

Design, synthesis and biological evaluation of novel β -caryophyllene derivatives as potential anti-cancer agents through the ROS-mediated apoptosis pathway

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Table S1. IC₅₀ values of **AC-1** - **AC-23** and β -caryolanol determined in three human normal cell lines, LO2 normal hepatocytes, MCF-10A mammary epithelial cells, and BEAS-2B bronchial epithelial cells, with β -CP, and 5-FU as the positive control. The selectivity index (SI) was calculated as the IC₅₀ ratio. IC₅₀ values listed as >500/1000 indicate that no 50% inhibition was observed at the 500/1000 μ M dose, nor was the maximum inhibition observed.

Cmpd	IC ₅₀ (μ M)	SI=LO2/ HepG2	IC ₅₀ (μ M)	SI=MCF-10A /MCF-7	IC ₅₀ (μ M)	SI=BEAS-2B/ A549
	LO2		MCF-10A		BEAS-2B	
AC-7	24.65 $\pm$ 1.56	1.8	11.71 $\pm$ 1.51	/	11.02 $\pm$ 0.44	0.7
AC-8	36.30 $\pm$ 27.72	2.4	15.88 $\pm$ 1.42	/	14.52 $\pm$ 1.01	/
AC-9	17.52 $\pm$ 0.80	2.9	13.02 $\pm$ 1.42	1.4	14.11 $\pm$ 0.65	1.4
AC-10	7.01 $\pm$ 0.46	/	8.81 $\pm$ 0.20	/	46.36 $\pm$ 12.42	/
AC-11	17.81 $\pm$ 4.68	2.7	14.14 $\pm$ 1.21	1.7	10.77 $\pm$ 0.33	1.4
AC-12	16.27 $\pm$ 0.56	2.9	15.17 $\pm$ 1.07	1.6	14.07 $\pm$ 1.08	1.4
AC-13	6.64 $\pm$ 0.23	2.3	6.27 $\pm$ 0.16	1.4	7.44 $\pm$ 0.34	1.0
AC-14	3.79 $\pm$ 0.11	1.7	3.10 $\pm$ 0.03	0.2	3.52 $\pm$ 0.19	0.6
AC-15	1.91 $\pm$ 0.01	0.9	1.82 $\pm$ 0.04	0.4	4.49 $\pm$ 0.21	1.0
AC-16	2.90 $\pm$ 0.27	0.7	5.63 $\pm$ 0.73	1.3	6.12 $\pm$ 0.09	0.9
AC-17	13.20 $\pm$ 3.26	2.8	6.67 $\pm$ 0.18	0.5	15.31 $\pm$ 6.20	1.1
AC-18	31.06 $\pm$ 0.98	1.8	20.24 $\pm$ 0.60	/	28.95 $\pm$ 3.16	/
AC-19	25.74 $\pm$ 4.47	3.5	15.77 $\pm$ 0.97	1.2	12.93 $\pm$ 0.61	1.1
AC-20	9.64 $\pm$ 1.15	1.8	4.42 $\pm$ 0.07	0.6	9.19 $\pm$ 0.22	0.7
AC-21	28.03 $\pm$ 2.38	3.8	15.77 $\pm$ 0.97	1.4	55.763 $\pm$ 2.229	/
AC-22	14.04 $\pm$ 1.75	1.5	6.24 $\pm$ 0.19	0.6	9.00 $\pm$ 0.29	/
AC-23	25.41 $\pm$ 0.46	/	13.59 $\pm$ 0.99	/	18.32 $\pm$ 1.20	/
β-CP	400.74 $\pm$ 37.07	1.4	> 1000	/	221.90 $\pm$ 6.07	1.1

<i>β</i>-Caryolanol	61.45 ± 6.55	0.6	97.37 ± 4.22	1.0	>500	/
5-FU	0.37 ± 0.02	0.3	4.42 ± 0.07	21	3.89 ± 0.28	1.7

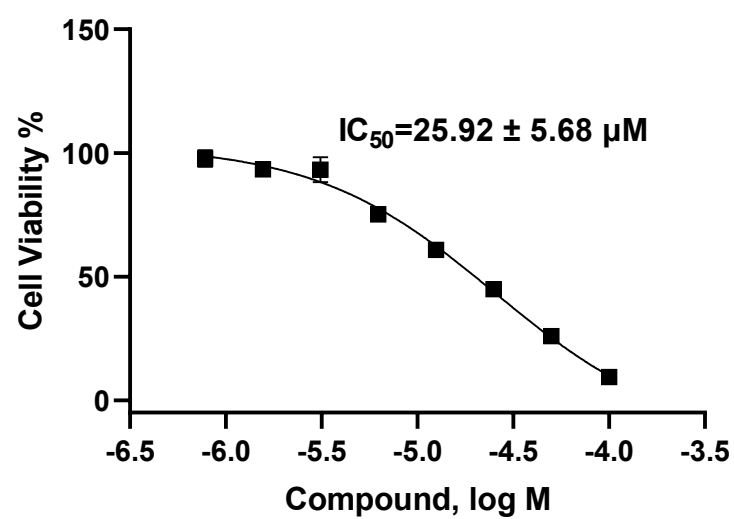
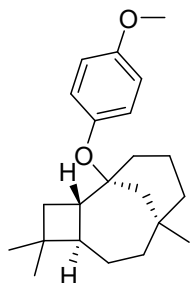


Figure S1. Cell viability of HT-29 after treatment with LY294002.

Characterization data of synthetic compounds

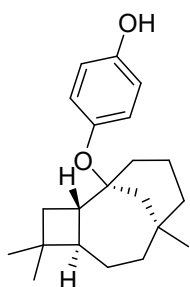
(1*R*,2*S*,5*R*,8*S*)-1-(4-methoxyphenoxy)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecane (**AC -1**).



According to the genenal procedure, compound **AC-1** could be obtained with 70% yield as white solid using β -Caryophyllene and 4-methoxyphenol as substrates;

¹H NMR (400 MHz, CDCl₃) δ 6.88 – 6.81 (m, 2H), 6.81 – 6.74 (m, 2H), 3.78 (s, 3H), 2.46 – 2.34 (m, 1H), 2.07 – 1.97 (m, 1H), 1.89 – 1.74 (m, 4H), 1.73 – 1.65 (m, 2H), 1.58 (m, 2H), 1.38 (m, 3H), 1.21 – 1.15 (m, 1H), 1.13(d, $J = 9.6$ Hz, 1H), 1.05(s, 3H), 1.04 (s, 3H), 1.02 – 0.95 (m, 1H), 0.89 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 153.76, 147.91, 122.81, 112.64, 79.20, 54.49, 45.77, 44.20, 39.60, 36.19, 36.11, 35.64, 33.94, 33.76, 33.70, 32.40, 29.38, 21.12, 19.95, 19.86.

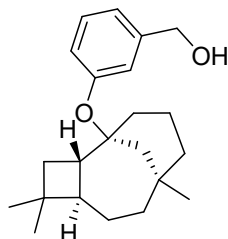
4-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)phenol (**AC -2**).



According to the genenal procedure, compound **AC-2** could be obtained with 70% yield as white solid using β -Caryophyllene and Hydroquinone as substrates; ¹H NMR (400 MHz, CDCl₃) δ 6.77 – 6.72 (m, 2H), 6.71 – 6.65 (m, 2H), 2.42 – 2.32 (m, 1H), 2.04 – 1.95 (m, 1H), 1.84-1.76 (m, 2H), 1.72-1.65 (m, 3H), 1.54 – 1.48 (m, 3H), 1.36 – 1.32 (m, 3H), 1.17 – 1.12 (m, 1H), 1.12 – 1.07 (m, 2H), 1.02 (s, 3H), 1.01 (s, 3H), 0.86 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 151.18 , 148.43 , 124.16 , 115.32 , 80.41 , 46.72 , 45.16 , 40.49 , 37.22, 37.15, 36.58 , 35.00 , 34.76, 34.74, 33.44 , 30.42 , 22.09 , 21.01,

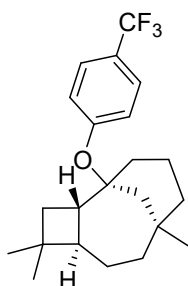
20.91.

(3-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)phenyl)methanol (**AC-3**).



According to the general procedure, compound **AC-3** could be obtained with 70% yield as white solid using β -Caryophyllene and 3-Hydroxybenzyl alcohol as substrates; ¹H NMR (400 MHz, CDCl₃) δ 7.16 (t, J = 7.9 Hz, 1H), 6.87 (m, 2H), 6.74 – 6.63 (m, 1H), 5.08 (s, 1H), 4.44 (d, J = 12.1 Hz, 1H), 4.32 (d, J = 12.1 Hz, 1H), 2.28 – 2.18 (m, 1H), 1.91 (m, 1H), 1.87 – 1.77 (m, 2H), 1.75 – 1.71 (m, 2H), 1.64 (d, J = 9.6 Hz, 1H), 1.52 (ddd, J = 10.3, 6.1, 2.5 Hz, 2H), 1.45 – 1.37 (m, 2H), 1.37 – 1.25 (m, 2H), 1.21 (d, J = 12.8 Hz, 1H), 1.16 – 1.05 (m, 2H), 1.00 (s, 6H), 0.89 (d, J = 2.8 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.64, 142.21, 129.39, 119.15, 113.93, 113.85, 63.82, 46.93, 46.00, 40.41, 37.75, 37.69, 36.78, 35.28, 34.69, 34.60, 33.92, 30.50, 22.76, 20.95, 20.64.

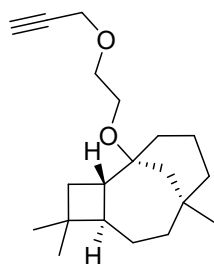
(1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyl-1-(4-(trifluoromethyl)phenoxy)tricyclo[6.3.1.0^{2,5}]dodecane (**AC-4**).



According to the general procedure, compound **AC-4** could be obtained with 91% yield as white solid using β -Caryophyllene and 4-(trifluoromethyl)phenol as substrates; ¹H NMR (400 MHz, CDCl₃) 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). ¹³C NMR (101 MHz,

CDCl₃) δ 158.86, 125.95 (q, $J=3.7$ Hz), 122.82 (t, $J=40.5$ Hz), 120.11, 81.92, 47.63, 46.15, 42.60, 38.87, 38.32, 36.06, 35.68, 34.67, 34.52, 33.43, 30.21, 23.12, 20.75, 20.69.

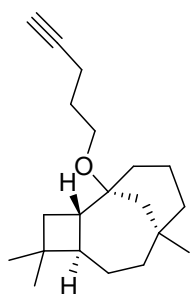
(1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyl-1-(2-(prop-2-yn-1-yloxy)ethoxy)tricyclo[6.3.1.0^{2,5}]dodecane (**AC-5**).



According to the genenal procedure, compound **AC-5** could be obtained with 70% yield as white solid using β -Caryophyllene and Propynol ethoxylate as substrates;

¹H NMR (400 MHz, CDCl₃) δ 4.22 (d, $J=2.4$ Hz, 2H), 3.64 (dd, $J=8.0, 3.2$ Hz, 2H), 3.61 – 3.54 (m, 1H), 3.40 (dt, $J=10.2, 5.1$ Hz, 1H), 2.41 (t, $J=2.4$ Hz, 1H), 2.19 – 2.09 (m, 1H), 1.88 – 1.81 (m, 1H), 1.66 – 1.57 (m, 3H), 1.56 – 1.47 (m, 3H), 1.47 – 1.41 (m, 2H), 1.34 – 1.28 (m, 3H), 1.15 – 1.08 (m, 3H), 0.99 (s, 3H), 0.98 (s, 3H), 0.87 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 80.00, 76.00, 74.22, 69.87, 61.33, 58.54, 46.92, 45.89, 40.19, 37.69, 36.65, 35.19, 34.61, 34.35, 33.86, 30.42, 22.72, 20.90, 20.62.

(1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyl-1-(pent-4-yn-1-yloxy)tricyclo[6.3.1.0^{2,5}]dodecane (**AC-6**).

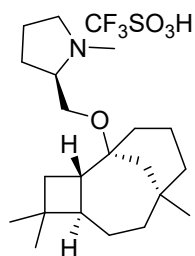


According to the genenal procedure, compound **AC-6** could be obtained with 70% yield as white solid using β -Caryophyllene and 4-Pentyn-1-ol as substrates;

¹H NMR (400 MHz, CDCl₃) δ 3.39 (dt, $J=9.0, 6.6$ Hz, 1H), 3.22 (dt, $J=9.0, 6.4$ Hz, 1H), 2.19 (td, $J=7.1, 2.6$ Hz, 2H), 2.14 – 2.02 (m, 1H), 1.85 (t, $J=2.7$ Hz, 1H), 1.79

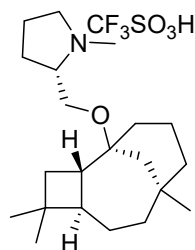
– 1.71 (m, 1H), 1.69 – 1.57 (m, 6H), 1.51 – 1.36 (m, 3H), 1.32 – 1.18 (m, 4H), 1.09 – 0.96 (m, 3H), 0.92 (s, 3H), 0.91 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 84.46, 75.46, 68.17, 60.22, 46.73, 45.89, 40.31, 37.74, 36.50, 35.13, 34.63, 34.36, 33.95, 30.47, 29.61, 22.74, 20.92, 20.64, 15.38.

(*R*)-1-methyl-2-((((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)pyrrolidine trifluoromethanesulfonate (**AC-7**).



According to the general procedure, compound **AC-7** could be obtained with 70% yield as white solid using β -Caryophyllene and (*R*)-(1-methylpyrrolidin-2-yl)methanol as substrates; HRMS(ESI): calcd for $\text{C}_{21}\text{H}_{37}\text{NO}$ $[\text{M} + \text{H}]^+$ m/z 320.2948, found 320.2740; ^1H NMR (400 MHz, CDCl_3) δ 3.98 (m, 1H), 3.80 (dd, $J = 10.8, 9.2$ Hz, 1H), 3.49 (dd, $J = 10.8, 3.2$ Hz, 1H), 3.40–3.28 (m, 1H), 3.09 (d, $J = 5.0$ Hz, 3H), 3.00 – 2.86 (m, 1H), 2.28 – 2.12 (m, 3H), 2.12 – 2.01 (m, 1H), 1.83 – 1.75 (m, 3H), 1.74 – 1.69 (m, 2H), 1.65 (d, $J = 9.1$ Hz, 1H), 1.63 – 1.59 (m, 1H), 1.53–1.43 (m, 3H), 1.41–1.34 (m, 2H), 1.32 – 1.28 (m, 1H), 1.26 (s, 1H), 1.17 (d, $J = 12.9$ Hz, 1H), 1.10 – 1.03 (m, 1H), 0.99 (s, 6H), 0.89 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 120.31 (q, $J = 318$ Hz), 77.20, 69.90, 61.27, 58.05, 45.93, 45.91, 42.59, 40.06, 37.66, 37.40, 36.53, 35.38, 34.74, 33.80, 33.32, 30.53, 27.01, 22.63, 22.28, 20.80, 20.52.

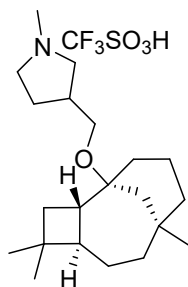
(*S*)-1-methyl-2-((((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)pyrrolidine trifluoromethanesulfonate (**AC-8**).



According to the general procedure, compound **AC-8** could be obtained with 60% yield

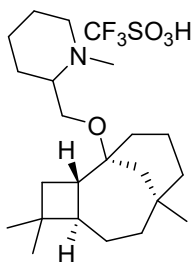
as white solid using β -Caryophyllene and (S)-(1-methylpyrrolidin-2-yl)methanol as substrates; HRMS(ESI): calcd for C₂₁H₃₇NO [M + H]⁺ *m/z* 320.2948, found 320.2743; ¹H NMR (400 MHz, CDCl₃) δ 3.85-3.72 (m, 1H), 3.72 – 3.61 (m, 2H), 3.42 – 3.27 (m, 1H), 3.17 – 2.99 (m, 1H), 2.98 (s, 3H), 2.27 – 2.11 (m, 3H), 2.12 – 1.94 (m, 2H), 1.82 – 1.69 (m, 3H), 1.67 – 1.55 (m, 3H), 1.51–1.43 (m, 3H), 1.43 – 1.28 (m, 4H), 1.18 – 1.10 (m, 2H), 1.09 – 1.02 (m, 1H), 0.99 (s, 3H), 0.98 (s, 3H), 0.89 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.31 (q, *J* = 318 Hz), 76.92, 60.39, 57.65, 45.85, 44.95, 40.26, 37.56, 37.39, 36.07, 35.23, 34.85, 33.87, 33.22, 30.62, 29.71, 26.91, 22.50, 22.12, 20.82, 20.52.

1-methyl-3-((((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)pyrrolidine trifluoromethanesulfonate (AC-9).



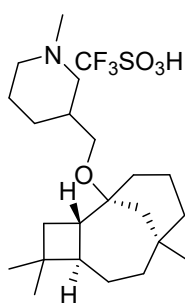
According to the genenal procedure, compound **AC-9** could be obtained with 68% yield as white solid using β -Caryophyllene and (1-methylpyrrolidin-3-yl)methanol as substrates; HRMS(ESI): calcd for C₂₁H₃₇NO [M + H]⁺ *m/z* 320.2953, found 320.2813; ¹H NMR (400 MHz, CDCl₃) δ 3.57 – 3.21 (m, 4H), 3.06 (brs, 1H), 2.89 (s, 3H), 2.70 – 2.59 (m, 1H), 2.23 – 2.05 (m, 2H), 2.00 – 1.83 (m, 1H), 1.75 – 1.66 (m, 1H), 1.66 – 1.58 (m, 2H), 1.57-1.50 (m, 2H), 1.45 – 1.36 (m, 2H), 1.35 – 1.27 (m, 2H), 1.28 – 1.19 (m, 3H), 1.10 – 0.95 (m, 3H), 0.92 (s, 3H), 0.91 (s, 3H), 0.81 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.31 (q, *J* = 318 Hz), 75.76, 75.72, 62.00, 61.81, 58.53, 58.36, 56.60, 56.46, 45.98, 45.88, 41.47, 41.43, 40.32, 40.30, 37.83, 37.73, 37.65, 37.60, 36.39, 36.35, 35.22, 34.73, 34.71, 33.95, 33.85, 30.63, 30.61, 29.67, 27.16, 27.05, 22.62, 20.84, 20.49.

1-methyl-2-((((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)piperidine trifluoromethanesulfonate (AC-10).



According to the genenal procedure, compound **AC-10** could be obtained with 98% yield as white solid using β -Caryophyllene and (1-methylpiperidin-2-yl)methanol as substrates; HRMS(ESI): calcd for C₂₂H₃₉NO [M+H]⁺ *m/z* 334.3110, found 334.2894; ¹H NMR (400 MHz, CDCl₃) δ 3.76 – 3.68 (m, 1H), 3.56 (dd, *J* = 10.2, 4.9 Hz, 0.6H), 3.42 (dd, *J* = 10.2, 4.8 Hz, 0.4H), 3.25 (dd, *J* = 10.7, 3.3 Hz, 1H), 2.70 (s, 1.8H), 2.62 (s, 1.2H), 2.59-2.48 (m, 2H), 2.23 – 2.09 (m, 1H), 1.92 – 1.73 (m, 5H), 1.72 – 1.65 (m, 3H), 1.66 – 1.57 (m, 3H), 1.55-1.49 (m, 1H), 1.49 – 1.43 (m, 2H), 1.42 – 1.34 (m, 3H), 1.34 – 1.28 (m, 2H), 1.15-1.07 (m, 2H), 1.07 – 1.01 (m, 1H), 1.00 – 0.95 (m, 6H), 0.89 – 0.87 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.31 (q, *J* = 318 Hz), 76.49, 76.23, 65.74, 65.29, 63.57, 62.59, 57.06, 46.22, 46.22, 45.94, 45.87, 45.79, 40.34, 40.17, 37.74, 37.57, 36.51, 36.34, 35.25, 35.21, 34.74, 33.95, 33.82, 30.56, 30.53, 29.71, 28.12, 23.95, 23.75, 22.87, 22.70, 22.89, 20.90, 20.86, 20.58.

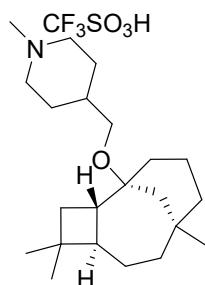
1-methyl-3-((((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)piperidine trifluoromethanesulfonate (AC-11).



According to the genenal procedure, compound **AC-11** could be obtained with 55% yield as white solid using β -Caryophyllene and (1-methylpiperidin-3-yl)methanol as substrates; HRMS(ESI): calcd for C₂₂H₃₉NO [M + H]⁺ *m/z* 334.3110, found 334.2943; ¹H NMR (400 MHz, CDCl₃) δ 7.71 (s, 1H), 7.44 (s, 1H), 3.43 – 3.33 (m, 2H), 3.29 (dd, *J* = 9.3, 4.8 Hz, 0.5H), 3.21 – 3.13 (m, 1H), 3.08 (dd, *J* = 9.2, 5.8 Hz, 0.5H), 2.77 (dq, *J* = 43.8, 10.7 Hz, 2H), 2.07 (dd, *J* = 19.1, 11.0 Hz, 1H), 2.01 - 1.91

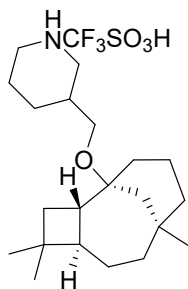
(m, 1H), 1.88 – 1.81 (m, 1H), 1.79 – 1.67 (m, 3H), 1.64 – 1.57 (m, 2H), 1.56 – 1.50 (m, 2H), 1.45 – 1.35 (m, 3H), 1.34 – 1.27 (m, 2H), 1.26 – 1.18 (m, 3H), 1.09 – 0.95 (m, 3H), 0.92 (s, 3H), 0.90 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 120.31 (q, $J = 318$ Hz), 75.60, 75.52, 63.39, 63.32, 58.22, 47.87, 47.85, 45.93, 45.84, 45.04, 40.32, 40.26, 37.73, 37.69, 37.63, 36.22, 36.16, 35.16, 34.66, 34.58, 34.47, 33.98, 33.94, 33.75, 30.45, 30.42, 25.68, 22.69, 22.64, 21.78, 21.74, 20.84, 20.55, 18.23.

1-methyl-4-((((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)piperidine trifluoromethanesulfonate (AC-12).



According to the genenal procedure, compound **AC-12** could be obtained with 63% yield as white solid using β -Caryophyllene and (1-methylpiperidin-4-yl)methanol as substrates; HRMS(ESI): calcd for $\text{C}_{22}\text{H}_{39}\text{NO}$ $[\text{M} + \text{H}]^+$ m/z 334.3110, found 334.2943; ^1H NMR (400 MHz, CDCl_3) δ 3.47 (d, $J = 10.1$ Hz, 2H), 3.22 – 3.14 (m, 1H), 3.12 – 3.03 (m, 1H), 2.79 (s, 3H), 2.78 – 2.60 (m, 2H), 2.08 (td, $J = 11.0, 7.9$ Hz, 1H), 2.02 – 1.87 (m, 3H), 1.75 – 1.69 (m, 1H), 1.65 – 1.59 (m, 4H), 1.57 – 1.51 (m, 3H), 1.45 – 1.36 (m, 3H), 1.26 – 1.23 (m, 2H), 1.08 – 1.03 (m, 1H), 1.02 – 0.96 (m, 2H), 0.91 (s, 3H), 0.91 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 120.20 (q, $J = 375.2$ Hz), 75.53, 64.90, 46.28, 45.99, 40.35, 37.74, 37.65, 36.37, 35.19, 34.70, 34.05, 34.00, 30.56, 29.70, 22.71, 20.87, 20.56.

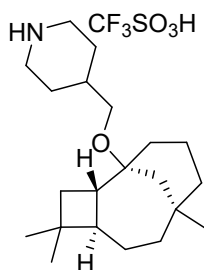
3-((((1R,2S,5R,8S)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)piperidine trifluoromethanesulfonate (AC-13).



