Supporting Information for

Palladium-catalyzed direct phosphonation of azoles with dialkyl phosphites

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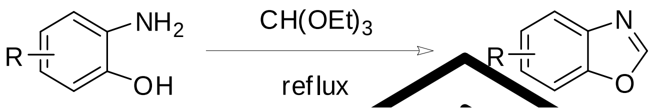
1. General information

All non-aqueous reactions and manipulations were performed using standard Schlenk techniques. All the chemicals were used as received without further purification. All solvents before use were dried and degassed by standard methods. All reactions were monitored by TLC and HPLC. Silica gel was purchased from Qing Dao Hai Lang Chemical Industry Co. NMR spectra of the products were recorded using a Bruker Avance TM Ⅲ spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C in $CDCl_3$ unless otherwise noted. ^{31}P NMR (162 MHz) spectra were taken on Bruker Avance TM Ⅲ spectrometer and were obtained in $CDCl_3$ or CD_3CN with H_3PO_4 ($\delta = 0$ ppm) as internal standard. NMR yields were determined by fine ^{31}P NMR spectra with diphenylphosphine oxide as an internal standard. High resolution mass spectra (HRMS) of the products were obtained on a Bruker Daltonics micrO TOF-Q Ⅱ spectrometer. High performance liquid chromatography (HPLC) analysis was performed by Agilent 1260 Infinity equipped with an Agilent ZORBAX SB-C18 column using aqueous methanol as eluent and 2, 3-dimethylindole as inner standard.

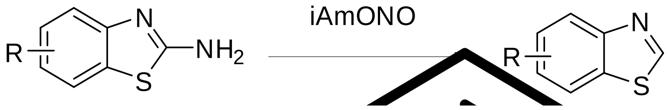
2. General procedures for the synthesis of substituted azoles

General procedure for the preparation of substituted benzoxazole[1]



2-Aminophenol derivative (5 mmol) and triethyl orthoformate(8 mL) were introduced into a 50 mL bake-dried Schlenk tube under an argon atmosphere, and the resulting mixture was refluxed for 12-18 h. After cooling to room temperature, the solvent was removed under reduced pressure, and then the residue was purified by column chromatography, affording the desired products in similar yields with the reported procedure.

General procedure for the preparation of substituted benzothiazole[2]



A 50 mL Schlenk tube was charged with 2-aminobenzothiazole derivative (6.5 mmol) and 10 mL of THF, and then isoamyl nitrite (14.3 mmol) was added slowly into the solution. The resultant mixture was refluxed for 30 minutes, and poured into ice-water, and the resultant aqueous mixture was extracted with ethyl acetate (3×30 mL). The organic extracts were combined and washed with brine, dried over $MgSO_4$, filtered, concentrated in vacuum and purified by column chromatography, giving the desired benzothiazoles in similar yields with the reported procedure.

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[1] S. M. Guo, B. Qian, Y. J. Xie, C. G. Xia and H. M. Huang, *Org. Lett.*, 2011, **13**, 522.

[2] A. Tsuruoka, Y. Kaku, H. Kakinuma, I. Tsukada, M.Yanagisawa, K. Nara and T. Naito, *Chem. Pharm. Bull.*, 1998, **46**, 623.

3. Experimental procedure for the Pd-catalyzed direct phosphonation of azoles

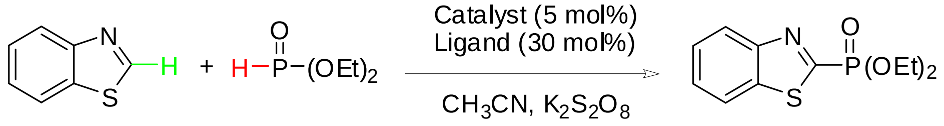
Catalyst (0.025 mmol, 5 mol%), ligand (0.15 mmol, 30 mol%), oxidant (1.5 mmol), azole (0.5 mmol), dialkyl phosphites (1.0 mmol), solvent (3.0 mL) were sequentially introduced into a 25 mL bake-dried Schlenk tube, and the resulting mixture was stirred in a preheated oil bath at 100 °C for 24h. Reaction mixture was cooled to r. t. and diluted with NH_4Cl solution, and then the aqueous solution was extracted with ethyl acetate (3×15 mL). The organic extracts were combined and dried over $MgSO_4$, filtered and concentrated in vacuum. The crude product was purified by column chromatography on silica gel (dichloromethane/petroleum ether 1:3−5:1), giving the desired 2-phosphonated azoles as an oil or pale yellow solid.

4. Optimization of the reaction conditions

L1 **L2** **L3** **L4**

L5 **L6** **L7** **L8**

Table S1: **Screening of catalysts**[a]



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

Entry	Catalyst	Ligand	Yield[b](%)
1	$Pd(OAc)_2$	-	12
2	**$Pd(OAc)_2$**	**L1**	**56**
3	$PdCl_2$	L1	27
4	$Pd(TFA)_2$	L1	47
5	$Pd(COD)Cl_2$	L1	47
6	$[Rh(COD)Cl]_2$	L1	12
7	$CuBr_2$	L1	Trace
8	CuI	L1	Trace

[a] General conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), catalyst (5 mol%), ligand (30 mol%), $K_2S_2O_8$ (1.5 mmol), CH_3CN (3.0 mL), 24 h, 100 ℃, air atmosphere. [b]HPLC yields using 2, 3-dimethylindole as an internal standard.

***Table S2:* Screening of oxidants**[a]

Entry	Oxidant	Yield[b](%)
1	**$K_2S_2O_8$**	**56**
2	I_2	7
3	$PhI(OAc)_2$	<5
4	Benzoyl peroxide	8
5	1,4-Benzoquinone	<5
6	Ag_2O	<5
7	AgOAc	5
8	TBP	<5
9	TBHP	<5
10	H_2O_2	<5
11	$Cu(OAc)_2$	<5
12	$CuBr_2$	<5

[a] General conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), $Pd(OAc)_2$ (5 mol%), **L1** (30 mol%), oxidant (1.5 mmol), CH_3CN (3.0 mL), 24 h, 100 ℃, air atmosphere. [b] HPLC yields using 2, 3-dimethylindole as an internal standard.

***Table S3:* Screening of Solvents**[a]

Entry	Solvent	Yield[b](%)
1	**CH_3CN**	**56**
2	CH_3OH	<5
3	Toluene	5
4	THF	9
5	NMP	<5
6	1,4-Dioxane	8
7	EtOAc	13
8	CH_3CN/Water (4/1)	21

[a] General conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), $Pd(OAc)_2$ (5 mol%), **L1** (30 mol%), $K_2S_2O_8$ (1.5 mmol), solvent (3.0 mL), 24 h, 100 ℃, air atmosphere. [b] HPLC yields using 2, 3-dimethylindole as an internal standard.

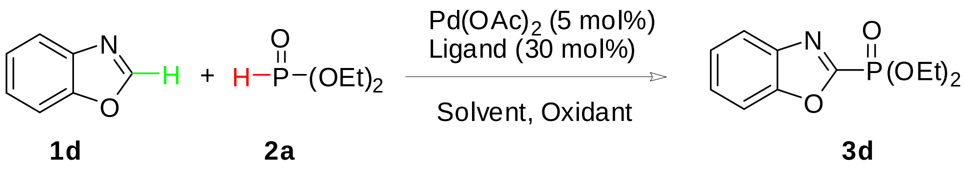
***Table S4:* Screening of Ligands**[a]

Entry	Ligand	Yield[b](%)
1	L2	48
2	L2 (10 mol%)	41
3	L1 (100 mol%)	33
4	L1 (50 mol%)	56
5	**L1**	**56**
6	L1(20 mol%)	53
7	L1(10 mol%)	43
8	L3	54
9	L4	34
10	L5	23
11	L6	41
12	L7	55
13	L8	16
14	Phenprobamate	34
15	Iminodiacetic acid	40
16	D-Alanine	43
17	Lactic acid	10
18	Malonic acid	22
19	Picolinic acid	23
20	Indole-2-carboxylic acid	16

21	2,6-Pyridinedicarboxylic acid	26

[a] General conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), $Pd(OAc)_2$ (5 mol%), ligand (30 mol%), $K_2S_2O_8$ (1.5 mmol), CH_3CN (3.0 mL), 24 h, 100 ℃, air atmosphere. [b] HPLC yields using 2, 3-dimethylindole as an internal standard.

Table S5: Optimization C-P bond formation of Substituted benzoxazole[a]



Entry	Ligand	Solvent	Oxidant	Yield[b](%)
1	NO	CH_3CN	$K_2S_2O_8$	8
2	**L1**	**CH_3CN**	**$K_2S_2O_8$**	**15**
3	L2 (20 m%)	CH_3CN	$K_2S_2O_8$	57
4	**L2**	**CH_3CN**	**$K_2S_2O_8$**	**60**
5	L2 (50 m%)	CH_3CN	$K_2S_2O_8$	56
6[c]	L2	CH_3CN	$K_2S_2O_8$	39
7[d]	L2	CH_3CN	$K_2S_2O_8$	12
8[e]	L2	CH_3CN	$K_2S_2O_8$	<5
9[f]	L2	CH_3CN	$K_2S_2O_8$	37
10[g]	L2	CH_3CN	$K_2S_2O_8$	49
11[h]	L2	CH_3CN	$K_2S_2O_8$	59
12	L2	Toluene	$K_2S_2O_8$	<5
13	L2	1,4-Dioxane	$K_2S_2O_8$	<5
14	L2	1,2-Dimethoxyethane	$K_2S_2O_8$	<5
15	L2	CH_3CN	TBHP	<5
16	L2	CH_3CN	$PhI(OAc)_2$	<5
17	L2	CH_3CN	1,4-Benzoquinone	<5
18	L3	CH_3CN	$K_2S_2O_8$	61
19	L4	CH_3CN	$K_2S_2O_8$	26
20	L5	CH_3CN	$K_2S_2O_8$	18
21	L6	CH_3CN	$K_2S_2O_8$	32
22	L7	CH_3CN	$K_2S_2O_8$	43
23	L8	CH_3CN	$K_2S_2O_8$	19

[a] General conditions: benzoxazole (**1d**) (0.5 mmol), **2a** (1.0 mmol), $Pd(OAc)_2$ (5 mol%), ligand (30 mol%), oxidant (1.5 mmol), solvent (3.0 mL), 24 h, 100 ℃, argon atmosphere. [b] ^{31}P NMR yields using an internal standard. [c] Air atmosphere. [d] Oxygen atmosphere. [e] 80 ℃. [f] 120 ℃. [g] 18 h. [h] 30 h.

5. Experiments for the investigation of mechanism

5.1 Pd-catalyzed direct phosphonation of 1a with 2a in the presence of a radical scavenger (TEMPO)

A 25 mL bake-dried Schlenk tube was charged with $Pd(OAc)_2$ (0.025 mmol, 5 mol%), **L1** (0.15 mmol, 30 mol%), $K_2S_2O_8$ (1.5 mmol), **1a** (0.5 mmol), **2a** (1.0 mmol), **TEMPO (0.5 mmol, 1.0 equiv.)** and 3.0 mL of CH_3CN. The resulting mixture was stirred in a preheated oil bath at 100 °C for 24 h. The crude reaction mixture was analyzed by HPLC and a 51% yield of **3a** was obtained. **This controll experiment possibly suggests that current oxidative C-P bond forming reaction may not be a radical involving reaction.**

5.2 The effect of addition of Et_3N for the Pd-catalyzed direct phosphonation of 1a with 2a

A 25 mL bake-dried Schlenk tube was charged with $Pd(OAc)_2$ (0.025 mmol, 5 mol%), **L1** (0.15 mmol, 30 mol%.), $K_2S_2O_8$ (1.5 mmol), **1a** (0.5 mmol), **2a** (1.0 mmol), **Et_3N (1.0 mmol, 2.0 equiv.)** and 3.0 mL of CH_3CN. The resulting mixture was stirred in a preheated oil bath at 100 °C for 24 h. The crude reaction mixture was analyzed by HPLC and an 18% yield of **3a** was obtained. **This experiment possibly indicates that the addition of a base (Et_3N) significantly obstructed the phosphonation, which is opposite to the radical C-P formation wherein base would help the abstraction of the H^+ from dialkyl H-phosphonate cation radical and increase the catalytic activity.**

5.3 The effect of addition of CH_3COOH for the Pd-catalyzed direct phosphonation of 1a with 2a

A 25 mL bake-dried Schlenk tube was charged with $Pd(OAc)_2$ (0.025 mmol, 5 mol%), **L1** (0.15 mmol, 30 mol%.), $K_2S_2O_8$ (1.5 mmol), **1a** (0.5 mmol), **2a** (1.0 mmol), **CH_3COOH (1.0 mmol, 2.0 equiv.)** and 3.0 mL of CH_3CN. The resulting mixture was stirred in a preheated oil bath at 100 °C for 24 h. The crude reaction mixture was analyzed by HPLC and an 8% yield of **3a** was obtained. **This experiment possibly suggests that the introducing of additional acid such as CH_3COOH into the reaction will greatly reduced the reactivity, which is inconsistent with Larhed's results.**

5.4 ESI-MS experiment for the Pd-catalyzed direct phosphonation of 1a with 2b

$Pd(OAc)_2$ (0.05 mmol, 5 mol%), **L2** (0.3 mmol, 30 mol%), **1a** (1.0 mmol), diisopropyl phosphate (**2b**) (2.0 mmol), $K_2S_2O_8$ (3.0 mmol) and CH_3CN (6.0 mL) were introduced into a 25 mL bake-dried tube under air. The resulting mixture was stirred in a preheated oil bath at 100 °C. The aliquots were taken from the reaction mixture at 20 min, 60 min after the start of reaction and diluted ten times with CH_3CN before ESI-MS analysis.

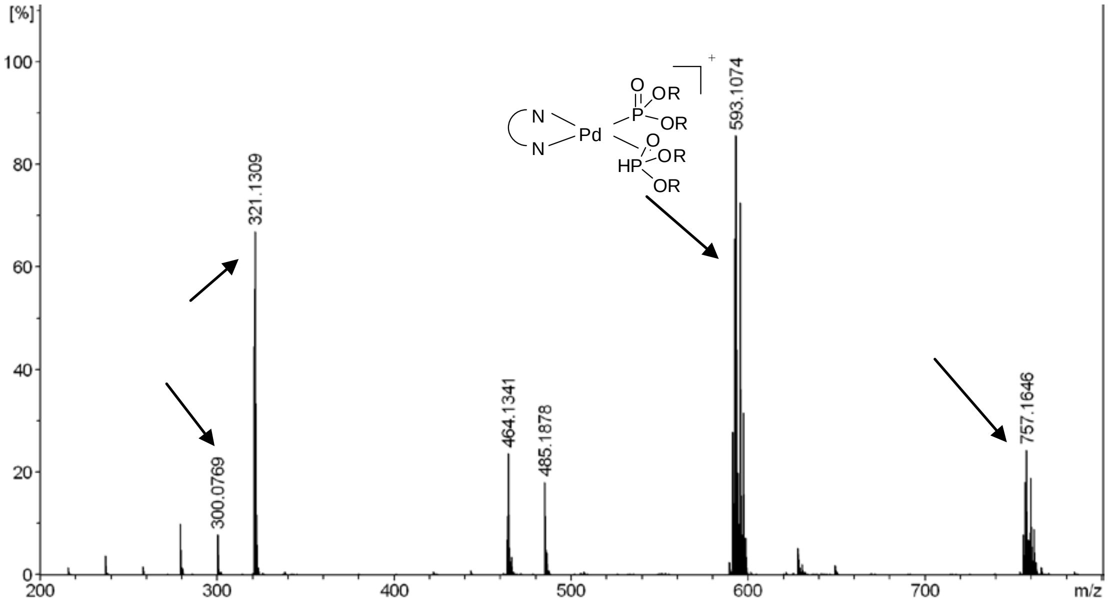


Figure S1 ESI-MS spectrum of the reaction mixture (20 min).

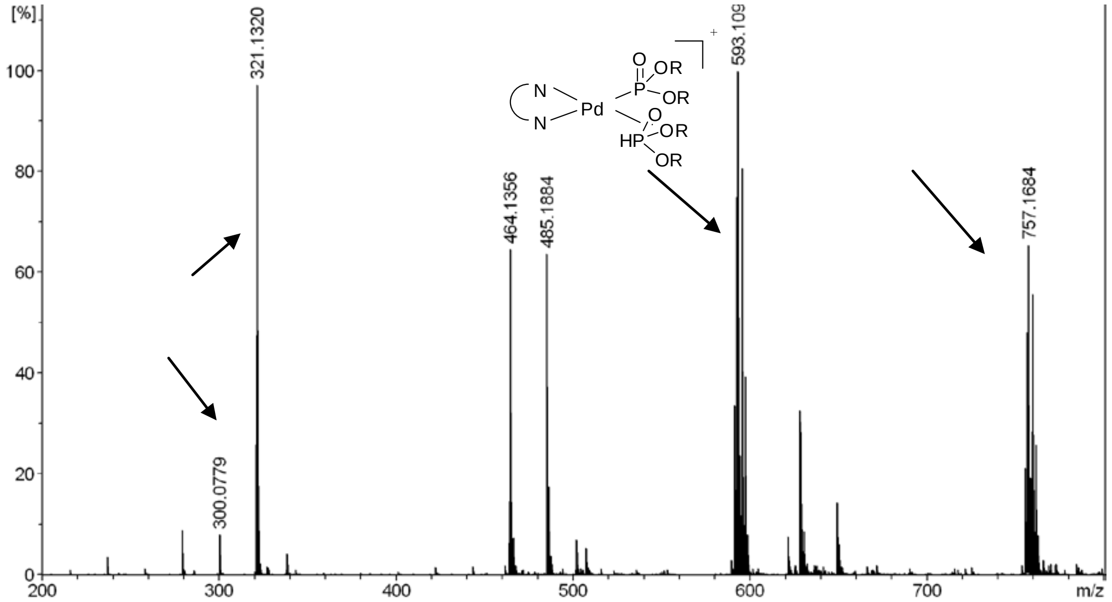


Figure S2 ESI-MS spectrum of the reaction mixture (60 min).

Figure S1 and S2 showed that two Pd species (**B** and **E**) were clearly detected and they are dominant in the reaction mixture

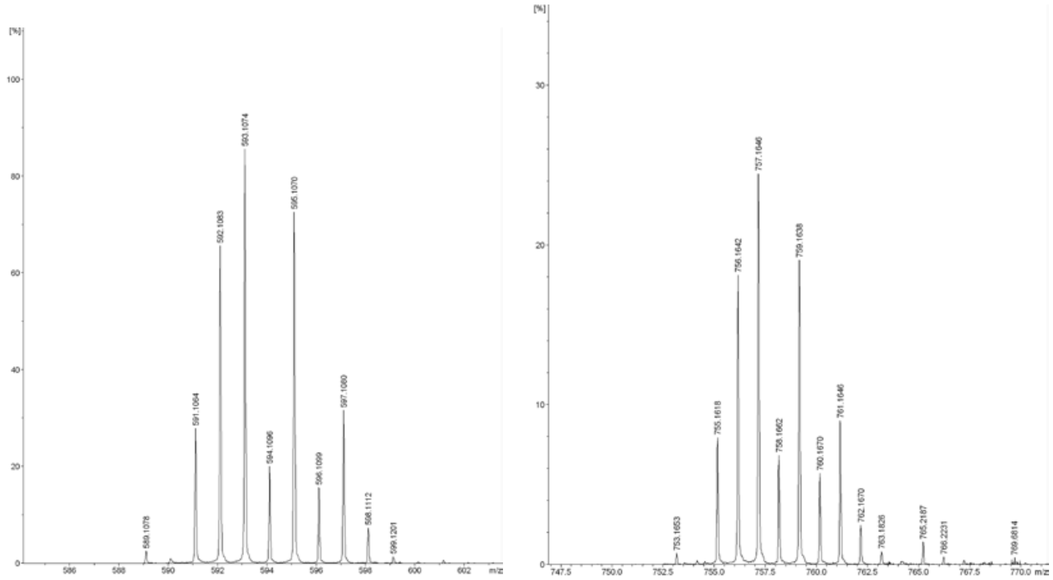


Figure S3 The magnification of peak around m/z 593 and 757.

