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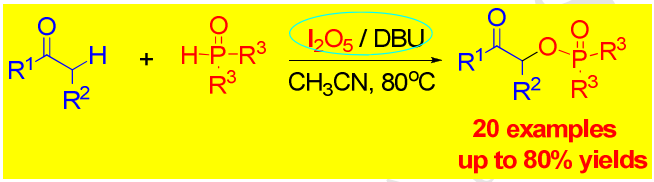

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I_2O_5/DBU mediated direct α-phosphoryloxylation of ketones with H-phosphonates leading to α-hydroxyketone phosphates

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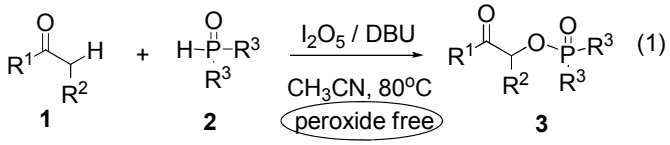
ABSTRACT

A simple and convenient procedure has been developed for the construction of α-hydroxyketone phosphates via I_2O_5/DBU mediated direct α-phosphoryloxylation of ketones with H-phosphonates. This new reaction proceeds through three steps involving α-iodination of ketones, oxidation of H-phosphonates, and nucleophilic substitution of α-iodo ketones to access a series of α-hydroxyketone phosphates of biological importance.

1. Introduction

Organophosphates are key structural motifs in living organisms such as DNA, RNA, ATP, and cell membranes.[1] They are also the important elements in drug discovery[2] and many agrochemicals such as insecticides and herbicides.[3] Moreover, some biologically active phosphates analog can be employed as the extremely useful tools in investigating mechanistic details of various enzymatic systems.[4] In particular, α-hydroxyketone phosphates have attracted great interest of chemists serving as sugar analogues[5] and the key intermediates in the synthesis of phospholipid and oligonucleotide[6] due to the selective hydrolytic removal of the ketoxide motif can be achieved under mildly basic conditions.[7] Generally, α-hydroxyketone phosphates are prepared by the treatment of 2,2,2-trialkoxy-1,3,2-dioxaphospholen with hydrogen chloride[8] or the *a*-phosphoryloxylation of ketones with the preformed [hydroxy(phosphoryloxy)iodo]arenes.[9] Alternative procedures have also been developed such as the conversion of terminal alkynes to ketol phosphates with [hydroxy((bis(pheny1oxy)phosphory1)oxy) idolbenzene,[10] oxyphosphorylation of silyl enol ethers with phosphoric acid and *p*-(dif1uoroiodo)toluene,[11] and iodobenzene promoted *a*-phosphoryloxylation of ketones with $(RO)_2PO_2H$ in the presence of stoichiometric amounts of *m*-chloroperbenzoic acid (*m*-CPBA[12]. However, most of these methods could suffer from some limitations such as extra steps for preparation of active precursors, low atom economy, the poor substrate scope, potentially dangerous peroxide oxidants, toxic chemical wastes, or low yields. Therefore, the development of simple, convenient and efficient methods for preparing ketol phosphates is still highly desirable in synthetic and pharmaceutical chemistry.

Iodine pentoxide (I_2O_5, IP), which are safe, reliable and promising single-electron oxidative surrogates for organic hypervalent iodines, have been recently employed for various organic transformations due to their particular stability, ready availability, and cost-effectiveness.[13] As part of our continuous interest in metal-free synthetic transformations,[14] here, we wish to report a new I_2O_5/DBU-mediated one-pot protocol for the synthesis of α-hydroxyketone phosphates via direct α-phosphoryloxylation reaction of ketones with H-phosphonates (Eq. 1). The present methodology provides a convenient and highly attractive approach to a variety of α-hydroxyketone phosphates in moderate to good yields under the metal and peroxide-free conditions.



2. Results and discussion

Initially, the model reaction of propiophenone **1a** with $(EtO)_2P(O)H$ **2a** was performed aiming to screen various iodine reagents in the presence of DABCO (1,4-Diazabicyclo[2.2.2]octane) in CH_3CN at 80°C. Gratifyingly, the desired ketol phosphate **3aa** was obtained in 33% yield when I_2O_5 was tested (Table 1, entry 5). Other iodine reagents such as

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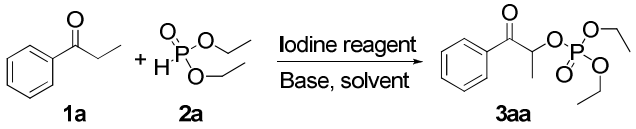
Table 1. Optimization of the reaction conditions[a]



Entry	Iodine reagent	Base	Solvent	Yield (%)[b]
1	I_2	DABCO	CH_3CN	0
2	KI	DABCO	CH_3CN	0
3	NaI	DABCO	CH_3CN	0
4	TBAI	DABCO	CH_3CN	0
5	I_2O_5	DABCO	CH_3CN	33
6	**I_2O_5**	**DBU**	**CH_3CN**	**80**
7	I_2O_5	Et_3N	CH_3CN	0
8	I_2O_5	KOH	CH_3CN	trace
9	I_2O_5	Na_2CO_3	CH_3CN	0
10	I_2O_5	Cs_2CO_3	CH_3CN	0
11	I_2O_5	DBU	THF(reflux)	51
12	I_2O_5	DBU	1,4-dioxane	58
13	I_2O_5	DBU	DCE	63
14	I_2O_5	DBU	DME	68
15	I_2O_5	DBU	Toluene	55
16	I_2O_5	DBU	EtOH	0
17	I_2O_5	DBU	DMF	0
18	I_2O_5	DBU	DMSO	0
19	I_2O_5	DBU	H_2O	0
20	I_2O_5	DBU	CH_3CN	0[c]
21	I_2O_5	DBU	CH_3CN	52[d]
22	--	DBU	CH_3CN	0
23	I_2O_5	--	CH_3CN	0

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.75 mmol), iodine reagent (1 equiv), base (1 equiv), solvent (2 mL), 80°C, 48 h. TBAI=$(n\text{-}Bu)_4NI$; DME: 1,2-Dimethoxyethane, DCE: 1,2-Dichloroethane.

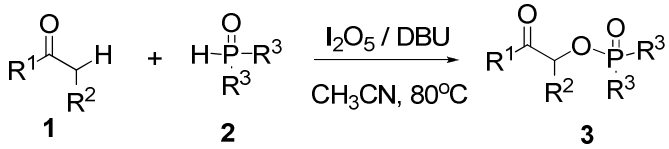
[b] Isolated yields based on **1a**.

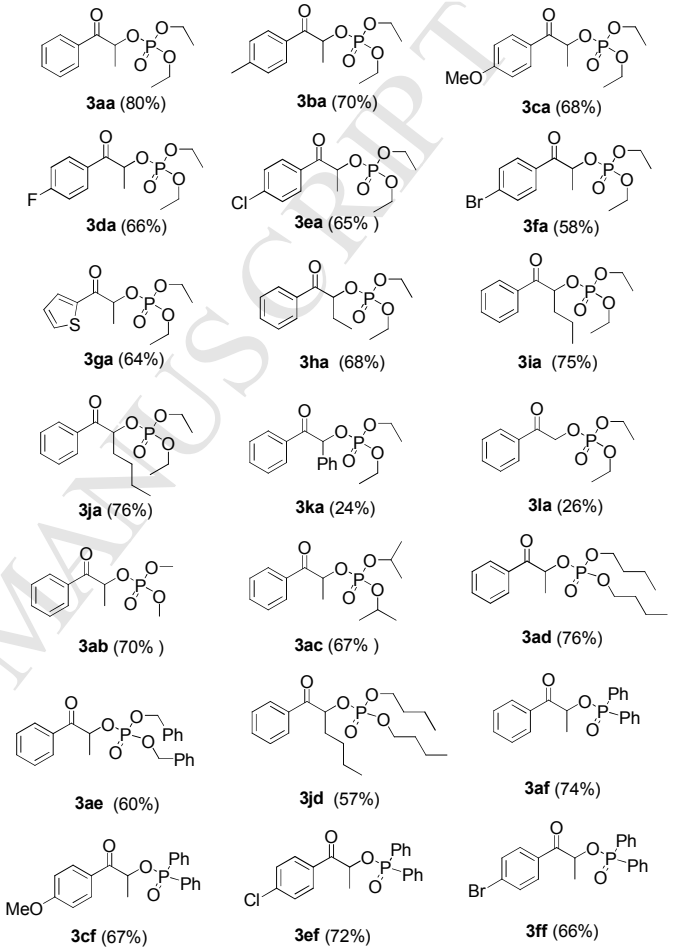
[c] 25°C

[d] 60°C.

I_2, KI, NaI, and TBAI did not promote the formation of product **3aa** (Table 1, entries 1-4). Further optimization of bases suggested that DBU (1,8-diazabicycloundec-7-ene) stood out to be the best choice, while the others such as Et_3N, KOH, Na_2CO_3, Cs_2CO_3 and DABCO were less effective (Table 1, entries 6-10). Also, the effects of various solvents were investigated. Among a range of solvents examined, CH_3CN was found to be the optimized reaction medium for this transformation, while THF, DME, 1,4-dioxane, DCE, and toluene performed with moderate efficiency (Table 1, entries 11-15). The reaction did not occur in EtOH, DMF, DMSO, and H_2O (Table 1, entries 16-19). Moreover, none of the desired product **3aa** was obtained when the reaction was performed at room temperature (Table 1, entry 20). The reaction efficiency was obviously improved with increasing of the reaction temperature and the best yield (80%) was achieved when the reaction proceeded at 80°C (Table 1, entries 6, 20-21). Additionally, no product was detected when the reaction was conducted in the absence of I_2O_5 or DBU (Table 1, entries 22 and 23).

Table 2. Results for I_2O_5/DBU mediated direct α-phosphoryloxylation of ketones with H-phosphonates[ab,]





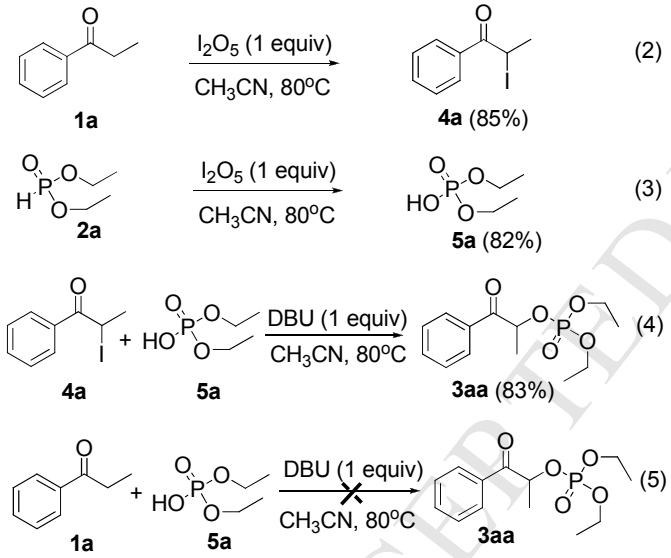
[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.75 mmol), I_2O_5 (0.25 mmol), DBU (0.25 mmol), CH_3CN (2 mL), 80°C, 48 h.

[b] Isolated yields based on **1**.

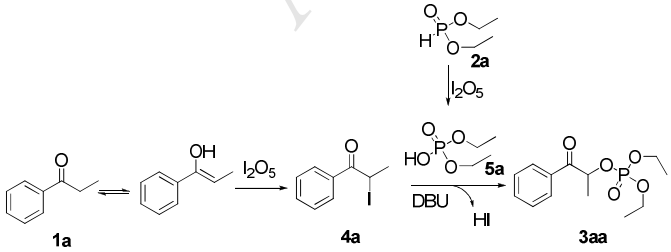
With the optimized conditions in hand, we next explored the scope and generality of this α-phosphoryloxylation reaction (Table 2). In general, propiophenone derivatives with both electron-donating and electron-withdrawing substituents on the benzene ring could be smoothly transformed into the desired products in moderate to good yields (**3aa**-**3fa**). Notably, halo substituents including F, Cl, and Br could be tolerated in this procedure, thus providing chances for further modification of these compounds (**3da**-**3fa**). Heteroaromatic ketone such as 1-(thiophen-2-yl)propan-1-one was also suitable for this process, with the corresponding product in 64% yield (**3ga**). Moreover, long chain alkyl substituted aromatic ketone did not hinder the reaction, affording the desired products in good yields (**3ha**-**3ja**).

Nevertheless, none of the desired product was obtained when dialkyl substituted aromatic ketone such as 2-methyl-1-phenylpropan-1-one was used as the substrate, which might be caused by the steric effect. Unfortunately, when 1,2-diphenylethanone and acetophenone were used as the substrates, the corresponding products were obtained in relatively low yields (**3ka** and **3la**). With respect to the H-phosphonates, dimethyl, diisopropyl, dibutyl, and dibenzyl phosphonates were discovered to be suitable substrates in addition to **2a**, which delivered the desired α-phosphoryloxylation products in moderate to good yields. In addition, this synthetic methodology was extended to $Ph_2P(O)H$, showing the corresponding products in good yields (**3af**-**3ff**).

In order to understand the detailed reaction mechanism, several control experiments were performed as shown in Eq. 2-5. When propiophenone **1a** independently reacted with I_2O_5, the 2-iodo-1-phenylpropan-1-one **4a** could be obtained in 85% yield (Eq. 2). On the other hand, the diethyl hydrogen phosphate **5a** was isolated in 82% yield when the reaction of diethyl phosphonate **2a** with I_2O_5 was performed in CH_3CN at 80°C (Eq. 3). Furthermore, treatment of 2-iodo-1-phenylpropan-1-one **4a** with diethyl hydrogen phosphate **5a** led to the formation of desired product **3aa** in the presence of DBU (Eq. 4). Nevertheless, the direct reaction of propiophenone **1a** with diethyl hydrogen phosphate **5a** did not give the desired α-phosphoryloxylation product **3aa** (Eq. 5). The above results indicated **4a** and **5a** might be two key intermediates in the present reaction system.



On the basis of the above results and previous reports,[13,15] a tentative reaction pathway was proposed in Scheme 1. Initially, α-iodination of propiophenone **1** with I_2O_5 formed the key intermediate α-iodo ketone **4a**, and the oxidation of diethyl phosphonate **2a** with I_2O_5 produced the corresponding diethyl



Scheme 1. Tentative reaction pathway

hydrogen phosphate **5a**. Then, the nucleophilic substitution of α-iodo ketone **4a** by **5a** in the presence of DBU would produce the desired α-phosphoryloxylation product **3aa**.

3. Conclusions

In conclusion, a novel and convenient synthesis method has been developed for the one-pot construction of α-hydroxyketone phosphates via direct α-phosphoryloxylation of ketones with H-phosphonates simply by using I_2O_5/DBU system. This reaction was constituted by three steps involving α-iodination of ketones, oxidation of H-phosphonates, and nucleophilic substitution of α-iodo ketones. A series of biologically important ketol phosphates could be conveniently and efficiently obtained in moderate to good yields from readily-available starting materials. The present protocol is expected to expand the potential applications of α-hydroxyketone phosphatess in the pharmaceutical and synthetic chemistry.

4. Experimental section

4.1. General remarks

All commercially available reagent grade chemicals were purchased from Aldrich, Acros, Alfa Aesar and Beijing Ouhe Chemical Company and used as received without further purification unless otherwise stated. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR were recorded in $CDCl_3$ on a Bruker Avance III 400 spectrometer with TMS as internal standard (400 MHz ^{1}H, 100 MHz ^{13}C, 162 MHz ^{31}P) at room temperature, the chemical shifts (δ) were expressed in ppm and J values were given in Hz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). All first order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). Mass analyses and HRMS were obtained on a Finnigan-LCQDECA mass spectrometer and a Bruker Daltonics Bio-TOF-Q mass spectrometer by the ESI method, respectively. Column chromatography was performed on silica gel (200-300 mesh).

4.2. Experimental Procedures:

General procedure for I_2O_5/DBU mediated direct α-phosphoryloxylation of ketones with H-phosphonates.

In a sealed tube (25 mL), ketones **1** (0.25 mmol), H-phosphonates **2** (0.75 mmol), I_2O_5 (0.25 mmol), DBU (0.25 mmol), and CH_3CN (2 mL) were added. The reaction vessel was allowed to stir at 80 °C for 48 h. After the reaction, the solution was concentrated in vacuum. The resulting mixture purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product **3**.

*The reaction of propiophenone **1a** with I_2O_5.*

In a sealed tube (25 mL), propiophenone **1a** (0.25 mmol), I_2O_5 (0.25 mmol), and CH_3CN (2 mL) were added. The reaction vessel was allowed to stir at 80 °C for 48 h. After the reaction, the solution was concentrated in vacuum. The resulting mixture purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired 2-iodo-1-phenylpropan-1-one **4a** in 85% yield.

*The reaction of diethyl phosphonate **2a** with I_2O_5.*

In a sealed tube (25 mL), diethyl phosphonate **2a** (0.25 mmol), I_2O_5 (0.25 mmol), and CH_3CN (2 mL) were added. The reaction vessel was allowed to stir at 80 °C for 12 h. After the reaction, the solution was concentrated in vacuum. The resulting mixture purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired diethyl hydrogen phosphate **5a** in 82% yield.

*The reaction of **4a** and **5a** in the presence of DBU.*

To a mixture of 2-iodo-1-phenylpropan-1-one **4a** (0.25 mmol), diethyl hydrogen phosphate **5a** (0.75 mmol) and DBU (0.25 mmol) in a 25 mL round-bottomed flack at room temperature, was added the CH_3CN (2 mL). The reaction vessel was allowed to stir at 80 °C for 12 h. After the reaction, the solution was concentrated in vacuum, the desired product **3aa** was obtained in 83% yield.

*The reaction of **1a** and **5a** in the presence of DBU.*

To a mixture of propiophenone **1a** (0.25 mmol), diethyl hydrogen phosphate **5a** (0.75 mmol) and DBU (0.25 mmol) in a 25 mL round-bottomed flack at room temperature, was added the CH_3CN (2 mL). The reaction vessel was allowed to stir at 80°C for 12 h. After the reaction, the solution was concentrated in vacuum, none of the desired product **3aa** was detected.

