Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Cobaltaelectro-Catalyzed Oxidative Allene Annulation by Electro-Removable Hydrazides

Ruhuai Mei,*[a,b] Xinyue Fang,[b] Liang He,[a] Junmei Sun,[a] Liang Zou,[c] Wenbo Ma[b] and Lutz Ackermann*[d]

[a] College of Pharmacy and Biological Engineering, Chengdu University, Chengdu 610106, P. R. China

[b] Antibiotics Research and Re-evaluation Key Laboratory of Sichuan Province, Sichuan Industrial Institute of Antibiotics, Chengdu University, Chengdu, 610052, P. R. China

[c] Affiliated Hospital & Clinical Medical College of Chengdu University, Chengdu 610081, P. R. China

[d] Institut für Organische und Biomolekulare Chemie, Georg-August-Universität, Tammannstraße 2, 37077 Göttingen, Germany

*rmei@cdu.edu.cn

*Lutz.Ackermann@chemie.uni-goettingen.de

Table of Contents

General Remarks S-3

Optimization of the Reaction Conditions S-4

General Procedure for the Electrochemical Cobalt–Catalyzed C–H Annulation with allenes S-5

Characterization Data of Products **3** S-6

X-Ray Crystallographic Analysis of **3aa** and **4ag'** S-28

Gram Scale Experiment S-32

Electrochemical Removal of the Directing Group S-33

Mechanistic Studies S-36

Cyclic Voltammetry S-43

References S-44

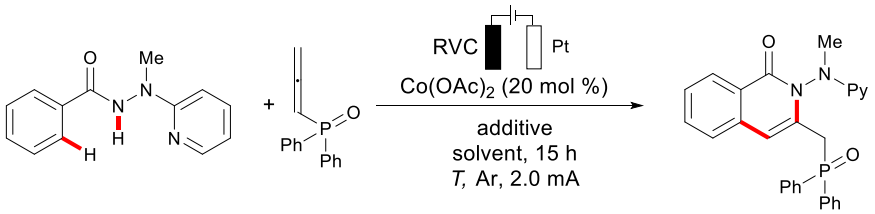
NMR-Spectra S-45

General Remarks

Catalytic reactions were carried out in undivided electrochemical cells under an Argon atmosphere using pre–dried glassware, if not noted otherwise. Benzhydrazides **1**[1] and allenes **2**[2] were synthesized according to a previously described method. Other chemicals were obtained from commercial sources and were used without further purification. Platinum electrodes (10 mm × 10 mm × 0.20 mm) and RVC electrodes (10 mm × 15 mm × 6 mm) are commercially available from Tianjin Aida. Electrolysis was conducted using an AXIOMET AX3003P potentiostat in constant current mode. Yields refer to isolated compounds, estimated to be > 95% pure as determined by ^{1}H-NMR. Chromatography separations were carried out on silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China). High resolution mass spectrometry (HRMS) was measured on Thermo-DFS mass spectrometer. NMR spectra were recorded on JEOL 600 NMR (^{1}H 600 MHz, ^{13}C 150 MHz, ^{31}P 243 MHz, ^{19}F 565 MHz) in $CDCl_3$. If not otherwise specified, chemical shifts (δ) are given in ppm. The cyclic voltammetry was carried out with a CHI650E workstation from Shanghai Chenhua.

Optimization of the Reaction Conditions

Table S-1 Optimization of the electrochemical cobalt-catalyzed oxidative C–H functionalization with allene **2a**.[a]



1a **2a** **3aa**

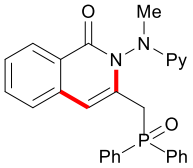
Entry	Solvent	Additive	T [℃]	Yield [%]
1	MeOH	NaOPiv	23	81
2	MeCN	NaOPiv	23	---[b]
3	DMF	NaOPiv	23	---[b]
4	DMSO	NaOPiv	23	---[b]
5	H_2O	NaOPiv	23	trace
6	HFIP	NaOPiv	23	45
7	**TFE**	NaOPiv	23	84
8	TFE	NaOPiv	40	87
9	TFE	NaOPiv	60	72
10	**TFE**	**NaOAc**	**40**	**91**
11	TFE	PivOH	40	81
12	TFE	---	40	48
13	TFE	NaOAc	40	69[c]
14	TFE	NaOAc	40	---[d]
15	TFE	NaOAc	40	trace[e]

[a] Reaction conditions: Undivided cell, **1a** (0.55 mmol), **2a** (0.50 mmol), $Co(OAc)_2$ (10 mol %), additive (2.0 equiv), solvent (3.5 mL), 2.0 mA, 15 h, RVC anode (1.0 × 1.5 cm), Pt-plate cathode (1.0 × 1.0 cm) under Ar. [b] *n*-Bu_4NPF_6 (0.30 mmol). [c] 4.0 mA, 8.0 h. [d] Without cobalt. [e] Without electricity.

General Procedure for the Electrochemical C–H Annulation with allenes

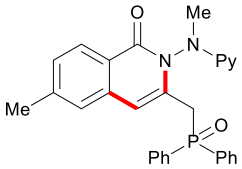
The electrolysis was carried out in an undivided cell, with a RVC anode (10 mm × 15 mm × 6 mm) and a platinum cathode (10 mm × 10 mm × 0.20 mm). $Co(OAc)_2$ (8.9 mg, 0.05 mmol, 10 mol %), NaOAc (82 mg, 1.00 mmol, 2.00 equiv), benzhydrazide **1** (0.55 mmol, 1.10 equiv) then the allene (0.50 mmol, 1.00 equiv) was dissolved in TFE (3.5 mL) under an argon atmosphere. At 40 ℃, electrolysis was started with a constant current of 2.0 mA which was then maintained for 15 h. The mixture was transferred to a flask and the electrodes were rinsed with acetone (3 × 5.0 mL). Then, Et_3N (0.5 mL) and silica gel (0.8 g) were added and the combined solvents were removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum/EtOAc, with 1% NEt_3) to yield the desired product **3**.

Characterization Data of 3



3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3aa)

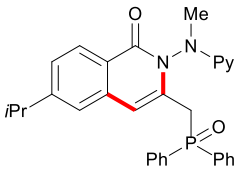
The general procedure was followed using hydrazide **1a** (125.0 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.25) yielded **3aa** (211.8 mg, 91%) as a colorless solid. M.P. = 153–154 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.25–8.23 (m, 1H), 8.21 (ddd, J = 4.9, 1.8, 0.8 Hz, 1H), 7.77–7.72 (m, 2H), 7.72–7.67 (m, 2H), 7.61–7.58 (m, 1H), 7.57–7.49 (m, 2H), 7.46–7.37 (m, 7H), 6.81–6.71 (m, 2H), 6.26 (d, J = 8.5 Hz, 1H), 3.93 (dd, J = 15.9, 13.7 Hz, 1H), 3.70 (dd, J = 16.0, 12.7 Hz, 1H), 3.33 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.4 (C_q), 159.0 (C_q), 148.0 (CH), 137.9 (CH), 136.2 (d, $^2J_{C\text{-}P}$ = 5.1 Hz, C_q), 136.1 (C_q), 132.9 (CH), 132.6 (d, $^1J_{C\text{-}P}$ = 101.3 Hz, C_q), 132.2 (d, $^4J_{C\text{-}P}$ = 3.3 Hz, CH), 132.2 (d, $^4J_{C\text{-}P}$ = 3.3 Hz, CH), 131.6 (d, $^1J_{C\text{-}P}$ = 101.6 Hz, C_q), 131.2 (d, $^3J_{C\text{-}P}$ = 9.2 Hz, CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.7 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.5 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.5 Hz, CH), 127.8 (CH), 126.6 (CH), 126.1 (CH), 126.0 (C_q), 115.8 (CH), 108.2 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.2 (d, $^1J_{C\text{-}P}$ = 67.7 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{25}N_3O_2P$ $[M+H^+]$ 466.1679, found 466.1671. The analytical data correspond with those reported in the literature.[3]



3-[(Diphenylphosphoryl)methyl]-6-methyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3ba)

The general procedure was followed using hydrazide **1b** (132.7 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.26) yielded **3ba** (160.6 mg, 67%) as a colorless solid. M.P. =

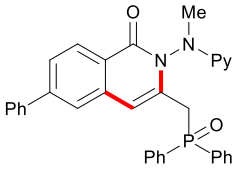
172–173 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.23–8.18 (m, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.77–7.72 (m, 2H), 7.71–7.67 (m, 2H), 7.54–7.48 (m, 2H), 7.44–7.41 (m, 4H), 7.38 (ddd, *J* = 8.8, 7.4, 1.8 Hz, 1H), 7.23–7.17 (m, 2H), 6.77–6.71 (m, 2H), 6.23 (d, *J* = 8.5 Hz, 1H), 3.92 (dd, *J* = 15.9, 13.7 Hz, 1H), 3.70 (dd, *J* = 16.0, 12.7 Hz, 1H), 3.34 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.3 (C_q), 159.0 (C_q), 147.9 (CH), 143.5 (C_q), 137.8 (CH), 136.2 (C_q), 136.1 (d, $^{2}J_{C\text{-}P}$ = 4.8 Hz, C_q), 132.7 (d, $^{1}J_{C\text{-}P}$ = 101.2 Hz, C_q), 132.1 (d, $^{4}J_{C\text{-}P}$ = 2.7 Hz, CH), 132.1 (d, $^{4}J_{C\text{-}P}$ = 2.7 Hz, CH), 131.6 (d, $^{1}J_{C\text{-}P}$ = 102.1 Hz, C_q), 131.1 (d, $^{3}J_{C\text{-}P}$ = 8.9 Hz, CH), 130.7 (d, $^{3}J_{C\text{-}P}$ = 9.3 Hz, CH), 128.8 (d, $^{2}J_{C\text{-}P}$ = 12.6 Hz, CH), 128. 7 (d, $^{2}J_{C\text{-}P}$ = 12.3 Hz, CH), 128.1 (CH), 127.7 (CH), 125.8 (CH), 123.7 (C_q), 115.6 (CH), 108.1 (d, $^{3}J_{C\text{-}P}$ = 5.9 Hz, CH) , 106.7 (CH), 38.1 (CH_3), 32.1 (d, $^{1}J_{C\text{-}P}$ = 67.8 Hz, CH_2), 21.7 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{27}N_3O_2P$ [M+H$^+$] 480.1835, found 480.1824.



3-[(diphenylphosphoryl)methyl]-6-isopropyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3ca)

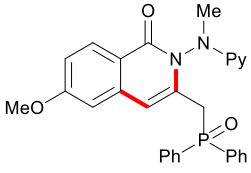
The general procedure was followed using hydrazide **1c** (148.1 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.26) yielded **3ca** (225.9 mg, 89%) as a colorless solid. M.P. = 174–175 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.23–8.20 (m, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.78–7.73 (m, 2H), 7.73–7.68 (m, 2H), 7.55–7.50 (m, 2H), 7.46–7.43 (m, 4H), 7.39 (ddd, *J* = 8.8, 7.3, 1.8 Hz, 1H), 7.29 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.27–7.25 (m, 1H), 6.84 (d, *J* = 2.6 Hz, 1H), 6.75 (dd, *J* = 6.9, 5.1 Hz, 1H), 6.24 (d, *J* = 8.5 Hz, 1H), 3.92 (dd, *J* = 16.0, 13.5 Hz, 1H), 3.71 (dd, *J* = 16.0, 13.0 Hz, 1H), 3.33 (s, 3H), 2.99 (h, *J* = 6.9 Hz, 1H), 1.28 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.3 (C_q), 159.1 (C_q), 154.3 (C_q), 148.0 (CH), 137.8 (CH), 136.4 (C_q), 136.0 (d, $^{2}J_{C\text{-}P}$ = 4.2 Hz, C_q), 132.7 (d, $^{1}J_{C\text{-}P}$ = 101.2 Hz, C_q), 132.1 (CH), 132.1 (CH), 131.2 (d, $^{1}J_{C\text{-}P}$ = 100.3 Hz, C_q), 131.1 (d, $^{3}J_{C\text{-}P}$ = 8.9 Hz, CH), 130.8 (d, $^{3}J_{C\text{-}P}$ = 9.7 Hz, CH), 128.8 (d, $^{2}J_{C\text{-}P}$ = 11.9 Hz, CH), 128.7 (d, $^{2}J_{C\text{-}P}$ = 12.5 Hz, CH), 127.9 (CH), 125.8 (CH), 124.1 (C_q), 123.3 (CH), 115.6 (CH), 108.4 (d, $^{3}J_{C\text{-}P}$ = 5.9 Hz, CH), 106.8 (CH), 38.2 (CH_3), 34.3 (CH), 32.0 (d, $^{1}J_{C\text{-}P}$ = 67.9 Hz, CH_2), 23.6

(CH_3), 23.6 (CH_3). **$^{31}P\{^1H\}$-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{31}H_{31}N_3O_2P$ $[M+H^+]$ 508.2148, found 508.2153.



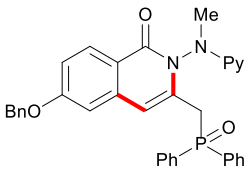
3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-6-phenylisoquinolin-1(2*H*)-one (3da)

The general procedure was followed using hydrazide **1d** (166.8 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.24) yielded **3da** (241.0 mg, 89%) as a colorless solid. M.P. = 75–76 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 8.3 Hz, 1H), 8.23–8.20 (m, 1H), 7.78–7.73 (m, 2H), 7.73–7.69 (m, 2H), 7.64–7.59 (m, 4H), 7.54–7.49 (m, 2H), 7.48–7.37 (m, 8H), 6.85 (d, *J* = 2.4 Hz, 1H), 6.76 (dd, *J* = 7.1, 5.1 Hz, 1H), 6.29 (d, *J* = 8.5 Hz, 1H), 3.95 (dd, *J* = 16.0, 13.7 Hz, 1H), 3.73 (dd, *J* = 16.0, 12.6 Hz, 1H), 3.36 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.3 (C_q), 159.0 (C_q), 148.0 (CH), 145.6 (C_q), 139.9 (C_q), 137.9 (CH), 136.7 (d, $^2J_{C\text{-}P}$ = 4.2 Hz, C_q), 136.5 (C_q), 132.7 (d, $^1J_{C\text{-}P}$ = 100.2 Hz, C_q), 132.1 (CH), 132.1 (CH), 131.7 (d, $^1J_{C\text{-}P}$ = 101.5 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.1 Hz, CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 128.9 (CH), 128.8 (d, $^2J_{C\text{-}P}$ = 11.8 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 11.7 Hz, CH), 128.4 (CH), 128.2 (CH), 127.4 (CH), 125.8 (CH), 124.8 (C_q), 124.2 (CH), 115.7 (CH), 108.3 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.2 (d, $^1J_{C\text{-}P}$ = 67.7 Hz, CH_2). **$^{31}P\{^1H\}$-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{34}H_{29}N_3O_2P$ $[M+H^+]$ 542.1992, found 542.1980.



3-[(diphenylphosphoryl)methyl]-6-methoxy-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3ea)

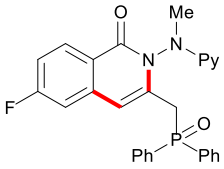
The general procedure was followed using hydrazide **1e** (141.5 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/1, R_f: 0.15) yielded **3ea** (175.9 mg, 71%) as a colorless solid. M.P. = 92–93 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.24–8.21 (m, 1H), 8.16 (d, J = 8.9 Hz, 1H), 7.78–7.73 (m, 2H), 7.72–7.68 (m, 2H), 7.56–7.50 (m, 2H), 7.50–7.40 (m, 4H), 7.40 (ddd, J = 8.7, 7.3, 1.8 Hz, 1H), 6.97 (dd, J = 8.9, 2.4 Hz, 1H), 6.84 (d, J = 2.4 Hz, 1H), 6.81 (d, J = 2.4 Hz, 1H), 6.76 (dd, J = 7.2, 5.0 Hz, 1H), 6.23 (d, J = 8.5 Hz, 1H), 3.91 (dd, J = 16.1, 13.5 Hz, 1H), 3.87 (s, 3H), 3.71 (dd, J = 16.1, 13.0 Hz, 1H), 3.32 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 163.2 (C_q), 161.0 (C_q), 159.1 (C_q), 148.0 (CH), 138.2 (C_q), 137.9 (CH), 136.7 (d, $^2J_{C\text{-}P}$ = 4.0 Hz, C_q), 132.6 (d, $^1J_{C\text{-}P}$ = 101.6 Hz, C_q), 132.2 (CH), 132.2 (CH), 131.6 (d, $^1J_{C\text{-}P}$ = 102.3 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.5 Hz，CH)，130.8 (d, $^3J_{C\text{-}P}$ = 9.7 Hz, CH), 129.8 (CH), 128.8 (d, $^2J_{C\text{-}P}$ = 11.8 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.2 Hz, CH), 119.7 (C_q), 116.2 (CH), 115.6 (CH), 108.0 (d, $^3J_{C\text{-}P}$ = 5.8 Hz, CH), 106.9 (CH), 106.8 (CH), 55.5 (CH_3), 38.2 (CH_3), 31.9 (d, $^1J_{C\text{-}P}$ = 67.9 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{27}N_3O_3P$ [M+H$^+$] 496.1785, found 496.1775.



6-(Benzyloxy)-3-[(diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3fa)

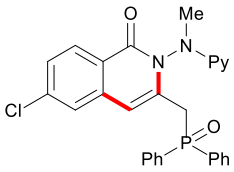
The general procedure was followed using hydrazide **1f** (183.4 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/1, R_f: 0.18) yielded **3fa** (185.8 mg, 65%) as a colorless solid. M.P. = 77–78 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.21 (ddd, J = 5.0, 1.8, 0.8 Hz, 1H), 8.16 (d, J = 8.9 Hz, 1H), 7.75–7.71 (m, 2H), 7.71–7.66 (m, 2H), 7.53–7.49 (m, 2H), 7.45–7.37 (m, 9H), 7.36–7.32 (m, 1H), 7.04 (dd, J = 8.9, 2.5 Hz, 1H), 6.86 (d, J = 2.4 Hz, 1H), 6.76 (d, J = 2.6 Hz, 1H), 6.74 (ddd, J = 7.2, 5.0, 0.7 Hz, 1H), 6.22 (d, J = 8.5 Hz, 1H), 5.12 (s, 2H), 3.89 (dd, J = 16.0, 13.5 Hz, 1H), 3.68 (dd, J = 16.1, 13.1 Hz, 1H), 3.30 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 162.3 (C_q), 161.0 (C_q), 159.1 (C_q), 148.0 (CH), 138.2 (C_q), 137.9 (CH), 136.8 (d, $^2J_{C\text{-}P}$ = 4.7 Hz, C_q), 136.1 (C_q), 132.6 (d, $^1J_{C\text{-}P}$ = 101.4

Hz, C_q), 132.2 (d, $^4J_{C\text{-}P}$ = 2.5 Hz, CH), 132.1 (d, $^4J_{C\text{-}P}$ = 2.4 Hz, CH), 131.6 (d, $^1J_{C\text{-}P}$ = 101.7 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 130.0 (CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.6 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.8 Hz, CH), 128.6 (CH), 128.2 (CH), 127.4 (CH), 119.9 (C_q), 116.7 (CH), 115.7 (CH), 108.1 (CH), 108.02 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 70.1 (CH_2), 38.2 (CH_3), 32.0 (d, $^1J_{C\text{-}P}$ = 67.7 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{35}H_{31}N_3O_3P$ [M+H$^+$] 572.2098, found 572.2086.



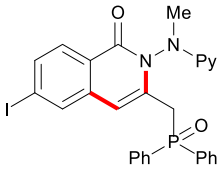
3-[(Diphenylphosphoryl)methyl]-6-fluoro-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3ga)

The general procedure was followed using hydrazide **1g** (134.9 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.30) yielded **3ga** (166.8 mg, 69%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.24 (dd, *J* = 8.8, 5.6 Hz, 1H), 8.20–8.17 (m, 1H), 7.75–7.72 (m, 2H), 7.70–7.67 (m, 2H), 7.55–7.49 (m, 2H), 7.47–7.40 (m, 5H), 7.08–7.05 (m, 1H), 7.00 (d, *J* = 9.2 Hz, 1H), 6.78–6.74 (m, 1H), 6.64 (s, 1H), 6.30 (d, *J* = 8.5 Hz, 1H), 3.93 (dd, *J* = 15.8, 13.7 Hz, 1H), 3.68 (dd, *J* = 15.9, 12.4 Hz, 1H), 3.33 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 165.5 (d, $^1J_{C\text{-}F}$ = 253.6 Hz, C_q), 160.7 (C_q), 158.9 (C_q), 148.1 (CH), 138.4 (d, $^3J_{C\text{-}F}$ = 10.0 Hz, C_q), 138.0 (d, $^2J_{C\text{-}P}$ = 4.9 Hz, C_q), 137.9 (CH), 132.6 (d, $^1J_{C\text{-}P}$ = 102.4 Hz, C_q), 132.2 (CH), 132.2 (CH), 131.6 (d, $^1J_{C\text{-}P}$ = 101.9 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 8.9 Hz, CH), 131.1 (d, $^3J_{C\text{-}F}$ = 8.9 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.3 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 11.9 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.0 Hz, CH), 122.6 (C_q), 115.9 (CH), 115.2 (d, $^2J_{C\text{-}F}$ = 23.7 Hz, CH), 110.9 (d, $^2J_{C\text{-}F}$ = 21.9 Hz, CH), 107.3 (dd, $^{3,4}J_{C\text{-}P/C\text{-}F}$ = 2.9, 2.3 Hz, CH), 106.8 (CH), 38.3 (CH_3), 32.4 (d, $^1J_{C\text{-}P}$ = 67.3 Hz, CH_2). **^{19}F-NMR** (565 MHz, $CDCl_3$) δ = -(105.34-150.30) (m). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{24}FN_3O_2P$ [M+H$^+$] 484.1585, found 484.1580.



6-Chloro-3-[(diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3ha)

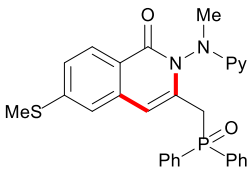
The general procedure was followed using hydrazide **1h** (143.9 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.29) yielded **3ha** (197.5 mg, 79%) as a colorless solid. M.P. = 177–178 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.19–8.17 (m, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.73 (ddd, J = 11.6, 8.1, 1.1 Hz, 2H), 7.71–7.66 (m, 2H), 7.56–7.49 (m, 2H), 7.47–7.41 (m, 5H), 7.35 (s, 1H), 7.31 (d, J = 8.6 Hz, 1H), 6.78–6.74 (m, 1H), 6.60 (d, J = 2.6 Hz, 1H), 6.30 (d, J = 8.5 Hz, 1H), 3.93 (dd, J = 15.8, 13.8 Hz, 1H), 3.68 (dd, J = 15.9, 12.4 Hz, 1H), 3.33 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.8 (C_q), 158.8 (C_q), 148.1 (CH), 139.3(C_q), 138.2 (d, $^2J_{C\text{-}P}$ = 5.4 Hz, C_q), 138.0 (CH), 137.3(C_q), 132.6 (d, $^1J_{C\text{-}P}$ = 106.7 Hz, C_q), 132.2 (CH), 132.2 (CH), 131.6 (d, $^1J_{C\text{-}P}$ = 101.8 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH) 131.1, 130.7 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH), 129.7 (CH), 128.9 (d, $^2J_{C\text{-}P}$ = 11.1 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 11.3 Hz, CH), 127.0 (CH), 125.2 (CH), 124.3 (C_q), 115.9 (CH), 106.9 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.4 (d, $^1J_{C\text{-}P}$ = 67.1 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{24}{}^{35}ClN_3O_2P$ [M+H$^+$] 500.1289, found 500.1280; calcd for $C_{28}H_{24}{}^{37}ClN_3O_2P$ [M+H$^+$] 502.1260, found 502.1253.



3-[(Diphenylphosphoryl)methyl]-6-iodo-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3ia)

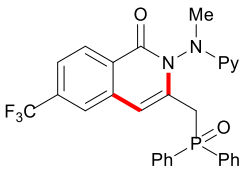
The general procedure was followed using hydrazide **1i** (194.2 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.32) yielded **3ia** (275.0 mg, 93%) as a colorless solid. M.P. =

238–239 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.18 (d, J = 4.7 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.77 (s, 1H), 7.73 (dd, J = 11.5, 7.9 Hz, 2H), 7.68 (dd, J = 12.8, 7.9 Hz, 3H), 7.56–7.50 (m, 2H), 7.47–7.42 (m, 5H), 6.79–6.74 (m, 1H), 6.58 (d, J = 2.0 Hz, 1H), 6.29 (d, J = 8.4 Hz, 1H), 3.93 (dd, J = 15.3, 13.5 Hz, 1H), 3.68 (dd, J = 15.8, 12.5 Hz, 1H), 3.32 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.2 (C_q), 158.7 (C_q), 148.1 (CH), 138.0 (CH), 137.9 (C_q), 137.5 (C_q), 135.4 (CH), 134.7 (CH), 132.6 (d, $^{1}J_{C\text{-}P}$ = 100.0 Hz , C_q), 132.2 (CH), 132.2 (CH), 131.5 (d, $^{1}J_{C\text{-}P}$ = 100.7 Hz , C_q), 131.1 (d, $^{3}J_{C\text{-}P}$ = 9.1 Hz, CH), 130.7 (d, $^{3}J_{C\text{-}P}$ = 9.3 Hz, CH), 129.3 (CH), 128.9 (d, $^{2}J_{C\text{-}P}$ = 11.2 Hz), 128.8 (d, $^{2}J_{C\text{-}P}$ = 10.2 Hz), 125.1 (C_q), 116.0 (CH), 106.8 (CH), 106.6 (d, $^{3}J_{C\text{-}P}$ = 6.0 Hz, CH), 100.9 (C_q), 38.2 (CH_3), 32.39 (d, $^{1}J_{C\text{-}P}$ = 67.0 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{24}IN_3O_2P$ [M+H$^+$] 592.0645, found 592.0630.



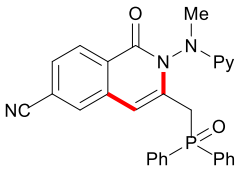
3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-6-(methylthio)isoquinolin-1(2*H*)-one (3ja)

The general procedure was followed using hydrazide **1j** (150.3 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/2, R_f: 0.10) yielded **3ja** (158.6 mg, 62%) as a colorless solid. M.P. = 204–205 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.25–8.17 (m, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.80–7.70 (m, 2H), 7.75–7.65 (m, 2H), 7.55–7.51 (m, 2H), 7.46–7.39 (m, 5H), 7.22 (d, J = 8.5 Hz, 1H), 7.15 (s, 1H), 6.83–6.75 (m, 1H), 6.76 (dd, J = 7.2, 5.0 Hz, 1H), 6.25 (d, J = 8.5 Hz, 1H), 3.92 (dd, J = 16.0, 13.5 Hz, 1H), 3.71 (dd, J = 16.0, 12.8 Hz, 1H), 3.33 (s, 3H), 2.51(s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.1 (C_q), 158.9 (C_q), 147.9 (CH), 145.7 (C_q), 137.8 (CH), 137.1 (d, $^{2}J_{C\text{-}P}$ = 4.4 Hz, C_q), 136.5 (C_q), 132.5 (d, $^{1}J_{C\text{-}P}$ = 101.4 Hz, C_q), 132.1 (CH), 132.1 (CH), 131.6 (d, $^{1}J_{C\text{-}P}$ = 102.0 Hz, C_q), 131.1 (d, $^{3}J_{C\text{-}P}$ = 9.4 Hz, CH), 130.7 (d, $^{3}J_{C\text{-}P}$ = 9.1 Hz, CH), 128.8 (d, $^{2}J_{C\text{-}P}$ = 11.2 Hz, CH), 128.7 (d, $^{2}J_{C\text{-}P}$ = 11.3 Hz, CH), 127.9 (CH), 124.3 (CH), 122.6 (C_q), 120.6 (CH), 115.7 (CH), 107.5 (d, $^{3}J_{C\text{-}P}$ = 5.9 Hz, CH), 106.7 (CH), 38.1 (CH_3), 32.0 (d, $^{1}J_{C\text{-}P}$ = 67.7 Hz, CH_2), 14.7 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{27}N_3O_2PS$ [M+H$^+$] 512.1556, found 512.1544.



3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-6-(trifluoromethyl)isoquinolin-1(2*H*)-one (3ka)

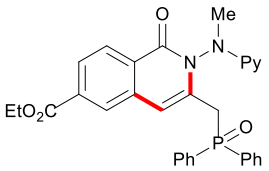
The general procedure was followed using hydrazide **1k** (162.4 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.31) yielded **3ka** (253.4 mg, 95%) as a colorless solid. M.P. = 186–187 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.34 (d, J = 8.3 Hz, 1H), 8.20–8.17 (m, 1H), 7.77–7.73 (m, 2H), 7.72–7.67 (m, 2H), 7.66 (s, 1H), 7.58–7.52 (m, 3H), 7.49–7.42 (m, 5H), 6.79 (dd, J = 7.1, 5.0 Hz, 1H), 6.73 (d, J = 2.6 Hz, 1H), 6.35 (d, J = 8.5 Hz, 1H), 3.97 (dd, J = 15.8, 13.8 Hz, 1H), 3.71 (dd, J = 15.9, 12.3 Hz, 1H), 3.35 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.7 (C_q), 158.7 (C_q), 148.1 (CH), 138.6 (d, $^2J_{C\text{-}P}$ = 5.4 Hz, C_q), 138.0 (CH), 136.1 (C_q), 134.4 (q, $^2J_{C\text{-}F}$ = 32.6 Hz, C_q), 132.3 (d, $^1J_{C\text{-}P}$ = 102.6 Hz, C_q), 132.3 (CH), 132.3 (CH), 131.5 (d, $^1J_{C\text{-}P}$ = 102.7 Hz, C_q), 131.1 (d, $^2J_{C\text{-}P}$ = 9.0 Hz, CH), 130.7 (d, $^2J_{C\text{-}P}$ = 9.7 Hz, CH), 129.0 (CH), 128.9 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH), 128.8 (d, $^3J_{C\text{-}P}$ = 8.8 Hz, CH), 128.1 (C_q), 123.6 (d, $^1J_{C\text{-}F}$ = 273.0 Hz, C_q), 123.3 (d, $^3J_{C\text{-}F}$ = 3.6 Hz, CH), 122.4 (d, $^3J_{C\text{-}F}$ = 2.0 Hz, CH), 116.1 (CH), 107.5 (d, $^3J_{C\text{-}P}$ = 6.1 Hz, CH), 106.8 (CH), 38.3 (CH_3), 32.5 (d, $^1J_{C\text{-}P}$ = 67.1 Hz, CH_2). **^{19}F-NMR** (565 MHz, $CDCl_3$) δ = -63.0 (s, 3F). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{24}F_3N_3O_2P$ [M+H$^+$] 534.1553, found 534.1540.



3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinoline-6-carbonitrile (3la)

The general procedure was followed using hydrazide **1l** (138.8 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel

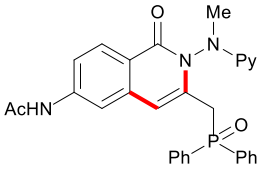
(petroleum/EtOAc 2/1, R_f: 0.15) yielded **3la** (164.3 mg, 67%) as a colorless solid. M.P. = 226–227 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.30 (d, J = 8.3 Hz, 1H), 8.17–8.14 (m, 1H), 7.76–7.72 (m, 2H), 7.71–7.66 (m, 3H), 7.57–7.51 (m, 3H), 7.49–7.43 (m, 5H), 6.80–6.77 (m, 1H), 6.59 (d, J = 2.8 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 3.98 (dd, J = 15.6, 13.9 Hz, 1H), 3.69 (dd, J = 15.8, 12.0 Hz, 1H), 3.35 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.4 (C_q), 158.5 (C_q), 148.1 (CH), 139.5 (d, $^2J_{C\text{-}P}$ = 5.8 Hz, C_q), 138.0 (CH), 136.2 (C_q), 132.5 (d, $^1J_{C\text{-}P}$ = 101.2 Hz, C_q), 132.3 (CH), 132.3 (CH), 131.5 (d, $^1J_{C\text{-}P}$ = 102.0 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.7 Hz, CH), 130.6 (CH), 129.0 (CH), 128.9 (d, $^2J_{C\text{-}P}$ = 10.0 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 9.3 Hz, CH), 128.3 (C_q), 128.0 (CH), 117.9 (C_q), 116.3 (C_q), 116.2 (CH), 106.8 (CH), 106.5 (d, $^3J_{C\text{-}P}$ = 6.1 Hz, CH), 38.3 (CH_3), 32.7 (d, $^1J_{C\text{-}P}$ = 66.5 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.9. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{24}N_4O_2P$ [M+H$^+$] 491.1631, found 491.1620.



Methyl 3-[(diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinoline-6-carboxylate (3ma)

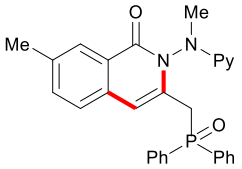
The general procedure was followed using hydrazide **1m** (156.9 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.19) yielded **3ma** (130.9 mg, 50%) as a colorless solid. M.P. = 183–184 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.27 (d, J = 8.3 Hz, 1H), 8.18–8.16 (m, 1H), 8.07–8.05 (m, 1H), 7.95 (dd, J = 8.3, 1.3 Hz, 1H), 7.76–7.71 (m, 2H), 7.71–7.66 (m, 2H), 7.55–7.48 (m, 2H), 7.46–7.41 (m, 5H), 6.75 (dd, J = 7.0, 5.1 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 6.33 (d, J = 8.5 Hz, 1H), 3.96 (dd, J = 15.7, 14.0 Hz, 1H), 3.92 (s, 3H), 3.70 (dd, J = 15.9, 12.1 Hz, 1H), 3.36 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 166.2 (C_q), 160.9 (C_q), 158.7 (C_q), 148.0 (CH), 137.9 (CH), 137.7 (d, $^2J_{C\text{-}P}$ = 5.5 Hz, C_q), 135.9 (C_q), 133.8 (C_q), 132.7 (d, $^1J_{C\text{-}P}$ = 101.1 Hz, C_q), 132.2 (d, $^4J_{C\text{-}P}$ = 2.7 Hz, CH), 132.2 (d, $^4J_{C\text{-}P}$ =2.3 Hz, CH), 131.6 (d, $^1J_{C\text{-}P}$ = 101.9 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 9.2 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 9.3 Hz, CH), 128.7 (C_q), 128.2 (CH), 127.9 (CH), 126.4 (CH), 115.9 (CH), 107.8 (d, $^2J_{C\text{-}P}$ = 6.4 Hz, CH), 106.8 (CH), 52.5 (CH_3), 38.2 (CH_3), 32.4 (d, $^1J_{C\text{-}P}$ = 67.3 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243

MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{27}N_3O_4P$ [M+H$^+$] 524.1734, found524.1723.



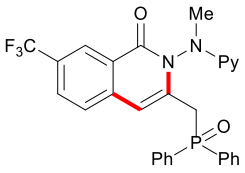
N-{3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinolin-6-yl}acetamide (3na)

The general procedure was followed using hydrazide **1n** (156.4 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/1, R_f: 0.22) yielded **3na** (214.2 mg, 82%) as a colorless solid. M.P. = 192–193 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 9.13 (s_{br} , 1H), 8.18–8.16 (m, 1H), 8.04–8.00 (m, 1H), 7.78 (s , 1H), 7.74–7.66 (m, 4H), 7.55–7.52 (m, 2H), 7.46–7.43 (m, 4H), 7.41–7.37 (m, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 6.78–6.71 (m, 1H), 6.56 (s , 1H), 6.25 (d, *J* = 8.5 Hz, 1H), 3.94 (dd, *J* = 15.7, 13.6 Hz, 1H), 3.70 (dd, *J* = 15.8, 12.5 Hz, 1H), 3.33(s , 3H), 2.03(s , 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 169.4 (C_q), 161.1 (C_q), 159.0 (C_q), 147.9 (CH), 142.9 (C_q), 137.9 (CH), 137.2 (C_q), 136.5 (d, $^2J_{C\text{-}P}$ = 6.0 Hz, C_q), 132.5 (d, $^1J_{C\text{-}P}$ = 101.0 Hz, C_q) 132.3 (CH), 132.3 (CH), 131.5 (d, $^1J_{C\text{-}P}$ = 101.9 Hz, C_q), 131.0 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 128.9 (d, $^2J_{C\text{-}P}$ = 10.8 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 10.9 Hz, CH), 128.6 (CH), 121.4 (C_q), 119.0 (CH), 115.8 (CH), 114.9 (CH), 108.5 (d, $^3J_{C\text{-}P}$ = 5.4 Hz, CH), 106.8 (CH), 38.3 (CH_3), 32.5 (d, $^1J_{C\text{-}P}$ = 67.3 Hz, CH_2), 24.3 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.9. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{28}N_4O_3P$ [M+H$^+$] 523.1894, found523.1881.



3-[(Diphenylphosphoryl)methyl]-7-methyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3oa)

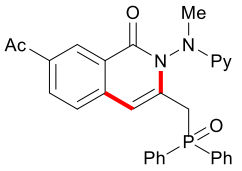
The general procedure was followed using hydrazide **1o** (132.7 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.31) yielded **3oa** (191.8 mg, 80%) as a colorless solid. M.P. = 117–118 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.20 (d, J = 4.7 Hz, 1H), 8.04 (s, 1H), 7.73 (dd, J = 11.6, 7.3 Hz, 2H), 7.69 (dd, J = 11.6, 7.3 Hz, 2H), 7.54–7.48 (m, 2H), 7.44–7.41 (m, 5H), 7.40–7.36 (m, 1H), 7.31 (d, J = 8.1 Hz, 1H), 6.76 (s, 1H), 6.75–6.72 (m, 1H), 6.22 (d, J = 8.5 Hz, 1H), 3.91 (dd, J = 16.0, 13.7 Hz, 1H), 3.68 (dd, J = 16.0, 12.7 Hz, 1H), 3.33 (s, 3H), 2.40 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.4 (C_q), 159.1 (C_q), 148.0 (CH), 137.9 (CH), 136.7 (C_q), 135.0 (d, $^2J_{C\text{-}P}$ = 5.0 Hz, C_q), 134.4 (CH), 133.8 (C_q), 132.8 (d, $^1J_{C\text{-}P}$ = 101.0 Hz, C_q), 132.1 (d, $^4J_{C\text{-}P}$ = 2.8 Hz, CH), 132.0 (d, $^4J_{C\text{-}P}$ = 3.1 Hz, CH), 131.8 (d, J = 102.4 Hz, C_q), 131.2 (d, $^3J_{C\text{-}P}$ = 9.3 Hz, CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.2 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.1 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.2 Hz, CH), 127.4 (CH), 126.1 (CH), 126.0 (C_q), 115.6 (CH), 108.2 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 38.1 (CH_3), 32.0 (d, $^1J_{C\text{-}P}$ = 67.8 Hz, CH_2), 21.3 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.2. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{27}N_3O_2P$ [M+H$^+$] 480.1835, found 480.1825.



3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-7-(trifluoromethyl)isoquinolin-1(2*H*)-one (3pa)

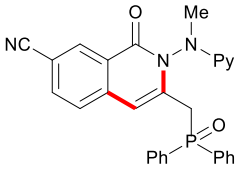
The general procedure was followed using hydrazide **1p** (162.4 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.30) yielded **3pa** (176.1 mg, 66%) as a colorless solid. M.P. = 223–224 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.34 (d, J = 8.3 Hz, 1H), 8.19–8.15 (m, 1H), 7.77–7.72 (m, 2H), 7.72–7.67 (m, 2H), 7.65 (s, 1H), 7.57–7.50 (m, 3H), 7.48–7.42 (m, 5H), 6.77 (ddd, J = 7.2, 5.1, 0.6 Hz, 1H), 6.73 (d, J = 2.8 Hz, 1H), 6.35 (d, J = 8.5 Hz, 1H), 3.97 (dd, J = 15.8, 13.8 Hz, 1H), 3.71 (dd, J = 15.9, 12.2 Hz, 1H), 3.35 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.7 (C_q), 158.6 (C_q), 148.1 (CH), 138.6 (d, $^2J_{C\text{-}p}$ = 5.4 Hz, C_q), 138.0 (CH), 136.1 (C_q), 134.4 (q, $^2J_{C\text{-}F}$ = 32.6 Hz, C_q), 132.6 (d, $^1J_{C\text{-}P}$ = 100.8 Hz, C_q), 132.3 (CH), 132.3 (CH), 131.6 (d, $^1J_{C\text{-}P}$ = 102.2 Hz, C_q), 131.1 (d, $^3J_{C\text{-}p}$ = 9.0 Hz, CH), 130.7 (d, $^3J_{C\text{-}p}$ = 9.0 Hz, CH), 129.0 (CH), 128.9 (d, $^2J_{C\text{-}p}$ = 9.7 Hz,

CH), 128.8 (d, $^{2}J_{C\text{-}p}$ = 9.0 Hz, CH), 128.1 (C_q), 123.5 (q, $^{1}J_{C\text{-}F}$ = 273.1 Hz, C_q), 123.3 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz, CH), 122.4 (q, $^{3}J_{C\text{-}F}$ = 2.1 Hz, CH), 116.1 (CH), 107.4 (d, $^{3}J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.5 (d, $^{1}J_{C\text{-}P}$ = 67.0 Hz, CH_2). **^{19}F-NMR** (565 MHz, $CDCl_3$) δ = -62.4 (s, 3F). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{24}F_3N_3O_2P$ [M+H$^+$] 534.1553, found 534.1541.



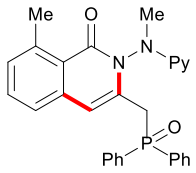
7-Acetyl-3-[(diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3qa)

The general procedure was followed using hydrazide **1q** (148.1 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.28) yielded **3qa** (172.6 mg, 68%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.78 (s, 1H), 8.20 – 8.16 (m, 2H), 7.74 (dd, *J* = 11.6, 8.1 Hz, 2H), 7.69 (dd, *J* = 11.7, 8.1 Hz, 2H), 7.56 – 7.49 (m, 2H), 7.48 – 7.41 (m, 6H), 6.78 (dd, *J* = 7.1, 3.6 Hz, 1H), 6.68 (s, 1H), 6.36 (d, *J* = 8.4 Hz, 1H), 4.02 – 3.95 (m, 1H), 3.72 (dd, *J* = 15.7, 12.4 Hz, 1H), 3.35 (s, 3H), 2.60 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 196.9 (C_q), 161.3 (C_q), 158.7 (C_q), 148.1 (CH), 139.7 (d, $^{2}J_{C\text{-}P}$ = 5.0 Hz, C_q), 139.6 (C_q), 138.0 (CH), 134.7 (C_q), 132.6 (d, $^{1}J_{C\text{-}P}$ = 97.9 Hz, C_q), 132.3 (CH), 132.3 (CH), 131.6 (d, $^{1}J_{C\text{-}P}$ = 102.1 Hz, C_q), 131.3 (CH), 130.7 (d, $^{3}J_{C\text{-}P}$ = 9.1 Hz, CH), 131.1 (d, $^{3}J_{C\text{-}P}$ = 9.1 Hz, CH), 129.5 (CH), 128.9 (d, $^{2}J_{C\text{-}P}$ = 12.1 Hz, CH), 128.8 (d, $^{2}J_{C\text{-}P}$ = 12.3 Hz, CH), 126.5 (CH), 125.5 (C_q), 116.1 (CH), 107.6 (d, $^{3}J_{C\text{-}P}$ = 6.1 Hz, CH), 106.9 (CH), 38.3 (CH_3), 32.8 (d, $^{1}J_{C\text{-}P}$ = 66.6 Hz, CH_2), 26.4 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{27}N_3O_3P$ [M+H$^+$] 508.1785, found 508.1775.



3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinoline-7-carbonitrile (3ra)

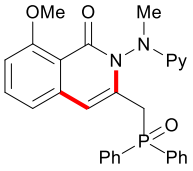
The general procedure was followed using hydrazide **1r** (138.8 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.21) yielded a mixture of isomers (174.1 mg, 71%, ratio: 14.3:1) as a colorless oil. Analytic data for the major isomer **3ra**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.51 (s, 1H), 8.15 (d, J = 4.8 Hz, 1H), 7.76 – 7.71 (m, 3H), 7.70–7.66 (m, 2H), 7.56–7.50 (m, 2H), 7.50–7.42 (m, 6H), 6.81–6.77 (m, 1H), 6.67 (d, J = 2.5 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 3.98 (dd, J = 15.6, 13.7 Hz, 1H), 3.70 (dd, J = 15.7, 12.3 Hz, 1H), 3.31 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.1 (C_q), 158.4 (C_q), 148.1 (CH), 141.0 (C_q), 141.0 (d, $^2J_{C\text{-}P}$ = 5.2 Hz, C_q), 139.1, 138.1 (CH), 134.4 (CH), 133.1 (CH), 132.5 (d, $^1J_{C\text{-}P}$ = 101.5 Hz, C_q), 132.3 (CH), 132.3 (CH), 131.6 (d, $^1J_{C\text{-}P}$ = 101.8 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.2 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.7 Hz, CH), 128.9 (d, $^2J_{C\text{-}P}$ = 11.5 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 11.7 Hz, CH), 127.0 (CH), 126.0 (C_q), 118.3 (C_q), 116.3 (CH), 109.6 (C_q), 107.0 (d, $^3J_{C\text{-}P}$ = 5.9 Hz, CH), 106.8 (CH), 38.3 (CH_3), 32.9 (d, $^1J_{C\text{-}P}$ = 66.3 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.2. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{24}N_4O_2P$ [M+H$^+$] 491.1631, found 491.1622.



3-[(Diphenylphosphoryl)methyl]-8-methyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3sa)

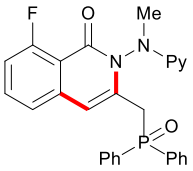
The general procedure was followed using hydrazide **1s** (132.7 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.30) yielded **3sa** (151.0 mg, 63%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.20 (d, J = 4.7 Hz, 1H), 7.75–7.66 (m, 4H), 7.53–7.48 (m, 2H), 7.46–7.37 (m, 6H), 7.19 (d, J = 7.9 Hz, 1H), 7.12 (d, J = 7.4 Hz, 1H), 6.73 (dd, J = 7.0, 5.1 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 6.25 (d, J = 8.4 Hz, 1H), 3.88 (dd, J = 15.9, 13.8 Hz, 1H), 3.65 (dd, J = 16.0, 12.5 Hz, 1H), 3.33 (s, 3H), 2.76 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.8 (C_q), 159.0 (C_q), 148.0 (CH), 142.0 (C_q), 137.8 (CH), 137.7 (C_q), 135.9 (d, $^2J_{C\text{-}P}$ = 4.6 Hz, C_q), 132.7 (d, $^1J_{C\text{-}P}$ = 101.1 Hz, C_q), 132. 1 (d, $^4J_{C\text{-}P}$ = 2.2 Hz, CH), 132.0 (d, $^4J_{C\text{-}P}$ = 2.2 Hz, CH), 132.0 (CH), 131.7 (d, $^1J_{C\text{-}P}$ = 102.0 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.2 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 129.5 (CH), 128. 8 (d, $^2J_{C\text{-}P}$ = 11.8 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.0 Hz, CH), 124.4 (CH), 115.5 (CH), 108.4 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.7 (CH), 38.0 (CH_3), 32.1 (d, $^1J_{C\text{-}P}$

= 67.9 Hz, CH_2), 23.5 (CH_3). **$^{31}P\{^1H\}$-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{27}N_3O_2P$ $[M+H^+]$ 480.1835, found 480.1824.



3-[(Diphenylphosphoryl)methyl]-8-methoxy-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3ta)

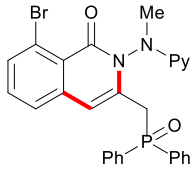
The general procedure was followed using hydrazide **1t** (141.5 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/2, R_f: 0.13) yielded **3ta** (128.8 mg, 52%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.16 (ddd, *J* = 4.9, 1.8, 0.7 Hz, 1H), 7.73–7.70 (m, 2H), 7.68 –7.63 (m, 2H), 7.52–7.45 (m, 3H), 7.44–7.38 (m, 4H), 7.36 (ddd, *J* = 8.8, 7.2, 1.9 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.71–6.67 (m, 2H), 6.24 (d, *J* = 8.5 Hz, 1H), 3.87 (dd, *J* = 16.2, 13.3 Hz, 1H), 3.87 (s, 3H), 3.63 (dd, *J* = 16.1, 13.3 Hz, 1H), 3.27 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.8 (C_q), 159.6 (C_q), 159.1 (C_q), 147.9 (CH), 139.0 (C_q), 137.8 (CH), 137.0 (d, $^2J_{C\text{-}P}$ = 4.5 Hz, C_q), 133.5 (CH), 132.6 (d, $^1J_{C\text{-}P}$ = 101.3 Hz, C_q), 132.1 (CH), 132.1 (CH), 131.7 (d, $^1J_{C\text{-}P}$ = 103.9 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 11.5 Hz, CH), 128.6 (d, $^2J_{C\text{-}P}$ = 11.6 Hz, CH), 118.4 (CH), 115.4 (CH), 115.2 (C_q), 107.8 (d, $^3J_{C\text{-}P}$ = 6.3 Hz, CH), 107.7 (CH), 106.7 (CH), 56.0 (CH_3), 38.2 (CH_3), 32.2 (d, $^1J_{C\text{-}P}$ = 67.5 Hz, CH_2). **$^{31}P\{^1H\}$-NMR** (243 MHz, $CDCl_3$) δ = 28.2. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{27}N_3O_3P$ $[M+H^+]$ 496.1785, found 496.1775.



3-[(Diphenylphosphoryl)methyl]-8-fluoro-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3ua)

The general procedure was followed using hydrazide **1u** (134.9 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel

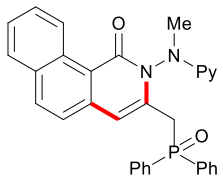
(petroleum/EtOAc 2/1, R_f: 0.33) yielded **3ua** (181.3 mg, 75%) as a colorless solid. M.P. = 209–210 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.19–8.16 (m, 1H), 7.76–7.71 (m, 2H), 7.70–7.65 (m, 2H), 7.54–7.47 (m, 3H), 7.46–7.40 (m, 5H), 7.14 (d, J = 8.0 Hz, 1H), 7.02–6.96 (m, 1H), 6.75 (ddd, J = 7.1, 5.0, 1.1 Hz, 1H), 6.69 (s, 1H), 6.32 (d, J = 8.5 Hz, 1H), 3.92 (dd, J = 15.8, 13.6 Hz, 1H), 3.66 (dd, J = 15.9, 12.7 Hz, 1H), 3.29 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 162.3 (d, $^1J_{C\text{-}F}$ = 264.8 Hz, C_q), 158.8 (C_q), 158.4 (d, $^2J_{C\text{-}F}$ = 4.5 Hz, C_q), 148.0 (CH), 138.7 (C_q), 137.9 (CH), 137.8 (C_q), 133.7 (d, $^3J_{C\text{-}F}$ = 9.8 Hz, CH), 132.6 (d, $^1J_{C\text{-}P}$ = 100.9 Hz, C_q), 132.2 (CH), 132.2 (CH), 131.7 (d, $^1J_{C\text{-}P}$ = 101.2 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.2 Hz, CH), 128.8 (d, $^2J_{C\text{-}p}$ = 11.6 Hz, CH), 128.7 (d, $^2J_{C\text{-}p}$ = 11.7 Hz, CH), 121.9 (d, $^4J_{C\text{-}F}$ = 3.8 Hz, CH), 115.9 (CH), 115.0 (d, $^2J_{C\text{-}p}$ = 5.3 Hz, C_q), 113.2 (d, $^2J_{C\text{-}F}$ = 21.4 Hz, CH), 107.3 (d, $^3J_{C\text{-}P}$ = 5.4 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.4 (d, $^1J_{C\text{-}P}$ = 67.1 Hz, CH_2). **^{19}F-NMR** (565 MHz, $CDCl_3$) δ = -110.4 (d, J = 9.2 Hz, 1F). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.2. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{24}FN_3O_2P$ [M+H$^+$] 484.1585, found 484.1574.



8-Bromo-3-[(diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3va)

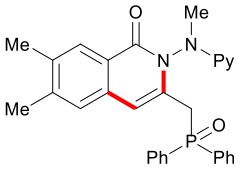
The general procedure was followed using hydrazide **1v** (168.4 mg, 0.55 mmol) , $Co(OAc)_2$ (17.7 mg, 0.1 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.31) yielded **3va** (209.6 mg, 77%) as a colorless solid. M.P. = 177–178 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.16 (d, J = 4.2 Hz, 1H), 7.75–7.70 (m, 2H), 7.70–7.65 (m, 2H), 7.61 (dd, J = 6.2, 2.7 Hz, 1H), 7.53–7.49 (m, 2H), 7.45–7.40 (m, 5H), 7.33–7.29 (m, 2H), 6.74 (dd, J = 7.1, 5.0 Hz, 1H), 6.66 (d, J = 2.5 Hz, 1H), 6.31 (d, J = 8.5 Hz, 1H), 3.89 (dd, J = 15.9, 13.4 Hz, 1H), 3.64 (dd, J = 16.0, 12.6 Hz, 1H), 3.30 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 159.4 (C_q), 158.7 (C_q), 148.0 (CH), 139.1 (C_q), 137.9 (CH), 137.7 (d, $^2J_{C\text{-}P}$ = 4.8 Hz, C_q), 133.4 (CH), 132.5 (d, $^1J_{C\text{-}P}$ = 101.5 Hz, C_q), 132.6 (CH), 132.2 (d, $^4J_{C\text{-}P}$ = 3.1 Hz, CH), 132.2 (d, $^4J_{C\text{-}P}$ = 3.1 Hz, CH), 131.7 (d, $^1J_{C\text{-}P}$ = 101.5 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 8.9 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.6 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.4 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.4 Hz,

CH), 126.1 (CH), 123.3 (C_q), 123.0 (C_q), 115.8 (CH), 107.5 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.7 (CH), 38.1 (CH_3), 32.4 (d, $^1J_{C\text{-}P}$ = 67.4 Hz, CH_2). **$^{31}P\{^1H\}$-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{24}{}^{79}BrN_3O_2P$ [M+H^+] 544.0784, found 544.0774; $C_{28}H_{24}{}^{81}BrN_3O_2P$ [M+H^+] 546.0764, found 546.0748.



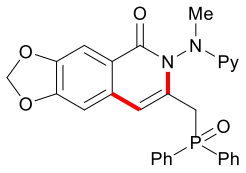
3-[(Diphenylphosphoryl)methyl]-2-[methyl(pyridin-2-yl)amino]benzo[h]isoquinolin-1(2*H*)-one (3wa)

The general procedure was followed using hydrazide **1w** (152.5 mg, 0.55 mmol), $Co(OAc)_2$ (17.7 mg, 0.1 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.24) yielded **3wa** (105.7 mg, 41%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 9.90 (d, *J* = 8.6 Hz, 1H), 8.22 (d, *J* = 4.4 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.75 (dd, *J* = 11.6, 7.7 Hz, 2H), 7.71 (dd, *J* = 11.6, 7.5 Hz, 2H), 7.62–7.58 (m, 1H), 7.54–7.48 (m, 3H), 7.46–7.41 (m, 4H), 7.39 (t, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 2.2 Hz, 1H), 6.75 (dd, *J* = 6.9, 5.1 Hz, 1H), 6.26 (d, *J* = 8.4 Hz, 1H), 4.03 (dd, *J* = 15.8, 13.7 Hz, 1H), 3.79 (dd, *J* = 15.8, 12.9 Hz, 1H), 3.40 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.5 (C_q), 159.0 (C_q), 148.0 (CH), 138.0 (d, $^2J_{C\text{-}P}$ = 5.4 Hz, C_q), 138.0 (C_q), 137.9 (CH), 134.3 (CH), 132.5 (d, $^1J_{C\text{-}P}$ = 102.3 Hz, C_q), 132.2 (CH), 132.2 (CH), 132.0 (C_q), 131.6 (d, $^1J_{C\text{-}P}$ = 102.2 Hz, C_q), 131.7 (C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.2 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 13.1 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 13.9 Hz, CH), 128.4 (CH), 128.1 (CH), 126.9 (CH), 126.3 (CH), 124.6 (CH), 119.4 (C_q), 115.7 (CH), 108.5 (d, $^3J_{C\text{-}P}$ = 5.7 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.6 (d, $^1J_{C\text{-}P}$ = 67.1 Hz, CH_2). **$^{31}P\{^1H\}$-NMR** (243 MHz, $CDCl_3$) δ = 28.3. **HR-MS** (ESI) *m/z* calcd for $C_{32}H_{27}N_3O_2P$ [M+H^+] 516.1835, found 516.1824.



