

Electronic Supplementary Information
for

**Copper-Catalyzed Cycloaddition between Hydrogen
Phosphonates and Activated Alkenes: Synthesis of
Phosphonoisoquinolinediones**

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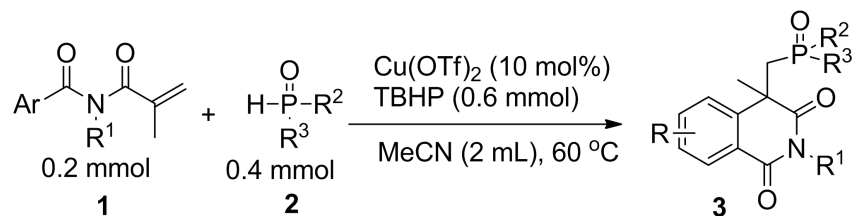
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1. General:

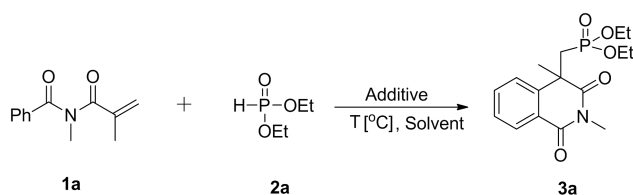
All reactions were carried out under nitrogen atmosphere. All reagents were purchased and used without further purification. All new compounds were further characterized by HRMS (ESI).

2. Experimental procedure for the synthesis of phosphonoisoquinolinediones:



An Schlenk tube containing $\text{Cu}(\text{OTf})_2$ (0.02 mmol, 10%) was evacuated and purged with nitrogen three times. methacryloylbenzamide (**1**, 0.20 mmol), H-phosphonate (**2**, 0.40 mmol), TBHP (0.6 mmol) and CH_3CN (2.0 mL) were sequentially added to the system at room temperature. The reaction mixture was heated with stirring at 60 °C for 24 hours. The reaction solution was concentrated in vacuo and then added 15 mL saturated sodium bicarbonate solution and extracted with EtOAc (3×10 mL). The combined organic layer was dried over MgSO_4 , filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography using petroleum ether–AcOEt (2:1-1:1, v/v) as the eluent to give the corresponding products.

3. Reaction conditions optimization^a

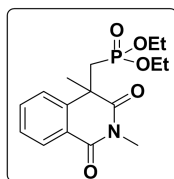


Entry	Additive (equiv)	Solvent	T [°C]	Yield[%]
1	Mn(OAc) ₃ ·2H ₂ O (3)	CH ₃ COOH	60	63
2	Mn(OAc) ₃ ·2H ₂ O (3)	CH ₃ COOH	70	59
3	Mn(OAc) ₃ ·2H ₂ O (3)	CH ₃ COOH	55	65
4	AgNO ₃ (0.05)+Mg(NO ₃) ₂ ·6H ₂ O(0.5)	CH ₃ CN	100	62
5 ^b	AgNO ₃ (0.05)+Mg(NO ₃) ₂ ·6H ₂ O(0.5)	CH ₃ CN	100	66
6	AgNO ₃ (0.05)+Mg(NO ₃) ₂ ·6H ₂ O(0.3)	CH ₃ CN	100	66
7	AgNO ₃ (0.1)+Mg(NO ₃) ₂ ·6H ₂ O(0.5)	CH ₃ CN	100	65
8	AgNO ₃ (0.05)+Mg(NO ₃) ₂ ·6H ₂ O(0.5)	CH ₃ CN	90	61
9	AgNO ₃ (0.05)+Mg(NO ₃) ₂ ·6H ₂ O(0.5)	CH ₃ CN	80	50
10	AgNO ₃ (0.05)+Mg(NO ₃) ₂ ·6H ₂ O(0.5)	CH ₃ CN	110	55
11	Cu(OAc) ₂ (0.1)+TBHP (3)	CH ₃ CN	60	40
12	CuCl ₂ (0.1)+TBHP (3)	CH ₃ CN	60	15
13	CuSO ₄ ·5H ₂ O (0.1)+TBHP (3)	CH ₃ CN	60	20
14	Cu(NO ₃) ₂ ·3H ₂ O (0.1)+TBHP (3)	CH ₃ CN	60	48
15	Cu(OTf)₂ (0.1)+TBHP (3)	CH₃CN	60	83
16	Cu(OTf) ₂ (0.05)+TBHP (3)	CH ₃ CN	60	70
17	Cu(OTf) ₂ (0.1)+TBHP (3)	CH ₃ CN	80	66
18	Cu(OTf) ₂ (0.1)+TBHP (3)	CH ₃ CN	60	49
19	CuCl (0.1)+TBHP (3)	CH ₃ CN	60	15
20	Cu(OTf) ₂ (0.2)	CH ₃ CN	60	25
21	TBHP (3)	CH ₃ CN	60	34
22	Cu (0.1)+TBHP (3)	CH ₃ CN	60	5

^a Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), additive in solvent (2.0 mL) stirring under nitrogen for 24 h. Oil bath. Yields were determined by ³¹P NMR based on Ph₃PO as internal standard. ^b Under air.

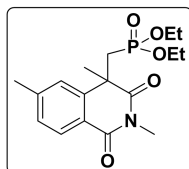
4. Spectral data

(3a) Diethyl((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.22 (dd, $J = 8.2$ Hz, $J = 1.60$ Hz, 1H), 7.62 – 7.58 (m, 1H), 7.43 – 7.39 (m, 2H), 3.76 – 3.66 (m, 3H), 3.57 – 3.50 (m, 1H), 3.37 (s, 3H), 2.96 (dd, $J = 17.8$ Hz, $J = 7.5$ Hz, 1H), 2.47 (dd, $J = 18.4$ Hz, $J = 15.5$ Hz, 1H), 1.60 (d, $J = 3.6$ Hz, 3H), 1.01 – 0.97 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.5, 164.2, 141.9, 133.4, 128.8, 127.6, 126.1, 124.6, 61.6 (d, $J = 6.6$ Hz), 61.3 (d, $J = 6.6$ Hz), 44.4 (d, $J = 4.0$ Hz), 37.6 (d, $J = 141.1$ Hz), 32.6 (d, $J = 19.2$ Hz), 27.3, 16.0 (q, $J = 6.0$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 25.2. HRMS-ESI: m/z 362.1136 ($[\text{M}+\text{Na}]^+$, $\text{C}_{16}\text{H}_{22}\text{NNaO}_5\text{P}^+$ calcd. 362.1133).

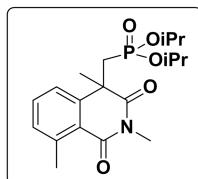
(3b) Diethyl ((2,4,6-trimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.13 (d, $J = 8.0$ Hz, 1H), 7.25 – 7.21 (m, 2H), 3.78 – 3.70 (m, 3H), 3.61 – 3.55 (m, 1H), 3.38 (s), 2.98 (dd, $J = 17.7$ Hz, $J = 15.3$ Hz, 1H), 2.52 – 2.44 (m, 4H), 1.61 (d, $J = 3.5$ Hz, 3H), 1.05 – 1.00 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.7 (d, $J = 1.6$ Hz), 164.3, 144.3, 134.5, 129.0, 128.7, 126.6, 122.1, 61.6 (d, $J = 6.3$ Hz), 61.3 (d, $J = 6.3$ Hz), 44.4 (d, $J = 3.8$ Hz), 37.5 (d, $J = 140.5$ Hz), 27.3, 22.0, 16.1 (dd, $J = 14.2$ Hz, $J = 6.1$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 25.0. HRMS-ESI: m/z 376.1253 ($[\text{M}+\text{Na}]^+$, $\text{C}_{17}\text{H}_{24}\text{NNaO}_5\text{P}^+$ calcd. 376.1290).

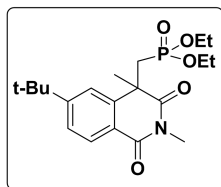
(3c)

Diisopropyl((2,4,8-trimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.45 (t, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 7.7$ Hz, 1H), 7.23 (d, $J = 7.4$ Hz, 1H), 4.49 – 4.41 (m, 1H), 4.36 – 4.28 (m, 1H), 3.37 (s, 3H), 2.94 (dd, $J = 17.7$ Hz, $J = 15.3$ Hz, 1H), 2.78 (s, 3H), 2.45 (dd, $J = 17.8$ Hz, $J = 15.4$ Hz, 1H), 1.62 (d, $J = 3.5$ Hz, 3H), 1.10 – 1.05 (m, 9H), 0.96 (d, $J = 6.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.4, 164.9, 143.4, 142.3, 132.3, 131.5, 124.6, 123.1, 70.1 (t, $J = 8.5$ Hz), 44.8 (d, $J = 4.1$ Hz), 39.1 (d, $J = 141.6$ Hz), 33.2 (d, $J = 19.3$ Hz), 27.4, 23.8 (t, $J = 3.8$ Hz), 18.4. ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 23.6. HRMS-ESI: m/z 404.1605 ($[\text{M}+\text{Na}]^+$, $\text{C}_{19}\text{H}_{28}\text{NNaO}_5\text{P}^+$ calcd. 404.1603).

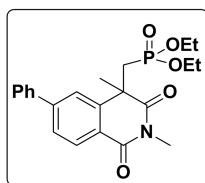
(3d) Diethyl((6-(tert-butyl)-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.26 (d, $J = 2.1$ Hz, 1H), 7.66 (dd, $J = 8.2$ Hz, $J = 2.1$ Hz, 1H), 7.36 (d, $J = 8.3$ Hz, 1H), 3.78 – 3.68 (m, 3H), 3.57 – 3.49 (m, 1H), 3.40 (s, 3H), 2.96 (dd, $J = 18.2$ Hz, $J = 15.5$ Hz, 1H), 2.47 (dd, $J = 17.7$ Hz, $J = 15.3$ Hz, 1H), 1.63 (d, $J = 3.6$ Hz, 3H), 1.36 (s, 9H), 1.00 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.8, 164.7, 151.0, 131.0, 126.0, 125.4, 124.2, 61.6 (d, $J = 6.4$ Hz), 61.3 (d, $J = 6.4$ Hz), 44.1 (d, $J = 3.8$ Hz), 37.8 (d, $J = 140.8$ Hz), 34.9, 32.6 (d, $J = 19.1$ Hz), 31.3, 27.5, 16.1 (dd, $J = 17.8$ Hz, $J = 6.4$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 25.5. HRMS-ESI: m/z 418.1755 ($[\text{M}+\text{Na}]^+$, $\text{C}_{20}\text{H}_{30}\text{NNaO}_5\text{P}^+$ calcd. 418.1759).

(3e)

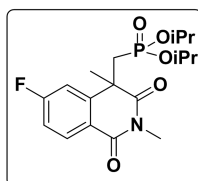
Diethyl((2,4-dimethyl-1,3-dioxo-6-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.49 (d, $J = 1.7$ Hz, 1H), 7.86 (dd, $J = 8.3$ Hz, $J = 1.8$ Hz, 1H), 7.64 (d, $J = 7.2$ Hz, 2H), 7.52 – 7.45 (m, 3H), 7.39 (t, $J = 7.3$ Hz, 1H), 3.81 – 3.72 (m, 3H), 3.66 – 3.56 (m, 1H), 3.42 (s, 3H), 3.02 (dd, $J = 18.0$ Hz, $J = 15.8$ Hz, 1H), 2.52 (dd, $J = 18.3$ Hz, $J = 15.7$ Hz, 1H), 1.67 (d, $J = 3.4$ Hz, 3H), 1.03 (t, $J = 6.9$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.5 (d, $J = 1.8$ Hz), 164.3, 140.7 (t, $J = 1.7$ Hz), 139.4, 132.0, 129.1, 128.1, 127.1, 126.8, 125.0, 61.7 (d, $J = 6.3$ Hz), 61.4 (d, $J = 6.4$ Hz), 44.3 (d, $J = 3.6$ Hz), 37.6 (d, $J = 140.7$ Hz), 32.6 (d, $J = 19.2$ Hz), 27.5, 16.1 (q, $J = 6.4$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 25.2. HRMS-ESI: m/z 416.1625 ($[\text{M}+\text{H}]^+$, $\text{C}_{22}\text{H}_{27}\text{NO}_5\text{P}^+$ calcd. 416.1627).

(3f)

Diisopropyl((6-fluoro-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate

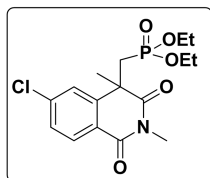


Yellow paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.27 (q, $J = 6.00$ Hz, 1H), 7.15 – 7.09 (m, 2H), 4.53 – 4.45 (m, 1H), 4.36 – 4.28 (m, 1H), 3.39 (s, 3H), 2.96 (t, $J = 16.0$ Hz, 1H), 2.39 (t, $J = 16.0$ Hz, 1H), 1.61 (d, $J = 3.4$ Hz, 3H), 1.13 (d, $J = 6.2$ Hz, 3H), 1.09 (t, $J = 5.9$ Hz, 6H), 0.95 (d, $J = 6.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.3, 166.0 (d, $J = 254.5$ Hz), 163.4, 145.1 (d,

$J = 2.1$ Hz), 131.9 (d, $J = 9.5$ Hz), 121.3 (d, $J = 1.5$ Hz), 115.4 (d, $J = 22.1$ Hz), 113.4 (d, $J = 22.8$ Hz), 70.5 (d, $J = 6.6$ Hz), 70.2 (d, $J = 6.9$ Hz), 45.0, 38.8 (d, $J = 141.7$ Hz), 32.7 (d, $J = 18.8$ Hz), 27.4, 23.8 (m). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 23.0. ^{19}F NMR (377 MHz, CDCl_3) δ (ppm) -116.8. HRMS-ESI: m/z 408.1350 ($[\text{M}+\text{Na}]^+$, $\text{C}_{18}\text{H}_{25}\text{FNNaO}_5\text{P}^+$ calcd. 408.1350).

(3g)

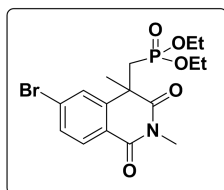
Diethyl((6-chloro-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.20 – 8.17 (m, 1H), 7.42 – 7.40 (m, 2H), 3.83 – 3.70 (m, 3H), 3.66 – 3.58 (m, 1H), 3.38 (s, 3H), 3.00 (dd, $J = 18.2$ Hz, $J = 15.52$ Hz, 1H), 2.43 (dd, $J = 17.5$ Hz, $J = 15.6$ Hz, 1H), 1.62 (d, $J = 3.5$ Hz, 3H), 1.07 (t, $J = 7.0$ Hz, 3H), 1.03 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.0, 163.4, 143.7 (d, $J = 2.1$ Hz), 140.0, 130.6, 128.2, 126.5, 123.2, 61.6 (t, $J = 5.6$ Hz), 44.6 (d, $J = 3.6$ Hz), 37.4 (d, $J = 140.4$ Hz), 32.6 (d, $J = 19.3$ Hz), 27.5, 16.1 (d, $J = 6.2$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 24.9. HRMS-ESI: m/z 374.0925 ($[\text{M}+\text{H}]^+$, $\text{C}_{16}\text{H}_{22}\text{ClNO}_5\text{P}^+$ calcd. 374.0924).