Diethyl 1-oxo-1-phenylpropan-2-yl phosphate, compound **3aa** was obtained in 80% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.99 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.9 Hz, 2H), 5.80-5.73 (m, 1H), 4.16-4.09 (m, 4H), 1.63 (d, J = 6.8 Hz, 3H), 1.35 (dt, J_1 = 7.1 Hz, J_2 = 0.9 Hz, 3H), 1.28 (dt, J_1 = 7.1Hz, J_2= 0.9Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.4 (d, J = 4.8 Hz), 134.3, 133.7, 130.9, 128.8, 74.6 (d, J = 5.4 Hz), 64.1 (q, J = 6.0 Hz), 19.4 (d, J = 5.0 Hz), 16.0 (t, J = 6.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.88; HRMS calc. for $C_{13}H_{19}O_5PNa$ $(M+Na)^+$, 309.0868; found, 309.0871.

Diethyl 1-oxo-1-p-tolylpropan-2-yl phosphate, compound **3ba** was obtained in 70% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.88 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.78-5.70 (m, 1H), 4.16-4.07 (m, 4H), 2.42 (s, 3H), 1.61 (d, J = 6.8 Hz, 3H), 1.33 (dt, J_1 = 7.1 Hz, J_2 = 0.8 Hz, 3H), 1.28 (dt, J_1 = 7.1 Hz, J_2 = 0.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 195.8 (d, J = 4.8 Hz), 144.6, 131.6, 129.4, 128.9, 74.5 (d, J = 5.4 Hz), 64.1 (q, J = 6.0 Hz), 21.7, 19.5 (d, J = 5.1 Hz), 16.0 (t, J = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.91; HRMS calc. for $C_{14}H_{21}O_5PNa$ $(M+Na)^+$, 323.1024; found, 323.1028.

Diethyl 1-(4-methoxyphenyl)-1-oxopropan-2-yl phosphate, compound **3ca** was obtained in 68% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.98 (d, J = 8.9 Hz, 2H), 6.96 (d, J = 8.9 Hz, 2H), 5.75-5.68 (m, 1H), 4.15-4.07 (m, 4H), 3.88 (s, 3H), 1.61 (d, J = 6.8 Hz, 3H), 1.33 (dt, J_1 = 7.0 Hz, J_2 = 0.8 Hz 3H), 1.27 (dt, J_1 = 7.0 Hz, J_2 = 0.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 194.6 (d, J = 4.8 Hz), 163.9, 131.1, 127.0, 114.0, 74.3 (d, J = 5.4 Hz), 64.0 (q, J = 6.0 Hz), 55.5, 19.5 (d, J = 5.0 Hz), 16.0 (t, J = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -2.01; HRMS calc. for $C_{14}H_{21}O_6PNa$ $(M+Na)^+$, 339.0973; found, 33.9.0977.

Diethyl 1-(4-fluorophenyl)-1-oxopropan-2-yl phosphate, compound **3da** was obtained in 66% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.06-8.03 (m, 2H), 7.17 (m, 2H), 5.73-5.66 (m, 1H), 4.16-4.07 (m, 4H), 1.62 (d, J = 6.8 Hz, 3H), 1.34 (dt, J_1 = 7.1 Hz, J_2 = 1.0 Hz, 3H), 1.28 (dt, J_1 = 7.1 Hz, J_2 = 1.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 194.8 (d, J = 5.0 Hz), 166.0 (d, J = 254.5 Hz), 131.6 (d, J = 9.4 Hz), 130.6 (d, J = 3.0 Hz), 115.9 (d, J = 21.8 Hz), 74.5 (d, J = 5.4 Hz), 64.1 (q, J = 6.0 Hz), 19.2 (d, J = 5.0 Hz), 16.0 (t, J = 6.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.88; HRMS calc. for $C_{13}H_{18}FO_5PNa$ $(M+Na)^+$, 327.0774; found, 327.0770.

1-(4-Chlorophenyl)-1-oxopropan-2-yl diethyl phosphate, compound **3ea** was obtained in 65% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.96 (d, J = 8.6 Hz, 2H), 7.48 (d, J = 8.6 Hz, 2H), 5.72-5.65 (m, 1H), 4.16-4.09 (m, 4H), 1.62 (d, J = 6.8 Hz, 3H), 1.35 (dt, J_1 = 7.1 Hz, J_2 = 0.7 Hz, 3H), 1.29 (dt, J_1 = 7.1 Hz, J_2 = 0.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 195.2 (d, J = 4.9 Hz), 140.2, 132.5, 130.3, 129.1, 74.6 (d, J = 5.4 Hz), 64.2 (q, J = 6.0 Hz), 19.2 (d, J = 5.1 Hz), 16.0 (t, J = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.92; HRMS calc. for $C_{13}H_{19}ClO_5P$ $(M+H)^+$, 321.0659; found, 321.0656.

1-(4-Bromophenyl)-1-oxopropan-2-yl diethyl phosphate, compound **3fa** was obtained in 58% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.88 (d, J = 8.6 Hz, 2H), 7.65 (d, J = 8.6 Hz, 2H), 5.72-5.65 (m, 1H), 4.16-4.10 (m, 4H), 1.62 (d, J = 6.8 Hz, 3H), 1.35 (dt, J_1 = 7.1 Hz, J_2 = 1.0 Hz, 3H), 1.30 (dt, J_1 = 7.1 Hz, J_2 = 1.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 195.5 (d, J = 5.0 Hz), 133.0, 132.1, 130.3, 128.9, 74.6 (d, J = 5.5 Hz), 64.2 (q, J = 6.1 Hz), 19.2 (d, J = 4.7 Hz), 16.0 (t, J = 6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.95; HRMS calc. for $C_{13}H_{18}BrO_5PNa$ $(M+Na)^+$, 386.9973; found, 386.9974.

Diethyl 1-oxo-1-(thiophen-2-yl)propan-2-yl phosphate, compound **3ga** was obtained in 64% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.93 (d, J = 3.8 Hz, 1H), 7.73 (d, J = 4.9 Hz, 1H), 7.18 (t, J = 4.2 Hz, 1H), 5.52-5.45 (m, 1H), 4.16-4.09 (m, 4H), 1.66 (d, J = 6.8 Hz, 3H), 1.34 (d, J = 7.0 Hz, 3H), 1.29 (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 189.5 (d, J = 5.1 Hz), 140.3, 135.0, 133.6, 128.4, 75.7 (d, J = 5.5 Hz), 64.2 (t, J = 6.4 Hz), 19.9 (d, J = 5.1 Hz), 16.1 (d, J = 4.6 Hz), 16.0 (d, J = 4.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -2.13; HRMS calc. for $C_{11}H_{17}O_5PSNa$ $(M+Na)^+$, 315.0432; found, 315.0428.

Diethyl 1-oxo-1-phenylbutan-2-yl phosphate, compound **3ha** was obtained in 68% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.97 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 5.63-5.58 (m, 1H), 4.17-4.09 (m, 4H), 2.06-1.99 (m, 1H), 1.96-1.89 (m, 1H), 1.34 (dt, J_1 = 7.0 Hz, J_2 = 0.9 Hz, 3H), 1.29 (dt, J_1 = 7.1 Hz, J_2 = 0.9 Hz, 3H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.4 (d, J = 2.7 Hz), 134.7, 133.6, 128.8, 128.6, 79.5 (d, J = 5.6 Hz), 64.1 (q, J = 6.0 Hz), 26.8 (d, J = 6.3 Hz), 16.0 (t, J = 6.8 Hz), 9.3; ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.64; HRMS calc. for $C_{14}H_{21}O_5PNa$ $(M+Na)^+$, 323.1024; found, 323.1019.

Diethyl 1-oxo-1-phenylpentan-2-yl phosphate, compound **3ia** was obtained in 75% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.96 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 5.64 (q, J = 7.1 Hz, 1H), 4.16-4.08 (m, 4H), 1.90-1.85(m, 2H), 1.55-1.49 (m, 2H), 1.32 (dt, J_1 = 7.0 Hz, J_2 = 0.7 Hz, 3H), 1.28 (dt, J_1 = 7.1 Hz, J_2 = 0.8 Hz, 3H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.5 (d, J = 2.4 Hz), 134.7, 133.6, 128.8, 128.6, 78.3 (d, J = 5.6 Hz), 64.0 (q, J = 6.0 Hz), 35.5 (d, J = 6.5 Hz), 18.3, 16.0 (t, J = 6.7 Hz), 13.6; ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.67; HRMS calc. for $C_{15}H_{24}O_5P$ $(M+H)^+$, 315.1361; found, 315.1364.

Diethyl 1-oxo-1-phenylhexan-2-yl phosphate, compound **3ja** was obtained in 76% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.97 (d, J = 7.4 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 5.67-5.62 (m, 1H), 4.19-4.10 (m, 4H), 1.94-1.86 (m, 2H), 1.51-1.46 (m, 2H), 1.38-1.27 (m, 8H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.6 (d, J = 2.4 Hz), 134.6, 133.6, 128.8, 128.6, 78.5 (d, J = 5.6 Hz), 64.1 (q, J = 6.0 Hz), 33.2 (d, J = 6.5 Hz), 27.1, 22.2, 16.0 (t, J = 6.6 Hz), 13.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.67; HRMS calc. for $C_{16}H_{25}O_5PNa$ $(M+Na)^+$, 351.1337; found, 351.1339.

Diethyl 2-oxo-1,2-diphenylethyl phosphate, compound **3ka** was obtained in 24% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.95 (d, J = 7.2 Hz, 2H), 7.54-7.50 (m, 3H), 7.43-7.34 (m, 5H), 6.67 (d, J = 8.0 Hz, 1H), 4.24-4.18(m, 2H), 3.96-3.89 (m, 2H), 1.34 (dt, J_1 = 7.1 Hz, J_2 = 0.9 Hz, 3H), 1.15 (dt, J_1 = 7.1 Hz, J_2 = 0.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 193.6 (d, J = 4.6 Hz), 134.9 (d, J = 5.3 Hz), 134.3, 133.6, 129.3, 129.1, 129.0, 128.6, 128.1, 80.1 (d, J = 4.8 Hz), 64.4 (d, J = 5.9 Hz), 64.0 (d, J = 6.1 Hz), 16.0 (d, J = 7.0 Hz), 15.8 (d, J = 7.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.92; HRMS calc. for $C_{18}H_{22}O_5P$ $(M+H)^+$, 349.1205; found, 349.1204.

Diethyl 2-oxo-2-phenylethyl phosphate

Compound **3la** was obtained in 26% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.91 (d, J = 7.3 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 5.34 (d, J = 9.9Hz, 2H), 4.28-4.20 (m, 4H), 1.38 (dt, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 192.3 (d, J = 5.2 Hz), 134.0, 133.9, 128.9, 127.8, 68.7 (d, J = 5.2 Hz), 64.4 (d, J = 6.0 Hz), 16.1 (d, J = 6.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -0.91; HRMS calc. for $C_{12}H_{17}O_5PNa$ $(M+Na)^+$, 295.0711; found, 295.0775.

Dimethyl 1-oxo-1-phenylpropan-2-yl phosphate, compound **3ab** was obtained in 70% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.99 (d, J = 7.2 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.9 Hz, 2H), 5.84-5.77 (m, 1H), 3.79 (t, J = 11.3 Hz, 6H), 1.64 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.2 (d, J = 4.7 Hz), 134.1, 133.8, 128.8, 128.7, 74.8 (d, J = 5.3 Hz), 54.5 (q, J = 6.1 Hz), 19.4 (d, J = 5.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 0.33; HRMS calc. for $C_{11}H_{15}O_5PNa$ $(M+Na)^+$, 281.0555; found, 281.0556.

Diisopropyl 1-oxo-1-phenylpropan-2-yl phosphate, compound **3ac** was obtained in 67% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.00 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 5.75-5.68 (m, 1H), 4.69-4.60 (m, 2H), 1.62 (d, J = 6.8 Hz, 3H), 1.33 (q, J = 6.2 Hz, 6H), 1.27 (t, J = 6.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.6 (d, J = 5.1 Hz), 134.3, 133.6, 128.8, 128.7, 74.5 (d, J = 5.5 Hz), 72.9 (q, J = 3.0 Hz), 23.6 (d, J = 4.8 Hz), 23.4 (d, J = 5.1 Hz), 19.4 (d, J = 4.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -3.48; HRMS calc. for $C_{15}H_{23}O_5PNa$ $(M+Na)^+$, 337.1181; found, 337.1176.

Dibutyl 1-oxo-1-phenylpropan-2-yl phosphate, compound **3ad** was obtained in 76% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.00 (d, J = 7.2 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 5.80-5.73 (m, 1H), 4.08-4.01 (m, 4H), 1.69-1.58 (m, 7H), 1.44-1.39 (m, 2H), 1.37-1.31 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.4 (d, J = 5.1 Hz), 134.2, 133.6, 128.8 128.7, 74.6 (d, J = 5.4 Hz), 67.8 (t, J = 6.3 Hz), 32.2 (dd, J_1 = 5.5 Hz, J_2 = 7.0 Hz), 19.3 (d, J = 4.9 Hz), 18.6 (d, J = 5.8 Hz), 13.6 (d, J = 3.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.74; ^{1}HRMS calc. for $C_{17}H_{27}O_5PNa$ $(M+Na)^+$, 365.1494; found, 365.1495.

Dibenzyl 1-oxo-1-phenylpropan-2-yl phosphate, compound **3ae** was obtained in 60% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.94 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.36 (s, 5H), 7.32 (s, 5H), 5.78-5.71 (m, 1H), 5.12-5.03 (m, 4H), 1.57 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.2 (d, J = 4.6 Hz), 135.7 (dd, J_1 = 1.8 Hz, J_2 = 7.3 Hz), 134.1, 133.7, 128.8 (d, J = 1.7 Hz), 128.6 (d, J = 4.6 Hz), 128.6, 128.5, 128.0 (d, J = 3.4 Hz), 74.9 (d, J = 5.4 Hz), 69.5 (q, J = 2.5 Hz), 19.3 (d, J = 5.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.92; ^{1}HRMS calc. for $C_{23}H_{24}O_5P$ $(M+H)^+$, 411.1361; found, 411.1364.

Dibutyl 1-oxo-1-phenylhexan-2-yl phosphate, compound **3jd** was obtained in 57% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.98 (d, J = 7.1 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.9 Hz, 2H), 5.67-5.62 (m, 1H), 4.09-4.04 (m, 4H), 1.93-1.87 (m, 2H), 1.67-1.57 (m, 4H), 1.50-1.30 (m, 8H), 0.95-0.87 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.2 (d, J = 2.5 Hz), 134.6, 133.6, 128.8, 128.7, 78.6 (d, J = 5.7 Hz), 67.8 (t, J = 6.1 Hz), 33.2 (d, J = 6.4 Hz), 32.2 (d, J = 5.1 Hz), 32.1 (d, J = 5.1 Hz), 27.1, 22.2, 18.6 (d, J = 3.8 Hz), 13.8, 13.6 (d, J = 1.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ -1.55; HRMS calc. for $C_{20}H_{33}O_5PNa$ $(M+Na)^+$, 407.1963; found, 407.1966.

1-Oxo-1-phenylpropan-2-yl diphenylphosphinate, compound **3af** was obtained in 74% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.95-7.87 (m, 4H), 7.79-7.74 (m, 2H), 7.59-7.54 (m, 2H), 7.52-7.47 (m, 2H), 7.45-7.41 (m, 3H), 7.39-7.35 (m, 2H), 5.92-5.84 (m, 1H), 1.63 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 196.7 (d, J = 4.8 Hz), 134.3, 133.5, 132.3 (d, J = 2.8 Hz), 132.2 (d, J = 2.9 Hz), 132.1 (d, J = 65.1 Hz), 131.8 (d, J = 7.9 Hz), 131.6 (d, J = 7.6 Hz), 130.8 (d, J = 62.9 Hz), 128.7 (d, J = 1.8 Hz), 128.6, 128.5 (d, J = 3.3 Hz), 128.4, 72.0 (d, J = 5.7 Hz), 20.2 (d, J = 3.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.12; HRMS calc. for $C_{21}H_{19}O_3PNa$ $(M+Na)^+$, 373.0970; found,373.0971.

1-(4-Methoxyphenyl)-1-oxopropan-2-yl diphenylphosphinate, compound **3cf** was obtained in 67% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.96-7.89 (m, 4H), 7.80-7.74 (m, 2H), 7.59-7.55 (m, 1H), 7.52-7.43 (m, 3H), 7.39-7.36 (m, 2H), 6.90 (d, J = 9.0 Hz, 2H), 5.89-5.81 (m, 1H), 3.87 (s, 3H), 1.62 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 195.0 (d, J = 4.8 Hz), 163.9, 132.3 (d, J = 2.8 Hz), 132.2 (d, J = 68.3 Hz), 132.2 (d, J = 2.8 Hz), 131.8 (d, J = 10.4 Hz), 131.7 (d, J = 10.4 Hz), 131.1, 130.8 (d, J = 64.7 Hz), 128.6 (d, J = 8.5 Hz), 128.4 (d, J = 9.5 Hz), 127.0, 113.9, 71.8 (d, J = 5.7 Hz), 55.5, 20.4 (d, J = 3.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.01; HRMS calc. for $C_{22}H_{21}O_4PNa$ $(M+Na)^+$, 403.1075; found, 403.1077.

1-(4-Chlorophenyl)-1-oxopropan-2-yl diphenylphosphinate, compound **3ef** was obtained in 72% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.93-7.88 (m, 2H), 7.87-7.84 (m, 2H), 7.77-7.71 (m, 2H), 7.59-7.55 (m, 1H), 7.51-7.45 (m, 3H), 7.40-7.35 (m, 4H), 5.87-5.80 (m, 1H), 1.60 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 195.6 (d, J = 4.7 Hz), 140.1, 132.6, 132.5 (d, J = 2.8 Hz), 132.4 (d, J = 2.8 Hz), 131.9 (d, J = 55.1 Hz), 131.7 (d, J = 1.6 Hz), 131.6 (d, J = 1.4 Hz), 130.5(d, J = 52.6 Hz), 130.2, 129.0, 128.7 (d, J = 11.6 Hz), 128.6 (d, J = 11.6 Hz), 72.0 (d, J = 5.7 Hz), 20.0 (d, J = 3.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.54;

HRMS calc. for $C_{21}H_{18}O_3ClPNa$ $(M+Na)^+$, 407.0580; found, 407.0584.

