Supporting Information

Design, Synthesis, and Insecticidal Activity of Novel 1-alkoxy-2-nitroguanidines

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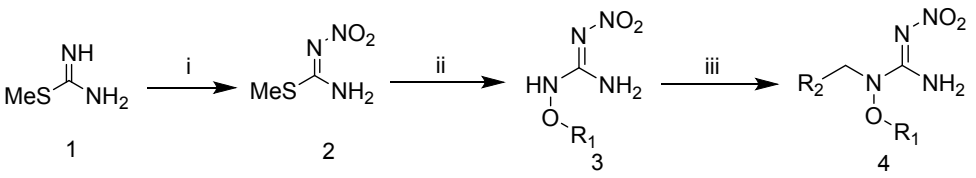


1 2 3 4

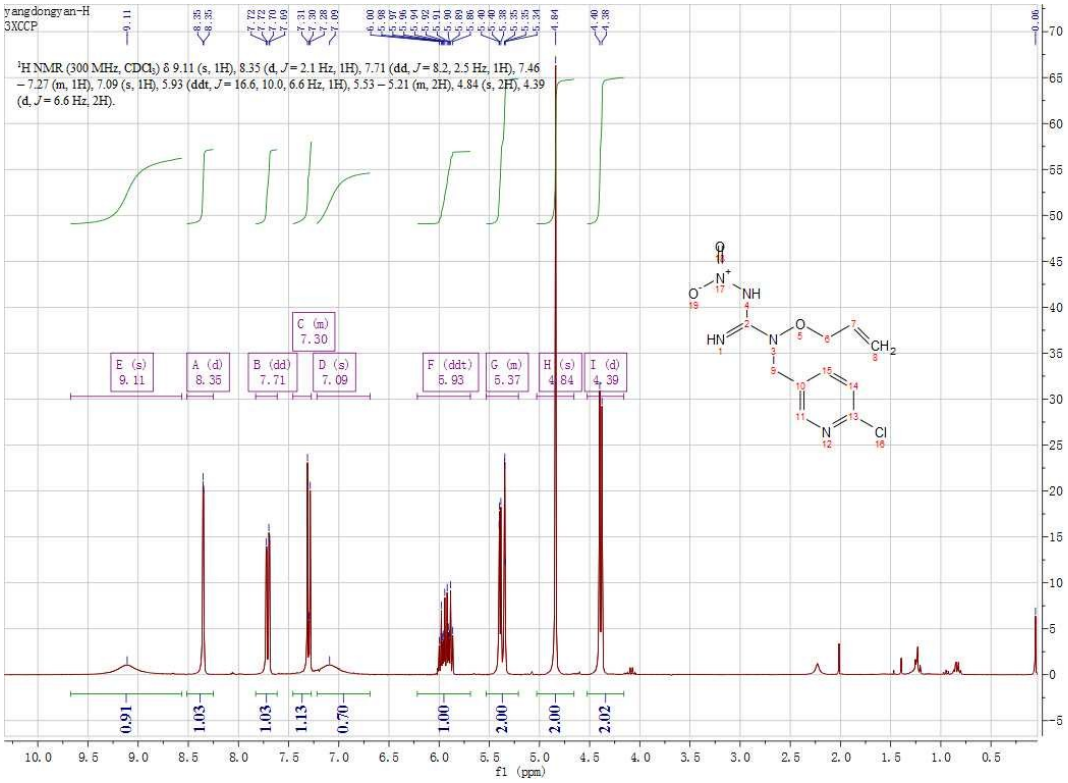
i. HNO_3,H_2SO_4, -15^{o}C; ii. R_1ONH_2, MeOH, 6-8h; iii.R_2CH_2X , NaH, KI, DMF, 0^{o}C-rt,22h

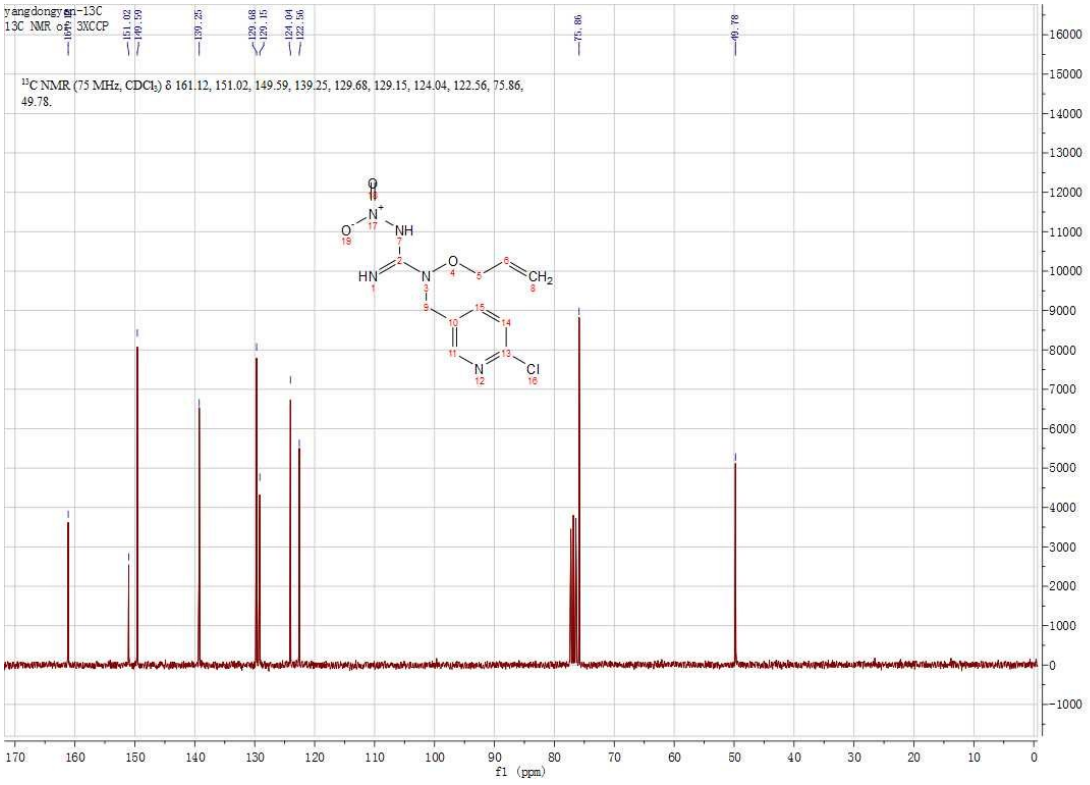
3-01 R_1=allyl 3-02 R_1=Et 3-03 R_1=*n*-Pr 3-04 R_1=*n*-Bu 3-05 R_1=*n*-Pentyl

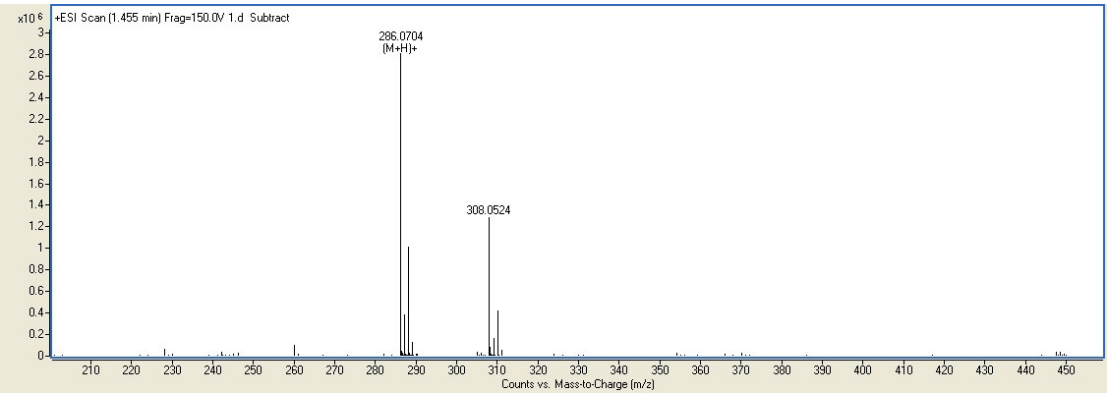
4-01 R_1=allyl, R_2=2-Cl-Pyridin-5-yl
4-02 R_1=Et, R_2=2-Cl-Pyridin-5-yl
4-03 R_1=*n*-Pr, R_2=2-Cl-Pyridin-5-yl
4-04 R_1=*n*-Bu, R_2=2-Cl-Pyridin-5-yl
4-05 R_1=*n*-Pentyl, R_2=2-Cl-Pyridin-5-yl
4-06 R_1=allyl, R_2=2-Cl-thiazol-5-yl
4-07 R_1=Et, R_2=2-Cl-thiazol-5-yl
4-08 R_1=*n*-Pr, R_2=2-Cl-thiazol-5-yl
4-09 R_1=*n*-Bu, R_2=2-Cl-thiazol-5-yl
4-10 R_1=*n*-Pentyl, R_2=2-Cl-thiazol-5-yl
4-11 R_1=allyl, R_2=4-ClC_6H_4
4-12 R_1=Et, R_2=4-ClC_6H_4
4-13 R_1=*n*-Pr, R_2=4-ClC_6H_4
4-14 R_1=*n*-Bu, R_2=4-ClC_6H_4
4-15 R_1=*n*-Pentyl, R_2=4-ClC_6H_4
4-16 R_1=allyl, R_2=4-$NO_2C_6H_4$
4-17 R_1=Et, R_2=4-$NO_2C_6H_4$
4-18 R_1=*n*-Pr, R_2=4-$NO_2C_6H_4$
4-19 R_1=*n*-Bu, R_2=4-$NO_2C_6H_4$
4-20 R_1=*n*-Pentyl, R_2=4-$NO_2C_6H_4$
4-21 R_1=allyl, R_2=4-CNC_6H_4
4-22 R_1=Et, R_2=4-CNC_6H_4
4-23 R_1=*n*-Pr, R_2=4-CNC_6H_4
4-24 R_1=*n*-Bu, R_2=4-CNC_6H_4
4-25 R_1=*n*-Pentyl, R_2=4-CNC_6H_4

^{1}H NMR,^{13}C NMR and HRMS spectrum of title compounds

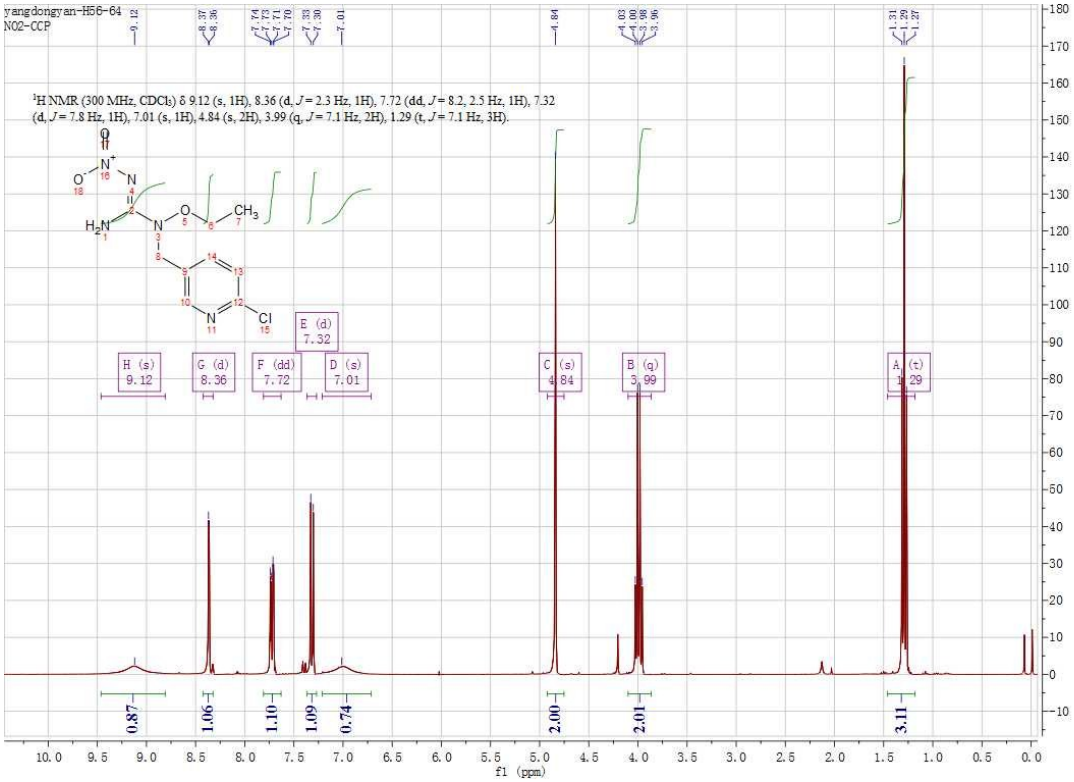
Data for (**4-01**): yield 72 %; white solid; mp 83-84 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.35 (d, *J* = 2.1 Hz, 1H), 7.71 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.46 – 7.27 (m, 1H), 7.09 (s, 1H), 5.93 (ddt, *J* = 16.6, 10.0, 6.6 Hz, 1H), 5.53 – 5.21 (m, 2H), 4.84 (s, 2H), 4.39 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.12, 151.02, 149.59, 139.25, 129.68, 129.15, 124.04, 122.56, 75.86, 49.78. HRMS (ESI) *m/z* calcd for $C_{10}H_{13}ClN_5O_3$ $(M+H)^+$ 286.0701, found 286.0704.

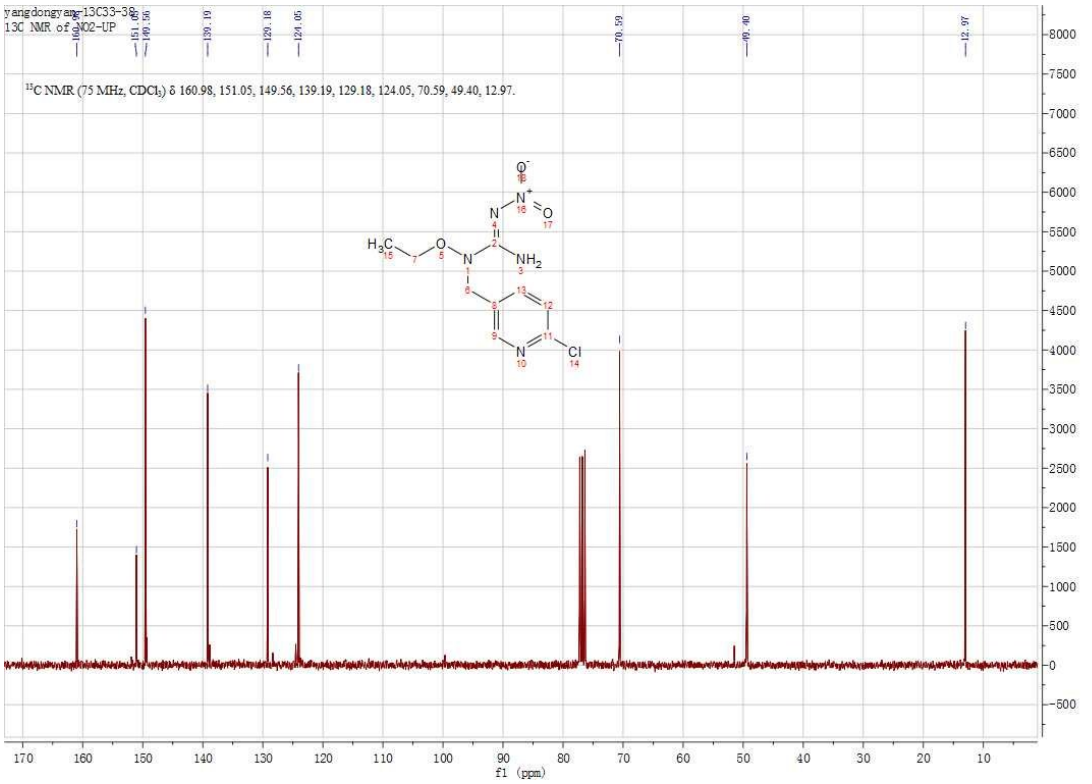


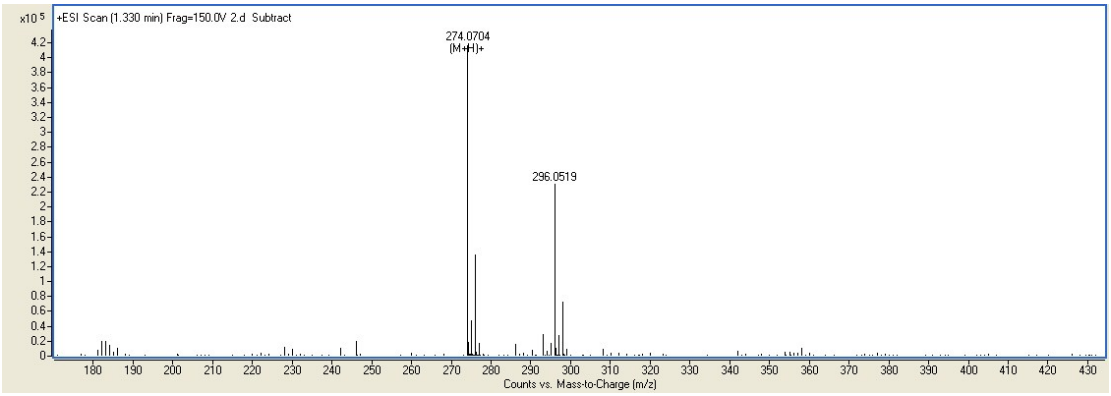




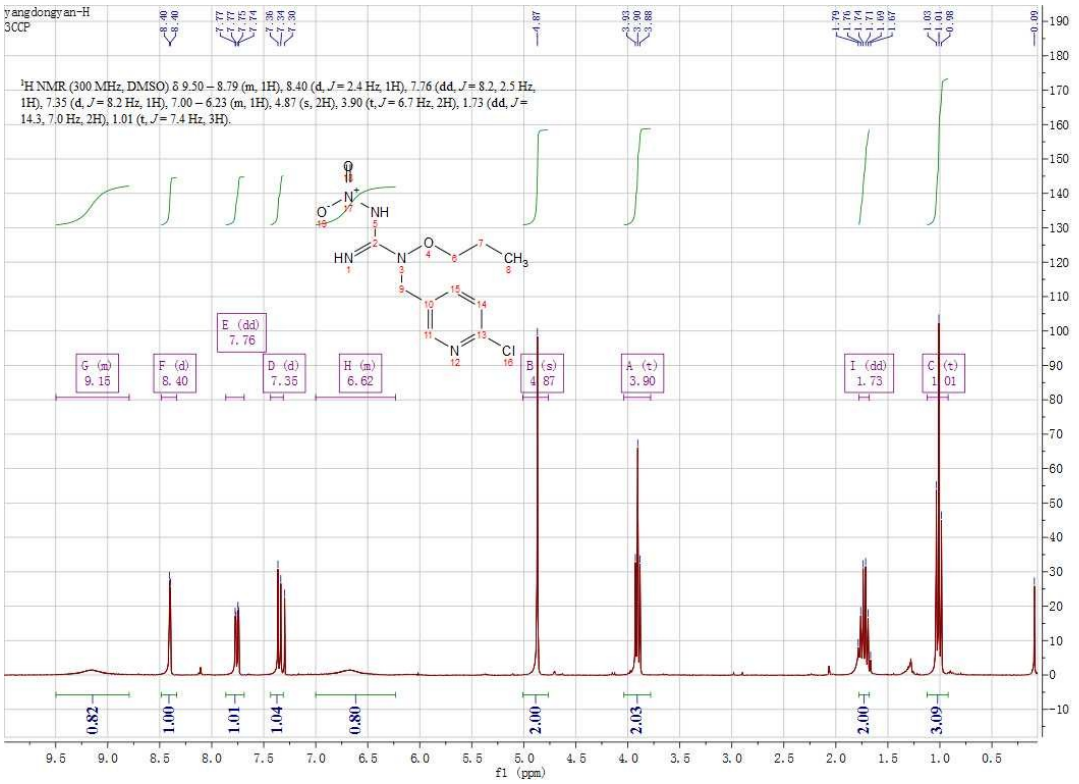
Data for (**4-02**): yield 78 %; white solid; mp 71-72 ℃;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.36 (d, *J* = 2.3 Hz, 1H), 7.72 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.01 (s, 1H), 4.84 (s, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.98, 151.05, 149.56, 139.19, 129.18, 124.05, 70.59, 49.40, 12.97. HRMS(ESI) *m/z* calcd for $C_9H_{13}ClN_5O_3$ $(M+H)^+$ 274.0701 , found 274.0704 .

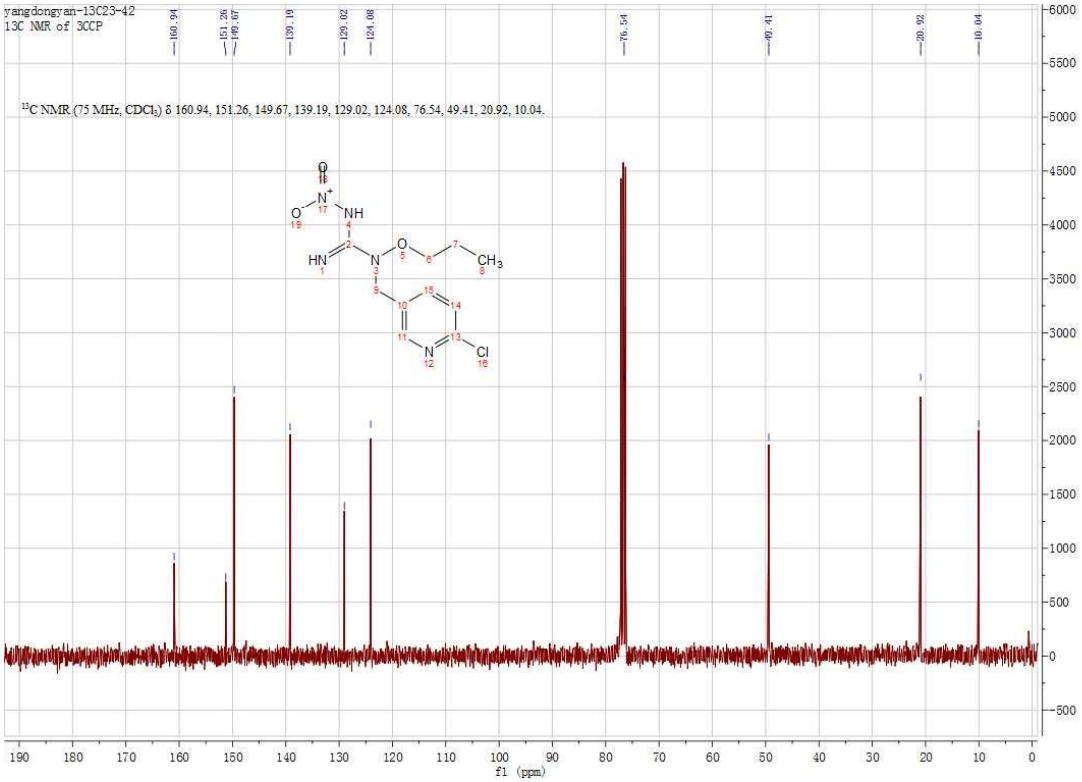


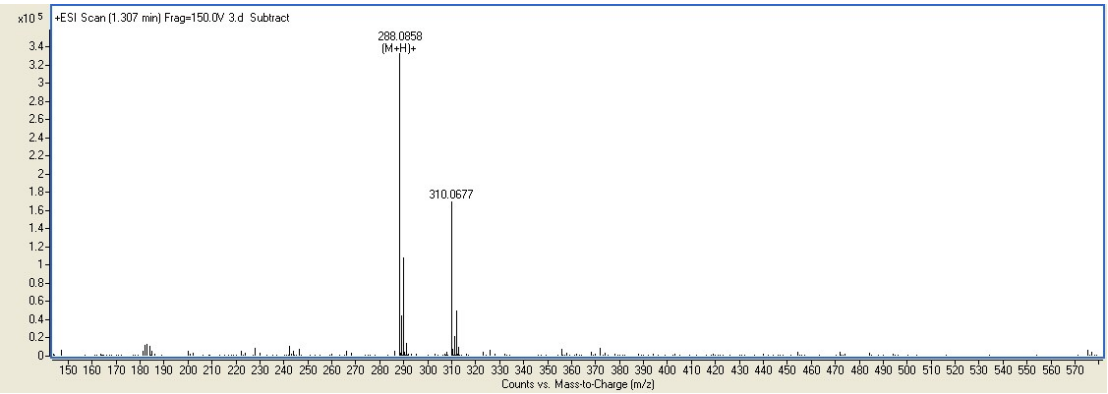




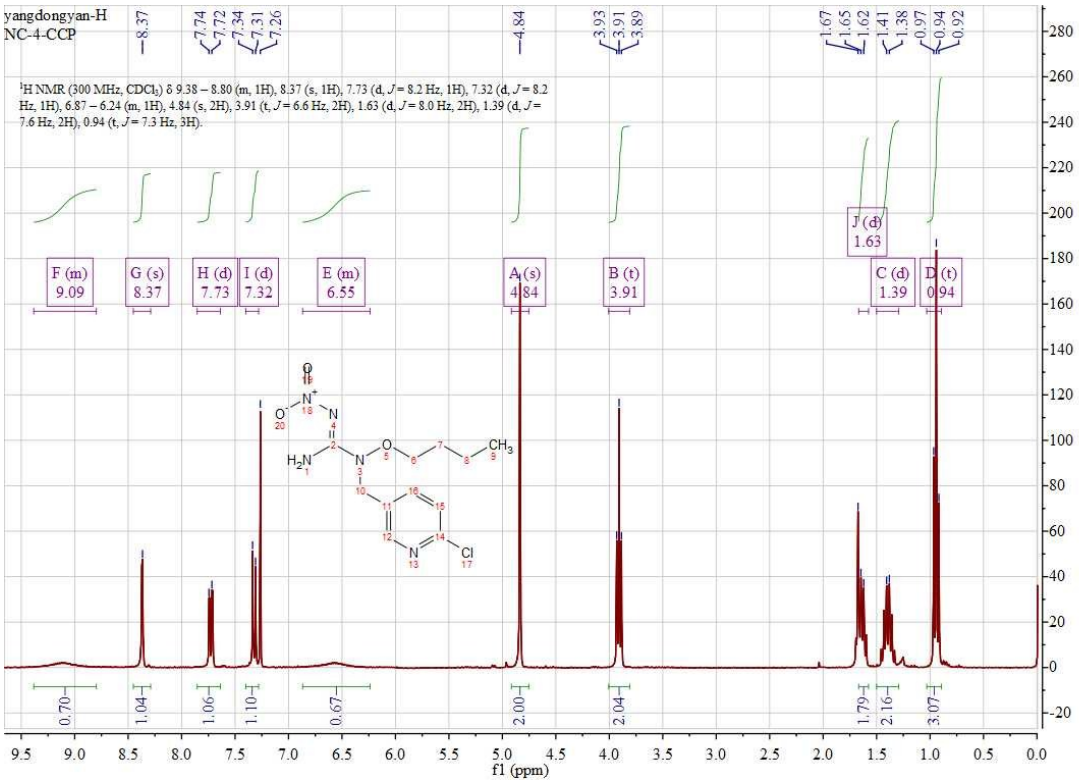
Data for (**4-03**): yield 59 %; white solid; mp 101-102 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 – 8.79 (m, 1H), 8.40 (d, *J* = 2.4 Hz, 1H), 7.76 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.00 – 6.23 (m, 1H), 4.87 (s, 2H), 3.90 (t, *J* = 6.7 Hz, 2H), 1.73 (dd, *J* = 14.3, 7.0 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.94, 151.26, 149.67, 139.19, 129.02, 124.08, 76.54, 49.41, 20.92, 10.04. HRMS (ESI) *m/z* calcd for $C_{10}H_{15}ClN_5O_3$ $(M+H)^+$ 288.0858 , found 288.0858 .