(3h)

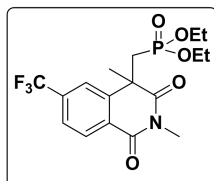
Diethyl((6-bromo-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.11 (d, $J = 8.3$ Hz, 1H), 7.59 – 7.56 (m, 2H), 3.86 – 3.78 (m, 2H), 3.76 – 3.68 (m, 1H), 3.66 – 3.58 (m, 1H), 3.38 (s, 3H), 3.00 (dd, $J = 18.0$ Hz, $J = 15.6$ Hz, 1H), 2.43 (dd, $J = 17.4$ Hz, $J = 15.7$ Hz, 1H), 1.62 (d, $J = 3.6$ Hz, 3H), 1.09 (t, $J = 7.0$ Hz, 3H), 1.04 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.0 (d, $J = 1.8$ Hz), 163.6, 143.7 (d, $J = 1.8$ Hz), 131.2, 130.6, 129.5, 128.6, 123.6, 61.6 (t, $J = 6.3$ Hz), 44.6 (d, $J = 4.5$ Hz), 37.4 (d, $J = 140.8$ Hz), 32.6 (d, $J = 19.4$ Hz), 27.5, 16.1 (d, $J = 6.3$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 24.9. HRMS-ESI: m/z 440.0243 ($[\text{M}+\text{Na}]^+$, $\text{C}_{16}\text{H}_{21}\text{BrNNaO}_5\text{P}^+$ calcd. 440.0238).

(3i)

Diethyl((2,4-dimethyl-1,3-dioxo-6-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate

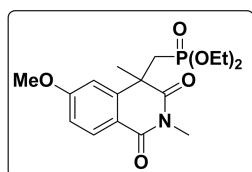


Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.40 (d, $J = 8.2$ Hz, 1H), 7.71 – 7.67 (m, 2H),

3.87 – 3.79 (m, 2H), 3.75 – 3.65 (m, 1H), 3.62 – 3.52 (m, 1H), 3.42 (s, 3H), 3.05 (dd, $J = 18.0$ Hz, $J = 15.6$ Hz, 1H), 2.50 (dd, $J = 18.2$ Hz, $J = 16.5$ Hz, 1H), 1.67 (d, $J = 3.4$ Hz, 3H), 1.08 (t, $J = 7.1$ Hz, 3H), 0.98 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 174.9 (d, $J = 1.8$ Hz), 163.2, 142.7 (d, $J = 1.8$ Hz), 135.0 (d, $J = 32.7$ Hz), 129.8, 127.6, 124.4 (q, $J = 3.6$ Hz), 123.5 (q, $J = 273.7$ Hz), 123.4 (q, $J = 3.6$ Hz), 61.7 (d, $J = 6.2$ Hz), 61.6 (d, $J = 6.3$ Hz), 44.7 (d, $J = 3.6$ Hz), 37.4 (d, $J = 140.5$ Hz), 32.6 (d, $J = 19.1$ Hz), 27.6, 16.0 (q, $J = 6.1$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 24.9. HRMS-ESI: m/z 408.1185 ($[\text{M}+\text{H}]^+$, $\text{C}_{17}\text{H}_{22}\text{F}_3\text{NO}_5\text{P}^+$ calcd. 408.1188).

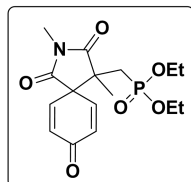
(3ja)

Diethyl((6-methoxy-2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.18 (d, $J = 8.82$ Hz, 1H), 6.96 – 6.87 (m, 2H), 3.88 (s, 3H), 3.81 – 3.70 (m, 3H), 3.68 – 3.58 (m, 1H), 3.36 (s, 3H), 2.99 (dd, $J = 17.6$ Hz, $J = 15.9$ Hz, 1H), 2.45 (dd, $J = 17.8$ Hz, $J = 15.7$ Hz, 1H), 1.61 (d, $J = 3.3$ Hz, 3H), 1.07 – 1.00 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.7 (d, $J = 1.6$ Hz), 163.98, 163.89, 144.1 (d, $J = 1.7$ Hz), 131.3, 117.6, 113.6, 111.3, 61.7 (d, $J = 6.2$ Hz), 61.4 (d, $J = 6.4$ Hz), 55.7, 44.8 (d, $J = 4.3$ Hz), 37.4 (d, $J = 140.8$ Hz), 32.9 (d, $J = 19.2$ Hz), 27.3, 16.1 (q, $J = 6.7$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 25.3. HRMS-ESI: m/z 392.1244 ($[\text{M}+\text{Na}]^+$, $\text{C}_{17}\text{H}_{24}\text{NNaO}_6\text{P}^+$ calcd. 392.1239).

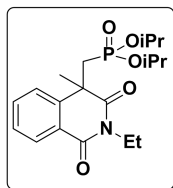
(3jb) Diethyl ((2,4-dimethyl-1,3,8-trioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 6.90 (dd, $J = 10.4$ Hz, $J = 3.0$ Hz, 1H), 6.75 (dd, $J = 10.4$ Hz, $J = 3.1$ Hz, 1H), 6.55 – 6.50 (m, 2H), 4.10 – 3.95 (m, 4H), 3.07 (s, 3H), 2.36 (dd, $J = 19.2$ Hz, $J = 16.0$ Hz, 1H), 2.07 (dd, $J = 19.7$ Hz, $J = 16.0$ Hz, 1H), 1.50 (d, $J = 0.7$ Hz, 3H), 1.30 – 1.23 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 184.3, 178.8 (d, $J = 13.5$ Hz), 172.5, 142.4 (d, $J = 60.6$ Hz), 133.3 (d, $J = 71.7$ Hz), 62.5 (d, $J = 6.6$ Hz), 62.3 (d, $J = 6.6$ Hz), 57.7 (d, $J = 1.7$ Hz), 51.5 (d, $J = 2.7$ Hz), 31.7 (d, $J = 144.0$ Hz), 26.2, 23.0 (d, $J = 9.3$ Hz), 16.3 (dd, $J = 10.0$ Hz, $J = 5.8$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 24.7. HRMS-ESI: m/z 378.1085 ($[\text{M}+\text{Na}]^+$, $\text{C}_{16}\text{H}_{22}\text{NNaO}_6\text{P}^+$ calcd. 378.1082).

(3k)

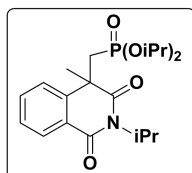
Diisopropyl((2-ethyl-4-methyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.21 (d, $J = 7.6$ Hz, 1H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.42 – 7.38 (m, 2H), 4.46 – 4.40 (m, 1H), 4.31 – 4.24 (m, 1H), 4.04 (q, $J = 7.0$ Hz, 2H), 2.93 (dd, $J = 17.7$ Hz, $J = 15.6$ Hz, 1H), 2.47 (dd, $J = 17.6$ Hz, $J = 15.6$ Hz, 1H), 1.57 (d, $J = 3.5$ Hz, 3H), 1.22 (d, $J = 7.1$ Hz, 3H), 1.07 – 1.03 (m, 9H), 0.89 (d, $J = 6.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.2 (d, $J = 1.7$ Hz), 163.8, 142.1 (d, $J = 1.7$ Hz), 133.3, 128.8, 127.4, 126.2, 124.9, 70.2 (d, $J = 6.2$ Hz), 70.0 (d, $J = 6.3$ Hz), 44.7 (d, $J = 4.2$ Hz), 38.2 (d, $J = 141.4$ Hz), 35.8, 33.1 (d, $J = 19.3$ Hz), 23.8 (q, $J = 3.6$ Hz), 23.6 (t, $J = 4.6$ Hz), 13.0. ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 23.6. HRMS-ESI: m/z 382.1789 ($[\text{M}+\text{H}]^+$, $\text{C}_{19}\text{H}_{29}\text{NO}_5\text{P}^+$ calcd. 382.1783).

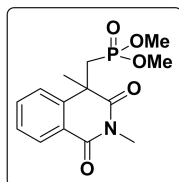
(31)

Diisopropyl((2-isopropyl-4-methyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.19 (d, $J = 7.3$ Hz, 1H), 7.56 (t, $J = 7.3$ Hz, 1H), 7.40 – 7.36 (m, 2H), 5.21 – 5.13 (m, 1H), 4.49 – 4.40 (m, 1H), 4.33 – 4.24 (m, 1H), 2.93 (dd, $J = 17.4$ Hz, $J = 15.4$ Hz, 1H), 2.46 (dd, $J = 17.3$ Hz, $J = 15.4$ Hz, 1H), 1.56 (d, $J = 3.6$ Hz, 3H), 1.48 (q, $J = 5.4$ Hz, 6H), 1.11 – 1.04 (m, 9H), 0.89 (d, $J = 6.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.7 (d, $J = 2.2$ Hz), 164.4, 142.1 (d, $J = 2.0$ Hz), 133.1, 128.8, 127.4, 126.0, 125.5, 70.2 (d, $J = 6.2$ Hz), 69.9 (d, $J = 6.5$ Hz), 45.6, 45.2 (d, $J = 3.7$ Hz), 37.9 (d, $J = 141.3$ Hz), 33.0 (d, $J = 19.5$ Hz), 23.8 (dd, $J = 9.5$ Hz, $J = 3.6$ Hz), 23.6 (d, $J = 4.6$ Hz), 19.5 (d, $J = 37.8$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 24.1. HRMS-ESI: m/z 396.1946 ($[\text{M}+\text{H}]^+$, $\text{C}_{20}\text{H}_{31}\text{NO}_5\text{P}^+$ calcd. 396.1940).

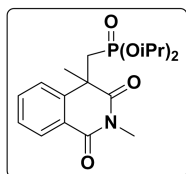
(3n) Dimethyl ((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.25 (d, $J = 8.0$ Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.43 (t, $J = 8.3$ Hz, 2H), 3.39 (s, 3H), 3.36 (d, $J = 11.0$ Hz, 3H), 3.25 (d, $J = 11.0$ Hz, 3H), 3.00 (dd, $J = 17.2$ Hz, $J = 15.4$ Hz, 1H), 2.48 (dd, $J = 17.2$ Hz, $J = 15.5$ Hz, 1H), 1.63 (d, $J = 3.6$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.5, 164.2, 141.8, 133.5, 129.0, 127.8, 125.9, 124.6, 52.3 (d, $J = 6.4$ Hz), 52.0 (d, $J = 6.4$ Hz), 44.4 (d, $J = 3.6$ Hz), 37.0 (d, $J = 140.2$ Hz), 32.44 (d, $J = 19.6$ Hz), 27.43. ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 28.0. HRMS-ESI: m/z 312.1000 ($[\text{M}+\text{H}]^+$,

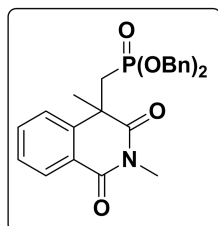
C₁₄H₁₉NO₅P⁺ calcd. 312.1001)

(3o) Diisopropyl ((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



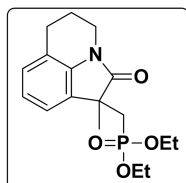
Yellow paste. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.21 (d, *J* = 8.2 Hz, 1H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.42 – 7.39 (m, 2H), 4.46 – 4.38 (m, 1H), 4.31 – 4.23 (m, 1H), 3.37 (s, 3H), 2.91 (dd, *J* = 17.2 Hz, *J* = 15.3 Hz, 1H), 2.45 (dd, *J* = 17.0 Hz, *J* = 15.4 Hz, 1H), 1.59 (d, *J* = 3.4 Hz, 3H), 1.06 – 1.03 (m, 9H), 0.90 (d, *J* = 6.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 175.6, 164.3, 142.1, 133.3, 128.8, 127.5, 126.3, 124.8, 70.1 (dd, *J* = 9.9 Hz, *J* = 6.5 Hz), 44.6 (d, *J* = 4.2 Hz), 38.8 (d, *J* = 141.4 Hz), 32.8 (d, *J* = 19.6 Hz), 27.4, 23.8 (t, *J* = 3.8 Hz), 23.6 (t, *J* = 5.5 Hz). ³¹P NMR (162 MHz, CDCl₃) δ (ppm) 23.3. HRMS-ESI: *m/z* 390.1447 ([M+Na]⁺, C₁₈H₂₆NNaO₅P⁺ calcd. 390.1446).

(3p) Dibenzyl ((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)phosphonate



Yellow paste. ¹H NMR (400 MHz, CDCl₃) δ (ppm) ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.20 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.28 – 7.26 (m, 6H), 7.10 – 7.04 (m, 4H), 4.67 – 4.58 (m, 3H), 4.46 (dd, *J* = 11.6 Hz, *J* = 9.3 Hz, 1H), 3.19 (s, 3H), 3.12 (dd, *J* = 17.6 Hz, *J* = 15.4 Hz, 1H), 2.57 (dd, *J* = 17.8 Hz, *J* = 15.5 Hz, 1H), 1.59 (d, *J* = 3.7 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 175.4 (d, *J* = 1.3 Hz), 163.9, 141.6 (d, *J* = 1.7 Hz), 135.8 (dd, *J* = 19.4 Hz, *J* = 6.1 Hz), 133.5, 128.9, 128.5, 128.4 (d, *J* = 3.1 Hz), 128.0 (d, *J* = 1.9 Hz), 127.7, 126.0, 124.5, 67.0 (dd, *J* = 9.1 Hz, *J* = 6.5 Hz), 44.6 (d, *J* = 3.9 Hz), 37.4 (d, *J* = 140.0 Hz), 32.9 (d, *J* = 19.7 Hz), 27.2. ³¹P NMR (162 MHz, CDCl₃) δ (ppm) 26.4. HRMS-ESI: *m/z* 486.1450 ([M+Na]⁺, C₂₆H₂₆NNaO₅P⁺ calcd. 486.1446).

(3q) Diethyl((1-methyl-2-oxo-2,4,5,6-tetrahydro-1H-pyrrolo[3,2,1-ij]quinolin-1-yl)methyl)phosphonate

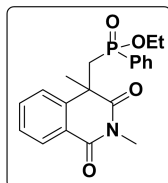


Yellow oil. ¹H NMR (400 MHz, CDCl₃) δ (ppm) ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.19 (d, *J* = 7.3 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 3.86 – 3.79 (m, 3H), 3.75 – 3.65 (m, 3H), 2.77 (t, *J* = 6.0 Hz, 2H), 2.41 – 2.28 (m, 2H), 2.02 – 1.97 (m, 2H), 1.42 (d, *J* = 2.1 Hz, 3H),

1.14 – 1.10 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 178.3 (d, $J = 6.5$ Hz), 139.0, 131.0 (d, $J = 1.8$ Hz), 126.9, 121.9, 121.7, 120.2, 67.0 (dd, $J = 41.7$ Hz, $J = 6.4$ Hz), 46.0 (d, $J = 3.6$ Hz), 39.0, 33.5 (d, $J = 143.5$ Hz), 25.7 (d, $J = 16.2$ Hz), 24.7, 21.2, 16.3 (dd, $J = 9.2$ Hz, $J = 6.2$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 26.2. HRMS-ESI: m/z 360.1343 ($[\text{M}+\text{Na}]^+$, $\text{C}_{17}\text{H}_{24}\text{NNaO}_4\text{P}^+$ calcd. 360.1341).