1-(4-Bromophenyl)-1-oxopropan-2-yl diphenylphosphinate, compound **3ff** was obtained in 66% yield according to the general procedure (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.93-7.87 (m, 2H), 7.78-7.71 (m, 4H), 7.60-7.55 (m, 3H), 7.52-7.45 (m, 3H), 7.40-7.35 (m, 2H), 5.87-5.79 (m, 1H), 1.60 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 195.8 (d, J = 4.8 Hz), 133.0, 132.5 (d, J = 2.8 Hz), 132.4 (d, J = 2.8 Hz), 132.0, 131.9 (d, J = 55.6 Hz), 131.7 (d, J = 1.9 Hz), 131.6 (d, J = 1.7 Hz), 130.5 (d, J = 53.2 Hz), 130.2, 128.8, 128.7 (d, J = 11.2 Hz), 128.5 (d, J = 11.2 Hz), 72.0 (d, J = 5.7 Hz), 20.0 (d, J = 3.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.55; HRMS calc. for $C_{21}H_{19}O_3BrP$ $(M+H)^+$, 429.0255; found, 429.0257.

2-Iodo-1-phenylpropan-1-one, compound **4a** was obtained in 85% yield from the reaction of propiophenone **1a** with I_2O_5 (48 h). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.04-8.02 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.9 Hz, 2H), 5.52 (q, J = 6.7 Hz, 1H), 2.10 (d, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 194.8, 133.7, 133.5, 128.7, 128.7, 22.0, 18.1; HRMS calc. for $C_9H_{10}OI$ $(M+H)^+$, 260.9776; found, 260.9771.

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Supplementary Information

I_2O_5/DBU mediated direct α-phosphoryloxylation of ketones with H-phosphonates leading to α-hydroxyketone phosphates

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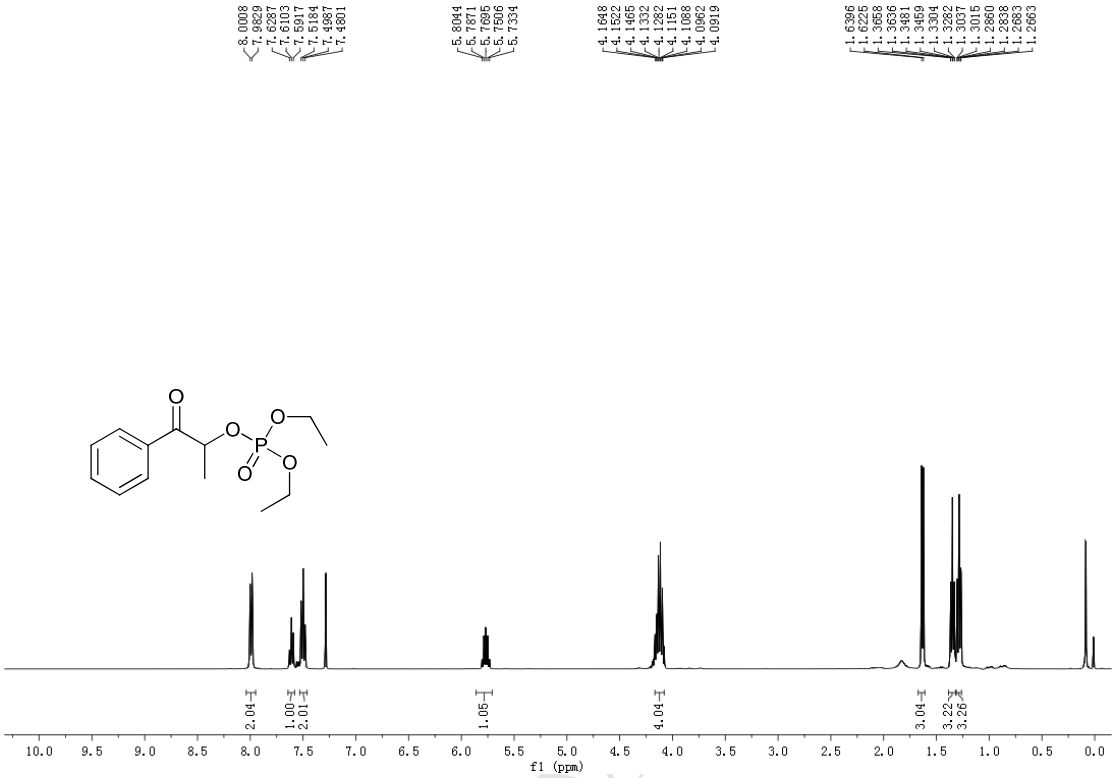
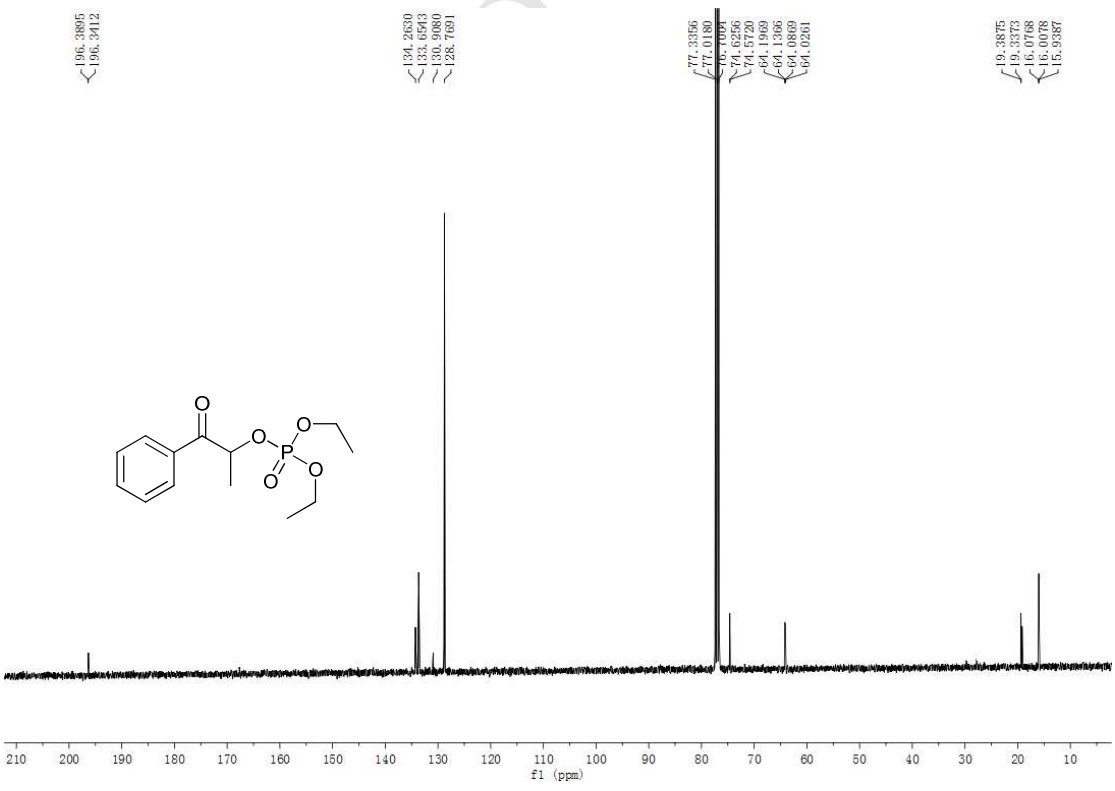
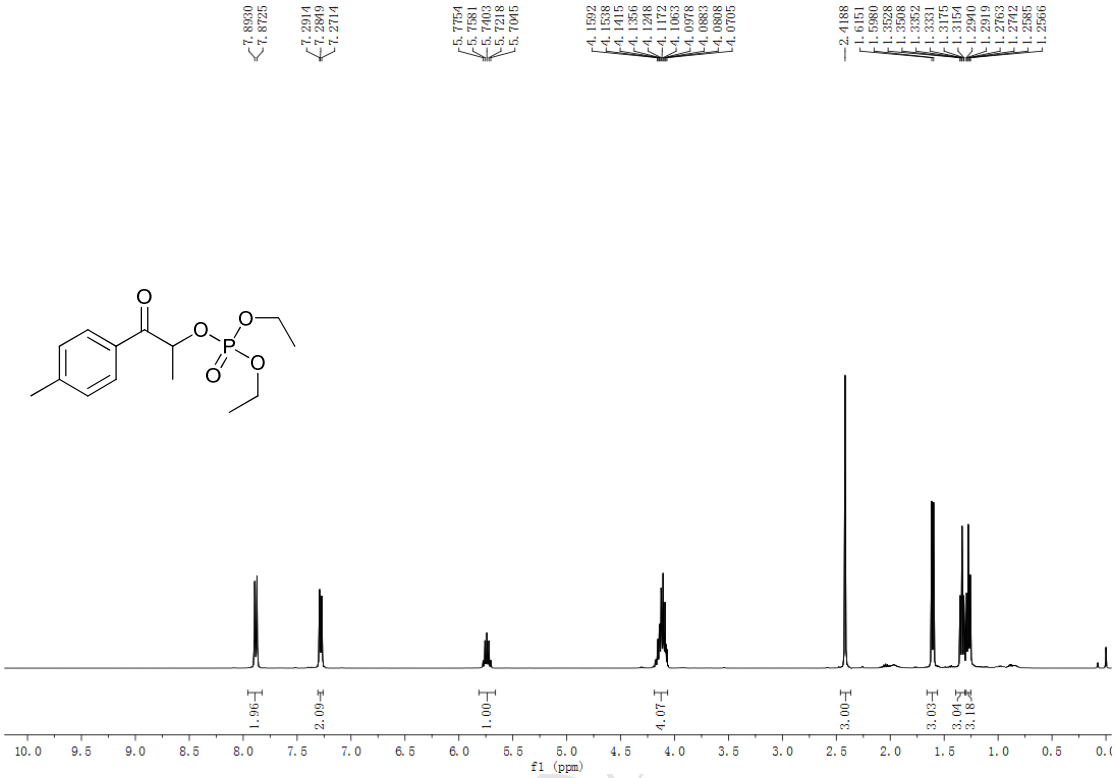
Contents

