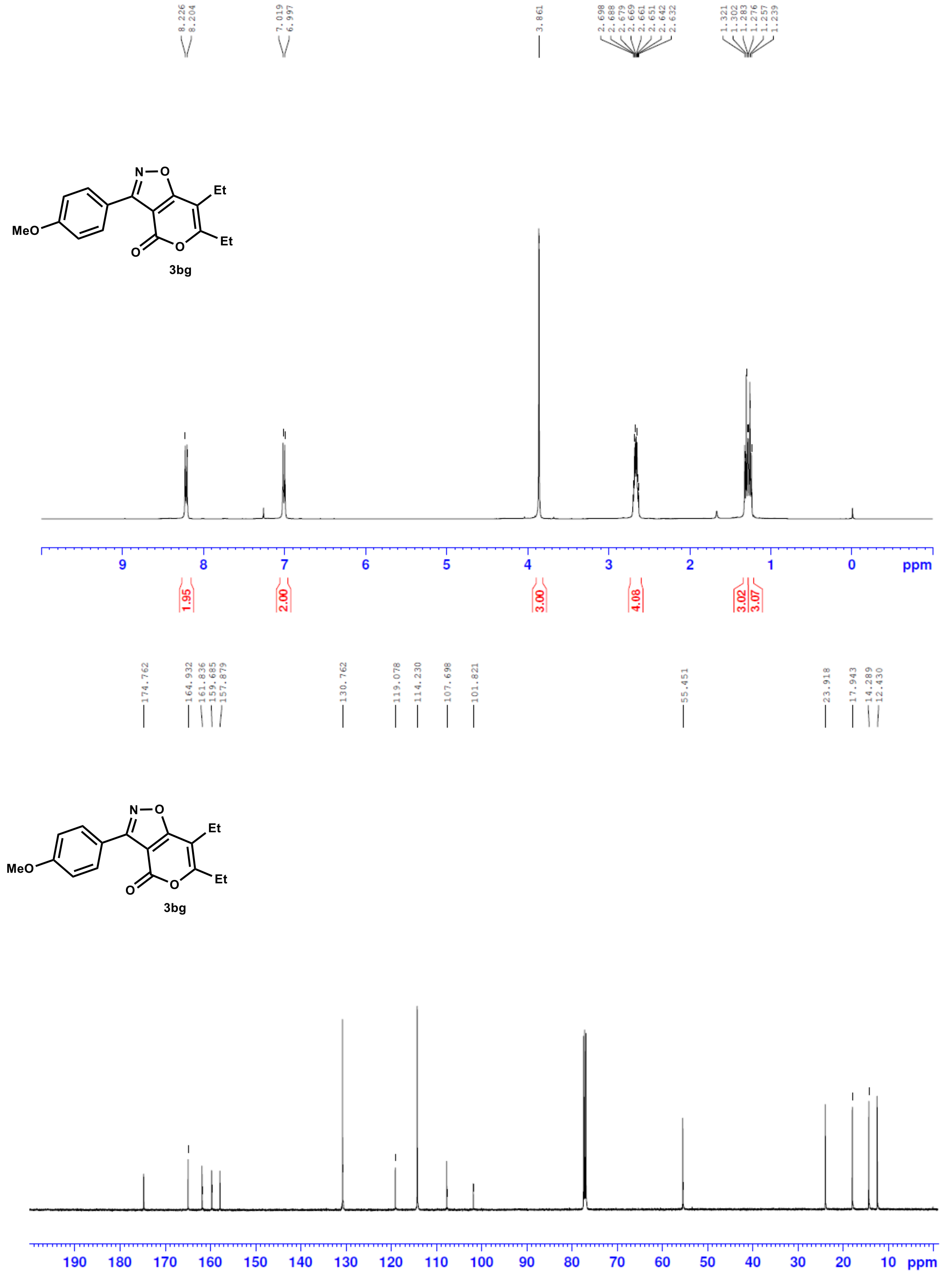


**Figure S25.** $^1$H and $^{13}$C NMR Spectra of compound **3bg**

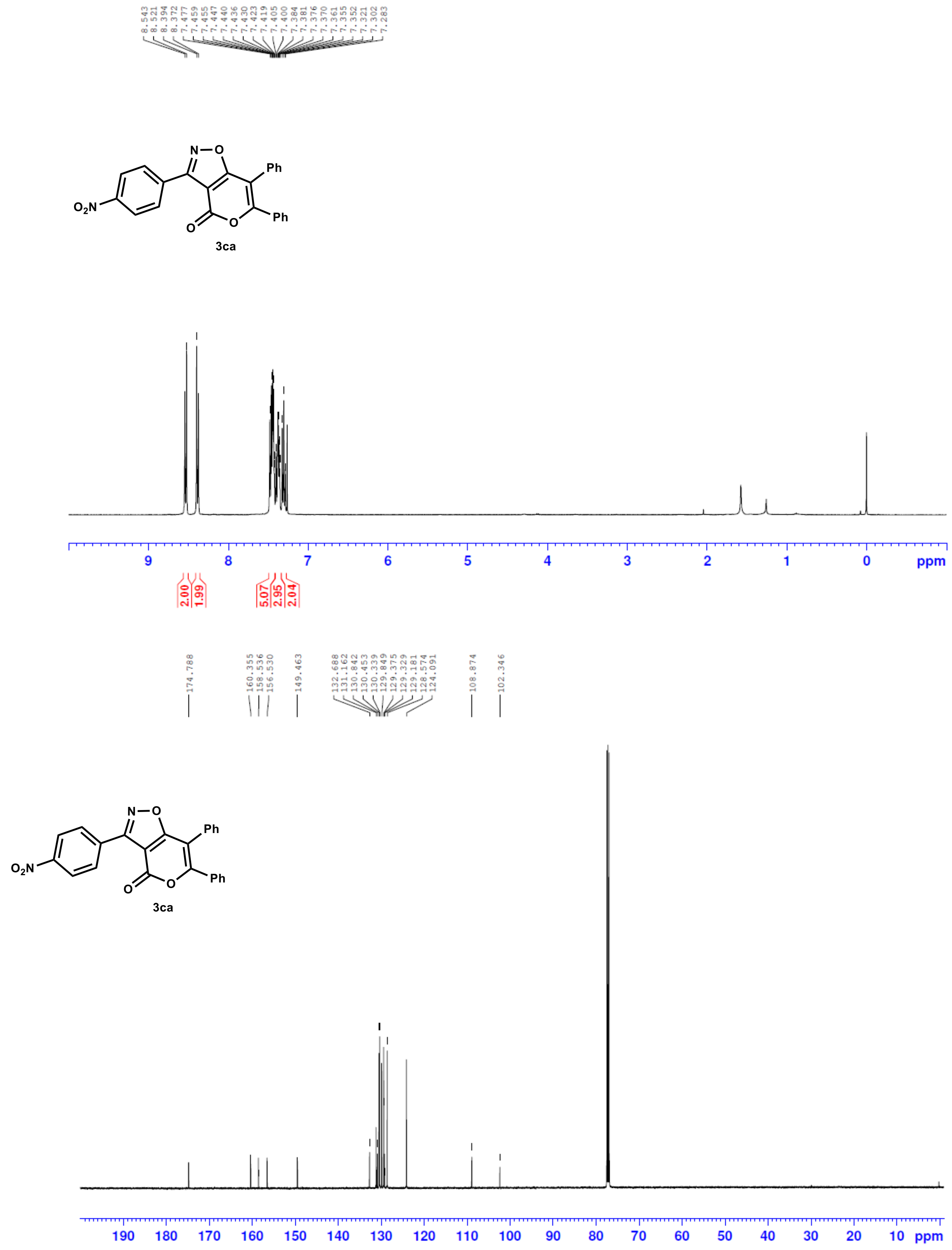


**Figure S26.** $^{1}$H and $^{13}$C NMR Spectra of compound **3ca**

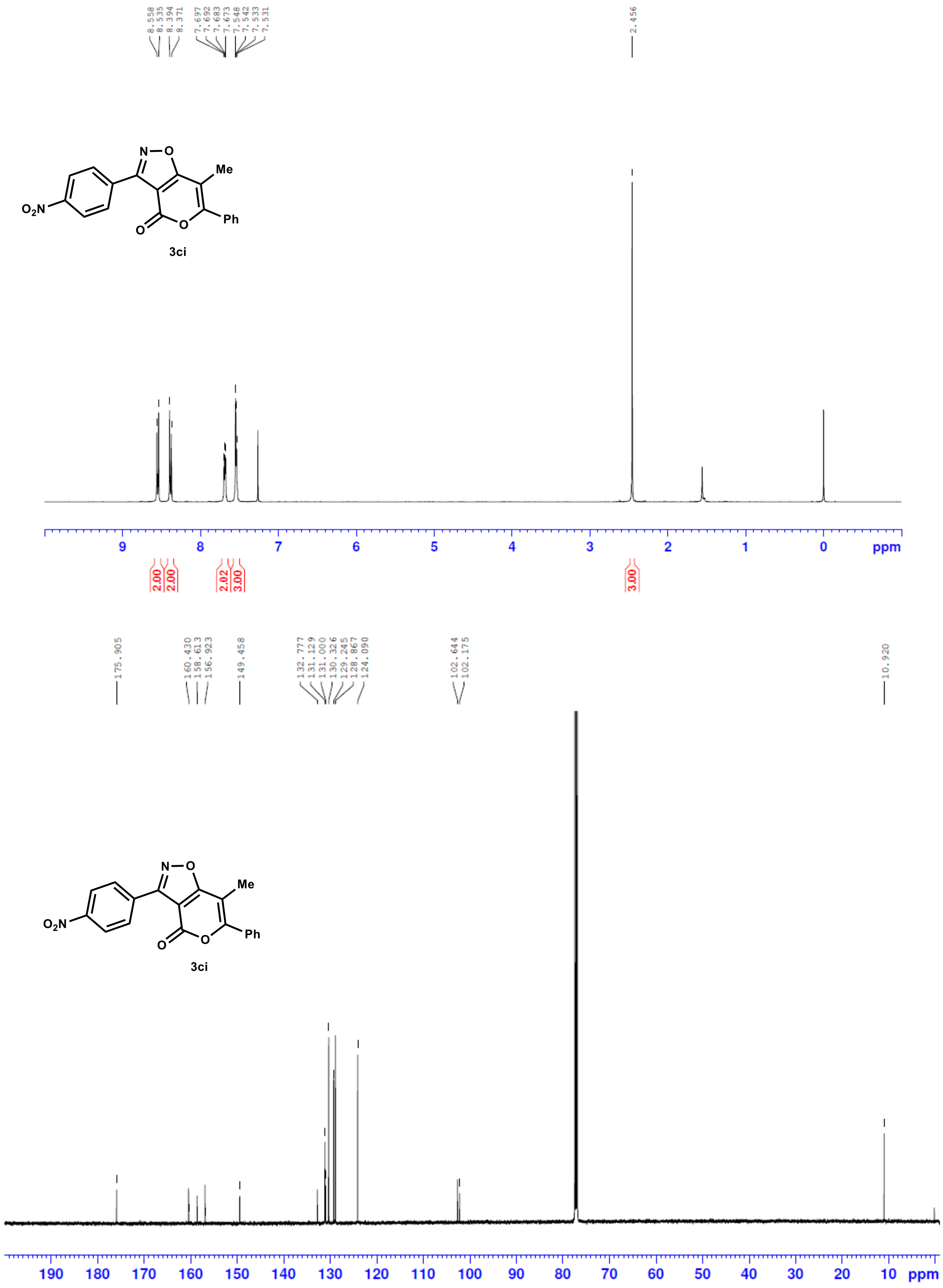


**Figure S27.** $^{1}H$ and $^{13}C$ NMR Spectra of compound **3ci**

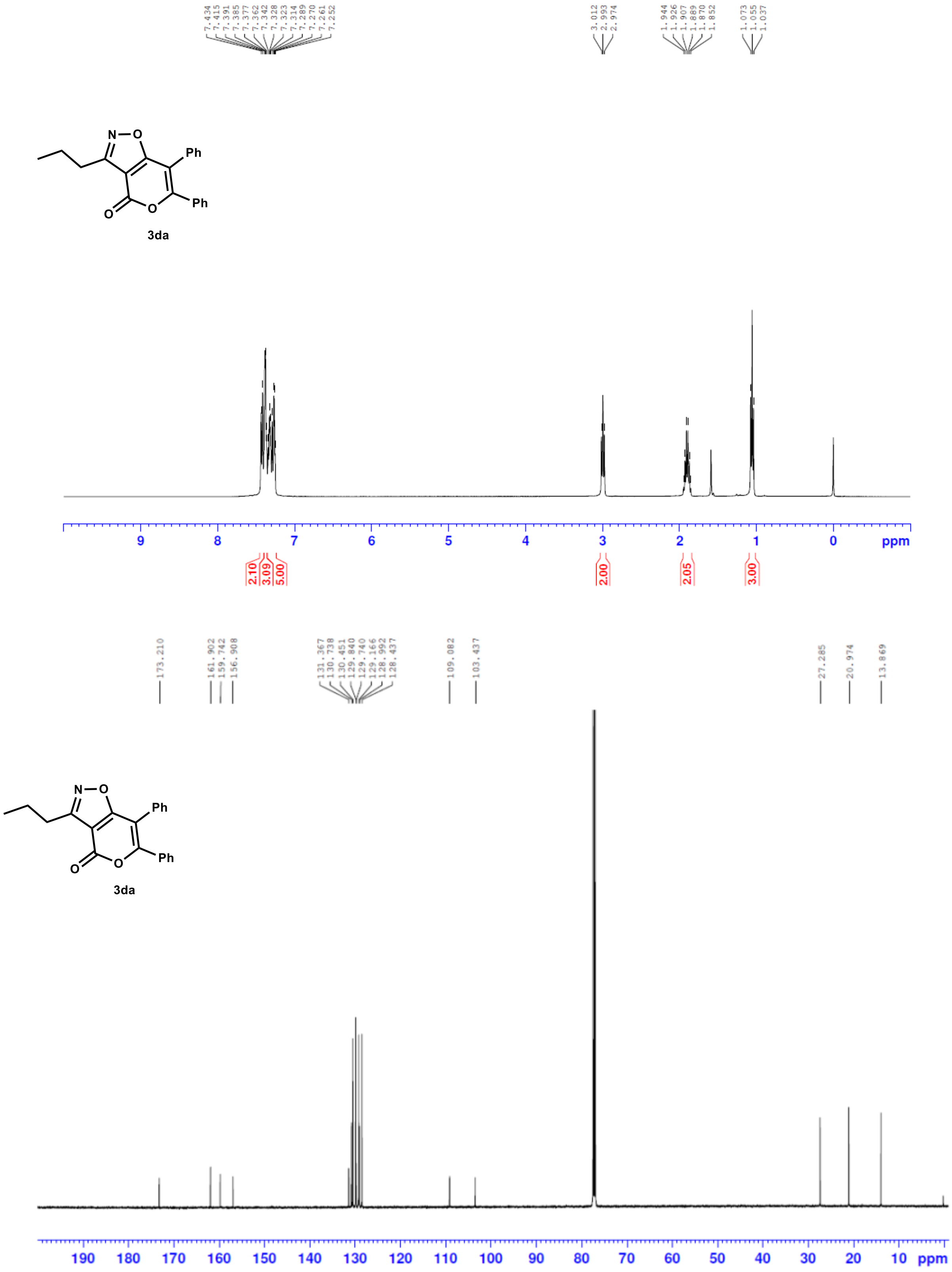
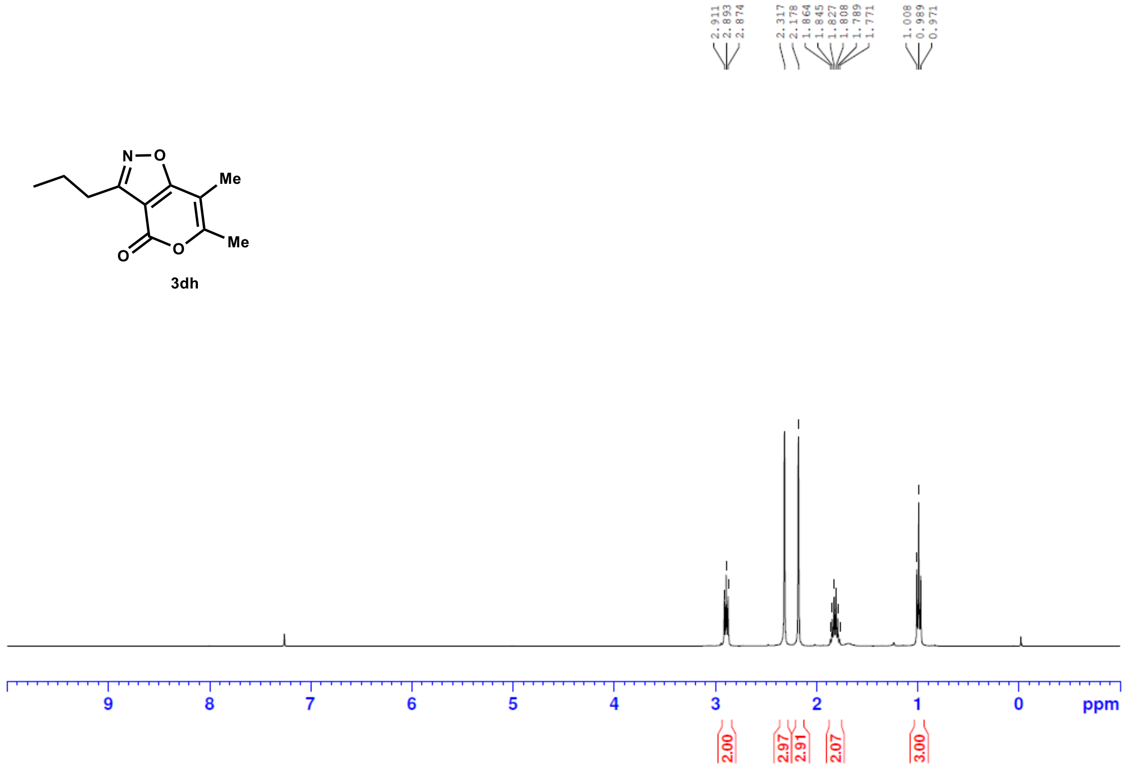
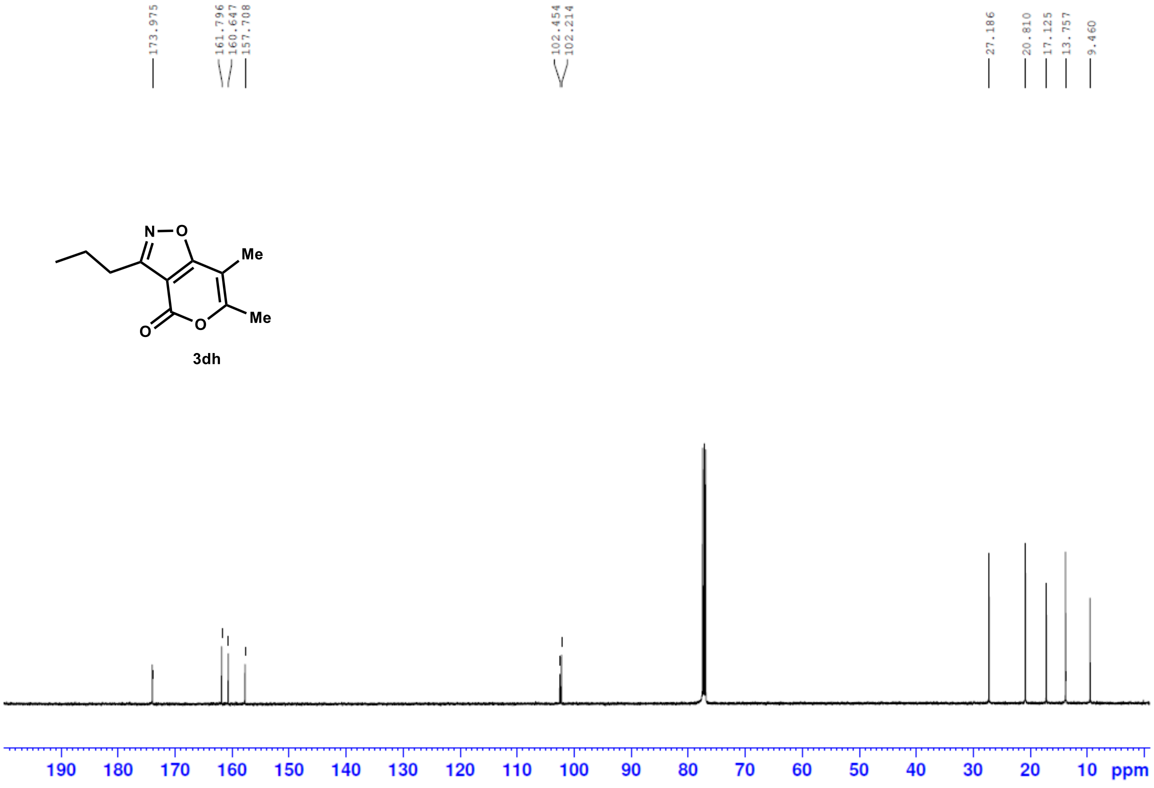


