Supporting Information

Bromide-Mediated, C2-Selective, and Oxygenative Alkylation of Pyridinium Salts using Alkenes and Molecular Oxygen†

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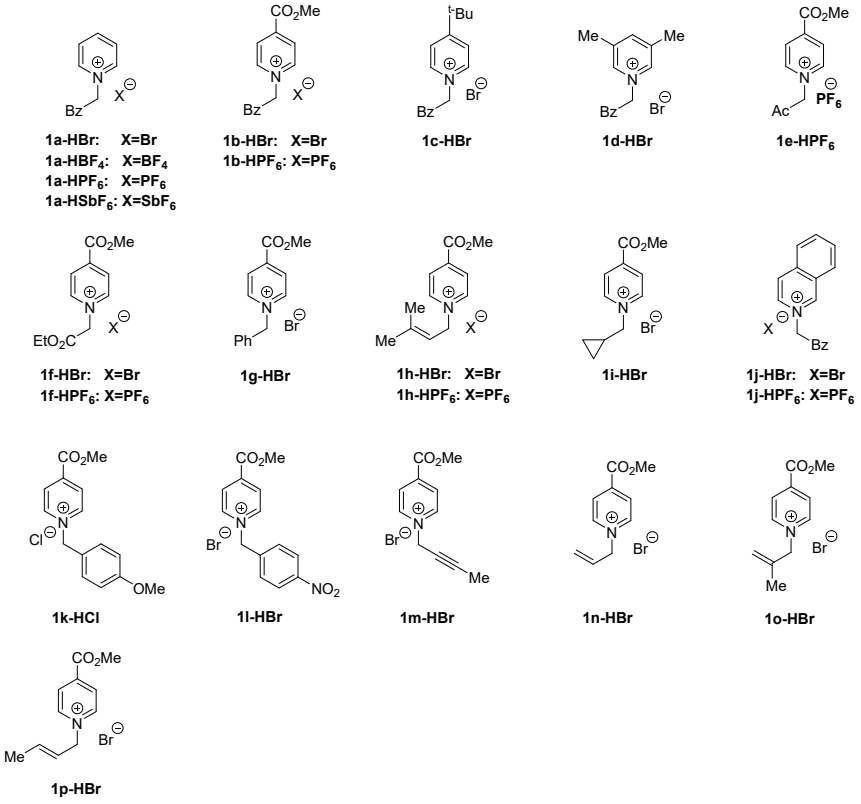
Table of Contents

1. General Procedures

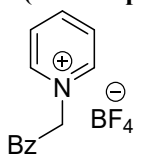
All the commercial available regents and solvents were used as received. NMR spectra were obtained with Avance TM III 400MHz instruments, the chemical shifts were quoted on the δ-scale in ppm. Multiplicities are reported as follows: singlet (s), doublet (d), triplet(t), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), doublet of quartets (dq), triplet of doublets (td), quartet (q), quartet of doublets (qd), and multiplet (m). Couplingconstants (J) are reported in Hz. High resolution mass spectra(HRMS) were measured at a Bruker micrOTOF-QII instruments.

2. Synthesis of Pyridinium Salts and Spectra Data

The starting materials of pyridinium salts are listed below. **1a-HBr**,[1] **1b-HBr**,[2] **1c-HBr**,[3] **1d-HBr**,[4] **1f-HBr**,[5] **1g-HBr**[6] and **1j-HBr**[7] were prepared following reported procedures.



1a-HBF$_4$:
1-(2-oxo-2-phenylethyl)pyridin-1-ium tetrafluoroborate



1a-HBF$_4$

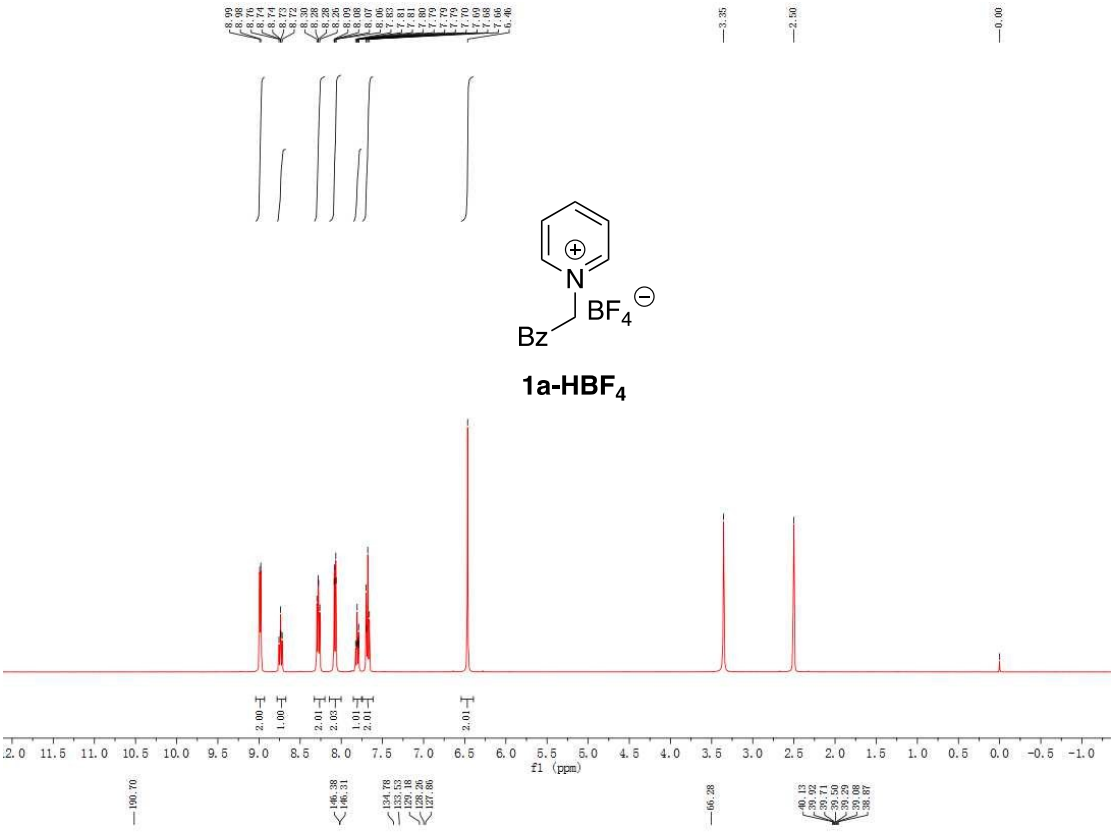
The procedure for synthesis of compound **1a-HBF$_4$:** A solution of 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide**1a-HBr** 1.39g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of $NaBF_4$ (1.1g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1a-HBF$_4$** as white powder (928mg, yield=69%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.98 (d, J = 5.1 Hz, 2H), 8.78 – 8.67 (m, 1H), 8.28 (dd, J = 7.8, 6.4 Hz, 2H), 8.14 – 8.00 (m, 2H), 7.85 – 7.75 (m, 1H), 7.68 (t, J = 7.7 Hz, 2H), 6.46 (s, 2H).

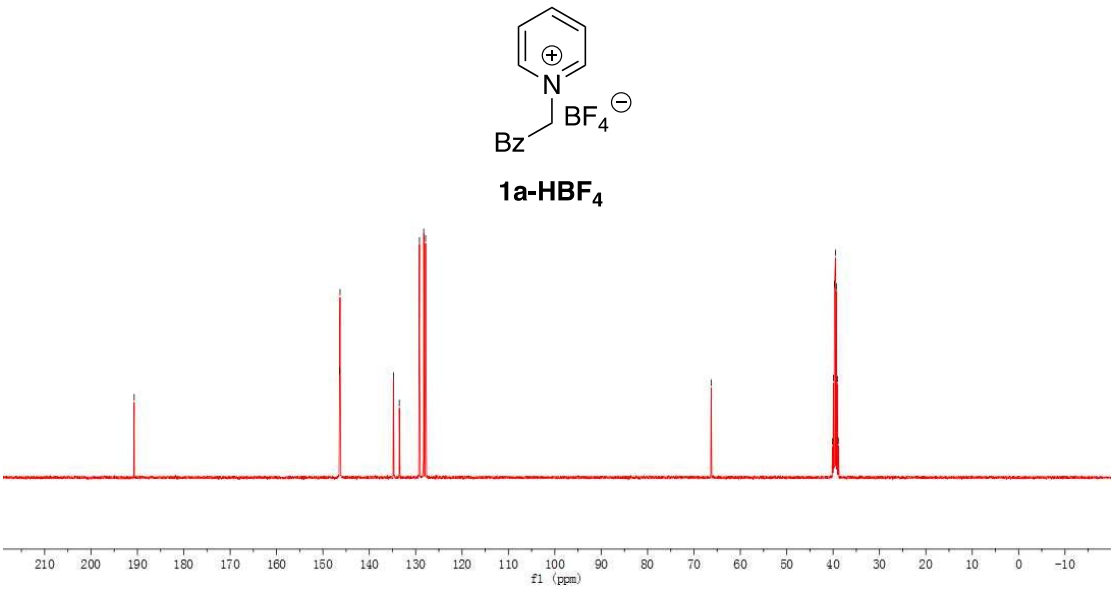
^{13}C NMR (101 MHz, DMSO-d_6): δ 190.7, 146.4, 146.3, 134.8, 133.5, 129.2, 128.3, 127.9, 66.3.

^{19}F NMR (376 MHz, DMSO): δ -148.20.

^{1}H, ^{13}C, ^{19}F NMR Spectra of **1a-HBF$_4$:**



1a-HBF$_4$



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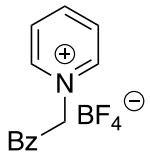
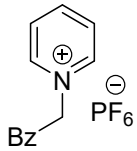


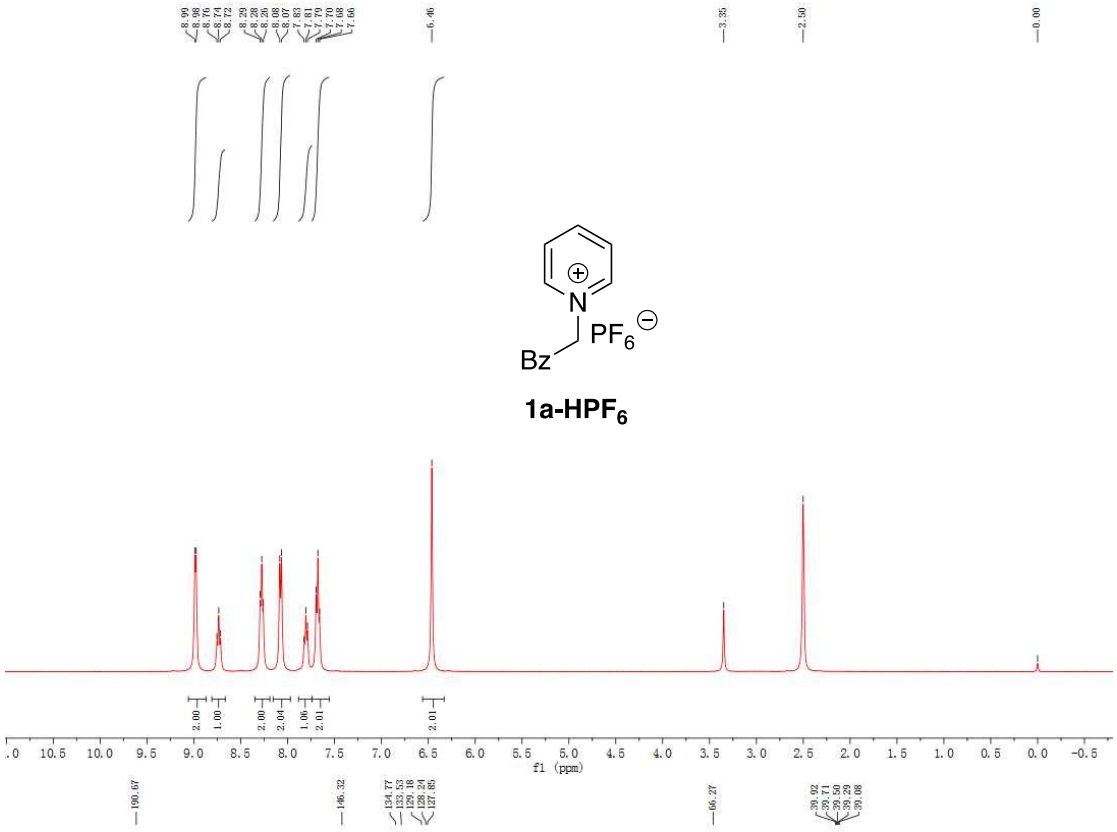
1a-HBF$_4$

1a-HPF$_6$:
1-(2-oxo-2-phenylethyl)pyridin-1-ium hexafluorophosphate

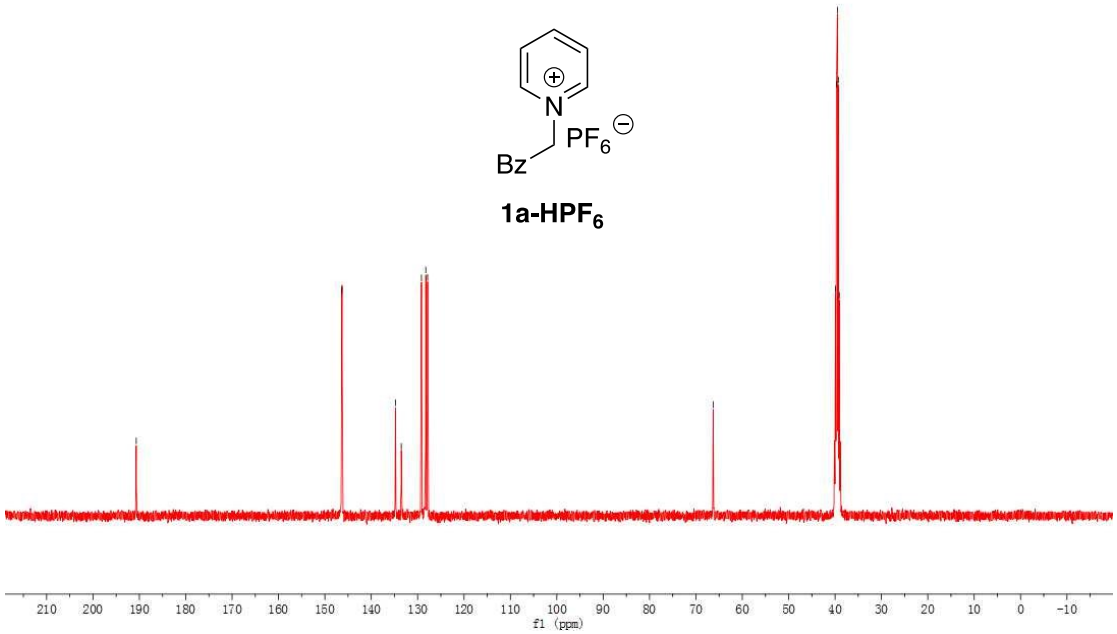


1a-HPF$_6$

The procedure for synthesis of compound **1a-HPF$_6$:** A solution of 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1a-HBr** (1.39g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of NH_4PF_6 (1.63g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1a-HPF$_6$** as white powder (1.58g, yield=92%).
^{1}H NMR (400 MHz, DMSO-d_6): δ 8.98 (d, J = 6.0 Hz, 2H), 8.74 (t, J = 7.8 Hz, 1H), 8.28 (t, J = 6.9 Hz, 2H), 8.07 (d, J = 7.7 Hz, 2H), 7.81 (t, J = 7.4 Hz, 1H), 7.68 (t, J = 7.6 Hz, 2H), 6.46 (s, 2H).
^{13}C NMR (101 MHz, DMSO-d_6): δ 190.7, 146.3, 134.8, 133.5, 129.2, 128.2, 127.9, 66.3.
^{19}F NMR (376 MHz, DMSO): δ -69.2, -71.0.
^{31}P NMR (162 MHz, DMSO): δ -130.98, -135.37, -139.76, -144.15, -148.55, -152.94, -157.33.
^{1}H, ^{13}C, ^{19}F, ^{31}P NMR Spectra of **1a-HPF$_6$:**



1a-HPF$_6$



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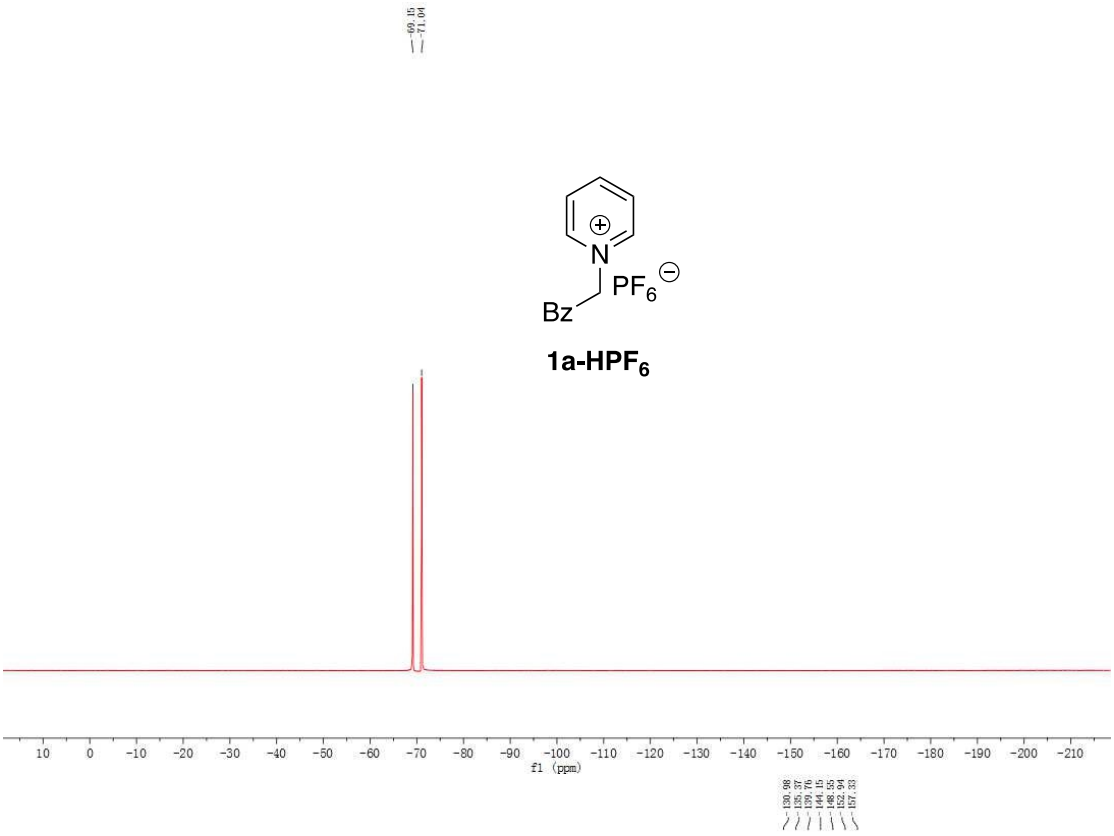
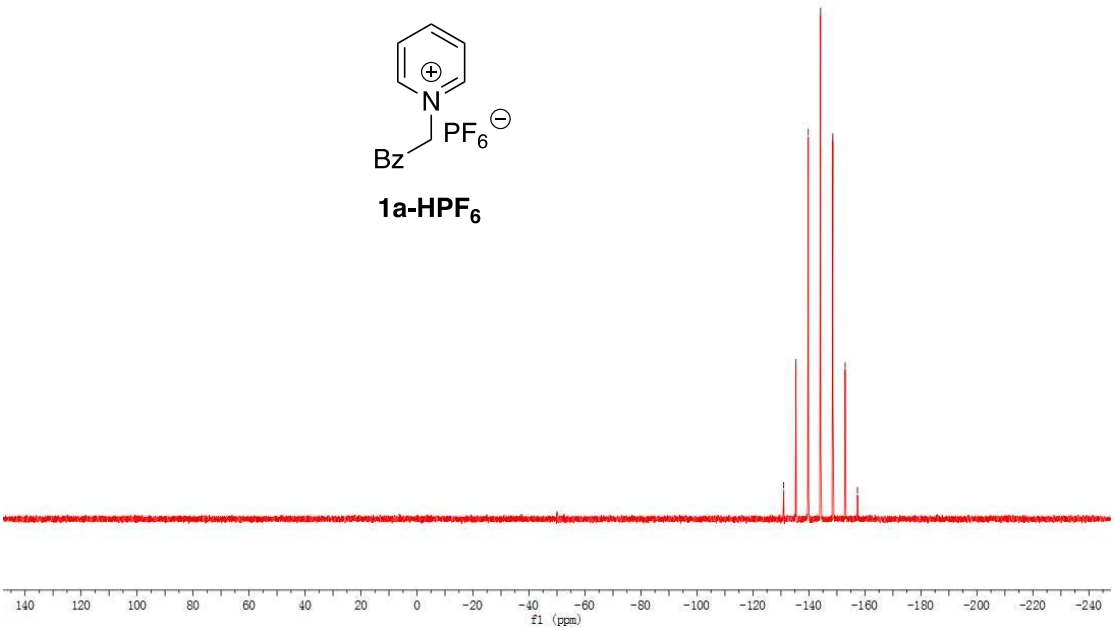
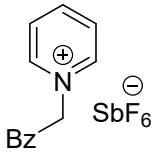


1a-HPF$_6$



1a-HPF$_6$

1a-HSbF$_6$:
1-(2-oxo-2-phenylethyl)pyridin-1-ium hexafluoroantimonate



1a-HSbF$_6$

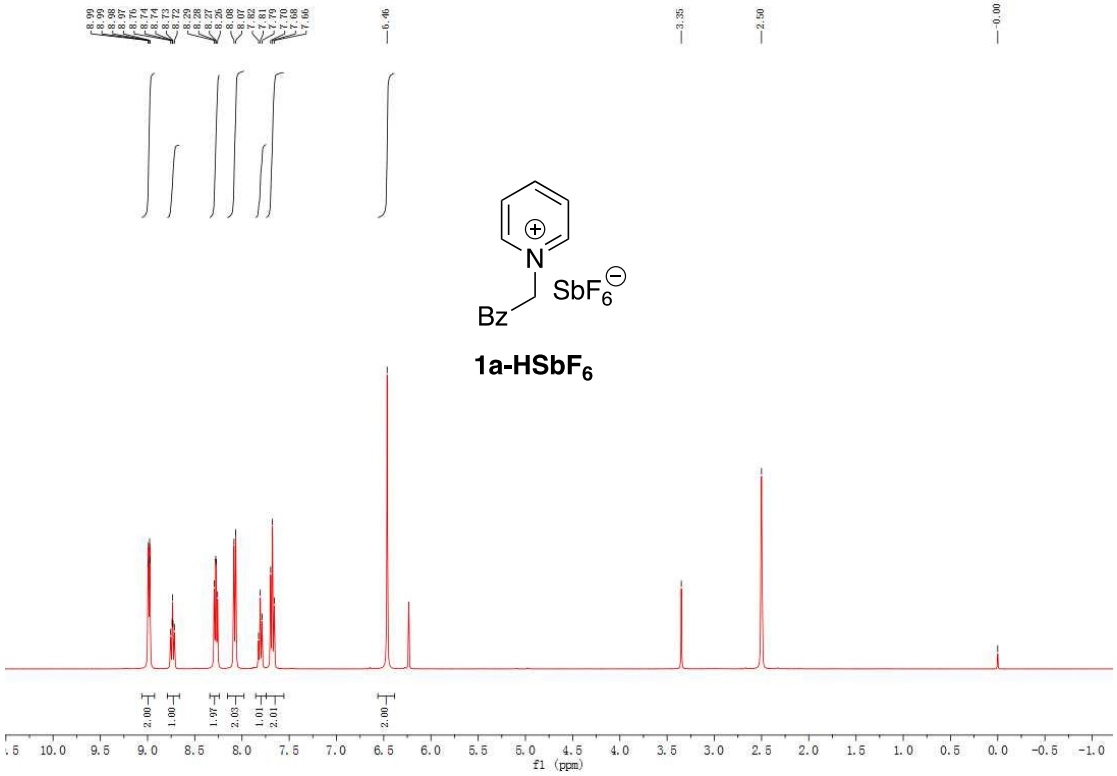
The procedure for synthesis of compound **1a-HSbF$_6$:**A solution of 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1a-HBr** (1.39g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of $NaSbF_6$ (2.59g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1a-HSbF$_6$** as white powder (1.67g, yield=77%).

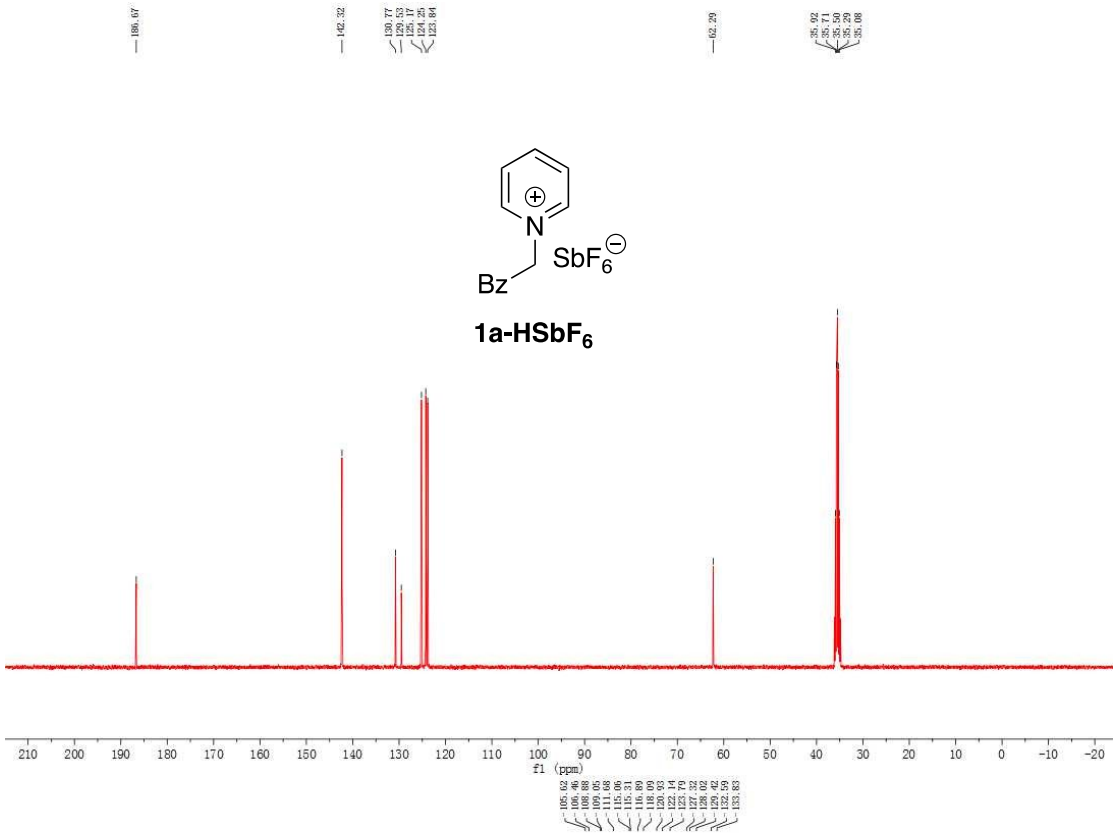
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.06 – 8.93 (m, 2H), 8.79 – 8.66 (m, 1H), 8.28 (dd, J = 7.7, 6.3 Hz, 2H), 8.08 (d, J = 7.0 Hz, 2H), 7.81 (t, J = 7.3 Hz, 1H), 7.68 (t, J = 7.7 Hz, 2H), 6.46 (s, 2H).

^{13}C NMR (101 MHz, DMSO): δ 186.7, 142.3, 130.8, 129.5, 125.2, 124.3, 123.8, 62.3.

^{19}F NMR (376 MHz, DMSO): δ -105.62-δ-133.83, m.

^{1}H, ^{13}C, ^{19}F NMR Spectra of **1a-HSbF$_6$:**





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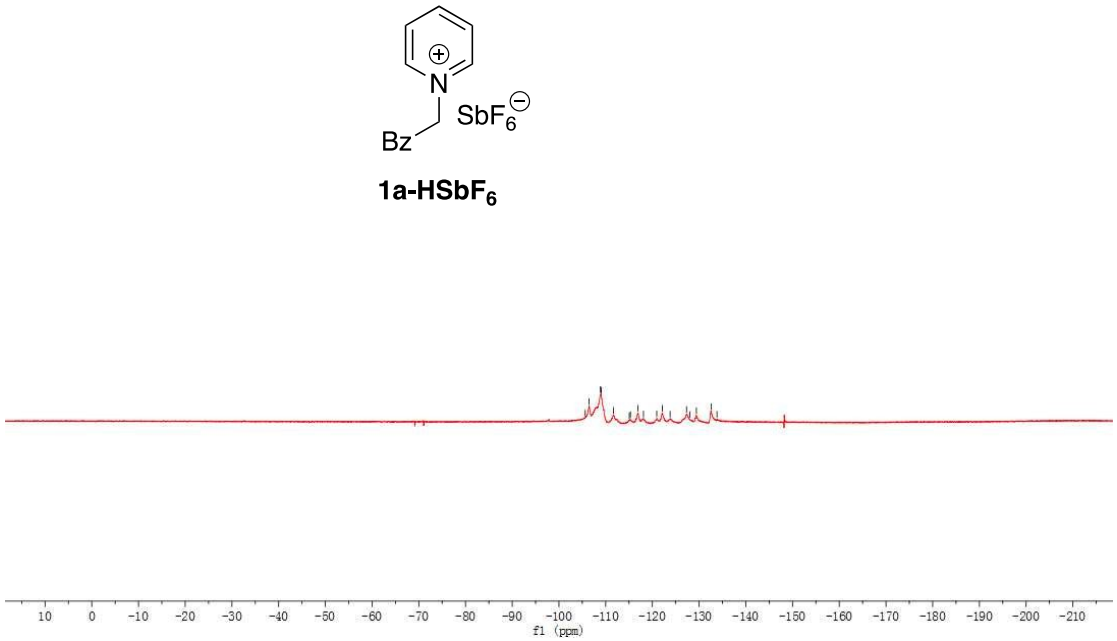
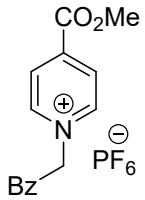


1a-HSbF$_6$

1b-HPF$_6$:
4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium hexafluorophosphate



1b-HPF$_6$

The procedure for synthesis of compound **1b-HPF$_6$:** A solution of 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (1.68g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of NH_4PF_6 (1.63g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1b-HPF$_6$** as colorless powder (1.64g, yield=82%).

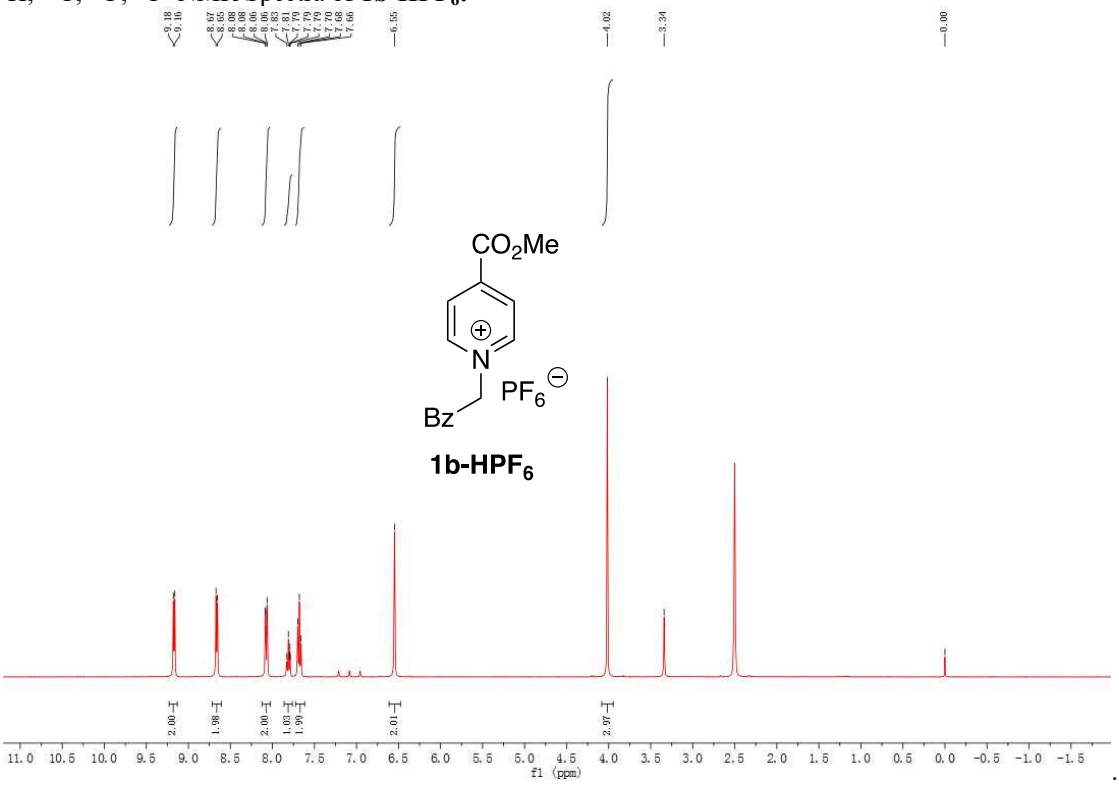
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.17 (d, J = 6.8 Hz, 2H), 8.66 (d, J = 6.8 Hz, 2H), 8.12 – 8.03 (m, 2H), 7.86 – 7.76 (m, 1H), 7.68 (t, J = 7.7 Hz, 2H), 6.55 (s, 2H), 4.02 (s, 3H).

^{13}C NMR (101 MHz, DMSO): δ 190.3, 162.5, 147.8, 144.5, 134.8, 133.5, 129.2, 128.3, 127.0, 66.7, 53.8.

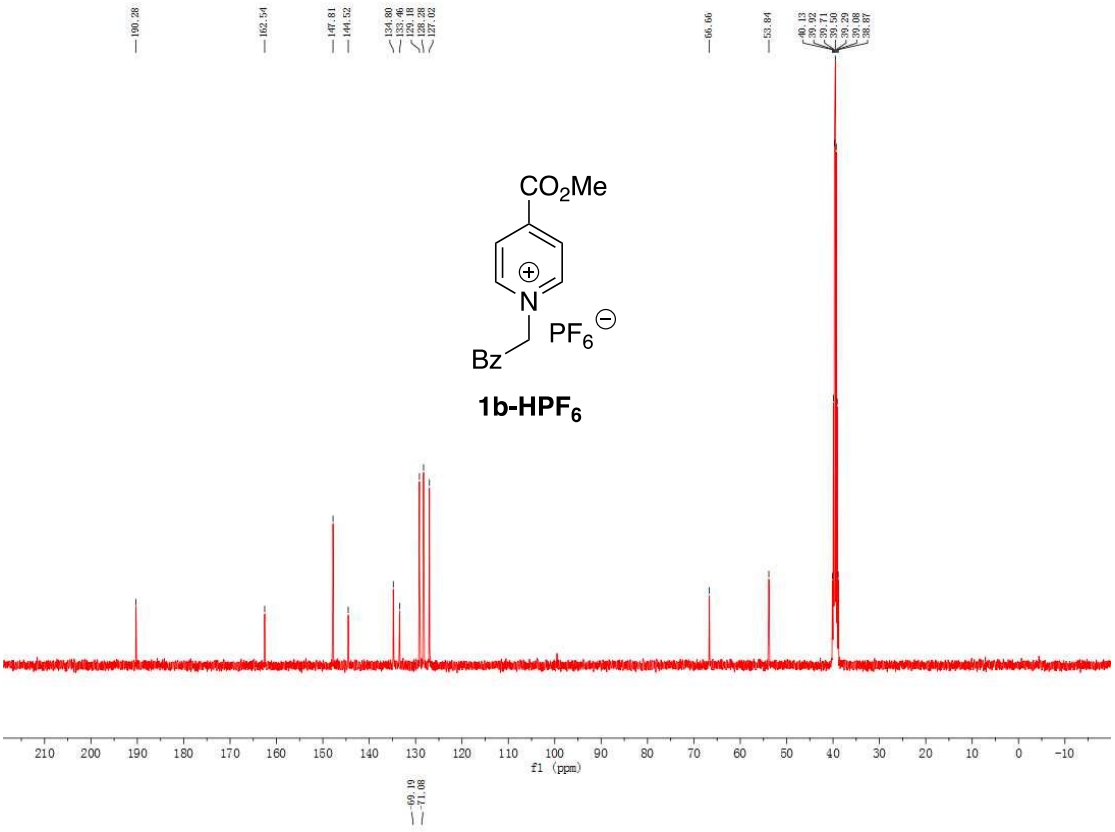
^{19}F NMR (376 MHz, DMSO): δ -69.19, -71.08.

^{31}P NMR (162 MHz, DMSO): δ -131.03, -135.42, -139.82, -144.21, -148.60, -152.99, -157.38.

^{1}H, ^{13}C, ^{19}F, ^{31}P NMR Spectra of **1b-HPF$_6$:**



1b-HPF$_6$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144.52
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129.18
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127.02
66.66
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40.13
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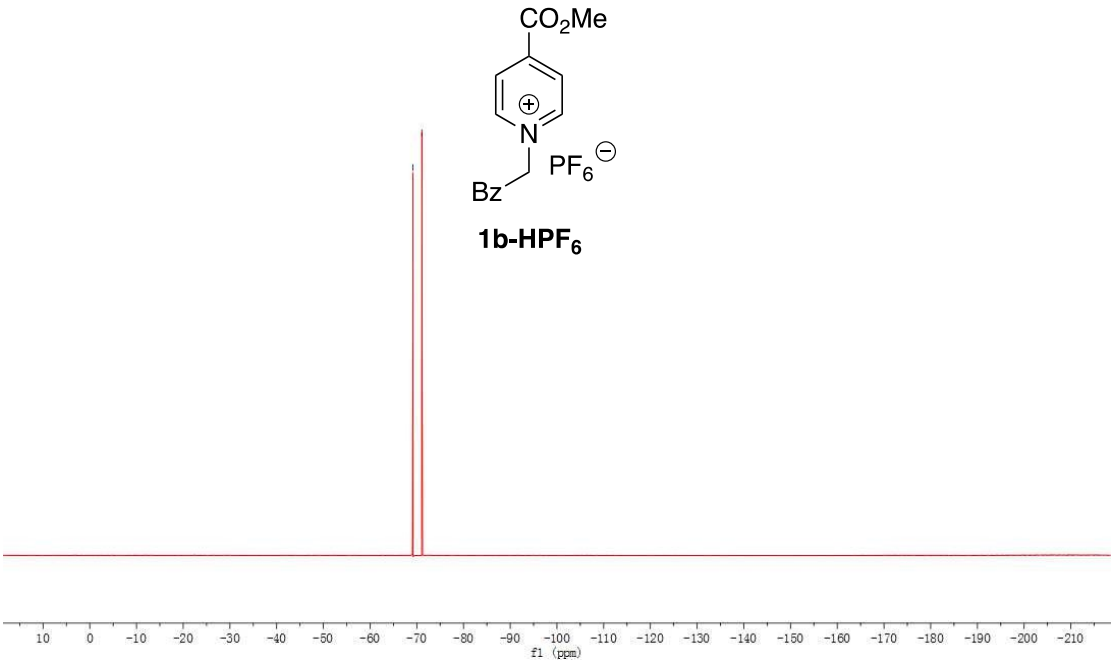
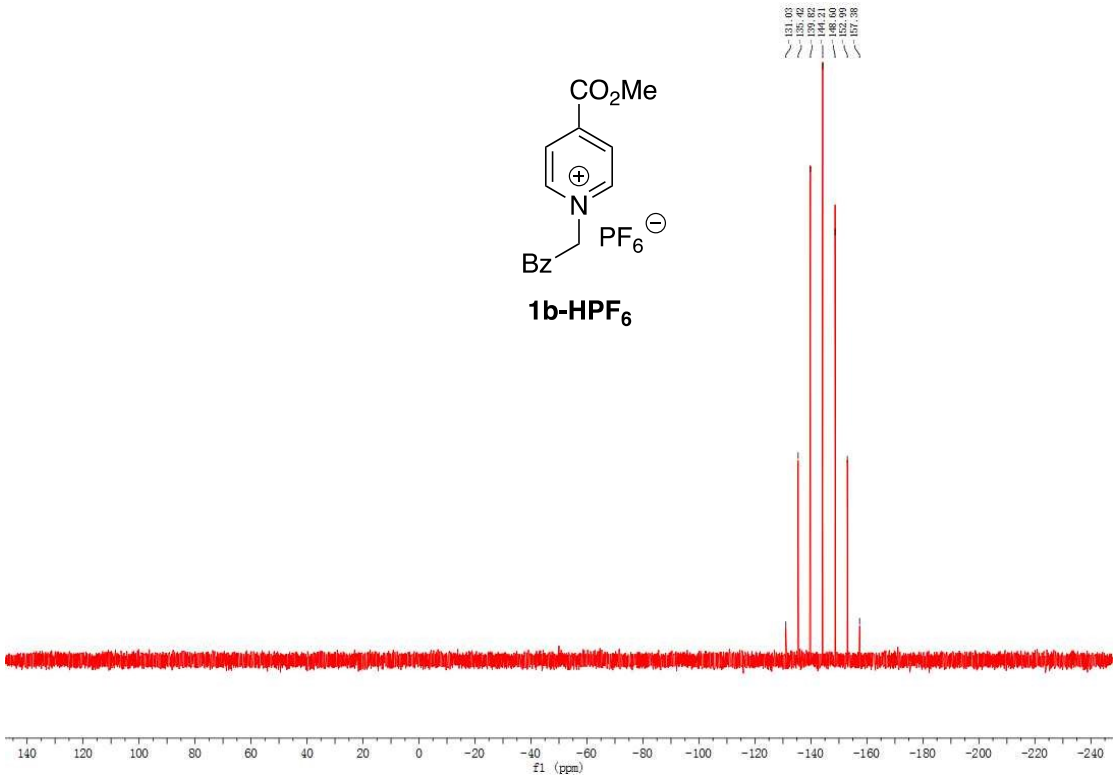
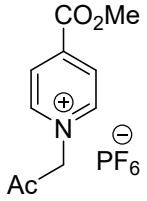
39.71
39.50
39.29
39.08
38.87
CO2Me
N
PF6
Bz
1b-HPF6
f1 (ppm)


-69.19
-71.08
CO2Me
N
PF6
Bz
1b-HPF6
f1 (ppm)



1e-HPF$_6$:
\4-(methoxycarbonyl)-1-(2-oxopropyl)pyridin-1-ium hexafluorophosphate



1e-HPF$_6$

The procedure for synthesis of compound **1e-HPF$_6$:** A solution of 4-(methoxycarbonyl)-1-(2-oxopropyl)pyridin-1-ium chloride **1e-HCl** (1.15g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of NH_4PF_6 (1.63g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1e-HPF$_6$** as white powder (1.16g, yield=68%).