Copies of NMR spectra for 3aa−3ff, 4a



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3.03
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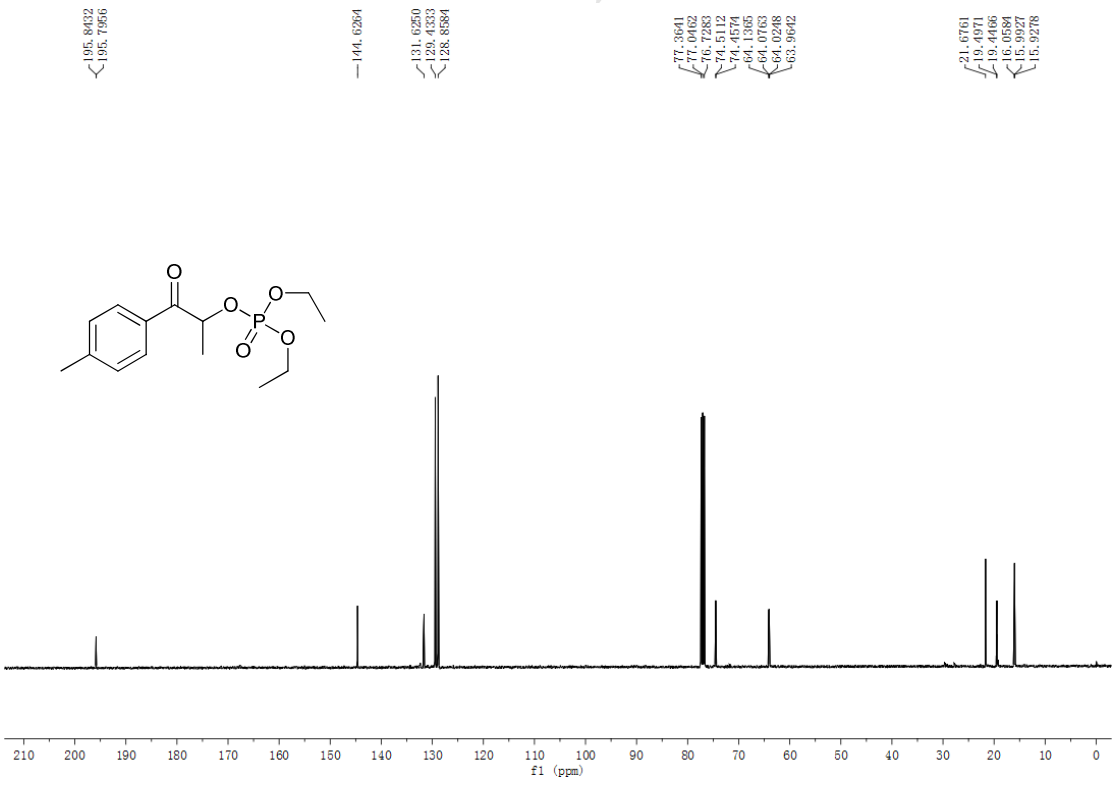
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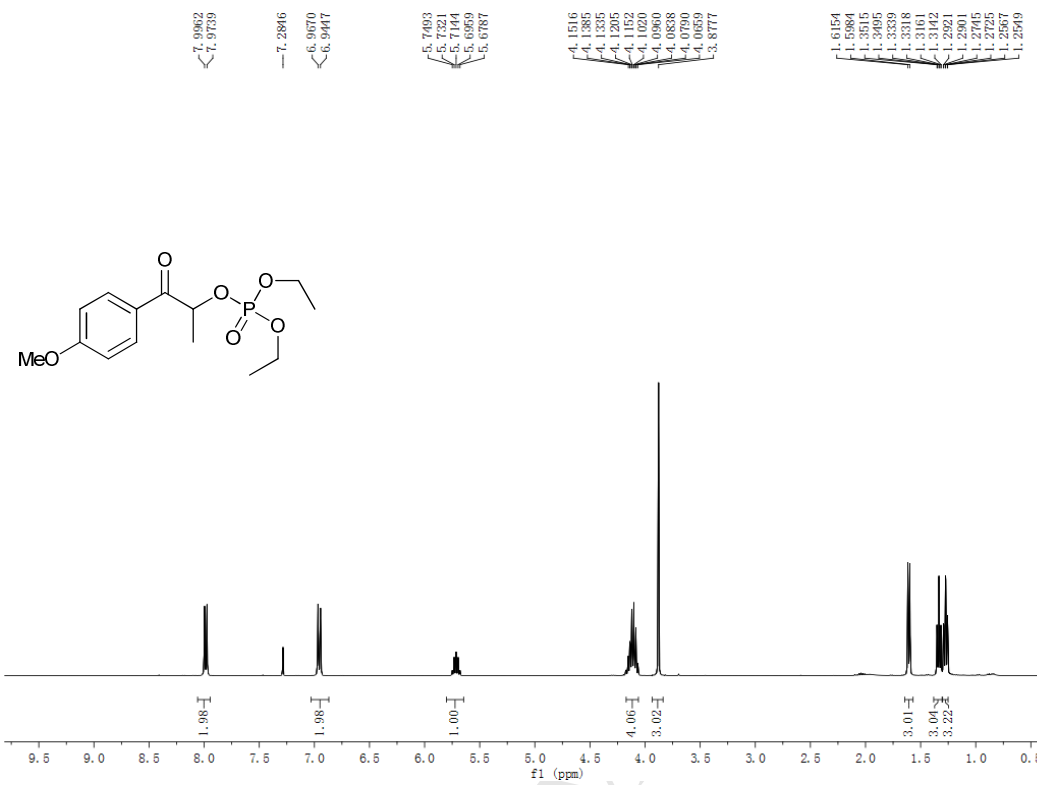
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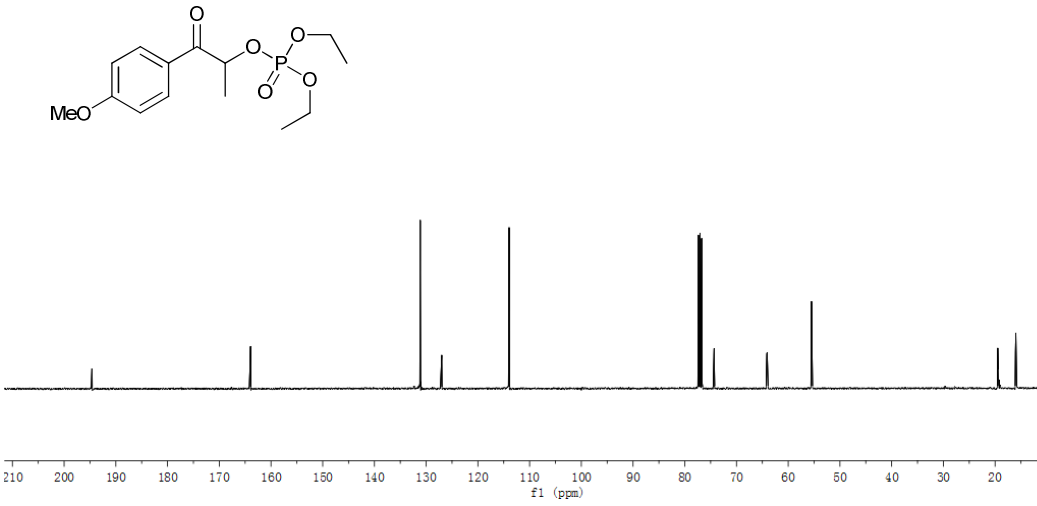
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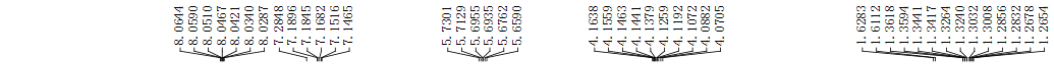
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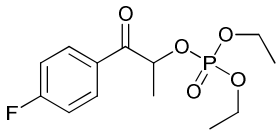
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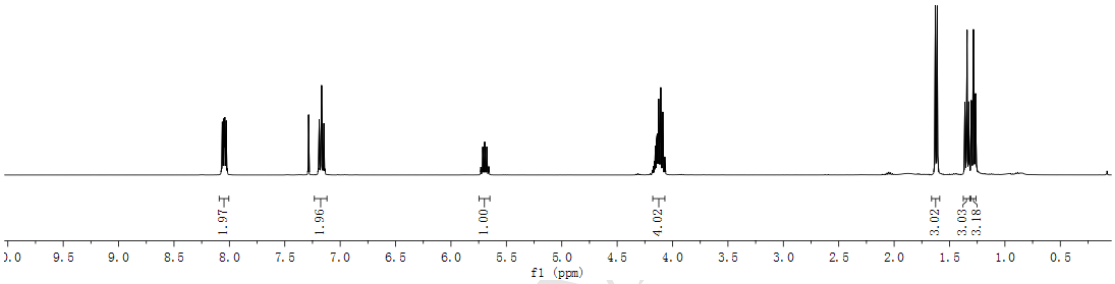
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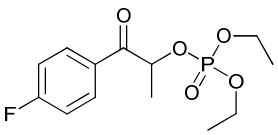
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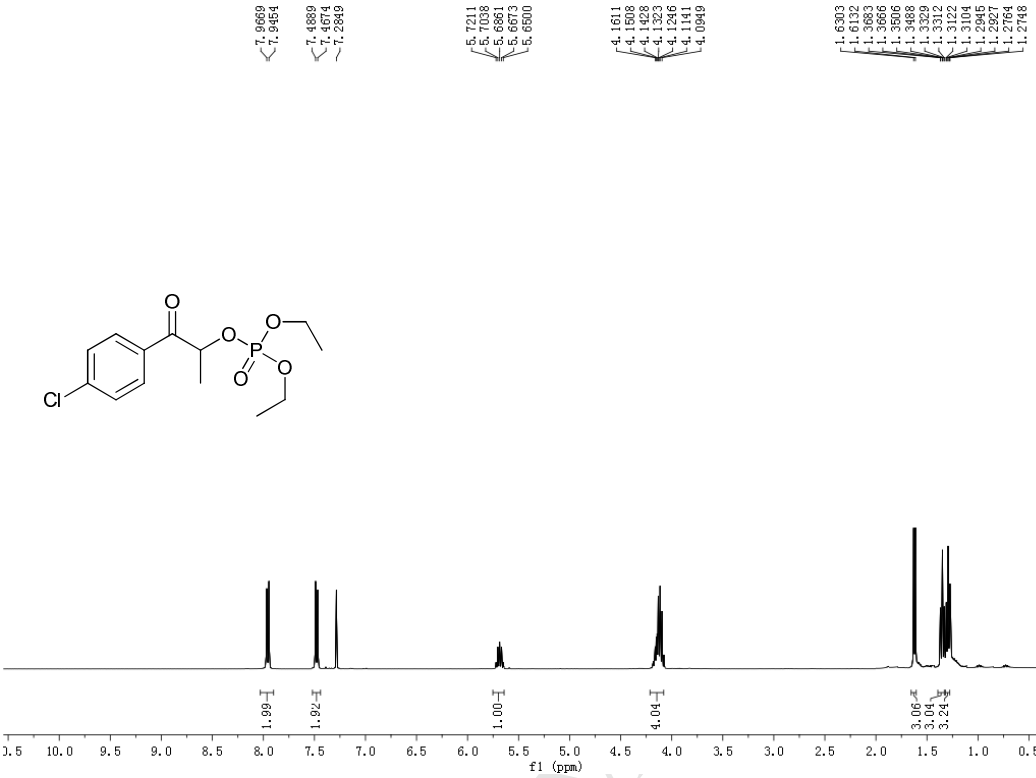
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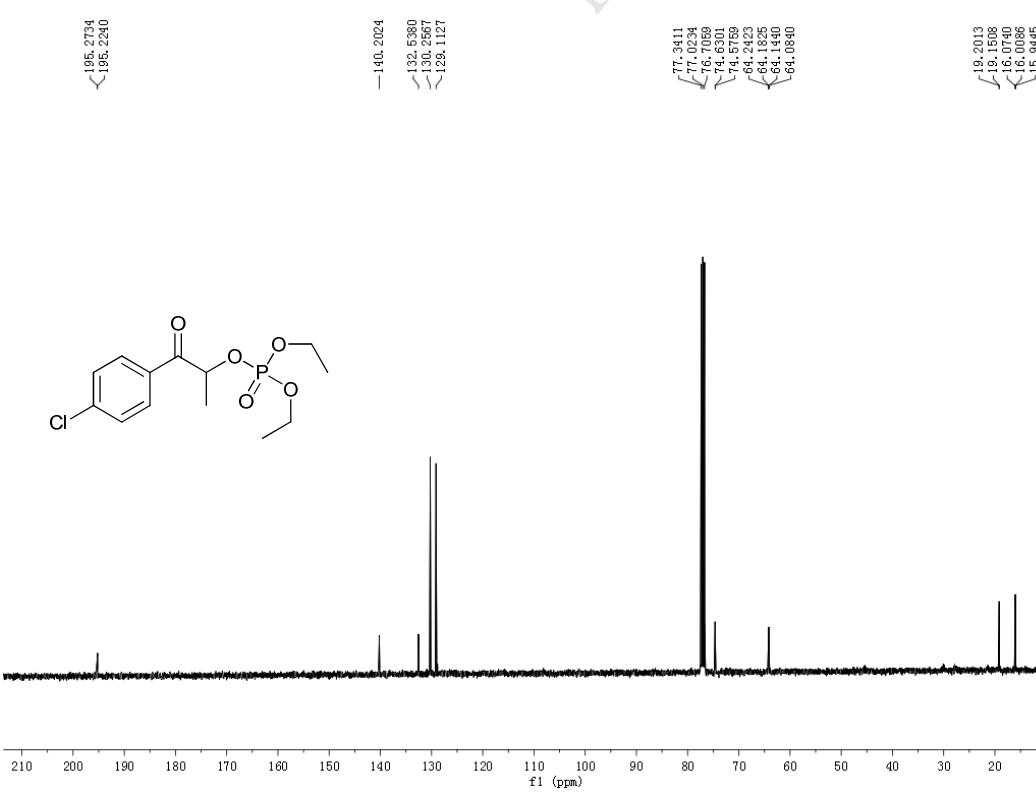
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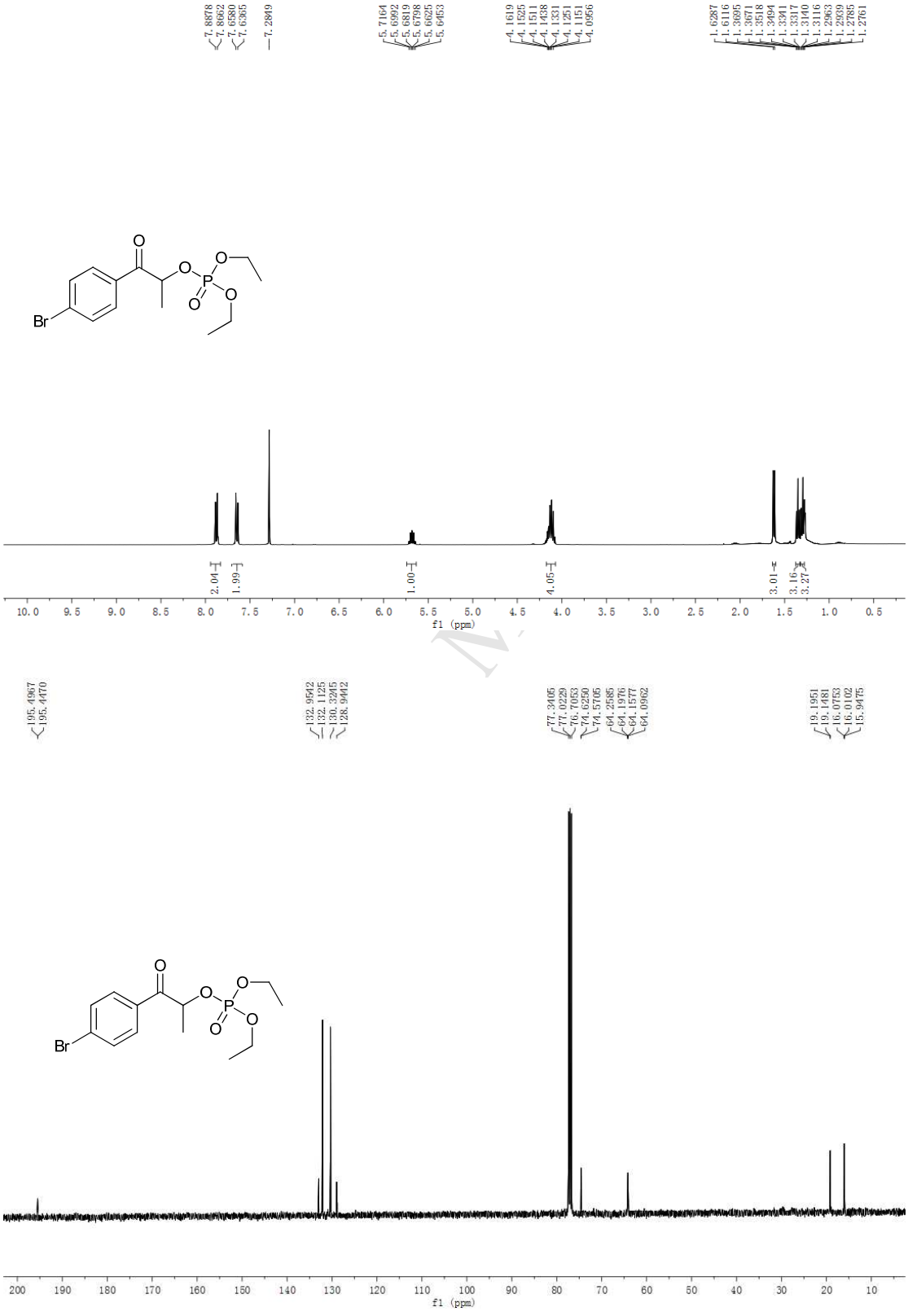