3-[(Diphenylphosphoryl)methyl]-6,7-dimethyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one (3xa)

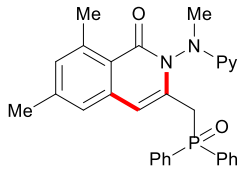
The general procedure was followed using hydrazide **1x** (140.4 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.35) yielded **3xa** (224.6 mg, 91%) as a colorless solid. M.P. = 180–181 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.24–8.21 (m, 1H), 8.01 (s, 1H), 7.77–7.72 (m, 2H), 7.72–7.68 (m, 2H), 7.56–7.50 (m, 2H), 7.46–7.43 (m, 4H), 7.38 (ddd, *J* = 8.7, 7.3, 1.8 Hz, 1H), 7.20 (s, 1H), 6.78–6.73 (m, 2H), 6.20 (d, *J* = 8.5 Hz, 1H), 3.91 (dd, *J* = 16.0, 13.7 Hz, 1H), 3.70 (dd, *J* = 16.0, 12.9 Hz, 1H), 3.33 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.3 (C_q), 159.1 (C_q), 148.0 (CH), 143.0 (C_q), 137.9 (CH), 136.2 (C_q), 135.8 (d, $^2J_{C\text{-}P}$ = 4.4 Hz, C_q), 134.3 (C_q), 132.1 (CH), 132.1 (CH), 132.7 (d, $^1J_{C\text{-}P}$ = 101.4 Hz, C_q), 131.7 (d, $^1J_{C\text{-}P}$ = 102.2 Hz, C_q), 131.2 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.7 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.4 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.6 Hz, CH), 127.8 (CH), 126.5 (CH), 124.1 (C_q), 115.6 (CH), 108.1 (d, $^3J_{C\text{-}P}$ = 6.0 Hz, CH), 106.8 (CH), 38.2 (CH_3), 32.0 (d, $^1J_{C\text{-}P}$ = 68.1 Hz, CH_2), 20.2 (CH_3), 19.7 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{29}N_3O_2P$ [M+H$^+$] 494.1992, found 494.1982.



7-[(Diphenylphosphoryl)methyl]-6-[methyl(pyridin-2-yl)amino]-[1,3]dioxolo[4,5-g]isoquinolin-5(6*H*)-one (3ya)

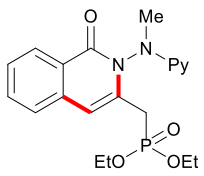
The general procedure was followed using hydrazide **1y** (149.2 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/2, R_f: 0.09) yielded **3ya** (188.5 mg, 74%) as a colorless solid. M.P. = 200–201 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.18 (d, *J* = 4.8 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.74–7.67 (m, 4H), 7.52–7.48 (m, 2H), 7.46–7.37 (m, 5H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.74–6.72 (m, 1H), 6.64 (s, 1H), 6.27 (d, *J* = 8.5 Hz, 1H), 6.05 (s. 2H), 3.92 (dd, *J* = 15.7, 13.7 Hz, 1H), 3.67 (dd, *J* = 15.8, 12.5 Hz, 1H), 3.31 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 160.8 (C_q), 159.0 (C_q), 150.2 (C_q), 148.0 (CH),

141.2 (C_q), 137.8 (CH), 136.9 (d, $^2J_{C\text{-}P}$ = 5.3 Hz, C_q), 132.8 (d, $^1J_{C\text{-}P}$ = 101.0 Hz, C_q), 132.1 (CH), 132.1 (CH), 131.8 (d, $^1J_{C\text{-}P}$ = 100.7 Hz, C_q), 131.1 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, CH), 130.7 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.6 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.1 Hz, CH), 123.3 (CH), 120.9 (C_q), 120.2 (C_q), 115.7 (CH), 108.5 (CH), 106.8 (CH), 100.2 (CH_2), 100.8 (d, $^3J_{C\text{-}P}$ = 6.6 Hz, CH), 38.3 (CH_3), 32.65 (d, $^1J_{C\text{-}P}$ = 67.1 Hz, CH_2). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 27.9. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{25}N_3O_4P$ [M+H$^+$] 510.1577, found 510.1569.



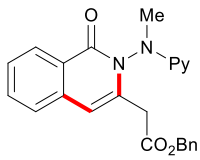
3-[(Diphenylphosphoryl)methyl]-6,8-dimethyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3za)

The general procedure was followed using hydrazide **1z** (140.4 mg, 0.55 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 2/1, R_f: 0.34) yielded **3za** (165.3 mg, 67%) as a colorless solid. M.P. = 164–165 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.22–8.19 (m, 1H), 7.75–7.66 (m , 4H), 7.53–7.49 (m, 2H), 7.44–7.41 (m, 4H), 7.39–7.35 (m, 1H), 6.99 (s, 1H), 6.96 (s, 1H), 6.74–6.70 (m, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 6.22 (d, *J* = 8.4 Hz, 1H), 3.85 (dd, *J* = 16.0, 13.7 Hz, 1H), 3.63 (dd, *J* = 16.1, 12.7 Hz, 1H), 3.32 (s, 3H), 2.72 (s, 3H), 2.34 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.7 (C_q), 159.1 (C_q), 148.0 (CH), 142.5 (C_q), 141.9 (C_q), 137.9 (C_q), 137.8 (CH), 135.8 (d, $^2J_{C\text{-}P}$ = 4.7 Hz, C_q), 132.7 (d, $^1J_{C\text{-}P}$ = 101.2 Hz, C_q), 132.1 (d, $^4J_{C\text{-}P}$ = 3.5 Hz, CH), 132.0 (d, $^4J_{C\text{-}P}$ = 3.3 Hz, CH), 131.74 (d, $^1J_{C\text{-}P}$ = 102.4 Hz, C_q), 131.2 (d, $^3J_{C\text{-}P}$ = 8.7 Hz, CH), 131. 1 (CH), 130.8 (d, $^3J_{C\text{-}P}$ = 9.0 Hz, CH), 128.8 (d, $^2J_{C\text{-}P}$ = 12.1 Hz, CH), 128.7 (d, $^2J_{C\text{-}P}$ = 12.1 Hz, CH), 124.3 (CH), 122.2 (C_q), 115.4 (CH), 108.3 (d, $^3J_{C\text{-}P}$ = 5.9 Hz, CH), 106.7 (CH), 77.2, 77.0, 76.8, 38.1 (CH_3), 32.0 (d, $^1J_{C\text{-}P}$ = 68.0 Hz, CH_2), 23.3 (CH_3), 21.4 (CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 28.4. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{29}N_3O_2P$ [M+H$^+$] 494.1992, found 494.1982.



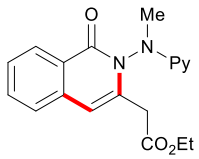
Diethyl {[2-(methyl[pyridin-2-yl]amino)-1-oxo-1,2-dihydroisoquinolin-3-yl]methyl}phosphonate (3ab)

The general procedure was followed using hydrazide **1a** (125.0 mg, 0.55 mmol) and allene **2b** (88.1 mg, 0.50 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 1/1, R_f: 0.08) yielded **3ab** (110.4 mg, 55%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.29 (d, *J* = 8.0 Hz, 1H), 8.22–8.20 (m, 1H), 7.66–7.62 (m, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.46 (ddd, *J* = 8.8, 7.3, 1.8 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 6.77–6.74 (m, 2H), 6.38 (d, *J* = 8.5 Hz, 1H), 4.14–4.04 (m, 4H), 3.58 (s, 3H), 3.42 (dd, *J* = 21.5, 15.9 Hz, 1H), 3.19 (dd, *J* = 22.9, 15.9 Hz, 1H), 1.29 (t, *J* = 6.2 Hz, 3H), 1.27 (t, *J* = 6.2 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.5 (C_q), 158.9 (C_q), 148.1 (CH), 137.8 (CH), 136.5 (d, $^2J_{C\text{-}P}$ = 6.2 Hz, C_q), 136.2 (d, $^4J_{C\text{-}P}$ = 2.9 Hz, C_q), 133.0 (CH), 128.0 (CH), 126.6 (CH), 126.1 (C_q), 125.9 (CH), 115.7 (CH), 107.3 (d, $^3J_{C\text{-}P}$ = 7.6 Hz, CH), 106.7 (CH), 62.5 (d, $^2J_{C\text{-}P}$ = 6.9 Hz, CH_2), 62.4 (d, $^2J_{C\text{-}P}$ = 6.9 Hz, CH_2), 38.3 (CH_3), 28.7 (d, $^1J_{C\text{-}P}$ = 143.1 Hz, CH_2), 16.4 (d, $^3J_{C\text{-}P}$ = 5.0 Hz, CH_3), 16.3 (d, $^3J_{C\text{-}P}$ = 5.0 Hz, CH_3). **^{31}P{^{1}H}-NMR** (243 MHz, $CDCl_3$) δ = 24.5. **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{25}N_3O_4P$ [M+H$^+$] 402.1577, found 402.1569.



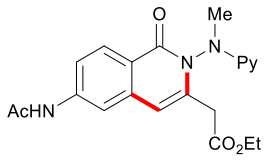
Benzyl 2-{2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinolin-3-yl}acetate (3ac)

The general procedure was followed using hydrazide **1a** (113.7 mg, 0.50 mmol) and allene **2c** (95.8 mg, 0.55 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 8/1, R_f: 0.30) yielded **3ac** (149.8 mg, 75%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.31 (d, *J* = 7.9 Hz, 1H), 8.23–8.21 (m, 1H), 7.67–7.63 (m, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.48–7.42 (m, 2H), 7.35–7.30 (m, 3H), 7.30–7.27 (m, 2H), 6.77 (dd, *J* = 7.1, 5.0 Hz, 1H), 6.52 (s, 1H), 6.40 (d, *J* = 8.5 Hz, 1H), 5.09 (d, *J* = 12.2 Hz, 1H), 5.00 (d, *J* = 12.2 Hz, 1H), 3.73 (d, *J* = 16.5 Hz, 1H), 3.61 (d, *J* = 16.5 Hz, 1H), 3.38 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 169.1 (C_q), 161.3 (C_q), 158.7 (C_q), 148.0 (CH), 138.7 (C_q), 137.8 (CH), 136.3 (C_q), 135.3 (C_q), 132.9 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128.0 (CH), 126.7 (CH), 126.4 (C_q), 125.9 (CH), 115.9 (CH), 107.8 (CH), 106.9 (CH), 67.0 (CH_2), 38.6 (CH_2), 38.3 (CH_3). **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3O_3$ [M+H$^+$] 400.1656, found 400.1652.



Ethyl 2-{2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinolin-3-yl}acetate (3ad)

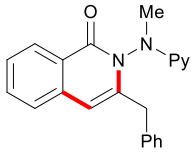
The general procedure was followed using hydrazide **1a** (113.7 mg, 0.50 mmol) and allene **2d** (61.7 mg, 0.55 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 8/1, R_f: 0.29) yielded **3ad** (161.9 mg, 96%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.31 (d, J = 8.2 Hz, 1H), 8.23–8.21 (m, 1H), 7.64 (t, J = 8.2 Hz, 1H), 7.55–7.44 (m, 1H), 7.48–7.42 (m, 2H), 6.79–6.75 (m,1H), 6.52 (s, 1H), 6.41 (d, J = 8.5 Hz, 1H), 4.12–4.01 (m, 2H), 3.67 (d, J = 16.3 Hz, 1H), 3.56 (d, J = 16.3 Hz, 1H), 3.48 (s, 3H), 1.18 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 169.2 (C_q), 161.3 (C_q), 158.7 (C_q), 148.0 (CH), 138.9 (C_q), 137.7 (CH), 136.4 (C_q), 132.9 (CH), 128.0 (CH), 126.7 (CH), 126.4 (C_q), 125.9 (CH), 115.8 (CH), 107.8 (CH), 106.9 (CH), 61.3 (CH_2), 38.7 (CH_2), 38.3 (CH_3), 14.1 (CH_3). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{20}N_3O_3$ [M+H$^+$] 338.1499, found 338.1492.



Ethyl 2-{6-acetamido-2-[methyl(pyridin-2-yl)amino]-1-oxo-1,2-dihydroisoquinolin-3-yl}acetate (3nd)

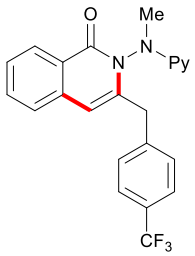
The general procedure was followed using hydrazide **1n** (142.2 mg, 0.50 mmol) and allene **2d** (61.7 mg, 0.55 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 5/1, R_f: 0.26) yielded **3nd** (181.4 mg, 92%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.23–8.20 (m, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.46 (ddd, J = 8.9, 7.3, 1.8 Hz, 1H), 7.26 (dd, J = 8.5, 1.8 Hz, 1H), 7.22 (d, J = 1.6 Hz, 1H), 6.78–6.74 (m, 1H), 6.42 (s, 1H), 6.40 (d, J = 8.5 Hz, 1H), 4.15–3.96 (m, 2H), 3.64 (d, J = 16.4 Hz, 1H), 3.54 (d, J = 16.4 Hz, 1H), 3.46 (s, 3H), 2.53 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 169.1 (C_q), 161.1 (C_q), 158.7 (C_q), 147.9 (CH), 145.7 (C_q), 139.7 (C_q), 137.7 (CH), 136.8 (C_q), 128.2 (CH), 124.4 (CH), 123.0 (C_q), 120.7 (CH), 115.8 (CH), 107.1 (CH), 106.9 (CH),

61.3 (CH_2), 38.7 (CH_2), 38.4 (CH_3), 14.8 (CH_3), 14.1 (CH_3). **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{23}N_4O_4$ [M+H^+] 395.1714, found 395.1711.



3-Benzyl-2-[methyl(pyridin-2-yl)amino]isoquinolin-1(2*H*)-one(3ae)

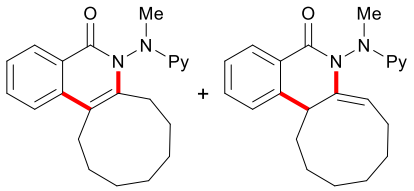
The general procedure was followed using hydrazide **1a** (113.6 mg, 0.50 mmol) and allene **2e** (63.9 mg, 0.55 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 15/1, R_f: 0.40) yielded **3ae** (99.0 mg, 58%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.31 (d, *J* = 7.9 Hz, 1H), 8.25–8.22 (m, 1H), 7.67–7.62 (m, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.44–7.40 (m, 1H), 7.40–7.36 (m, 1H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.23–7.17 (m, 3H), 6.74–6.70 (m, 1H), 6.39 (s, 1H), 6.23 (d, *J* = 8.4 Hz, 1H), 3.91 (s, 2H), 3.15 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.6 (C_q), 158.7 (C_q), 148.0 (CH), 144.9 (C_q), 137.7 (CH), 137.0 (C_q), 136.6 (C_q), 132.9 (CH), 129.1 (CH), 128.5 (CH), 128.0 (CH), 126.8 (CH), 126.3 (CH), 125.9 (C_q), 125.8 (CH), 115.1 (CH), 106.4 (CH), 106.2 (CH), 38.8 (CH_2), 37.8 (CH_3). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{20}N_3O$ [M+H^+] 342.1601, found 342.1594.



2-[Methyl(pyridin-2-yl)amino]-3-[4-(trifluoromethyl)benzyl]isoquinolin-1(2*H*)-one(3af)

The general procedure was followed using hydrazide **1a** (113.6 mg, 0.50 mmol) and allene **2f** (101.3 mg, 0.55 mmol). Purification by column chromatography on silica gel (petroleum/EtOAc 15/1, R_f: 0.38) yielded **3af** (135.1 mg, 66%) as a colorless solid. M.P. = 162–163 ℃ (recrystallization solvents: petroleum/EtOAc). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 7.9 Hz, 1H), 8.22–8.19 (m, 1H), 7.69–7.65 (m, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.44 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.36–7.32 (m, 1H), 7.30 (d, *J* = 8.0 Hz,

2H), 6.71 (dd, *J* = 7.1, 5.0 Hz, 1H), 6.44 (s, 1H), 6.16 (d, *J* = 8.4 Hz, 1H), 3.97 (s, 2H), 3.19 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 161.5 (C_q), 158.5 (C_q), 147.9 (CH), 143.9 (C_q), 141.2 (C_q), 137.7 (CH), 136.4 (C_q), 133.0 (CH), 129.4 (CH), 129.1 (q, $^2J_{C\text{-}F}$ = 32.6 Hz, C_q), 128.1 (CH), 126.6 (CH), 126.0 (C_q), 125.9 (CH), 125.4 (q, $^3J_{C\text{-}F}$ = 3.0 Hz, CH), 124.0 (q, $^1J_{C\text{-}F}$ = 271.8 Hz, C_q), 115.3 (CH), 106.7 (CH), 106.2 (CH), 38.8, 37.9 (CH_3). **^{19}F NMR** NMR (565 MHz, $CDCl_3$) δ = -62.31 (s). **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}F_3N_3O$ $[M+H^+]$ 410.1475, found 410.1465.



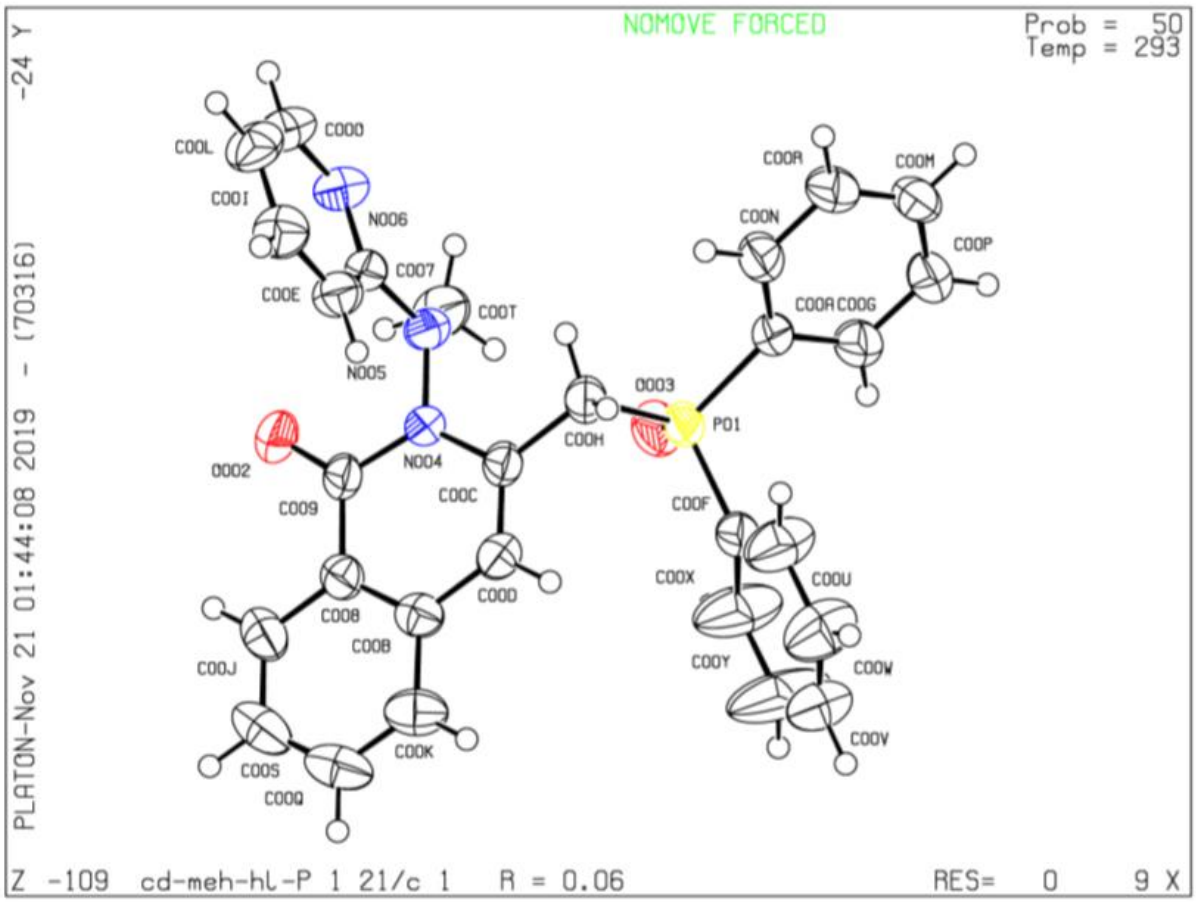
3ag **3ag'**

6-[Methyl(pyridin-2-yl)amino]-6,7,8,9,10,11,12,13-octahydro-5*H*-cyclonona[c]isoquinolin-5-one (3ag) and (S,E)-6-[Methyl(pyridin-2-yl)amino]-6,8,9,10,11,12,13,13a-octahydro-5*H*-cyclonona[c]isoquinolin-5-one (3ag')

The general procedure was followed using hydrazide **1a** (114.0 mg, 0.50 mmol) and allene **2g** (79.4mg, 0.65 mmol, 1.30 equiv). Purification by column chromatography on silica gel (petroleum/EtOAc 20/1, R_f: 0.40) yielded a column-inseparable mixture of **3ag'** and **3ag** as a pale yellow oil (119.9 mg, 69%, ratio by ^{1}H-NMR: 2.7:1).

X-Ray crystallographic data of 3aa and 4ag':

The structure of **3aa** was determined by the X-ray diffraction. Recrystallized from CH_2Cl_2 and petroleum ether. Further information can be found in the CIF file (Deposition number: **CCDC 1963954**).



Bond precision: C-C = 0.0040 A Wavelength=1.54184

Cell:	a=9.7656(3)	b=22.5128(5)	c=11.5704(3)
	alpha=90	beta=110.736(3)	gamma=90
Temperature:	293 K		

	Calculated	Reported
Volume	2378.98(12)	2379.00(11)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C28 H24 N3 O2 P	C28 H24 N3 O2 P
Sum formula	C28 H24 N3 O2 P	C28 H24 N3 O2 P
Mr	465.47	465.47
Dx,g cm-3	1.300	1.300
Z	4	4
Mu (mm-1)	1.268	1.268
F000	976.0	976.0
F000'	979.81	
h,k,lmax	12,27,14	11,27,14
Nref	4664	4561
Tmin,Tmax	0.665,0.684	0.624,1.000
Tmin'	0.418	

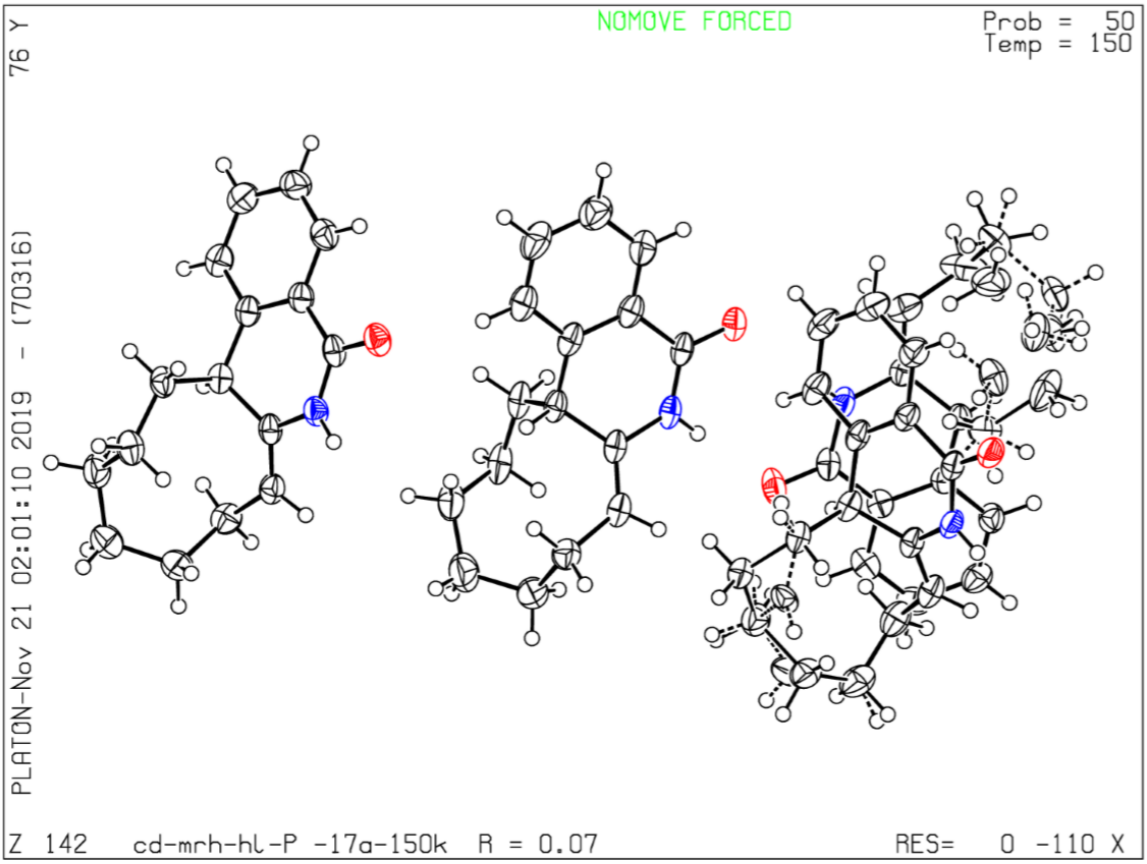
Correction method= # Reported T Limits: Tmin=0.624 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.978 Theta(max)= 71.900

R(reflections)= 0.0618(3742) wR2(reflections)= 0.1834(4561)

S = 1.016 Npar= 308

The structure of **4ag'** was determined by the X-ray diffraction. Recrystallized from EtOAc and petroleum ether. Further information can be found in the CIF file (Deposition number: **CCDC 1967120**).



Bond precision: C-C = 0.0031 A Wavelength=1.54184

Cell: a=9.6378(4) b=11.2515(5) c=24.9151(7)
alpha=87.202(3) beta=83.800(3) gamma=78.211(4)
Temperature: 150 K

	Calculated	Reported
Volume	2628.33(18)	2628.34(17)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C16 H19.73 N O, C16 H18.31 N O, 2(C16 H19 N O)	0.5(C16 H19 N O), 0.25(C16 H18.31 N O), 0.25(C16 H19.73 N O)
Sum formula	C64 H76.04 N4 O4	C16 H19 N O
Mr	965.32	241.32
Dx,g cm-3	1.220	1.220
Z	2	8
Mu (mm-1)	0.587	0.587
F000	1040.1	1040.0
F000'	1042.87	
h,k,lmax	11,13,30	11,13,30
Nref	10288	10083
Tmin,Tmax	0.738,0.943	0.426,1.000
Tmin'	0.631	

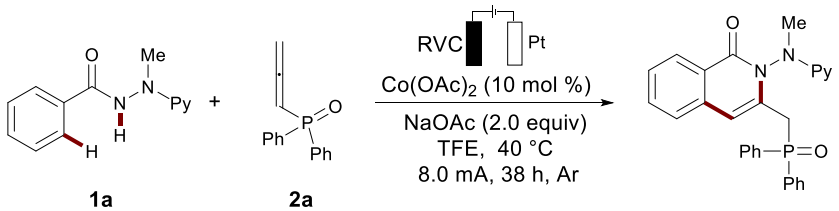
Correction method= # Reported T Limits: Tmin=0.426 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.980 Theta(max)= 71.847

R(reflections)= 0.0746(8519) wR2(reflections)= 0.2191(10083)

S = 1.037 Npar= 701

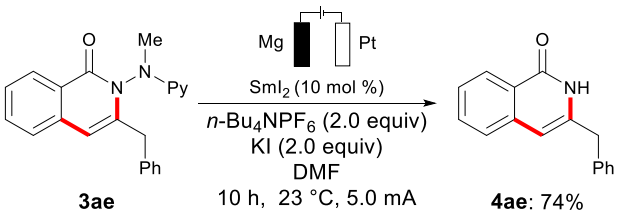
Gram Scale Experiment:



1a (5.5 mmol, 1.25 g) **2a** (5.0 mmol, 1.20 g) **3aa** (67%, 1.56 g)

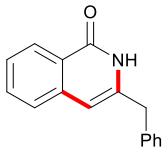
To a 50 mL three neck round bottom flask was added $Co(OAc)_2$ (88.5 mg, 0.50 mmol, 10 mol %), NaOAc (820 mg, 10 mmol, 2.0 equiv) and benzhydrazide **1a** (5.5 mmol, 1.25 g). Then, the flask was equipped with rubber stoppers, two pieces of platinum plates (15 × 10 mm) as cathode and one piece of reticulated vitreous carbon (30 × 10 mm) as anode. After flush the flask with argon 3 times, solvent TFE (36 mL) and allene **2a** (5.0 mmol, 1.20 g) was added *via* cannula under an argon atmosphere. At 40 ℃, electrolysis was started with a constant current of 8 mA which was then maintained for 38 h (Electricity = 2.24 F/mol). The mixture was then transferred to a flask and the electrodes were rinsed with acetone (3 × 15 mL). Then, Et_3N (2.0 mL) and silica gel (3.0 g) were added and the combined solvents were removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum/EtOAc = 2/1 to 1/1, with 1% NEt_3) to yield the desired product **3aa** as a light yellow solid (1.56 g, 67%) and re-isolated hydrazide **1a** (163 mg, 13%).

Electrochemical Removal of the Directing Group:



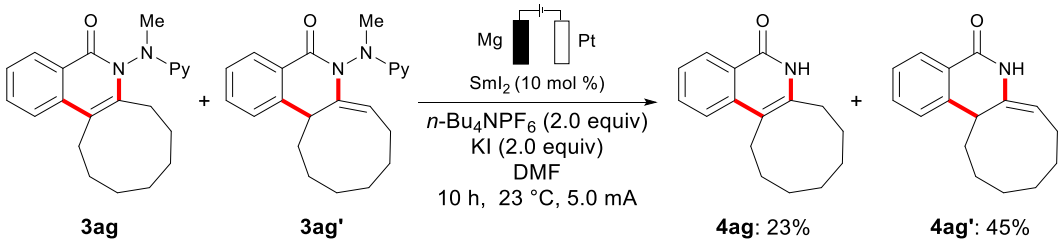
3ae **4ae**: 74%

The electrolysis was carried out in an undivided cell, with a magnesium anode (3.0 mm × 30 mm × 0.25 mm) and a platinum cathode (10 mm × 10 mm × 0.20 mm). Substrate **3ae** (170.7 mg, 0.50 mmol), KI (166.0 mg, 1.0 mmol) and *n*-Bu_4NPF_6 (387 mg, 1.0 mmol) were dissolved in DMF (5.0 mL) under an argon atmosphere, then SmI_2 (0.1 M in THF, 0.50 mL, 10 mol %) was added dropwise while stirring. At ambient temperature, electrolysis was started with a constant current of 5.0 mA which was maintained for 10 h. Then, H_2O (5.0 mL) was added to the mixture. The resulting slurry was filtrated through a celite pad, which was washed with EtOAc (20 mL × 3) and H_2O (5 mL). The organic phase were washed with H_2O (20.0 mL), brine (20.0 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography (petroleum/EtOAc 1/1, R_f: 0.24) on silica gel afforded the desired products **4ae** (87.0 mg, 74%) as a pale yellow solid. Analytic data for **4ae**:



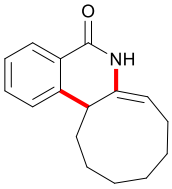
3-Benzylisoquinolin-1(2*H*)-one (4ae)

^{1}H NMR (600 MHz, $CDCl_3$) δ = 11.06 (s, 1H), 8.40–8.36 (m, 1H), 7.61 (ddd, J = 8.2, 7.1, 1.3 Hz, 1H), 7.47–7.41 (m, 2H), 7.38–7.34 (m, 2H), 7.31–7.29 (m, 2H), 7.26–7.22 (m, 1H), 6.28 (s, 1H), 3.97 (s, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 164.5 (C_q), 140.6 (C_q), 138.4 (C_q), 136.6 (C_q), 132.6 (CH), 129.3 (CH), 128.8 (CH), 127.3 (CH), 127.1 (CH), 126.0 (CH), 125.8 (CH), 124.5 (C_q), 104.9(CH), 39.5 (CH_2). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{14}NO$ [M+H$^+$] 236.1070, found 236.1065. The analytical data correspond with those reported in the literature.[4]



The electrolysis was carried out in an undivided cell, with a magnesium anode (3.0 mm × 30 mm × 0.25 mm) and a platinum cathode (10 mm × 10 mm × 0.20 mm). The mixture containing **3ag** (173.7 mg, 0.50 mmol), KI (166.0 mg, 1.0 mmol) and *n*-Bu_4NPF_6 (387 mg, 1.0 mmol) were dissolved in DMF (5.0 mL) under an argon atmosphere, then SmI_2 (0.1 M in THF, 0.50 mL, 10 mol %) was added dropwise while stirring. At ambient temperature, electrolysis was started with a constant current of 5.0 mA which was maintained for 10 h. Then, H_2O (5.0 mL) was added to the mixture. The resulting slurry was filtrated through a celite pad, which was washed with EtOAc (20 mL × 3) and H_2O (5 mL). The organic phase were washed with H_2O (20.0 mL), brine (20.0 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification by column chromatography (petroleum/EtOAc 1/1, R_f: 0.24, 0.32) on silica gel afforded the NH-free products **4ag'** (54.3 mg, 45%) and **4ag** (27.8 mg, 23%) as white solids.

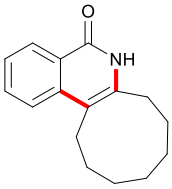
Analytic data for **4ag'**:



(S,E)-6,8,9,10,11,12,13,13a-Octahydro-5*H*-cyclonona[c]isoquinolin-5-one (4ag')

^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.08 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.80 (s, 1H), 7.49 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.24 (d, *J* = 7.3 Hz, 1H), 5.16 (dd, *J* = 10.1, 7.6 Hz, 1H), 4.03–3.96 (m, 1H), 2.24–2.19 (m, 1H), 2.16–2.09 (dtd, *J* = 12.9, 10.3, 2.5 Hz, 1H), 1.87–1.80 (m, 1H), 1.77–1.69 (m, 3H), 1.62–1.51 (m, 5H), 1.40–1.37 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 163.6 (C_q), 143.7 (C_q), 134.4 (C_q), 132.7 (CH), 127.9 (CH), 126.8 (CH), 126.7 (CH), 126.3 (C_q), 111.5 (CH), 39.0 (CH), 37.5 (CH_2), 26.3 (CH_2), 26.2 (CH_2), 25.5 (CH_2), 24.6 (CH_2), 23.5 (CH_2). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{20}NO$ [$M+H^+$] 242.1539, found 242.1532.

Analytic data for **4ag**:

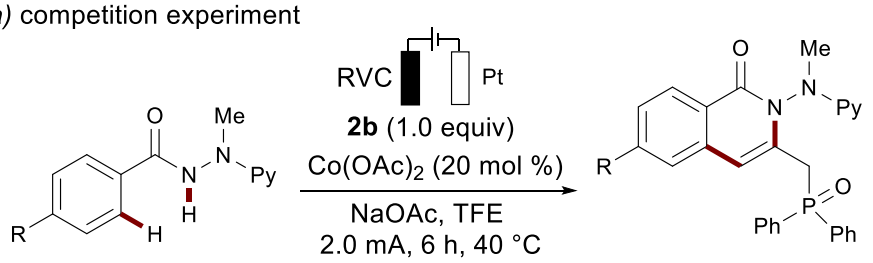


6,7,8,9,10,11,12,13-Octahydro-5*H*-cyclonona[c]isoquinolin-5-one (4ag)

^{1}H NMR (600 MHz, $CDCl_3$) δ = 10.89 (s_{br}, 1H), 8.47 (d, J = 7.9 Hz, 1H), 7.79–7.57 (m, 2H), 7.47–7.43 (m, 1H), 2.91–2.87 (m, 2H), 2.85–2.81 (m, 2H), 1.85 (p, J = 8.1 Hz, 2H), 1.78–1.73 (m, 2H), 1.47 (ddq, J = 23.5, 11.9, 4.9 Hz, 4H), 1.37 (p, J = 6.3 Hz, 2H). **^{13}C NMR** (150 MHz, D_6-DMSO, 100 ℃) δ = 162.4 (C_q), 139.6 (C_q), 138.2 (C_q), 132.6 (CH), 127.5 (CH), 126.0 (C_q), 125.5 (CH), 123.6 (CH), 111.9 (C_q), 29.5 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 24.8 (CH_2), 24.8 (CH_2), 24.7 (CH_2). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{20}NO$ [$M+H^+$] 242.1539, found 242.1527.

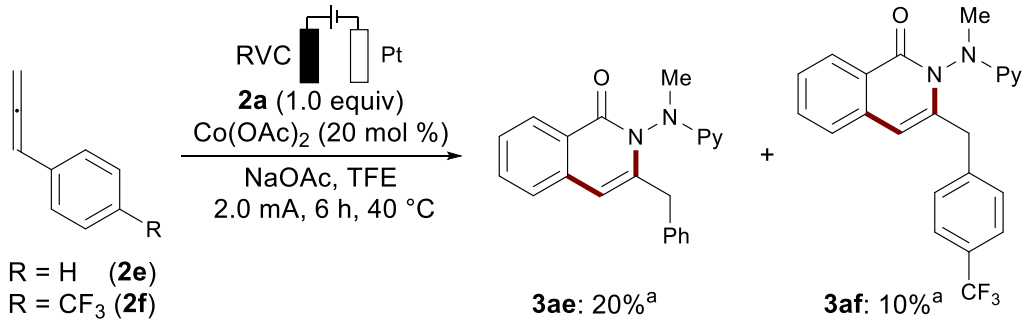
Mechanistic Studies

(a) competition experiment



R = Me (**1b**)
R = CF_3 (**1k**)

R = Me (**3ba**): 44%[a]
R = CF_3 (**3ka**): 18%[a]



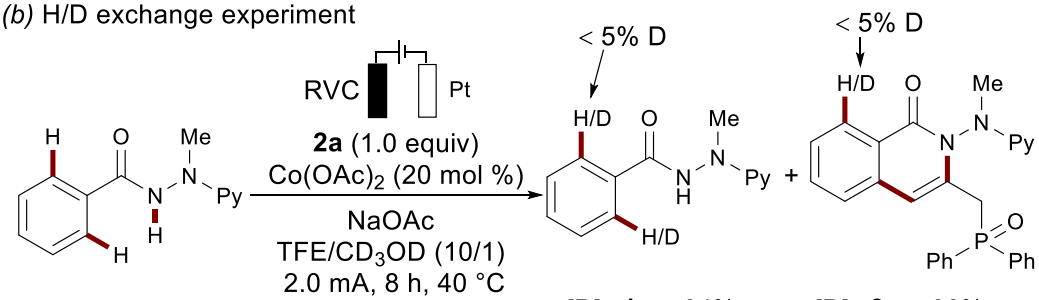
R = H (**2e**)
R = CF_3 (**2f**)

3ae: 20%[a]

3af: 10%[a]

[a] ^{1}H-NMR yield with 1,3,5-trimethoxybenzene as internal standard.

(b) H/D exchange experiment

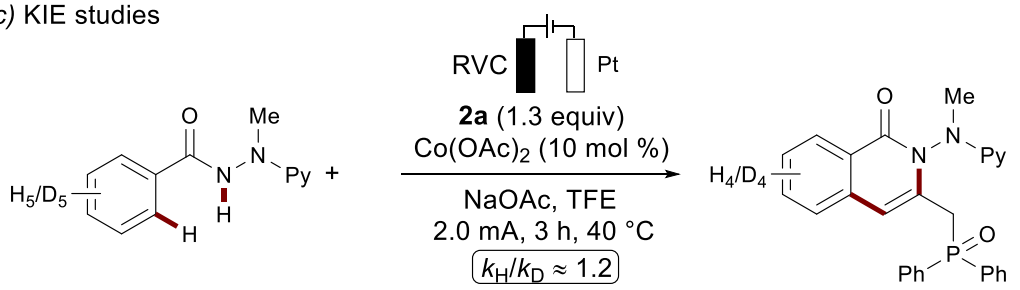


1a (2.0 equiv)

$[D]_n$-**1a**: 64%

$[D]_n$-**3aa**: 66%

(c) KIE studies

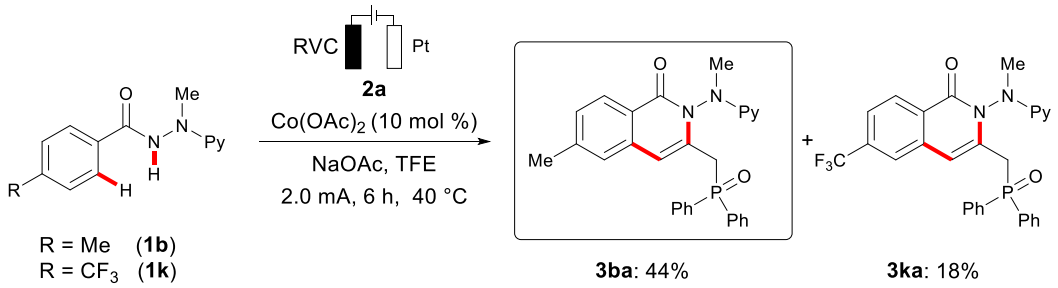


1a or $[D]_5$-**1a**

3aa or $[D]_4$-**3aa**

Scheme S1 Key Mechanistic Findings

Competition Experiments



The general procedure was followed using hydrazides **1b** (120.7 mg, 0.50 mmol), **1k** (147.6 mg, 0.50 mmol) and allene **2a** (120.1 mg, 0.50 mmol). Electrolysis was performed at 40 ℃ using a constant current of 2.0 mA which was maintained for 6 h. The mixture was diluted with a solvent mixture of petroleum/EtOAc/NEt_3 (200/100/3, 70 mL) and filtrated through a silica pad. After evaporation of the solvent, the crude mixture was analyzed by ^{1}H-NMR using 1,3,5- trimethoxybenzene (8.4 mg, 0.05 mmol) as the internal standard, which showed a product distribution of 2.4:1 in favor of **3ba**.

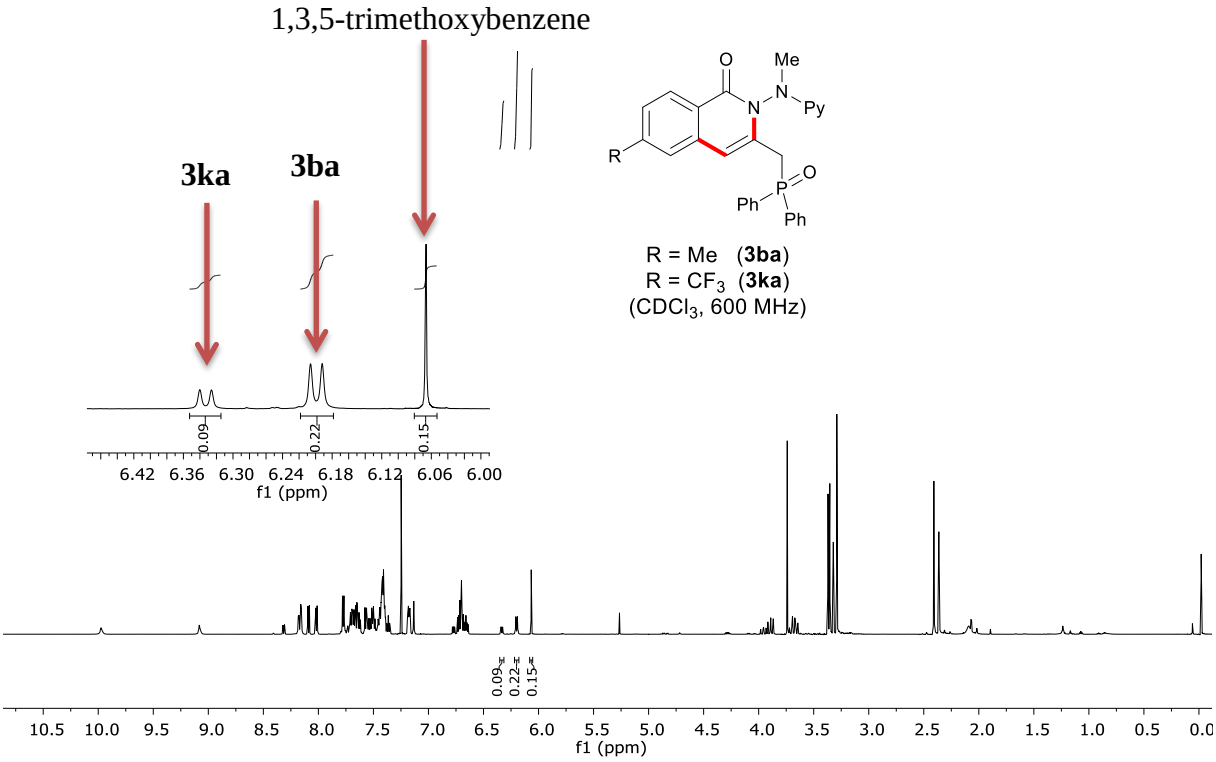
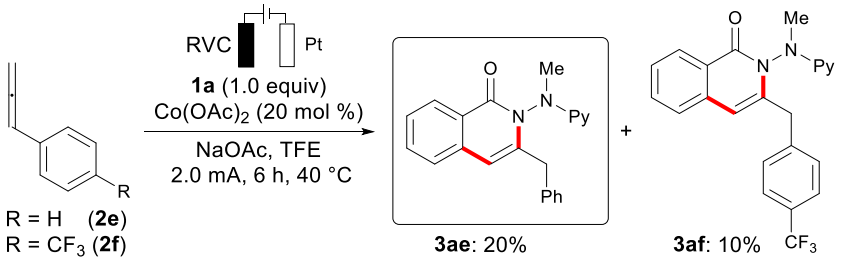


Figure S-2: ^{1}H-NMR Spectra of mixture of **3ba** and **3ka** with 1,3,5- trimethoxybenzene as internal standard**.**



The general procedure was followed using allenes **1b** (58.1 mg, 0.50 mmol), **1k** (92.1 mg, 0.50 mmol) and hydrazide **1a** (114.0 mg, 0.50 mmol). Electrolysis was performed at 40 ℃ using a constant current of 2.0 mA which was maintained for 6 h. The mixture was diluted with a solvent mixture of petroleum/EtOAc/NEt_3 (200/10/2, 70 mL) and filtrated through a silica pad. After evaporation of the solvent, the crude mixture was analyzed by ^{1}H-NMR using 1,3,5- trimethoxybenzene (16.8 mg, 0.10 mmol) as the internal standard, which showed a product distribution of 2.0:1 in favor of **3ae**.

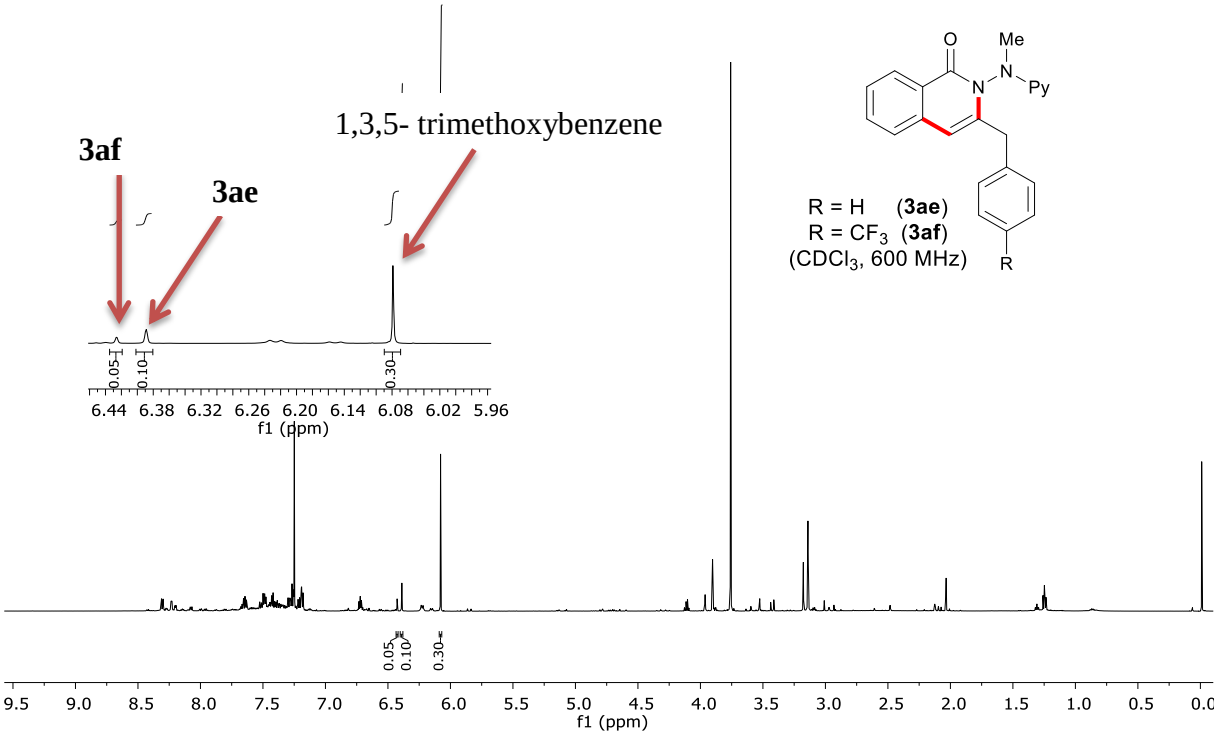
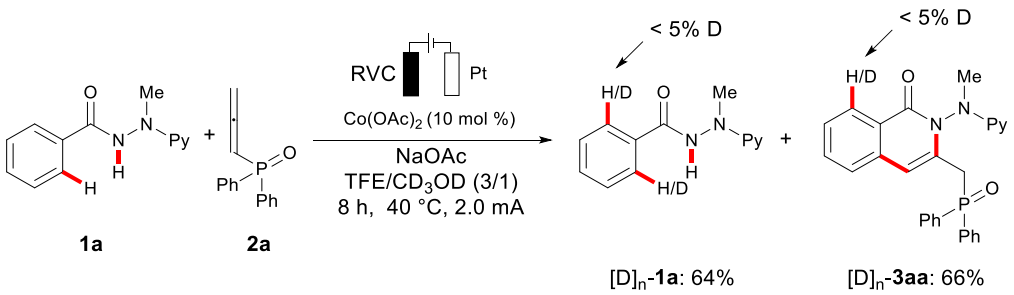


Figure S-3: ^{1}H-NMR Spectra of mixture of **3ae** and **3af** with 1,3,5- trimethoxybenzene as internal standard**.**

Deuteration Experiment



The general procedure was followed using allene **2a** (121 mg, 0.50 mmol) and hydrazide **1a** (227 mg, 1.0 mmol). Electrolysis was performed at 40 ℃ and a constant current of 2.0 mA in a solvent mixture of TFE/CD_3OD (3/1, 4.0 mL) for 8 h. The mixture was transferred to a flask and the electrodes were rinsed with acetone (3 × 5.0 mL). Then Et_3N (1.0 mL), silica gel (0.8 g) were added and the combined solvent was removed under reduced pressure. The residue solid sample was purified by column chromatography on silica gel (petroleum/EtOAc = 2/1 to 1/1) yielded the desired product $[D]_n$-**3aa** (155.0 mg, 66%) as a light yellow oil and re-isolated starting material $[D]_n$-**1a** (147.1 mg, 64%) as a white solid. No H/D-Scrambling could be detected in either compounds by ^{1}H-NMR spectroscopy.

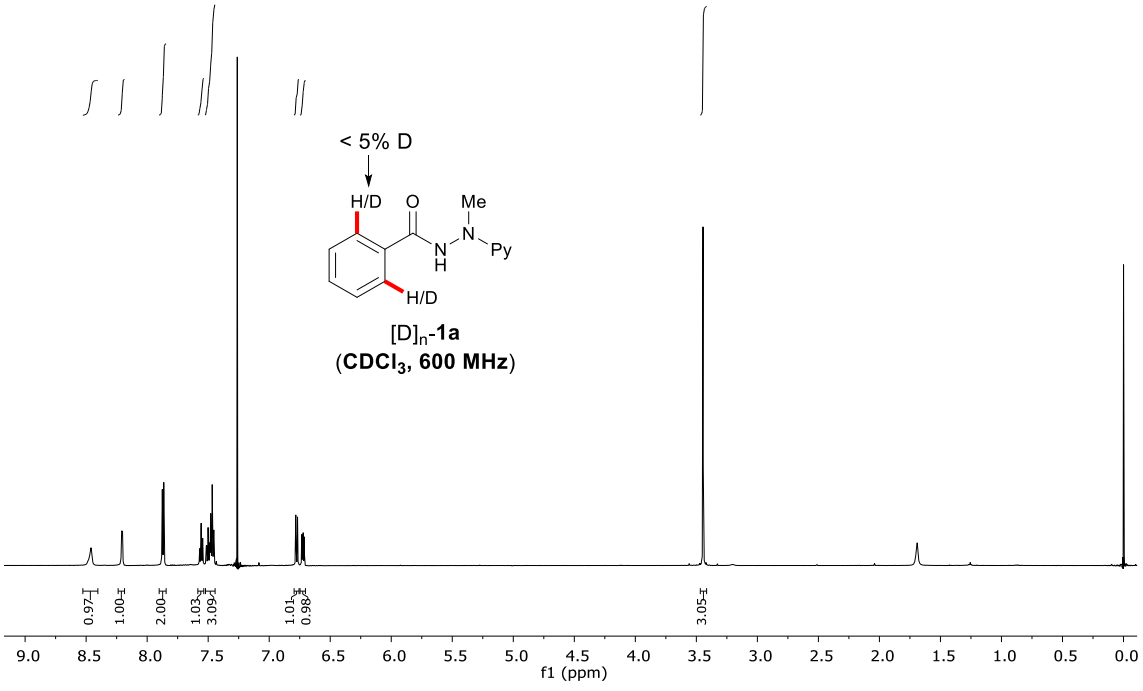


Figure S-4: ^{1}H-NMR Spectra of $[D]_n$-**1a** for the deuteration study.

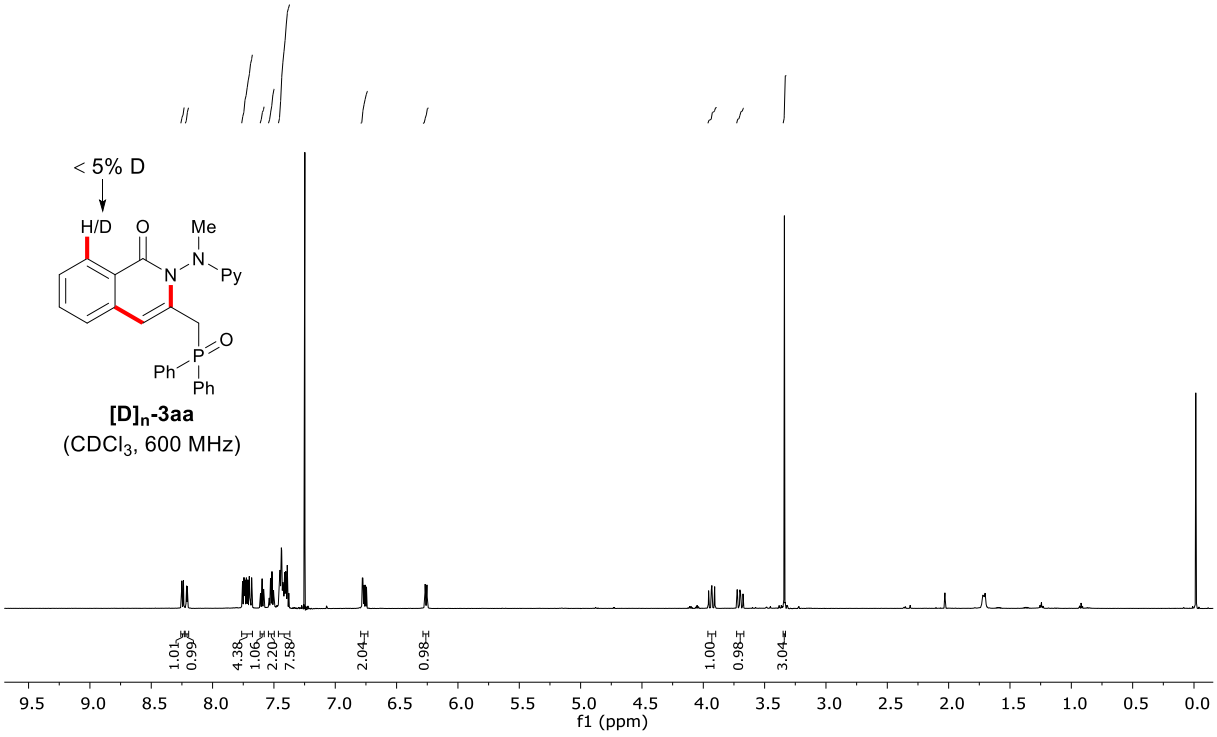
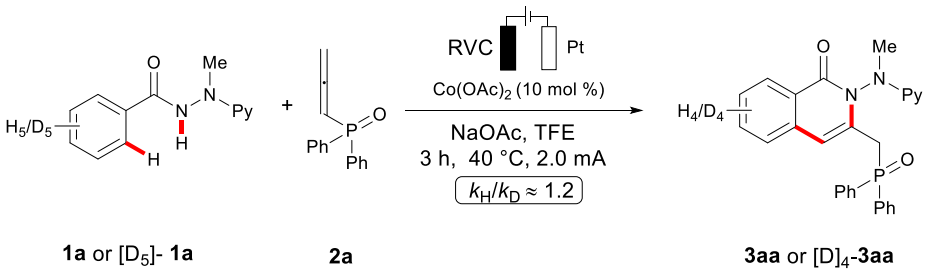


Figure S-5: ^{1}H-NMR Spectra of $[D]_n$-**3aa** for the deuteration study.