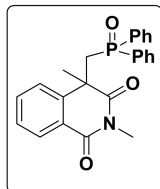
(3r)

Ethyl((2,4-dimethyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)(phenyl)phosphinate



White paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.2 (d, $J = 7.5$ Hz, 1H), 7.44 – 7.35 (m, 3H), 7.31 – 7.26 (m, 4H), 7.16 (d, $J = 8.0$ Hz, 1H), 3.79 – 3.70 (m, 1H), 3.59 – 3.49 (m, 1H), 3.41 (s, 3H), 3.29 (t, $J = 15.2$ Hz, 1H), 2.65 (dd, $J = 15.2$ Hz, $J = 11.2$ Hz, 1H), 1.61 (d, $J = 2.9$ Hz, 3H), 1.04 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 176.0 (d, $J = 1.5$ Hz), 164.4, 141.3 (d, $J = 2.4$ Hz), 133.3, 132.1 (d, $J = 2.6$ Hz), 131.5 (d, $J = 10.1$ Hz), 130.5, 128.8, 128.5 (d, $J = 12.6$ Hz), 127.7, 126.2, 124.5, 60.6 (d, $J = 6.3$ Hz), 44.7 (d, $J = 3.2$ Hz), 41.0 (d, $J = 99.5$ Hz), 33.0 (d, $J = 16.0$ Hz), 27.5, 16.1 (d, $J = 6.6$ Hz). ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 37.8. HRMS-ESI: m/z 372.1370 ($[\text{M}+\text{H}]^+$, $\text{C}_{20}\text{H}_{23}\text{NO}_4\text{P}^+$ calcd. 372.1365).

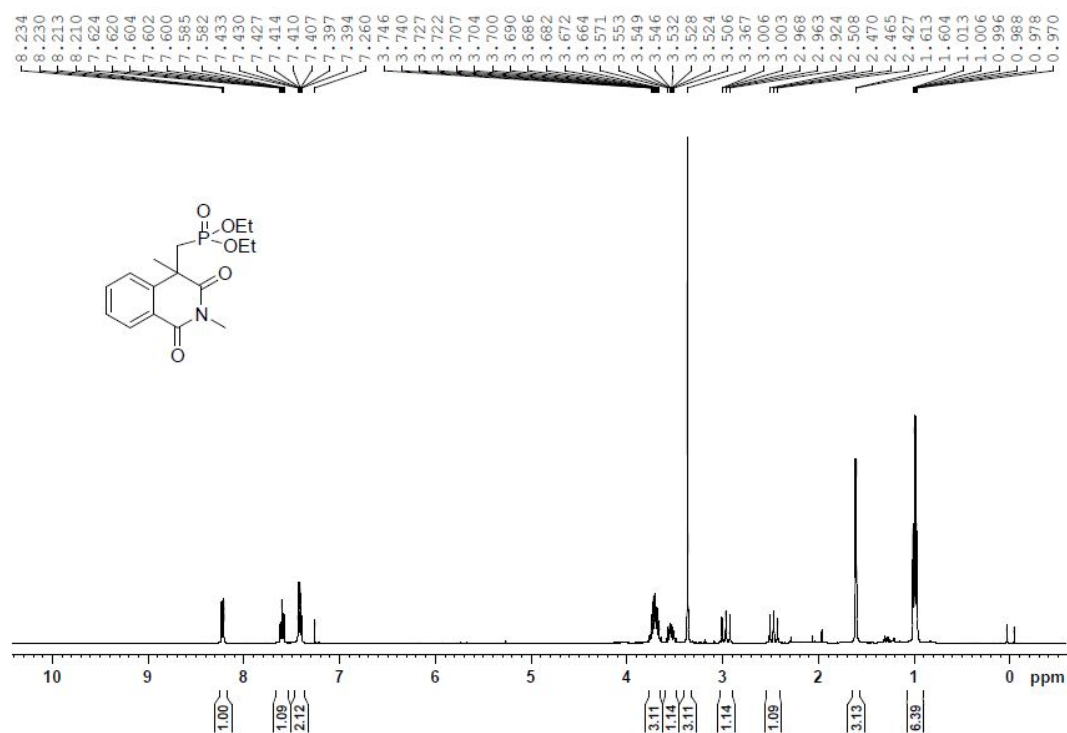
(3s) 4-((diphenylphosphoryl)methyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione



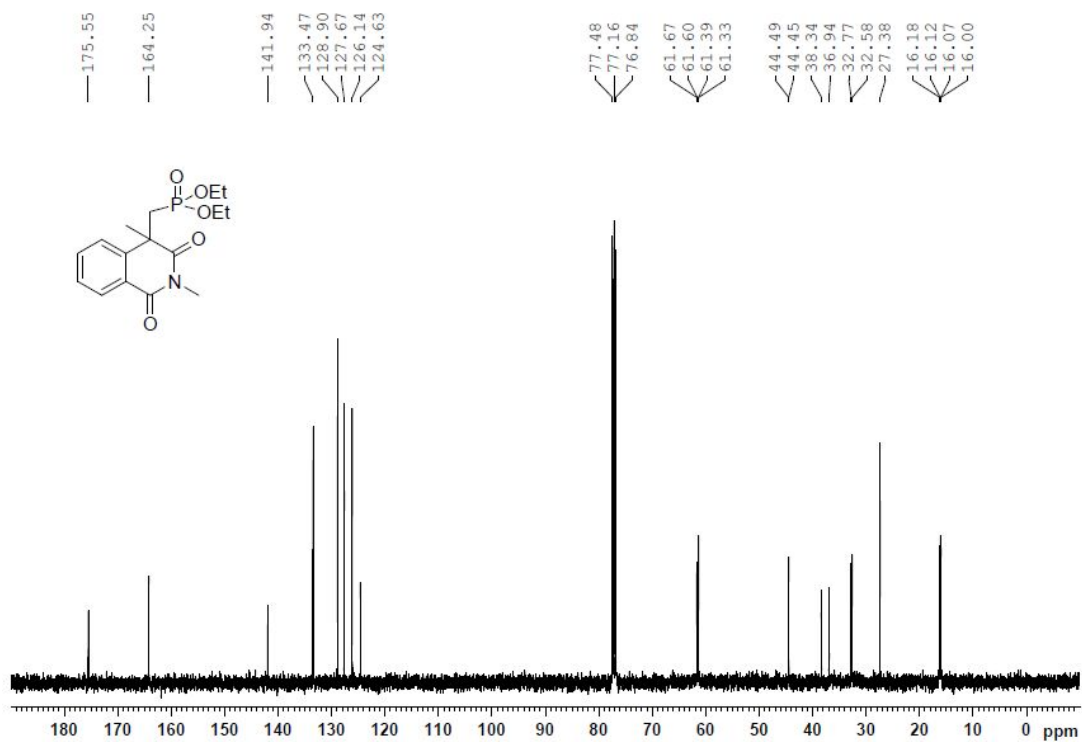
White paste. ^1H NMR (400 MHz, CDCl_3) δ (ppm) 8.14 (d, $J = 7.7$ Hz, 1H), 7.52 – 7.47 (m, 2H), 7.45 – 7.34 (m, 6H), 7.28 – 7.22 (m, 3H), 7.15 – 7.10 (m, 2H), 3.73 (dd, $J = 15.0$ Hz, $J = 10.8$ Hz, 1H), 3.30 (s, 3H), 2.96 (dd, $J = 15.0$ Hz, $J = 8.4$ Hz, 1H), 1.68 (d, $J = 2.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 175.9 (d, $J = 1.7$ Hz), 164.1, 140.7 (d, $J = 2.0$ Hz), 133.1 (d, $J = 99.9$ Hz), 132.7 (d, $J = 99.8$ Hz), 132.8, 131.8 (d, $J = 2.2$ Hz), 131.2 (d, $J = 2.5$ Hz), 130.8 (d, $J = 9.5$ Hz), 130.5 (d, $J = 9.2$ Hz), 128.6, 128.5 (d, $J = 8.6$ Hz), 128.3 (d, $J = 8.7$ Hz), 127.6, 126.4, 124.7, 44.9 (d, $J = 3.5$ Hz), 41.3 (d, $J = 69.3$ Hz), 33.1 (d, $J = 13.6$ Hz), 27.4. ^{31}P NMR (162 MHz, CDCl_3) δ (ppm) 26.3. HRMS-ESI: m/z 349.1547 ($[\text{M}+\text{Na}]^+$, $\text{C}_{17}\text{H}_{27}\text{NaO}_4\text{P}^+$ calcd. 349.1545).

