Supporting Information

Stereoselective Synthesis of 2,6-*cis*- and 2,6-*trans*-Piperidines through Organocatalytic Aza-Michael Reactions: A Facile Synthesis of (+)-Myrtine and (–)-Epimyrtine

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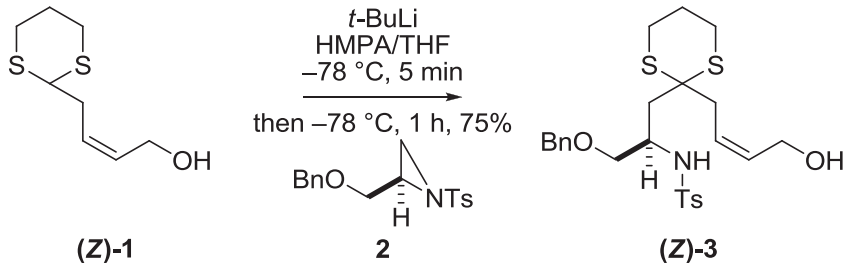
(*Z*)-Allyl Alcohol (*Z*)-3

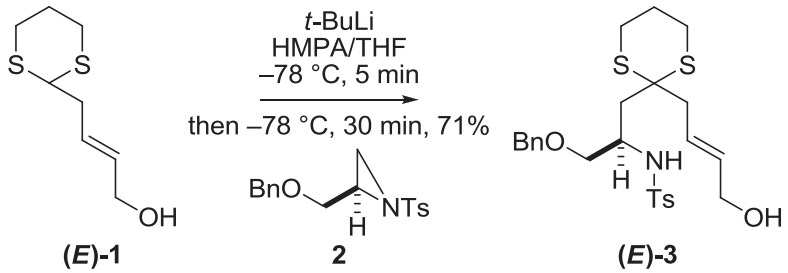


(*Z*)-1 2 (*Z*)-3

To a cooled (–78 ºC) solution of (*Z*)-**1** (100 mg, 0.53 mmol) in HMPA/THF (1:10, 11 mL) was added dropwise *t*-BuLi (0.63 mL, 1.7 M in pentane, 1.07 mmol), and the resulting mixture was stirred for 5 min before aziridine **2**[1] (167 mg, 0.53 mmol) was added. After stirred for 1 h at –78 ºC, the reaction mixture was quenched with saturated aqueous NH_4Cl and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1 to 1/1) to afford (*Z*)-**3** (201 mg, 75%): $[\alpha]^{26}_D$ = +11.5 (*c* 0.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.16–7.36 (m, 7H), 5.74 (ddd, *J* = 11.2, 7.2, 6.4 Hz, 1H), 5.60 (ddd, *J* = 11.2, 7.2, 6.4 Hz, 1H), 5.51 (d, *J* = 8.0 Hz, 1H), 4.29 (AB, J_{AB} = 12.0 Hz, $\Delta\nu_{AB}$ = 14.8 Hz, 2H), 4.15–4.22 (m, 1H), 4.03–4.10 (m, 1H), 3.71–3.78 (m, 1H), 3.36 (dd, *J* = 10.0, 3.2 Hz, 1H), 3.15 (dd, *J* = 10.0, 4.8 Hz, 1H), 2.61–2.83 (m, 5H), 2.55 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.38 (s, 3H), 2.31 (dd, *J* = 15.2, 4.8 Hz, 1H), 2.10 (dd, *J* = 15.6, 6.8 Hz, 1H), 1.77–1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.8, 137.5, 131.8, 129.5, 128.2, 127.7, 127.6, 127.0, 125.5, 72.9, 71.8, 58.2, 51.4, 51.1, 40.0, 36.3, 26.0, 25.8, 24.6, 21.4; IR (neat) 3273, 1156, 1090, 668 cm^{-1}; HRMS (FAB) found 525.1902 [calcd for $C_{25}H_{37}N_2O_4S_3$ $(M+NH_4)^+$ 525.1910].

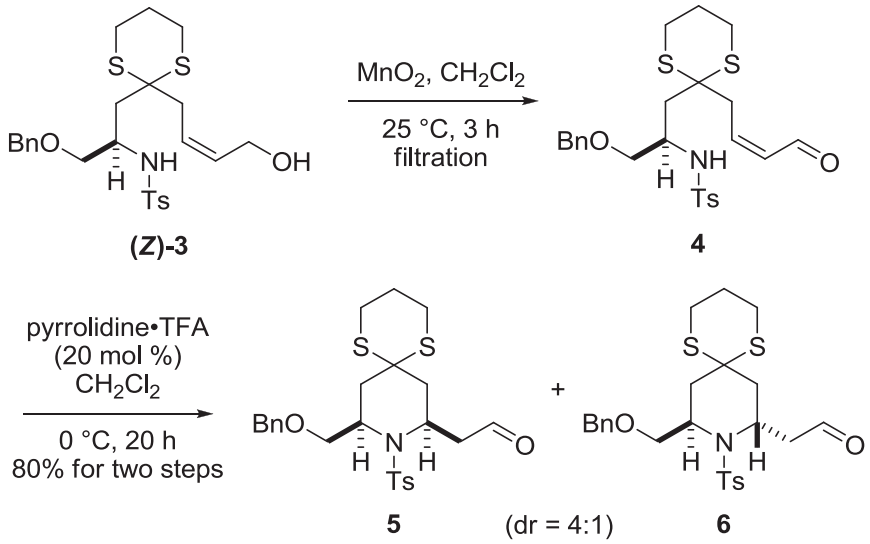
[1]Righi, P; Scardovi, N; Marotta, E; ten Holte, P; Zwanenburg, B. *Org. Lett.* **2002**, *4*, 497–500.

(*E*)-Allyl Alcohol (*E*)-3



To a cooled (–78 ºC) solution of (*E*)-**1** (150 mg, 0.79 mmol) in HMPA/THF (1:10, 11 mL) was added dropwise *t*-BuLi (0.93 mL, 1.7 M in pentane, 1.58 mmol), and the resulting mixture was stirred for 5 min before aziridine **2** (167 mg, 0.53 mmol) was added. After stirred for 0.5 h at –78 ºC, the reaction mixture was quenched with saturated aqueous NH_4Cl and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1 to 1/1) to afford (*E*)-**3** (285 mg, 71%): $[\alpha]^{26}_D$ = +22.5 (*c* 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.20–7.34 (m, 7H), 5.63–5.75 (m, 2H), 5.58 (d, *J* = 8.0 Hz, 1H), 4.29 (AB, J_{AB} = 12.0 Hz, $\Delta\nu_{AB}$ = 18.4 Hz, 2H), 4.04 (d, *J* = 4.4 Hz, 1H), 3.68–3.76 (m, 1H), 3.45 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.22 (dd, *J* = 9.6, 5.2 Hz, 1H), 2.60–2.82 (m, 4H), 2.54 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.43 (dd, *J* = 15.2, 6.4 Hz, 1H), 2.38 (s, 3H), 2.32 (dd, *J* = 15.2, 5.2 Hz, 1H), 2.11 (dd, *J* = 15.6, 6.8 Hz, 1H), 1.76–1.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.8, 137.5, 133.5, 129.5, 128.2, 127.6, 127.0, 125.7, 72.9, 71.8, 63.1, 51.2, 51.0, 41.3, 39.9, 26.0, 25.8, 24.6, 21.4; IR (neat) 3289, 1597, 1326, 1092 cm^{-1}; HRMS (FAB) found 525.1901 [calcd for $C_{25}H_{37}N_2O_4S_3$ $(M+NH_4)^+$ 525.1910].

Secondary Amine-Catalyzed Aza-Michael Reaction

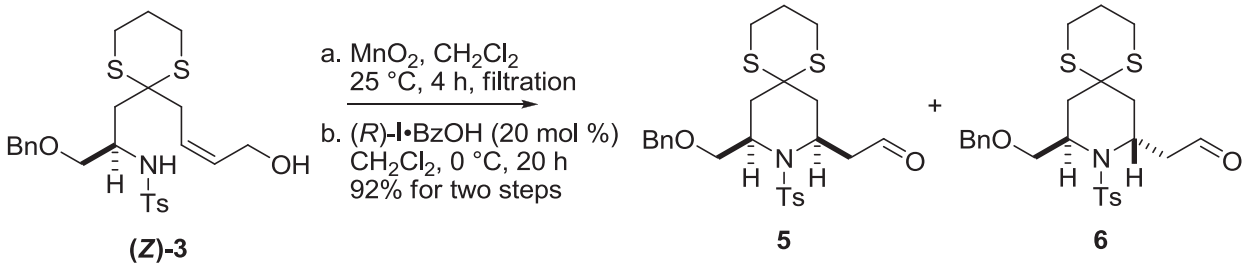


To a stirred solution of (*Z*)-**3** (10.0 mg, 0.0197 mmol) in CH_2Cl_2 (1.0 mL, 0.02 M) was added MnO_2 (34.3mg, 0.394 mmol) at 25 °C. After stirred for 3 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. The crude α,*β*-unsaturated aldehyde **4** was employed in the next step without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.19–7.34 (m, 7H), 6.68 (ddd, *J* = 11.2, 7.2, 4.0 Hz, 1H), 6.01 (ddd, *J* = 11.2, 8.0, 7.6 Hz, 1H), 5.22 (d, *J* = 8.4 Hz, 1H), 4.33 (s, 2H), 3.70 (brs, 1H), 3.41 (dd, *J* = 9.2, 2.8 Hz, 1H), 3.20 (dd, *J* = 9.2, 4.8 Hz, 1H), 3.08 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.96 (dd, *J* = 16.4, 7.2 Hz, 1H), 2.78–2.85 (m, 1H), 2.61–2.72 (m, 3H), 2.38 (s, 3H), 2.36 (dd, *J* = 15.2, 4.8 Hz, 1H), 2.12 (dd, *J* = 15.2, 6.8 Hz, 1H), 1.74–1.96 (m, 2H).

To a stirred solution of α,*β*-unsaturated aldehyde **4** (10.0 mg, 0.0197 mmol) in CH_2Cl_2 (1.0 mL, 0.02 M) was added pyrrolidine·TFA (0.1 mL, 7.3 mg pyrrolidine·TFA dissolved in 1.0 mL CH_2Cl_2) at 0 °C. After stirred for 20 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford an inseparable mixture of 2,6-*cis*-piperidine **5** and 2,6-*trans*-piperidine **6** (8.0 mg, 80%, **5**:**6** = 4:1) as a colorless oil: **[For 5]** $[\alpha]^{28}_D$ = +10.3 (*c* 0.32, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ

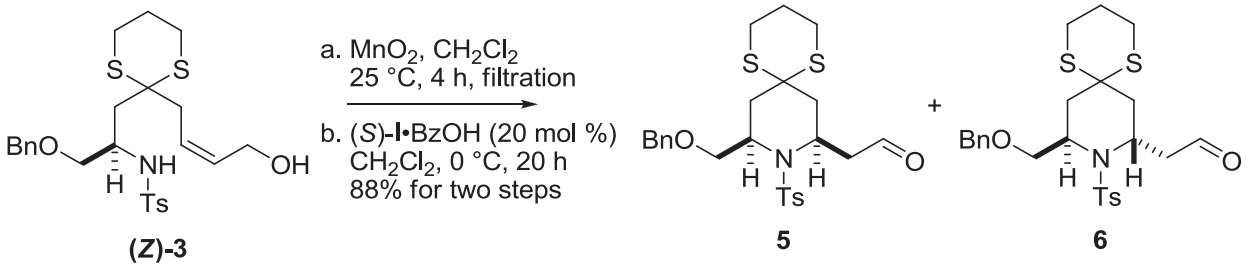
9.72 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.26–7.37 (m, 7H), 4.57 (AB, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 20.4 Hz, 2H), 4.46–4.53 (m, 1H), 4.15–4.22 (m, 1H), 3.97 (dd, J = 8.8, 8.8 Hz, 1H), 3.72 (dd, J = 8.8, 4.4 Hz, 1H), 3.23 (dd, J = 18.0, 8.8 Hz, 1H), 3.08 (dd, J = 18.0, 4.4 Hz, 1H), 2.71–2.86 (m, 4H), 2.51 (dd, J = 15.2, 4.0 Hz, 1H), 2.41 (s, 3H), 2.19 (dd, J = 14.8, 3.6 Hz, 1H), 1.94 (dd, J = 14.8, 6.4 Hz, 1H), 1.83–1.94 (m, 2H), 1.79 (dd, J = 15.2, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 143.7, 137.9, 136.7, 129.8, 128.4, 127.9, 127.7, 127.2, 73.3, 73.0, 51.6, 46.8, 44.3, 38.6, 35.3, 26.8, 26.7, 24.6, 21.5; IR (neat) 1721, 1327, 1098 cm^{-1}; HRMS (FAB) found 506.1482 [calcd for $C_{25}H_{32}NO_4S_3$ $(M+H)^+$ 506.1488]. **[For 6]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.26–7.37 (m, 5H), 7.14 (d, J = 8.8 Hz, 2H), 4.51 (AB, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 24.4 Hz, 2H), 4.37–4.47 (m, 2H), 4.03 (dd, J = 9.6, 7.2 Hz, 1H), 3.77 (dd, J = 10.0, 6.8 Hz, 1H), 3.12 (dd, J = 18.4, 6.4 Hz, 1H), 2.97 (dd, J = 18.4, 8.0 Hz, 1H), 2.72–2.90 (m, 4H), 2.35 (s, 3H), 2.26 (dd, J = 6.4, 5.6 Hz, 2H), 2.21 (d, J = 3.6 Hz, 1H), 2.20 (d, J = 6.8 Hz, 1H), 1.86–2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.9, 143.3, 139.4, 138.0, 129.5, 128.3, 127.8, 127.7, 127.6, 73.0, 70.6, 54.5, 47.7, 47.5, 46.5, 40.7, 37.8, 26.33, 26.29, 24.9, 21.5; IR (neat) 1722, 1326, 1305, 1085 cm^{-1}; HRMS (FAB) found 506.1489 [calcd for $C_{25}H_{32}NO_4S_3$ $(M+H)^+$ 506.1488].

Representative Procedures for Organocatalytic Allylic Oxidation/Aza-Michael Reactions



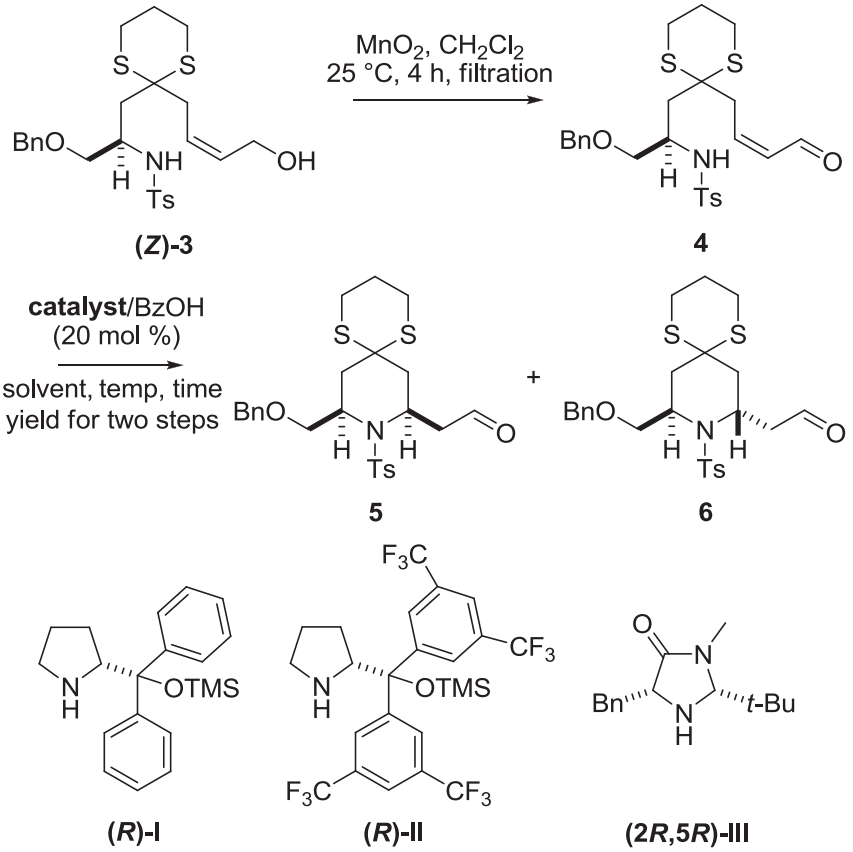
To a stirred solution of (*Z*)-**3** (13.0 mg, 0.0256 mmol) in CH_2Cl_2 (1.5 mL, 0.0171 M) was added MnO_2 (50.6mg, 0.512 mmol) at 25 °C. After stirred for 4 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. To a stirred solution of α,*β*-

unsaturated aldehyde **4** in CH_2Cl_2 (1.0 mL, 0.0256 M) was added (*R*)-**I**·BzOH (2.3 mg, 0.0051 mmol) at 0 °C. After stirred for 20 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford an inseparable mixture of 2,6-*cis*-piperidine **5** and 2,6-*trans*-piperidine **6** (12.1 mg, 92%, **5**:**6** = 11:1) as a colorless oil.



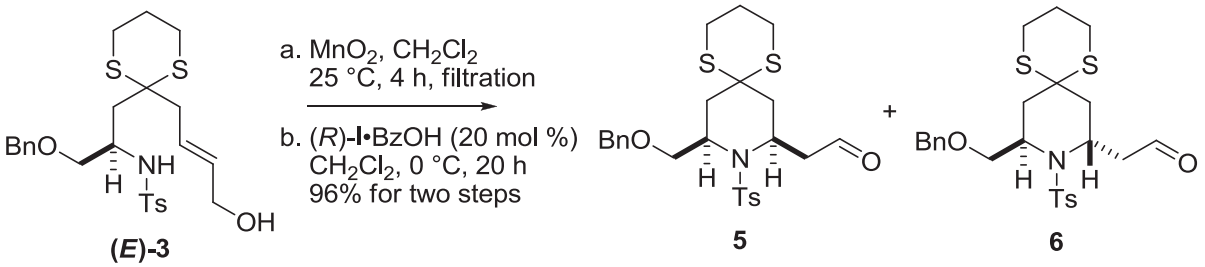
To a stirred solution of (*Z*)-**3** (13.0 mg, 0.0256 mmol) in CH_2Cl_2 (1.5 mL, 0.0171 M) was added MnO_2 (50.6mg, 0.512 mmol) at 25 °C. After stirred for 4 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. To a stirred solution of α,*β*-unsaturated aldehyde **4** in CH_2Cl_2 (1.0 mL, 0.0256 M) was added (*S*)-**I**·BzOH (2.3 mg, 0.0051 mmol) at 0 °C. After stirred for 20 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford an inseparable mixture of 2,6-*cis*-piperidine **5** and 2,6-*trans*-piperidine **6** (11.5 mg, 88%, **5**:**6** = 1:3) as a colorless oil.

Optimization of Reaction Conditions

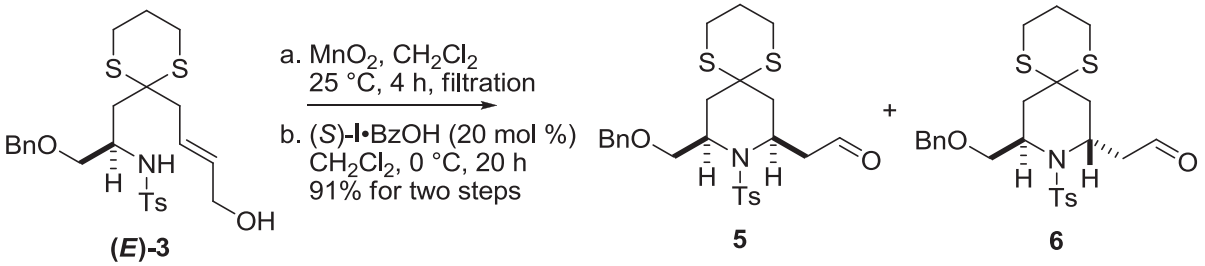


entry	catalyst	solvent	temp (ºC)	time (h)	yield (%)[a]	dr[b]
1	**(*R*)-I**	CH_2Cl_2	0	20	92	11:1
2	**(*R*)-II**	CH_2Cl_2	0	20	92	11:1
3	**(2*R*,5*R*)-III**	CH_2Cl_2	0	24	73	4:1
4	**(*R*)-I**	toluene	0	20	94	9:1
5	**(*R*)-I**	ether	0	48	45	4.5:1
6	**(*R*)-I**	MeOH	0	48	86	4:1
7	**(*R*)-I**	MeCN	0	48	86	4.5:1
8	**(*R*)-I**	DMF	0	72	28	4:1
9	**(*R*)-I**	THF	0	72	NR[c]	NA[d]
10	**(*R*)-I**	dioxane	25	72	NR[c]	NA[d]

[a] Combined yield of **5** and **6**. [b] Diastereomeric ratio (**5**:**6**) determined by integration of the ^{1}H NMR spectrum of the crude product. [c] No reaction. [d] Not applicable

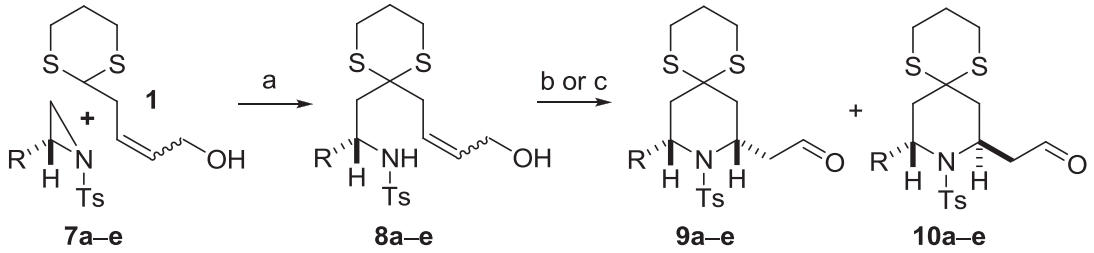


To a stirred solution of (*E*)-**3** (23.0 mg, 0.0453 mmol) in CH_2Cl_2 (1.5 mL, 0.0302 M) was added MnO_2 (89.6 mg, 0.906 mmol) at 25 °C. After stirred for 4 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. To a stirred solution of α,*β*-unsaturated aldehyde intermediate in CH_2Cl_2 (2.0 mL, 0.0227 M) was added (*R*)-**I**·BzOH (4.0 mg, 0.0091 mmol) at 0 °C. After stirred for 20 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford an inseparable mixture of 2,6-*cis*-piperidine **5** and 2,6-*trans*-piperidine **6** (22.0 mg, 96%, **5**:**6** = 15:1) as a colorless oil.



