Supporting Information

Synthesis and structure–activity relationships for cytotoxicity and apoptosis-inducing activity of (+)-halichonine B

Ichiro Hayakawa,*[a] Tomomi Nakamura,[b] Osamu Ohno,[c] Kiyotake Suenaga[d] and Hideo Kigoshi*[b]

[a] Division of Applied Chemistry, Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushima-naka, Kita-ku, Okayama 700-8530, Japan
E-mail: ichiro.hayakawa@okayama-u.ac.jp; Fax: +81-86-251-8215

[b] Department of Chemistry, Graduate School of Pure and Applied Sciences, University of Tsukuba 1-1-1 Tennodai, Tsukuba 305-8571, Japan
E-mail: kigoshi@chem.tsukuba.ac.jp; Fax: +81-29-853-4313

[c] Department of Chemistry and Life Science, School of Advanced Engineering, Kogakuin University, 2665-1 Nakano, Hachioji 192-0015, Japan

[d] Department of Chemistry, Faculty of Science and Technology, Keio University 3-14-1 Hiyoshi, Yokohama 223-8522, Japan.

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Table S1 GI_{50} values of halichonine B (**2**) against 39 human cancer cell lines

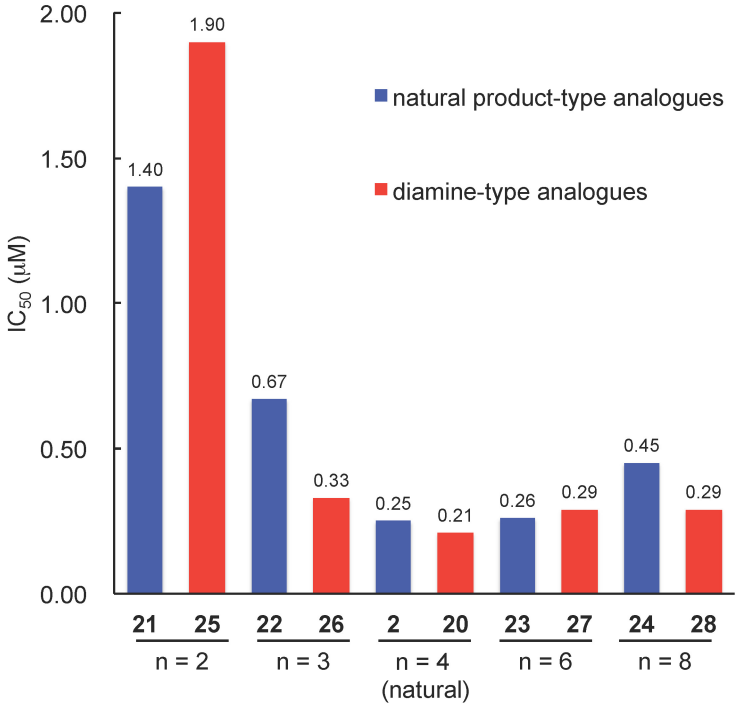
Type of cancer	Cell line	GI_{50}[a,b] (μM)	
		halichonine B free amine	halichonine B HCl salt
Breast	HBC-4	2.0	1.7
	BSY-1	2.0	1.6
	HBC-5	2.9	1.9
	MCF-7	3.4	1.9
	MDA-MB-231	12	1.8
Central nervous	U251	3.6	1.7
	SF-268	13	1.7
	SF-295	8.8	1.8
	SF-539	2.0	1.9
	SNB-75	16	1.9
	SNB-78	17	1.8
Colon	HCC2998	1.7	1.2
	KM-12	7.3	1.9
	HT-29	3.4	1.7
	HCT-15	11	1.8
	HCT-116	6.0	1.8
Lung	NCI-H23	13	1.8
	NCI-H226	14	2.0
	NCI-H522	2.5	1.7
	NCI-H460	3.5	1.8
	A549	16	1.9
	DMS273	4.7	1.9
	DMS114	1.9	1.6
Melanoma	LOX-IMVI	8.6	1.9
Ovary	OVCAR-3	13	1.7
	OVCAR-4	11	1.8
	OVCAR-5	3.5	1.7
	OVCAR-8	11	2.0
	SK-OV-3	18	2.1
Kidney	RXF-631L	13	1.8
	ACHN	17	1.8
Stomach	St-4	16	1.8
	MKN1	11	1.6
	MKN7	3.1	2.0
	MKN28	4.6	1.7
	MKN45	10	1.6
	MKN74	2.3	1.7
Prostate	DU-145	14	1.9
	PC-3	16	1.8
MG-MID[c]		–5.17	–5.75
Delta[d]		0.59	0.16
Range[e]		1.02	0.24

[a] Concentrations for the inhibition of cell growth at 50% relative to control.
[b] Cell growth was determined according to the sulforhodamine B assay.
[c] Mean GI_{50} value in all of the cell lines tested.
[d] Difference in the GI_{50} value between the most-sensitive cells and the MG-MID value.
[e] Difference in the log GI_{50} value between the most- and least-sensitive cells.

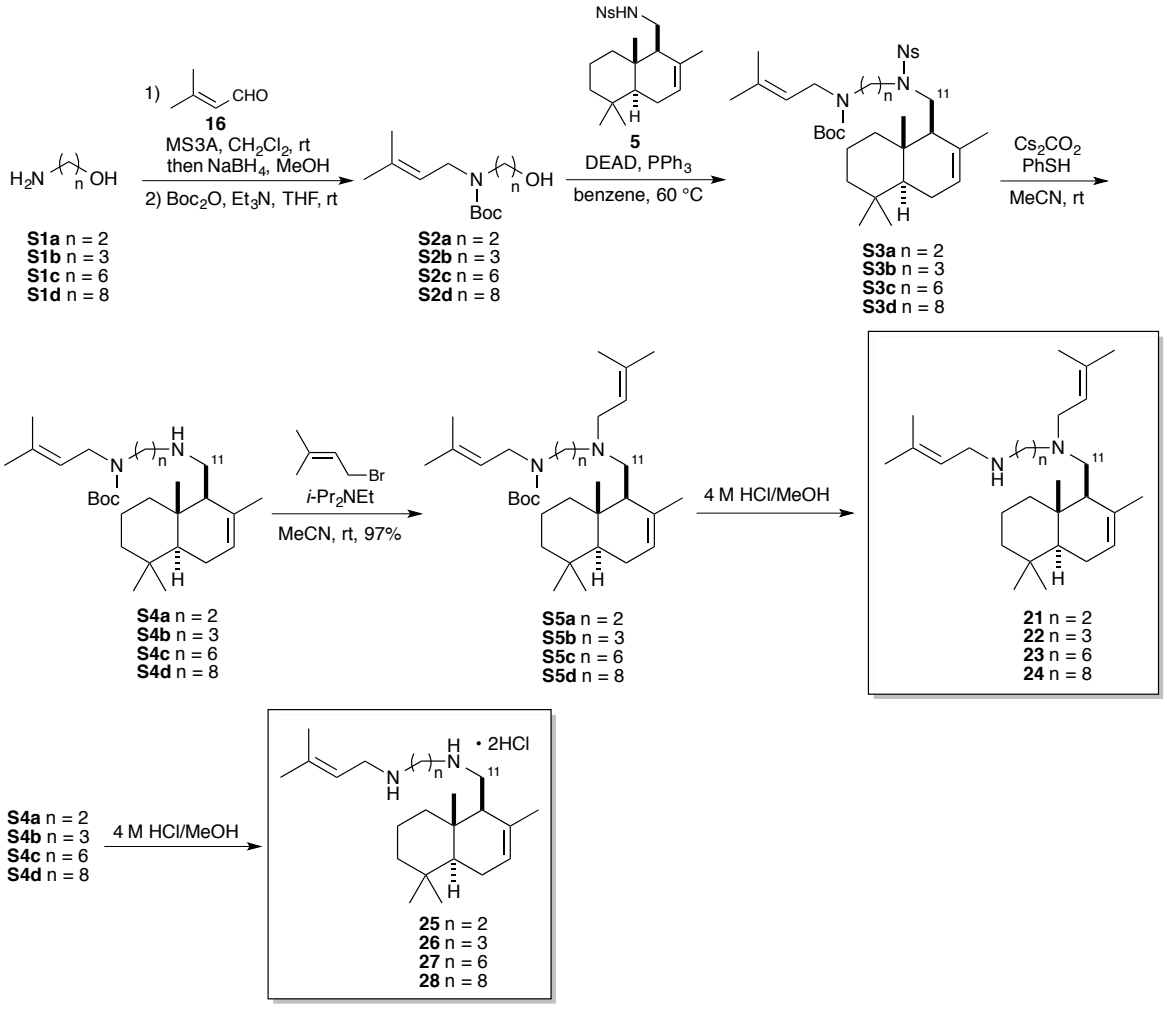
Table S2 Results of COMPARE

sample	known compounds	r (correlation coefficient)	molecular targets/drug type
halichonine B free amine	Tamoxifen citrate	0.724	Selective Estrogen Receptor Modulators (SERM), anticancer drugs, Protein Kinase C estrogen receptor
halichonine B HCl salt	Toremifene citrate	0.494	Selective Estrogen Receptor Modulators (SERM), anticancer drugs/estrogen antagonist
	Tamoxifen citrate	0.48	Selective Estrogen Receptor Modulators (SERM), anticancer drugs, Protein Kinase C estrogen receptor

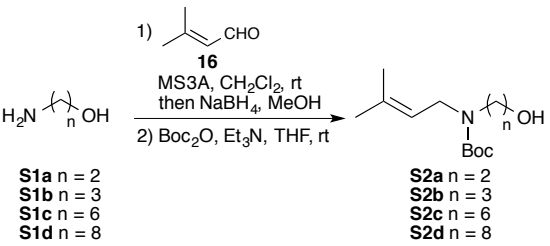
Figure S1 Relationship between the diamine chain length of halichonine B analogues and cytotoxicity against HL60 cells



Experimental protocols and characterization data of artificial analogues



General procedure for the preparation of alcohol **S2a**–**d**



To a stirred solution of amino alcohol **S1a**–**d** in CH_2Cl_2 (ca. 0.1 M) containing molecular sieves 3Å was added 3-methyl-2-butenal (**16**) (1.1 equiv.) at room temperature, and the mixture was stirred at room temperature for ca. 20 h. The mixture was filtered through a pad of Celite, and the residue was washed with CH_2Cl_2. Concentration of the filtrate and washings afforded the crude imine intermediate.

To a stirred solution of the crude imine intermediate in MeOH (ca. 1.0 M) was added $NaBH_4$ (2.0 equiv.) at 0 ºC. After being stirred at room temperature for 30 min, the reaction mixture was diluted with H_2O and extracted with CH_2Cl_2 (× 5). The combined extracts were washed with brine, dried

over Na_2SO_4, and filtered. Removal of the solvent afforded the crude amine, which was used for the next reaction without further purification.

To a stirred solution of the crude amine in THF (ca. 0.2 M) were added Boc_2O (1.2 equiv.) and Et_3N (2.0 equiv.) at 0 ºC. After being stirred at room temperature for ca. 1 h, the reaction mixture was diluted with saturated aqueous NH_4Cl and extracted with EtOAc (× 3). The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (*n*-hexane–Et_2O 5 : 1 → *n*-hexane–EtOAc 1 : 1 for **S2a**; *n*-hexane–EtOAc for **S2b**–**S2d**) to give alcohol **S2a**–**d**.

tert-butyl (2-hydroxyethyl)(3-methylbut-2-en-1-yl)carbamate [**S2a** (n = 2)]. Colorless oil (168 mg, 50% yield in 2 steps): R_f = 0.51 (*n*-hexane−EtOAc 2 : 1); IR ($CHCl_3$) 3429, 3010, 2980, 2934, 1665, 1455, 1415, 1252, 1166, 1050, 869 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.14 (m, 1H), 3.93–3.77 (br m, 2H), 3.74–3.63 (m, 2H), 3.42–3.20 (br m, 3H), 1.71 (s, 3H), 1.64 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.0, 135.4, 120.6, 80.0, 62.5, 49.6, 46.2, 28.4 (3C), 25.7, 17.8; HRMS (ESI) *m/z* 252.1568, calcd for $C_{12}H_{23}NNaO_3$ $[M+Na]^+$ 252.1576.

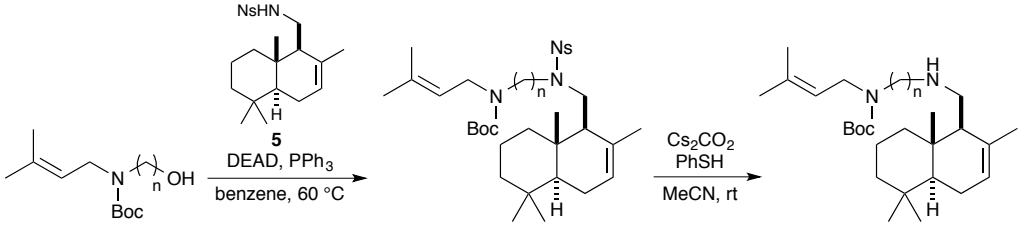
tert-butyl (3-hydroxypropyl)(3-methylbut-2-en-1-yl)carbamate [**S2b** (n = 3)]. Colorless oil (378 mg, quant. in 2 steps): R_f = 0.54 (*n*-hexane−EtOAc 1 : 1); IR ($CHCl_3$) 3411, 3009, 2980, 2937, 1661, 1478, 1420, 1253, 1164, 1076, 883 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.13 (m, 1H), 3.97–3.68 (br m, 3H), 3.62–3.44 (br m, 2H), 3.39–3.20 (br m, 2H), 1.79–1.37 (m, 2H), 1.71 (s, 3H), 1.64 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.0, 134.8, 120.7, 79.9, 58.4, 44.7, 42.1, 30.5, 28.4 (3C), 25.6, 17.7; HRMS (ESI) *m/z* 266.1746, calcd for $C_{13}H_{25}NNaO_3$ [M+Na]+ 266.1732.

tert-butyl (6-hydroxyhexyl)(3-methylbut-2-en-1-yl)carbamate [**S2c** (n = 6)]. Colorless oil (192 mg, 82% yield in 2 steps): R_f = 0.55 (*n*-hexane−EtOAc 2 : 1); IR ($CHCl_3$) 3626, 3449, 3008, 2978, 2935, 1668, 1454, 1419, 1251, 1168, 1077, 882 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.13 (m, 1H), 3.88–3.70 (br m, 2H), 3.62 (t, *J* = 6.5 Hz, 2H), 3.24–3.04 (br m, 2H), 1.71 (s, 3H), 1.65 (s, 3H), 1.61–1.23 (m, 8H), 1.44 (s, 9H). A signal due to one proton (OH) was not observed; ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.7, 134.7, 121.2, 79.1, 62.7, 46.0, 44.4, 32.7, 28.5 (3C), 28.2, 26.5, 25.6, 25.3, 17.7; HRMS (ESI) *m/z* 308.2201, calcd for $C_{16}H_{31}NNaO_3$ $[M+Na]^+$ 308.2202.

tert-butyl (8-hydroxyoctyl)(3-methylbut-2-en-1-yl)carbamate [**S2d** (n = 8)]. Colorless oil (202 mg, 78% yield in 2 steps): R_f = 0.42 (*n*-hexane−EtOAc 2 : 1); IR ($CHCl_3$) 3628, 3451, 3009, 2978, 2932, 1669, 1455, 1419, 1252, 1168, 1050, 880 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.14 (m, 1H), 3.89–3.69 (br m, 2H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.20–3.01 (br m, 2H), 1.71 (s, 3H), 1.65 (s, 3H), 1.59–1.18 (m, 12H), 1.44 (s, 9H). A signal due to one proton (OH) was not observed; ^{13}C NMR (150

MHz, $CDCl_3$) δ 155.6, 134.0, 121.2, 79.0, 62.8, 46.2, 44.1, 32.7, 29.3 (2C), 28.5 (3C), 28.2, 26.8, 25.6 (2C), 17.7; HRMS (ESI) *m/z* 336.2539, calcd for $C_{18}H_{35}NNaO_3$ $[M+Na]^+$ 336.2515.

General procedure for the preparation of amine **S4a**–**d**



S2a n = 2
S2b n = 3
S2c n = 6
S2d n = 8

S3a n = 2
S3b n = 3
S3c n = 6
S3d n = 8

S4a n = 2
S4b n = 3
S4c n = 6
S4d n = 8

To a stirred solution of Ns-amide **5**, alcohol **S2a**–**d** (3.0 equiv.), and PPh_3 (3.0 equiv.) in benzene (0.10 M) was added DIAD (3.0 equiv.) at room temperature. The mixture was stirred at reflux for ca. 15 h. Removal of the solvent afforded crude product, which was purified by column chromatography on silica gel to give coupling compound **S3a**–**d** (containing impurities). The coupling compound **S3a**–**d** was used for the next reaction without further purification.

To a stirred solution of coupling compounds **S3a**–**d** (containing impurities) and Cs_2CO_3 (1.7 equiv.) in MeCN (0.1 M) was added PhSH (1.4 equiv.) at 0 ºC. After being stirred at room temperature for ca. 15 h, the mixture was filtered through a pad of Celite, and the residue was washed with EtOAc. Concentration of the filtrate and washings afforded the crude product, which was purified by column chromatography on Al_2O_3 (*n*-hexane–Et_2O) to give amine **S4a**–**d**.

tert-butyl (3-methylbut-2-en-1-yl)(2-((((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)ethyl)carbamate [**S4a** (n = 2)]. Yellow oil (18.8 mg, 30% yield in 2 steps): R_f = 0.58 ($CHCl_3$–MeOH 8 : 1); $[\alpha]_D^{24}$ +2.8 (*c* 0.24, $CHCl_3$); IR ($CHCl_3$) 3360, 3020, 2927, 2850, 1682, 1456, 1416, 1366, 1251, 1166, 1138, 884 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.43 (m, 1H), 5.15 (m, 1H), 3.92–3.72 (br m, 2H), 3.38–3.14 (br m, 2H), 2.82–2.62 (m, 3H), 2.50 (m, 1H), 2.01–1.79 (m, 3H), 1.78–1.36 (m, 4H), 1.71 (s, 6H), 1.65 (s, 3H), 1.44 (s, 9H), 1.23–1.12 (m, 2H), 1.05 (ddd, *J* = 13.1, 13.1, 3.6 Hz, 1H), 0.87 (s, 3H), 0.85 (s, 3H), 0.76 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.7, 134.8, 134.3, 122.9, 121.1, 79.3, 55.5, 50.0, 48.6, 48.2, 46.5, 45.2, 42.2, 39.4, 36.2, 33.2, 32.9, 28.5 (3C), 25.7, 23.7, 21.9 (2C), 18.8, 17.8, 14.1; HRMS (ESI) *m/z* 433.3796, calcd for $C_{27}H_{49}N_2O_2$ $[M+H]^+$ 433.3789.

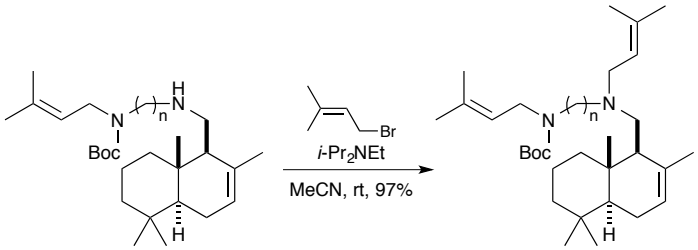
tert-butyl (3-methylbut-2-en-1-yl)(3-((((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)propyl)carbamate [**S4b** (n = 3)]. Yellow oil (21.5 mg, 63% yield in 2 steps): R_f = 0.47 ($CHCl_3$–MeOH 8 : 1); $[\alpha]_D^{24}$ +3.3 (*c* 0.57, $CHCl_3$); IR ($CHCl_3$) 3330,

3009, 2927, 2856, 1681, 1456, 1419, 1366, 1251, 1167, 1137, 869 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.42 (m, 1H), 5.13 (m, 1H), 3.88–3.68 (br m, 2H), 3.29–3.19 (br m, 2H), 2.67 (dd, *J* = 12.2, 1.5 Hz, 1H), 2.61 (ddd, *J* = 11.7, 7.1, 7.1 Hz, 1H), 2.56–2.41 (m, 2H), 2.00–1.22 (m, 9H), 1.72 (s, 3H), 1.70 (s, 3H), 1.64 (s, 3H), 1.44 (s, 9H), 1.20–1.11 (m, 2H), 1.06 (ddd, *J* = 13.1, 13.1, 3.4 Hz, 1H), 0.86 (s, 3H), 0.84 (s, 3H), 0.74 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 134.9, 134.3, 122.8, 121.1, 79.2, 55.2, 50.0, 48.2, 47.6, 44.5, 44.2, 42.2, 39.4, 36.2, 33.2, 32.9, 29.0, 28.5 (3C), 25.7, 23.7, 21.9 (2C), 18.8, 17.8, 14.0; HRMS (ESI) *m/z* 447.3964, calcd for $C_{28}H_{51}N_2O_2$ $[M+H]^+$ 447.3945.

tert-butyl (3-methylbut-2-en-1-yl)(6-((((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)hexyl)carbamate [**S4c** (n = 6)]. Yellow oil (19.6 mg, 53% yield in 2 steps): R_f = 0.50 ($CHCl_3$−MeOH 8 : 1); $[\alpha]_D^{24}$ +1.5 (*c* 0.13, $CHCl_3$); IR ($CHCl_3$) 3336, 3018, 2930, 2855, 1681, 1456, 1419, 1366, 1251, 1168, 1134, 880 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.42 (m, 1H), 5.13 (m, 1H), 3.85–3.70 (br m, 2H), 3.19–3.02 (br m, 2H), 2.69 (dd, *J* = 12.2, 1.6 Hz, 1H), 2.60 (ddd, *J* = 11.4, 7.2, 7.2 Hz, 1H), 2.50 (ddd, *J* = 11.4, 7.2, 7.2 Hz, 1H), 2.45 (dd, *J* = 12.2, 7.3 Hz, 1H), 2.00–1.12 (m, 17H), 1.71 (s, 3H), 1.71 (s, 3H), 1.64 (s, 3H), 1.44 (s, 9H), 1.07 (ddd, *J* = 13.2, 13.2, 3.7 Hz, 1H), 0.87 (s, 3H), 0.84 (s, 3H), 0.75 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 134.8, 134.3, 122.9, 121.2, 79.0, 55.3, 50.2, 50.0, 48.3, 46.2, 44.6, 42.2, 39.3, 36.2, 33.2, 33.0, 30.1, 28.5 (3C), 28.4, 27.2, 26.9, 25.7, 23.7, 21.9 (2C), 18.8, 17.8, 14.0; HRMS (ESI) *m/z* 489.4430, calcd for $C_{31}H_{57}N_2O_2$ $[M+H]^+$ 489.4415.

tert-butyl (3-methylbut-2-en-1-yl)(8-((((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)octyl)carbamate [**S4d** (n = 8)]. Yellow oil (38.9 mg, 67% yield in 2 steps): R_f = 0.53 ($CHCl_3$−MeOH 8 : 1); $[\alpha]_D^{24}$ +1.5 (*c* 0.13, $CHCl_3$); IR ($CHCl_3$) 3355, 3018, 2929, 2856, 1669, 1457, 1419, 1366, 1251, 1168, 881 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.42 (m, 1H), 5.13 (m, 1H), 3.87–3.68 (br m, 2H), 3.20–3.01 (br m, 2H), 2.69 (dd, *J* = 12.1, 1.2 Hz, 1H), 2.60 (ddd, *J* = 11.4, 7.2, 7.2 Hz, 1H), 2.50 (ddd, *J* = 11.4, 7.2, 7.2 Hz, 1H), 2.45 (dd, *J* = 12.1, 7.4 Hz, 1H), 2.00–1.79 (m, 3H), 1.77–1.12 (m, 18H), 1.72 (s, 3H), 1.70 (s, 3H), 1.64 (s, 3H), 1.44 (s, 9H), 1.07 (ddd, *J* = 13.1, 13.1, 3.6 Hz, 1H), 0.86 (s, 3H), 0.84 (s, 3H), 0.75 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 134.7, 134.3, 122.9, 121.2, 79.0, 55.3, 50.3, 50.0, 48.2, 46.2, 44.6, 42.2, 39.3, 36.2, 33.2, 33.0, 30.0, 29.5, 29.3, 28.5 (3C), 28.2, 27.4, 26.9, 25.7, 23.7, 21.9 (2C), 18.8, 17.8, 14.0; HRMS (ESI) *m/z* 517.4735, calcd for $C_{33}H_{61}N_2O_2$ $[M+H]^+$ 517.4728

General procedure for the preparation of **S5a**–**d**



S4a n = 2
S4b n = 3
S4c n = 6
S4d n = 8

S5a n = 2
S5b n = 3
S5c n = 6
S5d n = 8

To a stirred solution of amine **S4a**–**d** in MeCN (0.2 M) were added *i*-Pr_2NEt (1.0 equiv.) and prenyl bromide (2.4 equiv.) at 0 ºC. After being stirred at room temperature for ca. 1.5–20 h, the reaction mixture was diluted with H_2O and extracted with EtOAc (× 3). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by column chromatography on Al_2O_3 (*n*-hexane–Et_2O for **S5a**, **S5c**, and **S5d**; *n*-hexane–Et_2OAc 9 : 1 for **S5b**) to give compound **S5a**–**d**.

tert-butyl (3-methylbut-2-en-1-yl)(2-((3-methylbut-2-en-1-yl)(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)ethyl)carbamate [**S5a** (n = 2)]. Yellow oil (9.3 mg, 74% yield): R_f = 0.43 (*n*-hexane−Et_2O 4 : 1); $[\alpha]_D^{24}$ +26.6 (*c* 0.45, $CHCl_3$); IR ($CHCl_3$) 2926, 2851, 1680, 1457, 1416, 1366, 1251, 1169, 880 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.38 (m, 1H), 5.24 (m, 1H), 5.14 (m, 1H), 3.91–3.72 (br m, 2H), 3.33–3.06 (br m, 3H), 2.90 (br m, 1H), 2.70 (br m, 1H), 2.40–2.21 (m, 3H), 2.06–1.90 (br m, 2H), 1.88–1.32 (m, 5H), 1.74 (s, 3H), 1.72 (s, 3H), 1.71 (s, 3H), 1.66 (s, 3H), 1.62 (s, 3H), 1.45 (s, 9H), 1.23–1.10 (m, 2H), 1.01 (ddd, *J* = 13.1, 13.1, 3.3 Hz, 1H), 0.87 (s, 3H), 0.84 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 135.8, 134.9, 134.2, 122.0, 121.9, 121.2, 79.1, 53.9, 52.0, 51.8 (2C), 50.2, 45.6, 44.8, 42.3, 39.2, 36.1, 33.3, 33.0, 28.5 (3C), 25.9, 25.8, 23.7, 22.4, 22.0, 18.8, 18.0, 17.8, 13.7; HRMS (ESI) *m/z* 501.4401, calcd for $C_{32}H_{57}N_2O_2$ $[M+H]^+$ 501.4415.

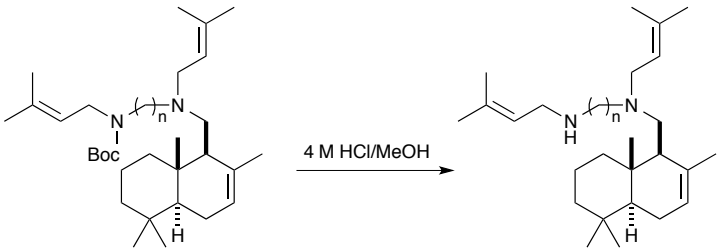
tert-butyl (3-methylbut-2-en-1-yl)(3-((3-methylbut-2-en-1-yl)(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)propyl)carbamate [**S5b** (n = 3)]. Yellow oil (8.0 mg, 53% yield): R_f = 0.61 (*n*-hexane−Et_2O 2 : 1); $[\alpha]_D^{24}$ +42.2 (*c* 0.65, $CHCl_3$); IR ($CHCl_3$) 2926, 2878, 1669, 1445, 1419, 1366, 1251, 1167, 869 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.38 (m, 1H), 5.22 (m, 1H), 5.14 (m, 1H), 3.88–3.69 (br m, 2H), 3.21–2.98 (br m, 3H), 2.87 (m, 1H), 2.49 (br m, 1H), 2.33–2.14 (m, 3H), 2.03–1.92 (br m, 2H), 1.87–1.36 (m, 7H), 1.74 (s, 3H), 1.71 (s, 6H), 1.65 (s, 3H), 1.62 (s, 3H), 1.44 (s, 9H), 1.23–1.11 (m, 2H), 0.99 (ddd, *J* = 13.1, 13.1, 3.3 Hz, 1H), 0.87 (s, 3H), 0.85 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 136.0, 134.7, 134.0, 121.9, 121.8, 121.3, 79.0, 53.8, 51.6, 51.1, 51.0, 50.2, 45.2, 44.3, 42.3, 39.2, 36.1, 33.3, 33.0, 28.5

(3C), 25.9, 25.7 (2C), 23.7, 22.4, 22.0, 18.8, 17.9, 17.8, 13.7; HRMS (ESI) *m/z* 515.4544, calcd for $C_{33}H_{59}N_2O_2[M+H]^+$ 515.4571.

tert-butyl (3-methylbut-2-en-1-yl)(6-((3-methylbut-2-en-1-yl)(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)hexyl)carbamate [**S5c** (n = 6)]. Yellow oil (12.1 mg, quant): R_f = 0.63 (*n*-hexane−Et_2O 4 : 1); $[\alpha]_D^{24}$ +36.6 (*c* 0.41, $CHCl_3$); IR ($CHCl_3$) 2929, 2857, 1669, 1454, 1419, 1366, 1251, 1168, 879 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.38 (m, 1H), 5.23 (m, 1H), 5.14 (m, 1H), 3.87–3.69 (br m, 2H), 3.19–3.03 (br m, 3H), 2.83 (dd, *J* = 14.2, 7.6 Hz, 1H), 2.48 (m, 1H), 2.32–2.24 (m, 2H), 2.18 (m, 1H), 2.05–1.92 (br m, 2H), 1.87–1.35 (m, 9H), 1.75 (s, 3H), 1.71 (s, 3H), 1.71 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.45 (s, 9H), 1.32–1.13 (m, 6H), 0.99 (ddd, *J* = 13.1, 13.1, 3.3 Hz, 1H), 0.87 (s, 3H), 0.85 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 136.2, 134.6, 133.7, 122.2, 121.9, 121.2, 79.0, 53.8, 53.6, 51.5, 51.2, 50.3, 46.2, 44.4, 42.3, 39.2, 36.2, 33.3, 33.0, 28.5 (3C), 28.4, 27.5, 27.0, 26.9, 25.9, 25.7, 23.7, 22.4, 22.0, 18.8, 17.9, 17.8, 13.7; HRMS (ESI) *m/z* 557.5031, calcd for $C_{36}H_{65}N_2O_2$ $[M+H]^+$ 557.5041.

tert-butyl (3-methylbut-2-en-1-yl)(8-((3-methylbut-2-en-1-yl)(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)amino)octyl)carbamate [**S5d** (n = 8)]. Yellow oil (21.7 mg, 79% yield): R_f = 0.49 (*n*-hexane−Et_2O 4 : 1); $[\alpha]_D^{24}$ +40.7 (*c* 0.44, $CHCl_3$); IR ($CHCl_3$) 2929, 2856, 1668, 1455, 1419, 1366, 1251, 1167, 1135, 881 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.38 (m, 1H), 5.23 (m, 1H), 5.14 (m, 1H), 3.87–3.69 (br m, 2H), 3.19–3.02 (br m, 3H), 2.84 (dd, *J* = 14.1, 7.6 Hz, 1H), 2.48 (m, 1H), 2.33–2.23 (m, 2H), 2.17 (m, 1H), 2.05–1.91 (br m, 2H), 1.88–1.35 (m, 9H), 1.75 (s, 3H), 1.71 (s, 6H), 1.65 (s, 3H), 1.62 (s, 3H), 1.45 (s, 9H), 1.32–1.11 (m, 10H), 0.98 (ddd, *J* = 13.1, 13.1, 3.3 Hz, 1H), 0.87 (s, 3H), 0.85 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 136.3, 134.7, 133.6, 122.2, 121.8, 121.2, 79.0, 53.8, 53.6, 51.6, 51.2, 50.3, 46.2, 44.0, 42.3, 39.2, 36.2, 33.3, 33.0, 29.7, 29.4, 28.5 (3C), 28.3, 27.7, 26.9, 26.8, 25.9, 25.7, 23.7, 22.4, 22.0, 18.9, 17.9, 17.8, 13.7.; HRMS (ESI) *m/z* 585.5359, calcd for $C_{38}H_{69}N_2O_2$ $[M+H]^+$ 585.5354.

General procedure for the preparation of natural product-type analogues **21**–**24**



S5a n = 2
S5b n = 3
S5c n = 6
S5d n = 8

21 n = 2
22 n = 3
23 n = 6
24 n = 8

The compound **S5a**–**d** was treated with 4.0 M HCl/MeOH at 0 ºC. After being stirred at room temperature for ca. 17 h, the reaction mixture was concentrated to afford **21**–**24** HCl salt. The **21**–**24** HCl salt was purified by column chromatography on Al_2O_3 ($CHCl_3$–MeOH for **21**, **23**, and **24**; *n*-hexane–EtOAc 5 : 1 for **22**) to give natural product-type analogues (free amine) **21**–**24**.

N^1,N^2-bis(3-methylbut-2-en-1-yl)-N^1-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)ethane-1,2-diamine [**21** (n = 2)]. Yellow oil (5.3 mg, quant.): R_f = 0.48 ($CHCl_3$−MeOH 9 : 1); $[\alpha]_D^{24}$ +26.6 (*c* 0.12, $CHCl_3$); IR ($CHCl_3$) 3307, 2960, 2925, 2850, 1675, 1456, 1378, 1224, 1093, 987 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 5.40 (m, 1H), 5.30–5.21 (m, 2H), 3.24–3.18 (m, 2H), 3.15 (dd, *J* = 14.2, 6.1 Hz, 1H), 2.92 (dd, *J* = 14.2, 7.8 Hz, 1H), 2.79–2.57 (m, 3H), 2.43–2.50 (m, 3H), 2.06–1.82 (br m, 4H), 1.74 (s, 6H), 1.73 (s, 3H), 1.68 (s, 3H), 1.66 (s, 3H), 1.58 (m, 1H), 1.49–1.39 (m, 2H), 1.27–1.17 (m, 2H), 1.10 (ddd, *J* = 13.2, 13.2, 3.4 Hz, 1H), 0.90 (s, 3H), 0.87 (s, 3H), 0.77 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (150 MHz, CD_3OD) δ 136.8, 136.4, 135.9, 123.4, 122.6, 122.5, 55.3, 53.5, 52.8, 52.7, 51.6, 47.5, 47.1, 43.4, 40.4, 37.4, 34.0, 33.8, 26.0, 25.9, 24.8, 23.0, 22.4, 19.8, 18.0 (2C), 14.2; HRMS (ESI) *m/z* 401.3860, calcd for $C_{27}H_{49}N_2$ $[M+H]^+$ 401.3890.