¹H and ¹³C NMR spectra

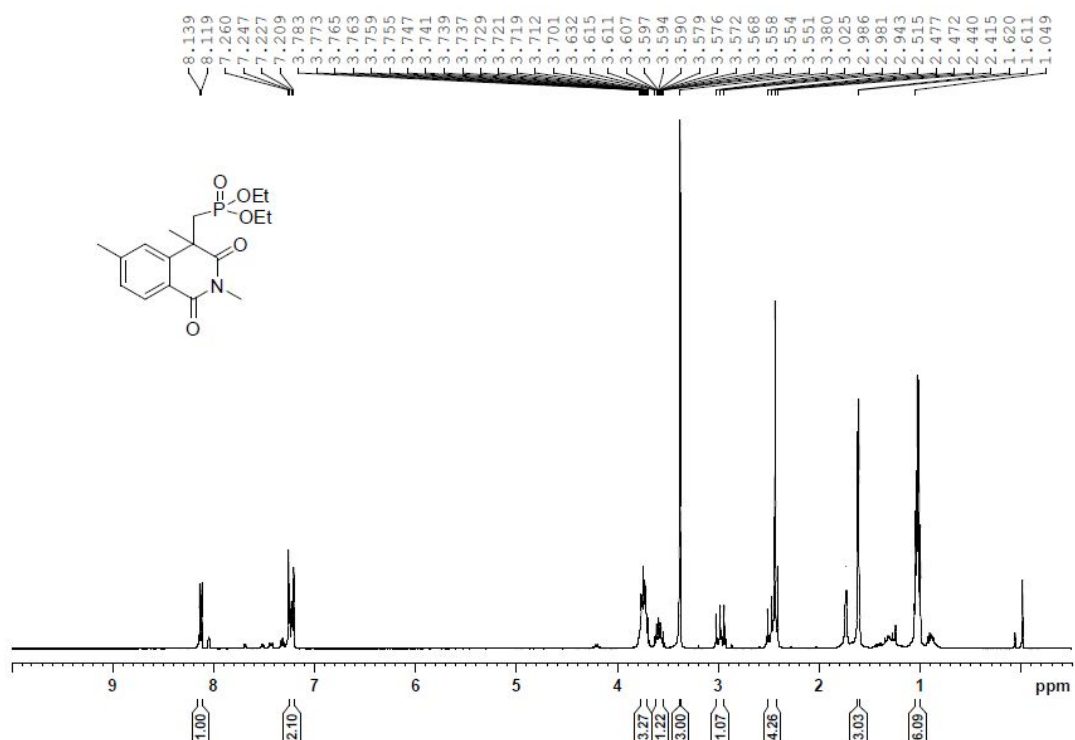
3a



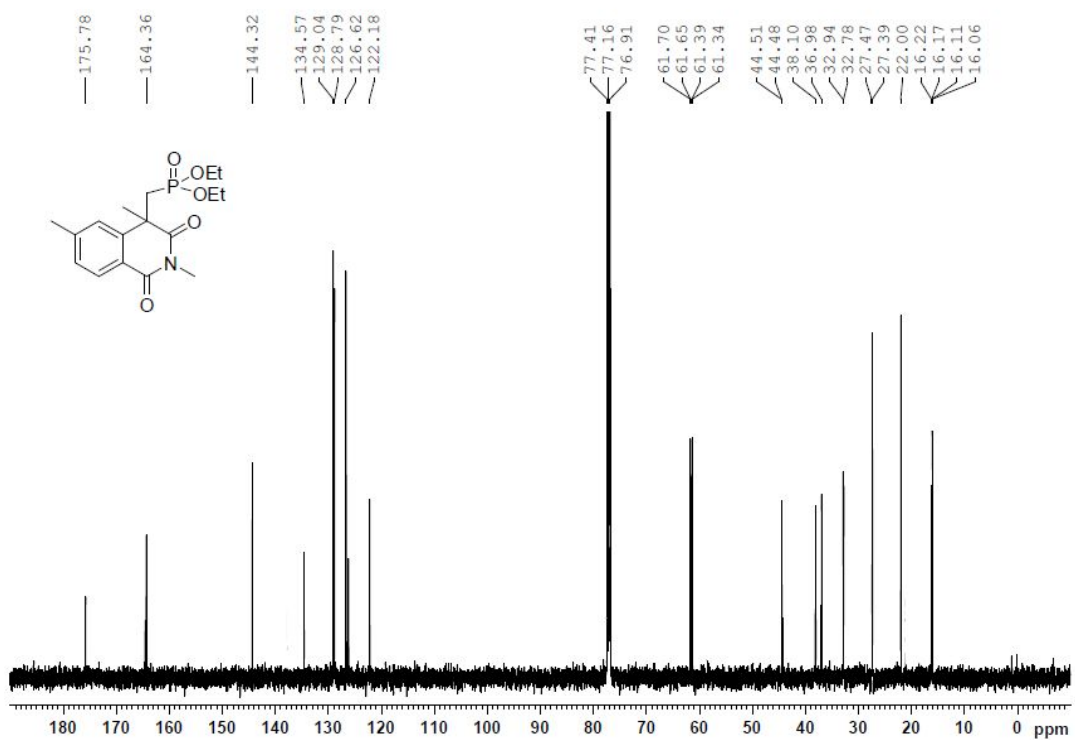
3a



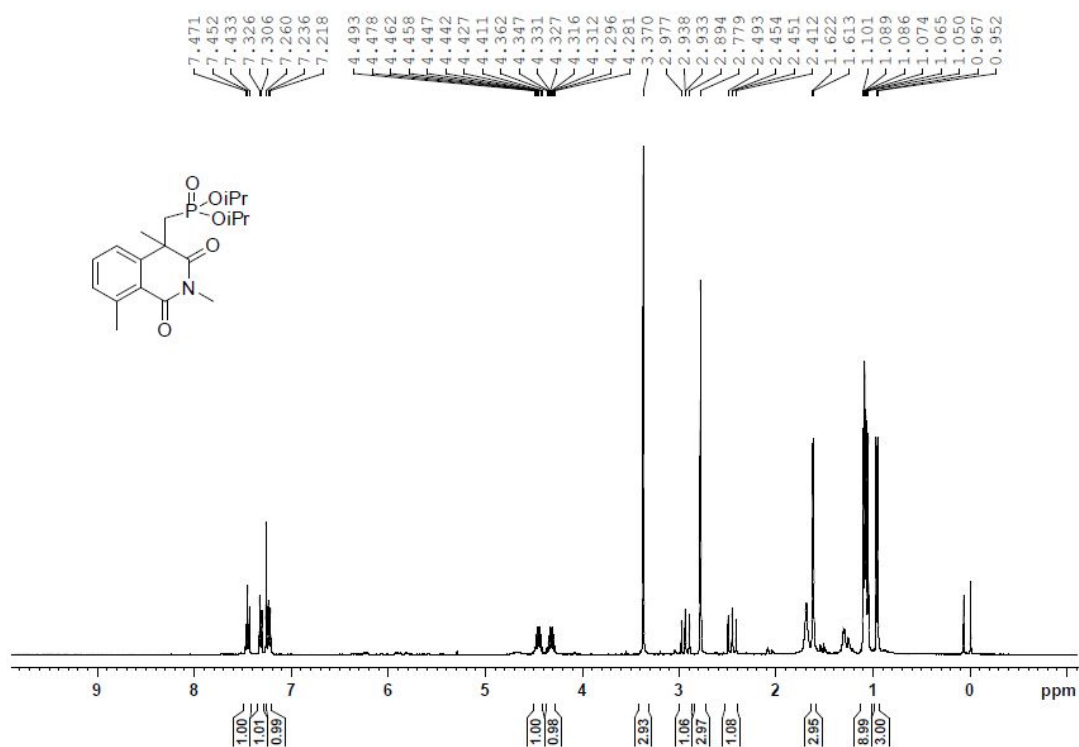
3b



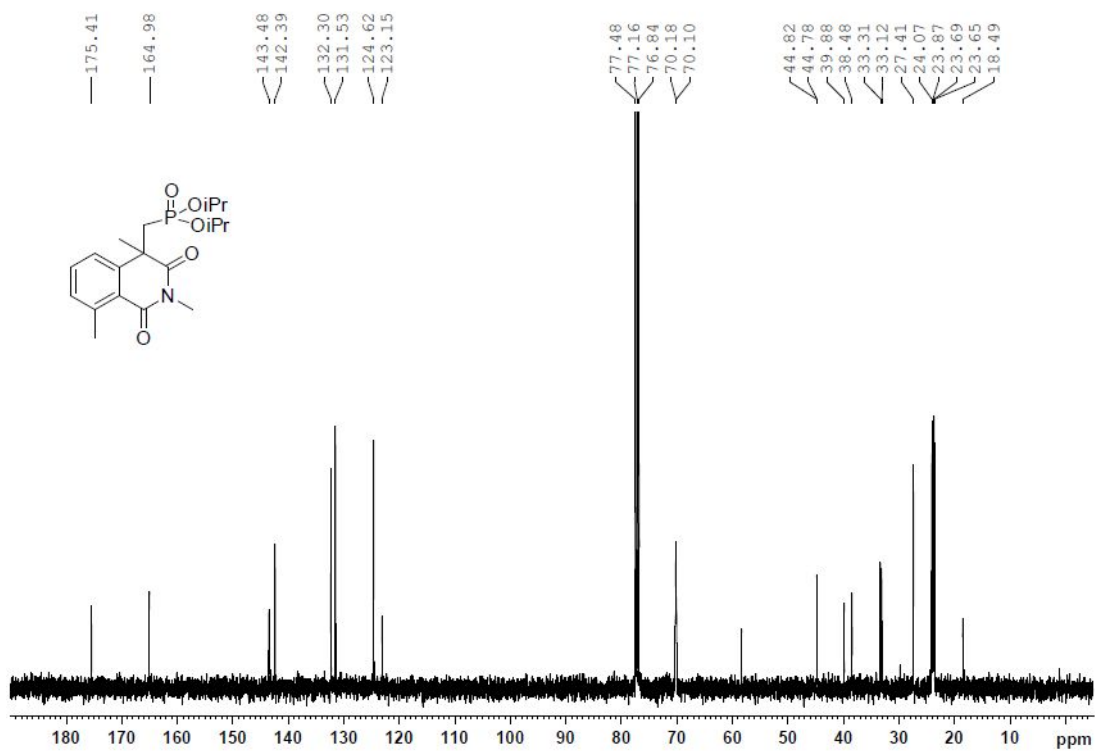
3b



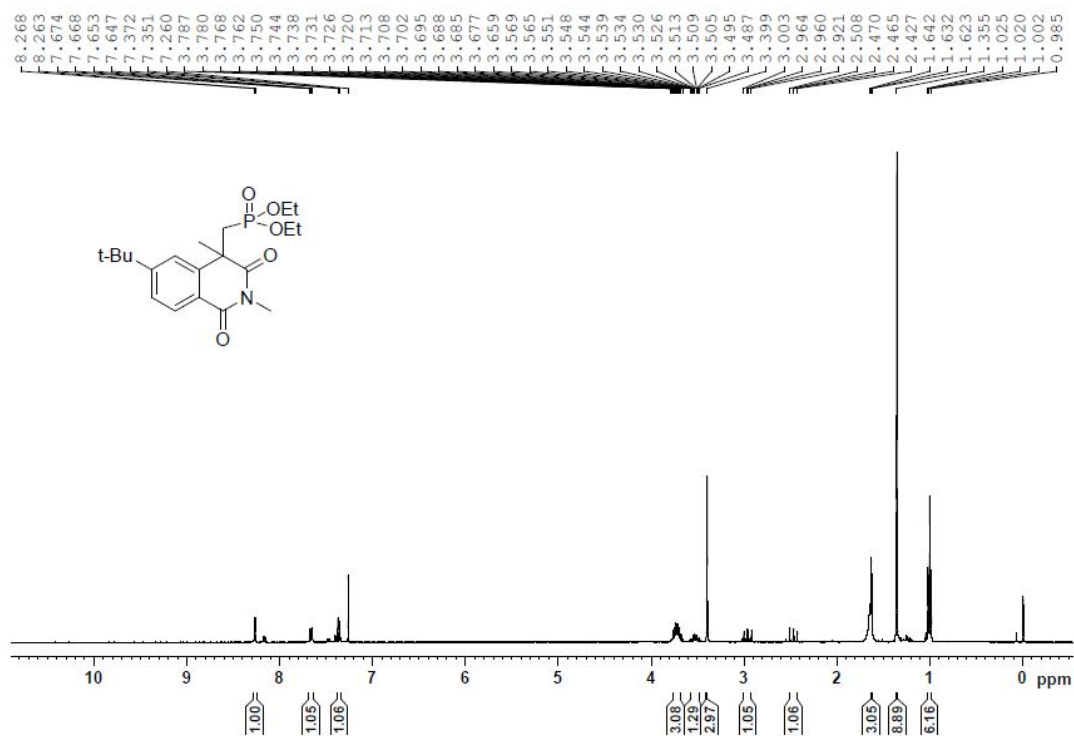
3c



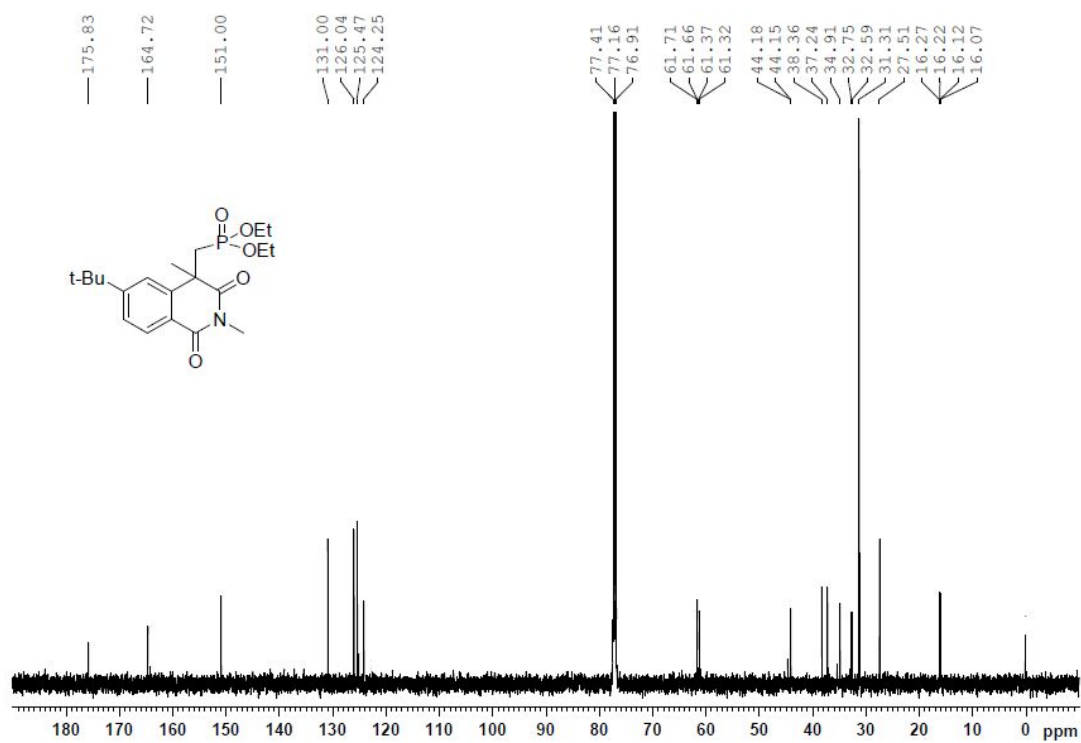
3c



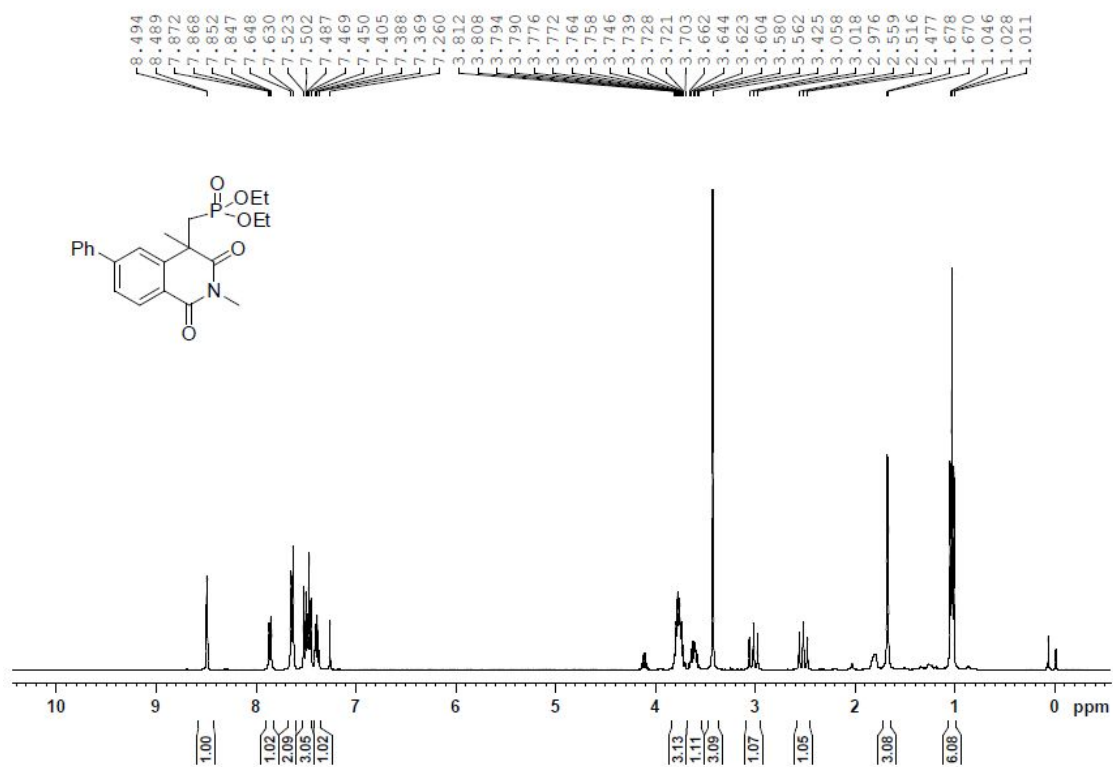
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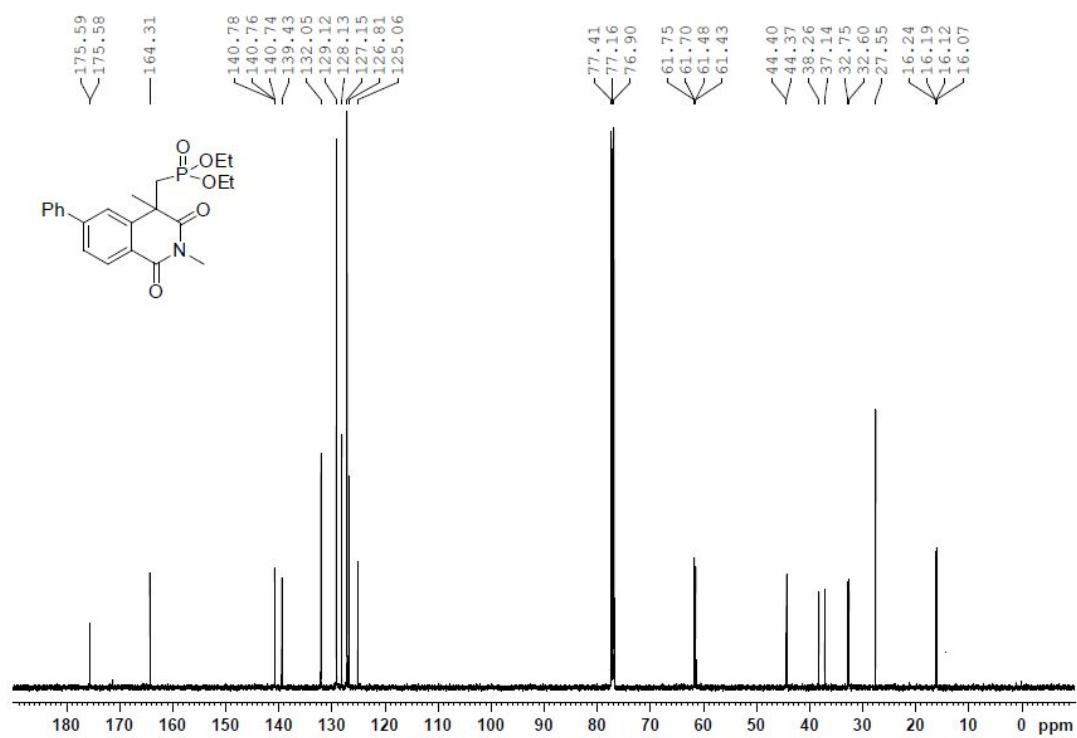
3d