To a stirred solution of (*E*)-**3** (23.0 mg, 0.0453 mmol) in CH_2Cl_2 (1.5 mL, 0.0302 M) was added MnO_2 (89.6 mg, 0.906 mmol) at 25 °C. After stirred for 4 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. To a stirred solution of α,*β*-unsaturated aldehyde intermediate in CH_2Cl_2 (2.0 mL, 0.0227 M) was added (*S*)-**I**·BzOH (4.0 mg, 0.0091 mmol) at 0 °C. After stirred for 20 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford an inseparable mixture of 2,6-*cis*-piperidine **5** and 2,6-*trans*-piperidine **6** (21.0 mg, 91%, **5**:**6** = 1:5) as a colorless oil.

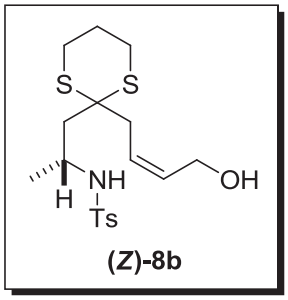
Substrate Scope of the Organocatalytic Aza-Michael Reaction



entry	R	allyl alcohol (yield)	Reaction conditions (time)[a]	major product (yield[b])	dr[c]
1	OBn	**(*Z*)-8a** (75%)	b (24 h)	**9a** (91%)	11:1
			c (24 h)	**10a** (82%)	1:3
		(*E*)-8a (81%)	b (20 h)	**9a** (93%)	15:1
			c (20 h)	**10a** (86%)	1:5
2	Me	**(*Z*)-8b** (60%)	b (7 h)	**9b** (90%)	>15:1
			c (10 h)	**10b** (75%)	1:2
		(*E*)-8b (66%)	b (7 h)	**9b** (97%)	>20:1
			c (9 h)	**10b** (80%)	1:4
3	*i*-Pr	**(*Z*)-8c** (30%)	b (45 h)	**9c** (78%)	10:1
			c (64 h)	**10c** (78%)	1:8
		(*E*)-8c (50%)	b (45 h)	**9c** (87%)	12:1
			c (67 h)	**10c** (79%)	1:10
4	$CH=CH_2$	**(*Z*)-8d** (30%)	b (15 h)	**9d** (90%)	15:1
			c (18 h)	**10d** (86%)	1:1
5	*t*-Bu	**(*Z*)-8e** (14%)	b (24 h)	NR[d]	NA[e]
			c (24 h)	NR[d]	

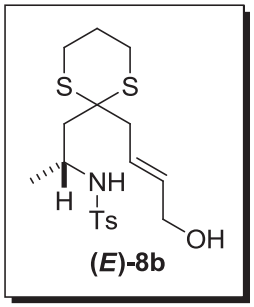
[a] *Reagents and conditions*: (a) *t*-BuLi, HMPA/THF (1:10), –78 °C, 5 min, then, **7a**–**e**,[2] –78 °C, 0.5–1 h, 14–81%; (b) MnO_2, CH_2Cl_2, 25 °C, 3 h, filtration; (*S*)-**I**·BzOH (20 mol %), CH_2Cl_2, 0 °C; (c) i. MnO_2, CH_2Cl_2, 25 °C, 3 h, filtration; ii. (*R*)-**I**·BzOH (20 mol %), CH_2Cl_2, 0 °C. [b] Combined yield of **9** and **10**. [c] Diastereomeric ratio (2,6-*cis*-piperidine:2,6-*trans*-piperidine) determined by integration of the ^1H NMR spectrum of the crude product. [d] No reaction. [e] Not applicable.

[2](a) Lapinsky, D. J; Bergmeier, S. C. *Tetrahedron Lett.* **2001**, *42*, 8583–8586. (b) Vicario, J. L; Badia, D; Carrillo, L. *ARKIVOC* **2007**, 304–311.



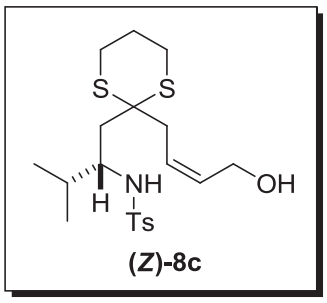
(*Z*)-8b

A colorless oil: $[\alpha]^{27}_{D} = -1.7$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.71 (ddd, *J* = 11.2, 7.2, 6.4 Hz, 1H), 5.66 (d, *J* = 6.4 Hz, 1H), 5.53 (ddd, *J* = 10.8, 7.2, 6.4 Hz, 1H), 4.15 (dd, *J* = 12.4, 7.6 Hz, 1H), 4.03 (dd, *J* = 12.4, 6.4 Hz, 1H), 3.52–3.62 (m, 1H), 2.62–2.80 (m, 5H), 2.46–2.52 (m, 1H), 2.36 (s, 3H), 2.12 (dd, *J* = 15.2, 8.0 Hz, 1H), 1.87 (dd, *J* = 15.2, 4.0 Hz, 1H), 1.78–1.94 (m, 2H), 1.00 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.8, 131.8, 129.5, 127.1, 125.6, 58.2, 51.2, 47.4, 44.6, 36.2, 26.0, 24.5, 23.0, 21.4; IR (neat) 3279, 1320, 1158, 668 cm^{-1}; HRMS (FAB) found 419.1491 [calcd for $C_{18}H_{31}N_2O_3S_3$ $(M+NH_4)^+$ 419.1491].



(*E*)-8b

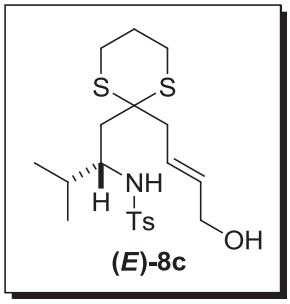
A colorless oil: $[\alpha]^{28.0}_{D} = -14.9$ (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 5.76 (d, *J* = 6.4 Hz, 1H), 5.60–5.73 (m, 2H), 4.07 (br s, 2H), 3.51–3.61 (m, 1H), 2.68–2.82 (m, 4H), 2.54 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.38–2.48 (m, 2H), 2.39 (s, 3H), 2.19 (dd, *J* = 15.2, 7.6 Hz, 1H), 1.79–1.96 (m, 3H), 1.08 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.7, 133.5, 129.5, 127.2, 125.6, 63.0, 51.0, 47.4, 44.6, 41.3, 26.0, 24.6, 23.1, 21.4; IR (neat) 3280, 1321, 1158, 1090, 668 cm^{-1}; HRMS (FAB) found 419.1487 [calcd for $C_{18}H_{31}N_2O_3S_3$ $(M+NH_4)^+$ 419.1491].



(*Z*)-8c

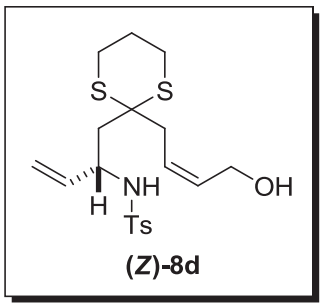
A colorless oil: $[\alpha]^{22}_{D} = -3.1$ (*c* 0.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 5.77 (ddd, *J* = 11.2, 7.2, 6.4 Hz, 1H), 5.58 (ddd, *J* = 11.2, 7.2, 6.0 Hz, 1H), 5.32 (d, *J* = 6.8 Hz, 1H), 4.18–4.24 (m, 1H), 4.04–4.10 (m, 1H), 3.56–3.62 (m, 1H), 2.69–2.81 (m, 5H), 2.56 (dd, *J* = 16.0, 5.6 Hz, 1H), 2.40 (s, 3H), 2.28 (br s, 1H), 1.82–1.99 (m, 5H), 0.80 (d, *J* = 7.2 Hz, 3H), 0.70 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 138.3, 131.9, 129.5, 127.1, 125.9, 58.3, 55.9,

51.3, 37.1, 36.0, 31.3, 26.2, 26.1, 24.6, 21.5, 18.2, 15.9; IR (neat) 3288, 1320, 1157, 1092, 668 cm^{-1}; HRMS (FAB) found 447.1793 [calcd for $C_{20}H_{35}N_2O_3S_3$ $(M+NH_4)^+$ 447.1804].



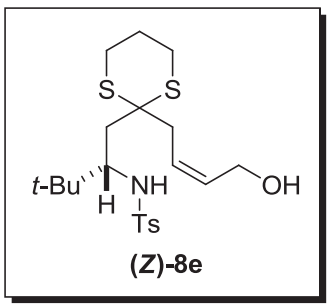
(*E*)-8c

A colorless oil: $[\alpha]^{28}_D$ = –9.5 (*c* 1.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 5.62–5.75 (m, 2H), 5.51 (d, *J* = 7.2 Hz, 1H), 4.08 (br s, 2H), 3.50–3.56 (m, 1H), 2.67–2.82 (m, 4H), 2.56 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.43 (dd, *J* = 14.0, 4.8 Hz, 1H), 2.39 (s, 3H), 1.84–2.01 (m, 5H), 0.79 (d, *J* = 7.2 Hz, 3H), 0.70 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 138.1, 133.3, 129.4, 127.1, 126.0, 63.1, 55.8, 51.1, 40.9, 37.6, 31.4, 26.1, 26.0, 24.6, 21.4, 18.0, 16.1; IR (neat) 3280, 1318, 1155, 666 cm^{-1}; HRMS (FAB) found 447.1793 [calcd for $C_{20}H_{35}N_2O_3S_3$ $(M+NH_4)^+$ 447.1804].



(*Z*)-8d

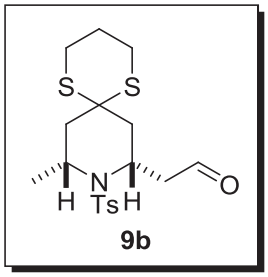
A colorless oil: $[\alpha]^{28}_D$ = +7.3 (*c* 0.48, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 5.78 (ddd, *J* = 11.6, 7.2, 5.2 Hz, 1H), 5.48–5.65 (m, 3H), 4.92 (d, *J* = 17.6 Hz, 1H), 4.86 (d, *J* = 10.0 Hz, 1H), 4.17–4.25 (m, 1H), 4.04–4.12 (m, 1H), 2.70–2.91 (m, 5H), 2.55 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.39 (s, 3H), 2.27 (dd, *J* = 15.2, 8.0 Hz, 1H), 2.03 (dd, *J* = 15.2, 4.4 Hz, 1H), 1.94–2.02 (m, 2H), 1.82–1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 138.1, 137.6, 132.0, 129.4, 127.5, 125.6, 116.3, 58.3, 54.4, 51.2, 42.7, 36.6, 26.2, 26.1, 24.7, 21.5; IR (neat) 3270, 1324, 1158, 1093, 668 cm^{-1}; HRMS (FAB) found 431.1482 [calcd for $C_{19}H_{31}N_2O_3S_3$ $(M+NH_4)^+$ 431.1491].



(*Z*)-8e

A colorless oil: $[\alpha]^{27}_D$ = –5.0 (*c* 0.14, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.77–5.83 (m, 1H), 5.67 (ddd, *J* = 12.0, 6.4, 5.6 Hz, 1H), 4.73 (d, *J* = 8.4 Hz, 1H), 4.16–4.26 (m, 1H), 4.07–4.16 (m, 1H), 3.77 (ddd, *J* = 9.2, 9.2, 1.6 Hz, 1H), 2.93 (dd, *J* = 17.2, 8.0 Hz, 1H), 2.70–2.86 (m, 5H),

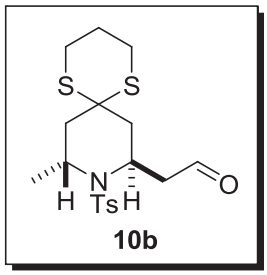
2.39 (s, 3H), 2.26 (dd, *J* = 15.6, 1.6 Hz, 1H), 2.09 (s, 1H), 1.89–1.99 (m, 2H), 1.89 (dd, *J* = 15.2, 10.0 Hz, 1H), 0.80 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 139.8, 131.4, 129.2, 127.0, 126.9, 60.7, 58.3, 51.8, 39.4, 36.5, 35.4, 27.0, 26.29, 26.25, 24.8, 21.5; IR (neat) 1653, 1153 cm^{-1}; HRMS (FAB) found 461.1962 [calcd for $C_{21}H_{33}N_2O_3S_3$ $(M+NH_4)^+$ 461.1961].



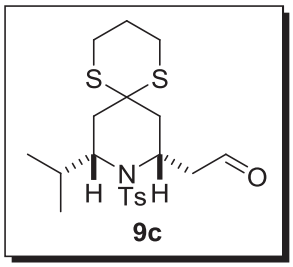
9b

An inseparable mixture (**9b**:**10b** > 20:1): $[\alpha]^{25}_D$ = +15.7 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.70 (d, *J* = 6.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.47–4.53 (m, 1H), 4.06–4.17 (m, 1H), 3.41 (dd, *J* = 18.0, 9.6 Hz, 1H), 3.17 (dd, *J* = 18.4, 4.8 Hz, 1H), 2.65–2.89 (m, 4H), 2.41(s, 3H), 2.35 (dd, *J* =15.2, 4.4 Hz, 1H), 1.82–2.03 (m, 5H), 1.54 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 143.5, 136.8, 129.8, 127.1, 51.3, 48.2, 47.1, 44.4, 41.3, 38.0, 26.8, 26.7, 24.8, 24.6, 21.5; IR (neat) 1720, 1160 cm^{-1}; HRMS (FAB) found 400.1067 [calcd for $C_{18}H_{26}NO_3S_3$ $(M+H)^+$ 400.1069].

An inseparable mixture (**9b**:**10b** = 1:4): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 4.74–4.81 (m, 1H), 3.98–4.08 (m, 1H), 3.13–3.27 (m, 2H), 2.68–2.95 (m, 4H), 2.41(s, 3H), 2.36 (dd, *J* =14.8, 5.6 Hz, 1H), 2.26 (dd, *J* =14.4, 4.4 Hz, 1H), 2.13 (dd, *J* =14.4, 4.0 Hz, 1H), 1.84–2.04 (m, 3H), 1.38 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 143.3, 139.9, 129.6, 127.0, 49.1, 48.5, 47.5, 47.1, 43.2, 39.8, 26.4, 26.3, 25.0, 21.5, 20.2.



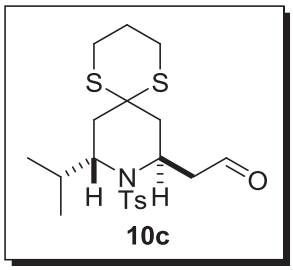
10b



9c

A colorless crystal: $[\alpha]^{27}_D$ = +69.6 (*c* 0.43, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.18–4.24 (m, 1H), 3.65–3.70 (m, 1H), 3.41 (dd, *J* = 18.4, 7.2 Hz, 1H), 2.89–3.01 (m, 2H), 2.87 (dd, *J* = 18.4, 8.0 Hz, 1H), 2.59–2.70 (m, 2H), 2.42 (s, 3H), 2.30 (dd, *J* = 14.0, 9.6 Hz, 1H), 2.20 (dd, *J* =

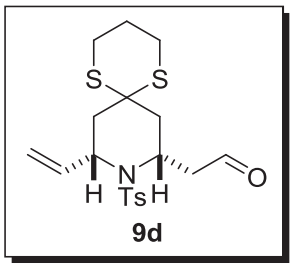
15.2, 2.0 Hz, 1H), 2.07 (dd, *J* = 14.8, 6.0 Hz, 1H), 1.92–2.00 (m, 1H), 1.72–1.82 (m, 1H), 1.43 (dd, *J* = 15.6, 6.4 Hz, 1H), 1.09 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 143.6, 136.6, 129.8, 127.4, 59.7, 50.9, 47.3, 44.4, 37.5, 36.5, 33.0, 27.0, 26.7, 24.5, 21.5, 20.9, 20.6; IR (neat) 1720, 1598, 1338, 1326, 1095 cm^{-1}; HRMS (FAB) found 428.1385 [calcd for $C_{20}H_{30}NO_3S_3$ $(M+H)^+$ 428.1381].



10c

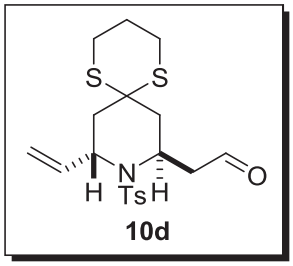
A colorless crystal: $[\alpha]^{23}_D$ = –9.10 (*c* 0.083, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 4.36–4.43 (m, 1H), 3.57–3.62 (m, 1H), 3.34 (dd, *J* = 18.4, 4.4 Hz, 1H), 3.24 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.81–2.95 (m, 2H), 2.54–2.66 (m, 2H), 2.42 (s, 3H), 2.31 (dd, *J* = 15.2, 9.6 Hz, 2H), 1.99–2.06 (m, 3H), 1.82–1.92 (m, 1H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.80 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.9, 143.5, 139.1, 129.6, 127.5, 63.2, 48.4, 47.5, 46.7, 40.7, 36.3, 29.6, 26.3, 25.0, 21.6, 20.7; IR (neat) 1724, 1155, 754 cm^{-1}.

An inseparable mixture (**9d**:**10d** = 15:1): $[\alpha]^{25}_D$ = +22.6 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz,



9d

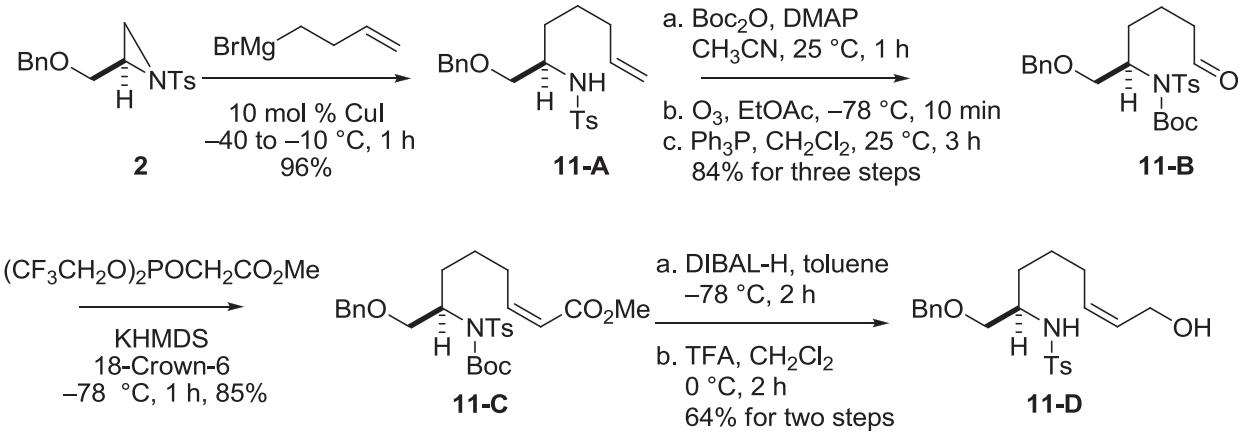
$CDCl_3$) δ 9.78 (s, 1H), 7.73 (d, *J* = 8.4 Hz, 2H),), 7.31 (d, *J* = 8.4 Hz, 2H), 6.07 (dddd, *J* = 16.8, 10.4, 5.6, 4.8 Hz, 1H), 5.39 (dd, *J* = 16.8, 2.0 Hz, 1H), 5.23 (dd, *J* = 10.4, 2.0 Hz, 1H), 4.44–4.57 (m, 2H), 3.35 (dd, *J* = 18.4, 4.0 Hz, 1H), 3.21 (dd, *J* = 18.0, 9.6 Hz, 1H), 2.80–2.93 (m, 2H), 2.62–2.71 (m, 2H), 2.43 (s, 3H), 2.31 (dd, *J* = 14.4, 6.4 Hz, 1H), 2.18 (dd, *J* = 15.2, 4.8 Hz, 2H), 1.93–2.00 (m, 1H), 1.80–1.87 (m, 1H), 1.76 (dd, *J* = 15.2, 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4, 143.8, 140.2, 136.5, 129.8, 127.4, 116.6, 53.5, 51.5, 47.7, 44.2, 40.5, 37.7, 27.0, 26.9, 24.5; IR (neat) 1721, 1325, 1162, 1094 cm^{-1}; HRMS (FAB) found 412.1070 [calcd for $C_{19}H_{26}NO_3S_3$ $(M+H)^+$ 412.1069].



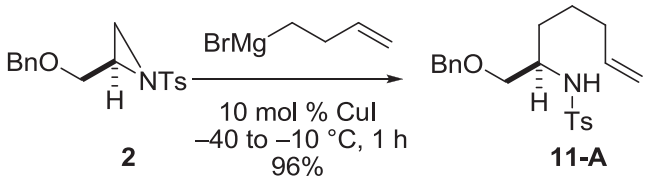
10d

An inseparable mixture (**9d**:**10d** = 1:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 2H),), 7.27 (d, *J* = 8.4 Hz, 2H), 5.96 (dddd, *J* = 16.8, 10.0, 5.2, 4.8 Hz, 1H), 5.25 (d, *J* = 10.4 Hz, 1H), 5.12 (d, *J* = 10.0 Hz, 1H), 4.58–4.64 (m, 2H), 3.27 (dd, *J* = 18.0, 6.4 Hz, 1H), 3.10 (dd, *J* = 18.4, 8.0 Hz, 1H), 2.80–2.93 (m, 2H), 2.71–2.79 (m, 2H), 2.41 (s, 3H), 2.22–2.30 (m, 2H), 2.20 (d, *J* = 3.2 Hz, 1H), 2.16 (d, *J* = 3.2 Hz, 1H), 1.95–2.04 (m, 1H), 1.78–1.88 (m, 1H).

