New Journal of Chemistry

Synthesis of 1,2,4-Oxadiazolidines via [3+2] Cycloaddition of Nitrones with Carbodiimides

Supporting information

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Content

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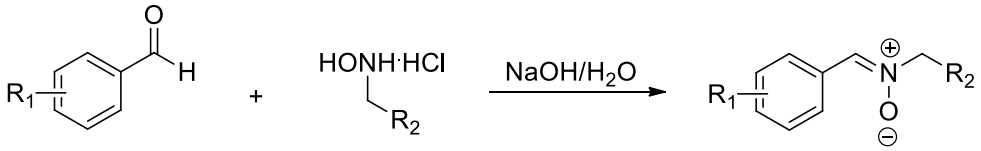
1 General Information

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring, unless otherwise specified. Dichloromethane was purified by passage through a bed of activated alumina. All other reagents and solvents were purchased from Sigma-Aldrich or J&K Chemical Company and used without any further purification. TLC information was recorded on GF 254 (Qingdao Haiyang Chemical Co., Ltd. P. R. China) plates and developed by staining with $KMnO_4$ or ceric ammonium molybdate (CAM). Purification of reaction products was carried out by flash chromatography using Silica gel (200 - 300 mesh, Qingdao Haiyang Chemical Co. Ltd. P. R. China). ^1H NMR spectra were measured on Varian 400 (400 MHz), spectrometers and are reported in ppm (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad; integration; coupling constant(s) in Hz), using TMS as an internal standard (TMS at 0.00 ppm) in $CDCl_3$. ^{13}C NMR spectra were recorded on V400 spectrometer and reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). High-resolution mass spectra were obtained using an Agilent 6230 TOF LC/MS with an (atmospheric pressure photo-ionization (APPI) or electrospray (ESI) source with purine and HP-0921 as an internal calibrants. HRMS (EI) was performed on an API-Qstar-Pulsar-1 spectrometer. Melting points were determined on a digital melting-point apparatus and uncorrected.

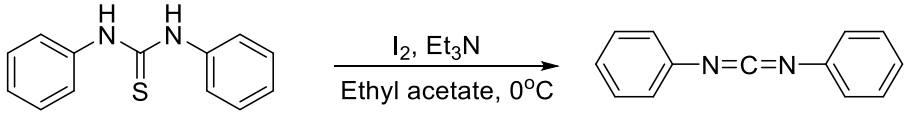
2.2 General procedure A for the synthesis of nitrones



R_1= H, Cl, F,CH_3, OCH_3, NO_2
R_2= H, Ph

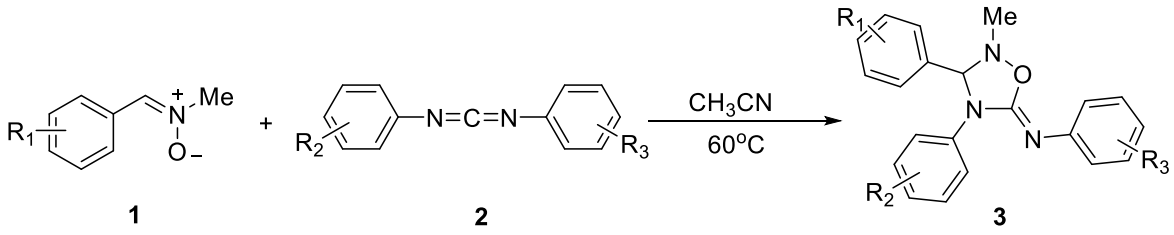
To a solution of hydroxylamine hydrochloride (1.0 mmol) in the water (2.0 mL) was added aldehyde (1.0 mmol) and NaOH (1.0 mmol), the reaction mixture was stirred at room temperature until completion, the aqueous phase extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phase was dried over $MgSO_4$ and concentrated in vacuo to give nitrones.

2.2 General procedure B for the synthesis of carbodiimides



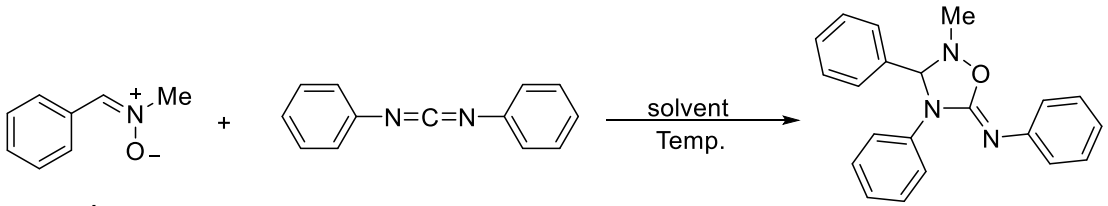
To a stirred and ice-cooled solution of 1,3-diphenylthiourea (2 mmol) in ethyl acetate (5 mL), was added triethylamine (4 mmol). To this was added iodine (2.2 mmol) portion-wise over a period of 30 min. A light yellow colour precipitate of sulfur started separating out during this period. The precipitated sulfur was filtered, the organic layer evaporated and then extracted with hexane (3 x 10 mL). The solution was concentrated under reduced pressure and purified by eluting through a short column of silica gel (100% hexane) to give oily carbodiimide (80%).

2.3 General procedure C for the [3+2]-cycloaddition of nitrones with carbodiimides:



To a solution of nitrones **1** (1.5 mmol) in CH_3CN (2.0 mL) was added carbodiimide **2** (1.0 mmol.) and stirred at 60°C and the reaction progress monitored by TLC (hexane : ethyl acetate = 10:1) until complete consumption of the carbodiimide (reaction time: see substrate tables). The mixture was filtered through the short pad of celite and the filtrate was concentrated under reduced pressure. The residue was purified via flash column chromatography (hexane : ethyl acetate = 100:1 to 20:1) to provide the desired cycloadducts.

2.1 Optimization of reaction conditions (Table 1)



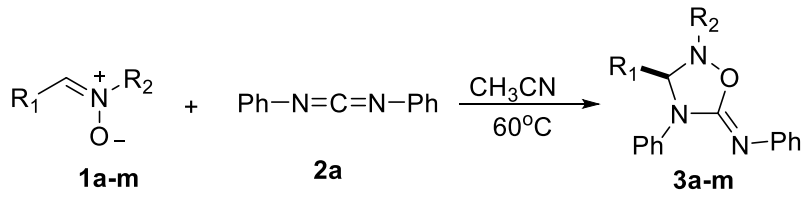
Entry[a]	Solvent	T/°C	T/h	Yilde[b]
1	CH_3CN	110	4	40%
2	CH_3CN	80	4	56%
3	CH_3CN	60	4	89%
4	CH_3CN	50	4	64%
5	CH_3CN	r.t.	24	24%
6	Tol.	60	24	50%
7	DMF	60	24	<5%
8	DMSO	60	24	<5%
9	1,4-dioxane	60	4	69%
10	CH_3CH_2OH	60	24	<5%
11	CH_3OH	r.t.	24	<5%
12	CH_3CO_2Et	r.t.	24	<5%
13	DCM	r.t.	24	<5%
14	THF	r.t.	24	<5%

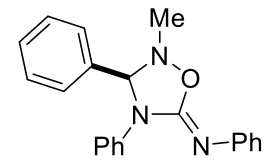
15	TFIP	r.t.	24	<5%

a Reaction conditions: a mixture of **1a** (1.5 mmol), **2a** (1.0 mmol) in solvent (2 mL) was stirred at the setting temperature for a certain period of time.

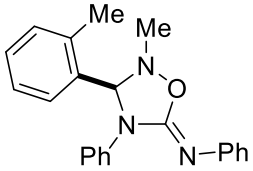
b Yield of isolated product.

Table 2. Scope of nitrones.[a]

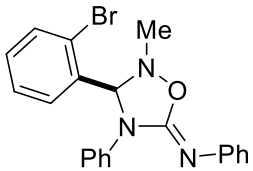




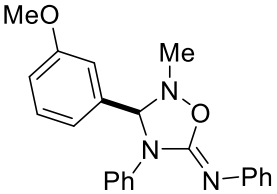
3a, 89%



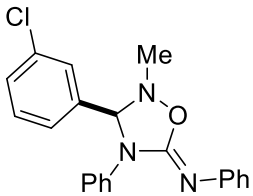
3b, 85%



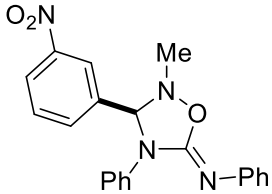
3c, 85%



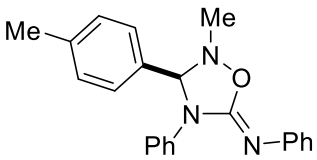
3d, 90%



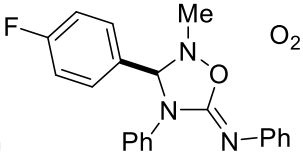
3e, 85%



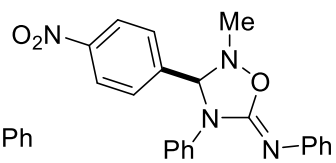
3f, 80%



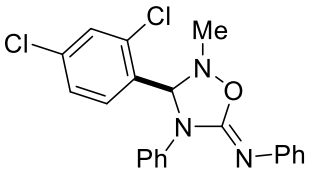
3g, 87%



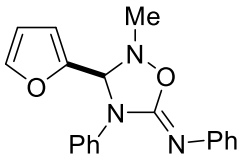
3h, 84%



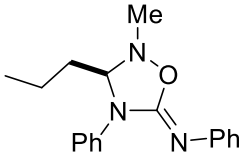
3i, 83%



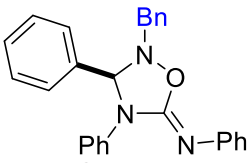
3j, 84%



3k, 89%

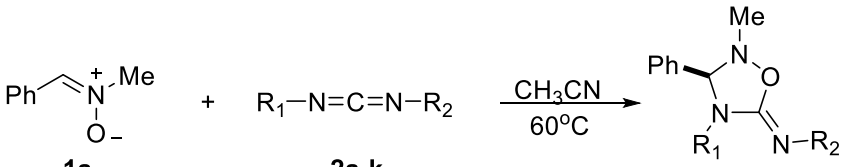


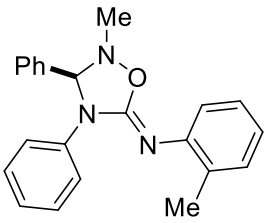
3l, 75%



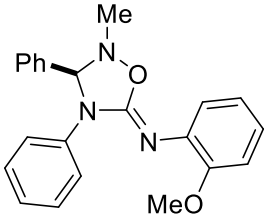
3m, 70%

Table 3. Scope of carbodiimides.[a]

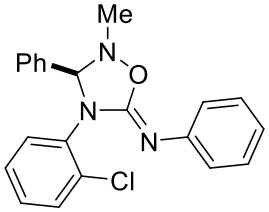




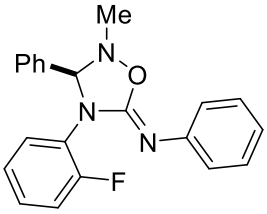
4a, 86%



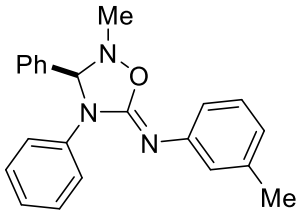
4b, 90%



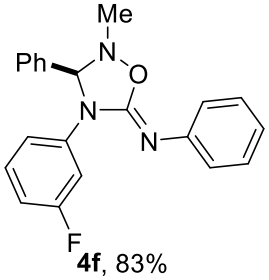
4c, 79%



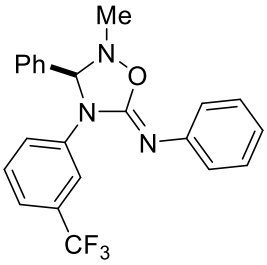
4d, 81%



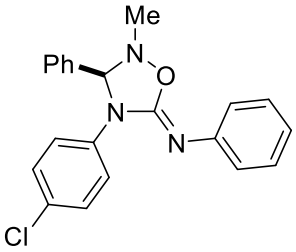
4e, 76%



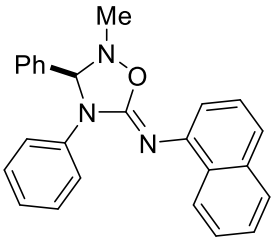
4f, 83%



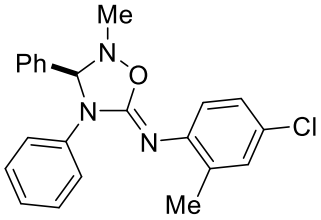
4g, 81%



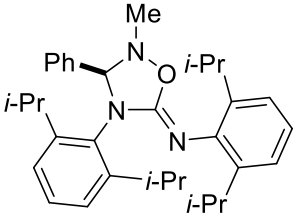
4h, 80%



4i, 81%

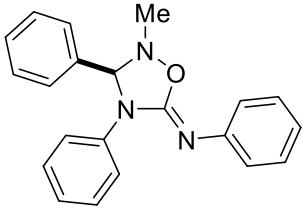


4j, 86%

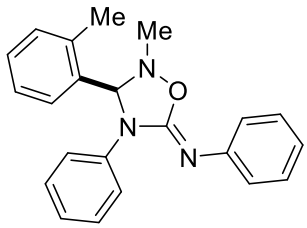


4k, 66%

3. Structure characterization

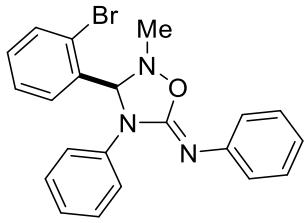


(R,Z)-2-methyl-N,3,4-triphenyl-1,2,4-oxadiazolidin-5-imine (**3a**) White solid, m. p. 78-80°C, 89% yield. Reaction time 4h.^{1}HNMR (400 MHz, $CDCl_3$): δ 7.60-7.58 (m, 2H), 7.48-7.40 (m, 5H), 7.35-7.31 (m, 4H), 7.30-7.28 (m, 2H) ,7.21-7.03 (m ,2H), 5.60 (s,1H), 3.06 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 147.6, 146.1, 138.2, 136.2, 129.6, 129.0, 128.6, 127.1, 124.1, 123.5, 122.9, 120.7, 85.1, 45.9. HRMS (EI) *m/z* 352.1428 $[M+Na]^+$ (calcd for $C_{21}H_{19}N_3ONa$ 352.1426).



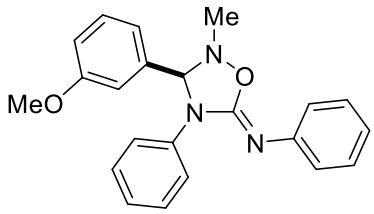
(R,Z)-2-methyl-N,4-diphenyl-3-(o-tolyl)-1,2,4-oxadiazolidin-5-imine(**3b**)

White solid, m. p. 84-85°C, 85% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.59 (m, 2H), 7.36-7.28 (m, 7H), 7.24-7.03 (m, 5H), 5.83 (s, 1H), 3.07 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 138.4, 136.3, 133.8, 131.3, 129.3, 129.0, 128.6, 125.9, 123.7, 123.6, 123.0, 119.5, 82.2, 46.1, 19.2. HRMS (EI) *m/z* 366.1584 $[M+Na]^+$ (calcd for $C_{22}H_{21}N_3ONa$ 366.1582).



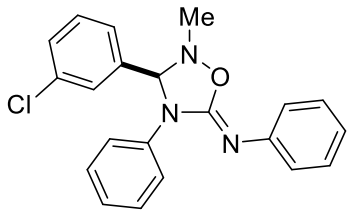
(R,Z)-3-(2-bromophenyl)-2-methyl-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3c**)

Coloeless oil, 85% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.62 (m, 3H), 7.42-7.21(m, 8H), 7.13-7.04 (m, 2H), 6.09 (s, 1H), 3.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 145.8, 138.1, 133.6, 130.9, 129.1, 128.6, 128.2, 127.6, 123.8, 123.6, 123.5, 123.1, 119.2, 83.1, 46.5. HRMS (EI) *m/z* 430.0531 $[M+Na]^+$ (calcd for $C_{21}H_{18}N_3ONa$ 430.0531).



(R,Z)-3-(3-methoxyphenyl)-2-methyl-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3d**)

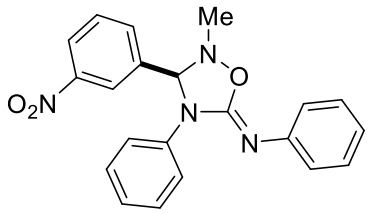
White solid, m. p. 75-77°C, 90% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.58 (m, 2H), 7.35-7.19 (m, 5H), 7.13-6.92 (m, 7H), 5.57 (s, 1H), 3.81 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 146.1, 138.2, 130.1, 129.0, 128.6, 124.2, 123.5, 122.9, 120.8, 119.4, 115.2, 112.5, 85.1, 55.3, 45.9. HRMS (EI) *m/z* 382.1531 $[M+Na]^+$ (calcd for $C_{22}H_{21}N_3O_2Na$ 382.1531).



(R,Z)-3-(3-chlorophenyl)-2-methyl-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3e**)

White solid, m. p. 74-76°C, 85% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.57 (m, 2H), 7.47 (s, 1H), 7.40-7.28 (m, 7H), 7.19-7.04 (m, 4H), 5.58 (s, 1H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 146.1, 138.0, 135.0, 130.3, 129.8, 129.2, 128.6, 127.4, 125.1, 124.4, 123.5, 123.5, 123.1, 120.5, 84.3, 46.0.

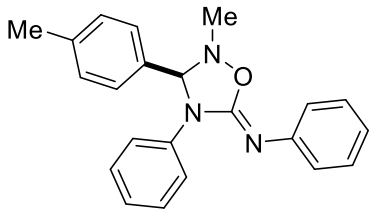
HRMS (EI) *m/z* 386.1034 $[M+Na]^+$ (calcd for $C_{21}H_{18}ClN_3ONa$ 386.1036).



(R,Z)-2-methyl-3-(3-nitrophenyl)-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3f**)

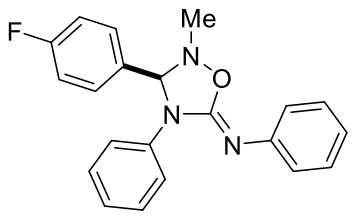
White solid, m. p. 84-86°C, 80% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37-8.36 (m, 1H), 8.29-8.26 (m, 1H), 7.78-7.76 (m, 1H), 7.62-7.58 (m, 3H), 7.39-7.29 (m, 4H), 7.19-7.07 (m, 4H), 5.74 (s, 1H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6, 145.6, 137.8, 132.8, 130.2, 129.4, 128.7, 124.7, 123.4, 123.3, 122.6, 120.5, 83.6, 29.7. HRMS (EI) *m/z*

397.1274 $[M+Na]^+$ (calcd for $C_{21}H_{18}N_4O_3Na$ 397.1277).



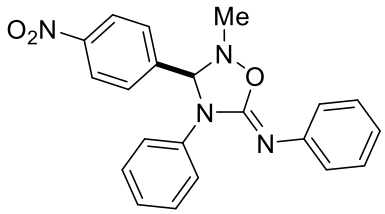
(R,Z)-2-methyl-N,4-diphenyl-3-(p-tolyl)-1,2,4-oxadiazolidin-5-imine(**3g**)

White solid, m. p. 71-73°C, 87% yield. Reaction time 4h. ^1H NMR (400 MHz, $CDCl_3$): δ 7.59-7.57 (d, 2H, *J* = 8.0 Hz), 7.36-7.30 (m, 6H), 7.22-7.18 (m, 4H), 7.12-7.03 (m, 2H), 5.56 (s, 1H), 3.03 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.2, 139.6, 138.2, 129.7, 128.9, 128.6, 127.1, 124.1, 123.6, 122.9, 120.8, 85.1, 45.7, 21.3. HRMS (EI) *m/z* 366.1580 $[M+Na]^+$ (calcd for $C_{22}H_{21}N_3ONa$ 366.1582).



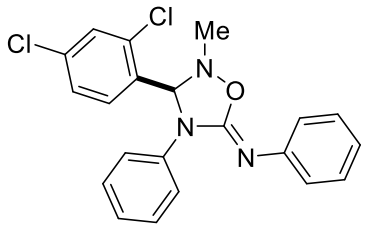
(R,Z)-3-(4-fluorophenyl)-2-methyl-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3h**)

White solid, m. p. 95-97°C, 84% yield. Reaction time 4h. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58-7.56 (m, 2H), 7.47-7.43 (m, 2H), 7.37-7.29 (m, 4H), 7.21-7.04 (m, 6H), 5.59 (s, 1H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.6, 162.1, 146.0, 138.0, 129.1, 128.6, 124.4, 123.5, 123.0, 120.9, 116.2, 116.0, 84.5, 45.7. HRMS (EI) *m/z* 370.1332 $[M+Na]^+$ (calcd for $C_{21}H_{18}FN_3ONa$ 370.1332).



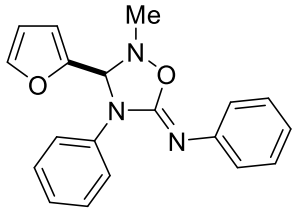
(R,Z)-2-methyl-3-(4-nitrophenyl)-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3i**)

White solid, m. p. 96-98°C, 83% yield. Reaction time 4h. ^1H NMR (400 MHz, Acetone-d_6): δ 8.33-8.31 (m, 1H), 8.12 (s, 1H), 7.82-7.79 (m, 3H), 7.57-7.55 (m, 2H), 7.40-7.21 (m, 4H), 7.15-6.99 (m, 2H), 6.47 (s, 1H), 3.15 (s, 3H); ^{13}C NMR (100 MHz, Acetone-d_6): δ 146.5, 140.0, 138.2, 128.9, 128.7, 128.5, 128.4, 123.9, 123.2, 122.7, 122.0, 120.1, 118.5, 82.3, 45.7. HRMS (EI) *m/z* 397.1275 $[M+Na]^+$ (calcd for $C_{21}H_{18}N_4O_3Na$ 397.1277).