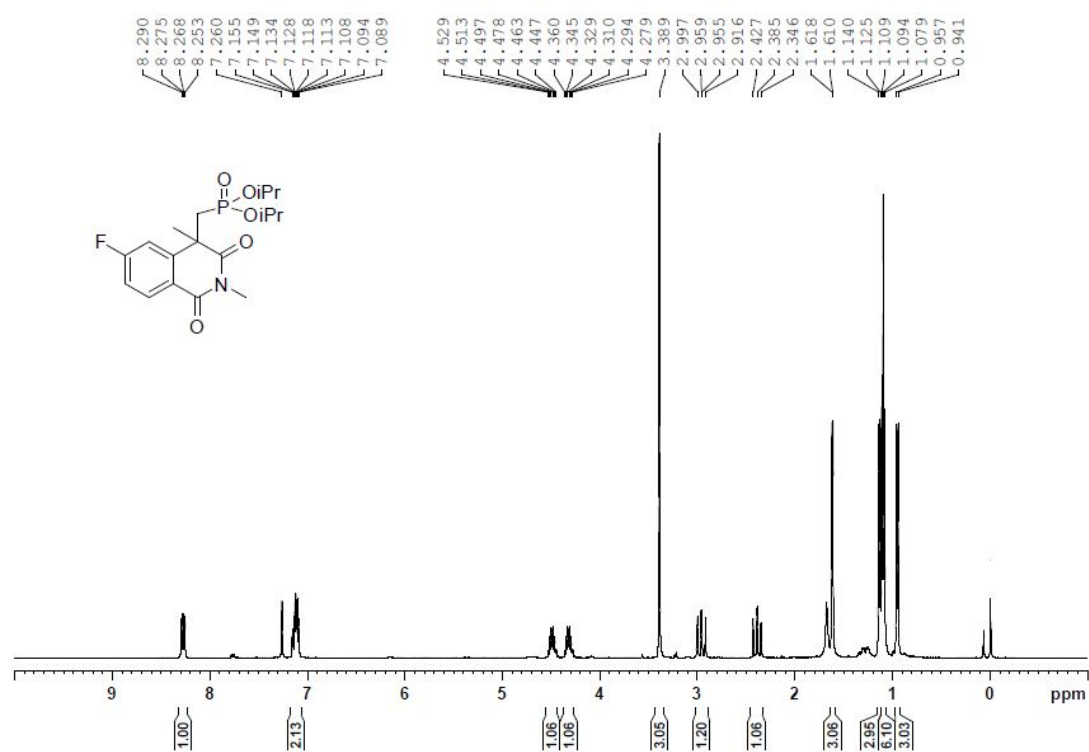
3e



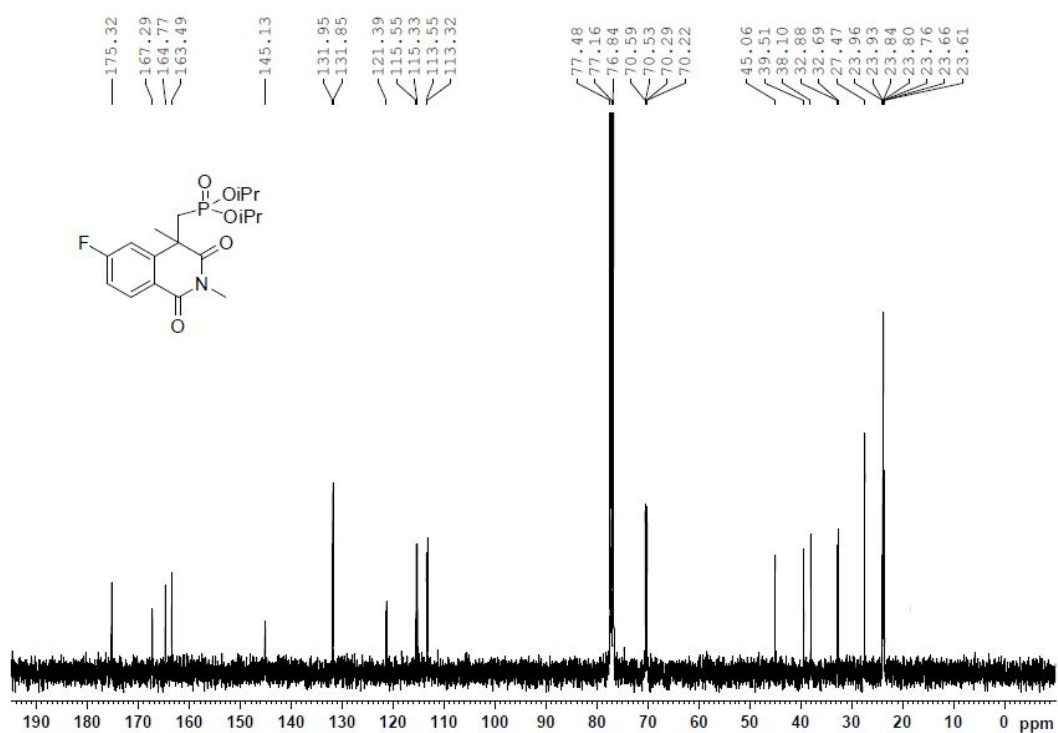
3e



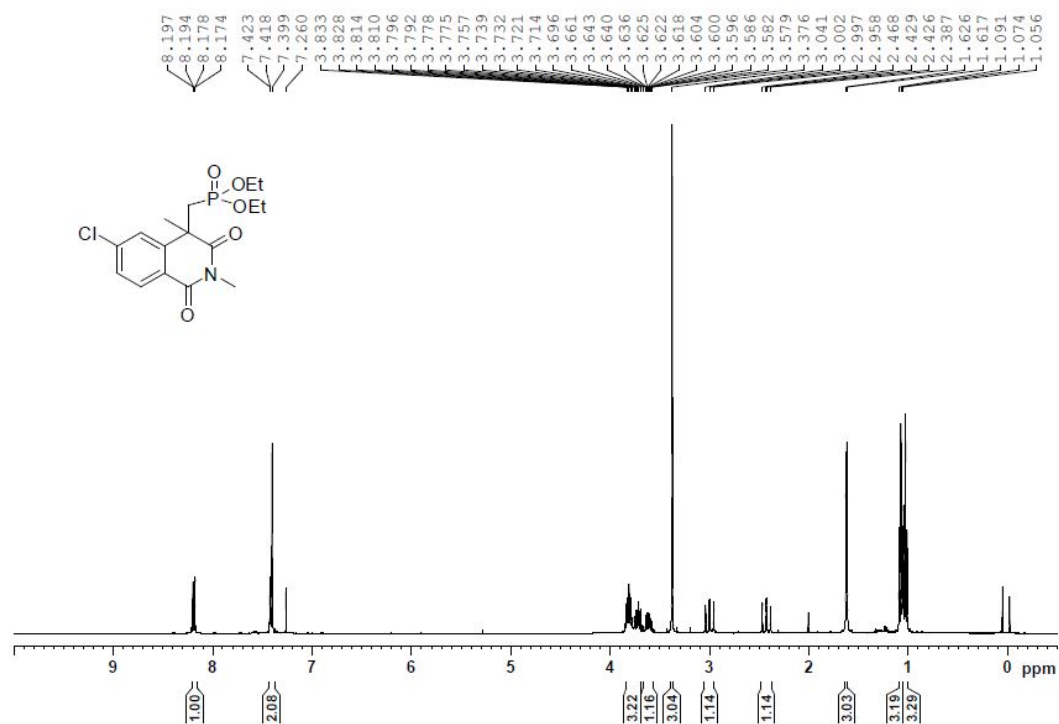
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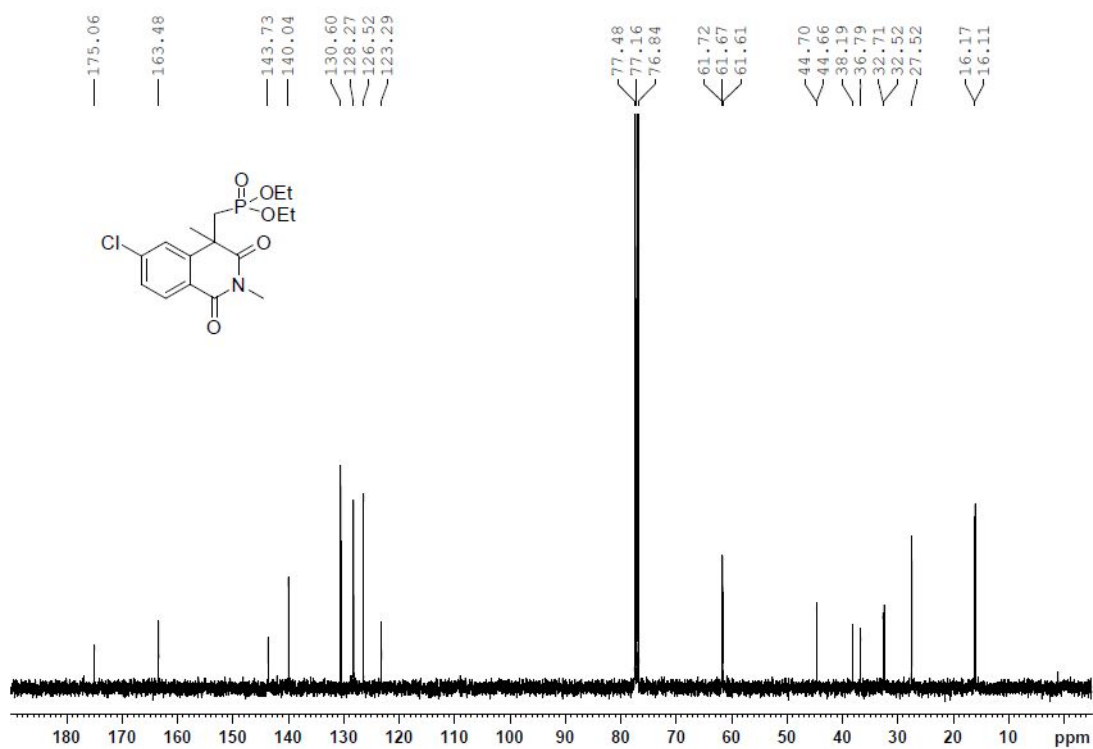
3f



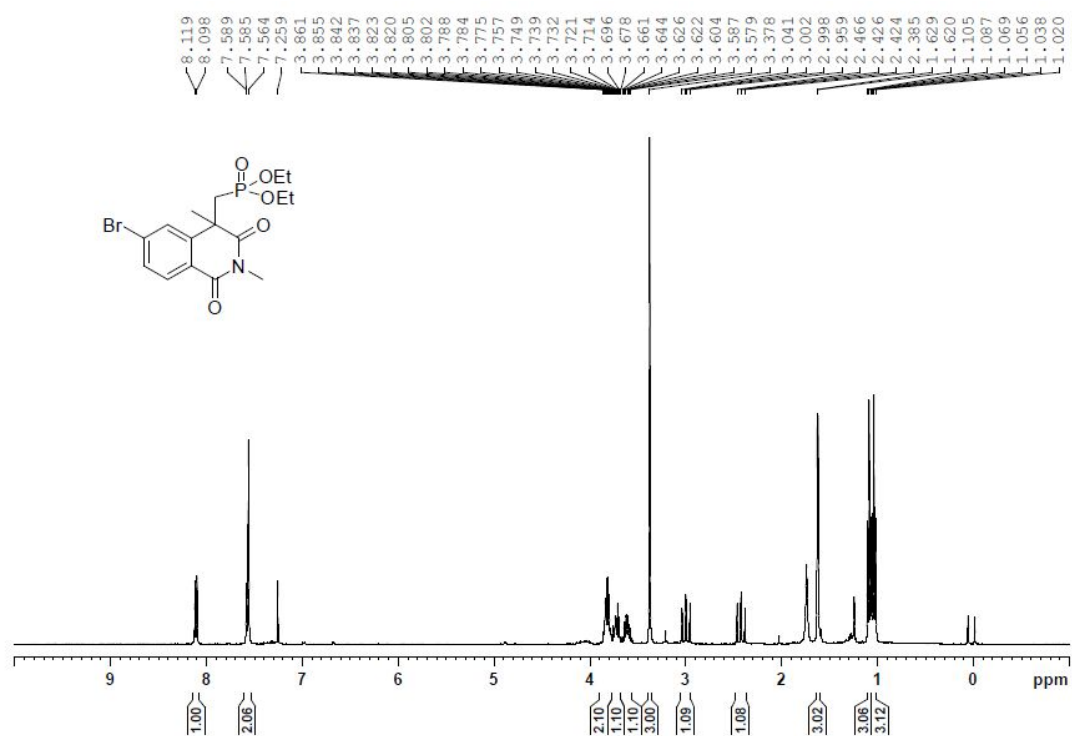
3g



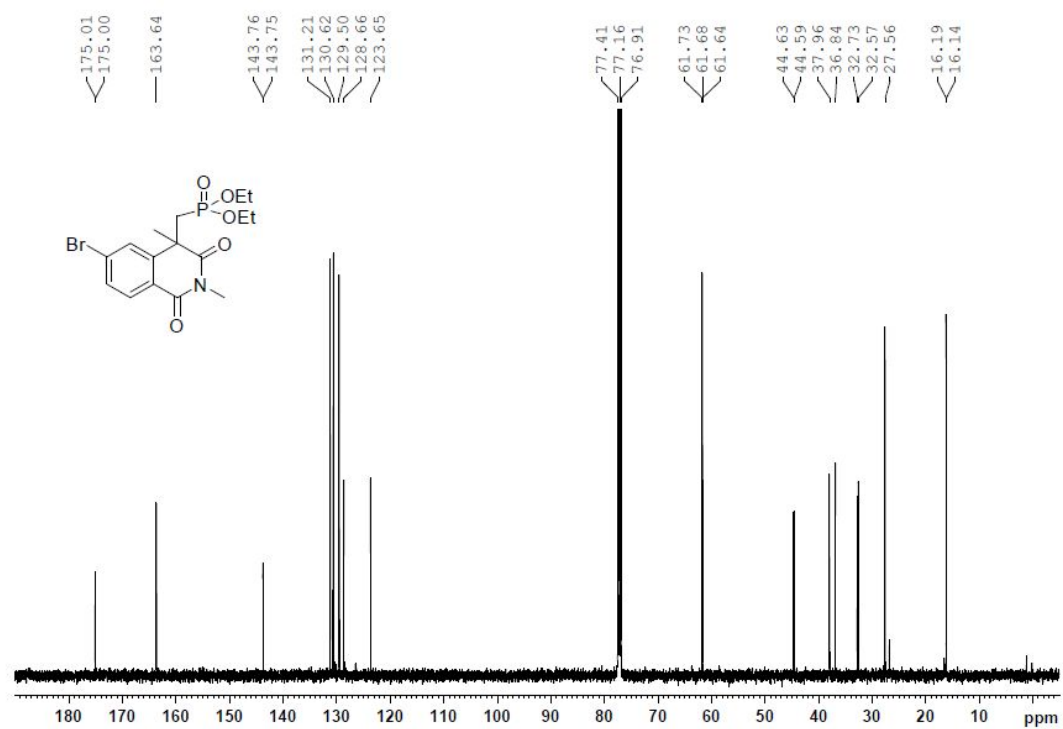
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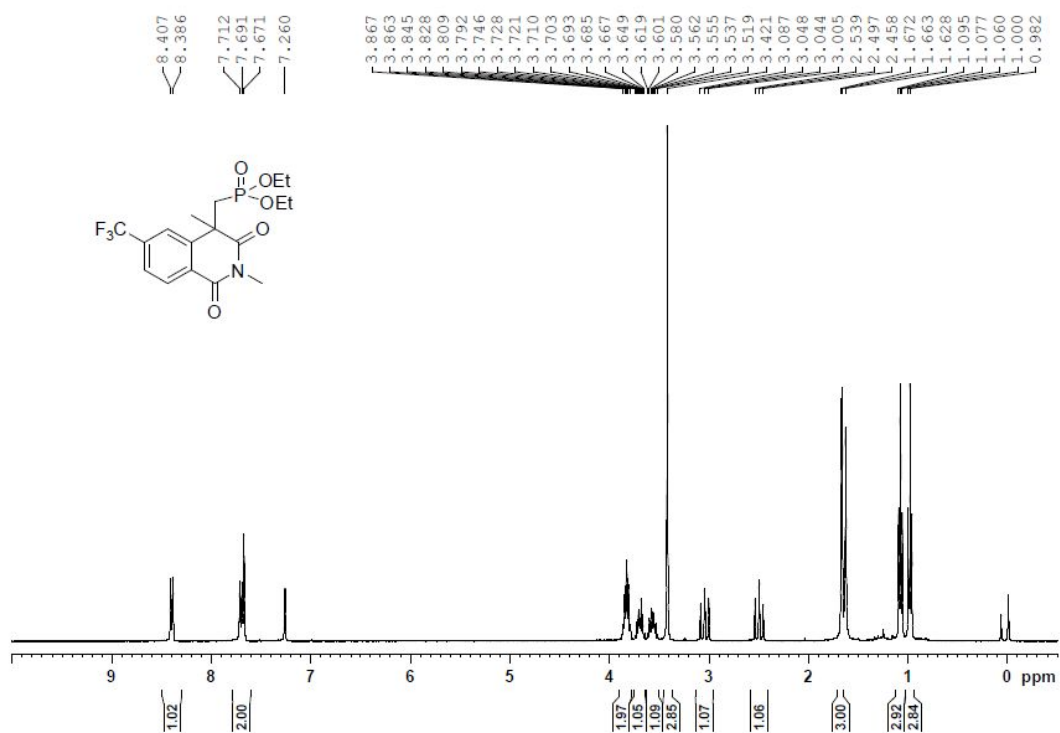
3h