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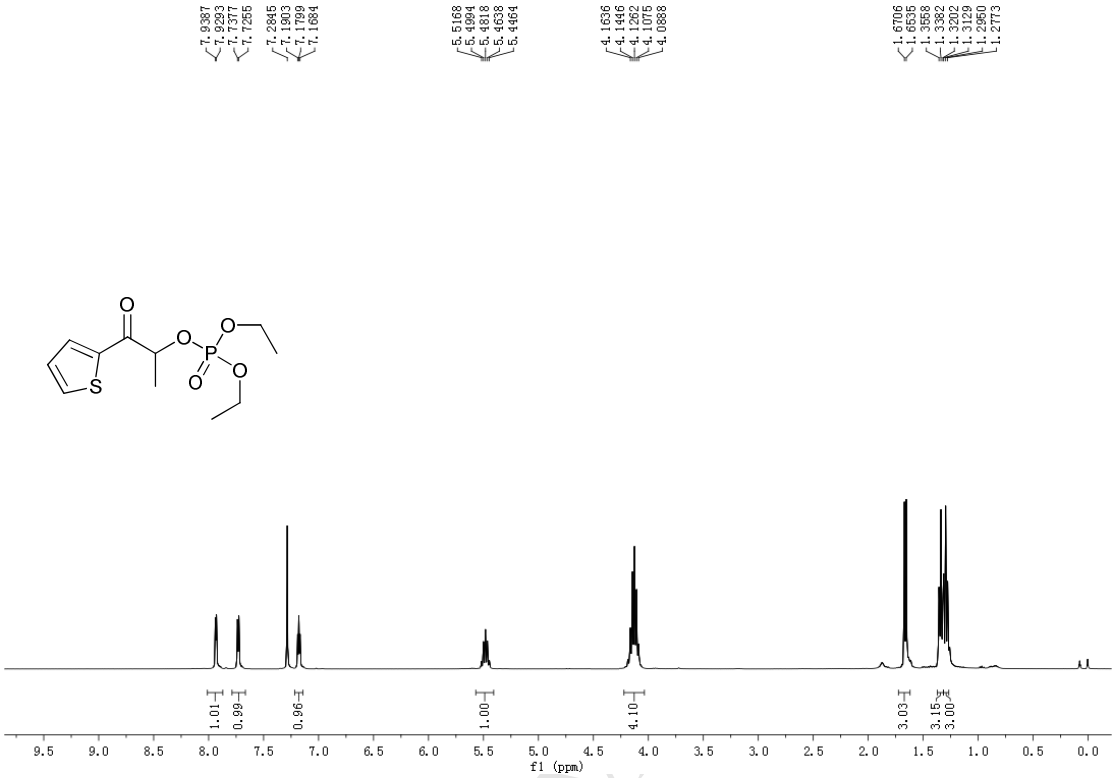
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3.03
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3.00
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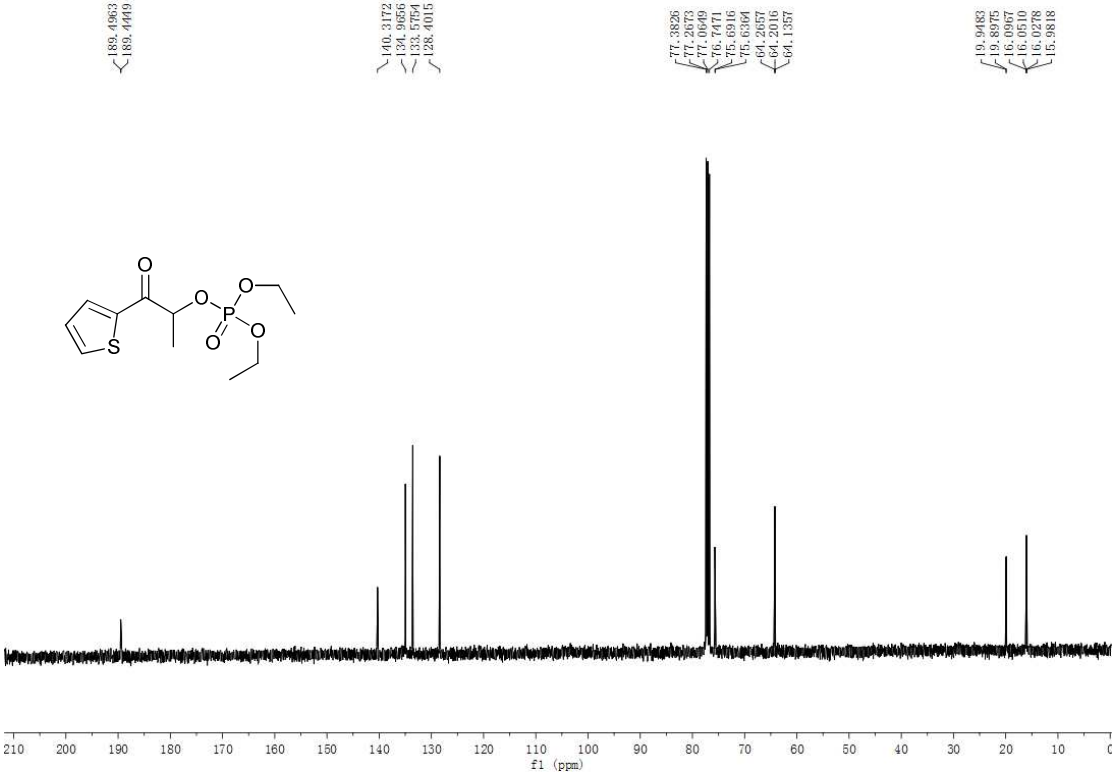
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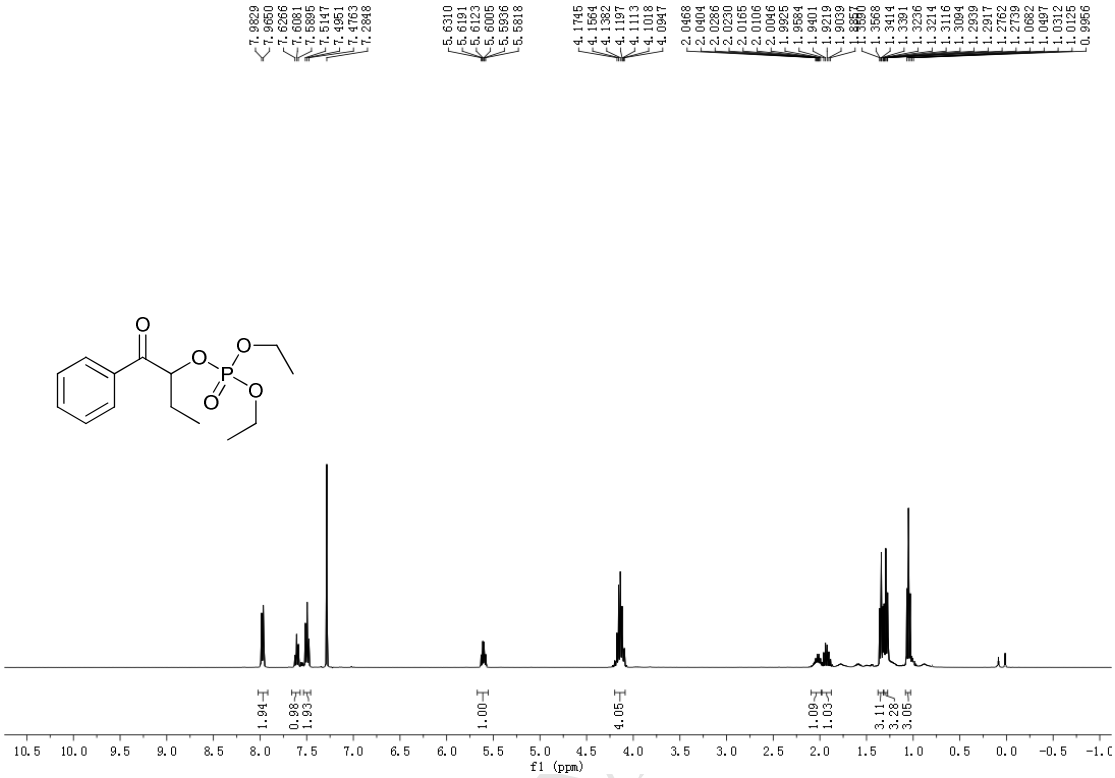
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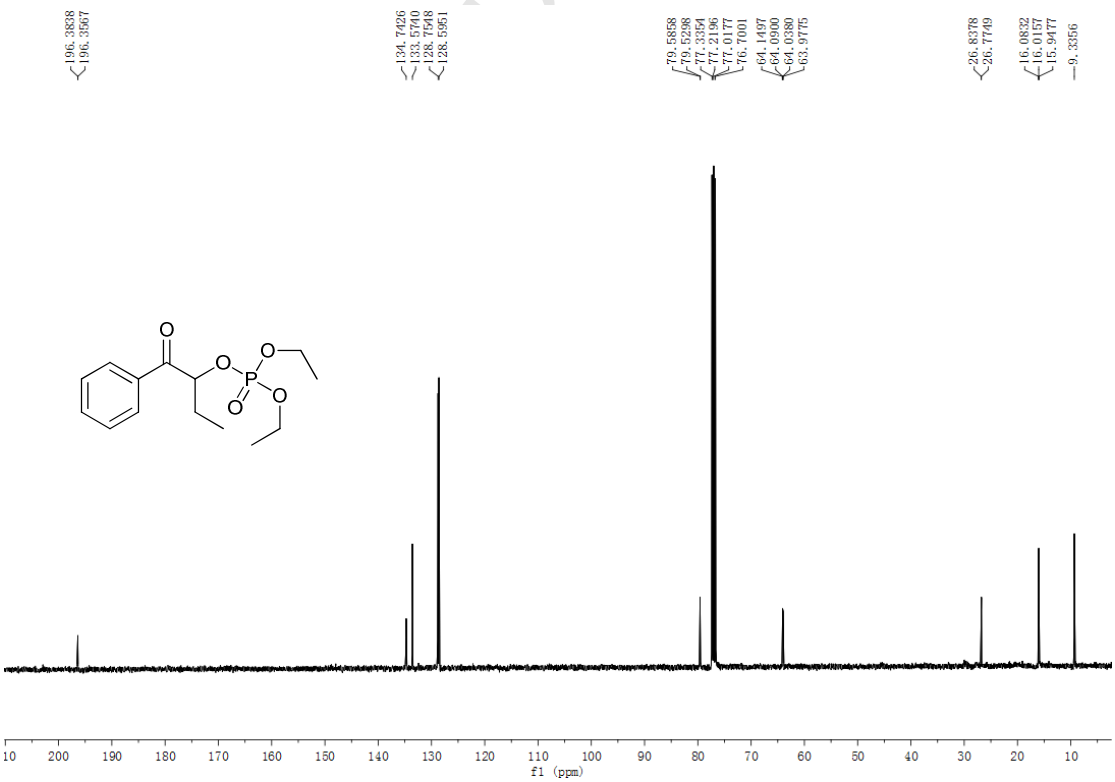
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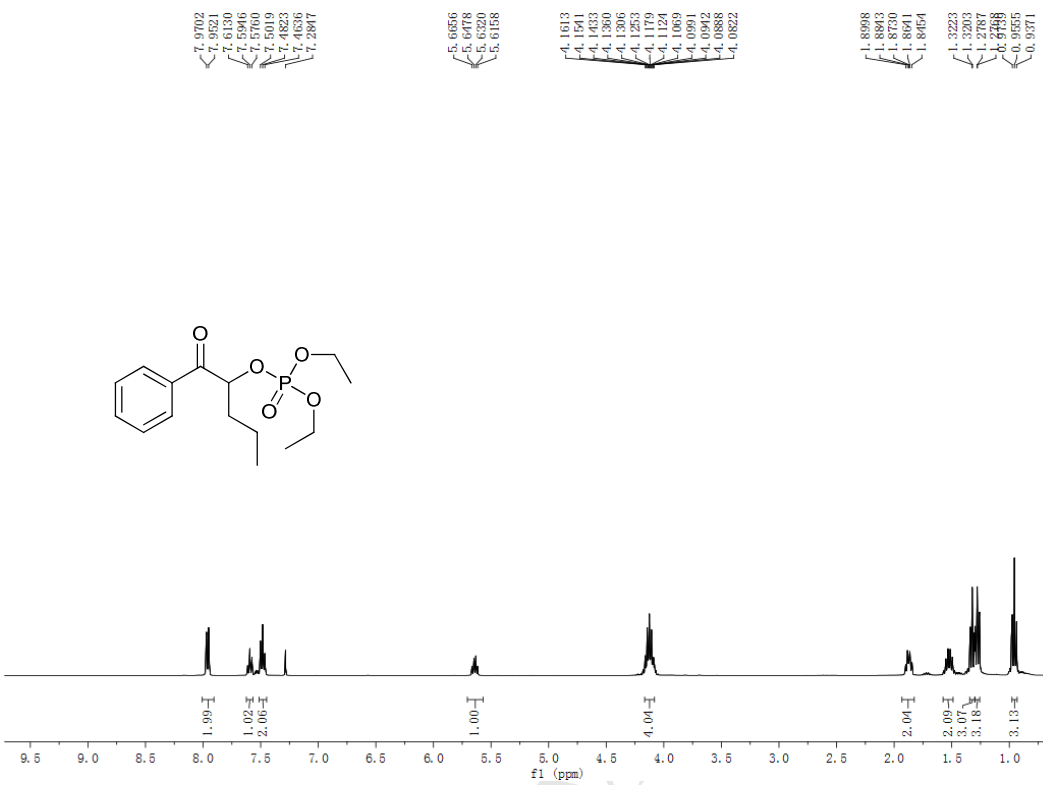
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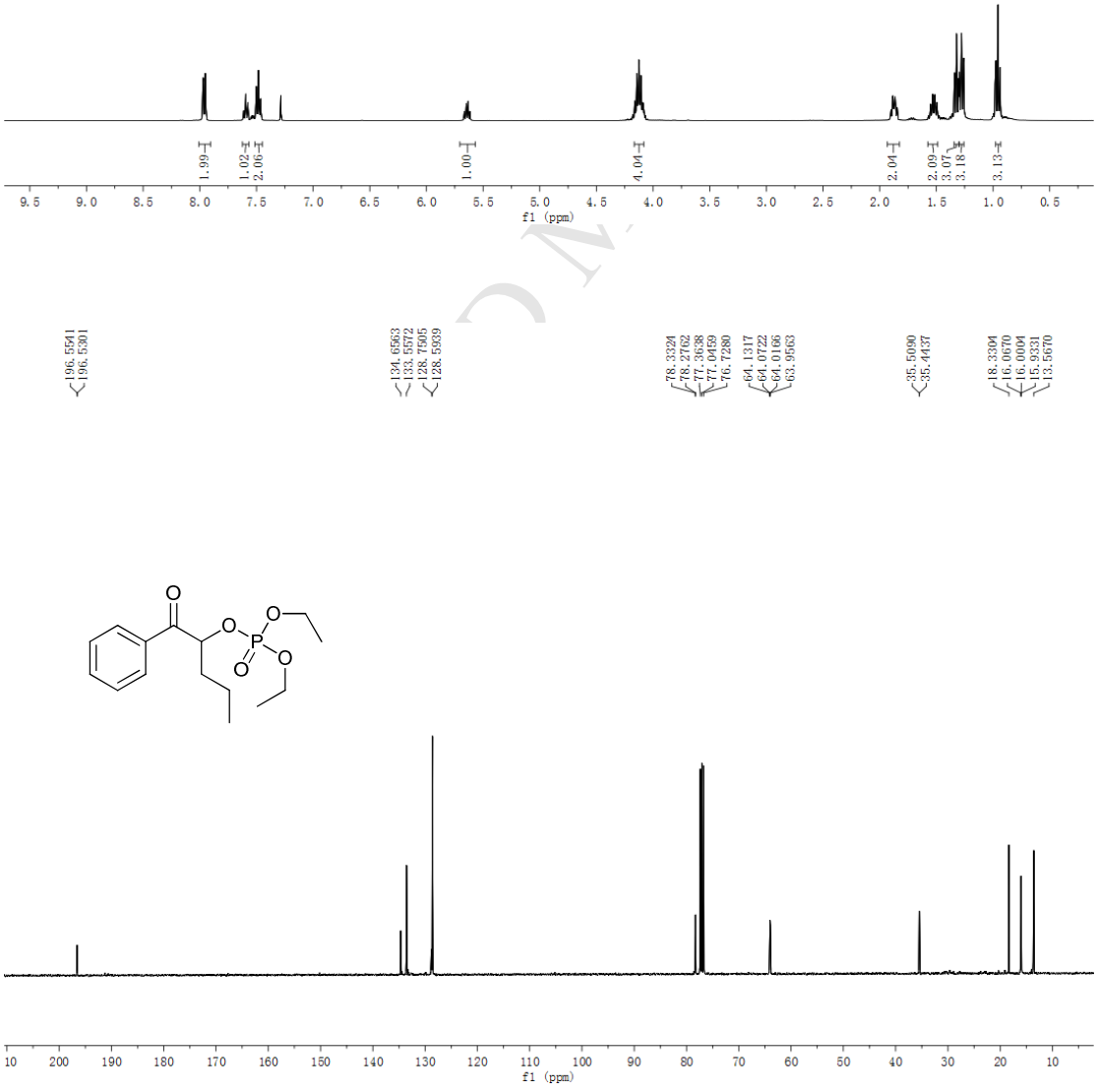
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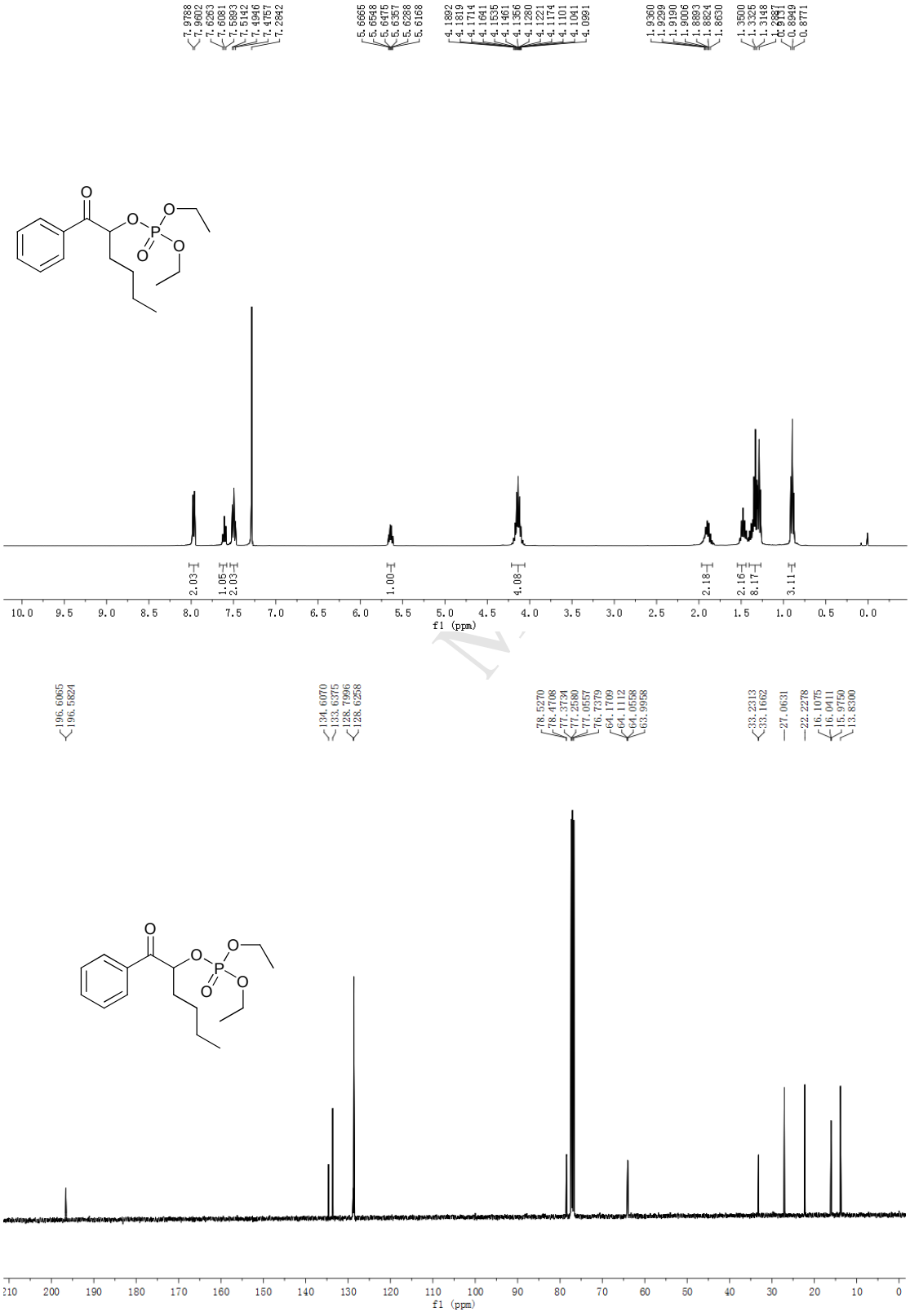
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P
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O
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f1 (ppm)