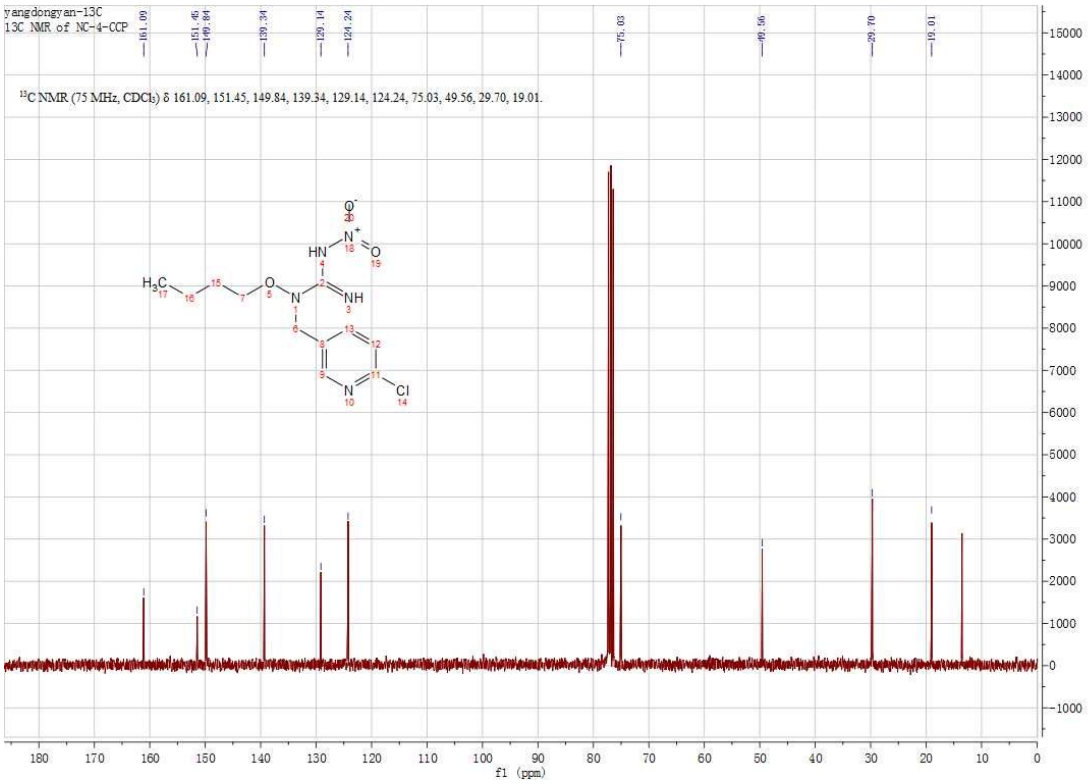

yangdongyan-H
3CCP
¹H NMR (300 MHz, DMSO) δ 9.50 – 8.79 (m, 1H), 8.40 (d, J = 2.4 Hz, 1H), 7.76 (dd, J = 8.2, 2.5 Hz, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.00 – 6.23 (m, 1H), 4.87 (s, 2H), 3.90 (t, J = 6.7 Hz, 2H), 1.73 (dd, J = 14.3, 7.0 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H).
G (m) 9.15
F (d) 8.40
E (dd) 7.76
D (d) 7.35
H (m) 6.62
B (s) 4.87
A (t) 3.90
I (dd) 1.73
C (t) 1.01
0.82
1.00
1.01
1.04
0.80
2.00
2.03
2.00
3.09
f1 (ppm)

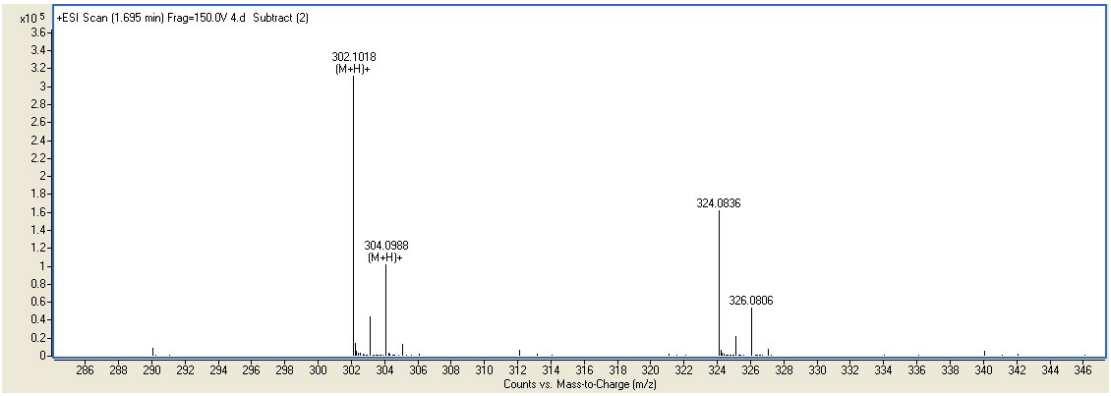

yangdongyan-13C23-42
13C NMR of 3CCP
¹³C NMR (75 MHz, CDCl₃) δ 160.94, 151.26, 149.67, 139.19, 129.02, 124.08, 76.54, 49.41, 20.92, 10.04.
f1 (ppm)



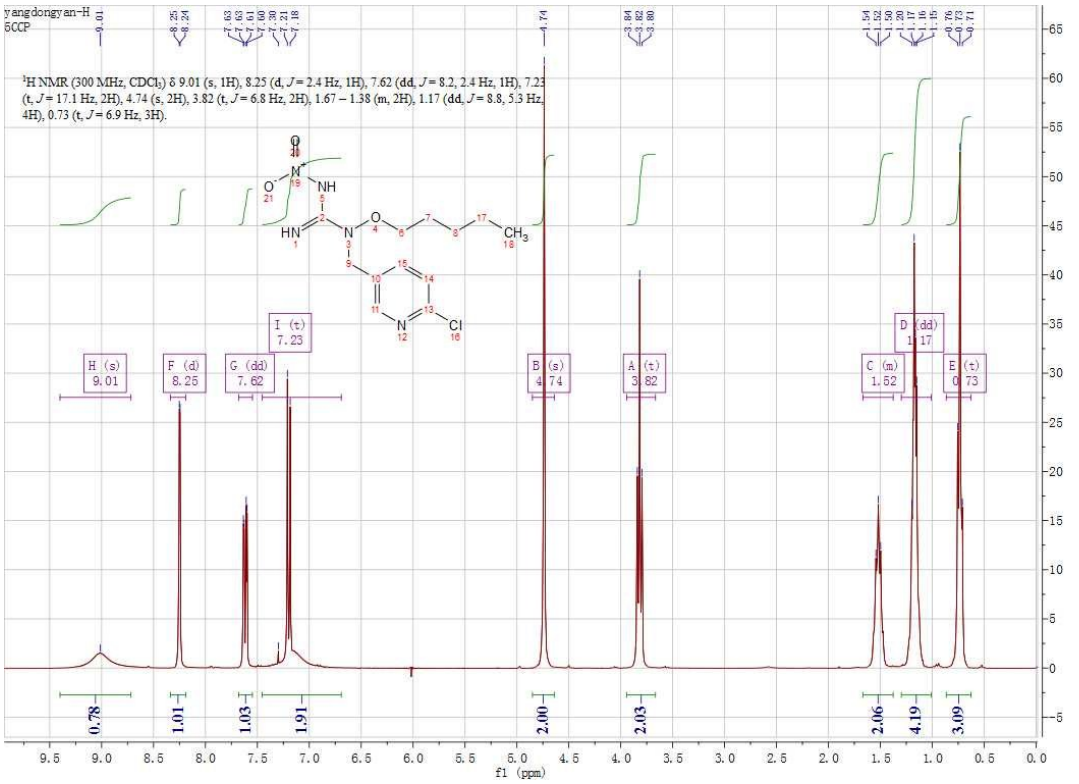
Data for (**4-04**): yield 60 %; white solid; mp 68-69 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 – 8.80 (m, 1H), 8.37 (s, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 6.87 – 6.24 (m, 1H), 4.84 (s, 2H), 3.91 (t, *J* = 6.6 Hz, 2H), 1.63 (d, *J* = 8.0 Hz, 2H), 1.39 (d, *J* = 7.6 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.09, 151.45, 149.84, 139.34, 129.14, 124.24, 75.03, 49.56, 29.70, 19.01. HRMS (ESI) *m/z* calcd for $C_{11}H_{17}ClN_5O_3$ $(M+H)^+$ 302.1014 , found 302.1018 .

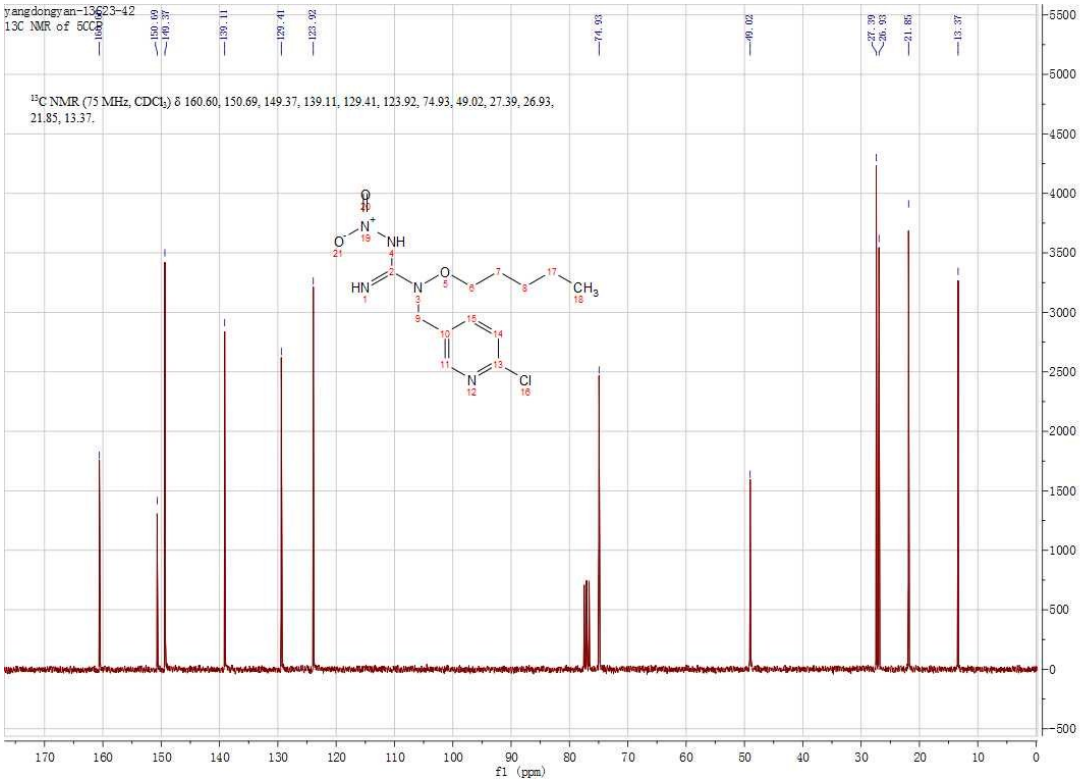


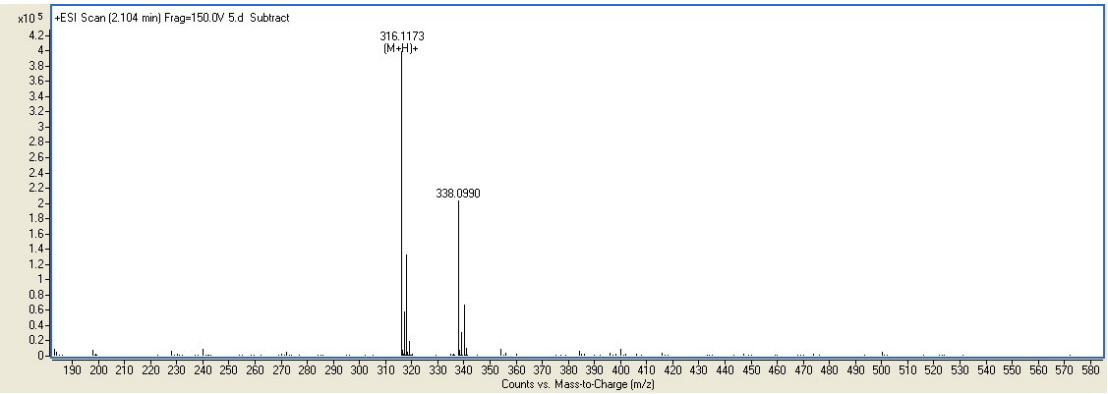




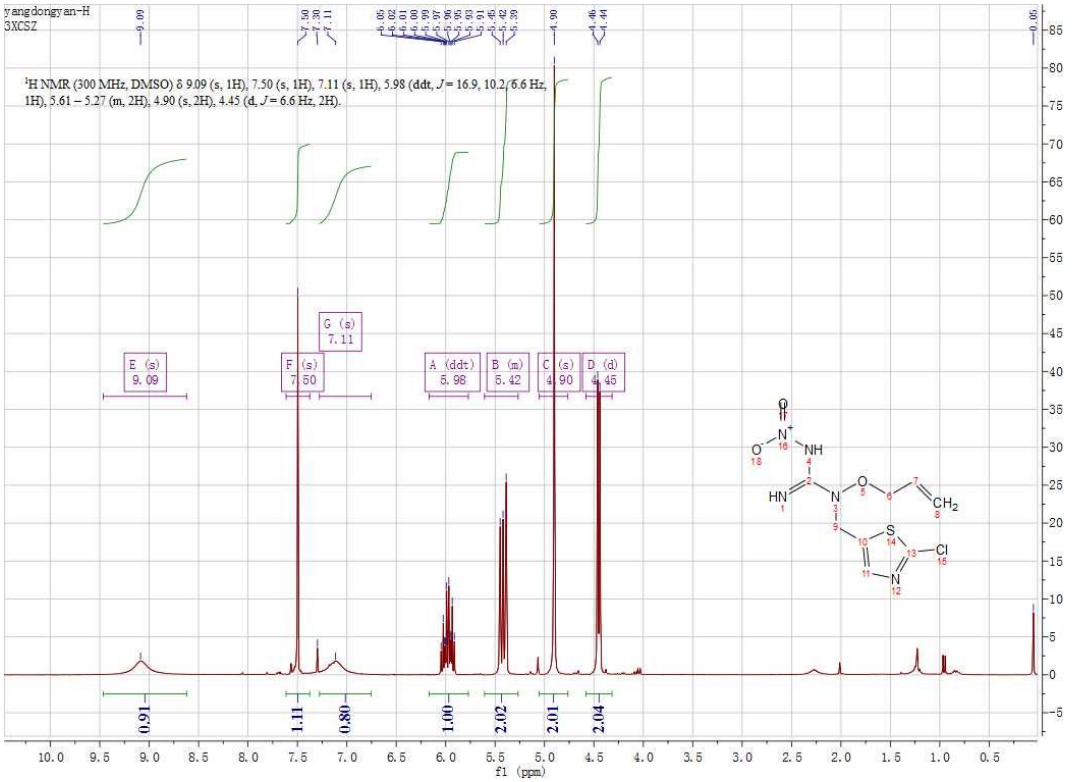
Data for (**4-05**): yield 57 %; white solid; mp 67-68 ℃;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.25 (d, *J* = 2.4 Hz, 1H), 7.62 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.23 (t, *J* = 17.1 Hz, 2H), 4.74 (s, 2H), 3.82 (t, *J* = 6.8 Hz, 2H), 1.67 – 1.38 (m, 2H), 1.17 (dd, *J* = 8.8, 5.3 Hz, 4H), 0.73 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.60, 150.69, 149.37, 139.11, 129.41, 123.92, 74.93, 49.02, 27.39, 26.93, 21.85, 13.37. HRMS (ESI) *m/z* calcd for $C_{12}H_{19}ClN_5O_3$ $(M+H)^+$ 316.1171 , found 316.1173 .

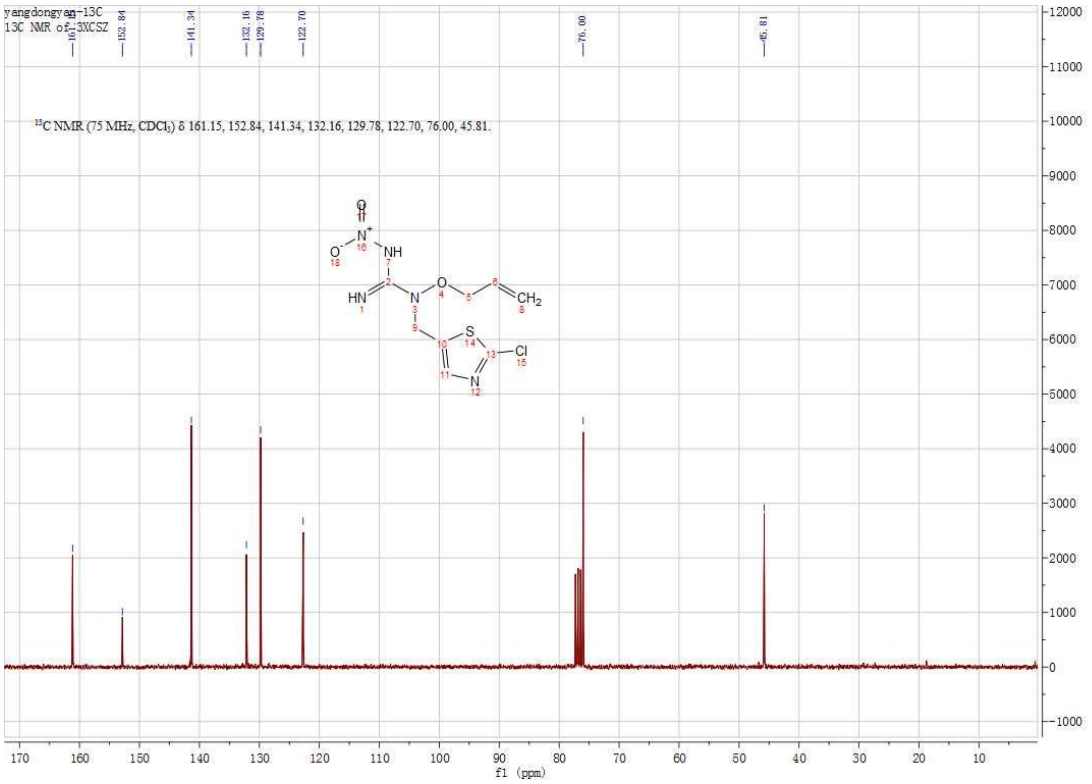

yangdongyan-H
5CCP
^{1}H NMR (300 MHz, CDCl$_3$) δ 9.01 (s, 1H), 8.25 (d, J = 2.4 Hz, 1H), 7.62 (dd, J = 8.2, 2.4 Hz, 1H), 7.23 (t, J = 17.1 Hz, 2H), 4.74 (s, 2H), 3.82 (t, J = 6.8 Hz, 2H), 1.67 – 1.38 (m, 2H), 1.17 (dd, J = 8.8, 5.3 Hz, 4H), 0.73 (t, J = 6.9 Hz, 3H).
H (s) 9.01
F (d) 8.25
G (dd) 7.62
I (t) 7.23
B (s) 4.74
A (t) 3.82
C (m) 1.52
D (dd) 1.17
E (t) 0.73
0.78
1.01
1.03
1.91
2.00
2.03
2.06
4.19
3.09
f1 (ppm)

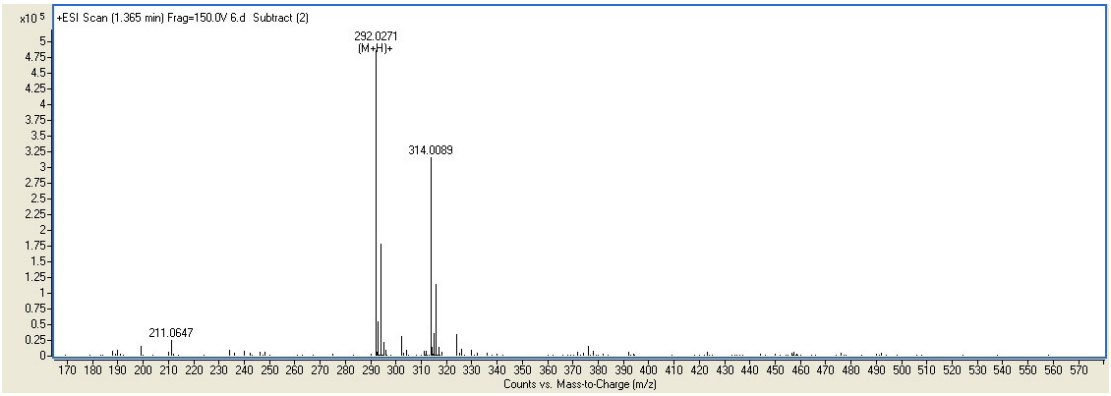

yangdongyan-13623-42
13C NMR of 5CCP
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.60, 150.69, 149.37, 139.11, 129.41, 123.92, 74.93, 49.02, 27.39, 26.93, 21.85, 13.37.
f1 (ppm)



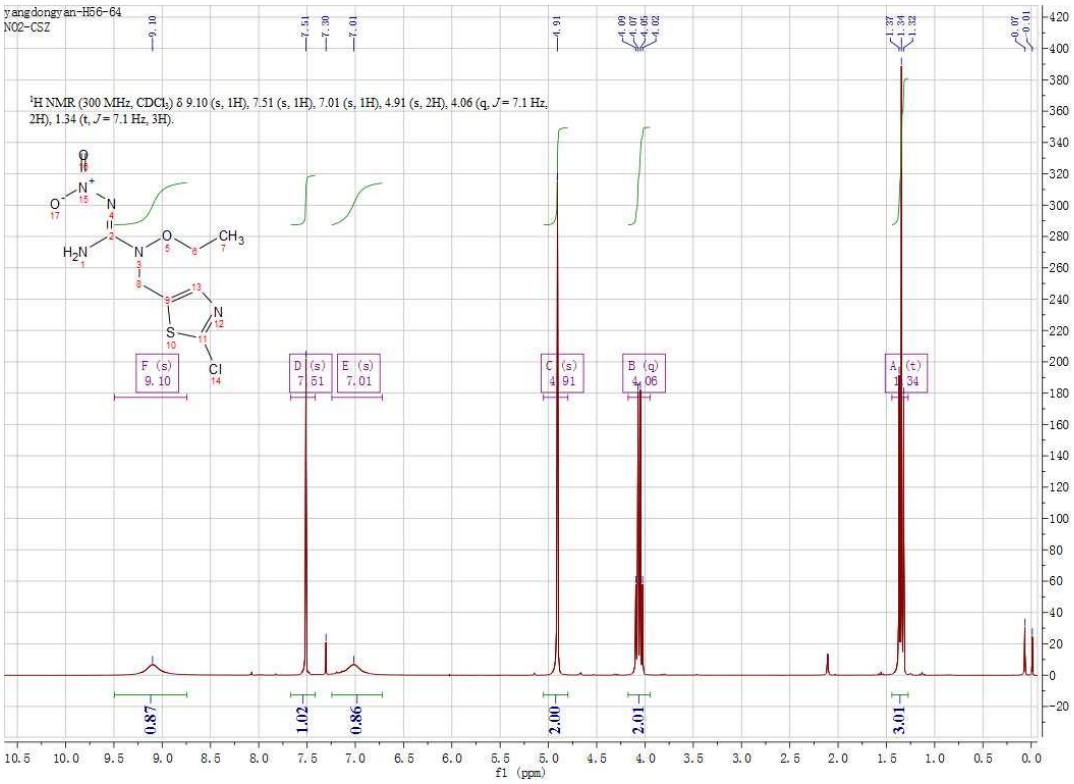
Data for (**4-06**): yield 64 %; yellow solid; mp 78-79℃;^{1}H NMR (300 MHz,$CDCl_3$) δ 9.09 (s, 1H), 7.50 (s, 1H), 7.11 (s, 1H), 5.98 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.61 – 5.27 (m, 2H), 4.90 (s, 2H), 4.45 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.15, 152.84, 141.34, 132.16, 129.78, 122.70, 76.00, 45.81. HRMS (ESI) *m/z* calcd for $C_8H_{11}ClN_5O_3S$ $(M+H)^+$ 292.0266 , found 292.0271 .

