

**β -Caryolane Derivatives as Novel Anti-Colorectal Cancer Agents: Synthesis and
in vitro Biological Evaluation**

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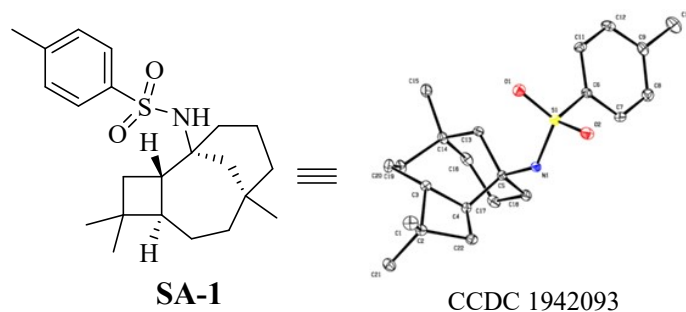
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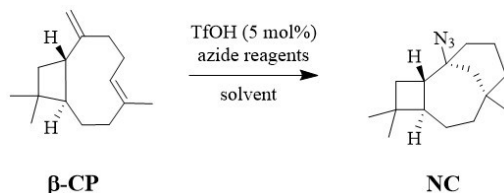
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Table S1. Crystal Structure of SA-1



Identification code	1942093
Empirical formula	C ₂₂ H ₃₃ NO ₂ S
Formula weight	375.57
Temperature (K)	100.0
a, b, c (Å)	a=8.7454(3) b=10.4909(4) c=12.6708(5)
Volume	1047.61(7)
Space group	P1
Z	2
μ (mm ⁻¹)	0.170
F000	408.0
h, k, lmax	11,13,16

Table S2. Optimization of the acid-catalyzed reaction conditions of azide reagents and β -CP. General procedure: Reactions were performed at 30°C for 16 h under air atmosphere using β -CP (0.2 mmol), azide reagents (0.1 mmol), and solvent (2 mL), with TfOH (5.0% equiv.) as catalyst, unless noted otherwise. The yield was calculated based on the ^1H NMR data with trimethoxybenzene as the internal standard and azide source as the reference.



Entry	Azide reagent	Solvent	Time (h)	yield
1	TMSN_3	1,4-dioxane	16	92%
2	NaN_3	1,4-dioxane	16	44%
3	DPPA	1,4-dioxane	16	43%
4	TMSN_3	DCM	16	96%
5	TMSN_3	1,2-DCE	16	76%
6	TMSN_3	1,4-dioxane	4	87%
7	TMSN_3	1,4-dioxane	8	91%

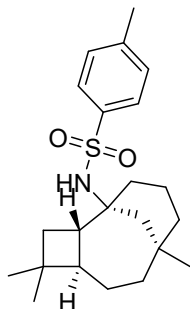
Table S3. Inhibition rate of β -caryolane derivatives (SA, CA and NC) on HT-29 cells at concentrations of 50 μ M and 10 μ M.

Cmpd	Inhibition rate %		Cmpd	Inhibition rate %		Cmpd	Inhibition rate %		Cmpd	Inhibition rate %	
	50 μ M	10 μ M		50 μ M	10 μ M		50 μ M	10 μ M		50 μ M	10 μ M
SA-1	94.62	< 50%	SA-18	93.86	< 50%	CA-1	99.42 ^a	< 50%	NC-11	16.83	< 50%
SA-2	97.68	< 50%	SA-19	100	< 50%	CA-2	74.88 ^a	< 50%	NC-12	89.88	< 50%
SA-3	87.18	< 50%	SA-20	96.14	< 50%	CA-3	98.56 ^a	< 50%	NC-13	32.3	< 50%
SA-4	98.94	< 50%	SA-21	89.3	50.38%	CA-7	66.32 ^a	< 50%	NC-14	78.27	53.38%
SA-5	99.49	< 50%	SA-22	77.15	< 50%	CA-8	62.38 ^a	< 50%	NC-15	72.3	62.69%
SA-6	97.4	< 50%	SA-23	79.82	< 50%	CA-9	61.52 ^a	< 50%	NC-16	98.53	91.64%
SA-7	15.84	-	SA-24	56.42	< 50%	CA-10	96.64 ^a	< 50%	NC-17	86.04	< 50%
SA-8	98.86	< 50%	SA-25	48.57	< 50%	NC-1	<50%	<50%	NC-18	74.43	68.09%
SA-9	48.26	< 50%	SA-26	98.64	< 50%	NC-2	44.79	< 50%	NC-19	78.51	66.86%
SA-10	83.75	< 50%	SA-27	71.37	< 50%	NC-3	36.17	< 50%	NC-20	92.96	80.20%
SA-11	75.89	< 50%	SA-28	51.78	< 50%	NC-4	44.95	< 50%	NC-21	78.32	66.28%
SA-12	70.66	< 50%	SA-29	-	82.55%	NC-5	40.42	< 50%	NC-22	75.15	67.31%
SA-13	98.14	< 50%	SA-30	-	73.98%	NC-6	93.83	< 50%	NC-23	84.11	75.65%
SA-14	98.3	< 50%	SA-31	-	55.24%	NC-7	88.8	< 50%	NC-24	83.74	76.62%
SA-15	100	< 50%	SA-32	-	78.01%	NC-8	45.77	< 50%			

“-”,	SA-16	98.72	< 50%	SA-33	47	< 50%	NC-9	54.99	< 50%				μM
	SA-17	93.54	< 50%	SA-34	90.18	< 50%	NC-10	72.94	< 50%	□	□	□	
	not		determined;			“a”,	measured		at	300			

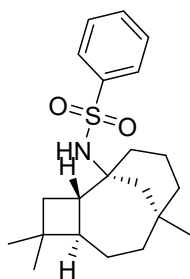
1. Characterization data of target compounds

4-Methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-1**)



According to the general procedure A, compound **SA-1** could be obtained with 100% yield as white solid using β -Caryophyllene and p-Toluenesulfonamide as substrates. Recrystallisation (DCM/hexane) of a portion of this material afforded an analytically pure sample of **SA-1** as fine white crystals. ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.26 (s, *J* = 8.3 Hz, 2H), 4.36 (s, 1H), 2.42 (s, 3H), 2.34 – 2.25 (m, 1H), 1.75–1.64 (m, 4H), 1.59 (d, *J* = 10.4 Hz, 2H), 1.52–1.48 (m, 1H), 1.46 – 1.39 (m, 3H), 1.32 – 1.25 (m, 3H), 1.22 (d, *J* = 12.9 Hz, 1H), 1.11 – 1.05 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.78 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 142.54, 141.47, 129.40, 126.79, 58.97, 45.78, 44.96, 40.05, 37.44, 36.99, 36.89, 35.13, 34.43, 34.28, 33.57, 30.48, 21.85, 21.50, 20.77, 20.06.

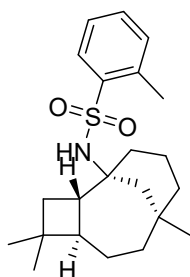
N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-2**)



According to the general procedure A, compound **SA-2** could be obtained with 88% yield as white solid using β -Caryophyllene and benzenesulfonamide as substrates. ¹H NMR (400 MHz, CDCl₃) δ 7.91 – 7.85 (m, 2H), 7.55 – 7.45 (m, 3H), 4.48 (s, 1H), 2.30 (td, *J* = 11.0, 8.2 Hz, 1H), 1.73 – 1.66 (m, 3H), 1.62 – 1.57 (m, 3H), 1.54 – 1.48 (m, 2H), 1.46 – 1.36 (m, 3H), 1.34 – 1.28 (m, 2H), 1.21 (d, *J* = 12.9 Hz, 1H), 1.11 – 1.04 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.78 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.29, 131.98, 128.82, 126.76, 59.12, 45.79, 45.02, 40.05, 37.41, 37.01, 36.88, 35.23, 34.46, 34.29, 33.55, 30.51, 21.85, 20.75, 20.06.

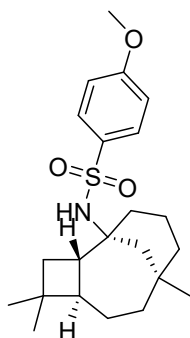
2-Methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-

yl)benzenesul fonamide (**SA-3**)



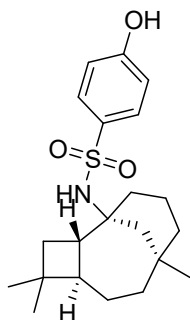
According to the general procedure A, compound **SA-3** could be obtained with 80% yield as white solid using β -Caryophyllene and 2-methylbenzene-1-sulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.99 (dd, $J = 5.6, 2.9$ Hz, 1H), 7.42 (td, $J = 7.5, 1.2$ Hz, 1H), 7.29 (dd, $J = 7.4, 3.6$ Hz, 2H), 4.34 (s, 1H), 2.68 (s, 3H), 2.32 (td, $J = 11.0, 8.2$ Hz, 1H), 1.80 – 1.71 (m, 2H), 1.70 – 1.62 (m, 2H), 1.60 (d, $J = 10.2$ Hz, 1H), 1.55 – 1.47 (m, 3H), 1.45 – 1.38 (m, 2H), 1.34 – 1.27 (m, 3H), 1.22 (d, $J = 13.6$ Hz, 1H), 1.09 – 1.04 (m, 1H), 1.02 (s, 3H), 0.99 (s, 3H), 0.76 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 141.99, 136.49, 132.28, 132.16, 128.80, 126.05, 59.16, 45.67, 45.03, 40.00, 37.36, 36.97, 36.83, 35.16, 34.52, 34.32, 33.50, 30.54, 21.81, 20.76, 20.35, 20.07.

4-Methoxy-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzene sulfonamide (**SA-4**)



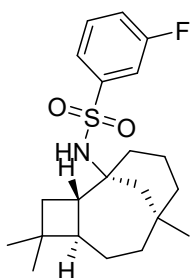
According to the general procedure A, compound **SA-4** could be obtained with 90% yield as white solid using β -Caryophyllene and p-methoxybenzenesulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.84 – 7.74 (m, 2H), 6.99 – 6.90 (m, 2H), 4.33 (s, 1H), 3.86 (s, 3H), 2.34 – 2.24 (m, 1H), 1.78 – 1.67 (m, 3H), 1.67 – 1.58 (m, 2H), 1.52 – 1.37 (m, 4H), 1.30–1.25 (m, 4H), 1.22(d, $J = 12.8$ Hz, 1H), 1.11 – 1.03 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.79 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.30, 136.12, 128.87, 113.91, 58.89, 55.56, 45.72, 44.99, 40.00, 37.44, 36.92, 36.86, 35.19, 34.46, 34.29, 33.57, 30.51, 21.83, 20.76, 20.07.

4-Hydroxy-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzene sulfonamide (**SA-5**)



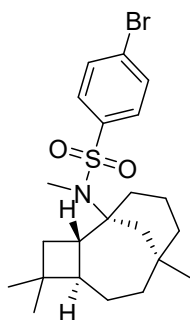
According to the general procedure A, compound **SA-5** could be obtained with 80% yield as white solid using β -Caryophyllene and 4-hydroxybenzenesulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.76 – 7.72 (m, 2H), 6.91 – 6.86 (m, 2H), 6.12 (s, 1H), 4.36 (s, 1H), 2.28 (ddd, J = 17.5, 10.4, 5.4 Hz, 1H), 1.78 – 1.69 (m, 3H), 1.62 – 1.58 (m, 1H), 1.53 – 1.42 (m, 4H), 1.37 – 1.30 (m, 3H), 1.28–1.25 (m, 2H), 1.22 (d, J = 12.9 Hz, 1H), 1.12 – 1.07 (m, 1H), 1.00 (s, 3H), 0.98 (s, 3H), 0.79 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.05, 135.93, 129.12, 115.55, 58.97, 45.70, 44.99, 39.99, 37.43, 36.91, 36.85, 35.19, 34.47, 34.29, 33.57, 30.52, 21.82, 20.76, 20.06.

3-Fluoro-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesul fonamide (**SA-6**)



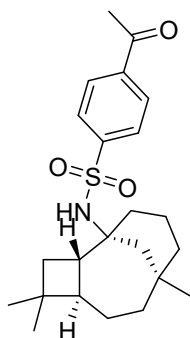
According to the general procedure A, compound **SA-6** could be obtained with 77% yield as white solid using β -Caryophyllene and 3-fluorobenzenesulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.47 (dt, J = 13.4, 6.7 Hz, 1H), 7.23 (td, J = 8.3, 1.1 Hz, 1H), 4.52 (s, 1H), 2.31 (dd, J = 19.5, 11.1 Hz, 1H), 1.77– 1.71 (m, 2H), 1.65– 1.58(m, 2H), 1.54–1.41 (m, 4H), 1.39 – 1.25 (m, 5H), 1.20 (d, J = 12.8 Hz, 1H), 1.11 – 1.06 (m, 1H), 1.01 (s, 3H), 0.99 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.28 (d, J = 250.7 Hz), 146.36 (d, J = 6.7 Hz), 130.60 (d, J = 7.6 Hz), 122.50 (d, J = 3.1 Hz), 119.18 (d, J = 21.5 Hz), 114.18 (d, J = 24.2 Hz), 59.45, 45.92, 45.11, 40.06, 37.37, 37.12, 36.90, 35.21, 34.46, 34.31, 33.55, 30.51, 21.88, 20.73, 20.04.

3-Bromo-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesul fonamide (**SA-7**)



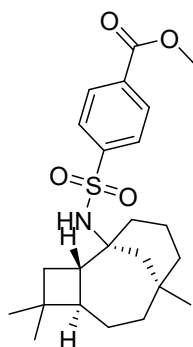
According to the general procedure A, compound **SA-7** could be obtained with 67% yield as white solid using β -Caryophyllene and 4-bromo-N-methylbenzenesulphonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.61 – 7.56 (m, 2H), 7.54 – 7.48 (m, 2H), 2.89 (s, 3H), 2.35 (d, J = 12.9 Hz, 1H), 2.17 – 2.00 (m, 2H), 1.96 – 1.87 (m, 1H), 1.76 (dd, J = 9.6, 7.9 Hz, 1H), 1.69 – 1.59 (m, 2H), 1.51 – 1.44 (m, 1H), 1.43 – 1.37 (m, 2H), 1.29 – 1.25 (m, 1H), 1.19 (d, J = 12.8 Hz, 1H), 1.11 – 1.02 (m, 2H), 0.94 (s, 3H), 0.90 (s, 3H), 0.87 – 0.78 (m, 2H), 0.73 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 143.87, 132.00, 128.01, 126.29, 65.40, 46.10, 44.68, 41.61, 39.08, 38.08, 36.48, 36.34, 34.50, 34.18, 34.12, 33.93, 30.37, 22.74, 20.89, 20.40.

5-Acetyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesul fonamide (**SA-8**)



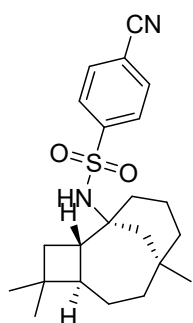
According to the general procedure A, compound **SA-8** could be obtained with 78% yield as white solid using β -Caryophyllene and 4-acetylbenzenesulphonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 8.06 (d, J = 8.6 Hz, 2H), 8.00 (d, J = 8.6 Hz, 2H), 5.22 (s, 1H), 2.66 (s, 3H), 2.29 (dt, J = 11.6, 6.9 Hz, 1H), 1.82– 1.64 (m, 6H), 1.55 – 1.45 (m, 2H), 1.44 – 1.40 (m, 1H), 1.36 – 1.26 (m, 4H), 1.14 (d, J = 12.9 Hz, 1H), 1.10 – 1.04 (m, 1H), 0.99 (s, 3H), 0.98 (s, 3H), 0.77 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 196.99, 148.42, 139.37, 128.78, 126.98, 59.46, 46.03, 44.85, 40.02, 37.37, 37.21, 36.86, 35.02, 34.34, 34.20, 33.54, 30.43, 26.87, 21.83, 20.76, 19.98.

Methyl-4-(N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)sulfamoyl) benzoate (**SA-9**)



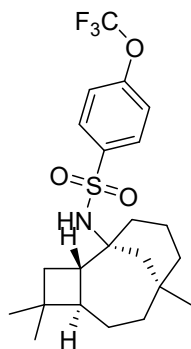
According to the general procedure A, compound **SA-9** could be obtained with 81% yield as white solid using β -Caryophyllene and methyl 4-sulphamoylbenzoate as substrates; ^1H NMR (400 MHz, CDCl_3) δ 8.20 – 8.07 (m, 2H), 8.02 – 7.91 (m, 2H), 4.67 (s, 1H), 3.96 (s, 3H), 2.30 (td, $J = 10.8, 8.3$ Hz, 1H), 1.78-1.67 (m, 4H), 1.64-1.61 (m, 1H), 1.56-1.43 (m, 2H), 1.46 – 1.37 (m, 2H), 1.36 – 1.28 (m, 3H), 1.28 – 1.23 (m, 1H), 1.17 (d, $J = 12.8$ Hz, 1H), 1.10 – 1.04 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.78 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.83, 148.27, 133.18, 130.13, 126.80, 59.45, 52.59, 45.90, 45.03, 40.02, 37.36, 37.10, 36.86, 35.26, 34.45, 34.29, 33.53, 30.50, 21.84, 20.73, 20.02.

4-Cyano-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-10**)



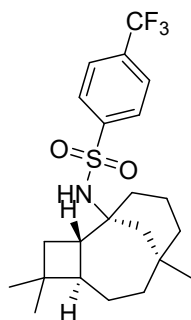
According to the general procedure A, compound **SA-10** could be obtained with 58% yield as white solid using β -Caryophyllene and 4-sulphamoylbenzonitrile as substrates; ^1H NMR (400 MHz, CDCl_3) δ 8.01 – 7.96 (m, 2H), 7.81 – 7.77 (m, 2H), 4.51 (s, 1H), 2.38 – 2.26 (m, 1H), 1.76 – 1.68 (m, 4H), 1.63 – 1.57 (m, 2H), 1.53 (s, 1H), 1.47-1.41 (m, 2H), 1.38 – 1.28 (m, 4H), 1.16 (d, $J = 12.8$ Hz, 1H), 1.13 – 1.06 (m, 1H), 1.02 (s, 3H), 0.99 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 148.44, 132.77, 127.41, 117.50, 115.75, 59.84, 46.12, 45.20, 40.07, 37.31, 37.25, 36.90, 35.31, 34.48, 34.34, 33.56, 30.54, 21.90, 20.69, 20.00.

4-(Trifluoromethoxy)-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-11**)



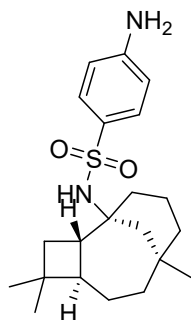
According to the general procedure A, compound **SA-11** could be obtained with 94% yield as white solid using β -Caryophyllene and 4-(trifluoromethoxy)benzenesulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.94 – 7.89 (m, 2H), 7.31 (d, J = 8.4 Hz, 2H), 4.48 (s, 1H), 2.37 – 2.26 (m, 1H), 1.76 – 1.67 (m, 4H), 1.1.63-1.58 (m, 2H), 1.53-1.48(m, 1H), 1.41-1.35(m, 2H), 1.35 – 1.25 (m, 4H), 1.19 (d, J = 12.8 Hz, 1H), 1.09-1.05(m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 151.59, 142.68, 128.86, 120.74, 59.48, 46.01, 45.13, 40.08, 37.37, 37.15, 36.92, 35.21, 34.46, 34.30, 33.55, 30.50, 26.92, 21.90, 20.72, 20.03.

4-(Trifluoromethyl)-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-12**)



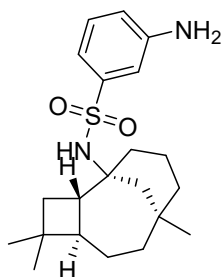
According to the general procedure A, compound **SA-12** could be obtained with 91% yield as white solid using β -Caryophyllene and 4-(trifluoromethyl)benzenesulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 8.00 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 8.3 Hz, 2H), 4.55 (s, 1H), 2.40 – 2.24 (m, 1H), 1.78 – 1.68 (m, 4H), 1.63 – 1.58 (m, 1H), 1.58 – 1.53 (m, 2H), 1.49-1.40 (m, 2H), 1.38 – 1.26 (m, 4H), 1.18 (d, J = 12.8 Hz, 1H), 1.12-1.08(m, 1H), 1.02 (s, 3H), 0.99 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 147.80, 133.75 (d), 133.57, 127.22, 126.05 (q, J = 3.7 Hz), 59.66, 46.11, 45.16, 40.11, 37.33, 37.23, 36.94, 35.20, 34.45, 34.32, 33.56, 30.51, 21.92, 20.71, 20.02.

4-Amino-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-13**)



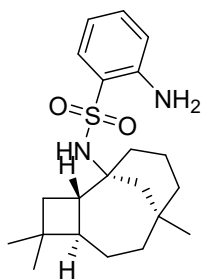
According to the general procedure A, compound **SA-13** could be obtained with 56% yield as white solid using β -Caryophyllene and p-aminobenzenesulfonamide as substrates. HRMS (ESI) for $C_{21}H_{32}N_2O_2S$: calculated, $[M+H]^+ = 377.2263$, found 377.2250; 1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, $J = 8.6$ Hz, 2H), 6.68 (d, $J = 8.6$ Hz, 2H), 4.32 (s, 1H), 2.37 – 2.26 (m, 1H), 1.78–1.70 (m, 2H), 1.69 – 1.59 (m, 4H), 1.58 – 1.49 (m, 3H), 1.48 – 1.39 (m, 3H), 1.34 – 1.30 (m, 3H), 1.24 (d, $J = 12.8$ Hz, 1H), 1.10 – 1.04 (m, 1H), 1.00 (s, 3H), 0.98 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.47, 133.22, 128.87, 114.18, 58.68, 45.63, 44.93, 39.99, 37.48, 36.86, 35.17, 34.45, 34.29, 33.58, 30.50, 29.71, 21.82, 20.78, 20.09.

3-Amino-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesul fonamide (**SA-14**)



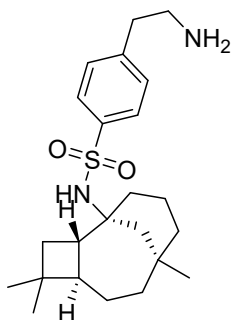
According to the general procedure A, compound **SA-14** could be obtained with 61% yield as white solid using β -Caryophyllene and m-aminobenzenesulfonamide as substrates. HRMS (ESI) for $C_{21}H_{32}N_2O_2S$: calculated, $[M+H]^+ = 377.2263$, found 377.2250; 1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, $J = 5.0$ Hz, 2H), 7.11 (s, 1H), 6.78 – 6.70 (m, 1H), 4.41 (s, 1H), 2.23 (td, $J = 10.8, 8.2$ Hz, 1H), 1.73 – 1.64 (m, 2H), 1.61 – 1.52 (m, 3H), 1.51 – 1.41 (m, 2H), 1.40 – 1.30 (m, 3H), 1.28 – 1.21 (m, 3H), 1.16 (d, $J = 8.9$ Hz, 1H), 1.04 – 0.98 (m, 1H), 0.94 (s, 3H), 0.91 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.55, 144.17, 128.71, 117.38, 115.72, 111.82, 58.03, 44.80, 43.97, 39.10, 36.40, 36.06, 35.91, 34.04, 33.38, 33.25, 32.56, 29.46, 20.87, 19.75, 19.05.

2-Amino-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesul fonamide (**SA-15**).



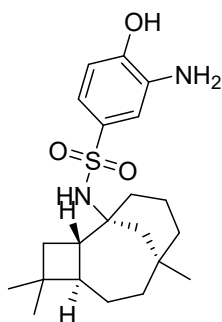
According to the general procedure A, compound **SA-15** could be obtained with 40% yield as white solid using β -Caryophyllene and o-aminobenzenesulfonamide as substrates. HRMS (ESI) for $C_{21}H_{32}N_2O_2S$: calculated, $[M+H]^+ = 377.2263$, found 377.2250; 1H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, $J = 8.0, 1.4$ Hz, 1H), 7.31 – 7.26 (m, 1H), 6.81 – 6.71 (m, 2H), 4.73 (s, 1H), 2.33 – 2.23 (m, 1H), 1.71 (ddd, $J = 15.4, 10.6, 5.7$ Hz, 2H), 1.66 – 1.59 (m, 3H), 1.59 – 1.46 (m, 3H), 1.44 – 1.36 (m, 2H), 1.34 – 1.24 (m, 3H), 1.22 (d, $J = 12.8$ Hz, 1H), 1.05 (ddd, $J = 8.6, 6.1, 2.9$ Hz, 1H), 0.99 (s, 3H), 0.97 (s, 3H), 0.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.52, 133.45, 129.08, 126.35, 117.74, 117.63, 59.04, 45.17, 44.75, 39.81, 37.46, 36.73, 36.57, 35.23, 34.46, 34.35, 33.52, 30.45, 21.68, 20.79, 20.14.

4-(2-Aminoethyl)-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-16**).



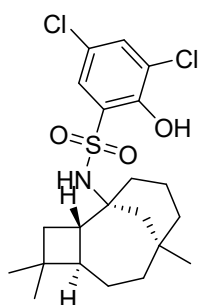
According to the general procedure A, compound **SA-16** could be obtained with 90% yield as yellow oil using β -Caryophyllene and 4-(2-aminoethyl)benzenesulfonamide as substrates; HRMS (ESI) for $C_{23}H_{36}N_2O_2S$: calculated, $[M+H]^+ = 405.2576$, found 405.2572; 1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, $J = 8.2$ Hz, 2H), 7.31 (d, $J = 8.2$ Hz, 2H), 4.65 (s, 1H), 3.13 (s, 2H), 3.08 – 3.02 (t, $J = 6.8$ Hz, 2H), 2.90 (t, $J = 6.8$ Hz, 2H), 2.30 (dd, $J = 19.8, 10.9$ Hz, 1H), 1.79 – 1.67 (m, 4H), 1.66–1.60 (m, 2H), 1.56 – 1.47 (m, 2H), 1.47 – 1.39 (m, 2H), 1.37–1.30 (m, 3H), 1.18 (d, $J = 12.9$ Hz, 1H), 1.11 – 1.04 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.31, 142.57, 129.33, 127.01, 59.22, 45.96, 45.01, 42.41, 40.12, 37.41, 37.20, 36.94, 35.10, 34.40, 34.27, 33.59, 30.51, 29.71, 21.90, 20.77, 20.05.

2-Amino-4-hydroxy-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl) benzenesulfonamide (**SA-17**)



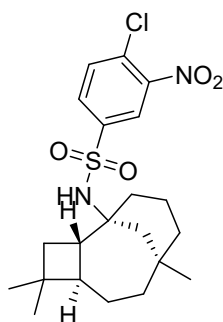
According to the general procedure A, compound **SA-17** could be obtained with 90% yield as white solid using β -Caryophyllene and 3-amino-4-hydroxybenzenesulphonamide as substrates; HRMS (ESI) for $C_{21}H_{32}N_2O_3S$: calculated, $[M+H]^+ = 393.2212$, found 393.1975; 1H NMR (400 MHz, DMSO) δ 9.83 (s, 1H), 7.03 (d, $J = 2.2$ Hz, 1H), 6.93 (s, 1H), 6.86 (dd, $J = 8.2, 2.2$ Hz, 1H), 6.70 (d, $J = 8.2$ Hz, 1H), 5.07 (s, 2H), 2.26 – 2.10 (m, 1H), 1.90 – 1.80 (m, 1H), 1.80 – 1.62 (m, 4H), 1.60 – 1.32 (m, 5H), 1.31 – 1.08 (m, 4H), 0.97 (s, 3H), 0.95 (s, 3H), 0.87 – 0.80 (m, 1H), 0.74 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 147.24, 136.51, 136.65, 115.80, 113.79, 112.32, 66.83, 58.01, 46.17, 44.01, 37.76, 37.75, 36.80, 34.37, 34.00, 33.88, 30.71, 21.87, 21.36, 19.88.

3,5-Dichloro-2-hydroxy-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-18**)



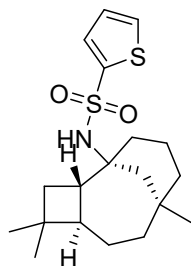
According to the general procedure A, compound **SA-18** could be obtained with 65% yield as white solid using β -Caryophyllene and 3,5-dichloro-2-hydroxybenzenesulfonamide as substrates; 1H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.53 (d, $J = 2.5$ Hz, 1H), 7.45 (d, $J = 2.5$ Hz, 1H), 4.66 (s, 1H), 2.31 – 2.22 (m, 1H), 1.69 – 1.62 (m, 4H), 1.621.56 (m, 2H), 1.47 – 1.37 (m, 4H), 1.36 – 1.29 (m, 3H), 1.14 (d, $J = 12.8$ Hz, 2H), 1.05–1.01 (m, 1H), 0.95 (s, 3H), 0.92 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.75, 132.99, 128.61, 125.45, 123.91, 123.05, 59.33, 44.69, 44.16, 38.90, 36.24, 36.07, 35.79, 34.06, 33.47, 33.36, 32.47, 29.47, 28.68, 20.78, 19.65, 19.01.

2-Chloro-3-nitro-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-19**)



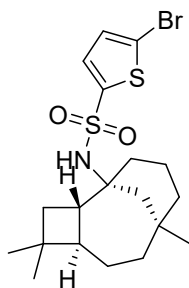
According to the general procedure A, compound **SA-19** could be obtained with 85% yield as white solid using β -Caryophyllene and 4-chloro-3-nitrobenzenesulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 8.36 (d, $J = 2.1$ Hz, 1H), 7.99 (dd, $J = 8.4$, 2.1 Hz, 1H), 7.69 (d, $J = 8.5$ Hz, 1H), 4.59 (s, 1H), 2.33 (td, $J = 10.9$, 8.2 Hz, 1H), 1.78-1.71 (m, 4H), 1.66 – 1.59 (m, 2H), 1.54 – 1.43 (m, 4H), 1.38 – 1.32 (m, 3H), 1.18 (d, $J = 12.8$ Hz, 1H), 1.13-1.09 (m, 1H), 1.02 (s, 3H), 1.00 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 147.69 , 144.52 , 132.72 , 130.84 , 130.74 , 124.25 , 60.16 , 46.19 , 45.24 , 40.10 , 37.33 , 37.29 , 36.94 , 35.31 , 34.49 , 34.37 , 33.57 , 30.51 , 21.93 , 20.69 , 20.01.

N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)thiophene-2-sulfonami de (**SA-20**)



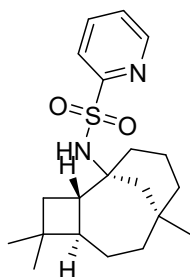
According to the general procedure A, compound **SA-20** could be obtained with 92% yield as white solid using β -Caryophyllene and 2-methylbenzene-1-sulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (dd, $J = 3.7$, 1.3 Hz, 1H), 7.53 (dd, $J = 5.0$, 1.3 Hz, 1H), 7.02 (dd, $J = 5.0$, 3.7 Hz, 1H), 4.51 (s, 1H), 2.38 – 2.28 (m, 1H), 1.77-1.72 (m, 2H), 1.70 – 1.65 (m, 3H), 1.59 – 1.56 (m, 2H), 1.54 – 1.48 (m, 3H), 1.48-1.44 (m, 2H), 1.33-1.29 (m, 2H), 1.11 – 1.08 (m, 1H), 1.01 (s, 3H), 0.99 (s, 3H), 0.82 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 146.07 , 131.37 , 131.00 , 126.92 , 59.65 , 45.37 , 44.99 , 40.04 , 37.42 , 36.91 , 36.88 , 35.09 , 34.49 , 34.34 , 33.58 , 30.49 , 21.84 , 20.76 , 20.10.

4-Bromo-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)thiophene-2-sulfonamide (**SA-21**)



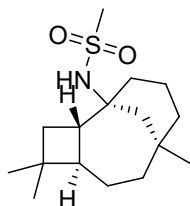
According to the general procedure A, compound **SA-21** could be obtained with 96% yield as white solid using β -Caryophyllene and 5-bromothiophene-2-sulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 7.32 (d, J = 3.7 Hz, 1H), 7.00 (d, J = 4.0 Hz, 1H), 4.55 (s, 1H), 2.39 – 2.26 (m, 1H), 1.81-1.75 (m, 2H), 1.72 – 1.66 (m, 2H), 1.64-1.59 (m, 1H), 1.59 – 1.52 (m, 3H), 1.52 – 1.45 (m, 2H), 1.36 – 1.24 (m, 4H), 1.15 – 1.10 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 146.85, 131.31, 129.90, 118.93, 59.95, 45.65, 45.09, 40.08, 37.39, 37.08, 36.94, 34.99, 34.48, 34.38, 33.60, 30.49, 21.90, 20.73, 20.07.

N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)pyridine-2-sulfonamide (**SA-22**)



According to the general procedure A, compound **SA-22** could be obtained with 78% yield as white solid using β -Caryophyllene and pyridine-2-sulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 8.64 (ddd, J = 4.7, 1.6, 0.8 Hz, 1H), 8.00 – 7.90 (m, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.42 (ddd, J = 7.6, 4.7, 1.1 Hz, 1H), 5.15 (s, 1H), 2.24 (dt, J = 12.0, 9.3 Hz, 1H), 1.79 – 1.73 (m, 1H), 1.70 - 1.65 (m, 1H), 1.63 – 1.58 (m, 2H), 1.46 – 1.35 (m, 3H), 1.27 – 1.17 (m, 3H), 1.07 (d, J = 12.8 Hz, 1H), 1.04 – 0.98 (m, 1H), 0.95 (s, 3H), 0.92 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.54, 149.76, 138.06, 126.21, 121.28, 63.76, 45.89, 44.80, 39.96, 37.41, 37.06, 36.87, 35.37, 34.30, 34.28, 33.54, 30.39, 21.84, 20.78, 20.08.

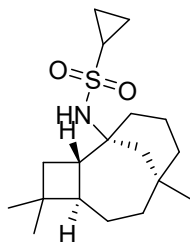
N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)methanesulfonamide (**SA-23**)



According to the general procedure A, compound **SA-23** could be obtained with 80% yield as white solid using β -Caryophyllene and methanesulfonamide as substrates; ^1H

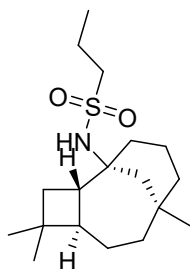
NMR (400 MHz, CDCl₃) δ 4.17 (s, 1H), 3.03 (s, 3H), 2.34 (ddd, J = 11.9, 10.7, 8.1 Hz, 1H), 1.90 – 1.85 (m, 1H), 1.83 – 1.76 (m, 2H), 1.76 – 1.73 (m, 1H), 1.72 – 1.66 (m, 2H), 1.59 – 1.46 (m, 3H), 1.45 – 1.39 (m, 2H), 1.37 – 1.26 (m, 2H), 1.19 – 1.11 (m, 2H), 1.01 (s, 3H), 0.99 (s, 3H), 0.90 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 58.91, 46.00, 45.48, 45.09, 40.09, 37.54, 37.14, 37.08, 35.64, 34.48, 34.40, 33.81, 30.45, 22.04, 20.75, 20.19.

N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)cyclopropanesulfonamide (**SA-24**).



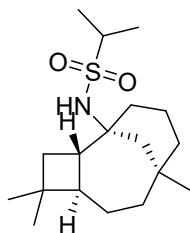
According to the general procedure A, compound **SA-24** could be obtained with 87% yield as white solid using β -Caryophyllene and cyclopropanesulfonamide as substrates; ¹H NMR (400 MHz, CDCl₃) δ 4.37 (s, 1H), 2.40 (tt, J = 8.0, 4.9 Hz, 1H), 2.25 (td, J = 10.7, 8.1 Hz, 1H), 1.83 – 1.76 (m, 2H), 1.76 – 1.71 (m, 2H), 1.60 (dd, J = 11.7, 6.1 Hz, 2H), 1.53 – 1.42 (m, 3H), 1.38 – 1.33 (m, 2H), 1.30 – 1.23 (m, 2H), 1.21 (d, J = 12.8 Hz, 1H), 1.12 – 1.06 (m, 3H), 1.06 – 1.03 (m, 1H), 0.94 (s, 3H), 0.92 (s, 3H), 0.89 (dd, J = 5.2, 2.9 Hz, 1H), 0.83 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 58.45, 46.45, 44.87, 40.05, 37.60, 37.12, 37.02, 36.25, 34.40, 34.33, 34.28, 33.83, 30.41, 22.00, 20.81, 20.25, 6.81, 6.51.

N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)propane-1-sulfonamide (**SA-25**)



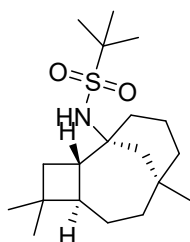
According to the general procedure A, compound **SA-25** could be obtained with 69% yield as white solid using β -Caryophyllene and propanesulfonamide as substrates; ¹H NMR (400 MHz, CDCl₃) δ 3.90 (s, 1H), 2.99 – 2.89 (m, 2H), 2.31 – 2.21 (m, 1H), 1.80 – 1.74 (m, 3H), 1.65 – 1.60 (m, 3H), 1.47 – 1.41 (m, 4H), 1.35 – 1.31 (m, 2H), 1.30 – 1.22 (m, 2H), 1.10 – 1.04 (m, 2H), 1.01 – 0.97 (m, 4H), 0.94 (s, 3H), 0.92 (s, 3H), 0.83 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 58.89, 58.77, 46.02, 45.13, 40.12, 37.54, 37.09, 37.07, 35.76, 34.49, 34.41, 33.80, 30.49, 22.03, 20.75, 20.20, 17.92, 13.00.

N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)propane-2-sulfonamide (**SA-26**)



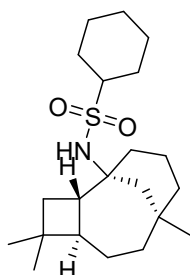
According to the general procedure A, compound **SA-26** could be obtained with 78% yield as white solid using β -Caryophyllene and isopropylsulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 4.02 (s, 1H), 3.03 (dt, J = 13.6, 6.8 Hz, 1H), 2.26 (td, J = 10.9, 8.2 Hz, 1H), 1.80 – 1.74 (m, 2H), 1.72 – 1.68 (m, 1H), 1.64 – 1.57 (m, 3H), 1.51 (d, J = 10.2 Hz, 1H), 1.49 – 1.43 (m, 2H), 1.42 – 1.37 (m, 1H), 1.35 (d, J = 5.7 Hz, 1H), 1.32 (d, J = 6.8 Hz, 3H), 1.30 (d, J = 6.9 Hz, 3H), 1.28 – 1.17 (m, 2H), 1.09 – 1.03 (m, 2H), 0.94 (s, 3H), 0.92 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 58.78, 56.29, 45.92, 45.01, 40.20, 37.52, 37.07, 37.05, 35.90, 34.42, 34.33, 33.80, 30.47, 22.02, 20.78, 20.21, 17.09, 16.74.

2-Methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)propane-2-sulfonamide (**SA-27**)



According to the general procedure A, compound **SA-27** could be obtained with 70% yield as white solid using β -Caryophyllene and *tert*-butylsulfonamide as substrates; ^1H NMR (400 MHz, CDCl_3) δ 3.42 (s, 1H), 2.31 (td, J = 11.1, 8.2 Hz, 1H), 1.81 – 1.71 (m, 3H), 1.71 – 1.65 (m, 2H), 1.64 (s, 1H), 1.61 – 1.55 (m, 1H), 1.53 – 1.43 (m, 4H), 1.42 – 1.38 (m, 1H), 1.31 (s, 9H), 1.29 – 1.23 (m, 1H), 1.10 – 1.03 (m, 2H), 0.94 (s, 3H), 0.93 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 60.27, 59.72, 46.29, 45.34, 40.87, 37.52, 37.29, 37.13, 36.14, 34.61, 34.38, 33.93, 30.58, 24.65, 22.19, 20.71, 20.49.

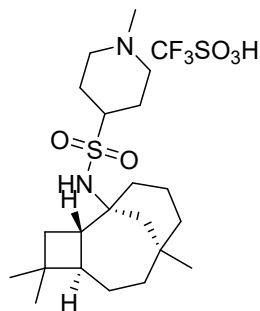
N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)cyclohexanesulfonamide (**SA-28**)



According to the general procedure A, compound **SA-28** could be obtained with 52% yield as white solid using β -Caryophyllene and cyclohexanesulfonamide as substrates;

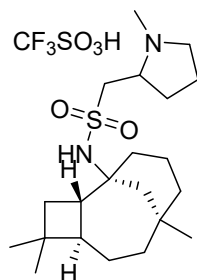
^1H NMR (400 MHz, CDCl_3) δ 3.90 (s, 1H), 2.70 (tt, $J = 12.0, 3.4$ Hz, 1H), 2.31 – 2.21 (m, 1H), 2.13 (t, $J = 12.8$ Hz, 2H), 1.85 – 1.77 (m, 3H), 1.75 – 1.68 (m, 2H), 1.67 – 1.59 (m, 4H), 1.50 – 1.42 (m, 4H), 1.36 – 1.29 (m, 3H), 1.28 – 1.16 (m, 4H), 1.10 – 1.01 (m, 3H), 0.94 (s, 3H), 0.92 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 64.44, 58.81, 46.27, 45.12, 40.32, 37.55, 37.21, 37.18, 35.83, 34.44, 34.32, 33.85, 30.48, 26.85, 26.60, 25.35, 25.24, 22.11, 20.77, 20.23.

1-Methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)piperidine-4-sulfonamide trifluoromethanesulfonate (**SA-29**)



According to the general procedure A, compound **SA-29** could be obtained with 43% yield as white solid using β -Caryophyllene and 1-Methyl-4-piperidinesulfonamide as substrates; HRMS (ESI) for $\text{C}_{21}\text{H}_{38}\text{N}_2\text{O}_2\text{S}$: calculated, $[\text{M}+\text{H}]^+ = 383.2732$, found 383.2544; ^1H NMR (400 MHz, CDCl_3) δ 4.66 (s, 1H), 3.55 – 3.31 (m, 4H), 3.10 – 2.85 (m, 3H), 2.75 (s, 3H), 2.33 – 2.22 (m, 3H), 2.12 (brs, 2H), 1.91 – 1.82 (m, 1H), 1.81 – 1.66 (m, 3H), 1.66 – 1.55 (m, 2H), 1.52 – 1.40 (m, 3H), 1.40 – 1.31 (m, 1H), 1.20 (d, $J = 12.6$ Hz, 2H), 1.12 – 1.00 (m, 2H), 0.94 (s, 3H), 0.92 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 120.20 (q, $J = 375.2$ Hz), 59.86, 53.08, 46.30, 45.04, 44.17, 40.33, 37.66, 37.45, 37.25, 35.63, 34.35, 34.22, 33.77, 30.43, 24.34, 24.12, 22.13, 20.75, 20.16.

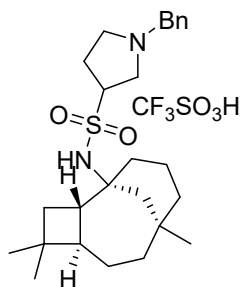
1-(1-Methylpyrrolidin-2-yl)-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)methanesulfonamide trifluoromethanesulfonate (**SA-30**)



According to the general procedure A, compound **SA-30** could be obtained with 36% yield as white solid using β -Caryophyllene and (1-methylpyrrolidin-2-yl)methanesulfonamide as substrates; HRMS (ESI) for $\text{C}_{21}\text{H}_{38}\text{N}_2\text{O}_2\text{S}$: calculated, $[\text{M}+\text{H}]^+ = 383.2732$, found 383.2540; ^1H NMR (400 MHz, CDCl_3) δ 8.93 (s, 1H), 5.10 (s, 1H), 3.93 (brs, 1H), 3.86 – 3.68 (m, 2H), 3.47 (d, $J = 9.3$ Hz, 1H), 3.16 (d, $J = 8.7$ Hz, 1H), 3.07 (s, 3H), 2.59 (brs, 1H), 2.41 – 2.28 (m, 1H), 2.27 – 2.08 (m, 3H), 2.00 (d,

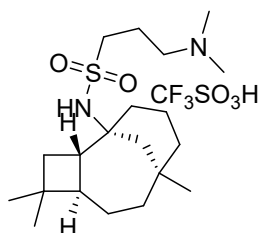
$J = 11.1$ Hz, 1H), 1.88 – 1.74 (m, 3H), 1.74 – 1.65 (m, 2H), 1.64 – 1.47 (m, 4H), 1.44 (d, $J = 13.4$ Hz, 1H), 1.38 – 1.30 (m, 2H), 1.20 – 1.10 (m, 2H), 1.02 (s, 3H), 1.00 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 65.68, 60.43, 60.25, 57.25, 57.14, 46.37, 45.03, 41.66, 40.16, 37.74, 37.49, 37.18, 35.59, 34.45, 34.23, 33.73, 30.68, 30.34, 22.14, 22.08, 21.06, 20.73, 20.17, 14.20.

1-Benzyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)pyrrolidine-3-sulfonamide trifluoromethanesulfonate (**SA-31**)



According to the general procedure A, compound **SA-31** could be obtained with 37% yield as white solid using β -Caryophyllene and 1-benzylpyrrolidine-3-sulfonamide as substrates; HRMS (ESI) for $\text{C}_{26}\text{H}_{40}\text{N}_2\text{O}_2\text{S}$: calculated, $[\text{M}+\text{H}]^+ = 445.2889$, found 445.2680; ^1H NMR (400 MHz, CDCl_3) δ 7.38 – 7.15 (m, 5H), 4.37 – 4.19 (m, 1H), 3.79 – 3.63 (m, 3H), 3.27 – 3.11 (m, 1H), 2.95 – 2.86 (m, 1H), 2.86 – 2.78 (m, 1H), 2.68 – 2.60 (m, 1H), 2.29 – 2.15 (m, 3H), 1.75 – 1.63 (m, 4H), 1.61 – 1.54 (m, 3H), 1.44 – 1.38 (m, 2H), 1.37 – 1.33 (m, 1H), 1.30 (d, $J = 3.1$ Hz, 1H), 1.28 – 1.22 (m, 2H), 1.08 – 1.01 (m, 2H), 0.92 (s, 1.5H), 0.91 (s, 1.5H), 0.90 (s, 3H), 0.89 (s, 1.5H), 0.81 (s, 3H), 0.80 (s, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 129.21, 128.62, 128.61, 127.85, 62.92, 62.88, 59.71, 59.66, 59.27, 59.23, 54.92, 54.49, 53.39, 53.25, 45.73, 44.96, 39.97, 39.92, 37.47, 36.98, 36.94, 36.92, 36.18, 36.10, 34.49, 34.41, 34.39, 33.75, 33.69, 30.52, 29.70, 27.02, 26.63, 21.92, 21.86, 20.20, 20.19.

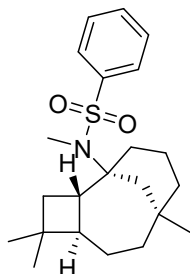
3-(Dimethylamino)-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)propane-1-sulfonamide trifluoromethanesulfonate (**SA-32**)



According to the general procedure A, compound **SA-32** could be obtained with 32% yield as white solid using β -Caryophyllene and 3-(dimethylamino)propane-1-sulfonamide as substrates; HRMS (ESI) for $\text{C}_{20}\text{H}_{38}\text{N}_2\text{O}_2\text{S}$: calculated, $[\text{M}+\text{H}]^+ = 371.2732$, found 371.2545; ^1H NMR (400 MHz, CDCl_3) δ 6.37 (s, 1H), 4.87 (s, 1H), 3.14 (dt, $J = 14.5, 6.6$ Hz, 4H), 2.77 (s, 6H), 2.29 – 2.11 (m, 3H), 1.87 (d, $J = 11.3$ Hz, 1H), 1.79 – 1.72 (m, 2H), 1.63 – 1.55 (m, 2H), 1.51 – 1.41 (m, 3H), 1.41 – 1.30 (m, 2H), 1.29 – 1.16 (m, 3H), 1.09 – 1.01 (m, 2H), 0.93 (s, 3H), 0.92 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 120.2 (q, $J = 375.2$ Hz), 59.52, 56.69, 53.69, 46.22,

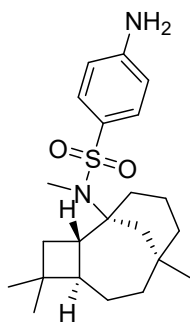
44.91, 43.79, 40.22, 37.64, 37.50, 37.20, 35.59, 34.33, 34.19, 33.79, 30.38, 22.10, 20.76, 20.26, 20.15.

N-Methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzene sulfonamide (**SA-33**)



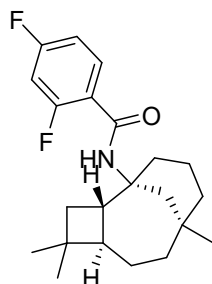
According to the general procedure A, compound **SA-33** could be obtained with 60% yield as white solid using β -Caryophyllene and N-methylbenzenesulfonamide as substrates; HRMS (ESI) for $C_{22}H_{33}NO_2S$: calculated, $[M+H]^+ = 376.2310$, found 376.2144; 1H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.67 (m, 2H), 7.48 – 7.33 (m, 3H), 2.90 (s, 3H), 2.34 (dd, $J = 12.8, 1.0$ Hz, 1H), 2.17 – 2.08 (m, 1H), 2.08 – 2.00 (m, 1H), 1.96 – 1.88 (m, 1H), 1.76 (dd, $J = 9.6, 7.9$ Hz, 1H), 1.63 – 1.56 (m, 2H), 1.49 – 1.43 (m, 1H), 1.39 (dt, $J = 6.1, 2.8$ Hz, 2H), 1.26 – 1.18 (m, 2H), 1.14 – 1.06 (m, 1H), 1.06 – 1.00 (m, 1H), 0.93 (s, 3H), 0.90 (s, 3H), 0.85 – 0.76 (m, 2H), 0.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.83, 131.65, 128.75, 126.41, 65.14, 45.99, 44.53, 41.59, 39.06, 37.99, 36.53, 36.21, 34.45, 34.13, 34.10, 33.94, 30.34, 22.67, 20.90, 20.38.

4-Amino-N-methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzenesulfonamide (**SA-34**)



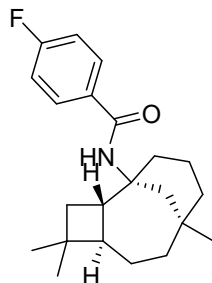
According to the general procedure A, compound **SA-34** could be obtained with 53% yield as white solid using β -Caryophyllene and N-methylbenzenesulfonamide as substrates; HRMS (ESI) for $C_{22}H_{34}N_2O_2S$: calculated, $[M+H]^+ = 391.2419$, found 391.2247; 1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.42 (m, 2H), 6.66 – 6.51 (m, 2H), 4.19 – 3.83 (brs, 2H), 2.83 (s, 3H), 2.29 (d, $J = 13.1$ Hz, 1H), 2.15 – 2.07 (m, 1H), 2.03 – 1.97 (m, 1H), 1.90 (ddd, $J = 12.0, 7.8, 6.5$ Hz, 1H), 1.74 (dd, $J = 9.5, 7.8$ Hz, 1H), 1.61 – 1.55 (m, 2H), 1.49 – 1.43 (m, 1H), 1.42 – 1.35 (m, 2H), 1.28 – 1.21 (m, 2H), 1.15 – 1.10 (m, 1H), 1.06 (d, $J = 12.8$ Hz, 1H), 1.04 – 0.99 (m, 1H), 0.92 (s, 3H), 0.89 (s, 3H), 0.86 – 0.79 (m, 1H), 0.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.58, 133.57, 128.50, 113.95, 64.81, 45.88, 44.44, 41.49, 39.10, 37.83, 36.68, 35.94, 34.46, 34.13, 34.08, 33.89, 30.31, 22.50, 20.90, 20.40.

2,4-Difluoro-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benz amide (**CA-1**).



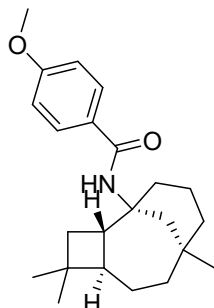
According to the general procedure B, compound **CA-1** could be obtained with 70% yield as white solid using β -Caryophyllene and 2,4-difluorobenzamide as substrates; HRMS (ESI) for $C_{22}H_{29}F_2NO$: calculated, $[M+H]^+ = 362.2295$, found 362.2070; 1H NMR (400 MHz, $CDCl_3$) δ 8.05 (td, $J = 9.0, 6.7$ Hz, 1H), 7.02 – 6.91 (m, 1H), 6.91 – 6.79 (m, 1H), 6.40 (d, $J = 12.9$ Hz, 1H), 2.45 (td, $J = 11.0, 8.0$ Hz, 1H), 2.34 (m, 1H), 1.89 – 1.74 (m, 4H), 1.71 – 1.63 (m, 2H), 1.63 – 1.55 (m, 2H), 1.48 (m, 2H), 1.39 (m, 1H), 1.32 (m, 1H), 1.17 (m, 2H), 1.01 (s, 3H), 0.98 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.68 (d, $J = 13.0$ Hz), 163.16 (d, $J = 12.5$ Hz), 161.82 (d, $J = 12.3$ Hz), 161.09 (d, $J = 3.8$ Hz), 133.63 (dd, $J = 10.0, 3.9$ Hz), 118.89, 112.21 (dd, $J = 21.0, 3.4$ Hz), 104.33, 104.06 (d, $J = 3.4$ Hz), 103.79, 56.32, 46.24, 45.87, 41.36, 38.11, 37.97, 37.31, 35.53, 34.42, 34.32, 34.04, 30.55, 23.01, 20.74, 20.07.

4-Fluoro-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzamide (**CA-2**)



According to the general procedure B, compound **CA-2** could be obtained with 44% yield as white solid using β -Caryophyllene and 4-fluorobenzamide as substrates; HRMS (ESI) for $C_{22}H_{30}FNO$: calculated, $[M+H]^+ = 344.2390$, found 344.2236; 1H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.64 (m, 2H), 7.11 – 7.00 (m, 2H), 5.83 (s, 1H), 2.50 – 2.48 (m, 2H), 1.95 – 1.88 (m, 1H), 1.88 – 1.74 (m, 3H), 1.70 – 1.60 (m, 1H), 1.60 – 1.48 (m, 3H), 1.42 – 1.36 (m, 2H), 1.34 – 1.25 (m, 2H), 1.22 – 1.10 (m, 2H), 1.01 (s, 3H), 0.97 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.60, 163.17, 132.31 (d, $J = 3.0$ Hz), 128.97 (d, $J = 8.8$ Hz), 115.41 (d, $J = 22$ Hz), 115.30, 55.93, 46.40, 46.16, 41.53, 38.19, 37.32, 35.77, 34.38, 34.31, 34.10, 30.58, 23.10, 20.73, 20.05.

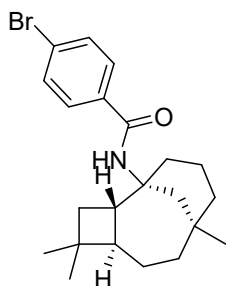
4-Methoxy-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzamide (**CA-3**)



According to the general procedure B, compound **CA-3** could be obtained with 30% yield as white solid using β -Caryophyllene and 4-methoxybenzamide as substrates;

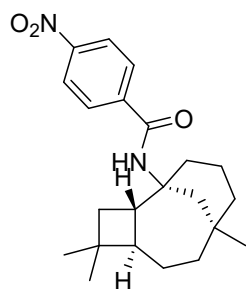
^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 5.73 (s, 1H), 3.76 (s, 3H), 2.42 – 2.30 (m, 2H), 1.85 – 1.71 (m, 4H), 1.61 – 1.56 (m, 1H), 1.53 – 1.48 (m, 2H), 1.44–1.40 (M, 1H), 1.34 (d, J = 12.7 Hz, 1H), 1.31 – 1.17 (m, 3H), 1.14 – 1.06 (m, 2H), 0.93 (s, 3H), 0.89 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 165.11, 160.76, 127.41, 112.60, 54.62, 54.36, 45.29, 45.15, 40.51, 37.13, 37.08, 36.34, 34.76, 33.35, 33.27, 33.06, 29.55, 22.04, 19.73, 19.05.

4-Bromo-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzamide (**CA-7**)



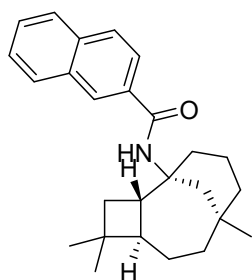
According to the general procedure B, compound **CA-7** could be obtained with 30% yield as white solid using β -Caryophyllene and 4-bromobenzamide as substrates; HRMS (ESI) for $\text{C}_{22}\text{H}_{30}\text{BrNO}$: calculated, $[\text{M}+\text{H}]^+ = 404.1589$, found 404.1417; ^1H NMR (400 MHz, CDCl_3) δ 7.56 – 7.41 (m, 4H), 5.74 (s, 1H), 2.41 – 2.30 (m, 2H), 1.86 – 1.81 (m, 1H), 1.78–1.68 (m, 2H), 1.61 – 1.53 (m, 1H), 1.53 – 1.37 (m, 4H), 1.36 – 1.28 (m, 2H), 1.24 – 1.16 (m, 2H), 1.15 – 1.04 (m, 2H), 0.94 (s, 3H), 0.89 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 164.62, 133.94, 130.64, 127.35, 124.51, 54.99, 45.39, 45.10, 40.49, 37.16, 37.13, 36.28, 34.70, 33.37, 33.30, 33.07, 29.56, 22.07, 19.69, 19.01.

4-Nitro-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzamide (**CA-8**)



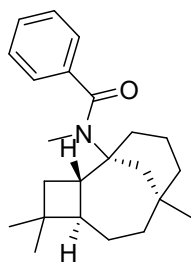
According to the general procedure B, compound **CA-8** could be obtained with 35% yield as white solid using β -Caryophyllene and 4-nitrobenzamide as substrates; HRMS (ESI) for $C_{22}H_{30}N_2O_3$: calculated, $[M+H]^+ = 371.2335$, found 371.2165; 1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, $J = 10.8$ Hz, 2H), 7.86 (d, $J = 12.1$ Hz, 2H), 5.91 (s, 1H), 2.46 (td, $J = 11.5, 8.1$ Hz, 2H), 1.95 (d, $J = 12.7$ Hz, 1H), 1.90 – 1.80 (m, 3H), 1.75 – 1.65 (m, 3H), 1.63 – 1.56 (m, 2H), 1.43 – 1.38 (m, 2H), 1.37 – 1.33 (m, 1H), 1.32 – 1.27 (m, 2H), 1.23 – 1.15 (m, 2H), 1.02 (s, 3H), 0.98 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.64, 149.29, 141.77, 127.91, 123.77, 123.72, 56.53, 46.54, 46.09, 41.54, 38.25, 38.23, 37.25, 35.72, 34.43, 34.38, 34.12, 30.60, 23.13, 20.69, 20.02.

N-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-2-naphthamide (**CA-9**)



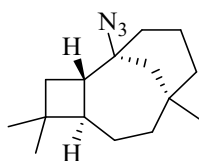
According to the general procedure B, compound **CA-9** could be obtained with 38% yield as white solid using β -Caryophyllene and 2-naphthamide as substrates; HRMS (ESI) for $C_{26}H_{33}NO$: calculated, $[M+H]^+ = 376.2640$, found 376.2463; 1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.93 – 7.87 (m, 1H), 7.85 (dd, $J = 8.7, 5.1$ Hz, 2H), 7.78 (dd, $J = 8.5, 1.8$ Hz, 1H), 7.56 – 7.48 (m, 2H), 6.03 (s, 1H), 2.55–2.40 (m, 2H), 1.98 (d, $J = 12.7$ Hz, 1H), 1.92–1.81 (m, 3H), 1.72 – 1.56 (m, 4H), 1.53 – 1.46 (m, 2H), 1.43 – 1.38 (m, 2H), 1.23 – 1.15 (m, 2H), 1.02 (s, 3H), 0.98 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.70, 134.53, 133.38, 132.69, 128.84, 128.35, 127.73, 127.38, 126.90, 126.66, 123.70, 58.16, 55.99, 46.41, 46.28, 41.61, 38.27, 38.23, 37.40, 35.87, 34.43, 34.35, 34.14, 30.62, 23.13, 20.79, 20.11.

N-Methyl-N-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)benzamide (**CA-11**)



According to the general procedure B, compound **CA-11** could be obtained with 20% yield as white solid using β -Caryophyllene and N-methylbenzamide as substrates; HRMS (ESI) for $C_{23}H_{33}NO$: calculated, $[M+H]^+ = 340.2640$, found 340.2476; 1H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.30 (m, 5H), 2.90 (s, 3H), 2.81 – 2.69 (m, 1H), 2.57 (d, $J = 12.8$ Hz, 1H), 2.41 (td, $J = 11.0, 8.1$ Hz, 1H), 2.03 – 1.93 (m, 1H), 1.89 (dd, $J = 9.7, 8.1$ Hz, 1H), 1.84 – 1.73 (m, 2H), 1.69–1.63 (m, 1H), 1.56 – 1.48 (m, 3H), 1.45 – 1.34 (m, 4H), 1.23 – 1.18 (m, 1H), 1.17 – 1.10 (m, 1H), 1.01 (s, 6H), 0.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.75, 139.52, 129.17, 128.29, 127.22, 61.53, 48.70, 44.27, 44.04, 40.08, 39.84, 36.62, 36.44, 35.93, 34.85, 34.58, 33.85, 30.89, 24.49, 20.83, 20.53.

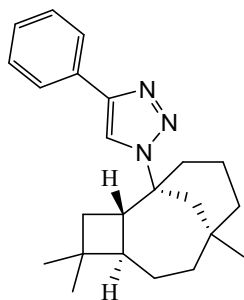
(1R,2S,5R,8S)-1-Azido-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecane (**NC**)



NC

A flask equipped with a septum and a magnetic stir bar was charged with β -CP (2.0 mmol), azidotrimethylsilane (1.0 mmol), and dichloromethane (5.0 mL). Then TfOH (4.4 μ L, 5 mol%) was added to the mixture. The mixture was stirred at 30 °C for 16 hours, then the reaction mixture was successively washed with saturated aq. $NaHCO_3$ and saturated brine and concentrated. The residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the product as colorless oil; 1H NMR (600 MHz, $CDCl_3$) δ 2.32 (ddd, $J = 12.1, 10.4, 8.0$ Hz, 1H), 1.90 – 1.85 (m, 1H), 1.85 – 1.81 (m, 1H), 1.79 (dt, $J = 13.1, 2.5$ Hz, 1H), 1.76 – 1.71 (m, 2H), 1.70 – 1.66 (m, 1H), 1.63 (d, $J = 10.1$ Hz, 1H), 1.57 – 1.53 (m, 1H), 1.54 – 1.50 (m, 1H), 1.49 – 1.41 (m, 2H), 1.39 – 1.34 (m, 1H), 1.19 – 1.15 (m, 1H), 1.14 – 1.08 (m, 2H), 1.04 (s, 3H), 1.01 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 63.12, 45.74, 45.33, 39.86, 37.46, 36.90, 36.10, 35.16, 34.73, 34.42, 33.37, 30.70, 21.97, 20.79, 20.27.