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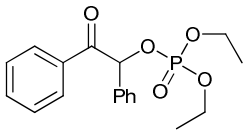
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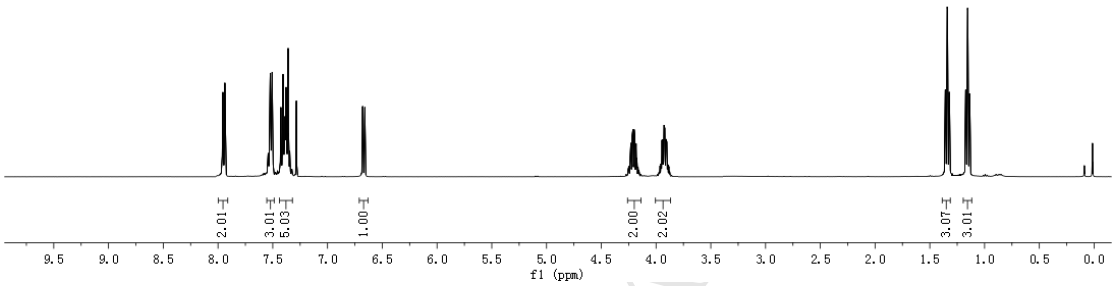
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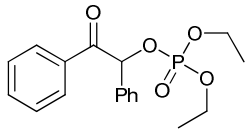
O
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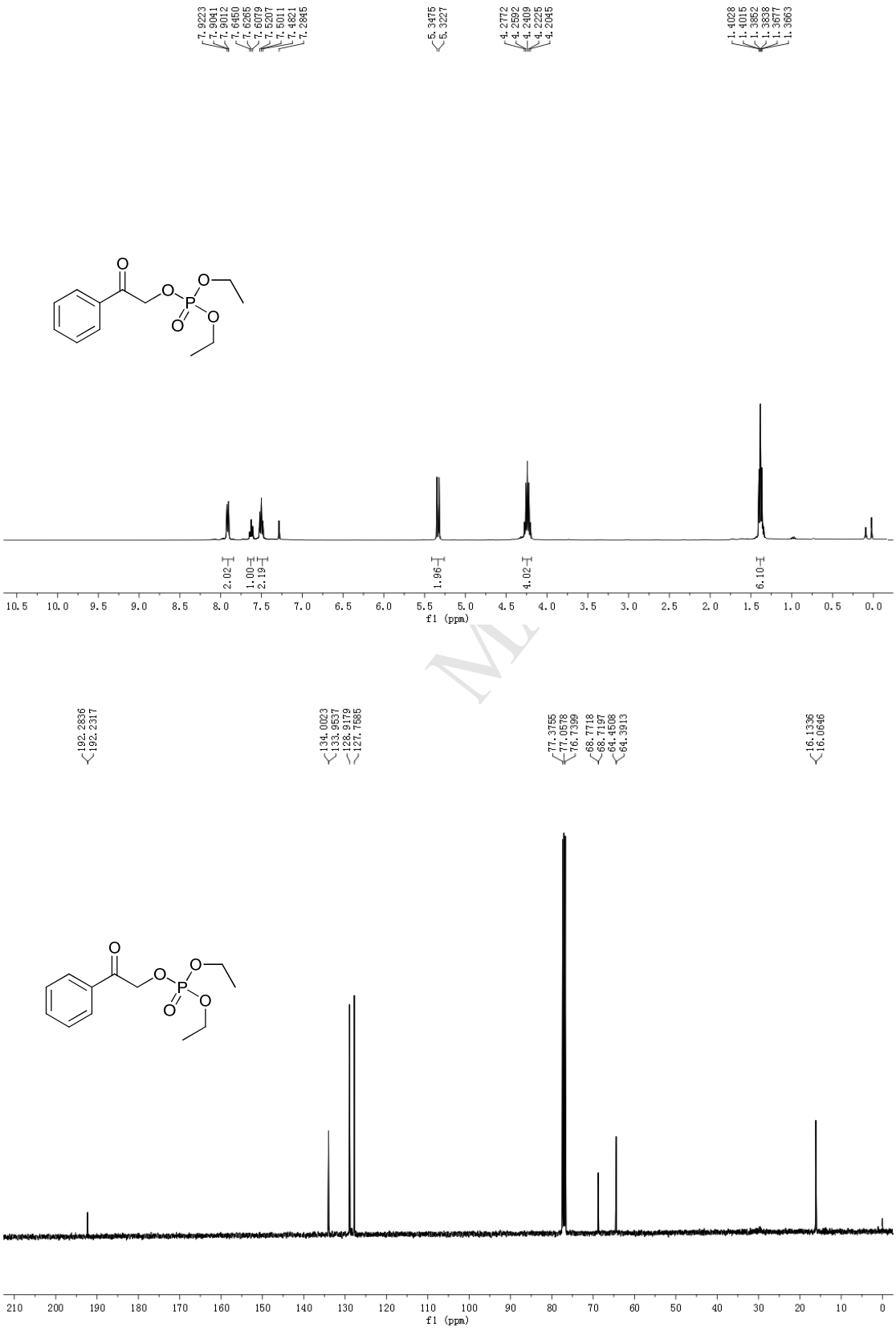
O
Ph