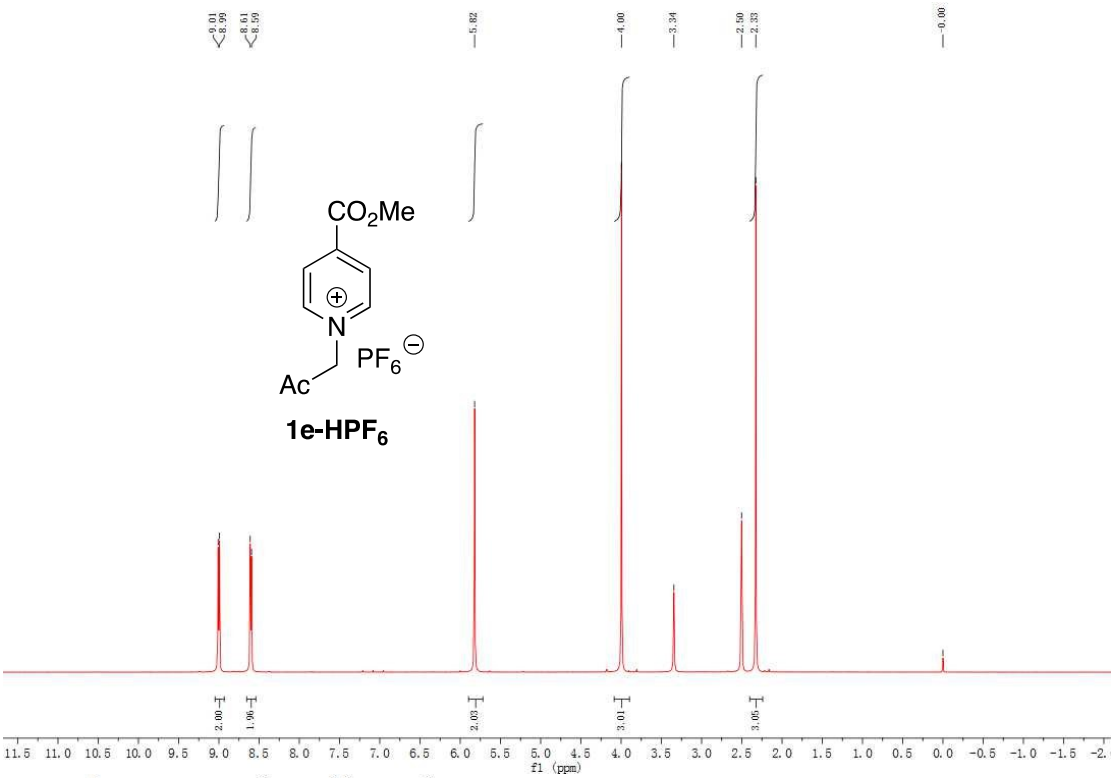
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.00 (d, J = 6.8 Hz, 2H), 8.60 (d, J = 6.8 Hz, 2H), 5.82 (s, 2H), 4.00 (s, 3H), 2.33 (s, 3H).

^{13}C NMR (101 MHz, DMSO): δ 198.9, 162.5, 147.4, 144.4, 126.9, 68.7, 53.8, 27.1.

^{19}F NMR (376 MHz, DMSO): δ -69.22, -71.11.

^{31}P NMR (162 MHz, DMSO): δ -131.05, -135.44, -139.83, -144.22, -148.62, -153.01, -157.40.

^{1}H, ^{13}C, ^{19}F, ^{31}P NMR Spectra of **1e-HPF$_6$:**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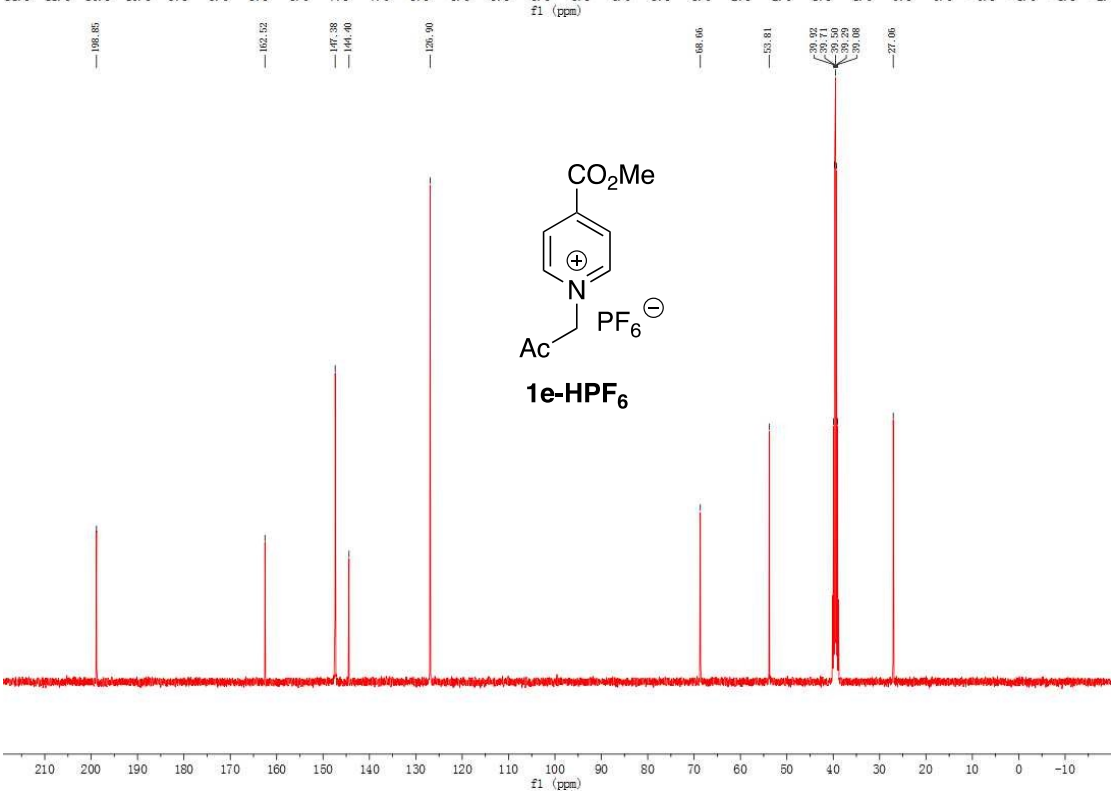
Ac
1e-HPF6
f1 (ppm)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Ac
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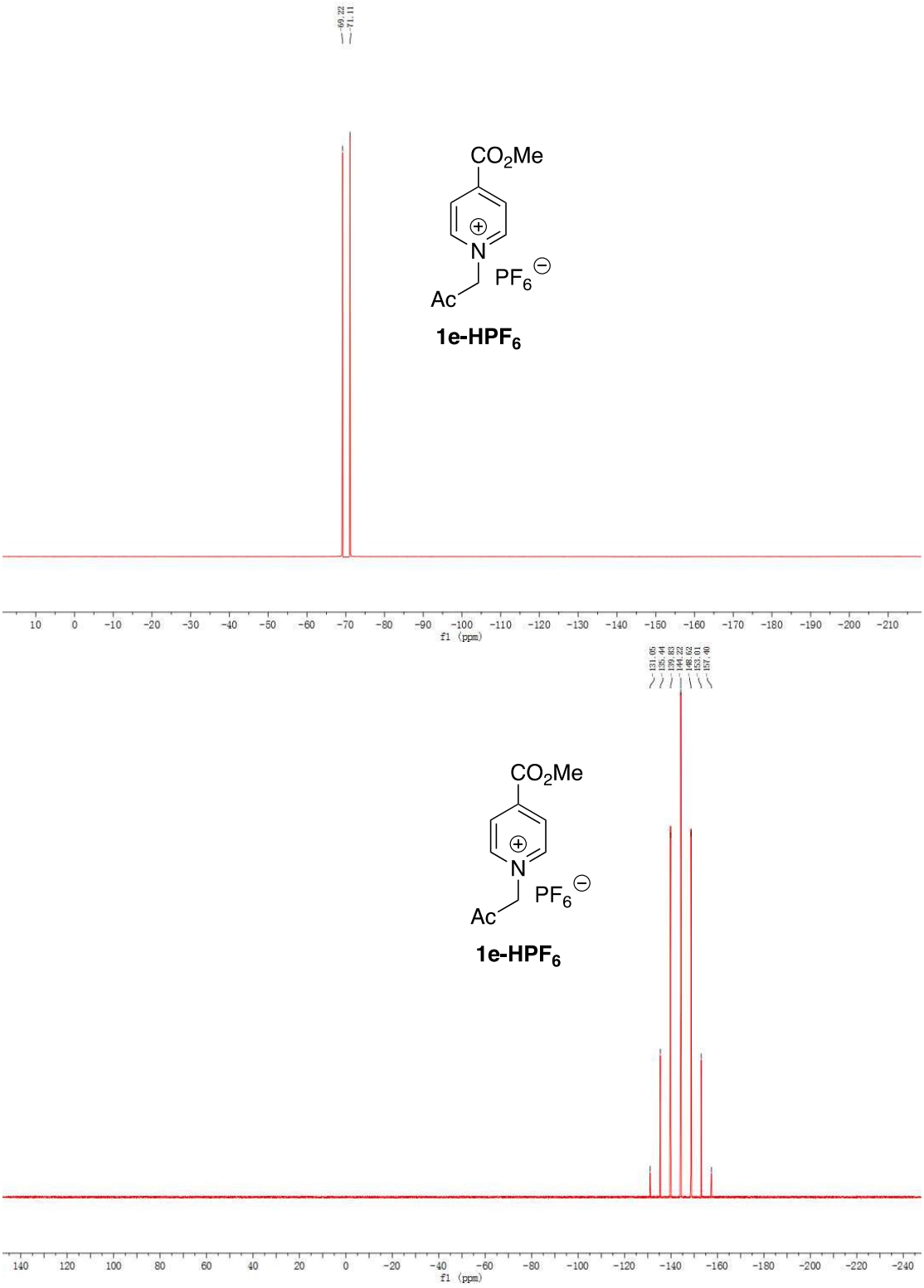
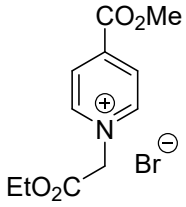
f1 (ppm)



1f-HBr:
1-(2-ethoxy-2-oxoethyl)-4-(methoxycarbonyl)pyridin-1-ium bromide



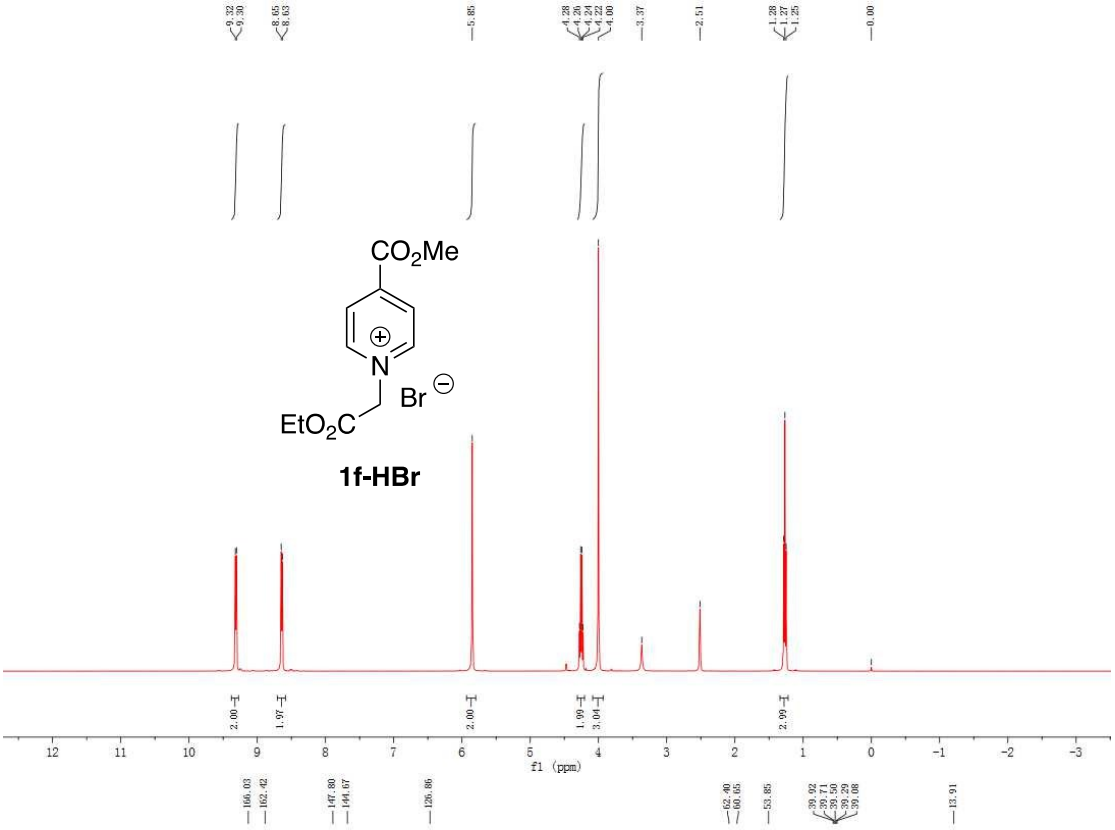
1f-HBr

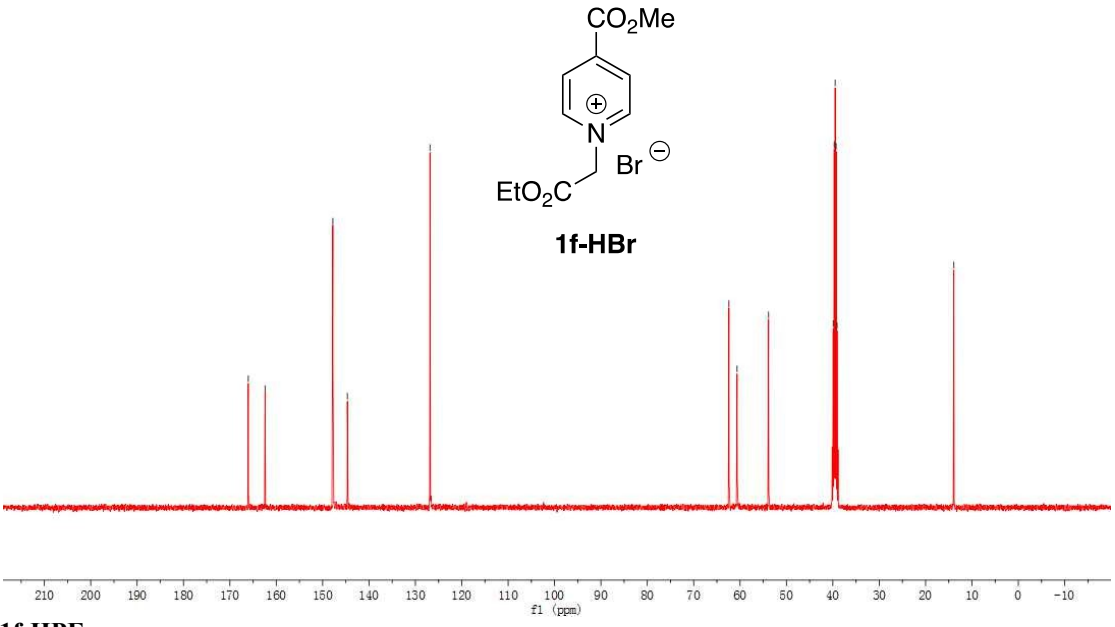
The procedure for synthesis of compound **1f-HBr**: Methyl isonicotinate (5.5mmol) and ethyl 2-bromoacetate (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 4 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1f-HBr,** as white solid (745mg, yield=49%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.31 (d, J = 6.7 Hz, 2H), 8.64 (d, J = 6.8 Hz, 2H), 5.85 (s, 2H), 4.25 (q, J = 7.1 Hz, 2H), 4.00 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 166.0, 162.4, 147.8, 144.7, 126.9, 62.4, 60.7, 53.9, 13.9.

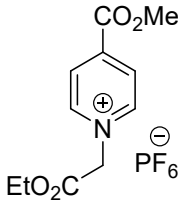
^{1}H, ^{13}C NMR Spectra of **1f-HBr:**





1f-HPF$_6$:

1-(2-ethoxy-2-oxoethyl)-4-(methoxycarbonyl)pyridin-1-ium hexafluorophosphate



1f-HPF$_6$

The procedure for synthesis of compound **1f-HPF$_6$:** A solution of 1-(2-ethoxy-2-oxoethyl)-4-(methoxycarbonyl)pyridin-1-ium bromide **1f-HBr** (1.52g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of NH_4PF_6 (1.63g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1f-HPF$_6$** as white powder (1.46g, yield=79%).

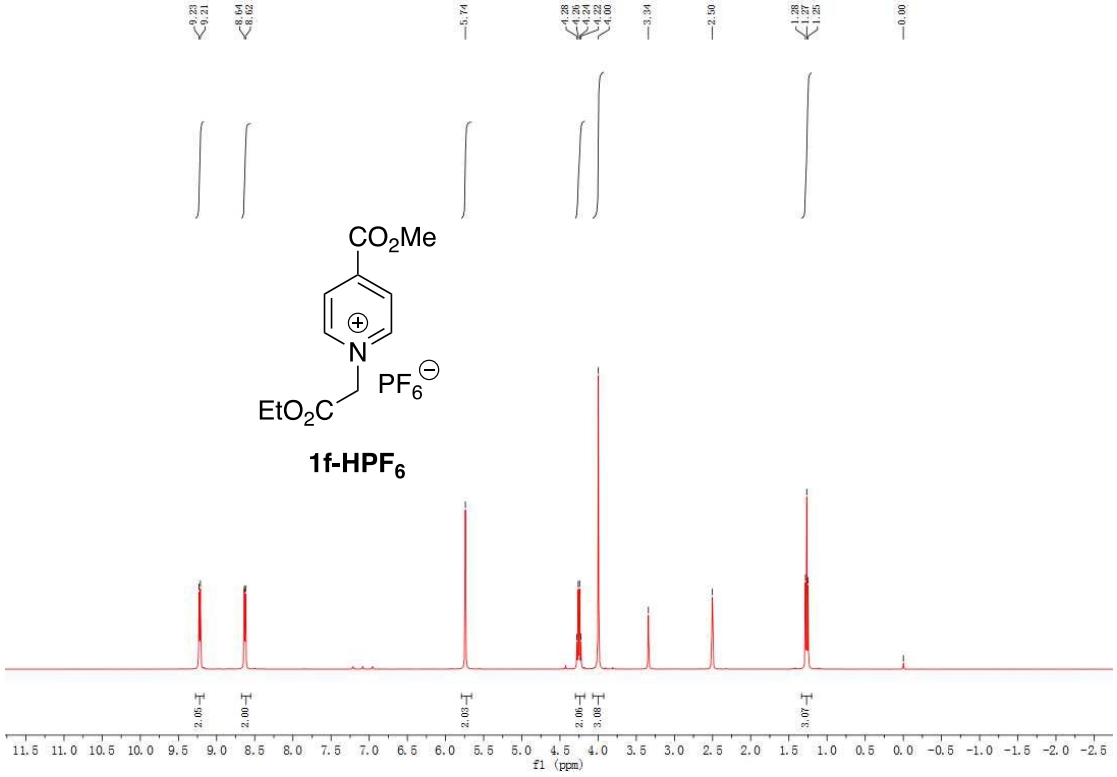
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.22 (d, J = 6.8 Hz, 2H), 8.63 (d, J = 6.3 Hz, 2H), 5.74 (s, 2H), 4.25 (q, J = 7.1 Hz, 2H), 4.00 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H).

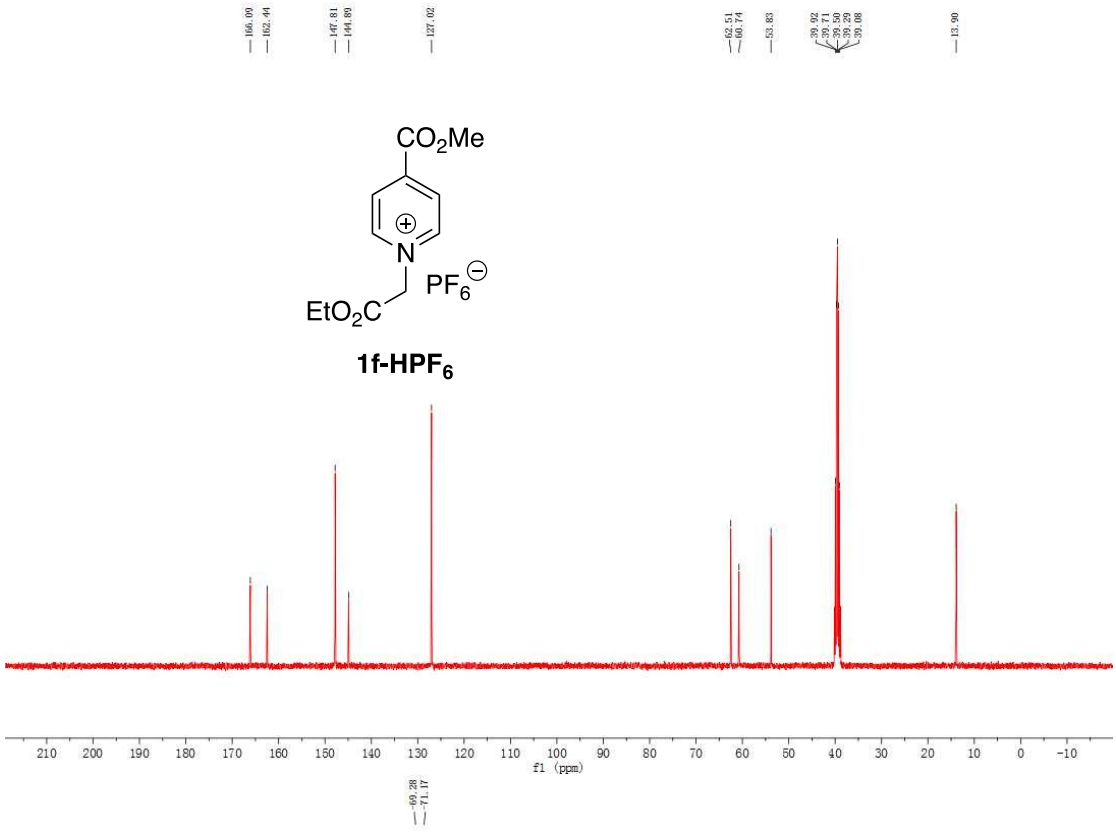
^{13}C NMR (101 MHz, DMSO-d_6): δ 166.1, 162.4, 147.8, 144.9, 127.0, 62.5, 60.7, 53.8, 13.9.

^{19}F NMR (376 MHz, DMSO): δ -69.28, -71.17.

^{31}P NMR (162 MHz, DMSO): δ -131.06, -135.45, -139.84, -144.23, -148.62, -153.01, -157.41.

^{1}H, ^{13}C, ^{19}F, ^{31}P NMR Spectra of **1f-HPF$_6$:**

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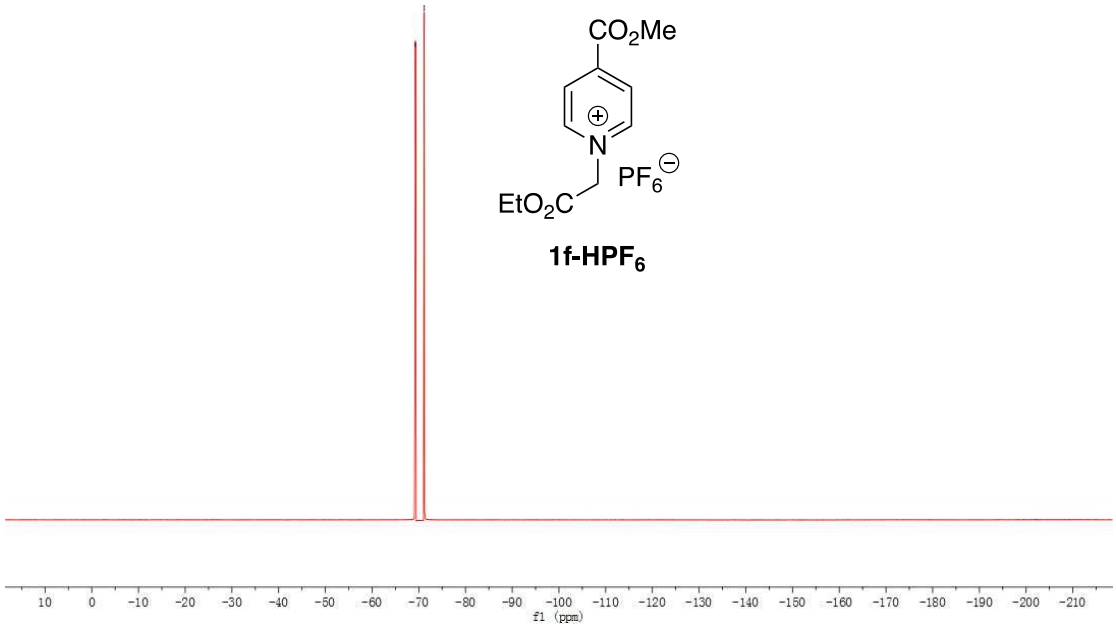
144.89
127.02
62.51
60.74
53.83
39.92
39.71
39.50
39.29
39.08
13.90
CO2Me
N
PF6
EtO2C
1f-HPF6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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-71.17
CO2Me
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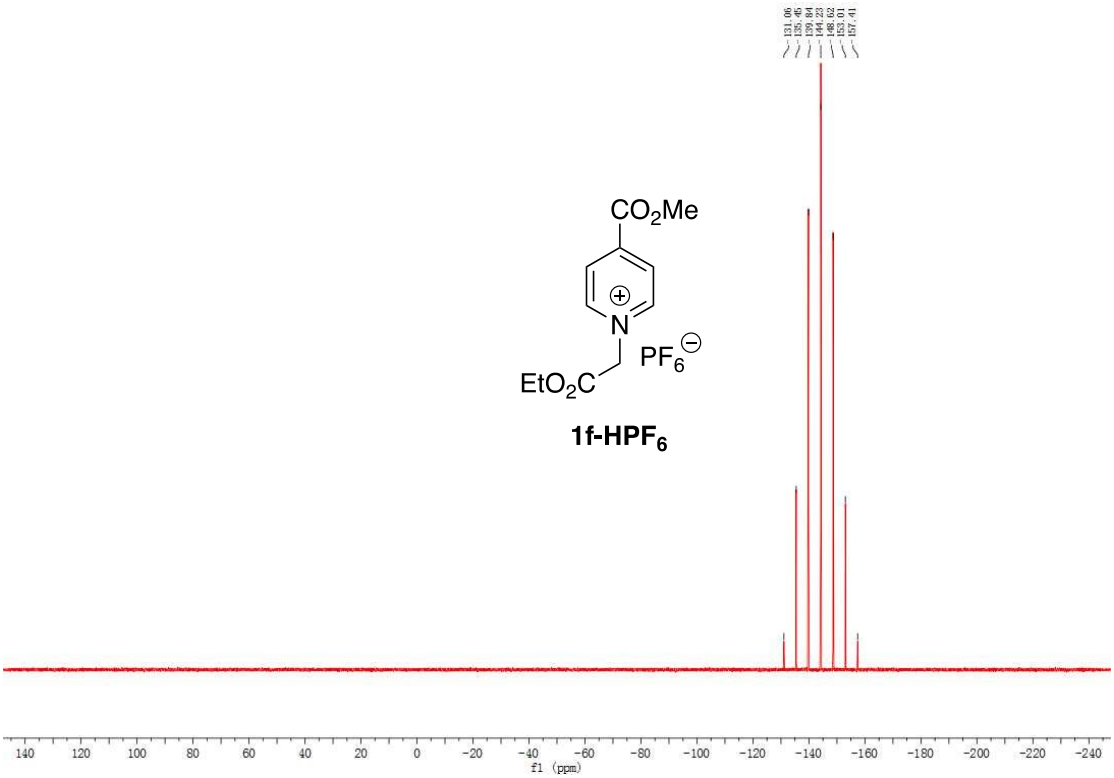
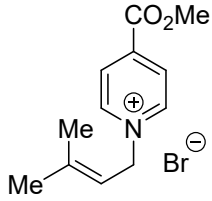
f1 (ppm)



1h-HBr:
4-(methoxycarbonyl)-1-(3-methylbut-2-en-1-yl)pyridin-1-ium bromide



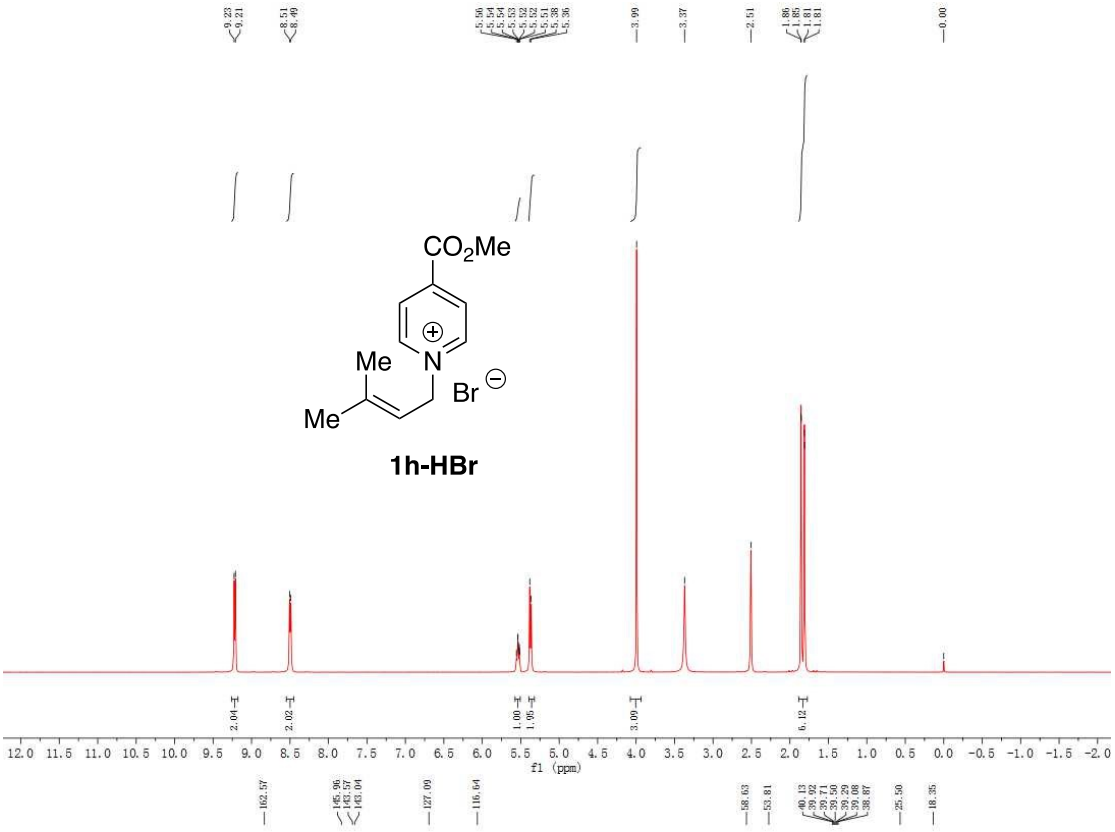
1h-HBr

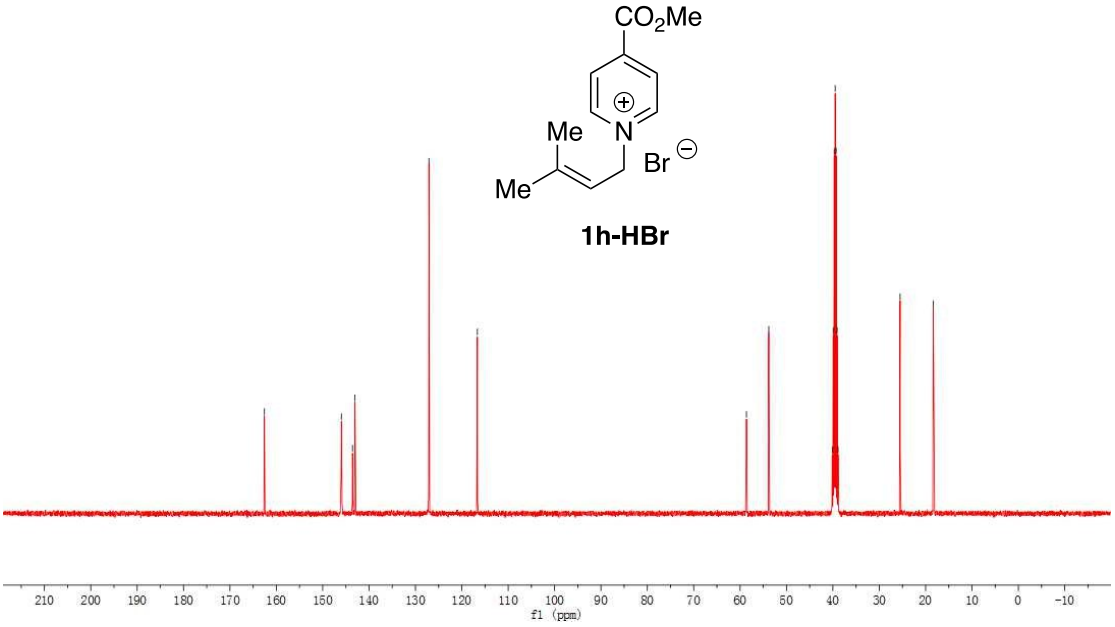
The procedure for synthesis of compound **1h-HBr**: Methyl isonicotinate (5.5mmol) and 3,3-Dimethylallyl bromide (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1h-HBr,** as white solid (959mg, yield=67%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.22 (d, J = 6.8 Hz, 2H), 8.50 (d, J = 6.3 Hz, 2H), 5.57 – 5.51 (m, 1H), 5.37 (d, J = 7.4 Hz, 2H), 3.99 (s, 3H), 1.83 (dd, J = 17.3, 1.3 Hz, 6H).

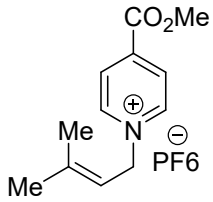
^{13}C NMR (101 MHz, DMSO-d_6): δ 162.6, 146.0, 143.6, 143.0, 127.1, 116.6, 58.6, 53.8, 25.5, 18.4.

^{1}H, ^{13}C NMR Spectra of **1h-HBr:**





1h-HPF_6:
4-(methoxycarbonyl)-1-(3-methylbut-2-en-1-yl)pyridin-1-ium hexafluorophosphate



1h-HPF$_6$

The procedure for synthesis of compound **1h-HPF$_6$:** A solution of 4-(methoxycarbonyl)-1-(3-methylbut-2-en-1-yl)pyridin-1-ium bromide **1h-HBr** (1.43g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of NH_4PF_6 (1.63g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1h-HPF$_6$** as white powder (1.25g, yield=71%).

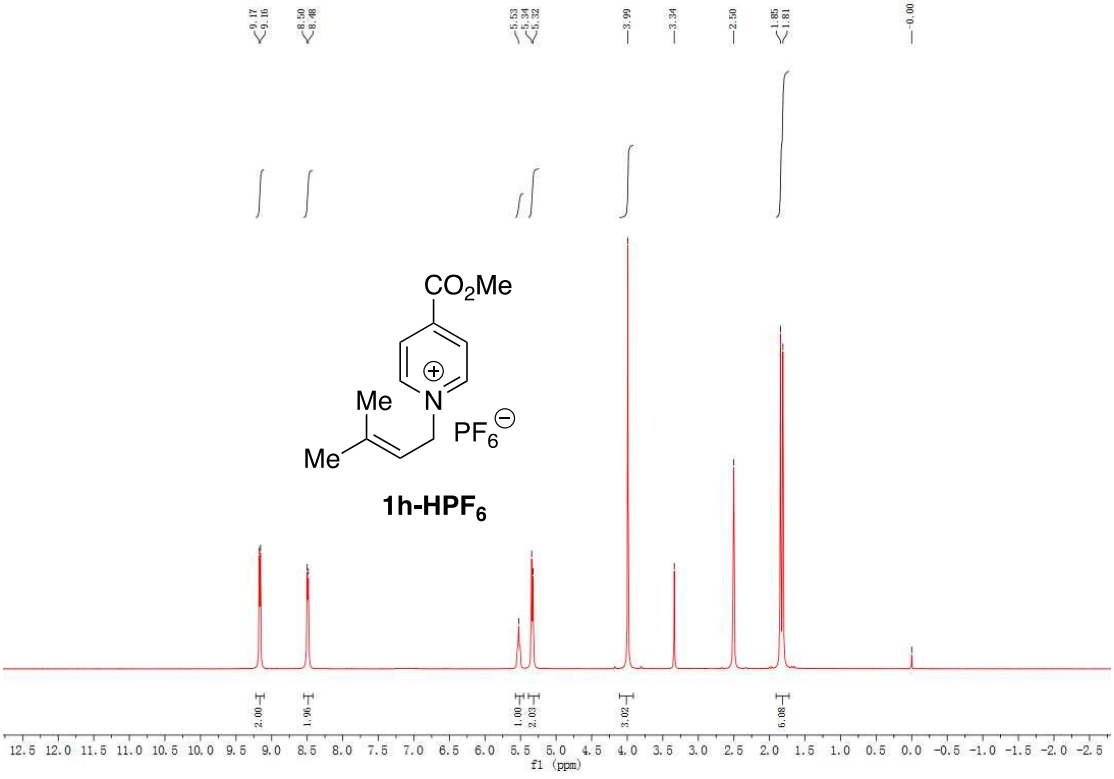
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.16 (d, J = 6.3 Hz, 2H), 8.49 (d, J = 6.1 Hz, 2H), 5.53 (s, 1H), 5.33 (d, J = 7.4 Hz, 2H), 3.99 (s, 3H), 1.83 (d, J = 13.8 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 162.5, 145.8, 143.8, 143.2, 127.2, 116.5, 58.7, 53.7, 25.4, 18.1.

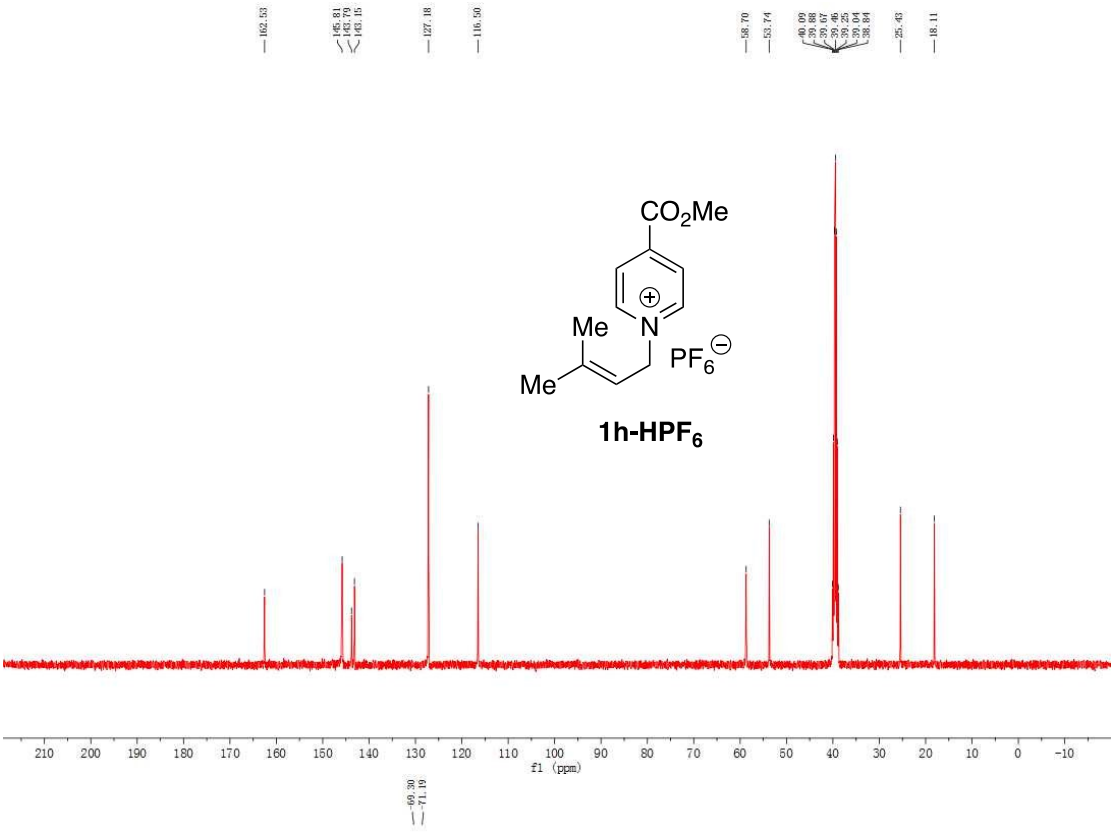
^{19}F NMR (376 MHz, DMSO): δ -69.30, -71.19.