KIE studies

Parallel experiment



Two independent reactions following the general procedure were carried out using substrates **1a**, $[D]_5$-**1a** (0.50 mmol each) and allene **2a** (120.1 mg, 0.50 mmol). Electrolysis was performed at 40 ℃ with a constant current of 2.0 mA for 3 h. At ambient temperature, these two reaction mixtures were combined and transferred to a flask. The electrodes were rinsed with acetone (3 × 5.0 mL). Then, Et_3N (1.0 mL) and silica gel (0.8 g) were added and the combined solvent was removed under reduced pressure. The residue solid sample was purified by column chromatography on silica gel (petroleum/EtOAc = 1/1 to 1/2) yielded the desired product $[D]_n$-**3aa** (58.2 mg, 25%) as a colorless solid. The k_H/k_D value was calculated based on ^{1}H-NMR analysis.

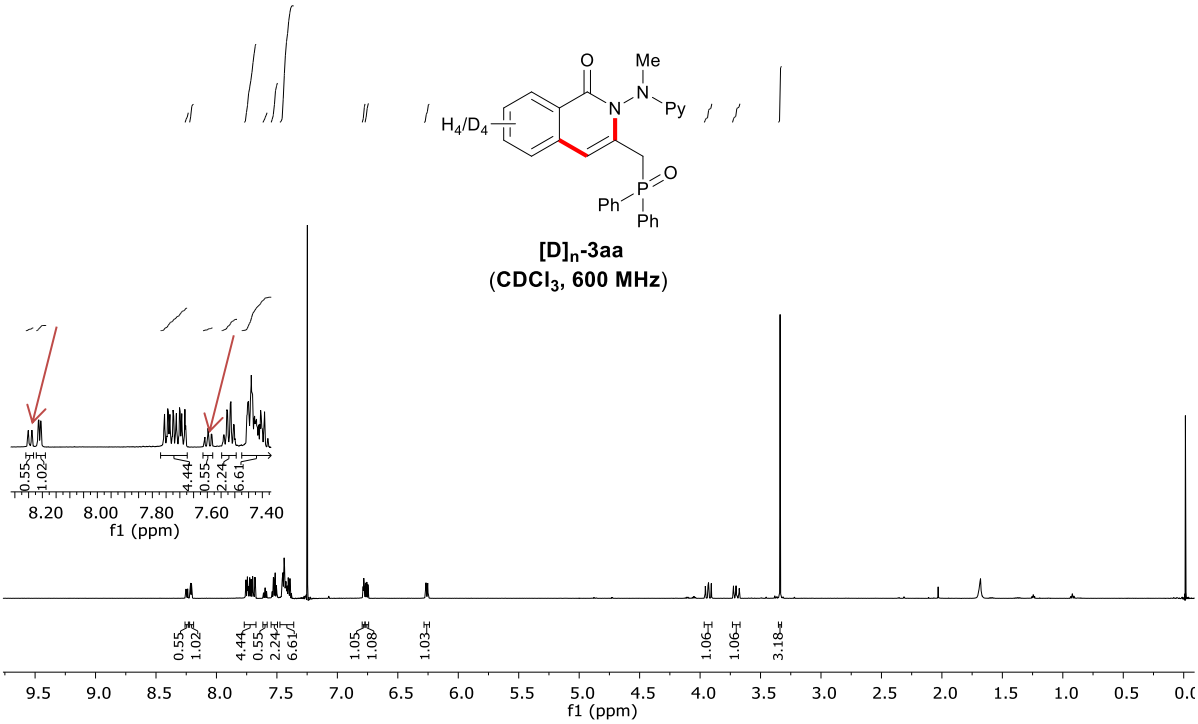


Figure S-6: ^{1}H-NMR Spectra of mixture of [D]$_4$-**3aa** and **3aa.**

Cyclic Voltammetry

The cyclic voltammetry was carried out with a CHI650E workstation. A glassy-carbon electrode (5 mm-diameter, disc-electrode) was used as the working electrode, a Pt wire as auxiliary electrode and a SCE electrode was used as the reference. The measurements were carried out at a scan rate of 100 mVs^{-1}.

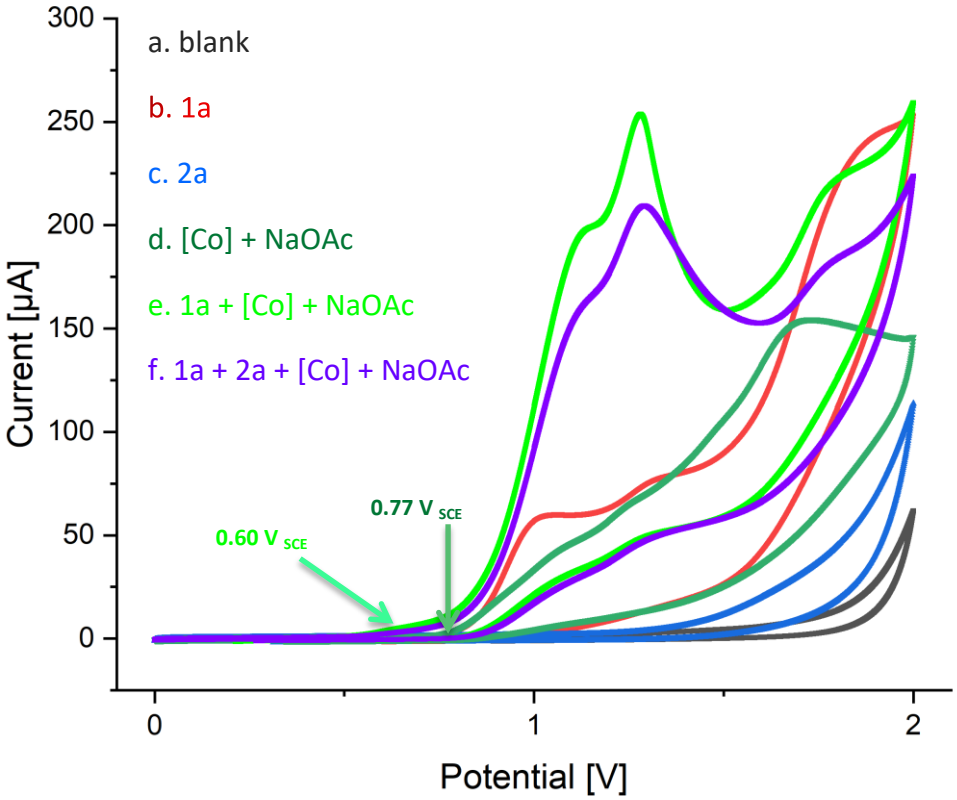


Figure S-7: Cyclic voltammogram at 100 mV/s.

Cyclic voltammograms at 100 mVs^{-1}: *n*-Bu_4NPF_6 (0.1 M in MeOH), concentration of substrates 2 mM (NaOAc 6 mM). (a) blank; (b) substrate **1a**; (c) substrate **2a**; (d) $Co(OAc)_2$ and NaOAc; (e) $Co(OAc)_2$, **1a** and NaOAc; (f) $Co(OAc)_2$, **1a**, **2a** and NaOAc.

Reference

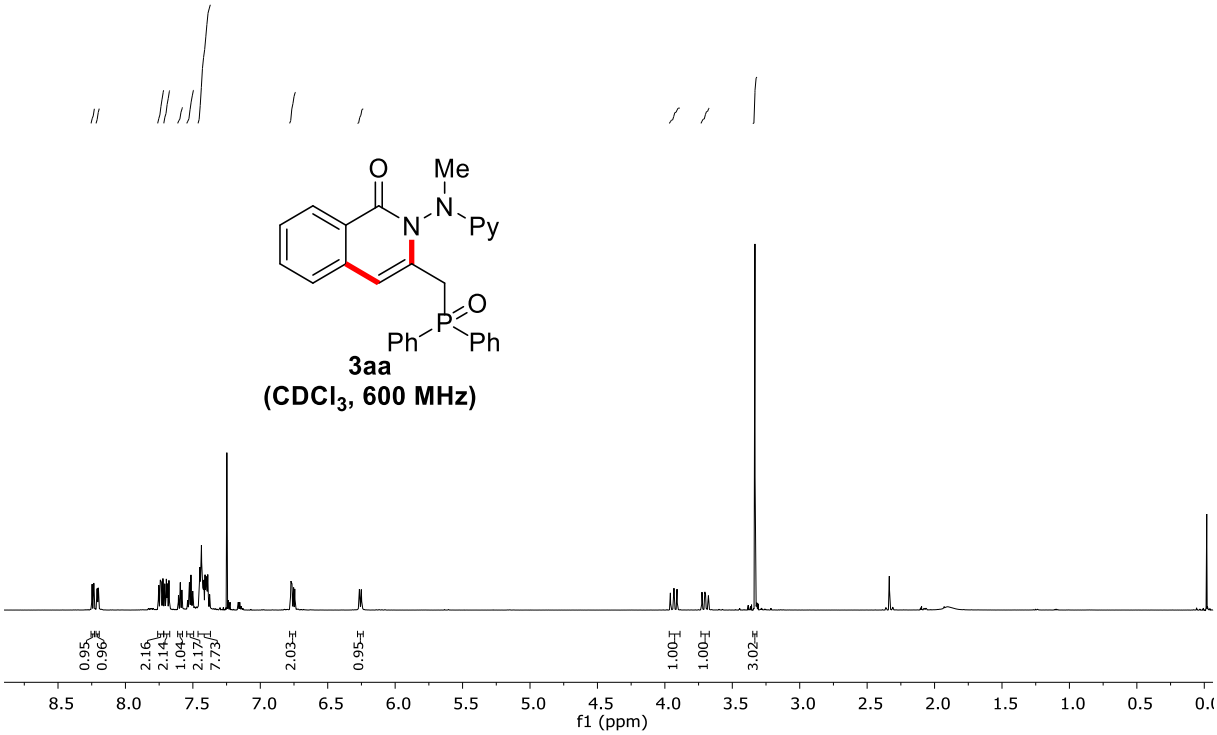
[1] (a) H. Zhao, X. Shao, T. Wang, S. Zhai, S. Qiu, C. Tao, H. Wang and H. Zhai, *Chem. Commun.*, 2018, **54**, 4927–4930; (b) R. Mei, N. Sauermann, J. C. Oliveira and L. Ackermann, *J. Am. Chem. Soc.*, 2018, **140**, 7913–7921.

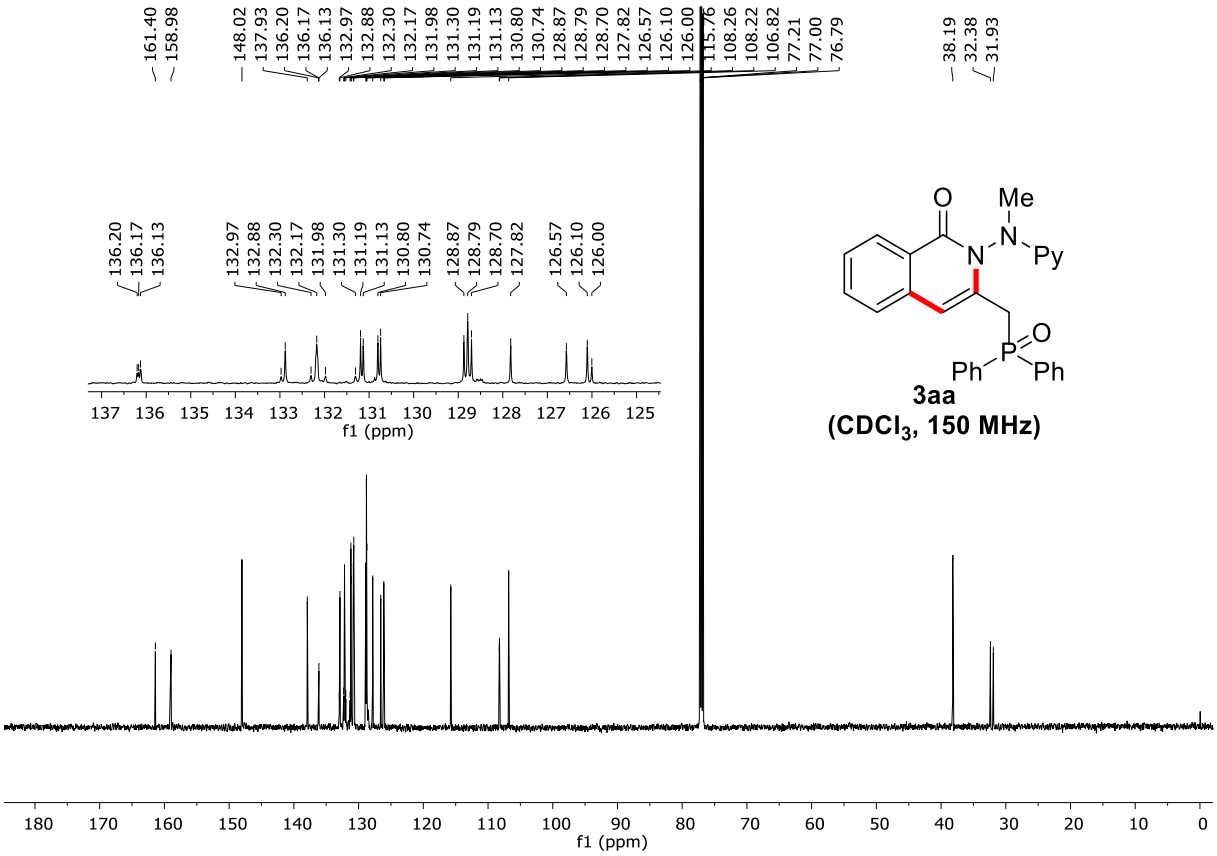
[2] (a) H. Guo, R. Qian, Y. Guo and S. Ma, *J. Org. Chem.*, 2008, **73**, 7934–7938; (b) S. Ma, H. Guo and F. Yu, *J. Org. Chem.*, 2006, **71**, 6634–6636; (c) T. Kippo, T. Fukuyama and I. Ryu, *Org. Lett.*, 2011, **13**, 3864–3867.

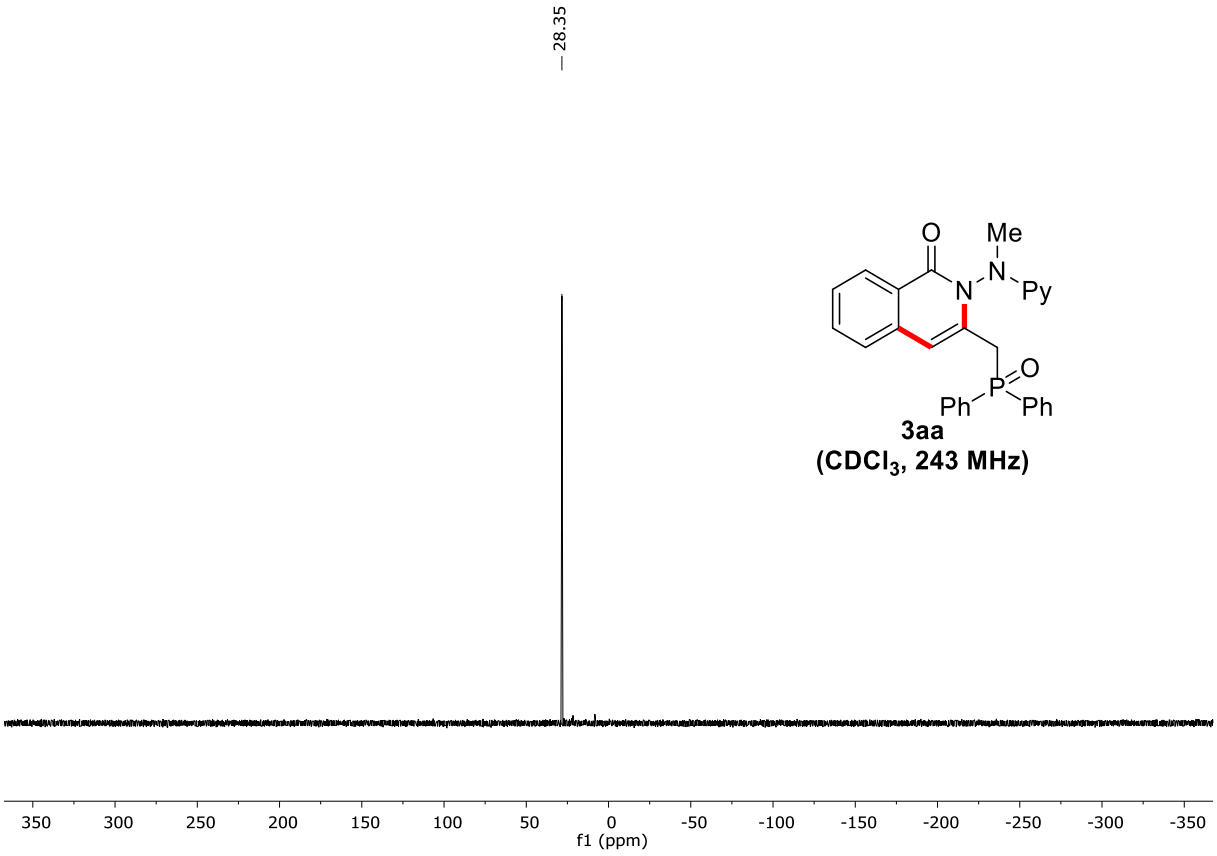
[3] T. H. Meyer, J. C. A. Oliveira, S. C. Sau, N. W. J. Ang and L. Ackermann, *ACS Catal.*, 2018, **8**, 9140–9147.

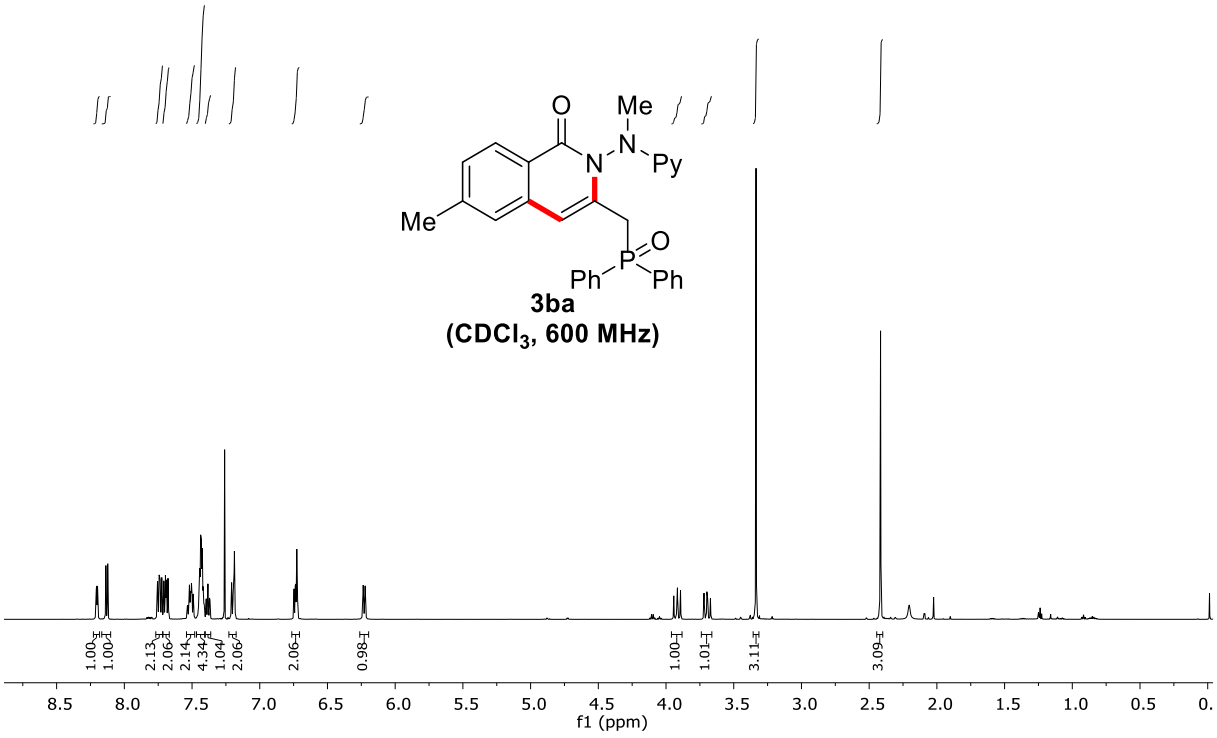
[4] G. Rouquet, D. E. Moore, M. Spain, D. M. Allwood, C. Battilocchio, D. C. Blakemore, P. V. Fish, S. Jenkinson, A. S. Jessiman, S. V. Ley, G. McMurray and R. I. Storer, *ACS Med. Chem. Lett.*, 2015, **6**, 329–333.

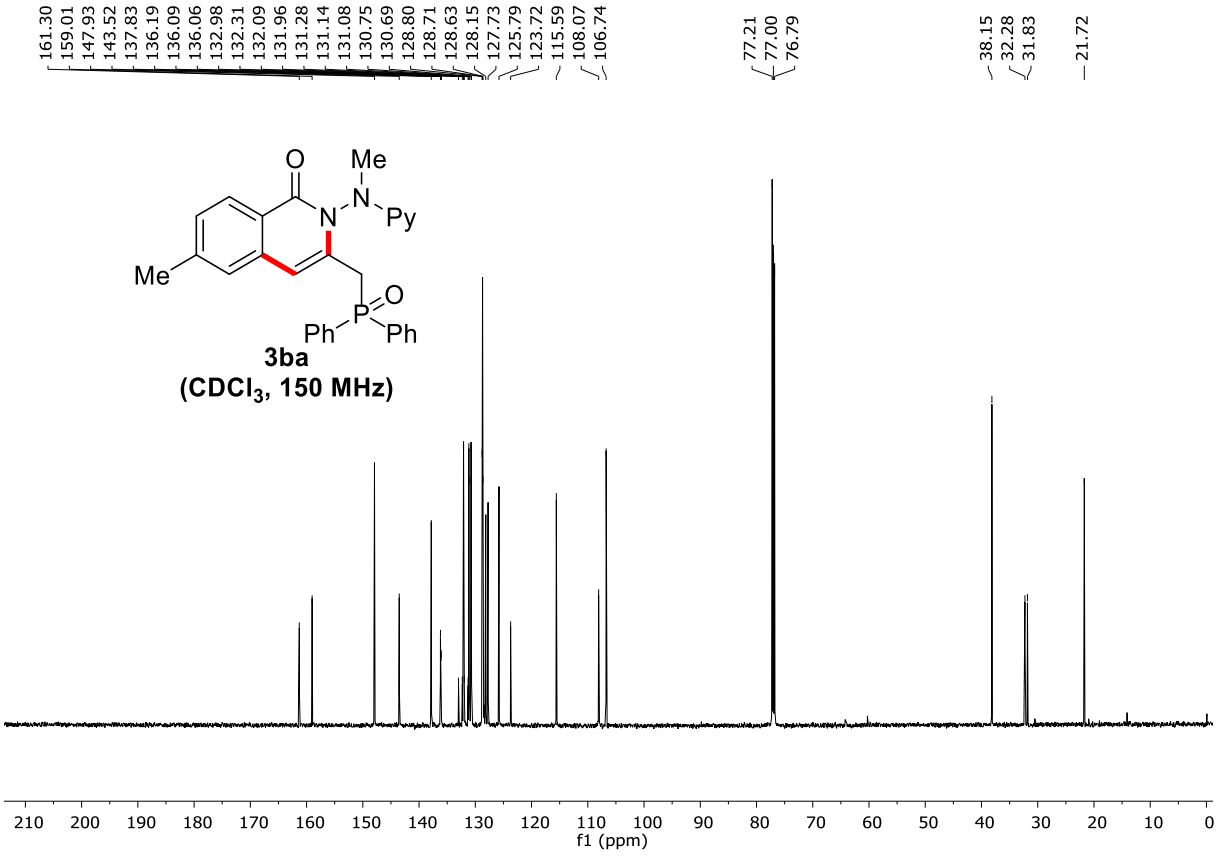
NMR spectra

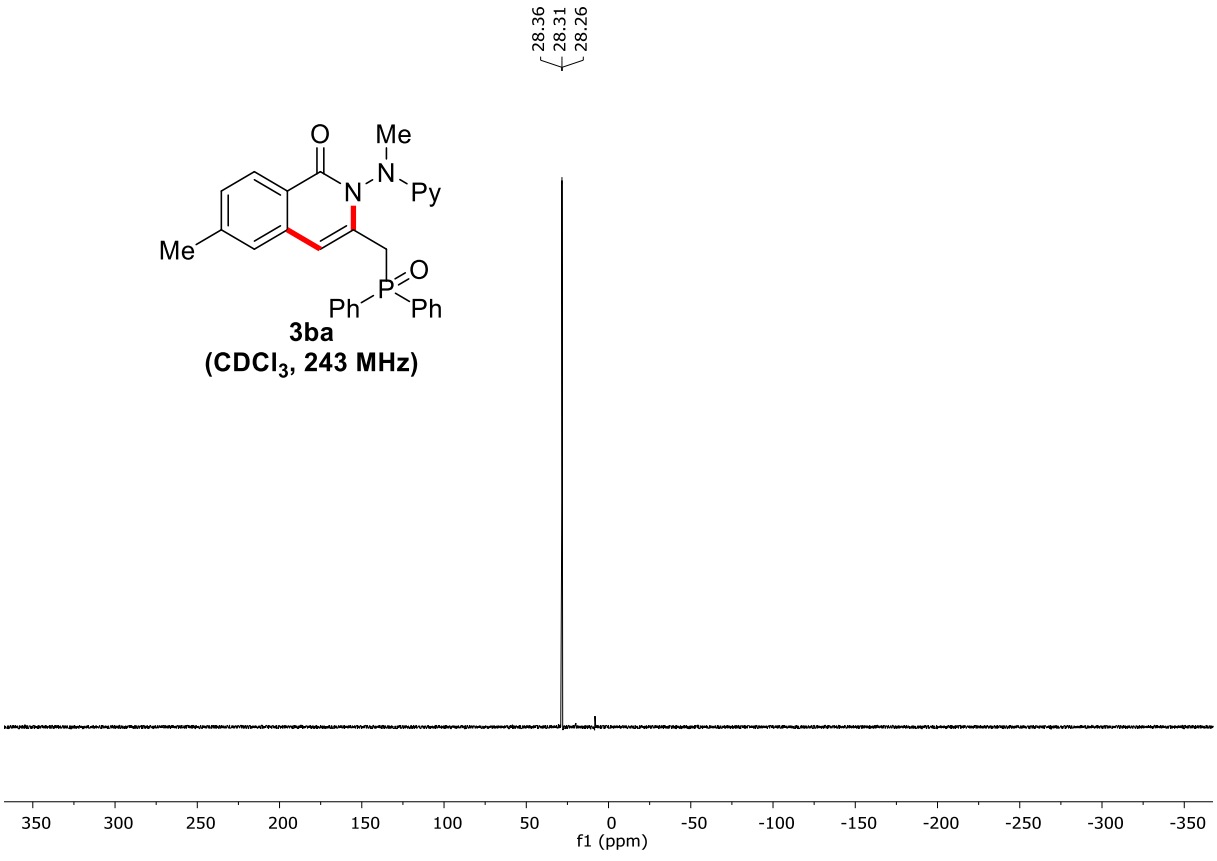


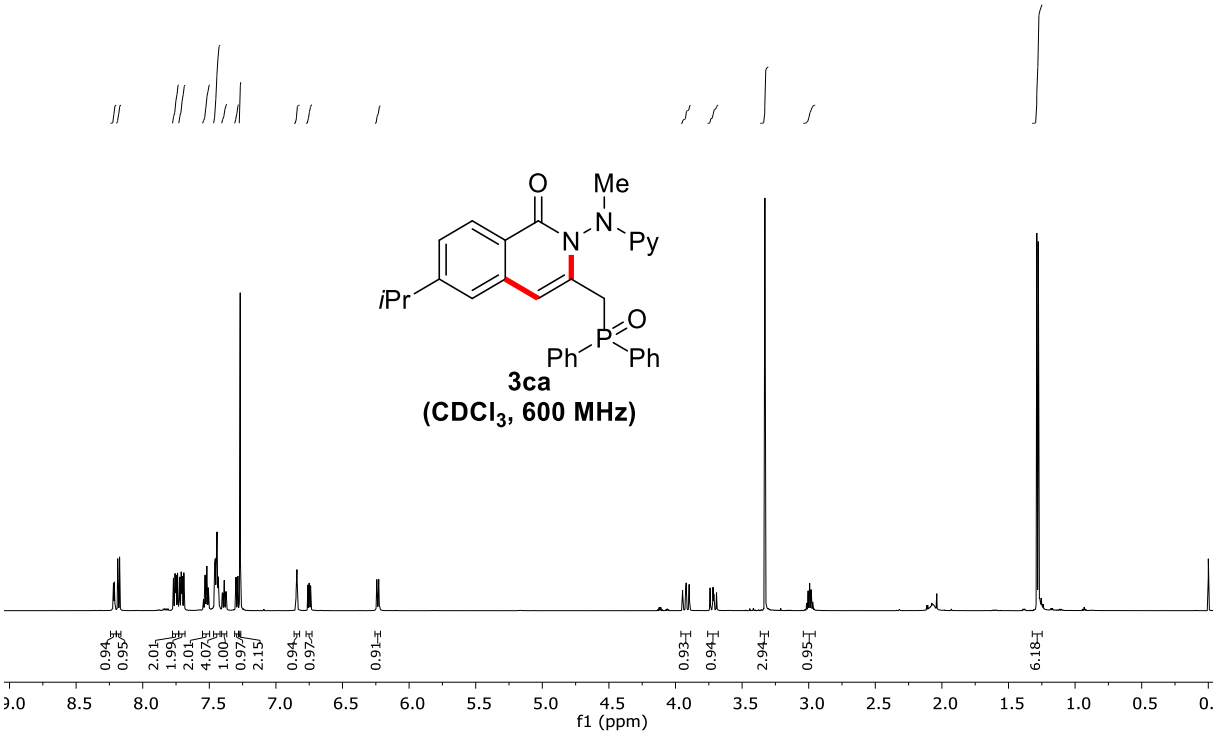


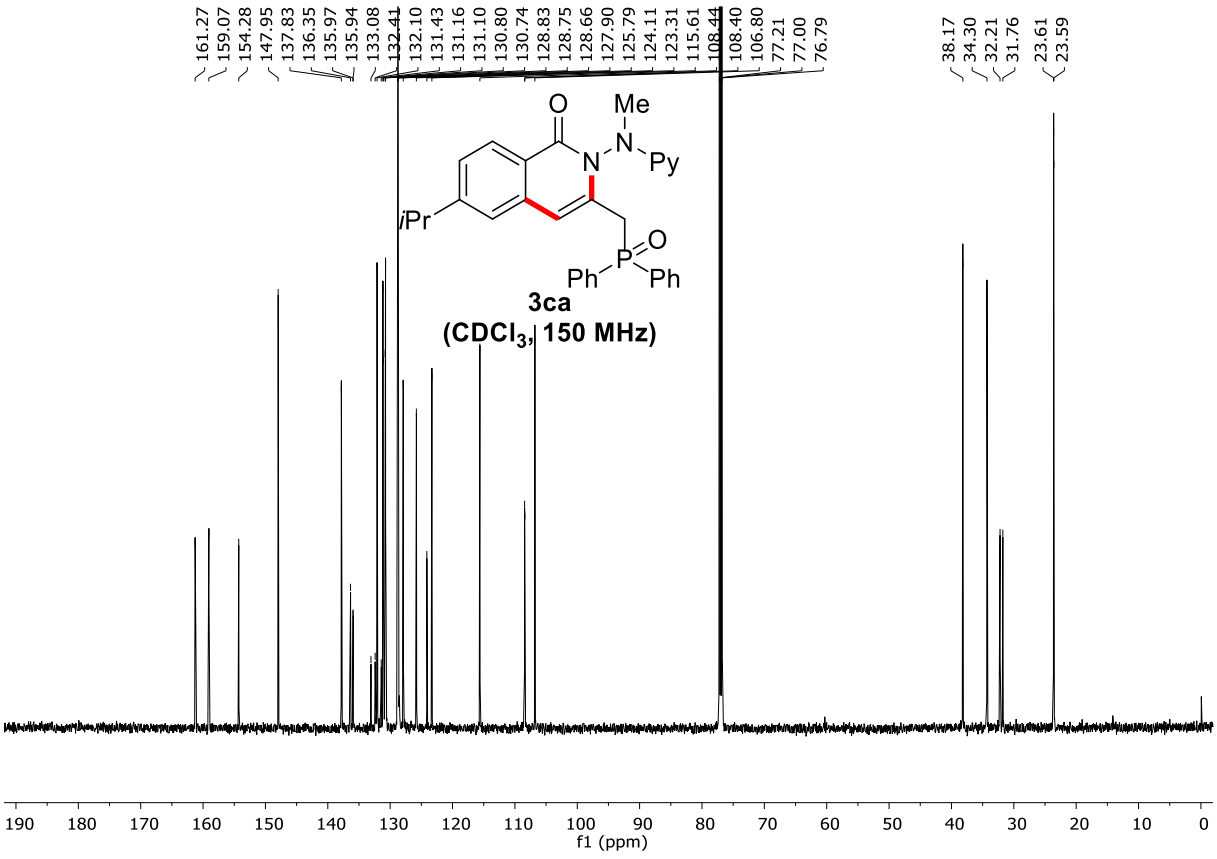

28.35
O
Me
N
N
Py
O
P
Ph
Ph
3aa
(CDCl3, 243 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)

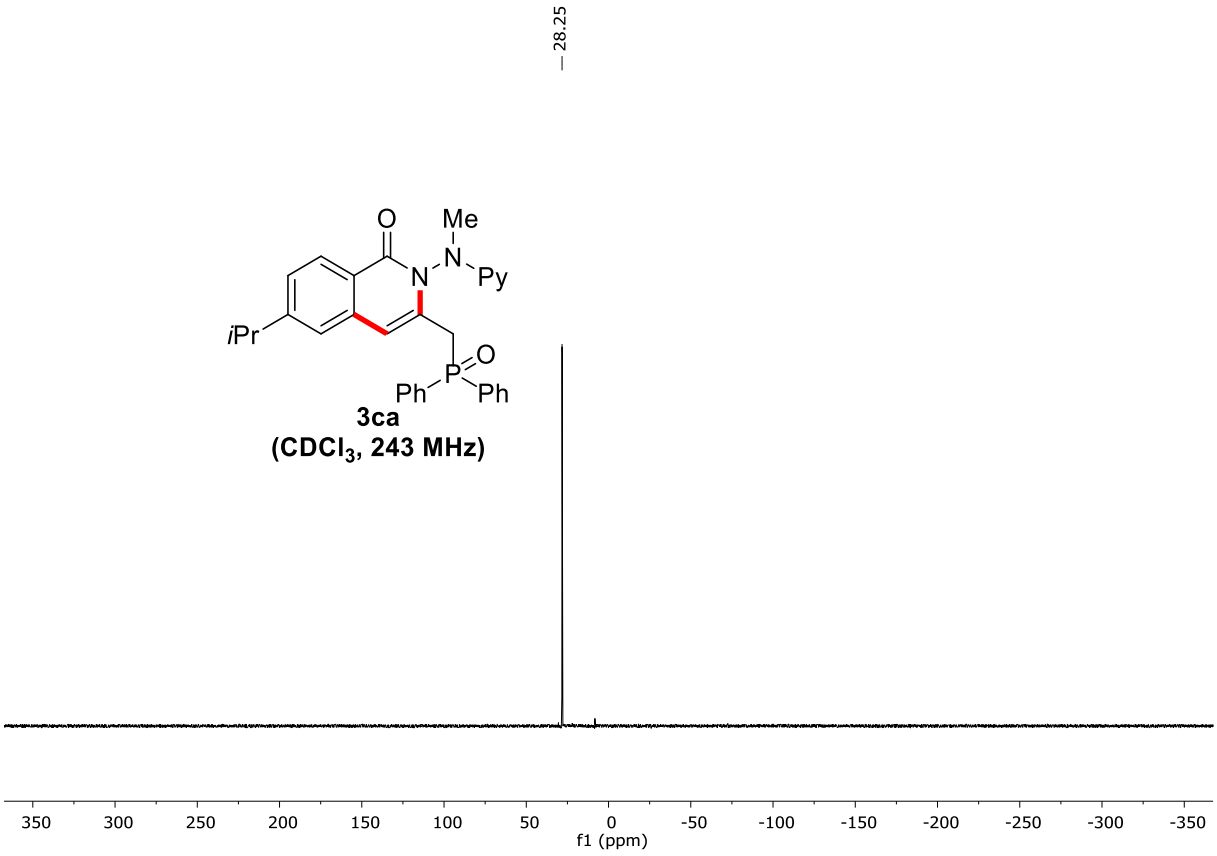

O
Me
N
N
Py
Me
O
P
Ph
Ph
3ba
(CDCl3, 600 MHz)
1.00
1.00
2.13
2.06
2.14
4.34
1.04
2.06
2.06
0.98
1.00
1.01
3.11
3.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

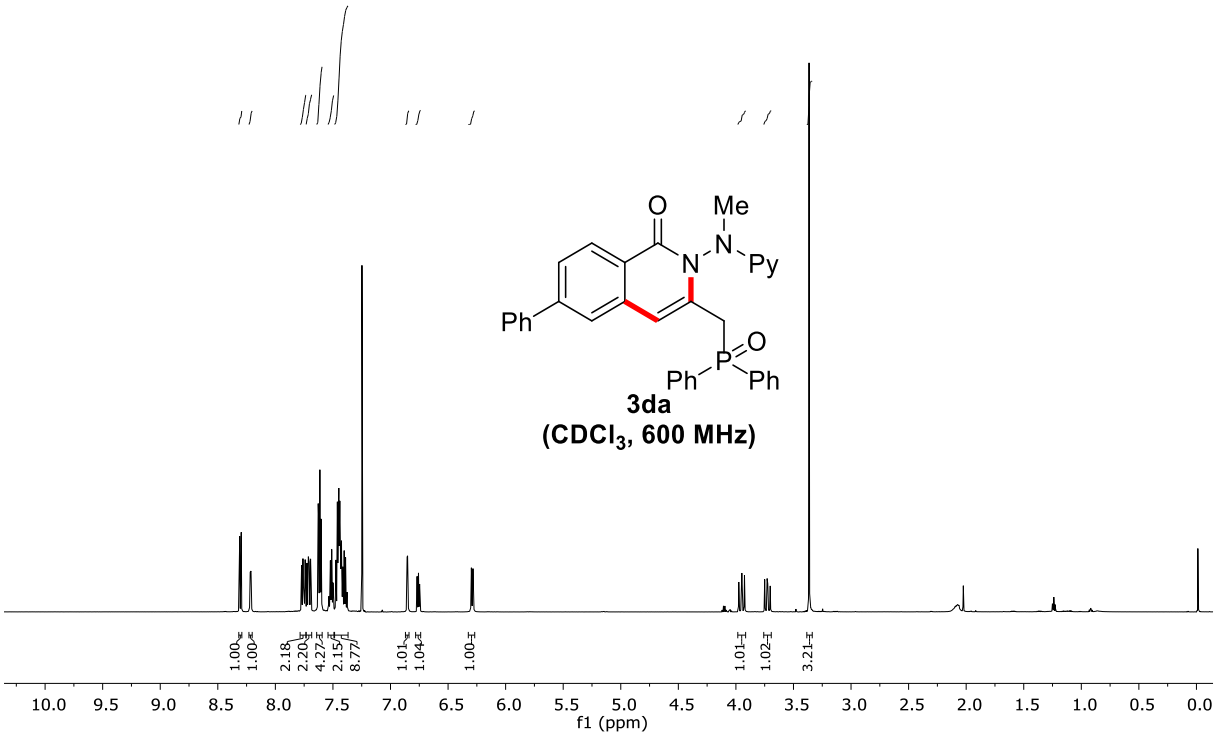

161.30
159.01
147.93
143.52
137.83
136.19
136.09
136.06
132.98
132.31
132.09
131.96
131.28
131.14
131.08
130.75
130.69
128.80
128.71
128.63
128.15
127.73
125.79
123.72
115.59
108.07
106.74
77.21
77.00
76.79
38.15
32.28
31.83
21.72
O
Me
N
N
Py
Me
P
O
Ph
Ph
3ba
(CDCl3, 150 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

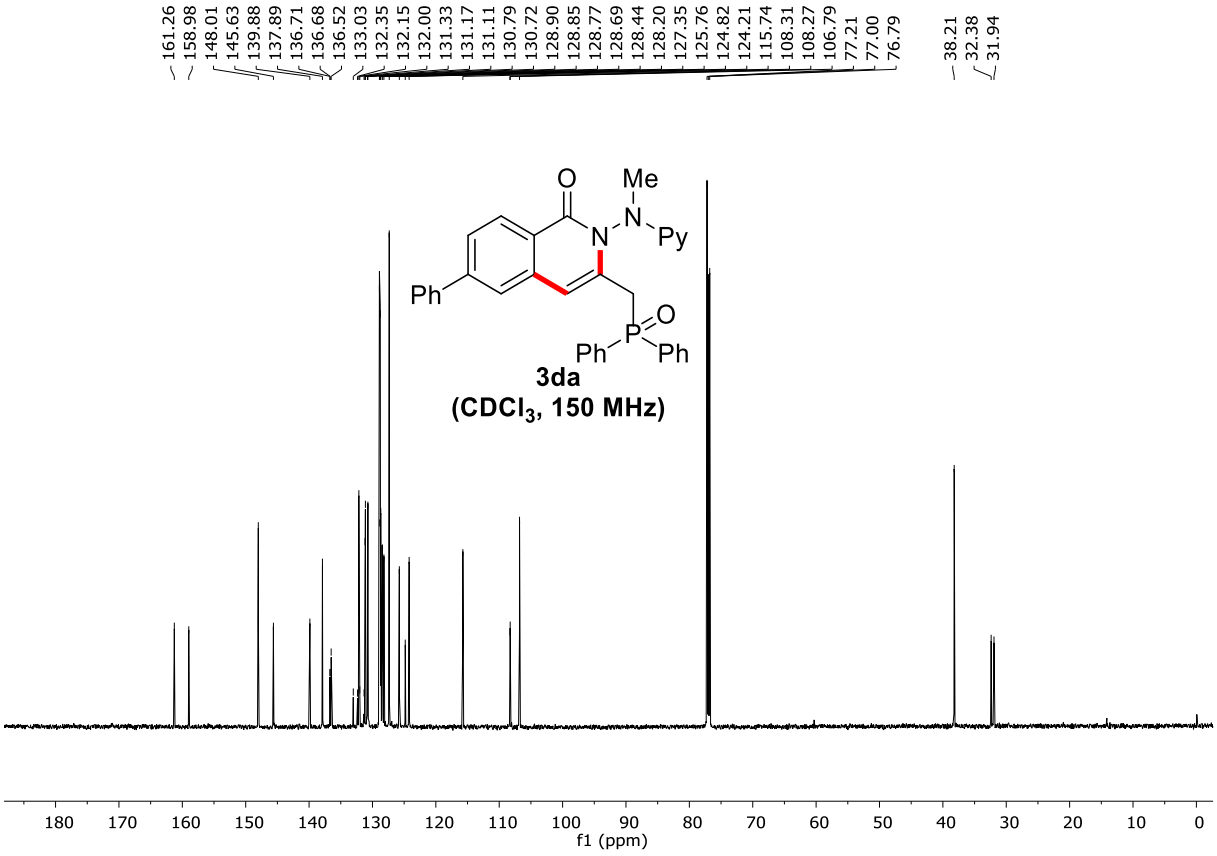

28.36
28.31
28.26
O
Me
N
N
Py
Me
P
O
Ph
Ph
3ba
(CDCl3, 243 MHz)
350 300 250 200 150 100 50 0 -50 -100 -150 -200 -250 -300 -350
f1 (ppm)

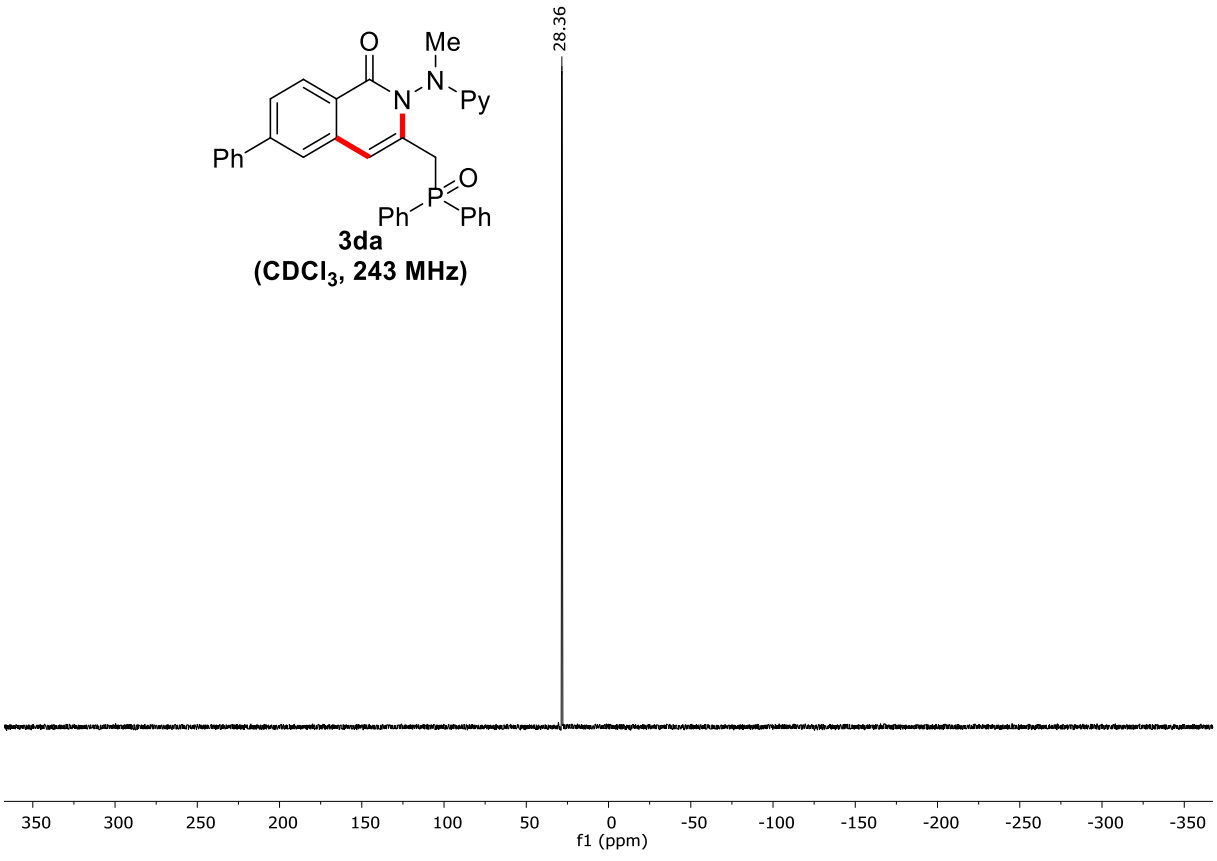

O
Me
N
N
Py
iPr
P
O
Ph
Ph
3ca
(CDCl3, 600 MHz)
0.94
0.95
2.01
1.99
2.01
4.07
1.00
0.97
2.15
0.94
0.97
0.91
0.93
0.94
2.94
0.95
6.18
f1 (ppm)

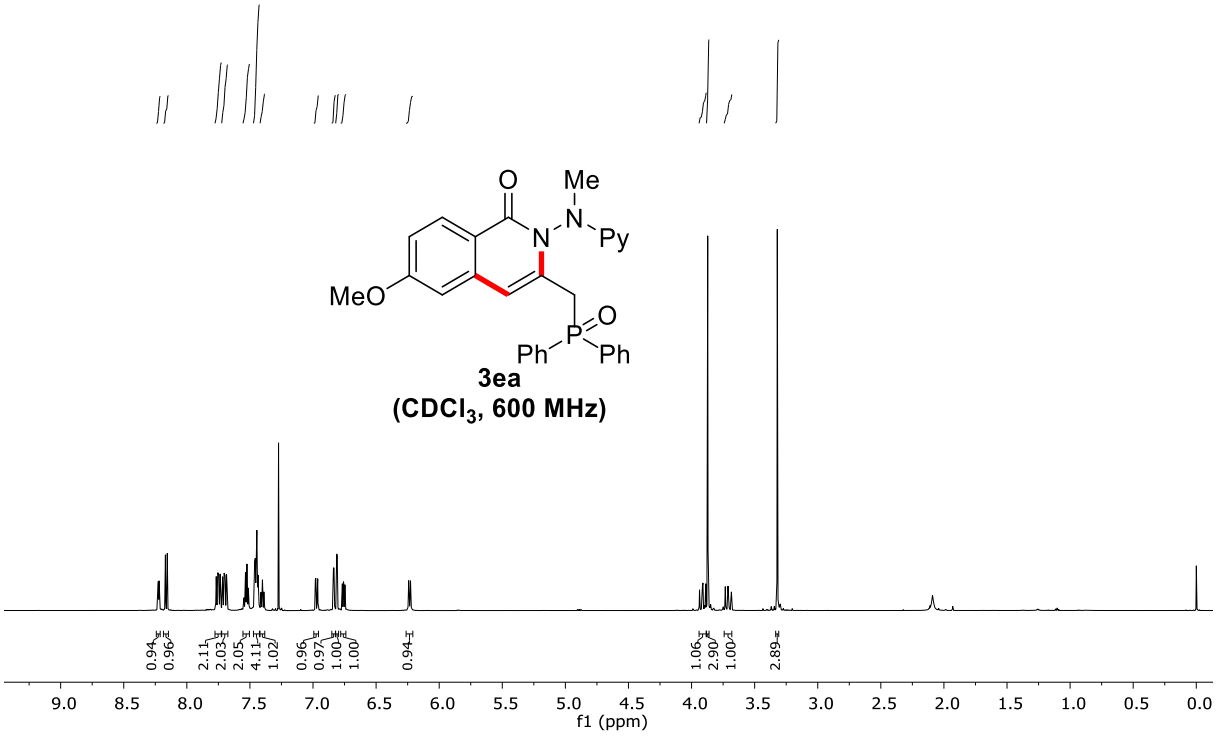

161.27
159.07
154.28
147.95
137.83
136.35
135.97
135.94
133.08
132.41
132.10
131.43
131.16
131.10
130.80
130.74
128.83
128.75
128.66
127.90
125.79
124.11
123.31
115.61
108.44
108.40
106.80
77.21
77.00
76.79
38.17
34.30
32.21
31.76
23.61
23.59
O
Me
N
N
Py
iPr
P
O
Ph
Ph
3ca
(CDCl3, 150 MHz)
f1 (ppm)

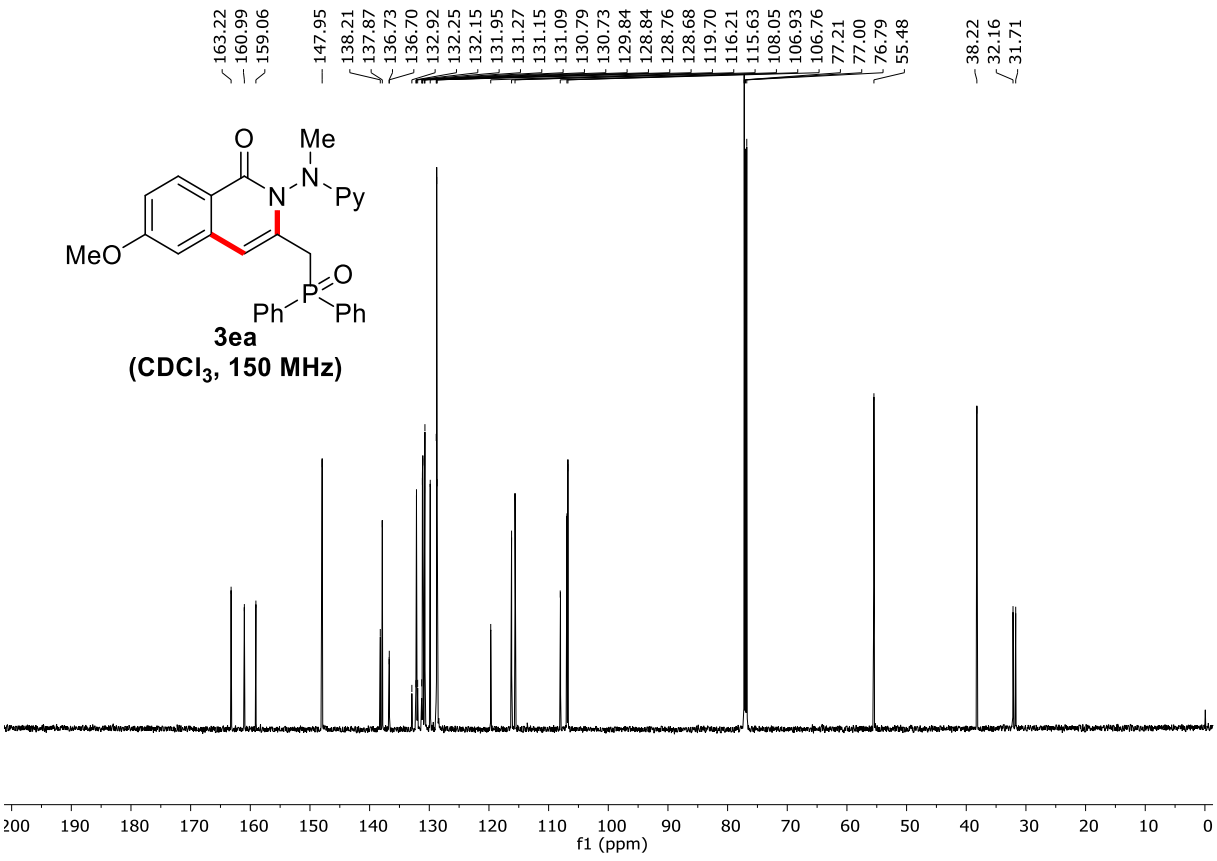

28.25
O
Me
N
N
Py
iPr
O
P
Ph
Ph
3ca
(CDCl3, 243 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)

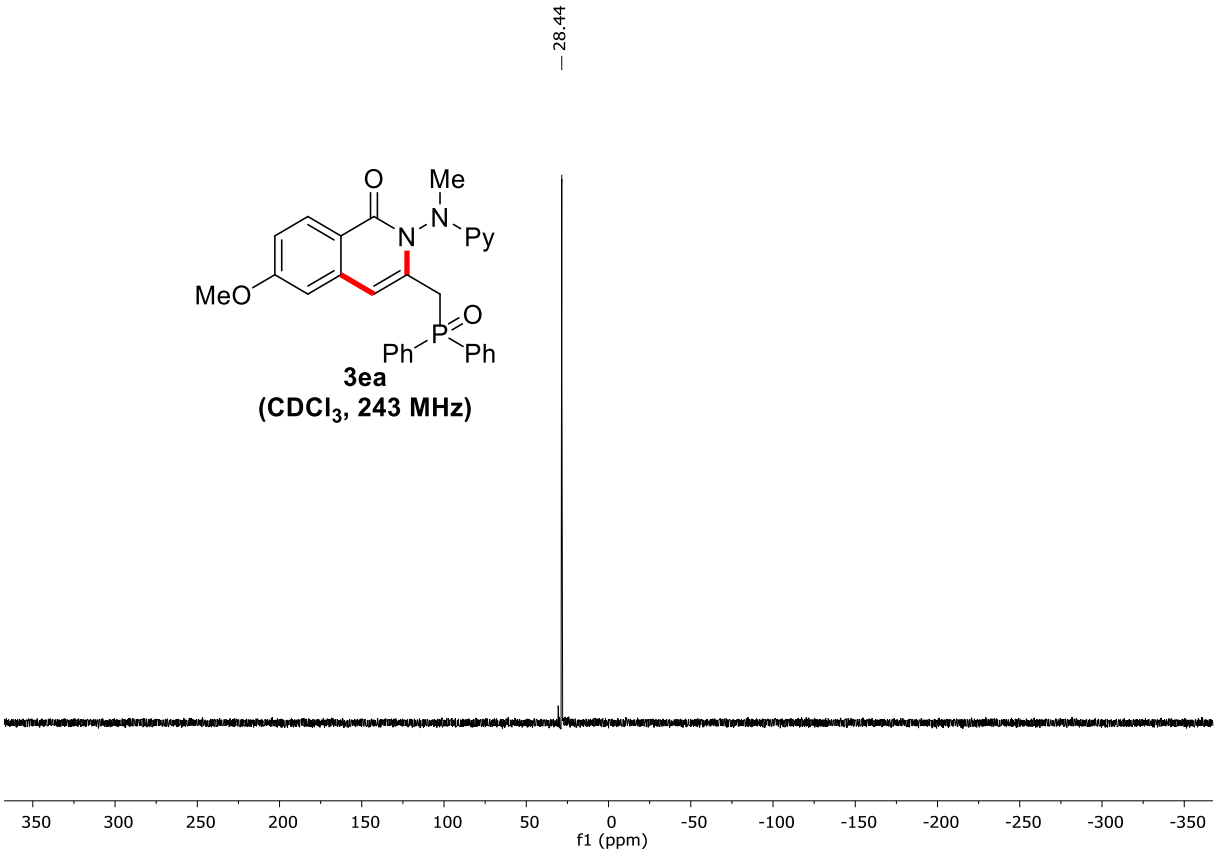

O
Me
N
N
Py
Ph
O
P
Ph
Ph
3da
(CDCl3, 600 MHz)
1.00
1.00
2.18
2.20
4.27
2.15
8.77
1.01
1.04
1.00
1.01
1.02
3.21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.26
158.98
148.01
145.63
139.88
137.89
136.71
136.68
136.52
133.03
132.35
132.15
132.00
131.33
131.17
131.11
130.79
130.72
128.90
128.85
128.77
128.69
128.44
128.20
127.35
125.76
124.82
124.21
115.74
108.31
108.27
106.79
77.21
77.00
76.79
38.21
32.38
31.94
O
Me
N
N
Py
Ph
O
P
Ph
Ph
3da
(CDCl3, 150 MHz)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

