Supporting Information

Base-promoted Lewis acid catalyzed synthesis of quinazoline derivatives

Fang-Peng Hu, Xin-Feng Cui, Guo-Qiang Lu and Guo-Sheng Huang*

State Key Laboratory of Applied Organic Chemistry, Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, Department of Chemistry, Lanzhou University, Lanzhou 730000, China. Fax: 86-931-8912596; E-mail: hgs@lzu.edu.cn

Table of contents

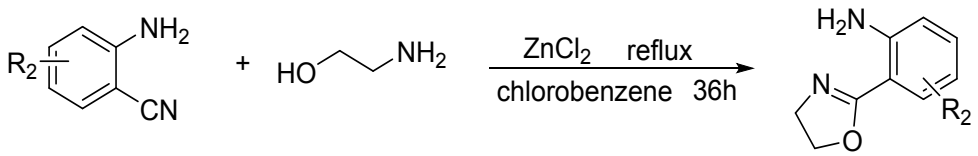
1. General information

^{1}H NMR, and ^{13}C NMR spectra were recorded on Mercury 400M in $CDCl_3$. All ^{1}H NMR and ^{13}C NMR chemical shifts were given as δ value (ppm) with reference to tetramethylsilane (TMS) as an internal standard. Copies of their ^{1}H NMR and ^{13}C NMR spectra were provided. Products were purified by flash chromatography on 200–300 mesh silica gels. All melting points were determined without correction. All reactions were carried out in oven-dried glassware, unless otherwise noted. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification.

2. Experimental section

2.1 General procedure for the synthesis of 1a-1be.[1]

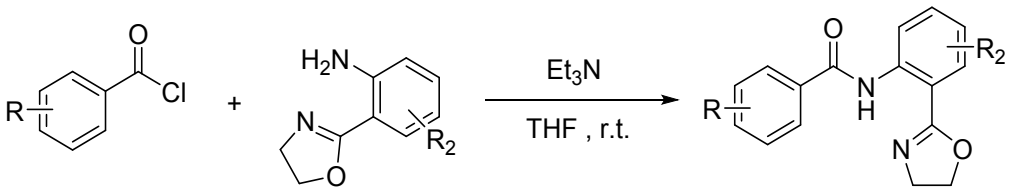
2.1.1 Synthesis of 2-(4,5-dihydrooxazol-2-yl)aniline.



2-aminobenzonitrile (19 g, 250 mmol) and $ZnCl_2$ (3.34 g, 25 mmol) was added to a 500 mL three-necked flask, and then suspended in chlorobenzene (350 mL) under nitrogen. 2-aminoethanol (45 mL, 750 mmol) was added to the suspension via a syringe. The mixture was

slowly heated to reflux until no gas was produced. After refluxing for 36 hours, the reaction mixture was cooled down to room temperature and the solvent was removed in a rotary evaporator. CH_2Cl_2 (250 mL) was added to the residue and washed with saturated $NaHCO_3$ (150 mL) and H_2O (150 mL). The aqueous fraction was extracted with CH_2Cl_2 (250 mL × 3). The combined organic phase was dried over Na_2SO_4, filtered and the solvent was removed in a rotary evaporator. The crude product was recrystallized from EtOAc/Hexane to give colorless crystals of the compound 2-(4,5-dihydrooxazol-2-yl)aniline 29 g (72%).

2.1.2 Preparation of Substrates 1a-1be.

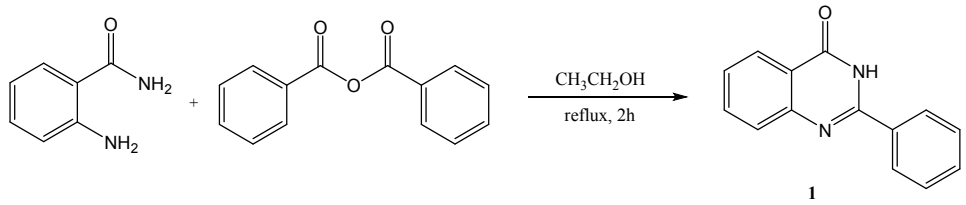


An acid chloride (5 mmol), prepared from the corresponding carboxylic acid and oxalyl chloride and 2-(4,5-dihydrooxazol-2-yl)aniline (5 mmol) were added to a 50 mL flask and then dissolved with THF (10 mL). Et_3N (7.5 mmol) was taken to the vigorously stirred solution via a syringe. The reaction mixture was stirred at room temperature for 6 h and quenched with saturated $NaHCO_3 \cdot H_2O$ (100 mL) was added to the mixture and extracted with EtOAc (150 mL × 3). Combined organic phase was washed with saturated NaCl (aq) and dried over Na_2SO_4, and then filtered, the solvent was removed in a rotary evaporator. The crude product was

recrystallized from EtOAc/Hexane to give colorless crystals of the product.

2.2 General procedure for the synthesis of A4. [2]

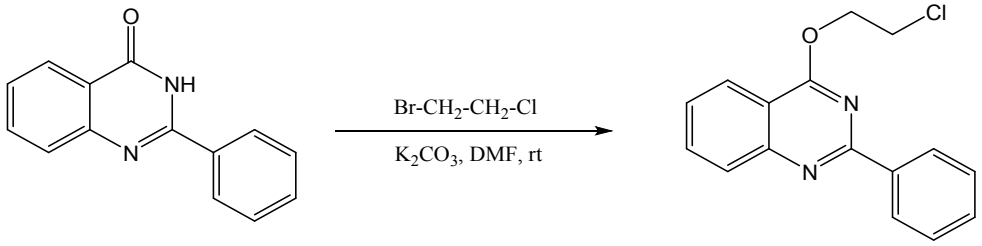
2.2.1 Synthesis of 2-Phenylquinazoli-4(3*H*)-one.



1

Anthranilamide (5.0 g, 36.7 mmol) was coupled with benzoic anhydride (9.3 g, 41.1 mmmol) in absolute ethanol (30 mL) at reflux for 2h. The reaction mixture was filtered to give a white solid, which was purified from 1 N aqueous NaOH and followed by 2 N aqueous HCl to afford **1** (6.8 g, 83%) as white crystals.

2.2.2 Preparation of Substrates A4.



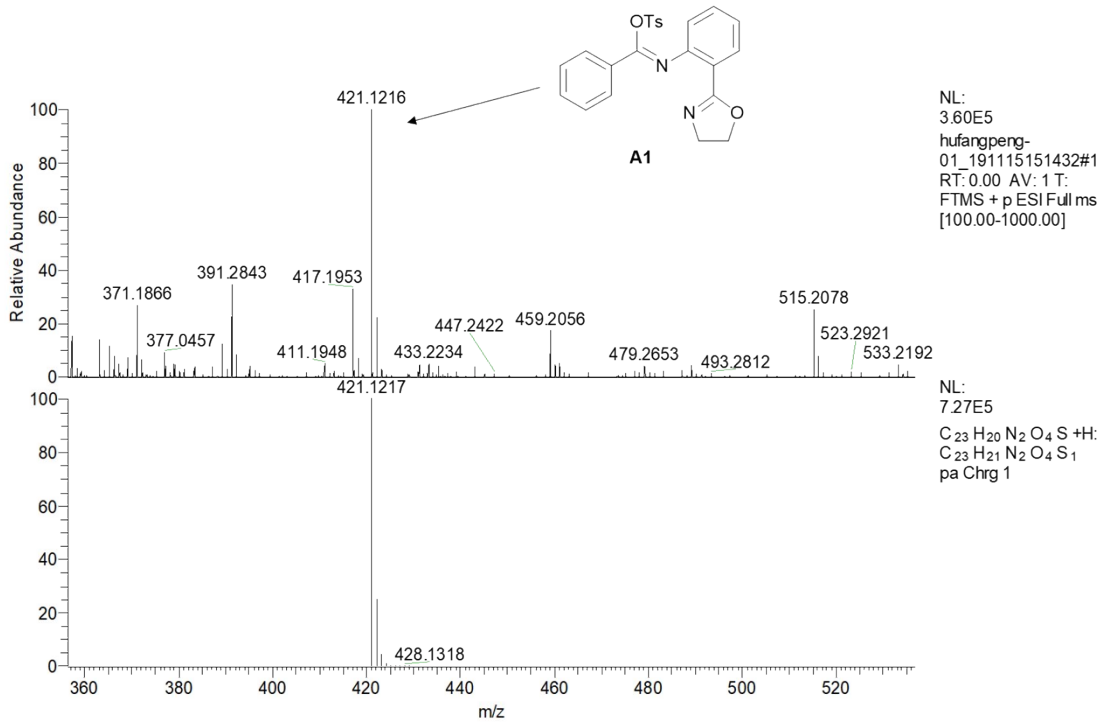
To a stirred mixture of **1** (4.5 mmol) and potassium carbonate (4.5 mmol) in DMF (10 mL) was added dropwise the appropriate bromochloroalkane (6.7 mmol) at room temperature for 24-48 h. The reaction was quenched by water (25 mL) and extracted with ethyl acetate (25 mL × 2).

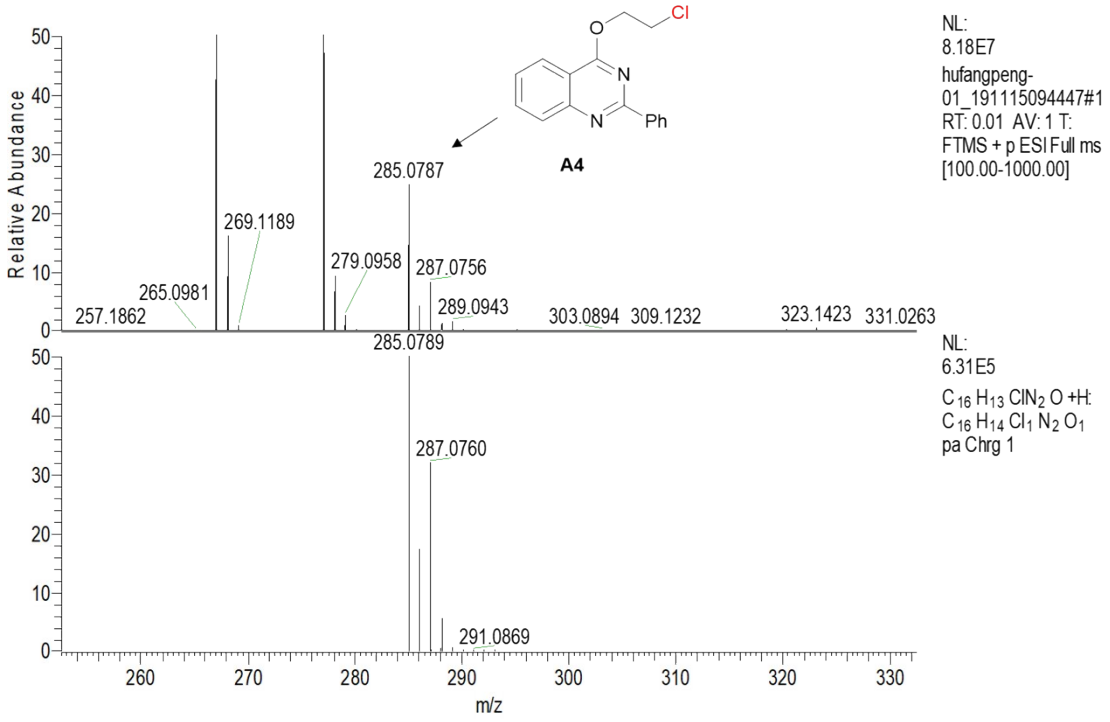
The combined organic extracts were washed with brine (25 mL × 3), dried by Na_2SO_4, and evaporated under reduced pressure. The residue was then purified by column chromatograph over silica gel eluting with ethyl acetate/n-hexane = 1/4.

2.3 General procedure to produce quinazolinones.

A mixture of amide-oxazolines **1a** (1 equiv, 0.1 mmol), TsCl **2** (0.13 mmol), $Cu(OAc)_2 \bullet H_2O$ (0.02 mmol), DMAP (0.02 mmol), DCE (1 mL), were stirred at 120℃ for 10 h (TLC monitored). Upon completion of the reaction, the reaction mixture was evaporated in vacuo and the crude product was purified by column chromatography, eluting with petroleum petroleum ether/ethyl acetate (4:1) to afford the desired **3a**.

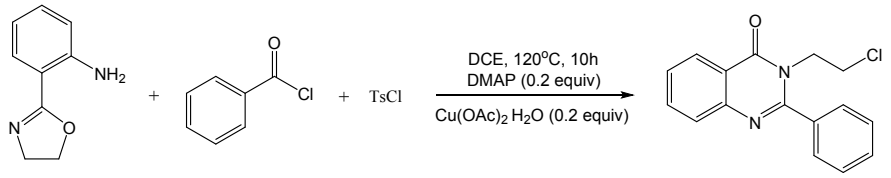
2.4 General Procedures for trapping A1 and A4 by HRMS-ESI.





2.5 Optimization of reaction conditions.

2.5.1 The reaction of 2-(4,5-dihydrooxazol-2-yl) aniline, benzoyl chloride with TsCl.

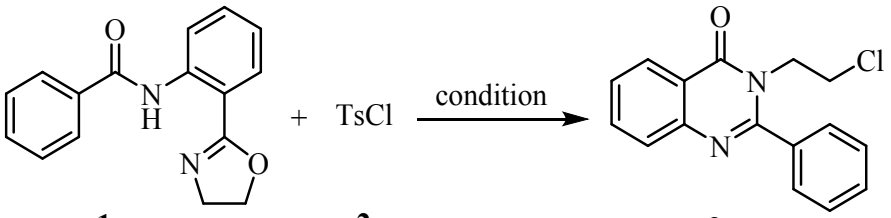


Entry	Base	Solvent	Lewis acid	T(℃)	Yield[a] (%)
1	DMAP	DCE	$Cu(OAc)_2 \cdot H_2O$	120	39
2	DMAP	THF	$Cu(OAc)_2 \cdot H_2O$	120	31
3	DMAP	DMF	$Cu(OAc)_2 \cdot H_2O$	120	0
4	DMAP	DMSO	$Cu(OAc)_2 \cdot H_2O$	120	O
5	DMAP	CH_3CN	$Cu(OAc)_2 \cdot H_2O$	120	trace
6	DMAP	Toluene	$Cu(OAc)_2 \cdot H_2O$	120	trace
7	DMAP	Dioxane	$Cu(OAc)_2 \cdot H_2O$	120	33
8	Et_3N	DCE	$Cu(OAc)_2 \cdot H_2O$	120	0
9	DABCO	DCE	$Cu(OAc)_2 \cdot H_2O$	120	trace
10	DBU	DCE	$Cu(OAc)_2 \cdot H_2O$	120	29
11	K_2CO_3	DCE	$Cu(OAc)_2 \cdot H_2O$	120	27
12	Na_2CO_3	DCE	$Cu(OAc)_2 \cdot H_2O$	120	23
13	$CaCO_3$	DCE	$Cu(OAc)_2 \cdot H_2O$	120	30
14	-	DCE	$Cu(OAc)_2 \cdot H_2O$	120	25
15	DMAP	DCE	$Zn(OAc)_2$	120	trace

16	DMAP	DCE	$FeCl_3$	120	0
17	DMAP	DCE	$Ni(OAc)_2$	120	trace
18	DMAP	DCE	$Cu(OAc)_2$	120	trace
19	DMAP	DCE	$NiCl_2$	120	trace
20	DMAP	DCE	$BF_3{\cdot}O(C_2H_5)_2$	120	trace
21	DMAP	DCE	-	120	0
22	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	140	34
23	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	100	8
24	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	80	trace
25	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	60	0

Reaction conditions: 2-(4,5-dihydrooxazol-2-yl)aniline (0.1 mmol), benzoyl chloride (0.12 mmol), TsCl (0.13 mmol), base (0.02 mmol), Lewis acid (0.02 mmol), solvent (1.0 mL). [a] Isolated yield.

2.5.2 The reaction of amide-oxazolines with TsCl.



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

Entry	Base	Solvent	Lewis acid	[Cl]	T [℃]	Yield [a] [%]
1	K_2CO_3	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	9
2	Na_2CO_3	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	39
3	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	84
4	DABCO	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	66
5	NEt_3	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	73
6	DBU	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	64
7	Pyridine	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	68
8		DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	46
9	DMAP	Toluene	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	65
10	DMAP	Hexane	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	41
11	DMAP	CH_3CN	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	78
12	DMAP	DMF	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	trace
13	DMAP	Dioxane	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	71
14	DMAP	THF	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	trace
15	DMAP	MeOH	$Cu(OAc)_2{\cdot}H_2O$	TsCl	120	trace
16	DMAP	DCE		TsCl	120	0

17	DMAP	DCE	$NiCl_2$	TsCl	120	0
18	DMAP	DCE	$ZnCl_2$	TsCl	120	42
19	DMAP	DCE	$Cu(OAc)_2$	TsCl	120	79
20	DMAP	DCE	$FeCl_3$	TsCl	120	0
21	DMAP	DCE	$BF_3{\cdot}O(C_2H_5)_2$	TsCl	120	19
22	DMAP	DCE	$AlCl_3$	TsCl	120	trace
23	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	NH_4Cl	120	0
24	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	NaCl	120	0
25	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	KCl	120	0
26	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	NCS	120	0
27	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	80	50
28	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	100	59
29	DMAP	DCE	$Cu(OAc)_2{\cdot}H_2O$	TsCl	140	66
30	-	DCE	$BF_3{\cdot}O(C_2H_5)_2$	TsCl	100	12
31	-	DCE	$BF_3{\cdot}O(C_2H_5)_2$	TsCl	80	trace
32	-	DCE	$BF_3{\cdot}O(C_2H_5)_2$	TsCl	60	trace

Reaction conditions: amide oxazoline **1a** (0.1 mmol), **2** (0.13 mmol), base (0.02 mmol), Lewis acid (0.02 mmol), solvent (1.0 mL), 120 °C for 10 h.[a] Isolated yield.

2.6 The X-ray data of 3a (CCDC 1966335).

An amount of 20 mg **3a** were dissolved in dichloromethane/petroleum ether/ethyl acetate (1:1:1) on the brown small reagent bottle (5 mL), which acted as good solvent, and a layer of ether was injected on the surface of acetonitrile, and the cap is covered with a thin film, white crystals will be presented after ten days.

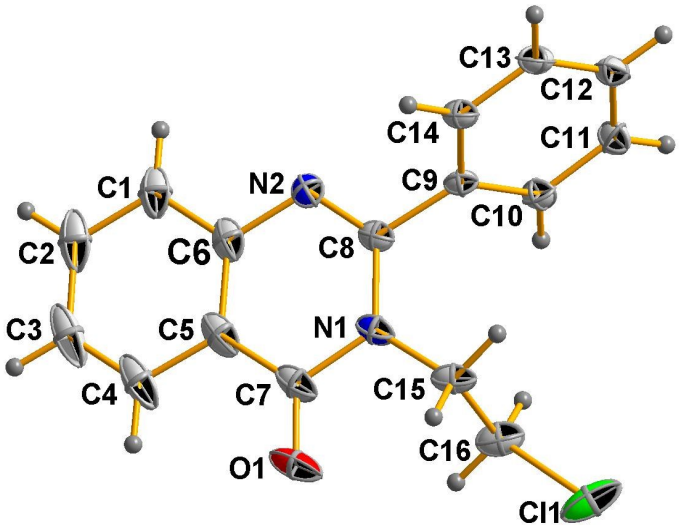


Figure S1. X-ray crystal structure of compound **3a**, thermal ellipsoids are drawn at 30% probability level.

Table 1 Crystal data and structure refinement for 3a.

Identification code	**3a**
Empirical formula	$C_{16}H_{13}N_2OCl$
Formula weight	284.73
Temperature/K	296(2)
Crystal system	orthorhombic
Space group	Pccn
a/Å	8.9470(18)
b/Å	16.934(3)
c/Å	18.608(4)
α/°	90
β/°	90

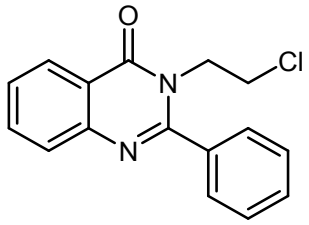
γ/°	90
Volume/Å^3	2819.4(10)
Z	8
ρ_{calc}g/cm^3	1.342
μ/mm^{-1}	0.267
F(000)	1184.0
Crystal size/mm^3	0.300 × 0.200 × 0.200
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.378 to 50.676
Index ranges	-10 ≤ h ≤ 10, -20 ≤ k ≤ 19, -22 ≤ l ≤ 10
Reflections collected	13695
Independent reflections	2588 [R_{int} = 0.0387, R_{sigma} = 0.0298]
Data/restraints/parameters	2588/0/181
Goodness-of-fit on F^2	1.003
Final R indexes [I>=2σ (I)]	R_1 = 0.0614, wR_2 = 0.1758
Final R indexes [all data]	R_1 = 0.0881, wR_2 = 0.2017
Largest diff. peak/hole / e Å^{-3}	0.56/-0.68

[1] M. Shang, S. Z. Sun, H. X. Dai, J. Q. Yu, *J Am Chem Soc,* **2014**, *136*, 3354-3357.

[2] G. S. Chen, S. Kalchar, C. W. Kuo, C. S. Chang, C. O. Usifoh, J. W. Chern, *J Org Chem,* 2003, **68**, 2502-2505.

3. Characterization data of products.

3-(2-chloroethyl)-2-phenylquinazolin-4(3*H*)-one (3a)

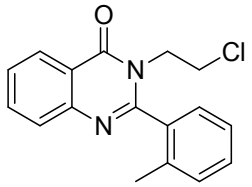


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 84% yield;

M.p. =127℃;

^{1}H NMR (400 MHz,) δ 8.33 (d, *J* = 8.1 Hz, 1H), 8.02 – 7.66 (m, 2H), 7.66 – 7.37 (m, 6H), 4.37 (t, *J* = 6.5 Hz, 2H), 3.74 (t, *J* = 6.6 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.26, 156.04, 147.18, 135.11, 134.83, 130.18, 129.05, 128.28, 127.74, 127.38, 126.82, 120.71, 47.20, 40.43.
HRMS (ESI) calcd for $C_{16}H_{13}ClN_2OH^+$: $[M+H]^+$ 285.0789, found:. 285.0792.

3-(2-chloroethyl)-2-(o-tolyl)quinazolin-4(3*H*)-one (3b)



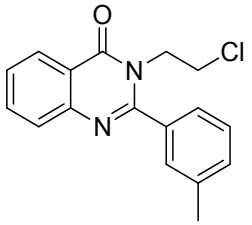
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 66% yield;

^{1}H NMR (400 MHz,) δ 8.34 (d, *J* = 7.8 Hz, 1H), 7.86 – 7.70 (m, 2H), 7.54 (m, *J* = 6.9, 6.0, 1.1 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.35 (dd, *J* = 11.0, 7.6 Hz, 2H), 4.49 (m, *J* = 12.6, 7.8, 4.7 Hz, 1H), 3.94 (m, *J* = 9.6, 7.1, 3.7 Hz, 1H), 3.71 (m, *J* = 8.5, 6.6, 2.4 Hz, 2H), 2.25 (s, 3H).

^{13}C NMR (101 MHz,) δ 162.14, 155.61, 147.26, 135.63, 134.82, 134.34, 130.87, 130.21, 128.47, 127.73, 127.41, 126.83, 126.48, 120.79, 46.71, 40.05, 19.37.

HRMS (ESI) calcd for $C_{17}H_{15}ClN_2OH^+$: $[M+H]^+$ 299.0946, found:.299.0947.

3-(2-chloroethyl)-2-(m-tolyl)quinazolin-4(3*H*)-one (3c)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 85% yield;

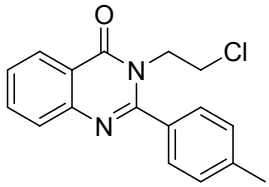
M.p. = 127℃;

^{1}H NMR (400 MHz,) δ 8.32 (d, *J* = 8.1 Hz, 1H), 7.93 – 7.70 (m, 2H), 7.58 – 7.48 (m, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.34 (dd, *J* = 14.9, 6.2 Hz, 3H), 4.37 (t, *J* = 6.6 Hz, 2H), 3.74 (t, *J* = 6.6 Hz, 2H), 2.44 (s, 3H).

^{13}C NMR (101 MHz,) δ 162.28, 156.24, 147.20, 139.07, 134.99, 134.80, 130.93, 128.89, 128.84, 127.72, 127.31, 126.81, 125.17, 120.69, 47.21, 40.43, 21.57.

HRMS (ESI) calcd for $C_{17}H_{15}ClN_2OH^+$: $[M+H]^+$ 299.0946, found:299.0947.

3-(2-chloroethyl)-2-(p-tolyl)quinazolin-4(3*H*)-one (3d)



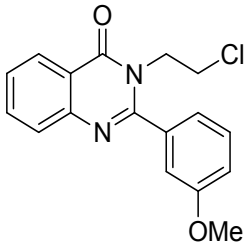
Following the general procedure the title compound was isolated by flash

chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 78% yield;

M.p. = 101℃;

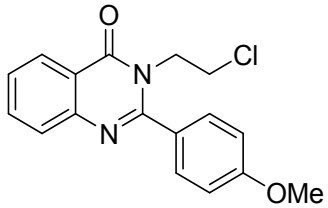
^{1}H NMR (400 MHz,) δ 8.32 (d, *J* = 7.7 Hz, 1H), 7.87 – 7.69 (m, 2H), 7.59 – 7.46 (m, 1H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.38 (t, *J* = 6.6 Hz, 2H), 3.73 (t, *J* = 6.6 Hz, 2H), 2.44 (s, 3H).
^{13}C NMR (101 MHz,) δ 162.36, 156.21, 147.25, 140.37, 134.76, 132.26, 129.66, 128.18, 127.71, 127.25, 126.80, 120.66, 47.17, 40.45, 21.55.
HRMS (ESI) calcd for $C_{17}H_{15}ClN_2OH^+$: $[M+H]^+$ 299.0946, found:299.0948.

3-(2-chloroethyl)-2-(3-methoxyphenyl)quinazolin-4(3*H*)-one (3e)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 68% yield;
^{1}H NMR (400 MHz,) δ 8.32 (d, *J* = 7.8 Hz, 1H), 7.86 – 7.71 (m, 2H), 7.60 – 7.50 (m, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.07 (dd, *J* = 13.7, 4.4 Hz, 3H), 4.37 (t, *J* = 6.6 Hz, 2H), 3.87 (s, 3H), 3.76 (t, *J* = 6.6 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.23, 159.94, 155.81, 147.14, 136.17, 134.83, 130.25, 127.74, 127.40, 126.82, 120.75, 120.32, 116.03, 113.84, 55.57, 47.25, 40.43.
HRMS (ESI) calcd for $C_{17}H_{15}ClN_2O_2H^+$: $[M+H]^+$ 315.0895, found:315.0895.

3-(2-chloroethyl)-2-(4-methoxyphenyl)quinazolin-4(3*H*)-one (3f)

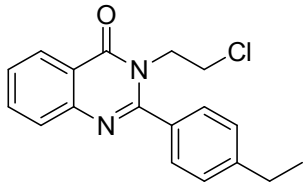


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 65% yield;

M.p. =106℃;

^{1}H NMR (400 MHz,) δ 8.31 (d, *J* = 8.1 Hz, 1H), 7.87 – 7.71 (m, 2H), 7.59 – 7.43 (m, 3H), 7.04 (d, *J* = 8.6 Hz, 2H), 4.41 (t, *J* = 6.6 Hz, 2H), 3.89 (s, 3H), 3.74 (t, *J* = 6.5 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.46, 160.92, 155.98, 147.26, 134.76, 129.89, 127.67, 127.47, 127.19, 126.80, 120.61, 114.40, 55.56, 47.22, 40.53.
HRMS (ESI) calcd for $C_{17}H_{15}ClN_2O_2H^+$: $[M+H]^+$ 315.0895, found: 315.0899.

3-(2-chloroethyl)-2-(4-ethylphenyl)quinazolin-4(3*H*)-one (3g)

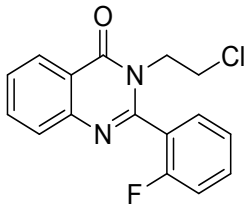


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 83% yield;

M.p. = 107℃;

^{1}H NMR (400 MHz,) δ 8.32 (d, *J* = 8.1 Hz, 1H), 7.77 (q, *J* = 8.3 Hz, 2H), 7.55 – 7.48 (m, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 4.39 (t, *J* = 6.6 Hz, 2H), 3.74 (t, *J* = 6.6 Hz, 2H), 2.74 (q, *J* = 7.6 Hz, 2H), 1.29 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR (101 MHz,) δ 162.37, 156.25, 147.26, 146.61, 134.77, 132.46, 128.54, 128.25, 127.72, 127.24, 126.80, 120.66, 47.19, 40.46, 28.89, 15.50.
HRMS (ESI) calcd for $C_{18}H_{17}ClN_2OH^+$: $[M+H]^+$ 313.1102, found:313.1103.

3-(2-chloroethyl)-2-(2-fluorophenyl)quinazolin-4(3*H*)-one (3h)

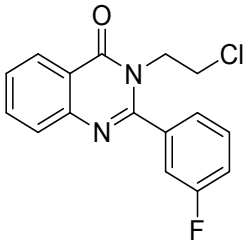


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 74% yield;

M.p. = 98℃;

^{1}H NMR (400 MHz,) δ 8.42 – 8.27 (m, 1H), 7.87 – 7.67 (m, 2H), 7.67 – 7.48 (m, 3H), 7.35 (m, *J* = 7.7, 1.0 Hz, 1H), 7.22 (t, *J* = 9.0 Hz, 1H), 4.71 – 4.47 (m, 1H), 4.14 – 3.97 (m, 1H), 3.87 (dd, *J* = 16.1, 9.1 Hz, 1H), 3.66 (dd, *J* = 10.4, 4.8 Hz, 1H).
^{13}C NMR (101 MHz,) δ 161.87, 159.07 (d, *J* = 248.6 Hz), 151.51, 147.22, 134.83, 132.47 (d, *J* = 8.2 Hz), 131.13 (d, *J* = 1.8 Hz), 127.74 (d, *J* = 9.1 Hz), 126.88, 125.18 (d, *J* = 3.1 Hz), 123.28, 123.13, 120.93, 116.12 (d, *J* = 20.6 Hz), 47.37, 40.50.
. HRMS (ESI) calcd for $C_{16}H_{12}ClFN_2OH^+$: $[M+H]^+$ 303.0695, found:303.0695.