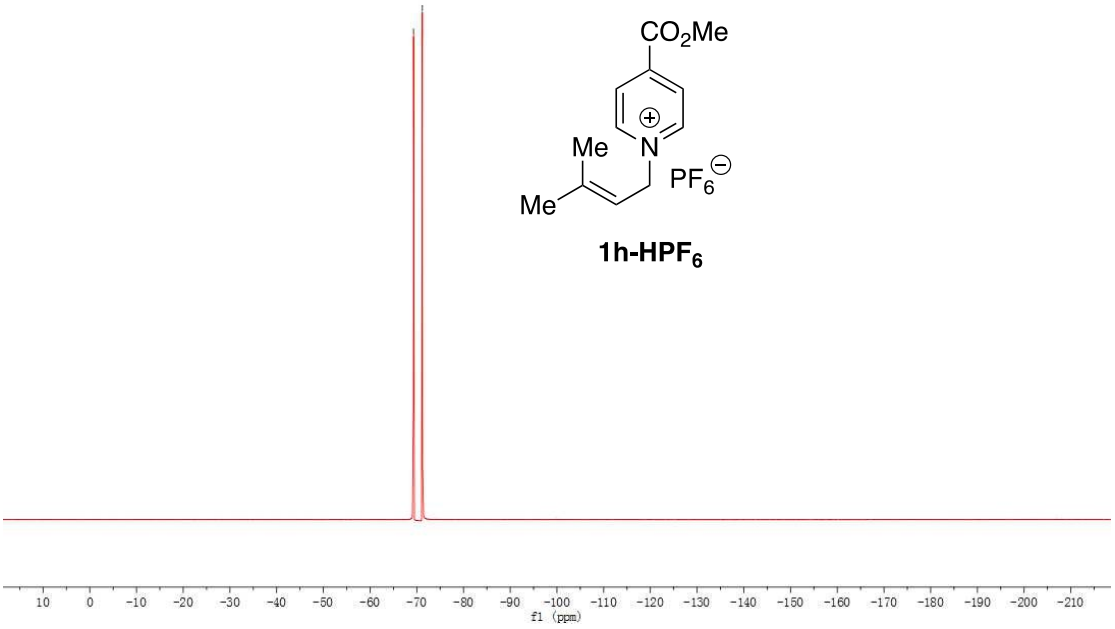
^{31}P NMR (162 MHz, DMSO): δ -131.06, -135.46, -139.85, -144.24, -148.63, -153.03, -157.42.

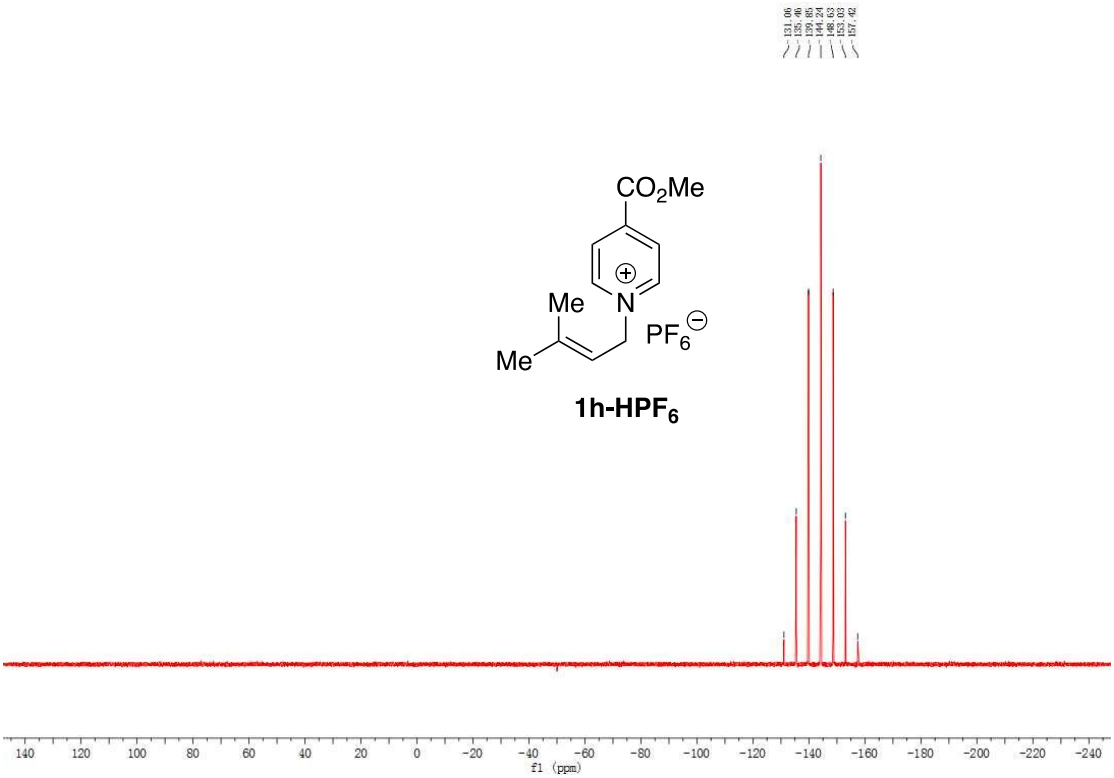
^{1}H, ^{13}C, ^{19}F, ^{31}P NMR Spectra of **1h-HPF$_6$:**



1h-HPF$_6$

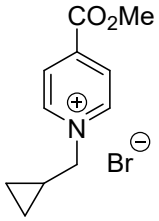

162.53
145.81
145.70
143.15
127.18
116.50
58.70
53.74
40.09
39.88
39.67
39.46
39.25
39.04
38.84
25.43
18.11
CO2Me
Me
N
PF6
Me
1h-HPF6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-69.30
-71.19
CO2Me
Me
N
PF6
Me
1h-HPF6
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)



1i-HBr:

1-(cyclopropylmethyl)-4-(methoxycarbonyl)pyridin-1-ium bromide



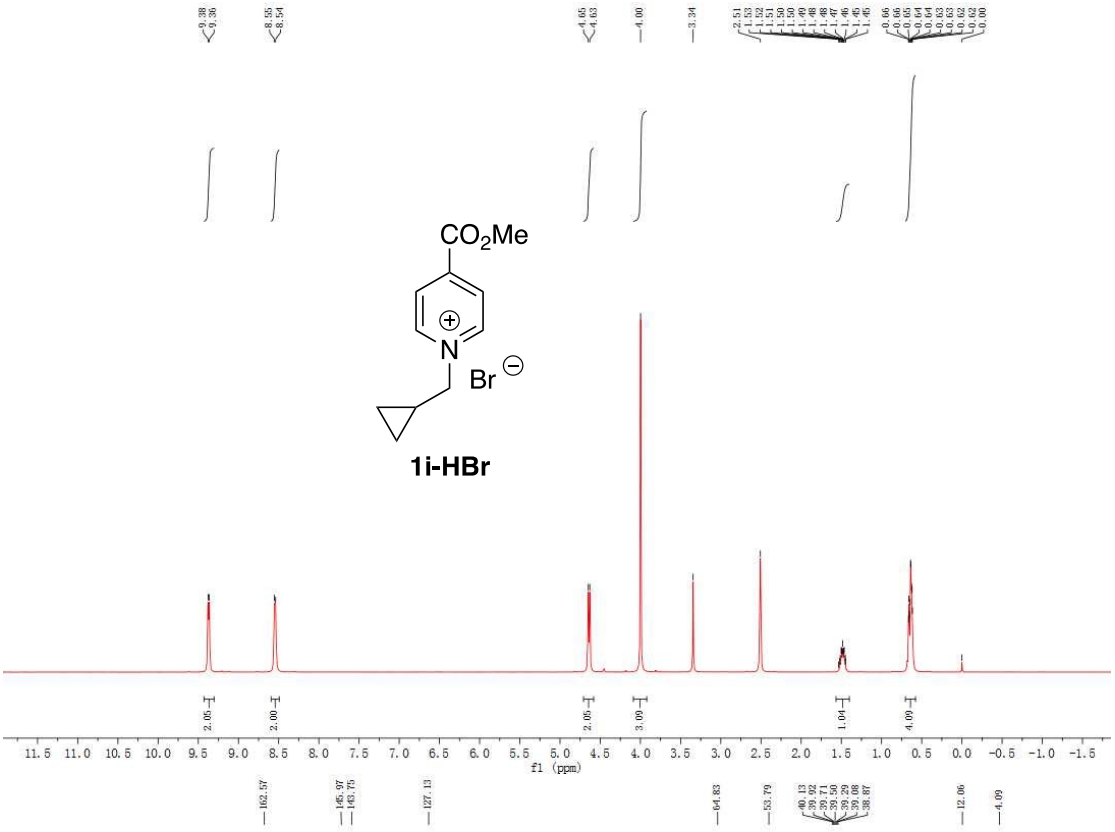
1i-HBr

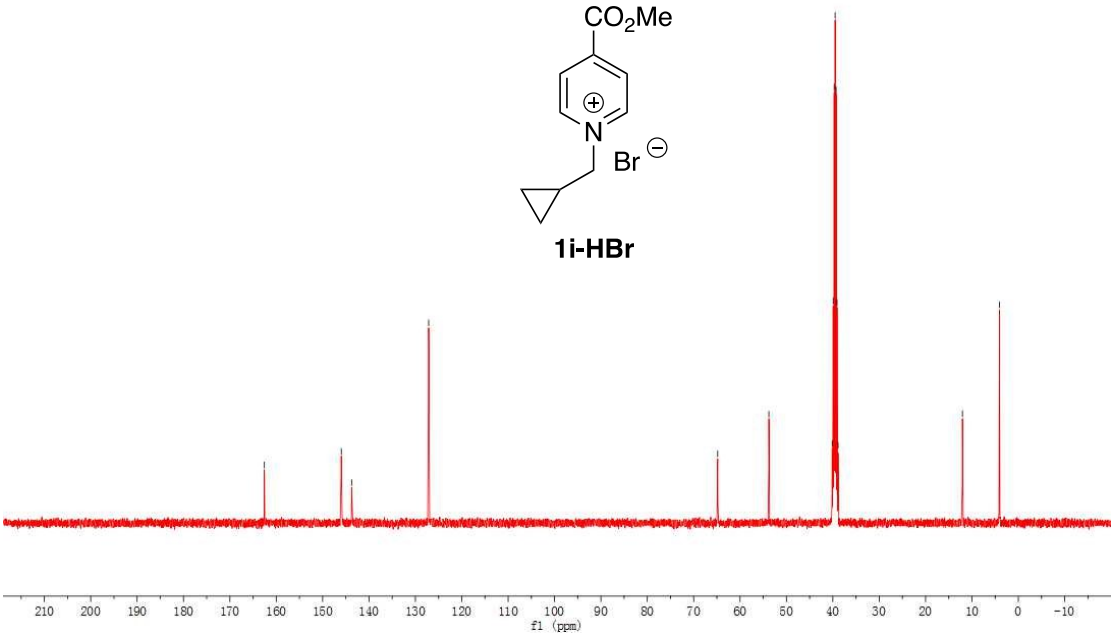
The procedure for synthesis of compound **1i-HBr**: Methyl isonicotinate (5.5mmol) and (Bromomethyl)cyclopropane (5mmol) were added in 3mL of ethyl acetate and stirred at 60℃ for 12 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1i-HBr,** as white solid (259mg, yield=19%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.37 (d, J = 6.1 Hz, 2H), 8.55 (d, J = 6.1 Hz, 2H), 4.64 (d, J = 7.5 Hz, 2H), 4.00 (s, 3H), 1.48 (tt, J = 7.7, 5.0 Hz, 1H), 0.70 – 0.58 (m, 4H).

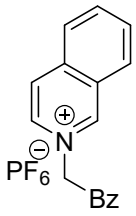
^{13}C NMR (101 MHz, DMSO-d_6): δ 162.6, 146.0, 143.8, 127.1, 64.8, 53.8, 12.1, 4.1.

^{1}H, ^{13}C NMR Spectra of **1i-HBr:**





1j-HPF_6:
2-(2-oxo-2-phenylethyl)isoquinolin-2-ium hexafluorophosphate



1j-HPF$_6$

The procedure for synthesis of compound **1j-HPF$_6$:** A solution of 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1j-HBr** (1.64g, 5mmol) in H_2O (5mL) was added dropwise under stirring to a solution of NH_4PF_6 (1.63g, 10mmol) in H_2O (5mL). The mixture was stirred at r.t. for 30min until the precipitate was completely formed. Then the insoluble solid were removed by filtration and washed with water to give pure products **1j-HPF$_6$** as colorless powder (1.67g, yield=85%).

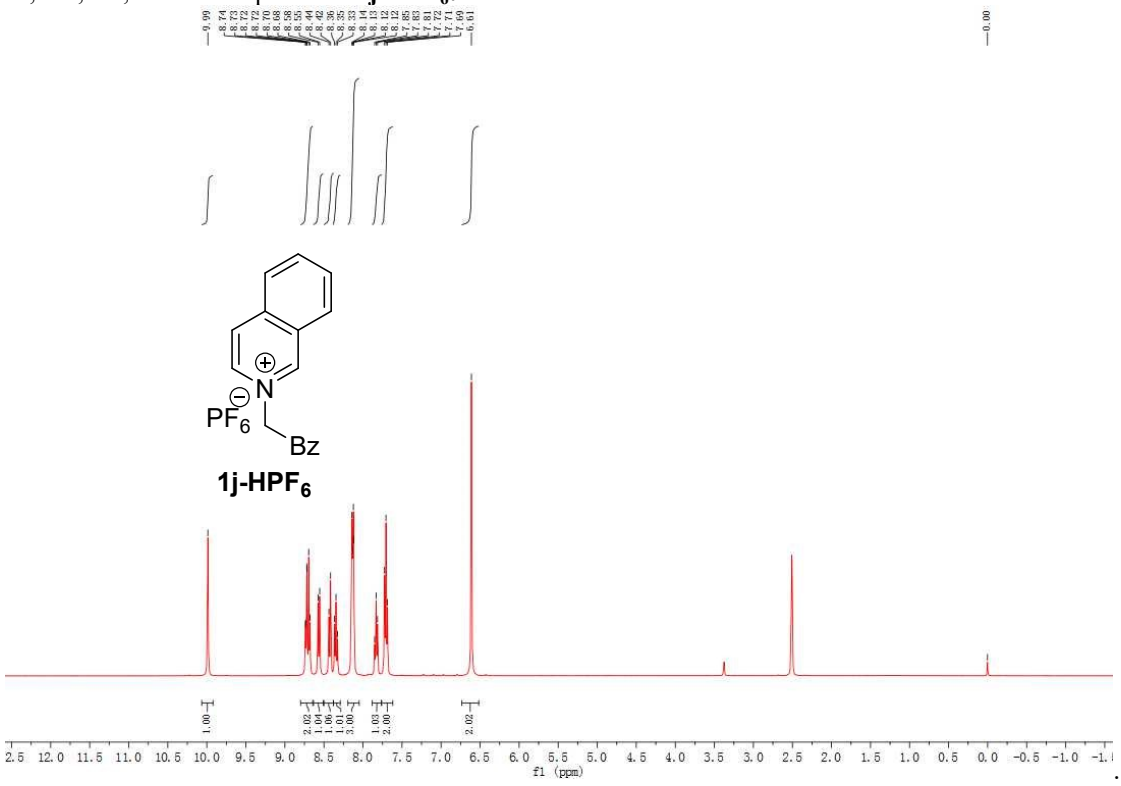
^{1}H NMR (400 MHz, DMSO-d_6): δ 9.99 (s, 1H), 8.80 – 8.64 (m, 2H), 8.57 (d, J = 8.3 Hz, 1H), 8.43 (d, J = 8.3 Hz, 1H), 8.35 (t, J = 7.6 Hz, 1H), 8.13 (dd, J = 6.2, 2.9 Hz, 3H), 7.83 (t, J = 7.4 Hz, 1H), 7.71 (t, J = 7.6 Hz, 2H), 6.61 (s, 2H).

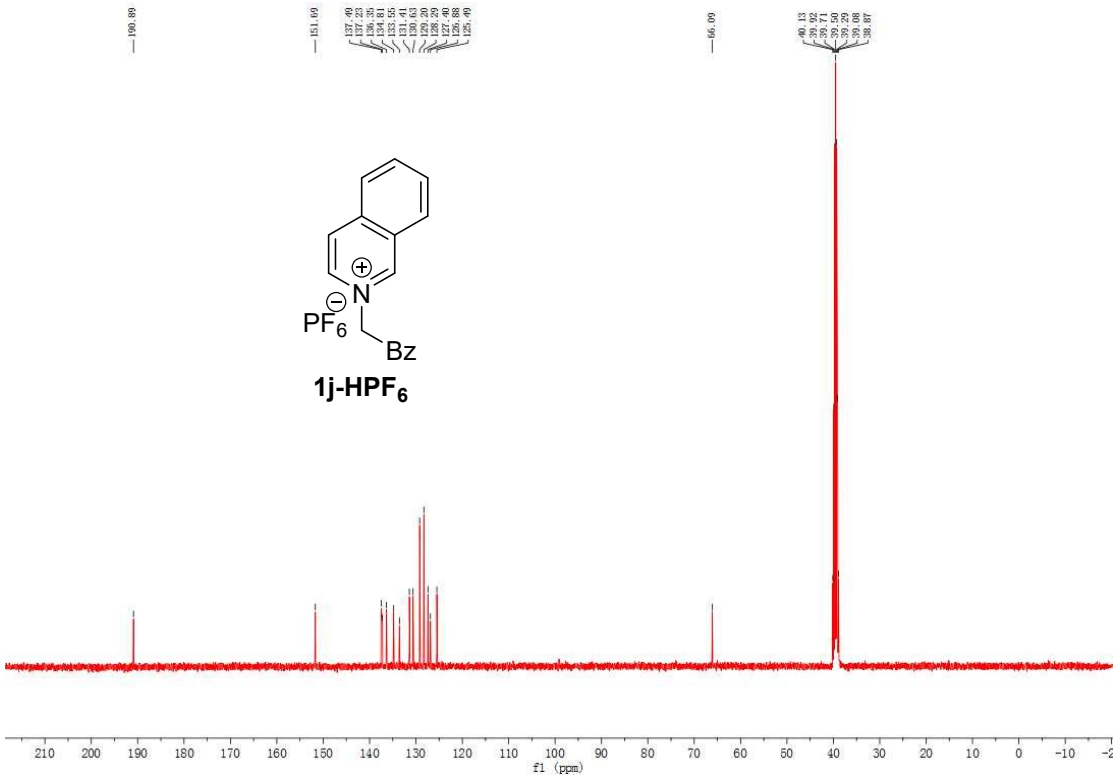
^{13}C NMR (101 MHz, DMSO-d_6): δ 190.9, 151.7, 137.5, 137.2, 136.4, 134.8, 133.6, 131.4, 130.6, 129.2, 128.3, 127.4, 126.9, 125.5, 66.1.

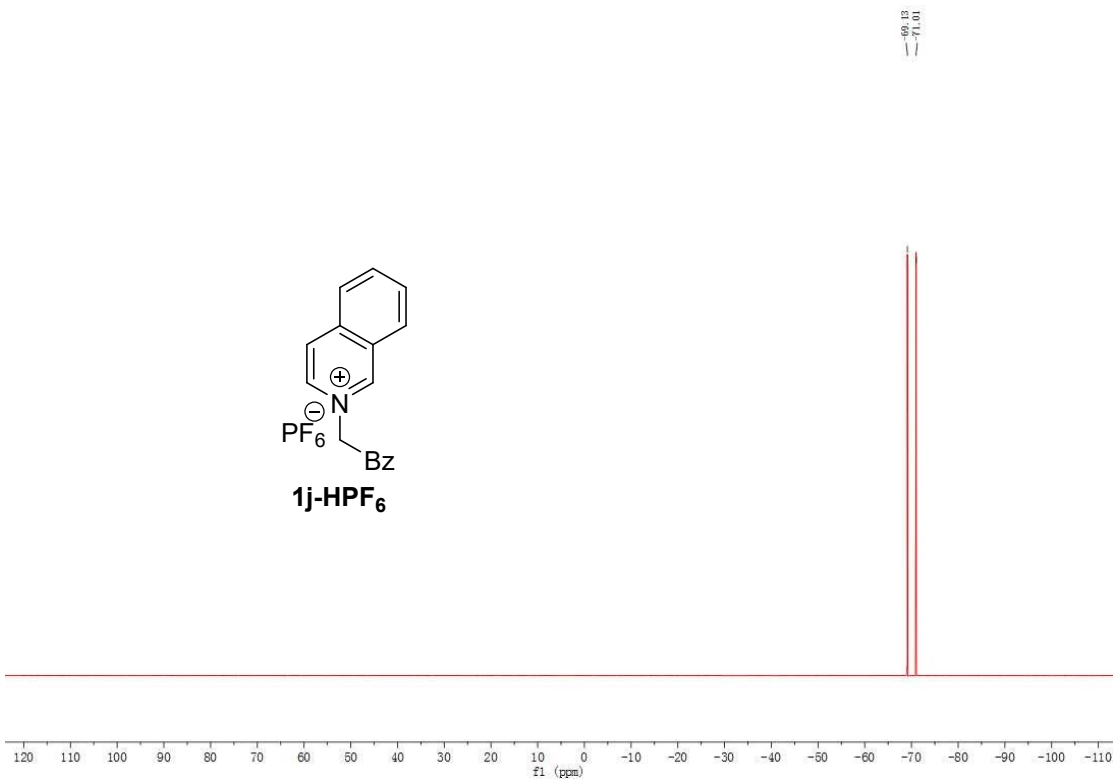
^{19}F NMR (377 MHz, DMSO): δ -69.13, -71.01.

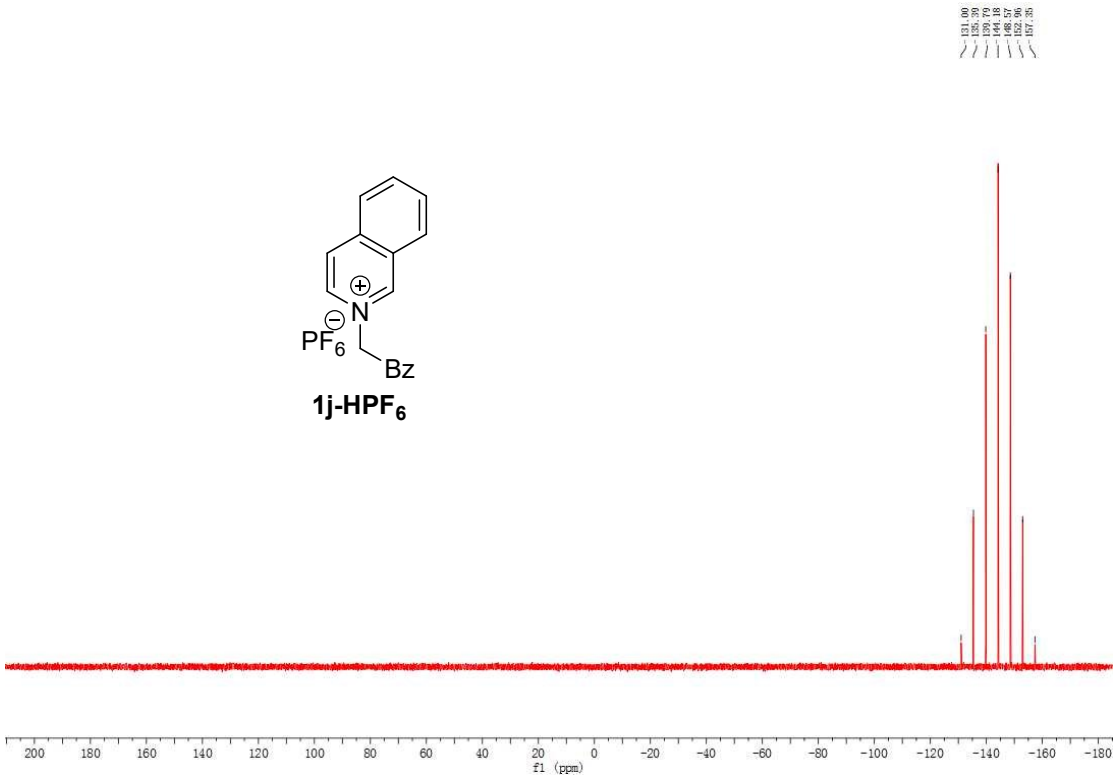
^{31}P NMR (162 MHz, DMSO): δ -131.00, -135.39, -139.79, -144.18, -148.57, -152.96, -157.35.

^{1}H, ^{13}C, ^{19}F, ^{31}P NMR Spectra of **1j-HPF$_6$:**




190.89
151.69
137.49
137.23
136.35
134.81
133.55
131.41
130.63
129.20
128.29
127.46
126.88
125.49
66.09
40.13
39.92
39.71
39.50
39.29
39.08
38.87
N
PF6
Bz
1j-HPF6
f1 (ppm)

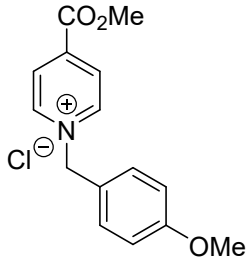

-69.13
-71.01
N
PF6
Bz
1j-HPF6
f1 (ppm)



1j-HPF$_6$

1k-HCl:

1-(4-methoxybenzyl)-4-(methoxycarbonyl)pyridin-1-ium chloride



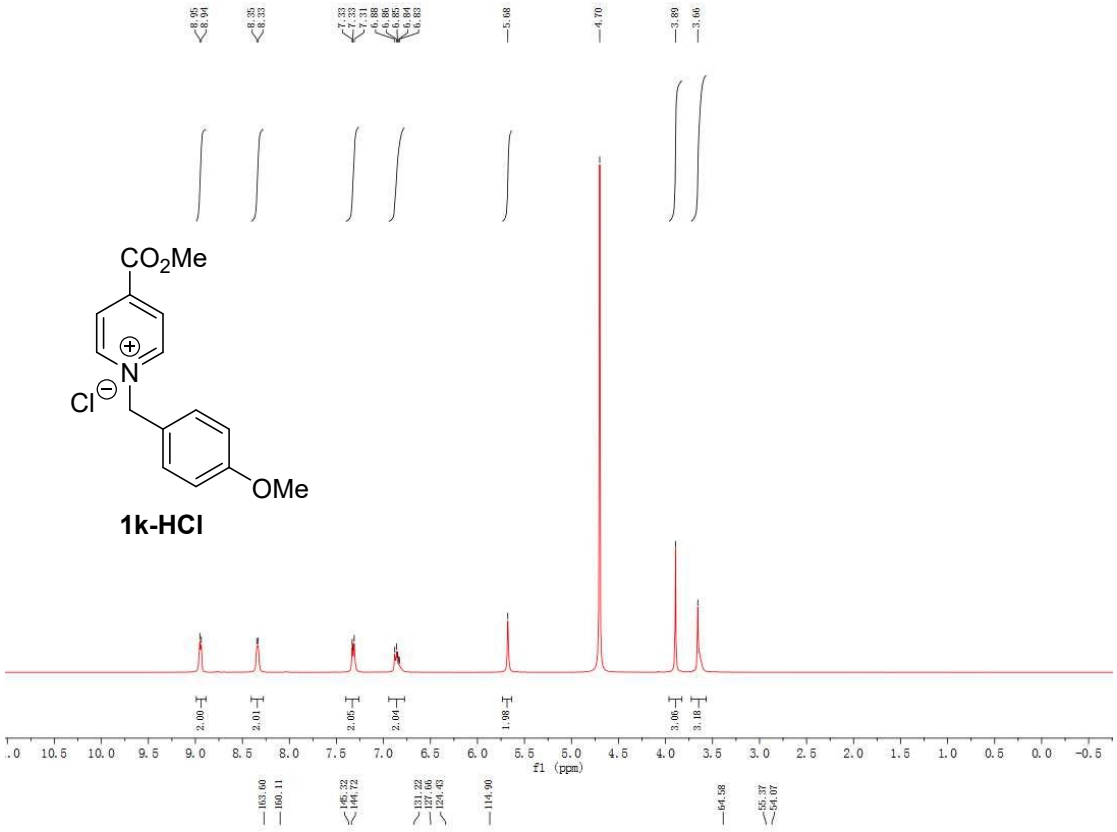
1k-HCl

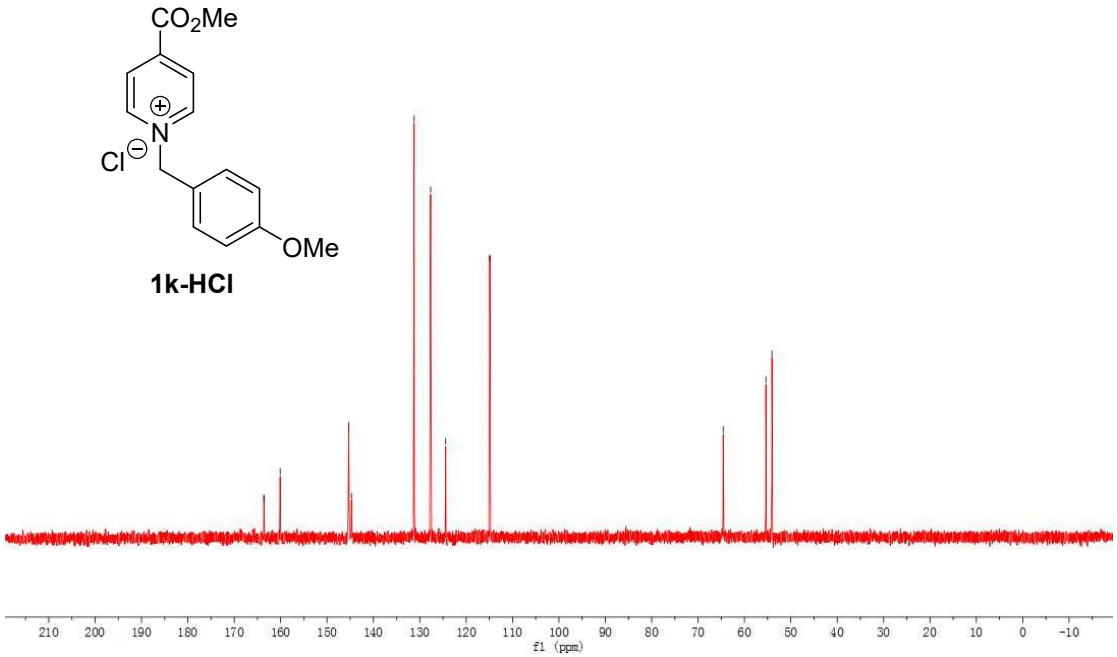
General procedure: The procedure for synthesis of compound **1k-HCl**: Methyl isonicotinate (5.5mmol) and 1-(chloromethyl)-4-methoxybenzene (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1k-HCl** as white solid.

^{1}H NMR (400 MHz, Deuterium Oxide) δ 8.94 (d, *J* = 6.2 Hz, 2H), 8.34 (d, *J* = 6.1 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 6.86 (t, *J* = 9.9 Hz, 2H), 5.68 (s, 2H), 3.89 (s, 3H), 3.66 (s, 3H).

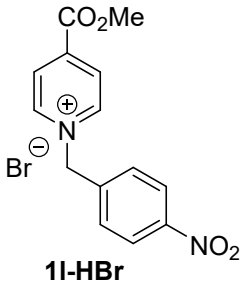
^{13}C NMR (101 MHz, Deuterium Oxide) δ 163.6, 160.1, 145.3, 144.7, 131.2, 127.7, 124.4, 114.9, 64.6, 55.4, 54.1.

1H, 13C NMR Spectra:





1l-HBr:
4-(methoxycarbonyl)-1-(4-nitrobenzyl)pyridin-1-ium bromide



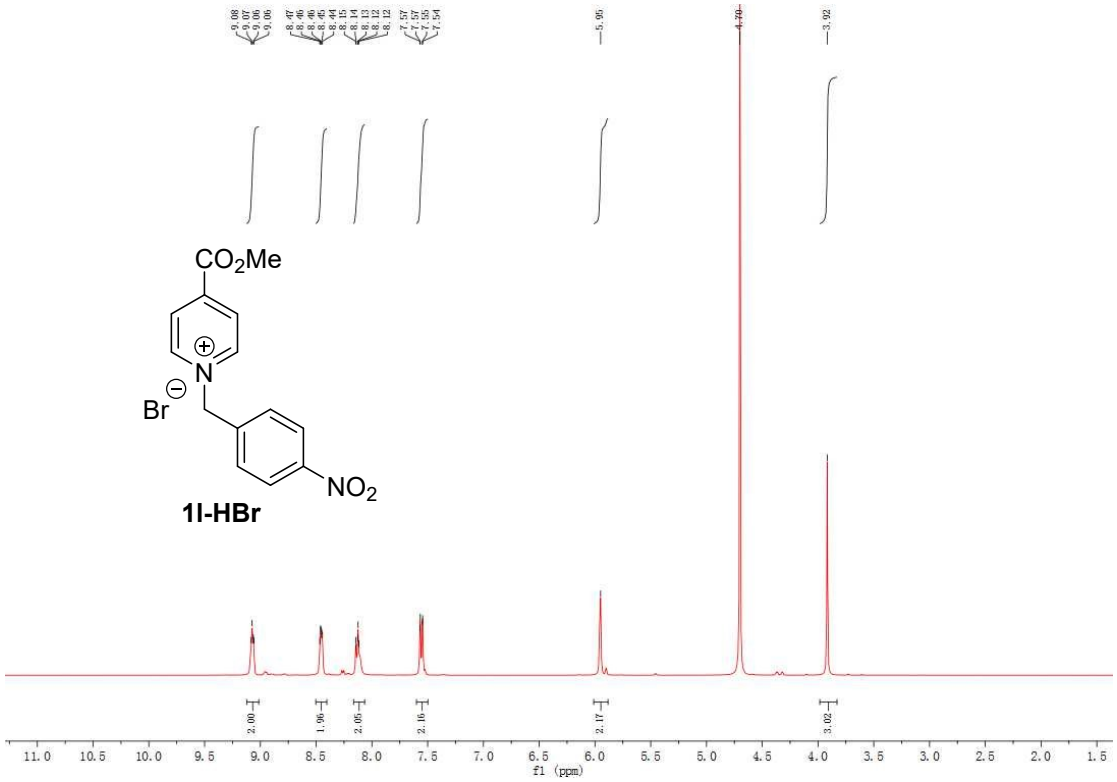
1l-HBr

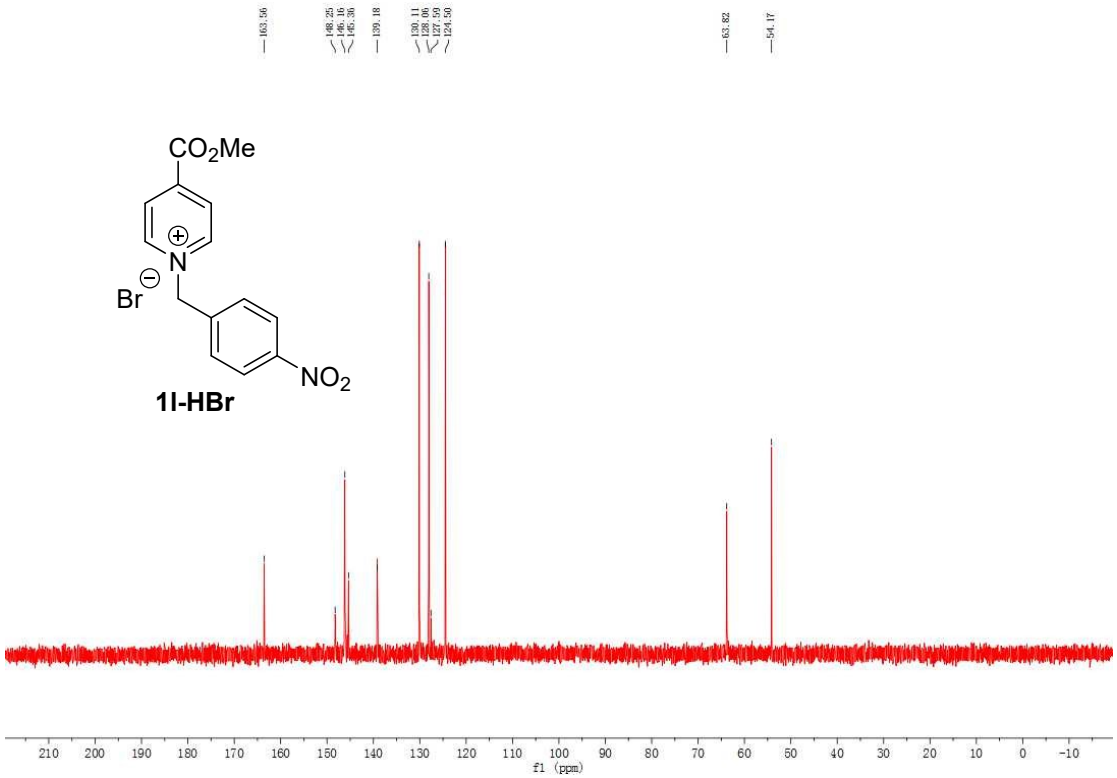
General procedure: The procedure for synthesis of compound **1l-HBr**: Methyl isonicotinate (5.5mmol) and 1-(bromomethyl)-4-nitrobenzene (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1l-HBr** as white solid.

^{1}H NMR (400 MHz, Deuterium Oxide): δ 9.12 – 9.01 (m, 2H), 8.50 – 8.40 (m, 2H), 8.16 – 8.07 (m, 2H), 7.60 – 7.50 (m, 2H), 5.95 (s, 2H), 3.92 (s, 3H).

^{13}C NMR (101 MHz, Deuterium Oxide): δ 163.6, 148.3, 146.2, 145.4, 139.2, 130.1, 128.1, 127.6, 124.5, 63.8, 54.2.

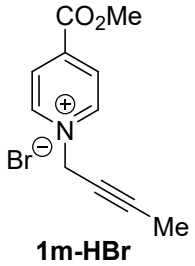
1H, 13C NMR Spectra:





1m-HBr:

1-(but-2-yn-1-yl)-4-(methoxycarbonyl)pyridin-1-ium bromide



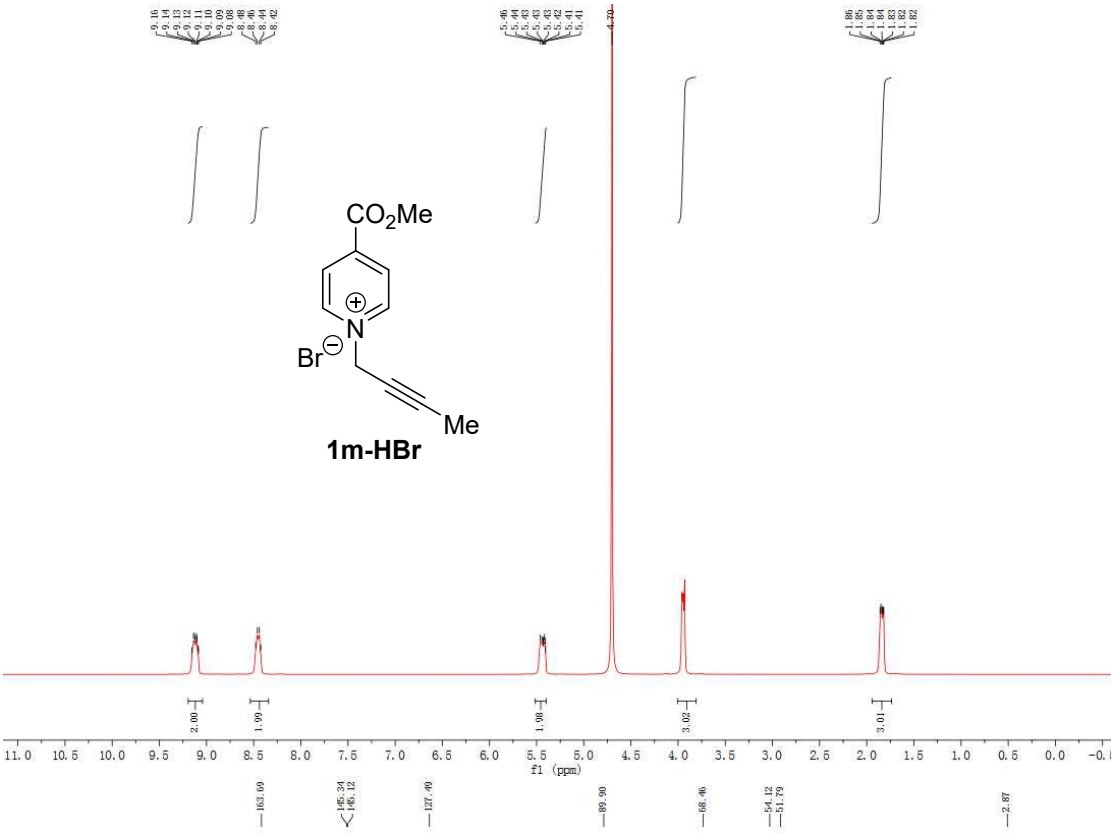
1m-HBr

General procedure: The procedure for synthesis of compound **1m-HBr**: Methyl isonicotinate (5.5mmol) and 1-bromobut-2-yne (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1m-HBr** as gray solid.

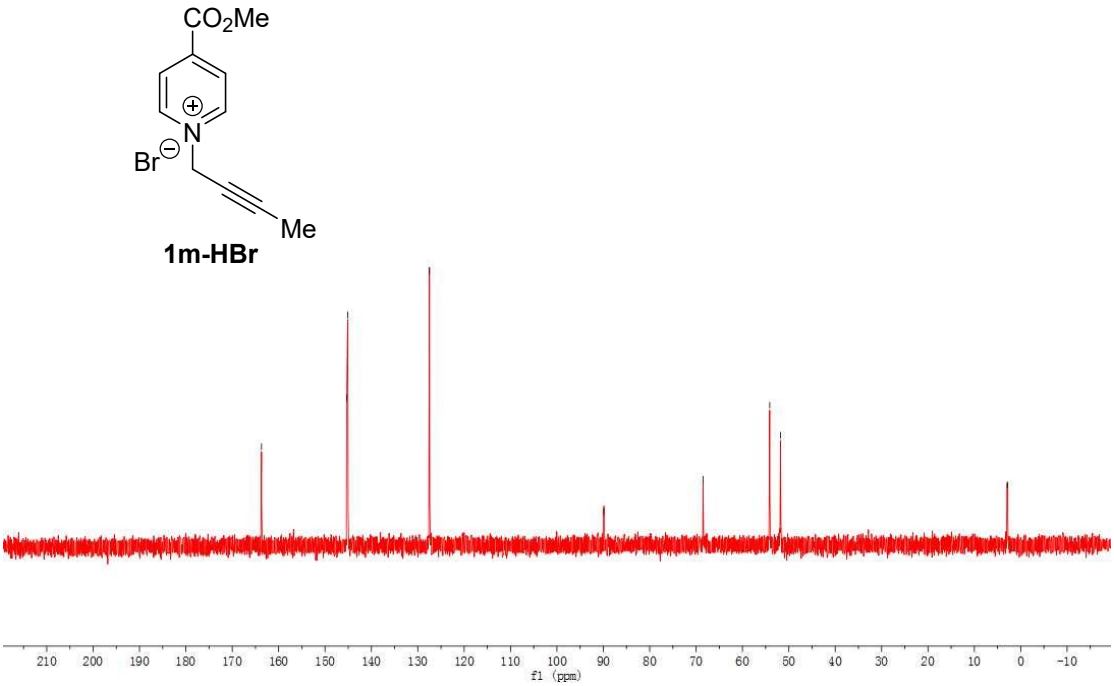
^{1}H NMR (400 MHz, Deuterium Oxide): δ 9.19-9.04 (m, 2H), 8.45 (q, J = 6.6, 6.0 Hz, 2H), 5.51 – 5.40 (m, 2H), 4.00 – 3.81 (m, 3H), 1.84 (dt, J = 8.2, 2.7 Hz, 3H).