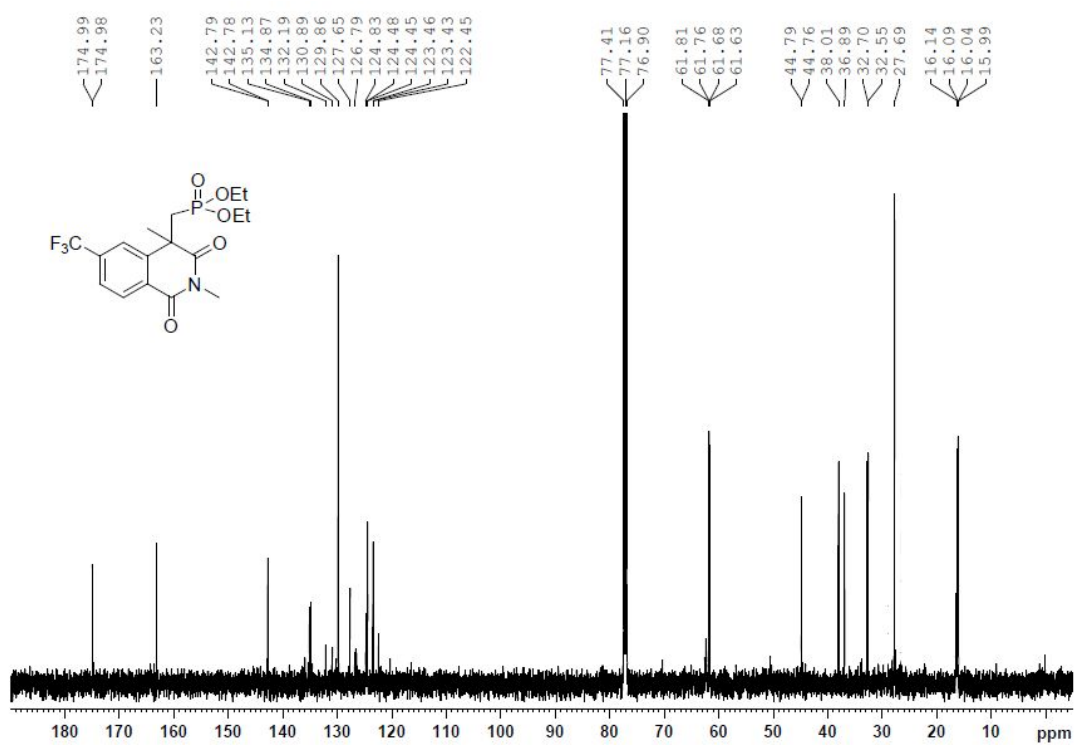
3h



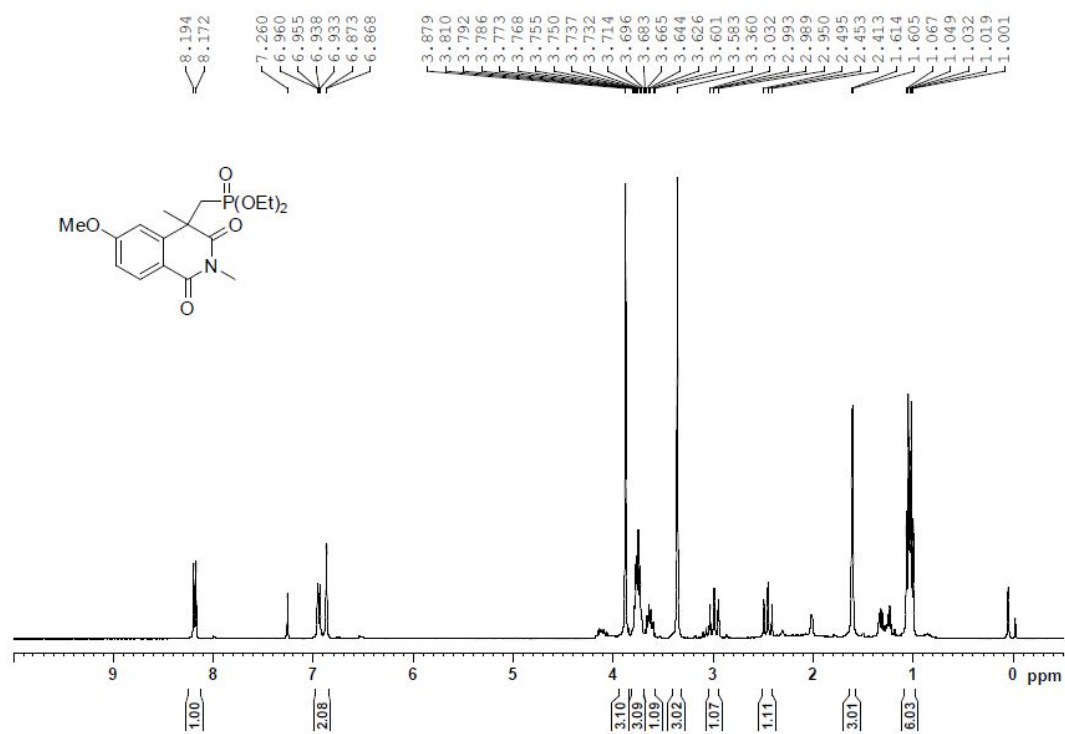
3i



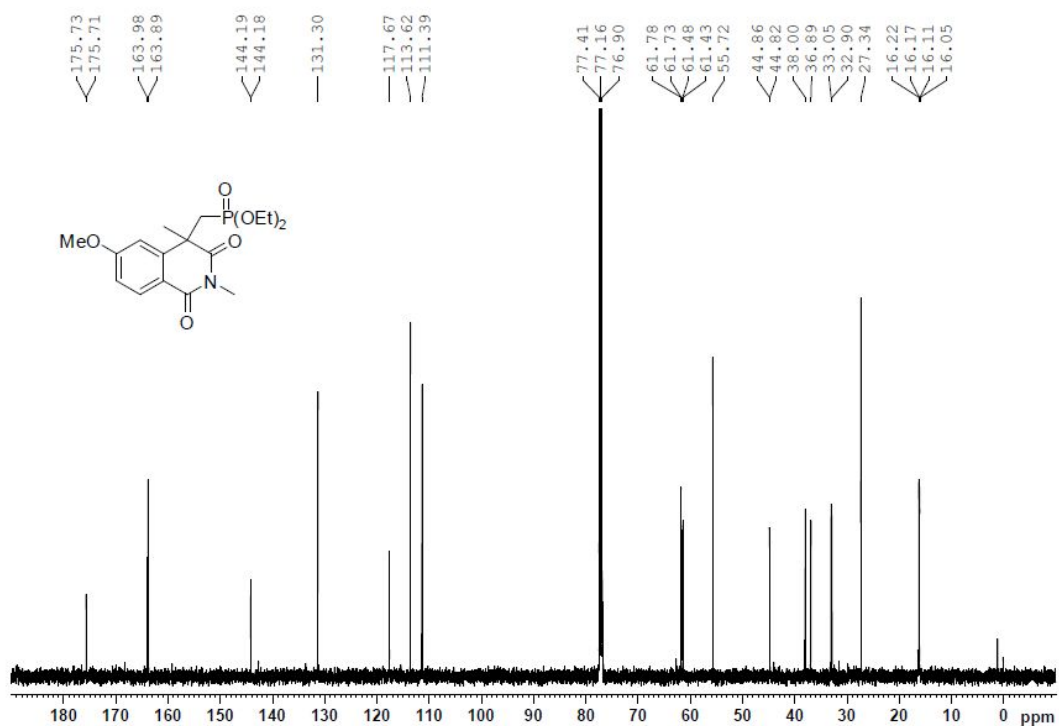
3i



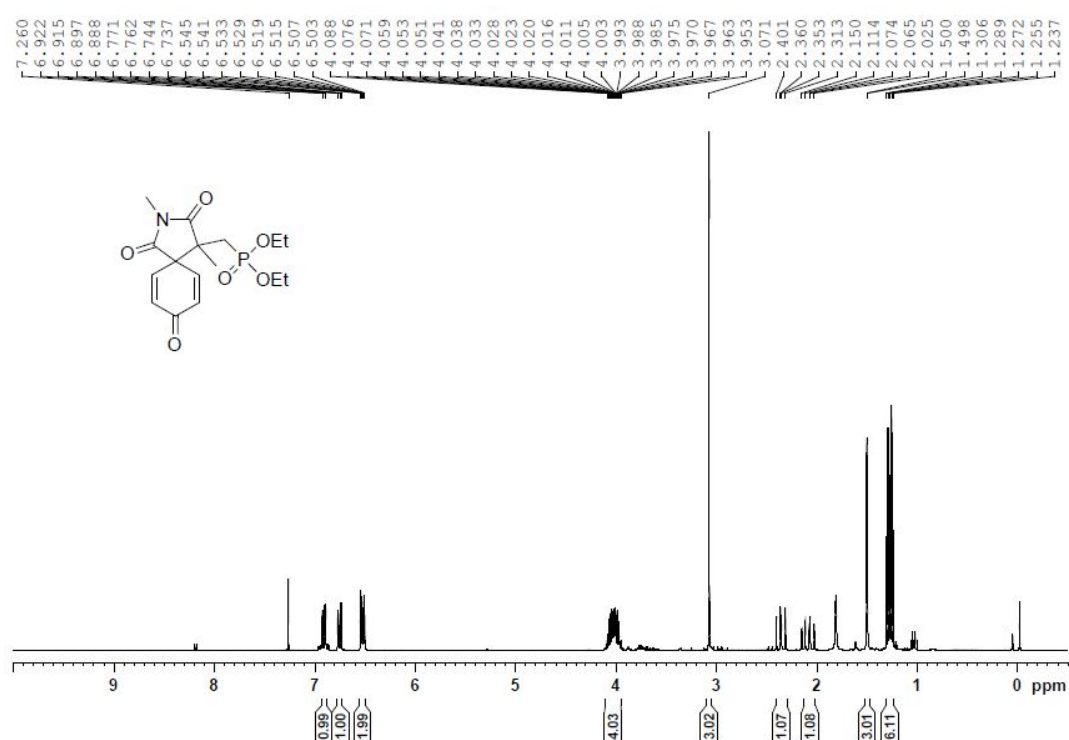
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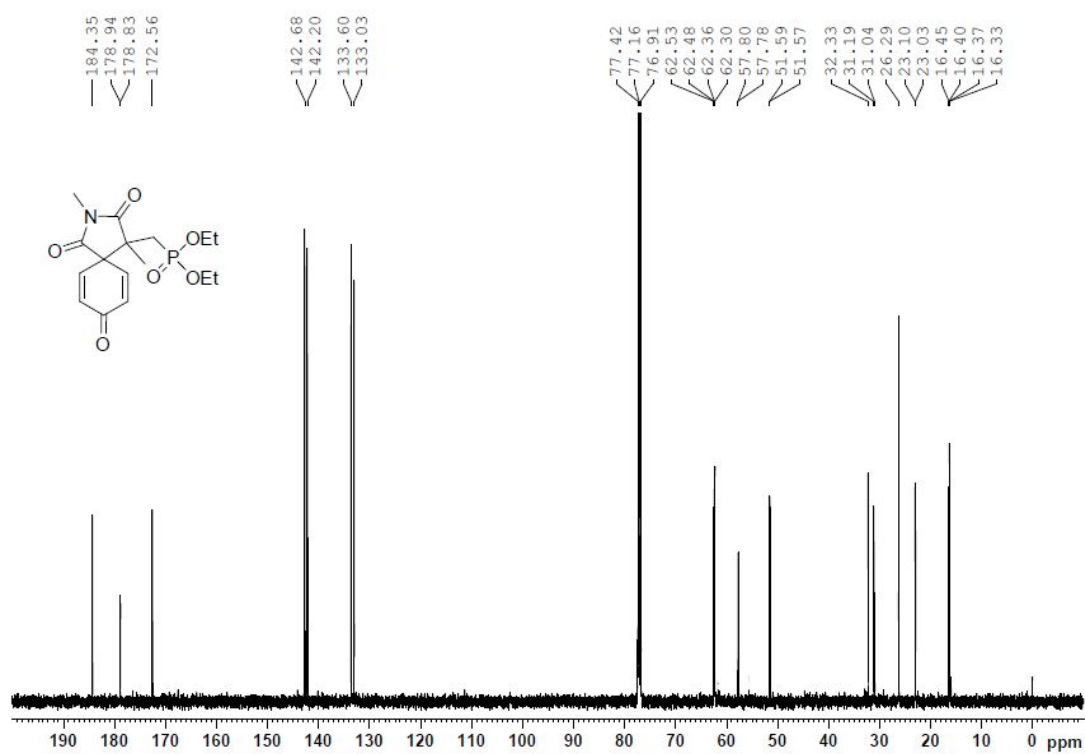
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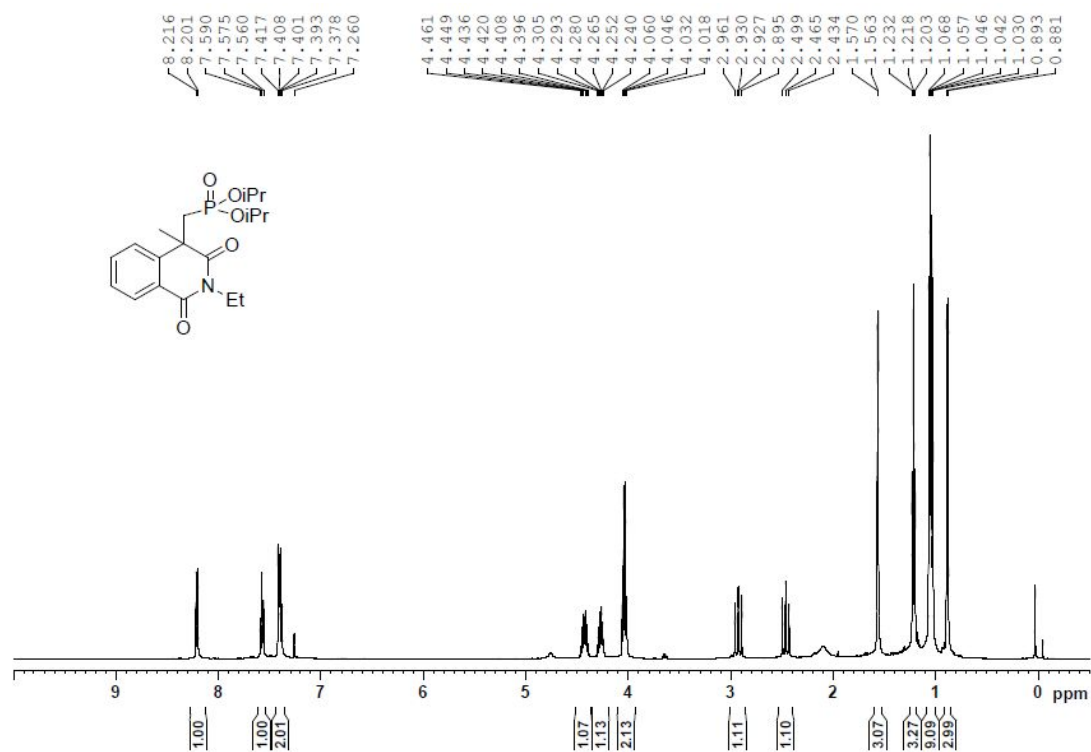
3jb