3-(2-chloroethyl)-2-(3-fluorophenyl)quinazolin-4(3*H*)-one (3i)



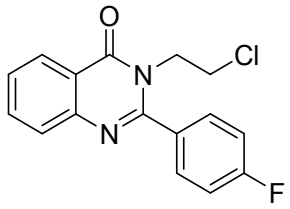
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 86% yield;

^{1}H NMR (400 MHz,) δ 8.37 – 8.29 (m, 1H), 7.84 – 7.77 (m, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.59 – 7.47 (m, 2H), 7.37 – 7.28 (m, 2H), 7.28 – 7.19 (m, 1H), 4.37 (t, *J* = 6.3 Hz, 2H), 3.77 (t, *J* = 6.4 Hz, 2H).

^{13}C NMR (101 MHz,) δ 163.94 – 161.46 (d, *J* = 250.5 Hz), 162.09, 154.65, 147.00, 136.93 (d, *J* = 7.7 Hz), 134.95, 130.88 (d, *J* = 8.2 Hz), 127.70 (d, *J* = 12.0 Hz), 126.86, 124.15, 120.76, 117.35 (d, *J* = 20.9 Hz), 116.15, 115.92, 47.31, 40.51.

HRMS (ESI) calcd for $C_{16}H_{12}ClFN_2OH^+$: $[M+H]^+$ 303.0695, found:303.0695.

3-(2-chloroethyl)-2-(4-fluorophenyl)quinazolin-4(3*H*)-one (3j)



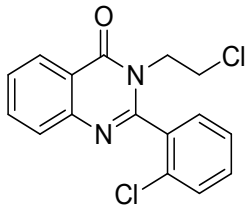
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 79% yield;

^{1}H NMR (400 MHz,) δ 8.32 (dd, *J* = 11.1, 3.1 Hz, 1H), 8.11 – 7.67 (m, 2H), 7.55 (m, *J* = 11.0, 7.8, 3.3 Hz, 3H), 7.25 (m, *J* = 15.0, 7.2 Hz, 2H), 4.38 (t, *J* = 6.0 Hz, 2H), 3.77 (q, *J* = 6.0 Hz, 2H).

^{13}C NMR (101 MHz,) δ 163.57 (d, *J* = 251.2 Hz), 162.22, 155.15, 147.06, 134.92, 131.29 (d, *J* = 3.5 Hz), 130.62 (d, *J* = 8.5 Hz), 127.61 (d, *J* = 18.7 Hz), 126.85, 120.69, 116.35, 116.13, 47.29, 40.57.

HRMS (ESI) calcd for $C_{16}H_{12}ClFN_2OH^+$: $[M+H]^+$ 303.0695, found:303.0695.

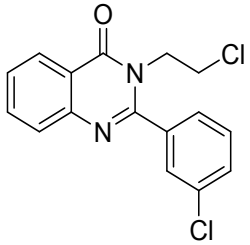
3-(2-chloroethyl)-2-(2-chlorophenyl)quinazolin-4(3*H*)-one (3k)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 75%

yield;
^{1}H NMR (400 MHz,) δ 8.35 (d, *J* = 7.8 Hz, 1H), 7.91 – 7.71 (m, 2H), 7.64 – 7.55 (m, 2H), 7.55 – 7.42 (m, 3H), 4.70 – 4.53 (m, 1H), 3.96 – 3.79 (m, 2H), 3.74 – 3.60 (m, 1H).
^{13}C NMR (101 MHz,) δ 161.87, 153.41, 147.21, 134.85, 134.04, 132.42, 131.54 131.06, 129.85, 127.82, 127.71, 127.62, 126.88, 121.02, 47.09, 40.43.
HRMS (ESI) calcd for $C_{16}H_{12}Cl_2N_2OH^+$: $[M+H]^+$ 319.0399, found: 319.0399.

3-(2-chloroethyl)-2-(3-chlorophenyl)quinazolin-4(3*H*)-one (3l)

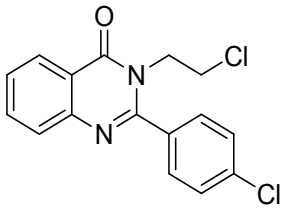


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 78% yield;

M.p. = 107℃;

^{1}H NMR (400 MHz,) δ 8.32 (d, *J* = 7.9 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.52 (m, *J* = 7.5, 6.4, 3.8 Hz, 2H), 7.49 – 7.38 (m, 2H), 4.36 (t, *J* = 6.3 Hz, 2H), 3.77 (t, *J* = 6.3 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.06, 154.61, 146.98, 136.67, 135.13, 134.97, 130.39, 130.33, 128.76, 127.74, 127.66, 126.86, 126.56, 120.74, 47.34, 40.57.
HRMS (ESI) calcd for $C_{16}H_{12}Cl_2N_2OH^+$: $[M+H]^+$ 319.0399, found:319.0402.

3-(2-chloroethyl)-2-(4-chlorophenyl)quinazolin-4(3*H*)-one (3m)

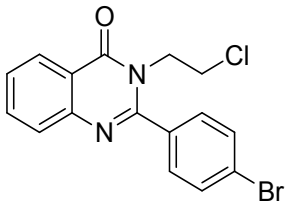


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 79% yield;

M.p. = 127℃;

^{1}H NMR (400 MHz,) δ 8.32 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.77 (m, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.60 – 7.45 (m, 5H), 4.37 (t, *J* = 6.3 Hz, 2H), 3.77 (t, *J* = 6.3 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.17, 155.03, 147.06, 136.42, 134.94, 133.54, 129.92, 129.32, 127.73, 127.59, 126.86, 120.70, 47.30, 40.60.
HRMS (ESI) calcd for $C_{16}H_{12}Cl_2N_2OH^+$: $[M+H]^+$ 319.0399, found:319.0400.

2-(4-bromophenyl)-3-(2-chloroethyl)quinazolin-4(3*H*)-one (3n)

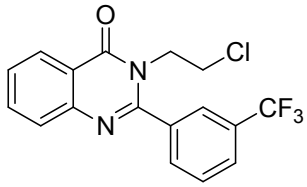


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 77% yield;

M.p. = 106℃;

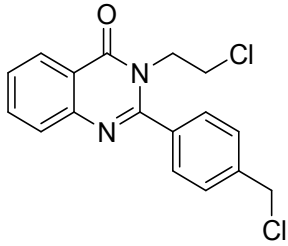
^{1}H NMR (400 MHz,) δ 8.39 – 8.25 (m, 1H), 7.84 – 7.76 (m, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.54 (m, *J* = 7.7, 1.0 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 4.36 (t, *J* = 6.3 Hz, 2H), 3.77 (t, *J* = 6.3 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.14, 155.07, 147.04, 134.95, 133.99, 132.27, 130.12, 127.72, 127.59, 126.86, 124.66, 120.69, 47.30, 40.61.
HRMS (ESI) calcd for $C_{16}H_{12}BrClN_2OH^+$: $[M+H]^+$ 362.9894, found:362.9897.

3-(2-chloroethyl)-2-(3-(trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (3o)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 69% yield;
^{1}H NMR (400 MHz,) δ 8.43 – 8.31 (m, 1H), 7.85 (s, 1H), 7.82 (dd, *J* = 10.9, 4.1 Hz, 2H), 7.76 (t, *J* = 7.2 Hz, 2H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.56 (dd, *J* = 11.0, 4.1 Hz, 1H), 4.35 (t, *J* = 6.1 Hz, 2H), 3.80 (t, *J* = 6.1 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.05, 154.59, 146.96, 135.90, 135.04, 131.06-132.04 (q, *J* = 32.3 Hz), 131.90, 129.64, 127.77, 126.96, 126.92, 126.89, 125.68 (d, J = 3.7 Hz), 127.70-119.56 (d, J = 273.7 Hz), 120.78, 47.44, 40.66.
HRMS (ESI) calcd for $C_{17}H_{12}ClF_3N_2OH^+$: $[M+H]^+$ 353.0663, found:353.0664.

3-(2-chloroethyl)-2-(4-(chloromethyl)phenyl)quinazolin-4(3*H*)-one (3p)



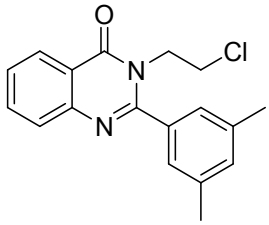
Following the general procedure the title compound was isolated by flash

chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 66% yield;

M.p. = 154℃;

^{1}H NMR (400 MHz,) δ 8.33 (d, *J* = 7.9 Hz, 1H), 7.79 (m, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.63 – 7.47 (m, 5H), 4.66 (s, 2H), 4.37 (t, *J* = 6.4 Hz, 2H), 3.76 (t, *J* = 6.4 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.21, 155.52, 147.14, 139.52, 135.13, 134.89, 129.18, 128.84, 127.74, 127.49, 126.84, 120.72, 47.27, 45.48, 40.55.
HRMS (ESI) calcd for $C_{17}H_{14}Cl_2N_2OH^+$: $[M+H]^+$ 333.0556, found: 333.0556.

3-(2-chloroethyl)-2-(3,5-dimethylphenyl)quinazolin-4(3*H*)-one (3q)

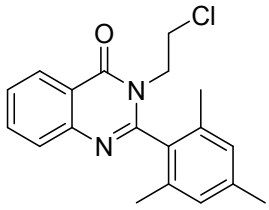


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 70% yield;

M.p. = 115℃;

^{1}H NMR (400 MHz,) δ 8.66 – 8.10 (m, 1H), 7.86 – 7.70 (m, 2H), 7.52 (m, *J* = 8.1, 6.5, 1.8 Hz, 1H), 7.14 (d, *J* = 7.7 Hz, 3H), 4.36 (t, *J* = 6.7 Hz, 2H), 3.74 (t, *J* = 6.7 Hz, 2H), 2.40 (s, 6H).
^{13}C NMR (101 MHz,) δ 162.29, 156.42, 147.22, 138.85, 134.89, 134.77, 131.78, 127.70, 127.24, 126.79, 125.78, 120.67, 47.22, 40.43, 21.45.
HRMS (ESI) calcd for $C_{18}H_{17}ClN_2OH^+$: $[M+H]^+$ 313.1102, found:313.1103.

3-(2-chloroethyl)-2-mesitylquinazolin-4(3*H*)-one (3r)



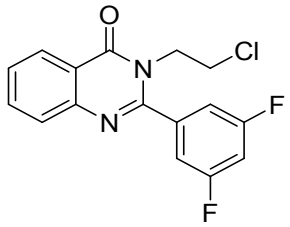
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 53% yield;

M.p. = 123℃;

^{1}H NMR (400 MHz,) δ 8.34 (d, *J* = 8.0 Hz, 1H), 7.88 – 7.67 (m, 2H), 7.65 – 7.48 (m, 1H), 6.98 (s, 2H), 4.16 (t, *J* = 7.1 Hz, 2H), 3.63 (t, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 2.17 (s, 6H).

^{13}C NMR (101 MHz,) δ 162.39, 155.21, 147.37, 139.85, 135.47, 134.75, 131.03, 129.12, 127.70, 127.34, 126.82, 120.72, 46.60, 39.58, 21.31, 19.68.
HRMS (ESI) calcd for $C_{19}H_{19}ClN_2OH^+$: $[M+H]^+$ 327.1259, found:327.1260.

3-(2-chloroethyl)-2-(3,5-difluorophenyl)quinazolin-4(3*H*)-one (3s)

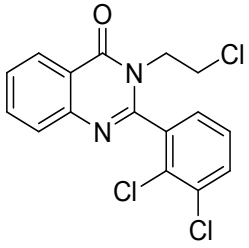


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 73% yield;

M.p. = 113℃;

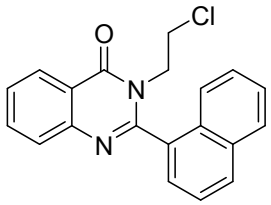
^{1}H NMR (400 MHz,) δ 8.33 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.89 – 7.78 (m, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.63 – 7.46 (m, 1H), 7.21 – 7.06 (m, 2H), 7.00 (m, *J* = 8.7, 2.2 Hz, 1H), 4.37 (t, *J* = 6.1 Hz, 2H), 3.80 (t, *J* = 6.1 Hz, 2H).
^{13}C NMR (101 MHz,) δ 164.41, 161.77 - 164.28 (d, *J* = 253.5 Hz), 161.93, 153.56, 146.82, 137.76 (t, *J* = 9.6 Hz), 135.08, 127.85 (d, *J* = 11.3 Hz), 126.91, 120.80, 112.31 (d, *J* = 8.1 Hz), 112.12 (d, *J* = 8.1 Hz), 47.41, 40.59.
HRMS (ESI) calcd for $C_{16}H_{11}ClF_2N_2OH^+$: $[M+H]^+$ 321.0601, found: 321.0602.

3-(2-chloroethyl)-2-(2,3-dichlorophenyl)quinazolin-4(3*H*)-one (3t)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 69% yield;
^{1}H NMR (400 MHz,) δ 8.36 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.87 – 7.78 (m, 1H), 7.75 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.65 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.57 (m, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.53 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 4.63 (m, *J* = 13.8, 5.7, 3.8 Hz, 1H), 3.93 (m, *J* = 10.9, 8.7, 5.7 Hz, 1H), 3.87 – 3.75 (m, 1H), 3.68 (m, *J* = 10.8, 6.1, 3.8 Hz, 1H).
^{13}C NMR (101 MHz,) δ 161.77, 152.79, 147.12, 135.96, 134.95, 133.84, 132.14, 131.10, 129.41, 128.31 , 127.90, 127.84, 126.91, 121.07, 47.25, 40.52.
HRMS (ESI) calcd for $C_{16}H_{11}Cl_3N_2OH^+$: $[M+H]^+$ 353.0010, found:353.0011.

3-(2-chloroethyl)-2-(naphthalen-1-yl)quinazolin-4(3*H*)-one (3u)



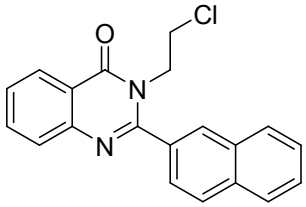
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 80% yield;

^{1}H NMR (400 MHz,) δ 8.40 (dd, *J* = 8.1, 1.1 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.96 (dd, *J* = 7.7, 2.2 Hz, 1H), 7.85 – 7.76 (m, 2H), 7.70 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.62 (dd, *J* = 8.1, 7.2 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.54 (s, 1H), 7.53 – 7.49 (m, 1H), 4.43 (m, *J* = 13.6, 7.1, 4.9 Hz, 1H), 3.89 – 3.79 (m, 1H), 3.72 (m, *J* = 10.9, 7.1 Hz, 1H), 3.57 (m, *J* = 11.0, 7.3, 4.8 Hz, 1H).

^{13}C NMR (101 MHz,) δ 162.16, 155.05, 147.37, 134.91, 133.56, 131.93, 130.60, 128.92, 127.88, 127.81, 127.61, 127.27, 126.92, 126.88, 125.39, 124.17, 120.96, 47.21, 40.27.

HRMS (ESI) calcd for $C_{20}H_{15}ClN_2OH^+$: $[M+H]^+$ 335.0946, found: 335.0946.

3-(2-chloroethyl)-2-(naphthalen-2-yl)quinazolin-4(3*H*)-one (3v)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 61% yield;

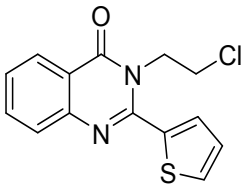
M.p. = 110℃;

^{1}H NMR (400 MHz,) δ 8.39 – 8.33 (m, 1H), 8.07 (d, *J* = 1.1 Hz, 1H), 8.01 (t, *J* = 9.3 Hz, 1H), 7.98 – 7.90 (m, 2H), 7.90 – 7.75 (m, 2H), 7.62 – 7.60 (m, 1H), 7.59 (dd, *J* = 3.4, 2.0 Hz, 1H), 7.57 – 7.51 (m, 1H), 4.43 (t, *J* = 6.5 Hz, 2H), 3.76 (t, *J* = 6.4 Hz, 2H).

^{13}C NMR (101 MHz,) δ 162.34, 156.12, 147.27, 134.87, 133.70, 132.91, 132.36, 128.99, 128.62, 128.55, 127.93, 127.77 (s), 127.66, 127.42, 127.23, 126.88, 124.95, 120.76, 47.34, 40.56.

HRMS (ESI) calcd for $C_{20}H_{15}ClN_2OH^+$: $[M+H]^+$ 335.0946, found:335.0946.

3-(2-chloroethyl)-2-(thiophen-2-yl)quinazolin-4(3*H*)-one (3w)

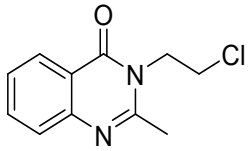


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 63% yield;

M.p. = 134℃;

^{1}H NMR (400 MHz,) δ 8.29 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.82 – 7.71 (m, 2H), 7.57 (dd, *J* = 5.0, 0.7 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.18 (dd, *J* = 5.0, 3.8 Hz, 1H), 4.58 (t, *J* = 7.0 Hz, 2H), 3.86 (t, *J* = 7.0 Hz, 2H).
^{13}C NMR (101 MHz,) δ 162.33, 149.81, 147.08, 136.25, 134.87, 129.54, 129.38, 127.76, 127.60, 127.55, 126.86, 120.40, 47.20, 40.30.
HRMS (ESI) calcd for $C_{14}H_{11}ClN_2OSH^+$: $[M+H]^+$ 291.0353, found:291.0356.

3-(2-chloroethyl)-2-methylquinazolin-4(3*H*)-one (3x)

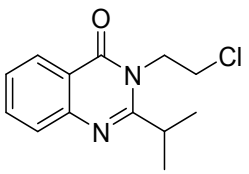


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 43% yield;

M.p. = 126℃;

^{1}H NMR (400 MHz,) δ 8.24 (d, *J* = 8.3 Hz, 1H), 7.75 (dd, *J* = 8.0, 7.3 Hz, 1H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 4.44 (t, *J* = 6.2 Hz, 2H), 3.92 (t, *J* = 6.3 Hz, 2H), 2.73 (s, 3H).
^{13}C NMR (101 MHz,) δ 162.11, 154.12, 147.32, 134.67, 126.91, 126.76, 126.74, 120.41, 46.39, 40.89, 23.90.
HRMS (ESI) calcd for $C_{11}H_{11}ClN_2OH^+$: $[M+H]^+$ 223.0633, found:223.0636.

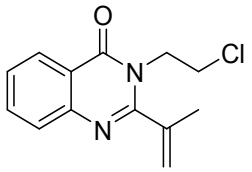
3-(2-chloroethyl)-2-isopropylquinazolin-4(3*H*)-one （3y）



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 53% yield;

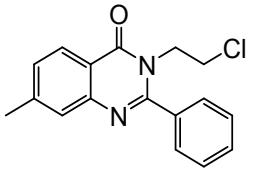
^{1}H NMR (400 MHz,) δ 8.24 (dd, *J* = 8.5, 0.9 Hz, 1H), 7.78 – 7.68 (m, 1H), 7.69 – 7.63 (m, 1H), 7.44 (dd, *J* = 11.0, 4.2 Hz, 1H), 4.49 (t, *J* = 6.5 Hz, 2H), 3.86 (t, *J* = 6.5 Hz, 2H), 3.33 (m, *J* = 13.3, 6.7 Hz, 1H), 1.38 (d, *J* = 6.6 Hz, 6H).
^{13}C NMR (101 MHz,) δ 162.52, 160.98, 147.44, 134.42, 127.35, 126.64, 126.53, 120.29, 44.56, 41.17, 32.04, 21.25.
HRMS (ESI) calcd for $C_{13}H_{15}ClN_2OH^+$: $[M+H]^+$ 251.0946, found:251.0948.

3-(2-chloroethyl)-2-(prop-1-en-2-yl)quinazolin-4(3*H*)-one (3z)



Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 51% yield;
^{1}H NMR (400 MHz,) δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.76 (m, *J* = 8.1, 4.1 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 7.9, 7.1 Hz, 1H), 5.56 (s, 1H), 5.35 (d, *J* = 0.5 Hz, 1H), 4.44 (t, *J* = 6.8 Hz, 2H), 3.84 (t, *J* = 6.7 Hz, 2H), 2.22 (d, *J* = 0.6 Hz, 3H).
^{13}C NMR (101 MHz,) δ 162.14, 156.93, 147.27, 139.68, 134.73, 127.52, 127.19, 126.73, 120.70, 120.03, 47.01, 40.32, 22.62.
HRMS (ESI) calcd for $C_{13}H_{13}ClN_2OH^+$: $[M+H]^+$ 249.0789, found:249.0791.

3-(2-chloroethyl)-7-methyl-2-phenylquinazolin-4(3*H*)-one (3ba)

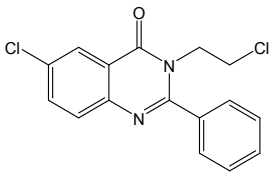


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 60% yield;

M.p. = 145℃;

^{1}H NMR (400 MHz,) δ 8.20 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.47 (m, 6H), 7.34 (dd, *J* = 8.1, 1.4 Hz, 1H), 4.35 (t, *J* = 6.6 Hz, 2H), 3.73 (t, *J* = 6.6 Hz, 2H), 2.50 (s, 3H).
^{13}C NMR (101 MHz,) δ 162.18, 156.09, 147.30, 145.88, 135.25, 130.09, 129.00, 128.94, 128.28, 127.47, 126.64, 118.32, 47.11, 40.50, 22.05.
HRMS (ESI) calcd for $C_{17}H_{15}ClN_2OH^+$: $[M+H]^+$ 299.0946, found: 299.0943.

6-chloro-3-(2-chloroethyl)-2-phenylquinazolin-4(3*H*)-one (3bb)

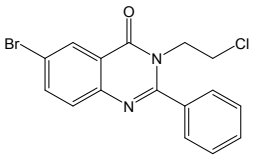


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 70% yield;

M.p. = 149℃;

^{1}H NMR (400 MHz,) δ 8.38 – 8.18 (m, 1H), 7.80 – 7.64 (m, 2H), 7.62 – 7.44 (m, 6H), 4.37 (t, *J* = 6.4 Hz, 2H), 3.73 (t, *J* = 6.5 Hz, 2H).
^{13}C NMR (101 MHz,) δ 161.31, 156.31 ,145.70, 135.24, 134.84, 133.16, 130.34 , 129.43, 129.09 , 128.28 , 126.19 , 121.73 , 47.33 , 40.33 .
HRMS (ESI) calcd for $C_{16}H_{12}Cl_2N_2OH^+$: $[M+H]^+$ 319.0400, found: 319.0401.

6-bromo-3-(2-chloroethyl)-2-phenylquinazolin-4(3*H*)-one (3bc)

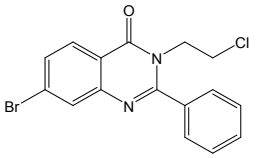


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 75% yield;

M.p. = 171℃;

^{1}H NMR (400 MHz,) δ 8.44 (d, *J* = 2.3 Hz, 1H), 7.85 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.46 (m, 5H), 4.37 (t, *J* = 6.4 Hz, 2H), 3.73 (t, *J* = 6.4 Hz, 2H).
^{13}C NMR (101 MHz,) δ 161.14, 156.47, 146.02, 137.98, 134.85, 130.35, 129.57, 129.37, 129.08 , 128.26, 122.05, 120.89, 47.35, 40.34.
HRMS (ESI) calcd for $C_{16}H_{12}BrClN_2OH^+$: $[M+H]^+$ 362.9895, found: 362.9892.

7-bromo-3-(2-chloroethyl)-2-phenylquinazolin-4(3*H*)-one (3bd)

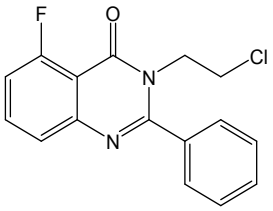


Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as white solid in 68% yield;

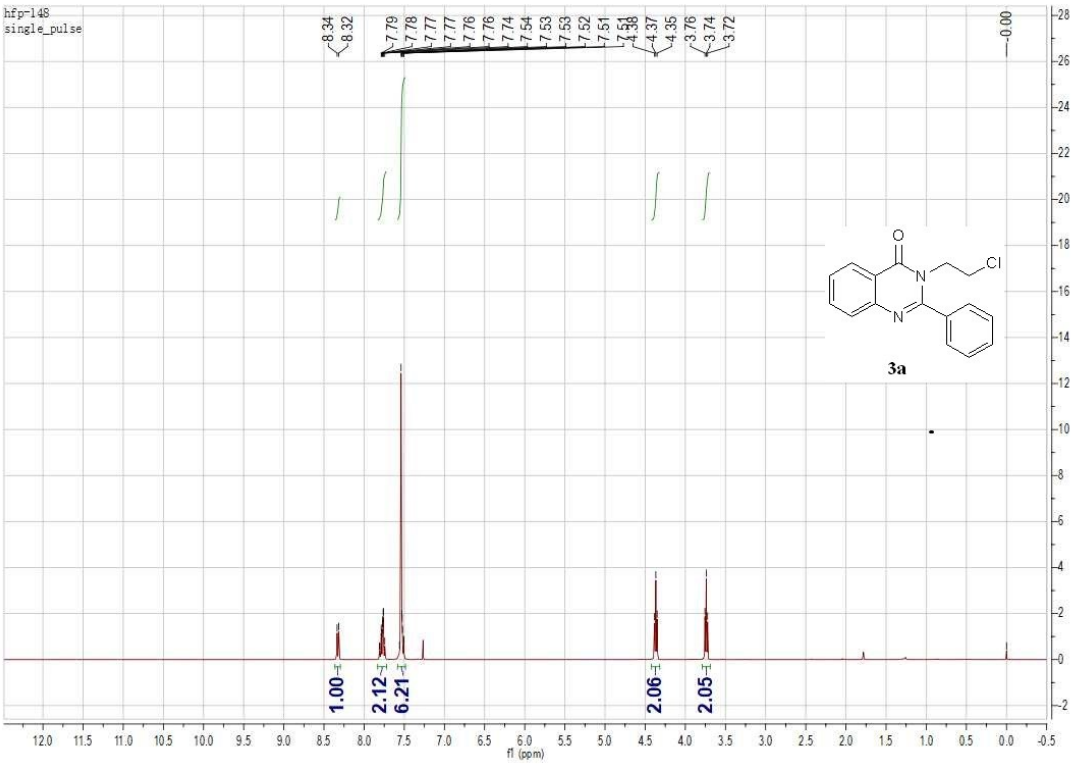
M.p. = 165℃;

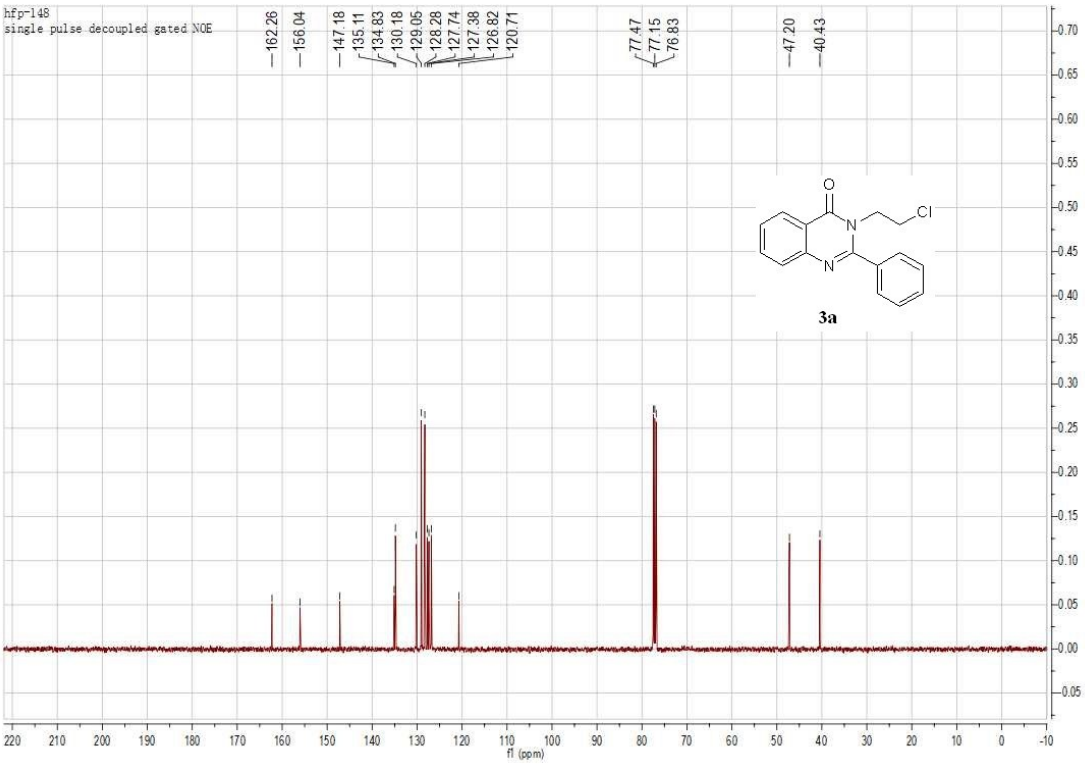
^{1}H NMR (400 MHz,) δ 8.16 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 1.8 Hz, 1H), 7.61 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.58 – 7.47 (m, 5H), 4.36 (t, *J* = 6.5 Hz, 2H), 3.72 (t, *J* = 6.5 Hz, 2H).
^{13}C NMR (101 MHz,) δ 161.81, 157.31, 148.14, 134.82, 130.73, 130.50, 130.38, 129.54, 129.08, 128.30, 128.25, 119.51, 47.28 , 40.35 .
HRMS (ESI) calcd for $C_{16}H_{12}BrClN_2OH^+$: $[M+H]^+$ 362.9895, found: 362.9896.

