Supporting Information

Synthesis of Isoquinolones via Rh-Catalyzed C–H Activation of Substituted Benzamides Using Air as the Sole Oxidant in Water

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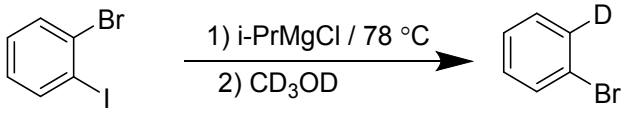
General. All reactions were conducted under a nitrogen atmosphere on a dual-manifold Schlenk line unless otherwise mentioned and in oven-dried glass wares. All solvents were dried according to known methods and distilled prior to use [1]. $[Cp^*Rh(CH_3CN)_3](BF_4)_2]$ was prepared from $RhCl_3.xH_2O$ following a literature procedure.[2] Other reagents were commercially available and used as purchased.

General Procedure for the Synthesis of Isoquinolones by Rhodium-Catalyzed C–H Activation.

To a screw-capped glass tube containing $[Cp^*Rh(CH_3CN)_3](BF_4)_2]$ (4.0 mol %), K_2CO_3 (0.20 mmol), *N*-alkyl benzamide **1** (0.40 mmol), and acetylene **2** (0.50 mmol) was added water (2.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 16 h. After completion, the reaction mixture was cooled and extracted with E.A. (ethyl acetate, 3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by a silica gel column using hexane/ethyl acetate (90/10) as eluent to yield the desired pure product **3**.

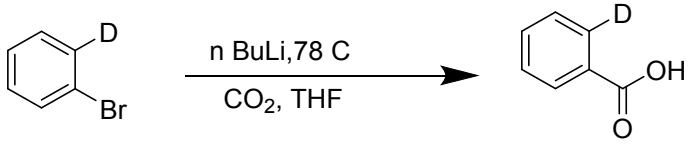
The spectral data and a copy of ^1H and ^{13}C NMR spectra for all compounds **3** are listed below (p. S26)

Synthesis of 2-deuteriobromobenzene.[4]



To a stirred solution of 1-bromo-2-iodobenzene (5.00 g, 17.7 mmol) in a mixture of THF and Et_2O (120 mL, 1:1) at -78 °C was added dropwise isopropyl magnesium chloride (2 M in Et_2O, 10.6 mL, 21.2 mmol). The mixture was stirred at that temperature for 2 h and then, CD_3OD (2.2 mL, 53.0 mmol) was added. The solution was slowly warmed to room temperature, then an aq. HCl (10%, 100 mL) solution was added and the resulting mixture was stirred for 30 min at room temperature. The aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic phase was dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The pure 2-deuteriobromobenzene was obtained by distillation.

Synthesis of 2-deuteriobenzoic acid.[4]



To a stirred solution of 2-deuteriobromobenzene (1.00 g, 6.32 mmol) in dry THF (20 mL) was added a solution of *n*-BuLi in *n*-hexane (3.0 mL, 2.5M, 7.59 mmol) dropwise at -78 °C for 30 min. The mixture was stirred at the same temperature for 30 min, and then CO_2 was bubbled through the mixture at -78 °C for 30 min. The mixture was allowed to warm to ambient temperature, quenched with H_2O (20 mL), acidified to pH = 1 with 1M HCl, and extracted with EtOAc (2 × 30 mL). The combined organic phase was dried over $MgSO_4$, filtered and the solvents were removed in vacuum to give product 2-deuteriobenzoic acid (550 mg, 70 %).

Synthesis of *N*-methyl -2-deuteriobenzamide 1a-d_1.[4]

To the solution of the 2-deuteriobenzoic acid (550 mg, 4.47 mmol) in dry E.A. (20 mL) at 0 °C under N_2 were added dropwise oxalyl chloride (372 mg, 6.70 mmol) and a catalytic amount of dry DMF (2 drops). The reaction was allowed to stir at room temperature for 5 h. The solvent was then removed under reduced pressure to afford the corresponding crude deuterated acid chloride. Methyl amine hydrochloride (450 mg, 5.36 mmol) was added to a biphasic mixture of K_2CO_3 (1.23 g, 8.92 mmol) in a 2:1 mixture of EtOAc (30 mL) and H_2O (15 mL). The resulting solution was cooled to 0°C followed by dropwise addition of the unpurified deuterated acid chloride dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at room temperature for 10 h. Afterwards the phases were extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated under reduced pressure to give the desired product without any further purification. ^{1}H NMR (400 MHz, CDCl3): δ 7.75-7.72 (m, 1 H), 7.40-7.36 (m, 1 H), 7.31-7.7.27 (m, 2 H), 7.19 (br, 1 H, NH), 2.88 (d, 3 H). HRMS (FAB+) calcd for C_8H_8DNO 136.074, found 136.073.

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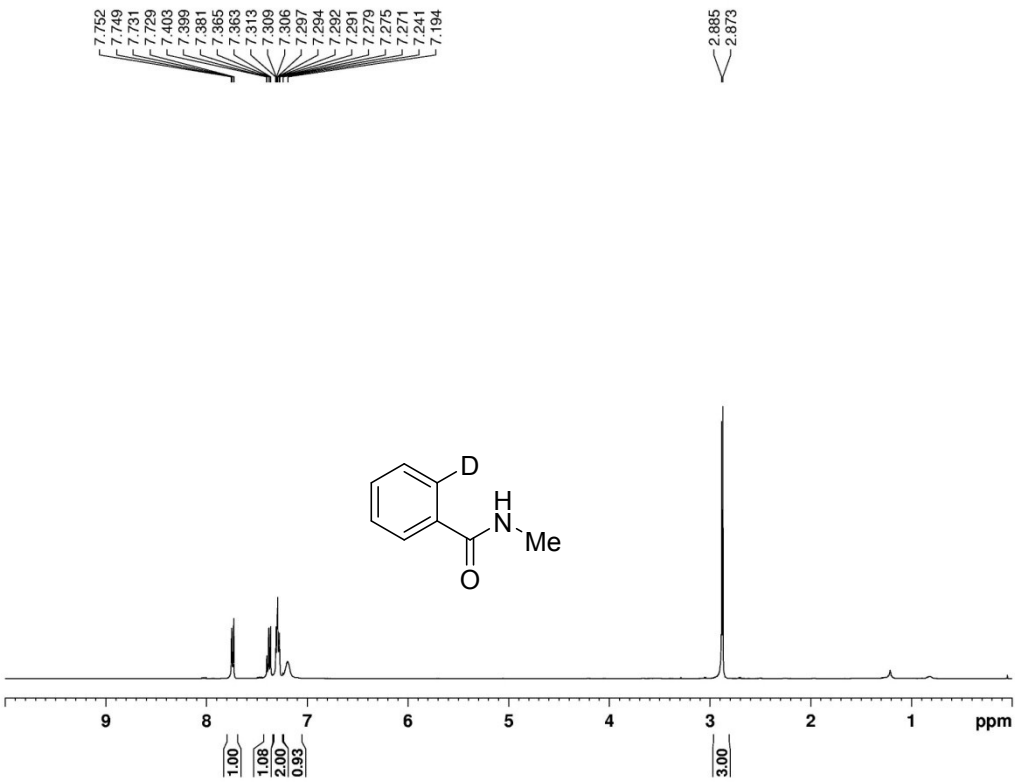
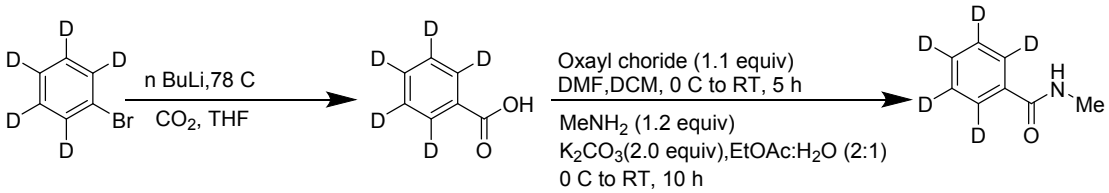
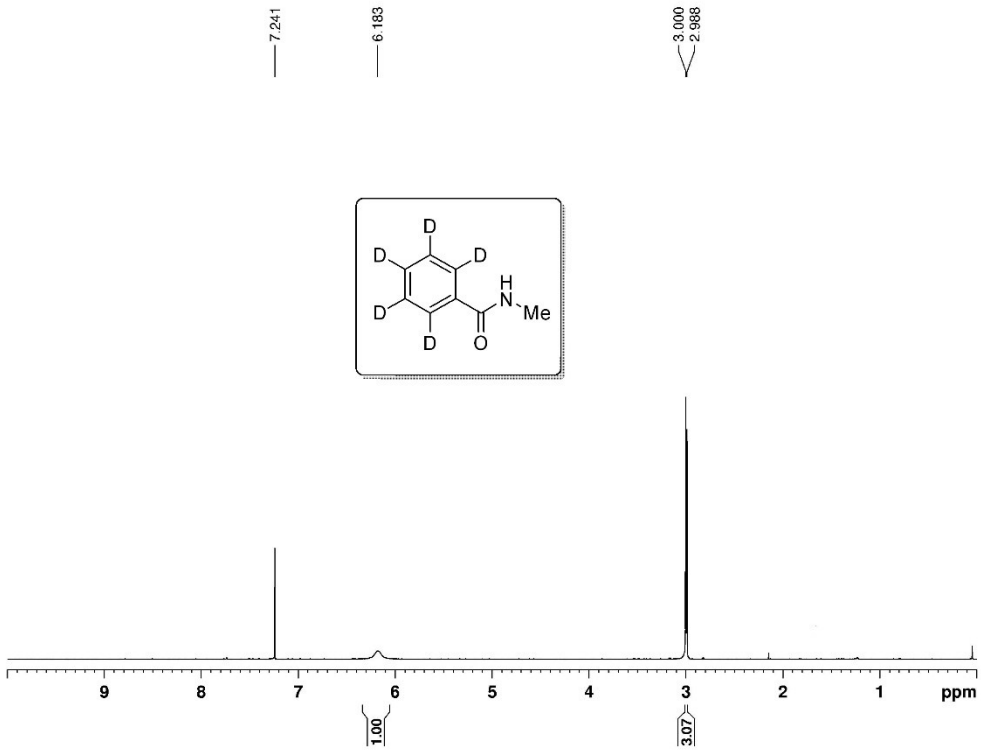


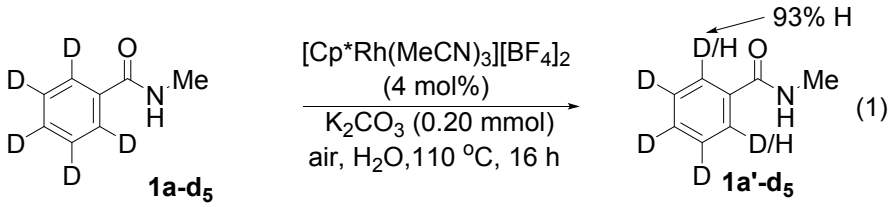
Synthesis of *N*-methyl-2,3,4,5,6-pentadeuteriobenzamide 1a-d_5.[4]



N-methyl-2,3,4,5,6-pentadeuteriobenzamide was prepared from 2,3,4,5,6-pentadeuteriobenzene using the same procedure as the synthesis of *N*-methyl-2-deuteriobenzamide, ^{1}H NMR (400 MHz, CDCl3): δ 6.18 (s, 1 H, NH), 2.99 (d, 3 H).

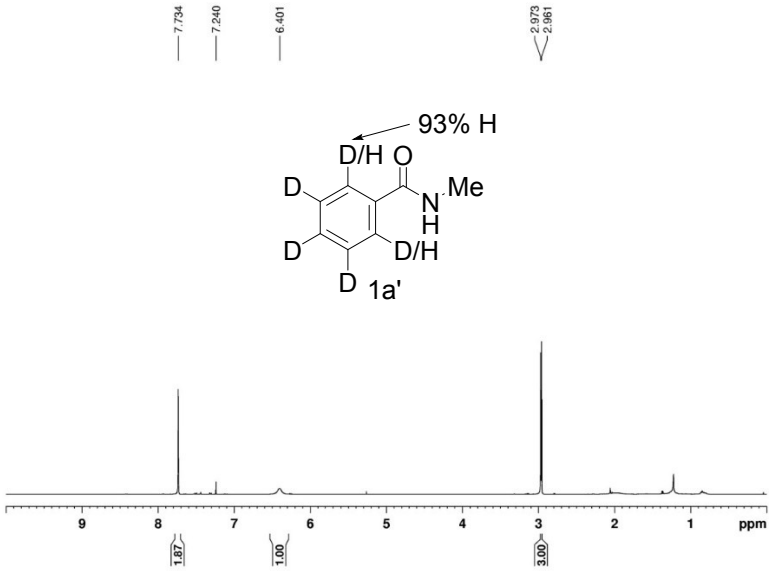


Reversible D/H exchange:

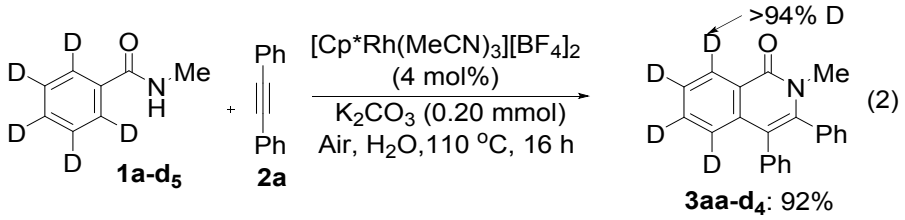


To a sealed tube containing $[Cp^*Rh(CH_3CN)_3](BF_4)_2$ (4.0 mol %), K_2CO_3 (0.20 mmol), *N*-methyl-2,3,4,5,6-pentadeueriobenzamide **1a-d$_5$** (0.40 mmol) was added water (2.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 16 h, when the reaction was complete, the mixture was cooled and the reaction mixture was extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to yield **1a'-d$_5$**.

The D/H incorporation in **1a'-d$_5$** was determined by ^{1}H-NMR spectroscopy.



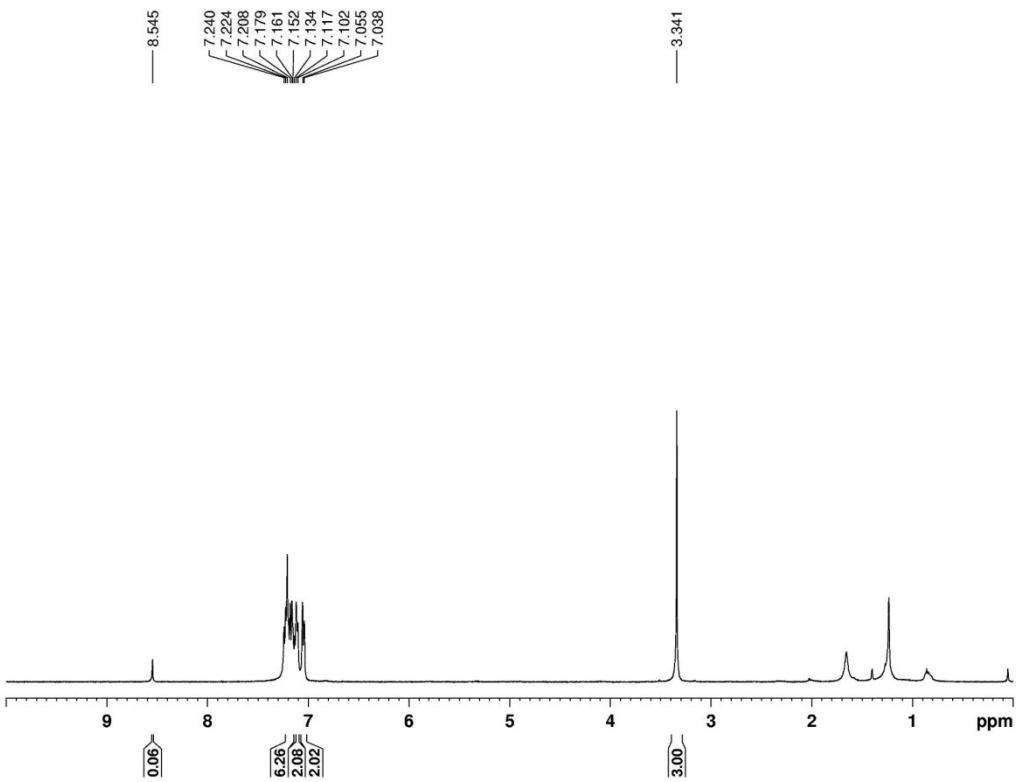
Rh-Catalyzed Isoquinolones from 1a-d_5:



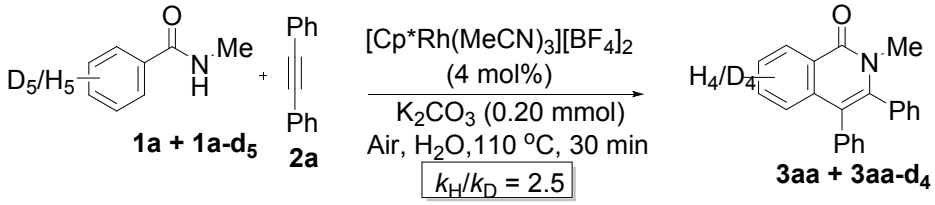
(2)

A sealed tube containing [Cp*Rh(CH_3CN)$_3$](BF_4)$_2$] (4.0 mol %), K_2CO_3 (0.20 mmol), *N*-methyl-2,3,4,5,6-pentadeueriobenzamide **1a-d_5** (0.40 mmol), diphenyl acetylene **2a** (0.50 mmol) then water (2.0 mL) was added to the system via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air in filled a balloon for 16 h, when the reaction was complete, the mixture was cooled and the reaction mixture was diluted and extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to yield **3aa-d_4**. The ortho deuterium content 92% was determined by ^{1}H-NMR spectroscopy

^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3aa-d$_4$**.



Intermolecular Kinetic Isotope Effect

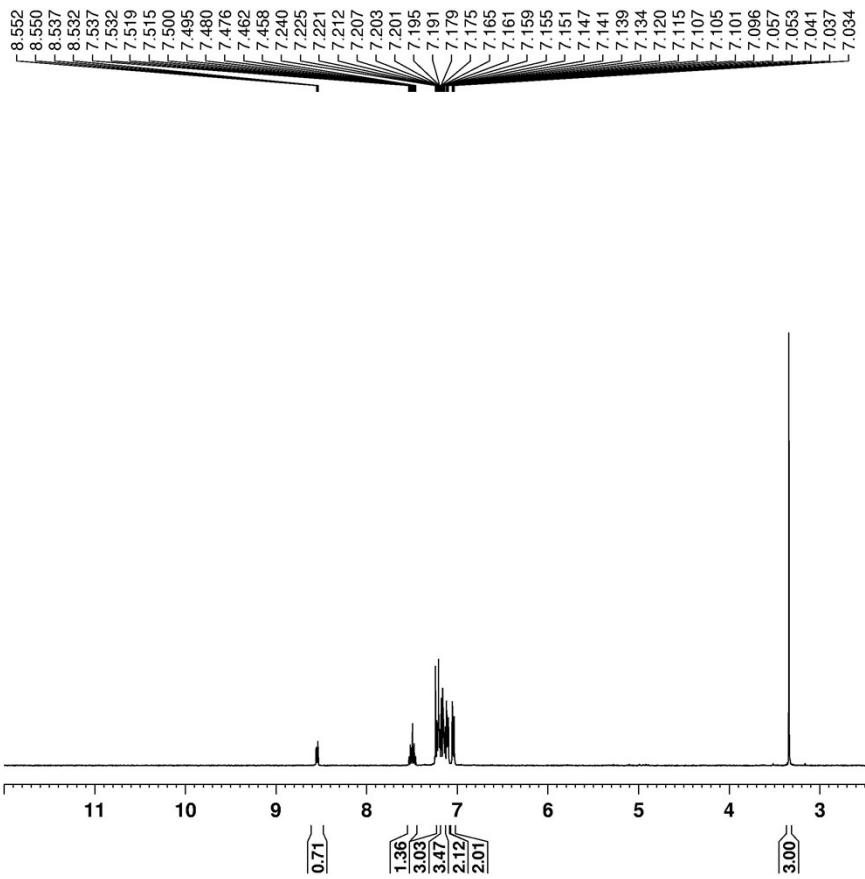


Competition Experiment:

A sealed tube containing [Cp*Rh(CH_3CN)$_3$](BF_4)$_2$] (4.0 mol %), K_2CO_3 (0.20 mmol), *N*-methyl benzamide **1a** (0.20 mmol), *N*-methyl-2,3,4,5,6-pentadeueriobenzamide **1a-d$_5$** (0.20 mmol), diphenyl acetylene **2a** (0.50 mmol) then water (2.0 mL) was added to the system via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 30 min, then the mixture was cooled and the reaction mixture was diluted and extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to afford a

mixture of products **3aa** and **3aa-d$_4$** in 26% yield. The ratio of two compounds was determined by ^{1}H NMR integration to give intermolecular kinetic isotopic effect (KIE) k_H/k_D = **2.5**

^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound

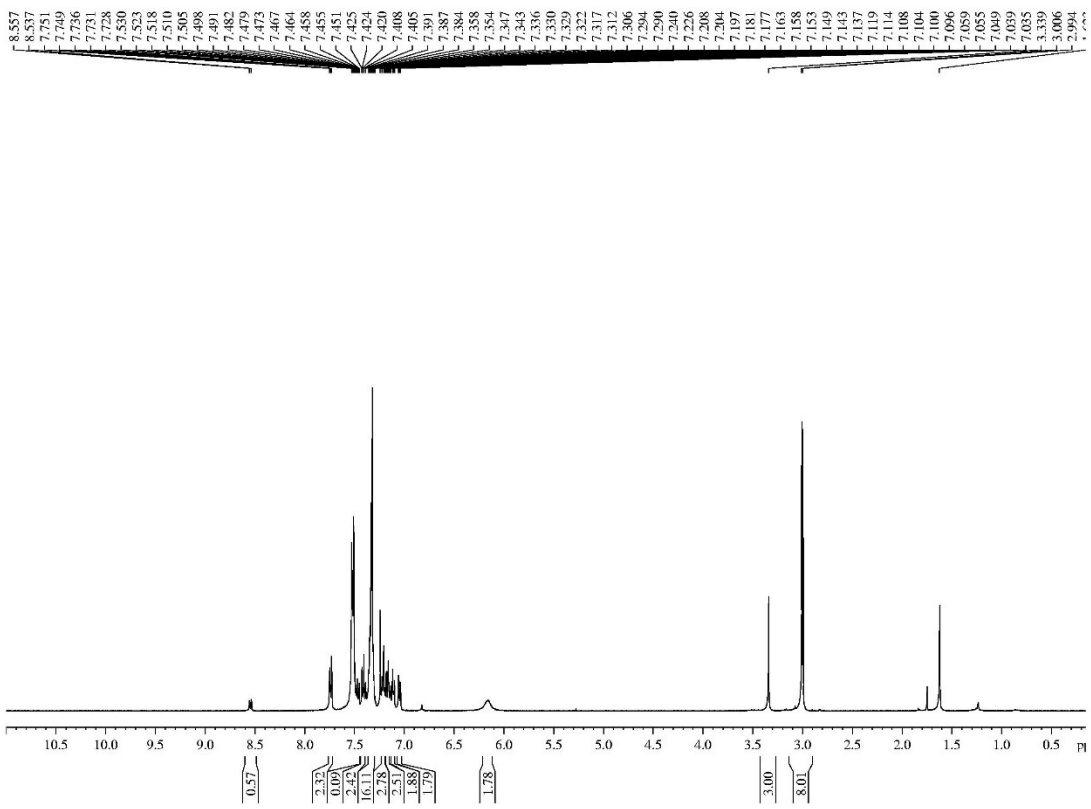


Parallel Experiment:

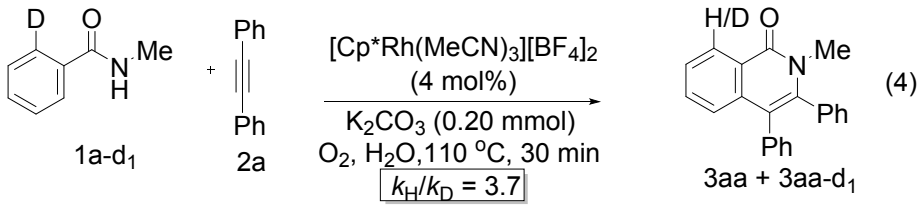
A sealed tube containing [Cp*Rh(CH_3CN)$_3$](BF_4)$_2$] (4.0 mol %), K_2CO_3 (0.20 mmol), *N*-methyl benzamide **1a** (0.40 mmol), diphenyl acetylene **2** (0.50 mmol) was sealed with a septum, then water (2.0 mL) was added to the system via syringe and similarly in another sealed tube *N*-methyl-2,3,4,5,6-pentadeueriobenzamide **1a-d$_5$** (0.40 mmol) was added instated of *N*-methyl benzamide **1a** (0.40 mmol), both tubes were allowed to stir at 110 °C under one atmosphere of air filled a balloon for 30 min, then the mixtures were cooled and both reaction mixtures were extracted with E.A. (3 x 10 mL). The combined organic layer was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to afford a mixture of products **3aa** and **3aa-d$_4$** in 27% yield. The ratio of two compounds was determined by ^{1}H NMR integration to give intermolecular kinetic

isotopic effect (KIE) k_H/k_D = **1.3**

^{1}H NMR (400 MHz, $CDCl_3$) crude spectra of compound **3aa** and **3aa-d$_4$**.



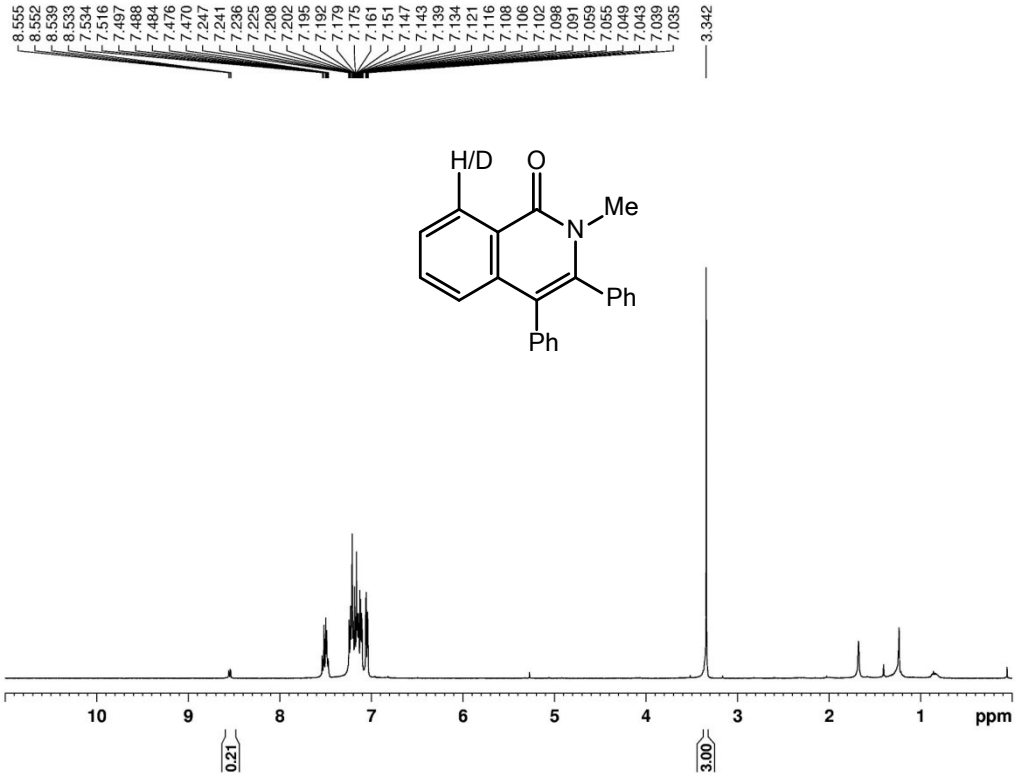
Intramolecular Kinetic Isotope Effect-



A sealed tube containing [Cp*Rh(CH_3CN)$_3$](BF_4)$_2$] (4.0 mol %), K_2CO_3 (0.20 mmol), *N*-methyl benzamide **[D$_1$]-1a** (0.40 mmol)**,** diphenyl acetylene **2** (0.50 mmol) was sealed with a septum, then water (2.0 mL) was added to the system via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled a balloon for 30 min, then the mixture was cooled and the reaction mixture was extracted with E.A. (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (Hexane /E.A.: 90/10) to afford a mixture of products **3aa** and **3aa-d$_1$** in 26%

yield. The ratio of two compounds was determined by ^{1}H NMR integration to give intermolecular kinetic isotopic effect (KIE) k_H/k_D = 3.7

^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **3aa** and **3aa-d$_1$**.