**Figure S28.** $^1$H and $^{13}$C NMR Spectra of compound **3da**



3dh



3dh

**Figure S29.** $^1$H and $^{13}$C NMR Spectra of compound **3dh**

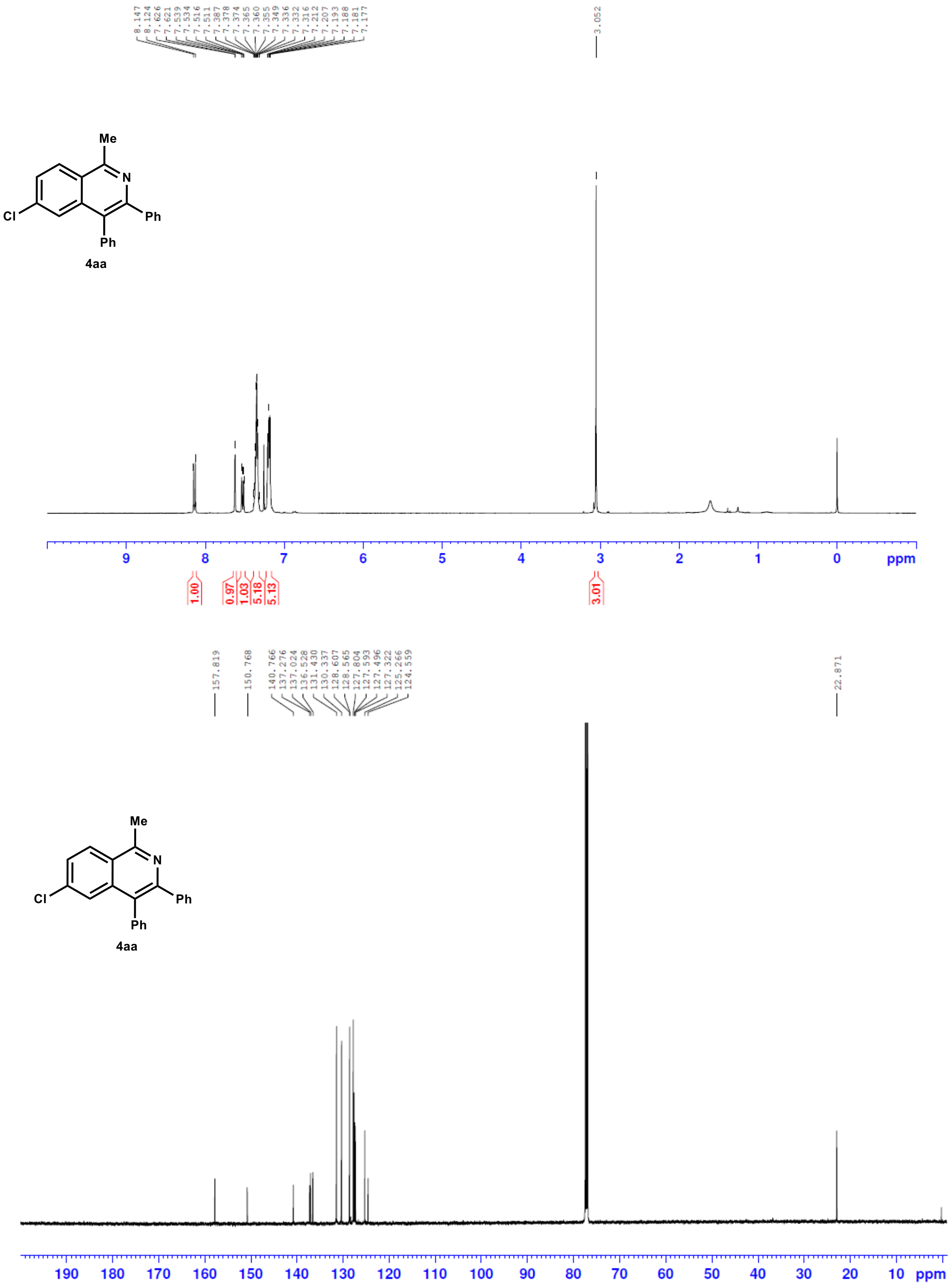
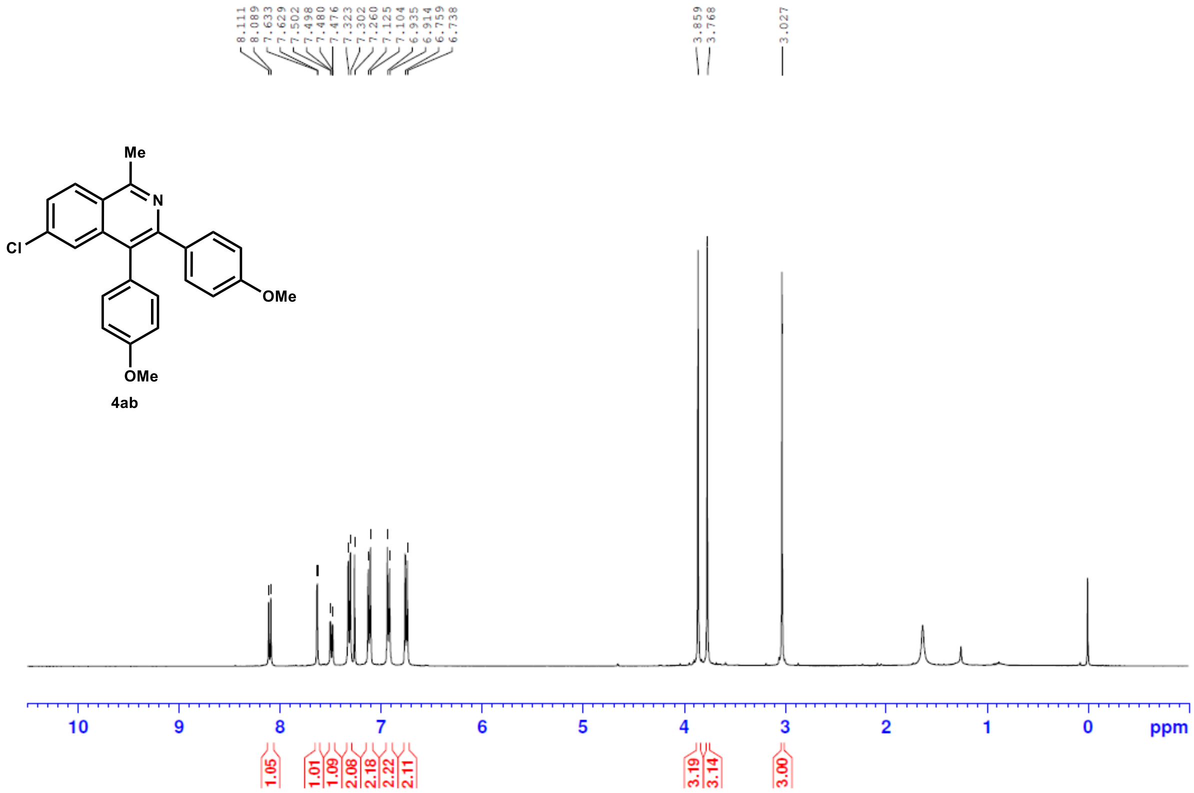


