Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Dearomatization-Rearomatization Strategy for Construction of 4*H*-Quinolizin-4-ones via C-H Bond Functionalization of Pyridines

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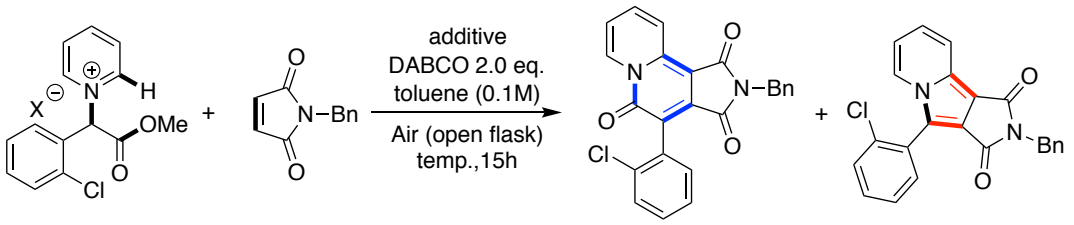
1. General Procedures and Bromide Effect

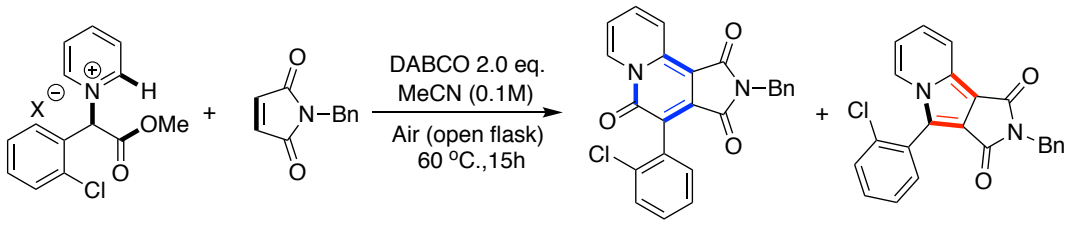
All the commercial available regents and solvents were used as received. NMR spectra were obtained with Avance TM III 400MHz instruments, the chemical shifts were quoted on the δ-scale in ppm. Multiplicities are reported as follows: singlet (s), doublet (d), triplet(t), doublet of doublets (dd), doublet 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.



1a (1.2 eq.) **2a** (0.3 mmol) **3aa** **5aa**

Entry	X	Additive	Temp.	yield (**3aa**)	yield (**5aa**)
1	PF_6	none	35 °C	0%	0%
2	Br	TBAB 5.0 eq.	35 °C	13%	28%

Scheme S1. Bromide Effect at 35 °C in toluene. [a], [b] [a] Reaction conditions: 1a (0.36 mmol), 2 (0.30 mmol), DABCO (0.60 mmol) in toluene (3.0 mL) under open-flask condition at 35 °C for 15h; [b] Yields determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard.



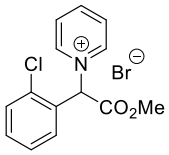
1a (1.2 eq.) **2a** (0.3 mmol) **3aa** **5aa**

Entry	X	yield (**3aa**)	yield (**5aa**)
1	PF_6	54%	n.d.
2	Br	81%	n.d.

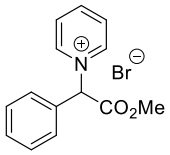
Scheme S2. Bromide Effect at 60 °C in MeCN. [a], [b] [a] Reaction conditions: 1a (0.36 mmol), 2 (0.30 mmol), DABCO (0.60 mmol) in MeCN (3.0 mL) under open-flask condition at 60 °C for 15h; [b] Yields determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard.

2. Synthesis of Pyridinium Salts and Spectra Data

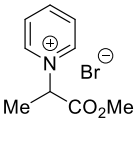
The starting materials of pyridinium salts are listed below. **1e** were prepared following reported procedures[1].



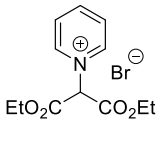
1a



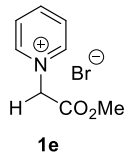
1b



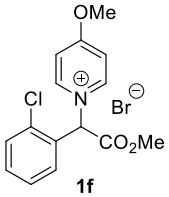
1c



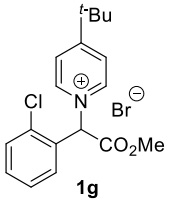
1d



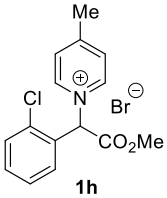
1e



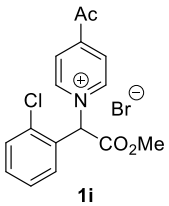
1f



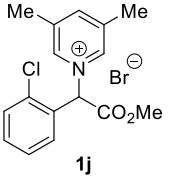
1g



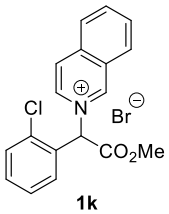
1h



1i

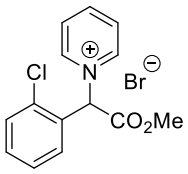


1j



1k

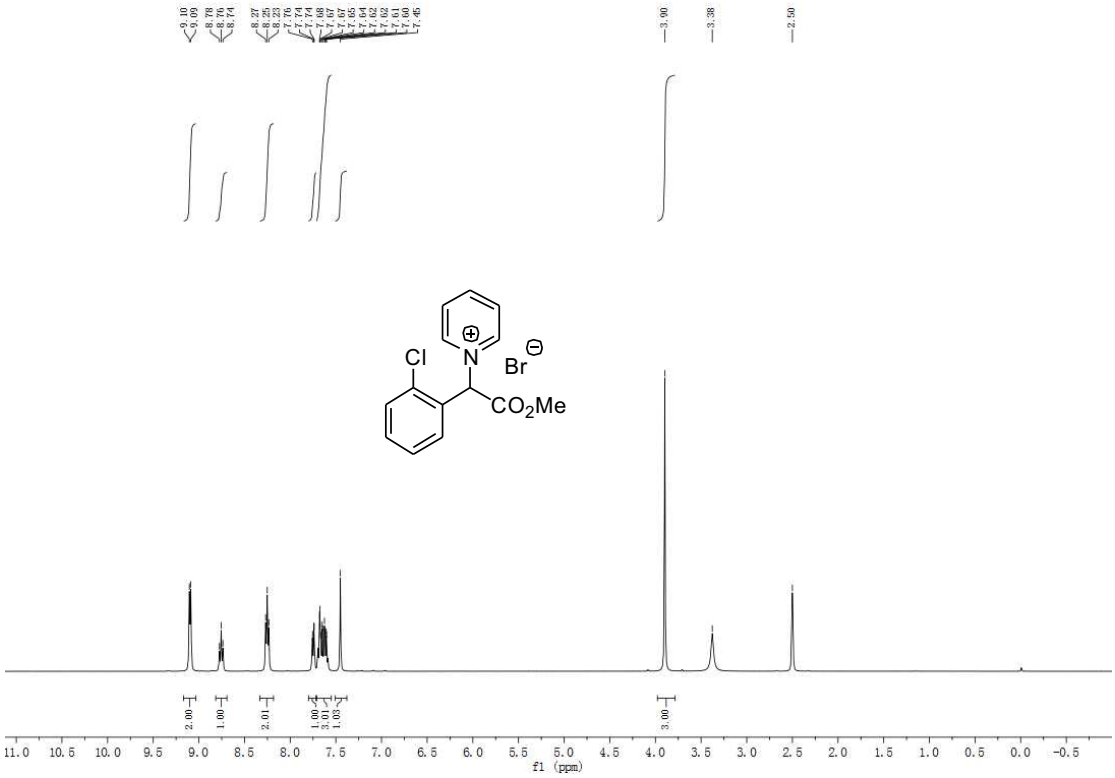
1a:
1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide

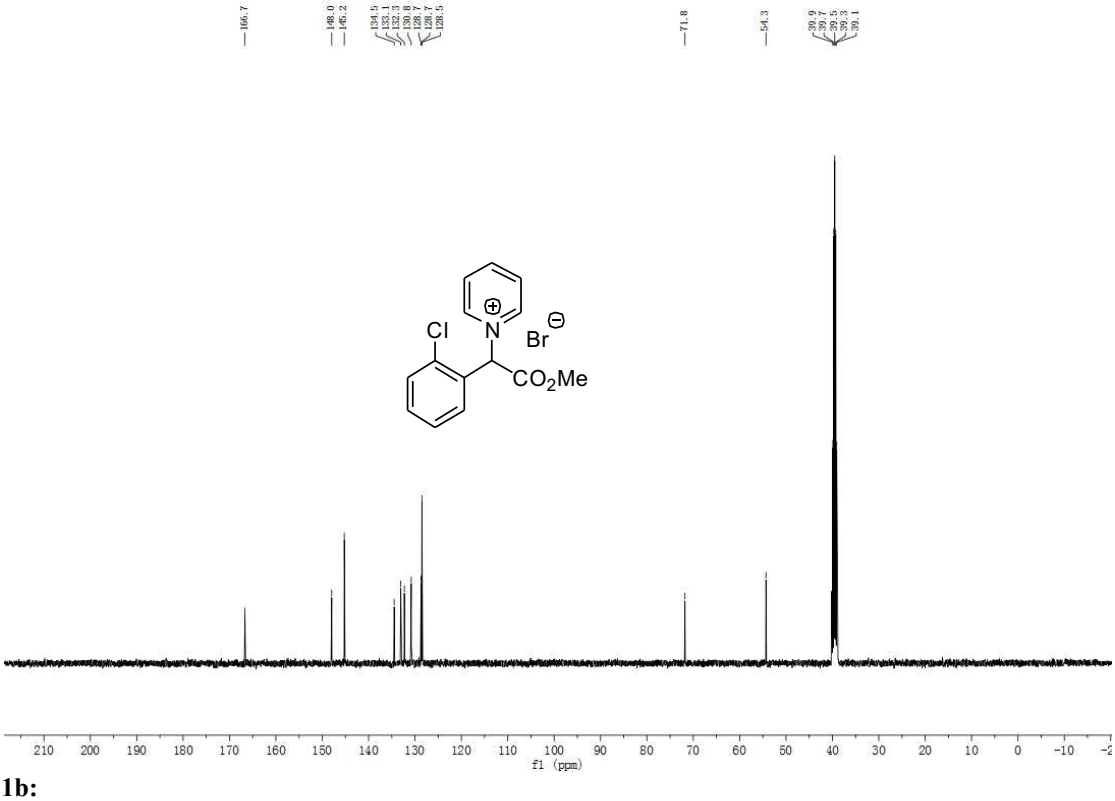


Synthesis procedure for **1a**: pyridine (5.5mmol) and ethyl methyl 2-bromo-2-(2-chlorophenyl)acetate (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 6 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1a,** as white solid (1.18g, yield=69%).

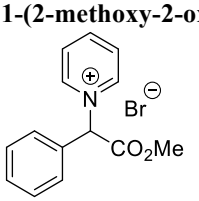
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.10 (d, J = 6.0 Hz, 2H), 8.76 (t, J = 7.8 Hz, 1H), 8.25 (t, J = 7.1 Hz, 2H), 7.80 – 7.72 (m, 1H), 7.71 – 7.55 (m, 3H), 7.45 (s, 1H), 3.90 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 166.7, 148.0, 145.2, 134.5, 133.1, 132.3, 130.8, 128.7, 128.7, 128.5, 71.8, 54.3.





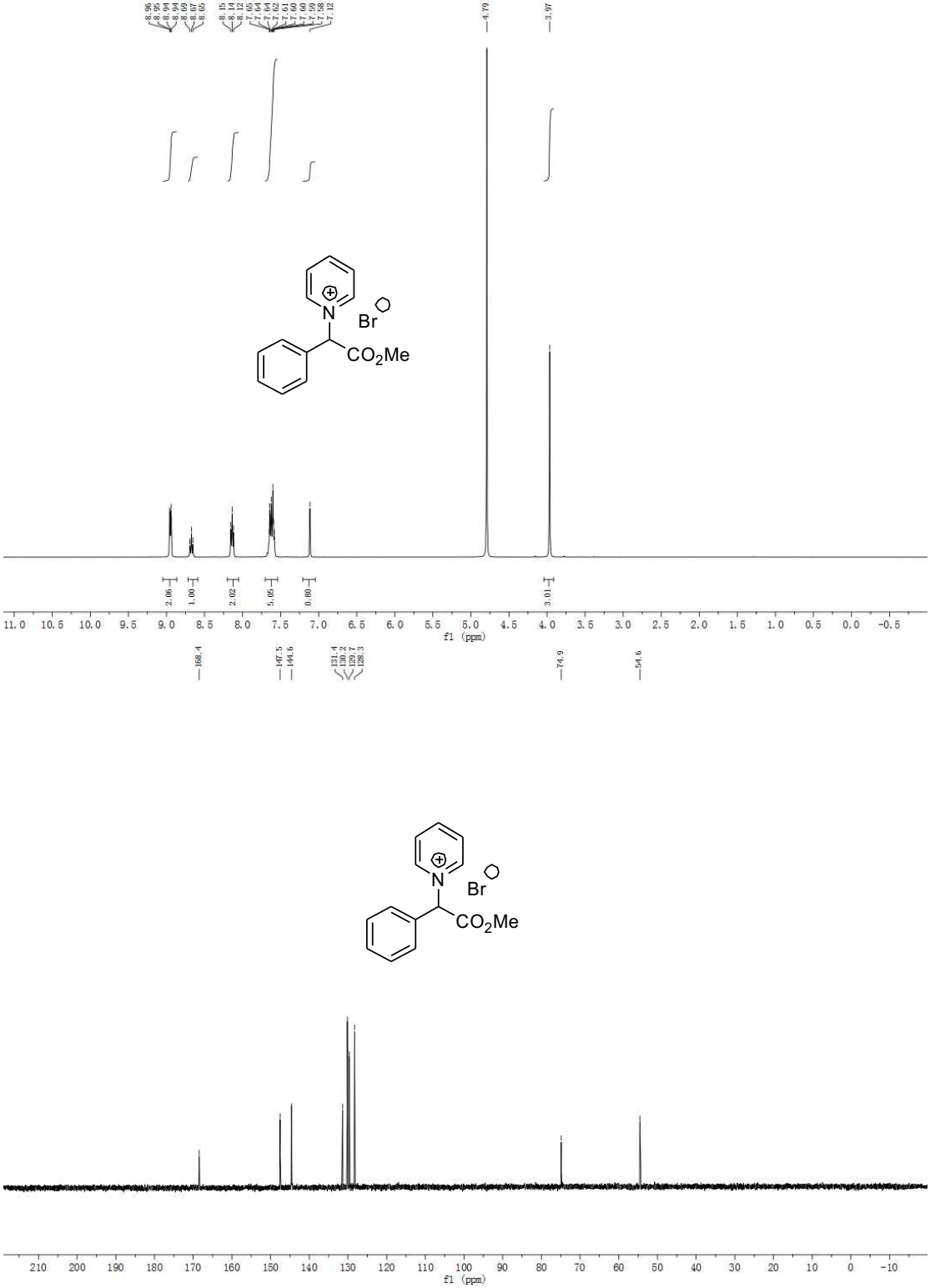
1b:
1-(2-methoxy-2-oxo-1-phenylethyl)pyridin-1-ium bromide



Synthesis procedure for **1b**: pyridine (10mmol) and methyl 2-bromo-2-phenylacetate (8mmol) were added in 4mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1b,** as white solid (1.575g, yield=64%).

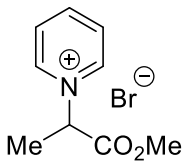
^{1}H NMR (400 MHz, Deuterium Oxide) δ 9.05 – 8.86 (m, 2H), 8.67 (t, *J* = 7.8 Hz, 1H), 8.14 (t, *J* = 7.1 Hz, 2H), 7.70 – 7.54 (m, 5H), 7.12 (s, 1H), 3.97 (s, 3H).

^{13}C NMR (101 MHz, Deuterium Oxide) δ 168.4, 147.5, 144.6, 131.4, 130.2, 129.7, 128.3, 74.9, 54.6.



1c:

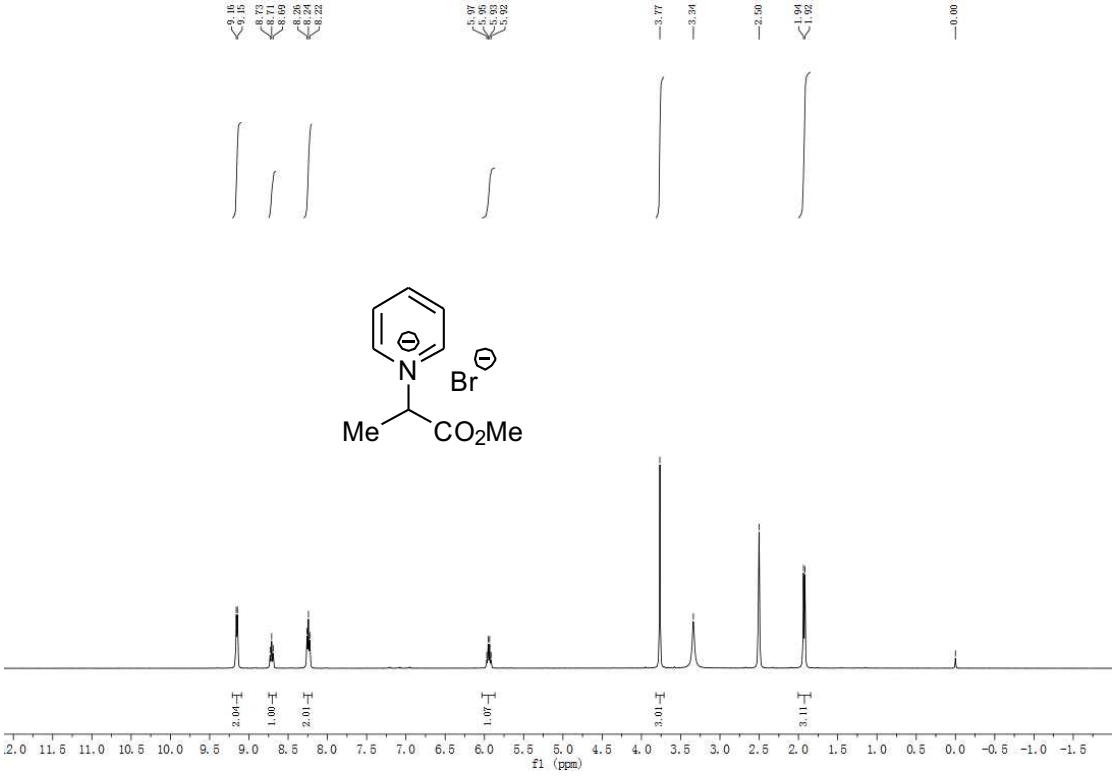
1-(1-methoxy-1-oxopropan-2-yl)pyridin-1-ium bromide

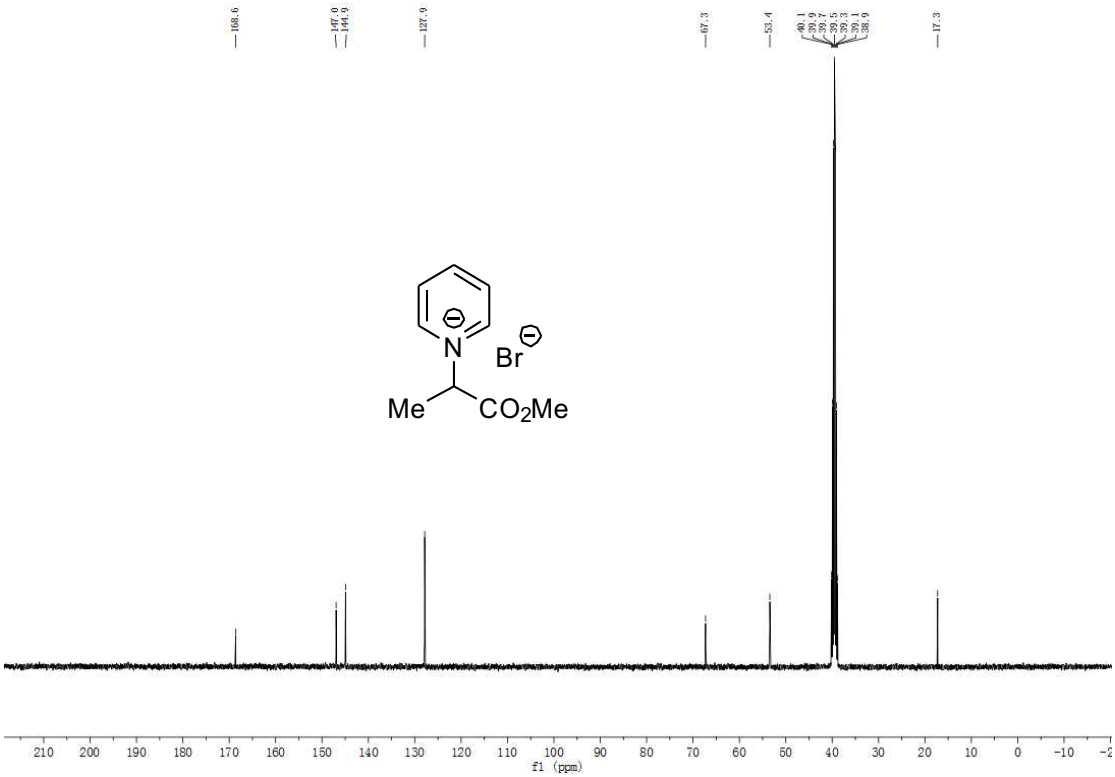


Synthesis procedure for **1c**: pyridine (10mmol) and methyl 2-bromopropanoate (8mmol) were added in 4mL of 1,4 dioxane and stirred at 35°C for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1c,** as colorless solid (1.18g, yield=60%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (d, J = 6.1 Hz, 2H), 8.71 (t, J = 7.8 Hz, 1H), 8.24 (t, J = 7.1 Hz, 2H), 5.94 (q, J = 7.3 Hz, 1H), 3.77 (s, 3H), 1.93 (d, J = 7.3 Hz, 3H).

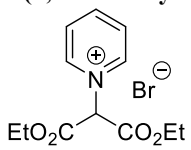
^{13}C NMR (101 MHz, DMSO-d_6) δ 168.6, 147.0, 144.9, 127.9, 67.3, 53.4, 17.3.





1d:

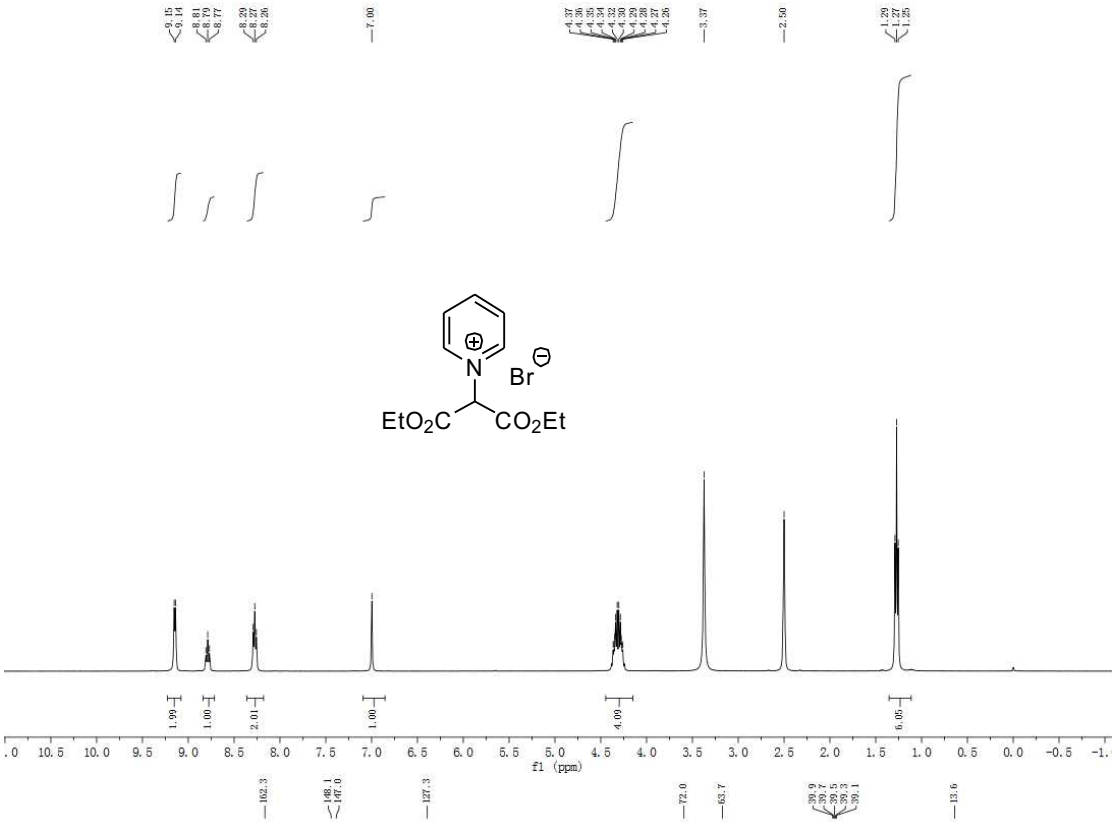
1-(1,3-diethoxy-1,3-dioxopropan-2-yl)pyridin-1-ium bromide

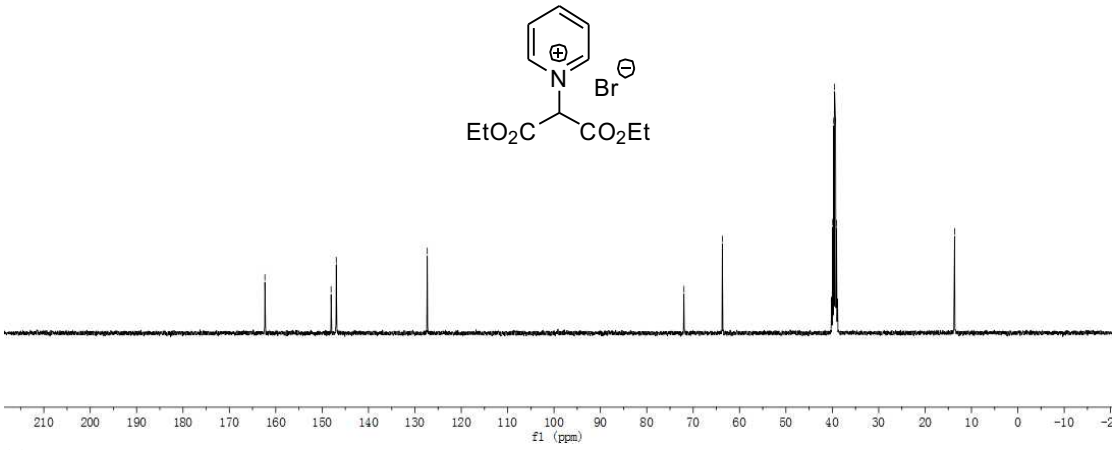


Synthesis procedure for **1d**: pyridine (12mmol) and diethyl 2-bromomalonate (10mmol) were added in 5mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1d,** as light orange solid (2.39g, yield=75%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (d, J = 6.1 Hz, 2H), 8.79 (t, J = 7.8 Hz, 1H), 8.27 (t, J = 7.1 Hz, 2H), 7.00 (s, 1H), 4.45 – 4.15 (m, 4H), 1.27 (t, J = 7.1 Hz, 6H).

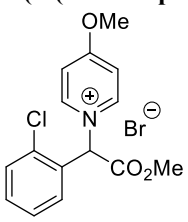
^{13}C NMR (101 MHz, DMSO-d_6) δ 162.3, 148.1, 147.0, 127.3, 72.0, 63.7, 13.6.