Preparation of Allyl Alcohol 11-D



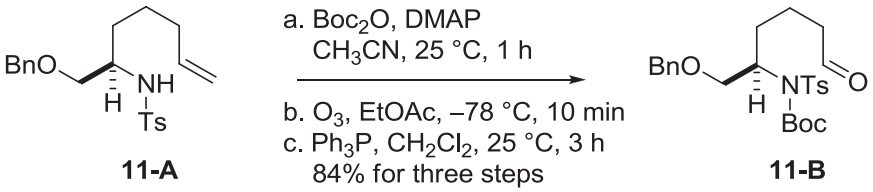
Preparation of Alkene 11-A



To a cooled (–40 ºC) solution of 3-butene magnesium bromide (0.13 M, 15 mL) in THF (15 mL, 0.13 M) was added CuI (18 mg, 0.095 mmol) and aziridine **2** (300 mg, 0.95 mmol). The resulting mixture was warmed to –10 ºC, stirred at –10 ºC for 1 h, and quenched with 4 mL NH_4Cl/NH_4OH (3:1). After stirred at 25 ºC for 2 h, the reaction mixture was diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined

organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford alkene **11-A** (340 mg, 96%): $[\alpha]^{26}_D$ = +18.1 (*c* 0.68, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.8 Hz, 2H), 7.17–7.34 (m, 7H), 5.68 (dddd, *J* = 17.2, 10.4, 6.8, 2.8 Hz, 1H), 4.97 (d, *J* = 8.4 Hz, 1H), 4.91 (d, *J* = 17.2 Hz, 1H), 4.90 (d, *J* = 9.2 Hz, 1H), 4.33 (s, 2H), 3.27–3.36 (m, 2H), 3.20 (dd, *J* = 9.6, 4.8 Hz, 1H), 2.39 (s, 3H), 1.93 (q, *J* = 6.8 Hz, 2H), 1.43–1.58 (m, 2H), 1.18–1.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 138.2, 138.1, 137.7, 129.5, 128.3, 127.6, 127.5, 126.9, 114.6, 73.0, 71.2, 53.4, 33.2, 31.9, 24.7, 21.4; IR (neat) 1640, 1598, 1453, 1416, 1323, 1157, 1090, 1022 cm^{-1}.

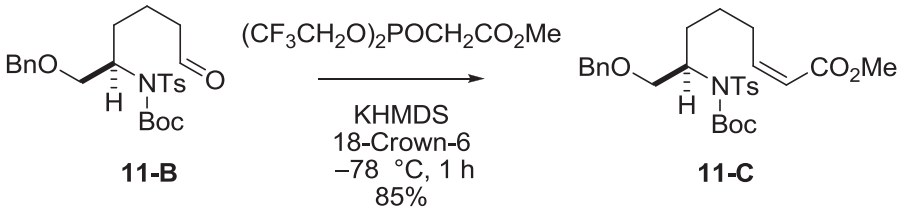
Preparation of Aldehyde 11-B



To a stirred solution of alkene **11-A** (297 mg, 0.795 mmol) in CH_3CN (15 mL, 0.053 M) was added Boc_2O (208 mg, 0.954 mmol) and DMAP (19 mg, 0.159 mmol) at 25 ºC. After stirred at 25 ºC for 1 h, the reaction mixture was concentrated and purified by purified by column chromatography (silica gel, hexanes/EtOAc, 10/1) to afford Boc-protected alkene (340 mg, 96%). To a cooled (–78 ºC) solution of the known Boc protected alkene (300 mg, 0.634 mmol) in EtOAc (50 mL, 0.013 M) was bubbled O_3 until blue color was persisted (ca. 10 min). After purging the reaction with N_2 gas, EtOAc was removed and the residue was dissolved in CH_2Cl_2 (10 mL) before Ph_3P was added. The resulting mixture was stirred at 25 ºC for 3 h and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 4/1) to afford aldehyde **11-B** (260 mg, 84% for three steps): ^{1}H NMR (400

MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.85 (d, J = 8.4 Hz, 2H), 7.21–7.30 (m, 5H), 7.05 (d, J = 8.0 Hz, 2H), 4.75–4.82 (m, 1H), 4.49 (AB, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 45.6 Hz, 2H), 3.97 (t, J = 9.6 Hz, 1H), 3.58 (dd, J = 10.0, 5.6 Hz, 1H), 2.44–2.57 (m, 2H), 1.94–2.04 (m, 1H), 1.58–1.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 150.5, 143.5, 137.8, 137.6, 128.7, 128.27, 128.25, 127.8, 127.5, 84.1, 73.0, 70.5, 58.1, 43.2, 29.7, 27.8, 21.5, 19.0.

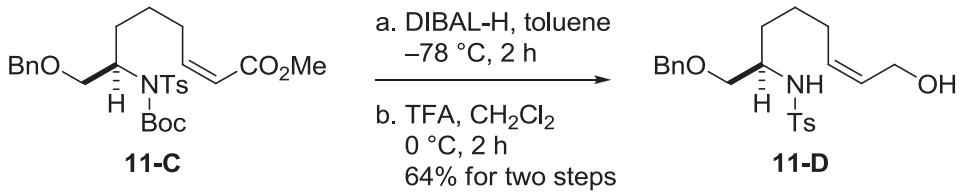
Preparation of Aldehyde 11-C



To a cooled (–78 ºC) solution of methyl bis(2,2,2-trifluoroethyl)phosphonoacetate (0.23 mL, 1.06 mmol) and 18-crown-6 (1.4 g, 5.3 mmol) in THF (30 mL, 0.035 M) was added KHMDS (0.5 M, 2.1 mL). After stirred at the same temperature for 0.5 h, aldehyde **11-B** (250 mg, 0.53 mmol) was added to the reaction mixture. After stirred for 1 h at –78 ºC, the reaction mixture was quenched with saturated aqueous NH_4Cl and diluted with EtOAc. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 8/1 to 4/1) to afford enoate **11-C** (236 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 6.4 Hz, 2H), 7.22–7.30 (m, 5H), 7.05 (d, J = 8.4 Hz, 2H), 6.22 (ddd, J = 11.2, 7.2, 4.4 Hz, 1H), 5.78 (ddd, J = 11.2, 2.0, 2.0 Hz, 1H), 4.75–4.83 (m, 1H), 4.49 (AB, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 47.6 Hz, 2H), 3.98 (dd, J = 9.6, 9.6 Hz, 1H), 3.69 (s, 3H), 3.57 (dd, J = 10.0, 5.6 Hz, 1H), 2.69–2.75 (m, 2H), 2.35 (s, 3H), 1.93–2.03 (m, 1H), 1.53–1.67 (m, 3H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 150.5, 150.0, 143.4,

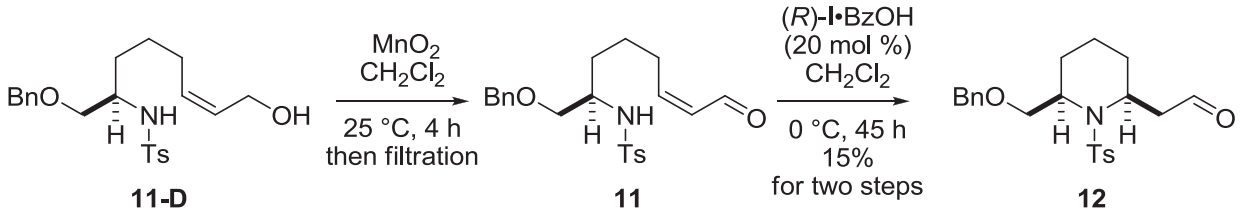
137.9, 137.7, 128.7, 128.3, 128.2, 127.8, 127.5, 119.6, 84.0, 72.9, 70.6, 58.4, 50.9, 29.9, 28.6, 27.8, 25.8, 21.5.

Preparation of Allylic Alcohol 11-D



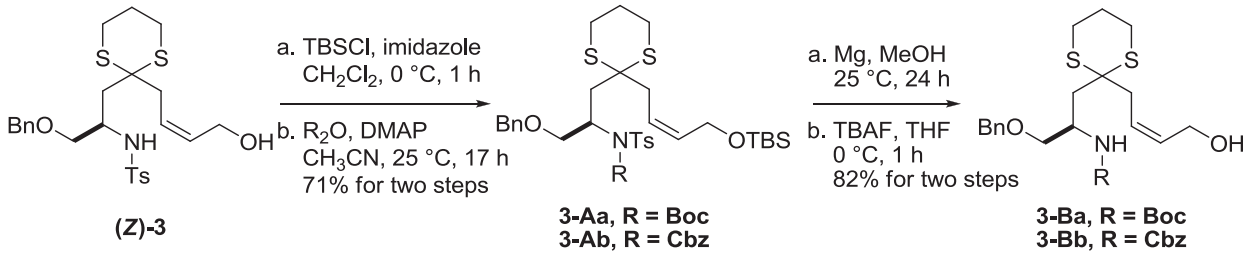
[DIBAL-H Reduction] To a cooled (–78 ºC) solution of enoate **11-C** (230 mg, 0.433 mmol) in toluene (8 mL, 0.054 M) was added DIBAL-H (1.73 mL, 1.0 M in toluene, 1.732 mmol). After stirred at the same temperature for 2 h, the reaction mixture was quenched with MeOH, and diluted with Et_2O. The resulting mixture was stirred for 5 h at 25 ºC, filtered through a pad of celite and concentrated *in vacuo*. This crude alcohol was employed in the next step without purification. **[Boc-Deprotection]** To the crude Boc-sulfonamide (105 mg, 0.21 mmol) in CH_2Cl_2 (4.2 mL) was added TFA (0.8 mL) at 0 ºC. After stirred at the same temperature for 2 h, the reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica gel, hexanes/EtOAc, 1/1) to afford **11-D** (54 mg, 64% for two steps) as a colorless oil: $[\alpha]^{26}_{D} = +8.5$ (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.18–7.35 (m, 7H), 5.58 (ddd, *J* = 12.8, 6.8, 6.0 Hz, 1H), 5.40 (ddd, *J* = 15.2, 10.4, 7.2 Hz, 1H), 5.02 (d, *J* = 8.4 Hz, 1H), 4.32 (s, 2H), 4.13 (d, *J* = 6.8 Hz, 2H), 3.28–3.38 (m, 1H), 3.28 (dd, *J* = 9.2, 4.0 Hz, 1H), 3.16 (dd, *J* = 8.8, 4.4 Hz, 1H), 2.40 (s, 3H), 2.17 (s, 1H), 1.92–2.06 (m, 2H), 1.44–1.58 (m, 2H), 1.21–1.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 138.0, 137.6, 132.1, 129.5, 128.8, 128.3, 127.7, 127.6, 126.9, 73.1, 71.1, 58.3, 53.3, 31.8, 26.7, 25.3, 21.4; IR (neat) 1598, 1453, 1323, 1157, 1091, 1024 cm^{-1}.

Allylic Oxidation/Aza-Michael Reaction of 11-D



[Allylic Oxiation] To a stirred solution of **11-D** (41 mg, 0.102 mmol) in CH_2Cl_2 (3.0 mL, 0.0331 M) was added MnO_2 (196.3 mg, 1.986 mmol) at 25 °C. After stirred for 4 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. This crude α,*β*-unsaturated aldehyde **11** (40 mg, 0.0998 mmol) was employed in the next step without purification. **[Aza-Michael Reaction]** To a stirred solution of α,*β*-unsaturated aldehyde **11** in CH_2Cl_2 (4.0 mL, 0.0248 M) was added (*R*)-**I**·BzOH (8.9 mg, 0.0197 mmol) at 0 °C. After stirred for 45 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel, hexanes/EtOAc, 3/1) to afford 2,6-*cis*-piperidine **12** as the major diastereomer (6 mg, 15% for two steps, dr = 11:1) as a colorless oil: **[For 11]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.19–7.34 (m, 8H), 6.51 (ddd, *J* = 11.2, 8.0, 3.2 Hz, 1H), 5.94 (dd, *J* = 11.2, 8.0 Hz, 1H), 4.76 (d, *J* = 8.8 Hz, 1H), 4.33 (brs, 2H), 3.30–3.39 (m, 1H), 3.26 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.14 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.51–2.57 (m, 2H), 2.41 (s, 3H); **[For 12]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71(s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.26–7.38 (m, 7H), 4.56 (d, *J* = 4.0 Hz, 2H), 4.18–4.25 (m, 1H), 3.61 (d, *J* = 8.0 Hz, 1H), 3.59 (d, *J* = 5.6 Hz, 1H), 2.76 (dd, *J* = 17.2, 5.6 Hz, 1H), 2.64 (ddd, *J* = 17.2, 8.8, 1.6 Hz, 1H), 2.42 (s, 3H), 1.80 (d, *J* = 12.8 Hz, 2H), 1.17–1.56 (m, 6H).

Preparation of Allyl Alcohols 3-Ba and 3-Bb



(*Z*)-3

3-Aa, R = Boc
3-Ab, R = Cbz

3-Ba, R = Boc
3-Bb, R = Cbz

To a stirred solution of sulfonamide **(*Z*)-3** (200 mg, 0.39 mmol) in CH_2Cl_2 (3 mL, 0.13 M) was added TBSCl (66 mg, 0.437 mmol) and imidazole (80 mg, 1.18 mmol) at 0 ºC. After stirred at 0 ºC for 1 h, the reaction mixture was concentrated and purified by purified by column chromatography (silica gel, hexanes/EtOAc, 10/1) to afford the corresponding TBS-protected allyl alcohol (210 mg, 86%). To a stirred solution of the TBS-protected allyl alcohol (105 mg, 0.17 mmol) in CH_3CN (6 mL, 0.03 M) was added Boc_2O (55 mg, 0.253 mmol) and DMAP (5 mg, 0.04 mmol) at 25 ºC. After stirred at 25 ºC for 17 h, the reaction mixture was concentrated and purified by purified by column chromatography (silica gel, hexanes/EtOAc, 10/1) to afford **3-Aa** (100 mg, 71% for two steps): **[For 3-Aa]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.0 Hz, 2H), 7.18–7.25 (m, 5H), 7.02 (d, J = 7.2 Hz, 2H), 5.64 (ddd, J = 12.0, 6.0, 5.6 Hz, 1H), 5.55 (ddd, J = 12.0, 6.8, 5.6 Hz, 1H), 5.03 (brs, 1H), 4.44 (AB, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 60.8 Hz, 2H), 4.21 (d, J = 6.0 Hz, 2H), 3.64 (dd, J = 9.6, 5.6 Hz, 1H), 2.87 (d, J = 11.2 Hz, 2H), 2.53–2.79 (m, 4H), 2.23–2.37 (m, 1H), 2.29 (s, 3H), 1.90–1.97 (m, 1H), 1.75–1.84 (m, 1H), 1.22 (s, 9H), 0.82 (s, 9H), 0.00 (s, 6H).

Cbz-protected sulfonamide **3-Ab** was prepared from **(*Z*)-3** in the same manner in 71% for two steps. **[For 3A-b]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 2H), 7.17–7.26 (m, 6H), 7.11 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 7.2 Hz, 2H), 6.88 (d, J = 7.2 Hz, 2H), 5.62 (ddd, J = 11.6, 5.6, 5.2 Hz, 1H), 5.50 (ddd, J = 12.0, 6.8, 5.6 Hz, 1H), 4.91–5.05 (m, 1H), 4.48 (d, J = 12.0 Hz,

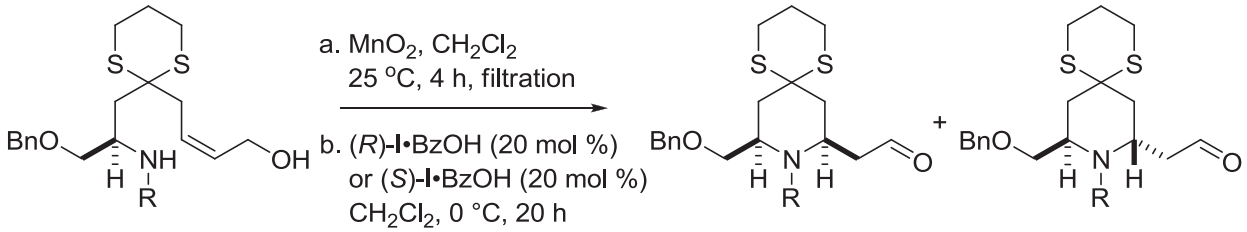
1H), 4.33 (s, 1H), 4.19 (d, *J* = 5.6 Hz, 2H), 3.59 (dd, *J* = 9.6, 5.2 Hz, 1H), 2.54–2.80 (m, 7H), 2.23–2.31 (m, 1H), 2.24 (s, 3H), 1.74–1.90 (m, 2H), 0.83 (s, 9H), 0.00 (s, 6H).

To a stirred solution of Boc-protected sulfonamide **3-Aa** (65mg, 0.09 mmol) in CH_3OH (3 mL, 0.03M) was added Mg powder (66mg, 2.7 mmol) and NH_4Cl (49 mg, 0.9 mmol) at room temperature. After stirring at room temperature for 24h, the reaction mixture was diluted with water and then extracted three times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 10/1) to afford the corresponding Boc-protected amine (44 mg, 86%). To a stirred solution of the Boc-protected amine (42mg, 0.074 mmol) in THF (3 mL, 0.025M) was added TBAF (1.0 M in THF, 0.11 mL) at 0 ºC. After stirring at 0 ºC for 1h, the reaction mixture was quenched with sat. NH_4Cl and then extracted three times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 2/1) to afford **3-Ba** (32 mg, 82% for two steps): **[For 3-Ba]** $[\alpha]^{21}_D$ = +9.0 (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.38 (m, 5H), 5.80 (ddd, *J* = 12.4, 6.8, 5.6 Hz, 1H), 5.69 (ddd, *J* = 12.4, 7.2, 5.2 Hz, 1H), 4.95 (d, *J* = 8.0 Hz, 1H), 4.18 (brs, 2H), 4.00–4.09 (m, 1H), 3.59 (brs, 1H), 3.45 (brs, 1H), 2.68–2.88 (m, 6H), 2.50 (s, 1H), 2.36 (dd, *J* = 14.8, 4.0 Hz, 1H), 2.02 (dd, *J* = 14.8, 7.2 Hz, 1H), 1.87–1.99 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 138.0, 131.8, 128.4, 127.7, 126.0, 79.6, 73.1, 72.9, 58.3, 51.4, 47.5, 40.1, 36.0, 28.4, 26.2, 26.1, 24.9. IR (neat) 1695, 1506, 1455, 1366, 1390, 1252, 1170, 1050 cm^{-1}; HRMS (FAB) found 454.2080 [calcd for $C_{23}H_{36}NO_4S_2$ $(M+H)^+$ 454.2080].

Cbz-protected allyl alcohol **3-Bb** was prepared from **3-Bb** in the same manner in 82% for two steps. **[For 3-Bb]** $[\alpha]^{27}_D$ = +18.6 (*c* 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.35 (m, 9H), 5.78 (ddd, *J* = 12.4, 7.2, 5.2 Hz, 1H), 5.68 (ddd, *J* = 12.4, 6.4, 5.6 Hz, 1H), 5.28 (d, *J* = 8.8

Hz, 1H), 5.10 (br s, 2H), 4.51 (s, 2H), 4.09–4.19 (m, 3H), 3.60 (dd, J = 8.8, 2.4 Hz, 1H), 3.47 (dd, J = 8.8, 4.0 Hz, 1H), 2.72–2.85 (m, 6H), 2.42 (s, 1H), 2.34 (dd, J = 15.2, 4.4 Hz, 1H), 2.08 (dd, J = 15.2, 7.6 Hz, 1H), 1.86–1.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 137.8, 136.4, 131.8, 128.4, 128.3, 128.0, 127.7, 125.9, 73.1, 72.6, 66.7, 58.3, 51.3, 48.2, 40.0, 36.1, 26.2, 26.1, 24.8. IR (neat) 1699, 1520, 1268, 1238, 1052 cm^{-1}; HRMS (FAB) found 488.1921 [calcd for $C_{26}H_{34}NO_4S_2$ $(M+H)^+$ 488.1924].

Aza-Michael Reaction with 3-Ba and 3-Bb



3-Ba, R = Boc
3-Bb, R = Cbz

3-Ca, R = Boc
3-Cb, R = Cbz

3-Da, R = Boc
3-Db, R = Cbz

entry	R	catalyst	yield (%)[a]	dr[b]
1	Ts	(*R*)-**I**	92	11:1
2	Ts	(*S*)-**I**	88	1:3
3	Boc	(*R*)-**I**	80	8:1
4	Boc	(*S*)-**I**	70	4:1
5	Cbz	(*R*)-**I**	67	20:1
6	Cbz	(*S*)-**I**	61	2:1

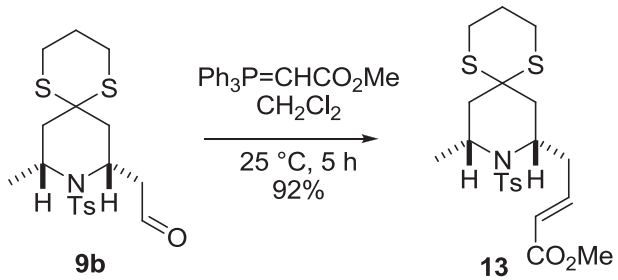
[a]Combined yield of **3-C** and **3-D**. [b]Diastereomeric ratio (2,6-*cis*-piperidine:2,6-*trans*-piperidine) determined by integration of the ^{1}H NMR spectrum of the crude product.