Gram-scale Synthesis of Isoquinolones via Rhodium-Catalyzed C–H Activation.

To a screw-capped glass tube containing [Cp*Rh(CH_3CN)$_3$](BF_4)$_2$] (4.0 mol %), K_2CO_3 (4.4 mmol), *N*-alkyl benzamide **1a** (1g, 7.4 mmol), and acetylene **2** (1.32g , 7.4 mmol) was added water (20.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 20 h. After completion, the reaction solution was cooled to room temperature, the precipitate was collected and was washed with H_2O (3 x 20 mL) and dried in vacuum to give the crude product which was further purified by a silica gel column using hexane/ethyl acetate (90/10) as eluent to yield the desired pure product **3** in 86 % (1.99 g).

Evaluation of Green metrics of the process.

Atom economy defined as “how much of the reactants remain in the final desired product"

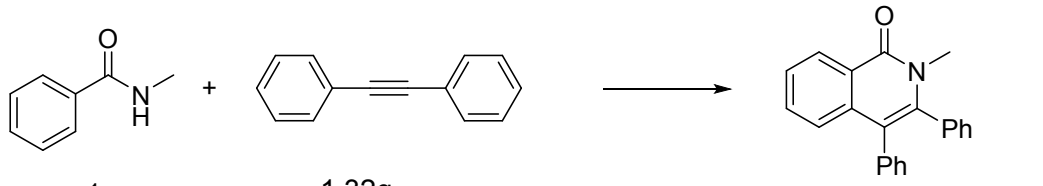
$$\text{Atom economy (AE)} = \frac{\text{Molecular mass of desired product}}{\text{Molecular mass of all reactants}} \times 100$$

Reaction mass efficiency (RME) defined as “the percentage of the mass of the reactants that remain in the product”

$$\text{Reaction mass efficiency (RME)} = \frac{\text{mass of desired product}}{\text{mass of all reactants}} \times 100$$

Evaluation of Green metrics for the current methodology.

Reaction scheme



1g + 1.32g → 1.99g

Chemical Formula: C_8H_9NO
Molecular Weight: 135.1632

Chemical Formula: $C_{14}H_{10}$
Molecular Weight: 178.2292

Chemical Formula: $C_{22}H_{17}NO$
Molecular Weight: 311.38

Product Yield: 86%

Total= 135.16+178.23 =313.39

Reactant 1	N-methylbenzamide (**1g**)	1g	0.0074 mol	FW 135.16
Reactant 2	1,2-diphenylethyne (**1.32g**)	1.32g	0.0074 mol	FW 178.22
Base	Potassium Carbonate **(0.51g)**	0.51g	0.0037 mol	FW 138.20
Solvent	H_2O	20 g	---	---
Auxiliary	---	---	---	---
Product	2-methyl-3,4-diphenylisoquinolin-1(2H)-one **(3aa)**	1.99g	0.0064 mol	FW 311.37

Product yield= 86%

E-factor $= \dfrac{1g + 1.32g + 20\ g + 0.51\ g - 1.99\ g}{1.99\ g}$ = 10.47 kg waste/ 1 kg product

Atom economy $= \dfrac{311}{313} \times 100$ = 99.4%

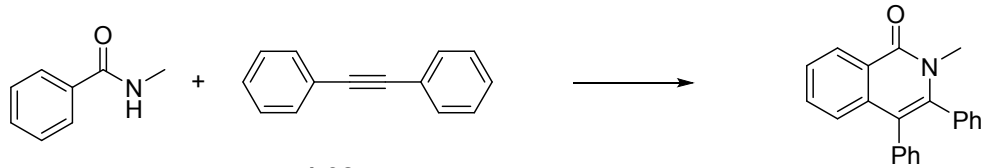
Atom efficiency = 86 X (99.4 / 100) = 85.5%

Carbon efficiency $= \dfrac{22}{8 + 14} \times 100$ = 100%

Reaction mass efficiency $= \dfrac{1.99\ g}{1g + 1.32g} \times 100$ = 85.8%

Evaluation of Green metrics for the reported methodology [6].

Reaction scheme



1g **1.32g** **1.56g**

Chemical Formula: C_8H_9NO
Molecular Weight: 135.1632

Chemical Formula: $C_{14}H_{10}$
Molecular Weight: 178.2292

Chemical Formula: $C_{22}H_{17}NO$
Molecular Weight: 311.3765

Product Yield: 68%

Total= 135.16+178.23 =313.39

Reactant 1	N-methylbenzamide (**1g**)	1g	0.0074 mol	FW 135.16
Reactant 2	1,2-diphenylethyne (**1.32g**)	1.32g	0.0074 mol	FW 178.22
Oxidant	$Cu(OAc)_2.H_20$	2.95g	0.0148 mol	FW 199.65
Solvent	*t*-amyl alcohol	40.25 g (50 mL)	---	---
Auxiliary	---	---	---	---
Product	2-methyl-3,4-diphenylisoquinolin-1(2H)-one	1.56g	0.005 mol	FW 311.37

Product yield= 68%

E-factor = $\frac{1g + 1.32g + 40.25g + 2.95g - 1.56\,g}{1.56\,g}$ = 28.18 kg waste/ 1 kg product

Atom economy = $\frac{311}{313}$ X 100 = 99.4%

Atom efficiency = 68 X (99.4 / 100) = 67.6%

Carbon efficiency = $\frac{22}{8 + 14}$ X 100 = 100%

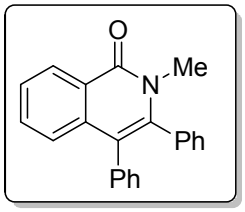
Reaction mass efficiency = $\frac{1.56\,g}{1g + 1.32g}$ X 100 = 67.2%

Procedure for the Synthesis of 5,6,13-Triphenyl-8H-isoquinolino[3,2-a]isoquinolin-8-one (3ta).

To a screw-capped glass tube containing $[Cp^*Rh(CH_3CN)_3](BF_4)_2$ (4.0 mol %), K_2CO_3 (0.20 mmol), primary benzamide **1t** (0.40 mmol), and diphenylacetylene **2a** (1.50 mmol) was added water (3.0 mL) via syringe and the reaction mixture was allowed to stir at 110 °C under one atmosphere of air filled in a balloon for 16 h. After completion, the reaction mixture was cooled and extracted with ethyl acetate, (3 x 10 mL). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The mixture was filtered through a Celite pad and the Celite pad was washed with E.A. (10 mL). After filtration and evaporation of the solvents in vacuo, the crude product was purified by a silica gel column using hexane/ethyl acetate (80/20) as eluent to yield the desired pure product **3ta**.

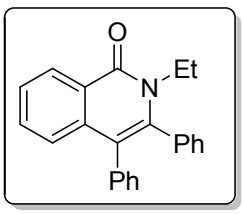
The spectral data and a copy of ^1H and ^{13}C NMR spectra for all compounds **3ta** are listed below (p. S56)

2-Methyl-3,4-diphenylisoquinolin-1(2H)-one (3aa)



White solid, m.p. 245-248 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 9.2 Hz 1 H), 7.52-7.45 (m, 2 H), 7.23-7.09 (m, 9 H), 7.05-7.03 (m, 2 H), 3.34 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.7 (C), 141.2 (C), 137.1 (C), 136.4 (C), 135.0 (C), 131.9 (CH), 131.5 (2CH), 129.9 (2CH), 128.1 (3CH), 127.8 (2CH), 127.7 (CH), 126.7 (CH), 126.5 (CH), 125.3 (CH), 124.9 (C), 118.8 (C), 34.3 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{17}NO$ 311.1310, found 311.1310; IR (KBr): 2923, 1648, 1604, 1550, 1425, 1030, 925, 698 cm^{-1}

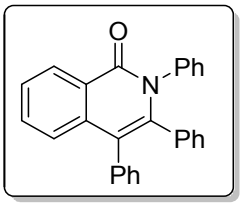
2-Ethyl-3,4-diphenylisoquinolin-1(2H)-one (3ba)



Yellow solid, m.p. 246-248 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.55-8.53 (m, 1 H), 7.51-7.45 (m, 2 H), 7.23-7.09 (m, 9 H), 7.04-7.02 (m, 2 H), 3.96-3.90 (q, 2 H), 1.15 (t, *J* = 14.0 Hz 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.0 (C), 141.0 (C), 137.1 (C), 136.5 (C), 134.7 (C), 131.9 (CH), 131.5 (2 CH), 130.1 (2 CH), 128.1 (CH), 127.8 (2 CH), 127.8 (2 CH), 127.7 (CH), 126.7 (CH), 126.5 (CH), 125.3

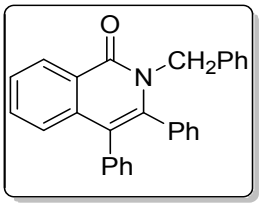
(CH), 125.2 (C), 119.0 (C), 41.3 (CH_2), 14.1 (CH_3); **HRMS** (ESI) cal. for $C_{23}H_{19}NO$ 325.1467, found 325.1467; IR (KBr): 2923, 1645, 1604, 1548, 1427, 1080, 925, 771, 698 cm^{-1}

2,3,4-Triphenylisoquinolin-1(2H)-one (3ca)



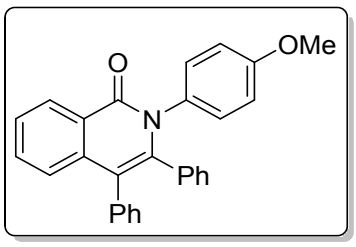
White solid, m.p. 167-170 °C; **^{1}H NMR** (400 MHz, CDCl3): δ 8.56 (d, *J* = 8.0 Hz 1 H), 7.59-7.49 (m, 2 H), 7.25-7.08 (m, 11 H), 6.87 (s, 5 H); **^{13}C NMR** (100 MHz, CDCl3): δ 162.6 (C), 141.0 (C), 139.4 (C), 137.6 (C), 136.3 (C), 134.7 (CH), 132.5 (CH), 131.6 (2 CH), 131.0 (2 CH), 129.5 (2 CH), 128.5 (2 CH), 128.2 (CH), 127.9 (2 CH), 127.5 (CH), 127.2 (CH), 127.0 (2 CH), 126.8 (CH), 125.5 (2 CH), 118.8 (C); **HRMS** (ESI) cal. for $C_{27}H_{19}NO$ 373.1467, found 373.1466; IR (KBr): 2923, 1648, 1604, 1550, 1425, 1030, 925, 698 cm^{-1}

2-Benzyl-3,4-diphenylisoquinolin-1(2H)-one (3da)



Yellow solid, m.p. 167-170 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.61-8.59 (m 1 H), 7.56-7.19 (m, 2 H), 7.17-7.09 (m, 8 H), 7.06-7.02 (m, 4 H), 6.89-6.82 (m, 4 H), 5.20 (s, 2 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.6 (C), 141.3 (C), 137.7 (C), 137.3 (C), 136.4 (C), 134.3 (C), 132.2 (CH), 131.4 (2 CH), 130.4 (2 CH), 128.2 (CH), 128.1 (2 CH), 128.0 (CH), 127.8 (CH), 127.5 (2 CH), 126.9 (2 CH), 126.8 (2 CH), 126.7 (CH), 126.7 (CH), 125.4 (CH), 125.1 (C), 119.4 (C), 49.0 (CH_2) **HRMS** (ESI) cal. for $C_{28}H_{21}NO$ 387.1623, found 387.1620; IR (KBr): 2854, 1645, 1604, 1548, 1427, 1080, 925, 771, 698 cm^{-1}

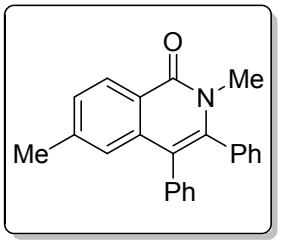
2-(4-Methoxyphenyl)-3,4-diphenylisoquinolin-1(2H)-one (3ea)



Yellow solid, m.p. 219-221 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.59-8.56 (m, 1 H), 7.57-7.47 (m, 2 H), 7.26-7.11 (m, 6 H), 7.04-6.90 (m, 2 H), 6.90 (m, 5 H), 6.74-6.70 (m, 2 H), 3.66 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ

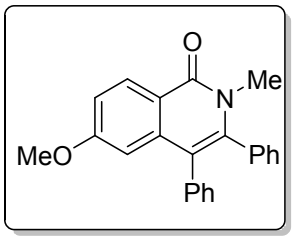
162.7 (C), 158.3 (C), 141.2 (C), 137.4 (C), 136.2 (C), 134.7 (C), 132.3 (CH), 132.0 (C), 131.4 (2 CH), 130.8 (2 CH), 130.2 (2 CH), 128.1 (CH), 127.8 (2 CH), 127.0 (2 CH), 127.0 (2 CH), 126.6 (CH), 125.4 (CH), 125.3 (CH), 118.5 (C), 113.7 (CH), 55.1 (CH_3); **HRMS** (ESI) cal. for $C_{28}H_{21}NO_2$ 403.1572, found 403.1572; IR (KBr): 2923, 1655, 1604, 1508, 1323, 1229, 1030, 771 cm^{-1}

2,6-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3fa)



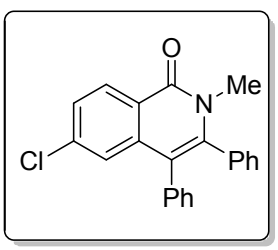
White solid, m.p. 263-265 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.0 Hz 1 H), 7.31-7.29 (d, *J* = 8.0 Hz 1 H), 7.21-7.02 (m, 10 H), 6.90 (s, 1 H), 3.32 (s, 3 H), 2.32 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.6 (C), 142.4 (C), 141.2 (C), 137.1 (C), 136.5 (C), 135.1 (C), 131.4 (2 CH), 131.3 (2 CH), 129.8 (2 CH), 128.1 (2CH), 128.0 (CH), 127.8 (CH), 126.6 (CH), 126.4 (CH), 124.9 (CH), 122.7 (C), 118.6 (C), 34.1 (CH_3), 21.8 (CH_3); **HRMS** (ESI) cal. for $C_{23}H_{19}NO$ 325.1467, found 325.1469; IR (KBr): 2931,1645, 1604, 1548, 1425, 1080, 925, 830, 771, 698 cm^{-1}

6-Methoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ga)



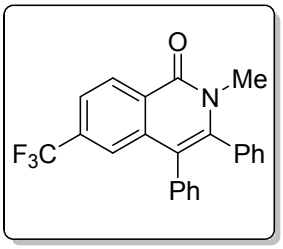
Yellow solid, m.p. 220-223 °C, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.47 (d, *J* = 8.8 Hz 1 H), 7.22-7.23 (m,10 H), 6.50-6.49 (m, 1 H), 3.65 (s, 3 H), 3.30 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.5 (C), 162.3 (C), 141.8 (C), 139.1 (C), 136.4 (C), 135.1 (C), 131.4 (2 CH), 129.9 (2 CH), 129.8 (2 CH), 128.1 (2 CH), 127.8 (2 CH), 126.7 (CH), 118.9 (C), 118.5 (C), 115.4 (CH), 106.9 (CH), 55.1 (CH_3), 34.0 (CH_3); **HRMS** (ESI) cal for $C_{23}H_{19}NO_2$ 341.1416, found 341.1414; IR (KBr): 2923, 1645, 1604, 1548, 1427, 1030, 1080, 925, 813, 771, 698 cm^{-1}

6-Chloro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ha)



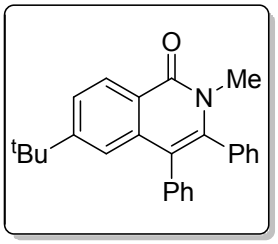
Yellow solid, m.p. 267-270 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.46 (d, *J* = 8.4 Hz 1 H), 7.41-7.38 (m, 1 H), 7.23-7.08 (m, 9 H), 7.03-7.01 (m, 2 H), 3.31 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.1 (C), 142.6 (C), 138.6 (C), 138.4 (C), 135.6 (C), 134.7 (C), 131.3 (2 CH), 129.6 (3 CH), 128.3 (CH), 128.2 (2 CH), 128.1 (2 CH), 127.0 (2 CH), 124.6 (CH), 123.2 (C), 117.9 (C), 34.3 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{16}ClNO$ 345.0920, found 345.0918; IR (KBr): 2923, 2854, 1651, 1614, 1548, 1427, 1002, 875, 833, 782 cm^{-1}

2-Methyl-3,4-diphenyl-6-(trifluoromethyl)isoquinolin-1(2H)-one (3ia)



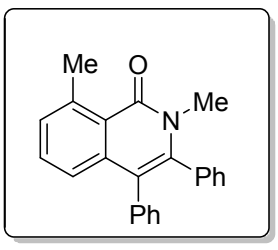
White solid, m.p. 175-178 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 8.4 Hz 1 H), 7.67-7.65 (m,1 H), 7.42 (s, 1 H), 7.26-7-14 (m, 7 H), 7.12-7.09 (m, 2 H), 7.04-7.02 (m, 2 H), 3.35 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.9 (C), 142.9 (C), 137.2 (C), 135.4 (C), 134.5 (C), 133.6 (CH, $J_{C\text{-}F}$ = 321 Hz), 131.3 (2 CH), 129.7 (2 CH), 129.0 (CH), 128.5 (CH), 128.3 (3 CH), 128.2 (2 CH), 127.3 (CH), 126.9 (C), 125.1 (C), 122.5 (C, $J_{C\text{-}F}$ = 222 Hz), 123.2 (CH), 118.6 (C), 34.5 (CH_3); **HRMS** (ESI) cal. for $C_{23}H_{16}F_3NO$ 379.1184, found 379.1183; IR (KBr): 2854, 1645, 1604, 1548, 1427, 1313, 1008, 785, 740 cm^{-1}

6-(Tert-butyl)-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ja)



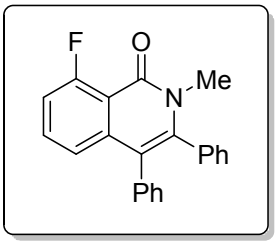
White solid, m.p. 135-138 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.48 (d, *J* = 8.0 Hz 1 H), 7.56 (dd, *J* = 8.0 Hz 1 H), 7.22-7.08 (m, 12 H), 3.32 (s, 3 H), 1.20 (t, 9 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.5 (C), 155.3 (C), 141.0 (C), 136.9 (C), 136.4 (C), 135.1 (C), 131.4 (2 CH), 129.9 (2 CH), 128.0 (2 CH), 128.0 (CH), 127.7 (2 CH), 127.5 (CH), 126.6 (CH), 124.6 (CH), 122.6 (C), 121.2 (CH), 119.1 (C), 35.0 (C), 34.1 (CH_3), 30.9 (3 CH_3); **HRMS** (ESI) cal. for $C_{26}H_{25}NO$ 367.1936, found 367.1934; IR (KBr): 2960.20, 1654.00, 1588.20, 1480.03, 1080.20, 925.40, 760.30, 698.30 cm^{-1}

2,8-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3ka)



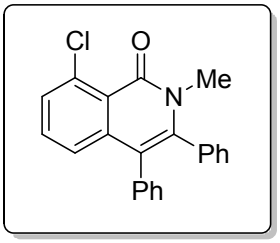
Yellow solid, m.p. 220-224 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.31-7.29 (m, 1 H), 7.23-7.18 (m, 9 H), 7.16-7.08 (m, 2 H), 7.04-6.95 (m, 1 H), 3.28 (s, 3 H), 3.02 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.4 (C), 141.5 (C), 141.1 (C), 138.8 (C), 137.1 (C), 135.2 (C), 131.5 (2 CH), 131.1 (CH), 129.7 (3 CH), 128.0 (2CH), 127.9 (2 CH), 127.8 (CH), 126.6 (CH), 123.6 (CH), 123.4 (CH), 118.7 (C), 34.2 (CH_3), 24.3 (CH_3); **HRMS** (ESI) cal. for $C_{23}H_{19}NO$ 325.1467, found 325.1467; IR (KBr): 2854, 1645, 1499, 1497, 1145, 948, 771, 730 cm^{-1}

8-Fluoro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3la)



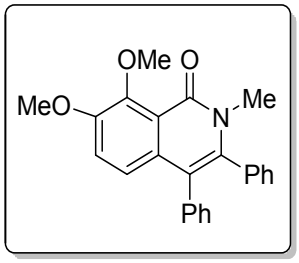
White solid, m.p. 228-230 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.40-7.35 (m, 1 H), 7.23-7.00 (m, 11 H), 6.88 (d, J = 8.0 Hz 1 H), 3.27 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.8 (C, $J_{C\text{-}F}$ = 381 Hz), 161.1 (C), 142.5 (C), 139.7 (C), 136.3 (C), 134.7 (C), 132.5 (CH, $J_{C\text{-}F}$ = 10 Hz), 131.4 (2 CH), 129.5 (2 CH), 128.2 (CH), 128.1 (2 CH),127.9 (2 CH), 126.8 (CH), 121.2 (CH, $J_{C\text{-}F}$ = 4 Hz), 117.0 (C), 114.1 (C, $J_{C\text{-}F}$ = 4 Hz), 113.2 (CH, $J_{C\text{-}F}$ = 21 Hz), 34.0 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{16}FNO$ 329.1216, found 329.1216; IR (KBr): 2923, 1651, 1611, 1483, 1417, 1134, 1048, 925, 781 cm^{-1}

8-Chloro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ma)



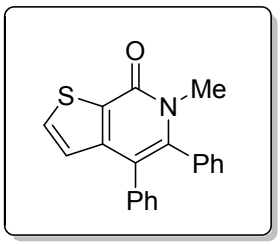
White solid, m.p. 220-222 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48-7.47 (m, 1 H), 7.46-7.29 (m, 1 H), 7.22-7.00 (m, 11 H), 3.29 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.8(C), 142.3 (C), 140.1 (C), 136.4 (C), 135.2 (C), 134.6 (C), 131.4 (2 CH), 131.3 (2 CH), 129.6 (2 CH), 129.4 (2 CH), 128.1 (CH),128.1 (CH), 127.9 (CH), 126.8 (CH), 124.5 (CH), 121.2 (C), 117.9 (C), 34.46 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{16}ClNO$ 345.0920, found 345.0919; IR (KBr): 2931, 1649, 1597, 1443, 1417, 1380, 1070, 935, 861, 784 cm^{-1}

7,8-Dimethoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3na)



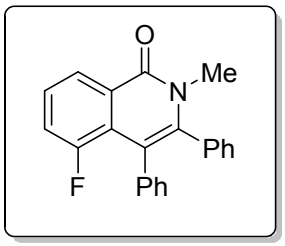
White solid, m.p. 221-223 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.20-7.09 (m, 7 H),, 7.08-7.05 (m, 2 H), 7.01-6.99 (m, 2 H), 6.85-6.83 (d, J = 8.4 Hz 1 H), 4.02 (s, 3 H), 3.87 (s, 3 H), 3.26 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.7 (C), 151.4 (C), 149.2 (C), 139.5 (C), 136.9 (C), 135.1 (C), 132.8 (C), 131.5 (2 CH), 129.9 (2 CH), 128.0 (2 CH), 127.9 (CH), 127.8 (2 CH), 126.6 (CH), 121.6 (CH), 119.8 (C), 118.1 (CH), 117.8 (C), 61.5 (OCH_3), 56.6 (CH_3), 34.2 (CH_3), 55.1 (CH_3); **HRMS** (ESI) cal. for $C_{24}H_{21}NO_3$ 371.1521, found 371.1520; IR (KBr): 2954, 1647, 1610, 1483, 1427, 1070, 1001, 771 cm^{-1}

6-Methyl-4,5-diphenylthieno[2,3-c]pyridin-7(6H)-one (3oa)



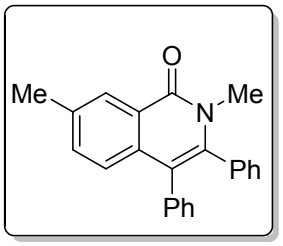
Yellow solid, m.p. 242-243 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.0 Hz 1 H), 7.26-7.23 (m, 3 H), 7.17-7.09 (m, 5 H), 7.05-7.03 (m, 2 H), 6.88 (d, J = 5.2 Hz 1 H), 3.37 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.8 (C), 145.5 (C), 142.3 (C), 136.8 (C), 134.6 (C), 132.7 (CH), 130.6 (CH), 130.1 (CH), 128.8 (CH), 128.4 (CH), 128.3 (C), 127.8 (CH), 126.7 (CH), 124.7 (CH), 117.7 (C), 34.2 (CH_3); **HRMS** (ESI) cal. for $C_{20}H_{15}NOS$ 317.0874, found 317.0872; IR (KBr): 2923, 1640, 1577, 1490, 1440, 780, 698 cm^{-1}

5-Fluoro-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3pa)



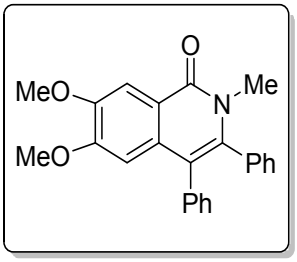
Yellow solid, m.p. 244-246 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.39 (d, J = 8.0 Hz 1 H), 7.45-7.39 (m, 1 H), 7.23-7.17 (m, 4 H), 7.11-7.02 (m, 7 H), 3.20 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.6 (C), 158.1 (C, $J_{C\text{-}F}$ = 253 Hz), 142.6 (C), 138.3 (2 C), 134.6 (C), 130.6 (CH, $J_{C\text{-}F}$ = 3 Hz), 129.8 (2 CH), 128.2 (CH), 128.1 (2 CH), 127.1 (3 CH), 126.3 (CH), 125.9 (C, $J_{C\text{-}F}$ = 9 Hz), 124.0 (CH $J_{C\text{-}F}$ = 4 Hz), 119.0 (CH), 118.7 (CH), 114.6 (C), 34.5 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{16}FNO$ 329.1216, found 329.1215; IR (KBr): 2954, 1651, 1611, 1548, 1416, 1002, 833, 782 cm^{-1}

2,7-Dimethyl-3,4-diphenylisoquinolin-1(2H)-one (3qa)



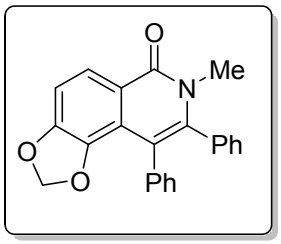
White solid, m.p. 232-234 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.35 (s, 1 H), 7.34-7.32 (m, 1 H), 7.24-7.02 (m, 11 H), 3.33 (s, 3 H), 2.47 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.6 (C), 140.2 (C), 136.6 (2 C), 135.1 (C), 134.8 (C), 133.4 (CH), 131.4 (2 CH), 130.0 (CH), 128.1 (3 CH), 127.8 (2 CH), 127.3 (2 CH), 126.6 (CH), 125.3 (CH), 124.8 (C), 118.7 (C), 34.3 (CH_3), 21.3 (CH_3); **HRMS** (ESI) cal. for $C_{23}H_{19}NO$ 325.1467, found 325.1467; IR (KBr): 2923, 1645, 1499, 1340, 1142, 948, 770, 730 cm^{-1}

6,7-Dimethoxy-2-methyl-3,4-diphenylisoquinolin-1(2H)-one (3ra)



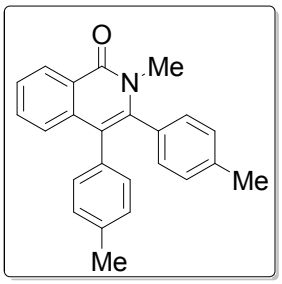
White solid, m.p. 240-242 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.90 (s, 1 H), 7.18-7.00 (m, 10 H), 6.40 (s, 1 H), 4.00 (s, 3 H), 3.64 (s, 3 H), 3.32 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.9 (C), 153.0 (C), 149.0 (C), 139.8 (C), 136.6 (C), 135.1 (C), 132.5 (2 CH), 131.3 (2 CH), 130.0 (2 CH), 128.0 (2 CH), 128.0 (2 CH), 127.8 (CH), 126.7 (CH), 118.9 (CH), 118.4 (CH), 107.6 (C), 105.5 (C), 55.6 (OCH_3), 55.1 (OCH_3), 34.3 (CH_3); **HRMS** (ESI) cal. for $C_{24}H_{21}NO_3$ 371.1521, found 371.1520; IR (KBr): 2954, 1645, 1604, 1483, 1415, 1230, 1143, 1072, 1001, 856, 781 cm^{-1}

7-Methyl-8,9-diphenyl-[1,3]dioxolo[4,5-f]isoquinolin-6(7H)-one (3sa)



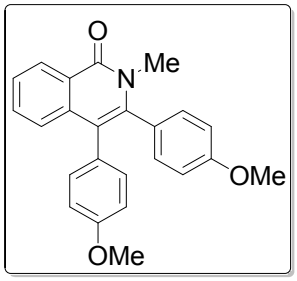
White solid, m.p. 248-250 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.4 Hz 1 H), 7.21-7.16 (M, 3 H), 7.07-7.00 (m, 8 H), 5.70 (s, 2 H), 3.26 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.0 (C), 150.5 (C), 142.0 (C), 141.8 (C), 137.4 (C), 134.8 (C), 131.2 (2 CH), 129.9 (2 CH), 128.0 (2 CH), 126.9 (2CH), 126.4 (CH), 123.6 (CH), 121.6 (C), 120.3 (C), 114.5 (C), 108.9 (CH), 101.4 (CH_2), 34.1 (CH_3); **HRMS** (ESI) cal. for $C_{23}H_{17}NO_3$ 355.1208, found 355.1206; IR (KBr): 2931, 1720, 1634, 1248, 1227, 1180, 925, 771, 705 cm^{-1}

2-Methyl-3,4-di-p-tolylisoquinolin-1(2H)-one (3ab)



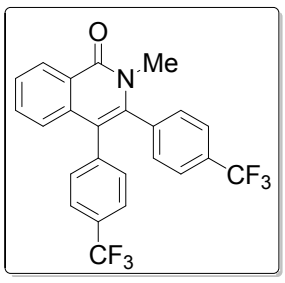
Yellow solid, m.p. 197-198 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (d, *J* = 7.2 Hz 1 H), 7.80-7.43 (M, 2 H), 7.14 (d, *J* = 7.6 Hz, 1 H), 7.03-6.91 (m, 8 H), 3.13 (s, 3 H), 2.26 (s, 3 H), 2.26 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.8 (C), 141.3 (C), 137.8 (C), 137.4 (C), 136.1 (C), 133.5 (C), 132.2 (2 CH), 131.8 (2 CH), 131.3 (2 CH), 129.7 (2CH), 128.8 (CH), 128.6 (CH), 127.7 (CH), 126.4 (CH), 125.3 (CH), 124.8 (C), 118.7 (C), 34.2 (CH_3), 21.2 (CH_3), 21.1 (CH_3); **HRMS** (ESI) cal. for $C_{24}H_{21}NO$ 339.1623, found 339.1621; IR (KBr): 2854, 1640, 1592, 1480, 1411, 1080, 817, 773 cm^{-1}.