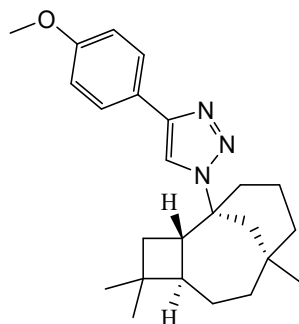
4-Phenyl-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole (**NC-1**)



NC-1

According to the general procedure C, compound **NC-1** could be obtained with 78% yield as white solid using **NC** and phenylacetylene as substrates; HRMS (ESI) for $C_{23}H_{32}N_3$: calculated, $[M+H]^+ = 350.2596$, found 350.2599; 1H NMR (600 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.79 (s, 1H), 7.45 (t, $J = 7.6$ Hz, 2H), 7.37 – 7.32 (m, 1H), 2.74 (dt, $J = 13.0, 2.4$ Hz, 1H), 2.61 (ddd, $J = 12.2, 10.4, 8.0$ Hz, 1H), 2.47 – 2.40 (m, 1H), 2.12 – 2.01 (m, 3H), 1.87 (dt, $J = 13.9, 4.1$ Hz, 2H), 1.80 – 1.61 (m, 5H), 1.61 – 1.56 (m, 1H), 1.51 (d, $J = 13.0$ Hz, 1H), 1.49 – 1.43 (m, 2H), 1.34 – 1.26 (m, 2H), 1.26 – 1.20 (m, 1H), 1.04 (s, 4H), 1.00 (s, 3H), 0.88 (s, 3H), 0.34 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.54, 131.05, 128.94, 128.08, 125.81, 117.23, 64.05, 45.21, 45.08, 40.56, 37.40, 37.03, 36.32, 36.07, 34.34, 34.32, 33.52, 30.39, 21.93, 20.85, 20.02.

4-(4-Methoxyphenyl)-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole (**NC-2**)

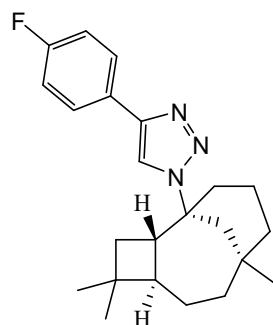


NC-2

According to the general procedure C, compound **NC-2** could be obtained with 52% yield as white solid using **NC** and 4-Ethynylanisole as substrates; HRMS (ESI) for $C_{24}H_{34}N_3O$: calculated, $[M+H]^+ = 380.2702$, found 380.2708; 1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, $J = 8.7$ Hz, 2H), 7.70 (s, 1H), 6.97 (d, $J = 8.8$ Hz, 2H), 3.85 (s, 3H), 2.72 (dt, $J = 13.0, 2.4$ Hz, 1H), 2.59 (ddd, $J = 12.1, 10.4, 8.0$ Hz, 1H), 2.41 (ddt, $J = 11.8, 5.3, 3.1$ Hz, 1H), 2.07 (dt, $J = 12.1, 7.3$ Hz, 1H), 2.01 (dtd, $J = 16.7, 7.4, 3.6$ Hz, 1H), 1.94 – 1.87 (m, 1H), 1.87 – 1.82 (m, 1H), 1.74 (td, $J = 12.1, 5.3$ Hz, 1H), 1.71 – 1.66 (m, 1H), 1.64 (td, $J = 6.7, 3.4$ Hz, 1H), 1.60 – 1.54 (m, 1H), 1.51 – 1.41 (m, 4H), 1.37 (d, $J = 22.9$ Hz, 1H), 1.33 – 1.25 (m, 4H), 1.20 (dd, $J = 13.1, 4.7$ Hz, 1H), 1.02 (s, 3H), 0.99 (s, 3H), 0.87 (s, 3H), 0.34 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.48, 146.45, 127.00, 124.05, 116.38, 114.28, 63.72, 55.43, 45.14, 45.05, 40.53,

37.38, 37.00, 36.25, 36.01, 34.26, 34.24, 33.48, 30.35, 21.89, 20.83, 19.98.

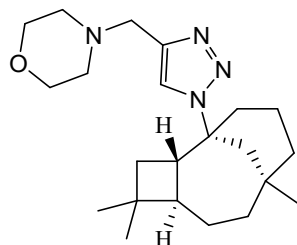
4-(4-Fluorophenyl)-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole (**NC-3**)



NC-3

According to the general procedure C, compound **NC-3** could be obtained with 45% yield as white solid using **NC** and 4-fluorophenylacetylene as substrates; HRMS (ESI) for C₂₃H₃₁FN₃: calculated, [M+H]⁺ = 368.2502, found 368.2505; ¹H NMR (600 MHz, CDCl₃) δ 7.82 (td, *J* = 6.0, 2.9 Hz, 2H), 7.67 (s, 1H), 7.17 – 7.07 (m, 2H), 4.67 (dd, *J* = 13.3, 5.6 Hz, 1H), 2.36 (t, *J* = 12.5 Hz, 1H), 1.95 (dd, *J* = 11.6, 5.6 Hz, 1H), 1.59 (s, 1H), 1.56 – 1.42 (m, 5H), 1.40 – 1.34 (m, 1H), 1.34 – 1.28 (m, 2H), 1.28 – 1.24 (m, 2H), 1.24 – 1.20 (m, 1H), 1.19 (s, 2H), 1.18 – 1.10 (m, 2H), 1.00 (s, 3H), 0.92 (s, 2H), 0.89 – 0.81 (m, 2H), 0.15 (td, *J* = 12.9, 4.8 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 163.53, 161.89, 146.11, 127.51, 127.46, 118.93, 115.97, 115.83, 69.93, 51.44, 45.14, 43.78, 43.11, 40.30, 38.18, 33.25, 32.85, 32.82, 30.90, 30.45, 24.77, 20.69, 18.49.

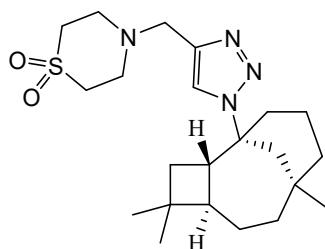
4-((1-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methyl)morpholine (**NC-4**)



NC-4

According to the general procedure C, compound **NC-4** could be obtained with 62% yield as white solid using **NC** and 4-prop-2-ynyl-morpholine as substrates; HRMS (ESI) for C₂₂H₃₇N₄O: calculated, [M+H]⁺ = 373.2967, found 373.2972; ¹H NMR (600 MHz, CD₃OD) δ 8.02 (s, 1H), 3.78 (s, 2H), 3.72 (t, *J* = 4.4 Hz, 4H), 2.73 – 2.65 (m, 2H), 2.60 (s, 4H), 2.47 (dt, *J* = 12.2, 3.2 Hz, 1H), 2.11 – 2.04 (m, 2H), 1.87 (dt, *J* = 14.5, 4.3 Hz, 1H), 1.79 – 1.63 (m, 4H), 1.62 – 1.55 (m, 1H), 1.49 (ddd, *J* = 14.0, 6.9, 2.7 Hz, 1H), 1.44 (s, 1H), 1.43 – 1.40 (m, 1H), 1.31 (ddd, *J* = 14.1, 6.4, 3.8 Hz, 1H), 1.24 (td, *J* = 13.0, 4.8 Hz, 1H), 1.03 (s, 3H), 1.01 (s, 3H), 0.87 (s, 3H), 0.09 (d, *J* = 10.0 Hz, 1H); ¹³C NMR (151 MHz, CD₃OD) δ 141.15, 122.02, 65.96, 64.01, 52.64, 52.43, 44.84, 44.50, 40.12, 36.92, 36.39, 35.76, 35.11, 33.76, 33.68, 32.28, 29.26, 21.21, 19.52, 19.38.

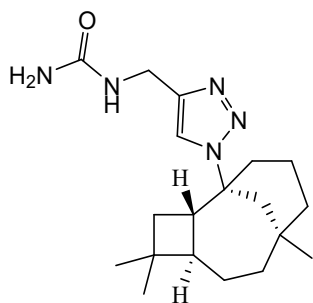
4-((1-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methyl)thiomorpholine 1,1-dioxide (**NC-5**)



NC-5

According to the general procedure C, compound **NC-5** could be obtained with 43% yield as white solid using **NC** and 4-(prop-2-yn-1-yl)thiomorpholine-1,1-dioxide as substrates; HRMS (ESI) for C₂₂H₃₇N₄O₂S: calculated, [M+H]⁺ = 421.2637, found 421.2637; ¹H NMR (600 MHz, CD₃OD) δ 8.01 (s, 1H), 3.86 (s, 2H), 3.11 (t, *J* = 5.0 Hz, 4H), 2.99 (dd, *J* = 7.2, 3.7 Hz, 4H), 2.74 – 2.62 (m, 2H), 2.46 (dp, *J* = 11.6, 3.0 Hz, 1H), 2.09 – 1.99 (m, 2H), 1.85 (dt, *J* = 15.1, 4.5 Hz, 1H), 1.78 – 1.61 (m, 4H), 1.60 – 1.54 (m, 1H), 1.48 (dtd, *J* = 13.9, 6.8, 4.0 Hz, 1H), 1.44 – 1.38 (m, 2H), 1.29 (ddd, *J* = 14.1, 6.4, 3.9 Hz, 2H), 1.26 – 1.20 (m, 1H), 1.02 (s, 3H), 1.00 (s, 3H), 0.85 (s, 3H), 0.05 (t, *J* = 10.0 Hz, 1H); ¹³C NMR (151 MHz, CD₃OD) δ 142.15, 121.64, 64.00, 51.03, 50.69, 50.68, 50.04, 44.85, 44.45, 40.18, 36.92, 36.40, 35.79, 35.10, 33.76, 33.67, 32.28, 29.32, 21.23, 19.52, 19.38.

1-((1-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methyl)urea (**NC-6**)

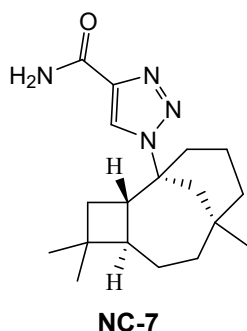


NC-6

According to the general procedure C, compound **NC-6** could be obtained with 56% yield as white solid using **NC** and 1-(prop-2-ynyl)urea as substrates; HRMS (ESI) for C₁₉H₃₂N₅O: calculated, [M+H]⁺ = 346.2607, found 346.2601; ¹H NMR (600 MHz, CD₃OD) δ 7.89 (s, 1H), 5.51 (s, 2H), 4.38 (s, 2H), 2.74 – 2.63 (m, 2H), 2.44 (d, *J* = 12.4 Hz, 1H), 1.87 (dd, *J* = 17.8, 9.4 Hz, 2H), 1.74 (dt, *J* = 16.1, 4.9 Hz, 2H), 1.72 – 1.61 (m, 3H), 1.57 (d, *J* = 14.0 Hz, 2H), 1.49 (ddd, *J* = 11.3, 7.1, 3.6 Hz, 2H), 1.45 – 1.39 (m, 2H), 1.37 – 1.30 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 2H), 1.03 (s, 3H), 1.01 (s, 3H), 0.87 (s, 3H), 0.12 (t, *J* = 10.0 Hz, 1H); ¹³C NMR (151 MHz, CD₃OD) δ 171.59, 116.72, 63.94, 60.13, 53.39, 44.82, 44.52, 40.07, 36.93, 36.40, 35.70, 35.19, 33.65, 32.28, 29.22, 21.21, 19.54, 13.05.

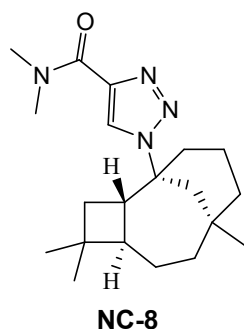
1-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-

triazole-4-carboxamide (**NC-7**)



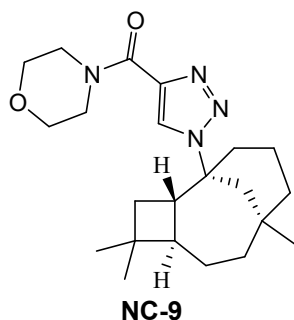
According to the general procedure C, compound **NC-7** could be obtained with 76% yield as white solid using **NC** and prop-2-ynamide as substrates; HRMS (ESI) for $C_{18}H_{29}N_4O$: calculated, $[M+H]^+ = 317.2341$, found 317.2340; 1H NMR (600 MHz, CD_3OD) δ 8.39 (s, 1H), 2.69 (ddt, $J = 12.2, 10.2, 2.4$ Hz, 2H), 2.51 – 2.44 (m, 1H), 2.10 – 2.02 (m, 2H), 1.90 – 1.82 (m, 1H), 1.78 – 1.62 (m, 3H), 1.60 – 1.54 (m, 1H), 1.49 (ddd, $J = 10.0, 6.9, 3.5$ Hz, 1H), 1.46 – 1.40 (m, 2H), 1.30 (ddd, $J = 14.1, 6.5, 3.8$ Hz, 1H), 1.23 (td, $J = 13.1, 4.8$ Hz, 1H), 1.02 (s, 3H), 1.00 (s, 3H), 0.86 (s, 3H), 0.11 (t, $J = 10.0$ Hz, 1H); ^{13}C NMR (151 MHz, CD_3OD) δ 165.05, 142.80, 125.09, 65.95, 46.29, 45.89, 41.45, 38.28, 37.84, 37.21, 36.62, 35.22, 35.14, 33.70, 30.62, 22.66, 20.90, 20.80.

N,N-Dimethyl-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxamide (**NC-8**)



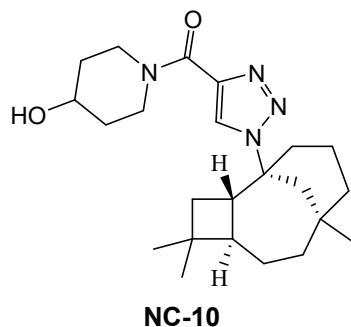
According to the general procedure C, compound **NC-8** could be obtained with 70% yield as white solid using **NC** and N,N-dimethyl-2-propynamide; HRMS (ESI) for $C_{20}H_{33}N_4O$: calculated, $[M+H]^+ = 345.2654$, found 345.2650; 1H NMR (600 MHz, $CDCl_3$) δ 8.10 (s, 1H), 3.59 (s, 4H), 3.11 (s, 4H), 2.65 (dt, $J = 13.0, 2.4$ Hz, 1H), 2.56 (ddd, $J = 12.2, 10.4, 8.0$ Hz, 1H), 2.37 (ddd, $J = 11.9, 5.2, 2.9$ Hz, 1H), 2.05 – 1.96 (m, 2H), 1.87 – 1.81 (m, 1H), 1.71 – 1.57 (m, 5H), 1.57 – 1.51 (m, 2H), 1.46 – 1.39 (m, 4H), 1.29 – 1.22 (m, 5H), 1.17 (ddt, $J = 13.4, 8.1, 4.0$ Hz, 2H), 0.99 (s, 3H), 0.96 (s, 3H), 0.85 (s, 3H), 0.20 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.74, 143.54, 125.78, 64.16, 45.07, 44.99, 40.34, 38.81, 37.21, 36.90, 36.48, 36.25, 35.77, 34.23, 34.19, 33.37, 30.25, 29.70, 21.80, 20.65, 19.86.

Morpholino(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-9**)



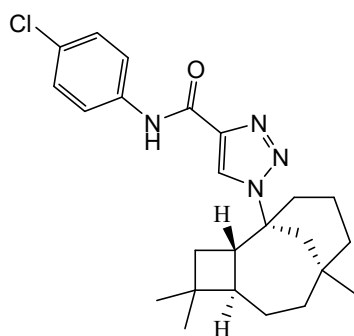
According to the general procedure D, compound **NC-9** could be obtained with 62% yield as white solid using **NC-13** and morpholine; HRMS (ESI) for $C_{22}H_{35}N_4O_2$: calculated, $[M+H]^+ = 387.2760$, found 387.2755; 1H NMR (600 MHz, $CDCl_3$) δ 8.12 (s, 1H), 4.44 (dd, $J = 6.2, 3.5$ Hz, 2H), 3.78 (s, 5H), 2.64 (dt, $J = 13.0, 2.4$ Hz, 1H), 2.57 (ddd, $J = 12.2, 10.4, 8.0$ Hz, 1H), 2.43 – 2.31 (m, 1H), 2.05 – 1.93 (m, 2H), 1.89 – 1.80 (m, 1H), 1.71 – 1.58 (m, 5H), 1.58 – 1.51 (m, 2H), 1.46 – 1.38 (m, 3H), 1.27 (ddt, $J = 12.2, 5.5, 3.0$ Hz, 2H), 1.22 – 1.15 (m, 2H), 0.99 (s, 3H), 0.97 (s, 3H), 0.86 (s, 3H), 0.22 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.20, 143.11, 126.23, 67.31, 66.96, 64.34, 47.31, 45.14, 45.04, 43.10, 40.32, 37.20, 36.90, 36.30, 35.83, 34.28, 34.22, 33.39, 30.26, 21.82, 20.64, 19.86.

(4-Hydroxypiperidin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-10**)



According to the general procedure D, compound **NC-10** could be obtained with 48% yield as white solid using **NC-13** and piperidin-4-ol; HRMS (ESI) for $C_{23}H_{37}N_4O_2$: calculated, $[M+H]^+ = 401.2917$, found 401.2924; 1H NMR (600 MHz, $CDCl_3$) δ 8.06 (s, 1H), 4.74 – 4.64 (m, 1H), 4.22 – 4.15 (m, 1H), 3.98 (dt, $J = 8.2, 4.2$ Hz, 1H), 3.82 – 3.74 (m, 1H), 3.69 (p, $J = 6.7$ Hz, 1H), 3.34 (dp, $J = 13.4, 3.8$ Hz, 1H), 3.16 (q, $J = 7.4$ Hz, 1H), 2.66 – 2.59 (m, 2H), 2.59 – 2.52 (m, 1H), 2.36 (d, $J = 11.8$ Hz, 1H), 2.03 – 1.92 (m, 5H), 1.86 – 1.79 (m, 1H), 1.62 (dddd, $J = 27.9, 14.2, 10.8, 5.6$ Hz, 6H), 1.53 (d, $J = 13.8$ Hz, 1H), 1.39 (dd, $J = 13.3, 5.7$ Hz, 9H), 1.25 (ddd, $J = 13.8, 6.9, 3.8$ Hz, 2H), 1.20 – 1.13 (m, 1H), 0.97 (s, 3H), 0.95 (s, 3H), 0.84 (s, 3H), 0.19 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.38, 142.96, 125.63, 67.11, 64.33, 55.31, 45.11, 45.09, 44.96, 43.95, 43.32, 40.32, 40.29, 37.15, 36.88, 36.28, 36.25, 35.78, 35.75, 34.85, 34.84, 34.21, 34.18, 33.94, 33.37, 30.25, 21.80, 20.61, 19.82, 12.55.

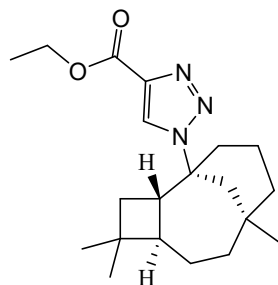
N-(4-Chlorophenyl)-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxamide (**NC-11**)



NC-11

According to the general procedure D, compound **NC-11** could be obtained with 89% yield as light yellow solid using **NC-13** and 4-chloroaniline; HRMS (ESI) for $C_{24}H_{32}ClN_4O$: calculated, $[M+H]^+ = 427.2265$, found 427.2267; 1H NMR (600 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.15 (s, 1H), 7.69 – 7.63 (m, 2H), 7.37 – 7.30 (m, 2H), 2.67 (dt, $J = 12.9, 2.4$ Hz, 1H), 2.59 (ddd, $J = 12.2, 10.3, 8.0$ Hz, 1H), 2.45 – 2.36 (m, 1H), 2.01 (ddd, $J = 17.5, 12.1, 9.0$ Hz, 2H), 1.90 – 1.81 (m, 1H), 1.74 – 1.59 (m, 4H), 1.59 – 1.53 (m, 1H), 1.48 – 1.38 (m, 3H), 1.29 (ddd, $J = 13.1, 6.6, 3.1$ Hz, 1H), 1.20 (td, $J = 13.0, 4.8$ Hz, 1H), 1.01 (s, 3H), 0.97 (s, 3H), 0.86 (s, 3H), 0.18 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.49, 142.18, 136.32, 129.48, 129.25, 123.52, 121.18, 64.98, 45.26, 45.10, 40.46, 37.27, 36.97, 36.41, 35.97, 34.41, 34.38, 33.47, 30.42, 21.89, 20.75, 19.96.

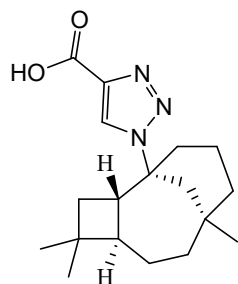
Ethyl-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxylate (**NC-12**)



NC-12

According to the general procedure C, compound **NC-12** could be obtained with 88% yield as white solid using **NC** and ethyl propiolate; HRMS (ESI) for $C_{20}H_{32}N_3O_2$: calculated, $[M+H]^+ = 346.2495$, found 346.2495; 1H NMR (600 MHz, $CDCl_3$) δ 8.03 (s, 1H), 4.36 (q, $J = 7.1$ Hz, 3H), 2.63 (dt, $J = 13.0, 2.4$ Hz, 1H), 2.52 (ddd, $J = 12.1, 10.3, 8.0$ Hz, 1H), 2.33 (ddd, $J = 12.1, 5.2, 2.8$ Hz, 1H), 2.02 – 1.87 (m, 3H), 1.83 – 1.74 (m, 2H), 1.66 – 1.46 (m, 6H), 1.40 – 1.32 (m, 7H), 1.27 – 1.17 (m, 2H), 1.17 – 1.08 (m, 2H), 0.94 (s, 4H), 0.91 (s, 4H), 0.87 – 0.82 (m, 1H), 0.80 (s, 4H), 0.14 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.29, 139.14, 124.99, 64.53, 61.14, 45.01, 44.94, 40.25, 37.17, 36.83, 36.17, 35.83, 34.25, 34.22, 33.32, 30.22, 21.73, 20.65, 19.81, 14.35.

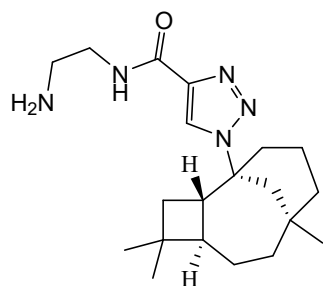
1-((1R,2S,5R,8S)-4,4,8-Trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxylic acid (**NC-13**)



NC-13

NC-12 (1.1 g, 3.2 mmol) dissolved in a mixture of THF (15 mL) and water (5 mL), then lithium hydroxide monohydrate (403 mg, 9.6 mmol) was added, and stirred at room temperature for 6 h. THF was distilled in vacuum, and 1 M HCl was added to adjusted the pH to 3-4, white solid was formed, and filtered, washed with water, dried under vacuum in 40 °C overnight, 965 mg **NC-13** was given as white solid, with 95% yield. HRMS (ESI) for $C_{18}H_{28}N_3O_2$: calculated, $[M+H]^+ = 318.2182$, found 318.2178; 1H NMR (600 MHz, $CDCl_3$) δ 8.19 – 8.15 (m, 1H), 2.67 (d, $J = 12.9$ Hz, 1H), 2.62 – 2.53 (m, 1H), 2.43 – 2.35 (m, 1H), 2.02 (td, $J = 11.3, 4.8$ Hz, 2H), 1.85 (dd, $J = 14.1, 5.2$ Hz, 2H), 1.72 – 1.49 (m, 7H), 1.47 – 1.40 (m, 4H), 1.32 – 1.23 (m, 2H), 1.22 – 1.15 (m, 2H), 1.00 (d, $J = 2.7$ Hz, 4H), 0.96 (s, 3H), 0.86 (d, $J = 2.8$ Hz, 3H), 0.18 (t, $J = 10.1$ Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.49, 138.47, 138.45, 125.93, 125.86, 65.12, 45.19, 45.04, 40.38, 37.25, 36.95, 36.36, 35.96, 34.41, 34.38, 33.44, 30.37, 21.86, 20.73, 19.93.

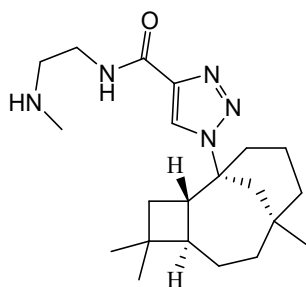
N-(2-Aminoethyl)-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxamide (**NC-14**)



NC-14

According to the general procedure C, compound **NC-14** could be obtained with 58% yield as white solid using **NC-13** and ethylenediamine; HRMS (ESI) for $C_{20}H_{34}N_5O$: calculated, $[M+H]^+ = 360.2763$, found 360.2766; 1H NMR (600 MHz, CD_3OD) δ 8.43 (d, $J = 1.4$ Hz, 1H), 3.68 (t, $J = 5.9$ Hz, 2H), 3.35 (s, 1H), 3.16 (t, $J = 6.1$ Hz, 2H), 2.75 – 2.65 (m, 2H), 2.47 (ddt, $J = 11.9, 5.6, 3.2$ Hz, 1H), 2.12 – 2.02 (m, 2H), 1.91 – 1.83 (m, 1H), 1.74 (ddd, $J = 19.9, 10.0, 4.8$ Hz, 1H), 1.71 – 1.62 (m, 2H), 1.60 – 1.54 (m, 1H), 1.48 (dtd, $J = 14.2, 6.8, 4.1$ Hz, 1H), 1.45 – 1.42 (m, 1H), 1.41 (s, 1H), 1.30 (ddd, $J = 14.2, 6.5, 3.9$ Hz, 1H), 1.27 – 1.20 (m, 1H), 1.02 (s, 3H), 1.00 (s, 3H), 0.85 (s, 3H), 0.10 (t, $J = 10.0$ Hz, 1H); ^{13}C NMR (151 MHz, CD_3OD) δ 163.92, 142.66, 124.99, 66.02, 46.30, 45.93, 41.41, 41.11, 38.38, 38.26, 37.80, 37.24, 36.65, 35.22, 35.14, 33.68, 30.63, 22.63, 20.89, 20.79.

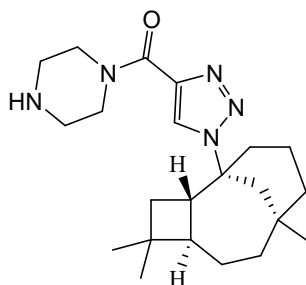
N-(2-(Methylamino)ethyl)-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxamide (**NC-15**)



NC-15

According to the general procedure D, compound **NC-15** could be obtained with 57% yield as white solid using **NC-13** and N-boc-N-methylethylenediamine; HRMS (ESI) for C₂₁H₃₆N₅O: calculated, [M+H]⁺ = 374.2920, found 374.2921; ¹H NMR (600 MHz, CDCl₃) δ 8.82 (s, 1H), 8.17 (s, 1H), 3.85 (s, 2H), 3.32 (s, 2H), 2.77 (s, 3H), 2.59 (t, *J* = 15.0 Hz, 2H), 2.46 – 2.31 (m, 1H), 1.97 (s, 2H), 1.84 (s, 1H), 1.60 (dt, *J* = 41.2, 14.1 Hz, 5H), 1.41 (t, *J* = 11.7 Hz, 3H), 1.34 – 1.25 (m, 1H), 1.20 (t, *J* = 13.1 Hz, 1H), 1.01 (s, 3H), 0.97 (s, 3H), 0.85 (s, 3H), 0.14 (s, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 161.77, 141.74, 123.45, 64.79, 49.18, 45.25, 44.98, 40.39, 37.24, 36.98, 36.40, 36.31, 35.96, 34.34, 33.55, 33.50, 30.40, 21.88, 20.71, 19.94.

Piperazin-1-yl(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-16**)

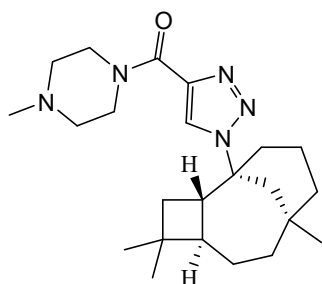


NC-16

According to the general procedure C, compound **NC-16** could be obtained with 66% yield as white solid using **NC-13** and piperazine; HRMS (ESI) for C₂₂H₃₆N₅O: calculated, [M+H]⁺ = 386.2920, found 386.2919; ¹H NMR (600 MHz, CDCl₃) δ 8.08 (d, *J* = 1.2 Hz, 1H), 4.32 (t, *J* = 5.0 Hz, 2H), 3.74 (q, *J* = 4.1 Hz, 2H), 2.95 (q, *J* = 4.8 Hz, 4H), 2.62 (dd, *J* = 13.0, 3.0 Hz, 1H), 2.55 (td, *J* = 11.3, 8.7 Hz, 1H), 2.40 – 2.31 (m, 1H), 1.98 (dq, *J* = 14.8, 7.3 Hz, 4H), 1.81 (dt, *J* = 14.6, 4.3 Hz, 1H), 1.71 – 1.55 (m, 3H), 1.53 (d, *J* = 13.5 Hz, 1H), 1.44 – 1.35 (m, 3H), 1.25 (ddd, *J* = 13.8, 6.8, 3.4 Hz, 1H), 1.16 (td, *J* = 13.1, 4.8 Hz, 1H), 0.97 (s, 3H), 0.95 (s, 3H), 0.84 (s, 3H), 0.21 (t, *J* = 10.1 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 160.32, 143.41, 126.14, 64.34, 48.14, 46.79, 46.16, 45.21, 45.13, 43.93, 40.41, 37.30, 37.00, 36.38, 35.90, 34.35, 34.30, 33.49, 30.35, 21.91, 20.74, 19.96.

(4-Methylpiperazin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-

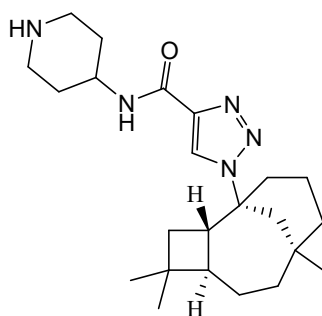
trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-17**)



NC-17

According to the general procedure C, compound **NC-17** could be obtained with 58% yield as white solid using **NC-13** and 1-methylpiperazine; HRMS (ESI) for C₂₃H₃₈N₅O: calculated, [M+H]⁺ = 400.3076, found 400.3100; ¹H NMR (600 MHz, CDCl₃) δ 8.11 (s, 1H), 4.41 (d, *J* = 6.0 Hz, 2H), 3.81 (d, *J* = 5.2 Hz, 3H), 2.65 (dt, *J* = 12.9, 2.4 Hz, 1H), 2.61 – 2.47 (m, 6H), 2.42 – 2.36 (m, 1H), 2.34 (d, *J* = 2.1 Hz, 4H), 2.01 (dd, *J* = 12.2, 7.1 Hz, 1H), 1.85 (ddt, *J* = 13.1, 6.7, 3.4 Hz, 1H), 1.67 (ddt, *J* = 12.3, 9.8, 3.5 Hz, 2H), 1.64 – 1.59 (m, 2H), 1.55 (dt, *J* = 14.3, 3.0 Hz, 1H), 1.43 (ddd, *J* = 9.9, 7.1, 4.0 Hz, 3H), 1.31 – 1.24 (m, 2H), 1.22 – 1.15 (m, 1H), 1.00 (d, *J* = 2.5 Hz, 3H), 0.97 (d, *J* = 2.1 Hz, 3H), 0.87 (d, *J* = 2.1 Hz, 3H), 0.23 (t, *J* = 10.1 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 160.13, 143.28, 126.07, 64.25, 55.51, 54.83, 46.47, 45.99, 45.10, 45.02, 42.58, 40.31, 37.20, 36.89, 36.27, 35.80, 34.25, 34.19, 33.38, 30.24, 21.81, 20.64, 19.85.

N-(Piperidin-4-yl)-1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazole-4-carboxamide (**NC-18**)

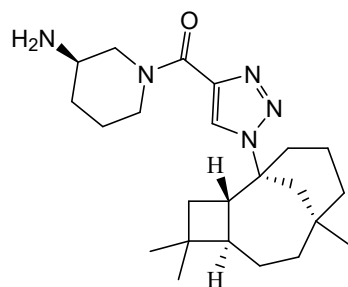


NC-18

According to the general procedure D, compound **NC-18** could be obtained with 57% yield as white solid using **NC-13** and 4-amino-cyclohexanecarboxylic acid tert-butyl ester; HRMS (ESI) for C₂₃H₃₈N₅O: calculated, [M+H]⁺ = 400.3076, found 400.3074; ¹H NMR (600 MHz, CDCl₃) δ 8.20 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 4.22 (dt, *J* = 7.5, 3.7 Hz, 1H), 3.63 – 3.54 (m, 3H), 3.18 – 3.10 (m, 3H), 2.60 (d, *J* = 12.9 Hz, 1H), 2.52 (td, *J* = 11.0, 8.1 Hz, 1H), 2.39 – 2.31 (m, 1H), 2.24 – 2.16 (m, 3H), 2.11 (t, *J* = 13.0 Hz, 3H), 1.99 – 1.91 (m, 2H), 1.78 (dt, *J* = 13.7, 4.1 Hz, 2H), 1.65 – 1.54 (m, 4H), 1.49 (d, *J* = 13.2 Hz, 2H), 1.37 (t, *J* = 11.9 Hz, 3H), 1.23 (ddd, *J* = 13.1, 6.3, 2.9 Hz, 2H), 1.17 – 1.09 (m, 2H), 0.95 (s, 4H), 0.91 (s, 3H), 0.81 (s, 3H), 0.14 (t, *J* = 10.2 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 160.33, 141.74, 123.47, 64.67, 50.54, 45.12, 44.97,

44.31, 43.31, 40.34, 37.20, 36.93, 36.34, 35.92, 34.29, 34.26, 33.43, 30.35, 30.33, 28.60, 21.83, 20.67, 19.89.

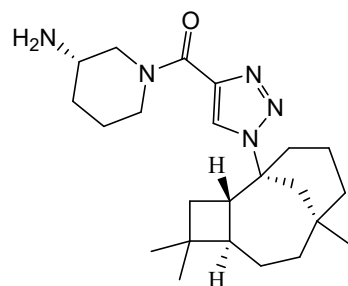
((R)-3-Aminopiperidin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-19**)



NC-19

According to the general procedure D, compound **NC-19** could be obtained with 67% yield as white solid using **NC-13** and (R)- 3-boc-aminopiperidine; HRMS (ESI) for C₂₃H₃₈N₅O: calculated, [M+H]⁺ = 400.3076, found 400.3077; ¹H NMR (600 MHz, CDCl₃) δ 8.11 (s, 1H), 5.00 – 4.93 (m, 1H), 4.91 – 4.81 (m, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 4.19 (dt, *J* = 13.7, 4.7 Hz, 1H), 3.54 – 3.35 (m, 1H), 3.21 – 3.07 (m, 1H), 3.01 (d, *J* = 10.1 Hz, 1H), 2.95 – 2.82 (m, 1H), 2.66 (t, *J* = 12.7 Hz, 1H), 2.58 (td, *J* = 11.1, 8.1 Hz, 1H), 2.39 (dq, *J* = 12.0, 3.6 Hz, 1H), 2.16 – 1.97 (m, 8H), 1.85 (tp, *J* = 8.7, 5.0 Hz, 3H), 1.73 – 1.59 (m, 5H), 1.56 (d, *J* = 13.7 Hz, 1H), 1.53 – 1.40 (m, 5H), 1.24 – 1.17 (m, 1H), 1.01 (s, 3H), 0.98 (s, 3H), 0.88 (s, 3H), 0.24 (t, *J* = 10.1 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 160.41, 143.38, 126.02, 125.97, 64.29, 64.27, 45.14, 45.08, 45.02, 43.25, 40.31, 37.20, 36.90, 36.30, 36.28, 35.80, 34.26, 34.20, 33.38, 30.26, 24.57, 23.23, 21.81, 20.64, 19.86.

((S)-3-Aminopiperidin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-20**)

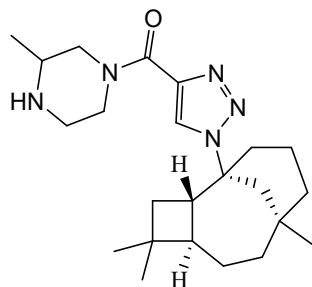


NC-20

According to the general procedure D, compound **NC-20** could be obtained with 70% yield as white solid using **NC-13** and (S)- 3-boc-aminopiperidine; HRMS (ESI) for C₂₃H₃₈N₅O: calculated, [M+H]⁺ = 400.3076, found 400.3075; ¹H NMR (600 MHz, CDCl₃) δ 8.09 (s, 1H), 5.01 – 4.79 (m, 2H), 4.47 – 4.35 (m, 1H), 4.19 (dd, *J* = 12.4, 5.2 Hz, 1H), 3.40 (ddd, *J* = 31.5, 13.1, 5.7 Hz, 2H), 3.12 (td, *J* = 11.4, 6.3 Hz, 1H), 3.05 (tt, *J* = 8.4, 3.7 Hz, 1H), 2.97 (dq, *J* = 8.9, 4.5 Hz, 1H), 2.83 (dd, *J* = 12.6, 9.2 Hz, 1H), 2.63 (d, *J* = 13.1 Hz, 2H), 2.60 – 2.50 (m, 2H), 2.41 – 2.19 (m, 8H), 2.05 – 1.93 (m, 6H), 1.88 – 1.77 (m, 5H), 1.71 – 1.49 (m, 11H), 1.48 – 1.37 (m, 8H), 1.31 – 1.21 (m,

5H), 1.20 – 1.13 (m, 2H), 0.97 (d, $J = 15.1$ Hz, 9H), 0.85 (s, 5H), 0.21 (s, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 160.53, 143.35, 126.03, 64.26, 64.22, 60.38, 54.39, 50.67, 48.31, 47.77, 46.95, 45.10, 44.98, 43.22, 40.30, 37.18, 36.89, 36.28, 35.80, 30.23, 21.80, 20.62, 19.84, 14.18.

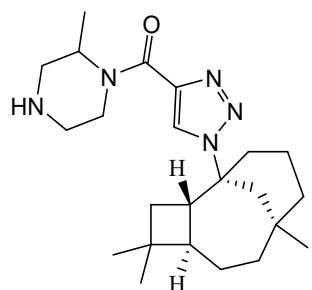
(3-Methylpiperazin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-21**)



NC-21

According to the general procedure D, compound **NC-21** could be obtained with 53% yield as white solid using **NC-13** and 1-boc-2-methylpiperazine; HRMS (ESI) for $\text{C}_{23}\text{H}_{38}\text{N}_5\text{O}$: calculated, $[\text{M}+\text{H}]^+ = 400.3076$, found 400.3074; ^1H NMR (600 MHz, CDCl_3) δ 8.08 (s, 1H), 5.37 – 5.23 (m, 1H), 4.57 (d, $J = 11.4$ Hz, 1H), 3.47 (d, $J = 1.1$ Hz, 2H), 3.32 (ddt, $J = 23.6, 13.2, 6.7$ Hz, 1H), 3.12 (d, $J = 15.6$ Hz, 1H), 3.05 – 2.86 (m, 4H), 2.64 (q, $J = 9.8$ Hz, 1H), 2.60 – 2.51 (m, 2H), 2.37 (td, $J = 13.0, 7.0$ Hz, 1H), 2.34 – 2.13 (m, 3H), 2.00 (td, $J = 15.1, 5.0$ Hz, 2H), 1.83 (dt, $J = 14.5, 4.2$ Hz, 1H), 1.70 – 1.57 (m, 4H), 1.54 (d, $J = 13.5$ Hz, 1H), 1.42 (tt, $J = 10.8, 4.8$ Hz, 3H), 1.27 (ddd, $J = 14.3, 7.2, 3.9$ Hz, 2H), 1.16 (td, $J = 10.7, 5.5$ Hz, 4H), 0.99 (s, 3H), 0.96 (s, 3H), 0.85 (s, 3H), 0.21 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 160.34, 160.25, 143.26, 143.19, 143.14, 126.20, 126.13, 126.07, 64.50, 53.49, 51.73, 51.68, 51.11, 50.93, 49.44, 47.01, 46.99, 46.48, 46.45, 45.67, 45.63, 45.30, 45.26, 45.23, 45.21, 45.13, 45.11, 42.87, 40.48, 40.44, 40.42, 37.32, 37.06, 37.02, 36.45, 36.43, 36.40, 35.96, 35.91, 34.39, 34.35, 34.34, 33.53, 33.50, 30.39, 21.97, 21.93, 20.76, 19.98, 19.37, 19.03.

(2-Methylpiperazin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-22**)

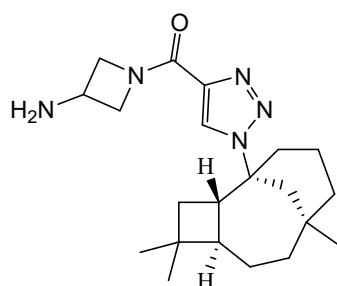


NC-22

According to the general procedure D, compound **NC-22** could be obtained with 67% yield as white solid using **NC-13** and 4-boc-2-methylpiperazine; HRMS (ESI) for $\text{C}_{23}\text{H}_{38}\text{N}_5\text{O}$: calculated, $[\text{M}+\text{H}]^+ = 400.3076$, found 400.3080; ^1H NMR (600 MHz,

CDCl₃) δ 8.15 – 8.03 (m, 1H), 5.65 – 5.39 (m, 1H), 5.18 (s, 1H), 4.83 (s, 1H), 4.47 (s, 1H), 3.46 (d, J = 1.7 Hz, 1H), 3.18 – 2.99 (m, 3H), 2.87 (dd, J = 28.1, 14.2 Hz, 2H), 2.69 – 2.60 (m, 1H), 2.56 (td, J = 11.2, 8.1 Hz, 1H), 2.37 (dt, J = 12.3, 3.9 Hz, 1H), 2.23 (d, J = 23.4 Hz, 3H), 1.99 (ddd, J = 18.7, 9.4, 4.0 Hz, 2H), 1.82 (dt, J = 14.5, 4.2 Hz, 1H), 1.71 – 1.56 (m, 4H), 1.53 (d, J = 13.7 Hz, 1H), 1.46 – 1.35 (m, 6H), 1.26 (ddd, J = 13.8, 7.3, 3.9 Hz, 2H), 1.17 (td, J = 13.1, 4.8 Hz, 1H), 0.98 (s, 3H), 0.96 (s, 3H), 0.85 (s, 3H), 0.22 (t, J = 10.1 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 160.60, 143.39, 126.09, 126.05, 64.41, 45.25, 45.23, 45.13, 45.12, 40.46, 40.42, 37.32, 37.05, 37.01, 36.42, 36.40, 35.95, 35.91, 34.38, 34.37, 34.32, 33.52, 33.50, 30.38, 30.36, 21.96, 21.93, 20.75, 19.98.

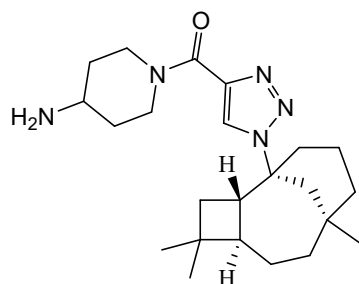
(3-Aminoazetidin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-23**)



NC-23

According to the general procedure D, compound **NC-23** could be obtained with 86% yield as white solid using **NC-13** and 3-N-boc-amino-azetidine; HRMS (ESI) for C₂₁H₃₄N₅O: calculated, [M+H]⁺ = 372.2763, found 372.2762; ¹H NMR (600 MHz, CDCl₃) δ 9.07 (d, J = 8.3 Hz, 1H), 8.42 (s, 1H), 5.30 – 5.17 (m, 1H), 4.54 (t, J = 8.8 Hz, 4H), 2.63 (d, J = 12.9 Hz, 1H), 2.56 (q, J = 10.2 Hz, 1H), 2.41 (d, J = 12.1 Hz, 1H), 1.95 (dq, J = 13.4, 6.9 Hz, 2H), 1.86 – 1.75 (m, 1H), 1.68 – 1.56 (m, 3H), 1.56 – 1.45 (m, 2H), 1.40 (q, J = 11.9 Hz, 3H), 1.31 – 1.22 (m, 2H), 1.16 (td, J = 13.0, 5.0 Hz, 2H), 0.98 (d, J = 5.4 Hz, 3H), 0.93 (s, 3H), 0.81 (s, 3H), 0.15 (t, J = 10.1 Hz, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 160.78, 141.47, 124.24, 64.89, 53.37, 45.21, 44.96, 41.54, 40.44, 37.27, 37.02, 36.49, 36.01, 34.35, 34.33, 33.53, 30.44, 21.93, 20.73, 19.98.

(4-Aminopiperidin-1-yl)(1-((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)-1H-1,2,3-triazol-4-yl)methanone (**NC-24**)



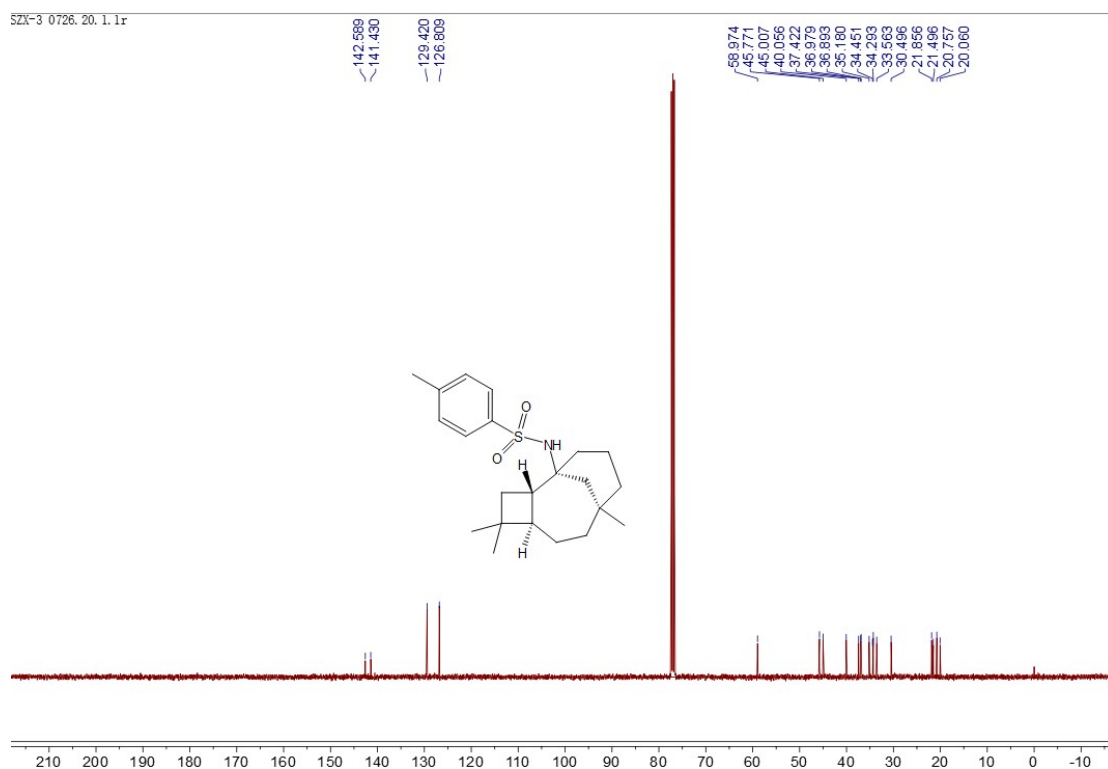
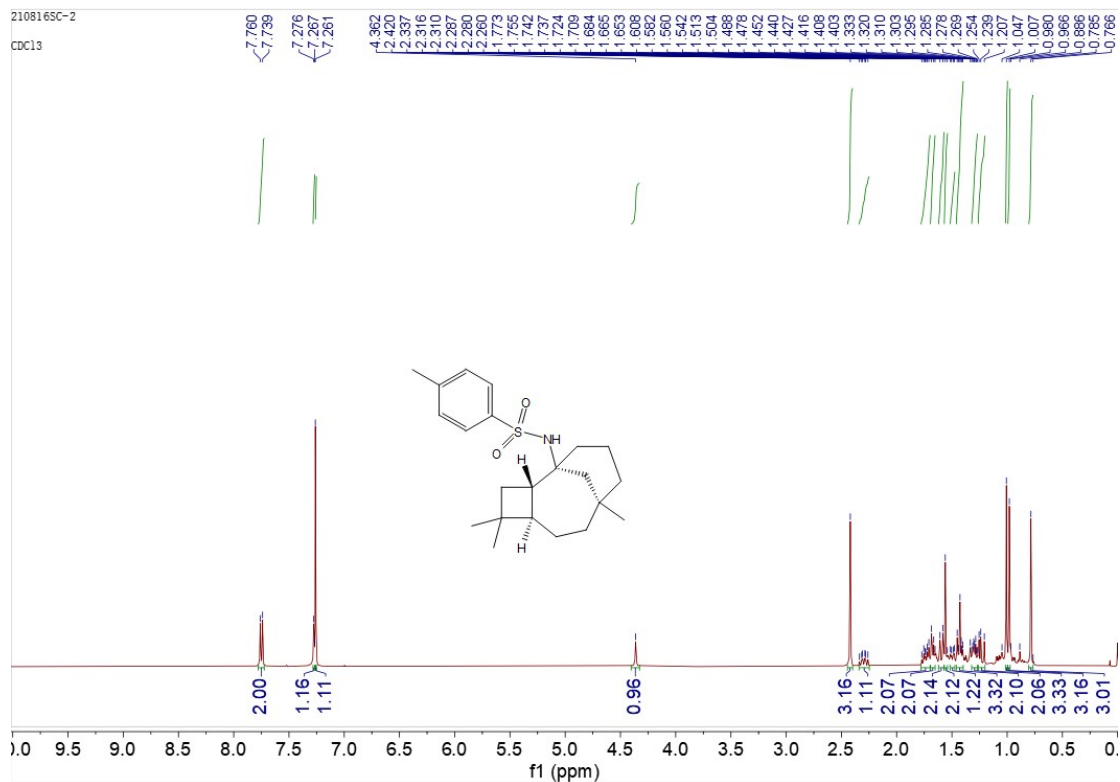
NC-24

According to the general procedure D, compound **NC-24** could be obtained with 52% yield as white solid using **NC-13** and 4-N-boc-aminopiperidine; HRMS (ESI) for

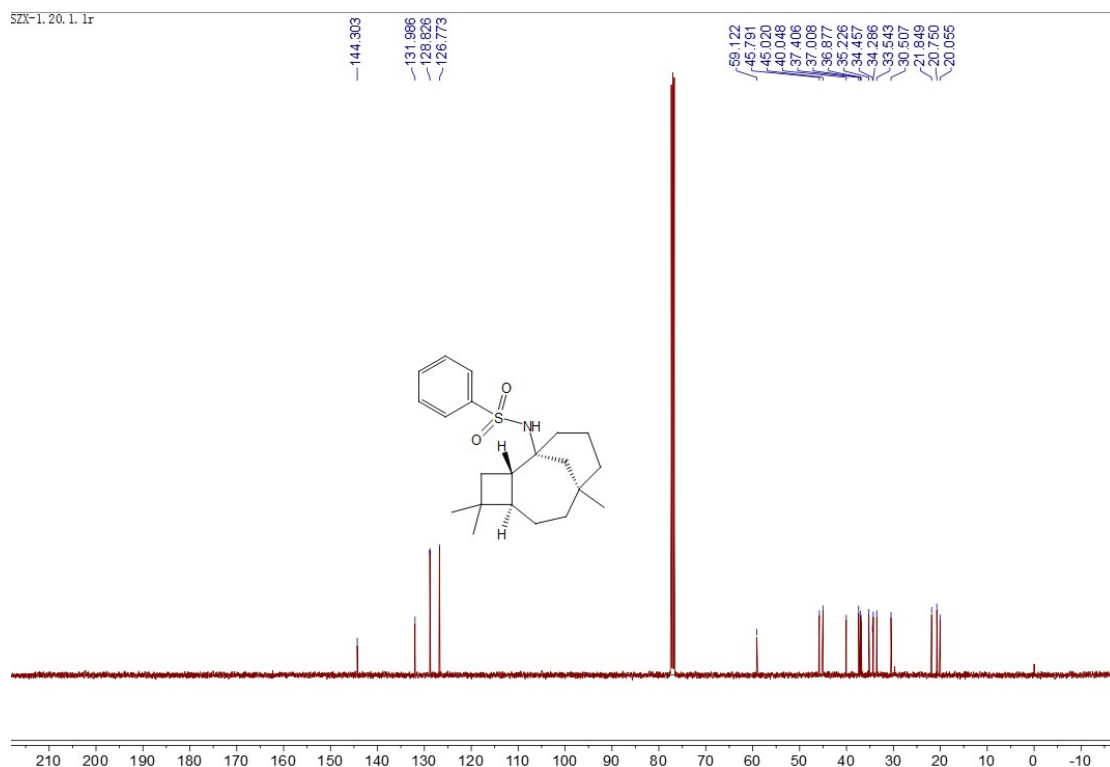
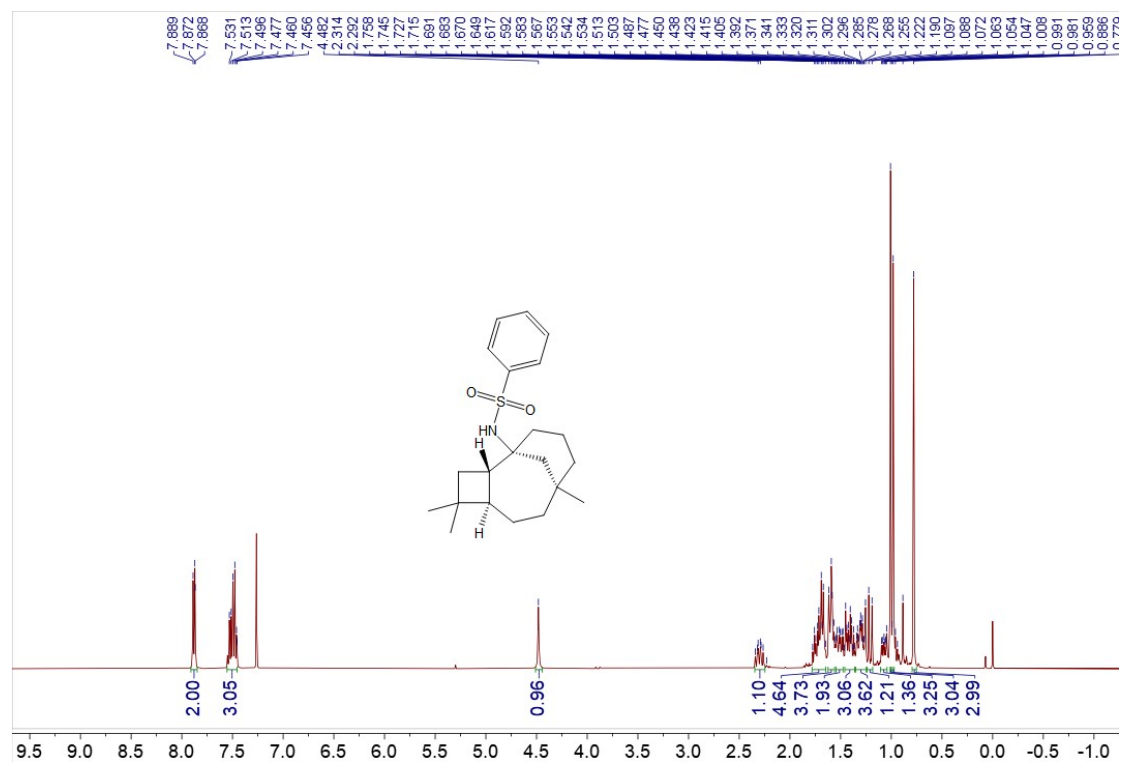
$C_{23}H_{38}N_5O$: calculated, $[M+H]^+ = 400.3076$, found 400.3076; 1H NMR (600 MHz, $CDCl_3$) δ 8.16 – 8.04 (m, 1H), 5.10 (d, $J = 14.4$ Hz, 1H), 4.65 (d, $J = 35.3$ Hz, 6H), 3.55 (d, $J = 11.5$ Hz, 1H), 3.30 (d, $J = 12.9$ Hz, 1H), 3.13 (q, $J = 7.1$ Hz, 3H), 2.90 (q, $J = 11.9$ Hz, 1H), 2.53 (t, $J = 15.1$ Hz, 1H), 2.25 (t, $J = 16.7$ Hz, 3H), 1.95 (dd, $J = 37.1$, 11.5 Hz, 2H), 1.79 (t, $J = 19.1$ Hz, 3H), 1.61 (dt, $J = 30.0$, 13.0 Hz, 3H), 1.54 – 1.45 (m, 2H), 1.36 (dt, $J = 16.1$, 10.4 Hz, 7H), 1.29 – 1.21 (m, 3H), 1.20 – 1.10 (m, 2H), 0.94 (s, 3H), 0.92 (s, 3H), 0.81 (s, 3H), 0.17 (t, $J = 10.1$ Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.61, 142.47, 142.42, 125.81, 64.44, 48.87, 46.18, 44.86, 41.21, 40.35, 37.15, 36.98, 35.77, 34.24, 34.21, 33.43, 30.62, 30.33, 29.72, 21.86, 20.63, 19.84, 8.77.

