Supporting Information

Total synthesis, structural revision and biological evaluation of γ-elemene-type sesquiterpenes

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Table S1. Comparison of ^{1}H NMR data of natural elem-1,3,7,8-tetraen-8,12-olide[1] (300 MHz) with those of synthetic elem-1,3,7,8-tetraen-8,12-olide (3) (600 MHz)

Position	Natural, 300 MHz, $CDCl_3$, δ_H (mult. *J* in Hz)	Synthetic, 600 MHz, $CDCl_3$, δ_H (mult. *J* in Hz)	$\Delta\delta^*$ (ppm)
1	5.80△ (5.81)◇ (dd, 10.5, 17.3)	5.84 (dd, 10.8, 17.4)	0.03
2a	5.05 (dd, 0.6, 10.5)	5.07 (d, 10.8)	0.02
2b	4.99 (dd, 0.6, 17.3)	5.01 (d, 17.4)	0.02
3a	4.90 (m)	4.93 (m)	0.03
3b	4.75 (br s)	4.78 (br s)	0.02
4	--	--	--
5	2.45 (dd, 5.2, 8.3)	2.47 (dd, 4.8, 8.4)	0.02
6a	2.76△ (2.72)◇ (dd, 5.3, 17.2)	2.74 (ddd, 1.2, 4.8, 16.8)	0.02
6b	2.65△ (2.61)◇ (dd, 8.2, 17.2)	2.63 (ddd, 1.2, 8.4, 17.3)	0.02
7	--	--	--
8	--	--	--
9	5.45 (s)	5.47 (s)	0.02
10	--	--	--
11	--	--	--
12	--	--	--
13	1.86 (br s)	1.89 (s)	0.03
14	1.13 (s)	1.15 (s)	0.02
15	1.68 (br s)	1.70 (s)	0.02

*The chemical shift of synthetic product minus the chemical shift of natural product.

△Wrong characterization data of natural product in reported paper.[1]

◇The correct characterization data of natural product is on the basis of the ESI† in reported paper.[1]

Table S2. Comparison of ^{13}C NMR data of natural elem-1,3,7,8-tetraen-8,12-olide[1] (75 MHz) with those of synthetic elem-1,3,7,8-tetraen-8,12-olide (3) (150 MHz)

Position	Natural, 75 MHz, $CDCl_3$, δ_C (ppm)	Synthetic, 150 MHz, $CDCl_3$, δ_C (ppm)	$\Delta\delta^*$ (ppm)
1	146.1	146.0	-0.1
2	113.7	113.6	-0.1
3	114.9	114.9	0.0
4	145.4	145.3	-0.1
5	50.9	50.9	0.0
6	25.6	25.6	0.0
7	149.1	149.0	-0.1
8	148.1	148.0	-0.1
9	114.6	114.5	-0.1
10	42.1	42.0	-0.1
11	120.6	120.5	-0.1
12	171.6	171.4	-0.2
13	8.7	8.6	-0.1
14	22.2	22.2	0.0
15	24.0	23.9	-0.1

*The chemical shift of synthetic product minus the chemical shift of Natural product.

Table S3. Comparison of ^{1}H NMR data of natural elema-1,3,7(11),8-tetraen-8,12-lactam[2] (600 MHz) with those of synthetic elema-1,3,7(11),8-tetraen-8,12-lactam (4) (600 MHz)

Position	Natural, 600 MHz, $CDCl_3$, δ_H (mult. *J* in Hz)	Synthetic, 600 MHz, $CDCl_3$, δ_H (mult. *J* in Hz)	$\Delta\delta^*$ (ppm)
1	5.84 (dd, 10.8, 17.4)	5.84 (dd, 10.2, 17.4)	0.00
2a	5.04 (d, 10.8)	5.04 (dd, 0.8, 10.8)	0.00
2b	4.99 (d, 17.4)	4.99 (dd, 0.8, 17.4)	0.00
3a	4.89 (s)	4.89 (s)	0.00
3b	4.75 (s)	4.76 (s)	0.01
4	--	--	--
5	2.45 (dd, 4.8, 9.0)	2.46 (dd, 5.4, 8.4)	0.01
6a	2.68 (dd, 4.8, 17.4)	2.69 (ddd, 1.0, 4.8, 16.8)	0.01
6b	2.58 (dd, 9.0, 17.4)	2.58 (ddd, 1.2, 10.2, 17.4)	0.00
7	--	--	--
8	--	--	--
9	5.27 (s)	5.29 (s)	0.02
10	--	--	--
11	--	--	--
12	--	--	--
13	1.85 (s)	1.86 (s)	0.01
14	1.12 (s)	1.12 (s)	0.00
15	1.69 (s)	1.69 (s)	0.00
NH	7.46 (br s)	7.68 (br s)	0.22

*The chemical shift of synthetic product minus the chemical shift of natural product.

Table S4. Comparison of ^{13}C NMR data of natural elema-1,3,7(11),8-tetraen-8,12-lactam[2] (150 MHz) with those of synthetic elema-1,3,7(11),8-tetraen-8,12-lactam (4) (150 MHz)

Position	Natural, 150 MHz, $CDCl_3$, δ_C (ppm)	Synthetic, 150 MHz, $CDCl_3$, δ_C (ppm)	$\Delta\delta^*$ (ppm)
1	146.6	146.7	0.1
2	113.0	113.0	0.0
3	114.3	114.3	0.0
4	146.1	146.1	0.0
5	51.3	51.4	0.1
6	25.3	25.3	0.0
7	141.3	141.3	0.0
8	136.6	136.6	0.0
9	116.1	115.9	-0.2
10	41.9	42.0	0.1
11	124.8	125.0	0.2
12	173.5	173.2	-0.3
13	8.5	8.3	-0.2
14	22.0	22.0	0.0
15	23.9	24.0	0.1

*The chemical shift of synthetic product minus the chemical shift of Natural product.

Table S5. Comparison of ^{1}H NMR data of natural hydroxyisogermafurenolide[3] (600 MHz) with those of synthetic hydroxyisogermafurenolide (5) (600 MHz)

Position	Natural, 600 MHz, $CDCl_3$, δ_H (mult. *J* in Hz)	Synthetic, 600 MHz, $CDCl_3$, δ_H (mult. *J* in Hz)	$\Delta\delta^*$ (ppm)
1	5.70	5.70 (dd, 10.8, 17.4)	0.00
2a	5.00	5.00 (d, 10.8)	0.00
2b	4.97	4.97 (d 16.8)	0.00
3a	4.98	4.99 (s)	0.01
3b	4.74	4.74 (s)	0.00
4	--	--	--
5	2.05	2.05 (dd, 3.0, 13.2)	0.00
6a	2.56	2.56 (dd, 3.6, 13.8)	0.00
6b	2.72	2.72 (t, 13.8)	0.00
7	--	--	--
8	--	--	--
9a	1.76 (d)	1.76 (d, 12.6)	0.00
9b	2.14 (d)	2.14 (d, 14.4)	0.00
10	--	--	--
11	--	--	--
12	--	--	--
13	1.83	1.83 (s)	0.00
14	1.27	1.27 (s)	0.00
15	1.77	1.77 (s)	0.01
-OH	3.01	2.95 (b s)	0.06

*The chemical shift of synthetic product minus the chemical shift of Natural product.

Table S6. Comparison of ^{13}C NMR data of natural hydroxyisogermafurenolide[3] (75 MHz) with those of synthetic hydroxyisogermafurenolide (5) (150 MHz)

Position	Natural, 400 MHz, $CDCl_3$, δ_C (ppm)	Synthetic, 150 MHz, $CDCl_3$, δ_C (ppm)	$\Delta\delta^*$ (ppm)
1	147.4	147.6	0.2
2	112.0	112.1	0.1
3	114.2	114.3	0.1
4	144.7	144.9	0.2
5	54.2	54.4	0.2
6	27.1	27.2	0.1
7	160.1	160.2	0.1
8	102.8	102.9	0.1
9	49.3	49.5	0.2
10	40.6	40.8	0.2
11	122.0	122.2	0.2
12	171.9	172.0	0.1
13	8.2	8.4	0.2
14	17.7	17.9	0.2
15	24.4	24.5	0.2

*The chemical shift of synthetic product minus the chemical shift of Natural product.

Table S7. Comparison of ^{1}H NMR data of natural 8β-methoxy-isogermafurenolide[4] (600 MHz) with those of synthetic 8β-methoxy-isogermafurenolide (6a) (600 MHz)

Position	Natural, 600 MHz, CD_3OD, δ_H (mult. *J* in Hz)	Synthetic, 600 MHz, CD_3OD, δ_H (mult. *J* in Hz)	$\Delta\delta^*$ (ppm)
1	5.76 (dd, 10.7, 17.6)	5.76 (dd, 10.8, 17.4)	0.00
2a	4.96 (d, 10.7)	4.96 (dd, 0.6, 11.4)	0.00
2b	4.95 (d, 17.6)	4.95 (dd, 1.2, 17.6)	0.00
3a	4.97 (s)	4.98 (s)	0.01
3b	4.76 (s)	4.77 (s)	0.01
4	--	--	--
5	2.13 (dd, 4.1, 13.4)	2.14 (dd, 3.6, 12.6)	0.01
6a	2.63 (dd, 4.1, 13.4)	2.63 (dd, 4.2, 13.8)	0.00
6b	2.58 (t, 13.4)	2.59 (dt, 1.2, 12.6)	0.01
7	--	--	--
8	--	--	--
9a	1.66 (d, 13.7)	1.67 (d, 13.8)	0.01
9b	2.10 (d, 13.7)	2.10 (d, 13.8)	0.00
10	--	--	--
11	--	--	--
12	--	--	--
13	1.84 (s)	1.85 (d, 1.2)	0.01
14	1.77 (s)	1.77 (s)	0.00
15	1.20 (s)	1.21 (s)	0.01
-O*Me*	3.14 (s)	3.15 (s)	0.01

*The chemical shift of synthetic product minus the chemical shift of Natural product.

Table S8. Comparison of ^{13}C NMR data of natural 8β-methoxy-isogermafurenolide[4] (75 MHz) with those of synthetic 8β-methoxy-isogermafurenolide (6a) (150 MHz)

Position	Natural, 75 MHz, CD_3OD, δ_C (ppm)	Synthetic, 150 MHz, CD_3OD, δ_C (ppm)	$\Delta\delta^*$ (ppm)
1	149.5	149.3	-0.2
2	112.3	112.2	-0.1
3	114.6	114.5	-0.1
4	146.6	146.4	-0.2
5	55.4	55.2	-0.2
6	28.5	28.3	-0.2
7	160.8	160.7	-0.1
8	107.7	107.5	-0.2
9	49.8	49.6	-0.2
10	42.0	41.8	-0.2
11	125.4	125.2	-0.2
12	173.8	173.6	-0.2
13	8.2	8.1	-0.1
14	25.0	24.9	-0.1
15	18.1	18.0	-0.1
O*Me*	50.8	50.6	-0.2

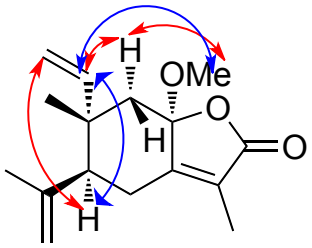
*The chemical shift of synthetic product minus the chemical shift of Natural product.

Table S9. ^{1}H and ^{13}C NMR data for compound 6b*

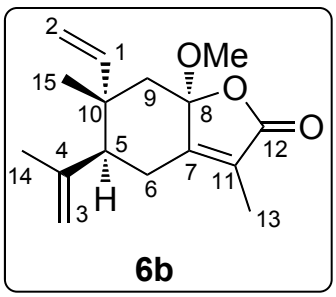
Position	δ_C (ppm)	δ_H (ppm, *J* in Hz)
1	148.7	6.22 (dd, 10.8, 17.4)
2	110.2	5.08 (d, 17.4); 4.97 (d, 11.4)
3	113.9	4.86 (s); 4.68 (s)
4	148.3	--
5	49.9	2.77 (t, 4.8)
6	28.0	2.69 - 2.68 (m)
7	159.4	--
8	107.7	--
9	46.6	*αH*, 2.26 (d, 14.4); *βH*, 1.89 (d, 14.4)
10	40.8	--
11	127.0	--
12	173.4	--
13	8.4	1.83 (s)
14	25.5	1.75 (t, 0.6 Hz)
15	26.3	1.00 (s)
O*Me*	50.4	3.07 (s)

*^{1}H NMR spectra recorded at 600 MHz, ^{13}C NMR spectra recorded at 150 MHz; the spectra of **6a** was obtained in CD_3OD.