^{13}C NMR (101 MHz, Deuterium Oxide): δ 163.7, 145.3, 145.1, 127.5, 89.9, 68.5, 54.1, 51.8, 2.9.

1H, 13C NMR Spectra:

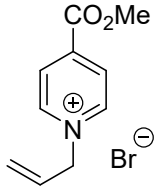


1m-HBr



1m-HBr

1n-HBr:
1-allyl-4-(methoxycarbonyl)pyridin-1-ium bromide



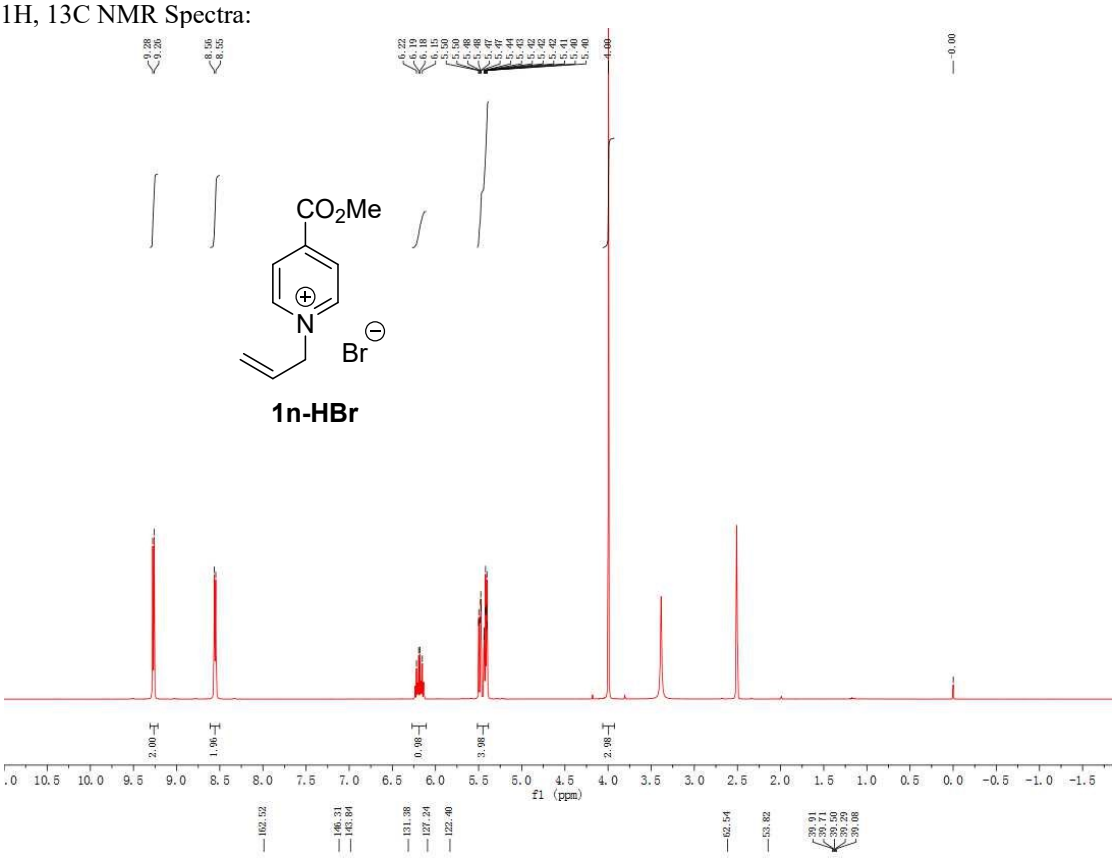
1n-HBr

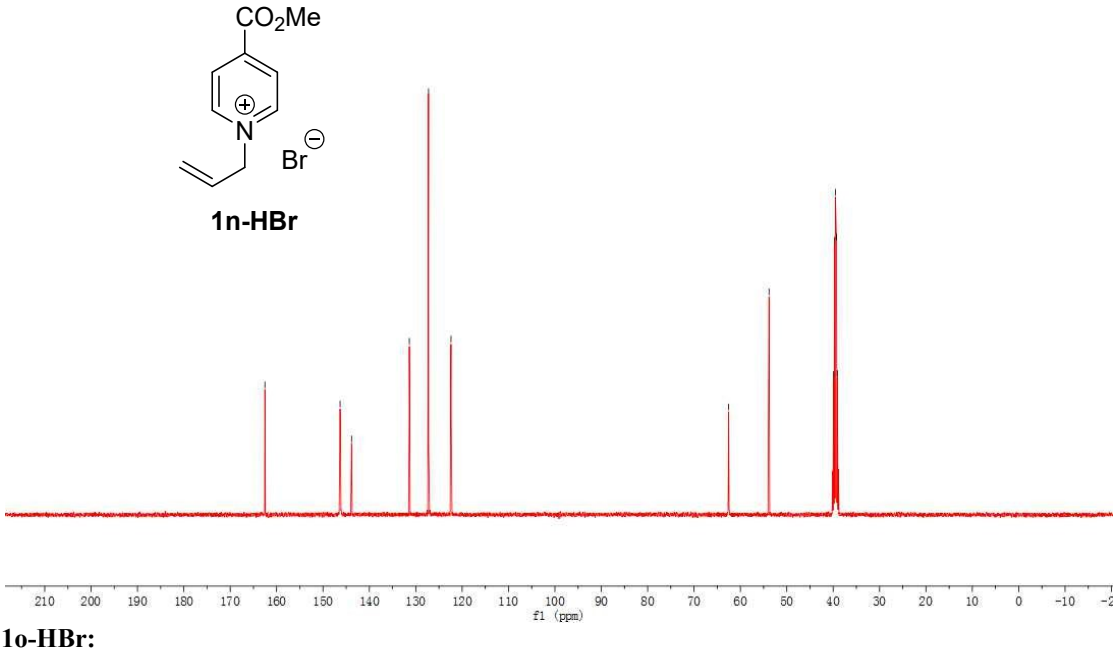
General procedure: The procedure for synthesis of compound **1n-HBr**: Methyl isonicotinate (5.5mmol) and Allyl bromide (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1n-HBr,** as gray solid (1.032g, yield=80%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.27 (d, J = 6.9 Hz, 2H), 8.55 (d, J = 6.8 Hz, 2H), 6.19 (dd, J = 16.9, 10.4 Hz, 1H), 5.51 – 5.39 (m, 4H), 4.00 (s, 3H).

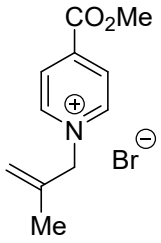
^{13}C NMR (101 MHz, DMSO-d_6): δ 162.5, 146.3, 143.8, 131.4, 127.2, 122.4, 62.5, 53.8.

1H, 13C NMR Spectra:





1o-HBr:
4-(methoxycarbonyl)-1-(2-methylallyl)pyridin-1-ium bromide



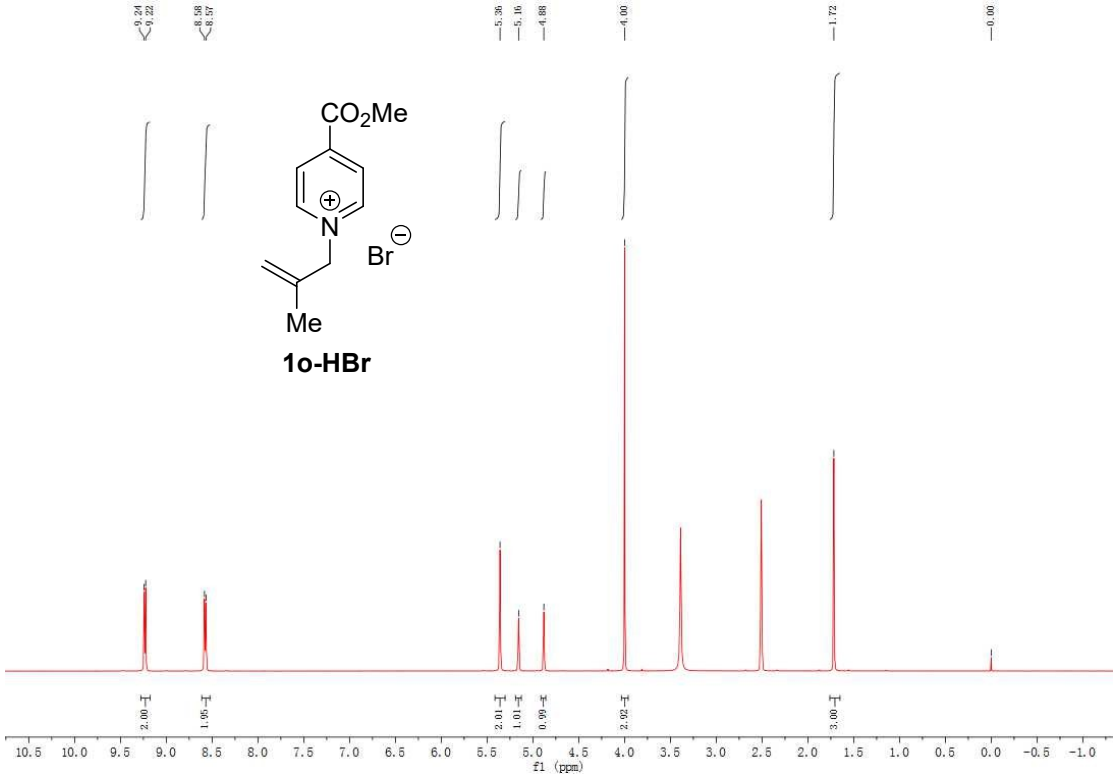
1o-HBr

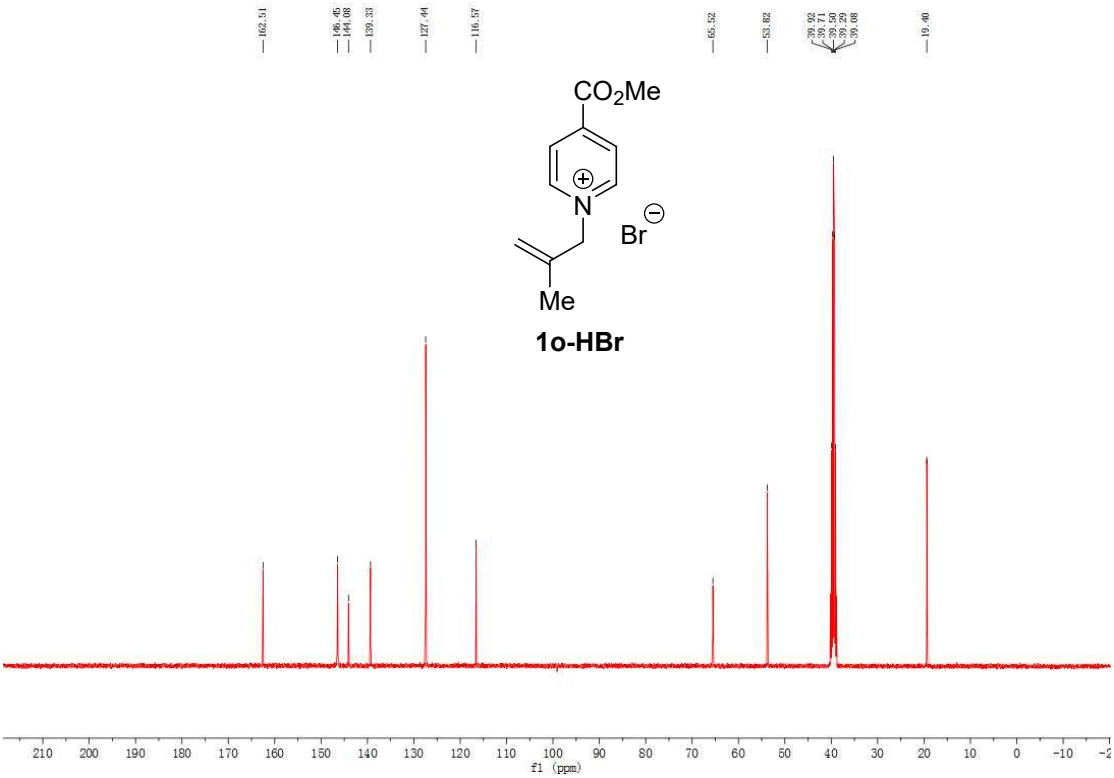
General procedure: The procedure for synthesis of compound **1o-HBr**: Methyl isonicotinate (5.5mmol) and 3-bromo-2-methylprop-1-ene (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 10 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1o-HBr,** as white solid (925.3mg, yield=68%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.23 (d, J = 6.8 Hz, 2H), 8.57 (d, J = 6.8 Hz, 2H), 5.36 (s, 2H), 5.16 (s, 1H), 4.88 (s, 1H), 4.00 (s, 3H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 162.5, 146.5 144.1, 139.3, 127.4, 116.6, 65.5, 53.8, 19.4.

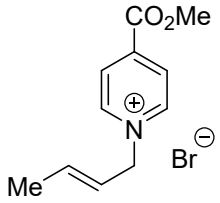
1H, 13C NMR Spectra:





1p-HBr:

1-(but-2-en-1-yl)-4-(methoxycarbonyl)pyridin-1-ium bromide



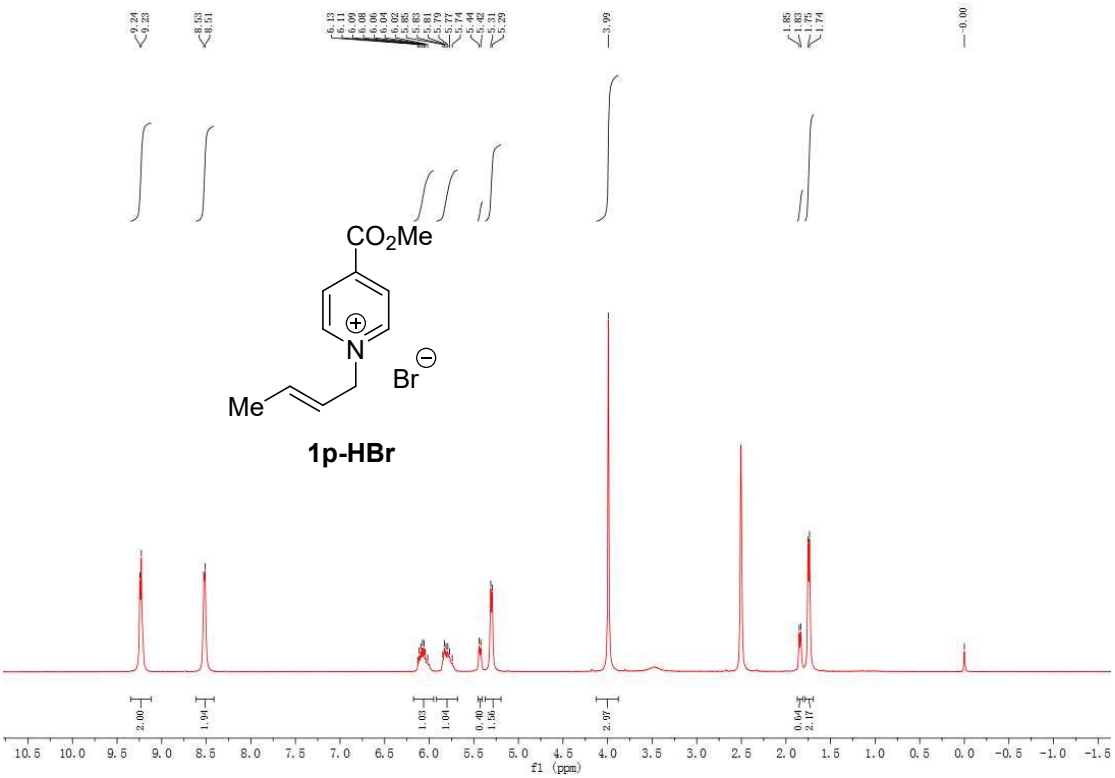
1p-HBr

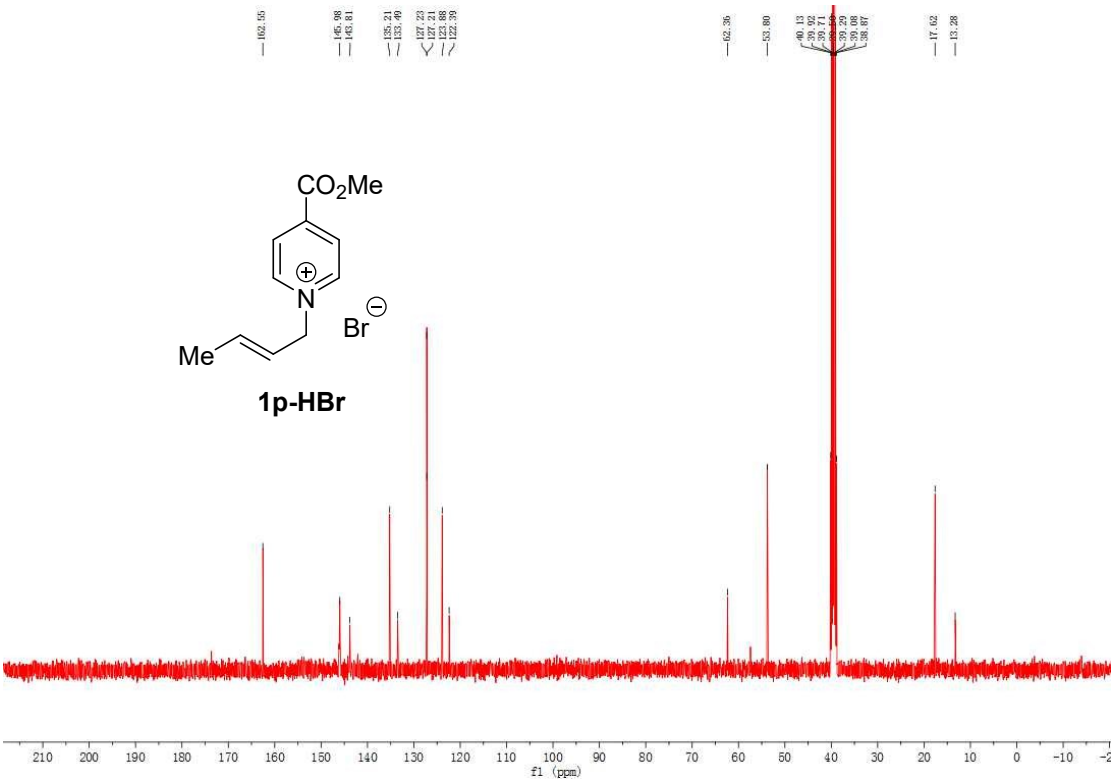
General procedure: The procedure for synthesis of compound **1p-HBr**: Methyl isonicotinate (5.5mmol) and 1-bromobut-2-ene (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1p-HBr,** as white solid (952mg, yield=70%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.24 (d, J = 6.4 Hz, 2H), 8.52 (d, J = 6.0 Hz, 2H), 6.08 (tt, J = 16.4, 8.2 Hz, 1H), 5.80 (dq, J = 19.8, 12.1, 9.5 Hz, 1H), 5.43 (d, J = 7.3 Hz, 0H), 5.30 (d, J = 6.8 Hz, 2H), 3.99 (s, 3H), 1.84 (d, J = 7.0 Hz, 1H), 1.74 (d, J = 6.6 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 162.6, 146.0, 143.8, 135.2, 133.5, 127.2, 127.2, 123.9, 122.4, 62.4, 53.8, 17.6, 13.3.

1H, 13C NMR Spectra:

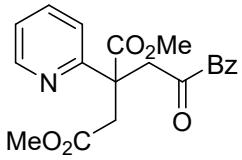




3. Synthesis of Products and Spectra Data

3aa:

dimethyl 2-(2,3-dioxo-3-phenylpropyl)-2-(pyridin-2-yl)succinate



3aa

General procedure: 1-(2-oxo-2-phenylethyl)pyridin-1-ium hexafluorophosphate **1a-HBr** (0.84mmol, 233.6mg, 2.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3aa** as brown oil (57.1mg, yield: 52%).

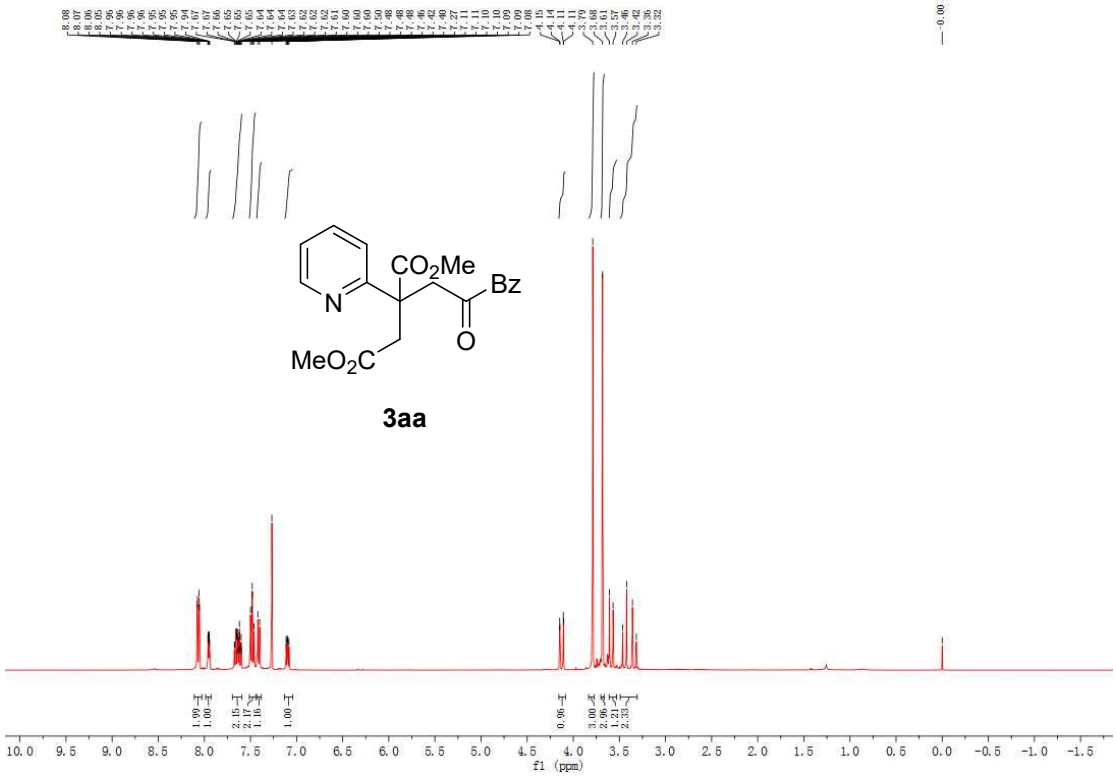
Instead of **1a-HBr**, **1a-HPF$_6$** provided **3aa** in < 5% NMR yield (1,3,5- trimethoxybenzene as internal standard) without the addition of tetrabutylammonium bromide.

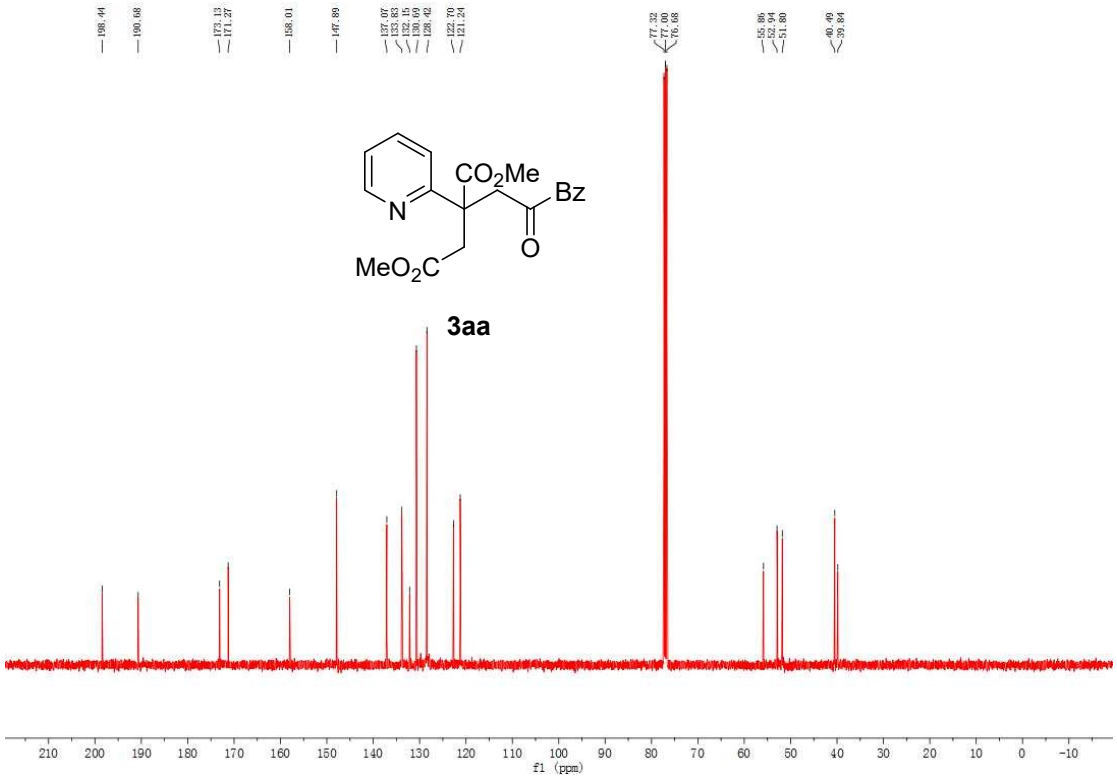
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.07 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.95 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.70 – 7.59 (m, 2H), 7.51 – 7.44 (m, 2H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.13 – 7.04 (m, 1H), 4.13 (dd, *J* = 15.6, 0.8 Hz, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.59 (d, *J* = 15.6 Hz, 1H), 3.49 – 3.31 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 198.4, 190.7, 173.1, 171.3, 158.0, 147.9, 137.1, 133.8, 132.2, 130.7, 128.4, 122.7, 121.2, 55.9, 52.9, 51.8, 40.5, 39.8.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{20}H_{20}NO_6$, 370.1285; found, 370.1294.

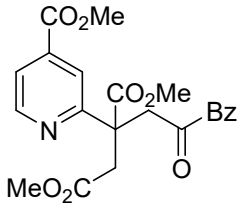
^{1}H, ^{13}C NMR Spectra of **3aa:**





3ba:

dimethyl 2-(2,3-dioxo-3-phenylpropyl)-2-(4-(methoxycarbonyl)pyridin-2-yl)succinate



3ba

General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.66mmol, 221.9mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and $^{i-}Pr_2NEt$ (0.6mmol, 100.0μL, 2.0eq.) were added sequentially to 3.0 mL of DCE. The reaction mixture was stirred at room temperature for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3ba** as brown oil (73.5mg, yield: 57%).

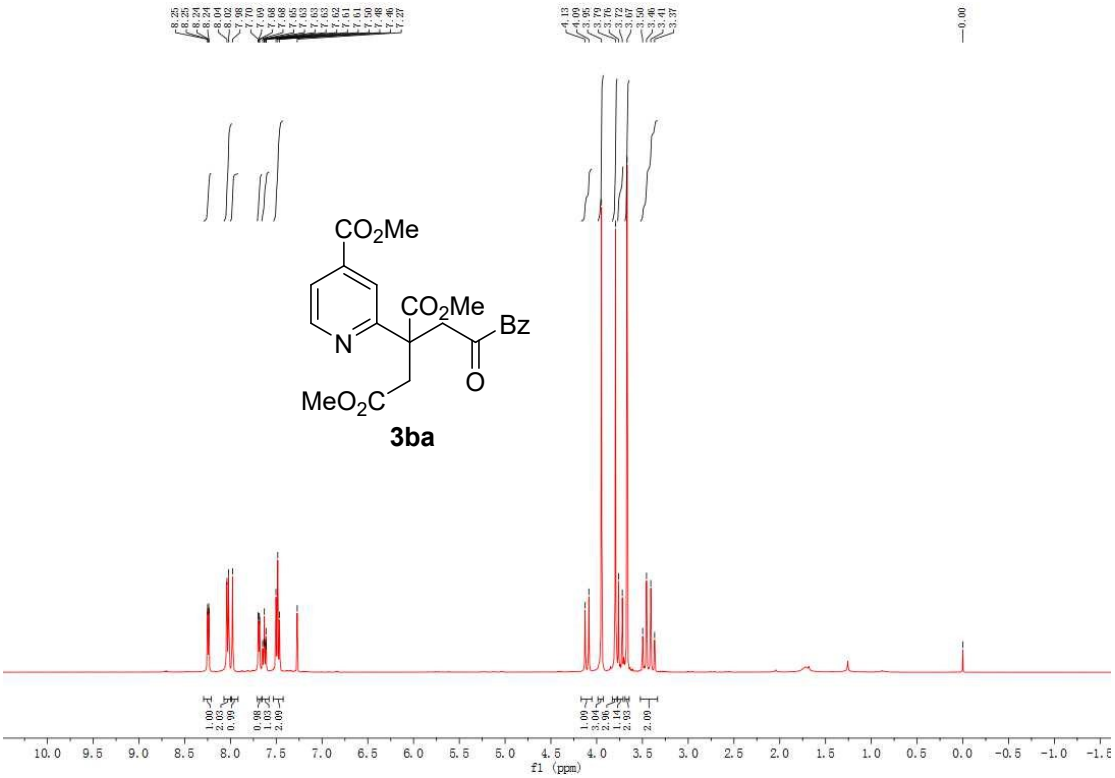
Instead of **1b-HBr**, **1b-HPF$_6$** provided **3ba** in 28% yield (35.7mg).

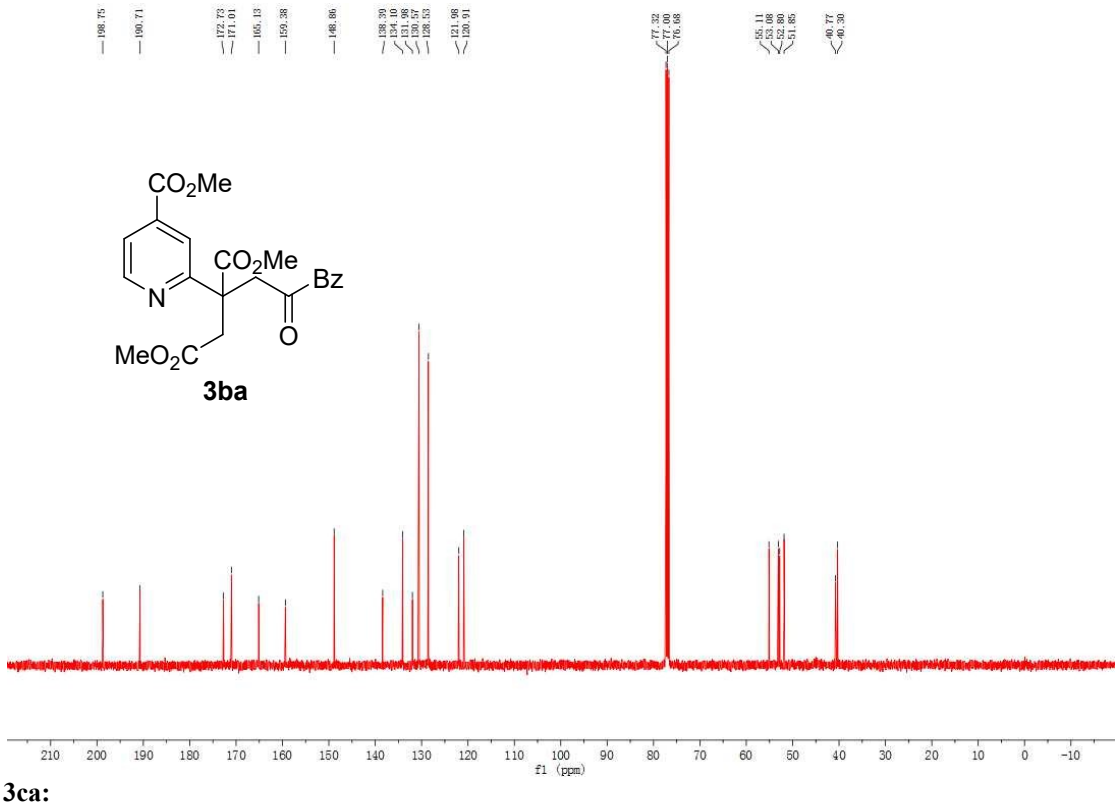
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.29 – 8.21 (m, 1H), 8.03 (d, *J* = 6.8 Hz, 2H), 7.98 (s, 1H), 7.69 (dd, *J* = 5.1, 1.4 Hz, 1H), 7.66 – 7.58 (m, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 4.11 (d, *J* = 16.4 Hz, 1H), 3.95 (s, 3H), 3.79 (s, 3H), 3.74 (d, *J* = 16.3 Hz, 1H), 3.67 (s, 3H), 3.52 – 3.33 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 198.8, 190.7, 172.7, 171.0, 165.1, 159.4, 148.9, 138.4, 134.1, 132.0, 130.6, 128.5, 122.0, 120.9, 55.1, 53.1, 52.8, 51.9, 40.8, 40.3.

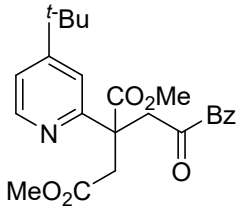
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{22}H_{22}NO_8$, 428.1340; found, 428.1348.

^{1}H, ^{13}C NMR Spectra of **3ba:**





3ca:
dimethyl 2-(4-(tert-butyl)pyridin-2-yl)-2-(2,3-dioxo-3-phenylpropyl)succinate



3ca

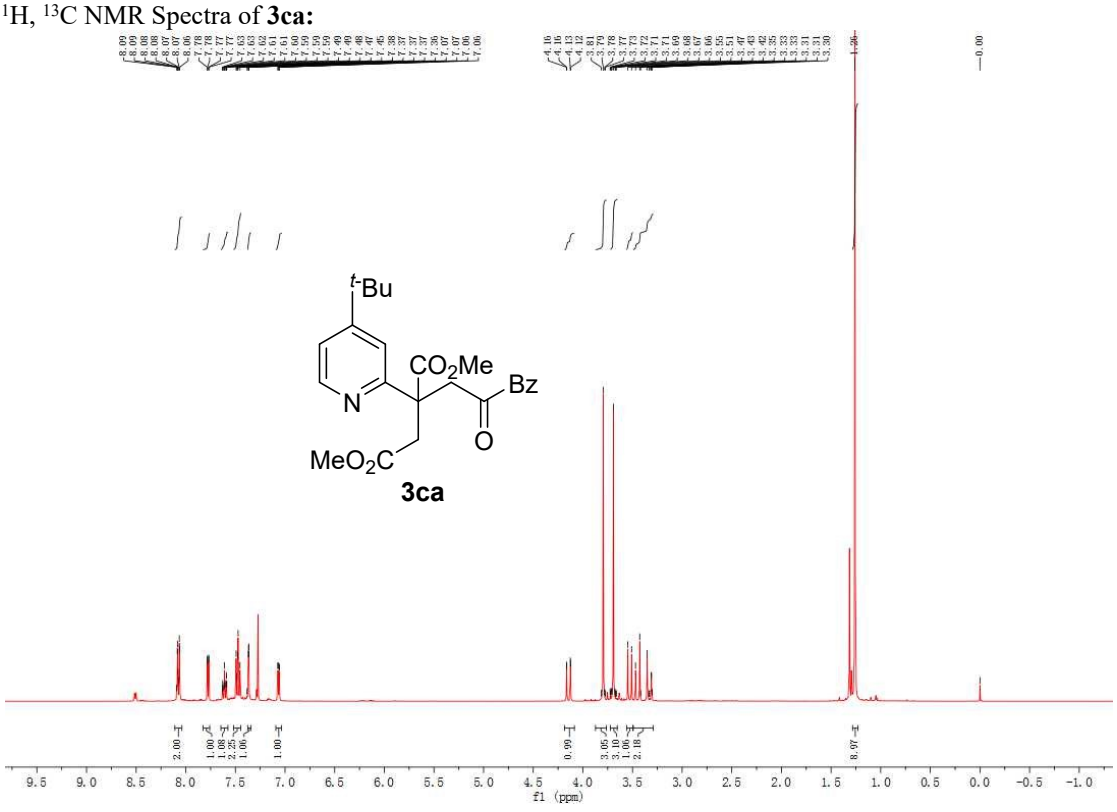
General procedure: 4-(tert-butyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1c-HBr** (0.84mmol, 280.8mg, 2.8eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and $^{i}Pr_2NEt$ (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.6) to afforded **3ca** as brown oil (77.0mg, yield: 60%).

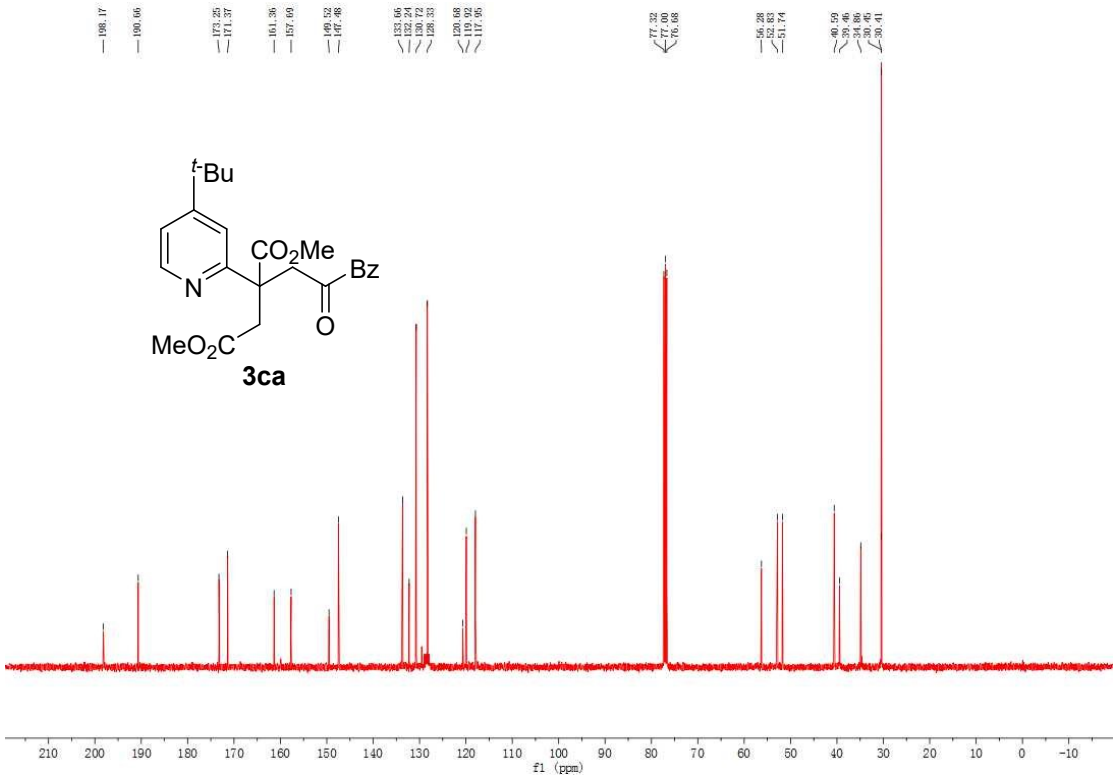
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.11 – 8.04 (m, 2H), 7.78 (dd, *J* = 5.3, 0.7 Hz, 1H), 7.65 – 7.58 (m, 1H), 7.47 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.37 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.06 (dd, *J* = 5.4, 1.8 Hz, 1H), 4.14 (dd, *J* = 15.2, 0.8 Hz, 1H), 3.79 (s, 3H), 3.69 (s, 3H), 3.53 (d, *J* = 15.2 Hz, 1H), 3.49 – 3.29 (m, 2H), 1.26 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 198.2, 190.7, 173.3, 171.4, 161.4, 157.7, 149.5, 147.5, 133.7, 132.2, 130.7, 128.3, 120.7, 119.9, 117.9, 56.3, 52.8, 51.7, 40.6, 39.5, 34.9, 30.5, 30.4.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{24}H_{28}NO_6$, 426.1911; found, 426.1912.