2. ^1H NMR and ^{13}C NMR spectra of β -caryolane derivatives

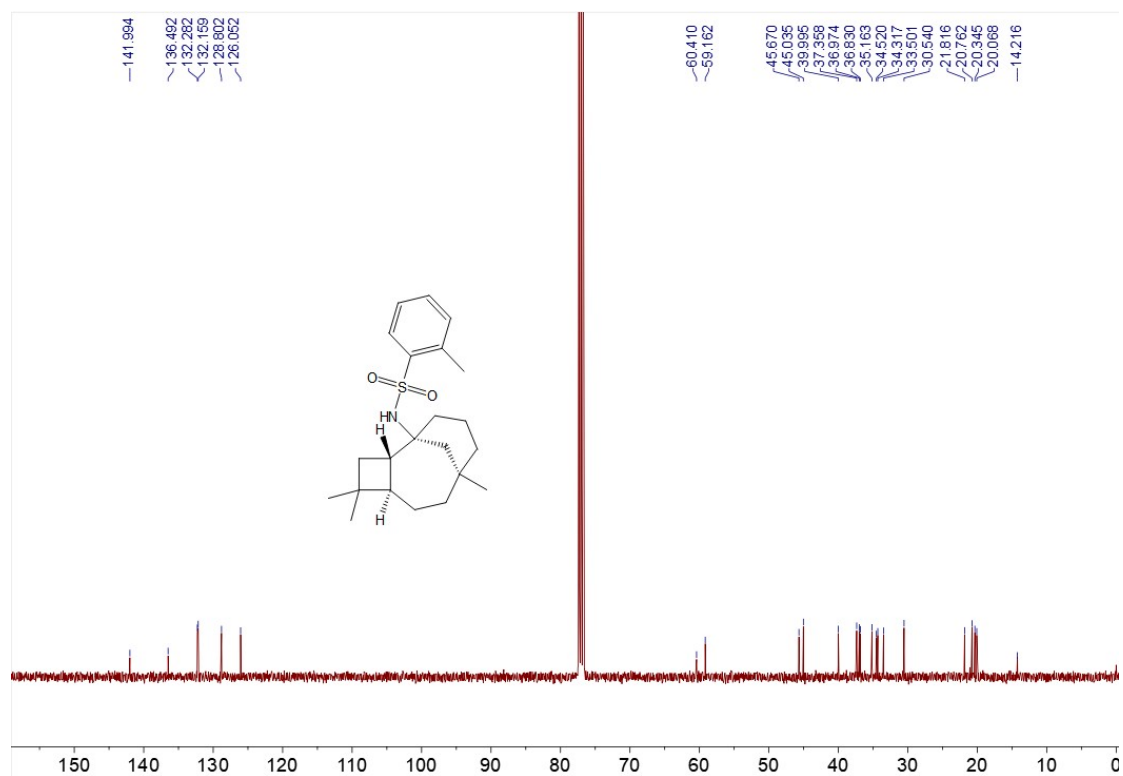
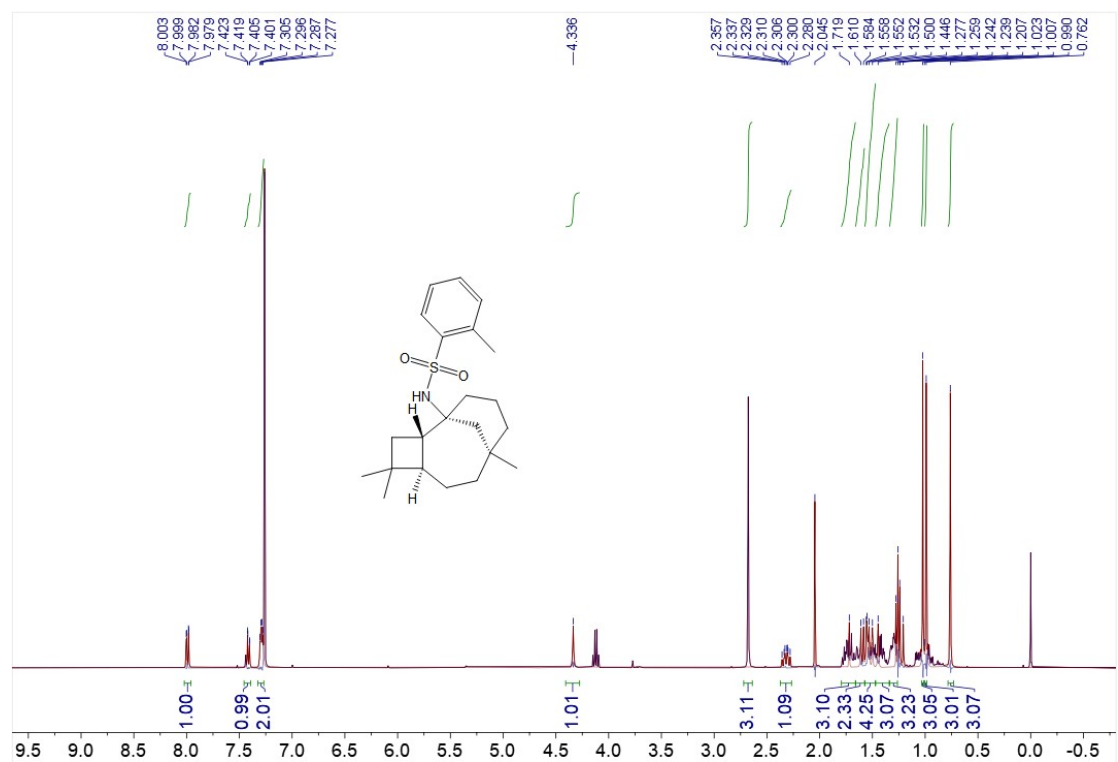
Compound SA-1



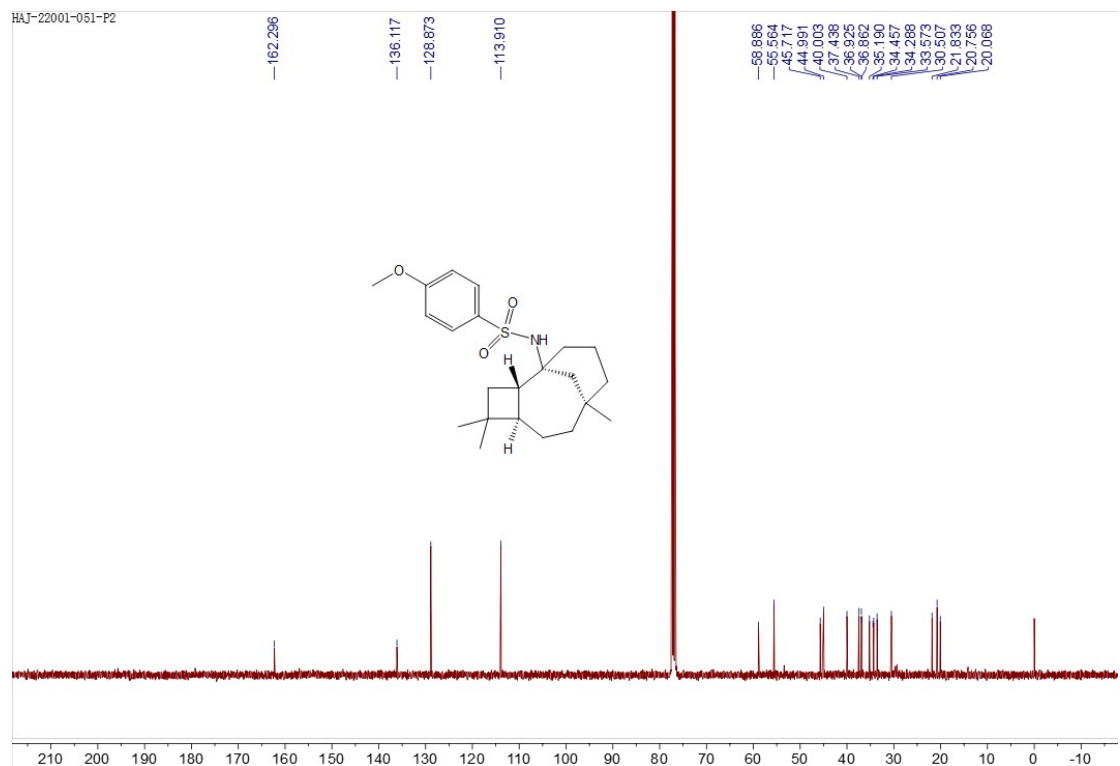
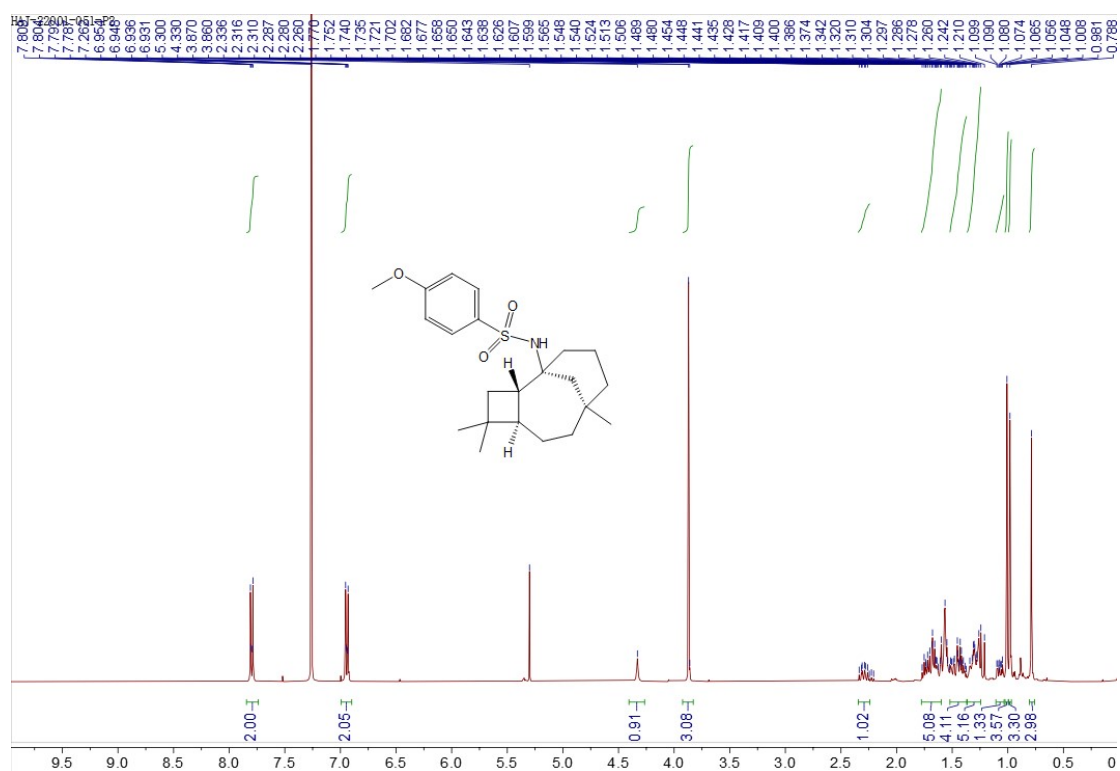
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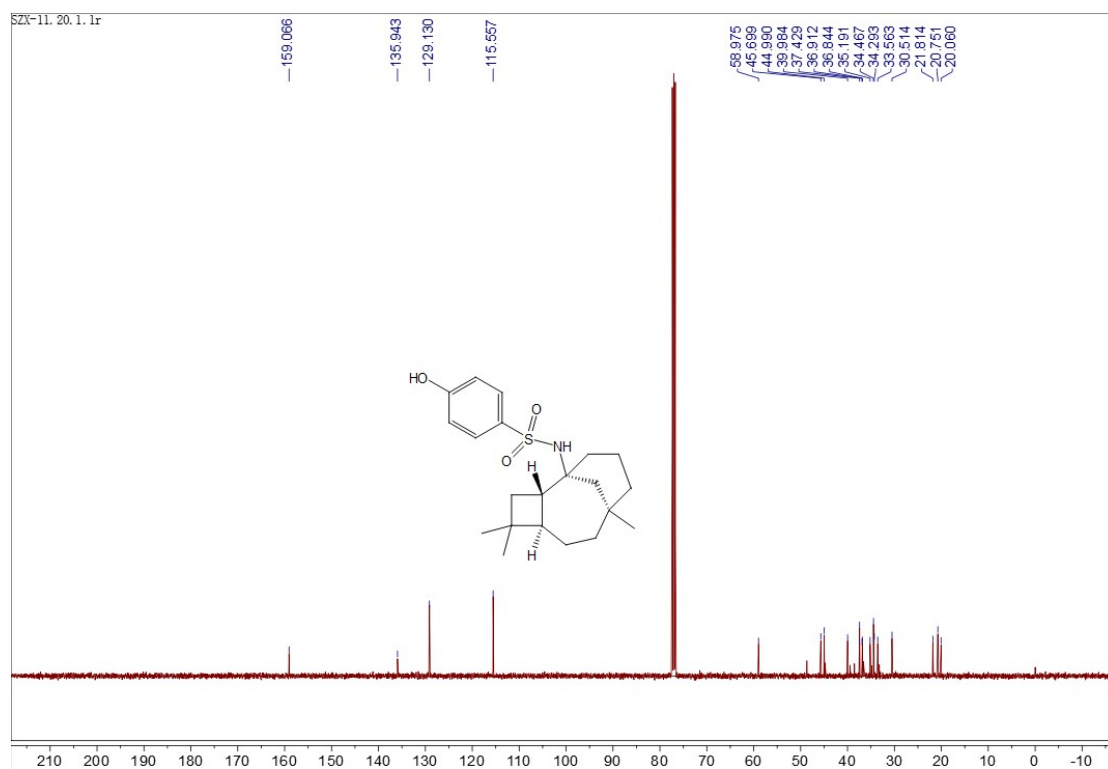
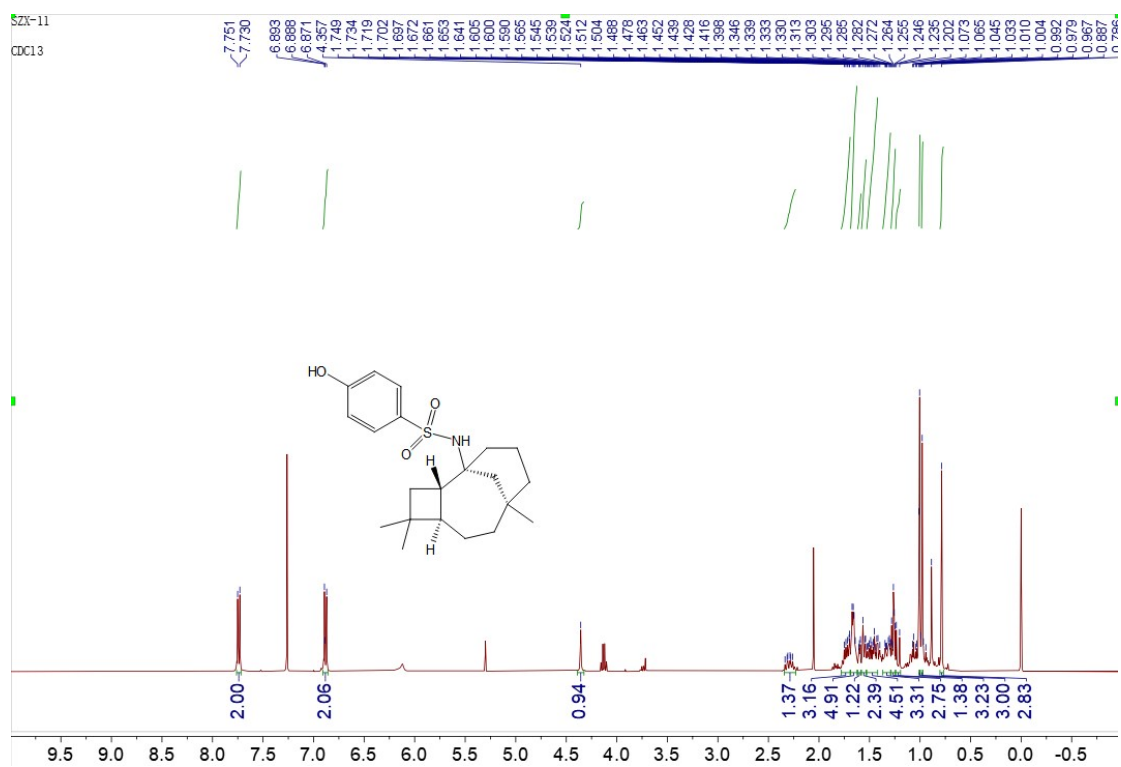
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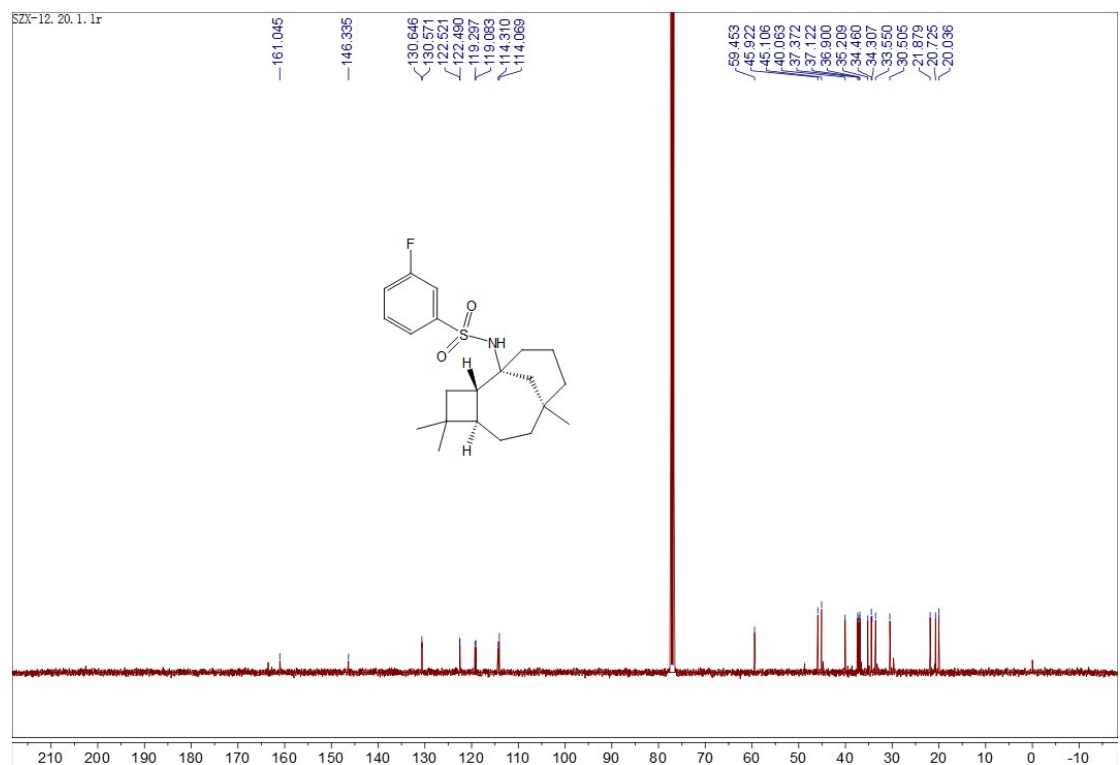
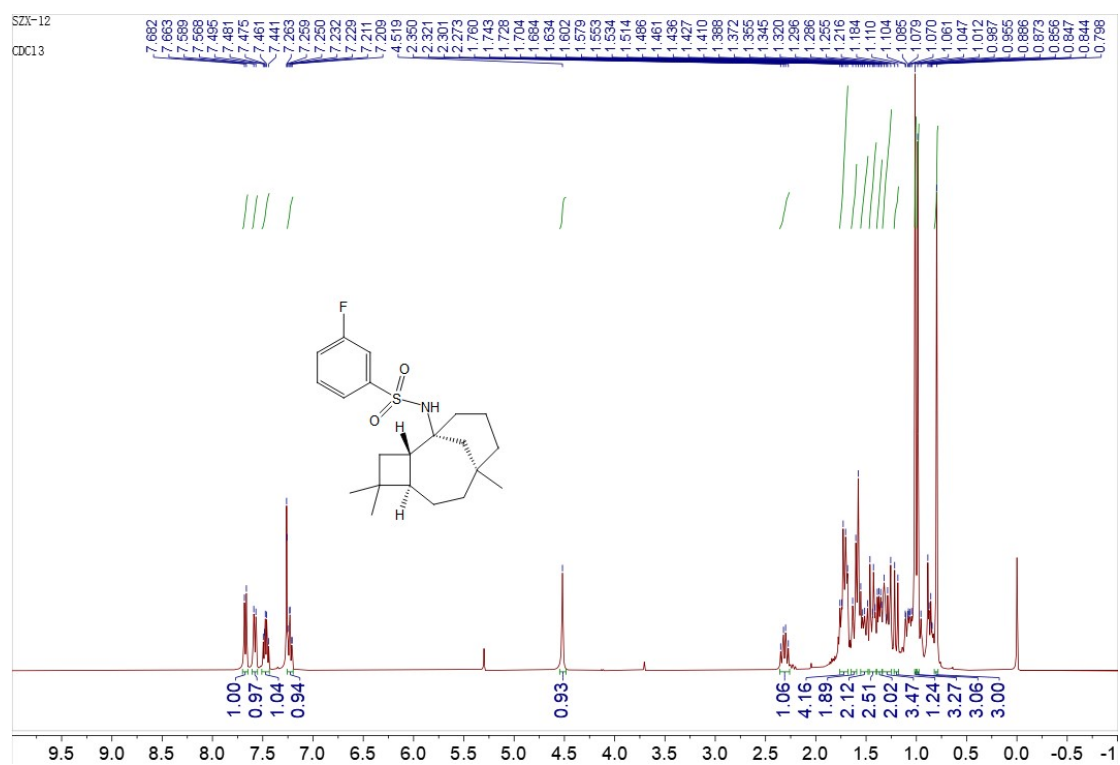
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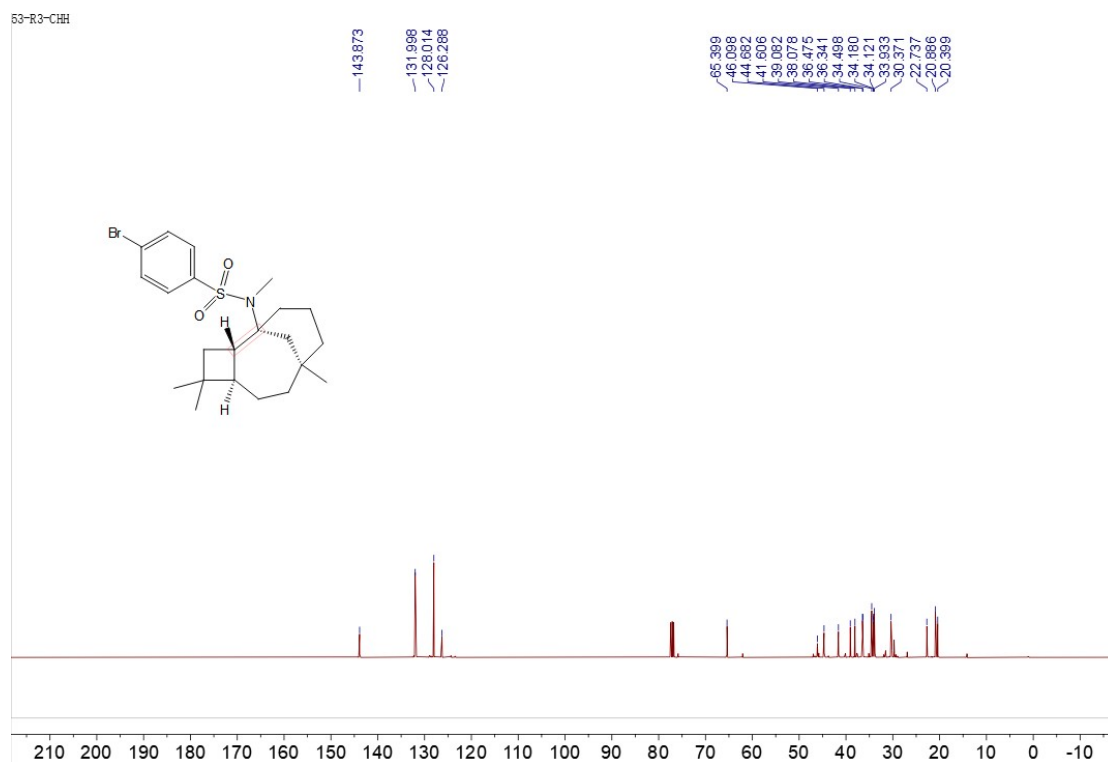
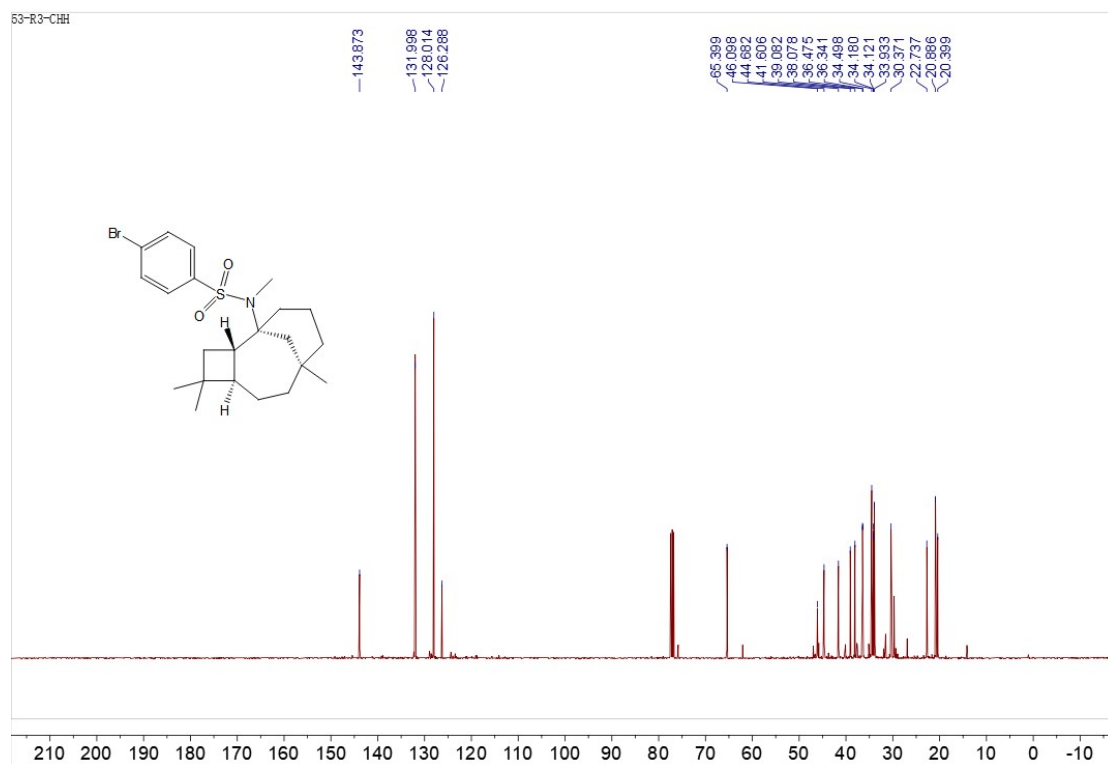
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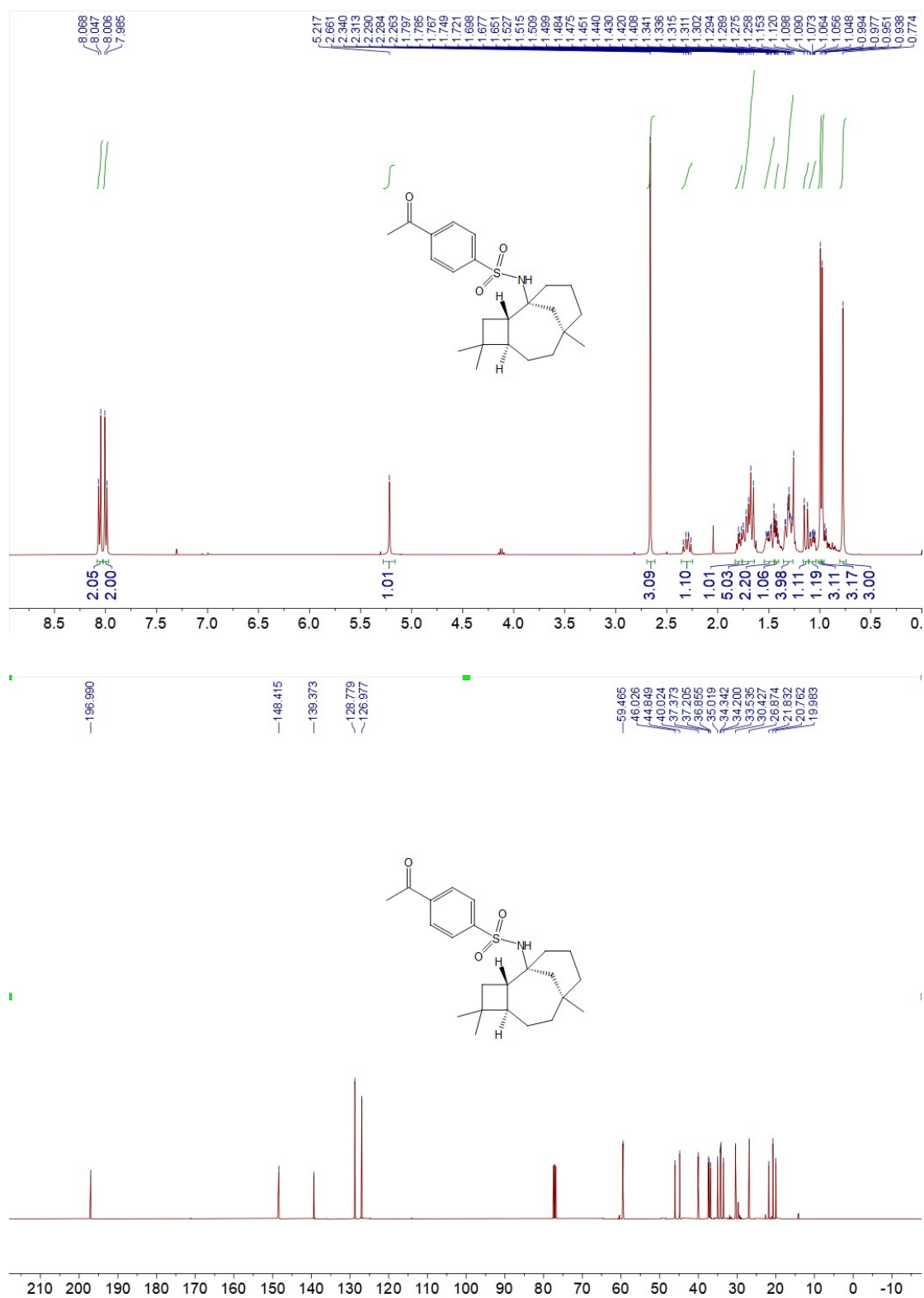
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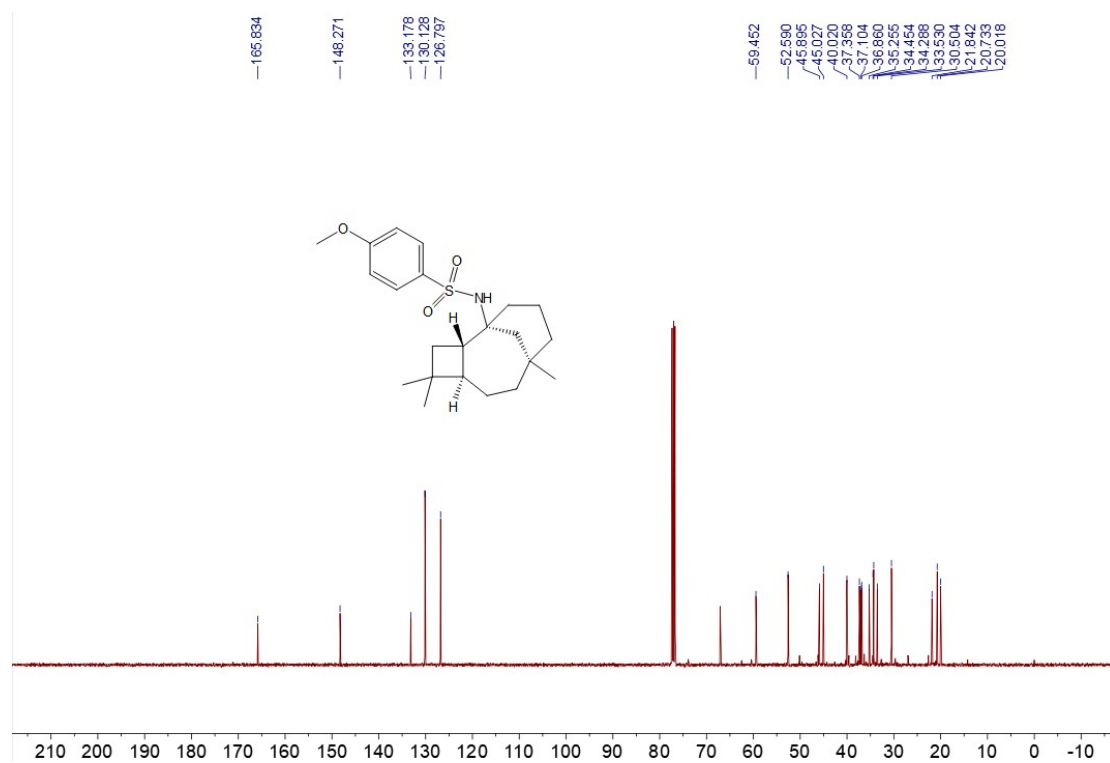
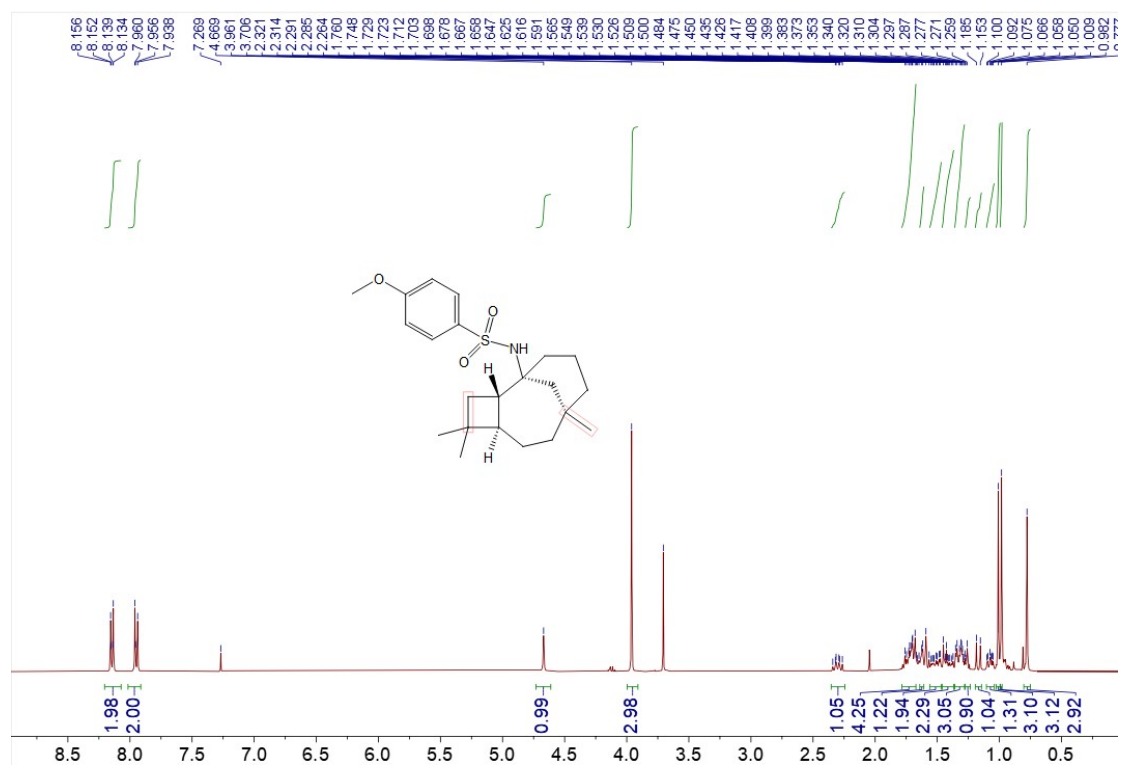
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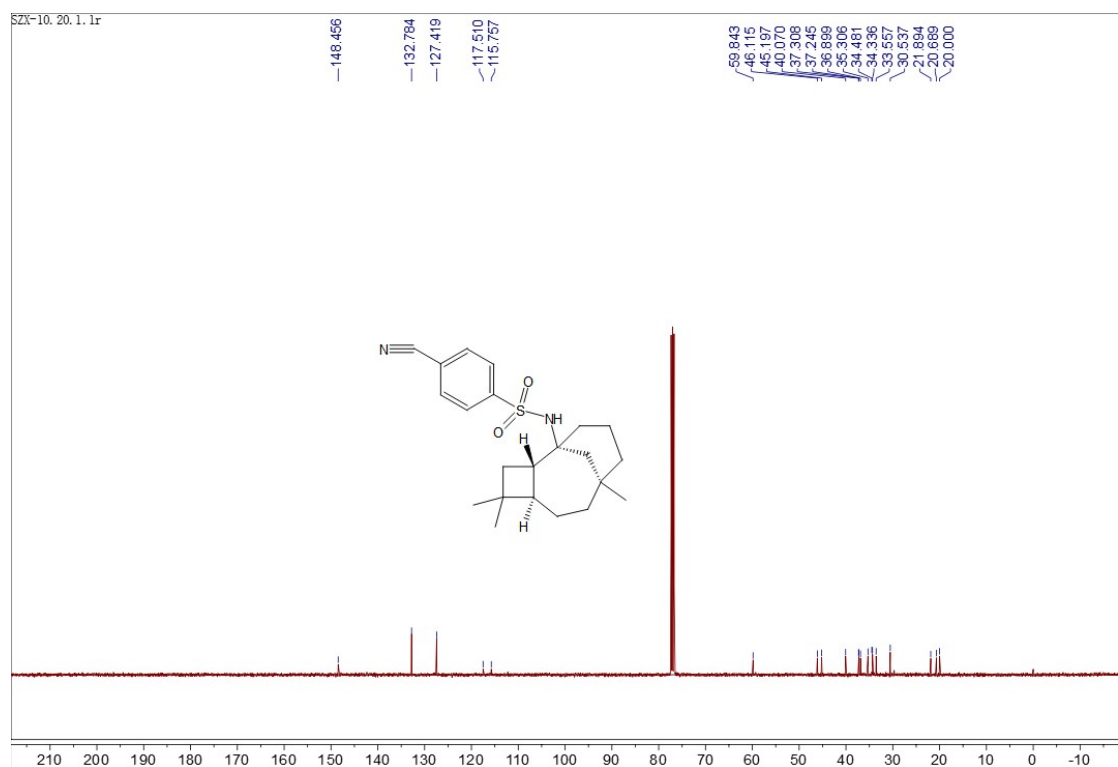
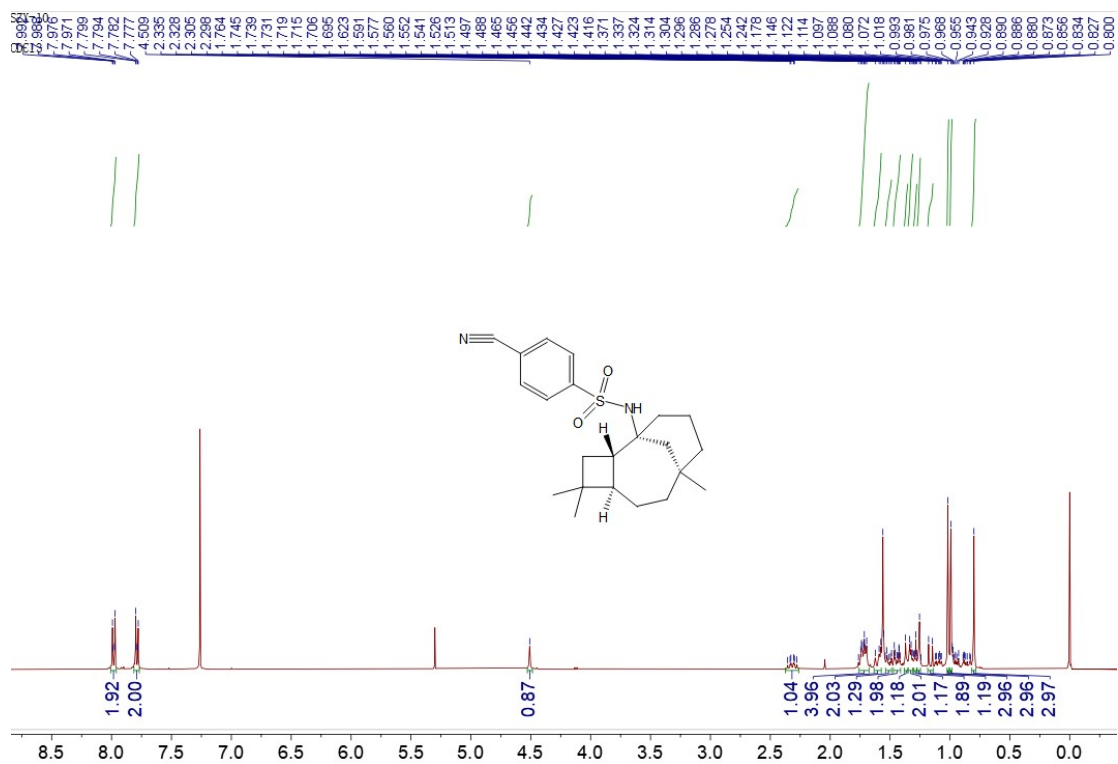
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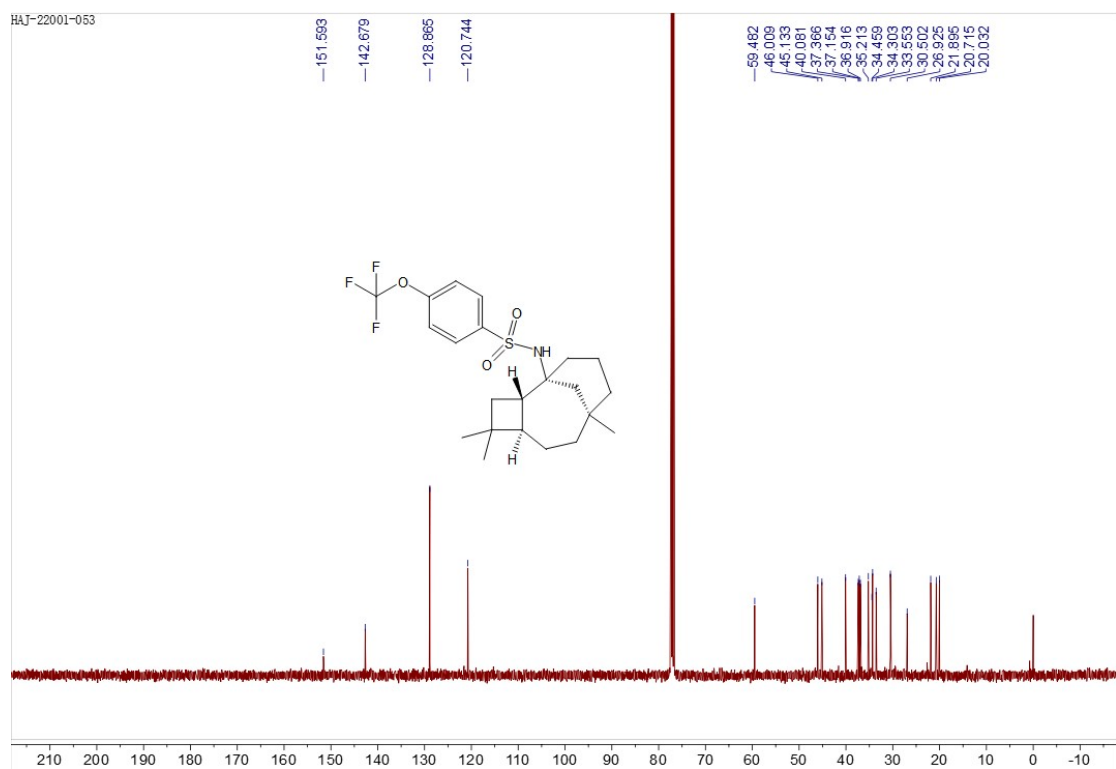
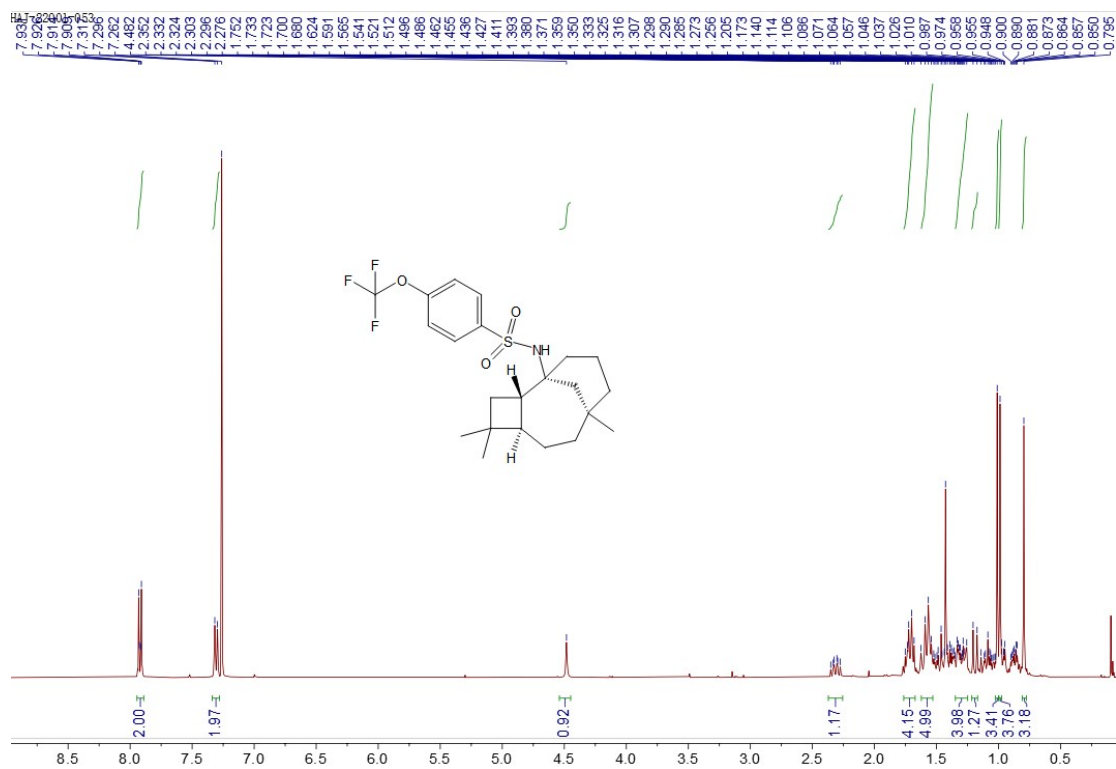
Compound SA-9



Compound SA-10

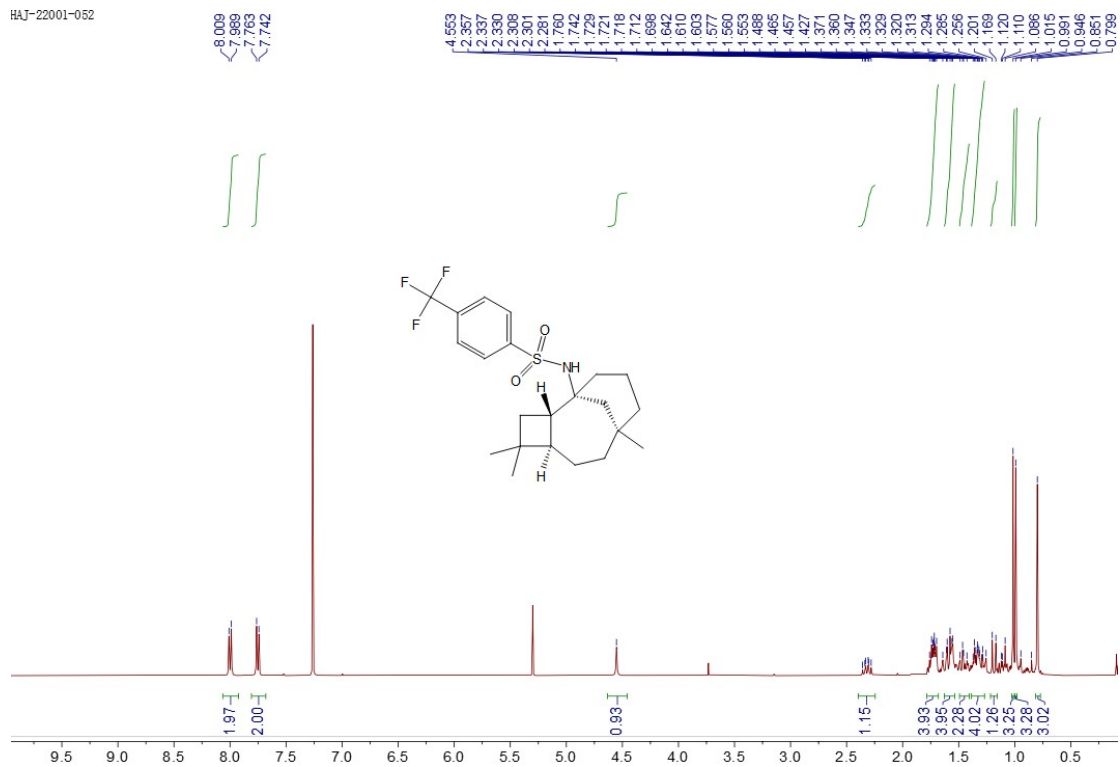


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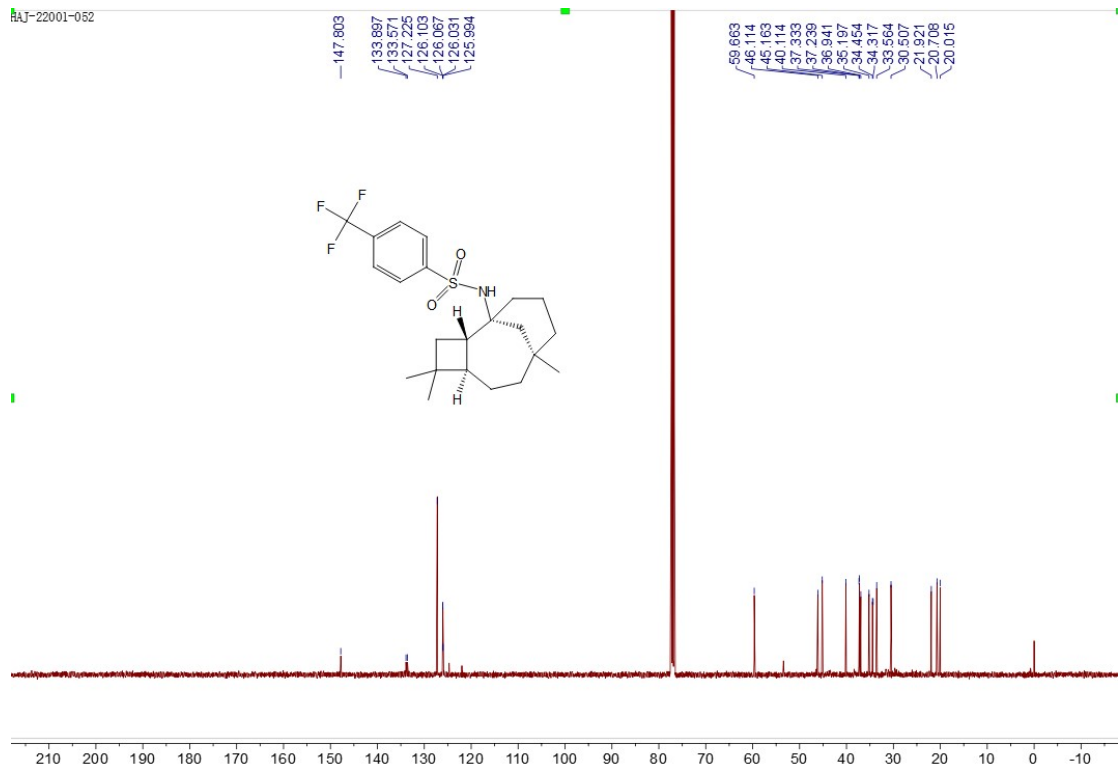


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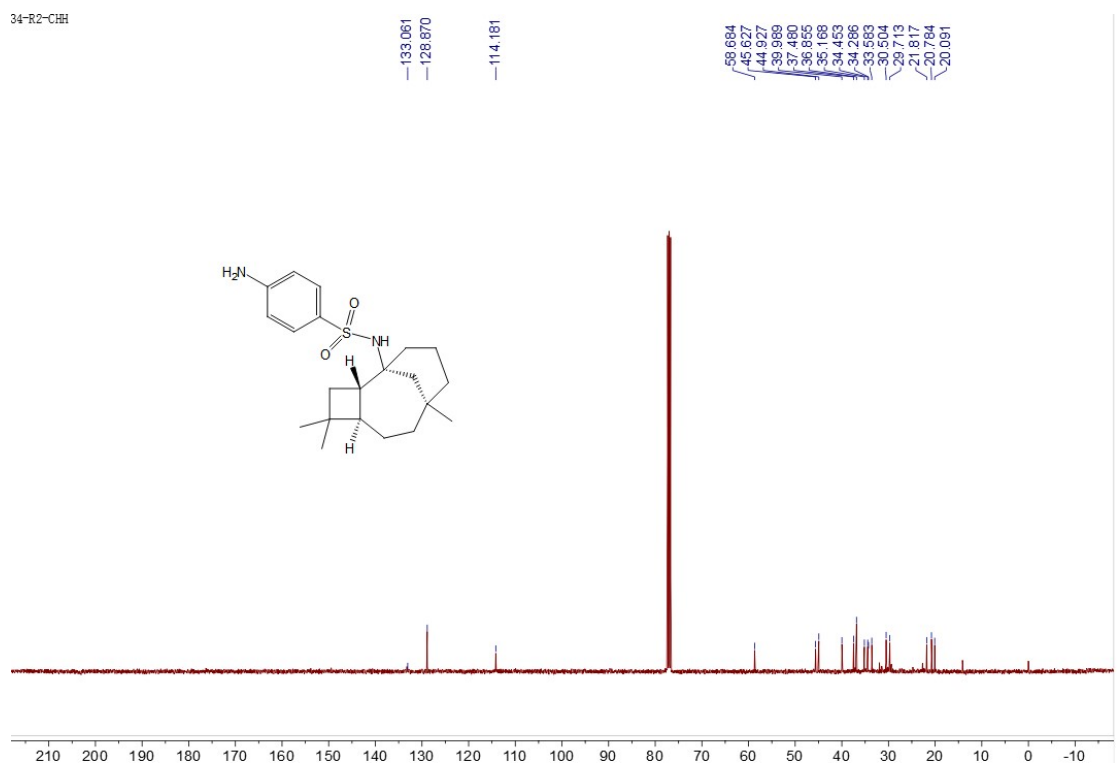
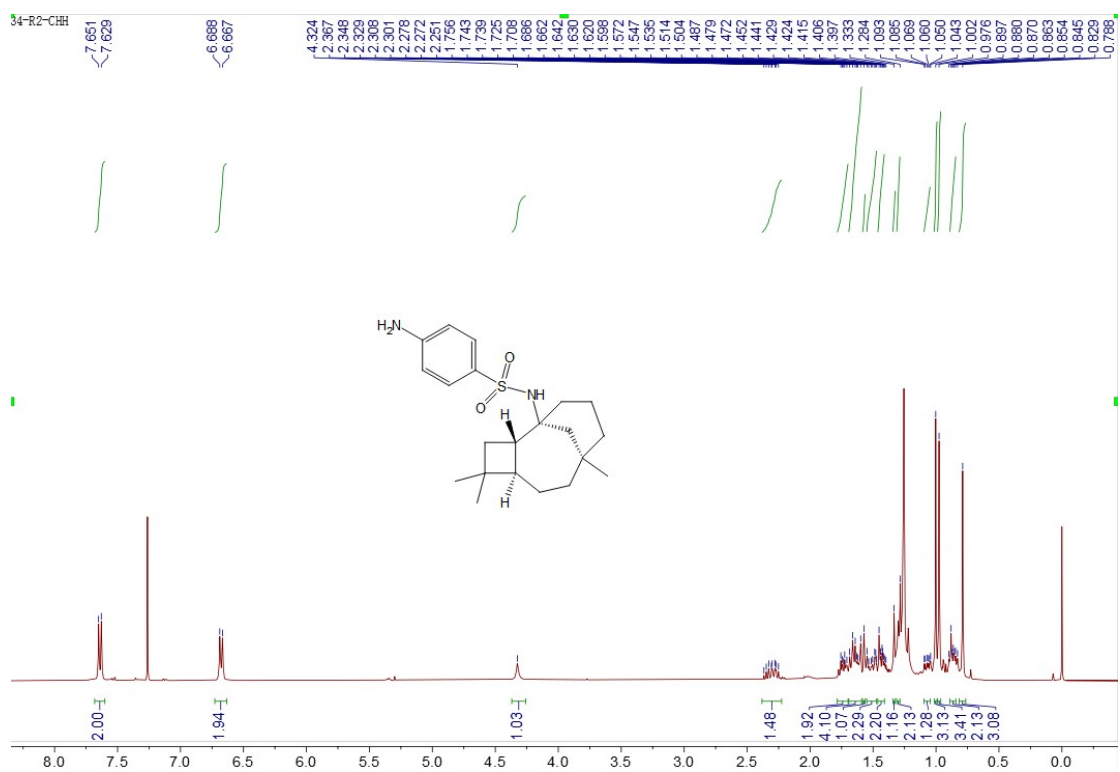
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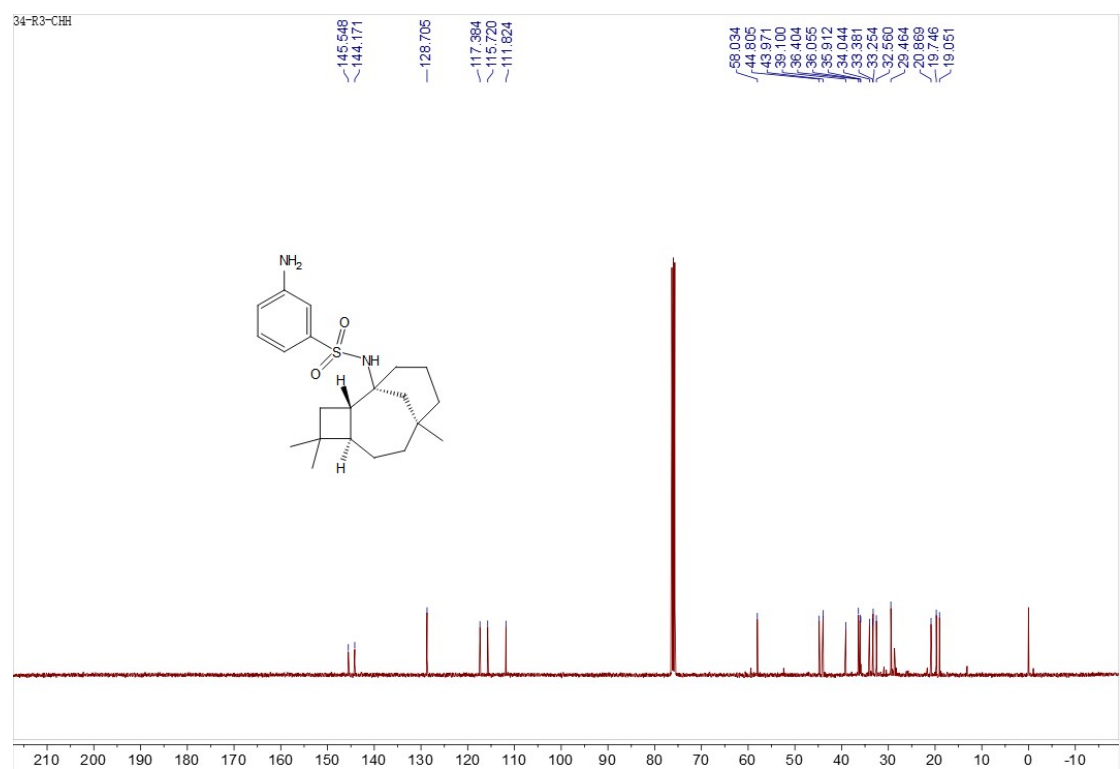
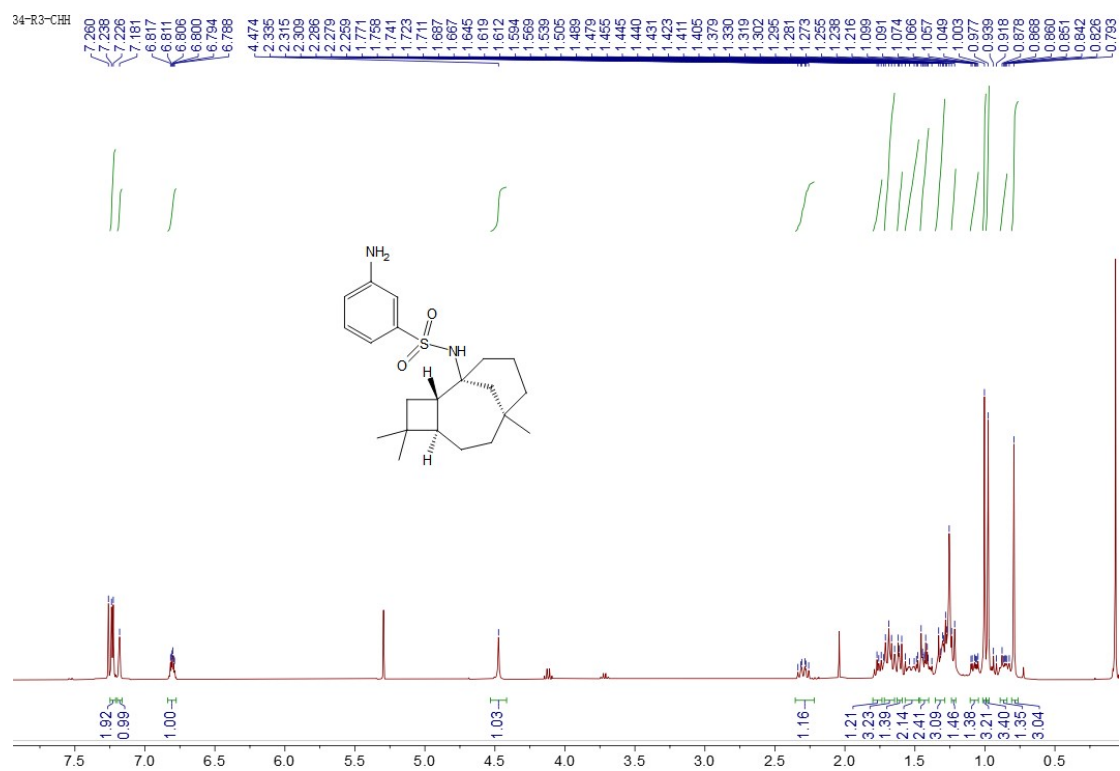
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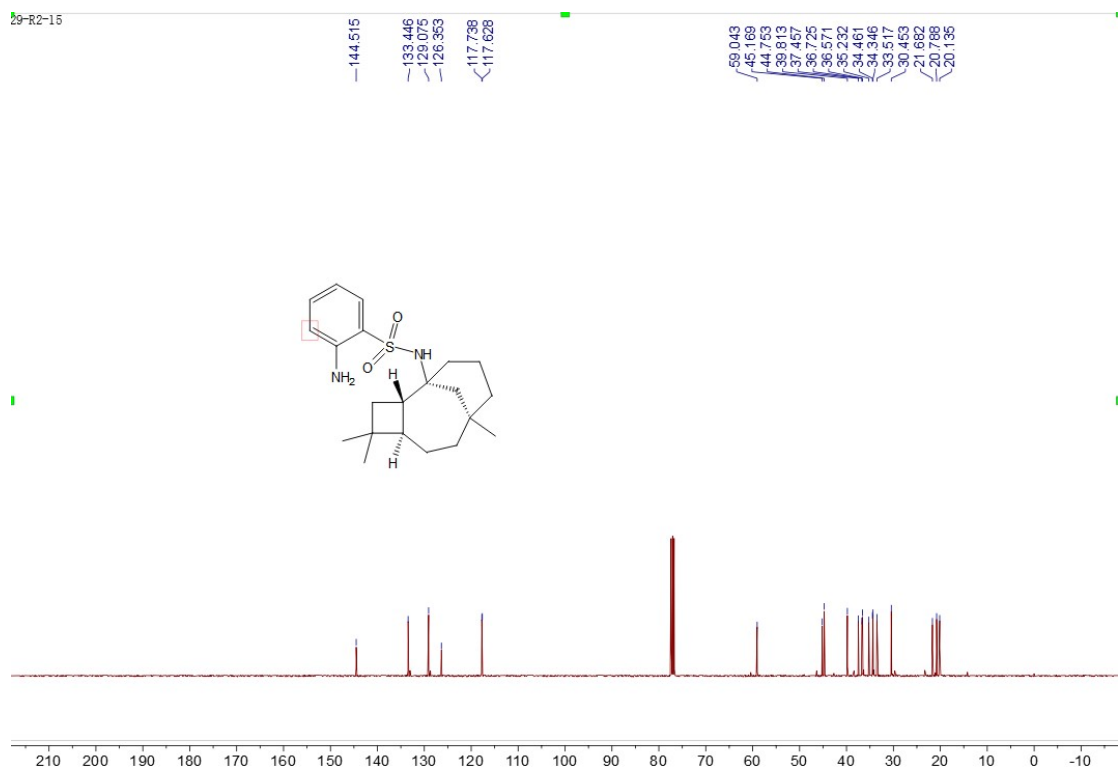
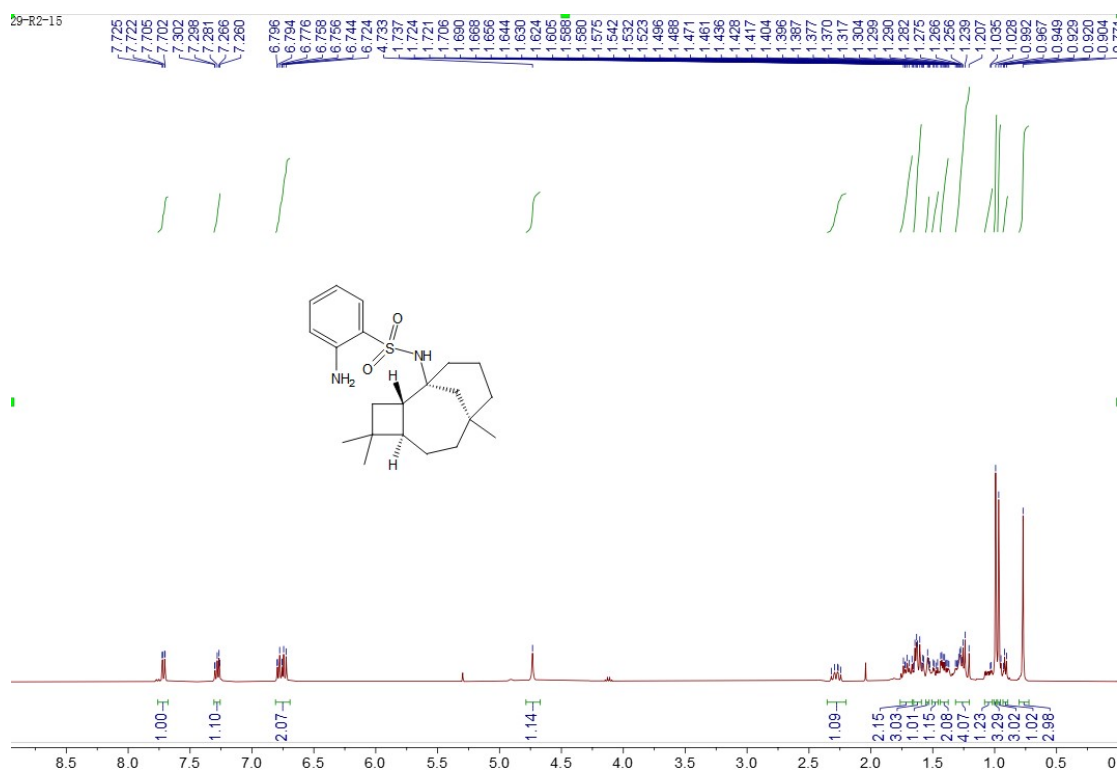
Compound SA-13