**Figure S30.** $^1$H and $^{13}$C NMR Spectra of compound **4aa**



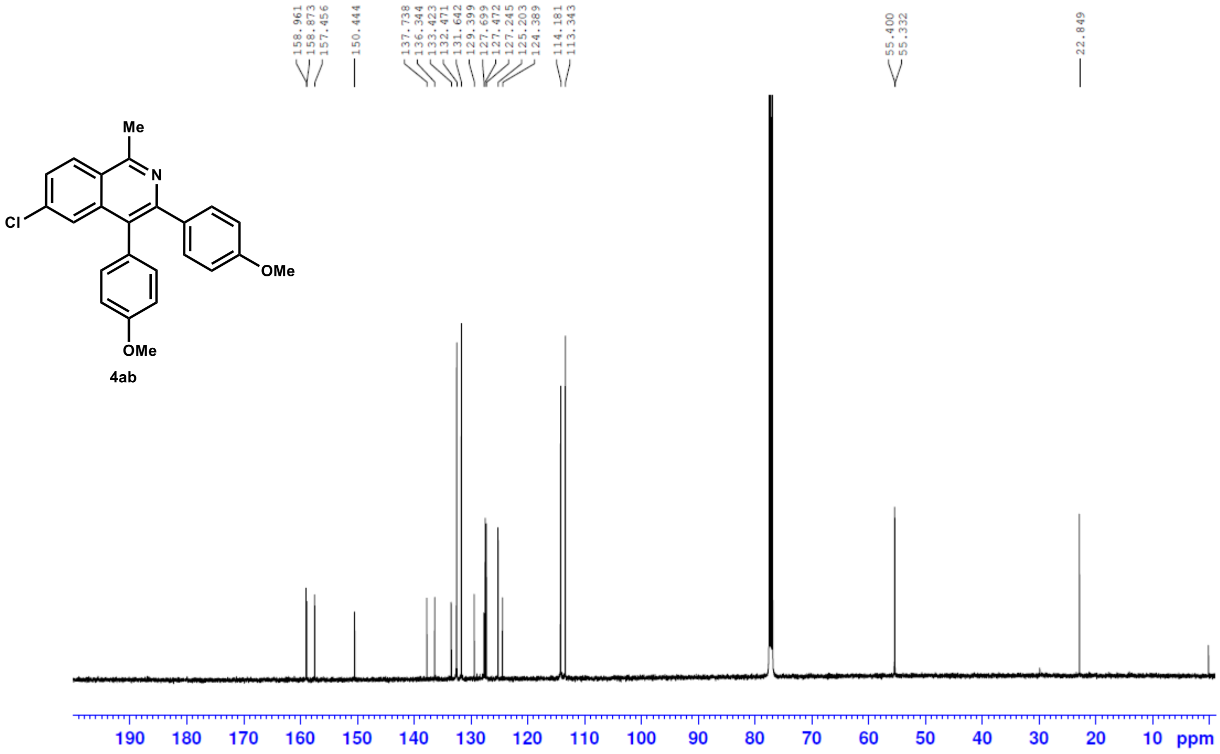


**Figure S31.** $^1$H and $^{13}$C NMR Spectra of compound **4ab**

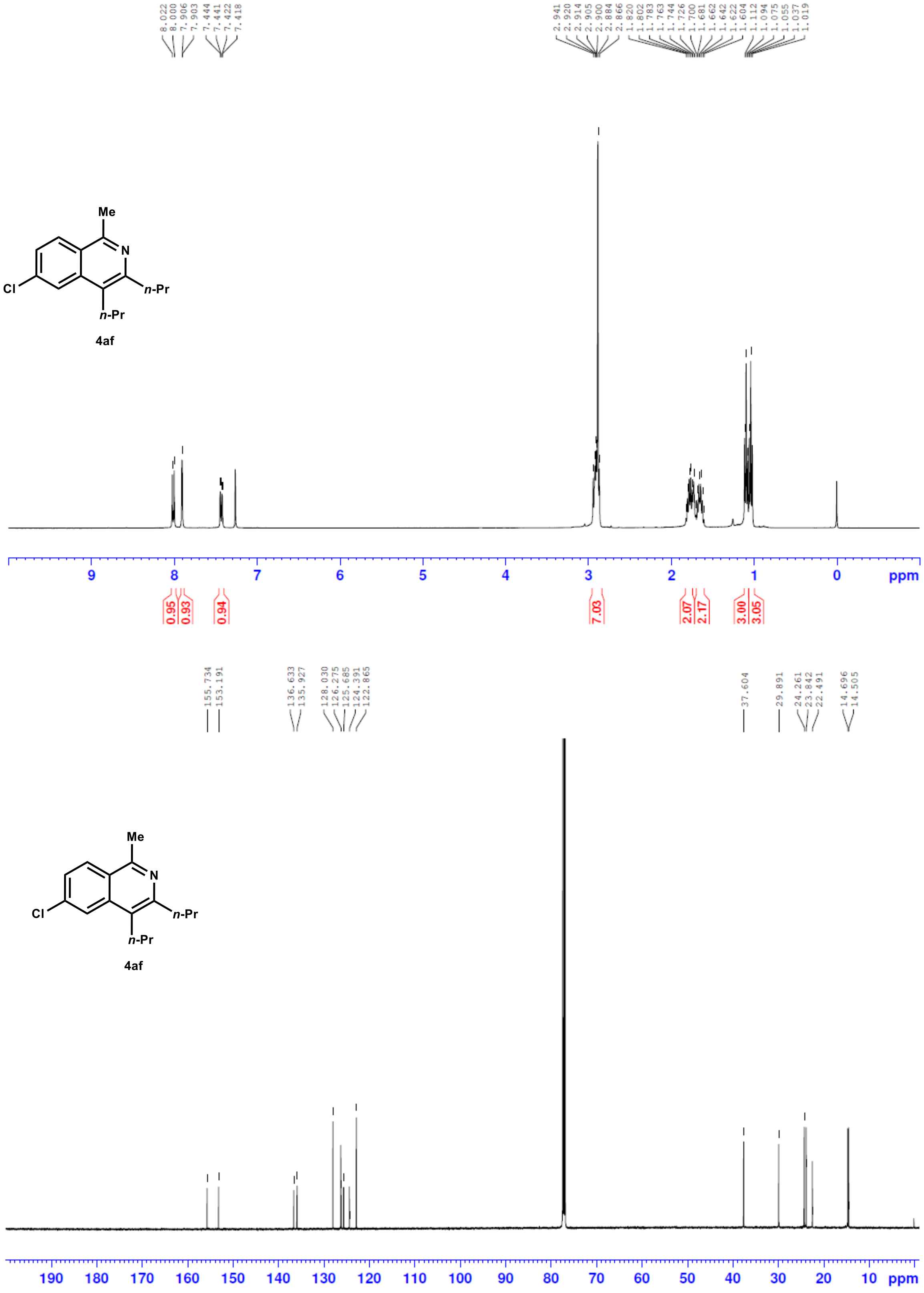


**Figure S32.** $^1$H and $^{13}$C NMR Spectra of compound **4af**

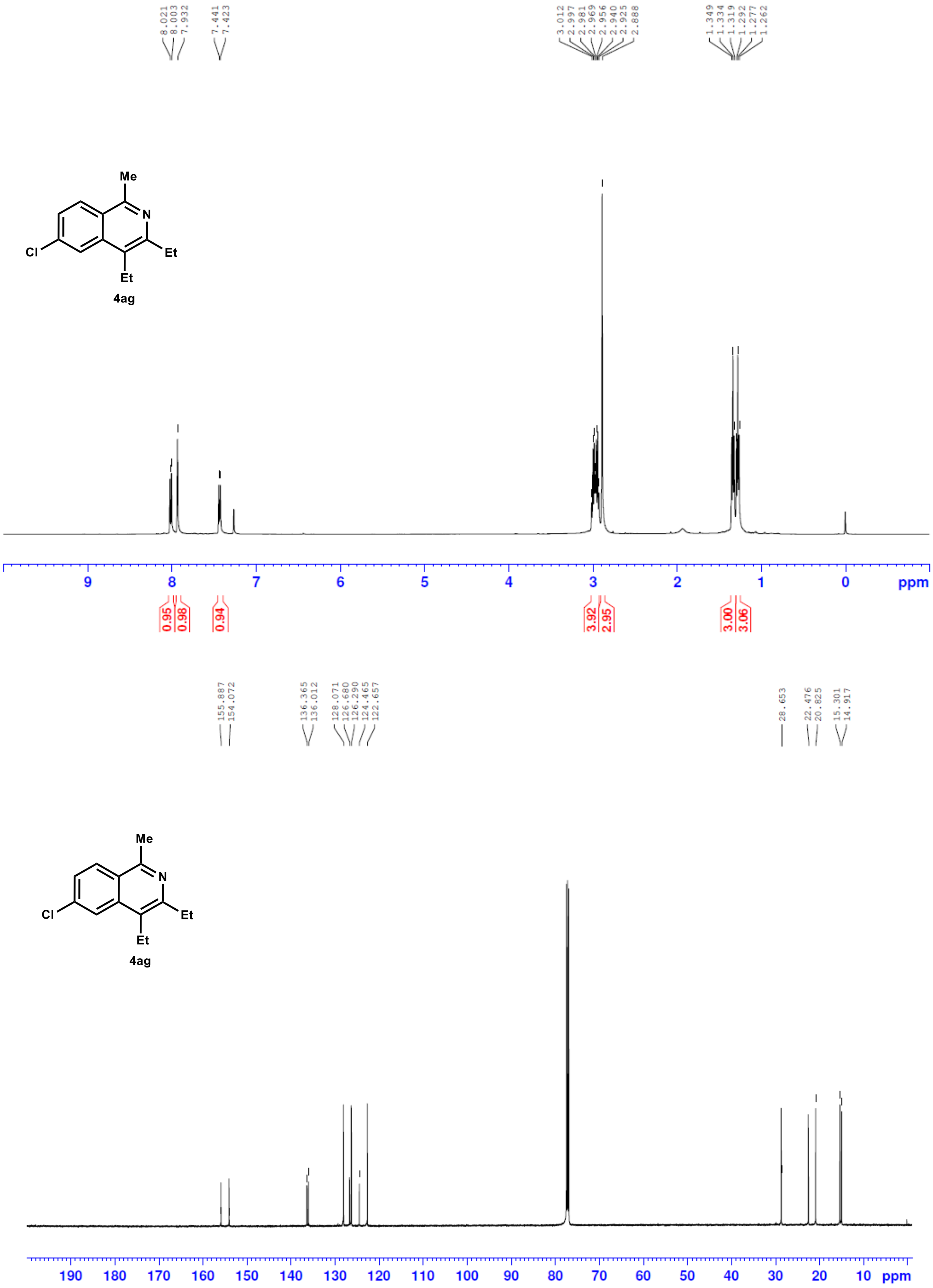


**Figure S33.** $^1$H and $^{13}$C NMR Spectra of compound **4ag**

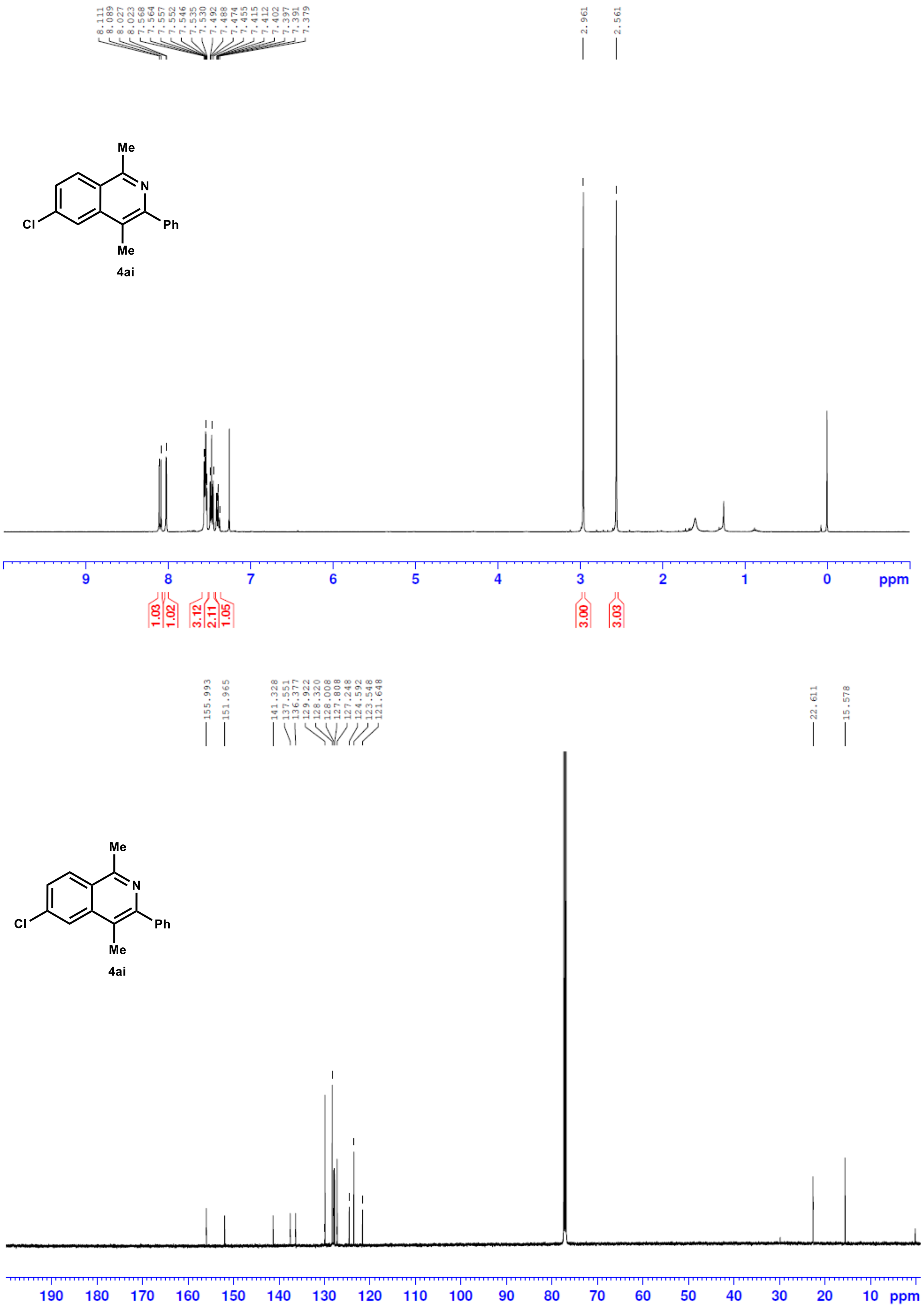
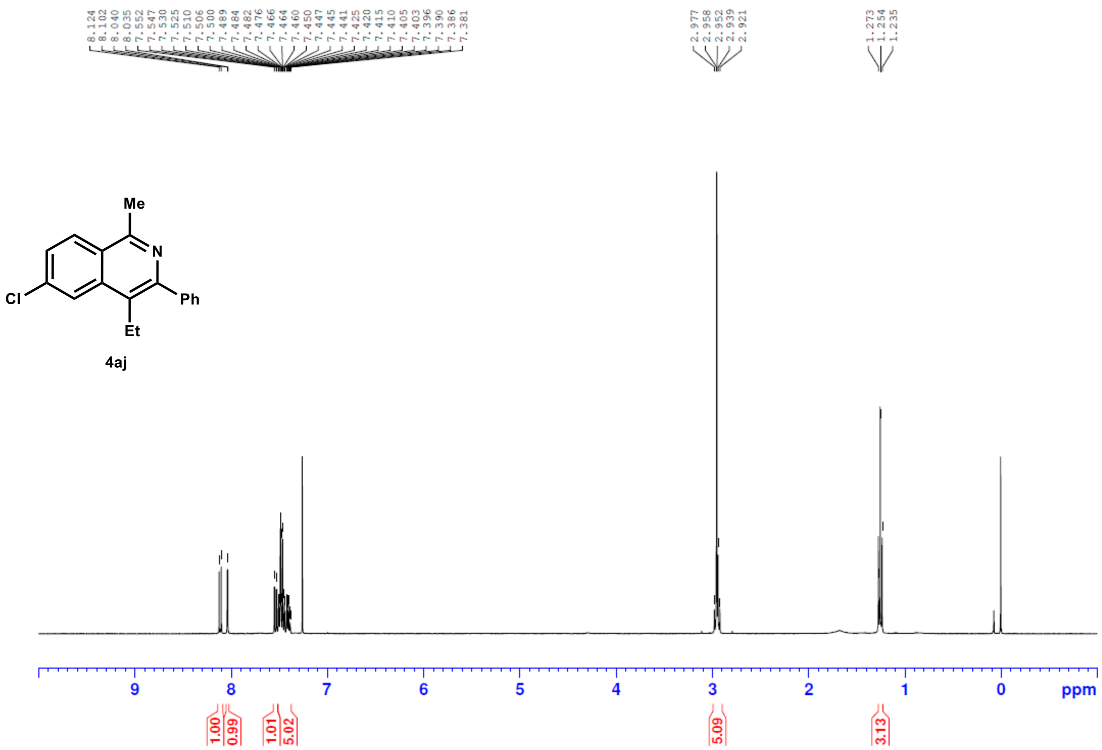