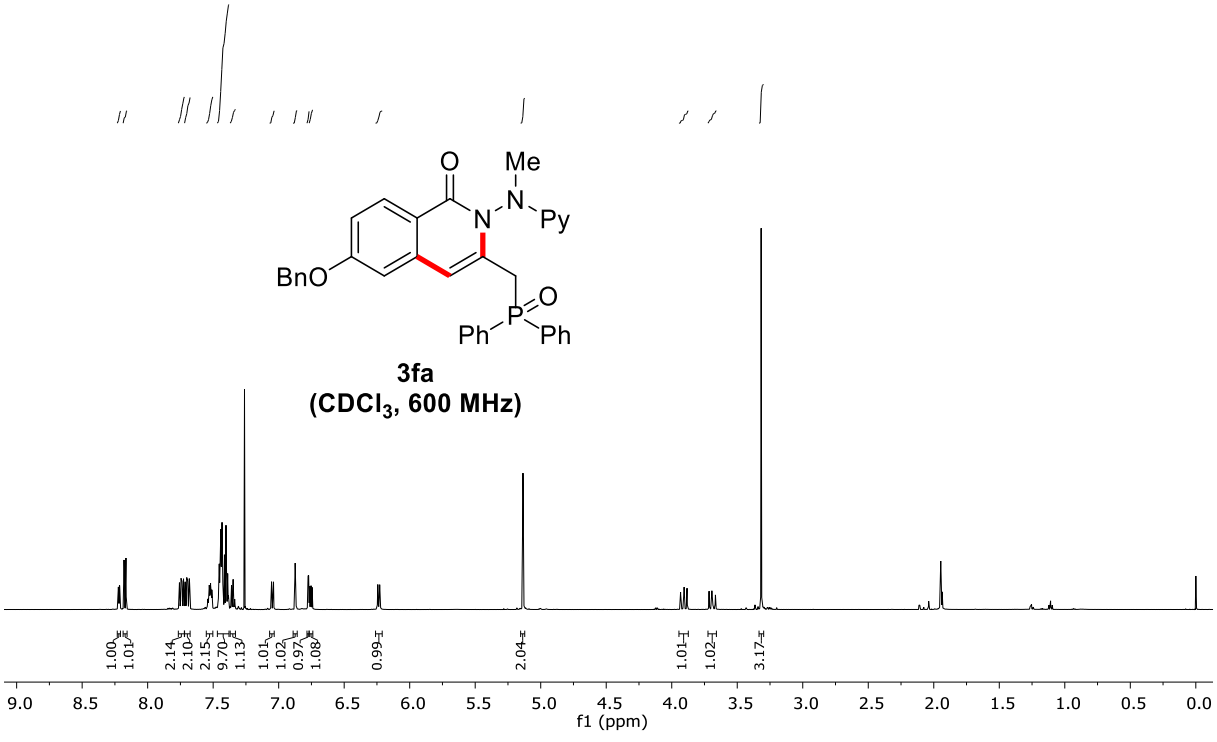

28.36
O
Me
N
N
Py
Ph
O
P
Ph
Ph
3da
(CDCl3, 243 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)


O
Me
N
N
Py
MeO
O
P
Ph
Ph
3ea
(CDCl3, 600 MHz)
0.94
0.96
2.11
2.03
2.05
4.11
1.02
0.96
0.97
1.00
1.00
0.94
1.06
2.90
1.00
2.89
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

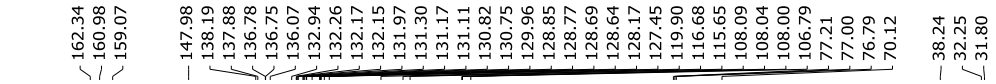

163.22
160.99
159.06
147.95
138.21
137.87
136.73
136.70
132.92
132.25
132.15
131.95
131.27
131.15
131.09
130.79
130.73
129.84
128.84
128.76
128.68
119.70
116.21
115.63
108.05
106.93
106.76
77.21
77.00
76.79
55.48
38.22
32.16
31.71
O
Me
N
N
Py
MeO
O
P
Ph
Ph
3ea
(CDCl3, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

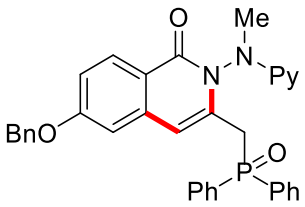


3ea
($CDCl_3$, 243 MHz)

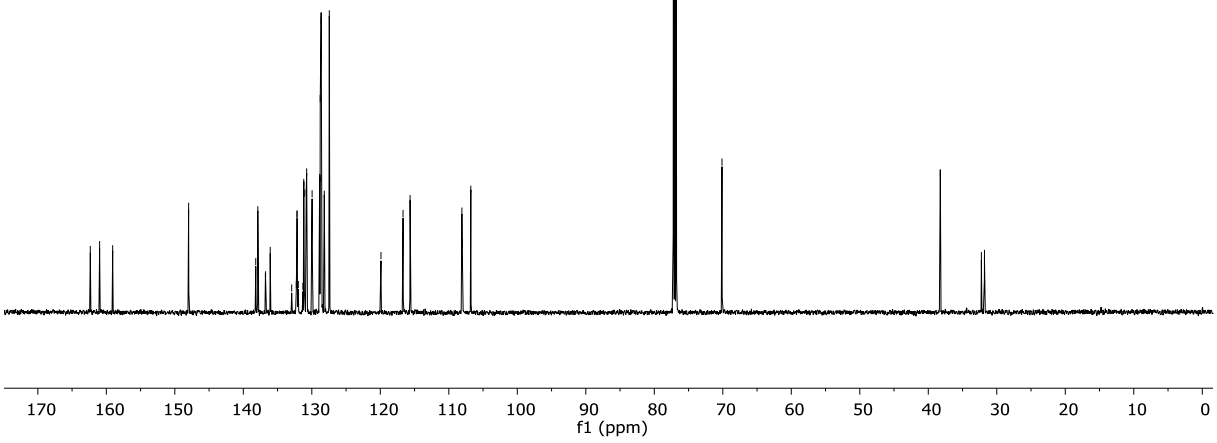


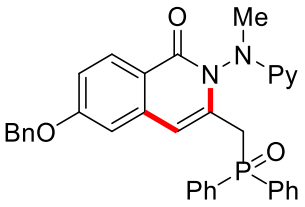
3fa
($CDCl_3$, 600 MHz)



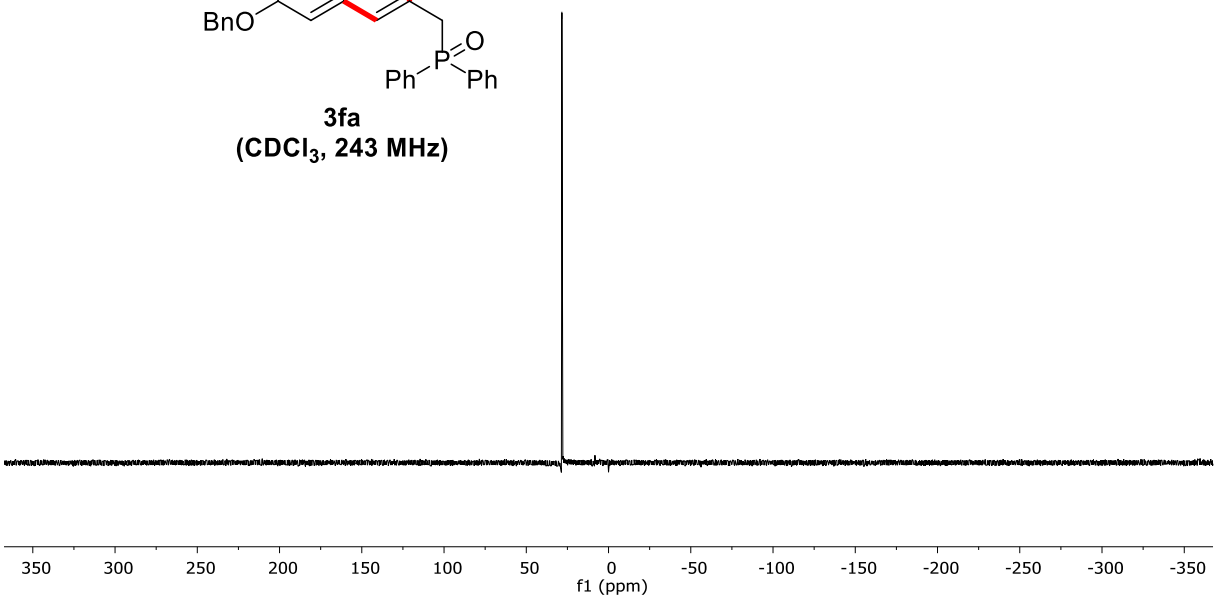


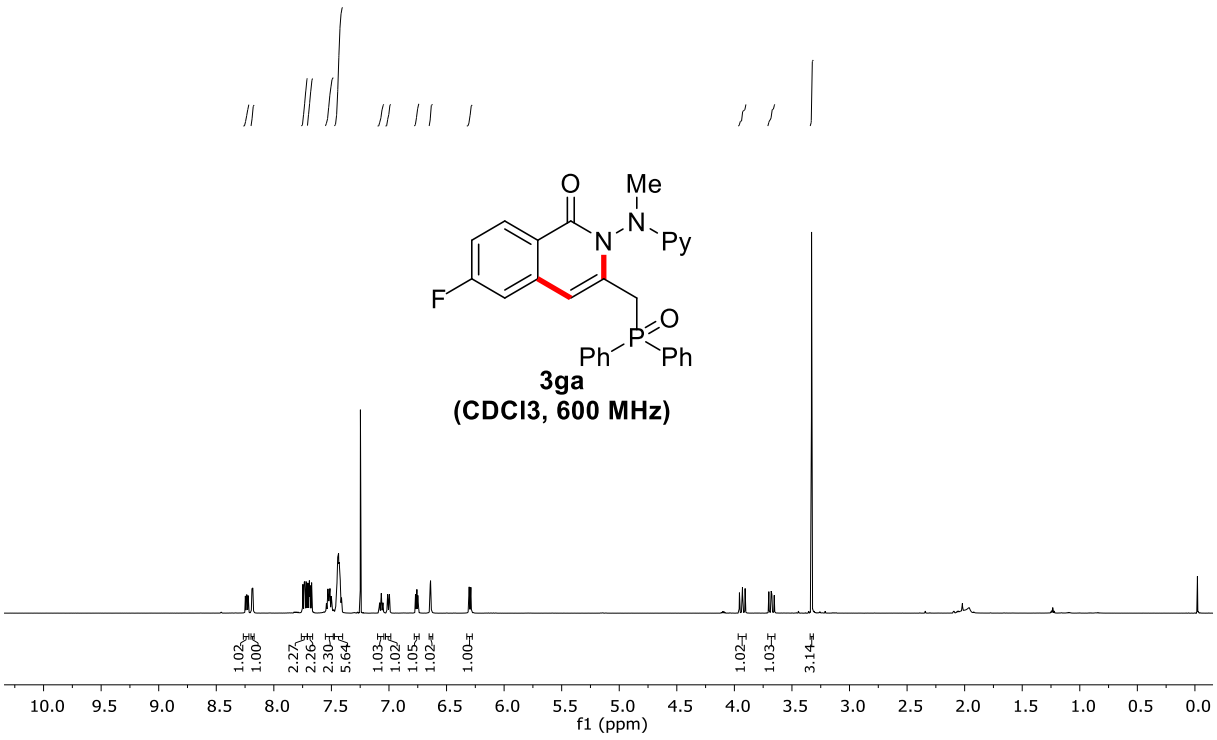
3fa
($CDCl_3$, 150 MHz)

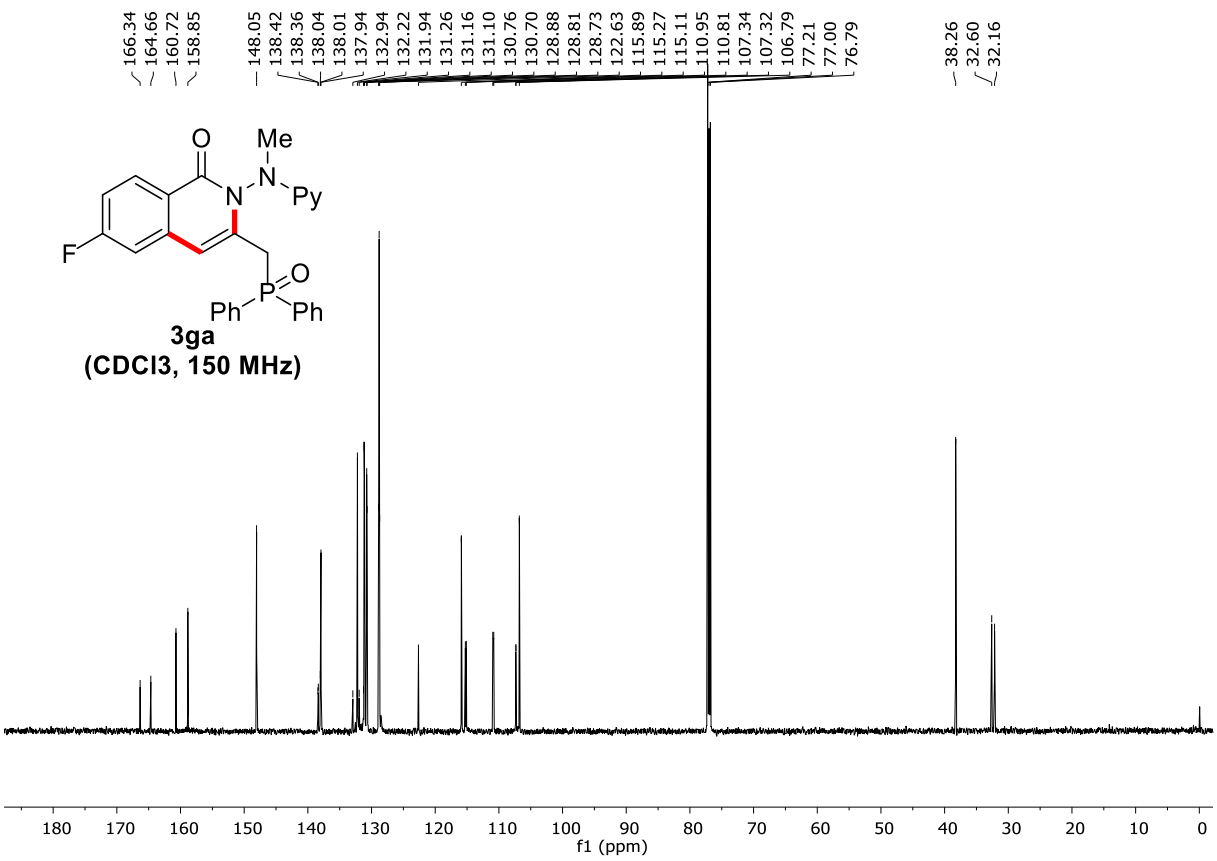


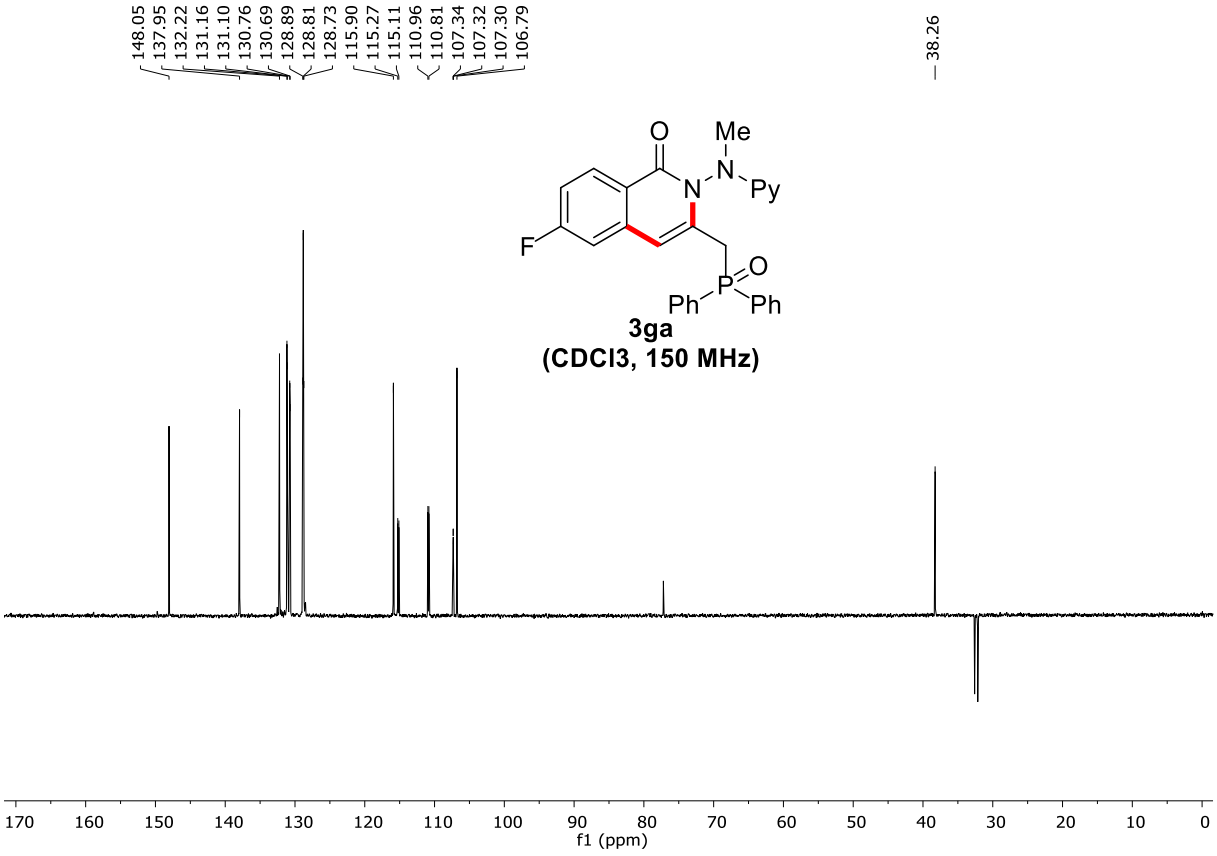


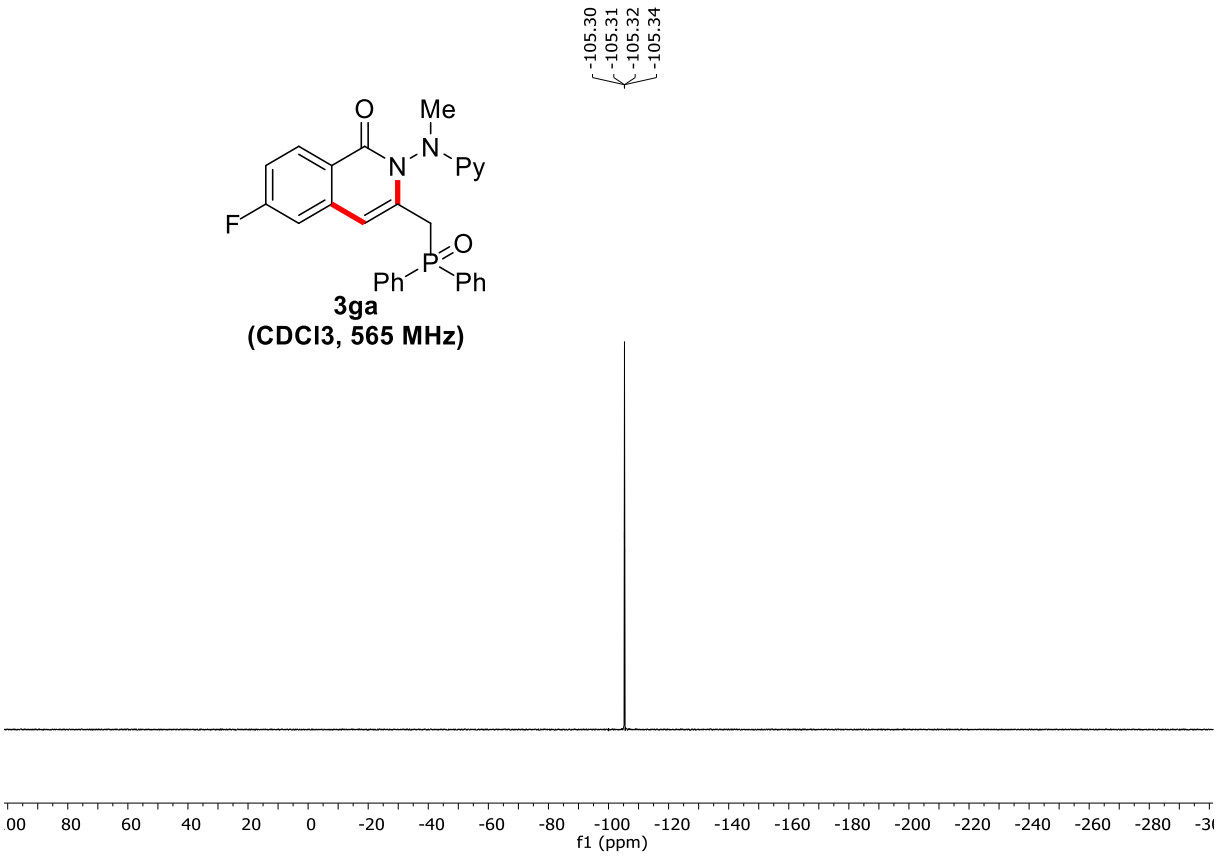
3fa
($CDCl_3$, 243 MHz)

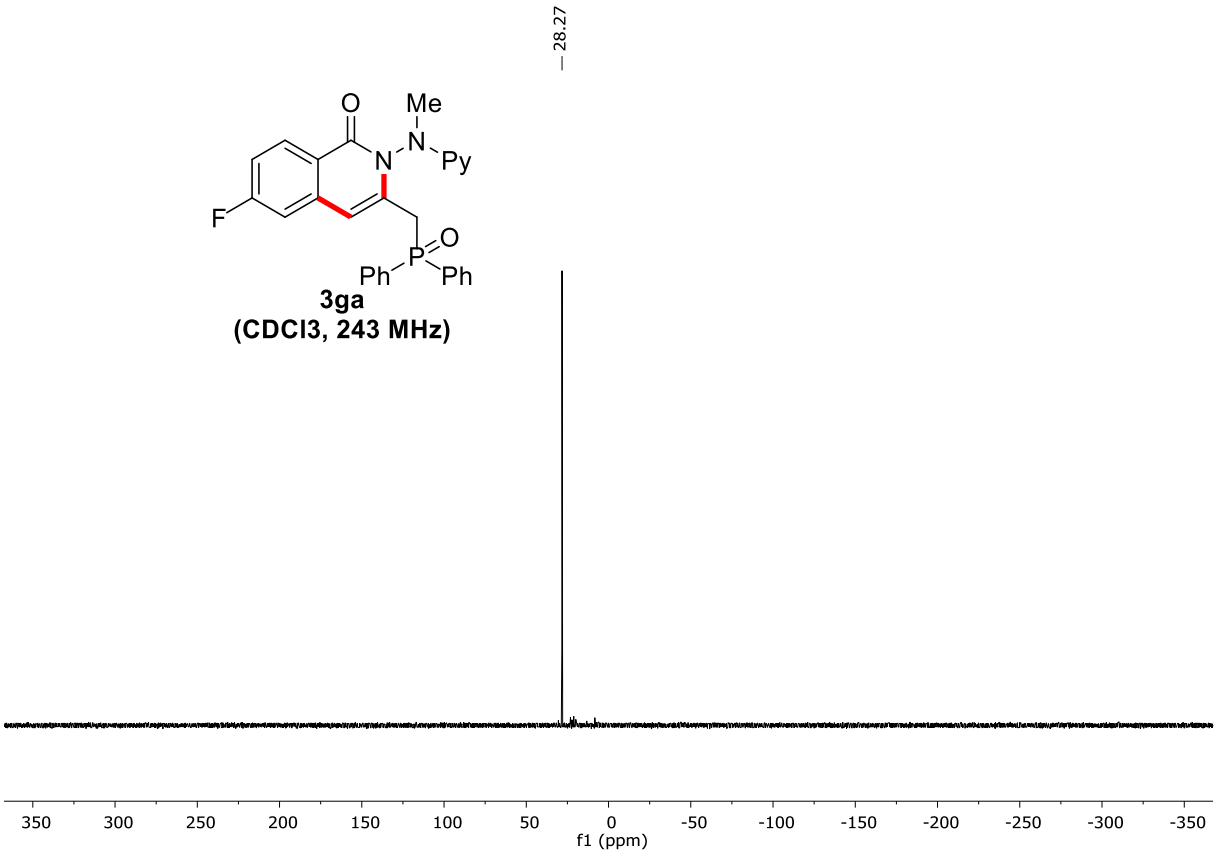



O
Me
N
N
Py
F
P
O
Ph
Ph
3ga
(CDCl3, 600 MHz)
1.02
1.00
2.27
2.26
2.30
5.64
1.03
1.02
1.05
1.02
1.00
1.02
1.03
3.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

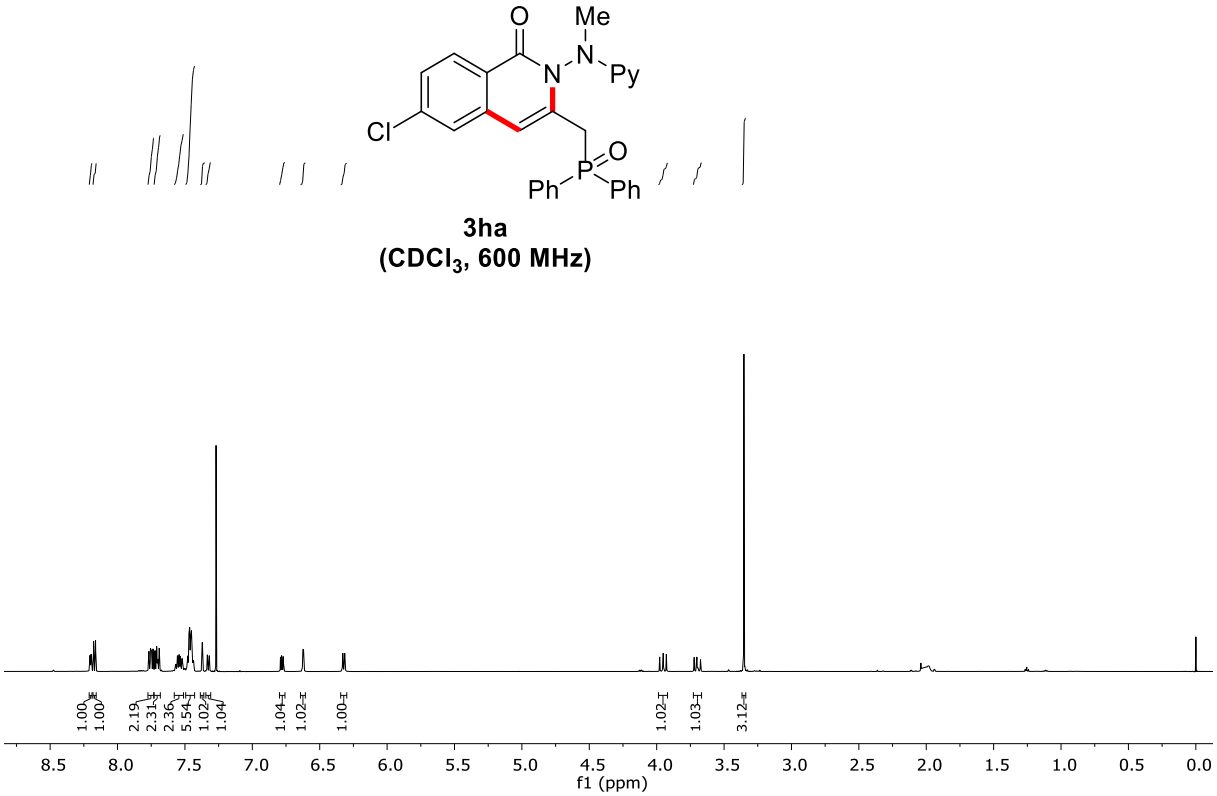

166.34
164.66
160.72
158.85
148.05
138.42
138.36
138.04
138.01
137.94
132.94
132.22
131.94
131.26
131.16
131.10
130.76
130.70
128.88
128.81
128.73
122.63
115.89
115.27
115.11
110.95
110.81
107.34
107.32
106.79
77.21
77.00
76.79
38.26
32.60
32.16
O
Me
N
N
Py
F
P
O
Ph
Ph
3ga
(CDCl3, 150 MHz)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


148.05
137.95
132.22
131.16
131.10
130.76
130.69
128.89
128.81
128.73
115.90
115.27
115.11
110.96
110.81
107.34
107.32
107.30
106.79
38.26
O
Me
N
N
Py
F
O
P
Ph
Ph
3ga
(CDCl3, 150 MHz)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

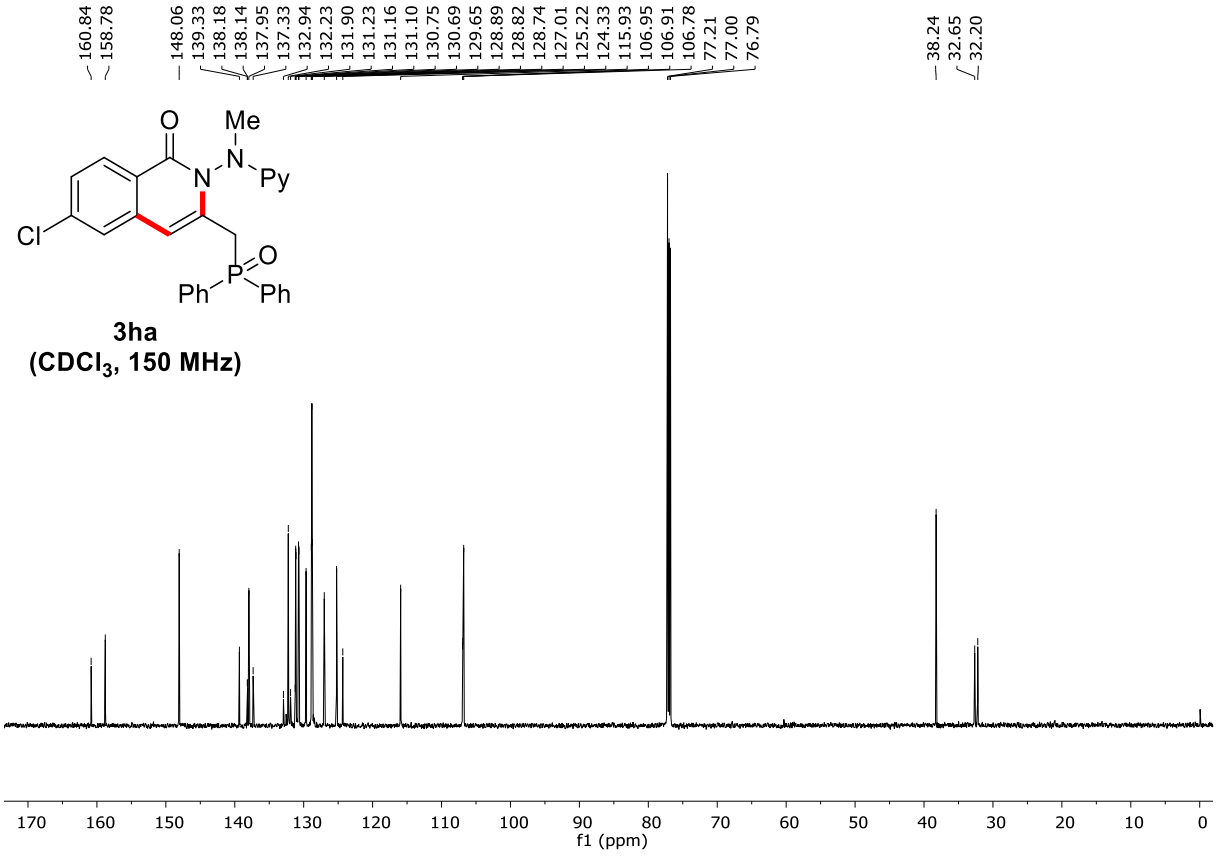

-105.30
-105.31
-105.32
-105.34
O
Me
N
N
Py
F
O
P
Ph
Ph
3ga
(CDCl3, 565 MHz)
00
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
-280
f1 (ppm)



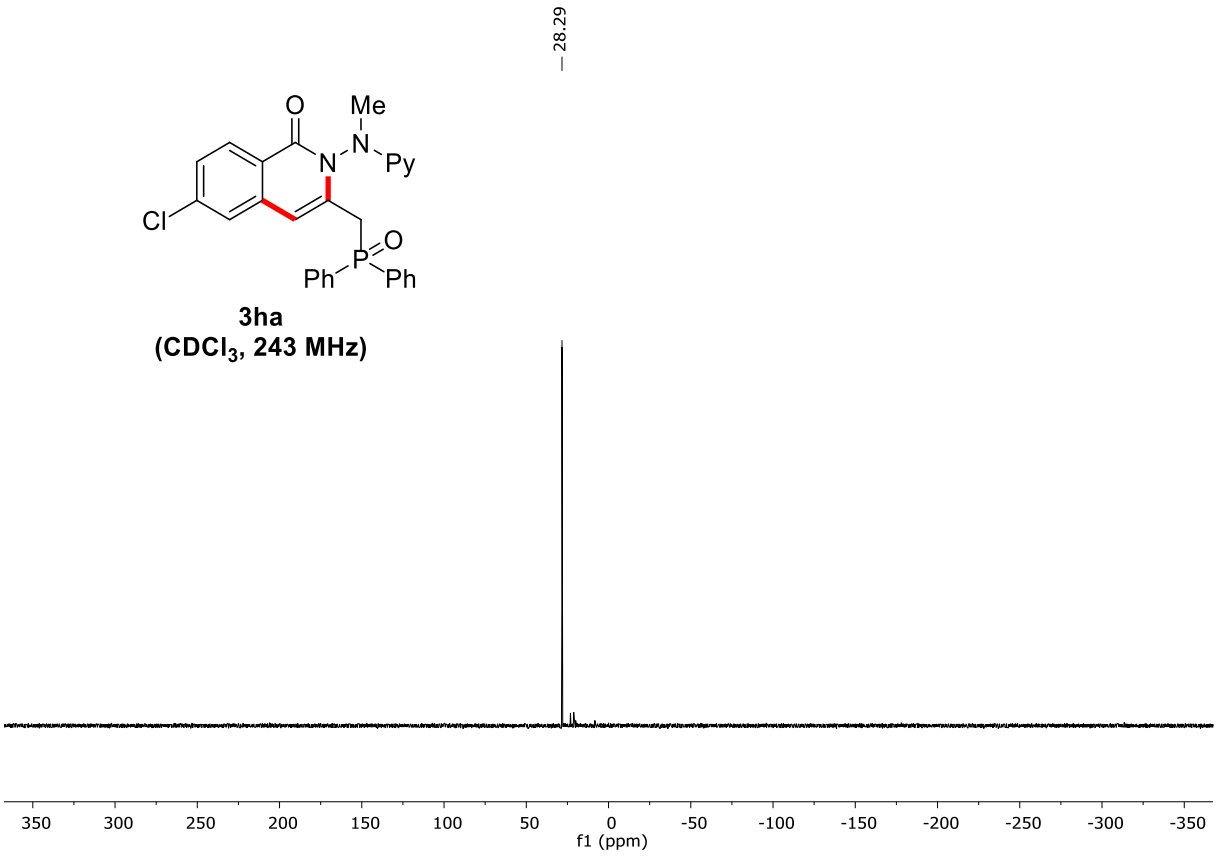
3ga
(CDCl3, 243 MHz)



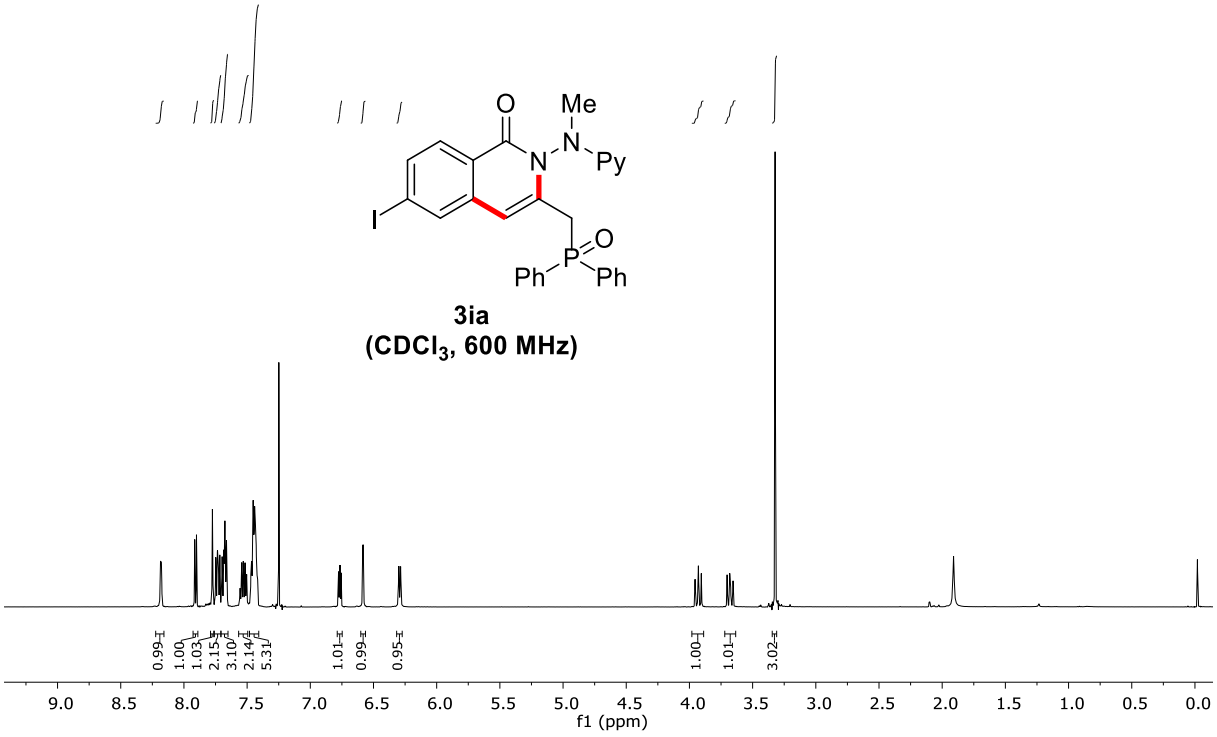
3ha
($CDCl_3$, 600 MHz)



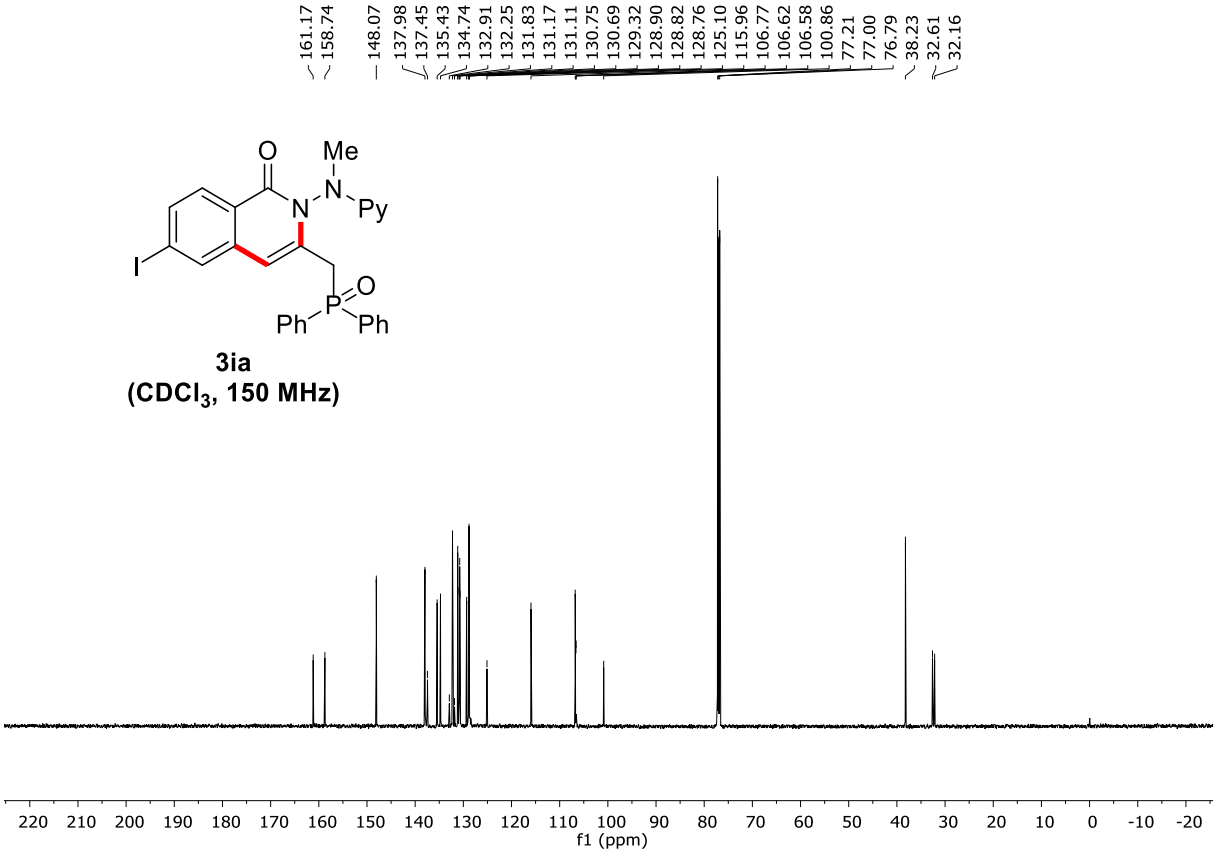
3ha
($CDCl_3$, 150 MHz)



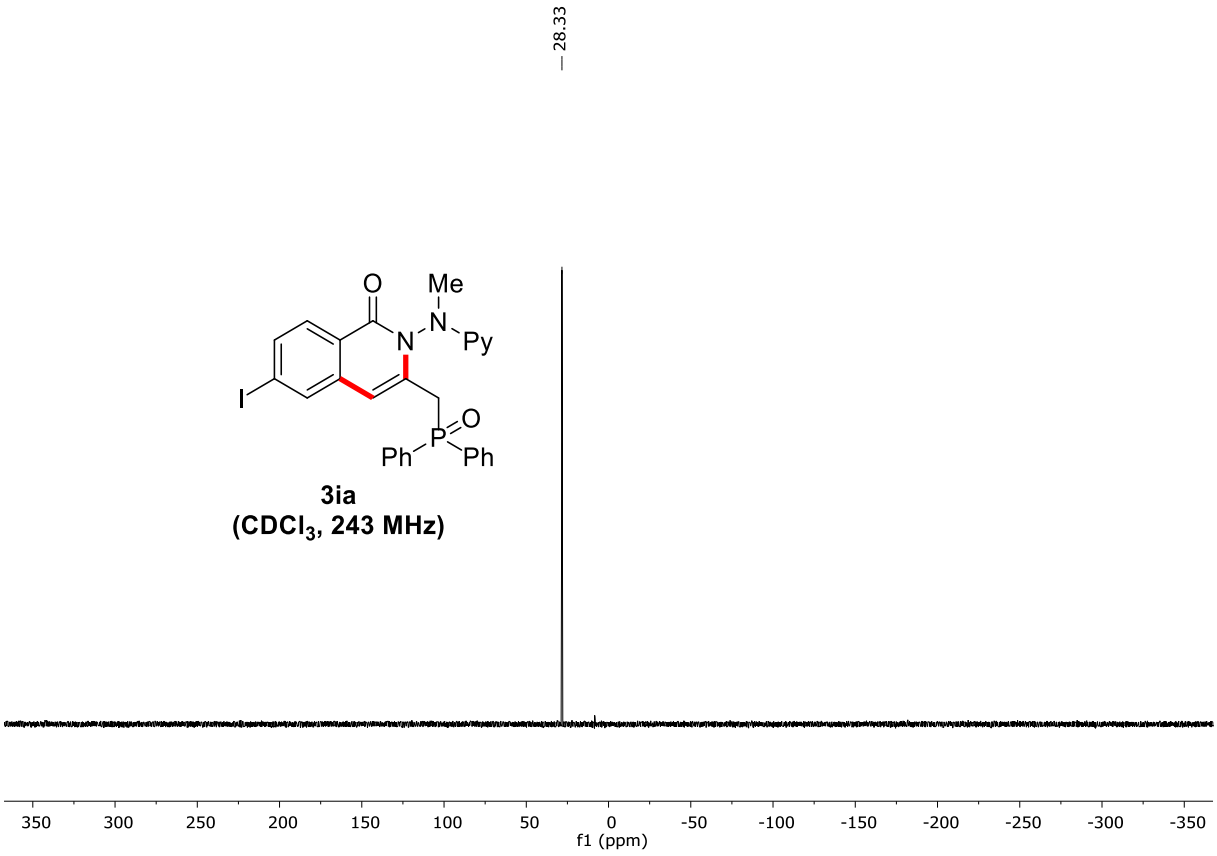
3ha
($CDCl_3$, 243 MHz)



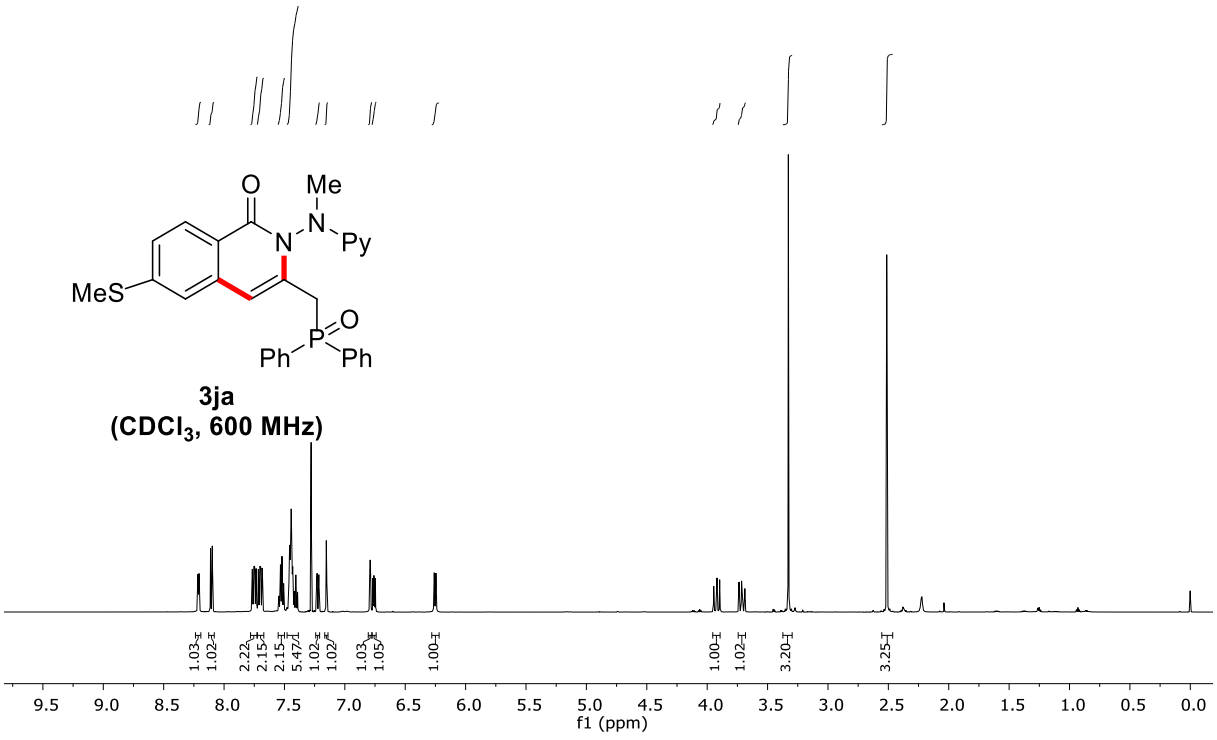
3ia
($CDCl_3$, 600 MHz)



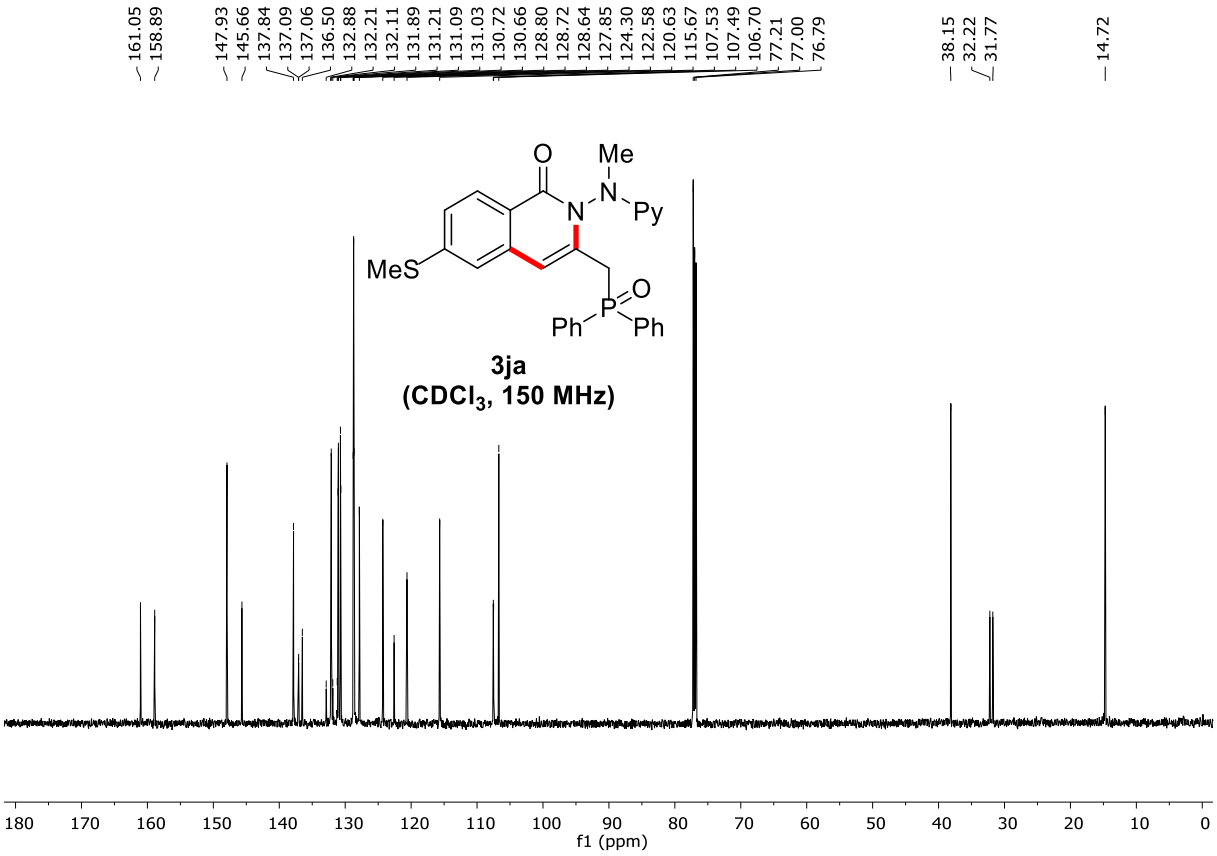
3ia
($CDCl_3$, 150 MHz)