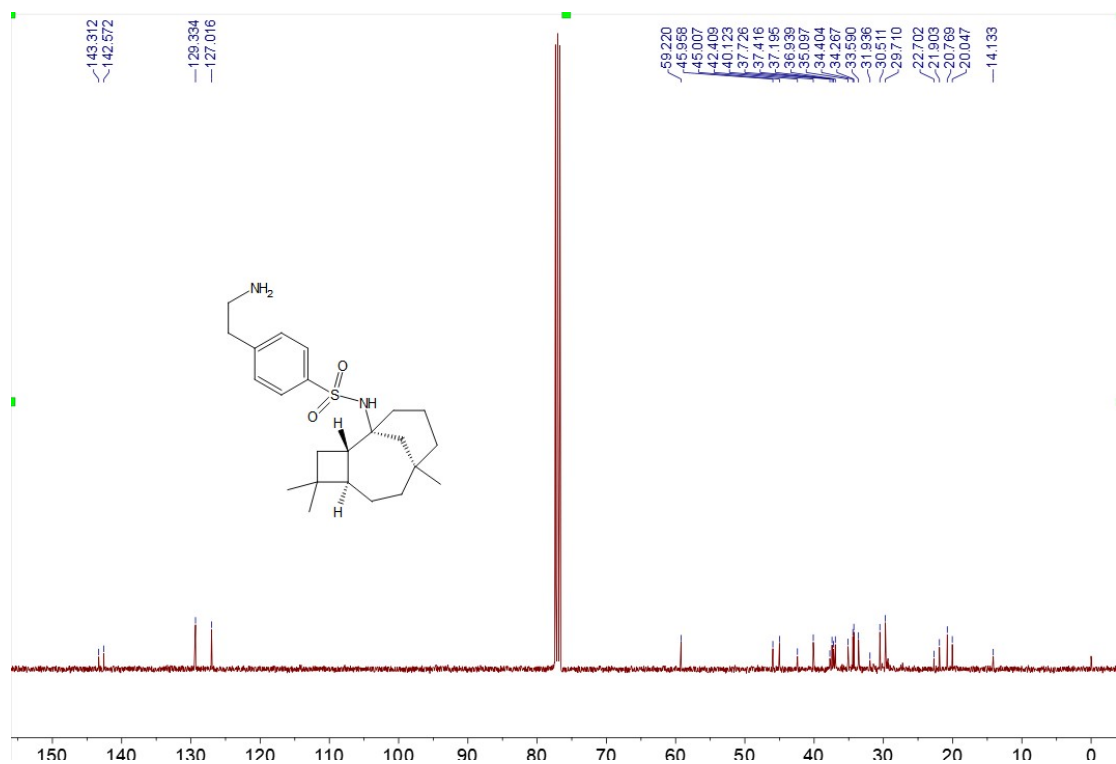
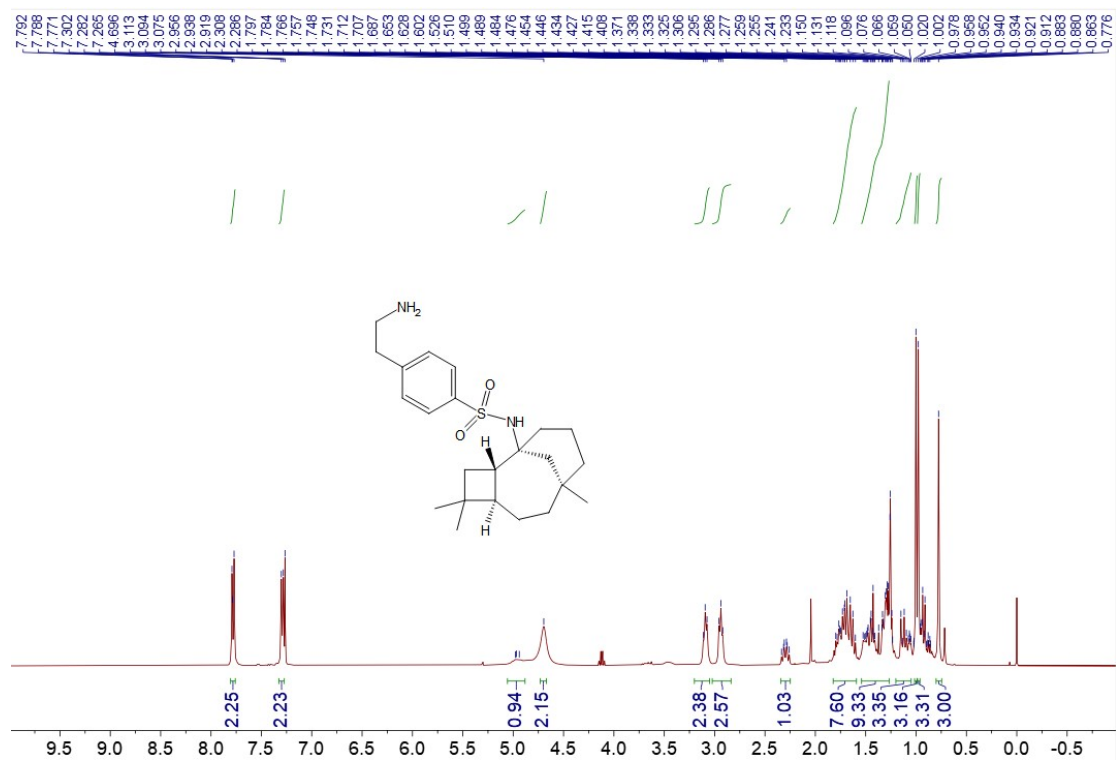
Compound SA-14



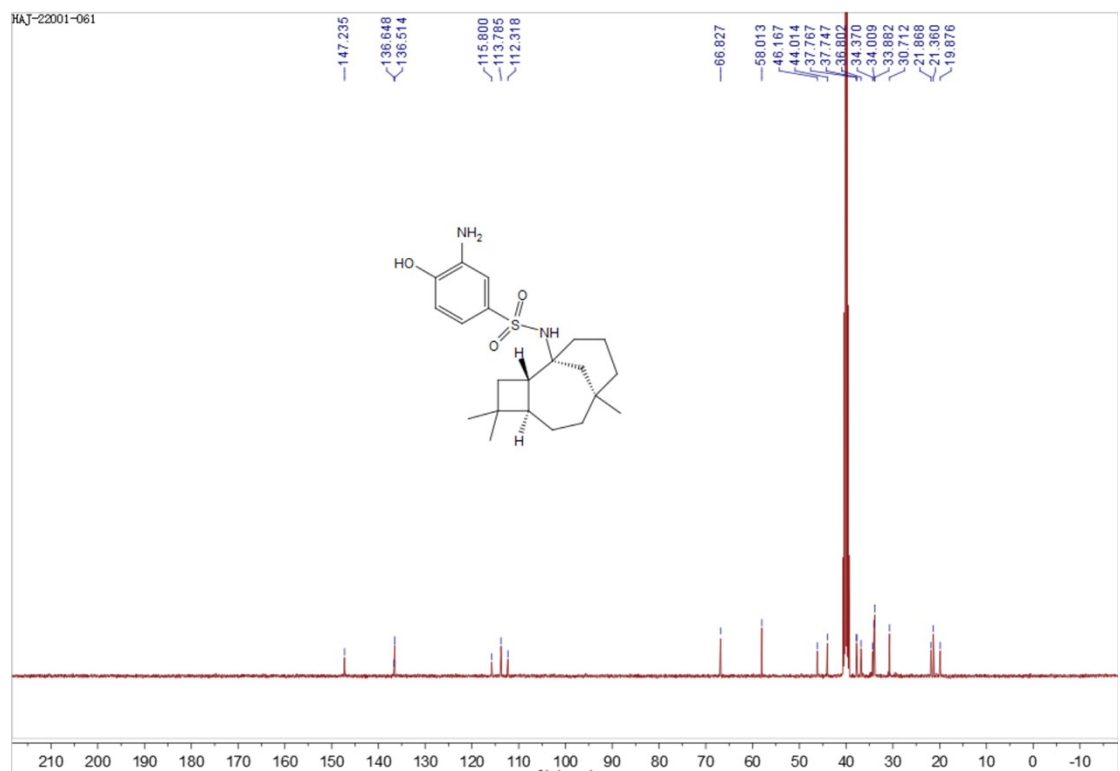
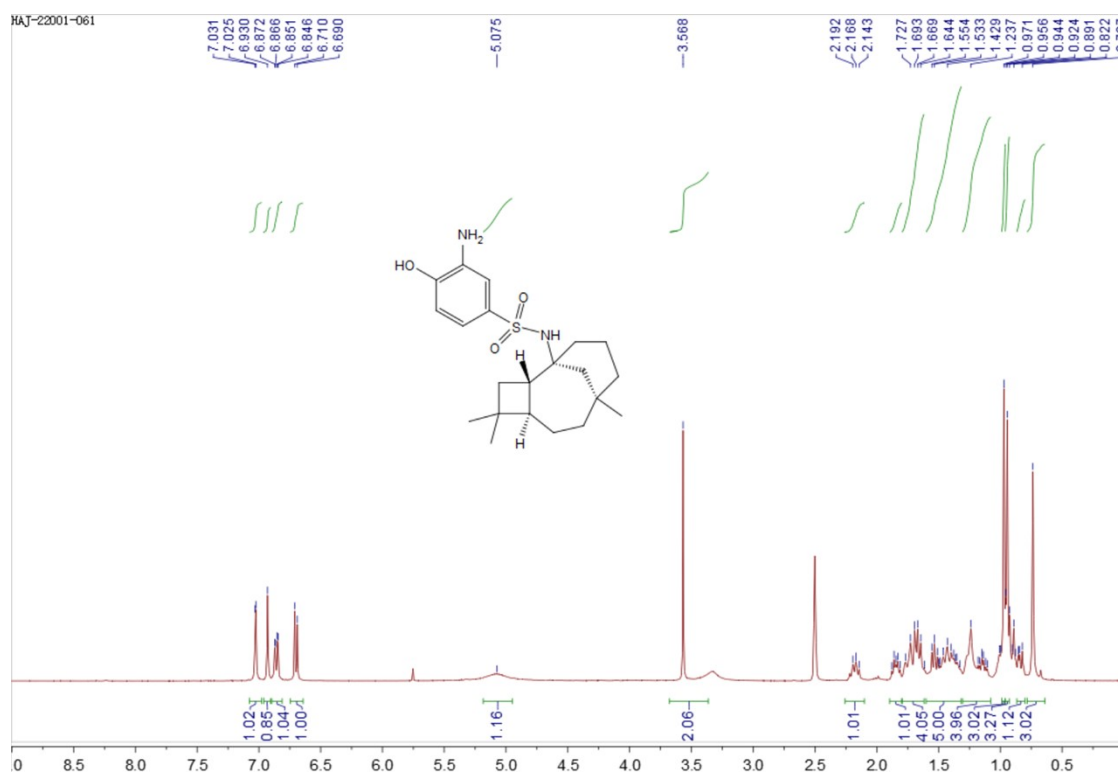
Compound SA-15



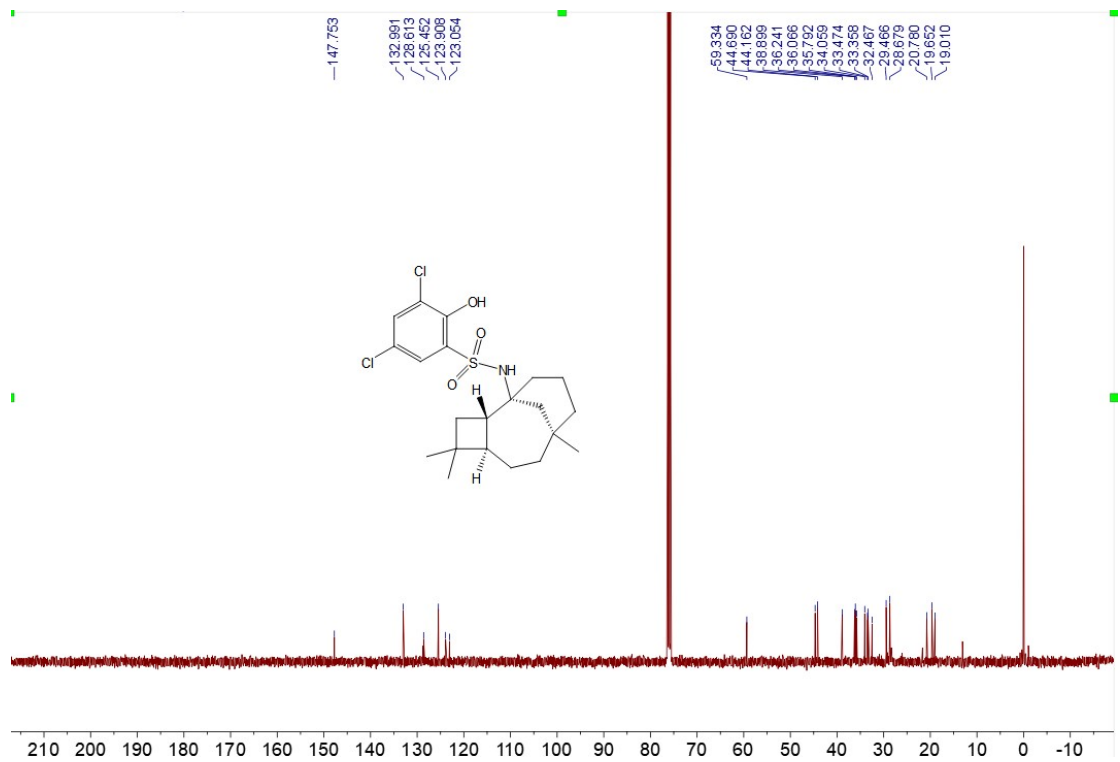
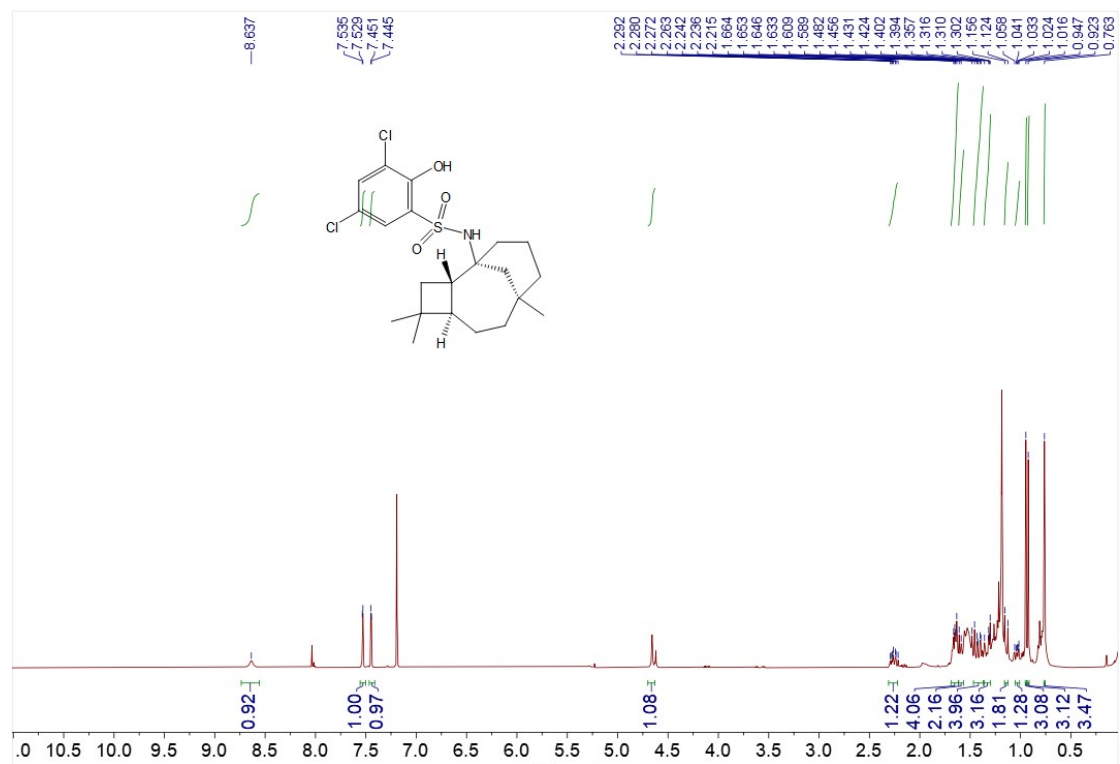
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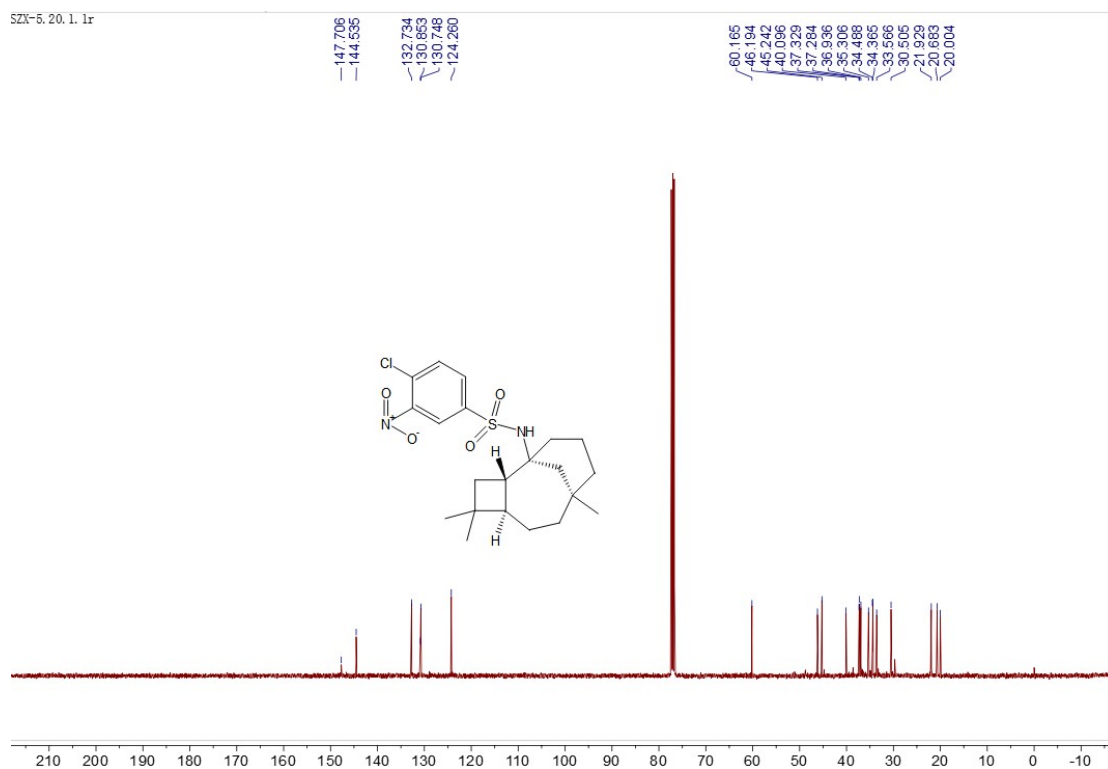
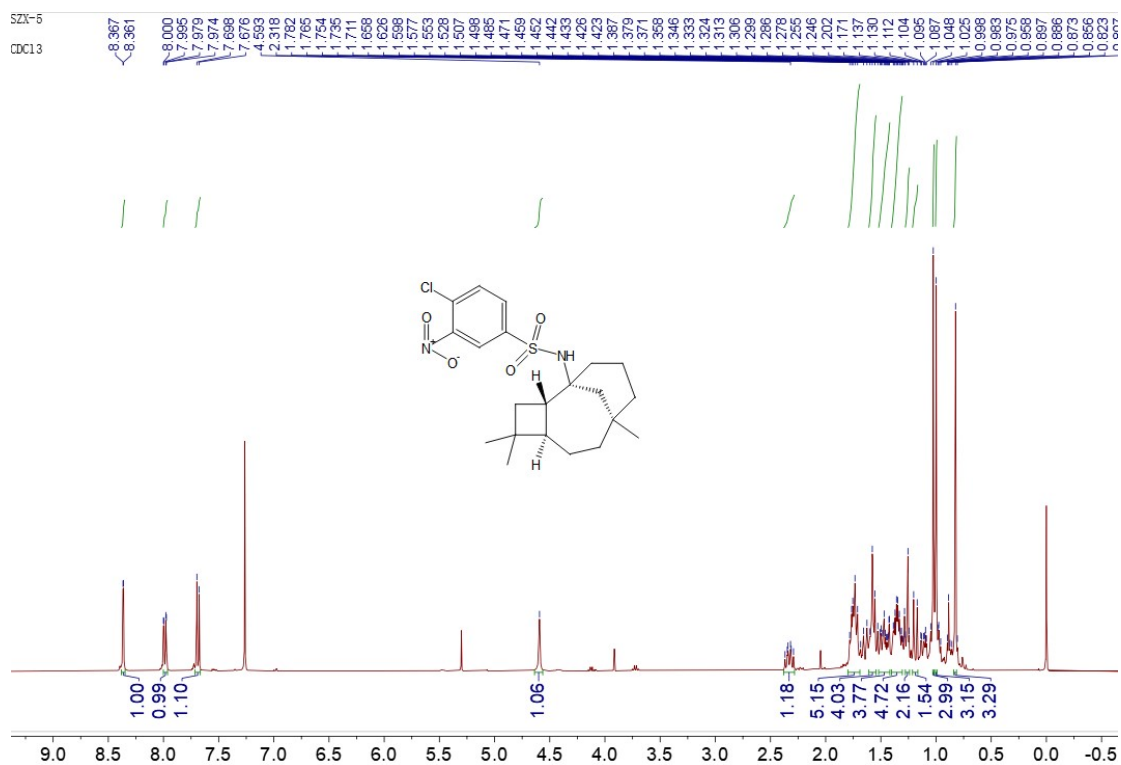
Compound SA-17



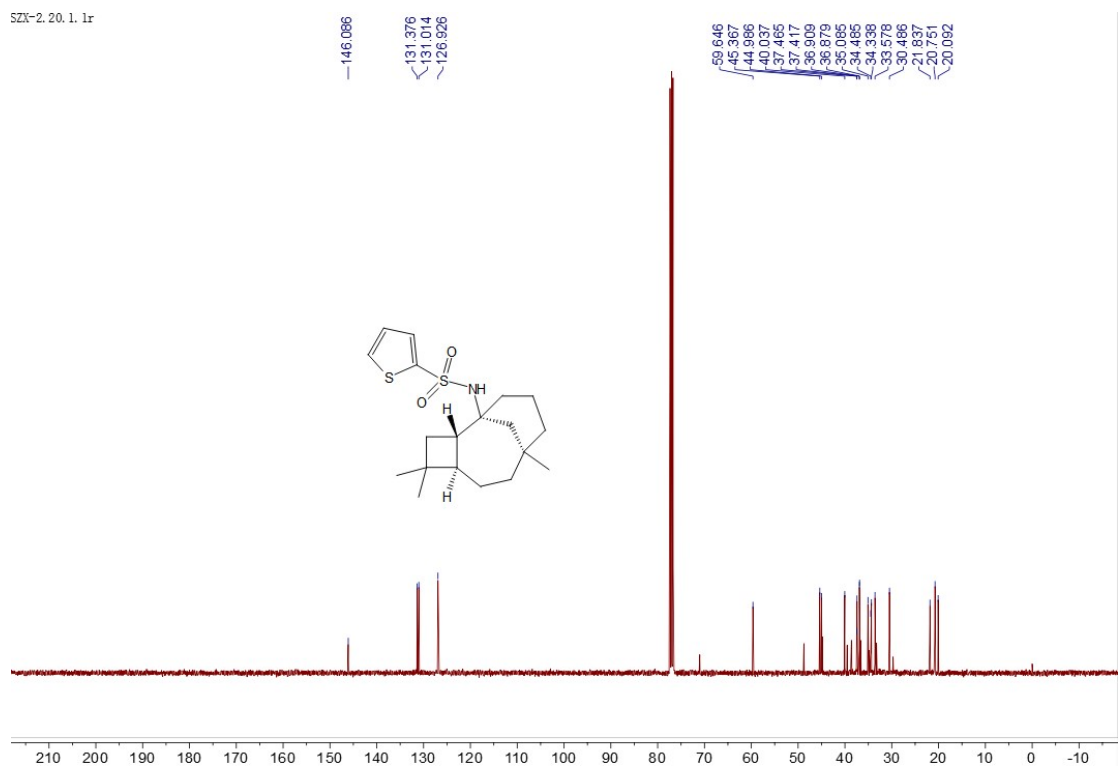
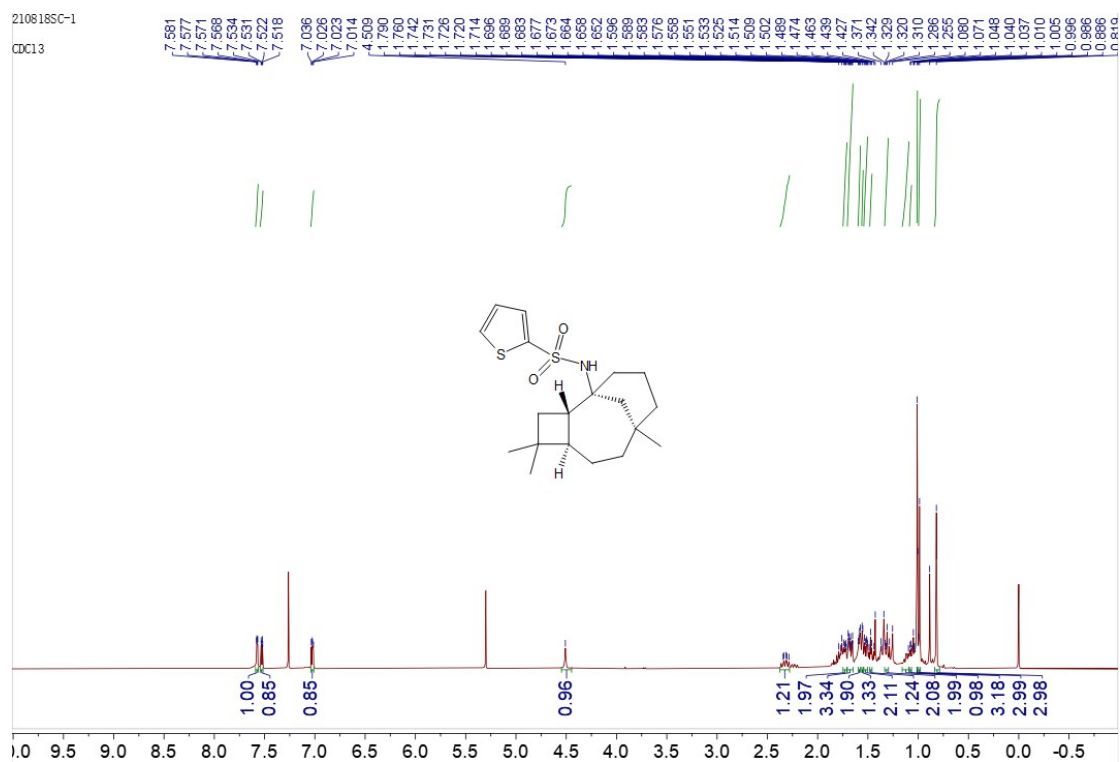
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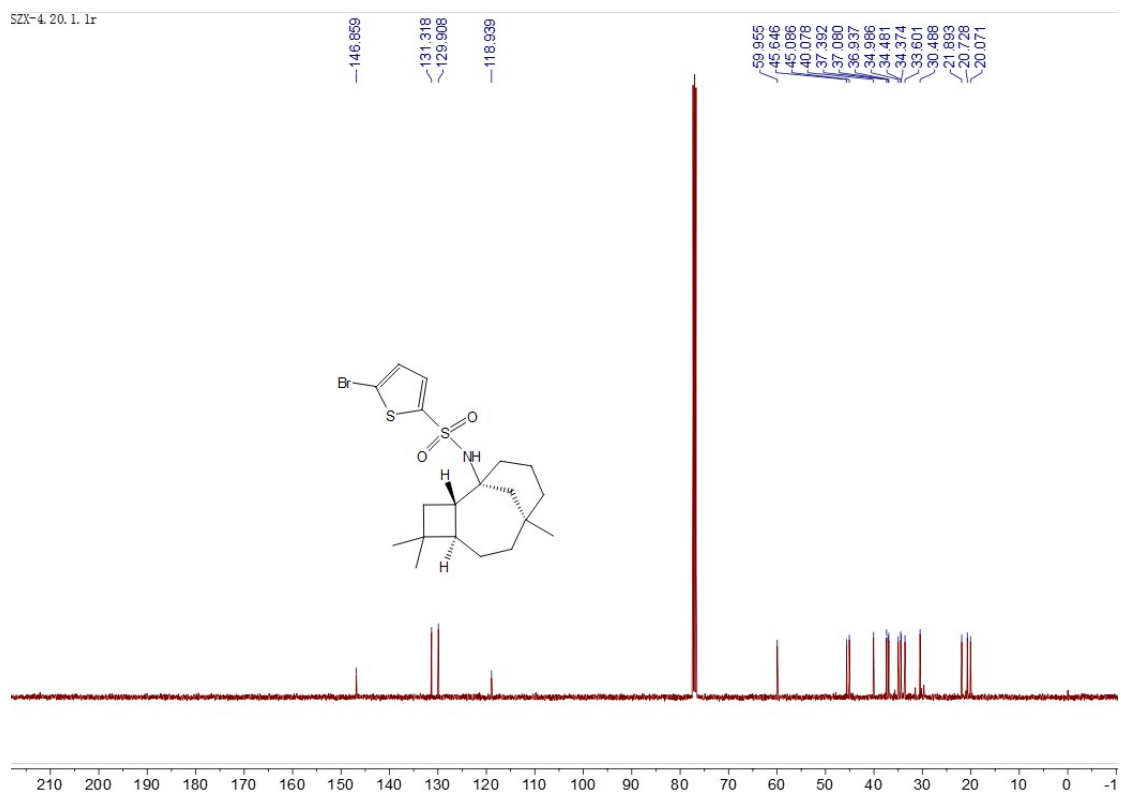
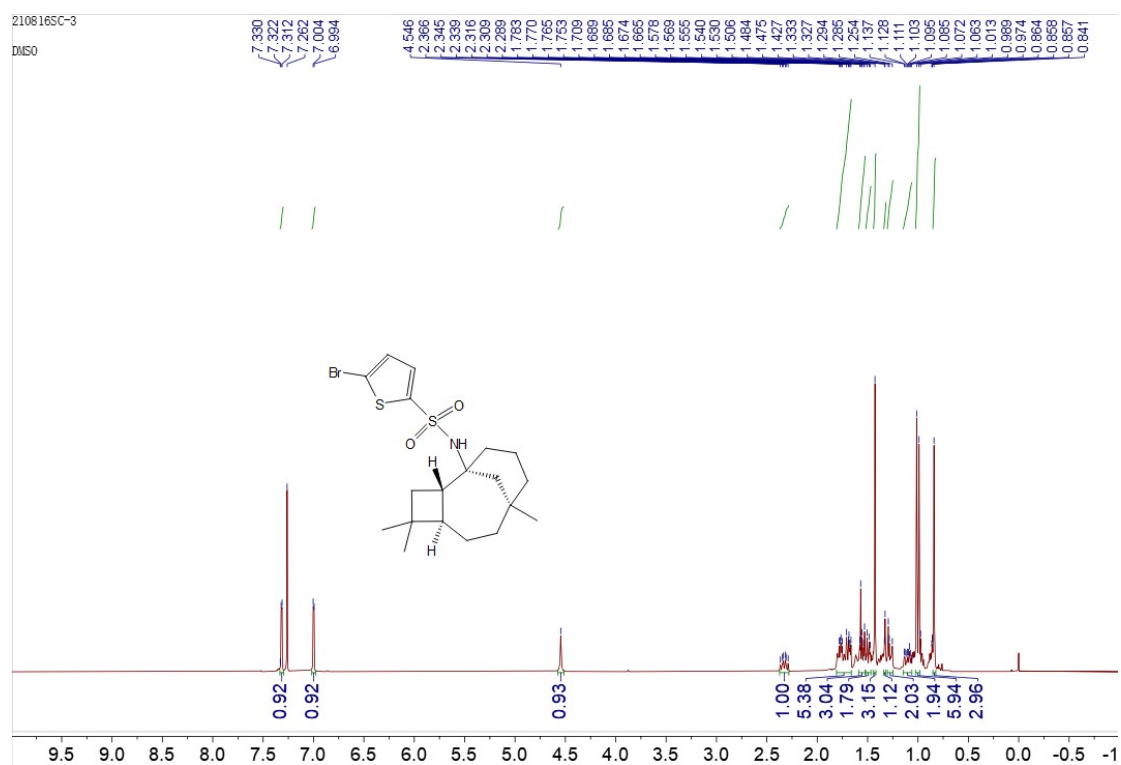
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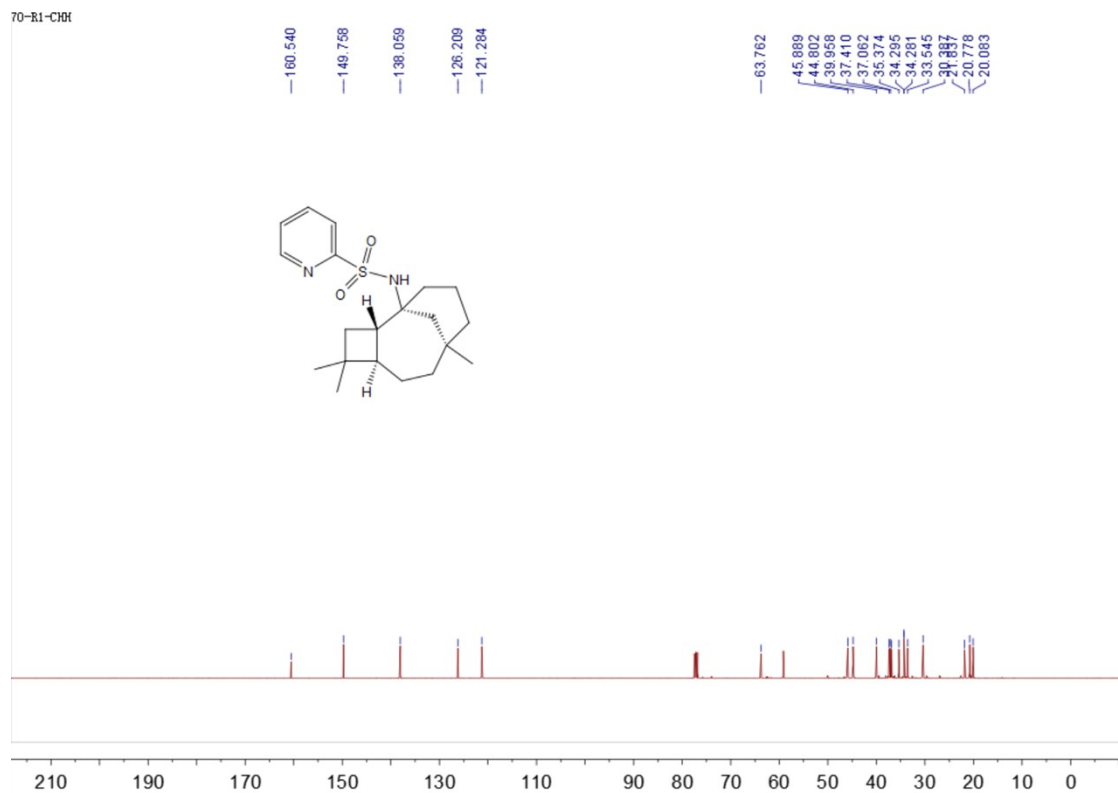
Compound SA-20



Compound SA-21



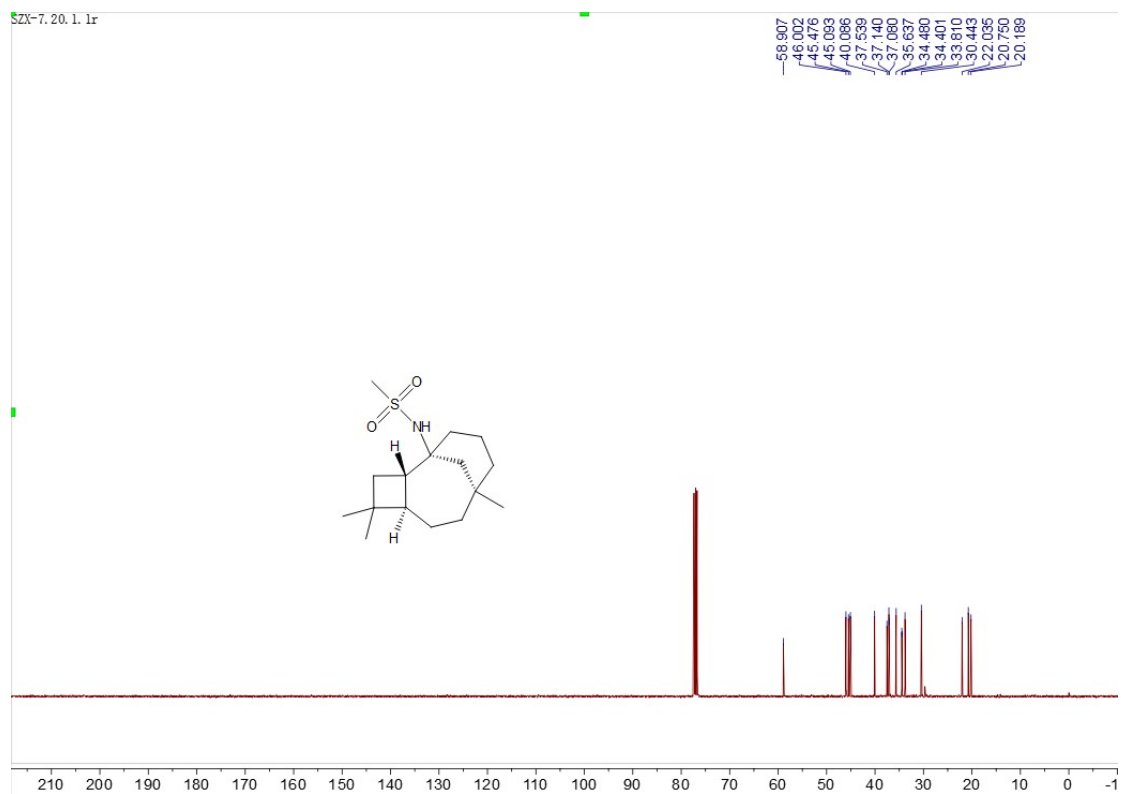
S61



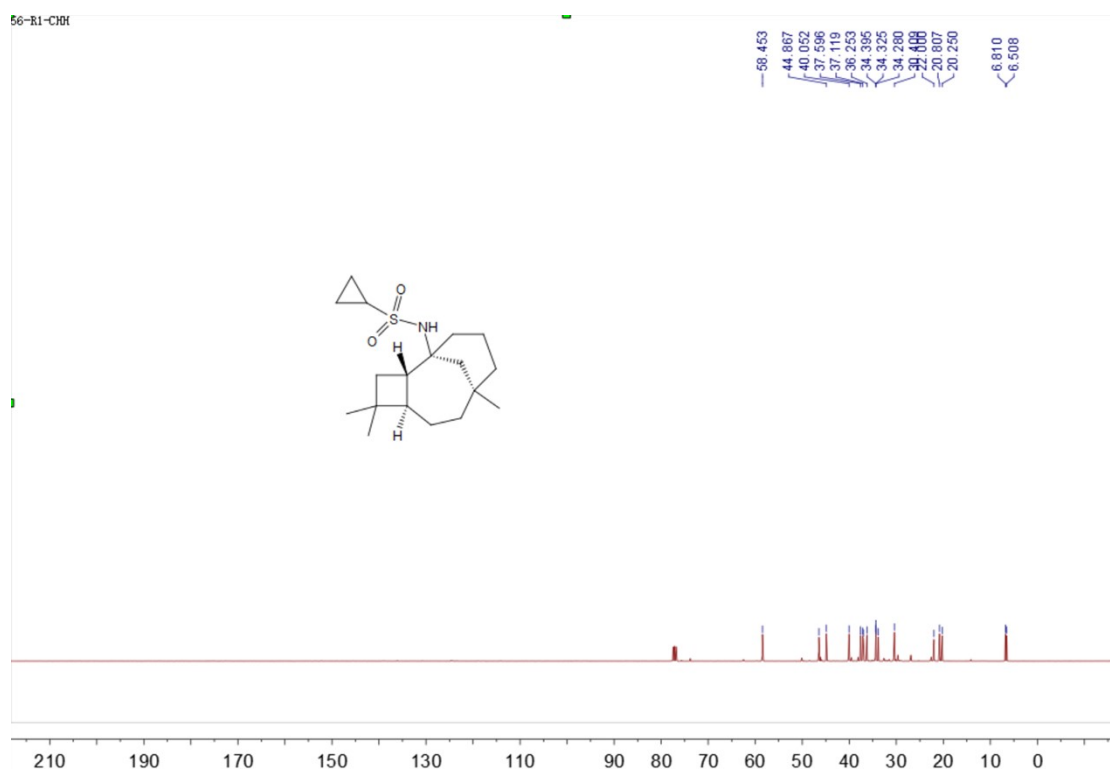
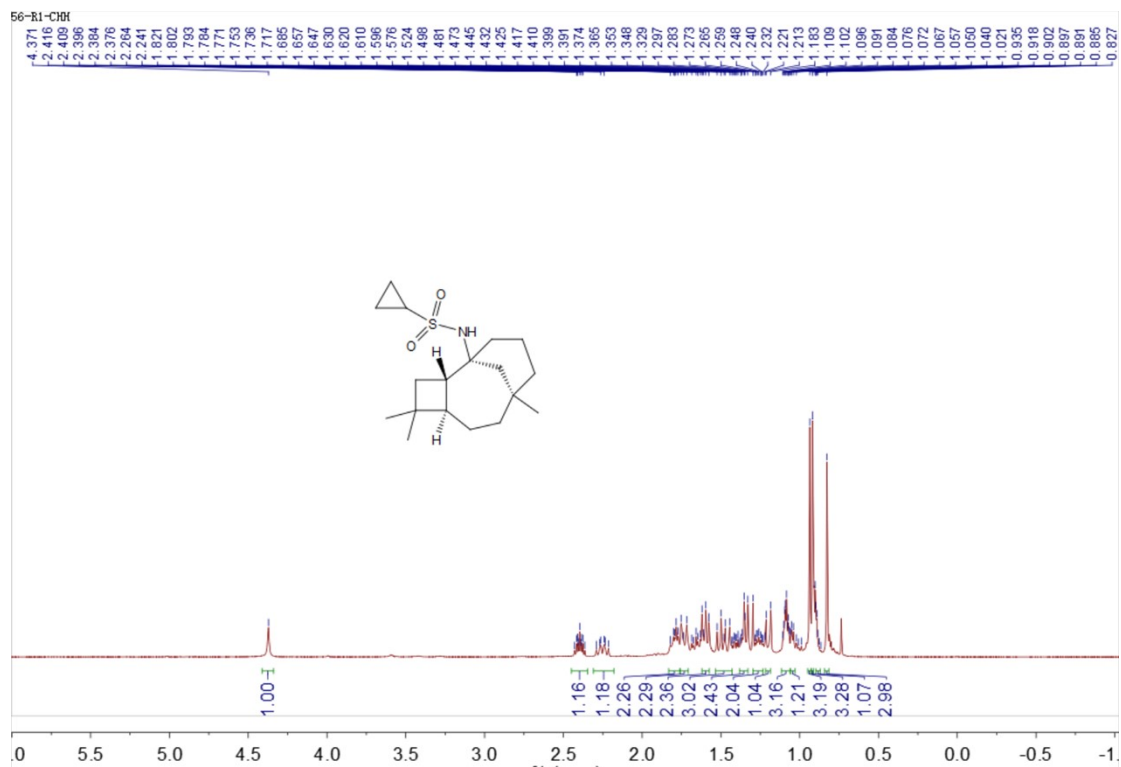
1H NMR spectrum of compound 10 in CDCl₃.

Chemical structure of compound 10: CC1(C)C2(C)CC(C1)C(S(=O)(=O)N)C2

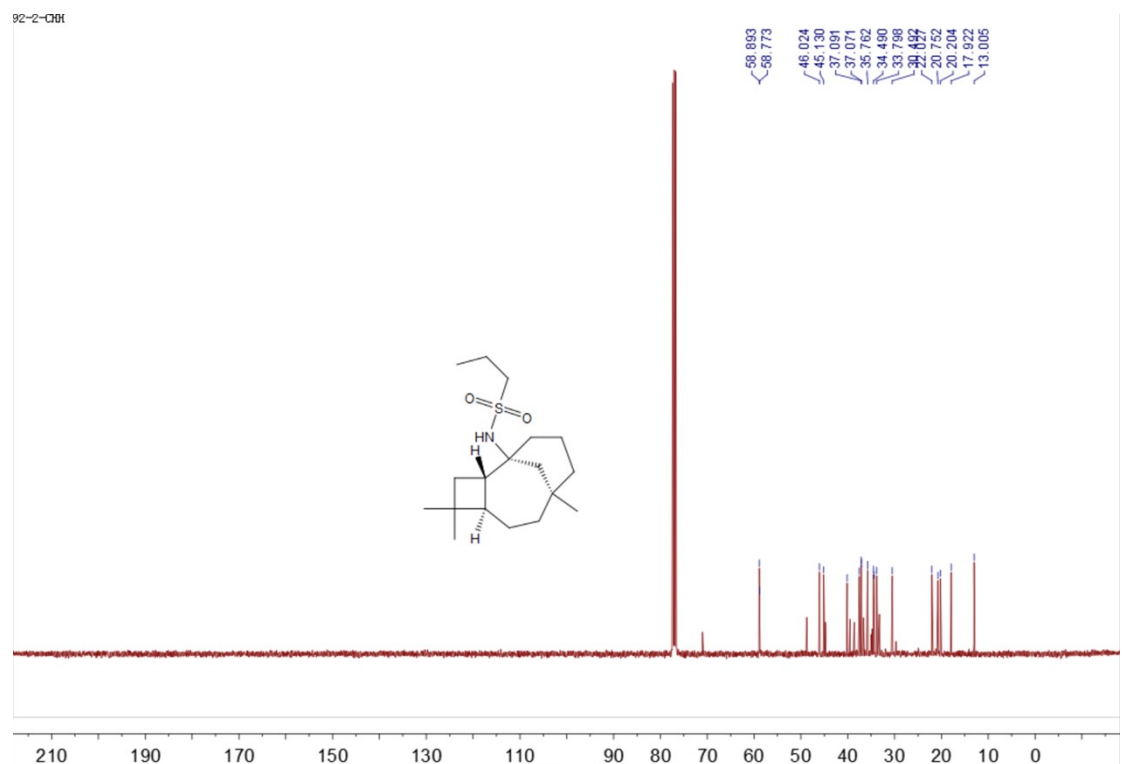
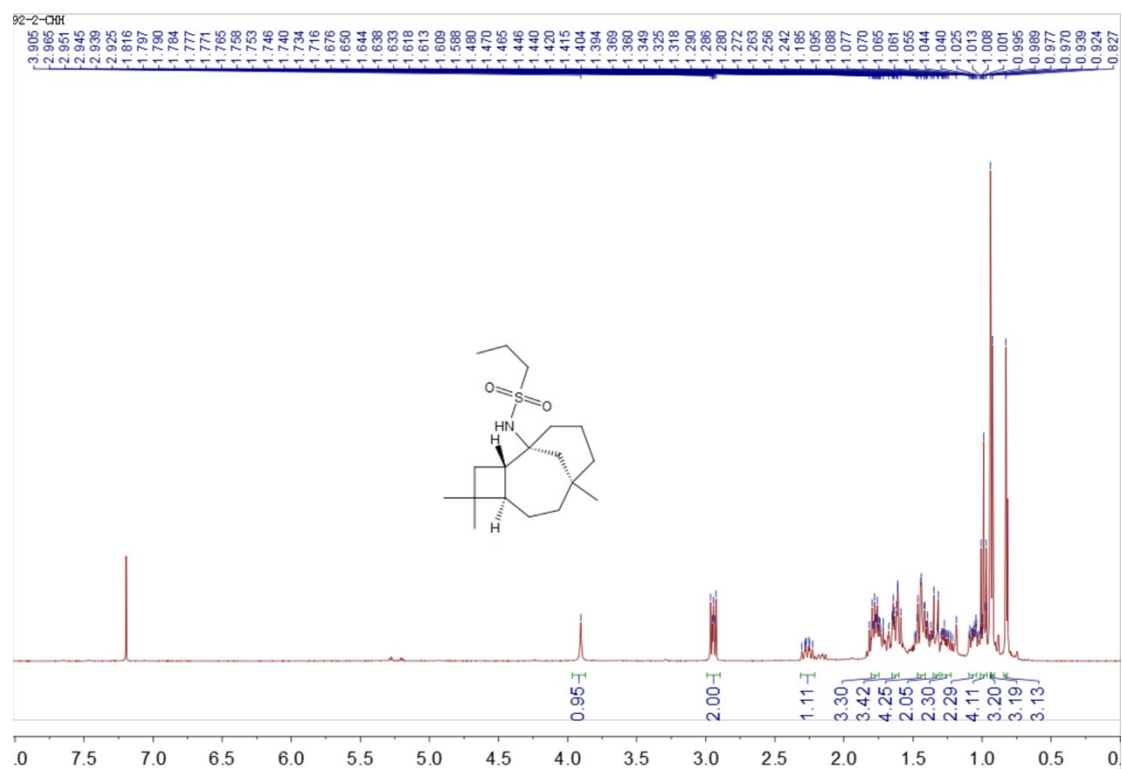
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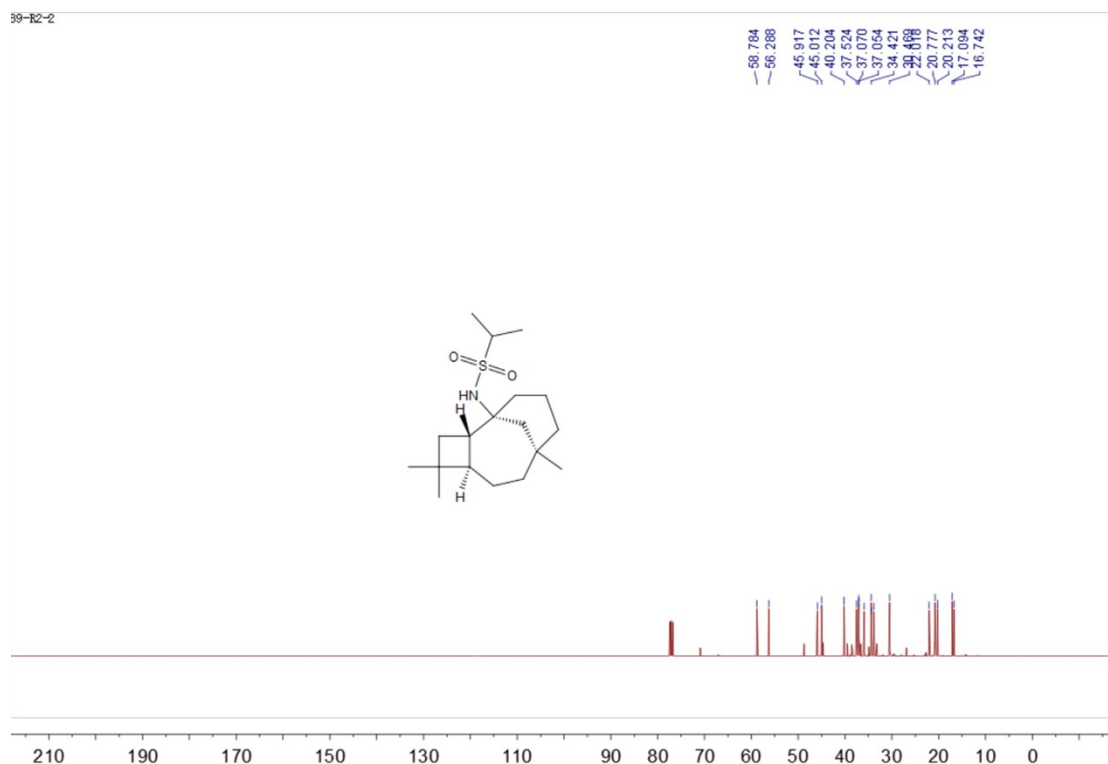
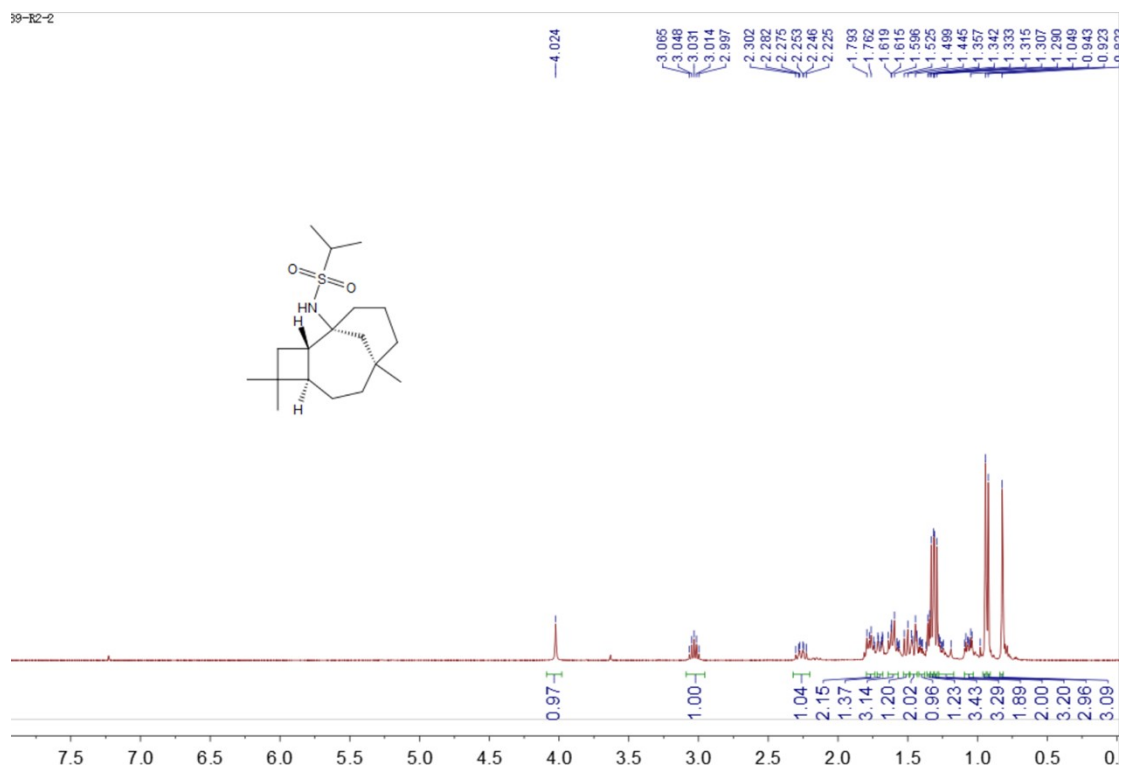
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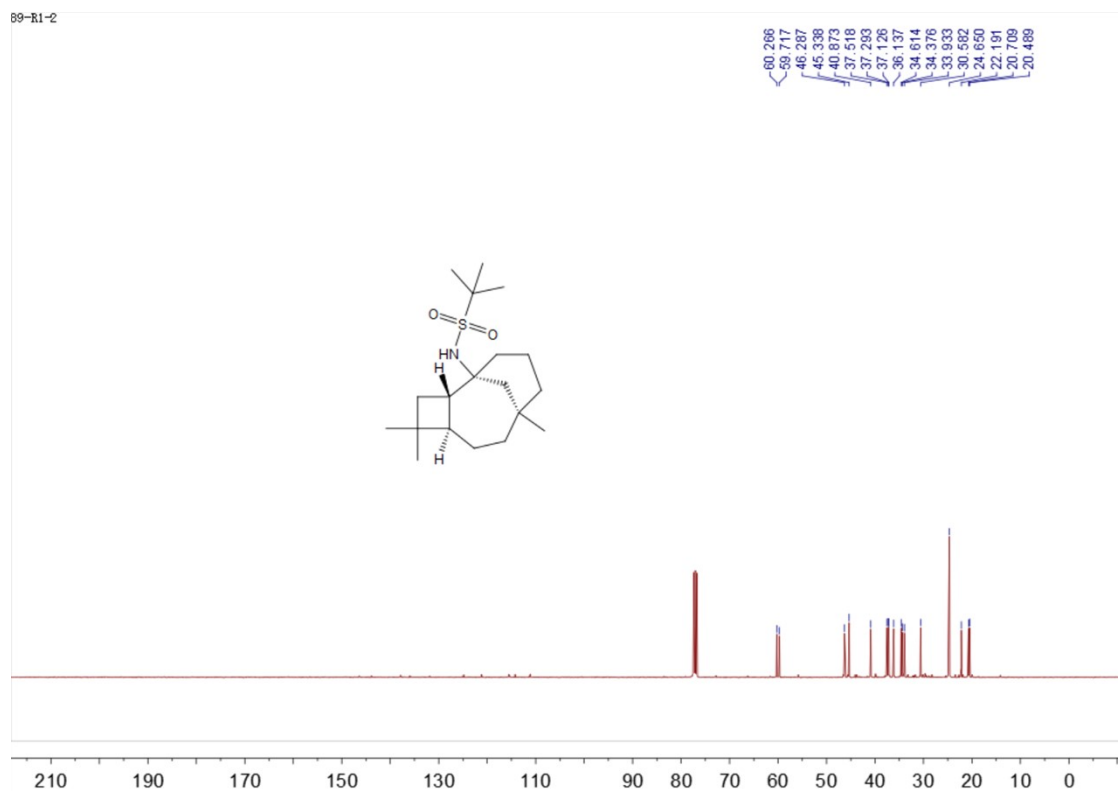
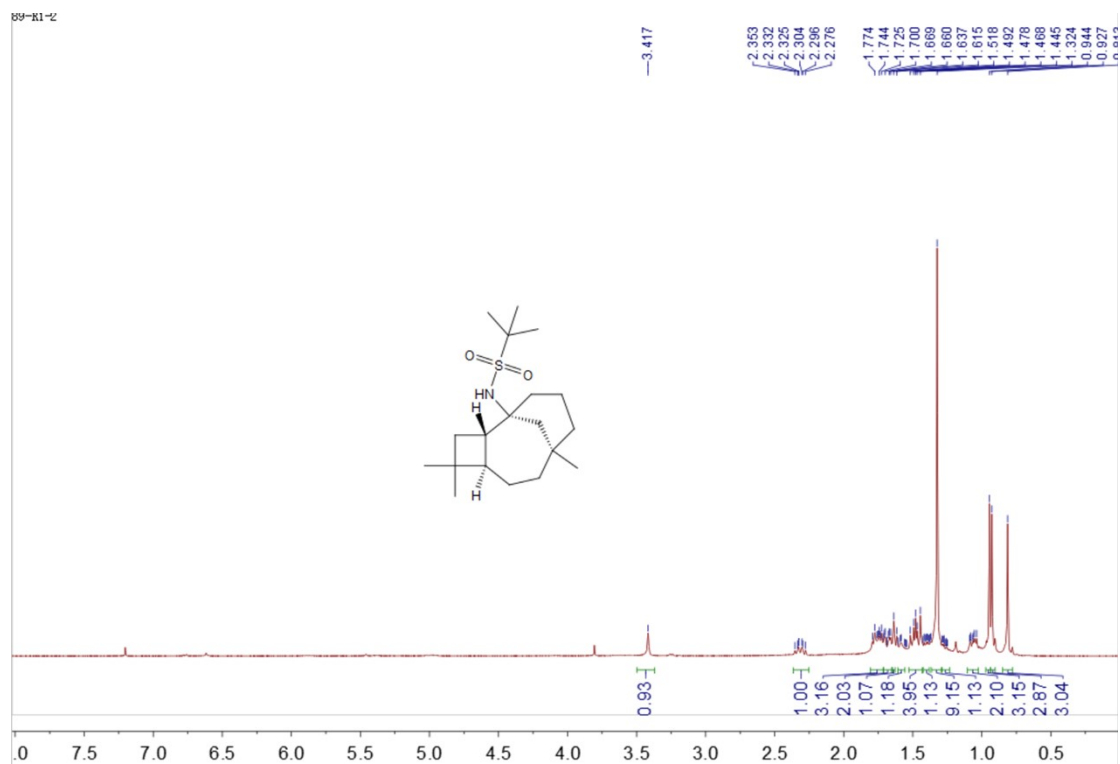
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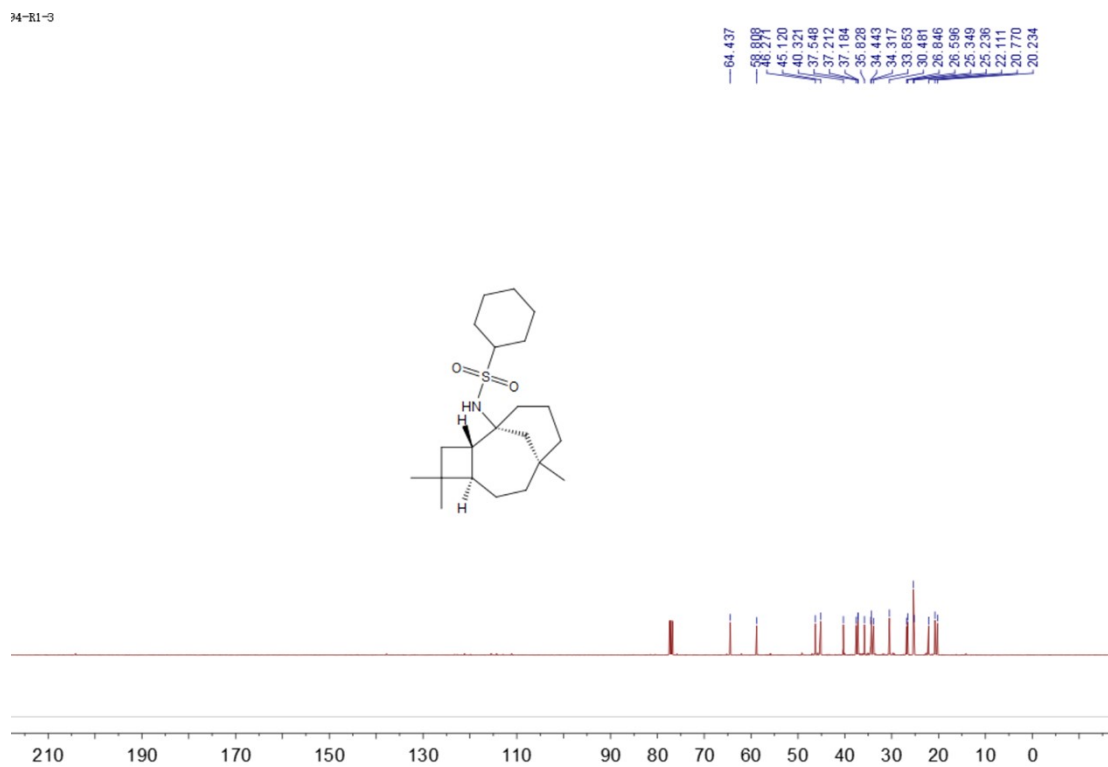
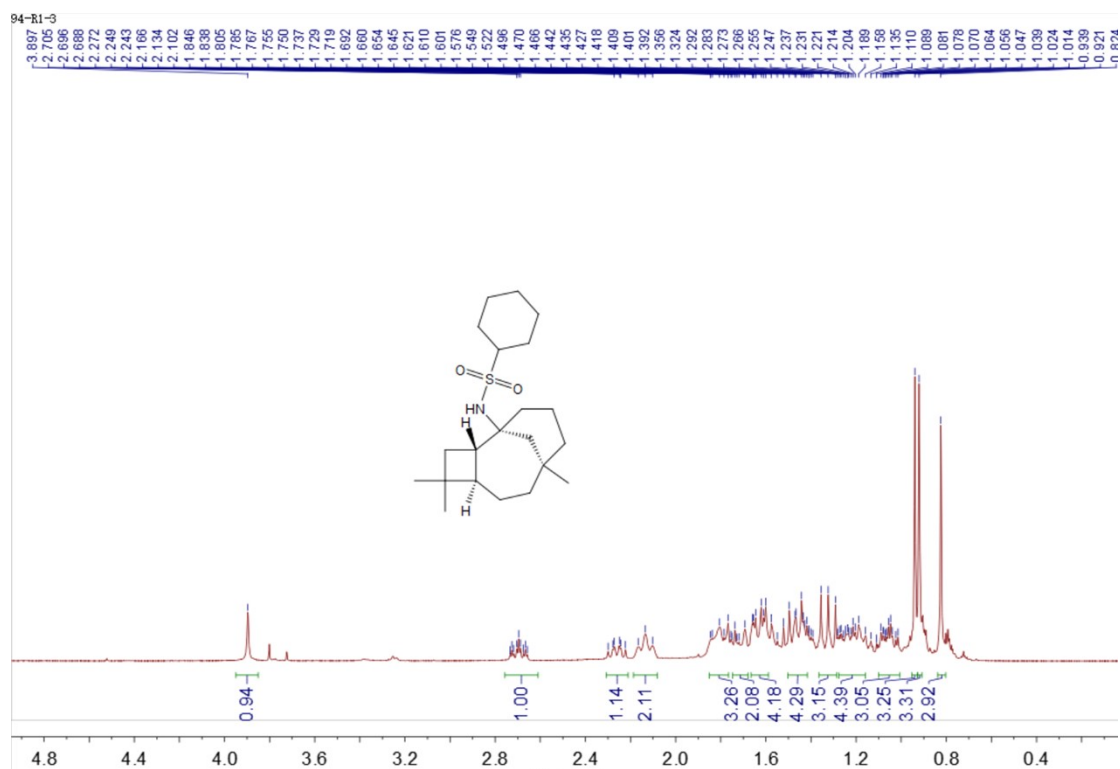
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Compound SA-27