According to the genenal procedure, compound **AC-13** could be obtained with 55% yield as white solid using β -Caryophyllene and piperidin-3-ylmethanol as substrates; HRMS(ESI): calcd for C₂₁H₃₇NO [M + H]⁺ *m/z* 320.2953, found 320.2793;

¹H NMR (400 MHz, CDCl₃) δ 7.71 (s, 1H), 7.44 (s, 1H), 3.43 – 3.33 (m, 2H), 3.29 (dd, *J* = 9.3, 4.8 Hz, 0.5H), 3.21 – 3.13 (m, 1H), 3.08 (dd, *J* = 9.2, 5.8 Hz, 0.5H), 2.77 (dq, *J* = 43.8, 10.7 Hz, 2H), 2.07 (dd, *J* = 19.1, 11.0 Hz, 1H), 2.01 - 1.91 (m, 1H), 1.88 – 1.81 (m, 1H), 1.79 – 1.67 (m, 3H), 1.64 – 1.57 (m, 2H), 1.56 – 1.50 (m, 2H), 1.45 – 1.35 (m, 3H), 1.34 – 1.27 (m, 2H), 1.26 – 1.18 (m, 3H), 1.09 – 0.95 (m, 3H), 0.92 (s, 3H), 0.90 (s, 3H), 0.80 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.31 (q, *J* = 318 Hz), 75.60, 75.52, 63.39, 63.32, 58.22, 47.87, 47.85, 45.93, 45.84, 45.04, 40.32, 40.26, 37.73, 37.69, 37.63, 36.22, 36.16, 35.16, 34.66, 34.58, 34.47, 33.98, 33.94, 33.75, 30.45, 30.42, 25.68, 22.69, 22.64, 21.78, 21.74, 20.84, 20.55, 18.23.

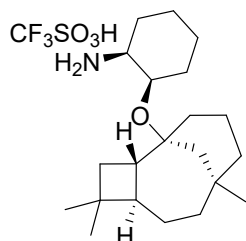
4-((((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)methyl)piperidine trifluoromethanesulfonate (**AC-14**).



According to the genenal procedure, compound **AC-14** could be obtained with 56% yield as white solid using β -Caryophyllene and piperidin-4-ylmethanol as substrates; HRMS(ESI): calcd for C₂₁H₃₇NO [M + H]⁺ *m/z* 320.2953, found 320.2796; ¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, *J* = 60.0 Hz, 2H), 3.78 (s, 1H), 3.31 (s, 2H), 3.15 (s, 2H), 2.22 - 2.08 (m, 1H), 1.90 (s, 2H), 1.75 – 1.56 (m, 5H), 1.56 – 1.46 (m, 3H), 1.46 – 1.35 (m, 3H), 1.35 – 1.20 (m, 3H), 1.10 – 1.01 (m, 2H), 1.01 – 0.95 (m, 1H), 0.92 (s, 3H),

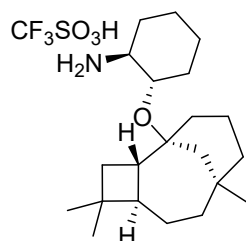
0.91 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 120.20(q, $J = 375.2$ Hz) , 76.95 , 60.61 , 45.49 , 45.41 , 41.28 , 41.24 , 40.27 , 37.76 , 37.45 , 35.45 , 35.03 , 34.97 , 34.55 , 34.08 , 30.63 , 30.54 , 30.36 , 22.35 , 21.06 , 20.65.

(1*S*,2*R*)-2-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)cyclohexan-1-amine trifluoromethanesulfonate (**AC-15**).



According to the general procedure, compound **AC-15** could be obtained with 71% yield as white solid using β -Caryophyllene and (1*R*,2*S*)-2-aminocyclohexan-1-ol as substrates; HRMS(ESI): calcd for $\text{C}_{21}\text{H}_{37}\text{NO}$ $[\text{M} + \text{H}]^+$ m/z 320.2953, found 320.2798; ^1H NMR (400 MHz, CDCl_3) δ 4.90 (brs, 3H), 3.85 – 3.75 (m, 1H), 3.30 (td, $J = 6.8, 3.1$ Hz, 1H), 2.19 (dd, $J = 20.1, 10.6$ Hz, 1H), 1.80-1.70 (m, 3H), 1.69-1.58 (m, 4H), 1.54 (d, $J = 10.1$ Hz, 1H), 1.49-1.36 (m, 7H), 1.32 – 1.21 (m, 5H), 1.19 – 1.16 (m, 2H), 1.07 (dd, $J = 10.0, 7.1$ Hz, 1H), 1.04 – 0.97 (m, 1H), 0.93 (s, 3H), 0.92 (s, 3H), 0.83 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 119.67 (q, $J = 375.2$ Hz), 77.27 , 67.10 , 65.17 , 53.59 , 45.29 , 44.63 , 40.52 , 37.68 , 37.41 , 35.29 , 35.12 , 35.05 , 34.59 , 33.71 , 30.88 , 30.44 , 29.71 , 25.96 , 22.21 , 21.27 , 20.64.

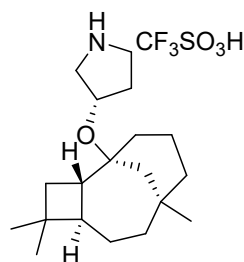
(1*S*,2*S*)-2-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)cyclohexan-1-amine trifluoromethanesulfonate (**AC-16**).



According to the general procedure, compound **AC-16** could be obtained with 67% yield as white solid using β -Caryophyllene and (1*S*,2*S*)-2-aminocyclohexan-1-ol as substrates; HRMS(ESI): calcd for $\text{C}_{21}\text{H}_{37}\text{NO}$ $[\text{M} + \text{H}]^+$ m/z 320.2953, found 320.2812; ^1H NMR (400 MHz, CDCl_3) δ 5.40 (s, 3H), 3.46 – 3.31 (m, 1H), 2.82 – 2.71 (m, 1H), 2.19 (dd, $J = 20.1, 10.3$ Hz, 1H), 2.06 (d, $J = 11.2$ Hz, 1H), 1.96 (d, $J = 9.6$

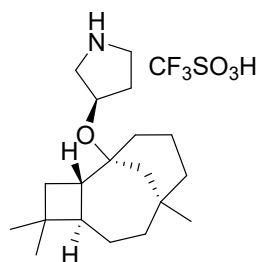
Hz, 1H), 1.78 – 1.59 (m, 5H), 1.56 – 1.46 (m, 4H), 1.45 – 1.33 (m, 3H), 1.31 – 1.20 (m, 7H), 1.03 (d, $J = 12.2$ Hz, 2H), 0.91 (s, 6H), 0.82 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 119.67 (q, $J = 375.2$ Hz), 70.23, 67.08, 56.43, 45.55, 44.45, 39.45, 37.31, 36.49, 35.32, 34.90, 34.70, 34.06, 33.55, 33.00, 30.58, 29.70, 28.44, 23.93, 23.86, 21.41, 20.81.

(*S*)-3-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)pyrrolidine trifluoromethanesulfonate (**AC-17**).



According to the general procedure, compound **AC-17** could be obtained with 63% yield as white solid using β -Caryophyllene and (*S*)-pyrrolidin-3-ol as substrates; HRMS(ESI): calcd for $\text{C}_{19}\text{H}_{33}\text{NO}$ [$\text{M} + \text{H}$] $^{+}$ m/z 292.2640, found 292.2494; ^1H NMR (400 MHz, CDCl_3) δ 7.93 (d, $J = 77.1$ Hz, 2H), 4.26 – 4.17 (m, 1H), 3.41 – 3.27 (m, 3H), 3.18–3.06 (m, 1H), 2.14 – 1.98 (m, 2H), 1.93 – 1.84 (m, 1H), 1.72 – 1.63 (m, 2H), 1.62 – 1.53 (m, 3H), 1.45 – 1.36 (m, 2H), 1.35 – 1.28 (m, 2H), 1.28 – 1.20 (m, 3H), 1.10 – 1.03 (m, 1H), 1.02 – 0.96 (m, 2H), 0.91 (s, 3H), 0.91 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 120.31 (q, $J = 318$ Hz), 78.10, 69.63, 52.71, 46.40, 46.03, 45.00, 40.15, 37.99, 37.80, 36.43, 35.63, 35.09, 34.86, 34.29, 33.63, 30.46, 22.86, 21.13, 20.46.

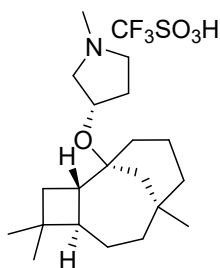
(*R*)-3-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)pyrrolidine trifluoromethanesulfonate (**AC-18**).



According to the general procedure, compound **AC-18** could be obtained with 56%

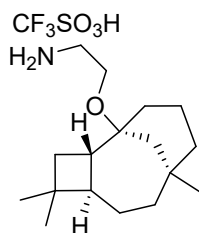
yield as white solid using β -Caryophyllene and (R)-pyrrolidin-3-ol as substrates; HRMS(ESI): calcd for C₁₉H₃₃NO [M + H]⁺ *m/z* 292.2640, found 292.2497; ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J* = 21.7 Hz, 2H), 4.19 (s, 1H), 3.35 (s, 3H), 3.13 (s, 1H), 2.16 – 2.01 (m, 2H), 1.95 (s, 1H), 1.74 – 1.68 (m, 1H), 1.62 – 1.50 (m, 4H), 1.44 – 1.35 (m, 3H), 1.33 – 1.23 (m, 4H), 1.08 – 1.02 (m, 1H), 0.99 (d, *J* = 12.9 Hz, 2H), 0.92 (s, 3H), 0.91 (s, 3H), 0.80 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.31 (q, *J* = 318 Hz), 77.14, 68.62, 52.22, 45.50, 44.87, 43.62, 39.05, 36.93, 36.77, 35.46, 34.53, 34.13, 33.80, 33.17, 31.80, 29.37, 28.68, 21.80, 20.16, 19.47.

(*S*)-1-methyl-3-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)pyrrolidine trifluoromethanesulfonate (**AC-19**).



According to the genenal procedure, compound **AC-19** could be obtained with 72% yield as white solid using β -Caryophyllene and (*S*)-1-methylpyrrolidin-3-ol as substrates; HRMS(ESI): calcd for C₂₀H₃₅NO [M + H]⁺ *m/z* 306.2797, found 306.2641; ¹H NMR (400 MHz, CDCl₃) δ 4.32 – 4.23 (m, 1H), 3.74 (dd, *J* = 12.1, 5.3 Hz, 1H), 3.64 (t, *J* = 8.0 Hz, 1H), 3.23 – 3.10 (m, 1H), 2.91 (s, 3H), 2.91 – 2.83 (s, 1H), 2.27 – 2.16 (m, 1H), 2.11 (td, *J* = 11.1, 7.8 Hz, 1H), 2.03 – 1.93 (m, 1H), 1.70 – 1.60 (m, 4H), 1.59 – 1.51 (m, 2H), 1.47 – 1.37 (m, 2H), 1.36 – 1.31 (m, 1H), 1.27 – 1.21 (m, 3H), 1.10 – 1.04 (m, 1H), 1.02 – 0.96 (m, 2H), 0.92 (s, 3H), 0.92 (s, 3H), 0.82 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.20 (q, *J* = 375.2 Hz), 78.52, 69.89, 63.13, 55.51, 46.49, 46.23, 42.96, 40.26, 38.08, 37.75, 36.72, 35.70, 35.21, 34.94, 34.51, 34.37, 30.58, 22.95, 21.13, 20.41.

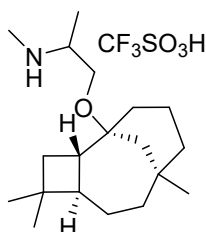
2-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)ethan-1-amine trifluoromethanesulfonate (**AC-20**).



According to the genenal procedure, compound **AC-20** could be obtained with 51% yield as white solid using β -Caryophyllene and 2-aminoethan-1-ol as substrates; HRMS(ESI): calcd for $C_{17}H_{31}NO$ $[M + H]^+$ m/z 266.2484, found 266.2363;

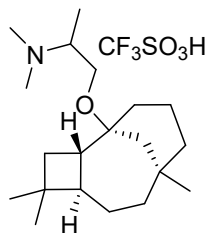
1H NMR (400 MHz, $CDCl_3$) δ 6.19 (s, 3H), 3.54 (dt, $J = 10.8, 5.4$ Hz, 1H), 3.46 – 3.30 (m, 1H), 3.16 – 3.02 (m, 2H), 2.08 (td, $J = 11.1, 7.9$ Hz, 1H), 1.79 – 1.69 (m, 1H), 1.65 – 1.54 (m, 4H), 1.47 – 1.34 (m, 3H), 1.34 – 1.26 (m, 2H), 1.26 – 1.19 (m, 2H), 1.10 – 0.95 (m, 3H), 0.92 (s, 3H), 0.91 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 120.20(q, $J = 375.2$ Hz), 76.85, 56.77, 45.84, 45.81, 41.03, 40.19, 37.78, 37.52, 36.24, 35.26, 34.68, 33.90, 33.86, 30.27, 22.72, 20.87, 20.52.

N-methyl-1-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)propan-2-amine trifluoromethanesulfonate (**AC-21**).



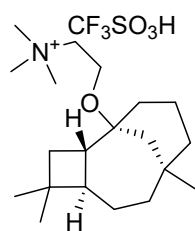
According to the genenal procedure, compound **AC-21** could be obtained with 49% yield as white solid using β -Caryophyllene and 2-(methylamino)propan-1-ol as substrates; HRMS(ESI): calcd for $C_{19}H_{35}NO$ $[M + H]^+$ m/z 294.2797, found 294.2646; 1H NMR (400 MHz, $CDCl_3$) δ 7.00 (brs, 2H), 3.58 – 3.39 (m, 1H), 3.37 – 3.21 (m, 2H), 2.71 (d, $J = 9.0$ Hz, 3H), 2.15 – 2.02 (m, 1H), 1.79 – 1.70 (m, 1H), 1.65 (d, $J = 7.9$ Hz, 1H), 1.59 – 1.52 (m, 2H), 1.46 – 1.36 (m, 3H), 1.34 – 1.19 (m, 7H), 1.10 – 1.02 (m, 2H), 1.02 – 0.95 (m, 1H), 0.92 (s, 3H), 0.90 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 120.31 (q, $J = 318$ Hz), 76.80, 76.72, 61.42, 60.78, 56.15, 45.83, 45.82, 45.70, 45.44, 40.28, 40.22, 37.78, 37.50, 36.28, 36.14, 35.25, 35.19, 34.71, 34.67, 33.91, 33.87, 33.69, 33.68, 31.12, 31.11, 30.38, 30.35, 22.70, 20.87, 22.83, 20.45, 13.82, 13.52.

N,N-dimethyl-1-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)propan-2-amine trifluoromethanesulfonate (**AC-22**).



According to the genenal procedure, compound **AC-22** could be obtained with 49% yield as white solid using β -Caryophyllene and 2-(dimethylamino)propan-1-ol as substrates; HRMS(ESI): calcd for C₂₀H₃₇NO [M + H]⁺ *m/z* 308.2953, found 308.2798; ¹H NMR (400 MHz, CDCl₃) δ 3.70 - 3.63 (m, 0.5H), 3.51 - 3.35 (m, 2.5H), 2.85 (s, 6H), 2.11 (tt, *J* = 11.0, 7.4 Hz, 1H), 1.77 - 1.69 (m, 1H), 1.67 - 1.63 (m, 2H), 1.60 - 1.53 (m, 2H), 1.45 - 1.38 (m, 2H), 1.38 - 1.33 (m, 2H), 1.33 - 1.26 (m, 5H), 1.08 - 1.03 (m, 2H), 1.01 - 0.96 (m, 1H), 0.92 (m, 6H), 0.82 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 120.31 (q, *J* = 318 Hz), 62.18, 62.03, 60.80, 60.62, 46.00, 45.72, 45.47, 40.21, 40.10, 37.70, 37.67, 37.48, 36.47, 36.36, 35.39, 35.30, 34.84, 34.79, 33.94, 33.92, 33.65, 33.50, 30.61, 30.54, 29.71, 22.65, 22.60, 20.86, 20.83, 20.45, 11.99, 11.84.

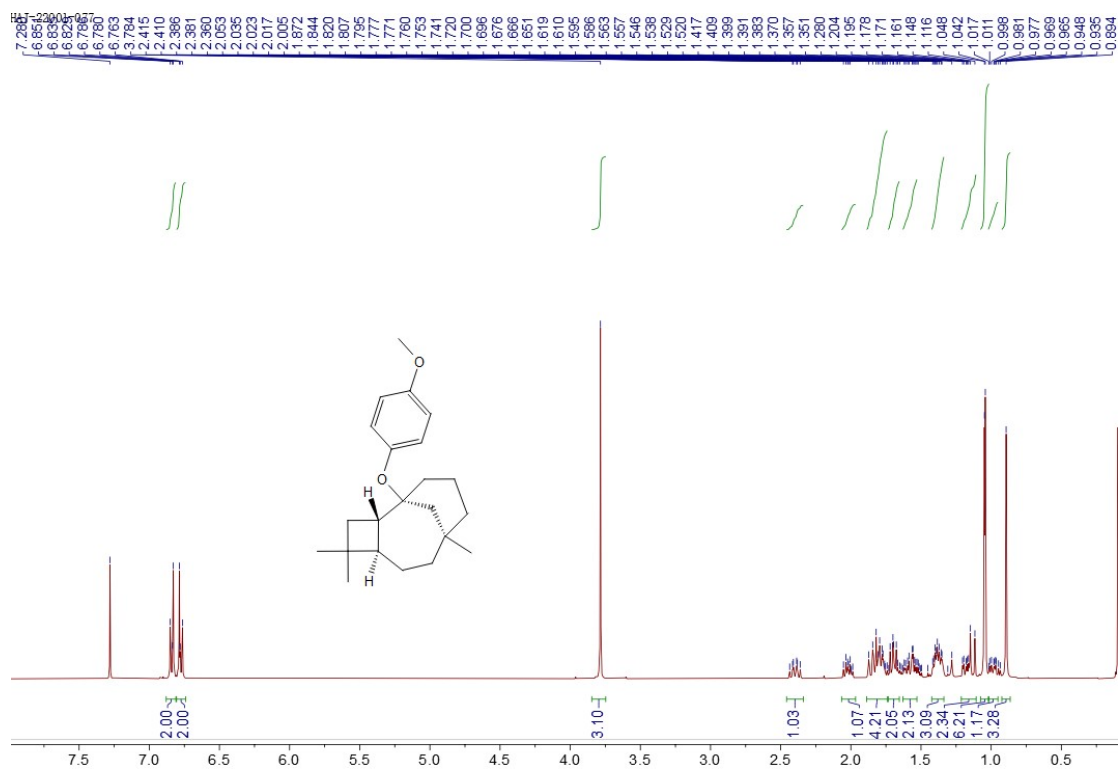
N,N,N-trimethyl-2-(((1*R*,2*S*,5*R*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-yl)oxy)ethan-1-aminium trifluoromethanesulfonate (**AC-23**).



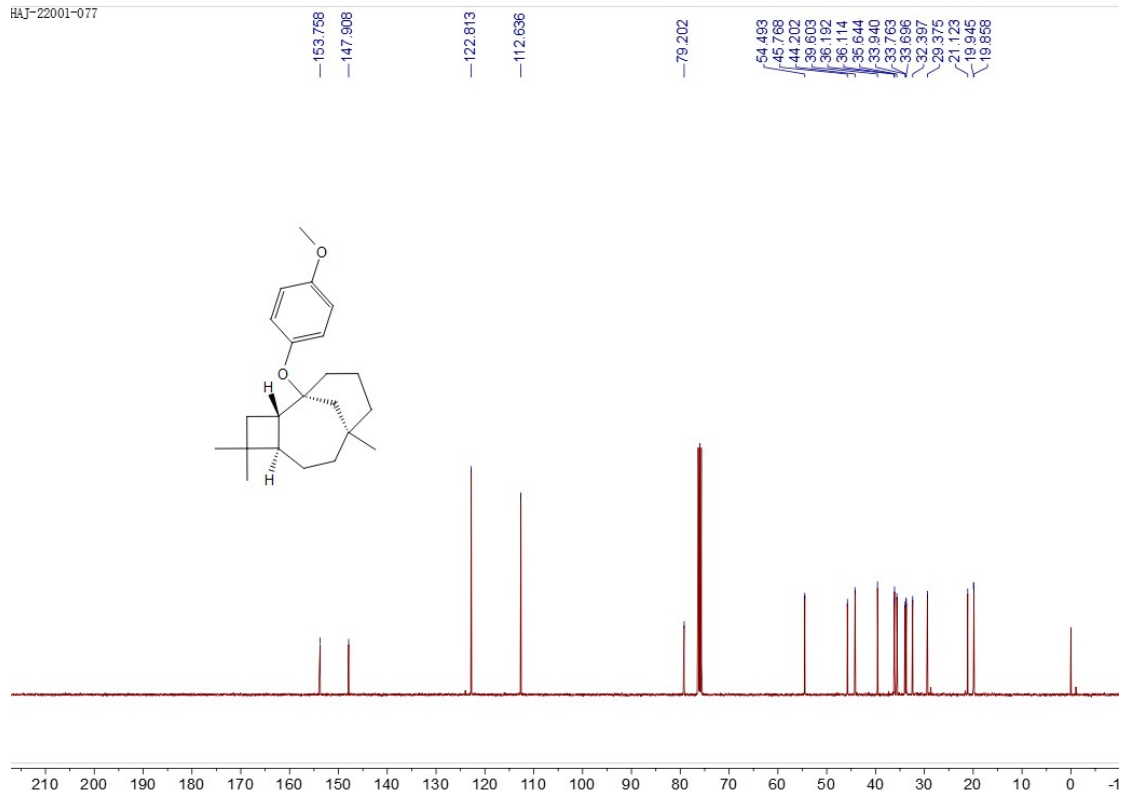
According to the genenal procedure, compound **AC-23** could be obtained with 43% yield as white solid using β -Caryophyllene and Choline hydroxide as substrates; HRMS(ESI): calcd for C₂₀H₃₈NO M⁺ *m/z* 308.2948, found 308.2799; ¹H NMR (400 MHz, CDCl₃) δ 3.76 (d, *J* = 7.1 Hz, 1H), 3.62 - 3.53 (m, 1H), 3.53 - 3.43 (m, 2H), 3.19 (s, 9H), 2.10 (td, *J* = 11.1, 7.9 Hz, 1H), 1.74 - 1.61 (m, 3H), 1.61 - 1.53 (m, 3H), 1.48 - 1.37 (m, 2H), 1.36 - 1.28 (m, 3H), 1.27 - 1.22 (m, 1H), 1.09 - 1.01 (m, 2H), 0.98 (dd, *J* = 8.7, 4.9 Hz, 1H), 0.92(s, 3H), 0.91(s, 3H), 0.81 (s, 3H). ¹³C NMR (101 MHz,

CDCl₃) δ 120.60(q, $J = 318$ Hz) , 77.49 , 66.65 , 56.20 , 54.45 , 54.42 , 54.39 , 45.93 , 45.64 , 39.97 , 37.61 , 37.44 , 36.38 , 35.28 , 34.80 , 33.91 , 33.46 , 30.49 , 22.56 , 20.79 , 20.47.