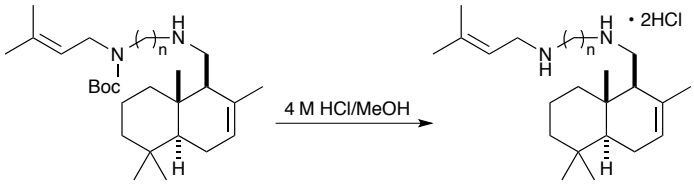
N^1,N^3-bis(3-methylbut-2-en-1-yl)-N^1-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)propane-1,3-diamine [**22** (n = 3)]. Yellow oil (1.9 mg, 40% yield): R_f = 0.24 ($CHCl_3$−MeOH 9 : 1); $[\alpha]_D^{24}$ +40.5 (*c* 0.19, $CHCl_3$); IR ($CHCl_3$) 3388, 2960, 2928, 2855, 1675, 1456, 1378, 1261, 1095, 1006 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 5.39 (m, 1H), 5.30–5.19 (m, 2H), 3.18 (d, *J* = 6.9 Hz, 2H), 3.13 (m, 1H), 2.94 (dd, *J* = 14.2, 7.9 Hz, 1H), 2.68–2.55 (m, 3H), 2.35–2.25 (m, 3H), 2.08–1.92 (br m, 4H), 1.78–1.38 (m, 5H), 1.75 (s, 3H), 1.74 (s, 6H), 1.66 (s, 3H), 1.58 (s, 3H), 1.25–1.15 (m, 2H), 1.06 (ddd, *J* = 13.1, 13.1, 3.3 Hz, 1H), 0.90 (s, 3H), 0.87 (s, 3H), 0.77 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (150 MHz, CD_3OD) δ 136.6, 135.7, 135.6, 123.3, 123.2, 122.7, 55.0, 53.2, 53.0, 52.3, 51.7, 49.6, 47.6, 43.5, 40.5, 37.4, 34.0, 33.8, 26.1, 25.9, 24.8, 22.9 (2C), 22.4, 19.9, 18.1, 18.0, 14.1; HRMS (ESI) *m/z* 415.4032, calcd for $C_{28}H_{51}N_2$ $[M+H]^+$ 415.4047.

N^1,N^6-bis(3-methylbut-2-en-1-yl)-N^1-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)hexane-1,6-diamine [**23** (n = 6)]. Yellow oil (4.1 mg, quant.): R_f = 0.20 ($CHCl_3$−MeOH 9 : 1); $[\alpha]_D^{24}$ –39.7 (*c* 0.33, $CHCl_3$); IR ($CHCl_3$) 3300, 2929, 2856, 1666, 1456, 1378, 1266, 1096, 986 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.37 (m, 1H), 5.31–5.21 (m, 2H), 3.20 (d, *J* = 7.0 Hz, 2H), 3.13 (dd, *J* = 13.9, 5.7 Hz, 1H), 2.88 (dd, *J* = 13.9, 7.6 Hz, 1H), 2.61–2.47 (m, 3H), 2.38–2.17 (m, 3H), 2.17–1.80 (m, 4H), 1.75 (s, 3H), 1.74 (s, 3H), 1.72 (s, 3H), 1.67 (s, 3H), 1.65 (s, 3H), 1.62–1.14 (m, 13H), 1.03 (ddd, *J* = 13.1, 13.1, 3.4 Hz, 1H), 0.90 (s, 3H), 0.87 (s,

3H), 0.76 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (100 MHz, CD_3OD) δ 136.9, 136.2, 135.1, 123.1, 123.0, 122.8, 54.9, 54.6, 53.0, 52.4, 51.7, 49.9, 47.6, 43.5, 40.6, 37.4, 34.0, 33.8, 30.3, 28.6, 28.4, 27.8, 26.1, 25.9, 24.8, 22.9, 22.4, 19.9, 18.0 (2C), 14.1; HRMS (ESI) *m/z* 457.4521, calcd for $C_{31}H_{57}N_2$ $[M+H]^+$ 457.4516.

N^1,N^8-bis(3-methylbut-2-en-1-yl)-N^1-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)octane-1,8-diamine [**24** (n = 8)]. Yellow oil (10.2 mg, 76% yield): R_f = 0.36 ($CHCl_3$–MeOH 9 : 1); $[\alpha]_D^{24}$ +41.1 (*c* 0.84, $CHCl_3$); IR ($CHCl_3$) 3305, 2929, 2855, 1670, 1456, 1381, 1271, 1095, 987 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 5.37 (m, 1H), 5.30–5.20 (m, 2H), 3.19 (d, *J* = 6.8 Hz, 2H), 3.13 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.88 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.62–2.48 (m, 3H), 2.40–2.18 (m, 3H), 2.11–1.81 (m, 4H), 1.75 (s, 3H), 1.74 (s, 3H), 1.72 (s, 3H), 1.67 (s, 3H), 1.65 (s, 3H), 1.62–1.16 (m, 17H), 1.04 (ddd, *J* = 13.1, 13.1, 3.4 Hz, 1H), 0.90 (s, 3H), 0.87 (s, 3H), 0.76 (s, 3H). A signal due to one proton (NH) was not observed; ^{13}C NMR (100 MHz, CD_3OD) δ 136.9, 136.1, 135.1, 123.2, 123.0, 122.9, 54.9, 54.6, 53.1, 52.4, 51.7, 50.0, 47.6, 43.5, 40.6, 37.4, 34.0, 33.9, 30.6 (2C), 30.4, 28.6, 28.4, 27.8, 26.1, 25.9, 24.8, 22.9, 22.4, 19.9, 18.0 (2C), 14.1; HRMS (ESI) *m/z* 485.4820, calcd for $C_{33}H_{61}N_2$ $[M+H]^+$ 485.4829.

General procedure for the preparation of diamine-type analogues **25**–**28**



S4a n = 2
S4b n = 3
S4c n = 6
S4d n = 8

25 n = 2
26 n = 3
27 n = 6
28 n = 8

The amine **S4a**–**d** was treated with 4.0 M HCl/MeOH at 0 ºC. After being stirred at room temperature for ca. 2.5–17 h, the reaction mixture was concentrated to afford diamine-type analogues **25**–**28**.

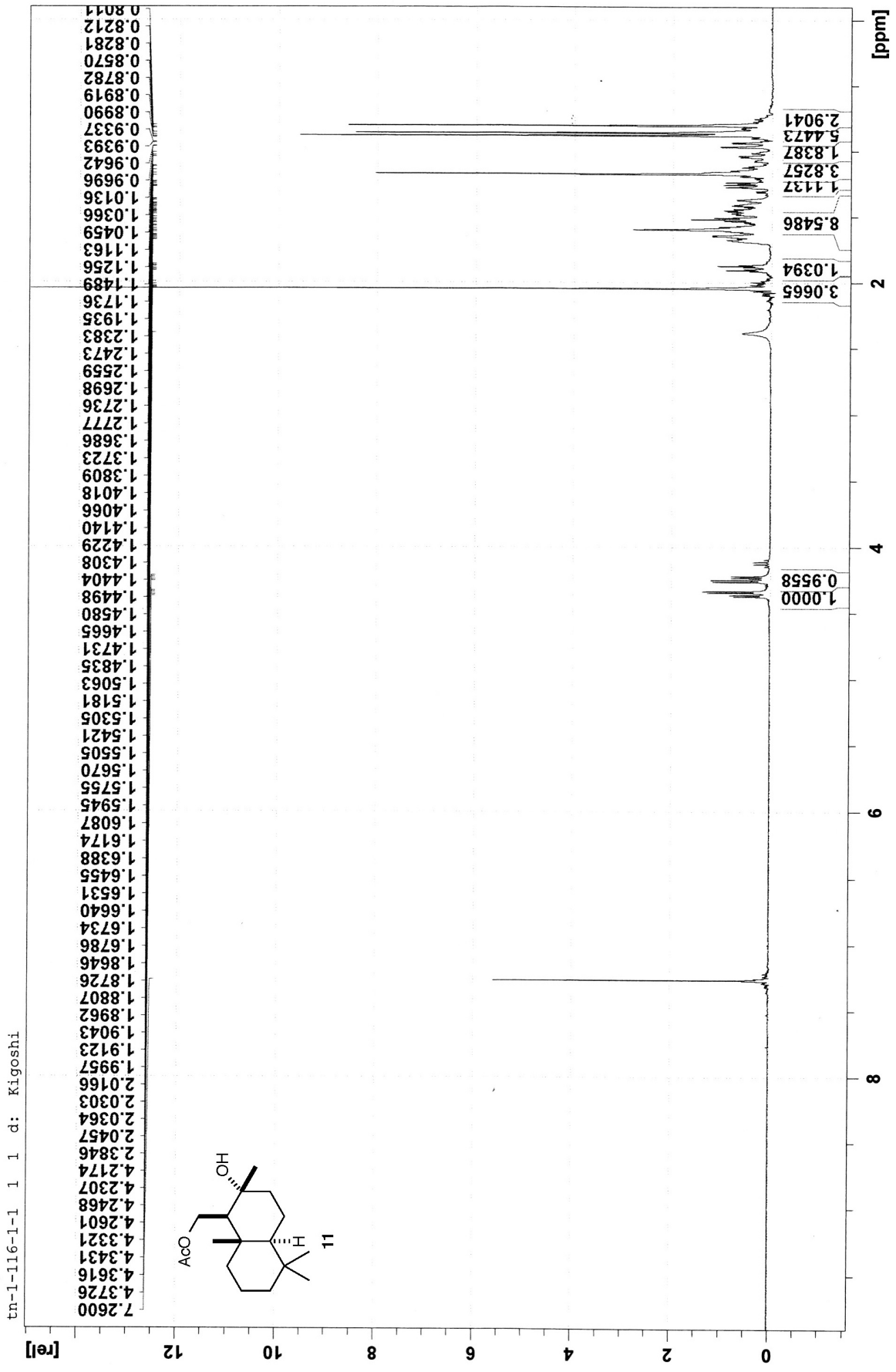
N^1-(3-methylbut-2-en-1-yl)-N^2-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)ethane-1,2-diamine [**25** (n = 2)]. Yellow oil (4.6 mg, 95% yield): R_f = 0.28 ($CHCl_3$–MeOH 4 : 1); $[\alpha]_D^{24}$ –10.8 (*c* 0.43, $CHCl_3$); IR ($CHCl_3$) 3372, 2965, 2855, 2777, 2450, 1589, 1442, 1389, 1236, 983 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 5.60 (m, 1H), 5.35 (t, *J* = 7.5 Hz, 1H), 3.73 (d, *J* = 7.5 Hz, 2H), 3.58–3.41 (m, 4H), 3.28–3.26 (m, 2H), 2.31–1.20 (m, 7H), 1.85 (s, 6H), 1.81 (s, 3H), 1,36–1.20 (m, 3H), 0.93 (s, 3H), 0.90 (s, 3H), 0.83 (s, 3H). Signals due to two proton (NH) were not observed; ^{13}C NMR (100 MHz, CD_3OD) δ 145.2, 131.5, 126.3, 114.5,

53.8, 50.9, 48.7, 46.7, 46.1, 43.5, 43.0, 40.1, 37.7, 33.9, 33.5, 26.0, 24.7, 22.1, 22.0, 19.6, 18.4, 14.0; HRMS (ESI) *m/z* 333.3278, calcd for $C_{22}H_{41}N_2$ $[M+H]^+$ 333.3264.

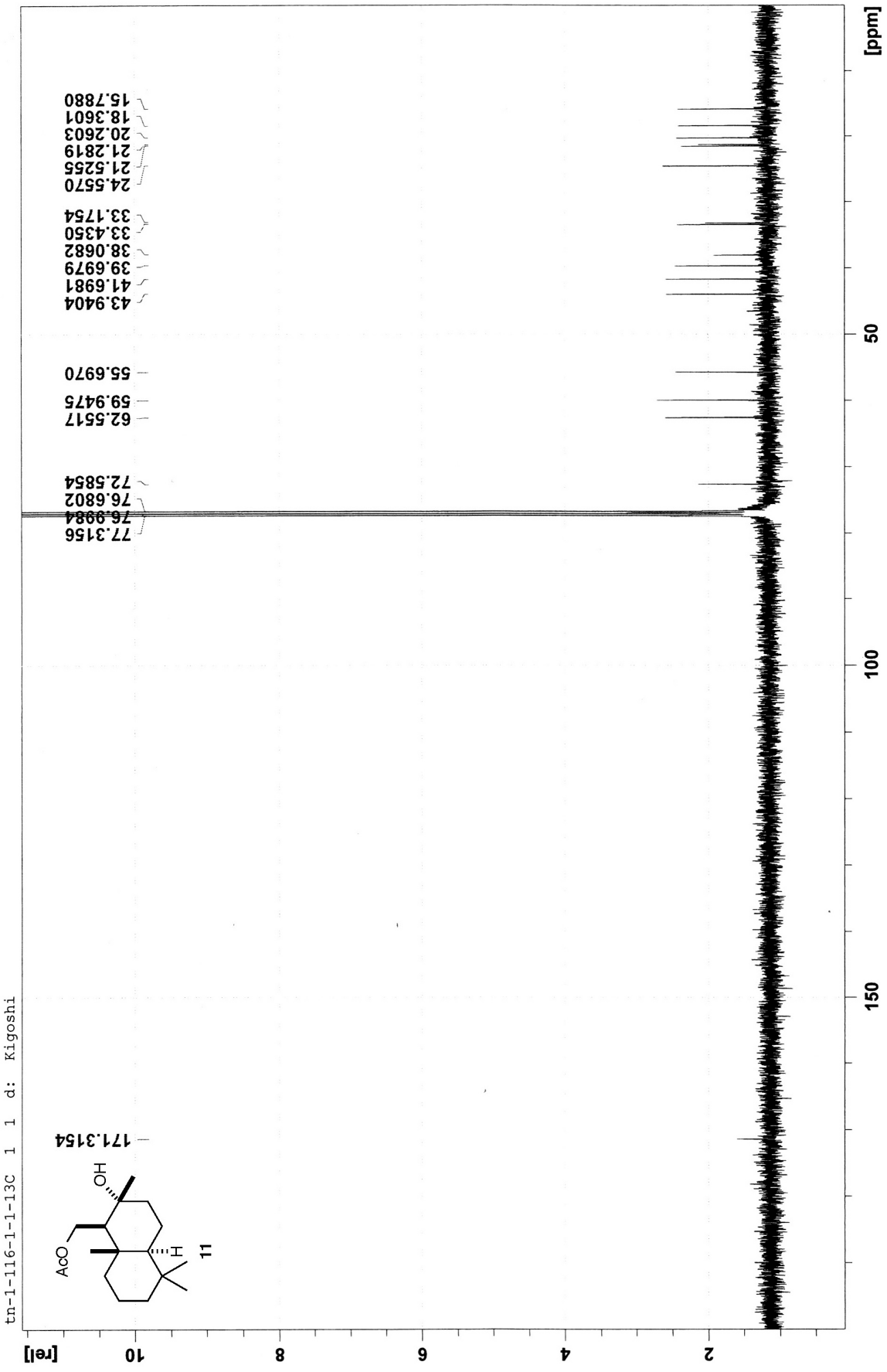
N^1-(3-methylbut-2-en-1-yl)-N^3-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)propane-1,3-diamine [**26** (n = 3)]. Yellow solid (10.8 mg, 91% yield): R_f = 0.42 ($CHCl_3$–MeOH 4 : 1); $[\alpha]_D^{24}$ –10.7 (*c* 0.88, $CHCl_3$); IR ($CHCl_3$) 3393, 3040, 2964, 2763, 2690, 1456, 1240, 1167 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.59 (m, 1H), 5.34 (m, 1H), 3.68 (d, *J* = 7.2 Hz, 2H), 3.28–3.05 (m, 6H), 2.30–1.41 (m, 9H), 1.84 (s, 6H), 1.80 (s, 3H), 1,37–1.17 (m, 3H), 0.92 (s, 3H), 0.89 (s, 3H), 0.83 (s, 3H). Signals due to two proton (NH) were not observed; ^{13}C NMR (100 MHz, CD_3OD) δ 144.4, 131.6, 126.2, 114.9, 53.7, 50.9, 48.2, 47.3, 46.5, 45.0, 43.0, 40.0, 37.7, 33.9, 33.5, 26.0, 24.7, 24.0, 22.1, 21.9, 19.6, 18.4, 14.0; HRMS (ESI) *m/z* 347.3423, calcd for $C_{23}H_{43}N_2$ $[M+H]^+$ 347.3421.

N^1-(3-methylbut-2-en-1-yl)-N^6-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)hexane-1,6-diamine [**27** (n = 6)]. Yellow oil (5.0 mg, 95% yield): R_f = 0.57 ($CHCl_3$–MeOH 4 : 1); $[\alpha]_D^{24}$ –7.6 (*c* 0.41, $CHCl_3$); IR ($CHCl_3$) 3409, 2964, 2861, 2774, 1592, 1457, 1385, 1241, 984 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 5.59 (m, 1H), 5.31 (m, 1H), 3.63 (d, *J* = 6.4 Hz, 2H), 3.21–2.93 (m, 6H), 2.20–1.42 (m, 15H), 1.83 (s, 3H), 1.81 (s, 3H), 1.78 (s, 3H), 1,32–1.15 (m, 3H), 0.92 (s, 3H), 0.89 (s, 3H), 0.82 (s, 3H). Signals due to two proton (NH) were not observed; ^{13}C NMR (150 MHz, CD_3OD) δ 144.1, 131.6, 126.2, 115.2, 53.8, 51.0, 50.3, 48.0, 47.9, 46.4, 43.1, 40.1, 37.7, 33.9, 33.5, 27.2, 27.1, 26.7, 26.6, 26.0, 24.7, 22.1, 21.8, 19.7, 18.4, 14.1; HRMS (ESI) *m/z* 389.3902, calcd for $C_{26}H_{49}N_2$ $[M+H]^+$ 389.3890.

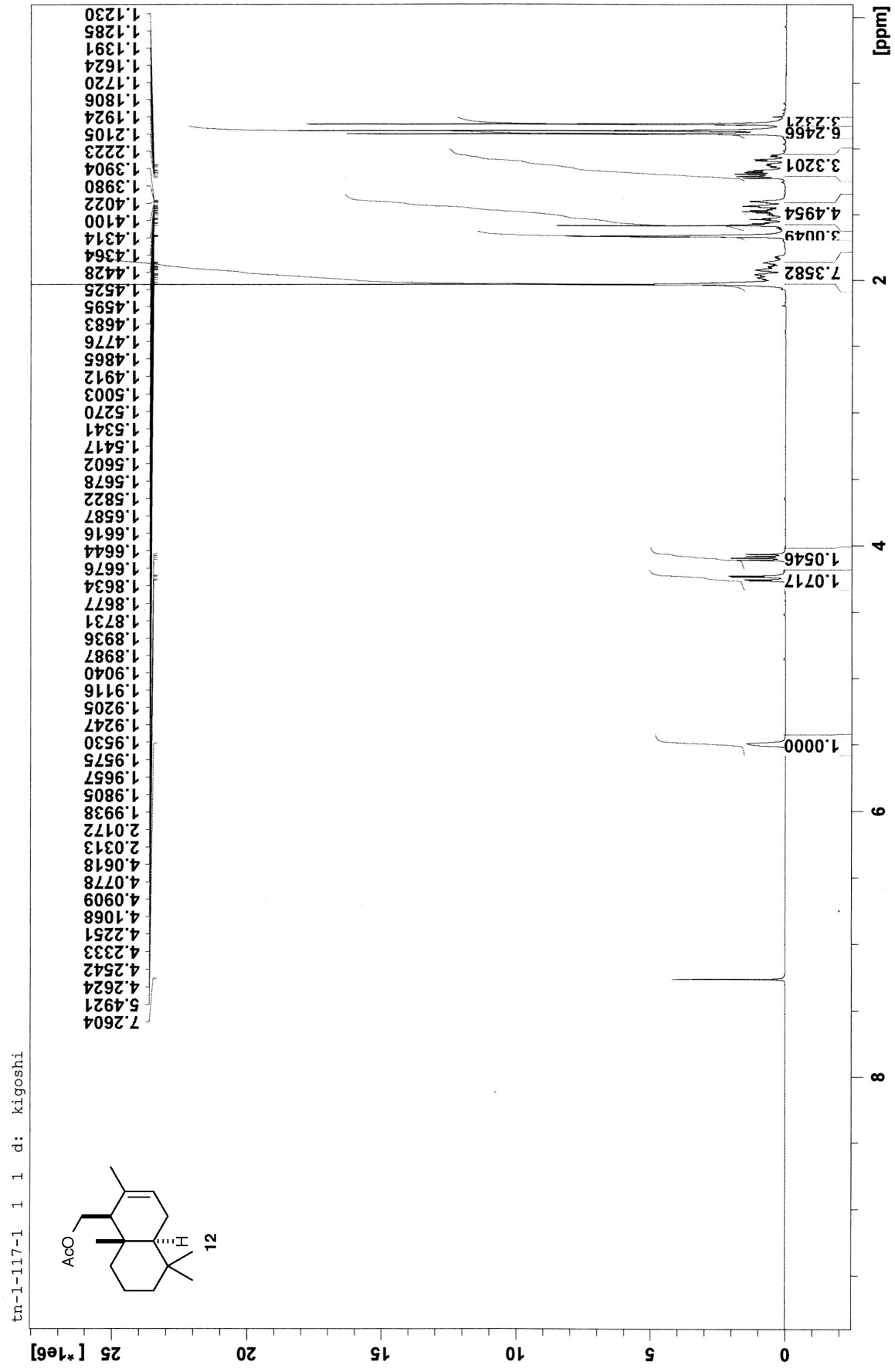
N^1-(3-methylbut-2-en-1-yl)-N^8-(((1*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl)octane-1,8-diamine [**28** (n = 8)]. Yellow solid (8.0 mg, 87% yield): R_f = 0.66 ($CHCl_3$–MeOH 4 : 1); $[\alpha]_D^{24}$ –9.5 (*c* 0.68, $CHCl_3$); IR ($CHCl_3$) 3398, 2938, 2859, 2773, 1559, 1462, 1382, 1232, 987 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 5.59 (m, 1H), 5.30 (m, 1H), 3.63 (d, *J* = 7.4 Hz, 2H), 3.21–2.93 (m, 6H), 2.14–2.04 (m, 2H), 1.97–1.35 (m, 17H), 1.83 (s, 3H), 1.80 (s, 3H), 1.78 (s, 3H), 1,32–1.16 (m, 3H), 0.92 (s, 3H), 0.89 (s, 3H), 0.82 (s, 3H). Signals due to two proton (NH) were not observed; ^{13}C NMR (150 MHz, CD_3OD) δ 144.0, 131.7, 126.2, 115.2, 53.8, 51.0, 50.3, 48.0, 47.7, 46.4, 43.1, 40.0, 37.7, 33.9, 33.5, 29.9 (2C), 27.5, 27.4, 27.3, 26.8, 26.0, 24.7, 22.1, 21.7, 19.7, 18.2, 14.0; HRMS (ESI) *m/z* 417.4195, calcd for $C_{28}H_{53}N_2$ $[M+H]^+$ 417.4203.



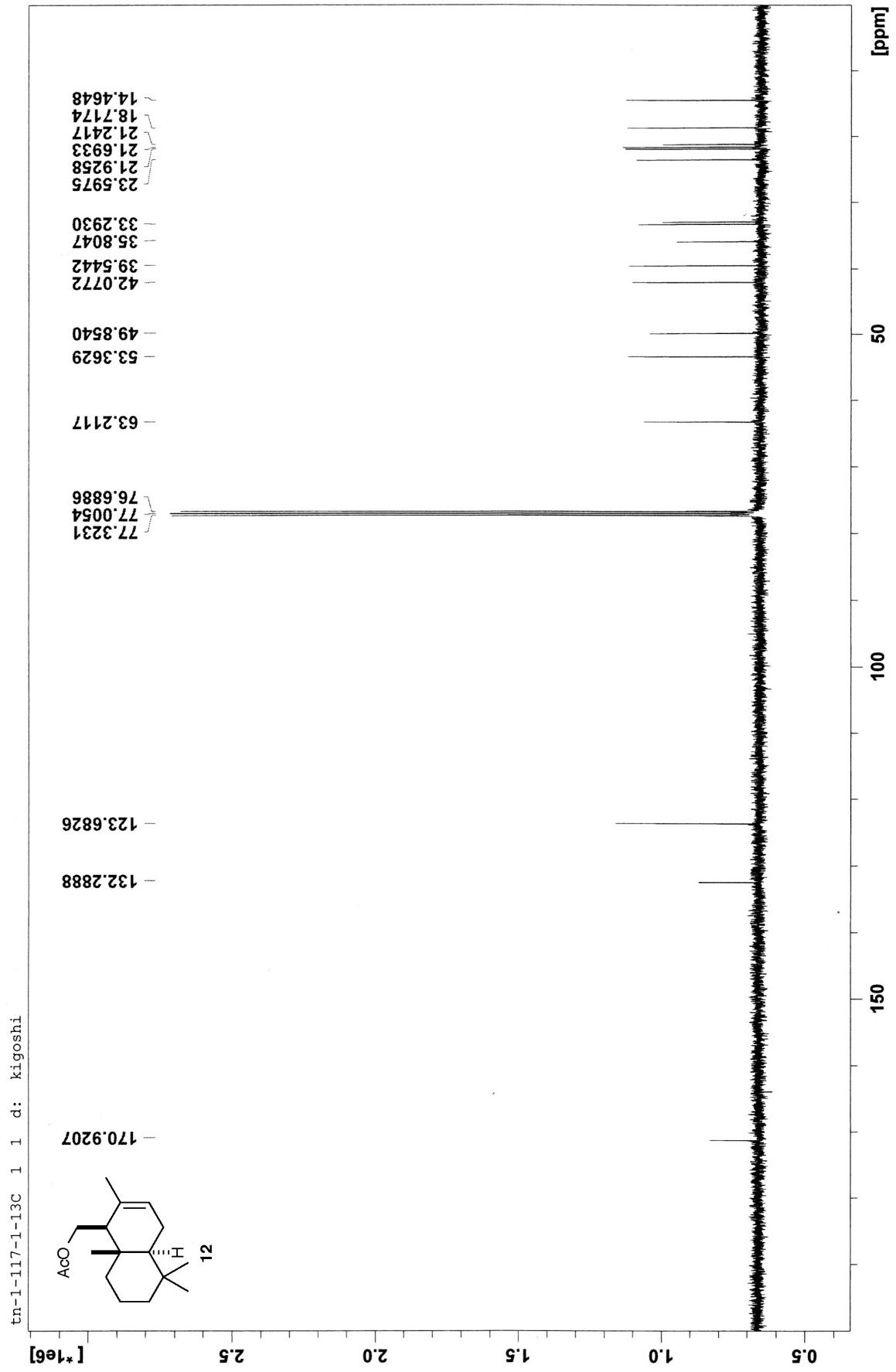
^{1}H NMR spectra of **11** (400 MHz, $CDCl_3$)



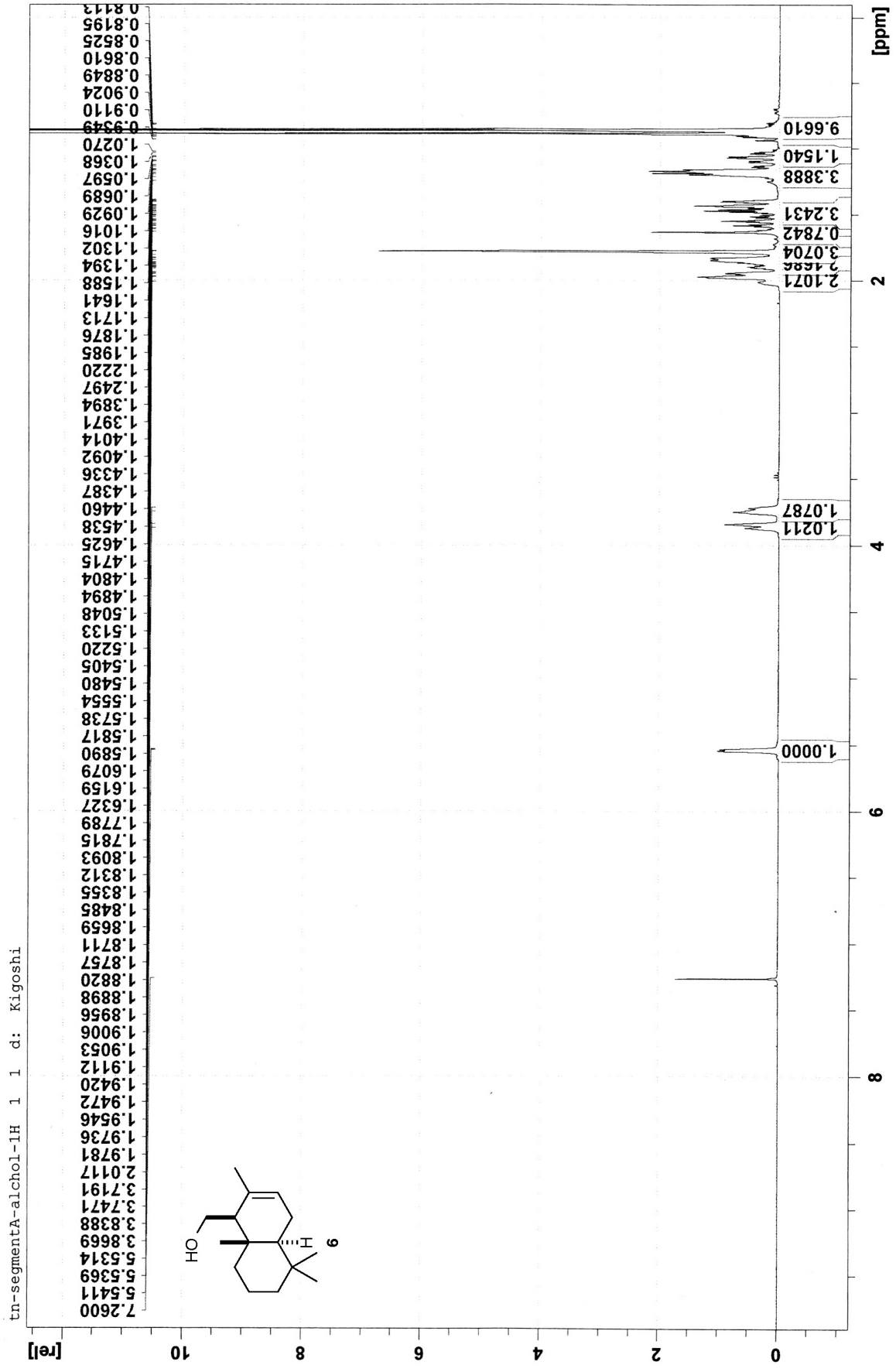
^{13}C NMR spectra of **11** (100 MHz, $CDCl_3$)



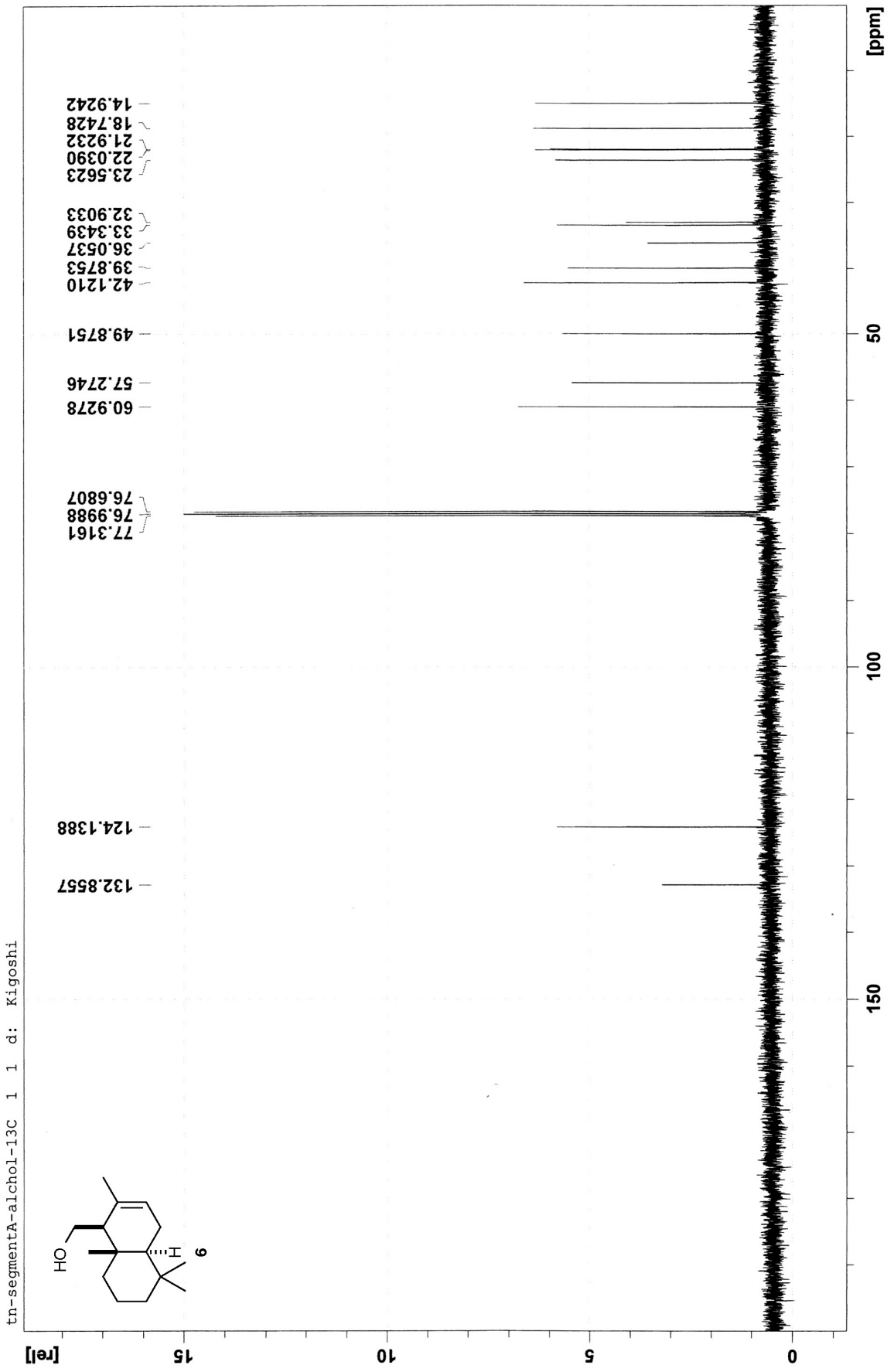
^{1}H NMR spectra of **12** (400 MHz, $CDCl_3$)



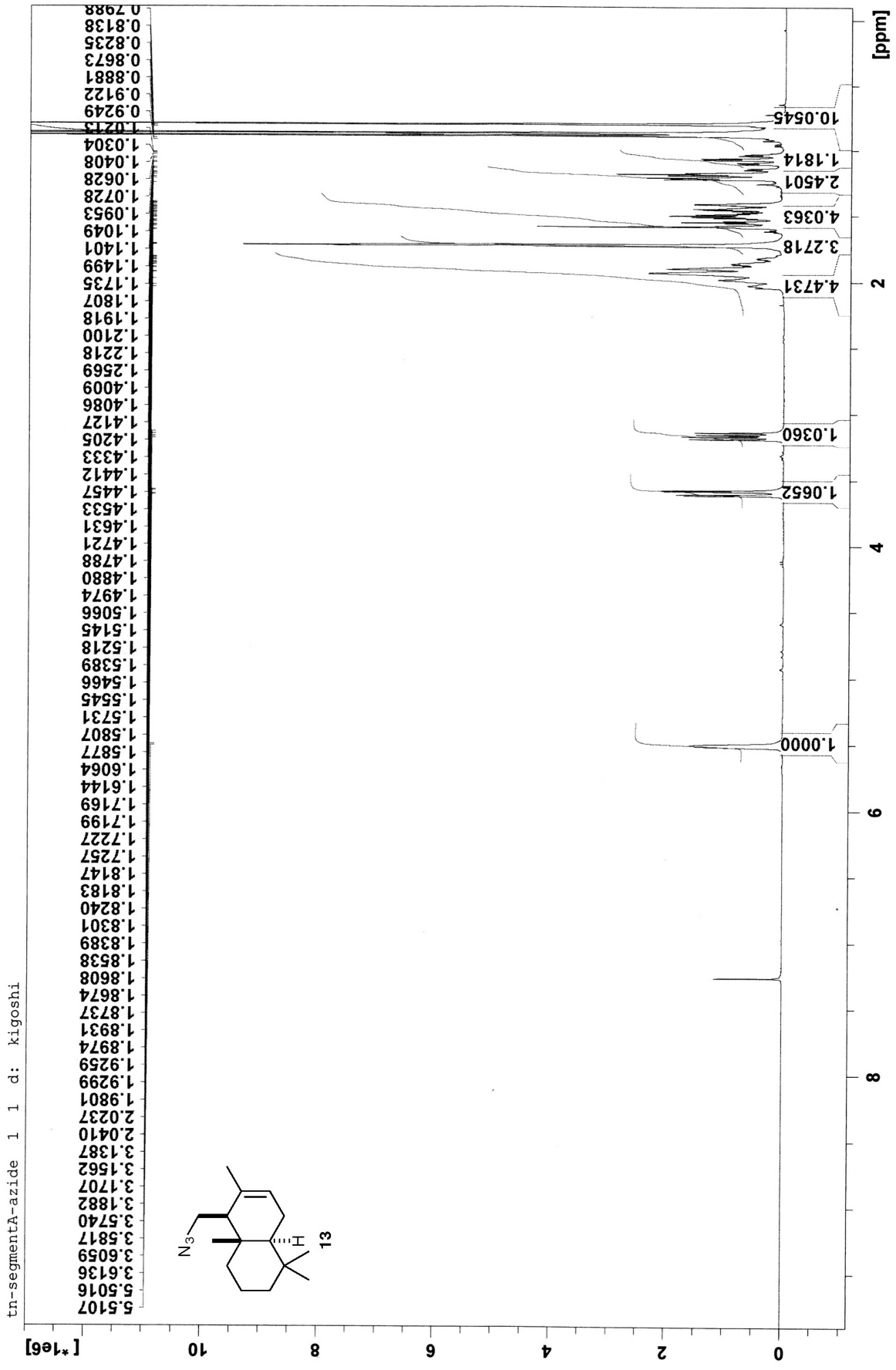
^{13}C NMR spectra of **12** (100 MHz, $CDCl_3$)