1f:

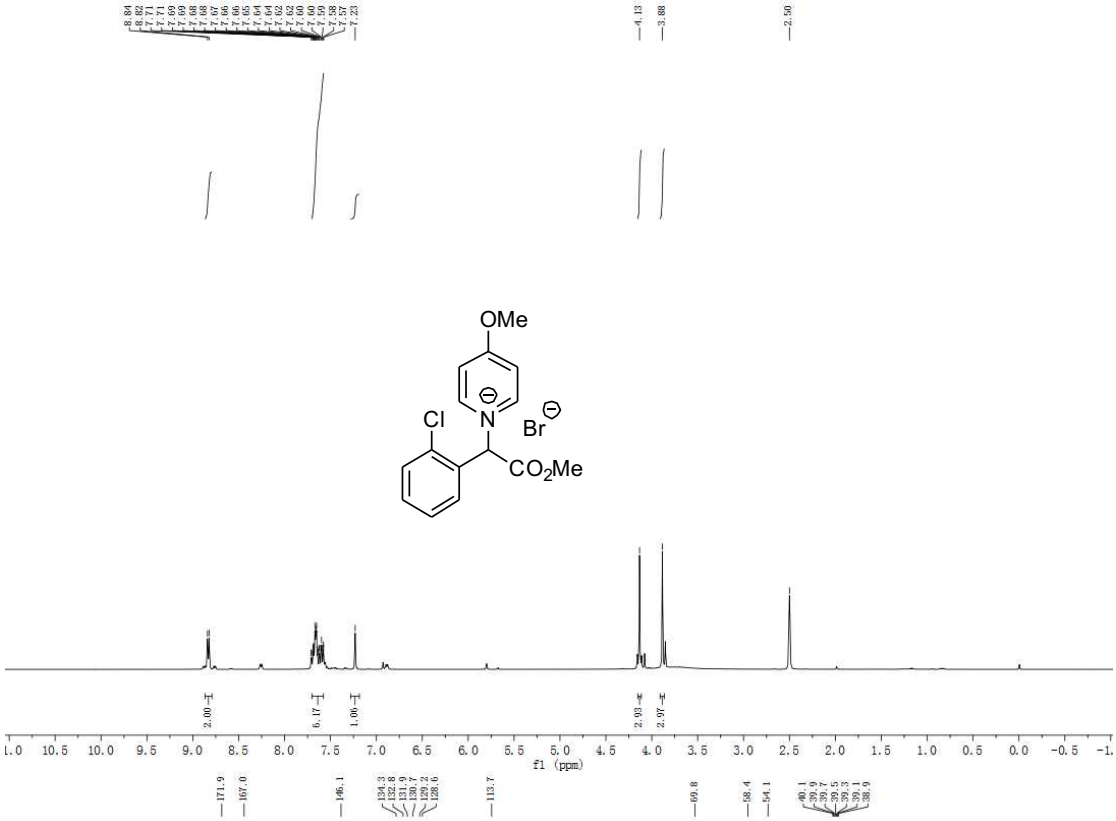
1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)-4-methoxypyridin-1-ium bromide

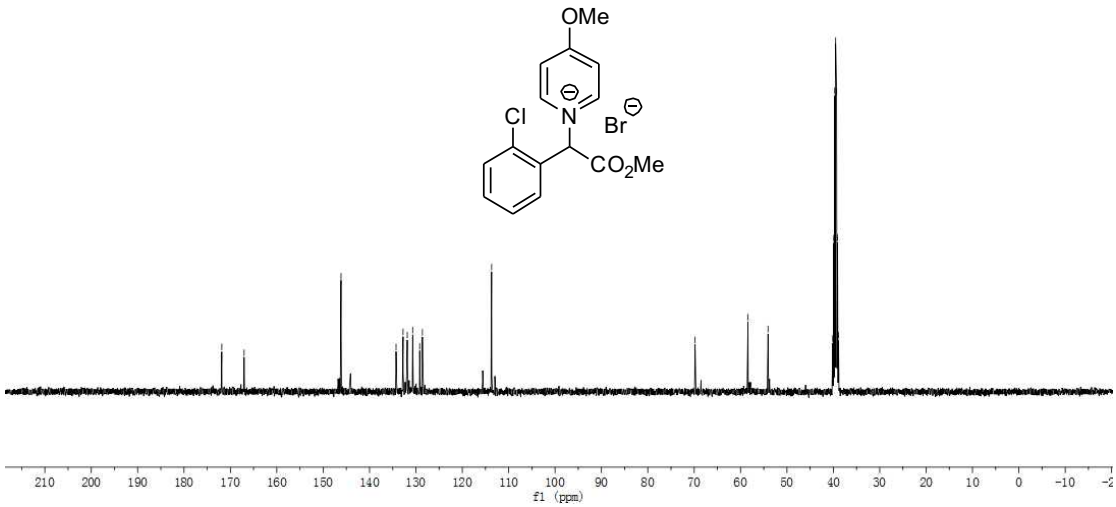


Synthesis procedure for **1f**: 4-methoxypyridine (8mmol) and methyl 2-bromo-2-(2-chlorophenyl)acetate (5mmol) were added in 4mL of ethyl acetate and stirred at room temperature for 10 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1f,** as colorless solid (1.373g, yield=74%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.83 (d, J = 7.5 Hz, 2H), 7.70 – 7.58 (m, 6H), 7.23 (s, 1H), 4.13 (s, 3H), 3.88 (s, 3H).

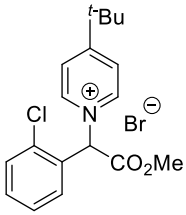
^{13}C NMR (101 MHz, DMSO-d_6) δ 171.9, 167.1, 146.2, 134.3, 132.8, 131.9, 130.7, 129.2, 128.6, 113.7, 69.81 , 58.4, 54.1.





1g:

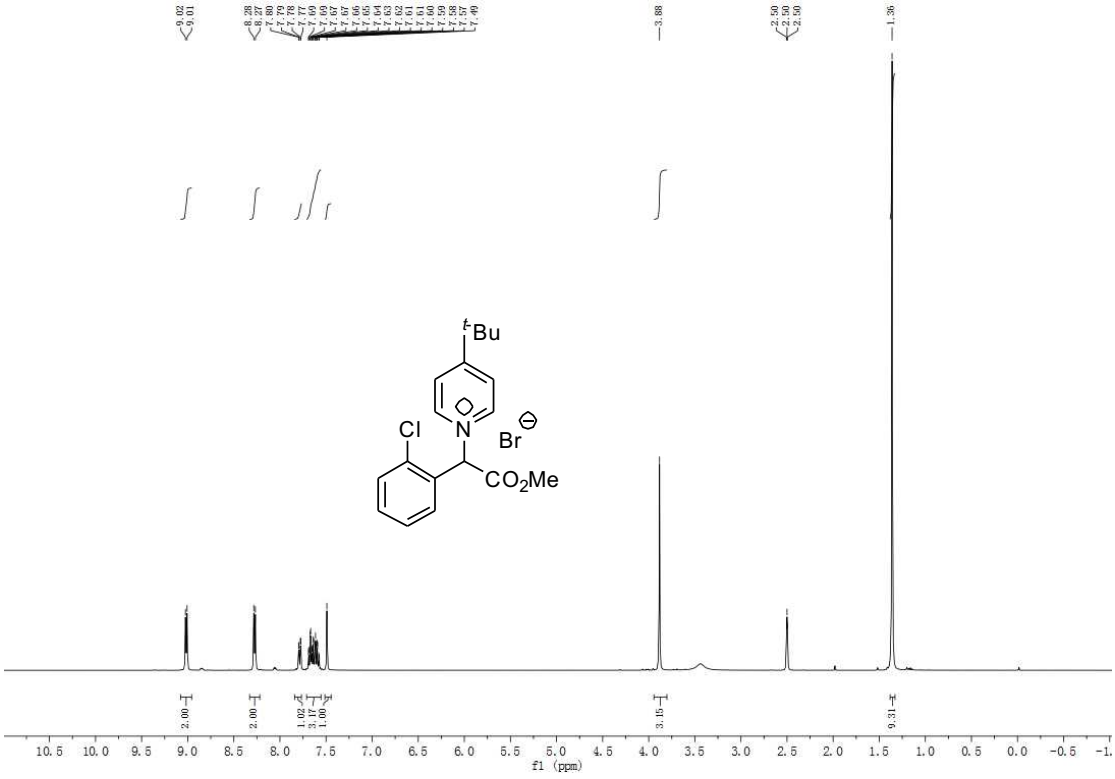
4-(tert-butyl)-1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide

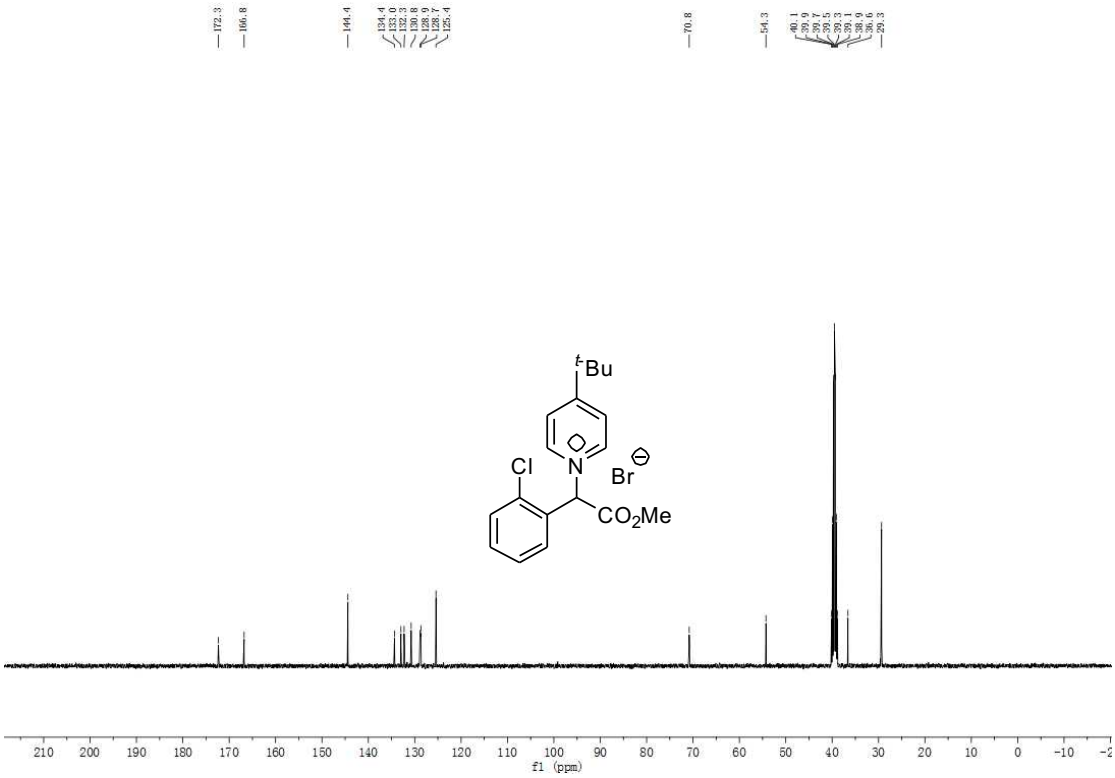


Synthesis procedure for **1g**: 4-(*tert*-butyl)pyridine (8mmol) and methyl 2-bromo-2-(2-chlorophenyl)acetate (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 8 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1g,** as white solid (1.546g, yield=78%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (d, J = 7.0 Hz, 2H), 8.28 (d, J = 7.0 Hz, 2H), 7.79 (dd, J = 7.4, 1.9 Hz, 1H), 7.71 – 7.55 (m, 3H), 7.49 (s, 1H), 3.88 (s, 3H), 1.36 (s, 9H).

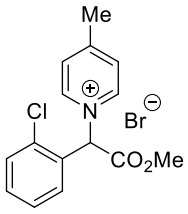
^{13}C NMR (101 MHz, DMSO-d_6) δ 172.3, 166.8, 144.4, 134.4, 133.0, 132.3, 130.8, 128.9, 128.7, 125.4, 70.8, 54.3, 36.6, 29.4.





1h:

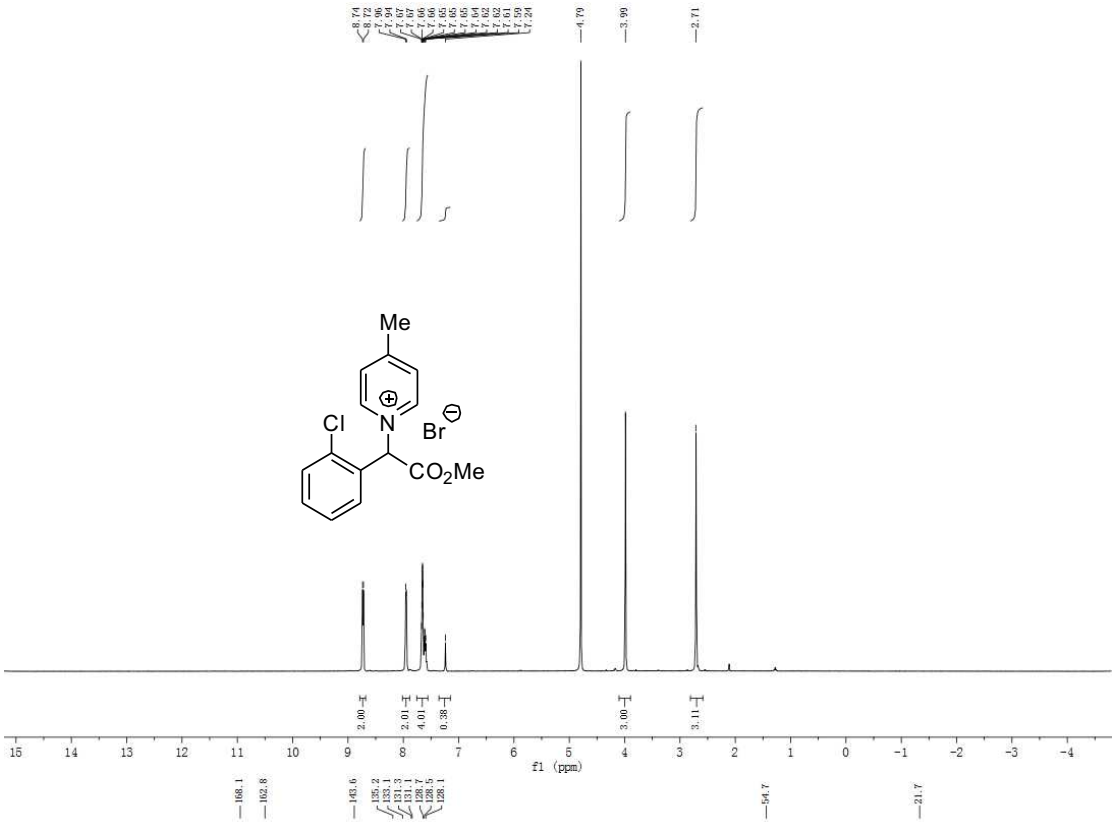
1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)-4-methylpyridin-1-ium bromide

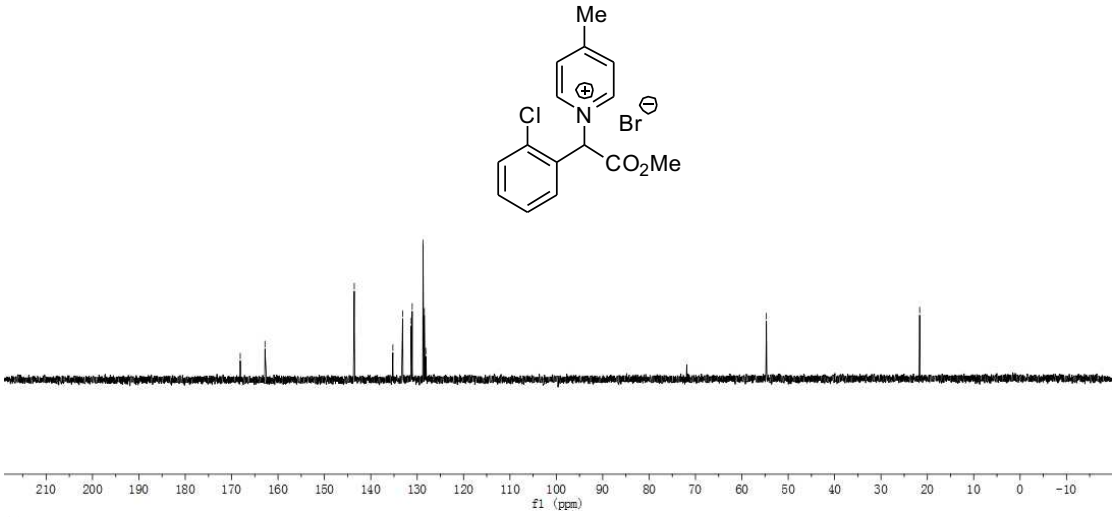


Synthesis procedure for **1h**: 4-methylpyridine (10mmol) and methyl 2-bromo-2-(2-chlorophenyl) acetate (8mmol) were added in 4mL of ethyl acetate and stirred at room temperature for 10 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1h,** as light pink solid (2.801g, yield=99%).

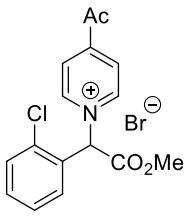
^{1}H NMR (400 MHz, Deuterium Oxide) δ 8.73 (d, *J* = 6.3 Hz, 2H), 7.95 (d, *J* = 6.3 Hz, 2H), 7.76 – 7.56 (m, 4H), 7.24 (s, 1H), 3.99 (s, 3H), 2.71 (s, 3H).

^{13}C NMR (101 MHz, Deuterium Oxide) δ 168.2, 162.8, 143.6, 135.2, 133.1, 131.3, 131.1, 128.7, 128.5, 128.1, 54.7, 21.7.





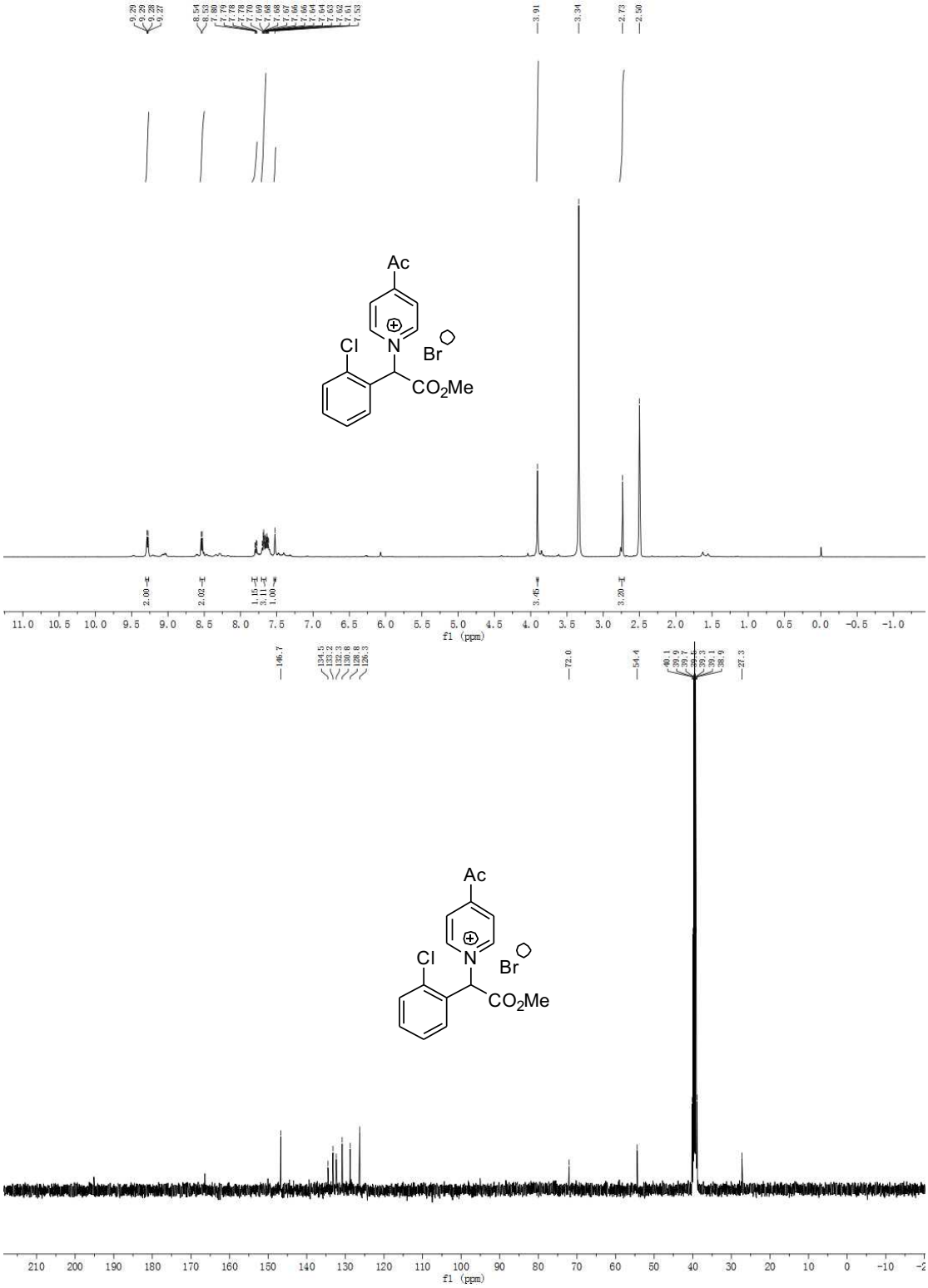
1i:
4-acetyl-1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide



Synthesis procedure for **1i**: 1-(pyridin-4-yl)ethan-1-one (8mmol) and methyl 2-bromo-2-(2-chlorophenyl)acetate (9mmol) were added in 4mL of ethyl acetate and stirred at room temperature for 10 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1i,** as brown solid (1.173g, yield=38%).

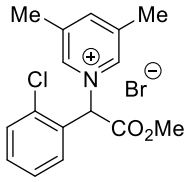
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.31 – 9.27 (m, 2H), 8.53 (d, J = 6.7 Hz, 2H), 7.79 (dd, J = 7.4, 1.9 Hz, 1H), 7.71 – 7.65 (m, 3H), 7.53 (s, 1H), 3.91 (s, 3H), 2.73 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 146.7, 134.5, 133.2, 132.3, 130.8, 128.8, 126.3, 72.0, 54.4, 27.3.



1j:

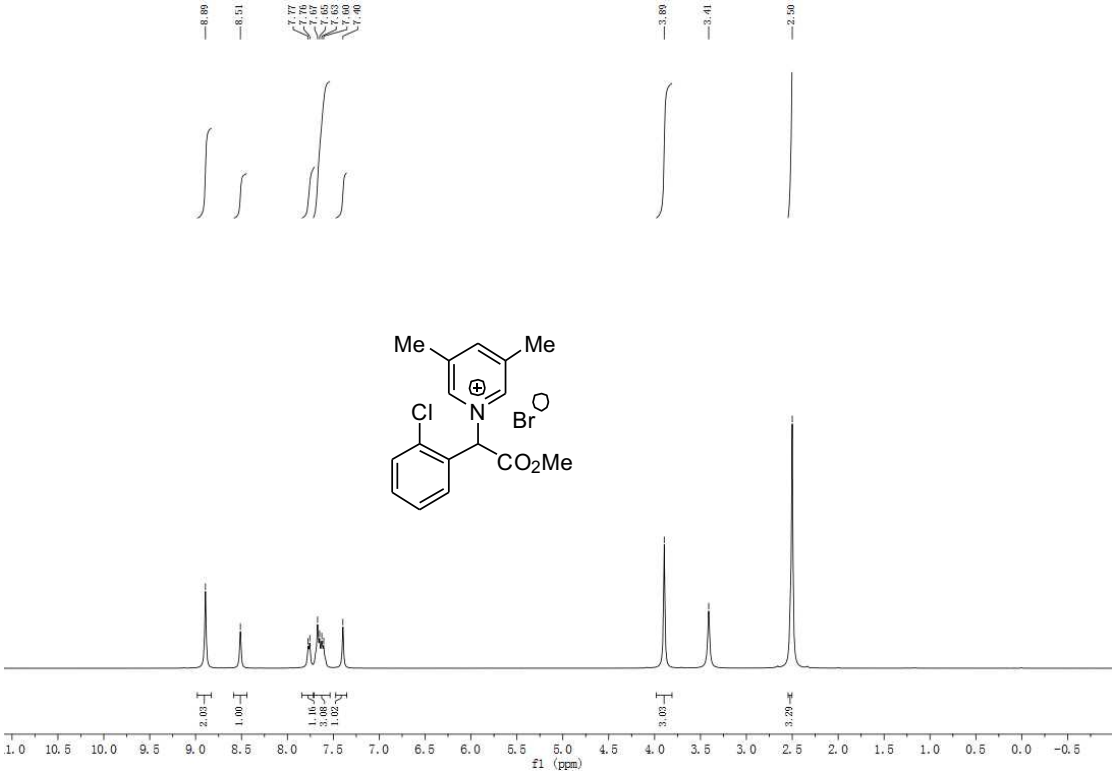
1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)-3,5-dimethylpyridin-1-ium bromide

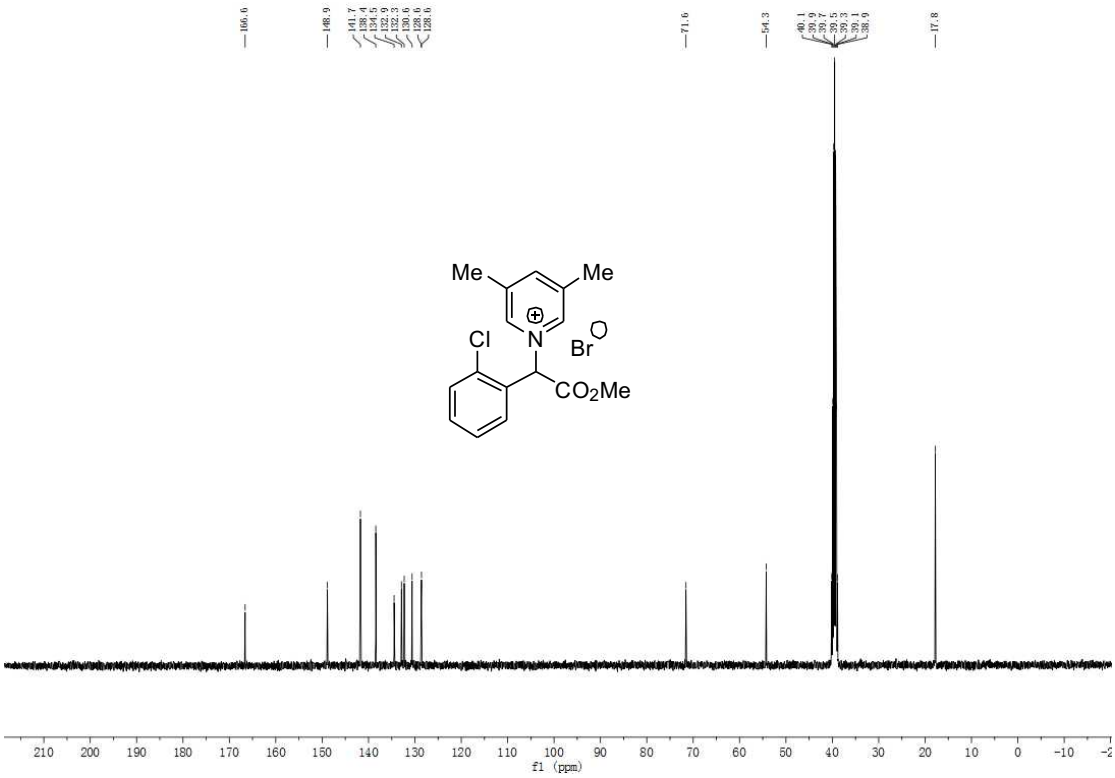


Synthesis procedure for **1j**: 3,5-dimethylpyridine (8mmol) and methyl 2-bromo-2-(2-chlorophenyl)acetate (5mmol) were added in 3mL of ethyl acetate and stirred at room temperature for 10 hours. Then the resulting precipitate was filtered and washed with ethyl acetate to afford **1j,** as brown solid (1.686g, yield=91%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.89 (s, 2H), 8.51 (s, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.72 – 7.54 (m, 3H), 7.40 (s, 1H), 3.89 (s, 3H), 2.51 (s, 3H).

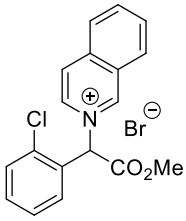
^{13}C NMR (101 MHz, DMSO-d_6) δ 166.6, 148.9, 141.7, 138.4, 134.5, 132.9, 132.3, 130.6, 128.6, 128.6, 71.6, 54.3, 17.8.





1k:

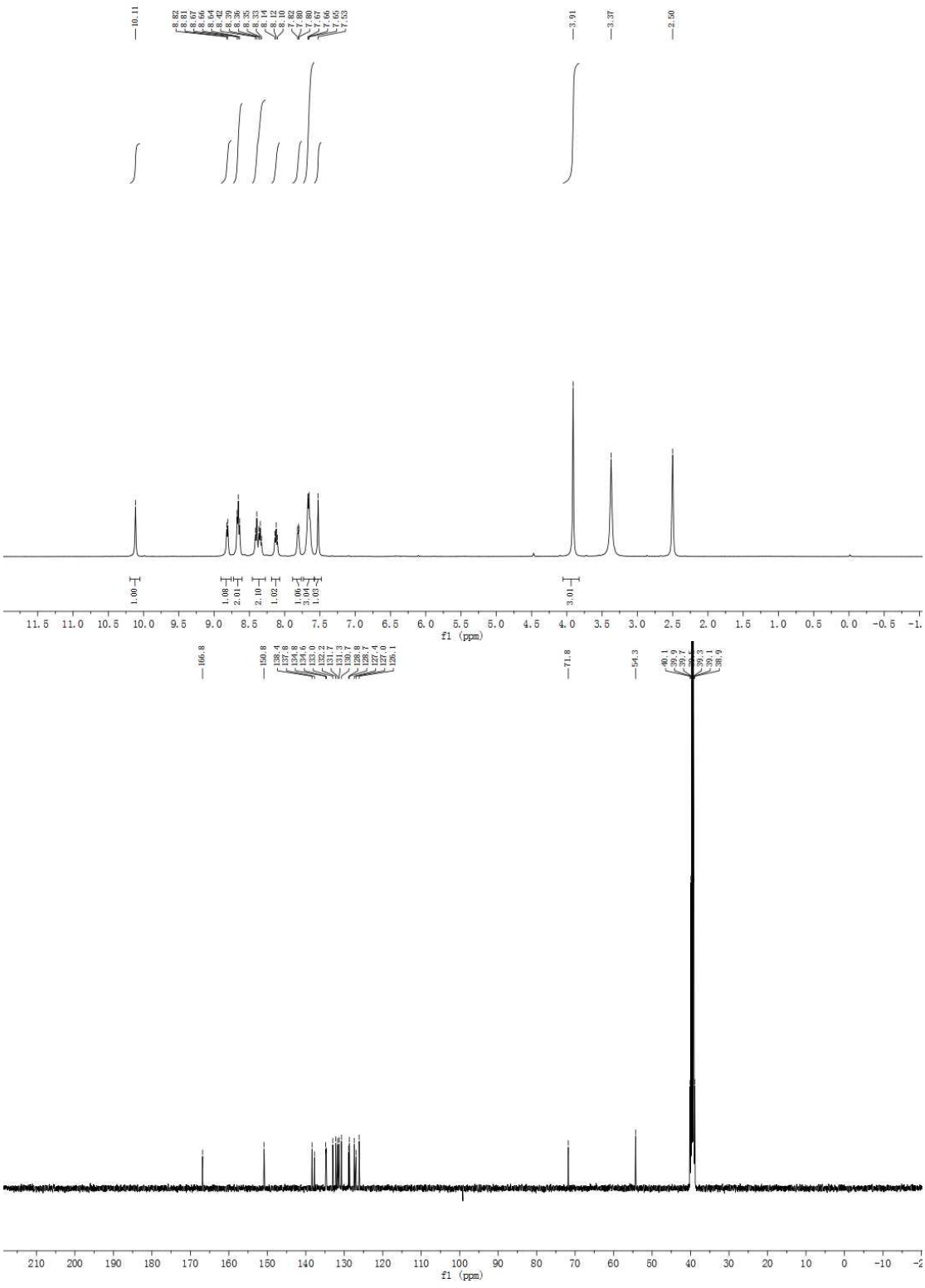
2-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)isoquinolin-2-ium bromide



Synthesis procedure for **1k**: isoquinoline (8mmol) and methyl 2-bromo-2-(2-chlorophenyl)acetate (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 **1k,** as orange solid (1.928g, yield=98%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.81 (d, J = 6.9 Hz, 1H), 8.66 (t, J = 7.2 Hz, 2H), 8.46 – 8.27 (m, 2H), 8.12 (t, J = 7.6 Hz, 1H), 7.89 – 7.76 (m, 1H), 7.73 – 7.58 (m, 3H), 7.53 (s, 1H), 3.91 (s, 3H).