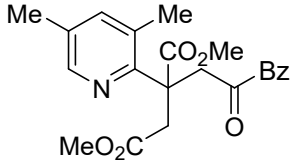
^{1}H, ^{13}C NMR Spectra of **3ca:**





3da:

methyl 2-(3,5-dimethylpyridin-2-yl)-2-(2,3-dioxo-3-phenylpropyl)-4-oxohexanoate



3da

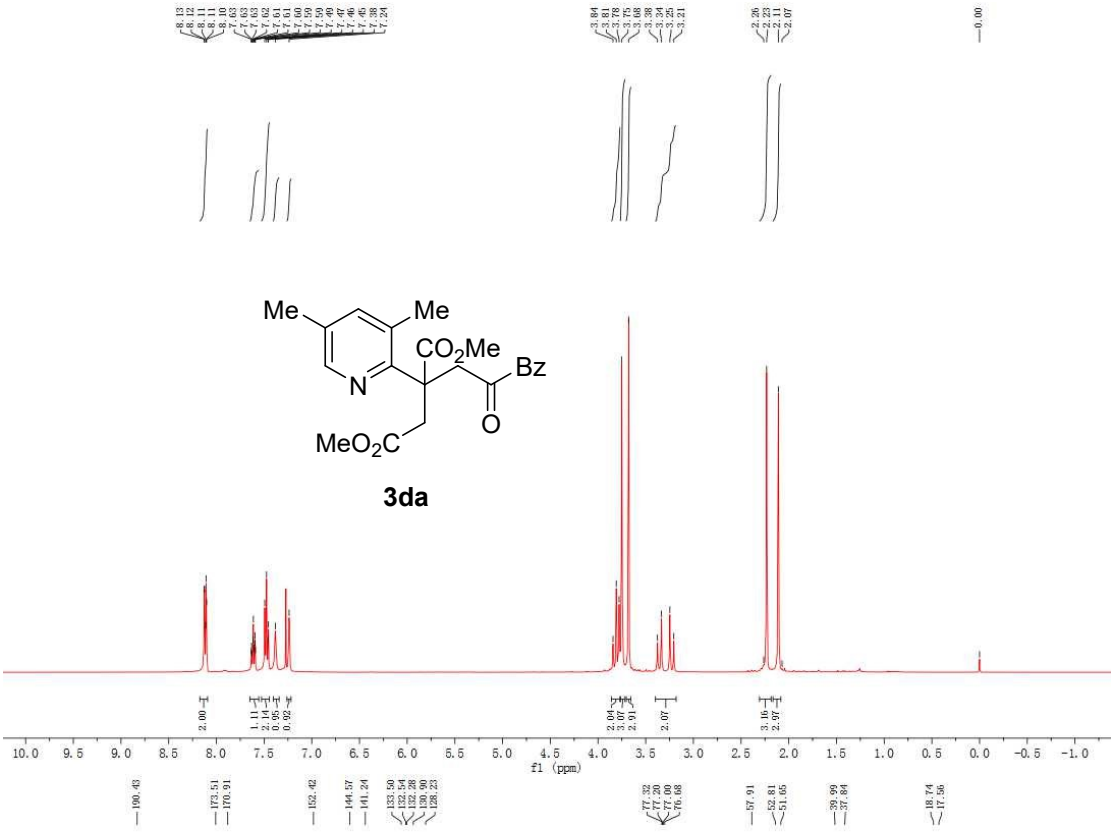
General procedure: 3,5-dimethyl-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1d-HBr** (0.84mmol, 256.2mg, 2.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=0:1, v/v; R_f=0.4) to afforded **3da** as brown oil (48.9 mg, yield: 41%).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.12 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.61 (td, *J* = 7.2, 1.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.38 (s, 1H), 7.24 (s, 1H), 3.84-3.78 (m, 2H), 3.75 (s, 3H), 3.68 (s, 3H), 3.40 – 3.18 (m, 2H), 2.23 (s, 3H), 2.11 (s, 3H).

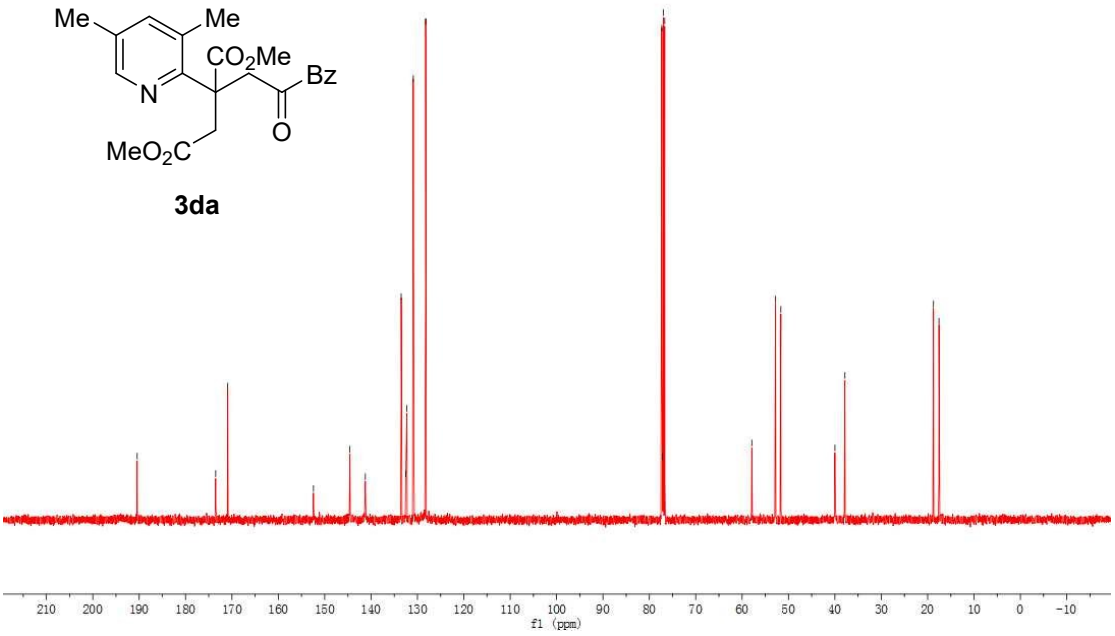
^{13}C NMR (101 MHz, Chloroform-*d*): δ 190.4, 173.5, 170.9, 144.6, 141.2, 133.5, 132.5, 132.3, 130.9, 128.2, 57.9, 52.8, 51.7, 40.0, 37.8, 18.7, 17.6.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{22}H_{24}NO_6$, 98.1598; found, 398.1600.

^{1}H, ^{13}C NMR Spectra of **3da:**

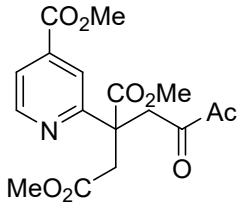


3da



3da

3ea:
dimethyl 2-(2,3-dioxobutyl)-2-(4-(methoxycarbonyl)pyridin-2-yl)succinate



3ea

General procedure: 4-(methoxycarbonyl)-1-(2-oxopropyl)pyridin-1-ium hexafluorophosphate **1e-HPF$_6$** (0.66mmol, 223.8mg, 2.2eq.), tetrabutylammonium bromide (0.9mmol, 290.1mg, 3.0eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}-Pr$_2$NEt (0.6mmol, 100.0μL, 2.0eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at room temperature for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.3) to afforded **3ea** as yellow oil (58.9mg, yield: 54%).

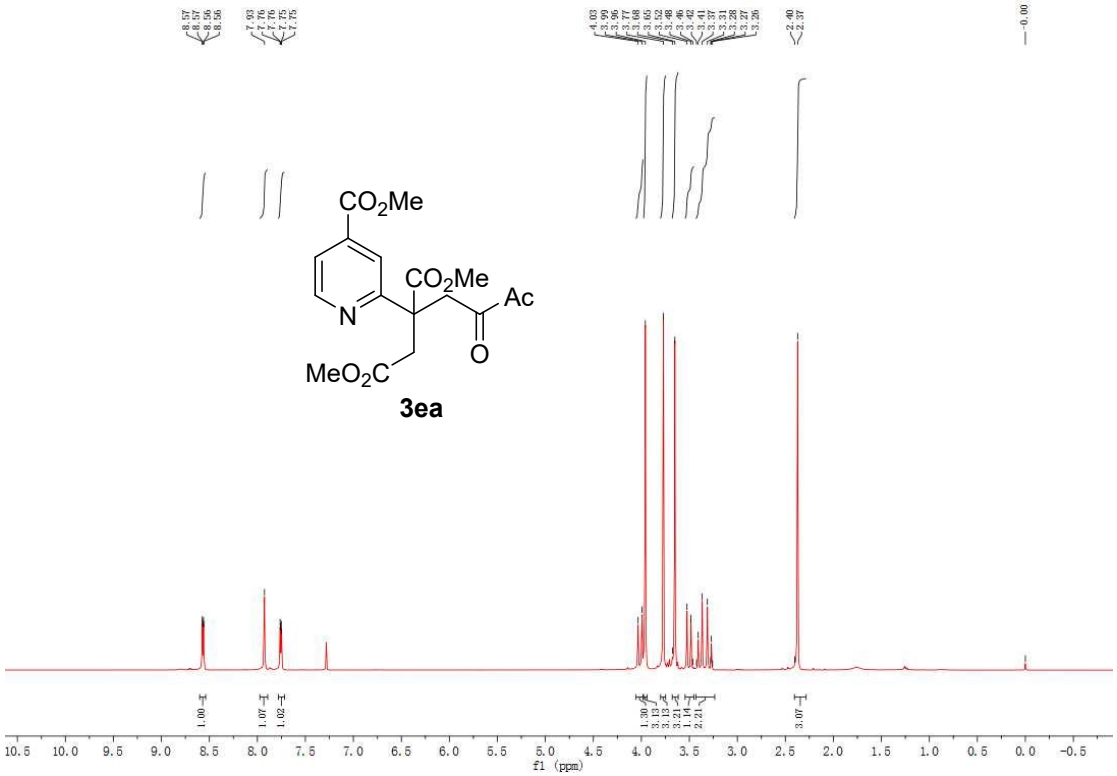
Without the addition of tetrabutylammonium bromide, **1e-HPF$_6$** provided **3ea** in 30% yield (33.0mg).

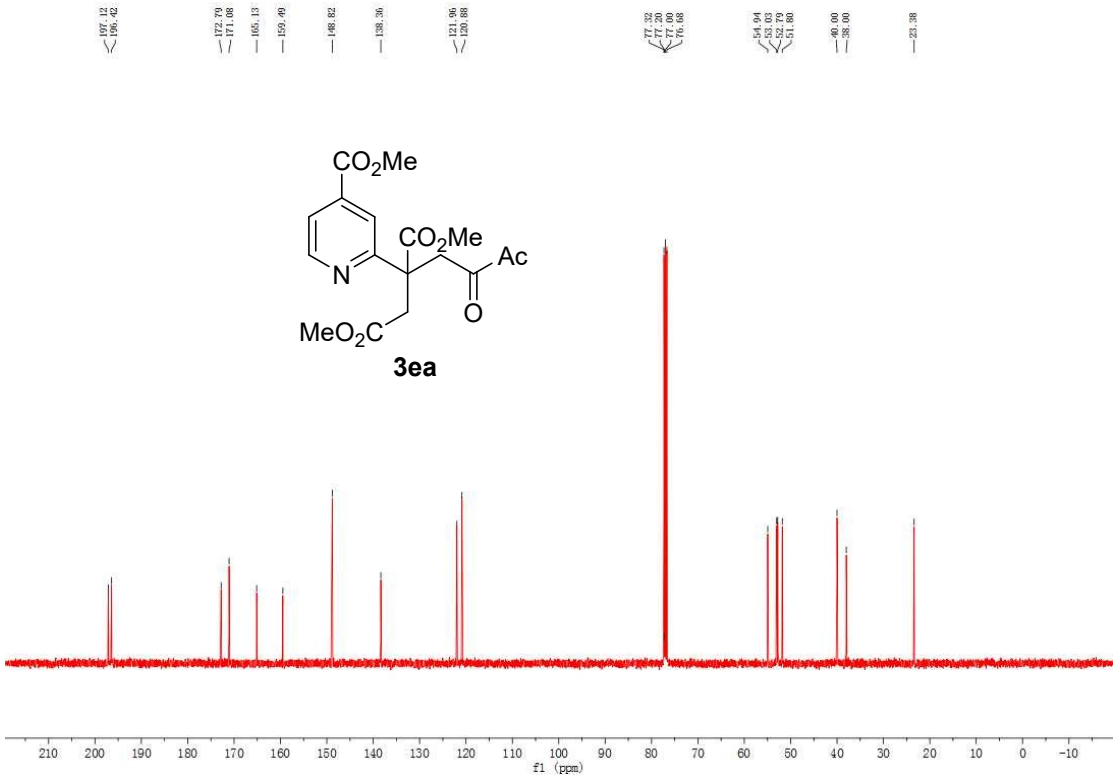
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.57 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.93 (s, 1H), 7.76 (dd, *J* = 5.0, 1.5 Hz, 1H), 4.01 (d, *J* = 16.6 Hz, 1H), 3.96 (s, 3H), 3.77 (s, 3H), 3.65 (s, 3H), 3.50 (d, *J* = 16.3 Hz, 1H), 3.43 – 3.24 (m, 2H), 2.37 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 197.1, 196.4, 172.8, 171.1, 165.1, 159.5, 148.8, 138.4, 122.0, 120.9, 54.9, 53.0, 52.8, 51.8, 40.0, 38.0, 23.4.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{17}H_{20}NO_8$, 366.1183; found, 366.1183.

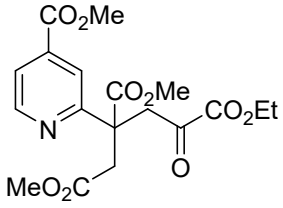
^{1}H, ^{13}C NMR Spectra of **3ea:**





3fa:

4-ethyl 1,2-dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-4-oxobutane-1,2,4-tricarboxylate



3fa

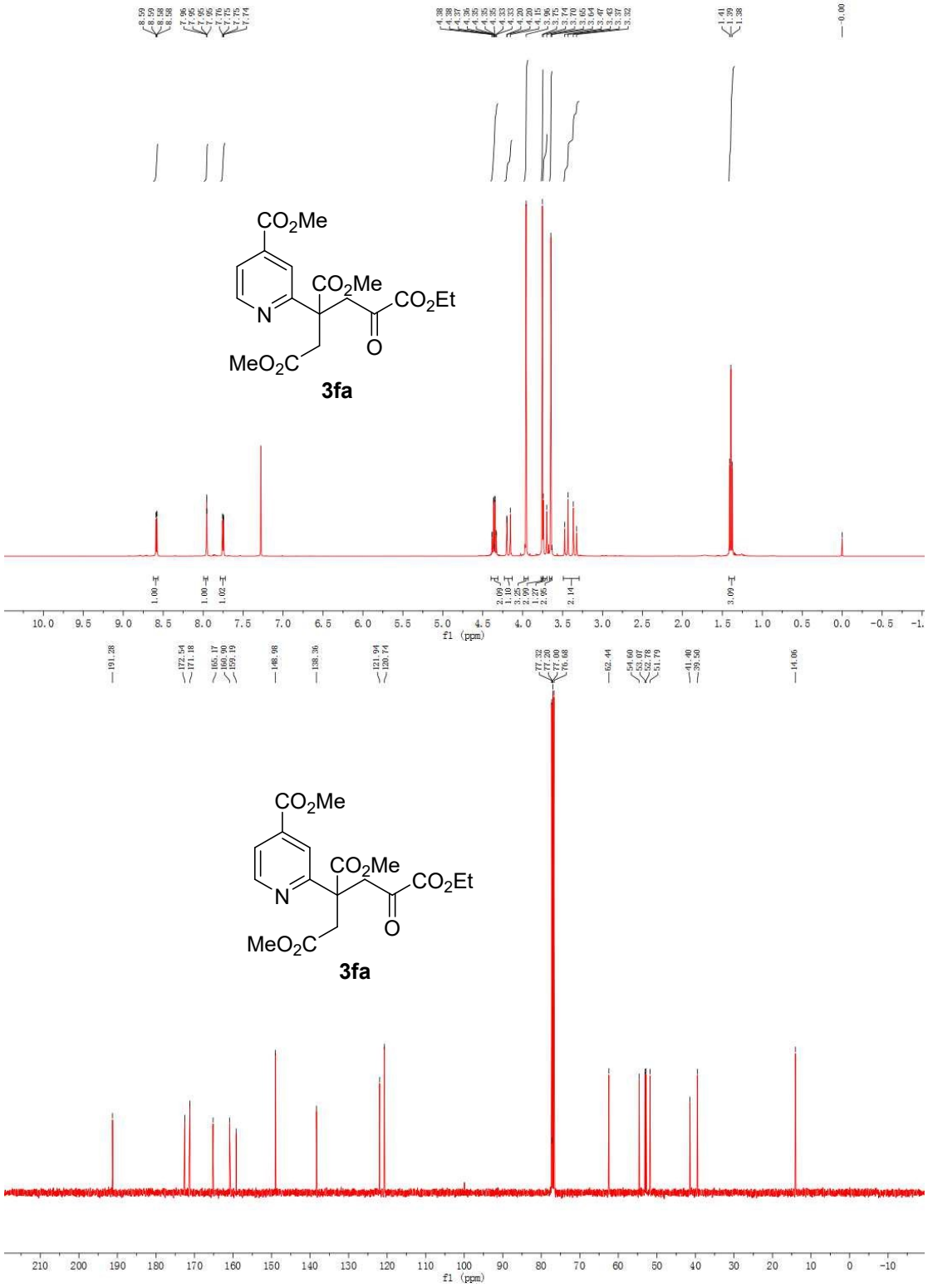
General procedure: 1-(2-ethoxy-2-oxoethyl)-4-(methoxycarbonyl)pyridin-1-ium bromide **1f-HPF$_6$** (0.84mmol, 310.1mg, 2.8eq.), tetrabutylammonium bromide (1.5mmol, 483.6mg, 5.0eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.2) to afforded **3fa** as yellow oil (50.9mg, yield: 43%).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.58 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.95 (dd, *J* = 1.4, 0.9 Hz, 1H), 7.75 (dd, *J* = 5.0, 1.5 Hz, 1H), 4.36 (qd, *J* = 7.2, 0.9 Hz, 2H), 4.23 – 4.13 (m, 1H), 3.96 (s, 3H), 3.75 (s, 3H), 3.72 (d, *J* = 17.4 Hz, 1H), 3.65 (s, 3H), 3.49 – 3.29 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).

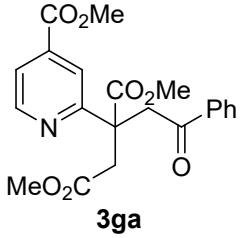
^{13}C NMR (101 MHz, $CDCl_3$): δ 191.3, 172.5, 171.2, 165.2, 160.9, 159.2, 149.0, 138.4, 121.9, 120.7, 62.4, 54.6, 53.1, 52.8, 51.8, 41.4, 39.5, 14.1.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{18}H_{22}NO_9$, 396.1289; found, 396.1295.

^{1}H, ^{13}C NMR Spectra of **3fa:**



3ga:
dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(2-oxo-2-phenylethyl)succinate



3ga

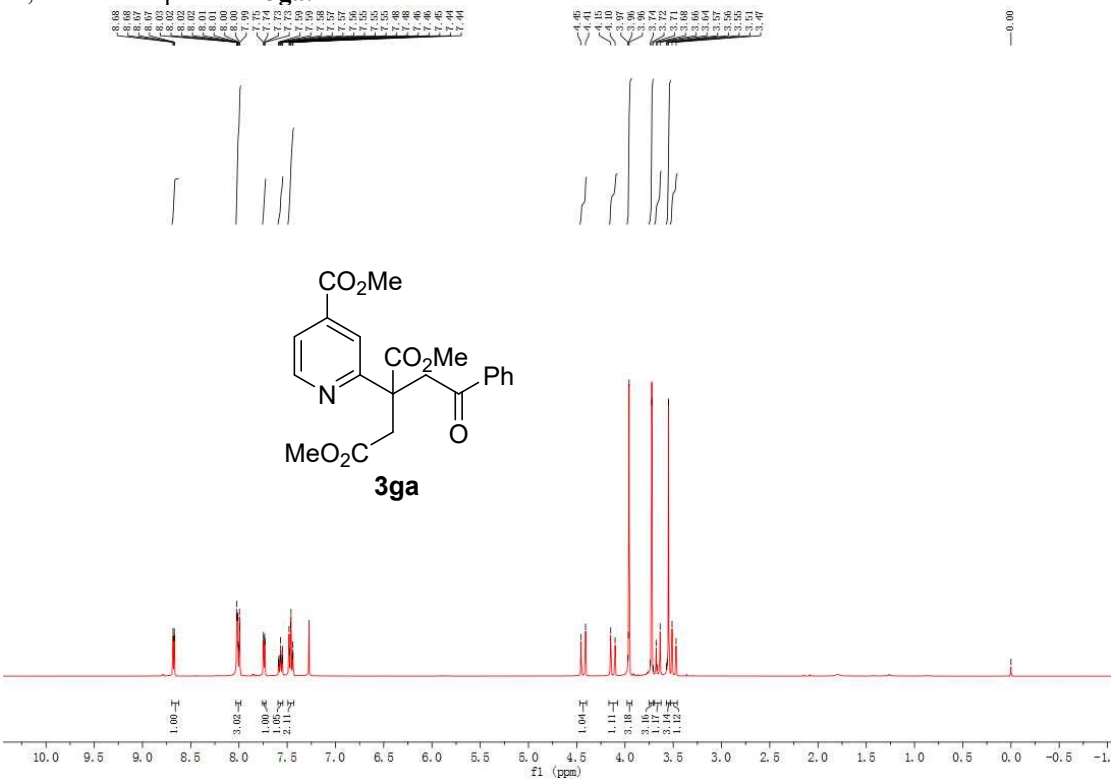
General procedure: 1-benzyl-4-(methoxycarbonyl)pyridin-1-ium bromide **1g-HBr** (0.84mmol, 258.9mg, 2.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3ga** as brown oil (79.5mg, yield: 66%).

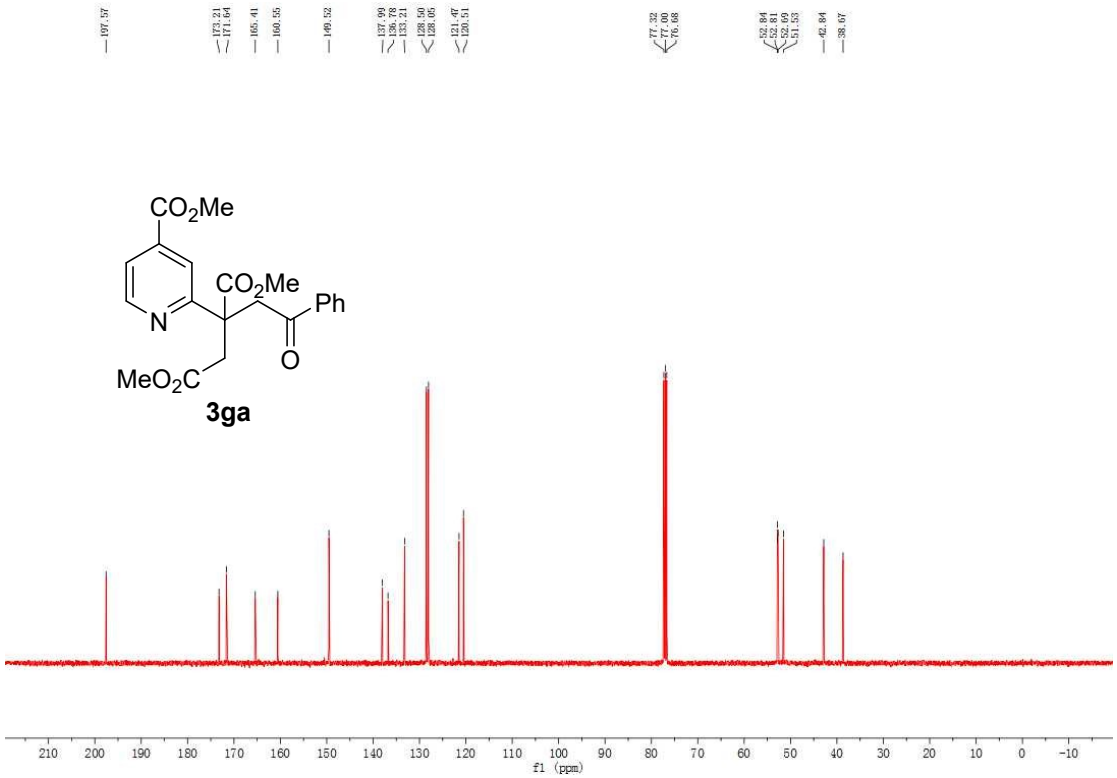
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.68 (dd, *J* = 5.0, 0.9 Hz, 1H), 8.03 – 7.98 (m, 3H), 7.74 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.49 – 7.43 (m, 2H), 4.43 (d, *J* = 18.3 Hz, 1H), 4.13 (d, *J* = 18.2 Hz, 1H), 3.96 (s, 3H), 3.72 (s, 3H), 3.66 (d, *J* = 16.5 Hz, 1H), 3.55 (s, 3H), 3.49 (d, *J* = 16.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 173.2, 171.6, 165.4, 160.6, 149.5, 138.0, 136.8, 133.2, 128.5, 128.1, 121.5, 120.5, 52.8, 52.8, 52.7, 51.5, 42.8, 38.7.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{21}H_{22}NO_7$, 400.1391; found, 400.1389.

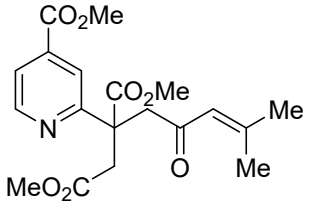
^{1}H, ^{13}C NMR Spectra of **3ga:**





3ha:

dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(4-methyl-2-oxopent-3-en-1-yl)succinate



3ha

General procedure: 4-(methoxycarbonyl)-1-(3-methylbut-2-en-1-yl)pyridin-1-ium bromide **1h-HBr** (0.66mmol, 188.9mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and *i*-Pr_2NEt (0.6mmol, 100.0μL, 2.0eq.) were added sequentially to 3.0 mL of DCE. The reaction mixture was stirred at room temperature for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3ha** as brown oil (49.0 mg, yield: 43%).

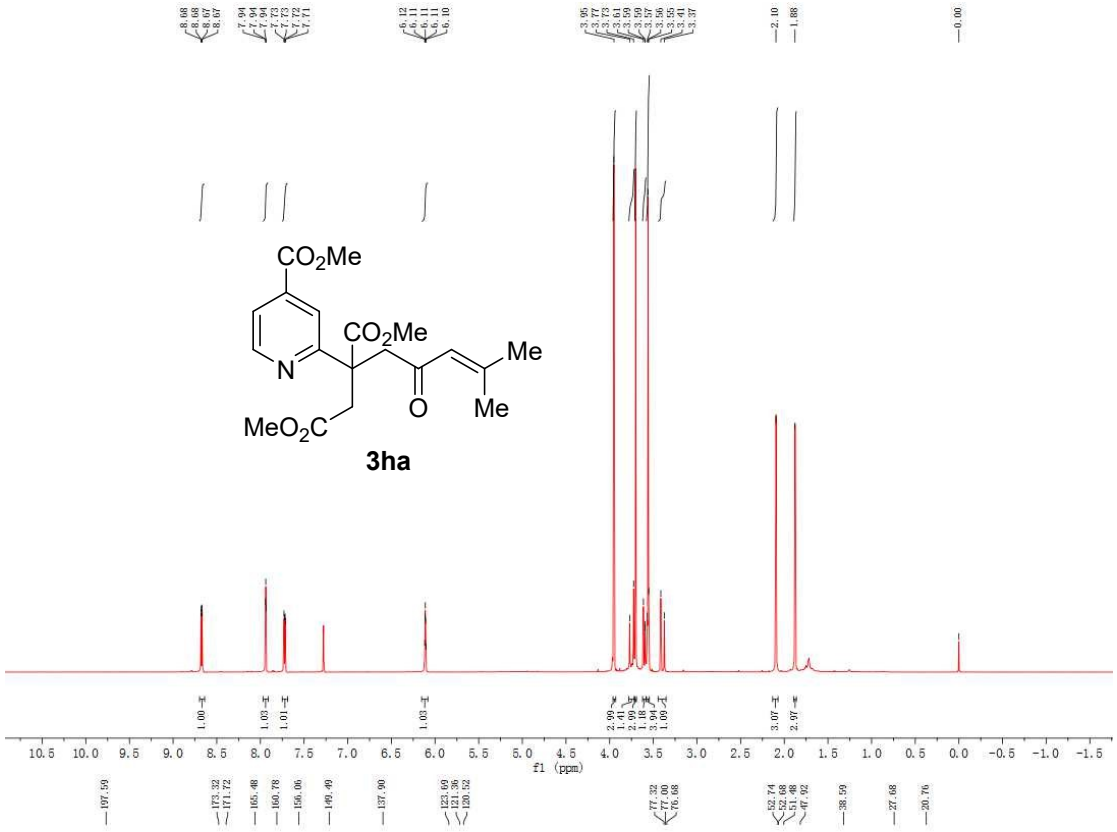
Instead of **1h-HBr**, **1h-HPF$_6$** provided **3ha** in 11% yield (13.1 mg).

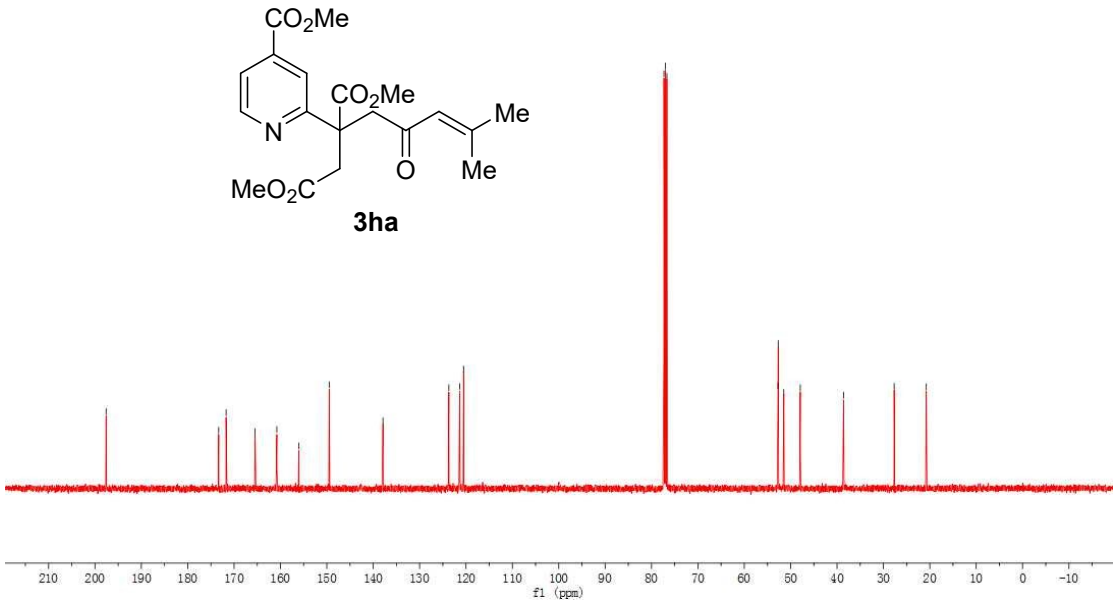
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.67 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.94 (t, *J* = 1.1 Hz, 1H), 7.72 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.11 (p, *J* = 1.3 Hz, 1H), 3.95 (s, 3H), 3.75 (d, *J* = 18.0 Hz, 1H), 3.70 (s, 3H), 3.60 (d, *J* = 7.6 Hz, 1H), 3.57-3.55 (M, 4H), 3.39 (d, *J* = 16.5 Hz, 1H), 2.09 (d, *J* = 1.2 Hz, 3H), 1.88 (d, *J* = 1.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 197.6, 173.3, 171.7, 165.5, 160.8, 156.1, 149.5, 137.9, 123.7, 121.4, 120.5, 52.7, 52.7, 51.5, 47.9, 38.6, 27.7, 20.8.

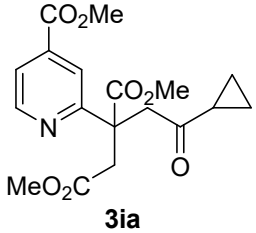
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{19}H_{24}NO_7$, 378.1547; found, 378.1546.

^{1}H, ^{13}C NMR Spectra of **3ha:**





3ia:
dimethyl 2-(2-cyclopropyl-2-oxoethyl)-2-(4-(methoxycarbonyl)pyridin-2-yl)succinate



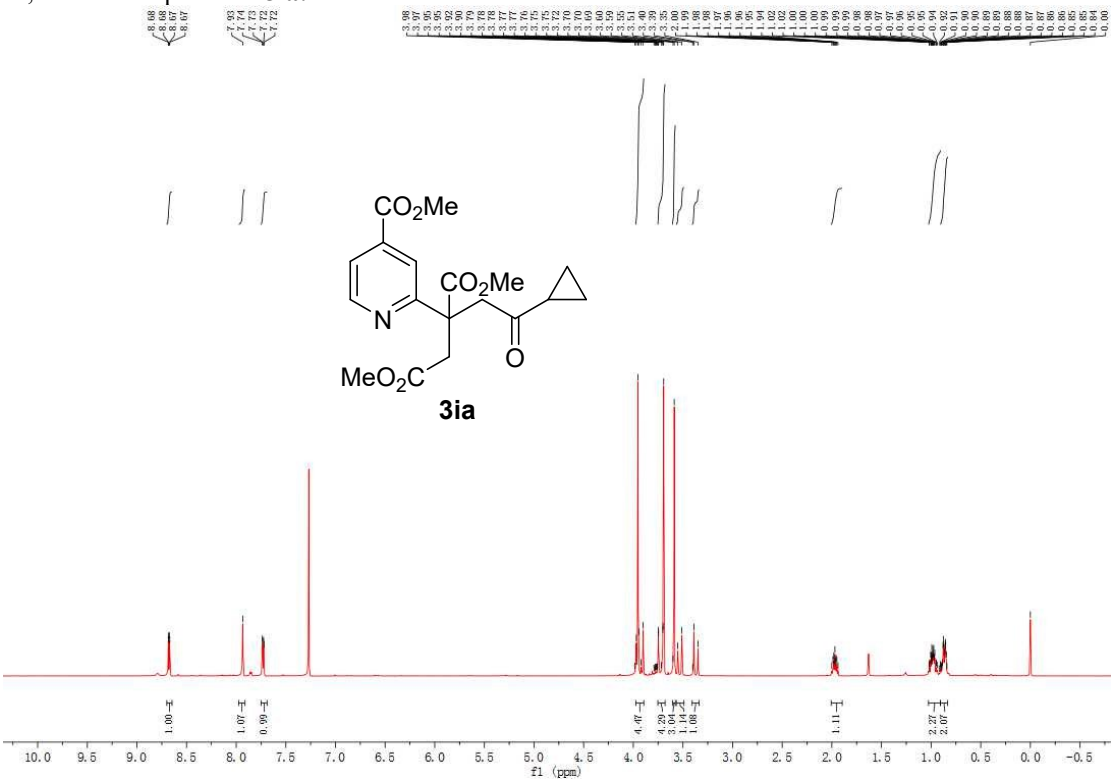
General procedure: 1-(cyclopropylmethyl)-4-(methoxycarbonyl)pyridin-1-ium bromide **1i-HPF$_6$** (0.84mmol, 283.2mg, 2.8eq.), tetrabutylammonium bromide (1.5mmol, 483.6mg, 5.0eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.6) to afforded **3ia** as brown oil (41.5mg, yield: 38%).

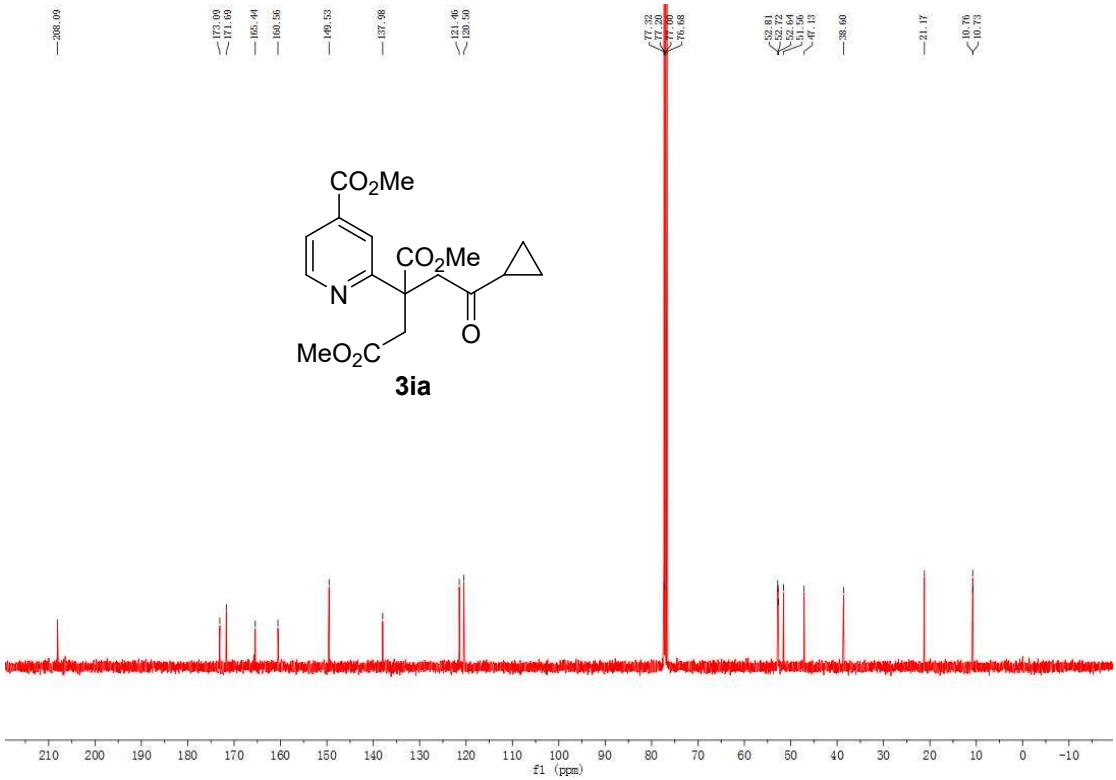
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.68 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.93 (s, 1H), 7.73 (dd, *J* = 5.0, 1.4 Hz, 1H), 3.98-3.90 (m, 4H), 3.75 – 3.68 (m, 4H), 3.59 (s, 3H), 3.53 (d, *J* = 16.5 Hz, 1H), 3.37 (d, *J* = 16.4 Hz, 1H), 1.97 (tt, *J* = 7.8, 4.6 Hz, 1H), 1.03 – 0.90 (m, 2H), 0.90 – 0.83 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 208.1, 173.1, 171.7, 165.4, 160.6, 149.5, 138.0, 121.5, 120.5, 52.8, 52.7, 52.6, 51.6, 47.1, 38.6, 21.2, 10.8, 10.7.

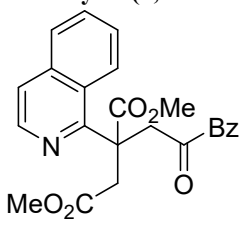
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{18}H_{22}NO_7$, 364.1391; found, 364.1391.