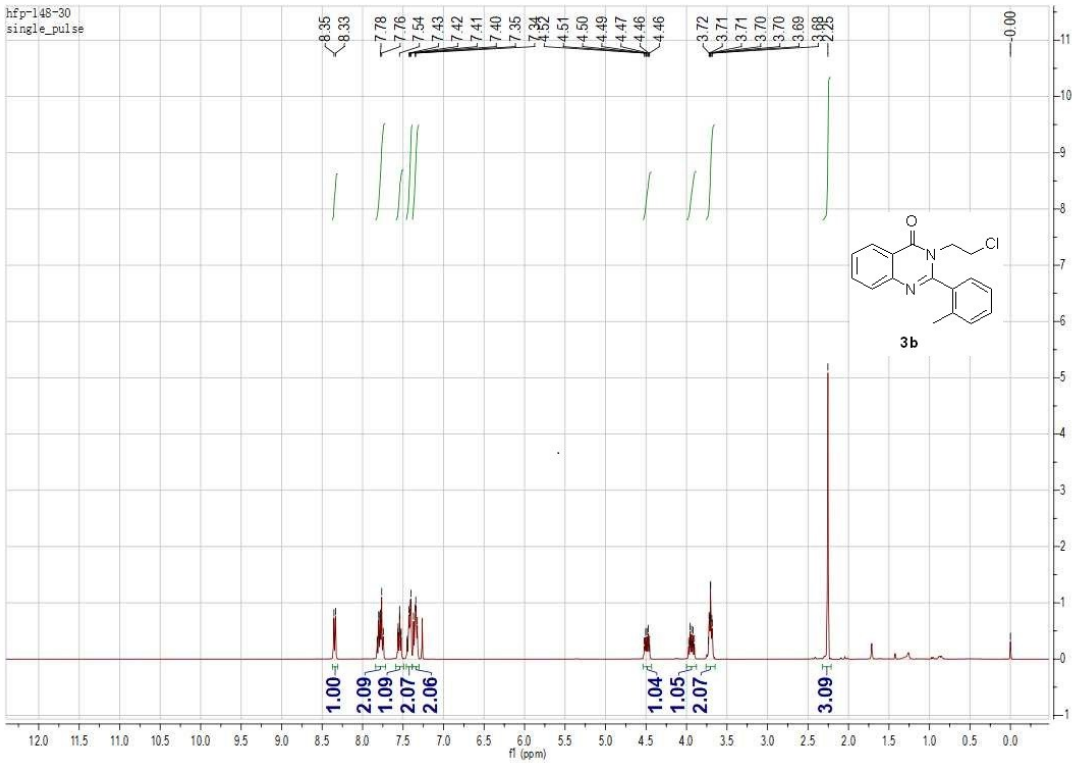
3-(2-chloroethyl)-5-fluoro-2-phenylquinazolin-4(3*H*)-one (3be)

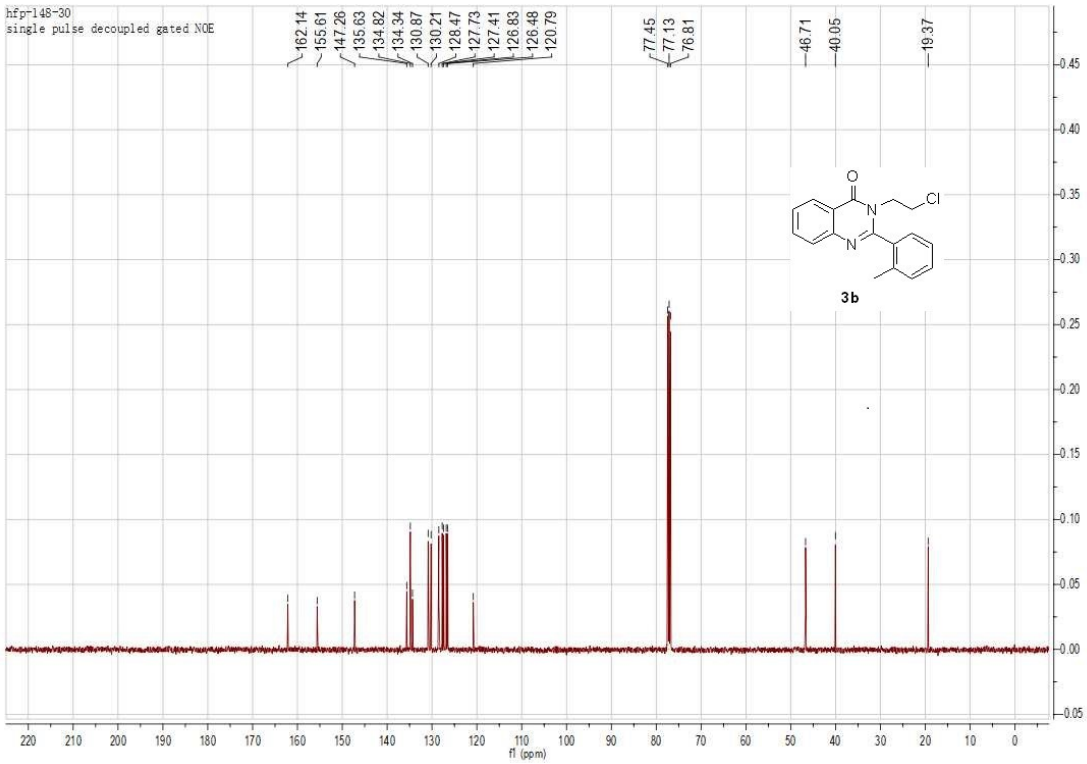


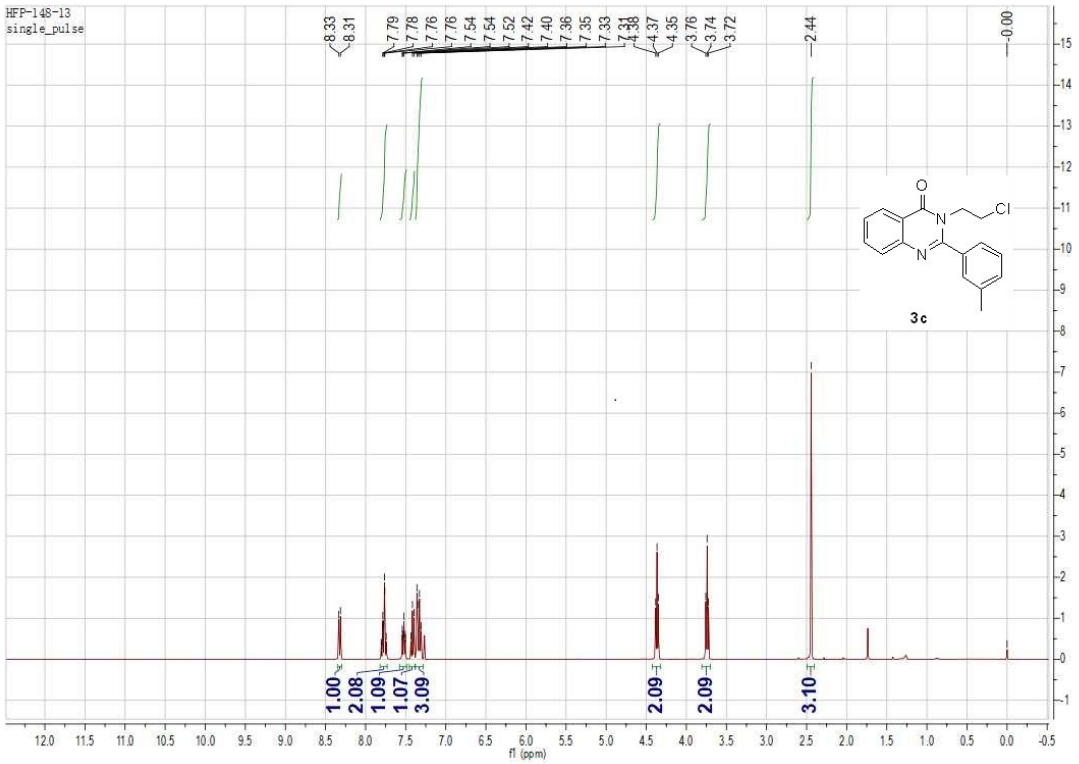
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/ Petroleum ether =1/4) as liquid in 43% yield;
^{1}H NMR (400 MHz,) δ 7.71 (m, *J* = 8.1, 5.4 Hz, 1H), 7.58 – 7.48 (m, 6H), 7.21 – 7.12 (m, 1H), 4.35 (t, *J* = 6.4 Hz, 2H), 3.76 (t, *J* = 6.4 Hz, 2H).
^{13}C NMR (101 MHz,) δ 161.29 (d, *J* = 266.5 Hz), 159.38, 157.11, 149.14, 135.15 (d, *J* = 10.4 Hz), 134.81, 130.35, 129.08, 128.24, 123.70 (d, *J* = 4.1 Hz), 113.87 (d, *J* = 20.9 Hz), 110.51, 47.18, 40.36.
HRMS (ESI) calcd for $C_{16}H_{12}ClFN_2OH^+$: $[M+H]^+$ 303.0695, found: 303.0694.

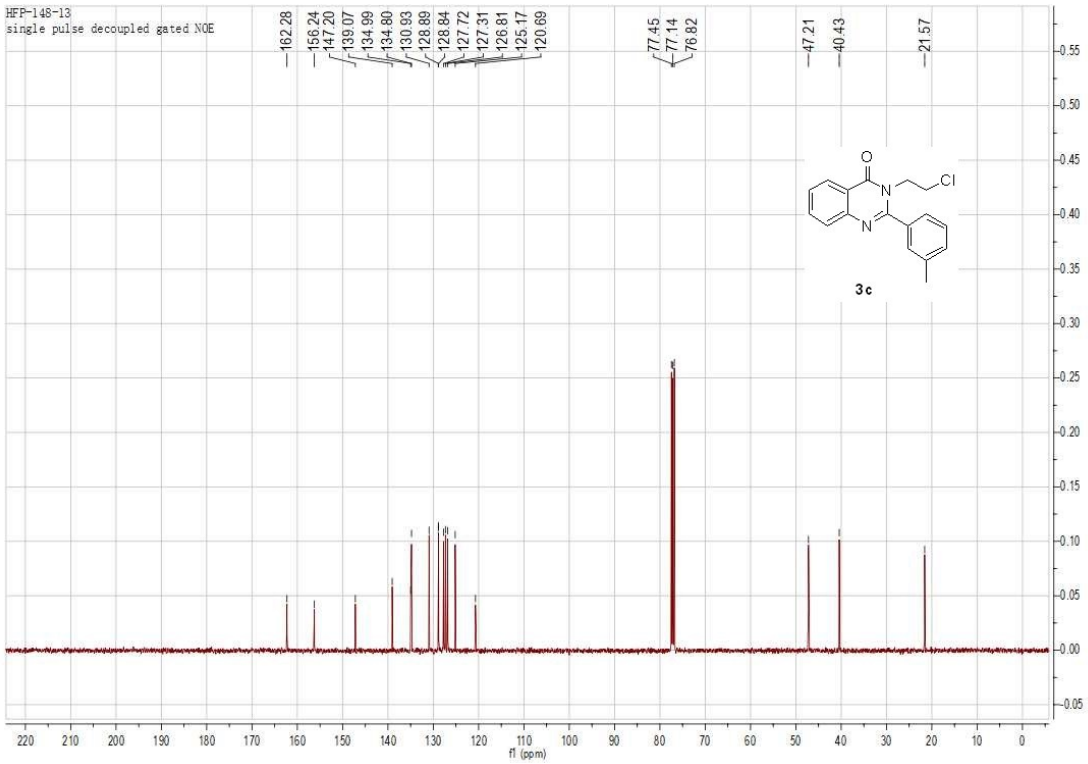

hfp-148
single_pulse
8.34
8.32
7.79
7.78
7.77
7.77
7.76
7.76
7.74
7.54
7.53
7.53
7.52
7.51
7.51
4.38
4.37
4.35
3.76
3.74
3.72
0.00
1.00
2.12
6.21
2.06
2.05
f1 (ppm)
O
N
N
Cl
3a

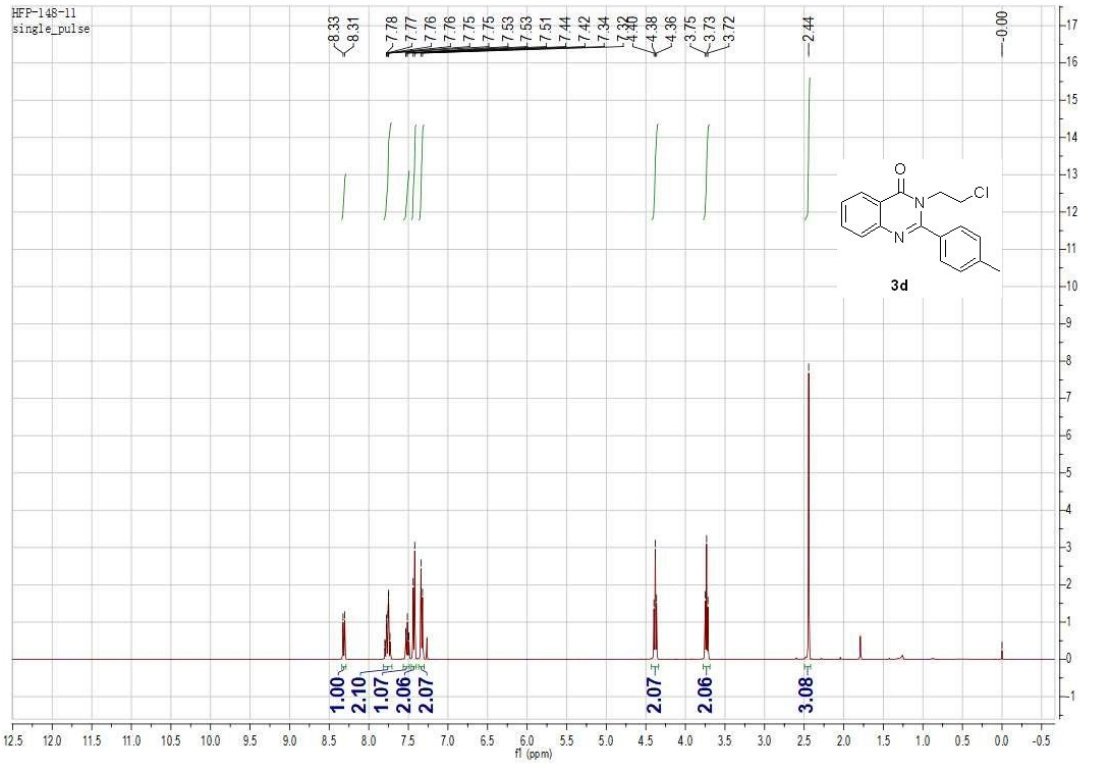

hfp-148
single pulse decoupled gated NOE
162.26
156.04
147.18
135.11
134.83
130.18
129.05
128.28
127.74
127.38
126.82
120.71
77.47
77.15
76.83
47.20
40.43
f1 (ppm)
O
N
N
Cl
3a

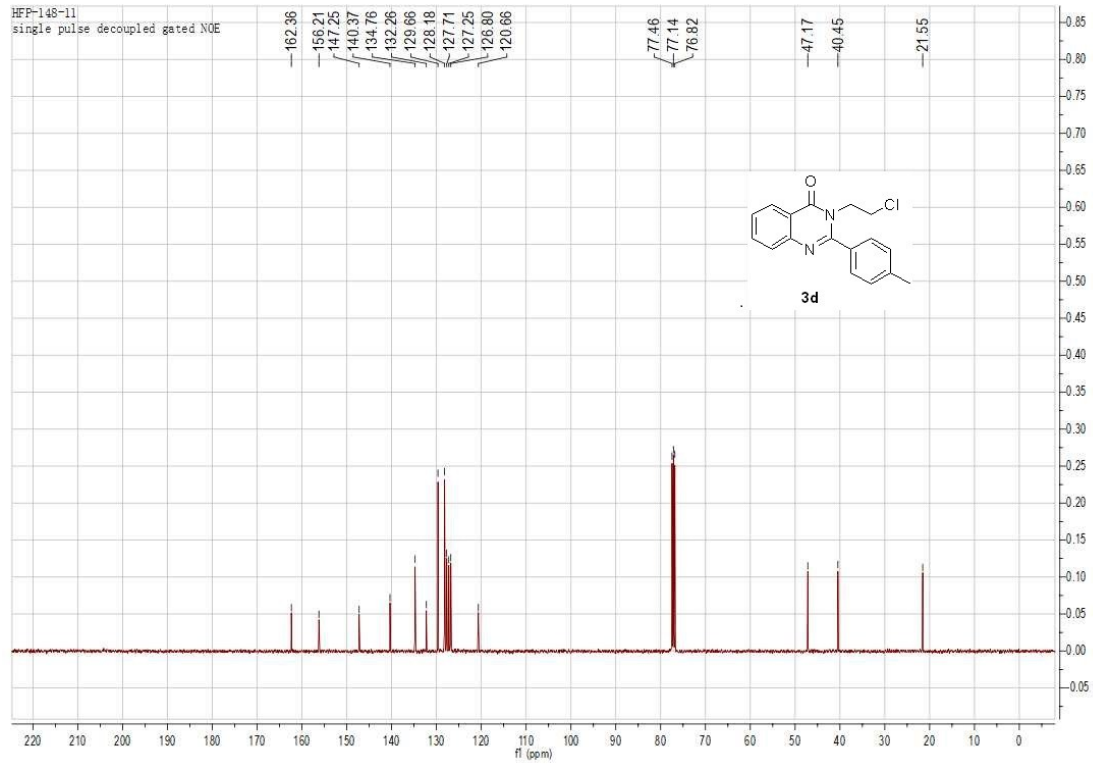

hfp-148-30
single_pulse
8.35
8.33
7.78
7.76
7.54
7.43
7.42
7.41
7.40
7.35
4.52
4.51
4.50
4.49
4.47
4.46
4.46
3.72
3.71
3.71
3.70
3.70
3.69
2.25
0.00
O
N
Cl
N
3b
1.00
2.09
1.09
2.07
2.06
1.04
1.05
2.07
3.09
f1 (ppm)

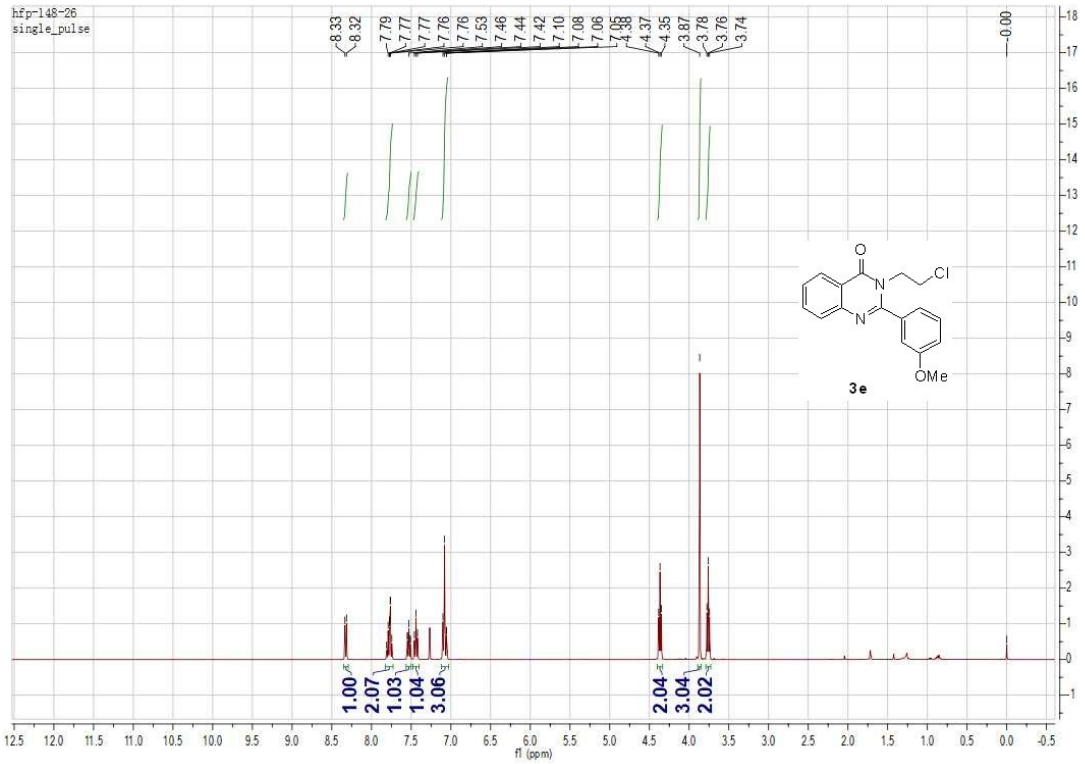

hfp-148-30
single pulse decoupled gated NOE
162.14
155.61
147.26
135.63
134.82
134.34
130.87
130.21
128.47
127.73
127.41
126.83
126.48
120.79
77.45
77.13
76.81
46.71
40.05
19.37
O
N
Cl
N
3b
f1 (ppm)

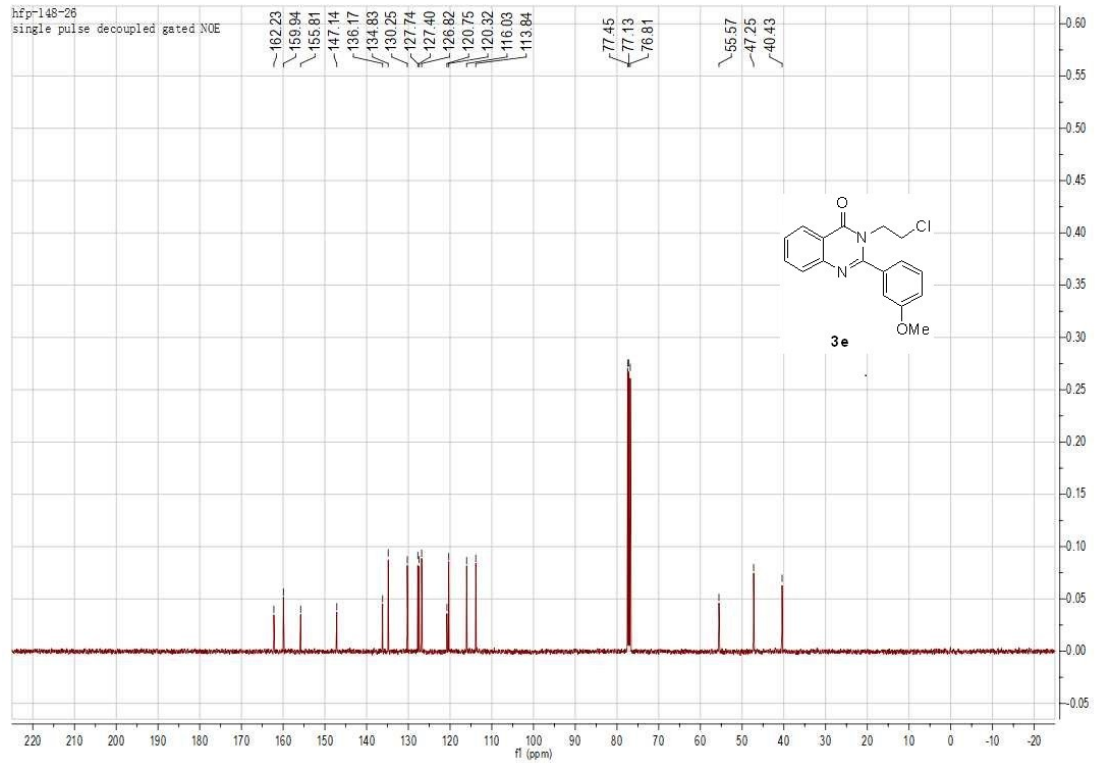

HFP-148-13
single_pulse
8.33
8.31
7.79
7.78
7.76
7.76
7.54
7.52
7.42
7.40
7.36
7.35
7.33
7.31
4.37
4.35
3.76
3.74
3.72
2.44
0.00
1.00
2.08
1.09
1.07
3.09
2.09
2.09
3.10
f1 (ppm)
3c

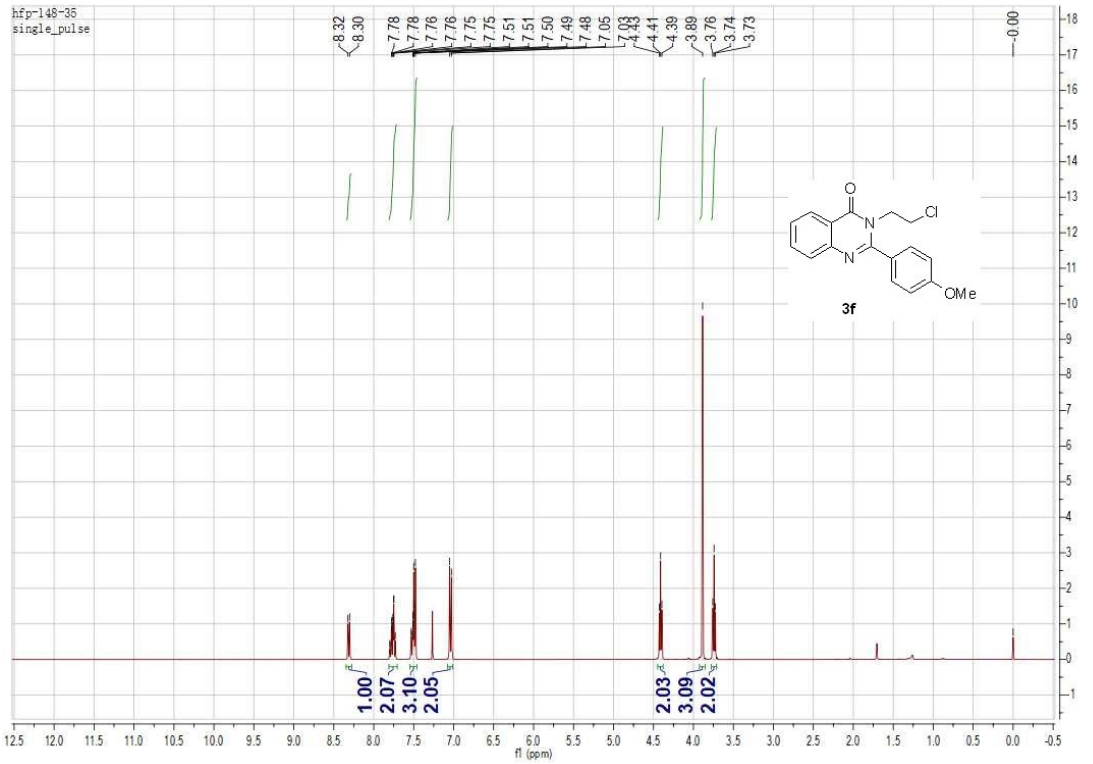

HFP-148-13
single pulse decoupled gated NOE
162.28
156.24
147.20
139.07
134.99
134.80
130.93
128.89
128.84
127.72
127.31
126.81
125.17
120.69
77.45
77.14
76.82
47.21
40.43
21.57
f1 (ppm)
3c

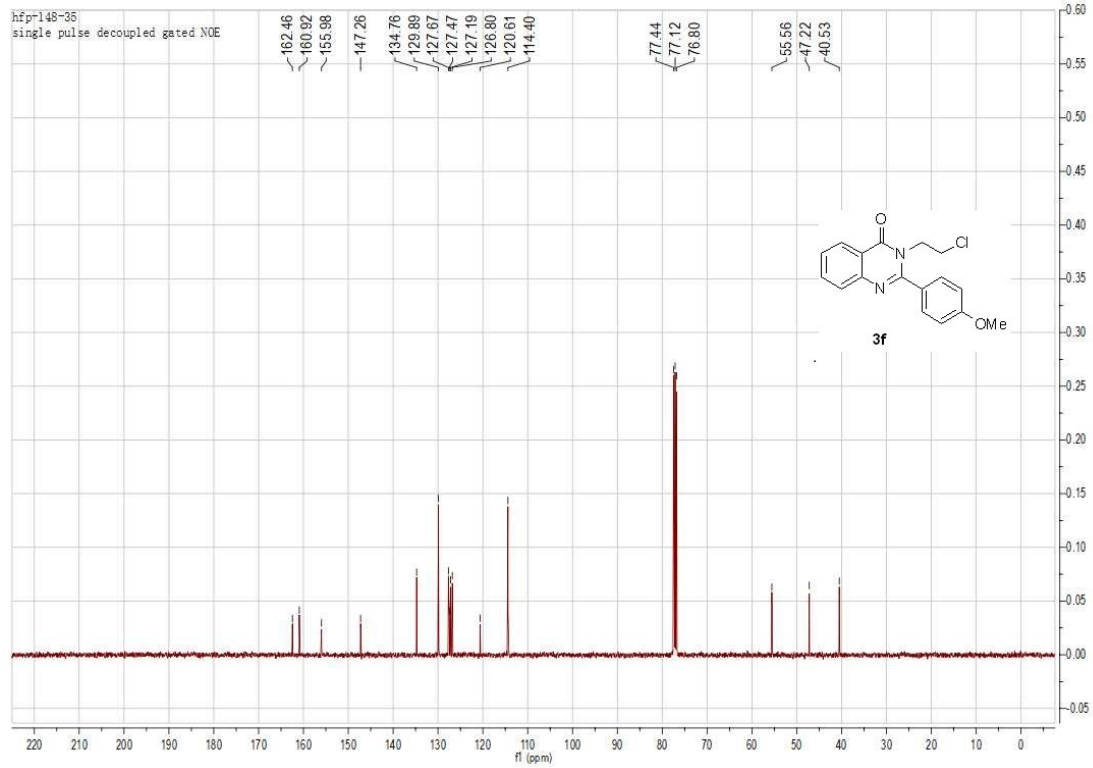

HFP-148-11
single_pulse
8.33
8.31
7.78
7.77
7.76
7.76
7.75
7.75
7.53
7.53
7.51
7.44
7.42
7.34
4.38
4.36
3.75
3.73
3.72
2.44
0.00
1.00
2.10
1.07
2.06
2.07
2.07
2.06
3.08
f1 (ppm)
3d