(R,Z)-3-(2,4-dichlorophenyl)-2-methyl-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3j**)

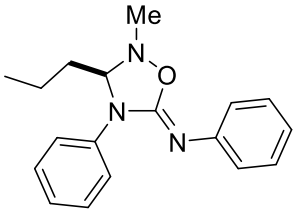
White solid, m. p. 85-87°C, 84% yield. Reaction time 4h. ^1H NMR (400 MHz, $CDCl_3$): δ 7.61-7.53 (m, 3H), 7.38-7.27 (m, 8H), 7.21-7.05 (m, 2H), 6.07 (s, 1H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3, 145.7, 137.9, 136.0, 134.4, 130.2, 129.2, 128.7, 128.6, 128.4, 127.9, 124.0, 123.5, 123.2, 119.3, 80.7, 46.4. HRMS (EI) *m/z* 420.0646 $[M+Na]^+$ (calcd for $C_{21}H_{17}Cl_2N_3ONa$ 420.0646).



(R,Z)-3-(furan-2-yl)-2-methyl-N,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**3k**)

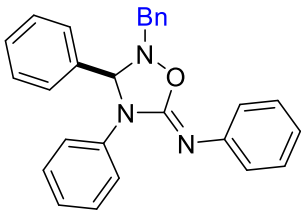
White solid, m. p. 83-85°C, 89% yield. Reaction time 4h. ^1H NMR (400 MHz, $CDCl_3$): δ 7.68-7.66 (m, 2H), 7.49(s,1H), 7.39-7.32 (m, 5H), 7.30-7.03 (m, 3H), 6.49 (s, 1H), 6.40 (s, 1H), 5.72 (s, 1H), 3.05

(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.4, 145.9, 143.7, 138.0, 129.0, 128.6, 124.2, 123.5, 123.0, 120.2, 110.7, 109.7, 78.7, 45.8. HRMS (EI) *m/z* 342.1220 $[M+Na]^+$ (calcd for $C_{19}H_{17}N_3O_2Na$ 342.1218).



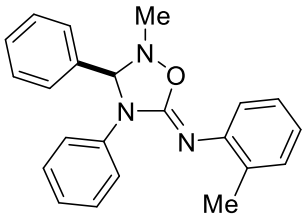
(R,Z)-2-methyl-N,4-diphenyl-3-propyl-1,2,4-oxadiazolidin-5-imine(**3l**)

Coloeless oil, 75% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, 2H, *J*= 8Hz), 7.47-7.43 (m, 2H), 7.33-7.29 (m, 2H), 7.18-7.16 (m, 3H), 7.08-7.04 (m, 1H), 4.76 (m, 1H), 2.94 (s, 3H), 1.85-1.79 (m, 2H), 1.68-48 (m, 2H), 1.00 (t, 3H, *J*= 8Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 146.4, 138.1, 129.3, 128.6, 123.9, 123.4, 122.8, 120.1, 82.9, 46.4, 34.3, 17.9, 13.8. HRMS (EI) *m/z* 318.1582 $[M+Na]^+$ (calcd for $C_{18}H_{21}N_3ONa$ 318.1582).



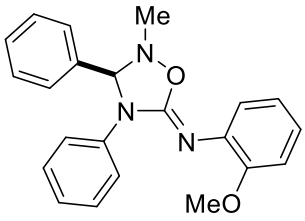
(R,Z)-2-benzyl-N,3,4-triphenyl-1,2,4-oxadiazolidin-5-imine(**3m**)

Coloeless oil, 70% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.62 (m, 2H), 7.41-7.20 (m, 16H), 7.12-7.03 (m, 2H), 5.82 (s, 1H), 4.50 (d, 1H, *J*= 11Hz), 4.20 (d, 1H, *J*= 11Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 146.0, 138.4, 134.2, 129.8, 129.1, 128.9, 128.8, 128.6, 128.5, 128.0, 126.7, 123.7, 123.5, 123.0, 119.6, 80.3, 62.3. HRMS (EI) *m/z* 428.4911 $[M+Na]^+$ (calcd for $C_{27}H_{23}N_3ONa$ 428.4908).



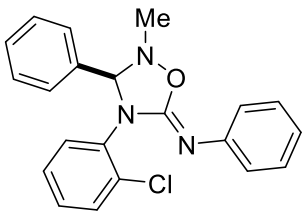
(R,Z)-2-methyl-3,4-diphenyl-N-(o-tolyl)-1,2,4-oxadiazolidin-5-imine(**4a**)

White solid, m. p. 80-81^{o}C, 86% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.62 (m, 2H), 7.48-7.31 (m, 7H), 7.20-6.97 (m, 5H), 5.62 (s, 1H), 3.01 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1, 138.3, 130.8, 130.0, 129.5, 129.0, 128.9, 127.1, 126.0, 123.9, 122.4, 120.3, 85.1, 46.0, 18.6. HRMS (EI) *m/z* 366.1582 $[M+Na]^+$ (calcd for $C_{22}H_{21}N_3ONa$ 366.1582).



(R,Z)-N-(2-methoxyphenyl)-2-methyl-3,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**4b**)

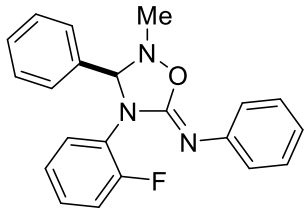
White solid, m. p. 81-83^{o}C, 90% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65-7.63 (m, 2H), 7.51-7.29 (m, 7H), 7.11-6.90 (m, 5H), 5.61 (s, 1H), 3.87 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 138.5, 136.7, 136.1, 129.4, 129.0, 127.0, 123.9, 123.7, 123.6, 120.6, 120.3, 111.4, 85.4, 55.6, 46.3. HRMS (EI) *m/z* 382.1530 $[M+Na]^+$ (calcd for $C_{22}H_{21}N_3O_2Na$ 382.1531).



(R,Z)-N-(2-chlorophenyl)-2-methyl-3,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**4c**)

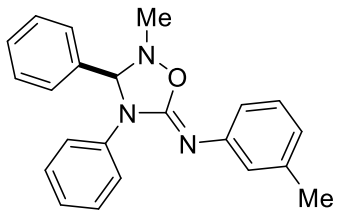
White solid, m. p. 82-84C, 79% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.64 (m, 2H), 7.48-7.28 (m, 8H),

7.21-7.11 (m, 3H), 7.01-6.97 (m, 1H), 5.63 (s, 1H), 3.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 144.1, 138.0, 136.2, 129.6, 129.4, 129.1, 127.7, 127.1, 127.0, 124.4, 124.2, 123.8, 120.7, 85.6, 46.3. HRMS (EI) *m/z* 386.1035 $[M+Na]^+$ (calcd for $C_{21}H_{18}ClN_3ONa$ 386.1036).



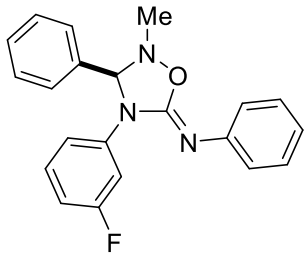
(R,Z)-4-(2-fluorophenyl)-2-methyl-N,3-diphenyl-1,2,4-oxadiazolidin-5-imine(**4d**)

White solid, m. p. 70-71^{o}C, 81% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33-8.30 (m, 1H), 7.57-7.48 (m, 3H), 7.45-7.30 (m, 10H), 5.67 (s, 1H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 138.2, 134.3, 129.6, 129.3, 129.1, 127.8, 127.2, 125.9, 125.7, 125.1, 124.3, 124.2, 122.9, 117.8, 85.3, 45.9. HRMS (EI) *m/z* 370.1332 $[M+Na]^+$ (calcd for $C_{21}H_{18}FN_3ONa$ 370.1332).



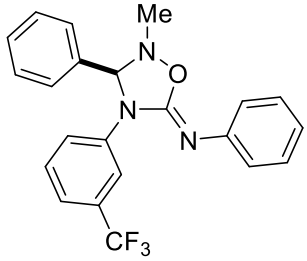
(R,Z)-2-methyl-3,4-diphenyl-N-(m-tolyl)-1,2,4-oxadiazolidin-5-imine(**4e**)

Coloeless oil, 76% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68-7.66 (m, 1H), 7.56-7.25 (m, 10H), 7.18-6.94 (m, 3H), 5.64 (s, 1H), 3.07 (s, 3H), 2.41 (d, 3H, *J*= 8Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.4, 146.2, 139.0, 138.4, 138.2, 136.5, 129.1, 129.0, 128.7, 128.5, 127.2, 125.2, 124.3, 124.2, 123.8, 123.6, 122.9, 121.6, 120.7, 120.6, 118.0, 85.1, 45.9, 21.7, 21.6. HRMS (EI) *m/z* 366.1584 $[M+Na]^+$ (calcd for $C_{22}H_{21}N_3ONa$ 366.1582).



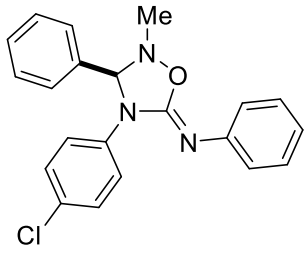
(R,Z)-4-(3-fluorophenyl)-2-methyl-N,3-diphenyl-1,2,4-oxadiazolidin-5-imine(**4f**)

White solid, m. p. 70-72^{o}C, 83% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.69 (m, 2H), 7.59-7.08 (m, 9H), 7.02-6.75 (m, 3H), 5.62 (s, 1H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 164.2, 161.9, 161.8, 145.8, 139.8, 139.7, 137.9, 129.7, 129.5, 129.2, 129.1, 129.0, 128.7, 127.2, 127.0, 124.6, 123.6, 121.2, 119.5, 110.9, 110.8, 110.6, 110.5, 109.7, 109.5, 84.8, 46.0, 45.8. HRMS (EI) *m/z* 370.1330 $[M+Na]^+$ (calcd for $C_{21}H_{18}FN_3ONa$ 370.1332).



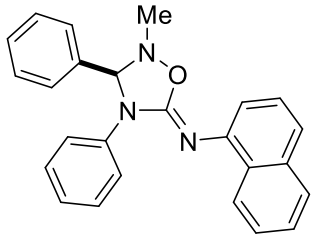
(R,Z)-2-methyl-N,3-diphenyl-4-(3-(trifluoromethyl)phenyl)-1,2,4-oxadiazolidin-5-imine(**4g**)

White solid, m. p. 59-61^{o}C, 81% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.70 (m, 1H), 7.56-7.07 (m, 13H), 5.63 (s, 1H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 138.7, 135.2, 129.9, 129.4, 129.2, 129.1, 129.0, 128.7, 127.2, 125.1, 123.6, 123.4, 123.3, 120.4, 84.9, 45.8. HRMS (EI) *m/z* 420.1304 $[M+Na]^+$ (calcd for $C_{22}H_{18}F_3N_3ONa$ 420.1300).



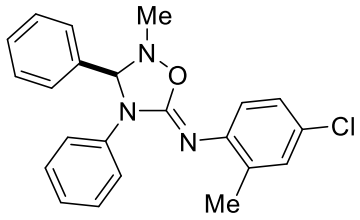
(R,Z)-4-(4-chlorophenyl)-2-methyl-N,3-diphenyl-1,2,4-oxadiazolidin-5-imine(**4h**)

White solid, m. p. 82-84C, 80% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.56 (m, 2H), 7.47-7.23 (m, 10H), 7.18-7.09 (m, 2H), 5.60 (d, 1H, *J*= 20Hz), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9, 144.9, 137.9, 136.7, 129.9, 129.7, 129.4, 129.2, 129.1, 129.0, 128.8, 128.6, 128.0, 127.3, 125.1, 124.5, 123.6, 123.1, 122.2, 121.1, 85.2, 45.6. HRMS (EI) *m/z* 386.1036 $[M+Na]^+$ (calcd for $C_{21}H_{18}ClN_3ONa$ 386.1036).



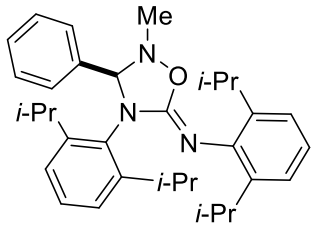
(R,Z)-2-methyl-N-(naphthalen-1-yl)-3,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**4i**)

White solid, m. p. 81-83^{o}C, 81% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.59 (m, 2H), 7.49-7.20 (m, 8H), 7.18-7.00 (m, 7H), 5.63 (s, 1H), 3.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 154.0, 138.0, 134.7, 129.6, 129.1, 127.1, 125.2, 125.1, 124.4, 123.9, 123.8, 123.7, 123.6, 120.8, 115.7, 115.5, 85.7, 46.1. HRMS (EI) *m/z* 402.1581 $[M+Na]^+$ (calcd for $C_{25}H_{21}N_3ONa$ 402.1582).



(R,Z)-N-(4-chloro-2-methylphenyl)-2-methyl-3,4-diphenyl-1,2,4-oxadiazolidin-5-imine(**4j**)

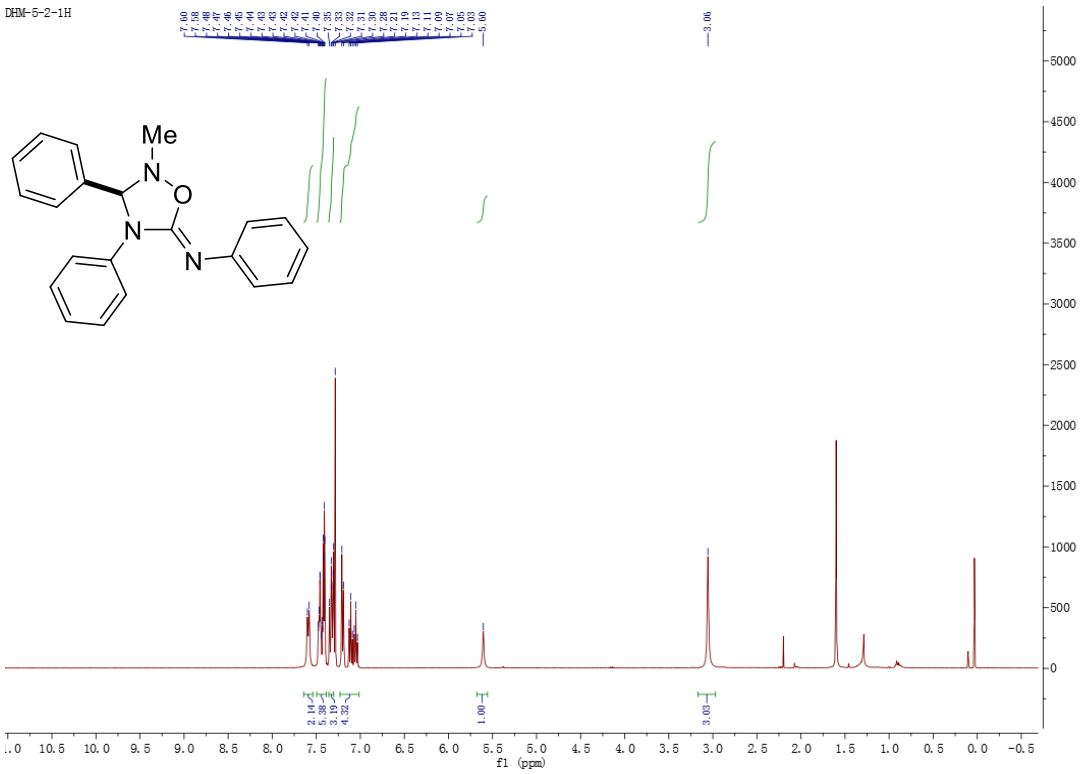
White solid, m. p. 58-60^{o}C, 86% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.58 (m, 2H), 7.47-6.99 (11H), 5.82 (s, 1H), 3.03 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.8, 138.0, 132.8, 131.3, `30.1, 129.8, 129.7, 129.6, 129.1, 129.0, 128.9, 128.5, 128.4, 127.7, 127.2, 126.7, 125.9, 124.3, 123.6, 123.5, 122.7, 120.7, 85.4, 45.8, 18.5. HRMS (EI) *m/z* 400.1196 $[M+Na]^+$ (calcd for $C_{22}H_{20}ClN_3ONa$ 400.1193).



(R,Z)-N,4-bis(2,6-diisopropylphenyl)-2-methyl-3-phenyl-1,2,4-oxadiazolidin-5-imine(**4k**)

White solid, m. p. 105-107^{o}C, 66% yield. Reaction time 4h. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.26 (m, 7H), 7.12-7.00 (m, 4H), 5.31 (s, 1H), 3.46-3.42 (m, 1H), 3.32-3.27 (m, 2H), 3.25-3.12 (m, 1H), 2.91 (s, 3H), 1.59-1.47 (m, 7H), 1.31-1.17 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 148.3, 147.8, 142.8, 140.4, 134.6, 129.7, 129.4, 128.7, 128.6, 124.5, 124.4, 122.8, 122.5, 88.2, 44.4, 29.0, 28.6, 27.9, 25.5, 24.6, 23.2. HRMS (EI) *m/z* 520.3303 $[M+Na]^+$ (calcd for $C_{33}H_{43}N_3ONa$ 520.3304).