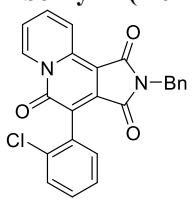
^{13}C NMR (101 MHz, DMSO-d_6) δ 166.8, 150.8, 138.4, 137.8, 134.8, 134.6, 133.0, 132.2, 131.7, 131.3, 130.7, 128.8, 128.7, 127.4, 127.0, 126.1, 71.8, 54.3.


10.11
8.82
8.81
8.67
8.66
8.54
8.42
8.39
8.36
8.35
8.33
8.14
8.12
8.10
7.82
7.80
7.80
7.67
7.66
7.65
7.63
3.91
3.37
2.50
1.00
1.08
2.01
2.10
1.02
1.06
3.04
1.03
3.01
f1 (ppm)
166.8
150.8
138.4
137.8
134.8
134.6
132.0
132.2
131.7
131.3
130.7
128.8
128.7
127.4
127.0
126.1
71.8
54.3
40.1
39.9
39.7
39.5
39.3
39.1
38.9
f1 (ppm)

3. Synthesis of Products and Spectra Data

3aa:

2-benzyl-4-(2-chlorophenyl)pyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

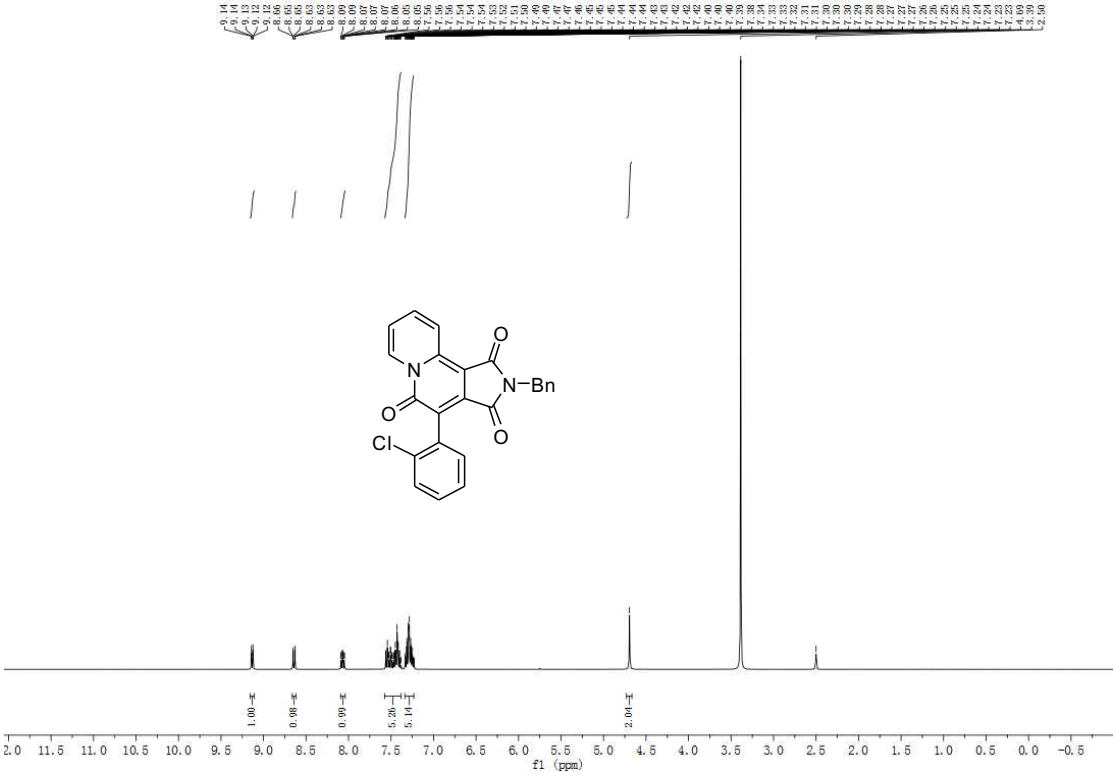


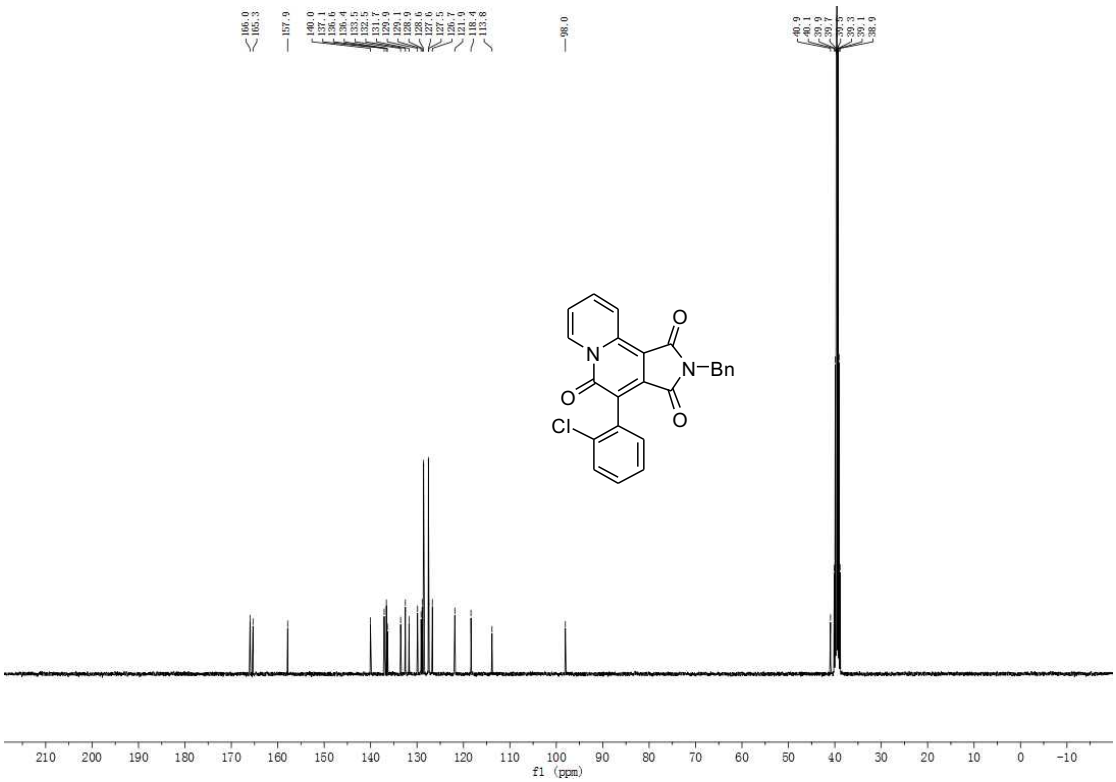
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; R_f=0.4) to afford compound **3aa** (yellow solid, m.p=87-89^{o}C, 117.1mg, yield=94%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{24}H_{16}ClN_2O_3$, 415.0844; found, 415.0842.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 – 9.11 (m, 1H), 8.64 (dt, J = 8.8, 1.2 Hz, 1H), 8.07 (ddd, J = 8.9, 6.8, 1.3 Hz, 1H), 7.57 – 7.38 (m, 5H), 7.34 – 7.23 (m, 5H), 4.69 (s, 2H).

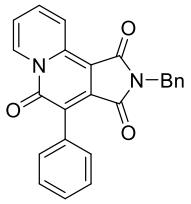
^{13}C NMR (101 MHz, DMSO-d_6) δ 166.0, 165.3, 157.9, 140.0, 137.1, 136.6, 133.5, 132.5, 131.7, 129.9, 129.1, 128.9, 128.6, 127.6, 127.5, 126.7, 121.9, 118.4, 98.1, 40.9.





3ba:

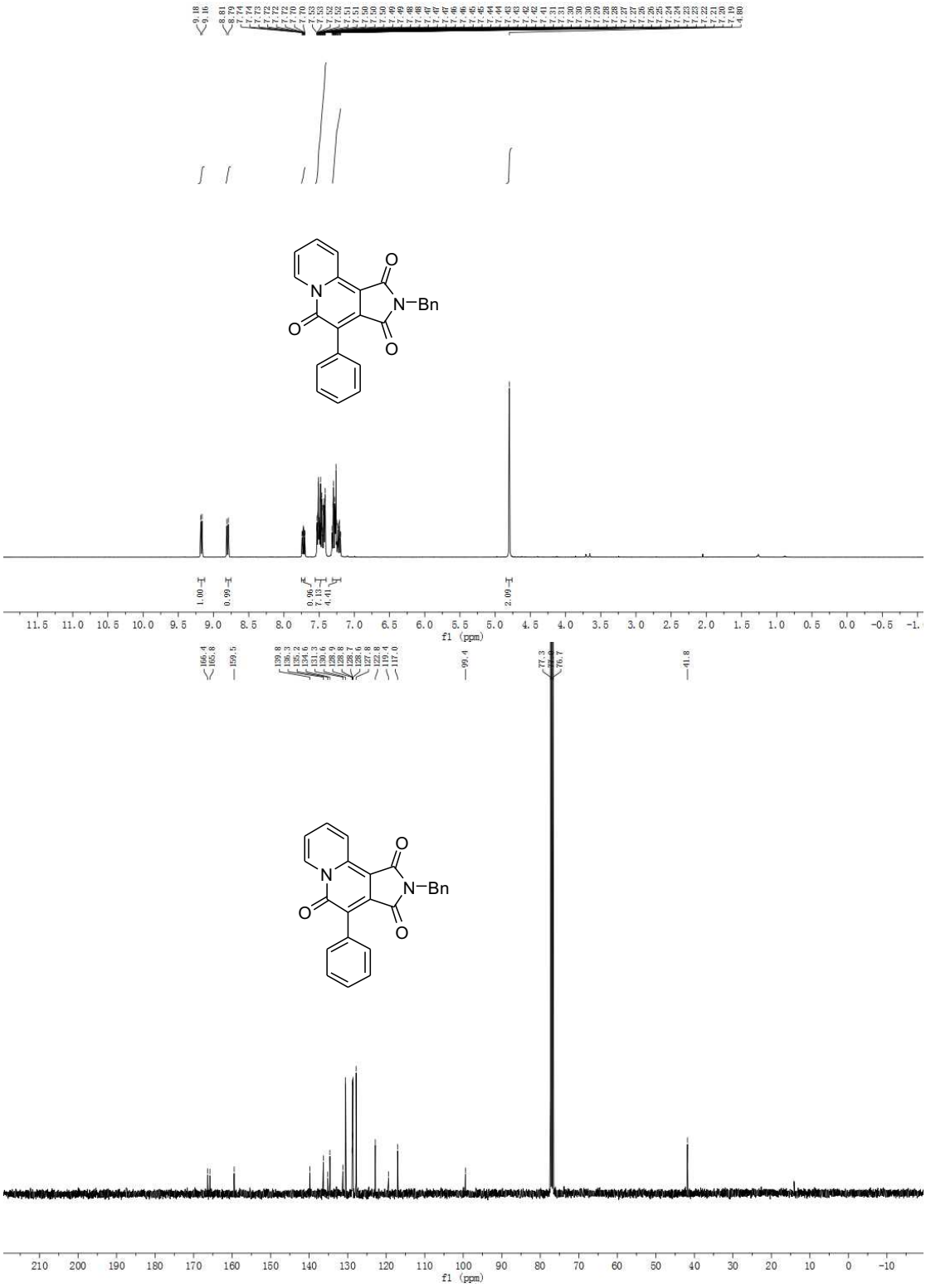
2-benzyl-4-phenylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



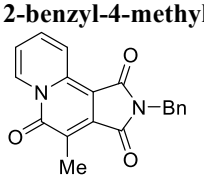
General procedure: 1-(2-methoxy-2-oxo-1-phenylethyl)pyridin-1-ium bromide **1b** (0.36mmol, 111.0mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.4) to afford compound **3ba** (yellow solid, m.p=109-111^{o}C, 89.2mg, yield=78%). HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{24}H_{17}N_2O_3$, 381.1234; found, 381.1234.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (d, *J* = 7.3 Hz, 1H), 8.80 (d, *J* = 8.9 Hz, 1H), 7.72 (ddd, *J* = 9.0, 6.7, 1.3 Hz, 1H), 7.55 – 7.40 (m, 7H), 7.31 – 7.19 (m, 4H), 4.80 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.4, 165.8, 159.5, 139.9, 136.3, 135.2, 134.6, 131.3, 130.6, 128.9, 128.8, 128.7, 128.6, 127.8, 122.8, 119.4, 117.0, 99.4, 41.8.



3ca:
2-benzyl-4-methylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



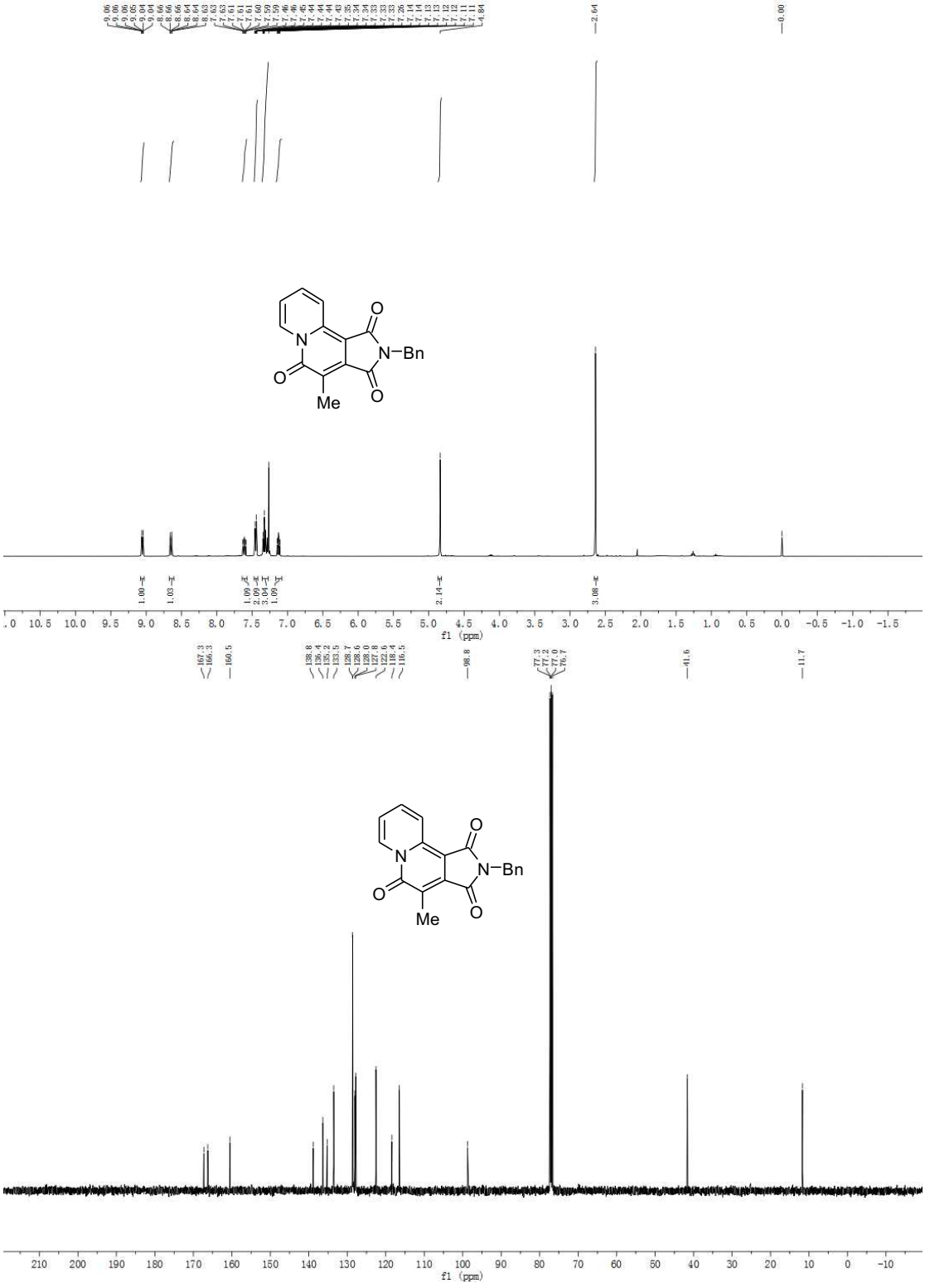
General procedure: 1-(1-methoxy-1-oxopropan-2-yl)pyridin-1-ium bromide **1c** (0.36mmol, 88.6mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2] octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of CH_3CN. The mixture

was stirred at 60°C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.45) to afford compound **3ca** (yellow solid, m.p=195-197°C, 56.2mg, yield=59%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{19}H_{15}N_2O_3$, 319.1077; found, 319.1074.

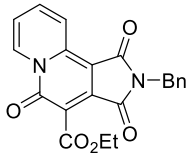
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.05 (dt, *J* = 7.4, 1.1 Hz, 1H), 8.65 (dt, *J* = 9.0, 1.1 Hz, 1H), 7.61 (ddd, *J* = 9.0, 6.6, 1.3 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.36 – 7.27 (m, 3H), 7.13 (ddd, *J* = 7.4, 6.6, 1.5 Hz, 1H), 4.84 (s, 2H), 2.64 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 166.3, 160.5, 138.8, 136.4, 135.2, 133.5, 128.7, 128.6, 128.0, 127.8, 122.6, 118.4, 116.5, 98.8, 77.2, 41.6, 11.7.



3da:

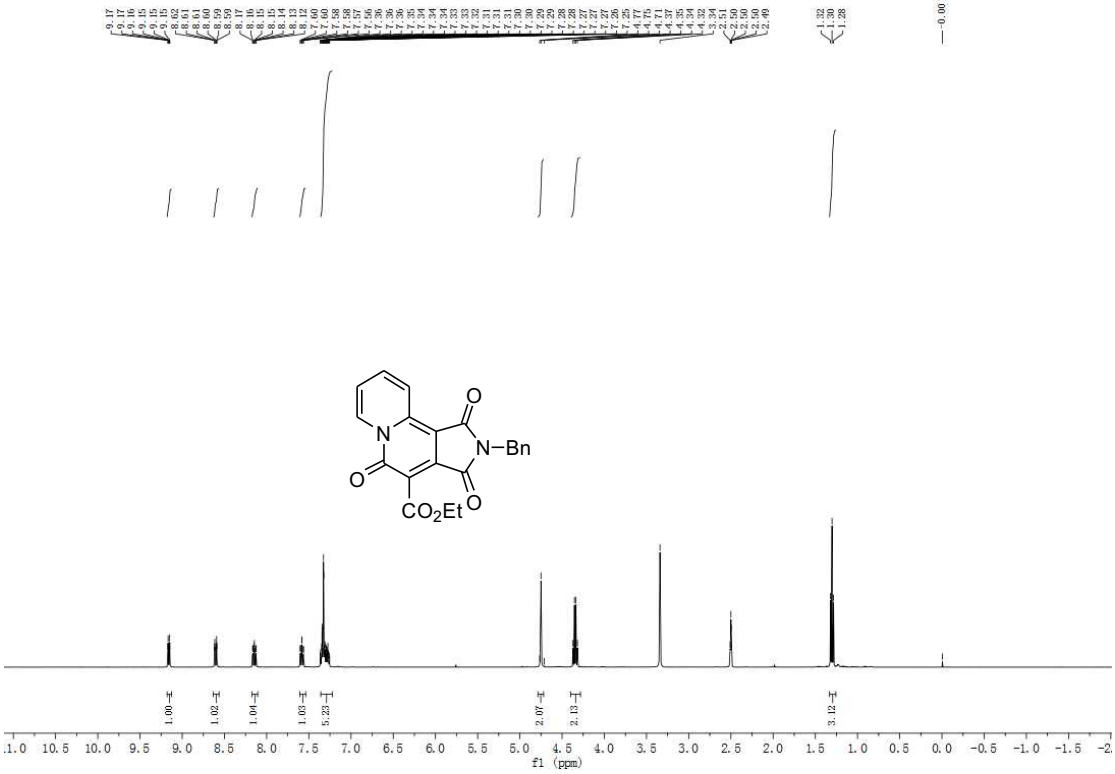
ethyl 2-benzyl-1,3,5-trioxo-1,2,3,5-tetrahydropyrrolo[3,4-a]quinolizine-4-carboxylate

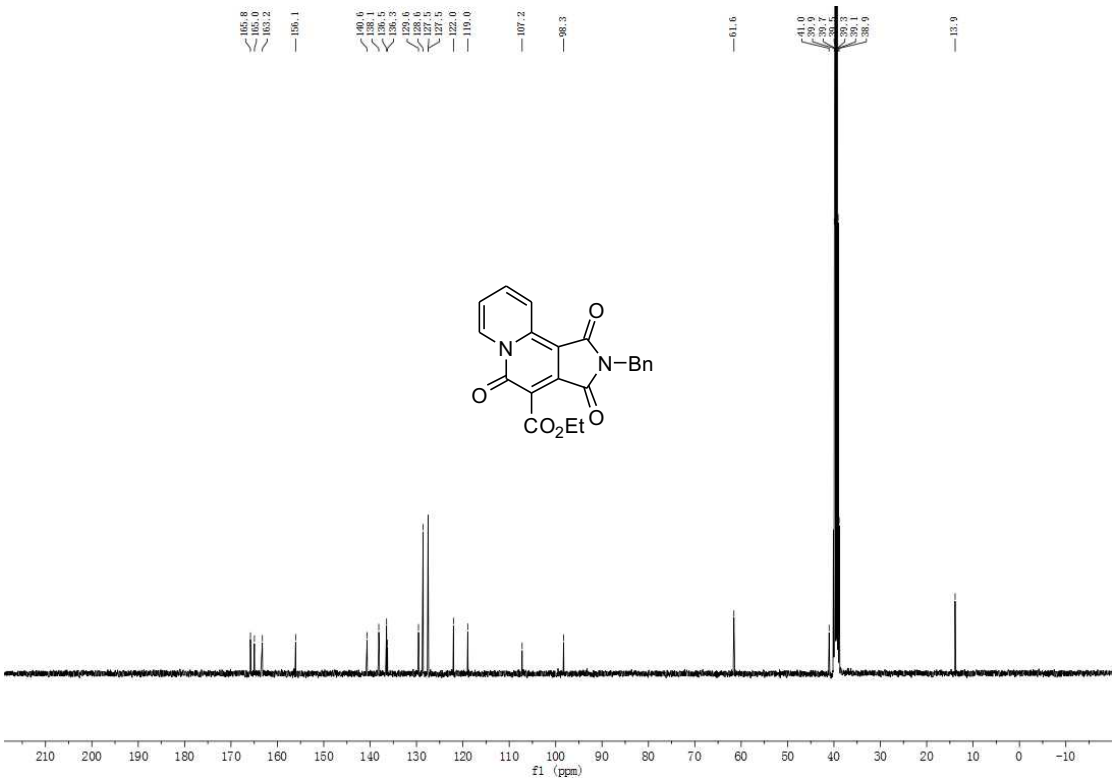


General procedure: 1-(1,3-diethoxy-1,3-dioxopropan-2-yl)pyridin-1-ium bromide **1d** (0.36mmol, 114.6mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.5) to afford compound **3da** (yellow solid, m.p=169-171^{o}C, 57.2mg, yield=51%). HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{21}H_{17}N_2O_5$, 377.1132; found, 377.1124.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 (dt, J = 7.2, 1.1 Hz, 1H), 8.60 (dt, J = 8.8, 1.2 Hz, 1H), 8.14 (ddd, J = 8.7, 6.9, 1.3 Hz, 1H), 7.58 (td, J = 7.0, 1.5 Hz, 1H), 7.36 – 7.22 (m, 5H), 4.75 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H).

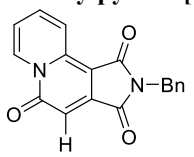
^{13}C NMR (101 MHz, DMSO-d_6) δ 165.8, 165.0, 163.2, 156.1, 140.7, 138.1, 136.5, 136.3, 129.6, 128.6, 127.51 , 127.5, 122.0, 119.0, 107.2, 98.3, 61.6, 41.0, 13.9.





3ea:

2-benzylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

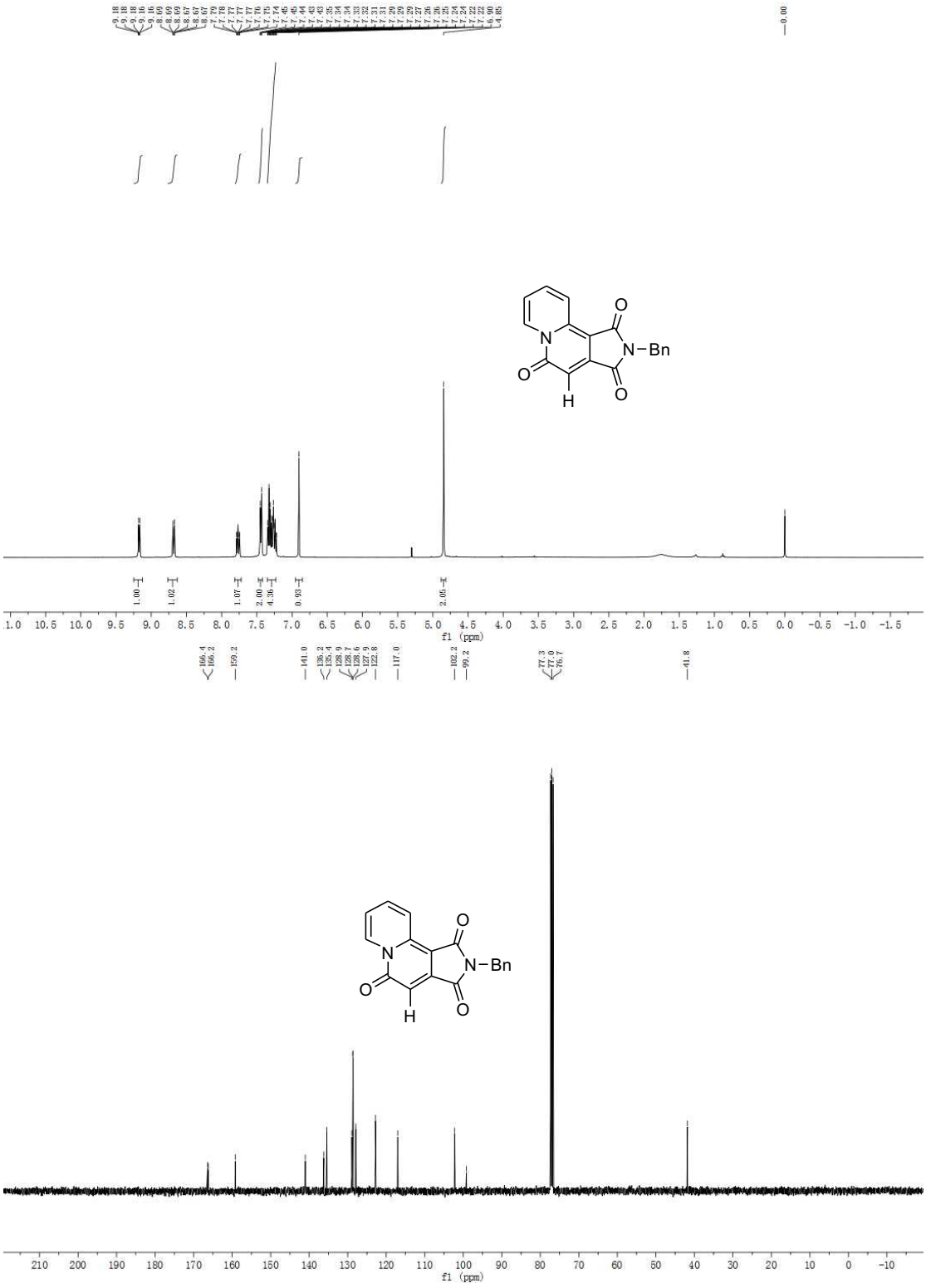


General procedure: 1-(2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1e** (0.36mmol, 83.6mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 2,2,6,6-Tetramethylpiperidoxyl (TEMPO, 0.6mmol, 93.8mg, 2.0equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.6mmol, 90.0μL, 2.0equiv) were added sequentially to 3.0mL of CH_3CN. The mixture was stirred at 80°C for 15h in N_2 atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.4) to afford compound **3ea** (yellow solid, m.p=171-174°C, 14.1mg, yield=15%).