3,4-Bis(4-methoxyphenyl)-2-methylisoquinolin-1(2H)-one (3ac)



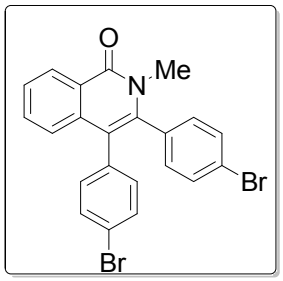
Yellow solid, m.p. 161-162 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.52 (d, *J* = 7.6 Hz 1 H), 7.51-7.42 (m, 2 H), 7.16 (d, *J* = 8.0 Hz, 1 H), 7.01 (dd, *J* = 7.6 Hz 2 H), 6.99 (dd, *J* = 7.6 Hz 2 H), 6.75-6.71 (m, 4 H), 3.73 (s, 6 H), 3.32 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.7 (C), 159.0 (C), 158.1 (C), 141.2 (C), 137.5 (C), 132.4 (2 CH), 131.8 (CH), 131.0 (2 CH), 128.8 (C), 127.7 (CH), 127.5 (C), 126.3 (CH), 125.3 (CH), 124.8 (C), 118.7 (C), 113.5 (2 CH), 113.3 (2 CH), 55.0 (OCH_3), 55.0 (OCH_3), 34.2 (CH_3); **HRMS** (ESI) cal. for $C_{24}H_{21}NO_3$ 371.1521, found 371.1518; IR (KBr): 2923, 1730, 1644, 1644, 1548, 1427, 1180, 925, 862, 731 cm^{-1}

2-Methyl-3,4-bis(4-(trifluoromethyl)phenyl)isoquinolin-1(2H)-one (3ad)



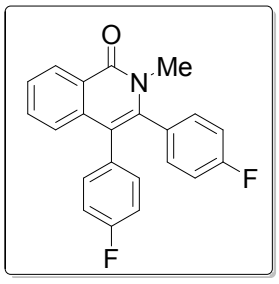
White solid, m.p. 198-200 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.56-8.54 (m, 1 H), 7.57-7.46 (m, 8 H), 7.27-7.25 (m, 2 H), 7.19-7.17 (m,2 H), 7.05-7.03 (m, 1 H), 3.31 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.4 (C), 139.9 (2 C), 138.1 (C), 136.3 (C), 132.4 (CH), 131.8 (2 CH), 130.8 (C, $J_{C\text{-}F}$ = 32 Hz), 130.3 (2 CH), 129.1 (C, $J_{C\text{-}F}$ = 32 Hz), 129.0 (C), 128.1 (CH), 127.3 (CH), 125.5 (CH), 125.2 (CH), 125.1 (CH), 125.0 (CH), 122.3 (C, $J_{C\text{-}F}$ = 35 Hz), 117.7 (C), 34.3 (CH_3); **HRMS** (ESI) cal. for $C_{24}H_{15}F_6NO$ 447.1058, found 447.1057; IR (KBr): 2923, 2399, 1639, 1604, 1548, 1447, 1080, 817, 771, 728 cm^{-1}

3,4-Bis(4-bromophenyl)-2-methylisoquinolin-1(2H)-one (3ae)



White solid, m.p. 202-204 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (d, J = 8.4 Hz 1 H), 7.39(dd, J =16.8 Hz 2 H), 7.39-7.33 (m, 4 H), 7.09-7.06 (m, 1 H), 6.99 (dd, J = 8.4 Hz 2 H), 6.92 (d, J = 8.4 Hz 2 H) , 3.30 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.5 (C), 140.1 (C), 136.6 (C), 135.1 (C), 133.6 (C), 133.0 (2 CH), 132.2 (CH), 131.7 (2 CH), 131.4 (4 CH), 127.9 (CH), 127.0 (CH), 125.0 (CH), 124.9 (C), 122.8 (C), 121.3 (C), 117.8 (2 C), 34.3 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{15}Br_2NO$ 468.9520, found 468.9519; IR (KBr): 2954, 1640, 1604, 1548, 1427, 1159, 1054, 771, 730 cm^{-1}

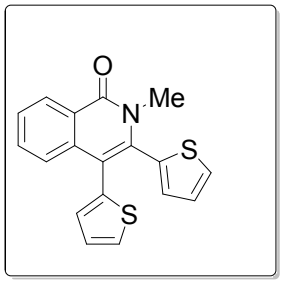
3,4-Bis(4-fluorophenyl)-2-methylisoquinolin-1(2H)-one (3af)



White solid, m.p. 173-175 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.54 (d, J = 8.0 Hz 1 H), 7.55-7.47 (m, 2 H), 7.11-7.06 (m, 3 H), 7.01-6.87 (m, 6 H),3.30 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.6 (C), 162.2 (C, $J_{C\text{-}F}$ = 248 Hz), 161.6 (C, $J_{C\text{-}F}$ = 246 Hz), 140.4 (C), 136.9 (C), 133.0 (2 CH, $J_{C\text{-}F}$ = 8 Hz), 132.2 (C), 132.1 (CH), 131.7 (2 CH, $J_{C\text{-}F}$ = 8 Hz), 130.9 (C), 127.9 (CH), 126.8 (CH), 125.1 (CH), 124.4 (C), 118.1 (C), 115.6 (CH), 115.4 (CH), 115.2 (CH),115.0 (CH), 34.2 (CH_3); **HRMS** (ESI) cal. for $C_{22}H_{15}F_2NO$ 347.1122, found 347.1121; IR (KBr): 2928,

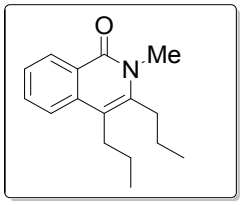
1640, 1604, 1508, 1482, 1080, 817, 771, 728 cm^{-1}

2-Methyl-3,4-di(thiophen-2-yl)isoquinolin-1(2H)-one (3ag)



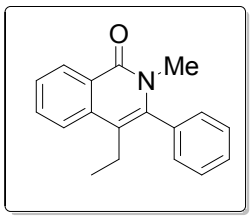
Brown solid, m.p. 228-230 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 7.6 Hz 1 H), 7.57-7.50 (m, 2 H), 7.36-7.31 (m, 2 H), 7.25-7.24 (m, 1 H), 6.94-6.91 (m, 3 H), 6.83-6.82 (m, 1 H), 3.31 (s, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.6 (C), 137.1 (C), 136.9 (C), 136.2 (C), 134.9 (C), 132.3 (CH), 130.1 (CH), 129.7 (CH), 127.7 (2 CH), 127.3 (CH), 126.6 (CH), 126.5 (2 CH), 125.4 (CH), 125.1 (C), 114.2 (C), 34.2 (CH_3); **HRMS** (ESI) cal. for $C_{18}H_{13}NOS_2$ 323.0439, found 323.0441; IR (KBr): 2957, 1640, 1604,1548,1470, 780, 760, 700 cm^{-1}

2-Methyl-3,4-dipropylisoquinolin-1(2H)-one (3ah)



Yellow solid, m.p. 60-62 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.44 (d, *J* = 8.0 Hz 1 H), 7.60-7.59 (m, 2 H), 7.41-7.36 (m, 1 H), 3.60 (s, 3 H), 2.71-2.64 (m, 4 H), 1.64-1.53 (m, 4 H) , 1.08-1.01 (m, 6 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.9 (C), 139.8 (C), 136.4 (C), 131.8 (C), 128.2 (C), 125.5 (2 CH), 124.7 (CH), 122.5 (2 CH), 113.8 (4 CH), 31.7 (CH), 31.2 (CH), 29.76 (CH), 23.60 (C), 22.5 (C), 14.3 (C), 14.1 (CH_3); **HRMS** (ESI) cal. for $C_{16}H_{21}NO$ 243.1623, found 243.1622; IR (KBr): 2931, 1645, 1547, 1457, 1057, 898, 740 cm^{-1}

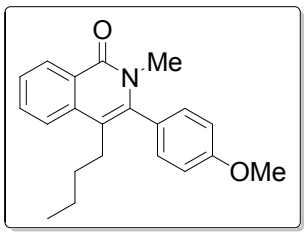
4-Ethyl-2-methyl-3-phenylisoquinolin-1(2H)-one (3ai)



Yellow solid, m.p. 130-132 °C; **^{1} H NMR** (400 MHz, $CDCl_3$): δ 8.52-8.50 (m, 1 H), 7.84-7.65 (m, 2 H), 7.52-7.44 (m, 4 H), 7.28-7.24 (m, 2 H), 3.21 (s, 3 H), 2.40 (q, 2 H), 1.05 (t, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.5 (C), 140.1 (C), 136.0 (C), 135.6 (C), 132.1 (CH), 129.1 (CH), 129.0 (2 CH), 128.7 (CH), 128.4

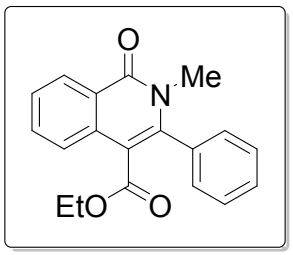
(CH), 127.7 (CH), 126.3 (CH), 125.7 (C), 123.1 (CH), 116.7 (C), 34.11 (CH_3), 22.6 (CH_2), 14.8 (CH_3); **HRMS** (ESI) cal. for $C_{18}H_{17}NO$ 263.1310, found 263.1310; IR (KBr): 3010, 1641, 1485, 1409, 1186, 1007, 840, 787, 704 cm^{-1}

4-Butyl-3-(4-methoxyphenyl)-2-methylisoquinolin-1(2H)-one (3aj)



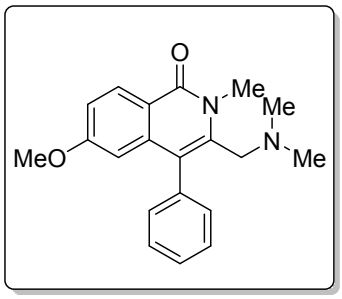
White semi-solid, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.51-8.49 (m, 1 H),, 7.67-7.61 (m, 2 H), 7.47-7.42 (m, 1 H), 7.16-7.14 (m, 2 H), 7.00-6.96 (m, 2 H), 3.84 (s, 3 H), 3.20 (s, 3 H), 2.39-2.35 (m, 2 H), 1.42-1.37 (m, 2 H), 1.20-1.16 (m, 2 H),0.77-0.73 (m, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.4 (C), 159.6 (C), 140.0 (C), 136.2 (C), 131.8 (CH), 130.3 (2 CH), 128.1 (CH), 127.7 (C), 126.1 (CH), 123.1 (CH), 115.9 (C), 114.1 (2 CH), 113.9 (C), 55.22 (OCH_3), 33.96 (CH_3), 32.49 (CH_3), 28.1 (CH_2), 22.7 (CH_2), 13.7 (CH_2); **HRMS** (ESI) cal. for $C2_1H_{23}NO_2$ 321.1729, found 321.1729; IR (KBr): 2957, 1642, 1611, 1518, 1411, 1180, 840, 771, 700 cm^{-1}

Ethyl 2-methyl-1-oxo-3-phenyl-1,2-dihydroisoquinoline-4-carboxylate (3ak)



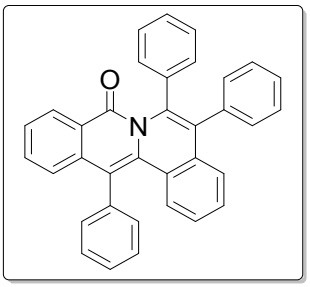
White solid, m.p. 167-170 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 7.6 Hz 1 H), 7.67-7.65 (m, 2 H), 7.53-7.49 (m, 1 H), 7.47-7.44 (m, 3 H), 7.36-7.33 (m, 2 H), 3.94 (q, 2 H), 3.30 (s, 3 H), 0.84 (t, 3 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.9 (C), 162.5 (C), 143.5 (C), 134.4 (C), 133.3 (C), 132.7 (CH), 129.3 (CH), 129.0 (2 CH), 128.6 (2 CH), 128.0 (CH), 127.2 (CH), 124.5 (C), 123.9 (CH), 112.5 (C), 61.0 (CH_2), 34.0 (CH_3), 13.4 (CH_3); **HRMS** (ESI) cal. for $C_{19}H_{17}NO_3$ 307.1208, found 307.1208; IR (KBr): 2923, 1730, 1644, 1284, 1247, 1193, 761, 705 cm^{-1}

3-((Dimethylamino)methyl)-6-methoxy-2-methyl-4-phenylisoquinolin-1(2H)-one (3fj)



White solid, m.p. 167-170 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 8.8 Hz 1 H), 7.46-7.40 (m, 3 H), 7.19-7.02 (m, 2 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.28 (s, 1 H), 3.81 (s, 3 H), 3.64 (s, 3 H), 3.24 (s, 2 H), 1.23 (s, 6 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.8 (C), 162.2 (C), 139.0 (C), 137.2 (C), 136.9 (C), 131.6 (2 CH), 129.9 (CH), 128.5 (2 CH), 127.6 (CH), 119.7 (C), 118.9 (C), 115.1 (CH), 107.3 (CH), 57.8 (OCH_3), 55.1 (CH_2), 44.6 (2 CH_3), 31.1 (CH_3); **HRMS** (ESI) cal. for $C_{20}H_{22}N_2O_2$ 322.1681, found 322.1682; IR (KBr): 2954, 1730.00, 1644.60, 1284.02, 1247.03, 1193.10, 761.80, 705.00 cm^{-1}

5,6,13-Triphenyl-8H-isoquinolino[3,2-a]isoquinolin-8-one (3ta)



Yellow solid, m.p. 165-167 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.0 Hz 1 H), 7.61-7.47 (m, 6 H), 7.42 (t, *J* = 16.0 Hz, 1 H), 7.33 (dd, *J* = 8.0 Hz 1 H), 7.27-7.06 (m, 13 H), 6.86 (t, *J* = 16.0 Hz, 1 H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.2 (C), 138.6 (C), 137.1 (2 C), 136.3 (C), 136.2 (C), 133.8 (C), 133.1 (C), 132.3 (CH), 132.2 (2 CH), 131.5 (2 CH), 129.7 (2 CH), 129.0 (CH), 128.9 (2 CH), 128.5 (CH), 128.1 (CH), 127.9 (2 CH), 127.6 (C), 127.4 (CH), 127.1 (2 CH), 126.9 (CH), 126.8 (CH), 126.7 (C), 126.4 (CH), 126.3 (CH), 125.8 (C), 125.6 (CH), 125.5 (CH), 116.9 (C); **HRMS** (ESI) cal. for $C_{35}H_{23}NO$ 473.1780, found 473.1778; IR (KBr): 2923, 1644, 1538, 1180, 925, 862, 701 cm^{-1}

References

1. D. D. Perrin, W. L. F. Armarego, In Purification of Laboratory Chemicals, 3rd ed.; Pergamon Press: New York, 1988.

2. B. Li and P. H. Dixneuf, *Chem. Soc. Rev.*, 2013

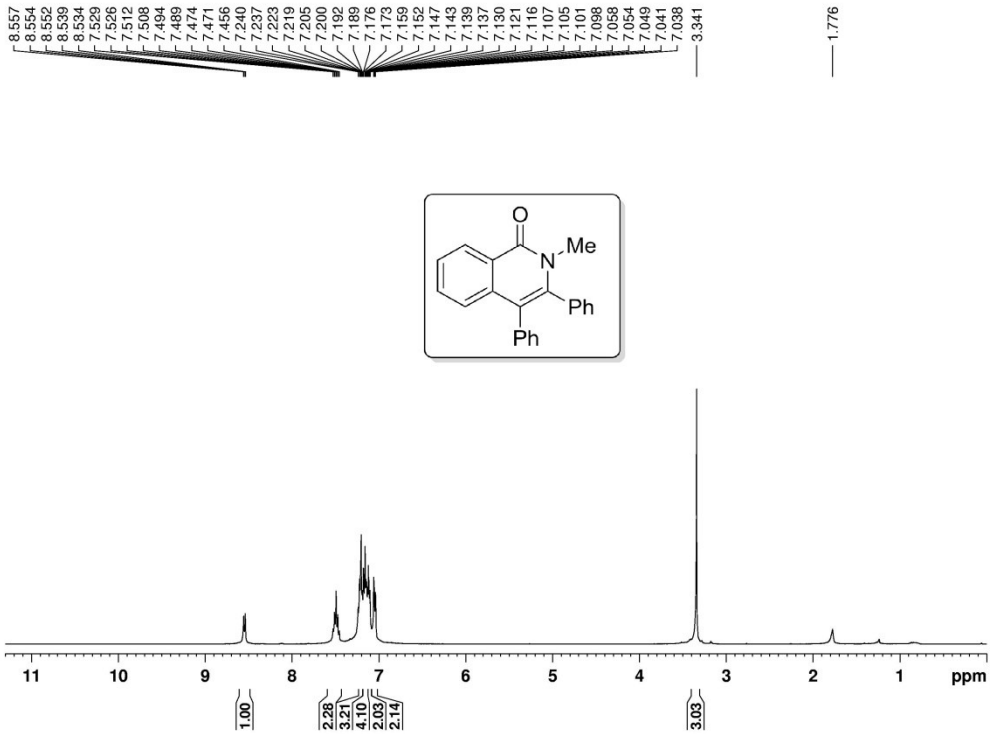
3 J. Wencel-Delord, T. Droge, F. Liu and F. Glorius, *Chem. Soc. Rev.*, 2011, **40**, 4740

4. L. Ackermann, A. V. Lygin and N. Hofmann, *Angew. Chem., Int. Ed.*, 2011, **50**, 6379

5. C.-C. Liu, K. Parthasarathy and C.-H. Cheng, *Org. Lett.*, 2010, **12**, 3518

6- T. K. Hyster and T. Rovis, *J. Am. Chem. Soc.*, 2010, **132**, 10565

^{1}H and ^{13}C NMR spectra of compound **3aa.**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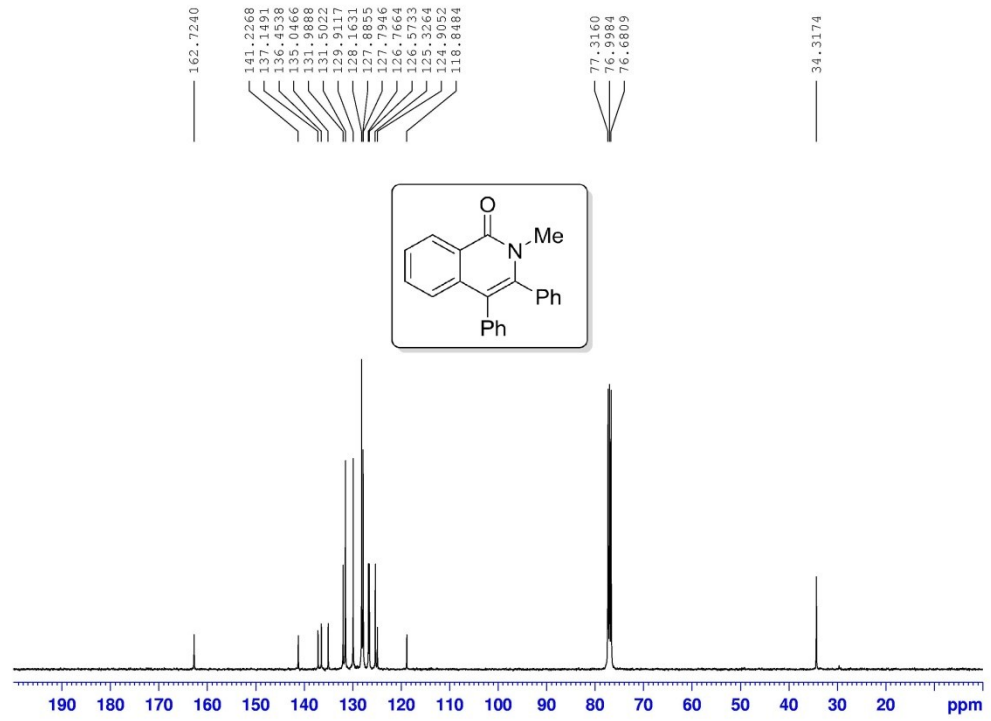
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Me
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160
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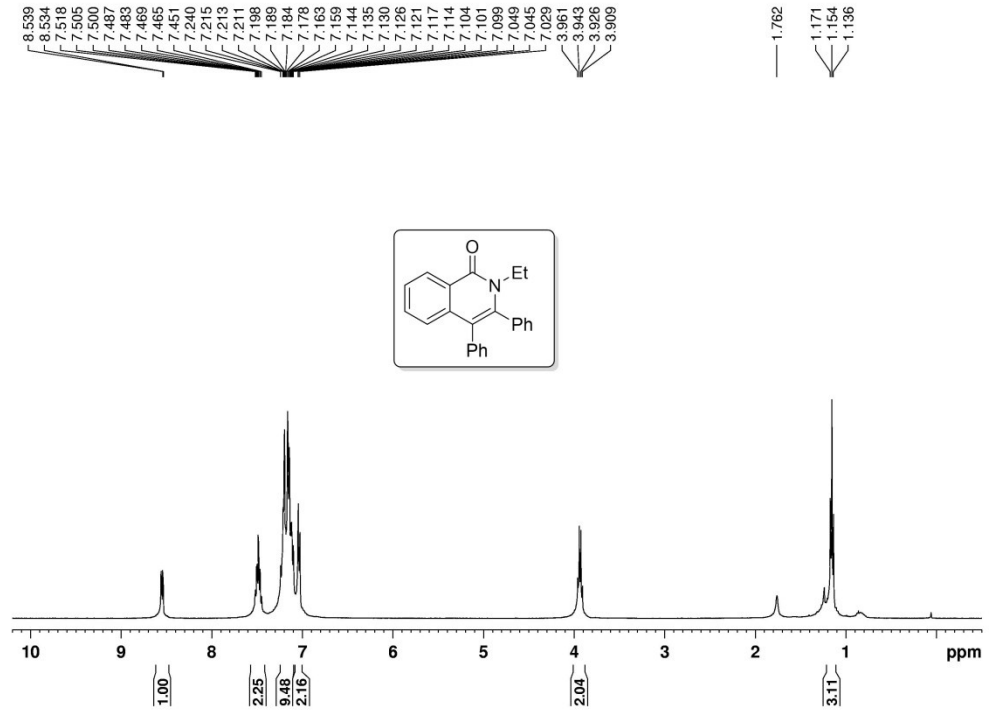
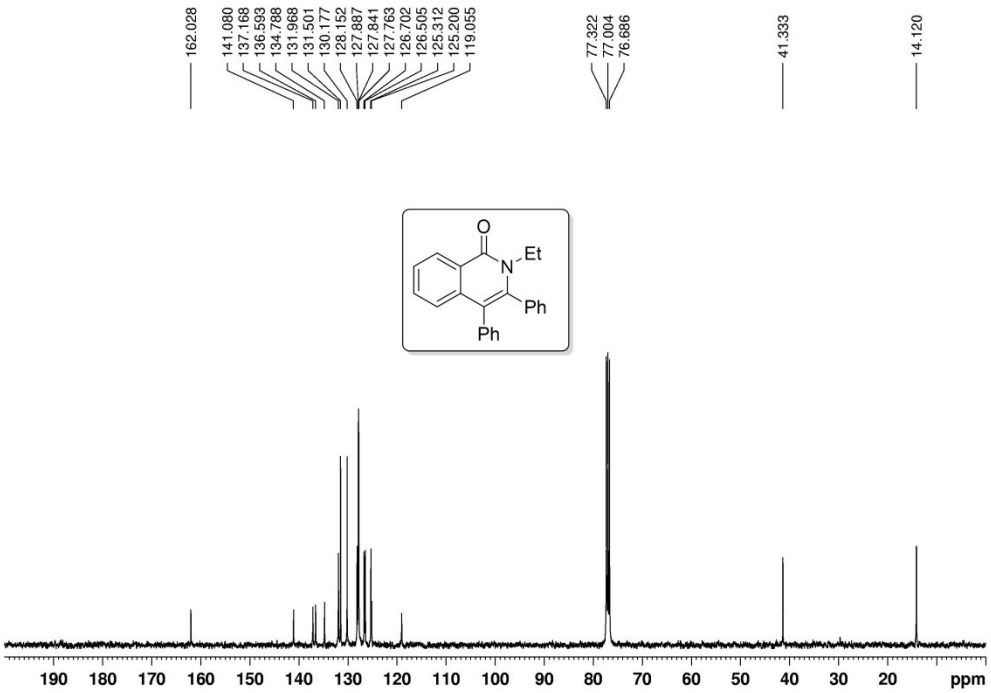
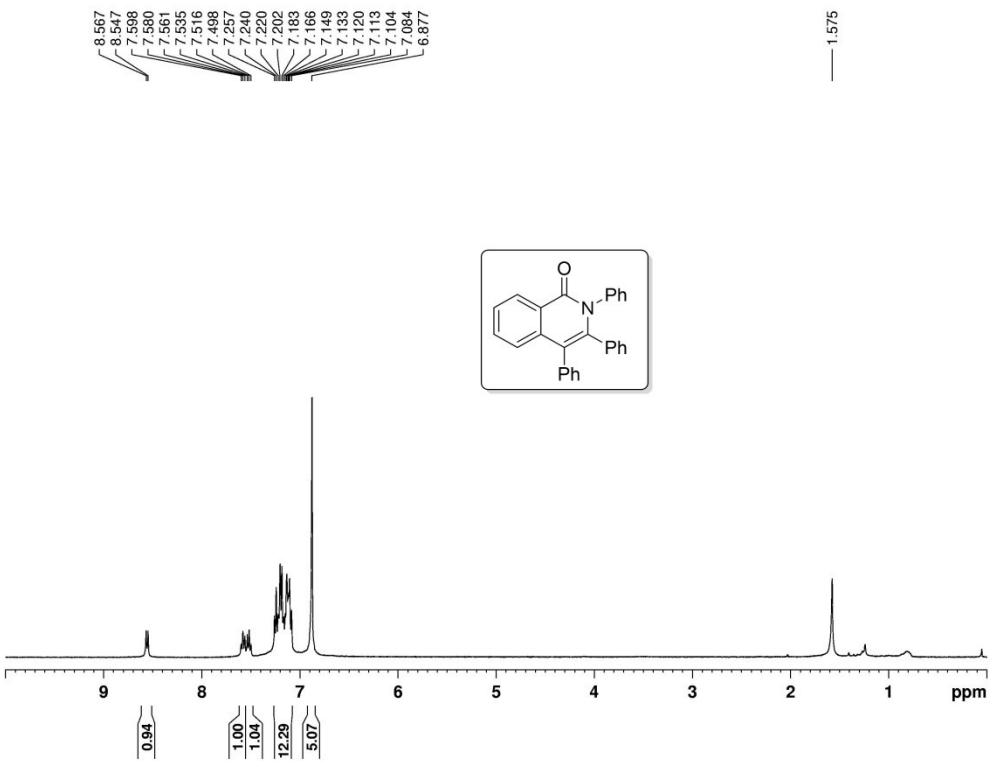
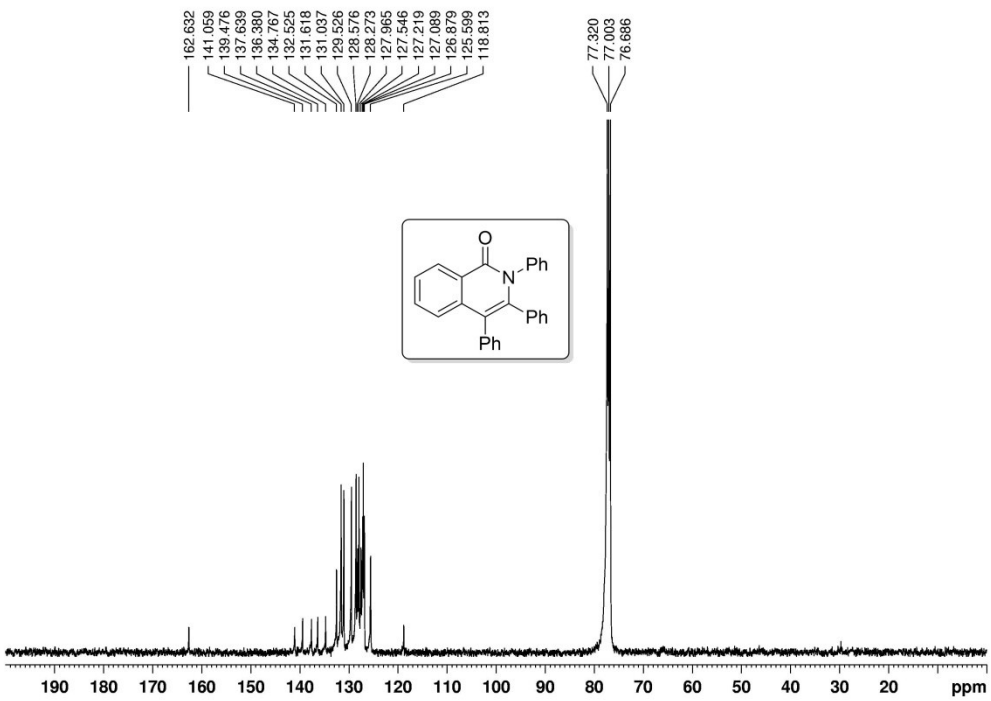
^{1}H and ^{13}C NMR spectra of compound **3ba**