4 NMR spectra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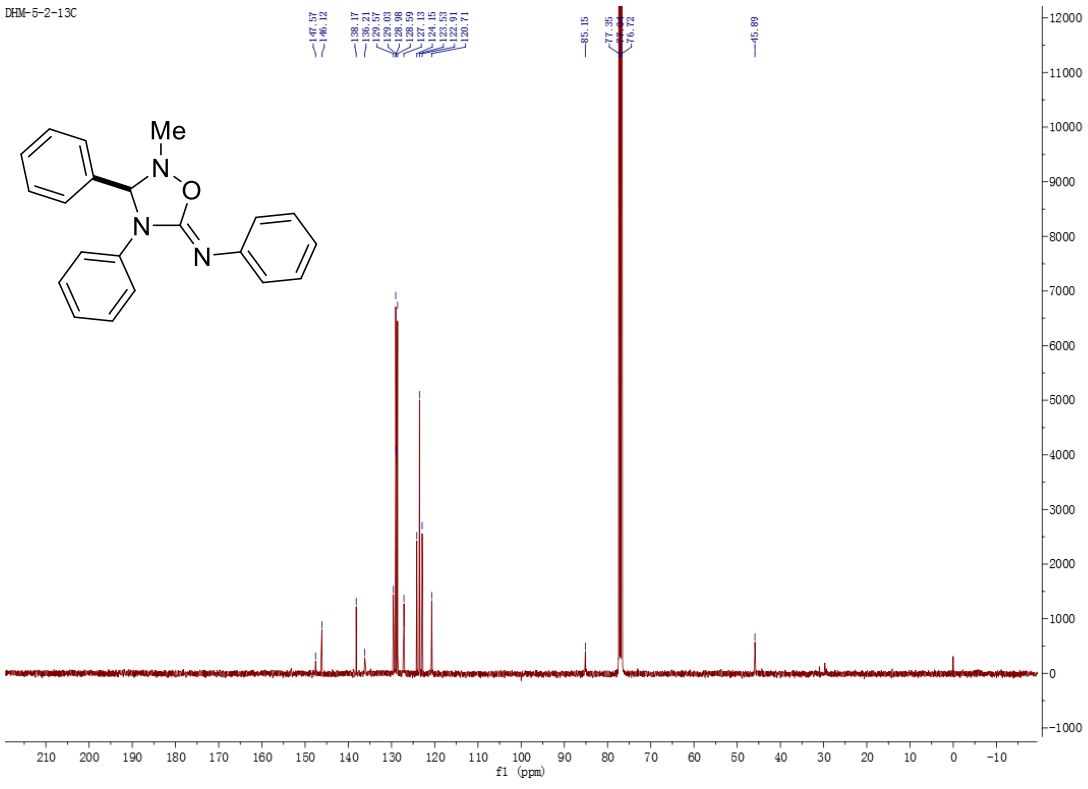
N
N
f1 (ppm)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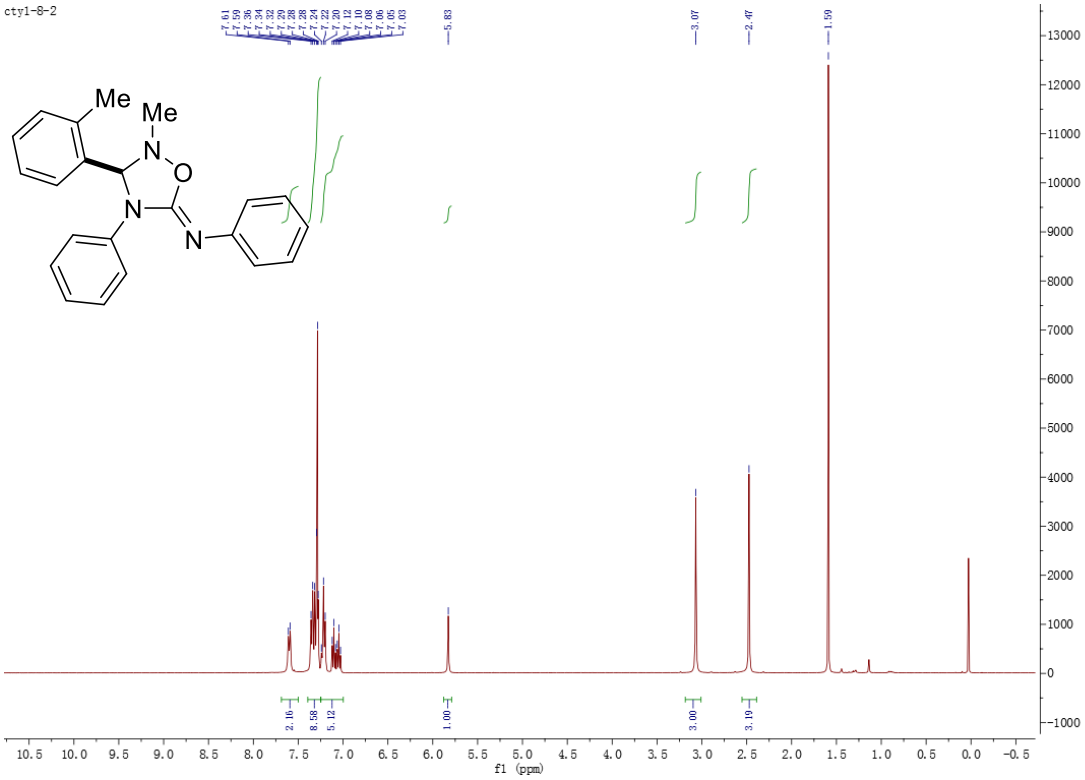
f1 (ppm)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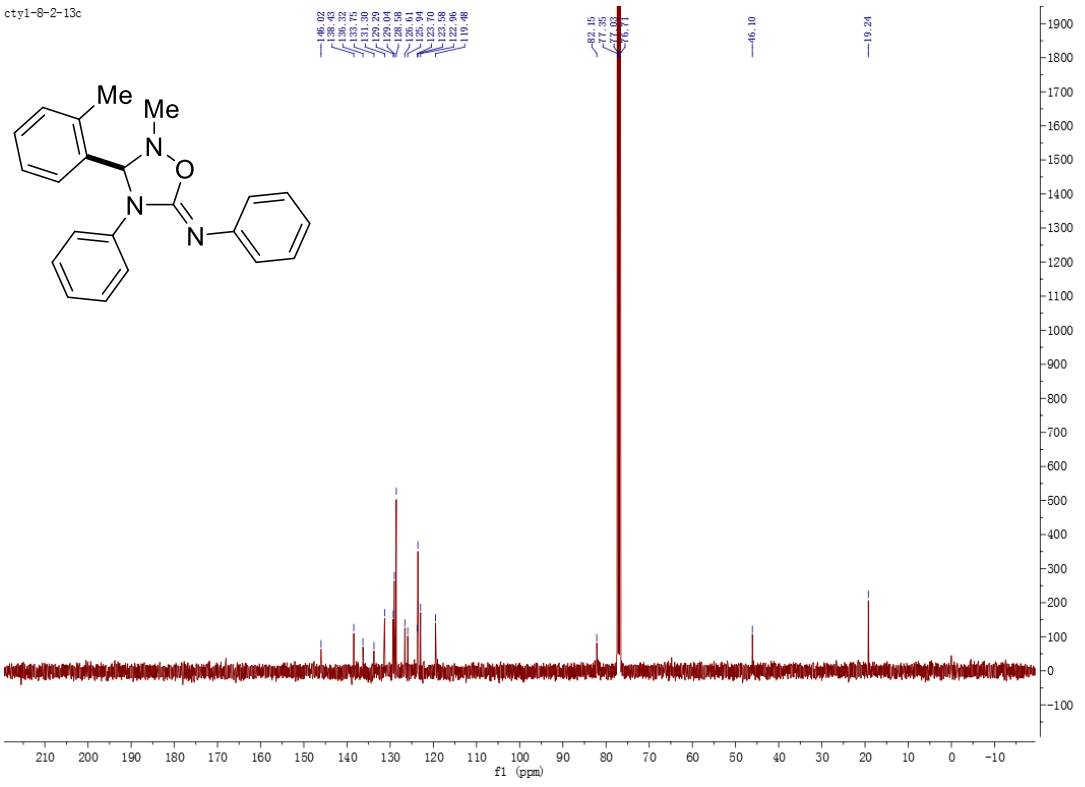
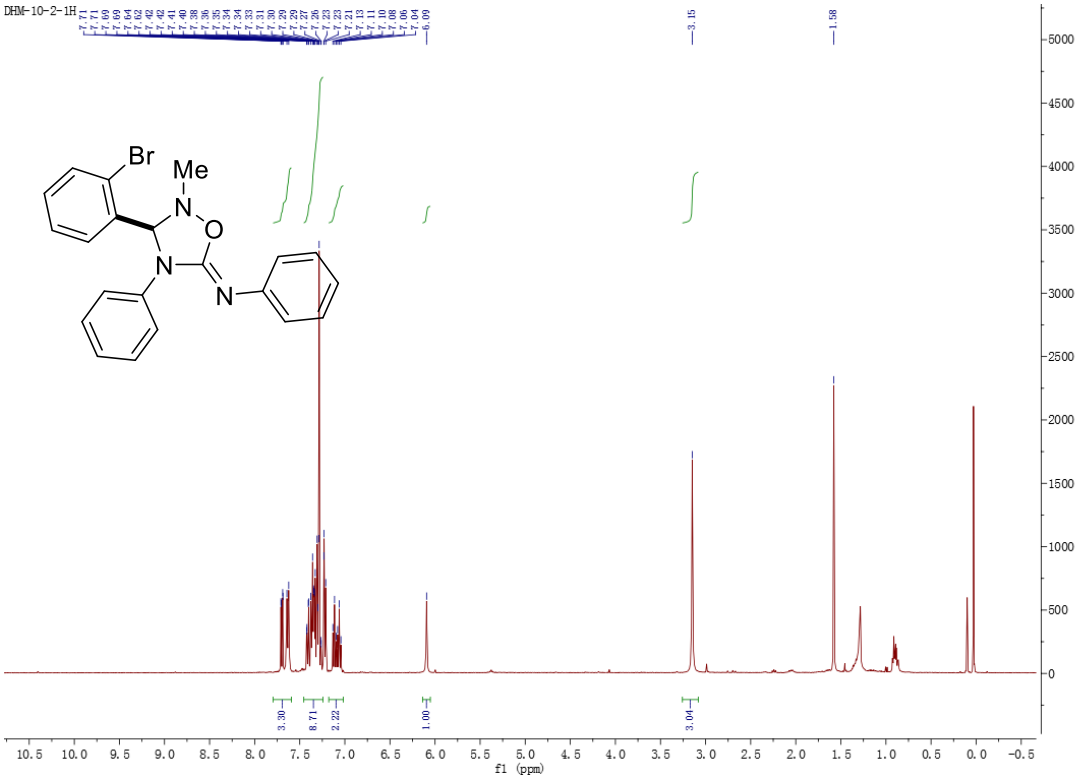
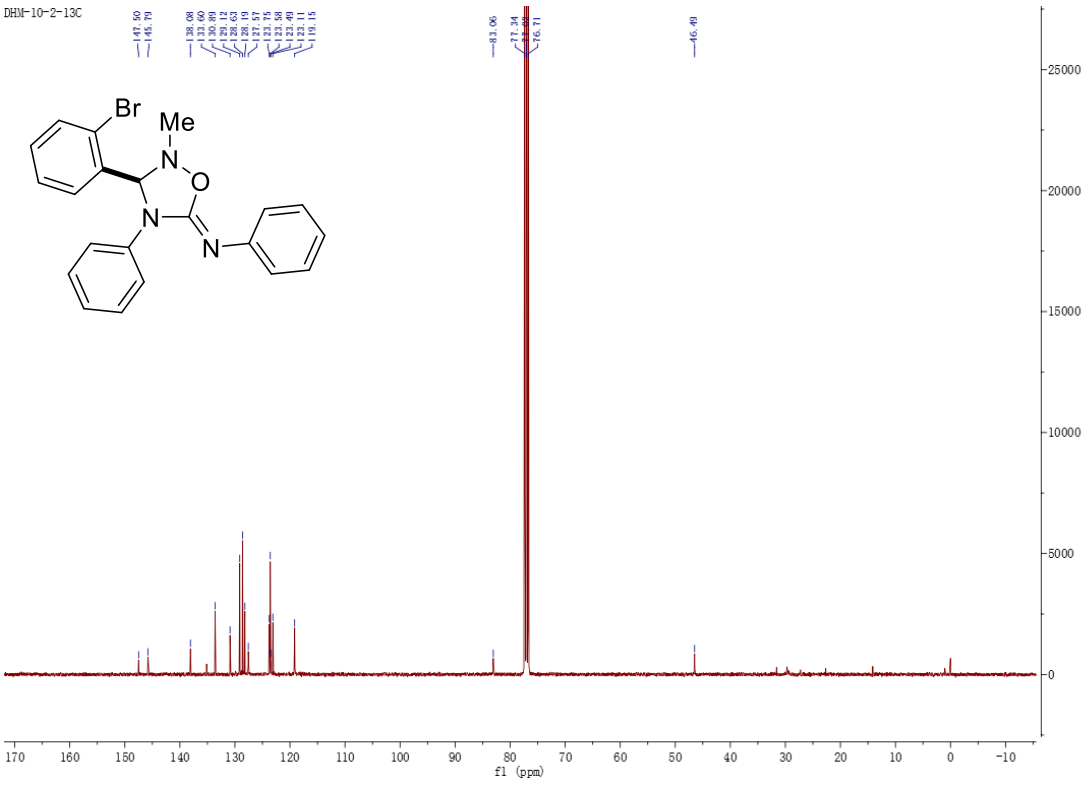
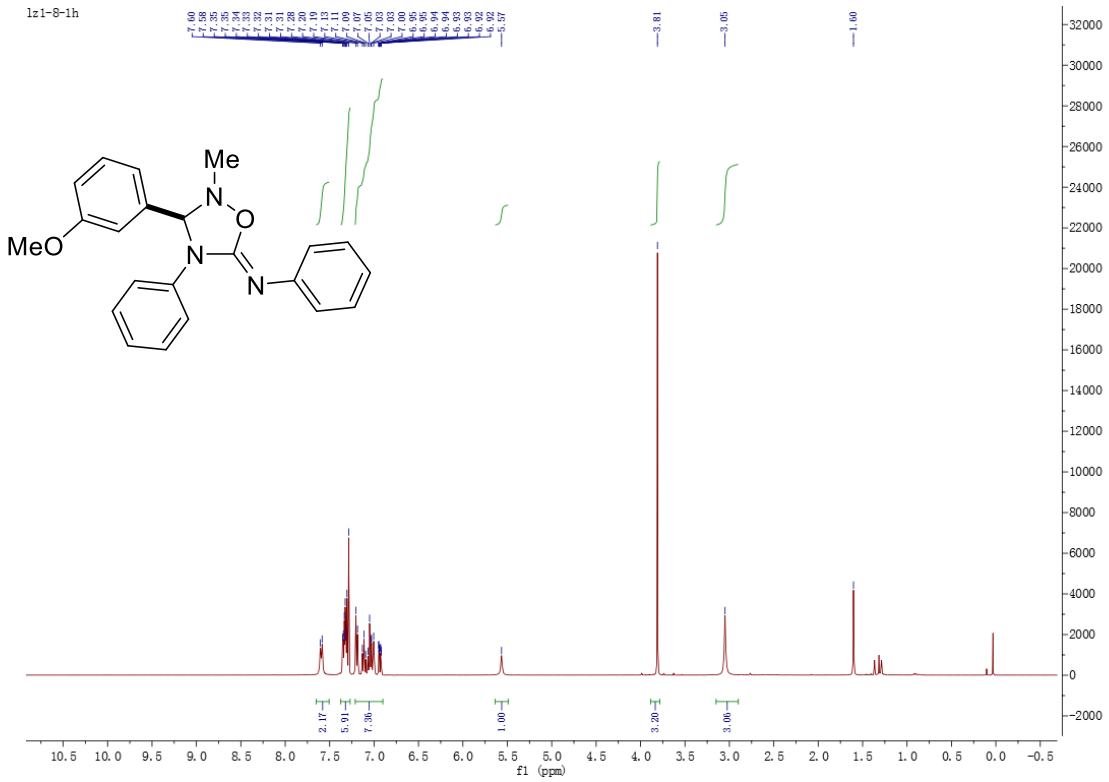
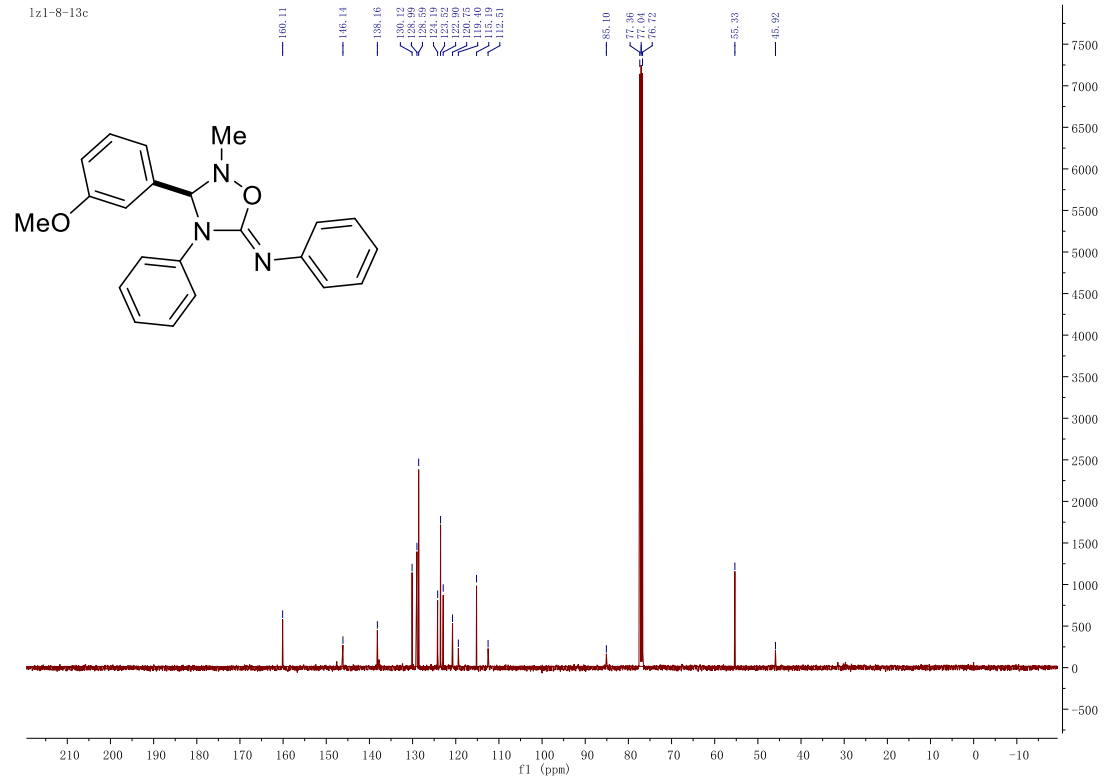
7.20
7.12
7.10
7.08
7.06
7.05
7.03
5.83
3.07
2.47
1.59
2.16
8.58
5.12
1.00
3.00
3.19
f1 (ppm)

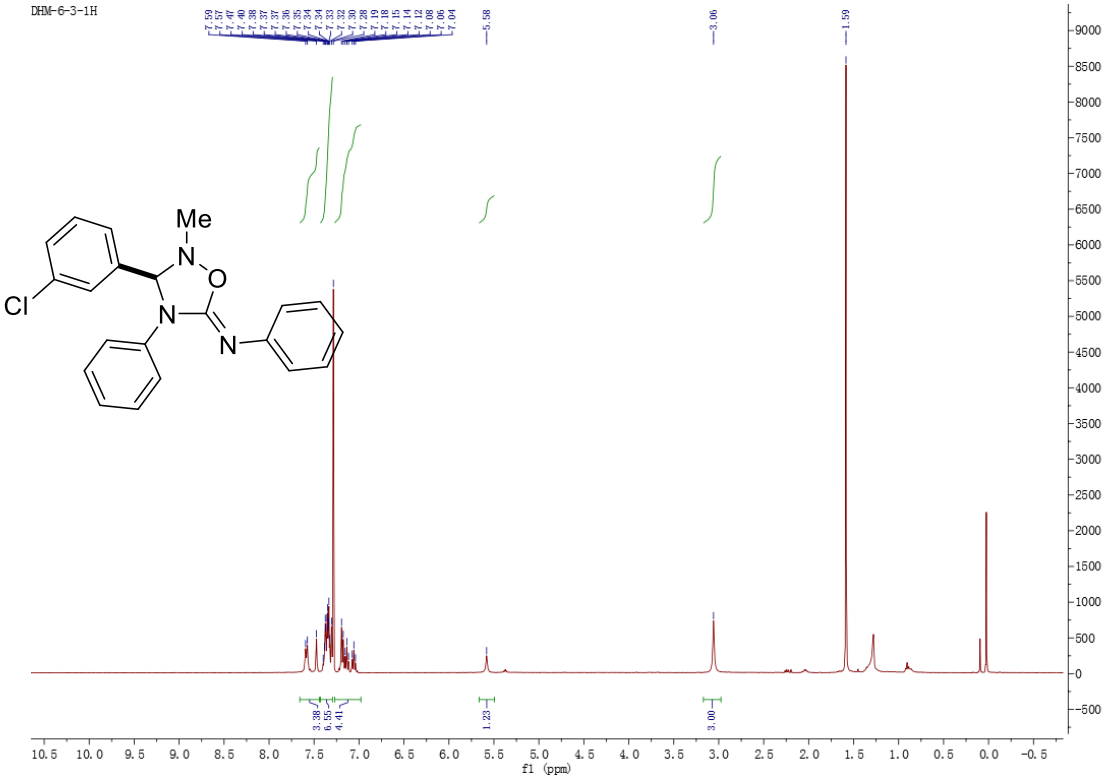

cty1-8-2-13c
Me
Me
N
O
N
N
146.02
138.43
136.32
133.75
131.39
129.29
129.04
128.58
126.64
125.94
123.70
123.58
122.96
119.46
82.15
77.35
77.03
76.71
46.10
19.24
f1 (ppm)

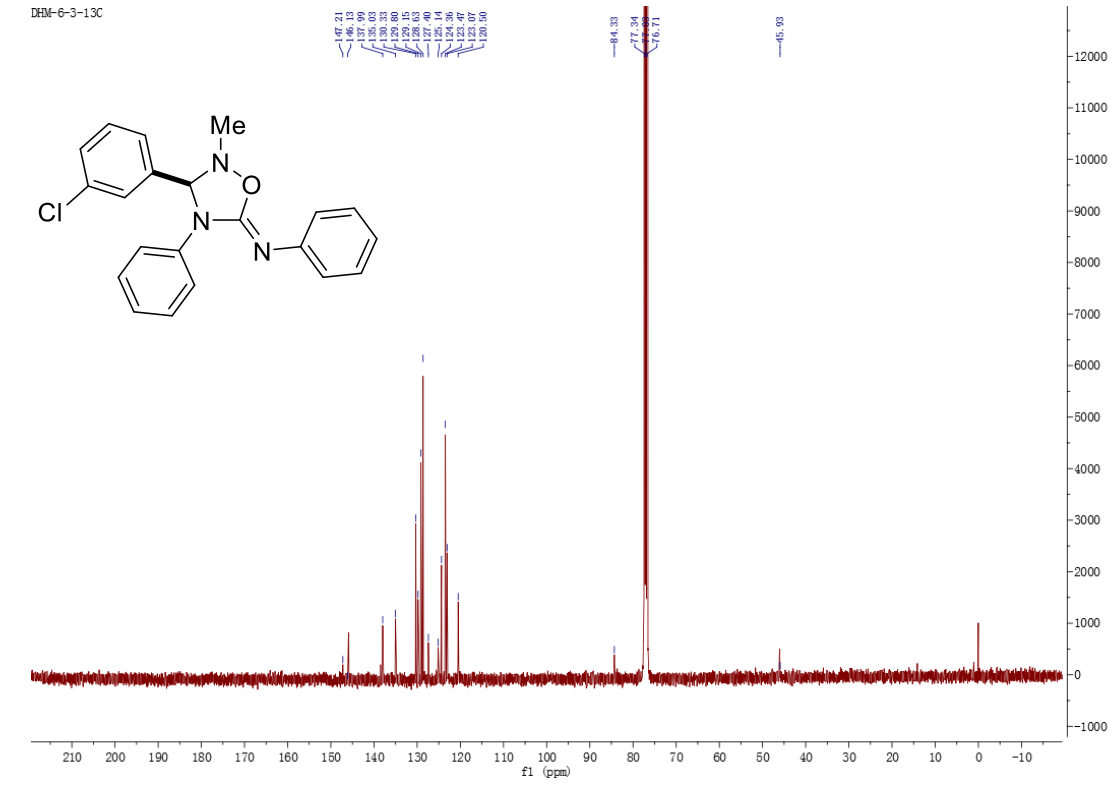

DHM-10-2-1H
Br
Me
N
O
N
N
3.15
1.58
3.30
8.71
2.22
1.00
3.04
f1 (ppm)

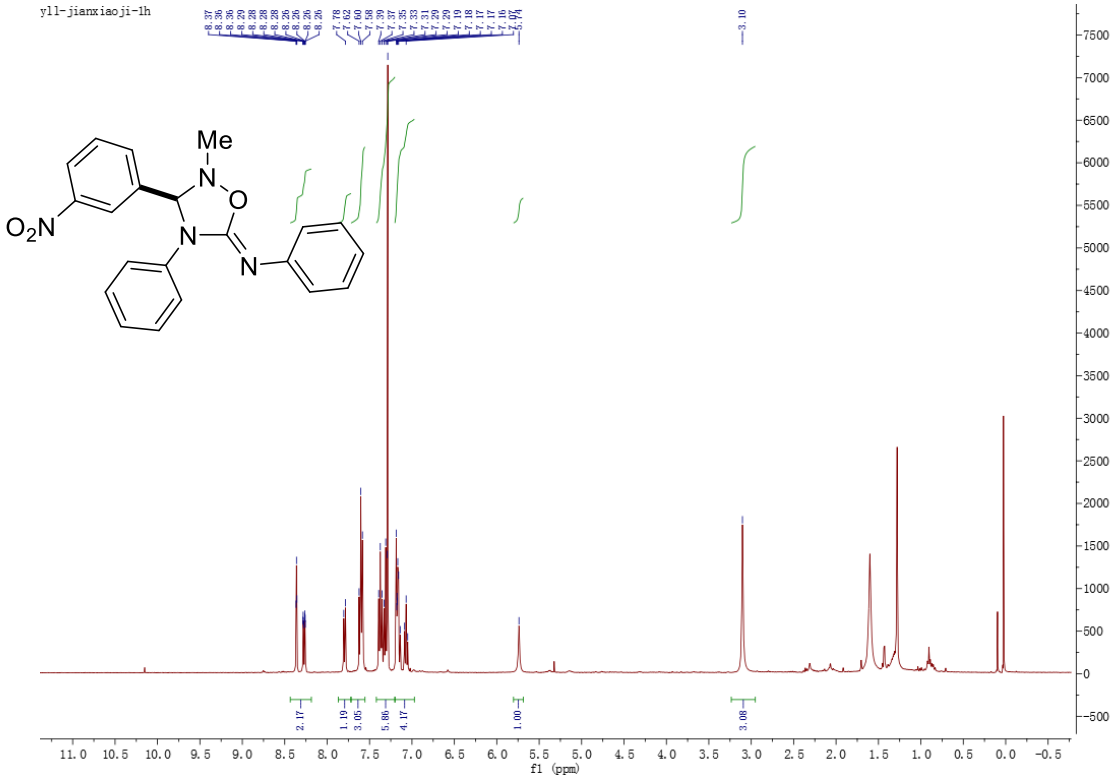

DHM-10-2-13C
Br
Me
N
O
N
N
f1 (ppm)