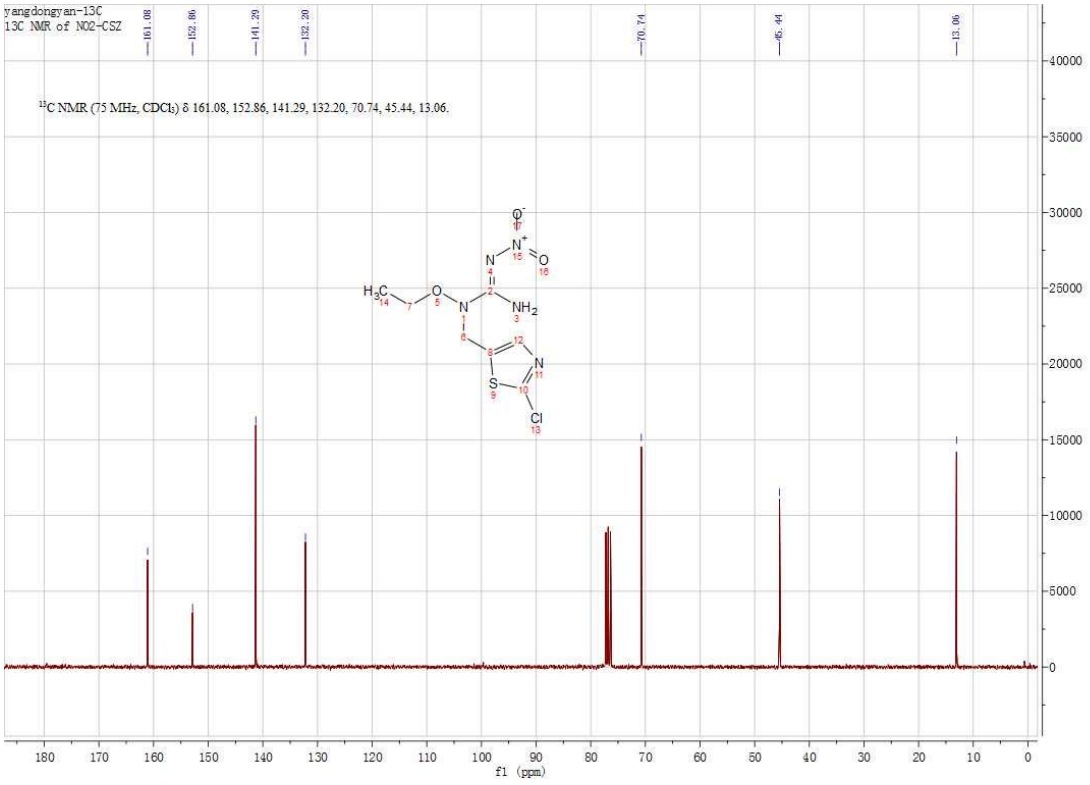


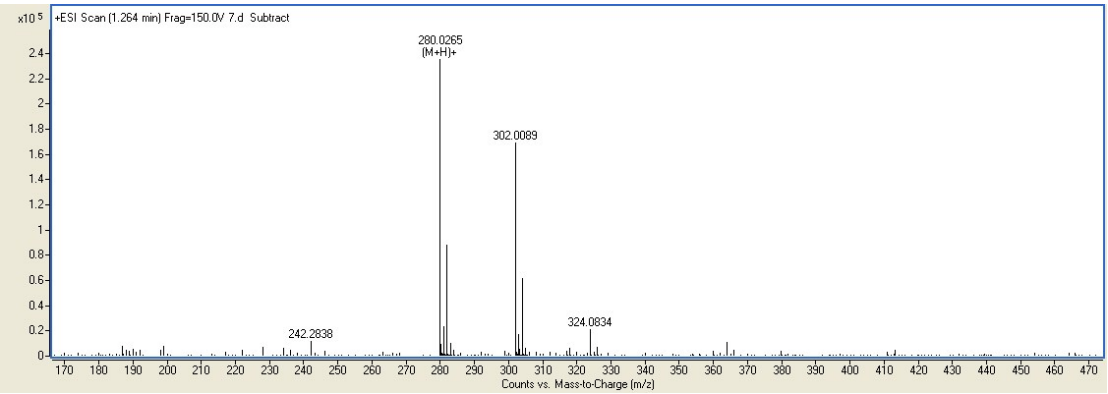




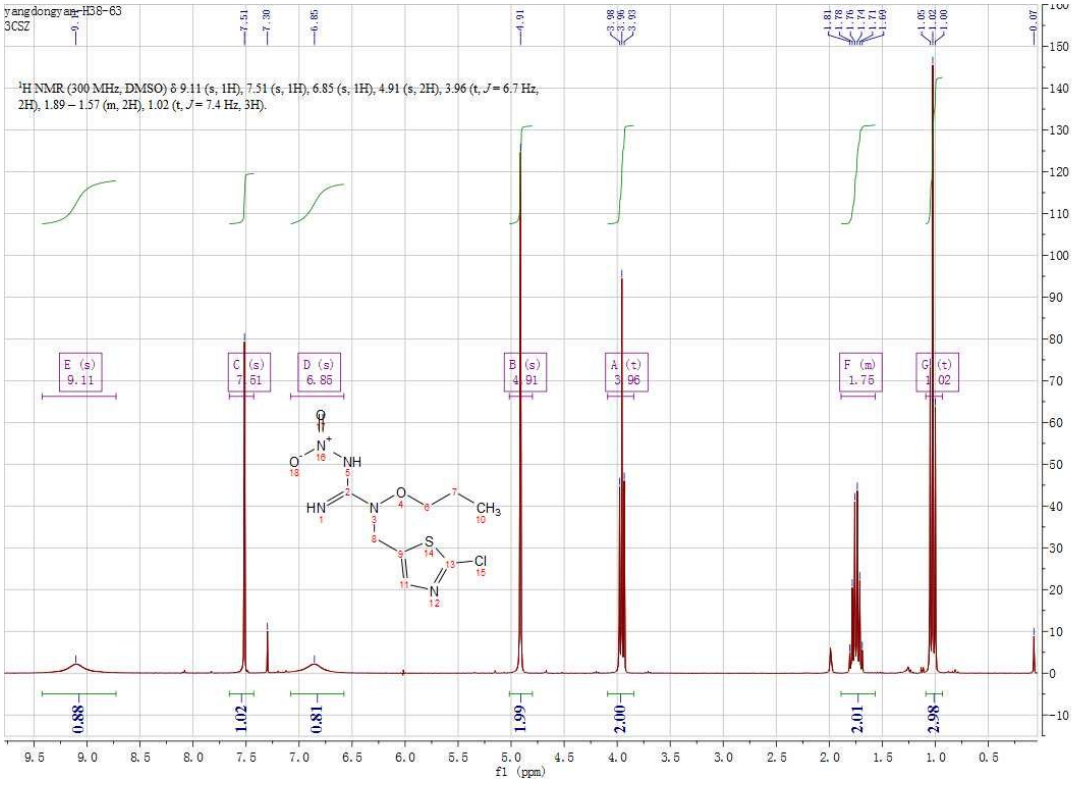
Data for (**4-07**): yield 53 %; white solid; mp 67-68 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.51 (s, 1H), 7.01 (s, 1H), 4.91 (s, 2H), 4.06 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.08, 152.86, 141.29, 132.20, 70.74, 45.44, 13.06. HRMS (ESI) *m/z* calcd for $C_7H_{11}ClN_5O_3S$ $(M+H)^+$ 280.0266 , found 280.0265 .

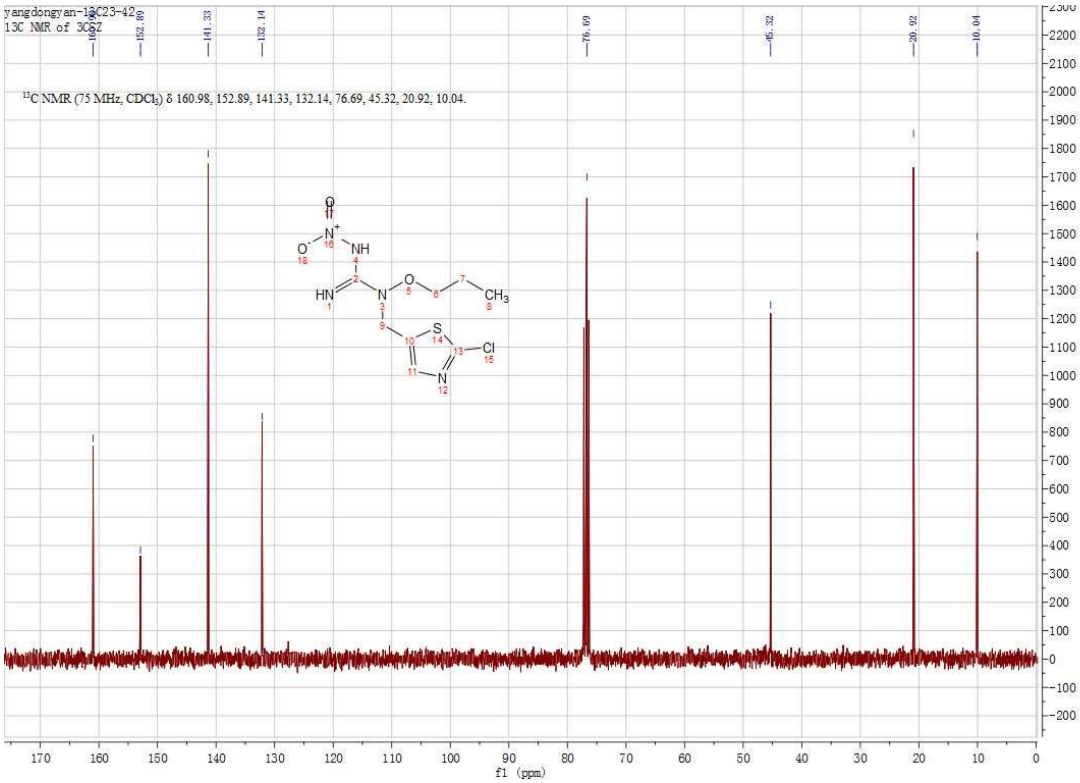

yangdongyan-H56-64
N02-CSZ
^{1}H NMR (300 MHz, CDCl$_3$) δ 9.10 (s, 1H), 7.51 (s, 1H), 7.01 (s, 1H), 4.91 (s, 2H), 4.06 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H).
F (s) 9.10
D (s) 7.51
E (s) 7.01
C (s) 4.91
B (q) 4.06
A (t) 1.34
0.87
1.02
0.86
2.00
2.01
3.01
f1 (ppm)

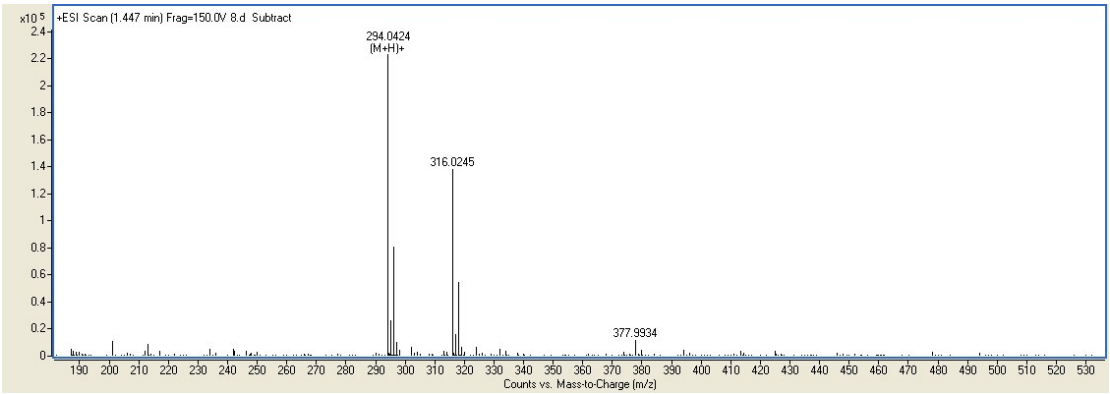

yangdongyan-13C
13C NMR of N02-CSZ
^{13}C NMR (75 MHz, CDCl$_3$) δ 161.08, 152.86, 141.29, 132.20, 70.74, 45.44, 13.06.
f1 (ppm)



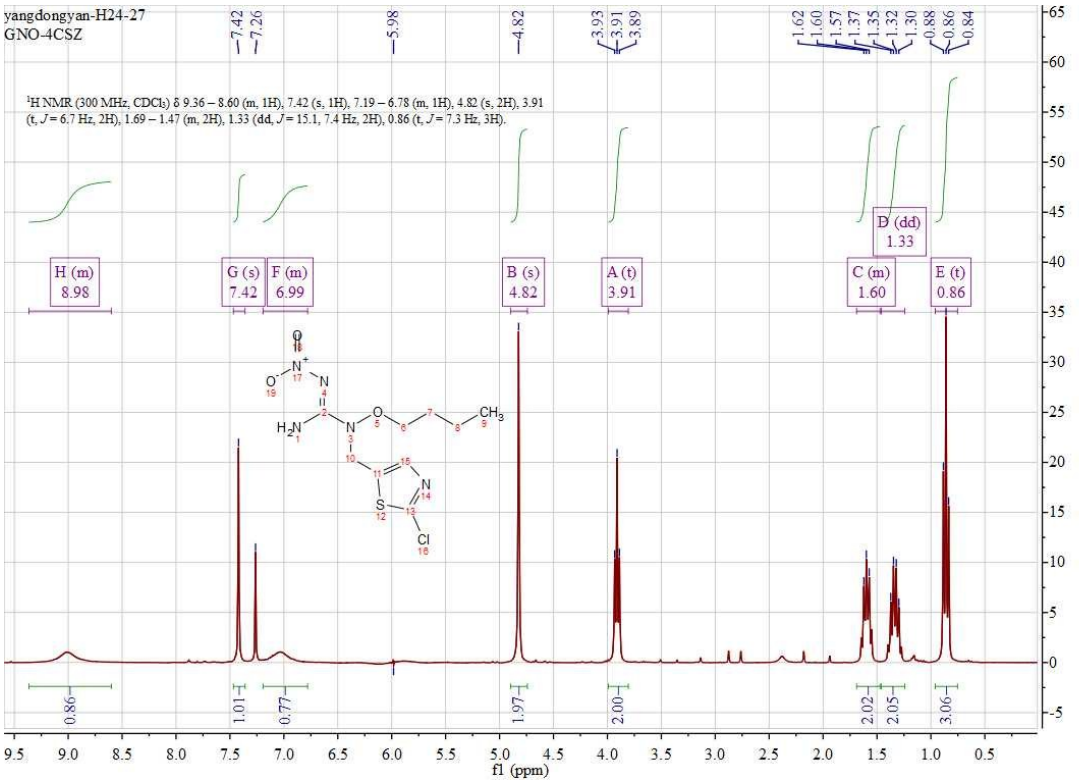
Data for (**4-08**): yield 61 %; white solid; mp 47-48 ℃;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.51 (s, 1H), 6.85 (s, 1H), 4.91 (s, 2H), 3.96 (t, *J* = 6.7 Hz, 2H), 1.89 – 1.57 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.98, 152.89, 141.33, 132.14, 76.69, 45.32, 20.92, 10.04. HRMS (ESI) *m/z* calcd for $C_8H_{13}ClN_5O_3S$ $(M+H)^+$ 294.0422 , found 294.0424 .

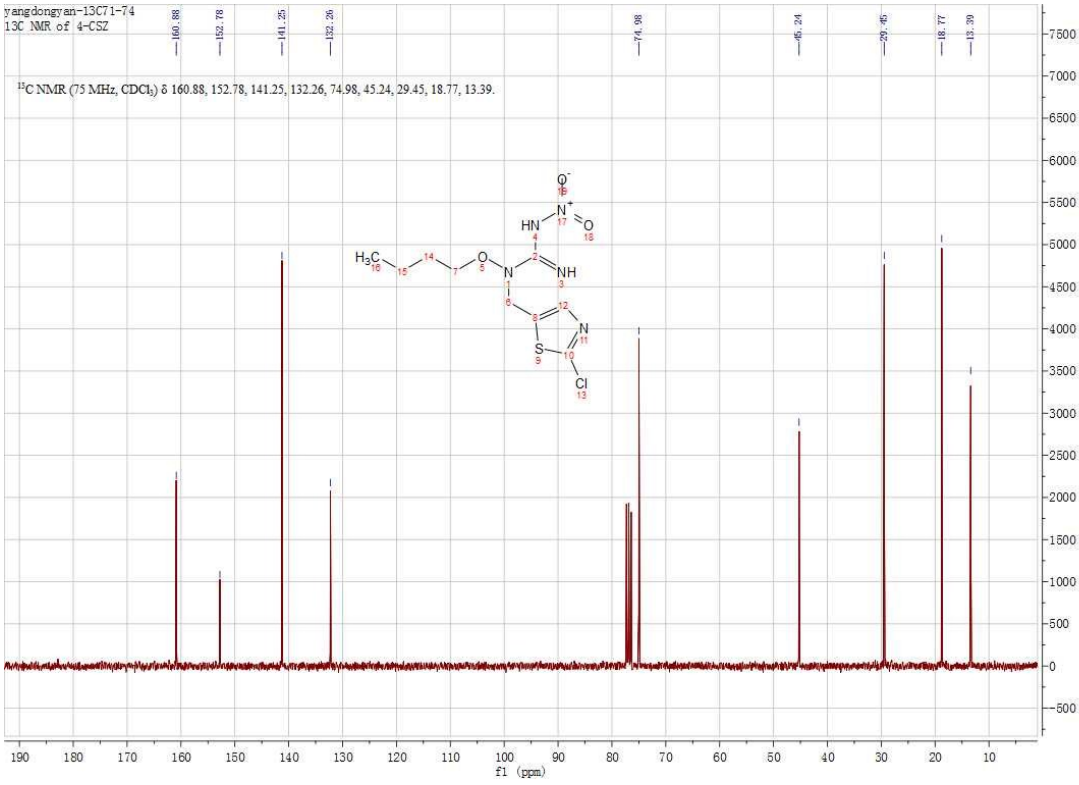


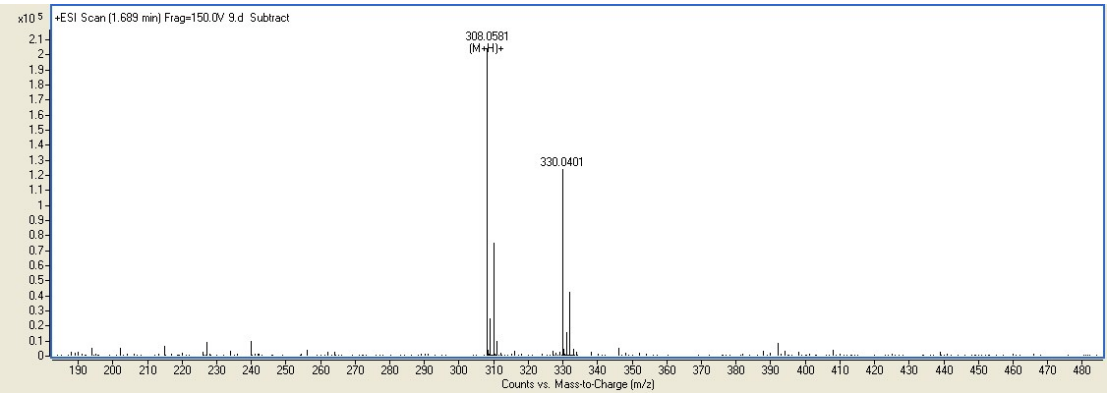




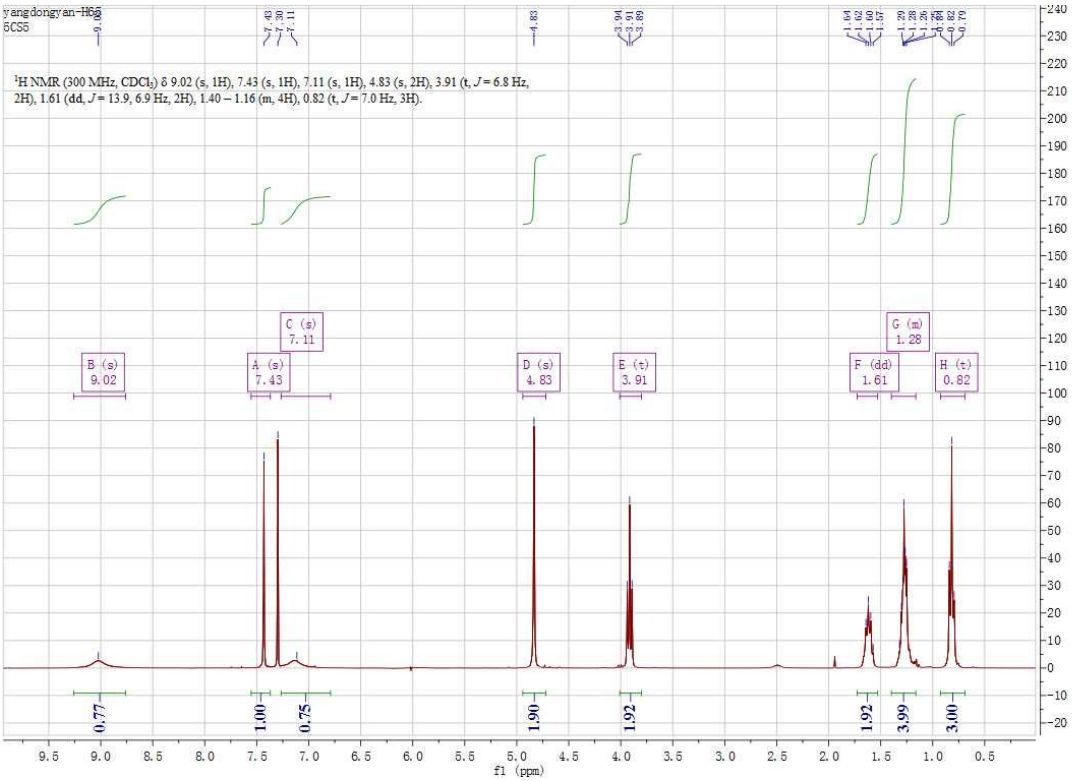
Data for (**4-09**): yield 62 %; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.36 – 8.60 (m, 1H), 7.42 (s, 1H), 7.19 – 6.78 (m, 1H), 4.82 (s, 2H), 3.91 (t, *J* = 6.7 Hz, 2H), 1.69 – 1.47 (m, 2H), 1.33 (dd, *J* = 15.1, 7.4 Hz, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.88, 152.78, 141.25, 132.26, 74.98, 45.24, 29.45, 18.77, 13.39. HRMS (ESI) *m/z* calcd for $C_9H_{15}ClN_5O_3S$ $(M+H)^+$ 308.0579 , found 308.0581.