**Figure S34.** $^{1}$H and $^{13}$C NMR Spectra of compound **4ai**



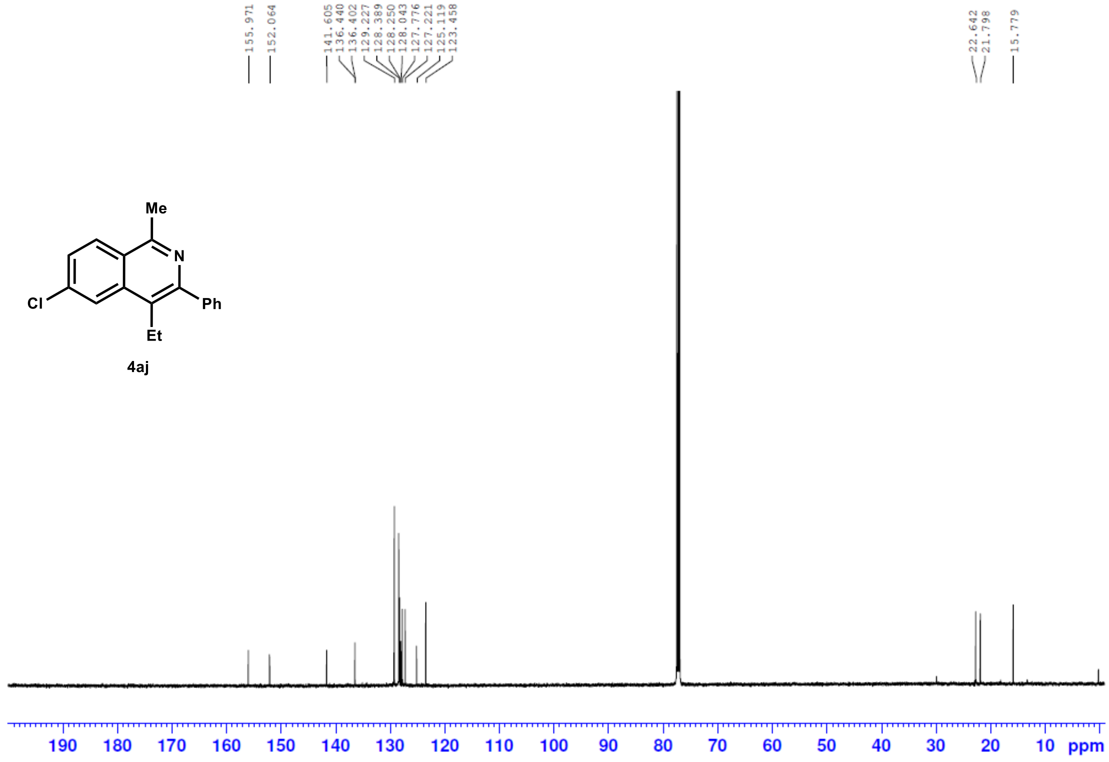


**Figure S35.** $^{1}$H and $^{13}$C NMR Spectra of compound **4aj**

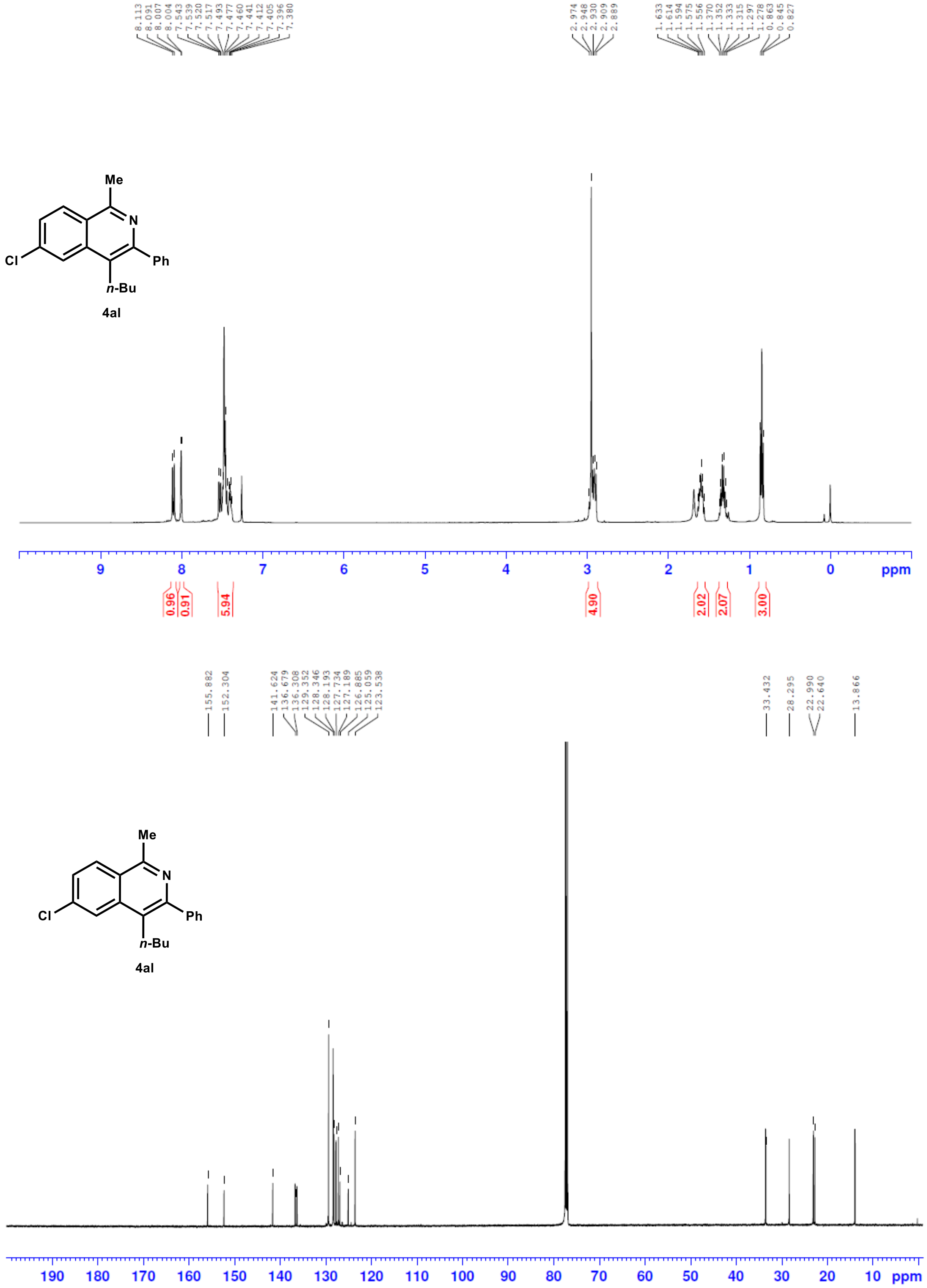


**Figure S36.** $^{1}H$ and $^{13}C$ NMR Spectra of compound **4al**

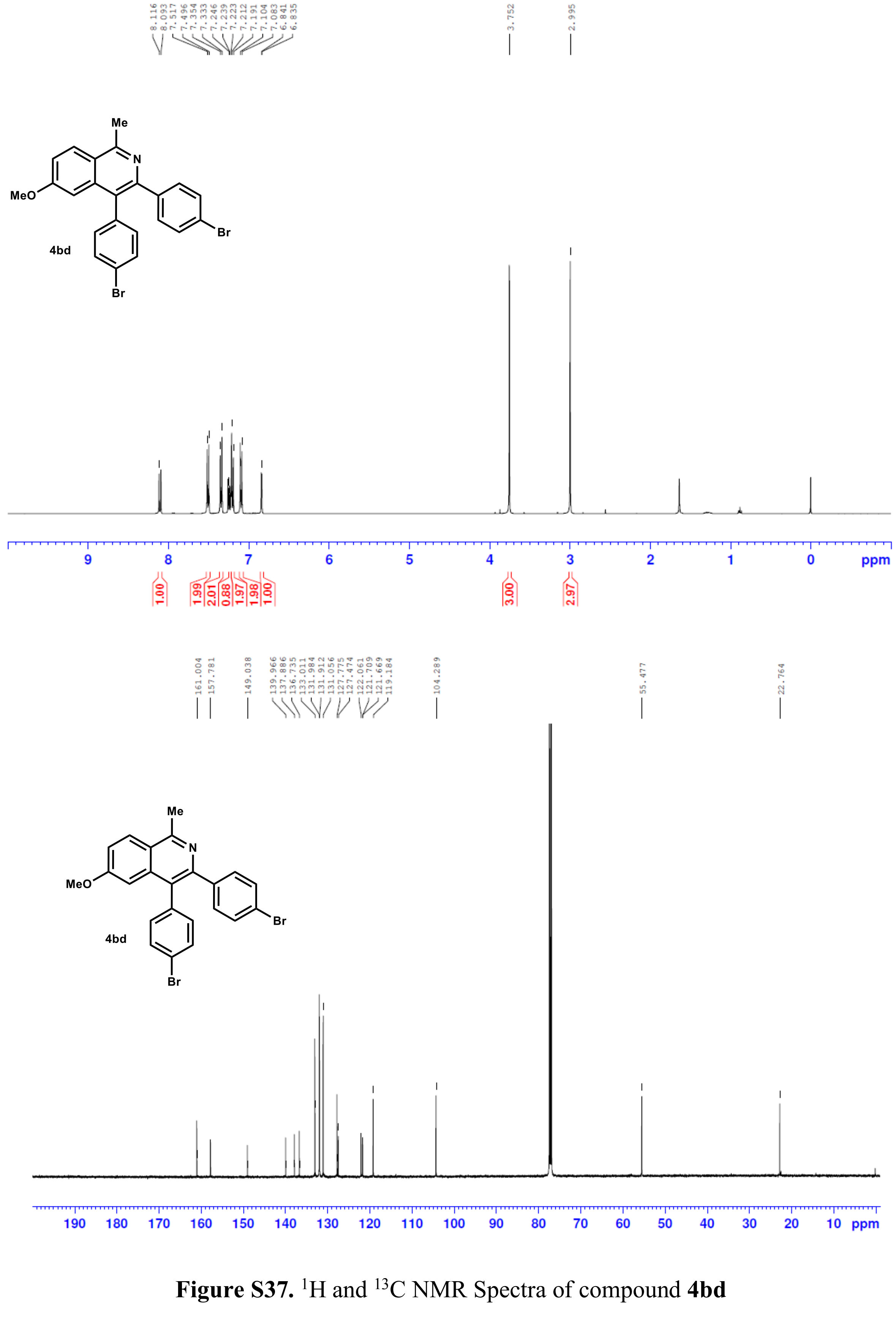


**Figure S37.** $^1$H and $^{13}$C NMR Spectra of compound **4bd**

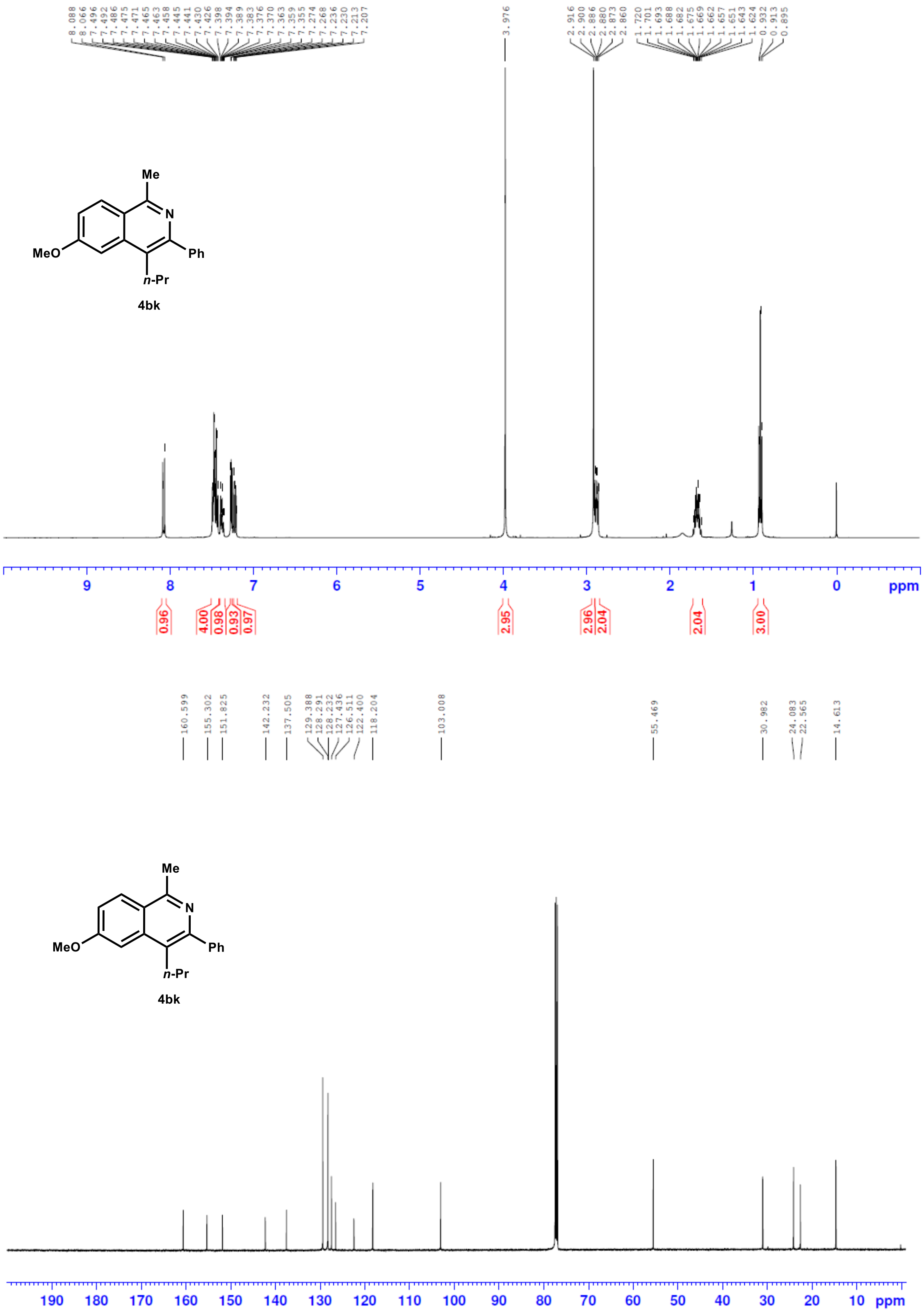


**Figure S38.** $^{1}$H and $^{13}$C NMR Spectra of compound **4bk**

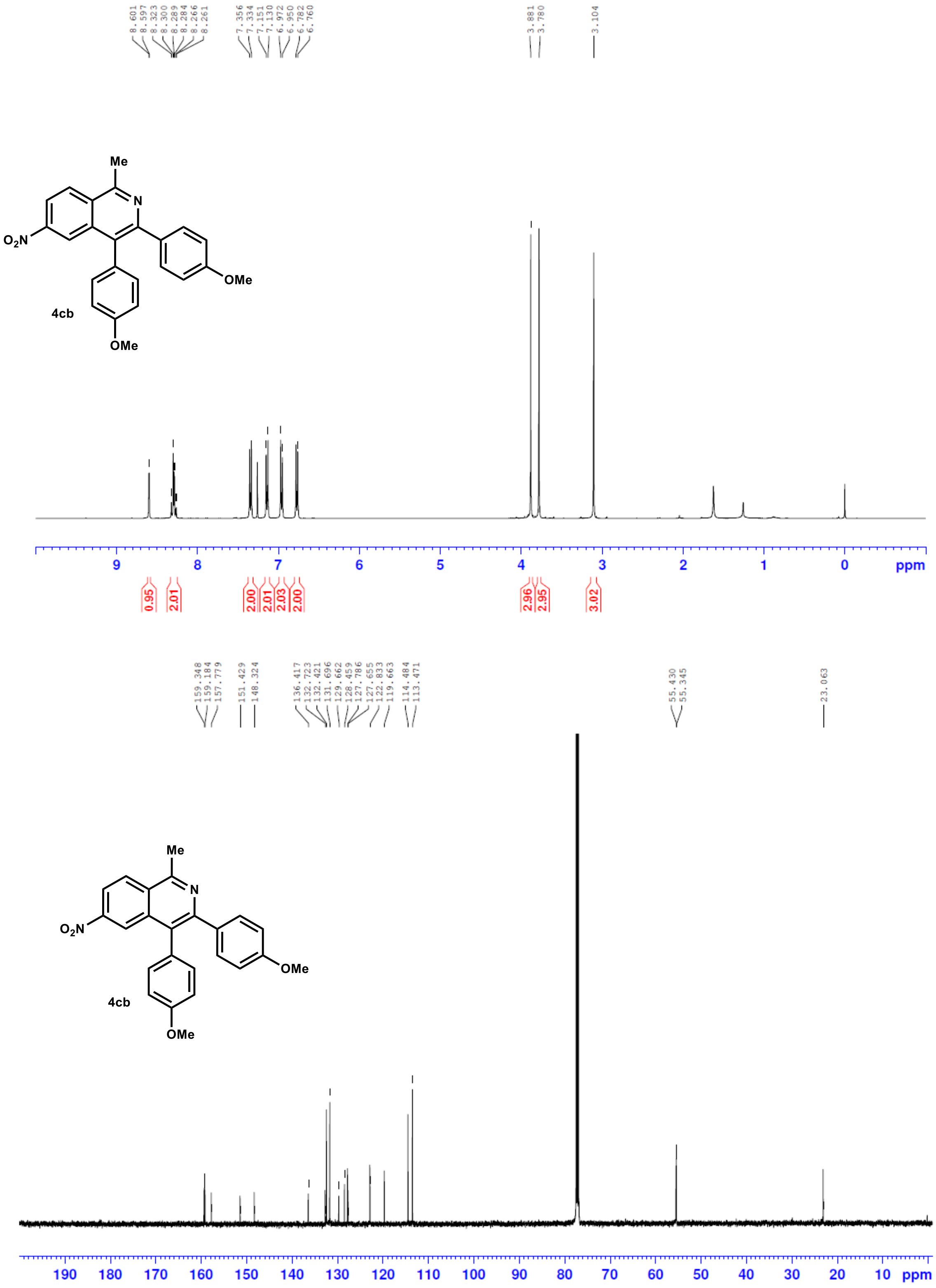