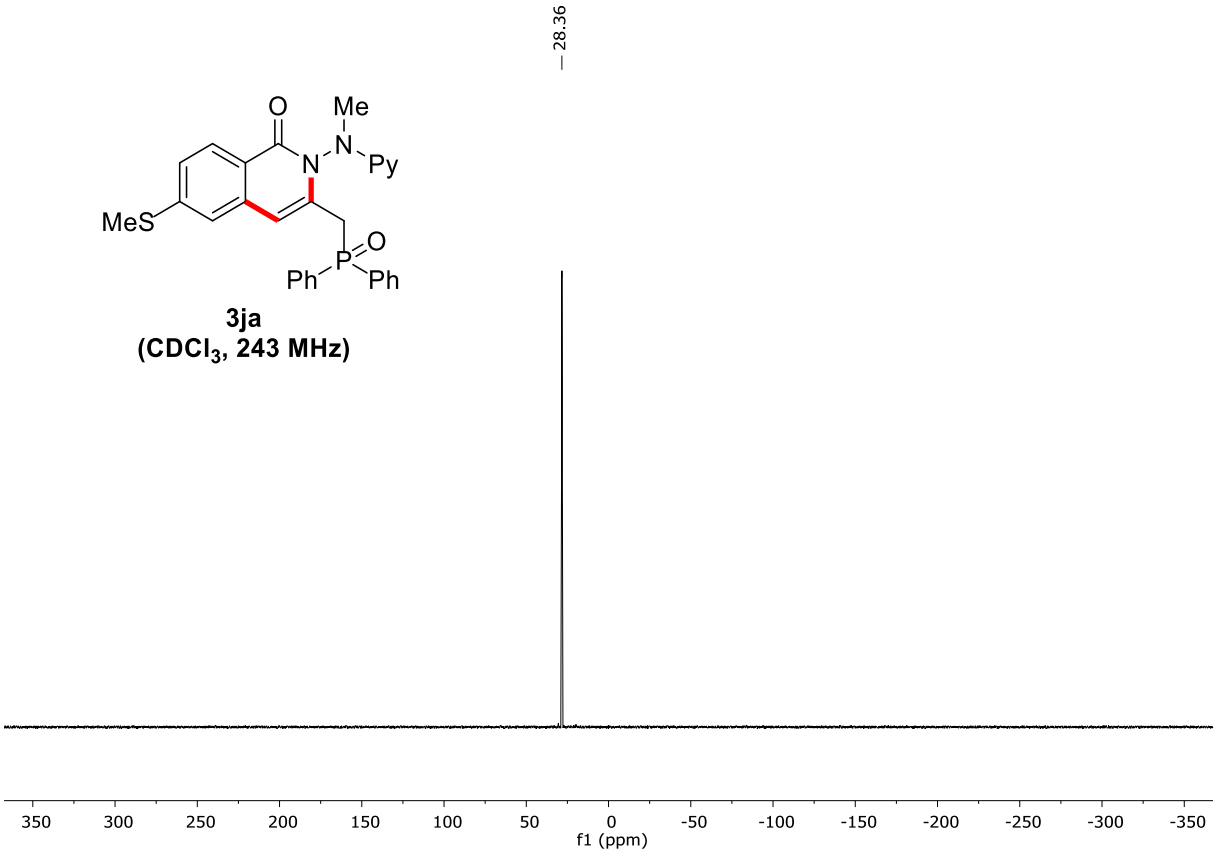


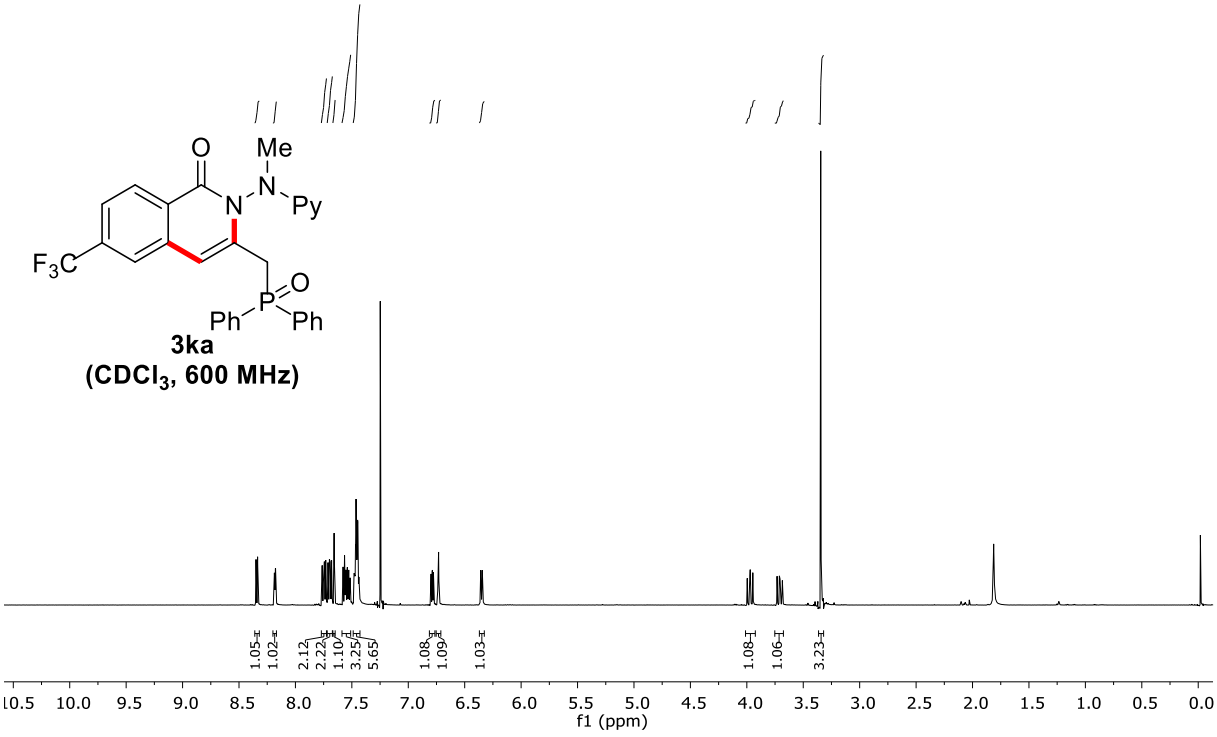
3ia
($CDCl_3$, 243 MHz)

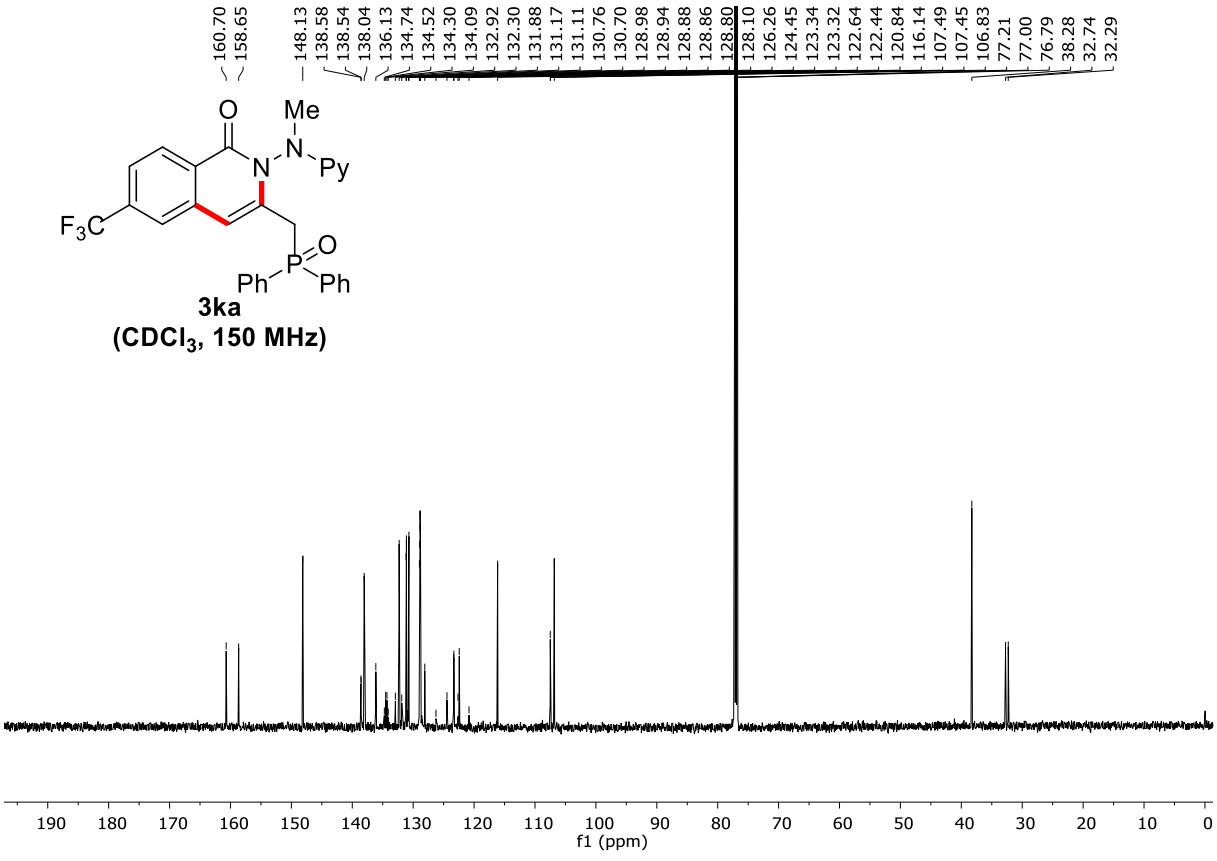


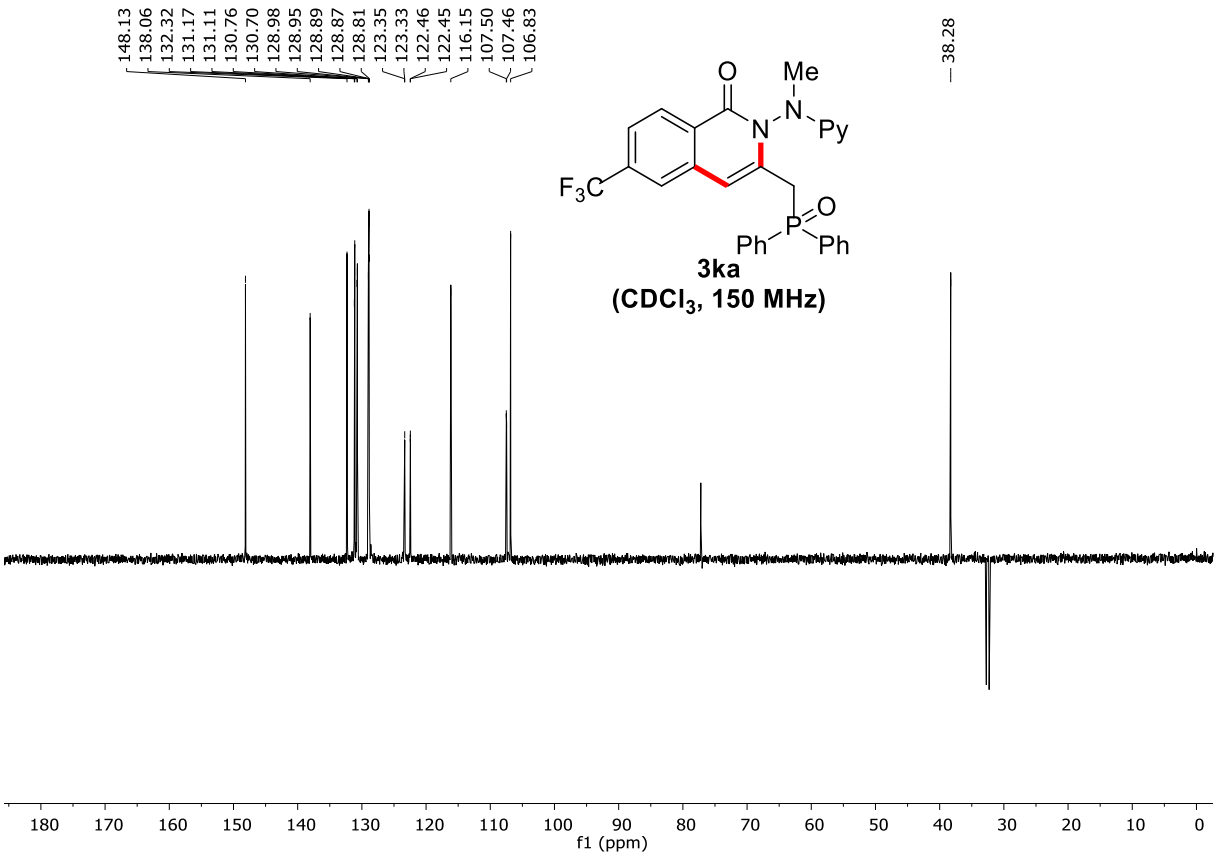
3ja
($CDCl_3$, 600 MHz)

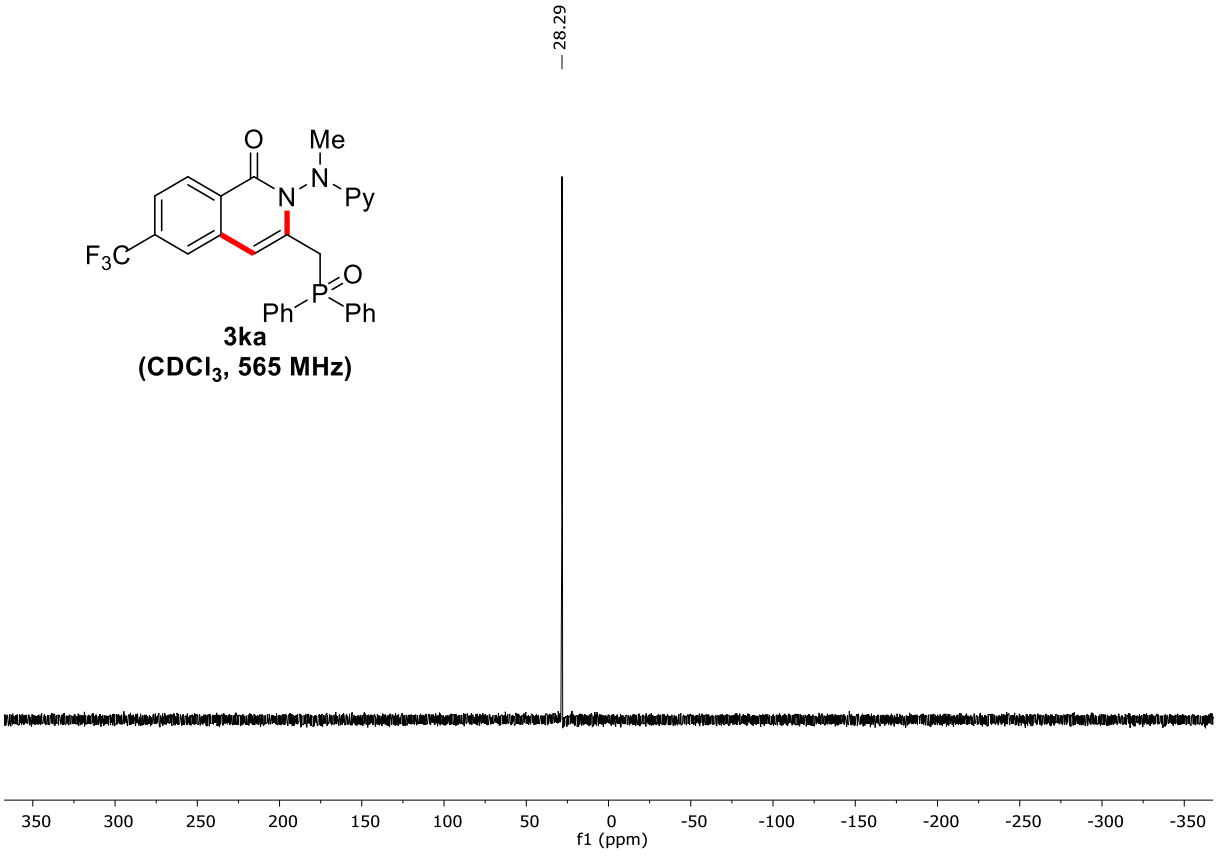

161.05
158.89
147.93
145.66
137.84
137.09
137.06
136.50
132.88
132.21
132.11
131.89
131.21
131.09
131.03
130.72
130.66
128.80
128.72
128.64
127.85
124.30
122.58
120.63
115.67
107.53
107.49
106.70
77.21
77.00
76.79
38.15
32.22
31.77
14.72
O
Me
N
N
Py
MeS
O
P
Ph
Ph
3ja
(CDCl3, 150 MHz)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

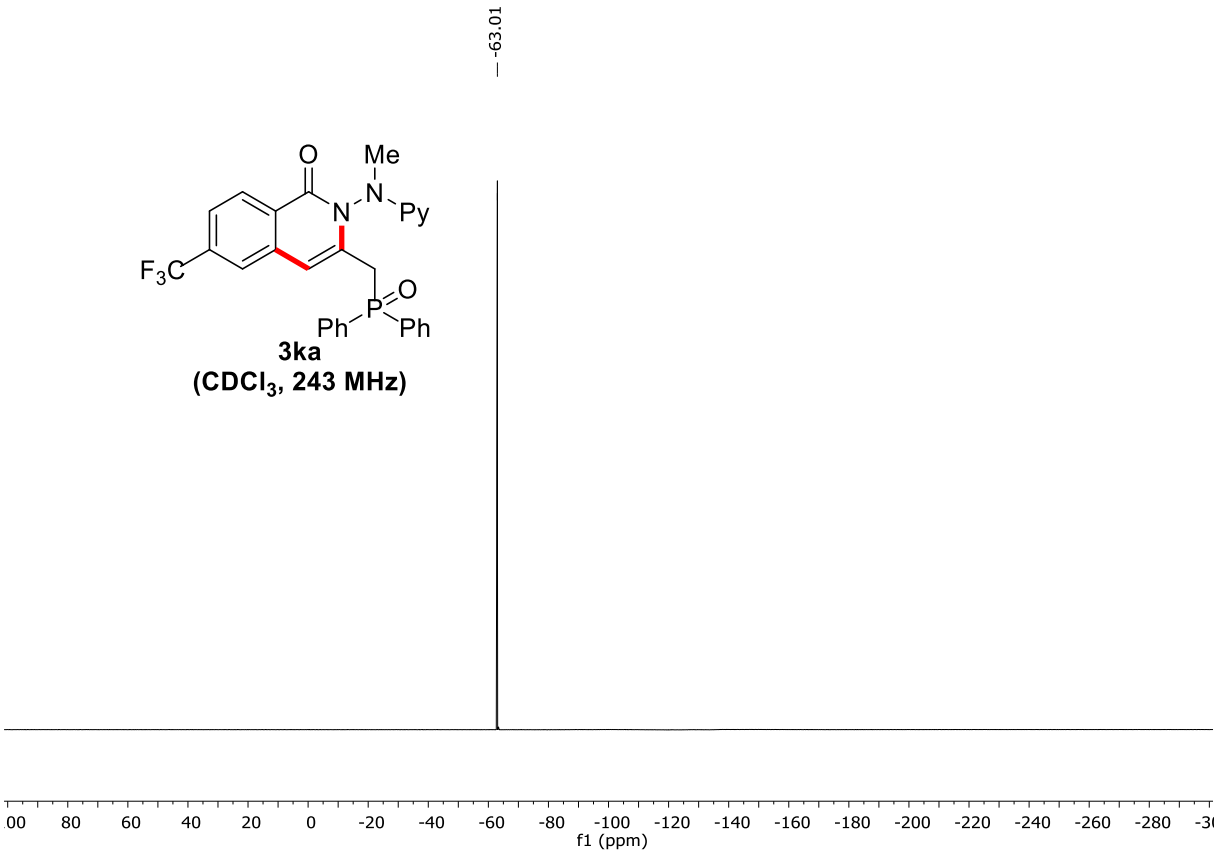

28.36
O
Me
N
N
Py
MeS
O
P
Ph
Ph
3ja
(CDCl3, 243 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)

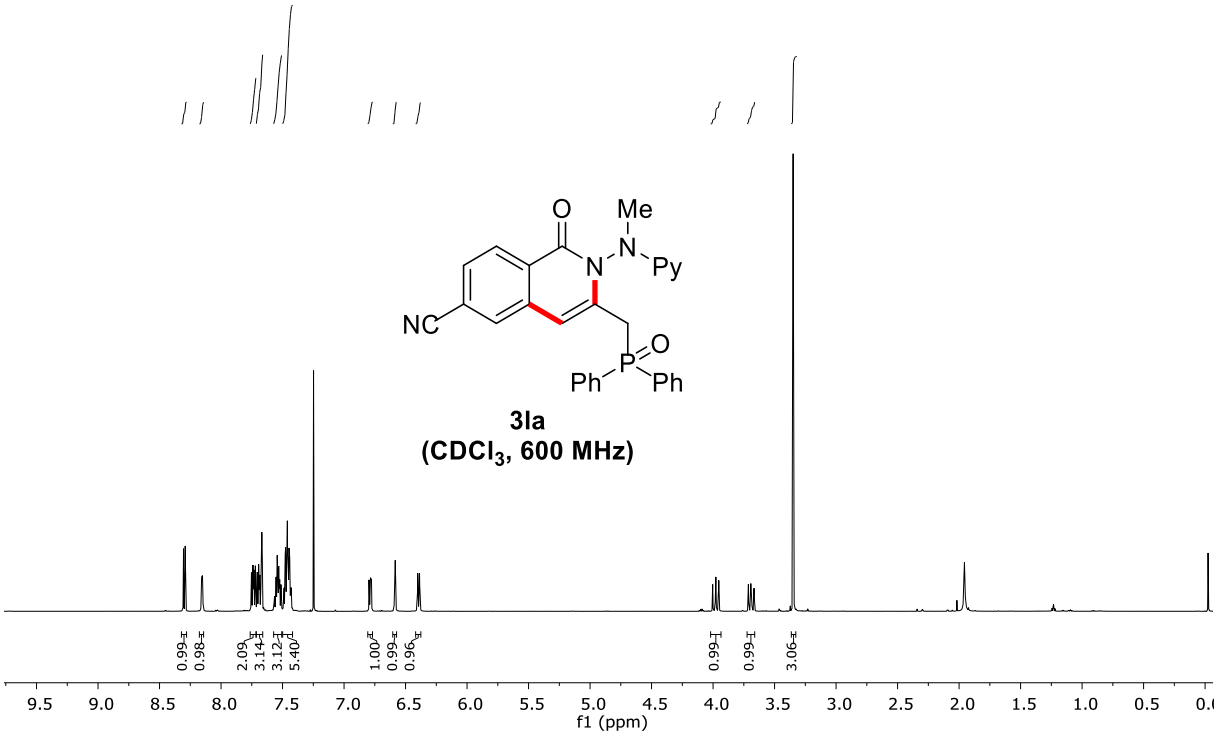

O
Me
N
Py
F3C
O
P
Ph
Ph
3ka
(CDCl3, 600 MHz)
1.05
1.02
2.12
2.22
1.10
3.25
5.65
1.08
1.09
1.03
1.08
1.06
3.23
f1 (ppm)

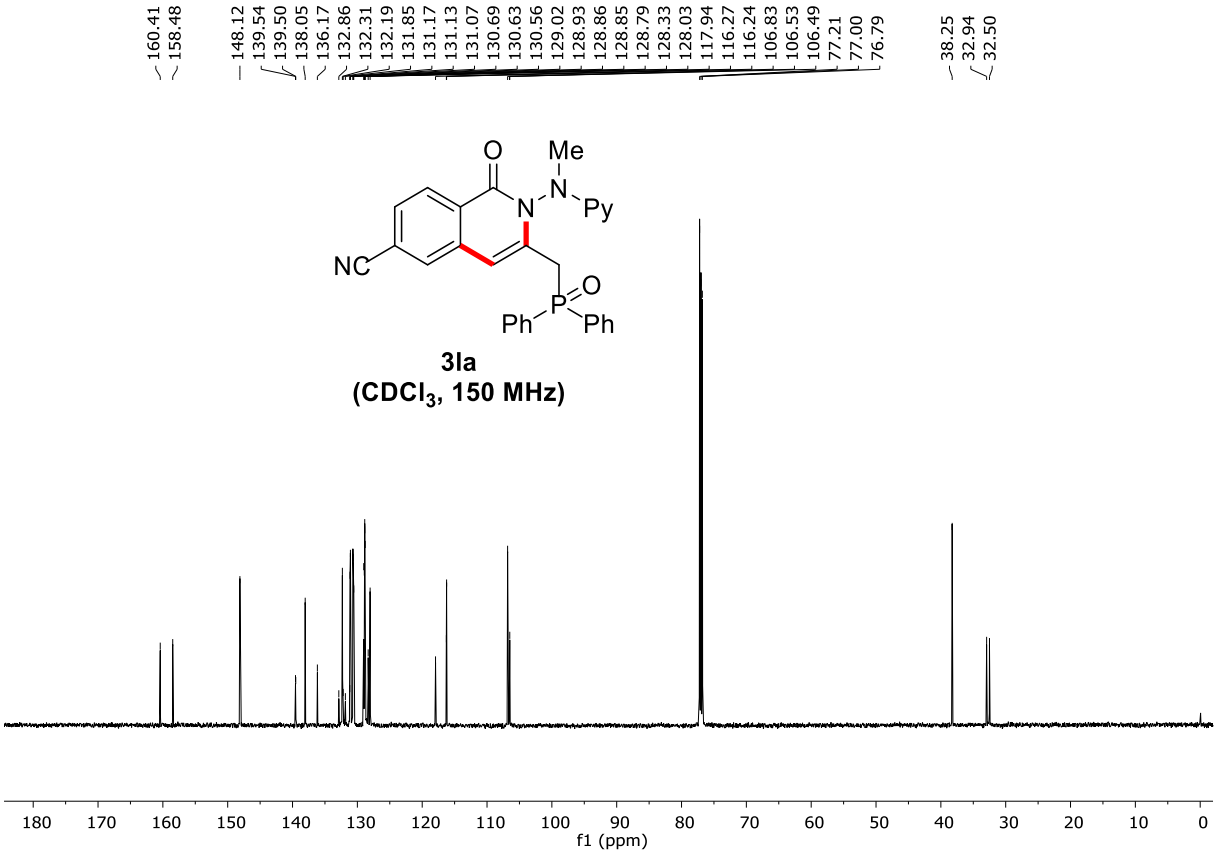

160.70
158.65
148.13
138.58
138.54
138.04
136.13
134.74
134.52
134.30
134.09
132.92
132.30
131.88
131.17
131.11
130.76
130.70
128.98
128.94
128.88
128.86
128.80
128.10
126.26
124.45
123.34
123.32
122.64
122.44
120.84
116.14
107.49
107.45
106.83
77.21
77.00
76.79
38.28
32.74
32.29
O
Me
N
Py
F3C
O
P
Ph
Ph
3ka
(CDCl3, 150 MHz)
f1 (ppm)

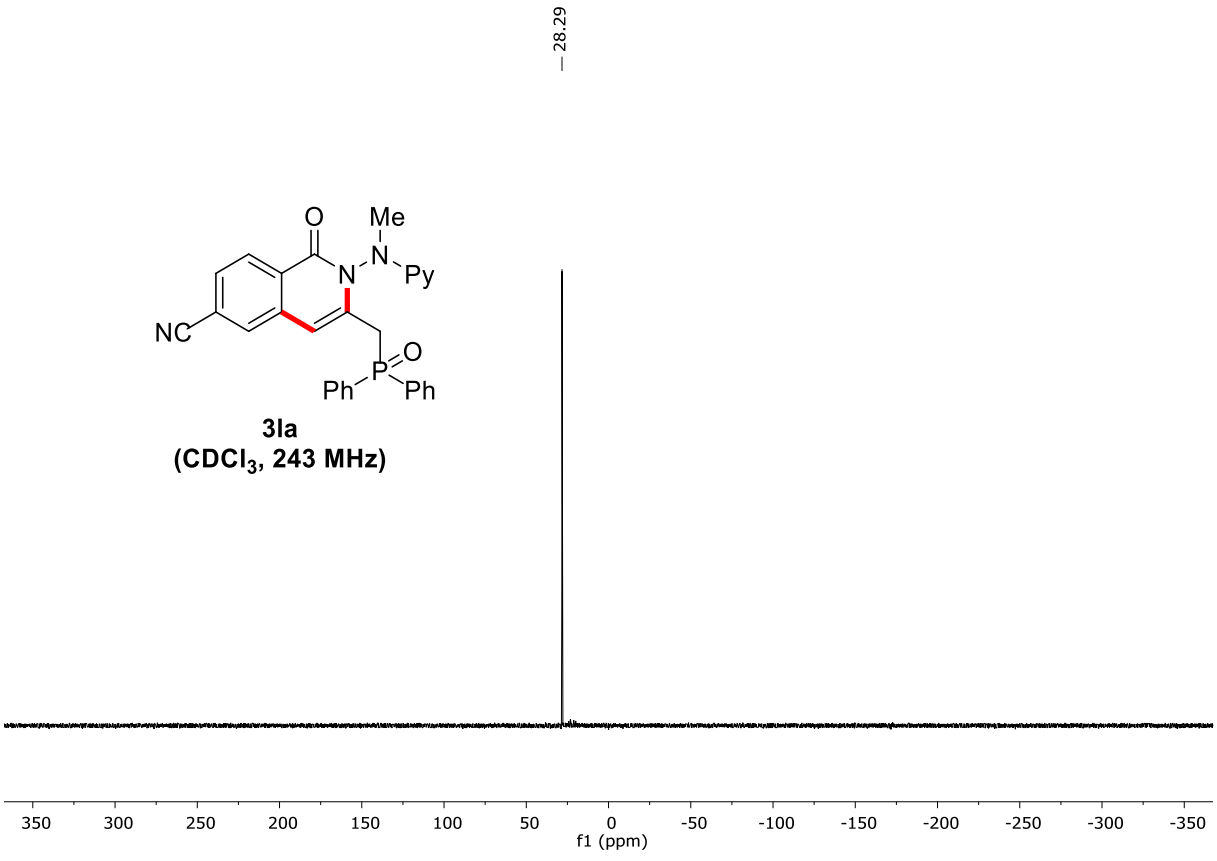

148.13
138.06
132.32
131.17
131.11
130.76
130.70
128.98
128.95
128.89
128.87
128.81
123.35
123.33
122.46
122.45
116.15
107.50
107.46
106.83
38.28
O
Me
N
N
Py
F3C
O
P
Ph
Ph
3ka
(CDCl3, 150 MHz)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

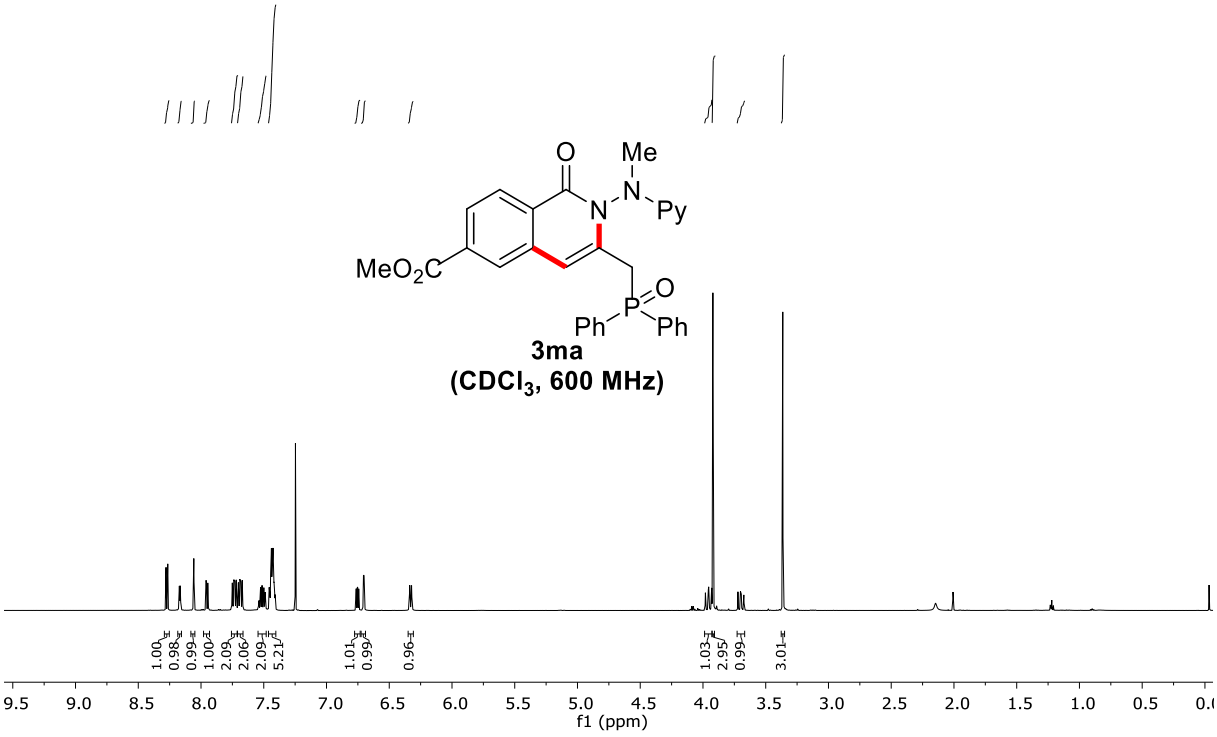

28.29
O
Me
N
N
Py
F3C
O
P
Ph
Ph
3ka
(CDCl3, 565 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)


-63.01
O
Me
N
N
Py
F3C
O
P
Ph
Ph
3ka
(CDCl3, 243 MHz)
f1 (ppm)

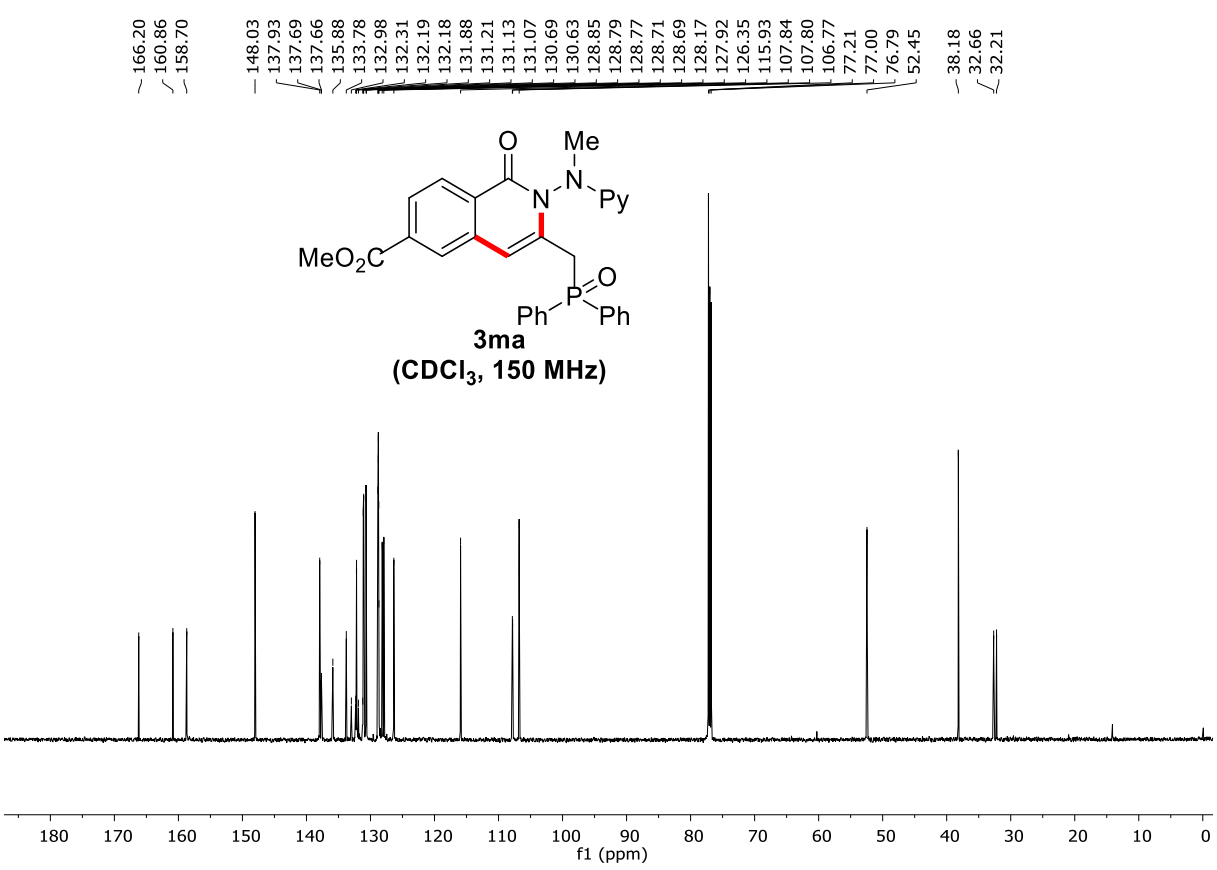

O
Me
N
N
Py
NC
O
P
Ph
Ph
3la
(CDCl3, 600 MHz)
0.99
0.98
2.09
3.14
3.12
5.40
1.00
0.99
0.96
0.99
0.99
3.06
f1 (ppm)


160.41
158.48
148.12
139.54
139.50
138.05
136.17
132.86
132.31
132.19
131.85
131.17
131.13
131.07
130.69
130.63
130.56
129.02
128.93
128.86
128.85
128.79
128.33
128.03
117.94
116.27
116.24
106.83
106.53
106.49
77.21
77.00
76.79
38.25
32.94
32.50
O
Me
N
N
Py
NC
O
P
Ph
Ph
3Ia
(CDCl3, 150 MHz)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

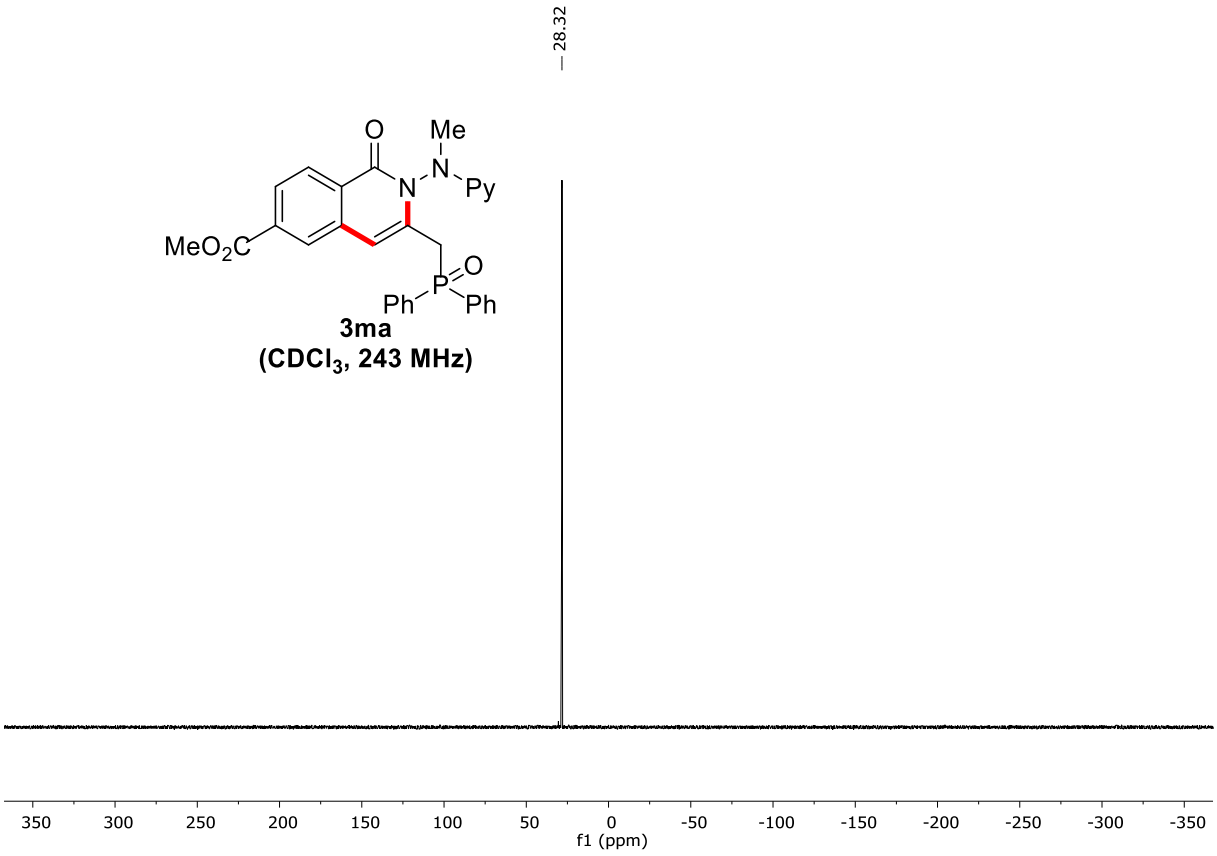

28.29
O
Me
N
N
Py
NC
O
P
Ph
Ph
3Ia
(CDCl3, 243 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)



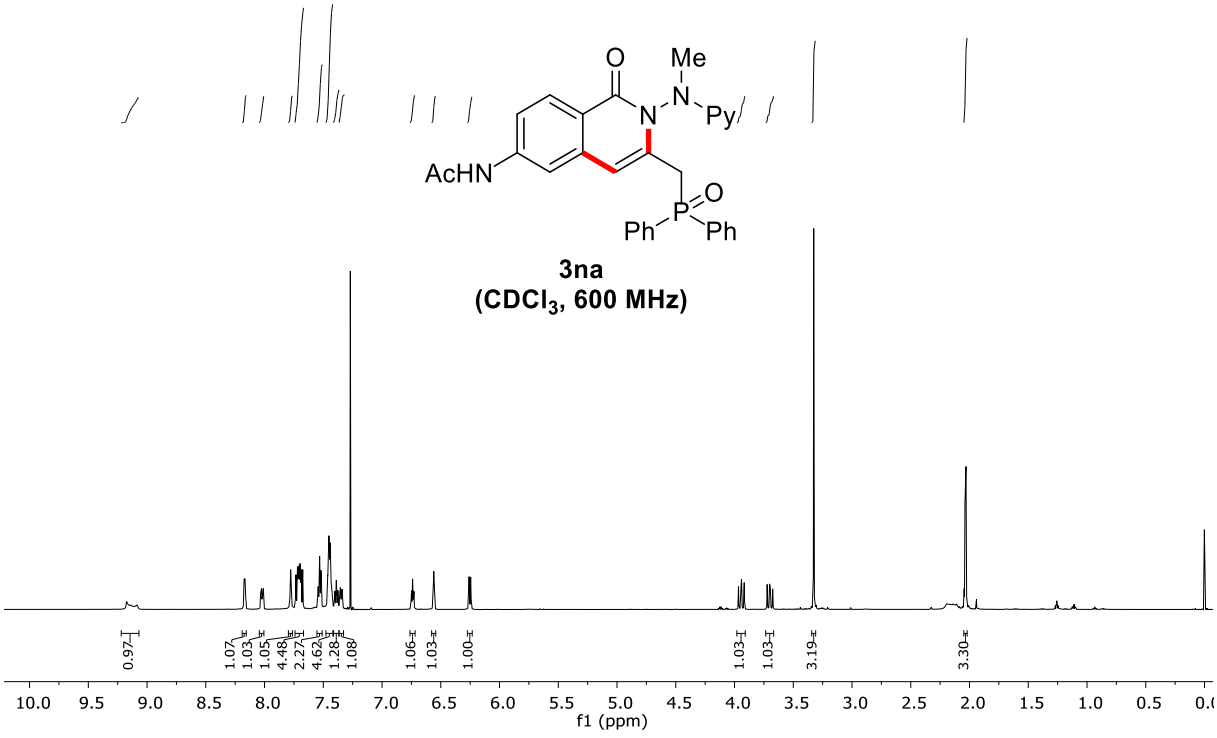
3ma
($CDCl_3$, 600 MHz)



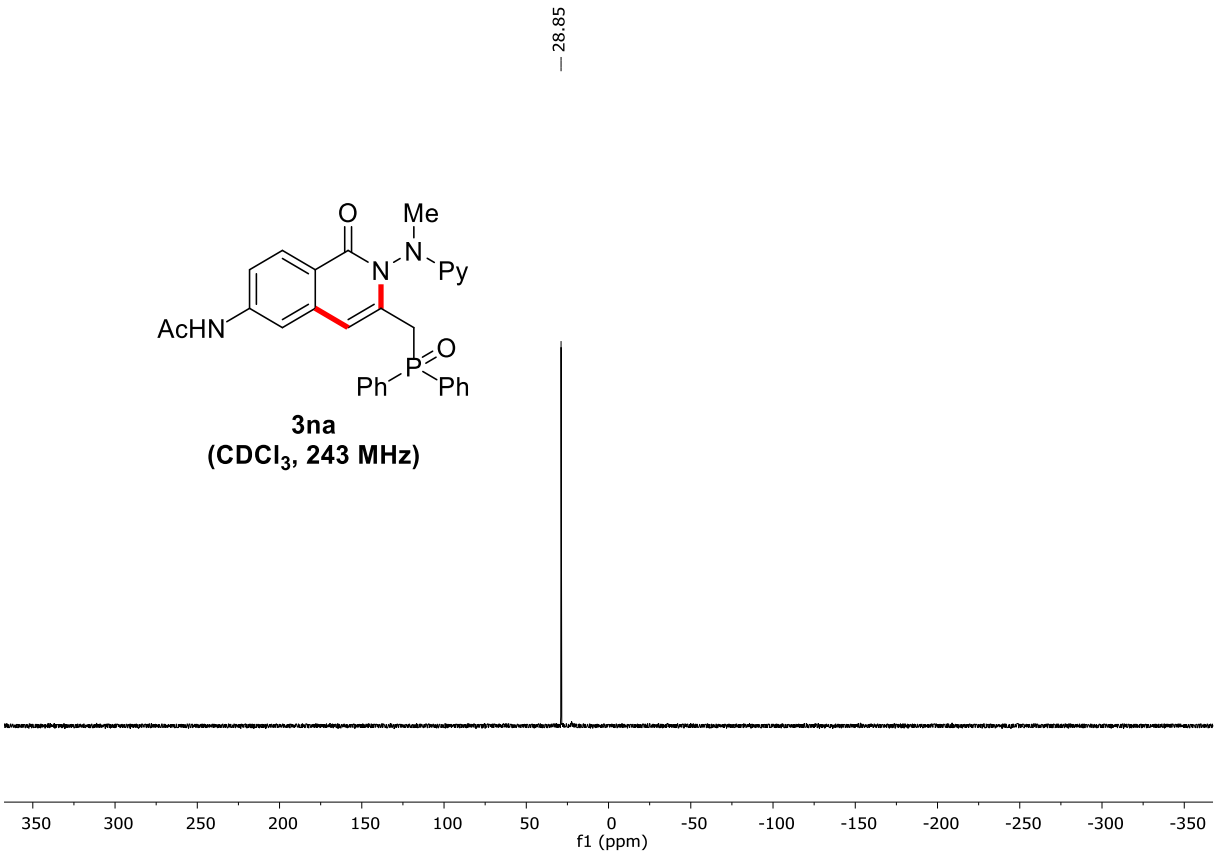
3ma
($CDCl_3$, 150 MHz)



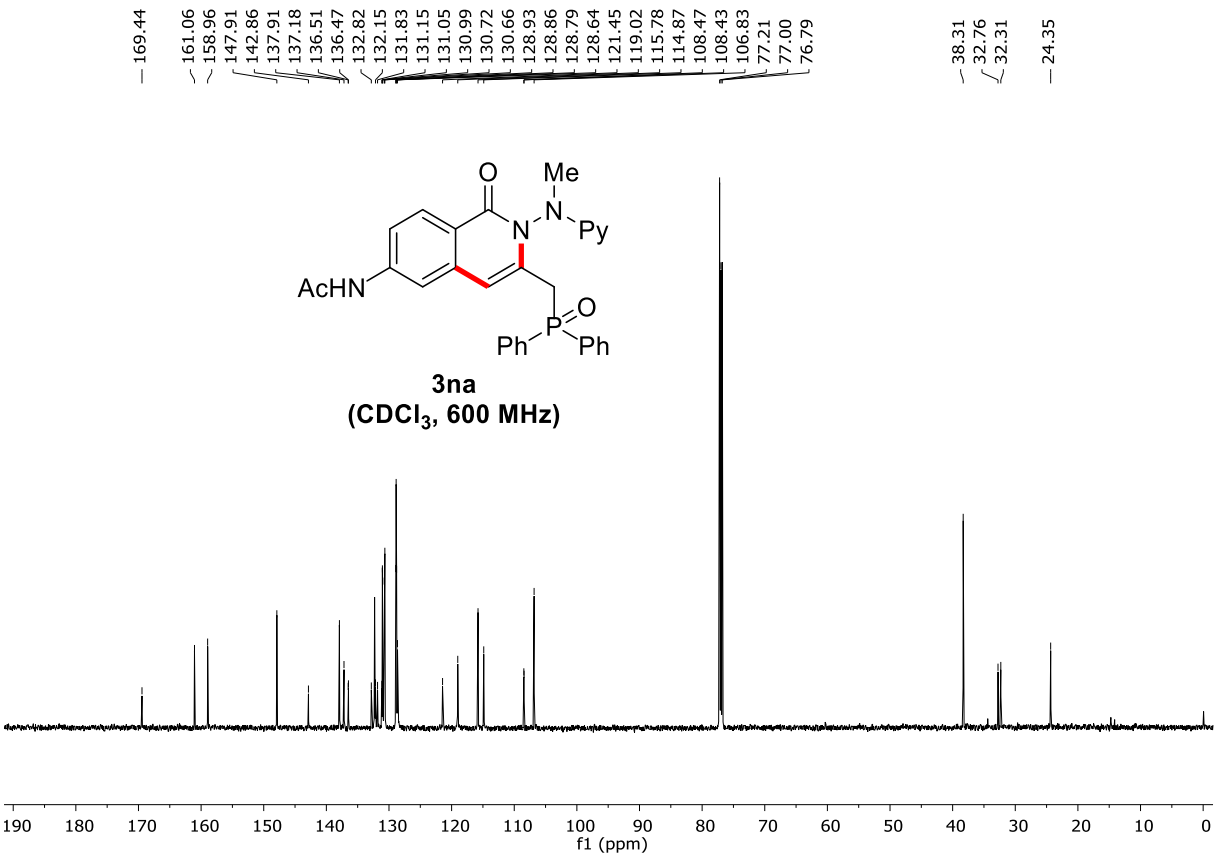
3ma
($CDCl_3$, 243 MHz)



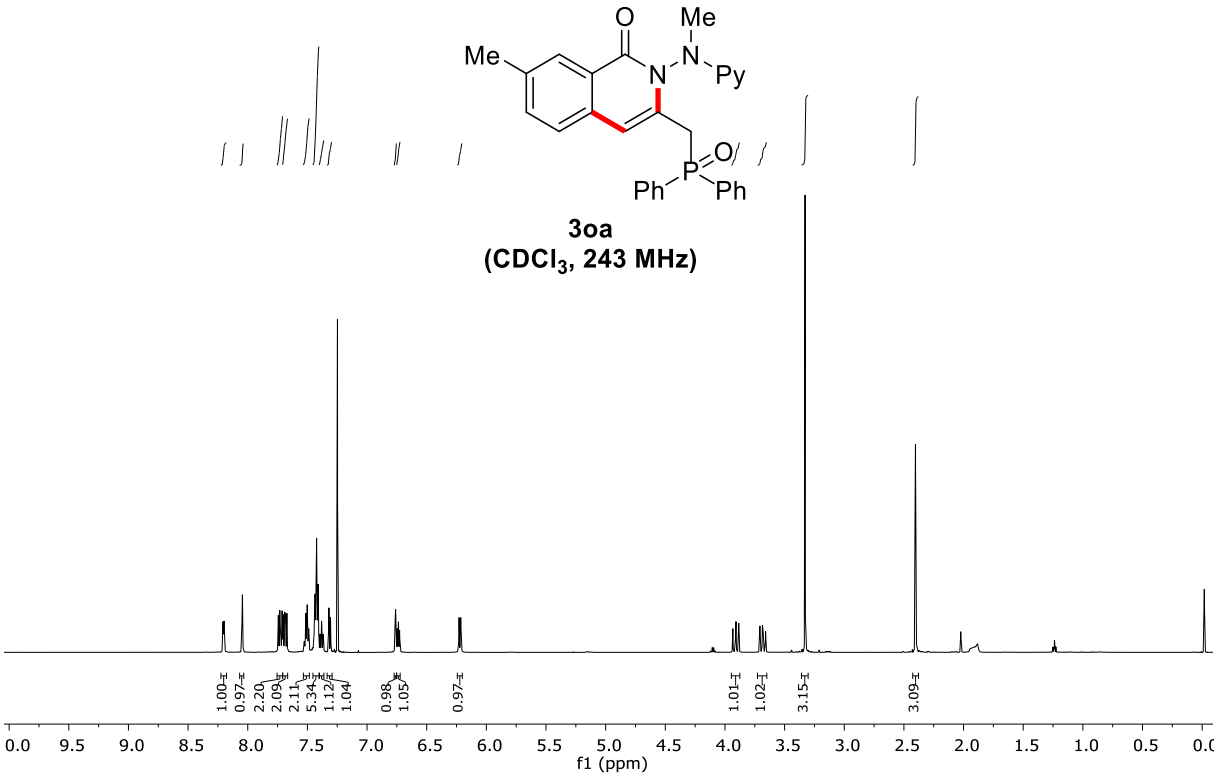
3na
($CDCl_3$, 600 MHz)



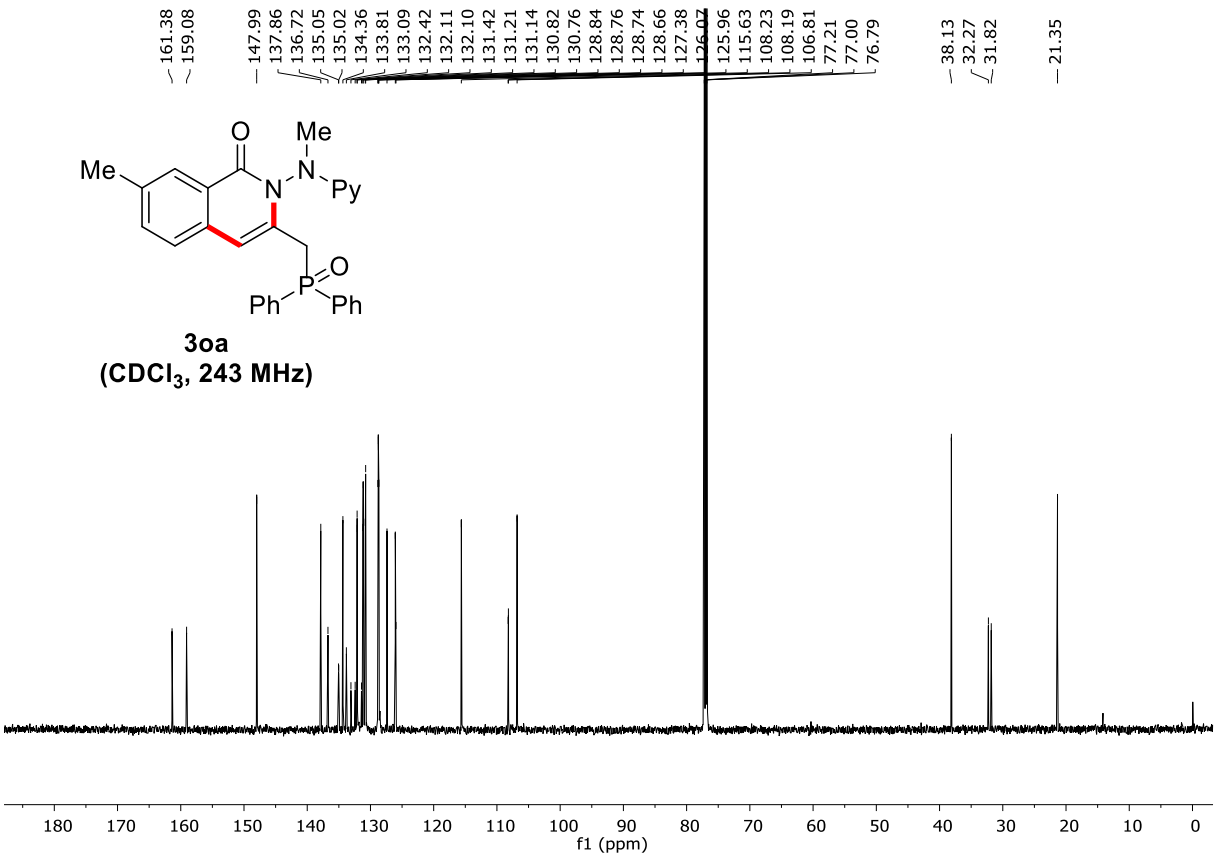
3na
($CDCl_3$, 243 MHz)



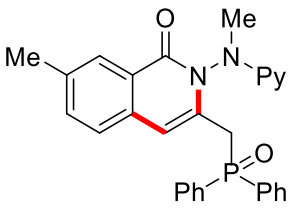
3na
($CDCl_3$, 600 MHz)



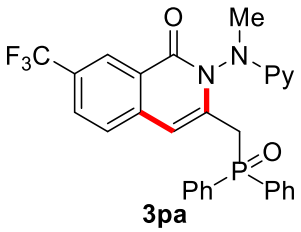
3oa
($CDCl_3$, 243 MHz)