This figure demonstrates that these two peaks (m/z 593 of **B** and m/z 757 of **E**) are monocationic Pd species.

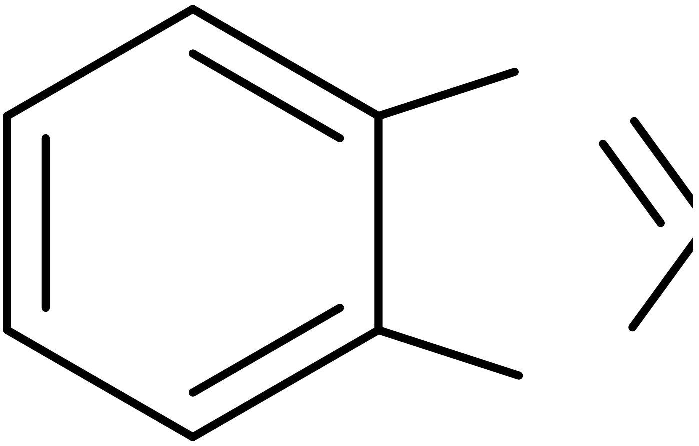


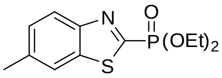
Figure S4 Proposed mechanism for the direct phosphonation of azole with dialkyl phosphite.

6. Characterization data for products

Diethyl benzothiazole-2-ylphosphonate (3a)

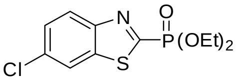
A light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.9 Hz, 1H), 8.14 – 7.95 (m, 1H), 7.57 (m, 2H), 4.33 (m, 4H), 1.40 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9 (s), 154.7 (s), 154.5 (s), 136.42 (s), 126.9 (d, *J* = 16.1 Hz), 125.0 (s), 122.0 (d, *J* = 1.5 Hz), 64.1 (d, *J* = 5.9 Hz), 16.3 (d, *J* = 6.3 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ 4.07 (s). HRMS (ESI) Calcd for $C_{11}H_{14}NNaO_3PS$: $[M+Na]^+$, 294.0324; Found: 294.0318

Diethyl 6-methylbenzothiazole-2-ylphosphonate (3b)



A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.5 Hz, 1H), 7.79 (s, 1H), 7.39 (dd, *J* = 8.5, 1.2 Hz, 1H), 4.44 – 4.21 (m, 4H), 2.53 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR(101 MHz, $CDCl_3$) δ 159.9 (s), 153.00 (s), 152.7 (s), 137.5 (s), 136.8 (s), 128.7 (s), 124.4 (s), 121.5 (d, *J* = 1.7 Hz), 64.0 (d, *J* = 5.9 Hz), 21.7 (s), 16.3 (d, *J* = 6.3 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ 4.38 (s). HRMS (ESI) Calcd for $C_{12}H_{16}NNaO_3PS$: $[M+Na]^+$, 308.0481; Found: 308.0478.

Diethyl 6-chlorobenzothiazole-2-ylphosphonate (3c)



A brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.8 Hz, 1H), 7.99 (s, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 4.49 – 4.21 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0 (s), 159.6 (s), 137.6 (d, *J* = 1.6 Hz), 133.3 (s), 127.9 (s), 125.6 (s), 121.5 (d, *J* = 1.6 Hz), 64.3 (d, *J* = 5.9 Hz), 16.3 (d, *J* = 6.2 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ 3.37 (s). HRMS (ESI) Calcd for $C_{11}H_{13}ClNClNaO_3PS$: $[M+Na]^+$, 327.9934; Found: 327.9936.

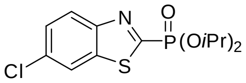
Diisopropyl benzothiazole-2-ylphosphonate (3d)

A pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 – 8.14 (m, 1H), 8.08 – 7.94 (m, 1H), 7.67 – 7.43 (m, 2H), 4.93 (m, 1.4 Hz, 2H), 1.43 (d, *J* = 6.2 Hz, 6H), 1.34 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7 (s), 160.29 (s), 154.8 (s), 154.5 (s), 136.5 (d, *J* = 1.4 Hz), 126.8 (d, *J* = 13.2 Hz), 124.9 (s), 121.9 (d, *J* = 1.5 Hz), 73.2 (d, *J* = 6.0 Hz), 24.1 (d, *J* = 4.1 Hz), 23.8 (d, *J* = 5.0 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ 1.97 (s). HRMS (ESI) Calcd for $C_{13}H_{18}NNaO_3PS$: $[M+Na]^+$, 322.0637; Found: 322.0634.

Diisopropyl 6-methylbenzothiazole-2-ylphosphonate (3e)

A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.70 (s, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 4.83 (m, 2H), 2.45 (s, 3H), 1.35 (d, *J* = 6.2 Hz, 6H), 1.26 (d, *J* = 6.2 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3 (s), 158.9 (s), 137.3 (s), 136.8 (d, *J* = 1.3 Hz), 128.5 (s), 124.4 (s), 121.4 (d, *J* = 1.6 Hz), 73.1 (d, *J* = 5.9 Hz), 24.0 (d, *J* = 4.1 Hz), 23.8 (d, *J* = 4.9 Hz), 21.7 (s). ^{31}P NMR (162 MHz, $CDCl_3$) δ 2.27 (s). HRMS (ESI) Calcd for $C_{14}H_{20}NNaO_3PS$: $[M+Na]^+$, 336.0795; Found: 336.0794.

Diisopropyl 6-chlorobenzothiazole-2-ylphosphonate (3f)



A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 2.0 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.0 Hz, 1H), 4.93 (ddd, *J* = 12.4, 6.2, 1.3 Hz, 2H), 1.44 (d, *J* = 6.2 Hz, 6H), 1.35 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4 (s), 161.0 (s), 137.6 (d, *J* = 1.4 Hz), 133.2 (s), 127.8 (s), 125.6 (s), 121.5 (d, *J* = 1.7 Hz), 73.4 (d, *J* = 6.0 Hz), 24.0 (d, *J* = 4.1 Hz), 23.8 (d, *J* = 4.9 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ 1.32 (s). HRMS (ESI) Calcd for $C_{13}H_{17}ClNNaO_3PS$: $[M+Na]^+$, 356.0255; Found: 356.0247.

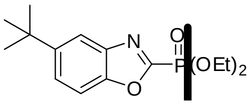
Diethyl benzoxazole-2-ylphosphonate (3g)

A tan oil. ^{1}H NMR (400 MHz, CDCl3) δ 7.87 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.46 (m, 2H), 4.51 – 4.29 (m, 4H), 1.44 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, CDCl3) δ 155.4 (s), 151.1 (d, J = 5.8 Hz), 140.2 (d, J = 16.3 Hz), 127.4 (s), 125.3 (s), 121.6 (s), 111.6 (s), 64.6 (d, J = 5.8 Hz), 16.3 (d, J = 6.3 Hz).^{31}P NMR (162 MHz, CDCl3) δ -2.17 (s). HRMS (ESI) Calcd for $C_{11}H_{14}NNaO_4P$: $[M+Na]^+$, 278.0553; Found: 278.0551.

Diethyl 5-methylbenzoxazole-2-ylphosphonate (3h)

A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 9.6 Hz, 1H), 4.46 – 4.27 (m, 4H), 2.50 (s, 3H), 1.43 (td, *J* = 7.1, 0.4 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0 (s), 155.4 (s), 149.4 (d, *J* = 5.9 Hz), 135.4 (d, *J* = 0.9 Hz), 128.8(s), 121.2 (s), 110.9 (s), 64.6 (d, *J* = 5.8 Hz), 21.5 (s), 16.3 (d, *J* = 6.3 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ -1.95 (s). HRMS (ESI) Calcd for $C_{12}H_{16}NNaO_4P$: $[M+Na]^+$, 292.0709; Found: 292.0709.

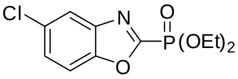
Diethyl 5-tert-butylbenzoxazole-2-ylphosphonate (3i)



A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.57 (d, *J* = 1.0 Hz, 2H), 4.50 – 4.28 (m, 4H), 1.44 (dd, *J* = 7.3, 6.9 Hz, 6H), 1.39 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1 (s), 155.4 (s), 149.1 (dd, *J* = 14.3, 3.3 Hz), 140.2 (d, *J* = 16.3 Hz), 125.5 (s), 117.74 (s), 110.7 (s), 64.5

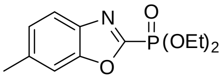
(d, *J* = 5.9 Hz), 35.0 (s), 31.7 (s), 16.3 (d, *J* = 6.3 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ -2.08 (s). HRMS (ESI) Calcd for $C_{12}H_{22}NNaO_4P$: $[M+Na]^+$, 334.1179; Found: 334.1179.

Diethyl 5-chlorobenzoxazole-2-ylphosphonate (3j)



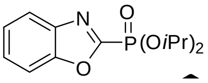
A tan oil. ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.85 (d, *J* = 2.0 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.47 (m, 1H), 4.50 – 4.30 (m, 4H), 1.45 (td, *J* = 7.1, 0.5 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9 (s), 149.7 (d, *J* = 5.9 Hz), 141.3 (d, *J* = 16.5 Hz), 131.0 (d, *J* = 1.5 Hz), 127.9 (s), 121.4 (s), 112.4 (s), 64.8 (d, *J* = 5.9 Hz), 16.3 (d, *J* = 6.2 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ -2.89 (s). HRMS (ESI) Calcd for $C_{11}H_{13}ClNNaO_4P$: $[M+Na]^+$, 312.0156; Found: 312.0163.

Diethyl 6-methylbenzoxazole-2-ylphosphonate (**3k**)



A brown oil. ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.72 (d, *J* = 8.2 Hz, 1H), 7.44 (s, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 4.48 – 4.24 (m, 4H), 2.52 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4 (s), 154.75 (s), 151.5 (d, *J* = 5.7 Hz), 138.3 (s), 126.8 (s), 120.9 (s), 111.5 (s), 64.5 (d, *J* = 5.9 Hz), 21.9 (s), 16.3 (d, *J* = 6.3 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ -1.94 (s). HRMS (ESI) Calcd for $C_{12}H_{16}NNaO_4P$: $[M+Na]^+$, 292.0709; Found: 292.0719.

Diisopropyl benzoxazole-2-ylphosphonate (3l)



A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.37 (m, 2H), 5.10 – 4.87 (m, 2H), 1.45 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0 (s), 156.4 (s), 151.1 (d, *J* = 5.8 Hz), 140.3 (d, *J* = 16.4 Hz), 127.3 (s), 125.2 (s), 121.6 (s), 111.5 (s), 73.9 (d, *J* = 5.9 Hz), 24.0 (d, *J* = 4.1 Hz), 23.7 (d, *J* = 5.0 Hz).^{31}P NMR (162 MHz, $CDCl_3$) δ -4.29 (s). HRMS (ESI) Calcd for $C_{13}H_{18}NNaO_4P$: $[M+Na]^+$, 306.0870; Found: 306.0866.

Diisopropyl 5-methylbenzoxazole-2-ylphosphonate (**3m**)

A pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 1H), 5.09 – 4.80 (m, 2H), 2.49 (s, 3H), 1.45 (d, *J* = 6.2 Hz, 6H), 1.39 (d, *J* = 6.2 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 156.3 (s), 149.4 (d, *J* = 5.8 Hz), 140.6 (d, *J* = 16.3 Hz), 135.2 (s), 128.6 (s), 121.3 (s), 110.8 (s), 73.8 (d, *J* = 5.9 Hz), 24.0 (d, *J* = 4.1 Hz), 23.7 (d, *J* = 5.0 Hz), 21.4 (s).^{31}P NMR (162 MHz, $CDCl_3$) δ -4.15 (s). HRMS (ESI) Calcd for $C_{14}H_{20}NNaO_4P$: $[M+Na]^+$, 320.1022; Found: 320.1013.

Diisopropyl 5-tert-butylbenzoxazole-2-ylphosphonate (3n)

A light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.55 (s, 2H), 4.95 (d, *J* = 7.7 Hz, 2H), 1.45 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 5.2 Hz, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0 (s), 156.4 (s), 149.1 (d, *J* = 5.8 Hz), 148.7 (s), 140.2 (d, *J* = 16.3 Hz), 125.2 (s), 117.7 (s), 110.6 (s), 73.7 (d, *J* = 5.9 Hz), 65.7 (s), 34.9 (s), 31.6 (s), 23.9 (d, *J* = 4.1 Hz), 23.6 (d, *J* = 5.0 Hz), 15.2 (s). ^{31}P NMR (162 MHz, $CDCl_3$) δ -4.18 (s). HRMS (ESI) Calcd for $C_{17}H_{26}NNaO_4P$: $[M+Na]^+$, 362.1492; Found: 362.1478.

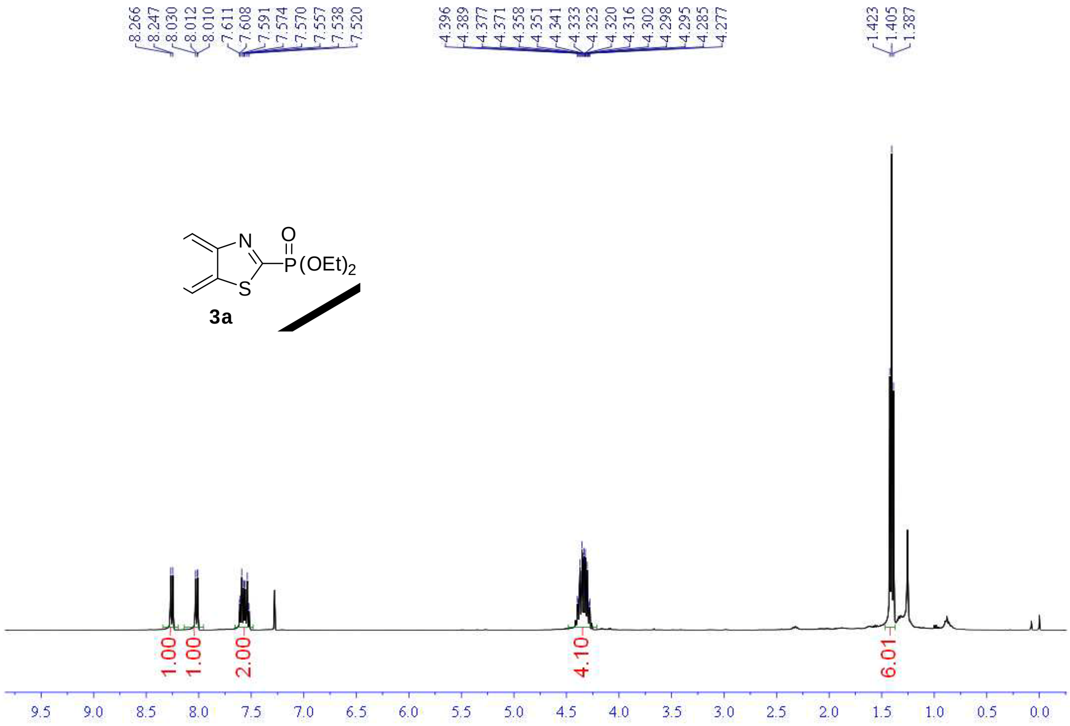
Diisopropyl 5-chlorobenzoxazole-2-ylphosphonate (3o)

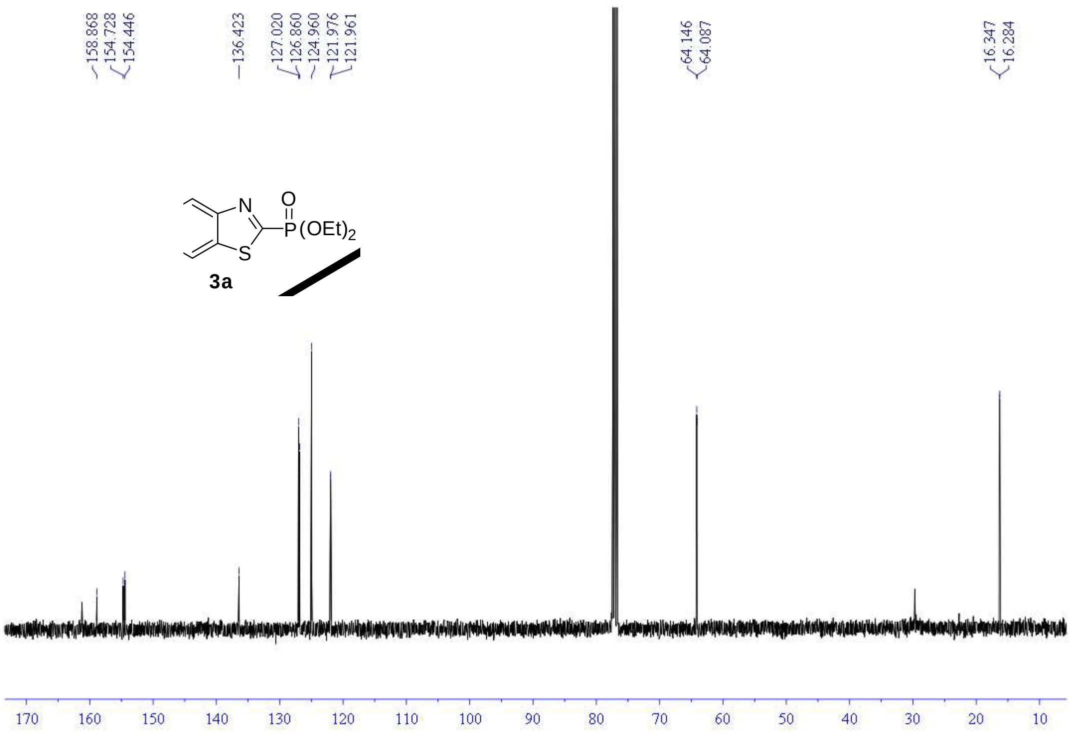
A tan oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 2.0 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.45 (m, 1H), 5.03 – 4.90 (m, 2H), 1.46 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5 (s), 157.9 (s), 149.6 (d, *J* = 5.9 Hz), 141.4 (d, *J* = 16.5 Hz), 130.8 (d, *J* = 1.4 Hz), 127.7 (s), 121.4 (s), 112.3 (s), 74.2 (d, *J* = 6.0 Hz), 24.0 (d, *J* = 4.1 Hz), 23.7 (d, *J* = 5.0 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ -5.03 (s). HRMS (ESI) Calcd for $C_{13}H_{27}ClNNaO_4P$: $[M+Na]^+$, 340.0476; Found: 340.0463.

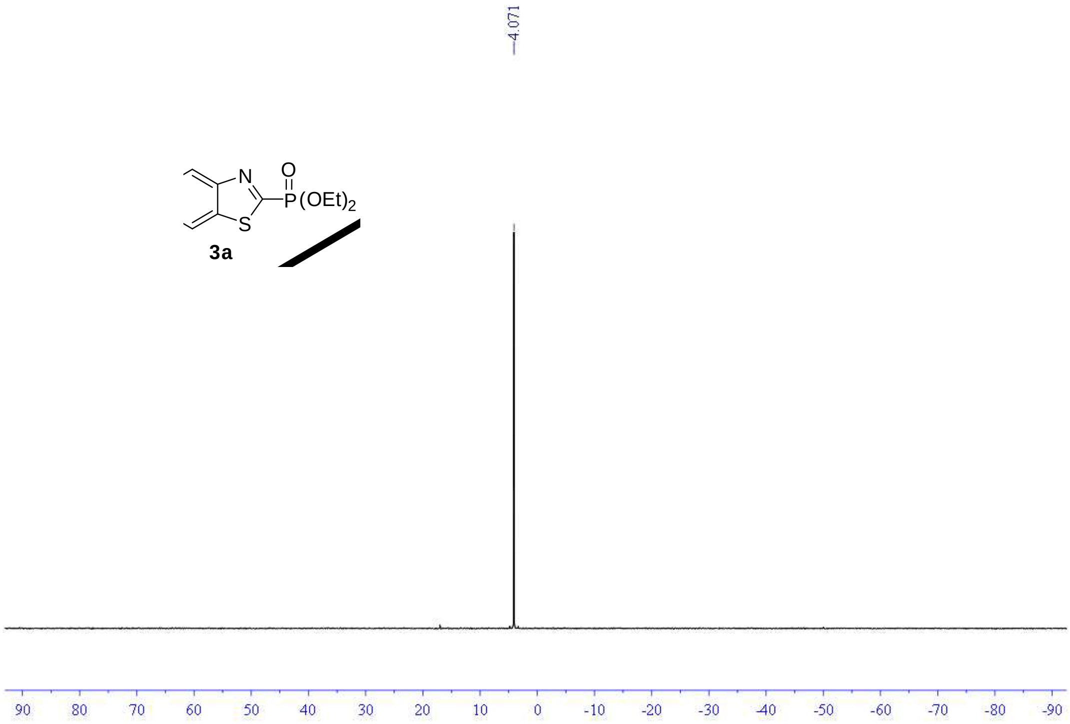
Diisopropyl 6-methylbenzoxazole-2-ylphosphonate (3p)

A tan oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 1H), 7.43 (s, 1H), 7.23 (dd, *J* = 8.2, 0.8 Hz, 1H), 5.11 – 4.82 (m, 2H), 2.52 (s, 3H), 1.44 (d, *J* = 6.2 Hz, 6H), 1.39 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (s), 155.7 (s), 151.5 (d, *J* = 5.7 Hz), 138.0 (s), 126.7 (s), 120.9 (s), 111.4 (s), 73.8 (d, *J* = 5.9 Hz), 24.0 (d, *J* = 4.1 Hz), 23.7 (d, *J* = 5.0 Hz), 21.9 (s). ^{31}P NMR (162 MHz, $CDCl_3$) δ -4.16 (s). HRMS (ESI) Calcd for $C_{14}H_{20}NNaO_4P$: $[M+Na]^+$, 320.1022; Found: 320.1015.