f1 (ppm)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5.3475
5.3227
4.2772
4.2592
4.2409
4.2225
4.2045
1.4028
1.4015
1.3852
1.3838
1.3677
1.3663
O
O
O
P
O
O
2.02
1.00
2.19
1.96
4.02
6.10
f1 (ppm)
192.2836
192.2317
134.0023
133.9537
128.9179
127.7685
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68.7197
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64.3913
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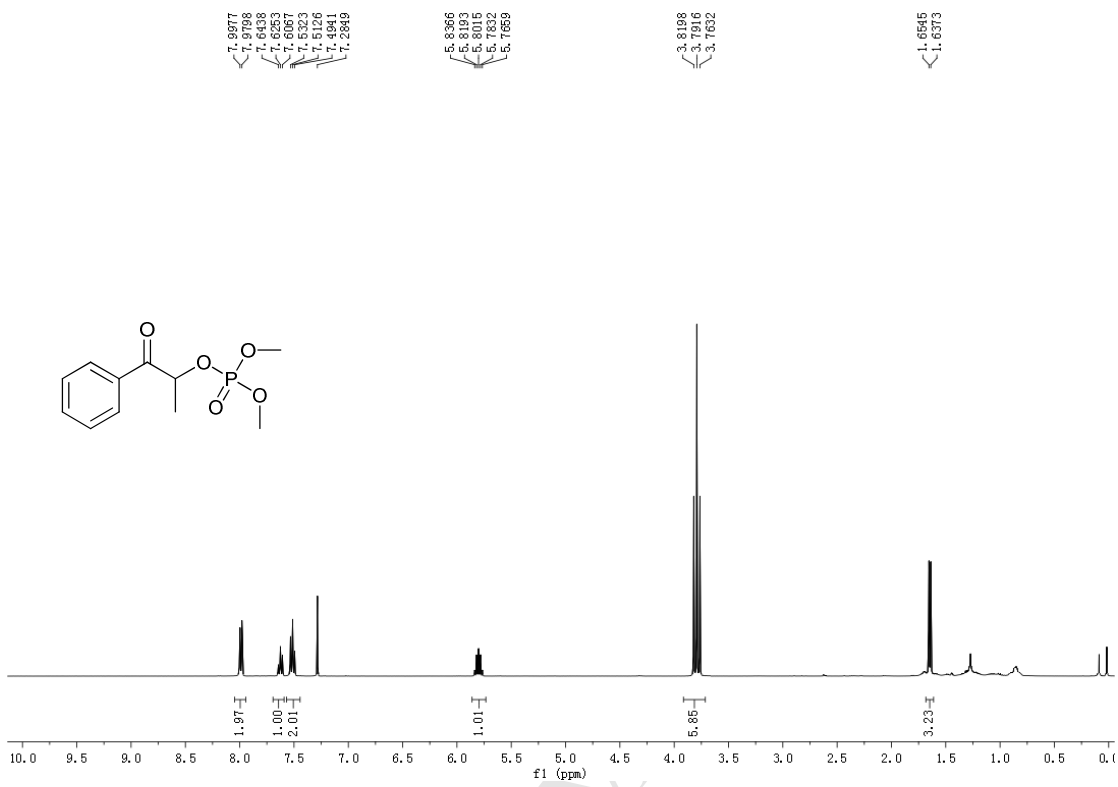
f1 (ppm)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7.2849
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5.8193
5.8015
5.7832
5.7659
3.8198
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1.6373
1.97
1.00
2.01
1.01
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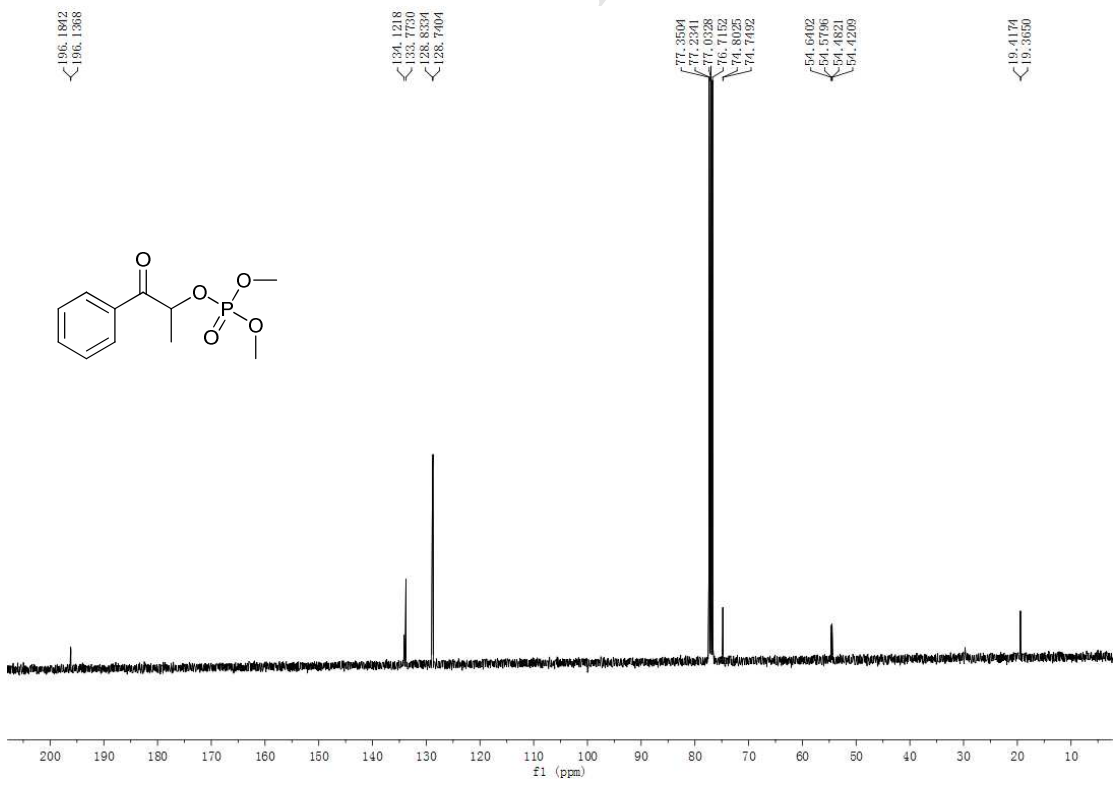
3.23
f1 (ppm)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54.4209
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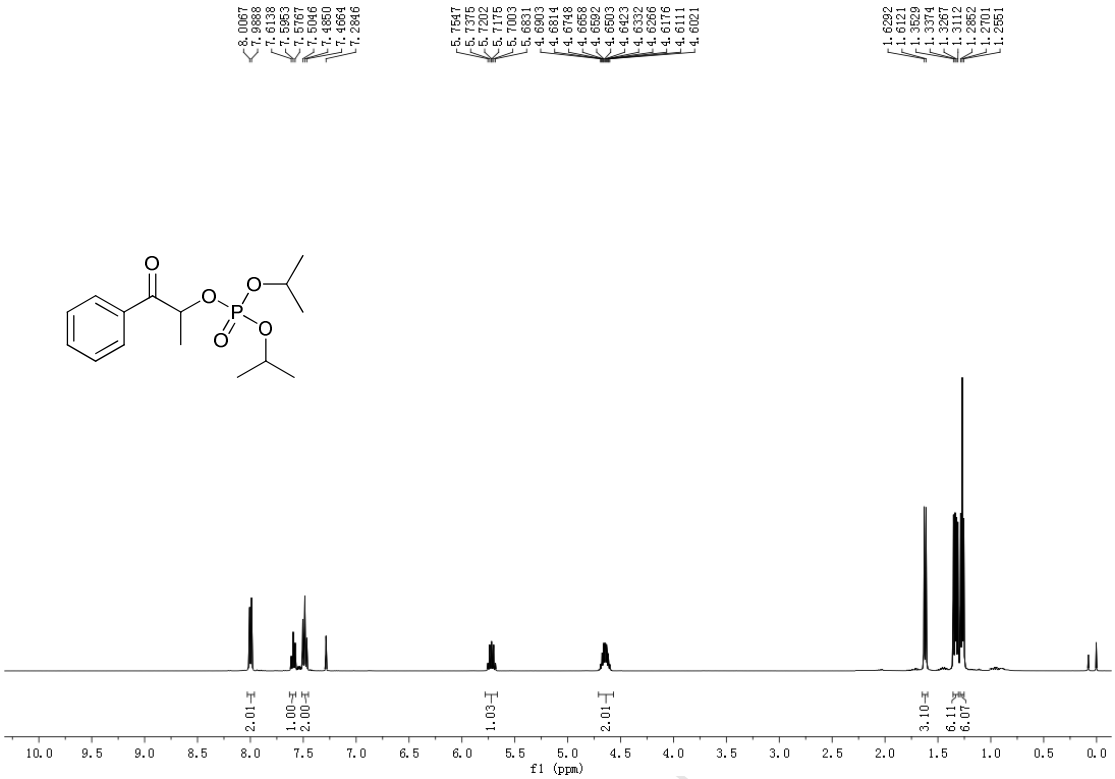
f1 (ppm)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5.7375
5.7202
5.7175
5.7003
5.6831
4.6903
4.6814
4.6748
4.6658
4.6592
4.6503
4.6423
4.6332
4.6266
4.6176
4.6111
4.6021
1.6292
1.6121
1.3629
1.3374
1.3267
1.3112
1.2862
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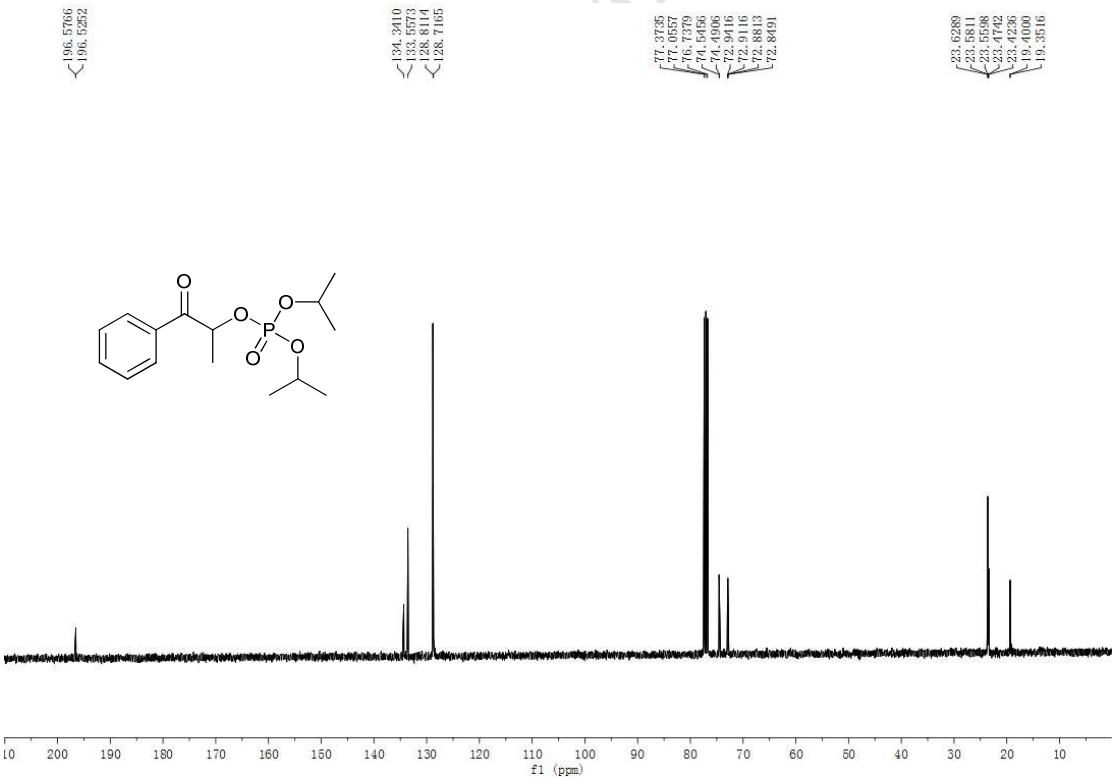
2.01
1.00
2.00
1.03
2.01
3.10
6.11
6.07
f1 (ppm)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72.9416
72.9116
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23.5598
23.4742
23.4236
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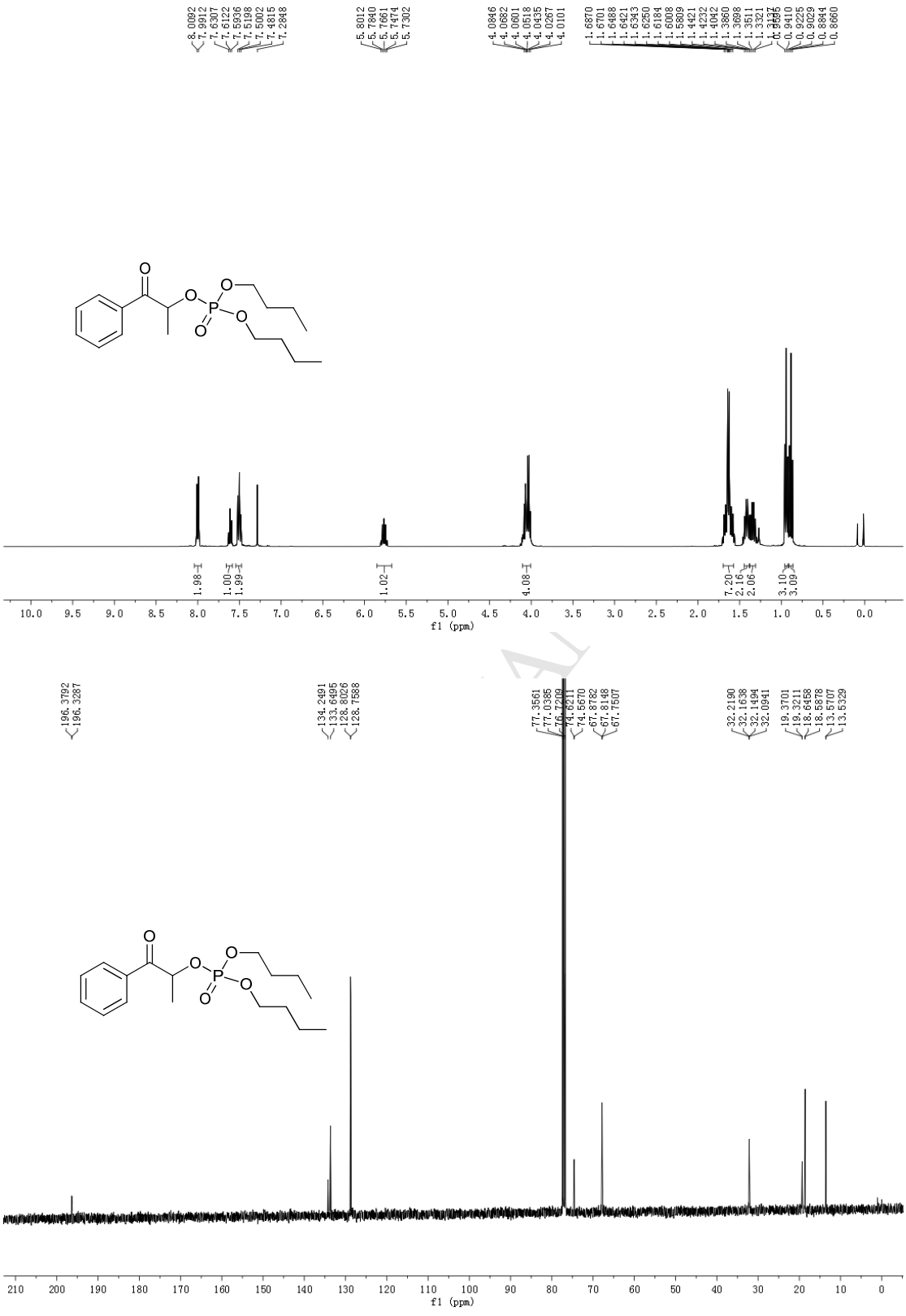
19.3516
f1 (ppm)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7.2848
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5.7840
5.7661
5.7474
5.7302
4.0846
4.0682
4.0601
4.0518
4.0435
4.0267
4.0101
1.6870
1.6701
1.6488
1.6421
1.6343
1.6250
1.6184
1.6008
1.5809
1.4421
1.4232
1.4042
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1.3511
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0.9410
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0.8844
0.8660
1.98
1.00
1.99
1.02
4.08
7.20
2.16
2.06
3.10
3.09
f1 (ppm)
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196.3287
134.2491
133.6495
128.8026
128.7588
77.3561
77.0385
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74.6211
74.5670
67.8782
67.8148
67.7507
32.2190
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32.0941
19.3701
19.3211
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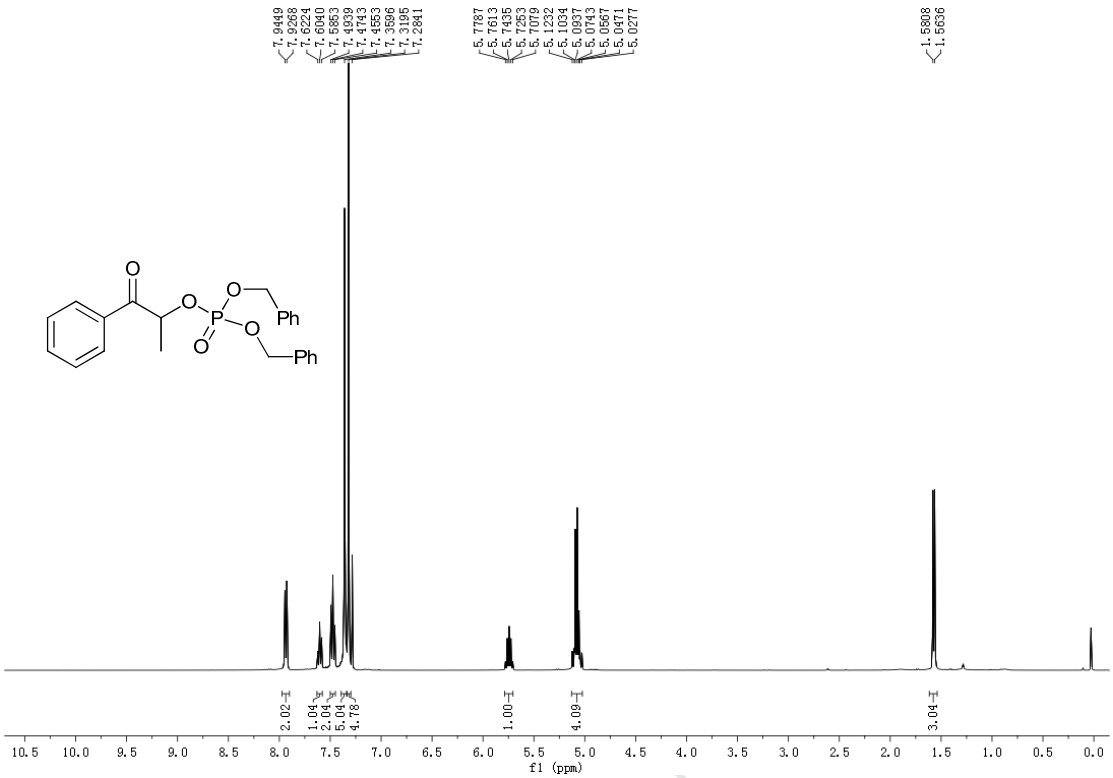
13.5329
f1 (ppm)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7.4743
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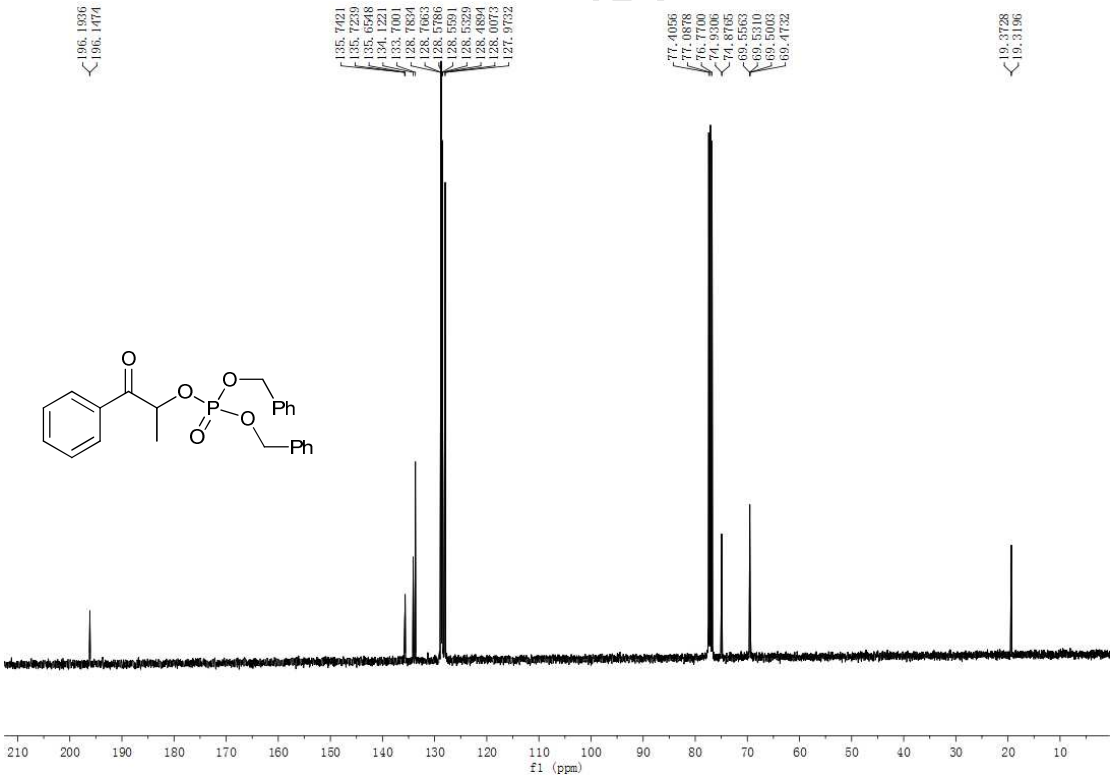
7.3596
7.3195
7.2841
5.7787
5.7613
5.7436
5.7253
5.7070
5.1232
5.1034
5.0937
5.0743
5.0567
5.0471
5.0277
1.5808
1.5636
O
O
O
P
O
O
Ph
Ph
2.02
1.04
2.04
5.04
4.78
1.00
4.09
3.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.5329
128.4894
128.0073
127.9732
77.4056
77.0878
76.7700
74.9506
74.8765
69.5563
69.5310
69.5003
69.4732
19.3728
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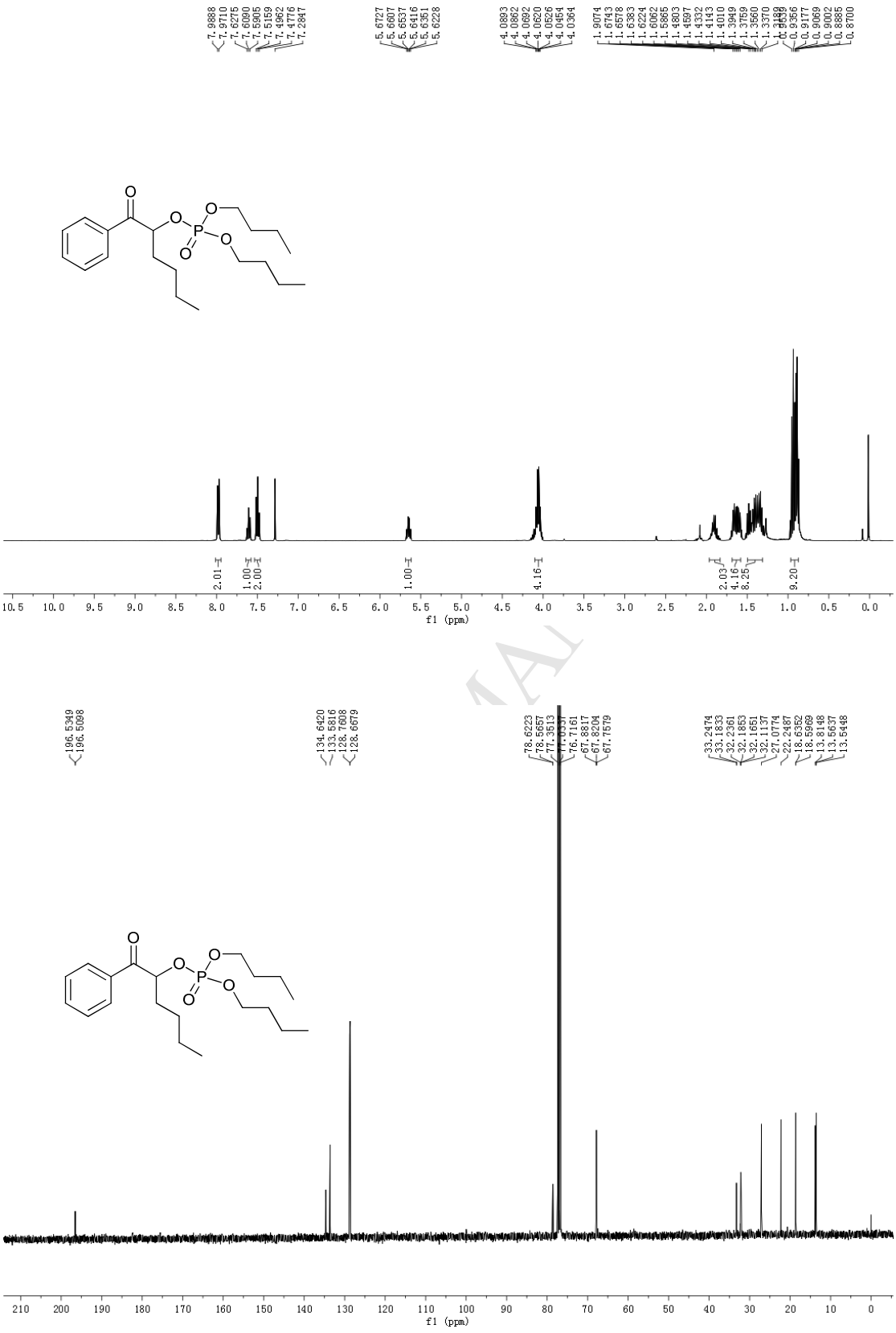
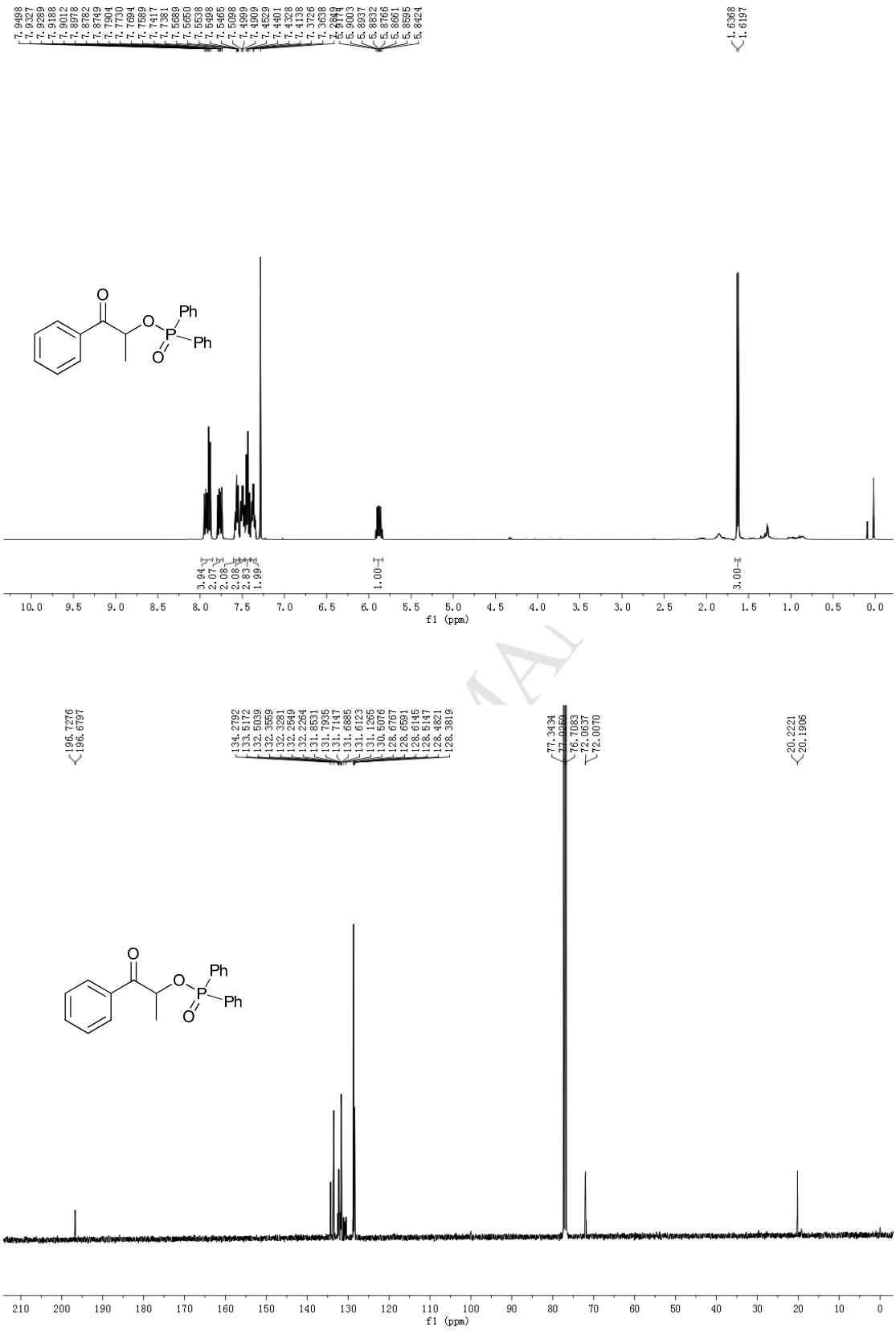
O
O
P
O
O
Ph
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