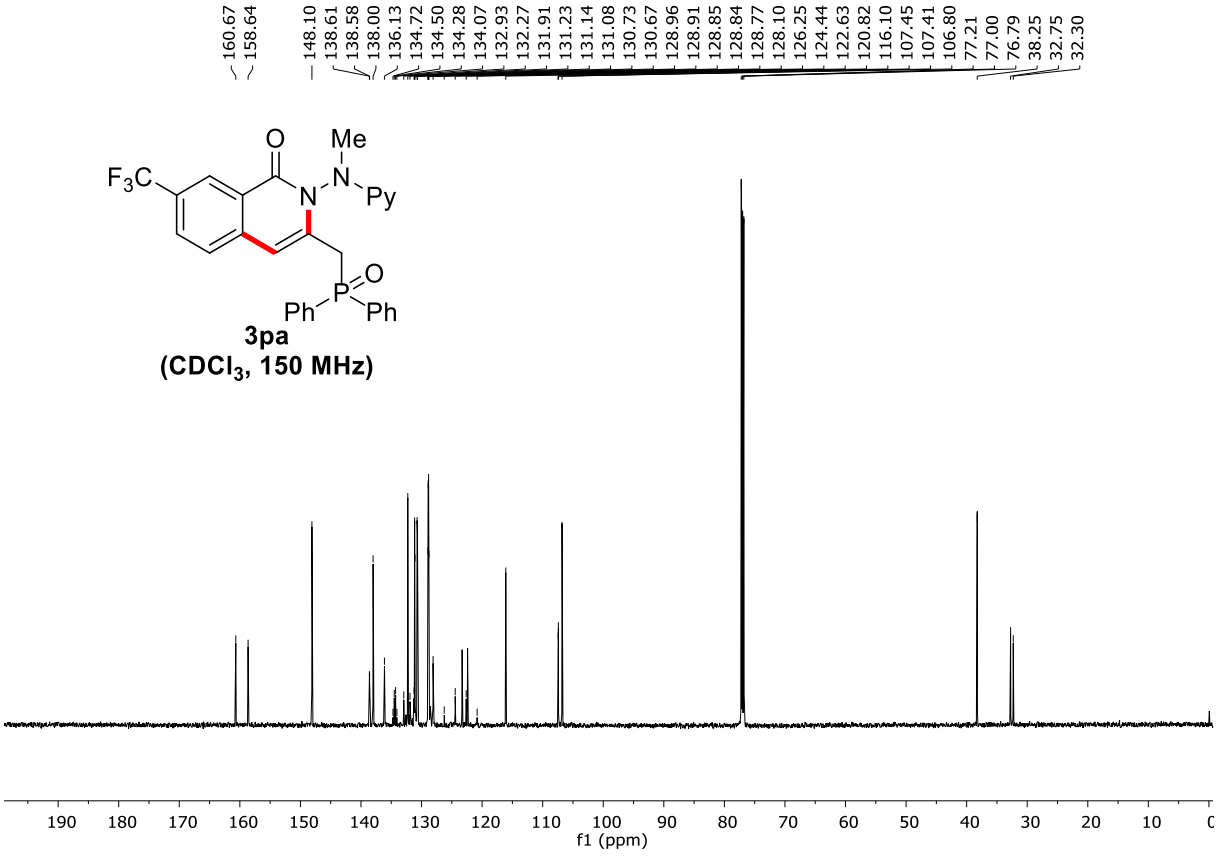
3oa
($CDCl_3$, 243 MHz)

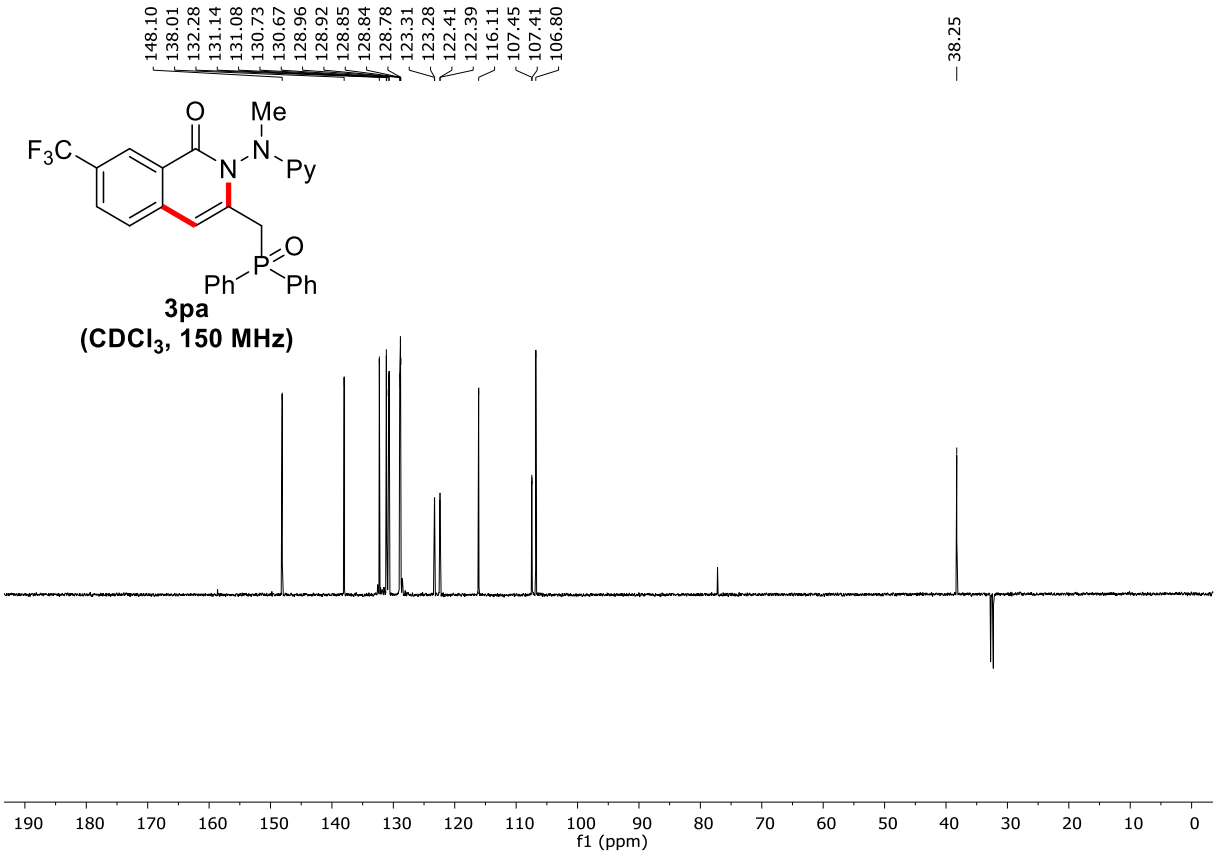


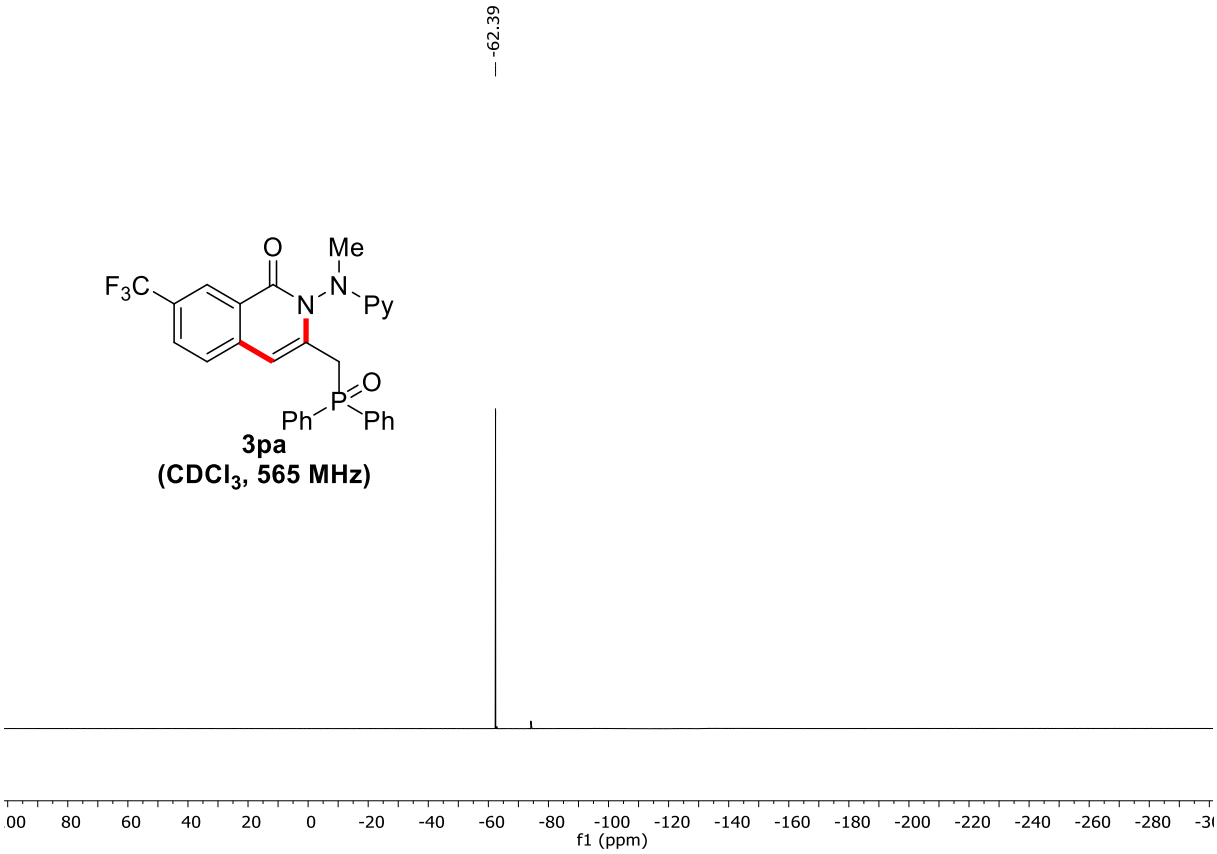
3oa
($CDCl_3$, 243 MHz)



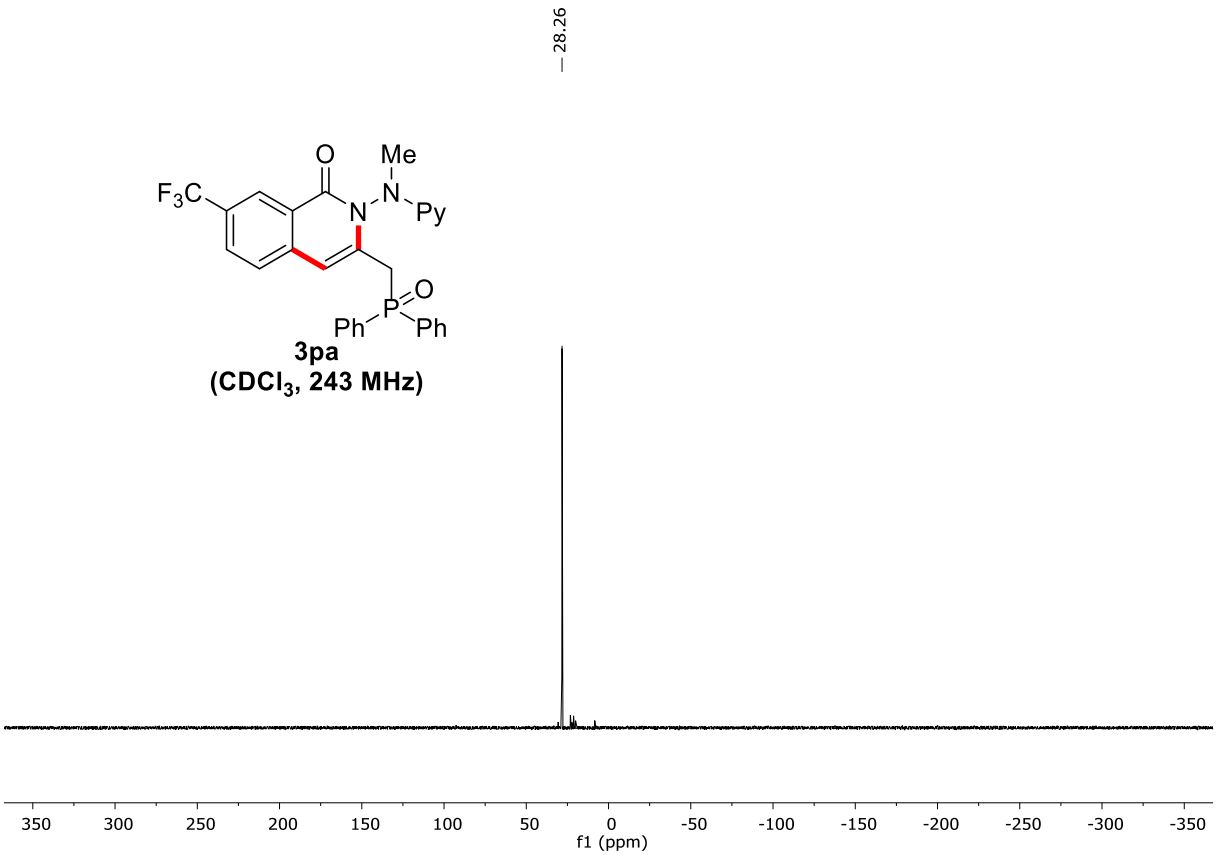
3pa
($CDCl_3$, 600 MHz)


160.67
158.64
148.10
138.61
138.58
138.00
136.13
134.72
134.50
134.28
134.07
132.93
132.27
131.91
131.23
131.14
131.08
130.73
130.67
128.96
128.91
128.85
128.84
128.77
128.10
126.25
124.44
122.63
120.82
116.10
107.45
107.41
106.80
77.21
77.00
76.79
38.25
32.75
32.30
O
Me
N
N
Py
F3C
O
P
Ph
Ph
3pa
(CDCl3, 150 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

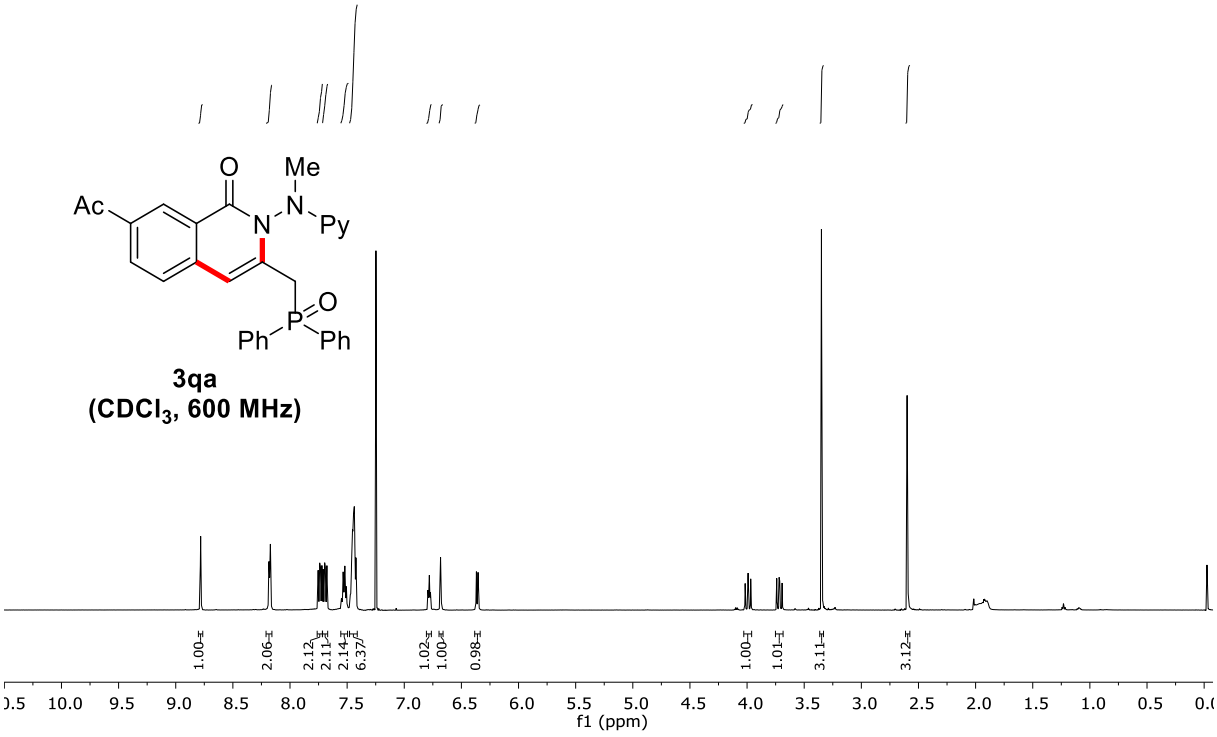

148.10
138.01
132.28
131.14
131.08
130.73
130.67
128.96
128.92
128.85
128.84
128.78
123.31
123.28
122.41
122.39
116.11
107.45
107.41
106.80
38.25
O
Me
N
N
Py
F3C
O
P
Ph
Ph
3pa
(CDCl3, 150 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

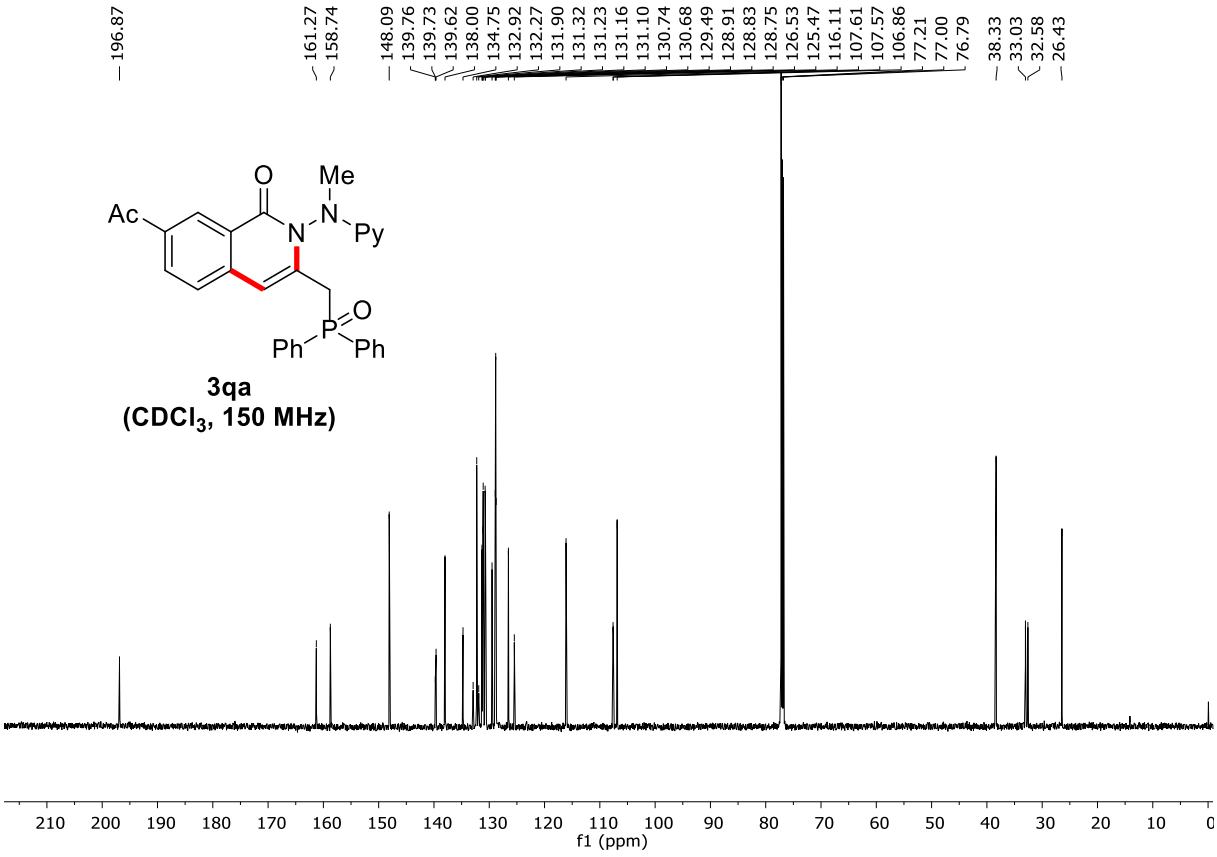


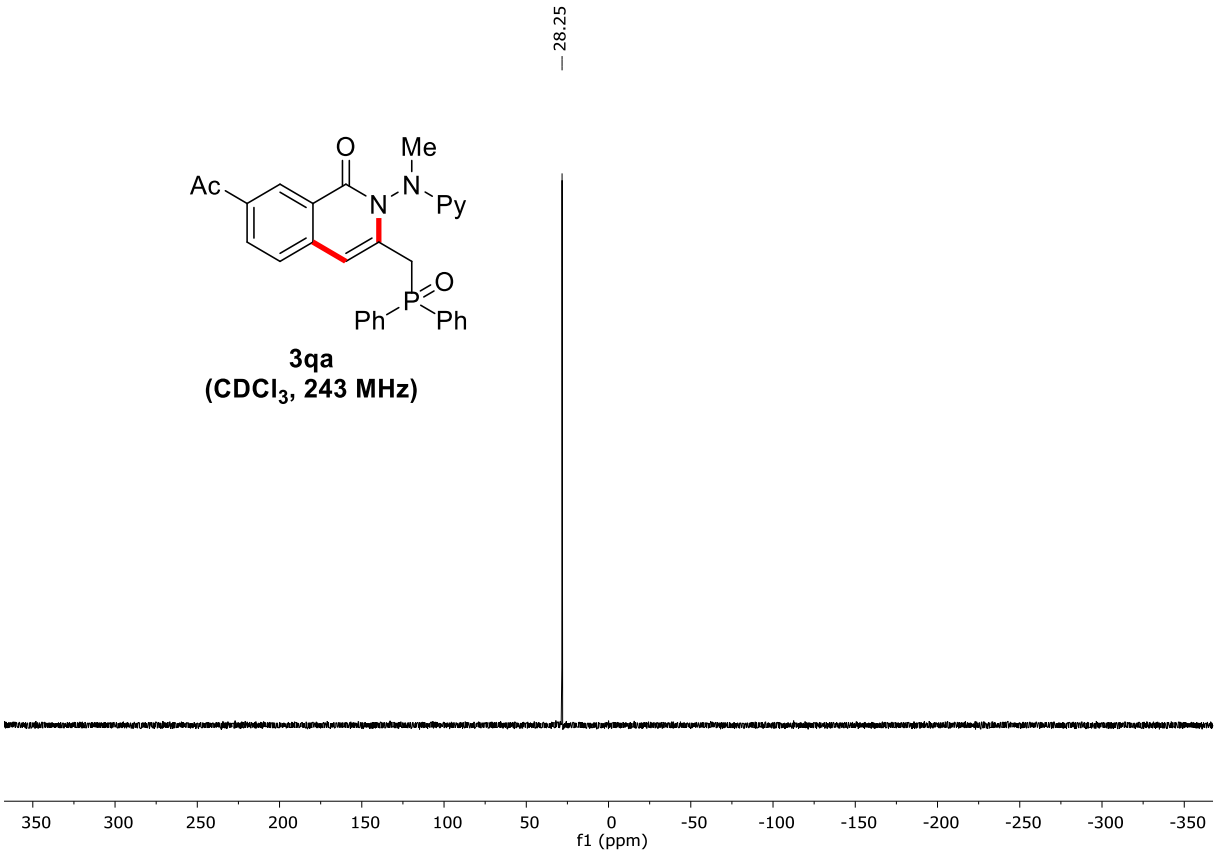
3pa
($CDCl_3$, 565 MHz)



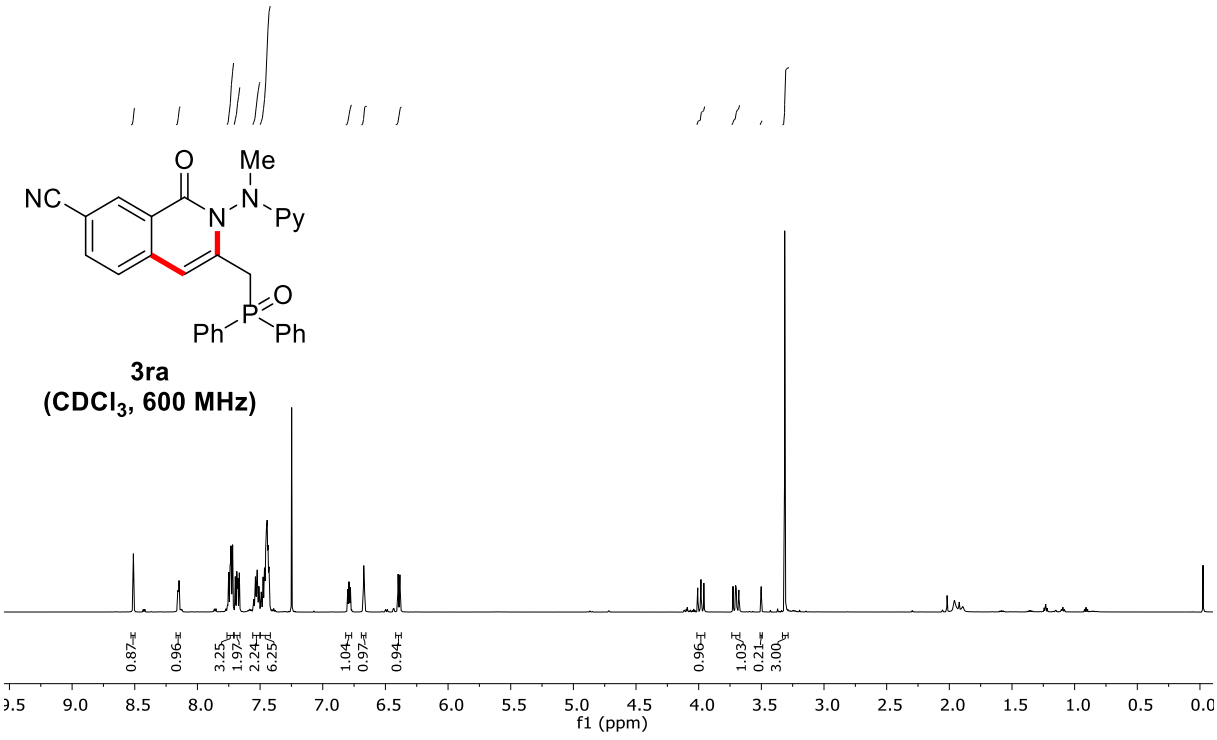
3pa
($CDCl_3$, 243 MHz)


Ac
O
Me
N
N
Py
P
O
Ph
Ph
3qa
(CDCl3, 600 MHz)
1.00
2.06
2.12
2.11
2.14
6.37
1.02
1.00
0.98
1.00
1.01
3.11
3.12
f1 (ppm)

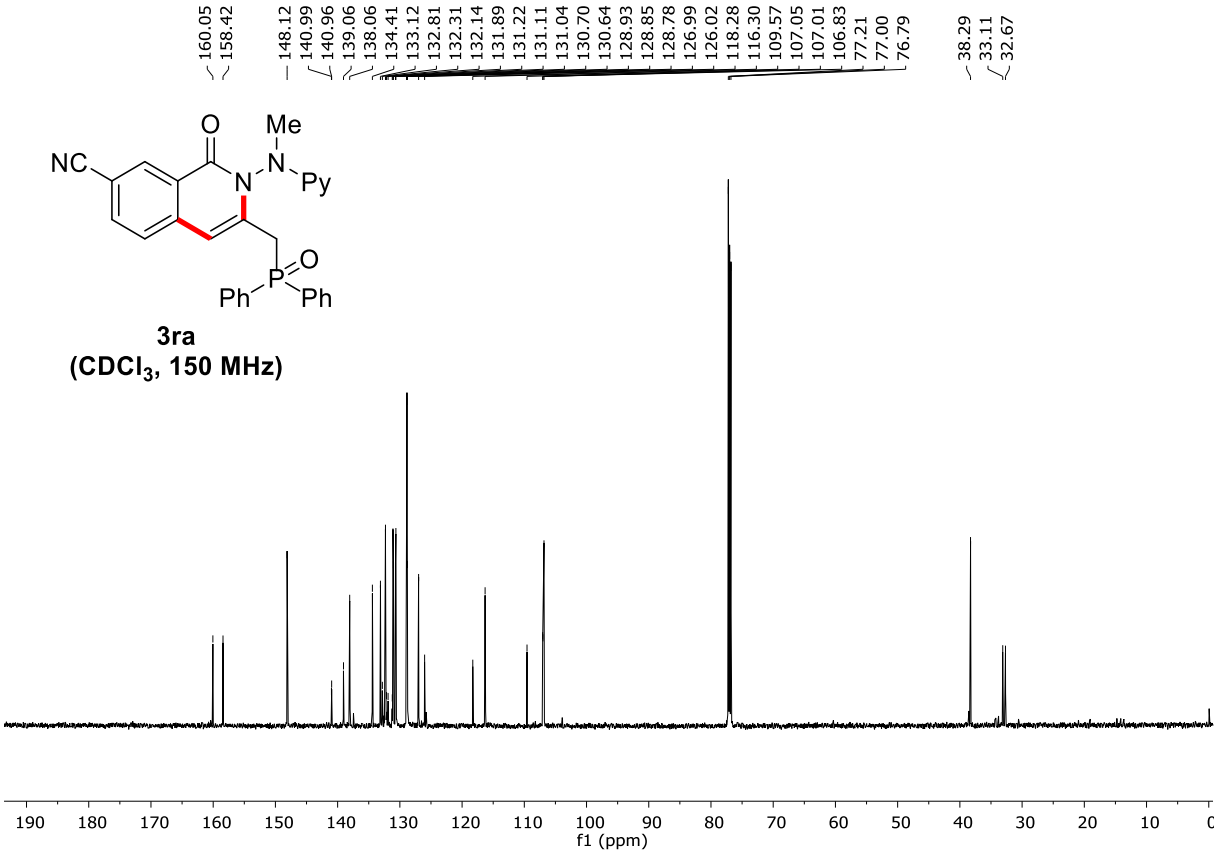

196.87
161.27
158.74
148.09
139.76
139.73
139.62
138.00
134.75
132.92
132.27
131.90
131.32
131.23
131.16
131.10
130.74
130.68
129.49
128.91
128.83
128.75
126.53
125.47
116.11
107.61
107.57
106.86
77.21
77.00
76.79
38.33
33.03
32.58
26.43
Ac
O
Me
N
N
Py
P
O
Ph
Ph
3qa
(CDCl3, 150 MHz)
f1 (ppm)



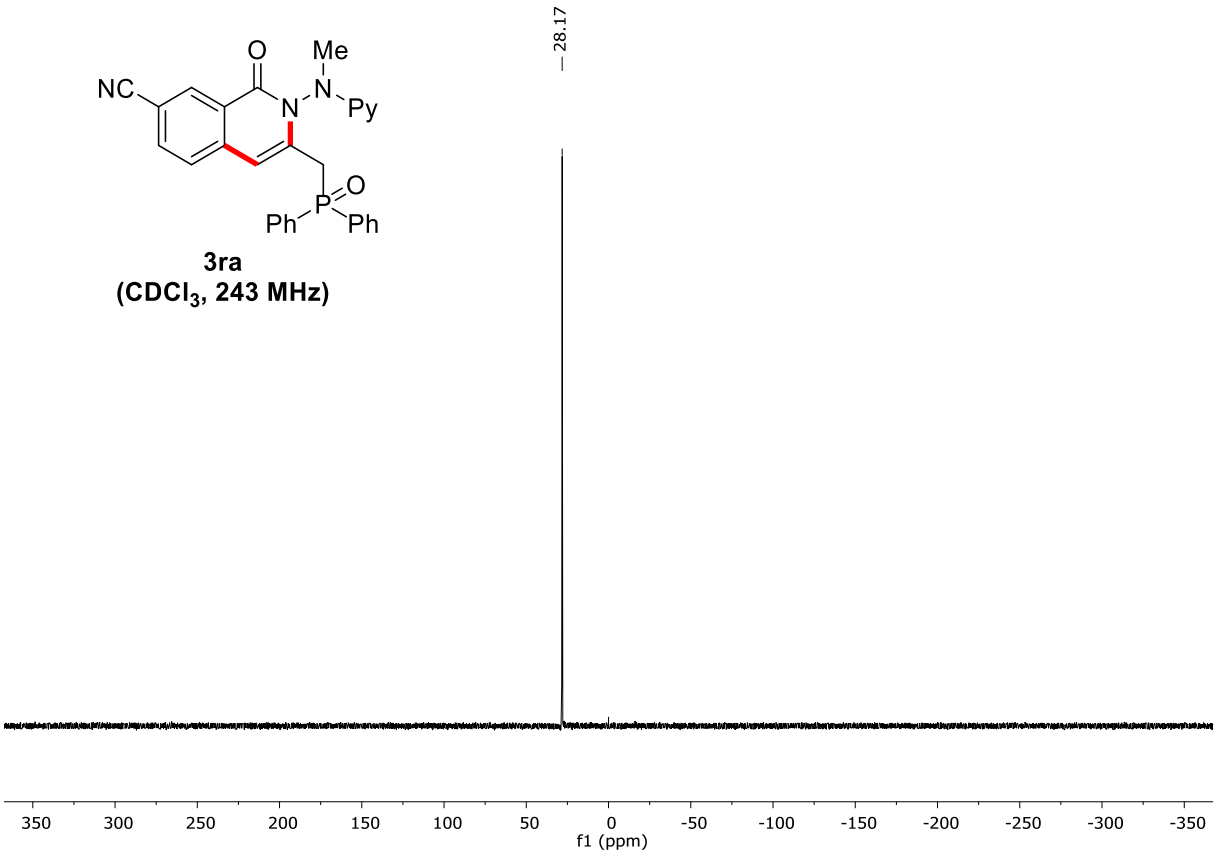
3qa
($CDCl_3$, 243 MHz)



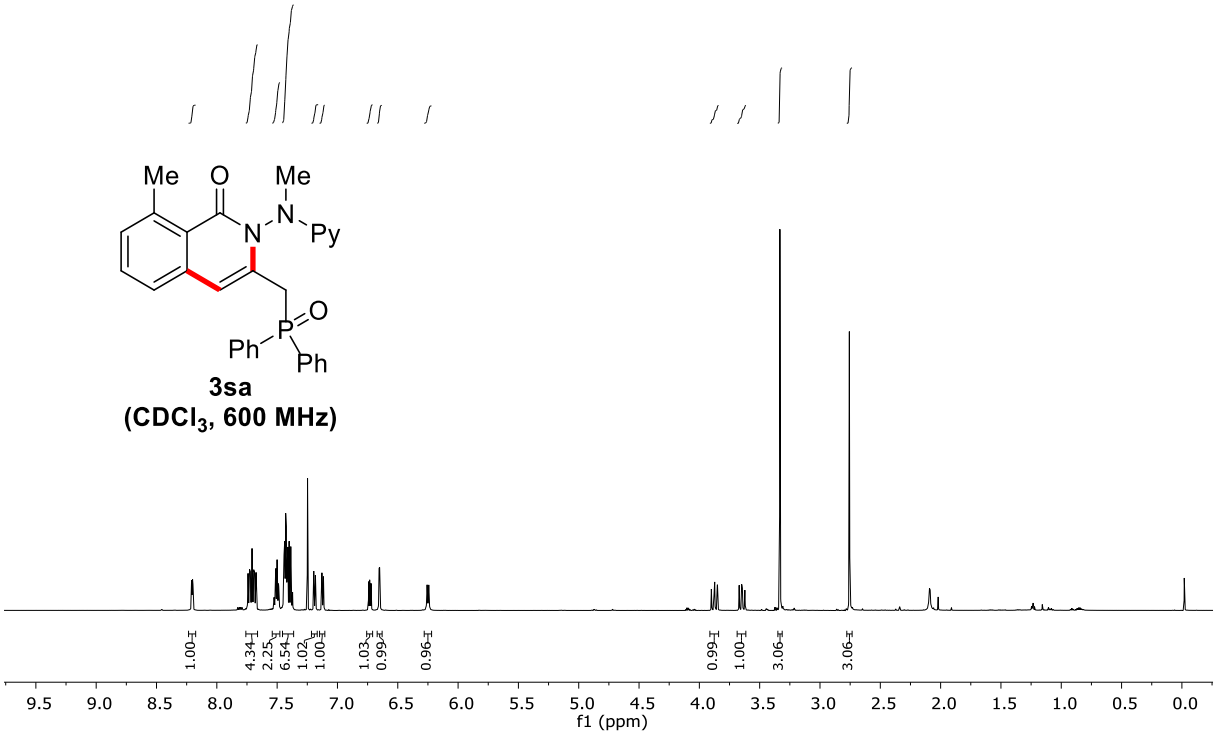
3ra
($CDCl_3$, 600 MHz)



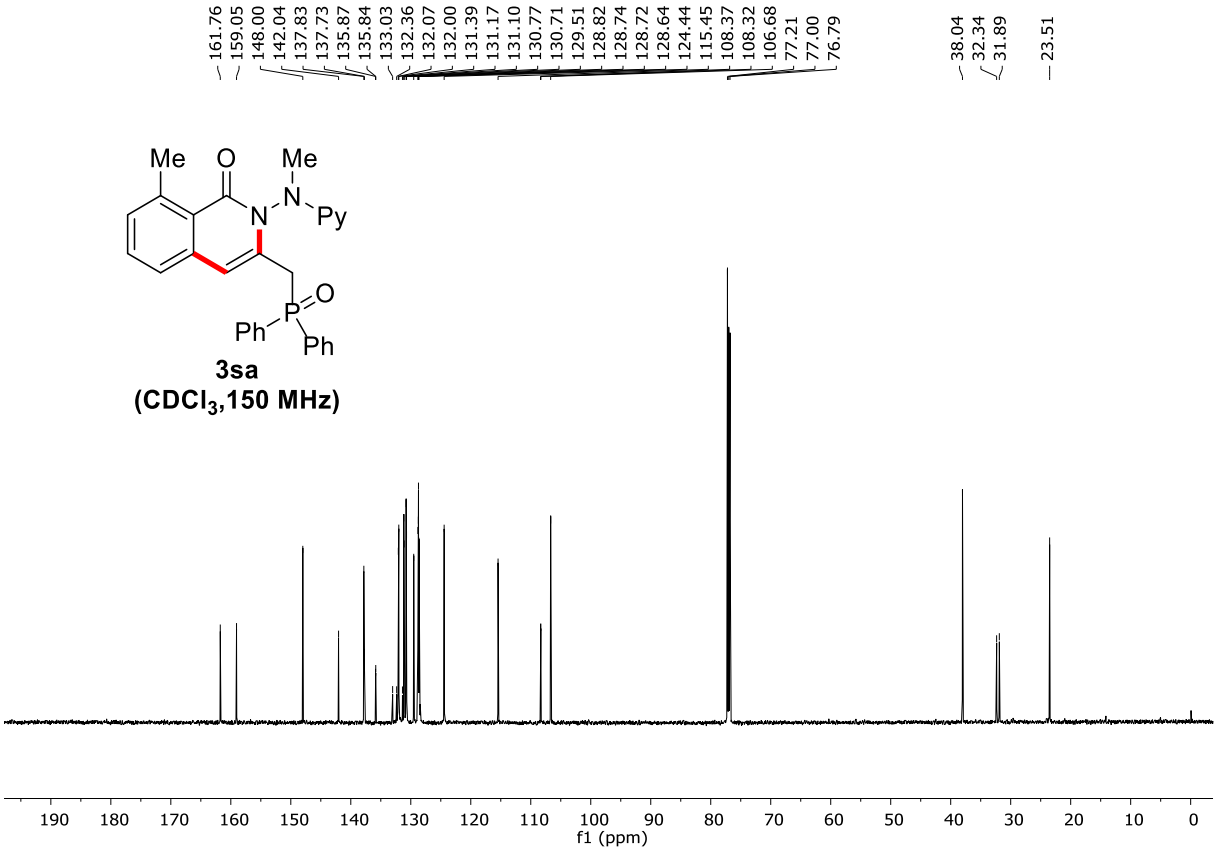
3ra
($CDCl_3$, 150 MHz)



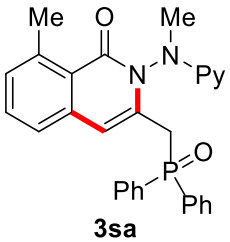
3ra
($CDCl_3$, 243 MHz)



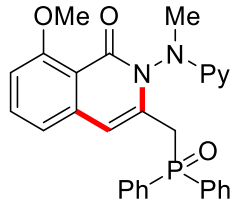
3sa
($CDCl_3$, 600 MHz)



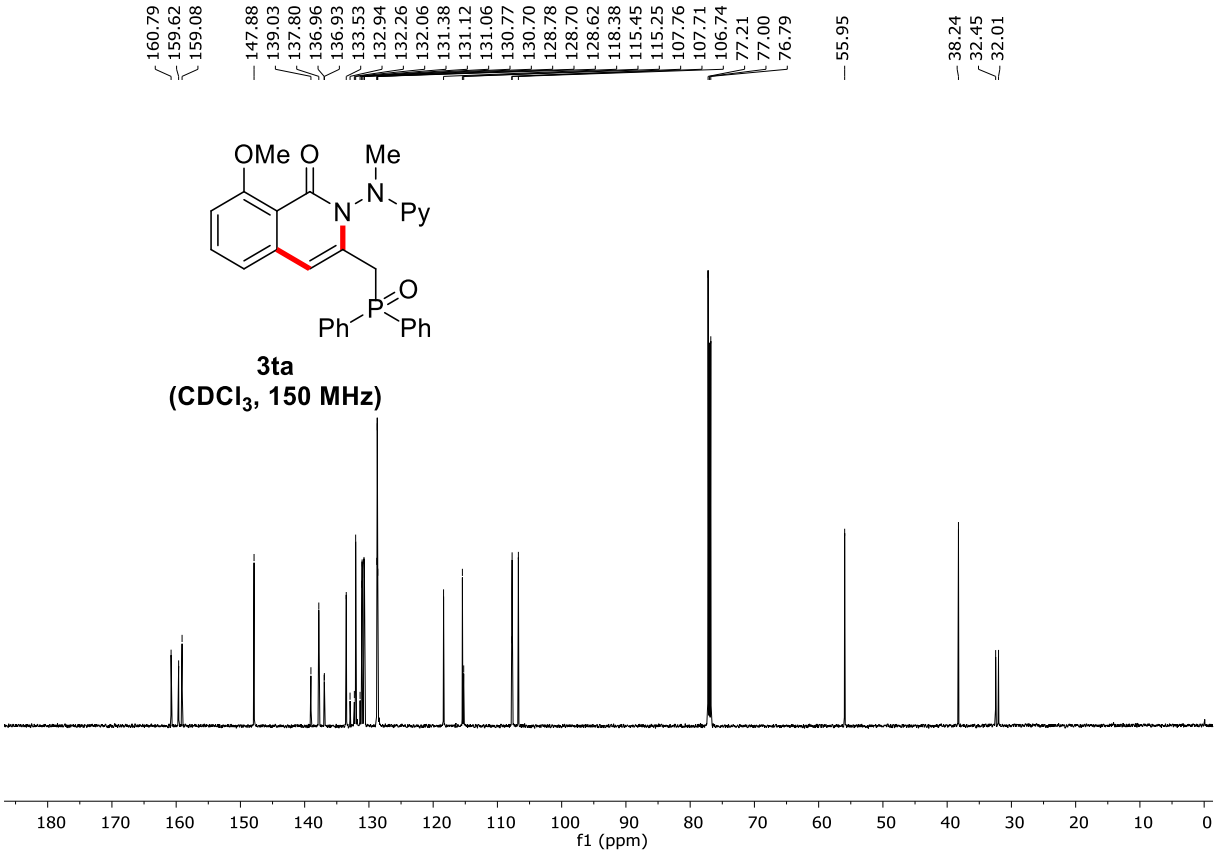
3sa
($CDCl_3$,150 MHz)

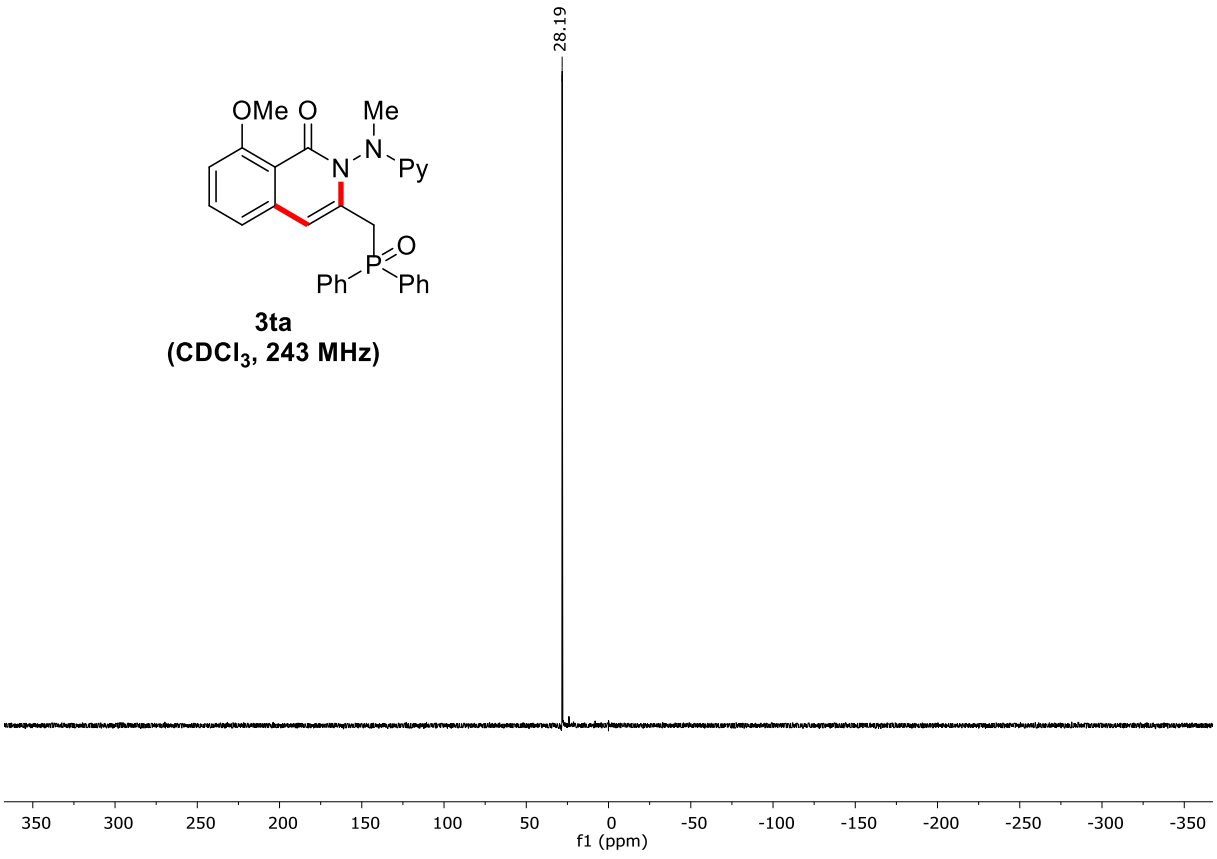


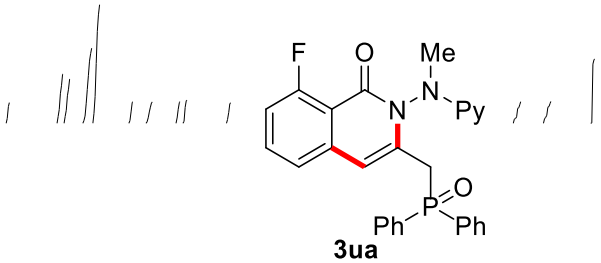
3sa
($CDCl_3$,243 MHz)



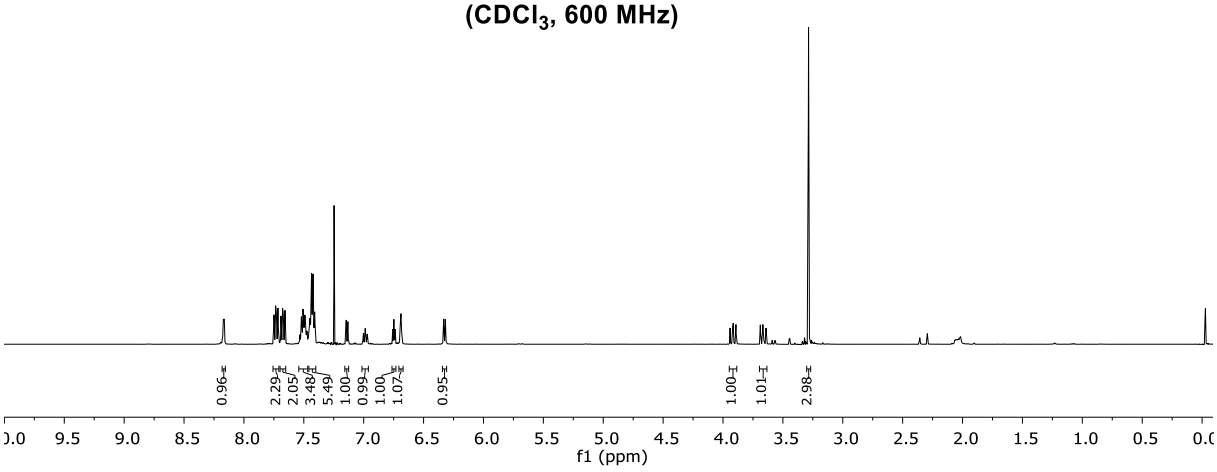
3ta
($CDCl_3$, 600 MHz)

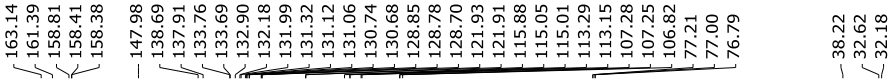

160.79
159.62
159.08
147.88
139.03
137.80
136.96
136.93
133.53
132.94
132.26
132.06
131.38
131.12
131.06
130.77
130.70
128.78
128.70
128.62
118.38
115.45
115.25
107.76
107.71
106.74
77.21
77.00
76.79
55.95
38.24
32.45
32.01
OMe O
Me
N
N
Py
O
P
Ph
Ph
3ta
(CDCl3, 150 MHz)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

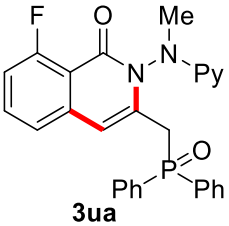

28.19
OMe O
Me
N
N
Py
O
P
Ph
Ph
3ta
(CDCl3, 243 MHz)
350 300 250 200 150 100 50 0 -50 -100 -150 -200 -250 -300 -350
f1 (ppm)



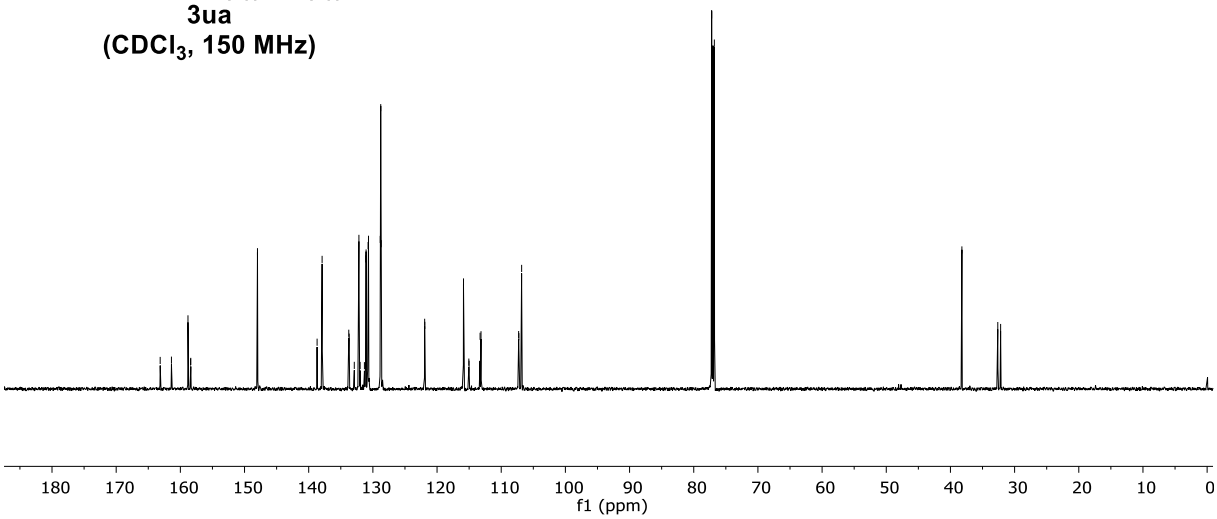
3ua
($CDCl_3$, 600 MHz)

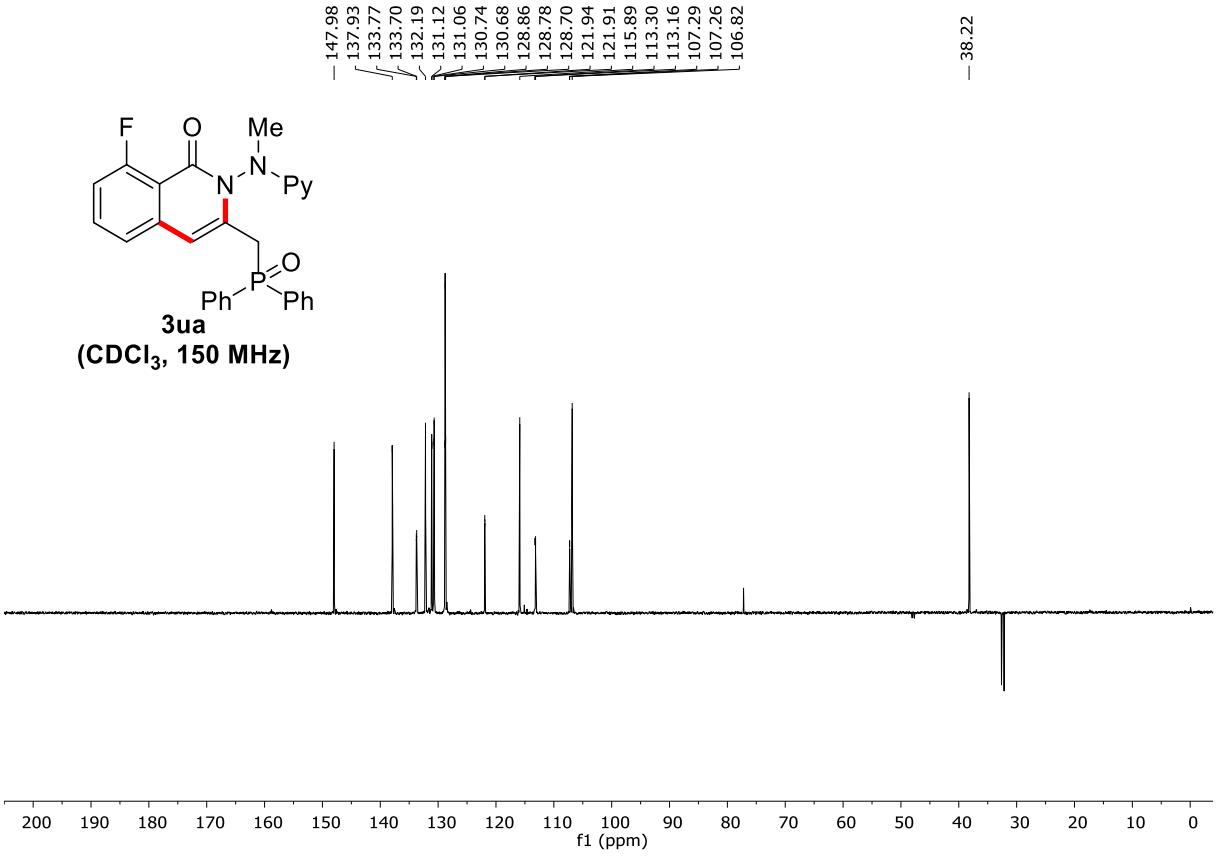




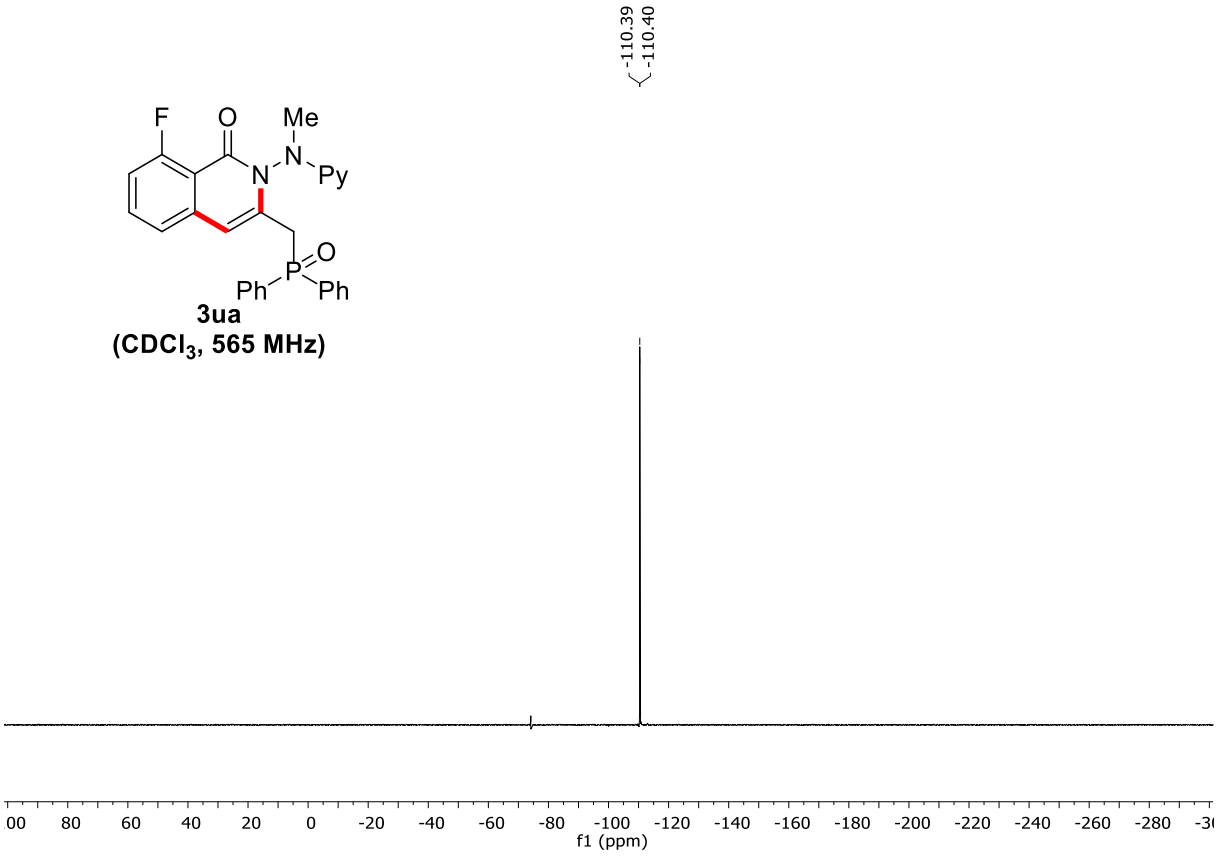


3ua
($CDCl_3$, 150 MHz)