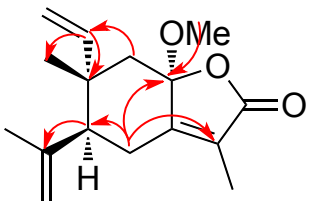
Figure 1 Key NOESY correlations and selected HMBC correlations of compound 6b



key NOESY correlations of compound **6b**



6b



selected HMBC correlations of compound **6b**

References:

[1] G. Xia, L. Zhou, J. Ma, Y. Wang, L. Ding, F. Zhao, L. Chen, F. Qiu, *Fitoterapia* **2015**, *103*, 143-148.

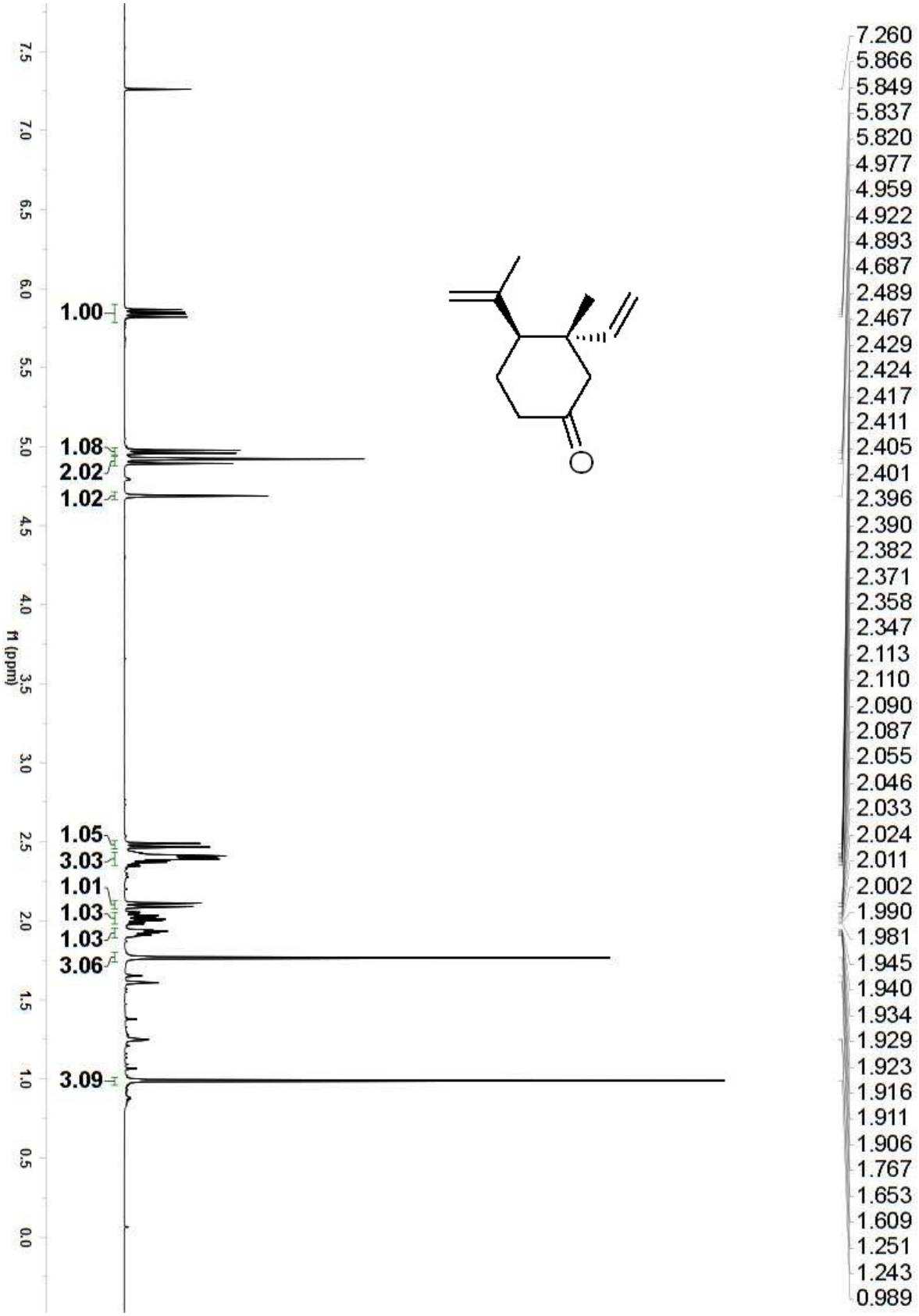
[2] G. Qiu, P. Yan, W. Shao, J. Zhou, W. Lin, L. Fang, X. Zhao, J. Dong, *Chem. Pharm. Bull.* **2013**, *61*, 983-986.

[3] D. Friedrich, F. Bohlmann, *Tetrahedron* **1988**, *44*, 1369-1392.

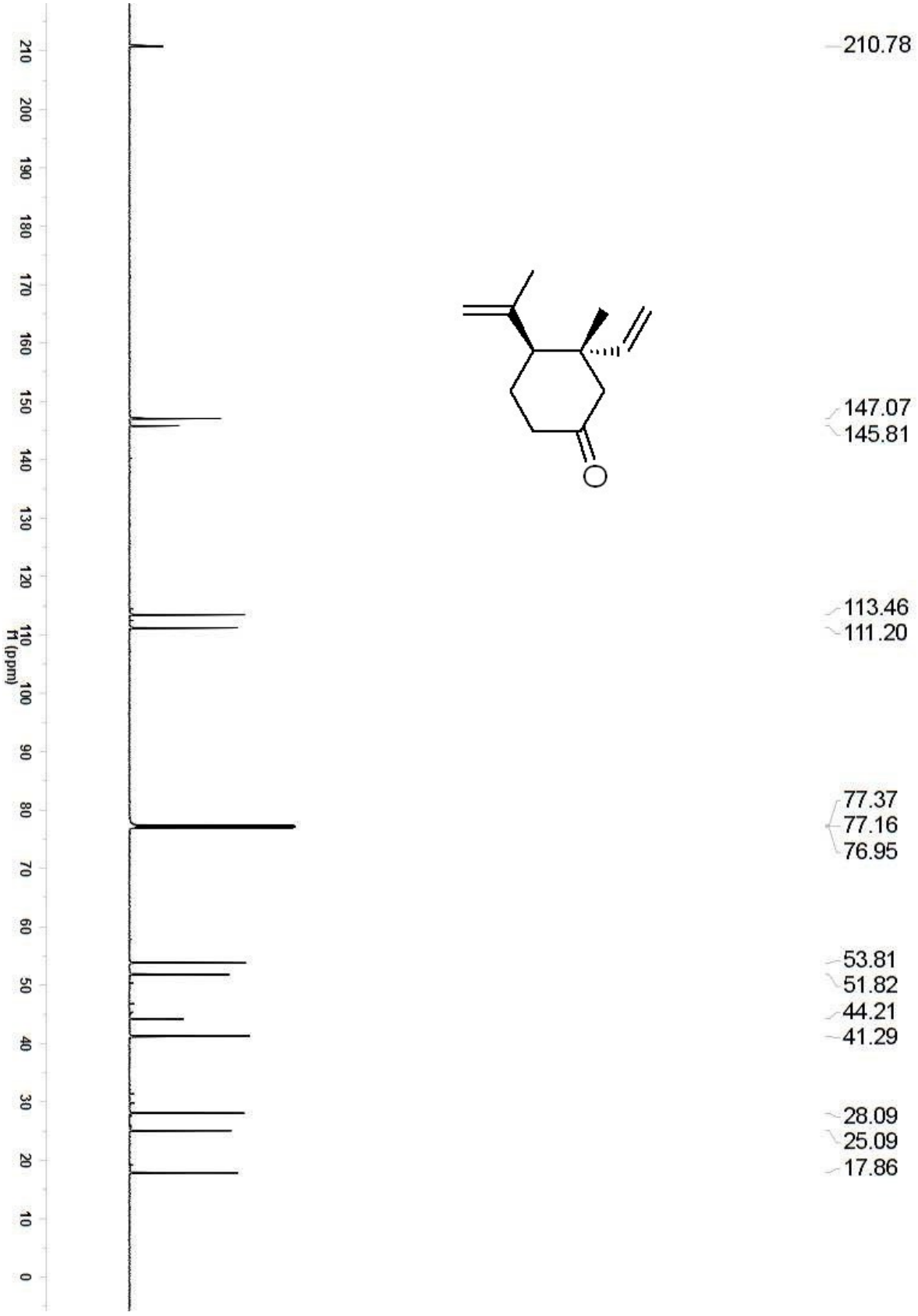
[4] J. -Hao, Ma, F. Zhao, Y. Wang, Y. Liu, S. -Y. Gao, L. -Q. Ding, L. -X. Chen, F. Qiu, *Org. Biomol. Chem.* **2015**, *13*, 8349-8358.

Spectra for Compounds

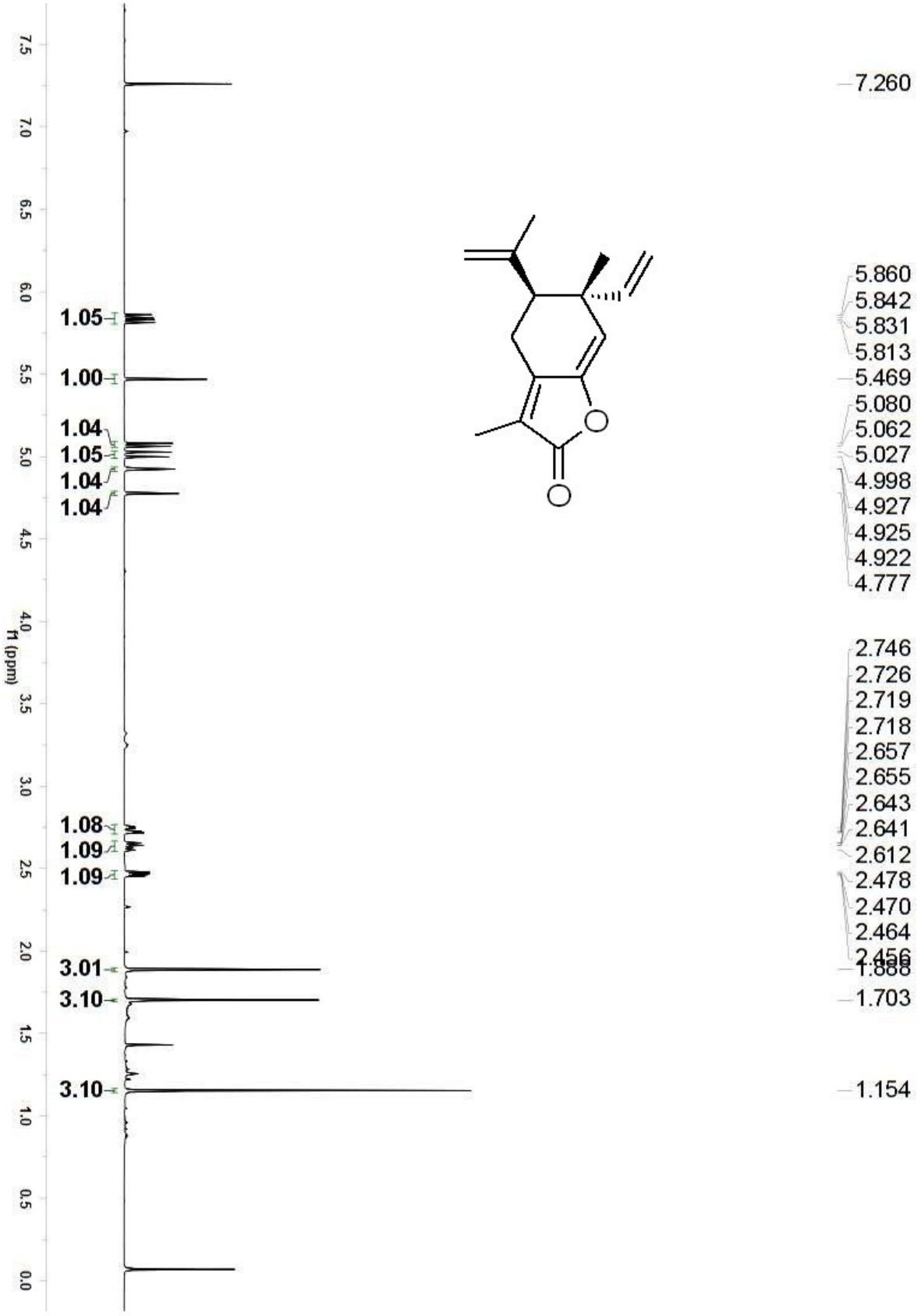
^{1}H NMR spectra of compound **12** in $CDCl_3$ (600 MHz)