7. ^{1}H NMR and ^{13}C NMR copies of products.



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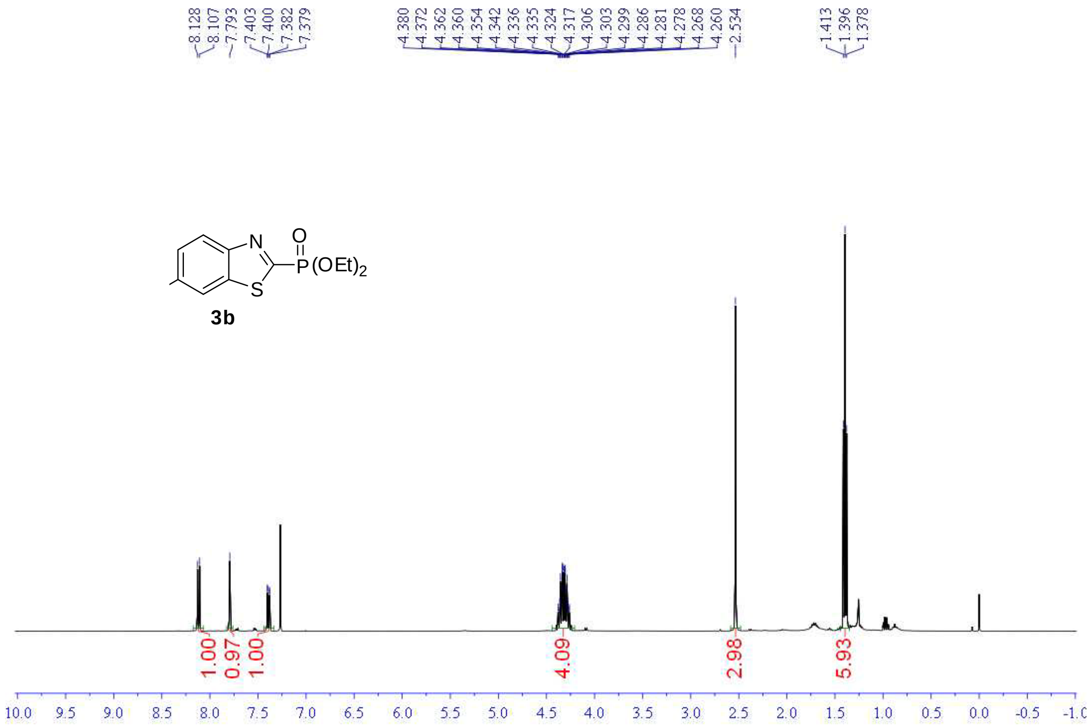
N
S
O
P(OEt)$_2$
3a
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90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8.107
7.793
7.403
7.400
7.382
7.379
4.380
4.372
4.362
4.360
4.354
4.342
4.336
4.335
4.324
4.317
4.306
4.303
4.299
4.286
4.281
4.278
4.268
4.260
2.534
1.413
1.396
1.378
N
S
O
P(OEt)$_2$
3b
1.00
0.97
1.00
4.09
2.98
5.93
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
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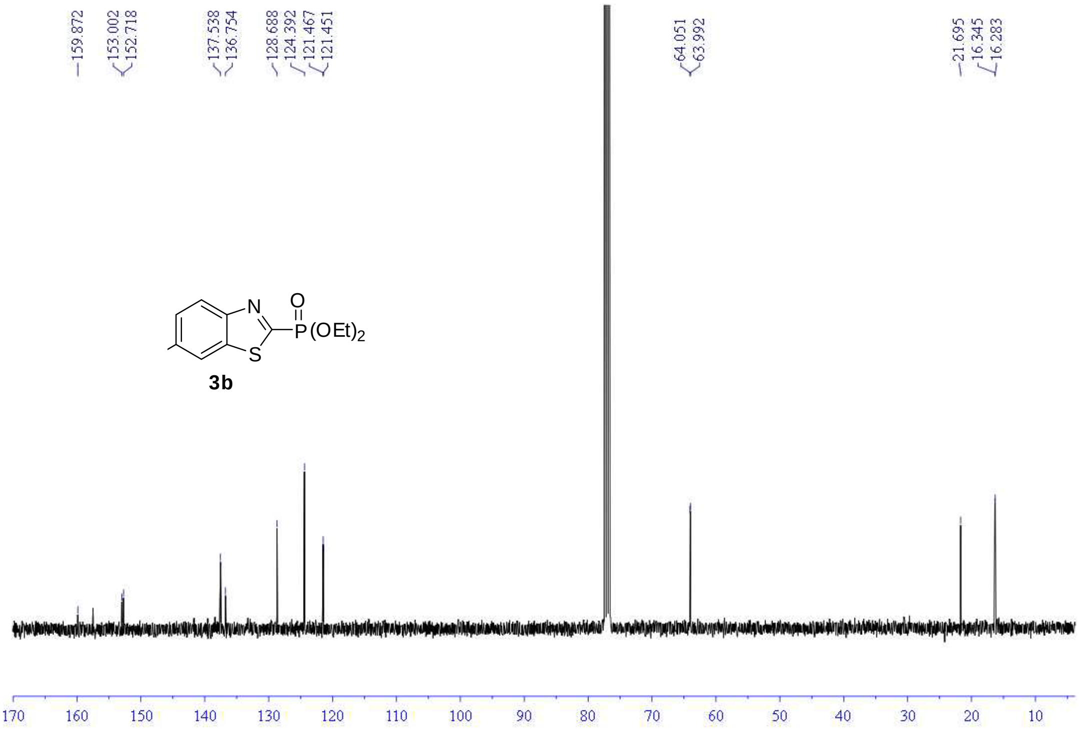
1.0
0.5
0.0
-0.5
-1.0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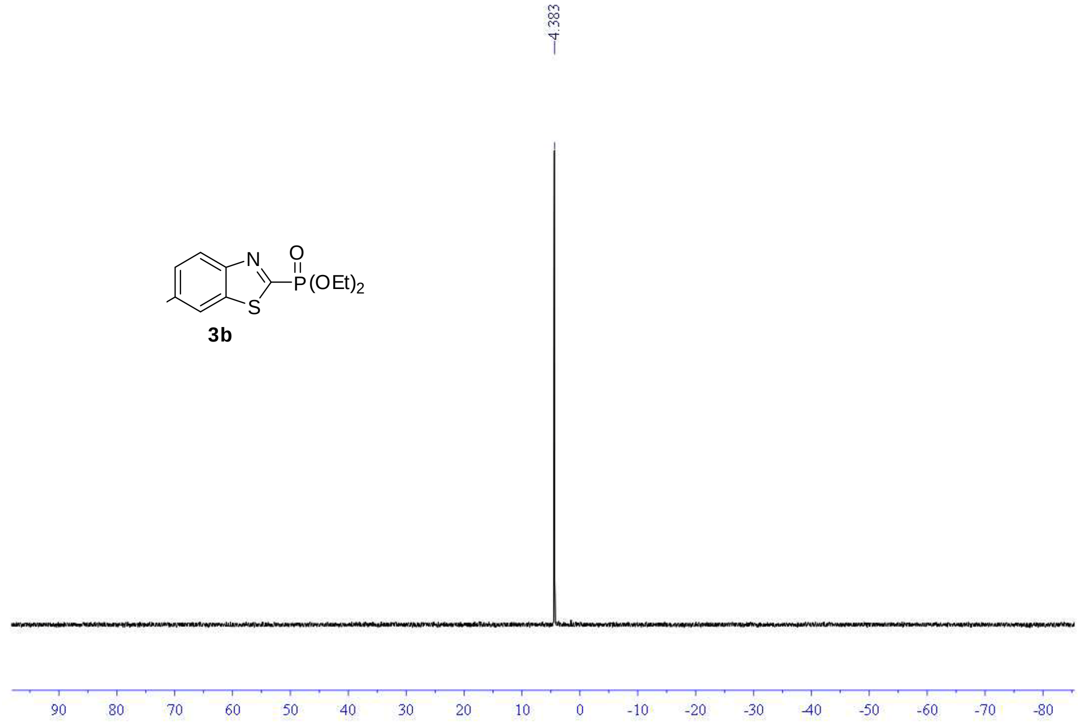
152.718
137.538
136.754
128.688
124.392
121.467
121.451
64.051
63.992
21.695
16.345
16.283
N
O
P(OEt)$_2$
S
3b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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O
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S
3b
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80
70
60
50
40
30
20
10
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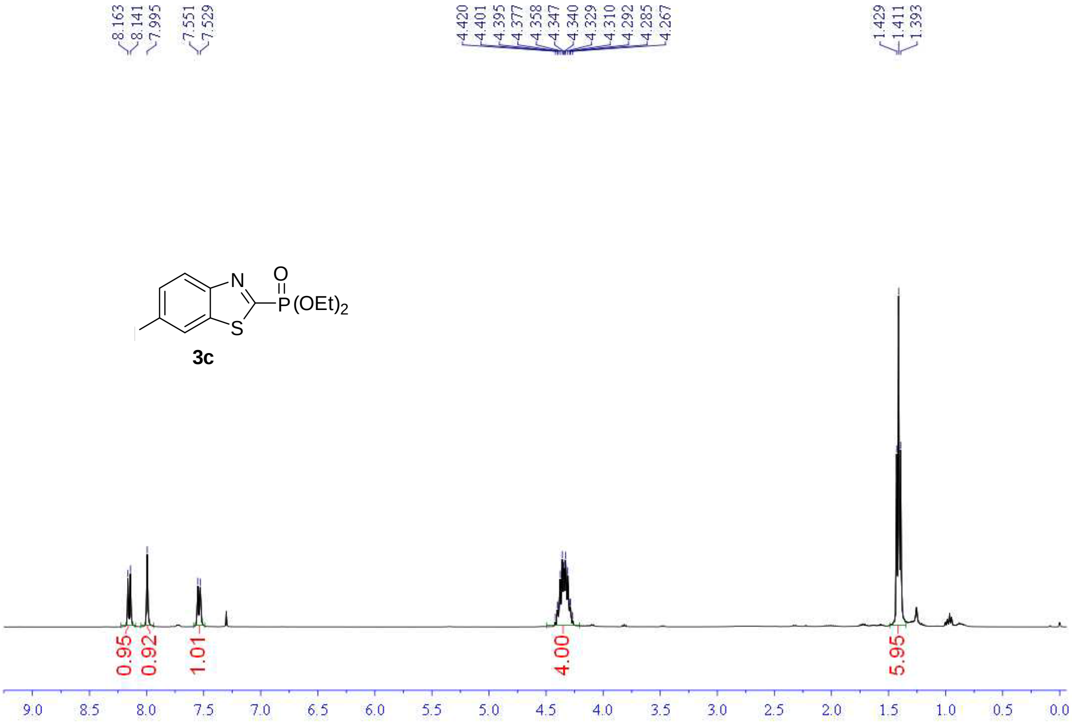
-30
-40
-50
-60
-70
-80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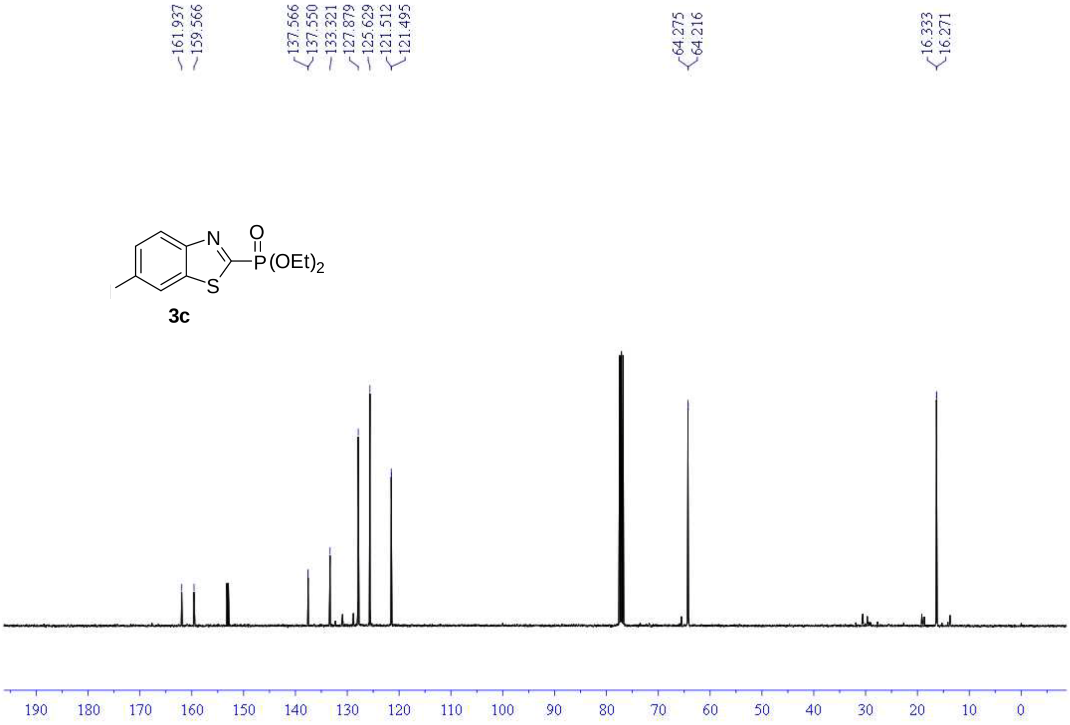
8.141
7.995
7.551
7.529
4.420
4.401
4.395
4.377
4.358
4.347
4.340
4.329
4.310
4.292
4.285
4.267
1.429
1.411
1.393
N
O
P(OEt)2
S
3c
0.95
0.92
1.01
4.00
5.95
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0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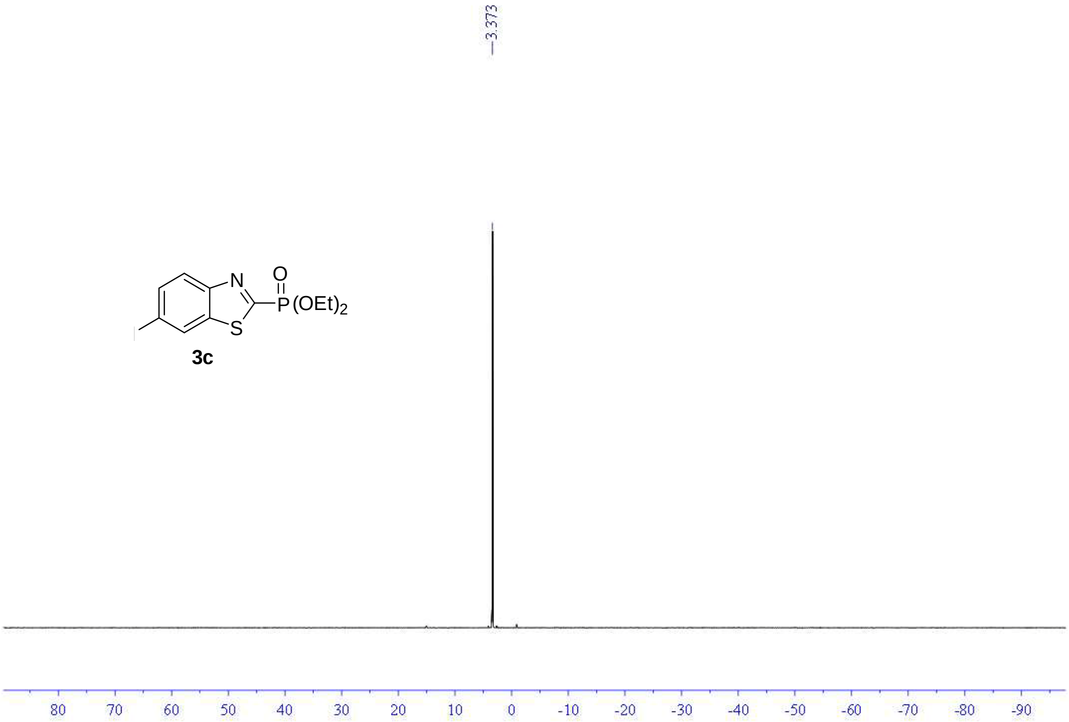
159.566
137.566
137.550
133.321
127.879
125.629
121.512
121.495
64.275
64.216
16.333
16.271
N
O
P(OEt)2
S
3c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



3c

-3.373
N
S
O
P(OEt)2
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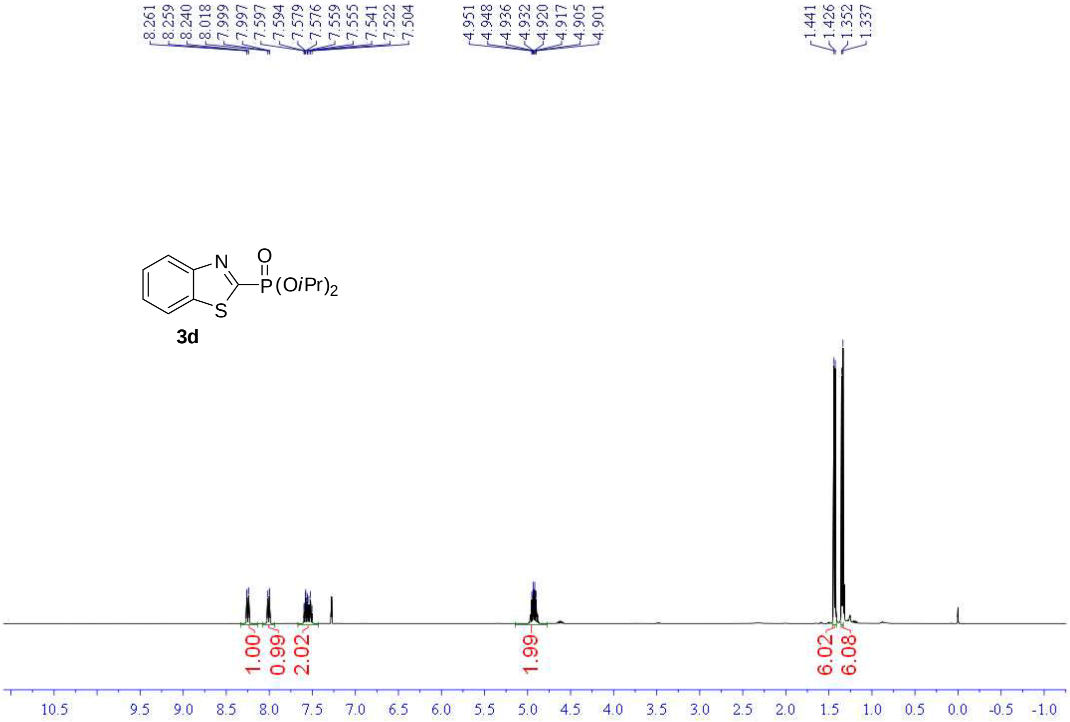
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90