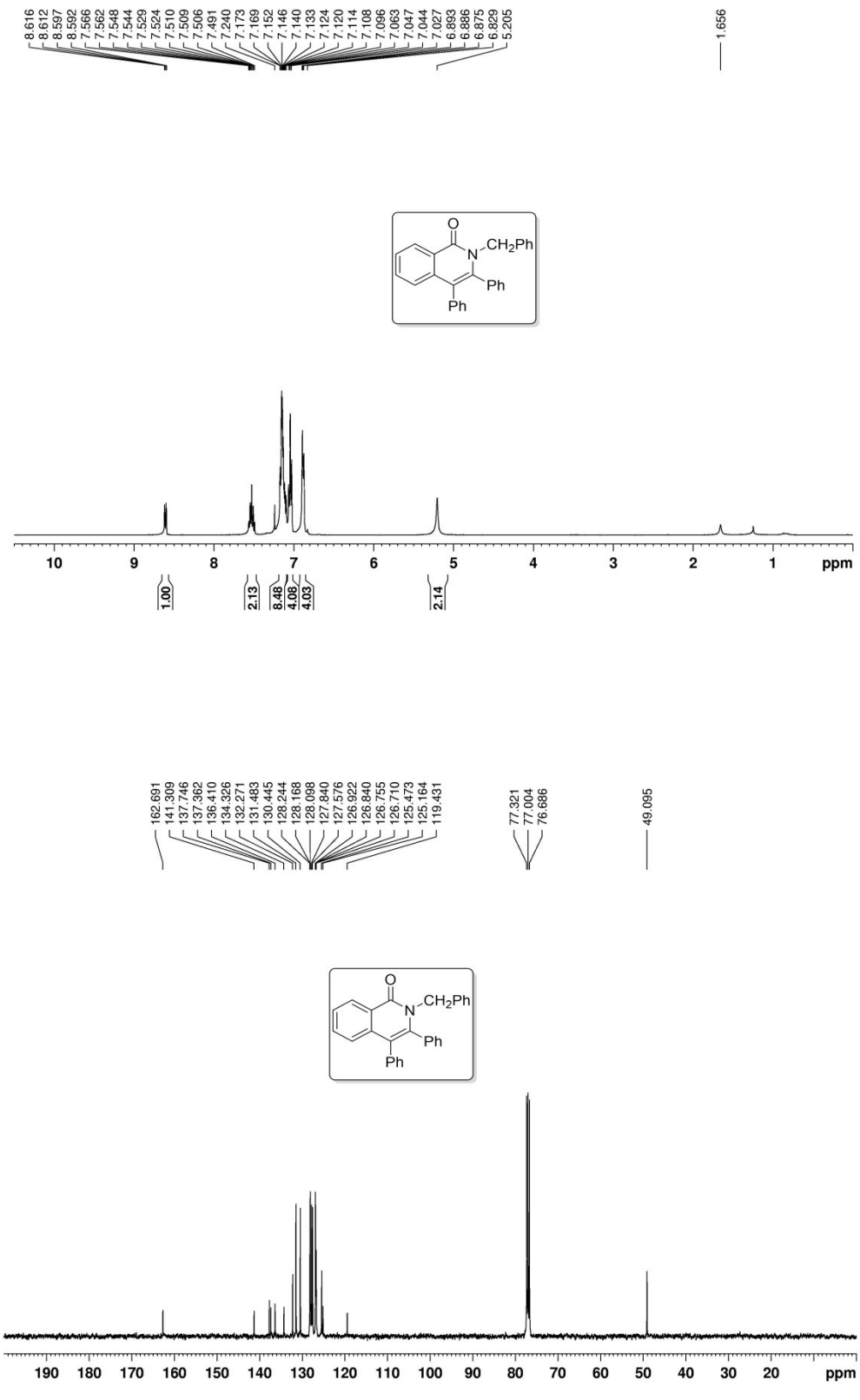


^{1}H and ^{13}C NMR spectra of compound **3ca.**

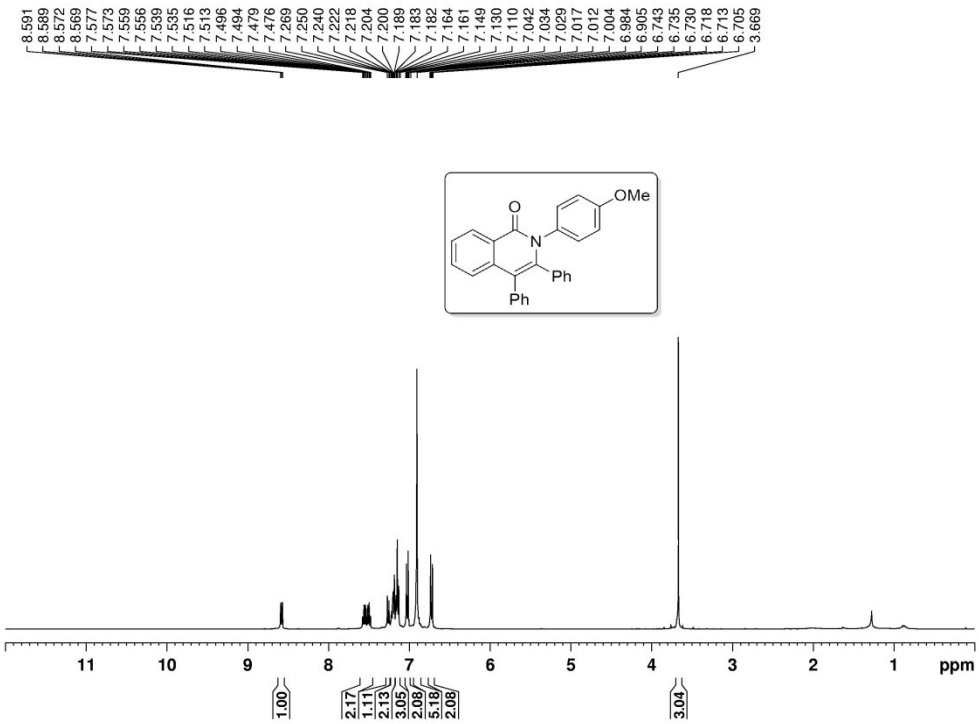


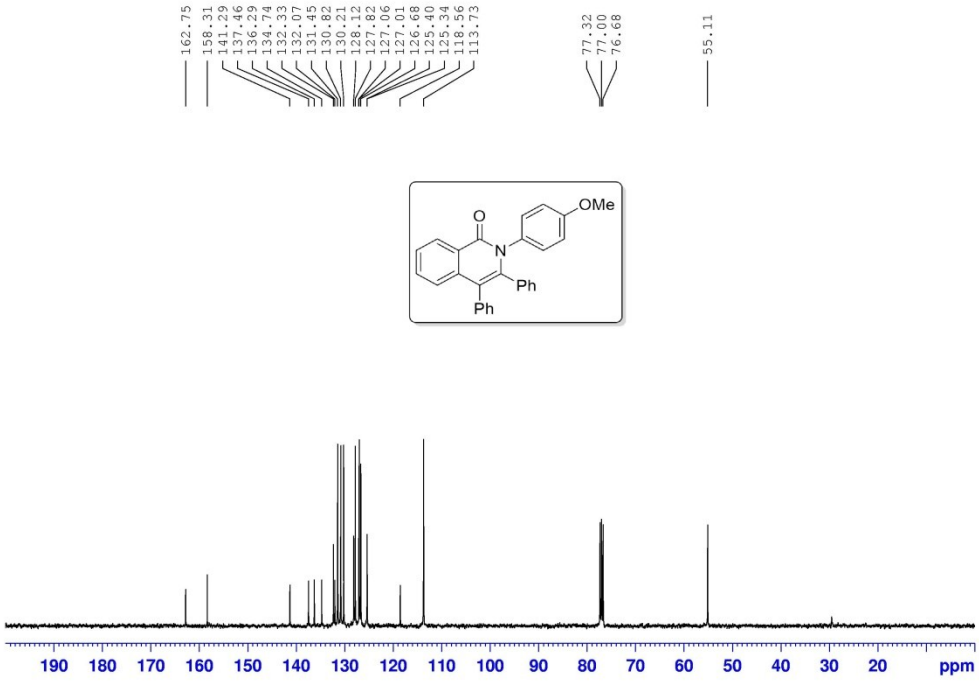


^{1}H and ^{13}C NMR spectra of compound **3da.**

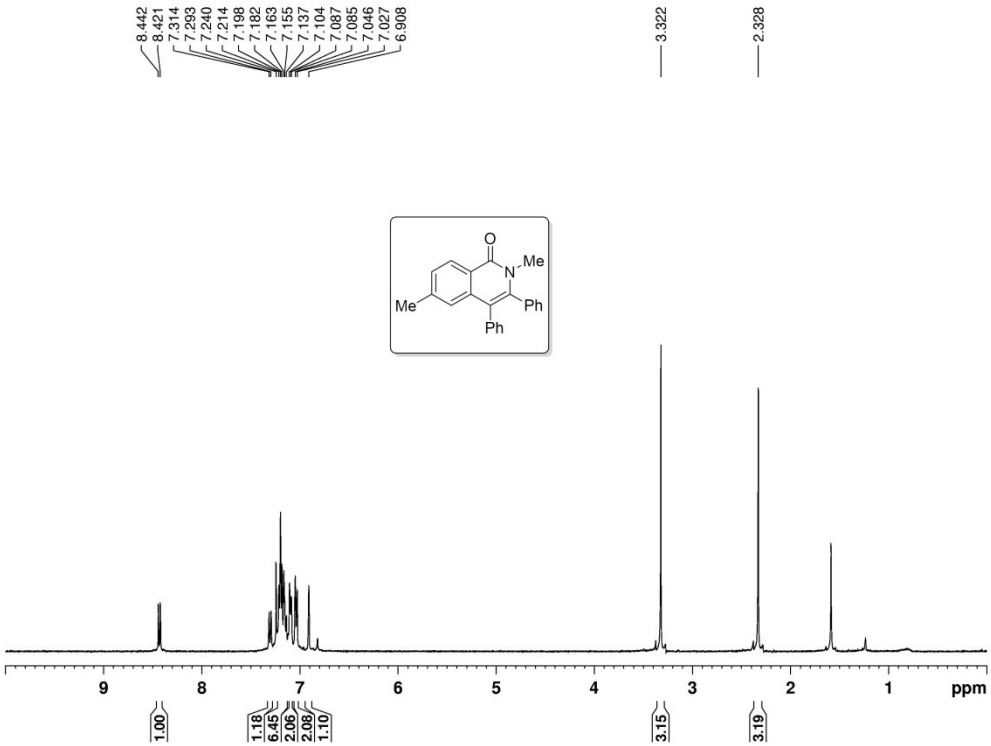


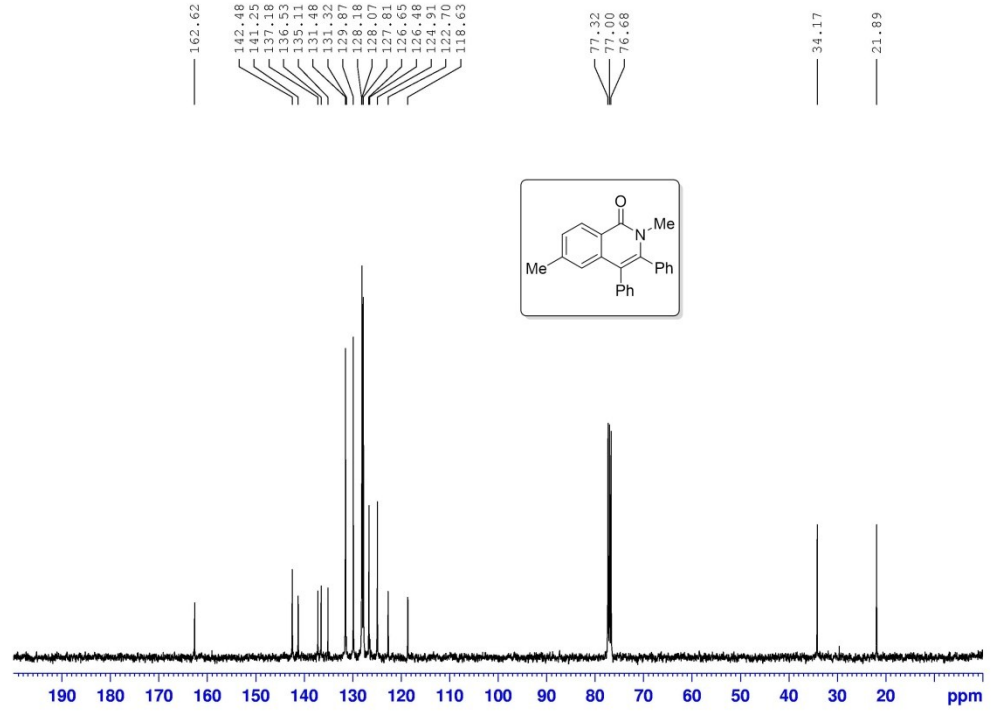
^{1}H and ^{13}C NMR spectra of compound **3ea.**



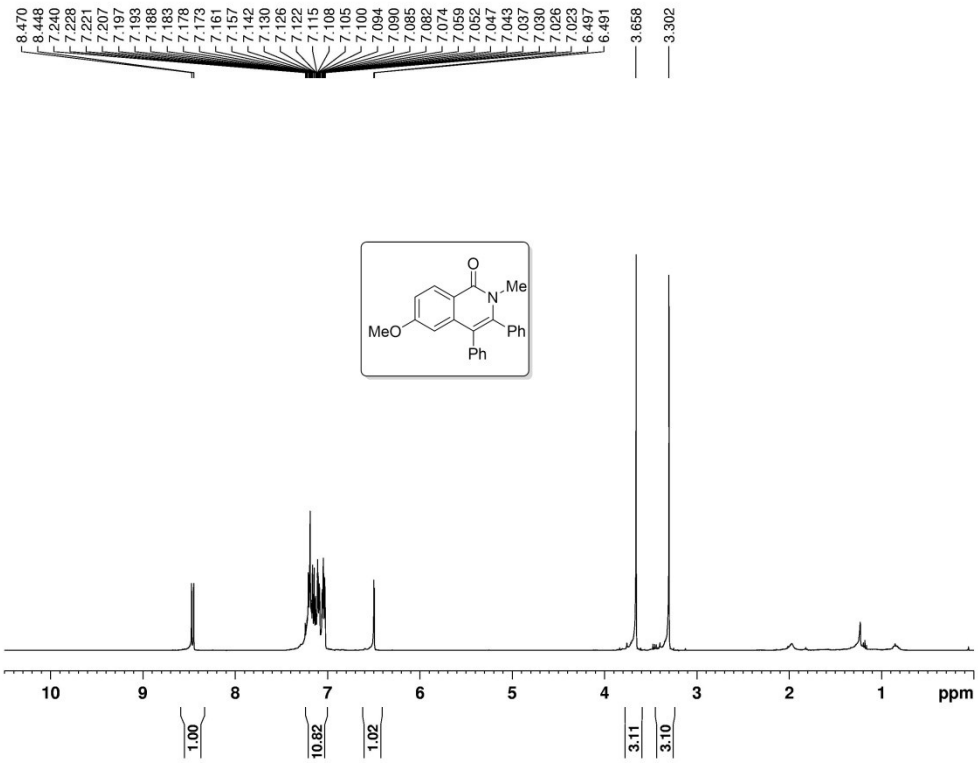


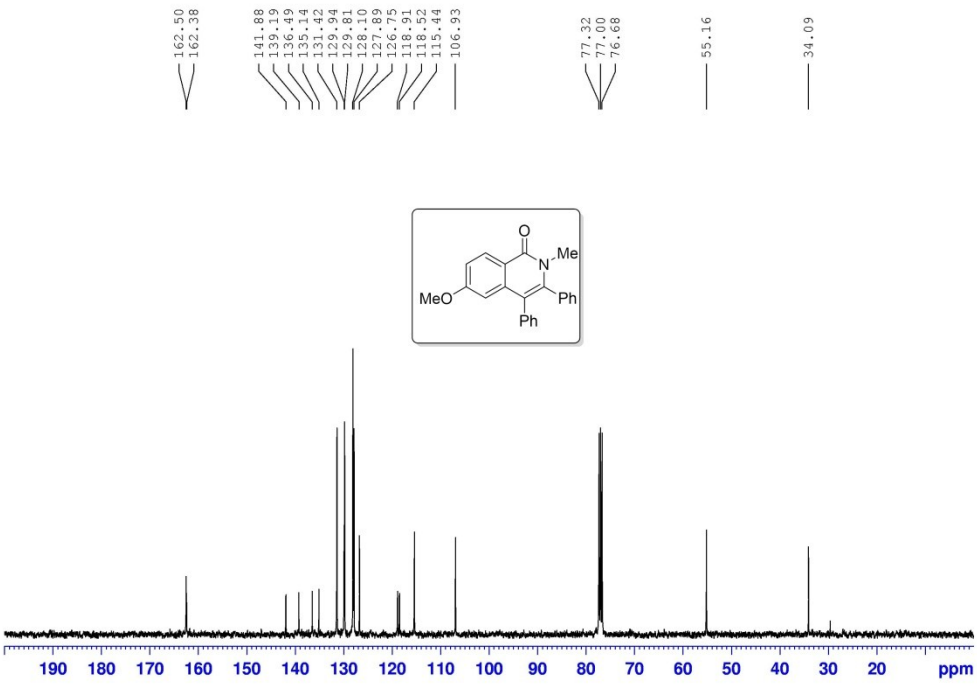
^{1}H and ^{13}C NMR spectra of compound **3fa.**



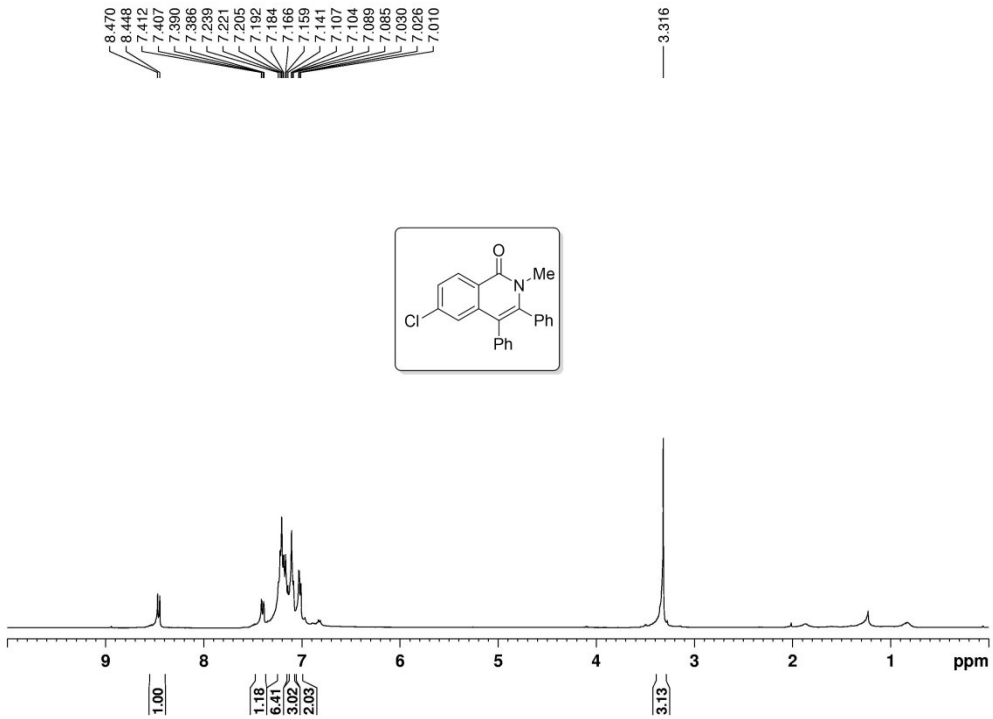


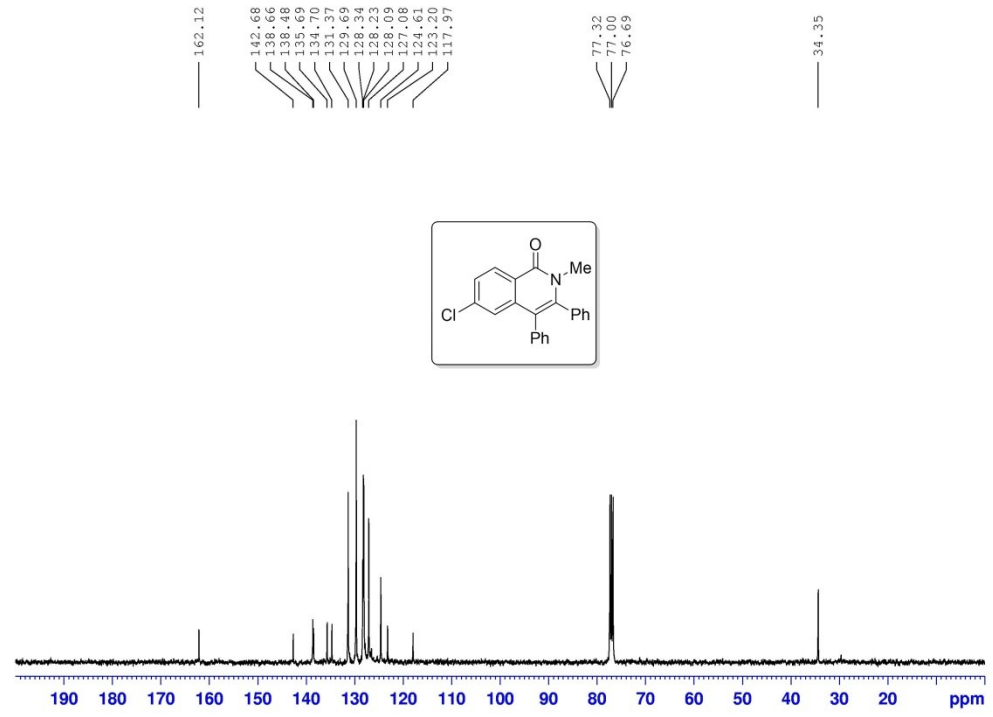
^{1}H and ^{13}C NMR spectra of compound **3ga.**