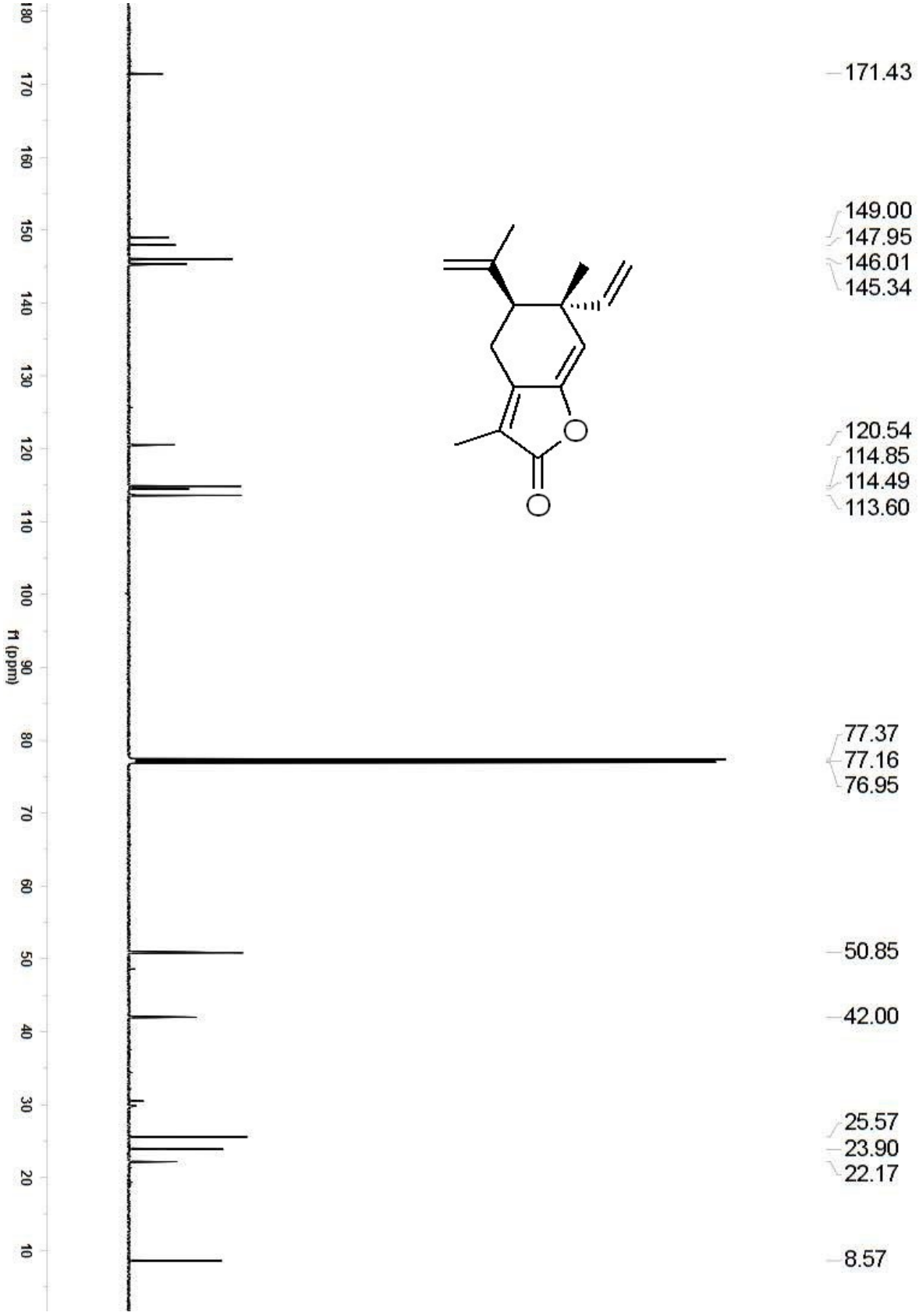
^{13}C NMR spectra of compound **12** in $CDCl_3$ (150 MHz)



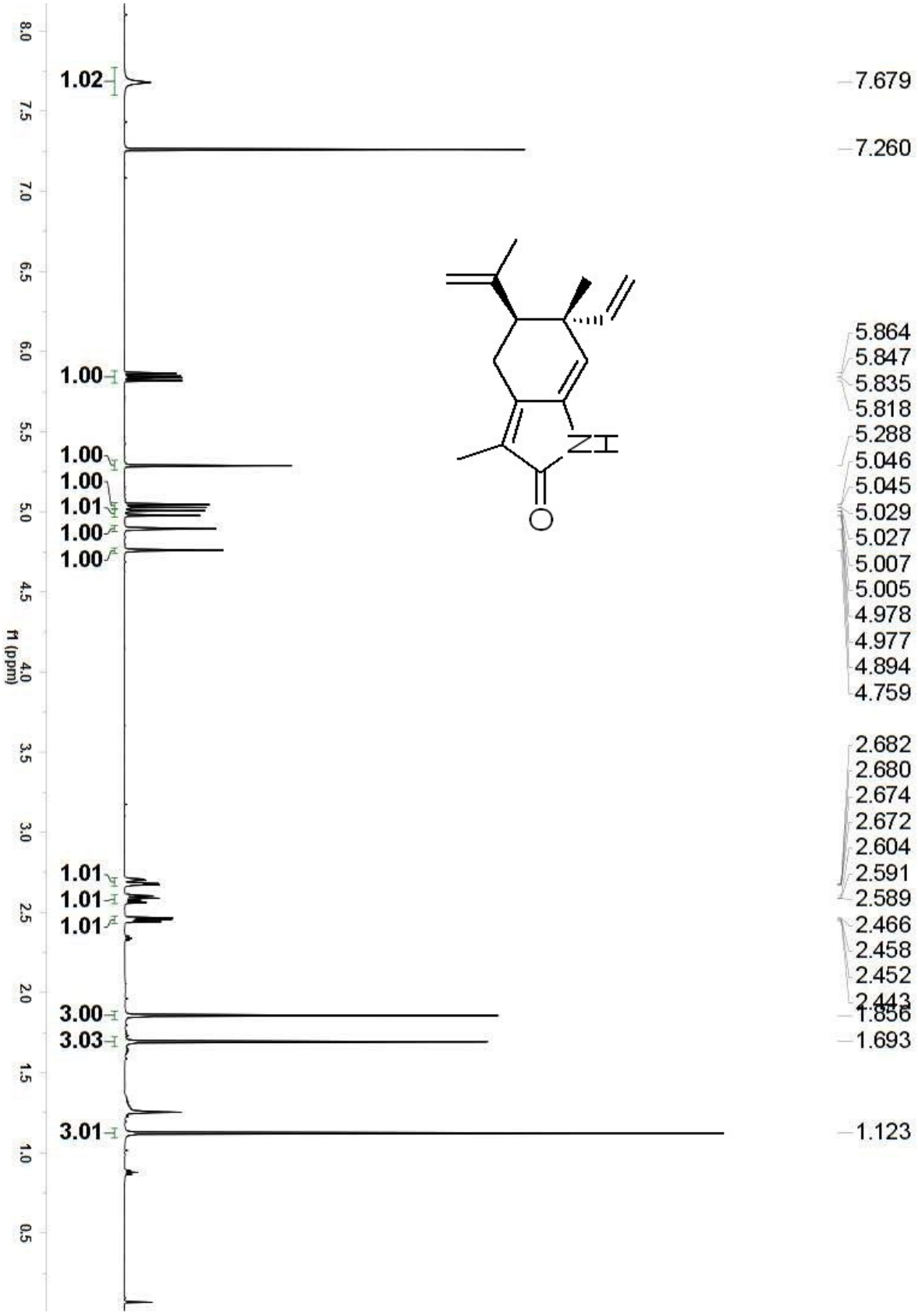
^{1}H NMR spectra of compound **3** in $CDCl_3$ (600 MHz)



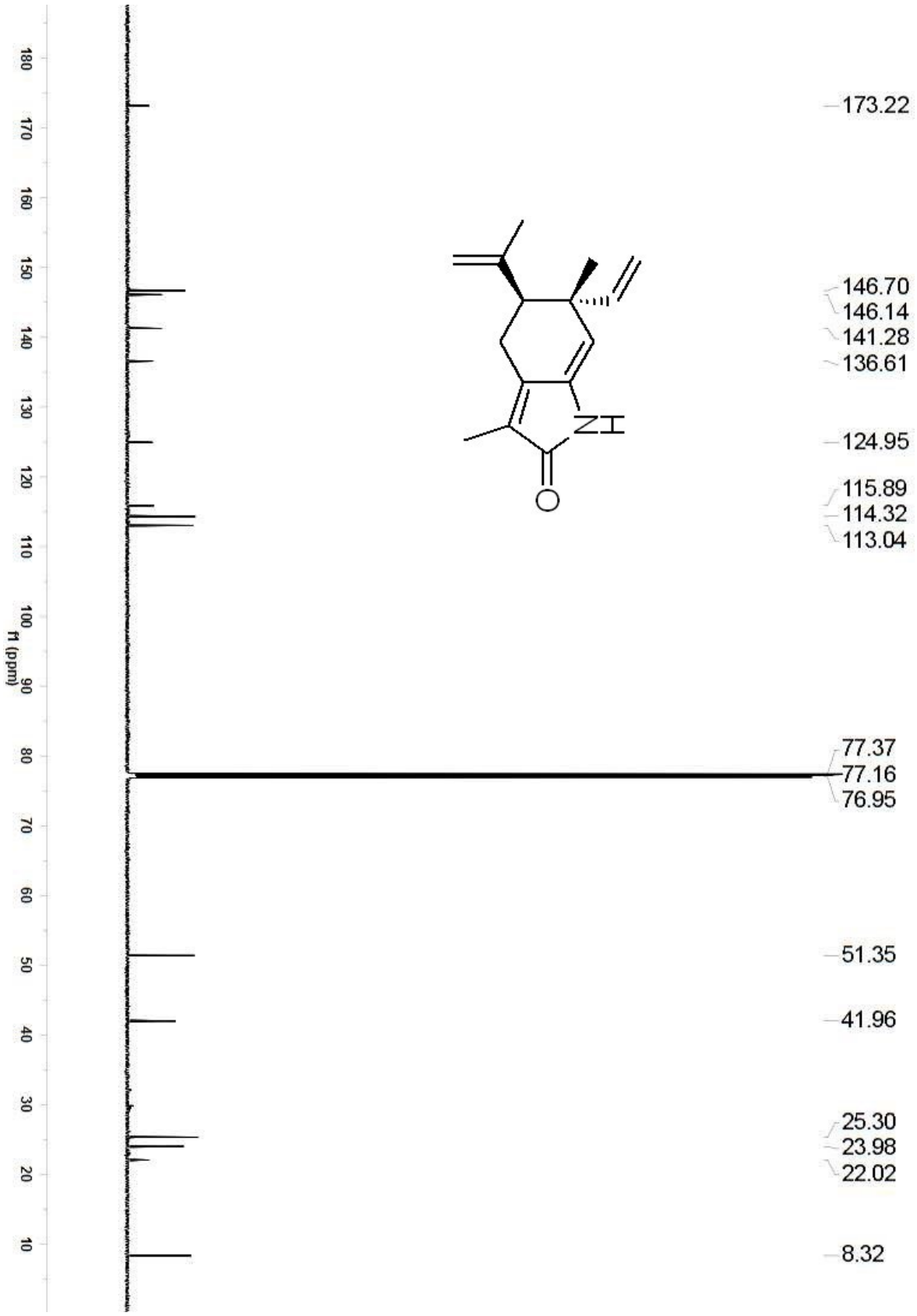
^{13}C NMR spectra of compound **3** in $CDCl_3$ (150 MHz)