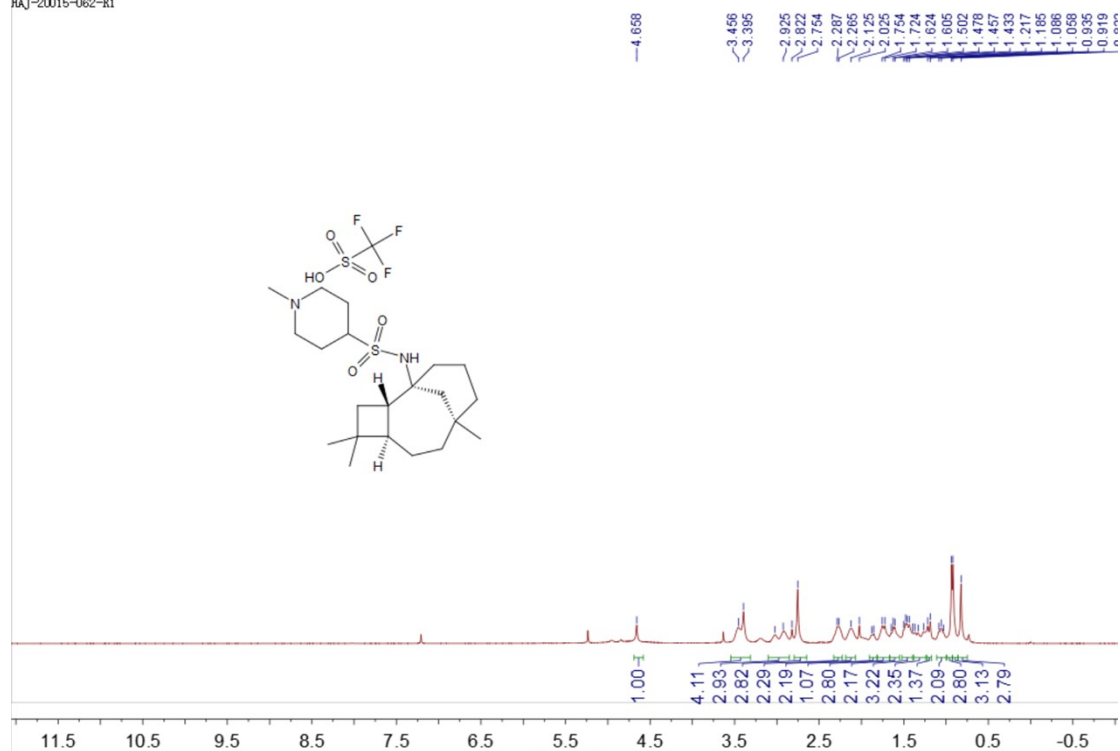


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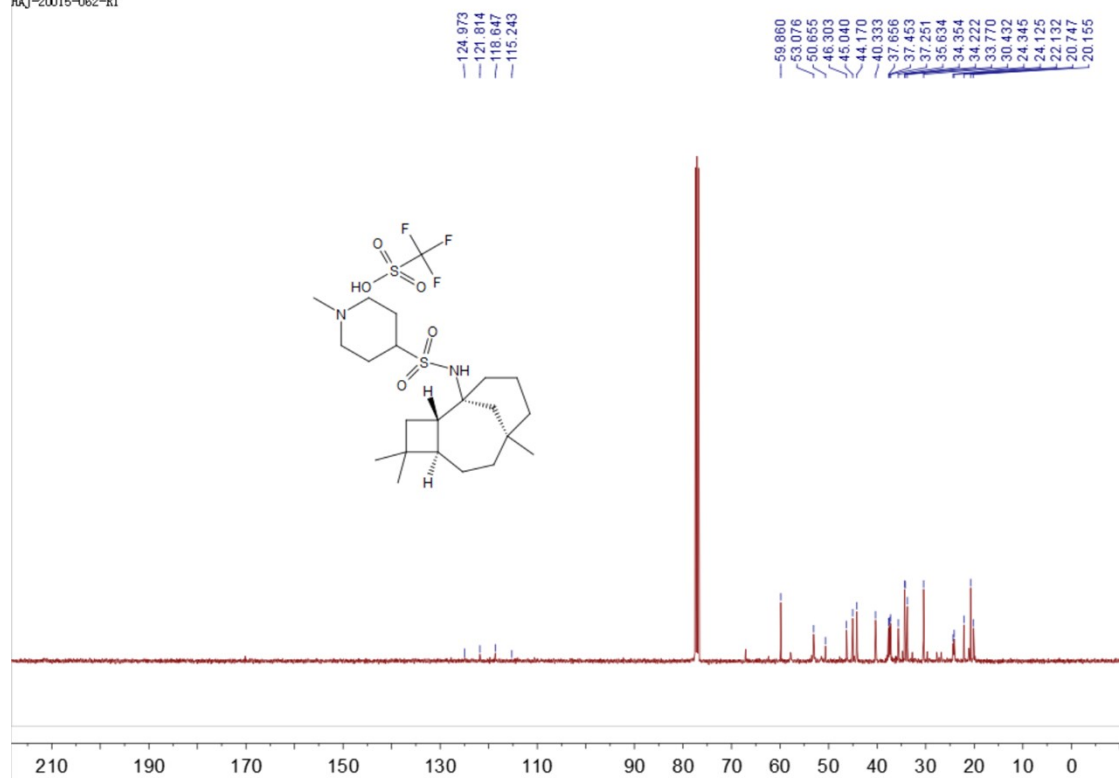