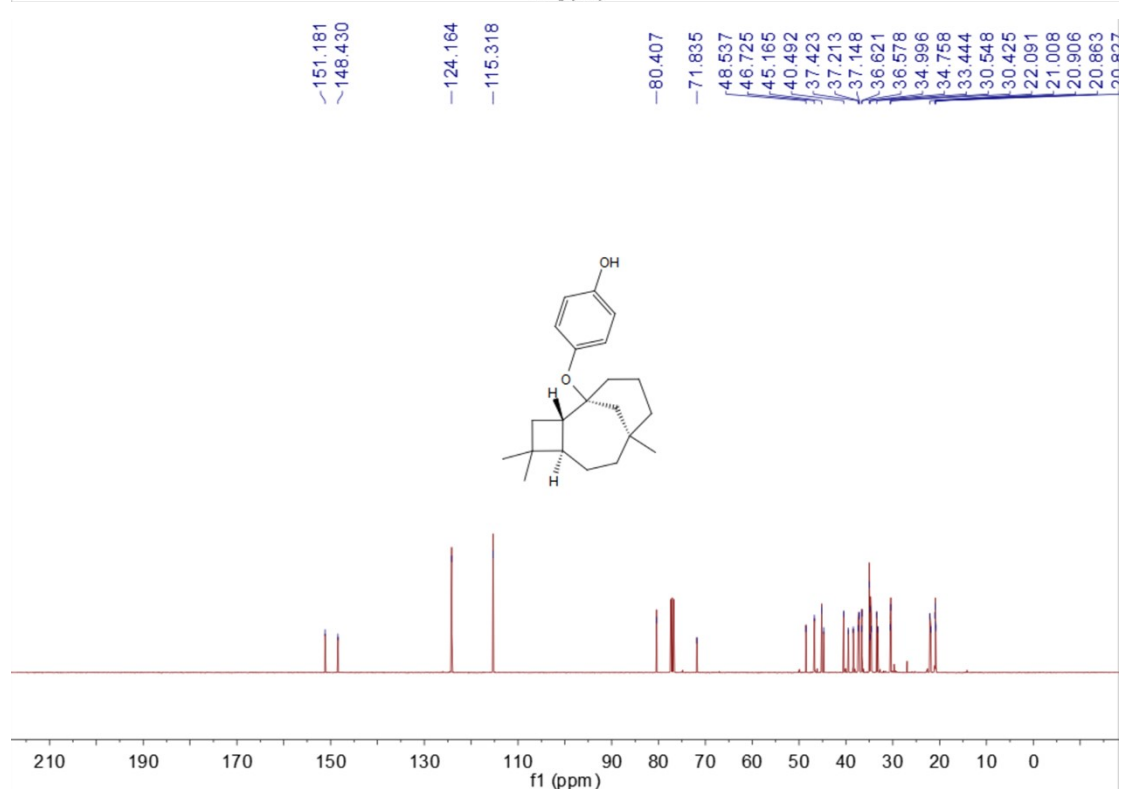
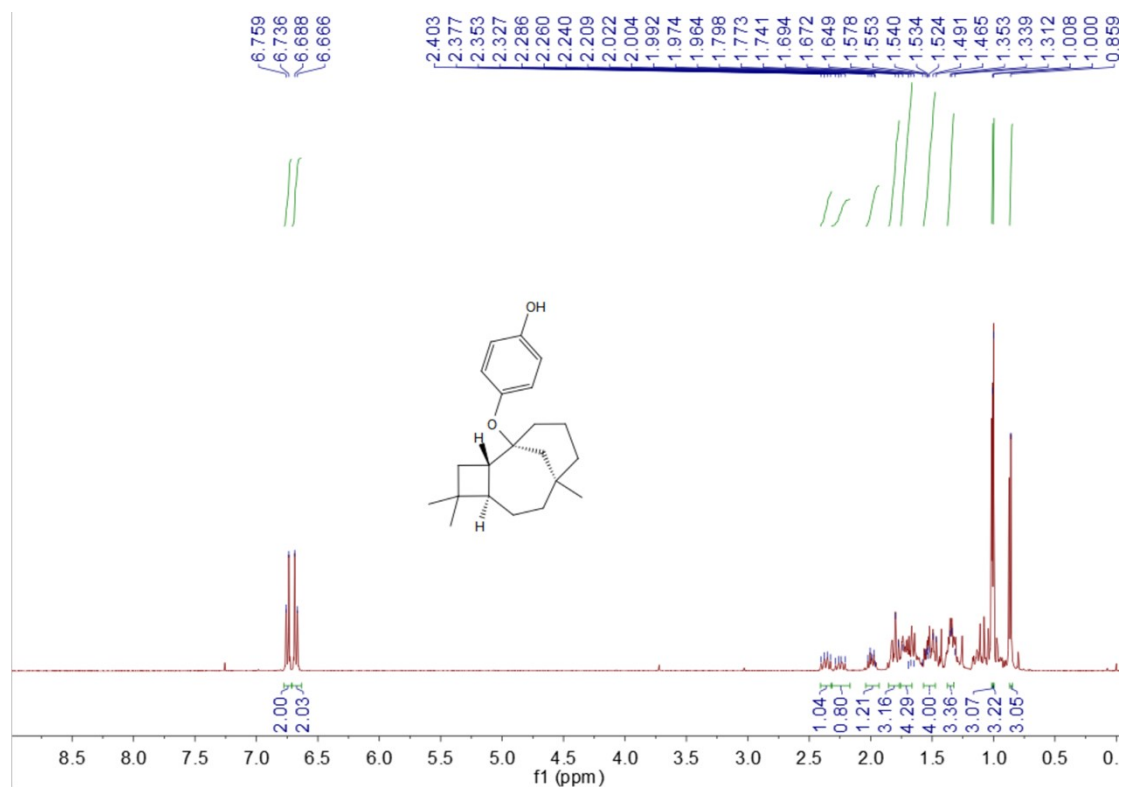
Compound AC-1



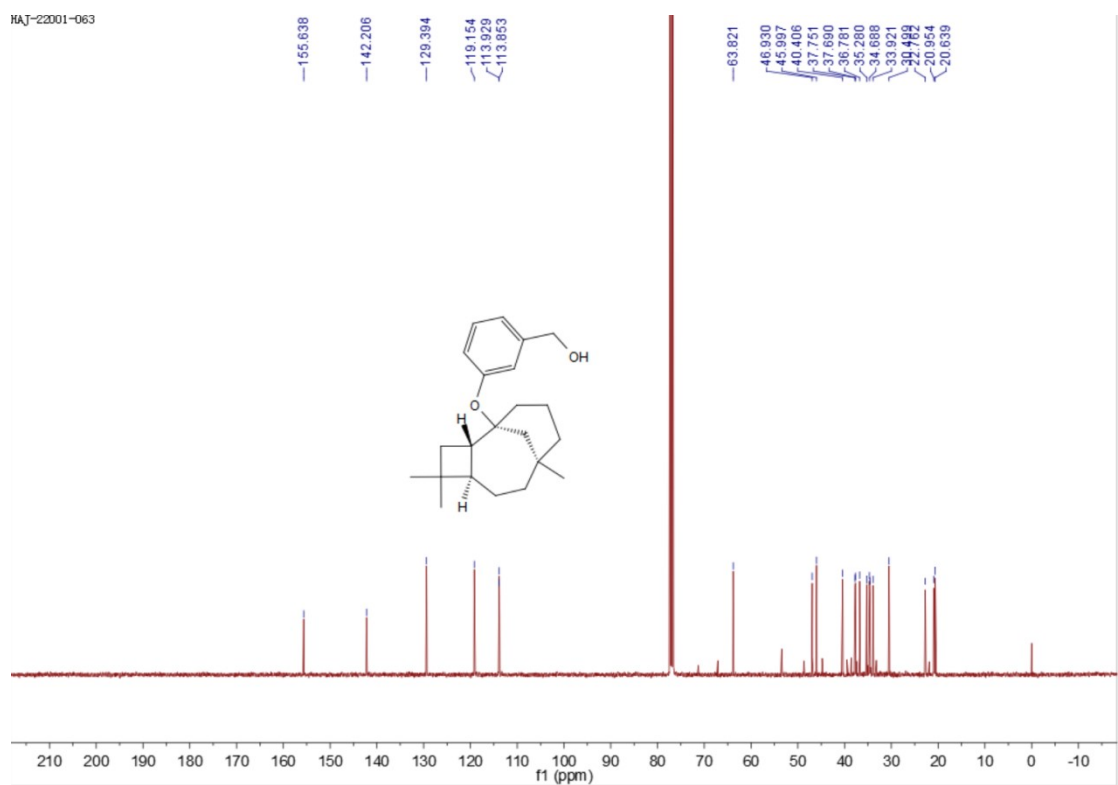
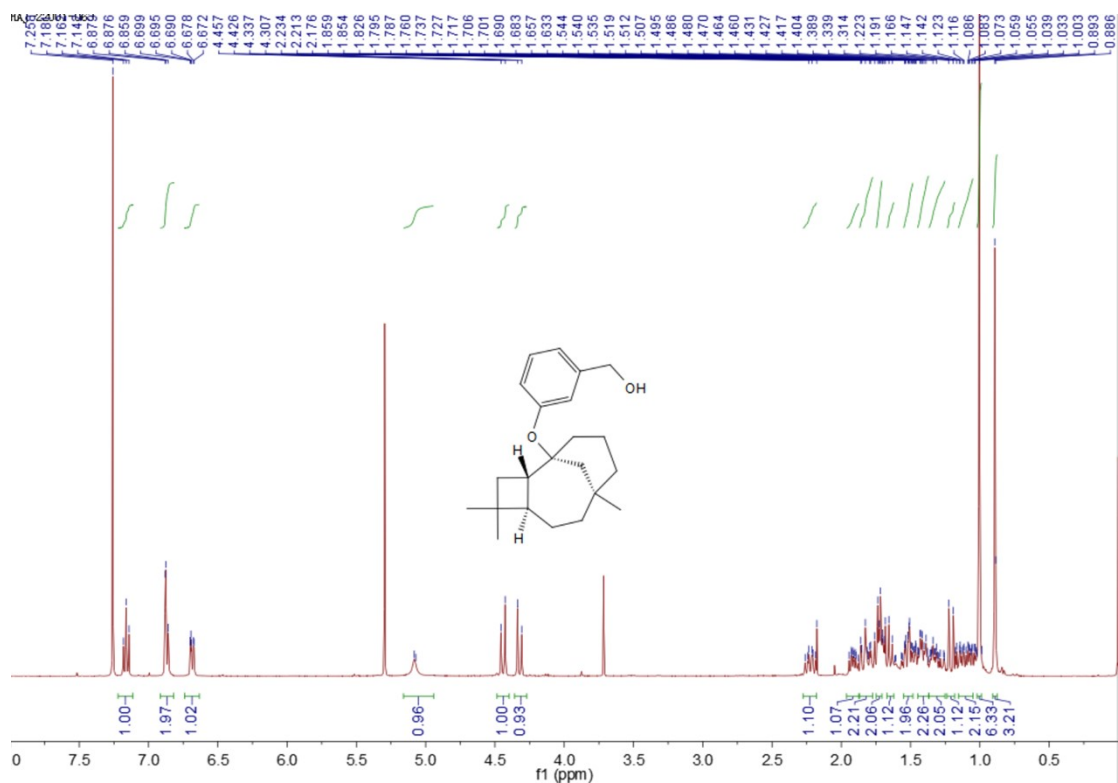
H4J-22001-077



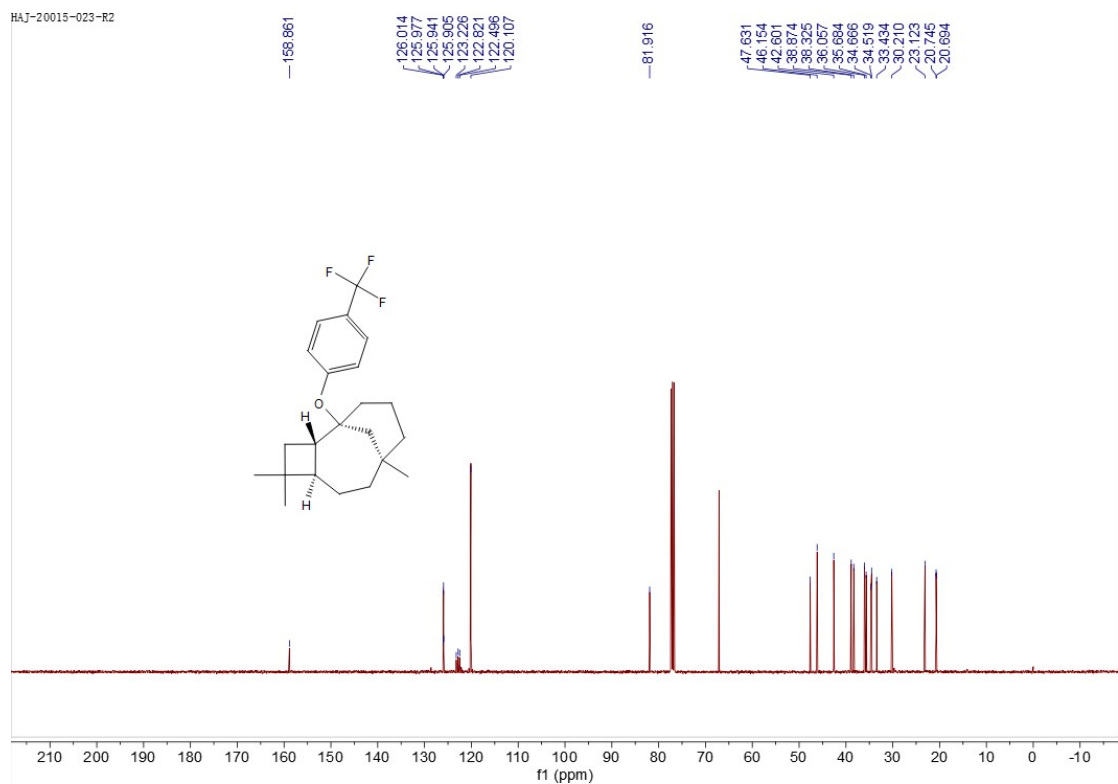
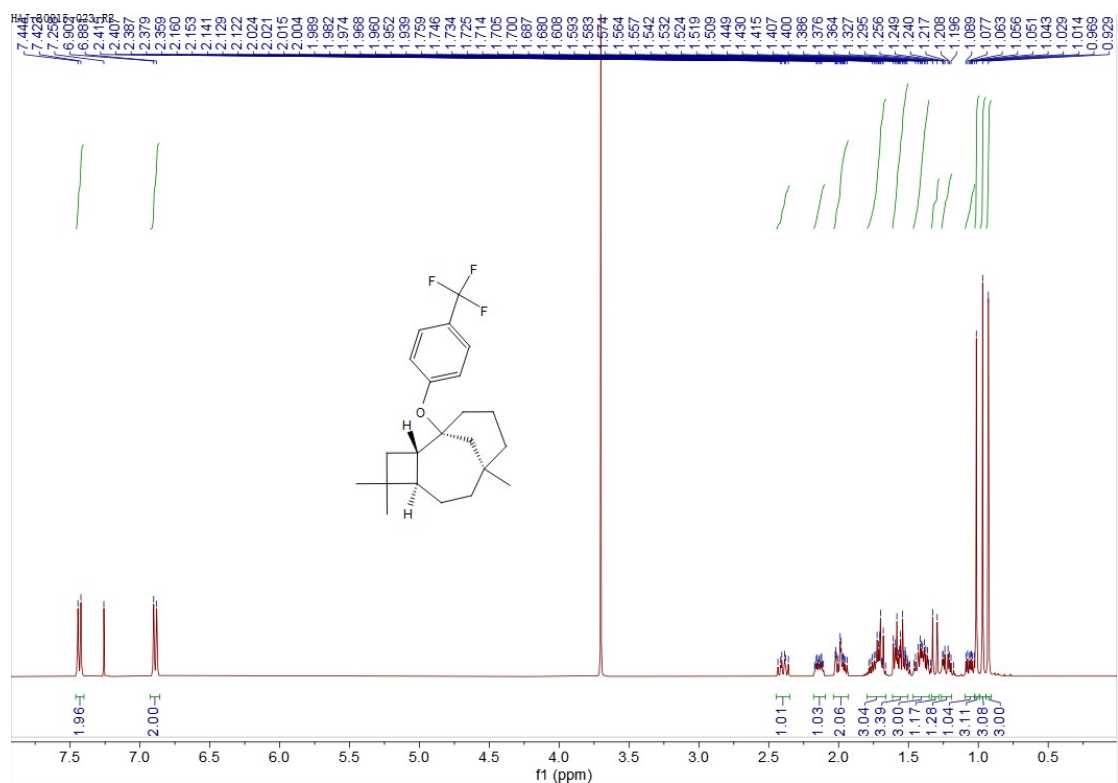
Compound AC-2



Compound AC-3



Compound AC-4



Chemical structure of compound 10 is shown above the spectrum. The structure is a complex polycyclic molecule with a terminal alkyne group.

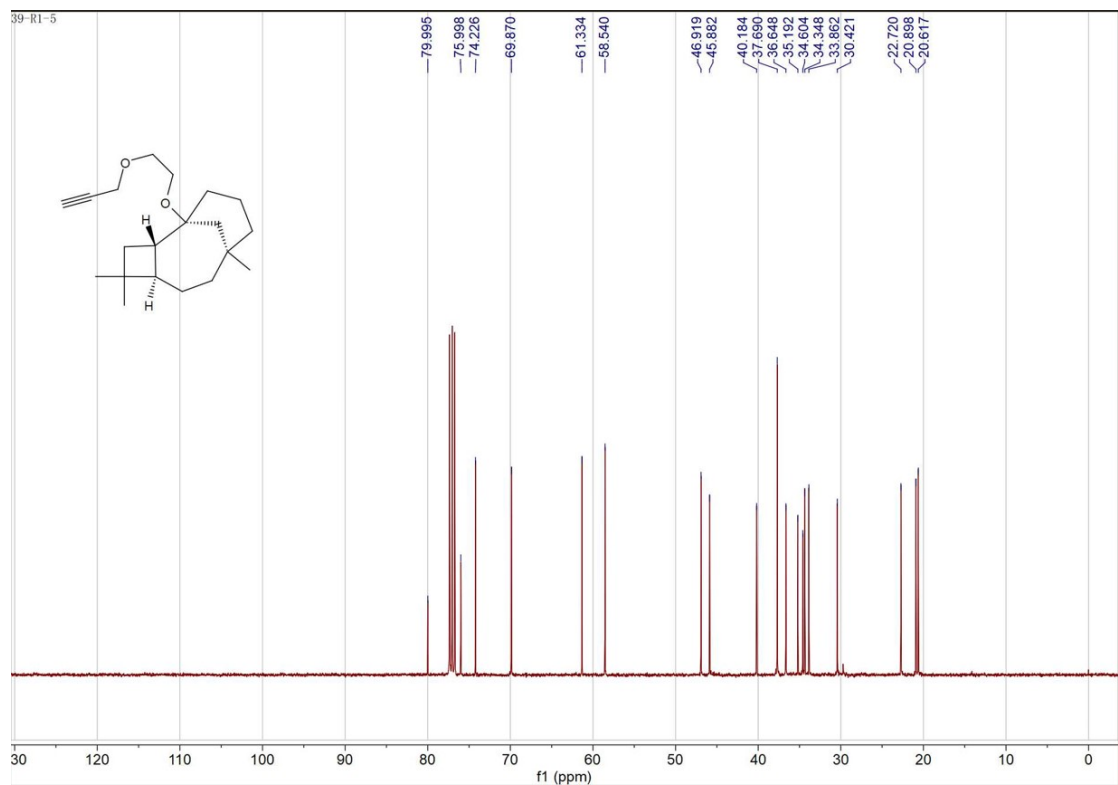
¹H NMR spectrum (CDCl₃) showing chemical shifts (δ) and integration values.

Chemical shifts (δ) listed on the right side of the spectrum (from top to bottom):

- 7.268, 4.221, 4.216, 3.653, 3.650, 3.641, 3.638, 3.625, 3.600, 3.589, 3.572, 3.563, 3.560, 3.548, 3.425, 3.412, 3.400, 3.387, 3.375, 2.417, 2.411, 2.405, 2.147, 2.127, 1.861, 1.858, 1.847, 1.770, 1.764, 1.737, 1.720, 1.711, 1.692, 1.682, 1.683, 1.671, 1.664, 1.660, 1.640, 1.605, 1.579, 1.555, 1.515, 1.505, 1.487, 1.483, 1.478, 1.465, 1.450, 1.427, 1.397, 1.368, 1.363, 1.357, 1.343, 1.317, 1.308, 1.284, 1.254, 1.171, 1.153, 1.135, 1.125, 1.114, 1.105, 1.092, 1.071, 1.068, 1.045, 0.990, 0.979, 0.871.

Integration values listed below the baseline (from left to right):

- 1.98
- 1.96
- 1.06
- 1.00
- 0.91
- 1.06
- 1.12
- 4.04
- 0.95
- 2.16
- 4.09
- 2.22
- 0.95
- 3.02
- 3.00
- 3.04

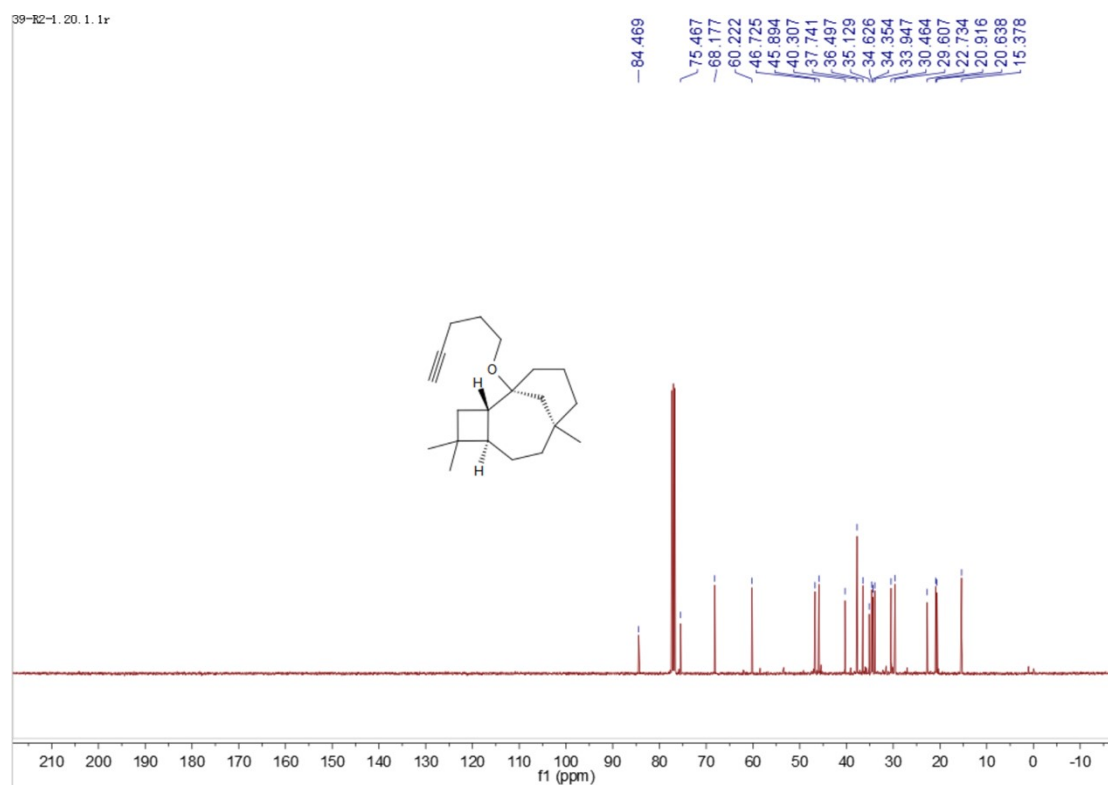


Chemical structure of compound 10 is shown above the spectrum. The structure is a bicyclic ether with a methyl group, a propargyl group, and a propyl group.

¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm, ranging from 0 to 3.9. The spectrum shows several peaks, with integration values provided for each major peak. The peak positions (ppm) are listed on the right side of the spectrum.

Integration values (from left to right): 1.00, 0.98, 1.99, 1.14, 0.90, 5.20, 1.05, 1.03, 2.03, 2.13, 1.99, 0.94, 1.96, 3.18, 3.33, 3.12.