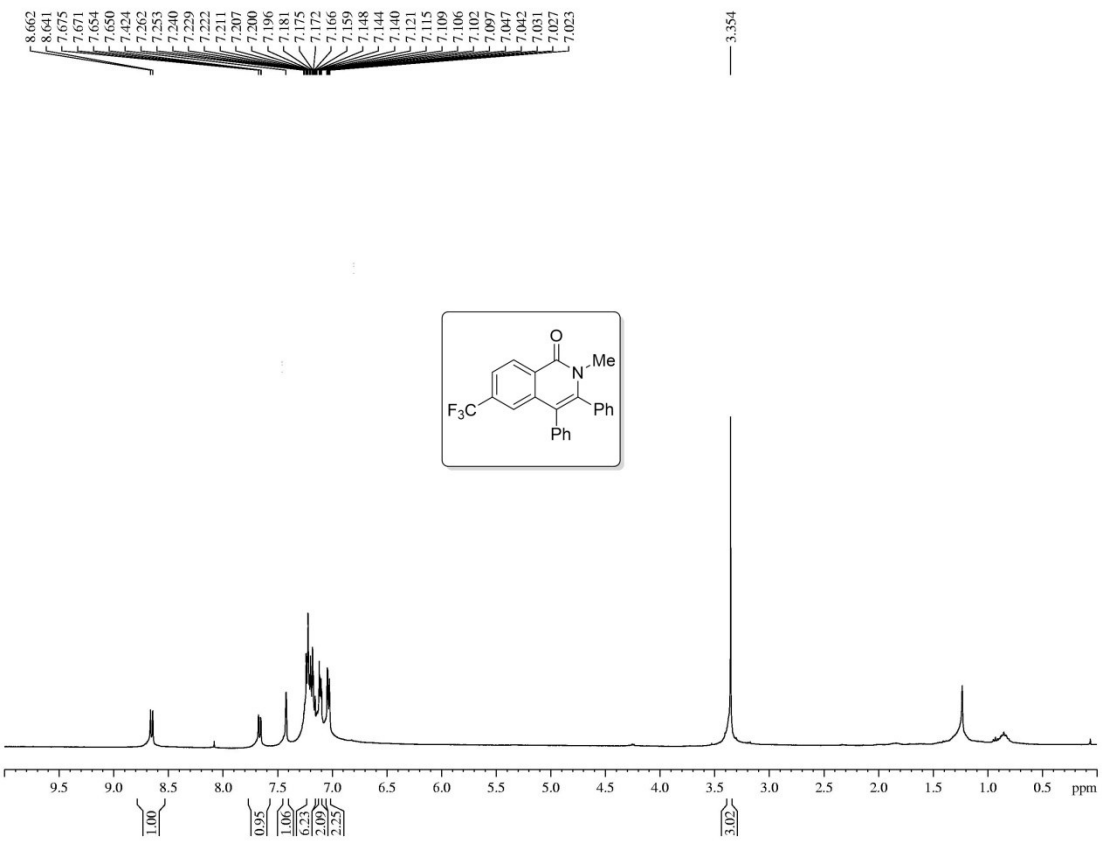


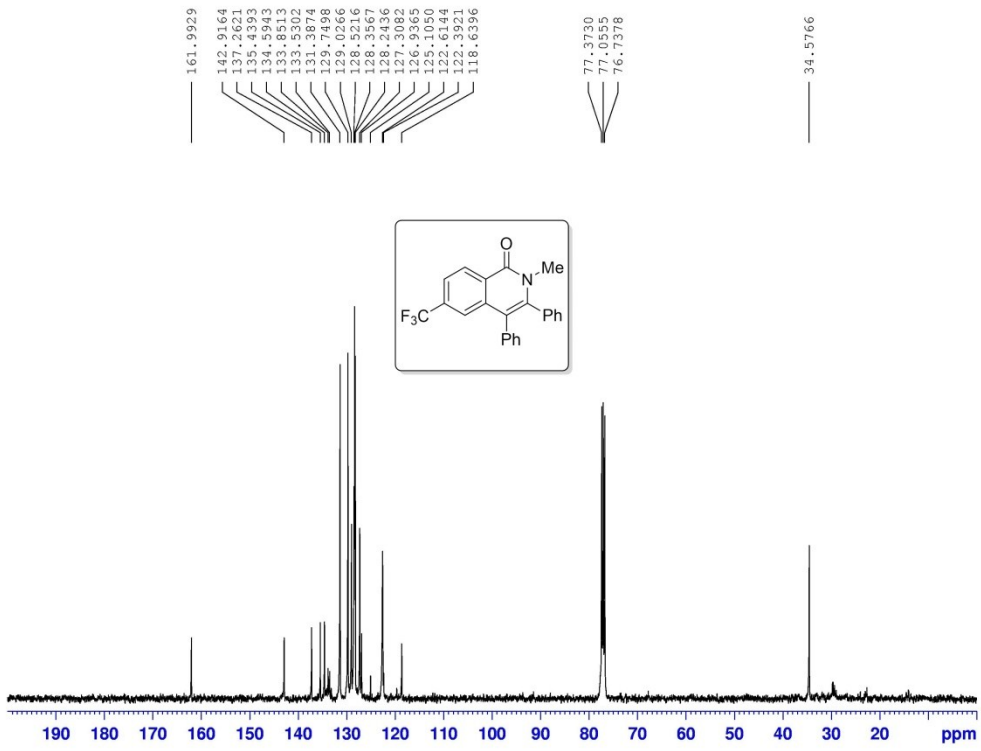
^{1}H and ^{13}C NMR spectra of compound **3ha.**



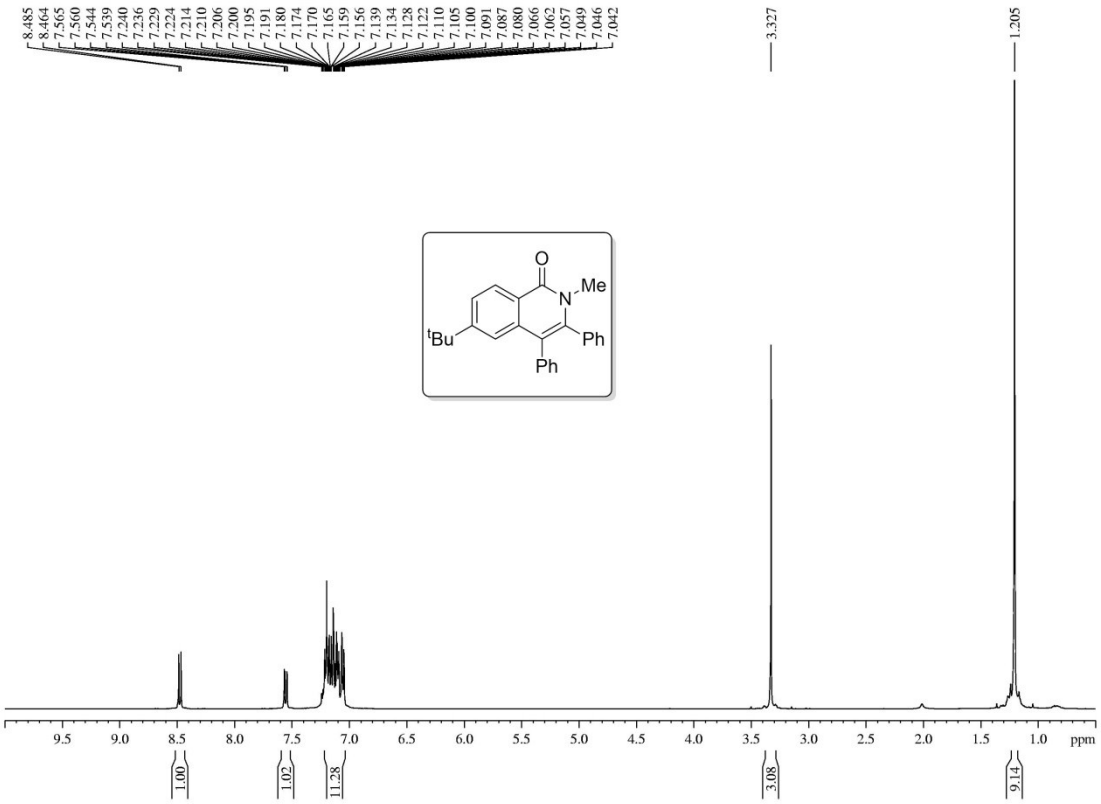


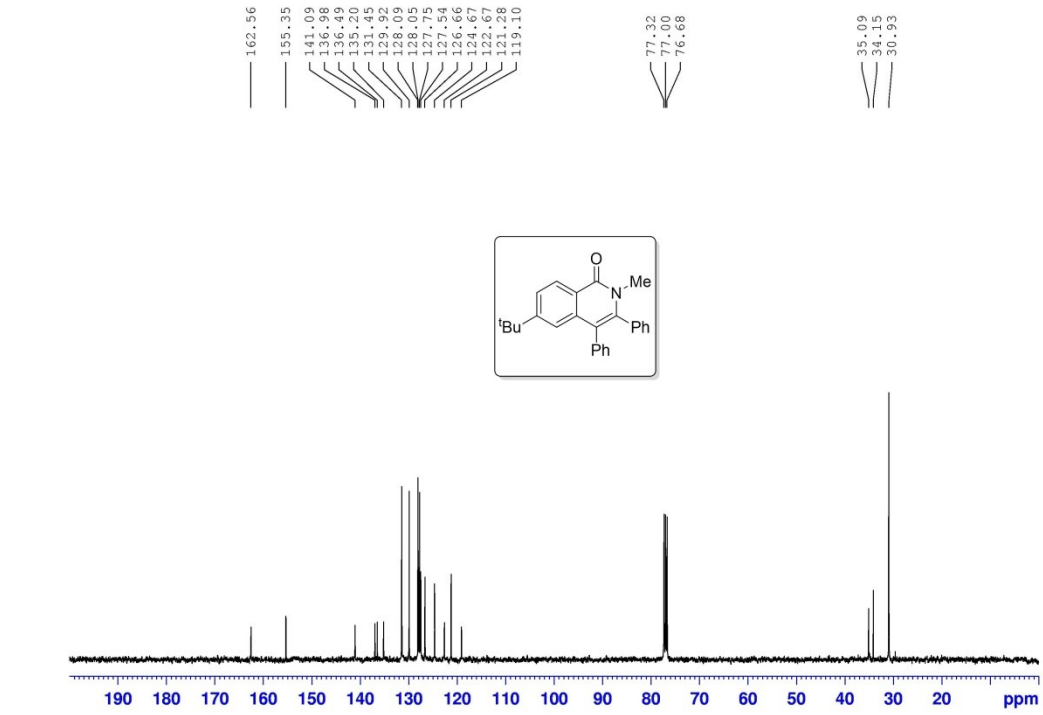
^{1}H and ^{13}C NMR spectra of compound **3ia.**



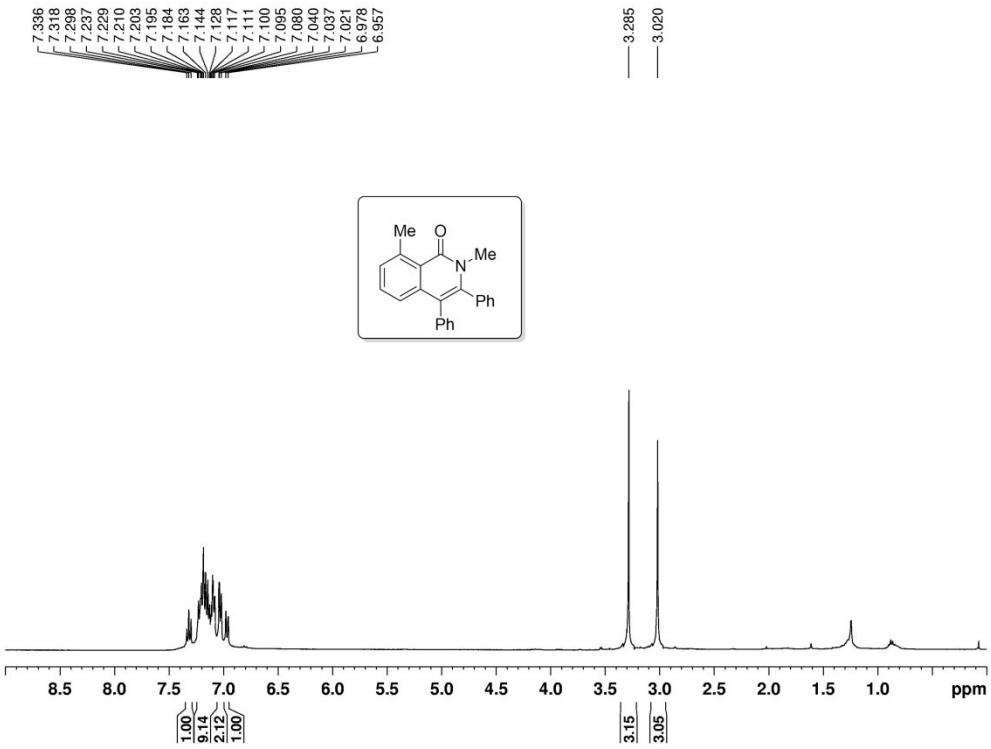


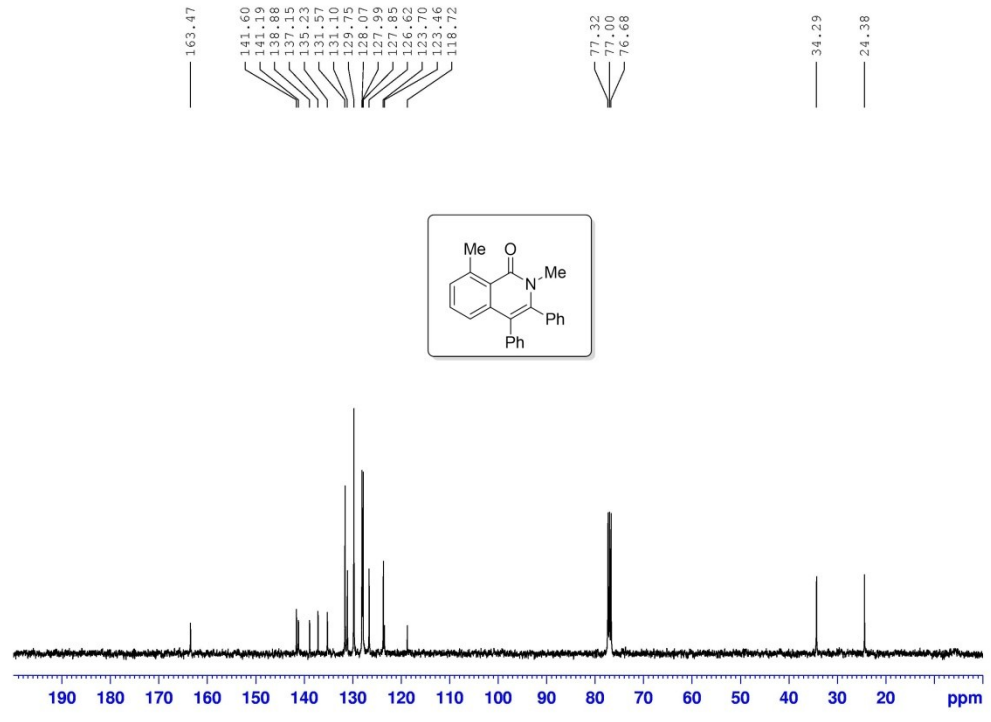
^{1}H and ^{13}C NMR spectra of compound **3ja**



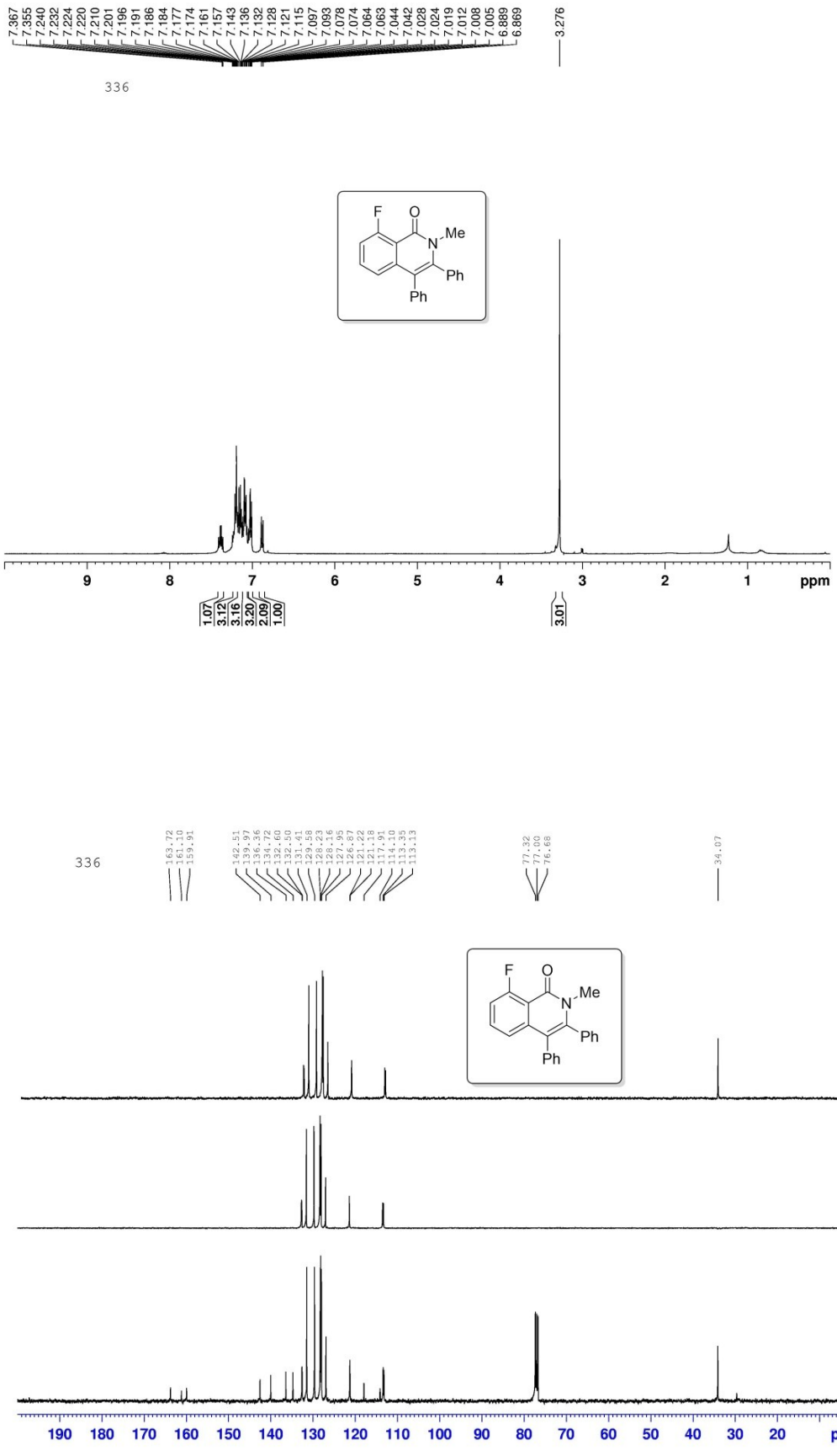


^{1}H and ^{13}C NMR spectra of compound **3ka.**

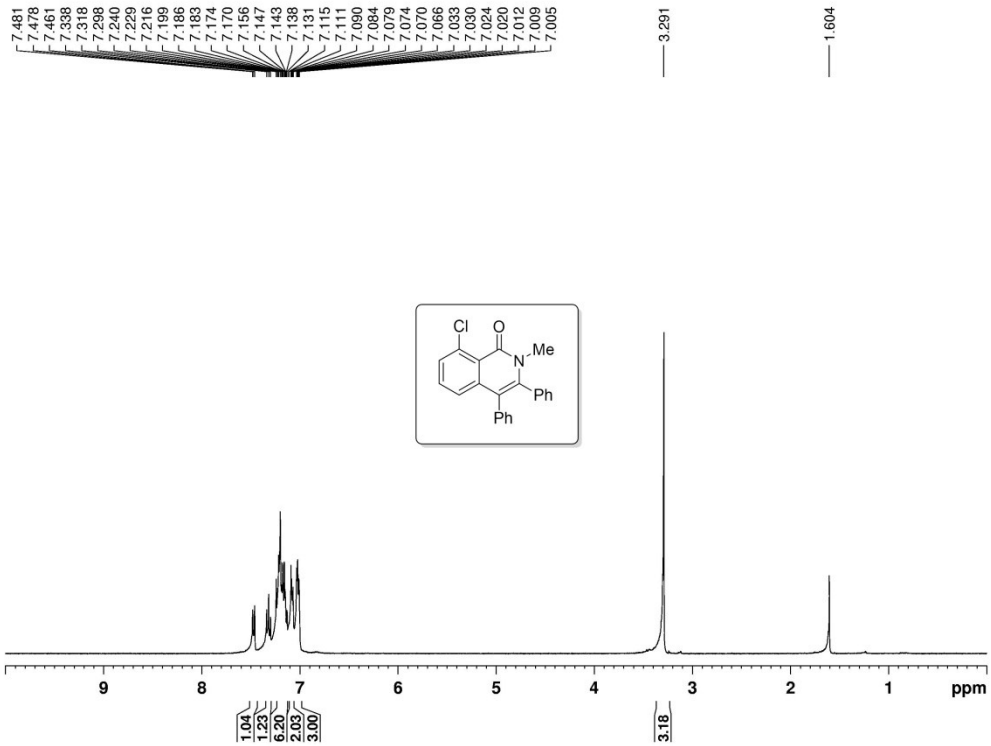


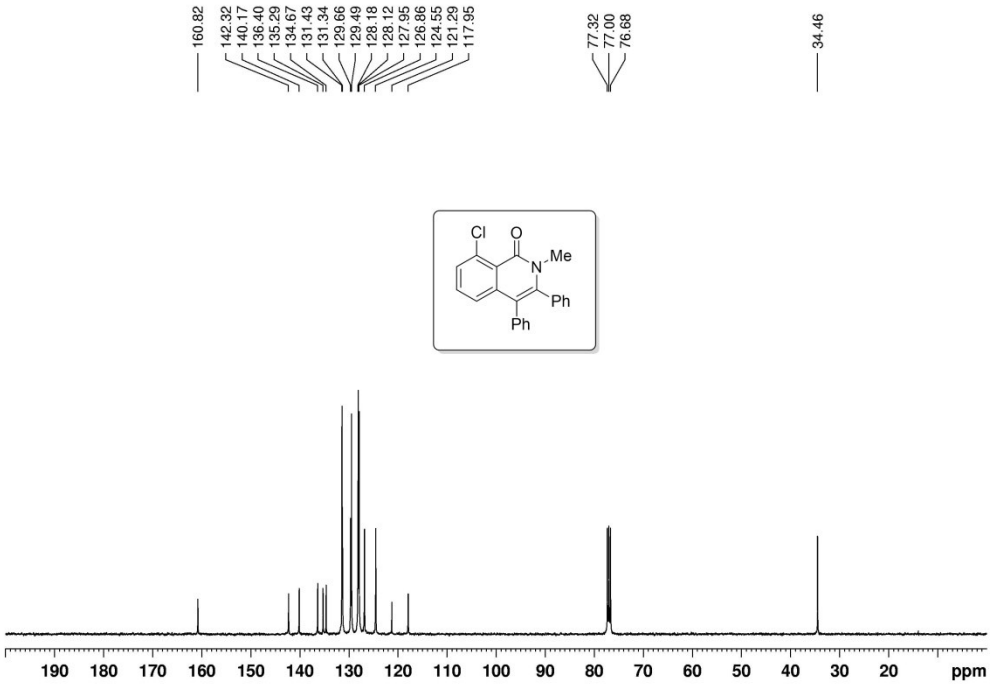


^{1}H and ^{13}C NMR spectra of compound **3la**

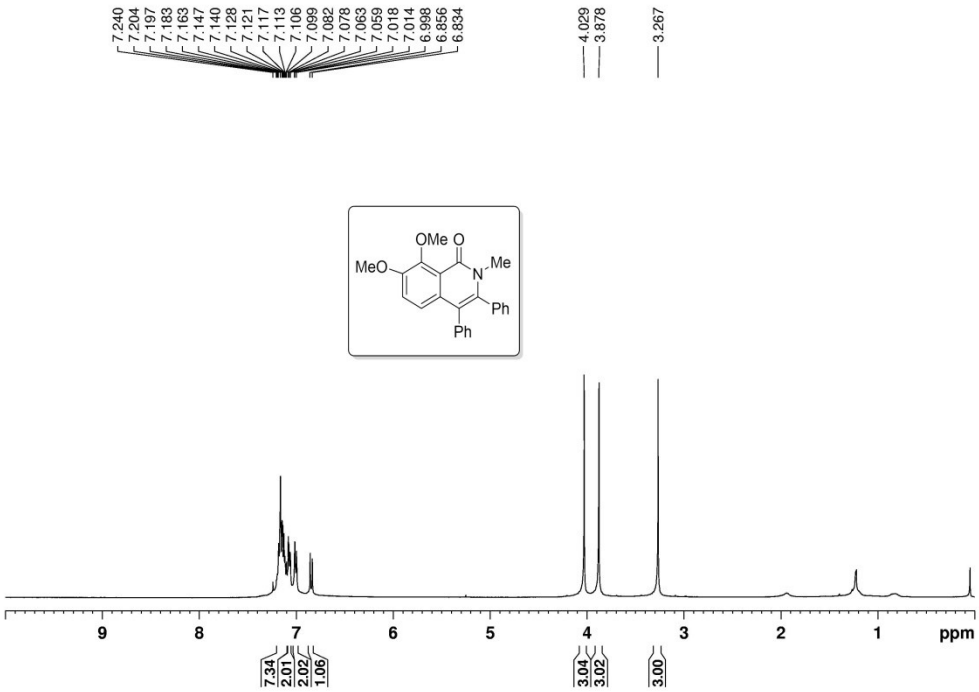


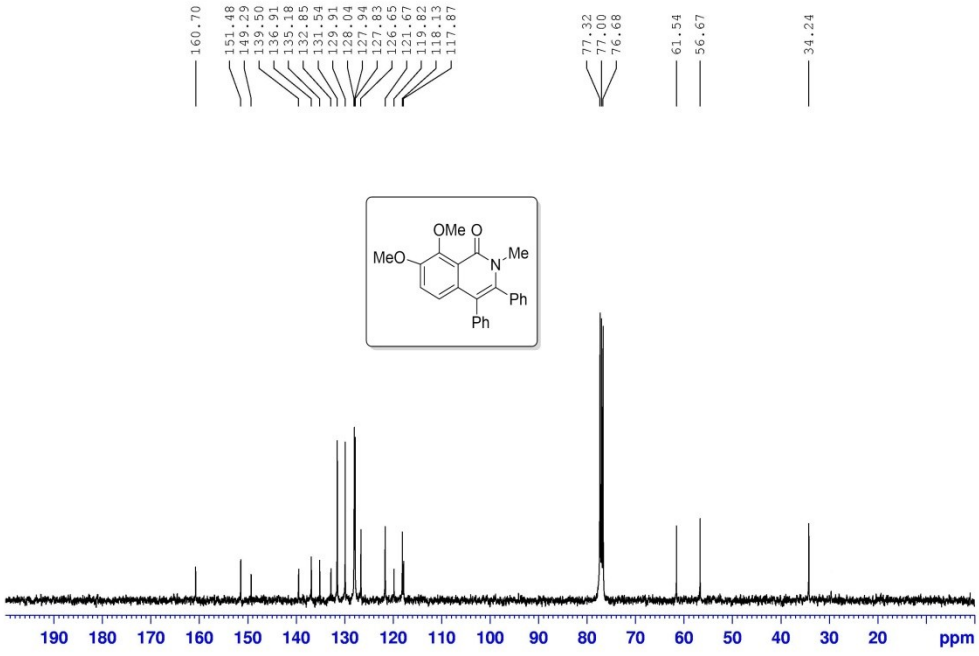
^{1}H and ^{13}C NMR spectra of compound **3ma.**