**Figure S39.** $^1$H and $^{13}$C NMR Spectra of compound **4cb**

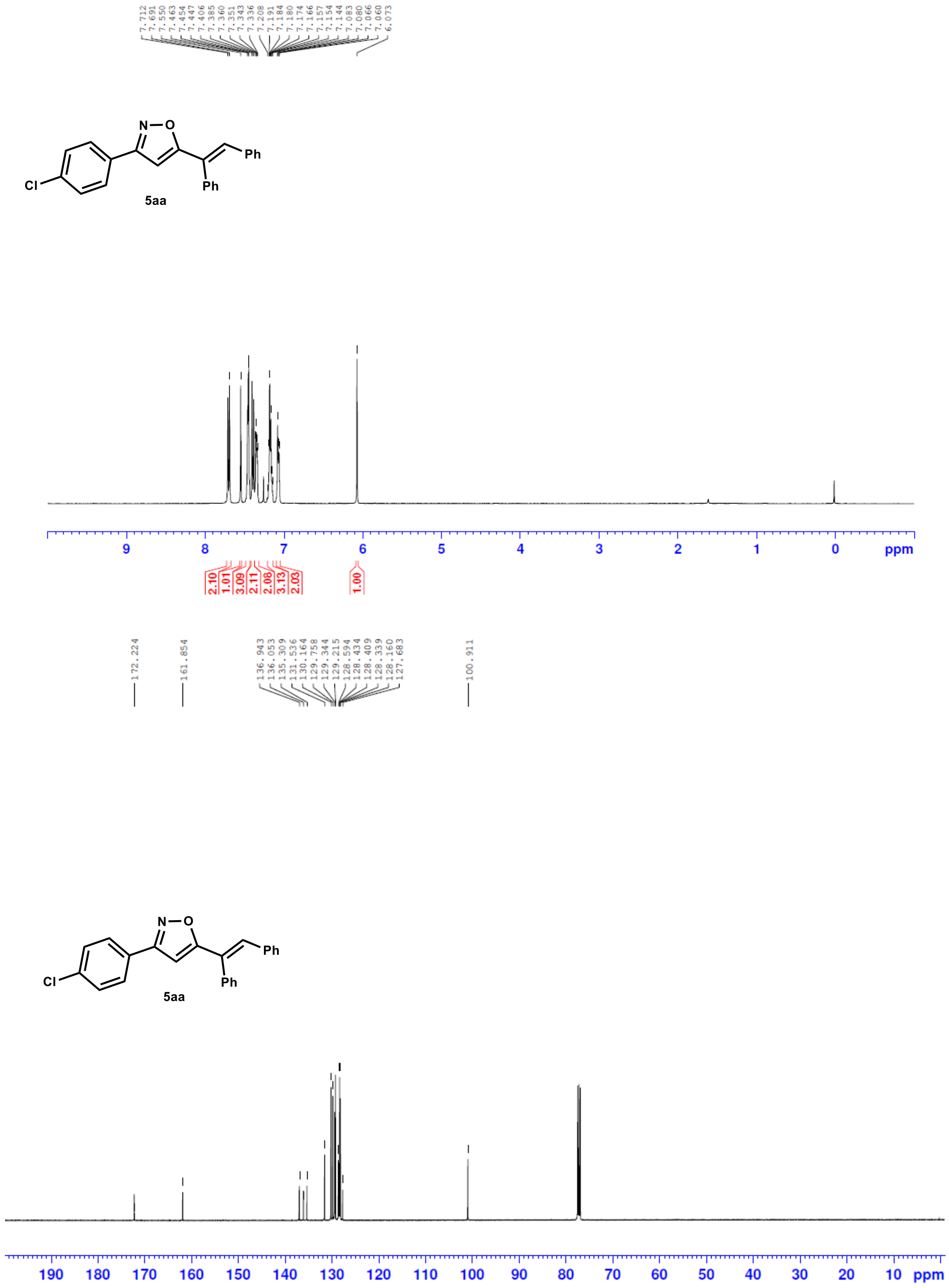


**Figure S40.** $^1$H and $^{13}$C NMR Spectra of compound **5aa**

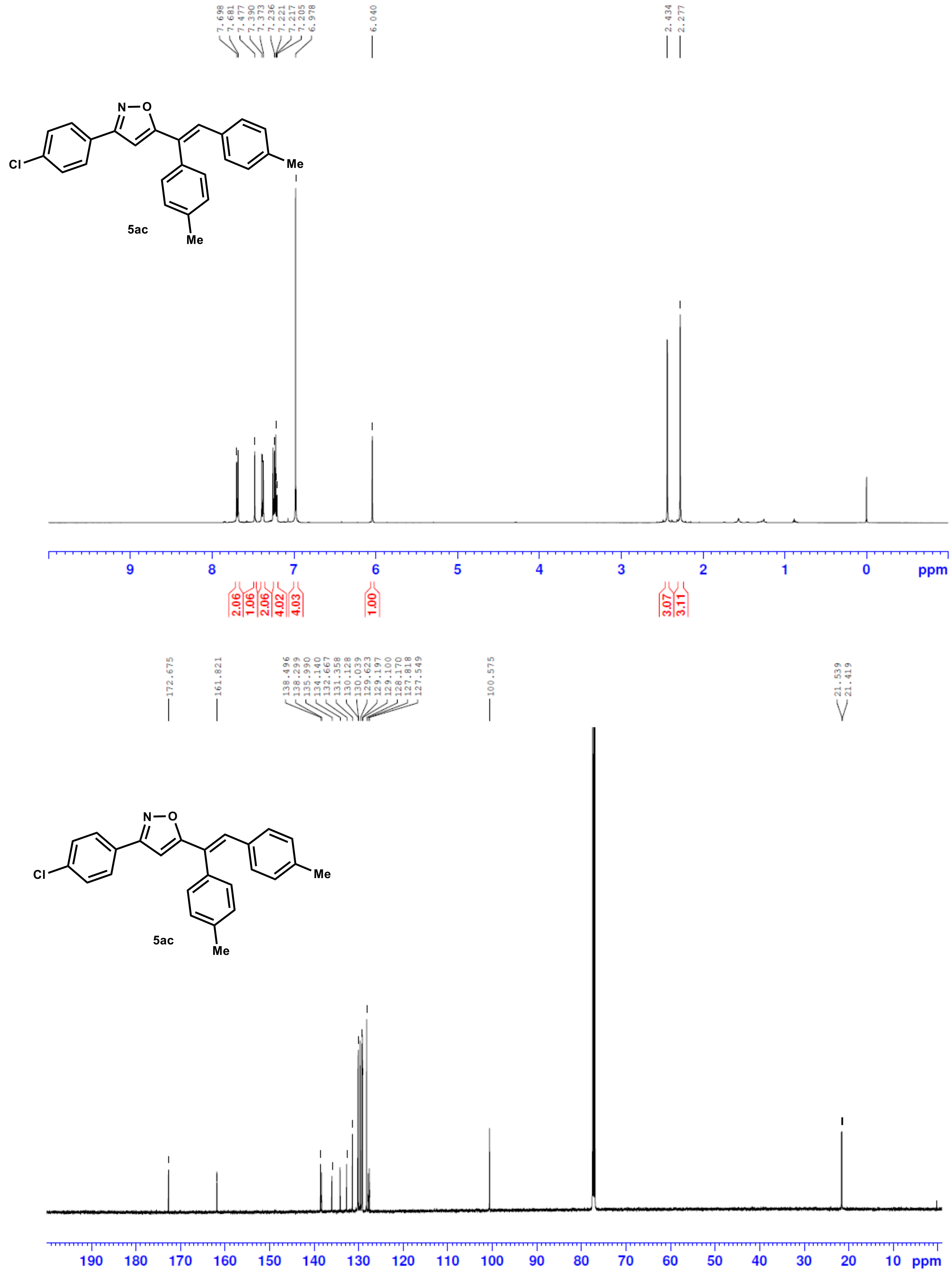


**Figure S41.** $^{1}$H and $^{13}$C NMR Spectra of compound **5ac**

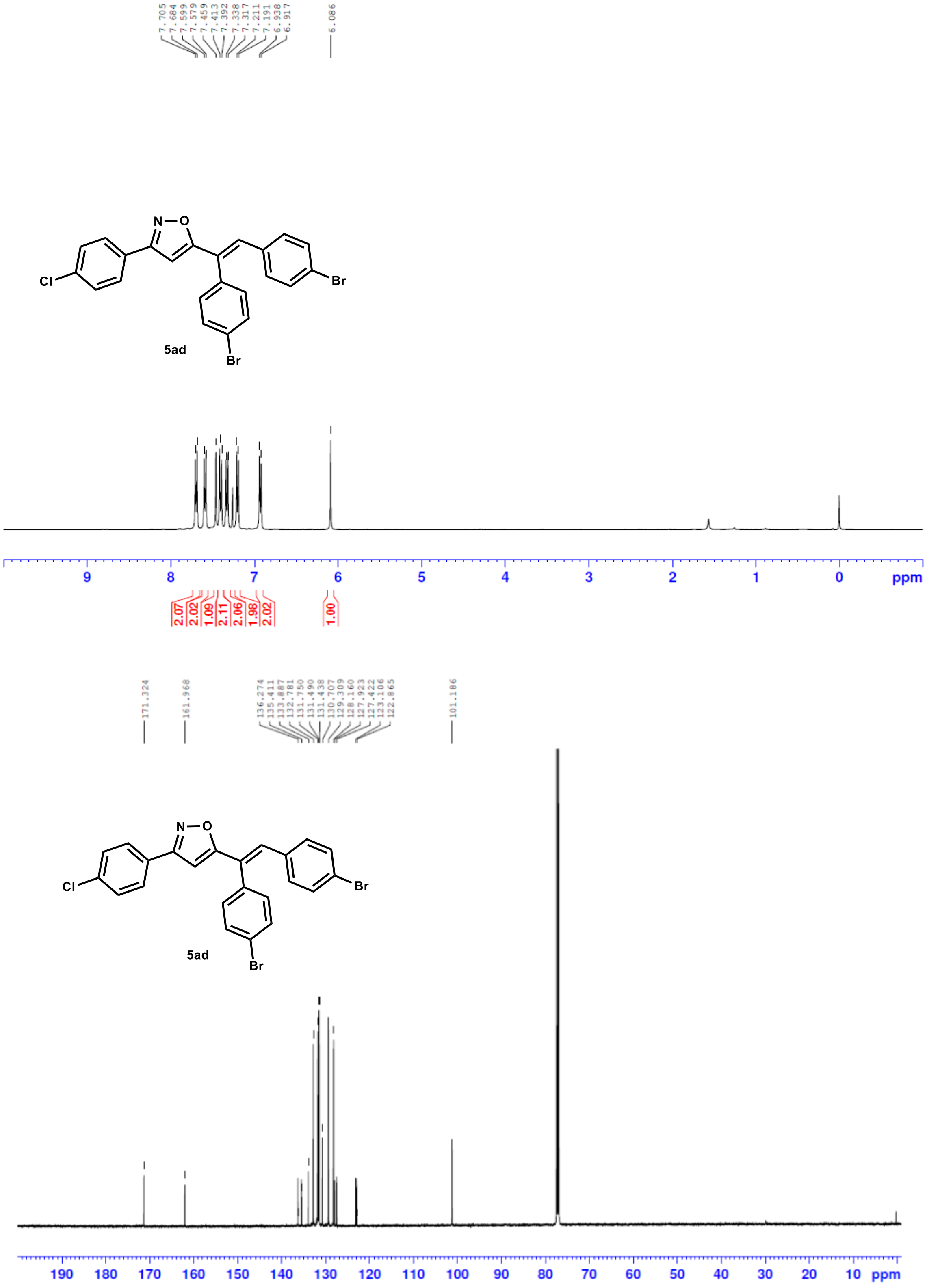


**Figure S42.** $^1$H and $^{13}$C NMR Spectra of compound **5ad**

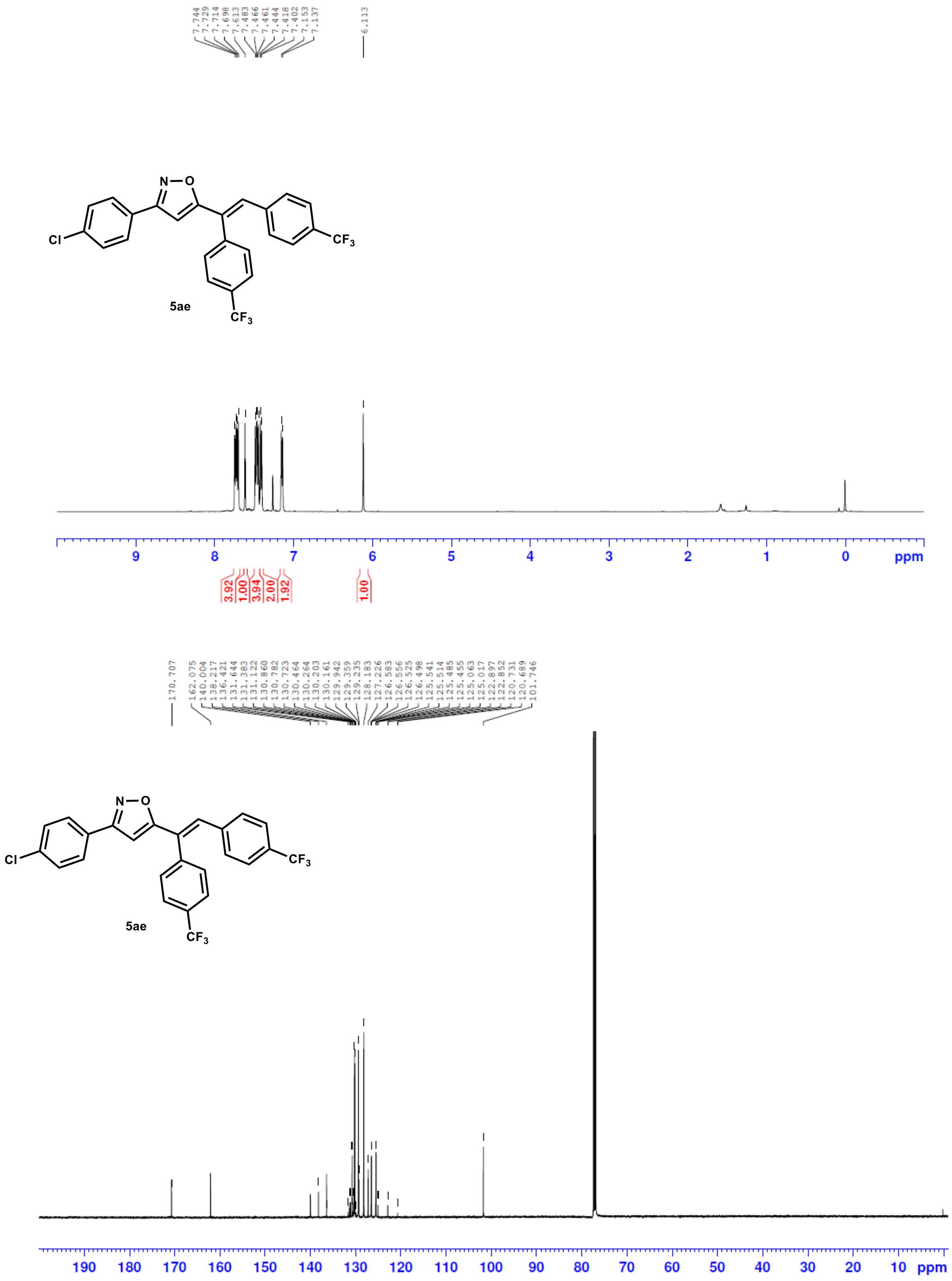
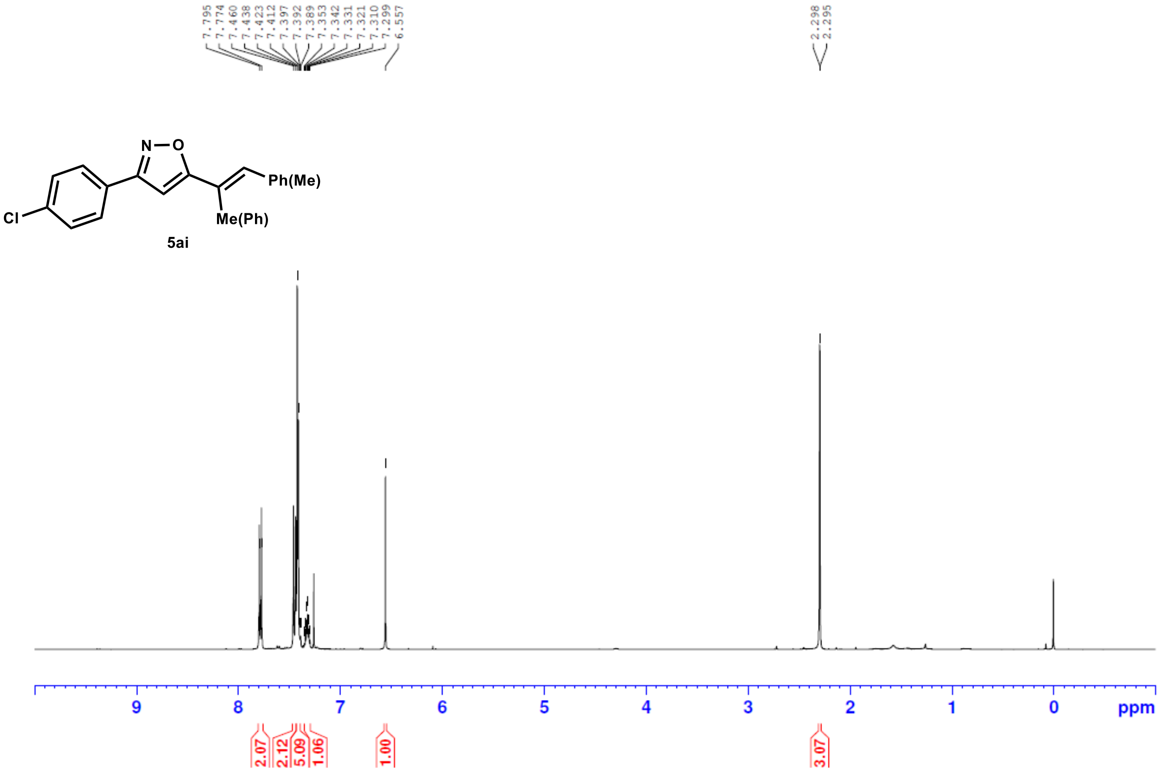