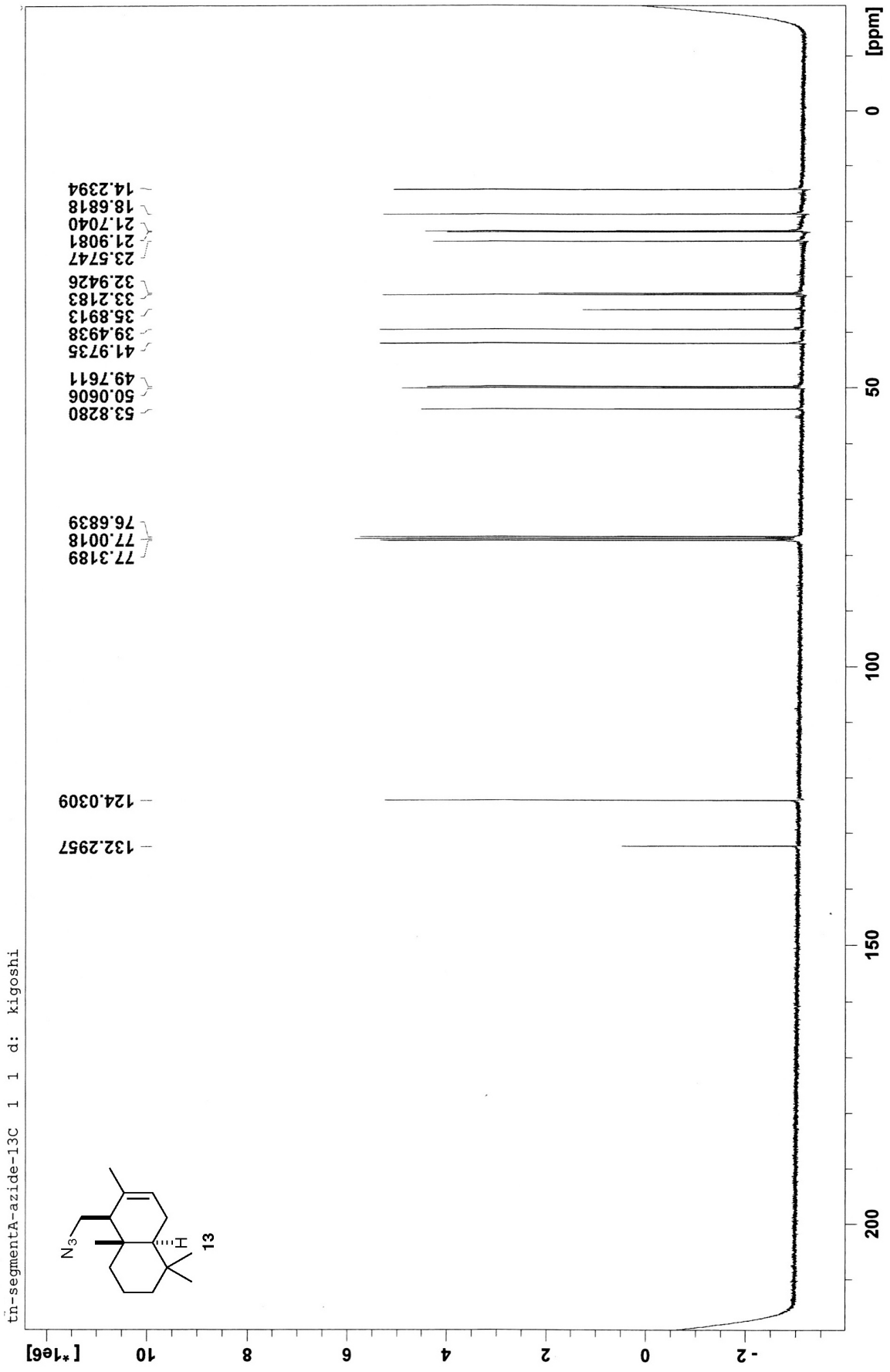
^{1}H NMR spectra of **6** (400 MHz, $CDCl_3$)



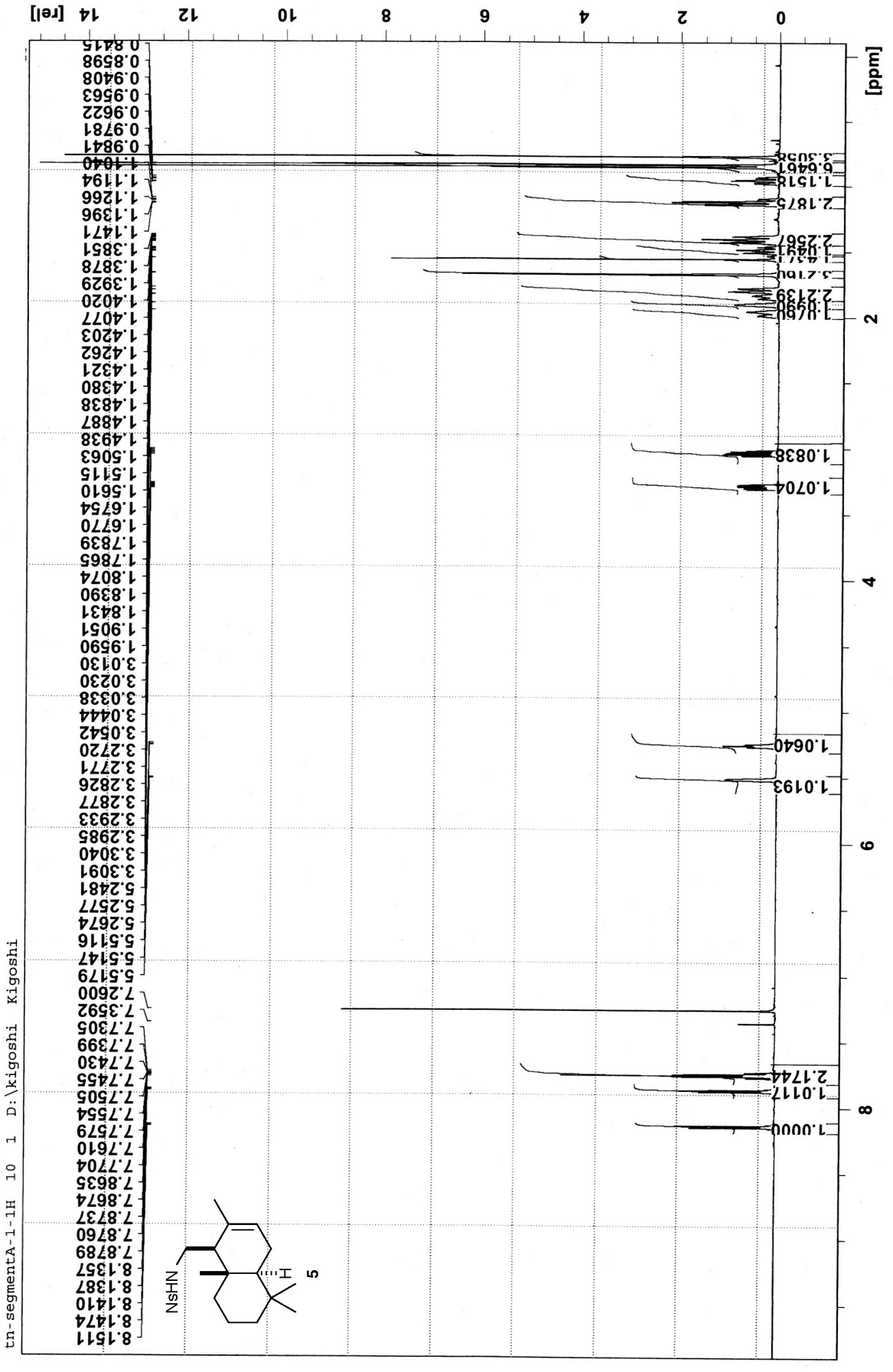
^{13}C NMR spectra of **6** (100 MHz, $CDCl_3$)



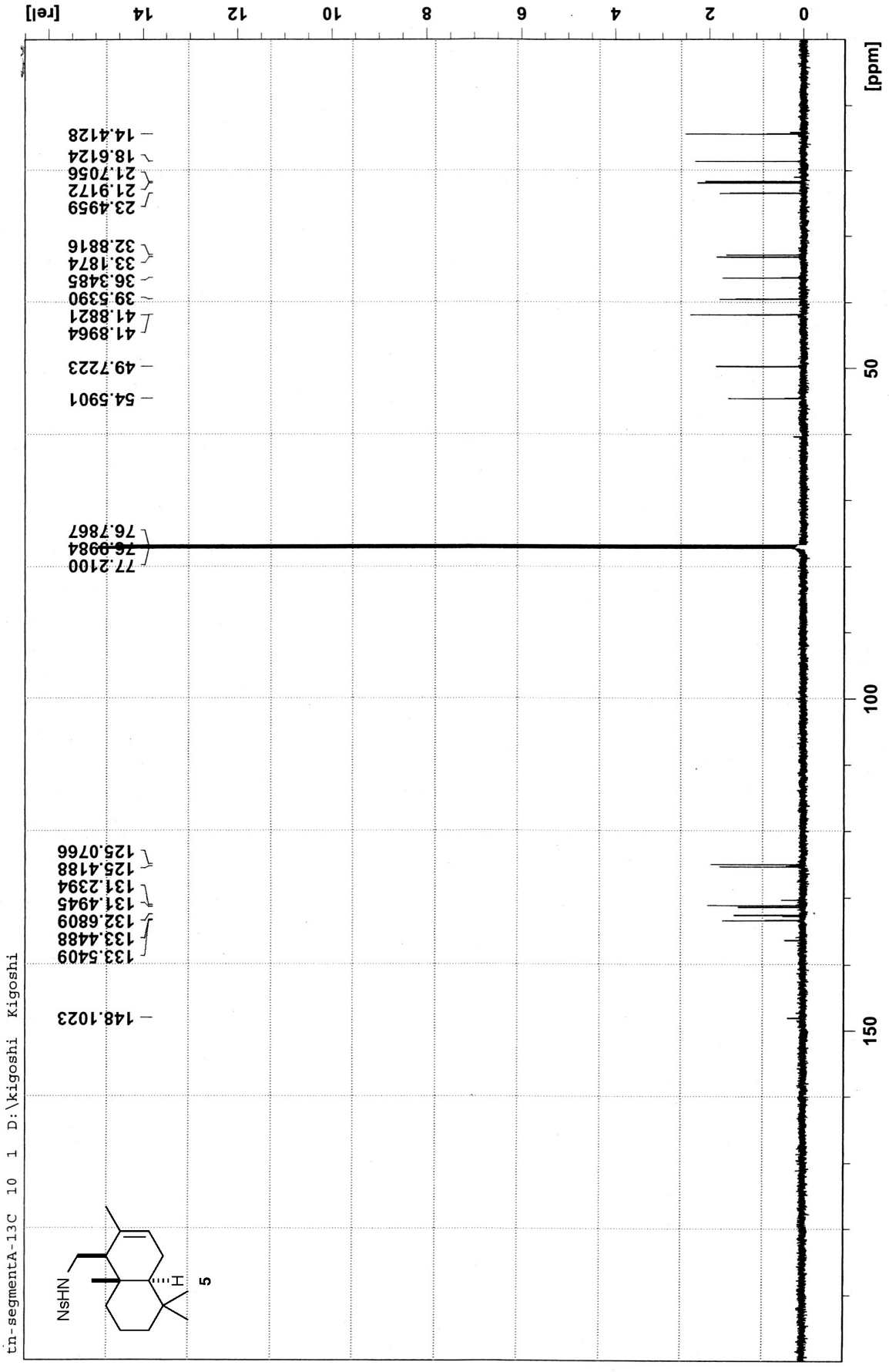
^{1}H NMR spectra of **13** (400 MHz, $CDCl_3$)



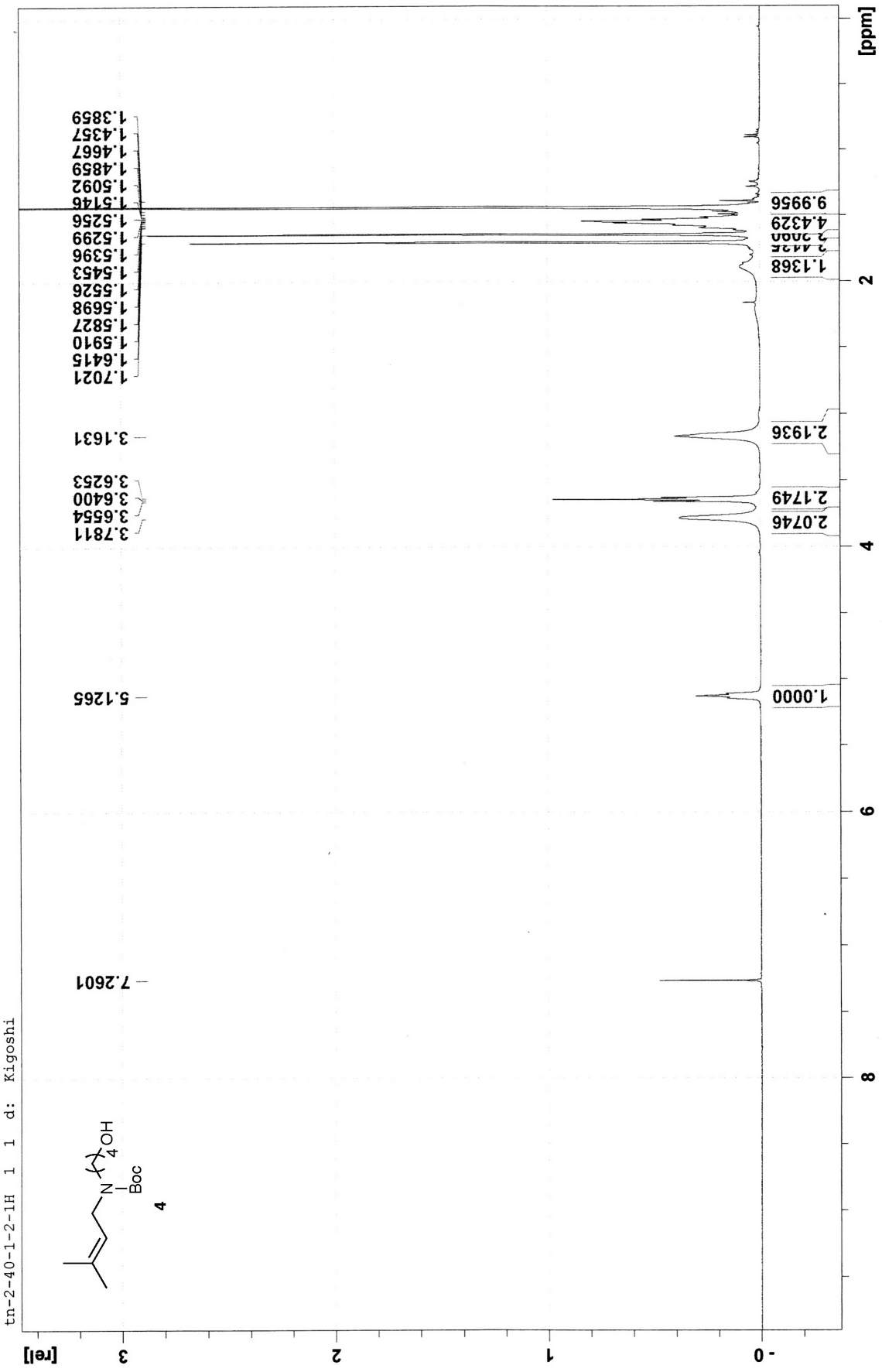
^{13}C NMR spectra of **13** (100 MHz, $CDCl_3$)



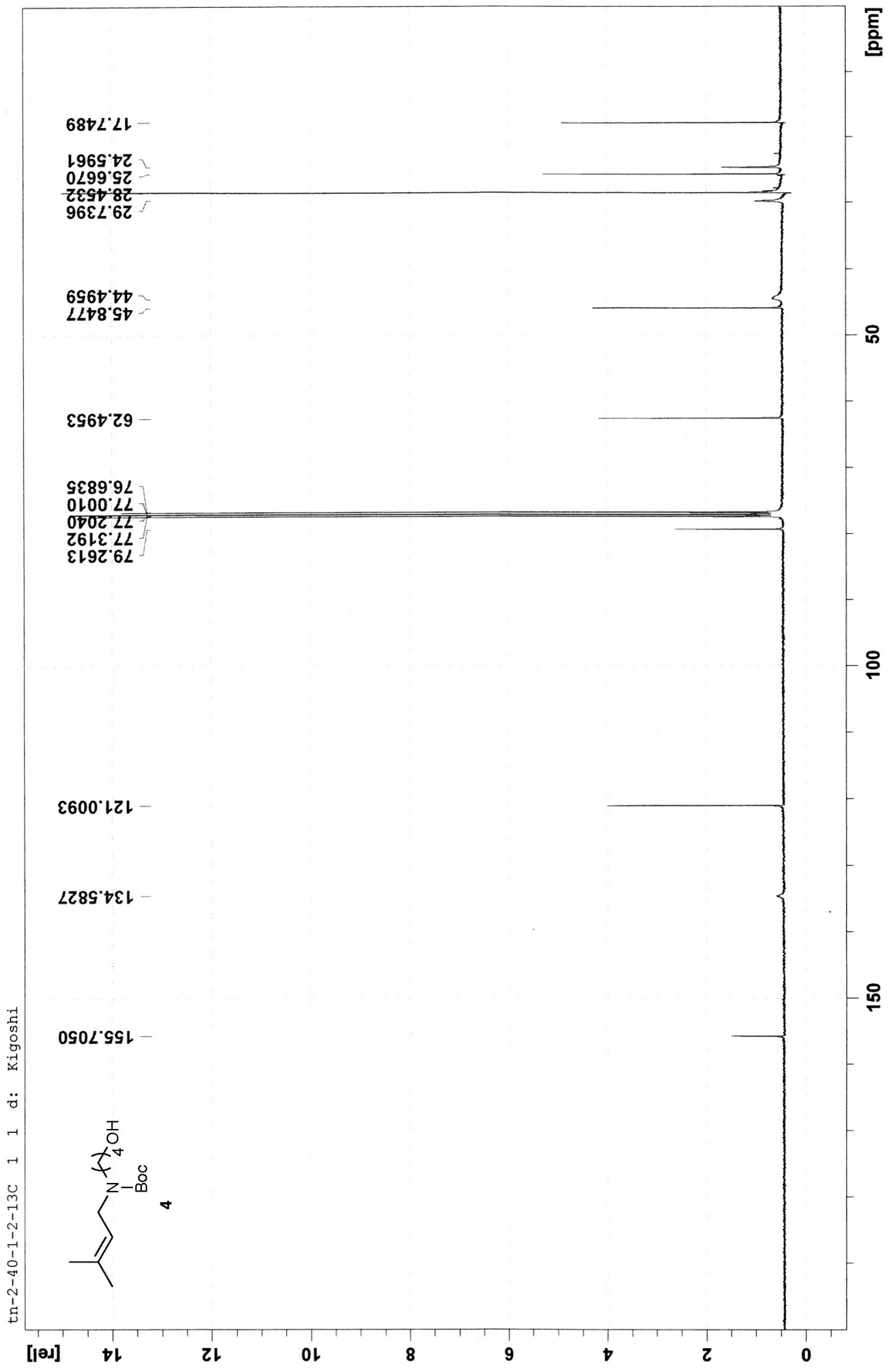
^{1}H NMR spectra of **5** (600 MHz, $CDCl_3$)



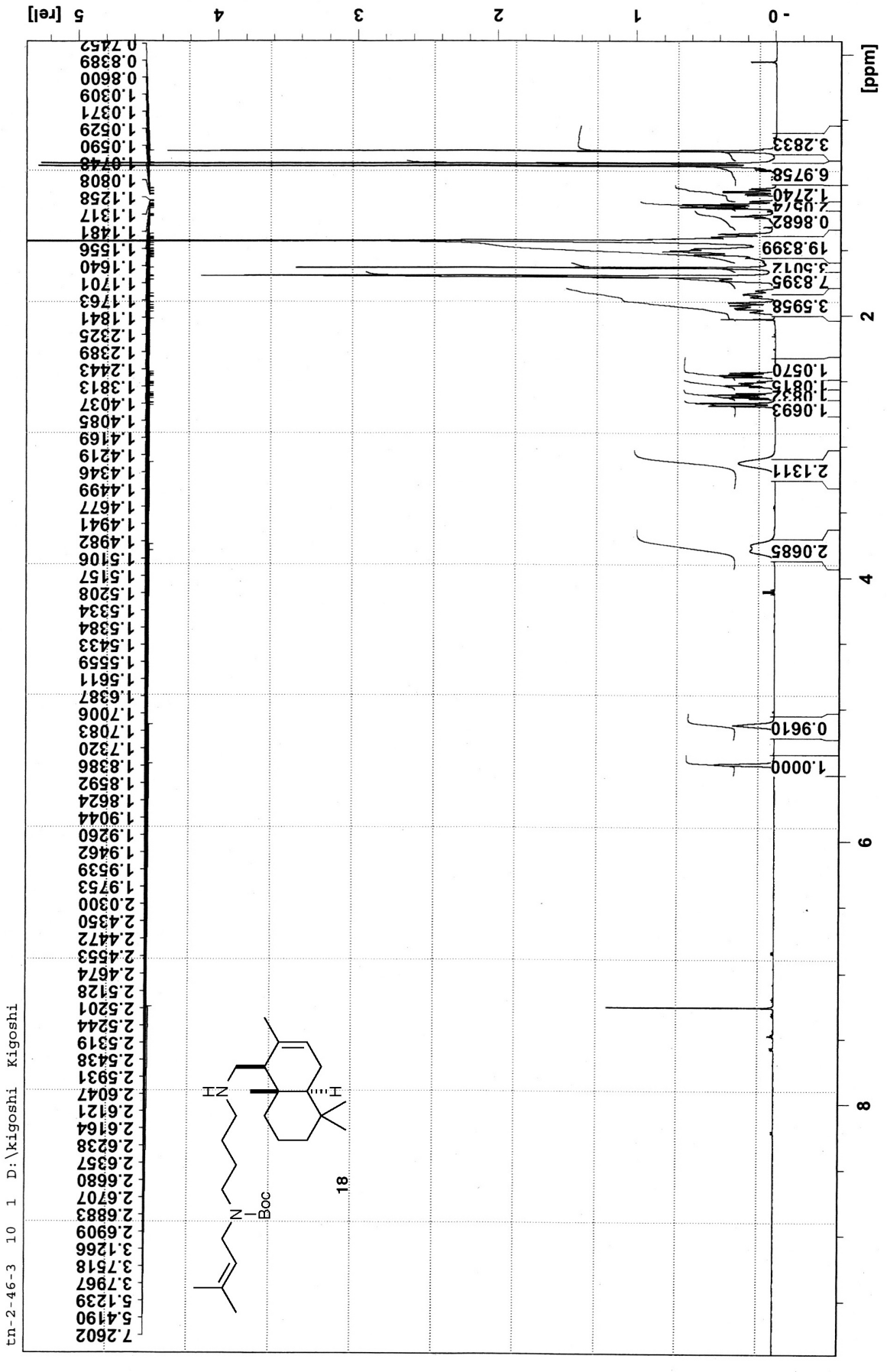
^{13}C NMR spectra of **5** (150 MHz, $CDCl_3$)



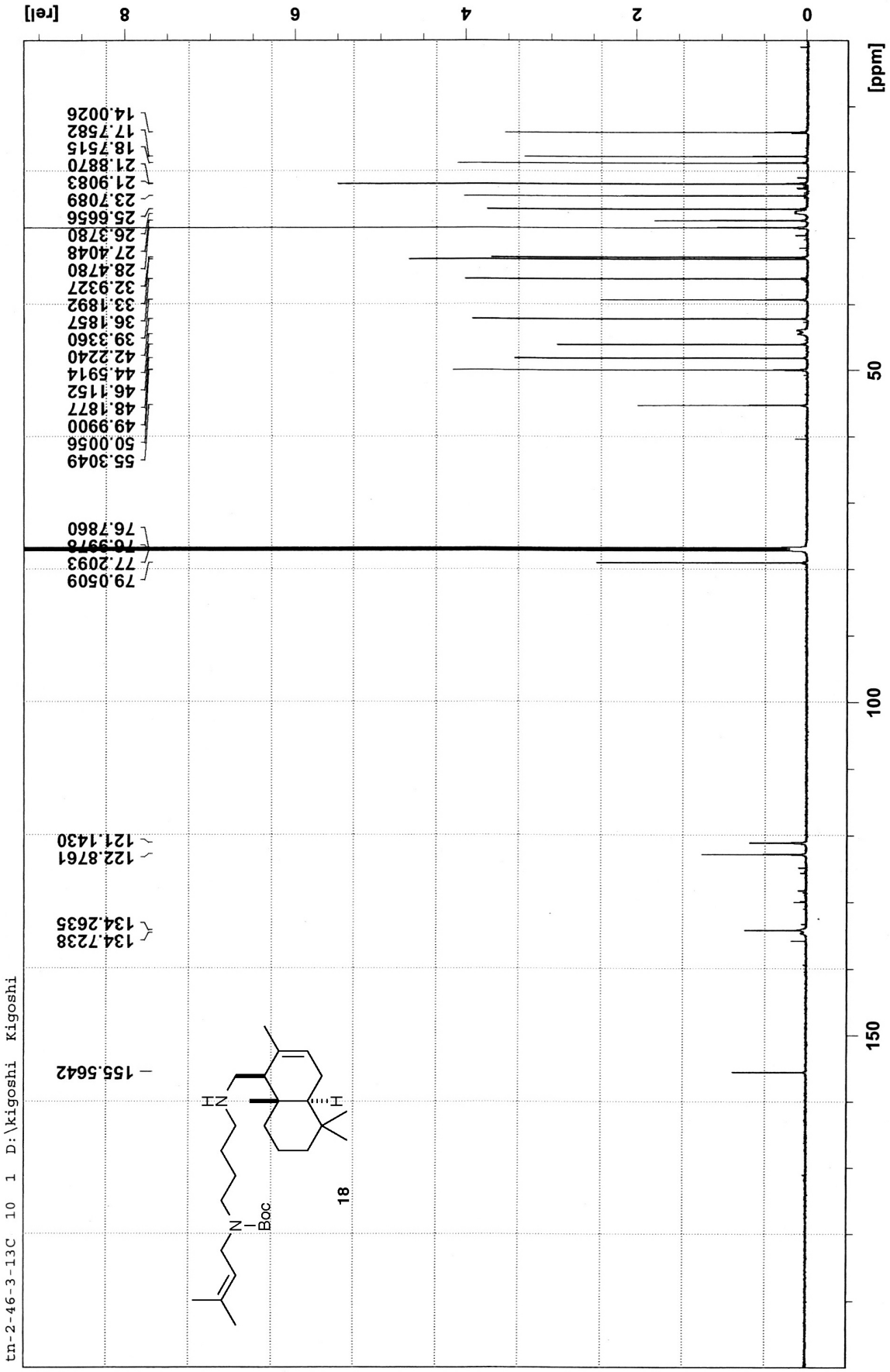
^{1}H NMR spectra of **4** (400 MHz, $CDCl_3$)



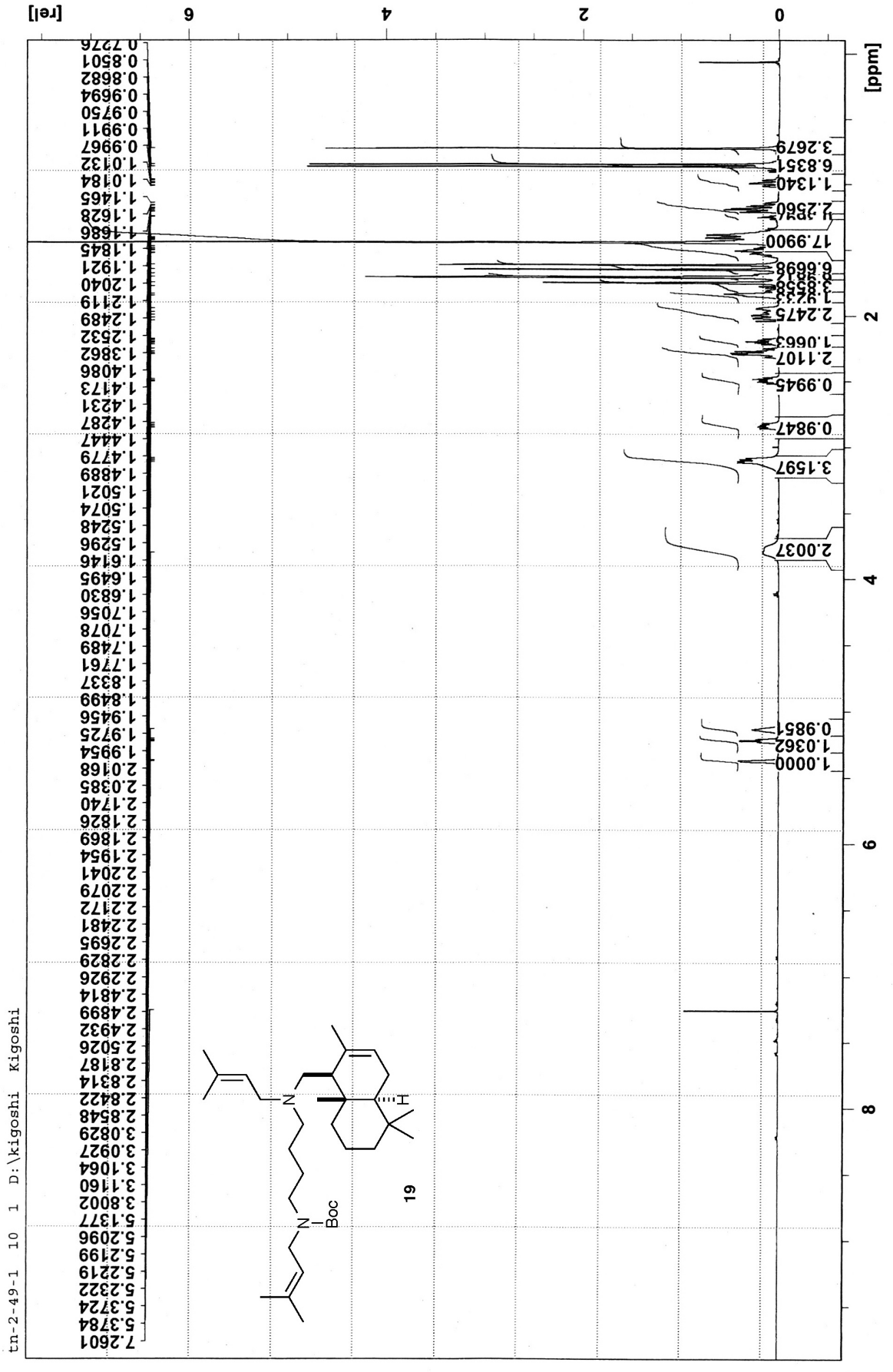
^{13}C NMR spectra of **4** (100 MHz, $CDCl_3$)



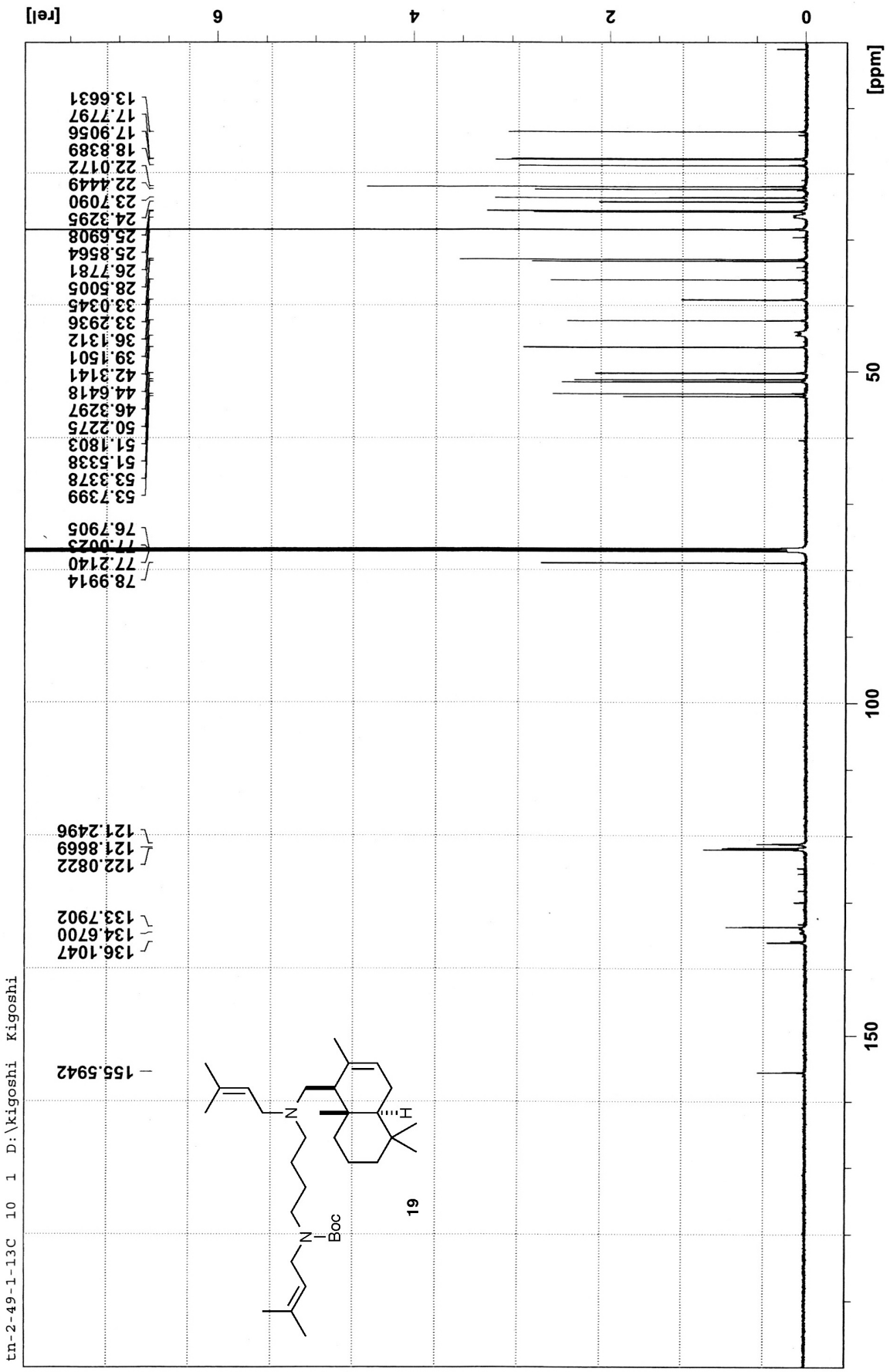
^{1}H NMR spectra of **18** (600 MHz, $CDCl_3$)