^{1}H, ^{13}C NMR Spectra of **3ia:**



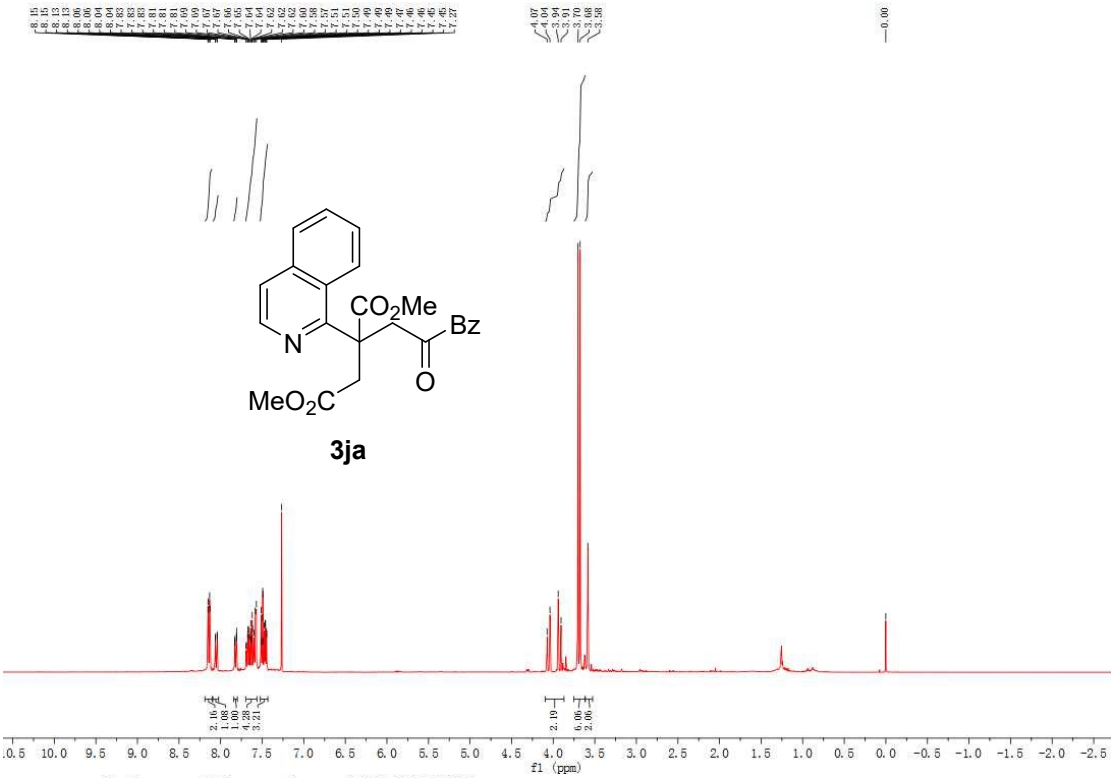


3ja:
dimethyl 2-(2,3-dioxo-3-phenylpropyl)-2-(isoquinolin-1-yl)malonate

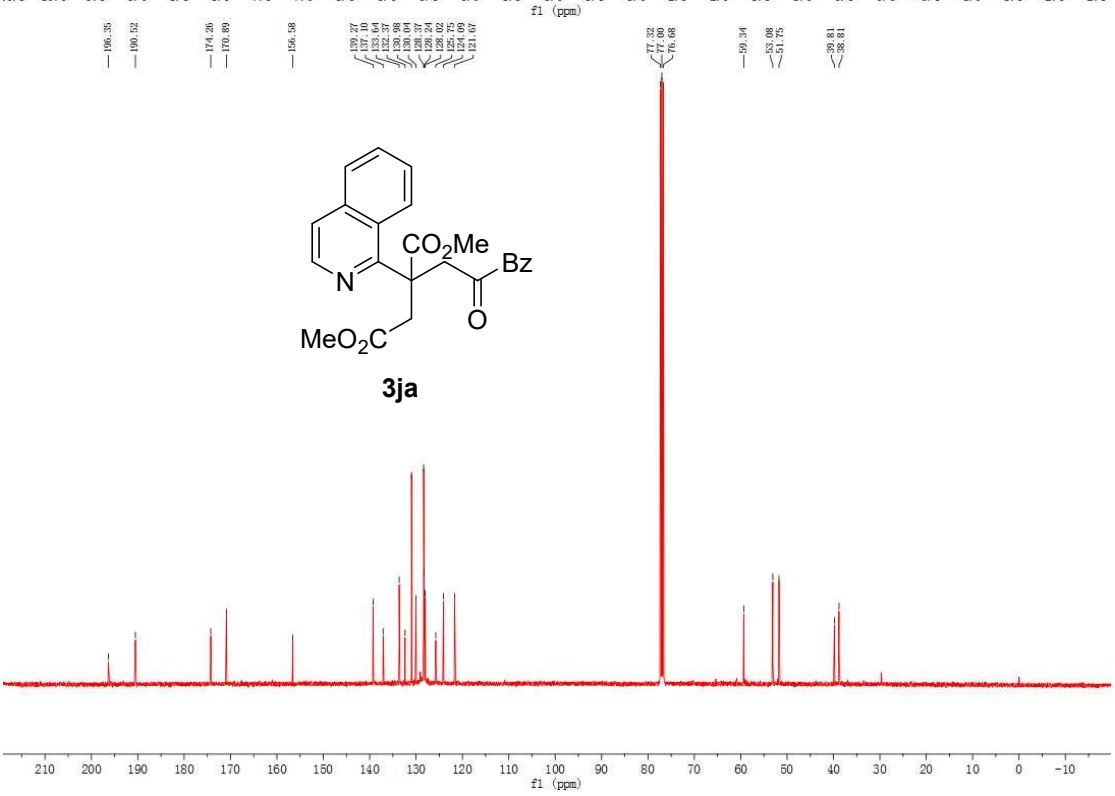


3ja

General procedure: 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium bromide **1j-HBr** (0.84mmol, 275.7mg, 2.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}-Pr_2NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=0:1, v/v; R_f=0.5) to afforded **3ja** as yellow oil (65.9mg, yield: 52%).
Instead of **1j-HBr**, **1j-HPF$_6$** provided **3ja** in <10% yield.
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.14 (dd, *J* = 8.4, 1.4 Hz, 2H), 8.05 (dd, *J* = 8.6, 1.0 Hz, 1H), 7.82 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.70 – 7.56 (m, 4H), 7.52 – 7.43 (m, 3H), 4.10 – 3.87 (m, 2H), 3.69 (d, *J* = 10.6 Hz, 6H), 3.58 (s, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*): δ 196.4, 190.5, 174.4, 170.9, 156.6, 139.3, 137.1, 133.6, 132.4, 131.0, 130.0, 128.4, 128.2, 128.0, 125.8, 124.1, 121.7, 59.3, 53.1, 51.8, 39.8, 38.8.
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{24}H_{22}NO_6$, 420.1442; found, 420.1441.
1H, 13C NMR Spectra:

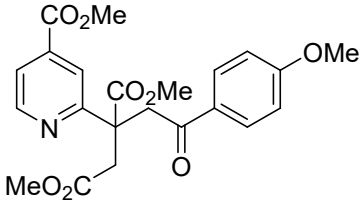


3ja



3ja

3ka:
dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(2-(4-methoxyphenyl)-2-oxoethyl)succinate



3ka

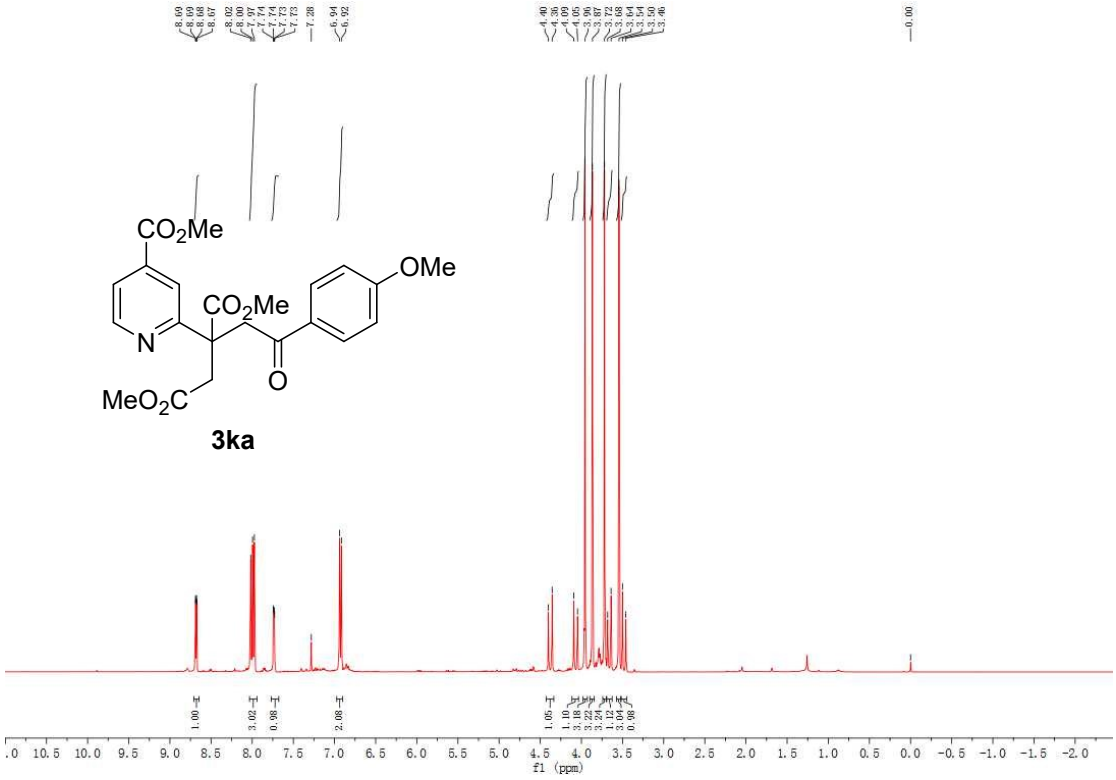
General procedure: 1-(4-methoxybenzyl)-4-(methoxycarbonyl)pyridin-1-ium chloride **1k-HCl** (0.84mmol, 246.7mg, 2.8eq.), tetrabutylammonium bromide (1.5mmol, 483.6mg, 5.0eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3ka** as yellow oil (61.5mg, yield: 48%).

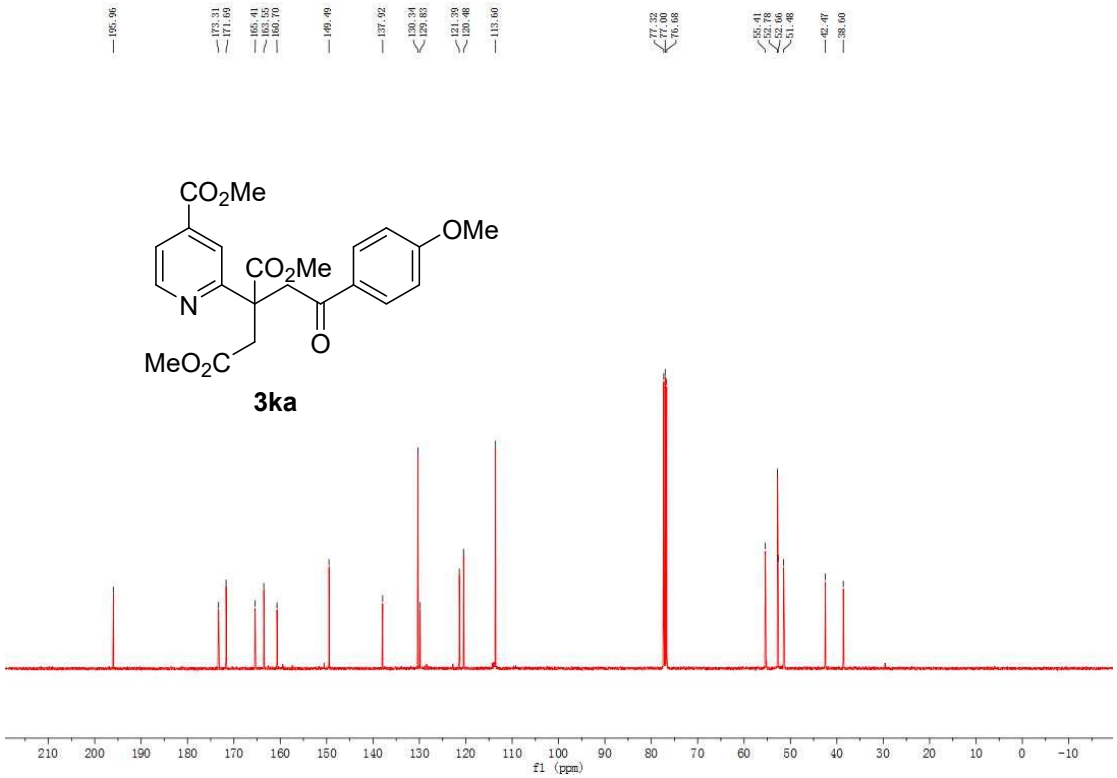
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.68 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.03 – 7.94 (m, 3H), 7.74 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 4.38 (d, *J* = 18.1 Hz, 1H), 4.07 (d, *J* = 18.1 Hz, 1H), 3.96 (s, 3H), 3.87 (s, 3H), 3.72 (s, 3H), 3.66 (d, *J* = 16.5 Hz, 1H), 3.54 (s, 3H), 3.48 (d, *J* = 16.5 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 196.0, 173.3, 171.7, 165.4, 163.6, 160.7, 149.5, 137.9, 130.3, 129.8, 121.4, 120.5, 113.6, 55.4, 52.8, 52.7, 51.5, 42.5, 38.6.

HRMS(ESI+)m/z: $[M+Na]^+$ calcd for $C_{22}H_{23}NNaO_8$, 452.1316; found, 452.1315.

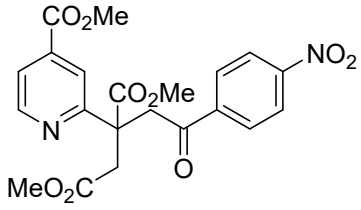
1H, 13C NMR Spectra:





3la:

dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(2-(4-nitrophenyl)-2-oxoethyl)succinate



3la

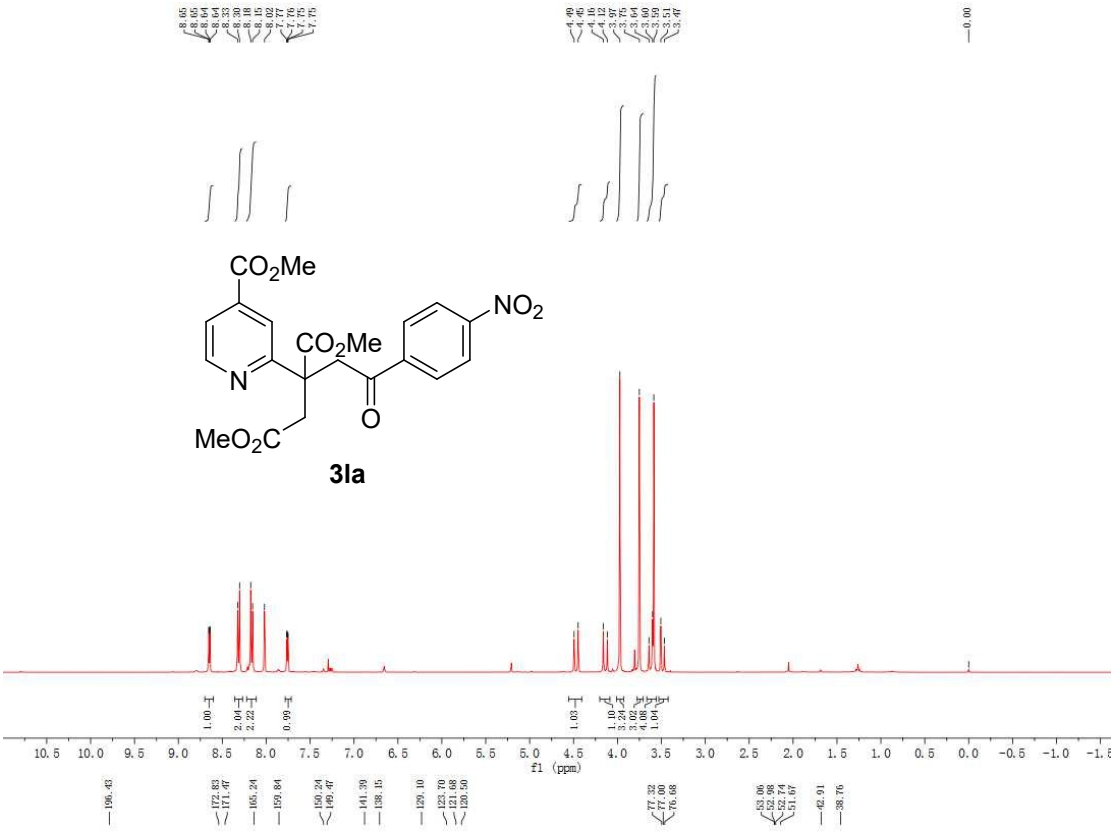
General procedure: 4-(methoxycarbonyl)-1-(4-nitrobenzyl)pyridin-1-ium bromide **1l-HBr** (0.84mmol, 296.5mg, 2.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 45℃ for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3la** as yellow oil (54.3mg, yield: 41%).

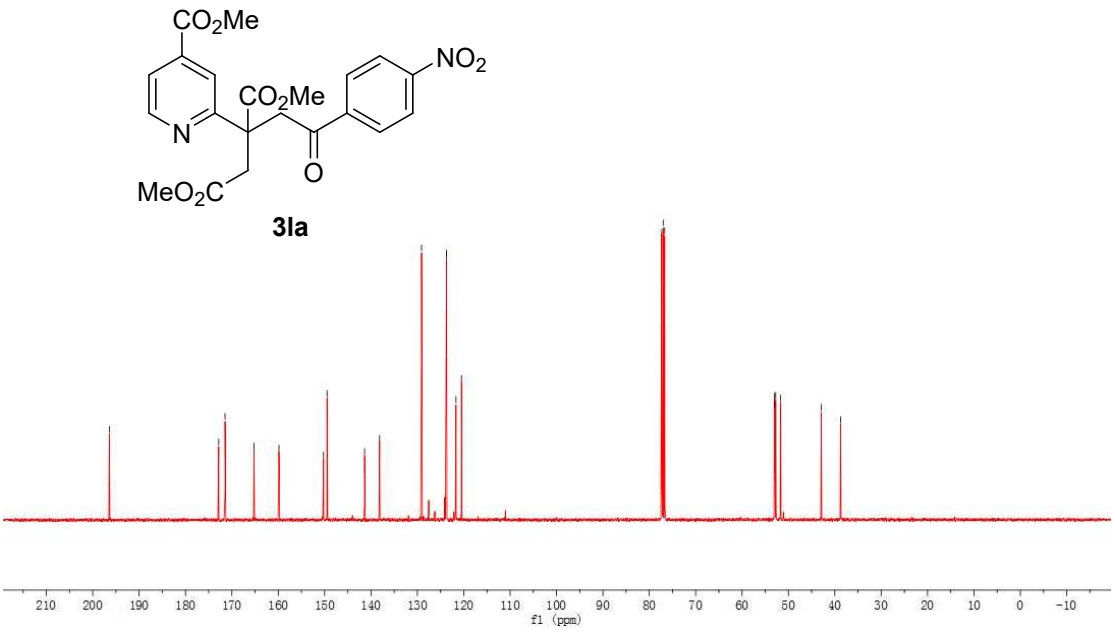
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.65 (dd, *J* = 5.0, 0.9 Hz, 1H), 8.31 (d, *J* = 8.8 Hz, 2H), 8.17 (d, *J* = 8.8 Hz, 2H), 7.76 (dd, *J* = 5.0, 1.4 Hz, 1H), 4.47 (d, *J* = 18.3 Hz, 1H), 4.14 (d, *J* = 18.2 Hz, 1H), 3.97 (s, 3H), 3.75 (s, 3H), 3.67 – 3.56 (m, 4H), 3.49 (d, *J* = 16.5 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 196.4, 172.8, 171.5, 165.2, 159.8, 150.2, 149.5, 141.4, 138.2, 129.1, 123.7, 121.7, 120.5, 53.1, 53.0, 52.7, 51.7, 42.9, 38.8.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{21}H_{21}N_2O_9$, 445.1242; found, 370.1236.

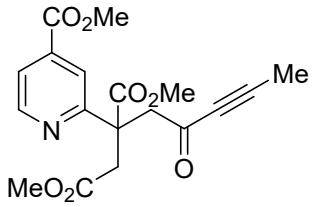
1H, 13C NMR Spectra:


CO2Me
NO2
CO2Me
N
O
MeO2C
3la
f1 (ppm)


CO2Me
NO2
CO2Me
N
O
MeO2C
3la
f1 (ppm)

3ma:

dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(2-oxopent-3-yn-1-yl)succinate



3ma

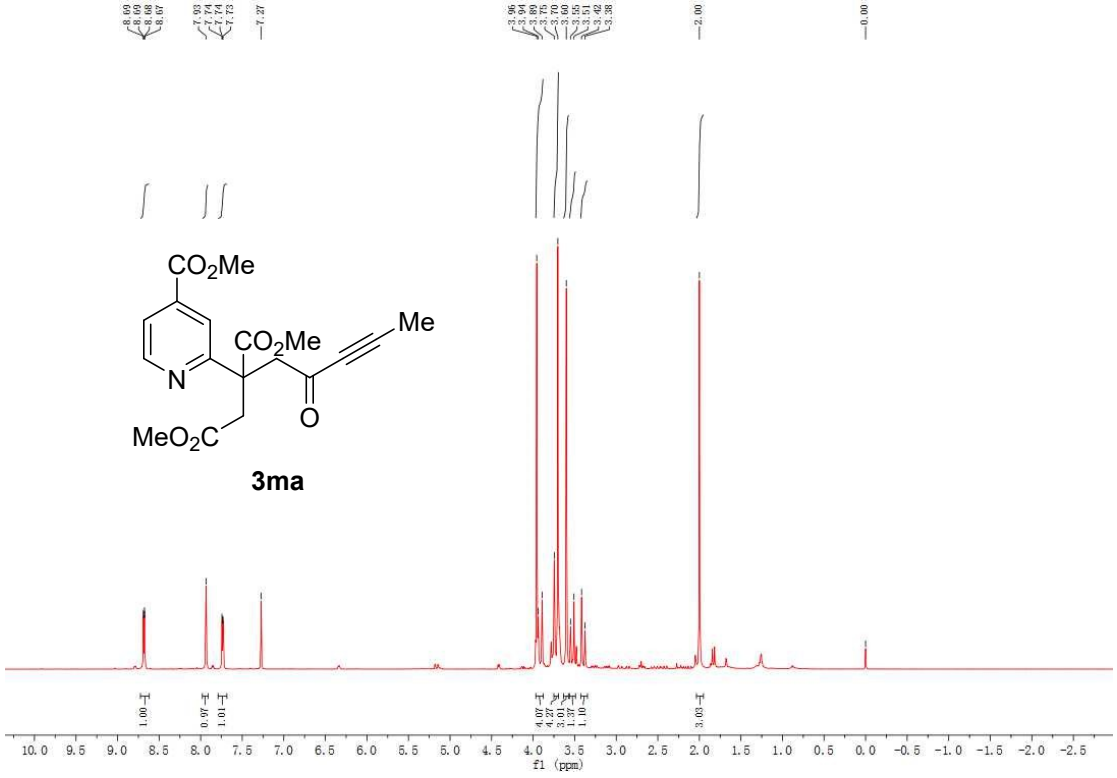
General procedure: 1-(but-2-yn-1-yl)-4-(methoxycarbonyl)pyridin-1-ium bromide **1m-HBr** (0.66mmol, 178.3mg, 2.2eq.), tetrabutylammonium bromide (0.84mmol, 270.8mg, 2.8eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}-Pr_2NEt (0.6mmol, 100.0μL, 2.0eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 25℃ for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3ma** as yellow oil (18.1mg, yield: 17%).

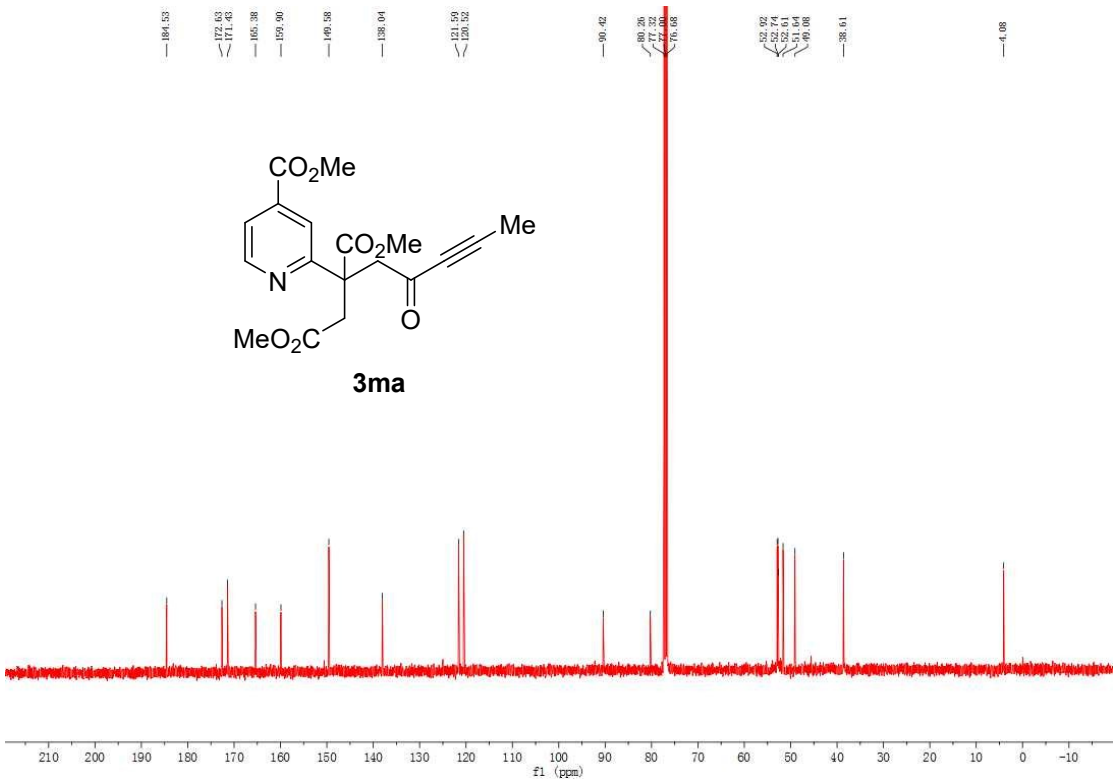
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.72 – 8.62 (m, 1H), 7.93 (s, 1H), 7.79 – 7.68 (m, 1H), 3.92 (m, 4H), 3.72 (m, 4H), 3.60 (s, 3H), 3.53 (d, *J* = 16.6 Hz, 1H), 3.40 (d, *J* = 16.6 Hz, 1H), 2.00 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 184.5, 172.6, 171.4, 165.4, 159.9, 149.6, 138.0, 121.6, 120.5, 90.4, 80.3, 52.9, 52.7, 52.6, 51.6, 49.1, 38.6, 4.1.

HRMS(ESI+)m/z: $[M+Na]^+$ calcd for $C_{18}H_{19}NNaO_7$, 384.1054; found, 384.1053.

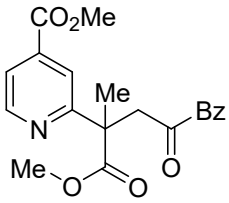
1H, 13C NMR Spectra :





3bb:

methyl 2-(1-methoxy-2-methyl-1,4,5-trioxo-5-phenylpentan-2-yl)isonicotinate



3bb

General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.66mmol, 221.9mg, 2.2eq.), methyl methacrylate **2b** (0.3mmol, 33.0μL, 1.0eq.) and $^{i}Pr_2NEt$ (0.6mmol, 100.0μL, 2.0eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at room temperature for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.4) to afforded **3bb** as yellow oil (56.0mg, yield: 51%).

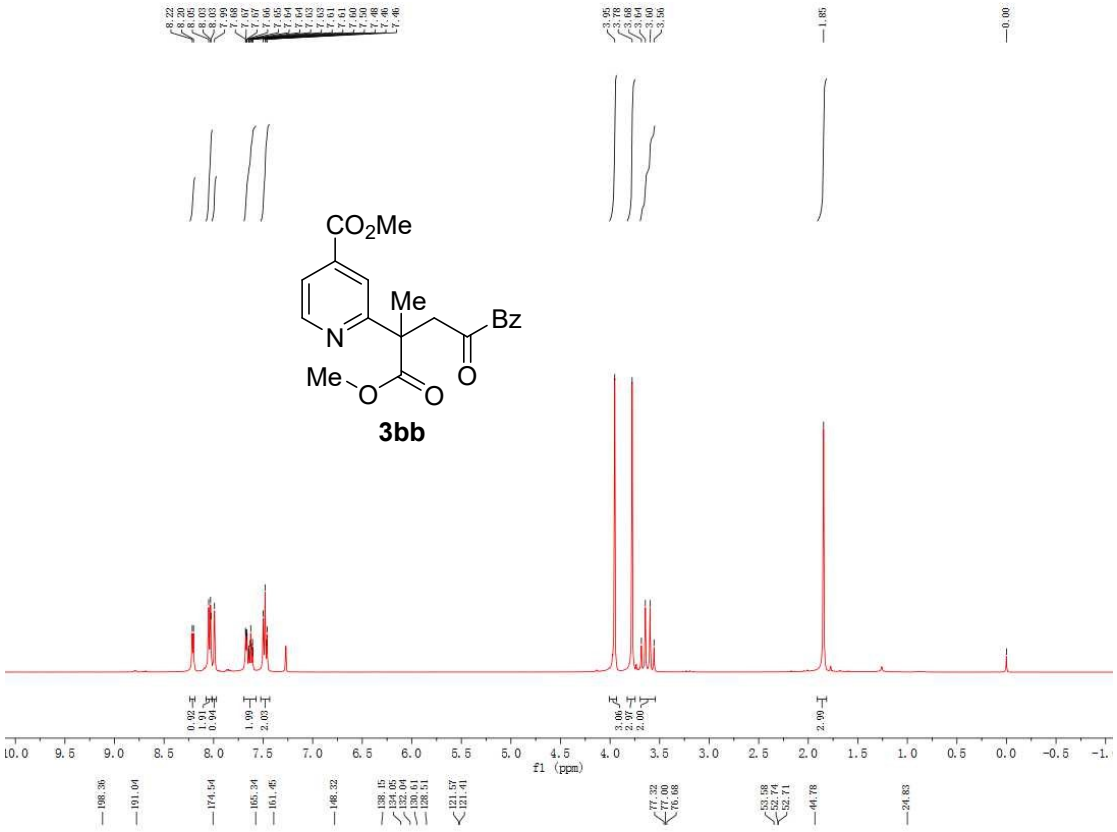
Instead of **1b-HBr**, **1b-HPF$_6$** provided **3bb** in 20% yield (22.1mg).

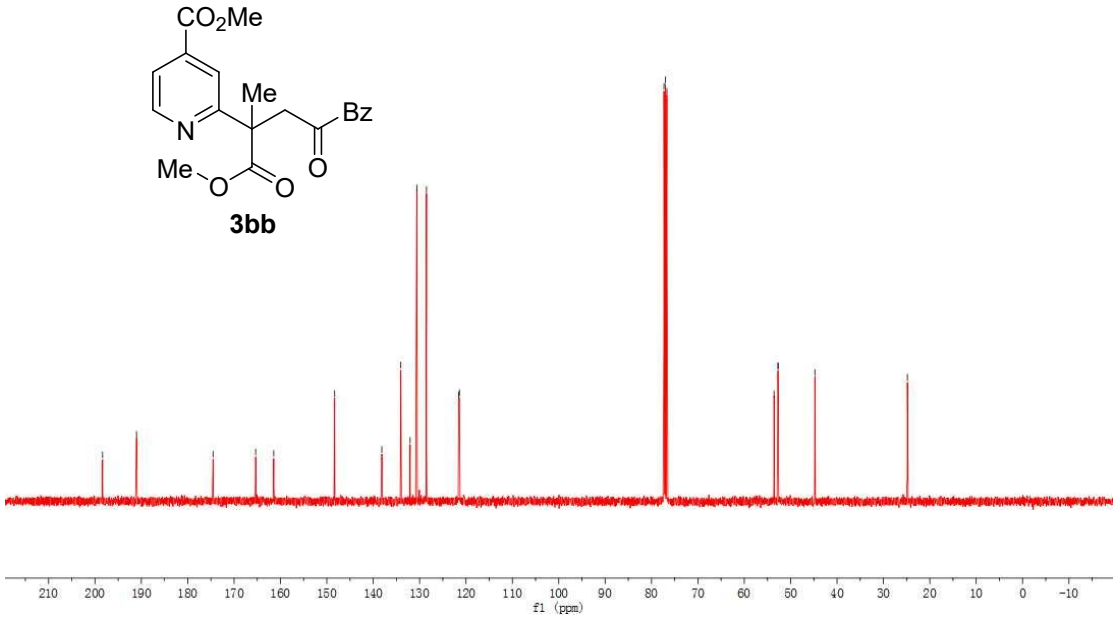
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.21 (d, *J* = 5.1 Hz, 1H), 8.08 – 8.01 (m, 2H), 7.99 (s, 1H), 7.69 – 7.57 (m, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 3.95 (s, 3H), 3.78 (s, 3H), 3.70 – 3.55 (m, 2H), 1.85 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 198.4, 191.0, 174.5, 165.3, 161.5, 148.3, 138.2, 134.1, 132.0, 130.6, 128.5, 121.6, 121.4, 53.6, 52.7, 52.7, 44.8, 24.8.

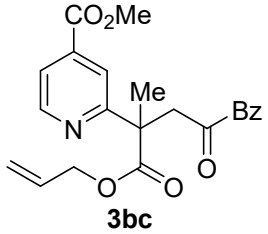
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{20}H_{20}NO_6$, 370.1285; found, 370.1282.

^{1}H, ^{13}C NMR Spectra of **3bb:**





3bc:
methyl 2-(1-(allyloxy)-2-methyl-1,4,5-trioxo-5-phenylpentan-2-yl)isonicotinate



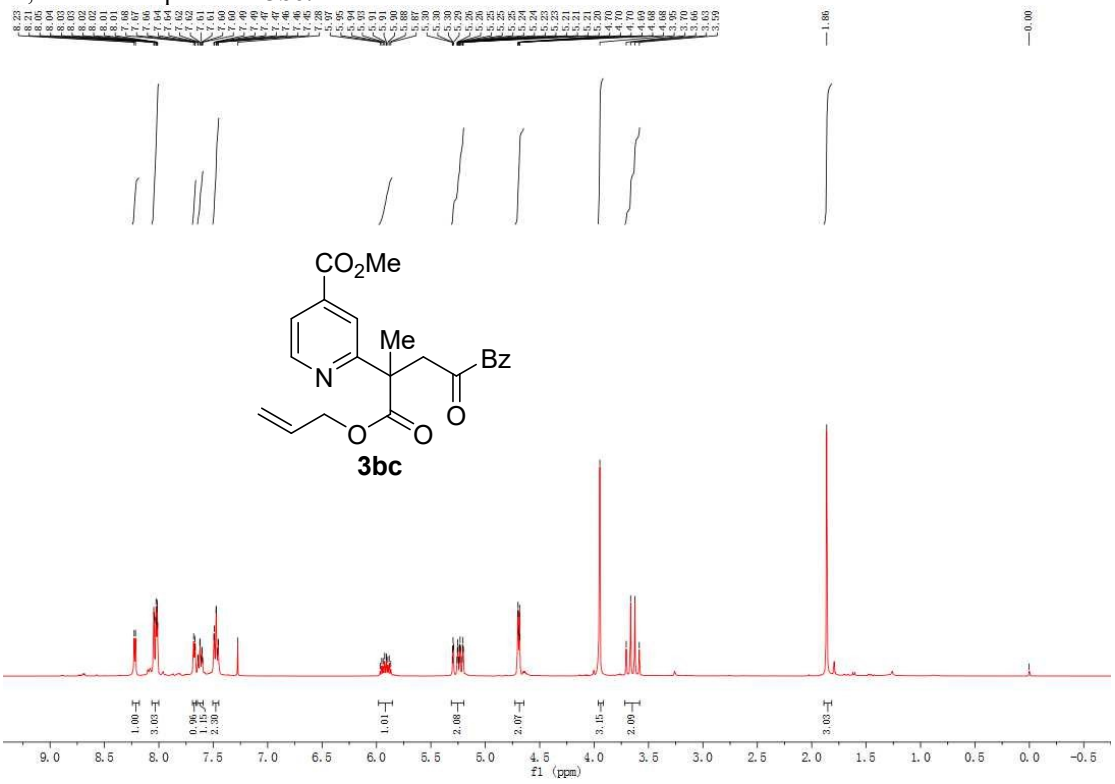
General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.84mmol, 282.4mg, 2.8eq.), allyl methacrylate **2c** (0.3mmol, 41.0μL, 1.0eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.) and $^{i}Pr_2NEt$ (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.5) to afforded **3bc** as yellow oil (77.2mg, yield: 65%).

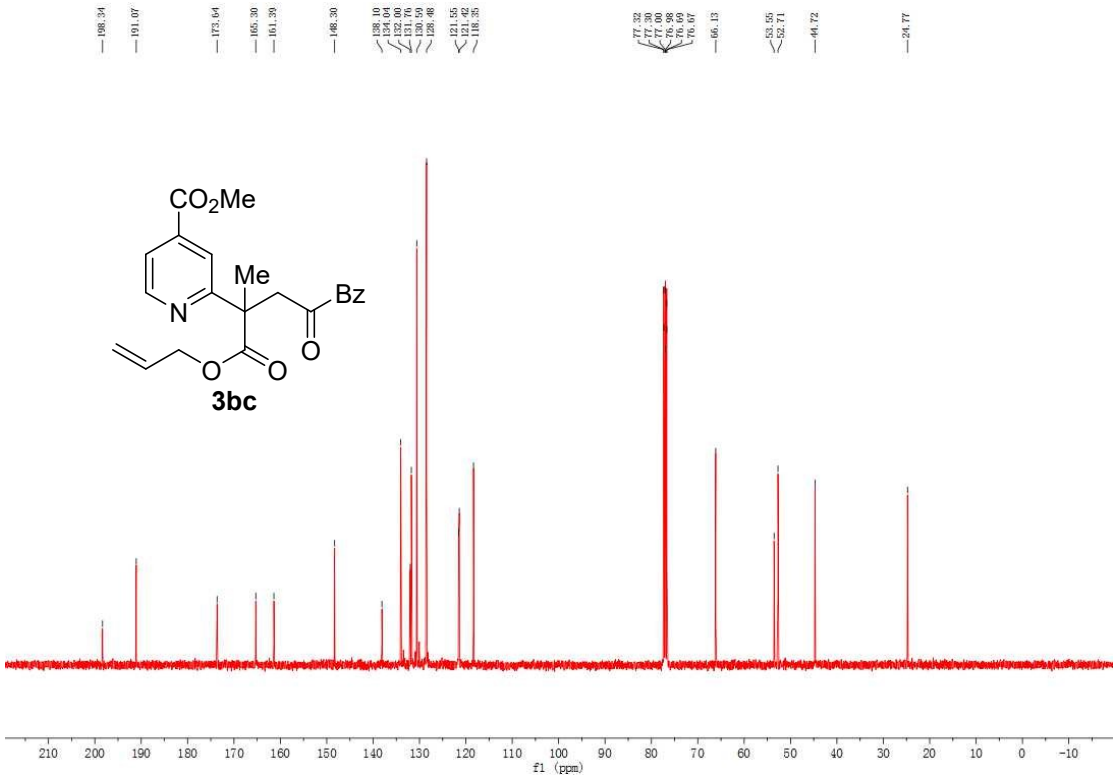
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.22 (d, *J* = 5.0 Hz, 1H), 8.06 – 8.00 (m, 3H), 7.67 (d, *J* = 4.8 Hz, 1H), 7.62 (td, *J* = 7.5, 1.6 Hz, 1H), 7.47 (td, *J* = 7.8, 1.6 Hz, 2H), 5.98 – 5.85 (m, 1H), 5.31 – 5.20 (m, 2H), 4.69 (dt, *J* = 5.7, 1.4 Hz, 2H), 3.95 (s, 3H), 3.64 (q, *J* = 16.2 Hz, 2H), 1.86 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 198.3, 191.1, 173.6, 165.3, 161.4, 148.3, 138.1, 134.0, 132.0, 131.8, 130.6, 128.5, 121.6, 121.4, 118.4, 66.1, 53.6, 52.7, 44.7, 24.8.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{22}H_{22}NO_6$, 396.1442; found, 396.1444.

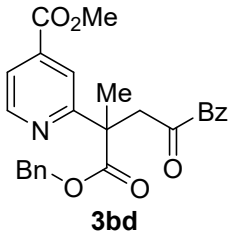
^{1}H, ^{13}C NMR Spectra of **3bc:**





3bd:

methyl 2-(1-(benzyloxy)-2-methyl-1,4,5-trioxo-5-phenylpentan-2-yl)isonicotinate



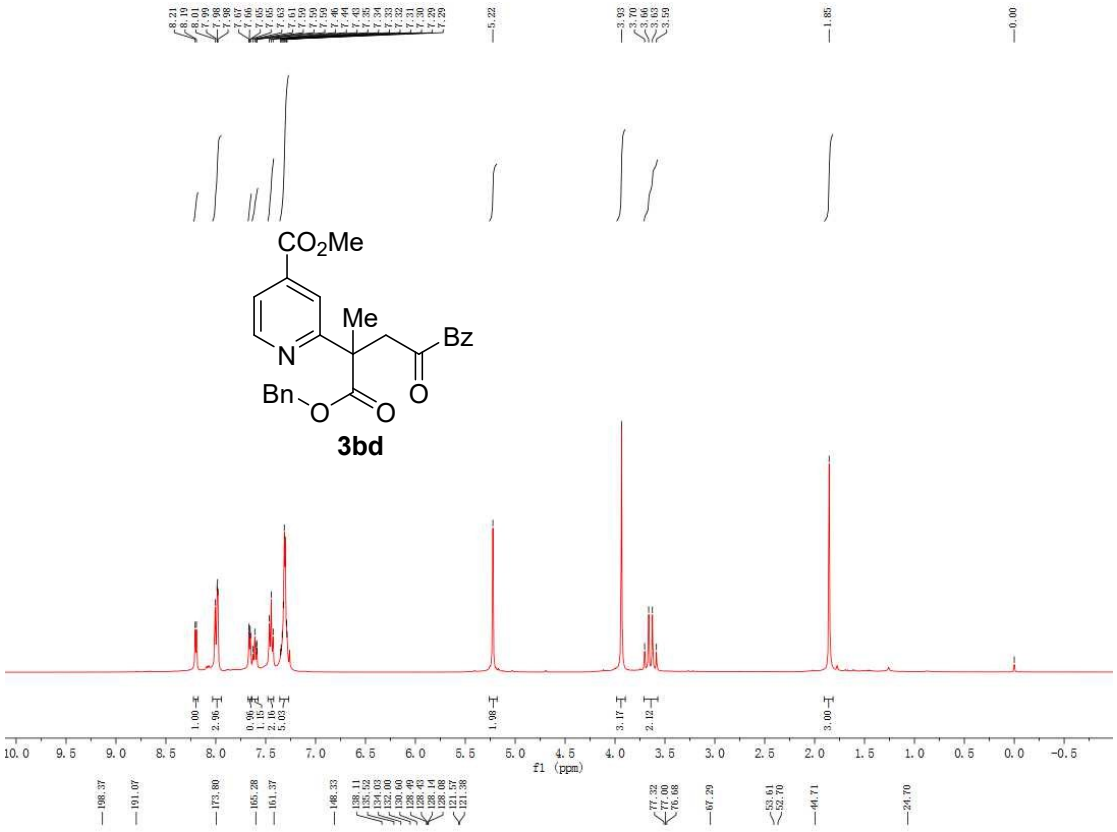
General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.84mmol, 282.4mg, 2.8eq.), Benzyl methacrylate **2d** (0.3mmol, 51.0μL, 1.0eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.) and ^{i}-Pr_2NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.45) to afforded **3bd** as yellow oil (58.1mg, yield: 43%).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.20 (d, *J* = 5.1 Hz, 1H), 8.03 – 7.94 (m, 3H), 7.66 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.35-7.29 (m, 5H), 5.22 (s, 2H), 3.93 (s, 3H), 3.64 (q, *J* = 16.1 Hz, 2H), 1.85 (s, 3H).