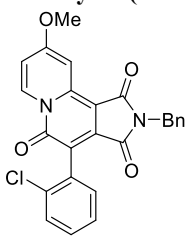
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{18}H_{13}N_2O_3$, 305.0921; found, 305.0912.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (dd, *J* = 7.4, 1.1 Hz, 1H), 8.68 (dt, *J* = 8.9, 1.2 Hz, 1H), 7.77 (ddd, *J* = 8.9, 6.7, 1.4 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.35 – 7.23 (m, 4H), 6.90 (s, 1H), 4.85 (s, 2H).

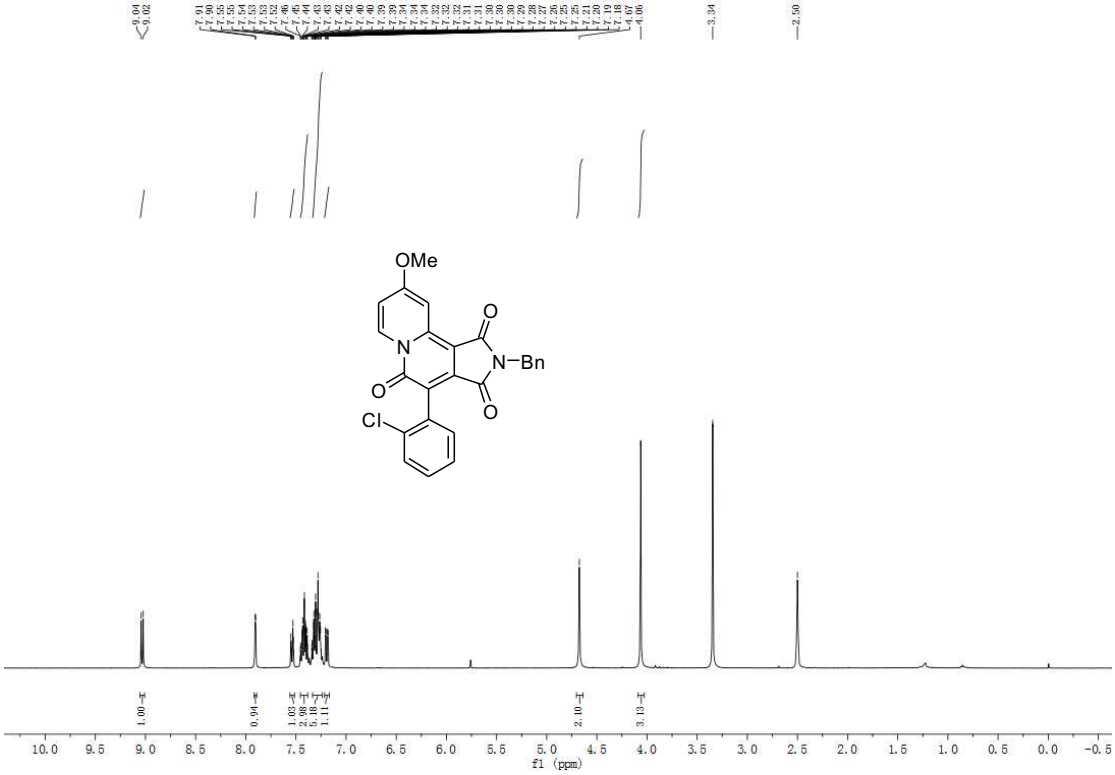
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.4, 166.2, 159.2, 141.0, 136.2, 135.4, 128.9, 128.7, 128.6, 127.9, 122.8, 117.0, 102.2, 99.2, 41.8.

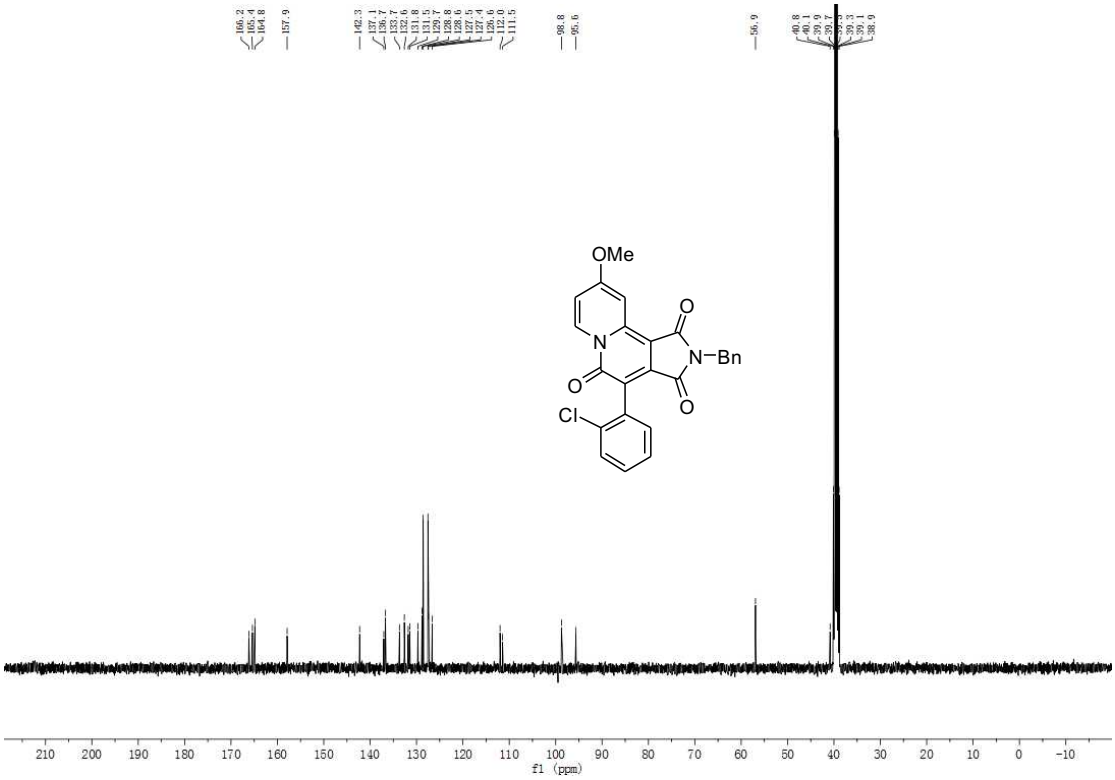


3fa:
2-benzyl-4-(2-chlorophenyl)-9-methoxypyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



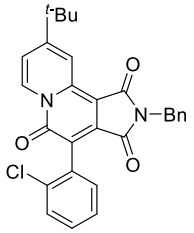
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)-4-methoxypyridin-1-ium bromide **1f** (0.36mmol, 134.3mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.75mmol, 113.0μL, 2.5equiv) were added sequentially to 2.0mL of CH_3CN. The mixture was stirred at 60°C for 20h in O_2 atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.3) to afford compound **3fa** (yellow solid, m.p=88-90°C, 47.9mg, yield=36%).
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{25}H_{18}ClN_2O_4$, 445.0950; found, 445.0945.
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 2.8 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.46 – 7.38 (m, 3H), 7.33 – 7.24 (m, 5H), 7.19 (dd, J = 8.0, 2.9 Hz, 1H), 4.67 (s, 2H), 4.06 (s, 3H).
^{13}C NMR (101 MHz, DMSO-d_6) δ 166.2, 165.4, 164.8, 157.9, 142.3, 137.1, 136.7, 133.7, 132.6, 131.8, 131.5, 129.7, 128.8, 128.6, 127.5, 127.4, 126.6, 112.0, 111.5, 98.8, 95.6, 56.9, 40.8.





3ga:

2-benzyl-9-(*tert*-butyl)-4-(2-chlorophenyl)pyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

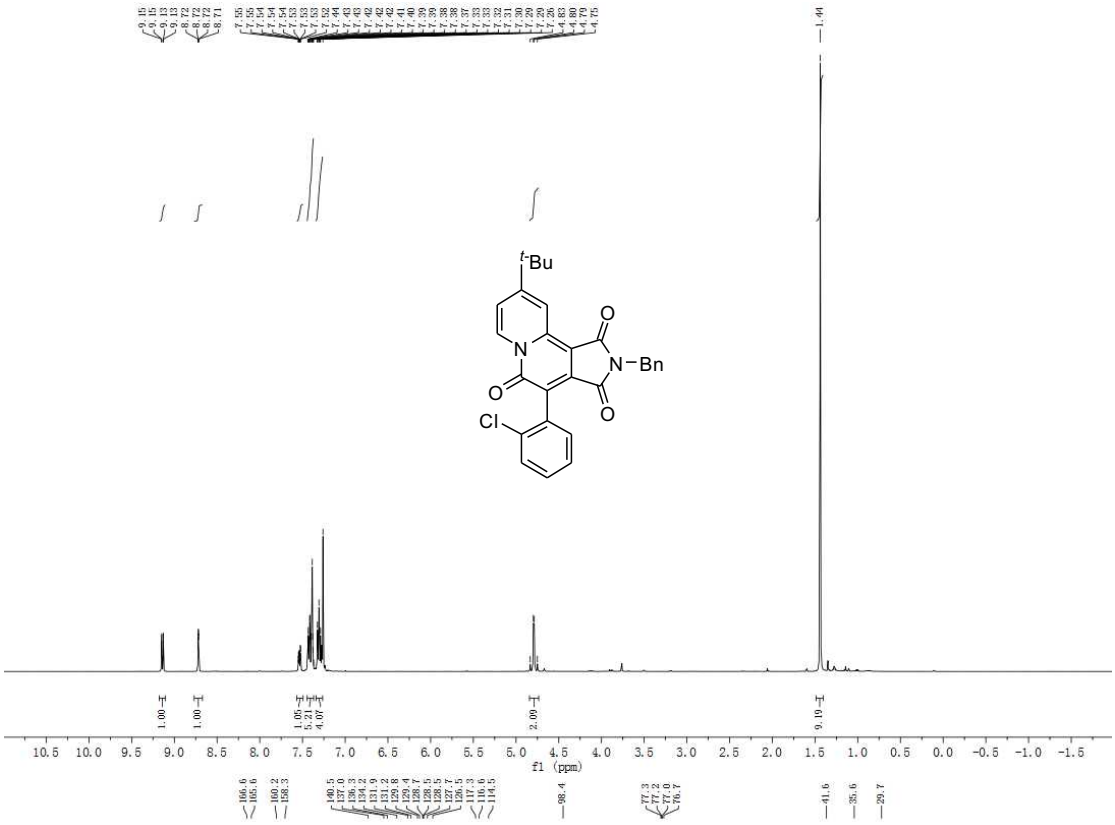


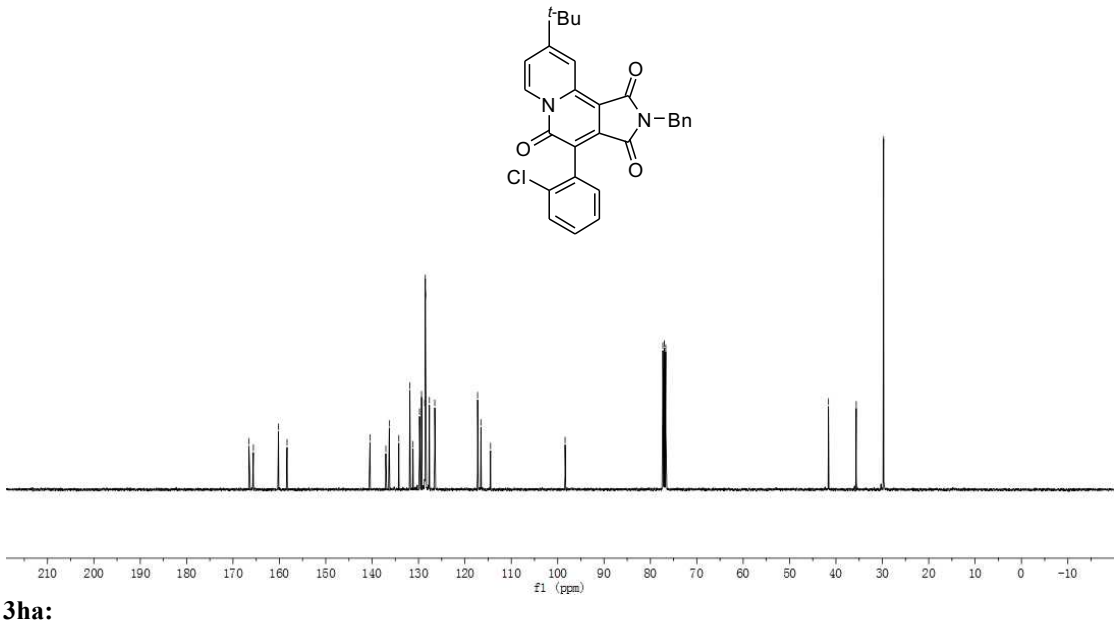
General procedure: 4-(*tert*-butyl)-1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1g** (0.36mmol, 143.6mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=5:1, v/v; Rf=0.3) to afford compound **3ga** (yellow solid, m.p=82-85^{o}C, 133.2mg, yield=94%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{28}H_{24}ClN_2O_3$, 471.1470; found, 471.1472.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.14 (dd, *J* = 7.7, 0.7 Hz, 1H), 8.72 (dd, *J* = 2.3, 0.8 Hz, 1H), 7.53 (ddd, *J* = 5.8, 2.8, 1.7 Hz, 1H), 7.45 – 7.37 (m, 5H), 7.34 – 7.26 (m, 4H), 4.84 – 4.73 (m, 2H), 1.44 (s, 9H).

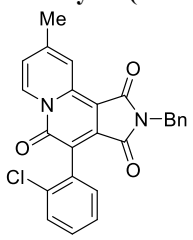
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 165.6, 160.2, 158.4, 140.5, 137.1, 136.3, 134.3, 131.9, 131.2, 129.8, 129.4, 128.7, 128.5, 128.5, 127.7, 126.5, 117.3, 116.6, 114.5, 98.4, 77.20 , 41.6, 35.6, 29.7.





3ha:

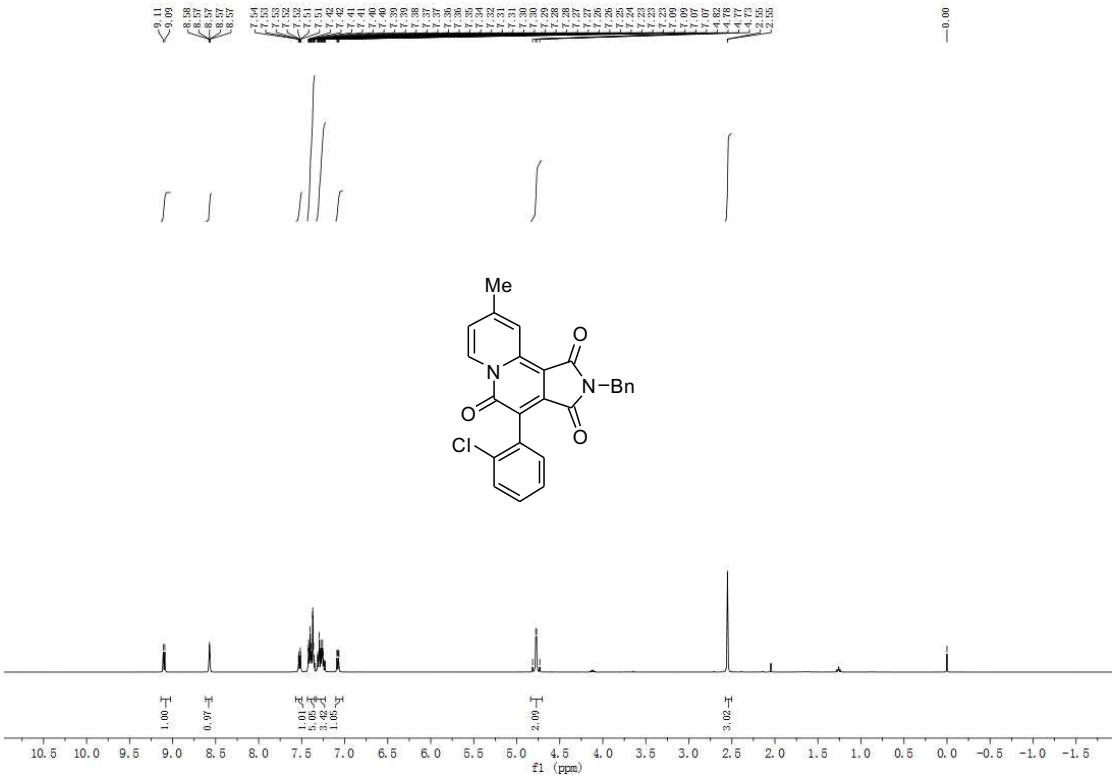
2-benzyl-4-(2-chlorophenyl)-9-methylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

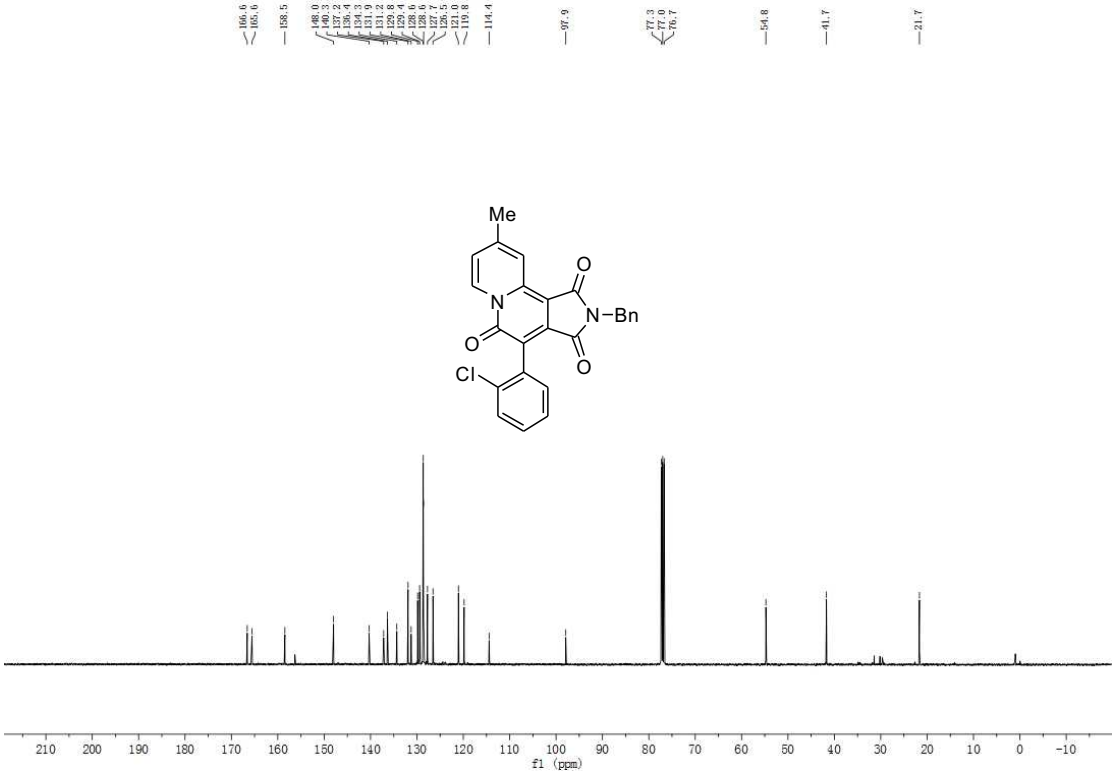


General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)-4-methylpyridin-1-ium bromide **1h** (0.36mmol, 128.4mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.4) to afford compound **3ha** (yellow solid, m.p=235-237^{o}C, 55.8mg, yield=43%). HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{25}H_{18}ClN_2O_3$, 429.1000; found, 429.0999.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.10 (d, *J* = 7.4 Hz, 1H), 8.57 (dt, *J* = 2.1, 1.1 Hz, 1H), 7.57 – 7.50 (m, 1H), 7.43 – 7.35 (m, 5H), 7.33 – 7.23 (m, 3H), 7.08 (dd, *J* = 7.5, 2.0 Hz, 1H), 4.84 – 4.71 (m, 2H), 2.55 (d, *J* = 1.1 Hz, 3H).

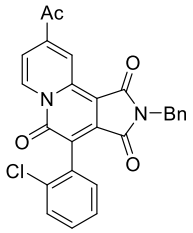
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 165.6, 158.5, 148.0, 140.3, 137.2, 136.4, 134.3, 131.9, 131.2, 129.8, 129.4, 128.6, 128.6, 127.7, 126.5, 121.1, 119.8, 114.4, 97.9, 54.8, 41.7, 21.7.



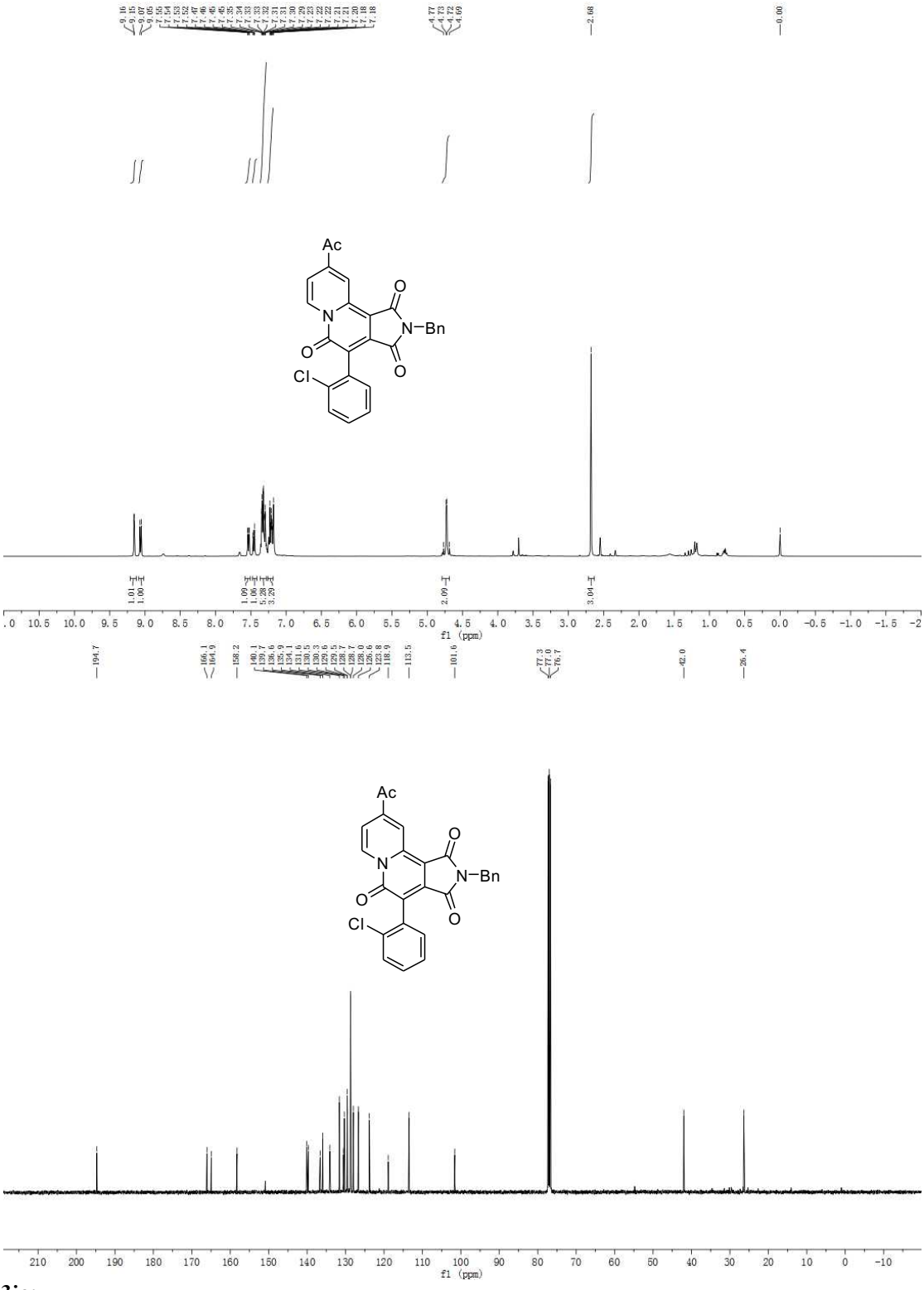


3ia:

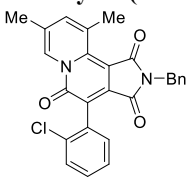
9-acetyl-2-benzyl-4-(2-chlorophenyl)pyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



General procedure: 4-acetyl-1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1i** (0.36mmol, 138.5mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.4) to afford compound **3ia** (yellow solid, m.p=100-102^{o}C, 72.5mg, yield=53%).
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{26}H_{18}ClN_2O_4$, 457.0950; found, 457.0957.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.15 (d, *J* = 1.9 Hz, 1H), 9.06 (d, *J* = 7.6 Hz, 1H), 7.53 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.46 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.37 – 7.28 (m, 5H), 7.26 – 7.18 (m, 3H), 4.73 (d, *J* = 4.5 Hz, 2H), 2.68 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.7, 166.1, 164.9, 158.3, 140.1, 139.7, 136.6, 136.0, 134.1, 131.6, 130.6, 130.3, 129.6, 129.5, 128.7, 128.7, 128.0, 126.7, 123.8, 118.9, 113.5, 101.6, 42.0, 26.4.



3ja:
2-benzyl-4-(2-chlorophenyl)-8,10-dimethylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



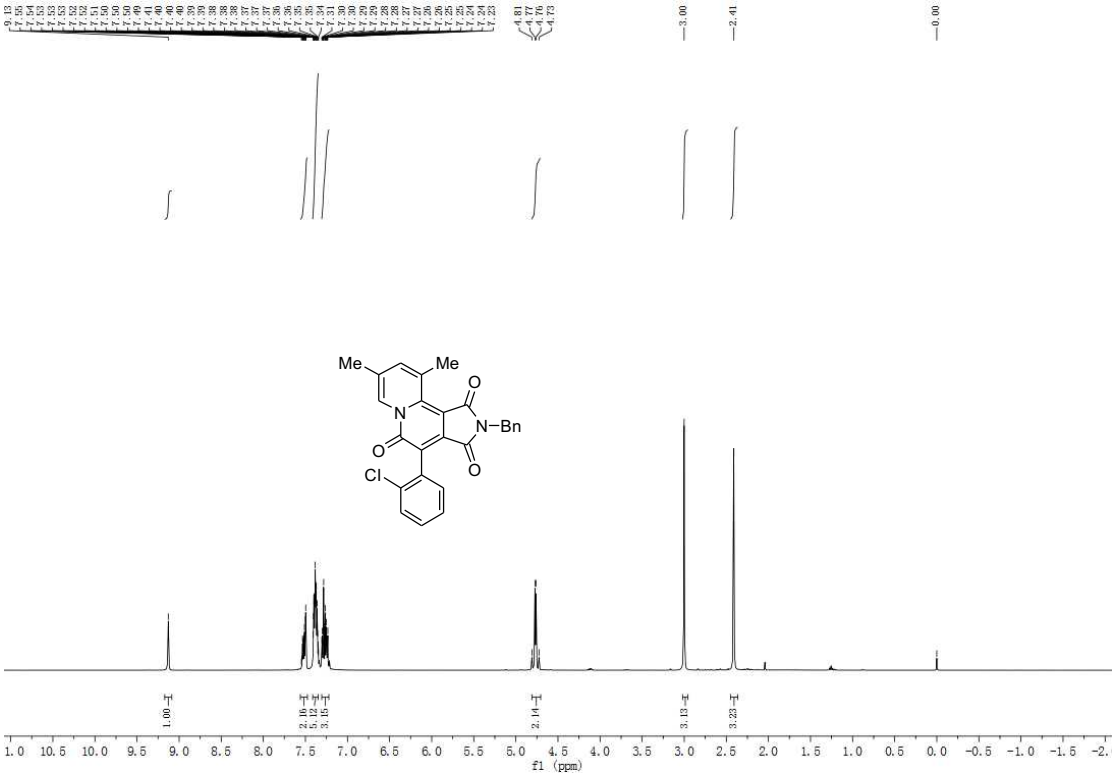
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)-3,5-dimethylpyridin-1-ium bromide **1j** (0.36mmol, 133.5mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg,

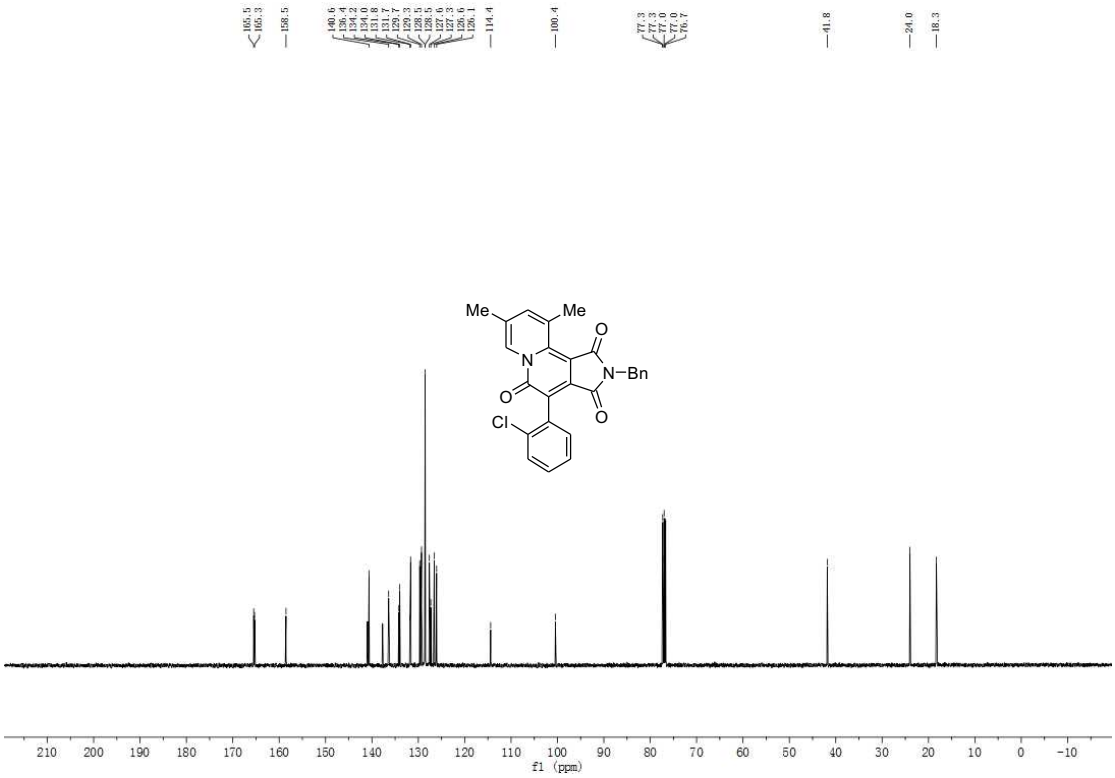
1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of CH_3CN. The mixture was stirred at 60°C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.55) to afford compound **3ja** (yellow solid, m.p=183-185°C, 112.9mg, yield=85%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{26}H_{20}ClN_2O_3$, 443.1157; found, 443.1153.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.13 (s, 1H), 7.56 – 7.48 (m, 2H), 7.38 (ddt, *J* = 7.3, 6.3, 2.2 Hz, 5H), 7.31 – 7.22 (m, 3H), 4.81 – 4.71 (m, 2H), 3.00 (s, 3H), 2.41 (s, 3H).