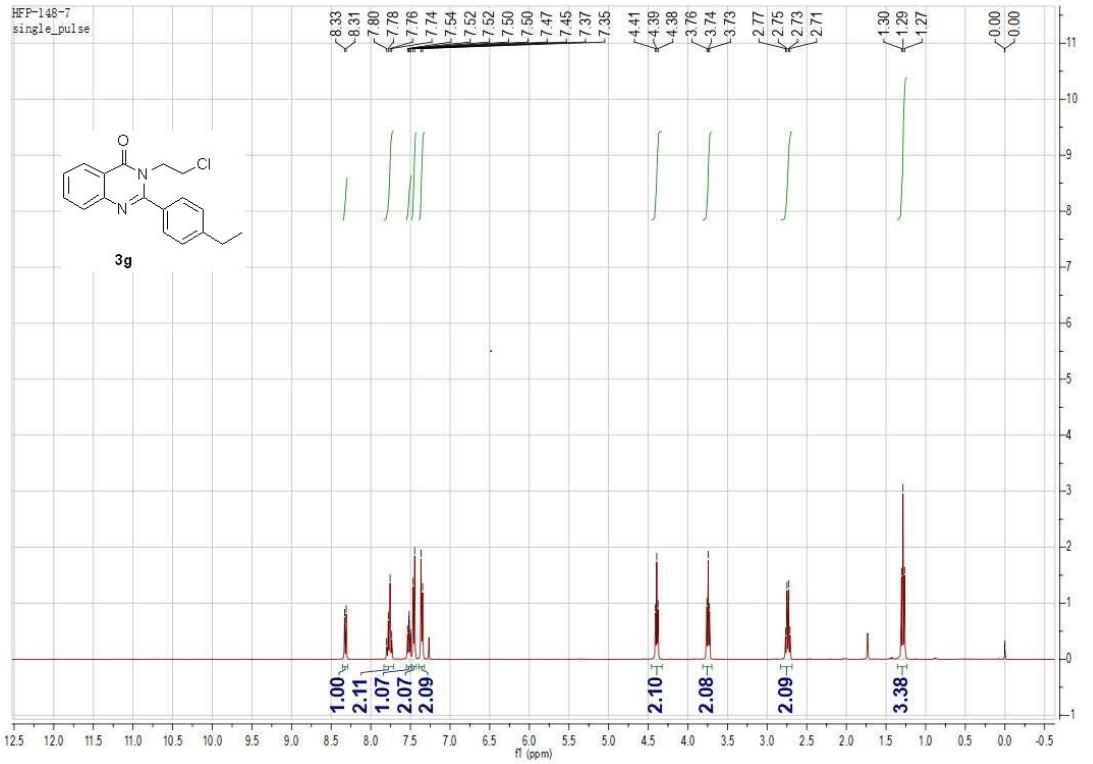

HFP-148-11
single pulse decoupled gated NOE
162.36
156.21
147.25
140.37
134.76
132.26
129.66
128.18
127.71
127.25
126.80
120.66
77.46
77.14
76.82
47.17
40.45
21.55
f1 (ppm)
3d

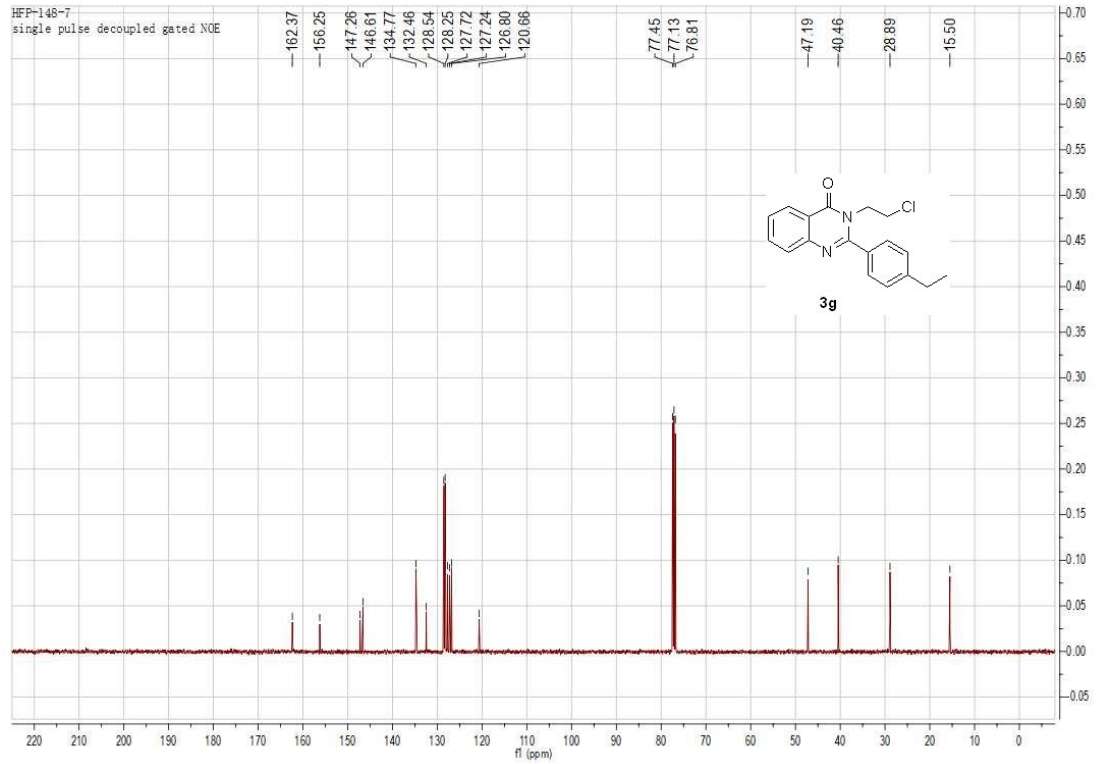

hfp-148-26
single_pulse
8.33
8.32
7.79
7.77
7.77
7.76
7.76
7.53
7.46
7.44
7.42
7.10
7.08
7.06
4.37
4.35
3.87
3.78
3.76
3.74
0.00
1.00
2.07
1.03
1.04
3.06
2.04
3.04
2.02
f1 (ppm)
O
N
N
Cl
OMe
3e

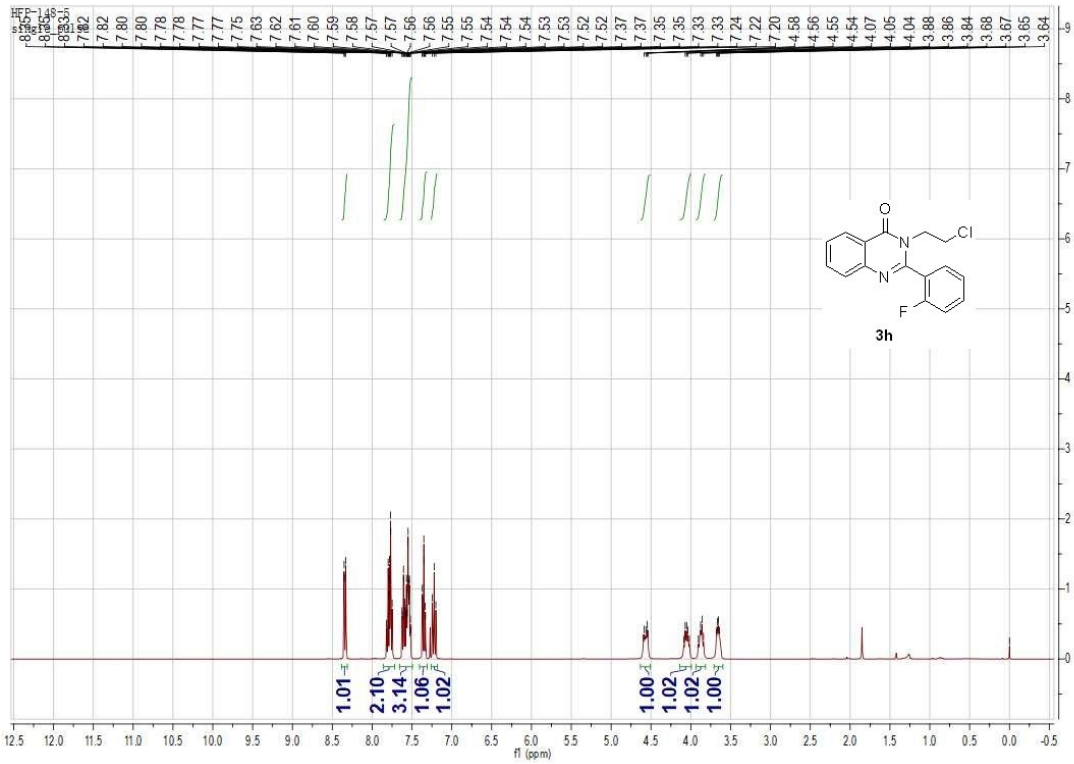

hfp-148-26
single pulse decoupled gated NOE
162.23
159.94
155.81
147.14
136.17
134.83
130.25
127.74
127.40
126.82
120.75
120.32
116.03
113.84
77.45
77.13
76.81
55.57
47.25
40.43
f1 (ppm)
O
N
N
Cl
OMe
3e

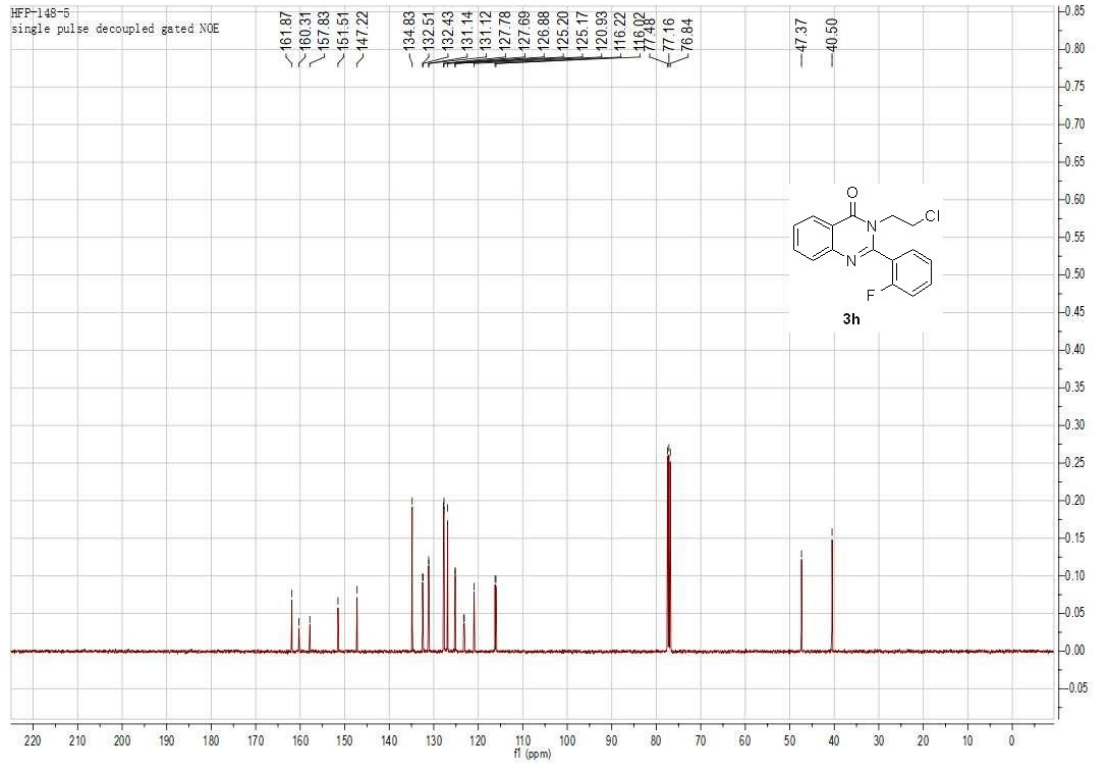

hfp-148-35
single_pulse
8.32
8.30
7.78
7.78
7.76
7.76
7.75
7.75
7.51
7.51
7.50
7.49
7.48
7.05
7.03
4.43
4.41
4.39
3.89
3.76
3.74
3.73
0.00
1.00
2.07
3.10
2.05
2.03
3.09
2.02
f1 (ppm)
3f

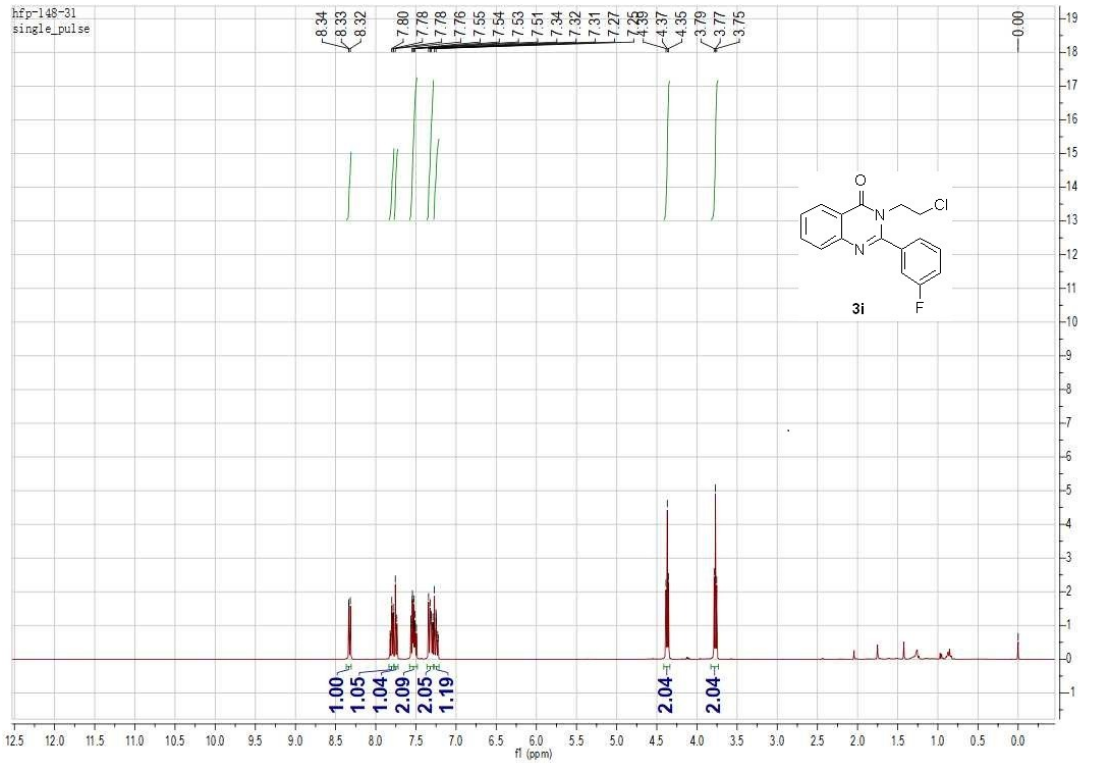

hfp-148-35
single pulse decoupled gated NOE
162.46
160.92
155.98
147.26
134.76
129.89
127.67
127.47
127.19
126.80
120.61
114.40
77.44
77.12
76.80
55.56
47.22
40.53
f1 (ppm)
3f

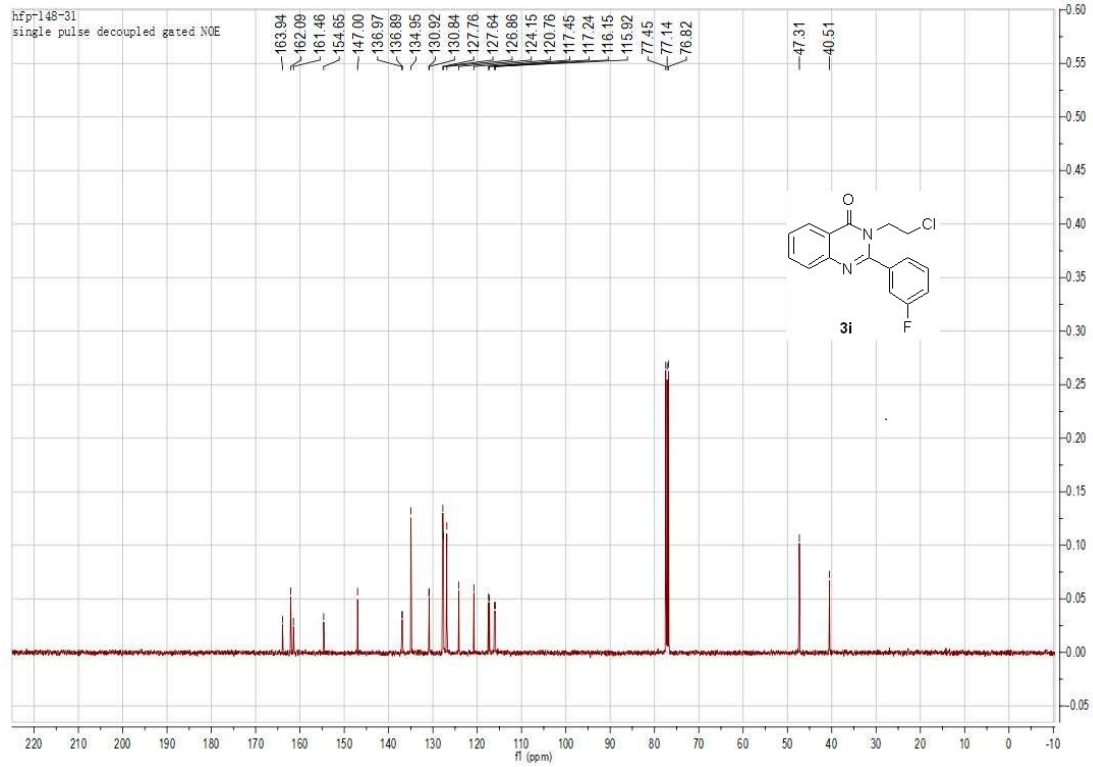

HFP-148-7
single_pulse
3g
1.00
2.11
1.07
2.07
2.09
2.10
2.08
2.09
3.38
f1 (ppm)

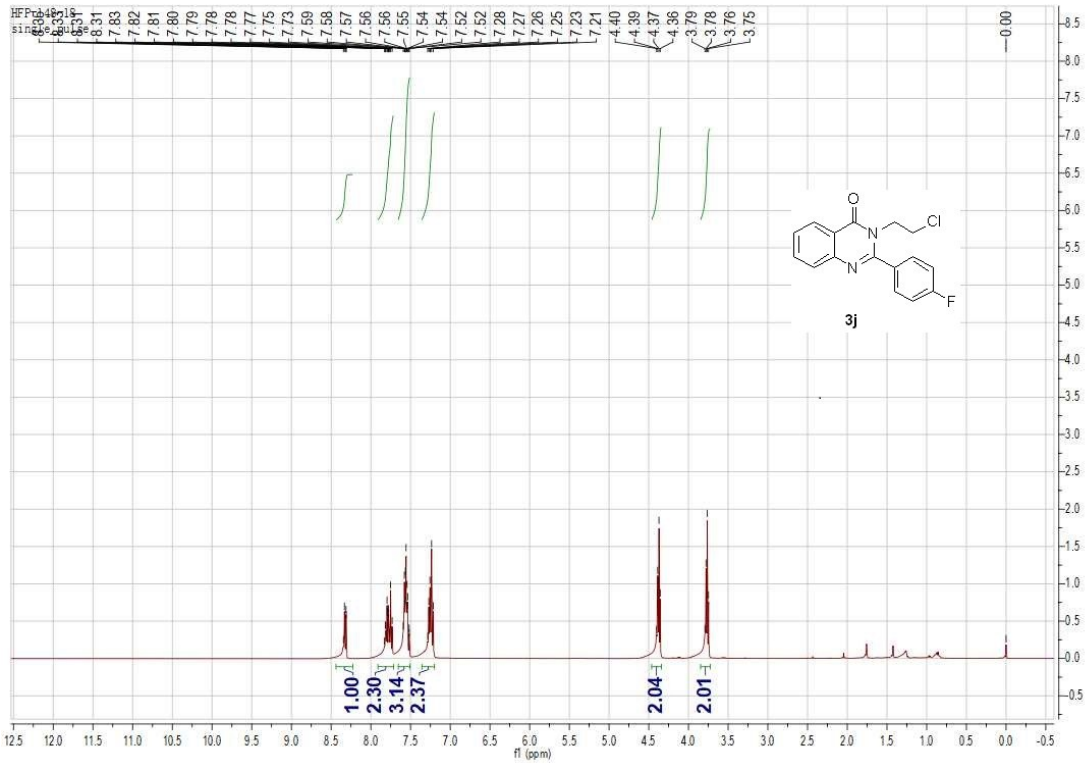

HFP-148-7
single pulse decoupled gated NOE
3g
f1 (ppm)

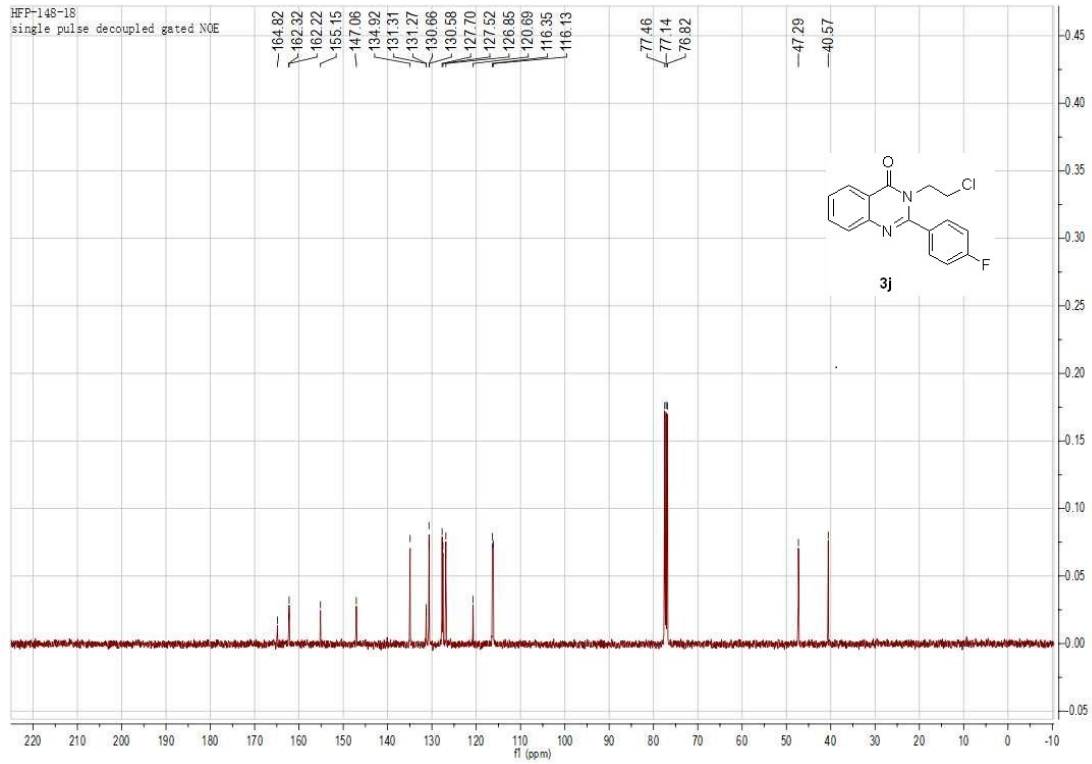

3h
1.01
2.10
3.14
1.06
1.02
1.00
1.02
1.02
1.00
f1 (ppm)

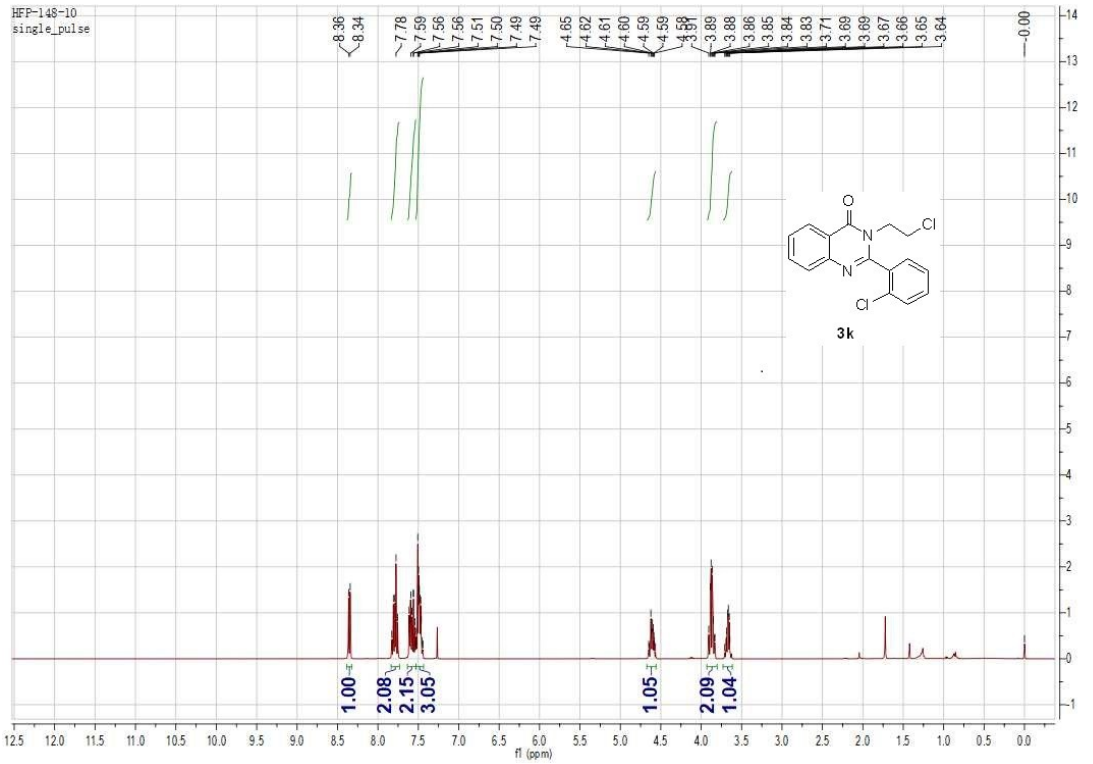

HFP-148-5
single pulse decoupled gated NOE
161.87
160.31
157.83
151.51
147.22
134.83
132.51
132.43
131.14
131.12
127.78
127.69
126.88
125.20
125.17
120.93
116.22
116.02
77.48
77.16
76.84
47.37
40.50
3h
f1 (ppm)

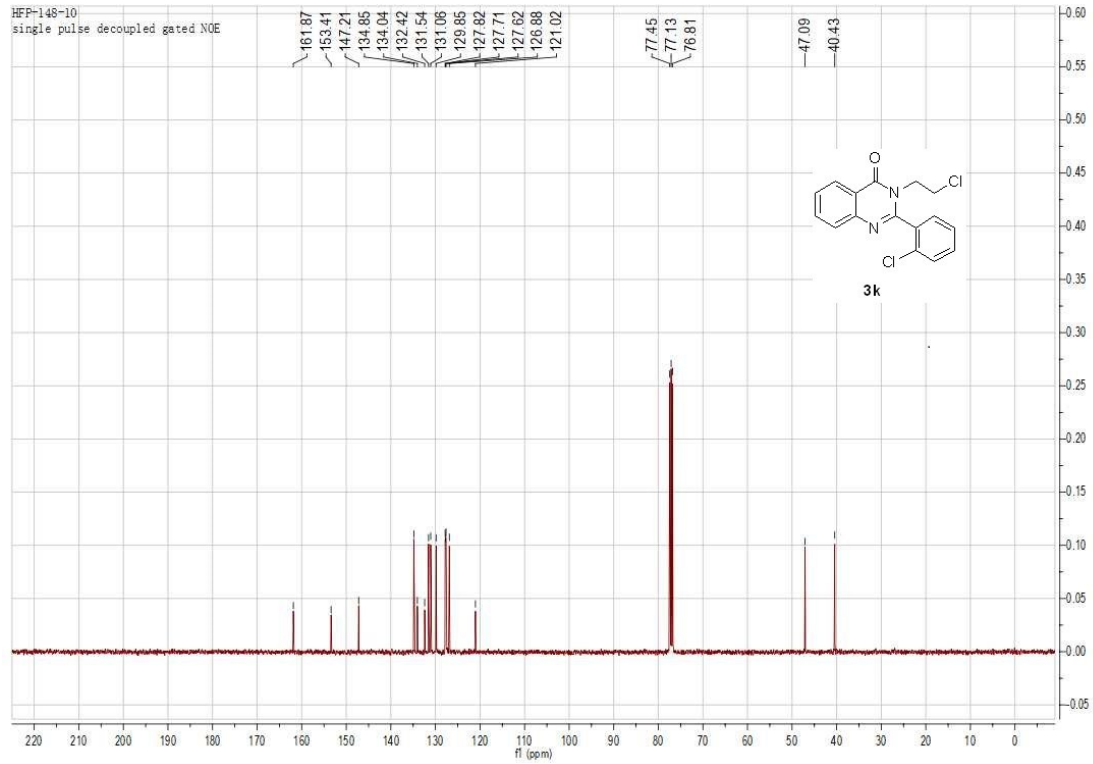

hfp-148-31
single_pulse
8.34
8.33
8.32
7.80
7.78
7.78
7.76
7.55
7.54
7.53
7.51
7.34
7.32
7.31
7.27
4.37
4.35
3.79
3.77
3.75
0.00
1.00
1.05
1.04
2.09
2.05
1.19
2.04
2.04
f1 (ppm)
3i