To a stirred solution of **3-Ba** (10 mg, 0.022 mmol) in CH_2Cl_2 (1.0 mL, 0.02 M) was added MnO_2 (220 mg, 0.55 mmol) at 25 °C. After stirred for 4 h at the same temperature, the reaction mixture was then filtered through celite and concentrated *in vacuo*. To a stirred solution of α,*β*-unsaturated aldehyde intermediate (9 mg, 0.02 mmol) in CH_2Cl_2 (1.0 mL, 0.02 M) was added (*R*)-**I**·BzOH (1.8 mg, 0.004 mmol) at 0 °C. After stirred for 20 h at the same temperature, the reaction mixture was concentrated and purified by column chromatography (silica gel,

hexanes/EtOAc, 3/1) to afford 2,6-*cis*- piperidine **3-Ca** as the major diastereomer (8 mg, 80% for two steps, **3-Ca**:**3-Da** = 8:1, Entry 3) as a colorless oil: **[For 3-Ca]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (t, *J* = 1.6 Hz, 1H), 7.27–7.37 (m, 5H), 4.67 (ddd, *J* = 14.4, 7.6, 6.4 Hz, 1H), 4.54 (AB, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 30.8 Hz, 2H), 4.47 (ddd, *J* = 14.0, 7.6, 5.6 Hz, 1H), 3.67 (dd, *J* = 9.6, 6.8 Hz, 1H), 3.48 (dd, *J* = 9.2, 4.8 Hz, 1H), 2.80–2.94 (m, 4H), 2.73 (dd, *J* = 16.4, 5.6 Hz, 1H), 2.56 (dd, *J* = 15.6, 7.2 Hz, 1H), 2.34 (dd, *J* = 14.4, 8.0 Hz, 1H), 2.22 (dd, *J* = 14.8, 5.2 Hz, 1H), 1.90–2.04 (m, 3H), 1.42 (s, 9H); HRMS (FAB) found 452.1924 [calcd for $C_{23}H_{34}NO_4S_2$ $(M+H)^+$ 452.1924].

2,6-*cis*-piperidine **3-Cb** was prepared as the major diastereomer from **13-Bb** in the same manner in 67% for two steps (**3-Cb**:**3-Db** = 20:1, Entry 5): **[For 3-Cb]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (t, *J* = 1.6 Hz, 1H), 7.27–7.36 (m, 10H), 5.14 (s, 2H), 4.75 (ddd, *J* = 14.8, 7.6, 7.2 Hz, 1H), 4.51–4.58 (m, 1H), 4.51 (AB, J_{AB} = 12.4 Hz, $\Delta\nu_{AB}$ = 30.4 Hz, 2H), 3.66 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.48 (dd, *J* = 9.6, 5.2 Hz, 1H), 2.72–2.96 (m, 5H), 2.62 (ddd, *J* = 14.4, 8.0, 2.0 Hz, 1H), 2.36 (ddd, *J* = 14.8, 8.4, 1.6 Hz, 1H), 2.19 (dd, *J* = 14.4, 5.6 Hz, 1H), 1.88–2.04 (m, 3H); HRMS (FAB) found 486.1766 [calcd for $C_{26}H_{32}NO_4S_2$ $(M+H)^+$ 486.1767].

Preparation of (*E*)-Enoate 13

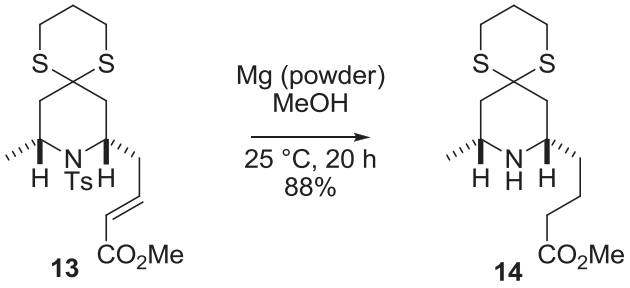


9b **13**

To a solution of aldehyde **9b** (104.8 mg, 0.262 mmol) in CH_2Cl_2 (4 mL) was added methyl 2-(triphenylphosphoranylidene)acetate at 25 ºC, and the resulting mixture was stirred at the same temperature for 5 h before concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 10/1) to afford (*E*)-enoate **13** (119.5 mg, 92%) as a

colorless oil: $[\alpha]^{25}_{D}$ = +42.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 6.91 (ddd, *J* = 16.0, 7.5, 7.5 Hz, 1H), 5.90 (d, *J* = 15.5 Hz, 1H), 4.03–4.12 (m, 2H), 3.73 (s, 3H), 2.96 (ddd, *J* = 14.5, 8.5, 8.5 Hz, 1H), 2.68–2.84 (m, 5H), 2.17 (dd, *J* = 15.5, 4.5 Hz, 1H), 2.05 (dd, *J* = 15.0, 5.0 Hz, 1H),1.94 (dd, *J* = 14.5, 6.5 Hz, 1H), 1.82–1.91 (m, 3H), 1.50 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 145.0, 144.3, 136.7, 129.5, 127.0, 123.7, 51.6, 51.4, 48.0, 44.3, 40.9, 40.3, 37.5, 26.77, 26.69, 24.47, 24.44, 21.4; IR (neat) 2947, 1716, 1158 cm^{-1}; HRMS (ESI) found 456.1328 [calcd for $C_{21}H_{30}NO_4S_3$ $(M+H)^+$ 456.1331].

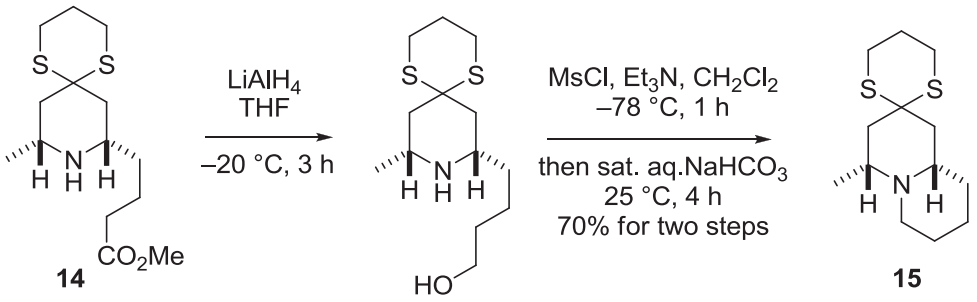
Preparation of Ester 14



To a solution of (*E*)–enoate **13** (102.0 mg, 0.224 mmol) in anhydrous MeOH (4 mL) was added Mg powder (272.0 mg, 11.2 mmol) at 25 ºC. After stirred at the same temperature for 20 h, the reaction mixture was diluted with diethyl ether and saturated aqueous $NaHCO_3$. The resulting cloudy mixture was stirred vigorously for 1 h, filtered through a pad of Celite, concentrated *in vacuo*, and partitioned between CH_2Cl_2 and H_2O. The layers were separated, and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 10/1 to 5:1) to give ester **14** as a colorless oil (60.0 mg, 88%): $[\alpha]^{28}_{D}$ = +31.5 (*c* 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.11 (ddddd, *J* = 12.8, 6.8, 6.8, 6.8, 2.8 Hz, 1H), 2.99 (dddd, *J* = 13.2, 6.8, 6.8, 2.4 Hz, 1H), 2.86

(dd, J = 6.4, 4.8 Hz, 2H), 2.73 (dd, J = 6.0, 6.0 Hz, 2H), 2.29 (dd, J = 7.6, 7.6 Hz, 2H), 2.20–2.29 (m, 2H), 1.91–1.99 (m, 2H), 1.62–1.71 (m, 2H), 1.34–1.43 (m, 4H), 1.06 (d, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 51.5, 48.8, 47.3, 45.5, 43.4, 35.7, 33.9, 26.00, 25.86, 25.63, 22.0, 21.2; IR (neat) 2930, 1730 cm^{-1}; HRMS (ESI) found 304.1394 [calcd for $C_{14}H_{26}NO_2S_2$ $(M+H)^+$ 304.1399].

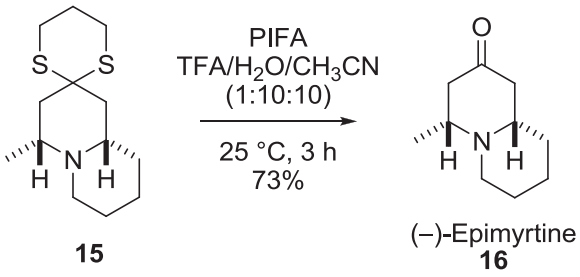
Preparation of Quinolizidine 15



[$LiAlH_4$-Reduction] To a cooled (–20 ºC) solution of ester **14** (60.0 mg, 0.198 mmol) in anhydrous THF (6 mL) was added $LiAlH_4$ (0.2 mL, 2.0 M in THF, 0.4 mmol). After stirred at the same temperature for 3 h, the reaction mixture was quenched with MeOH and diluted with THF (20 mL) and saturated aqueous $NaHCO_3$. The resulting cloudy mixture was stirred vigorously for 2 h, filtered through a pad of Celite, and concentrated *in vacuo* to afford crude alcohol, which was employed in next step without further purification. **[Cyclization]** To a cooled (–78 ºC) solution of crude alcohol in CH_2Cl_2 (10 mL) were added Et_3N (0.14 mL, 0.99 mmol) and MsCl (2.38 mL, 0.1 M in CH_2Cl_2, 0.24 mmol). The reaction mixture was allowed to warm to –20 ºC for 1 h and quenched with saturated aqueous $NaHCO_3$. The resulting mixture was allowed to warm to 25 ºC over 4 h with continuous stirring. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc only) to give quinolizidine **15** as a colorless oil (35.4 mg,

70% for two steps): $[\alpha]^{25}_{D} = -21.4$ (*c* 0.57, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.22 (br d, *J* = 11.5 Hz, 1H), 2.83–2.87 (m, 2H), 2.72–2.75 (m, 2H), 2.49–2.53 (m, 1H), 2.32 (dd, *J* = 9.5, 9.5 Hz, 2H), 2.19 (ddd, *J* = 14.0, 2.0, 2.0 Hz, 1H), 2.15 (ddd, *J* = 14.5, 3.0, 3.0 Hz, 1H), 1.93–1.99 (m, 2H), 1.64–1.83 (m, 5H), 1.50–1.57 (m, 2H), 1.22–1.34 (m, 2H), 1.09 (d, *J* = 5.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 57.6, 53.8, 51.1, 48.2, 46.1, 45.0, 33.1, 26.21, 26.04, 25.97, 25.69, 24.3, 20.0; IR (neat) 2930, 1423 cm^{-1}; HRMS (ESI) found 258.1347 [calcd for $C_{13}H_{24}NS_2$ $(M+H)^+$ 258.1344].

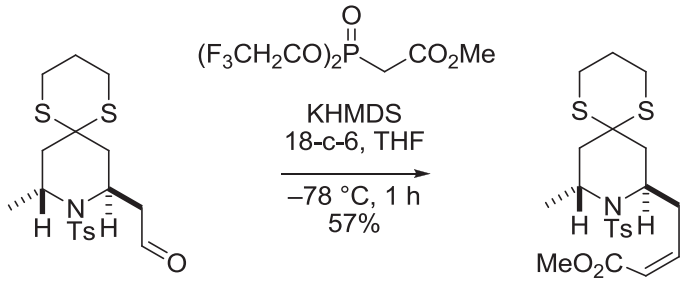
Completion of Synthesis (–)-Epimyrtine 16



To a solution of quinolizidine **15** (35.4 mg, 0.137 mmol) in $TFA/H_2O/CH_3CN$ (1:10:10, total 2.1 mL) was added [bis(trifluoroacetoxy)iodo]benzene (PIFA) (178.3 mg, 0.411 mmol) at 25 ºC. After stirred at the same temperature for 3 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc only) to give (–)-epimyrtine **16** as a colorless oil (16.8 mg, 73%): $[\alpha]^{25}_{D} = -17.8$ (*c* 0.18, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32 (br d, *J* = 11.5 Hz, 1H), 2.33–2.44 (m, 3H), 2.22–2.29 (m, 2H), 2.17 (dd, *J* = 11.0, 11.0 Hz, 1H), 1.82 (ddd, *J* = 11.0, 11.0, 2.5 Hz, 1H), 1.69–1.77 (m, 2H), 1.55–1.68 (m, 2H), 1.36–1.45 (m, 1H), 1.21–1.31 (m, 1H), 1.19 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 208.4, 62.0, 59.3, 51.0, 49.7, 48.6, 34.0, 25.8, 23.9, 20.6; IR (neat) 2930, 1716 cm^{-1}; HRMS (ESI) found 168.1378 [calcd for $C_{10}H_{18}NO$ $(M+H)^+$ 168.1382].

Preparation of (*Z*)-Enoate 17

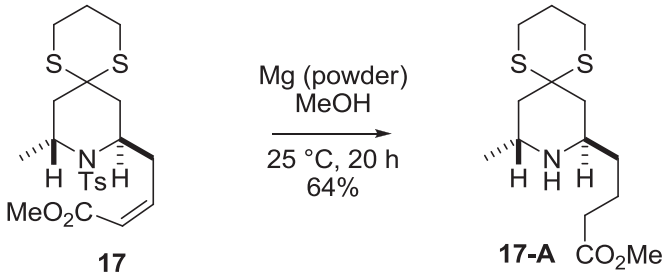


(10b:9b = 4:1) **17**

To a cooled (–78 ºC) solution of methyl 2-(bis(2,2,2-trifluoroethoxy)phosphoryl)acetate (0.15 mL, 0.702 mmol) and 18-Crown-6 (264.3 mg, 1.05 mmol) in THF (10 mL, 0.19 M) was added KHMDS (0.7 mL, 1.0 M in THF, 0.7 mmol). The resulting mixture was stirred at the same temperature for 30 min. A mixture of aldehydes **10b** and **9b** (4:1, 140.3 mg) was added, and the resulting mixture was stirred at the same temperature for 1 h before quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/ EtOAc, 1/1) to give (*Z*)-enoate ester **17** as a colorless oil (90.5 mg, 57%): $[\alpha]^{25}_D$ = –25.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 2H), 6.20 (ddd, *J* = 11.0, 7.5, 7.5 Hz, 1H), 5.82 (dd, *J* = 11.0, 1.0 Hz, 1H), 4.43–4.49 (m, 1H), 3.95–4.01 (m, 1H), 3.68 (s, 3H), 3.58 (ddd, *J* = 15.5, 9.0, 9.0 Hz, 1H), 3.02 (ddd, *J* = 16.0, 7.0, 7.0 Hz, 1H), 2.72–2.88 (m, 4H), 2.23 (dd, *J* = 15.0, 3.5 Hz, 1H), 2.16 (dd, *J* = 14.5, 6.0 Hz, 1H), 2.11 (d, *J* = 14.0 Hz, 1H), 1.91–1.99 (m, 3H), 1.34 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 146.5, 142.9, 129.4, 127.0, 121.0, 54.6, 51.1,

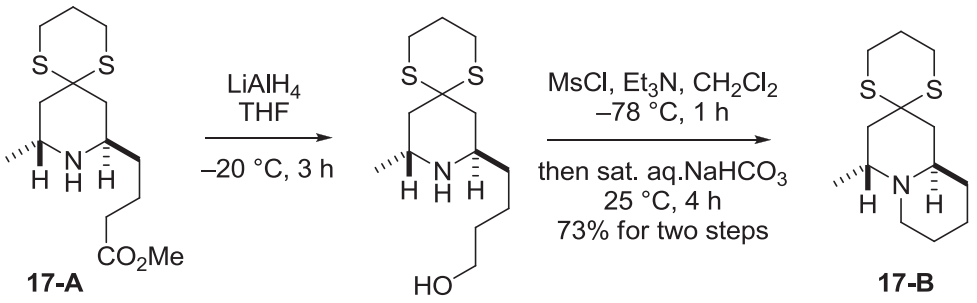
48.1, 47.8, 43.2, 39.9, 32.6, 26.39, 26.26, 25.1, 21.4, 19.7; IR (neat) 1716, 1147 cm^{-1}; HRMS (ESI) found 456.1333 [calcd for $C_{21}H_{30}NO_4S_3$ $(M+H)^+$ 456.1331].

Preparation of Ester 17-A



To a solution of (*E*)-enoate **17** (70.1 mg, 0.154 mmol) in anhydrous MeOH (4 mL, 0.044 M) was added Mg powder (50 mesh, 187.0 mg, 7.7 mmol). After stirred at room temperature for 20 h, the reaction mixture was diluted with diethyl ether (10 mL) and saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/ EtOAc, 1/1) to give ester **17-A** as a colorless oil (30.0 mg, 64%): $[\alpha]^{28}_D$ = +11.5 (*c* 0.47, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.24–3.32 (m, 1H), 3.11–3.14 (m, 1H), 2.79–2.89 (m, 4H), 1.91–1.98 (m, 2H), 1.78 (dd, *J* = 14.0, 7.5 Hz, 1H), 1.62–1.72 (m, 4H), 1.23 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 51.5, 49.8, 47.7, 44.4, 44.1, 41.0, 34.3, 33.8, 26.43, 26.42, 25.3, 22.1, 21.6; IR (neat) 2930, 1732, 1158 cm^{-1}; HRMS (ESI) found 304.1395 [calcd for $C_{14}H_{26}NO_2S_2$ $(M+H)^+$ 304.1399].

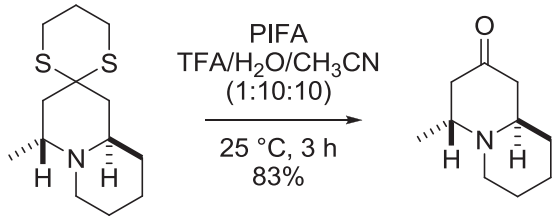
Preparation of Quinolizidine 17-B



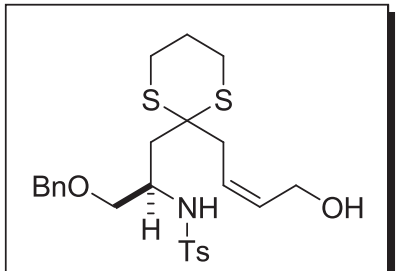
[$LiAlH_4$-Reduction] To a cooled (–20 ºC) solution of ester **17-A** (38.4 mg, 0.127 mmol) in anhydrous THF (5 mL) was added $LiAlH_4$ (0.51 mL, 2.0 M in THF, 1.02 mmol). After stirred at the same temperature for 3 h, the reaction mixture was quenched with MeOH and diluted with THF (10 mL) and saturated aqueous $NaHCO_3$. The cloudy mixture was stirred vigorously for 2 h, filtered through a pad of Celite, and concentrated *in vacuo* to afford crude amino alcohol, which was employed in next step without further purification. **[Cyclization]** To a cooled (–20 ºC) solution of crude alcohol in CH_2Cl_2 (5 mL) were added Et_3N (0.07 mL, 0.50 mmol) and MsCl (1.40 mL, 0.1 M in CH_2Cl_2, 0.140 mmol). After stirred at the same temperature for 1 h, the reaction mixture was quenched saturated aqueous $NaHCO_3$. The resulting mixture was allowed to warm to 25 ºC over 4 h with continuous stirring. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc only) to give quinolizidine **17-B** as a colorless oil (23.9 mg, 73%):$[\alpha]^{25}_D$ = +19.3 (*c* 0.41, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.23 (ddddd, *J* = 7.5, 7.5, 7.5, 7.5, 2.5 Hz, 1H), 2.96 (ddd, *J* = 17.5, 8.5, 5.0 Hz, 1H), 2.78–2.88 (m, 2H), 2.68–2.74 (m, 3H), 2.48 (ddd, *J* = 11.5, 11.5, 3.5 Hz, 1H), 2.33 (ddd, *J* = 13.5, 2.5, 2.5 Hz, 1H), 2.28 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.20 (ddd, *J* = 14.0, 2.5, 2.5 Hz, 1H), 1.87–2.02 (m, 3H), 1.76 (dd, *J* = 14.0, 10.5 Hz, 1H), 1.72 (br d, *J* = 13.0 Hz, 1H), 1.56–1.63 (m, 3H), 1.21–1.41 (m, 2H), 1.27 (d, *J* =

7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.9, 51.3, 50.2, 47.4, 45.0, 43.3, 32.7, 26.54, 26.35, 25.4, 24.1, 14.6; IR (neat) 2928, 1436, 1422, 1309, 1272, 1123 cm^{-1}; HRMS (ESI) found 258.1345 [calcd for $C_{13}H_{24}NS^2$ $(M+H)^+$ 258.1344].