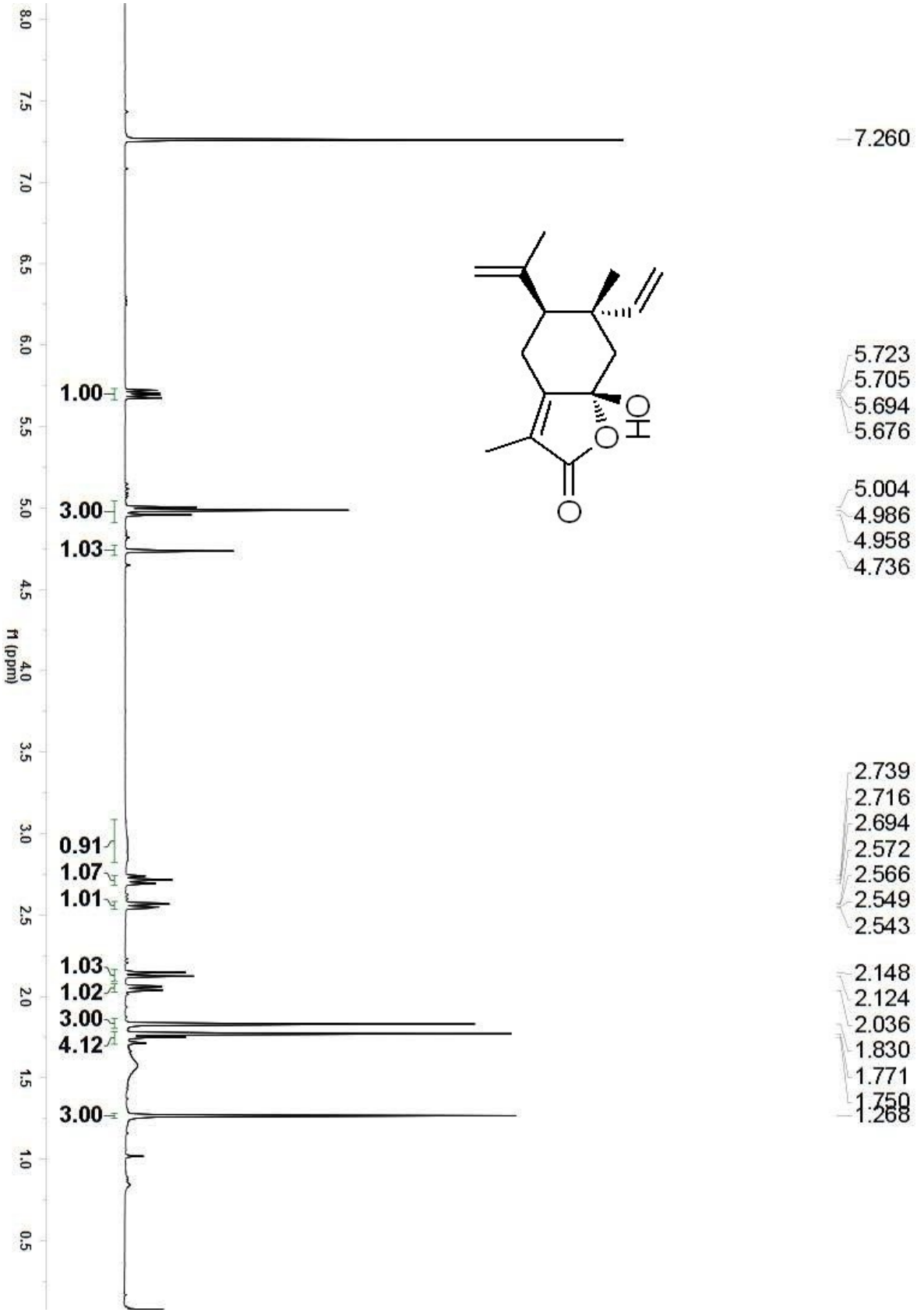
^{1}H NMR spectra of compound **4** in $CDCl_3$ (600 MHz)



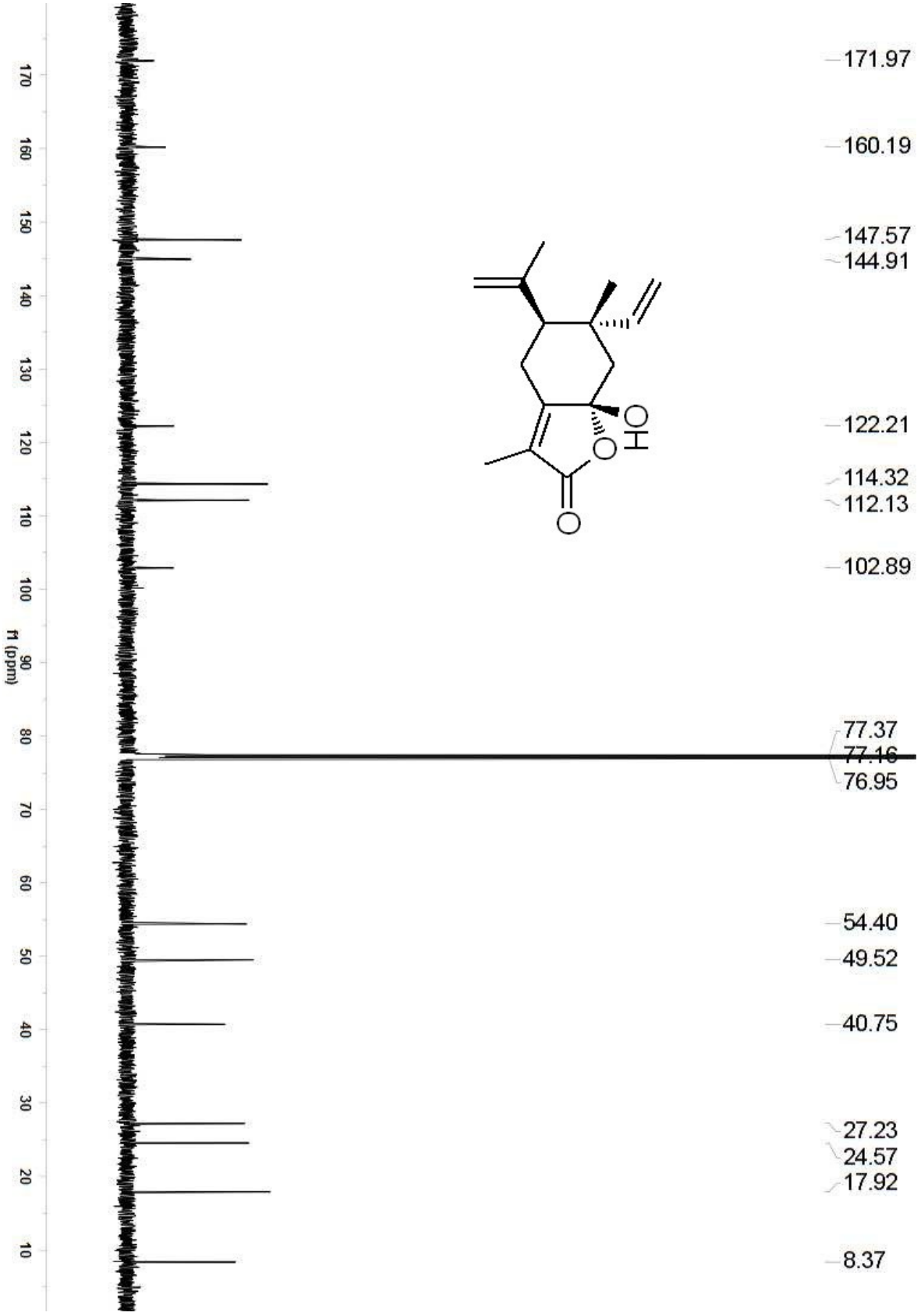
^{13}C NMR spectra of compound **4** in $CDCl_3$ (150 MHz)



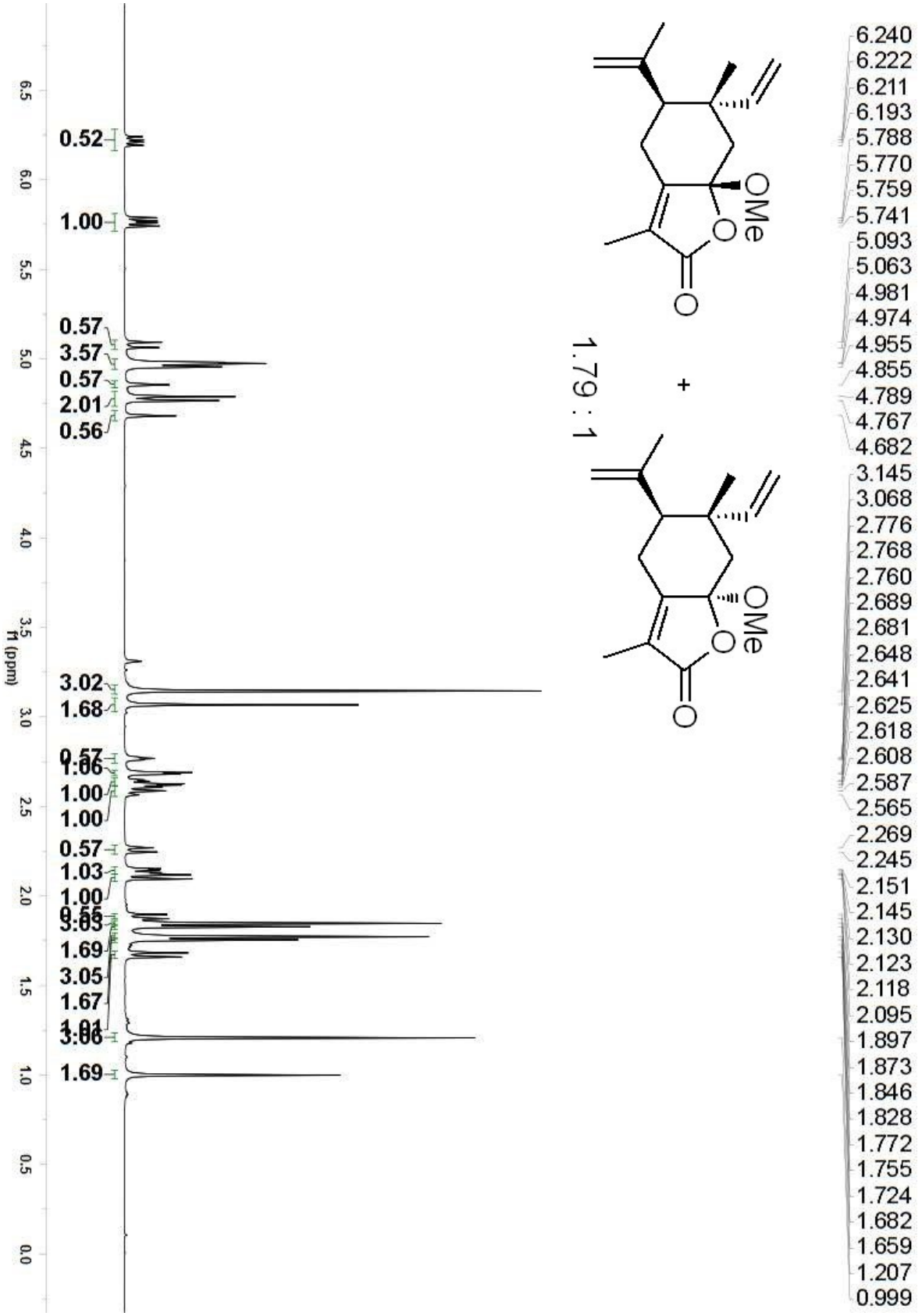
^{1}H NMR spectra of compound **5** in $CDCl_3$ (600 MHz)