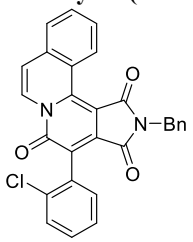
^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.5, 165.3, 158.5, 141.0, 140.6, 137.7, 136.4, 134.2, 134.0, 131.7, 129.7, 129.3, 128.5, 127.6, 127.3, 126.6, 126.1, 114.4, 100.5, 41.8, 24.0, 18.3.





3ka:

2-benzyl-4-(2-chlorophenyl)pyrrolo[3',4':3,4]pyrido[2,1-a]isoquinoline-1,3,5(2H)-trione

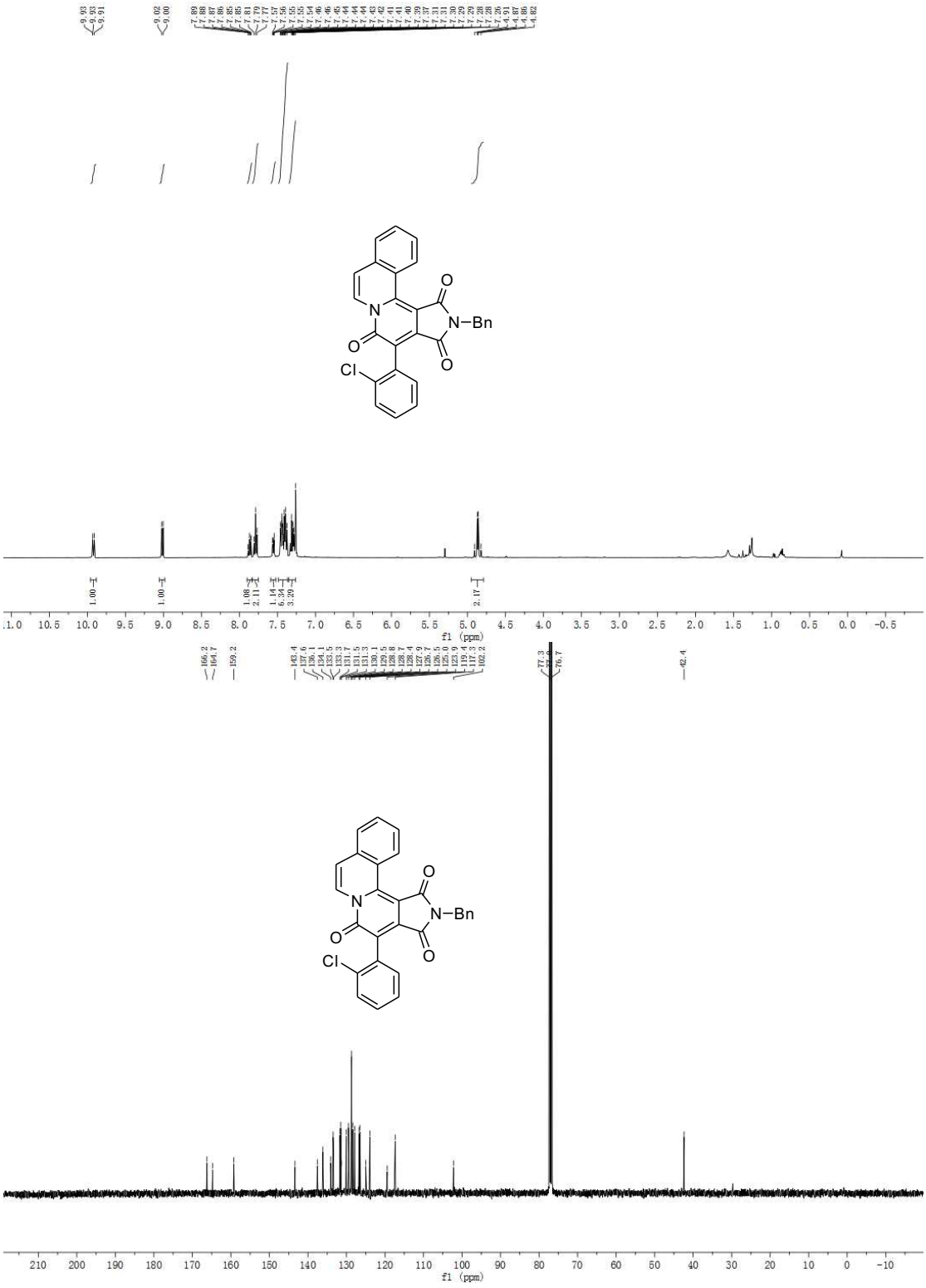


General procedure: 2-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)isoquinolin-2-ium bromide **1k** (0.36mmol, 141.4mg, 1.2equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 2,2,6,6-Tetramethylpiperidoxyl (TEMPO, 0.6mmol, 93.8mg, 2.0equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.6mmol, 90.0μL, 2.0equiv) were added sequentially to 3.0mL of CH_3CN. The mixture was stirred at 80°C for 15h in N_2 atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.5) to afford compound **3ka** (yellow solid, m.p=86-89°C, 31.2mg, yield=22%).

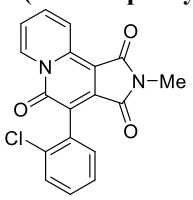
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{28}H_{18}ClN_2O_3$, 465.1000; found, 465.1008.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.96 – 9.88 (m, 1H), 9.01 (d, *J* = 7.7 Hz, 1H), 7.87 (td, *J* = 7.4, 1.2 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 2H), 7.59 – 7.52 (m, 1H), 7.49 – 7.37 (m, 6H), 7.35 – 7.26 (m, 3H), 4.95 – 4.79 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.2, 164.7, 159.3, 143.4, 137.6, 136.1, 134.1, 133.5, 133.3, 131.7, 131.5, 131.3, 130.1, 129.5, 128.8, 128.7, 128.4, 127.9, 126.7, 126.5, 125.0, 124.0, 119.4, 117.3, 102.2, 42.4.



3ab:
4-(2-chlorophenyl)-2-methylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

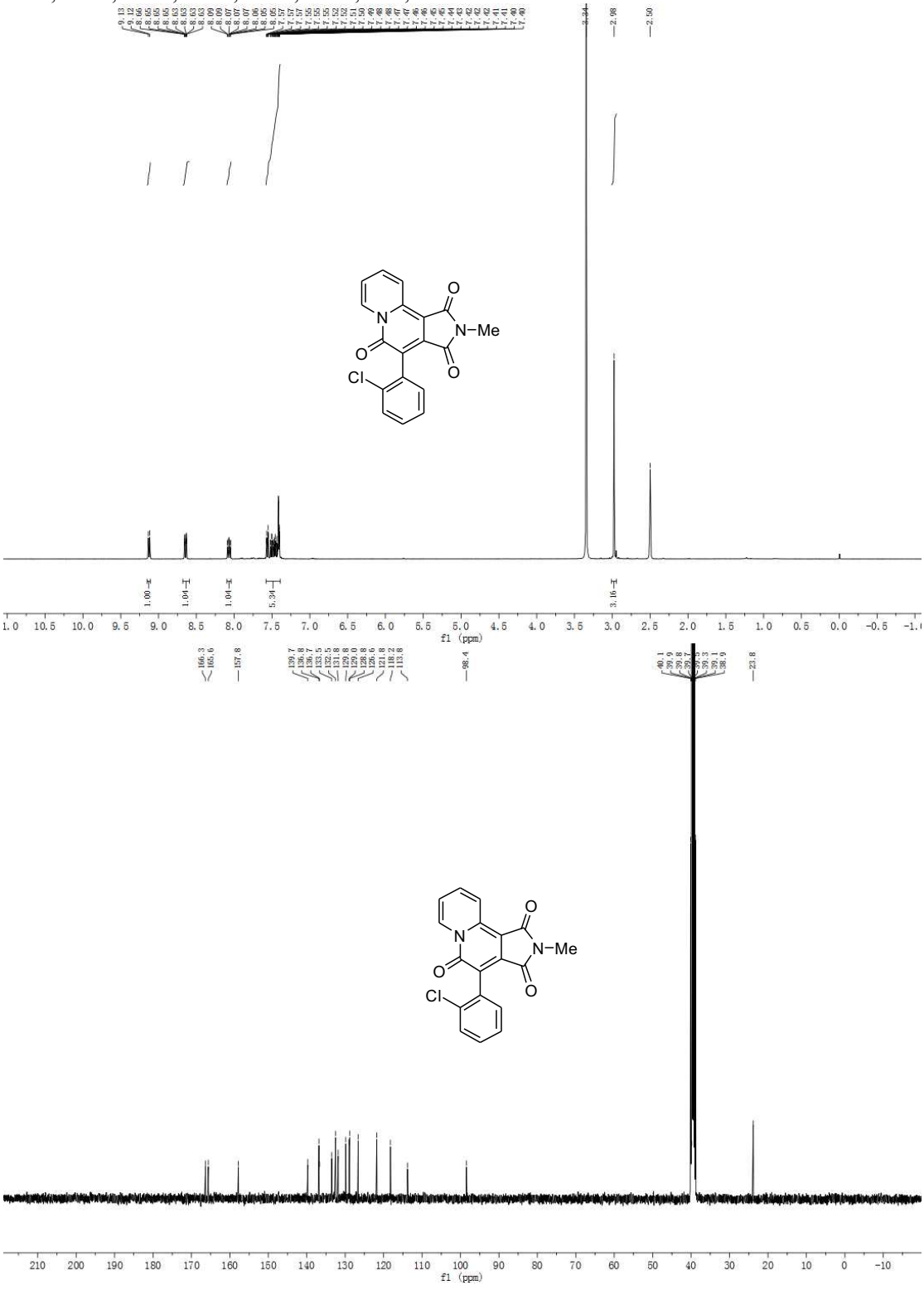


General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-methyl-1H-pyrrole-2,5-dione **2b** (0.3mmol, 34.0mg, 1.0equiv), 1,4-

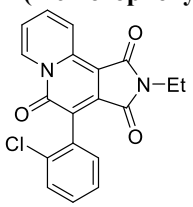
Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60°C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.45) to afford compound **3ab** (yellow solid, m.p=183-186°C, 85.8mg, yield=84%). HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{18}H_{12}ClN_2O_3$, 339.0531; found, 339.0525.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (d, J = 7.2 Hz, 1H), 8.64 (ddd, J = 8.9, 1.5, 0.9 Hz, 1H), 8.07 (ddd, J = 8.9, 6.8, 1.3 Hz, 1H), 7.58 – 7.39 (m, 5H), 2.98 (s, 3H).

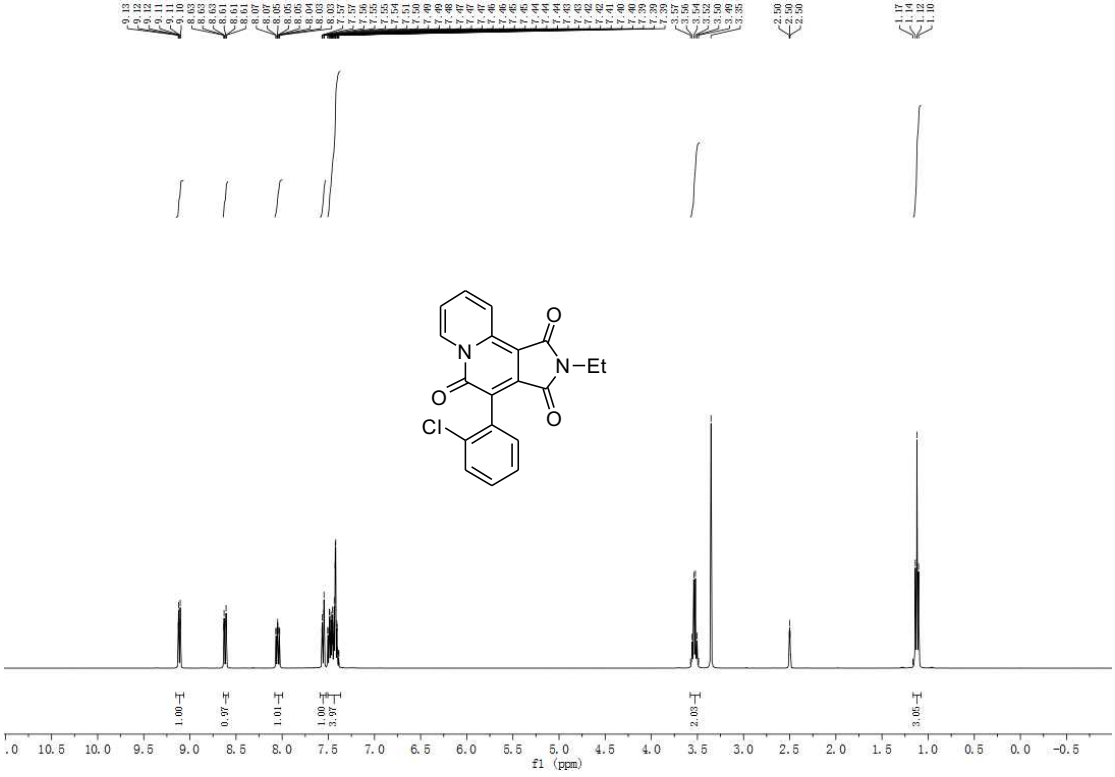
^{13}C NMR (101 MHz, DMSO-d_6) δ 166.3, 165.6, 157.8, 139.7, 136.8, 136.7, 133.5, 132.5, 131.8, 129.9, 129.0, 128.8, 126.6, 121.8, 118.2, 113.8, 98.5, 23.8.

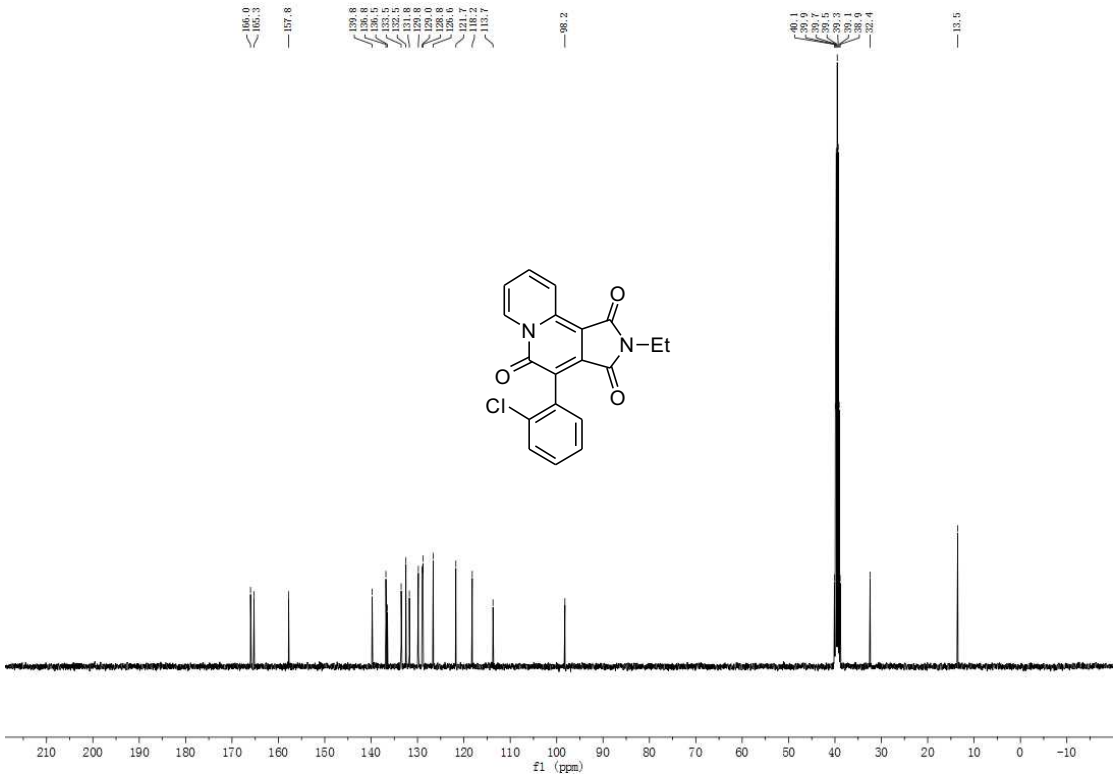


3ac:
4-(2-chlorophenyl)-2-ethylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



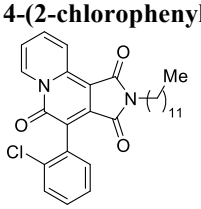
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-ethyl-1H-pyrrole-2,5-dione **2c** (0.3mmol, 37.6mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.6) to afford compound **3ac** (yellow solid, m.p=161-163^{o}C, 97.8mg, yield=92%).
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{19}H_{14}ClN_2O_3$, 353.0687; found, 353.0676.
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.11 (dt, J = 7.2, 1.1 Hz, 1H), 8.62 (dt, J = 8.7, 1.2 Hz, 1H), 8.05 (ddd, J = 8.9, 6.8, 1.3 Hz, 1H), 7.56 (dt, J = 7.8, 1.0 Hz, 1H), 7.51 – 7.37 (m, 4H), 3.53 (q, J = 7.1 Hz, 2H), 1.12 (t, J = 7.2 Hz, 3H).
^{13}C NMR (101 MHz, DMSO-d_6) δ 166.0, 165.3, 157.8, 139.8, 136.8, 136.5, 133.5, 132.5, 131.8, 129.8, 129.0, 128.8, 126.6, 121.7, 118.2, 113.7, 98.2, 32.4, 13.5.





3ad:

4-(2-chlorophenyl)-2-dodecylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

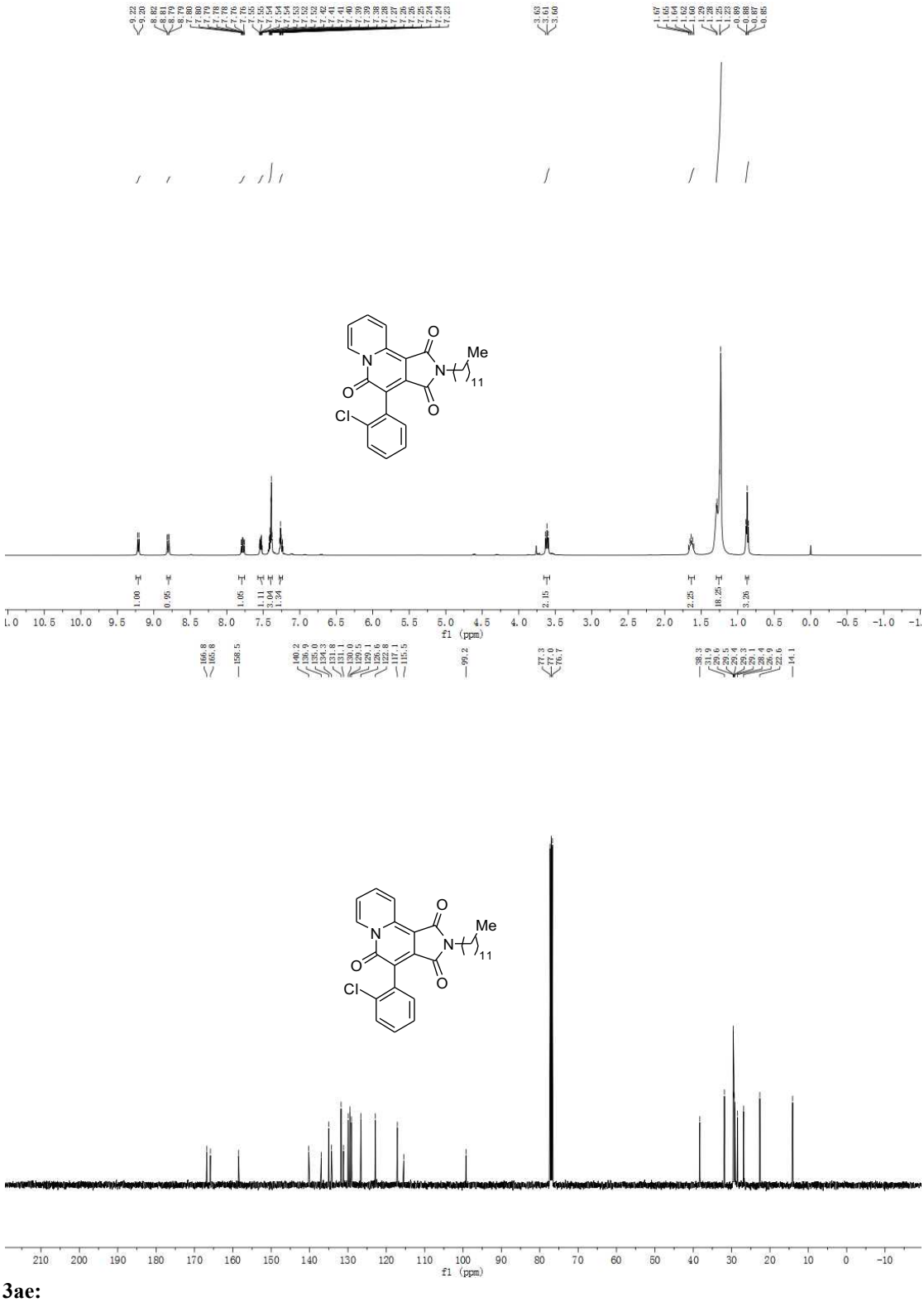


General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-dodecyl-1H-pyrrole-2,5-dione **2d** (0.3mmol, 79.6mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.5) to afford compound **3ad** (yellow oil, 98.9mg, yield=67%).

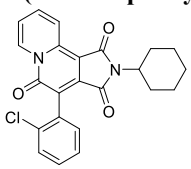
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{29}H_{34}ClN_2O_3$, 493.2252; found, 493.2248.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.21 (d, *J* = 7.3 Hz, 1H), 8.82 – 8.78 (m, 1H), 7.78 (ddd, *J* = 8.6, 6.7, 1.4 Hz, 1H), 7.58 – 7.50 (m, 1H), 7.43 – 7.38 (m, 3H), 7.28 – 7.24 (m, 1H), 3.61 (t, *J* = 7.4 Hz, 2H), 1.64 (p, *J* = 7.2 Hz, 2H), 1.29 – 1.22 (m, 18H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.8, 165.8, 158.5, 140.2, 137.0, 135.0, 134.3, 131.8, 131.1, 130.0, 129.5, 129.1, 126.6, 122.8, 117.1, 115.5, 99.2, 38.3, 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 28.4, 26.9, 22.7, 14.1.

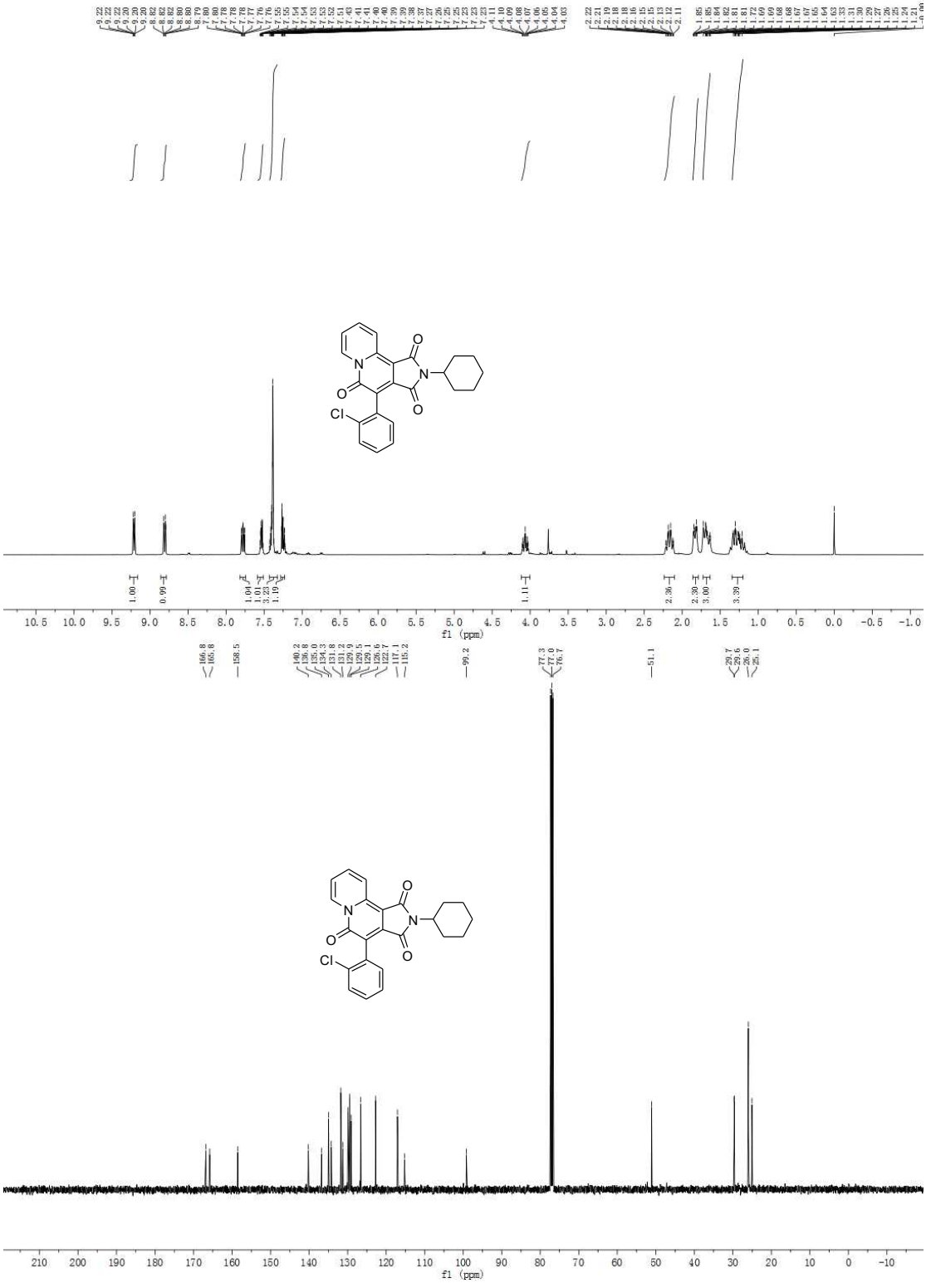


3ae:
4-(2-chlorophenyl)-2-cyclohexylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



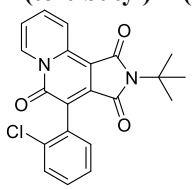
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-cyclohexyl-1H-pyrrole-2,5-dione **2e** (0.3mmol, 54.0mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL

of 1,2-Dichloroethane. The mixture was stirred at 60°C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.8) to afford compound **3ae** (yellow solid, m.p=89-91°C, 95.2mg, yield=78%).
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{23}H_{20}ClN_2O_3$, 407.1157; found, 407.1149.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.21 (dt, *J* = 7.3, 1.1 Hz, 1H), 8.81 (dt, *J* = 9.0, 1.2 Hz, 1H), 7.78 (ddd, *J* = 8.9, 6.7, 1.3 Hz, 1H), 7.59 – 7.51 (m, 1H), 7.43 – 7.33 (m, 3H), 7.28 – 7.23 (m, 1H), 4.07 (tt, *J* = 12.3, 3.9 Hz, 1H), 2.17 (tdd, *J* = 15.8, 11.1, 3.1 Hz, 2H), 1.86 – 1.79 (m, 2H), 1.73 – 1.63 (m, 3H), 1.34 – 1.20 (m, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.8, 165.8, 158.5, 140.2, 136.8, 135.0, 134.3, 131.8, 131.2, 129.9, 129.5, 129.1, 126.6, 122.8, 117.1, 115.3, 99.2, 51.1, 29.7, 29.6, 26.0, 25.1.