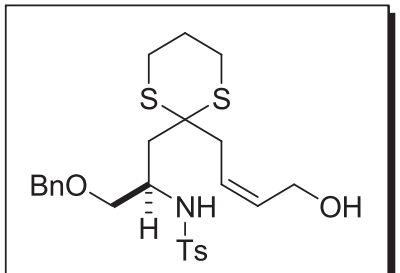
Completion of Synthesis (+)-Myrtine 18



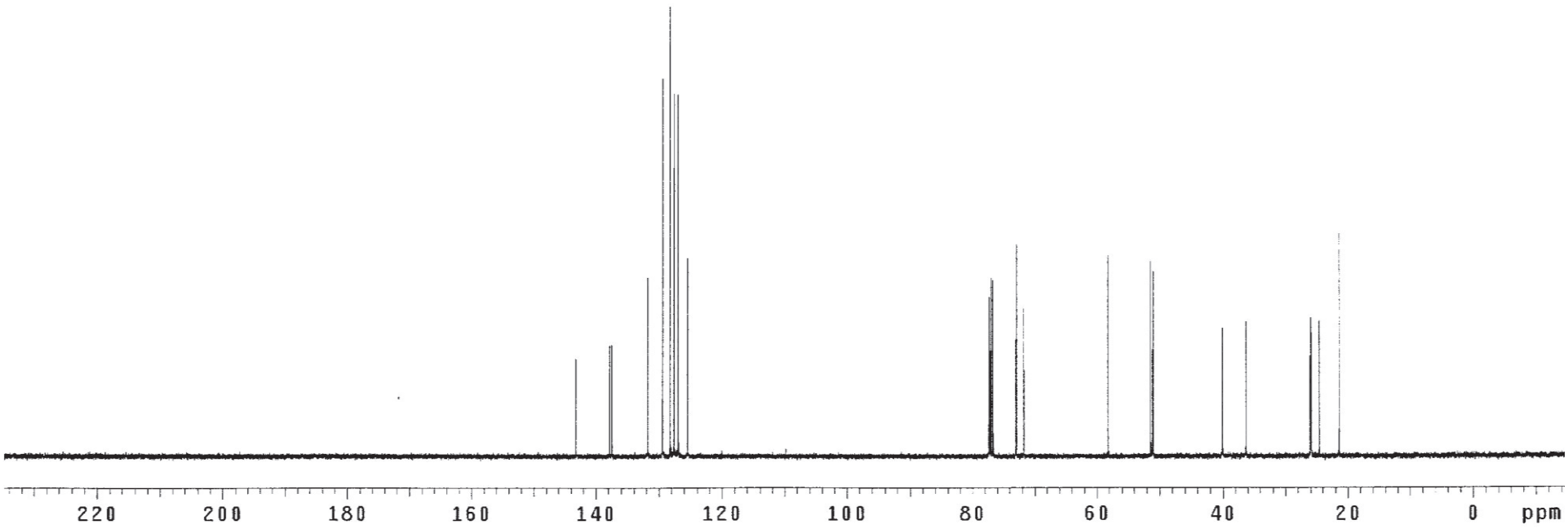
To a solution of quinolizidine **17-B** (23.9 mg, 0.093mmol) in $TFA/H_2O/CH_3CN$ (1:10:10, total 2.1 mL) was added [bis(trifluoroacetoxy)iodo]benzene (PIFA, 120.8 mg, 0.278 mmol) at 25 ºC. After stirred at the same temperature for 3 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc only) to give (+)-myrtine **18** as a colorless oil (12.8 mg, 83%): $[\alpha]^{25}_D$ = +14.1 (*c* 0.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (ddddd, *J* = 6.5, 6.5, 6.5, 6.5, 2.0 Hz, 1H), 2.85 (dd, *J* = 14.0, 6.5 Hz, 1H), 2.79 (br d, *J* = 11.0 Hz, 1H), 2.66 (dddd, *J* = 10.0, 10.0, 5.0, 3.0 Hz, 1H), 2.48 (ddd, *J* = 11.0, 11.0, 2.5 Hz, 1H), 2.23–2.27 (m, 2H), 2.19 (ddd, *J* = 13.5, 2.0, 2.0 Hz, 1H), 1.57–1.73 (m, 4H), 1.14–1.36 (m, 3H), 0.97 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5, 57.0, 53.5, 51.4, 48.6, 48.0, 34.1, 25.7, 23.4, 11.1; IR (neat) 2930, 1716, 1335, 1289, 1279, 1173, 1114 cm^{-1}; HRMS (ESI) found 168.1380 [calcd for $C_{10}H_{18}NO$ $(M+H)^+$ 168.1382].