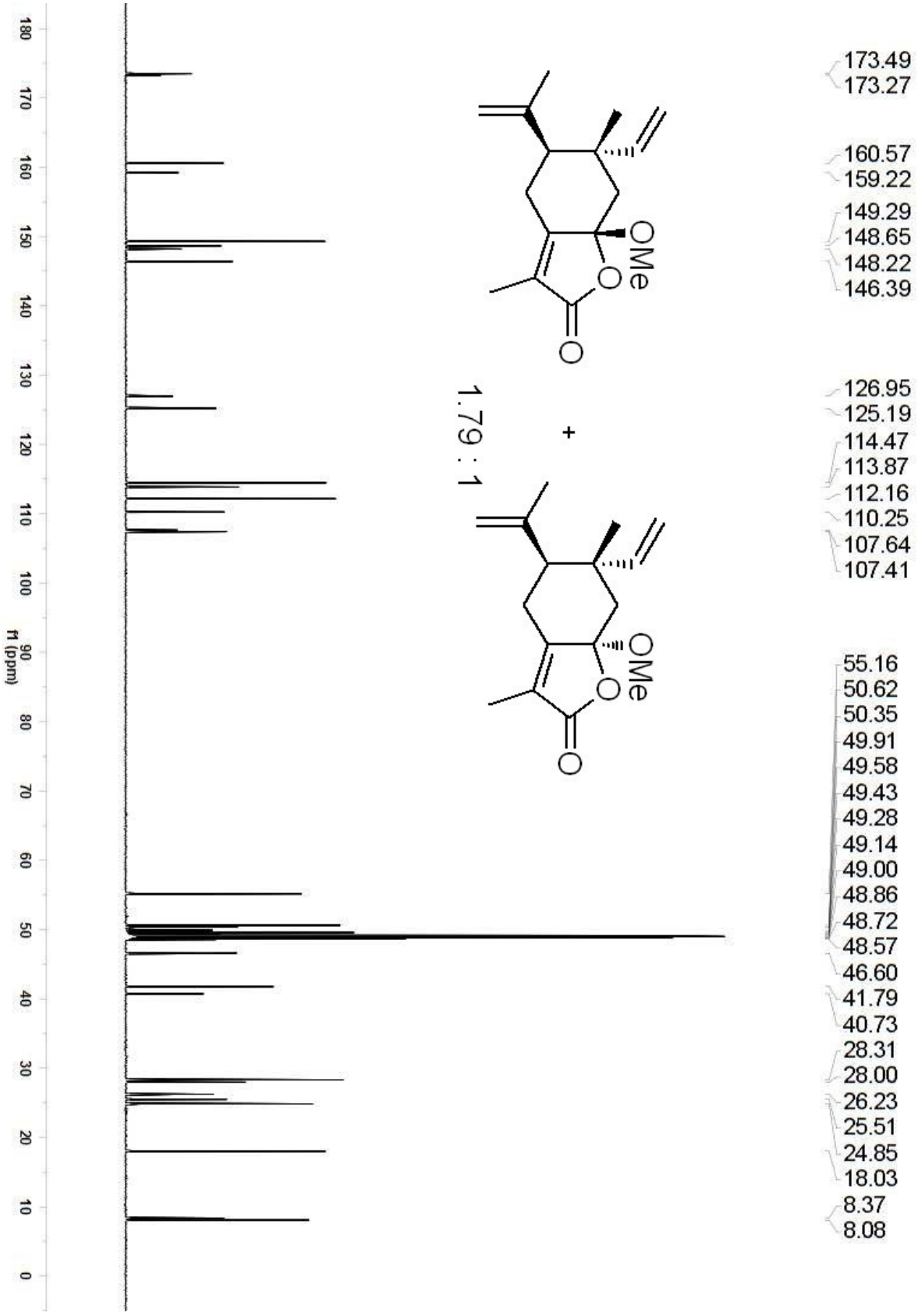
^{13}C NMR spectra of compound **5** in $CDCl_3$ (150 MHz)



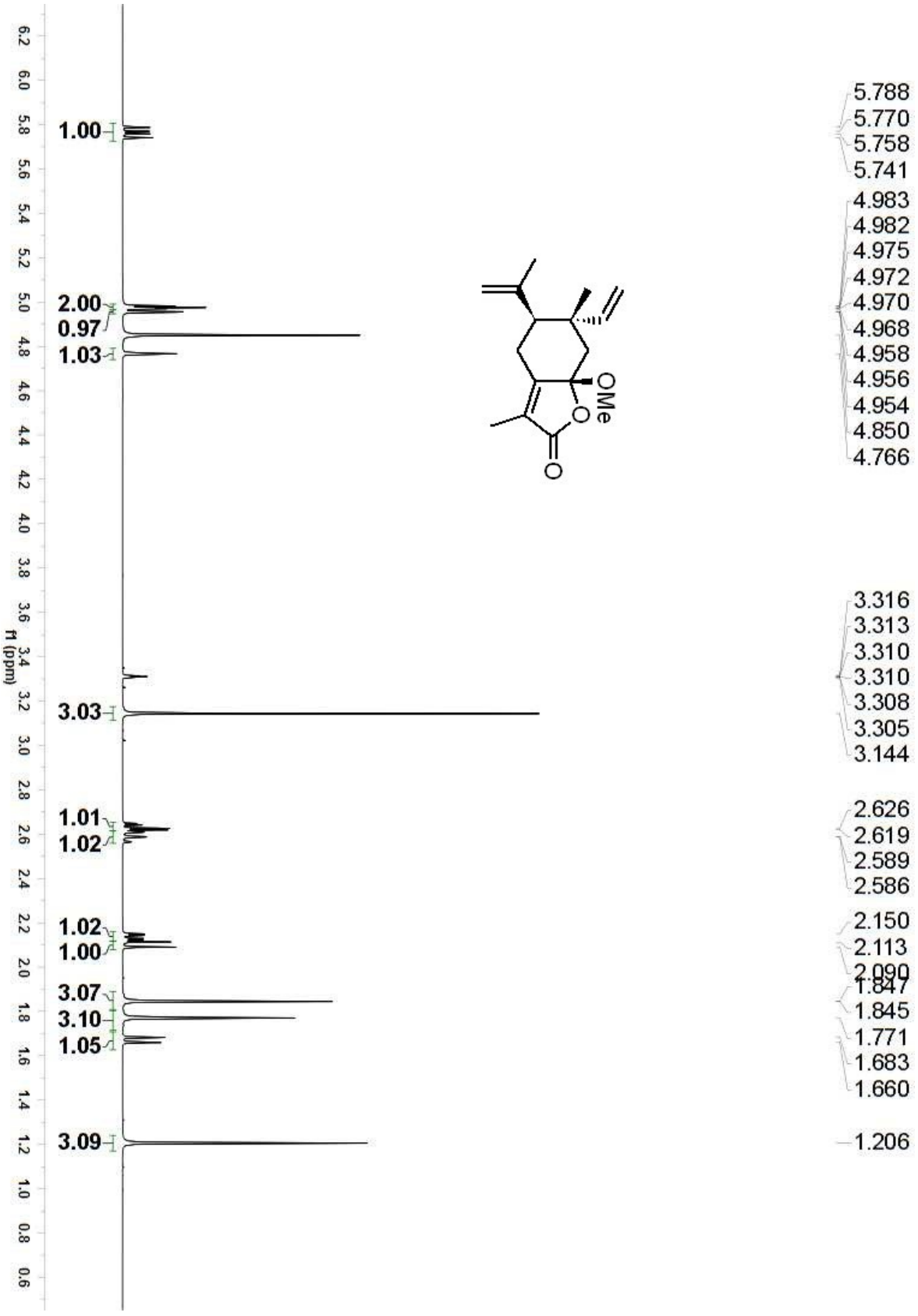
^{1}H NMR spectra of compounds **6a** and **6b** (diastereomixture) in CD_3OD (600 MHz)



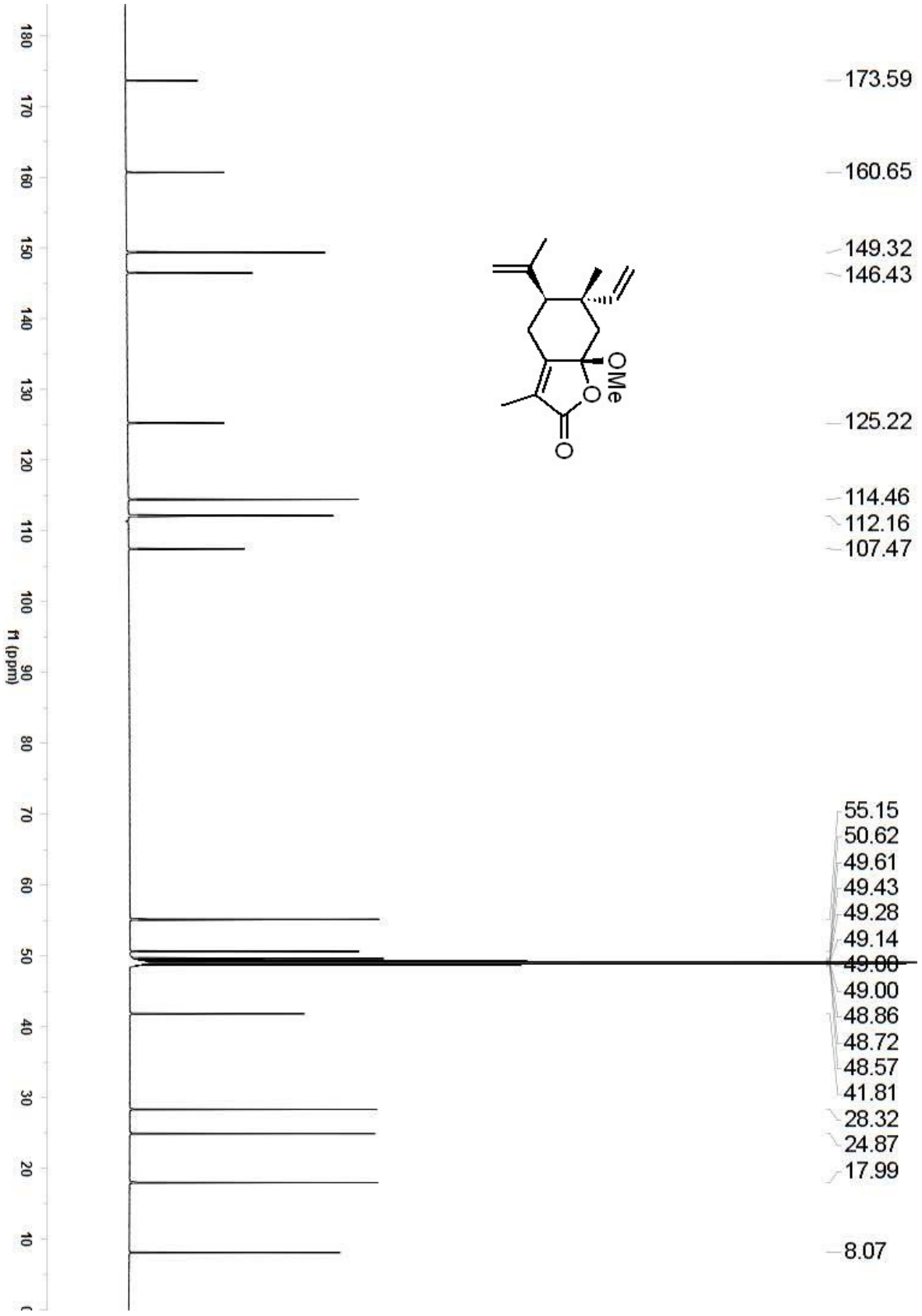
^{13}C NMR spectra of compounds **6a** and **6b** (diastereomixture) in CD_3OD (150 MHz)