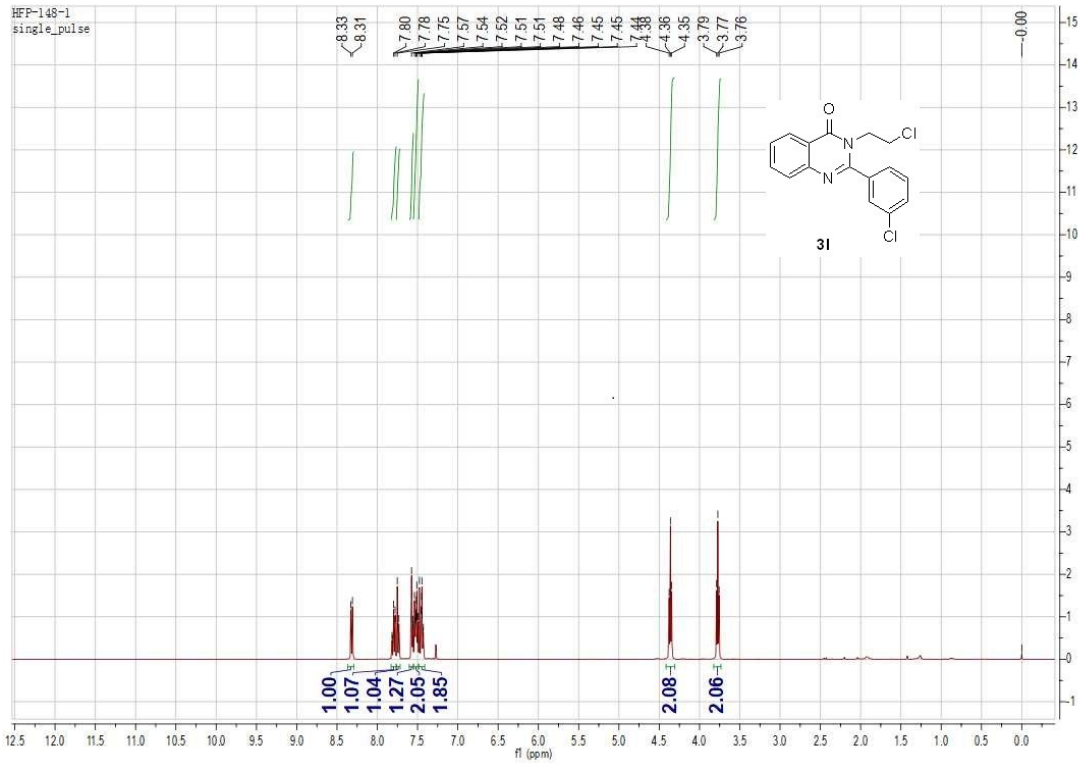

hfp-148-31
single pulse decoupled gated NOE
163.94
162.09
161.46
154.65
147.00
136.97
136.89
134.95
130.92
130.84
127.76
127.64
126.86
124.15
120.76
117.45
117.24
116.15
115.92
77.45
77.14
76.82
47.31
40.51
f1 (ppm)
3i

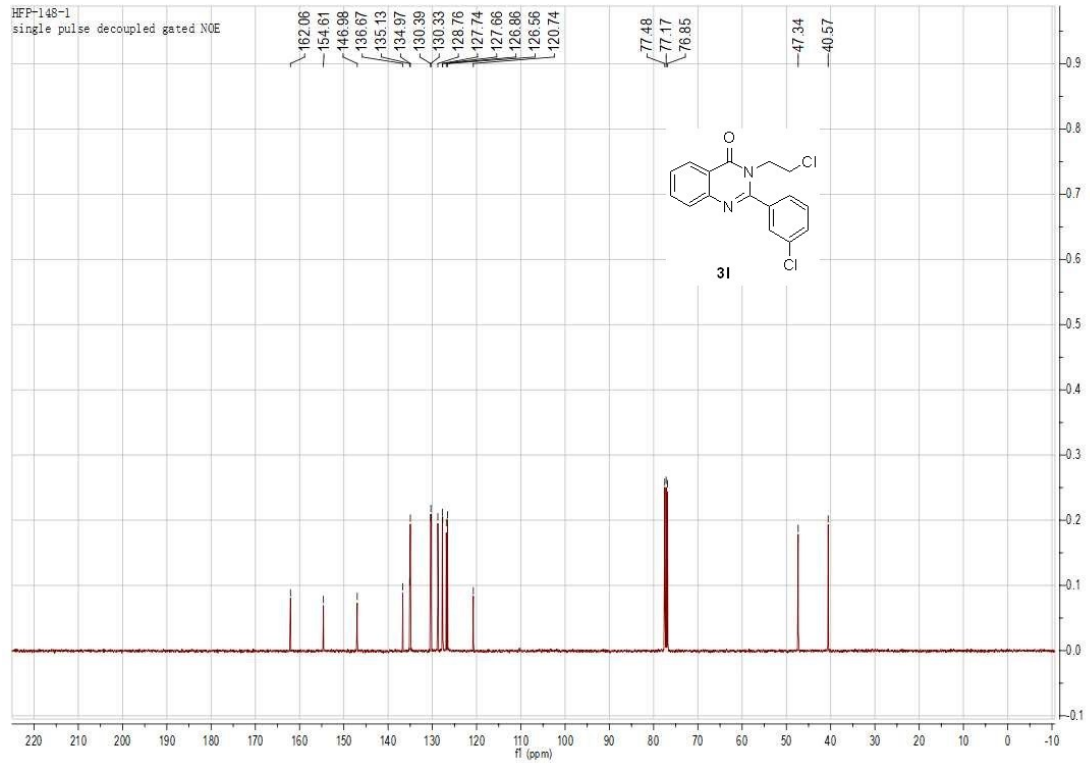

8.31
7.83
7.82
7.81
7.80
7.79
7.78
7.78
7.77
7.75
7.73
7.59
7.58
7.57
7.56
7.56
7.55
7.54
7.54
7.52
7.52
7.28
7.27
7.26
7.25
7.23
7.21
4.40
4.39
4.37
4.36
3.79
3.78
3.76
3.75
0.00
1.00
2.30
3.14
2.37
2.04
2.01
f1 (ppm)
3j

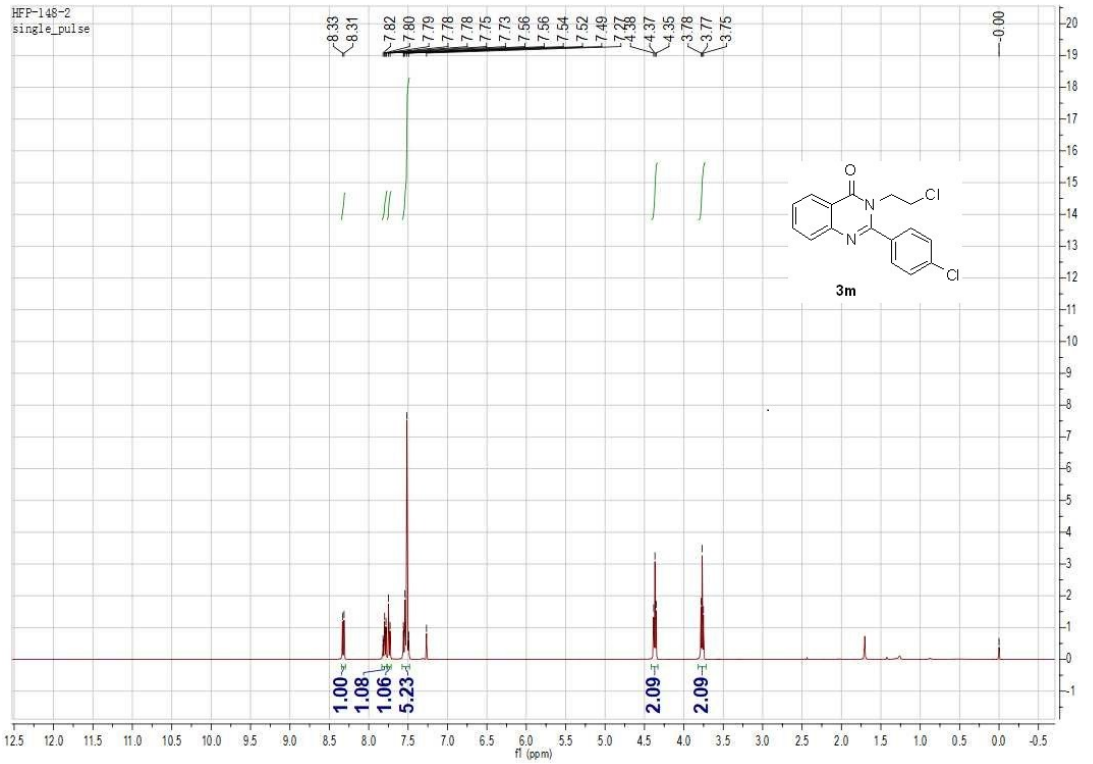

HFP-148-18
single pulse decoupled gated NOE
164.82
162.32
162.22
155.15
147.06
134.92
131.31
131.27
130.66
130.58
127.70
127.52
126.85
120.69
116.35
116.13
77.46
77.14
76.82
47.29
40.57
f1 (ppm)
3j

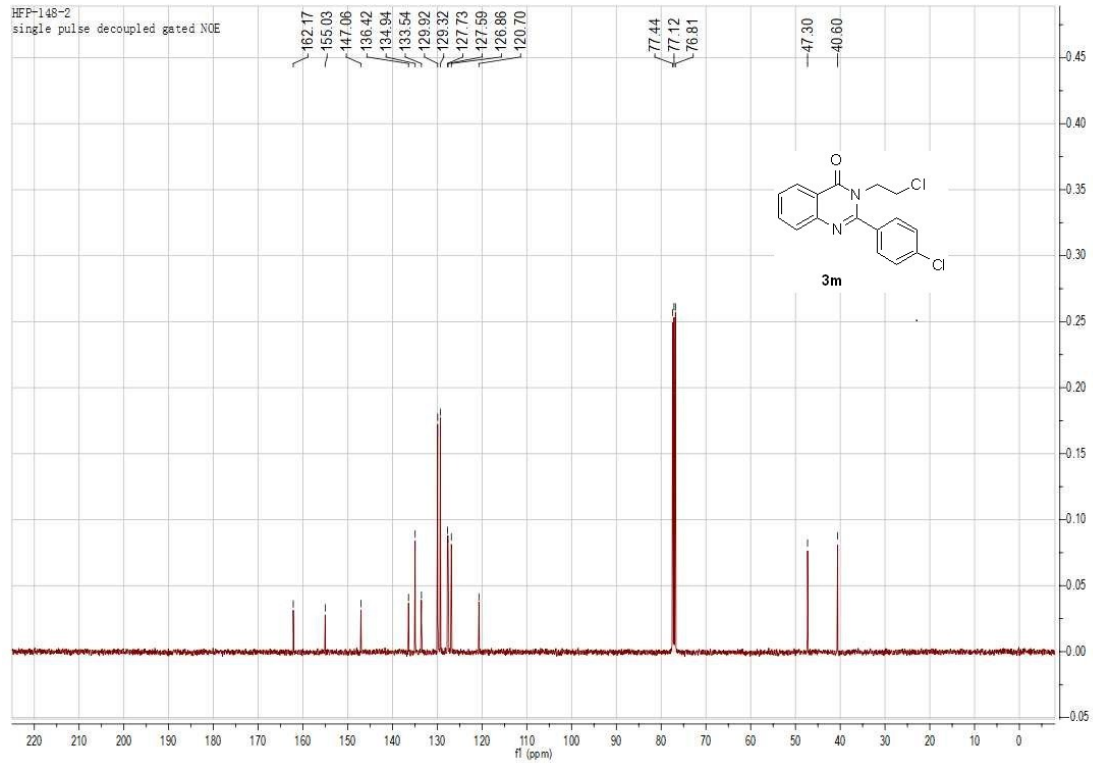

HFP-148-10
single_pulse
8.36
8.34
7.78
7.59
7.56
7.56
7.51
7.50
7.49
7.49
4.65
4.62
4.61
4.60
4.59
4.59
4.58
3.91
3.89
3.88
3.86
3.85
3.84
3.83
3.71
3.69
3.69
3.67
3.66
3.65
3.64
0.00
1.00
2.08
2.15
3.05
1.05
2.09
1.04
f1 (ppm)
3k

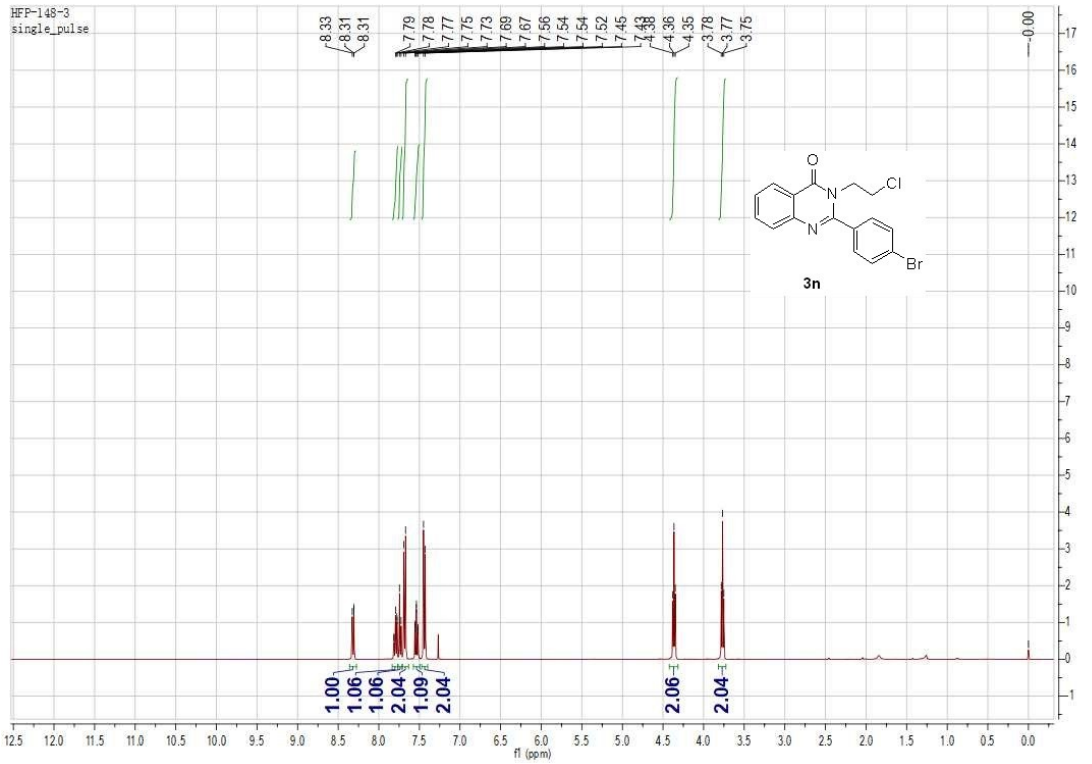

HFP-148-10
single pulse decoupled gated NOE
161.87
153.41
147.21
134.85
134.04
132.42
131.54
131.06
129.85
127.82
127.71
127.62
126.88
121.02
77.45
77.13
76.81
47.09
40.43
f1 (ppm)
3k

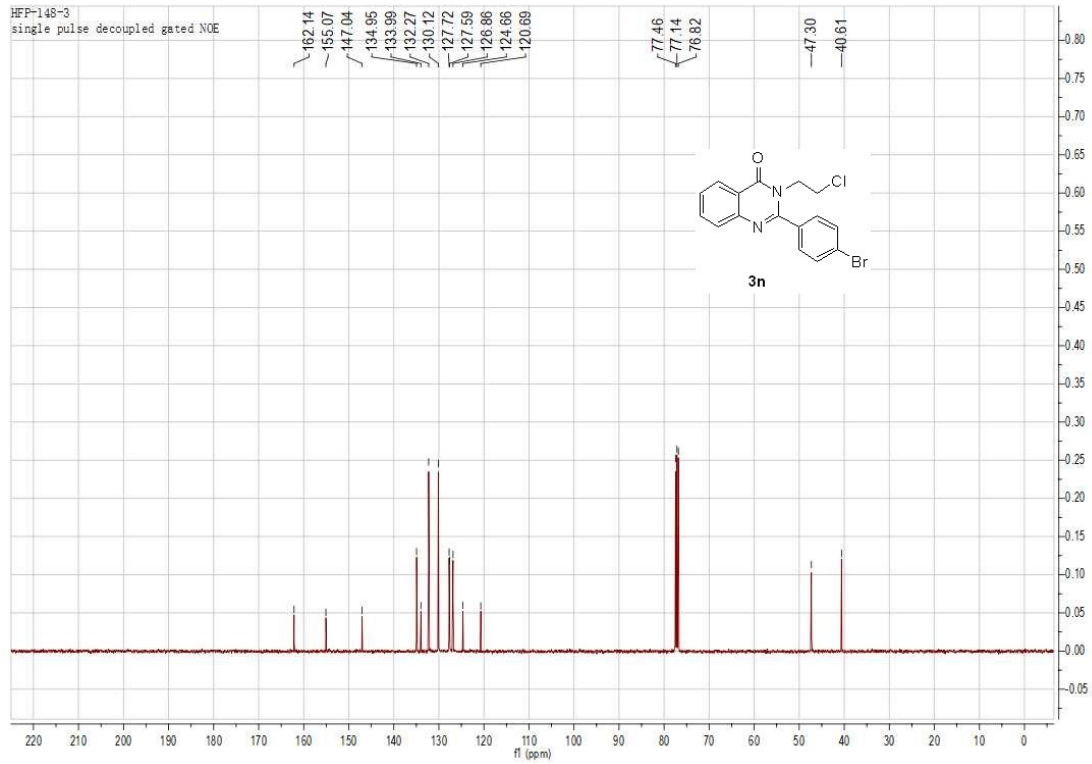

HFP-148-1
single_pulse
8.33
8.31
7.80
7.78
7.75
7.57
7.54
7.52
7.51
7.51
7.48
7.46
7.45
7.45
4.36
4.35
3.79
3.77
3.76
0.00
1.00
1.07
1.04
1.27
2.05
1.85
2.08
2.06
f1 (ppm)
3l

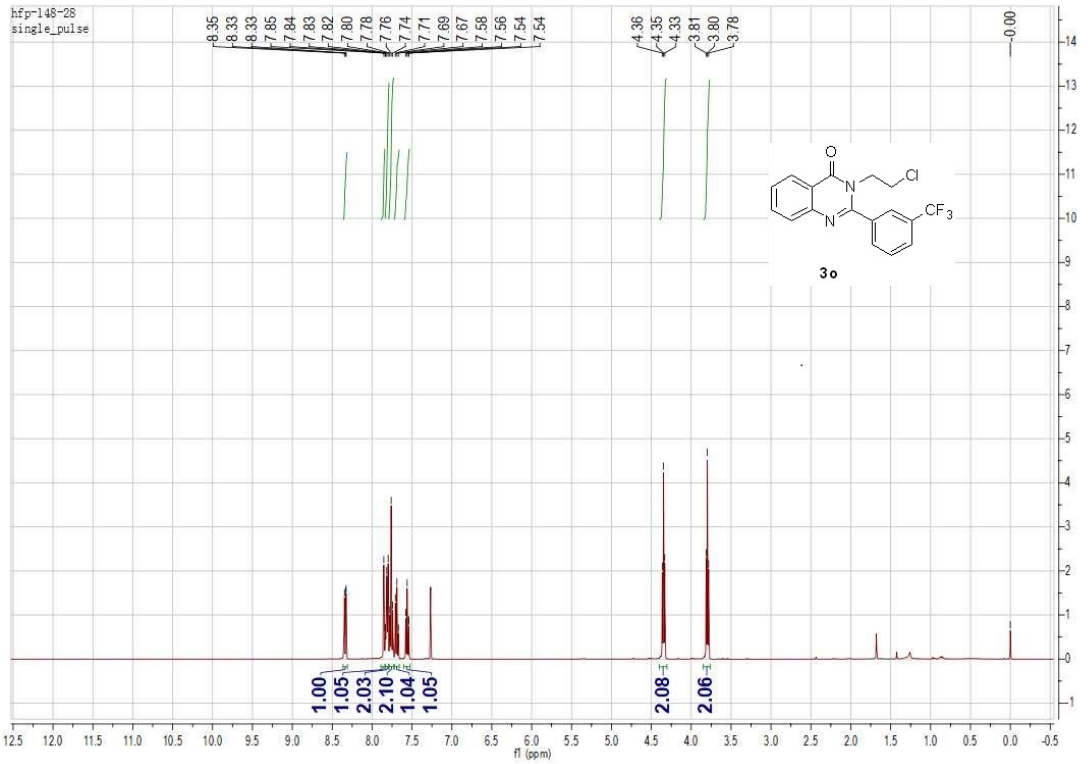

HFP-148-1
single pulse decoupled gated NOE
162.06
154.61
146.98
136.67
135.13
134.97
130.39
130.33
128.76
127.74
127.66
126.86
126.56
120.74
77.48
77.17
76.85
47.34
40.57
f1 (ppm)
3l

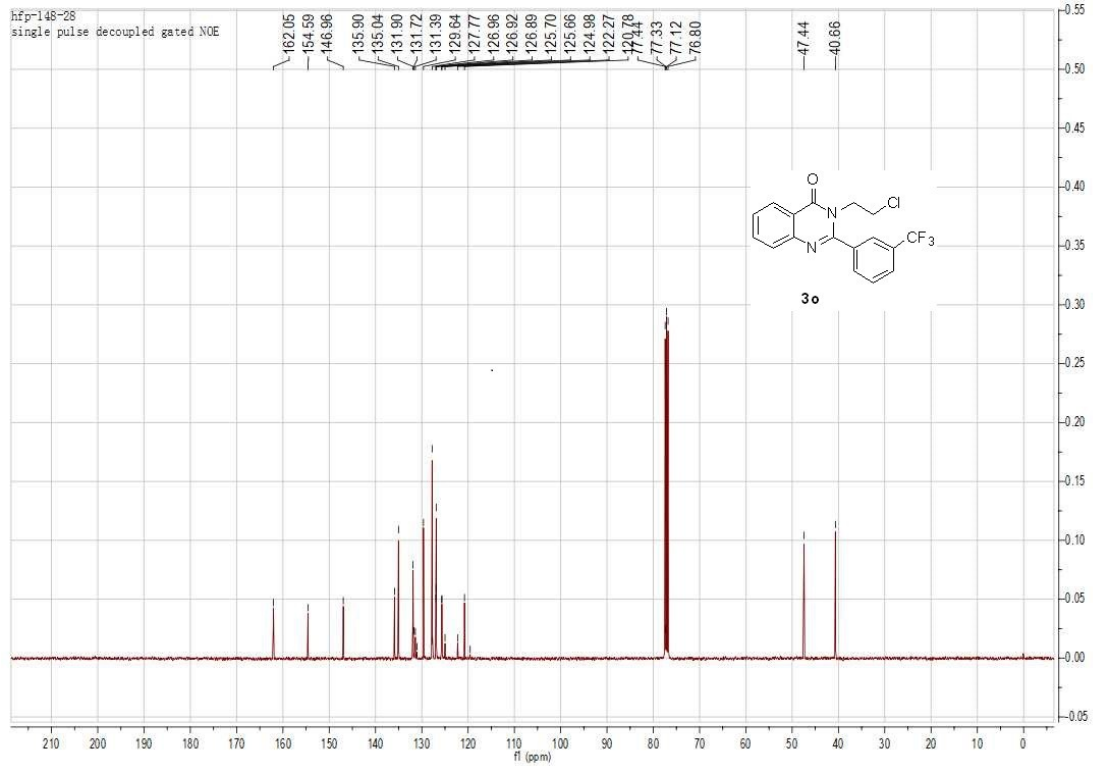

HFP-148-2
single_pulse
8.33
8.31
7.82
7.80
7.79
7.78
7.78
7.75
7.73
7.56
7.56
7.54
7.52
7.49
4.38
4.37
4.35
3.78
3.77
3.75
0.00
1.00
1.08
1.06
5.23
2.09
2.09
f1 (ppm)
3m

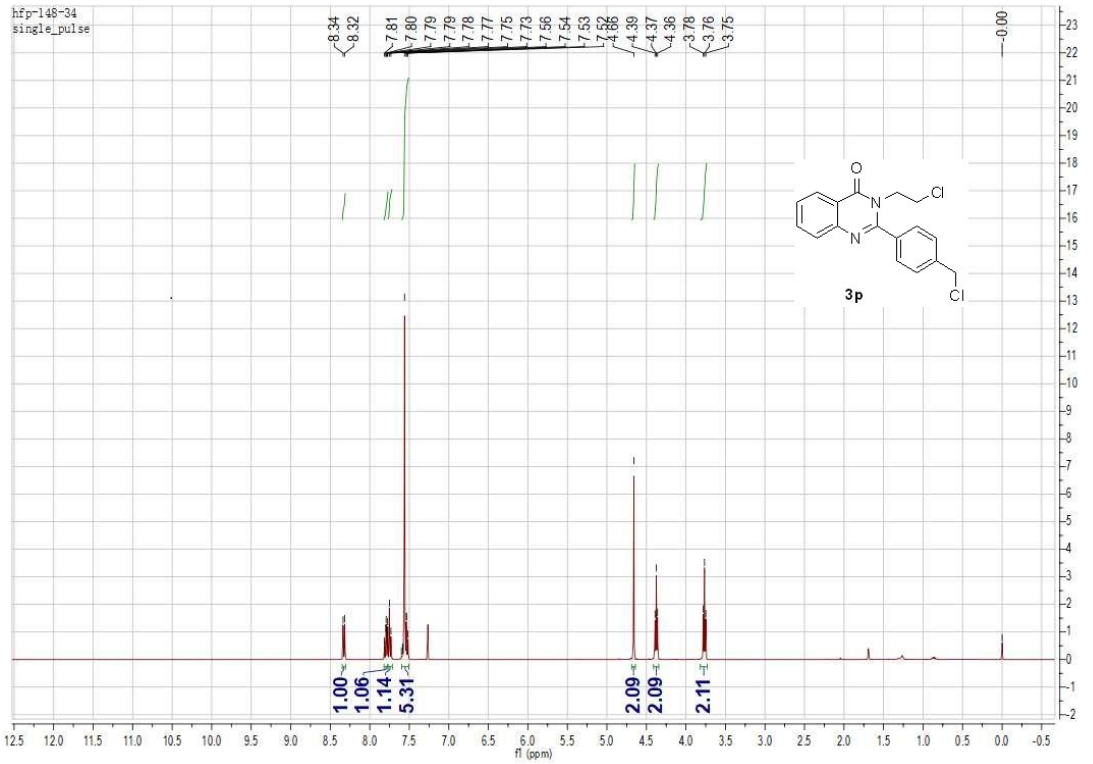

HFP-148-2
single pulse decoupled gated NOE
162.17
155.03
147.06
136.42
134.94
133.54
129.92
129.32
127.73
127.59
126.86
120.70
77.44
77.12
76.81
47.30
40.60
f1 (ppm)
3m

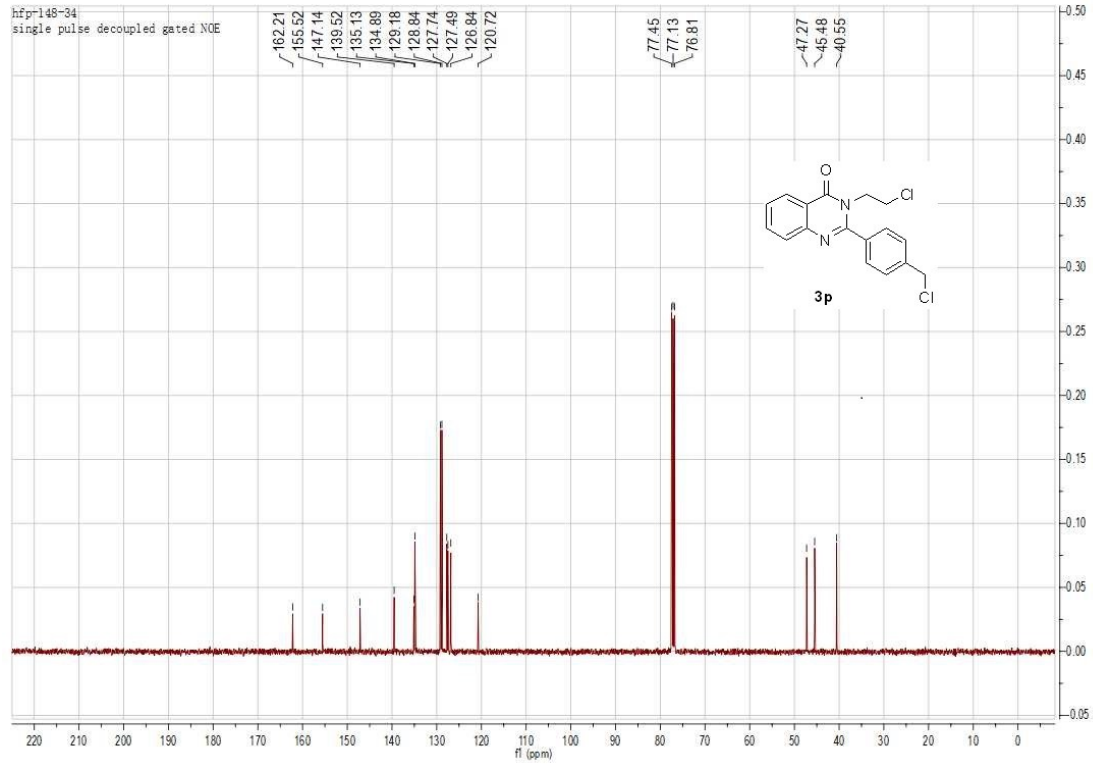

HFP-148-3
single_pulse
8.33
8.31
8.31
7.79
7.78
7.77
7.75
7.73
7.69
7.67
7.56
7.54
7.54
7.52
7.45
7.43
7.38
4.36
4.35
3.78
3.77
3.75
0.00
1.00
1.06
1.06
2.04
1.09
2.04
2.06
2.04
f1 (ppm)
O
N
N
Cl
Br
3n