3af:

2-(tert-butyl)-4-(2-chlorophenyl)pyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione

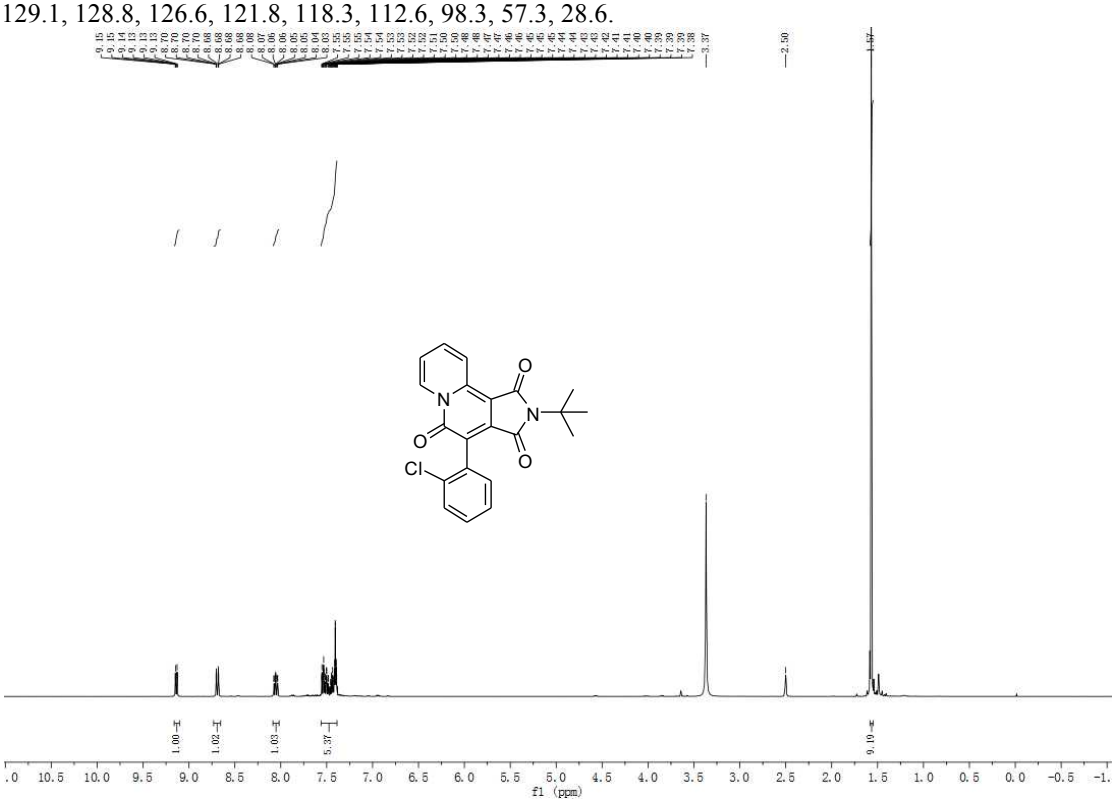


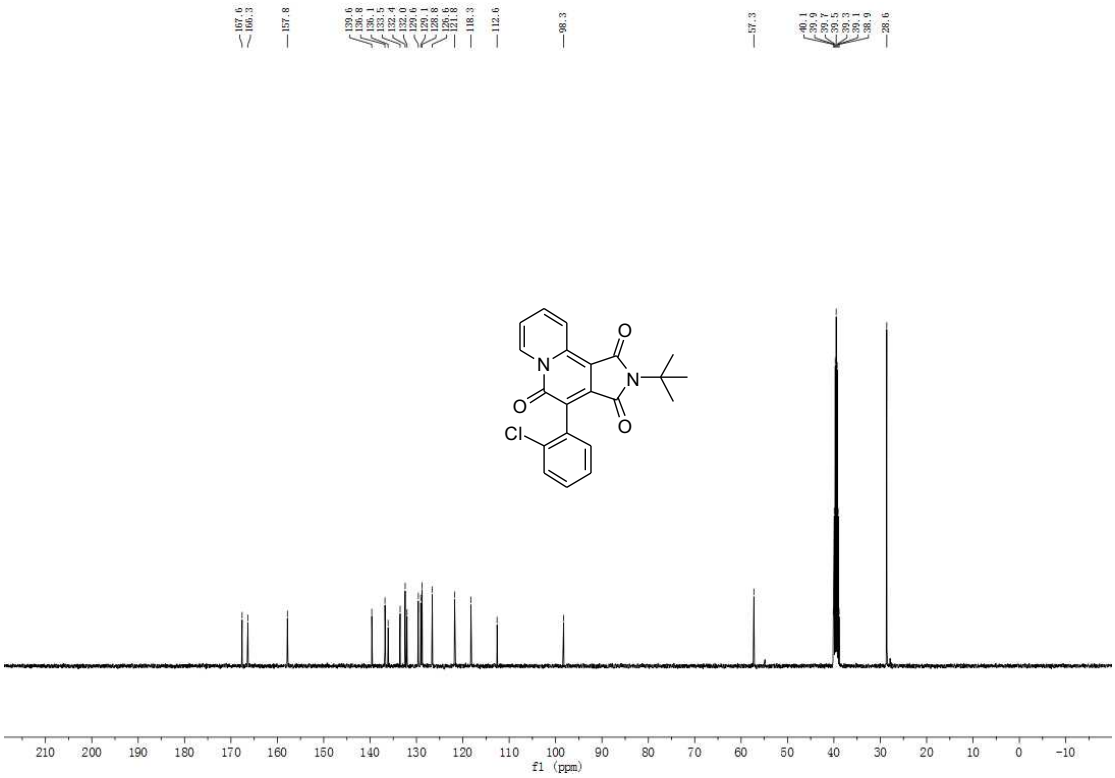
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-(*tert*-butyl)-1H-pyrrole-2,5-dione **2f** (0.3mmol, 44.0μL, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60°C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.8) to afford compound **3af** (yellow solid, m.p=166-168°C, 99.1mg, yield=87%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{21}H_{18}ClN_2O_3$, 381.1000; found, 381.0994.

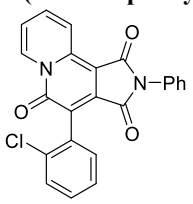
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.14 (dt, J = 7.3, 1.2 Hz, 1H), 8.69 (ddd, J = 8.9, 1.4, 0.9 Hz, 1H), 8.05 (ddd, J = 8.9, 6.8, 1.3 Hz, 1H), 7.56 – 7.39 (m, 5H), 1.57 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 167.6, 166.3, 157.8, 139.6, 136.8, 136.1, 133.5, 132.4, 132.0, 129.6, 129.1, 128.8, 126.6, 121.8, 118.3, 112.6, 98.3, 57.3, 28.6.





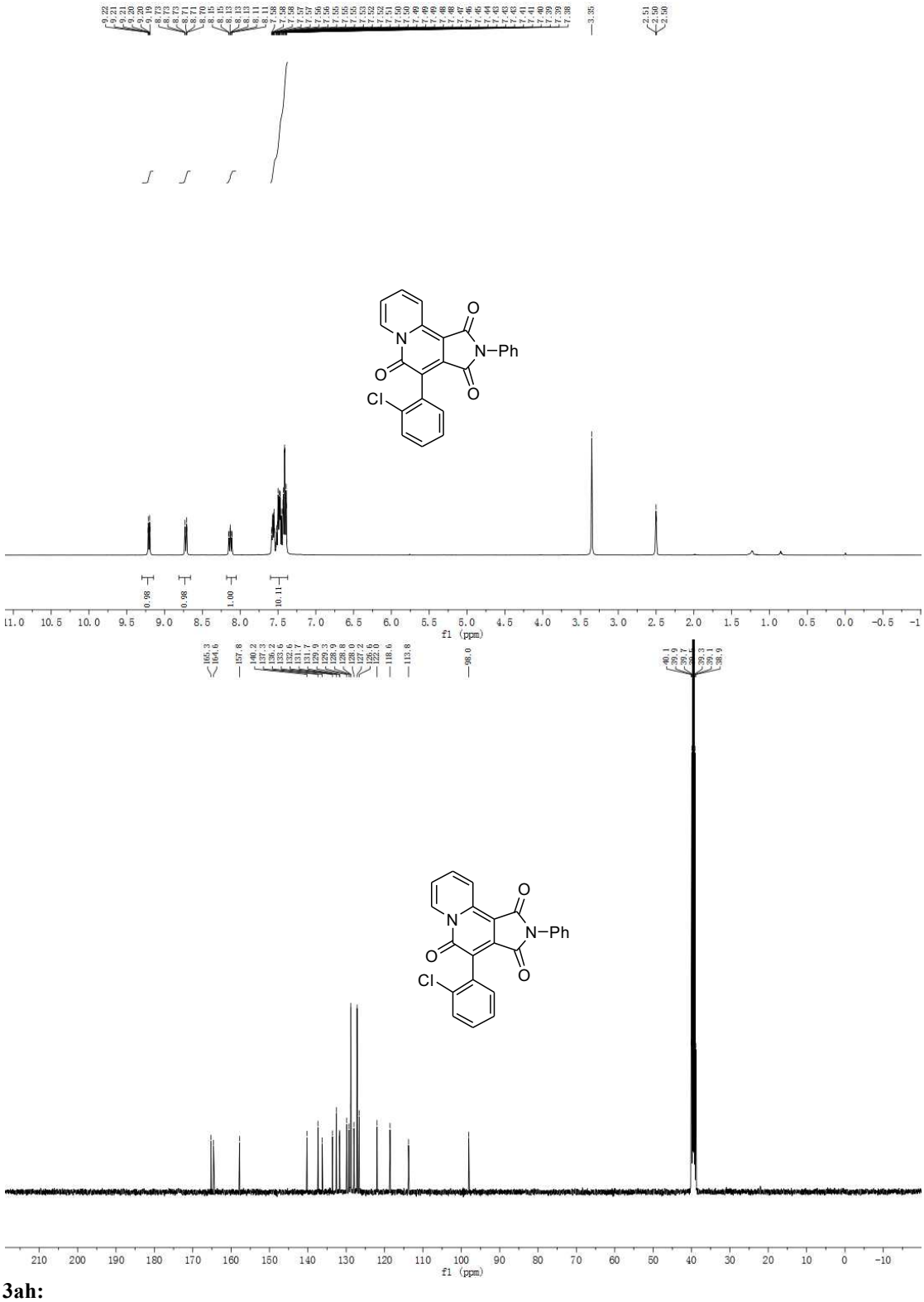
3ag:
4-(2-chlorophenyl)-2-phenylpyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



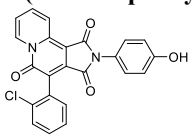
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-phenyl-1H-pyrrole-2,5-dione **2g** (0.3mmol, 51.9mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60^{o}C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.45) to afford compound **3ag** (yellow solid, m.p=188-191^{o}C, 99.5mg, yield=83%). HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{23}H_{14}ClN_2O_3$, 401.0687; found, 401.0679.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.21 (dt, J = 7.3, 1.2 Hz, 1H), 8.72 (dt, J = 8.9, 1.2 Hz, 1H), 8.13 (ddd, J = 8.6, 6.8, 1.3 Hz, 1H), 7.60 – 7.37 (m, 10H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 165.3, 164.6, 157.8, 140.2, 137.3, 136.3, 133.6, 132.6, 131.8, 131.7, 129.9, 129.3, 128.9, 128.8, 128.0, 127.2, 126.6, 122.0, 118.6, 113.8, 98.1.



3ah:
4-(2-chlorophenyl)-2-(4-hydroxyphenyl)pyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



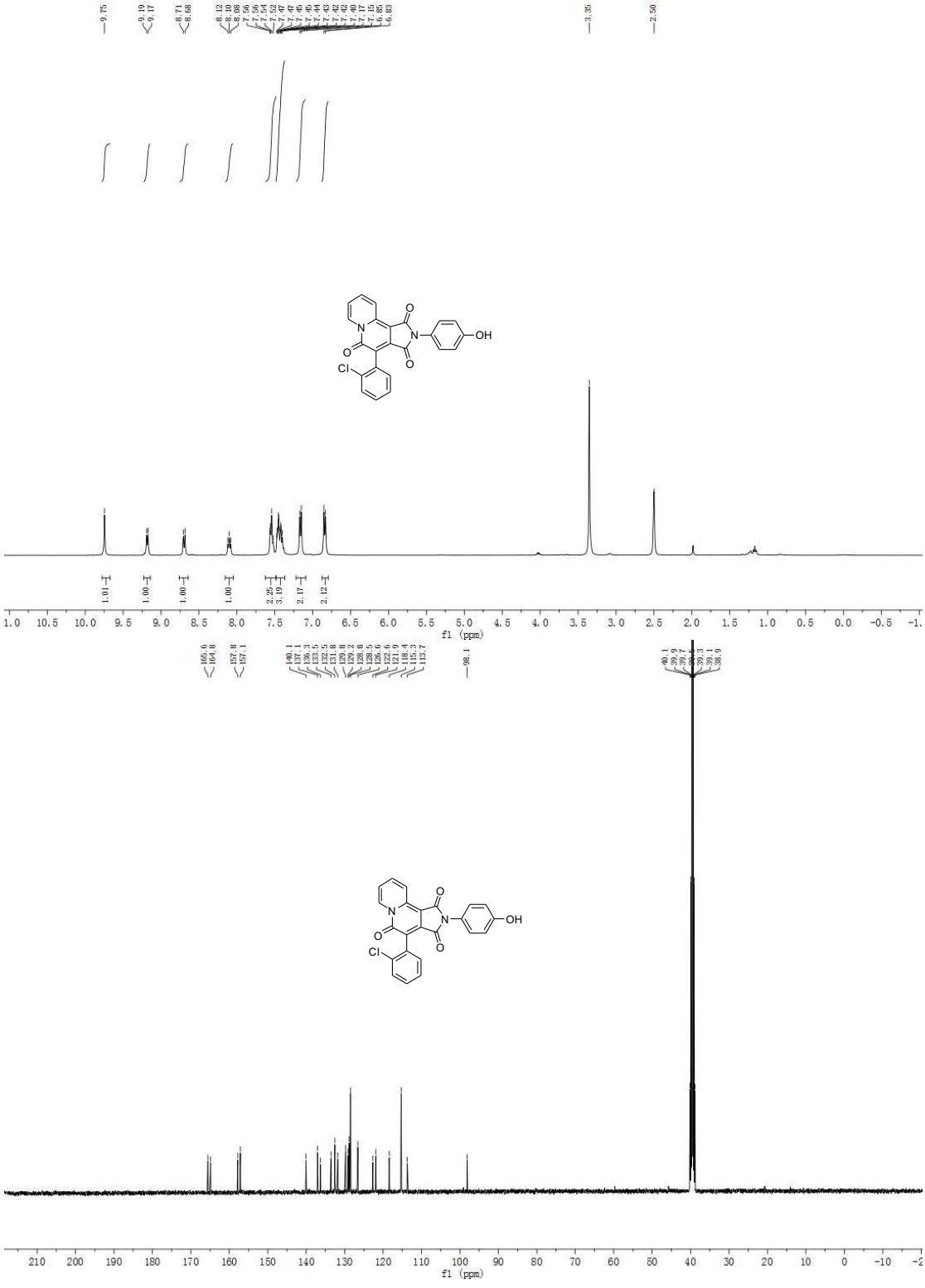
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1-(4-hydroxyphenyl)-1H-pyrrole-2,5-dione **2h** (0.3mmol, 56.7mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of CH_3CN. The mixture was stirred at 60°C for 20h in open flask. Then solvent

was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.3) to afford compound **3ah** (yellow solid, m.p=310-313^oC, 113.0mg, yield=90%).

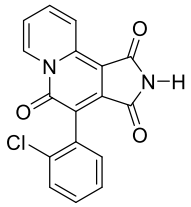
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{23}H_{14}ClN_2O_4$, 417.0637; found, 417.0642.

^1H NMR (400 MHz, DMSO-d_6) δ 9.75 (s, 1H), 9.18 (d, J = 7.3 Hz, 1H), 8.70 (d, J = 8.8 Hz, 1H), 8.10 (t, J = 7.8 Hz, 1H), 7.62 – 7.48 (m, 2H), 7.48 – 7.37 (m, 3H), 7.16 (d, J = 8.3 Hz, 2H), 6.84 (d, J = 8.3 Hz, 2H).

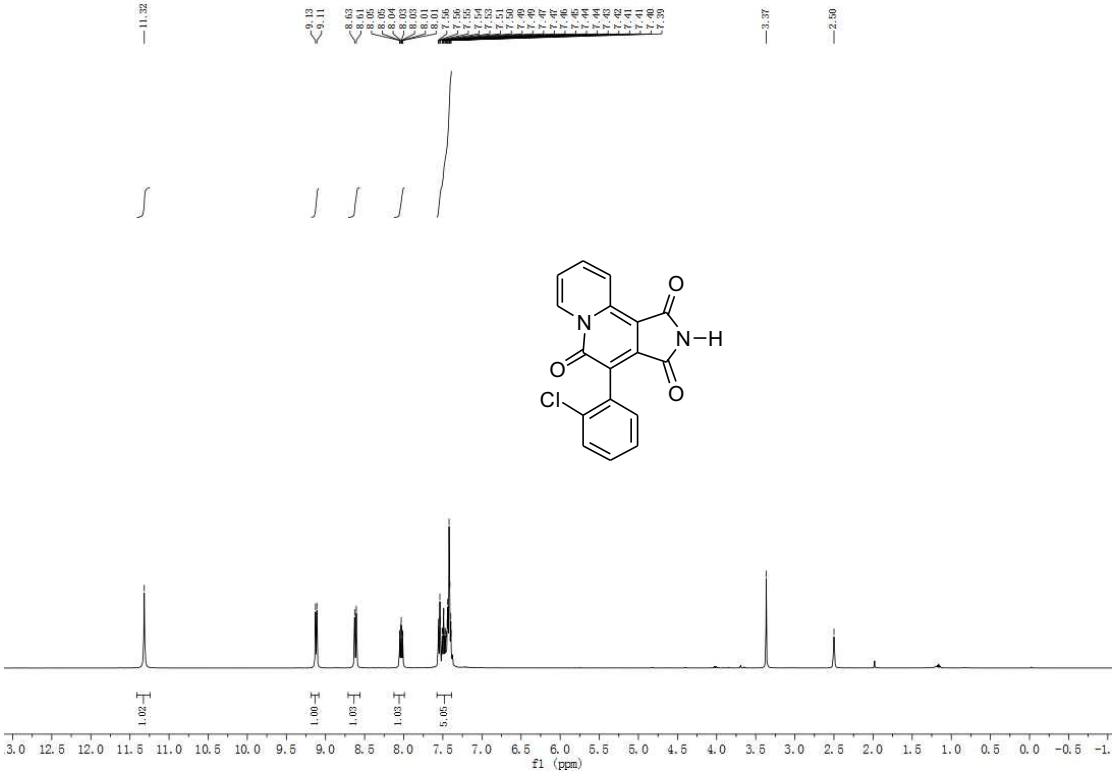
^{13}C NMR (101 MHz, DMSO-d_6) δ 165.6, 164.8, 157.8, 157.1, 140.1, 137.1, 136.3, 133.5, 132.5, 131.8, 129.8, 129.2, 128.8, 128.5, 126.6, 122.6, 121.9, 118.4, 115.3, 113.7, 98.1.

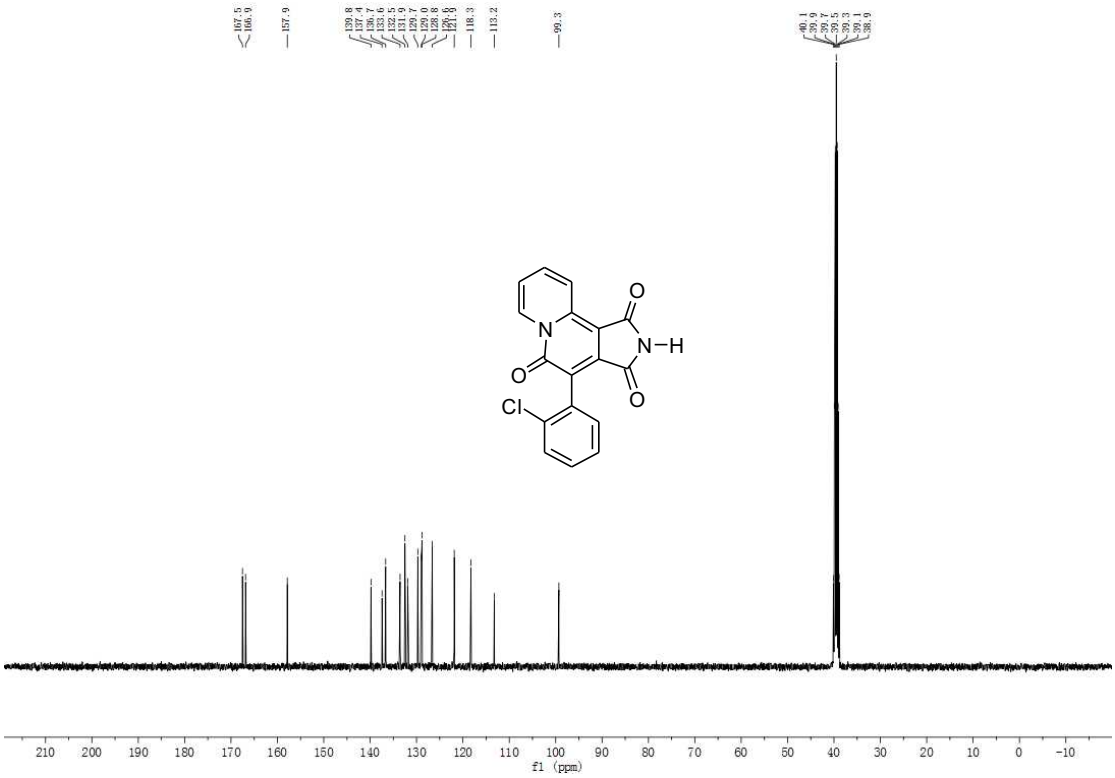


3ai:
4-(2-chlorophenyl)pyrrolo[3,4-a]quinolizine-1,3,5(2H)-trione



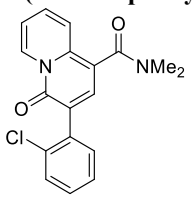
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), 1H-pyrrole-2,5-dione **2i** (0.3mmol, 29.1mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of CH_3CN. The mixture was stirred at 60^oC for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.4) to afford compound **3ai** (yellow solid, m.p=288-290^oC, 68.5mg, yield=70%).
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{17}H_{10}ClN_2O_3$, 325.0374; found, 415.325.0378.
^1H NMR (400 MHz, DMSO-d_6) δ 11.32 (s, 1H), 9.12 (d, J = 7.1 Hz, 1H), 8.62 (d, J = 8.4 Hz, 1H), 8.03 (ddd, J = 8.5, 6.8, 1.3 Hz, 1H), 7.58 – 7.39 (m, 5H).
^{13}C NMR (101 MHz, DMSO-d_6) δ 167.5, 166.9, 157.9, 139.8, 137.4, 136.7, 133.6, 132.5, 131.9, 129.7, 129.0, 128.8, 126.6, 121.9, 118.3, 113.2, 99.3.





3aj:

3-(2-chlorophenyl)-N,N-dimethyl-4-oxo-4H-quinolizine-1-carboxamide

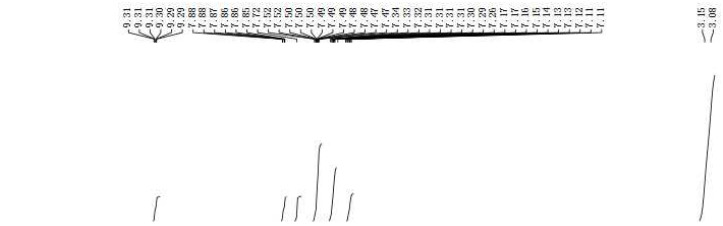


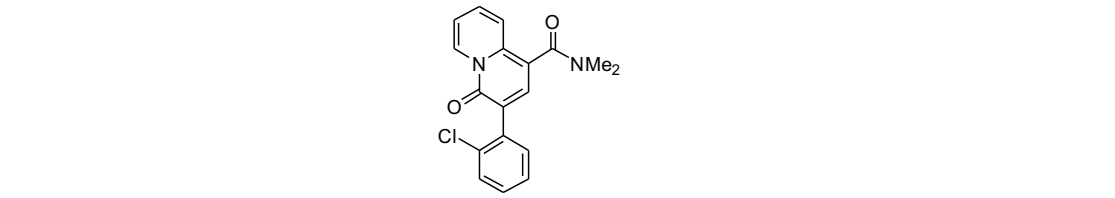
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.3mmol, 102.8mg, 1.0equiv), N,N-dimethylacrylamide **2j** (0.6mmol, 61.8μL, 2.0equiv), 2,2,6,6-Tetramethylpiperidoxyl (TEMPO, 0.75mmol, 117.2mg, 2.5equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.9mmol, 134.4μL, 3.0equiv) were added sequentially to 3.0mL of DMSO. The mixture was stirred at 120°C for 40h in open flask. After the reaction liquid was cooled to room temperature, 100ml of water was added and extracted by 50ml of ethyl acetate for three times. The organic phase was isolated and ethyl acetate was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.3) to afford compound **3aj** (yellow oil, 39.7mg, yield=40%).

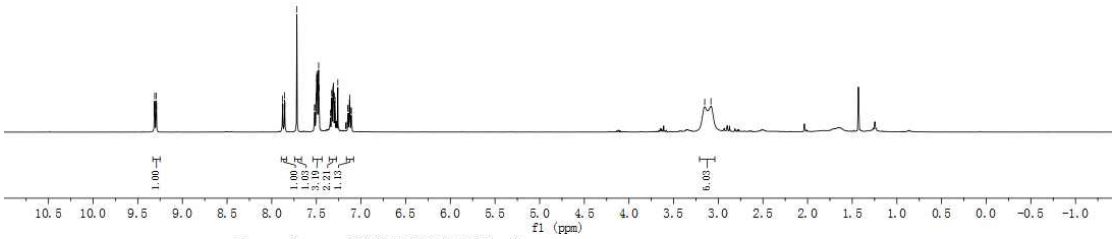
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{18}H_{16}ClN_2O_2$, 327.0895; found, 327.0897.

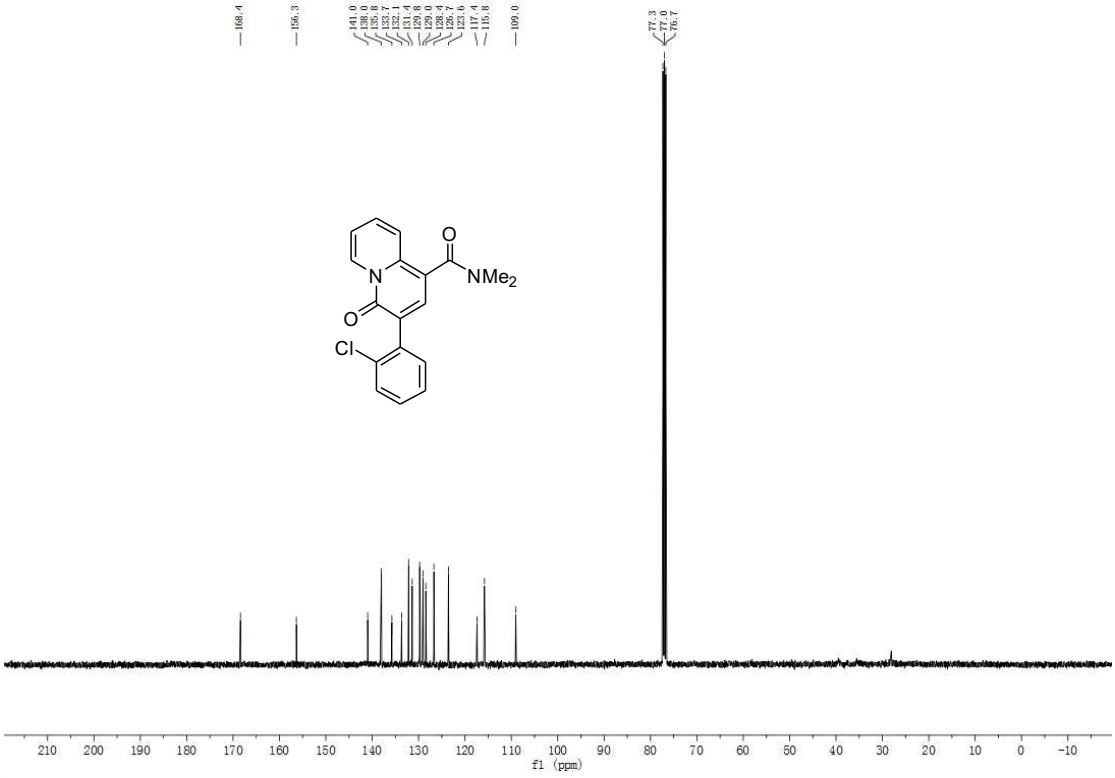
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.30 (dt, *J* = 7.4, 1.2 Hz, 1H), 7.87 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.72 (s, 1H), 7.54 – 7.44 (m, 3H), 7.36 – 7.28 (m, 2H), 7.13 (ddd, *J* = 7.8, 6.6, 1.5 Hz, 1H), 3.12 (d, *J* = 27.8 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.4, 156.3, 141.0, 138.0, 135.8, 133.7, 132.2, 131.4, 129.8, 129.1, 128.5, 126.7, 123.6, 117.4, 115.8, 109.0.