**Figure S43.** $^1$H and $^{13}$C NMR Spectra of compound **5ae**



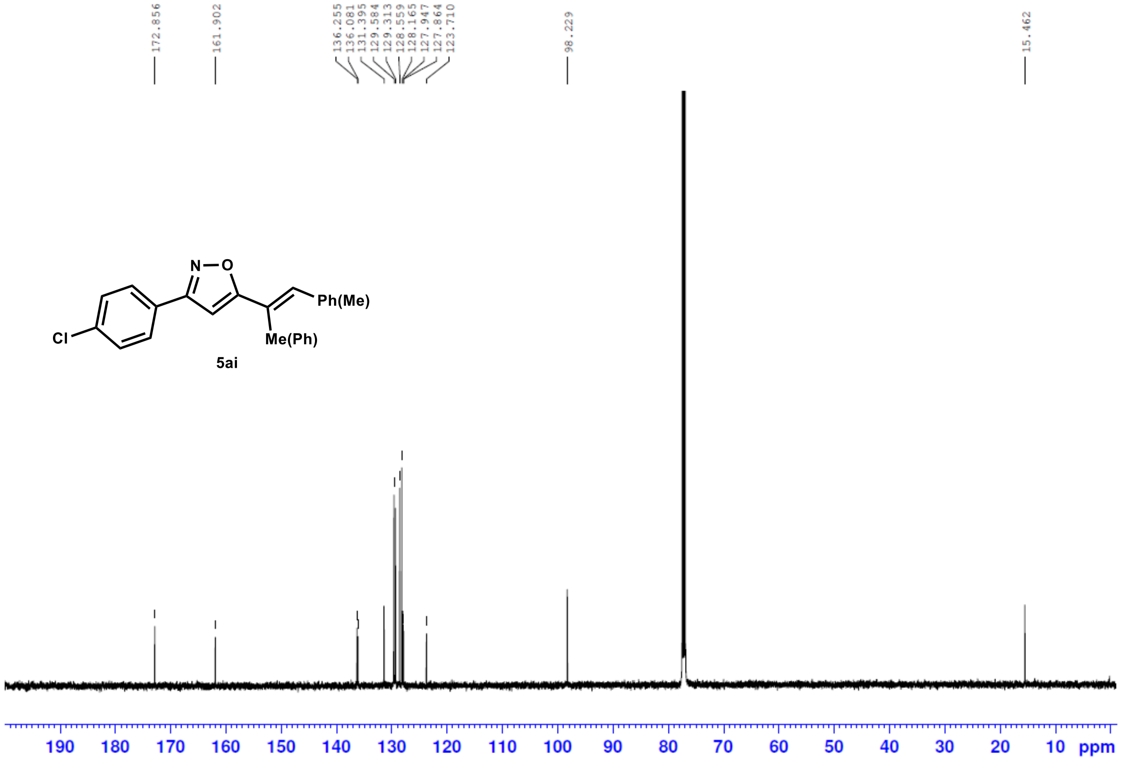


**Figure S44.** $^{1}H$ and $^{13}C$ NMR Spectra of compound **5ai**

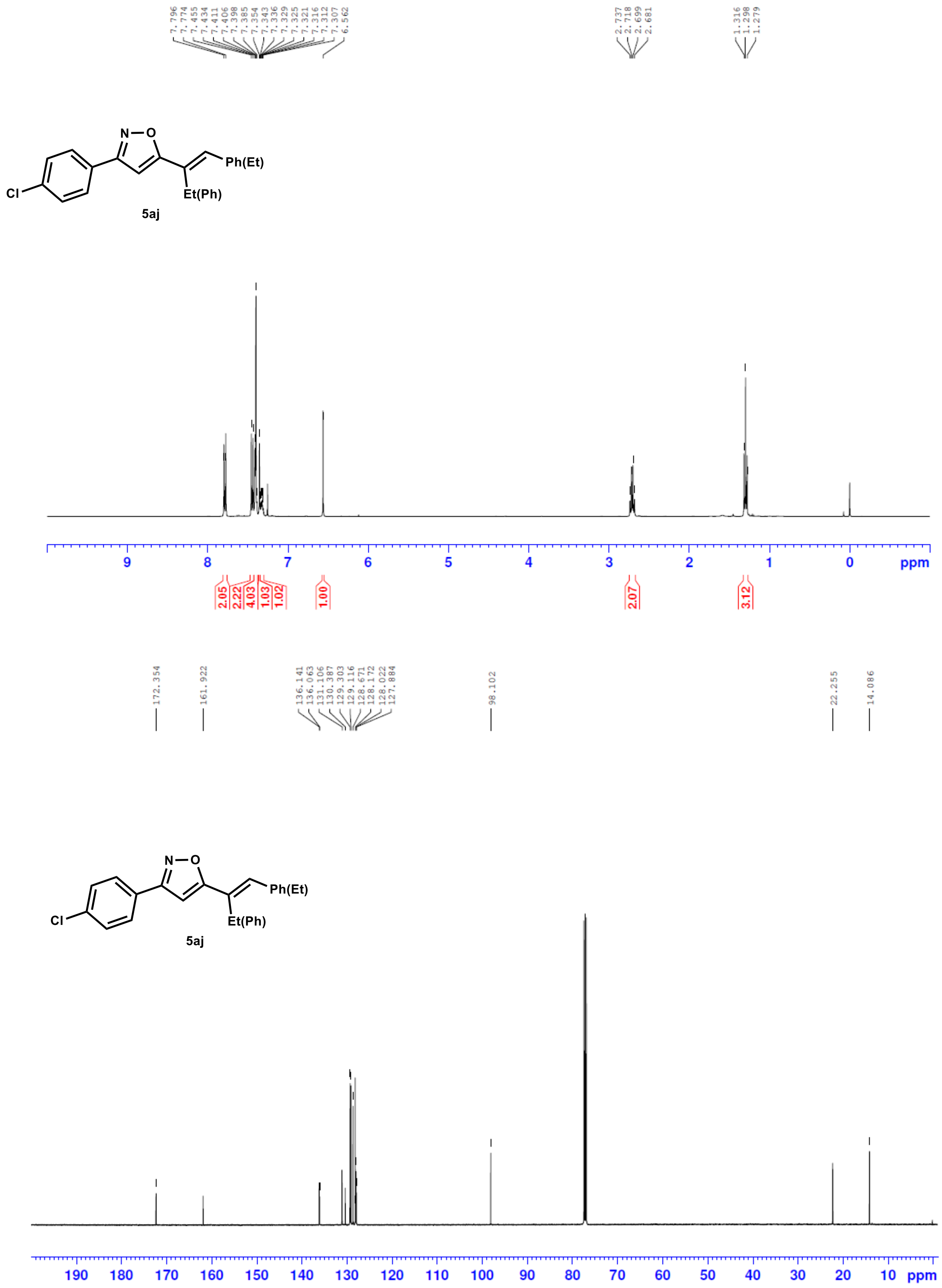


**Figure S45.** $^1$H and $^{13}$C NMR Spectra of compound **5aj**

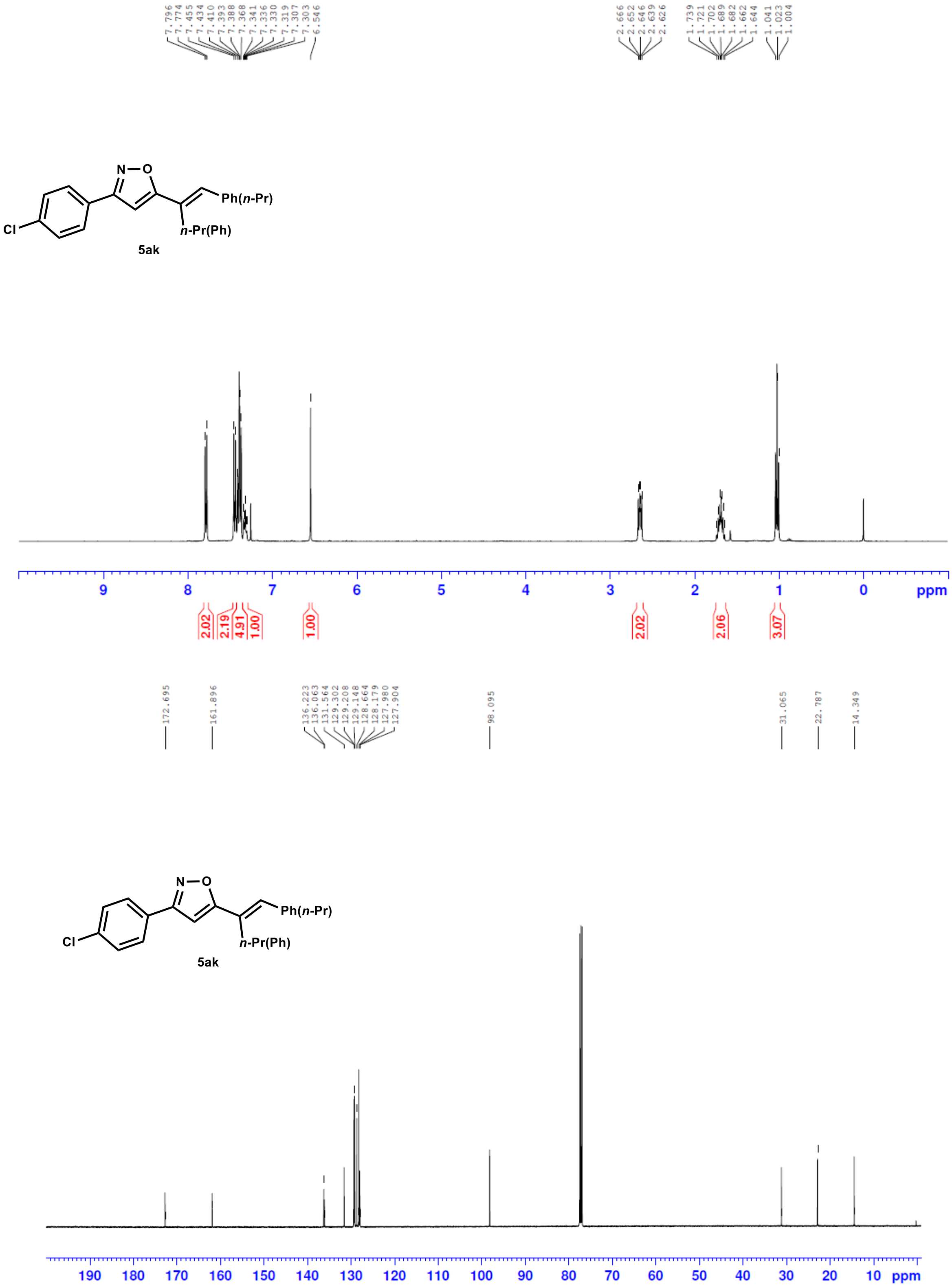


**Figure S46.** $^1$H and $^{13}$C NMR Spectra of compound **5ak**

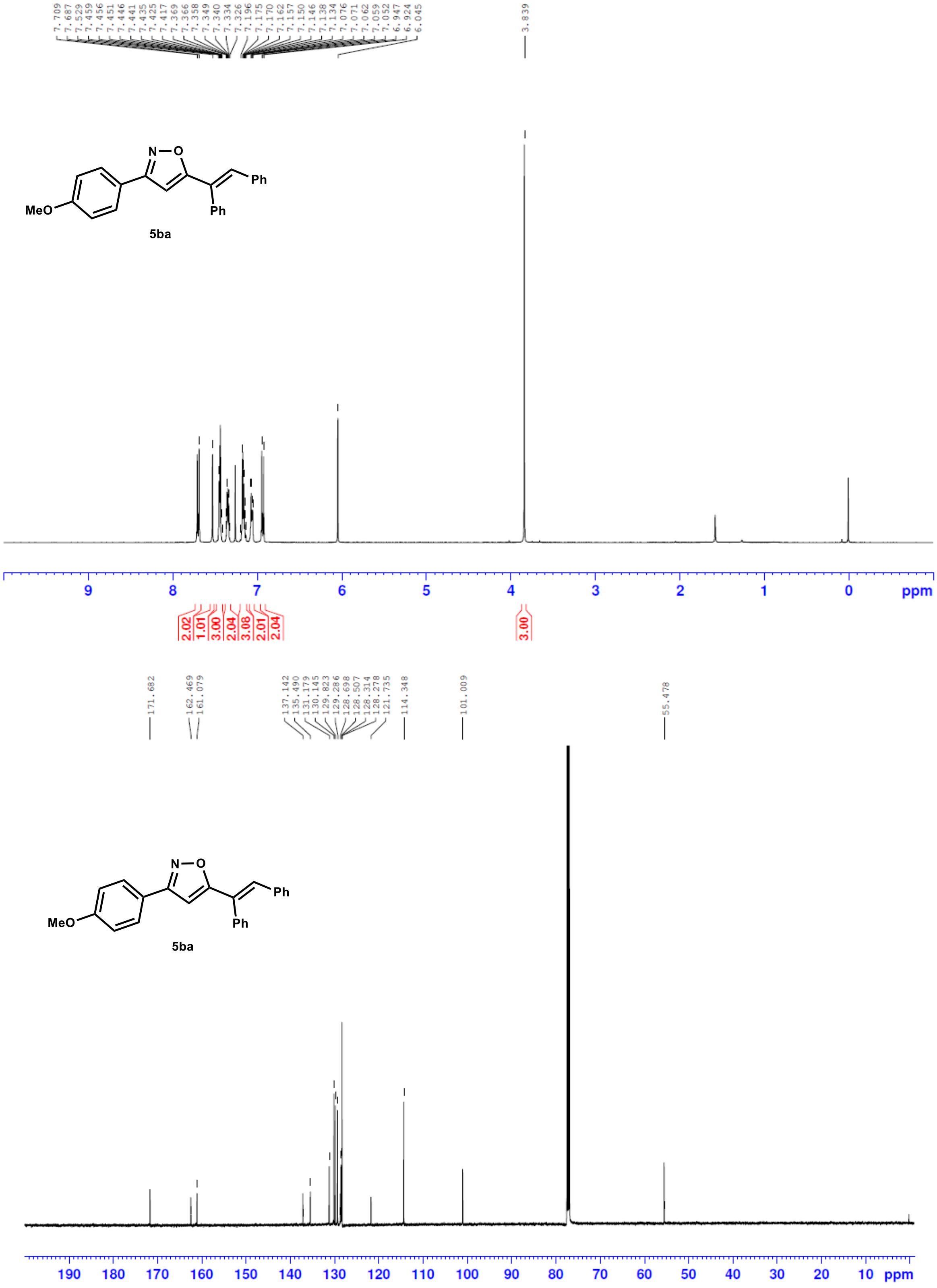