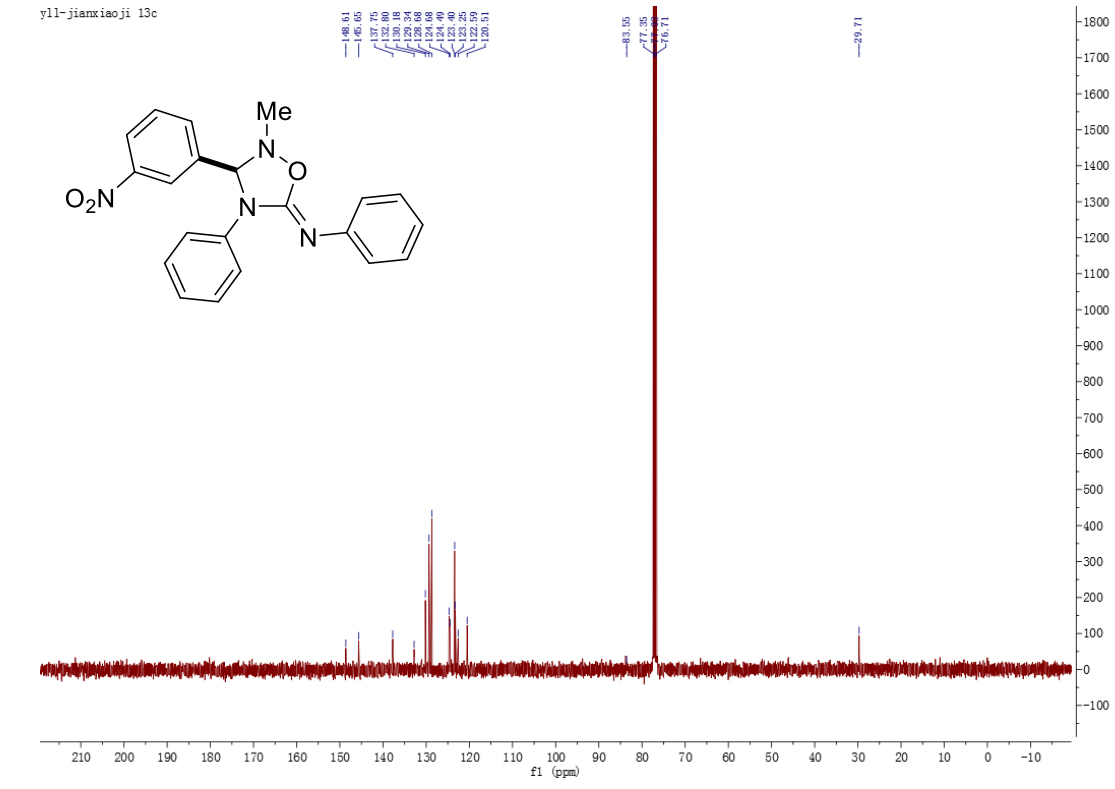

lz1-8-1h
Me
N
O
MeO
N
N
7.60
7.58
7.35
7.35
7.34
7.33
7.32
7.31
7.31
7.28
7.20
7.19
7.13
7.11
7.09
7.07
7.05
7.03
7.00
6.96
6.95
6.94
6.93
6.92
6.92
5.57
3.81
3.05
1.60
2.17
5.91
7.30
1.00
3.20
3.06
f1 (ppm)

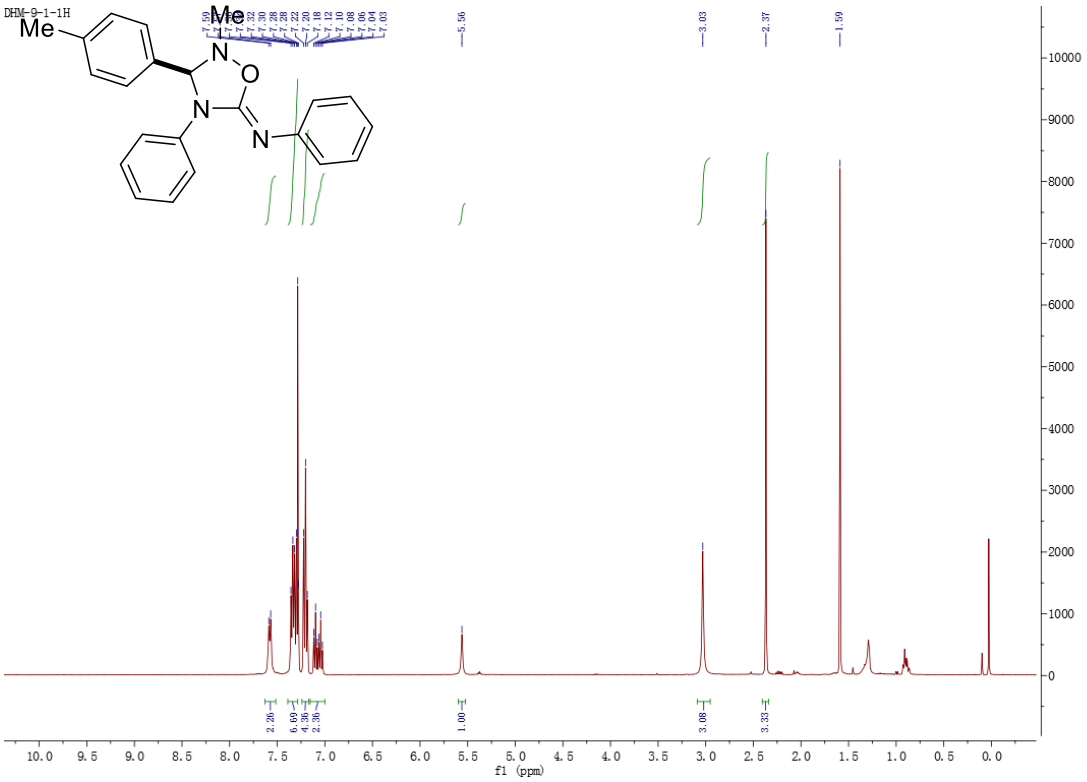

lz1-8-13c
Me
N
O
MeO
N
N
160.11
146.14
138.16
130.12
128.99
128.59
124.19
123.52
122.99
120.75
119.40
115.19
112.51
85.10
77.36
77.04
76.72
55.33
45.92
f1 (ppm)

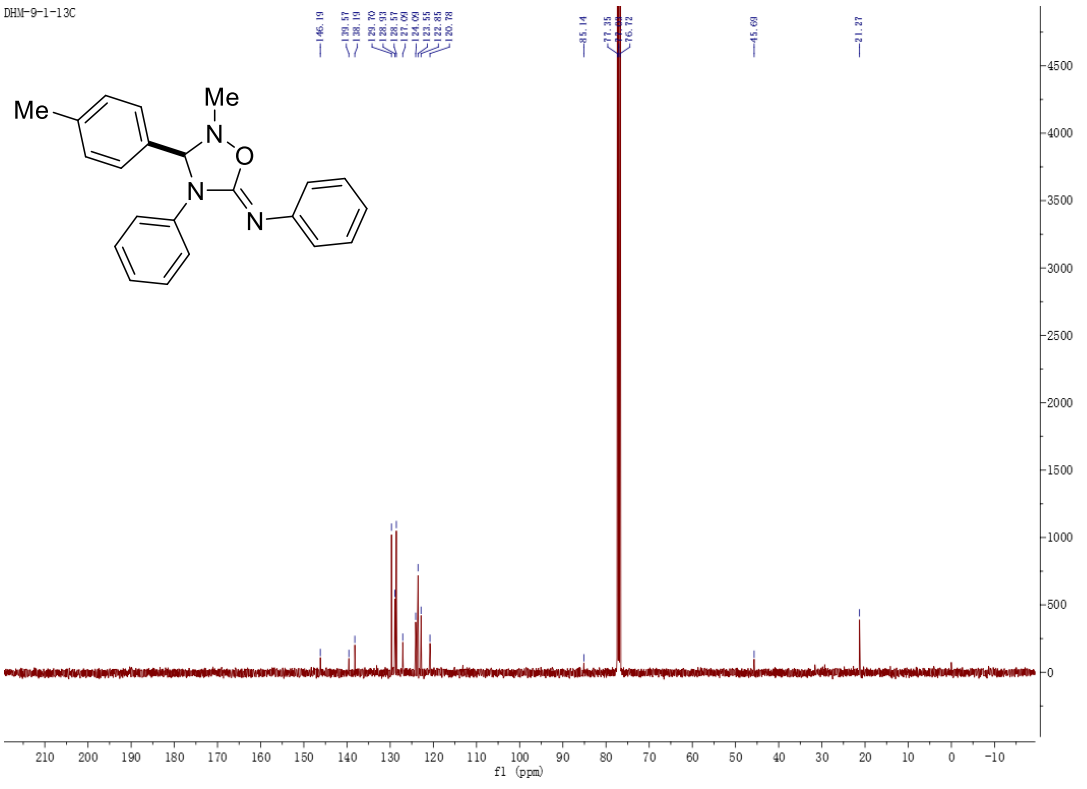

DHM-6-3-1H
Me
N
O
Cl
N
N
f1 (ppm)

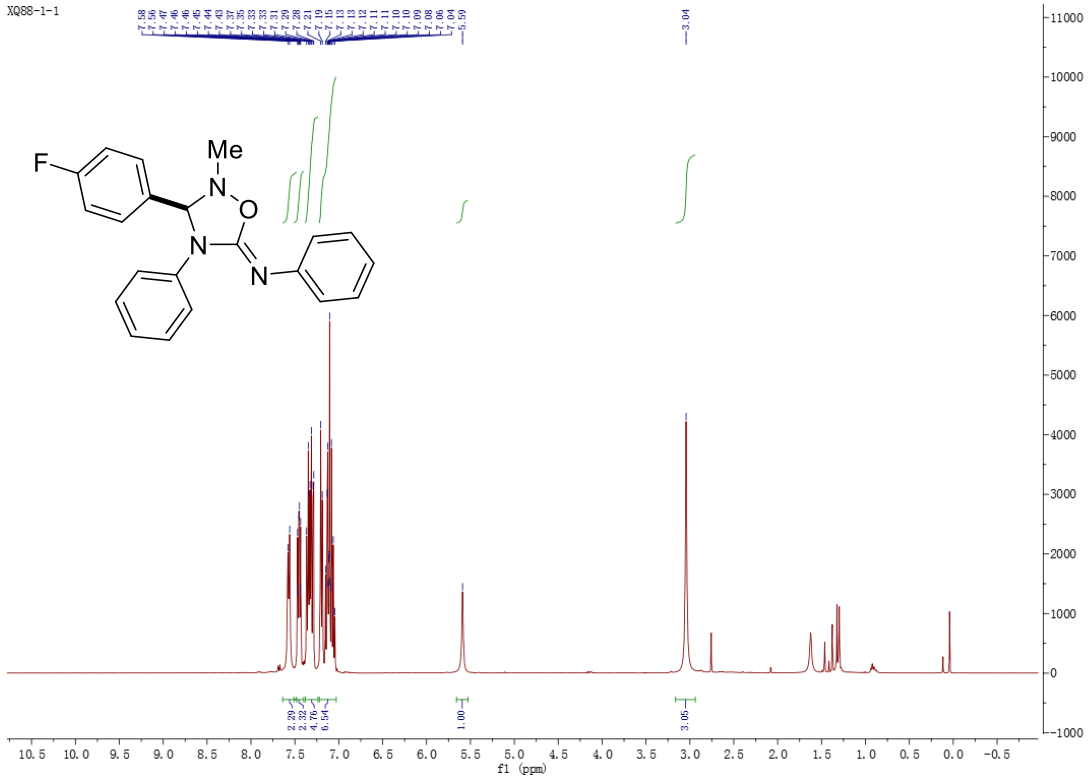

DHM-6-3-13C
Me
N
O
Cl
N
N
f1 (ppm)

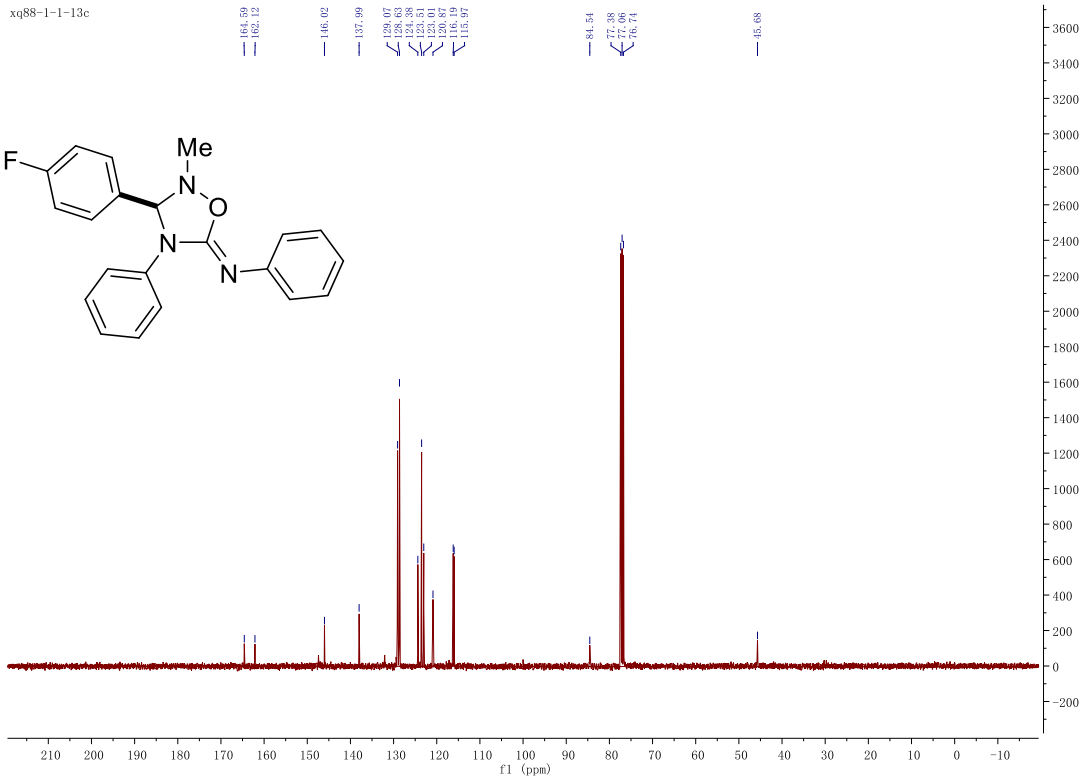

yll-jianxiaoji-1h
Me
N
O
N
N
O_2N
f1 (ppm)

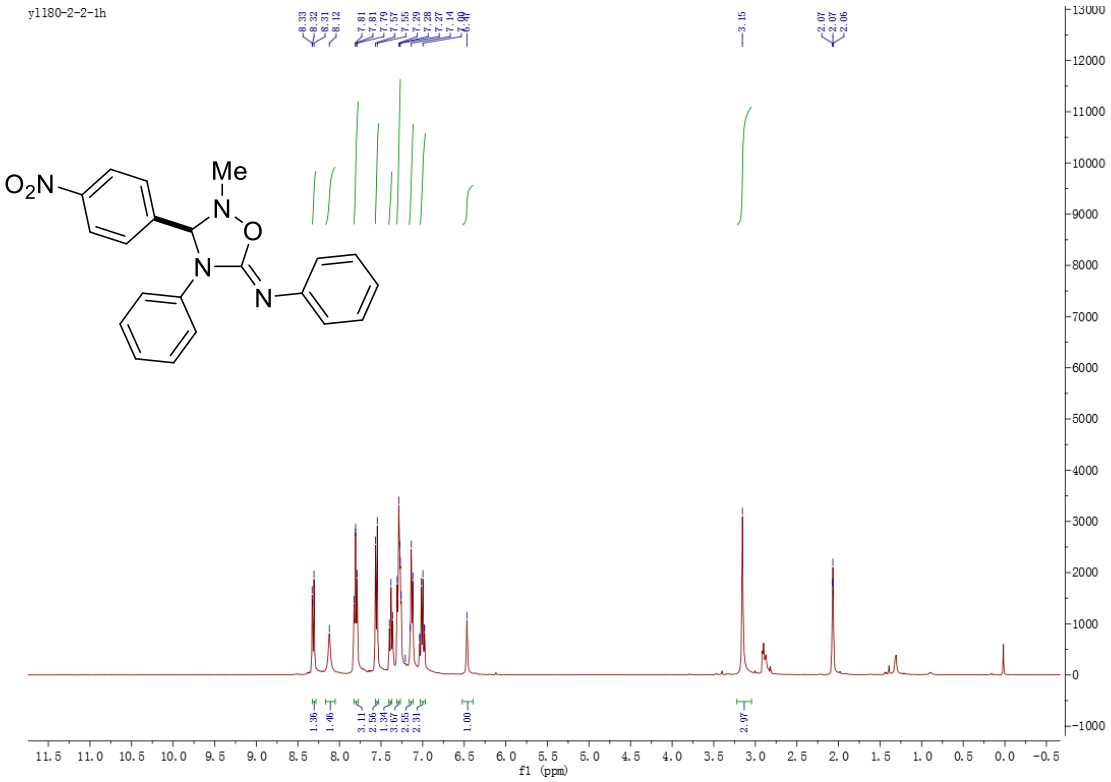

yll-jianxiaoji 13c
Me
N
O
N
N
O_2N
f1 (ppm)

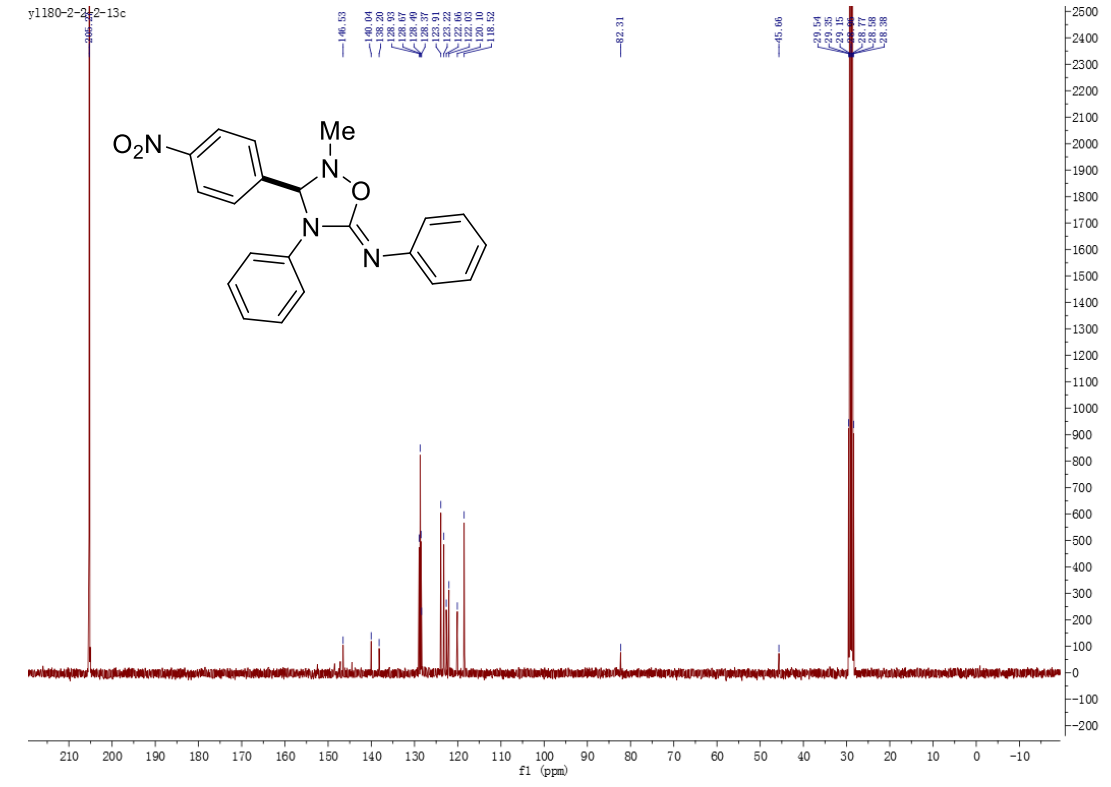

DHM-9-1-1H
Me
Me
N
O
N
N
7.59
7.57
7.32
7.30
7.28
7.23
7.22
7.20
7.18
7.12
7.10
7.08
7.06
7.04
7.03
5.56
3.03
2.37
1.59
2.20
6.69
4.36
2.36
1.00
3.08
3.33
f1 (ppm)

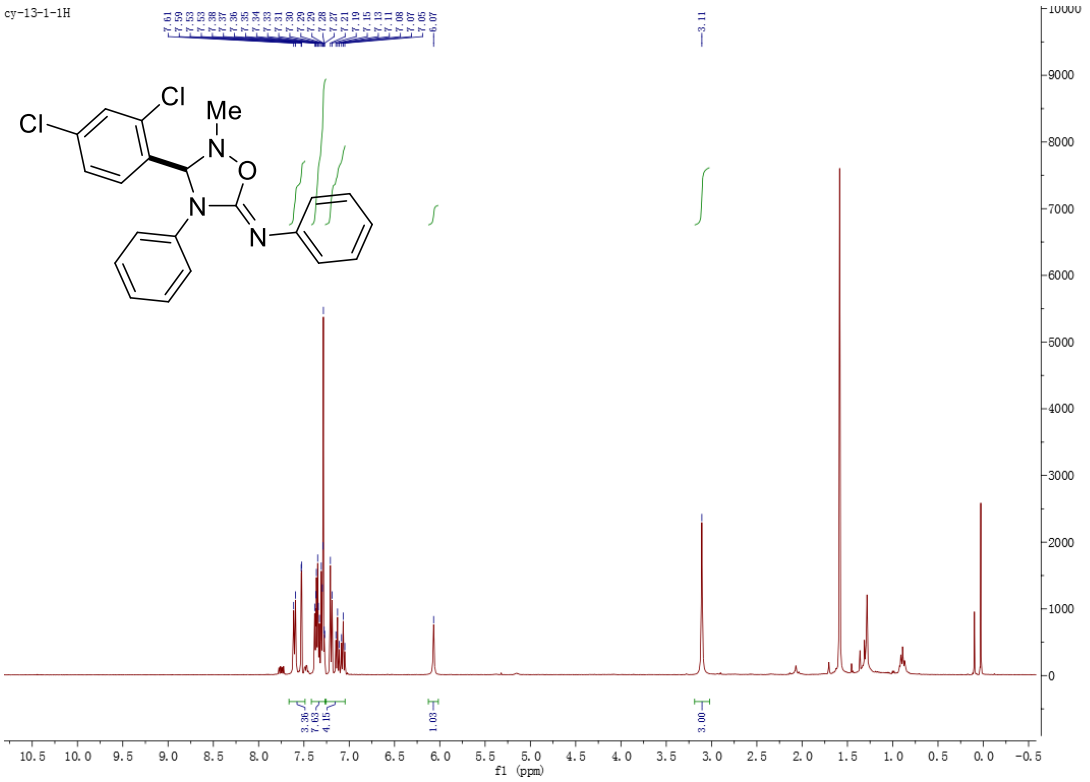

DHM-9-1-13C
Me
Me
N
O
N
N
146.19
139.57
138.19
129.70
128.93
128.57
127.09
124.09
123.55
122.85
120.78
85.14
77.35
77.04
76.72
45.69
21.27
f1 (ppm)