Peak positions (ppm) (from left to right): 3.398, 3.392, 3.375, 3.225, 3.215, 3.206, 2.214, 2.208, 2.197, 2.190, 2.179, 2.172, 1.861, 1.855, 1.848, 1.681, 1.664, 1.662, 1.654, 1.648, 1.644, 1.627, 1.621, 1.599, 1.591, 1.579, 1.575, 1.556, 1.503, 1.477, 1.452, 1.440, 1.418, 1.410, 1.396, 1.327, 1.301, 1.284, 1.269, 1.264, 1.258, 1.249, 1.238, 1.216, 1.185, 1.068, 1.049, 1.044, 1.035, 1.025, 1.016, 1.002, 0.982, 0.918, 0.910, 0.892, 0.805.

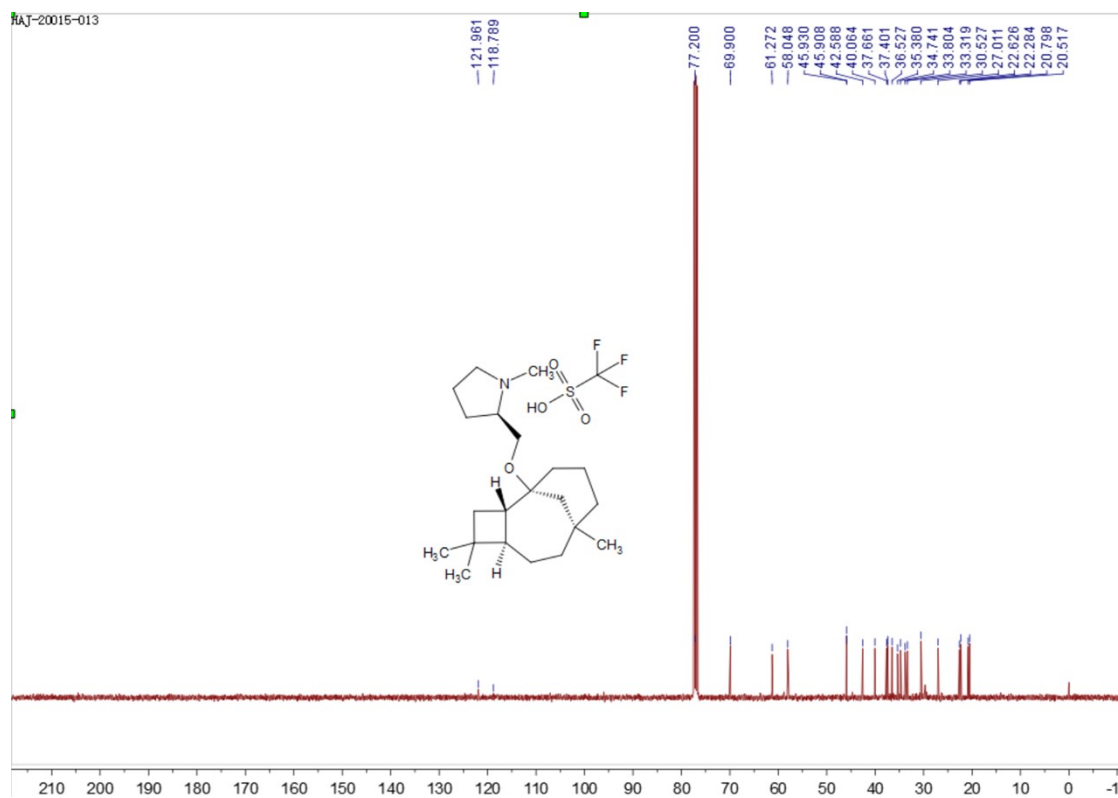


Chemical structure of compound 10 is shown above the spectrum. The structure is a complex bicyclic molecule with a sulfonamide group and a cyclopentyl ring.

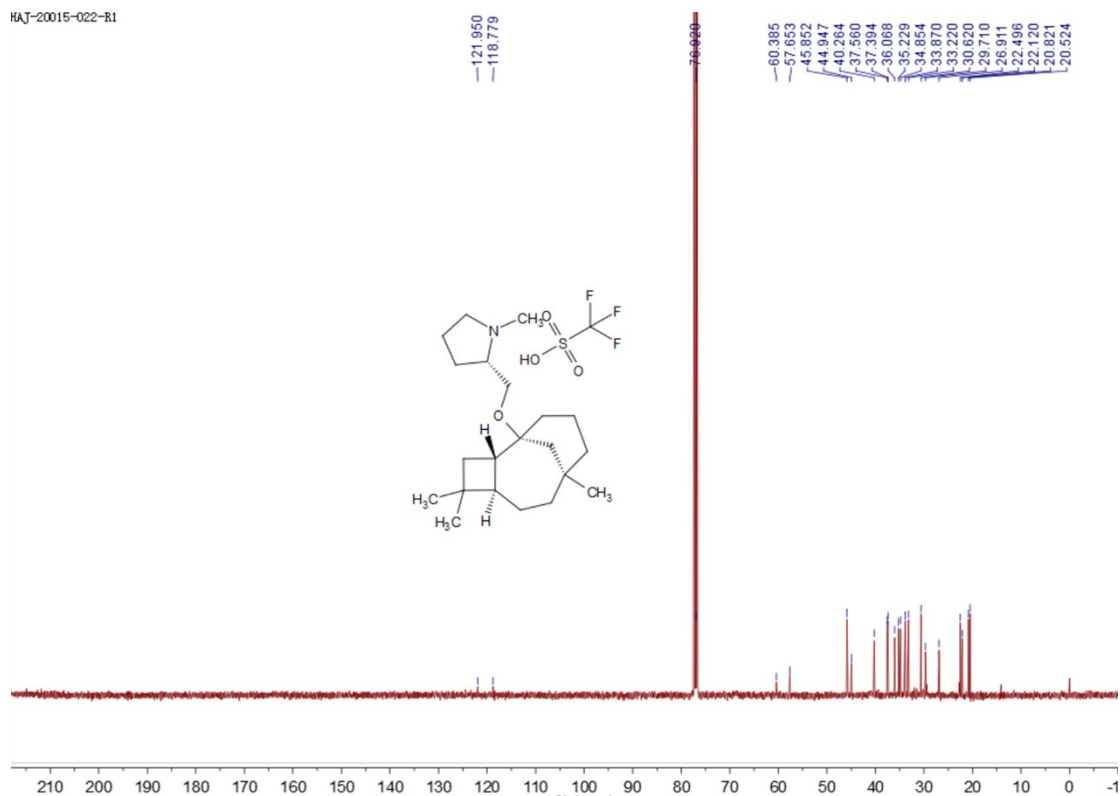
¹H NMR spectrum (CDCl₃) showing peaks from 0 to 12 ppm. The spectrum includes integration values below the peaks and a list of chemical shifts (delta) on the right side.

Chemical shifts (delta): 3.967, 3.971, 3.962, 3.824, 3.818, 3.798, 3.775, 3.507, 3.499, 3.480, 3.472, 3.340, 3.333, 3.095, 3.082, 2.964, 2.942, 2.936, 2.929, 2.915, 2.234, 2.222, 2.214, 2.204, 2.193, 2.178, 2.165, 2.157, 2.138, 2.082, 2.076, 1.837, 1.821, 1.816, 1.801, 1.792, 1.773, 1.732, 1.724, 1.715, 1.705, 1.699, 1.663, 1.641, 1.621, 1.609, 1.600, 1.513, 1.503, 1.493, 1.482, 1.473, 1.466, 1.459, 1.395, 1.369, 1.355, 1.346, 1.333, 1.311, 1.290, 1.285, 1.255, 1.184, 1.152, 1.119, 1.115, 0.988, 0.906, 0.888.

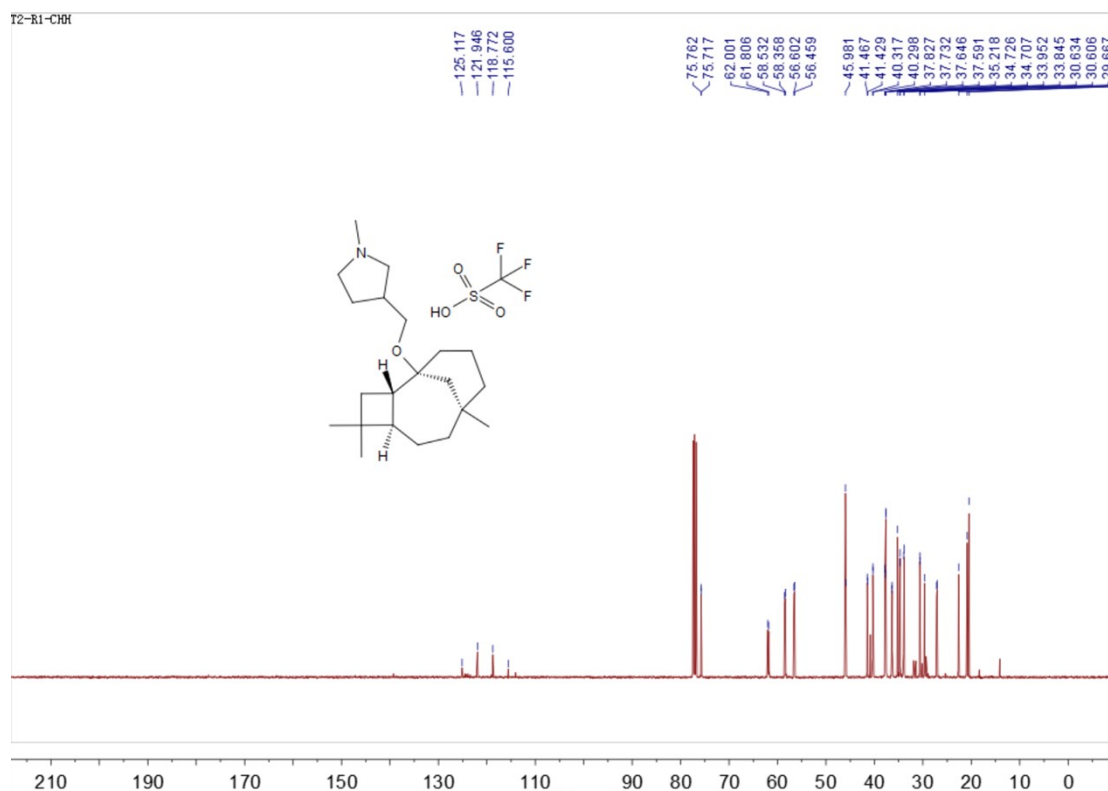
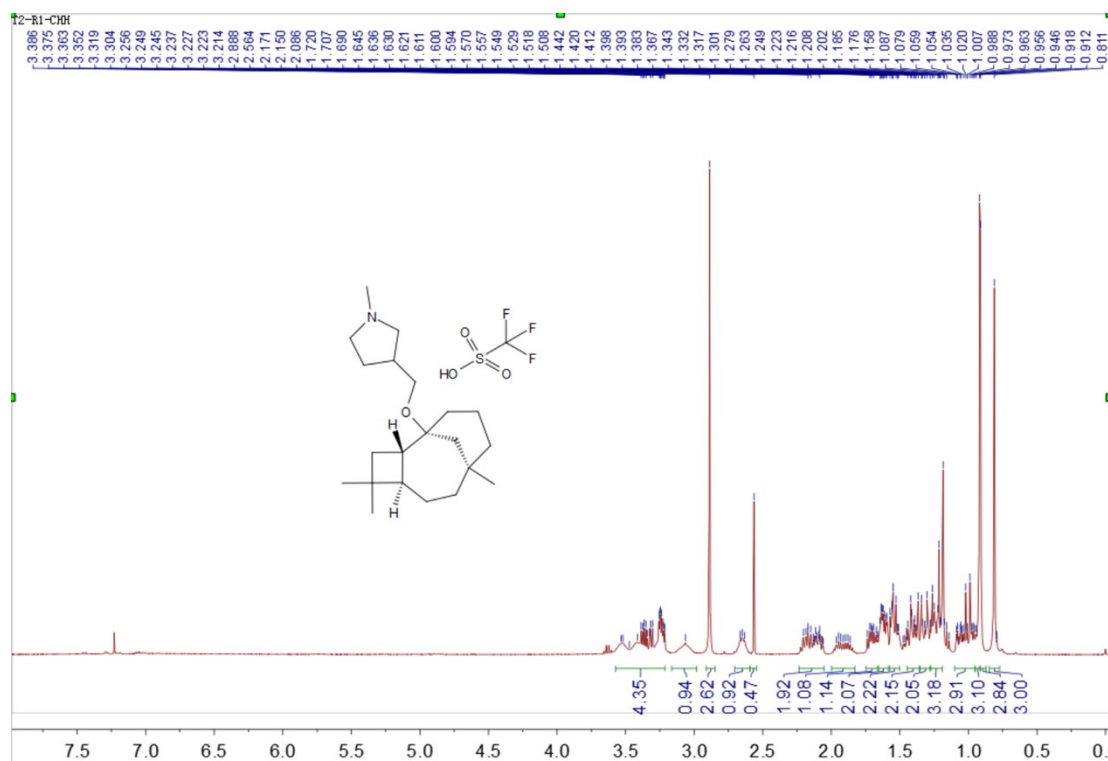
Integration values: 1.00, 0.98, 0.96, 2.88, 1.21, 3.20, 1.11, 3.07, 2.19, 1.23, 1.07, 3.19, 2.25, 1.39, 1.34, 0.99, 6.12, 3.04.



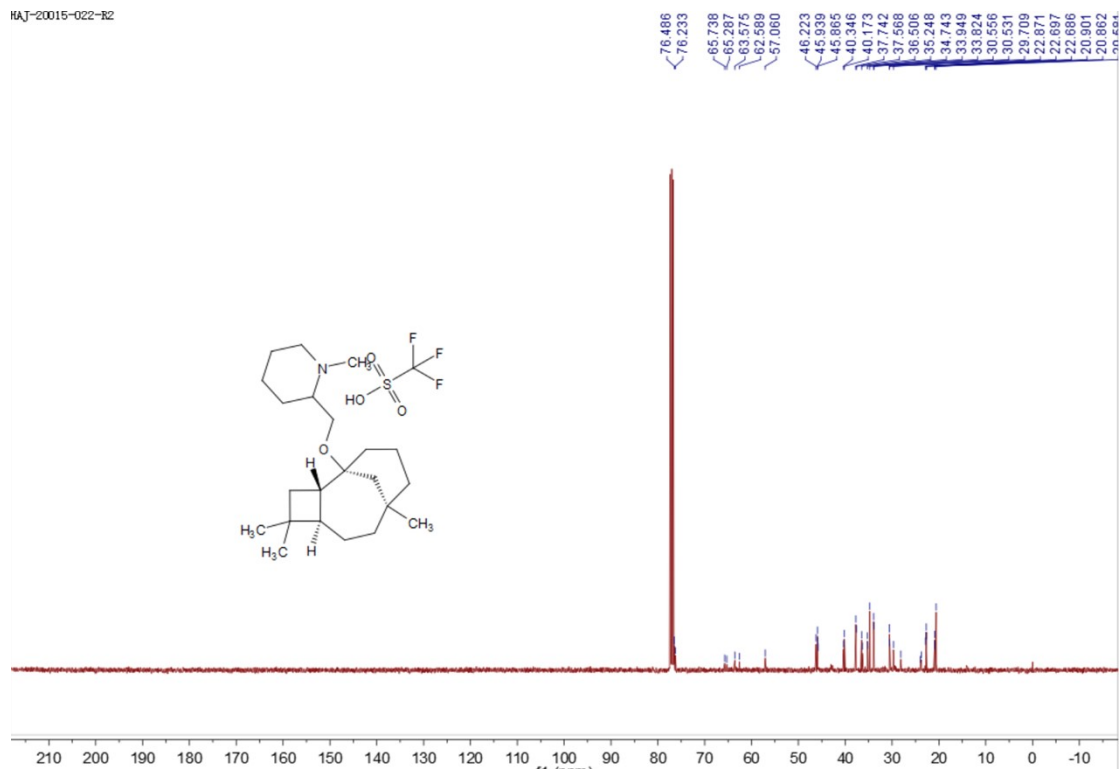
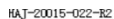
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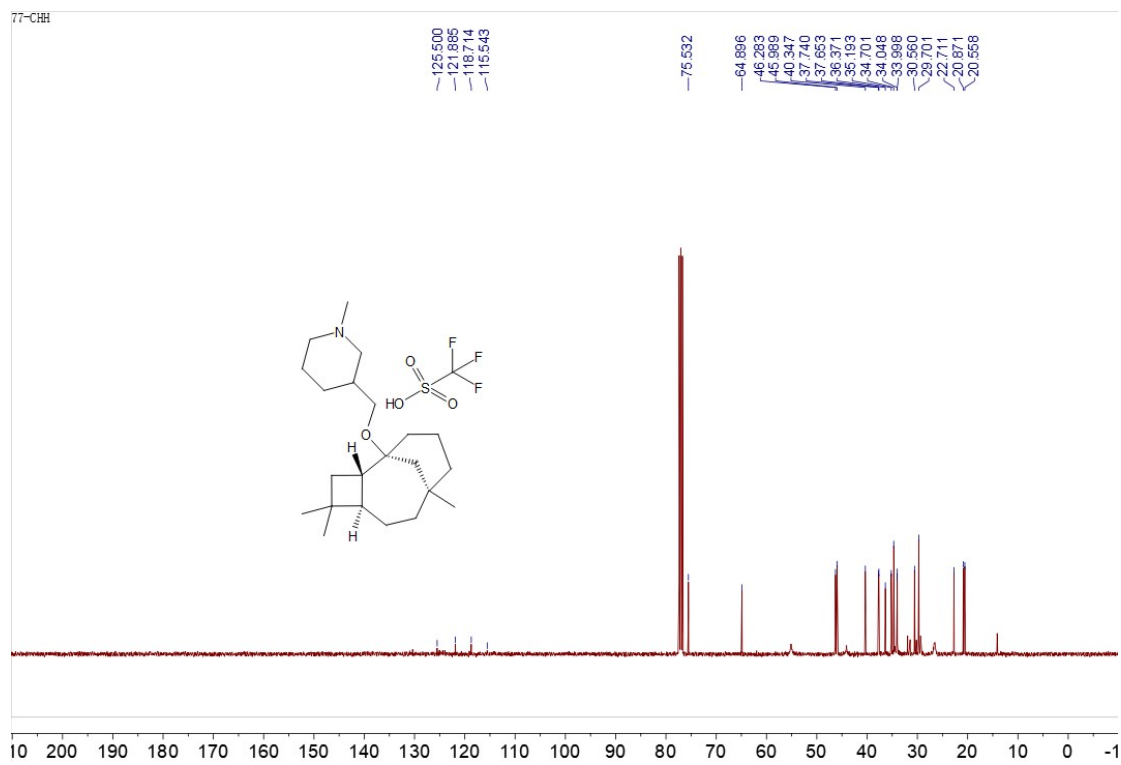
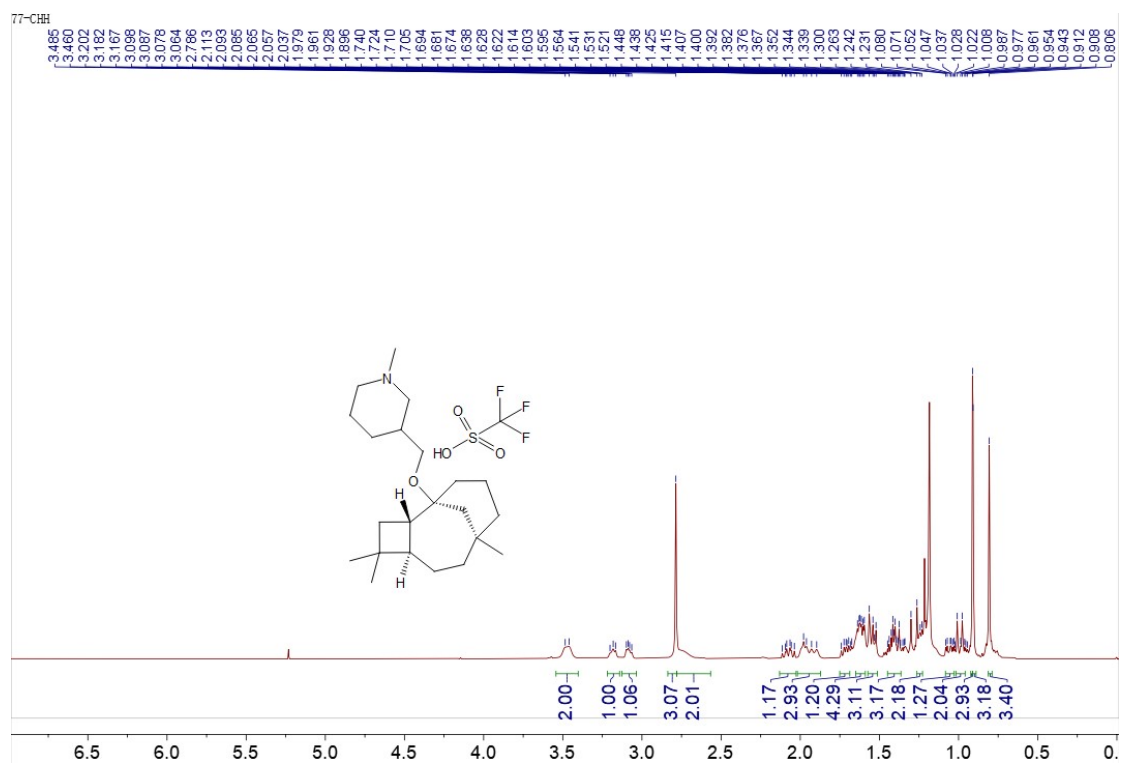
Compound AC-9