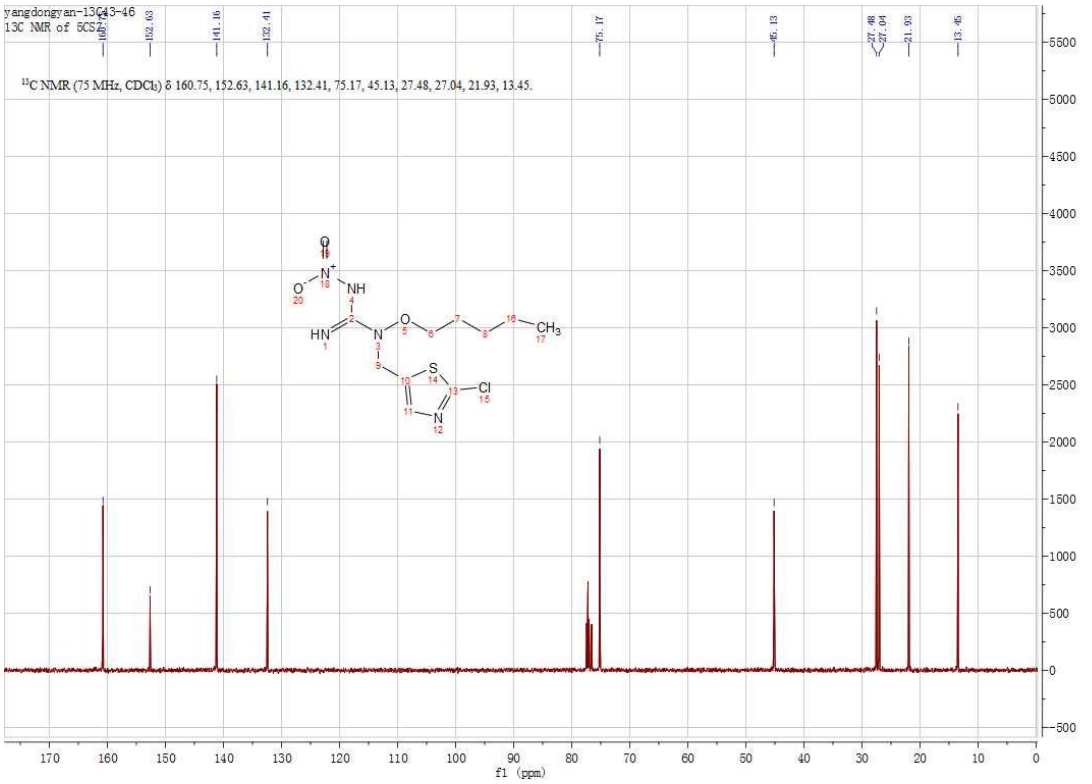

yangdongyan-H24-27
GNO-4CSZ
7.42
7.26
5.98
4.82
3.93
3.91
3.89
1.62
1.60
1.57
1.37
1.35
1.32
1.30
0.88
0.86
0.84
^{1}H NMR (300 MHz, CDCl$_3$) δ 9.36 – 8.60 (m, 1H), 7.42 (s, 1H), 7.19 – 6.78 (m, 1H), 4.82 (s, 2H), 3.91 (t, J = 6.7 Hz, 2H), 1.69 – 1.47 (m, 2H), 1.33 (dd, J = 15.1, 7.4 Hz, 2H), 0.86 (t, J = 7.3 Hz, 3H).
H (m) 8.98
G (s) 7.42
F (m) 6.99
B (s) 4.82
A (t) 3.91
D (dd) 1.33
C (m) 1.60
E (t) 0.86
0.86
1.01
0.77
1.97
2.00
2.02
2.05
3.06
f1 (ppm)

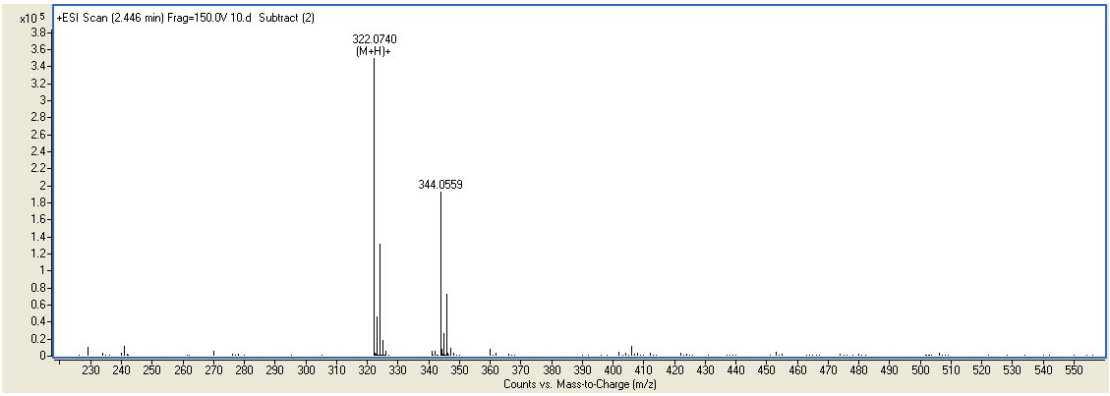

yangdongyan-13C71-74
13C NMR of 4-CSZ
160.88
152.78
141.25
132.26
74.98
45.24
29.45
18.77
13.39
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.88, 152.78, 141.25, 132.26, 74.98, 45.24, 29.45, 18.77, 13.39.
f1 (ppm)



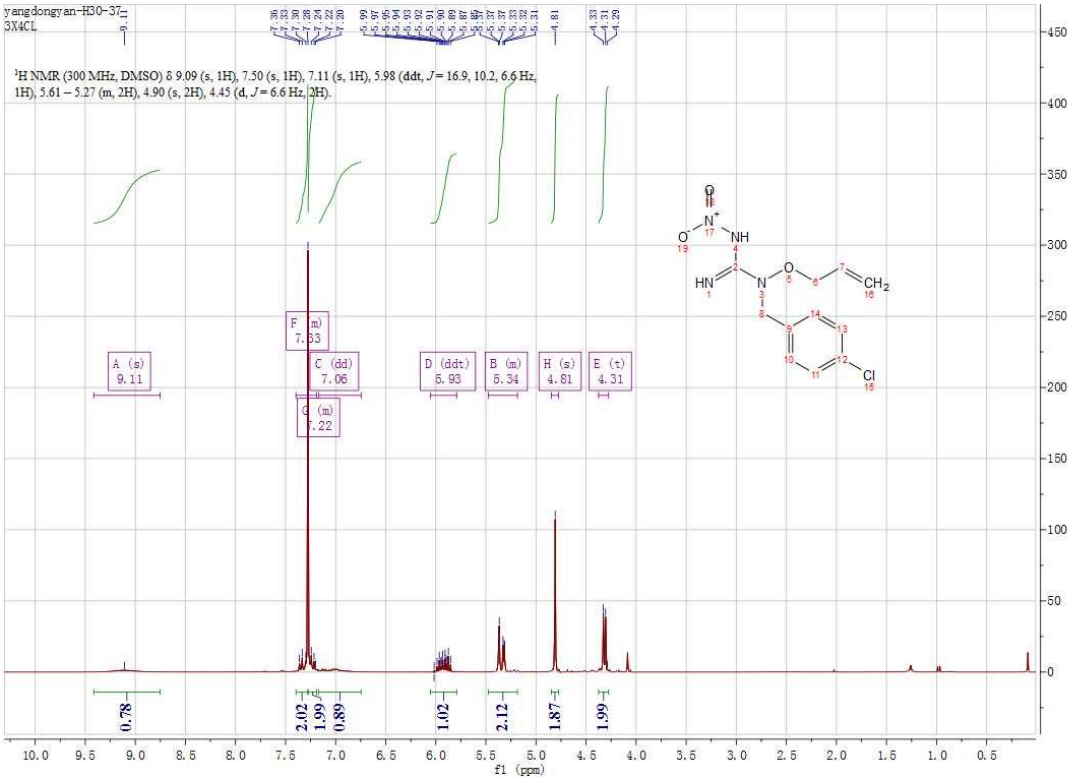
Data for (**4-10**): yield 43 %; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (s, 1H), 7.43 (s, 1H), 7.11 (s, 1H), 4.83 (s, 2H), 3.91 (t, *J* = 6.8 Hz, 2H), 1.61 (dd, *J* = 13.9, 6.9 Hz, 2H), 1.40 – 1.16 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.75, 152.63, 141.16, 132.41, 75.17, 45.13, 27.48, 27.04, 21.93, 13.45. HRMS (ESI) *m/z* calcd for $C_{10}H_{17}ClN_5O_3S$ $(M+H)^+$ 322.0735 , found 322.0740 .

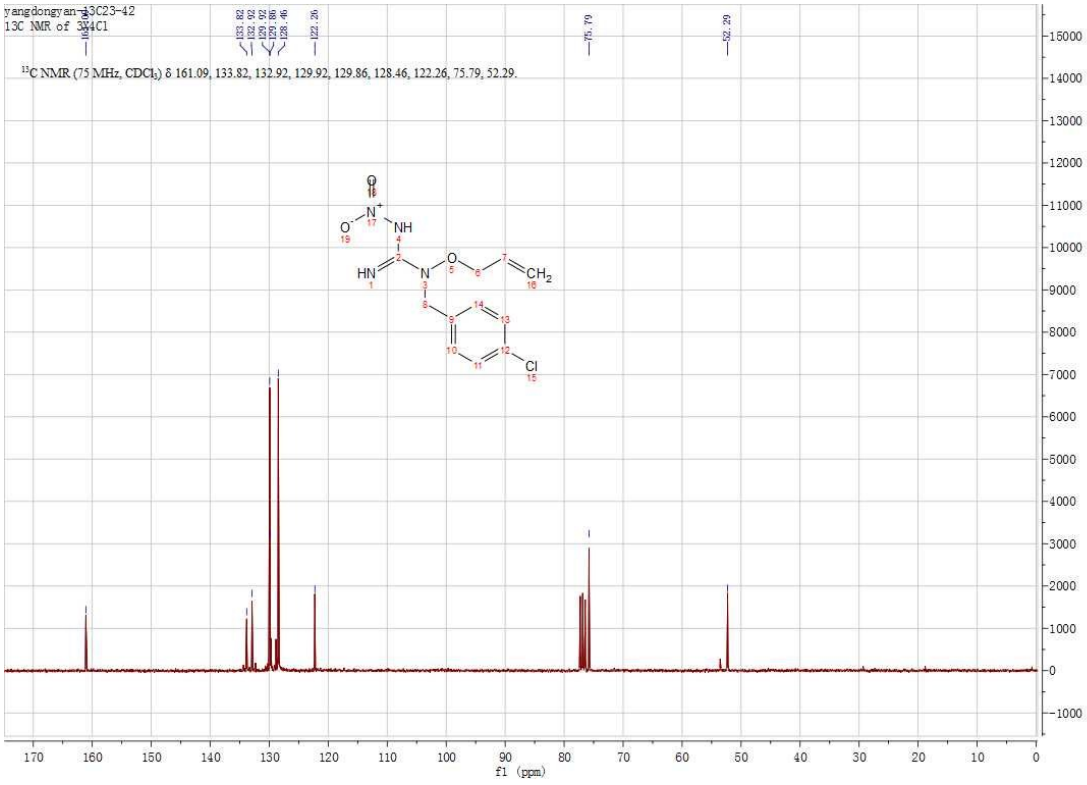


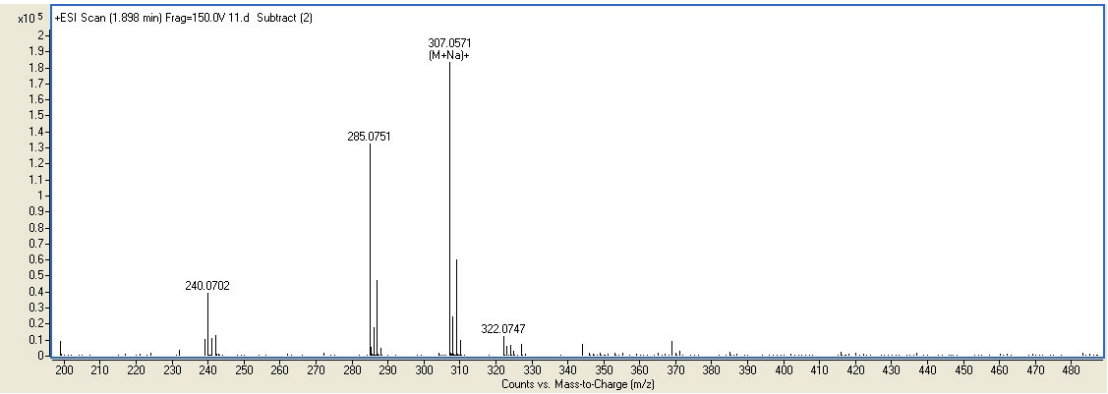




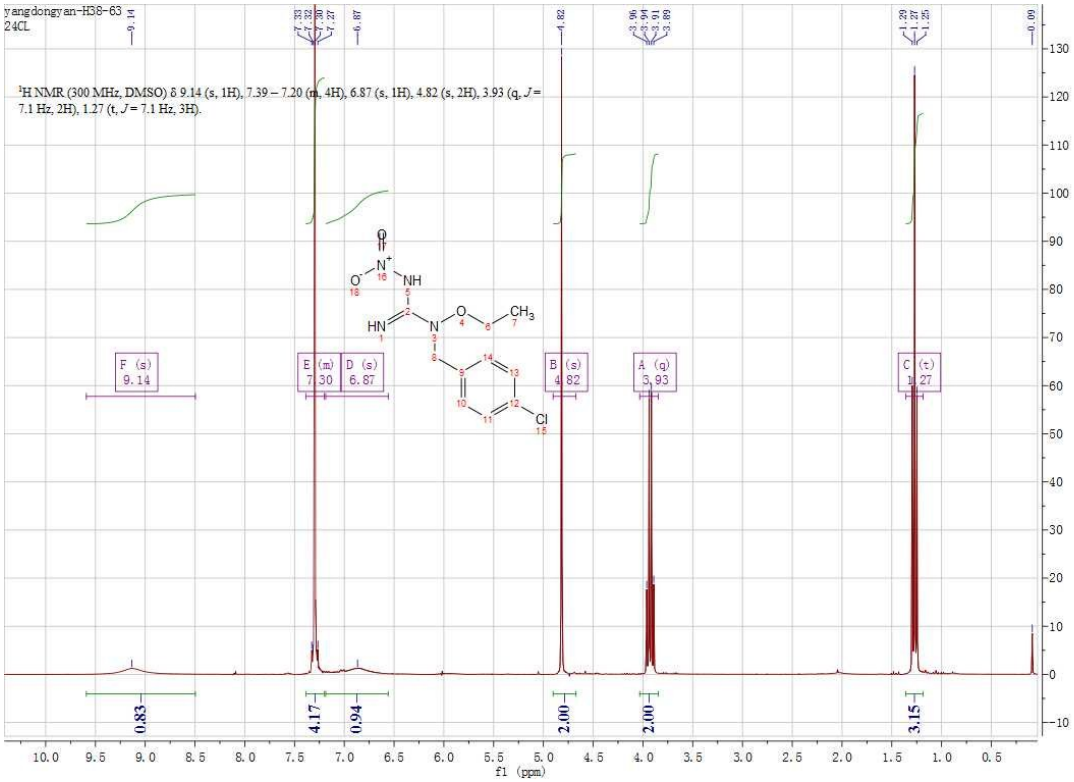
Data for (**4-11**): yield 64 %; white solid; mp 80-81 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.50 (s, 1H), 7.11 (s, 1H), 5.98 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.61 – 5.27 (m, 2H), 4.90 (s, 2H), 4.45 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.09, 133.82, 132.92, 129.92, 129.86, 128.46, 122.26, 75.79, 52.29. HRMS (ESI) *m/z* calcd for $C_{11}H_{13}ClN_4NaO_3$ $(M+Na)^+$ 307.0568, found 307.0571 .

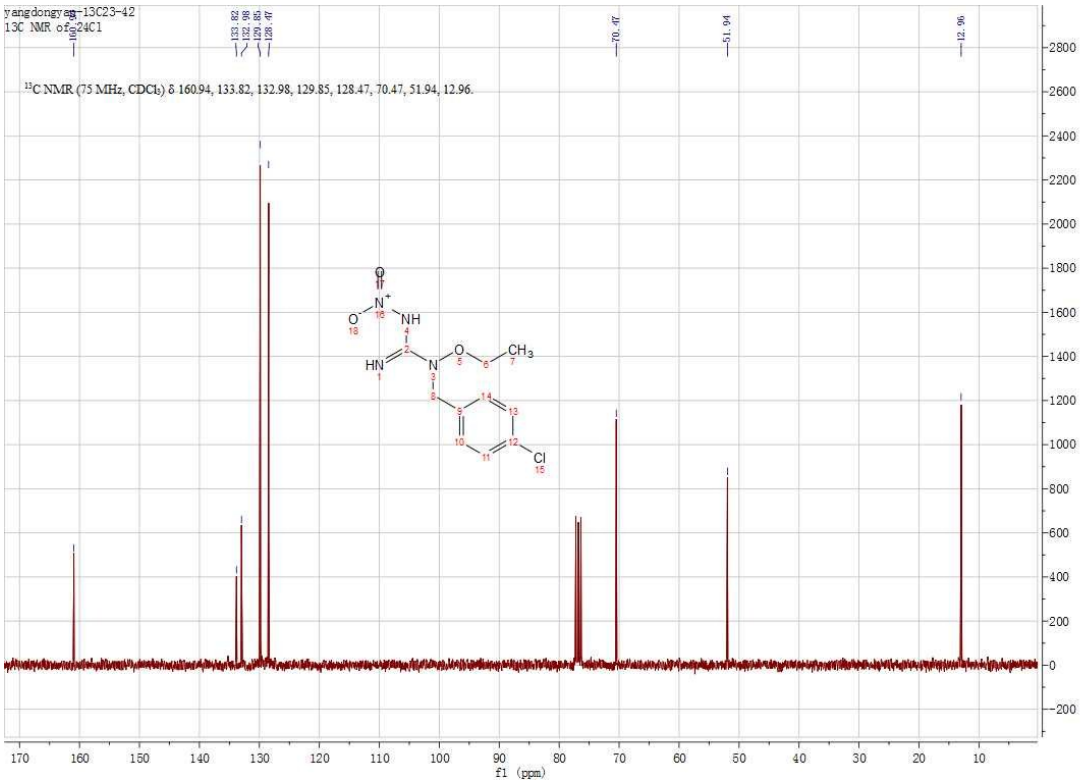

yangdongyan-H30-37
3X4Cl
^{1}H NMR (300 MHz, DMSO) δ 9.09 (s, 1H), 7.50 (s, 1H), 7.11 (s, 1H), 5.98 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.61 – 5.27 (m, 2H), 4.90 (s, 2H), 4.45 (d, J = 6.6 Hz, 2H).
A (s) 9.11
F (m) 7.33
C (dd) 7.06
G (m) 7.22
D (ddt) 5.93
B (m) 5.34
H (s) 4.81
E (t) 4.31
0.78
2.02
1.99
0.89
1.02
2.12
1.87
1.99
f1 (ppm)

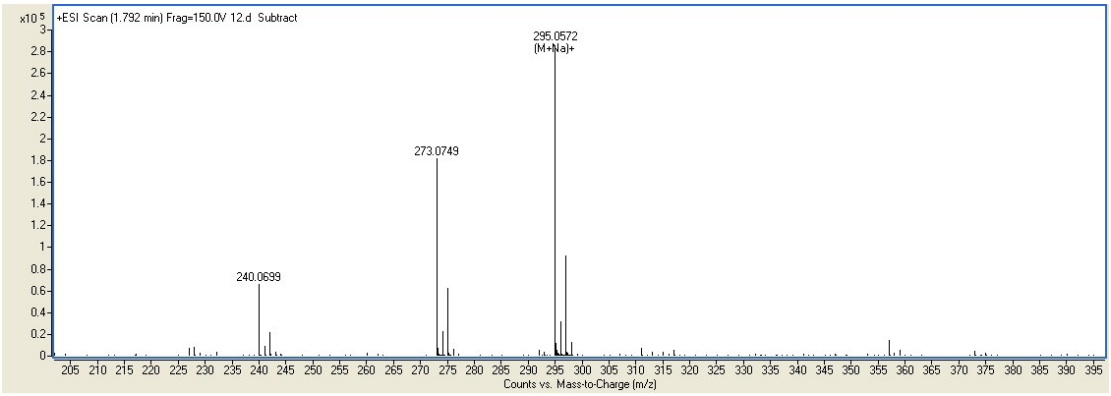

yangdongyan-13C23-42
13C NMR of 3X4Cl
^{13}C NMR (75 MHz, CDCl$_3$) δ 161.09, 133.82, 132.92, 129.92, 129.86, 128.46, 122.26, 75.79, 52.29.
f1 (ppm)



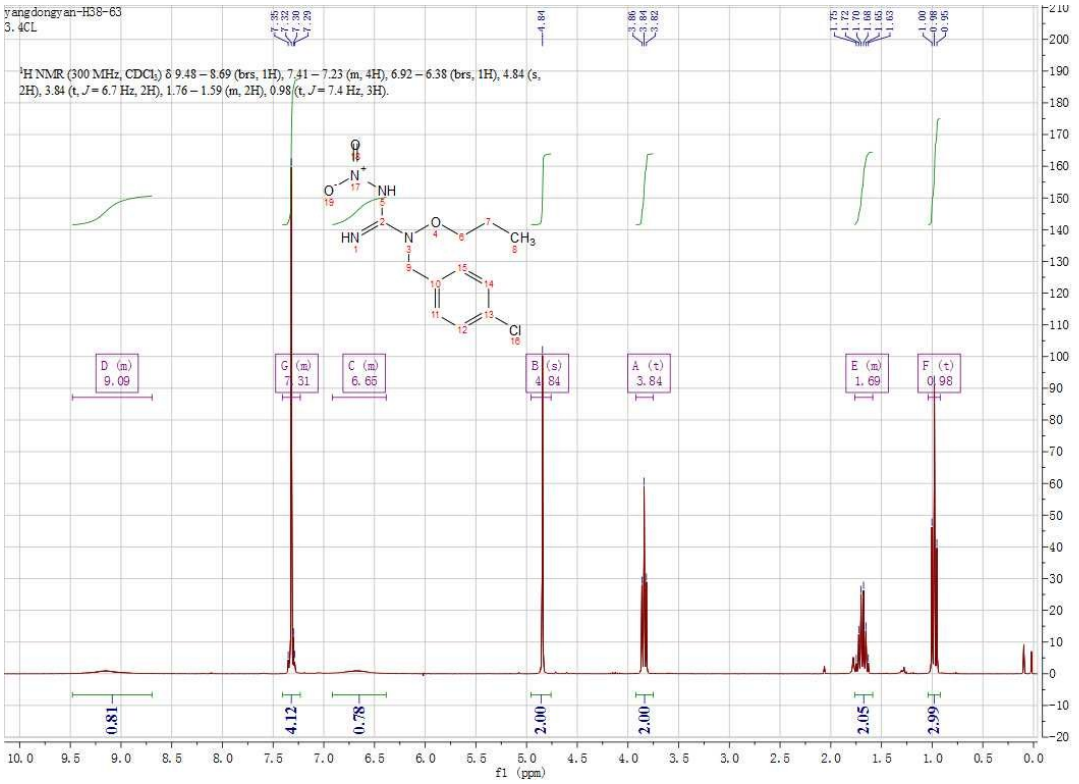
Data for (**4**-**12**): yield 63 %; white solid; mp 73-74 ℃;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.39 – 7.20 (m, 4H), 6.87 (s, 1H), 4.82 (s, 2H), 3.93 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.94, 133.82, 132.98, 129.85, 128.47, 70.47, 51.94, 12.96. HRMS (ESI) *m/z* calcd for $C_{10}H_{13}ClN_4NaO_3$ $(M+Na)^+$ 295.0568 , found 295.0572 .

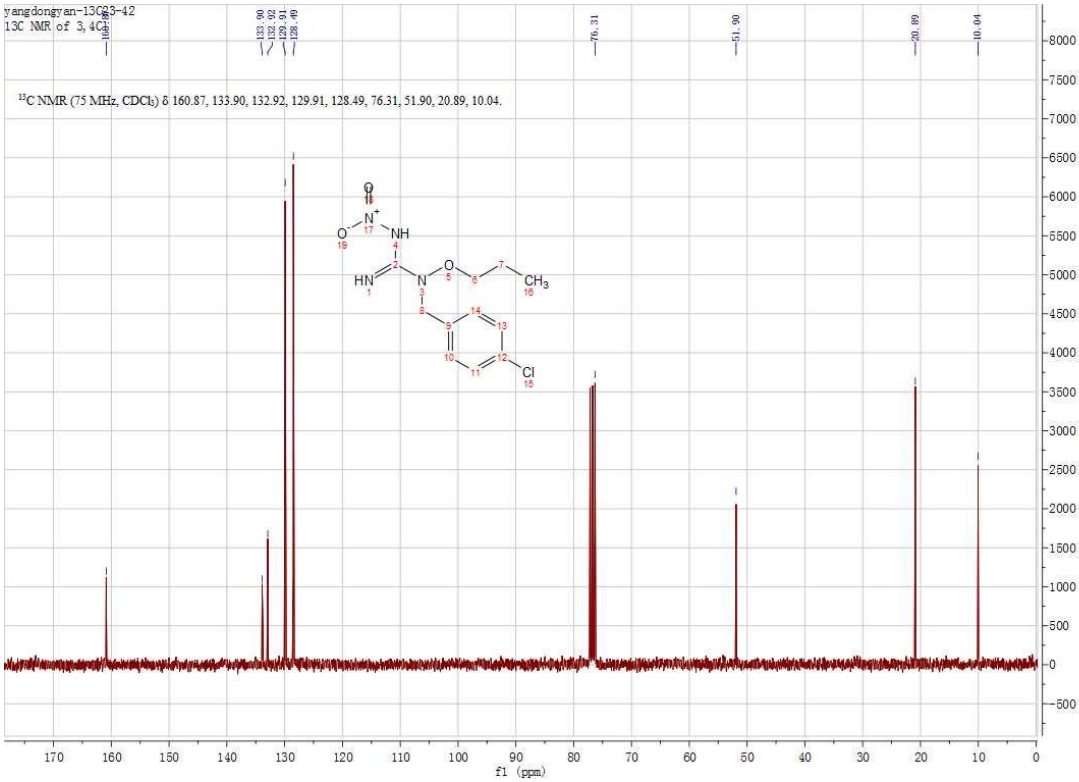


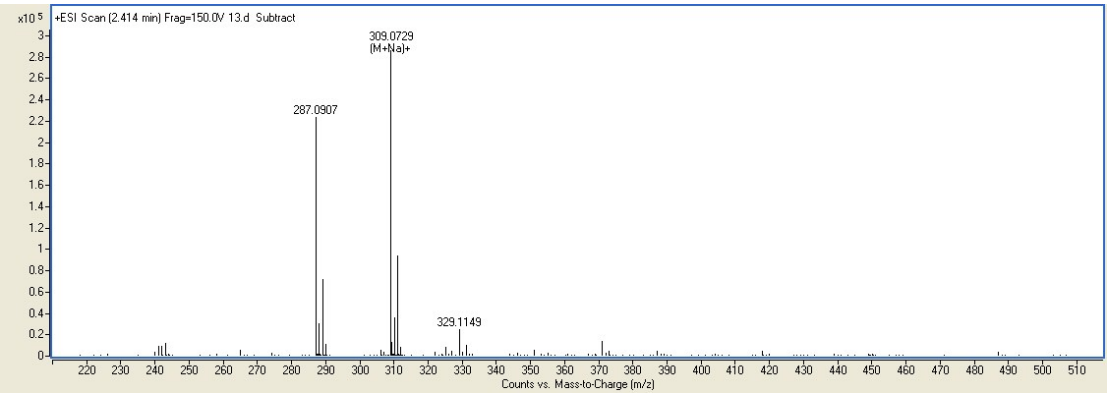




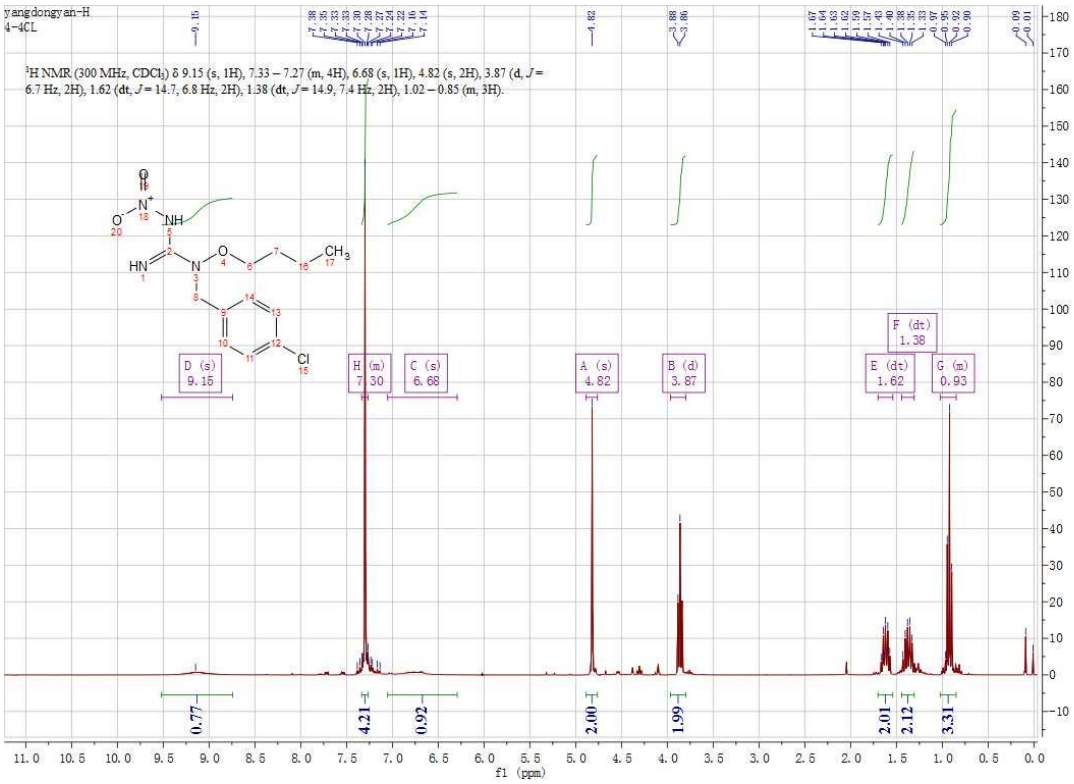
Data for (**4-13**): yield 45 %; white solid; mp 106-107℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48 – 8.69 (brs, 1H), 7.41 – 7.23 (m, 4H), 6.92 – 6.38 (brs, 1H), 4.84 (s, 2H), 3.84 (t, *J* = 6.7 Hz, 2H), 1.76 – 1.59 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.87, 133.90, 132.92, 129.91, 128.49, 76.31, 51.90, 20.89, 10.04. HRMS (ESI) *m/z* calcd for $C_{11}H_{15}ClN_4NaO_3$ $(M+Na)^+$ 309.0725 , found 309.0729.