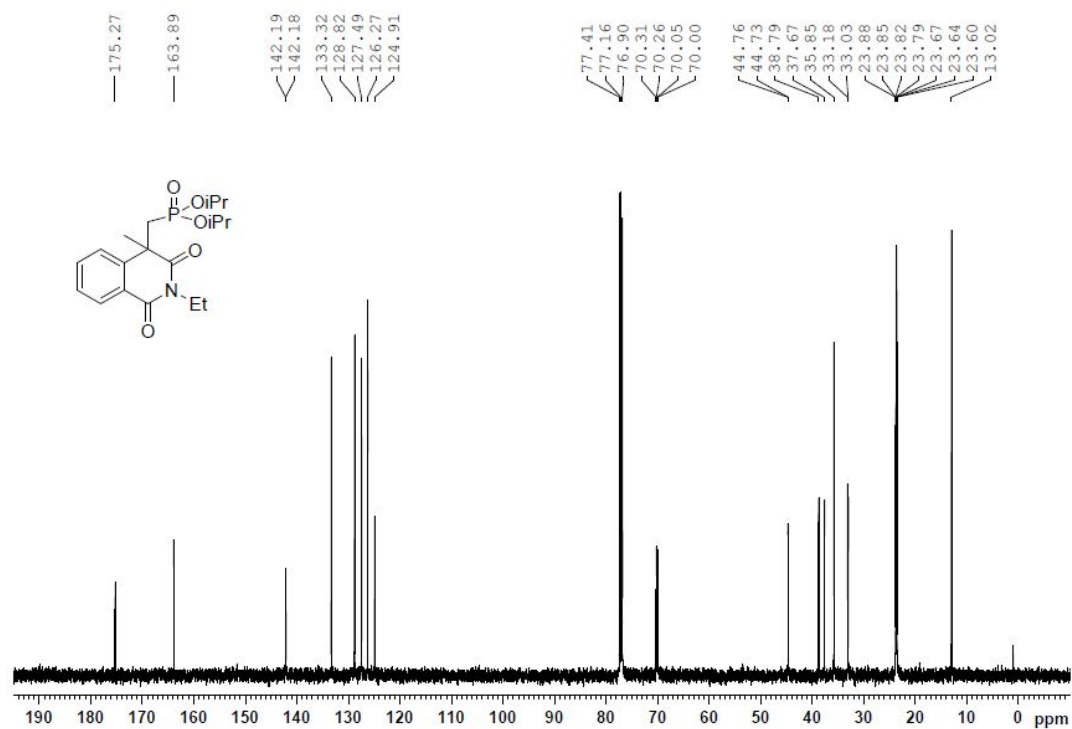
3jb



3k



3k



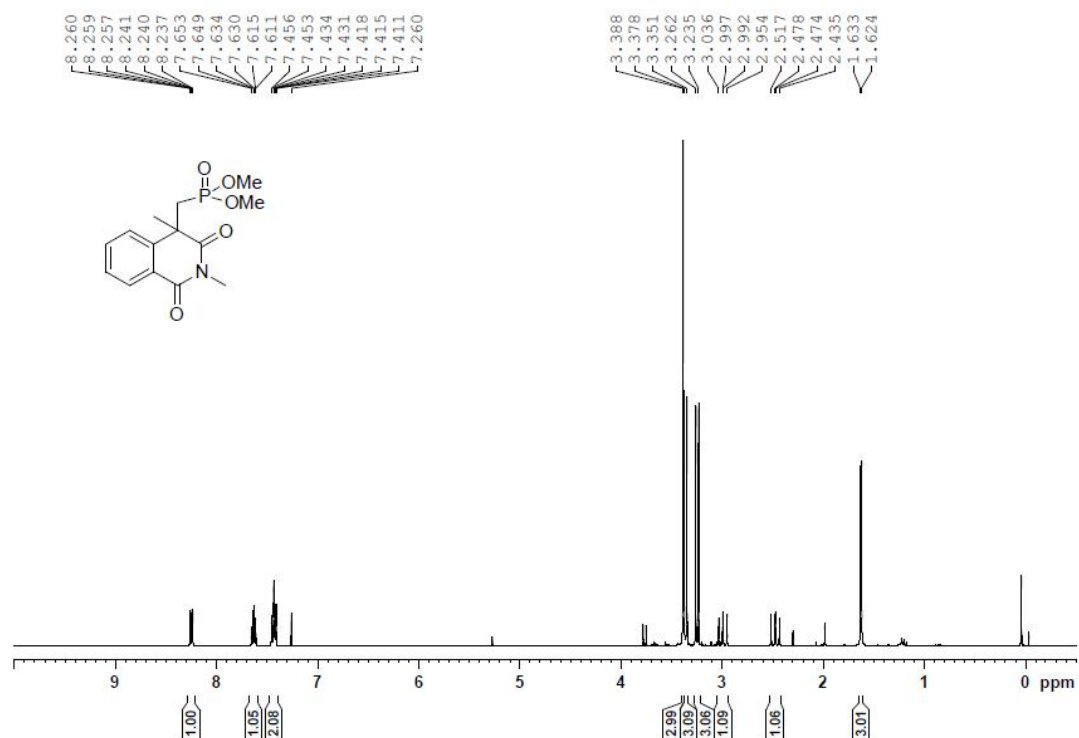
Chemical structure of compound 10 is shown in the inset. The ^1H NMR spectrum (CDCl₃) displays the following peaks (ppm) and integrations:

Chemical Shift (ppm)	Integration
8.196, 8.183, 8.181, 8.181, 7.574, 7.572, 7.557, 7.544, 7.541, 7.402, 7.397, 7.386, 7.382, 7.367, 7.365, 7.266	1.00, 1.09, 2.12
5.194, 5.180, 5.167, 5.153, 5.139, 4.700, 4.467, 4.457, 4.454, 4.445, 4.441, 4.432, 4.429, 4.301, 4.298, 4.289, 4.285, 4.276, 4.273, 4.264, 4.260	1.03, 1.05, 1.06
2.927, 2.924, 2.893, 2.488, 2.457, 2.453, 2.423, 1.561, 1.554, 1.498, 1.485, 1.474, 1.460, 1.107, 1.095, 1.077, 1.064, 1.050, 1.038, 0.897, 0.885	1.07, 1.10, 3.04, 6.03, 9.12, 3.02

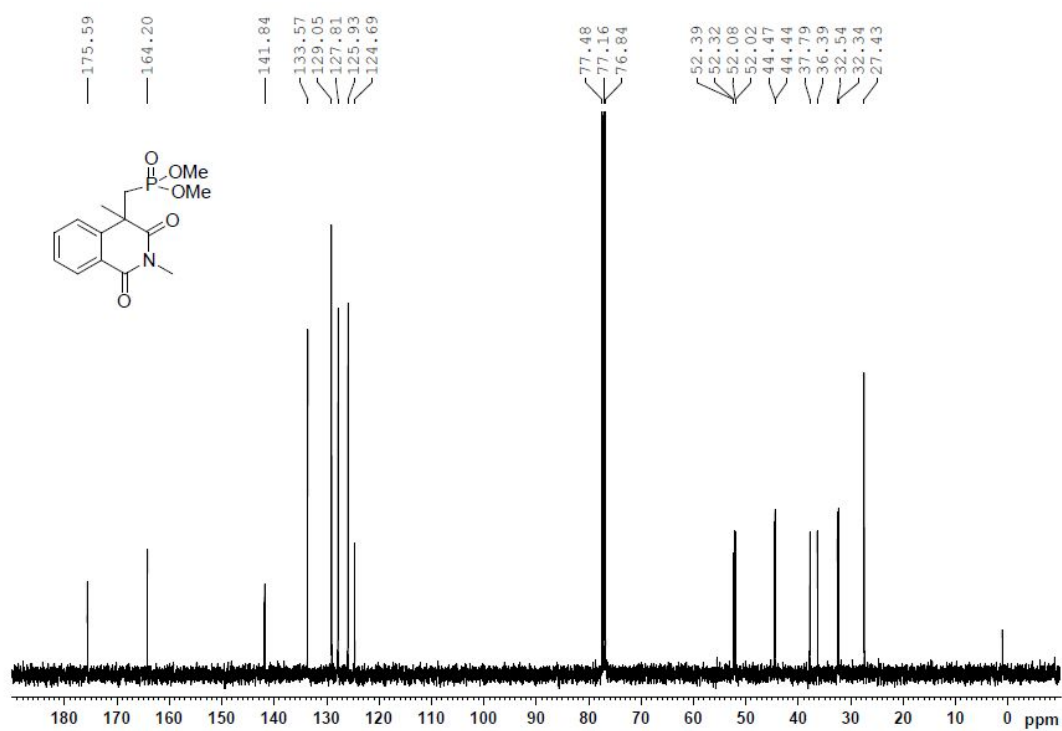
Chemical structure of compound 10 is shown above the ^{13}C NMR spectrum. The spectrum displays peaks corresponding to the following chemical shifts (ppm):

- 175.73
- 175.72
- 164.44
- 142.17
- 142.15
- 133.13
- 128.87
- 127.42
- 126.05
- 125.53
- 77.41
- 77.16
- 76.91
- 70.29
- 70.24
- 69.94
- 69.89
- 45.66
- 45.25
- 45.22
- 38.53
- 37.41
- 33.12
- 32.97
- 23.94
- 23.91
- 23.87
- 23.84
- 23.69
- 23.68
- 23.64
- 19.74
- 19.44