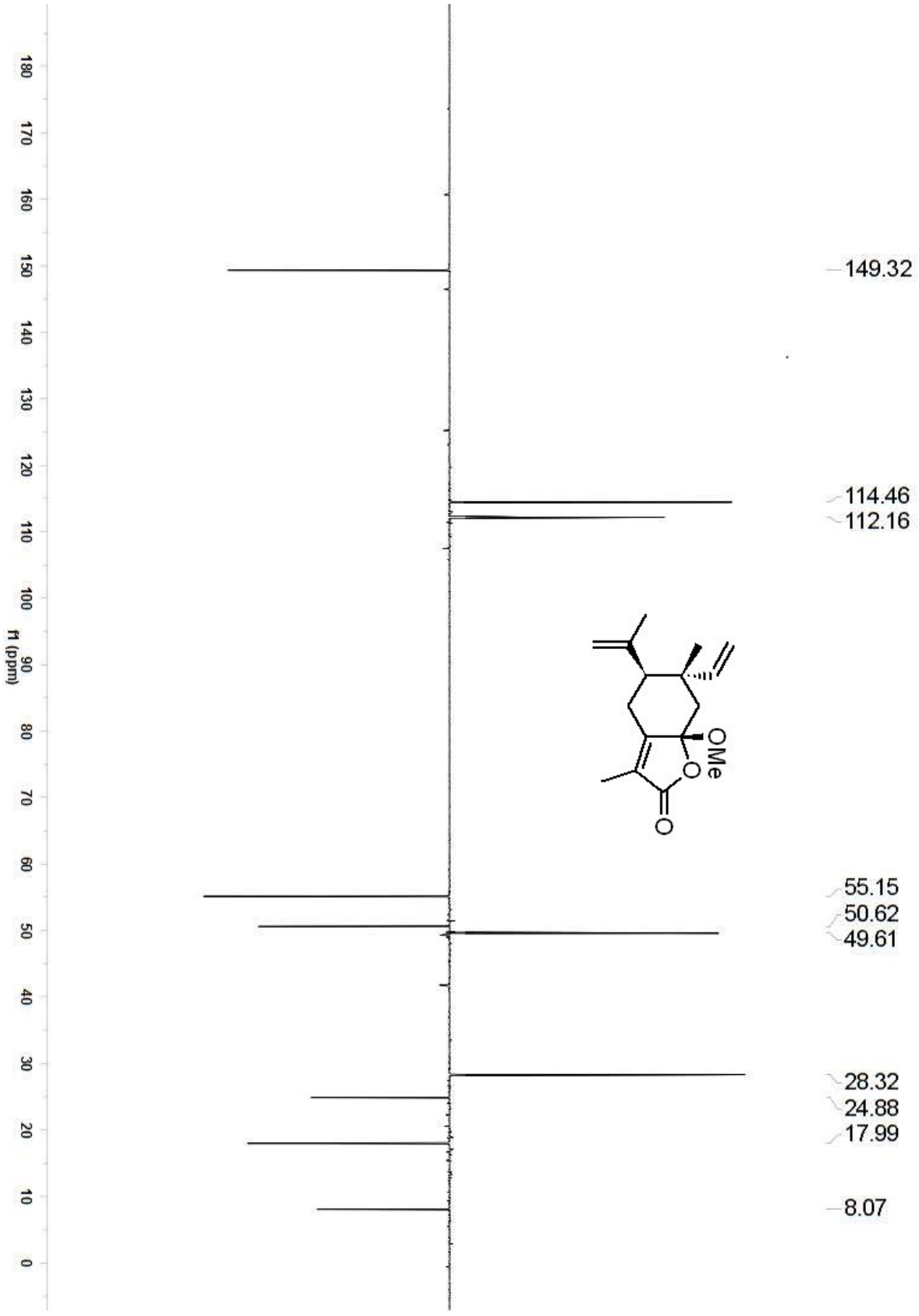
^{1}H NMR spectra of compound **6a** in CD_3OD (600 MHz)



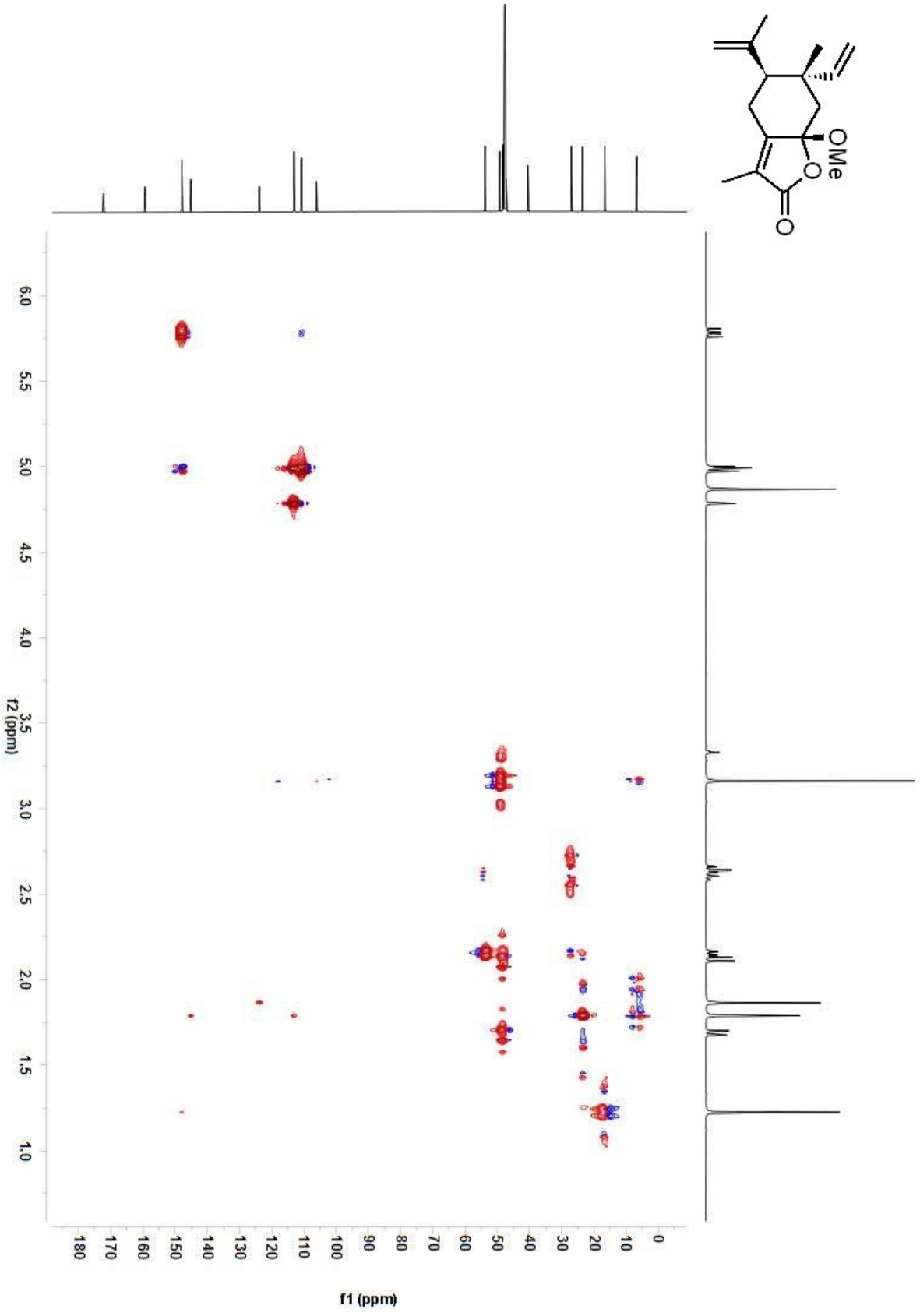
^{13}C NMR spectra of compound **6a** in CD_3OD (150 MHz)



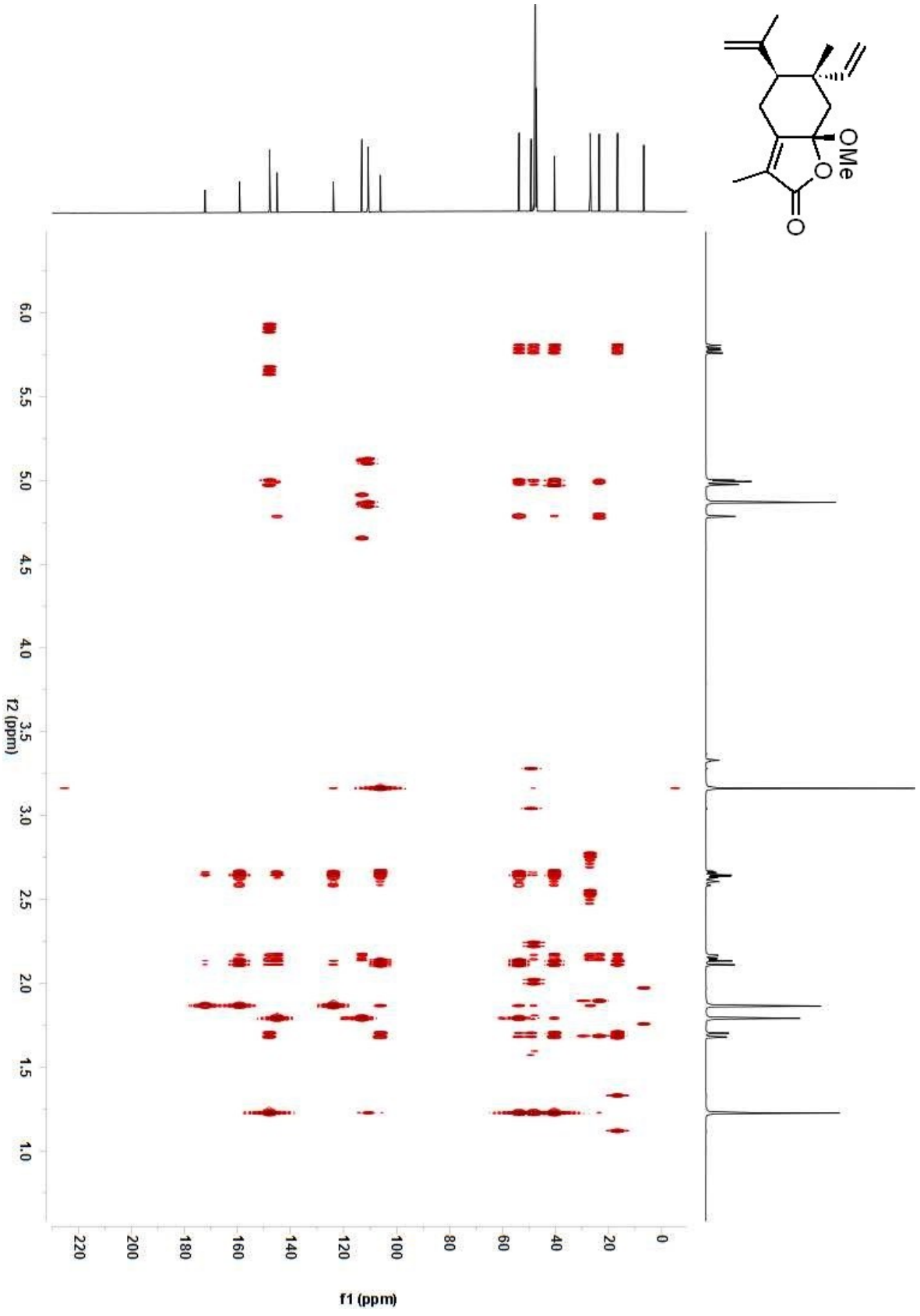
DEPT spectra of compound **6a** in CD_3OD