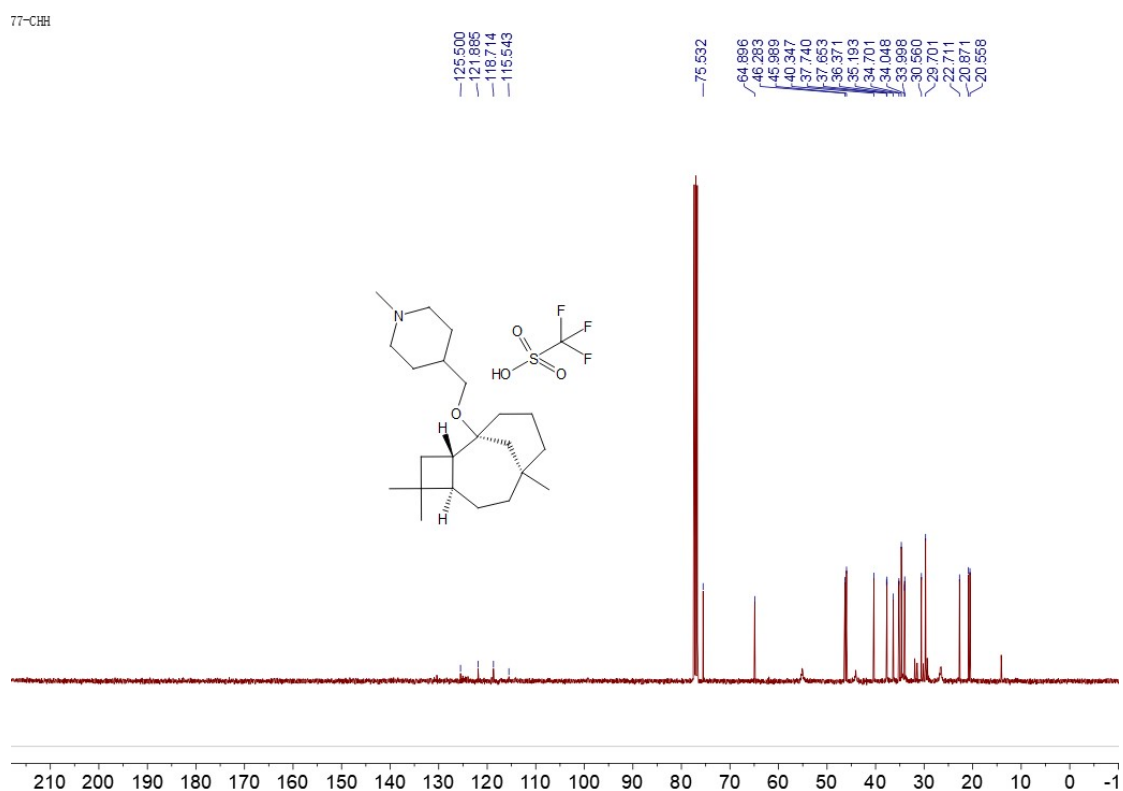
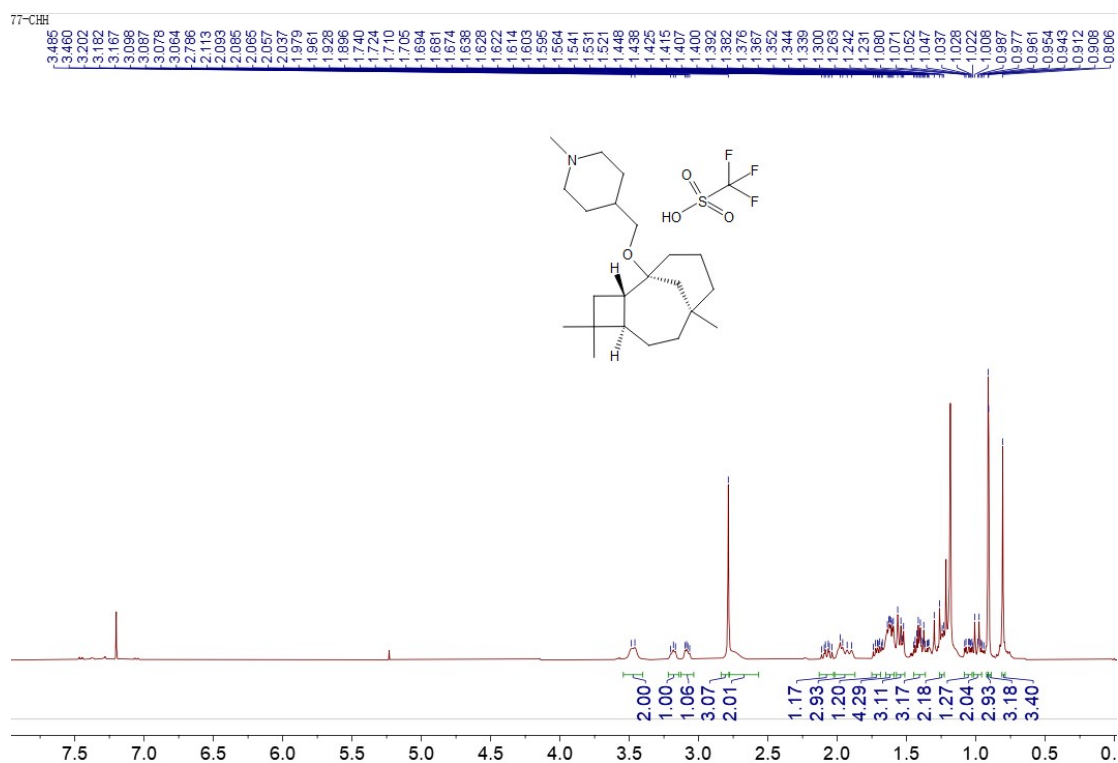
3.73	3.74	3.75	3.76	3.77	3.78	3.79	3.80	3.81	3.82	3.83	3.84	3.85	3.86	3.87	3.88	3.89	3.90	3.91	3.92	3.93	3.94	3.95	3.96	3.97	3.98	3.99	4.00	4.01	4.02	4.03	4.04	4.05	4.06	4.07	4.08	4.09	4.10	4.11	4.12	4.13	4.14	4.15	4.16	4.17	4.18	4.19	4.20	4.21	4.22	4.23	4.24	4.25	4.26	4.27	4.28	4.29	4.30	4.31	4.32	4.33	4.34	4.35	4.36	4.37	4.38	4.39	4.40	4.41	4.42	4.43	4.44	4.45	4.46	4.47	4.48	4.49	4.50	4.51	4.52	4.53	4.54	4.55	4.56	4.57	4.58	4.59	4.60	4.61	4.62	4.63	4.64	4.65	4.66	4.67	4.68	4.69	4.70	4.71	4.72	4.73	4.74	4.75	4.76	4.77	4.78	4.79	4.80	4.81	4.82	4.83	4.84	4.85	4.86	4.87	4.88	4.89	4.90	4.91	4.92	4.93	4.94	4.95	4.96	4.97	4.98	4.99	5.00	5.01	5.02	5.03	5.04	5.05	5.06	5.07	5.08	5.09	5.10	5.11	5.12	5.13	5.14	5.15	5.16	5.17	5.18	5.19	5.20	5.21	5.22	5.23	5.24	5.25	5.26	5.27	5.28	5.29	5.30	5.31	5.32	5.33	5.34	5.35	5.36	5.37	5.38	5.39	5.40	5.41	5.42	5.43	5.44	5.45	5.46	5.47	5.48	5.49	5.50	5.51	5.52	5.53	5.54	5.55	5.56	5.57	5.58	5.59	5.60	5.61	5.62	5.63	5.64	5.65	5.66	5.67	5.68	5.69	5.70	5.71	5.72	5.73	5.74	5.75	5.76	5.77	5.78	5.79	5.80	5.81	5.82	5.83	5.84	5.85	5.86	5.87	5.88	5.89	5.90	5.91	5.92	5.93	5.94	5.95	5.96	5.97	5.98	5.99	6.00	6.01	6.02	6.03	6.04	6.05	6.06	6.07	6.08	6.09	6.10	6.11	6.12	6.13	6.14	6.15	6.16	6.17	6.18	6.19	6.20	6.21	6.22	6.23	6.24	6.25	6.26	6.27	6.28	6.29	6.30	6.31	6.32	6.33	6.34	6.35	6.36	6.37	6.38	6.39	6.40	6.41	6.42	6.43	6.44	6.45	6.46	6.47	6.48	6.49	6.50	6.51	6.52	6.53	6.54	6.55	6.56	6.57	6.58	6.59	6.60	6.61	6.62	6.63	6.64	6.65	6.66	6.67	6.68	6.69	6.70	6.71	6.72	6.73	6.74	6.75	6.76	6.77	6.78	6.79	6.80	6.81	6.82	6.83	6.84	6.85	6.86	6.87	6.88	6.89	6.90	6.91	6.92	6.93	6.94	6.95	6.96	6.97	6.98	6.99	7.00	7.01	7.02	7.03	7.04	7.05	7.06	7.07	7.08	7.09	7.10	7.11	7.12	7.13	7.14	7.15	7.16	7.17	7.18	7.19	7.20	7.21	7.22	7.23	7.24	7.25	7.26	7.27	7.28	7.29	7.30	7.31	7.32	7.33	7.34	7.35	7.36	7.37	7.38	7.39	7.40	7.41	7.42	7.43	7.44	7.45	7.46	7.47	7.48	7.49	7.50	7.51	7.52	7.53	7.54	7.55	7.56	7.57	7.58	7.59	7.60	7.61	7.62	7.63	7.64	7.65	7.66	7.67	7.68	7.69	7.70	7.71	7.72	7.73	7.74	7.75	7.76	7.77	7.78	7.79	7.80	7.81	7.82	7.83	7.84	7.85	7.86	7.87	7.88	7.89	7.90	7.91	7.92	7.93	7.94	7.95	7.96	7.97	7.98	7.99	8.00	8.01	8.02	8.03	8.04	8.05	8.06	8.07	8.08	8.09	8.10	8.11	8.12	8.13	8.14	8.15	8.16	8.17	8.18	8.19	8.20	8.21	8.22	8.23	8.24	8.25	8.26
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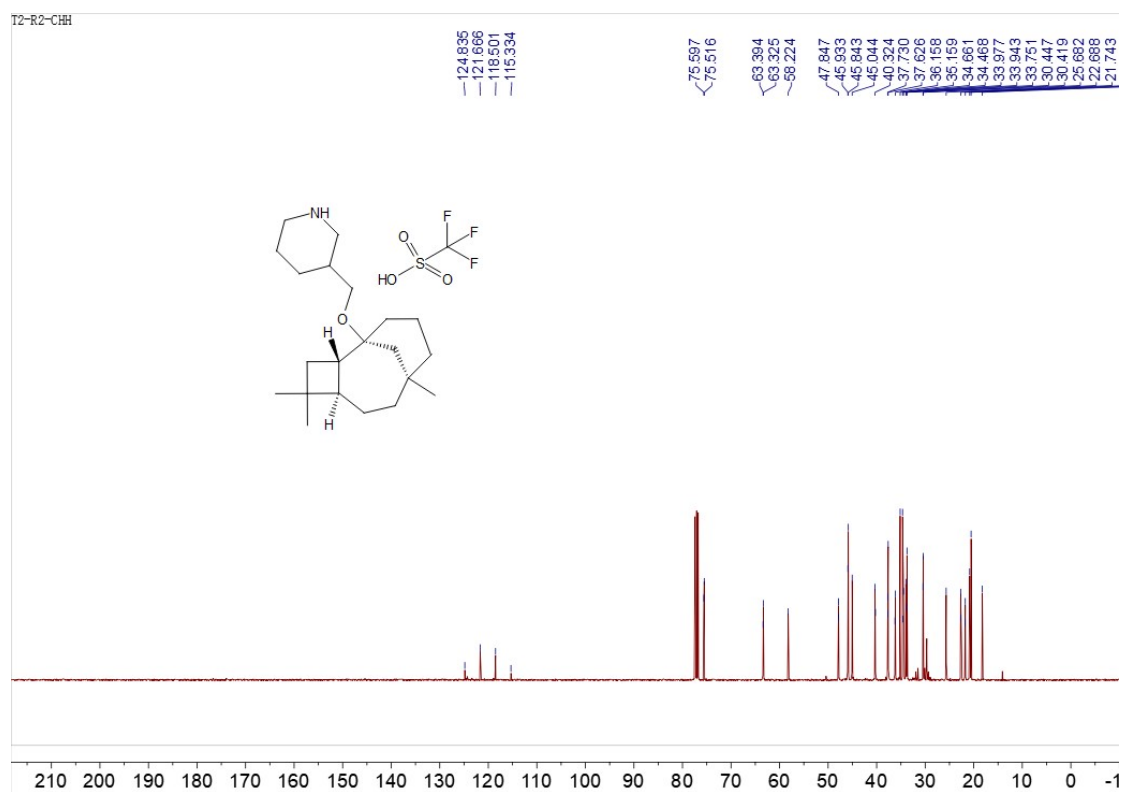
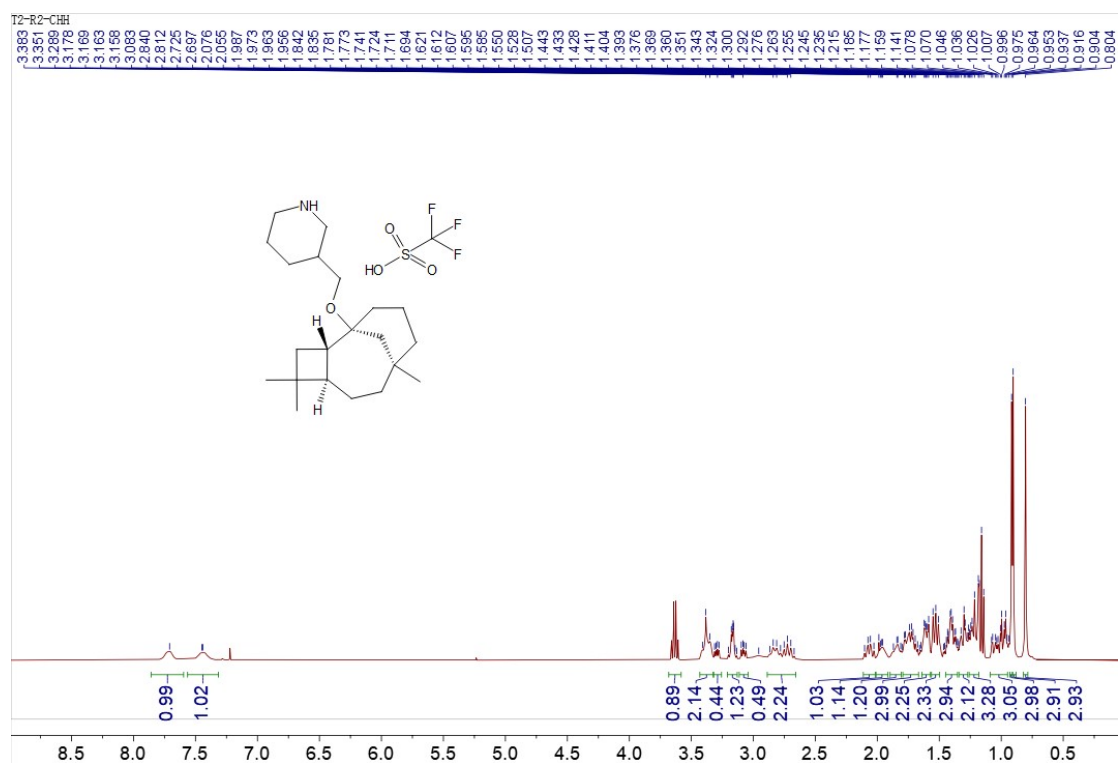
Compound AC-11



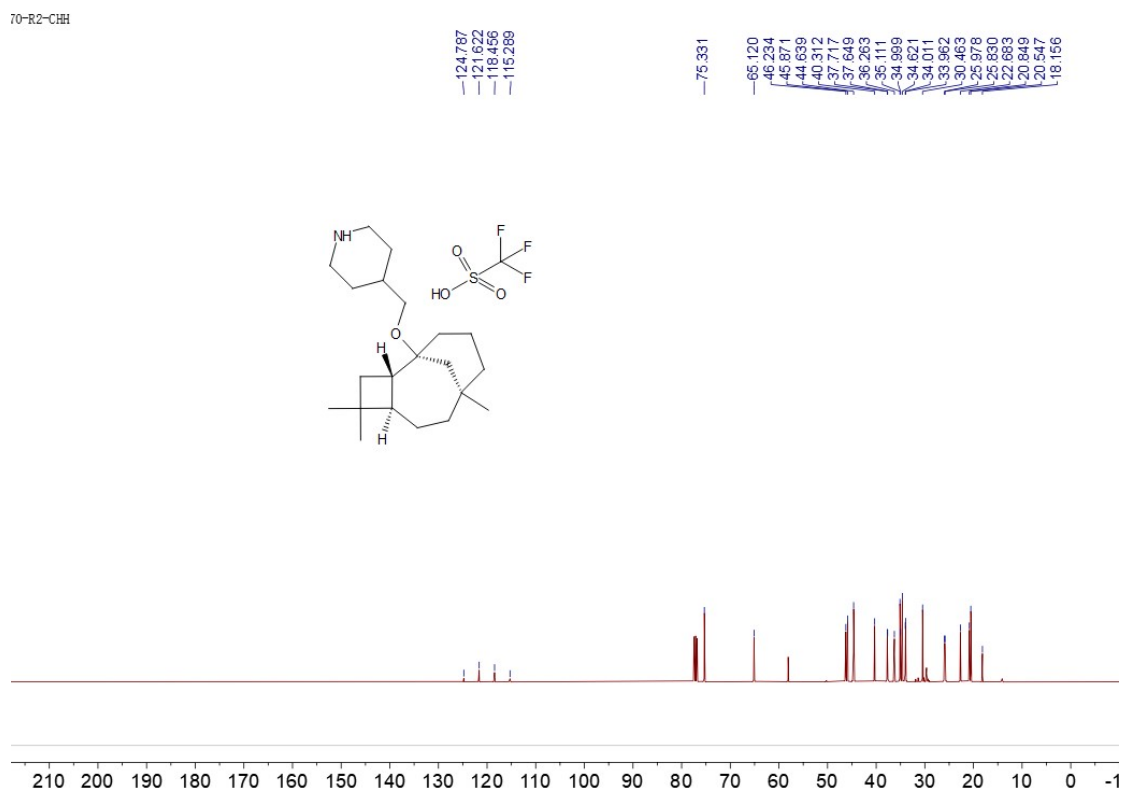
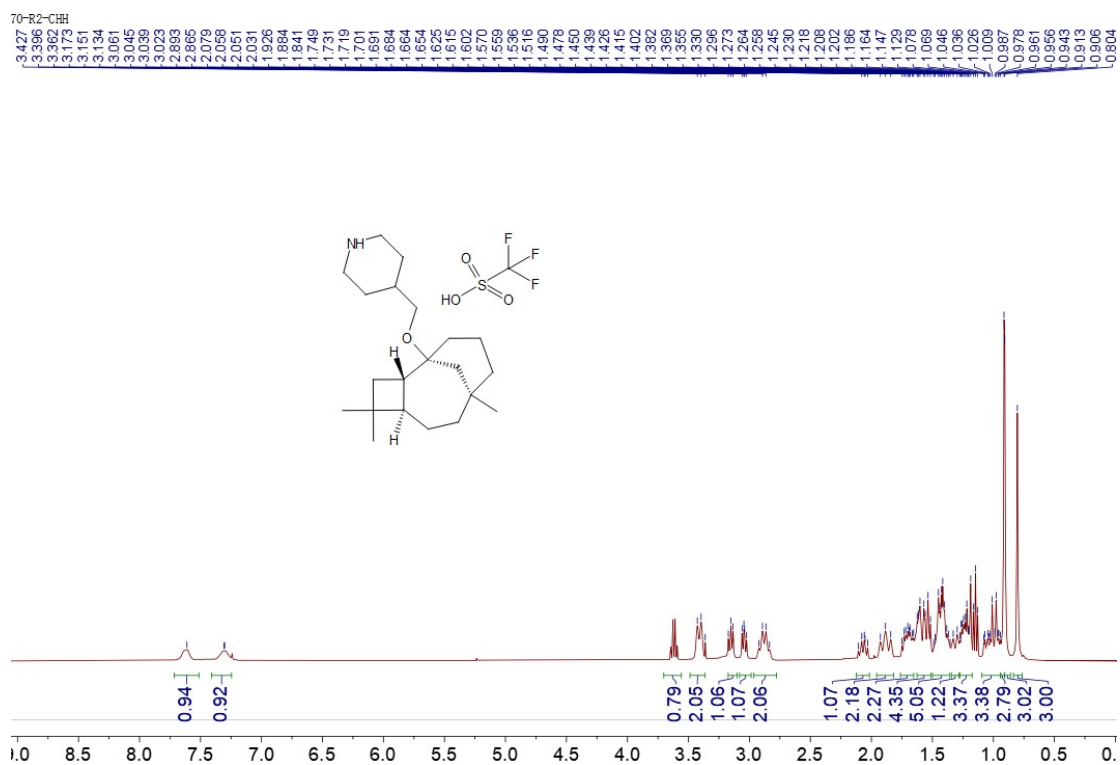
Compound AC-12



Compound AC-13

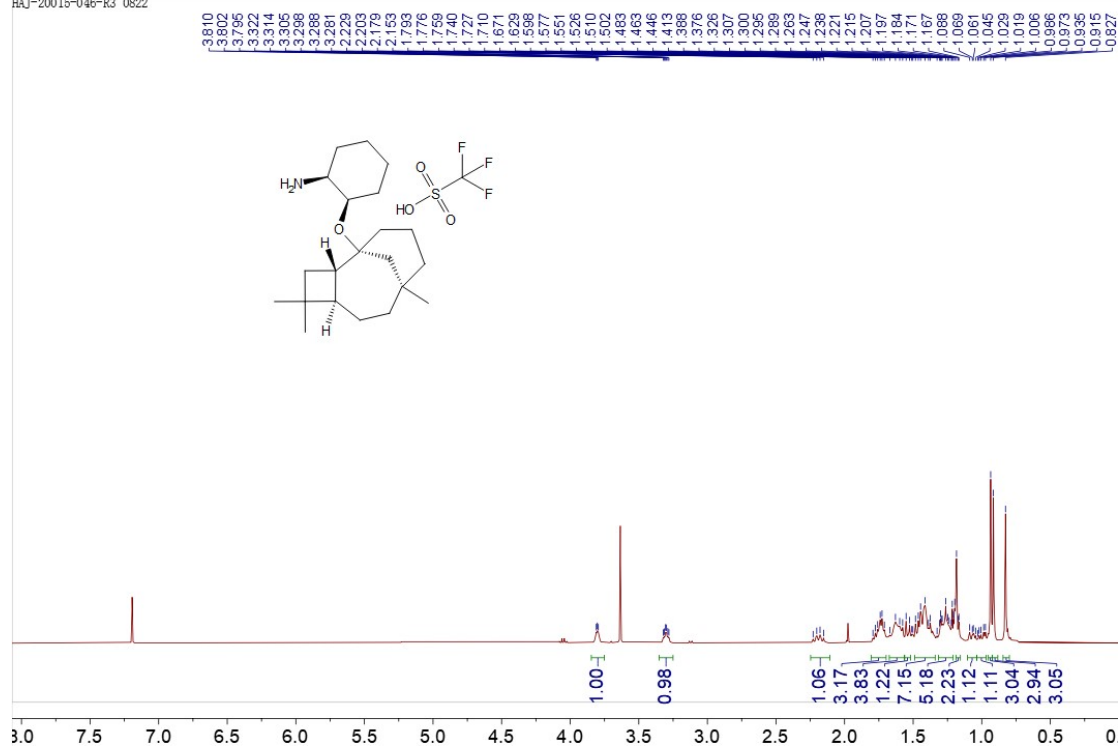


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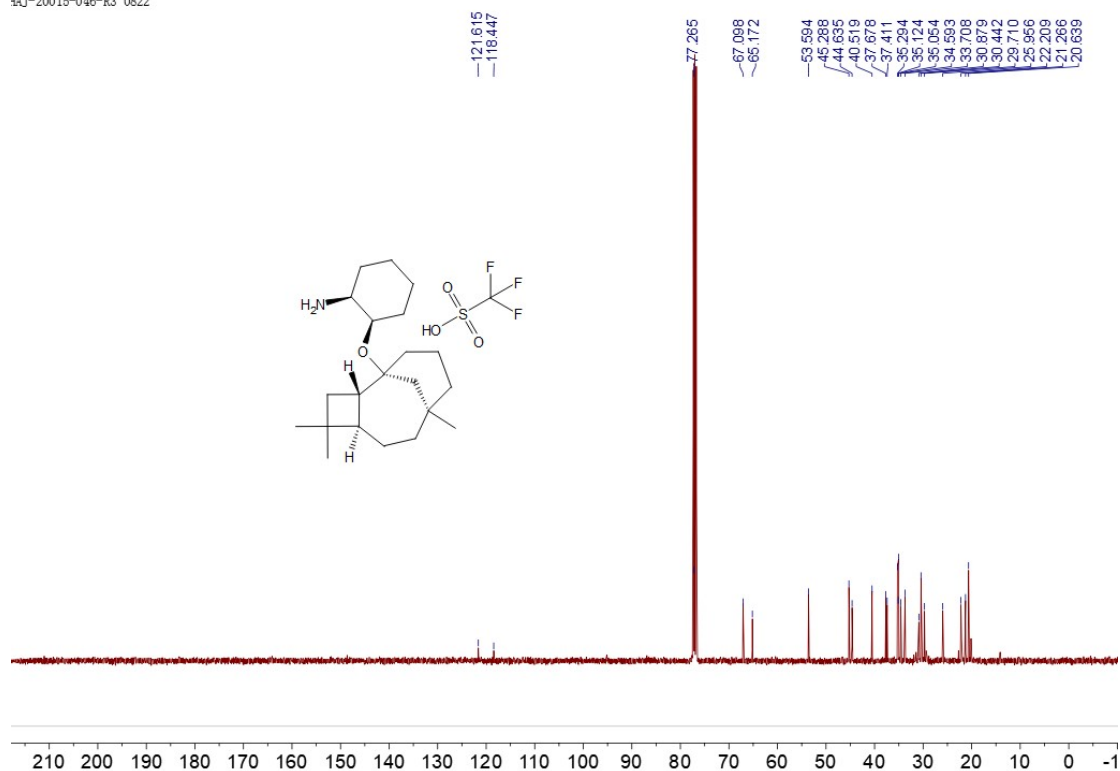