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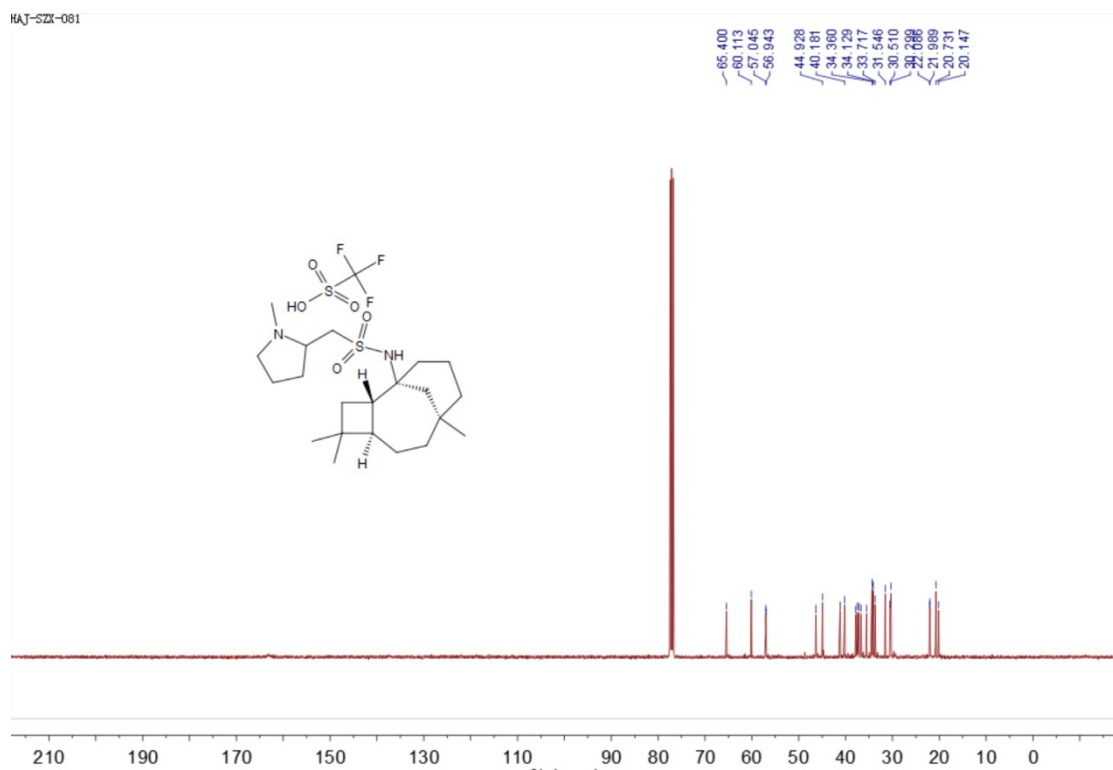
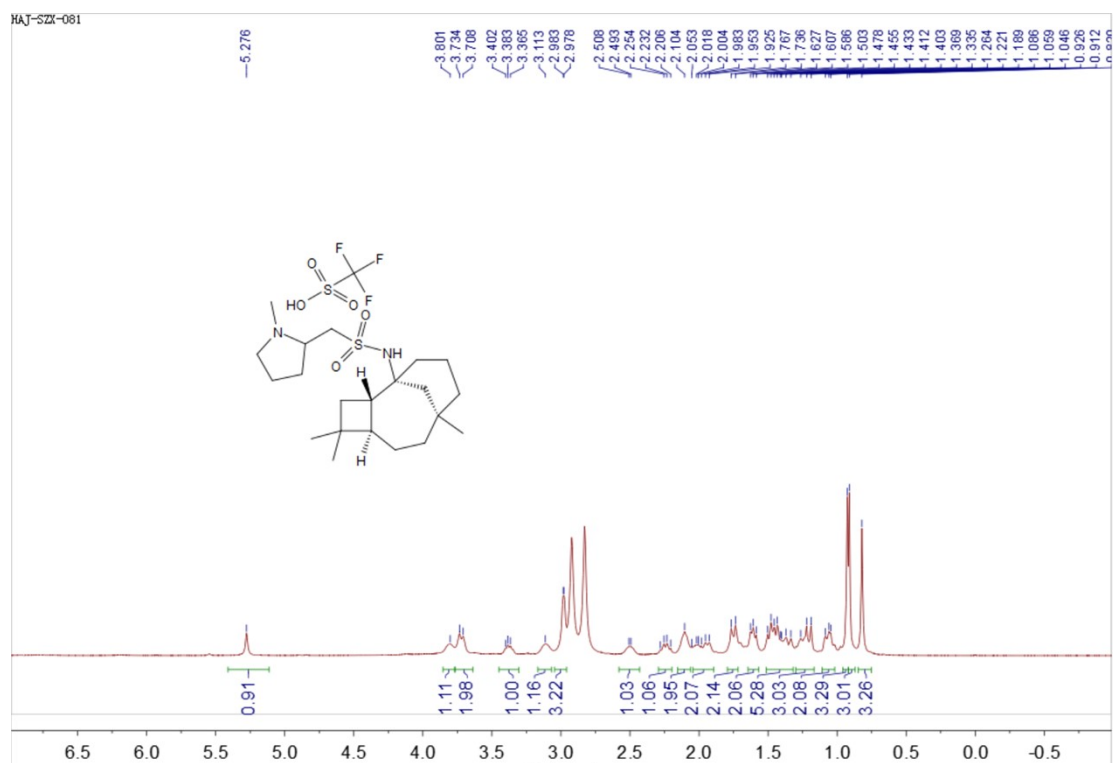
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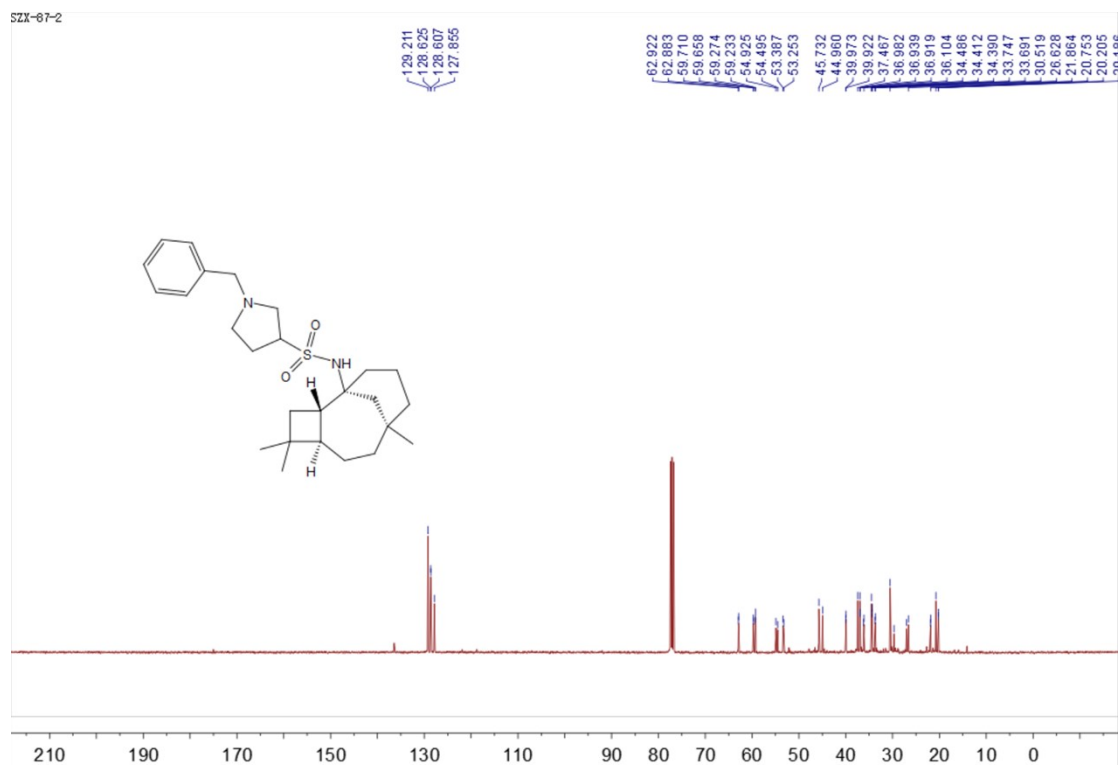
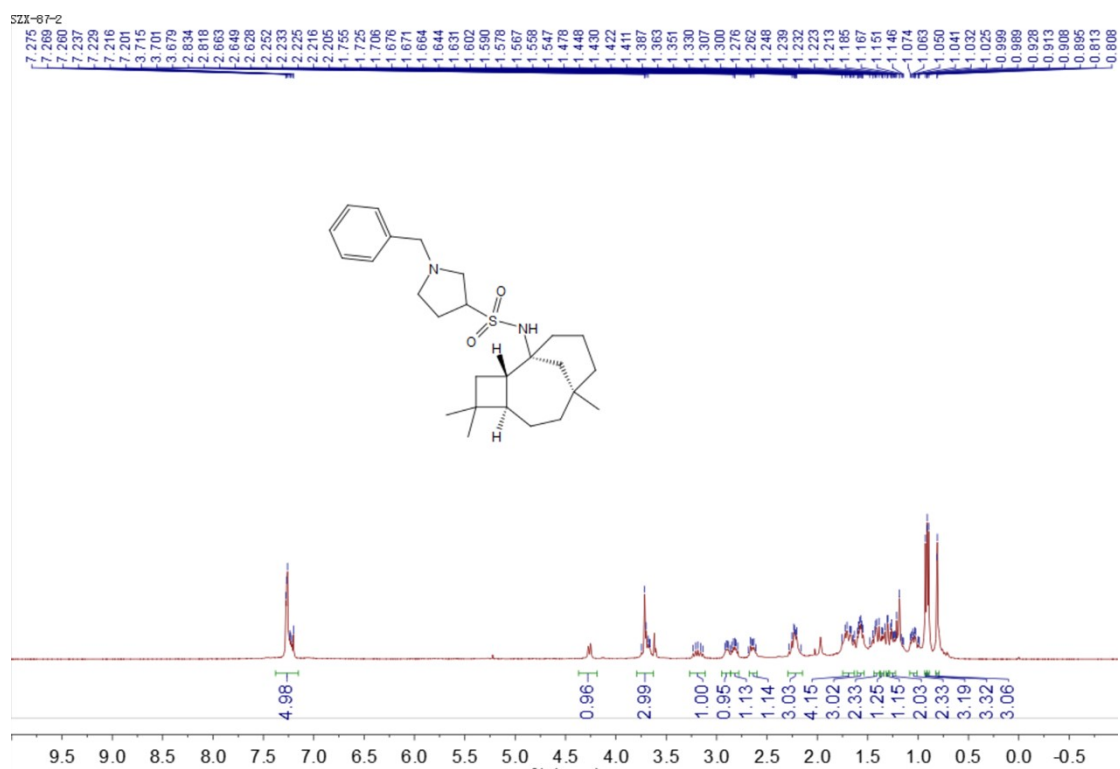
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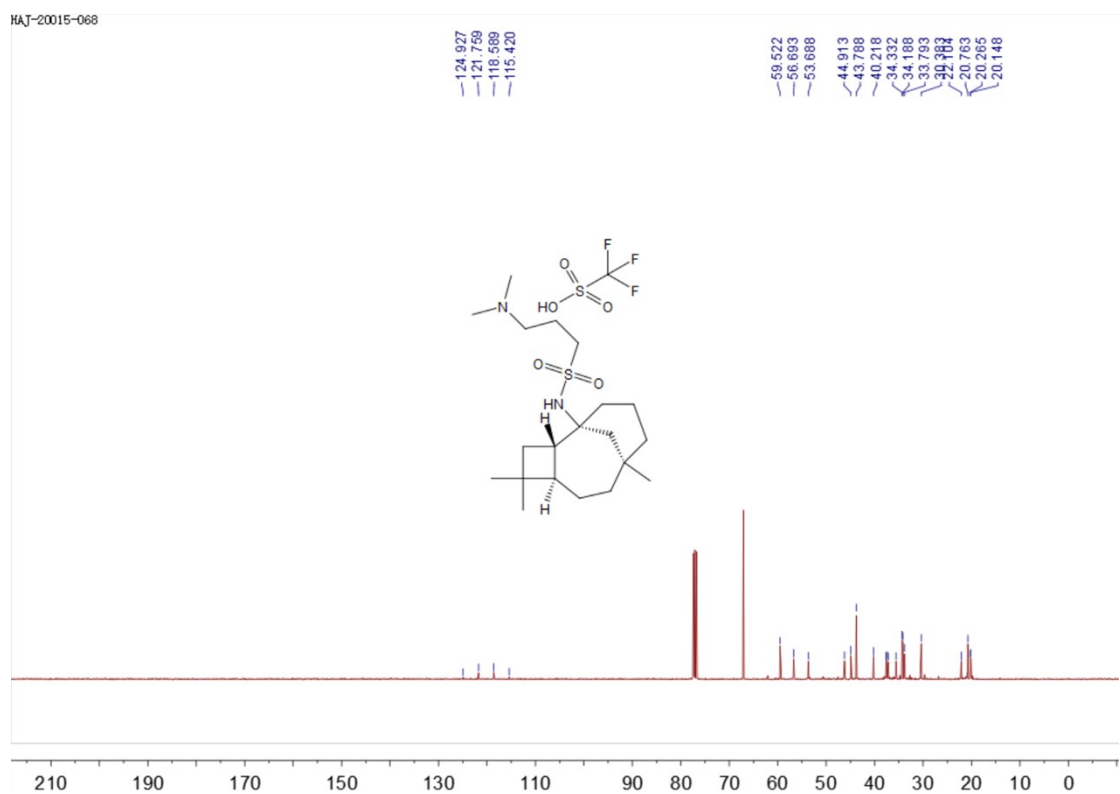
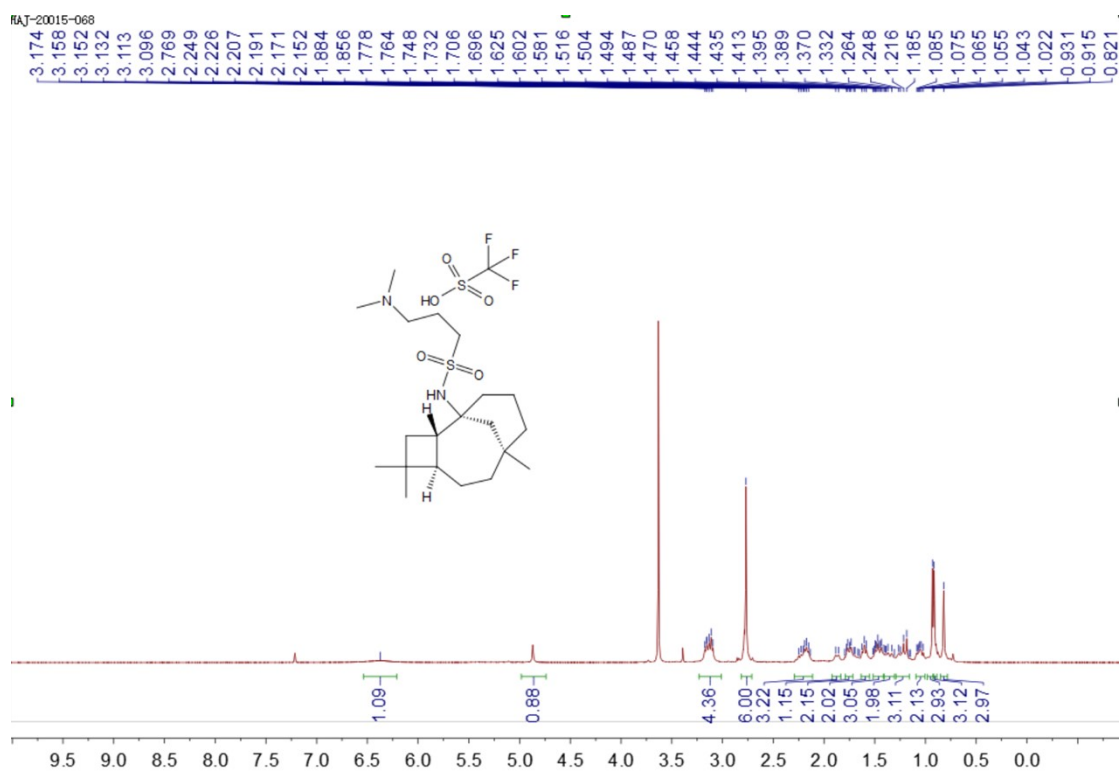
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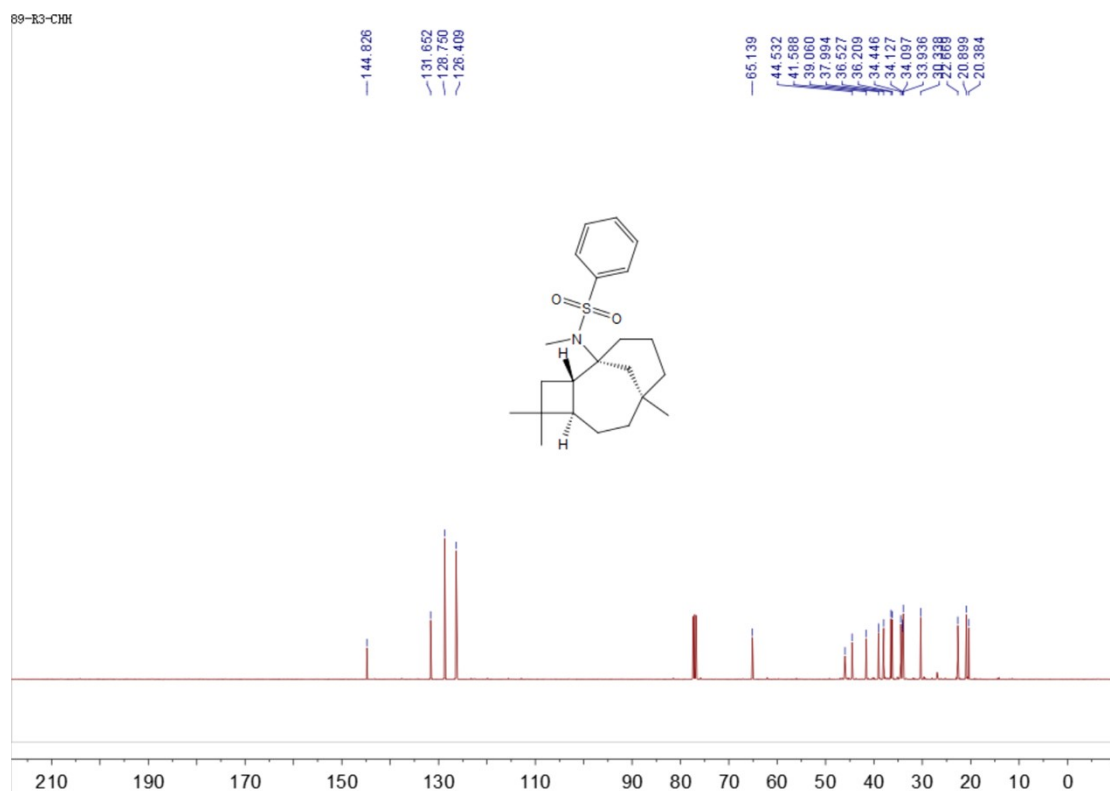
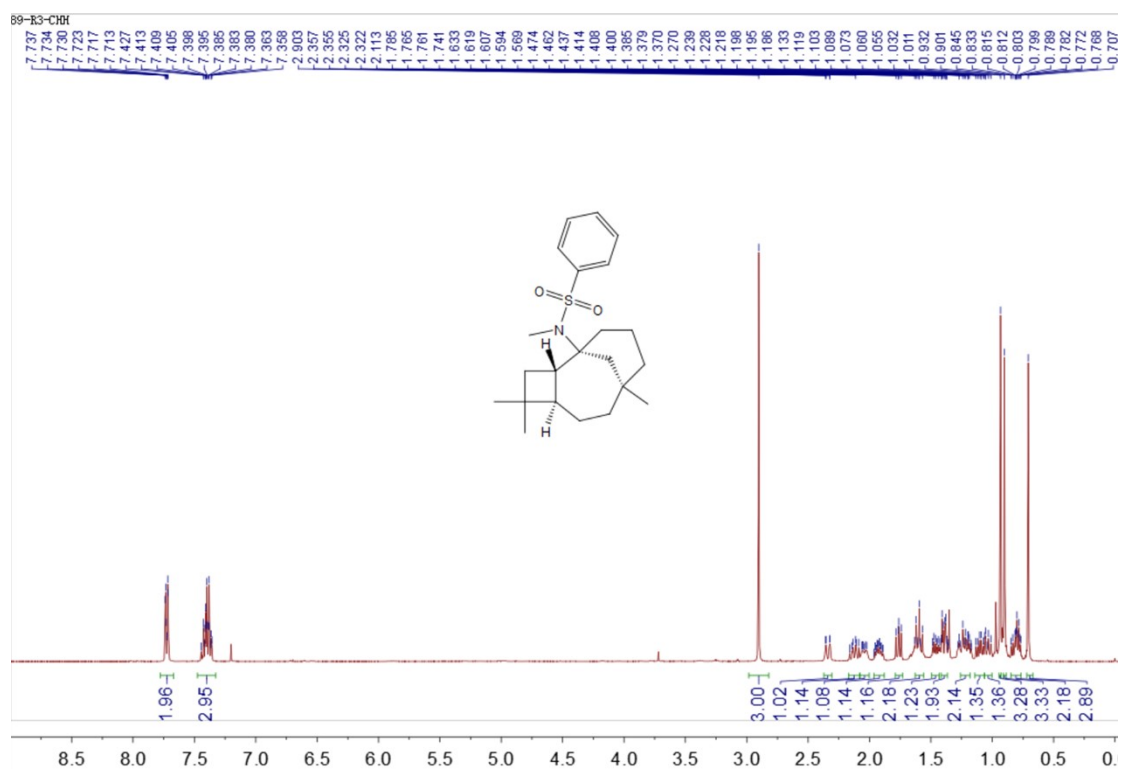
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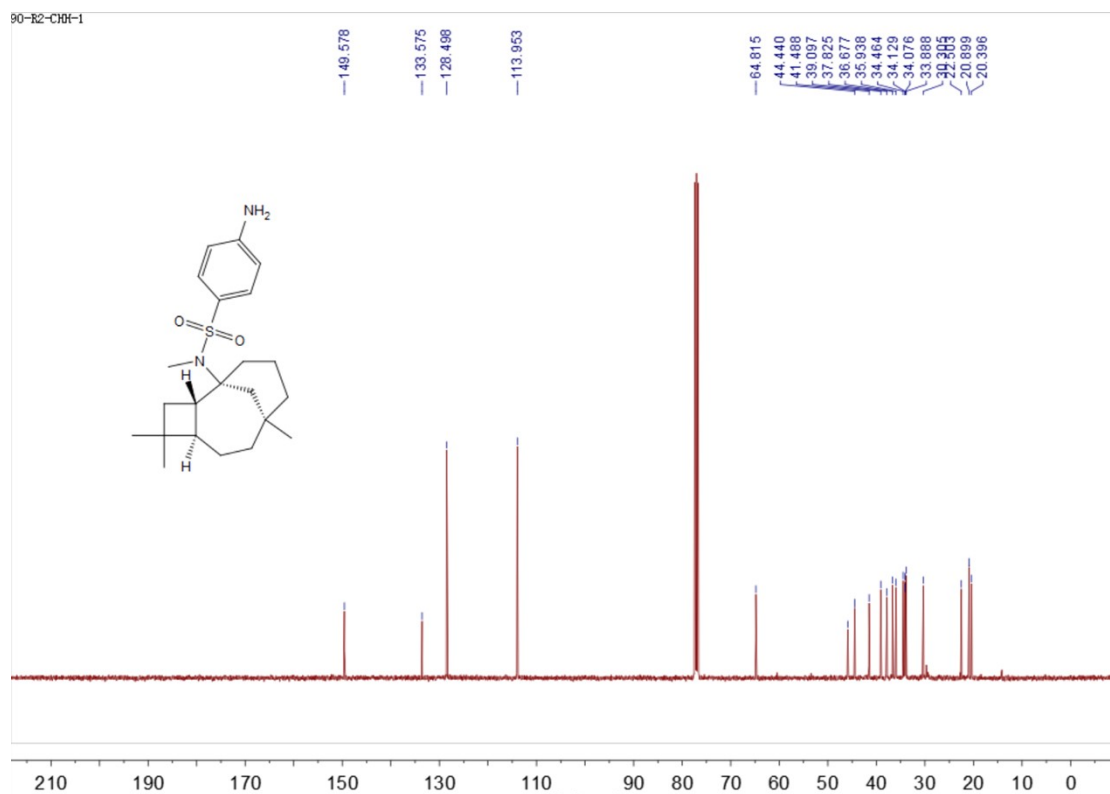
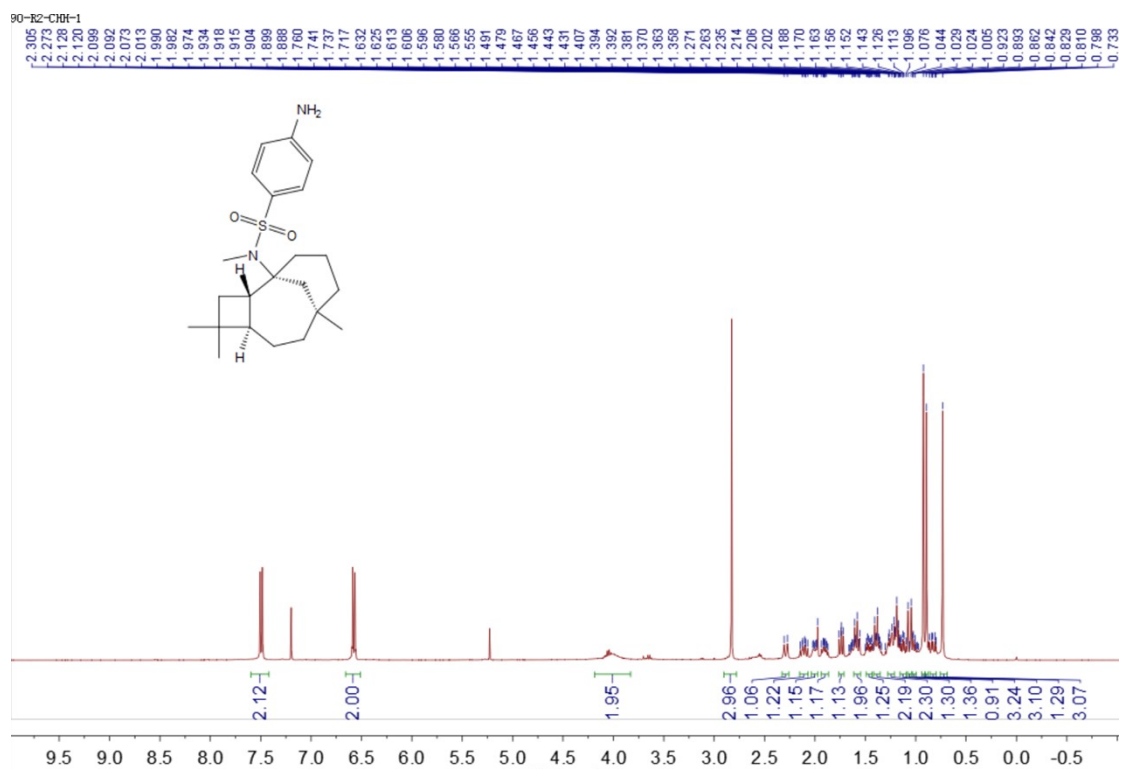
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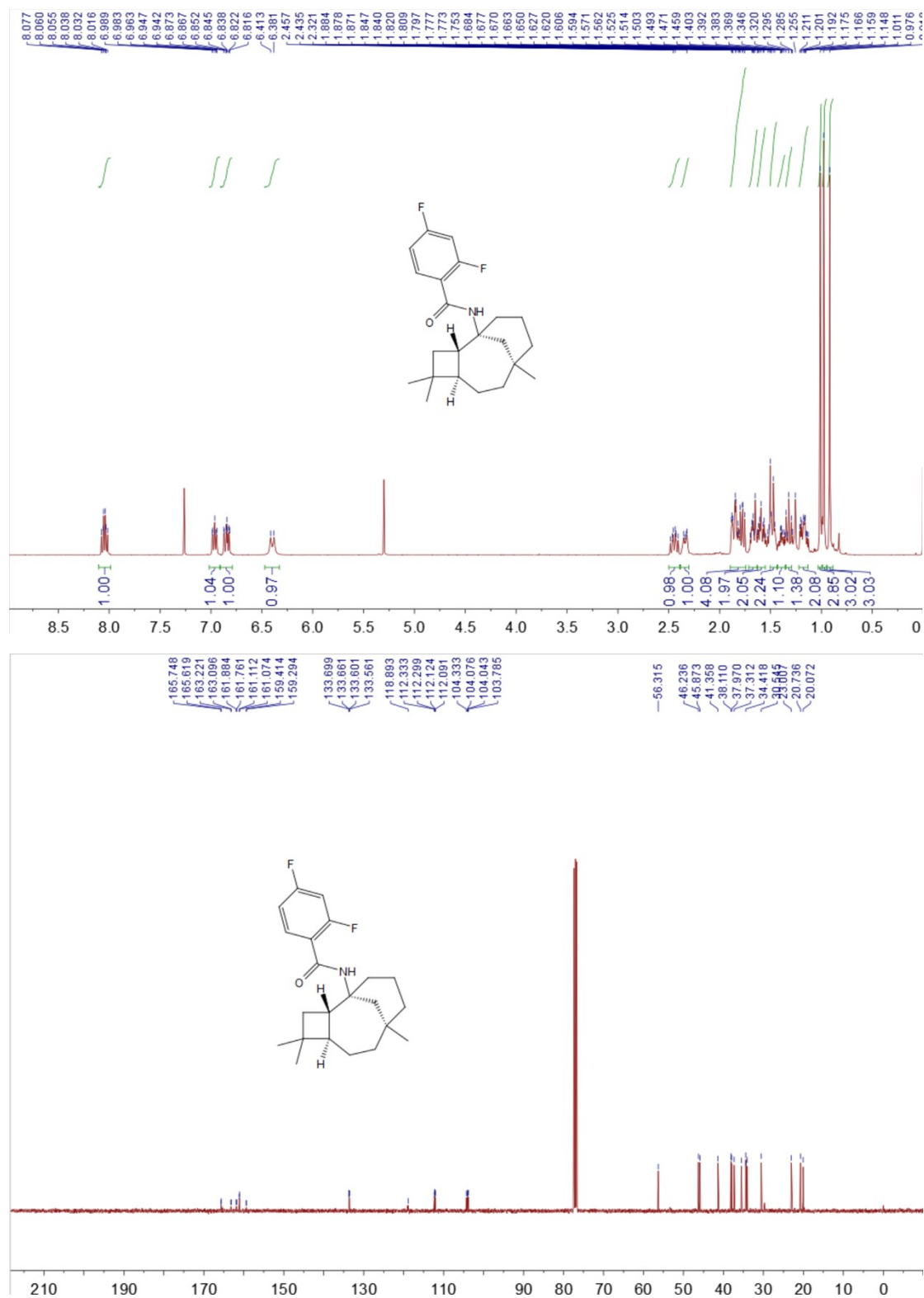
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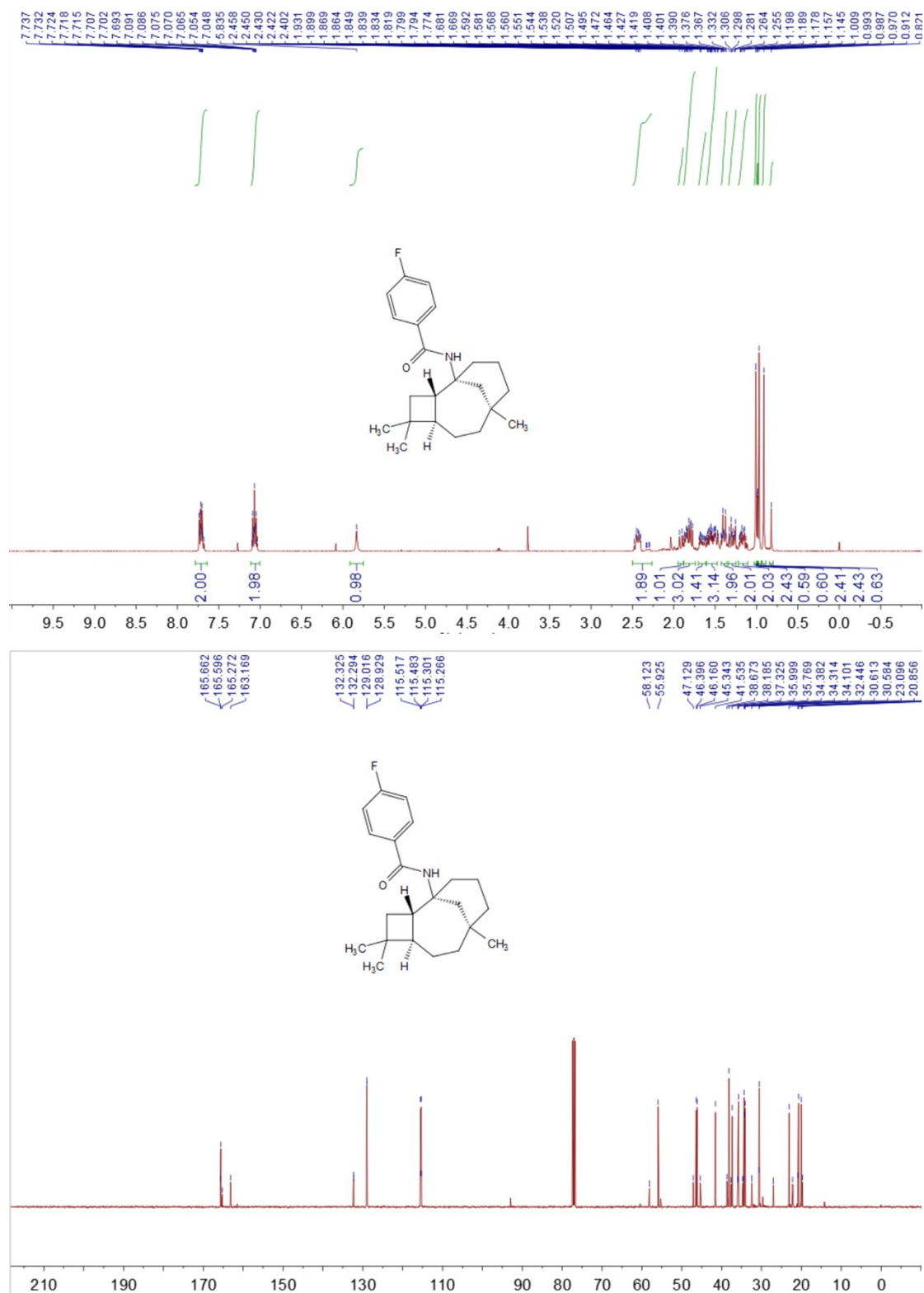
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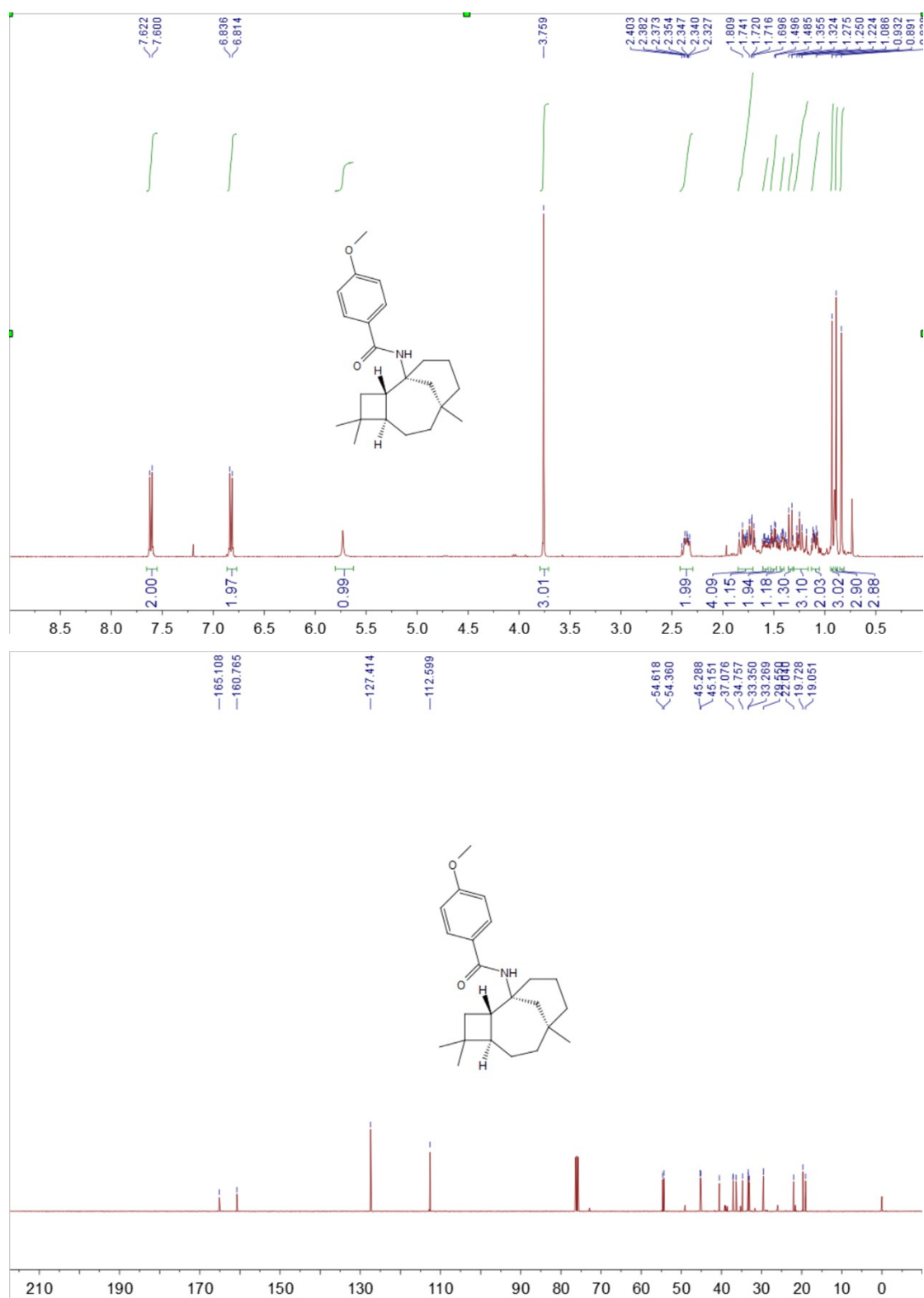
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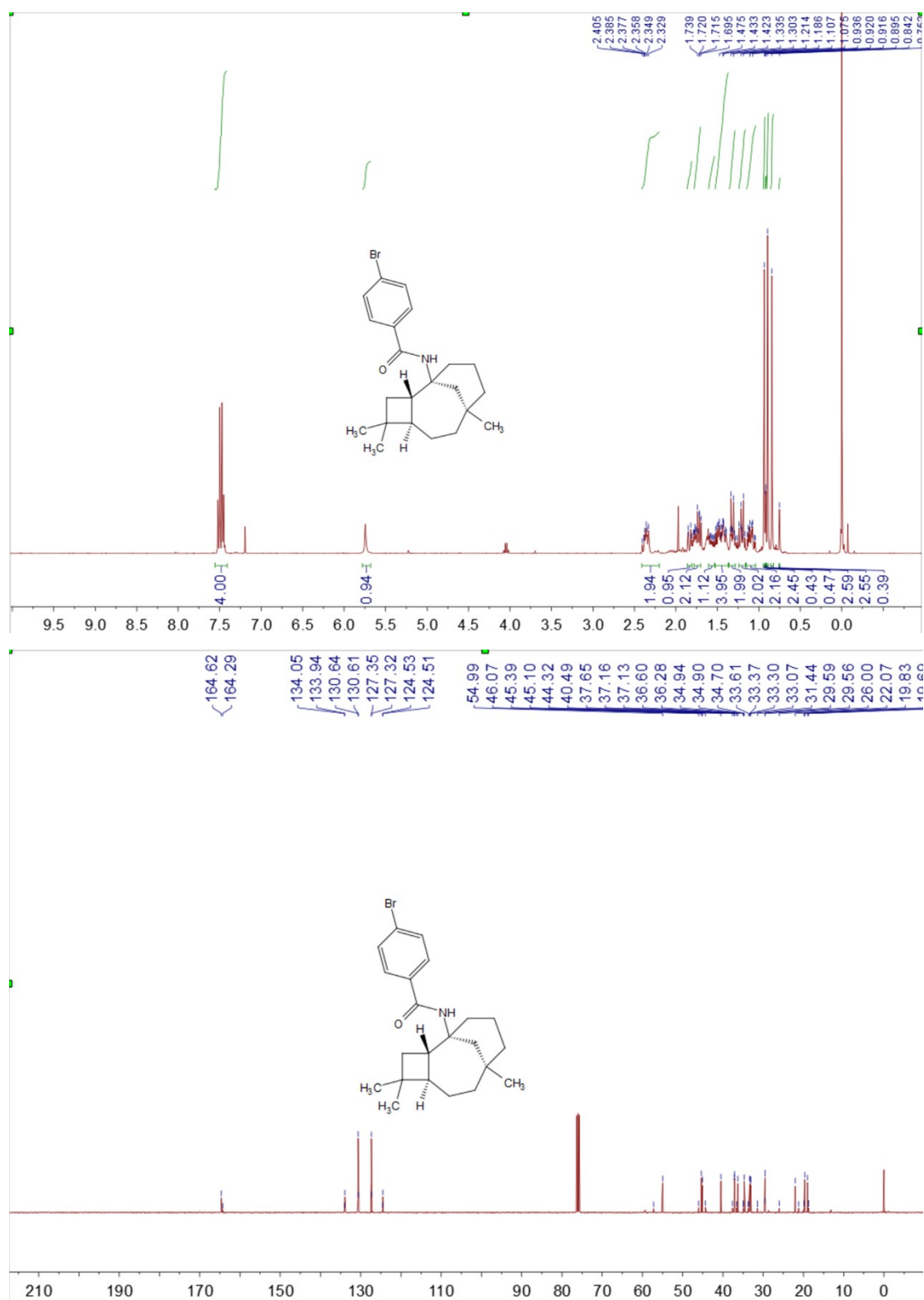
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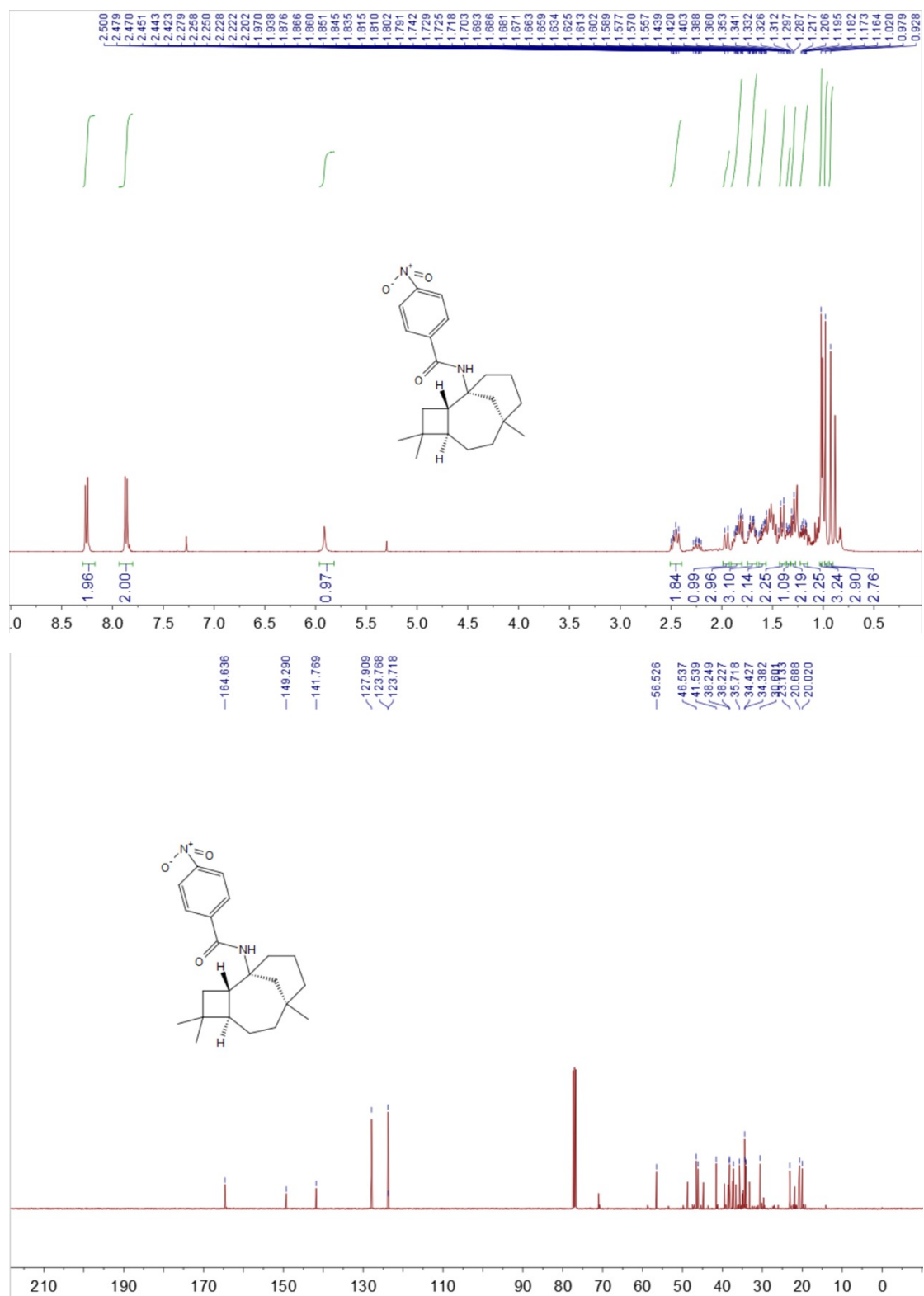
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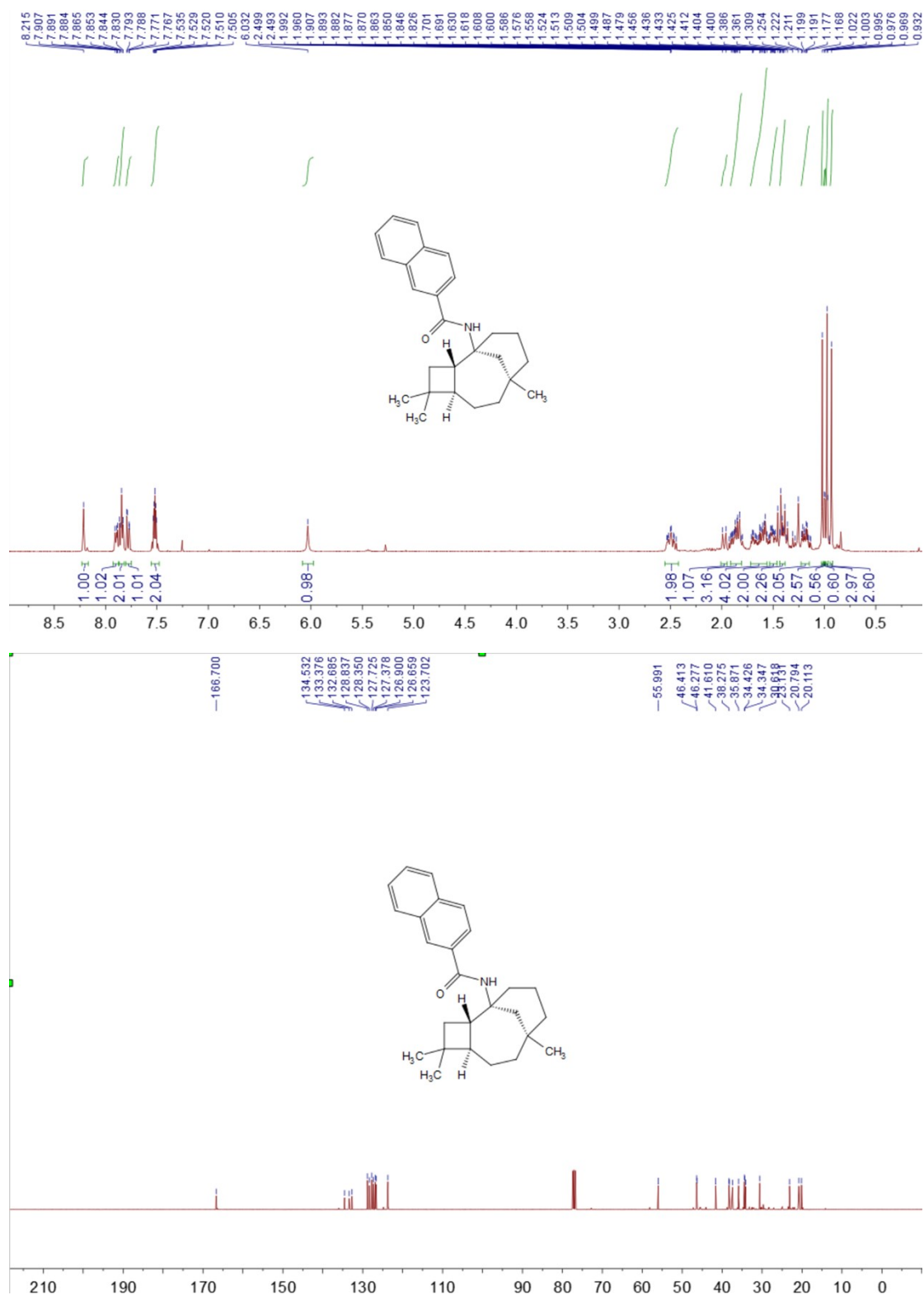
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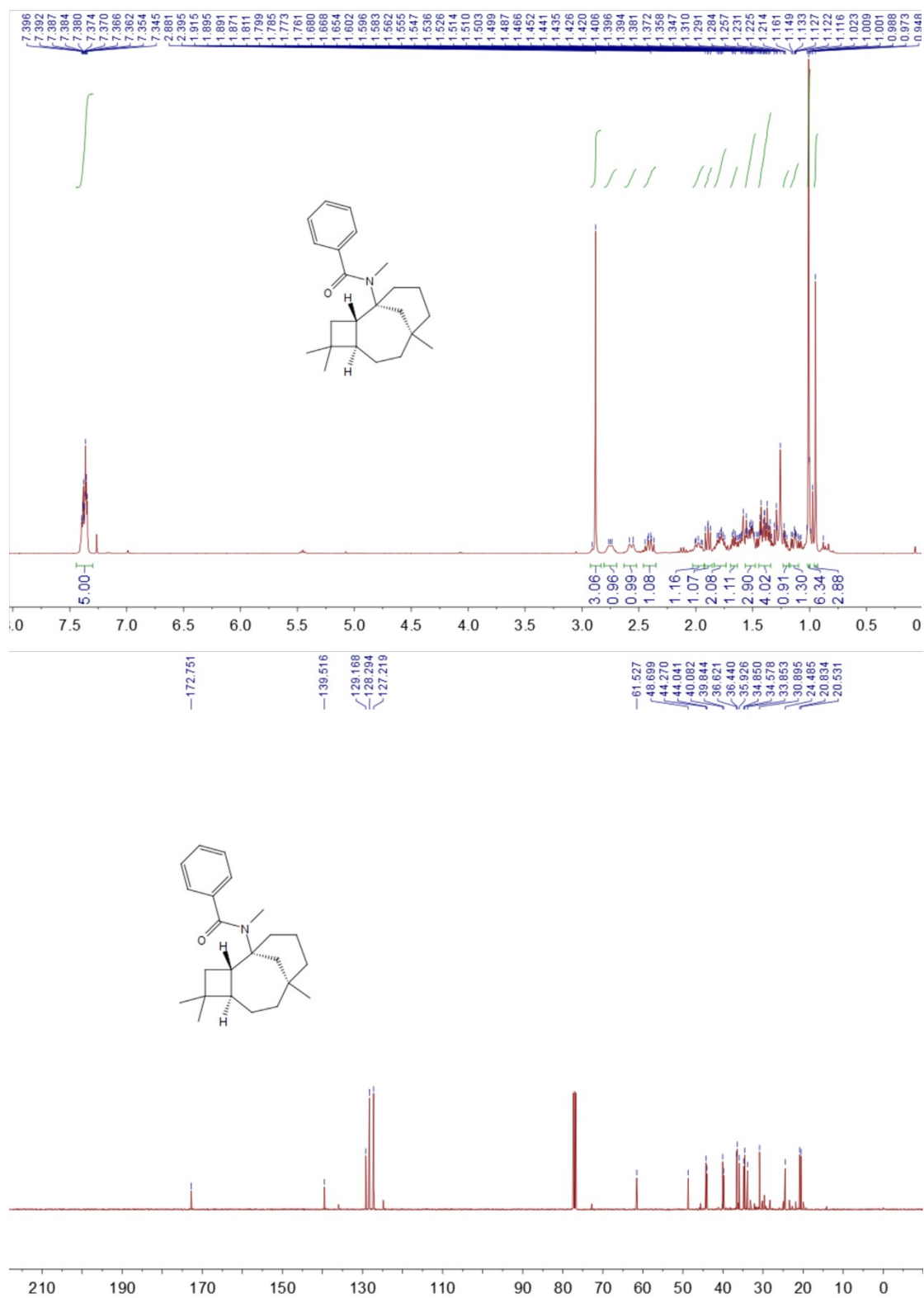
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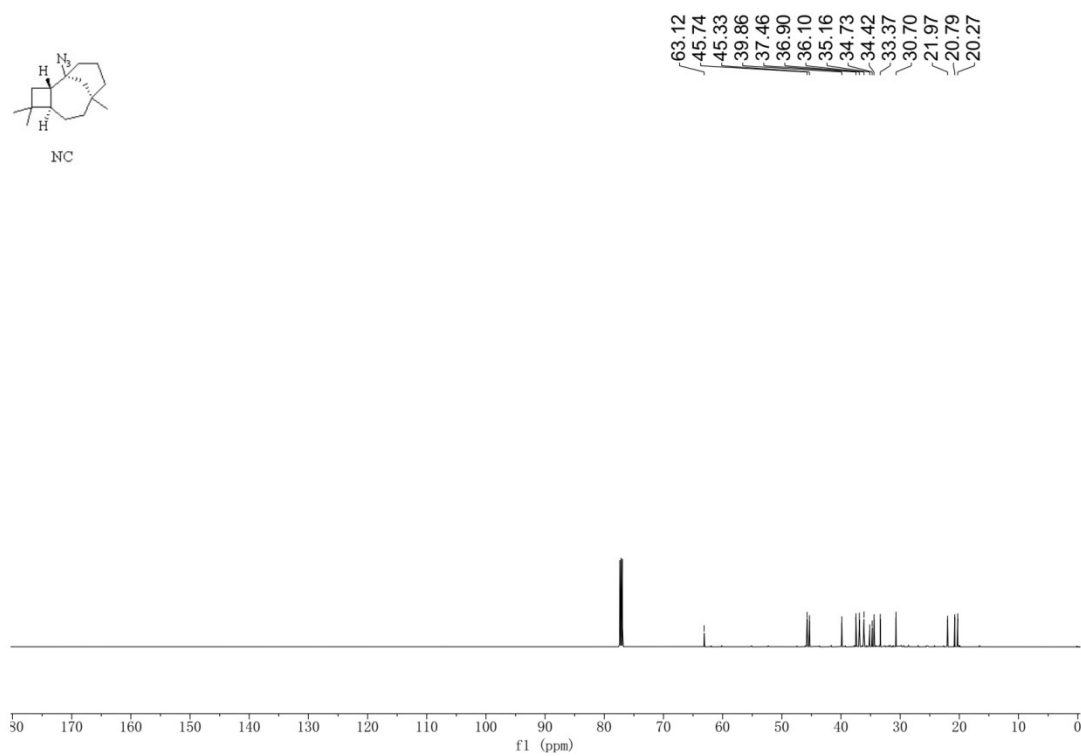
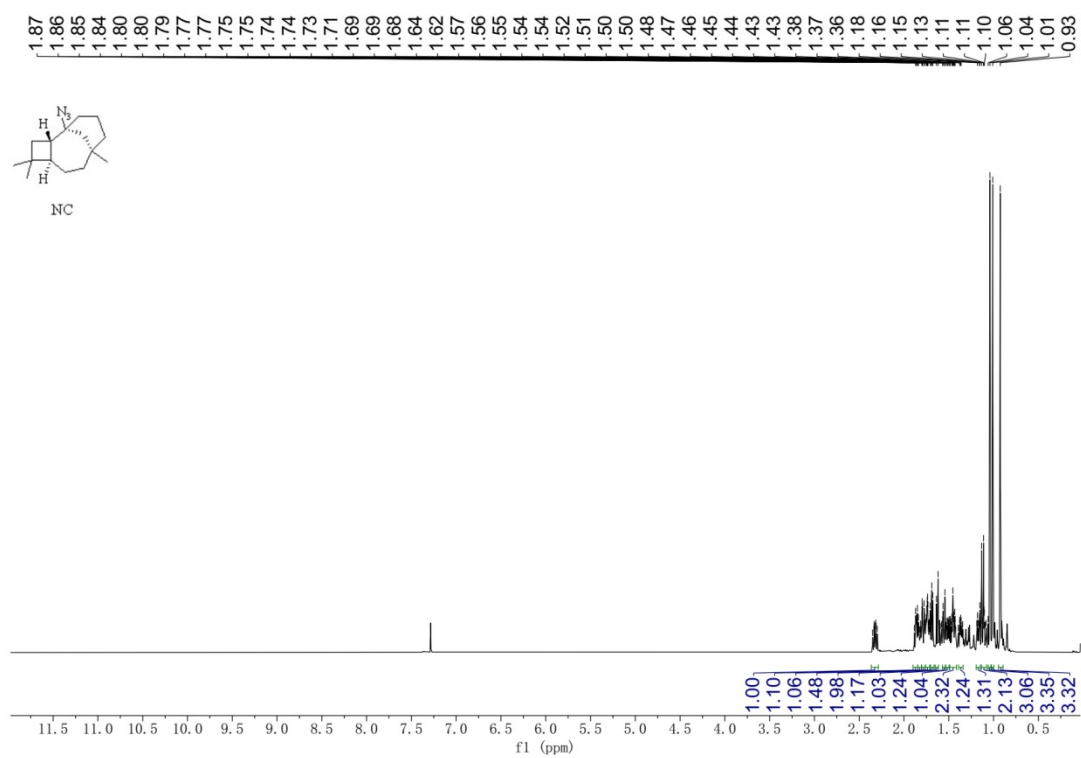
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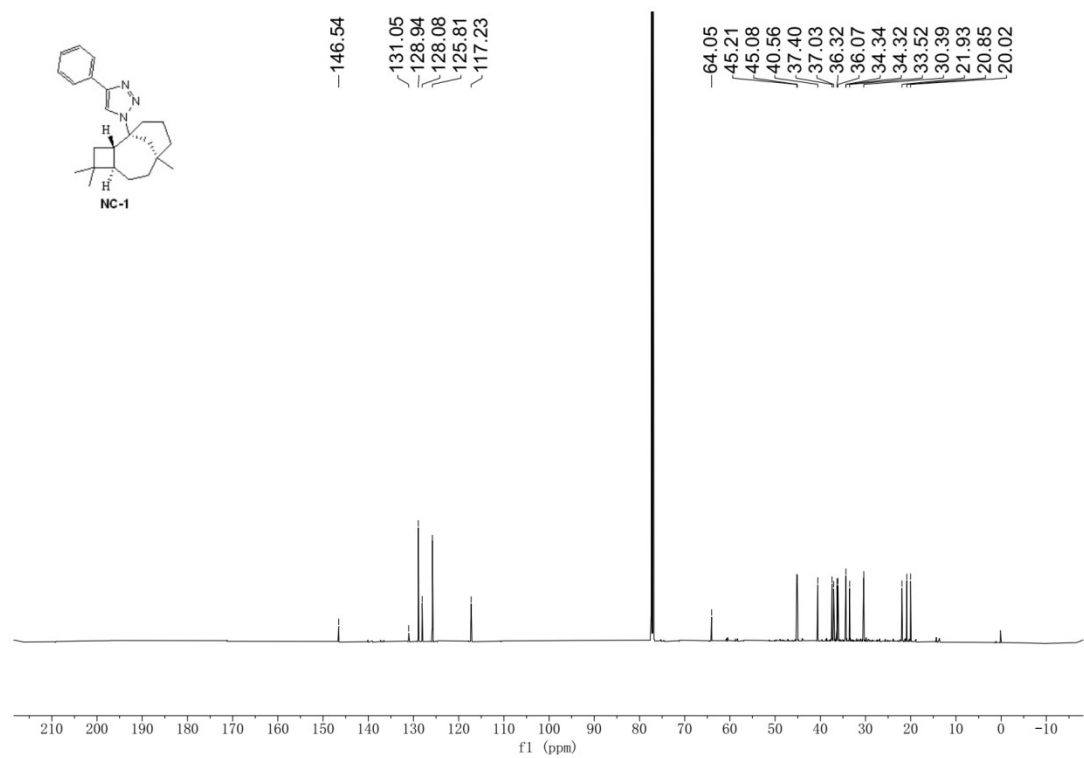
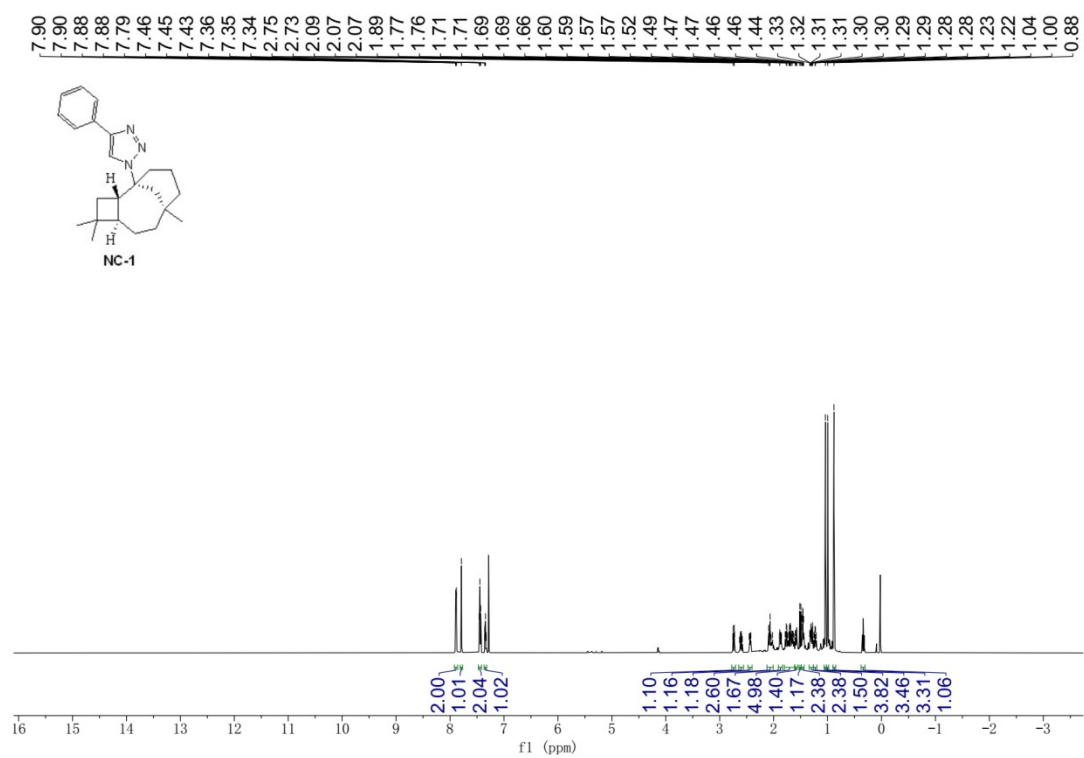
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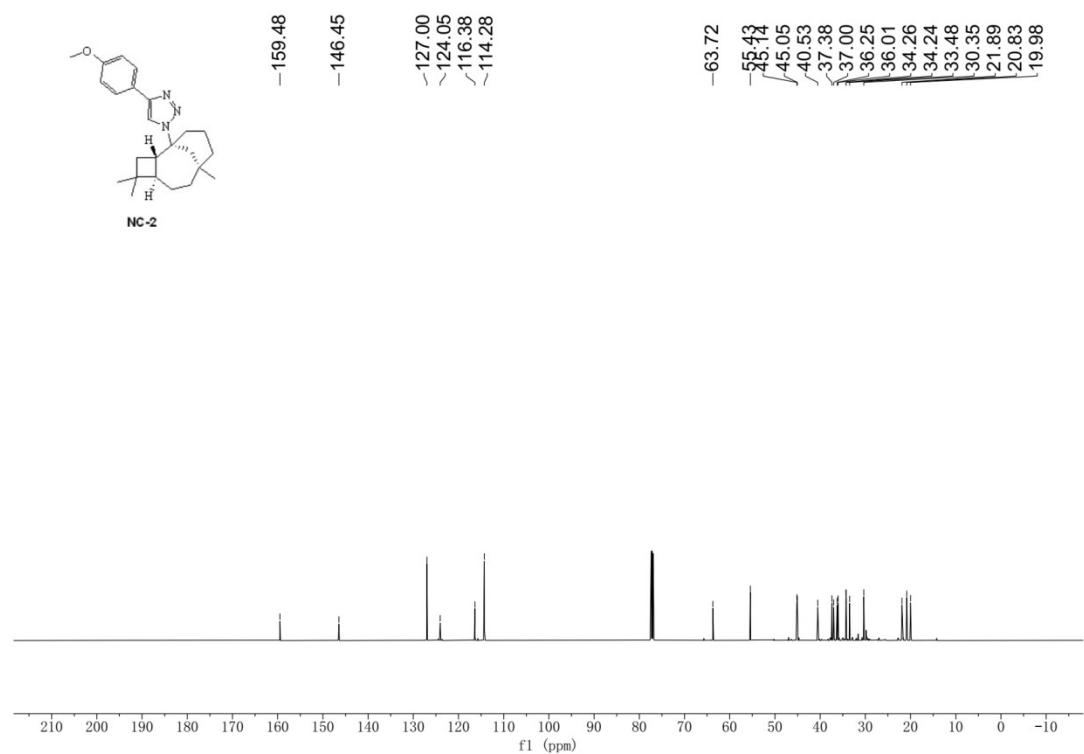
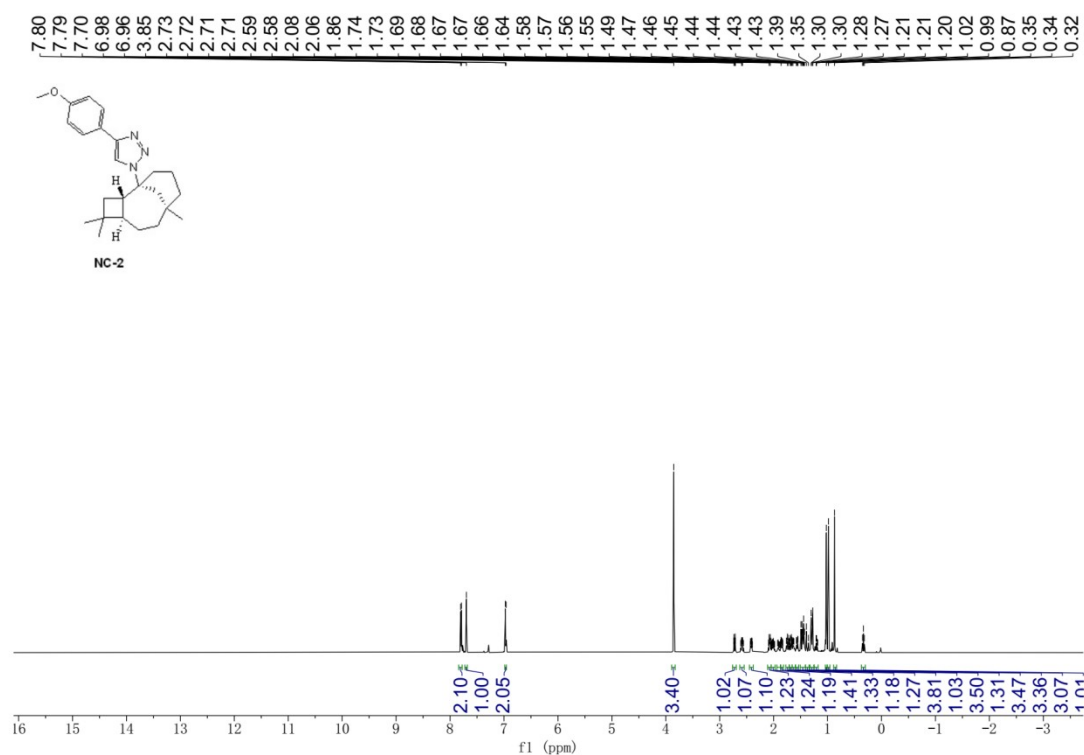
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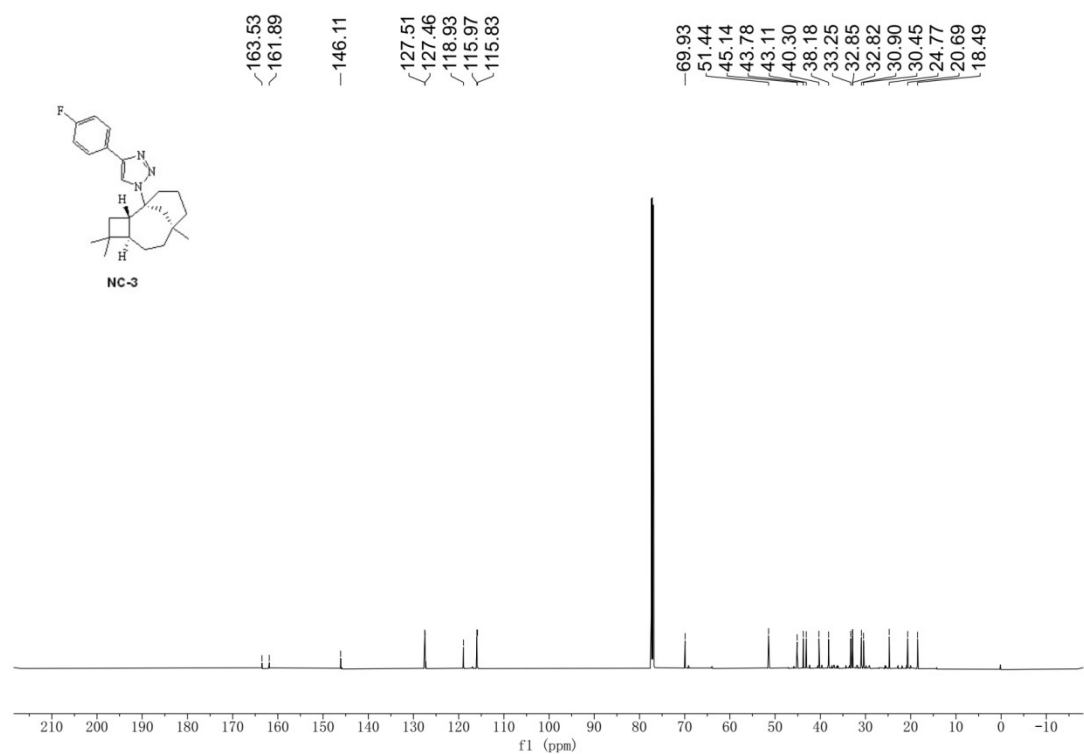
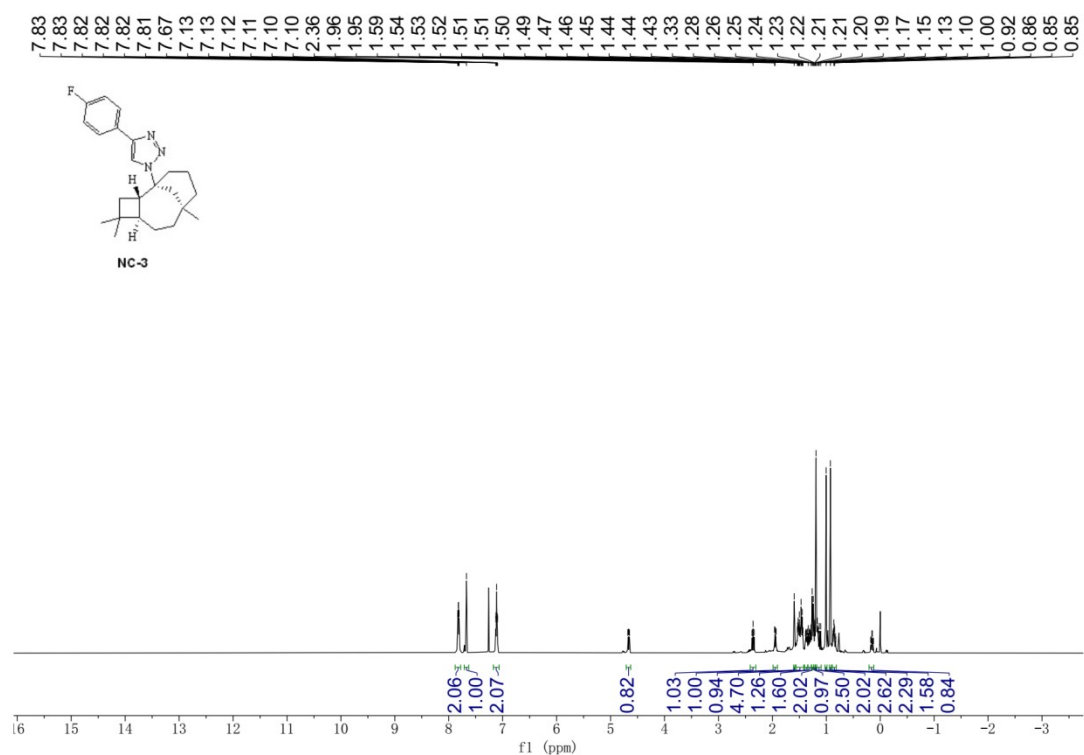
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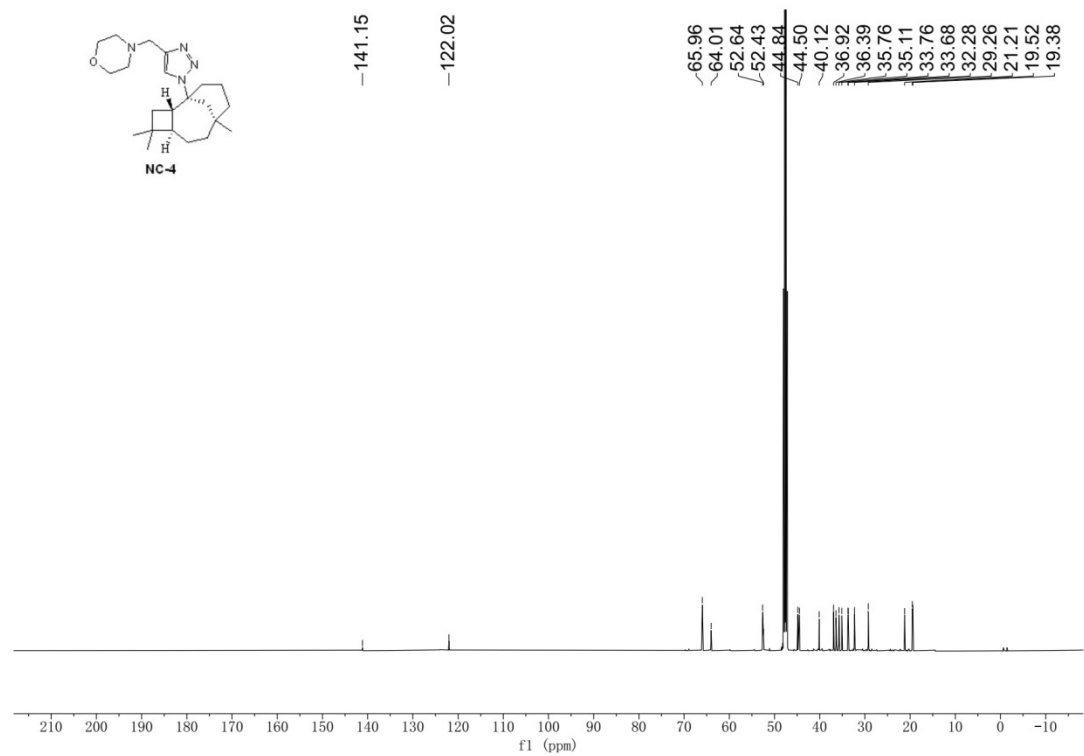
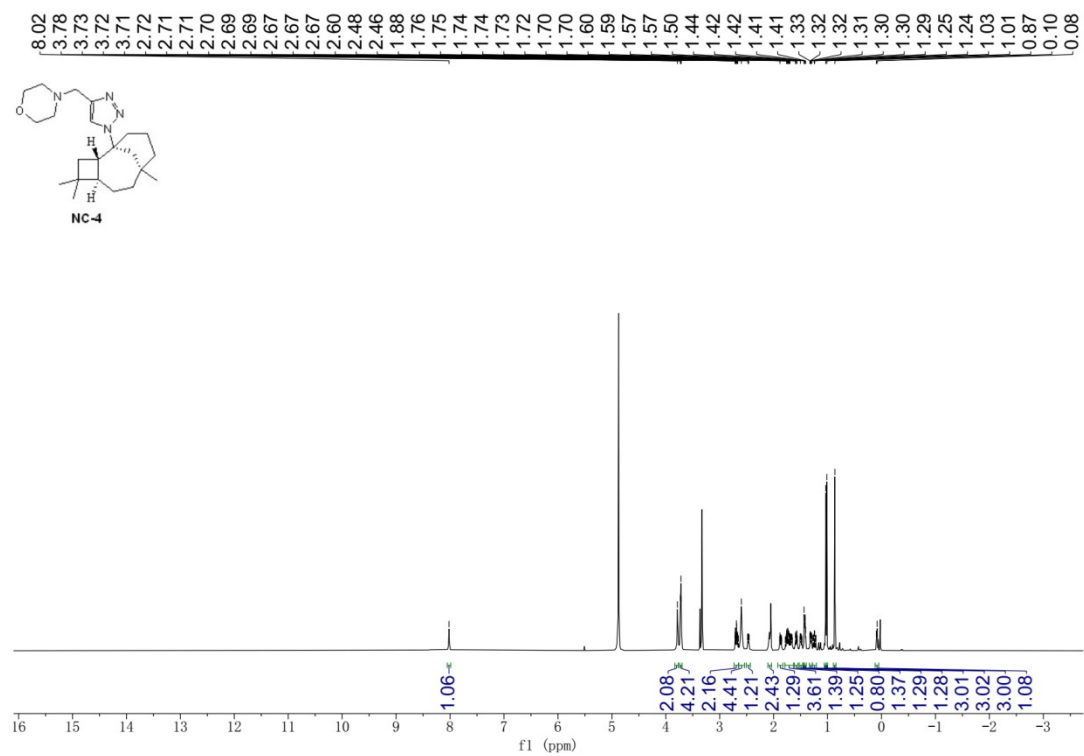
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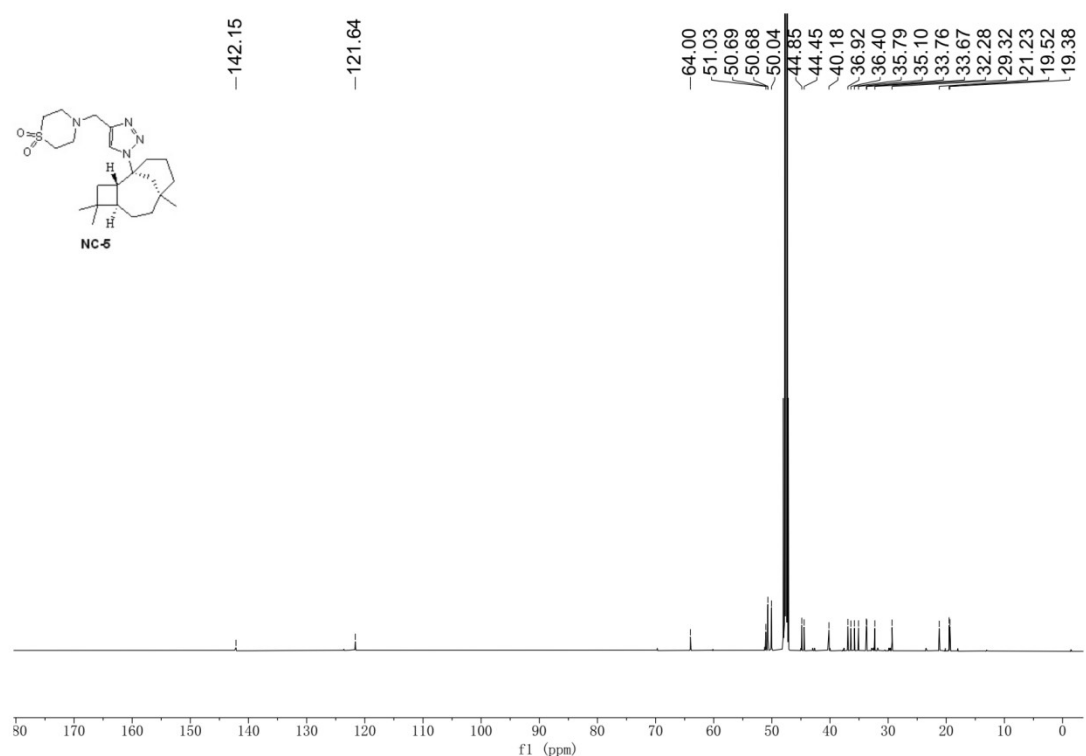
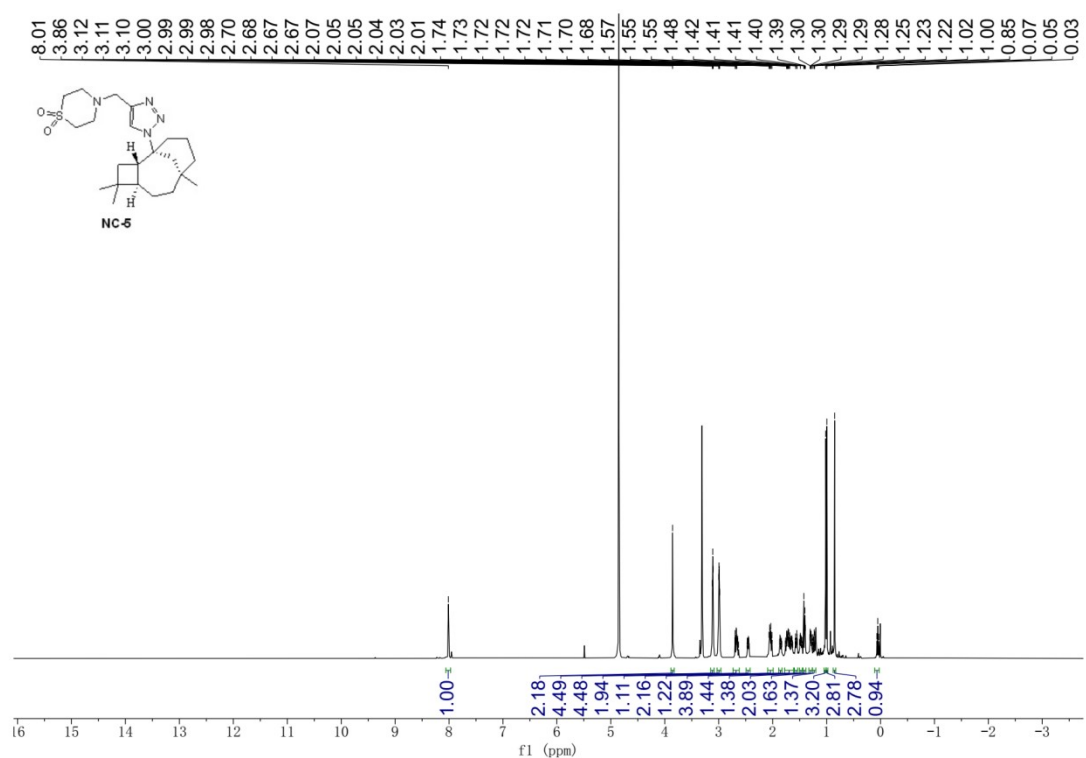
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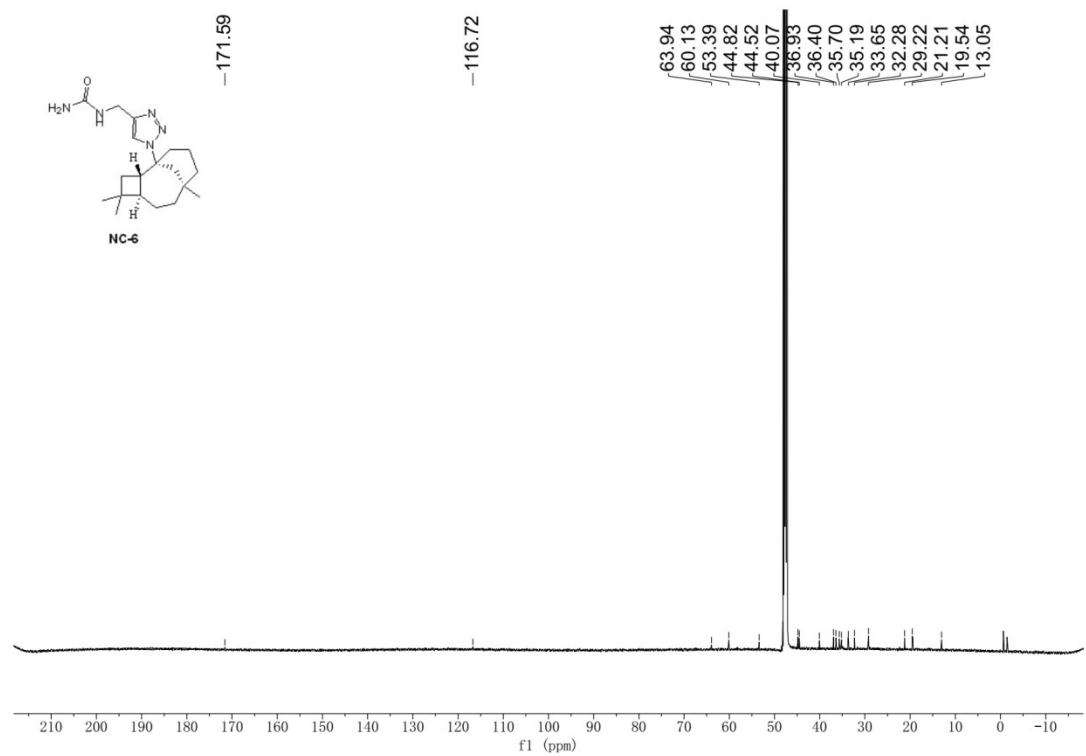
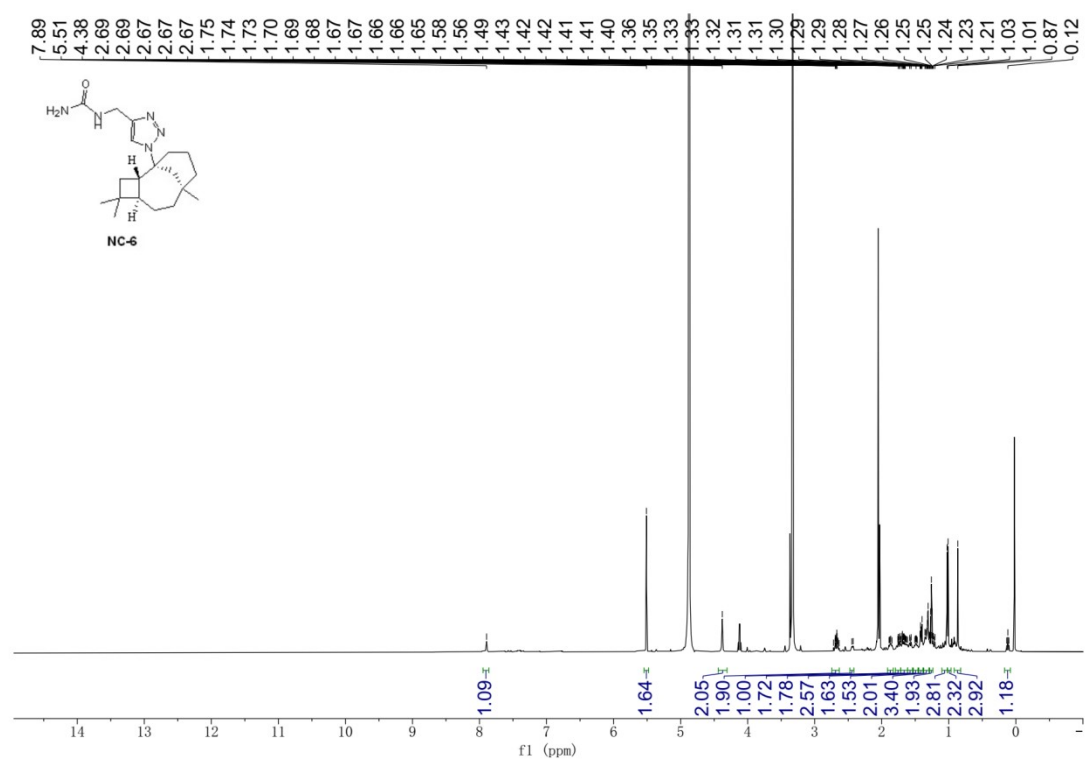
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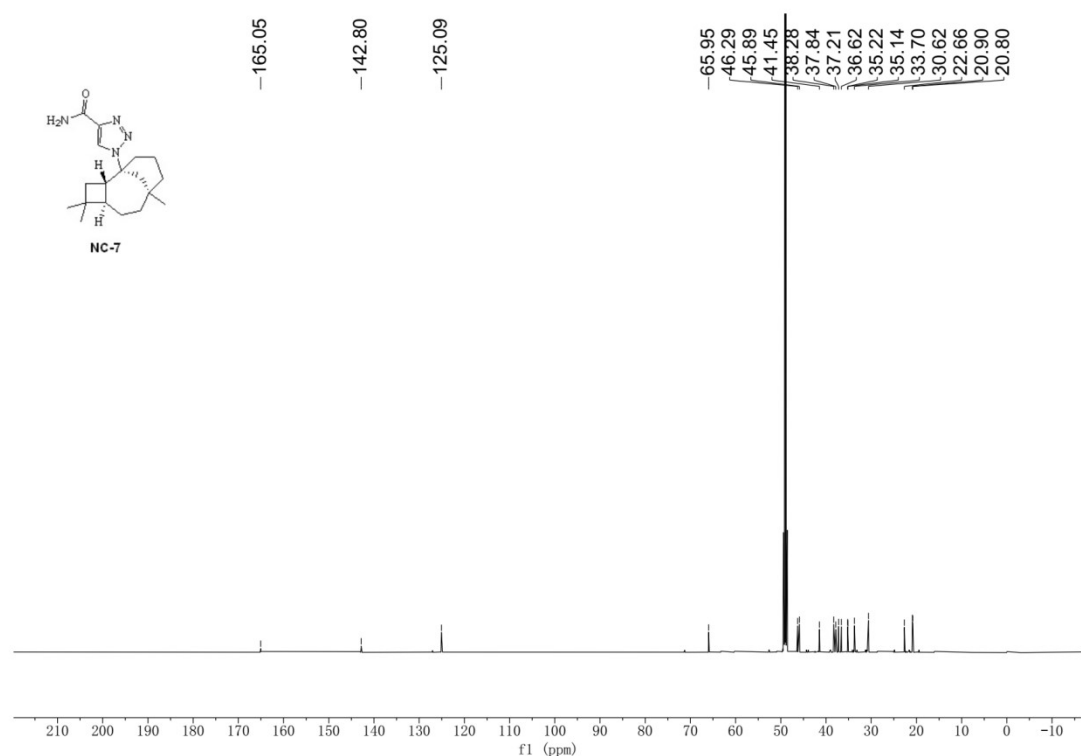
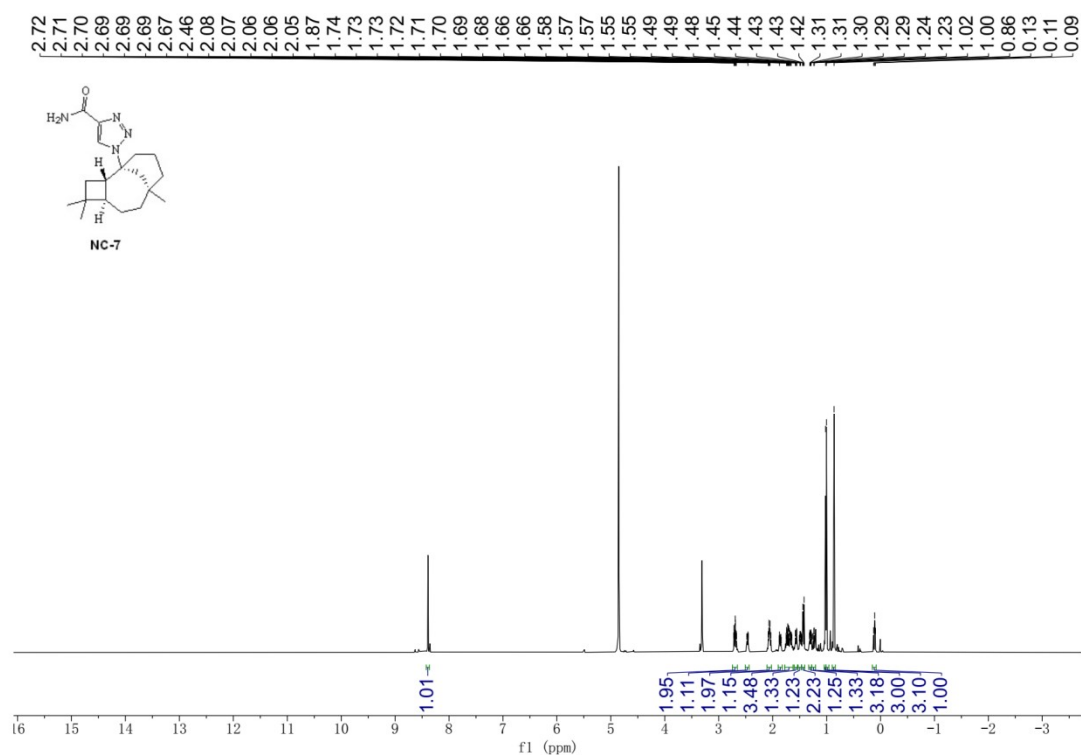
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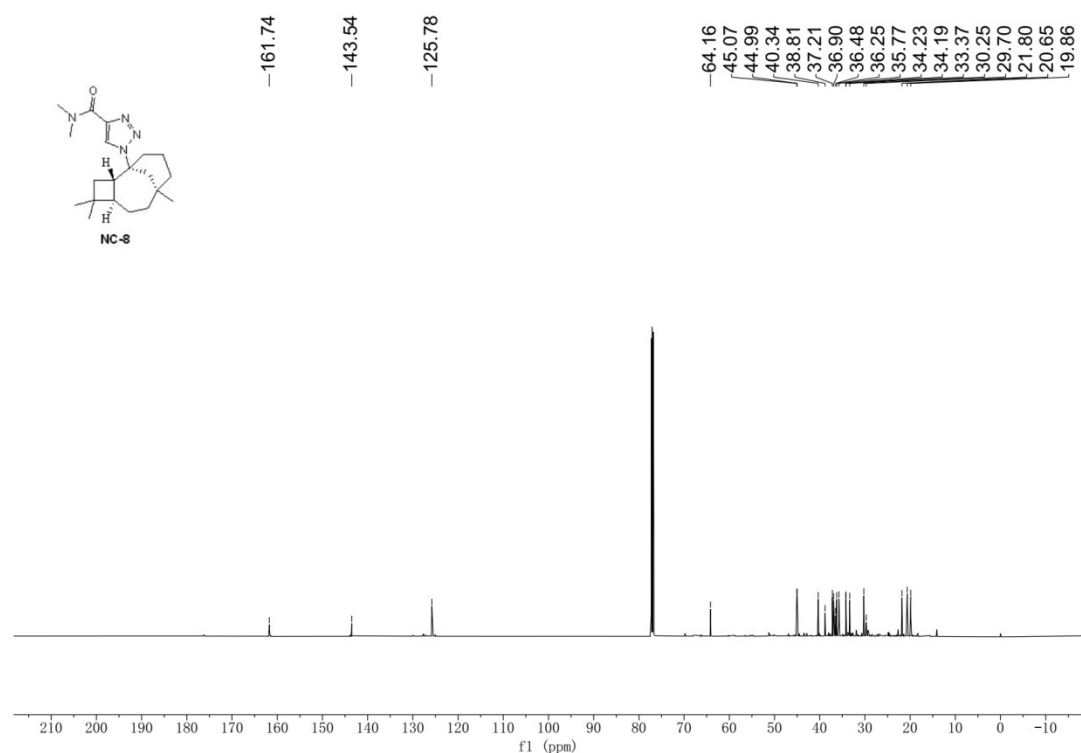
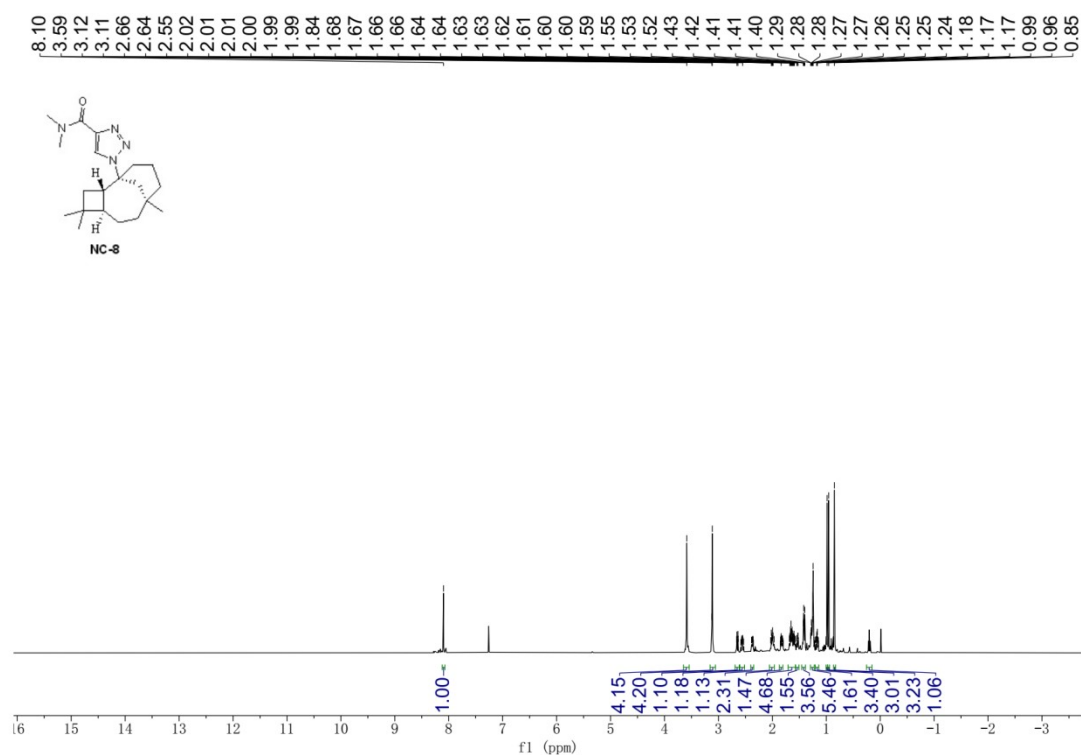
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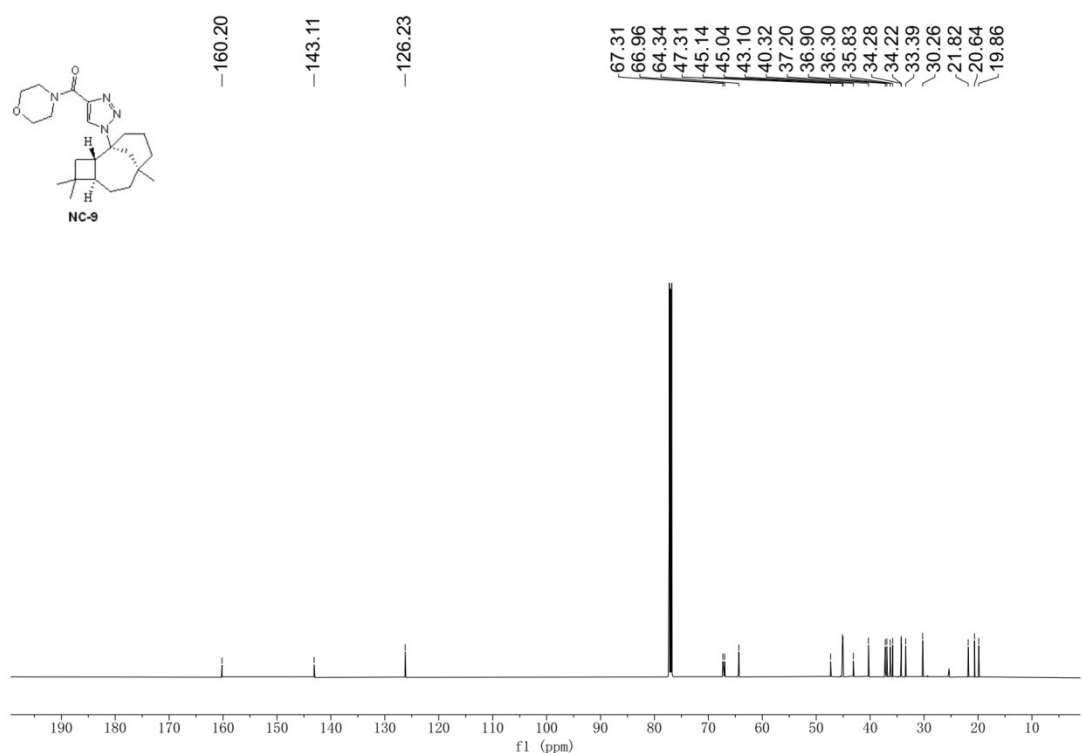
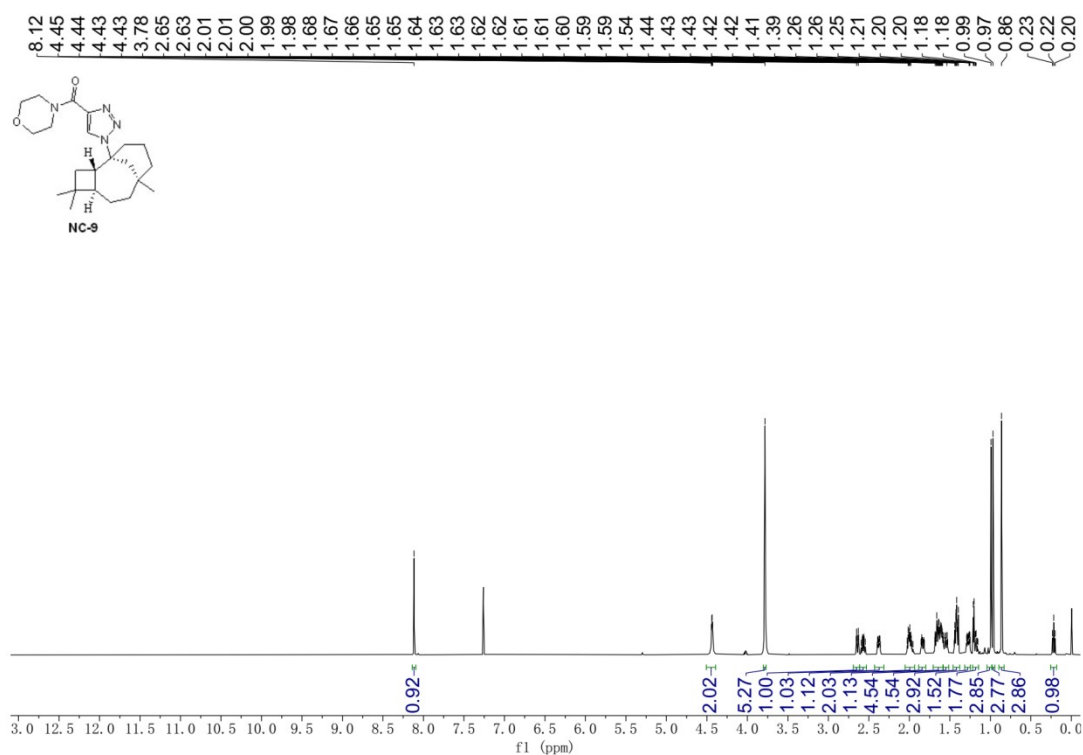
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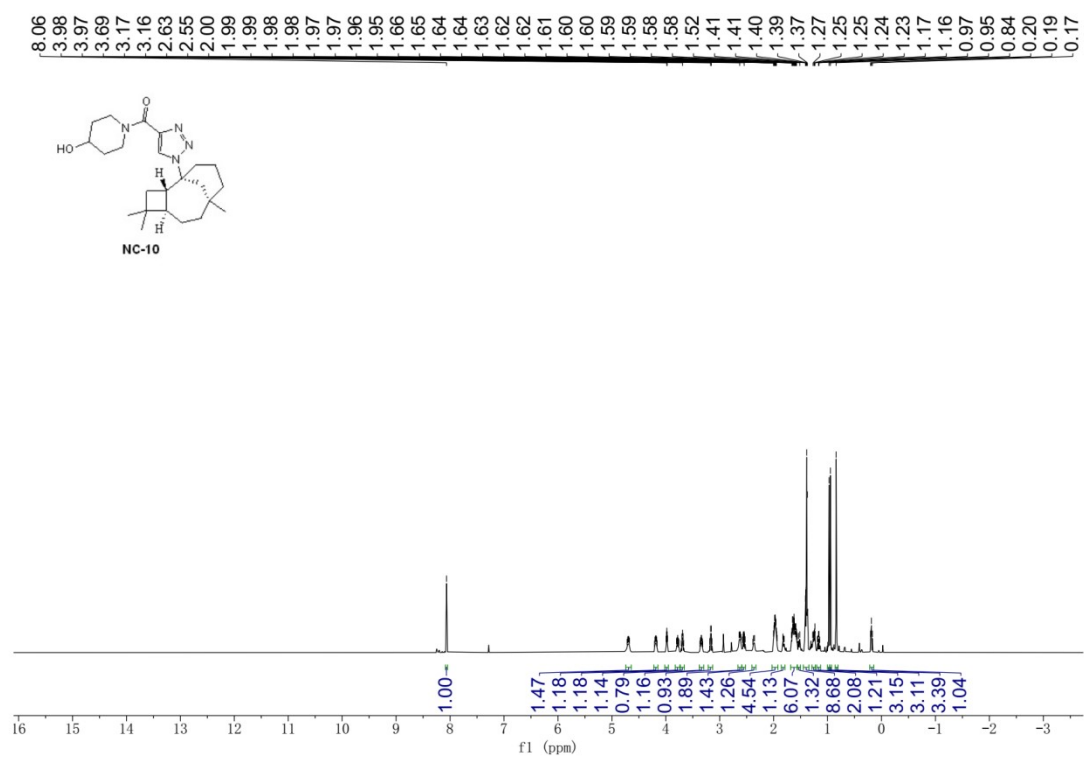
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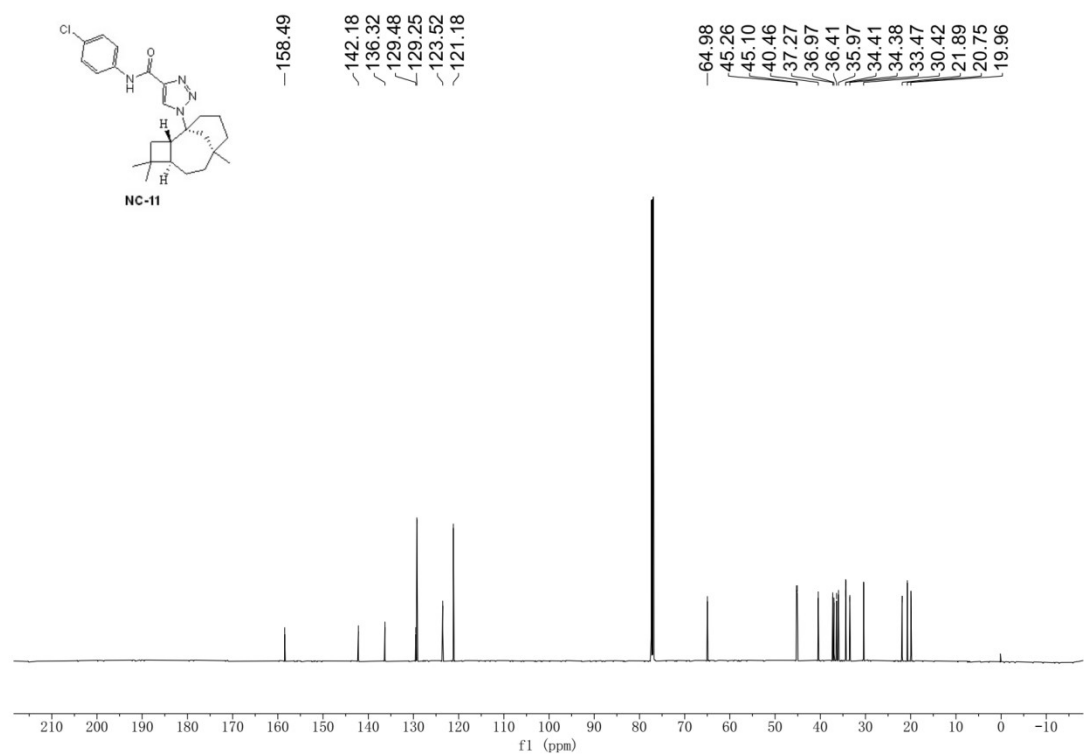
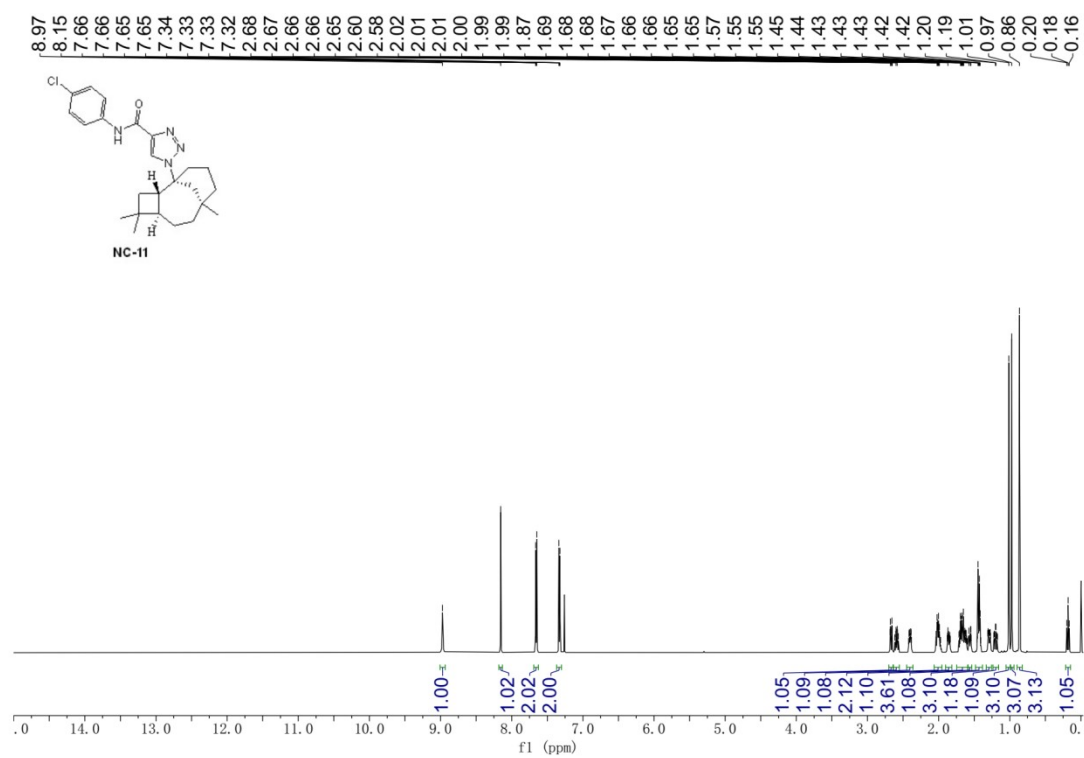
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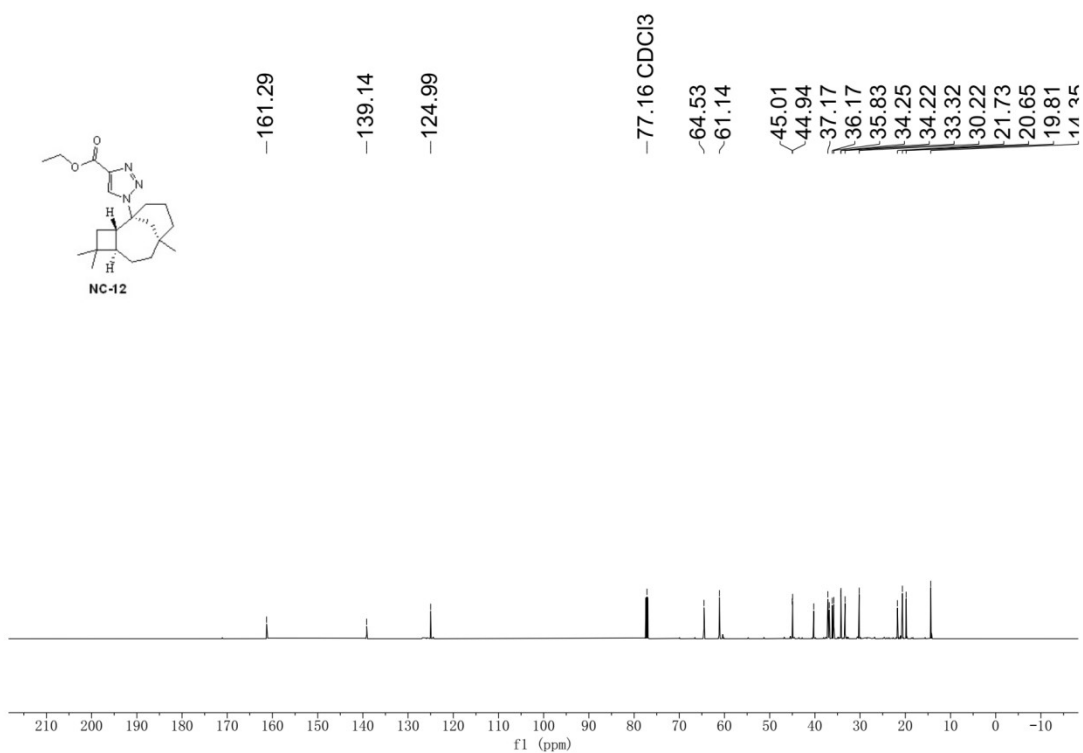
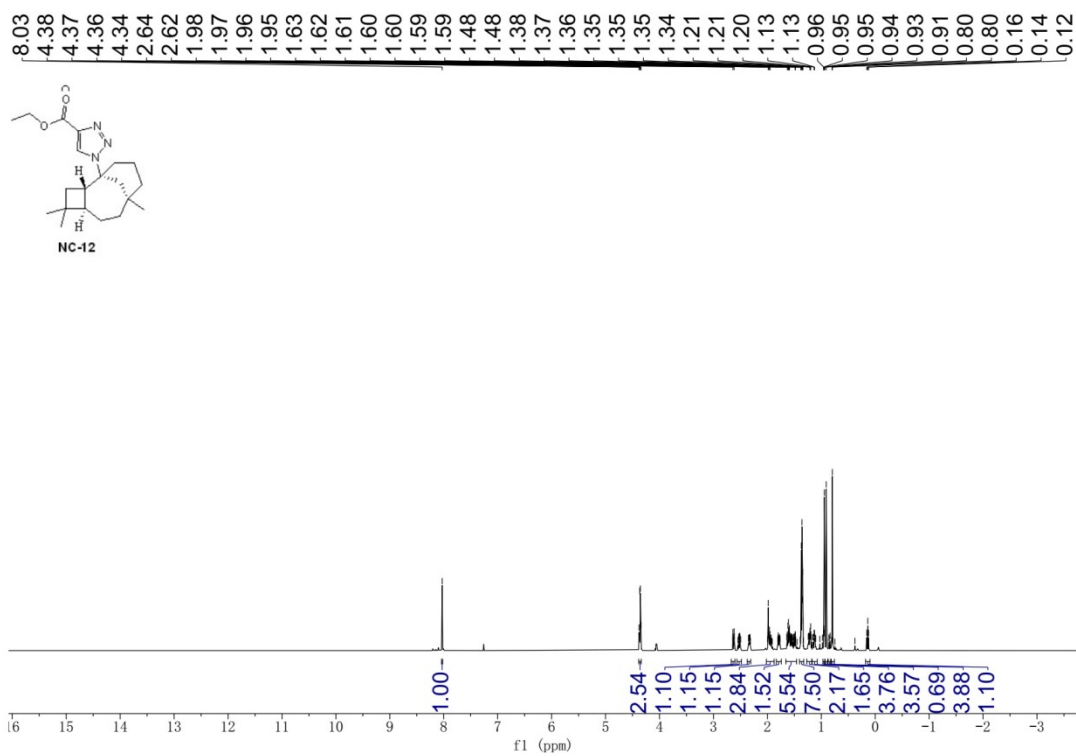
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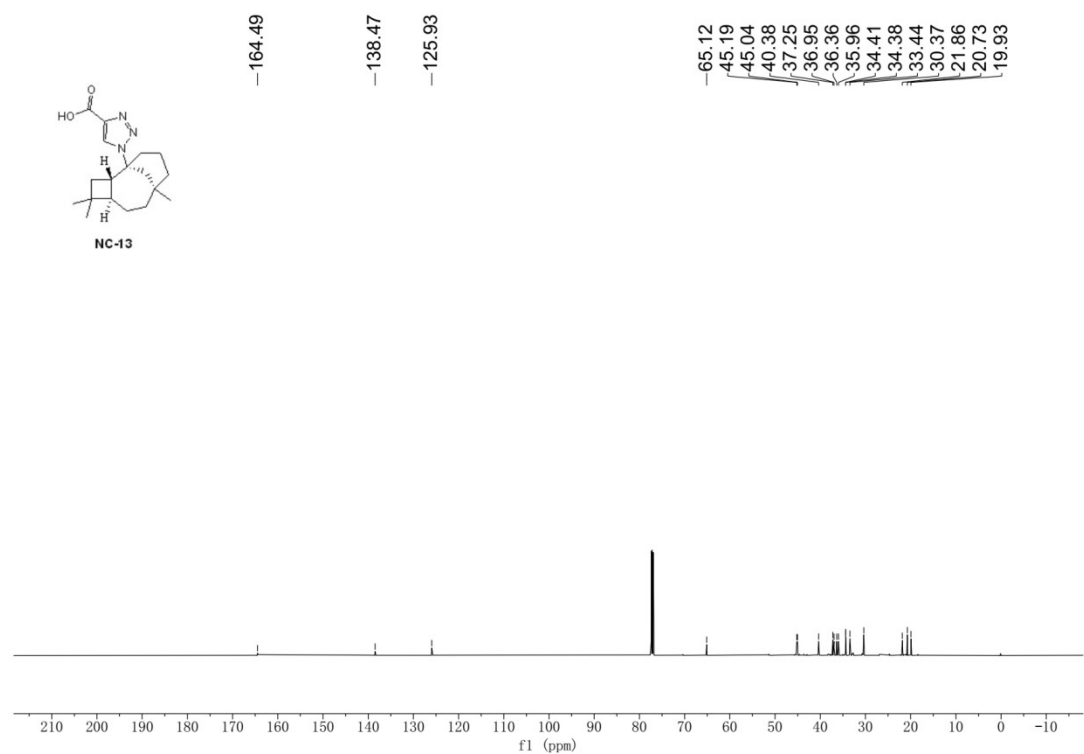
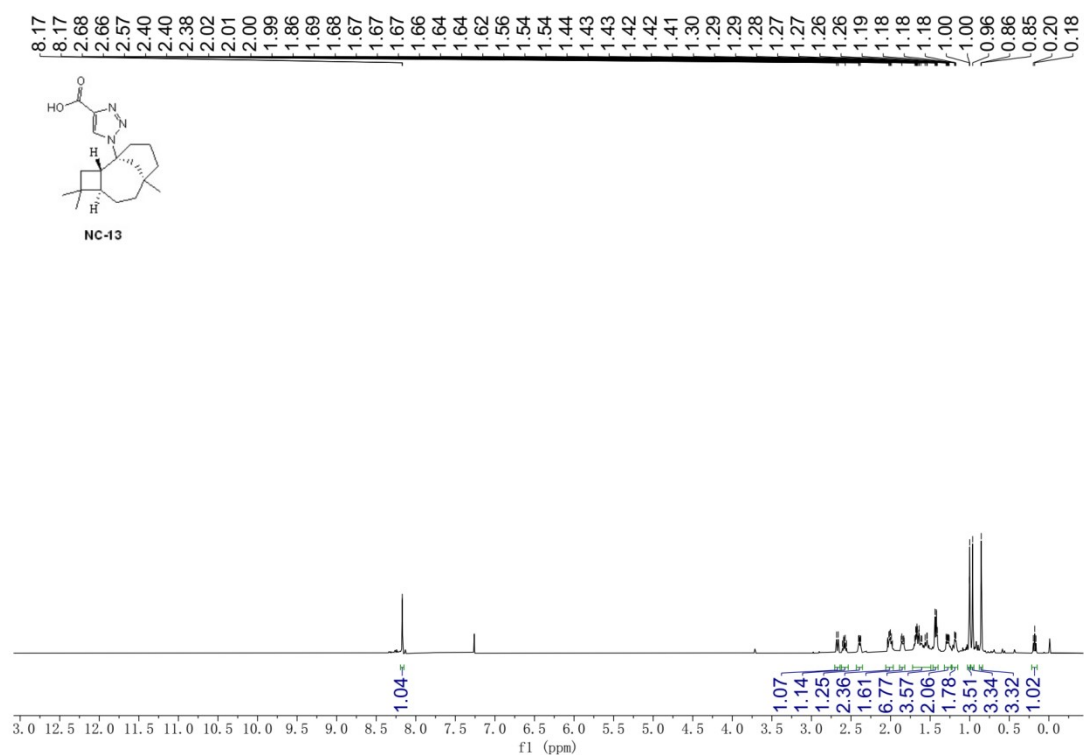
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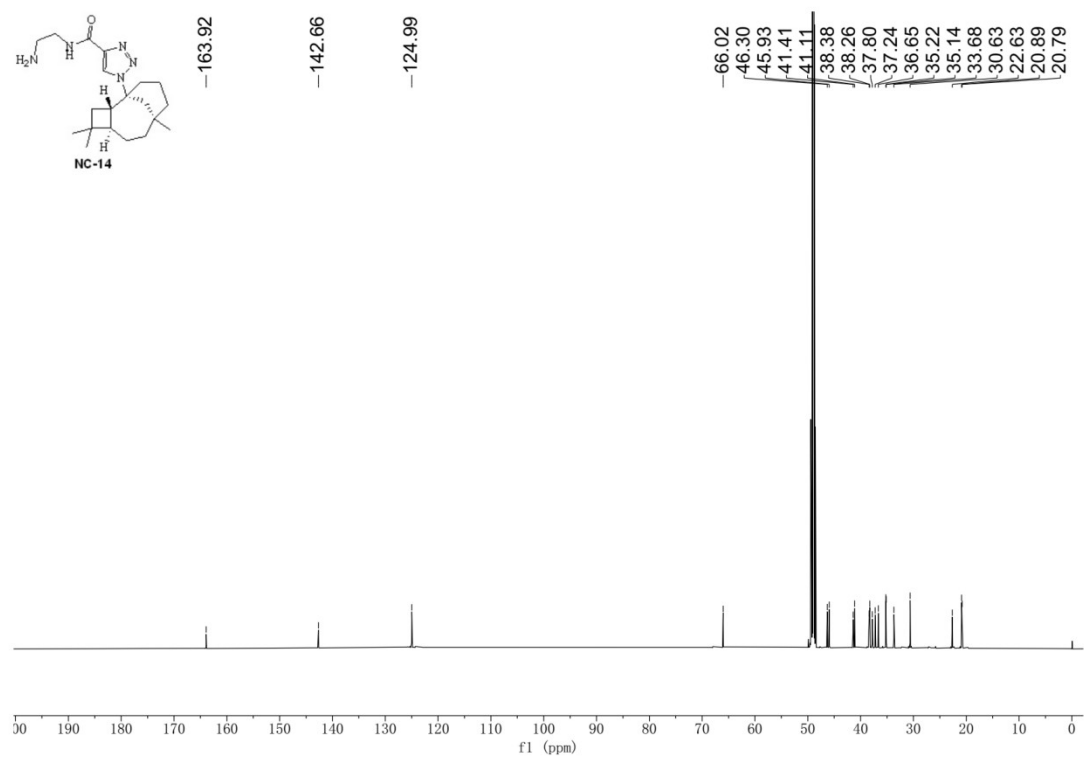
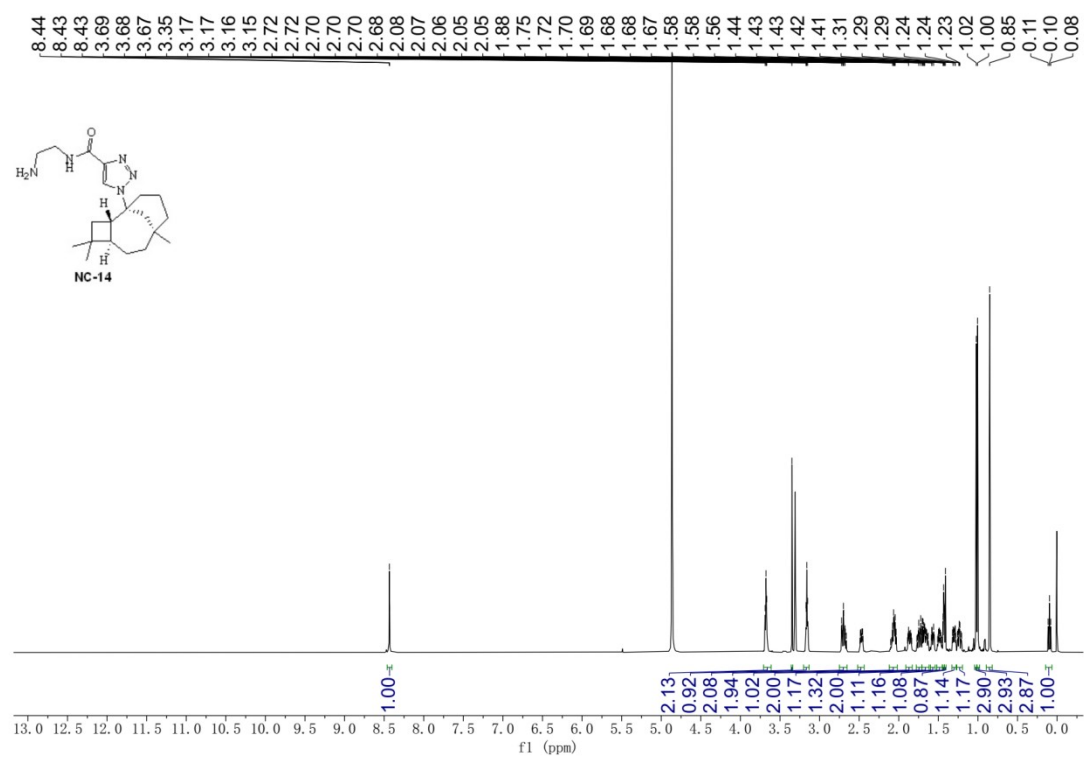
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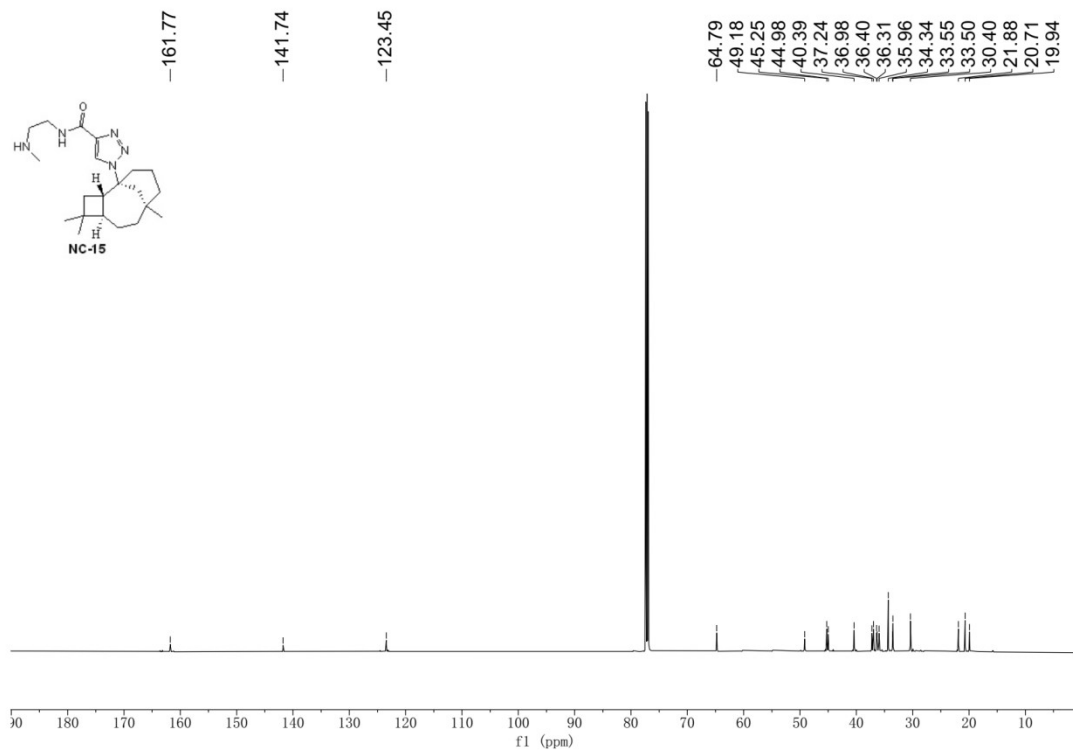
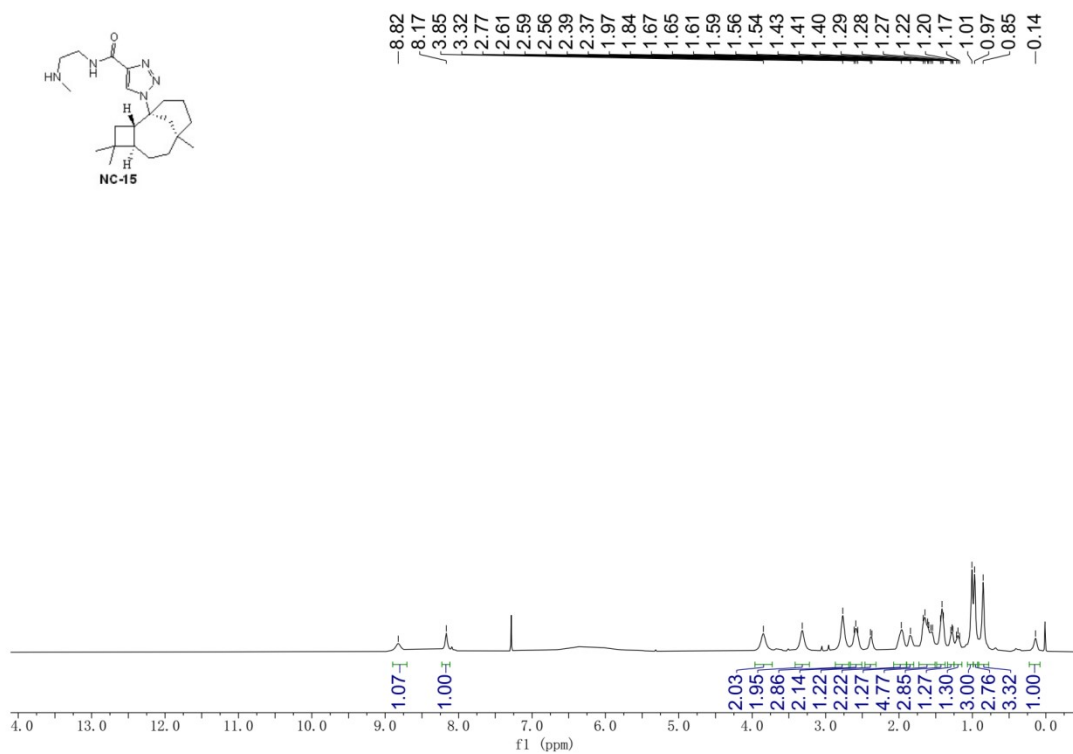
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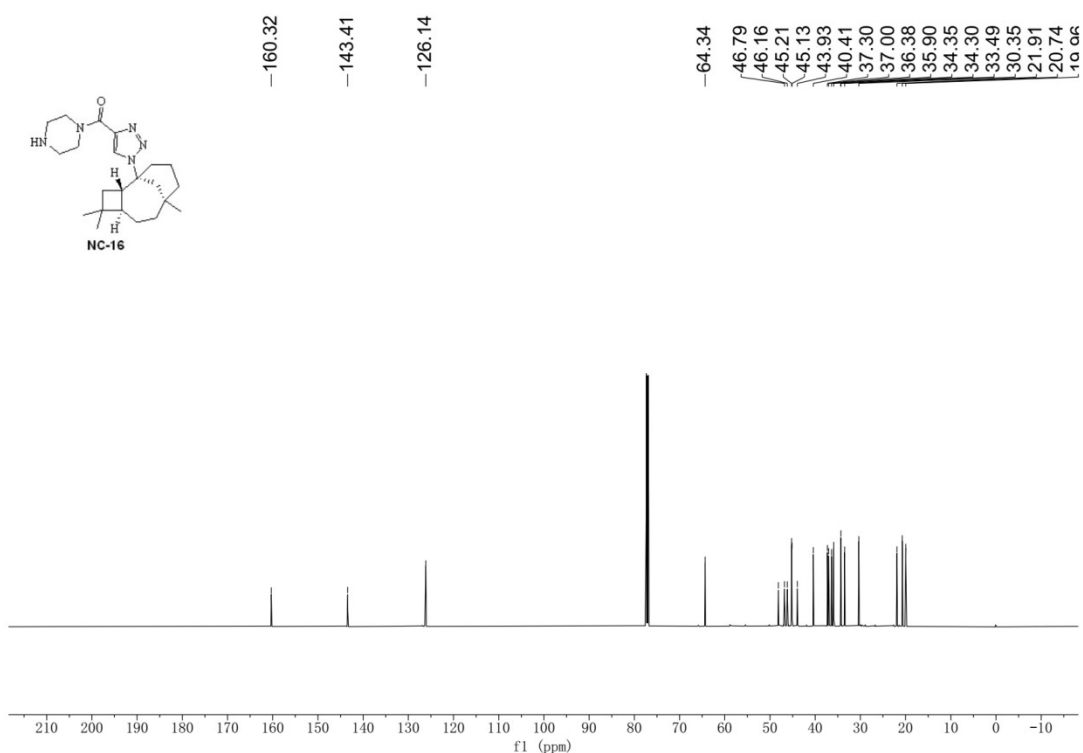
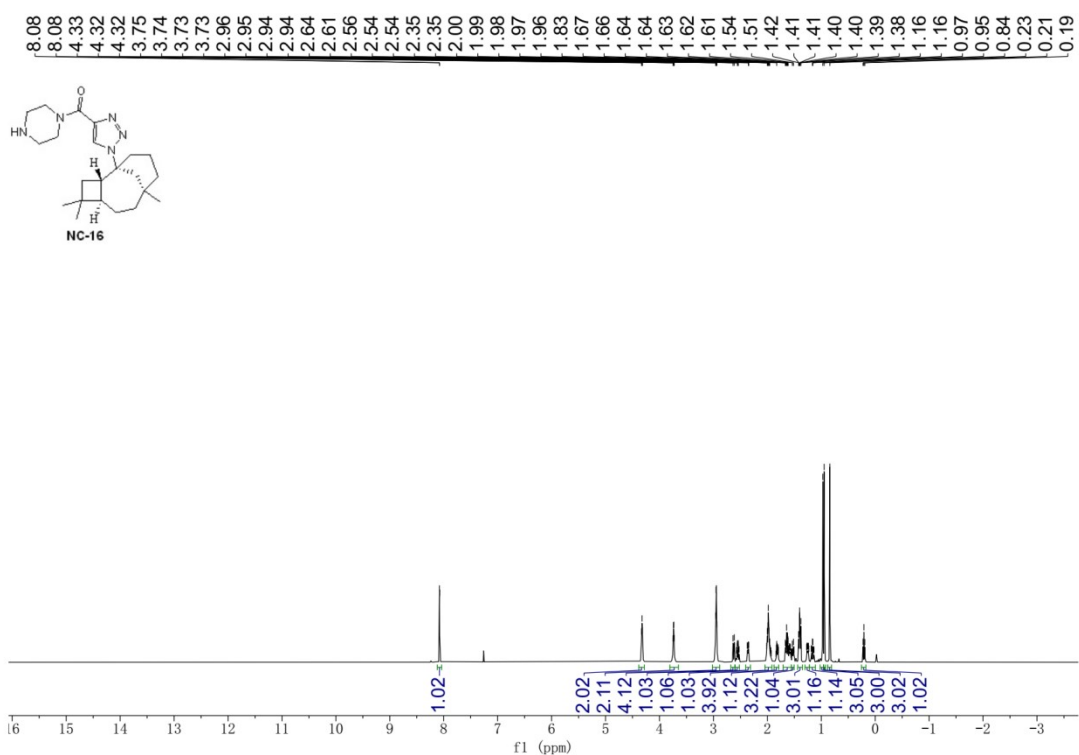
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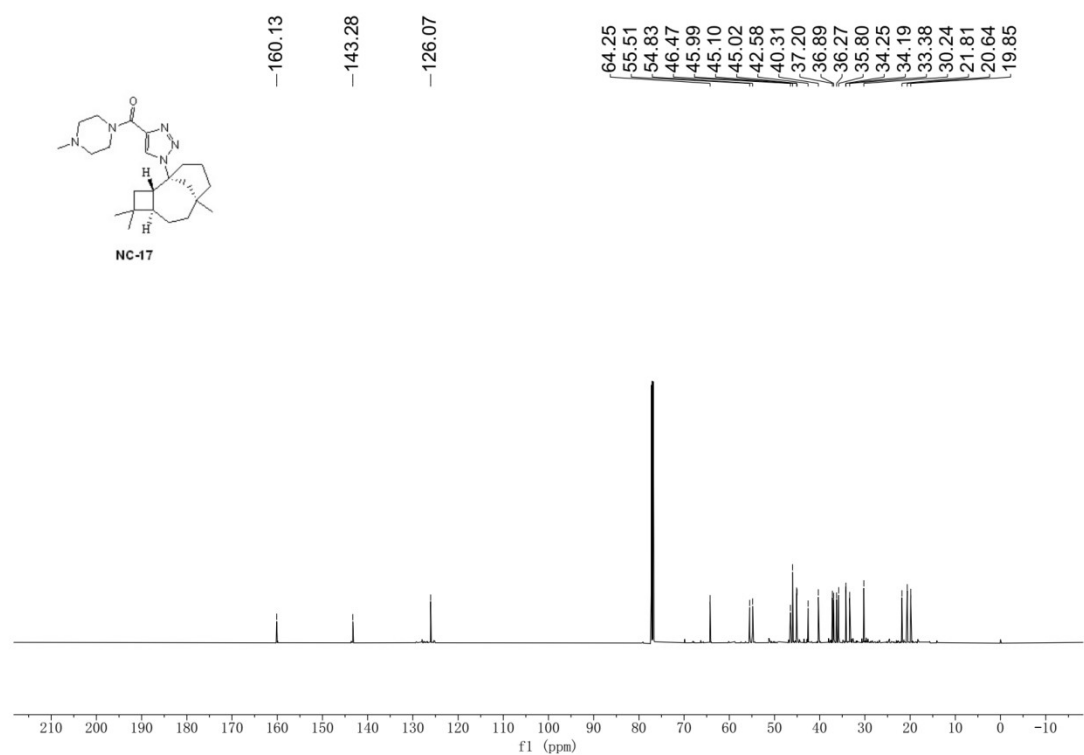
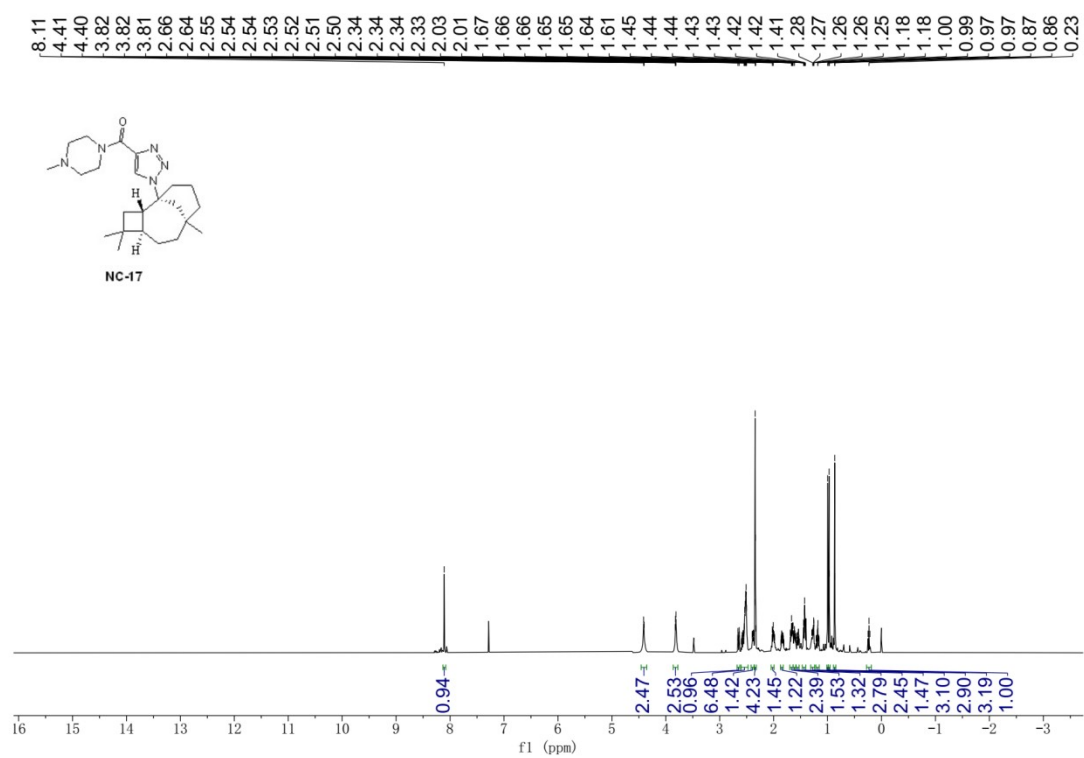
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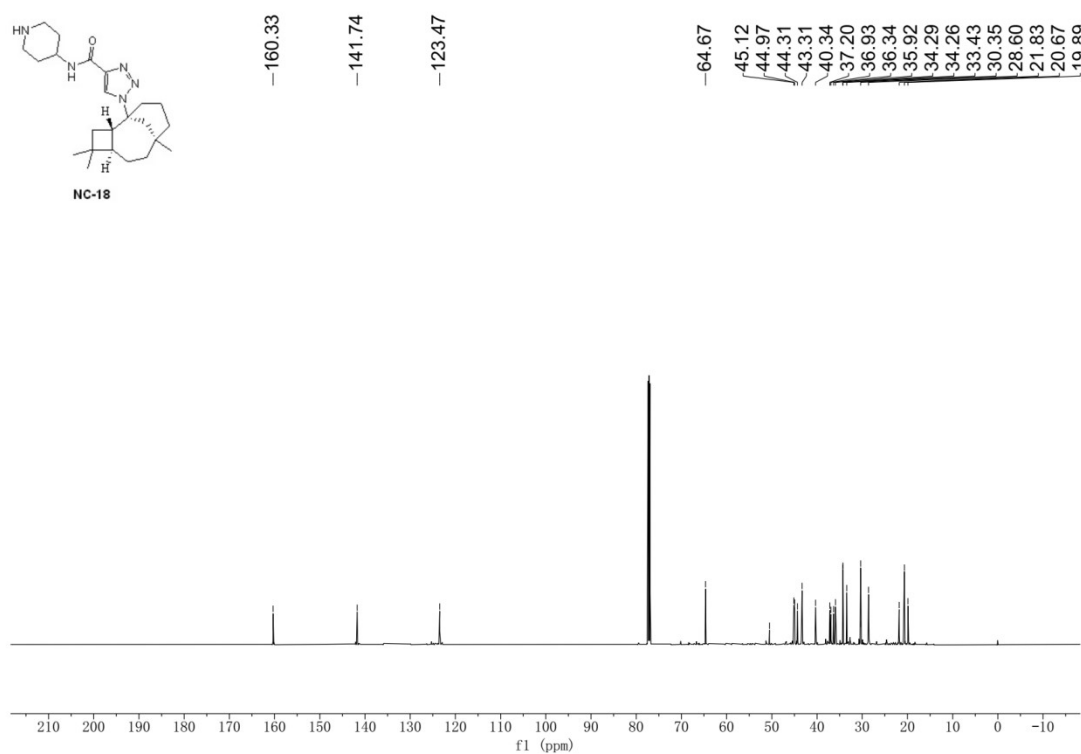
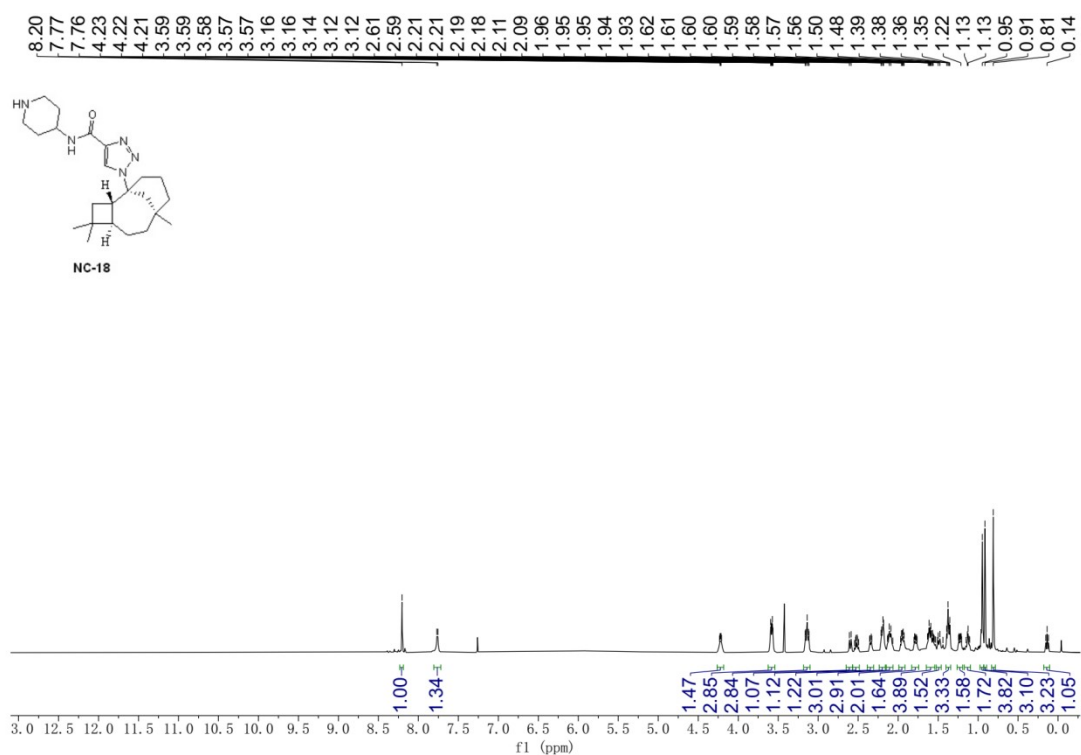
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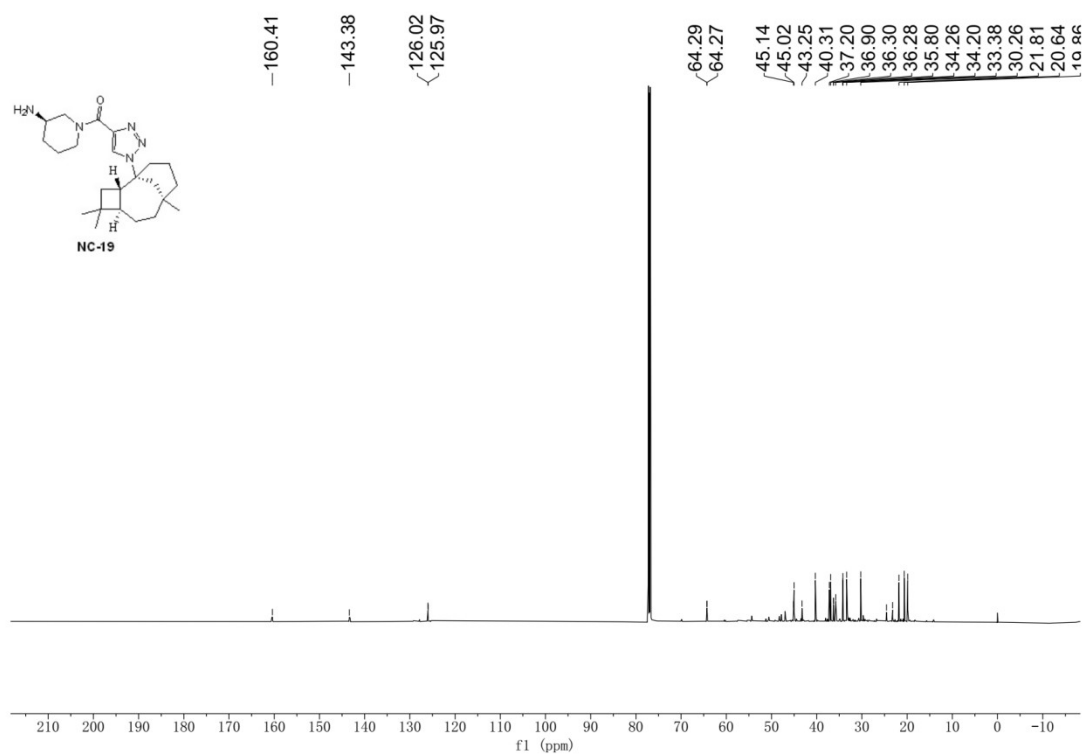
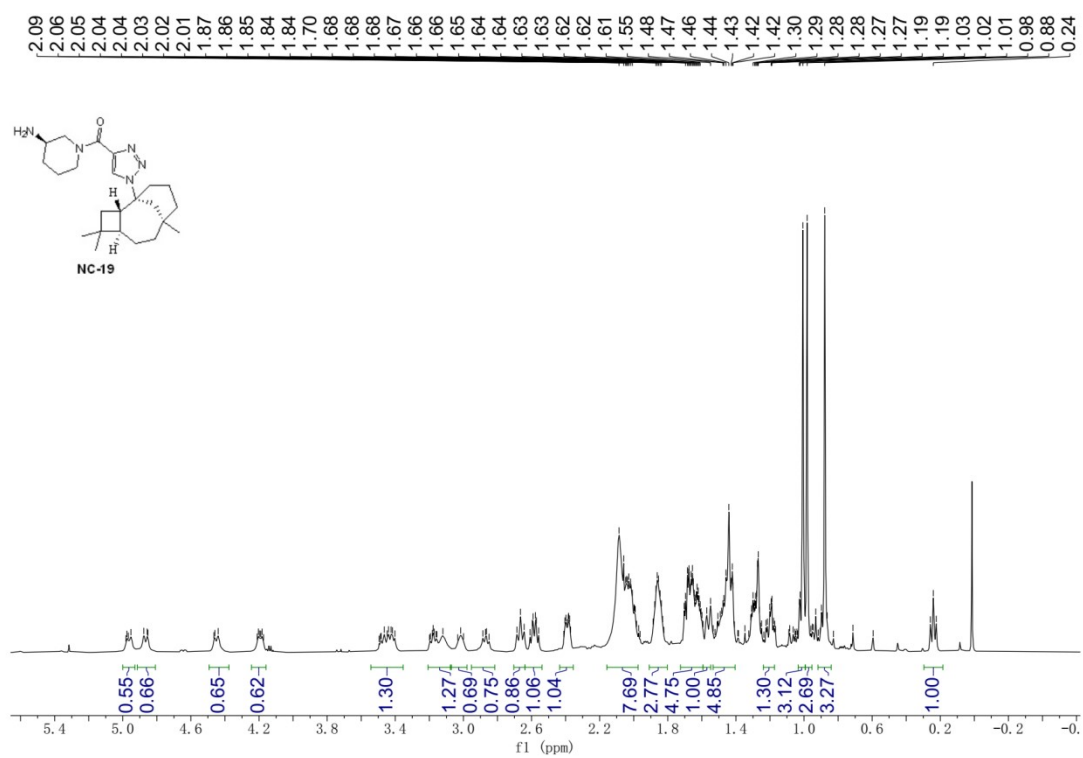
Compound NC-17