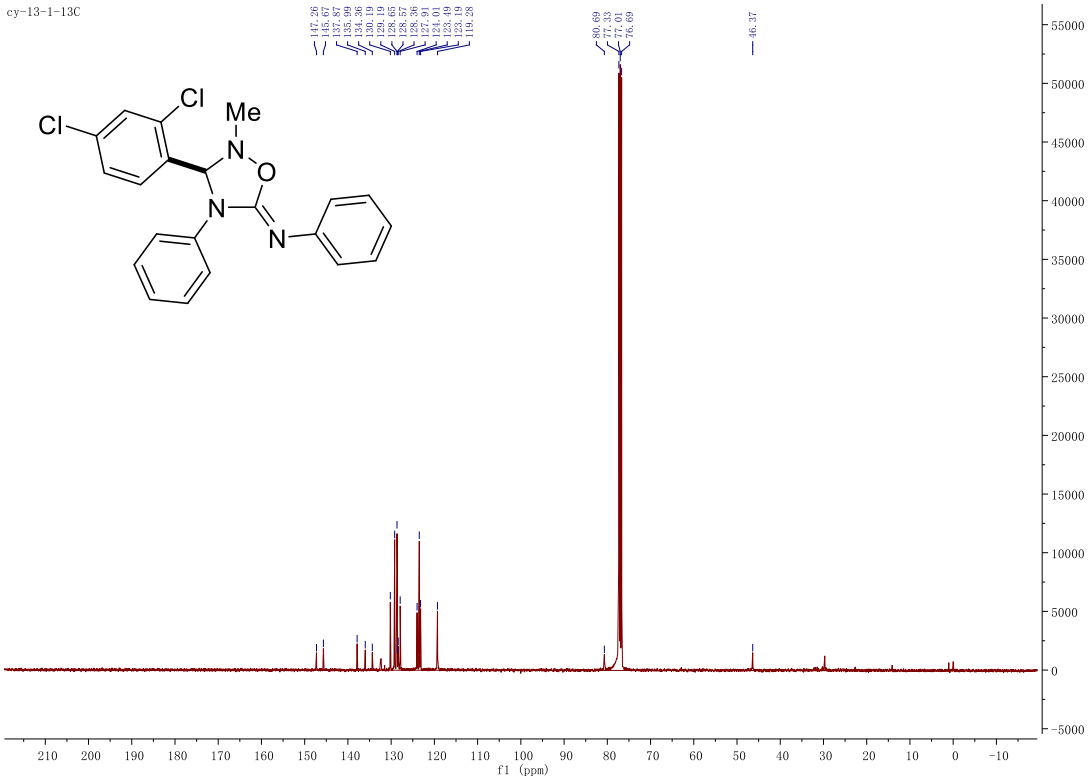

XQ88-1-1
F
Me
N
O
N
N
f1 (ppm)

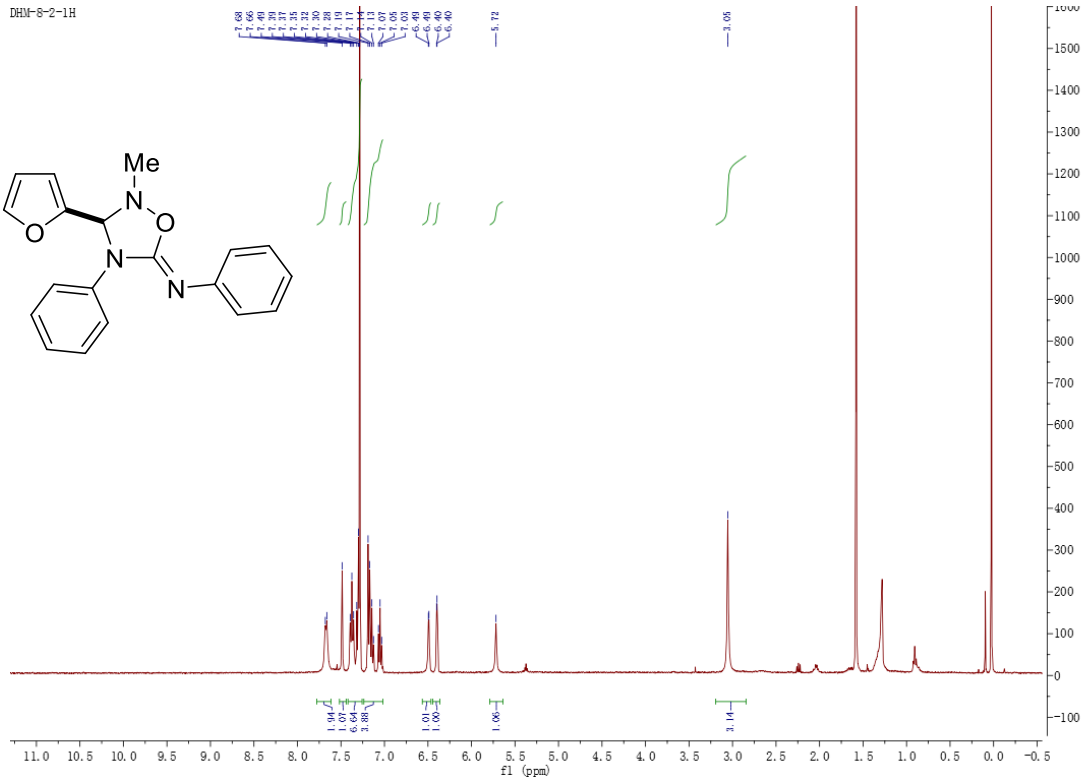

xq88-1-1-13c
F
Me
N
O
N
N
f1 (ppm)

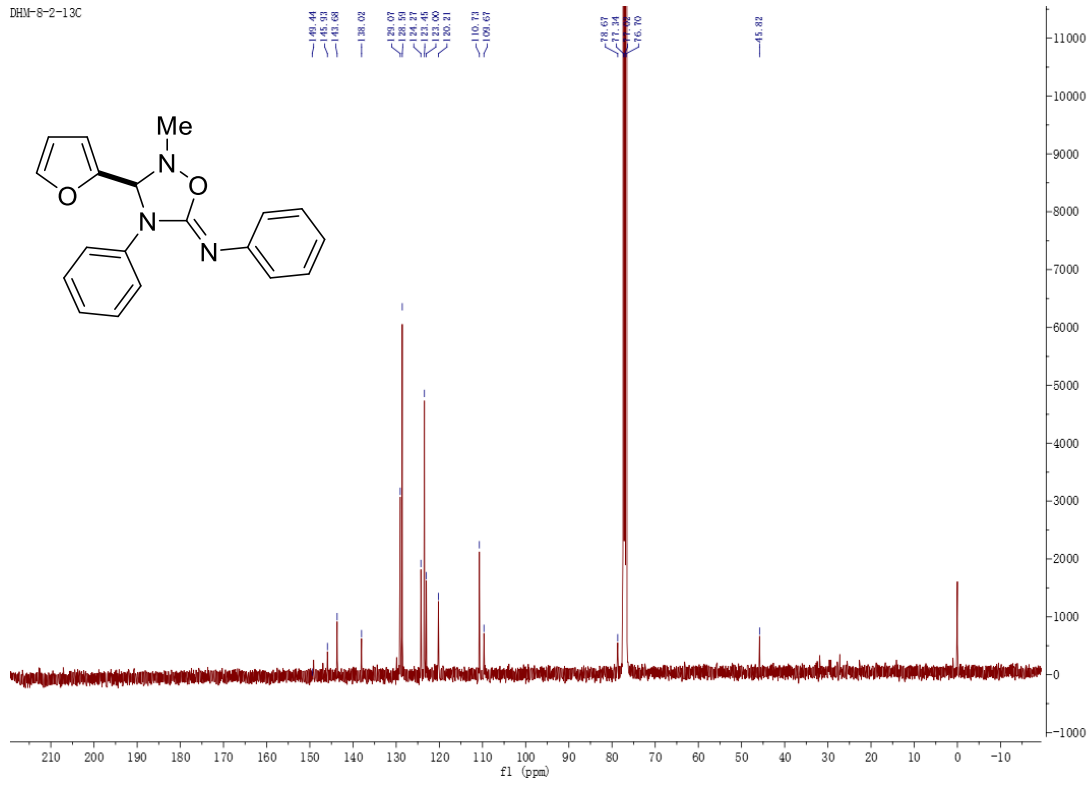

yl180-2-2-1h
8.33
8.32
8.31
8.12
7.81
7.81
7.79
7.57
7.55
7.29
7.28
7.27
7.14
7.00
6.99
3.15
2.07
2.07
2.06
Me
N
O
N
N
O_2N
1.36
1.46
3.11
2.56
1.34
3.67
2.55
2.31
1.00
2.97
f1 (ppm)

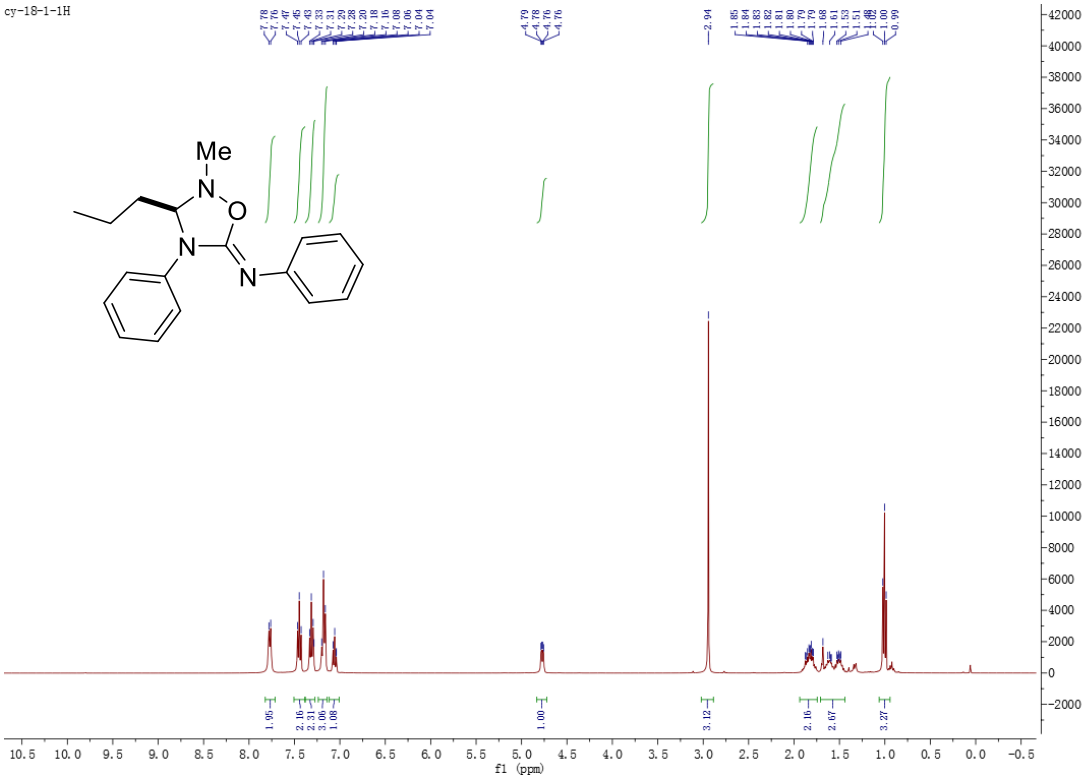

yl180-2-2-13c
146.53
140.04
138.20
128.93
128.67
128.49
128.37
123.91
123.22
122.66
122.03
120.10
118.52
82.31
45.66
29.54
29.35
29.15
28.77
28.58
28.38
Me
N
O
N
N
O_2N
f1 (ppm)

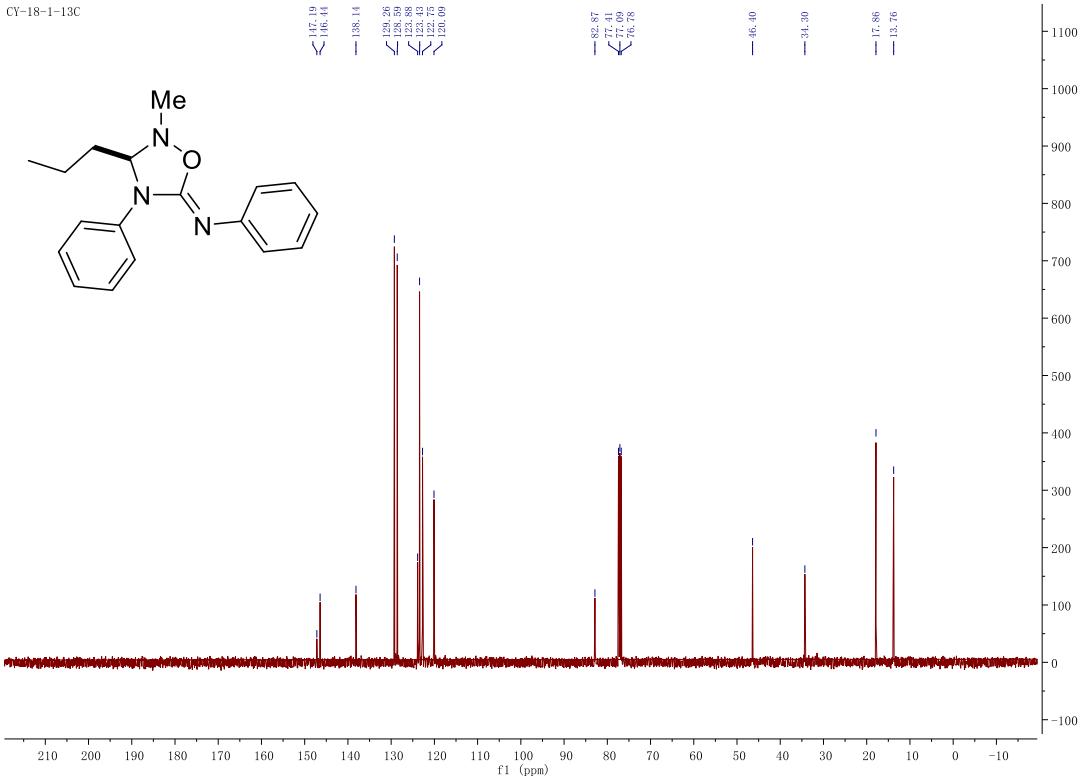

cy-13-1-1H
Cl
Cl
Me
N
O
N
N
f1 (ppm)

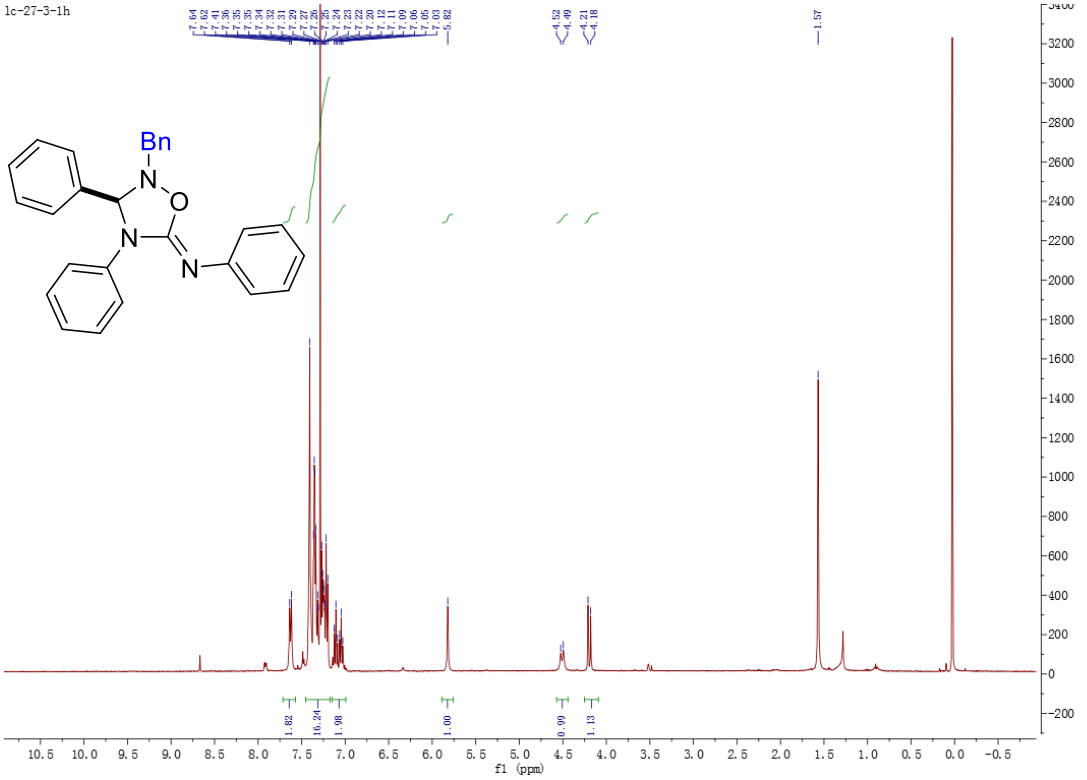

cy-13-1-13C
Cl
Cl
Me
N
O
N
N
f1 (ppm)

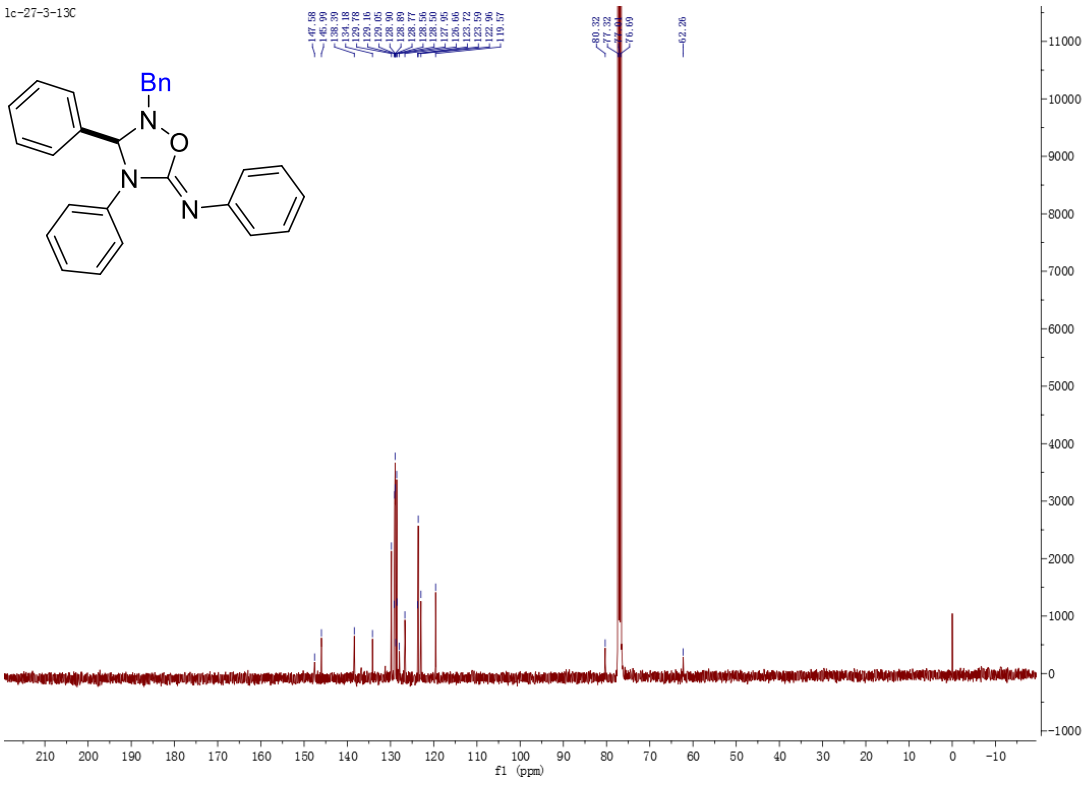

DHM-8-2-1H
Me
O
N
O
N
N
7.68
7.66
7.49
7.39
7.37
7.35
7.32
7.30
7.28
7.19
7.17
7.13
7.11
7.07
7.05
7.03
6.49
6.48
6.40
6.40
5.72
3.06
1.94
1.07
6.64
3.88
1.01
1.00
1.06
3.14
f1 (ppm)

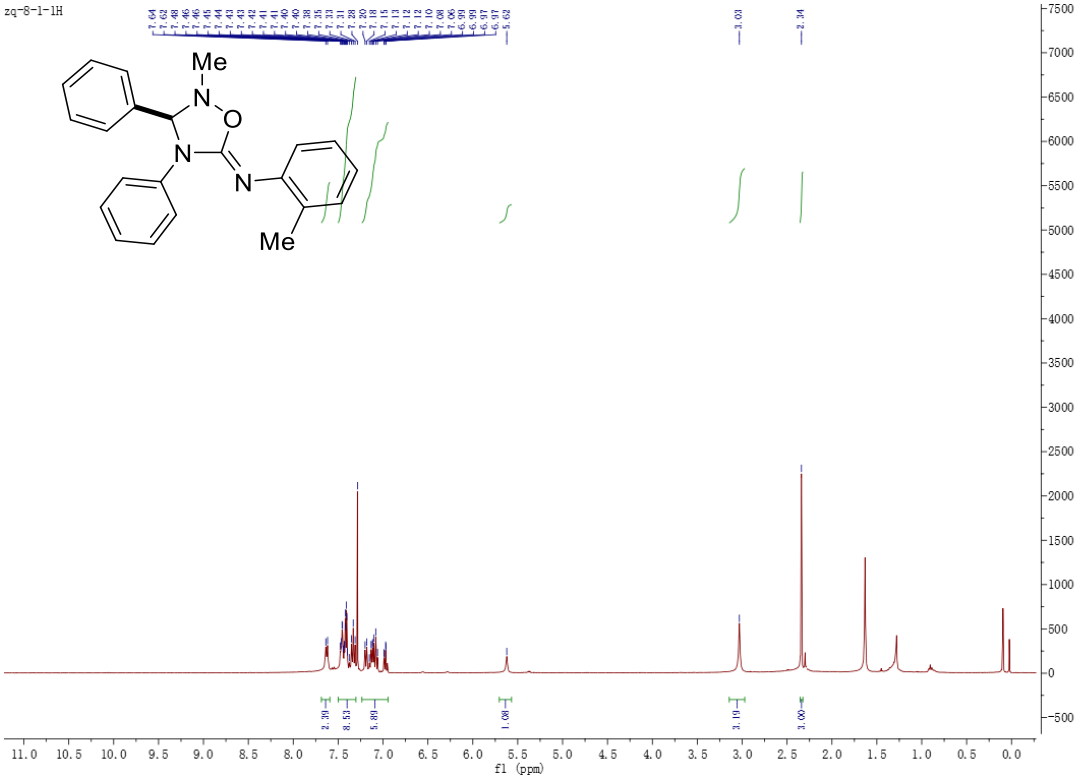

DHM-8-2-13C
Me
O
N
O
N
N
149.44
145.93
143.68
138.02
129.07
128.59
124.27
123.45
123.00
120.21
110.73
109.67
78.67
77.34
76.70
45.82
f1 (ppm)