**Figure S47.** $^{1}H$ and $^{13}C$ NMR Spectra of compound **5ba**

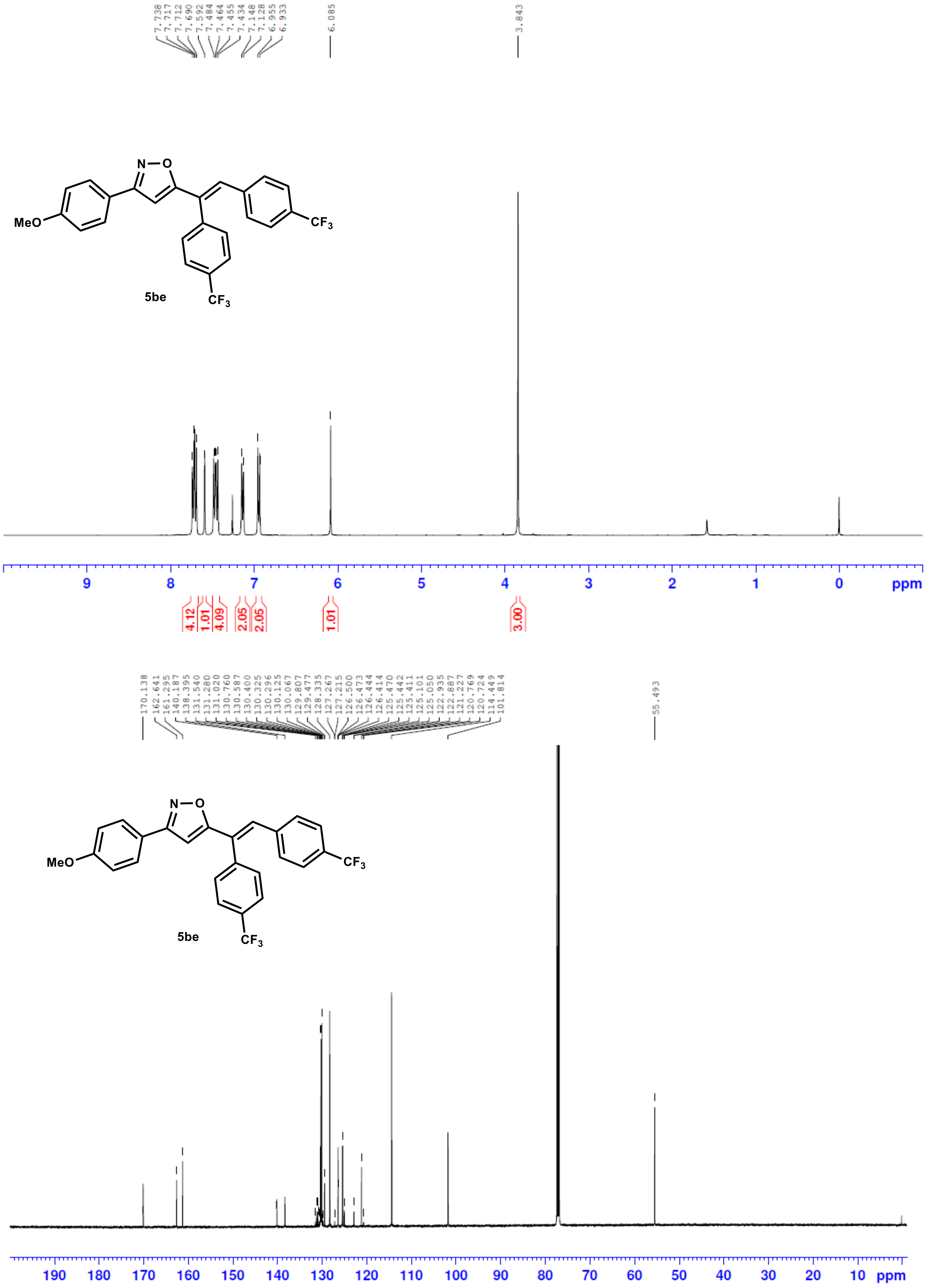


**Figure S48.** $^1$H and $^{13}$C NMR Spectra of compound **5be**

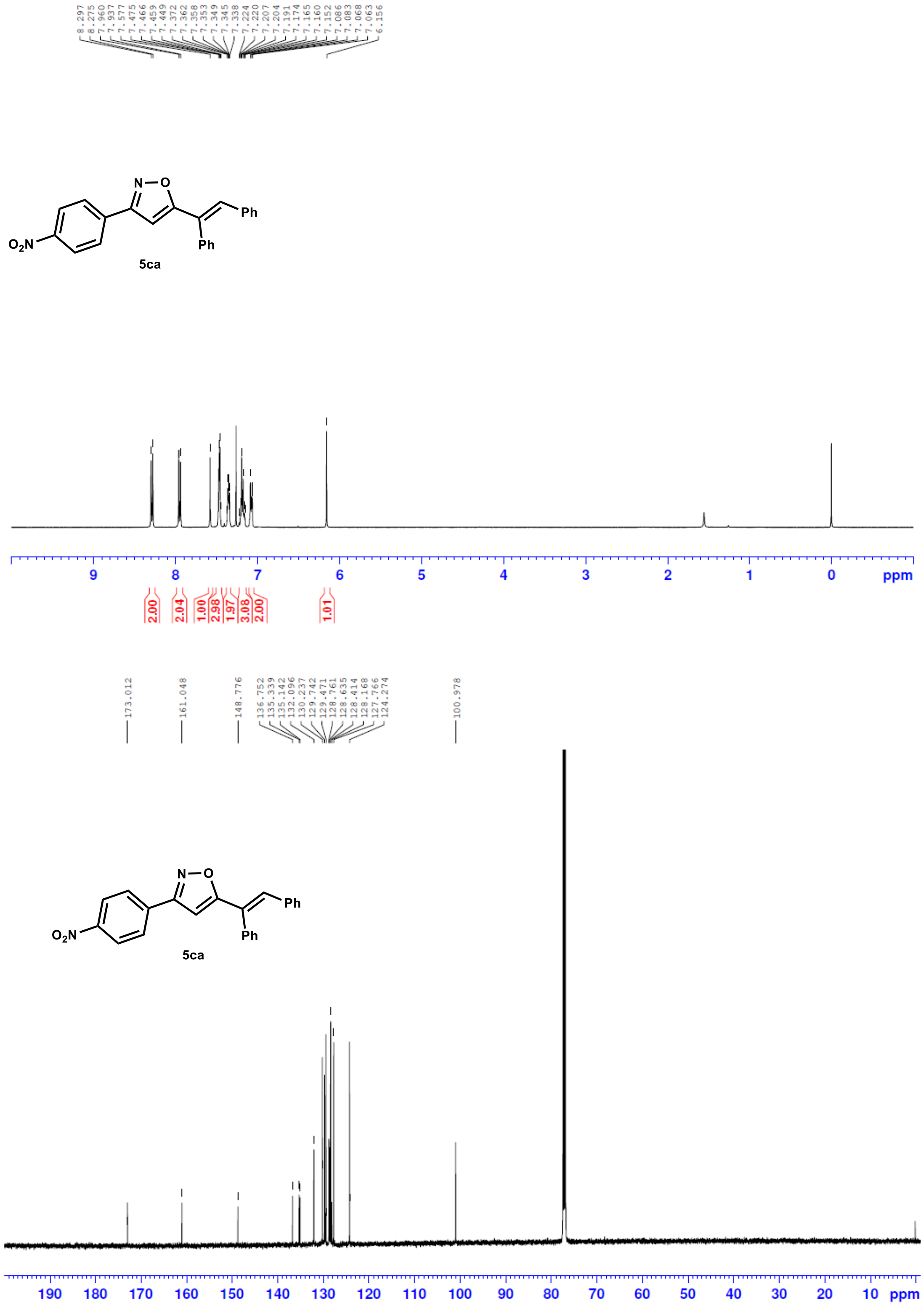


**Figure S49.** $^1$H and $^{13}$C NMR Spectra of compound **5ca**

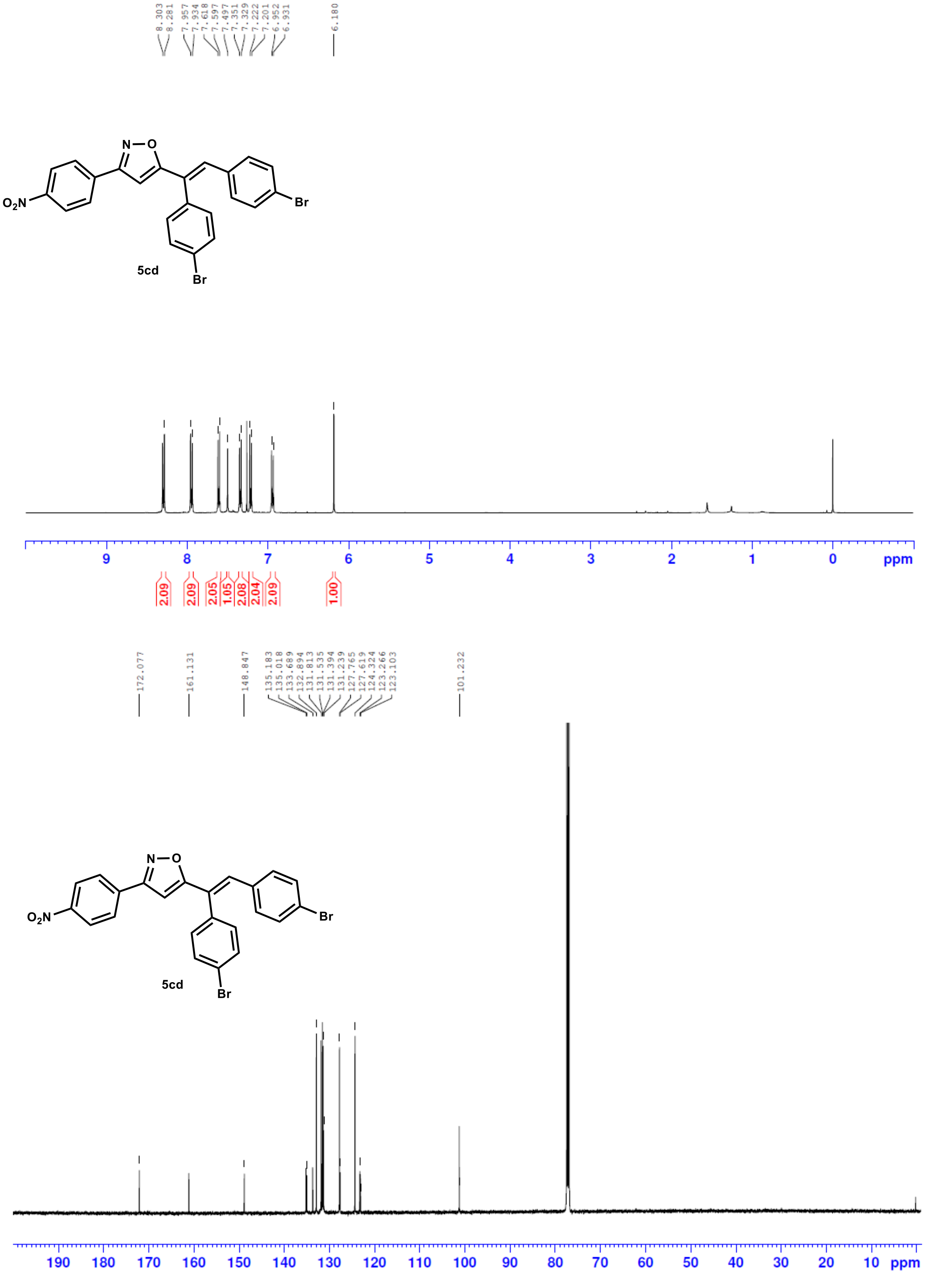


**Figure S50.** $^1$H and $^{13}$C NMR Spectra of compound **5cd**

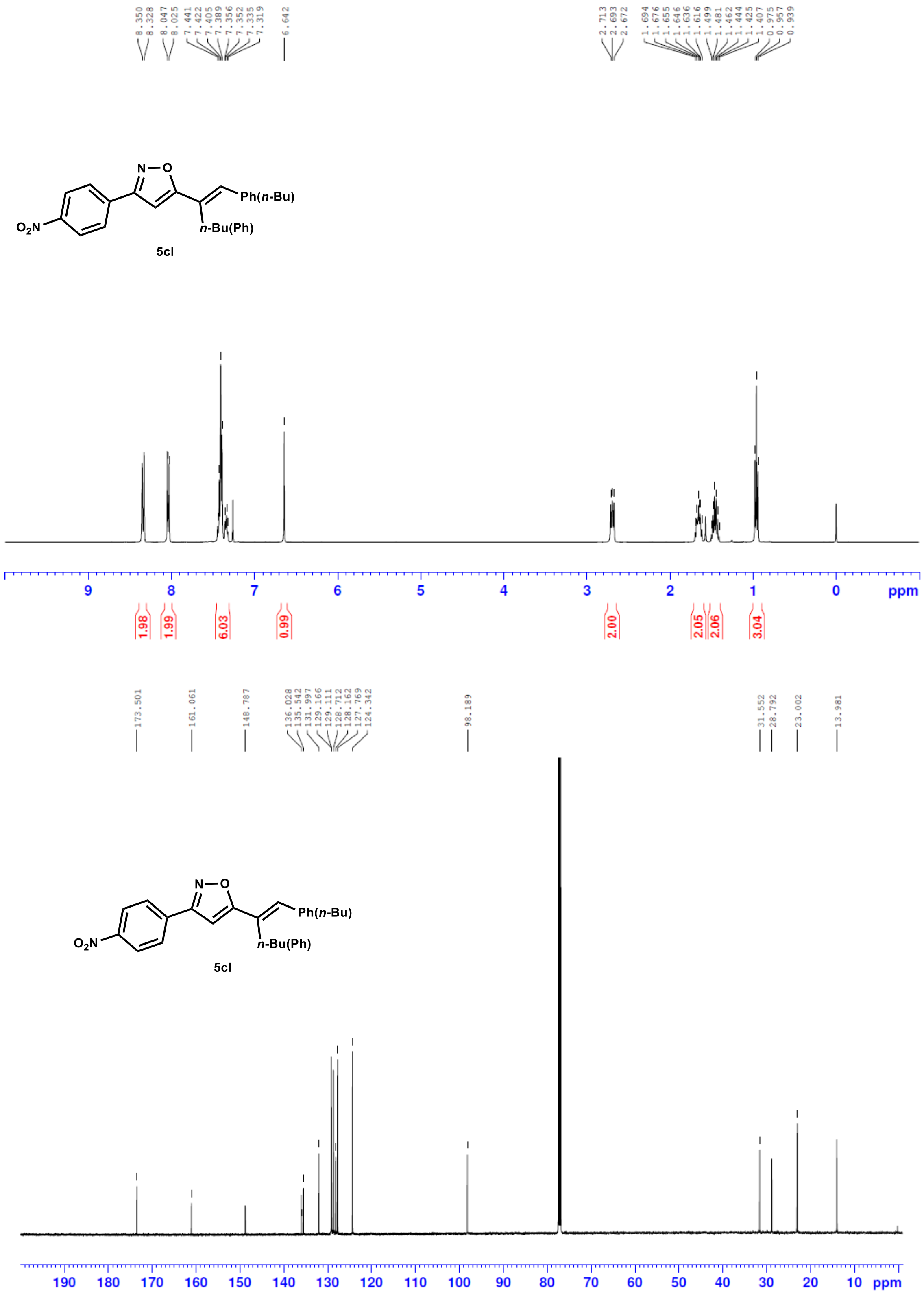


**Figure S51.** $^1$H and $^{13}$C NMR Spectra of compound **5cl**

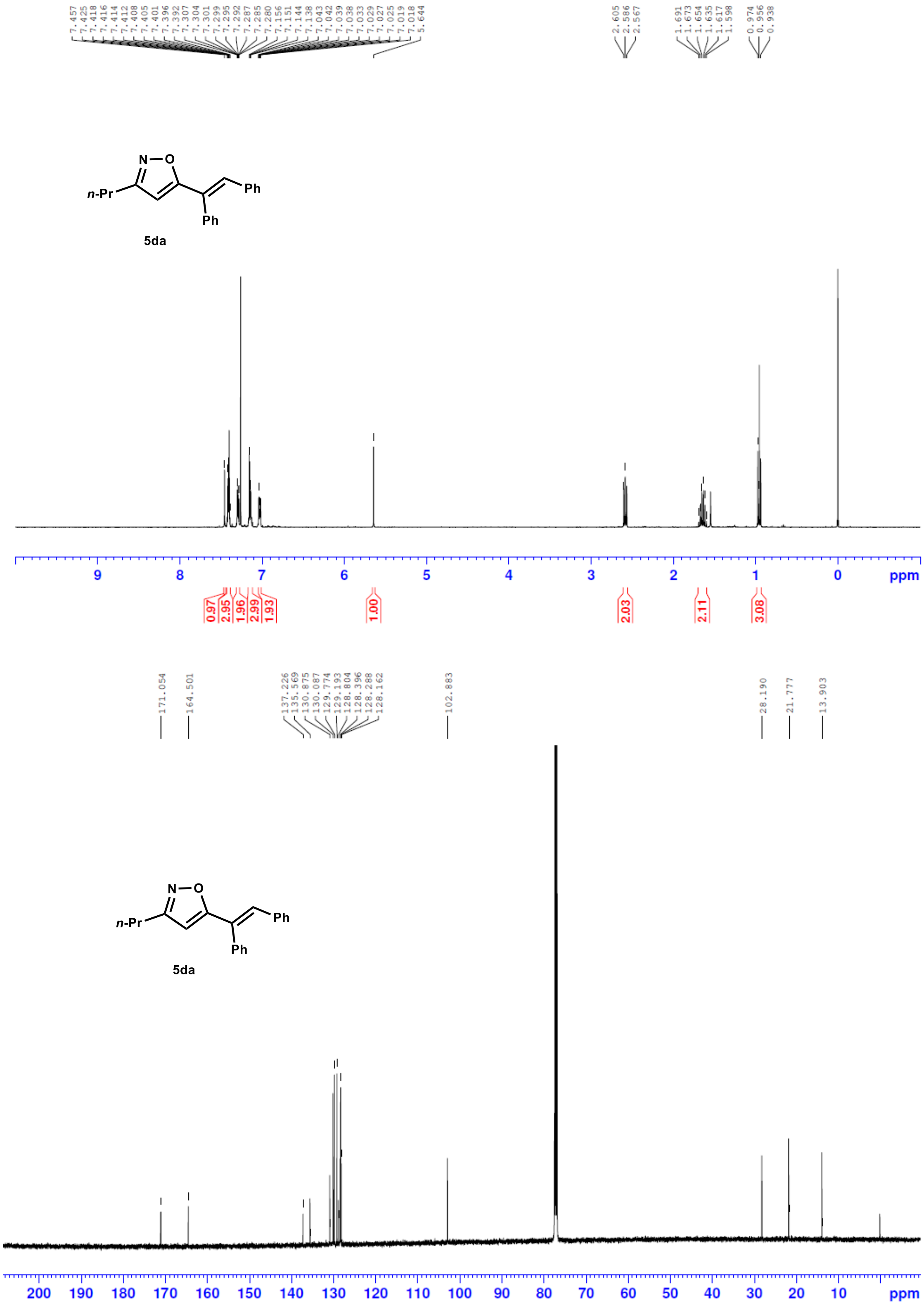