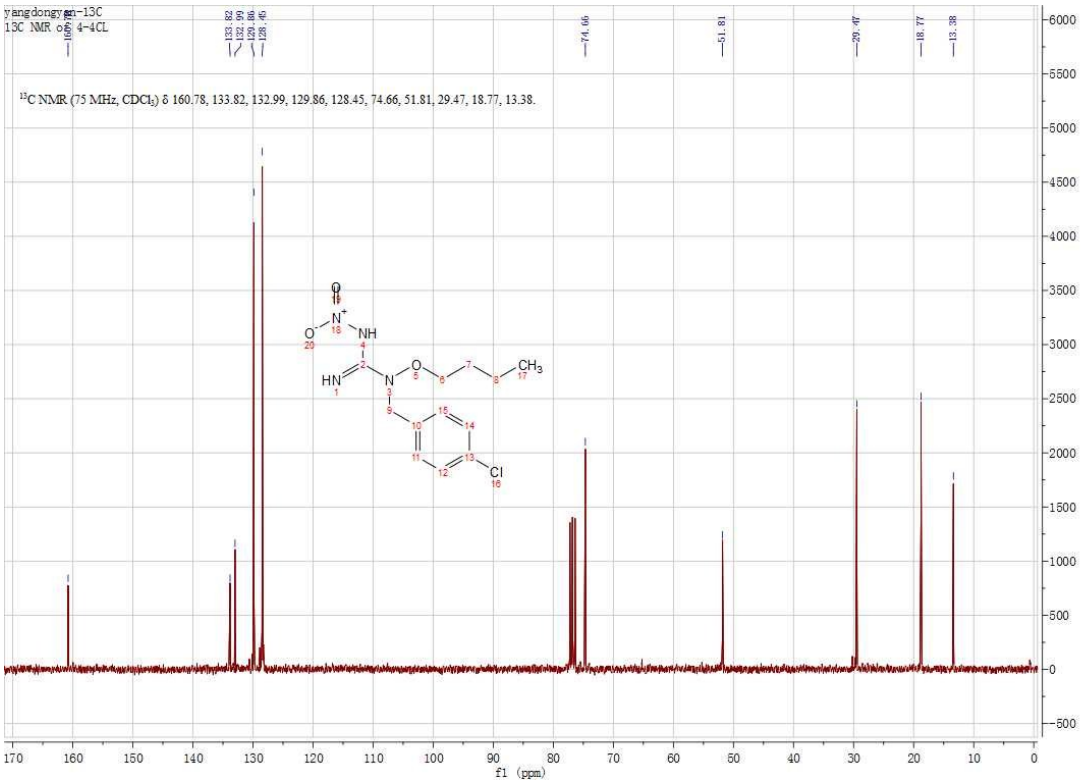

yangdongyan-H38-63
3.4CL
¹H NMR (300 MHz, CDCl₃) δ 9.48 – 8.69 (brs, 1H), 7.41 – 7.23 (m, 4H), 6.92 – 6.38 (brs, 1H), 4.84 (s, 2H), 3.84 (t, J = 6.7 Hz, 2H), 1.76 – 1.59 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H).
D (m) 9.09
G (m) 7.31
C (m) 6.66
B (s) 4.84
A (t) 3.84
E (m) 1.69
F (t) 0.98
0.81
4.12
0.78
2.00
2.00
2.05
2.99
f1 (ppm)

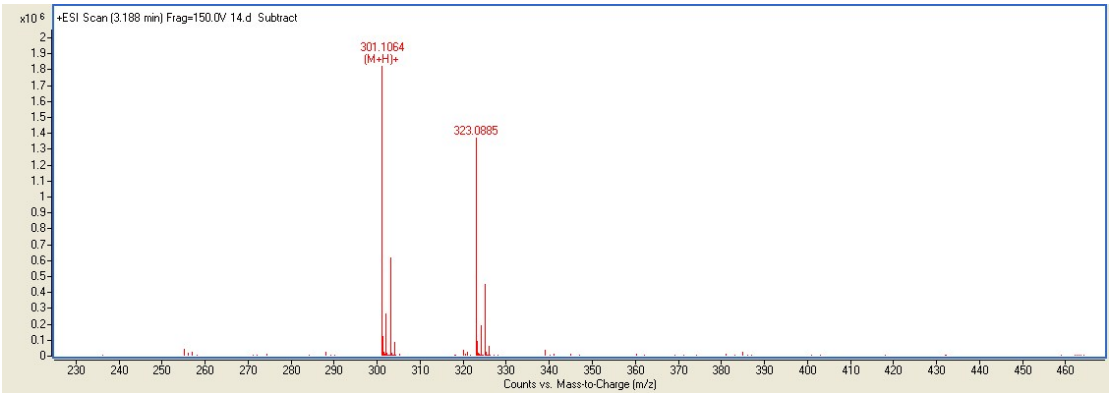

yangdongyan-13C83-42
13C NMR of 3,4Cl
¹³C NMR (75 MHz, CDCl₃) δ 160.87, 133.90, 132.92, 129.91, 128.49, 76.31, 51.90, 20.89, 10.04.
f1 (ppm)



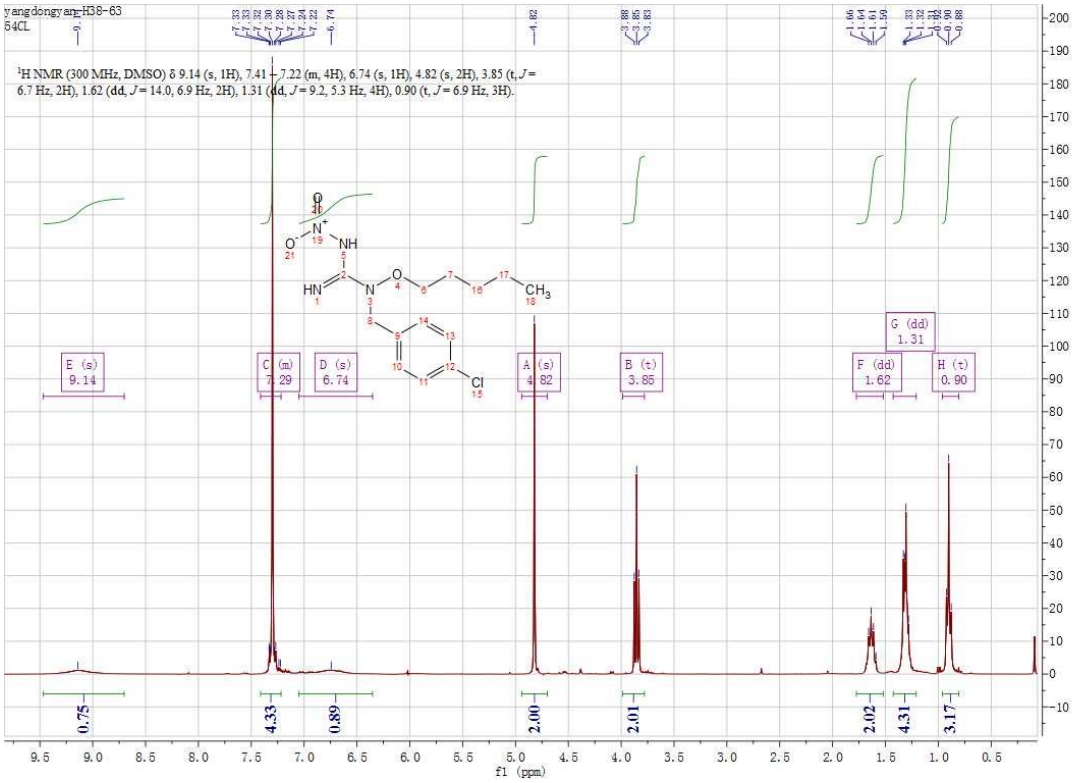
Data for (**4-14**): yield 65 %; white solid; mp 92-93 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.33 – 7.27 (m, 4H), 6.68 (s, 1H), 4.82 (s, 2H), 3.87 (d, *J* = 6.7 Hz, 2H), 1.62 (dt, *J* = 14.7, 6.8 Hz, 2H), 1.38 (dt, *J* = 14.9, 7.4 Hz, 2H), 1.02 – 0.85 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.78, 133.82, 132.99, 129.86, 128.45, 74.66, 51.81, 29.47, 18.77, 13.38. HRMS (ESI) *m/z* calcd for $C_{12}H_{18}ClN_4O_3$ $(M+H)^+$ 301.1062 , found 301.1064 .

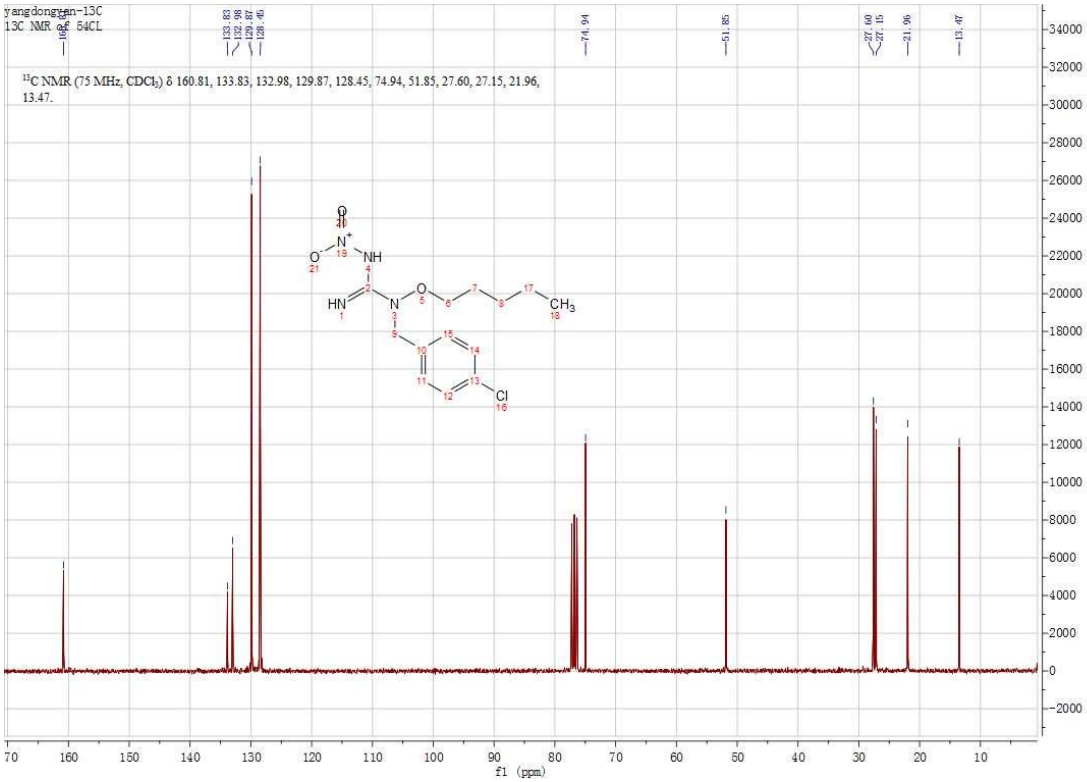


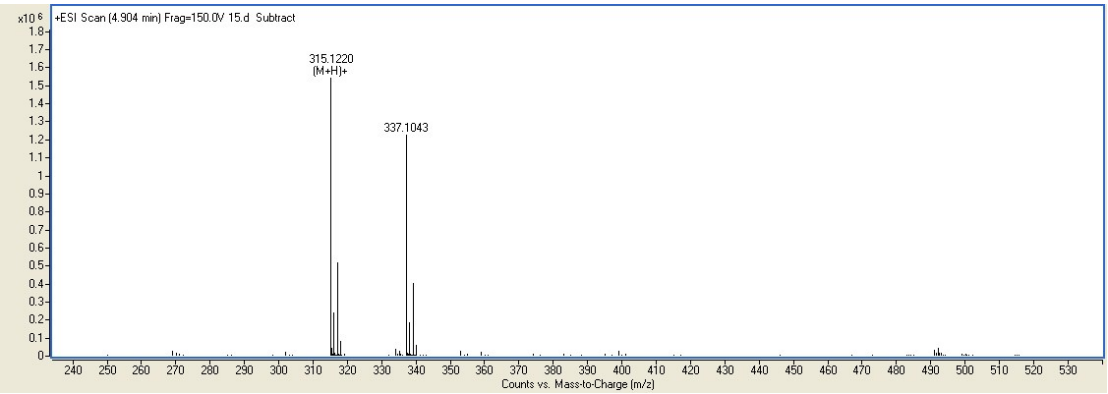




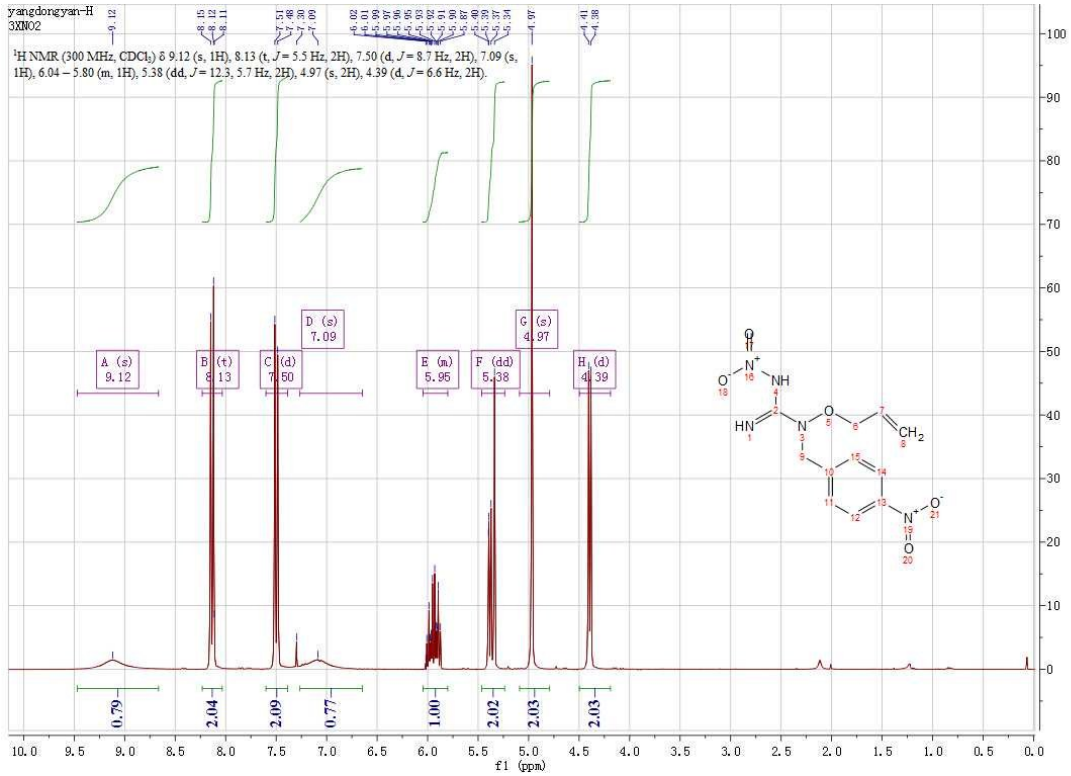
Data for (**4-15**): yield 58 %; white solid; mp 78-79℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.41 – 7.22 (m, 4H), 6.74 (s, 1H), 4.82 (s, 2H), 3.85 (t, *J* = 6.7 Hz, 2H), 1.62 (dd, *J* = 14.0, 6.9 Hz, 2H), 1.31 (dd, *J* = 9.2, 5.3 Hz, 4H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.81, 133.83, 132.98, 129.87, 128.45, 74.94, 51.85, 27.60, 27.15, 21.96, 13.47. HRMS (ESI) *m/z* calcd for $C_{13}H_{20}ClN_4O_3$ $(M+H)^+$ 315.1218 , found 315.1220 .

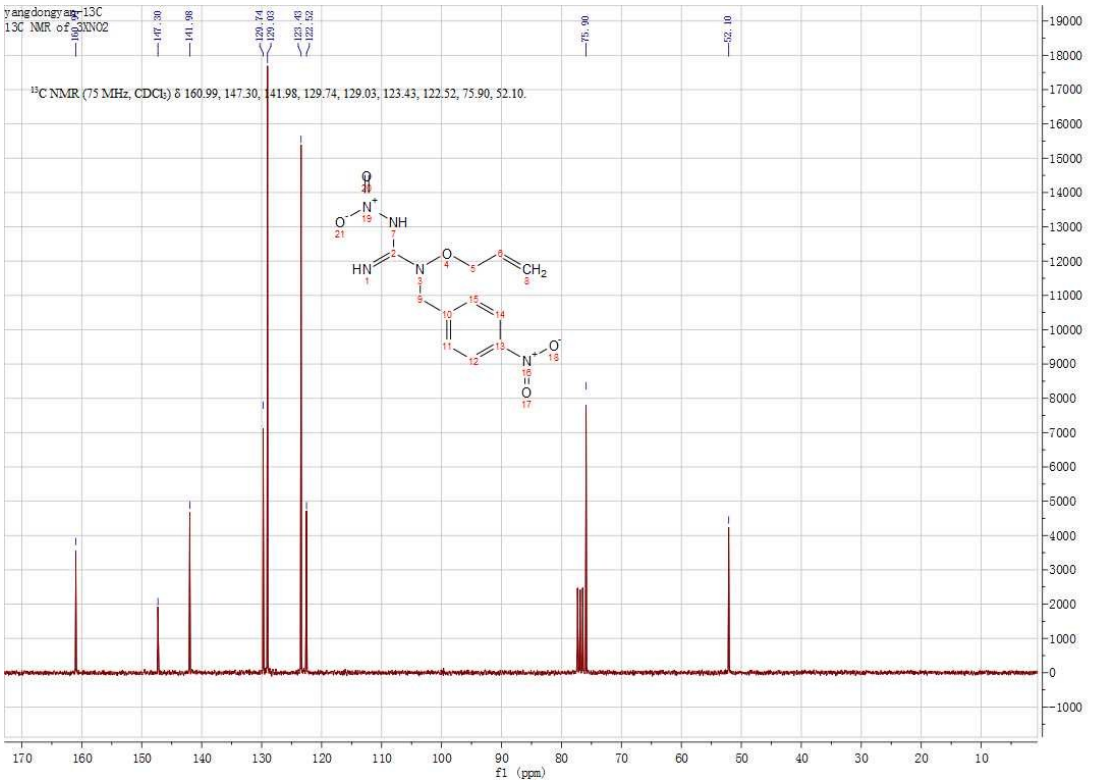

yangdongyan-H38-63
54CL
^{1}H NMR (300 MHz, DMSO) δ 9.14 (s, 1H), 7.41 – 7.22 (m, 4H), 6.74 (s, 1H), 4.82 (s, 2H), 3.85 (t, J = 6.7 Hz, 2H), 1.62 (dd, J = 14.0, 6.9 Hz, 2H), 1.31 (dd, J = 9.2, 5.3 Hz, 4H), 0.90 (t, J = 6.9 Hz, 3H).
E (s) 9.14
C (m) 7.29
D (s) 6.74
A (s) 4.82
B (t) 3.85
F (dd) 1.62
G (dd) 1.31
H (t) 0.90
0.75
4.33
0.89
2.00
2.01
2.02
4.31
3.17
f1 (ppm)

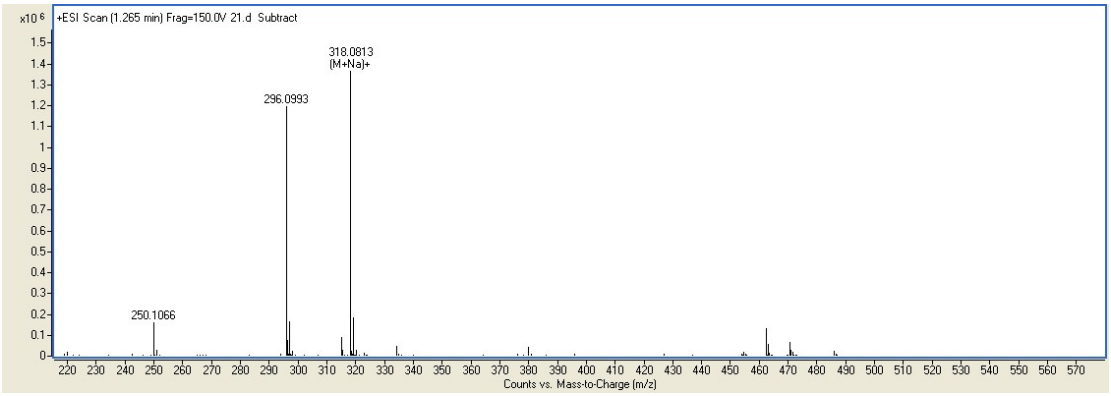

yangdongyan-13C
13C NMR
54CL
^{13}C NMR (75 MHz, $CDCl_3$) δ 160.81, 133.83, 132.98, 129.87, 128.45, 74.94, 51.85, 27.60, 27.15, 21.96, 13.47.
f1 (ppm)



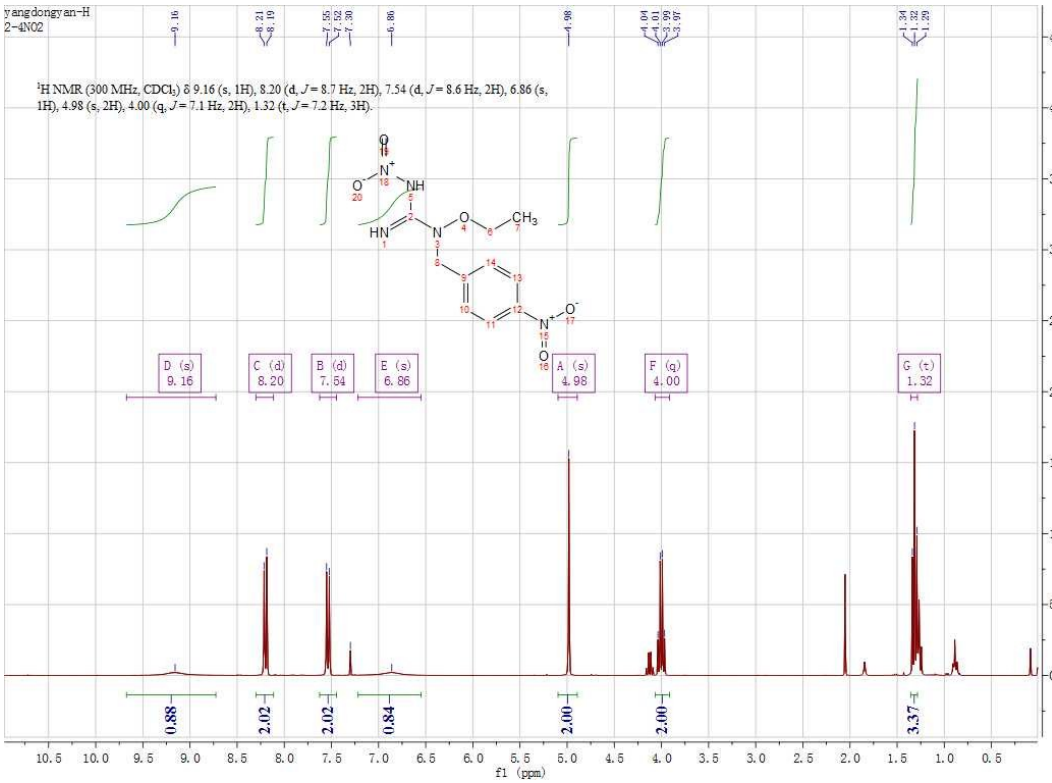
Data for (**4-16**): yield 56 %; white solid; mp 76-77℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.13 (t, *J* = 5.5 Hz, 2H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.09 (s, 1H), 6.04 – 5.80 (m, 1H), 5.38 (dd, *J* = 12.3, 5.7 Hz, 2H), 4.97 (s, 2H), 4.39 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.99, 147.30, 141.98, 129.74, 129.03, 123.43, 122.52, 75.90, 52.10. HRMS (ESI) *m/z* calcd for $C_{11}H_{13}N_5NaO_5$ $(M+Na)^+$ 318.0809 , found 318.0813.