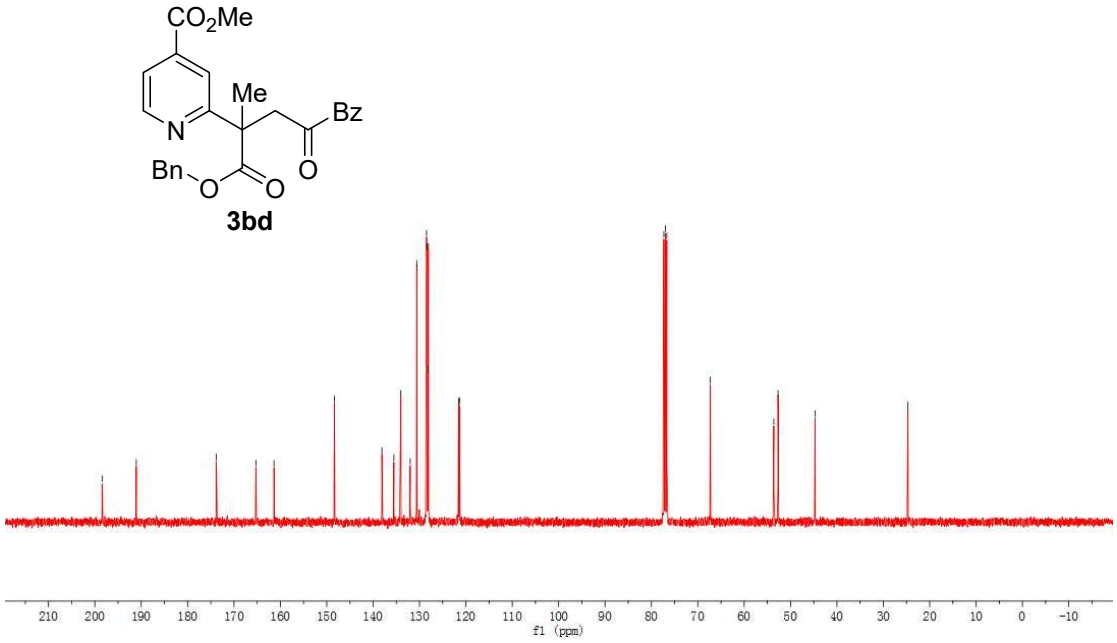
^{13}C NMR (101 MHz, $CDCl_3$): δ 198.4, 191.1, 173.8, 165.3, 161.4, 148.3, 138.1, 135.5, 134.0, 132.0, 130.6, 128.5, 128.4, 128.1, 128.1, 121.6, 121.4, 67.3, 53.6, 52.7, 44.7, 24.7.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{26}H_{24}NO_6$, 446.1598; found, 446.1597.

^{1}H, ^{13}C NMR Spectra of **3bd:**

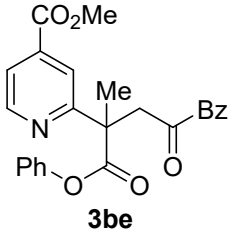


3bd



3bd

3be:
methyl 2-(2-methyl-1,4,5-trioxo-1-phenoxy-5-phenylpentan-2-yl)isonicotinate



3be

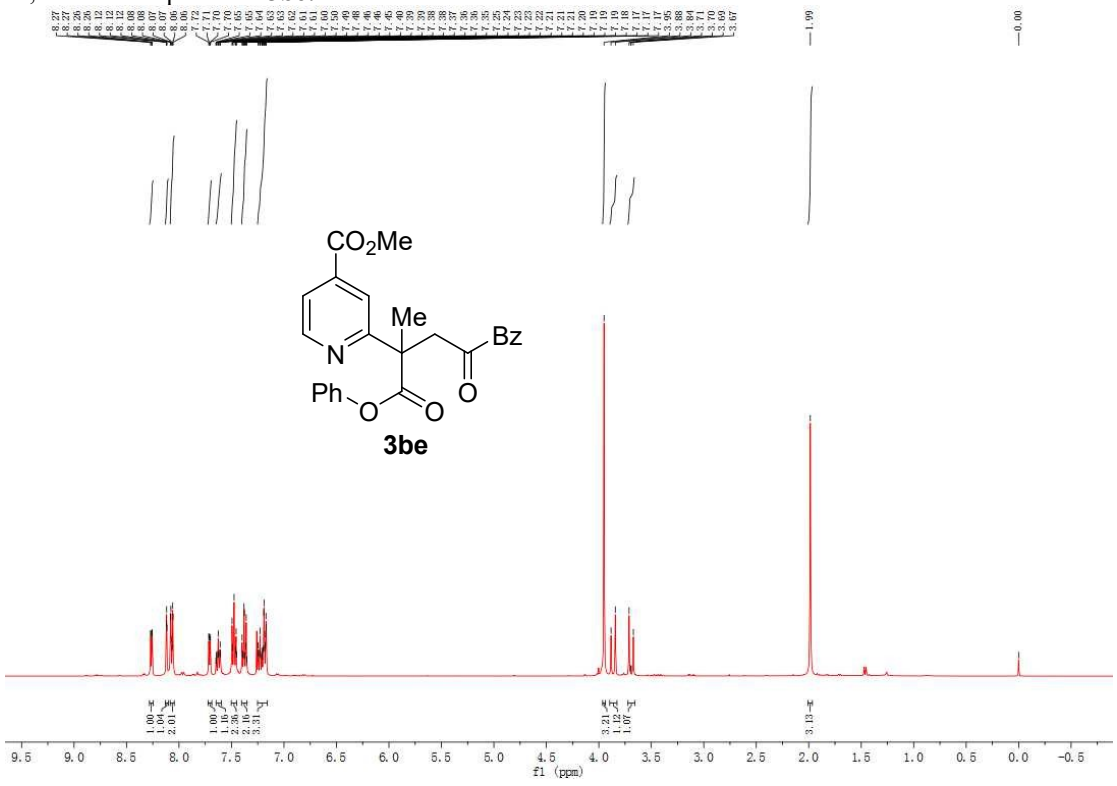
General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.84mmol, 282.4mg, 2.8eq.), Phenyl methacrylate **2e** (0.3mmol, 47.0μL, 1.0eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.) and $^{i}Pr_2NEt$ (0.75mmol, 125.0μL, 2.0eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.45) to afforded **3be** as brown oil (63.6mg, yield: 49%).

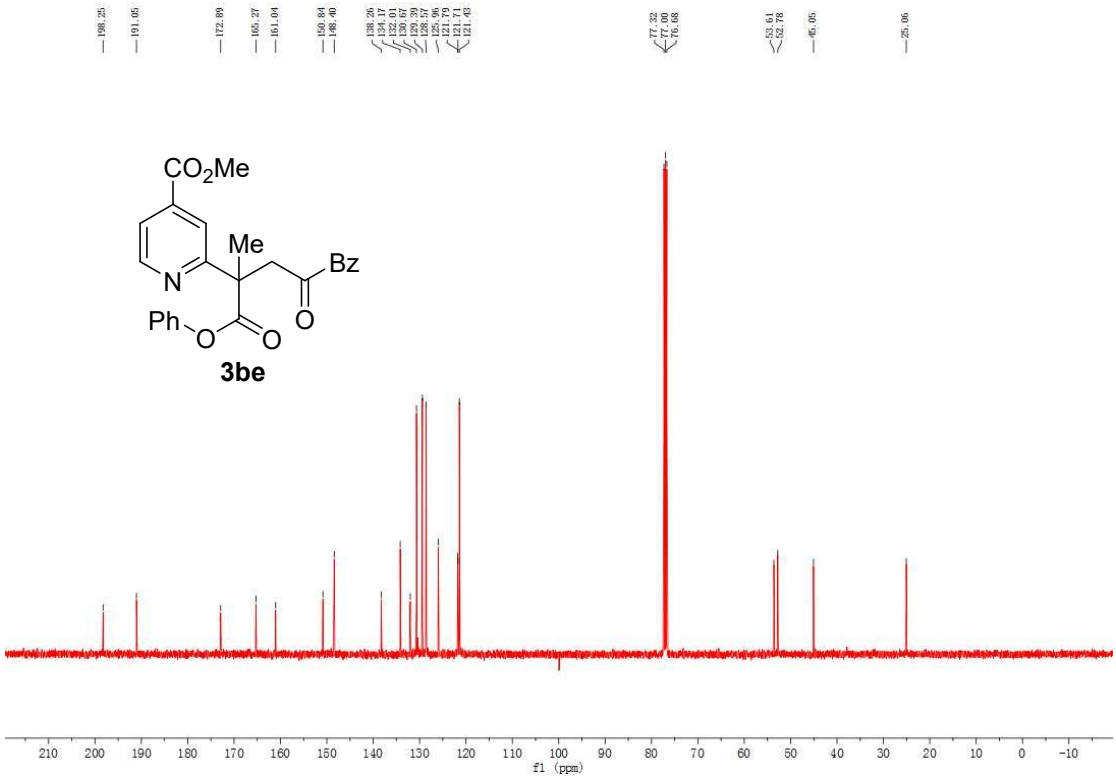
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.26 (dd, *J* = 5.0, 0.9 Hz, 1H), 8.12 (t, *J* = 1.2 Hz, 1H), 8.08 – 8.05 (m, 2H), 7.71 (dd, *J* = 5.1, 1.5 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.40 – 7.35 (m, 2H), 7.25 – 7.16 (m, 3H), 3.95 (s, 3H), 3.86 (d, *J* = 16.3 Hz, 1H), 3.69 (d, *J* = 16.3 Hz, 1H), 1.99 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 198.3, 191.1, 172.9, 165.3, 161.0, 150.8, 148.4, 138.3, 134.2, 132.0, 130.7, 129.4, 128.6, 126.0, 121.8, 121.7, 121.4, 53.6, 52.8, 45.1, 25.1.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{25}H_{22}NO_6$, 432.1442; found, 432.1437.

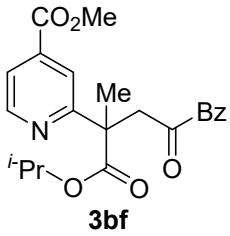
^{1}H, ^{13}C NMR Spectra of **3be:**





3bf:

methyl 2-(1-isopropoxy-2-methyl-1,4,5-trioxo-5-phenylpentan-2-yl)isonicotinate



General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.66mmol, 221.9mg, 2.2eq.), methacrylic acid isopropyl ester **2f** (0.3mmol, 44.0μL, 1.0eq.) and $^{i-}Pr_2NEt$ (1.05mmol, 175.0μL, 3.5eq.) were added sequentially to 3.0 mL of DCE. The reaction mixture was stirred at room temperature for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.6) to afforded **3bf** as yellow oil (53.0mg, yield: 45%).

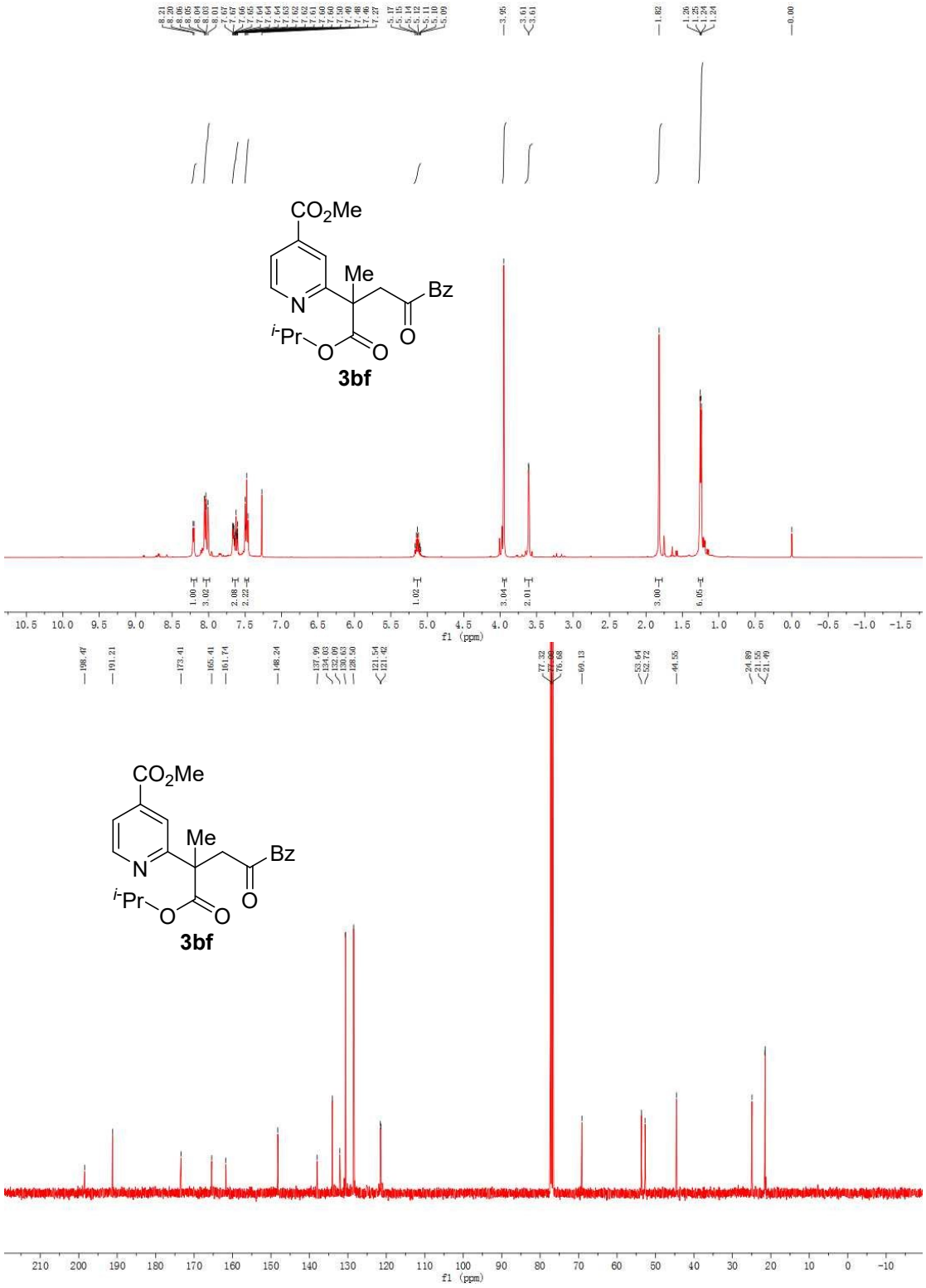
Instead of **1b-HBr**, **1b-HPF$_6$** provided **3bf** in 29% yield (34.2mg).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.21 (d, *J* = 5.1 Hz, 1H), 8.07 – 7.99 (m, 3H), 7.63 (ddt, *J* = 16.2, 6.9, 1.4 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 5.14 (dt, *J* = 12.7, 6.4 Hz, 1H), 3.95 (s, 3H), 3.61 (d, *J* = 2.3 Hz, 2H), 1.82 (s, 3H), 1.25 (dd, *J* = 6.3, 2.5 Hz, 6H).

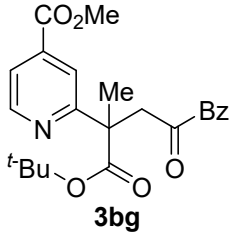
^{13}C NMR (101 MHz, Chloroform-*d*): δ 198.5, 191.2, 173.4, 165.4, 161.7, 148.2, 138.0, 134.0, 132.1, 130.6, 128.5, 121.5, 121.4, 69.1, 53.6, 52.7, 44.6, 24.9, 21.6, 21.5.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{22}H_{24}NO_6$, 398.1598; found, 398.1602.

^{1}H, ^{13}C NMR Spectra of **3bf:**



3bg:
methyl 2-(1-(tert-butoxy)-2-methyl-1,4,5-trioxo-5-phenylpentan-2-yl)isonicotinate



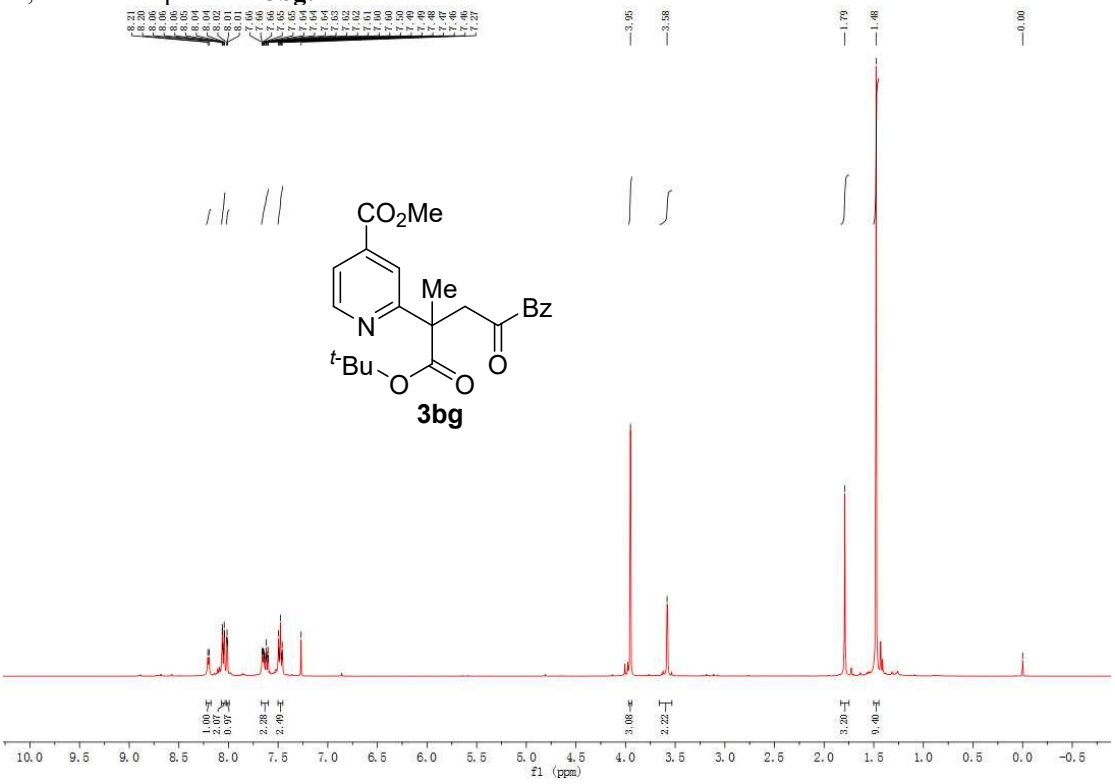
General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.84mmol, 282.4mg, 2.8eq.), tert-butyl methacrylate **2g** (0.3mmol, 49.0μL, 1.0eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.) and $^{i}Pr_2NEt$ (0.75mmol, 125.0μL, 2.5 eq.) were added sequentially to 2.0 mL of dioxnae. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=5:1, v/v; R_f=0.7) to afforded **3bg** as yellow oil (62.4mg, yield: 51%).

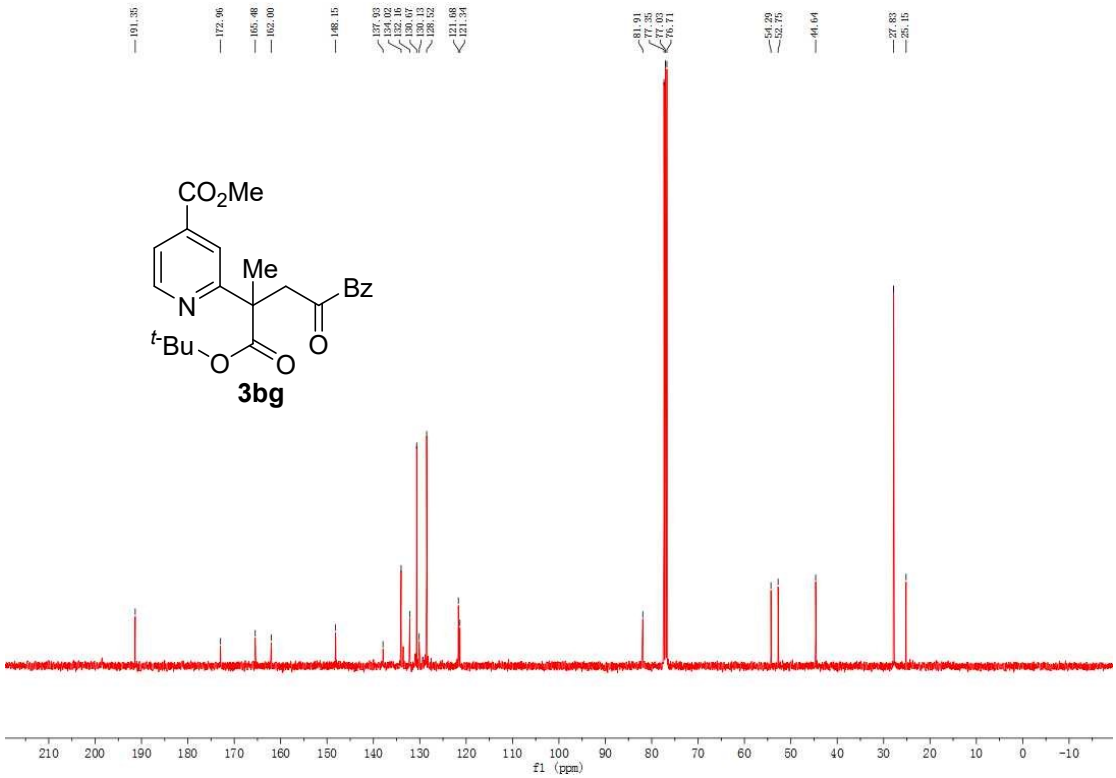
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.20 (d, *J* = 5.1 Hz, 1H), 8.05 (dt, *J* = 7.1, 1.4 Hz, 2H), 8.01 (t, *J* = 1.2 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 3.95 (s, 3H), 3.58 (d, *J* = 1.9 Hz, 2H), 1.79 (s, 3H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 191.4, 173.0, 165.5, 162.0, 148.2, 137.9, 134.0, 132.2, 130.7, 130.1, 128.5, 121.7, 121.3, 81.9, 54.3, 52.8, 44.6, 27.8, 25.2.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{23}H_{26}NO_6$, 412.1755; found, 412.1752.

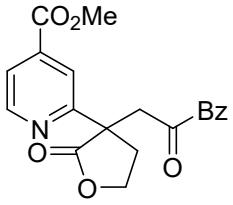
^{1}H, ^{13}C NMR Spectra of **3bg:**





3bh:

methyl 2-(3-(2,3-dioxo-3-phenylpropyl)-2-oxotetrahydrofuran-3-yl)isonicotinate



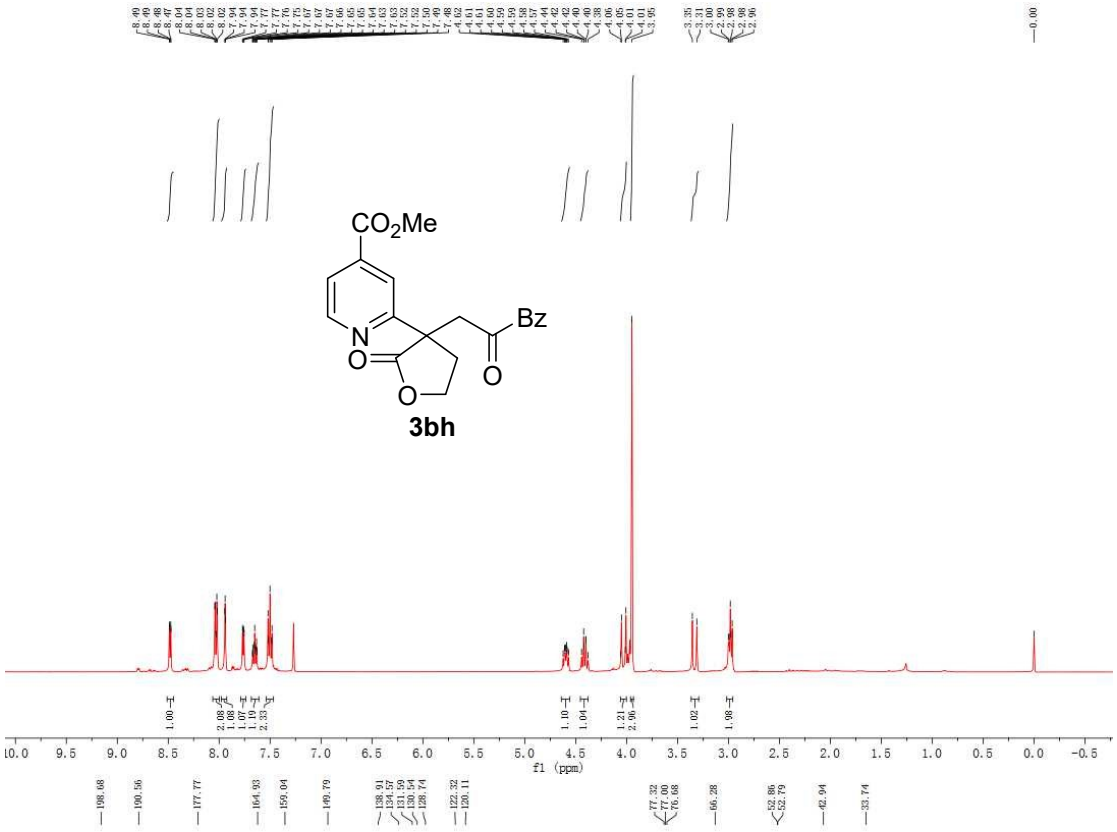
General procedure: 4-(methoxycarbonyl)-1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1b-HBr** (0.84mmol, 282.4mg, 2.8eq.), tulipalin A **2h** (0.3mmol, 27.0μL, 1.0eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.) and ^{i}-Pr_2NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3bh** as yellow oil (70.0mg, yield: 62%).

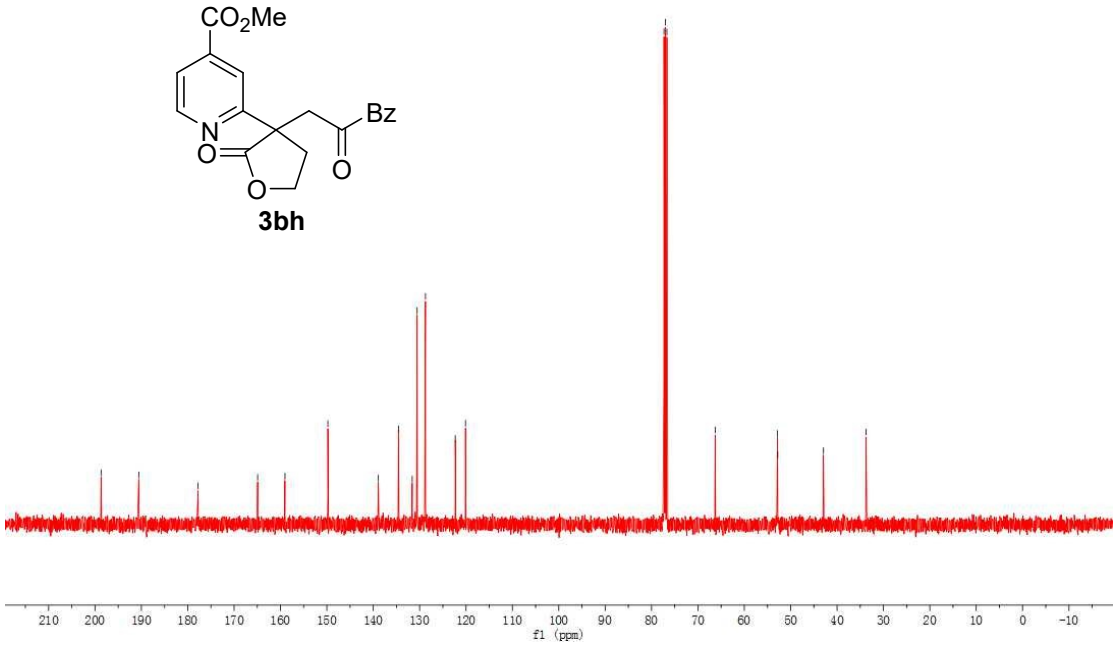
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.51 – 8.45 (m, 1H), 8.03 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.98 – 7.93 (m, 1H), 7.76 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.68 – 7.61 (m, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 4.60 (ddd, *J* = 9.0, 7.0, 5.1 Hz, 1H), 4.45 – 4.38 (m, 1H), 4.03 (d, *J* = 17.5 Hz, 1H), 3.95 (s, 3H), 3.33 (d, *J* = 17.6 Hz, 1H), 3.02 – 2.96 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 198.7, 190.6, 177.8, 164.9, 159.0, 149.8, 138.9, 134.6, 131.6, 130.5, 128.7, 122.3, 120.1, 66.3, 52.9, 52.8, 42.9, 33.7.

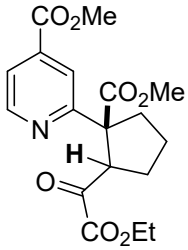
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{20}H_{18}NO_6$, 368.1129; found, 368.1129.

^{1}H, ^{13}C NMR Spectra of **3bh:**





3fi:
methyl 2-((1S)-2-(2-ethoxy-2-oxoacetyl)-1-(methoxycarbonyl)cyclopentyl)isonicotinate



3fi

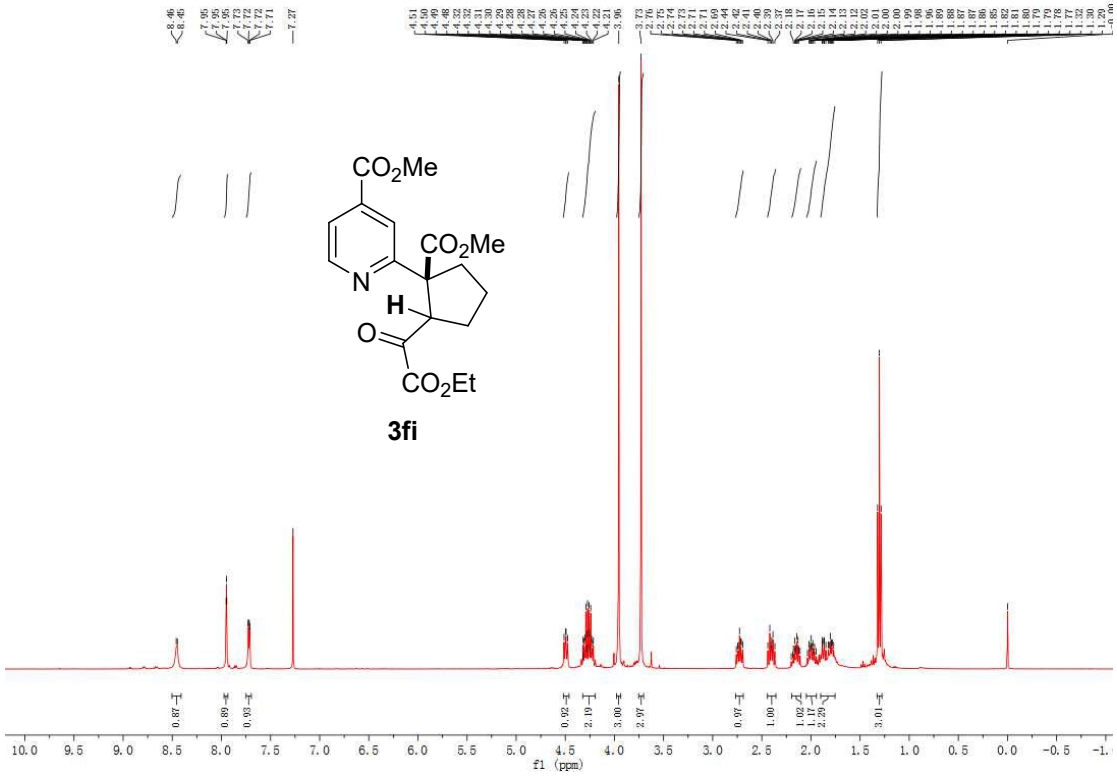
General procedure: 1-(2-ethoxy-2-oxoethyl)-4-(methoxycarbonyl)pyridin-1-ium bromide **1f-PF$_6$** (0.84mmol, 310.1mg, 2.8eq.), methyl 1-cyclopentenoate **2i** (0.3mmol, 37.0μL, 1.0eq.), tetrabutylammonium bromide (1.5mmol, 483.6mg, 5.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3fi** as yellow oil (24.2mg, yield: 22%).

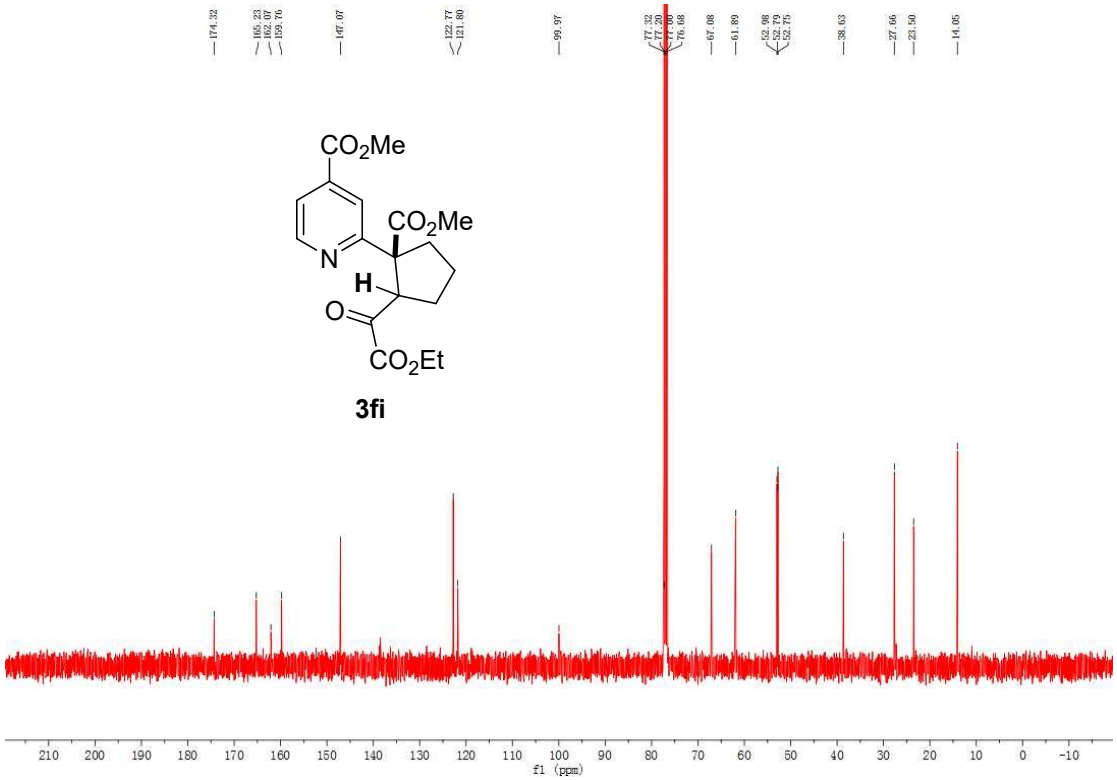
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.45 (d, *J* = 5.0 Hz, 1H), 7.95 (t, *J* = 1.2 Hz, 1H), 7.72 (dd, *J* = 5.2, 1.5 Hz, 1H), 4.49 (dd, *J* = 8.4, 6.2 Hz, 1H), 4.32 – 4.20 (m, 2H), 3.96 (s, 3H), 3.73 (s, 3H), 2.73 (ddd, *J* = 12.9, 7.8, 5.2 Hz, 1H), 2.40 (dt, *J* = 12.8, 7.9 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.99 (ddt, *J* = 13.2, 9.0, 6.3 Hz, 1H), 1.90 – 1.75 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.3, 165.2, 162.1, 159.8, 147.1, 122.8, 121.8, 100.0, 67.1, 61.9, 53.0, 52.8, 52.8, 38.6, 27.7, 23.5, 14.1.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{18}H_{22}NO_7$, 364.1391; found, 364.1394.

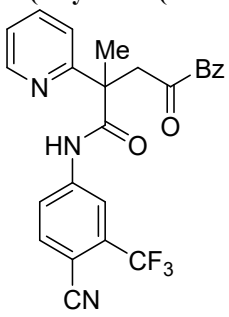
^{1}H, ^{13}C NMR Spectra of **3fi:**





3fi

3aj:
N-(4-cyano-3-(trifluoromethyl)phenyl)-2-methyl-4,5-dioxo-5-phenyl-2-(pyridin-2-yl)pentanamide



3aj

General procedure: 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **1a-HBr** (0.75mmol, 208.5mg, 1.5eq.), tetrabutylammonium bromide (0.75mmol, 241.8mg, 1.5eq.), N-(4-cyano-3-(trifluoromethyl)phenyl)methacrylamide **2j** (0.5mmol, 127.1mg, 1.0eq.) and DABCO (1.25mmol, 140.3mg, 2.5eq.) were added sequentially to 5.0 mL of dioxane. The reaction mixture was stirred at 50℃ for 15h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3aj** as yellow oil (43.3mg, yield: 31%).

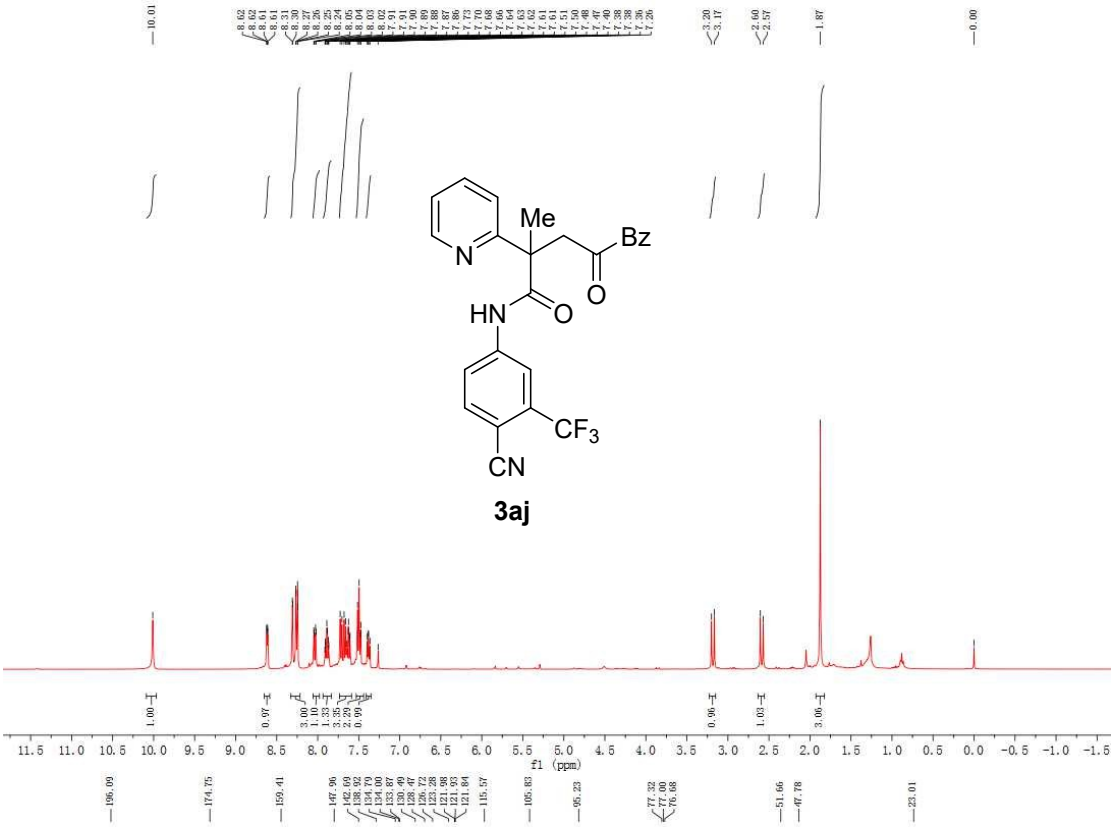
^{1}H NMR (400 MHz, Chloroform-*d*): δ 10.01 (s, 1H), 8.62 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.33 – 8.22 (m, 3H), 8.03 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.89 (td, *J* = 7.7, 1.8 Hz, 1H), 7.73 – 7.59 (m, 3H), 7.49 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.35 (m, 1H), 3.18 (d, *J* = 13.8 Hz, 1H), 2.59 (d, *J* = 13.9 Hz, 1H), 1.87 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 196.1, 174.8, 159.4, 148.0, 142.7, 138.9, 134.8, 134.0, 133.9, 133.0 (q, *J* = 32.7 Hz), 130.5, 128.5, 126.7, 123.3, 122.1 (q, *J* = 272.0 Hz), 121.9 (q, *J* = 5.0 Hz), 121.8, 115.6, 105.8, 95.2, 51.7, 47.8, 23.0.

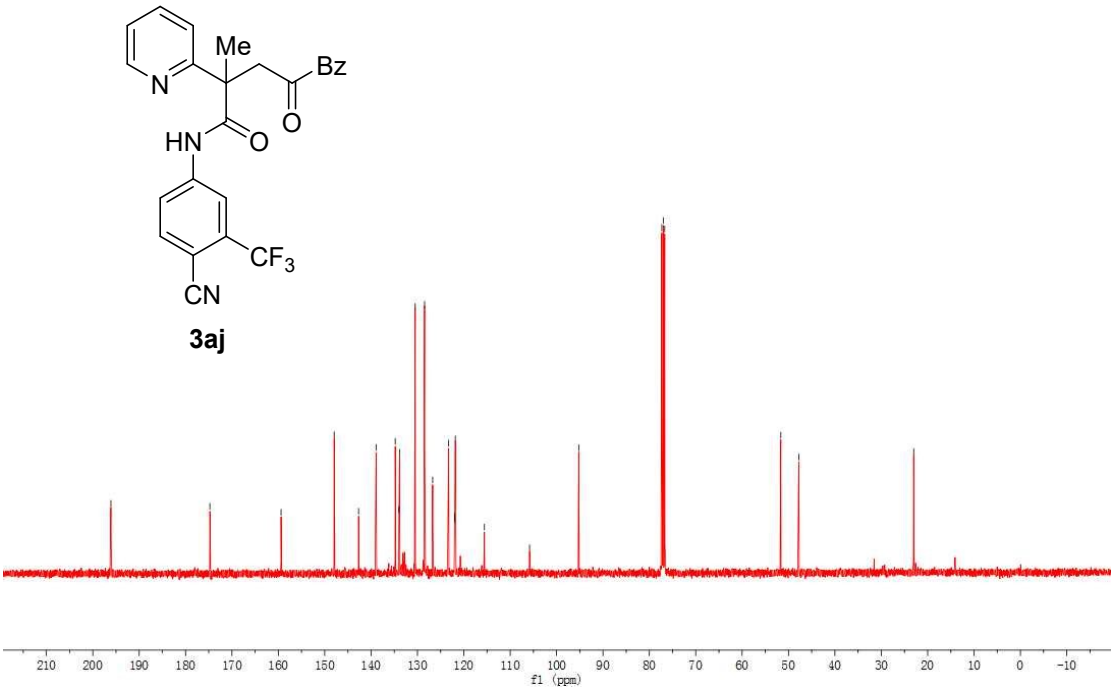
^{19}F NMR (376 MHz, $CDCl_3$): δ -62.00.

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{25}H_{19}F_3N_3O_3$, 466.1373; found, 466.1380.