Compound AC-15

HAJ-20015-046-R3 0822

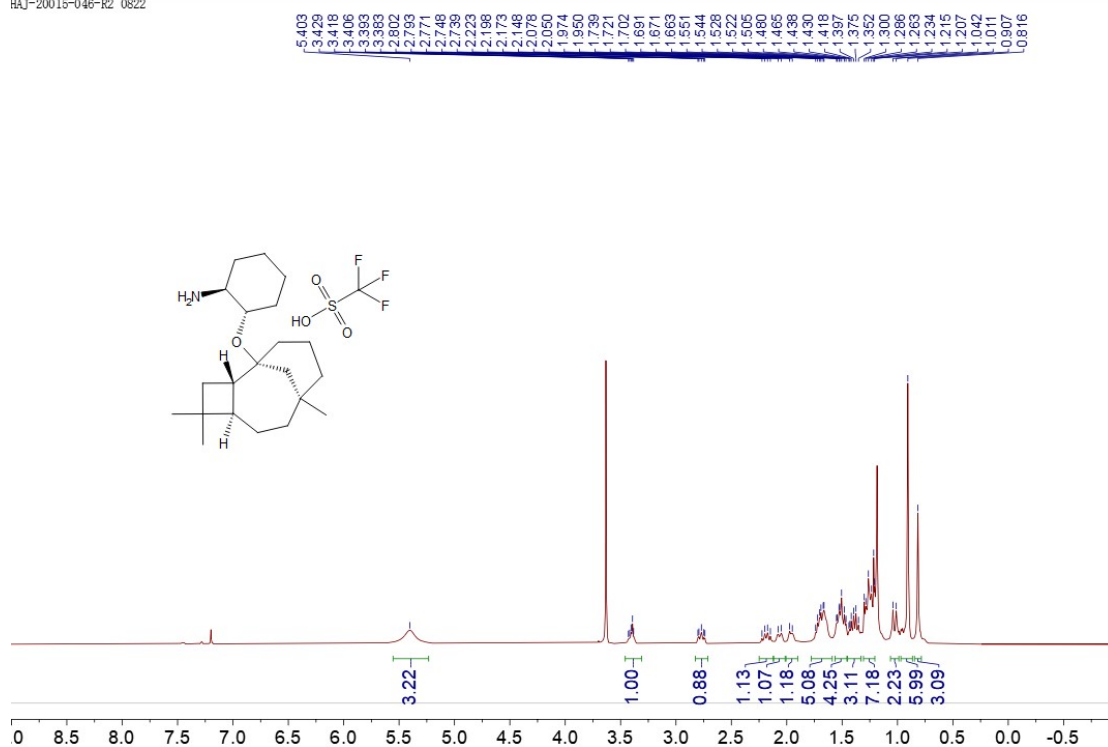


HAJ-20015-046-R3 0822

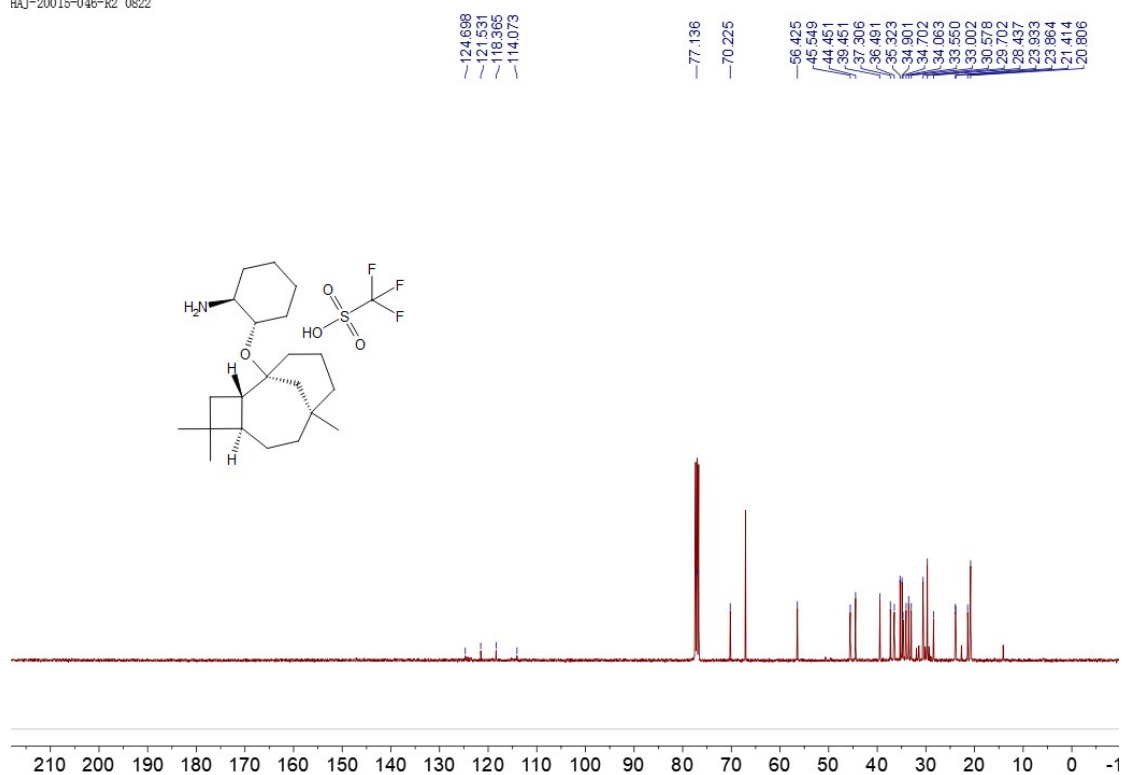


Compound AC-16

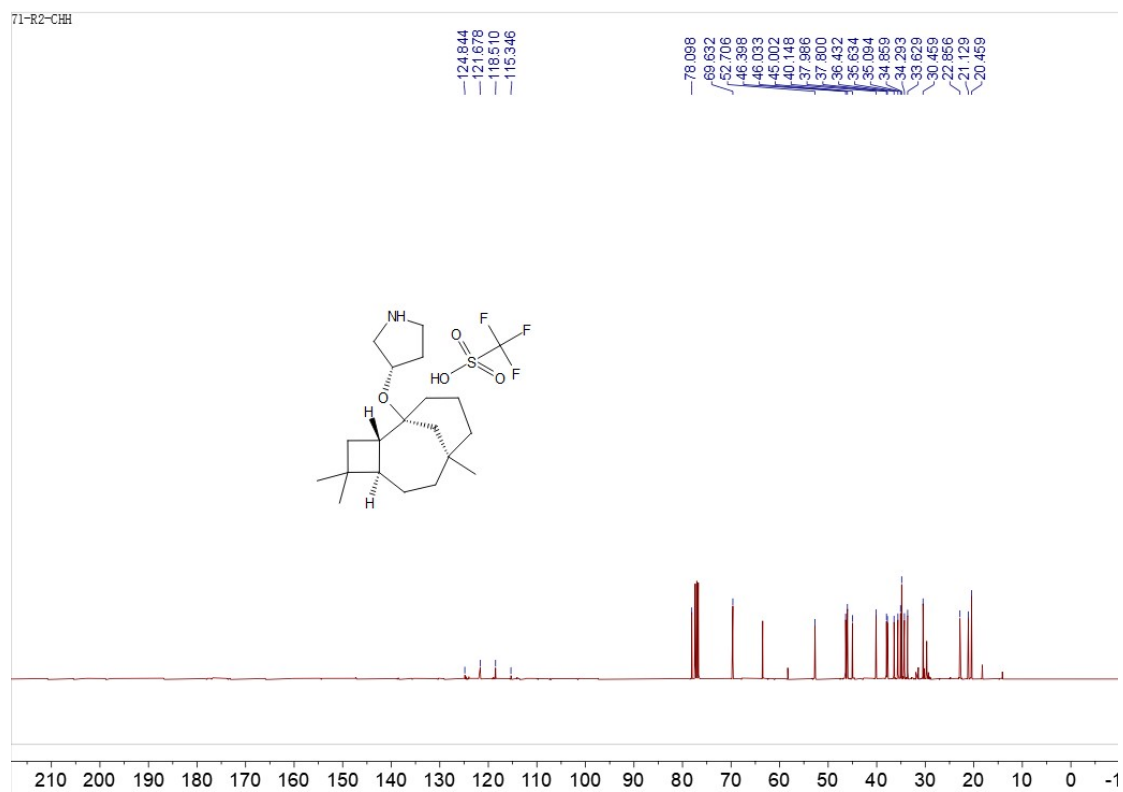
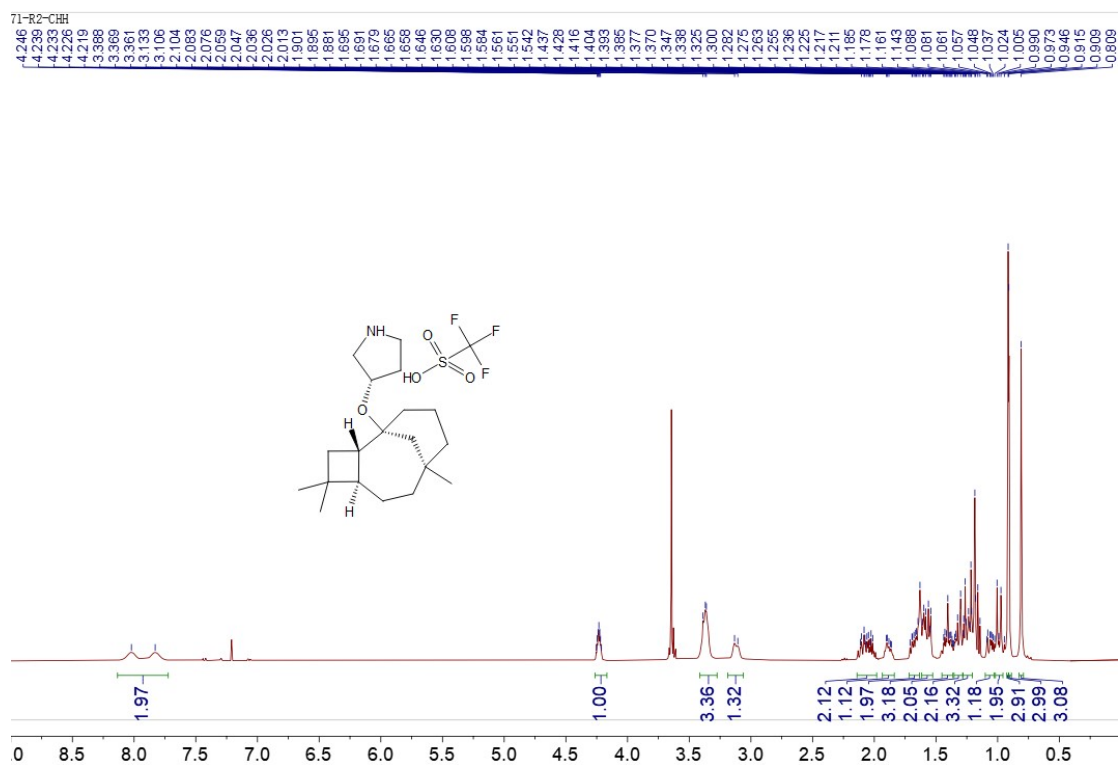
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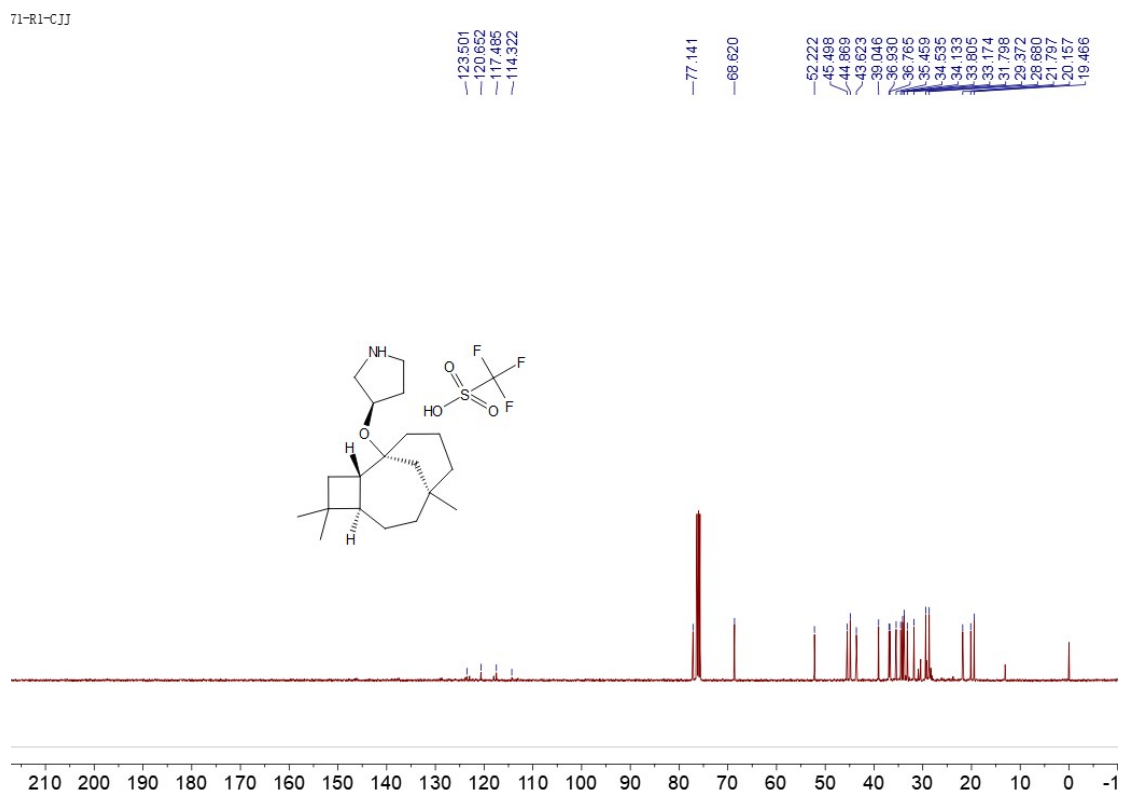
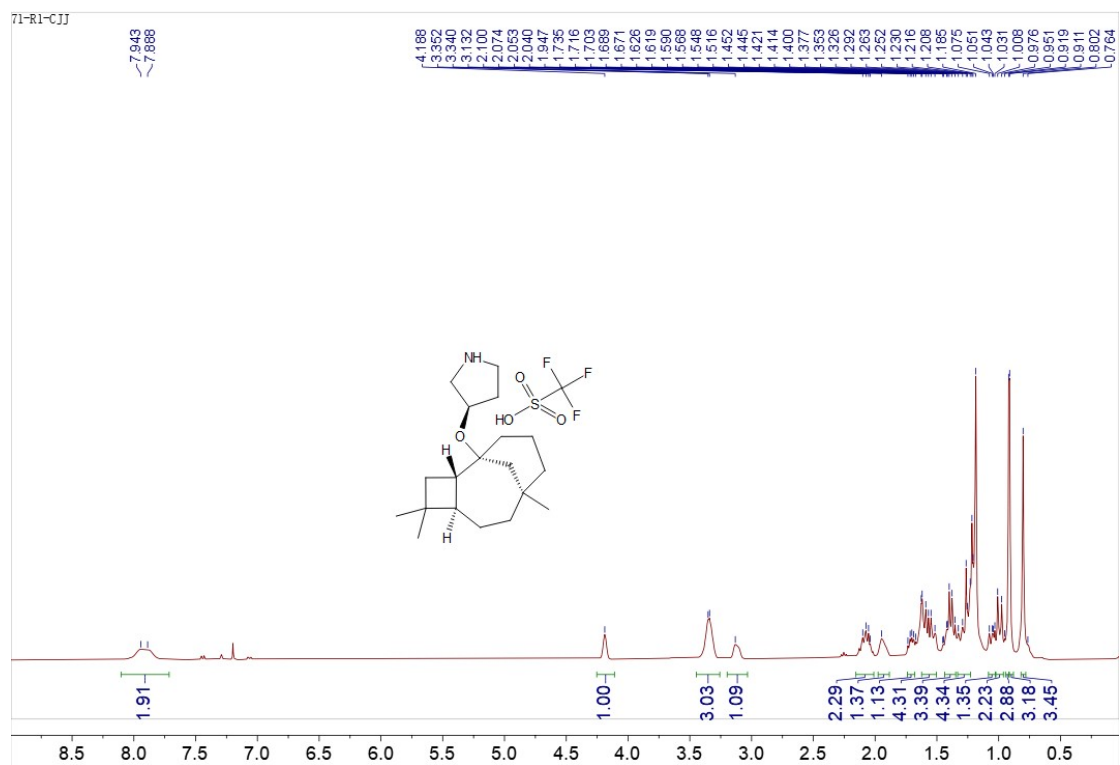
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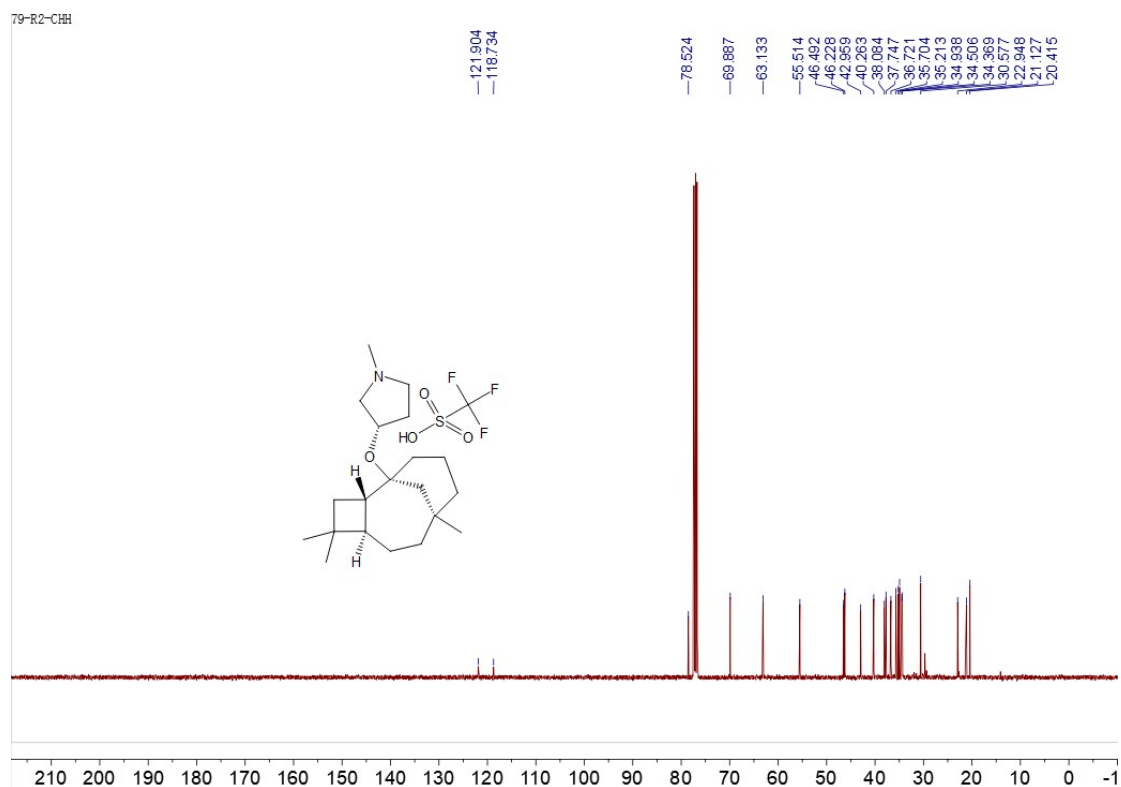
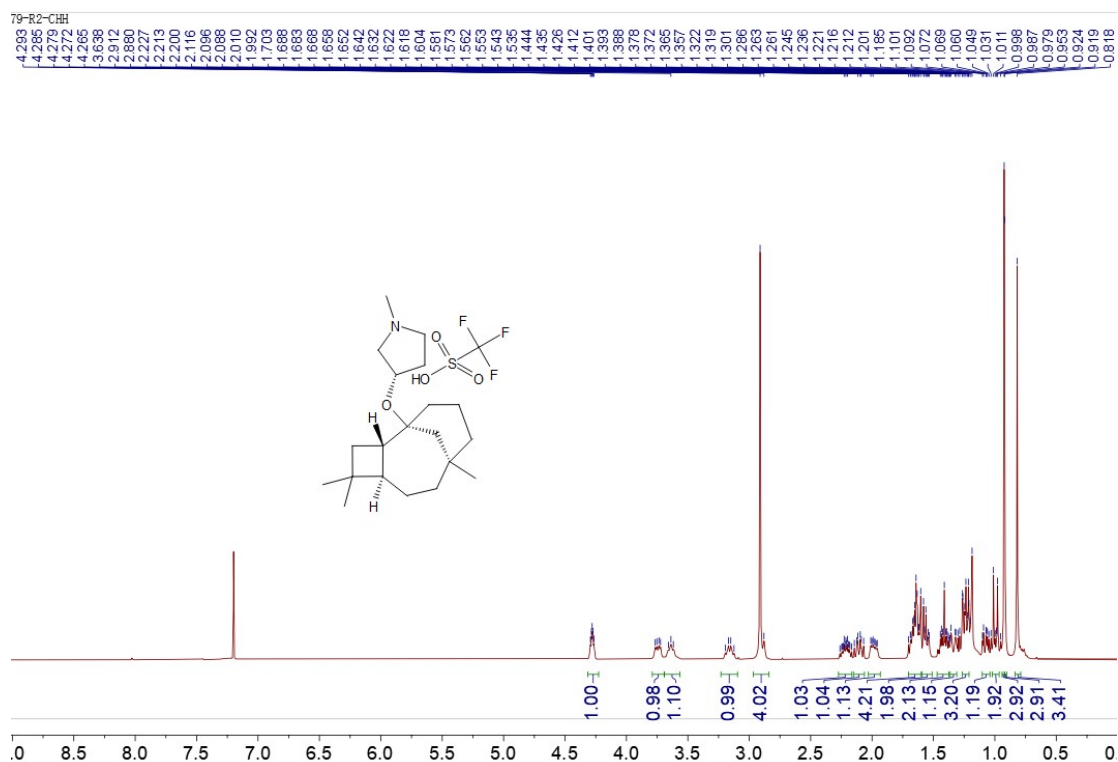
Compound AC-17