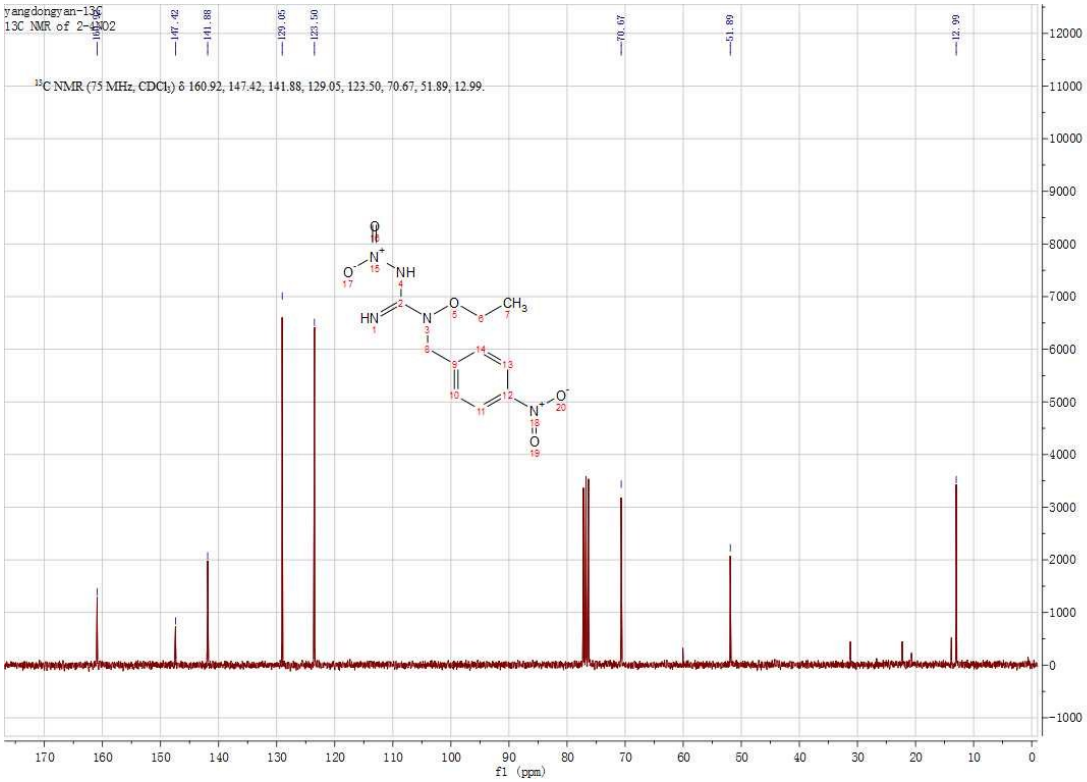


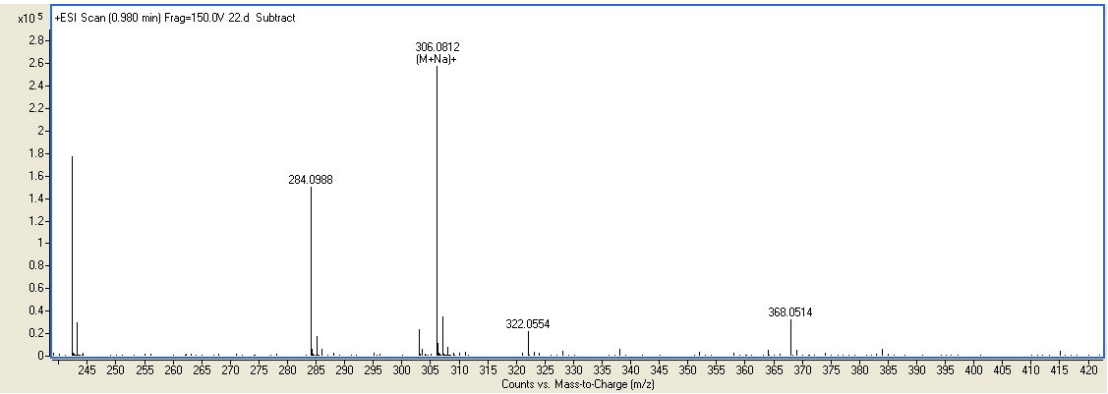




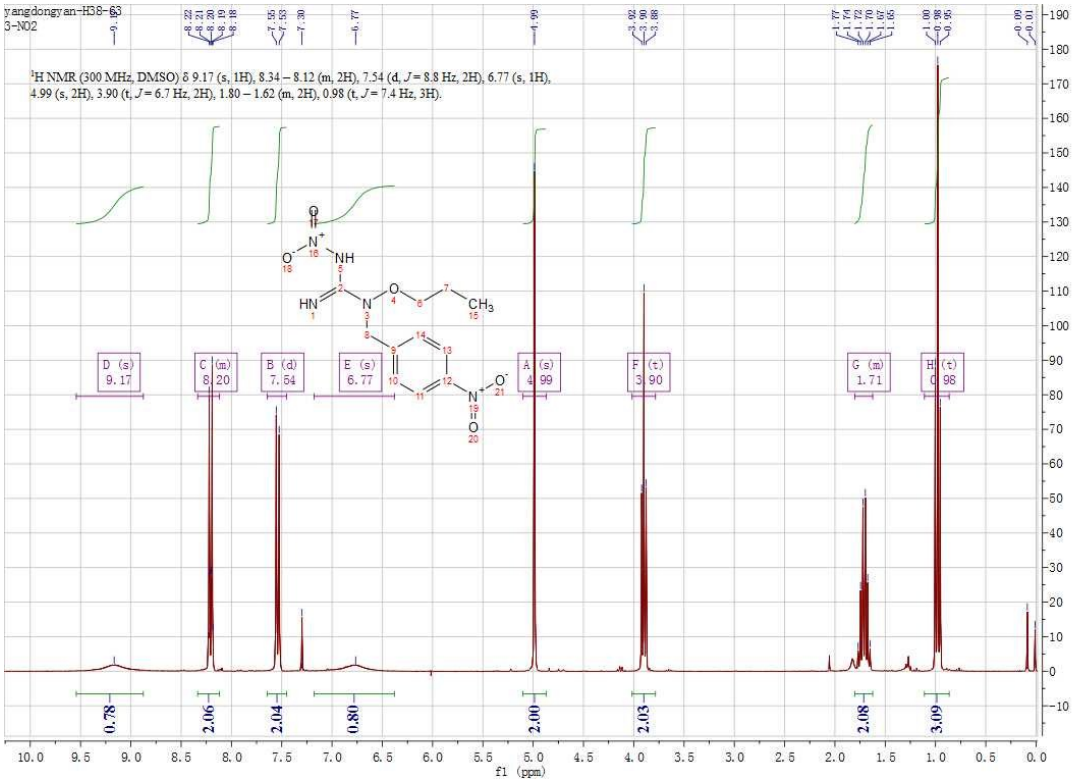
Data for (**4**-**17**): yield 64 %; white solid; mp 76-77 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.20 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 6.86 (s, 1H), 4.98 (s, 2H), 4.00 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.92, 147.42, 141.88, 129.05, 123.50, 70.67, 51.89, 12.99. HRMS (ESI) *m/z* calcd for $C_{10}H_{13}N_5NaO_5$ $(M+H)^+$ 306.0809, found 306.0812 .

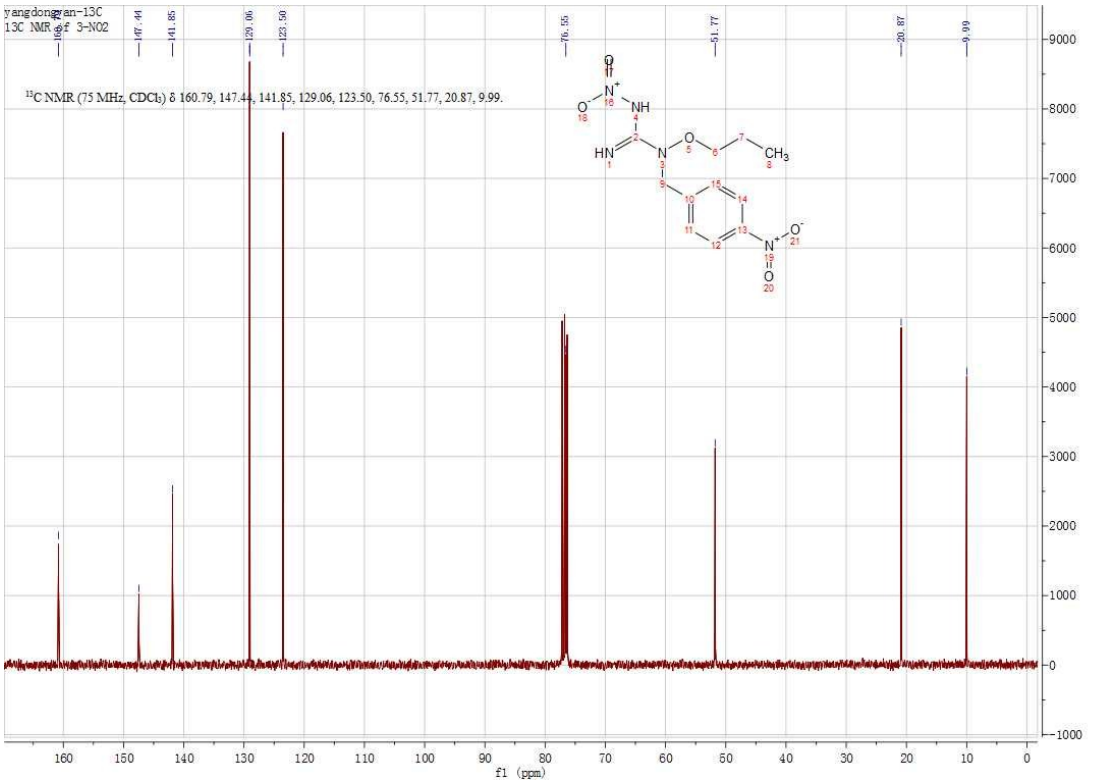

yangdongyan-H
2-4N02
^{1}H NMR (300 MHz, CDCl$_3$) δ 9.16 (s, 1H), 8.20 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 6.86 (s, 1H), 4.98 (s, 2H), 4.00 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H).
D (s) 9.16
C (d) 8.20
B (d) 7.54
E (s) 6.86
A (s) 4.98
F (q) 4.00
G (t) 1.32
0.88
2.02
2.02
0.84
2.00
2.00
3.37
f1 (ppm)

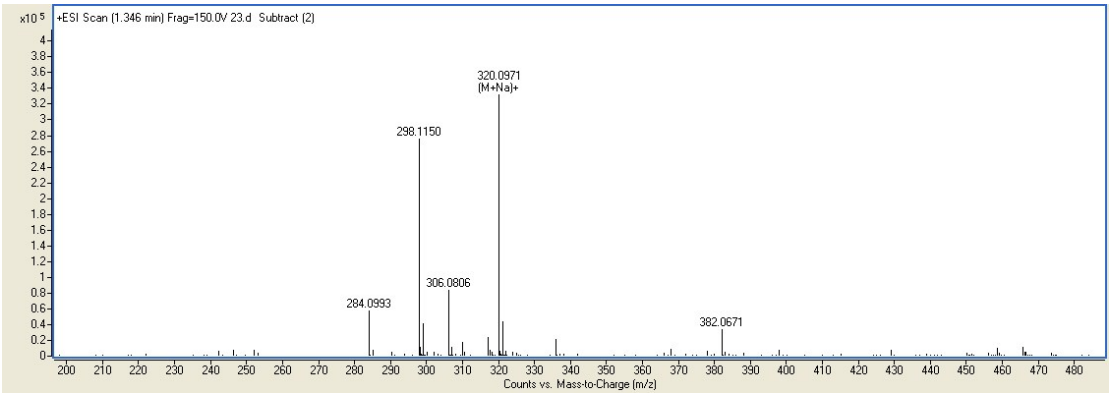

yangdongyan-13C
13C NMR of 2-4N02
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.92, 147.42, 141.88, 129.05, 123.50, 70.67, 51.89, 12.99.
f1 (ppm)



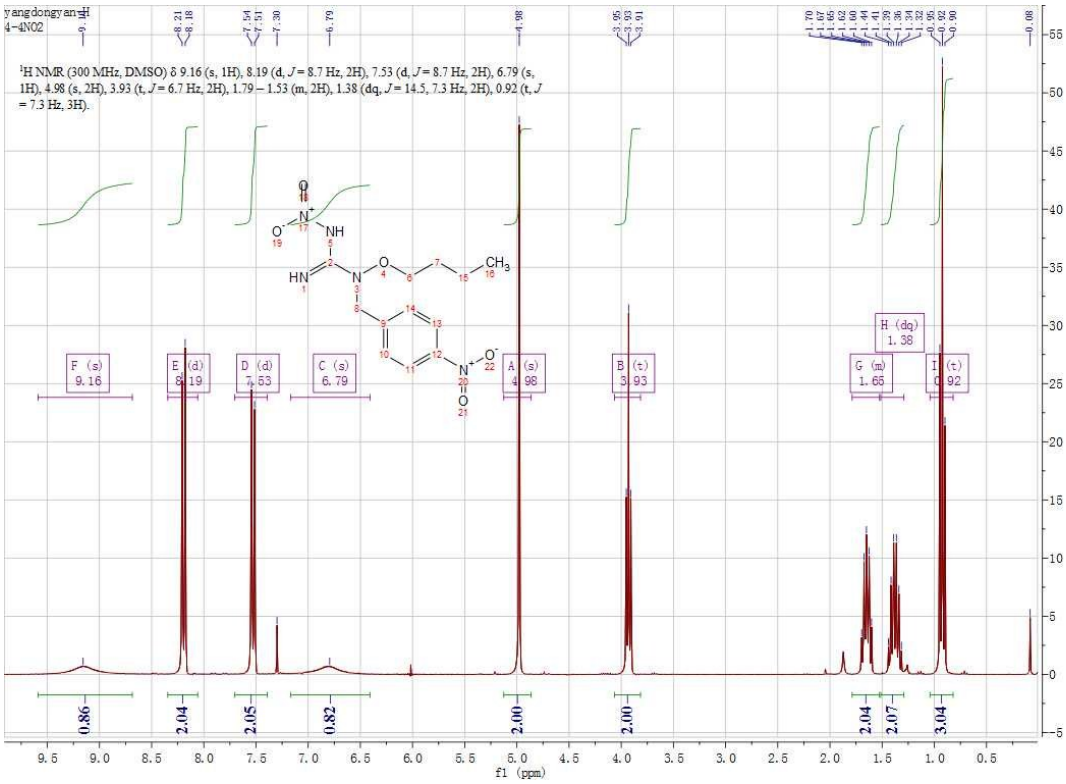
Data for (**4-18**): yield 48 %; yellow solid; mp 74-75℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.34 – 8.12 (m, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 6.77 (s, 1H), 4.99 (s, 2H), 3.90 (t, *J* = 6.7 Hz, 2H), 1.80 – 1.62 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.79, 147.44, 141.85, 129.06, 123.50, 76.55, 51.77, 20.87, 9.99. HRMS (ESI) *m/z* calcd for $C_{11}H_{15}N_5NaO_5$ $(M+Na)^+$ 320.0965 , found 320.0971.

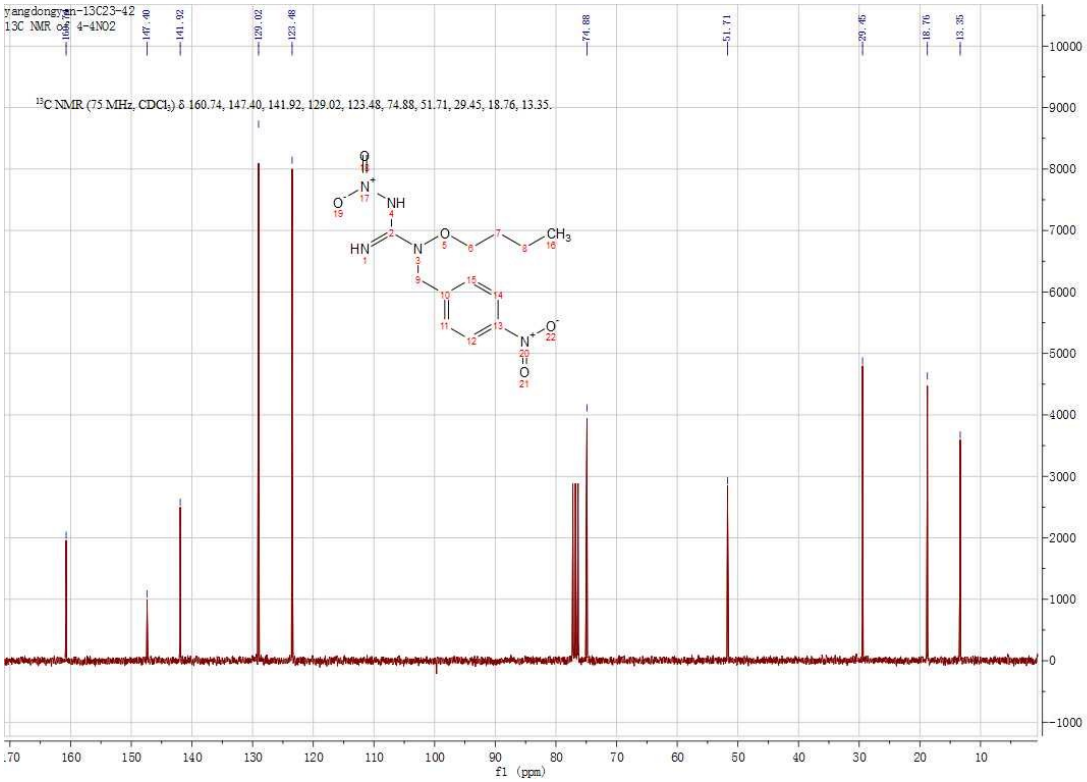


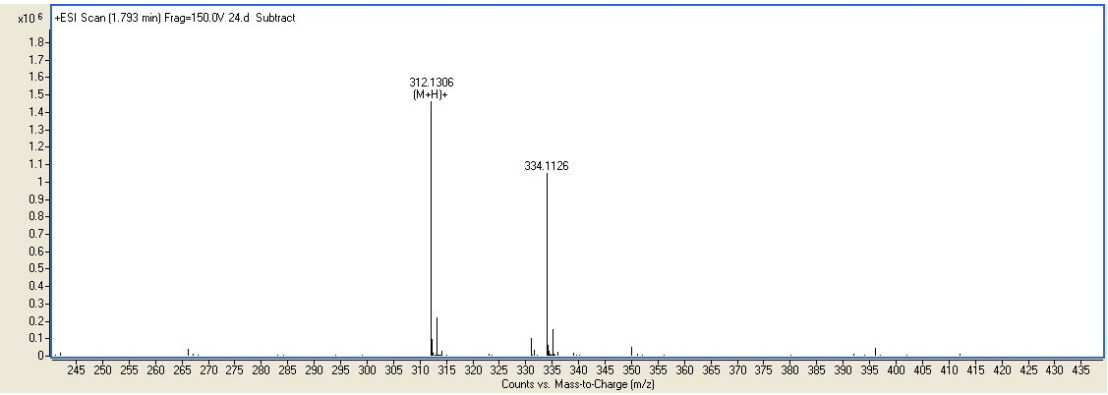




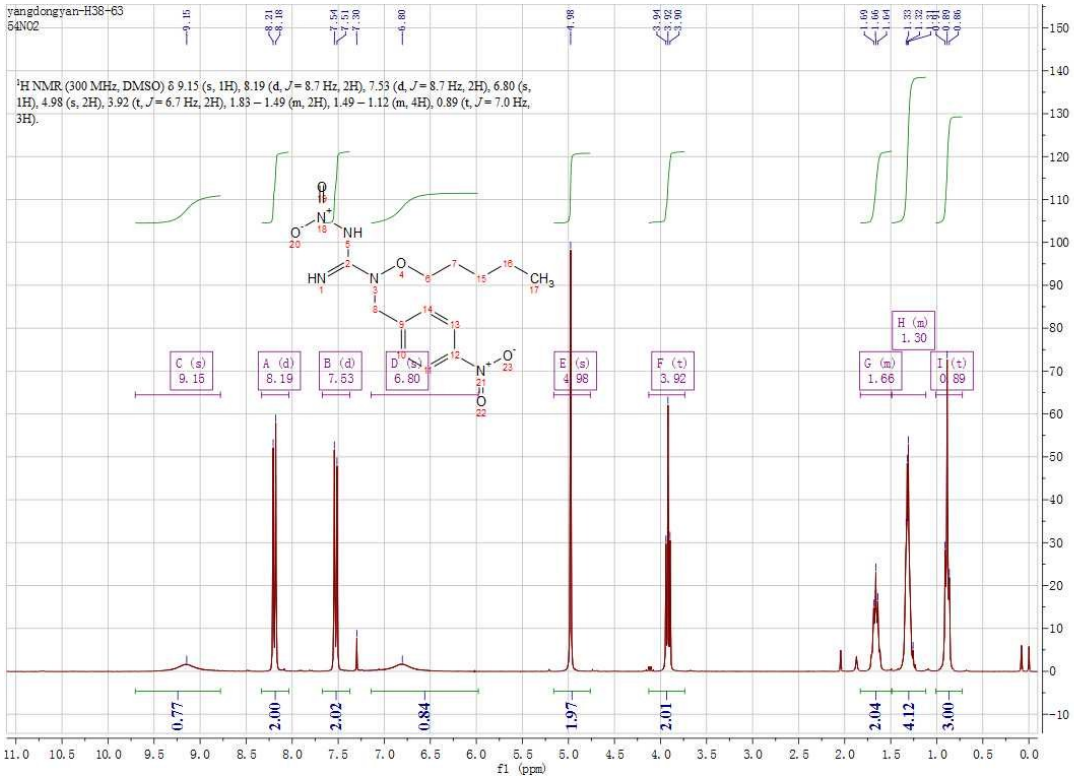
Data for (**4-19**): yield 69 %; white solid; mp 93-94℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.19 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 6.79 (s, 1H), 4.98 (s, 2H), 3.93 (t, *J* = 6.7 Hz, 2H), 1.79 – 1.53 (m, 2H), 1.38 (dq, *J* = 14.5, 7.3 Hz, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.74, 147.40, 141.92, 129.02, 123.48, 74.88, 51.71, 29.45, 18.76, 13.35. HRMS (ESI) *m/z* calcd for $C_{12}H_{18}N_5O_5$ $(M+H)^+$ 312.1302, found 312.1306.