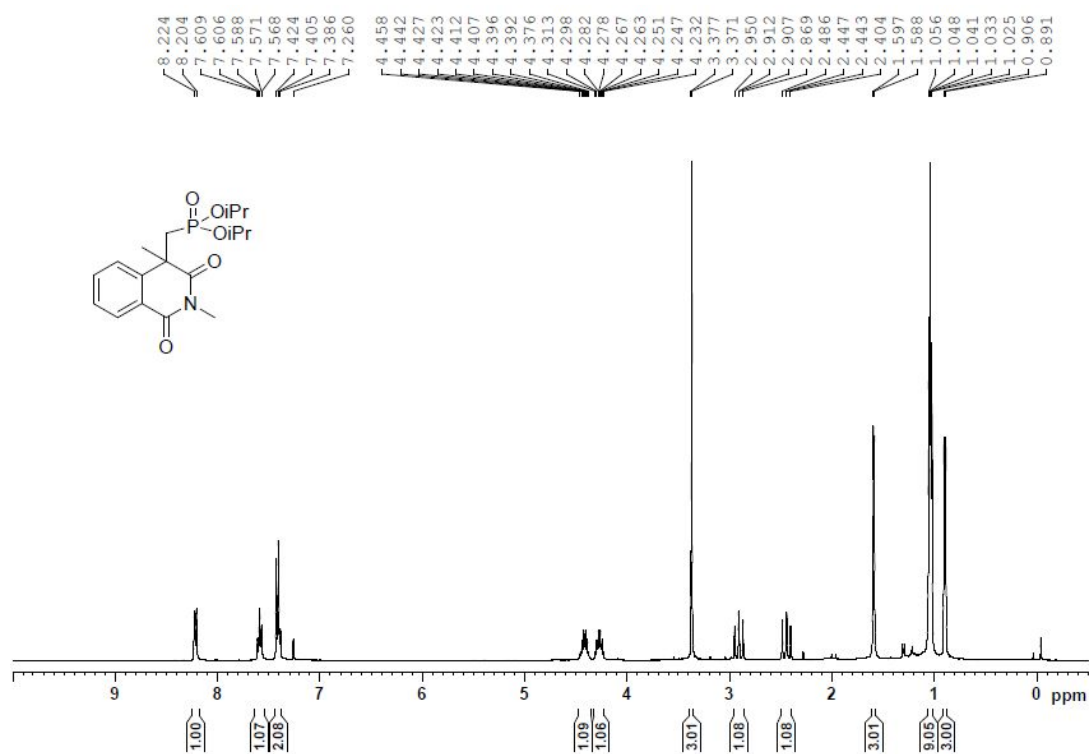
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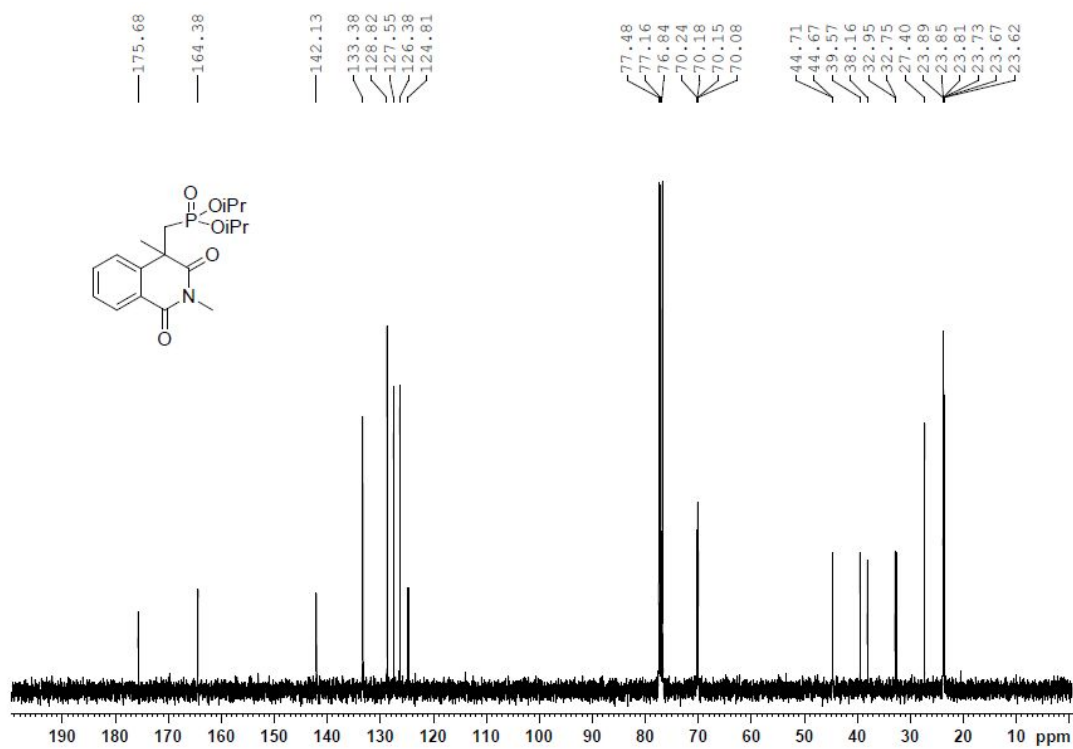
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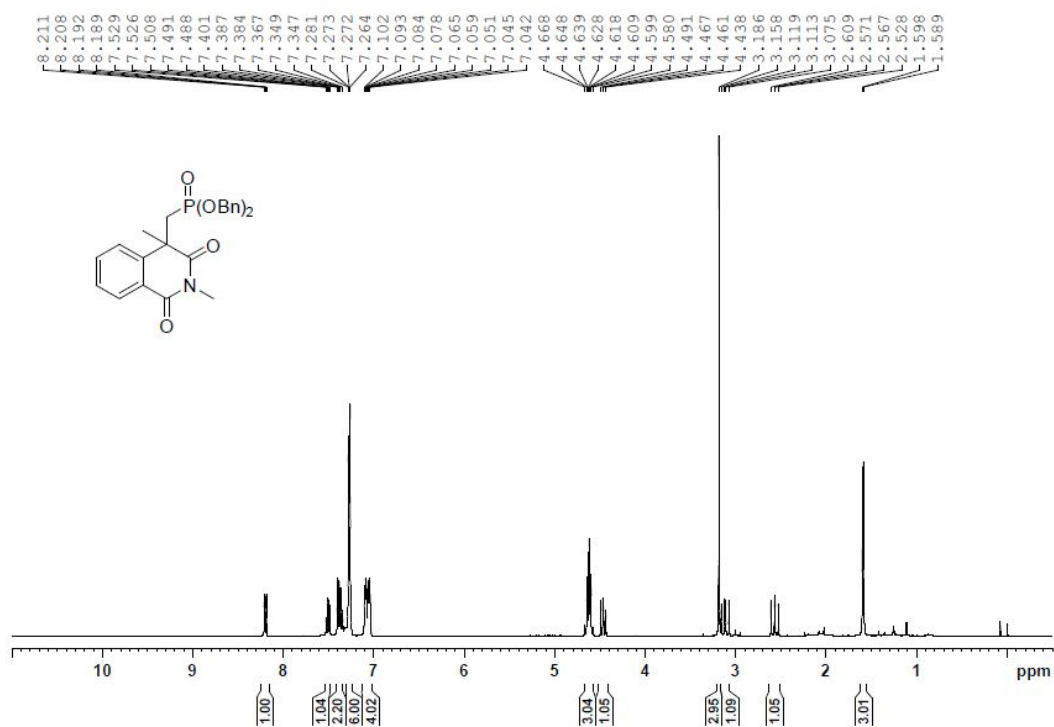
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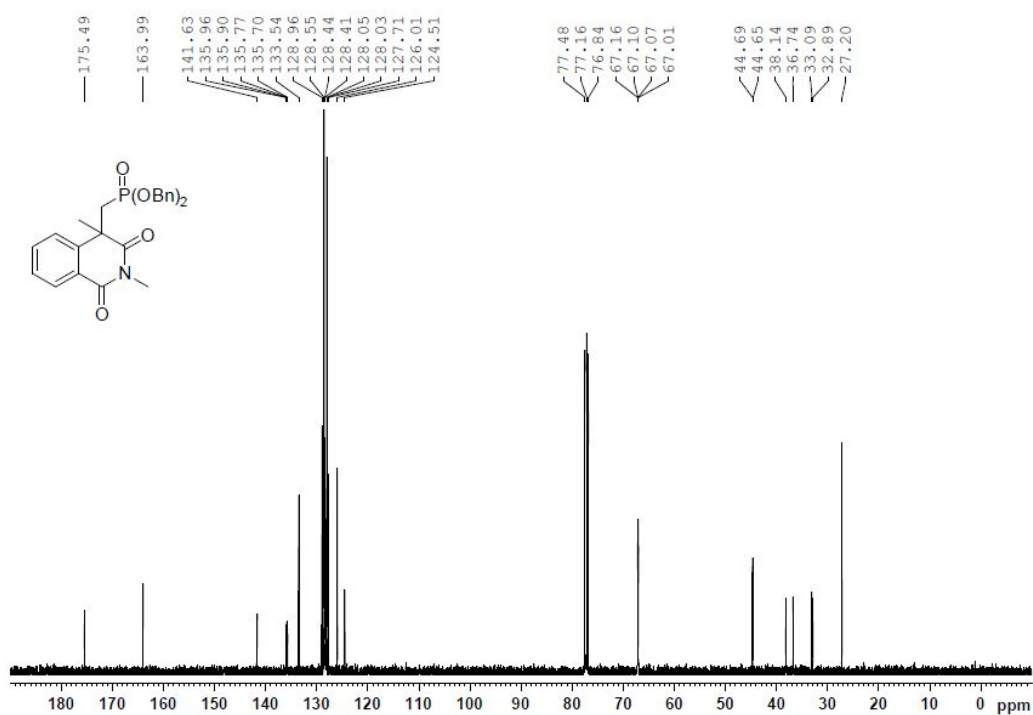
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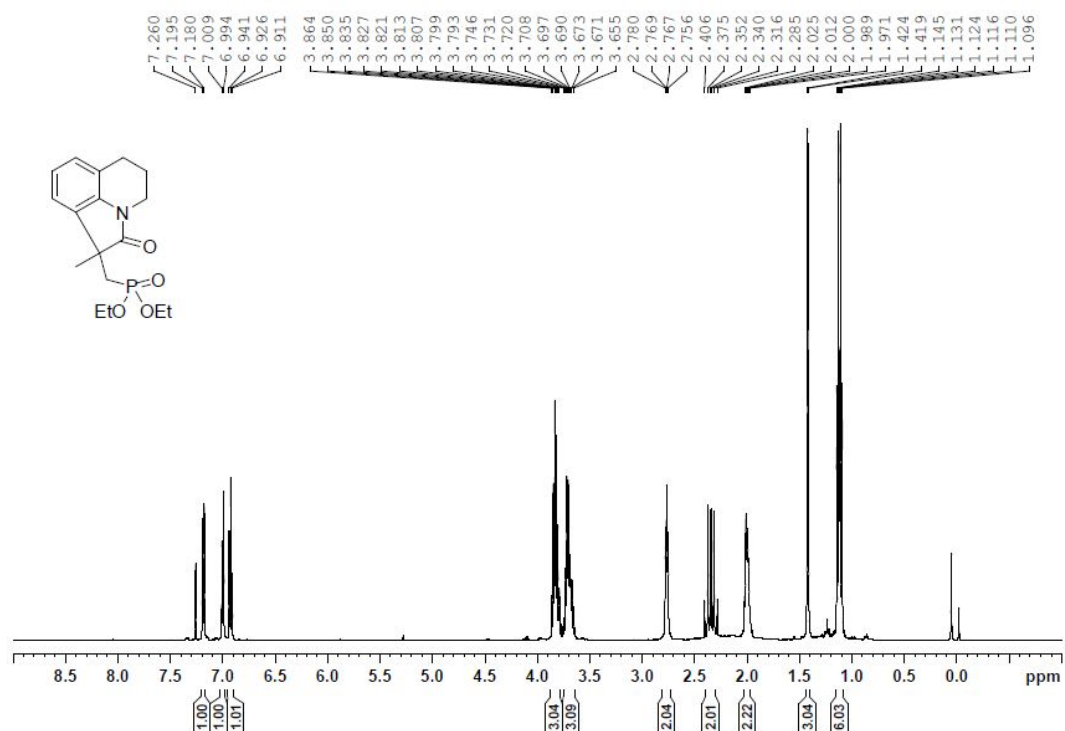
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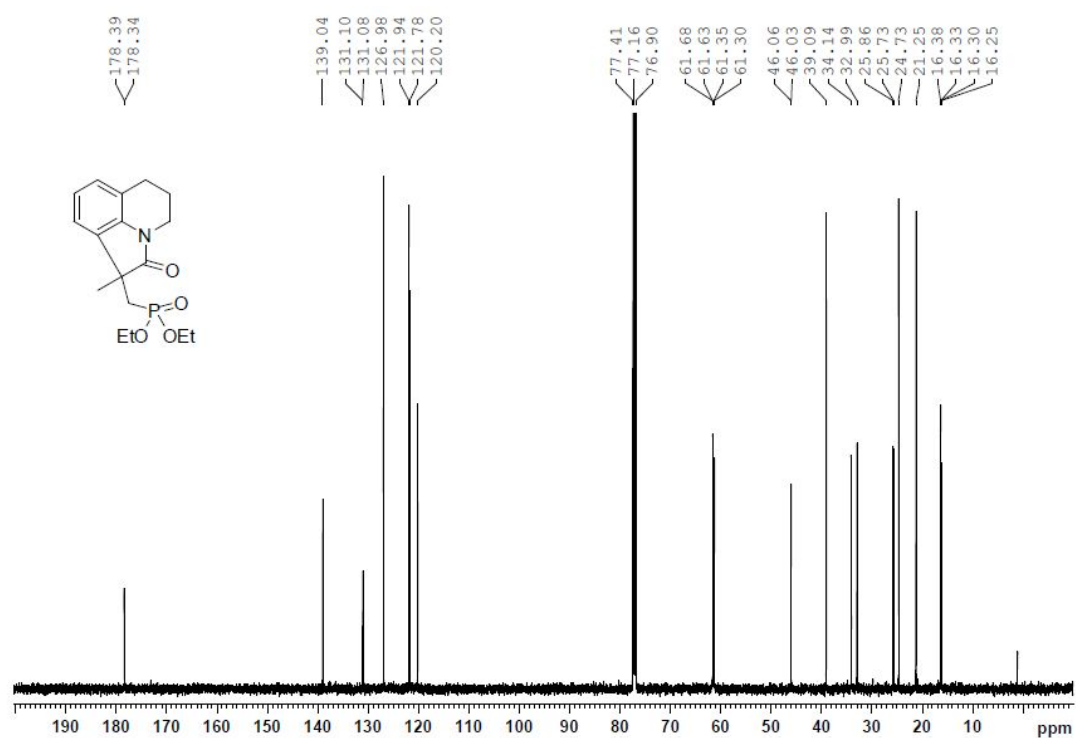
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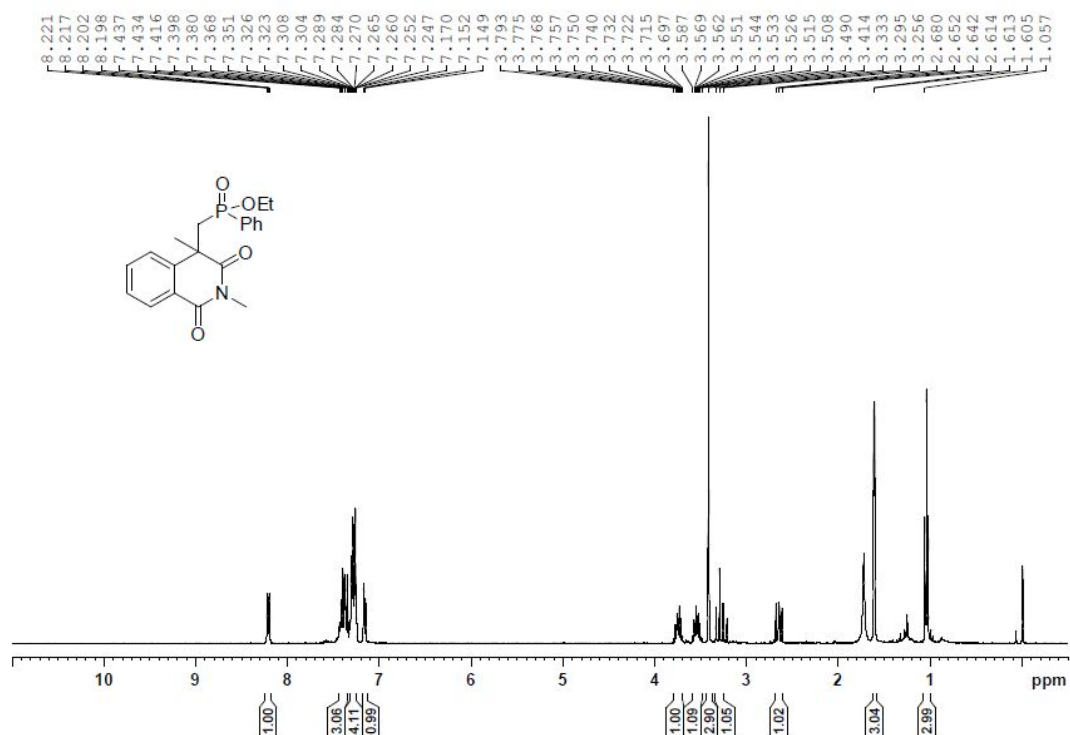
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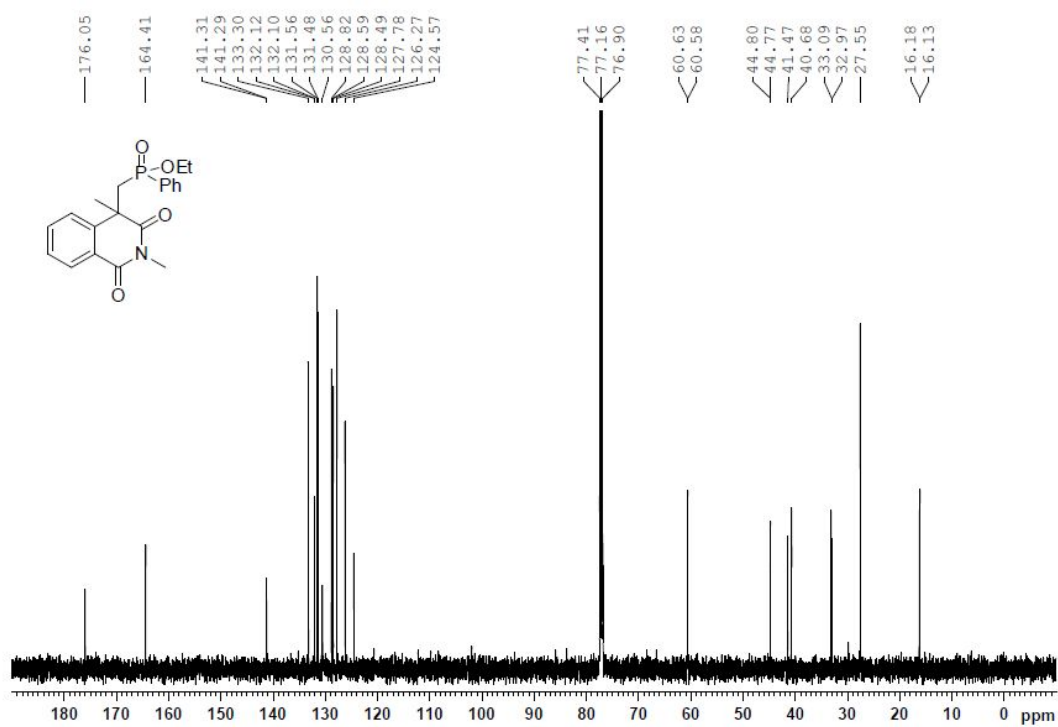
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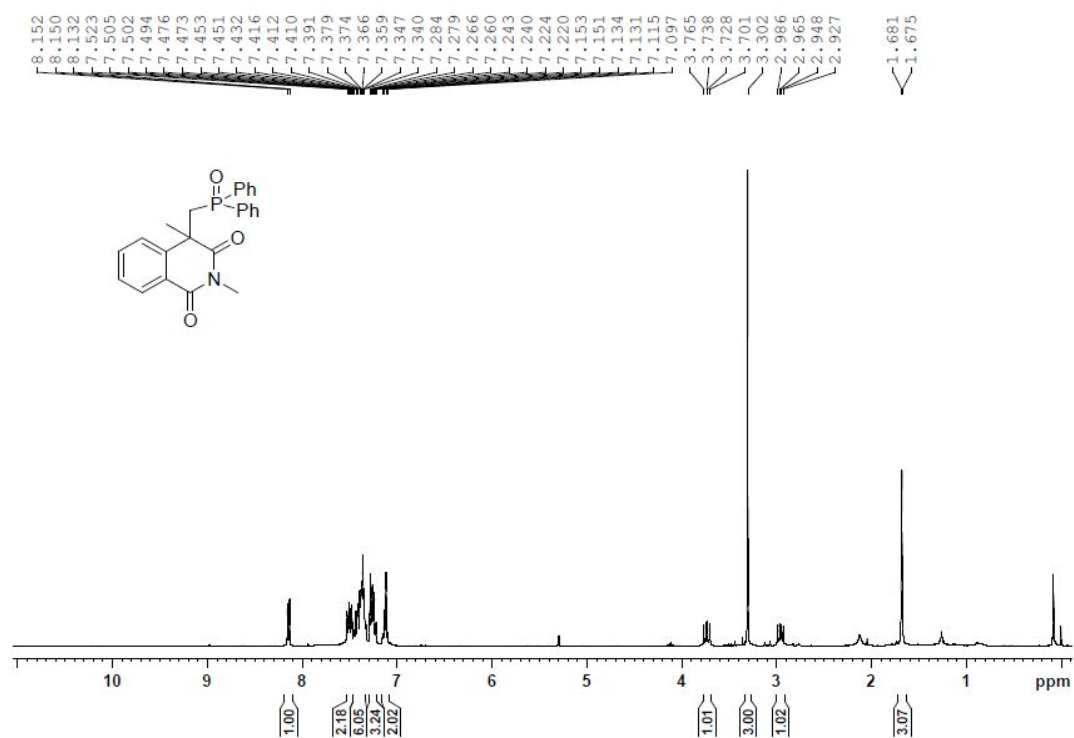
3r



3r



3s



3s