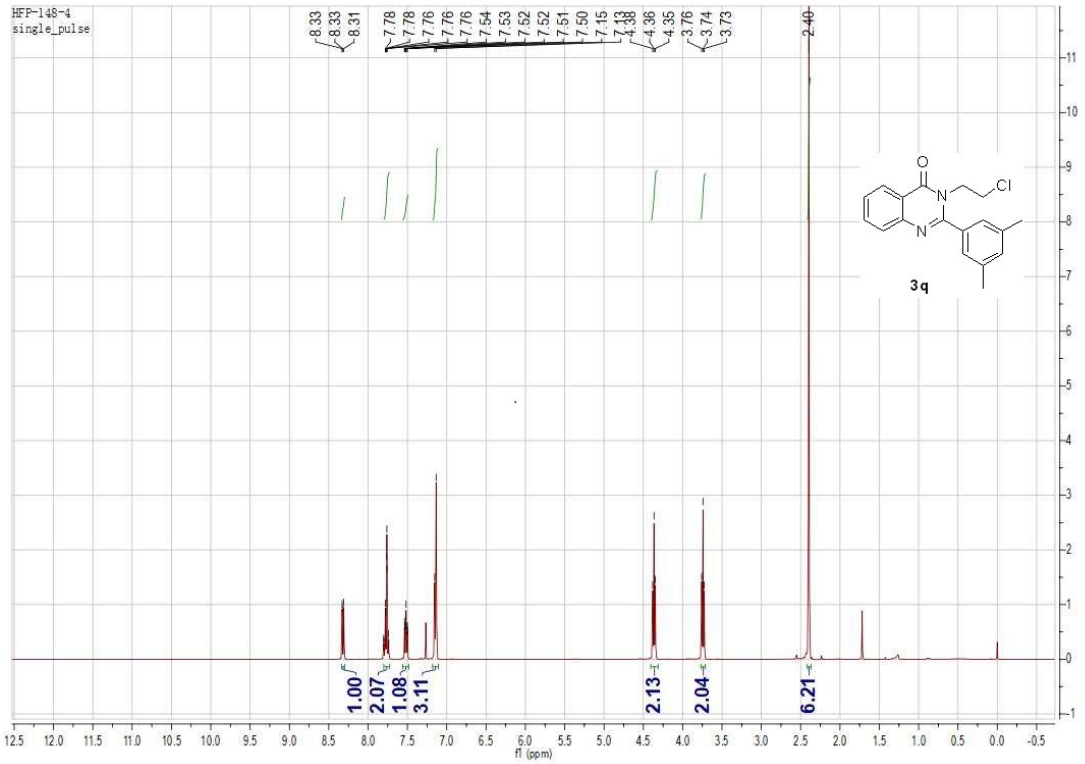

HFP-148-3
single pulse decoupled gated NOE
162.14
155.07
147.04
134.95
133.99
132.27
130.12
127.72
127.59
126.86
124.66
120.69
77.46
77.14
76.82
47.30
40.61
f1 (ppm)
O
N
N
Cl
Br
3n

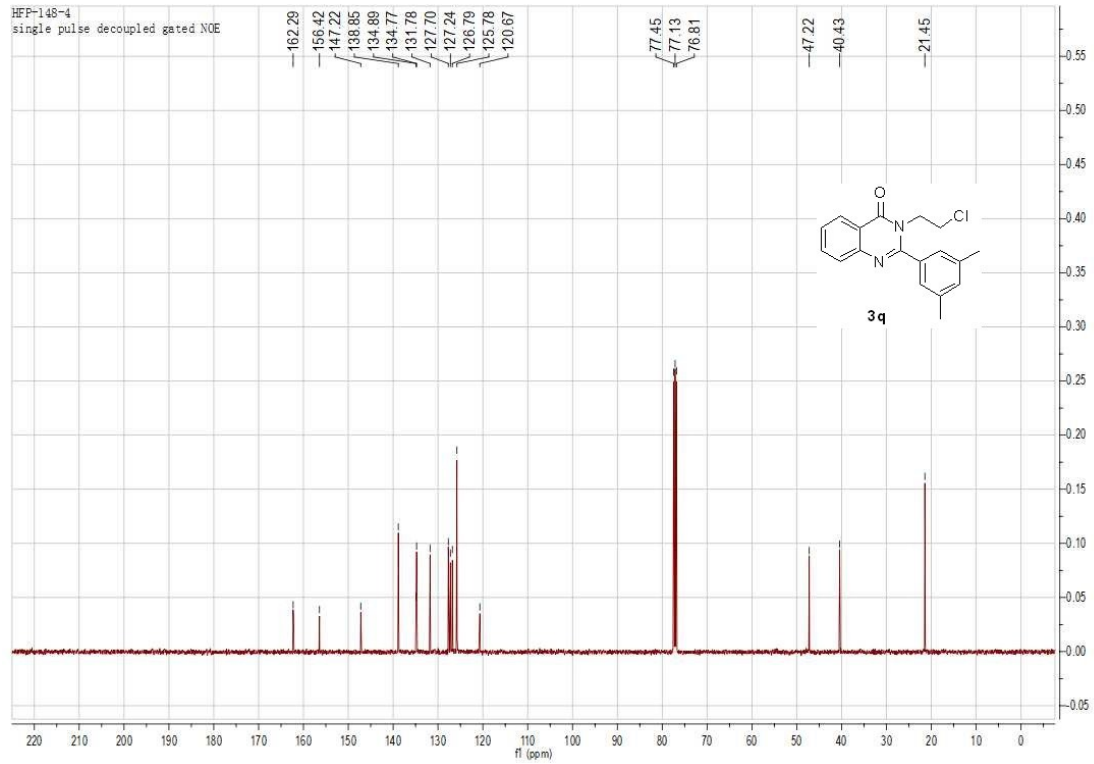

hfp-148-28
single_pulse
8.35
8.33
8.33
7.85
7.84
7.83
7.82
7.80
7.78
7.76
7.74
7.71
7.69
7.67
7.58
7.56
7.54
7.54
4.36
4.35
4.33
3.81
3.80
3.78
0.00
1.00
1.05
2.03
2.10
1.04
1.05
2.08
2.06
f1 (ppm)
3o

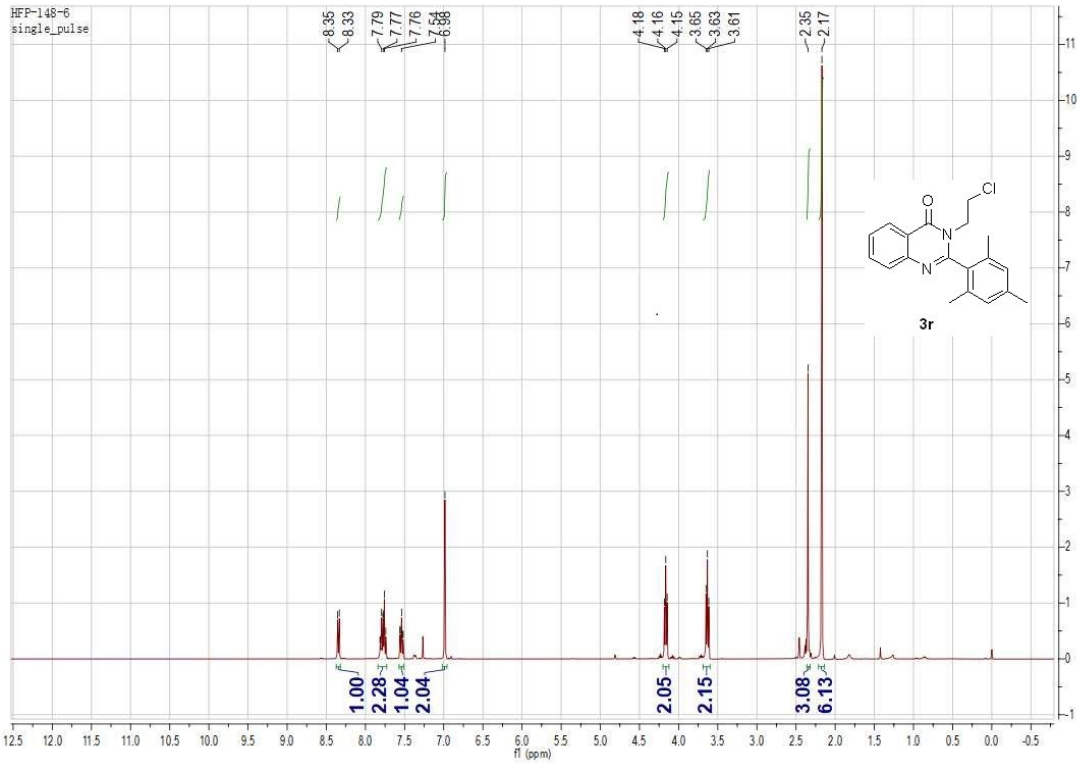

hfp-148-28
single pulse decoupled gated NOE
162.05
154.59
146.96
135.90
135.04
131.90
131.72
131.39
129.64
127.77
126.96
126.92
126.89
125.70
125.66
124.98
122.27
120.78
77.44
77.33
77.12
76.80
47.44
40.66
f1 (ppm)
3o

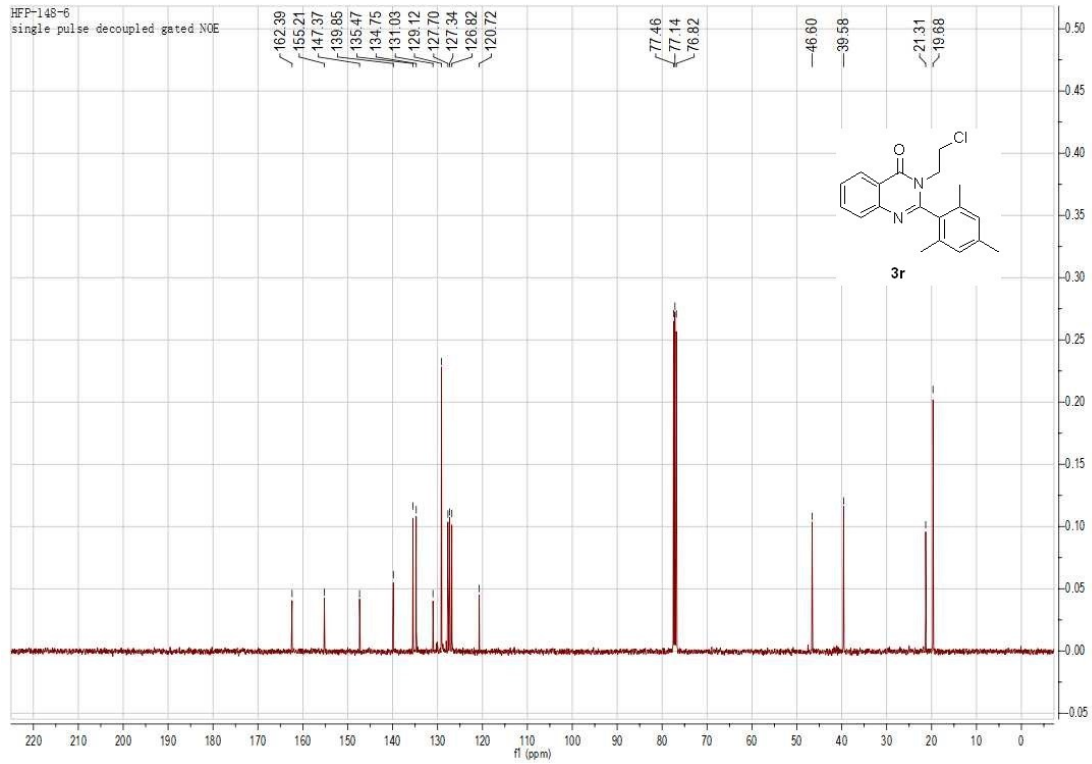

hfp-148-34
single_pulse
8.34
8.32
7.81
7.80
7.79
7.79
7.78
7.77
7.75
7.73
7.56
7.54
7.53
7.52
4.39
4.37
4.36
3.78
3.76
3.75
0.00
1.00
1.06
1.14
5.31
2.09
2.09
2.11
f1 (ppm)
3p

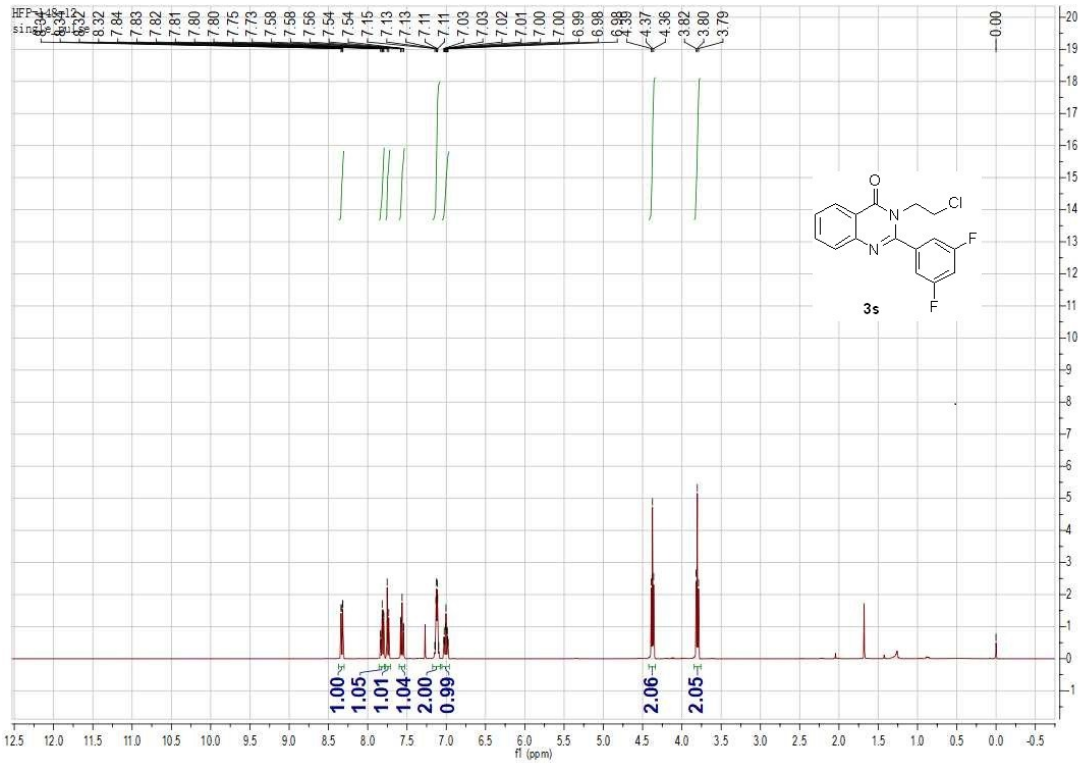

hfp-148-34
single pulse decoupled gated NOE
162.21
155.52
147.14
139.52
135.13
134.89
129.18
128.84
127.74
127.49
126.84
120.72
77.45
77.13
76.81
47.27
45.48
40.55
f1 (ppm)
3p

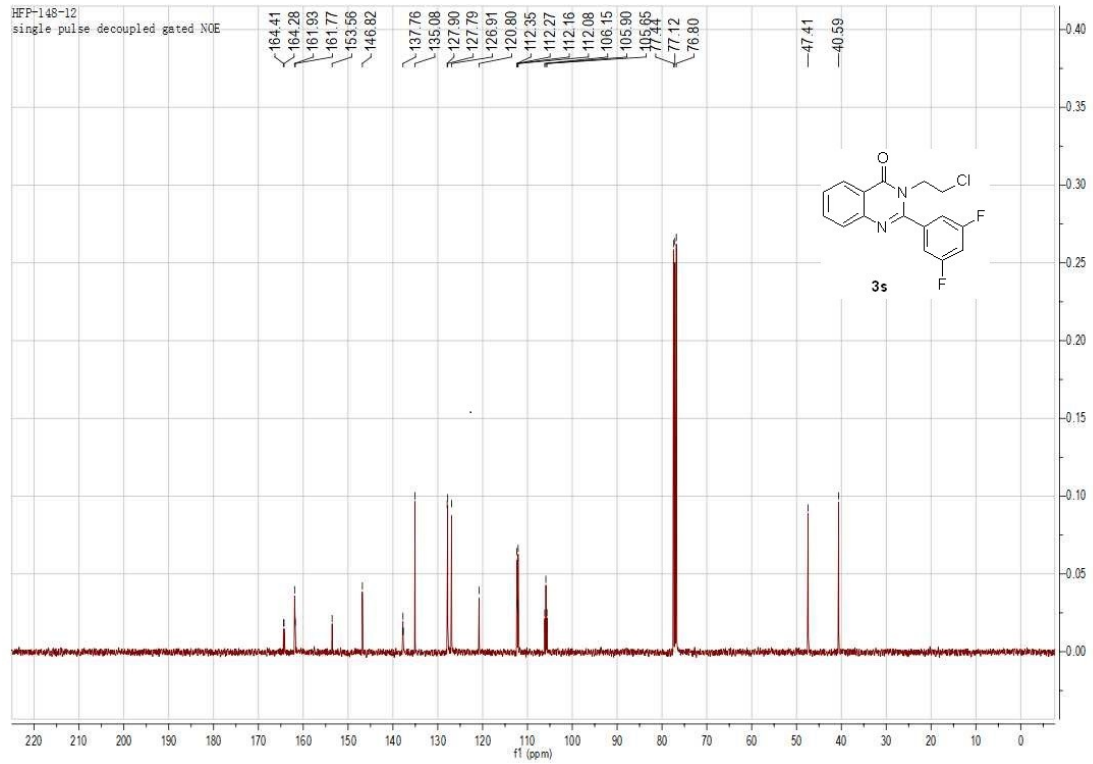

HFP-148-4
single_pulse
8.33
8.33
8.31
7.78
7.78
7.76
7.76
7.76
7.54
7.53
7.52
7.52
7.51
7.50
7.15
4.38
4.36
4.35
3.76
3.74
3.73
2.40
1.00
2.07
1.08
3.11
2.13
2.04
6.21
f1 (ppm)
3q

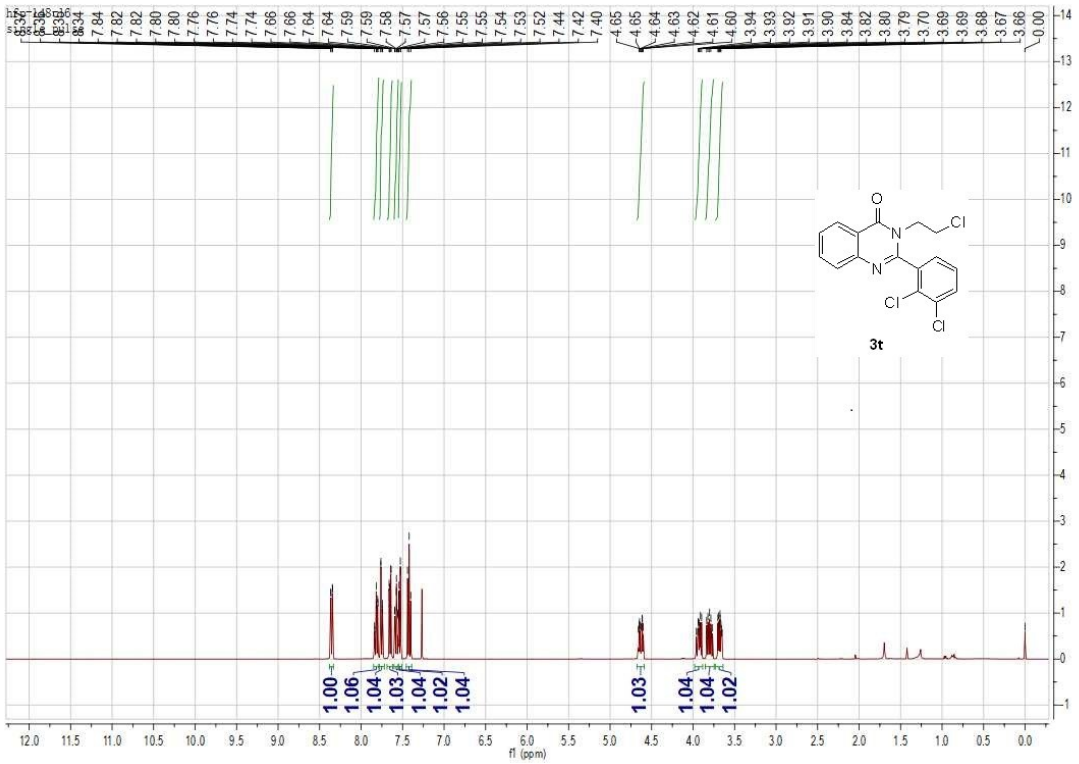

HFP-148-4
single pulse decoupled gated NOE
162.29
156.42
147.22
138.85
134.89
134.77
131.78
127.70
127.24
126.79
125.78
120.67
77.45
77.13
76.81
47.22
40.43
21.45
f1 (ppm)
3q

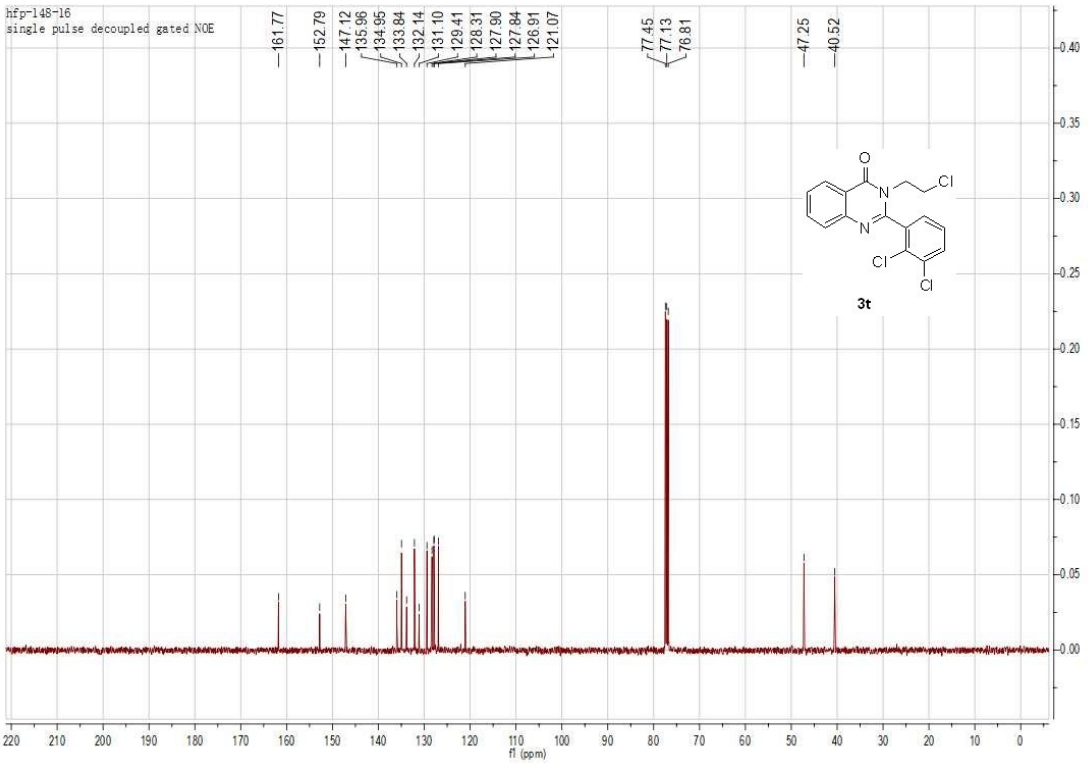

HFP-148-6
single_pulse
8.35
8.33
7.79
7.77
7.76
7.54
6.98
4.18
4.16
4.15
3.65
3.63
3.61
2.35
2.17
1.00
2.28
1.04
2.04
2.05
2.15
3.08
6.13
f1 (ppm)
3r

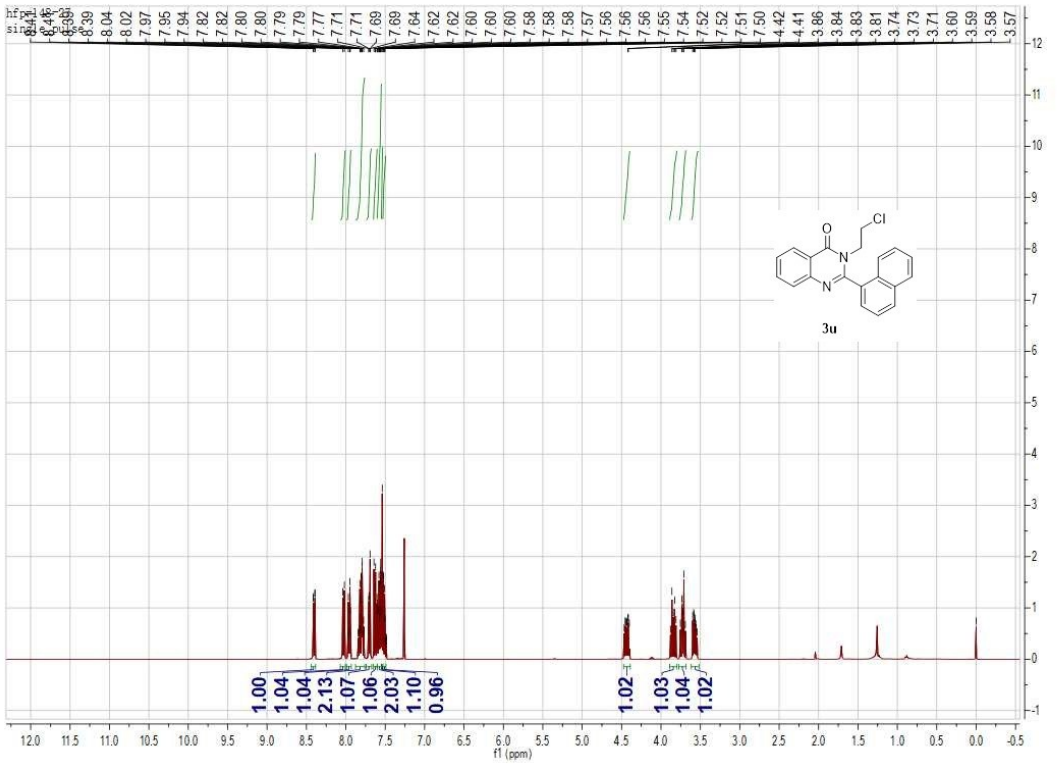

HFP-148-6
single pulse decoupled gated NOE
162.39
155.21
147.37
139.85
135.47
134.75
131.03
129.12
127.70
127.34
126.82
120.72
77.46
77.14
76.82
46.60
39.58
21.31
19.68
f1 (ppm)
3r

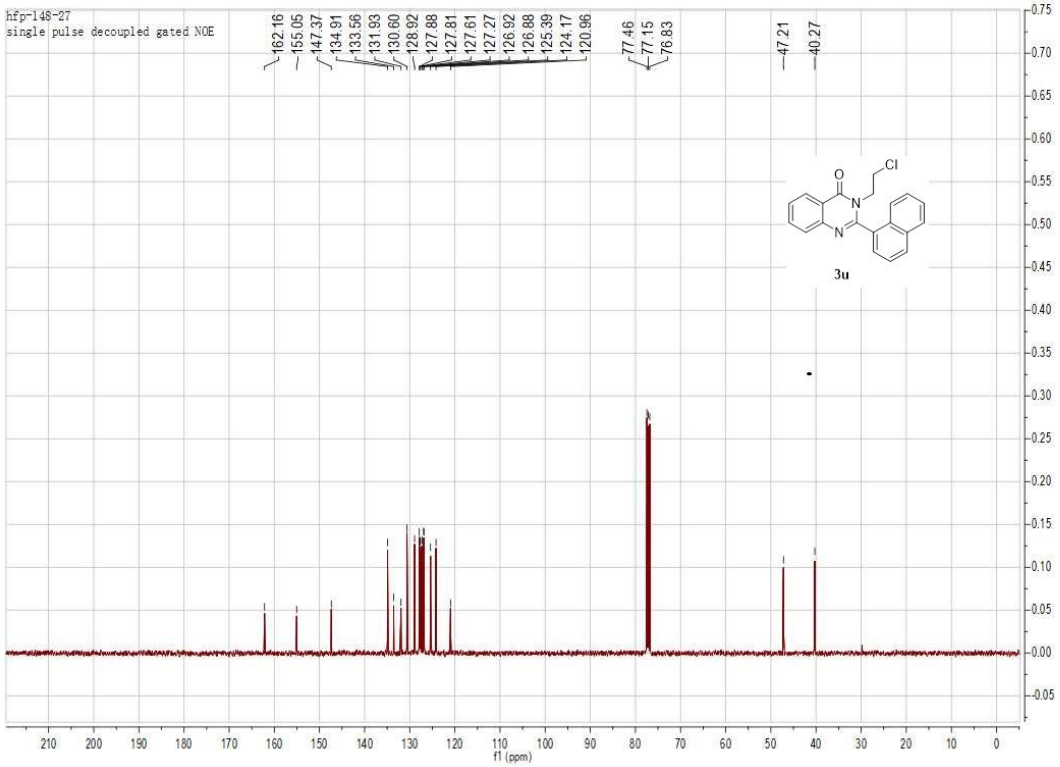

8.32
7.84
7.83
7.82
7.81
7.80
7.80
7.75
7.73
7.58
7.58
7.56
7.54
7.54
7.15
7.13
7.13
7.11
7.11
7.03
7.03
7.02
7.01
7.00
7.00
6.99
6.98
4.37
4.36
3.82
3.80
3.79
0.00
1.00
1.05
1.01
1.04
2.00
0.99
2.06
2.05
f1 (ppm)
3s