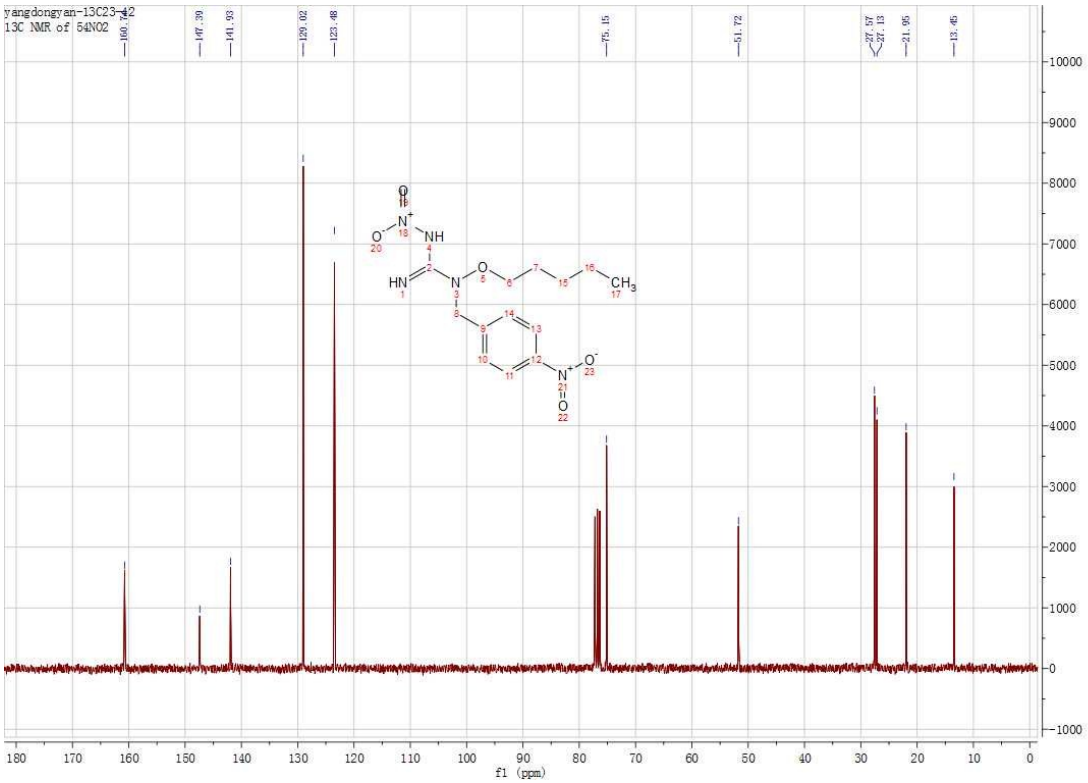

yangdongyan-H
4-4N02
^{1}H NMR (300 MHz, DMSO) δ 9.16 (s, 1H), 8.19 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.7 Hz, 2H), 6.79 (s, 1H), 4.98 (s, 2H), 3.93 (t, J = 6.7 Hz, 2H), 1.79 – 1.53 (m, 2H), 1.38 (dq, J = 14.5, 7.3 Hz, 2H), 0.92 (t, J = 7.3 Hz, 3H).
F (s) 9.16
E (d) 8.19
D (d) 7.53
C (s) 6.79
A (s) 4.98
B (t) 3.93
H (dq) 1.38
G (m) 1.65
I (t) 0.92
0.86
2.04
2.05
0.82
2.00
2.00
2.04
2.07
3.04
f1 (ppm)

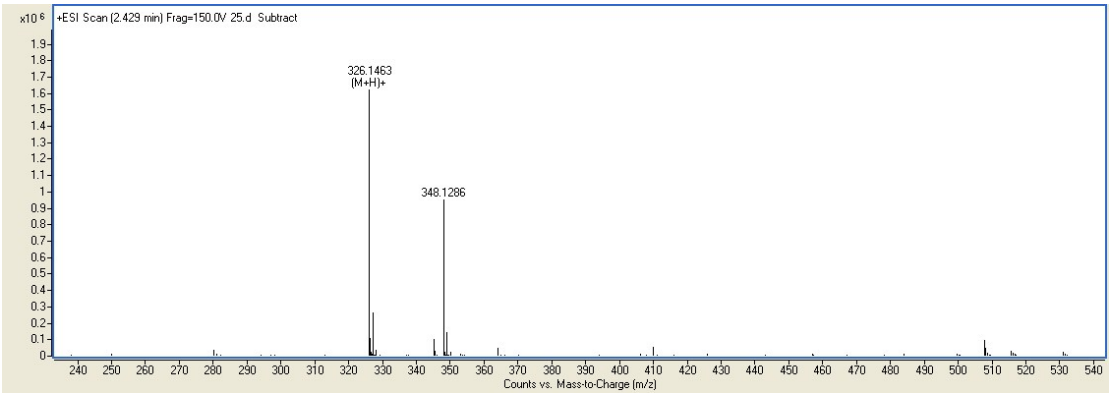

yangdongyan-13C23-42
13C NMR 6
4-4N02
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.74, 147.40, 141.92, 129.02, 123.48, 74.88, 51.71, 29.45, 18.76, 13.35.
f1 (ppm)



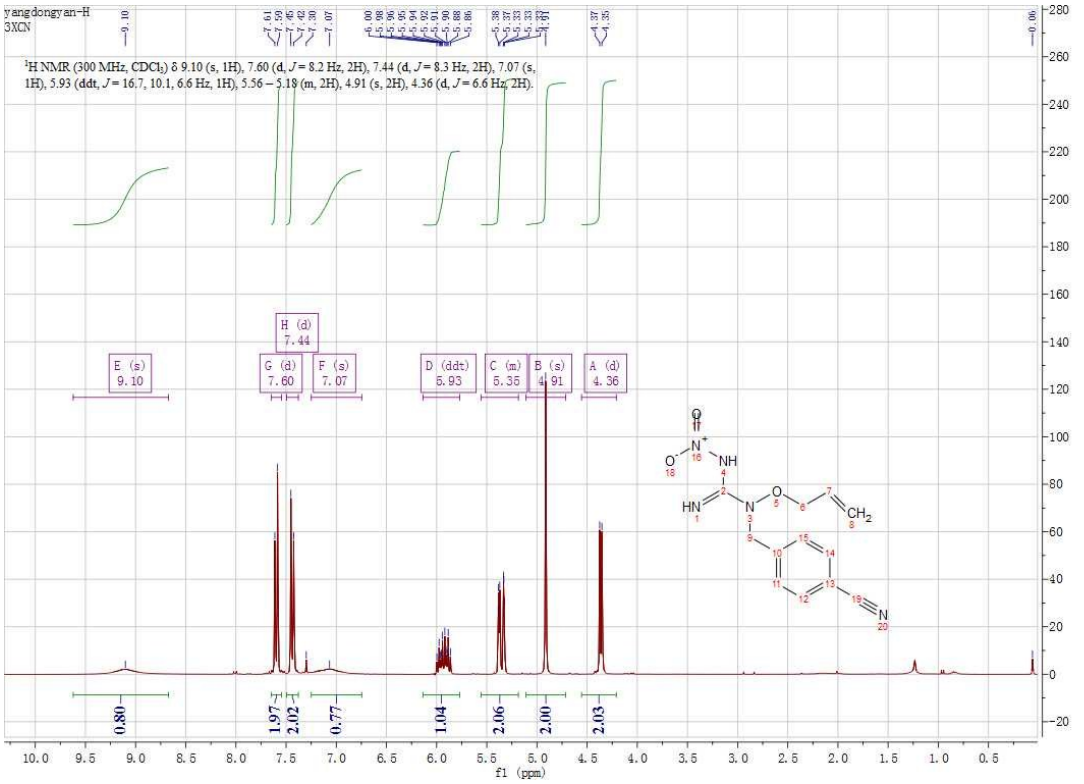
Data for (**4-20**): yield 57 %; white solid; mp 88-89℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.19 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 6.80 (s, 1H), 4.98 (s, 2H), 3.92 (t, *J* = 6.7 Hz, 2H), 1.83 – 1.49 (m, 2H), 1.49 – 1.12 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.74, 147.39, 141.93, 129.02, 123.48, 75.15, 51.72, 27.57, 27.13, 21.95, 13.45. HRMS (ESI) *m/z* calcd for $C_{13}H_{20}N_5O_5$ $(M+H)^+$ 326.1459 , found 326.1463 .

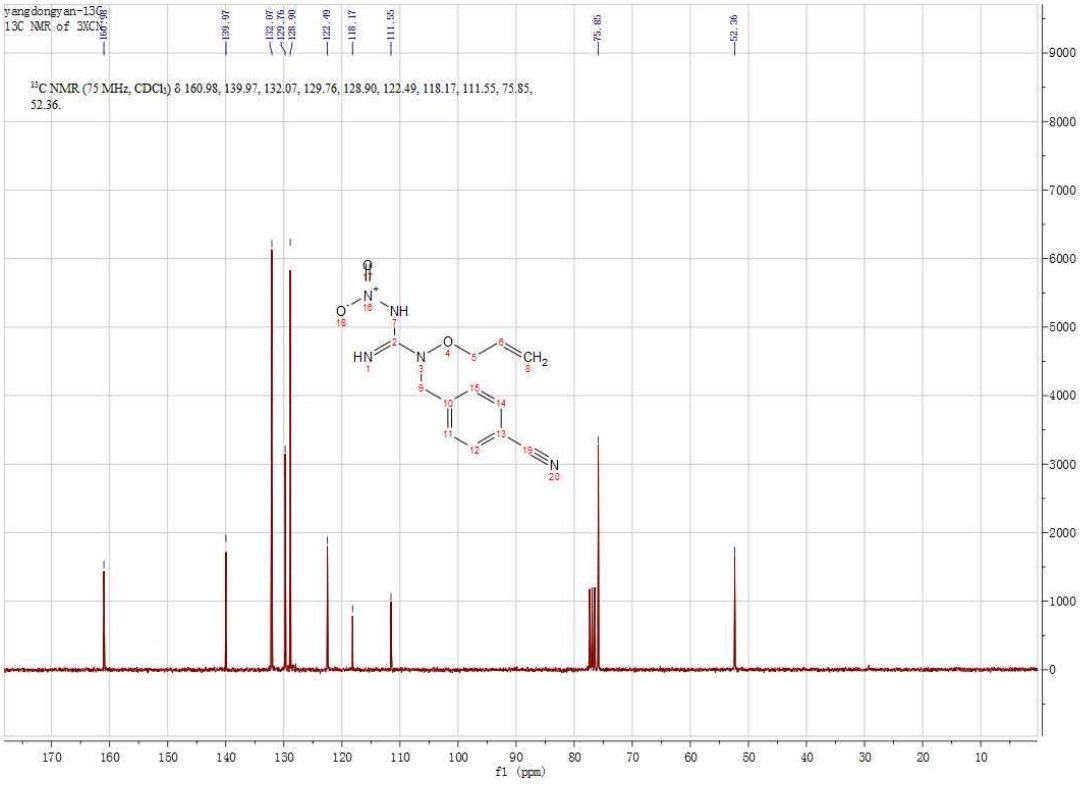


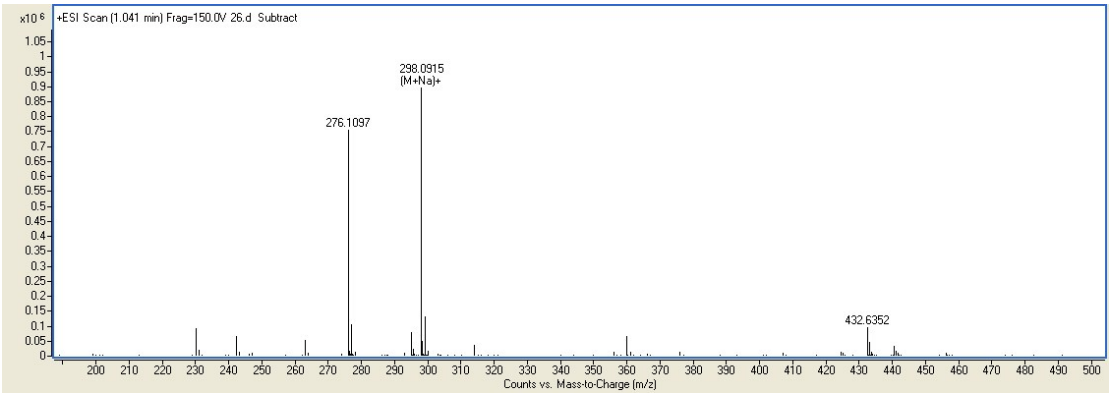




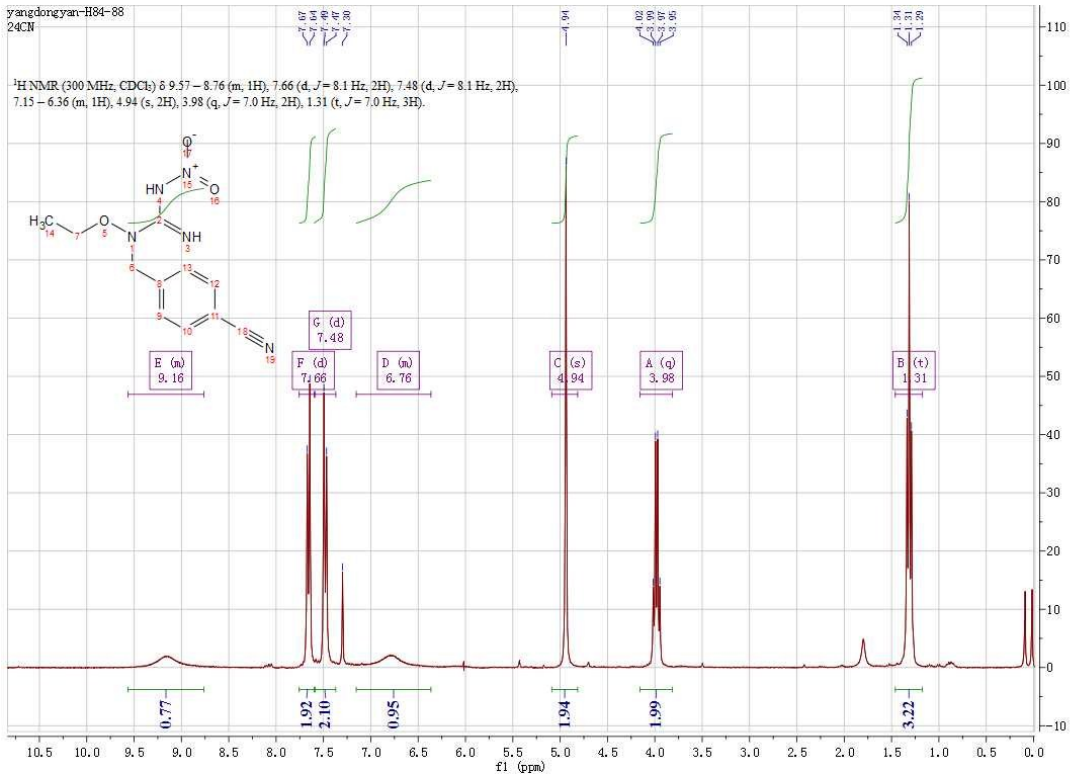
Data for (**4-21**): yield 52 %; white solid; mp 91-92℃;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.07 (s, 1H), 5.93 (ddt, *J* = 16.7, 10.1, 6.6 Hz, 1H), 5.56 – 5.18 (m, 2H), 4.91 (s, 2H), 4.36 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.98, 139.97, 132.07, 129.76, 128.90, 122.49, 118.17, 111.55, 75.85, 52.36. HRMS (ESI) *m/z* calcd for $C_{12}H_{13}N_5NaO_3$ $(M+H)^+$ 298.0911, found 298.0915 .

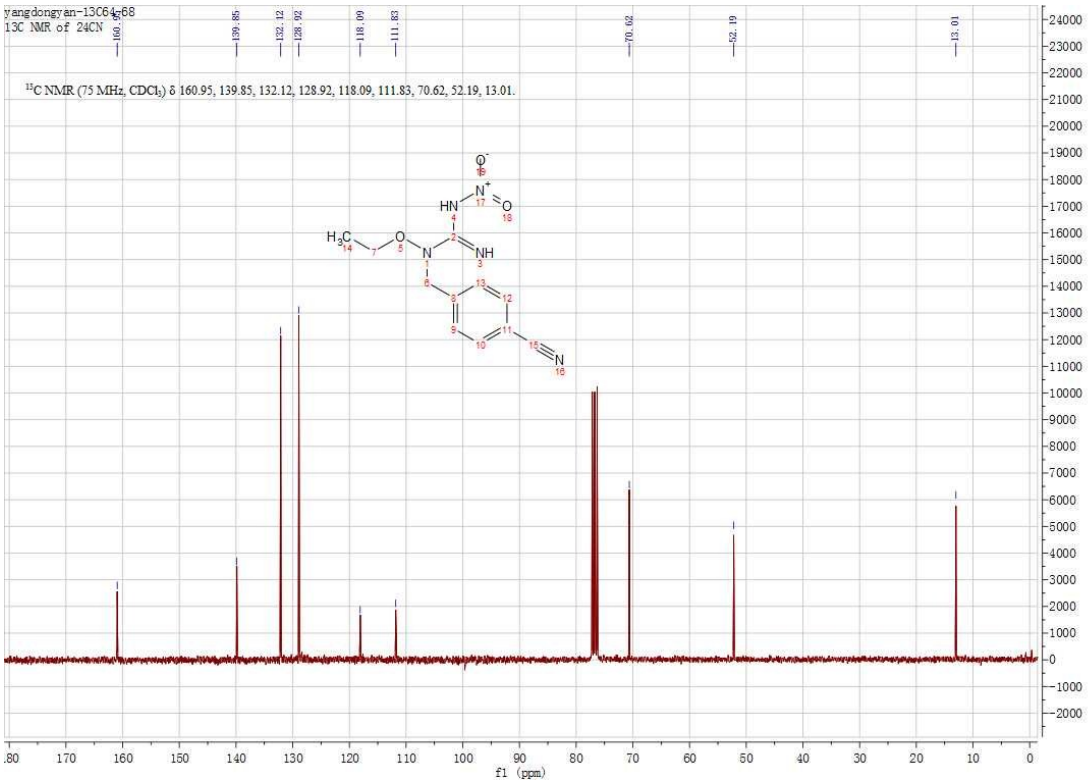

yangdongyan-H
3XCN
^{1}H NMR (300 MHz, CDCl$_3$) δ 9.10 (s, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 8.3 Hz, 2H), 7.07 (s, 1H), 5.93 (ddt, J = 16.7, 10.1, 6.6 Hz, 1H), 5.56 – 5.18 (m, 2H), 4.91 (s, 2H), 4.36 (d, J = 6.6 Hz, 2H).
H (d) 7.44
E (s) 9.10
G (d) 7.60
F (s) 7.07
D (ddt) 5.93
C (m) 5.36
B (s) 4.91
A (d) 4.36
0.80
1.97
2.02
0.77
1.04
2.06
2.00
2.03
f1 (ppm)

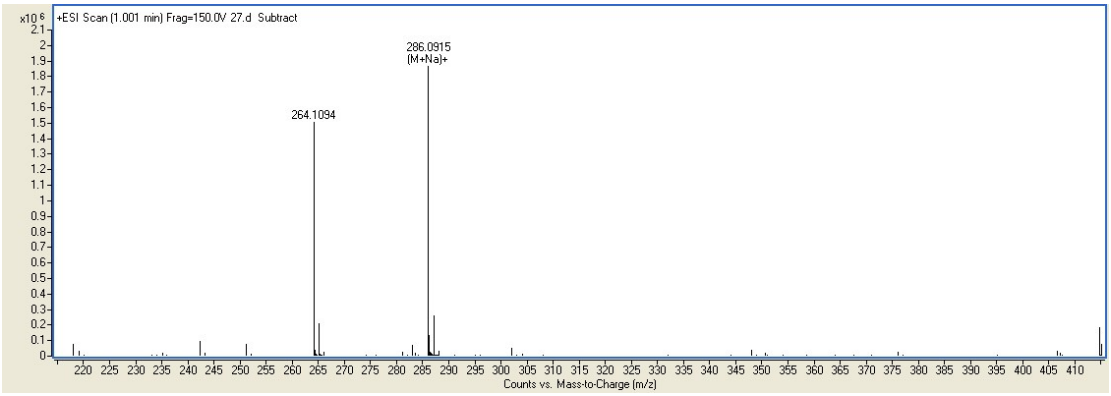

yangdongyan-13C
13C NMR of 3XCN
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.98, 139.97, 132.07, 129.76, 128.90, 122.49, 118.17, 111.55, 75.85, 52.36.
f1 (ppm)



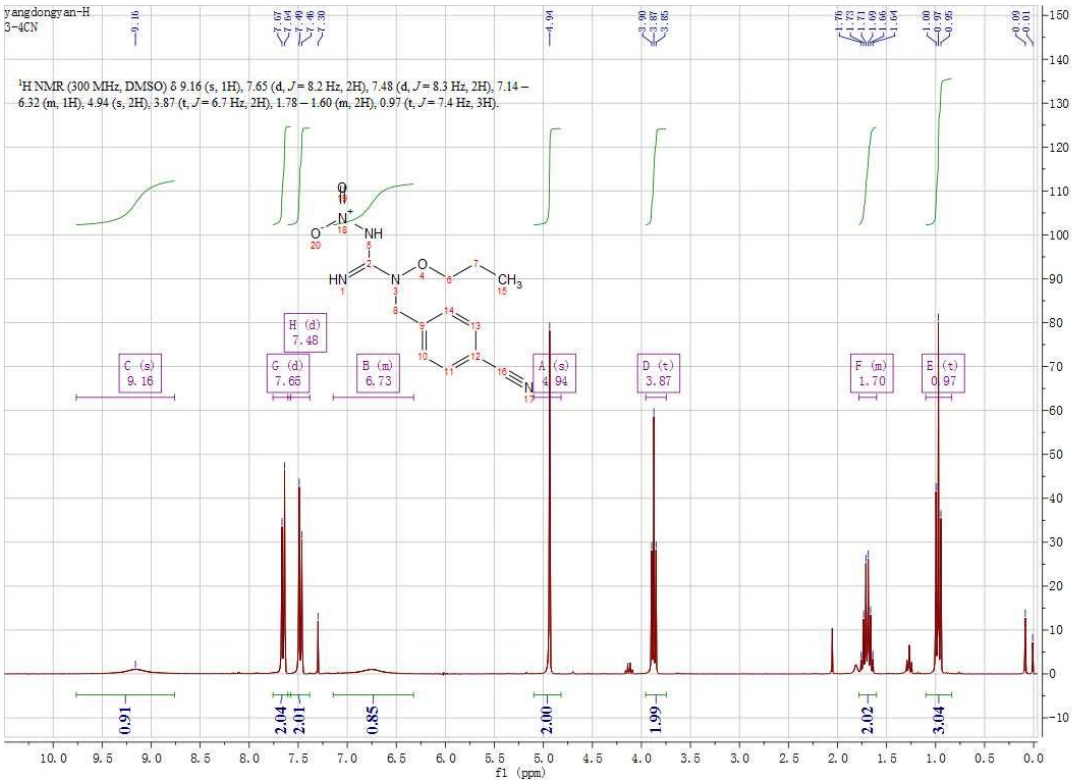
Data for (**4-22**): yield 45 %;white solid; mp 111-113℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 – 8.76 (m, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.15 – 6.36 (m, 1H), 4.94 (s, 2H), 3.98 (q, *J* = 7.0 Hz, 2H), 1.31 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.95, 139.85, 132.12, 128.92, 118.09, 111.83, 70.62, 52.19, 13.01. HRMS (ESI) *m/z* calcd for $C_{11}H_{13}N_5NaO_3$ $(M+Na)^+$ 286.0911 , found 286.0915 .

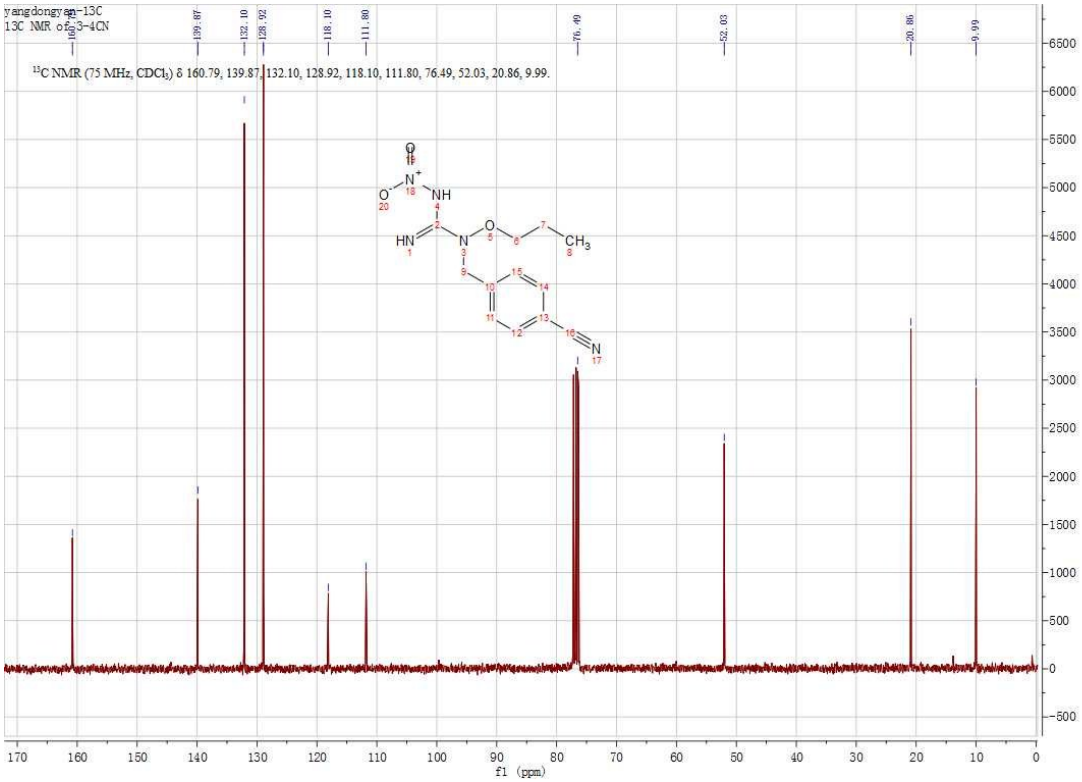


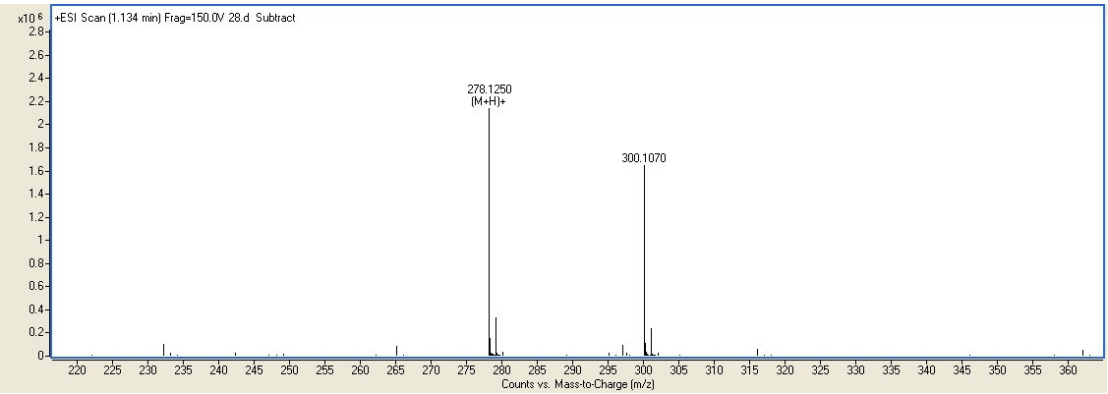




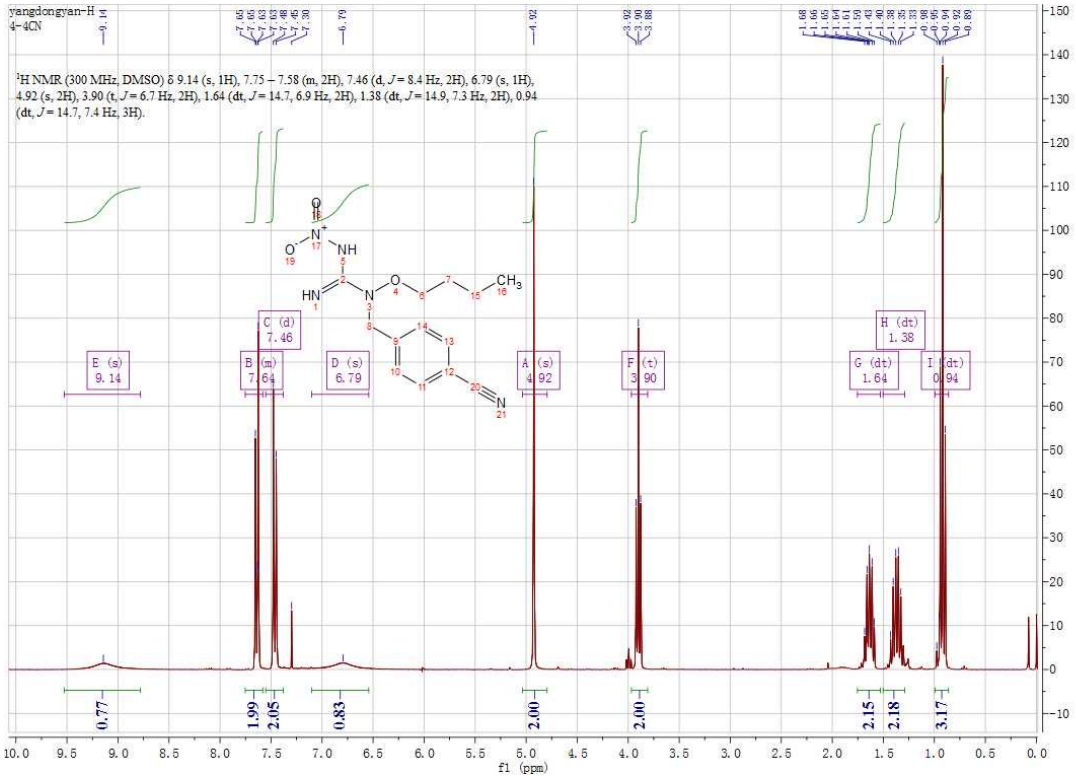
Data for (**4-23**): yield 59 %; white solid; mp 64-65℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.14 – 6.32 (m, 1H), 4.94 (s, 2H), 3.87 (t, *J* = 6.7 Hz, 2H), 1.78 – 1.60 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.79, 139.87, 132.10, 128.92, 118.10, 111.80, 76.49, 52.03, 20.86, 9.99. HRMS (ESI) *m/z* calcd for $C_{12}H_{16}N_5O_3$ $(M+H)^+$ 278.1248 , found 278.1250.