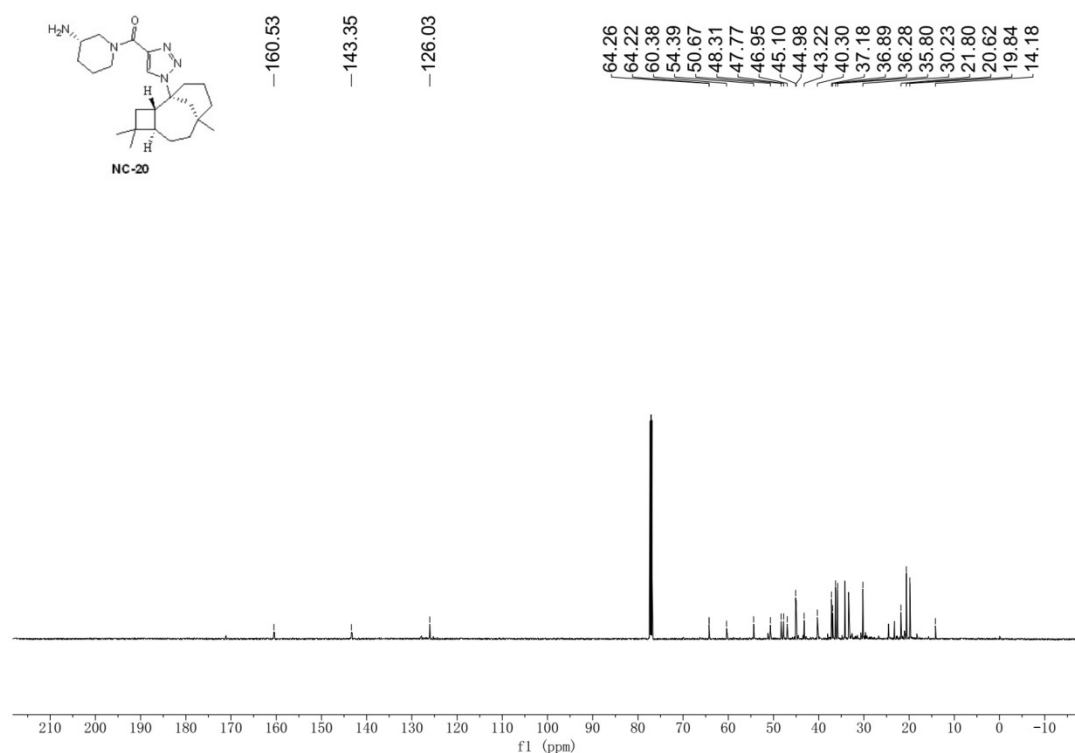
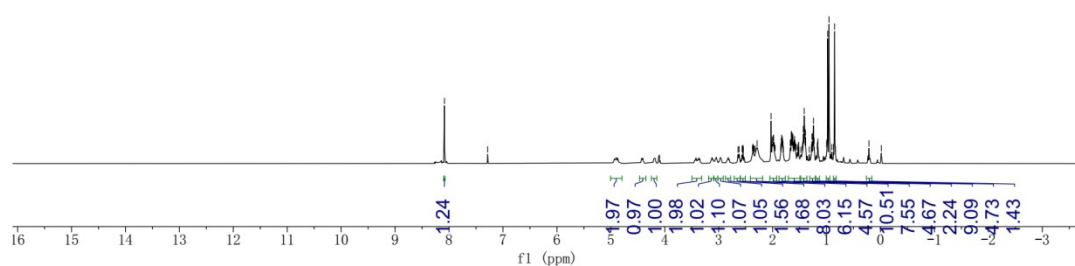
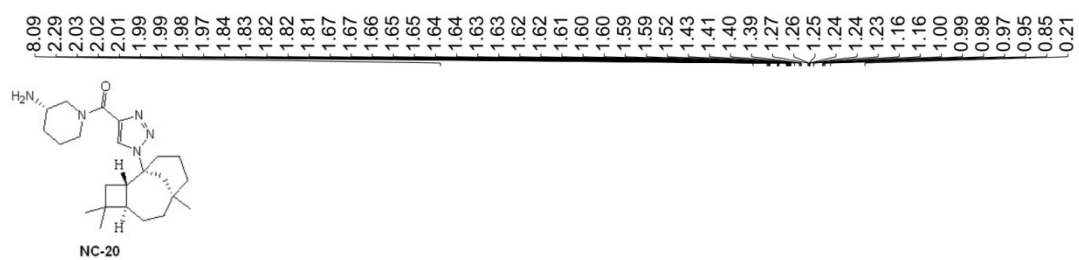
Compound NC-18



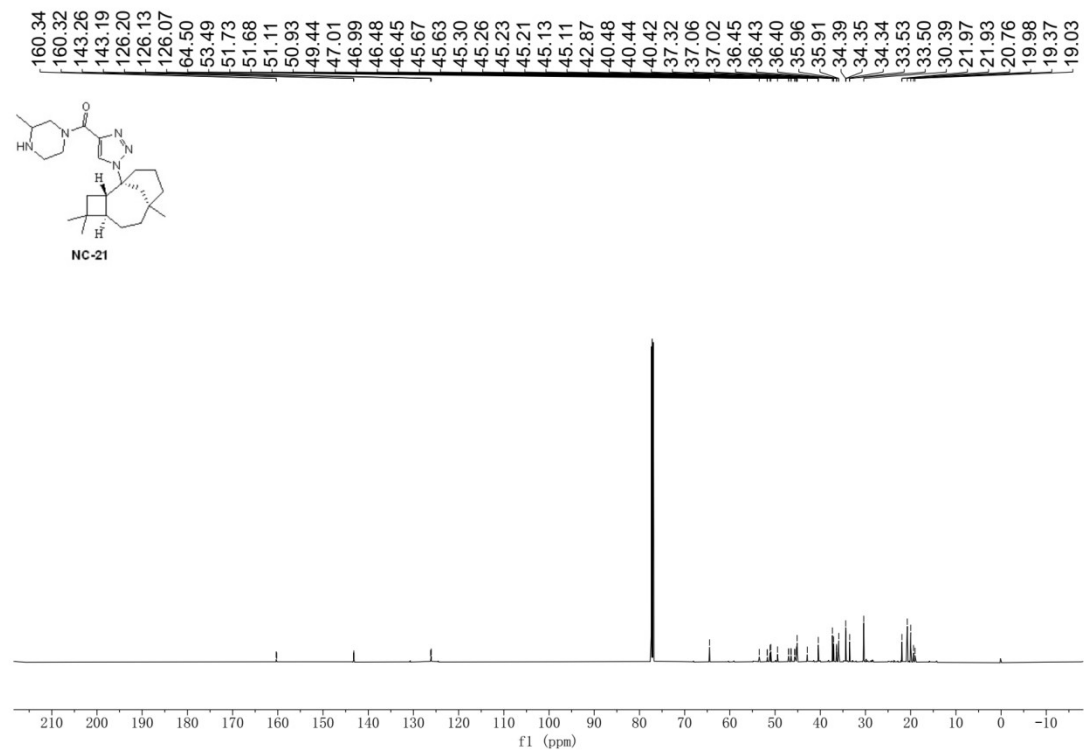
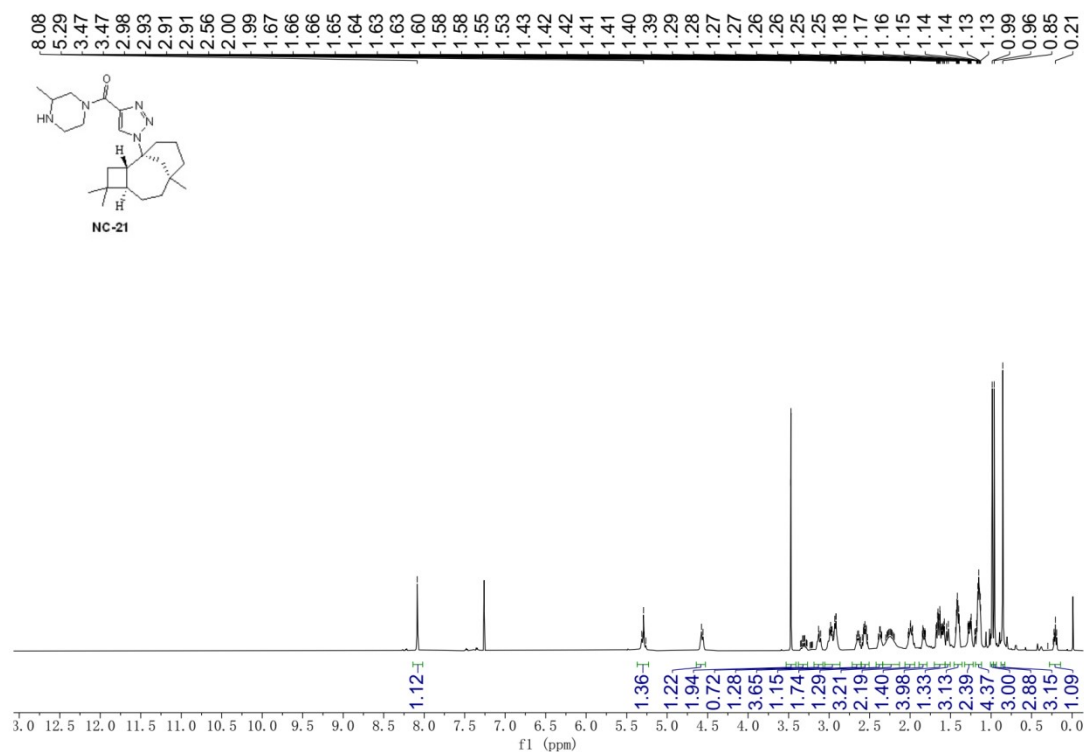
Compound NC-19



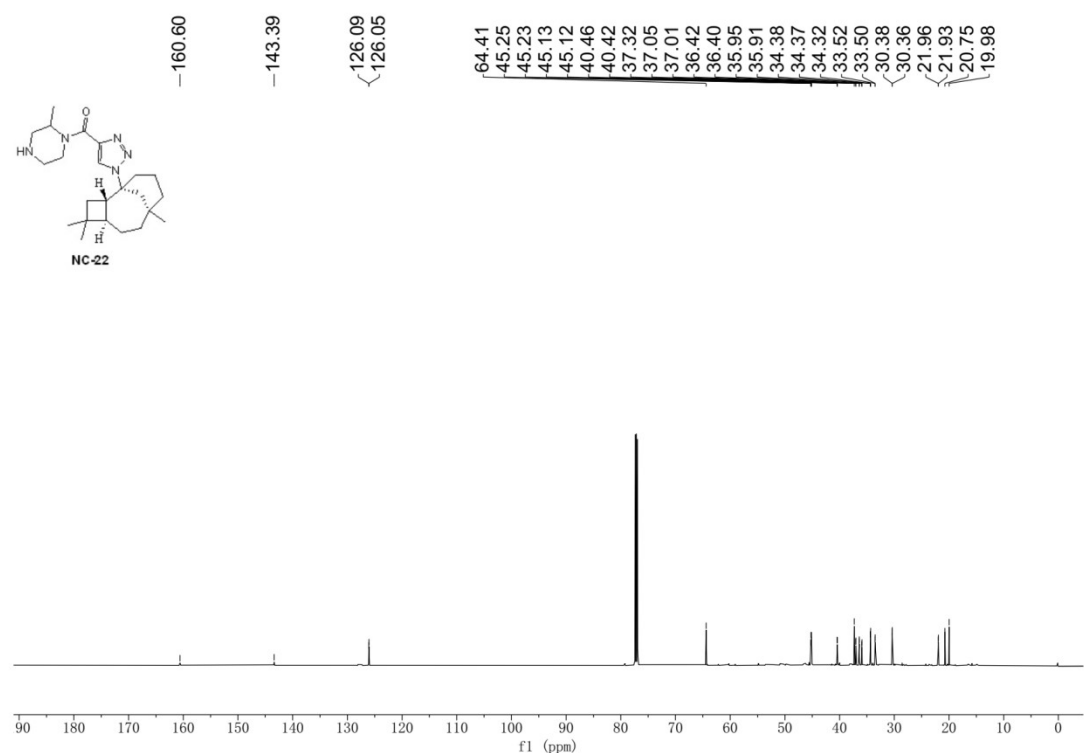
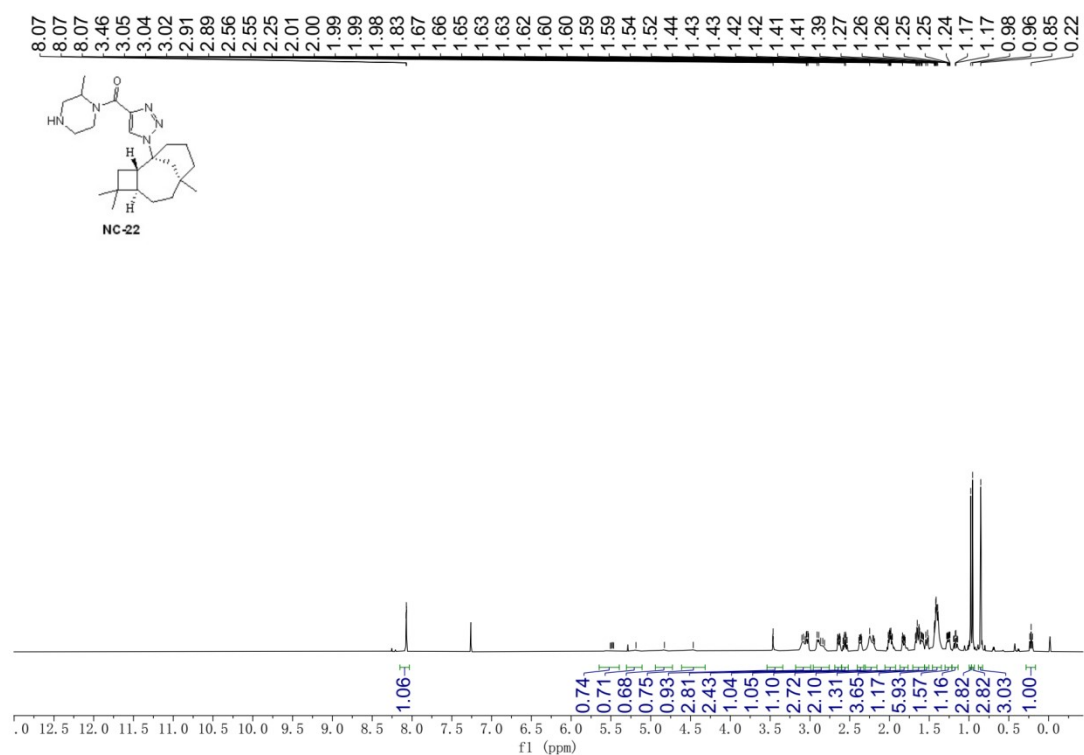
Compound NC-20



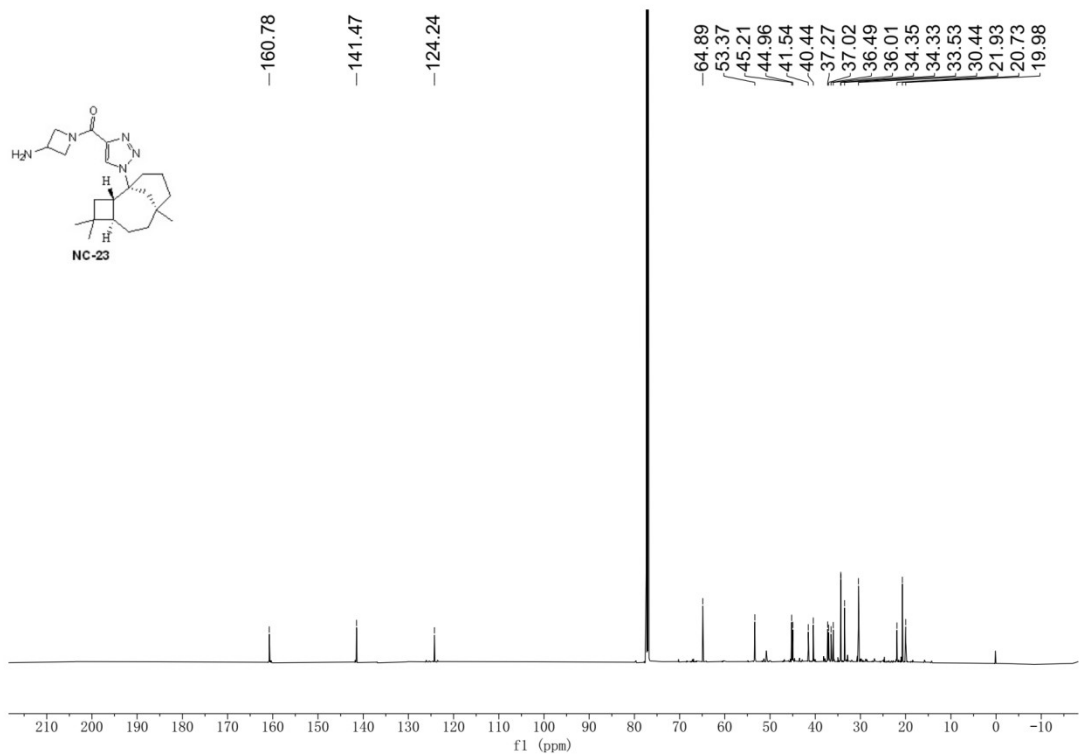
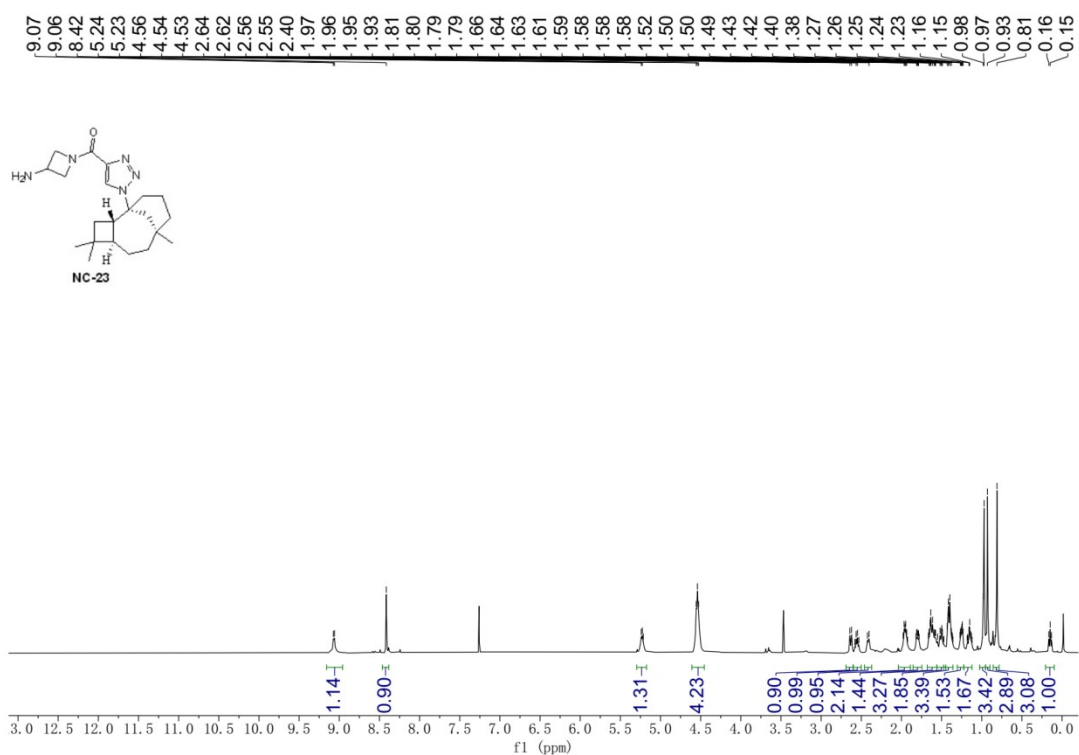
Compound NC-21



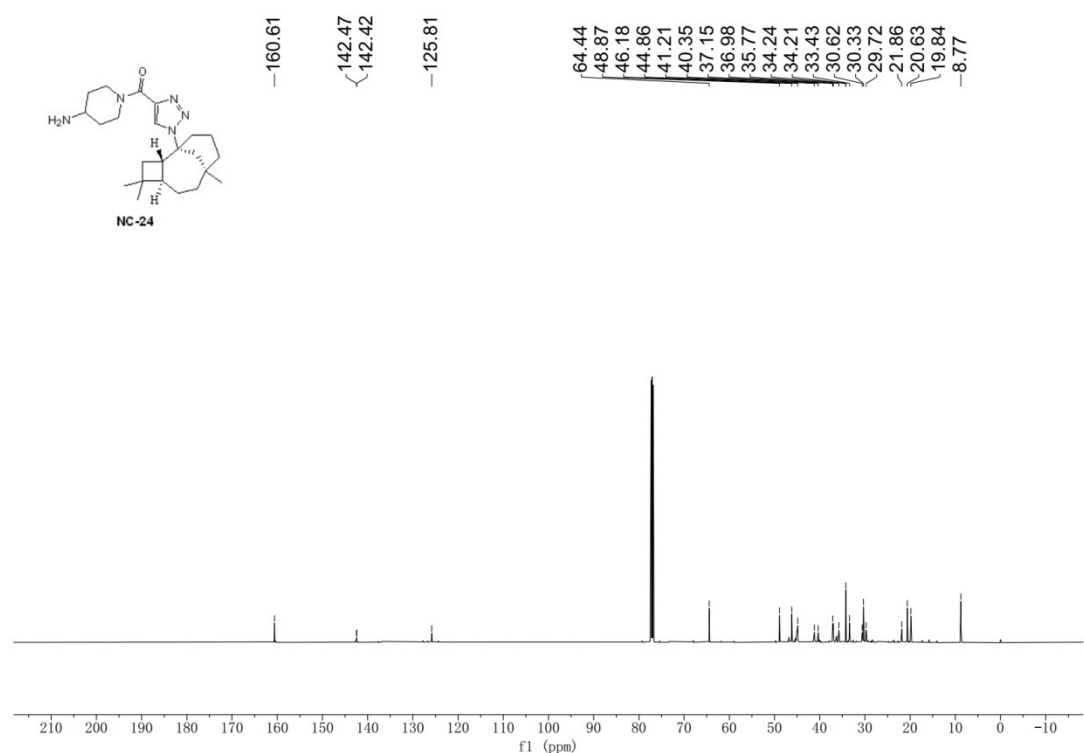
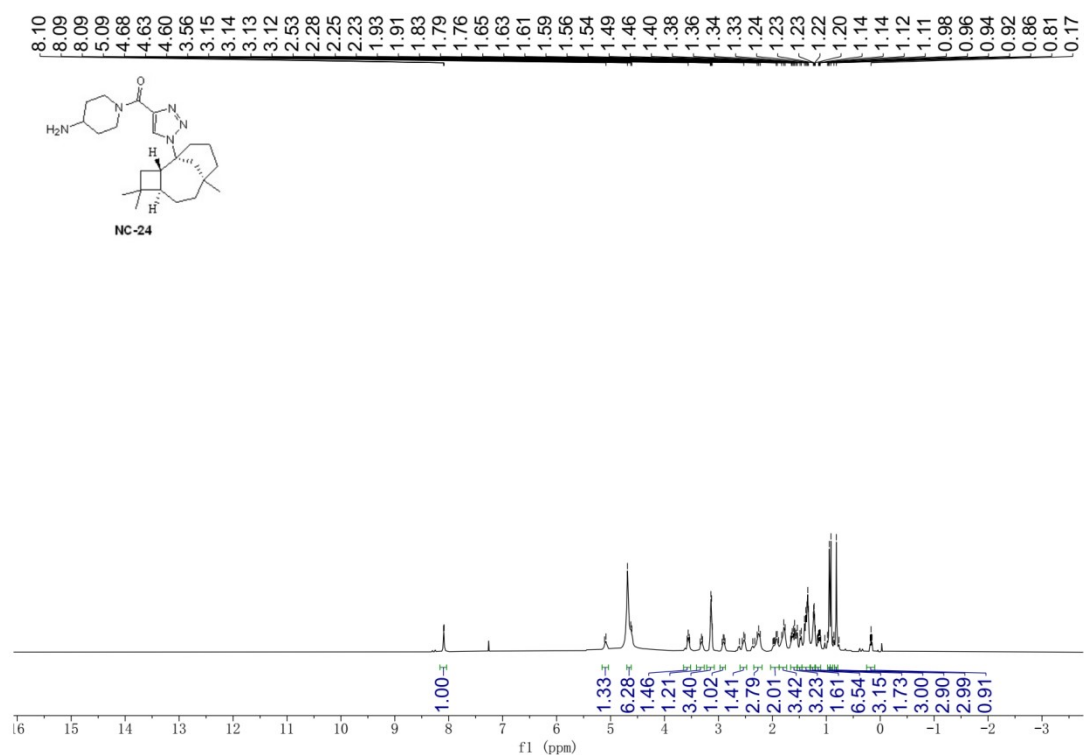
Compound NC-22