3d

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8.259
8.240
8.018
7.999
7.997
7.597
7.594
7.579
7.576
7.559
7.555
7.541
7.522
7.504
4.951
4.948
4.936
4.932
4.920
4.917
4.905
4.901
1.441
1.426
1.352
1.337
N
S
O
P(OiPr)2
1.00
0.99
2.02
1.99
6.02
6.08
10.5
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
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0.5
0.0
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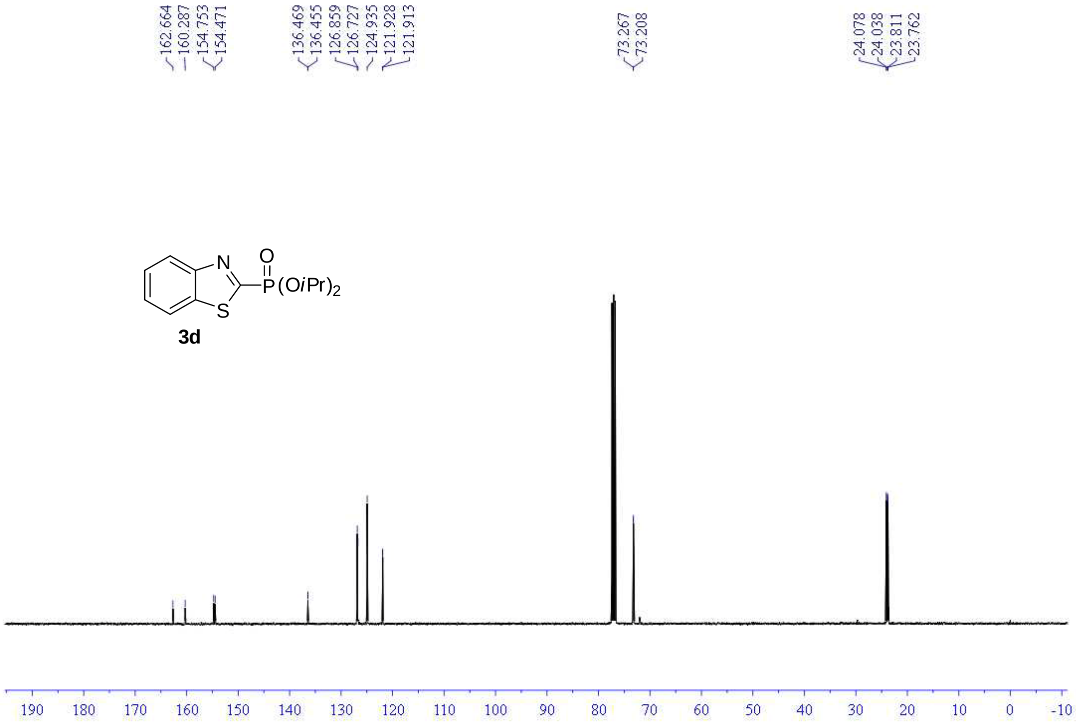
-1.0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154.753
154.471
136.469
136.455
126.859
126.727
124.935
121.928
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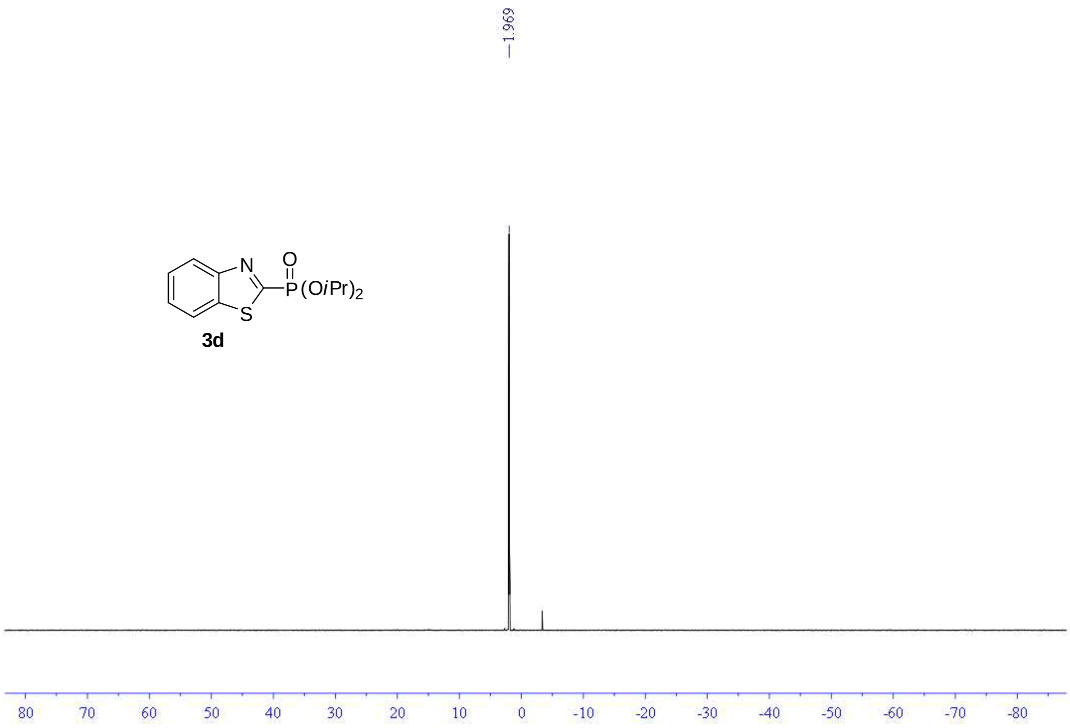
73.267
73.208
24.078
24.038
23.811
23.762
N
O
P(O*i*Pr)$_2$
S
3d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


1.969
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O
P(O*i*Pr)$_2$
S
3d
80
70
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50
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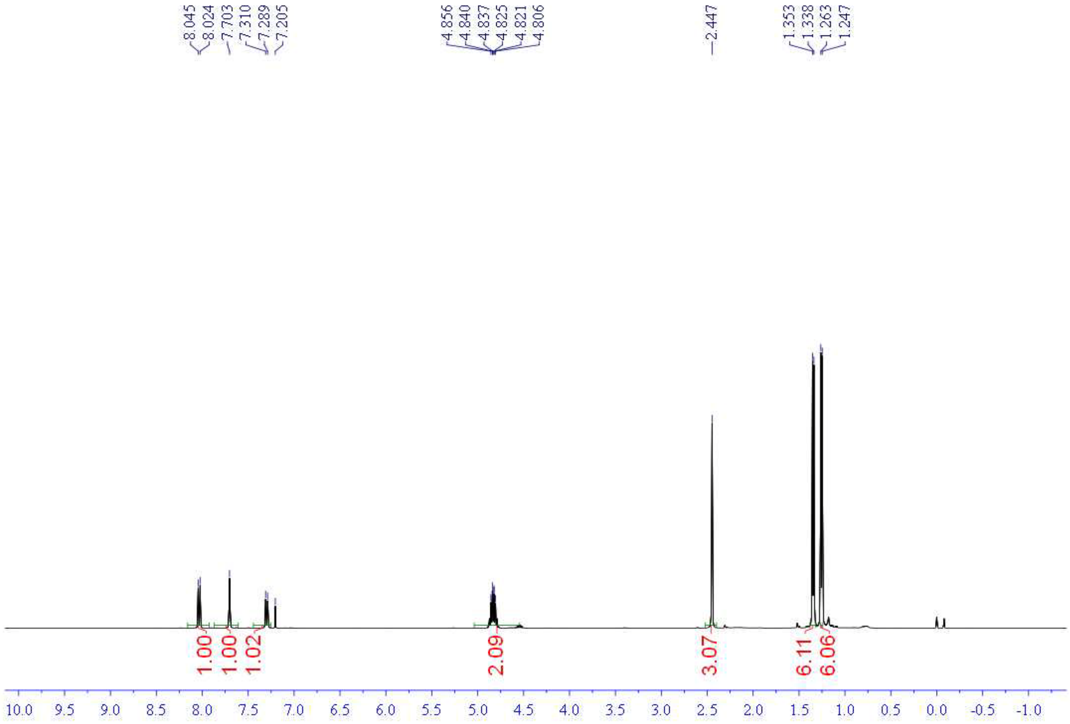
10
0
-10
-20
-30
-40
-50
-60
-70
-80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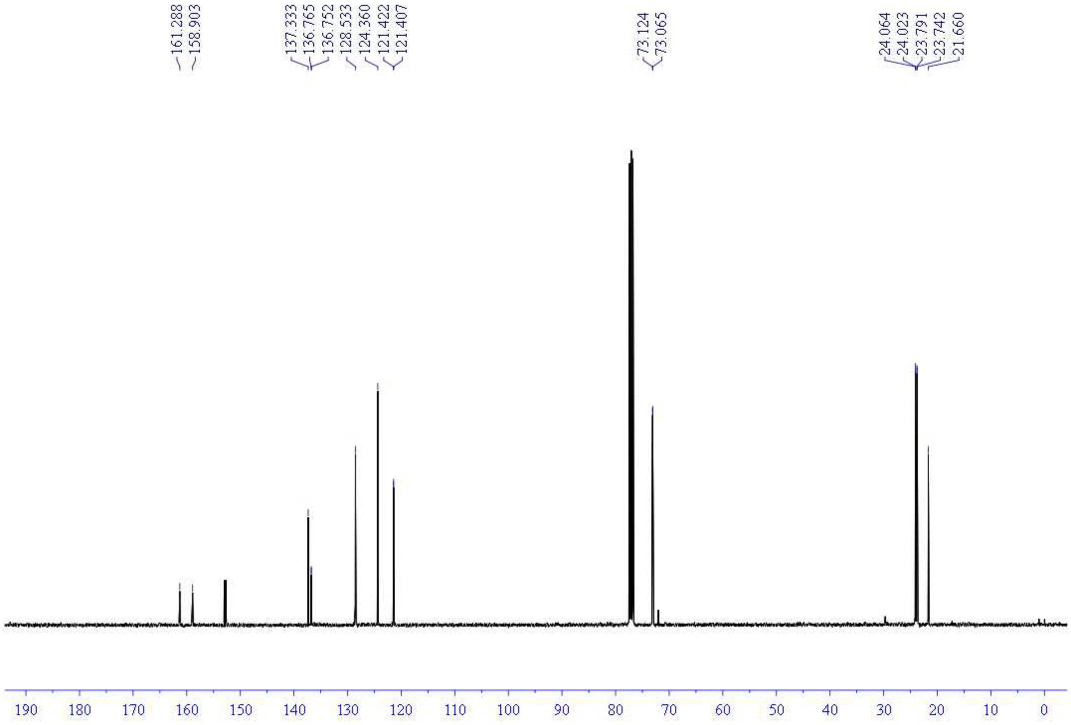
7.205
4.856
4.840
4.837
4.825
4.821
4.806
2.447
1.353
1.338
1.263
1.247
1.00
1.00
1.02
2.09
3.07
6.11
6.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0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128.533
124.360
121.422
121.407
73.124
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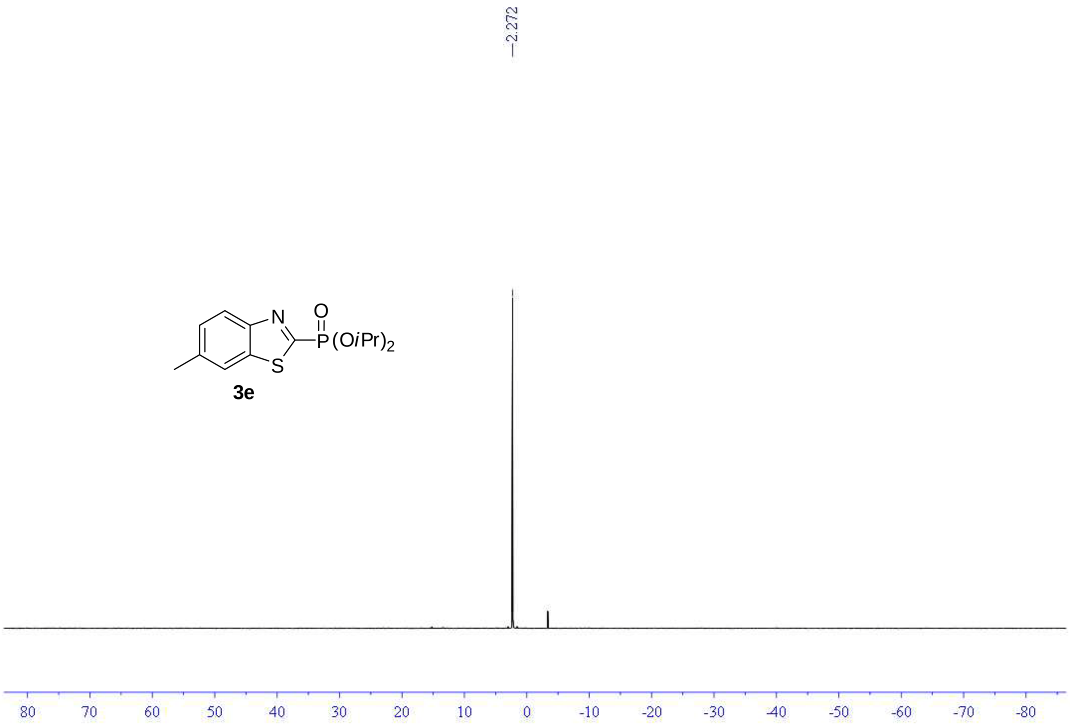
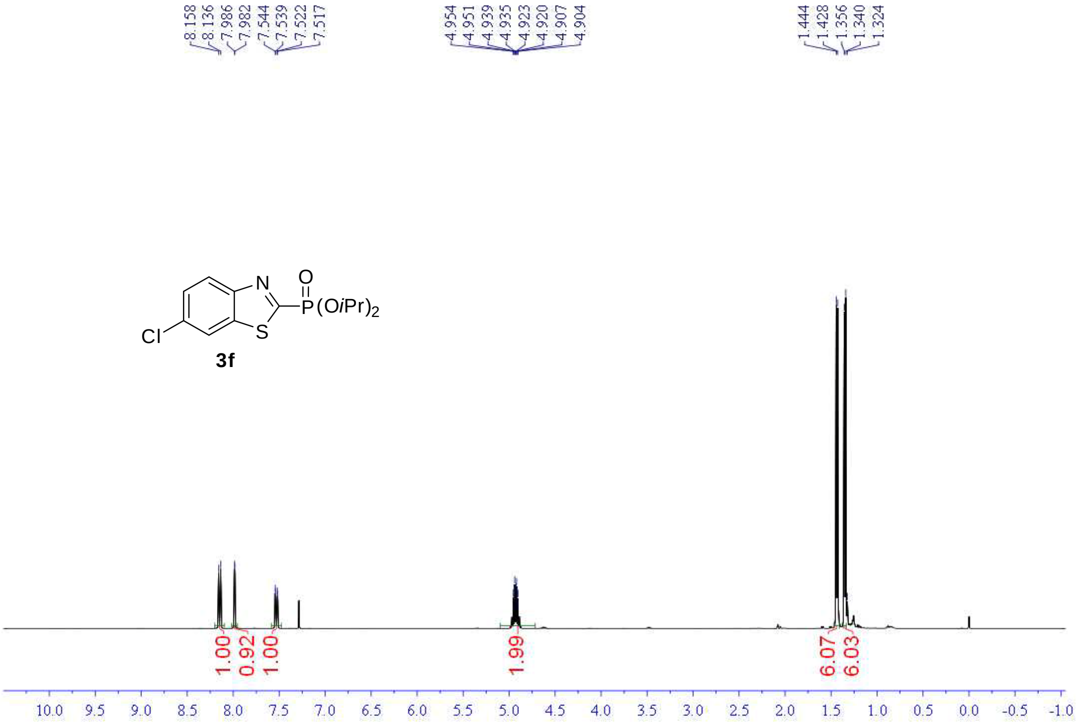
24.064
24.023
23.791
23.742
21.660
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


2.272
N
O
P(O*i*Pr)₂
S
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80

3e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8.136
7.986
7.982
7.544
7.539
7.522
7.517
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4.951
4.939
4.935
4.923
4.920
4.907
4.904
1.444
1.428
1.356
1.340
1.324
N
O
P(O*i*Pr)₂
Cl
S
1.00
0.92
1.00
1.99
6.07
6.03
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
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2.5
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1.5
1.0
0.5
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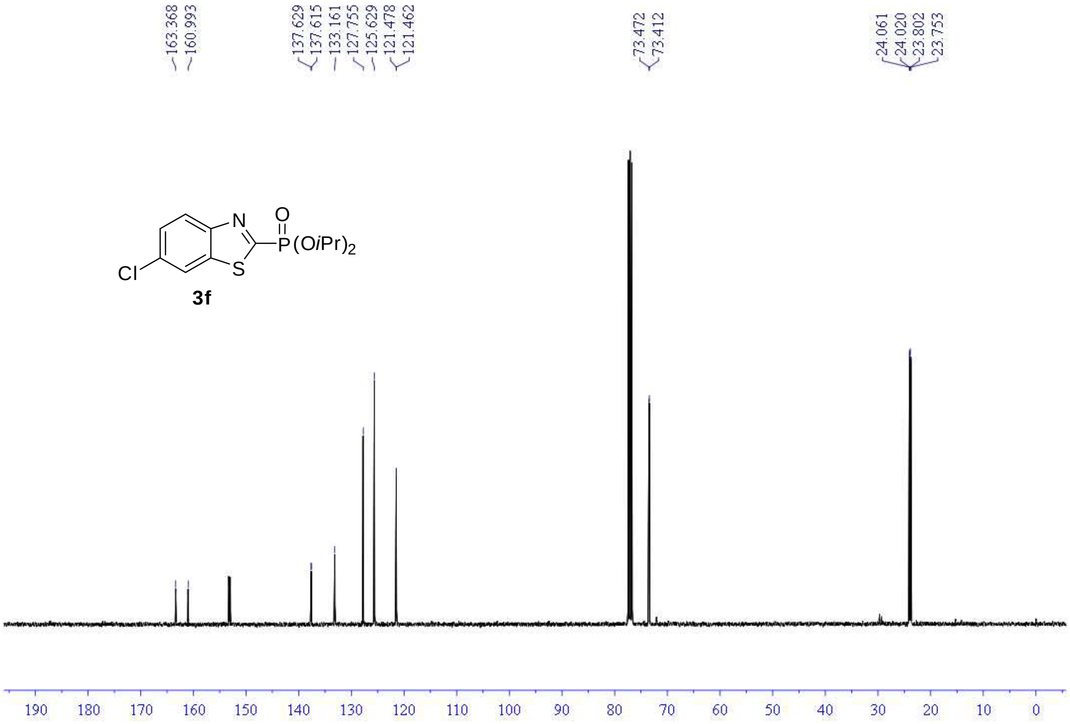
-0.5
-1.0