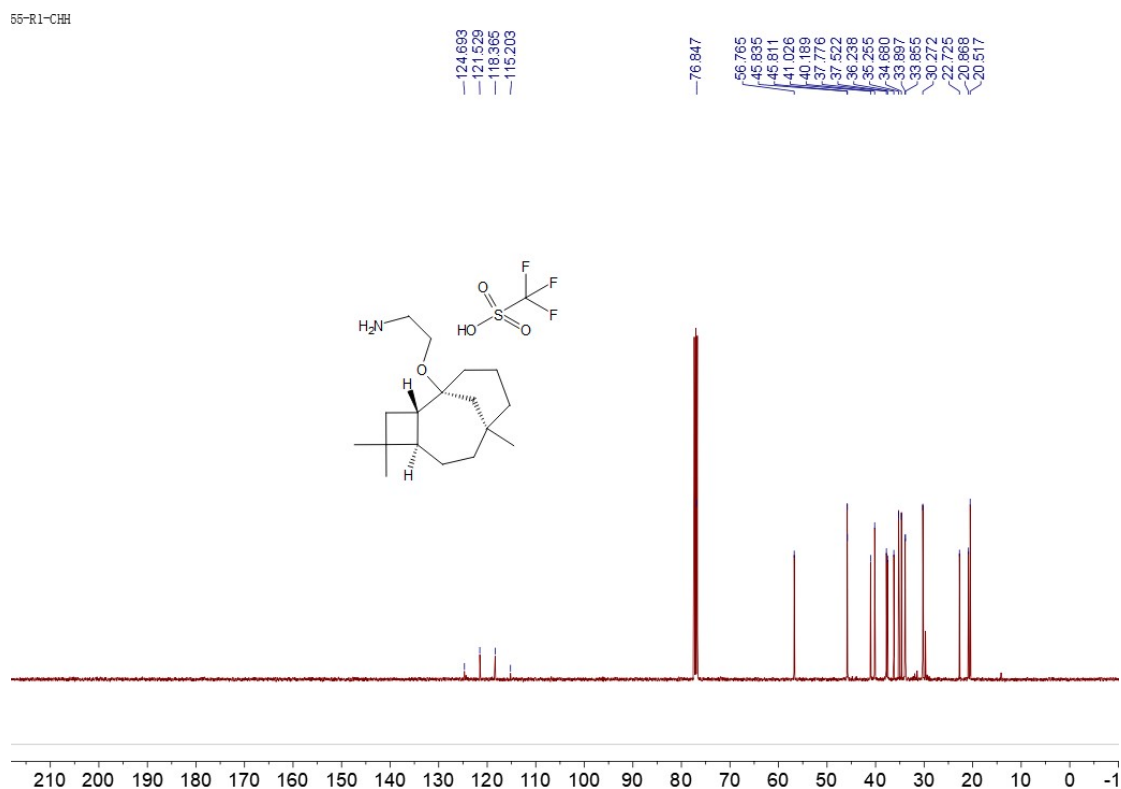
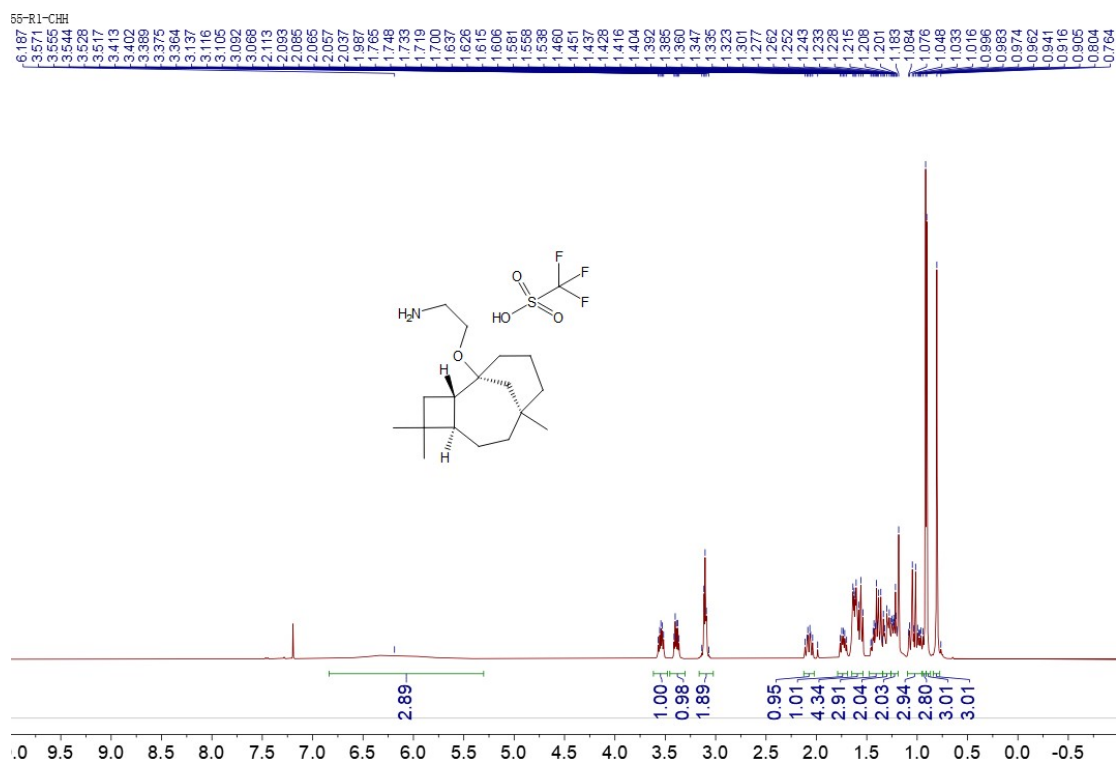
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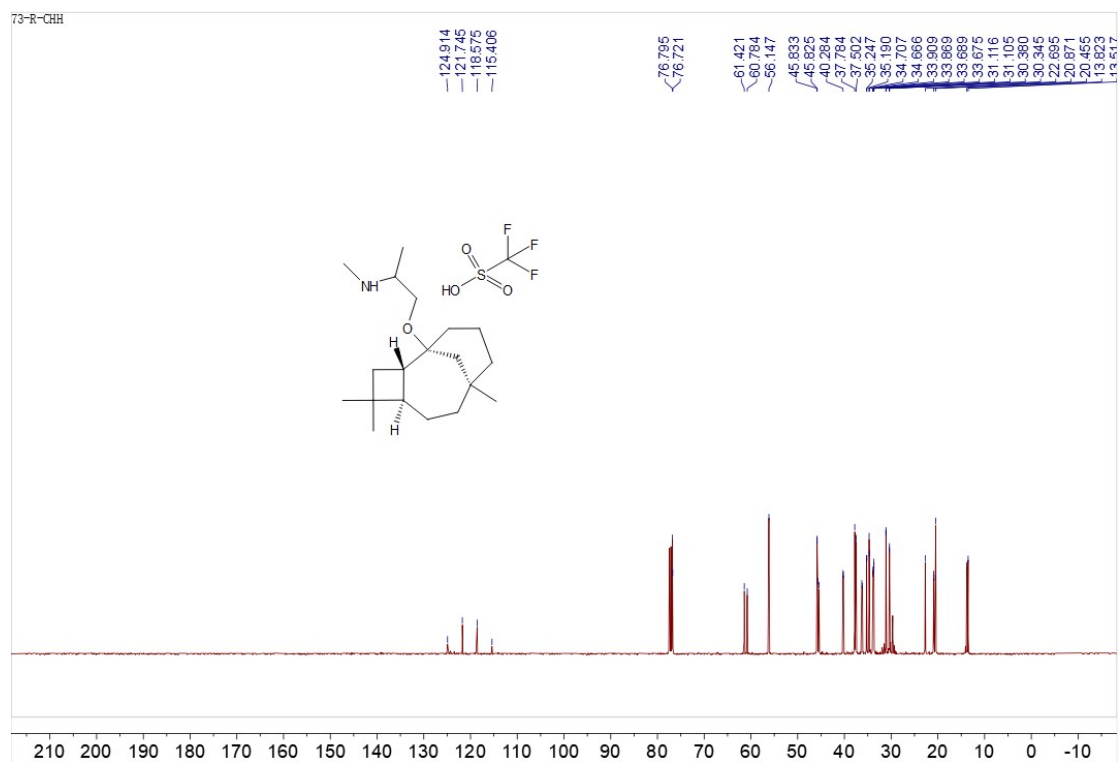
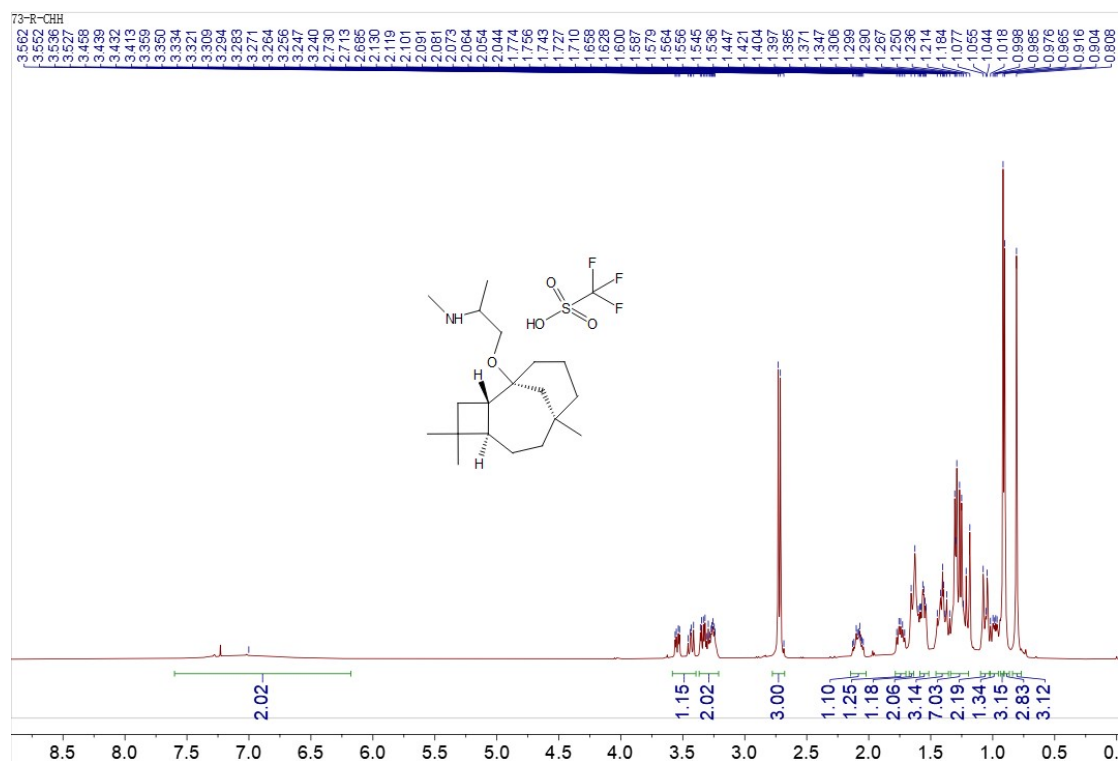
Compound AC-19



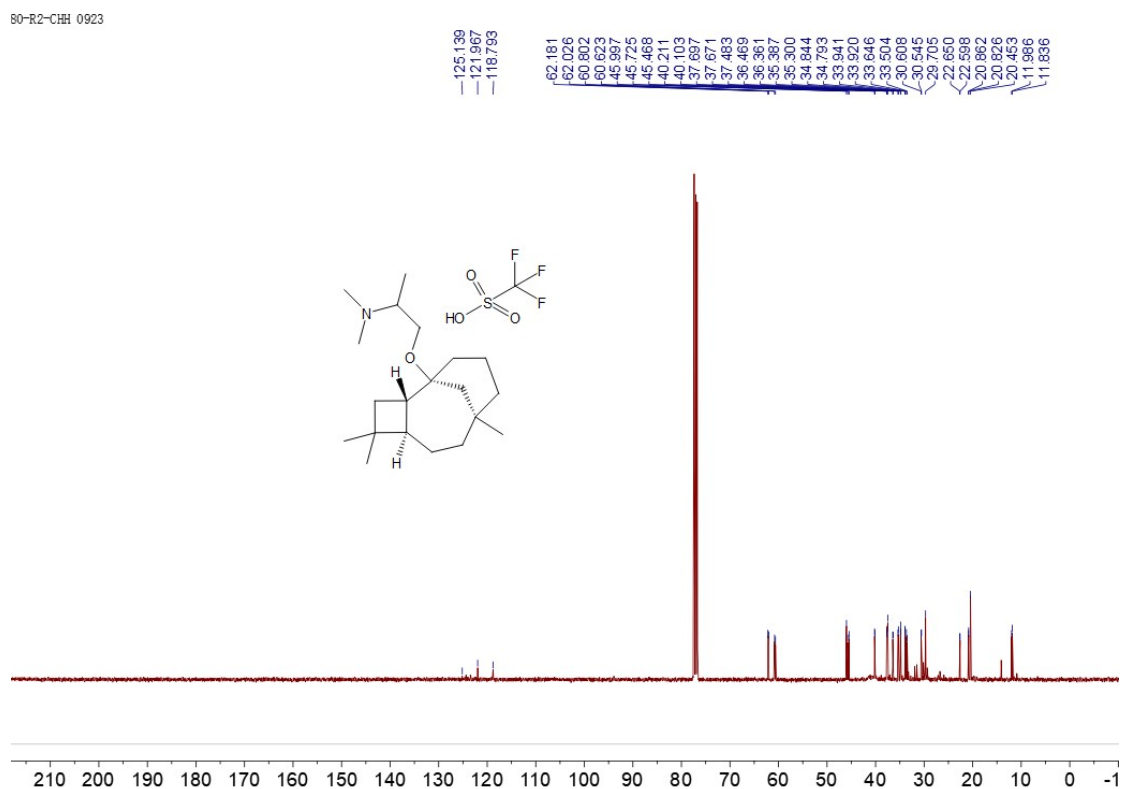
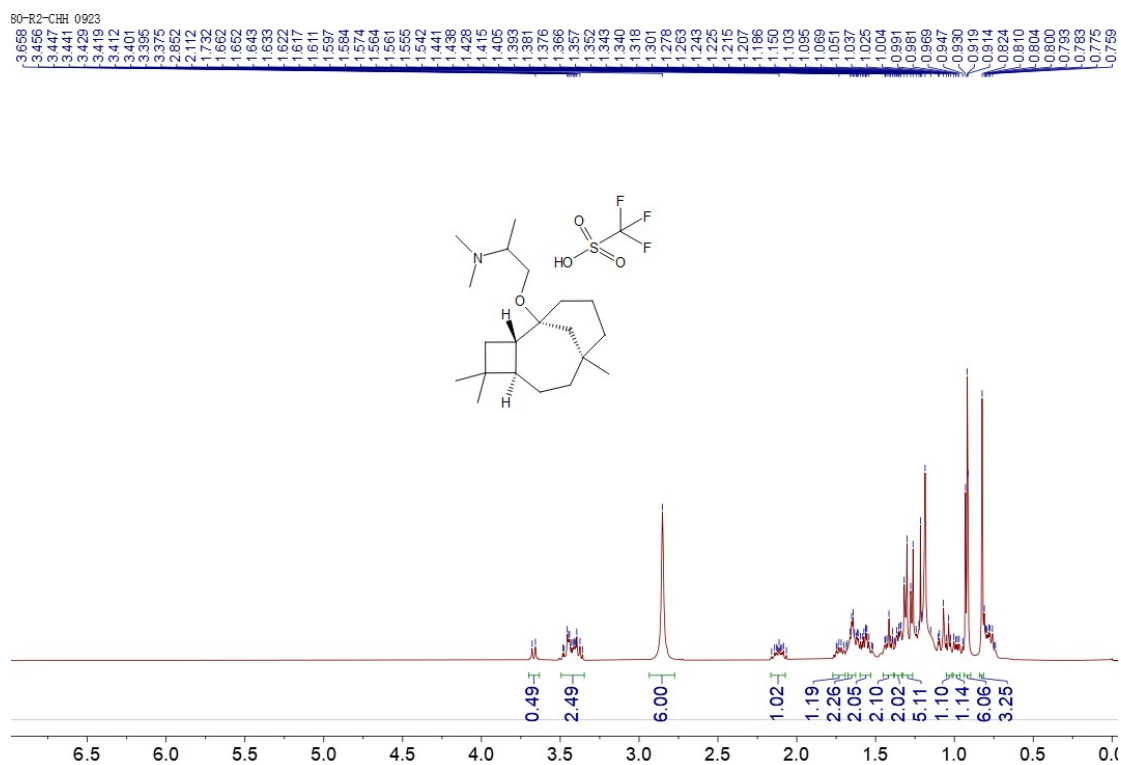
Compound AC-20



Compound AC-21



Compound AC-22



Compound AC-23

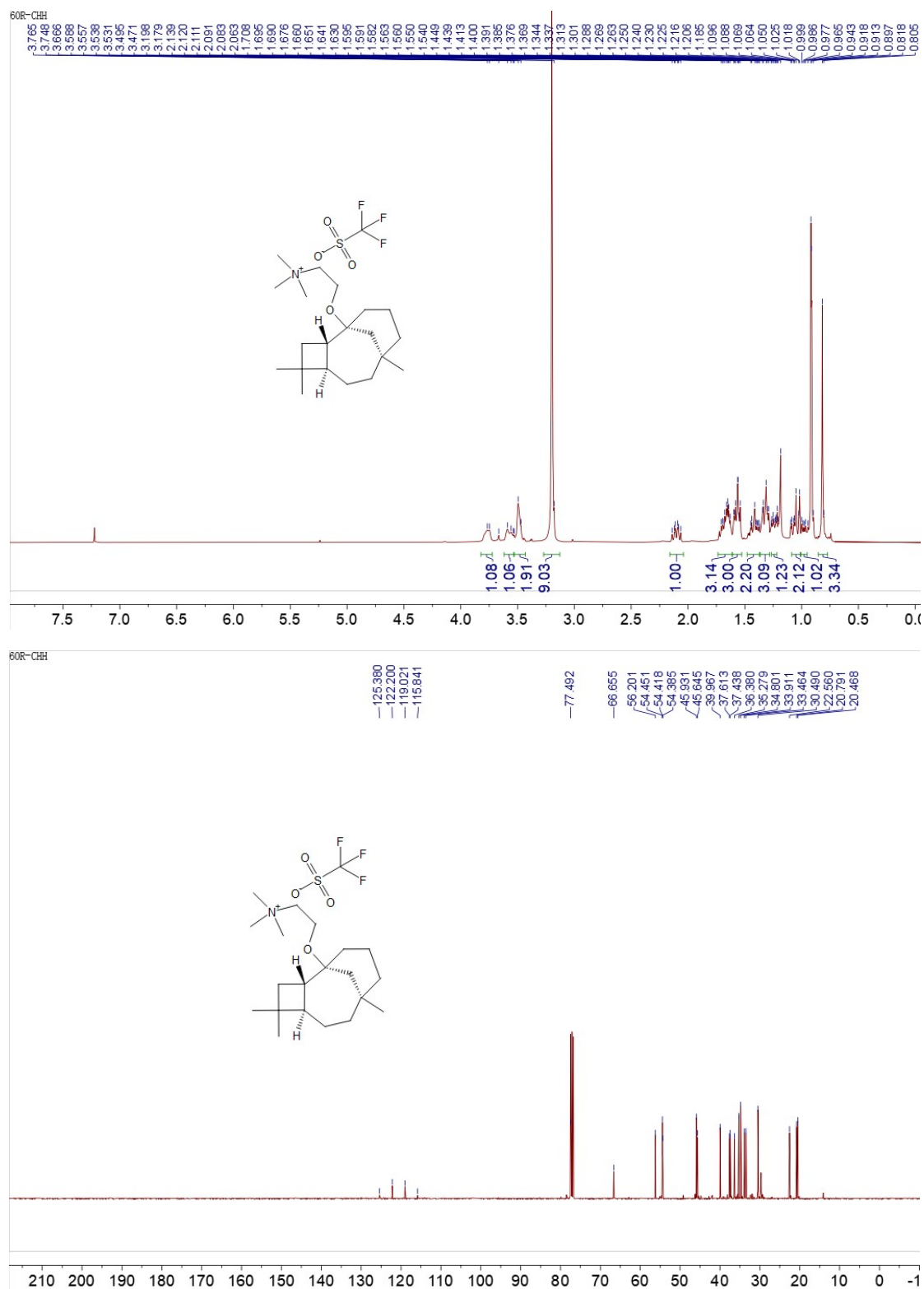
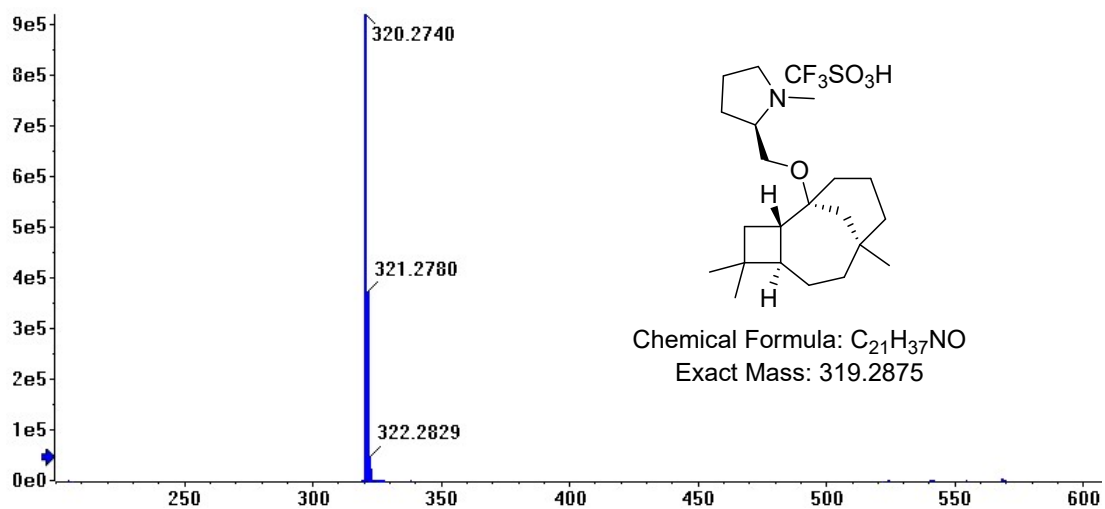
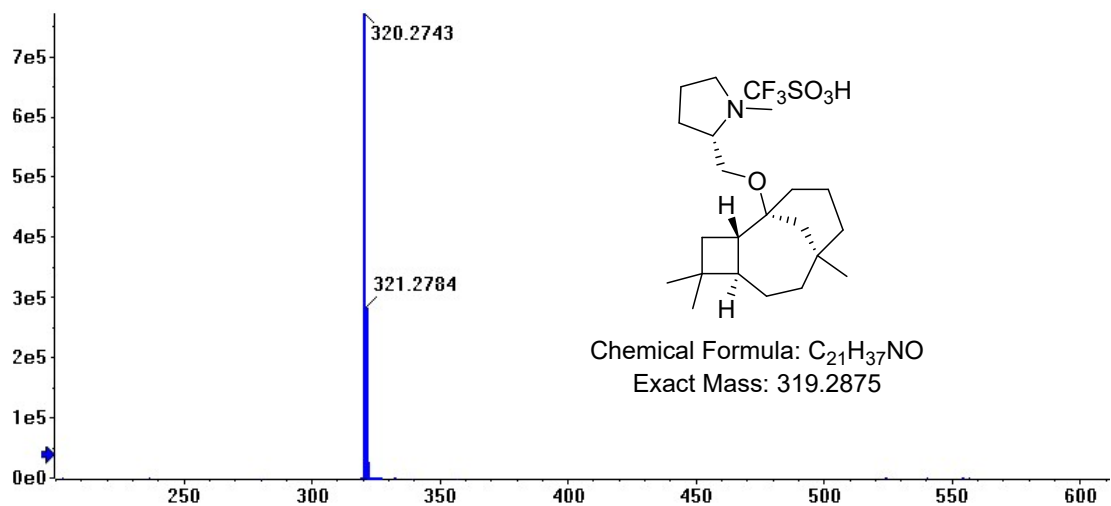


Fig S2. ¹H and ¹³C NMR spectra of AC-1 to AC-23.