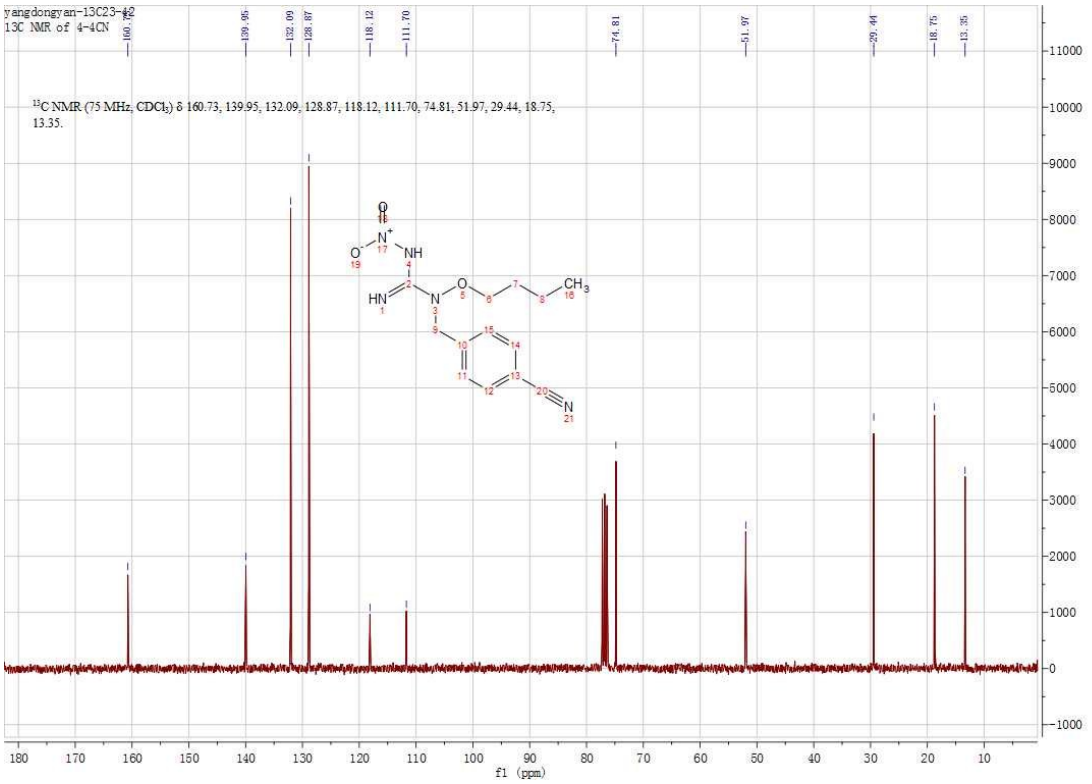

yangdongyan-H
3-4CN
^{1}H NMR (300 MHz, DMSO) δ 9.16 (s, 1H), 7.65 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.3 Hz, 2H), 7.14 – 6.32 (m, 1H), 4.94 (s, 2H), 3.87 (t, J = 6.7 Hz, 2H), 1.78 – 1.60 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H).
C (s) 9.16
G (d) 7.65
H (d) 7.48
B (m) 6.73
A (s) 4.94
D (t) 3.87
F (m) 1.70
E (t) 0.97
0.91
2.04
2.01
0.85
2.00
1.99
2.02
3.04
f1 (ppm)

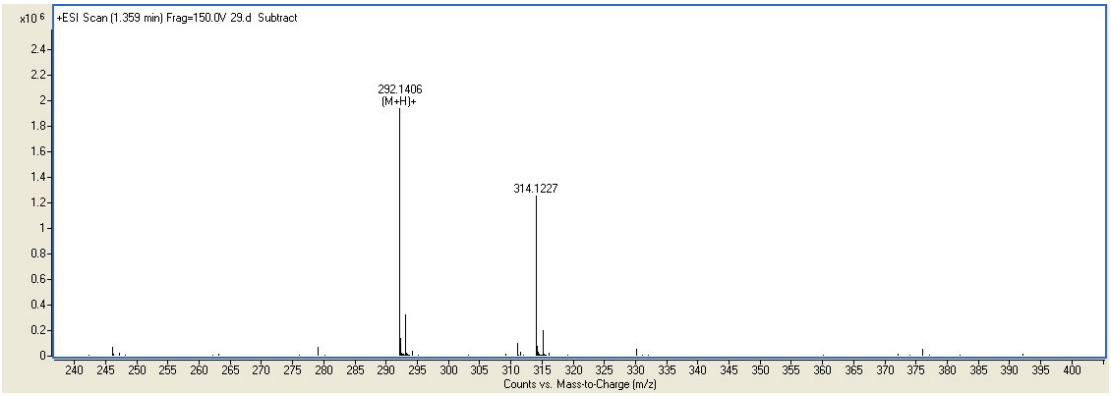

yangdongyan-13C
13C NMR of 3-4CN
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.79, 139.87, 132.10, 128.92, 118.10, 111.80, 76.49, 52.03, 20.86, 9.99.
f1 (ppm)



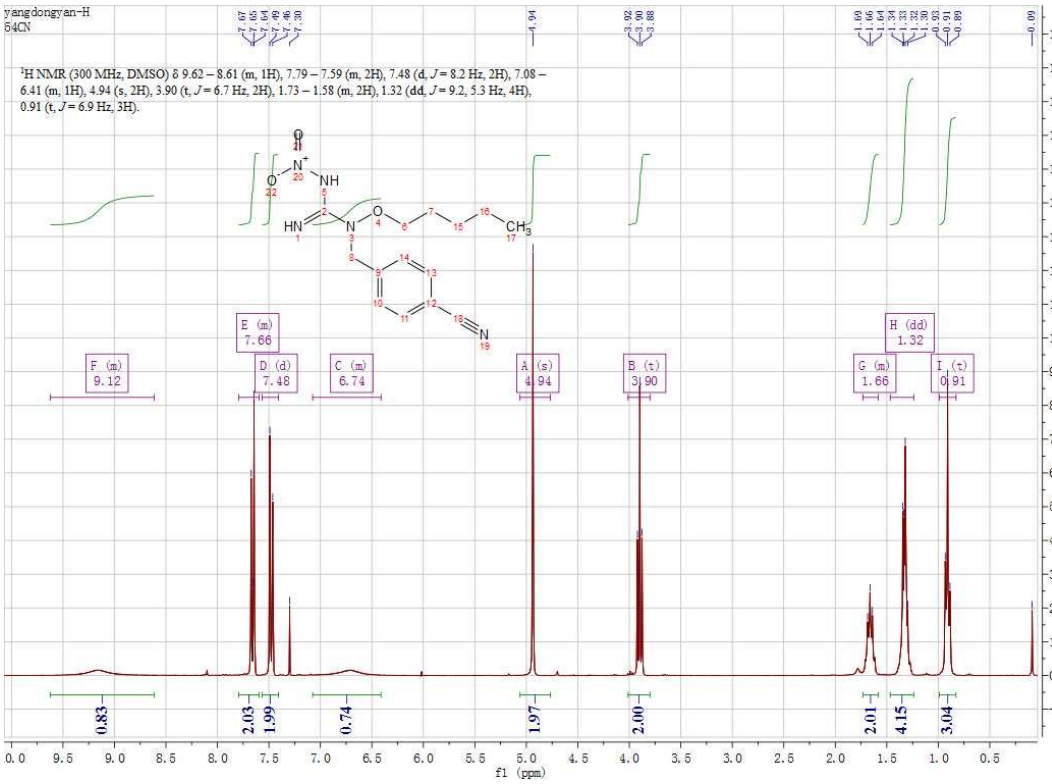
Data for (**4-24**): yield 52 %; white crystal; mp 88-89 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.75 – 7.58 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 6.79 (s, 1H), 4.92 (s, 2H), 3.90 (t, *J* = 6.7 Hz, 2H), 1.64 (dt, *J* = 14.7, 6.9 Hz, 2H), 1.38 (dt, *J* = 14.9, 7.3 Hz, 2H), 0.94 (dt, *J* = 14.7, 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.73, 139.95, 132.09, 128.87, 118.12, 111.70, 74.81, 51.97, 29.44, 18.75, 13.35. HRMS (ESI) *m/z* calcd for $C_{13}H_{18}N_5O_3$ $(M+H)^+$ 292.1404, found 292.1406.

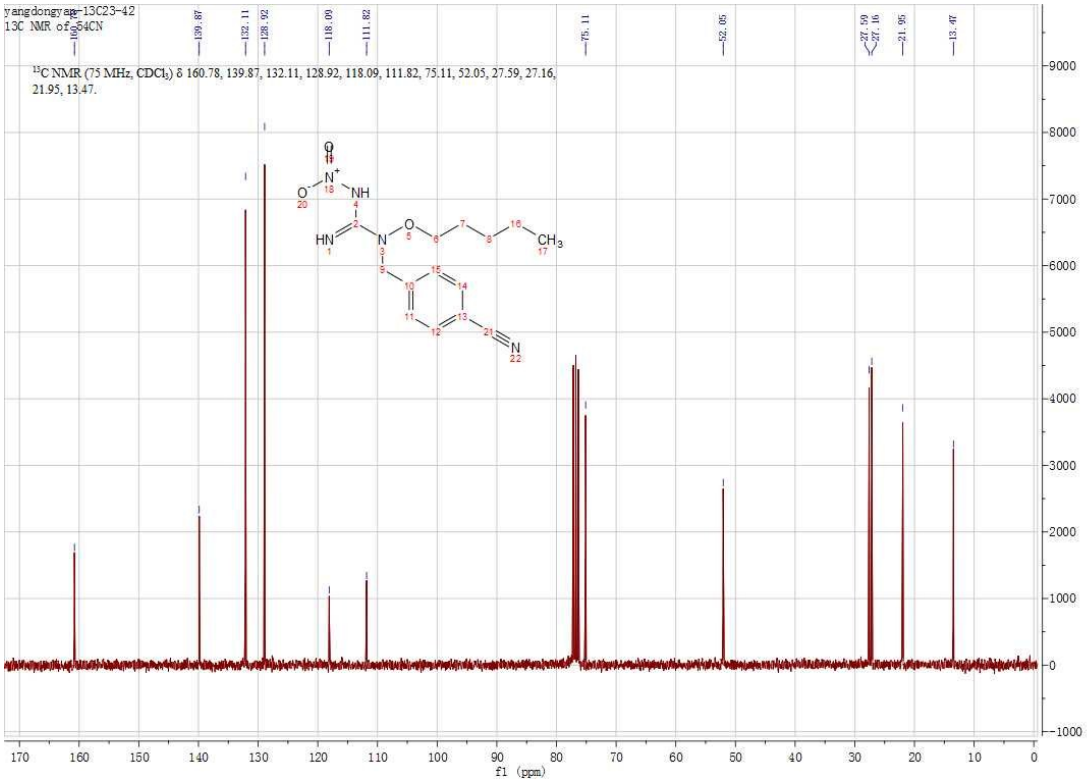


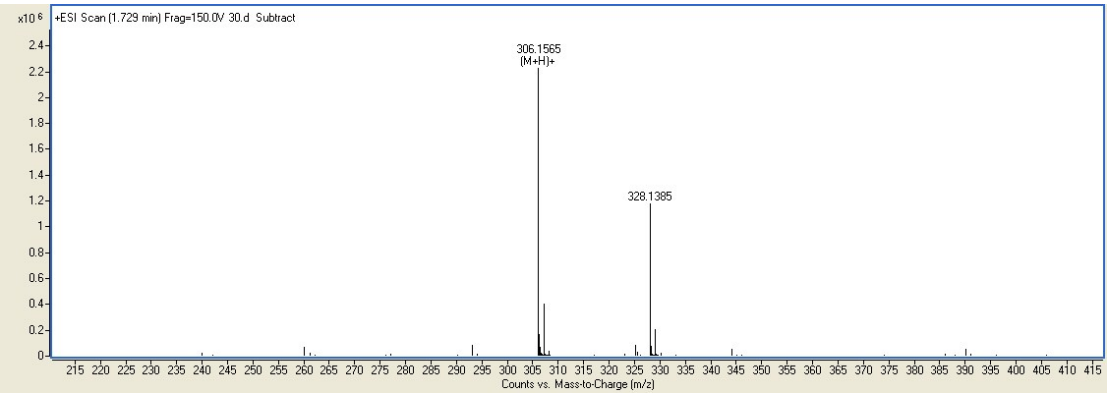




Data for (**4-25**): yield 62 %; white solid; mp 70-71℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.62 – 8.61 (m, 1H), 7.79 – 7.59 (m, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.08 – 6.41 (m, 1H), 4.94 (s, 2H), 3.90 (t, *J* = 6.7 Hz, 2H), 1.73 – 1.58 (m, 2H), 1.32 (dd, *J* = 9.2, 5.3 Hz, 4H), 0.91 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.78, 139.87, 132.11, 128.92, 118.09, 111.82, 75.11, 52.05, 27.59, 27.16, 21.95, 13.47. HRMS (ESI) *m/z* calcd for $C_{14}H_{20}N_5O_3$ $(M+H)^+$ 306.1561, found 306.1565 .


yangdongyan-H
54CN
^{1}H NMR (300 MHz, DMSO) δ 9.62 – 8.61 (m, 1H), 7.79 – 7.59 (m, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.08 – 6.41 (m, 1H), 4.94 (s, 2H), 3.90 (t, J = 6.7 Hz, 2H), 1.73 – 1.58 (m, 2H), 1.32 (dd, J = 9.2, 5.3 Hz, 4H), 0.91 (t, J = 6.9 Hz, 3H).
F (m) 9.12
E (m) 7.66
D (d) 7.48
C (m) 6.74
A (s) 4.94
B (t) 3.90
H (dd) 1.32
G (m) 1.66
I (t) 0.91
0.83
2.03
1.99
0.74
1.97
2.00
2.01
4.15
3.04
f1 (ppm)


yangdongyan-13C23-42
13C NMR of 54CN
^{13}C NMR (75 MHz, CDCl$_3$) δ 160.78, 139.87, 132.11, 128.92, 118.09, 111.82, 75.11, 52.05, 27.59, 27.16, 21.95, 13.47.
f1 (ppm)


x10 6
+ESI Scan (1.729 min) Frag=150.0V 30.d Subtract
306.1565
(M+H)+
328.1385
Counts vs. Mass-to-Charge (m/z)

Single crystal X-Ray data for compound 4-02

Crystal Data. $C_9H_{12}ClN_5O_3$, M =273.69, monoclinic, a = 11.7756(4) Å, b = 9.1501(3) Å, c = 11.4455(4) Å, β = 103.010(3)°, U = 1201.57(7) Å^3, T = 105.2, space group $P2_1/c$ (no. 14), Z = 4, μ(Mo Kα) = 0.328, 4458 reflections measured, 2357 unique (R_{int} = 0.0201) which were used in all calculations. The final $wR(F_2)$ was 0.1039 (all data).

Table 1: Crystal data and structure refinement for exp_4503

Identification code	exp_4503
Empirical formula	$C_9H_{12}ClN_5O_3$
Formula weight	273.69
Temperature / K	105.2
Crystal system	monoclinic
Space group	$P2_1/c$
a / Å, b / Å, c / Å	11.7756(4), 9.1501(3),
α/°, β/°, γ/°	90.00, 103.010(3), 90.00
Volume / Å^3	1201.57(7)
Z	4
ρ_{calc} / mg mm^{-3}	1.513
μ / mm^{-1}	0.328
F(000)	568
Crystal size / mm^3	0.34 × 0.30 × 0.25
2Θ range for data collection	6.32 to 51.98°
Index ranges	-14 ≤ h ≤ 14, -11 ≤ k ≤ 6, -7
Reflections collected	4458
Independent reflections	2357[R(int) = 0.0201 (inf-
Data/restraints/parameters	2357/0/164
Goodness-of-fit on F²	1.067
Final R indexes [I>2σ (I) i.e. F_o>4σ (F_o)]	R_1 = 0.0411, wR_2 = 0.0984
Final R indexes [all data]	R_1 = 0.0497, wR_2 = 0.1039
Largest diff. peak/hole / e Å^{-3}	0.404/-0.493
Flack Parameters	N
Completeness	0.999

Table 2 Fractional Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å²×10³) for exp_4503. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1	6876.9(5)	137.9(6)	4516.8(6)	33.69(18)
O1	2439.5(12)	4521.3(15)	5582.2(12)	20.4(3)
O3	174.1(13)	515.0(17)	2008.7(13)	28.1(4)
N5	347.5(15)	1016.8(18)	3041.9(15)	21.3(4)
O2	-200.5(14)	542.3(18)	3780.8(14)	32.1(4)
N2	2028.3(14)	3953.3(18)	4422.9(14)	18.5(4)
C6	2806.8(16)	4207(2)	3610.0(17)	19.0(4)
N4	1151.7(14)	2092.8(17)	3279.6(14)	18.5(4)
C4	3839.7(16)	3181(2)	3835.2(17)	17.6(4)
N1	5591.0(16)	2252(2)	5144.8(16)	28.0(4)
C1	5669.9(17)	1311(2)	4253.6(19)	22.1(4)
N3	929.6(14)	2407.3(19)	5315.2(15)	21.1(4)
C7	1332.5(16)	2756(2)	4362.9(17)	17.5(4)
C5	4662.0(17)	3182(2)	4921.7(18)	20.5(4)
C3	3989.3(18)	2162(2)	2982.9(18)	25.0(5)
C2	4911.5(17)	1225(2)	3180.0(18)	21.0(4)
C8	1925.2(18)	5957(2)	5667.3(19)	23.9(5)
C9	2428(2)	6496(2)	6922.0(19)	30.0(5)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for exp_4503. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka \times b \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	26.7(3)	25.9(3)	49.5(4)	8.0(3)	10.7(3)	7.2(2)
O1	20.8(7)	22.3(7)	15.4(7)	-2.4(6)	-1.5(6)	2.3(6)
O3	34.3(9)	33.6(9)	16.2(7)	-6.2(7)	5.0(6)	-11.7(7)
N5	21.0(9)	22.2(9)	20.0(9)	2.5(8)	3.4(7)	-1.2(7)
O2	38.3(9)	38.0(9)	23.1(8)	-0.7(7)	13.6(7)	-17.3(7)
N2	19.7(8)	21.7(9)	12.7(8)	-1.8(7)	0.6(7)	-1.4(7)
C6	19.2(10)	21.5(10)	15.7(9)	1.9(8)	2.5(8)	-2.9(8)
N4	18.5(8)	19.2(8)	17.2(8)	-0.4(7)	2.9(7)	-2.5(7)
C4	17.9(9)	16.6(9)	18.7(10)	1.5(8)	4.8(8)	-5.2(7)
N1	27.7(10)	31.3(10)	24.7(10)	1.4(8)	5.6(8)	-0.1(8)
C1	21.8(10)	18.1(10)	27.8(11)	2.4(9)	8.3(9)	0.1(8)
N3	23.7(9)	22.9(9)	17.8(9)	-1.5(7)	6.9(7)	-2.6(7)
C7	14.8(9)	19.6(10)	17.2(10)	3.6(8)	1.7(8)	4.6(7)
C5	21.1(10)	20.2(10)	19.4(10)	-3.0(8)	2.8(8)	-1.3(8)
C3	26.6(11)	29.6(12)	16.2(10)	-4.1(9)	-0.5(9)	-1.7(9)
C2	21.3(10)	21.3(10)	19.2(10)	-9.2(9)	2.0(8)	1.2(8)
C8	25.3(11)	20.6(10)	25.2(11)	-0.5(9)	4.8(9)	3.0(8)
C9	37.3(13)	28.0(11)	24.2(12)	-5.2(10)	5.8(10)	-3.1(10)

Table 4 Bond Lengths for exp_4503.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl1	C1	1.752(2)	N4	C7	1.354(2)
O1	N2	1.406(2)	C4	C5	1.393(3)
O1	C8	1.459(2)	C4	C3	1.389(3)
O3	N5	1.242(2)	N1	C1	1.354(3)
N5	O2	1.251(2)	N1	C5	1.364(3)
N5	N4	1.351(2)	C1	C2	1.349(3)
N2	C6	1.464(2)	N3	C7	1.322(2)
N2	C7	1.360(2)	C3	C2	1.362(3)
C6	C4	1.512(3)	C8	C9	1.508(3)

Table 5 Bond Angles for exp_4503.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N2	O1	C8	109.63(14)	C1	N1	C5	116.35(18)
O3	N5	O2	121.07(16)	N1	C1	Cl1	116.78(16)
O3	N5	N4	114.76(16)	C2	C1	Cl1	117.75(16)
O2	N5	N4	124.17(17)	C2	C1	N1	125.46(19)
O1	N2	C6	114.15(14)	N4	C7	N2	112.09(16)
C7	N2	O1	114.89(15)	N3	C7	N2	118.48(18)
C7	N2	C6	123.50(16)	N3	C7	N4	129.43(18)
N2	C6	C4	112.83(16)	N1	C5	C4	122.24(18)
N5	N4	C7	118.03(16)	C2	C3	C4	121.93(19)
C5	C4	C6	121.50(17)	C1	C2	C3	116.97(19)
C3	C4	C6	121.43(17)	O1	C8	C9	106.16(16)
C3	C4	C5	117.03(18)				

Table 6 Torsion Angles for exp_4503.

A	B	C	D	Angle/°
Cl1	C1	C2	C3	-178.90(16)
O1	N2	C6	C4	77.4(2)
O1	N2	C7	N4	-167.91(14)
O1	N2	C7	N3	12.6(2)
O3	N5	N4	C7	175.85(16)
N5	N4	C7	N2	-170.83(15)
N5	N4	C7	N3	8.6(3)
O2	N5	N4	C7	-3.8(3)
N2	O1	C8	C9	-178.86(15)
N2	C6	C4	C5	-62.7(2)
N2	C6	C4	C3	115.1(2)
C6	N2	C7	N4	-19.9(2)
C6	N2	C7	N3	160.55(17)
C6	C4	C5	N1	179.17(18)
C6	C4	C3	C2	-179.46(19)
C4	C3	C2	C1	1.1(3)
N1	C1	C2	C3	-0.2(3)
C1	N1	C5	C4	-0.5(3)
C7	N2	C6	C4	-70.8(2)
C5	C4	C3	C2	-1.6(3)
C5	N1	C1	Cl1	178.63(15)
C5	N1	C1	C2	-0.1(3)
C3	C4	C5	N1	1.3(3)
C8	O1	N2	C6	96.07(18)
C8	O1	N2	C7	-112.90(17)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for exp_4503.

Atom	*x*	*y*	*z*	U(eq)
H6A	3087	5207	3703	23
H6B	2370	4088	2790	23
H3A	483	1659	5294	25
H3B	1114	2928	5955	25
H5	4575	3840	5515	25
H3	3444	2118	2257	30
H2	5014	555	2601	25
H8A	1083	5883	5525	29
H8B	2121	6620	5081	29
H9A	2112	7442	7027	45
H9B	3260	6566	7048	45
H9C	2233	5825	7491	45