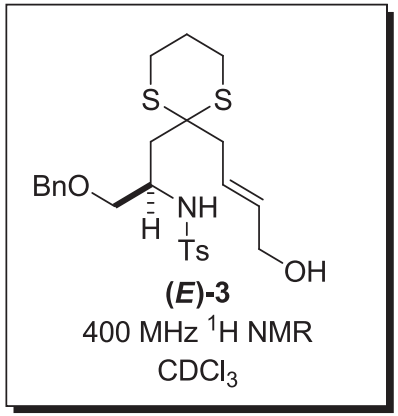


(*Z*)-3
400 MHz ^{1}H NMR
$CDCl_3$



(*Z*)-3
100 MHz ^{13}C NMR
$CDCl_3$

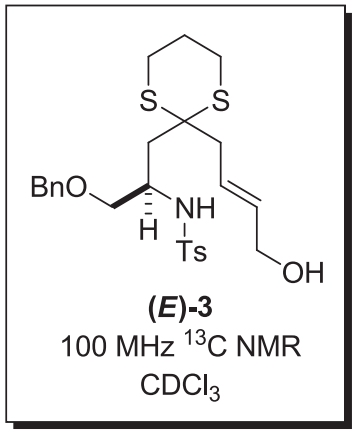




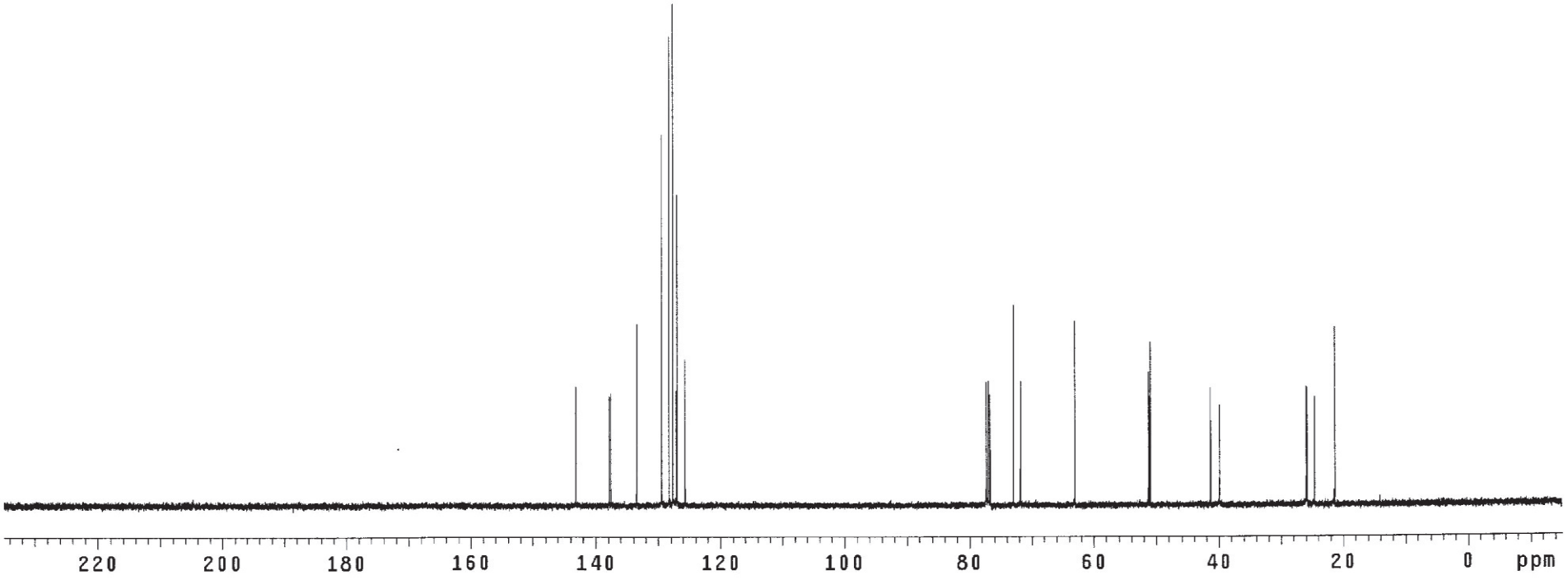
(*E*)-3

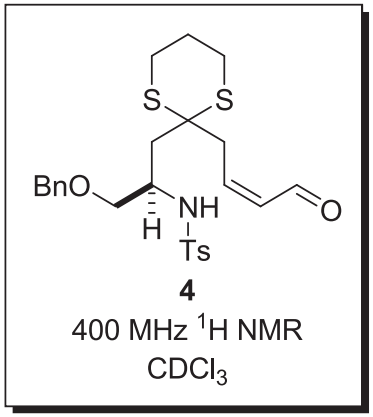
400 MHz ^{1}H NMR

$CDCl_3$



(*E*)-3
100 MHz ^{13}C NMR
$CDCl_3$

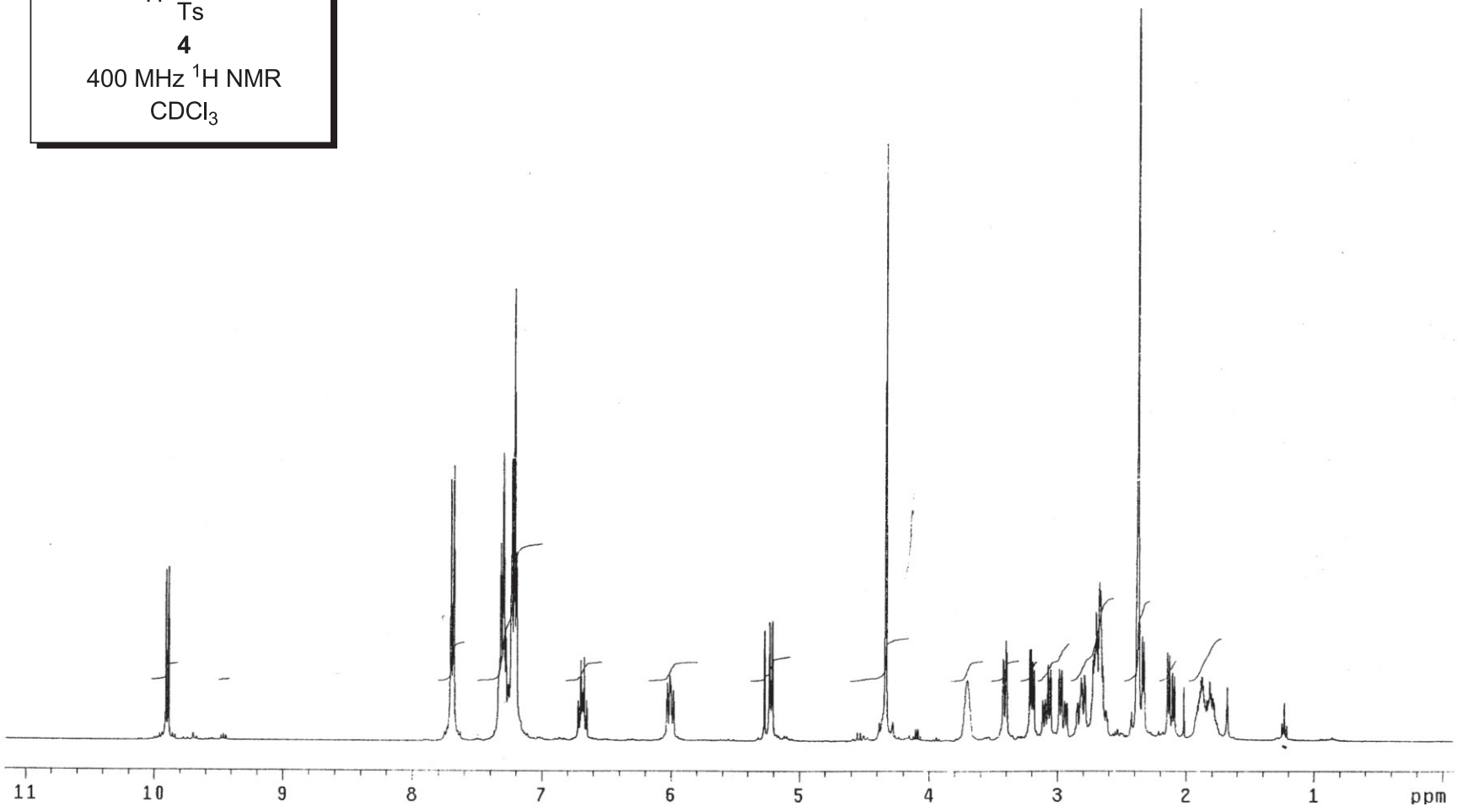


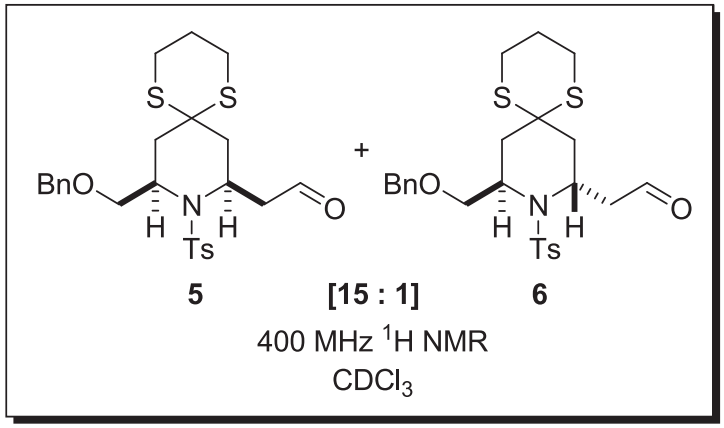


4

400 MHz ^{1}H NMR

$CDCl_3$

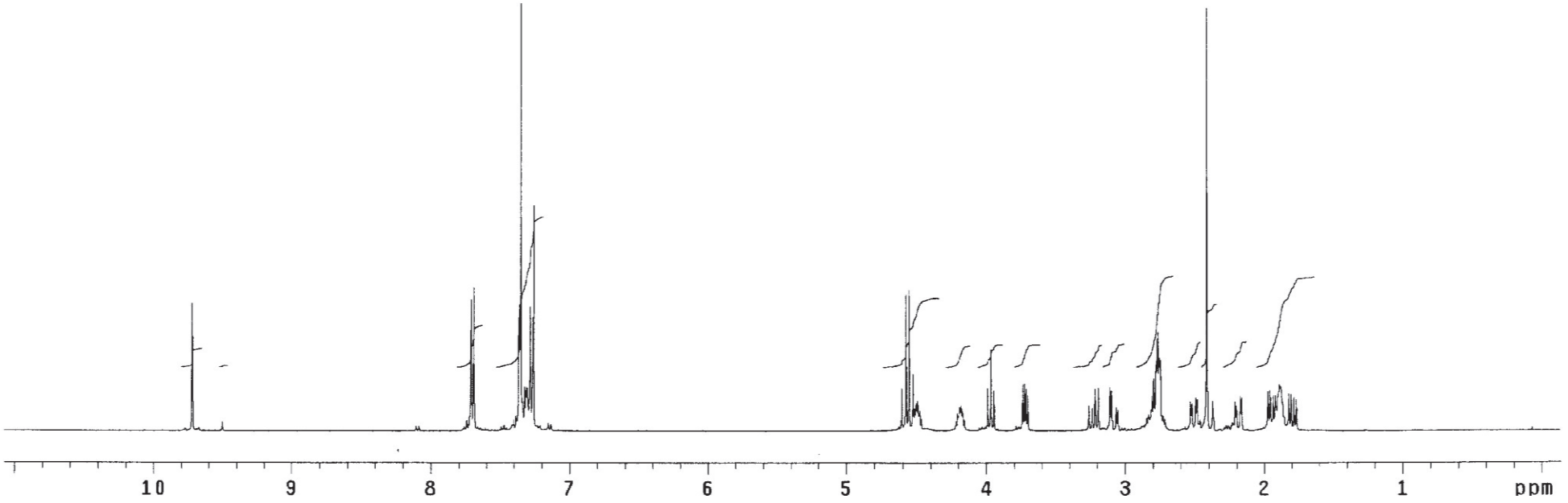


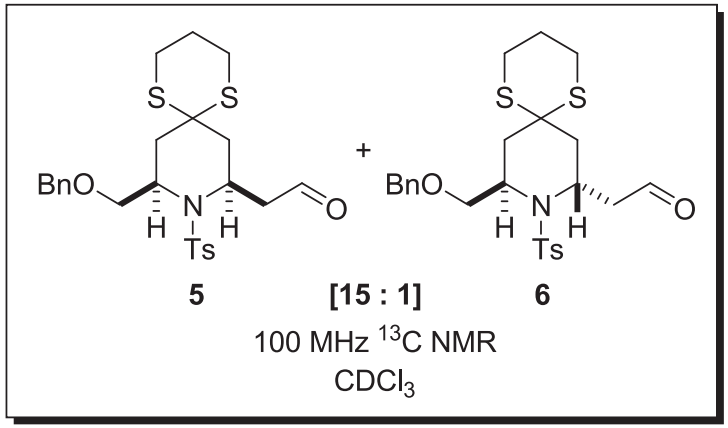


5 **[15 : 1]** **6**

400 MHz ^{1}H NMR

$CDCl_3$

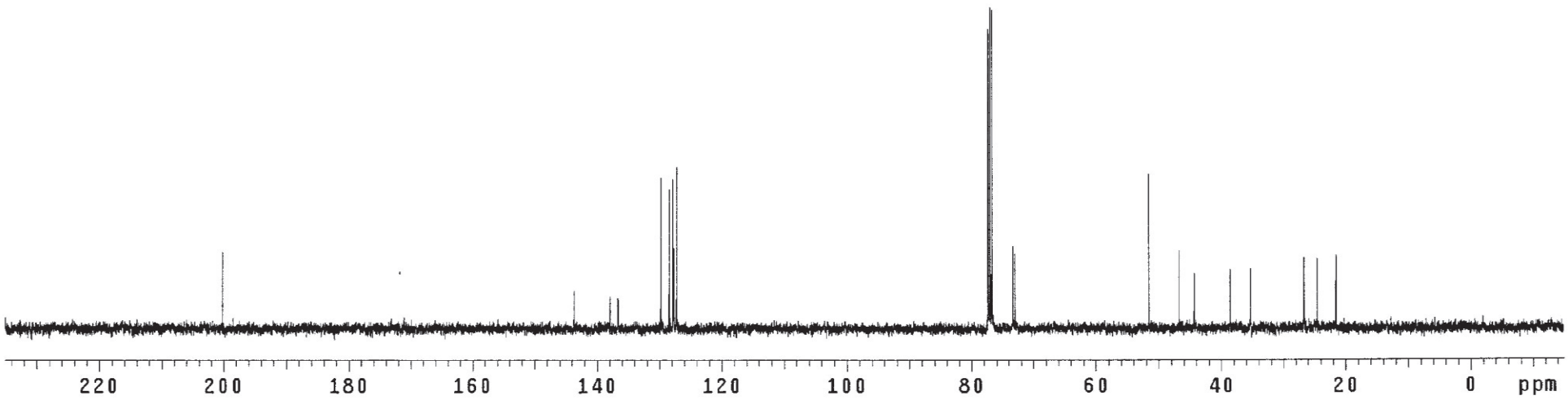


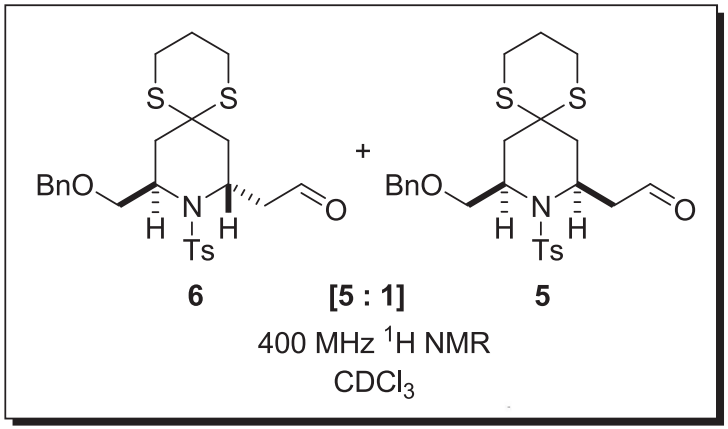


5 **[15 : 1]** **6**

100 MHz ^{13}C NMR

$CDCl_3$

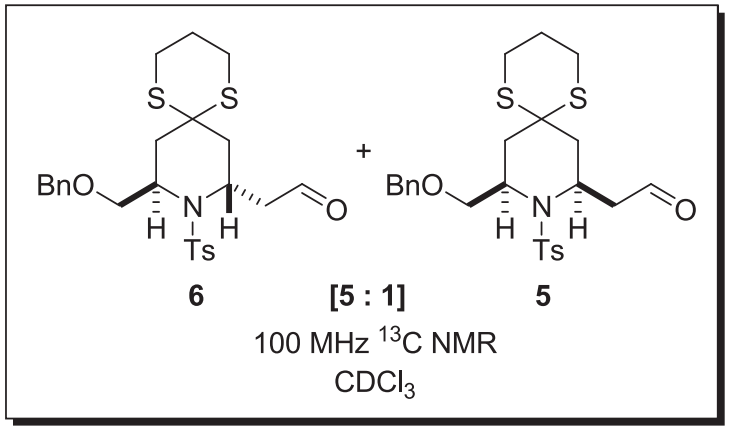




6 **[5 : 1]** **5**

400 MHz ^{1}H NMR

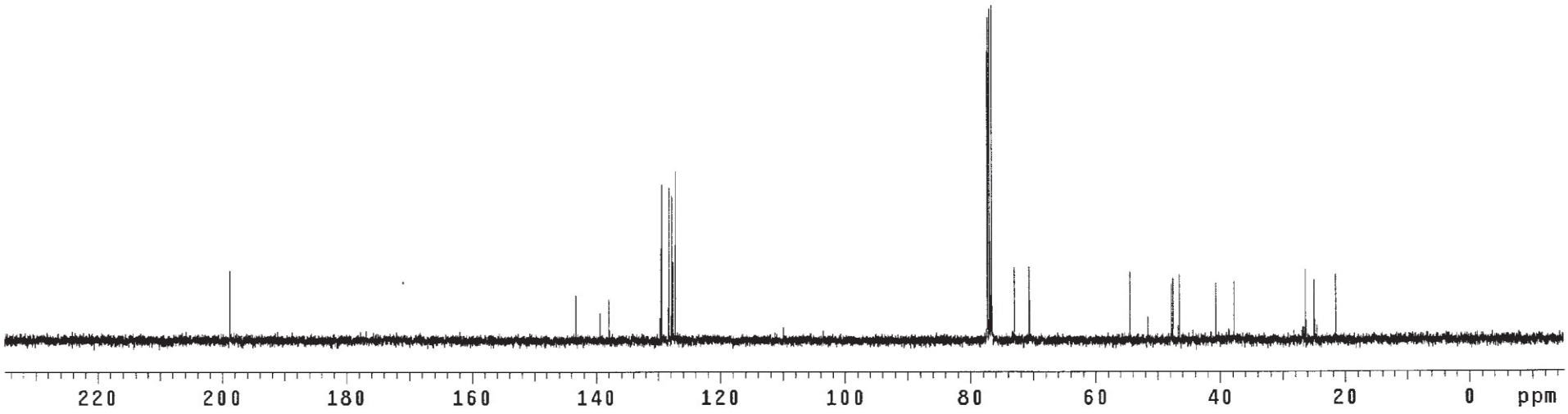
$CDCl_3$

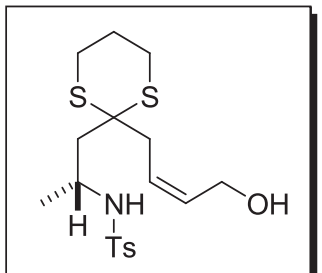


6 **[5 : 1]** **5**

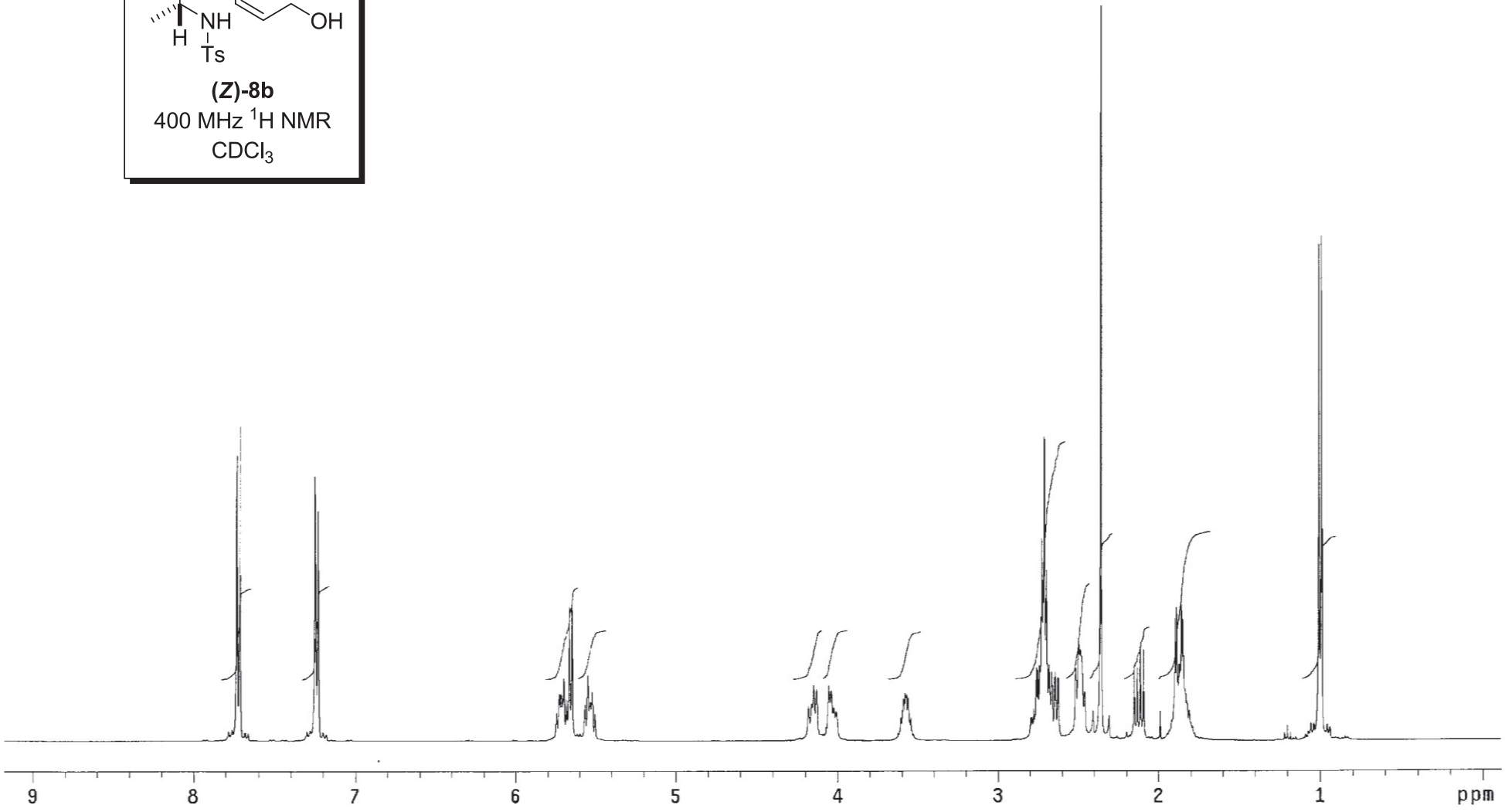
100 MHz ^{13}C NMR

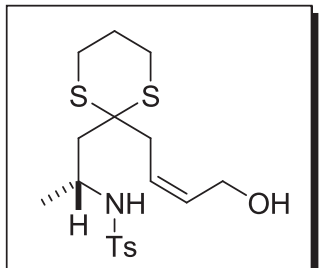
$CDCl_3$



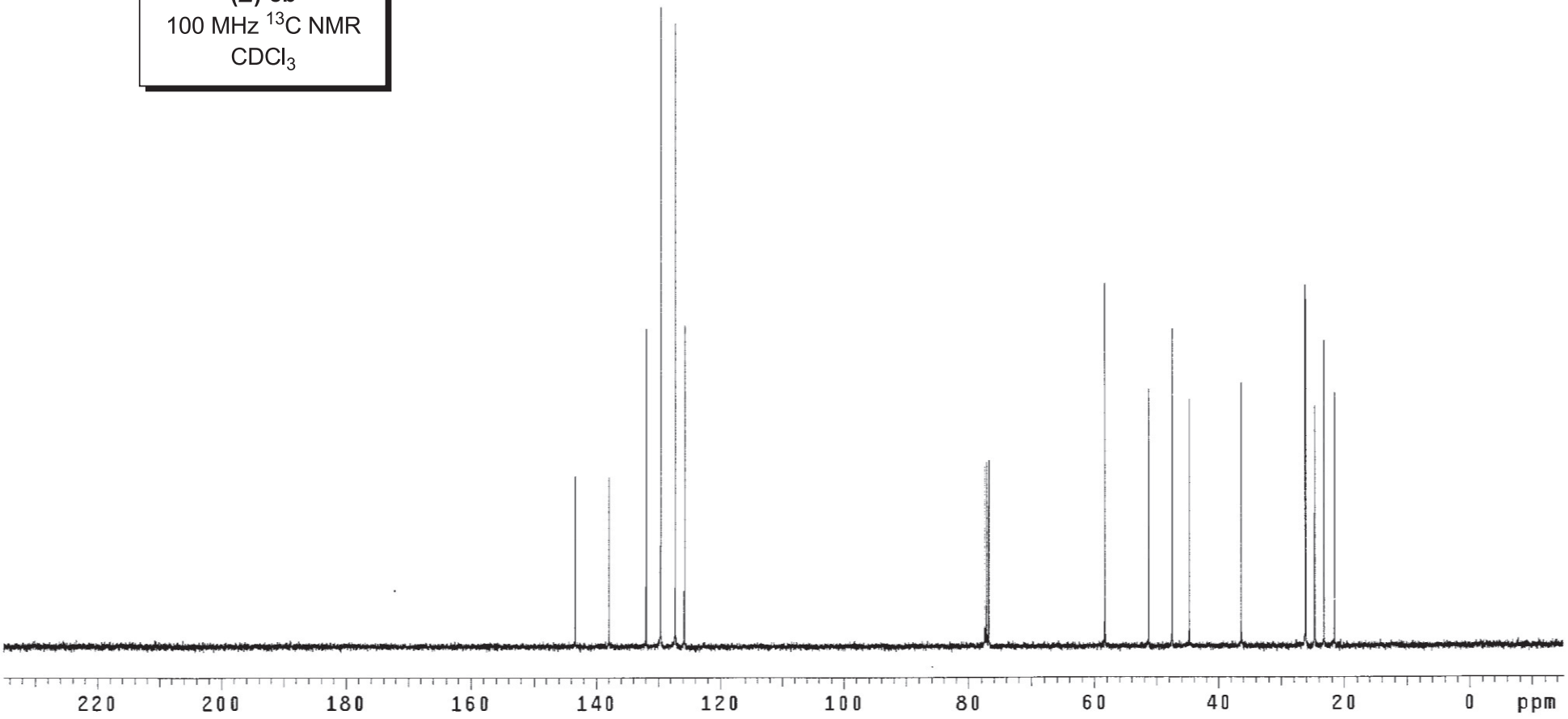


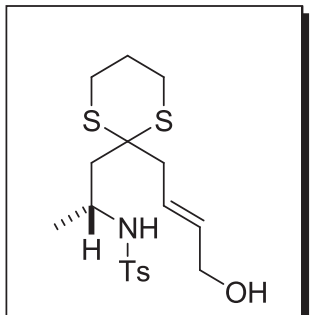
(*Z*)-8b
400 MHz ^{1}H NMR
$CDCl_3$



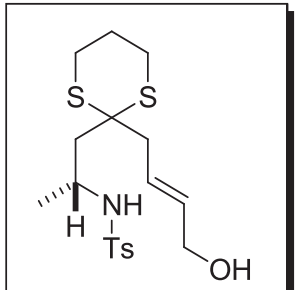


(*Z*)-8b
100 MHz ^{13}C NMR