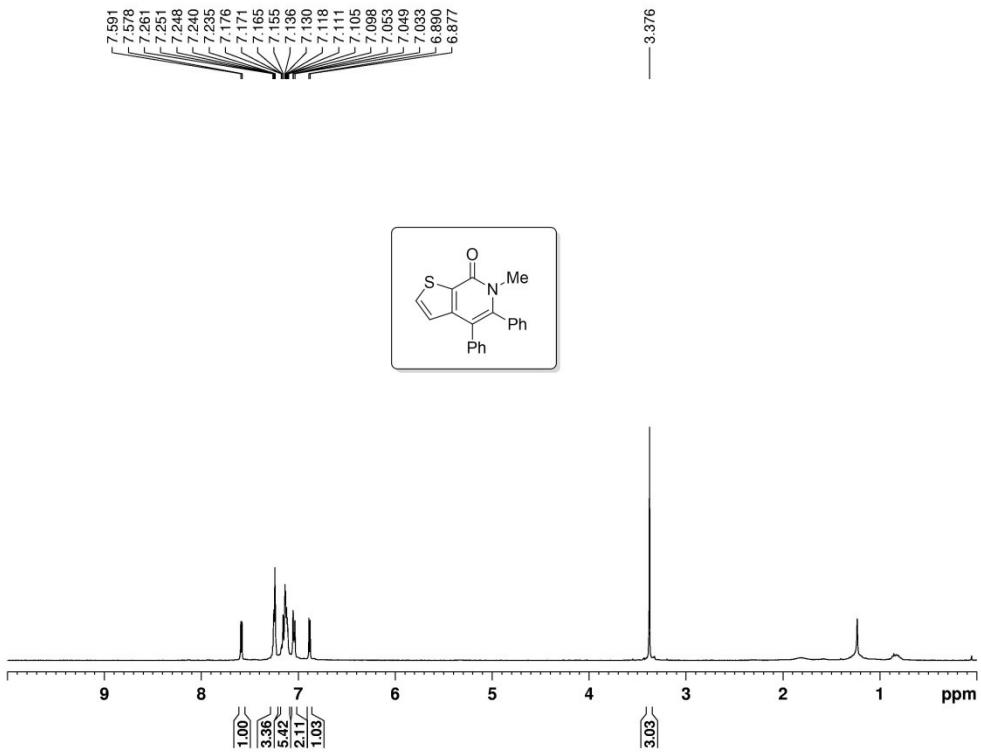


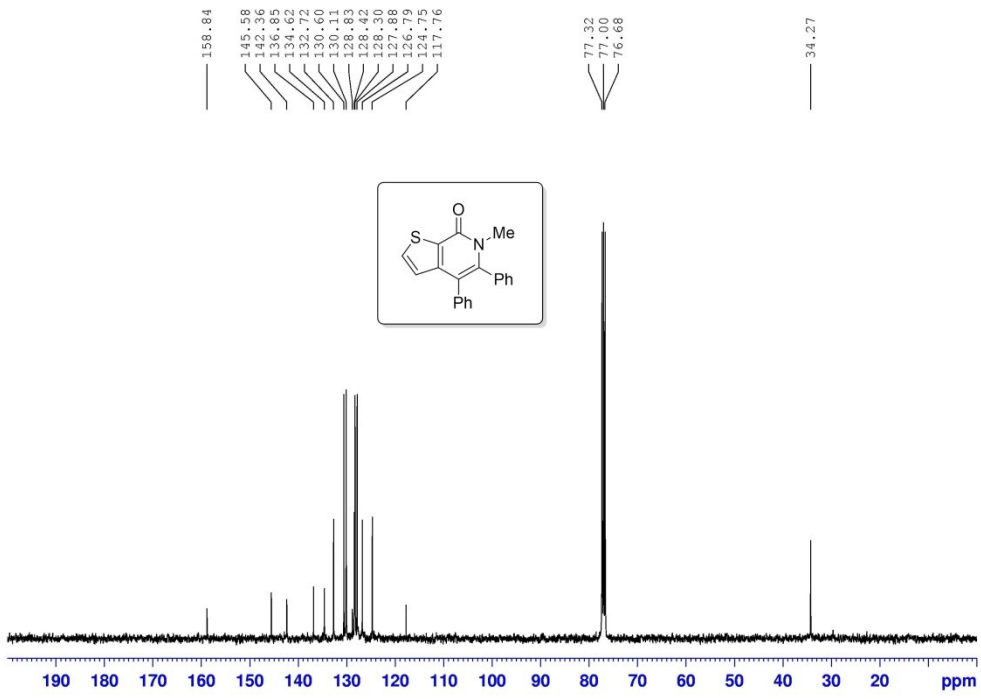
^{1}H and ^{13}C NMR spectra of compound **3na**



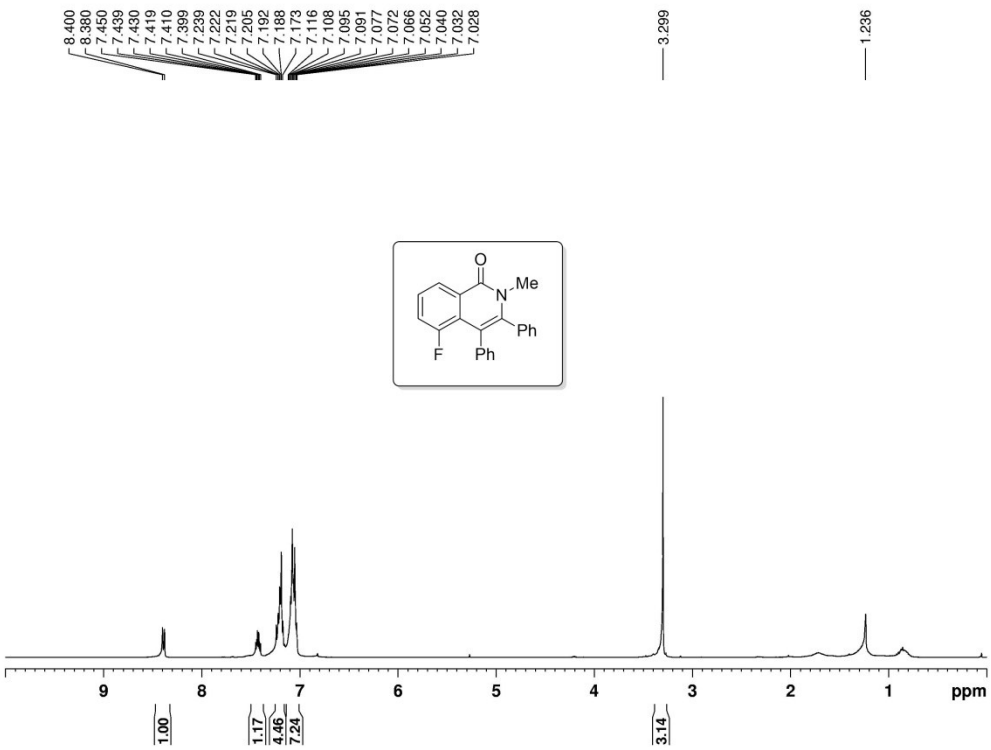


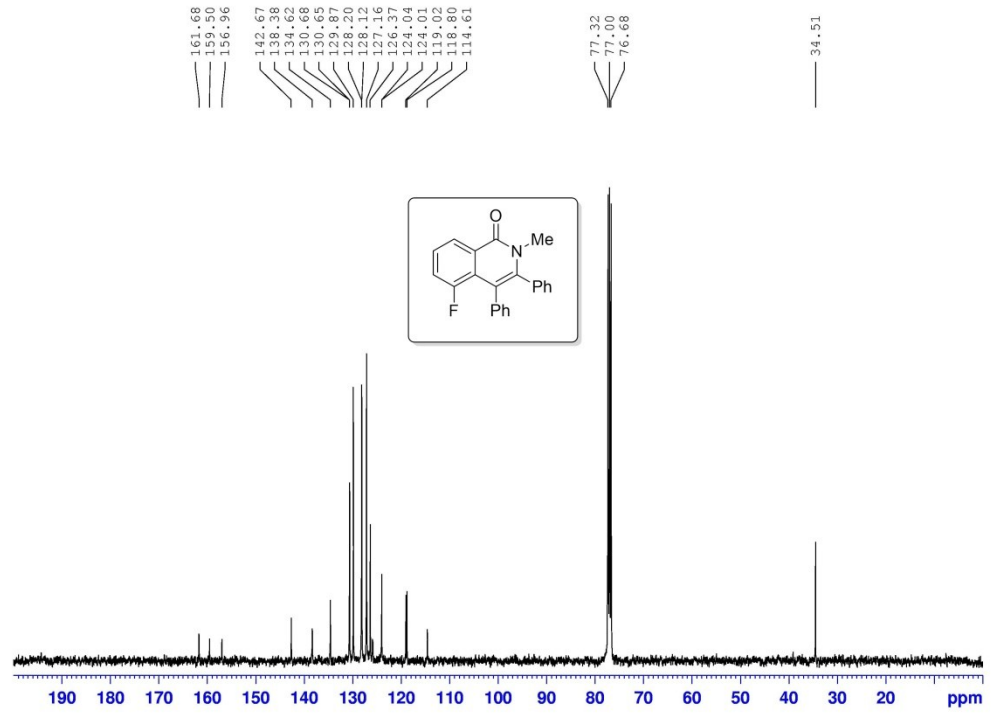
^{1}H and ^{13}C NMR spectra of compound **3oa**



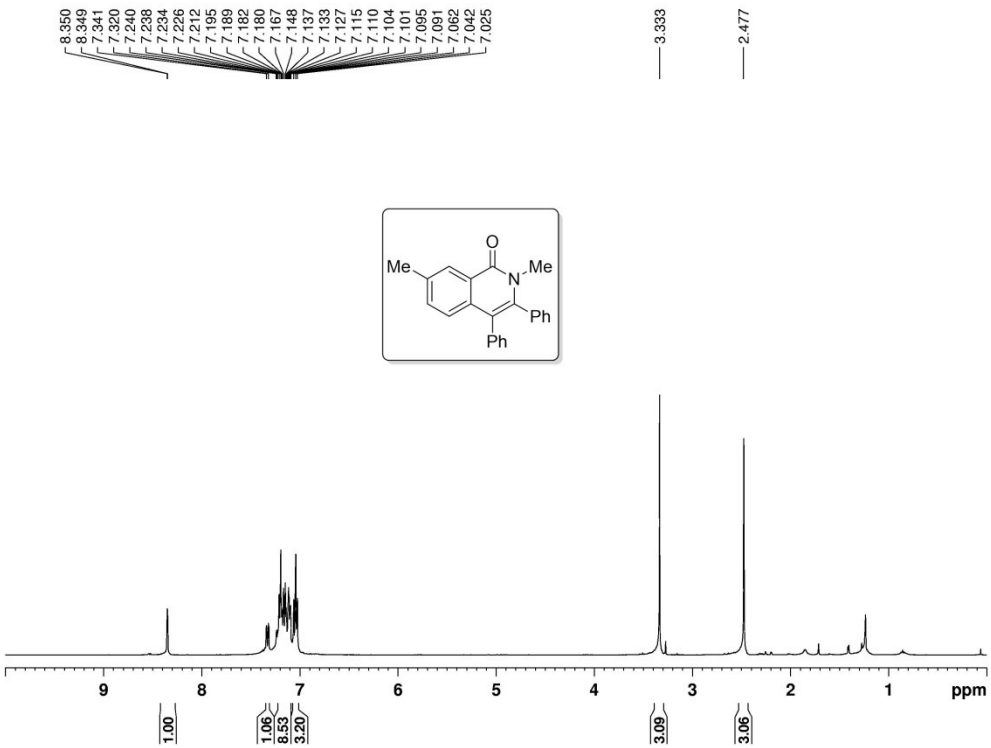


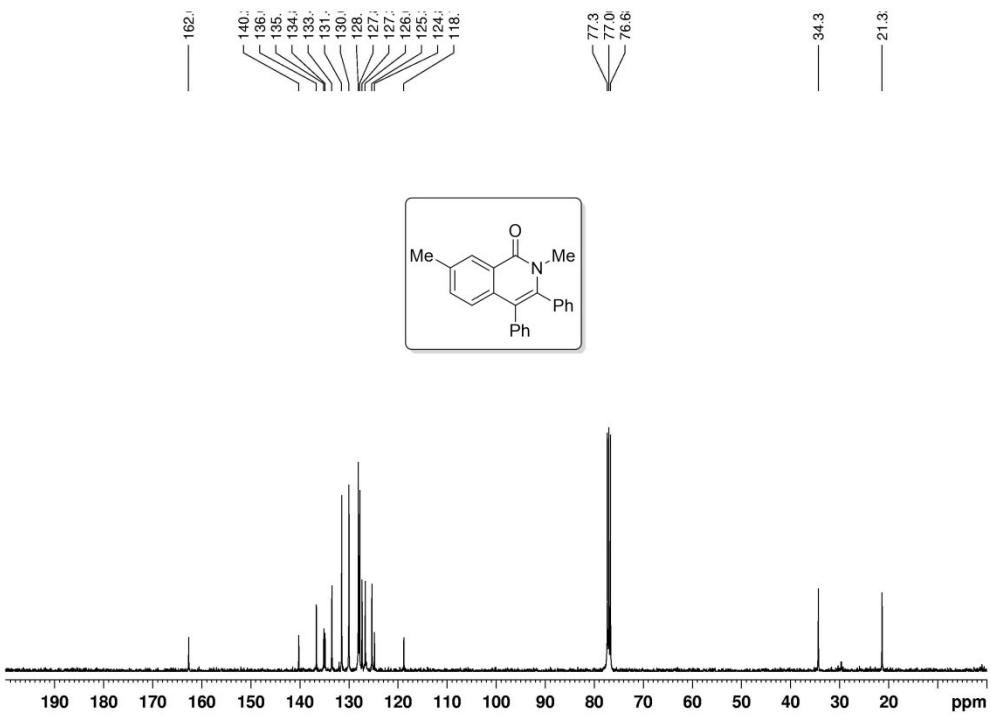
^{1}H and ^{13}C NMR spectra of compound **3pa.**



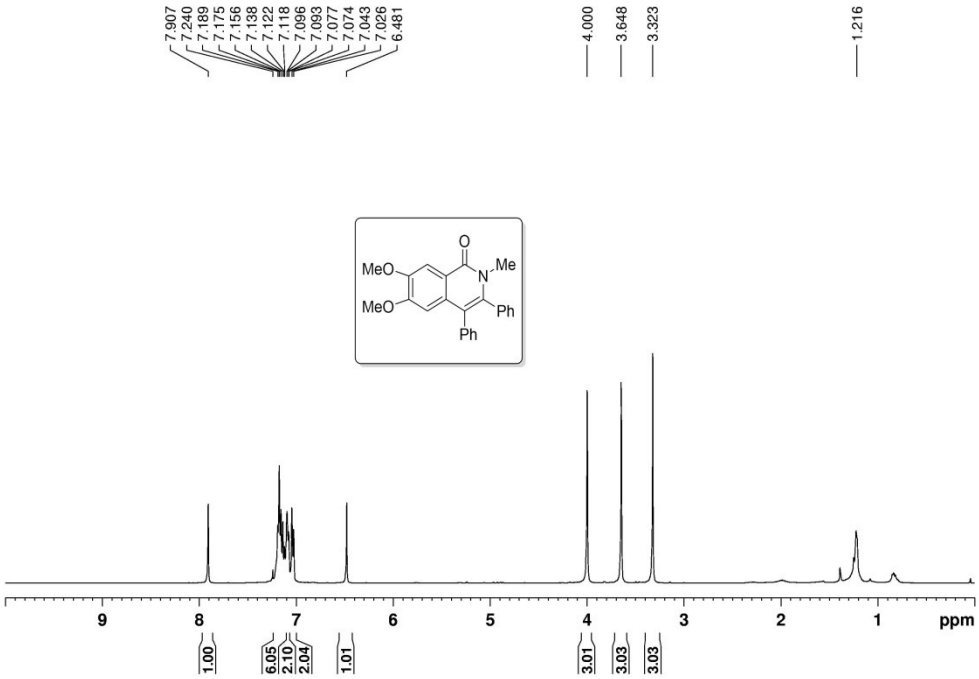


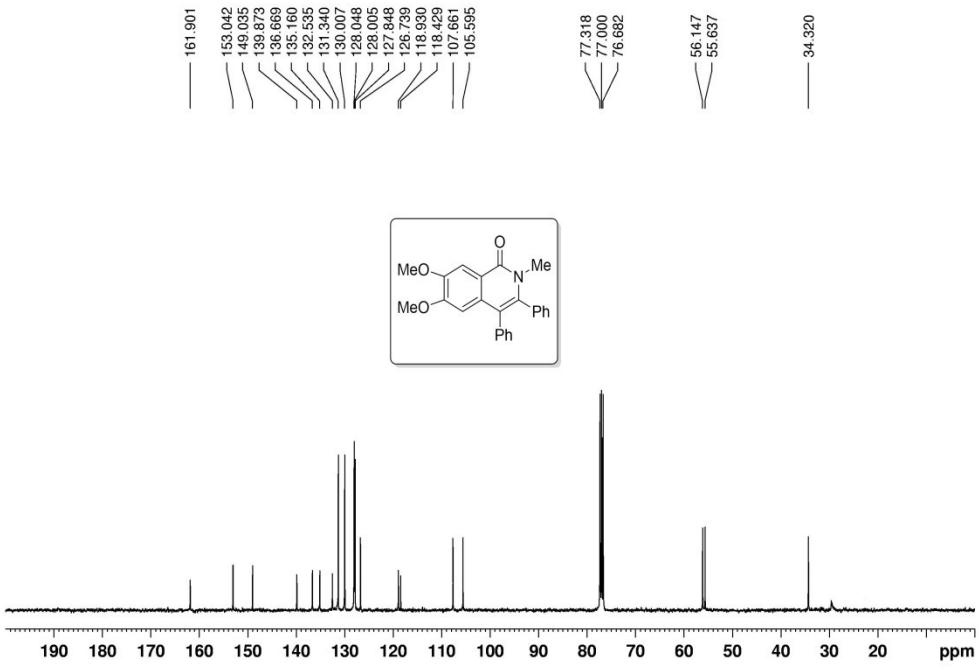
^{1}H and ^{13}C NMR spectra of compound **3qa.**



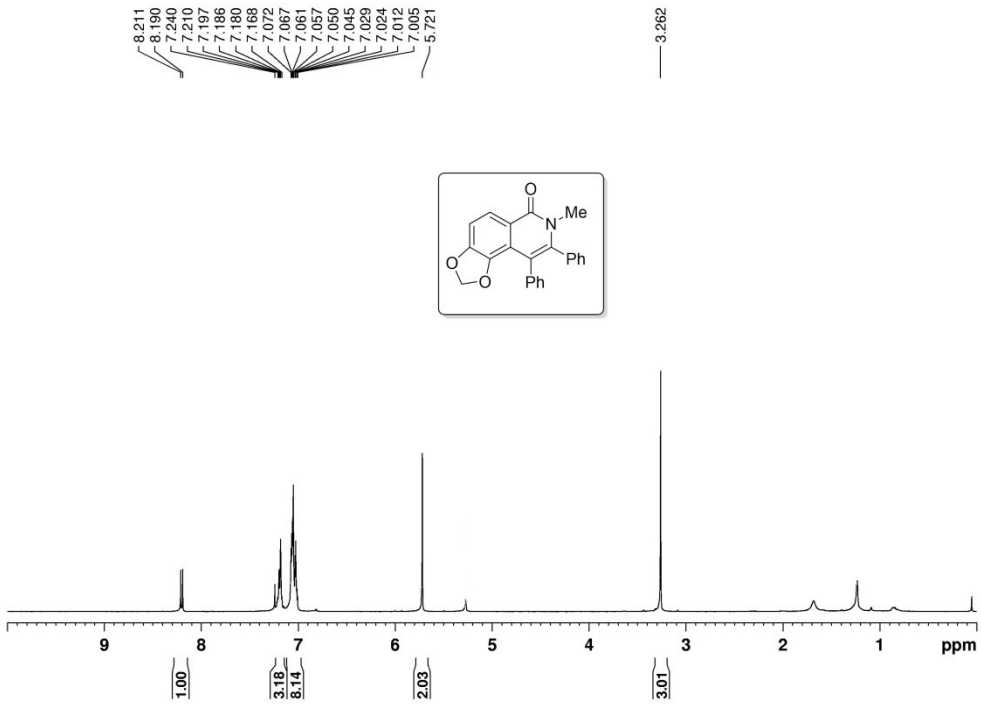


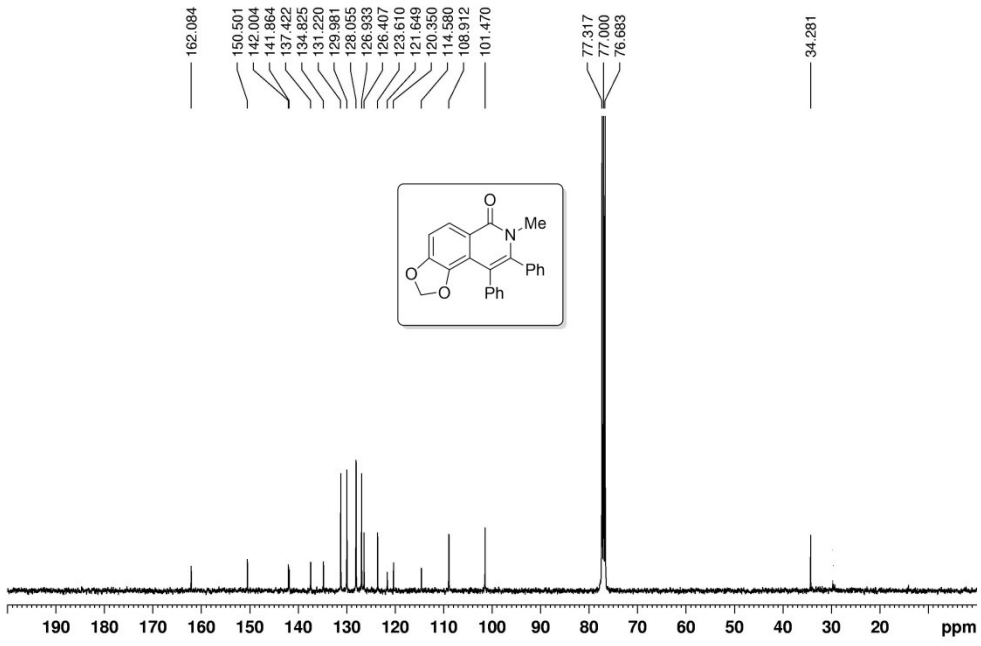
.^{1}H and ^{13}C NMR spectra of compound **3ra.**



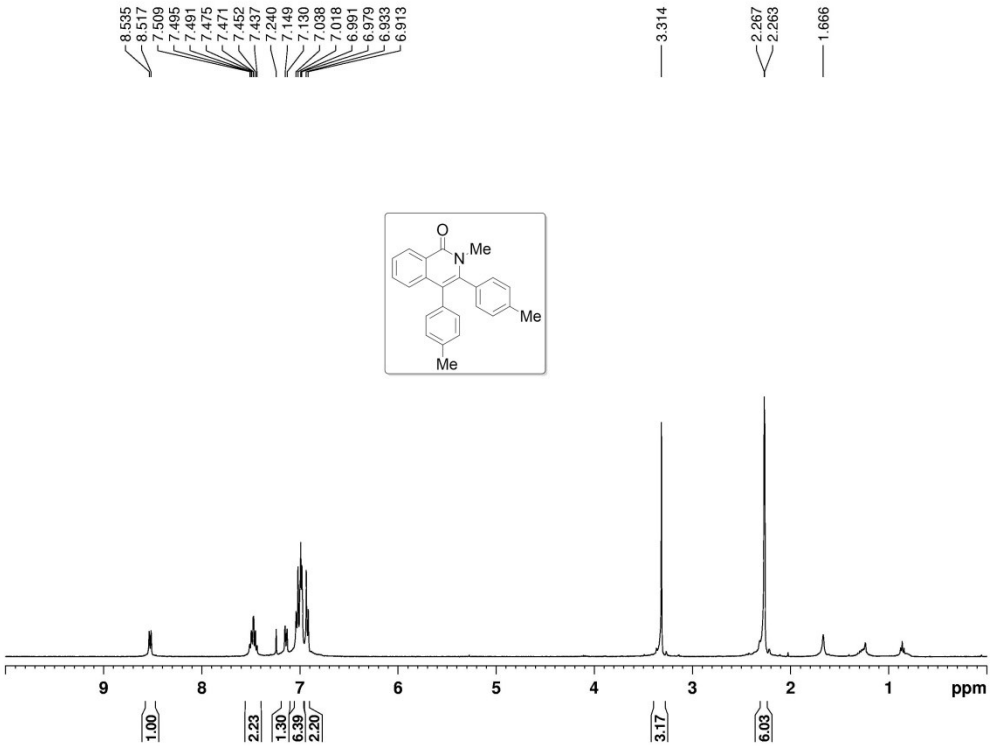


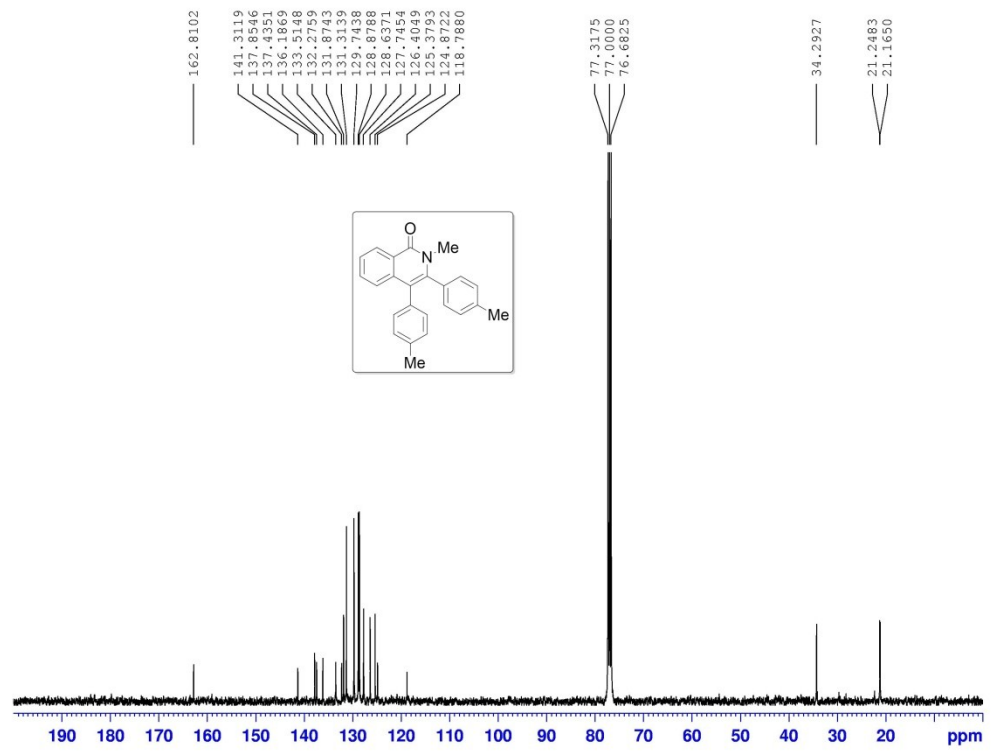
^{1}H and ^{13}C NMR spectra of compound **3sa**