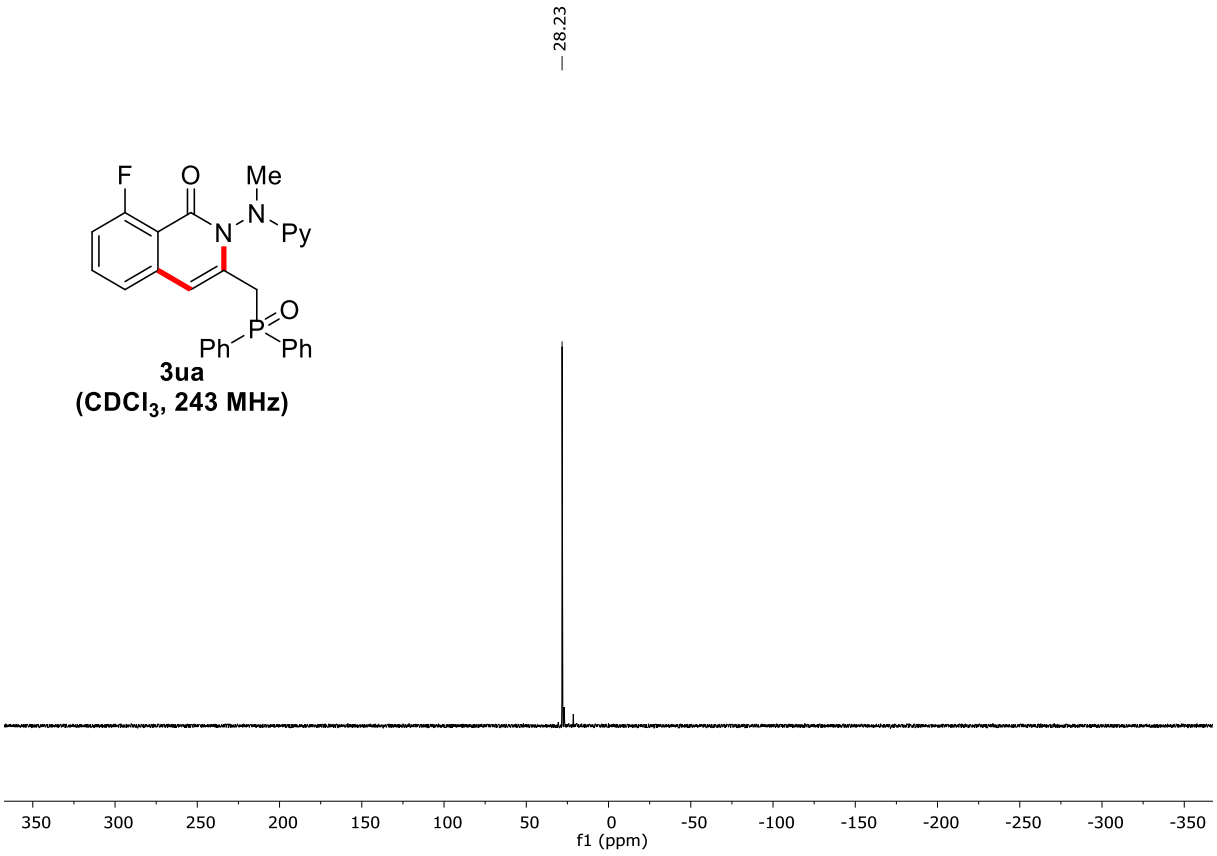




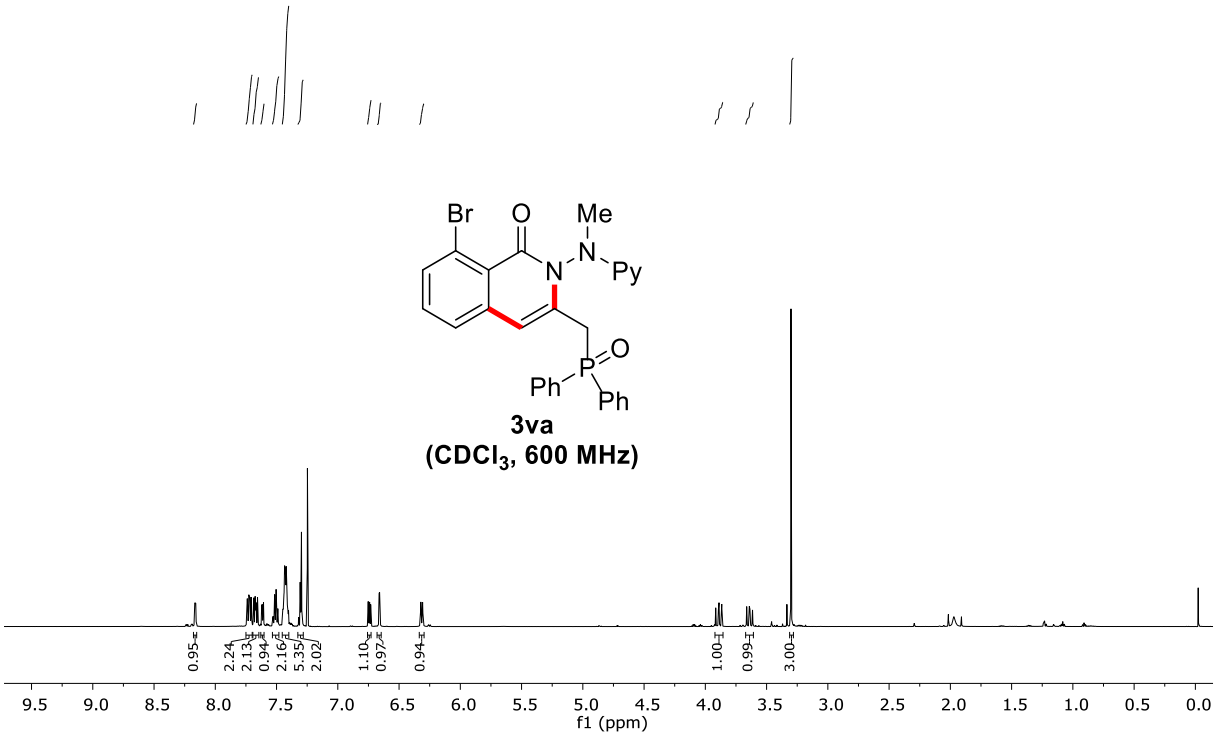
3ua
($CDCl_3$, 150 MHz)



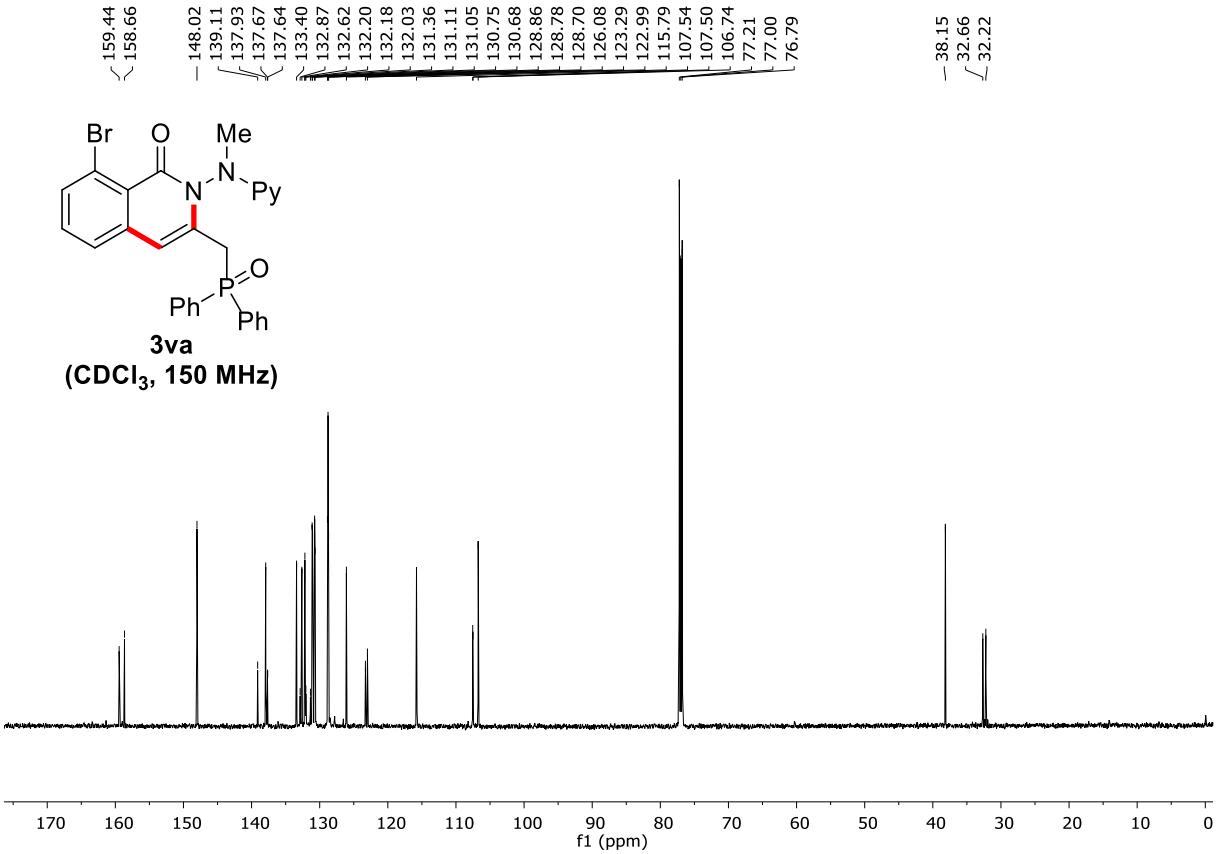
3ua
($CDCl_3$, 565 MHz)

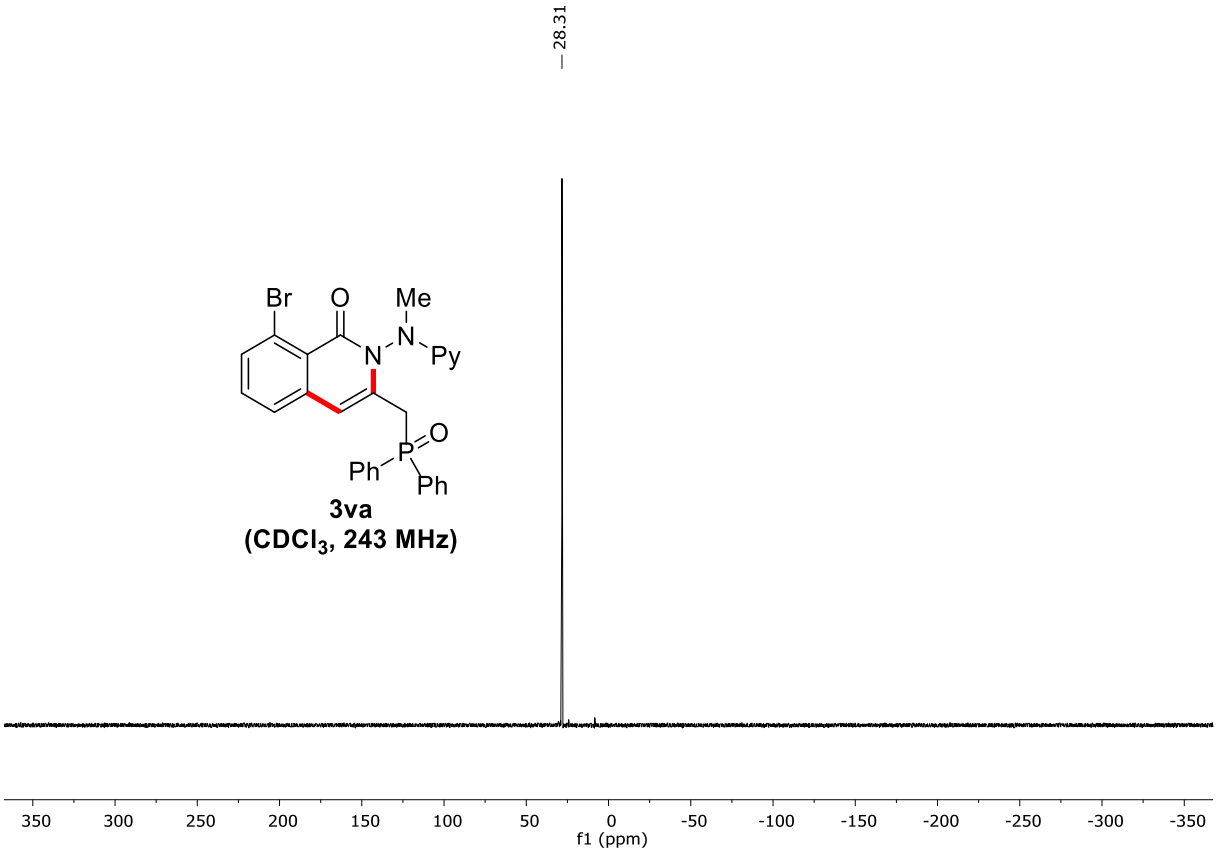


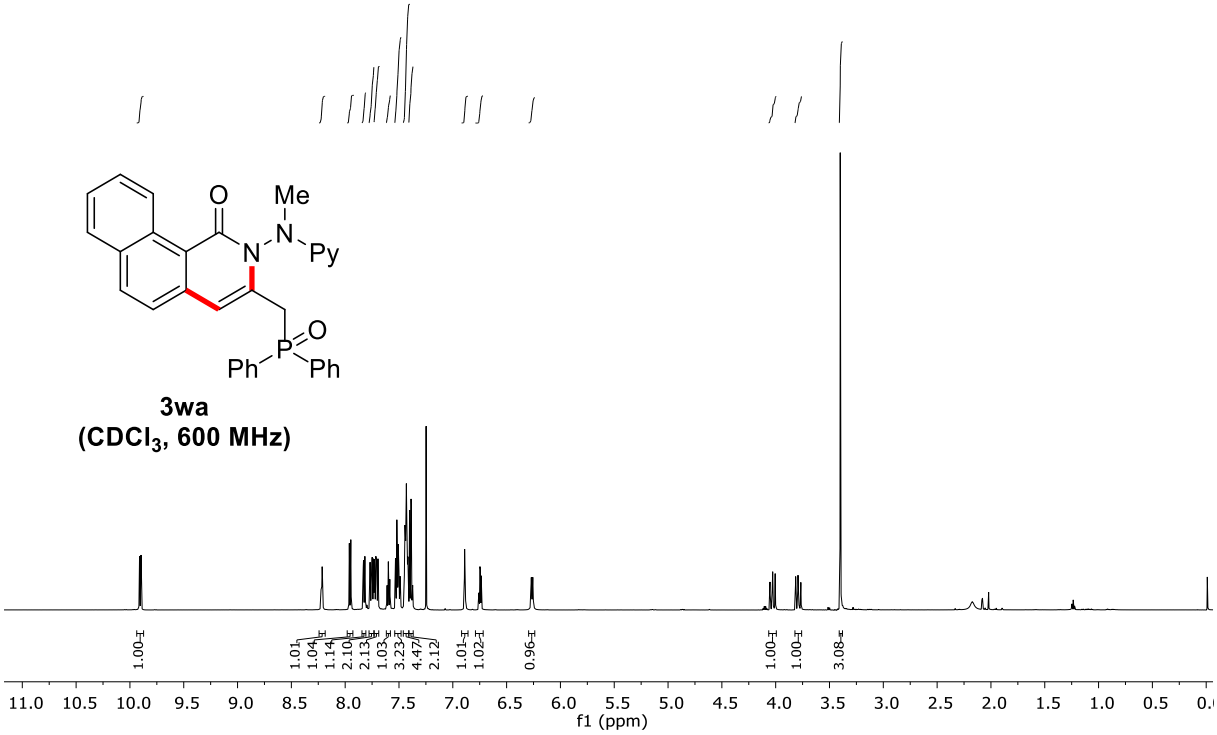
3ua
($CDCl_3$, 243 MHz)



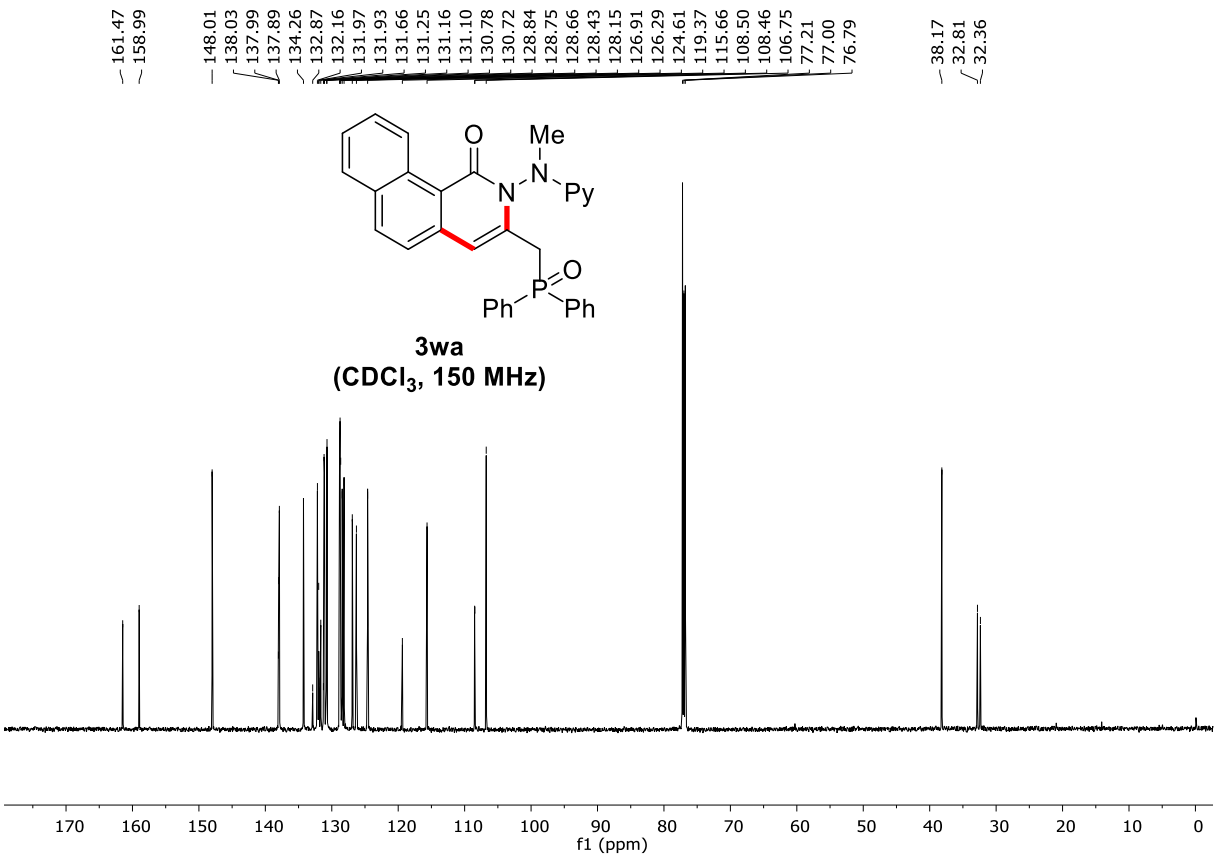
3va
($CDCl_3$, 600 MHz)


159.44
158.66
148.02
139.11
137.93
137.67
137.64
133.40
132.87
132.62
132.20
132.18
132.03
131.36
131.11
131.05
130.75
130.68
128.86
128.78
128.70
126.08
123.29
122.99
115.79
107.54
107.50
106.74
77.21
77.00
76.79
38.15
32.66
32.22
Br
O
Me
N
N
Py
O
P
Ph
Ph
3va
(CDCl3, 150 MHz)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

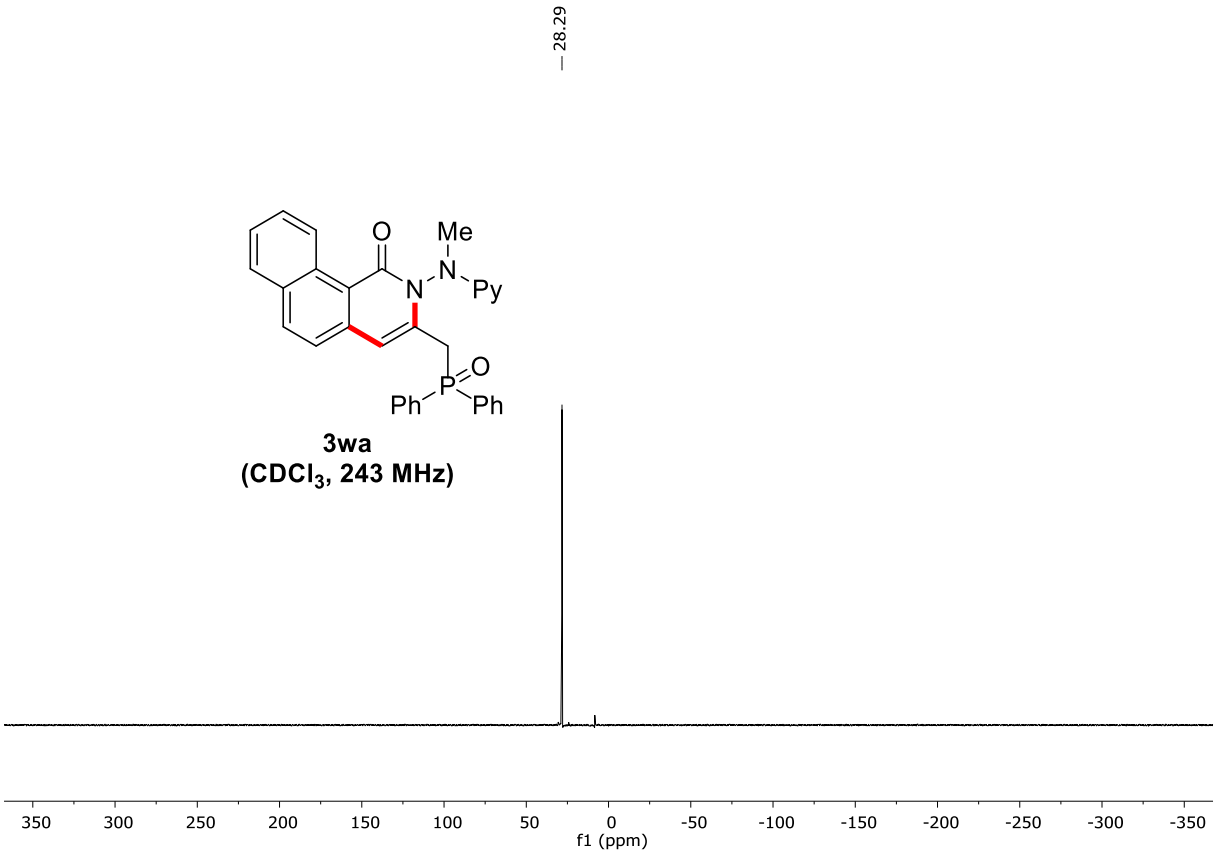

28.31
Br
O
Me
N
N
Py
O
P
Ph
Ph
3va
(CDCl3, 243 MHz)
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)



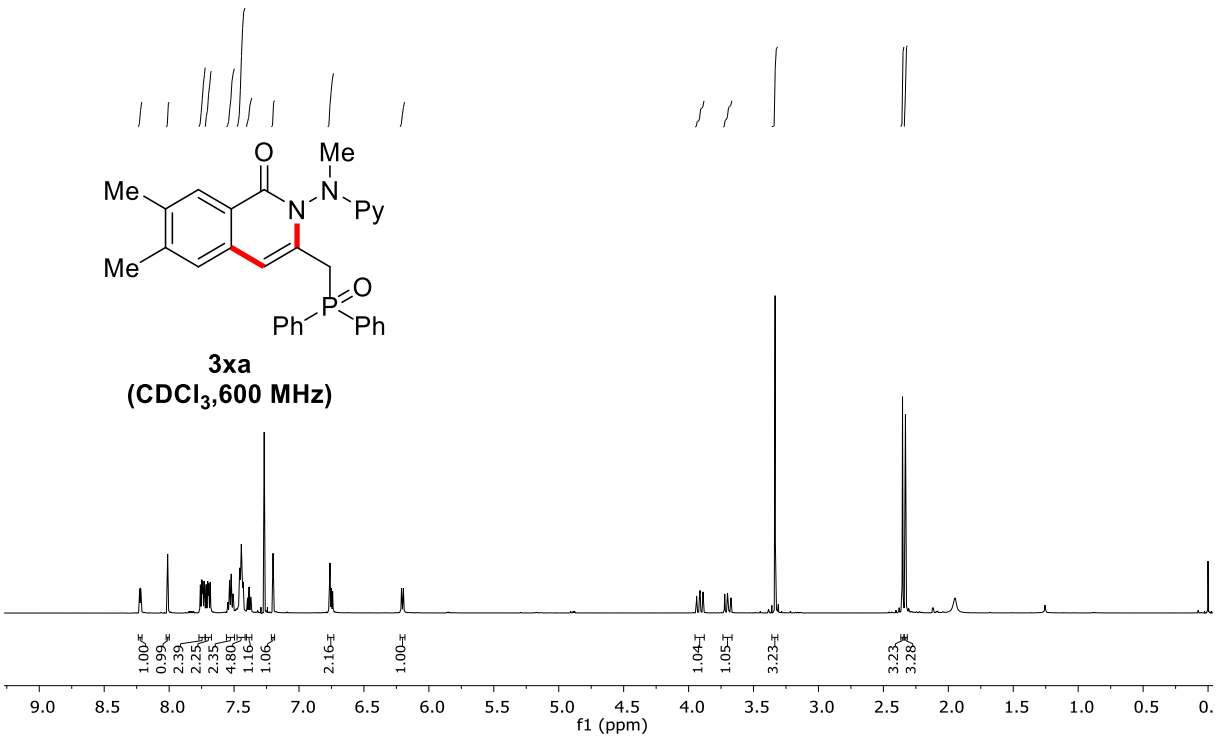
3wa
($CDCl_3$, 600 MHz)



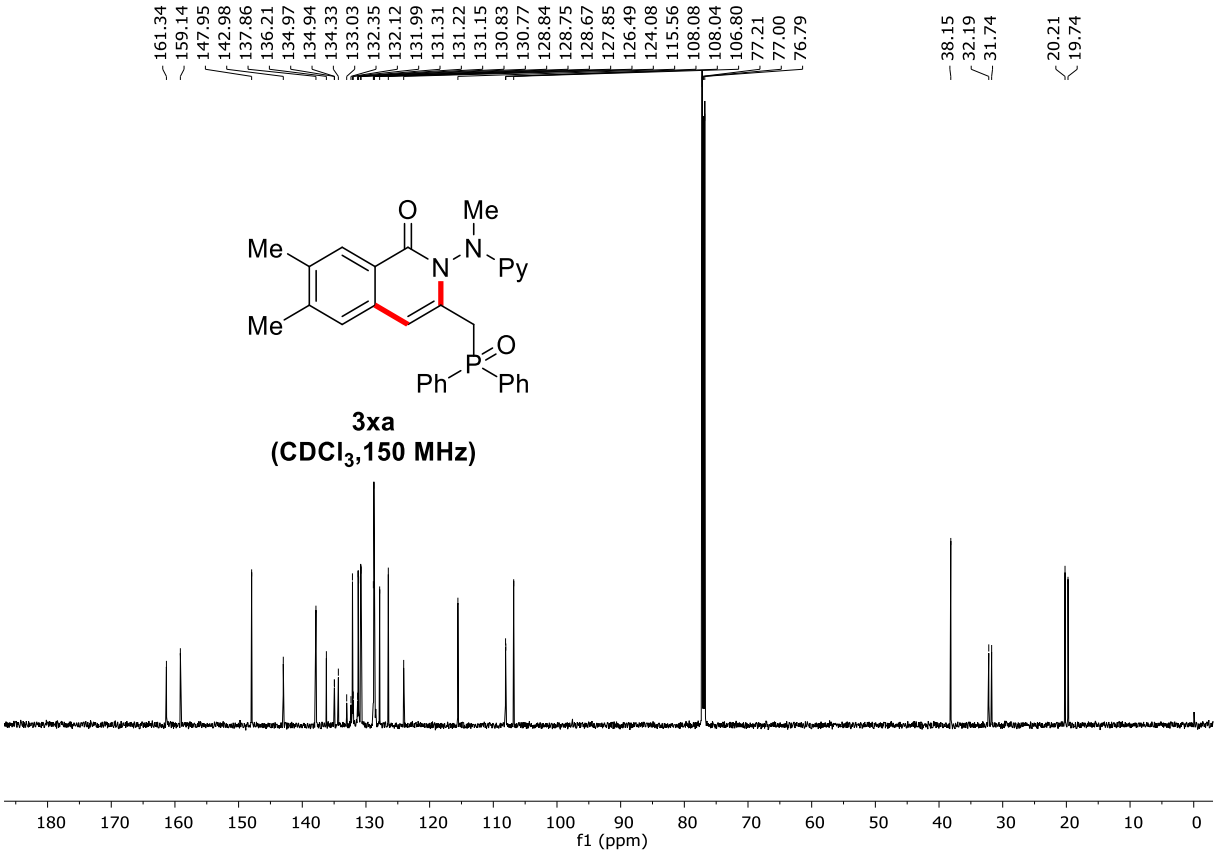
3wa
($CDCl_3$, 150 MHz)



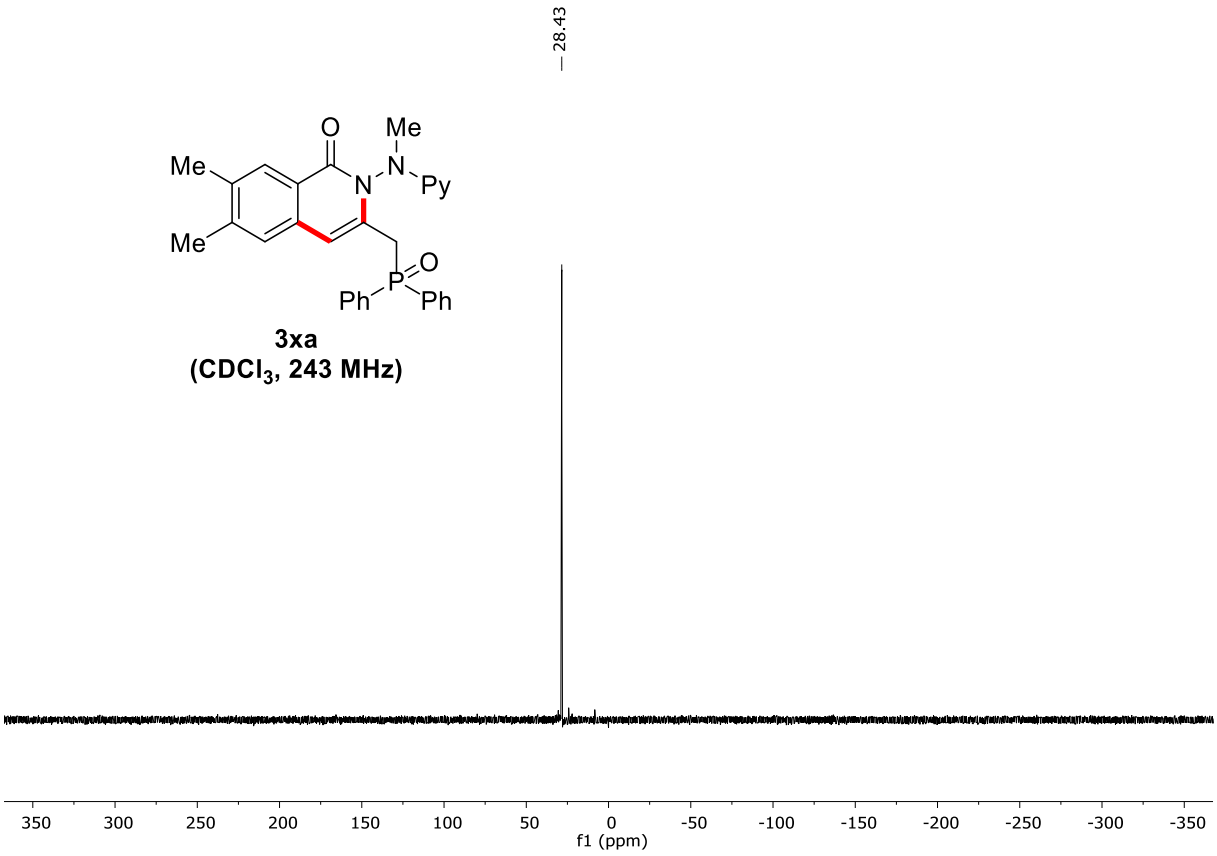
3wa
($CDCl_3$, 243 MHz)



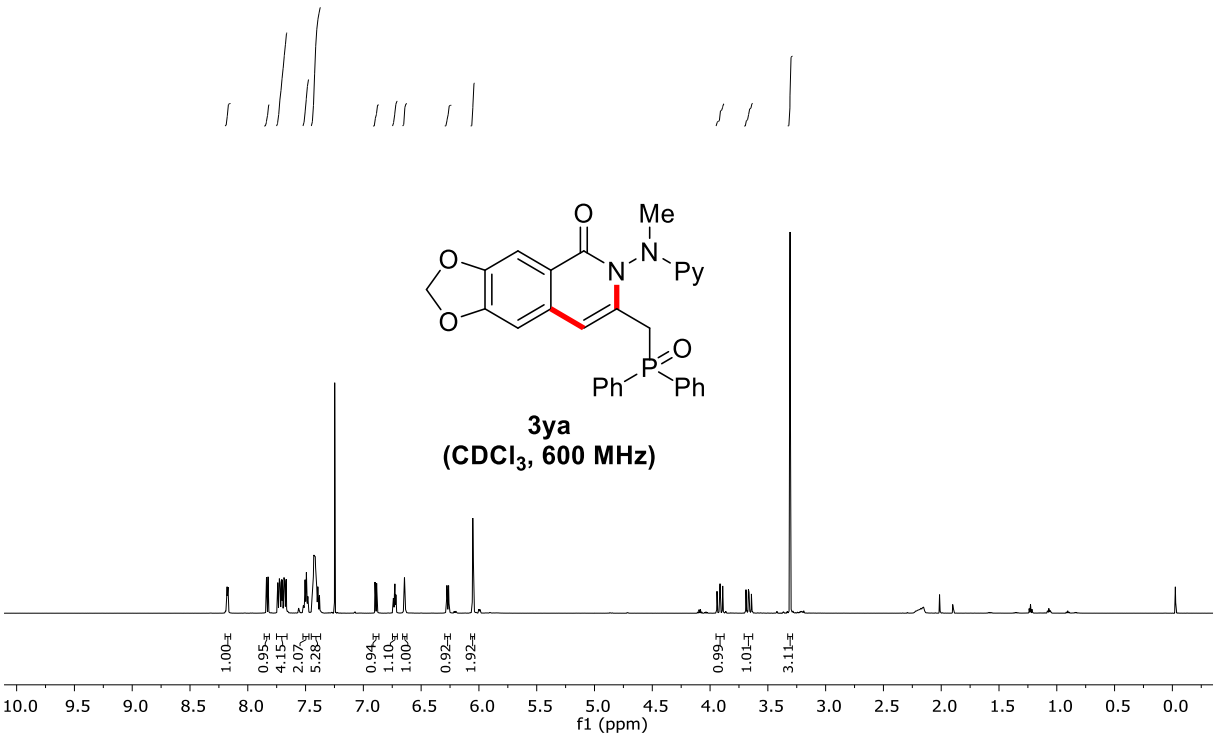
3xa
($CDCl_3$,600 MHz)



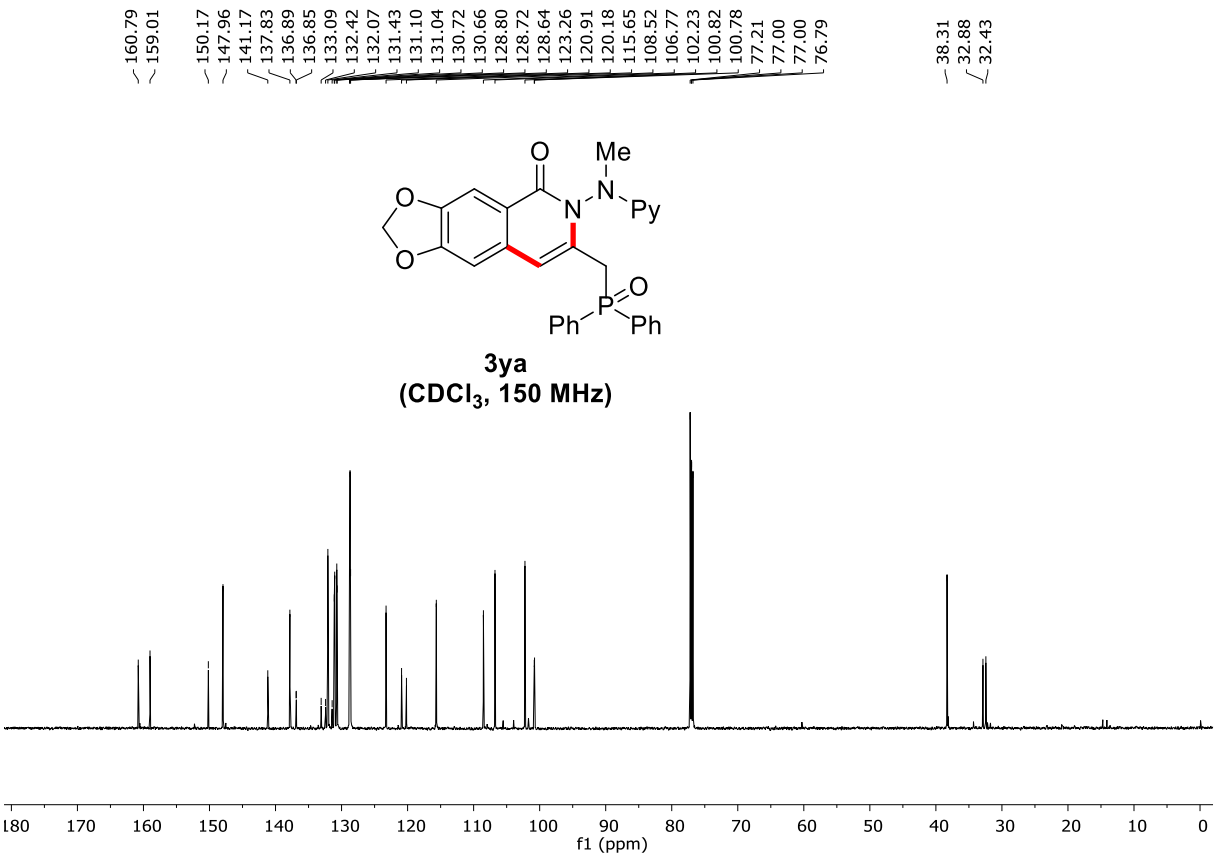
3xa
($CDCl_3$,150 MHz)



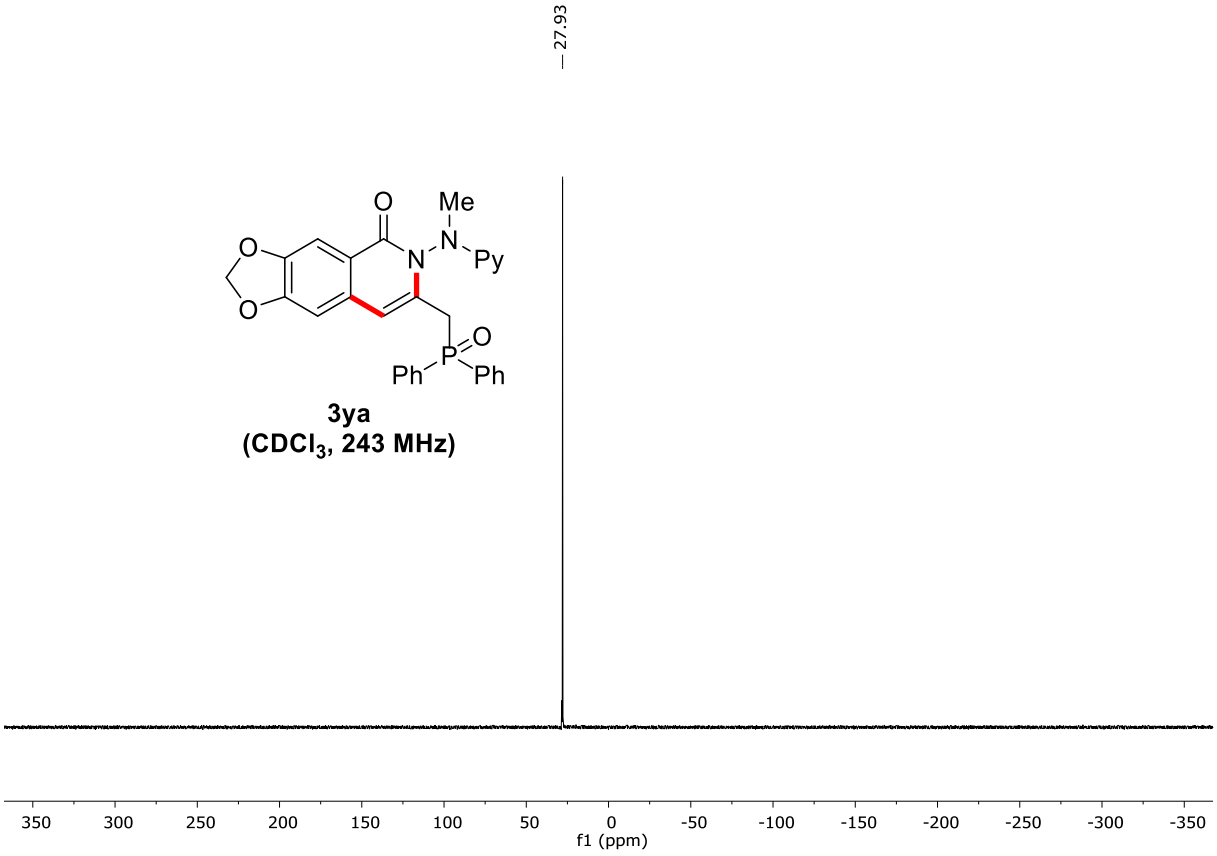
3xa
($CDCl_3$, 243 MHz)



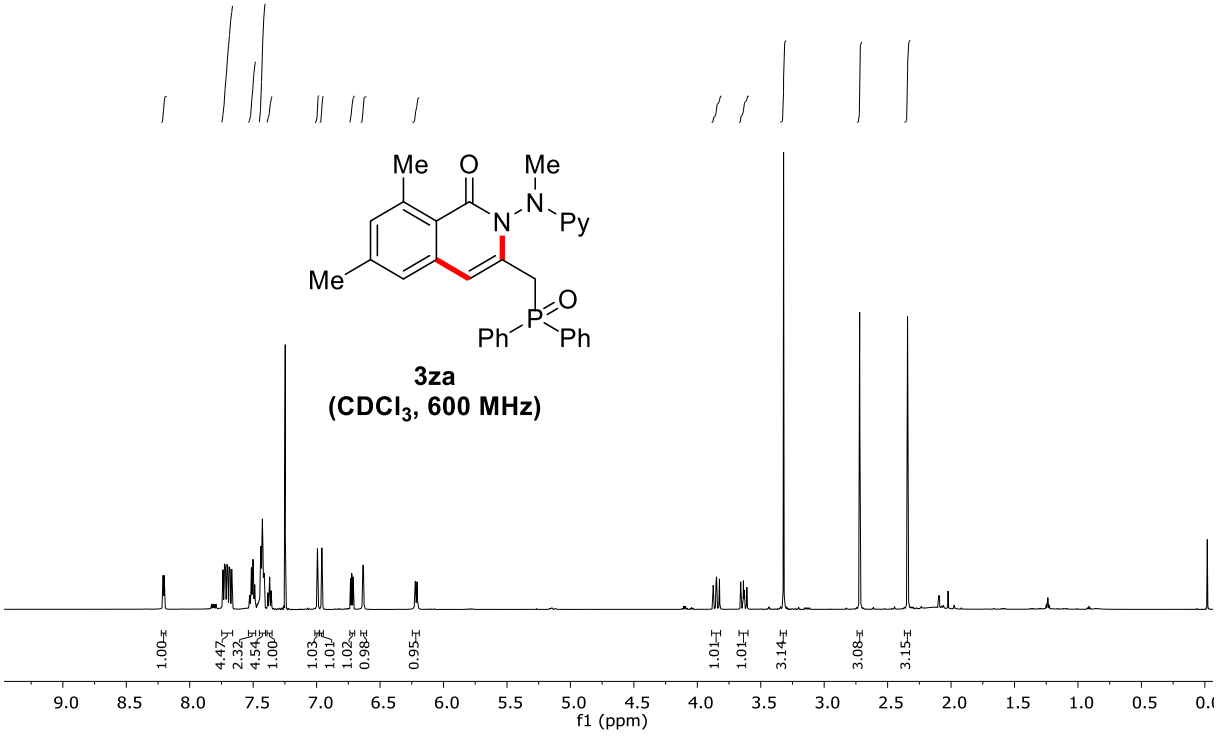
3ya
($CDCl_3$, 600 MHz)



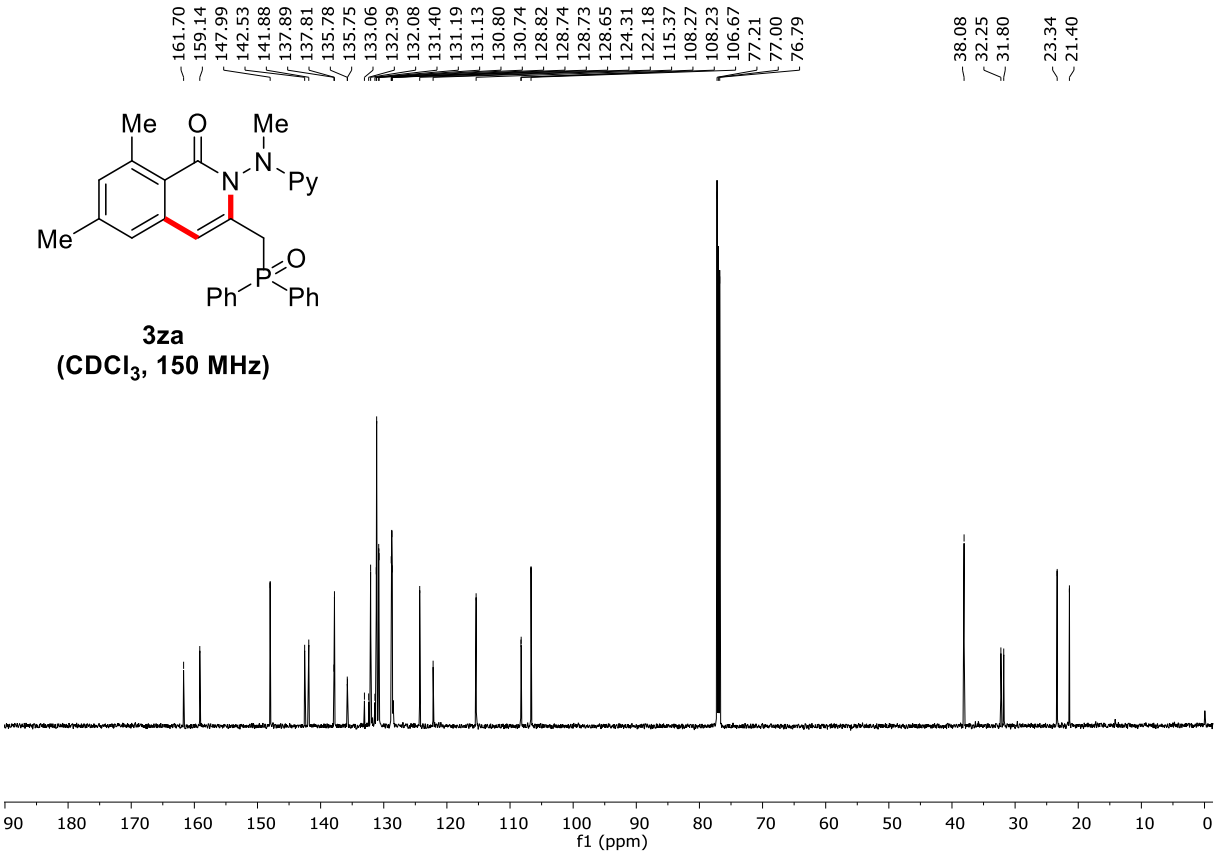
3ya
($CDCl_3$, 150 MHz)



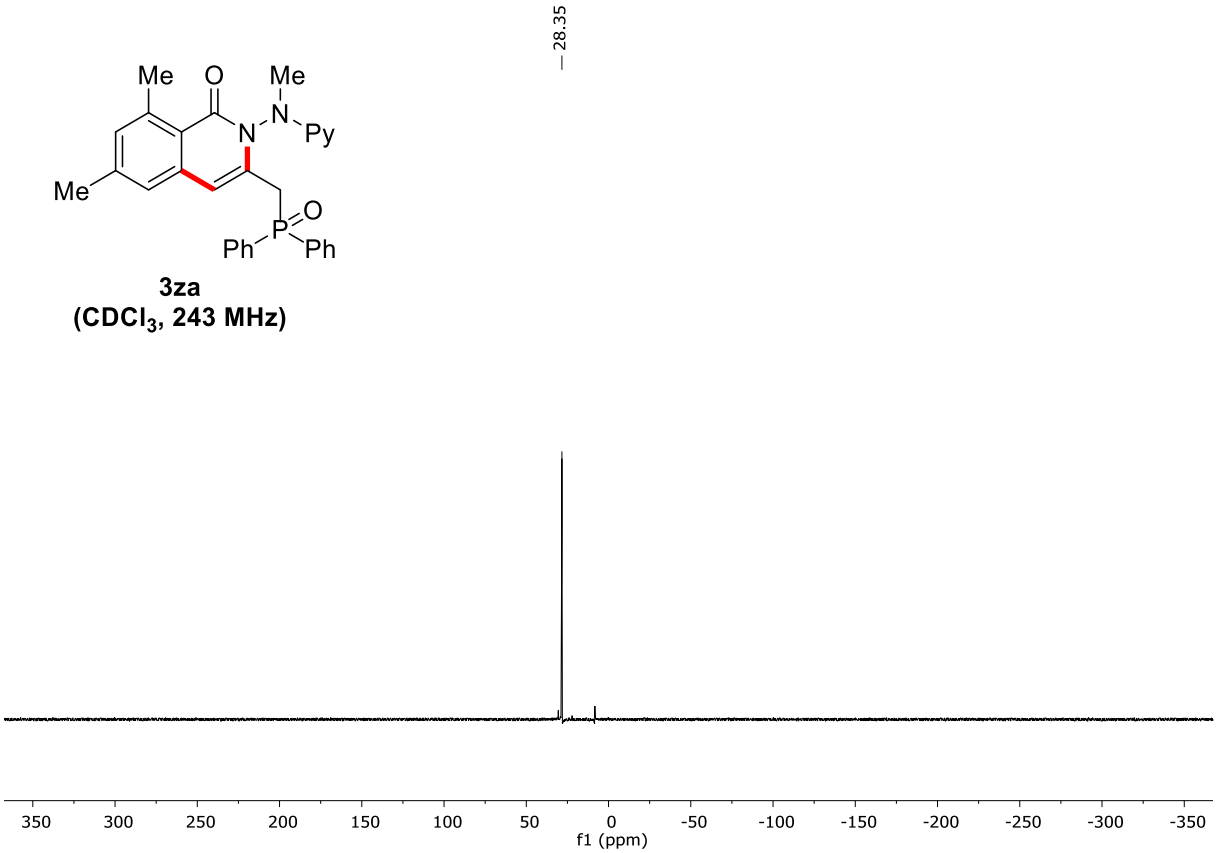
3ya
($CDCl_3$, 243 MHz)



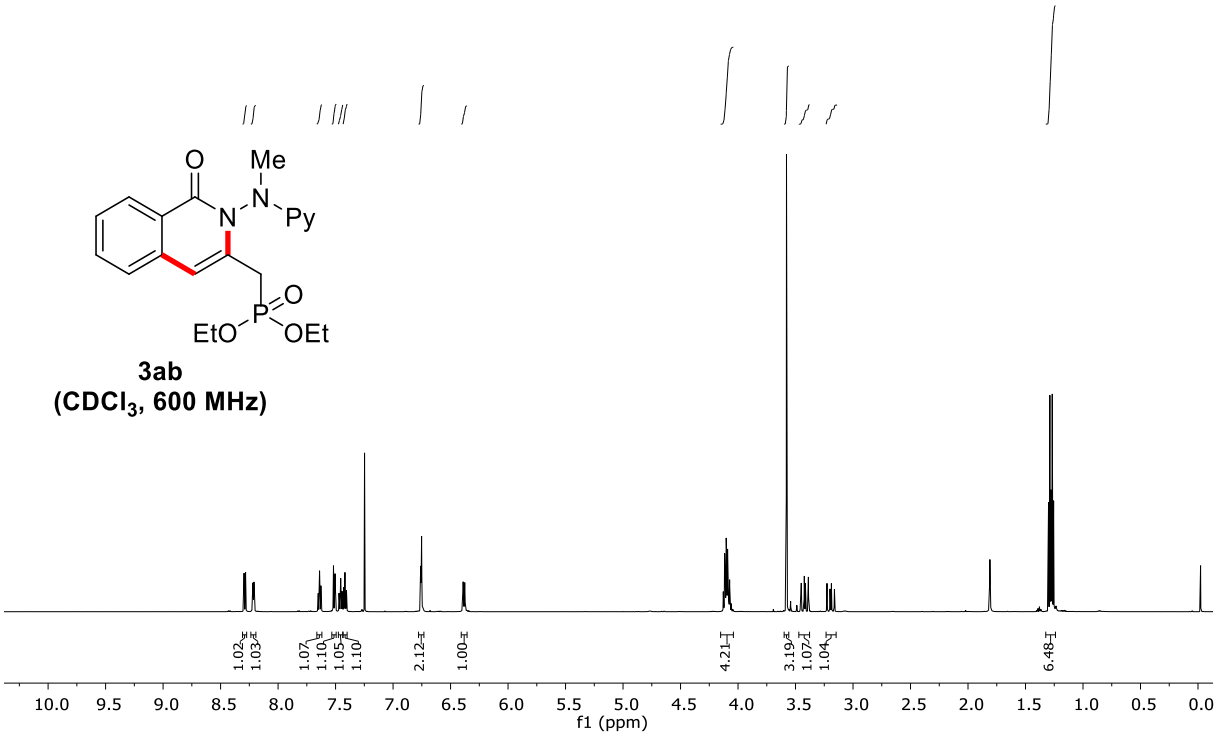
3za
($CDCl_3$, 600 MHz)