f1 (ppm)
f1 (ppm)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7.7589
7.7417
7.7381
7.5689
7.5650
7.5538
7.5498
7.5465
7.5098
7.4999
7.4909
7.4529
7.4401
7.4328
7.4138
7.3726
7.3638
5.9013
5.8837
5.8532
5.8766
5.8661
5.8595
5.8424
1.6368
1.6197
O
O
P
Ph
Ph
O
3.94
2.07
2.08
2.08
2.83
1.99
1.00
3.00
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)
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196.6797
134.2792
133.5172
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132.2549
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128.5147
128.4821
128.3819
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76.7083
72.0637
72.0070
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O
O
P
Ph
Ph
O
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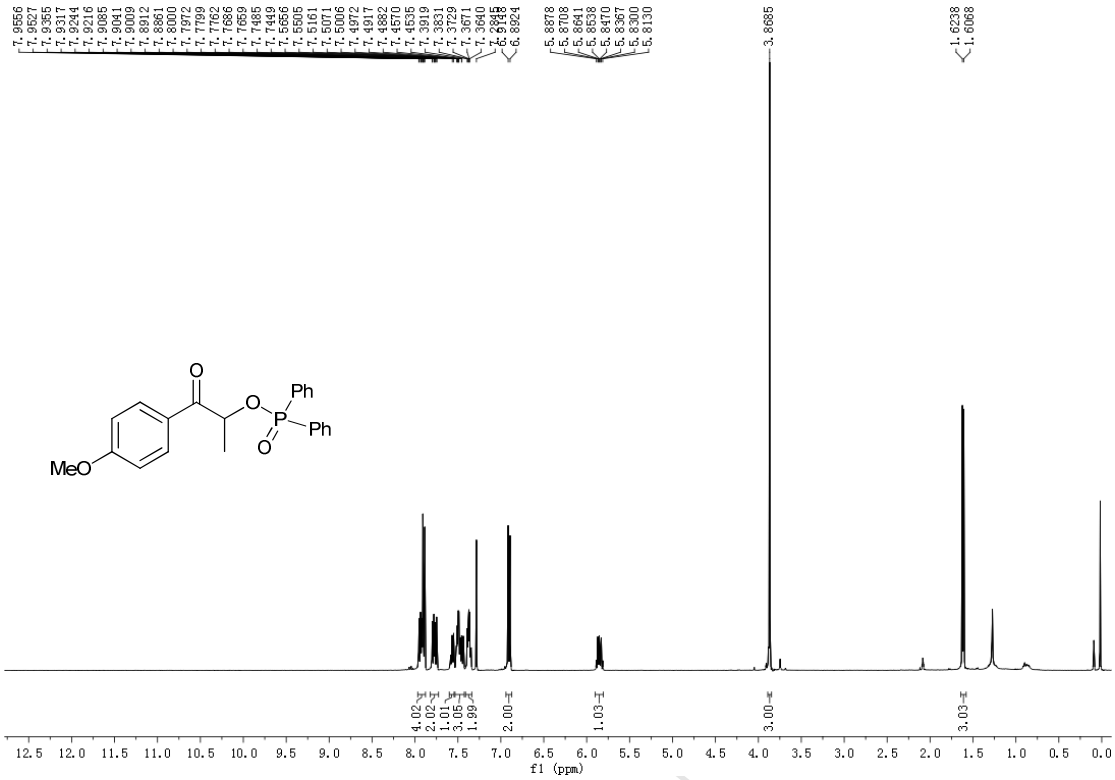
f1 (ppm)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7.5006
7.4972
7.4917
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7.4570
7.4535
7.3919
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7.3729
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7.3640
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5.8641
5.8538
5.8470
5.8367
5.8300
5.8130
3.8685
1.6238
1.6068
O
O
P
Ph
Ph
O
MeO
4.02
2.02
1.01
3.05
1.99
2.00
1.03
3.00
3.03
12.5 12.0 11.5 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
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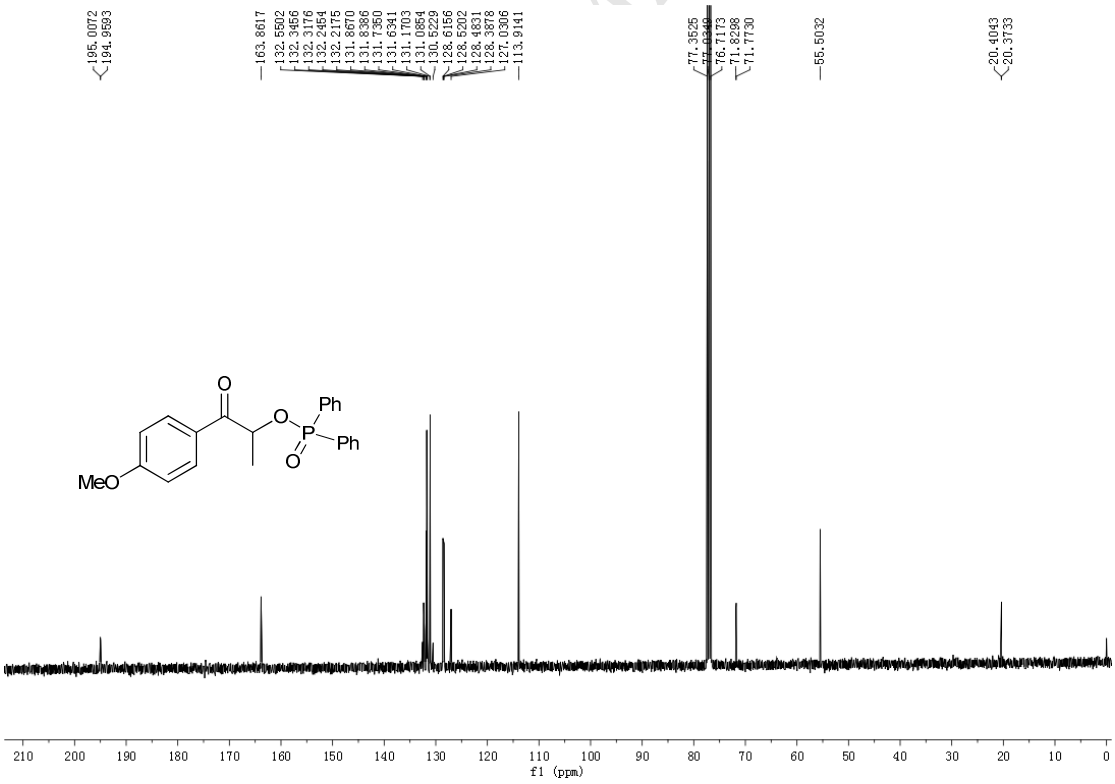
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55.5032
20.4043
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O
P
Ph
Ph
O
MeO
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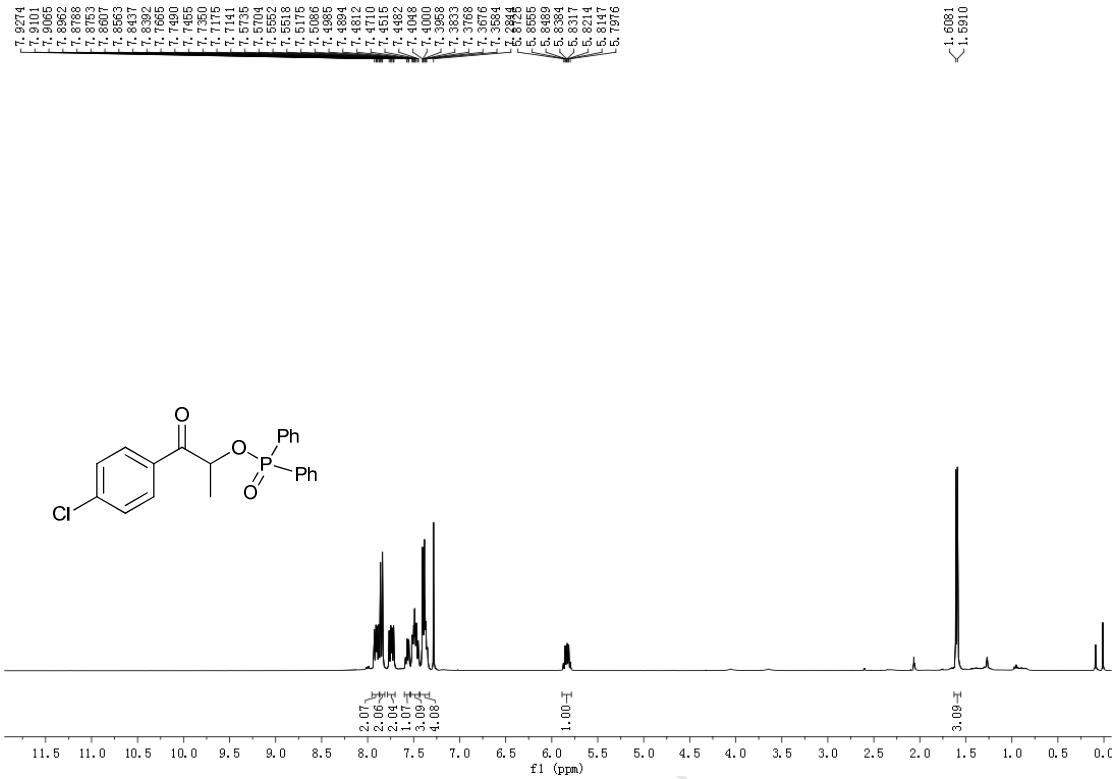
f1 (ppm)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7.7490
7.7455
7.7360
7.7175
7.7141
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7.5175
7.5086
7.4985
7.4894
7.4812
7.4710
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7.4482
7.4048
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5.8555
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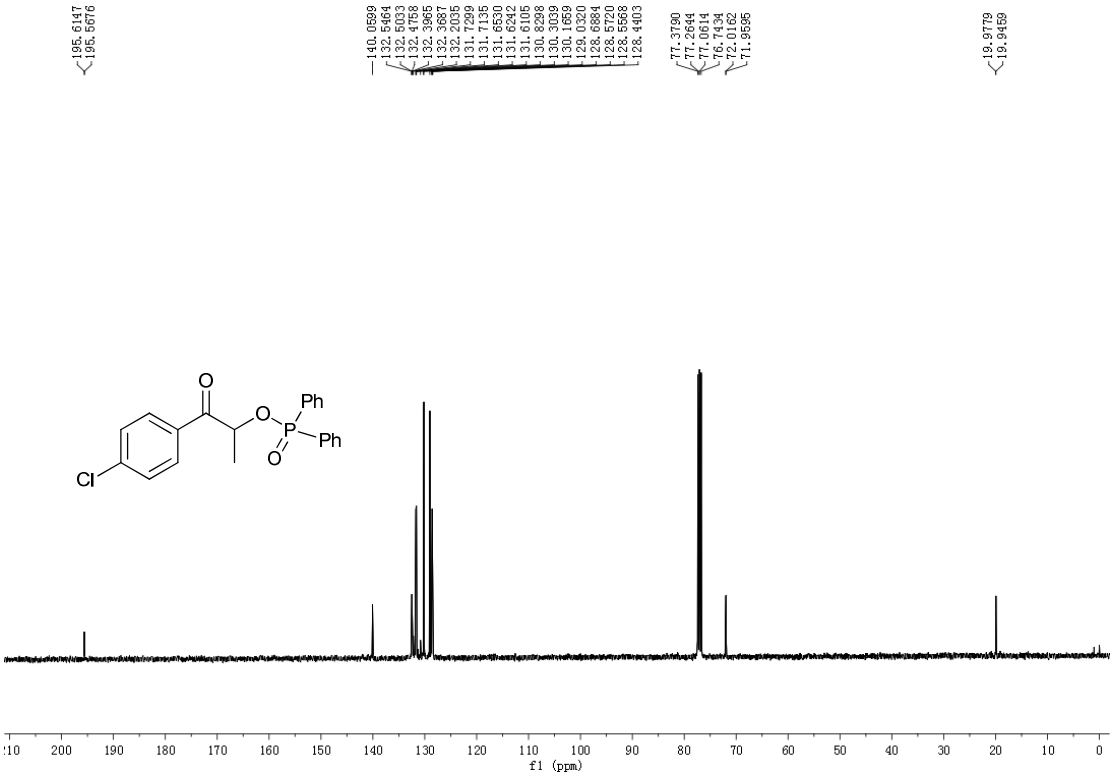
5.8317
5.8214
5.8147
5.7976
1.6081
1.5910
O
O
P
Ph
Ph
O
Cl
2.07
2.06
2.04
1.07
3.09
4.08
1.00
3.09
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.5568
128.4403
77.3790
77.2644
77.0614
76.7434
72.0162
71.9595
19.9779
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O
P
Ph
Ph
O
Cl
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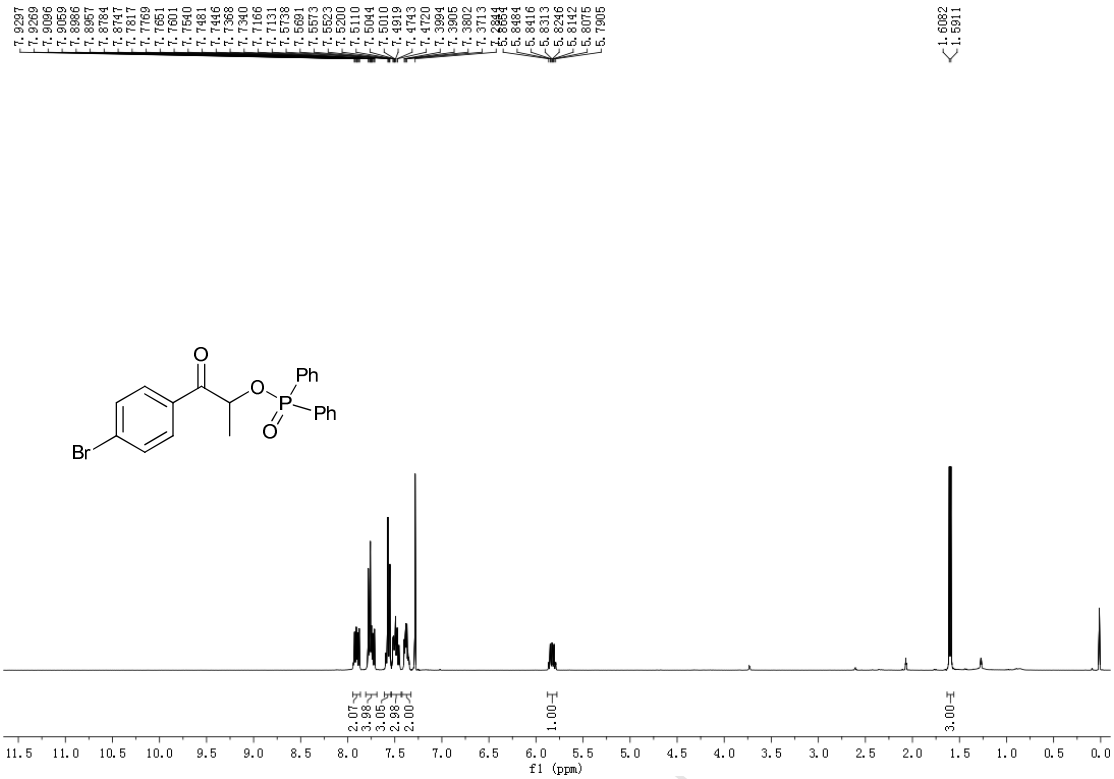
f1 (ppm)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7.5738
7.5691
7.5573
7.5523
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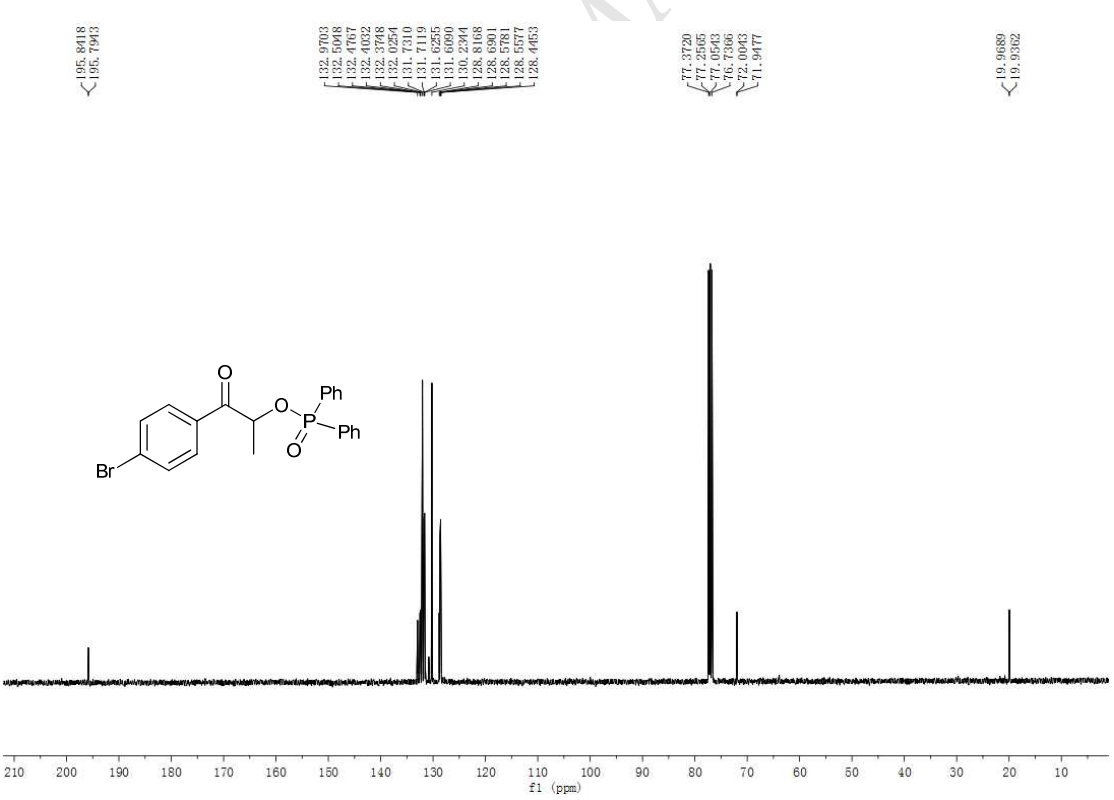
1.5911
O
O
P
Ph
Ph
O
Br
2.07
3.98
3.06
2.98
2.00
1.00
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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72.0943
71.9477
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Ph
O
Br
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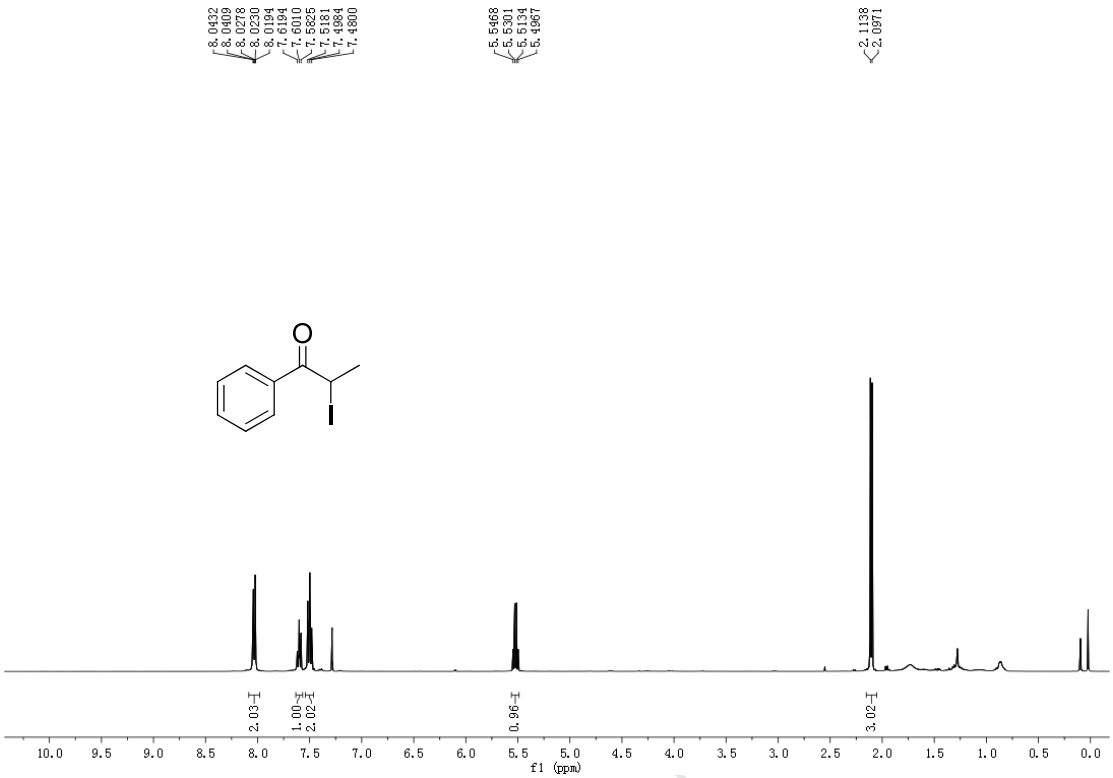
f1 (ppm)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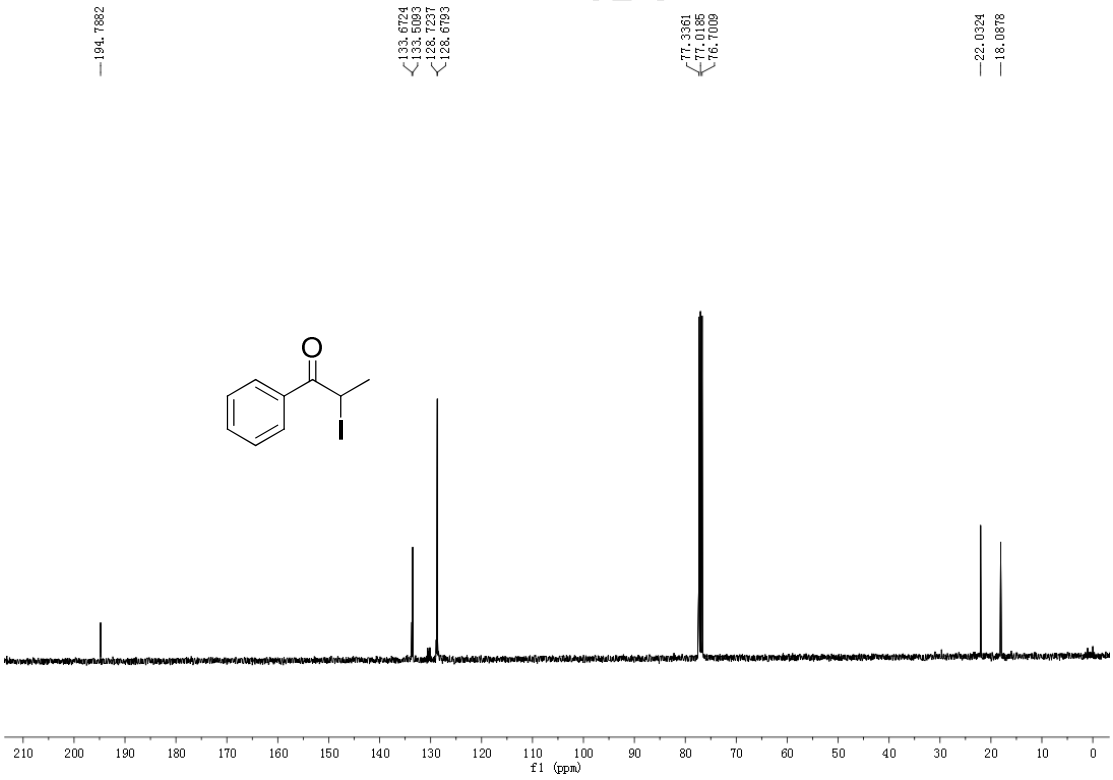
5.5301
5.5134
5.4967
2.1138
2.0971
O
2.03
1.00
2.02
0.96
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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18.0878
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210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)