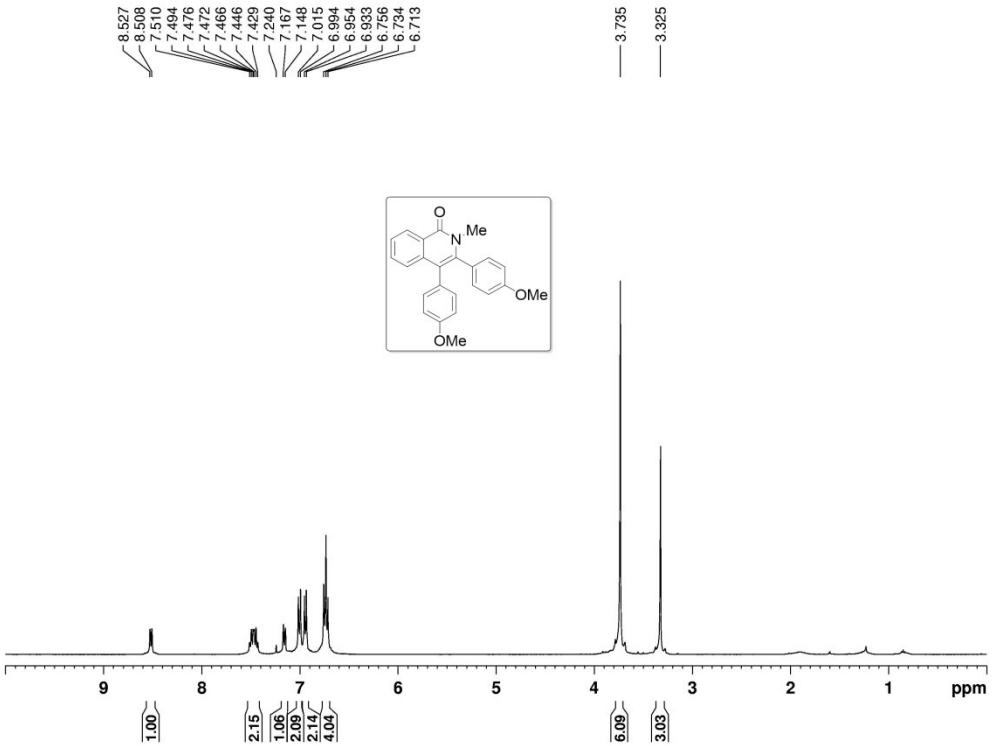


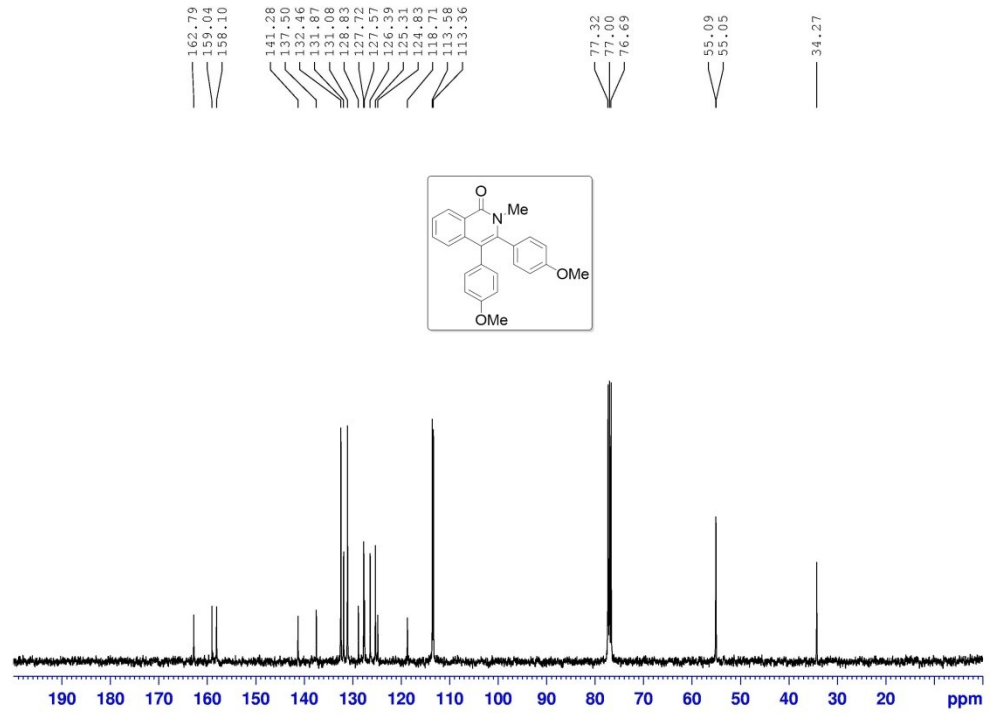
^{1}H and ^{13}C NMR spectra of compound **3ab.**



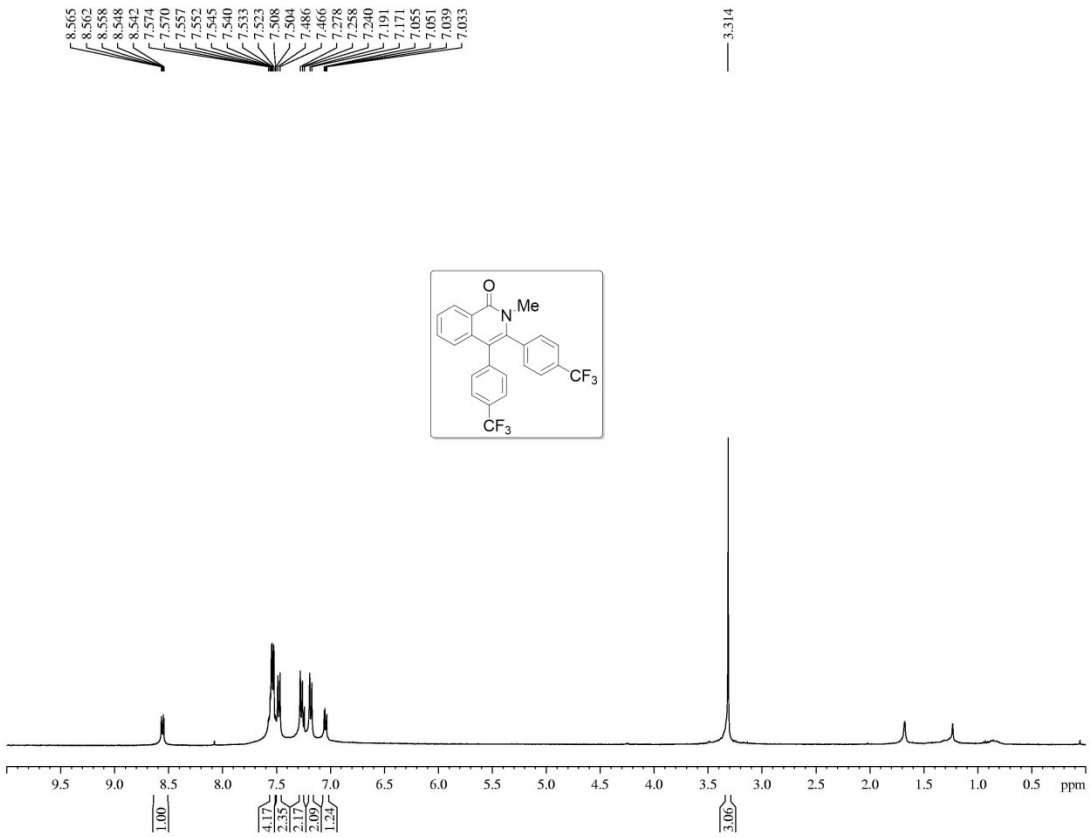


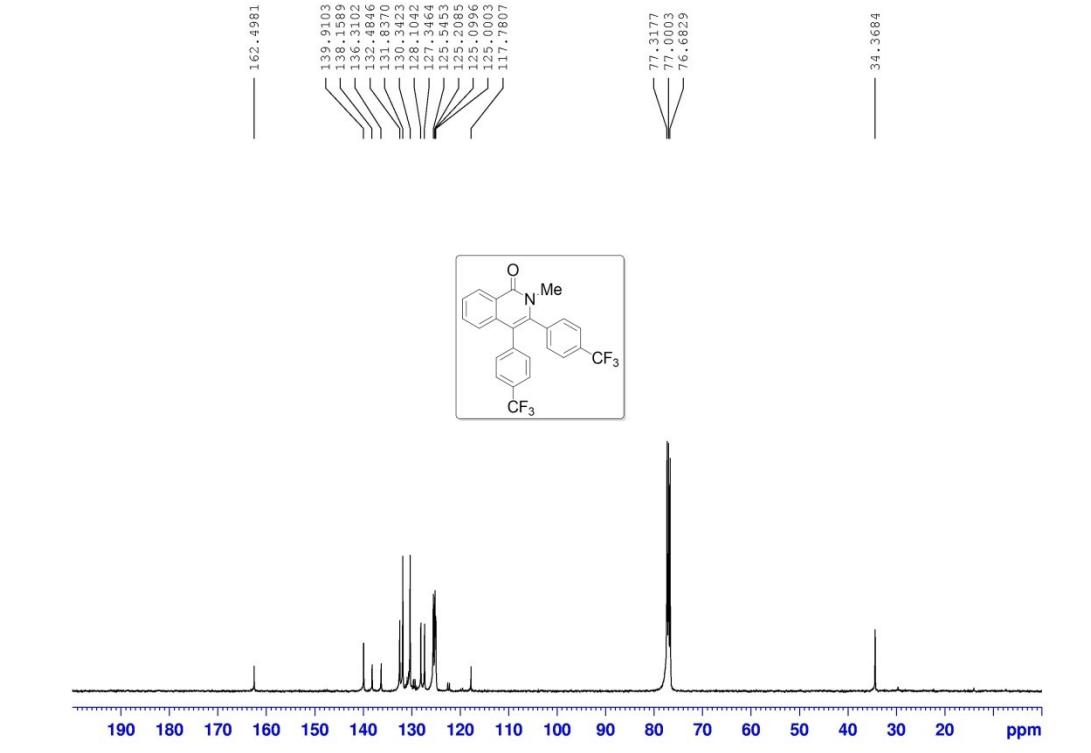
^{1}H and ^{13}C NMR spectra of compound **3ac.**



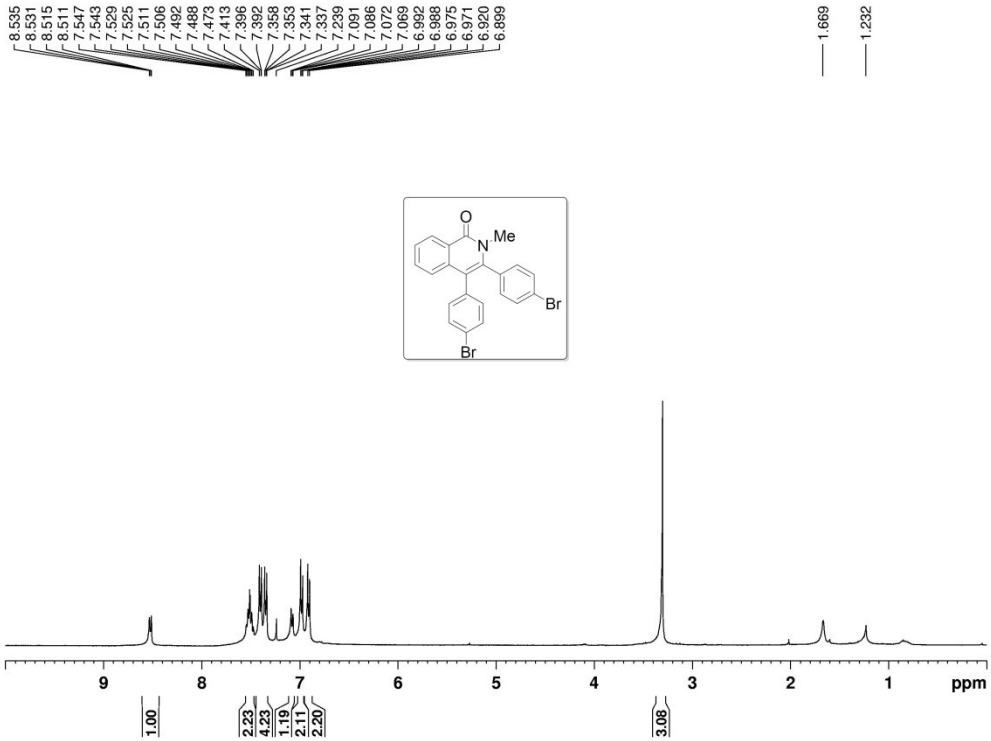


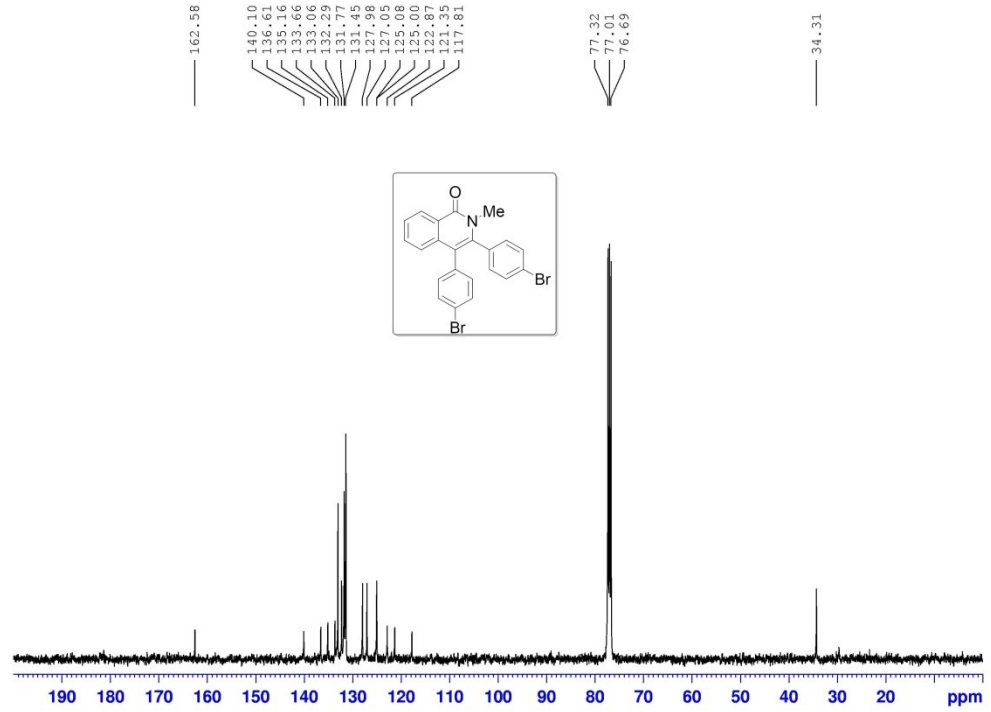
^{1}H and ^{13}C NMR spectra of compound **3ad.**



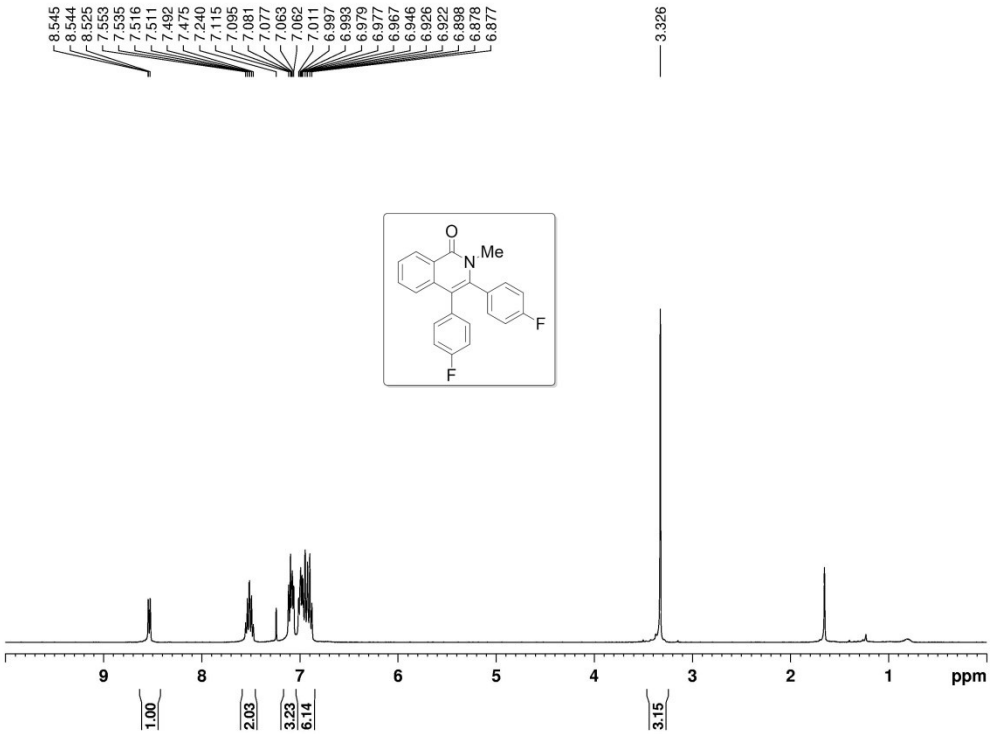


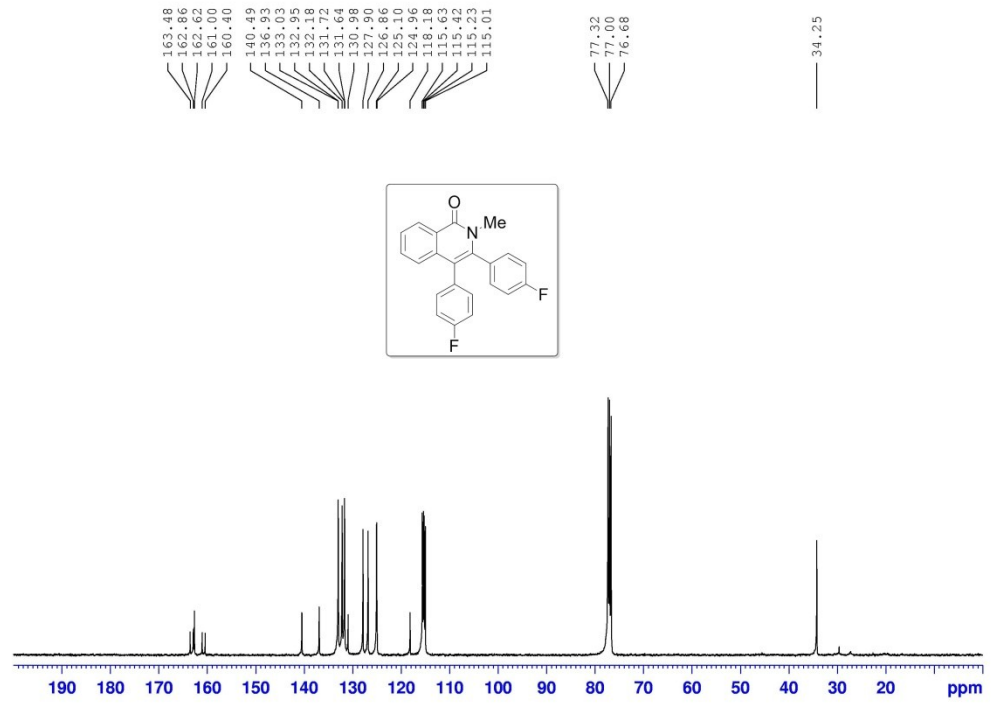
^{1}H and ^{13}C NMR spectra of compound **3ae.**



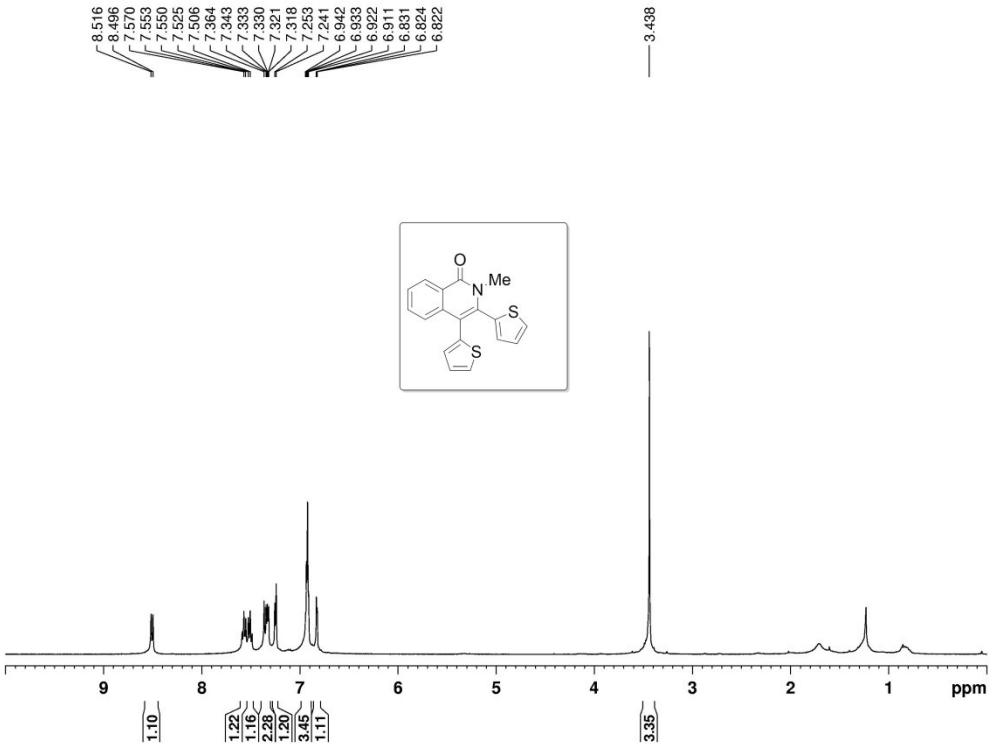


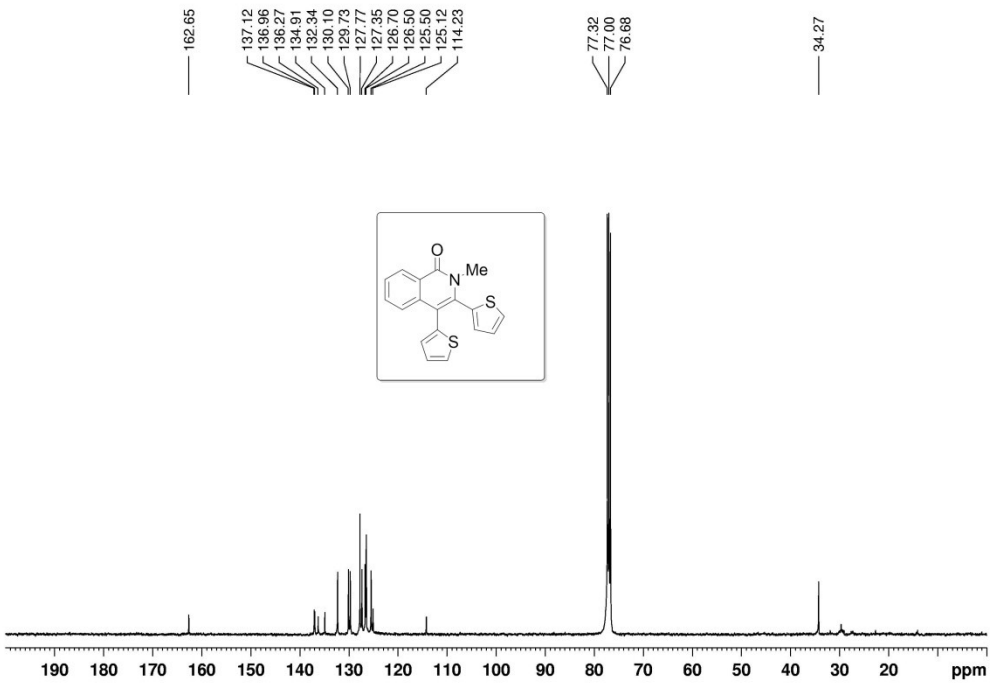
^{1}H and ^{13}C NMR spectra of compound **3af.**



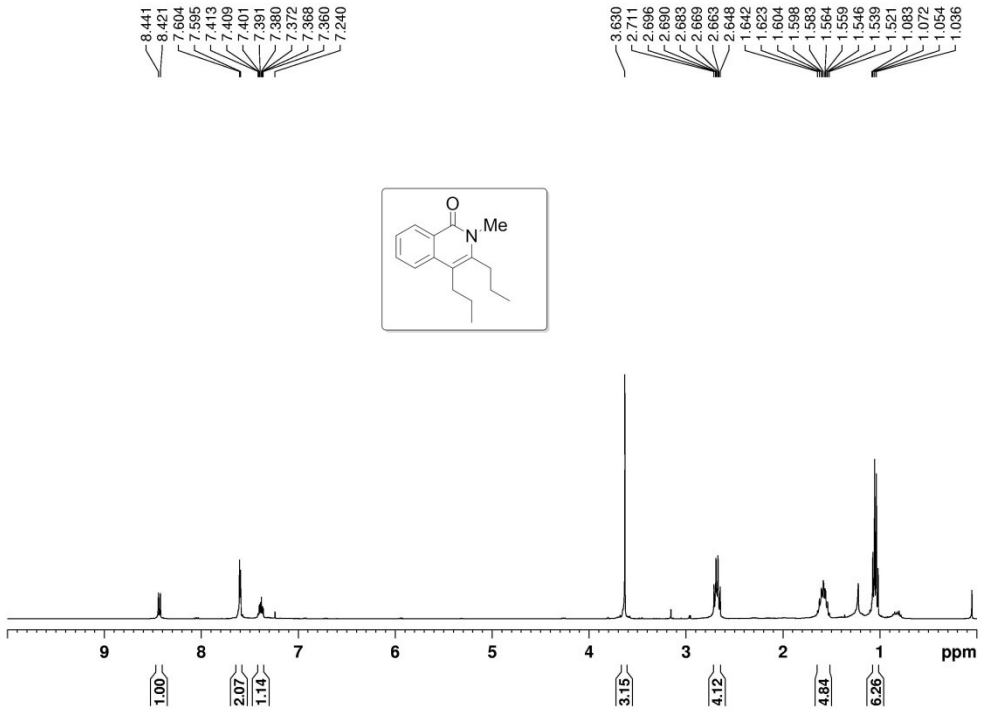


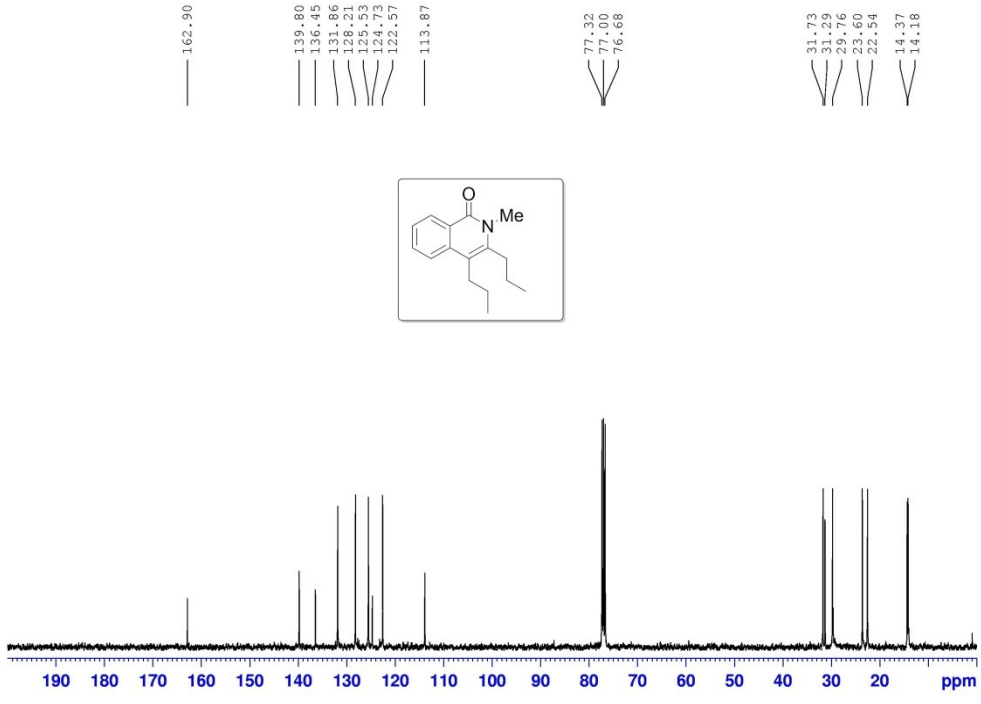
^{1}H and ^{13}C NMR spectra of compound **3ag.**