3f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133.161
127.755
125.629
121.478
121.462
73.472
73.412
24.061
24.020
23.802
23.753
N
O
P(OiPr)2
Cl
S
3f
190
180
170
160
150
140
130
120
110
100
90
80
70
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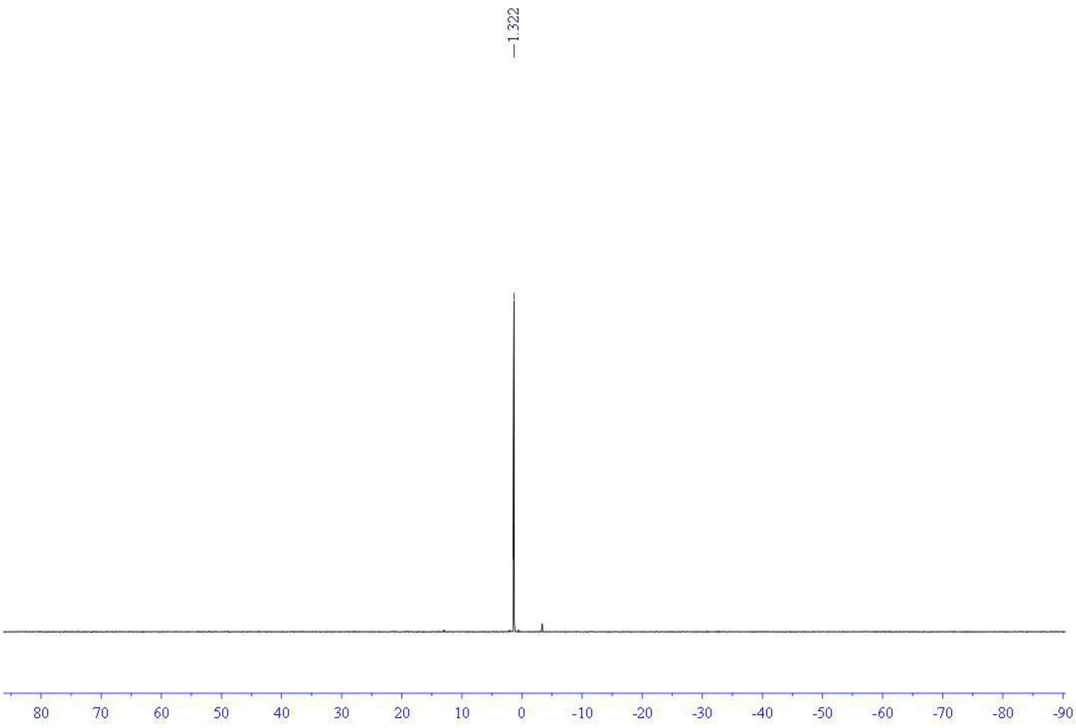
50
40
30
20
10
0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80
70
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50
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30
20
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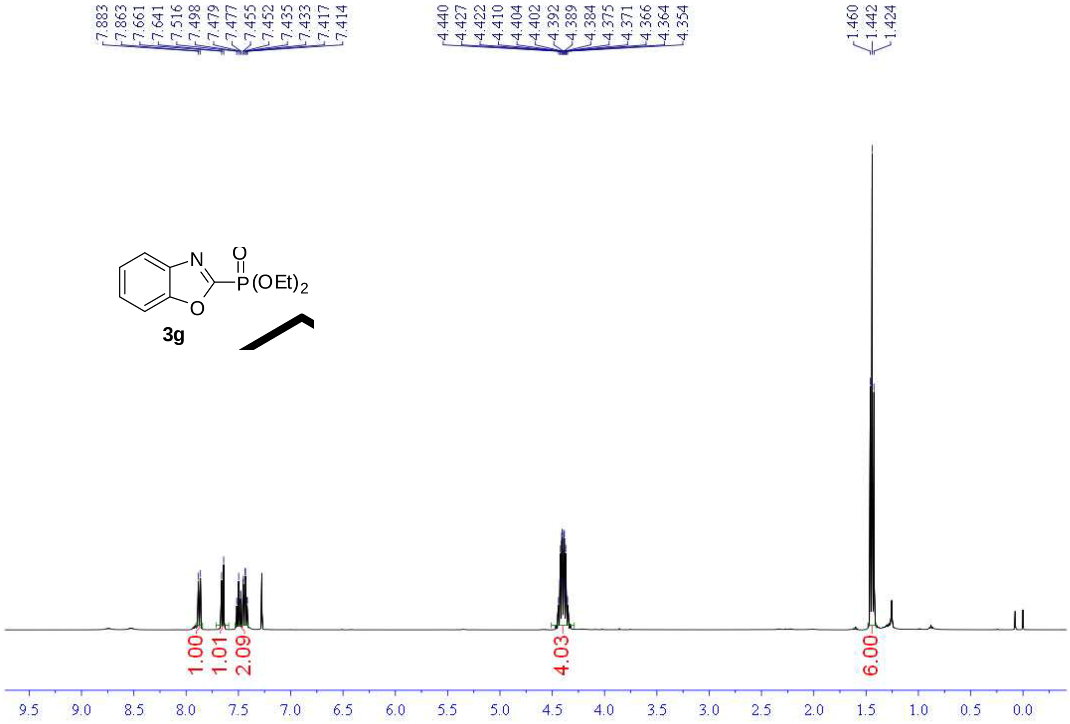
-10
-20
-30
-40
-50
-60
-70
-80
-90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7.863
7.661
7.641
7.516
7.498
7.479
7.477
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7.433
7.417
7.414
4.440
4.427
4.422
4.410
4.404
4.402
4.392
4.389
4.384
4.375
4.371
4.366
4.364
4.354
1.460
1.442
1.424
N
O
P(OEt)2
3g
1.00
1.01
2.09
4.03
6.00
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
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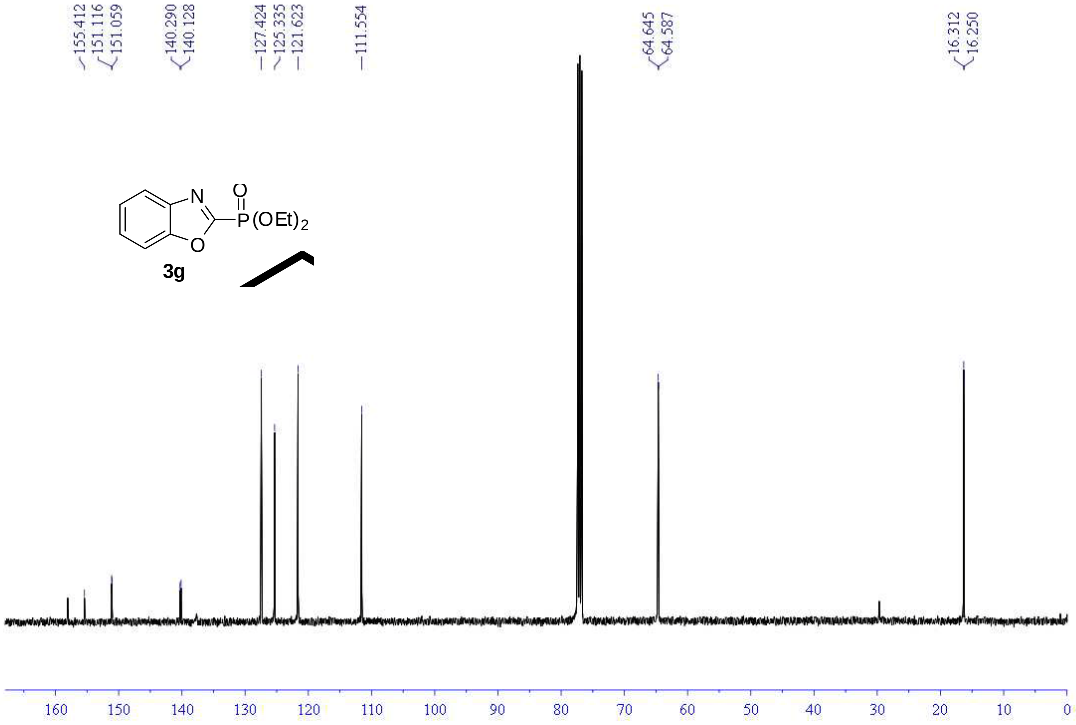
1.0
0.5
0.0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64.587
16.312
16.250
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O
P(OEt)2
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140
130
120
110
100
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70
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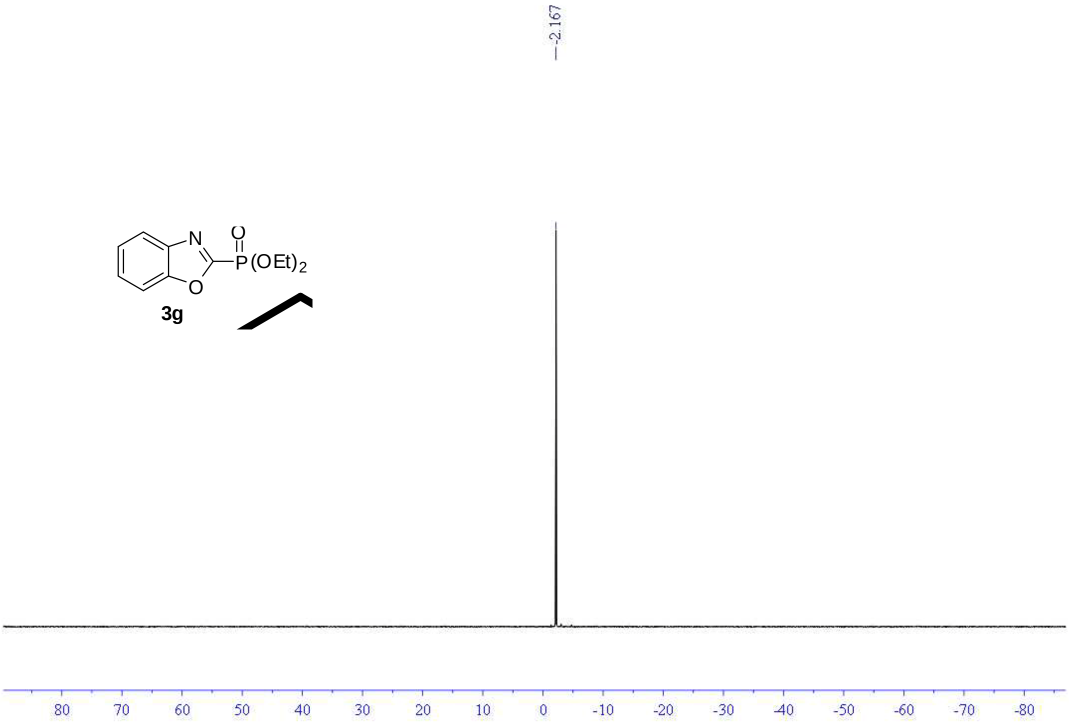
40
30
20
10
0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O
P(OEt)2
O
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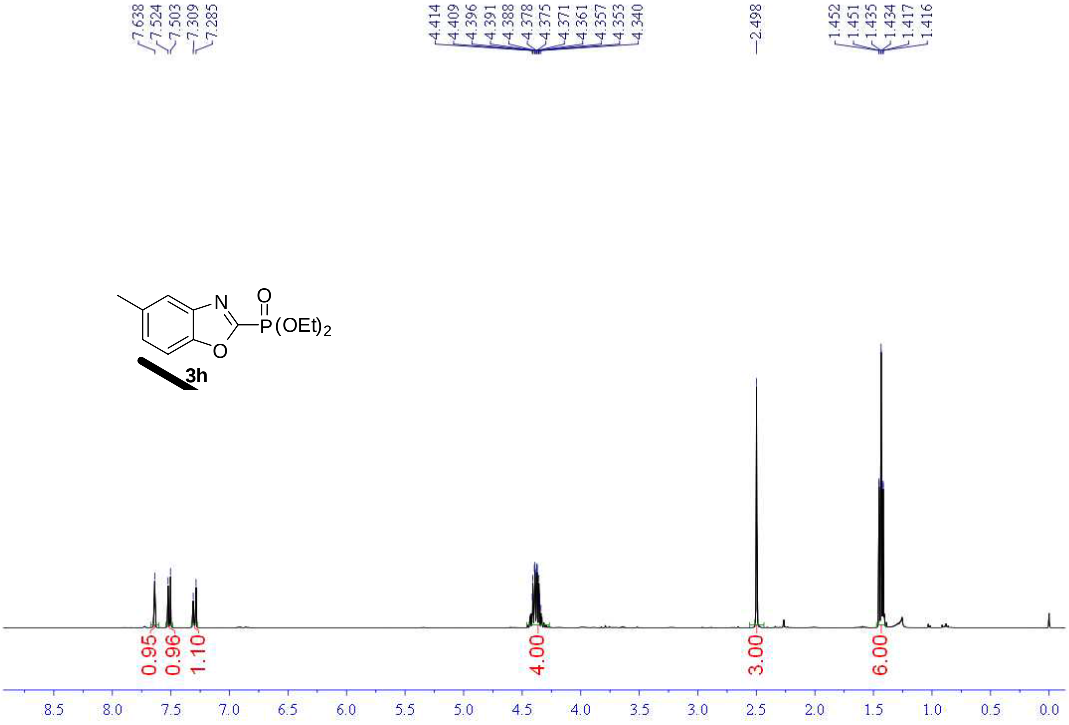
-60
-70
-80

3g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4.396
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4.388
4.378
4.375
4.371
4.361
4.357
4.353
4.340
2.498
1.452
1.451
1.435
1.434
1.417
1.416
N
O
P(OEt)2
O
0.95
0.96
1.10
4.00
3.00
6.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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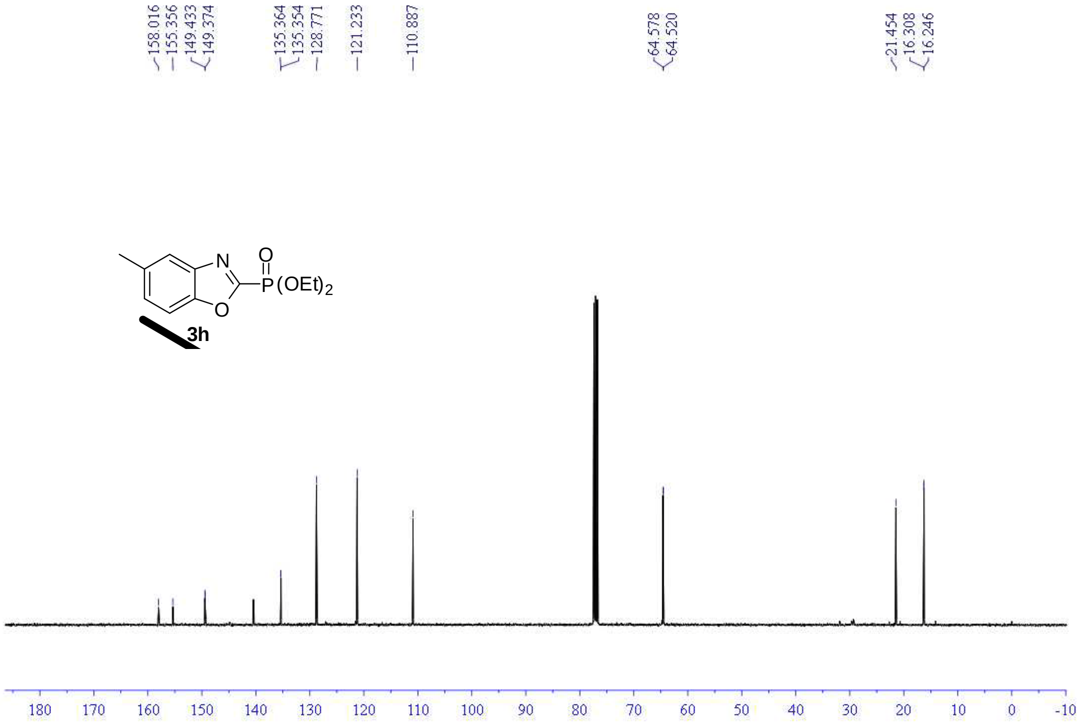
0.0