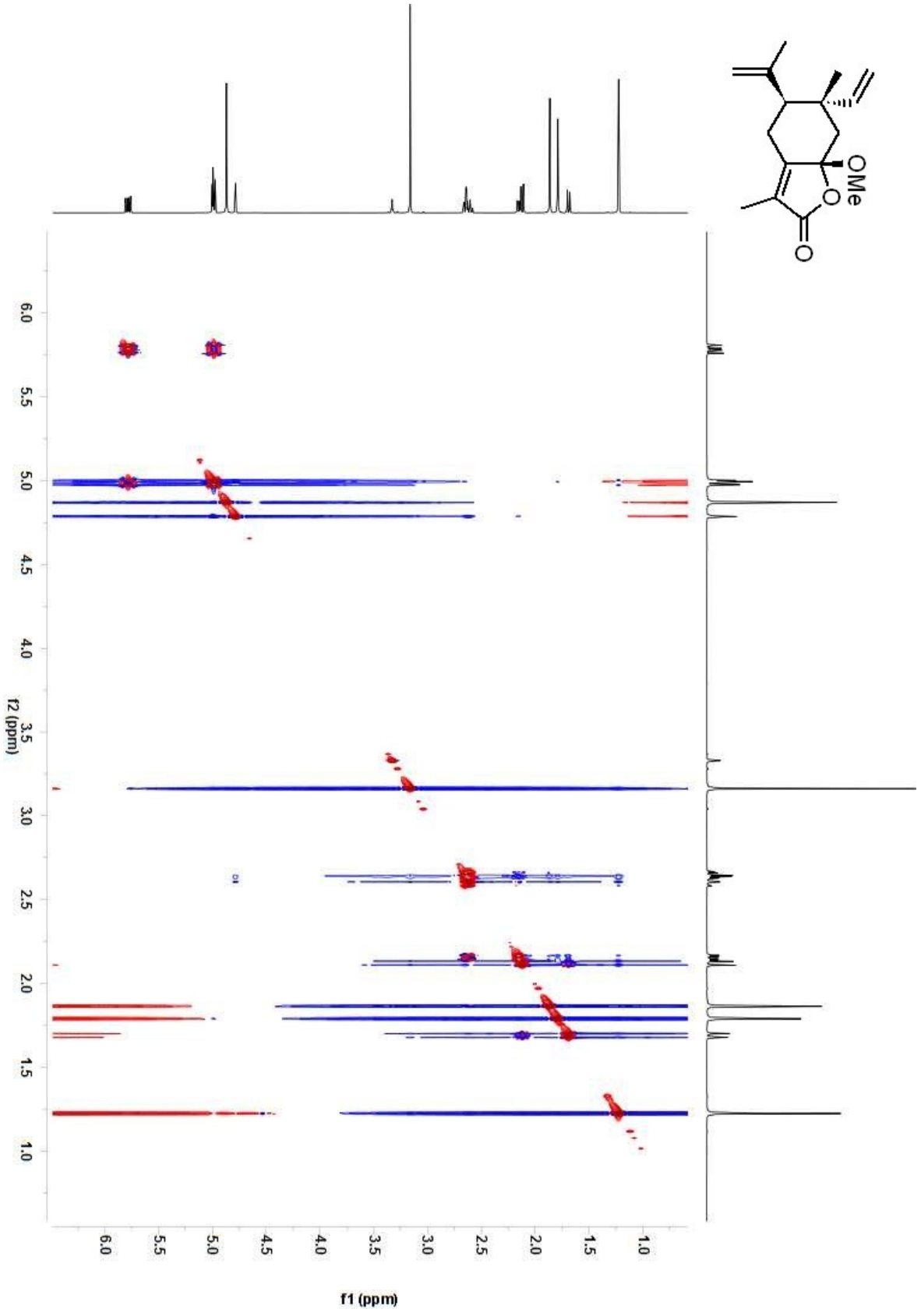
HSQC spectra of compound **6a** in CD_3OD



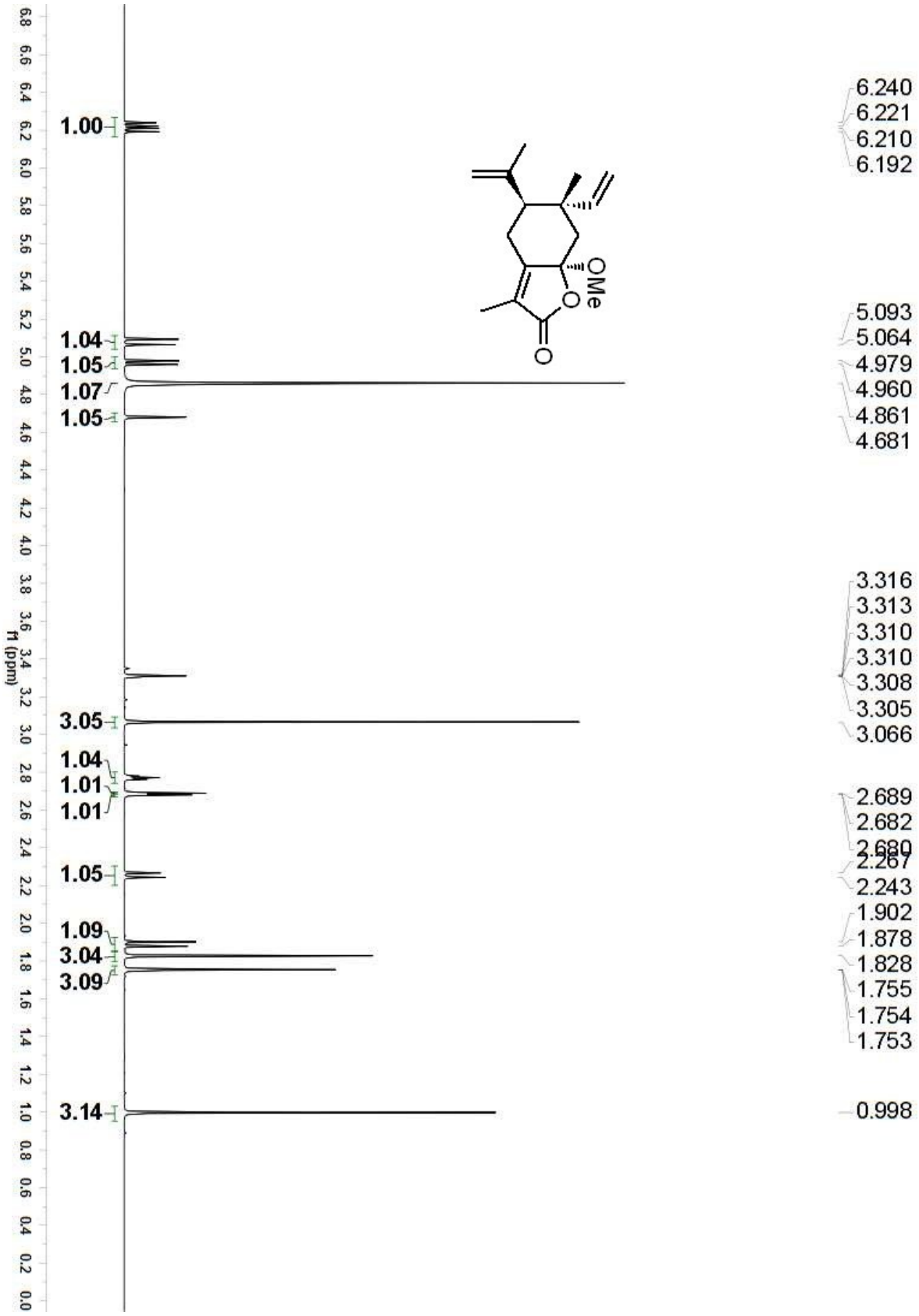
HMBC spectra of compound **6a** in CD_3OD



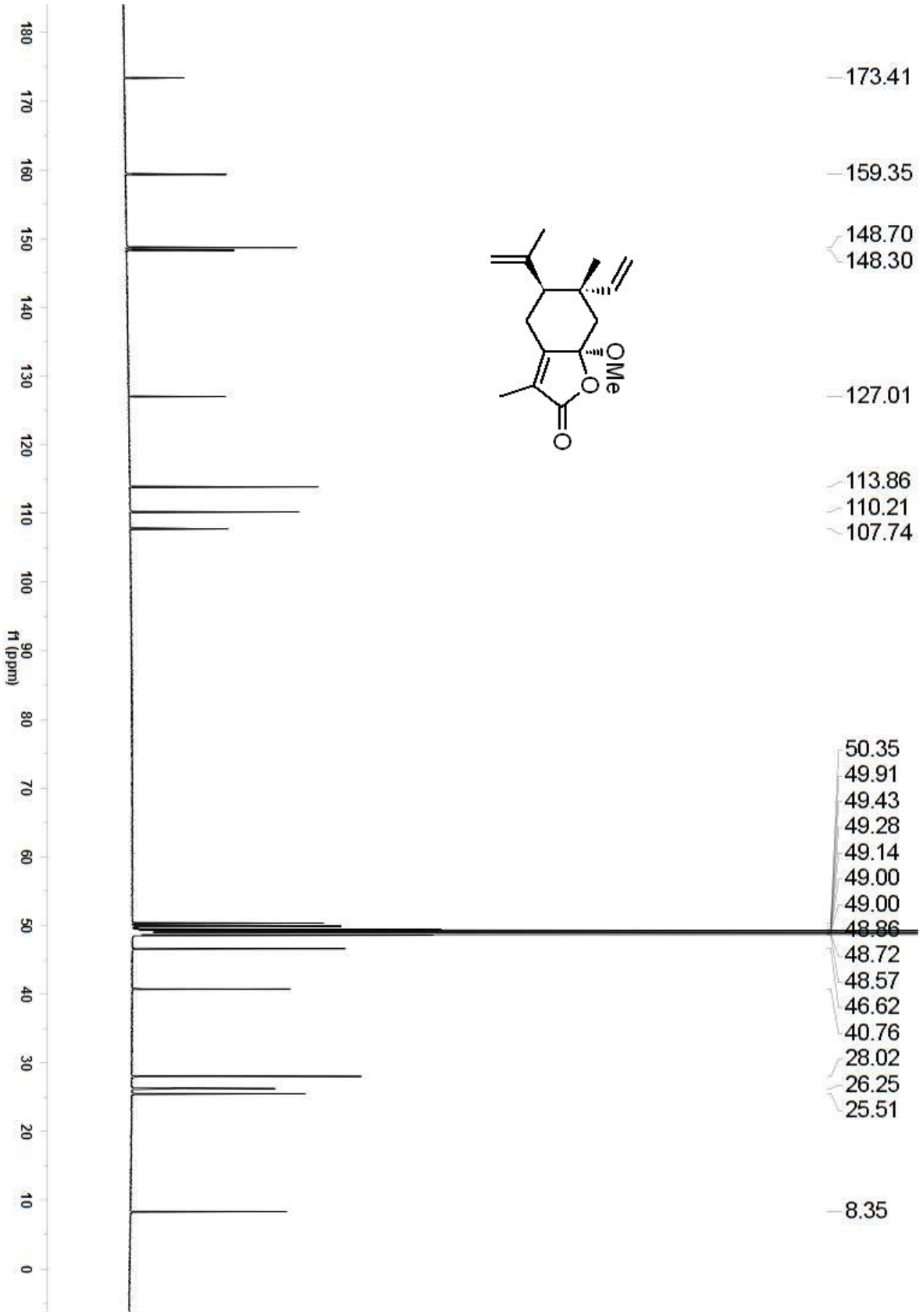
NOESY spectra of compound **6a** in CD_3OD