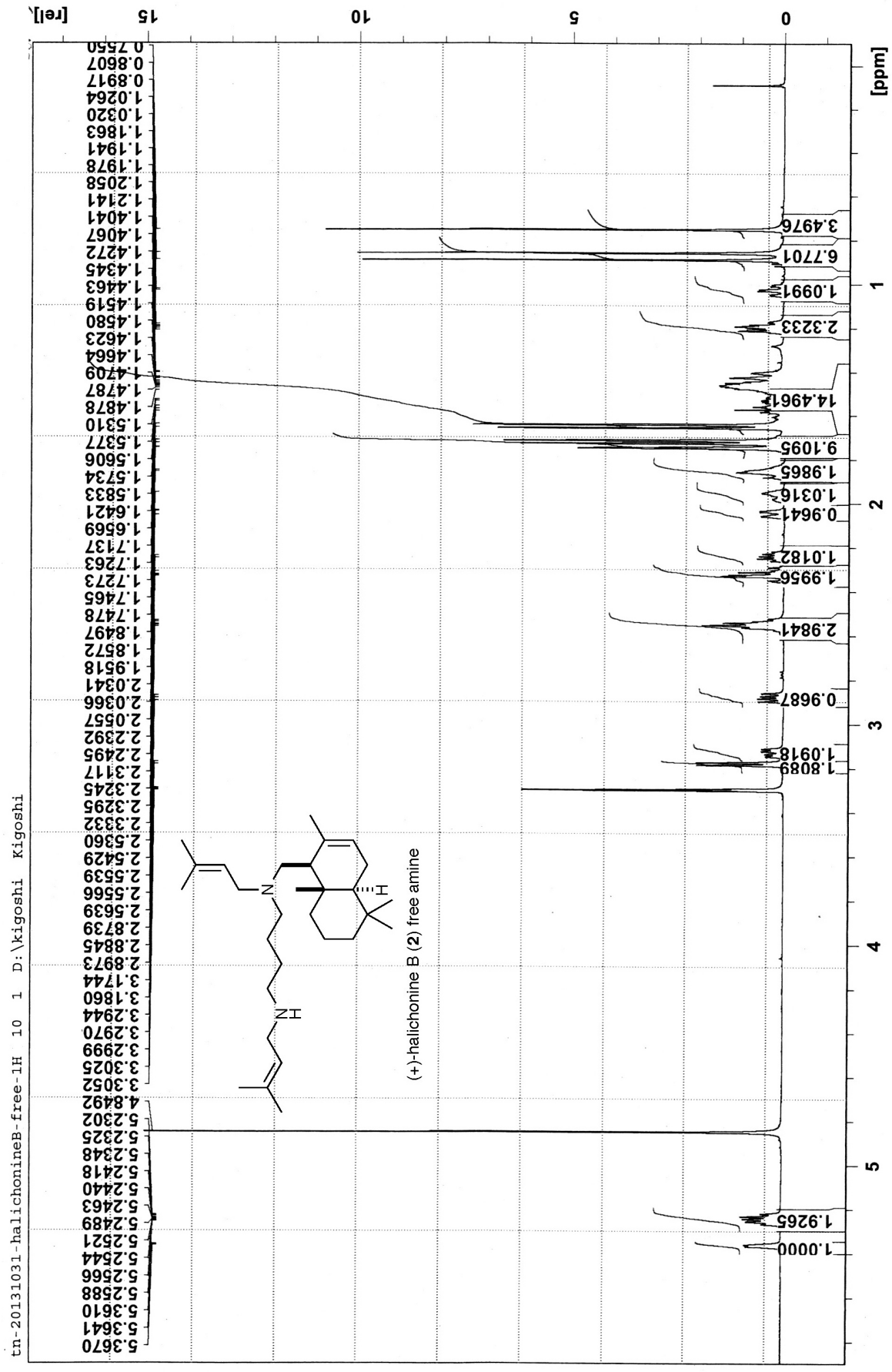
^{13}C NMR spectra of **18** (150 MHz, $CDCl_3$)



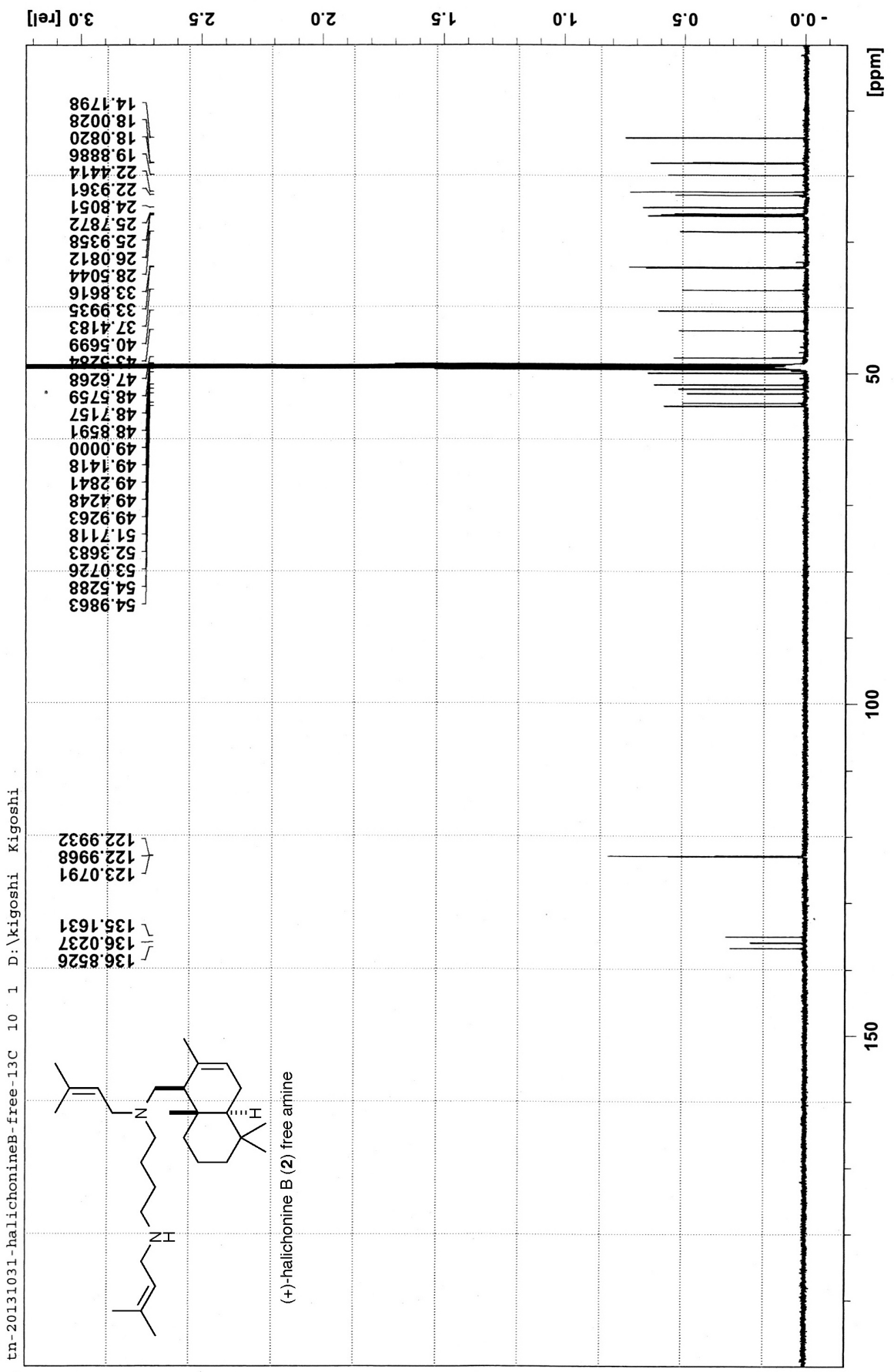
^{1}H NMR spectra of **19** (600 MHz, $CDCl_3$)



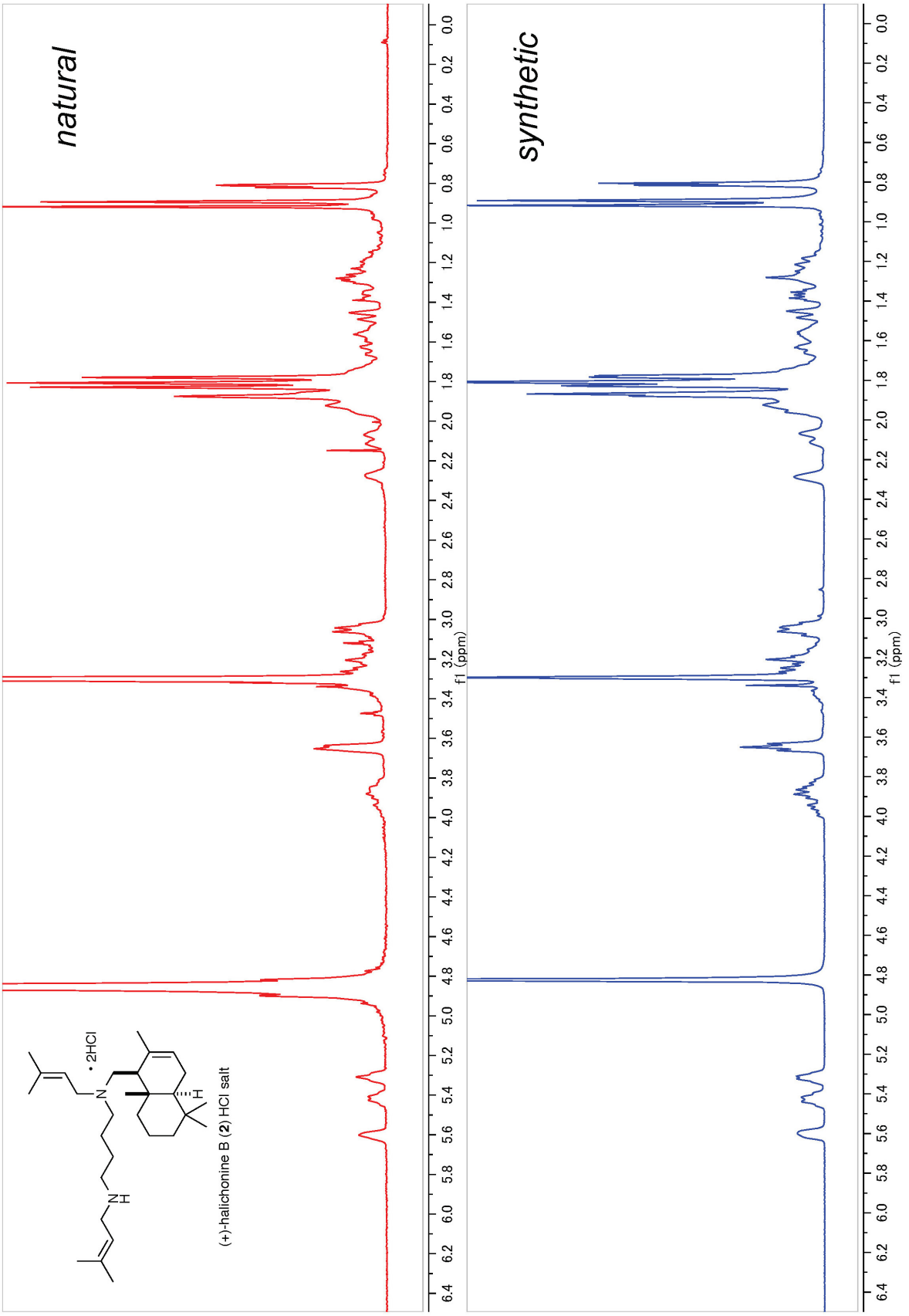
^{13}C NMR spectra of **19** (150 MHz, $CDCl_3$)



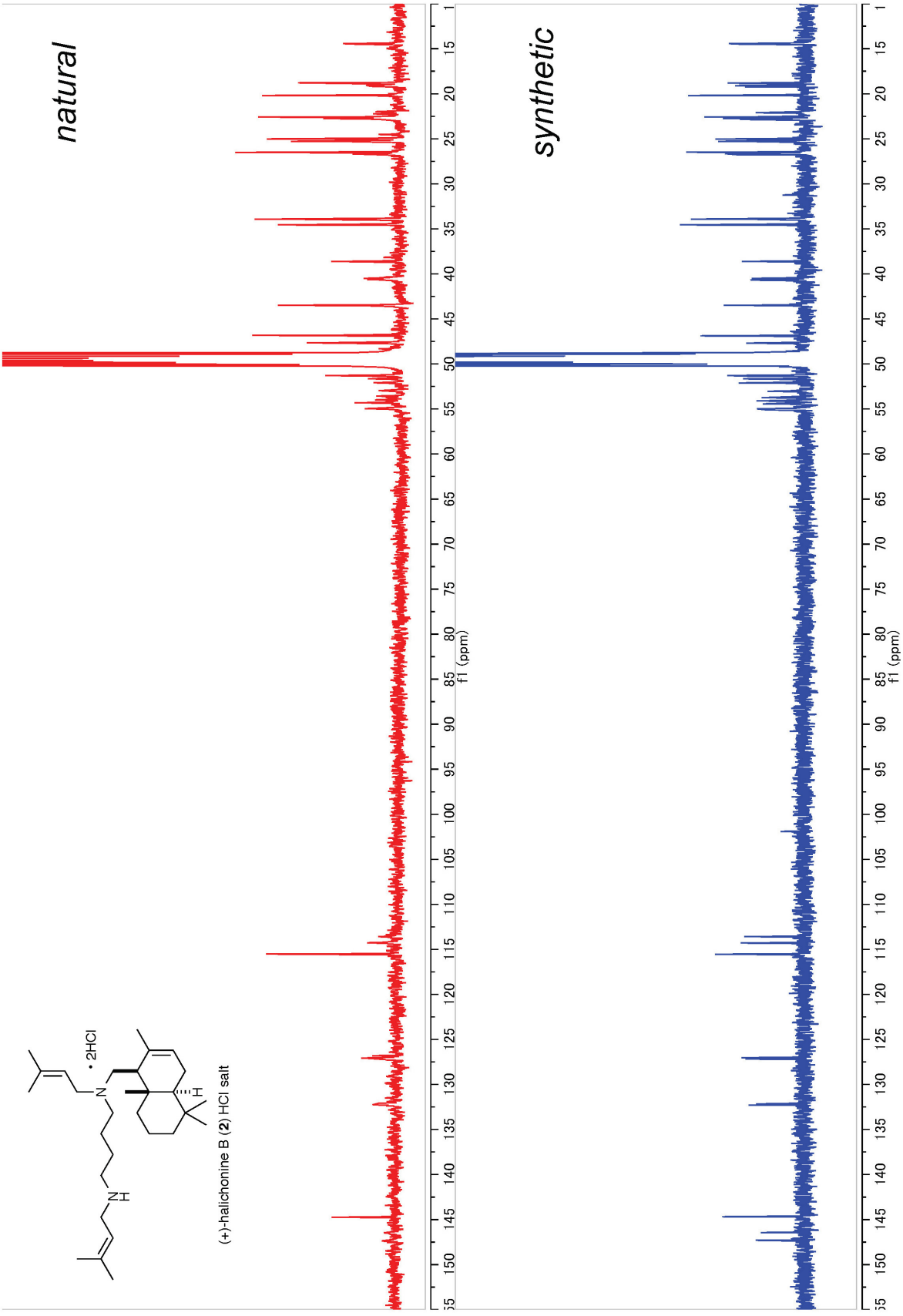
^{1}H NMR spectra of (+)-halichonine B (**2**) free amine (600 MHz, CD_3OD)



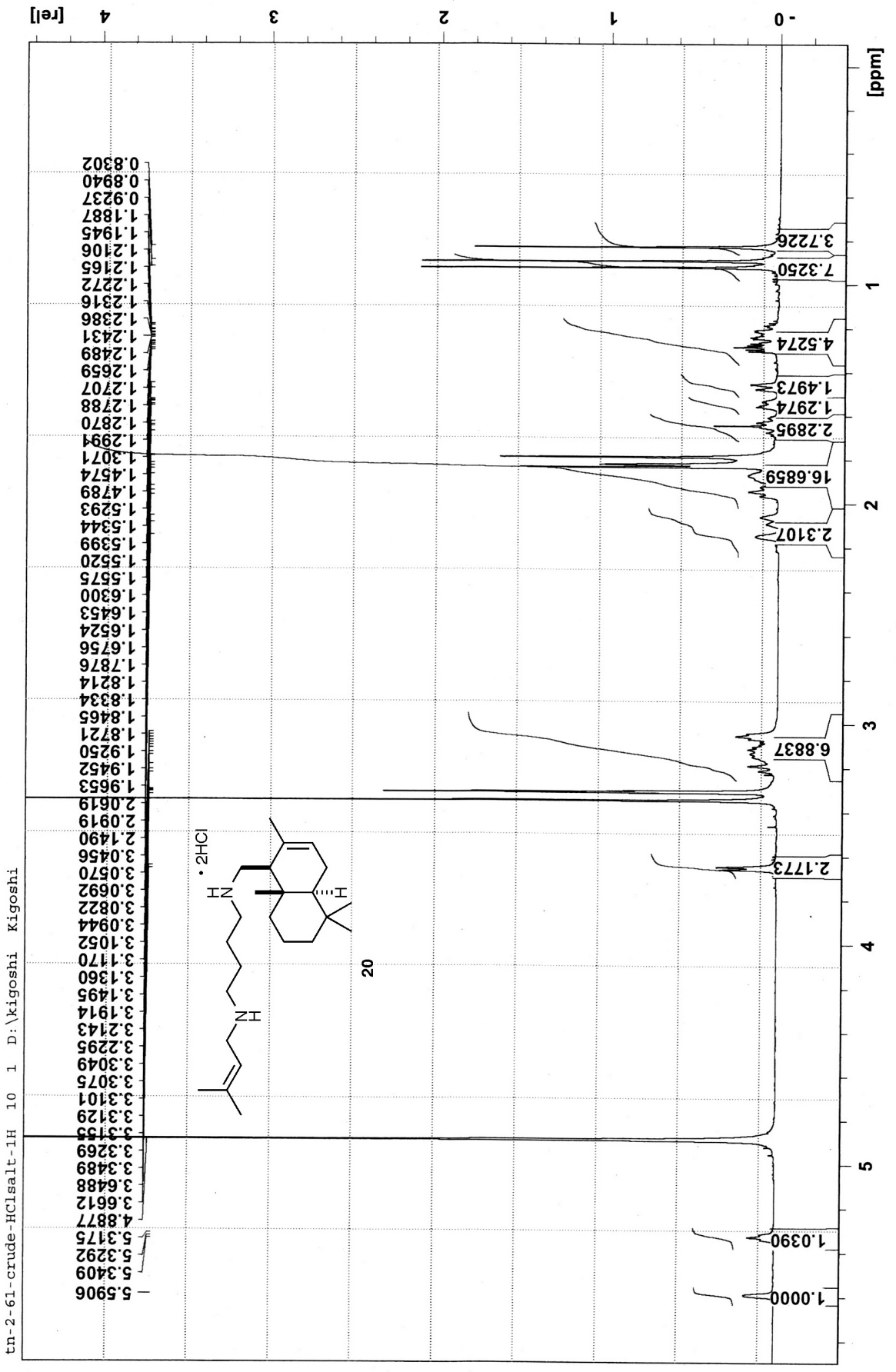
^{13}C NMR spectra of (+)-halichonine B (**2**) free amine (150 MHz, CD_3OD)



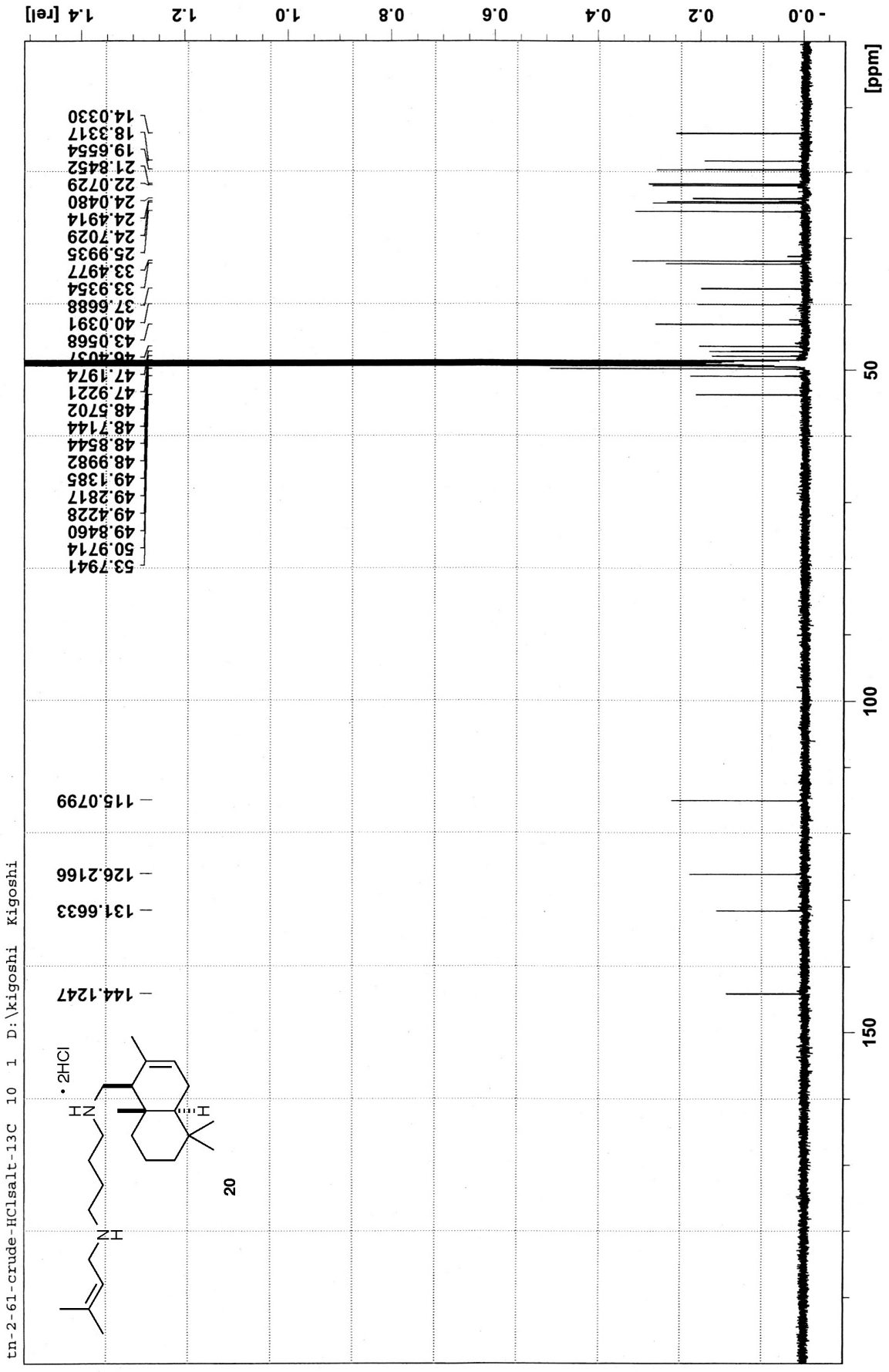
^{1}H NMR spectra of (+)-halichonine B (**2**) HCl salt (400 MHz, CD_3OD)



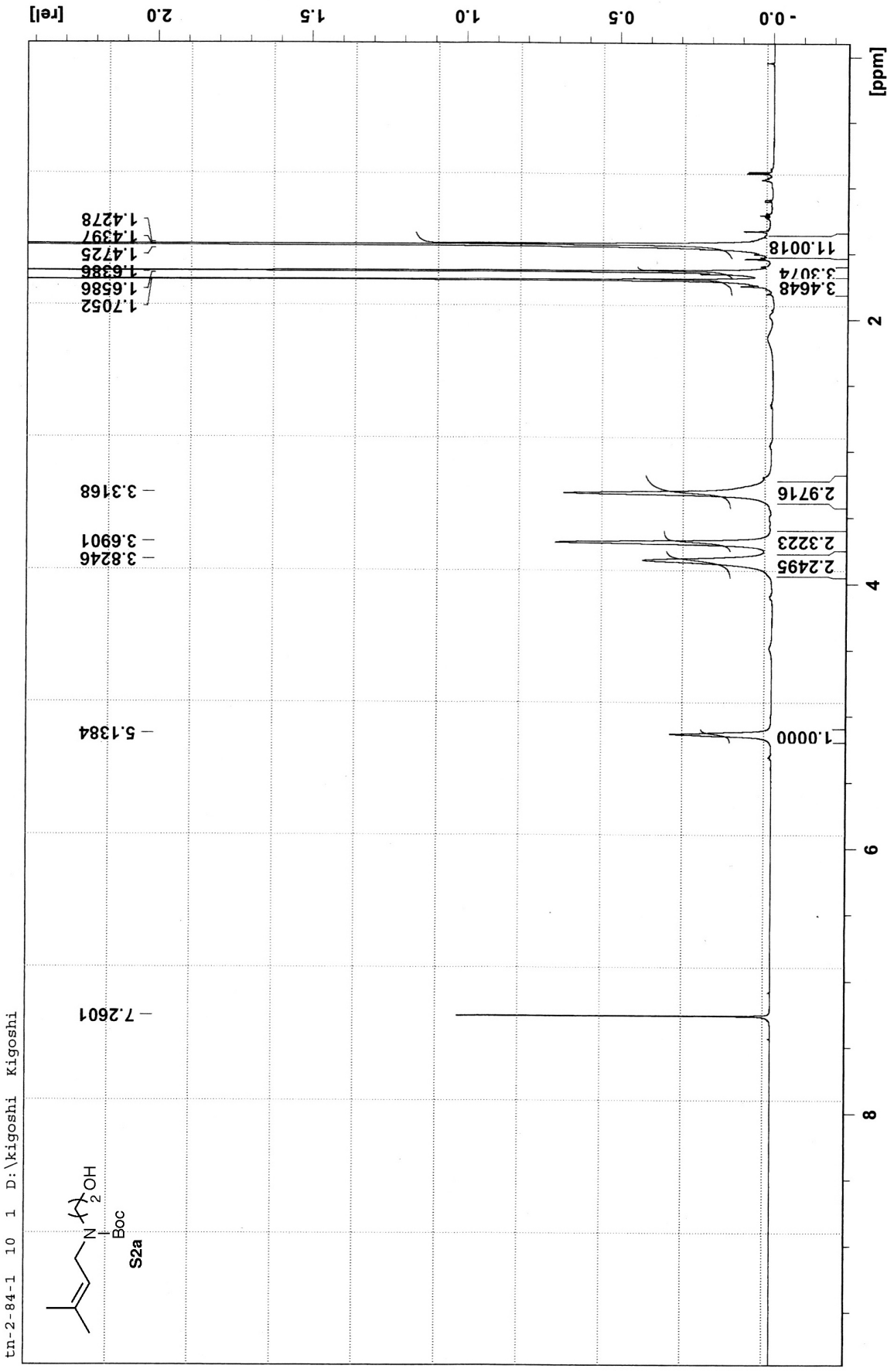
^{13}C NMR spectra of (+)-halichonine B (**2**) HCl salt (100 MHz, CD_3OD)



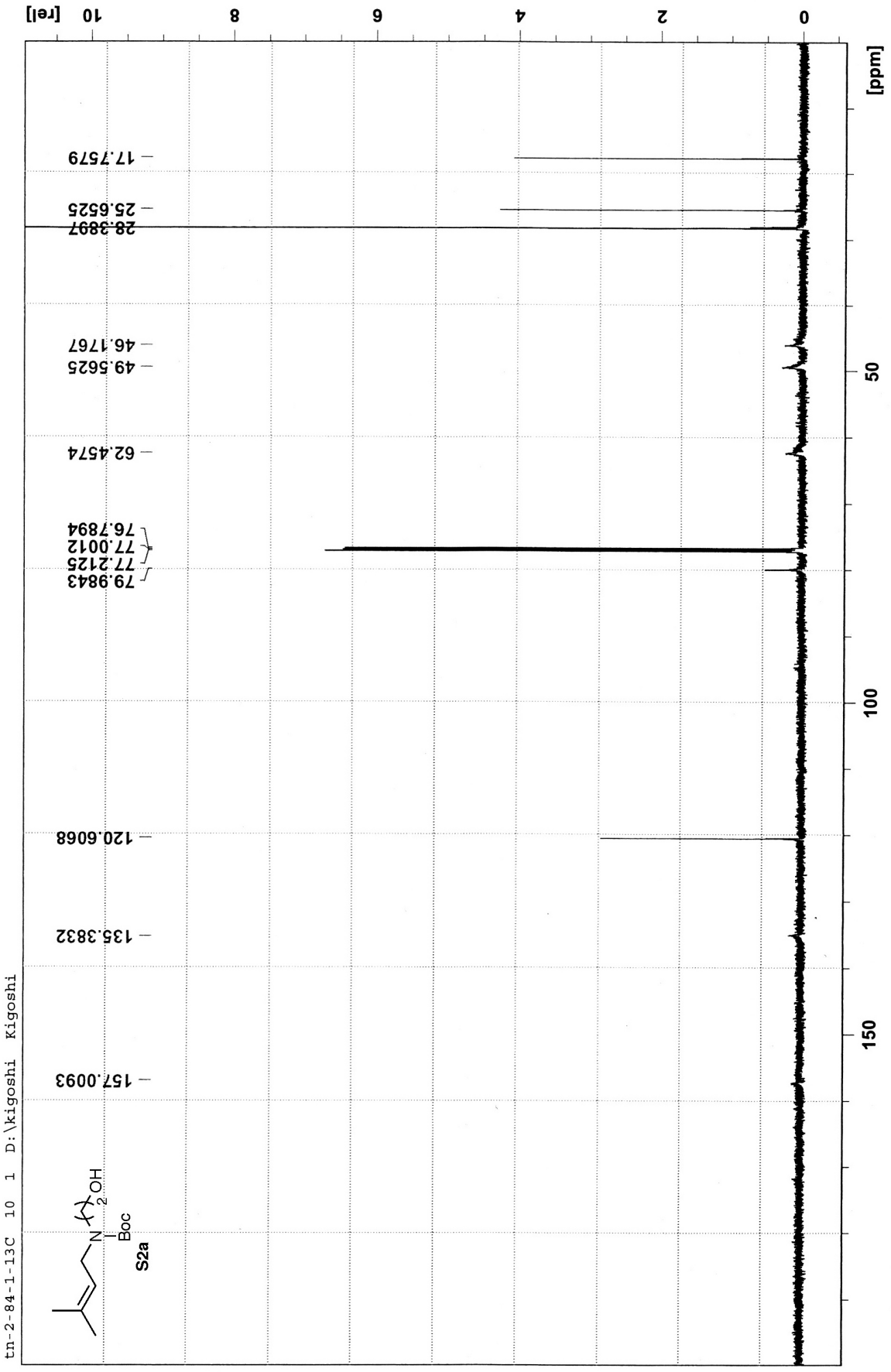
^{1}H NMR spectra of **20** (600 MHz, CD_3OD)



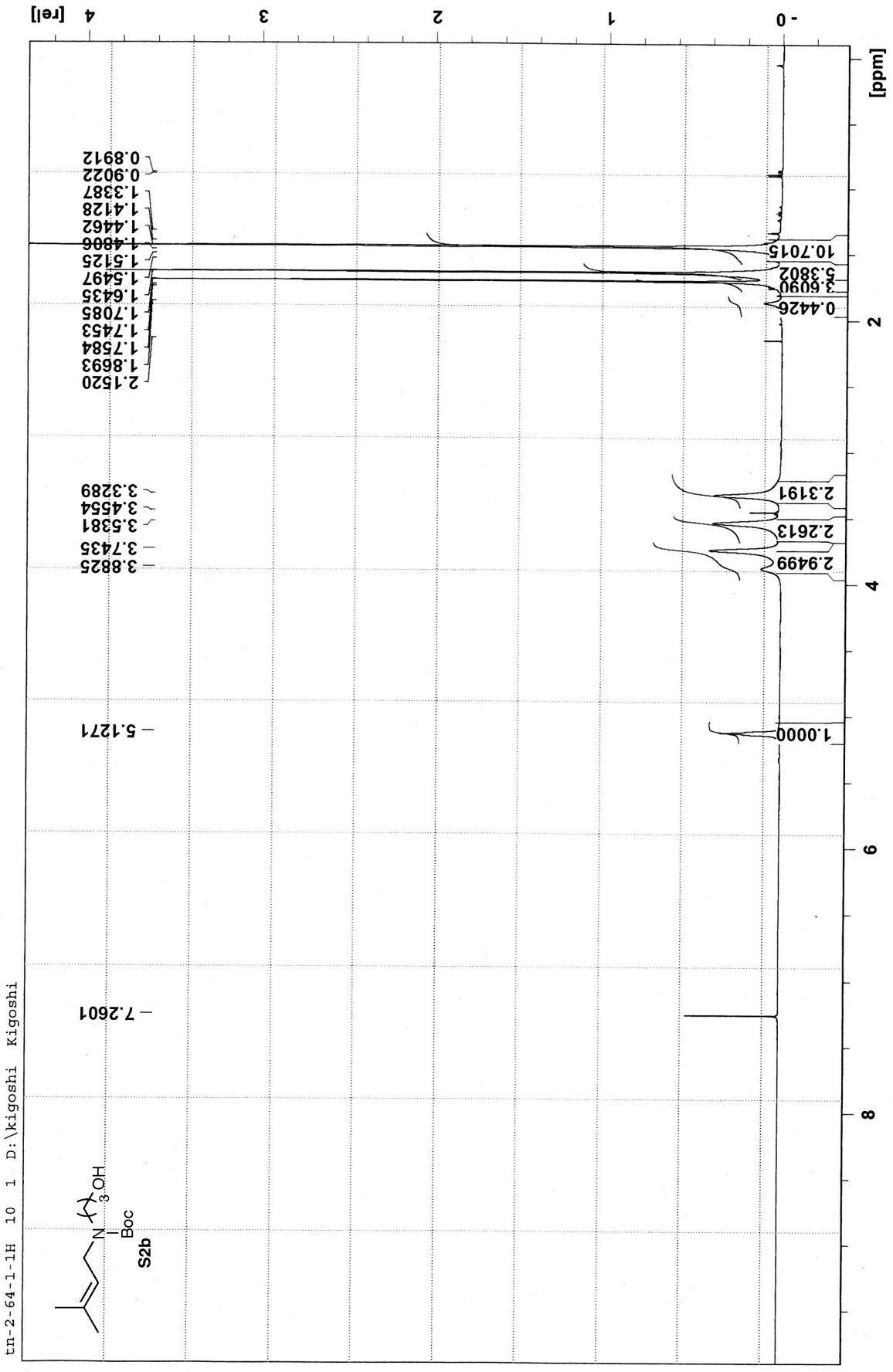
^{13}C NMR spectra of **20** (150 MHz, CD_3OD)