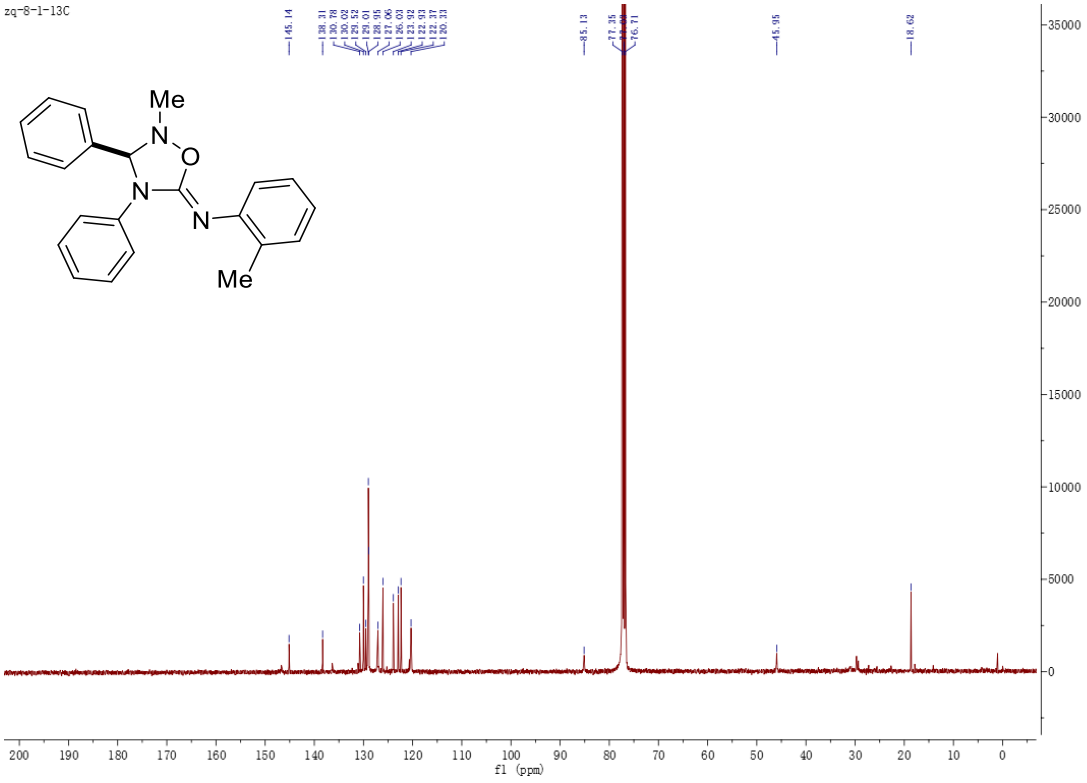

cy-18-1-1H
Me
N
O
N
N
f1 (ppm)

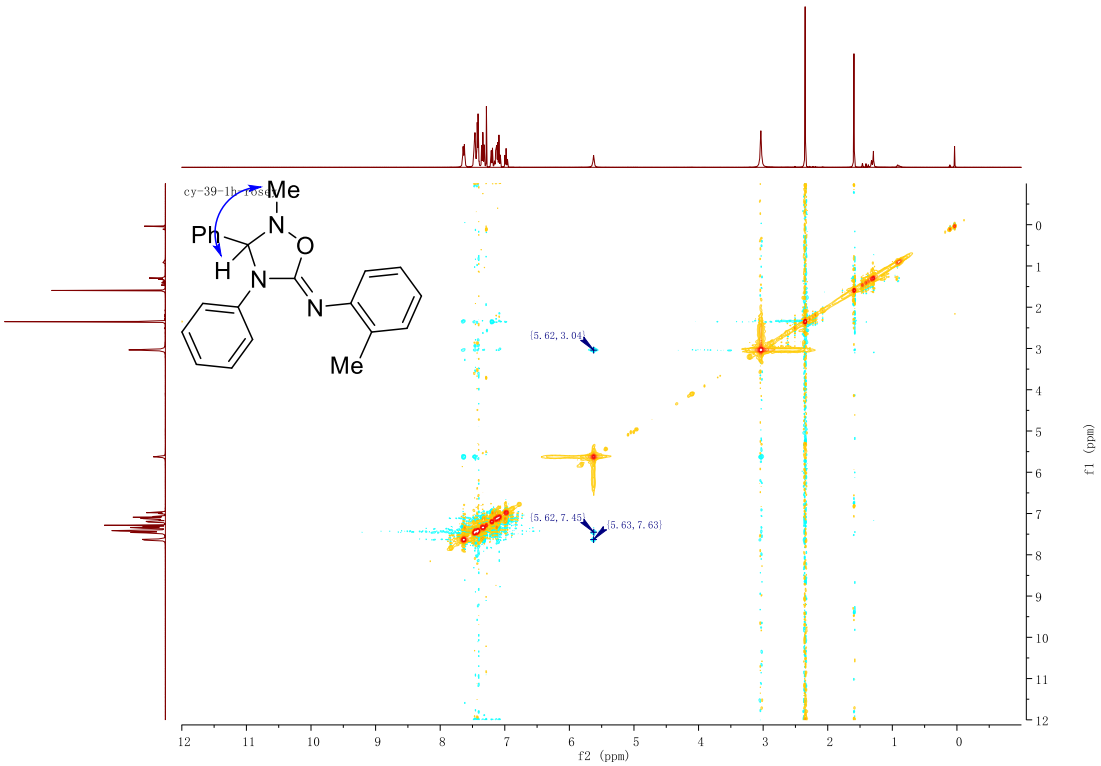

CY-18-1-13C
Me
N
O
N
N
f1 (ppm)

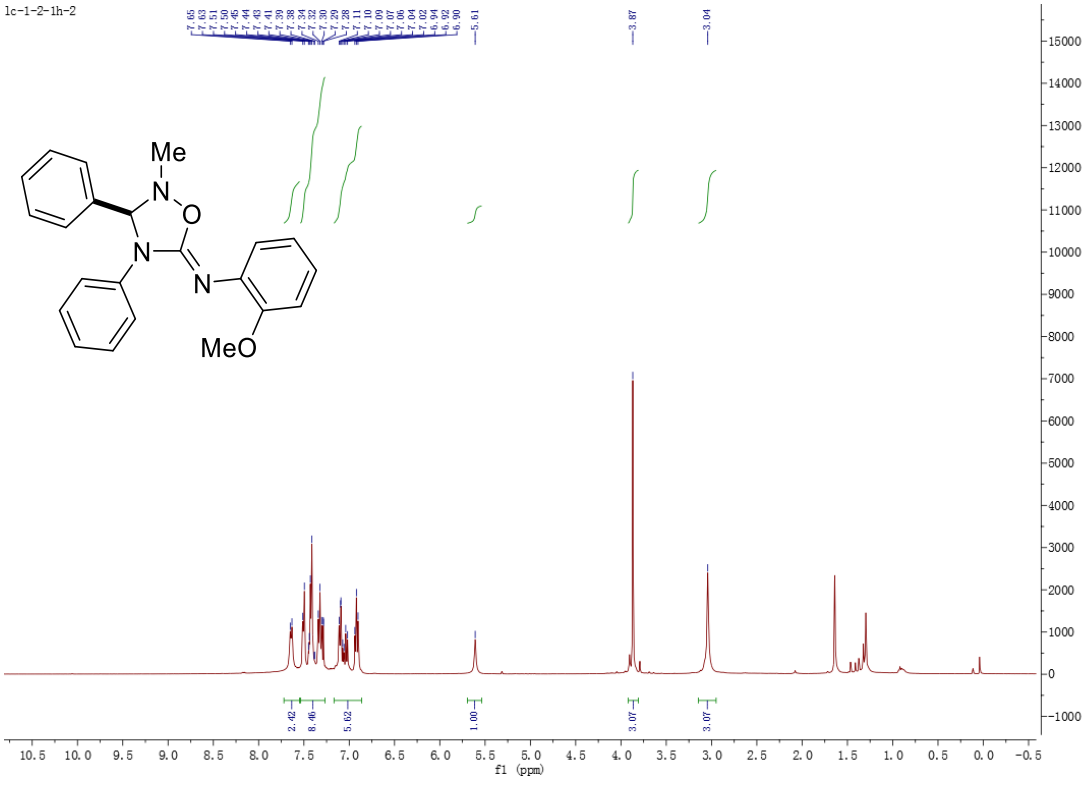

1c-27-3-1h
Bn
N
O
N
N
7.64
7.62
7.41
7.36
7.35
7.34
7.32
7.31
7.29
7.27
7.26
7.25
7.24
7.23
7.22
7.20
7.12
7.11
7.09
7.06
7.05
7.03
5.82
4.52
4.49
4.21
4.18
1.57
1.82
16.24
1.98
1.00
0.99
1.13
f1 (ppm)

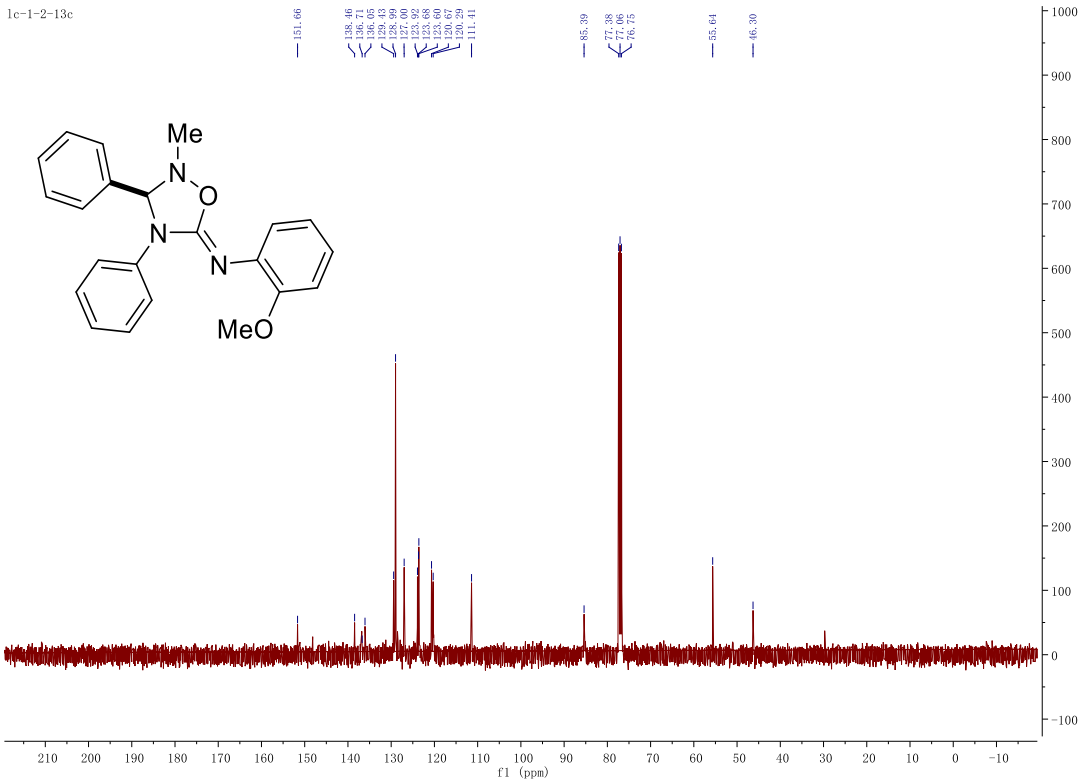

1c-27-3-13C
Bn
N
O
N
N
147.58
146.99
138.39
134.18
129.78
129.16
129.05
128.90
128.89
128.77
128.56
128.50
127.95
126.66
123.72
123.59
122.96
119.57
80.32
77.32
77.00
76.69
62.26
f1 (ppm)

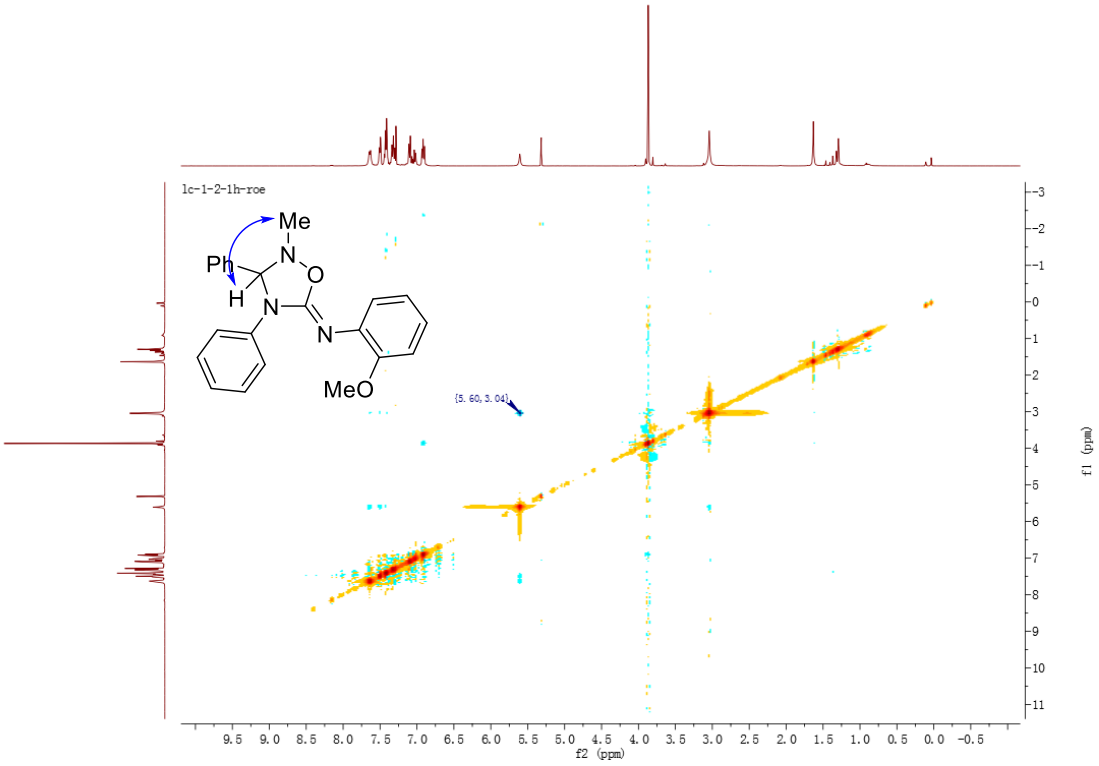

zq-8-1-1H
Me
N
O
N
N
Me
fl (ppm)

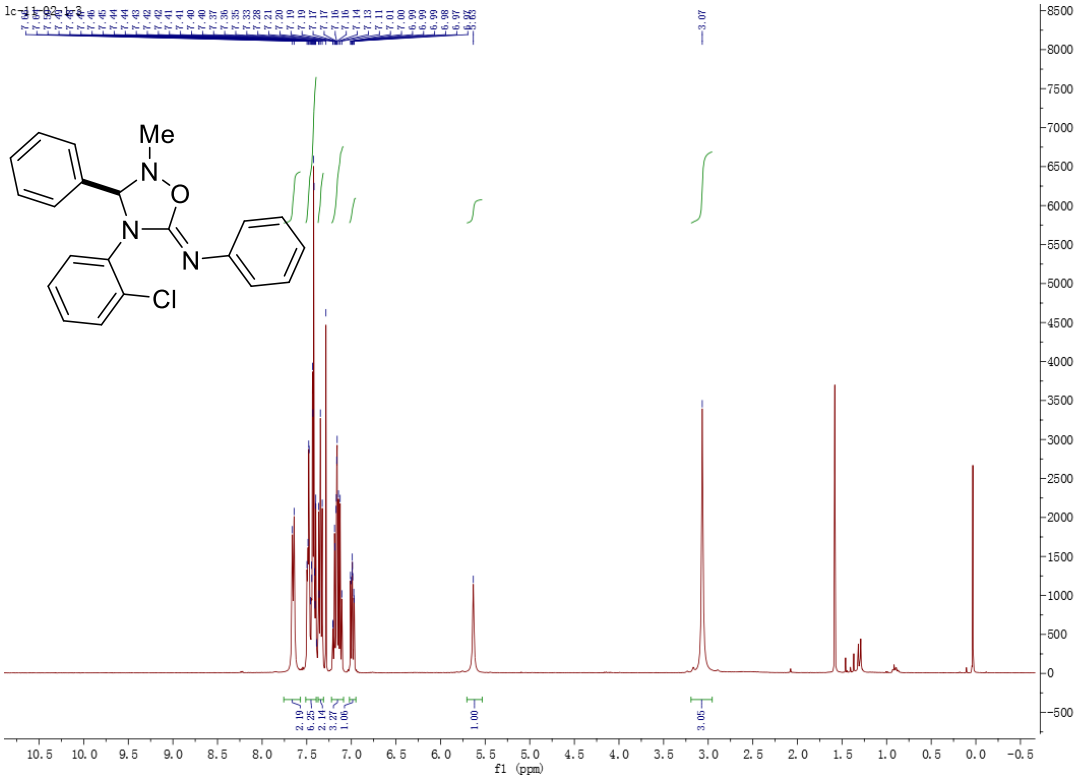

zq-8-1-13C
Me
N
O
N
N
Me
fl (ppm)

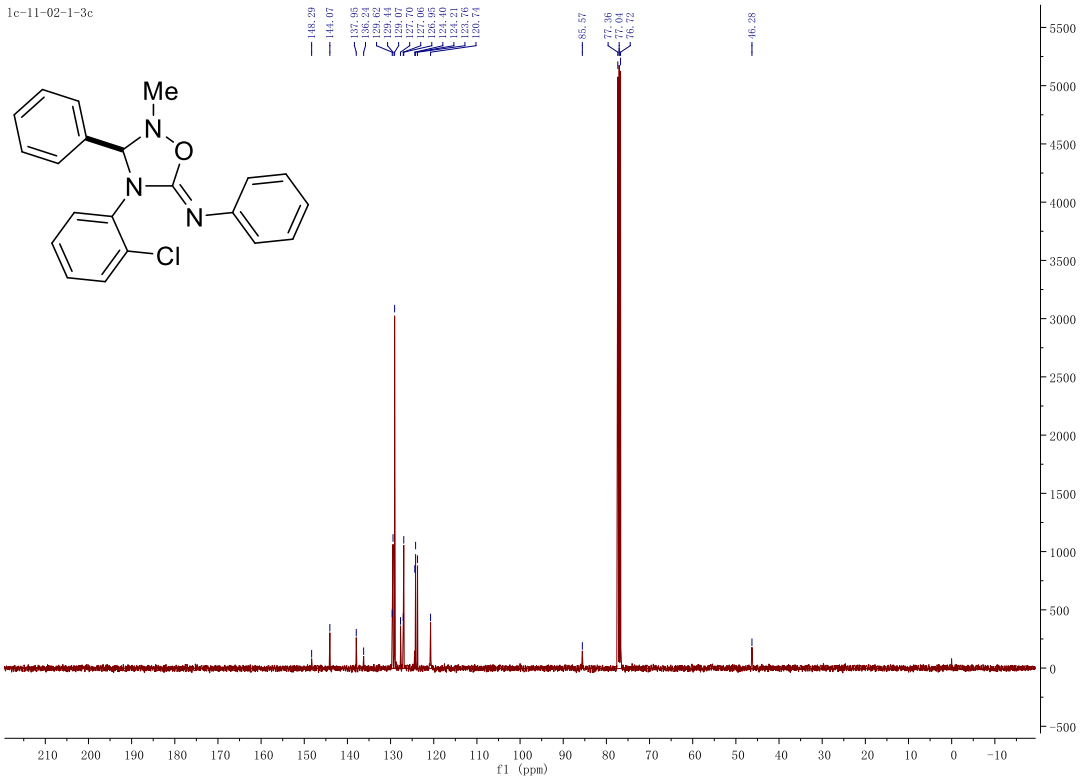

Me
Ph
H
N
O
N
N
Me
{5.62, 3.04}
{5.62, 7.45}
{5.63, 7.63}
f2 (ppm)
f1 (ppm)

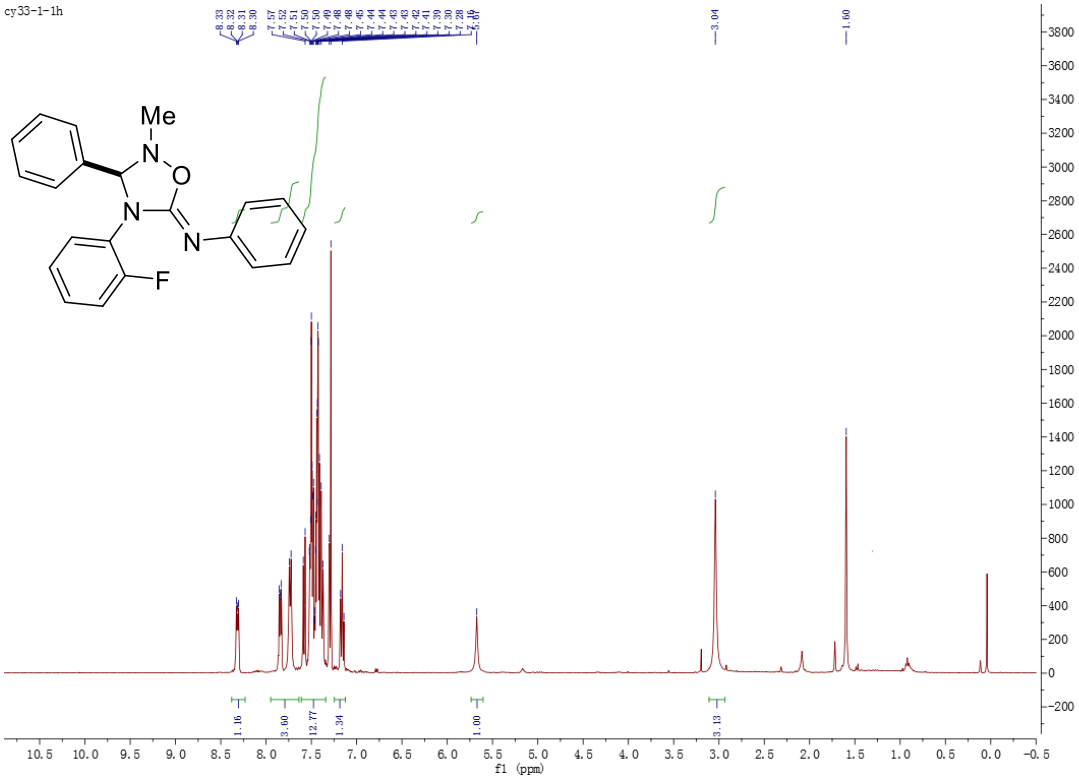

1c-1-2-1h-2
Me
N
O
N
N
MeO
5.61
3.87
3.04
2.42
8.46
5.62
1.00
3.07
3.07
f1 (ppm)