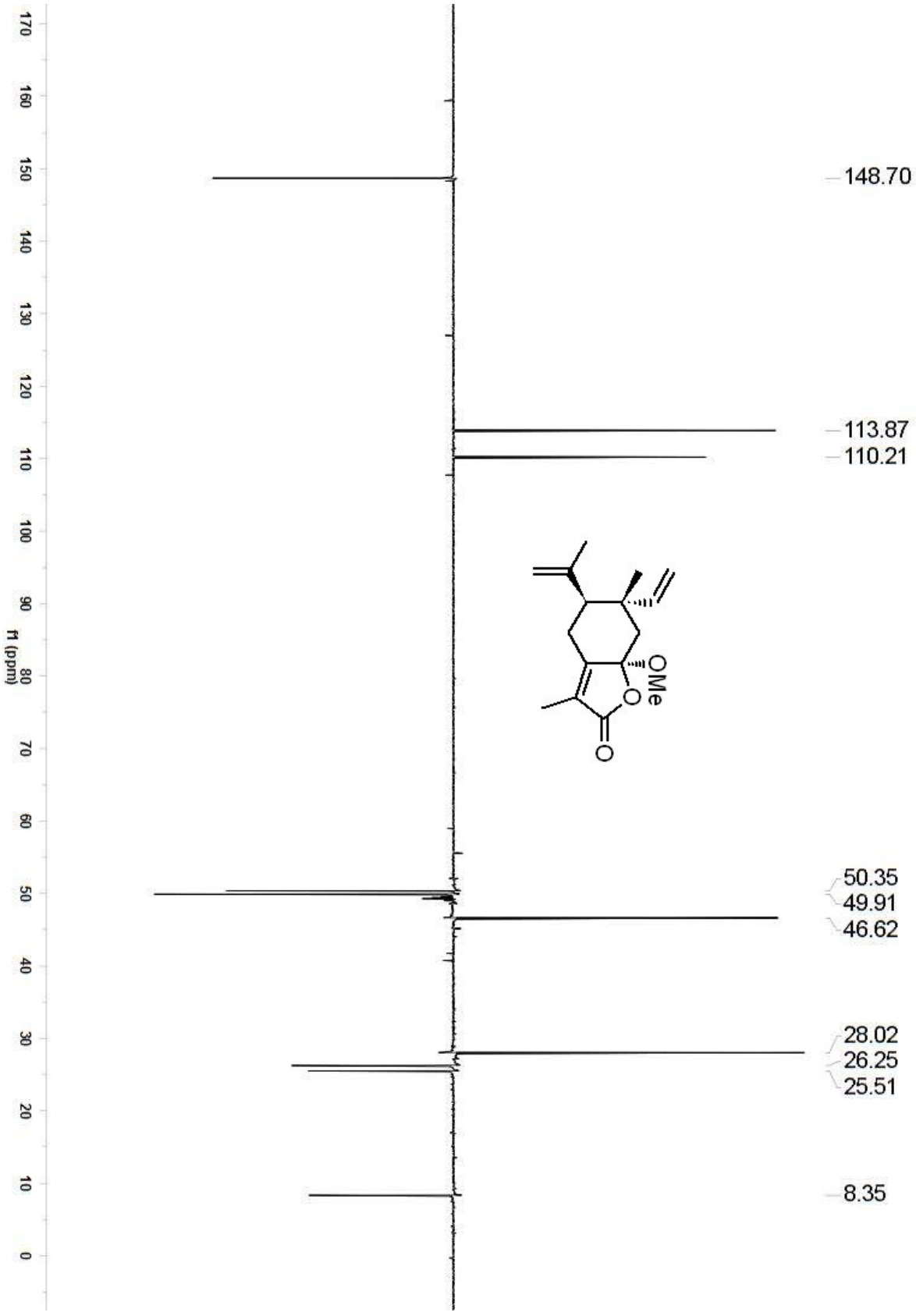
^{1}H NMR spectra of compound **6b** in CD_3OD (600 MHz)



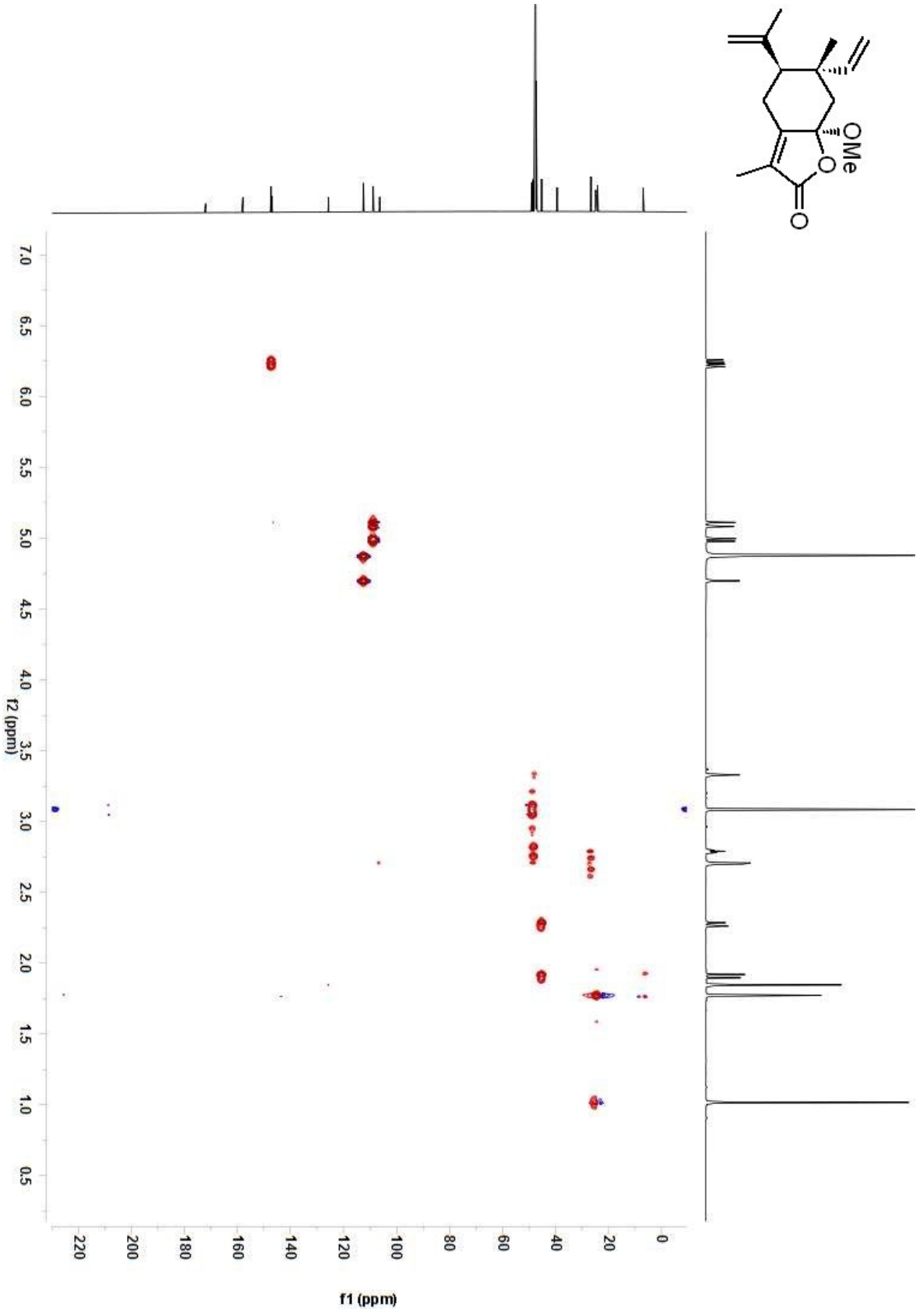
^{13}C NMR spectra of compound **6b** in CD_3OD (150 MHz)



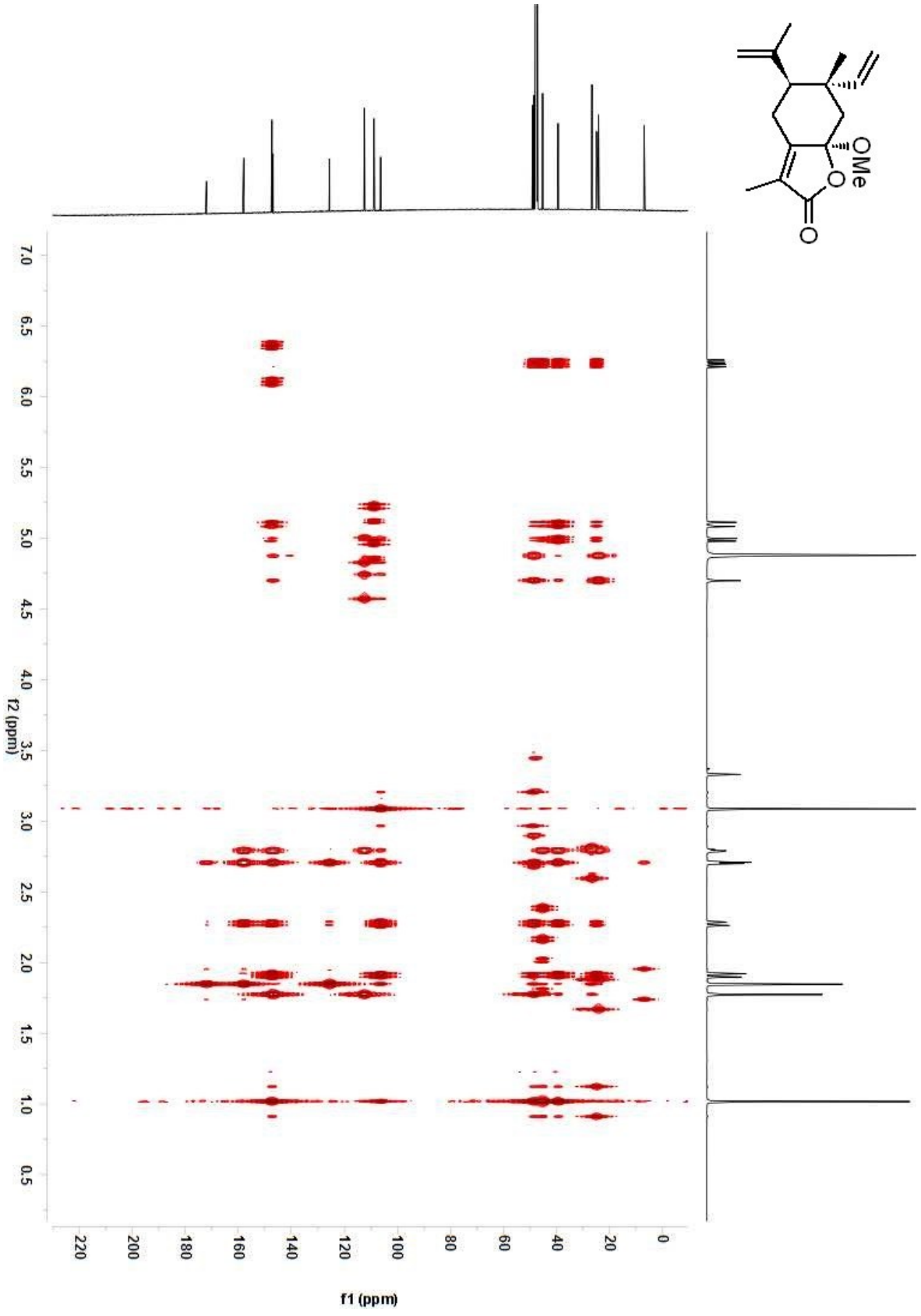
DEPT spectra of compound **6b** in CD_3OD



HSQC spectra of compound **6b** in CD_3OD



HMBC spectra of compound **6b** in CD_3OD



NOESY spectra of compound **6b** in CD_3OD