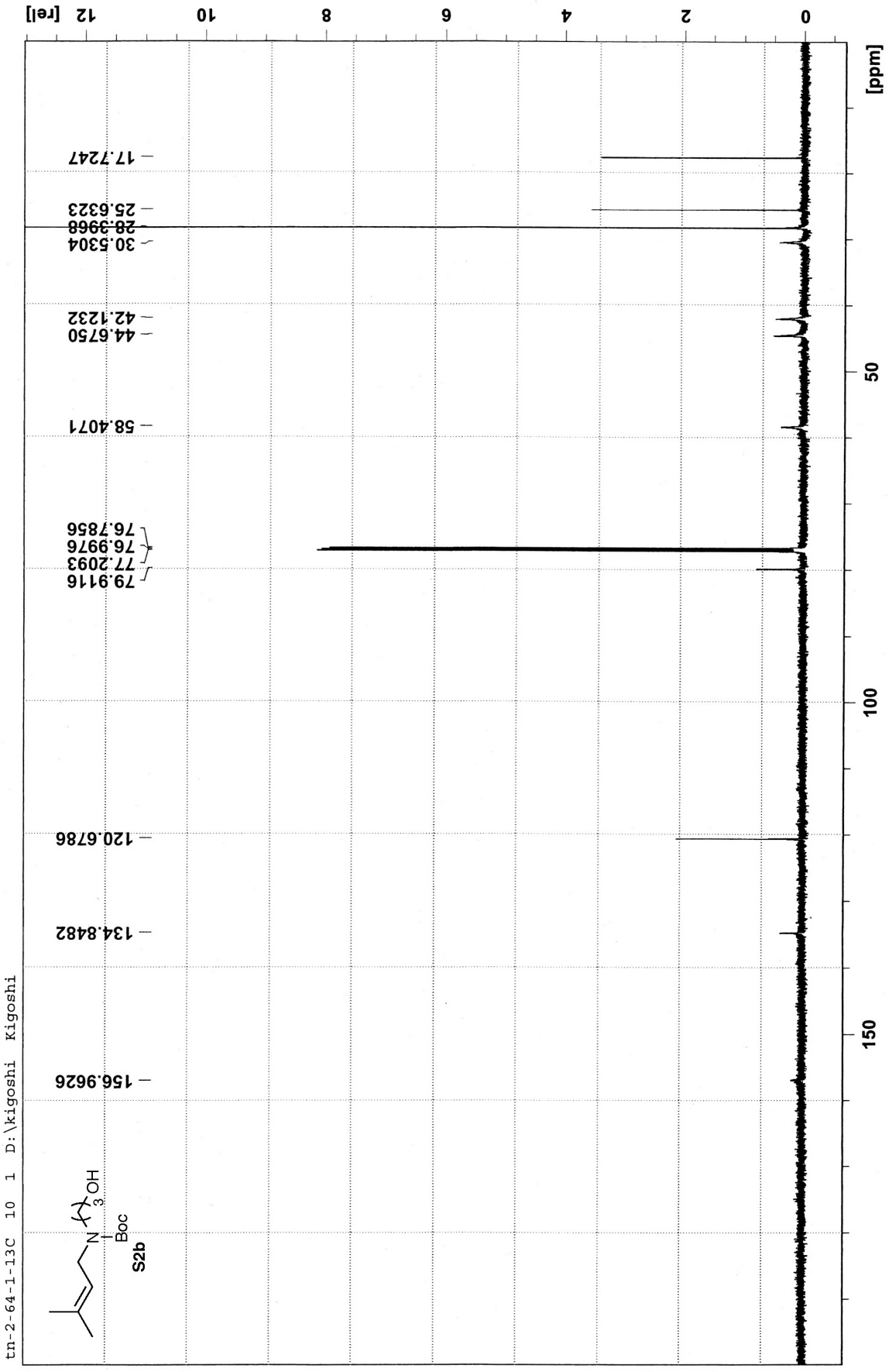
^{1}H NMR spectra of **S2a** (600 MHz, $CDCl_3$)



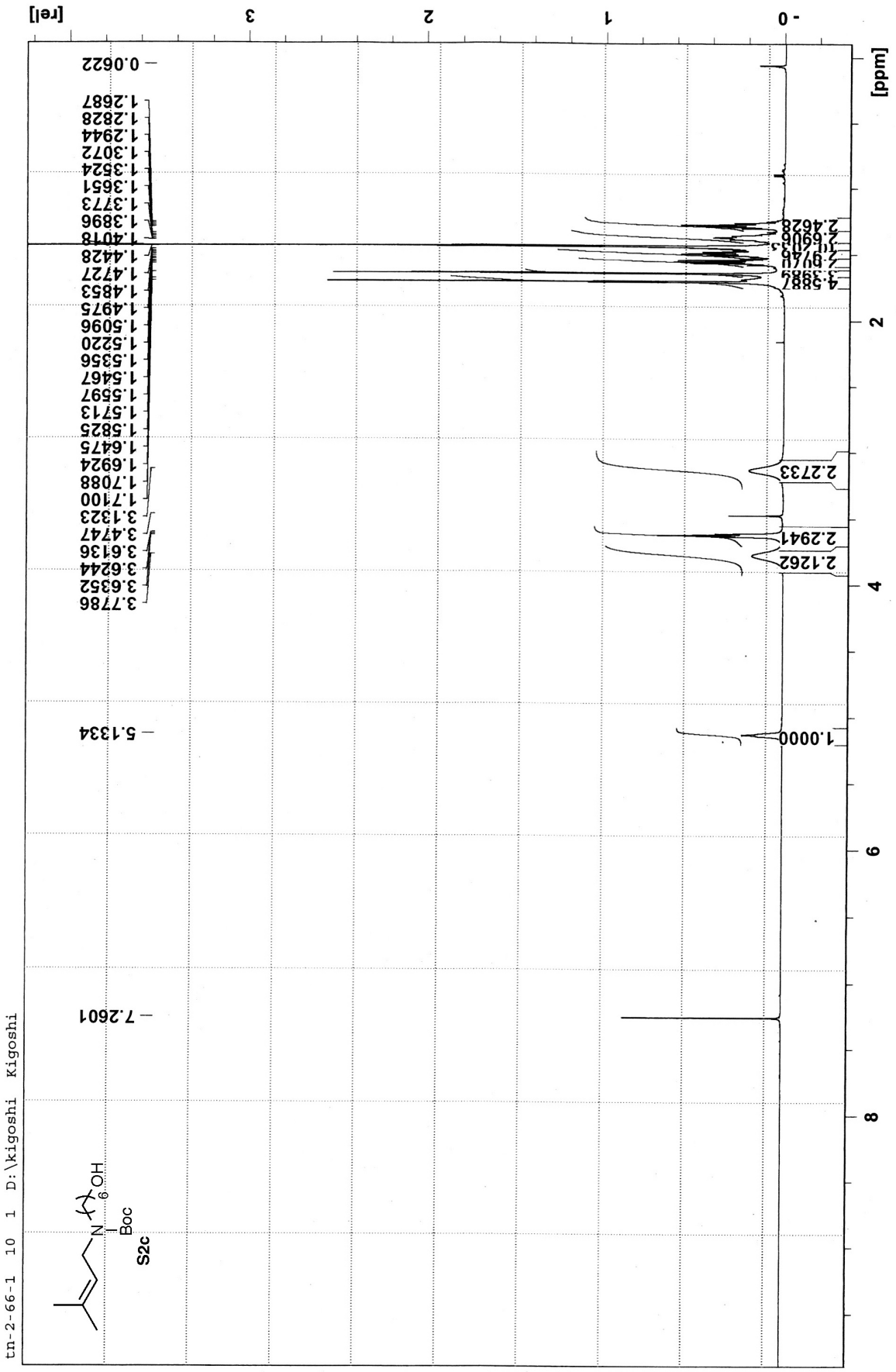
^{13}C NMR spectra of **S2a** (150 MHz, $CDCl_3$)



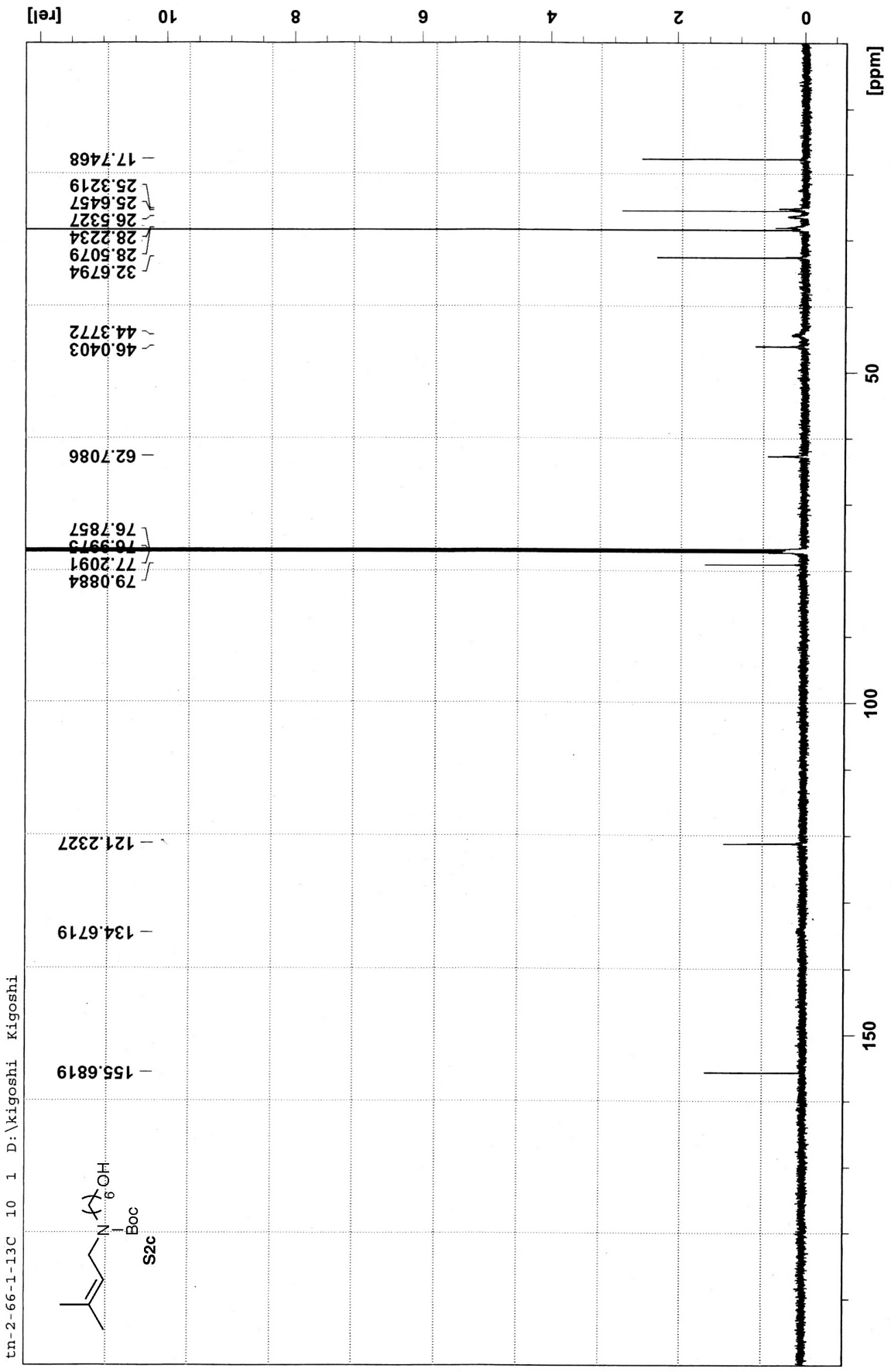
^{1}H NMR spectra of **S2b** (600 MHz, $CDCl_3$)



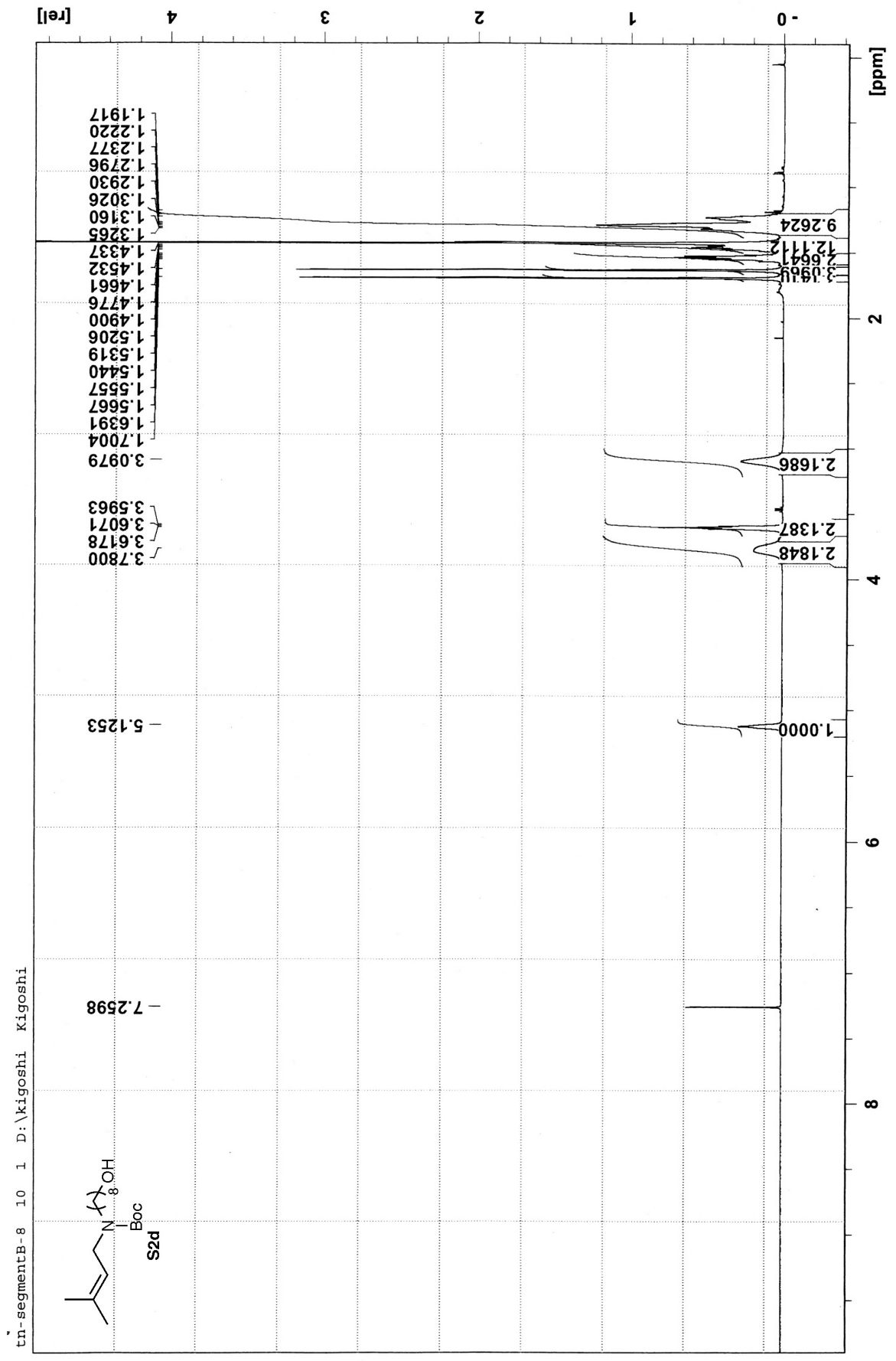
^{13}C NMR spectra of **S2b** (150 MHz, $CDCl_3$)



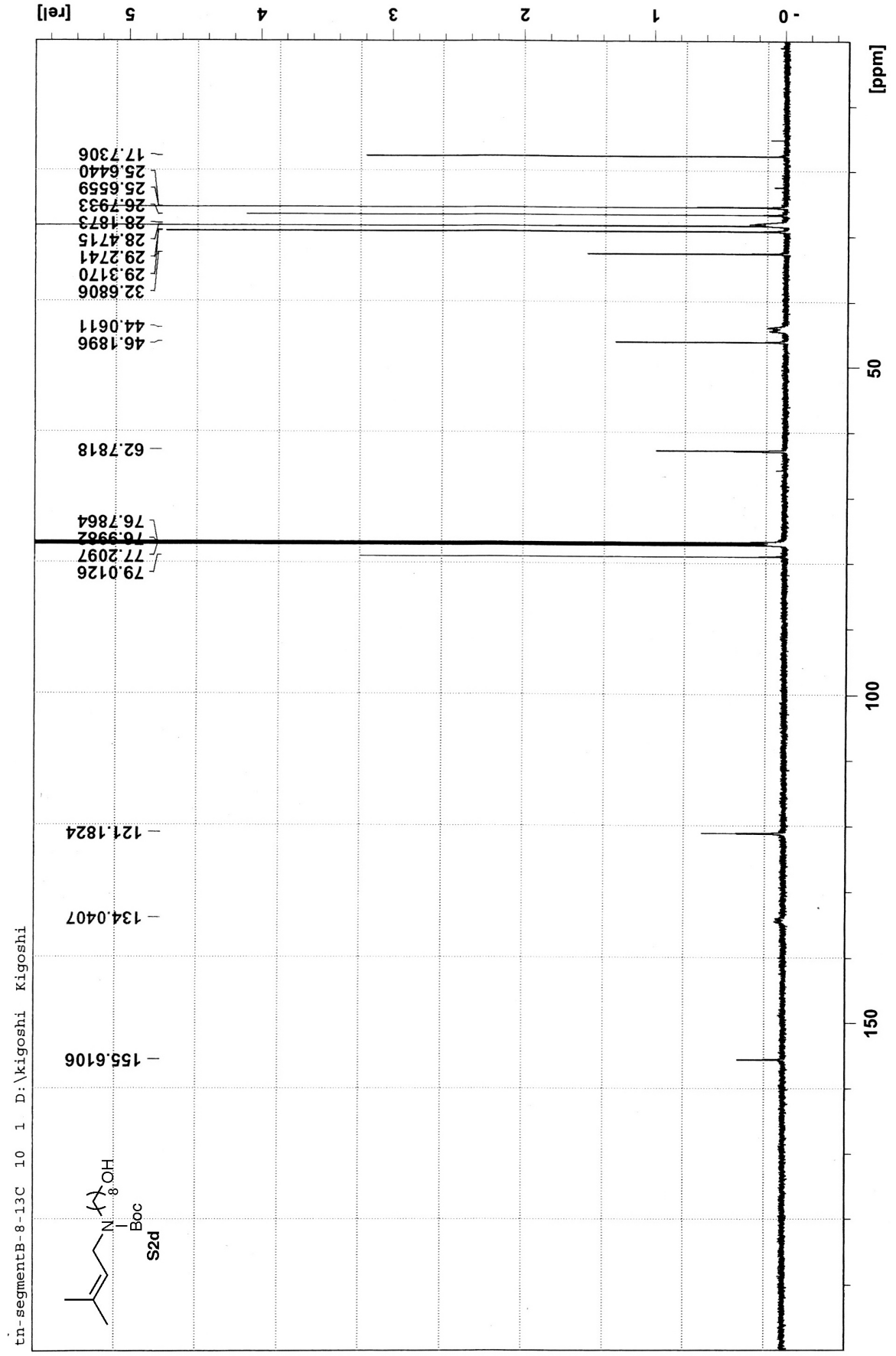
^{1}H NMR spectra of **S2c** (600 MHz, $CDCl_3$)



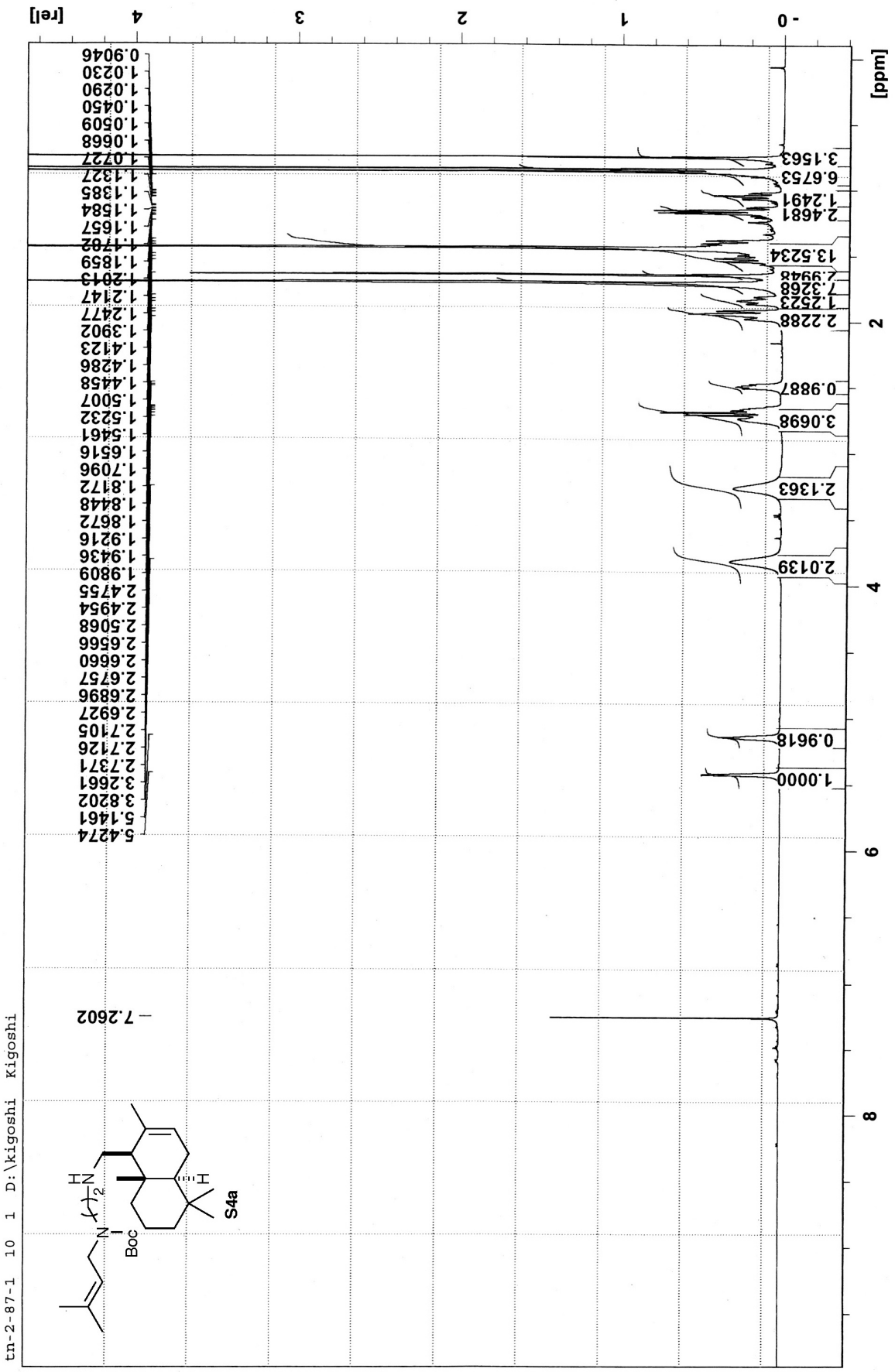
^{13}C NMR spectra of **S2c** (150 MHz, $CDCl_3$)



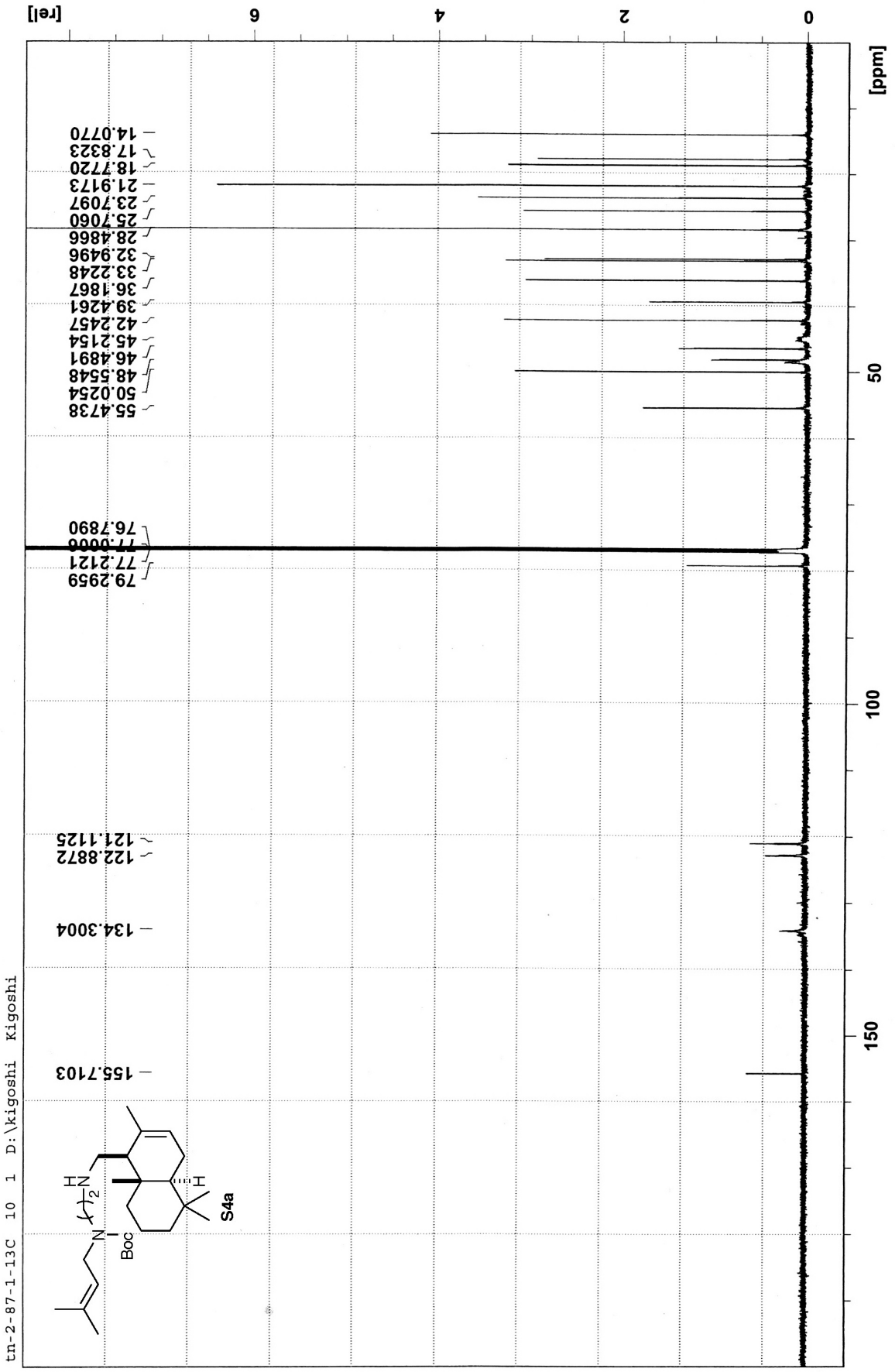
^{1}H NMR spectra of **S2d** (600 MHz, $CDCl_3$)



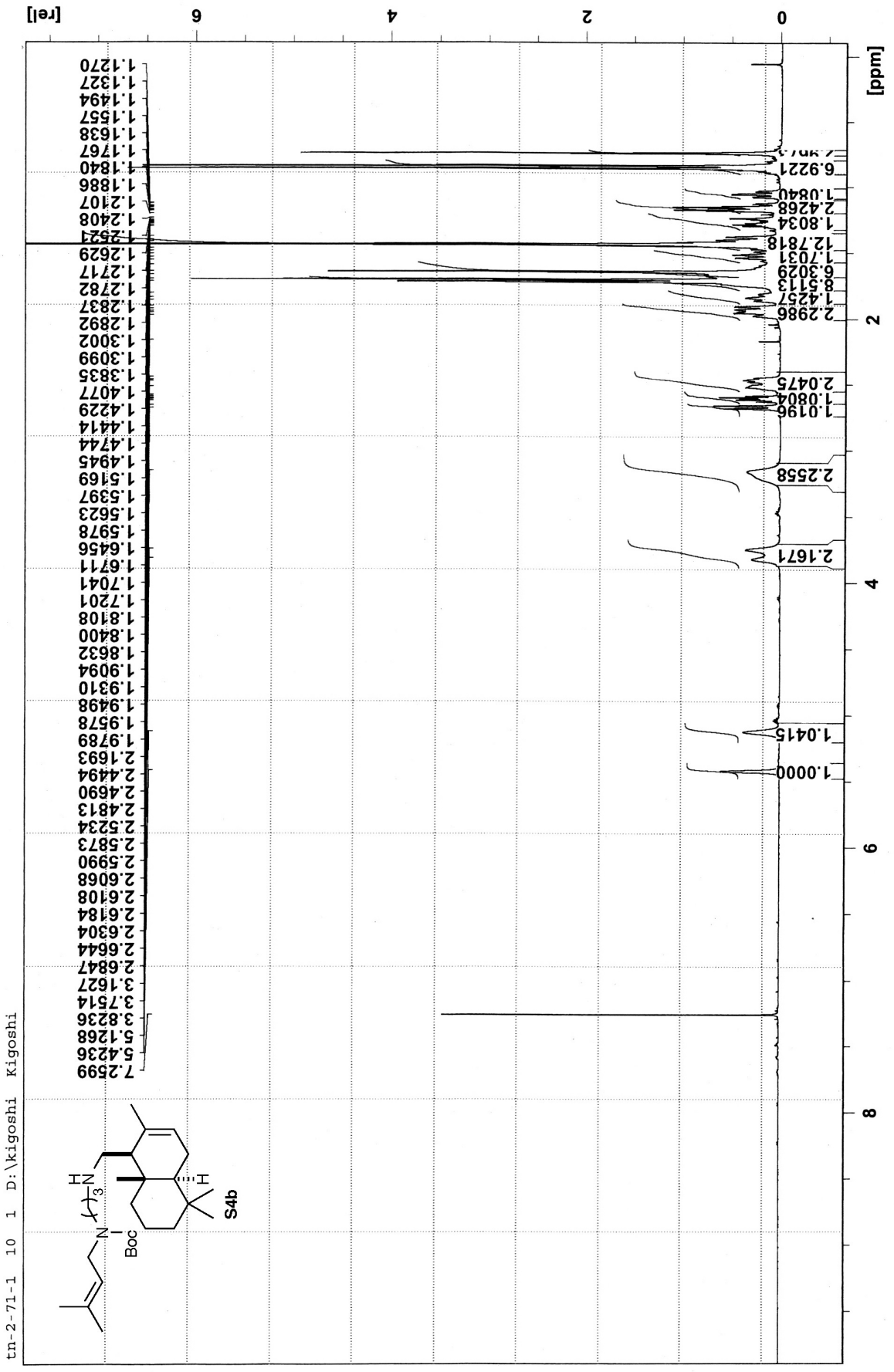
^{13}C NMR spectra of **S2d** (150 MHz, $CDCl_3$)



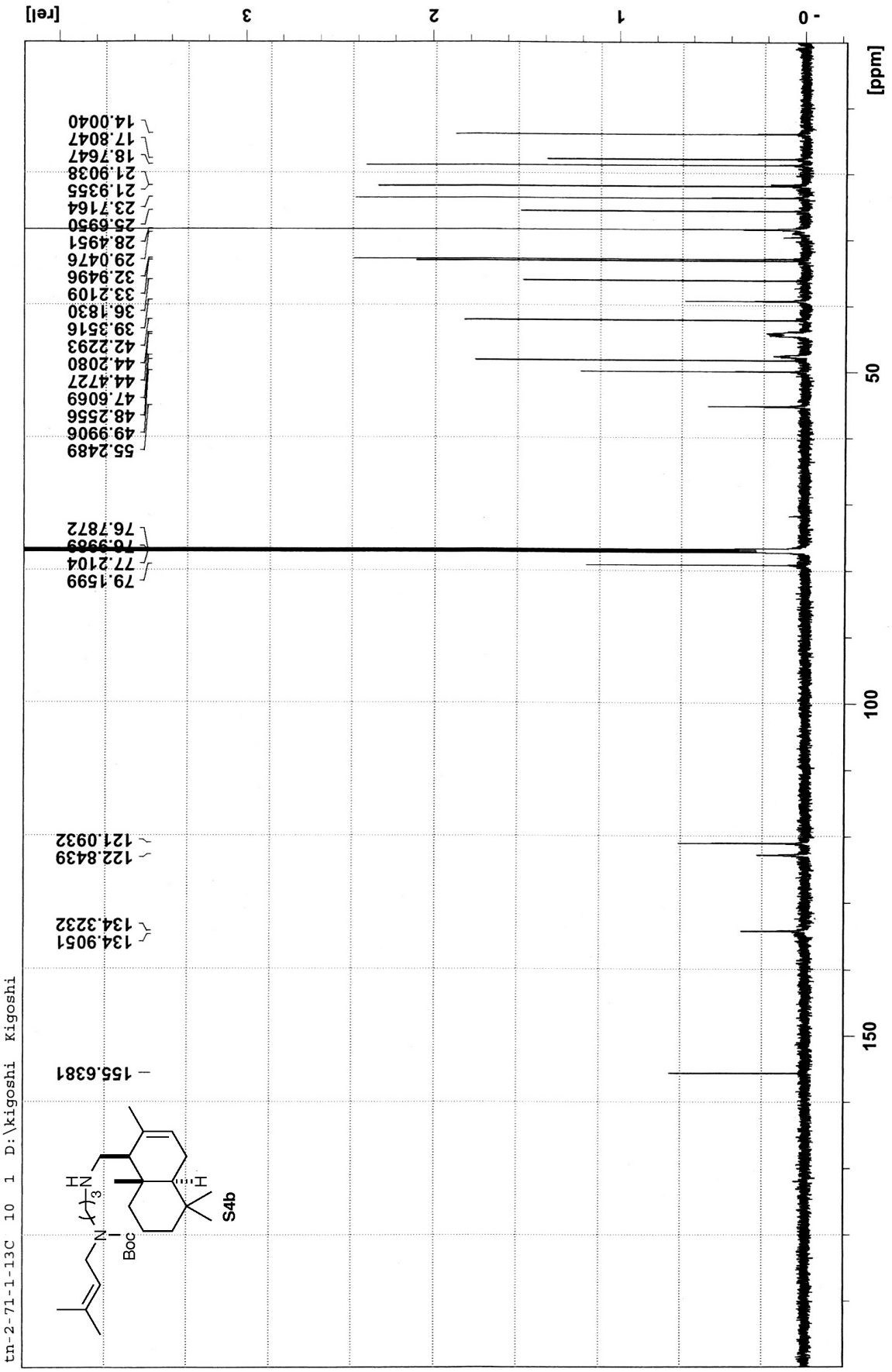
^{1}H NMR spectra of **S4a** (600 MHz, $CDCl_3$)