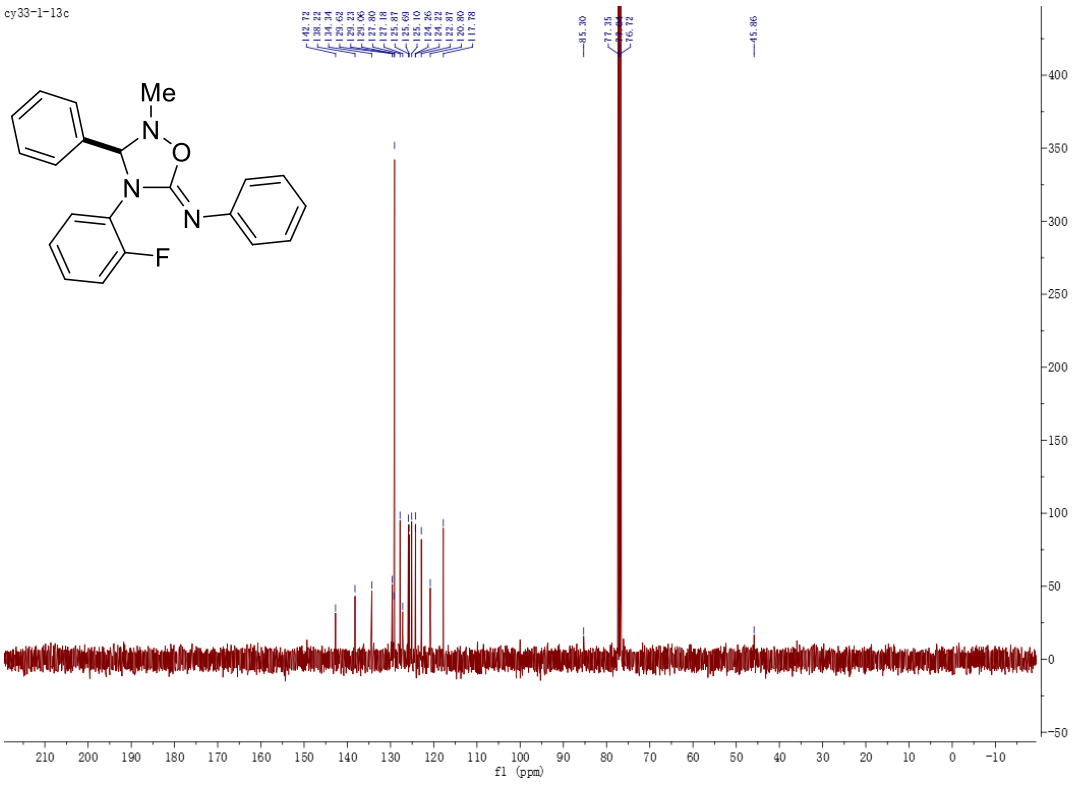

1c-1-2-13c
151.66
138.46
136.71
136.05
129.43
128.98
127.00
123.92
123.68
121.60
120.67
120.29
111.41
85.39
77.38
77.06
76.75
55.64
46.30
Me
N
O
N
N
MeO
f1 (ppm)

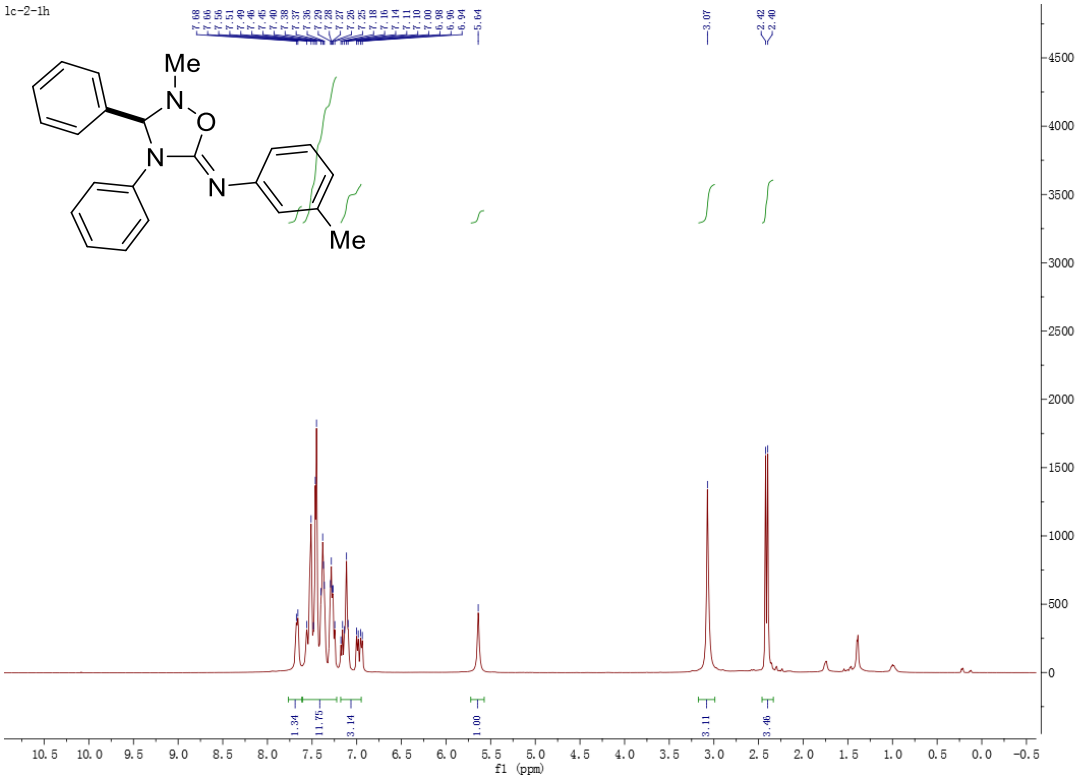

1c-1-2-1h-roe
Me
Ph
H
N
O
N
N
MeO
{5.60,3.04}
f2 (ppm)
f1 (ppm)

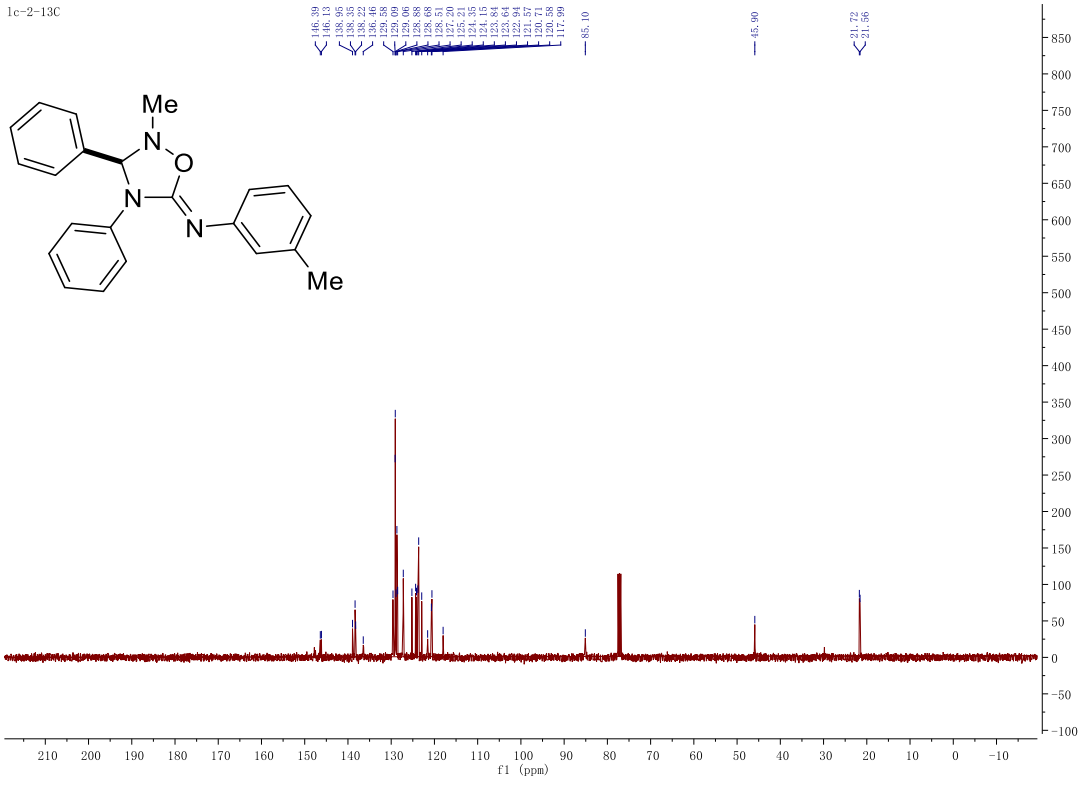

Me
N
O
N
N
Cl
3.07
2.19
2.23
2.14
3.27
1.06
1.00
3.05
f1 (ppm)

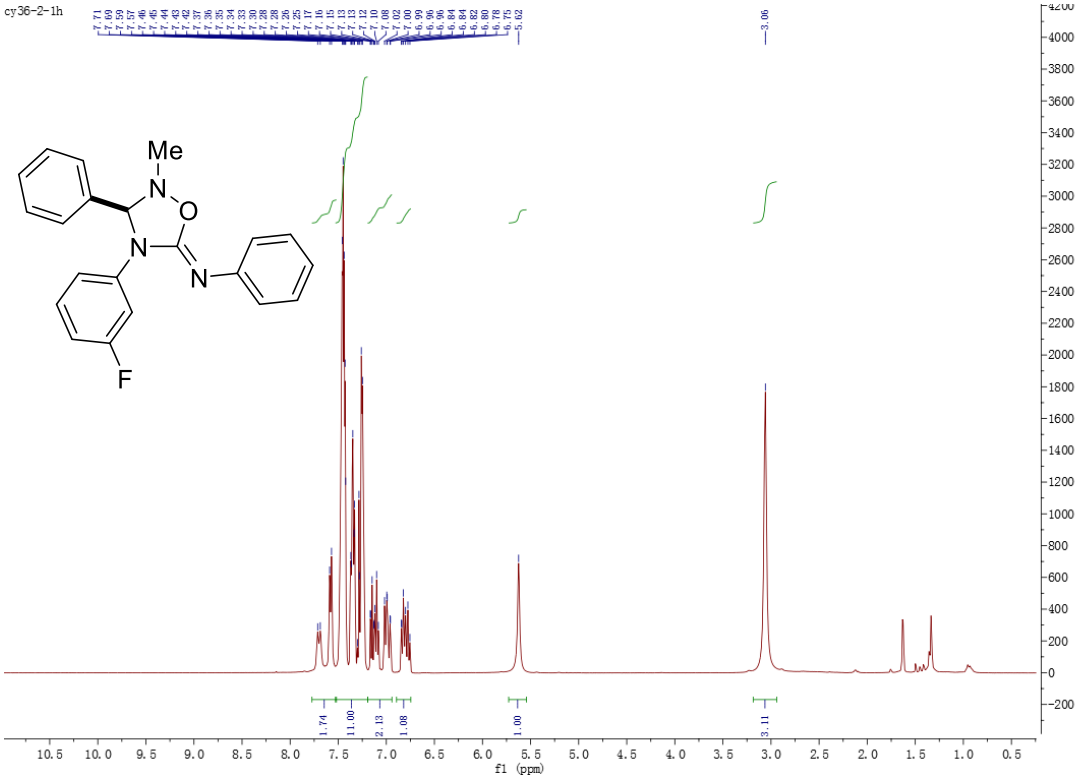

1c-11-02-1-3c
148.29
144.07
137.95
136.24
129.62
129.44
129.07
127.70
127.06
126.95
124.40
124.21
123.76
120.74
85.57
77.36
77.04
76.72
46.28
Me
N
O
N
N
Cl
f1 (ppm)

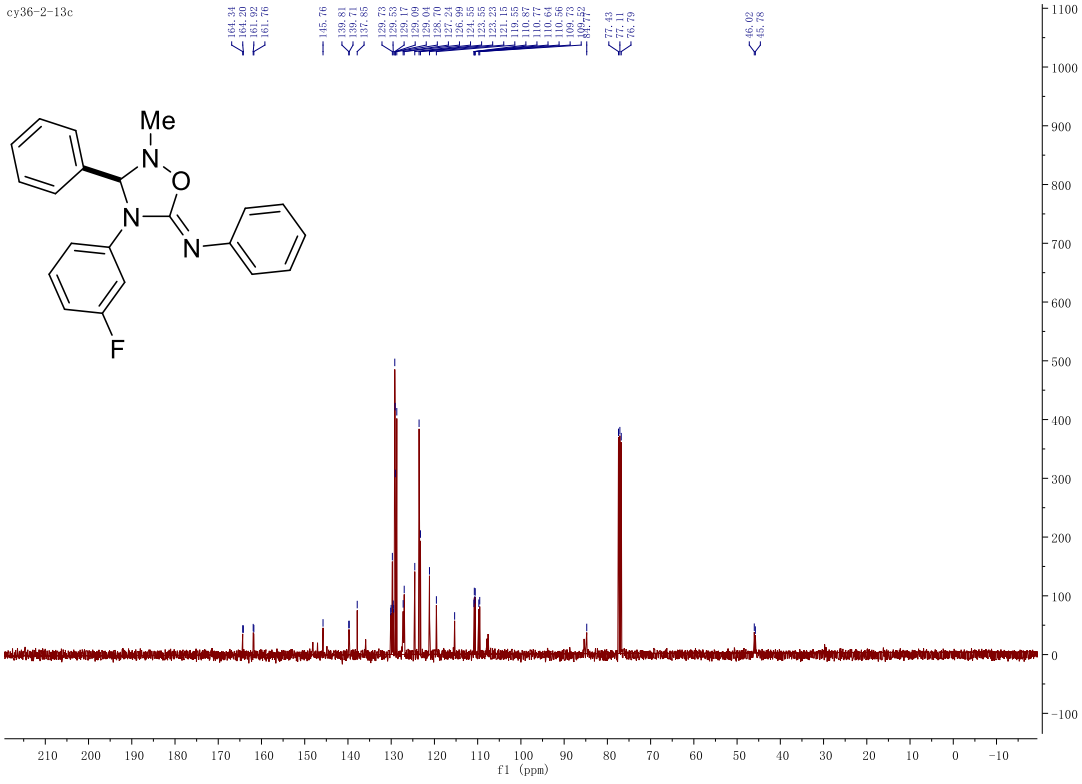

cy33-1-1h
Me
N
O
N
N
F
fl (ppm)

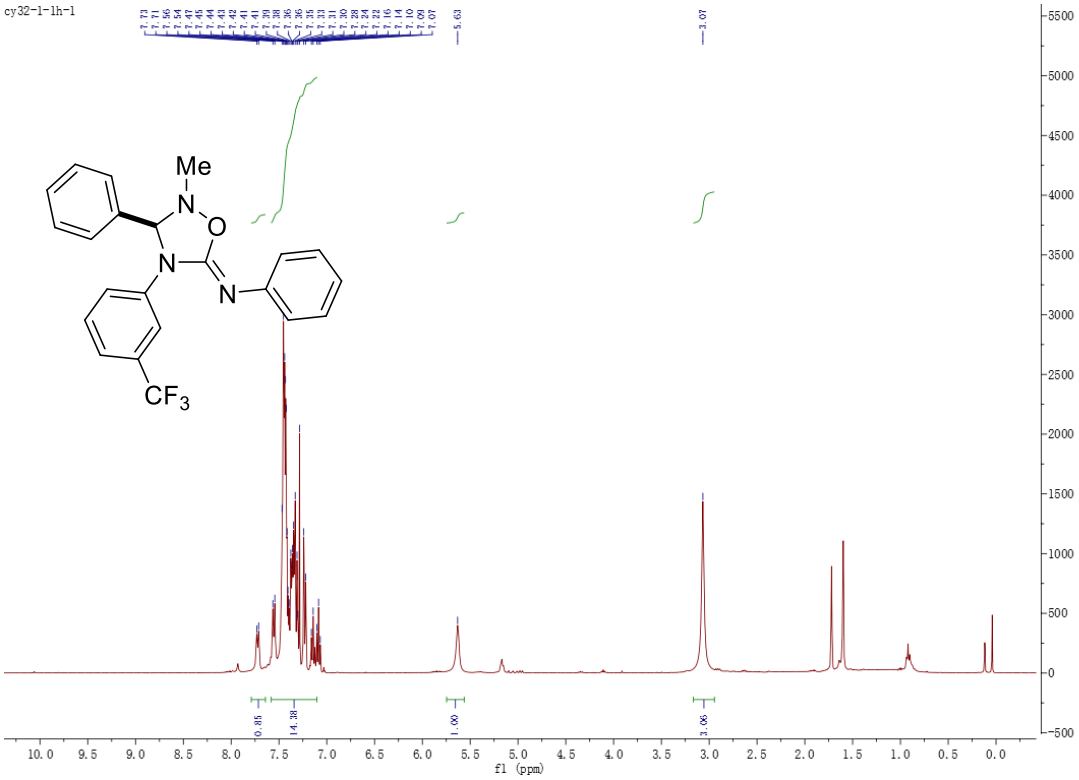

cy33-1-13c
Me
N
O
N
N
F
fl (ppm)

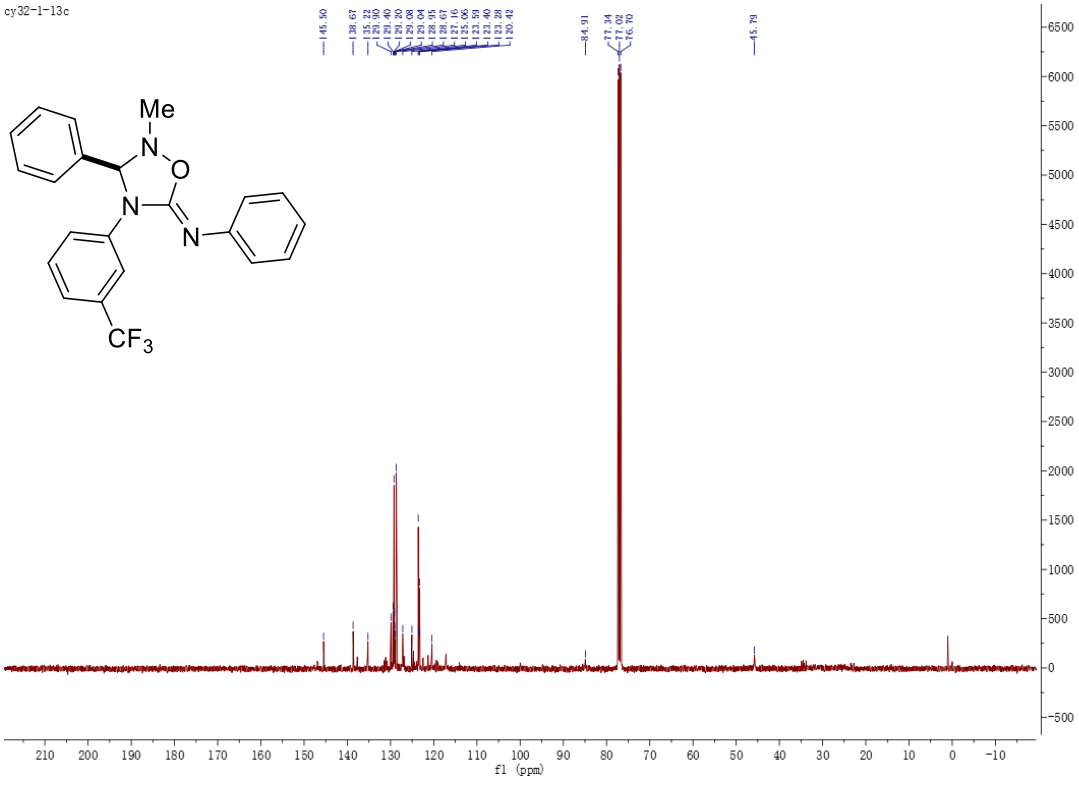

1c-2-1h
Me
N
O
N
N
Me
f1 (ppm)