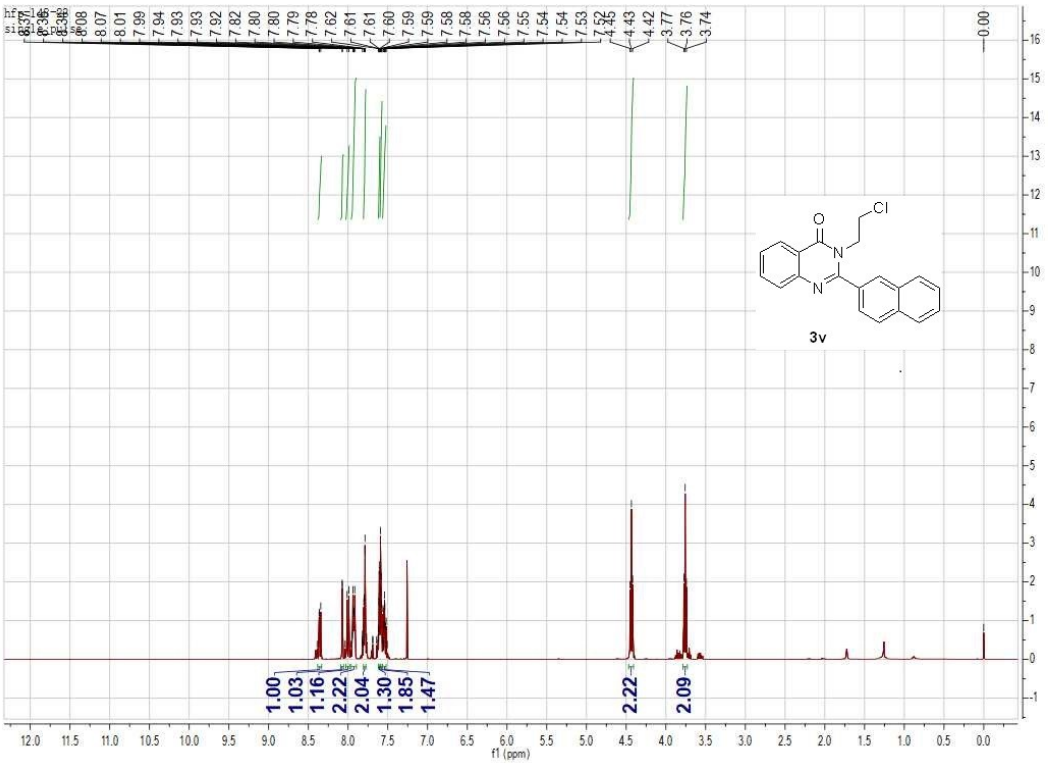

HFP-148-12
single pulse decoupled gated NOE
164.41
164.28
161.93
161.77
153.56
146.82
137.76
135.08
127.90
127.79
126.91
120.80
112.35
112.27
112.16
112.08
106.15
105.90
77.12
76.80
47.41
40.59
f1 (ppm)
3s

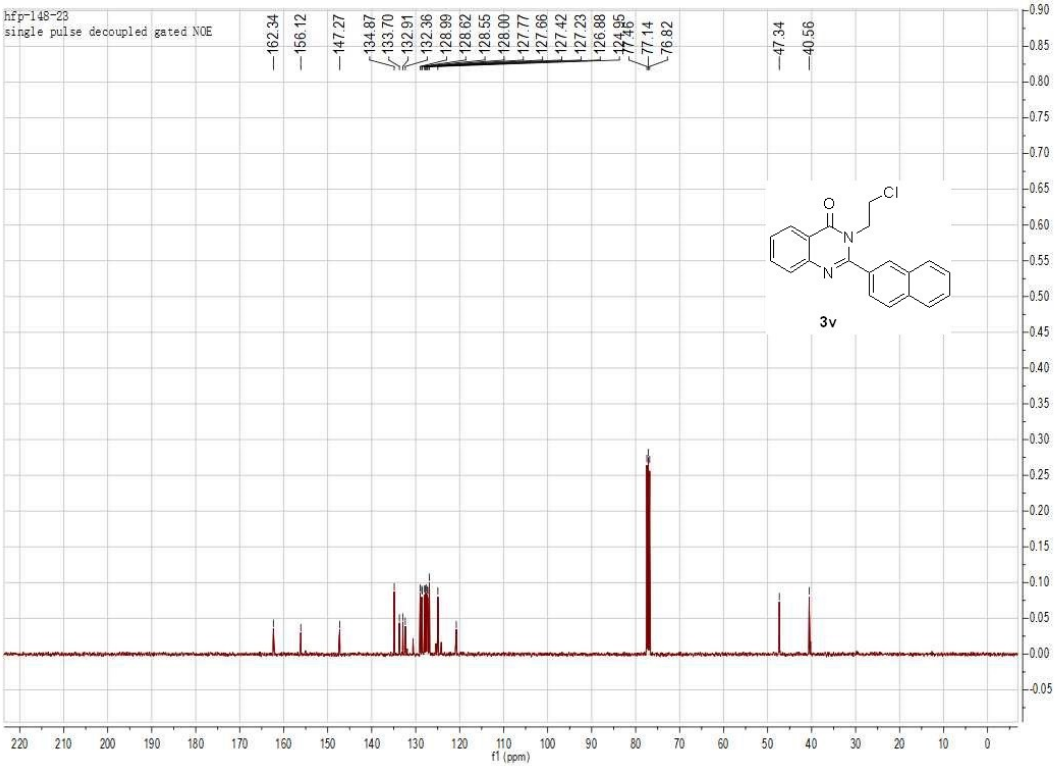

3t
1.00
1.06
1.04
1.03
1.04
1.02
1.04
1.03
1.04
1.04
1.02
f1 (ppm)

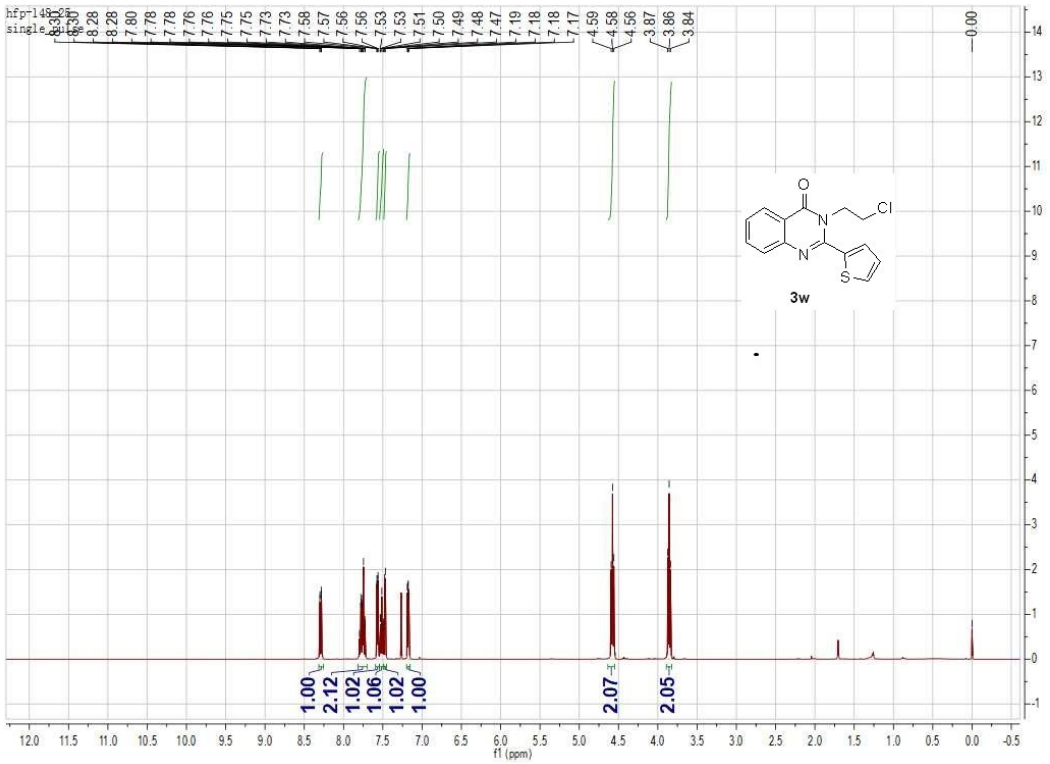

hfp-148-16
single pulse decoupled gated NOE
161.77
152.79
147.12
135.96
134.95
133.84
132.14
131.10
129.41
128.31
127.90
127.84
126.91
121.07
77.45
77.13
76.81
47.25
40.52
3t
f1 (ppm)

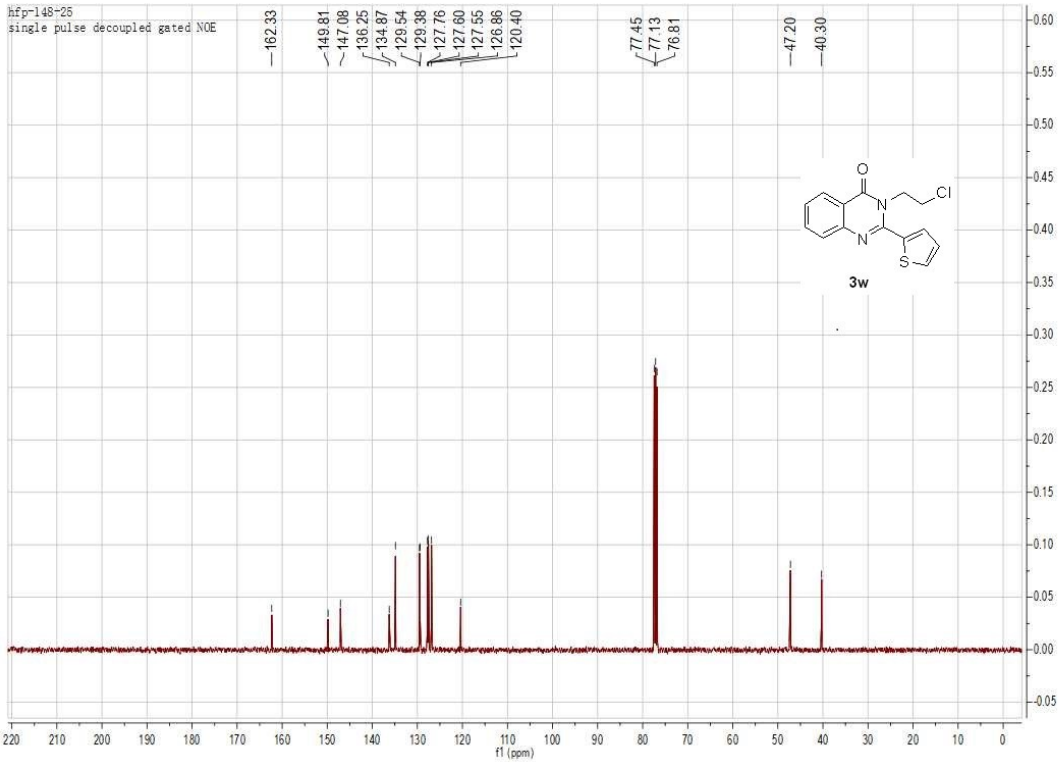

1.00
1.04
1.04
2.13
1.07
1.06
2.03
1.10
0.96
1.02
1.03
1.04
1.02
f1 (ppm)
3u

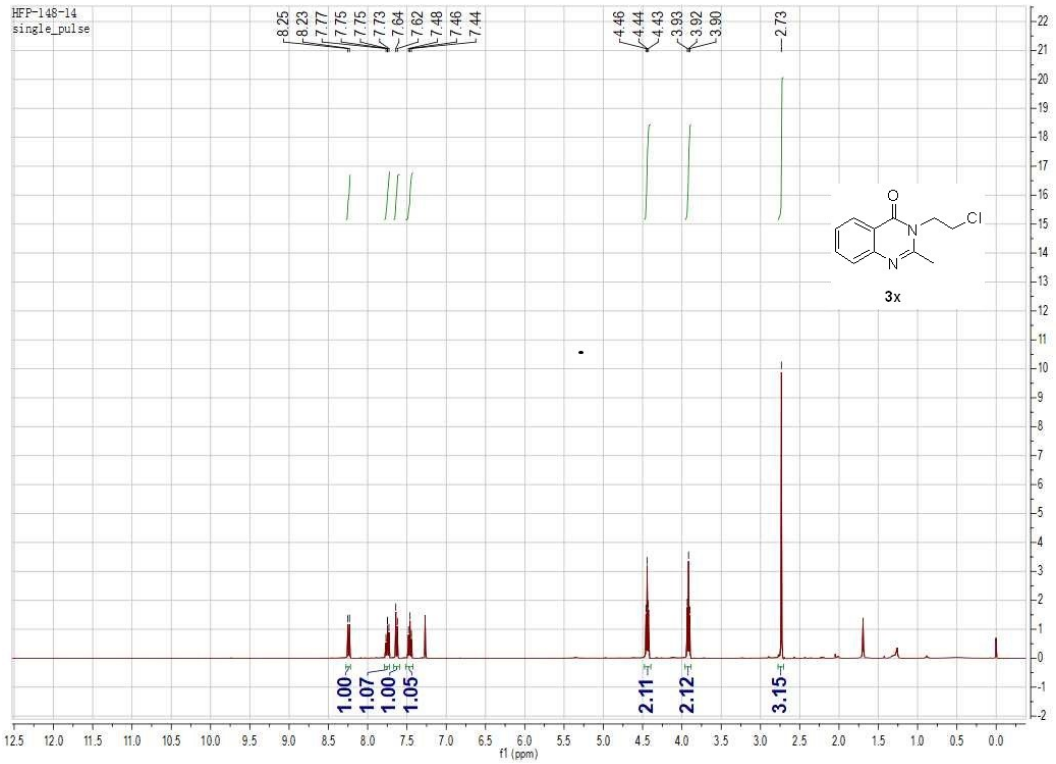

hfp-148-27
single pulse decoupled gated NOE
162.16
155.05
147.37
134.91
133.56
131.93
130.60
128.92
127.88
127.81
127.61
127.27
126.92
126.88
125.39
124.17
120.96
77.46
77.15
76.83
47.21
40.27
f1 (ppm)
3u

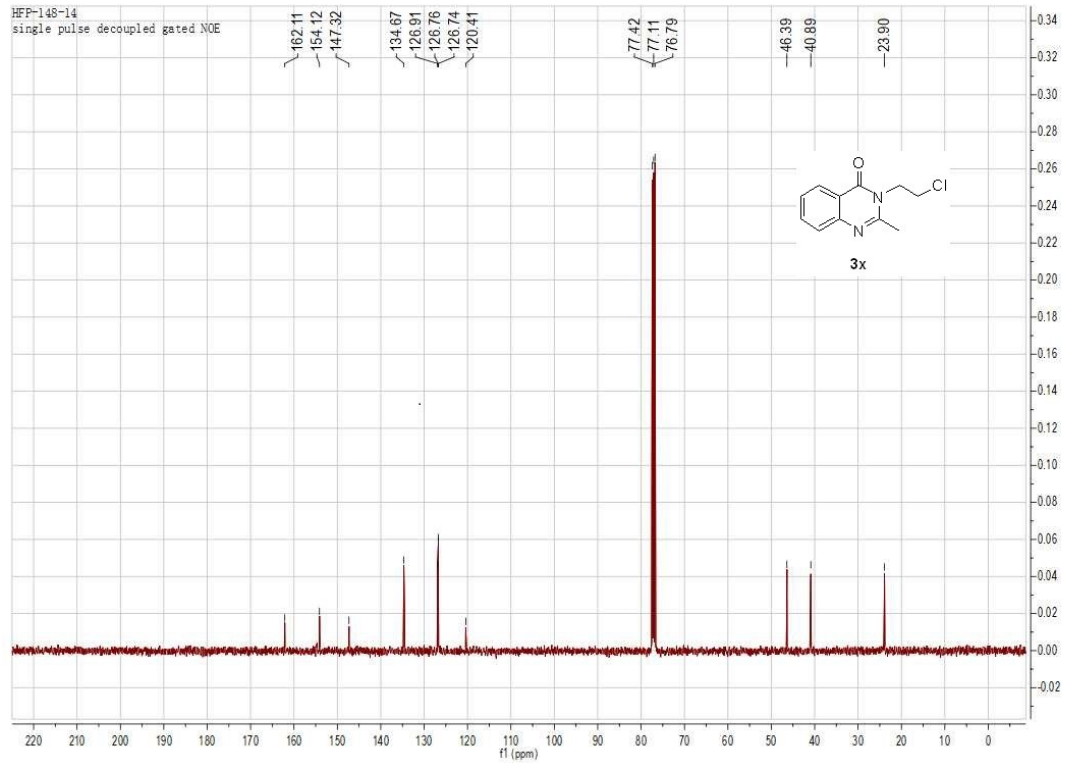

3v
1.00
1.03
1.16
2.22
2.04
1.30
1.85
1.47
2.22
2.09
f1 (ppm)

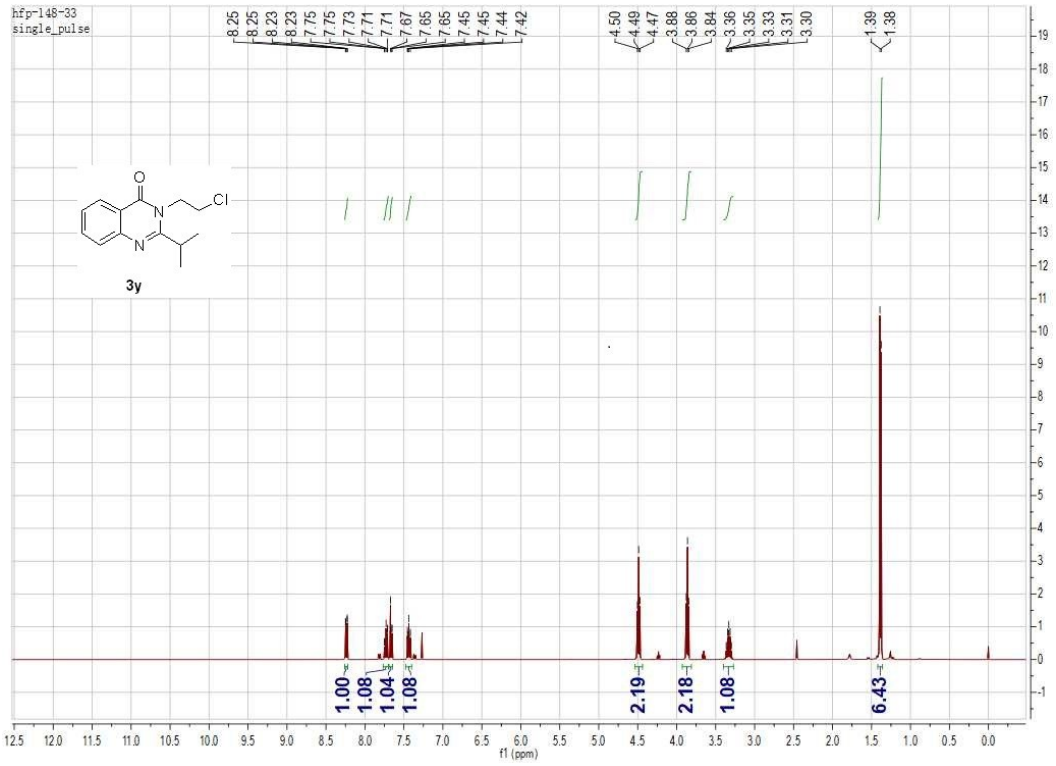

hfp-148-23
single pulse decoupled gated NOE
162.34
156.12
147.27
134.87
133.70
132.91
132.36
128.99
128.62
128.55
128.00
127.77
127.66
127.42
127.23
126.88
124.95
77.46
77.14
76.82
47.34
40.56
3v
f1 (ppm)

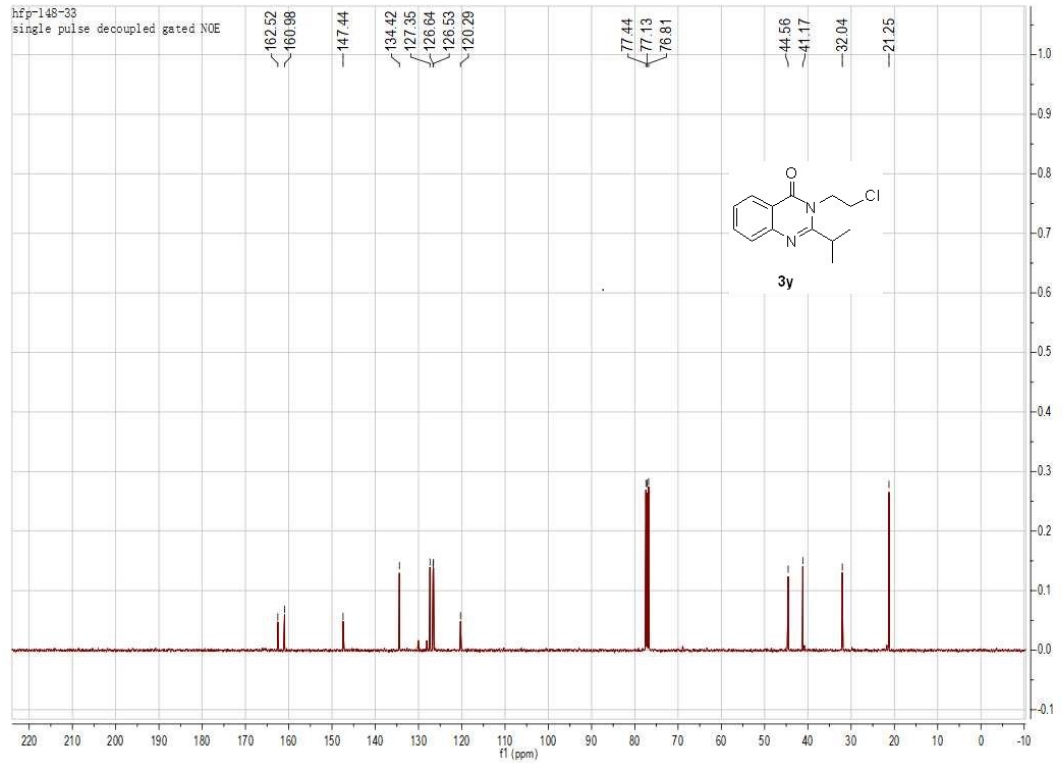

3w
1.00
2.12
1.02
1.06
1.02
1.00
2.07
2.05
f1 (ppm)

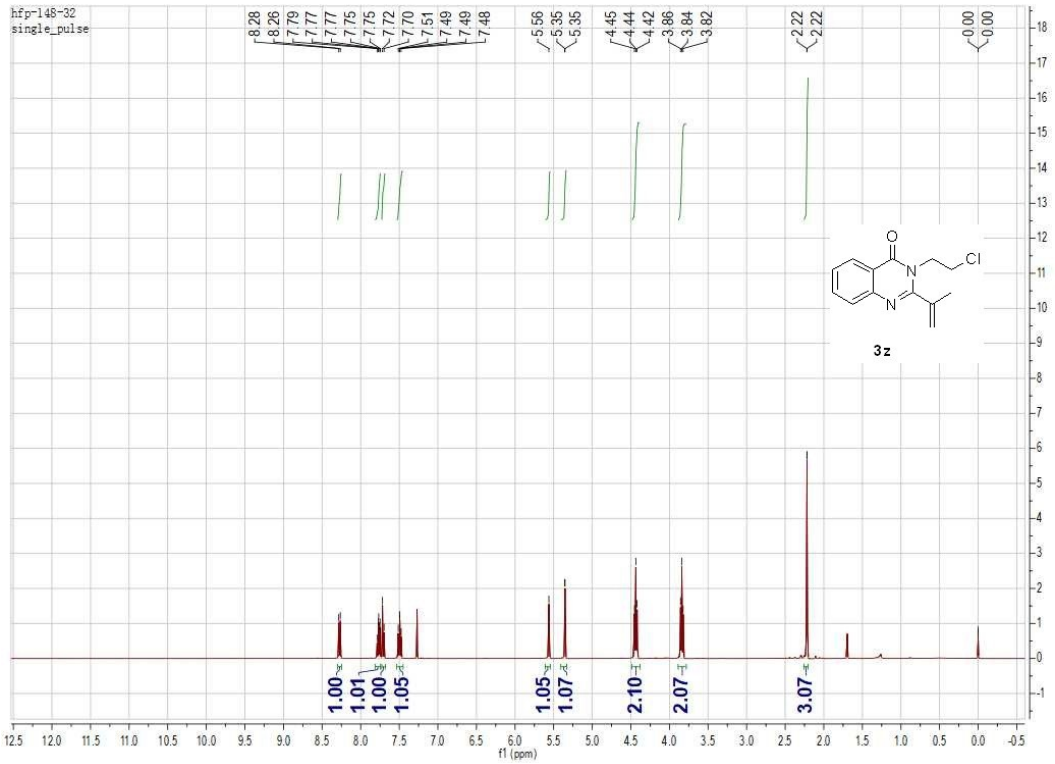

hfp-148-25
single pulse decoupled gated NOE
162.33
149.81
147.08
136.25
134.87
129.54
129.38
127.76
127.60
127.55
126.86
120.40
77.45
77.13
76.81
47.20
40.30
3w
f1 (ppm)

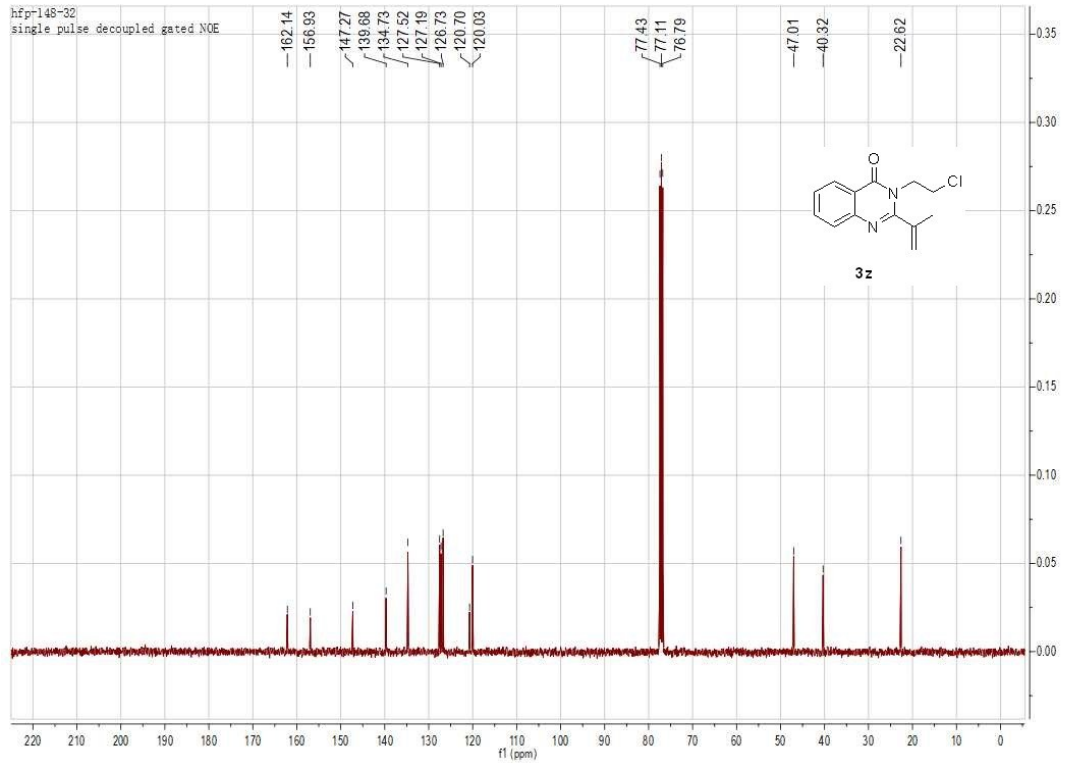

HFP-148-14
single_pulse
8.25
8.23
7.77
7.75
7.75
7.73
7.64
7.62
7.48
7.46
7.44
4.46
4.44
4.43
3.93
3.92
3.90
2.73
1.00
1.07
1.00
1.05
2.11
2.12
3.15
f1 (ppm)
3x