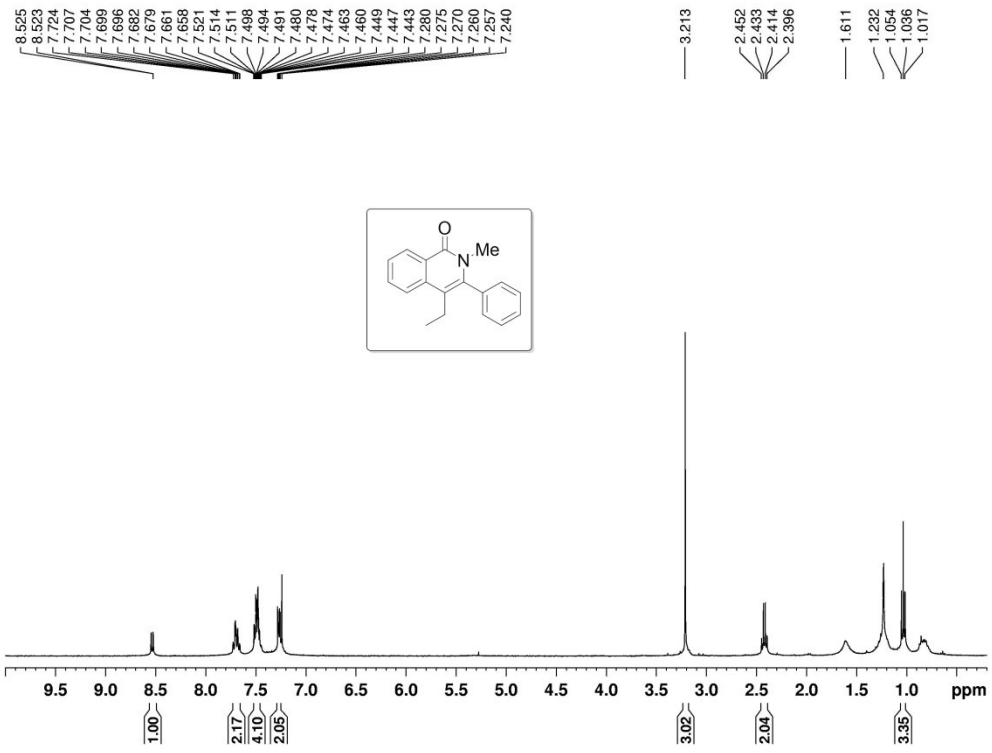


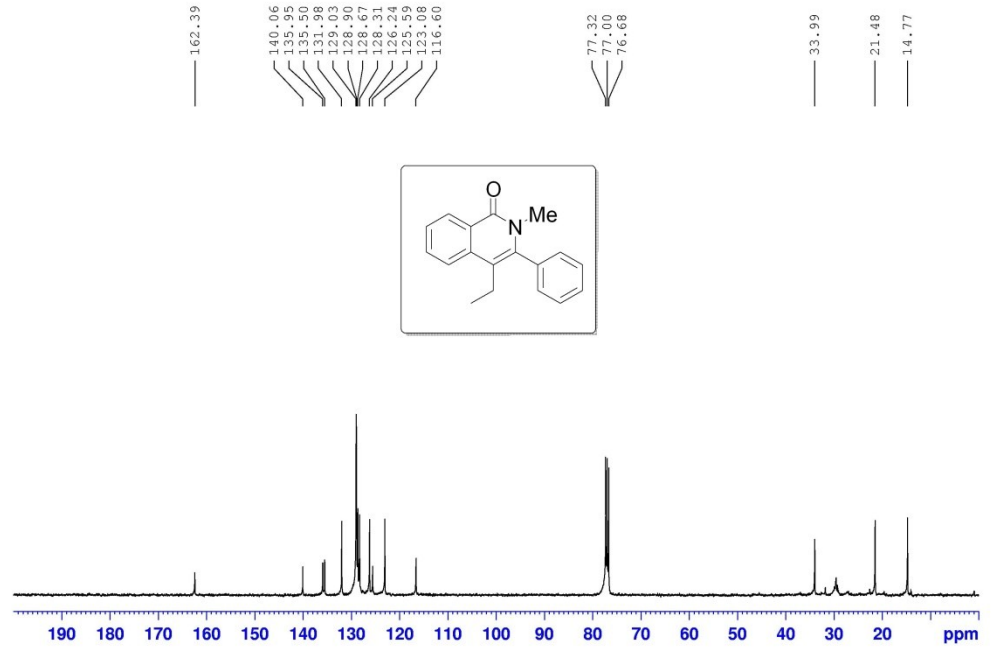
^{1}H and ^{13}C NMR spectra of compound **3ah.**



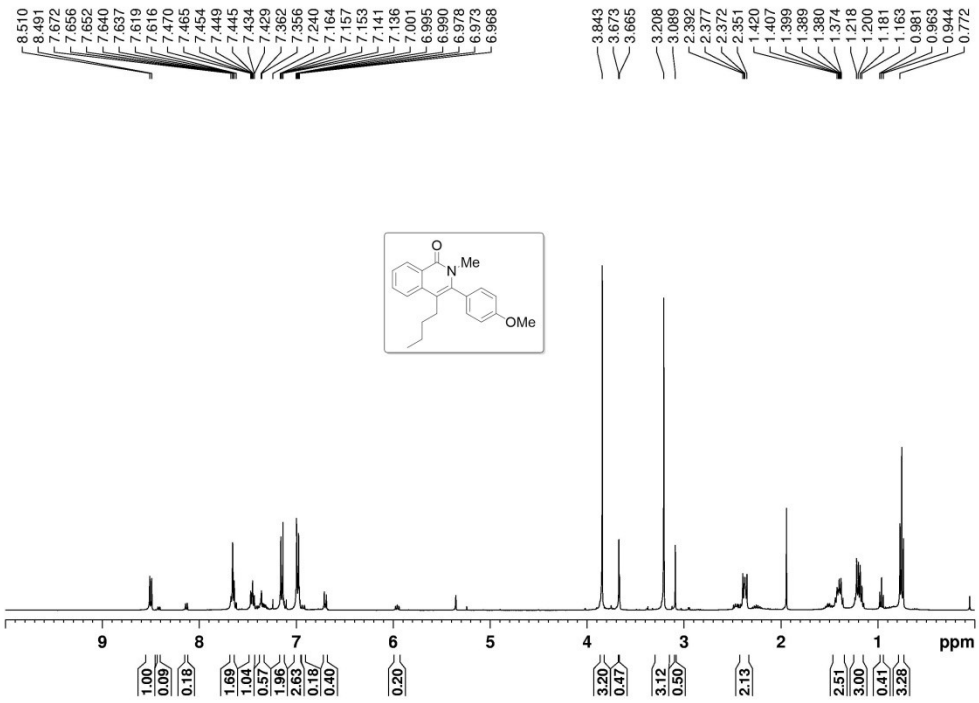


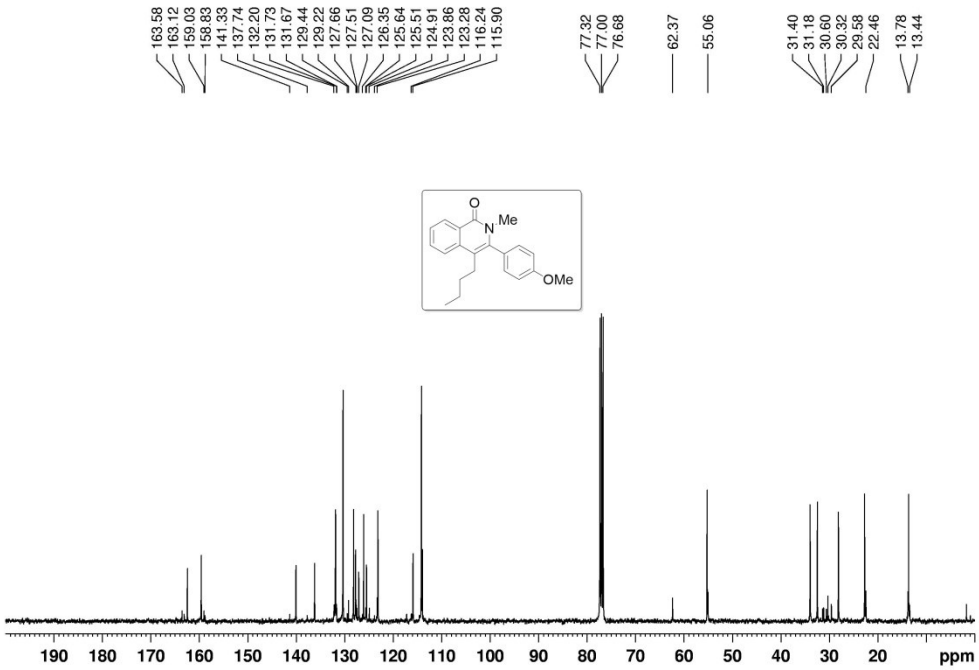
^{1}H and ^{13}C NMR spectra of compound **3ai.**



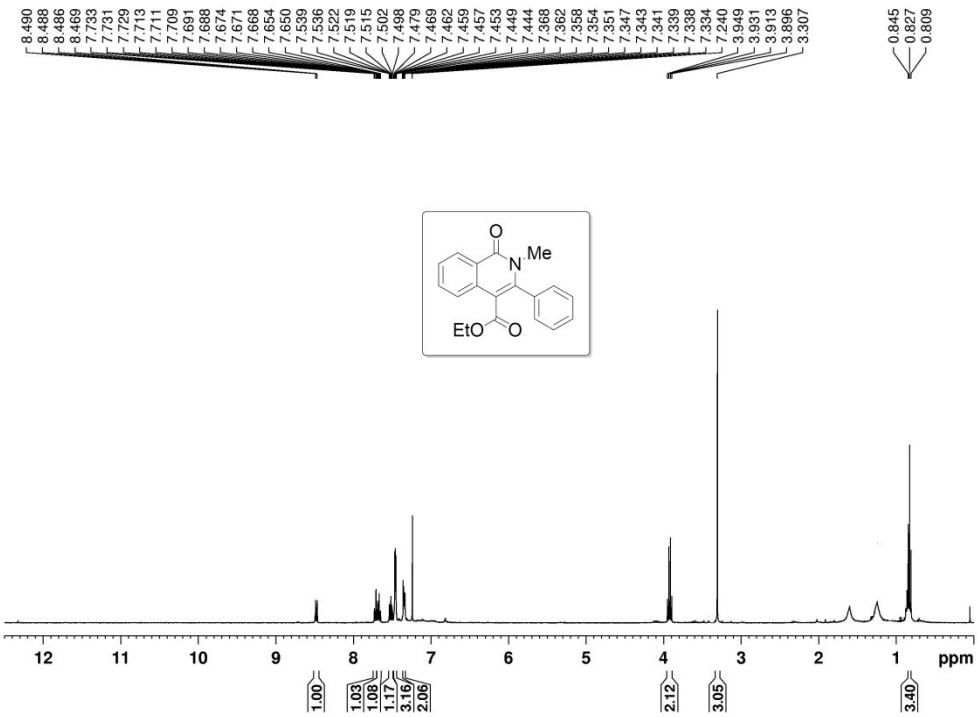


^{1}H and ^{13}C NMR spectra of compound **3aj**





^{1}H and ^{13}C NMR spectra of compound **3ak**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8.469
7.733
7.731
7.729
7.713
7.711
7.709
7.691
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7.674
7.671
7.668
7.654
7.650
7.539
7.536
7.522
7.519
7.515
7.502
7.498
7.479
7.469
7.462
7.459
7.457
7.453
7.449
7.444
7.368
7.362
7.358
7.354
7.351
7.347
7.343
7.341
7.339
7.338
7.334
7.240
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3.931
3.913
3.896
3.307
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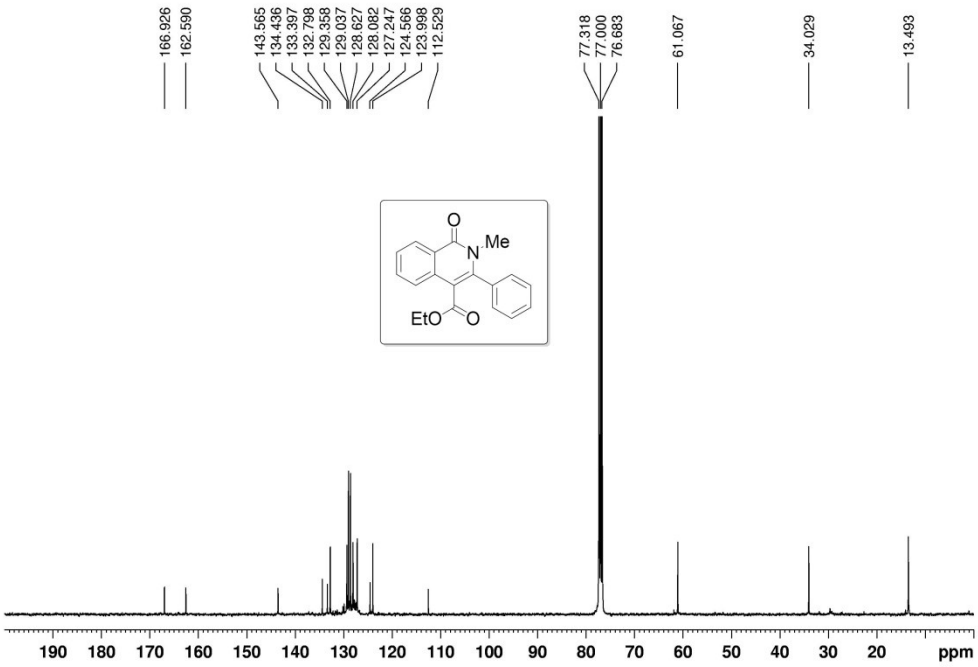
3.16
2.06
2.12
3.05
3.40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132.798
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112.529
77.318
77.000
76.683
61.067
34.029
13.493
O
N
Me
EtO
O
190
180
170
160
150
140
130
120
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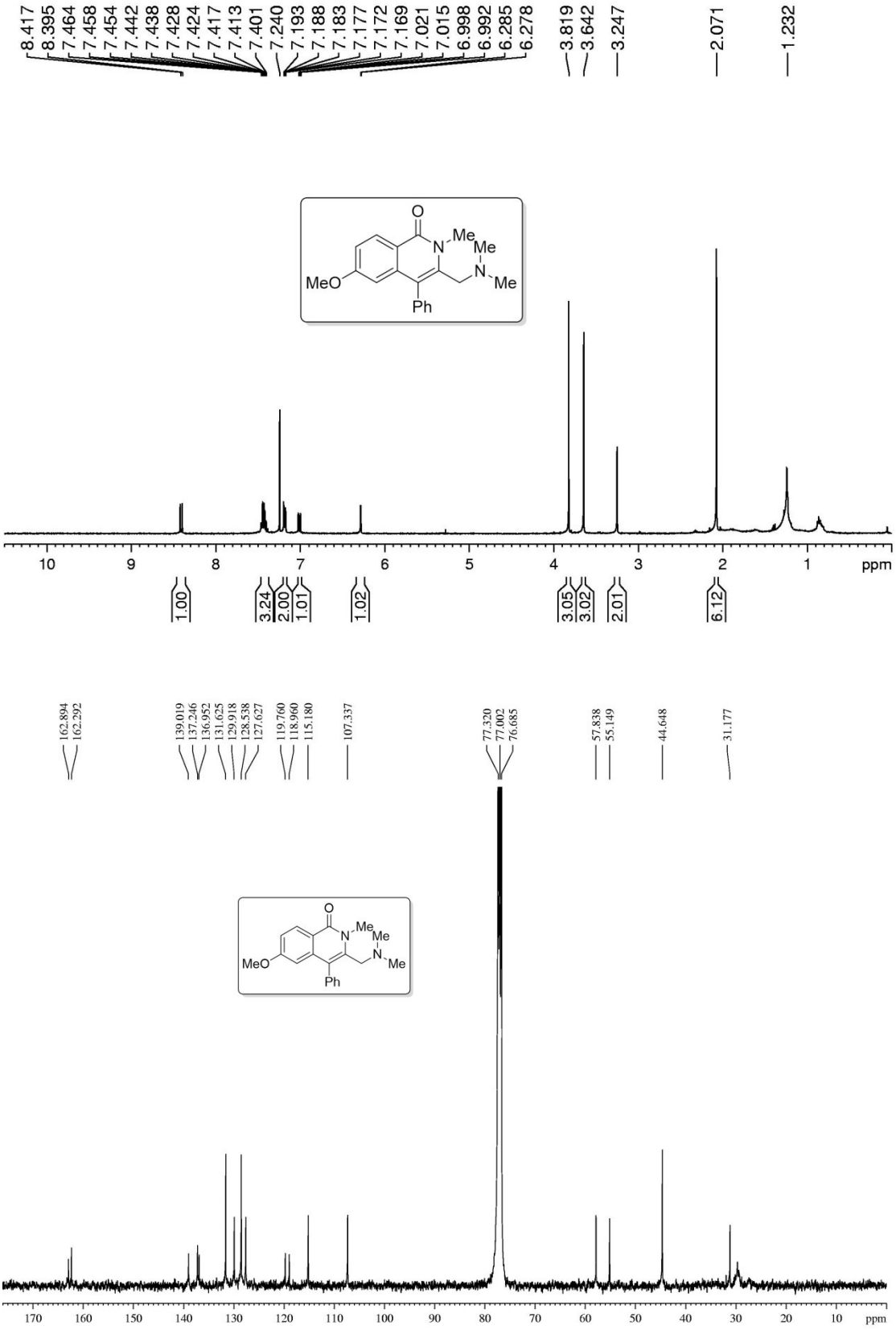
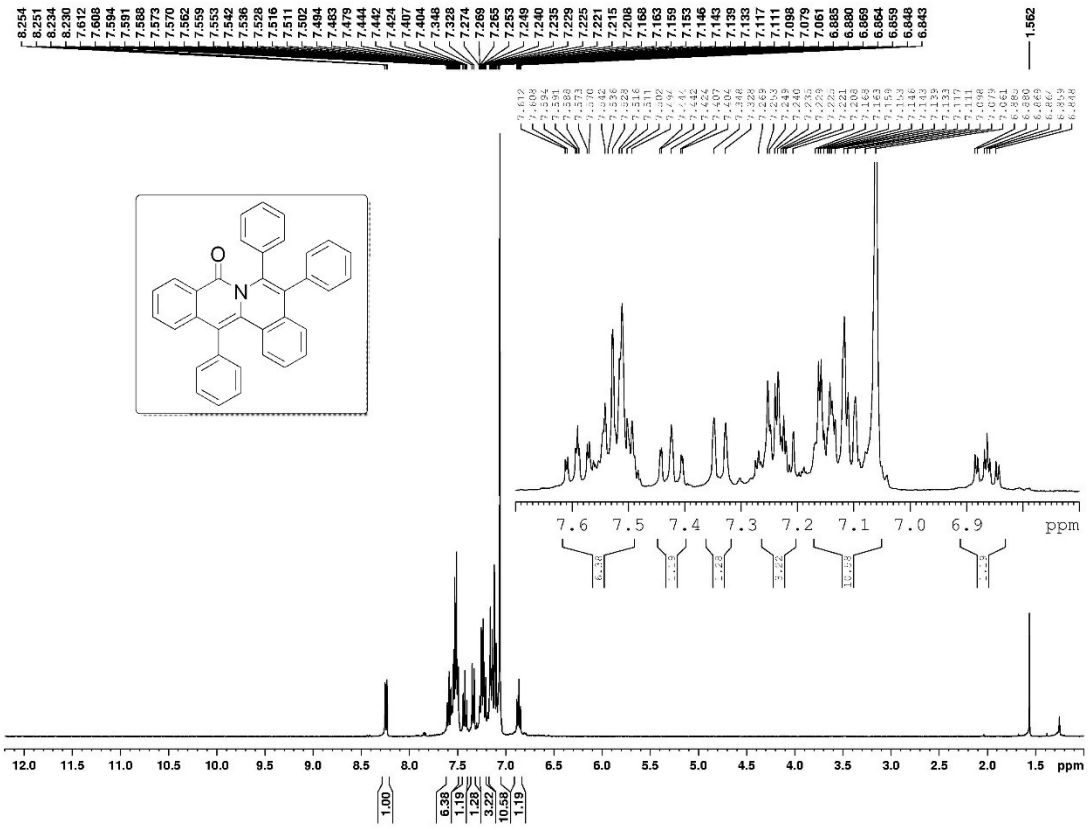
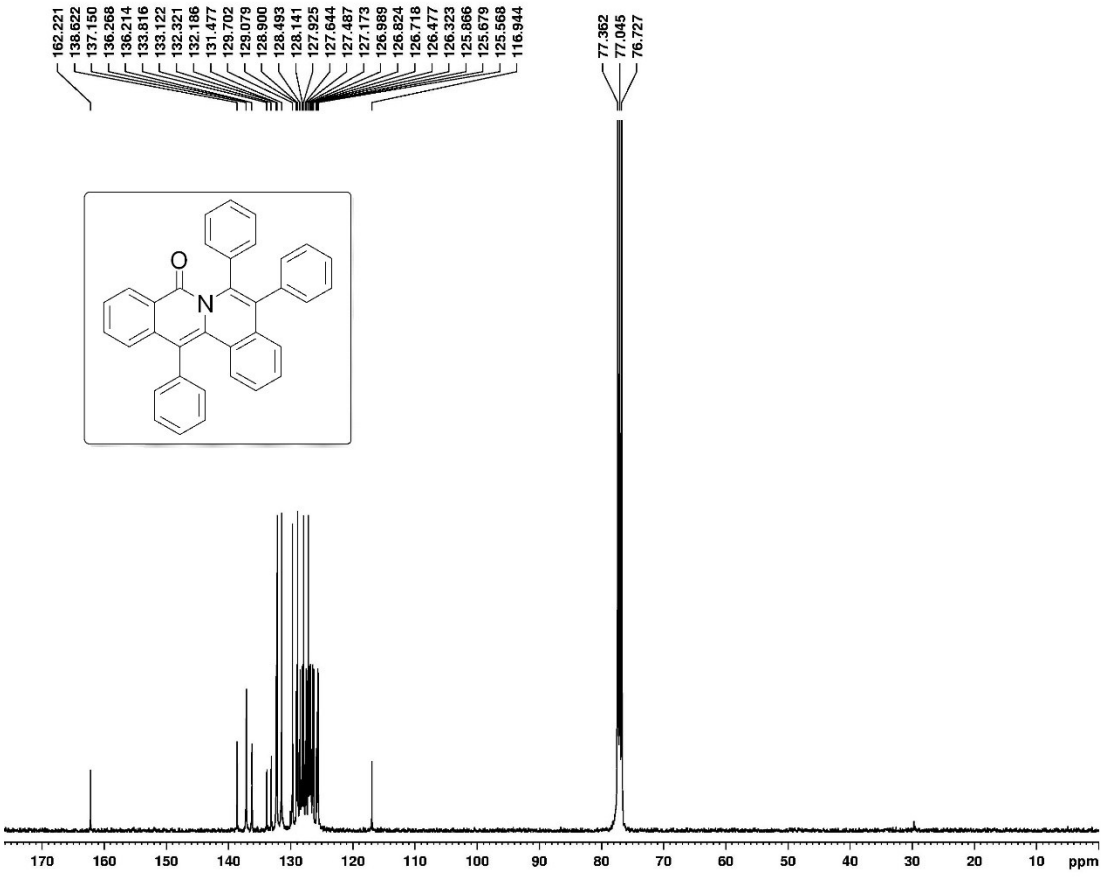
100
90
80
70
60
50
40
30
20
ppm

^{1}H and ^{13}C NMR spectra of compound **3fl.**



^{1}H and ^{13}C NMR spectra of compound **3ta.**





ORTEP diagram of compound **3aa**

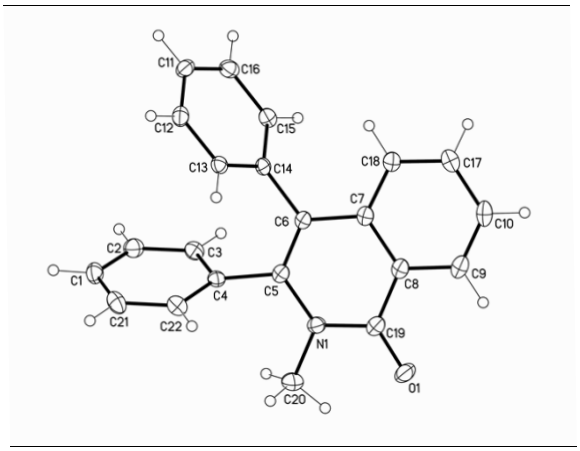


Table 1. Crystal data and structure refinement for mo_150714lt_0m (**3aa**).

Identification code	mo_150714lt_0m
Empirical formula	C22 H17 N O
Formula weight	311.36
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 9.3178(12) Å
	b = 9.5222(12) Å
	c = 10.9385(14) Å
Volume	789.02(18) $Å^3$
Z	2
Density (calculated)	1.311 Mg/m^3
Absorption coefficient	0.080 mm^{-1}
F(000)	328
Crystal size	0.20 x 0.20 x 0.15 mm^3
Theta range for data collection	2.102 to 26.485°.
Index ranges	-11<=h<=8, -11<=k<=11, -13<=l<=13
Reflections collected	12357
Independent reflections	3208 [R(int) = 0.0214]
Completeness to theta = 25.242°	99.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9485 and 0.8621
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3208 / 0 / 218
Goodness-of-fit on F^2	1.043

Final R indices [I>2sigma(I)]	R1 = 0.0354, wR2 = 0.0897
R indices (all data)	R1 = 0.0422, wR2 = 0.0944
Extinction coefficient	n/a
Largest diff. peak and hole	0.277 and -0.191 e.Å^{-3}

ORTEP diagram of compound **3ak**

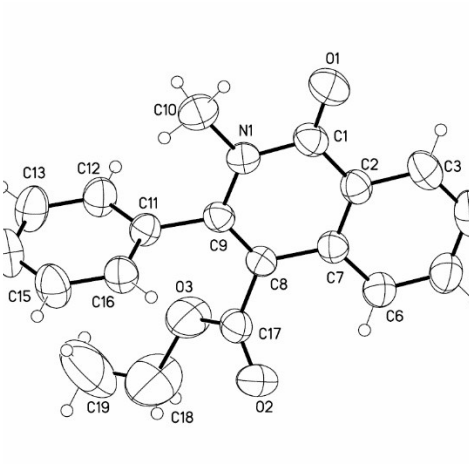


Table 2. Crystal data and structure refinement for mo_160743_0m_a (**3ak**).

Identification code	mo_160743_0m_a
Empirical formula	C19 H17 N O3
Formula weight	307.33
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 9.4992(7) Å
	b = 12.0176(9) Å
	c = 14.7148(11) Å
Volume	1600.6(2) Å^3
Z	4
Density (calculated)	1.275 Mg/m^3
Absorption coefficient	0.087 mm^{-1}
F(000)	648
Crystal size	0.22 x 0.18 x 0.16 mm^3
Theta range for data collection	2.232 to 26.457°.

Index ranges	-11<=h<=11, -14<=k<=15, -18<=l<=18
Reflections collected	13301
Independent reflections	3284 [R(int) = 0.0487]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9485 and 0.8834
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3284 / 0 / 210
Goodness-of-fit on F^2	1.030
Final R indices [I>2sigma(I)]	R1 = 0.0588, wR2 = 0.1424
R indices (all data)	R1 = 0.1079, wR2 = 0.1690
Extinction coefficient	n/a
Largest diff. peak and hole	0.309 and -0.329 e.$Å^{-3}$

ORTEP diagram of compound **3fl**

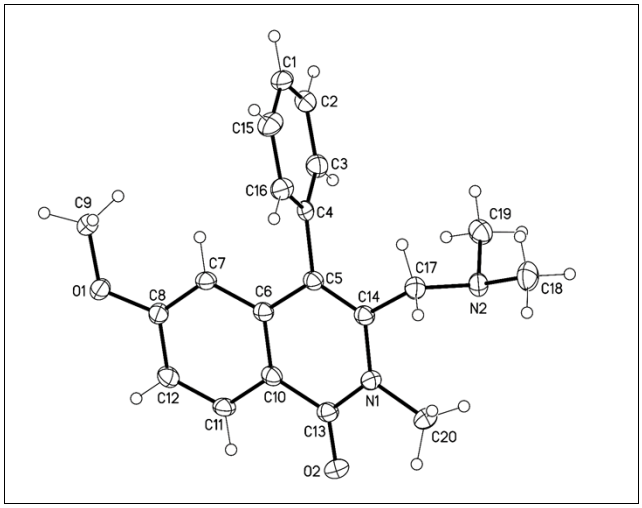


Table 3. Crystal data and structure refinement for 160602LT_0M (**3fl**).

Identification code	160602lt_0m
Empirical formula	C20 H22 N2 O2
Formula weight	322.39
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a=10.0712(6) Å
	b = 9.0247(5) Å

	c = 19.0587(9) Å
Volume	1706.90(16) $Å^3$
Z	4
Density (calculated)	1.255 Mg/m^3
Absorption coefficient	0.082 mm^{-1}
F(000)	688
Crystal size	0.20 x 0.18 x 0.18 mm^3
Theta range for data collection	2.169 to 26.406°.
Index ranges	-12<=h<=12, -11<=k<=11, -23<=l<=23
Reflections collected	14501
Independent reflections	3493 [R(int) = 0.0362]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9485 and 0.8976
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3493 / 0 / 221
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)]	R1 = 0.0424, wR2 = 0.1059
R indices (all data)	R1 = 0.0539, wR2 = 0.1133
Extinction coefficient	n/a
Largest diff. peak and hole	0.325 and -0.327 $e.Å^{-3}$