3h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121.233
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64.520
21.454
16.308
16.246
N
O
O
P(OEt)2
3h
180
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120
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100
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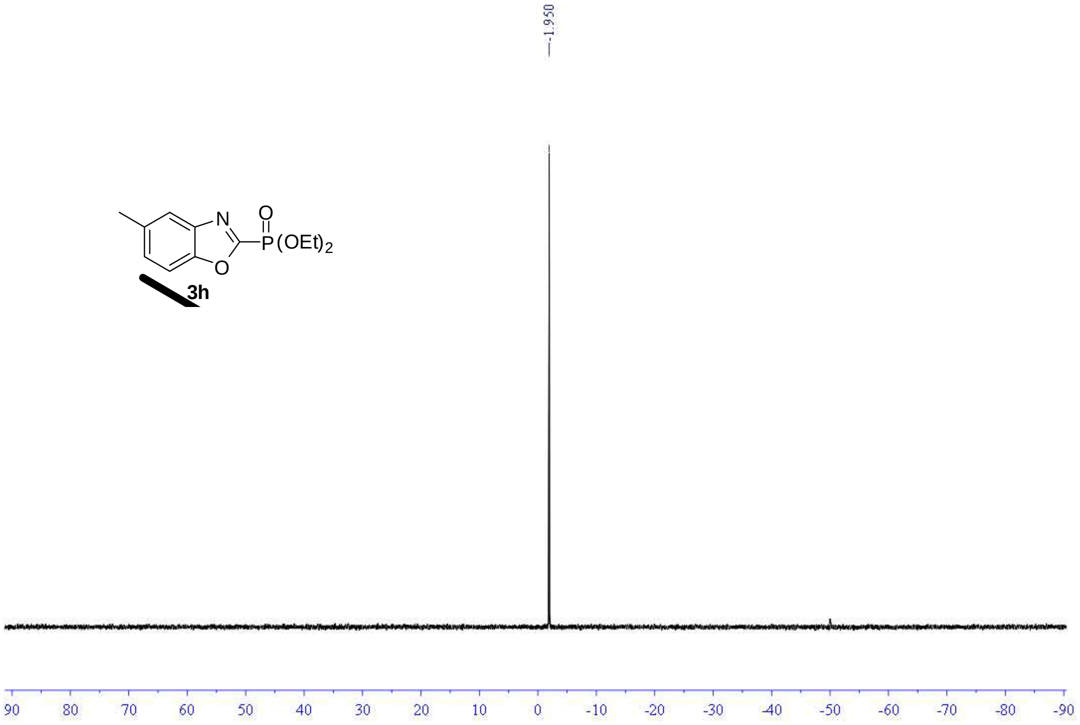
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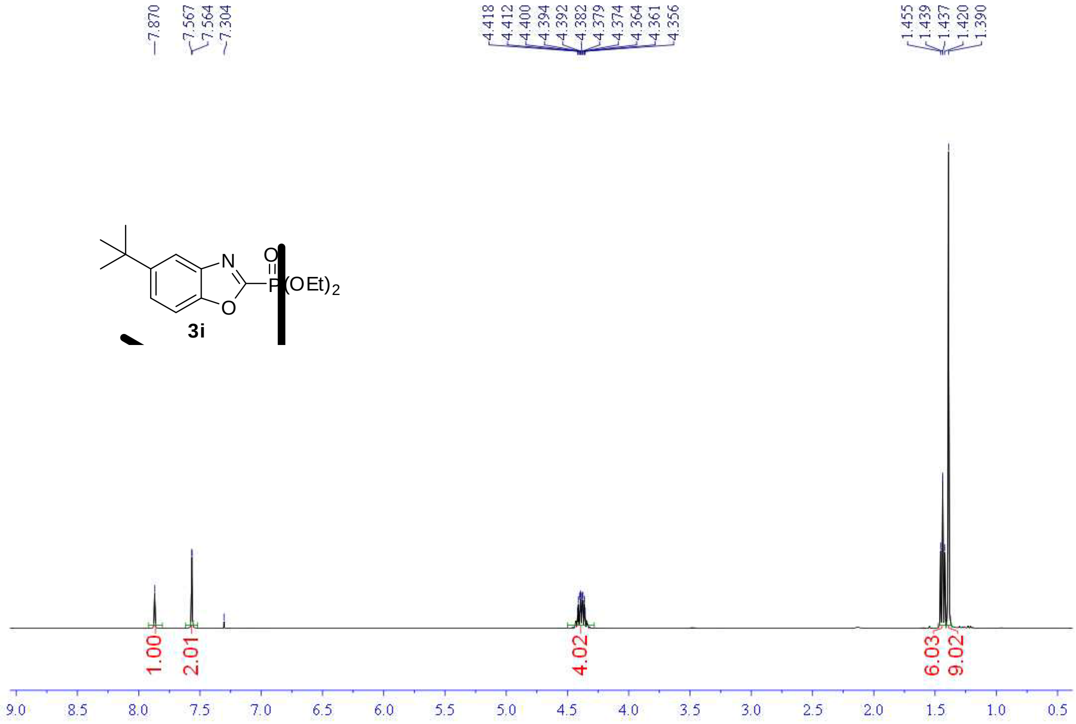
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4.394
4.392
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4.379
4.374
4.364
4.361
4.356
1.455
1.439
1.437
1.420
1.390
N
O
P(OEt)2
O
3i
1.00
2.01
4.02
6.03
9.02
9.0
8.5
8.0
7.5
7.0
6.5
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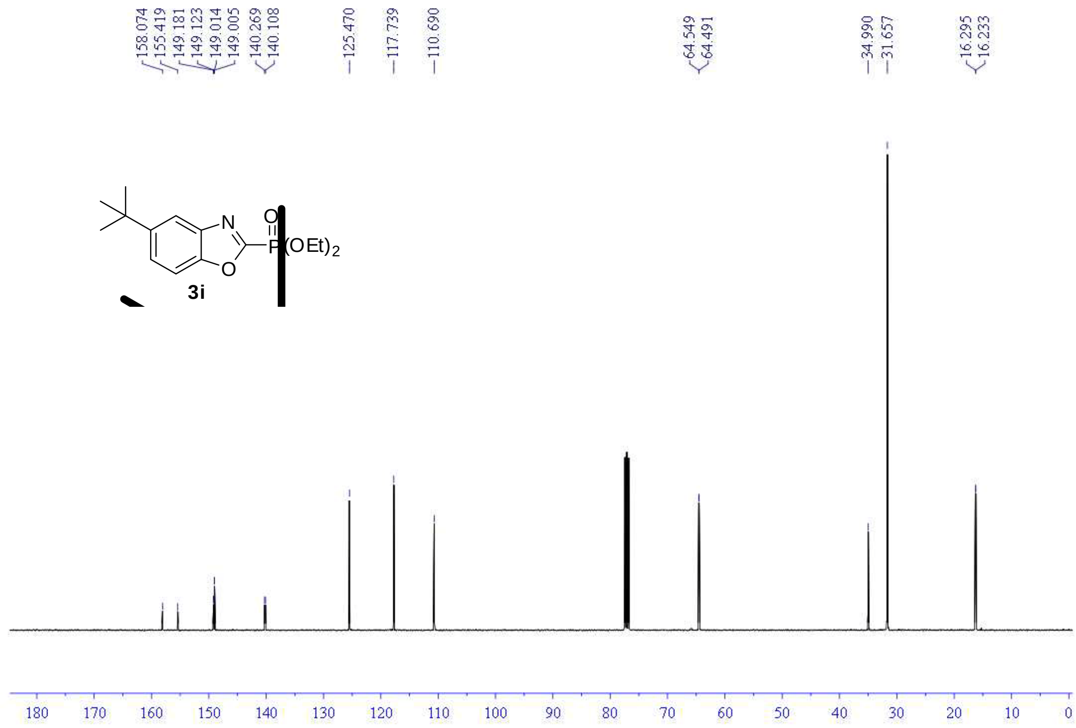
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140.108
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64.549
64.491
34.990
31.657
16.295
16.233
N
O
P(OEt)2
O
3i
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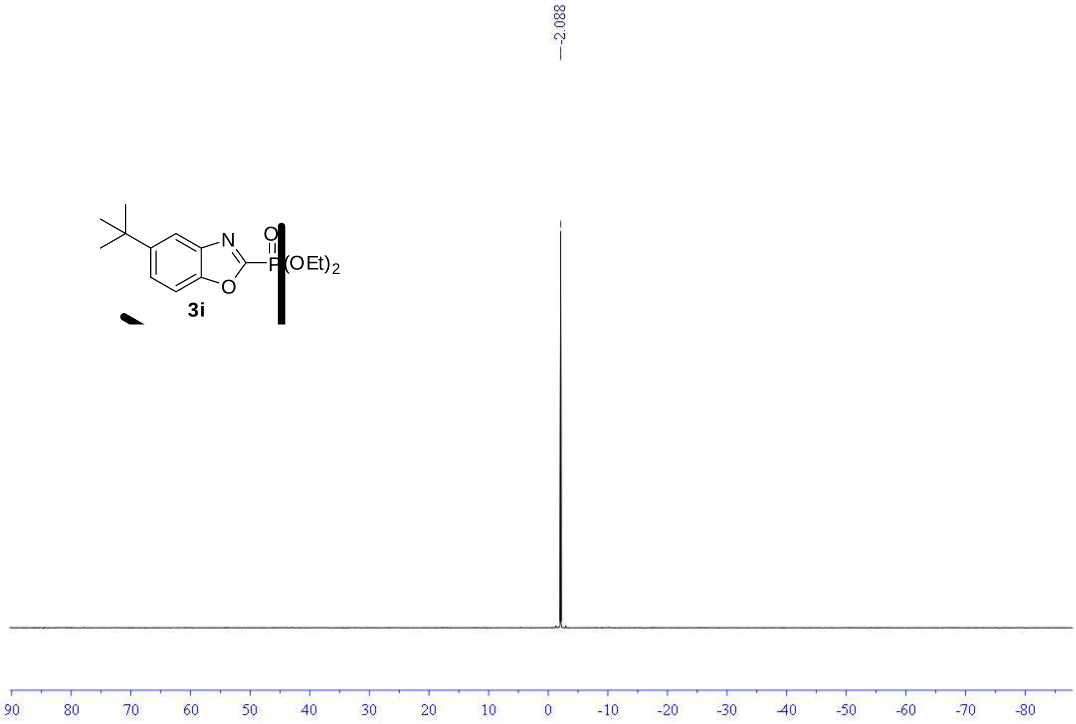
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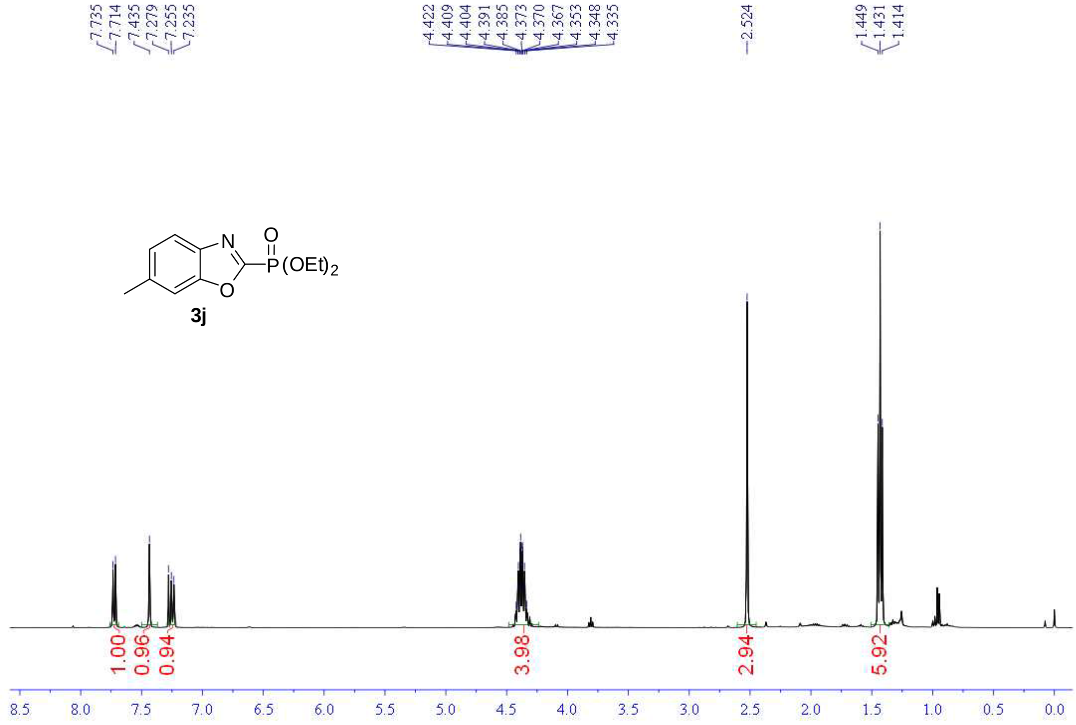
-40
-50
-60
-70
-80

3i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7.235
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4.409
4.404
4.391
4.385
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4.370
4.367
4.353
4.348
4.335
2.524
1.449
1.431
1.414
N
O
P(OEt)2
O
1.00
0.96
0.94
3.98
2.94
5.92
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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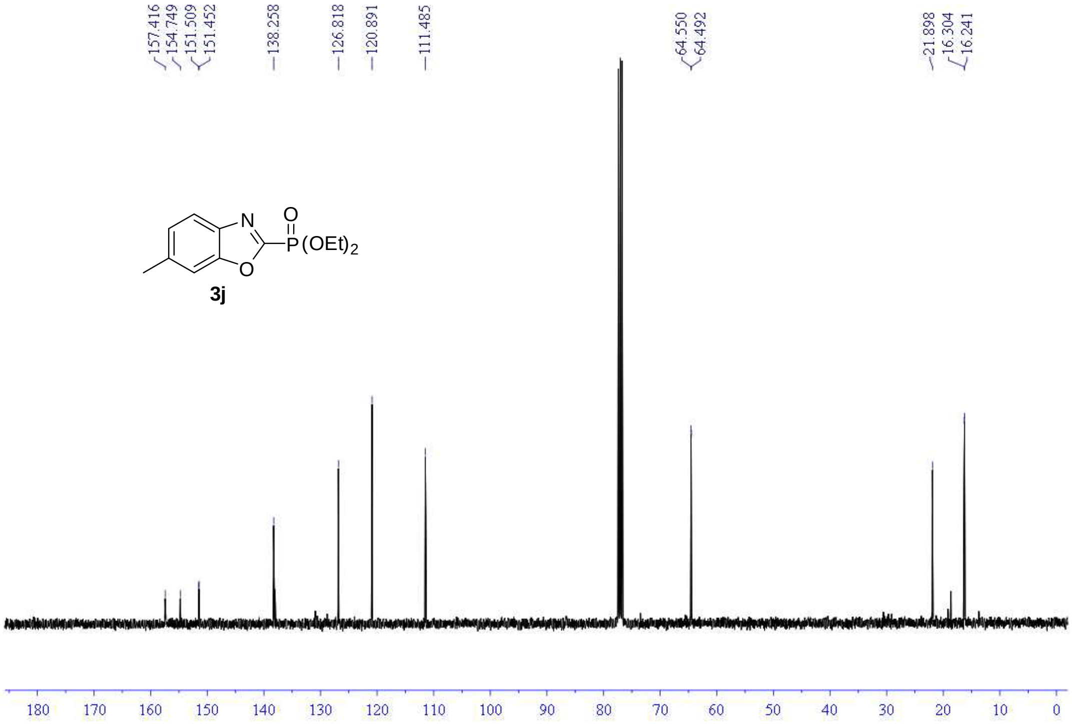
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