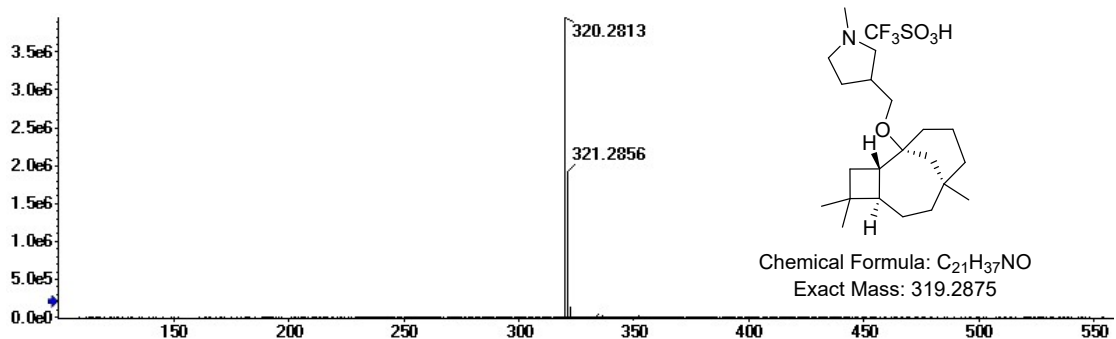
AC-7



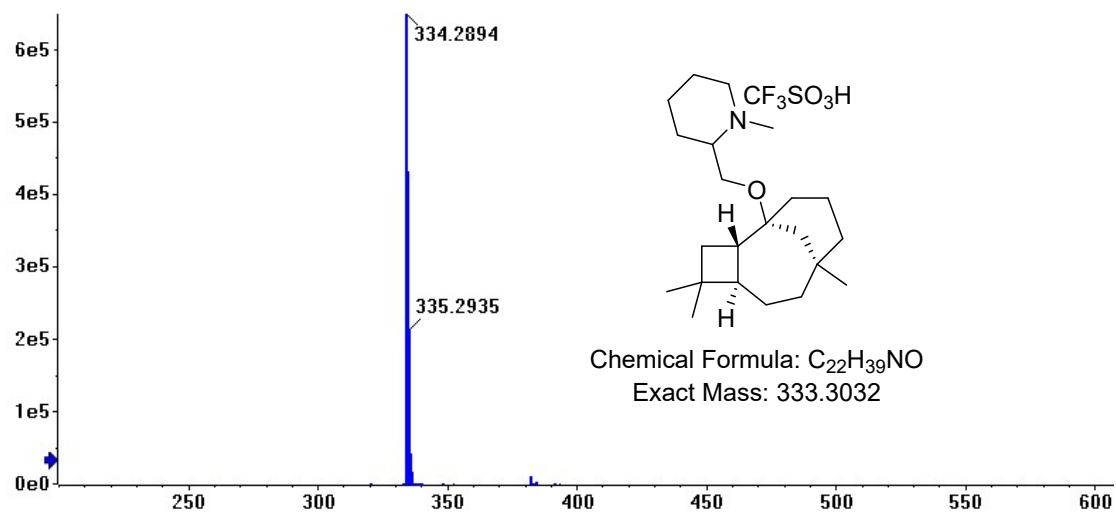
AC-8



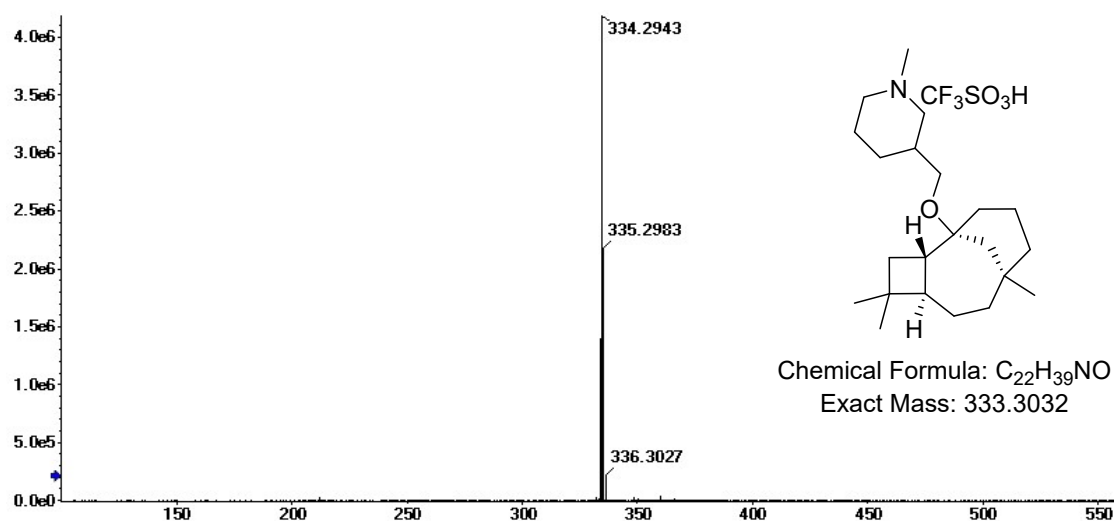
AC-9



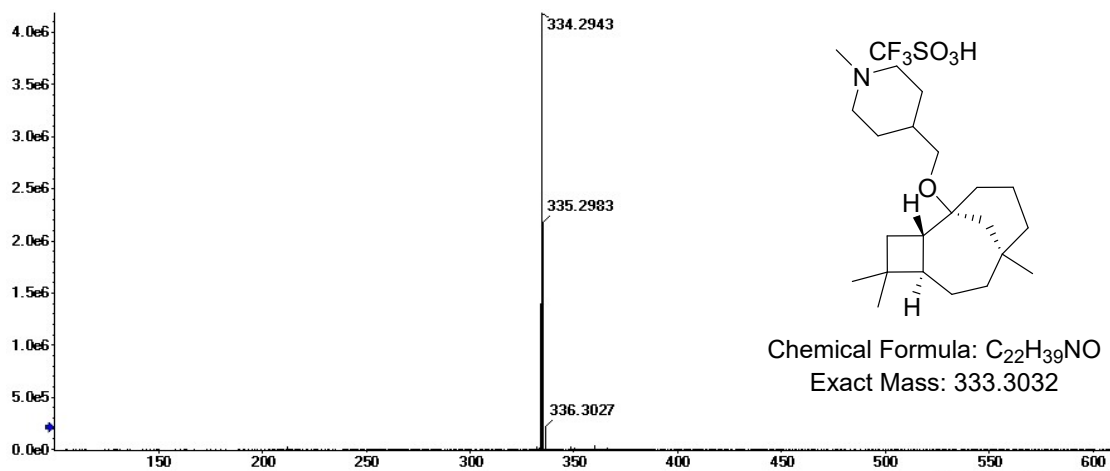
AC-10



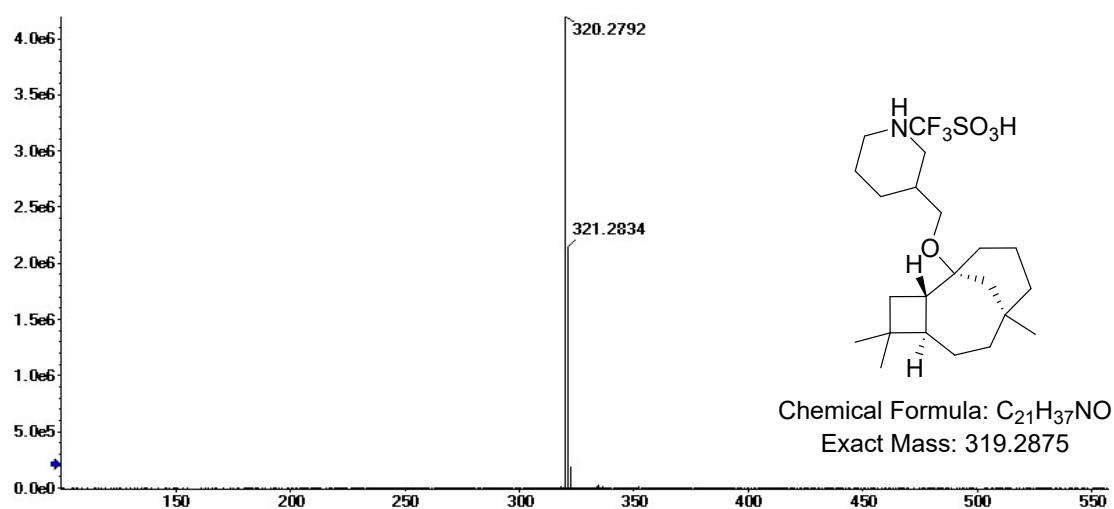
AC-11



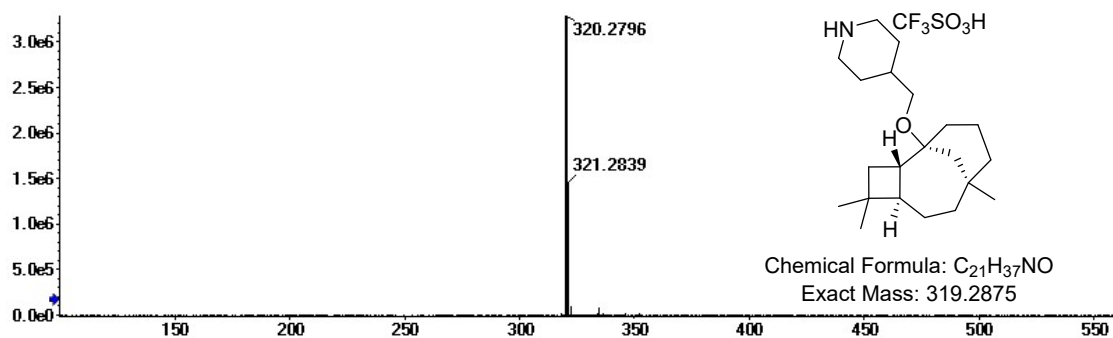
AC-12



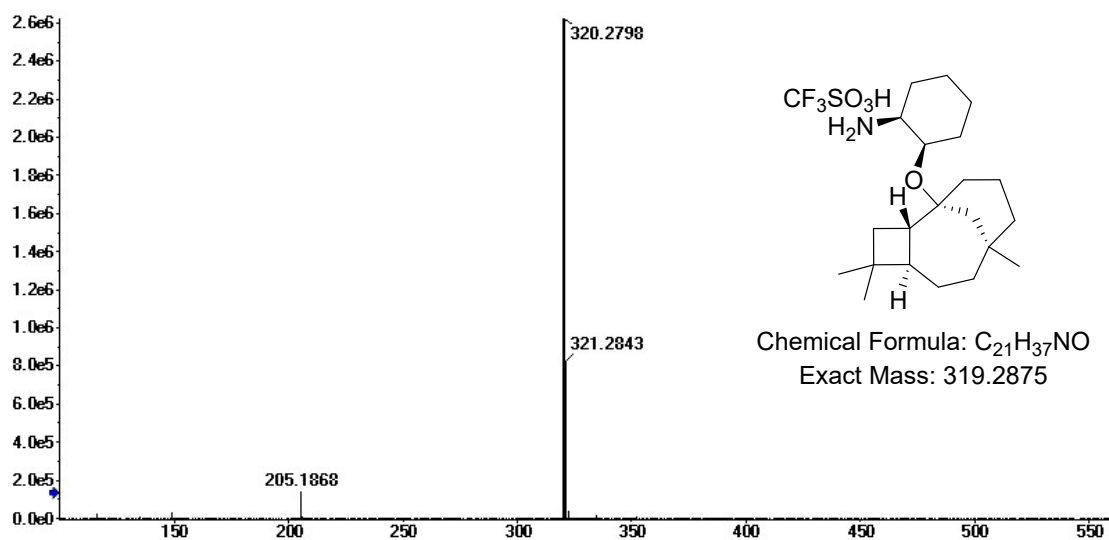
AC-13



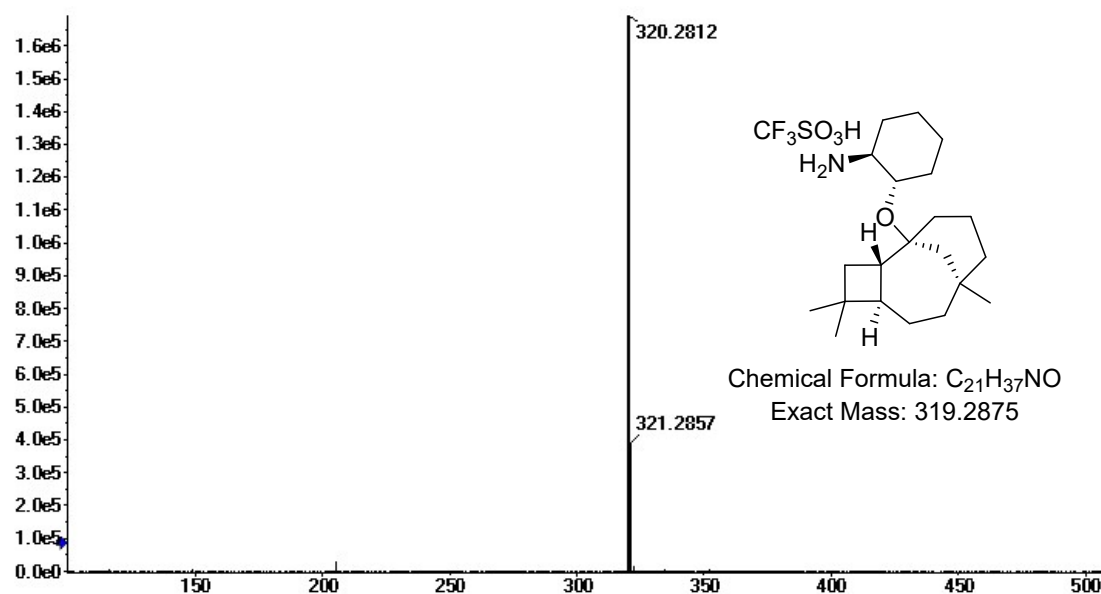
AC-14



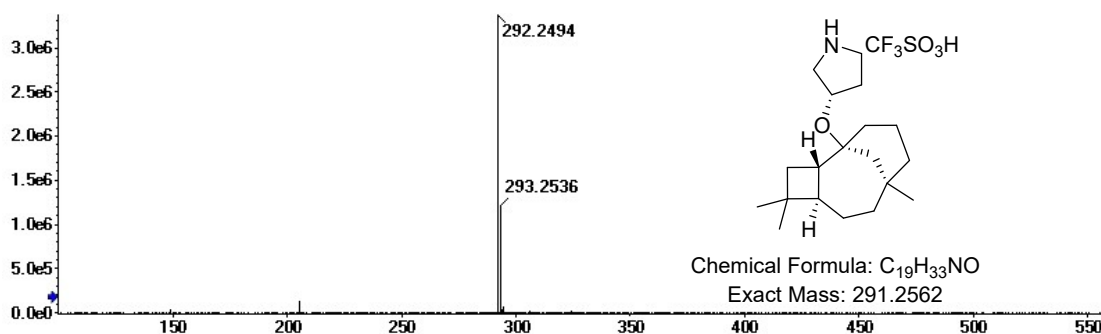
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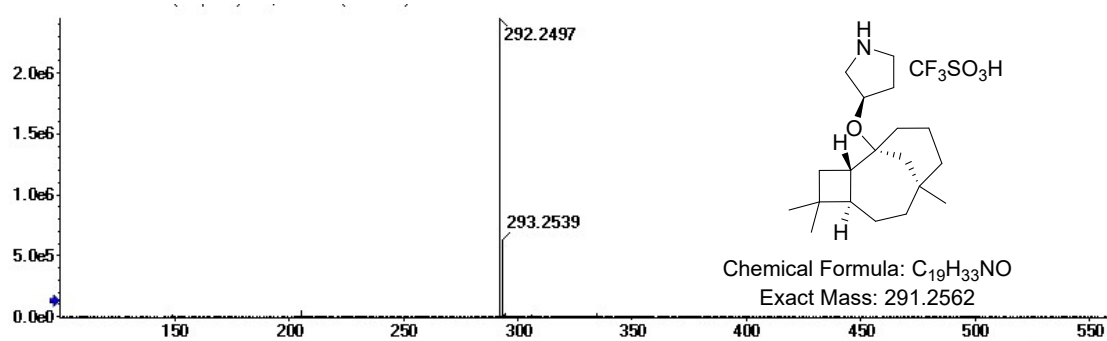
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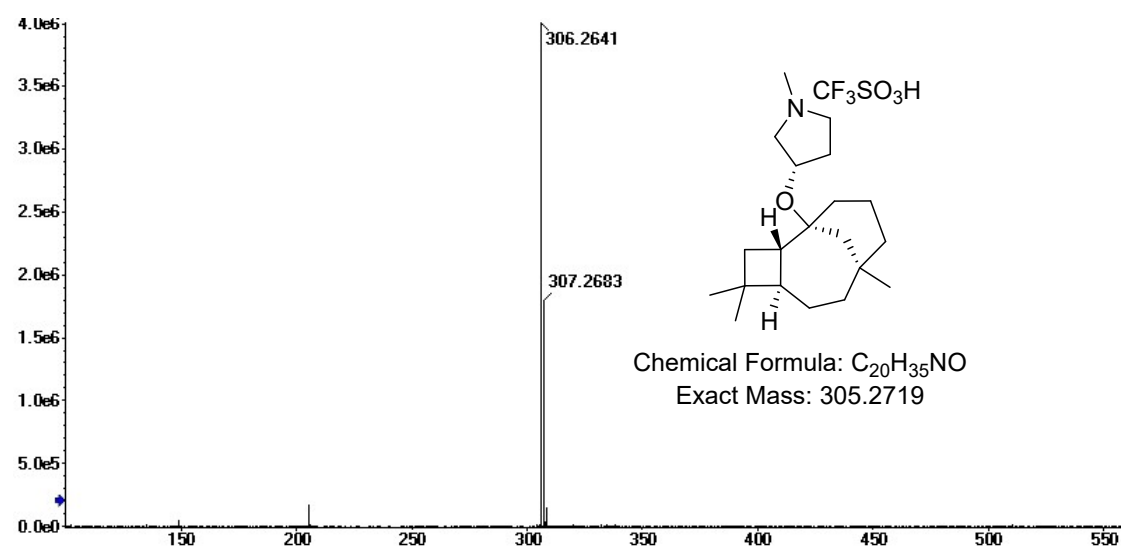
AC-17



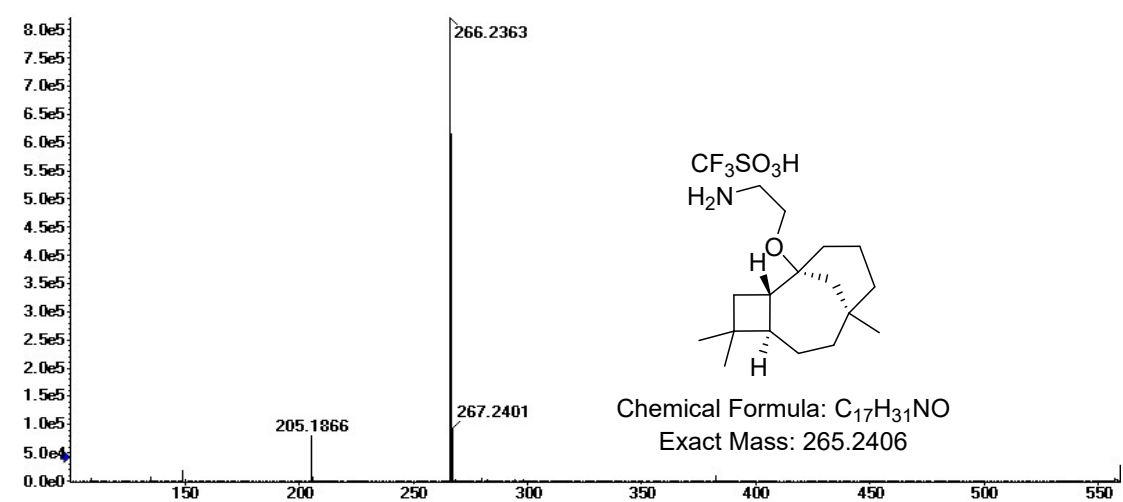
AC-18



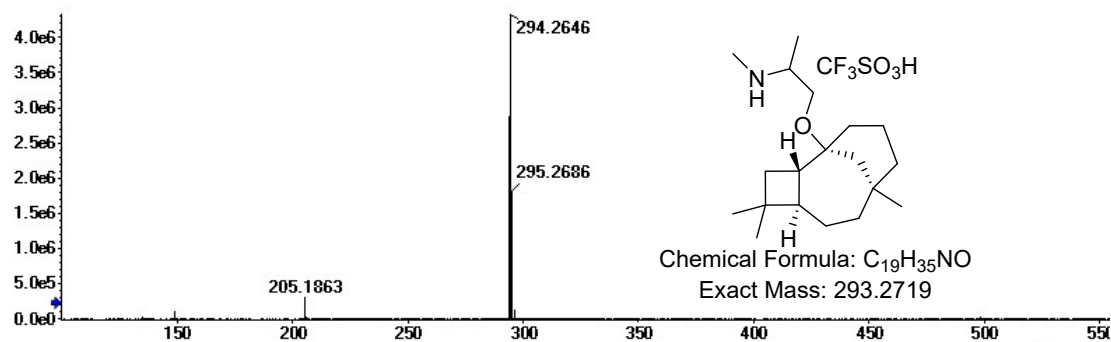
AC-19



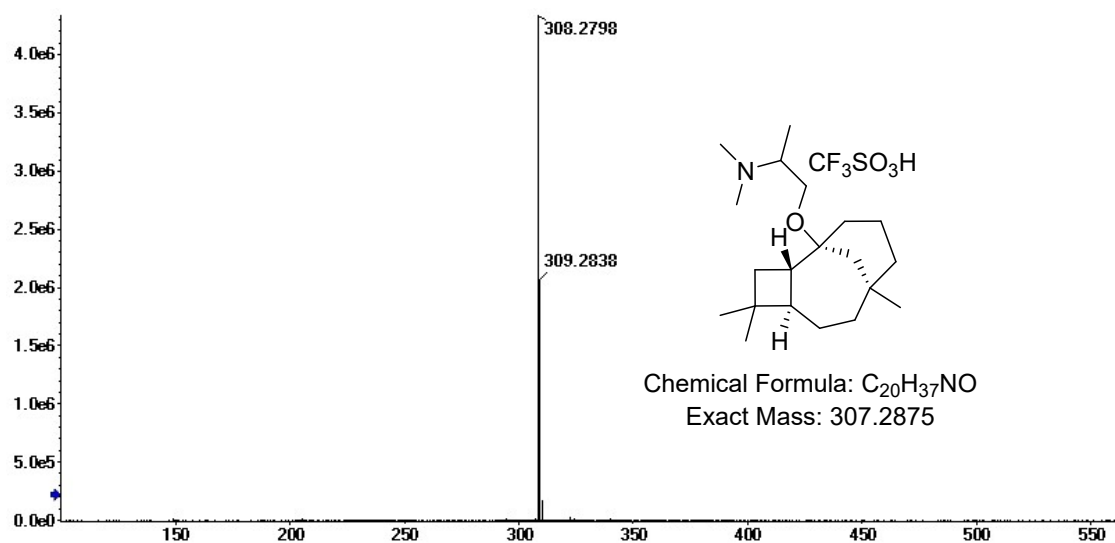
AC-20



AC-21



AC-22



AC-23

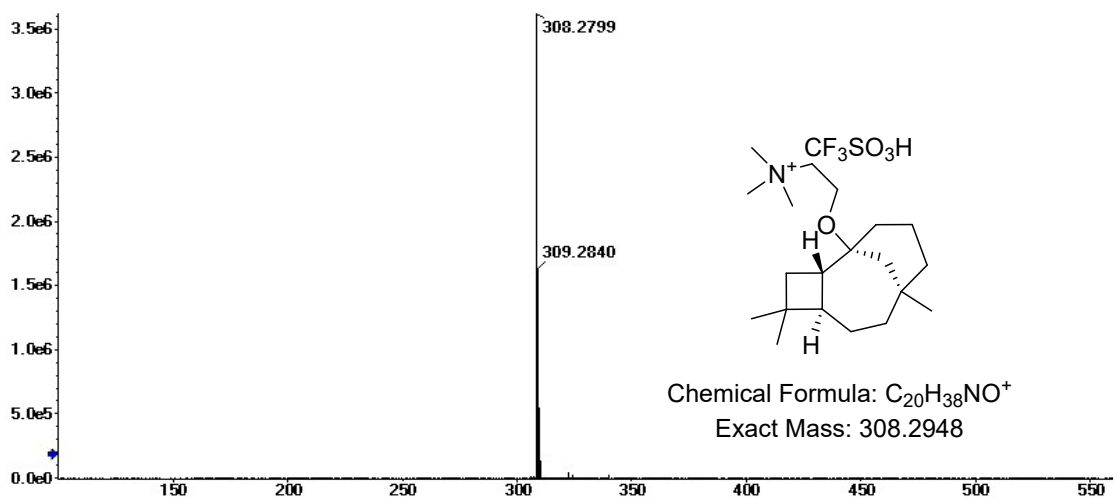


Fig S3. HRMS-ESI spectra of AC-7 to AC-23.