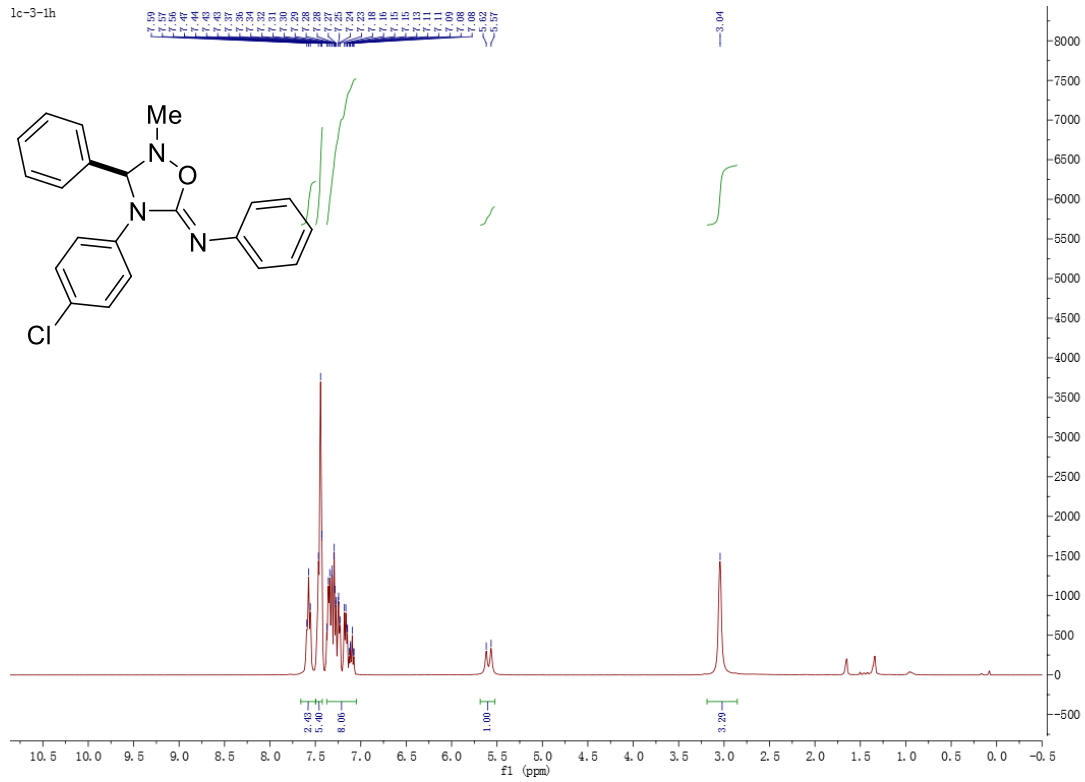

1c-2-13C
Me
N
O
N
N
Me
f1 (ppm)

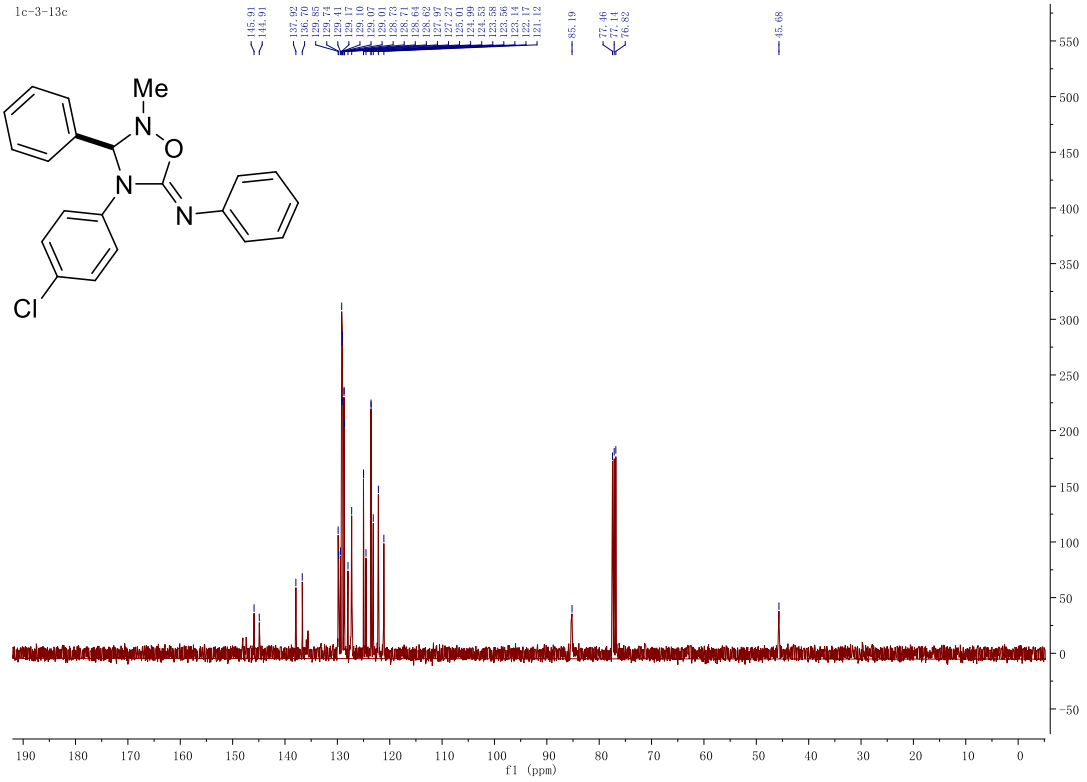

cy36-2-1h
Me
N
O
N
N
F
f1 (ppm)

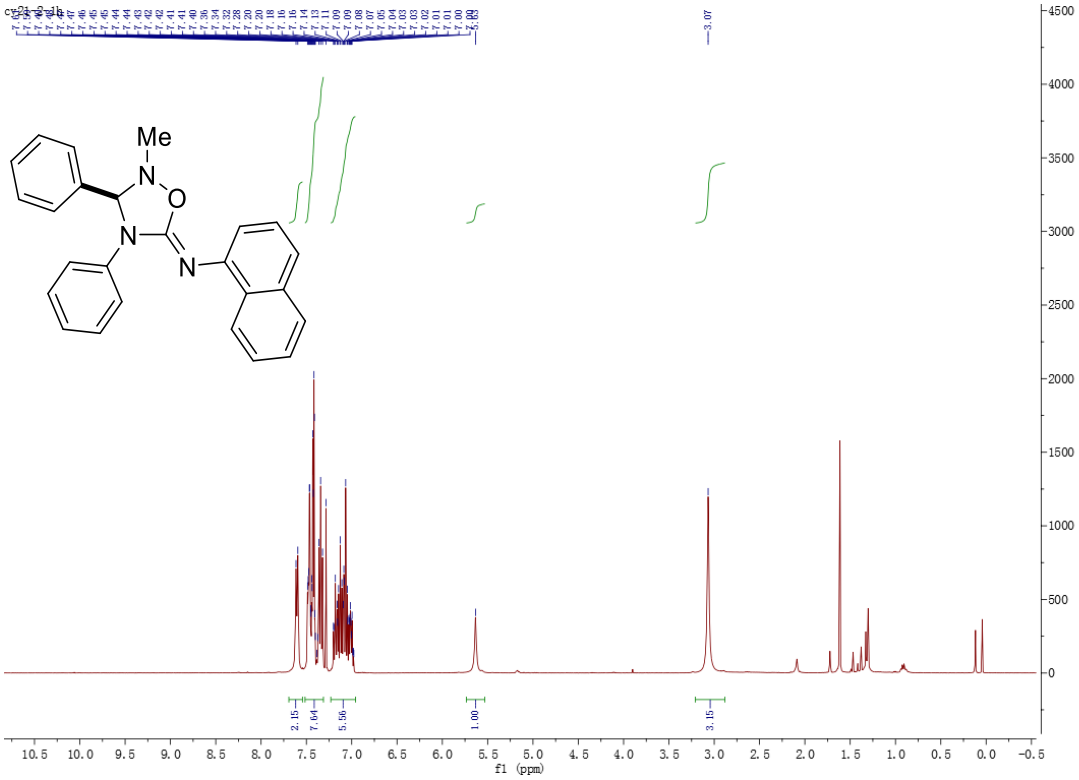

cy36-2-13c
Me
N
O
N
N
F
f1 (ppm)

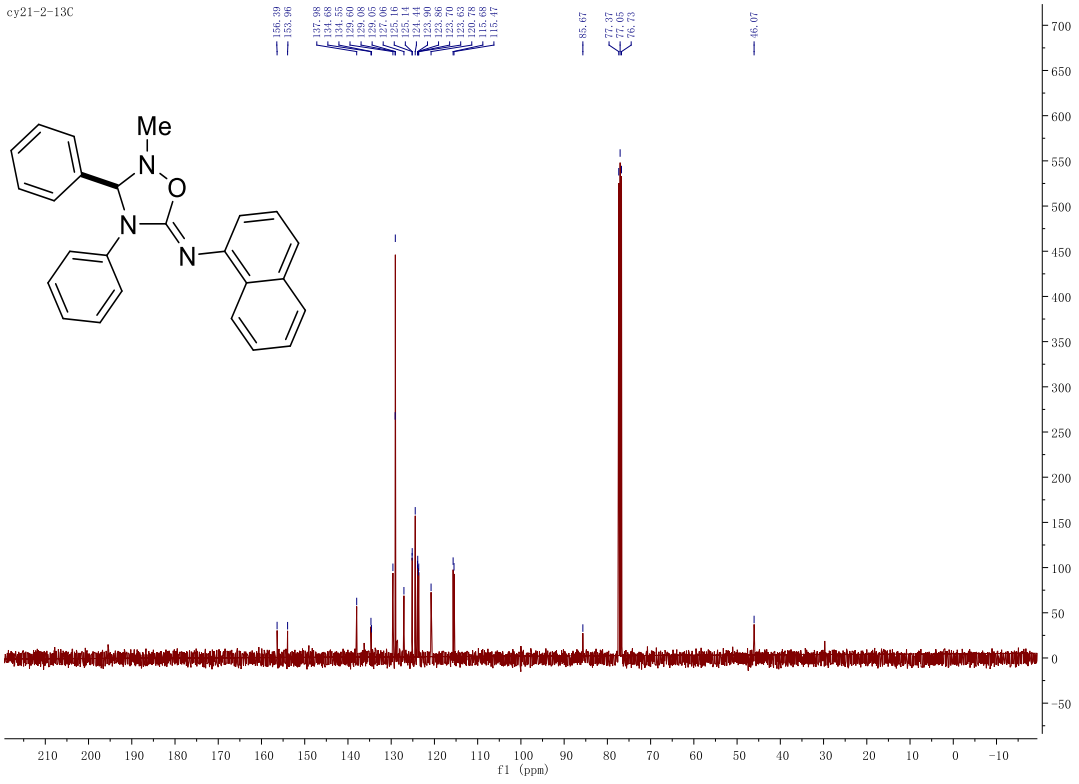

cy32-1-1h-1
Me
N
O
N
N
CF3
fl (ppm)

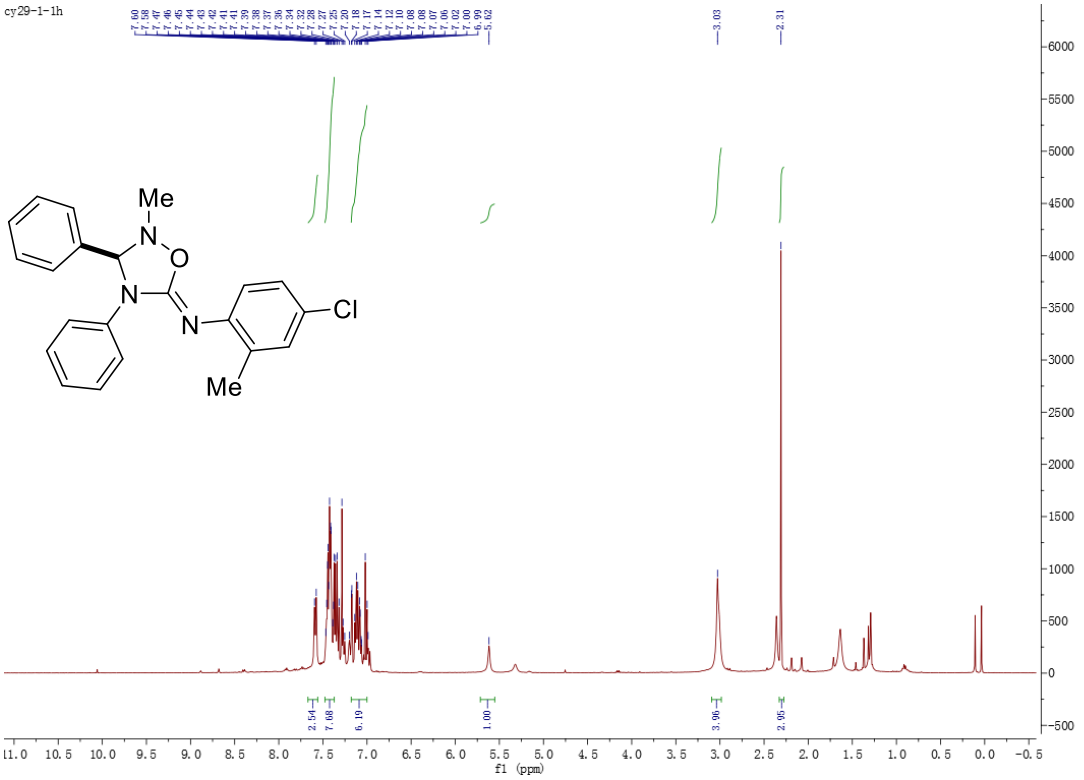

cy32-1-13c
Me
N
O
N
N
CF3
fl (ppm)

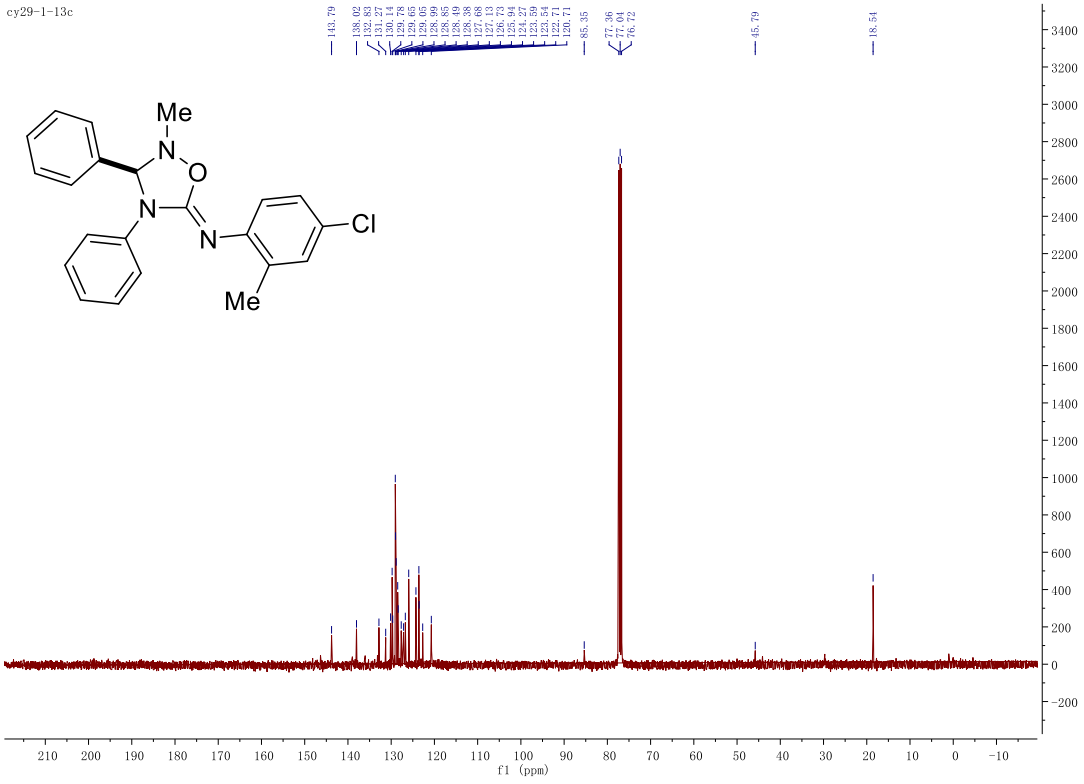

1c-3-1h
Me
N
O
N
N
Cl
f1 (ppm)

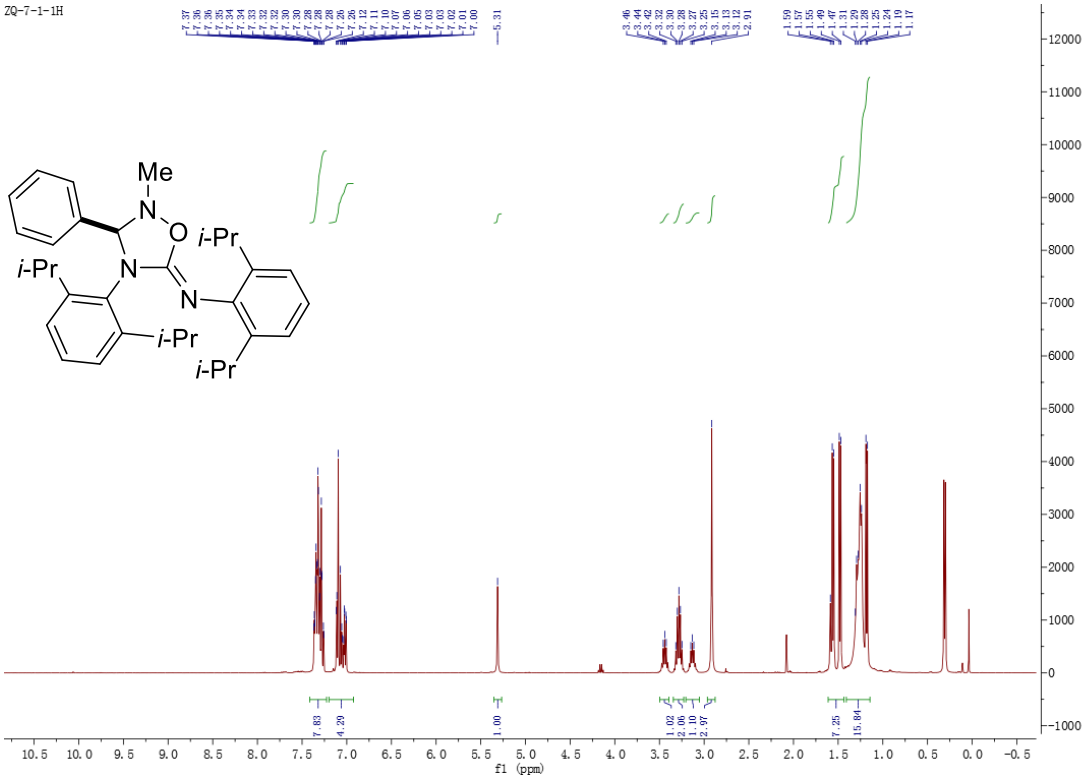

1c-3-13c
Me
N
O
N
N
Cl
f1 (ppm)

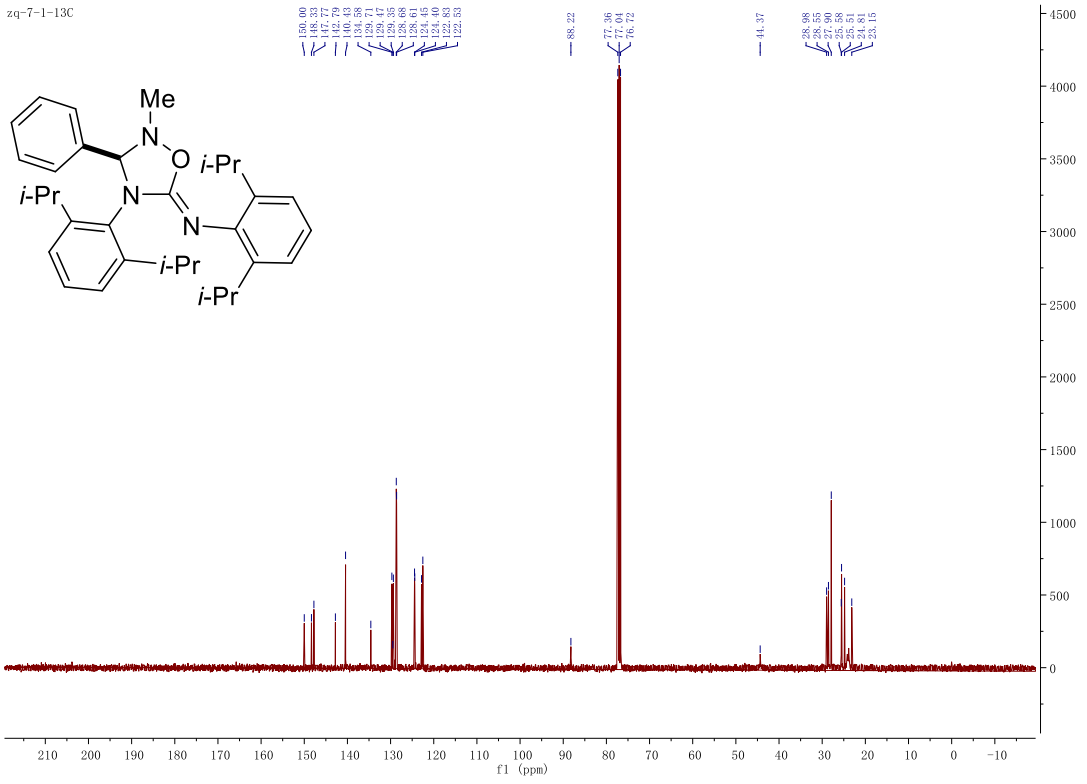

Me
N
O
N
N
2.15
7.64
5.56
1.00
3.15
f1 (ppm)


cy21-2-13C
Me
N
O
N
N
f1 (ppm)

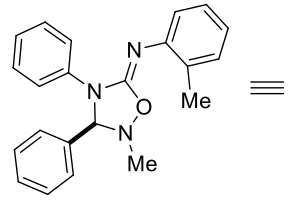

cy29-1-1h
Me
N
O
N
N
Cl
Me
f1 (ppm)


cy29-1-13c
Me
N
O
N
N
Cl
Me
f1 (ppm)


ZQ-7-1-1H
Me
N
O
i-Pr
i-Pr
N
N
i-Pr
i-Pr
f1 (ppm)


zq-7-1-13C
Me
N
O
i-Pr
i-Pr
N
N
i-Pr
i-Pr
f1 (ppm)

5 X-Ray diffraction of



4a

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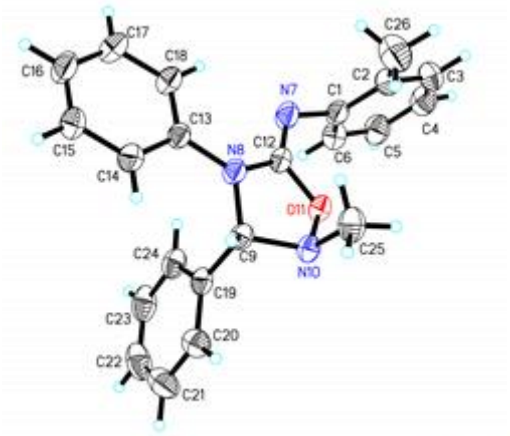

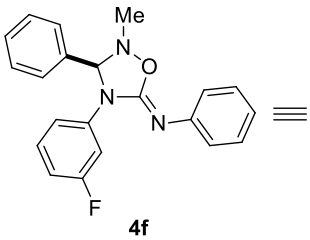

4f

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