$CDCl_3$

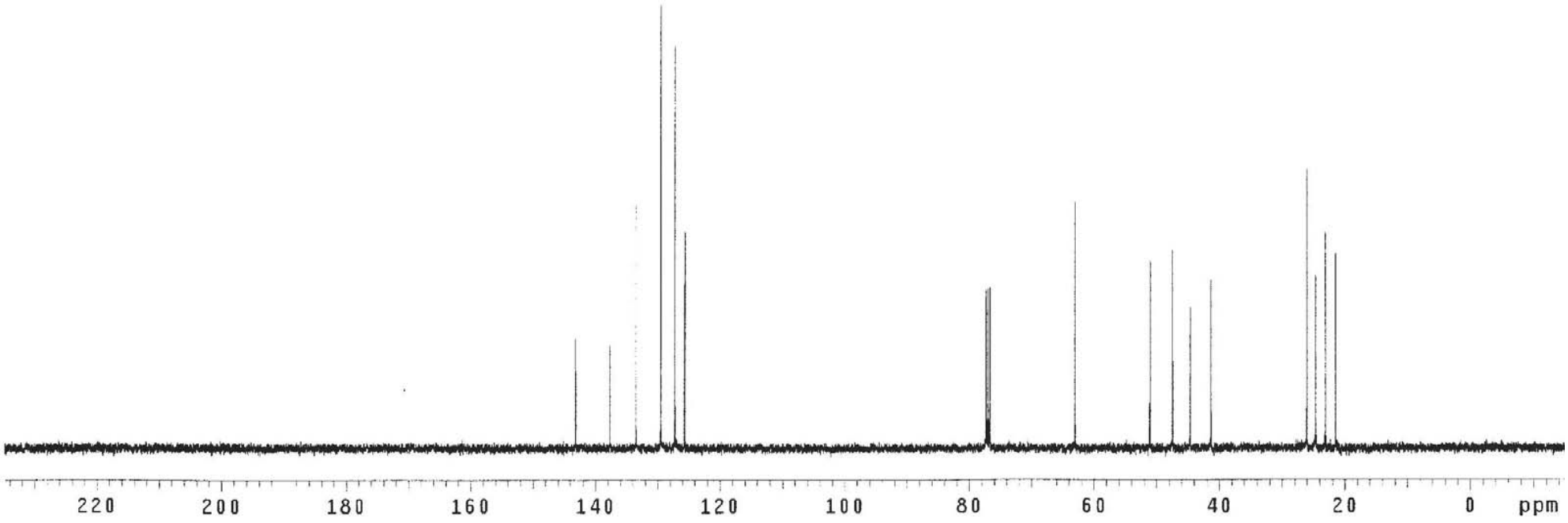


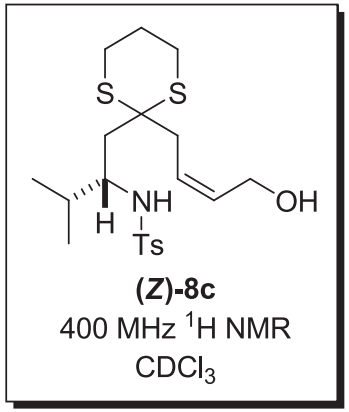


(*E*)-8b
400 MHz ^{1}H NMR
$CDCl_3$

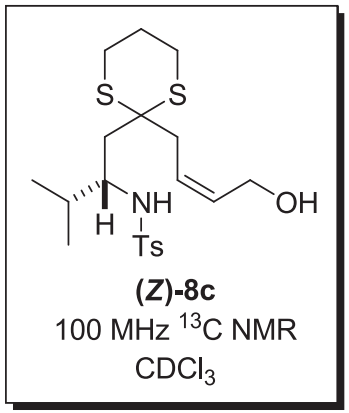


(*E*)-8b
100 MHz ^{13}C NMR
$CDCl_3$

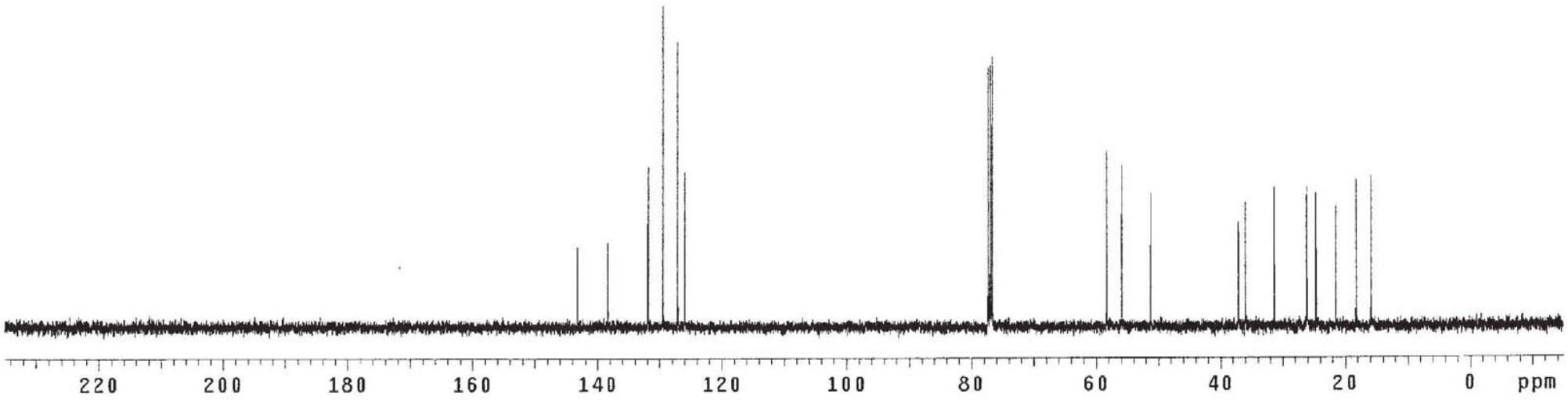


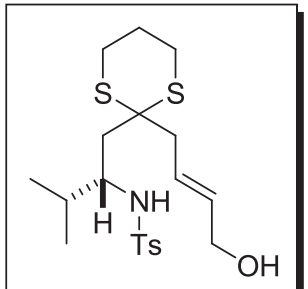


(*Z*)-8c
400 MHz ^{1}H NMR
$CDCl_3$

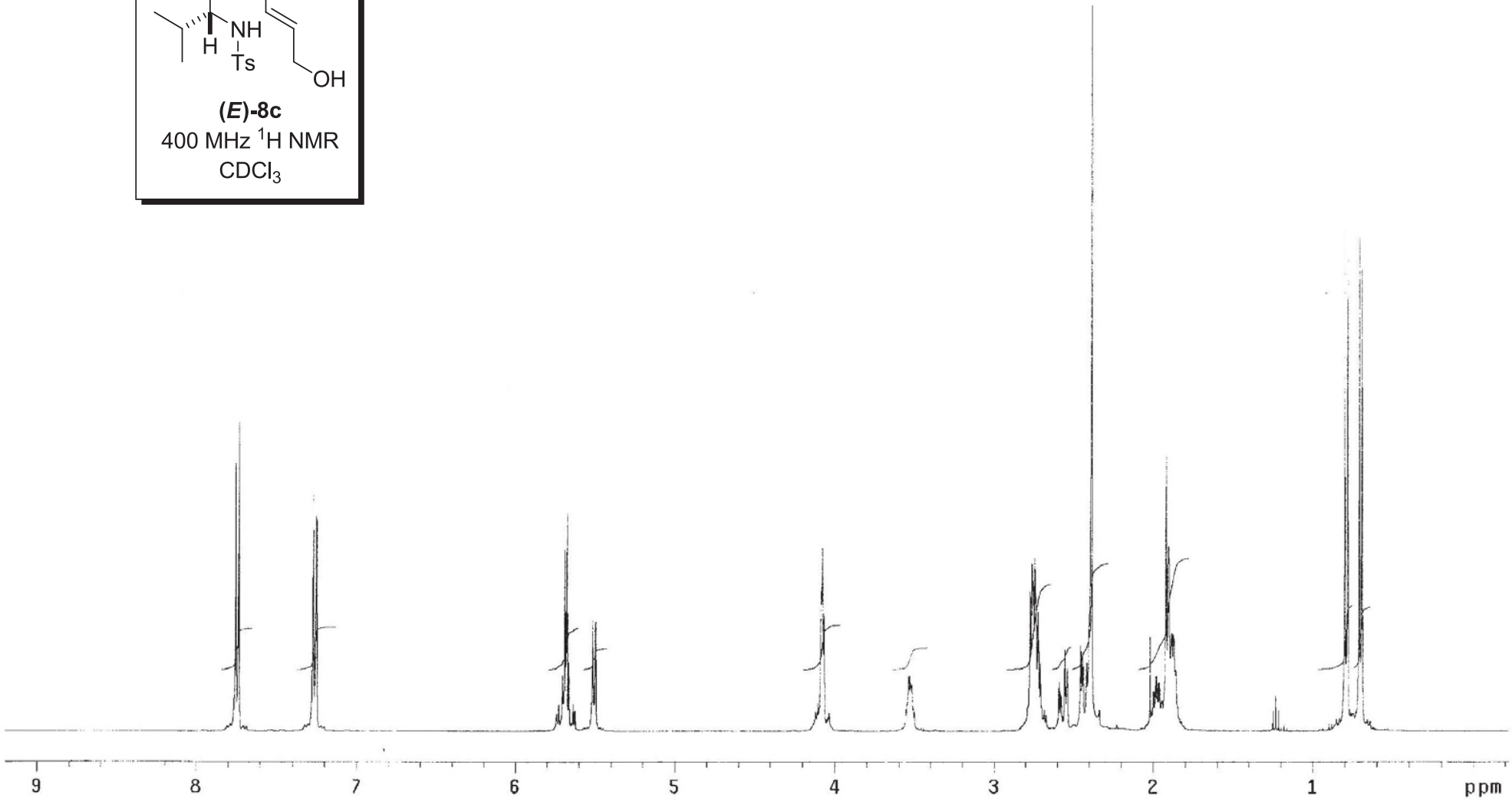


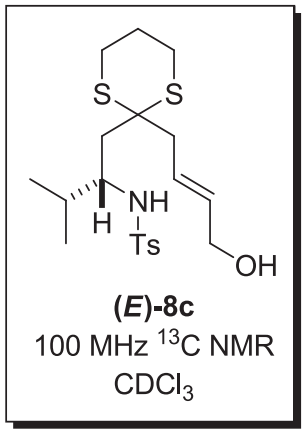
(*Z*)-8c
100 MHz ^{13}C NMR
$CDCl_3$



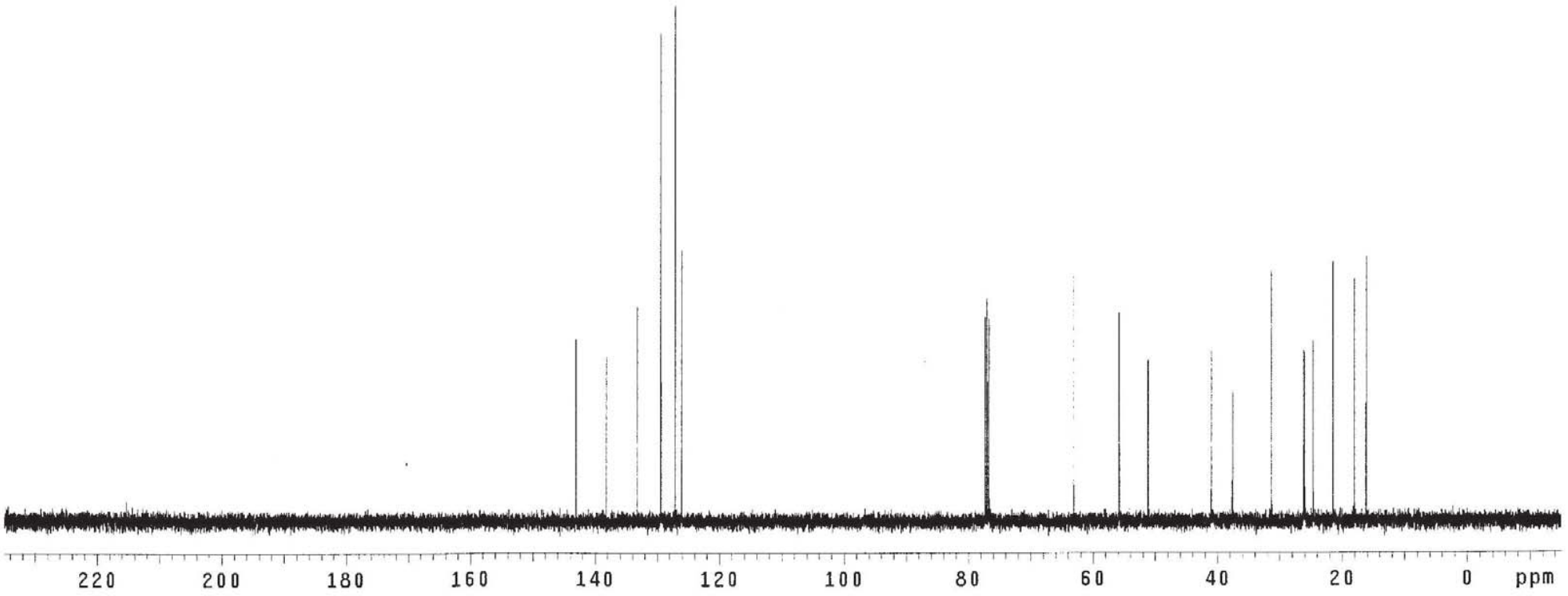


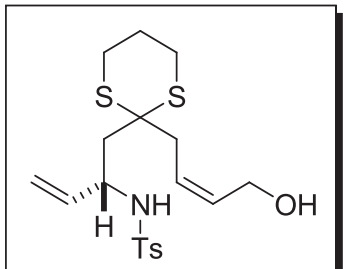
(*E*)-8c
400 MHz ^{1}H NMR
$CDCl_3$



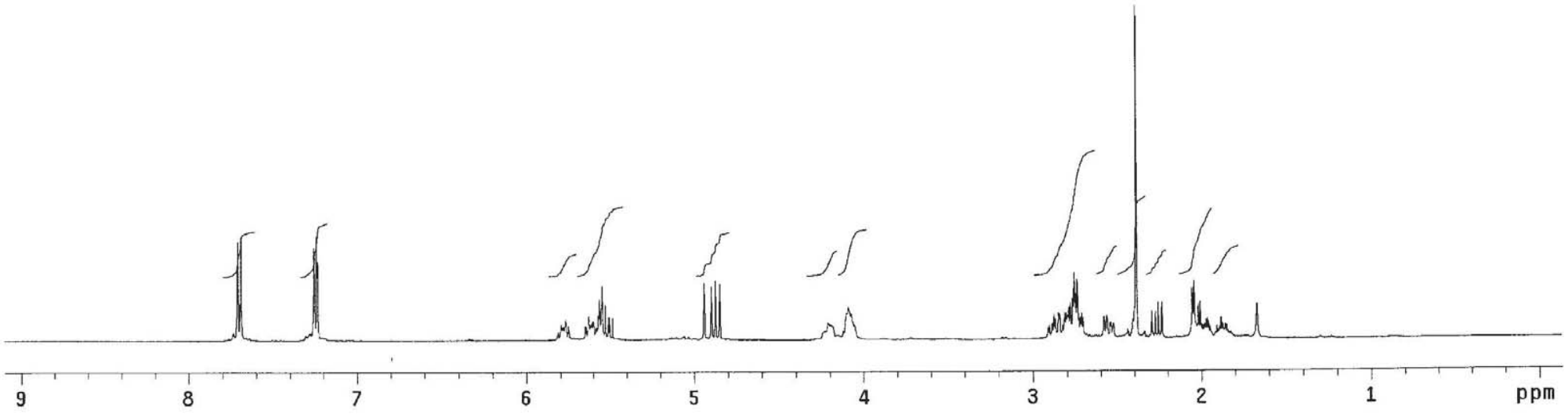


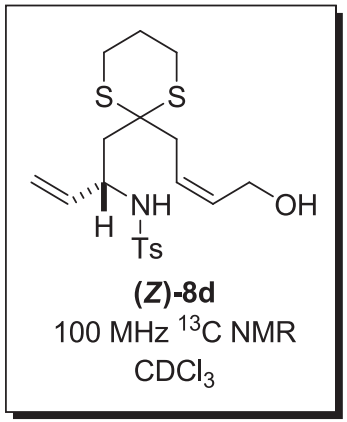
(*E*)-8c
100 MHz ^{13}C NMR
$CDCl_3$



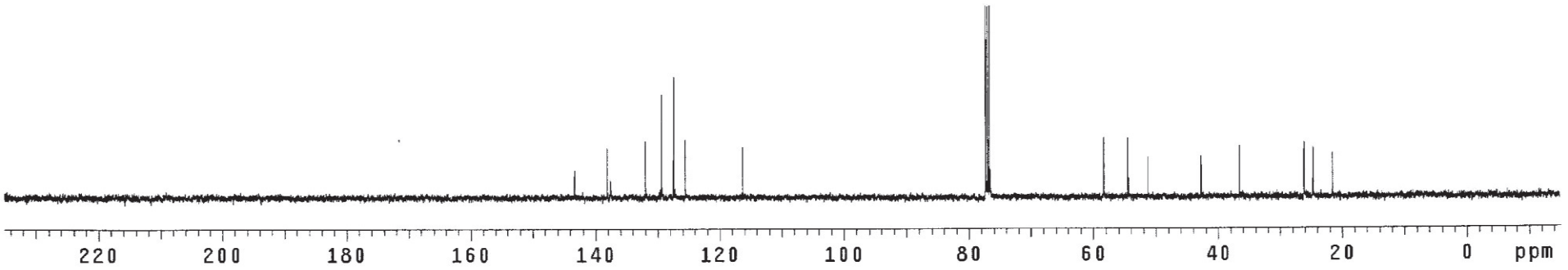


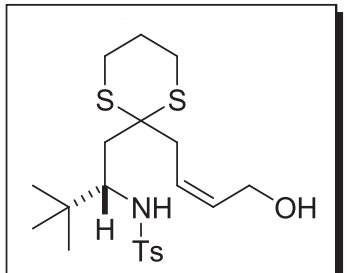
(*Z*)-8d
400 MHz ^{1}H NMR
$CDCl_3$



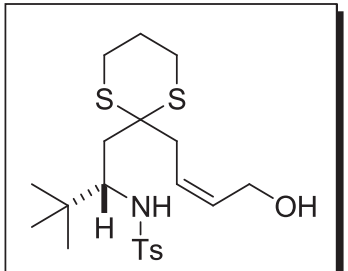


(*Z*)-8d
100 MHz ^{13}C NMR
$CDCl_3$

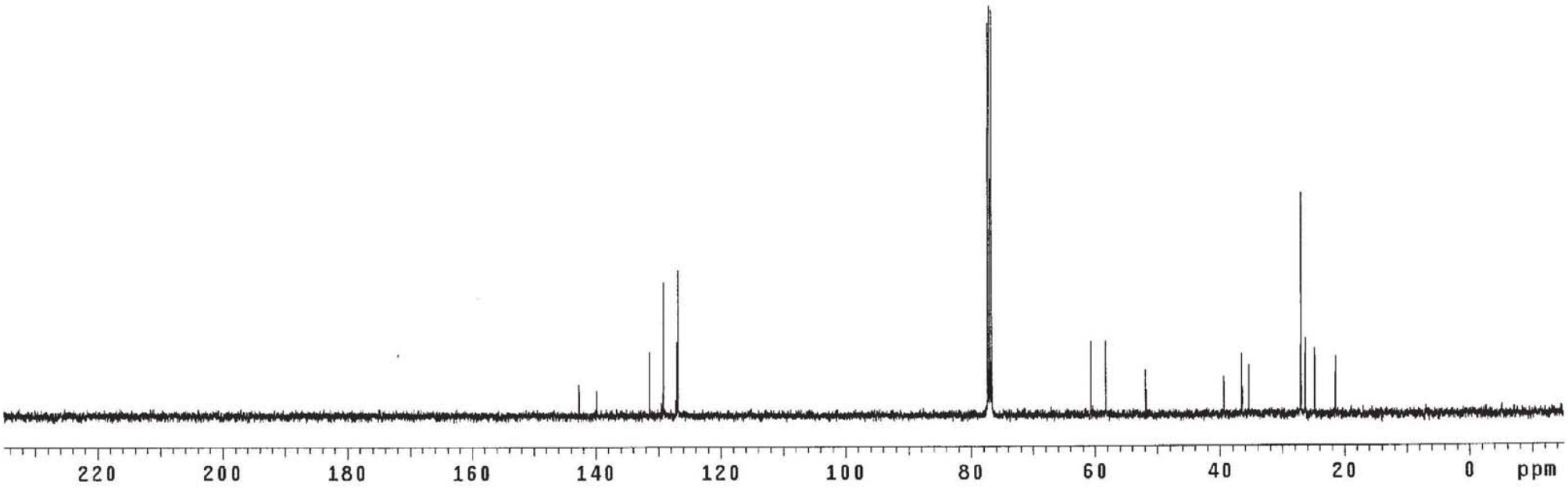


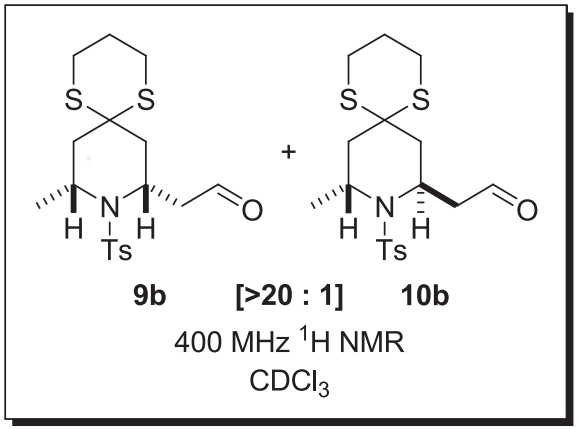


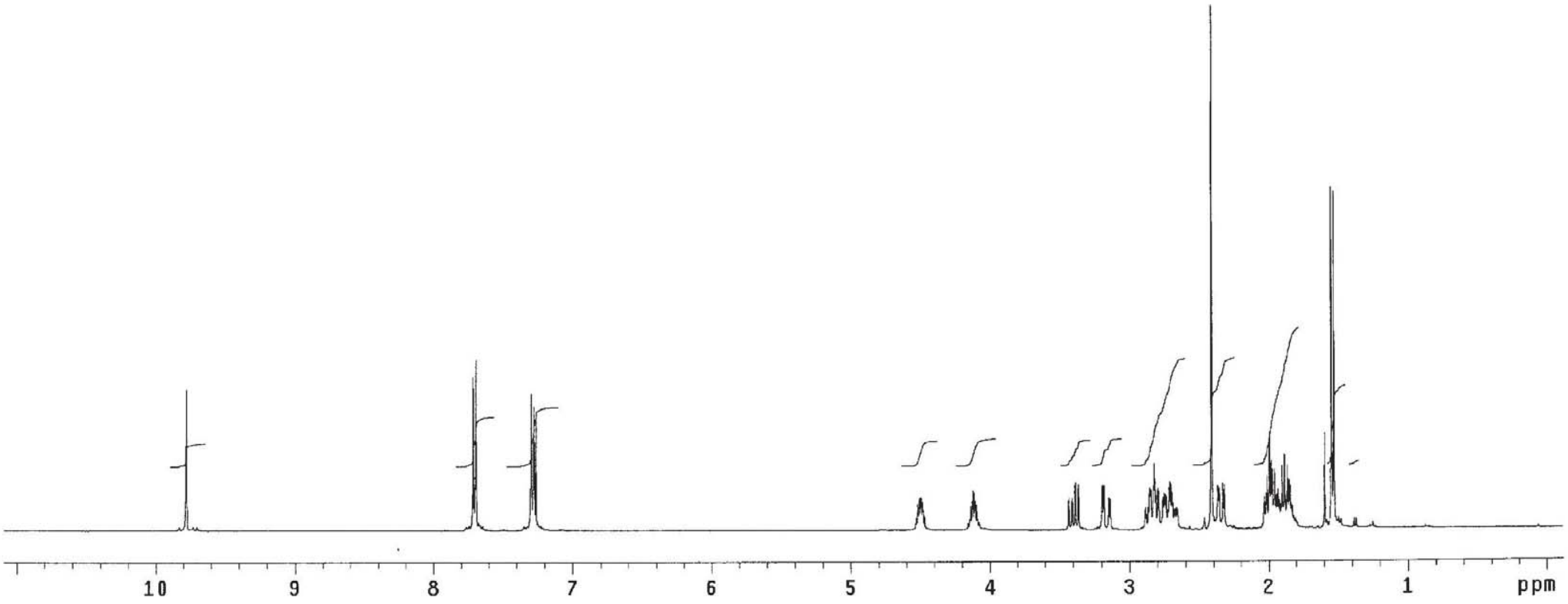
(*Z*)-8e
400 MHz ^{1}H NMR
$CDCl_3$

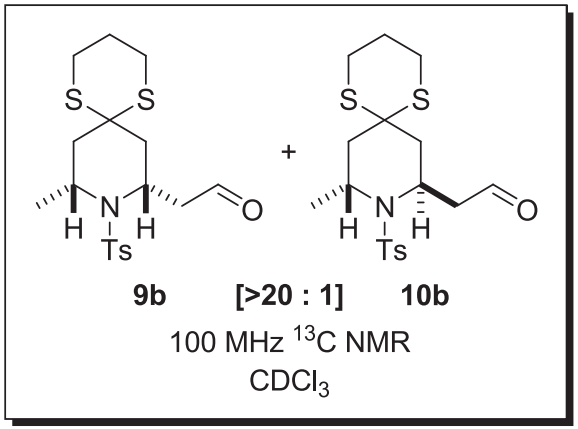


(*Z*)-8e
100 MHz ^{13}C NMR
$CDCl_3$




S
S
+
H
N
H
Ts
O
9b
[>20 : 1]
10b
400 MHz ^{1}H NMR
$CDCl_3$