Compound NC-23

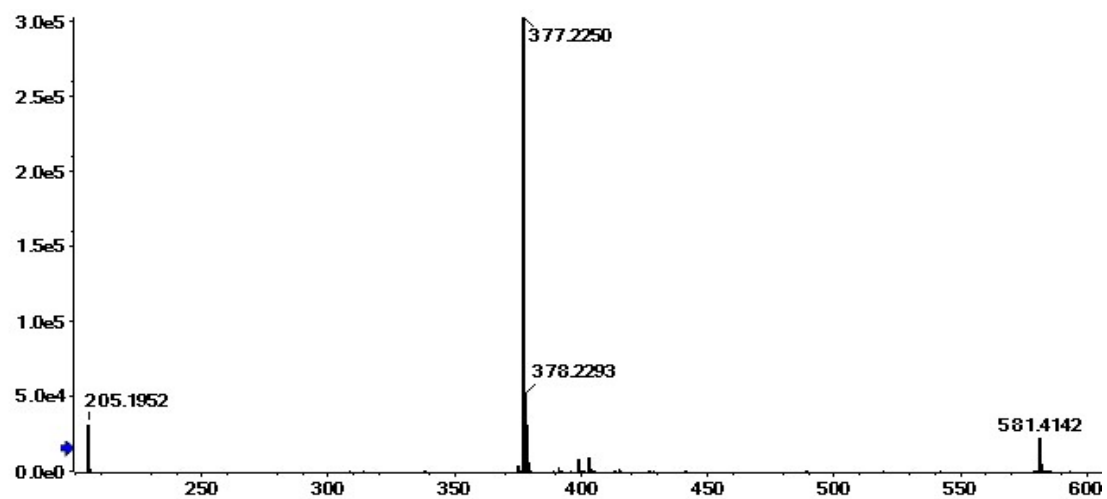


Compound NC-24

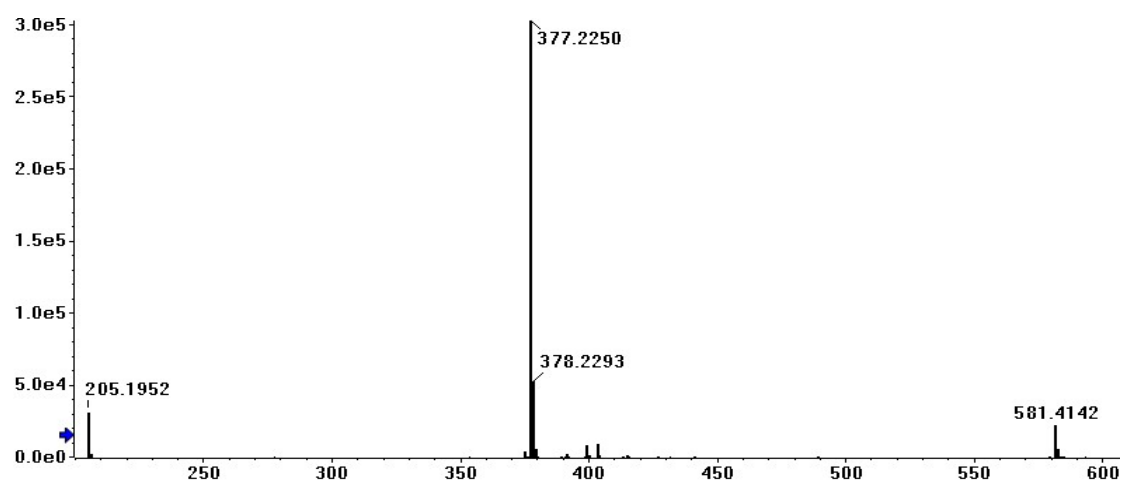


3. HRMS-ESI spectra of β -caryolane derivatives

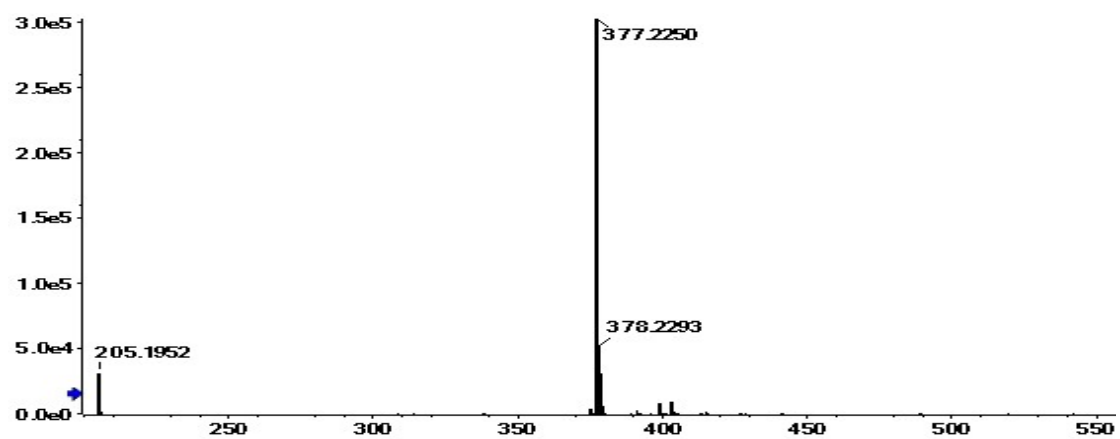
SA-13



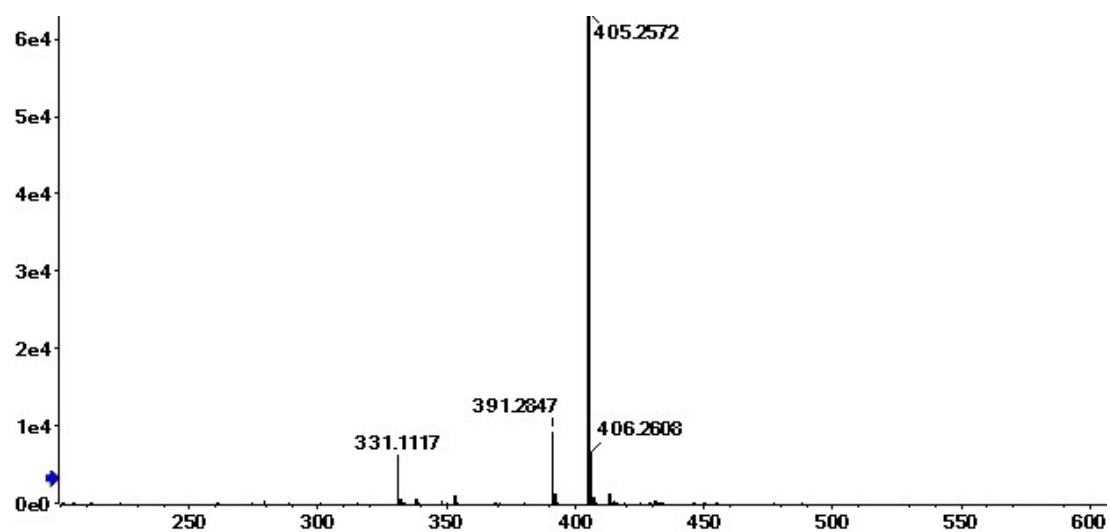
SA-14



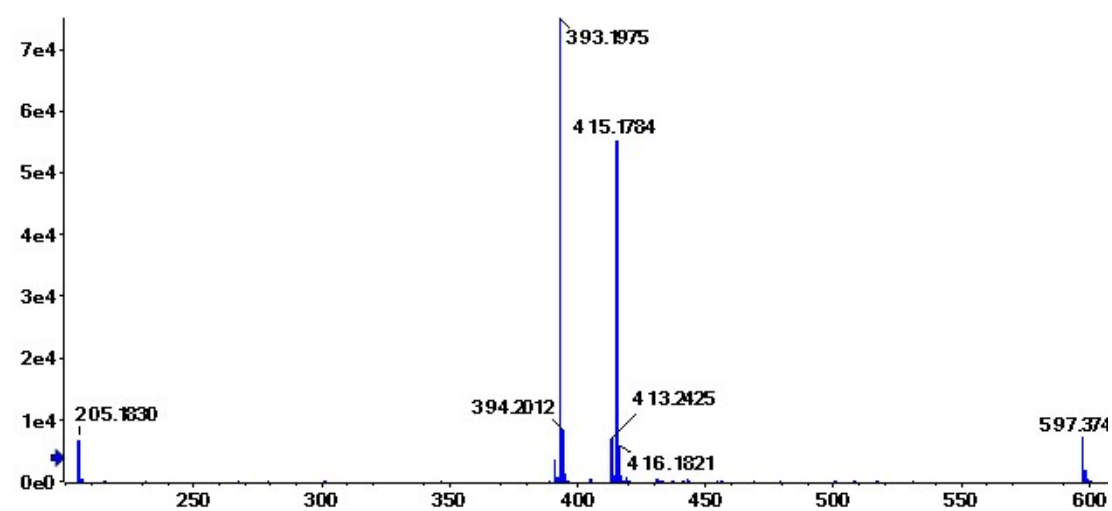
SA-15



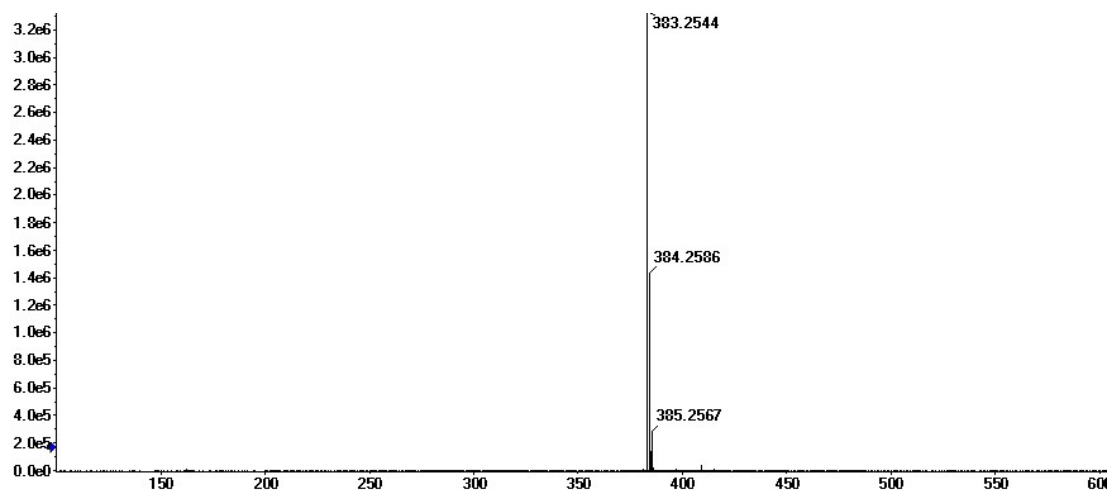
SA-16



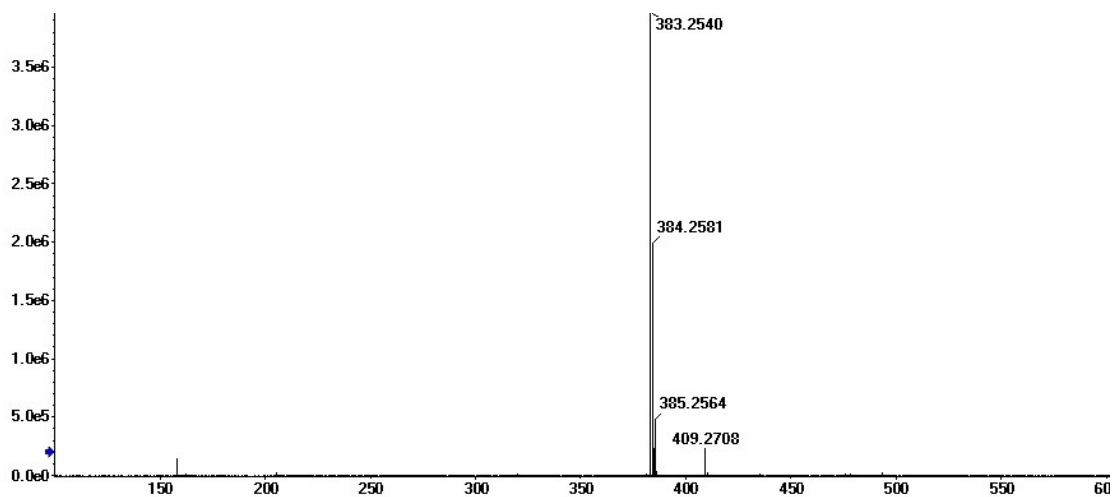
SA-17



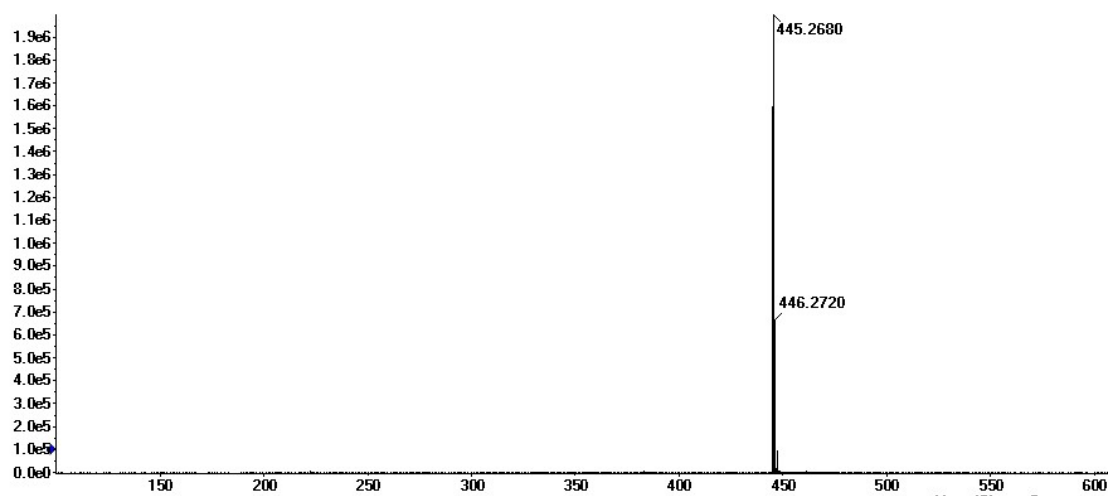
SA-29



SA-30

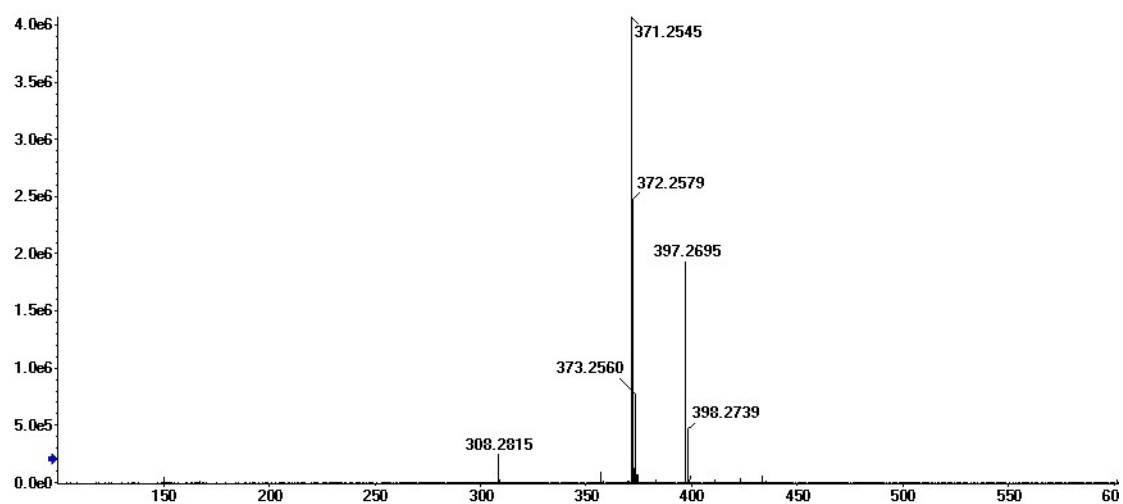


SA-31

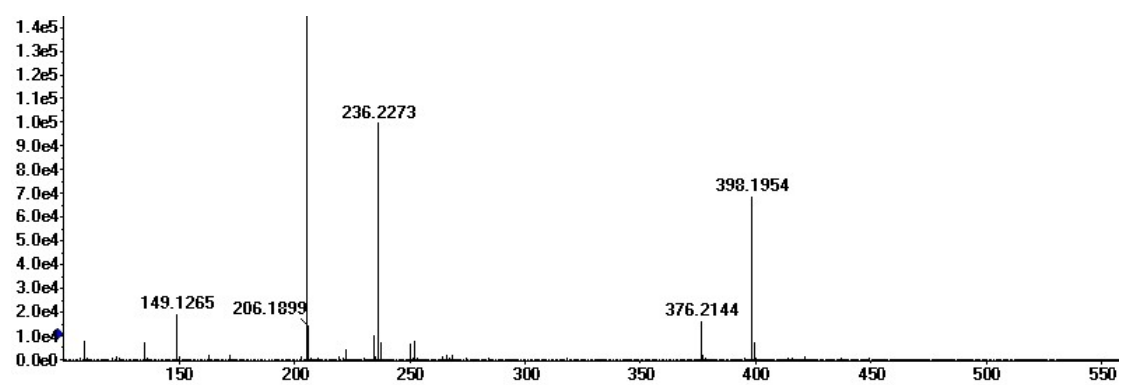


SA-32

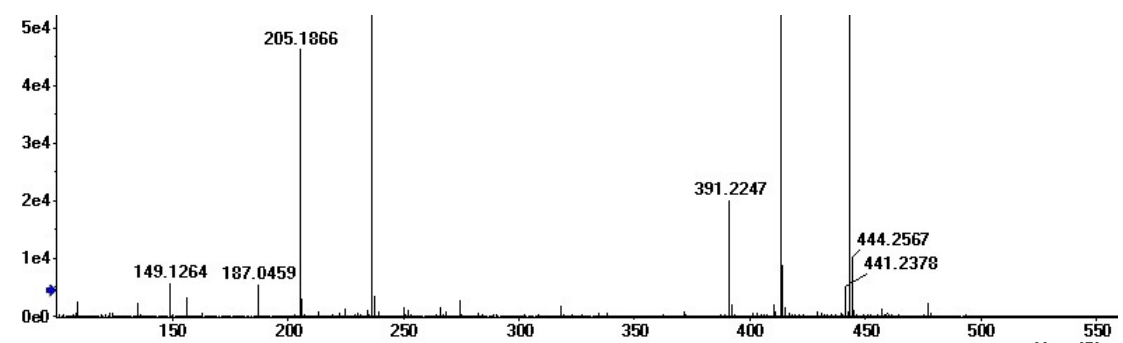
S109



SA-33

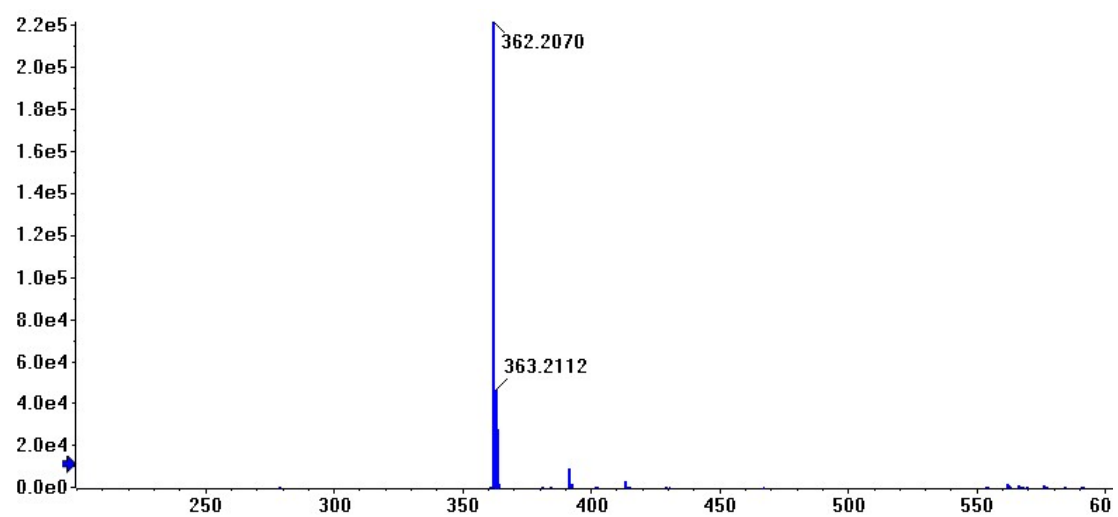


SA-34

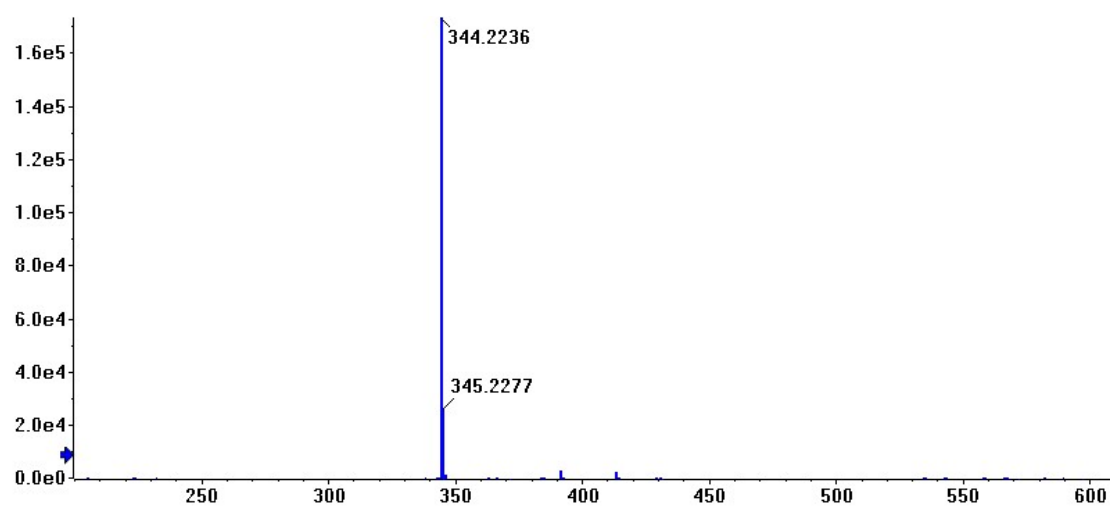


CA-1

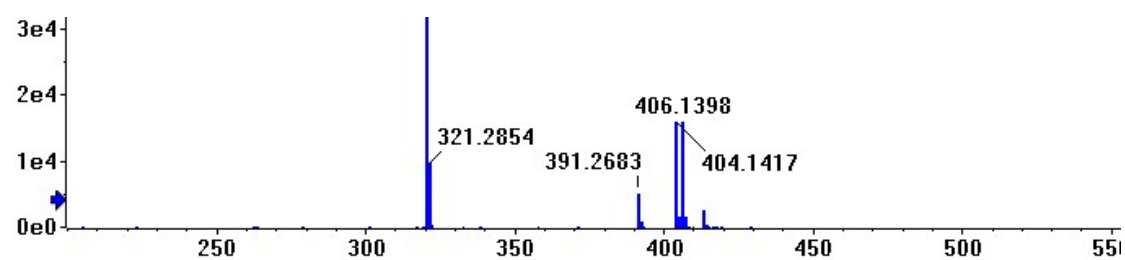
S110



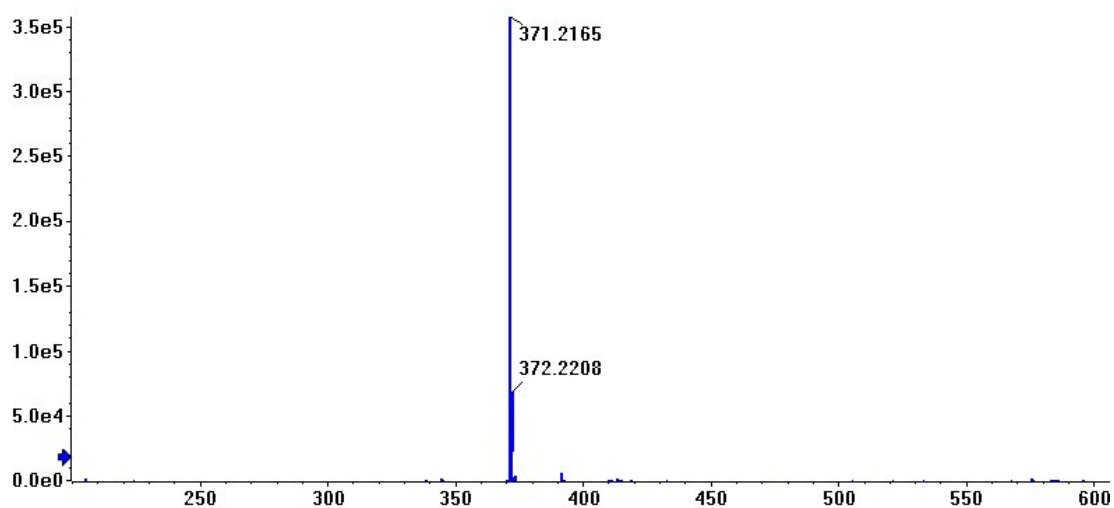
CA-2



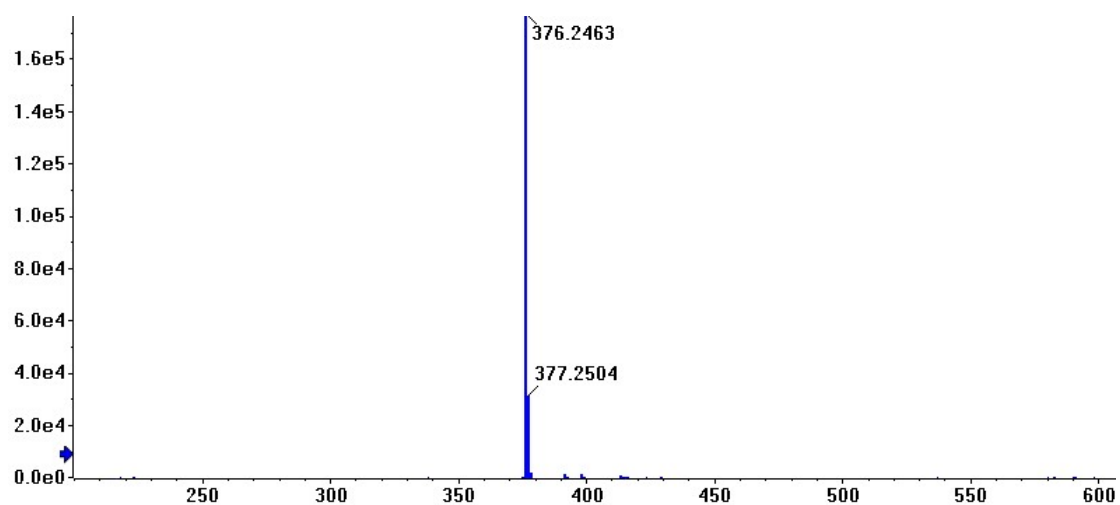
CA-7



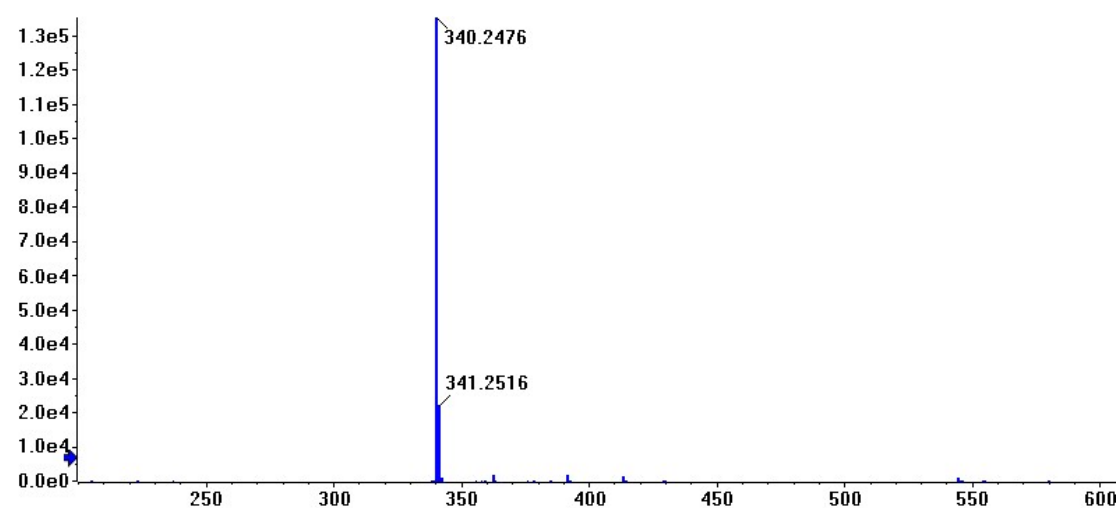
CA-8



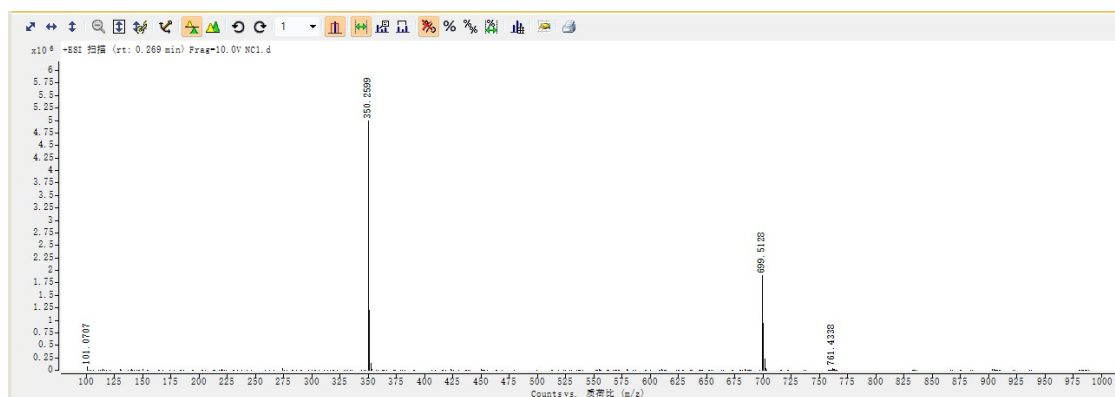
CA-9



CA-10

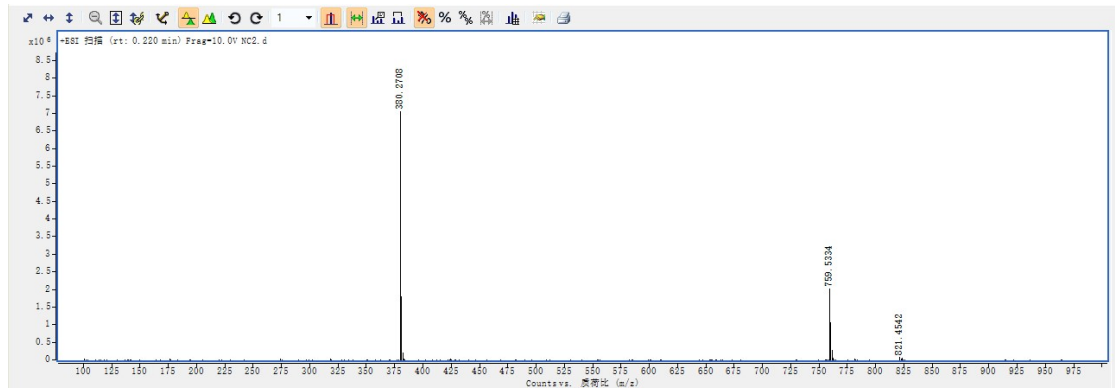


NC-1

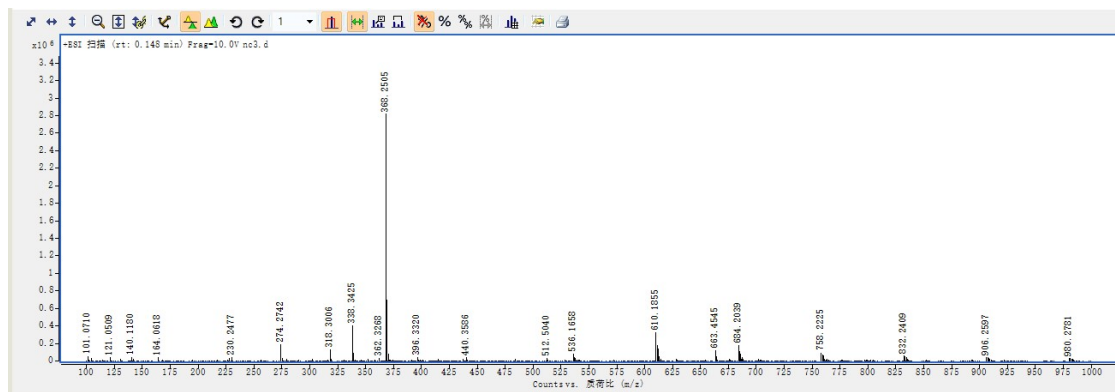


NC-2

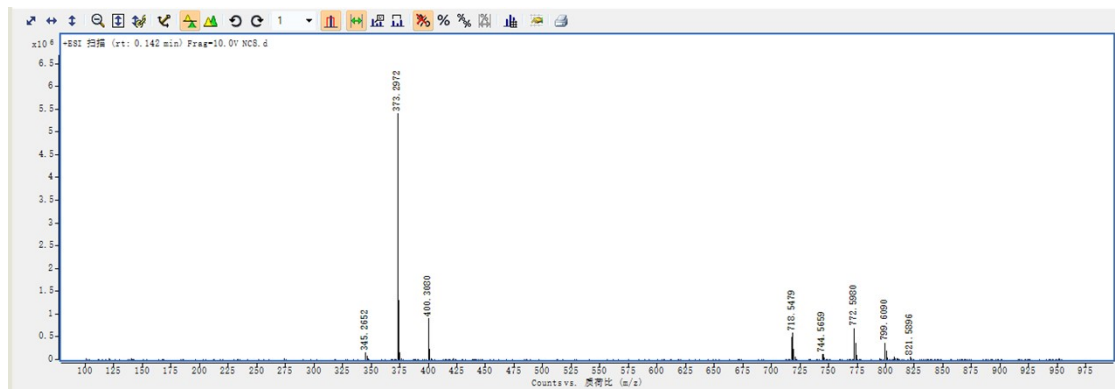
S113



NC-3

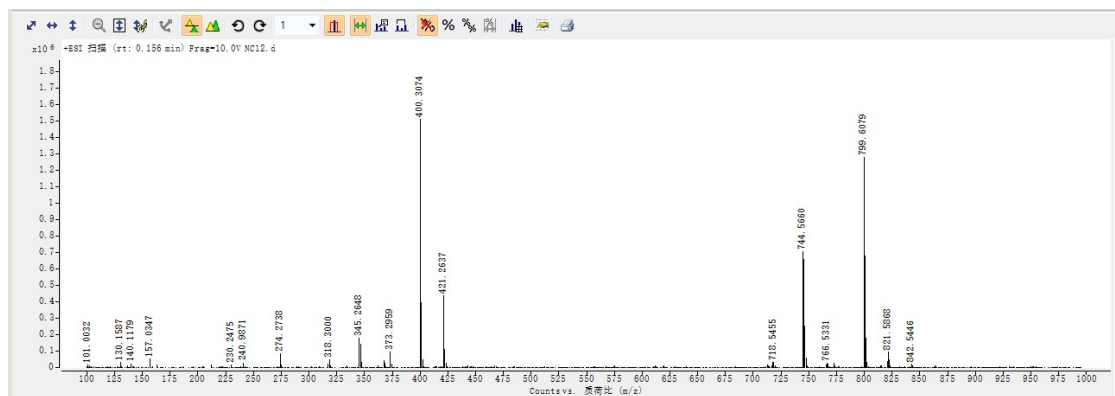


NC-4

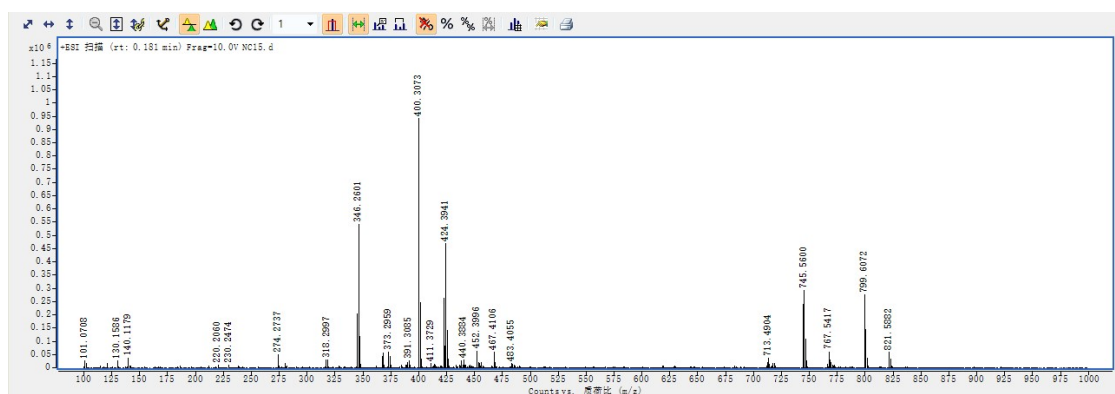


NC-5

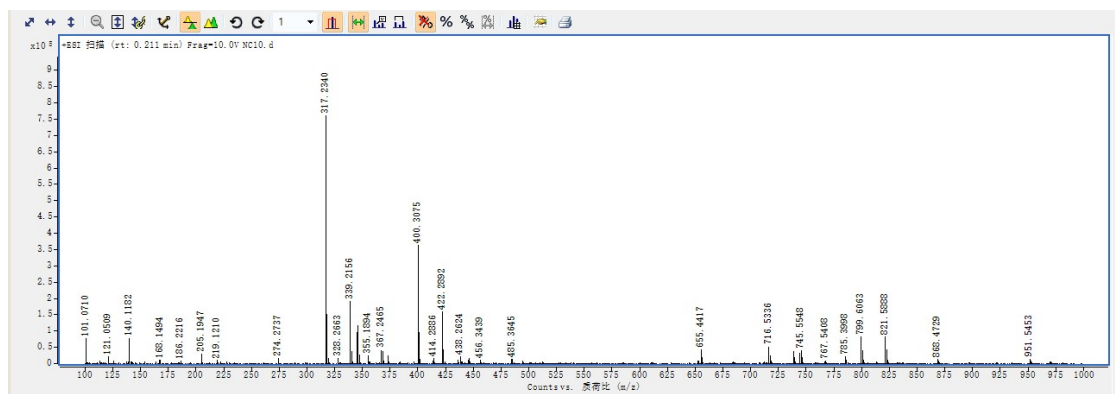
S114



NC-6

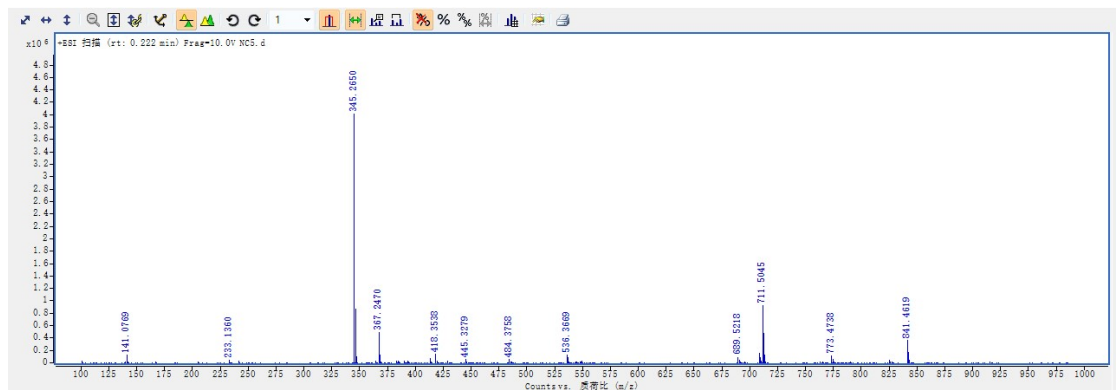


NC-7

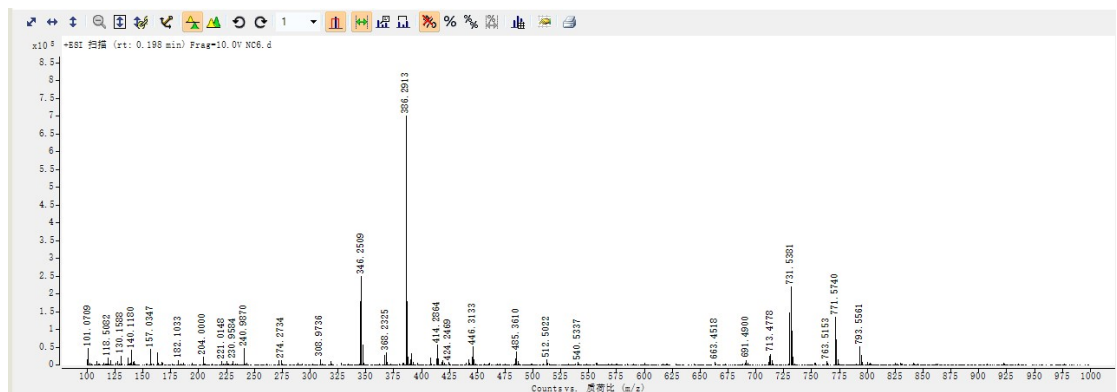


NC-8

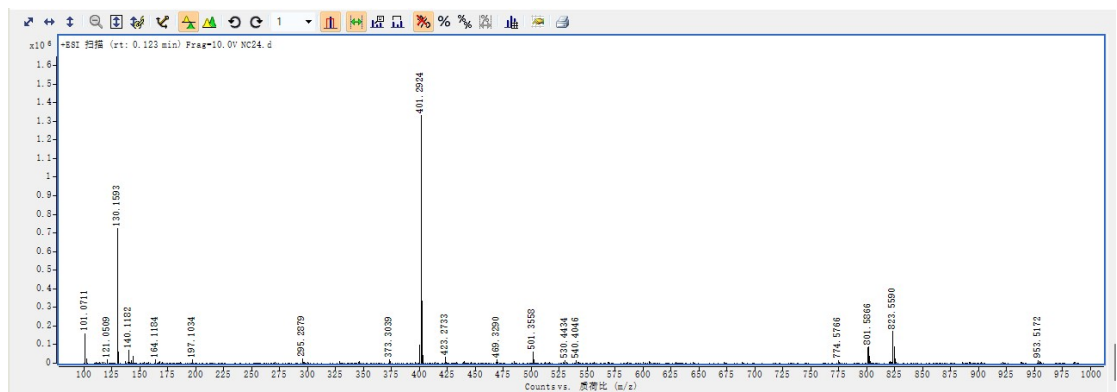
S115



NC-9

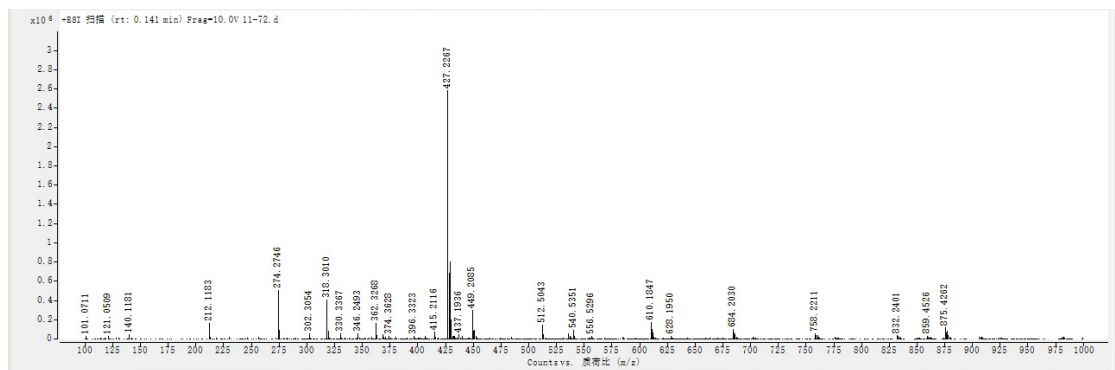


NC-10

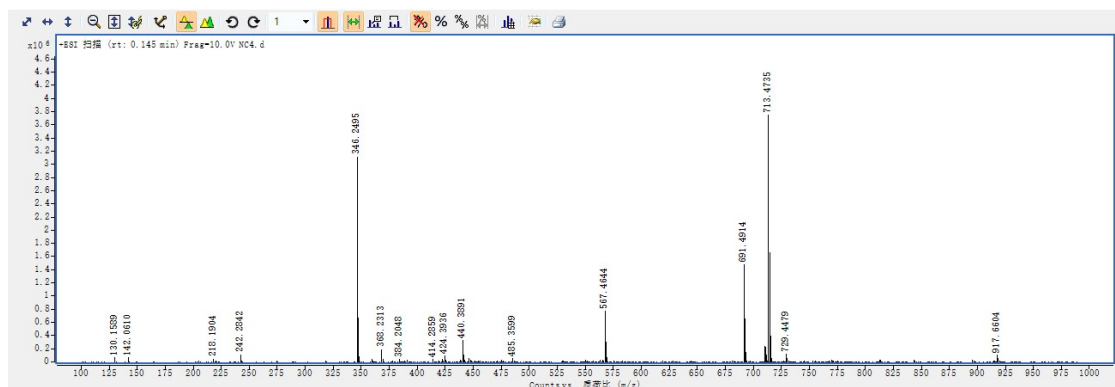


NC-11

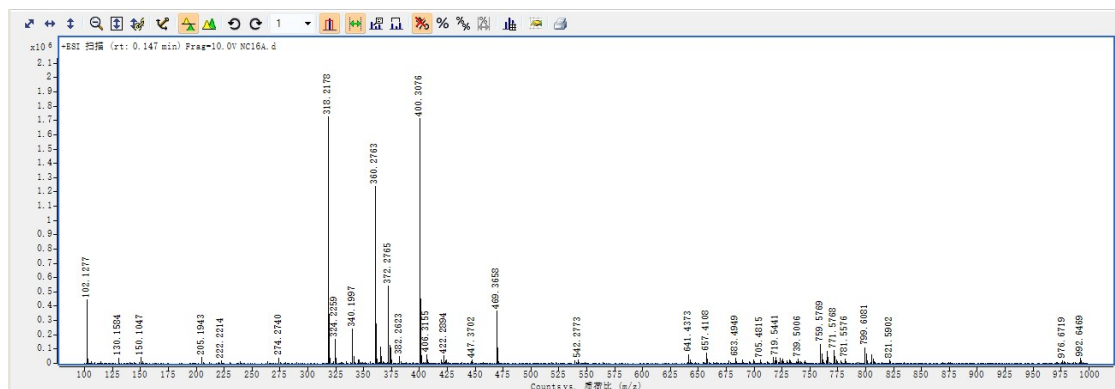
S116



NC-12

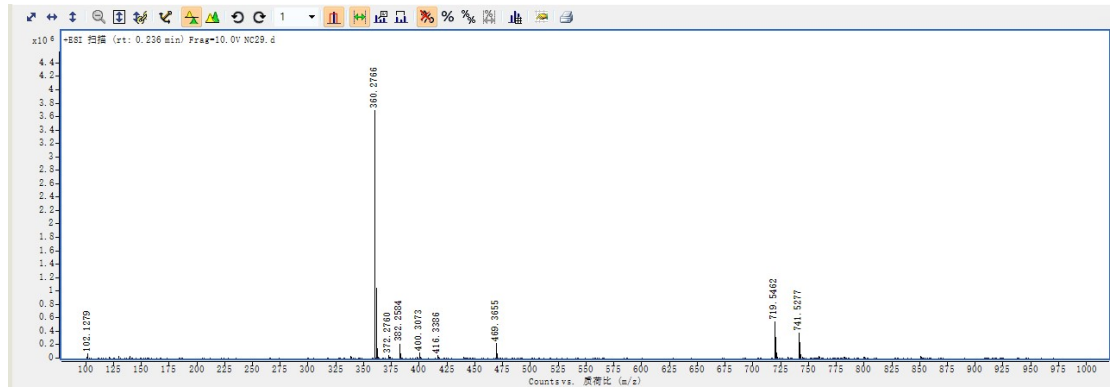


NC-13

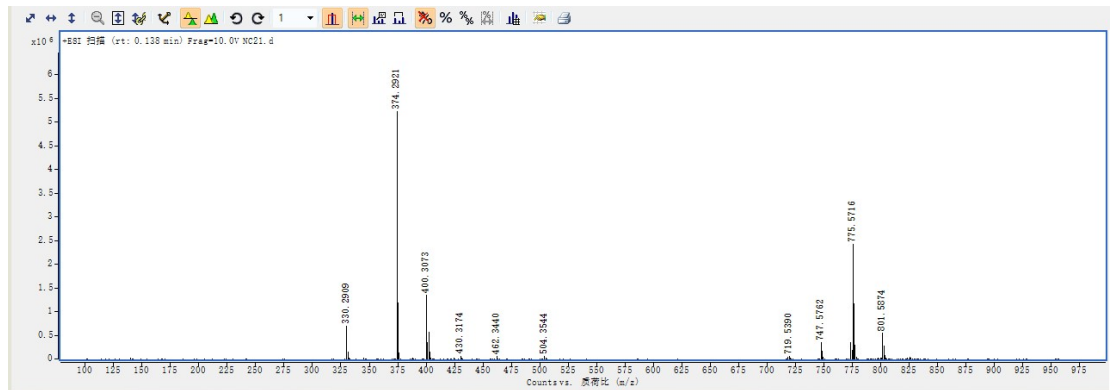


NC-14

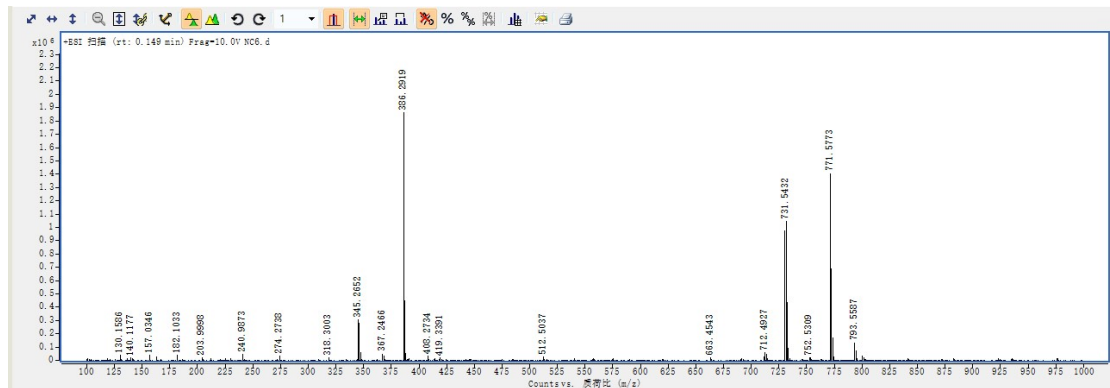
S117



NC-15

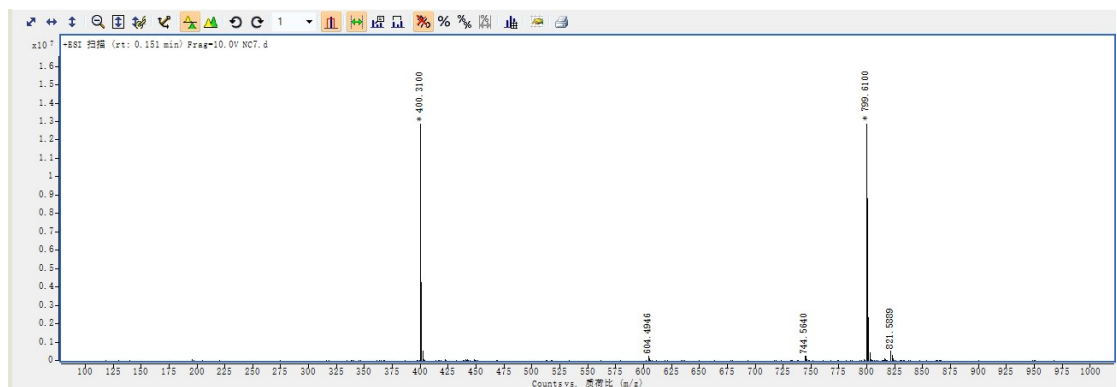


NC-16

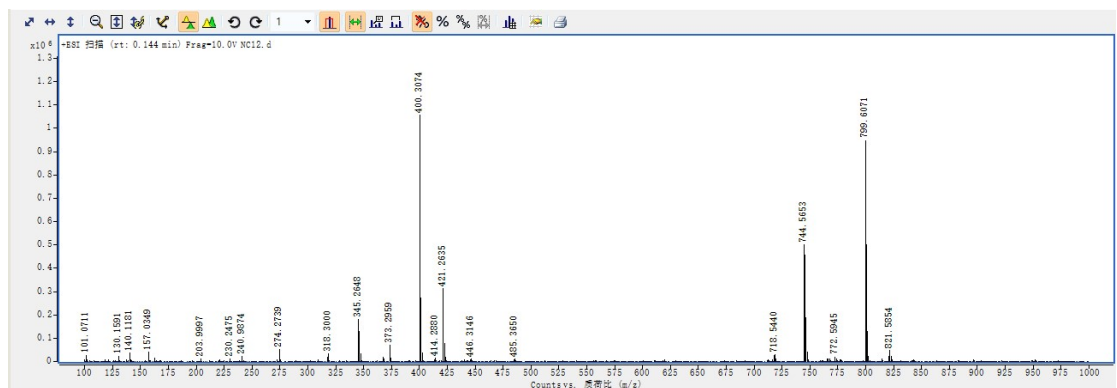


NC-17

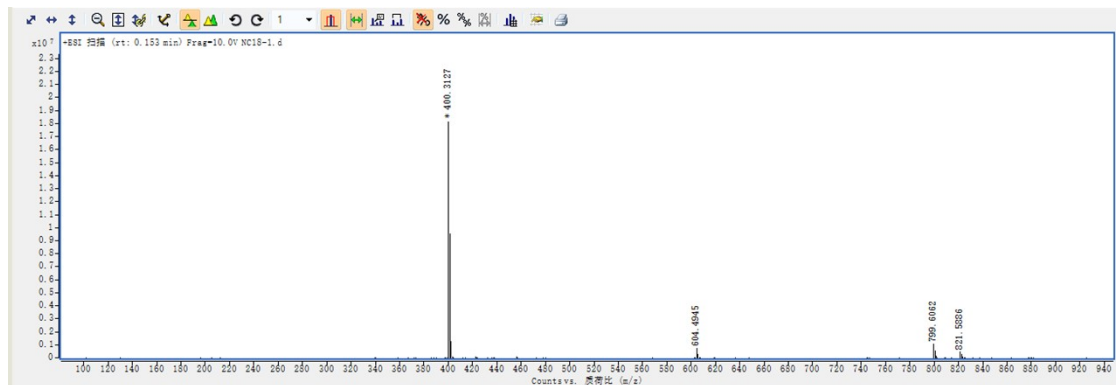
S118



NC-18

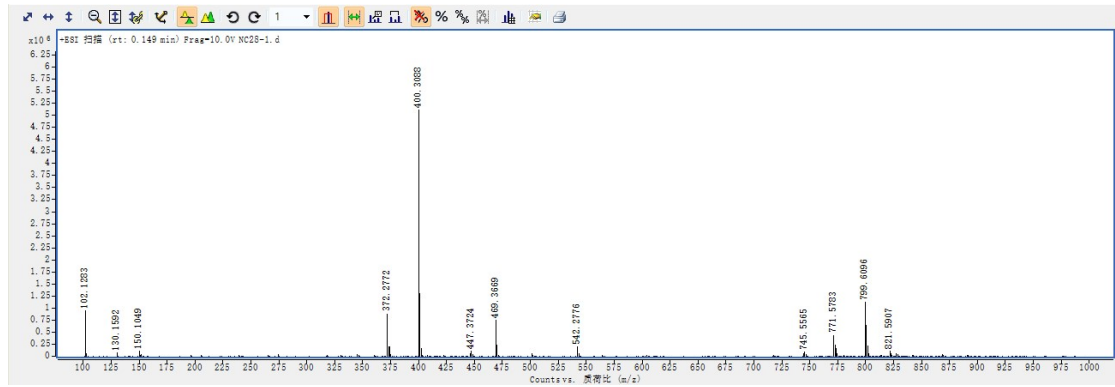


NC-19

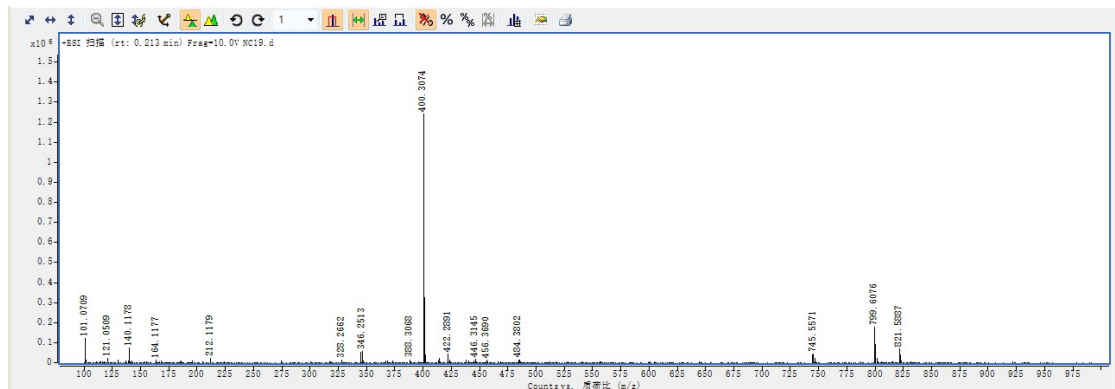


NC-20

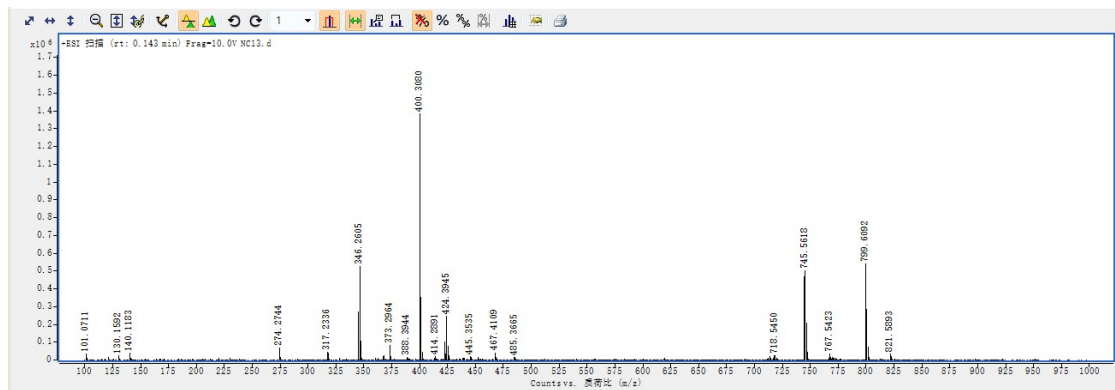
S119



NC-21

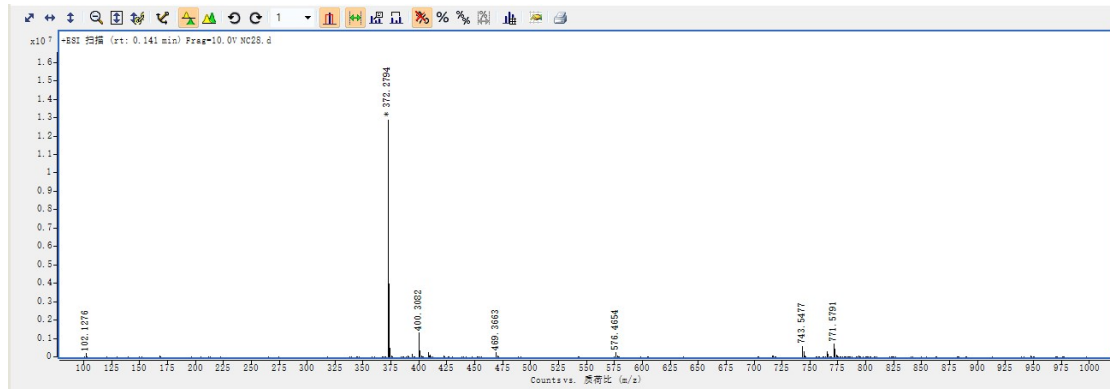


NC-22

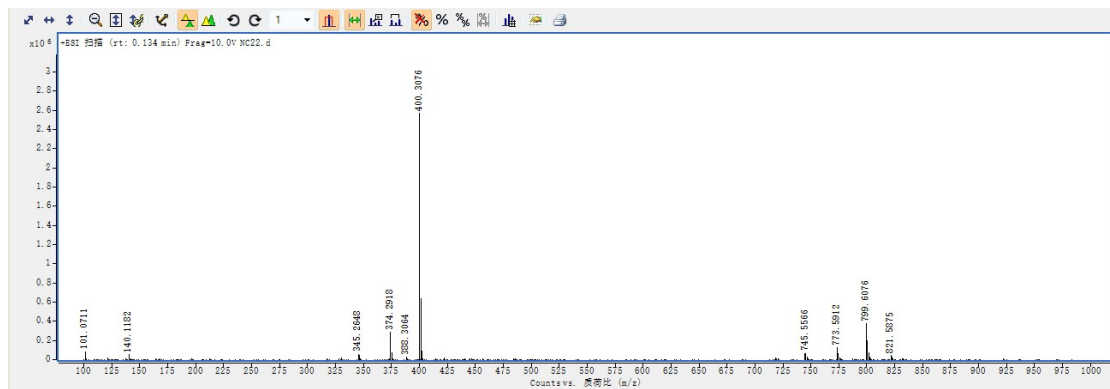


NC-23

S120



NC-24



S121