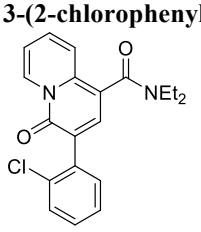








3ak:
3-(2-chlorophenyl)-N,N-diethyl-4-oxo-4H-quinolizine-1-carboxamide

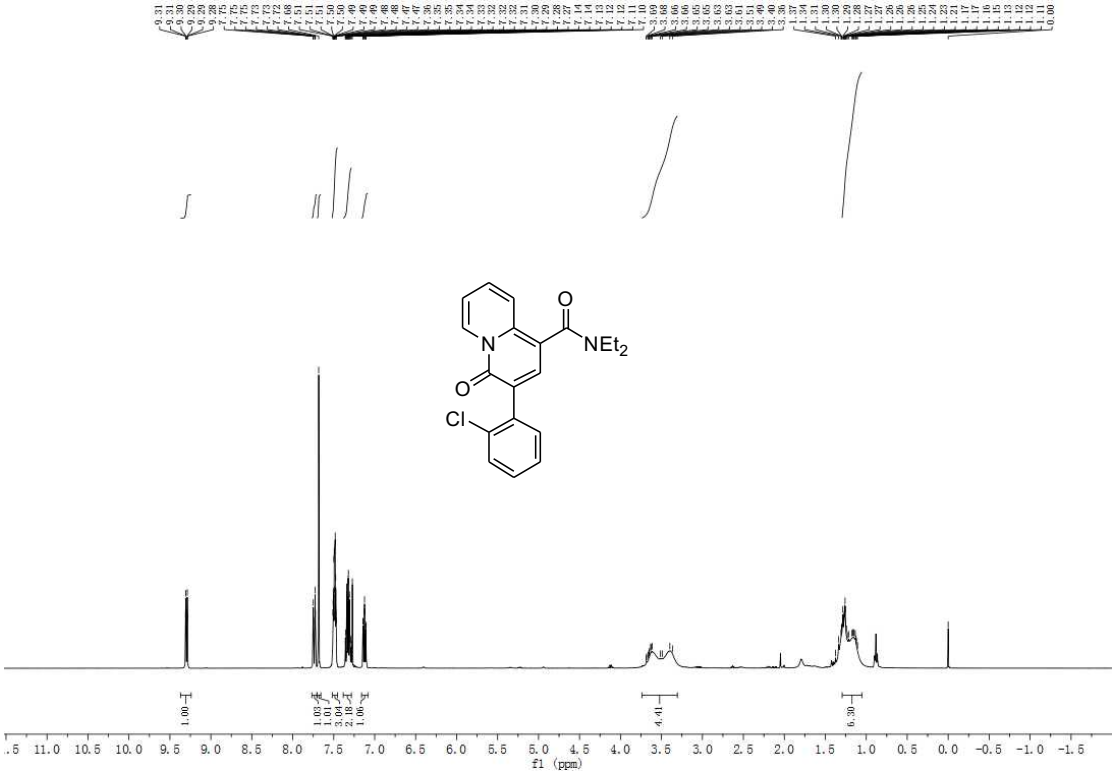


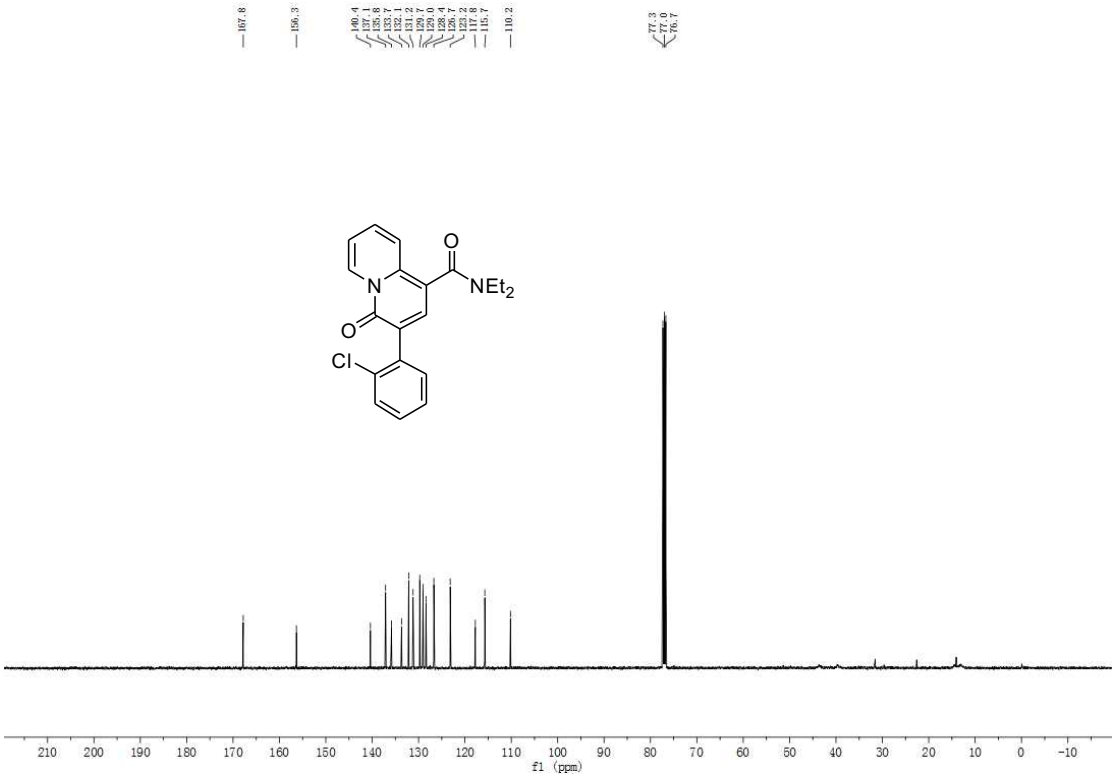
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.45mmol, 154.2mg, 1.5equiv), N,N-diethylacrylamide **2k** (0.3mmol, 41.3μL, 1.0equiv), 2,2,6,6-Tetramethylpiperidoxyl (TEMPO, 0.75mmol, 117.2mg, 2.5equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.9mmol, 134.4μL, 3.0equiv) were added sequentially to 3.0mL of DMSO. The mixture was stirred at 120°C for 40h in Ar. After the reaction liquid was cooled to room temperature, 100ml of water was added and extracted by 50ml of ethyl acetate for three times. The organic phase was isolated and ethyl acetate was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.3) to afford compound **3ak** (yellow oil, 29.0mg, yield=27%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{20}H_{20}ClN_2O_2$, 355.1208; found, 355.1202.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.30 (dt, *J* = 7.4, 1.1 Hz, 1H), 7.74 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.68 (s, 1H), 7.52 – 7.45 (m, 3H), 7.38 – 7.28 (m, 2H), 7.12 (ddd, *J* = 7.8, 6.6, 1.4 Hz, 1H), 3.74 – 3.31 (m, 4H), 1.29 – 1.05 (m, 6H).

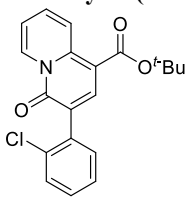
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.8, 156.3, 140.4, 137.1, 135.8, 133.7, 132.1, 131.2, 129.8, 129.0, 128.4, 126.7, 123.2, 117.8, 115.7, 110.2.





3al:

***tert*-butyl 3-(2-chlorophenyl)-4-oxo-4H-quinolizine-1-carboxylate**

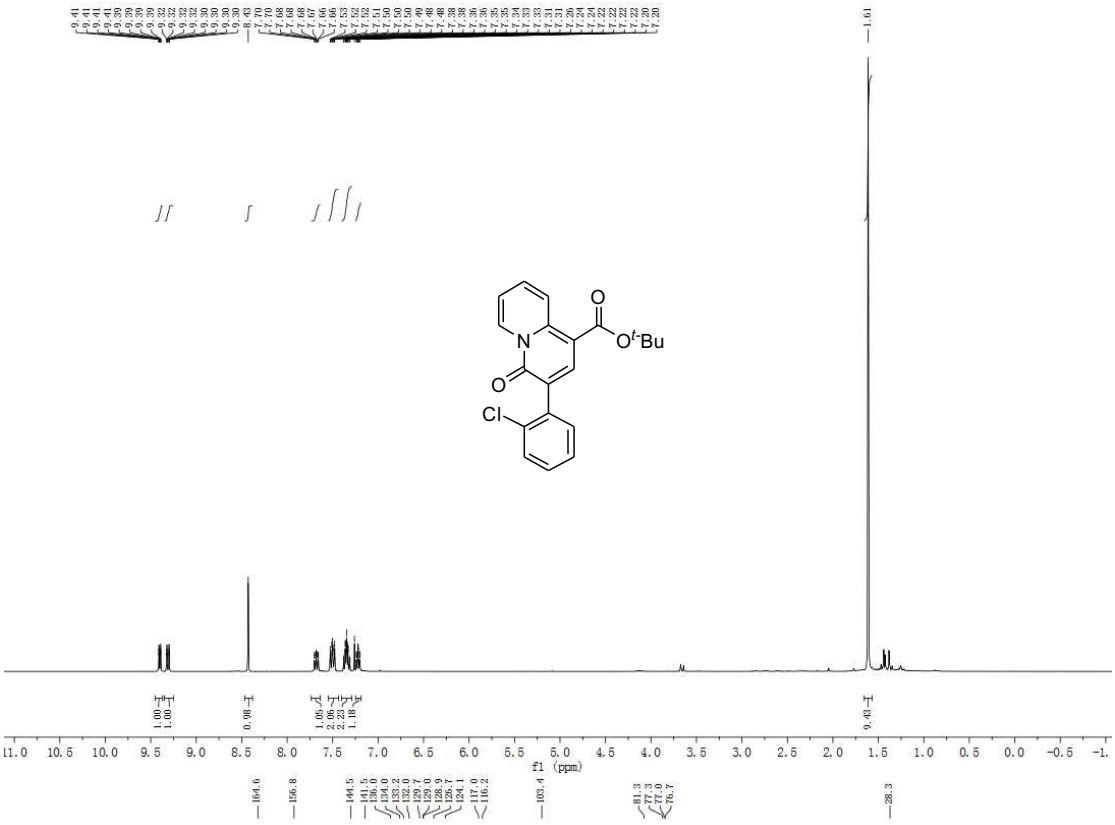


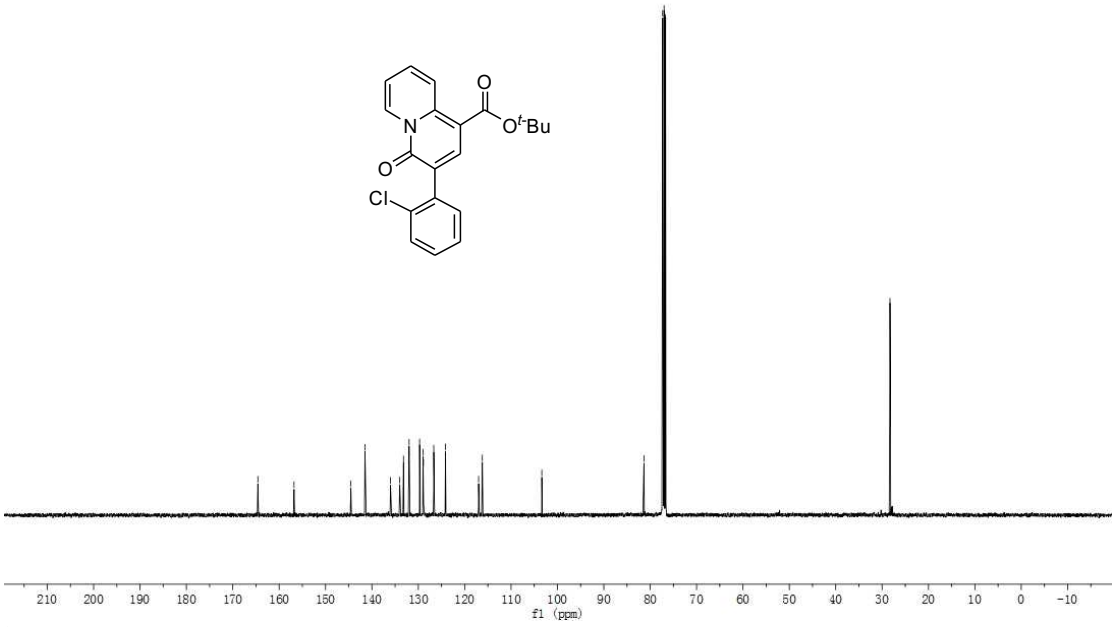
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.3mmol, 102.8mg, 1.0equiv), *tert*-butyl acrylate **2l** (0.6mmol, 88.0μL, 2.0equiv), 2,2,6,6-Tetramethylpiperidoxyl (TEMPO, 0.75mmol, 117.2mg, 2.5equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.9mmol, 134.4μL, 3.0equiv) were added sequentially to 3.0mL of toluene. The mixture was stirred at 100^{o}C for 40h in Ar atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; Rf=0.5) to afford compound **3al** (yellow oil, 34.4mg, yield=32%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{20}H_{19}ClNO_3$, 356.1048; found, 356.1051.

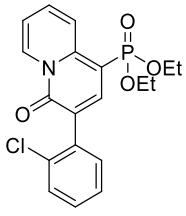
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.40 (ddd, *J* = 7.3, 1.4, 0.8 Hz, 1H), 9.31 (ddd, *J* = 9.3, 1.4, 0.9 Hz, 1H), 8.43 (s, 1H), 7.68 (ddd, *J* = 9.3, 6.6, 1.5 Hz, 1H), 7.55 – 7.43 (m, 2H), 7.40 – 7.29 (m, 2H), 7.22 (ddd, *J* = 7.3, 6.6, 1.5 Hz, 1H), 1.61 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.6, 156.8, 144.5, 141.5, 136.0, 134.0, 133.2, 132.0, 129.7, 129.0, 128.9, 126.7, 124.1, 117.0, 116.2, 103.4, 81.3, 28.3.





3am:
diethyl (3-(2-chlorophenyl)-4-oxo-4H-quinolizin-1-yl)phosphonate



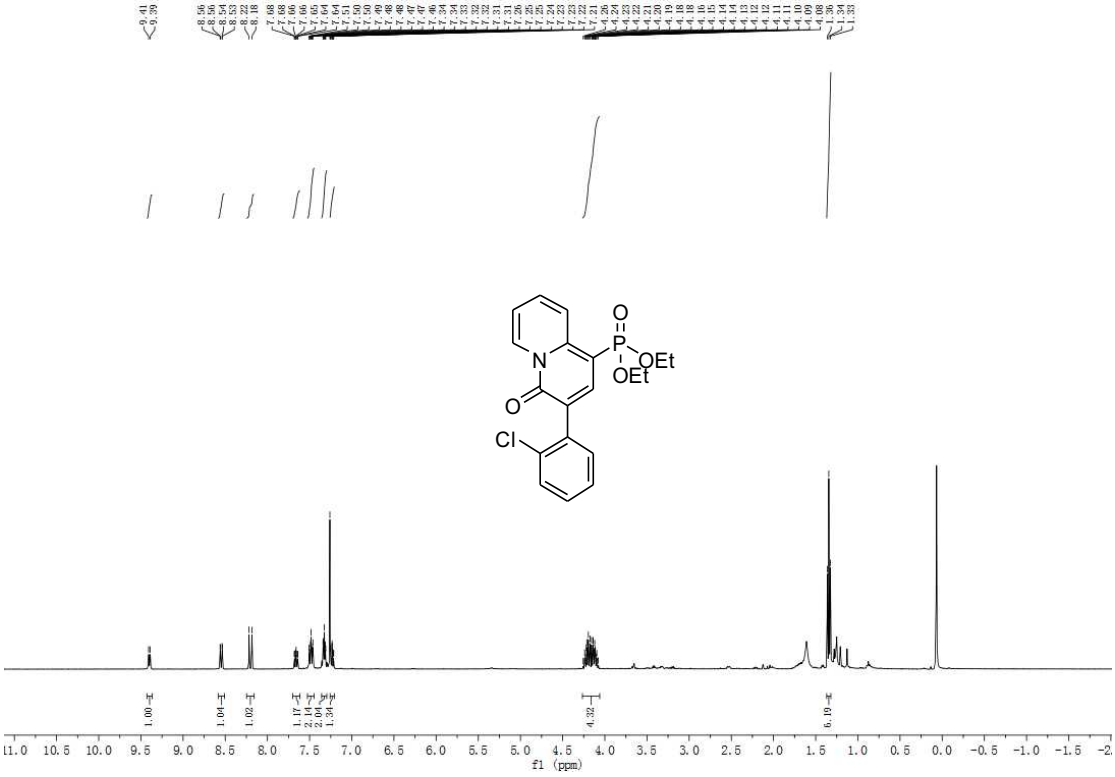
General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.6mmol, 205.6mg, 2.0equiv), diethyl vinylphosphonate **2m** (0.3mmol, 46.3μL, 1.0equiv), 2,2,6,6-Tetramethylpiperidoxyl (TEMPO, 0.75mmol, 117.2mg, 2.5equiv), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 1.2mmol, 179.2μL, 4.0equiv) were added sequentially to 3.0mL of toluene. The mixture was stirred at 100°C for 20h in N_2 atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=0:1, v/v; Rf=0.5) to afford compound **3am** (yellow oil, 13.0mg, yield=11%).

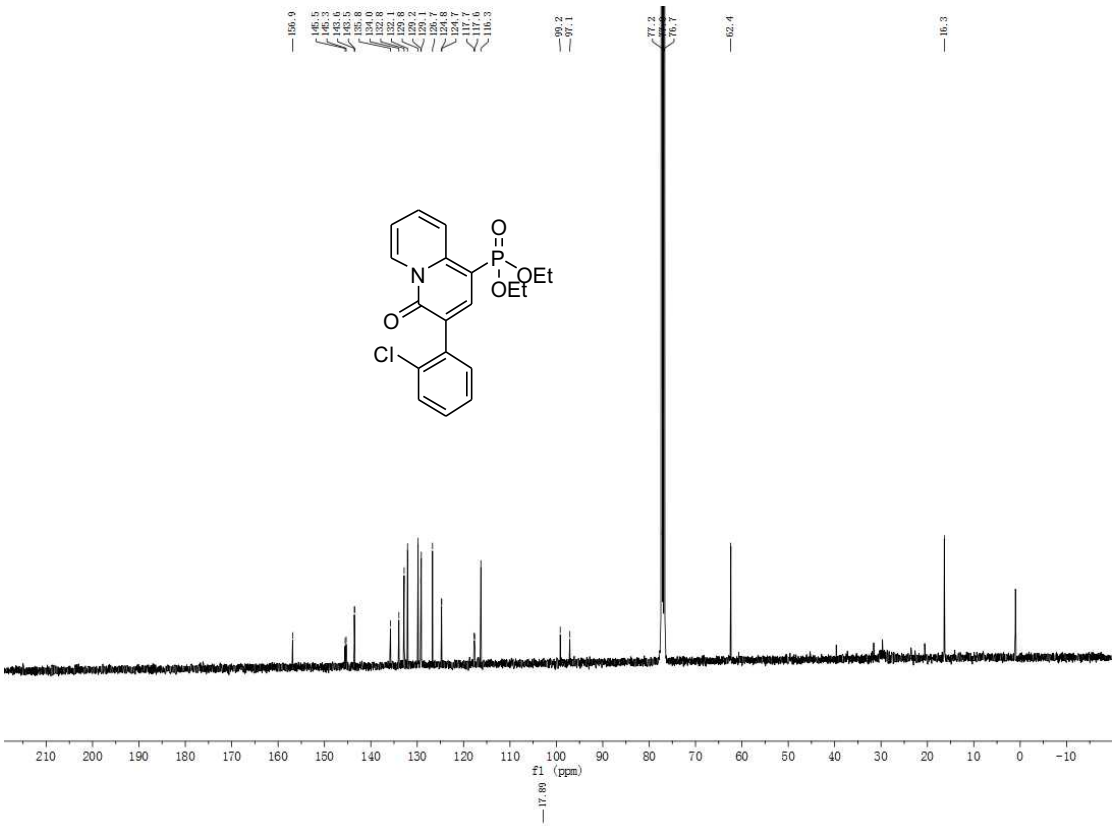
HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{19}H_{20}ClNO_4P$, 392.0813; found, 392.0808.

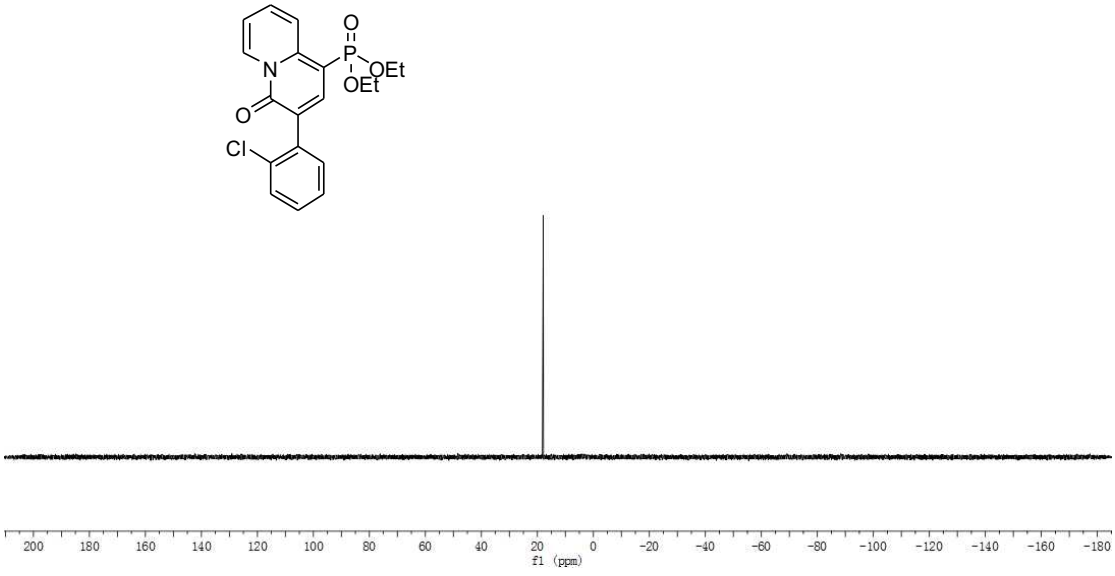
^1H NMR (400 MHz, Chloroform-*d*) δ 9.40 (d, *J* = 7.2 Hz, 1H), 8.55 (dd, *J* = 9.2, 1.3 Hz, 1H), 8.20 (d, *J* = 13.7 Hz, 1H), 7.66 (ddd, *J* = 8.7, 6.7, 1.4 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.36 – 7.30 (m, 2H), 7.26 – 7.21 (m, 1H), 4.27 – 4.06 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.9, 145.4, 143.6, 143.5, 135.8, 134.0, 132.8, 132.1, 129.8, 129.2, 129.1, 126.7, 124.8, 124.7, 117.8, 117.6, 116.3, 99.2, 97.1, 77.2, 62.4, 16.3.

^{31}P NMR (162 MHz, $CDCl_3$) δ 17.89.




156.9
145.5
145.3
142.6
135.8
134.0
132.8
131.1
129.8
129.2
129.1
124.8
124.7
117.7
117.6
116.3
99.2
97.1
77.2
62.4
16.3
17.89
O
P
OEt
OEt
N
O
Cl
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)


O
P
OEt
OEt
N
O
Cl
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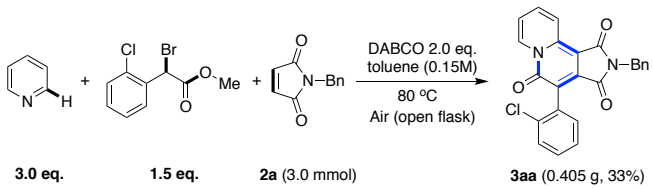
f1 (ppm)

4. Three-Component Reaction and Mechanism Study

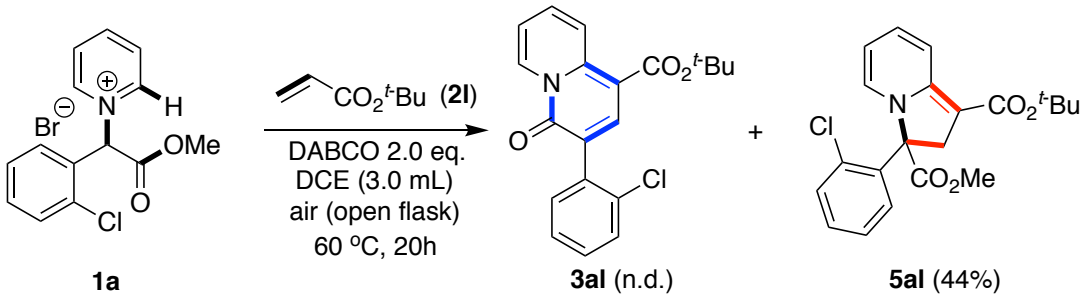
Scheme 4:



General procedure: pyridine (9.0 mmol, 728.0 uL), methyl 2-bromo-2-(2-chlorophenyl)acetate (4.5 mmol, 757.0 uL), 1-benzyl-1H-pyrrole-2,5-dione **2a** (3.0 mmol, 562.0 mg, 1.0equiv), and 1,4-Diazabicyclo[2.2.2]octane (DABCO, 6.0 mmol, 673.0 mg, 2.0equiv) were added sequentially to 20.0mL of toluene. The mixture was stirred at 80°C for 72h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=2:1, v/v; R_f=0.4) to afford compound **3aa** (yellow solid, 405.0 mg, yield=33%).

Scheme 5:

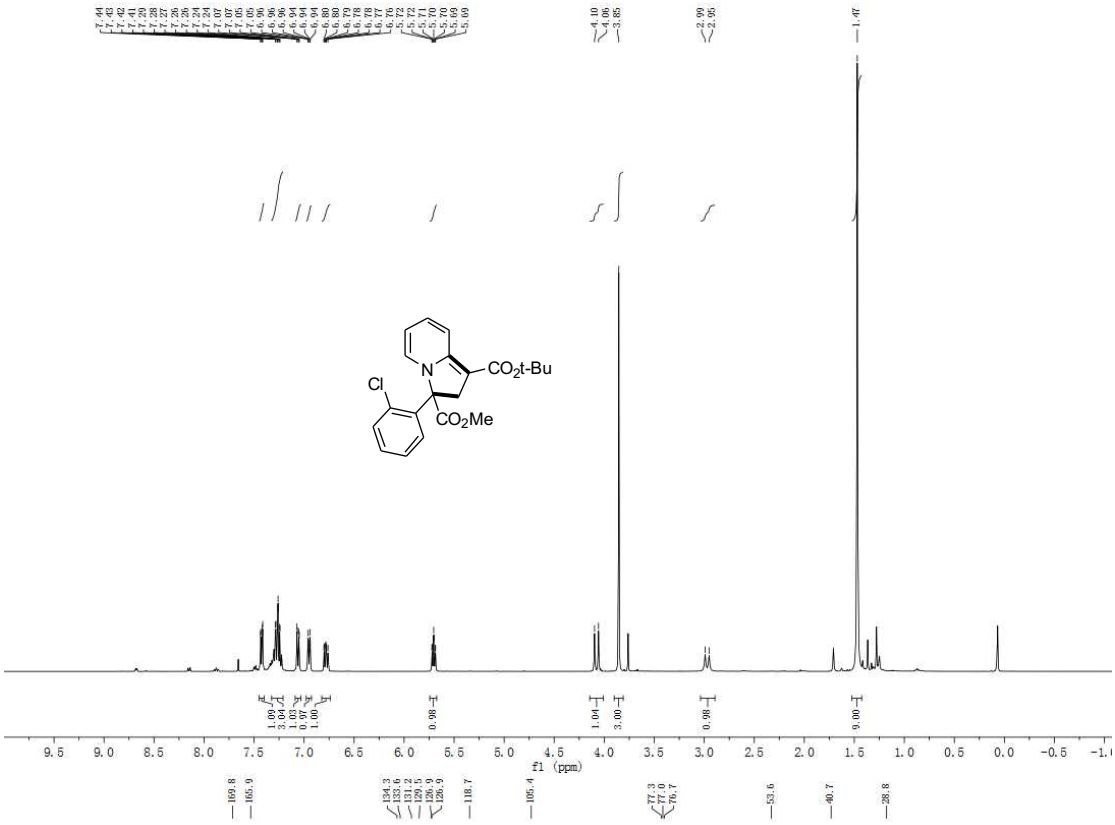
1-(tert-butyl) 3-methyl 3-(2-chlorophenyl)-2,3-dihydroindolizine-1,3-dicarboxylate (5al)