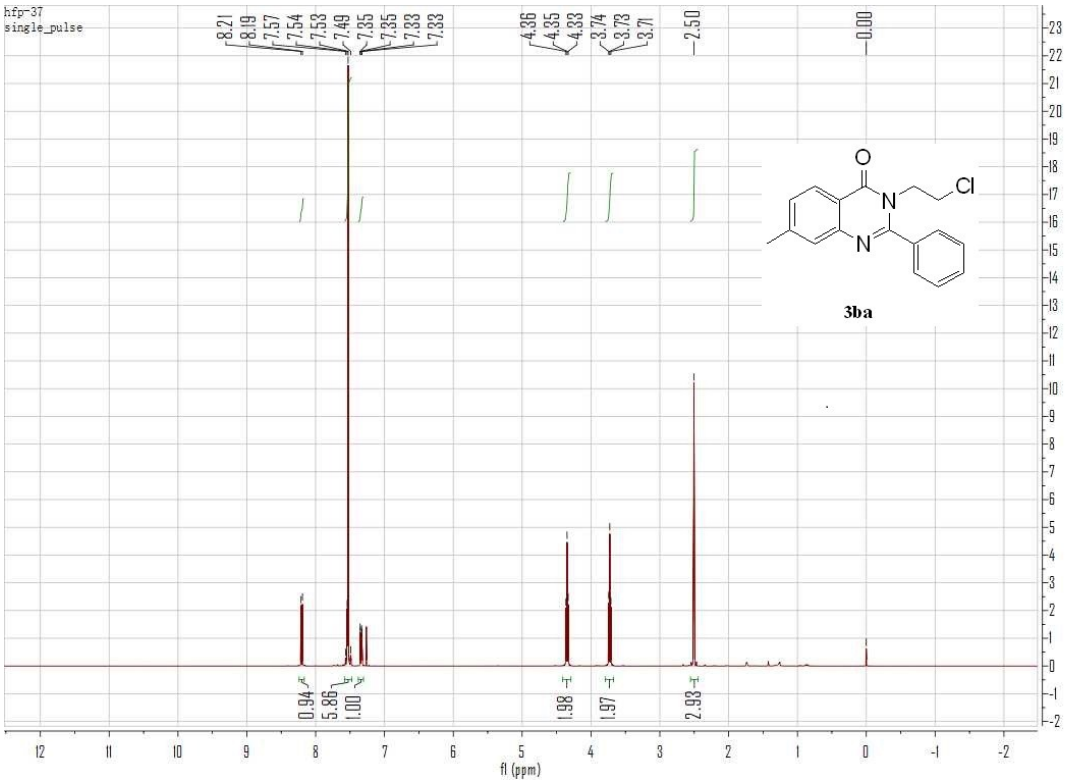

HFP-148-14
single pulse decoupled gated NOE
162.11
154.12
147.32
134.67
126.91
126.76
126.74
120.41
77.42
77.11
76.79
46.39
40.89
23.90
f1 (ppm)
3x

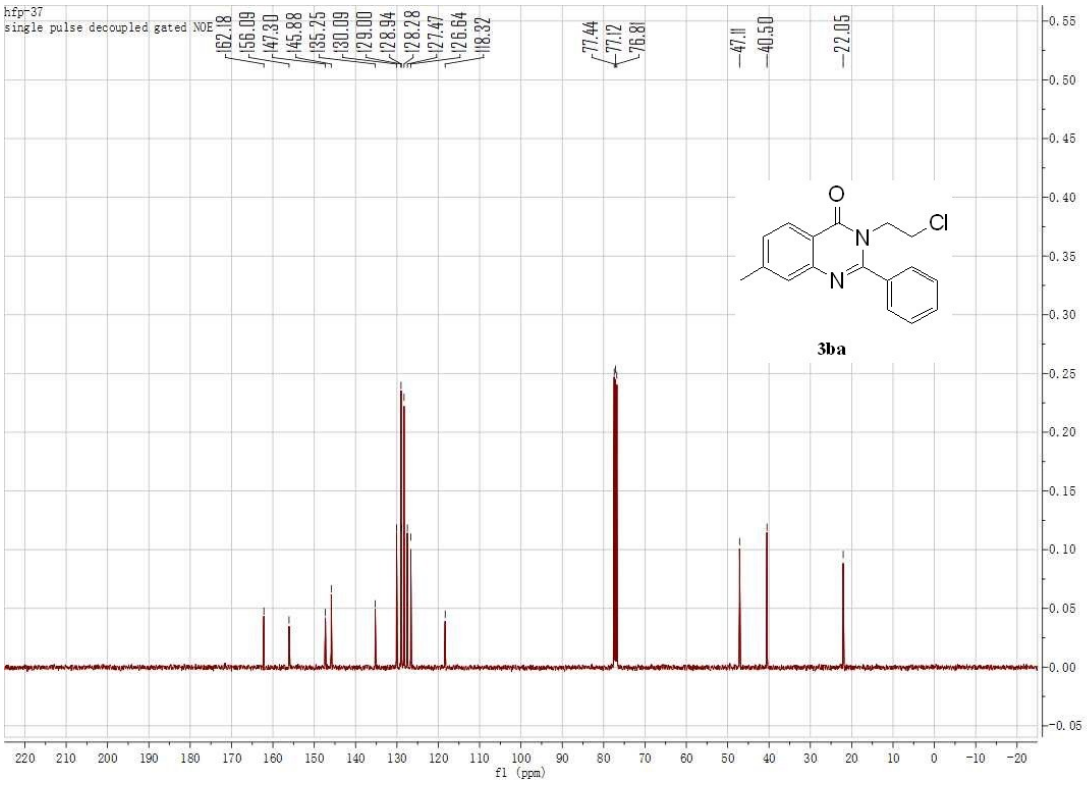

hfp-148-33
single_pulse
8.25
8.25
8.23
8.23
7.75
7.75
7.73
7.71
7.71
7.67
7.65
7.65
7.45
7.45
7.44
7.42
4.50
4.49
4.47
3.88
3.86
3.84
3.36
3.35
3.33
3.31
3.30
1.39
1.38
3y
1.00
1.08
1.04
1.08
2.19
2.18
1.08
6.43
f1 (ppm)

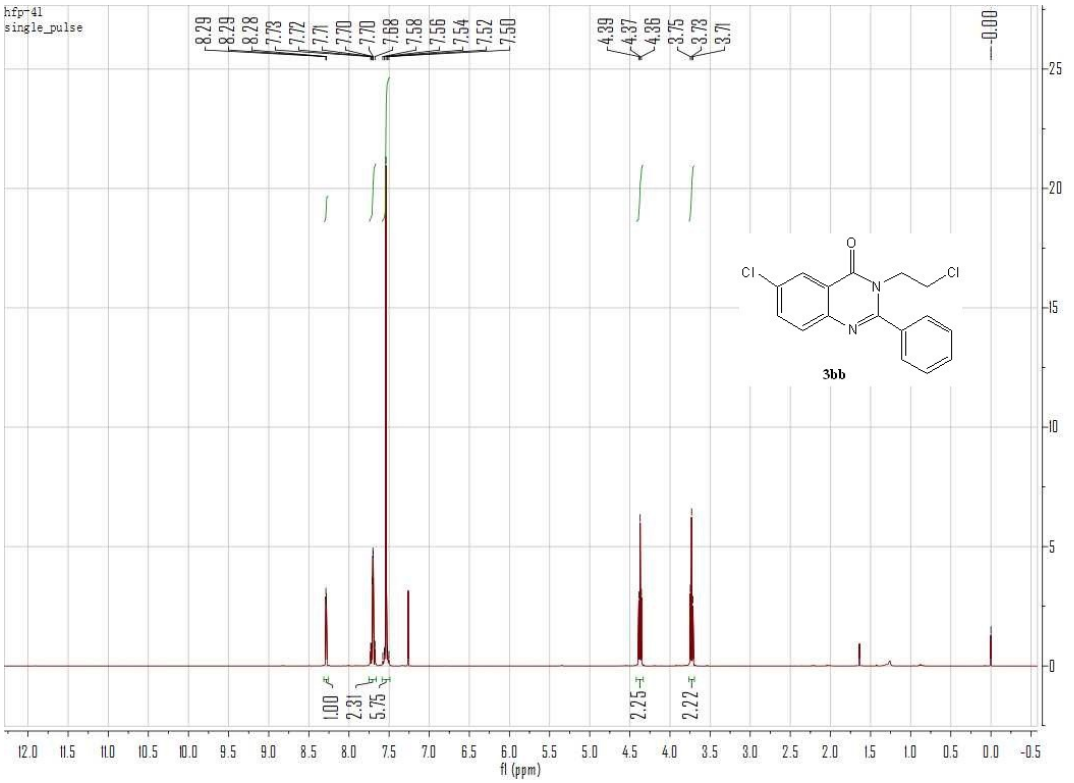

hfp-148-33
single pulse decoupled gated NOE
162.52
160.98
147.44
134.42
127.35
126.64
126.53
120.29
77.44
77.13
76.81
44.56
41.17
32.04
21.25
3y
f1 (ppm)

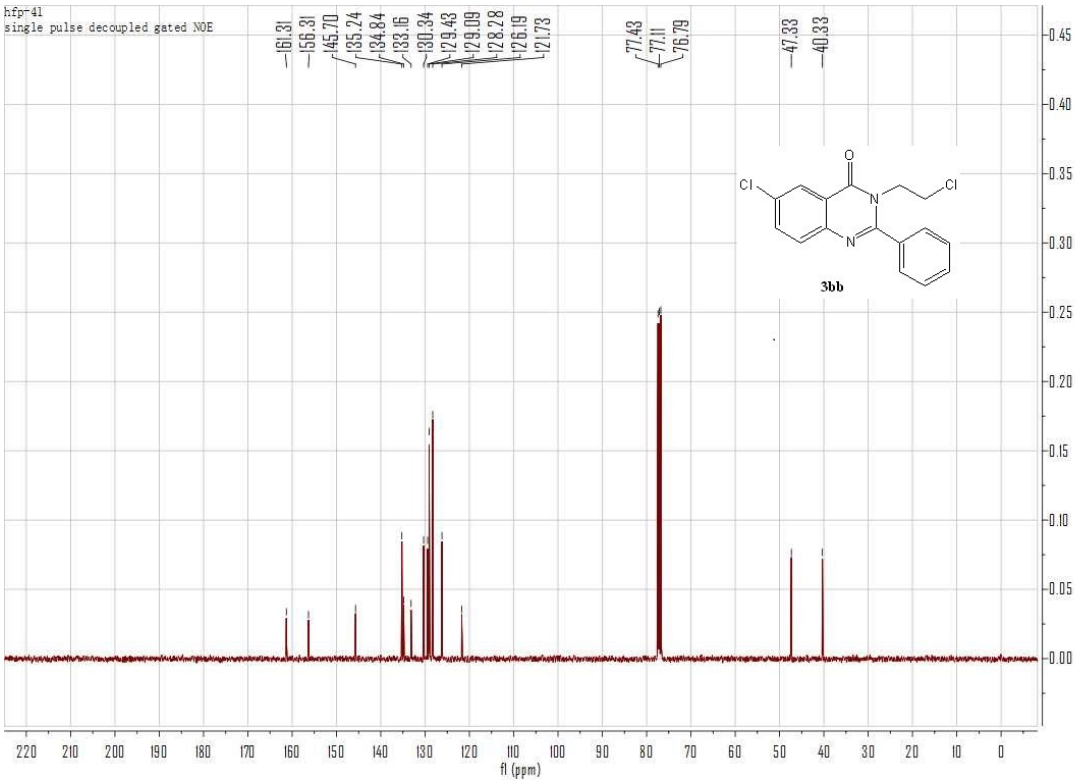

hfp-148-32
single_pulse
8.28
8.26
7.79
7.77
7.77
7.75
7.75
7.72
7.70
7.51
7.49
7.49
7.48
5.56
5.35
5.35
4.45
4.44
4.42
3.86
3.84
3.82
2.22
2.22
0.00
0.00
1.00
1.01
1.00
1.05
1.05
1.07
2.10
2.07
3.07
f1 (ppm)
3z

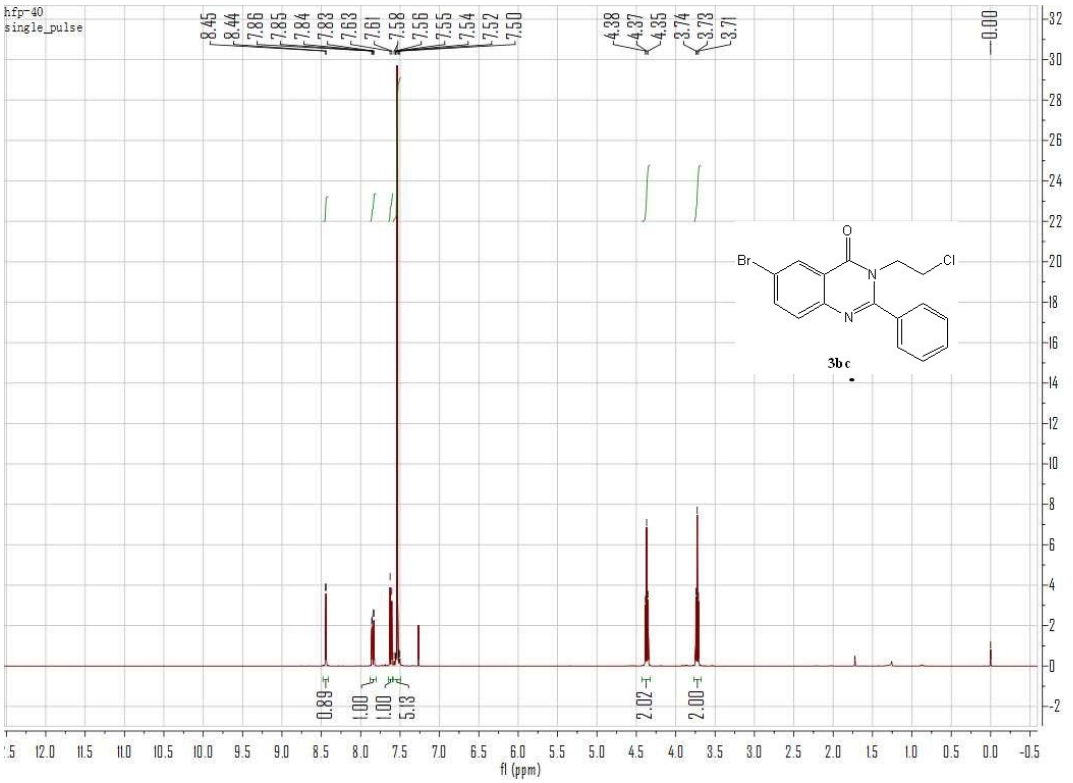

hfp-148-32
single pulse decoupled gated NOE
162.14
156.93
147.27
139.68
134.73
127.52
127.19
126.73
120.70
120.03
77.43
77.11
76.79
47.01
40.32
22.62
f1 (ppm)
3z

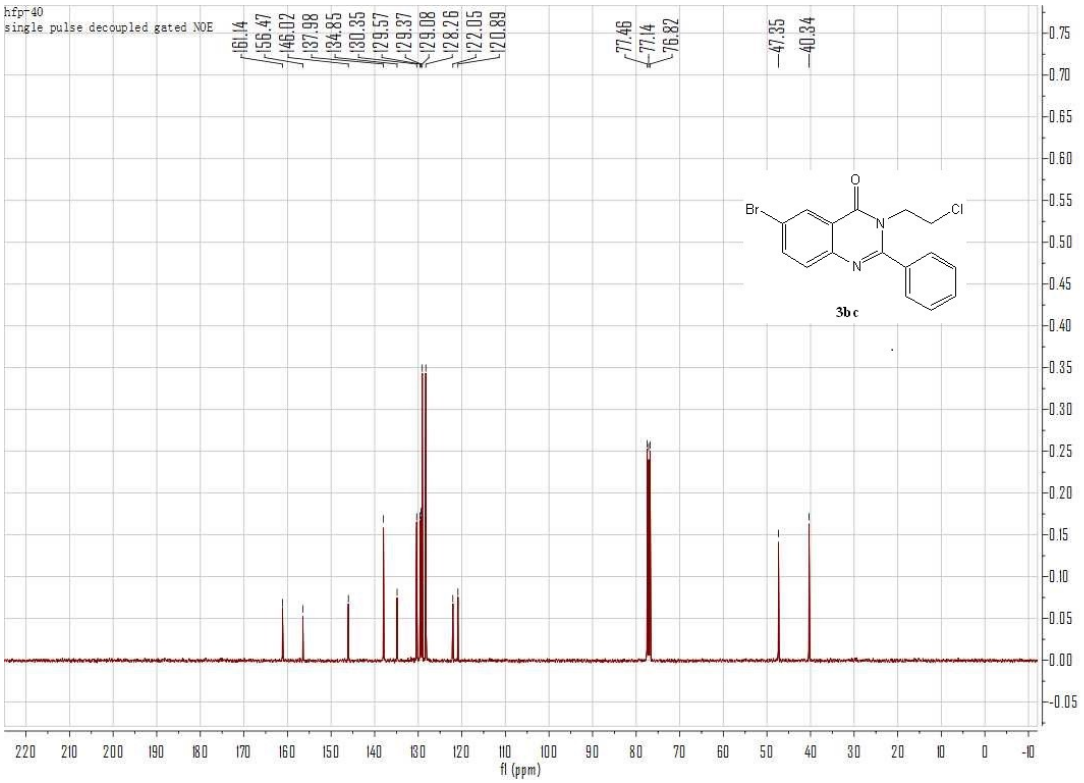

hfp-37
single_pulse
8.21
8.19
7.57
7.54
7.53
7.49
7.35
7.35
7.33
7.33
4.36
4.35
4.33
3.74
3.73
3.71
2.50
0.00
0.94
5.86
1.00
1.98
1.97
2.93
f1 (ppm)
O
N
Cl
N
3ba

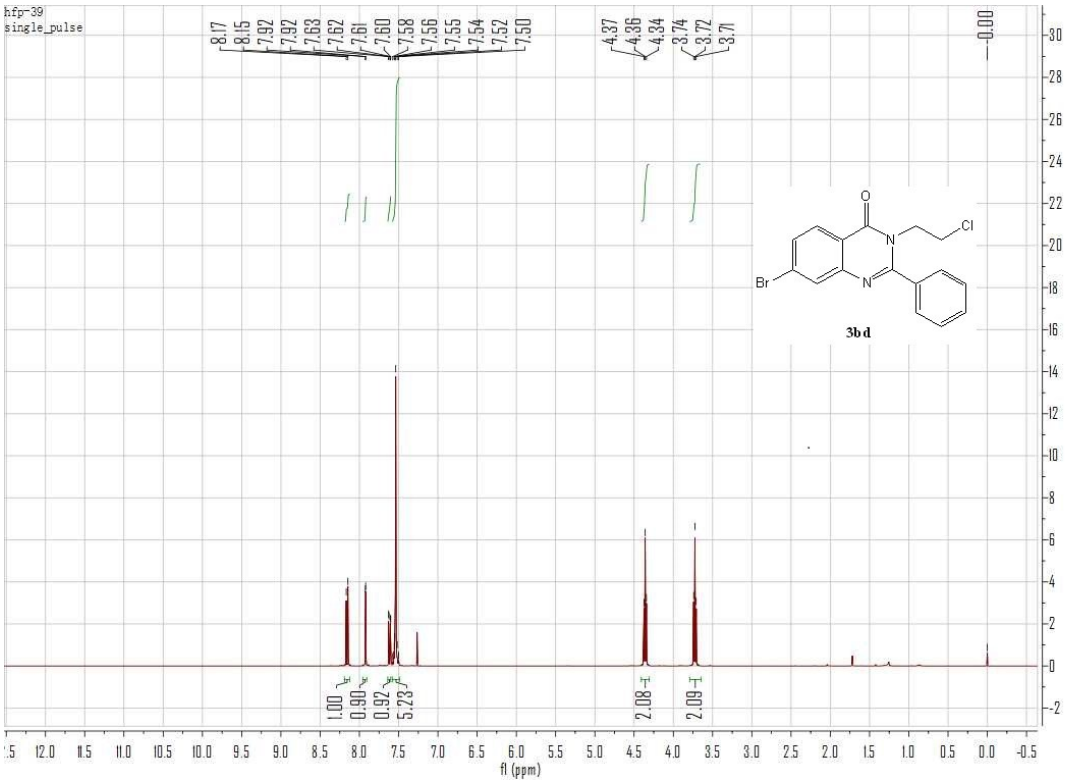

hfp-37
single pulse decoupled gated NOE
162.18
156.09
147.30
145.88
135.25
130.09
129.00
128.94
128.28
127.47
126.64
118.32
77.44
77.12
76.81
47.11
40.50
22.05
f1 (ppm)
O
N
Cl
N
3ba

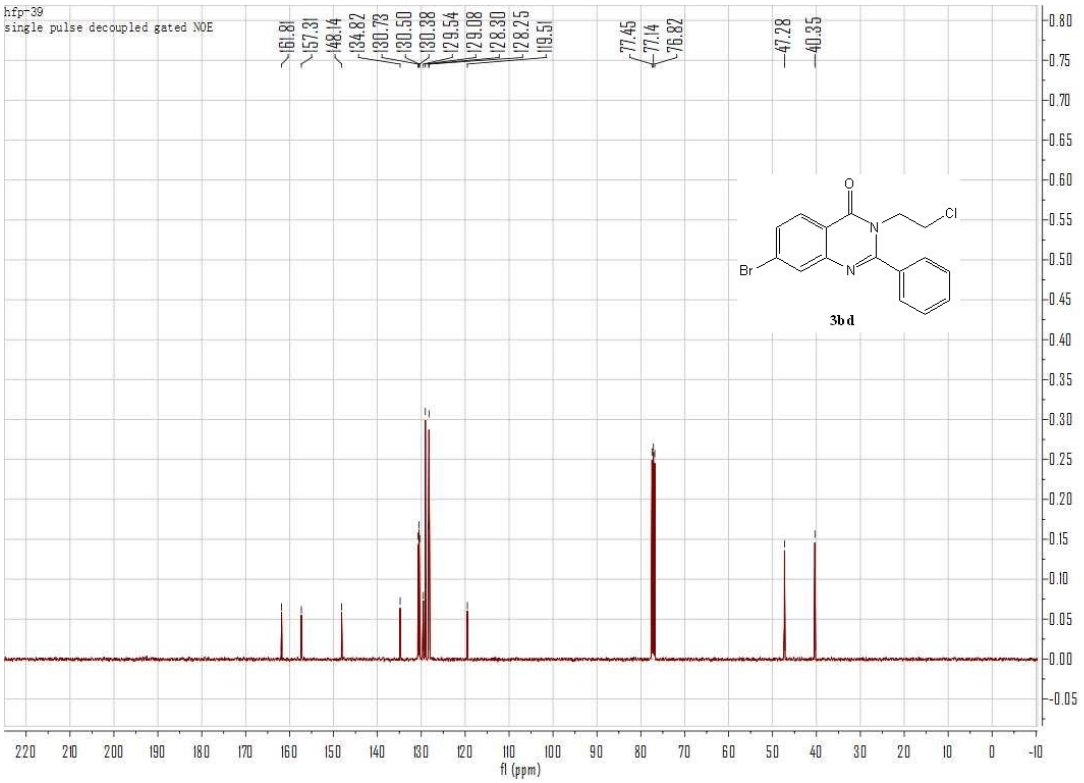

hfp-41
single_pulse
8.29
8.29
8.28
7.73
7.72
7.71
7.70
7.70
7.68
7.58
7.56
7.54
7.52
7.50
4.39
4.37
4.36
3.75
3.73
3.71
0.00
1.00
2.31
5.75
2.25
2.22
f1 (ppm)
3bb

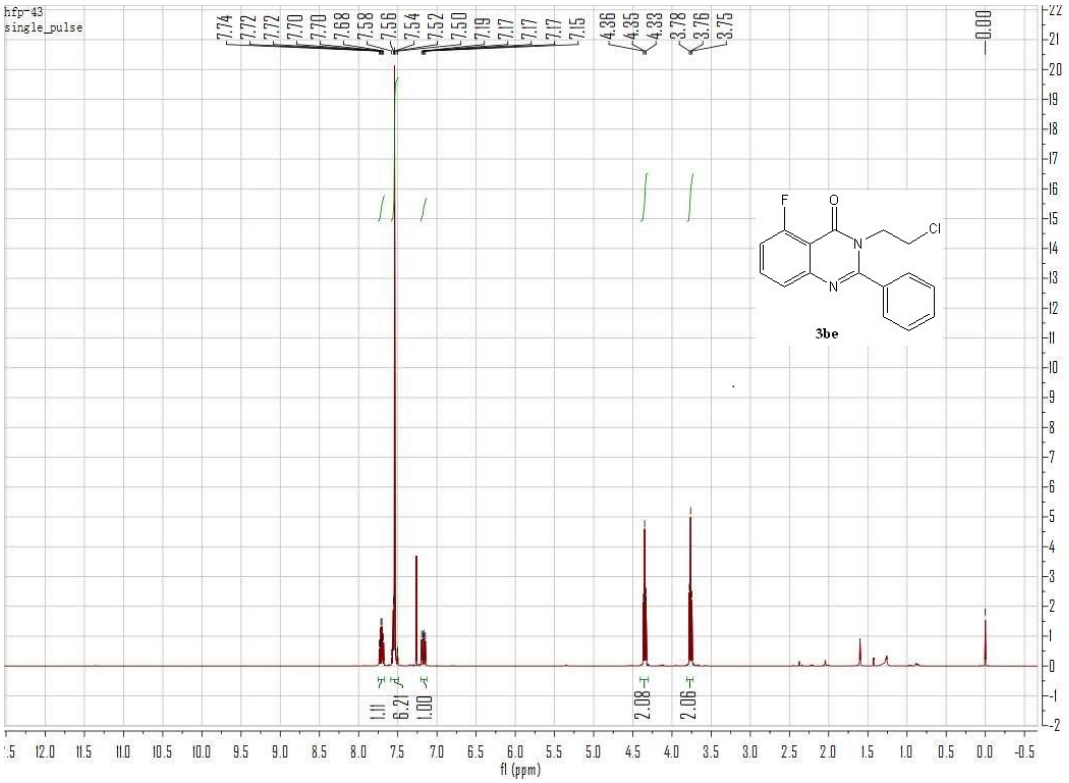

hfp-41
single pulse decoupled gated NOE
161.31
156.31
145.70
135.24
134.84
133.16
130.34
129.43
129.09
128.28
126.19
121.73
77.43
77.11
76.79
47.33
40.33
f1 (ppm)
3bb

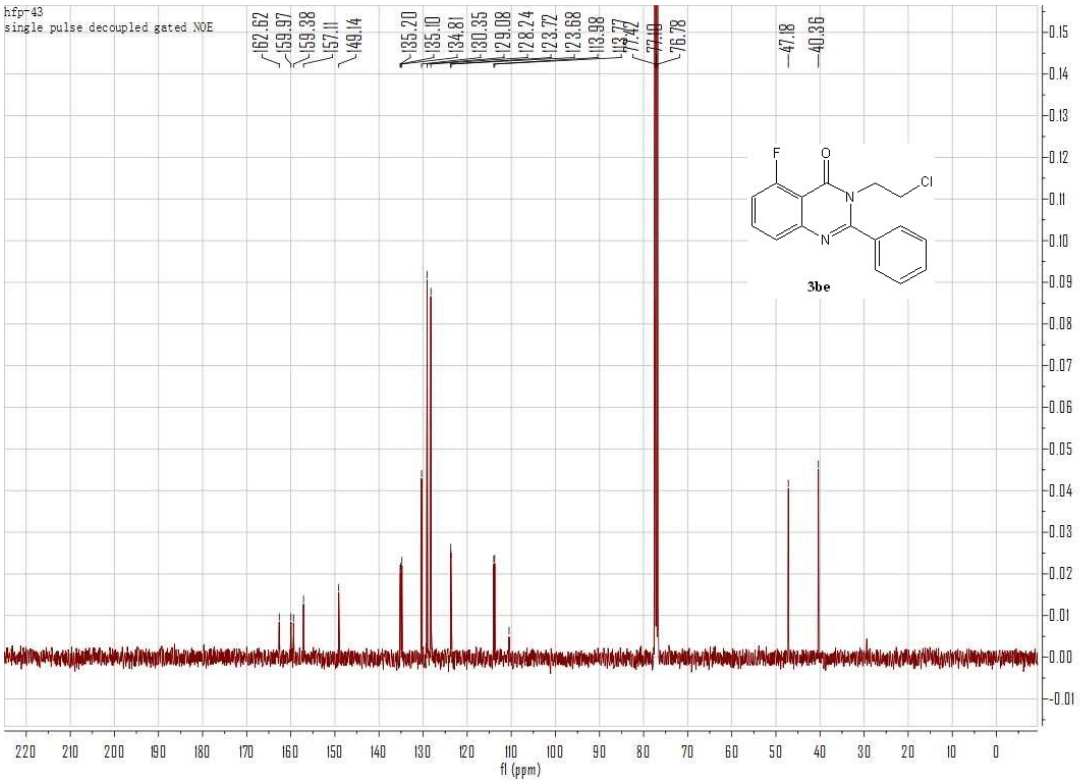

hfp-40
single_pulse
8.45
8.44
7.86
7.85
7.84
7.83
7.63
7.61
7.58
7.56
7.55
7.54
7.52
7.50
4.38
4.37
4.35
3.74
3.73
3.71
0.00
0.89
1.00
1.00
5.13
2.02
2.00
f1 (ppm)
Br
Cl
O
N
N
3bc


hfp-40
single pulse decoupled gated NOE
161.14
156.47
146.02
137.98
134.85
130.35
129.57
129.37
129.08
128.26
122.05
120.89
77.46
77.14
76.82
47.35
40.34
f1 (ppm)
Br
Cl
O
N
N
3bc


hfp-39
single_pulse
8.17
8.15
7.92
7.92
7.63
7.62
7.61
7.60
7.58
7.56
7.55
7.54
7.52
7.50
4.37
4.36
4.34
3.74
3.72
3.71
0.00
1.00
0.90
0.92
5.23
2.08
2.09
f1 (ppm)
O
N
Cl
Br
N
3b d


hfp-39
single pulse decoupled gated NOE
161.81
157.31
148.14
134.82
130.73
130.50
130.38
129.54
129.08
128.30
128.25
119.51
77.45
77.14
76.82
47.28
40.35
f1 (ppm)
O
N
Cl
Br
N
3b d


hfp-43
single_pulse
7.74
7.72
7.72
7.70
7.70
7.68
7.58
7.56
7.54
7.52
7.50
7.19
7.17
7.17
7.17
7.15
4.36
4.35
4.33
3.78
3.76
3.75
0.00
F
O
N
N
Cl
3be
1.11
6.21
1.00
2.08
2.06
f1 (ppm)


hfp-43
single_pulse decoupled gated NOE
162.62
159.97
159.38
157.11
149.14
135.20
135.10
134.81
130.35
129.08
128.24
123.72
123.68
113.98
113.77
113.42
77.10
76.78
47.18
40.36
F
O
N
N
Cl
3be
f1 (ppm)