3j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151.452
138.258
126.818
120.891
111.485
64.550
64.492
21.898
16.304
16.241
N
O
P(OEt)2
O
3j
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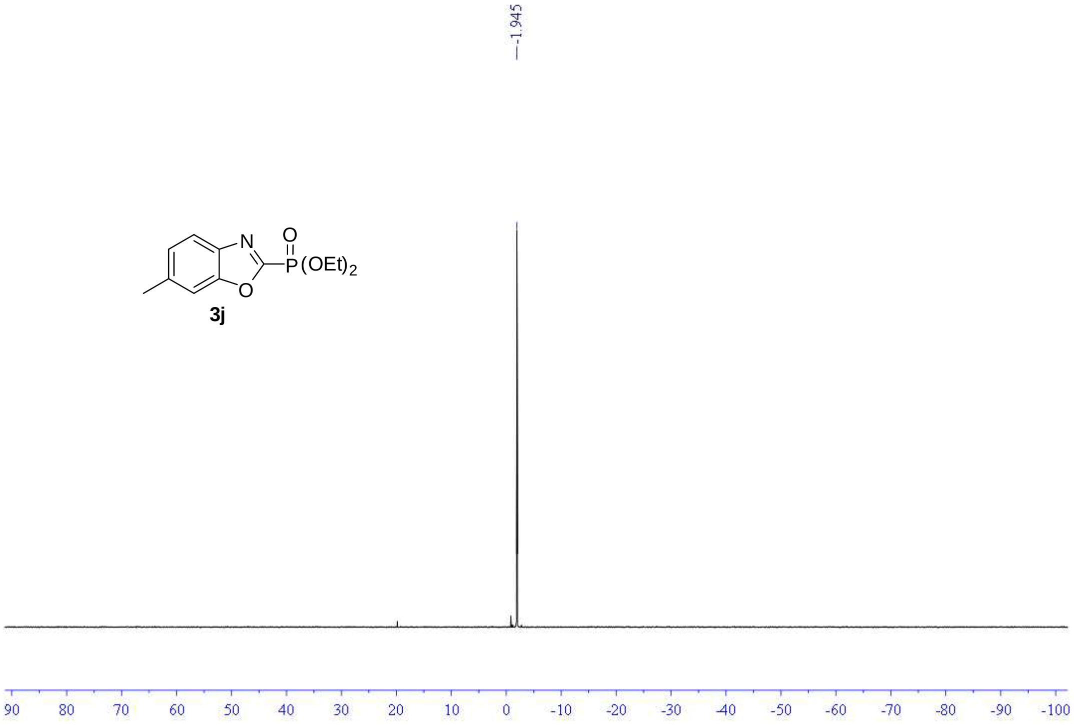
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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P(OEt)2
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3j
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-20
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-50
-60
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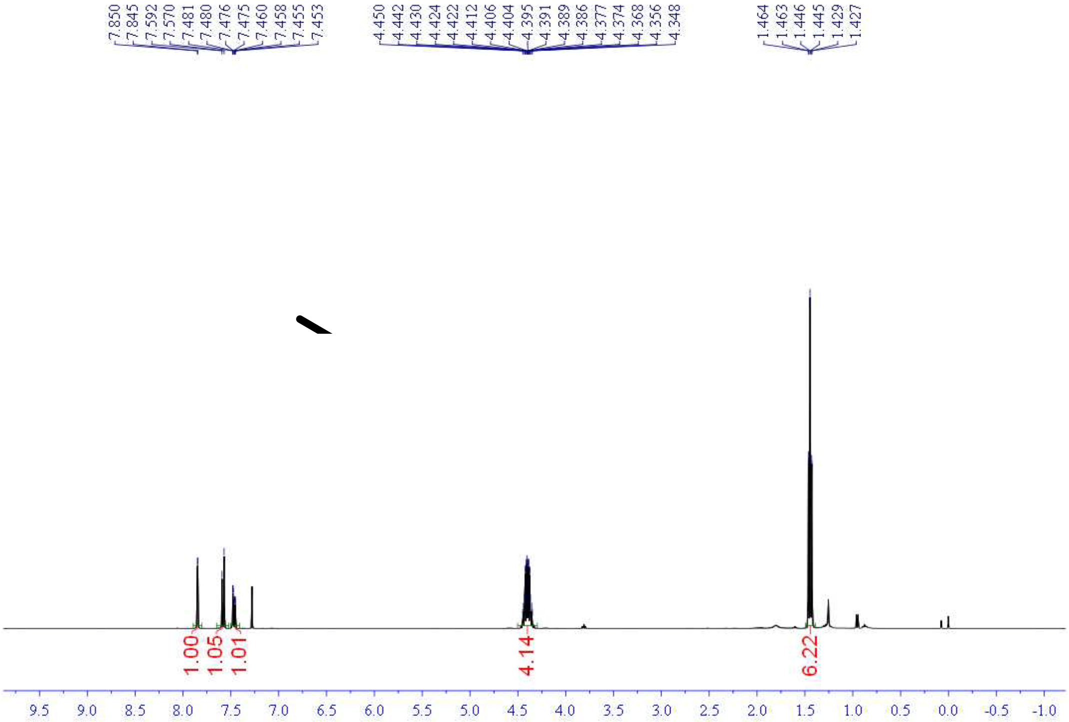
-80
-90
-100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7.592
7.570
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7.480
7.476
7.475
7.460
7.458
7.455
7.453
4.450
4.442
4.430
4.424
4.422
4.412
4.406
4.404
4.395
4.391
4.389
4.386
4.377
4.374
4.368
4.356
4.348
1.464
1.463
1.446
1.445
1.429
1.427
1.00
1.05
1.01
4.14
6.22
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.0
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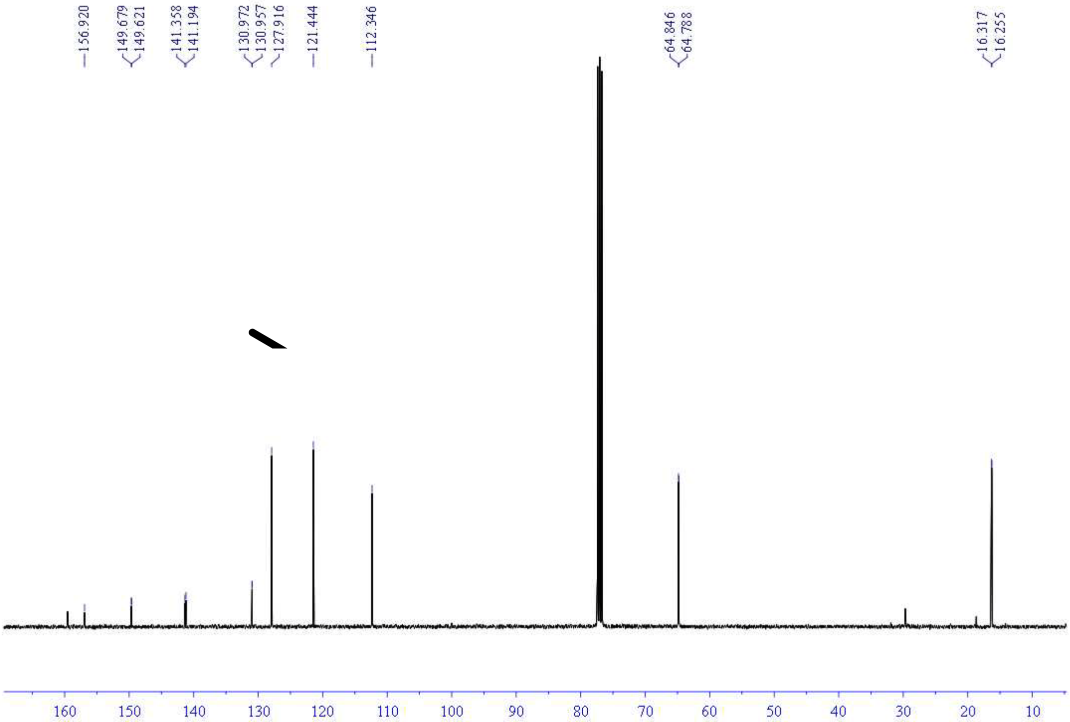
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149.621
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121.444
112.346
64.846
64.788
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150
140
130
120
110
100
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80
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30
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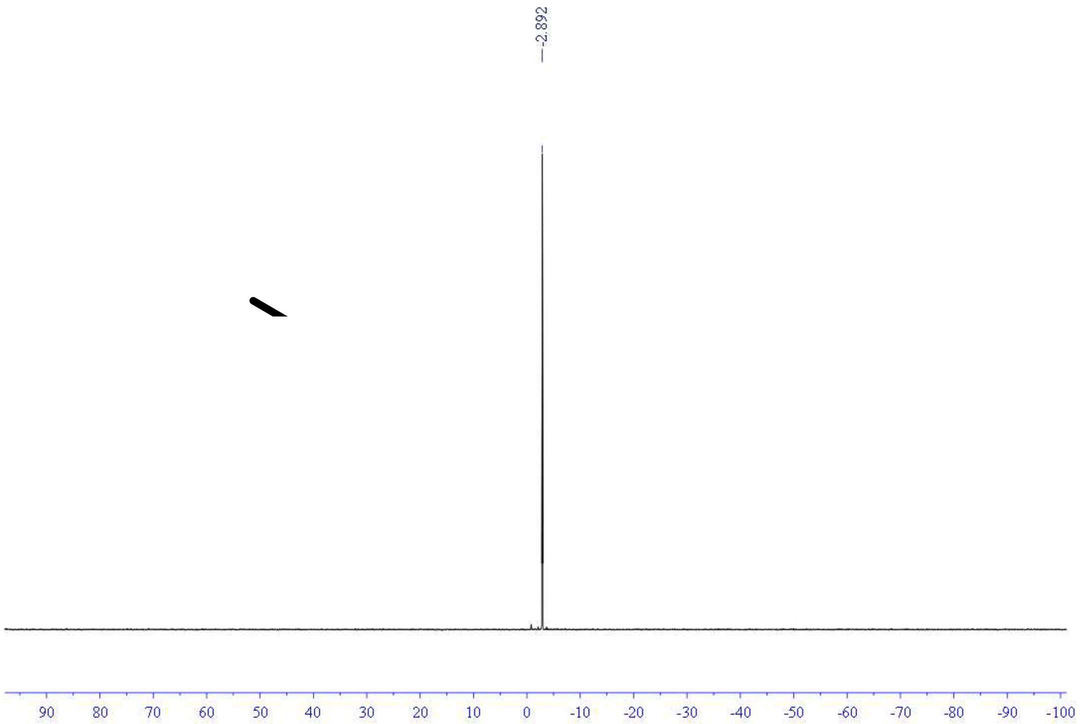
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80
70
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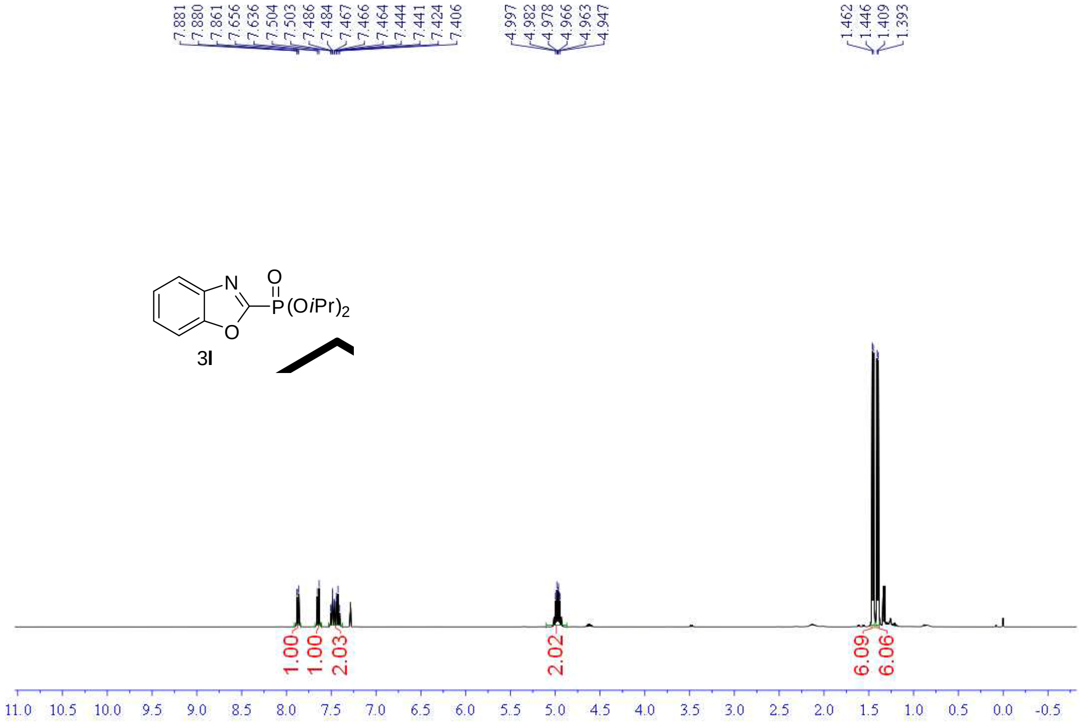
-50
-60
-70
-80
-90
-100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7.880
7.861
7.656
7.636
7.504
7.503
7.486
7.484
7.467
7.466
7.464
7.444
7.441
7.424
7.406
4.997
4.982
4.978
4.966
4.963
4.947
1.462
1.446
1.409
1.393
N
O
P(O*i*Pr)$_2$
O
3l
1.00
1.00
2.03
2.02
6.09
6.06
11.0
10.5
10.0
9.5
9.0
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
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1.0
0.5
0.0
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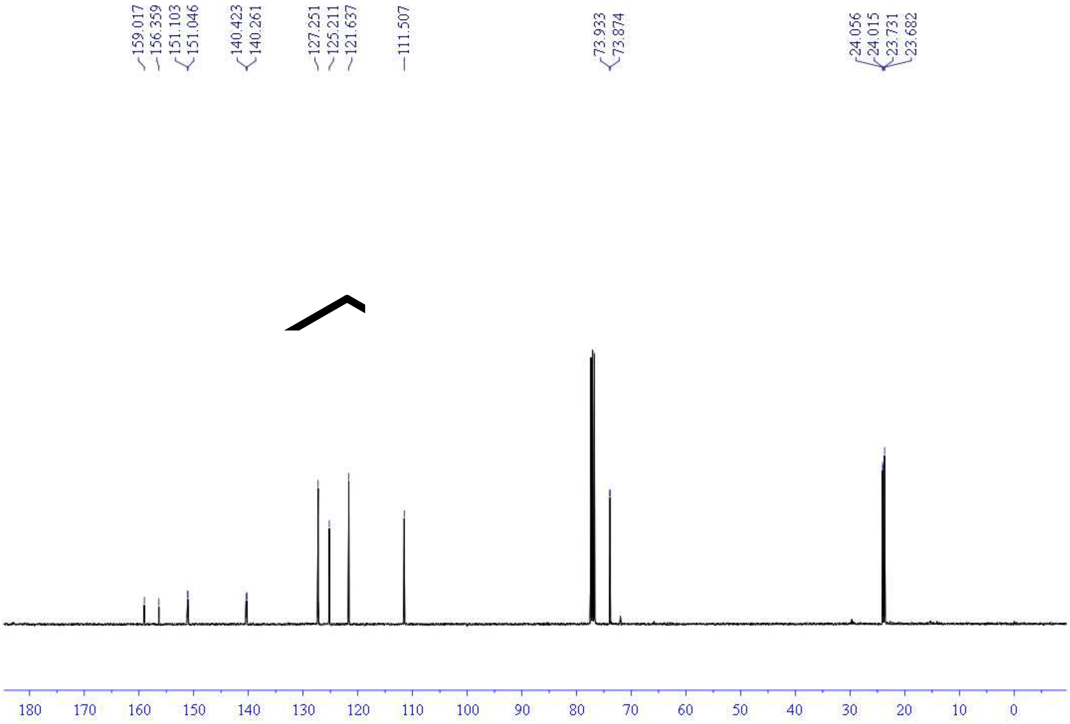
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125.211
121.637
111.507
73.933
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24.056
24.015
23.731
23.682
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150
140
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110
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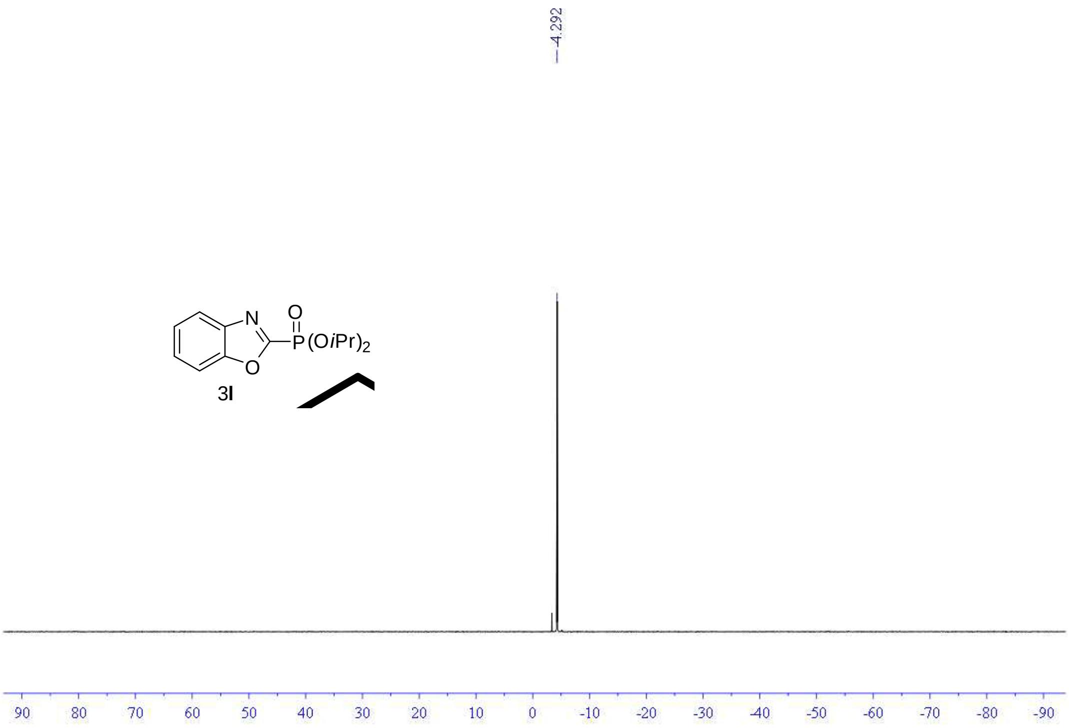
30
20
10
0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O
P(O*i*Pr)$_2$
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80
70
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20
10
0
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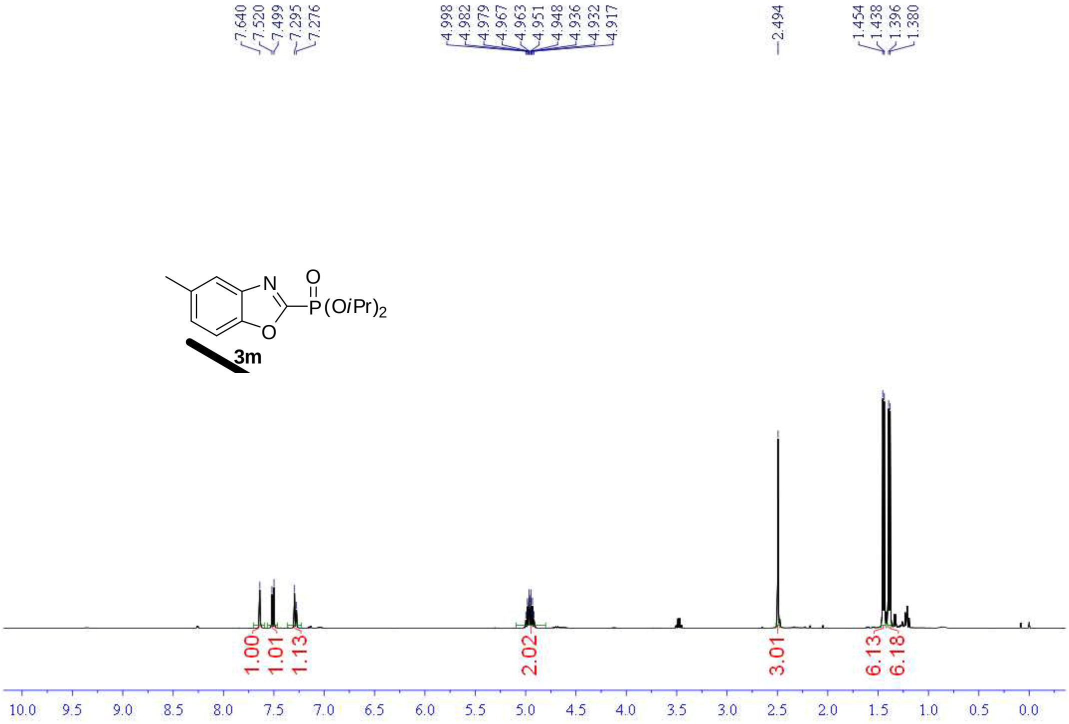
-20
-30
-40
-50
-60
-70
-80
-90