General procedure: 1-(1-(2-chlorophenyl)-2-methoxy-2-oxoethyl)pyridin-1-ium bromide **1a** (0.36mmol, 123.3mg, 1.2equiv), *tert*-butyl acrylate **2l** (0.3mmol, 44.0μL, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 67.3mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60°C for 20h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=5:1, v/v; Rf=0.65) to afford compound **5al** (orange oil, 50.6mg, yield=44%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.32 – 7.21 (m, 3H), 7.06 (dd, *J* = 7.6, 1.9 Hz, 1H), 6.95 (dt, *J* = 7.1, 1.2 Hz, 1H), 6.82 – 6.74 (m, 1H), 5.70 (ddd, *J* = 7.3, 6.3, 1.3 Hz, 1H), 4.08 (d, *J* = 15.9 Hz, 1H), 3.85 (s, 3H), 2.97 (d, *J* = 15.8 Hz, 1H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.8, 165.9, 134.3, 133.6, 131.2, 129.5, 126.9, 118.7, 105.4, 53.6, 40.7, 28.8.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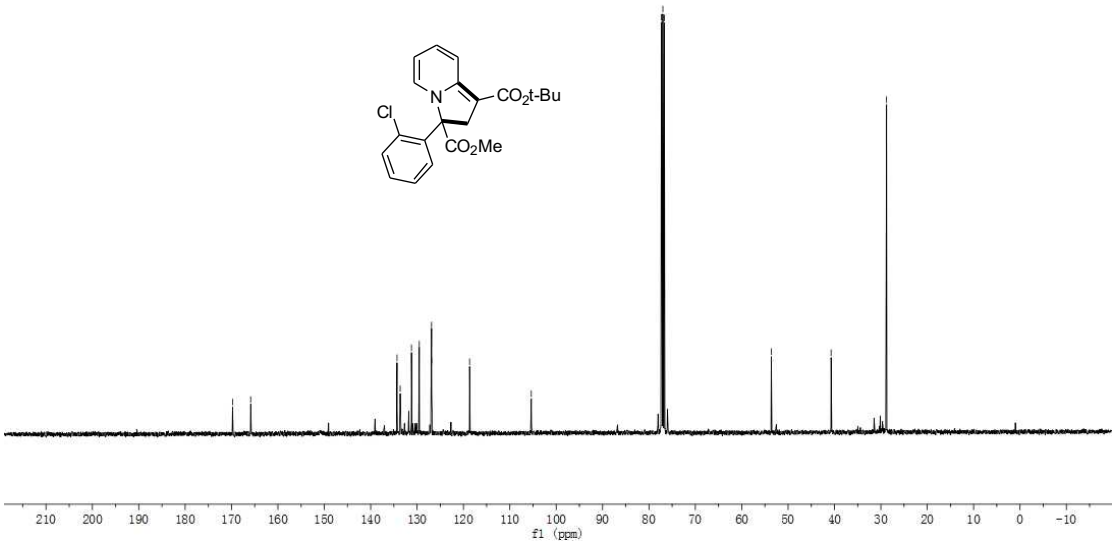
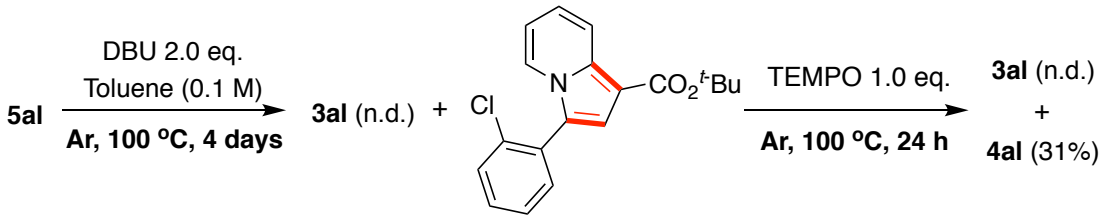
Cl
N
CO2Me
f1 (ppm)

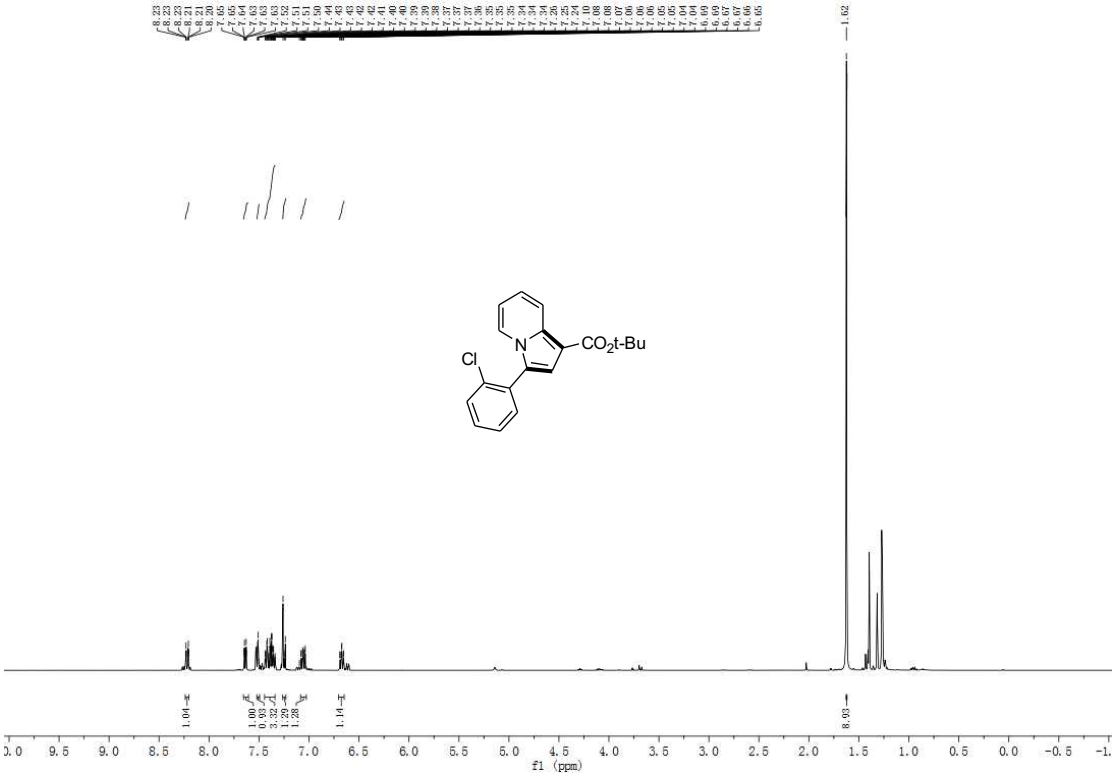

CO2t-Bu
Cl
N
CO2Me
f1 (ppm)

***tert*-butyl 3-(2-chlorophenyl)indolizine-1-carboxylate (4al)**

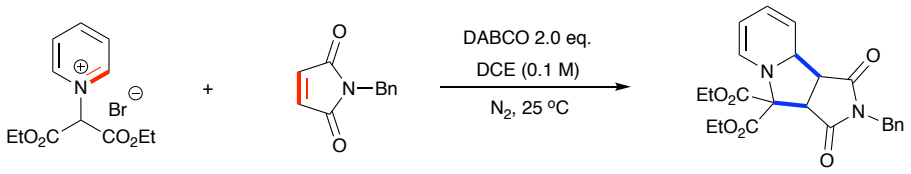


Synthesis procedure: 5al (0.45mmol, 174.6mg, 1.0equiv) and DBU (0.9mmol, 135.0 uL, 2.0equiv) were added to 4.5mL of toluene. The mixture was stirred at 100 °C for 4 days in Ar atmosphere. Neither 4*H*-quinolizin-4-one (**3al**) nor indolizine (**4al**) were observed by TLC. Then TEMPO (0.45 mmol, 70.3mg, 1.0equiv) was added in the reaction mixture. After 24 hours, solvent was removed by rotary evaporator, the residual crude products were purified by column chromatography (SiO_2, PE/EA=5:1, v/v; Rf=0.8) to afford compound **4al** (orange oil, 45.4mg, yield=31%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.64 (dt, *J* = 7.0, 1.1 Hz, 1H), 7.52 – 7.49 (m, 1H), 7.44 – 7.34 (m, 3H), 7.26 – 7.23 (m, 1H), 7.08 – 7.03 (m, 1H), 6.67 (td, *J* = 6.8, 1.4 Hz, 1H), 1.62 (s, 9H).

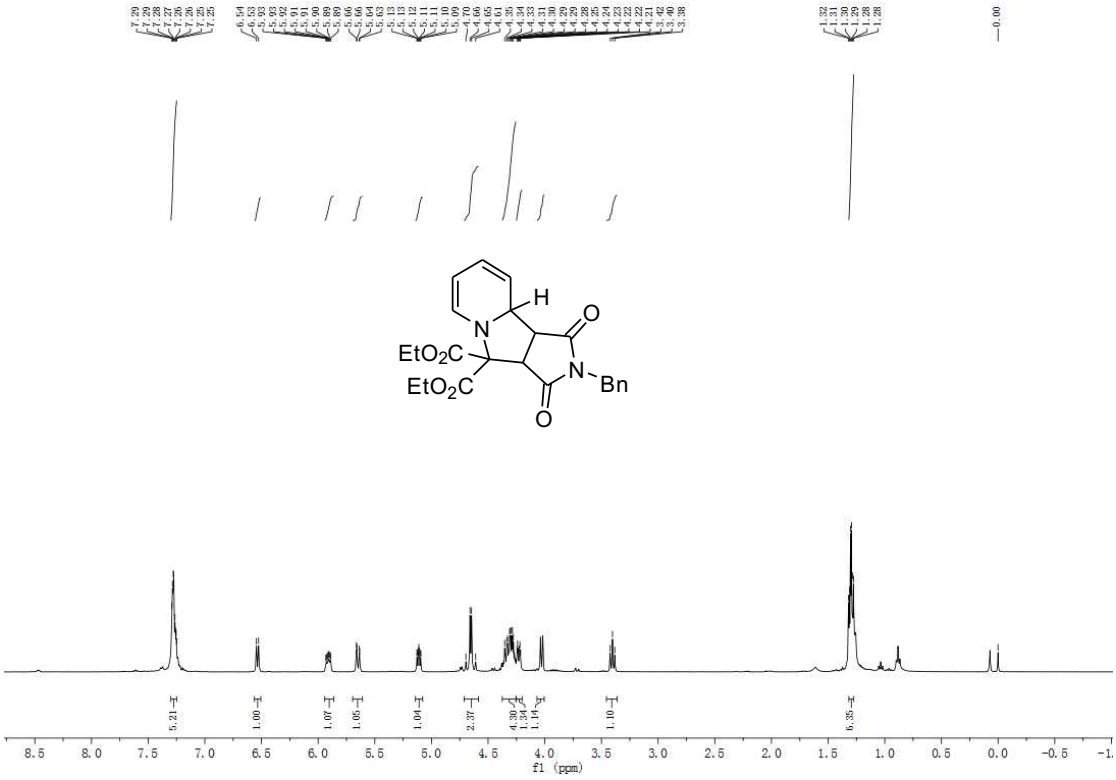


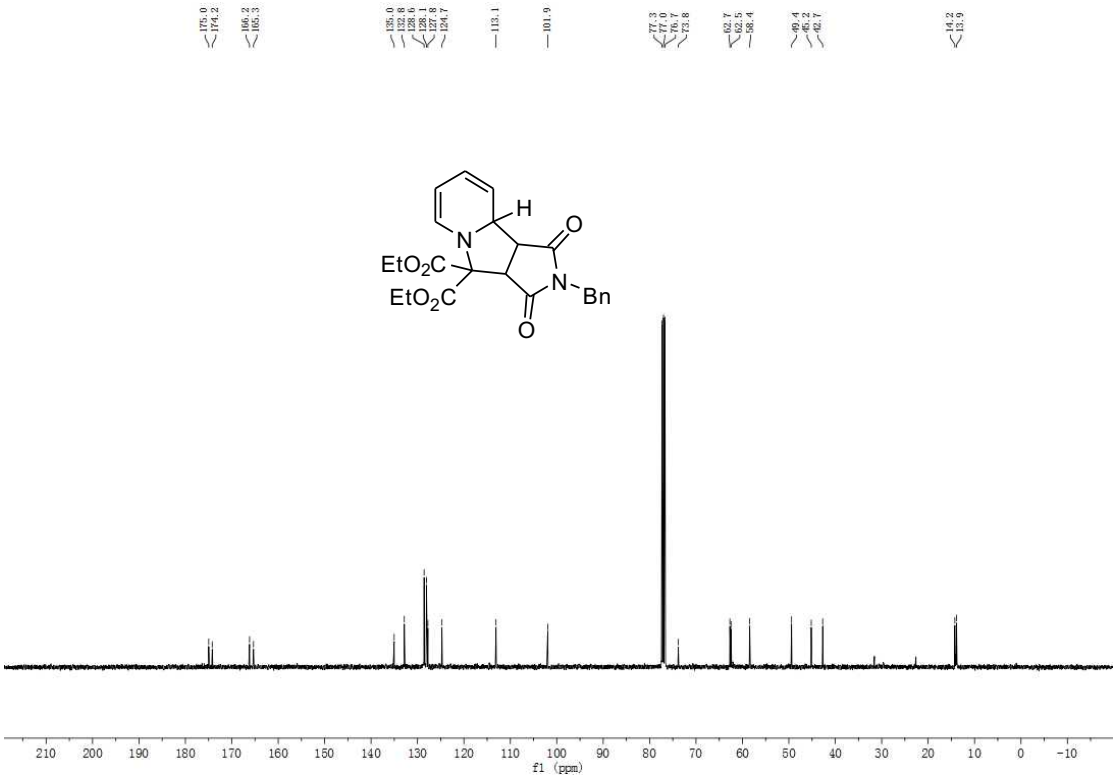
Scheme 6A:
diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate (6da)



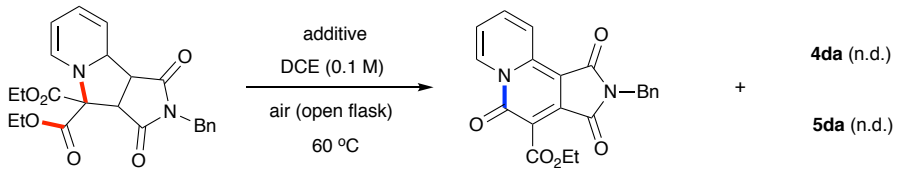
1d (1.2 eq.) **2a** **6da** (67%)

Synthesis procedure: 1-(1,3-diethoxy-1,3-dioxopropan-2-yl)pyridin-1-ium bromide **1d** (0.36 mmol, 114.6 mg, 1.2 equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3 mmol, 56.2 mg, 1.0 equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6 mmol, 67.3 mg, 2.0 equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 25 °C for 2 h under a nitrogen atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO2, PE/EA=5:1, v/v; Rf=0.5) to afford compound **6da** (yellow oil, 85.6 mg, yield= 67%).
HRMS(ESI+)m/z: [M+Na]+ calcd for $C_{23}H_{25}N_2O_6Na$, 447.1527; found, 447.1522.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 5H), 6.53 (d, *J* = 7.5 Hz, 1H), 5.94 – 5.86 (m, 1H), 5.65 (dd, *J* = 9.8, 1.8 Hz, 1H), 5.11 (ddd, *J* = 7.1, 5.4, 1.3 Hz, 1H), 4.71 – 4.58 (m, 2H), 4.38 – 4.25 (m, 4H), 4.25 – 4.20 (m, 1H), 4.03 (d, *J* = 7.9 Hz, 1H), 3.40 (t, *J* = 8.1 Hz, 1H), 1.29 (dt, *J* = 7.3, 3.7 Hz, 6H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.0, 174.2, 166.2, 165.3, 135.0, 132.8, 128.6, 128.1, 127.8, 124.7, 113.1, 101.94 , 73.8, 62.7, 62.5, 58.4, 49.4, 45.2, 42.7, 14.3, 13.9.





Scheme 6B: NMR Yield.



6da **3da**

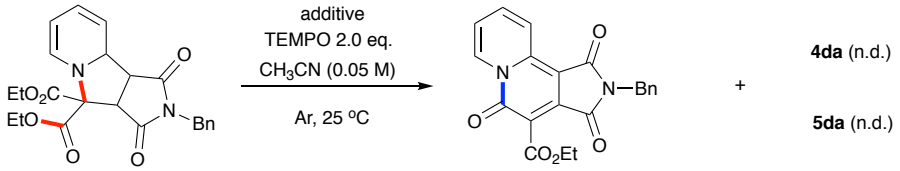
(A) additive = none, yield = 28% (conversion = 100%)
(B) additive = DABCO 1.0 eq., yield = 42% (conversion = 100%)
(C) additive = DABCO 1.0 eq. & **1d** 50 mol%, yield = 56% (conversion = 100%)

(A) diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate **6da** (0.3 mmol, 127.4mg) were added to 3.0mL of DCE. The mixture was stirred at 60 °C for 40h under open-flsk conditions. 28% NMR Yield of **3da** was obtained using 1,3,5-trimethoxybenzene as internal standard.

(B) diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate **6da** (0.3 mmol, 127.4mg) and DABCO (0.3mmol, 33.6mg) were added to 3.0mL of DCE. The mixture was stirred at 60 °C for 40h under open-flsk conditions. 42% NMR Yield of **3da** was obtained using 1,3,5- trimethoxybenzene as internal standard.

(C) diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate **6da** (0.3 mmol, 127.4mg), DABCO (0.3mmol, 33.6mg) and **1d** (0.15mmol, 47.7mg, 0.5equiv.) were added to 3.0mL of DCE. The mixture was stirred at 60 °C for 40h under open-flsk conditions. 42% NMR Yield of **3da** was obtained using 1,3,5- trimethoxybenzene as internal standard..

Scheme 6C:



(A) additive = none, yield = 45% (conversion = 100%)
(B) additive = DABCO 3.0 eq., yield = 47% (conversion = 100%)
(C) additive = DABCO 3.0 eq. & **1d** 50 mol%, yield = 76% (conversion = 100%)

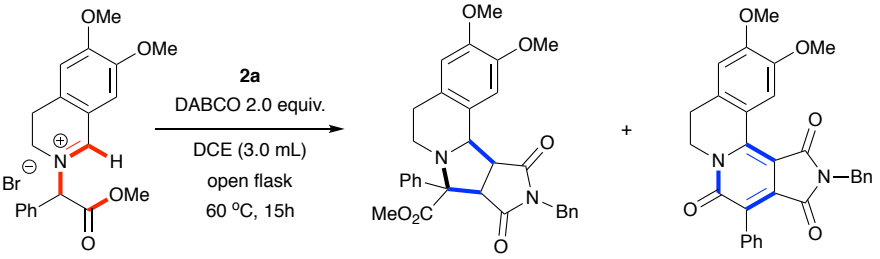
(A) diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate **6da** (0.3 mmol, 127.4mg) and TEMPO (0.6mmol, 93.8mg, 2.0equiv) were added sequentially to 6.0mL of CH_3CN. The mixture was stirred at 25 °C for 20h in an Argon atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.5) to afford compound **3da** (yellow solid, m.p=169-171°C, 51.2mg, yield=45%).

(B) diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate **6da** (0.3 mmol, 127.4mg), DABCO (0.9mmol, 101.0mg) and TEMPO (0.6mmol, 93.8mg, 2.0equiv) were added sequentially to 6.0mL of CH_3CN. The mixture was stirred at 25 °C for 20h in an Argon atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.5) to afford compound **3da** (yellow solid, m.p=169-171°C, 53.2mg, yield=47%).

(C) diethyl 2-benzyl-1,3-dioxo-1,2,3,3a,9a,9b-hexahydro-4H-pyrrolo[3,4-a]indolizine-4,4-dicarboxylate **6da** (0.3 mmol, 127.4mg), DABCO (0.9mmol, 101.0mg), **1d** (0.15mmol, 47.7mg, 0.5equiv.) and TEMPO (0.6mmol, 93.8mg, 2.0equiv) were added sequentially to 6.0mL of CH_3CN. The mixture was stirred at 25 °C for 20h in an Argon atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=1:1, v/v; Rf=0.5) to afford compound **3da** (yellow solid, m.p=169-171°C, 85.8mg, yield=76%).

Scheme 7A:

methyl 10-benzyl-2,3-dimethoxy-9,11-dioxo-8-phenyl-5,8,8a,9,10,11,11a,11b-octahydro-6H-pyrrolo[3',4':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate (6la)



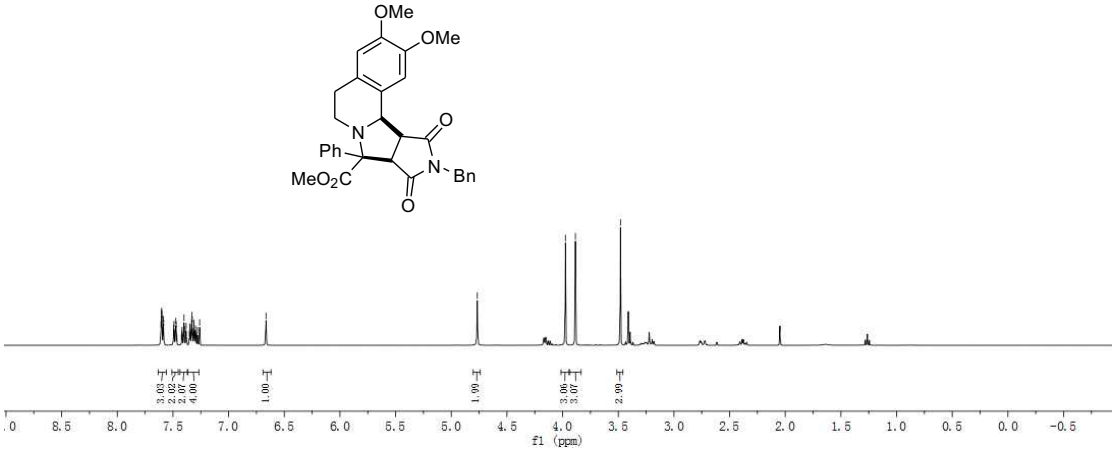
1l **6la** (91%) **3la** (not found)

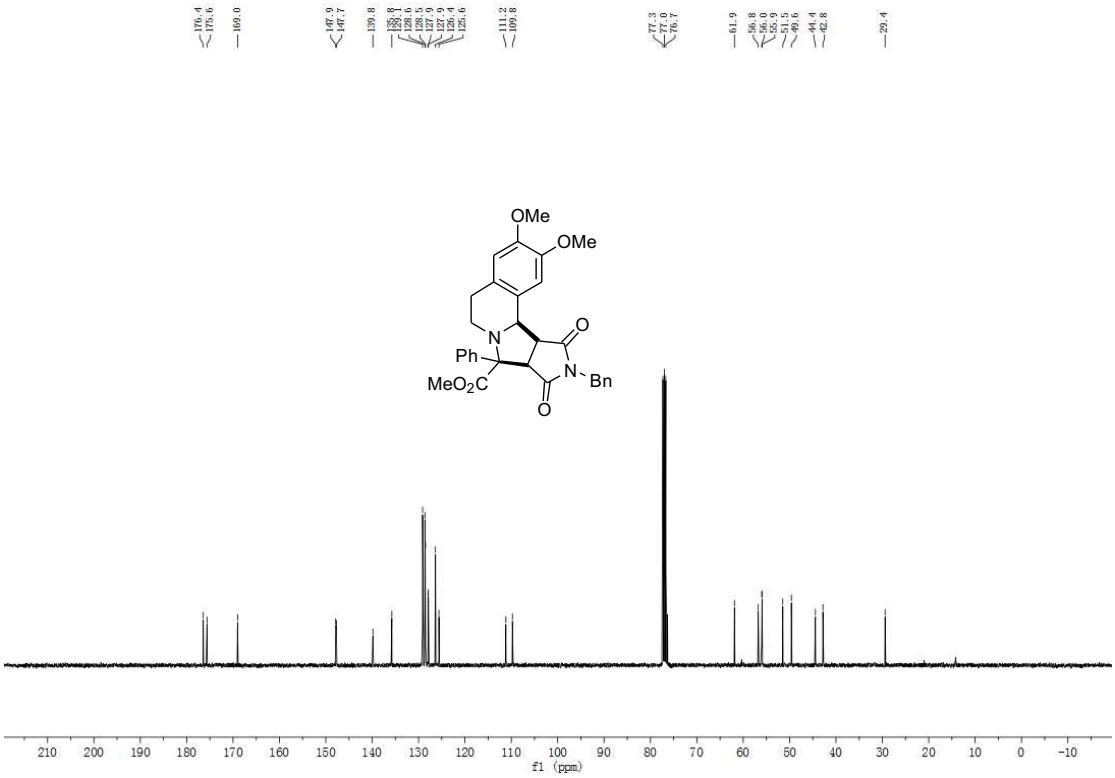
General procedure: 6,7-dimethoxy-2-(2-methoxy-2-oxo-1-phenylethyl)-3,4-dihydroisoquinolin-2-ium bromide **1l** (0.25mmol, 107.5mg, 1.25equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.2mmol, 37.5mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 0.6mmol, 44.9mg, 2.0equiv) were added sequentially to 3.0mL of 1,2-Dichloroethane. The mixture was stirred at 60°C for 15h in open flask. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=5:1, v/v; Rf=0.6) to afford compound **6la** (yellow oil, 95.9mg, yield=91%).

HRMS(ESI+)m/z: $[M+H]^+$ calcd for $C_{31}H_{31}N_2O_6$, 527.2177; found, 527.2185.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 – 7.56 (m, 3H), 7.51 – 7.45 (m, 2H), 7.44 – 7.37 (m, 2H), 7.37 – 7.27 (m, 4H), 6.66 (s, 1H), 4.77 (s, 2H), 3.97 (s, 3H), 3.89 (s, 3H), 3.48 (s, 3H).

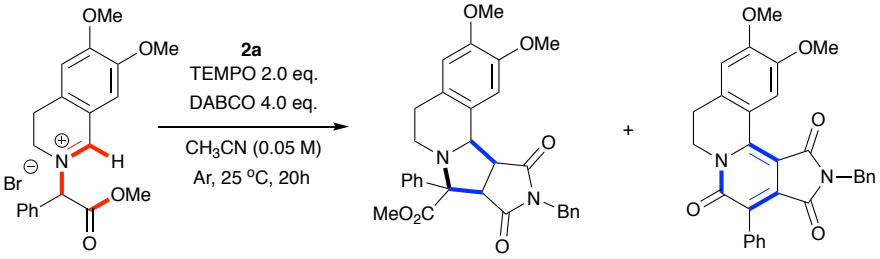
^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.4, 175.6, 169.0, 147.9, 147.7, 139.9, 135.8, 129.1, 128.6, 128.5, 127.9, 127.9, 126.4, 125.6, 111.2, 109.8, 61.9, 56.8, 56.0, 55.9, 51.5, 49.6, 44.4, 42.8, 29.4.





Scheme 7B:

methyl 10-benzyl-2,3-dimethoxy-9,11-dioxo-8-phenyl-5,8,8a,9,10,11,11a,11b-octahydro-6H-pyrrolo[3',4':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate (6la)

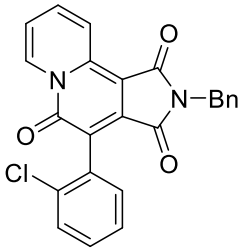


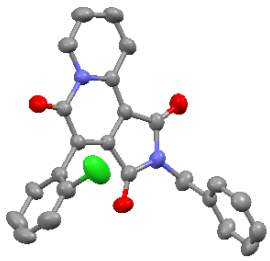
1l **6la** (71%) **3la** (not found)

General procedure: 6,7-dimethoxy-2-(2-methoxy-2-oxo-1-phenylethyl)-3,4-dihydroisoquinolin-2-ium bromide **1l** (0.45mmol, 189.1mg, 1.5equiv), 1-benzyl-1H-pyrrole-2,5-dione **2a** (0.3mmol, 56.2mg, 1.0equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO, 1.2mmol, 134.6mg, 4.0equiv), TEMPO (0.6mmol, 93.8mg, 2.0equiv) were added sequentially to 6.0mL of CH_3CN. The mixture was stirred at 25°C for 20h under an argon atmosphere. Then solvent was removed by rotary evaporator, the residual crude products was purified by column chromatography (SiO_2, PE/EA=5:1, v/v; Rf=0.6) to afford compound **6la** (yellow oil, 111.7mg, yield=71%).

5. X-ray Information for 3aa

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





3aa CCDC:2282683

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 1_a

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

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Bond precision:      C-C = 0.0035 A          Wavelength=0.71073
Cell:           a=9.8715(15) b=10.2631(15) c=10.4758(15)
                alpha=92.848(2) beta=100.885(2)
gamma=108.048(2)
Temperature:    296 K
                     Calculated              Reported
Volume               984.3(3)                984.3(3)
Space group          P -1                    P -1
Hall group          -P 1                    -P 1
Moiety formula       C24 H15 Cl N2 O3        ?
Sum formula          C24 H15 Cl N2 O3        C24 H15 Cl N2 O3
Mr                   414.83                  414.83
Dx,g cm-3            1.400                   1.400
Z                    2                       2
Mu (mm-1)            0.224                   0.224
F000                 428.0                   428.0
F000'                428.48
h,k,lmax             14,15,15                13,13,15
Nref                 6438                    5127
Tmin,Tmax            0.948,0.956             0.656,0.746
Tmin'                0.935
Correction method= # Reported T Limits: Tmin=0.656 Tmax=0.746
AbsCorr = MULTI-SCAN
Data completeness= 0.796       Theta(max)= 31.324
R(reflections)= 0.0603( 3475)
wR2(reflections)=
0.1930( 5127)
S = 0.998            Npar= 271
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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

PLAT230_ALERT_2_C Hirshfeld Test Diff for C4 --C5 . 6.0 s.u.
PLAT242_ALERT_2_C Low 'MainMol' Ueq as Compared to Neighbors of C6 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ..... 3.890 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.600 33 Report
PLAT992_ALERT_5_C Repd & Actual _reflns_number_gt Values Differ by 14 Check

Alert level G

PLAT154_ALERT_1_G The s.u.'s on the Cell Angles are Equal ..(Note) 0.002 Degree
PLAT432_ALERT_2_G Short Inter X...Y Contact Cl1 ..C10 . 3.25 Ang. 1-x,1-y,1-z = 2_666 Check
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 1155 Note
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ..... 1.3 Low
PLAT951_ALERT_5_G Calculated (ThMax) and CIF-Reported Kmax Differ 2 Units
PLAT957_ALERT_1_G Calculated (ThMax) and Actual (FCF) Kmax Differ 2 Units
PLAT965_ALERT_2_G The SHELXL WEIGHT Optimisation has not Converged Please Check
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 7 Info
0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
5 **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
5 ALERT type 2 Indicator that the structure model may be wrong or deficient
3 ALERT type 3 Indicator that the structure quality may be low
1 ALERT type 4 Improvement, methodology, query or suggestion
2 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 06/07/2023; check.def file version of 30/06/2023

6. Reference

1 Shi. -Z. Zhu, Chao. -Y. Qin, Yan. -L. Wang, Qian. -l. Chu, *Journal of Fluorine Chemistry.* 1999, ***99(2),*** 183-187.