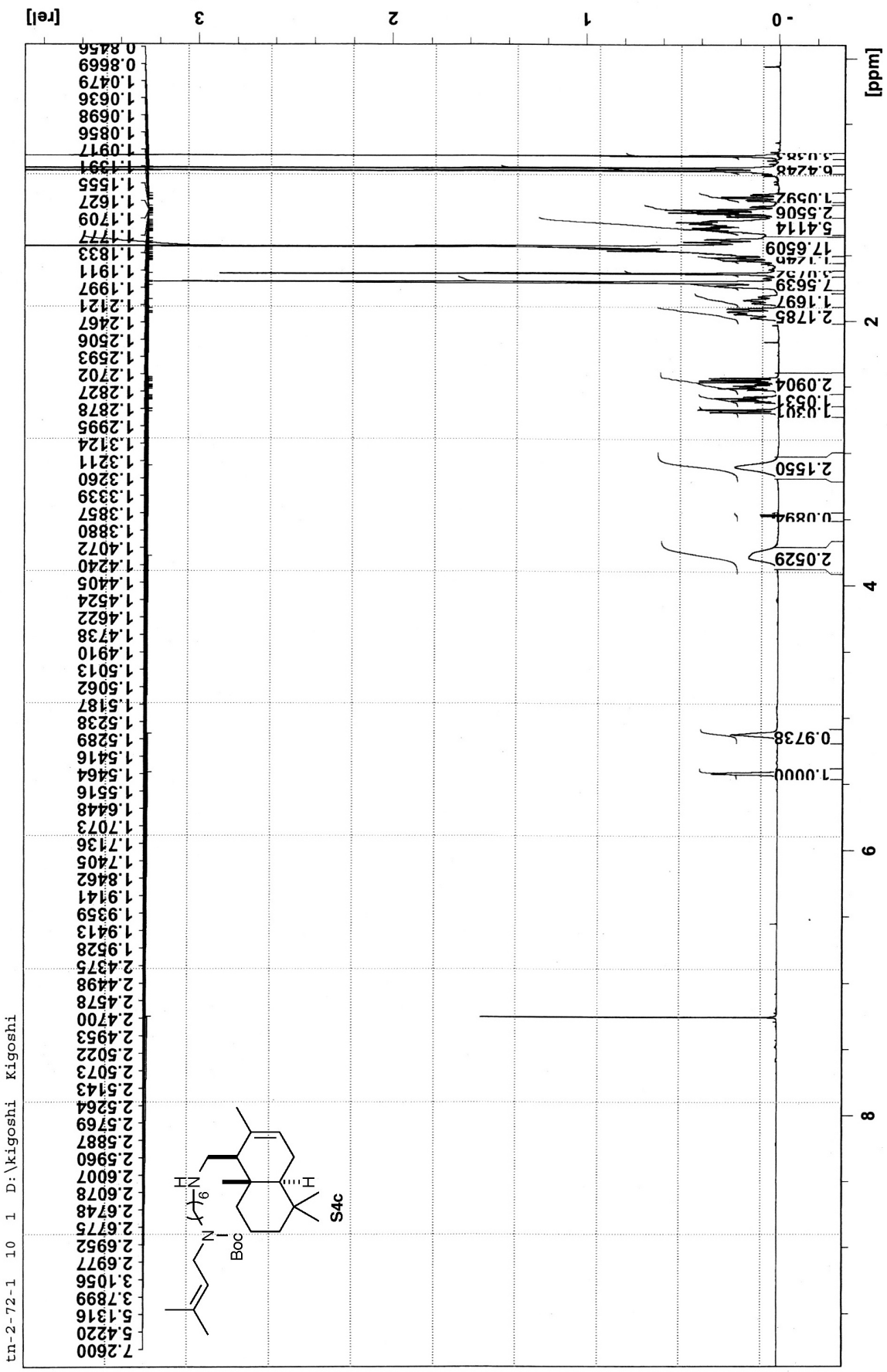
^{13}C NMR spectra of **S4a** (150 MHz, $CDCl_3$)



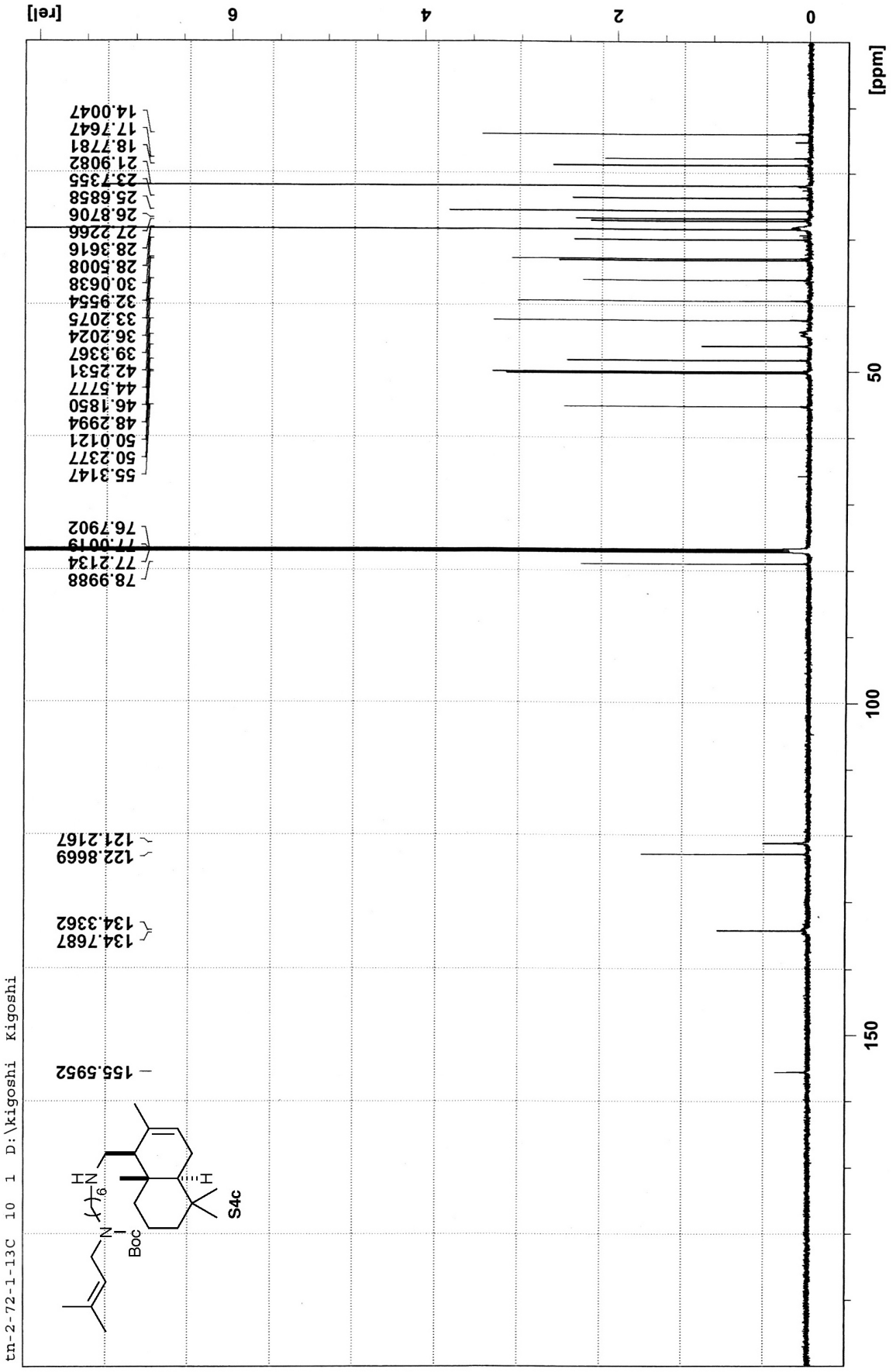
^{1}H NMR spectra of **S4b** (600 MHz, $CDCl_3$)



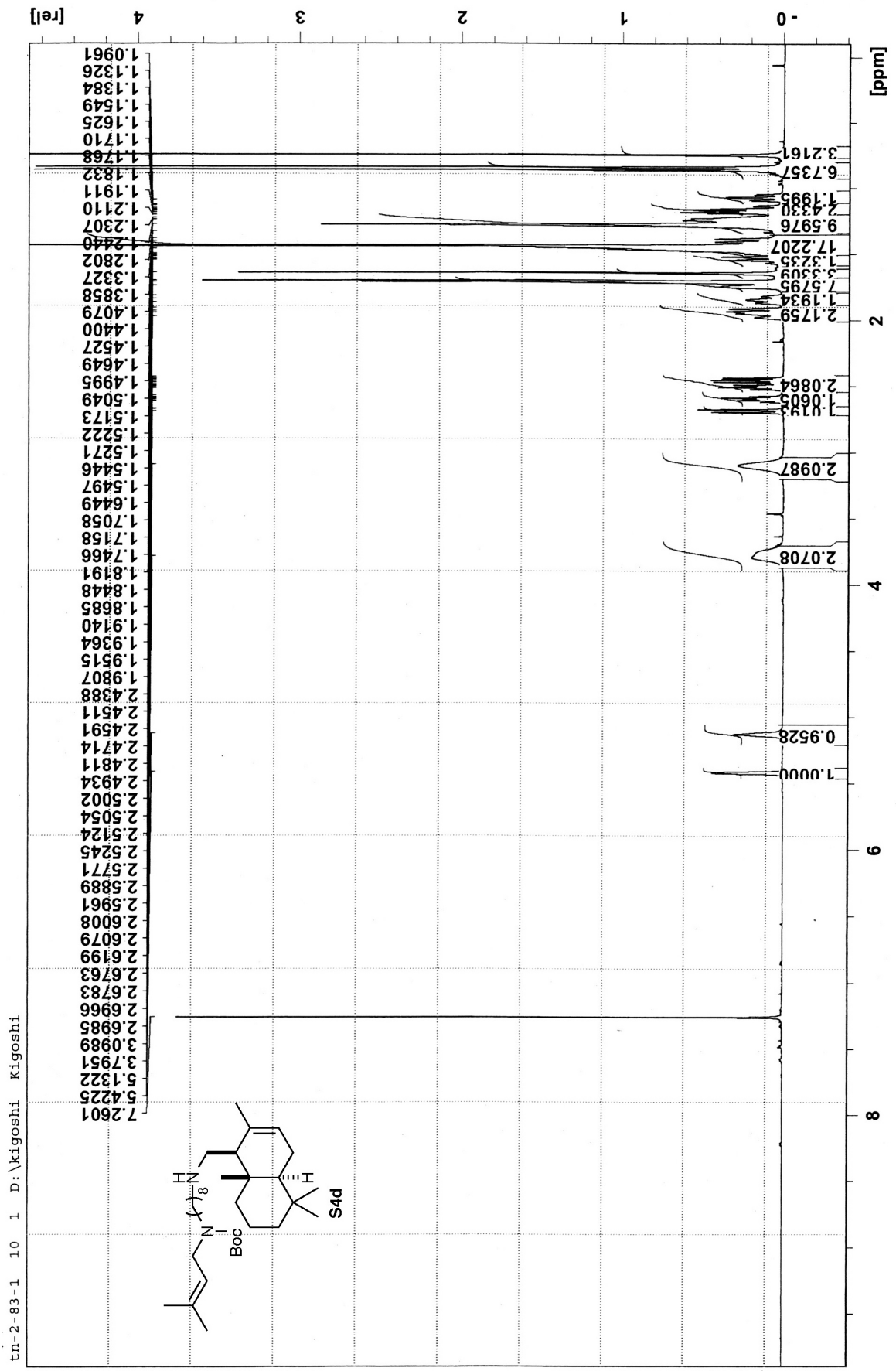
^{13}C NMR spectra of **S4b** (150 MHz, $CDCl_3$)



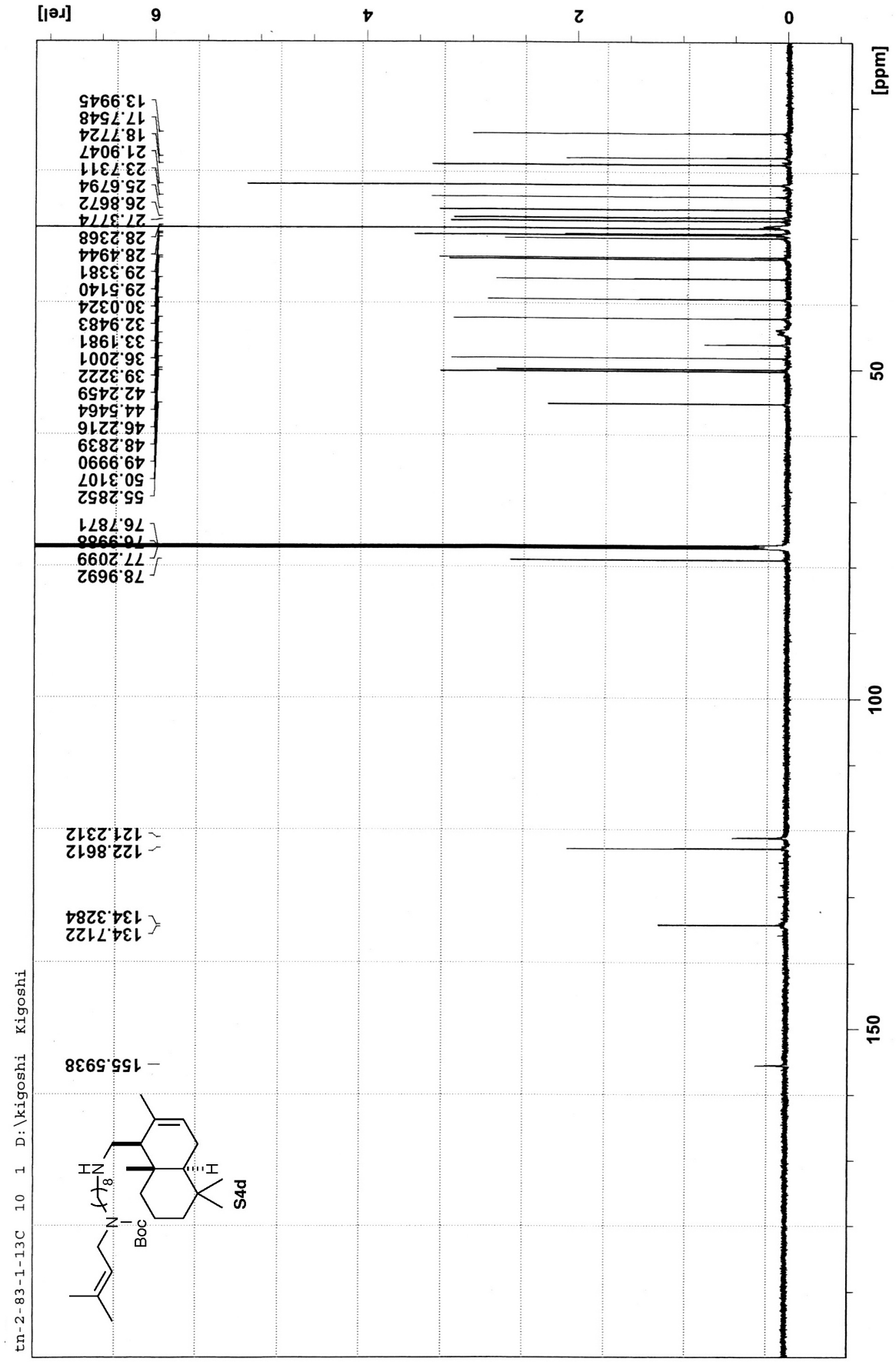
^{1}H NMR spectra of **S4c** (600 MHz, $CDCl_3$)



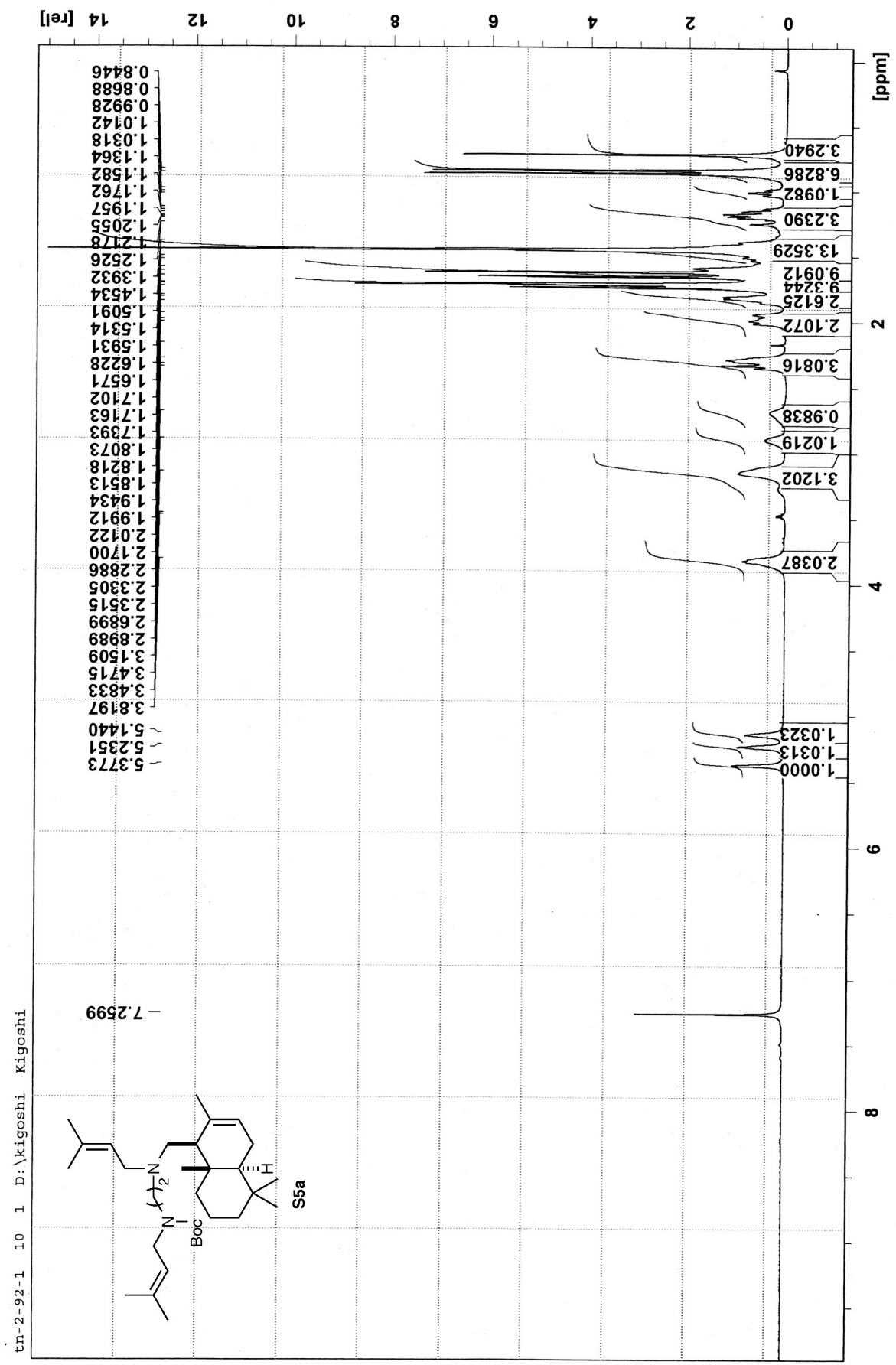
^{13}C NMR spectra of **S4c** (150 MHz, $CDCl_3$)



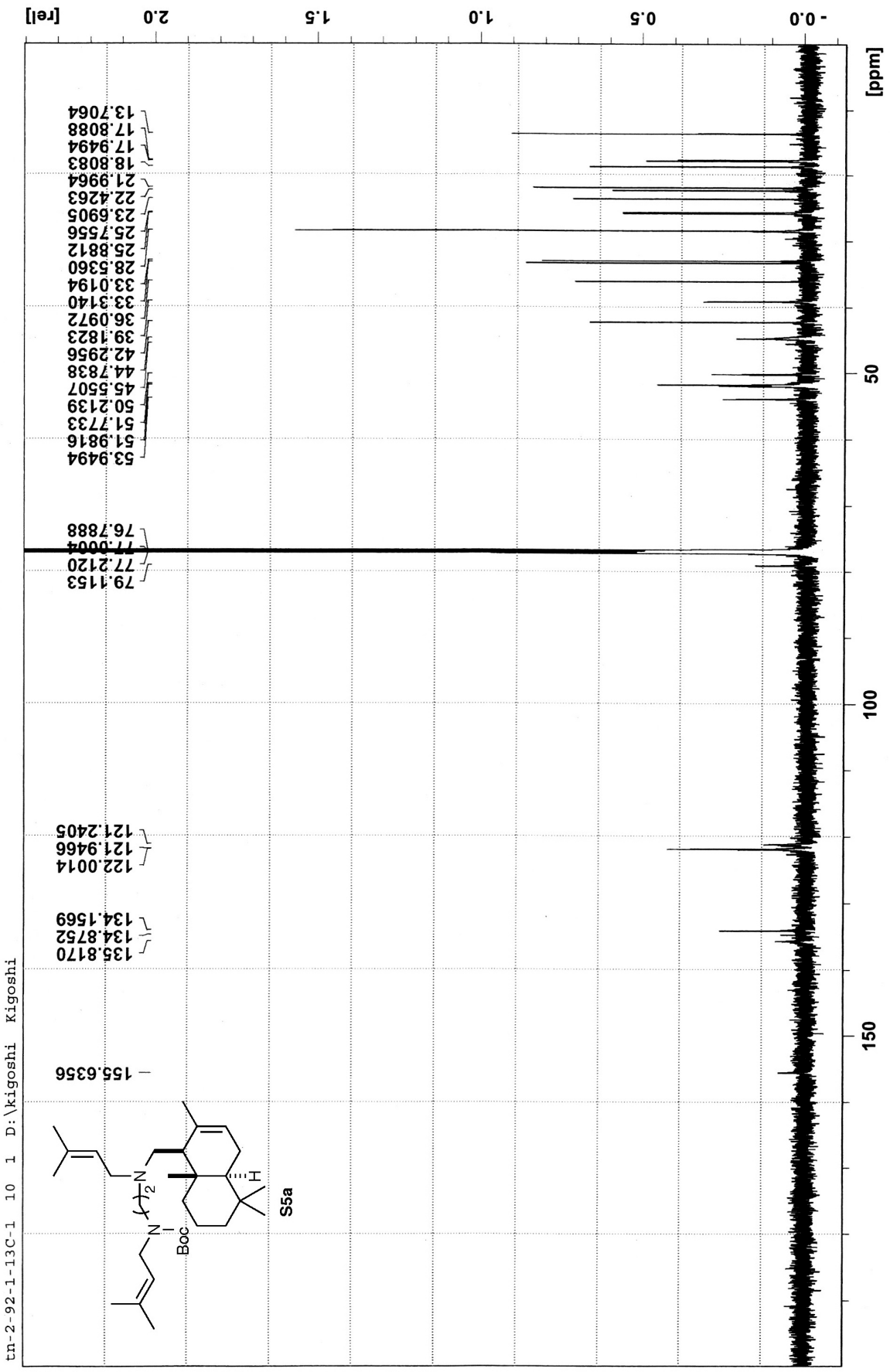
^{1}H NMR spectra of **S4d** (600 MHz, $CDCl_3$)



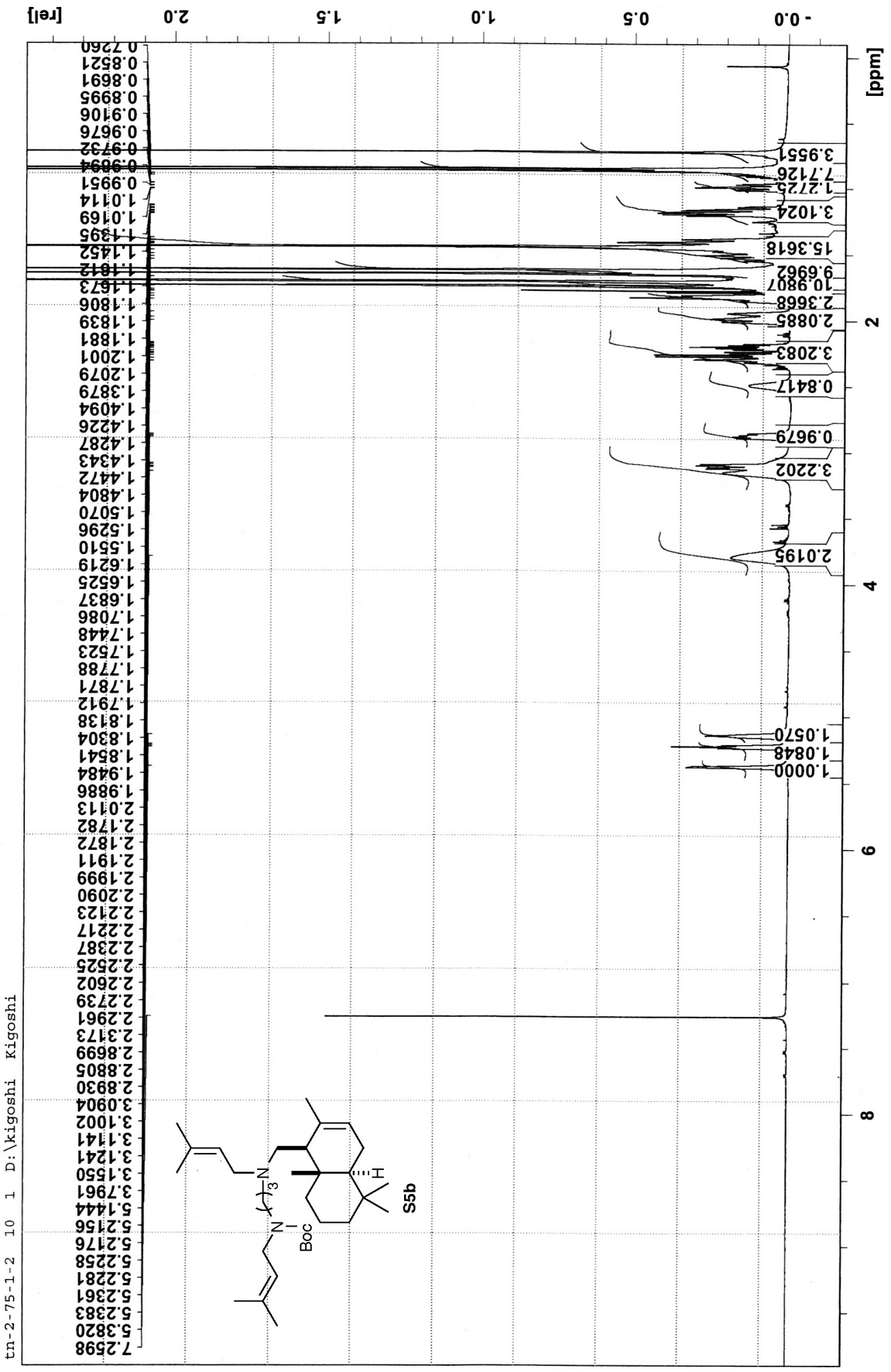
^{13}C NMR spectra of **S4d** (150 MHz, $CDCl_3$)



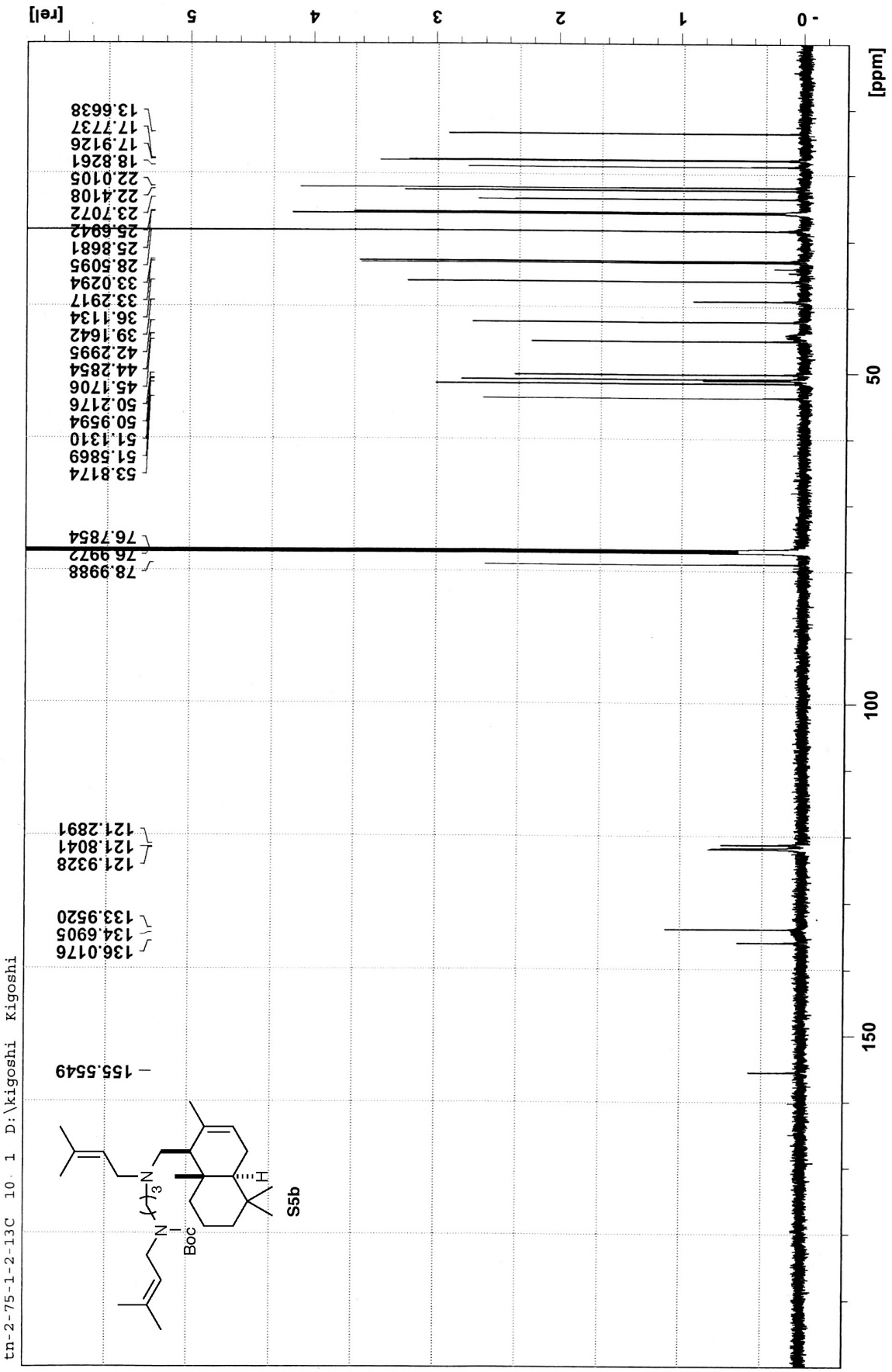
^{1}H NMR spectra of **S5a** (600 MHz, $CDCl_3$)



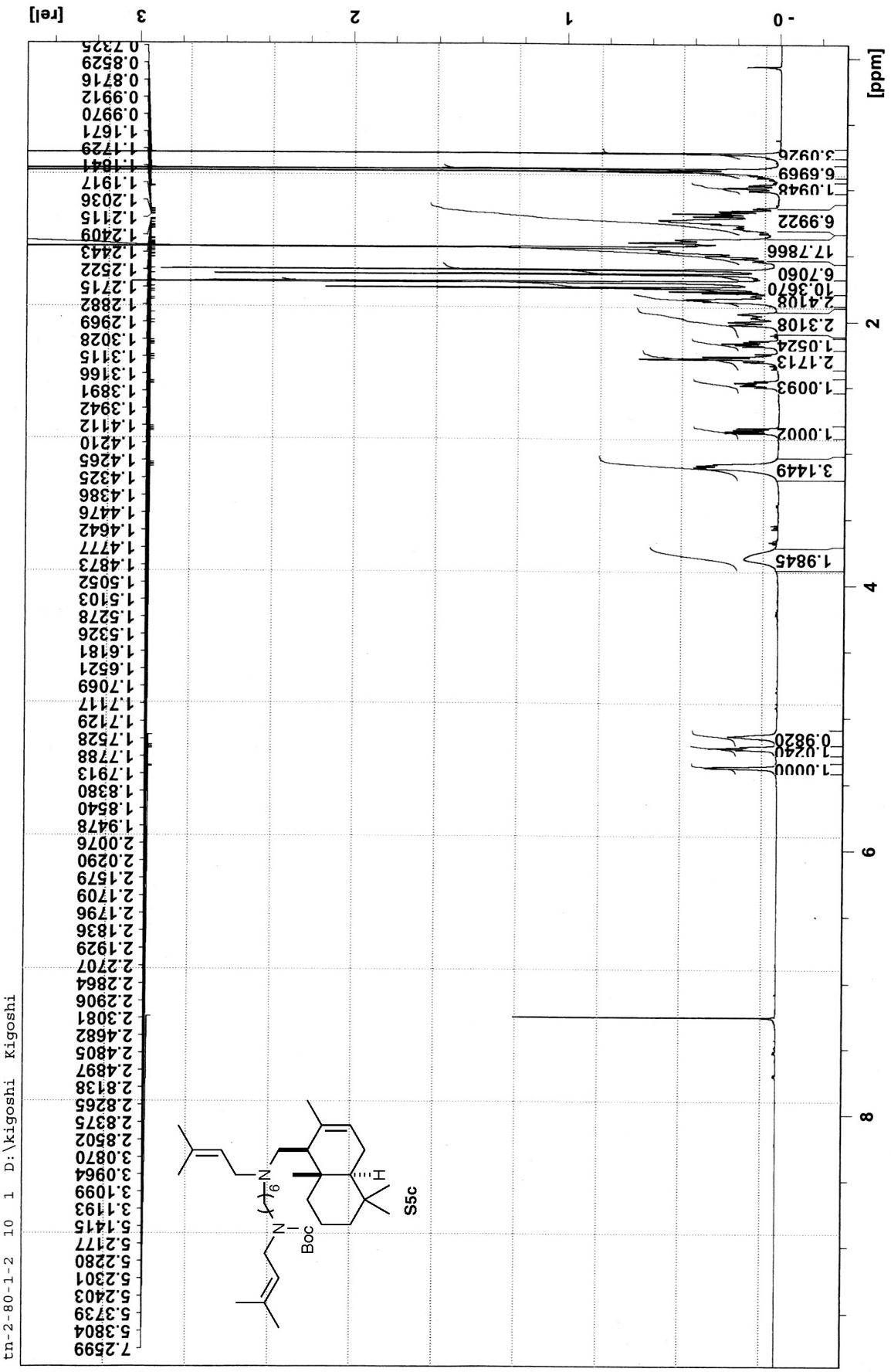
^{13}C NMR spectra of **S5a** (150 MHz, $CDCl_3$)



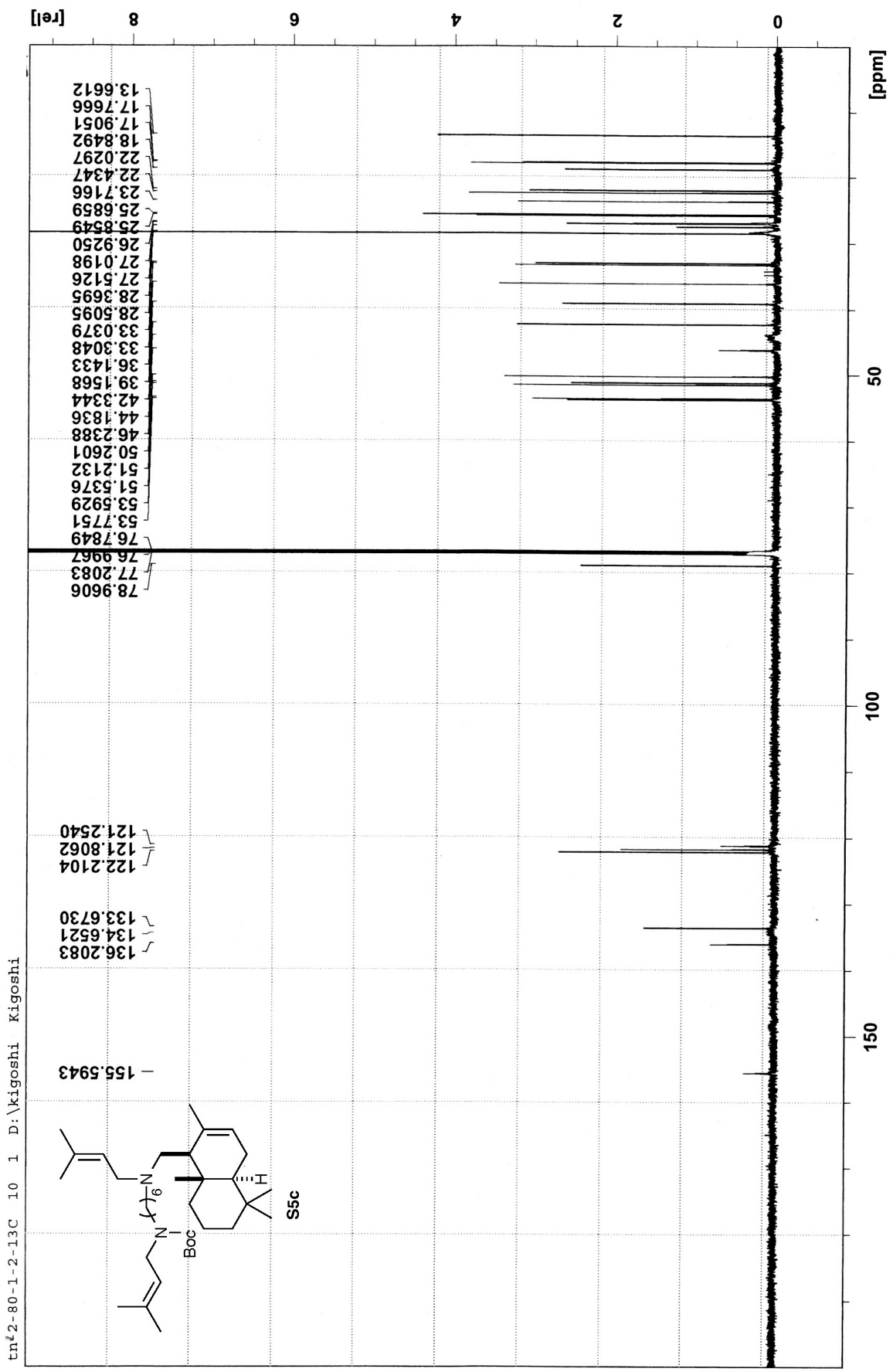
^{1}H NMR spectra of **S5b** (600 MHz, $CDCl_3$)