3l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7.499
7.295
7.276
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4.982
4.979
4.967
4.963
4.951
4.948
4.936
4.932
4.917
2.494
1.454
1.438
1.396
1.380
N
O
P(OiPr)$_2$
O
3m
1.00
1.01
1.13
2.02
3.01
6.13
6.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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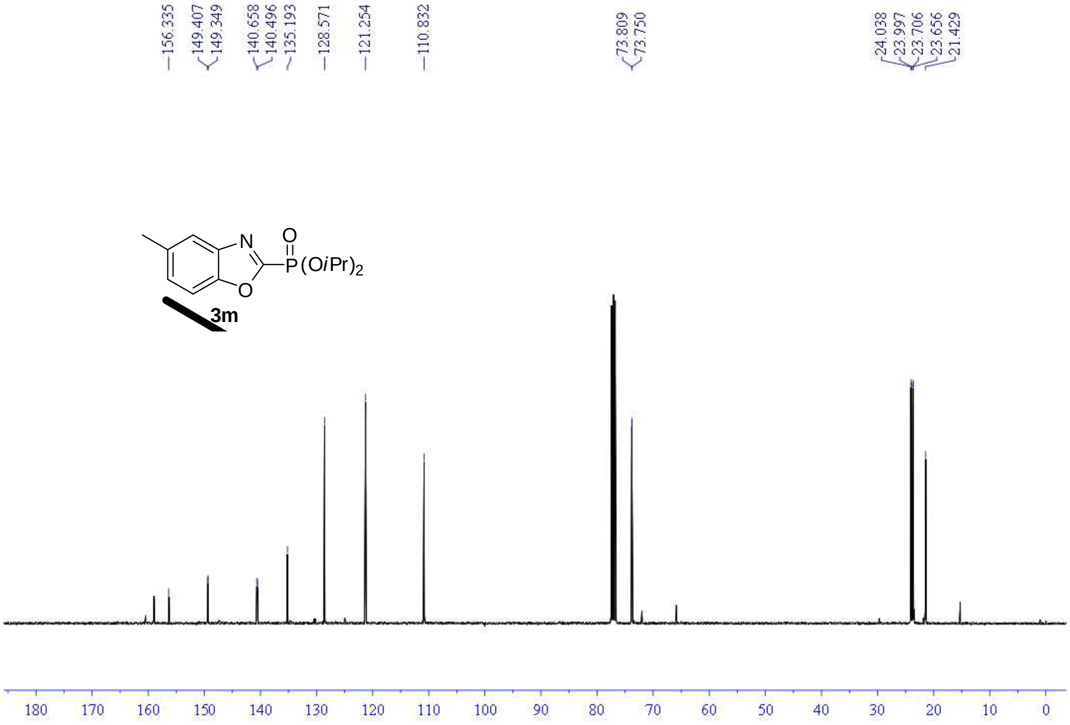
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24.038
23.997
23.706
23.656
21.429
N
O
P(OiPr)$_2$
O
3m
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150
140
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110
100
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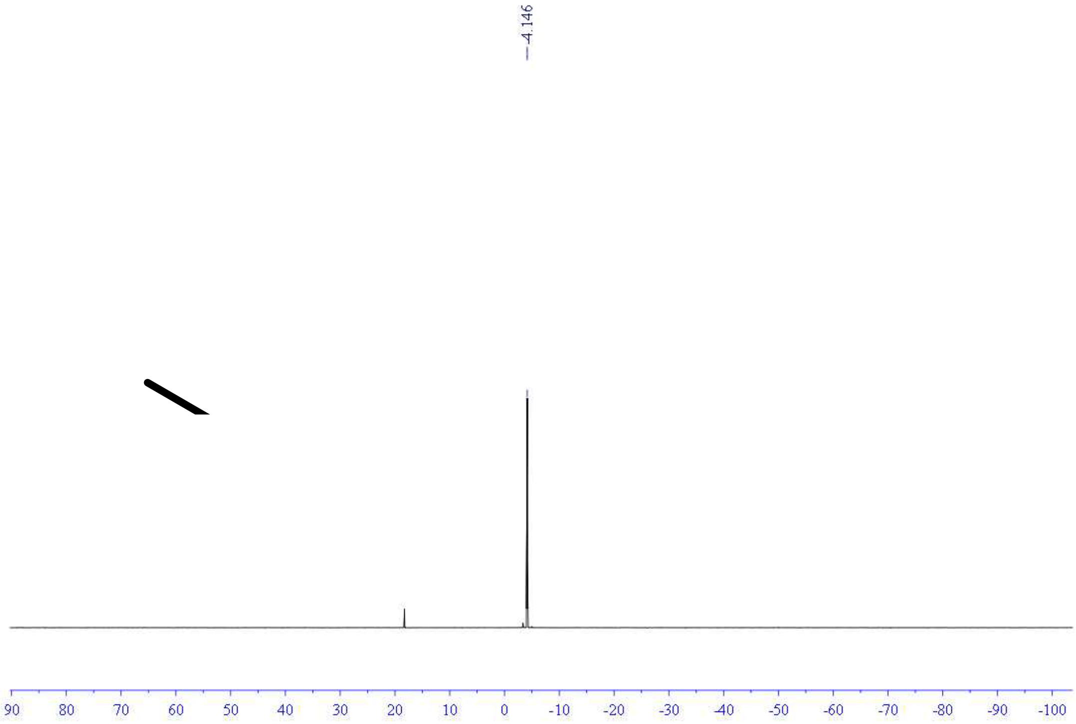
0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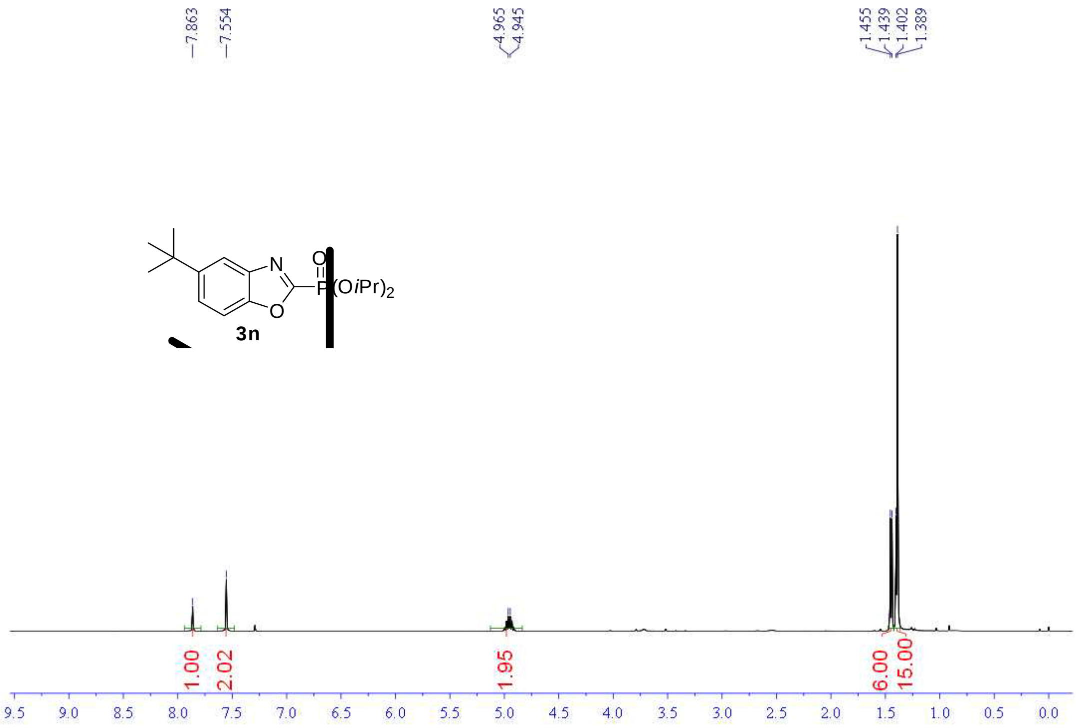
-100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1.402
1.389
N
O
O
P
(O*i*Pr)$_2$
3n
1.00
2.02
1.95
6.00
15.00
9.5
9.0
8.5
8.0
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7.0
6.5
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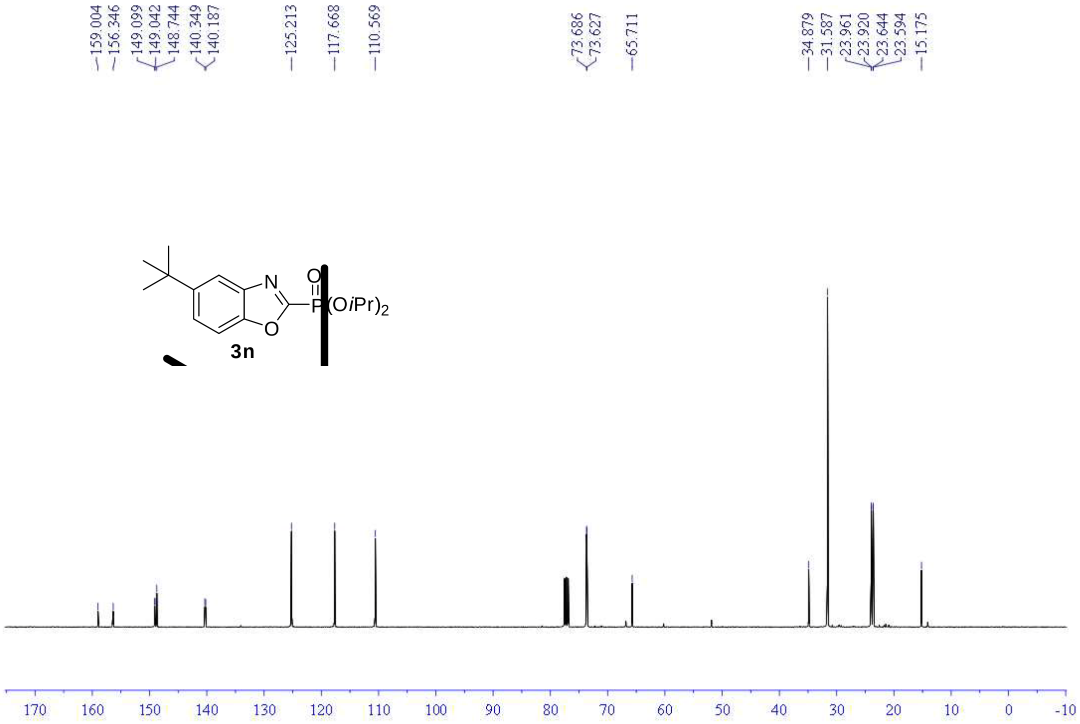
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65.711
34.879
31.587
23.961
23.920
23.644
23.594
15.175
N
O
P(OiPr)2
O
3n
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140
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120
110
100
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60
50
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20
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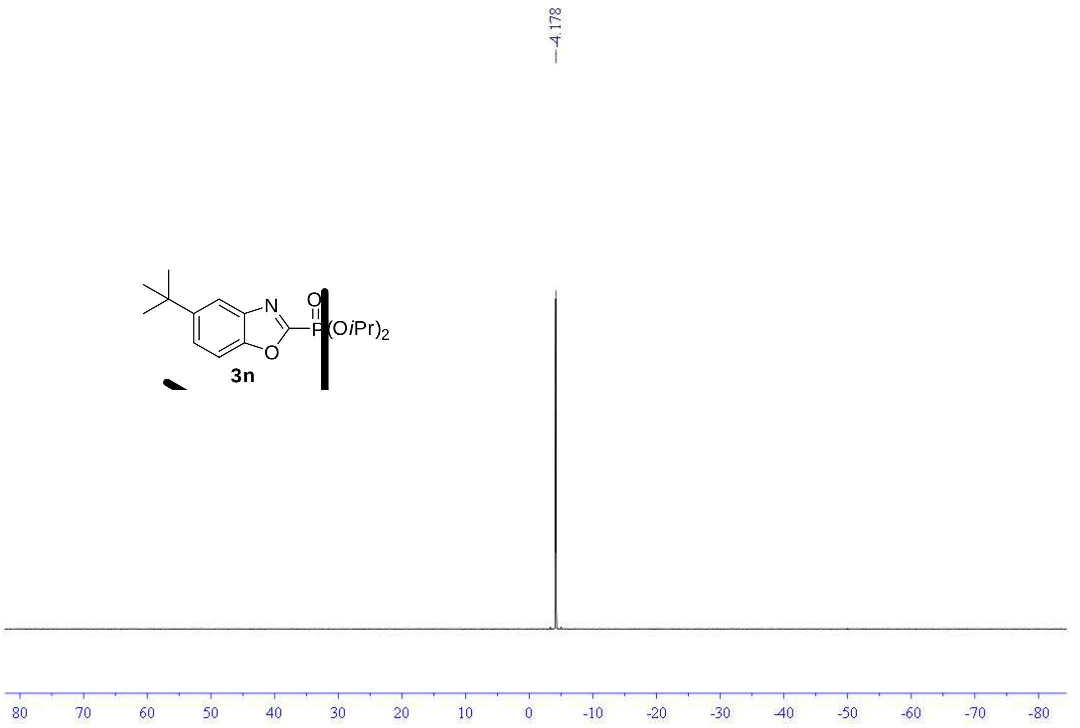
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40
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0
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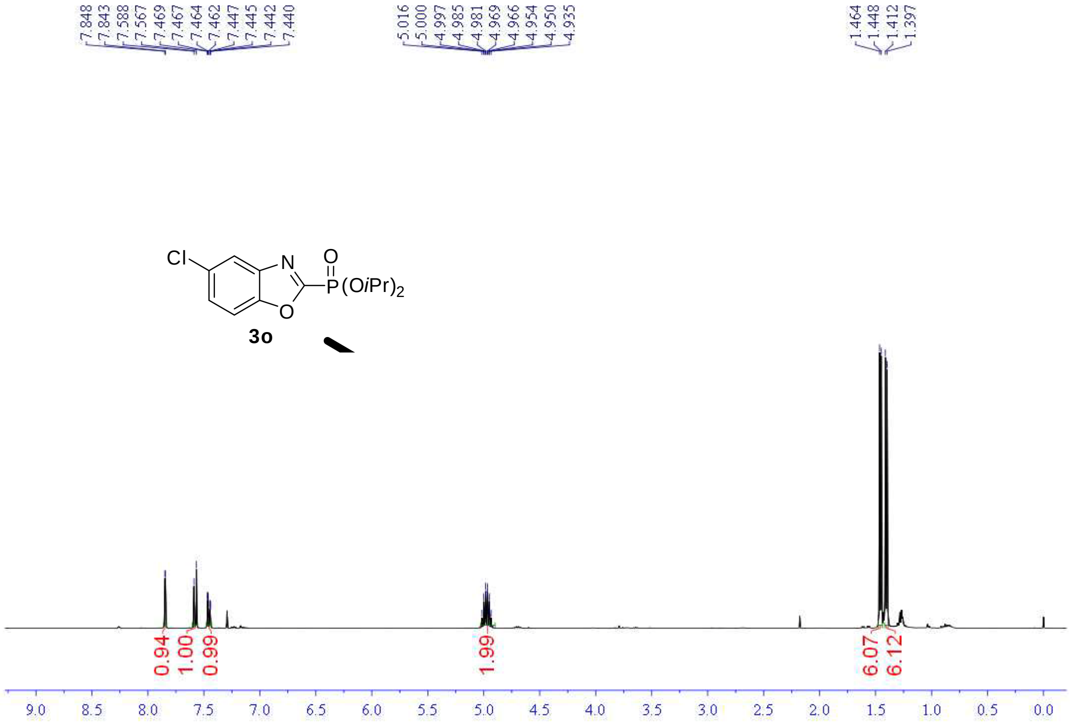
-40
-50
-60
-70
-80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7.462
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7.440
5.016
5.000
4.997
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4.981
4.969
4.966
4.954
4.950
4.935
1.464
1.448
1.412
1.397
Cl
N
O
P(O*i*Pr)$_2$
O
3o
0.94
1.00
0.99
1.99
6.07
6.12
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
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2.5
2.0
1.5
1.0
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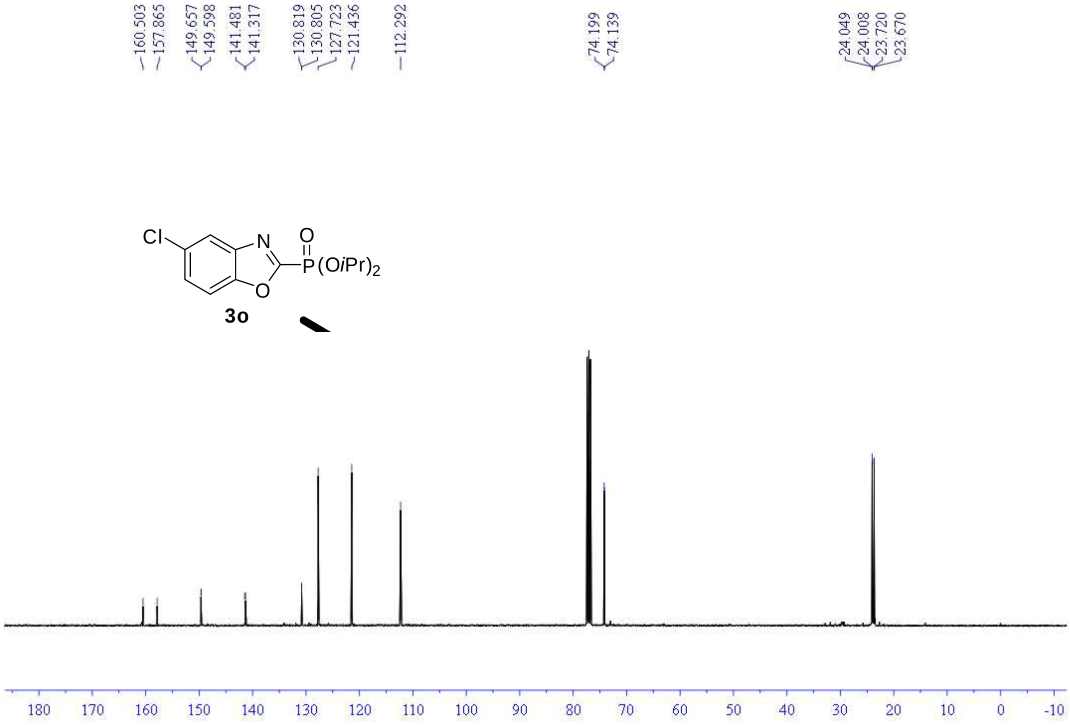
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121.436
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74.199
74.139
24.049
24.008
23.720
23.670
Cl
N
O
P(O*i*Pr)$_2$
O
3o
180
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140
130
120
110
100
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80
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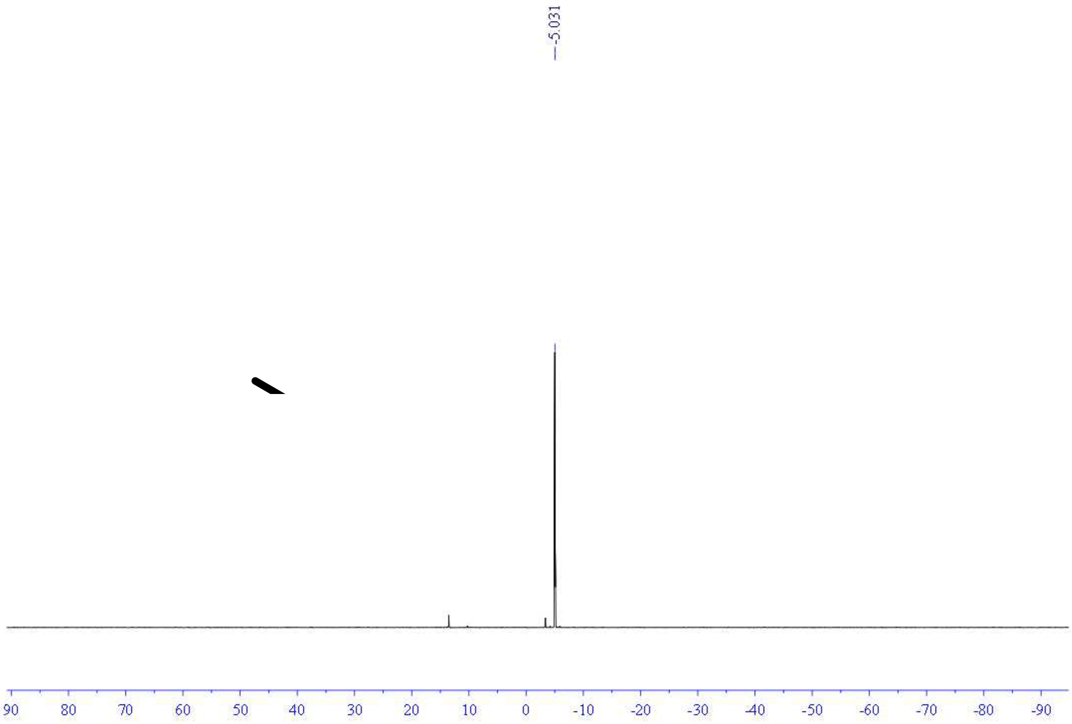
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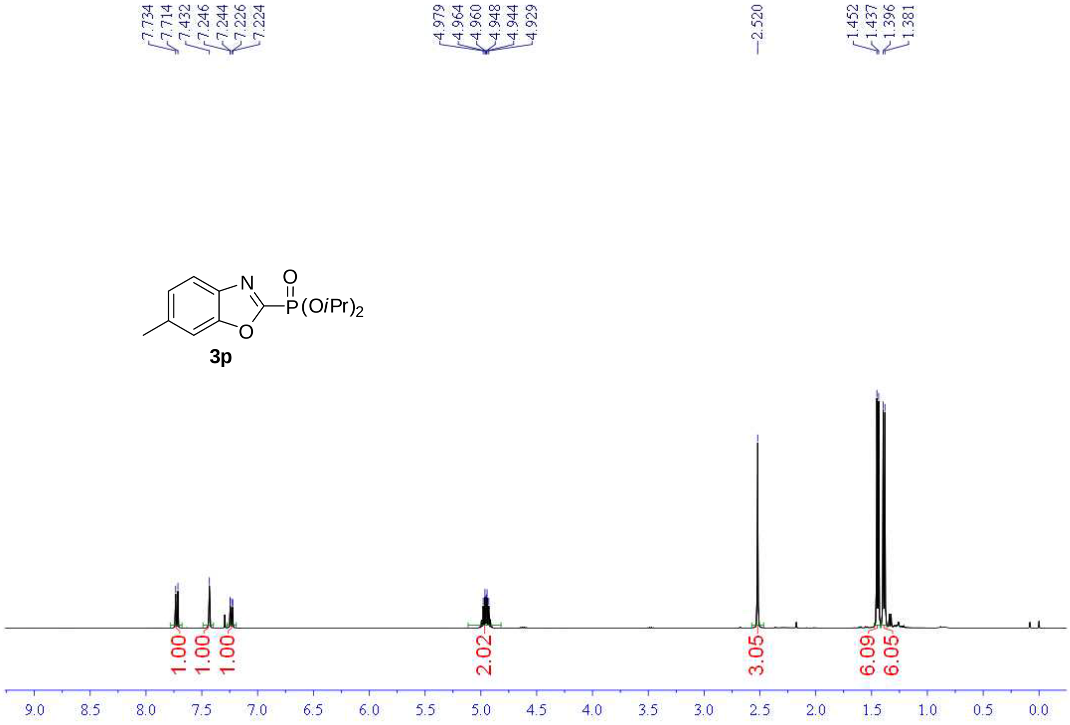
-90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4.929
2.520
1.452
1.437
1.396
1.381
N
O
P(OiPr)2
O
3p
1.00
1.00
1.00
2.02
3.05
6.09
6.05
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8.5
8.0
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7.0
6.5
6.0
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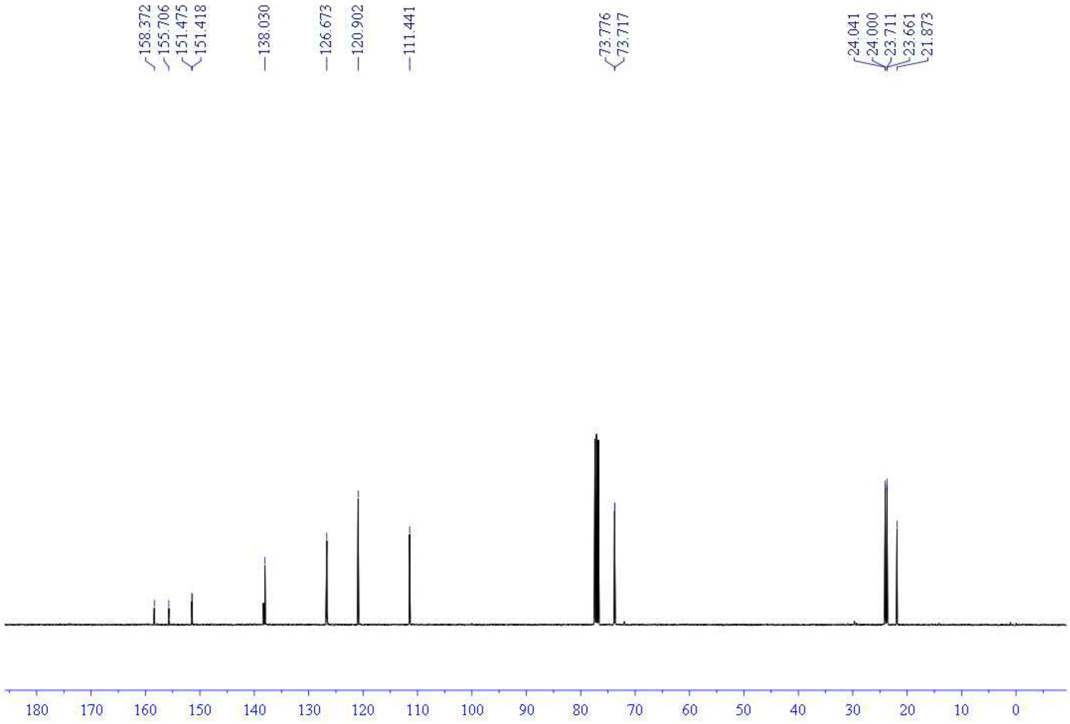
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23.661
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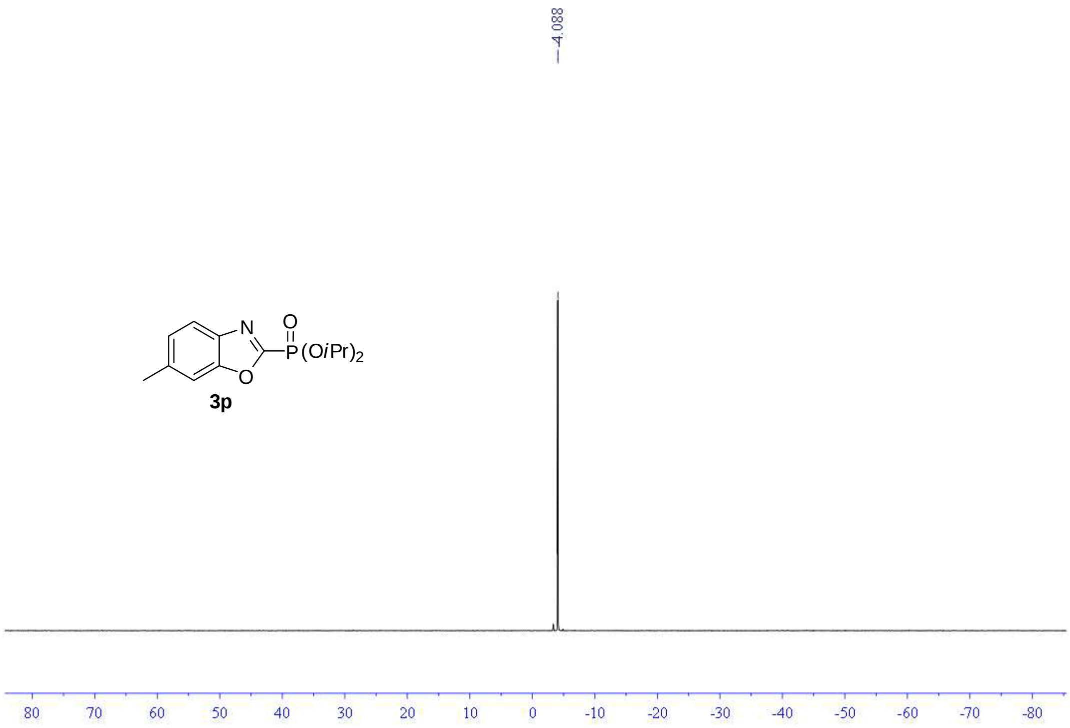
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N
O
O
P(O*i*Pr)$_2$
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80

3p