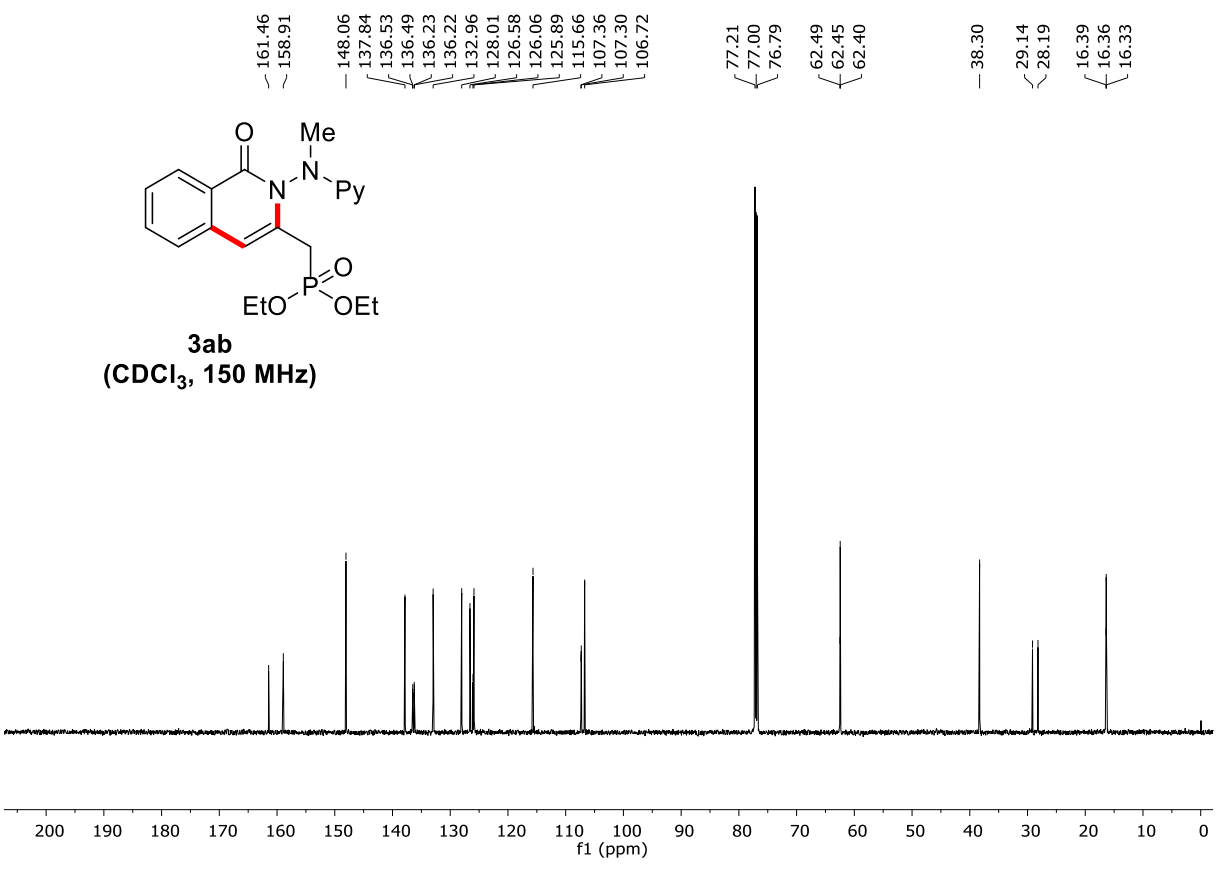
3za
($CDCl_3$, 150 MHz)



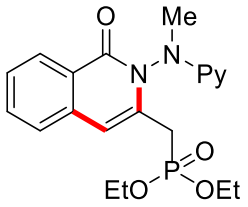
3za
($CDCl_3$, 243 MHz)



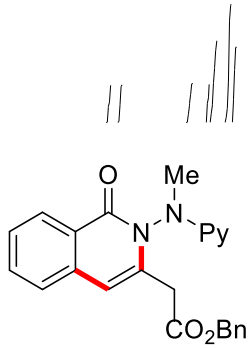
3ab
($CDCl_3$, 600 MHz)



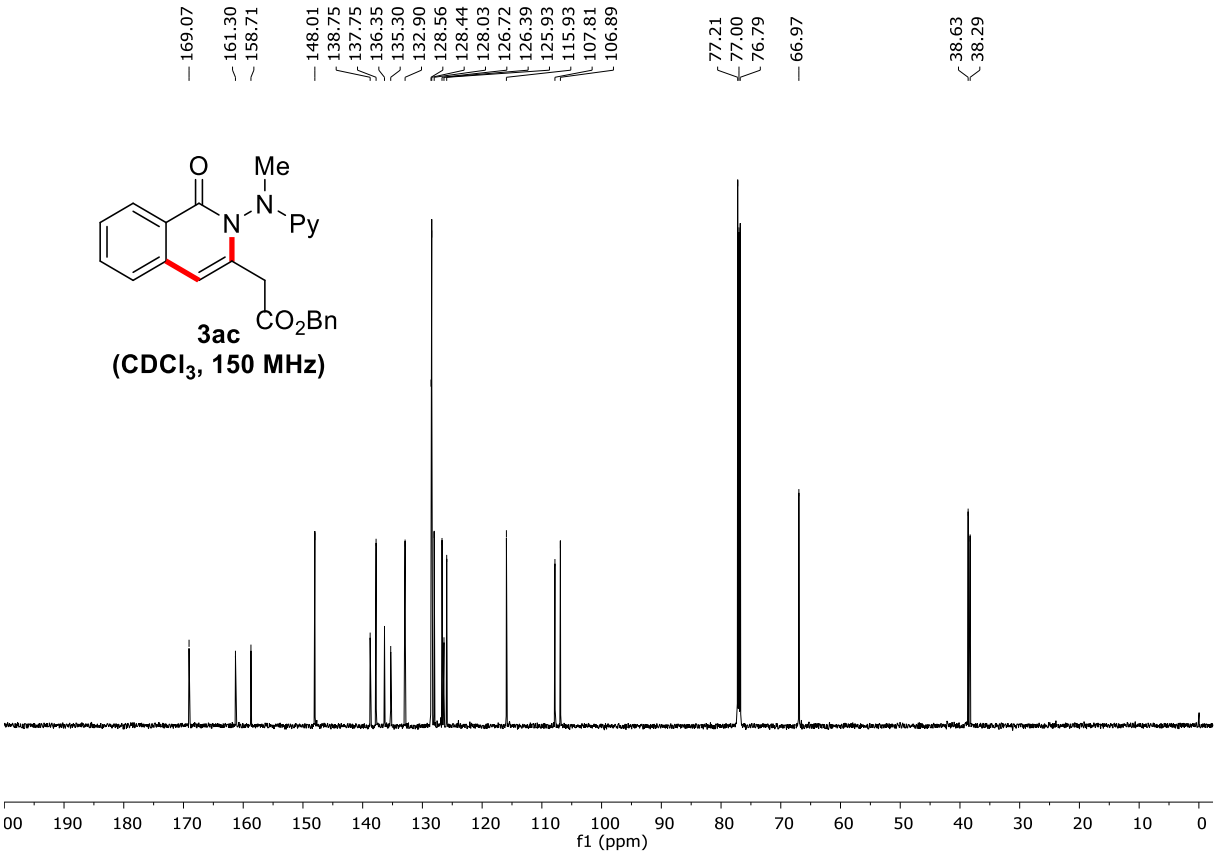
3ab
($CDCl_3$, 150 MHz)

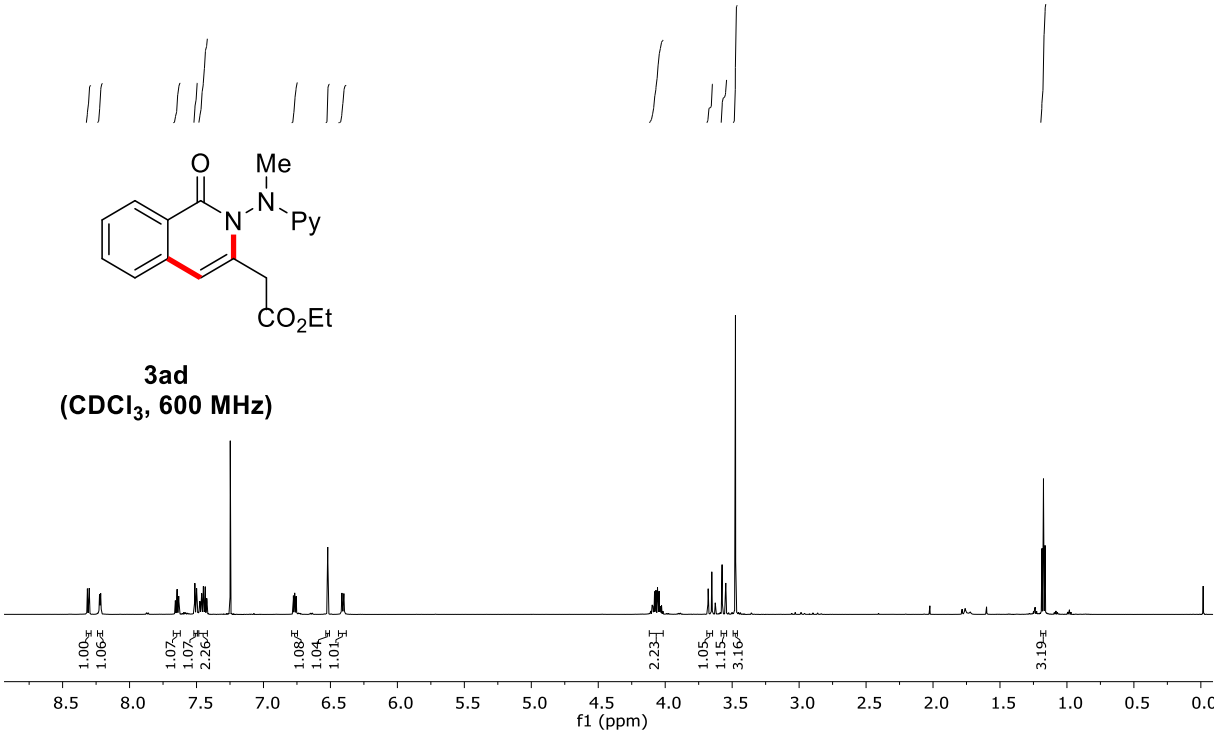


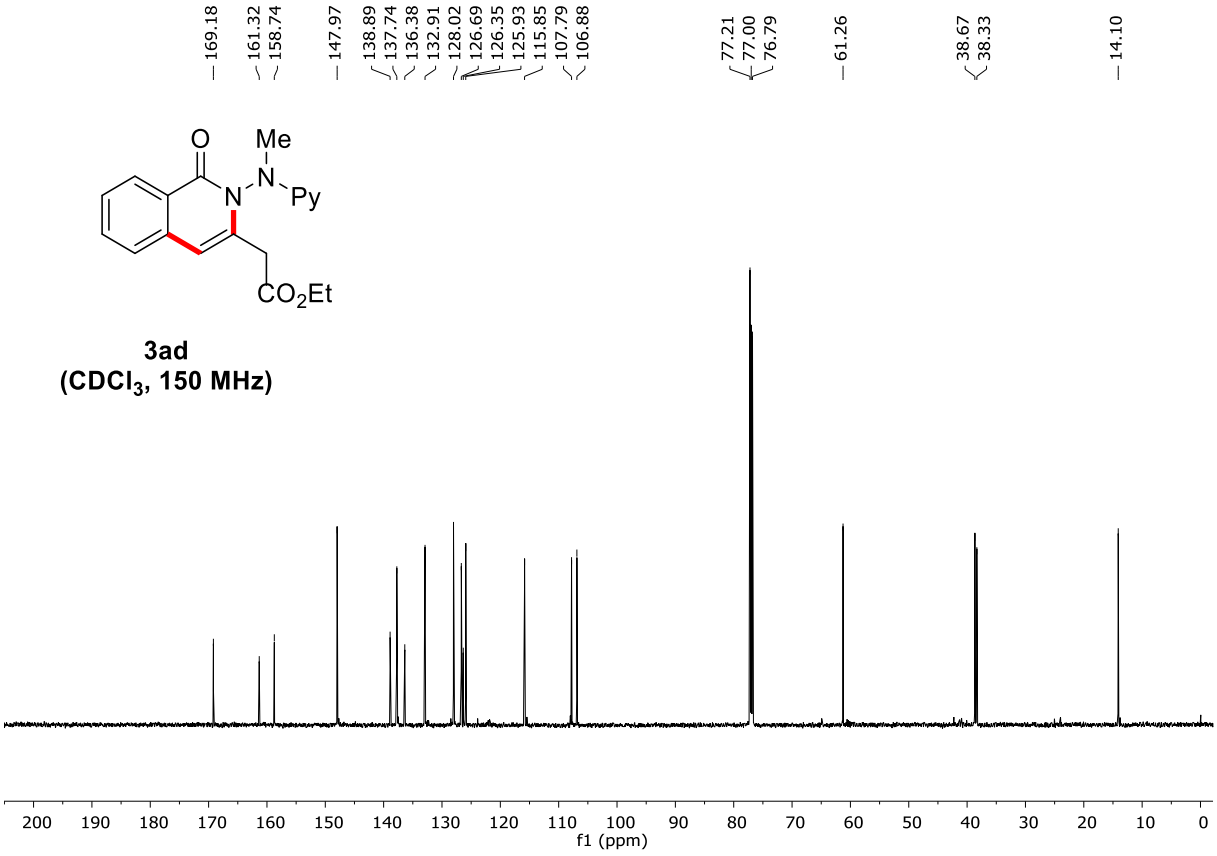
3ab
($CDCl_3$, 243 MHz)



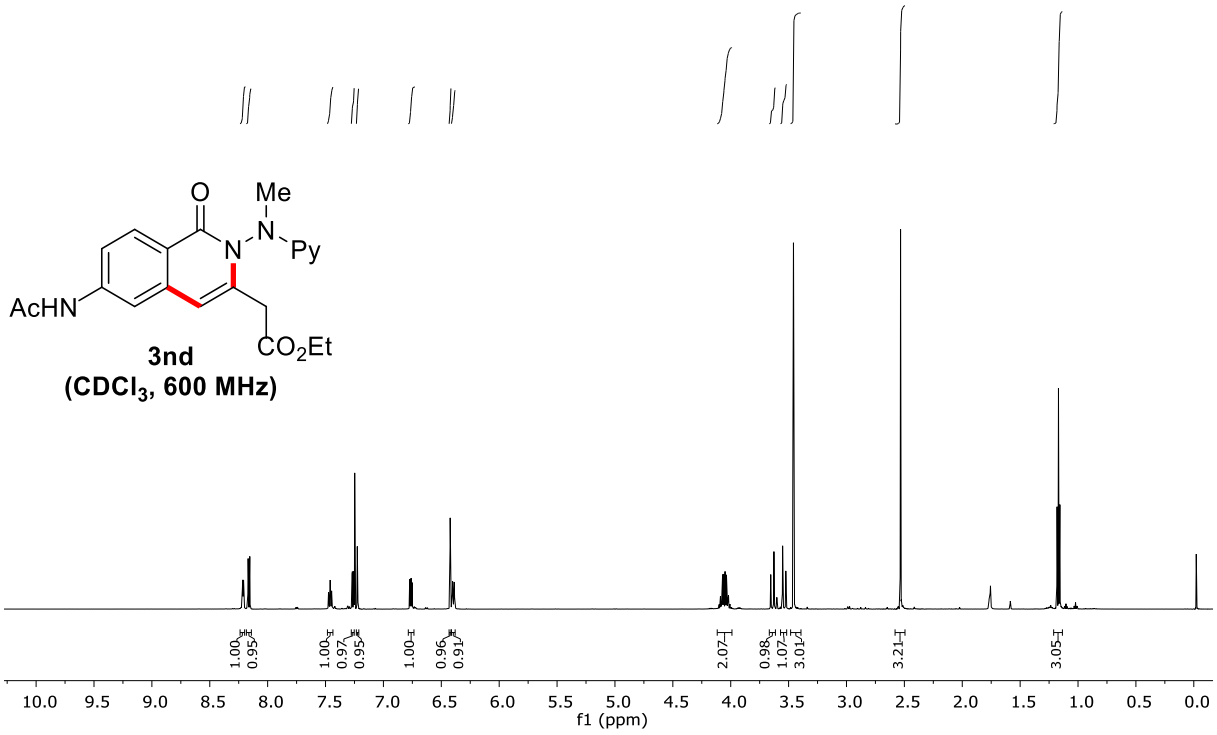
3ac
($CDCl_3$, 600 MHz)


169.07
161.30
158.71
148.01
138.75
137.75
136.35
135.30
132.90
128.56
128.44
128.03
126.72
126.39
125.93
115.93
107.81
106.89
77.21
77.00
76.79
66.97
38.63
38.29
O
Me
N
N
Py
CO2Bn
3ac
(CDCl3, 150 MHz)
f1 (ppm)

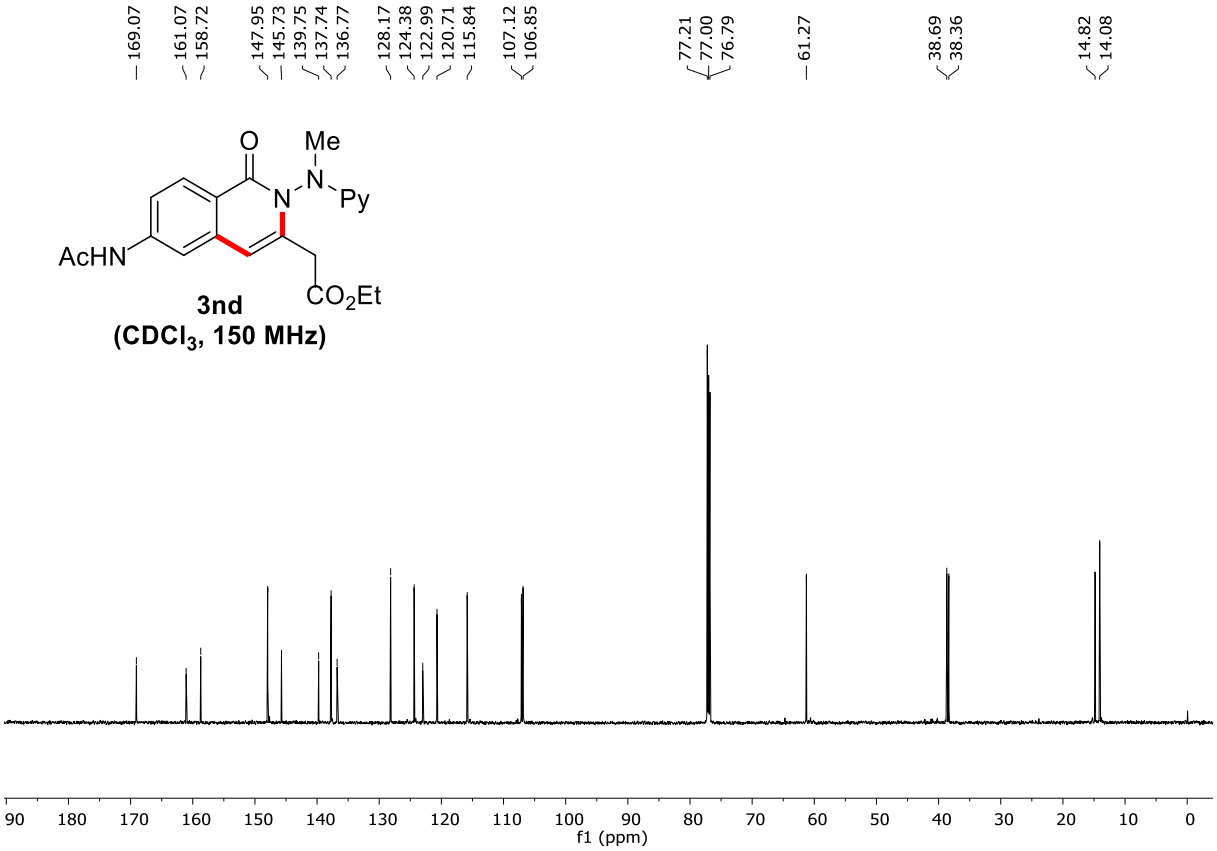

O
Me
N
N
Py
CO2Et
3ad
(CDCl3, 600 MHz)
1.00
1.06
1.07
1.07
2.26
1.08
1.04
1.01
2.23
1.05
1.15
3.16
3.19
f1 (ppm)

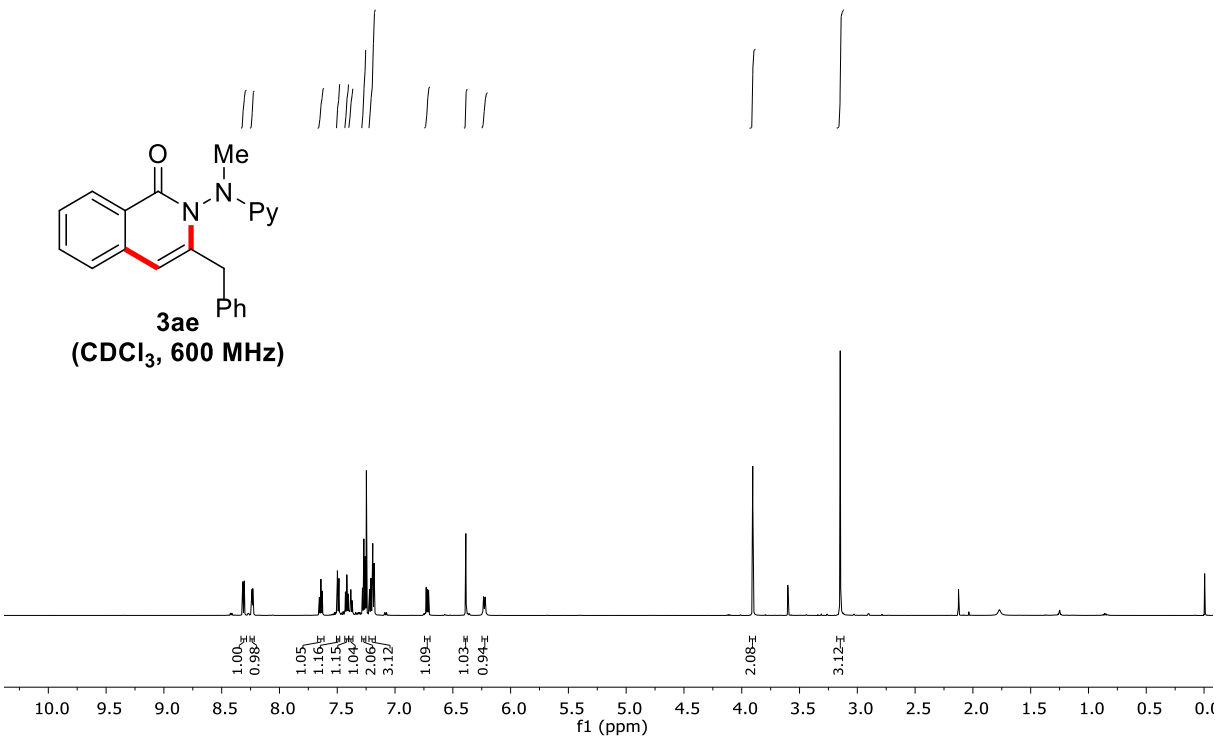


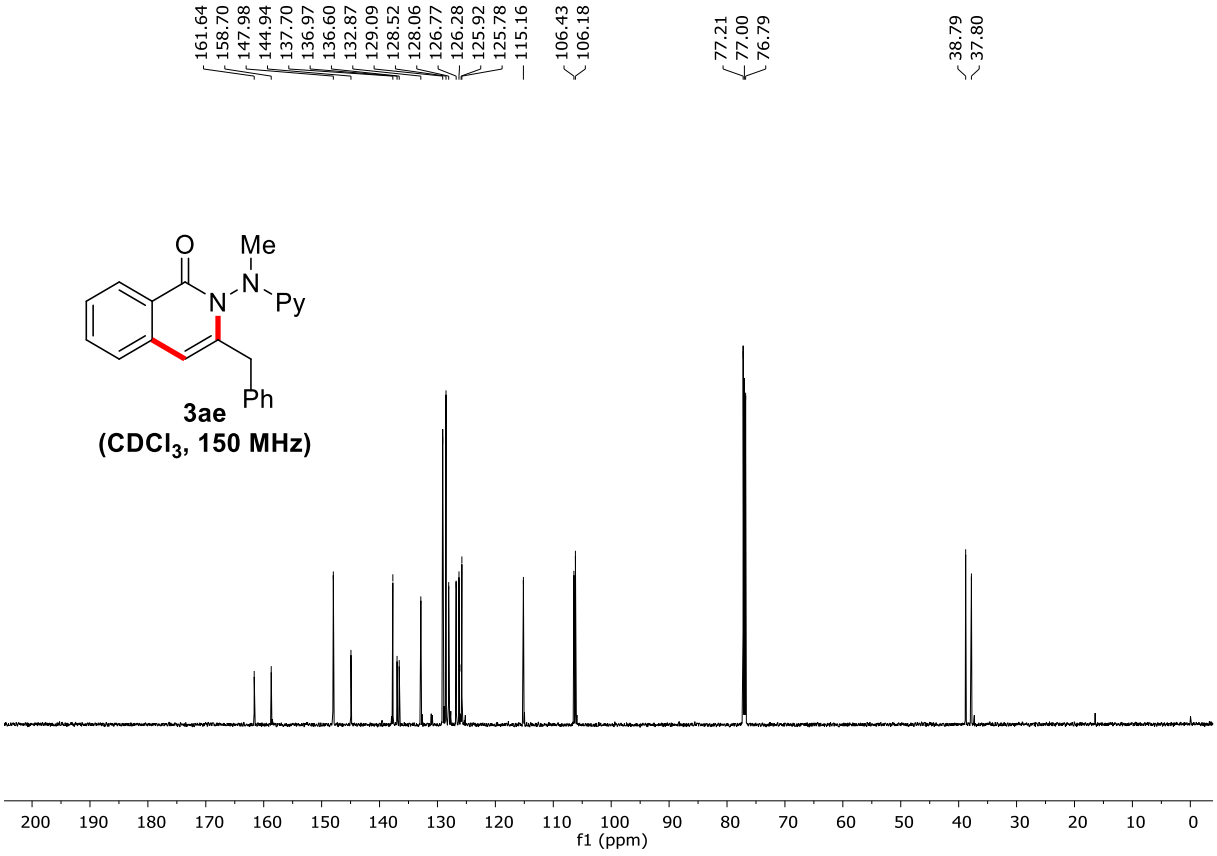
3ad
($CDCl_3$, 150 MHz)

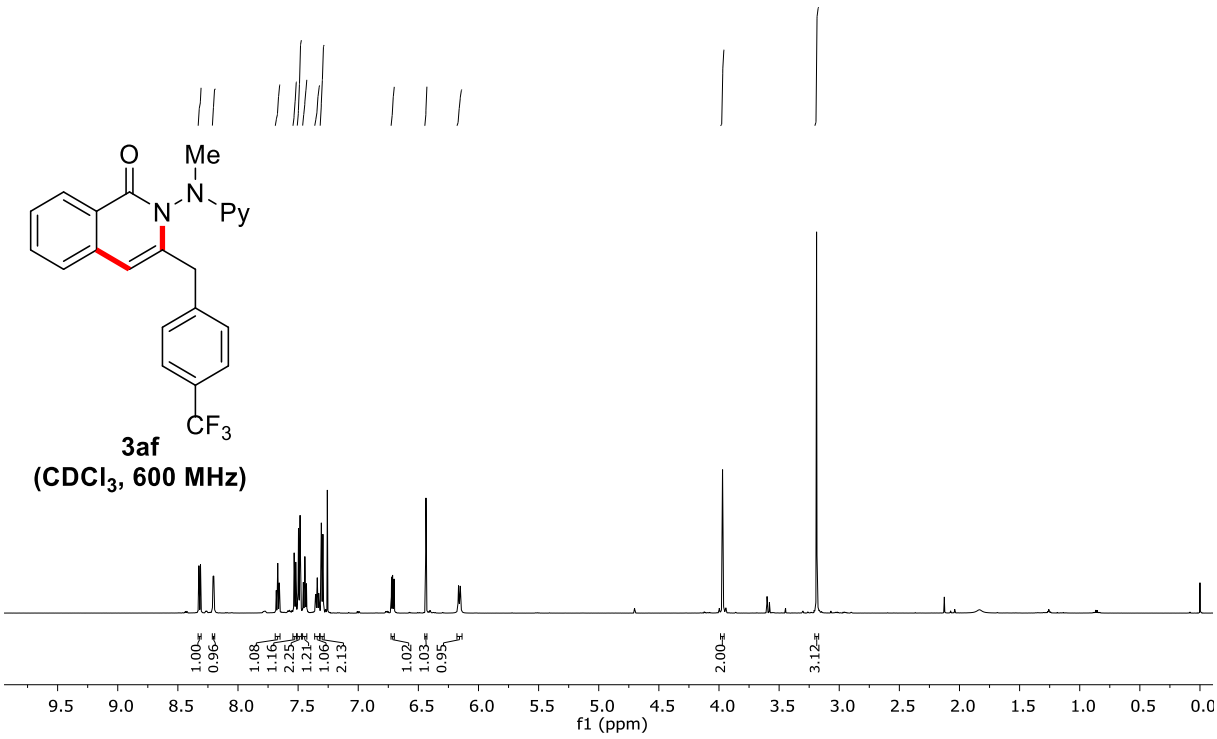


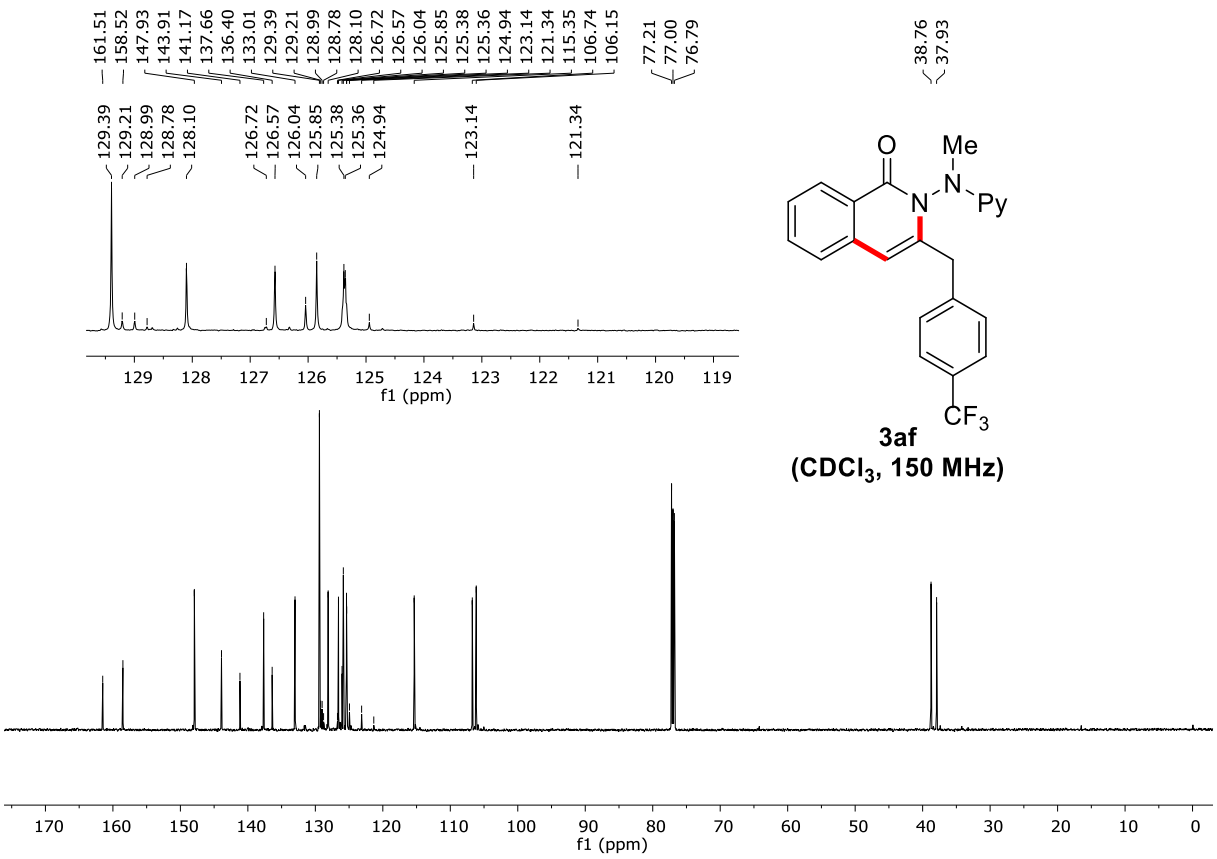
3nd
($CDCl_3$, 600 MHz)

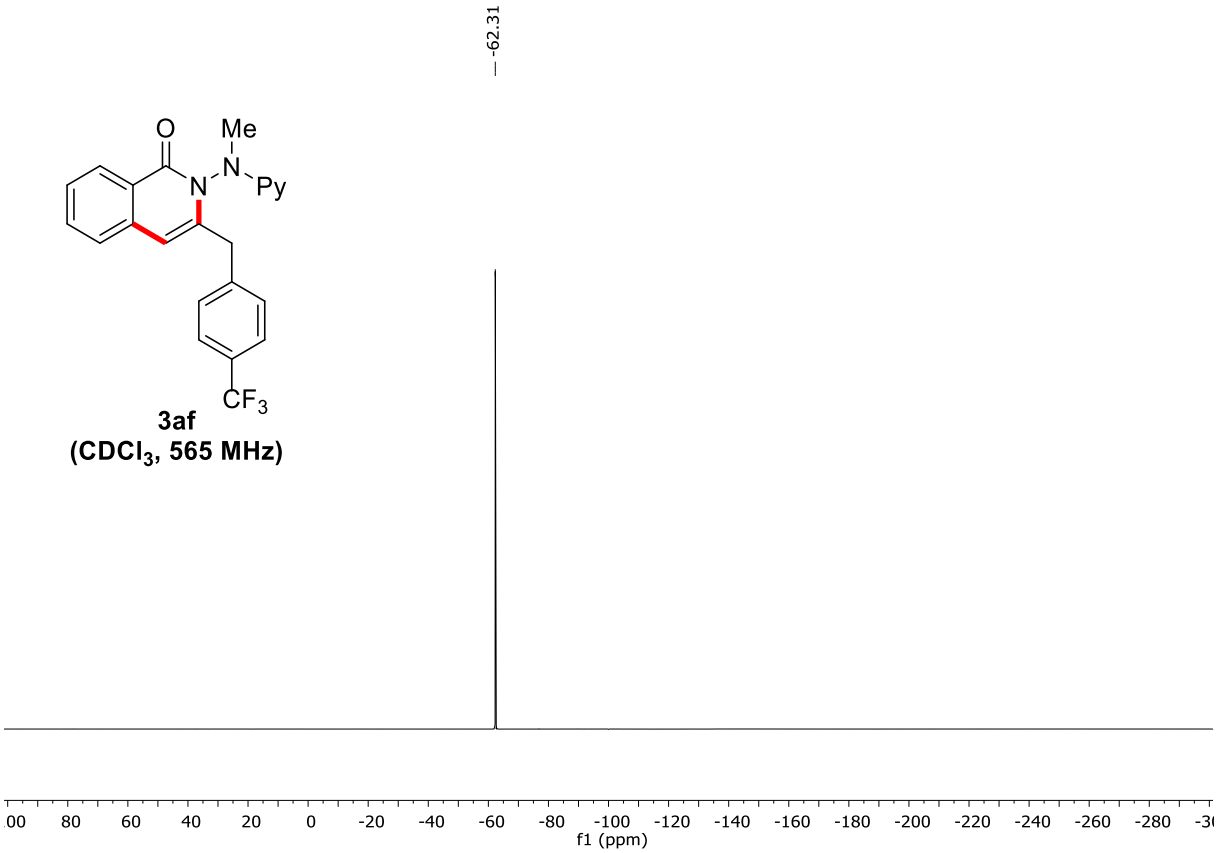

169.07
161.07
158.72
147.95
145.73
139.75
137.74
136.77
128.17
124.38
122.99
120.71
115.84
107.12
106.85
77.21
77.00
76.79
61.27
38.69
38.36
14.82
14.08
O
Me
N
N
Py
AcHN
CO2Et
3nd
(CDCl3, 150 MHz)
f1 (ppm)

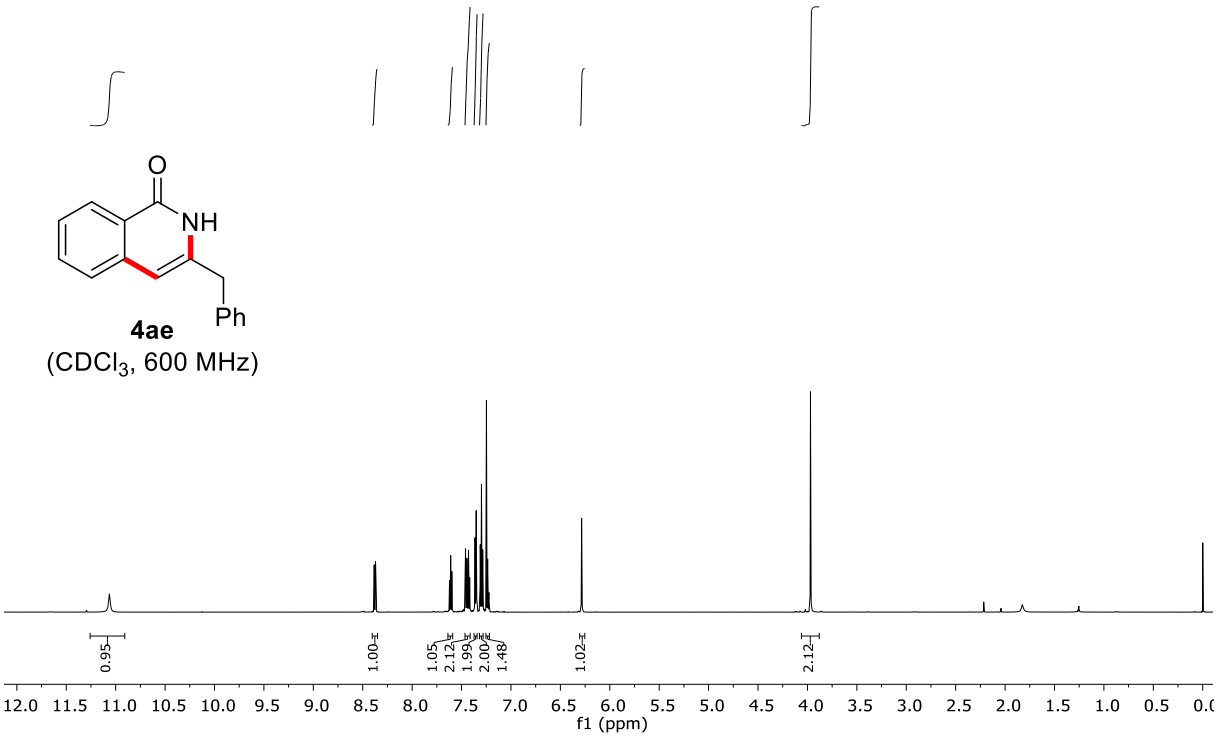

O
Me
N
N
Py
Ph
3ae
(CDCl3, 600 MHz)
1.00
0.98
1.05
1.16
1.15
1.04
2.06
3.12
1.09
1.03
0.94
2.08
3.12
f1 (ppm)


161.64
158.70
147.98
144.94
137.70
136.97
136.60
132.87
129.09
128.52
128.06
126.77
126.28
125.92
125.78
115.16
106.43
106.18
77.21
77.00
76.79
38.79
37.80
O
Me
N
N
Py
Ph
3ae
(CDCl3, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
Me
N
N
Py
CF3
3af
(CDCl3, 600 MHz)
1.00
0.96
1.08
1.16
2.25
1.21
1.06
2.13
1.02
1.03
0.95
2.00
3.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

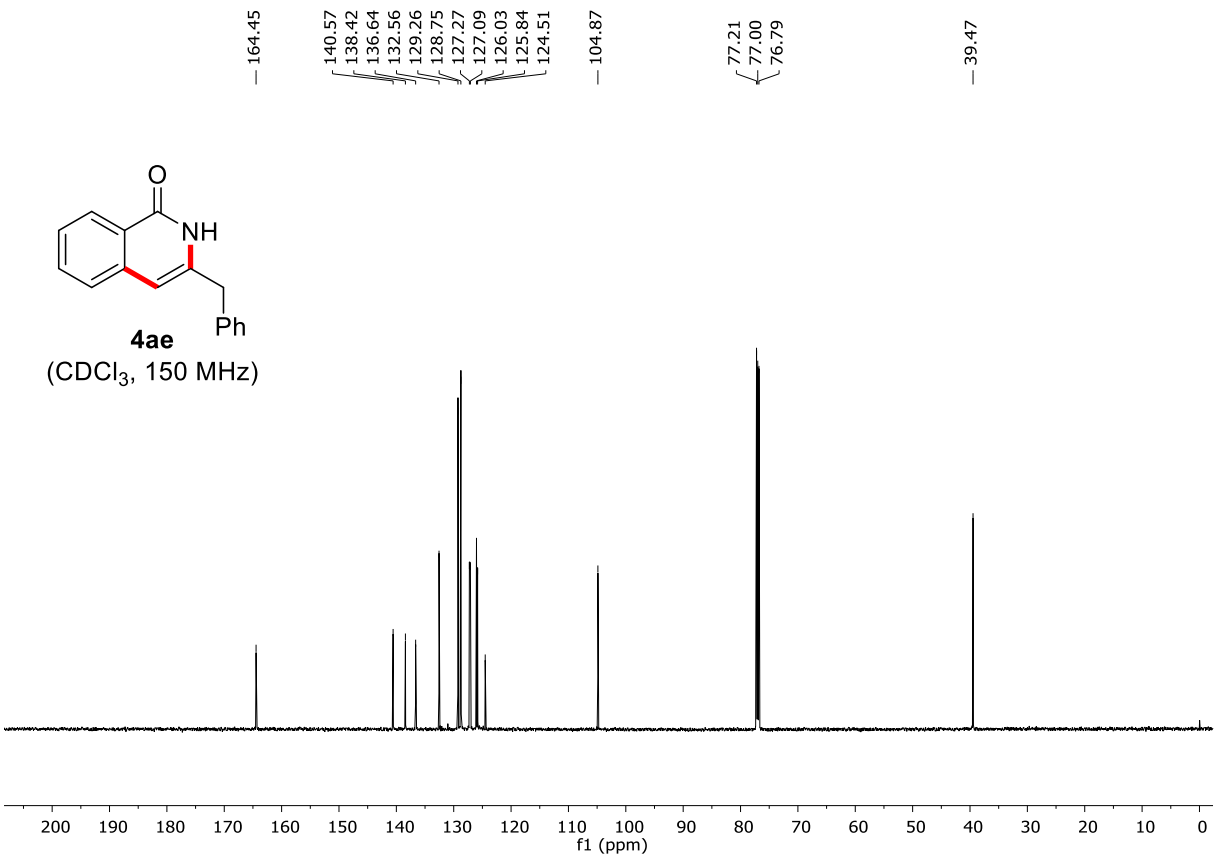

161.51
158.52
147.93
143.91
141.17
137.66
136.40
133.01
129.39
129.21
128.99
128.78
128.10
126.72
126.57
126.04
125.85
125.38
125.36
124.94
123.14
121.34
115.35
106.74
106.15
77.21
77.00
76.79
38.76
37.93
f1 (ppm)
O
Me
N
N
Py
CF3
3af
(CDCl3, 150 MHz)


-62.31
f1 (ppm)
O
Me
N
N
Py
CF3
3af
(CDCl3, 565 MHz)



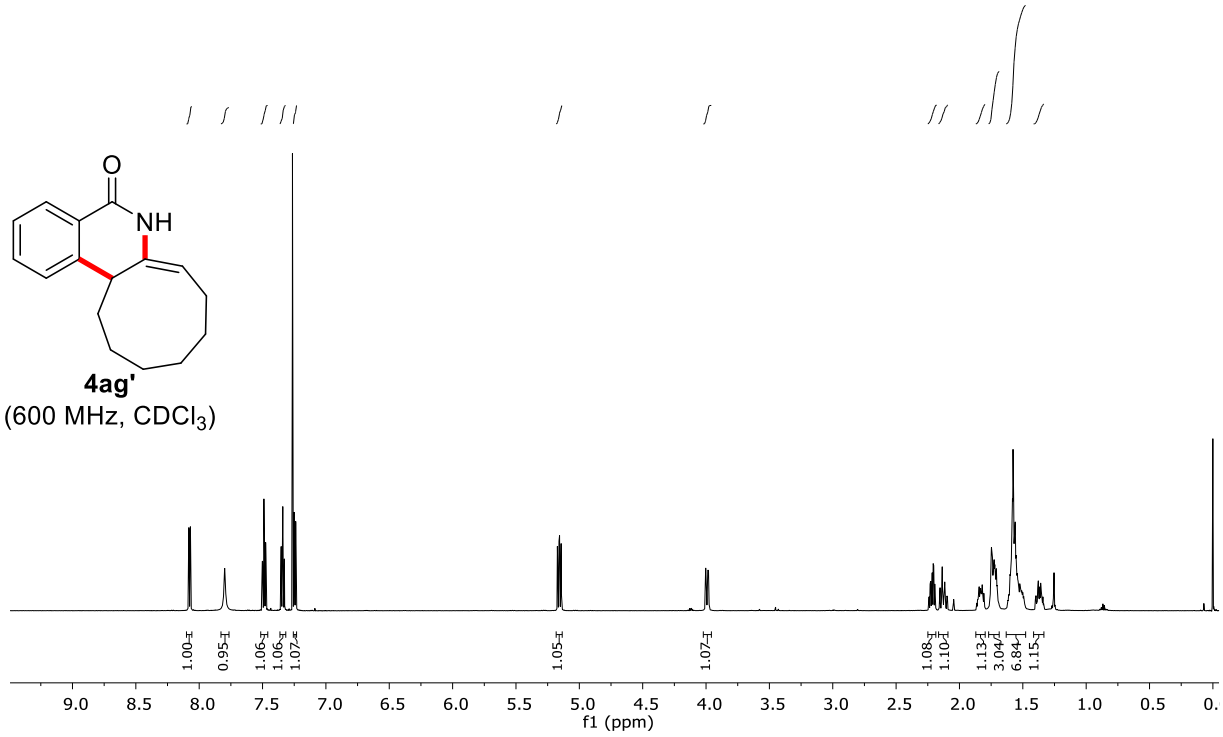
4ae

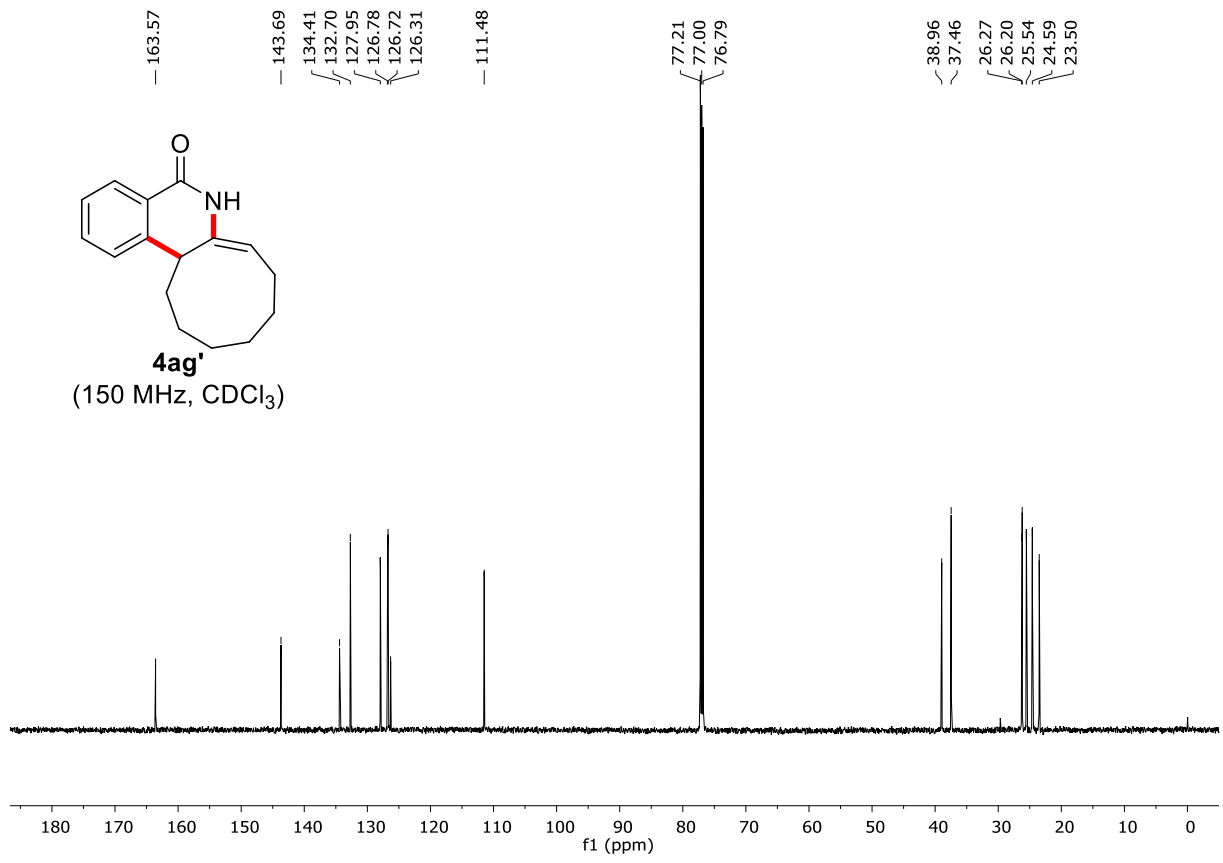
($CDCl_3$, 600 MHz)

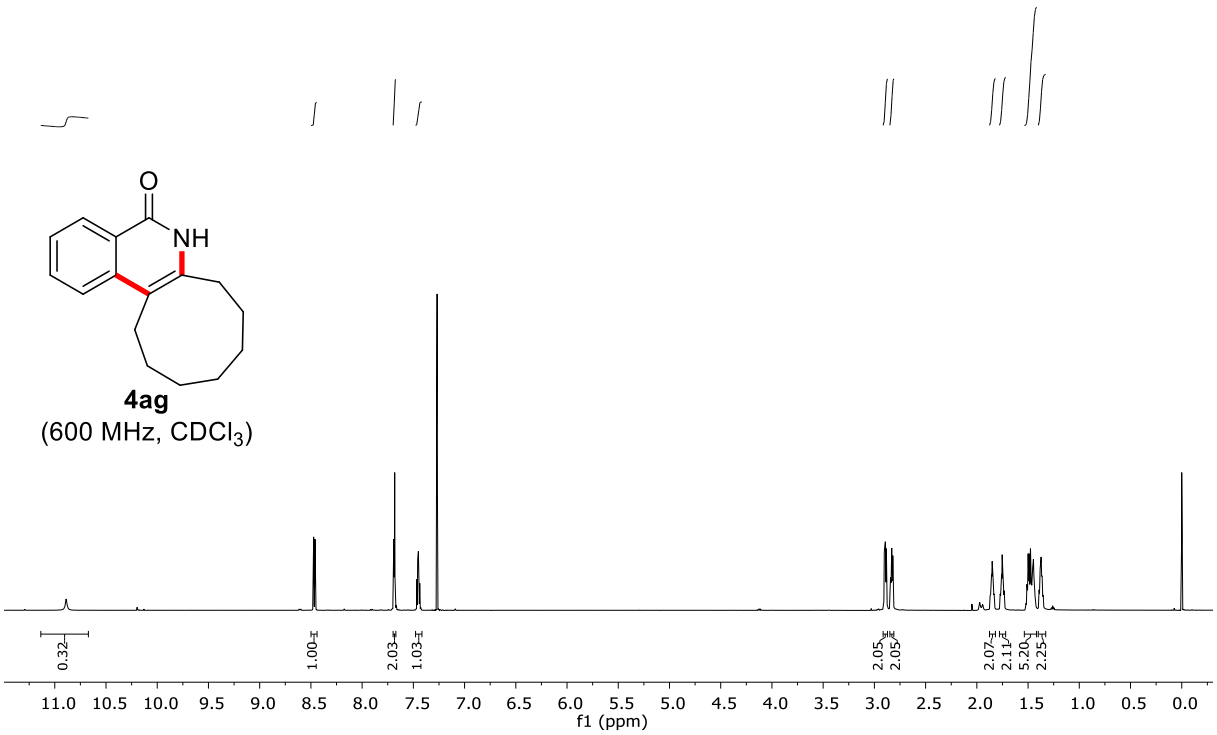


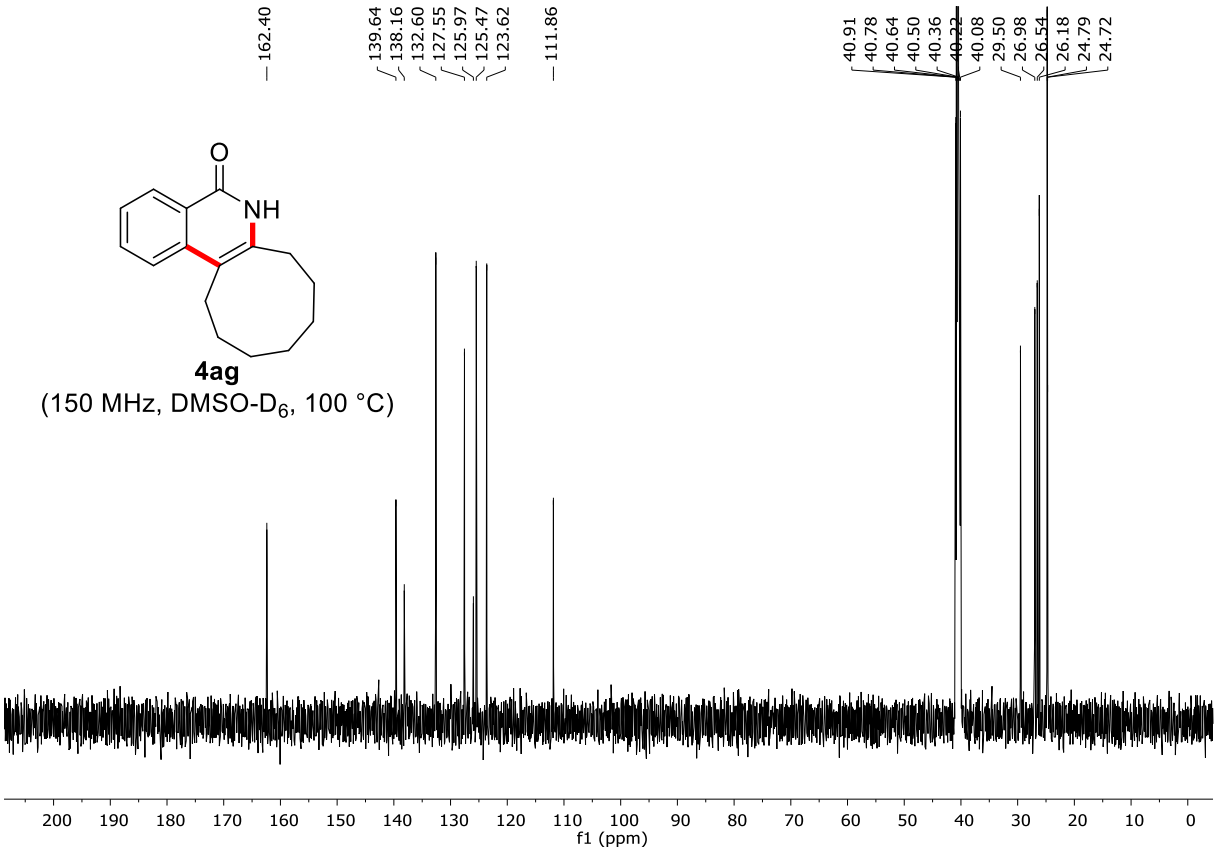
4ae

($CDCl_3$, 150 MHz)


O
NH
4ag'
(600 MHz, CDCl3)
1.00
0.95
1.06
1.06
1.07
1.05
1.07
1.08
1.10
1.13
3.04
6.84
1.15
f1 (ppm)


163.57
143.69
134.41
132.70
127.95
126.78
126.72
126.31
111.48
77.21
77.00
76.79
38.96
37.46
26.27
26.20
25.54
24.59
23.50
O
NH
4ag'
(150 MHz, CDCl3)
f1 (ppm)


O
NH
4ag
(600 MHz, CDCl3)
0.32
1.00
2.03
1.03
2.05
2.05
2.07
2.11
5.20
2.25
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.40
139.64
138.16
132.60
127.55
125.97
125.47
123.62
111.86
40.91
40.78
40.64
40.50
40.36
40.22
40.08
29.50
26.98
26.54
26.18
24.79
24.72
O
NH
4ag
(150 MHz, DMSO-D6, 100 °C)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)