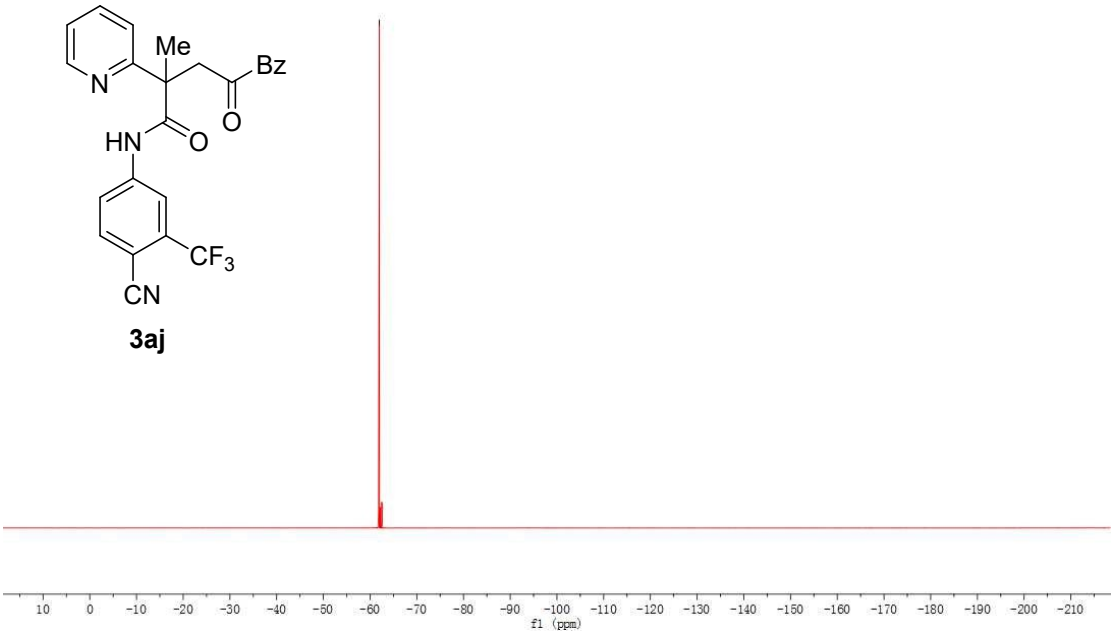
1H, 13C and ^{19}F NMR Spectra :



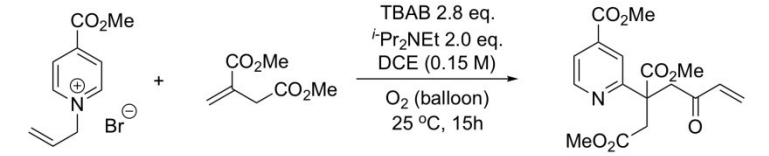
3aj



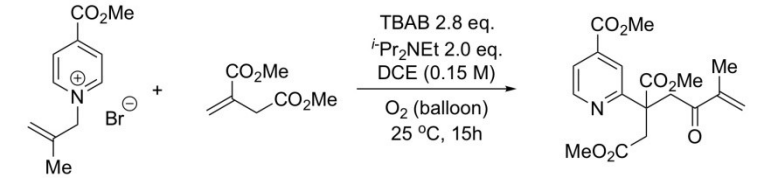
3aj



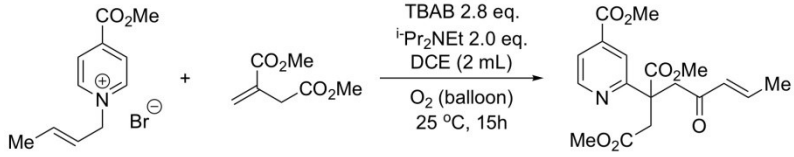
Other products :



1n-HBr (2.2 eq.) **2a** (0.3 mmol) **3na** (Not Detected)



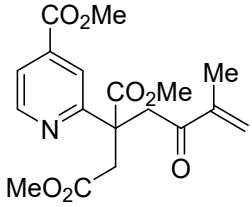
1o-HBr (2.2 eq.) **2a** (0.3 mmol) **3oa** (NMR Yield = 25%)



1p-HBr (2.2 eq.) **2a** (0.3 mmol) **3pa** (NMR Yield = 22%)

3oa:

dimethyl 2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(3-methyl-2-oxobut-3-en-1-yl)succinate



3oa

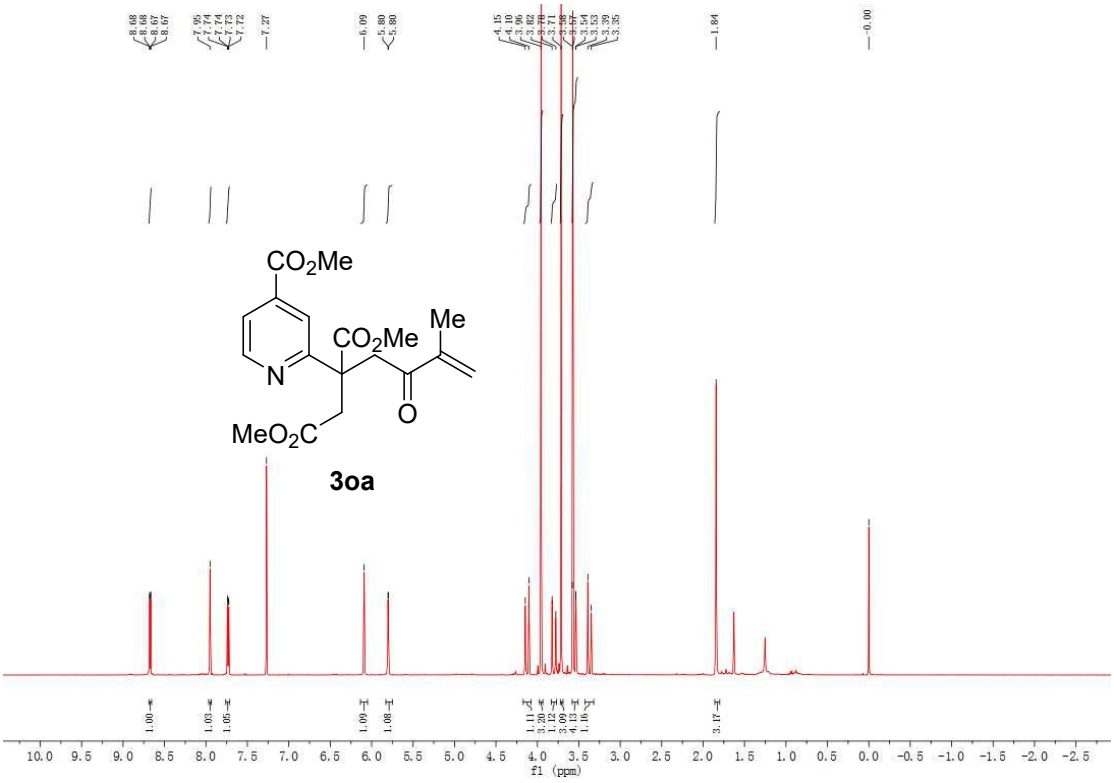
General procedure: 4-(methoxycarbonyl)-1-(2-methylallyl)pyridin-1-ium bromide **1o-HBr** (0.66mmol, 179.6mg, 2.2eq.), tetrabutylammonium bromide (0.84mmol, 270.8mg, 2.8eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were

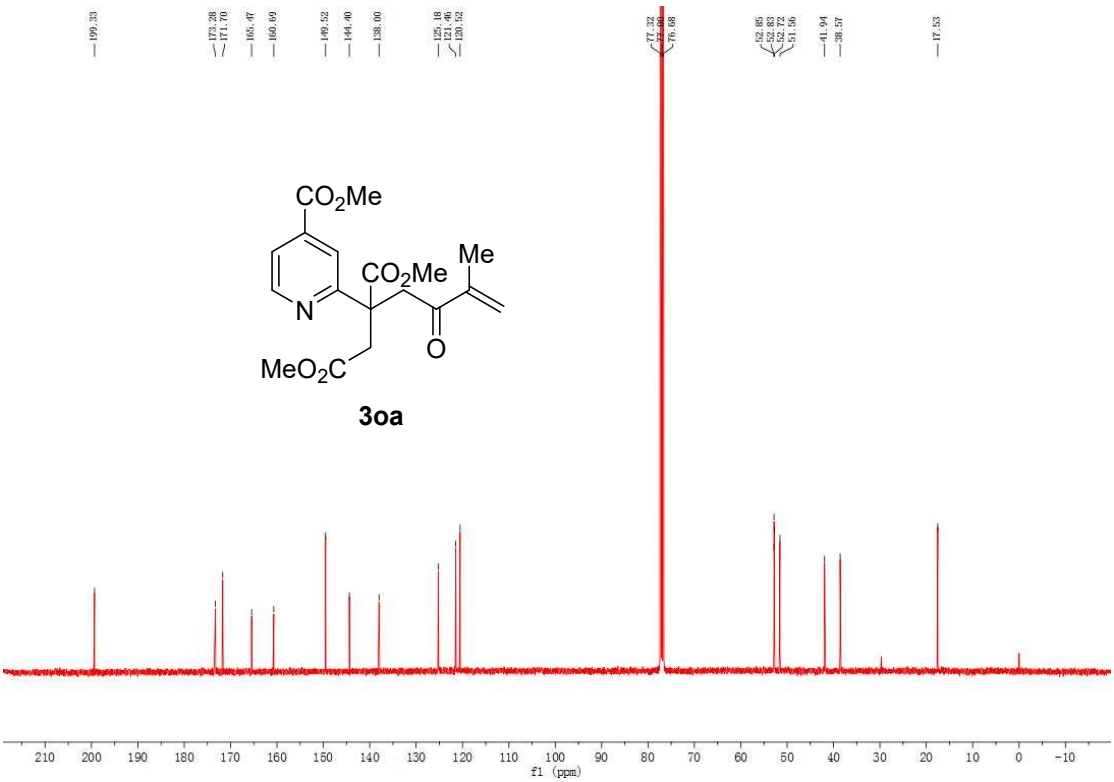
added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 25℃ for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=2:1, v/v; R_f=0.5) to afforded **3oa** as yellow oil (NMR yield: 25%, 1,3,5-trimethoxybenzene as internal standard).

^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.67 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.95 (s, 1H), 7.73 (dd, *J* = 5.0, 1.4 Hz, 1H), 6.09 (s, 1H), 5.80 (d, *J* = 1.4 Hz, 1H), 4.12 (d, *J* = 18.1 Hz, 1H), 3.96 (s, 3H), 3.80 (d, *J* = 18.0 Hz, 1H), 3.71 (s, 3H), 3.57 (s, 4H), 3.37 (d, *J* = 16.4 Hz, 1H), 1.84 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 199.3, 173.3, 171.7, 165.5, 160.7, 149.5, 144.4, 138.0, 125.2, 121.5, 120.5, 52.9, 52.8, 52.7, 51.6, 41.9, 38.6, 17.5.

1H, 13C NMR Spectra :

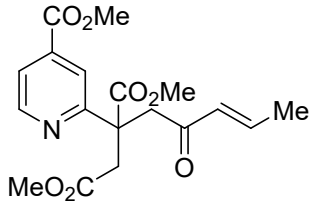




3oa

3pa:

dimethyl (E)-2-(4-(methoxycarbonyl)pyridin-2-yl)-2-(2-oxopent-3-en-1-yl)succinate



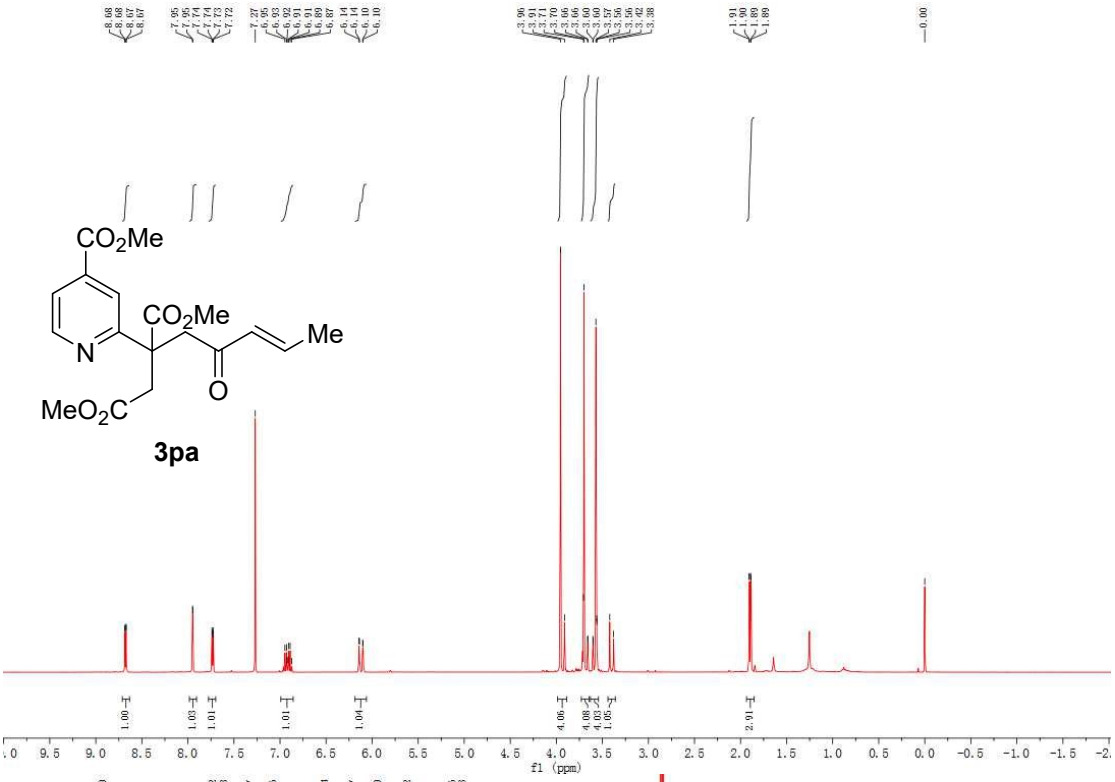
3pa

General procedure: 1-(but-2-en-1-yl)-4-(methoxycarbonyl)pyridin-1-ium bromide **1p-HBr** (0.66mmol, 179.6mg, 2.2eq.), tetrabutylammonium bromide (0.84mmol, 270.8mg, 2.8eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of DCE. The reaction mixture was stirred at 25℃ for 15h under O_2 atmosphere. Then DCE was removed and the residue was purified by column chromatography (SiO2, hexane/EA=2:1, v/v; Rf=0.5) to afforded **3pa** as yellow oil (NMR yield: 22%, 1,3,5-trimethoxybenzene as internal standard).

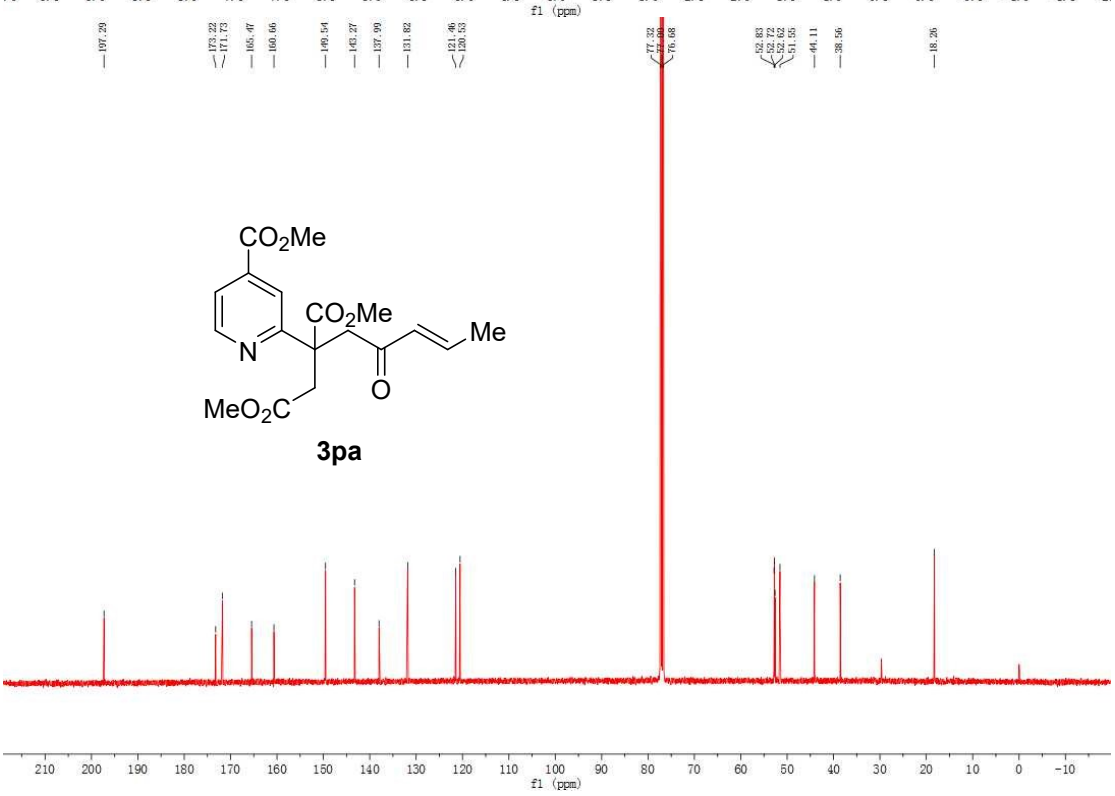
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.68 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.95 (d, *J* = 0.5 Hz, 1H), 7.73 (dd, *J* = 5.0, 1.5 Hz, 1H), 6.99 – 6.86 (m, 1H), 6.12 (dd, *J* = 15.8, 1.7 Hz, 1H), 3.96 (s, 4H), 3.70 (s, 4H), 3.63 – 3.54 (m, 4H), 3.40 (d, *J* = 16.5 Hz, 1H), 1.90 (dd, *J* = 6.8, 1.7 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.3, 173.2, 171.7, 165.5, 160.7, 149.5, 143.3, 138.0, 131.8, 121.5, 120.5, 52.8, 52.7, 52.6, 51.6, 44.1, 38.6, 18.3.

1H, 13C NMR Spectra:



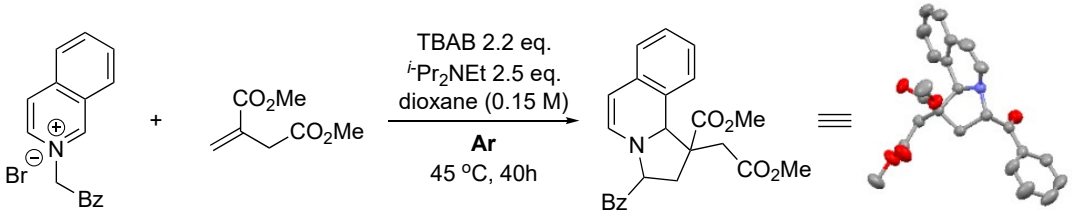
3pa



3pa

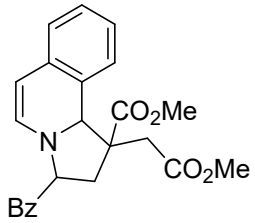
4. Mechanism Study

Synthesis of 4ja:



1j-HBr (2.8 eq.) **2a** **4ja** (NMR yield = 96%)

4ja: methyl 3-benzoyl-1-(2-methoxy-2-oxoethyl)-1,2,3,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1-carboxylate.(known)[8]



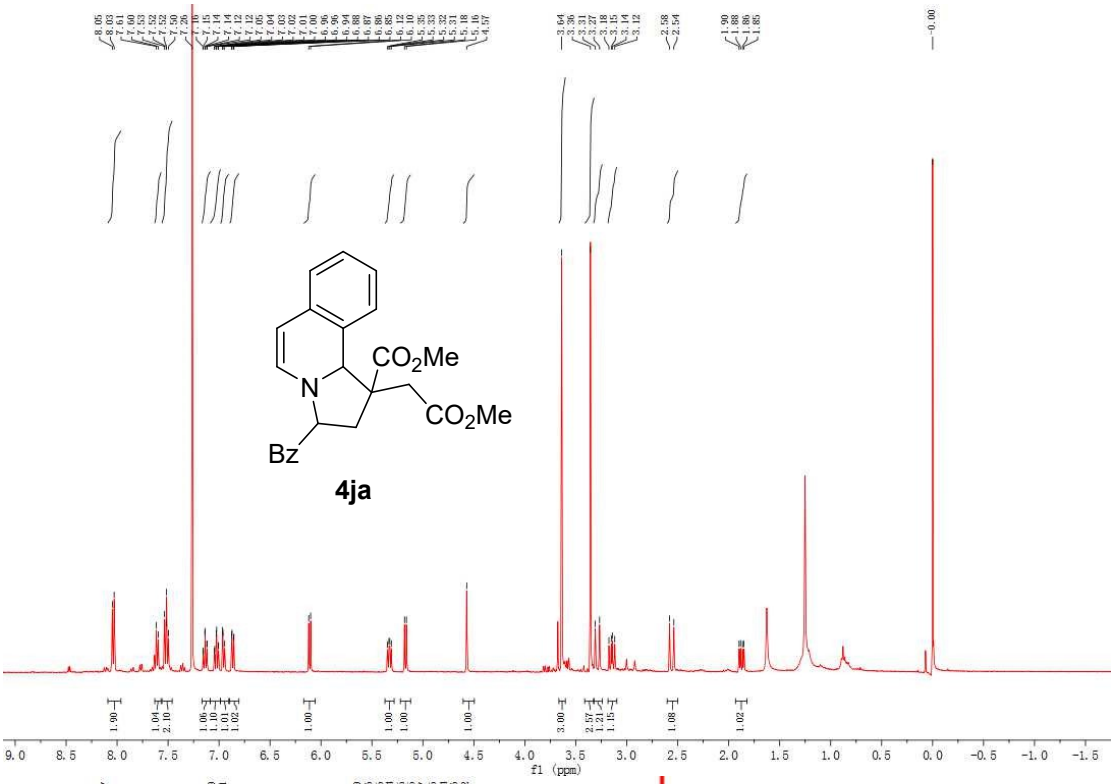
4ja

General procedure: 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium bromide **1j-HBr** (0.84mmol, 275.7mg, 2.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), dimethyl 2-methylenesuccinate **2a** (0.3mmol, 47.5mg, 1.0eq.) and ^{i}Pr$_2$NEt (0.75mmol, 125.0μL, 2.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under argon atmosphere. 96% NMR yield of **4ja** was obtained with 1,3,5-trimethoxy-benzene as internal standard. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=0:1, v/v; R_f=0.5) to afforded **4ja** as yellow solid (117.1mg, yield: 96%, not 100% purity because of slow decomposition on silica gel).

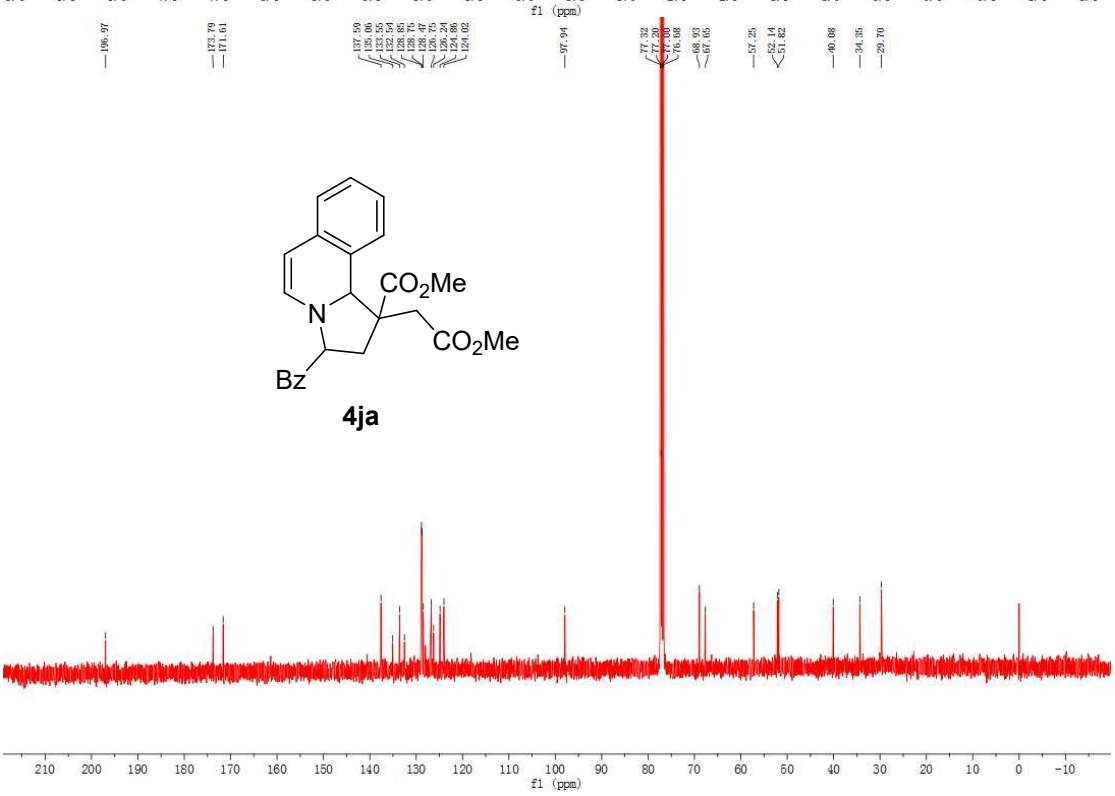
^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.04 (d, *J* = 7.1 Hz, 2H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.52 (dd, *J* = 8.2, 6.9 Hz, 2H), 7.14 (td, *J* = 7.5, 1.3 Hz, 1H), 7.02 (td, *J* = 7.5, 1.3 Hz, 1H), 6.99 – 6.90 (m, 1H), 6.86 (dd, *J* = 7.5, 1.3 Hz, 1H), 6.11 (d, *J* = 7.5 Hz, 1H), 5.33 (dd, *J* = 9.4, 5.6 Hz, 1H), 5.17 (d, *J* = 7.6 Hz, 1H), 4.57 (s, 1H), 3.64 (s, 3H), 3.36 (s, 3H), 3.29 (d, *J* = 16.9 Hz, 1H), 3.15 (dd, *J* = 13.4, 9.4 Hz, 1H), 2.56 (d, *J* = 16.9 Hz, 1H), 1.87 (dd, *J* = 13.4, 5.7 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*): δ 197.0, 173.8, 171.6, 137.6, 133.6, 132.5, 128.9, 128.8, 128.5, 126.8, 126.2, 124.9, 124.0, 97.9, 77.2, 68.9, 67.7, 57.3, 52.1, 51.8, 40.1, 34.4, 29.7.

1H, 13C NMR Spectra:

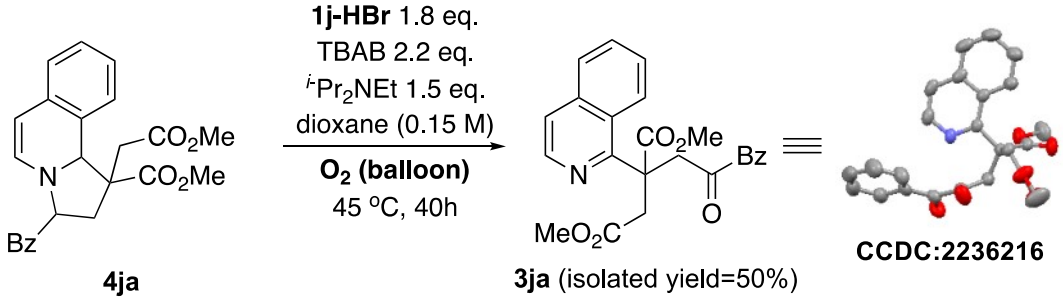


4ja



4ja

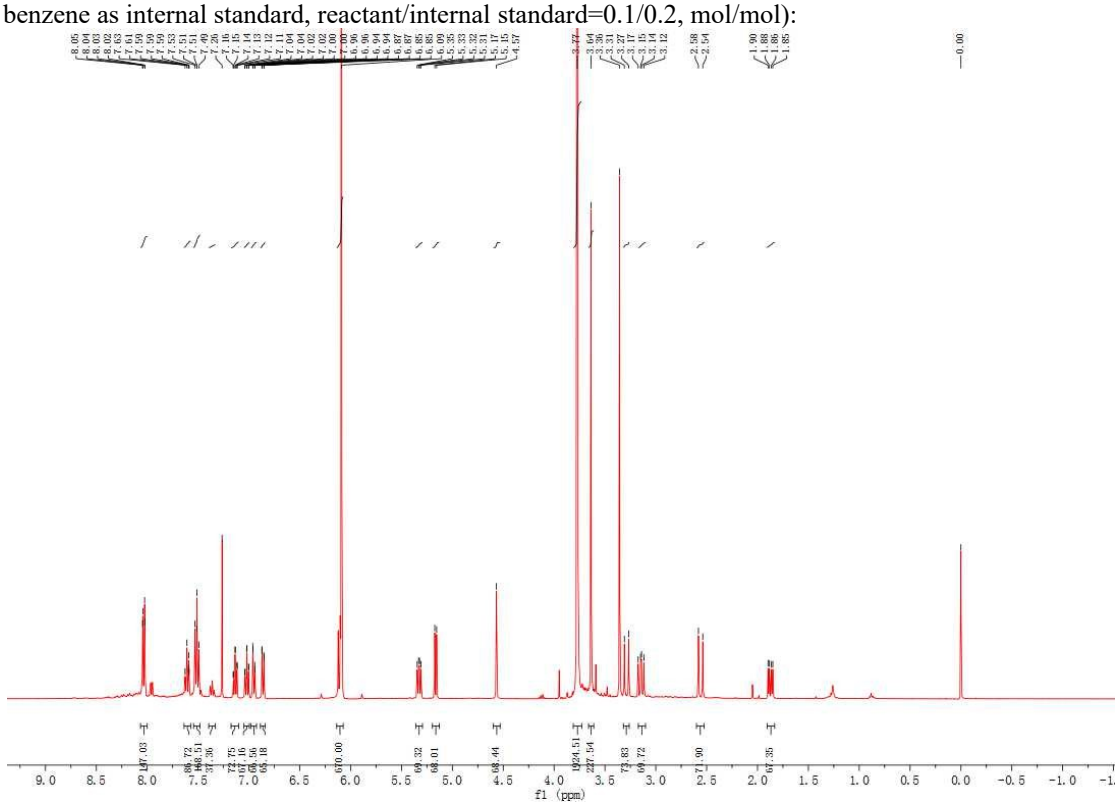
4ja to 3ja:



4ja **3ja** (isolated yield=50%) **CCDC:2236216**

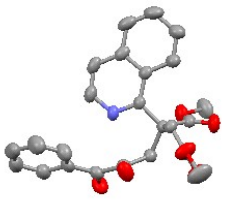
General procedure: methyl 3-benzoyl-1-(2-methoxy-2-oxoethyl)-1,2,3,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1-carboxylate **4ja** (0.3mmol, 121.5mg, 1.0eq.), 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium bromide **1j-HBr** (0.54mmol, 177.2mg, 1.8eq.), tetrabutylammonium bromide (0.66mmol, 212.8mg, 2.2eq.), and $^{i}Pr_2NEt$ (0.45mmol, 75.0μL, 1.5eq.) were added sequentially to 2.0 mL of dioxane. The reaction mixture was stirred at 45℃ for 40h under O_2 atmosphere. Then dioxane was removed and the residue was purified by column chromatography (SiO_2, hexane/EA=0:1, v/v; R_f=0.5) to afforded **3ja** as yellow oil (43.2mg, yield: 49%, based on 70% purity of **4ja**).

Note: The purity of **4ja** which used above was determined to be 70% by ^1H NMR (1,3,5-trimethoxybenzene as internal standard, reactant/internal standard=0.1/0.2, mol/mol):

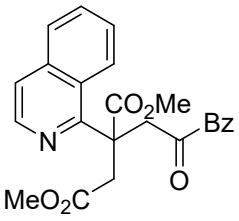


5. X-ray Information for 3ja and 4ja

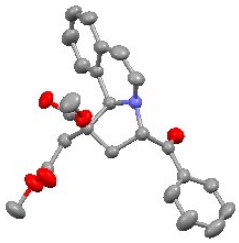
Crystals suitable of **3ja** and **4ja** for X-ray analysis could be successfully grown by slow volatilization in ethyl acetate.



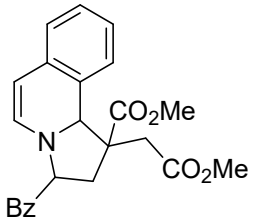
CCDC:2236216



3ja



CCDC:2236219



4ja

checkCIF/PLATON report(3ja)

Structure factors have been supplied for datablock(s) 1

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 1

Bond precision: C-C = 0.0025 A Wavelength=0.71073

Cell: a=9.4202(7) b=18.5520(13) c=12.6365(9)
alpha=90 beta=110.294(1) gamma=90

Temperature: 296 K

	Calculated	Reported
Volume	2071.3(3)	2071.3(3)
Space group	P 21/n	P2(1)/n
Hall group	-P 2yn	?
Moiety formula	C24 H21 N O6	?
Sum formula	C24 H21 N O6	C24 H21 N O6
Mr	419.42	419.42
Dx,g cm-3	1.345	1.345
Z	4	4
Mu (mm-1)	0.097	0.097
F000	880.0	880.0
F000'	880.48	
h,k,lmax	11,22,15	11,22,15
Nref	3644	3642
Tmin,Tmax	0.977,0.981	0.971,0.981
Tmin'	0.971	

Correction method= # Reported T Limits: Tmin=0.971 Tmax=0.981 AbsCorr = MULTI-SCAN

Data completeness= 0.999 Theta(max)= 25.000

R(reflections)= 0.0371(2992) wR2(reflections)= 0.0822(3642)

S = 1.001 Npar= 283

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT369_ALERT_2_C Long C(sp2)-C(sp2) Bond C7 - C8 . 1.53 Ang.

Alert level G

PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 2 Report
PLAT005_ALERT_5_G No Embedded Refinement Details Found in the CIF Please Do !
PLAT066_ALERT_1_G Predicted and Reported Tmin&Tmax Range Identical ? Check

PLAT093_ALERT_1_G No s.u.'s on H-positions, Refinement Reported as mixed Check
PLAT432_ALERT_2_G Short Inter X...Y Contact O2 ..C22 . 3.00 Ang.
1/2-x,1/2+y,1/2-z = 2_555 Check
PLAT793_ALERT_4_G Model has Chirality at C10 (Centro SPGR) S Verify
PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 13 Note
PLAT899_ALERT_4_G SHELXL97 is Deprecated and Succeeded by SHELXL- 2019/2 Note

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
1 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
8 **ALERT level G** = General information/check it is not something unexpected

2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
1 ALERT type 3 Indicator that the structure quality may be low
2 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

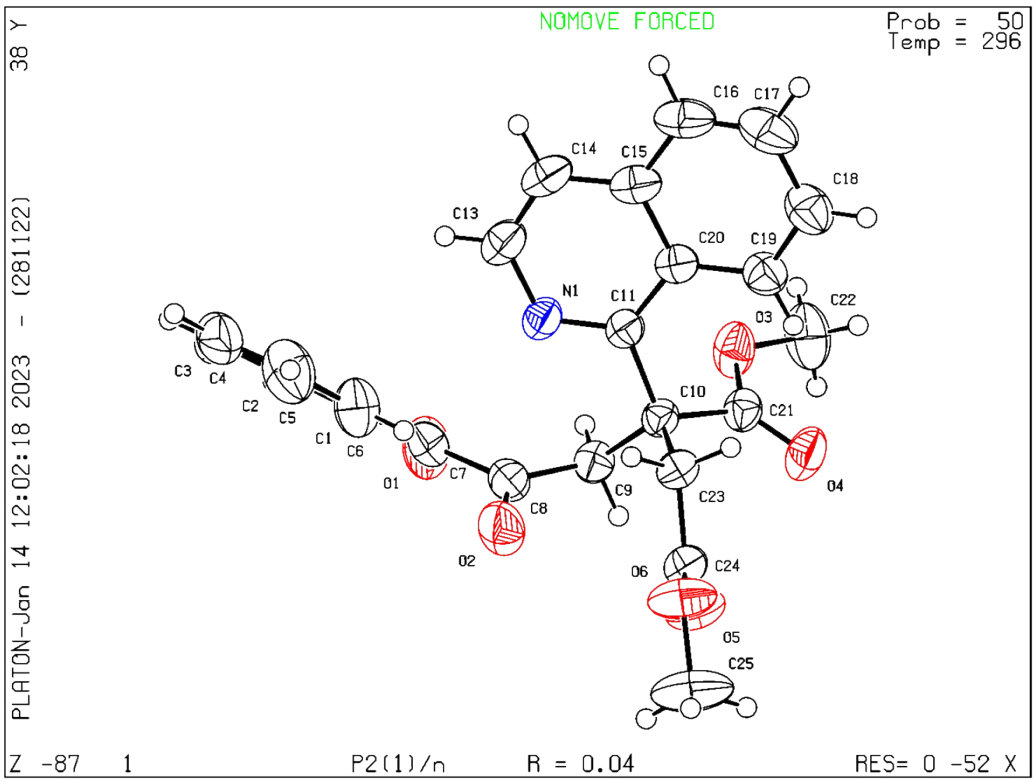
Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 28/11/2022; check.def file version of 28/11/2022
Datablock 1 - ellipsoid plot



checkCIF/PLATON report(4ja)

Structure factors have been supplied for datablock(s) 1

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: 1

Bond precision: C-C = 0.0043 A Wavelength=0.71073

Cell: a=7.713(2) b=13.434(4) c=19.831(6)
alpha=90 beta=90 gamma=90

Temperature: 296 K

	Calculated	Reported
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Hall group	P 2c -2n	?
Moiety formula	C24 H23 N O5	?
Sum formula	C24 H23 N O5	C24 H23 N O5
Mr	405.43	405.43
Dx,g cm-3	1.311	1.311
Z	4	4
Mu (mm-1)	0.092	0.092
F000	856.0	856.0
F000'	856.44	
h,k,lmax	9,16,24	9,16,24
Nref	3867[1993]	3690
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Tmin'	0.973	

Correction method= # Reported T Limits: Tmin=0.973 Tmax=0.982 AbsCorr = MULTI-SCAN

Data completeness= 1.85/0.95 Theta(max)= 25.580

R(reflections)= 0.0383(3116) wR2(reflections)= 0.1291(3690)
S = 1.001 Npar= 273

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

STRVA01_ALERT_4_C Flack test results are ambiguous.
From the CIF: _refine_ls_abs_structure_Flack 0.600
From the CIF: _refine_ls_abs_structure_Flack_su 1.300
PLAT089_ALERT_3_C Poor Data / Parameter Ratio (Zmax < 18) ..... 7.30 Note
PLAT242_ALERT_2_C Low 'MainMol' Ueq as Compared to Neighbors of C21 Check
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.00435 Ang.
PLAT907_ALERT_2_C Flack x > 0.5, Structure Needs to be Inverted? . 0.60 Check

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Alert level G

PLAT005_ALERT_5_G No Embedded Refinement Details Found in the CIF Please Do !
PLAT032_ALERT_4_G Std. Uncertainty on Flack Parameter Value High . 1.300 Report
PLAT066_ALERT_1_G Predicted and Reported Tmin&Tmax Range Identical ? Check
PLAT093_ALERT_1_G No s.u.'s on H-positions, Refinement Reported as mixed Check
PLAT792_ALERT_1_G Model has Chirality at C8 (Polar SPGR) S Verify
And 2 other PLAT792 Alerts
More ...
PLAT899_ALERT_4_G SHELXL97 is Deprecated and Succeeded by SHELXL- 2019/2 Note

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run on the final version of your CIF prior to submission.

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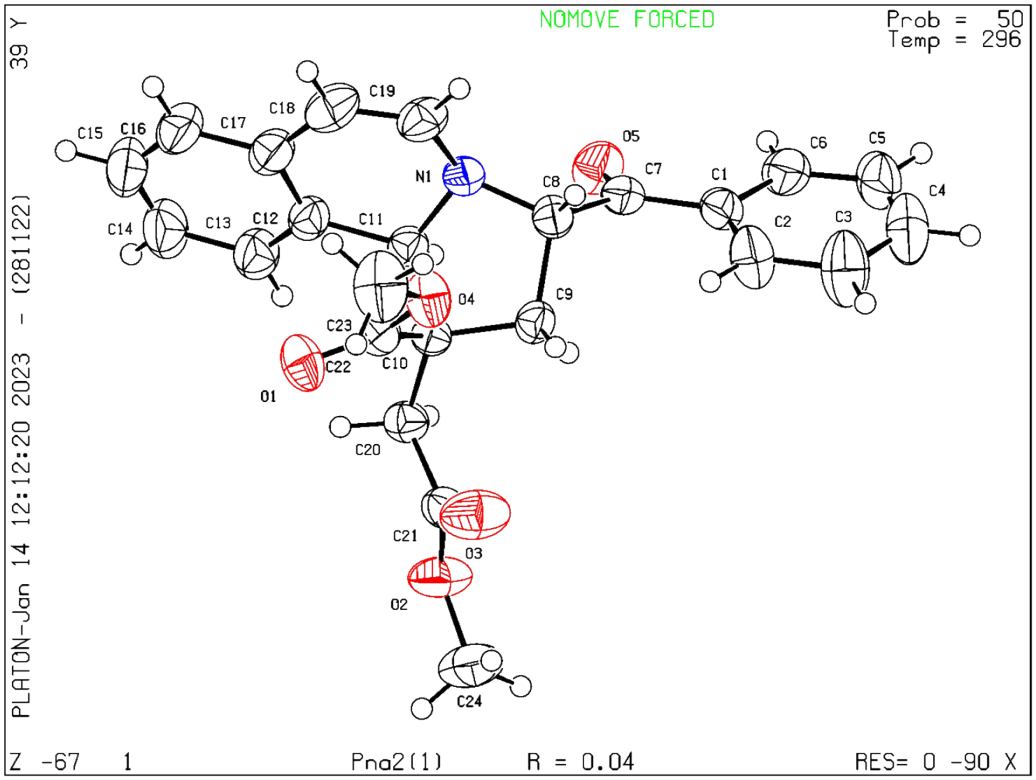
Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 28/11/2022; check.def file version of 28/11/2022
Datablock 1 - ellipsoid plot



6. Reference

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