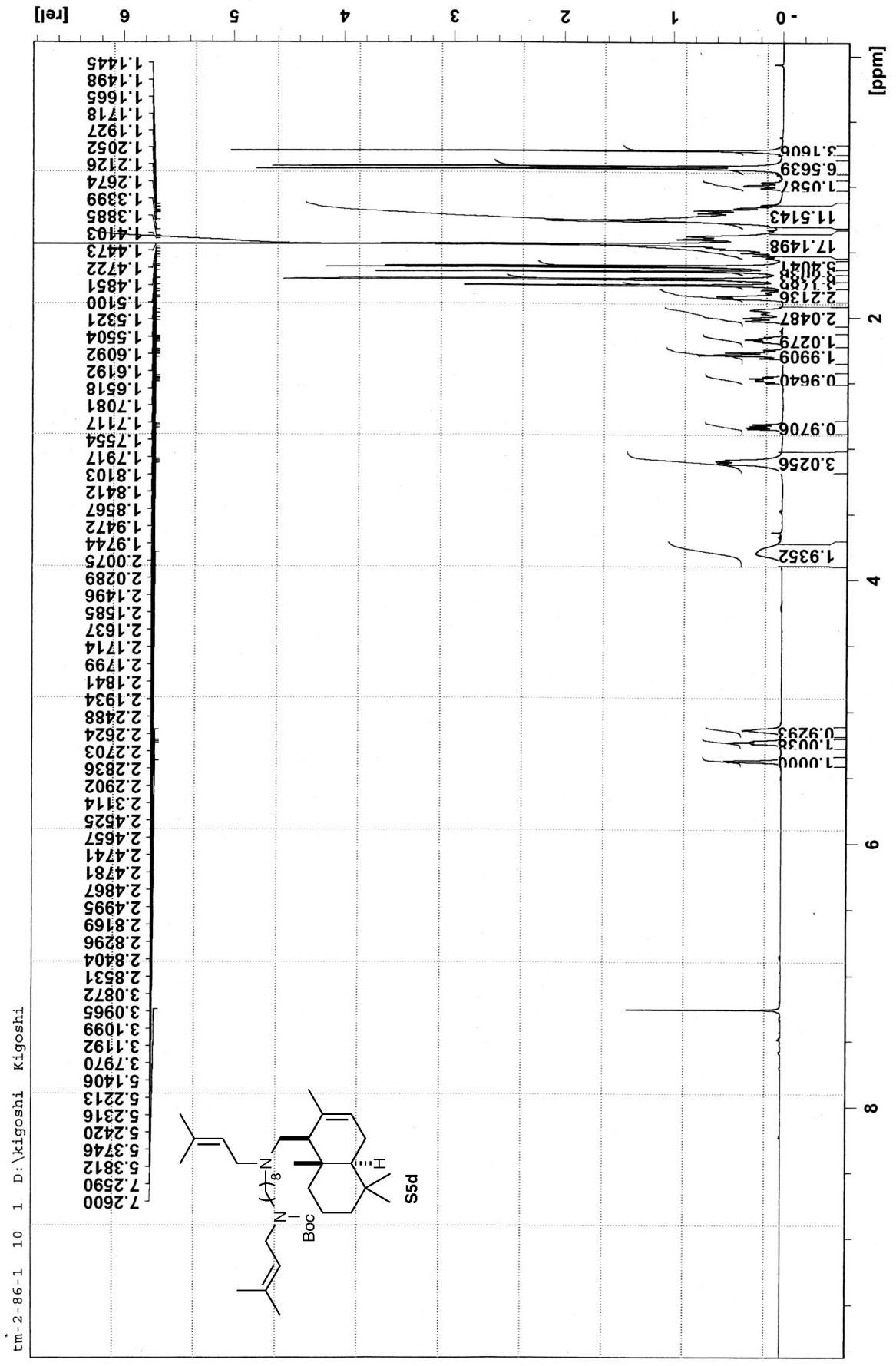
^{13}C NMR spectra of **S5b** (150 MHz, $CDCl_3$)



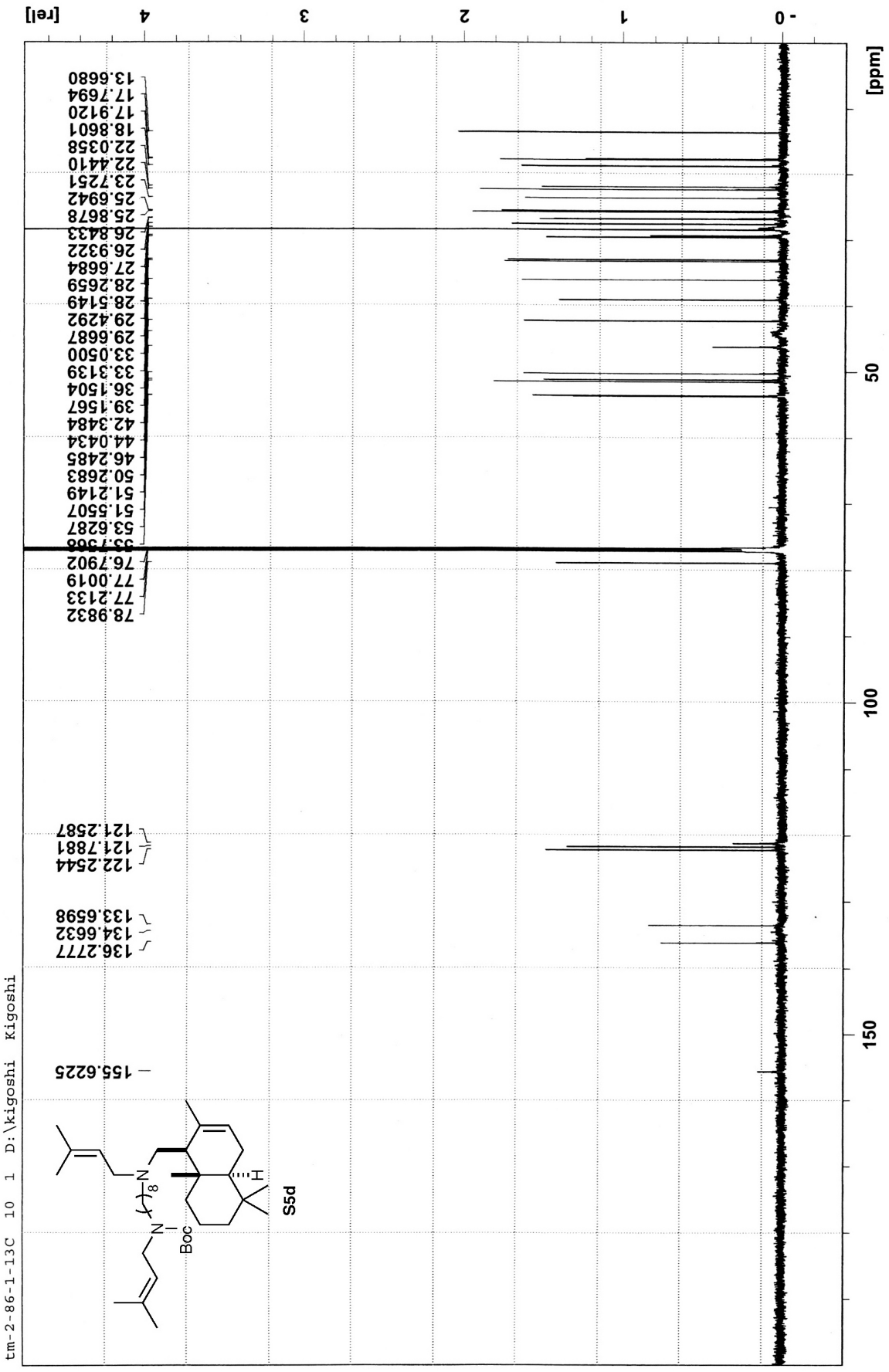
^{1}H NMR spectra of **S5c** (600 MHz, $CDCl_3$)



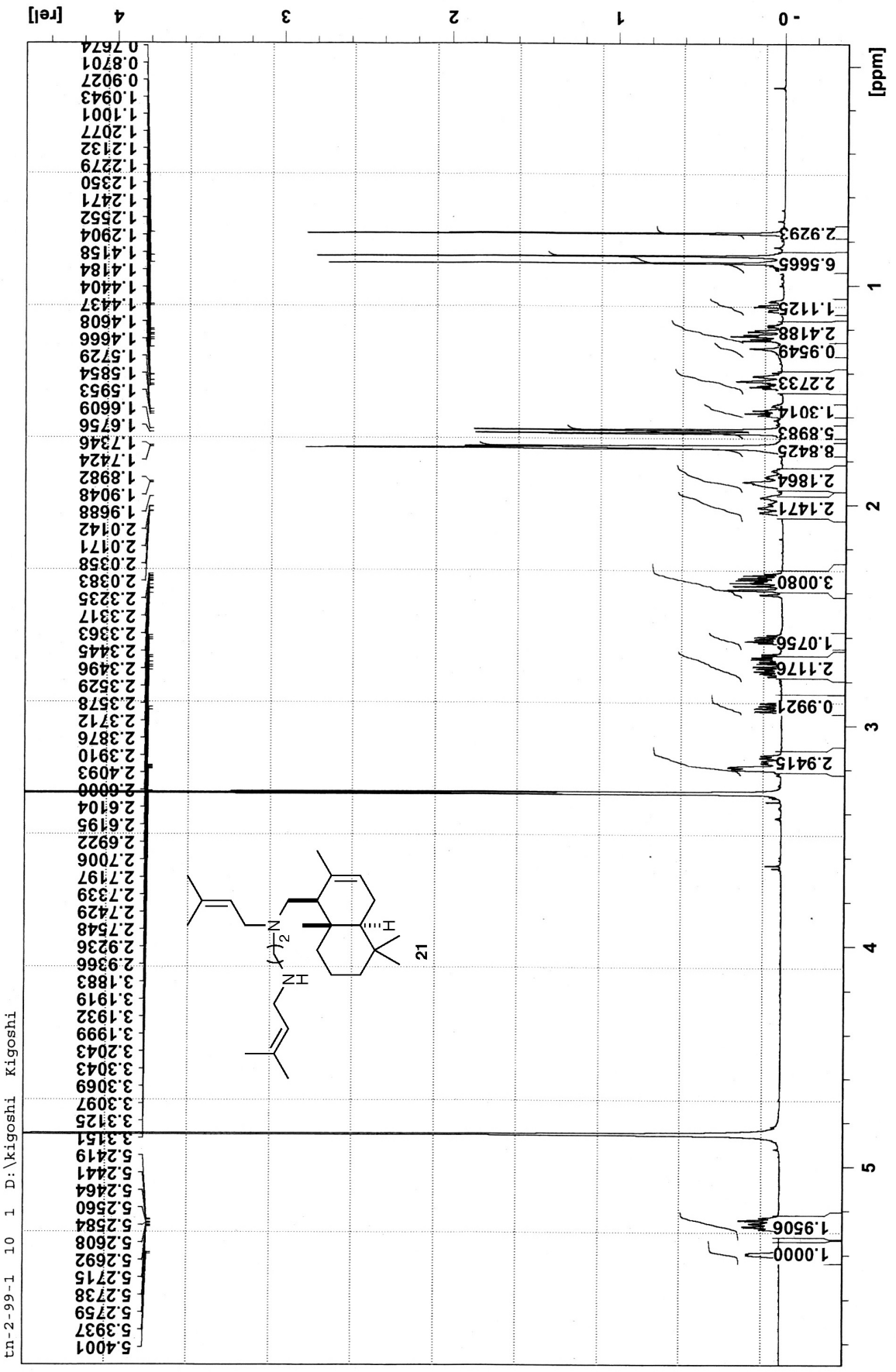
^{13}C NMR spectra of **S5c** (150 MHz, $CDCl_3$)



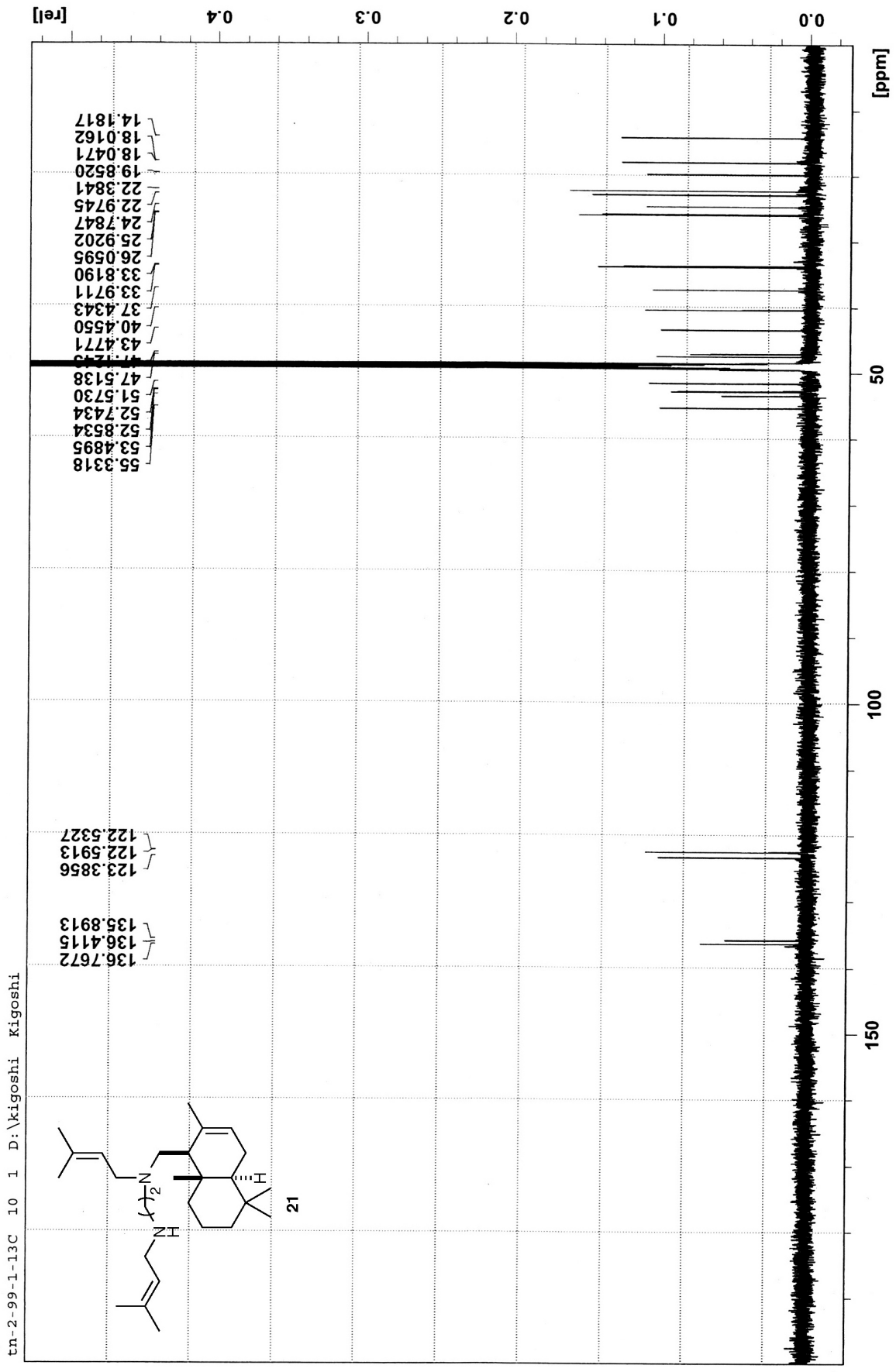
^{1}H NMR spectra of **S5d** (600 MHz, $CDCl_3$)



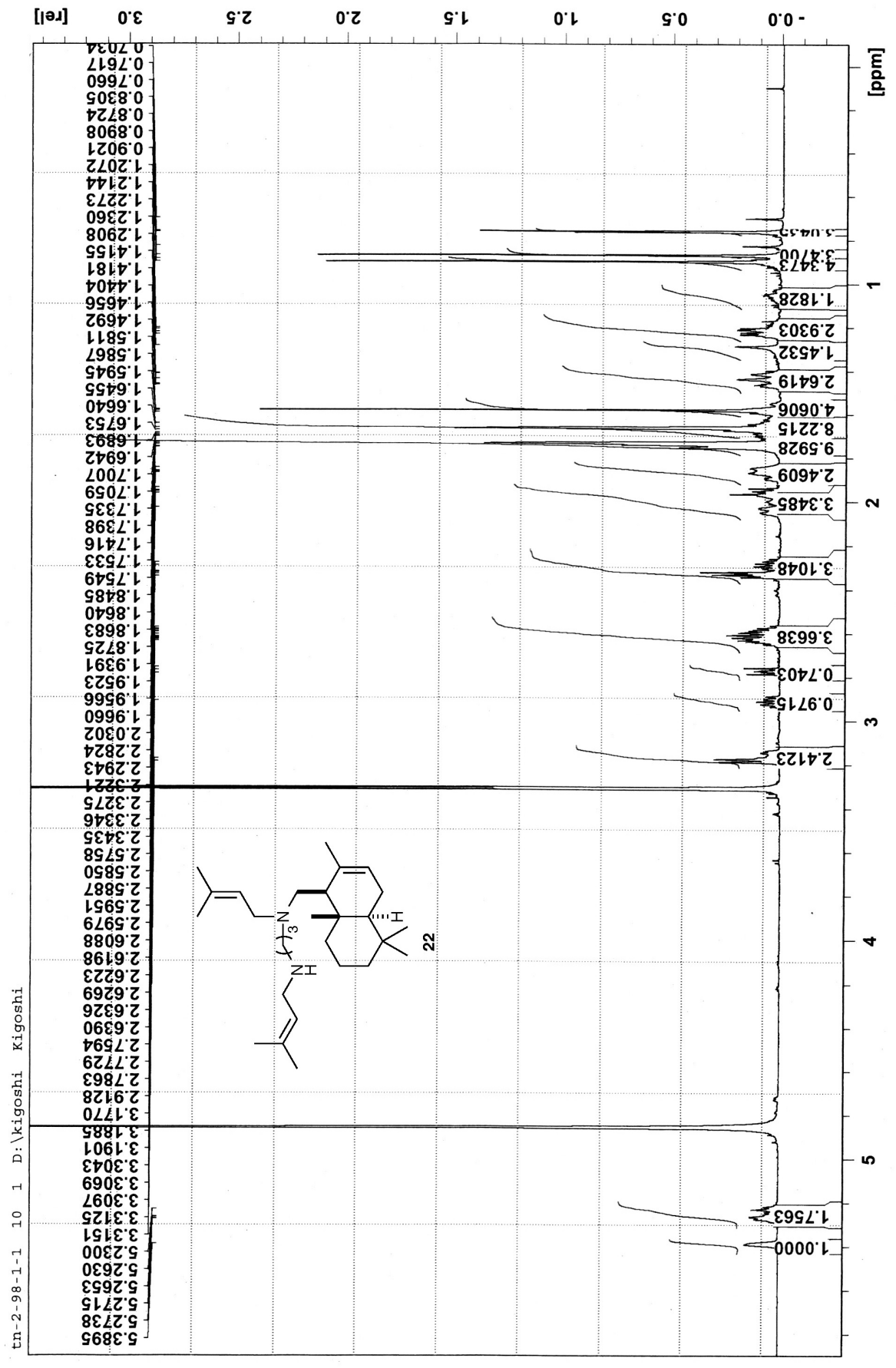
^{13}C NMR spectra of **S5d** (150 MHz, $CDCl_3$)



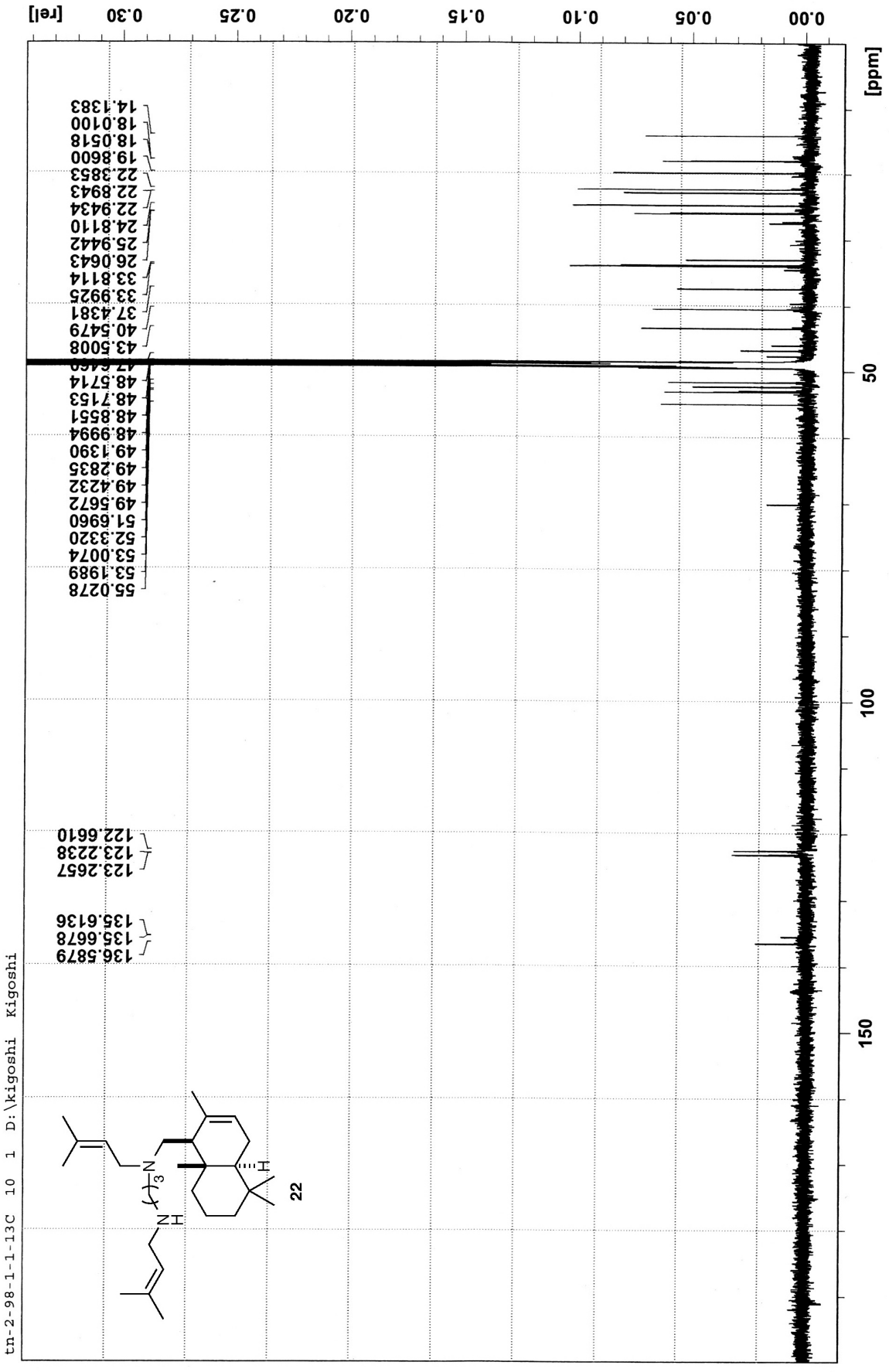
^{1}H NMR spectra of **21** (600 MHz, CD_3OD)



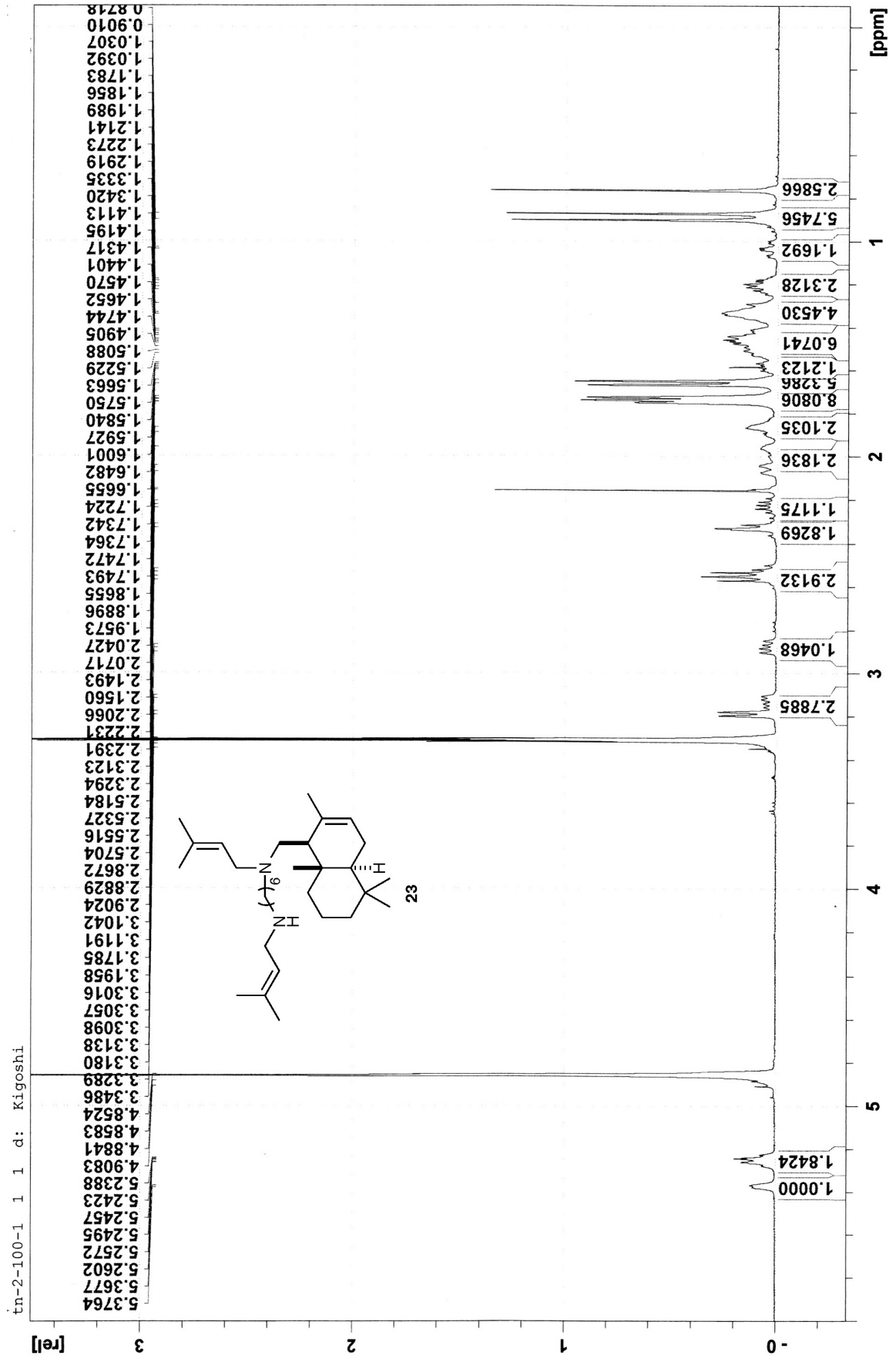
^{13}C NMR spectra of **21** (150 MHz, CD_3OD)



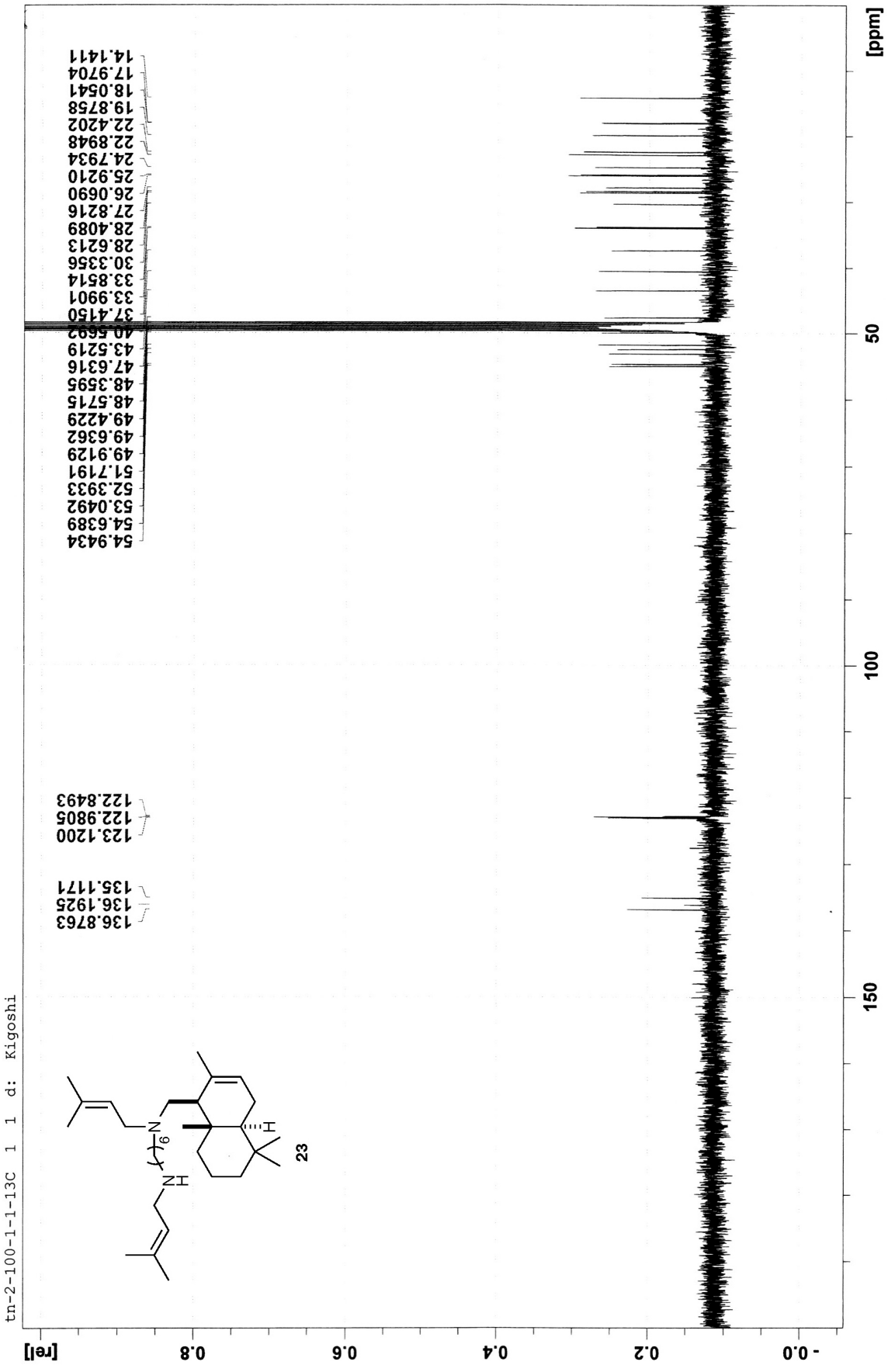
^{1}H NMR spectra of **22** (600 MHz, CD_3OD)



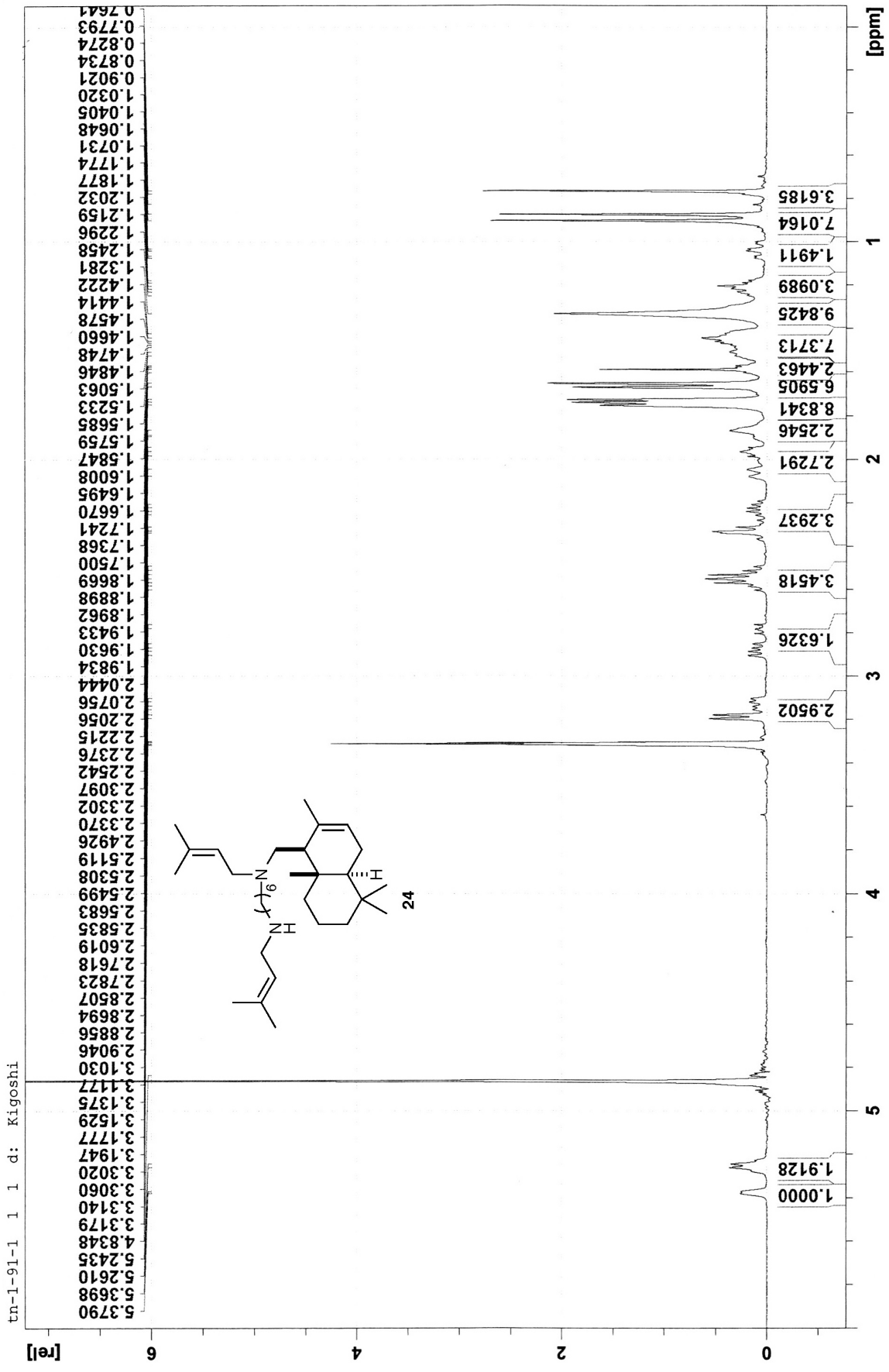
^{13}C NMR spectra of **22** (150 MHz, CD_3OD)