**Figure S52.** $^1$H and $^{13}$C NMR Spectra of compound **5da**

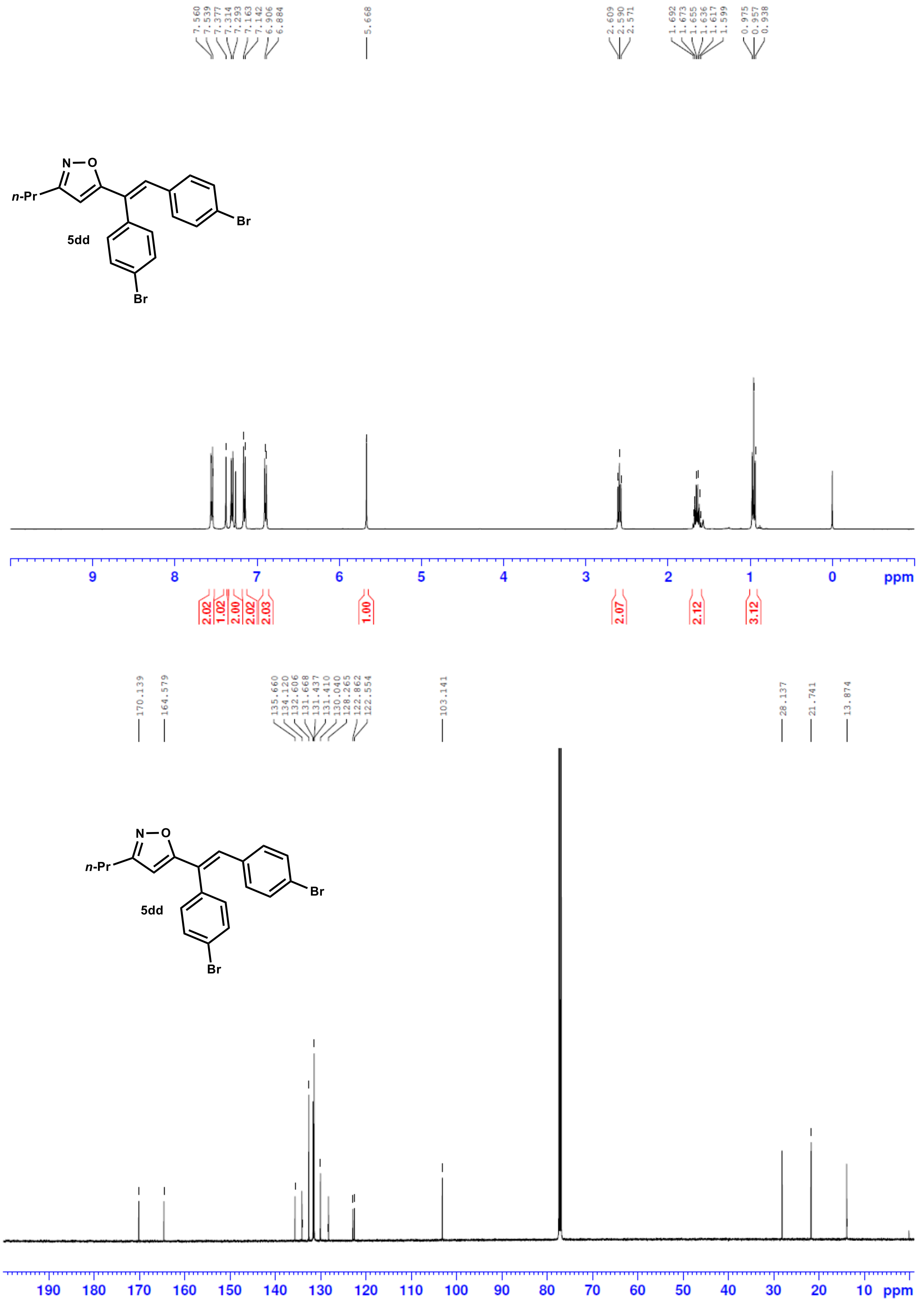


**Figure S53.** $^1$H and $^{13}$C NMR Spectra of compound **5dd**

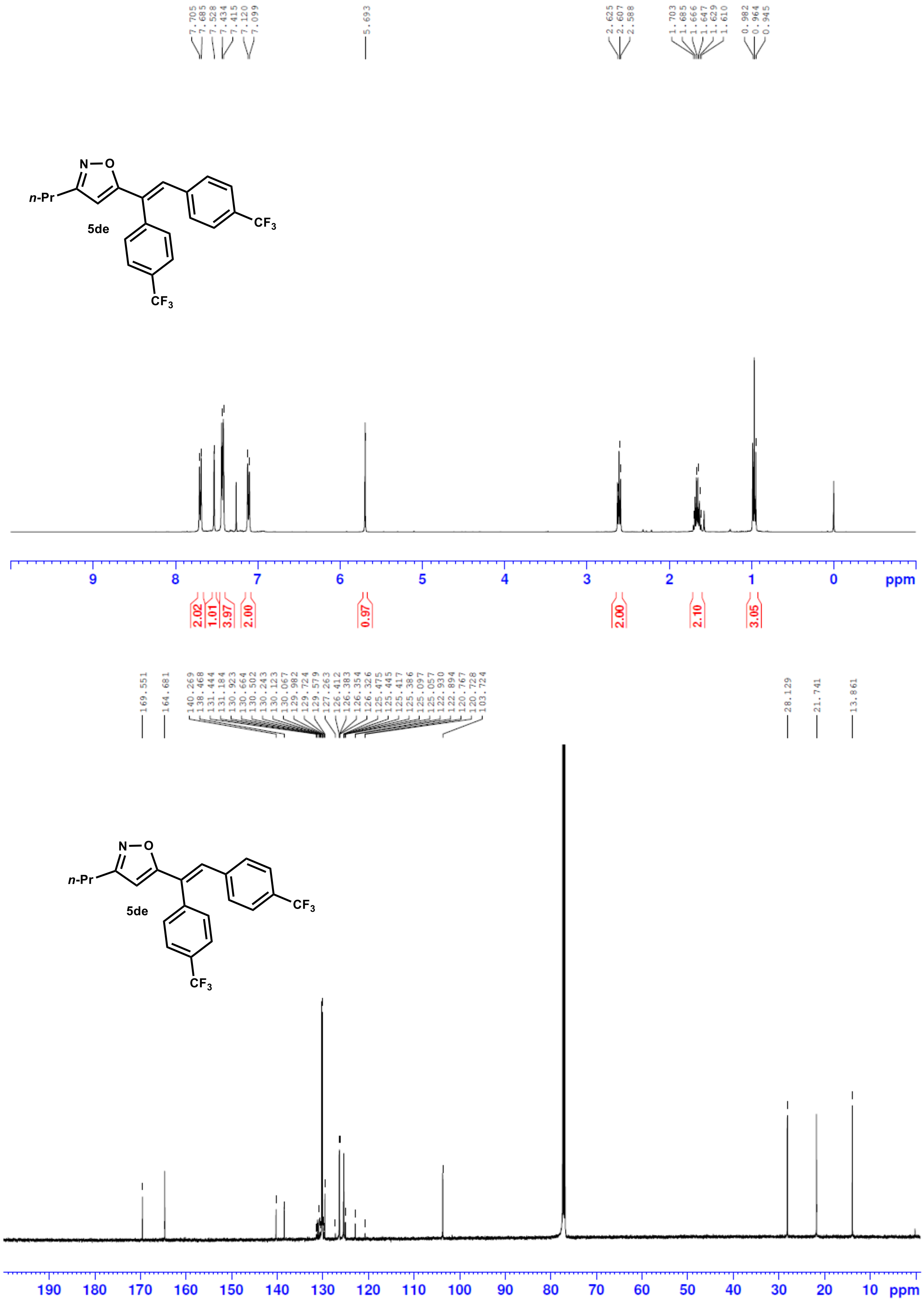


**Figure S54.** $^1$H and $^{13}$C NMR Spectra of compound **5de**

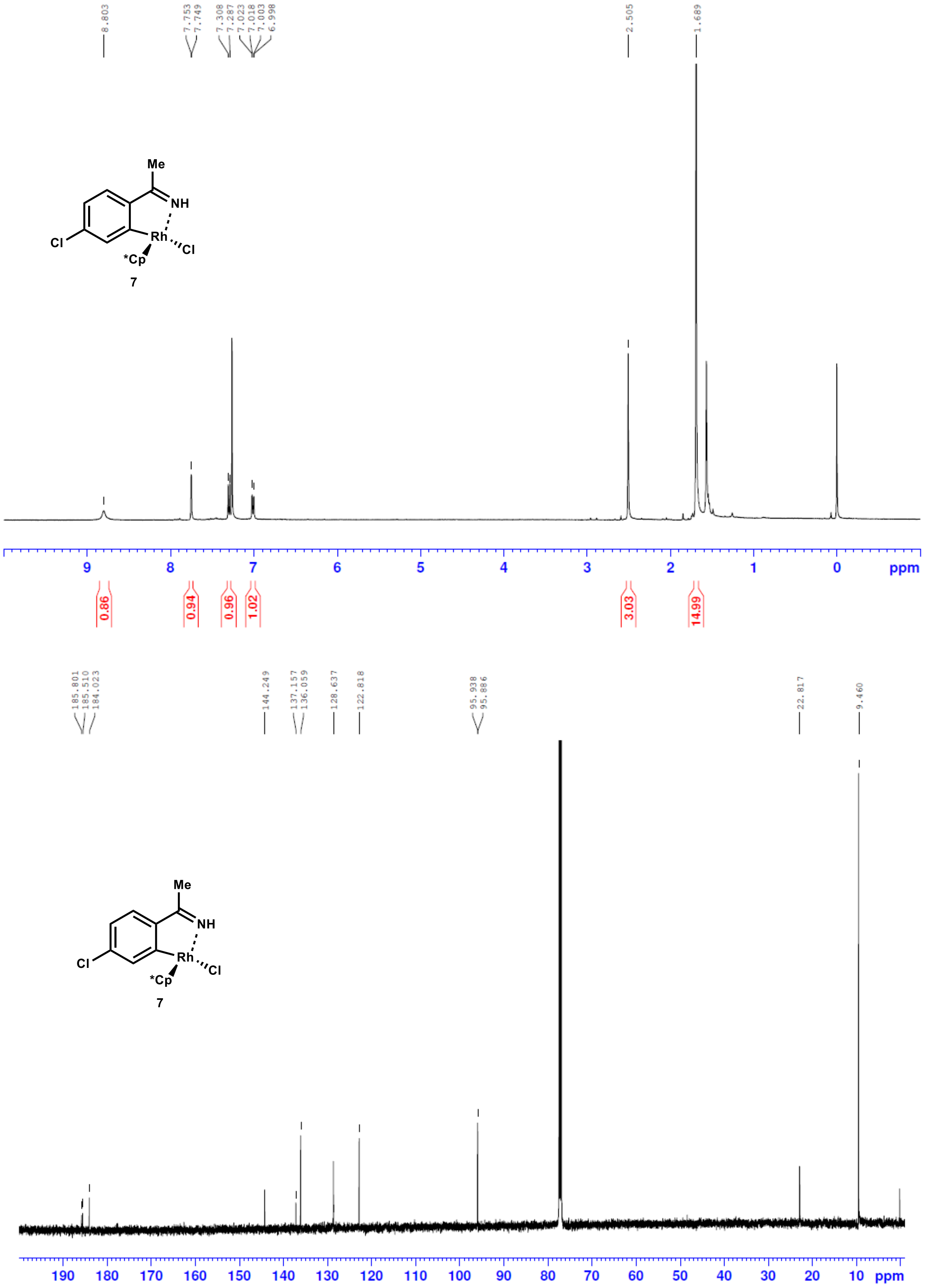


**Figure S55.** $^1$H and $^{13}$C NMR Spectra of compound **7**

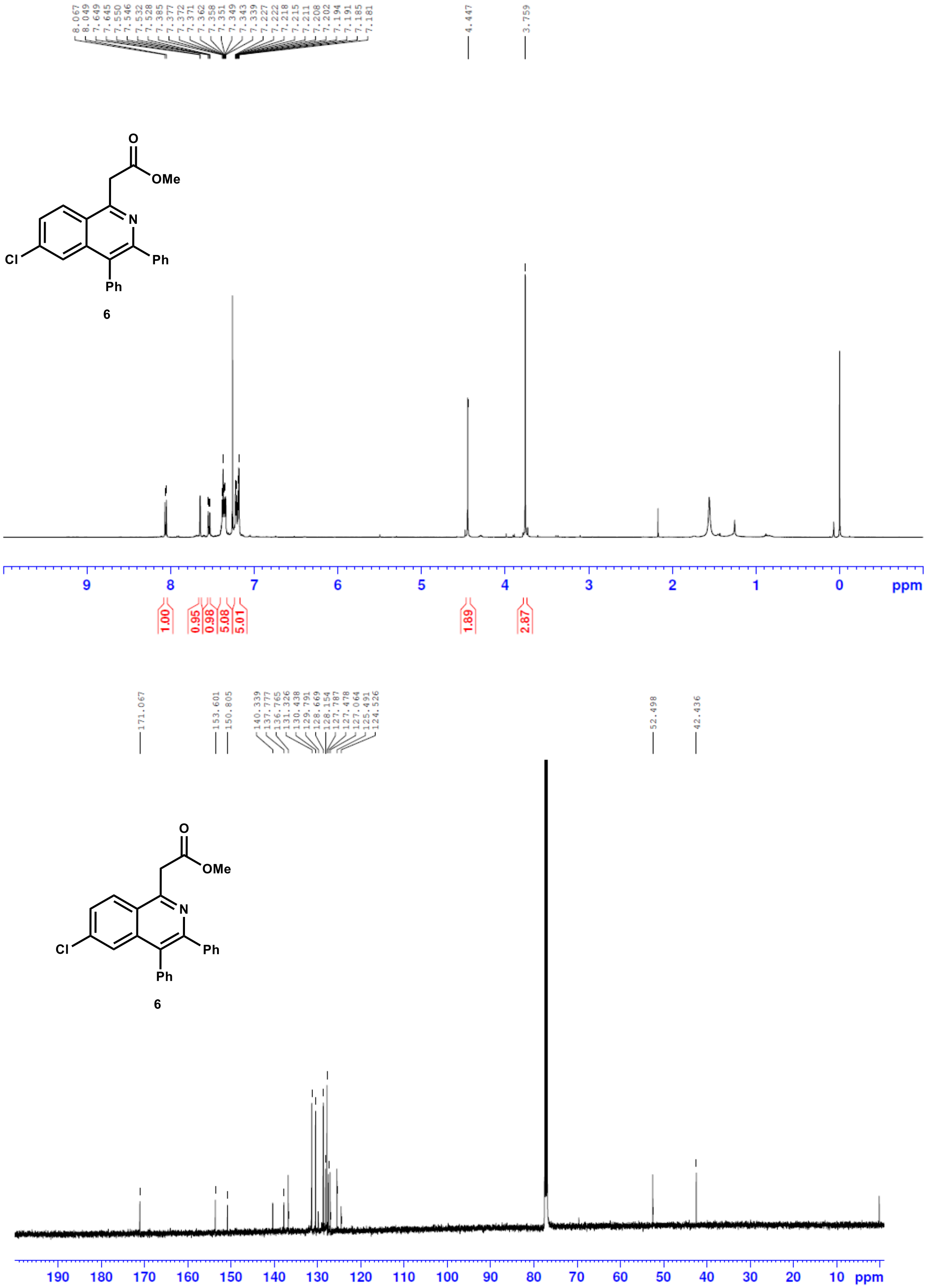


**Figure S57.** $^1$H and $^{13}$C NMR Spectra of compound **6**