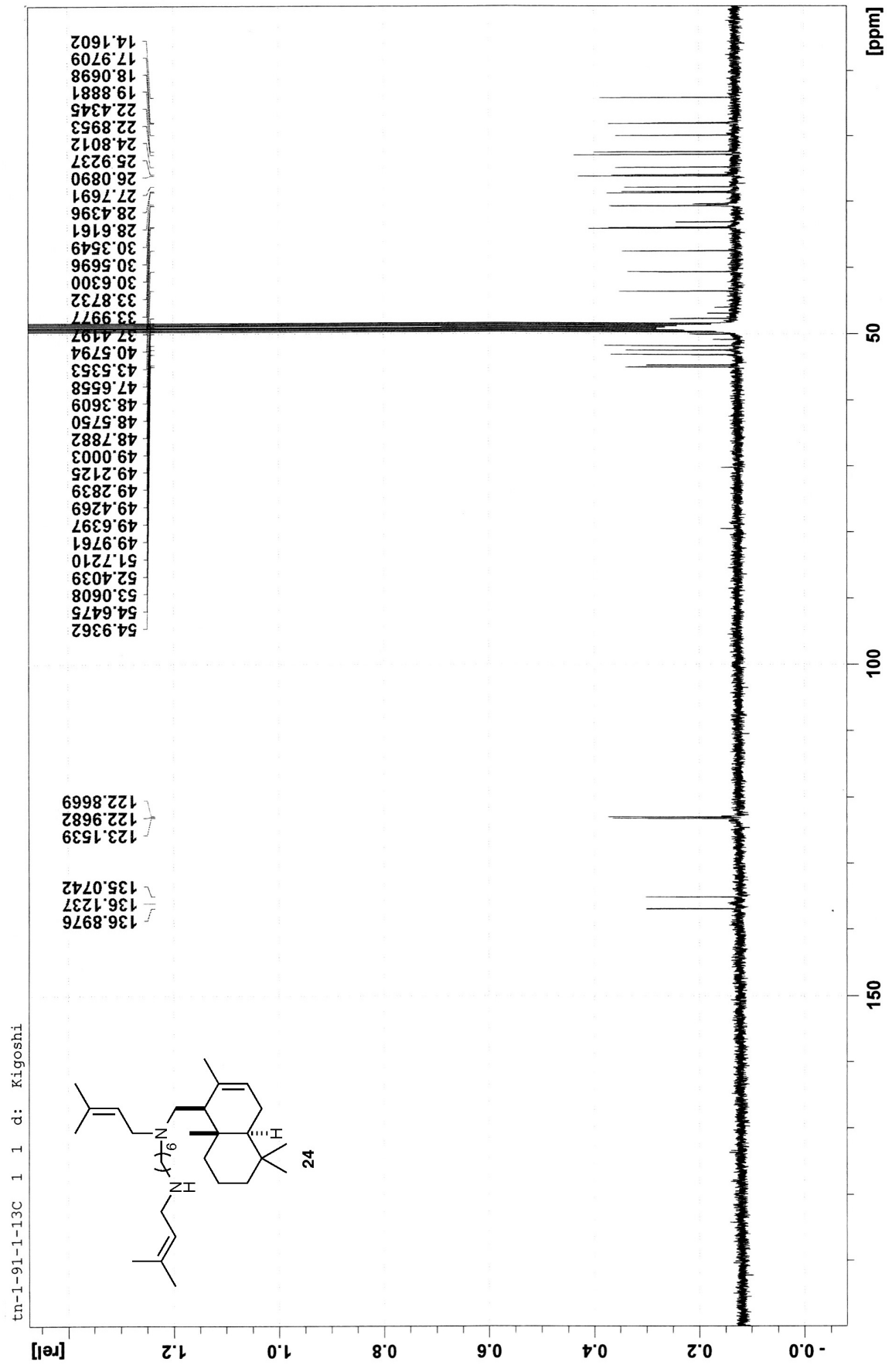
^{1}H NMR spectra of **23** (400 MHz, CD_3OD)



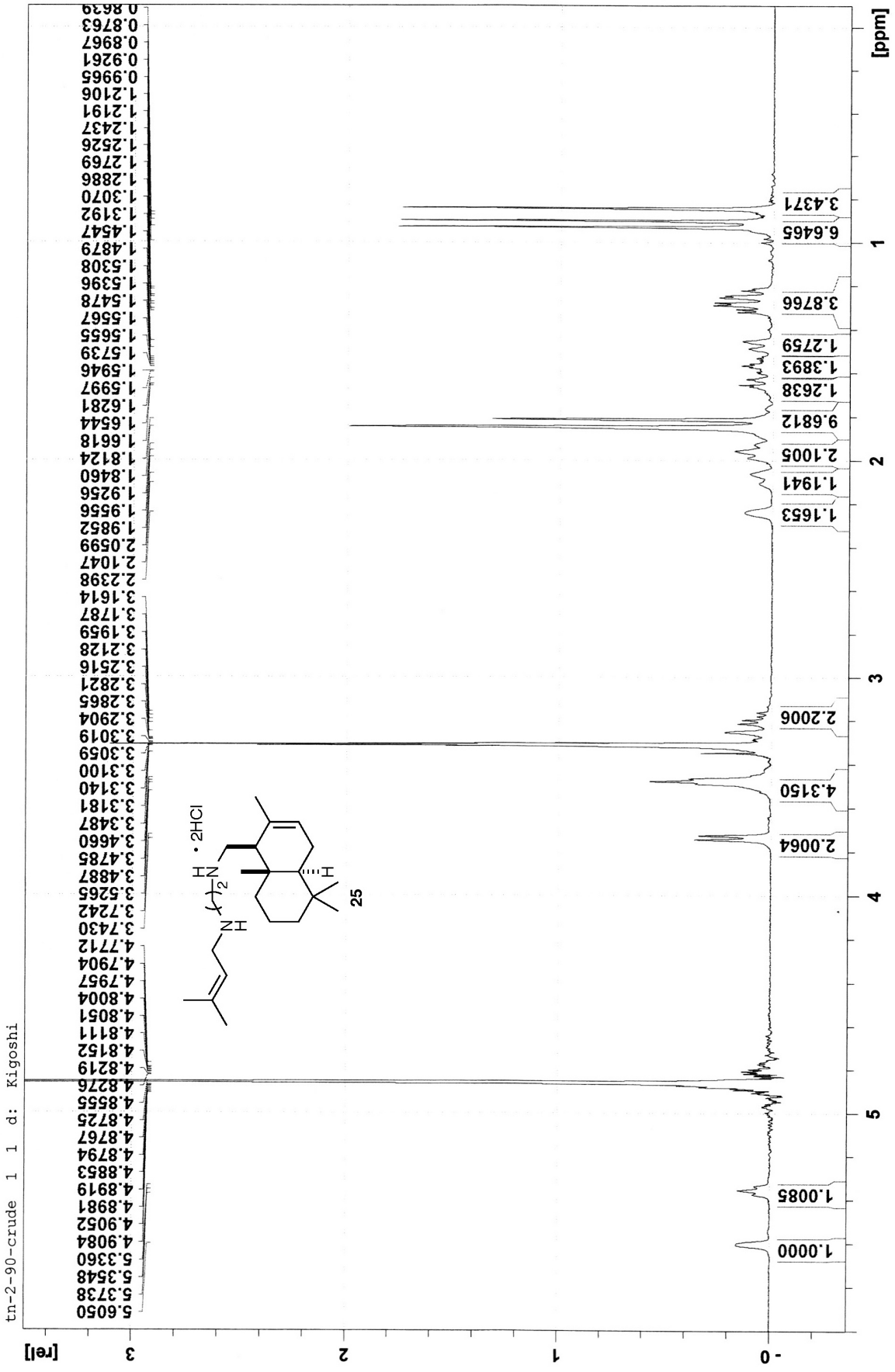
^{13}C NMR spectra of **23** (100 MHz, CD_3OD)



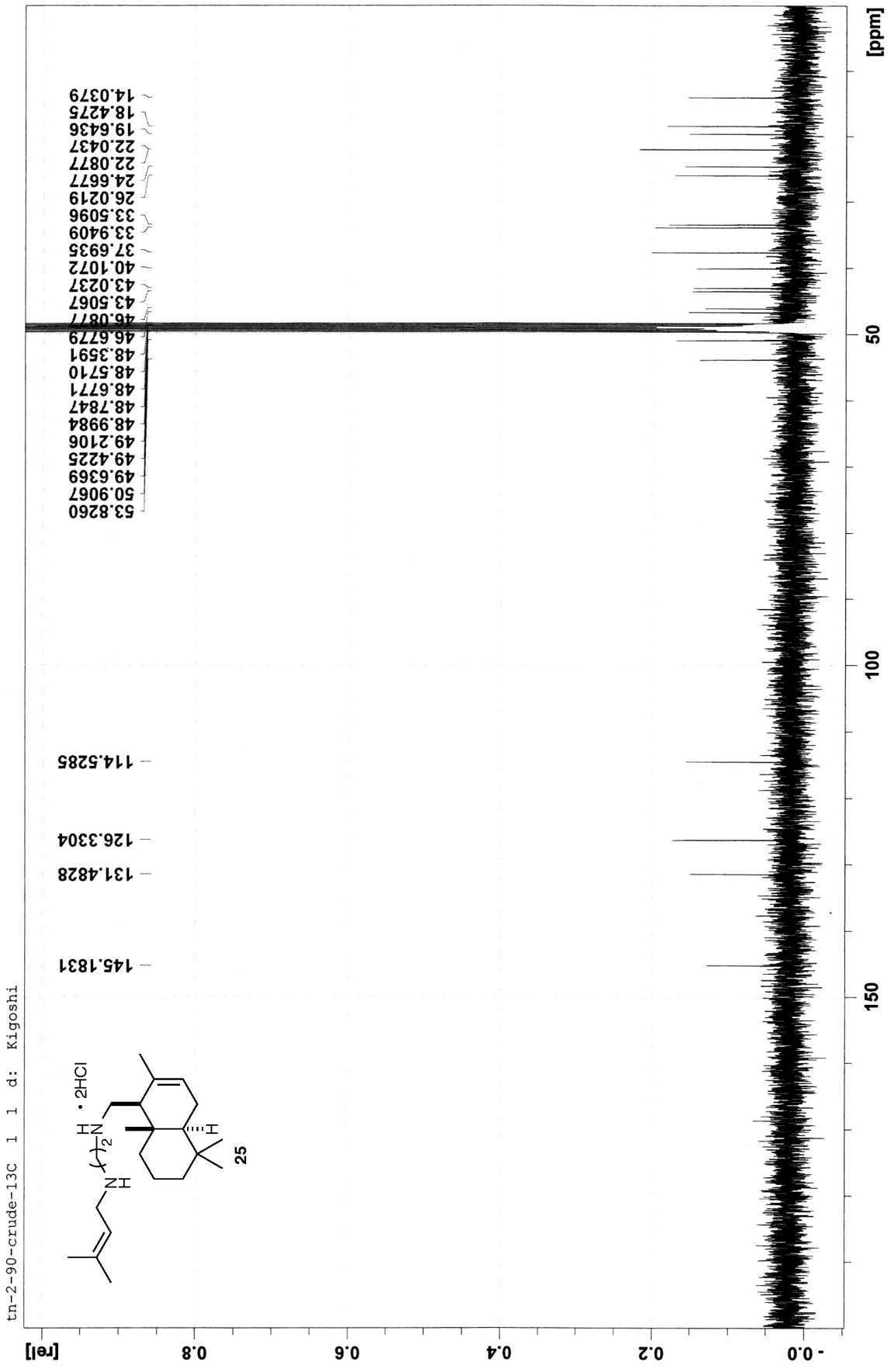
^{1}H NMR spectra of **24** (400 MHz, CD_3OD)



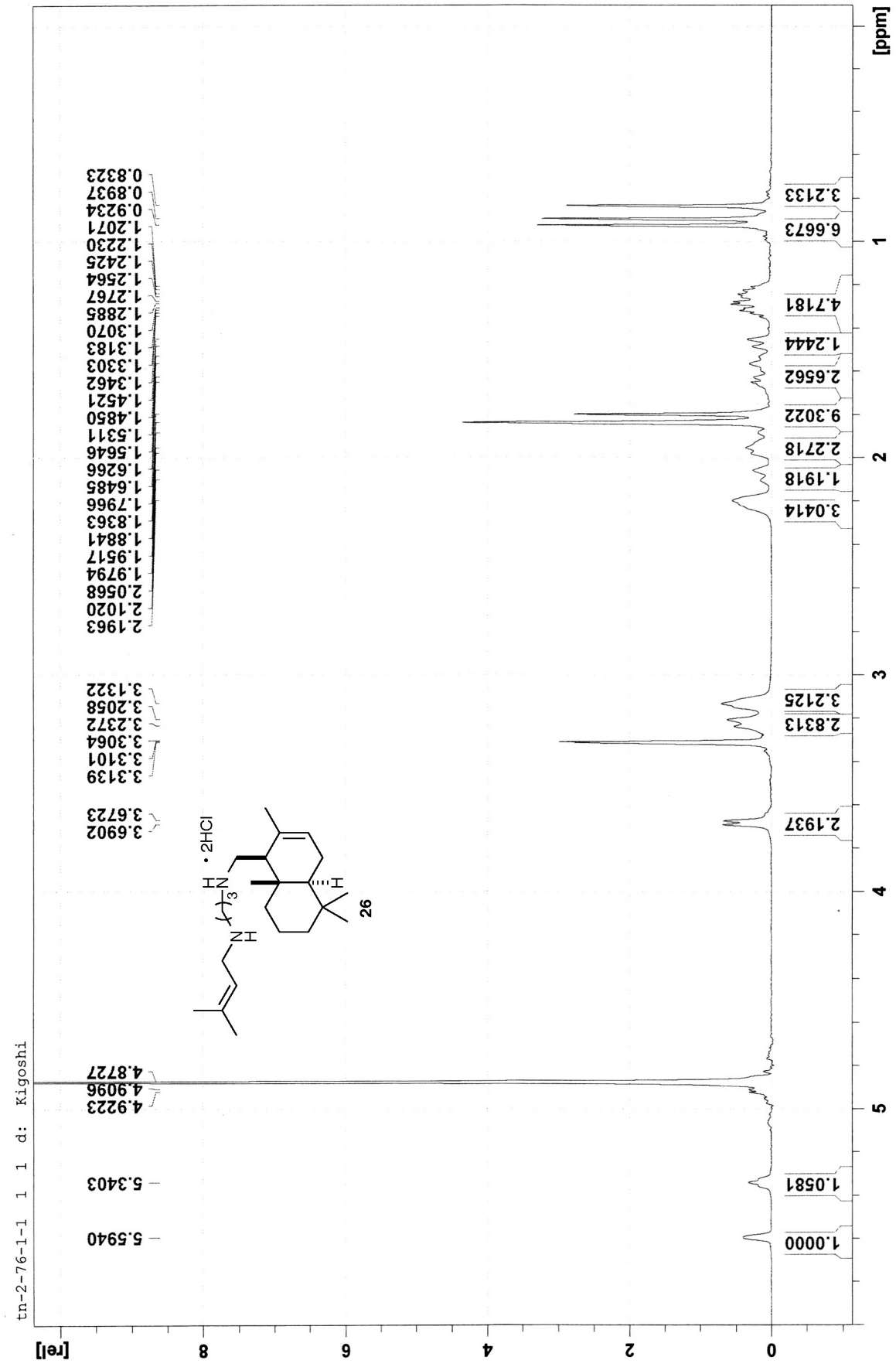
^{13}C NMR spectra of **24** (100 MHz, CD_3OD)



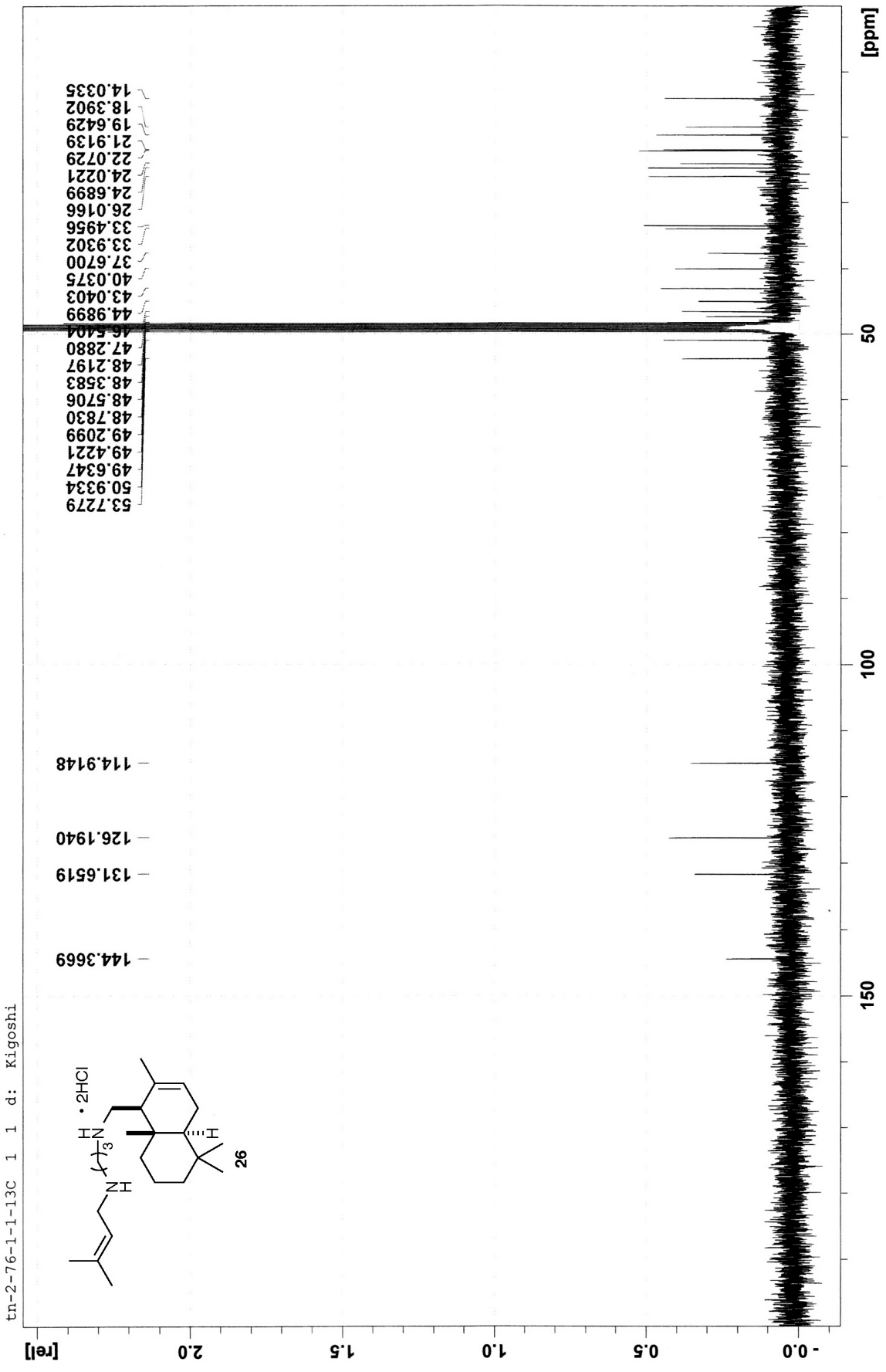
^{1}H NMR spectra of **25** (400 MHz, CD_3OD)



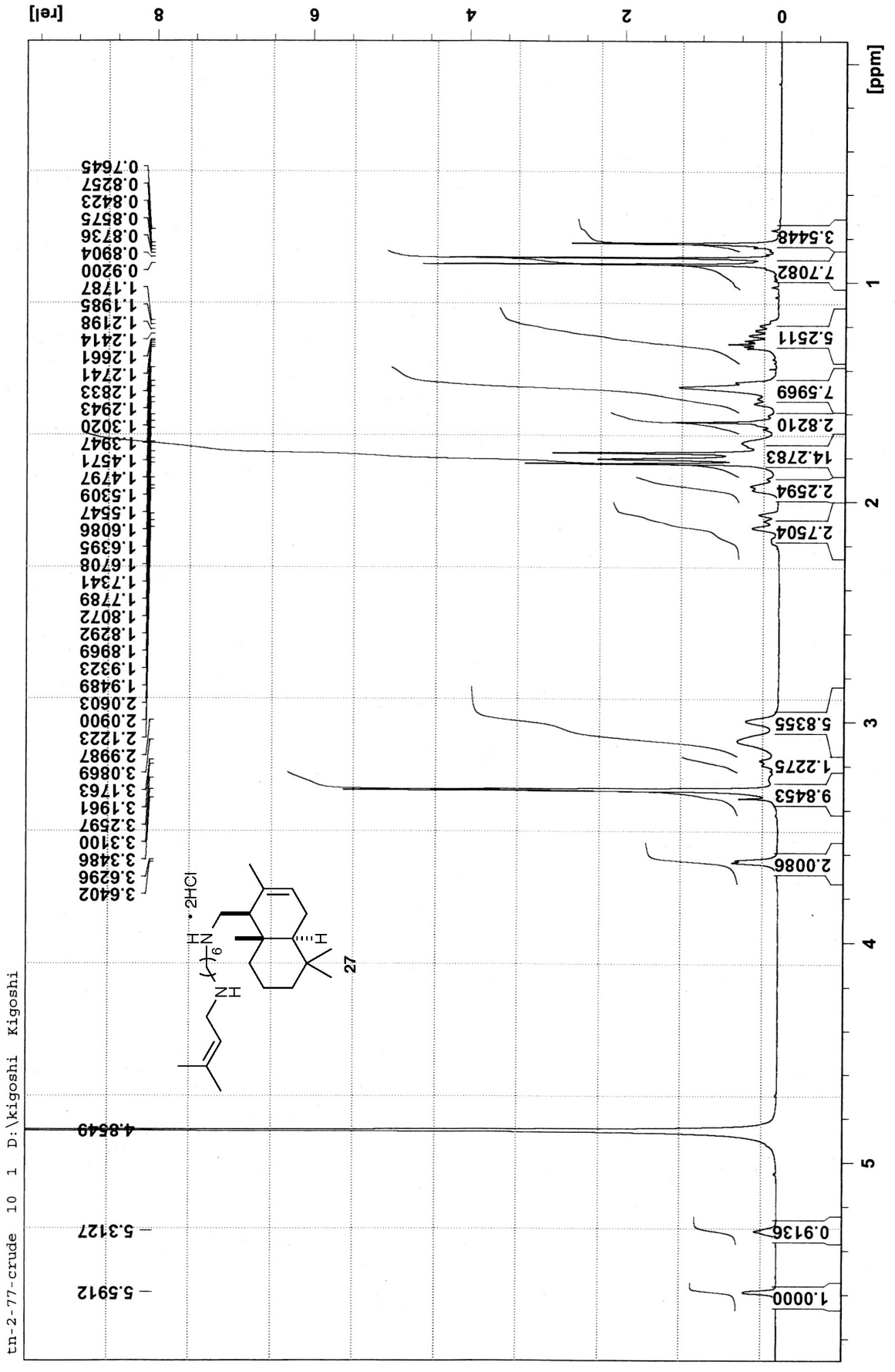
^{13}C NMR spectra of **25** (100 MHz, CD_3OD)



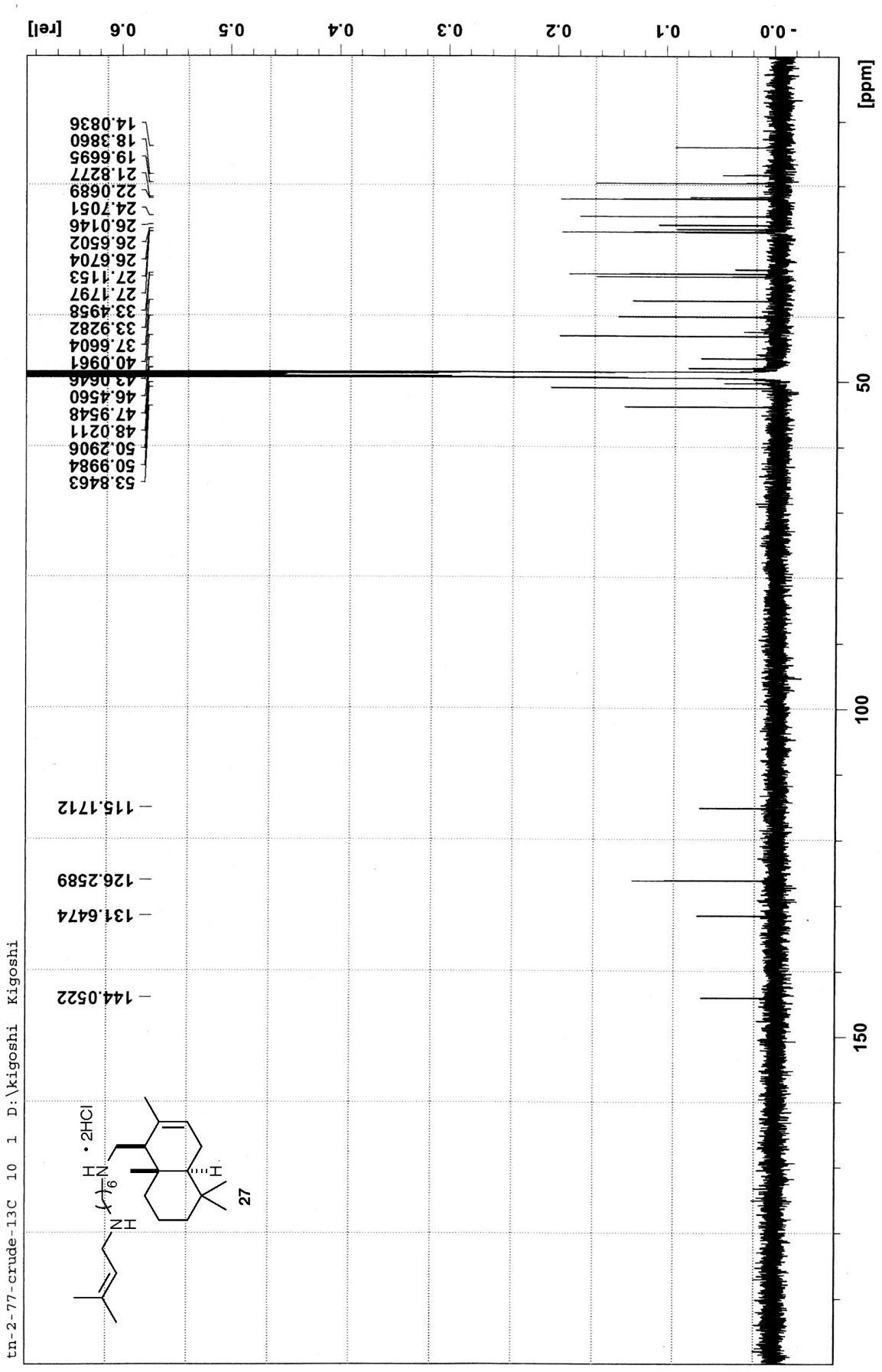
^{1}H NMR spectra of **26** (400 MHz, CD_3OD)



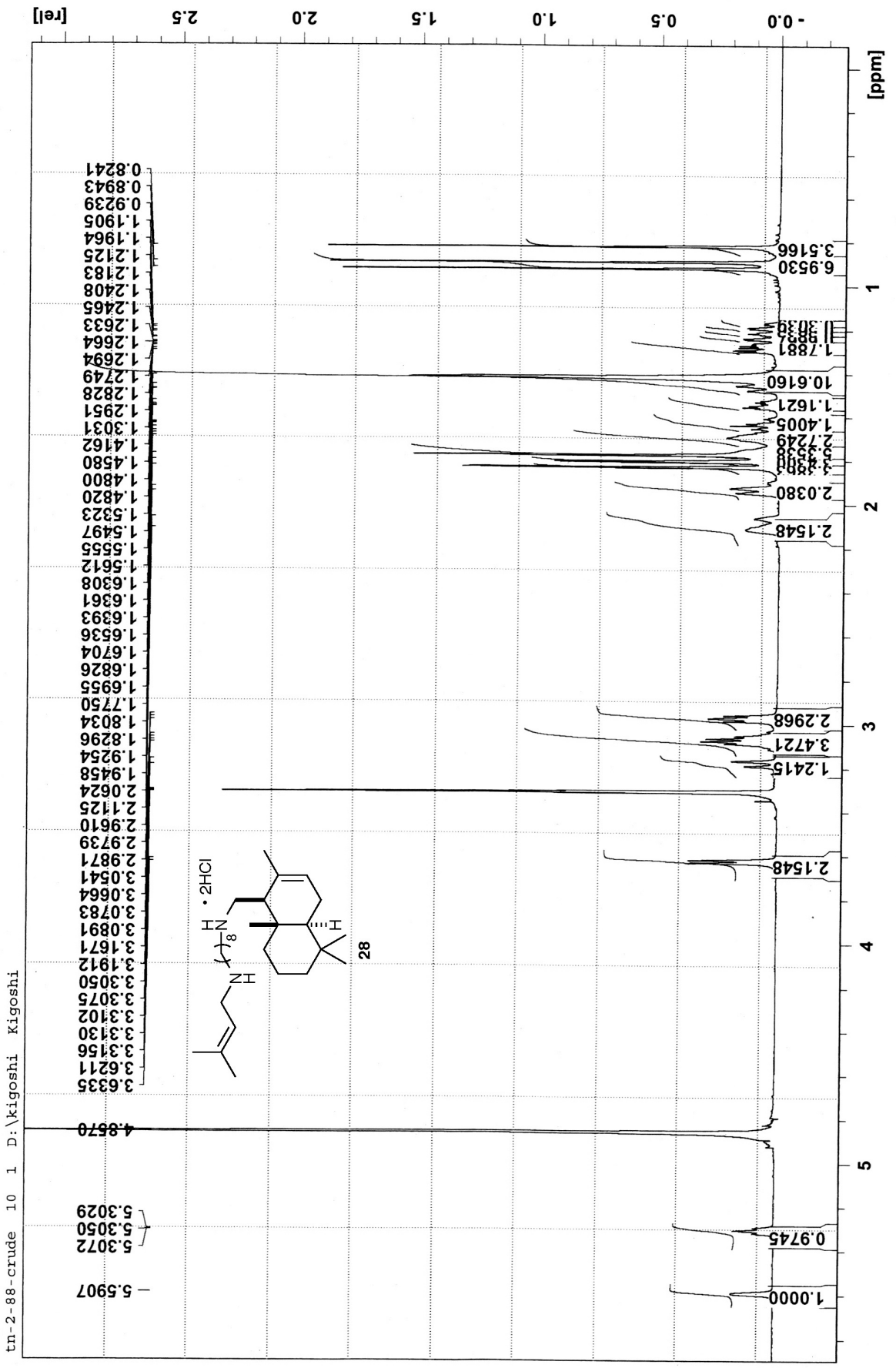
^{13}C NMR spectra of **26** (100 MHz, CD_3OD)



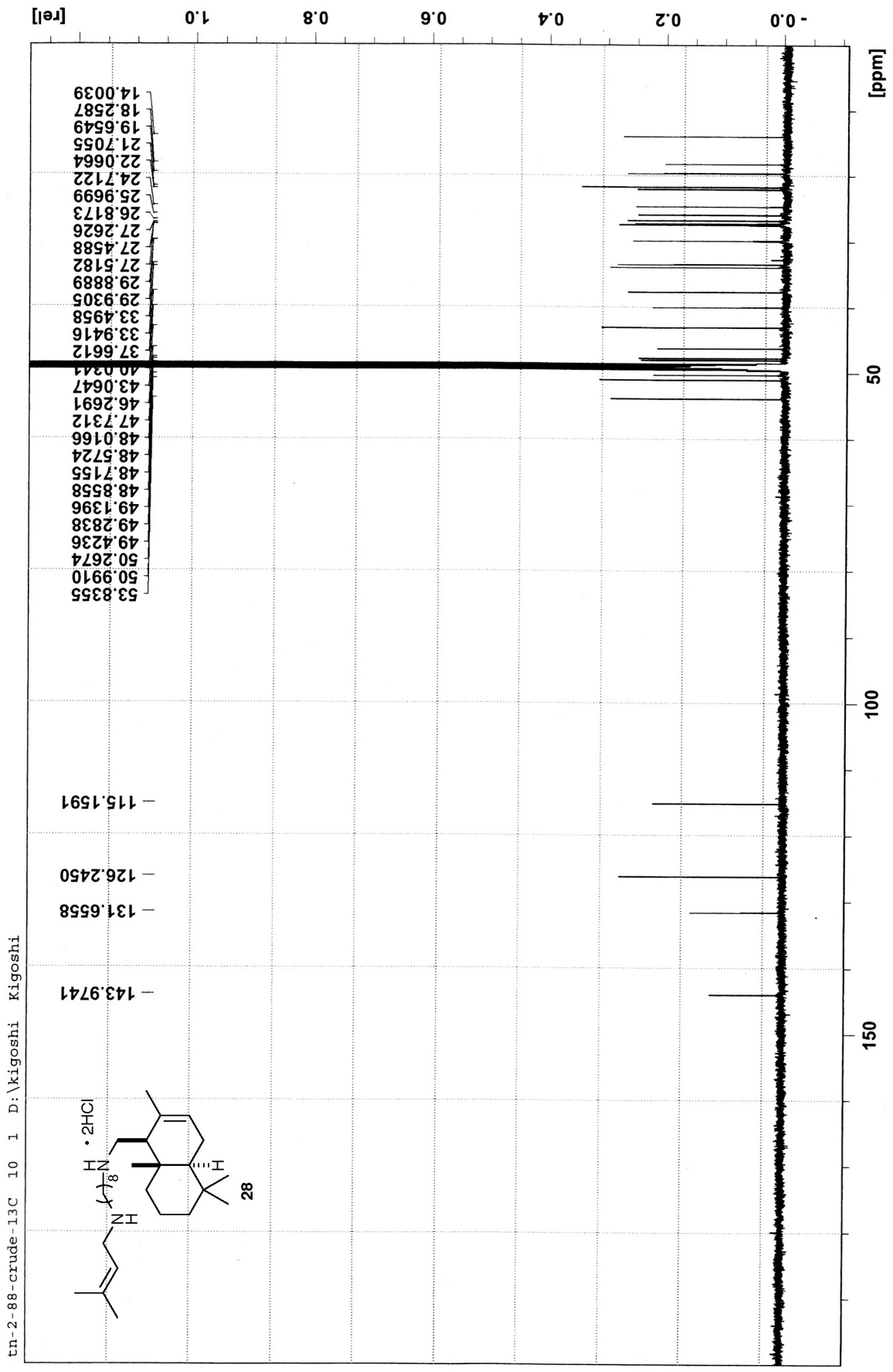
^{1}H NMR spectra of **27** (600 MHz, CD_3OD)



^{13}C NMR spectra of **27** (150 MHz, CD_3OD)



^{1}H NMR spectra of **28** (600 MHz, CD_3OD)



^{13}C NMR spectra of **28** (150 MHz, CD_3OD)