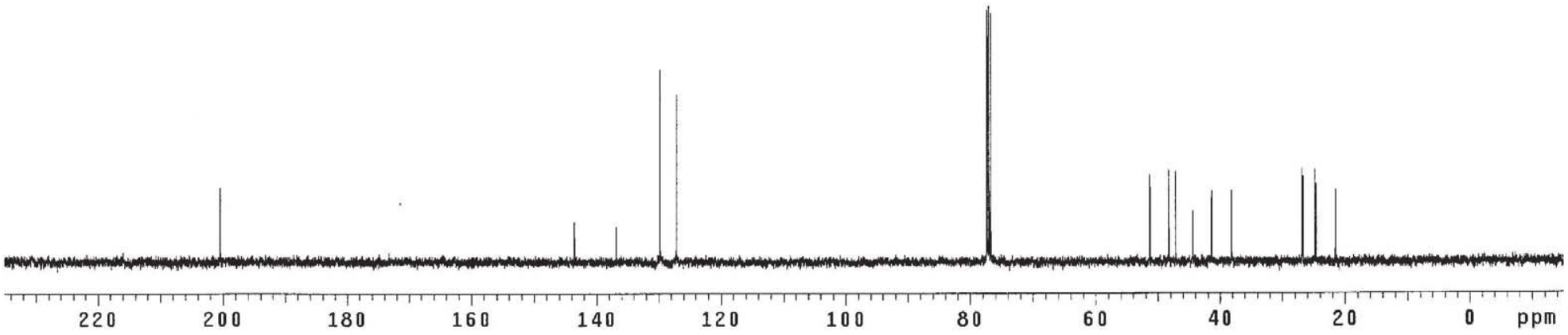

10
9
8
7
6
5
4
3
2
1
ppm

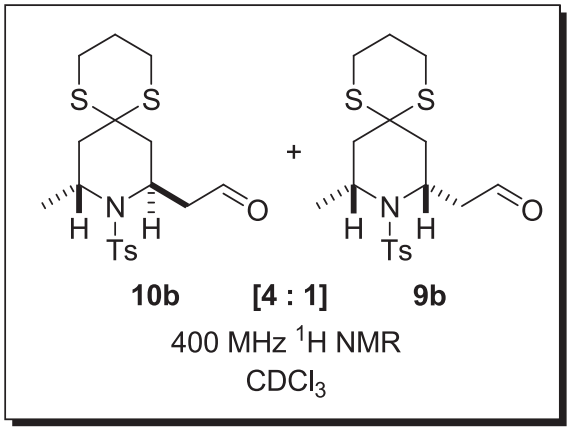


9b **[>20 : 1]** **10b**

100 MHz ^{13}C NMR

$CDCl_3$

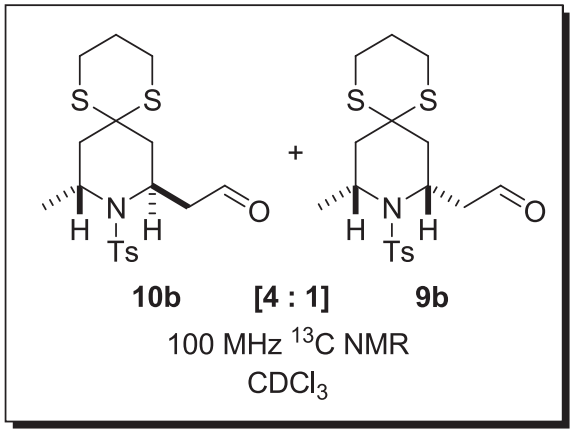




10b **[4 : 1]** **9b**

400 MHz ^{1}H NMR

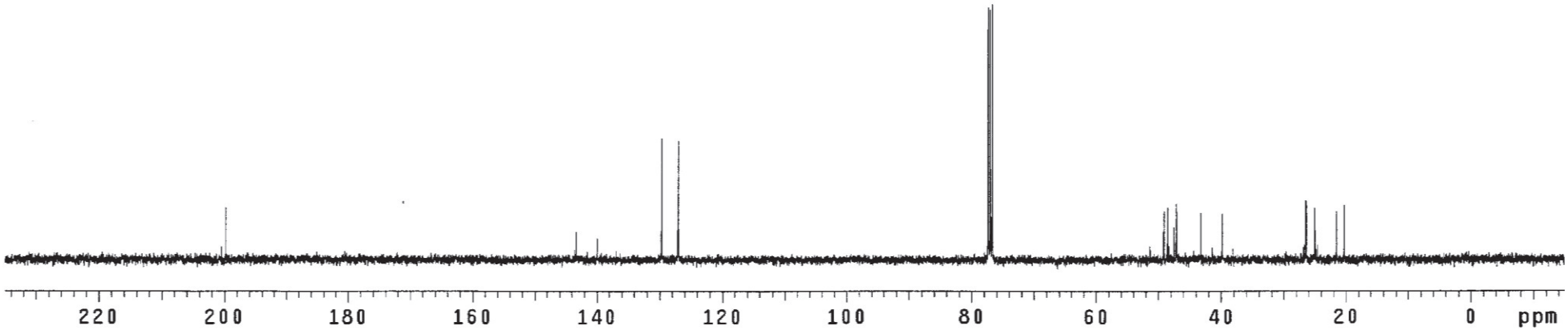
$CDCl_3$

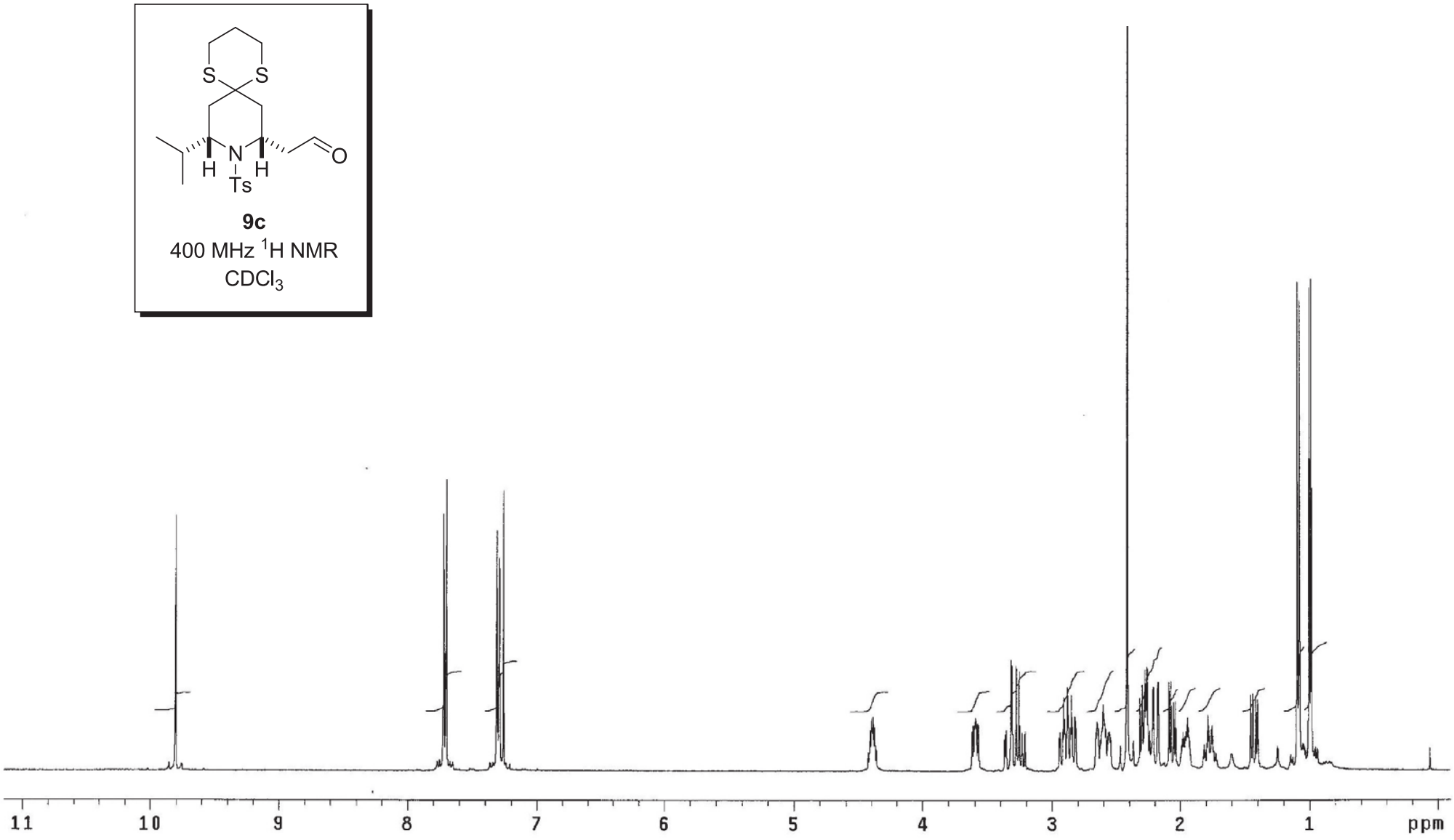


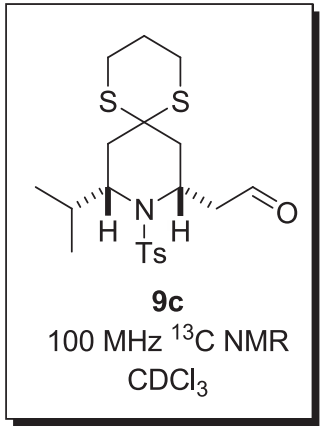
10b **[4 : 1]** **9b**

100 MHz ^{13}C NMR

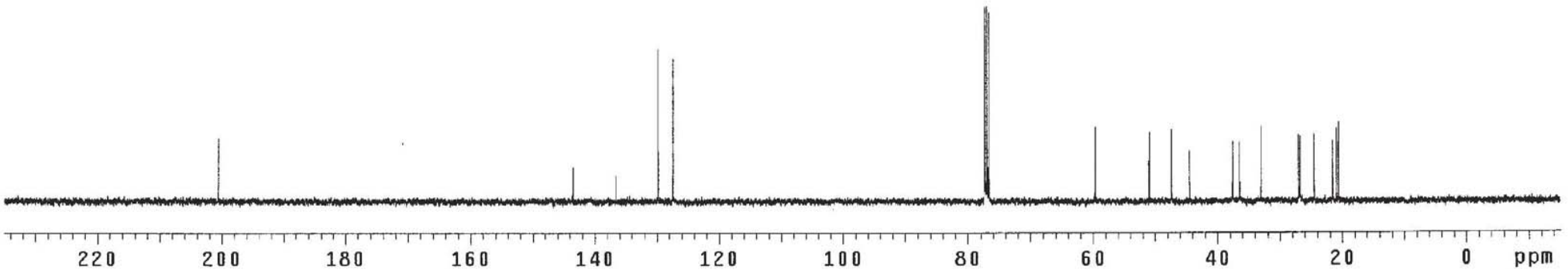
$CDCl_3$

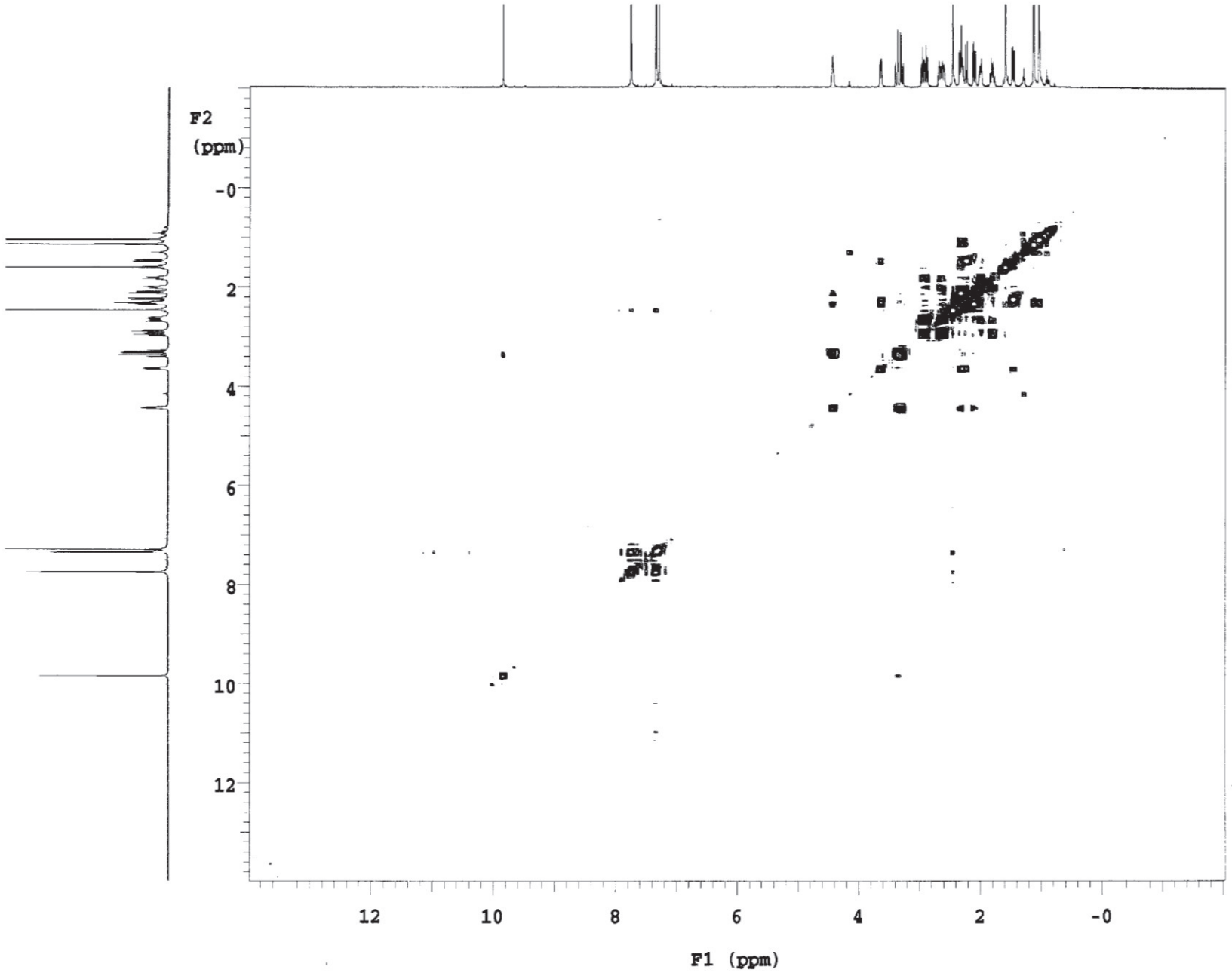


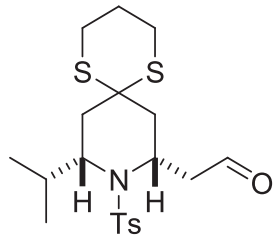

S
S
N
H
H
Ts
O
9c
400 MHz 1H NMR
CDCl3
11
10
9
8
7
6
5
4
3
2
1
ppm



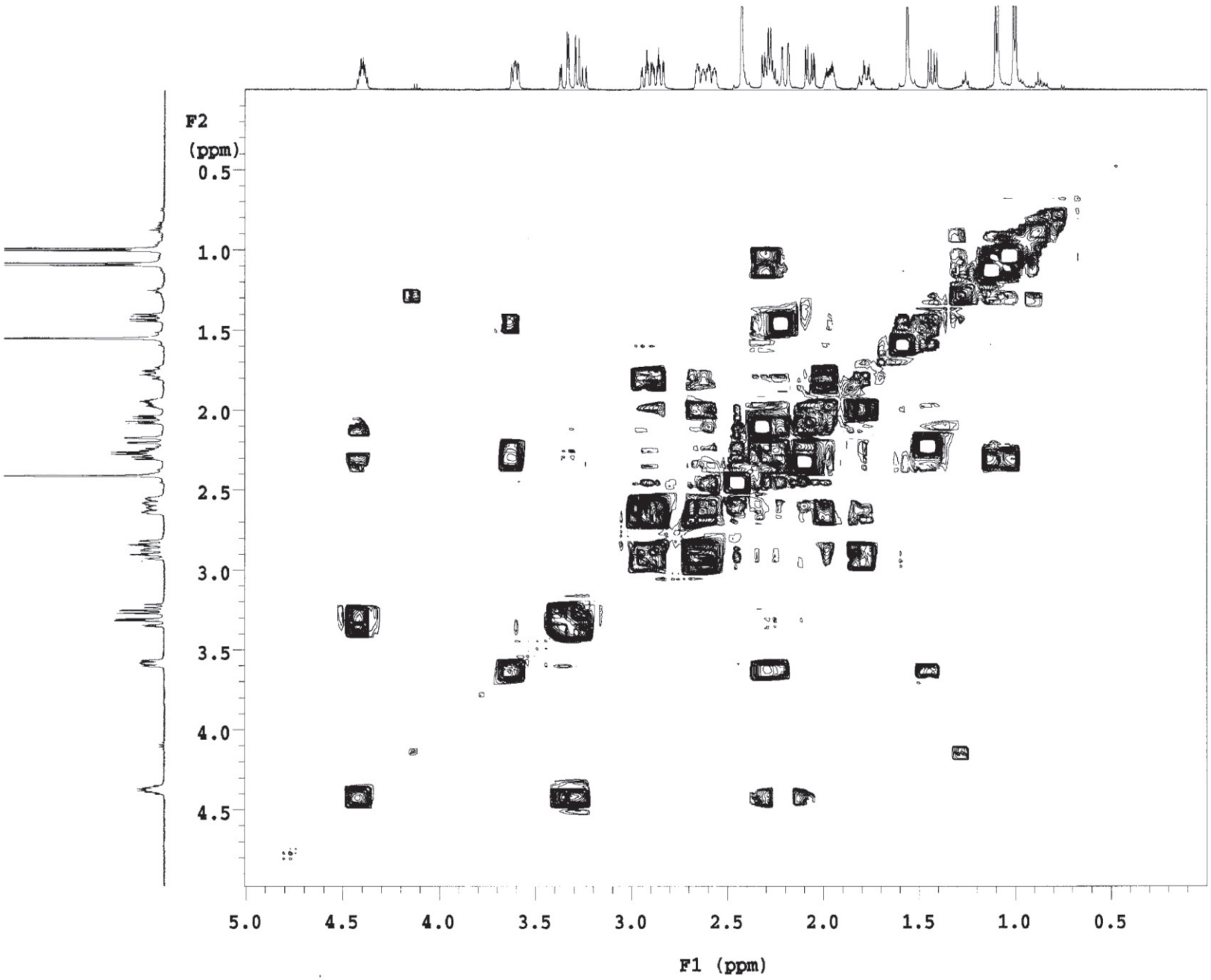
9c
100 MHz ^{13}C NMR
$CDCl_3$

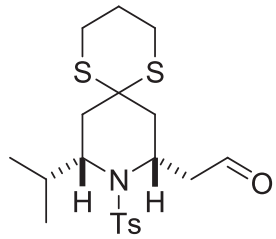




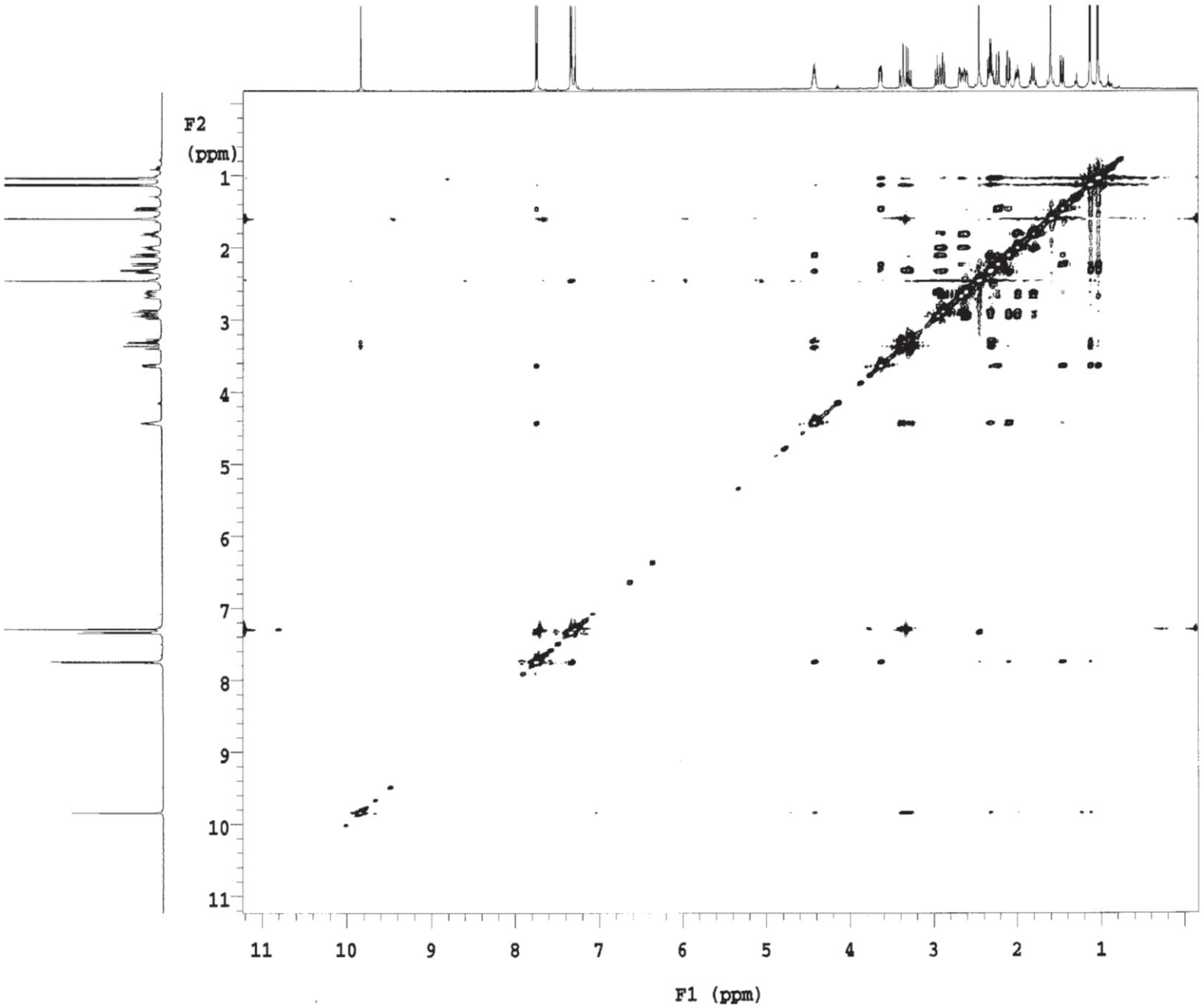


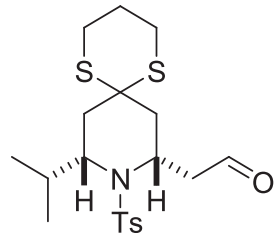
9c
500 MHz ^{1}H-^{1}H COSY NMR
$CDCl_3$





9c
500 MHz ^{1}H-^{1}H COSY NMR
$CDCl_3$

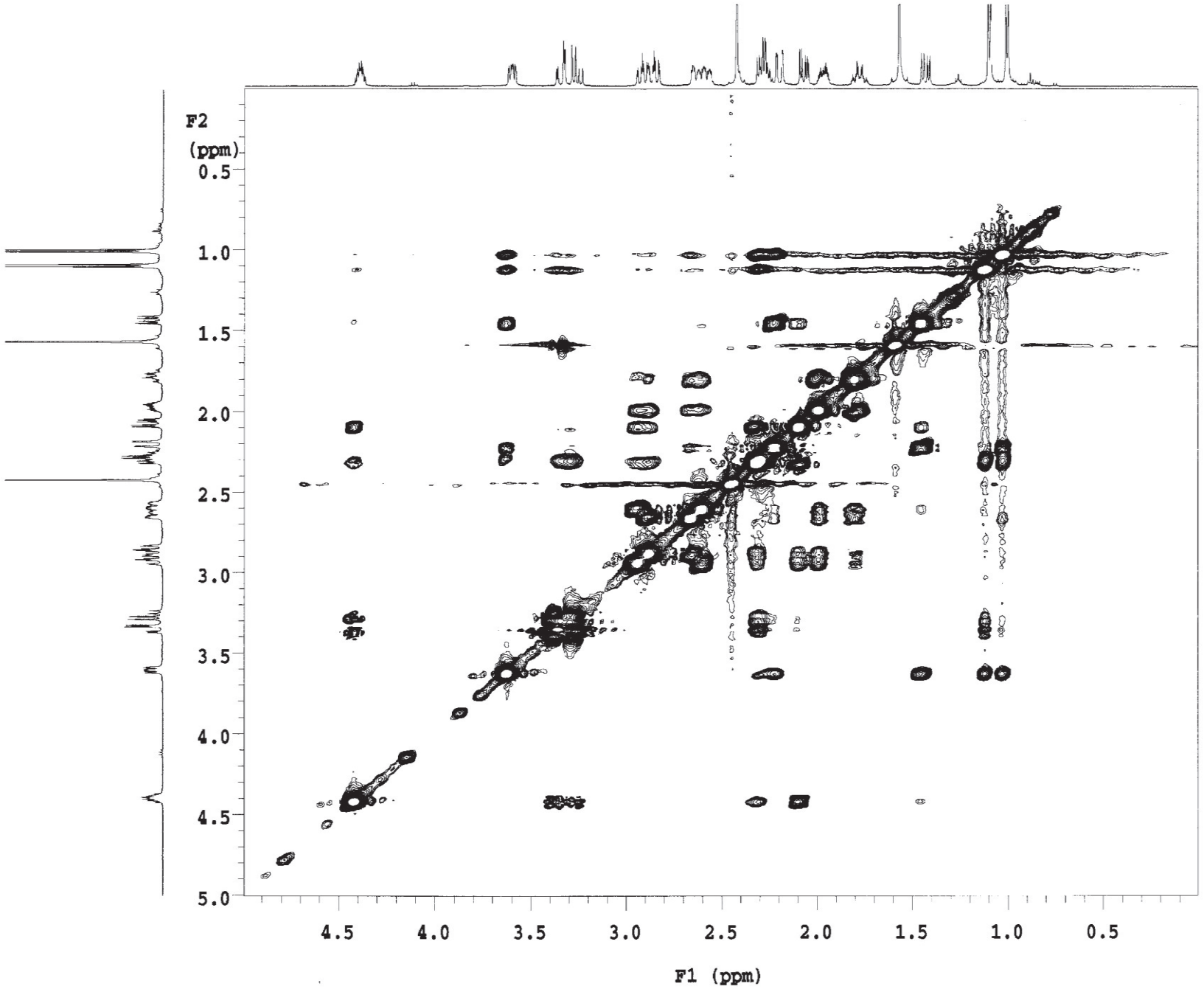


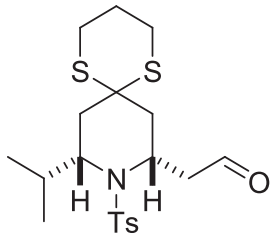


9c

500 MHz ^{1}H-^{1}H NOESY NMR

$CDCl_3$

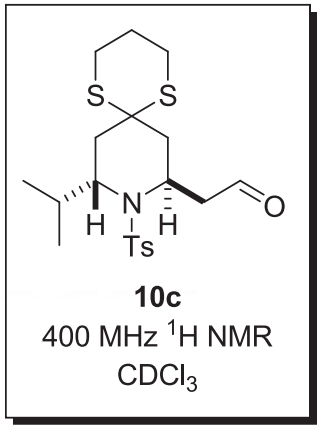




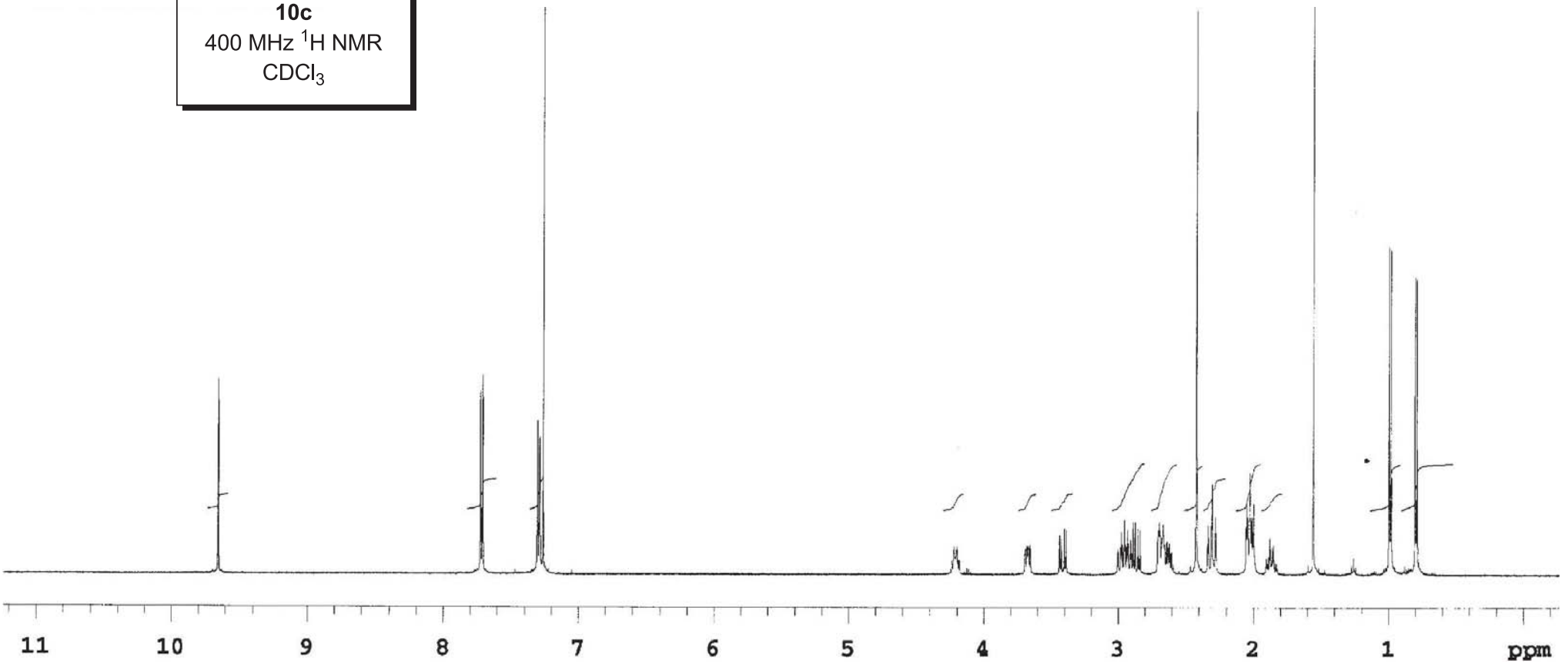
9c

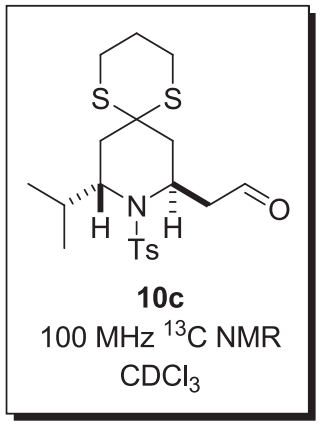
500 MHz ^{1}H-^{1}H NOESY NMR

$CDCl_3$

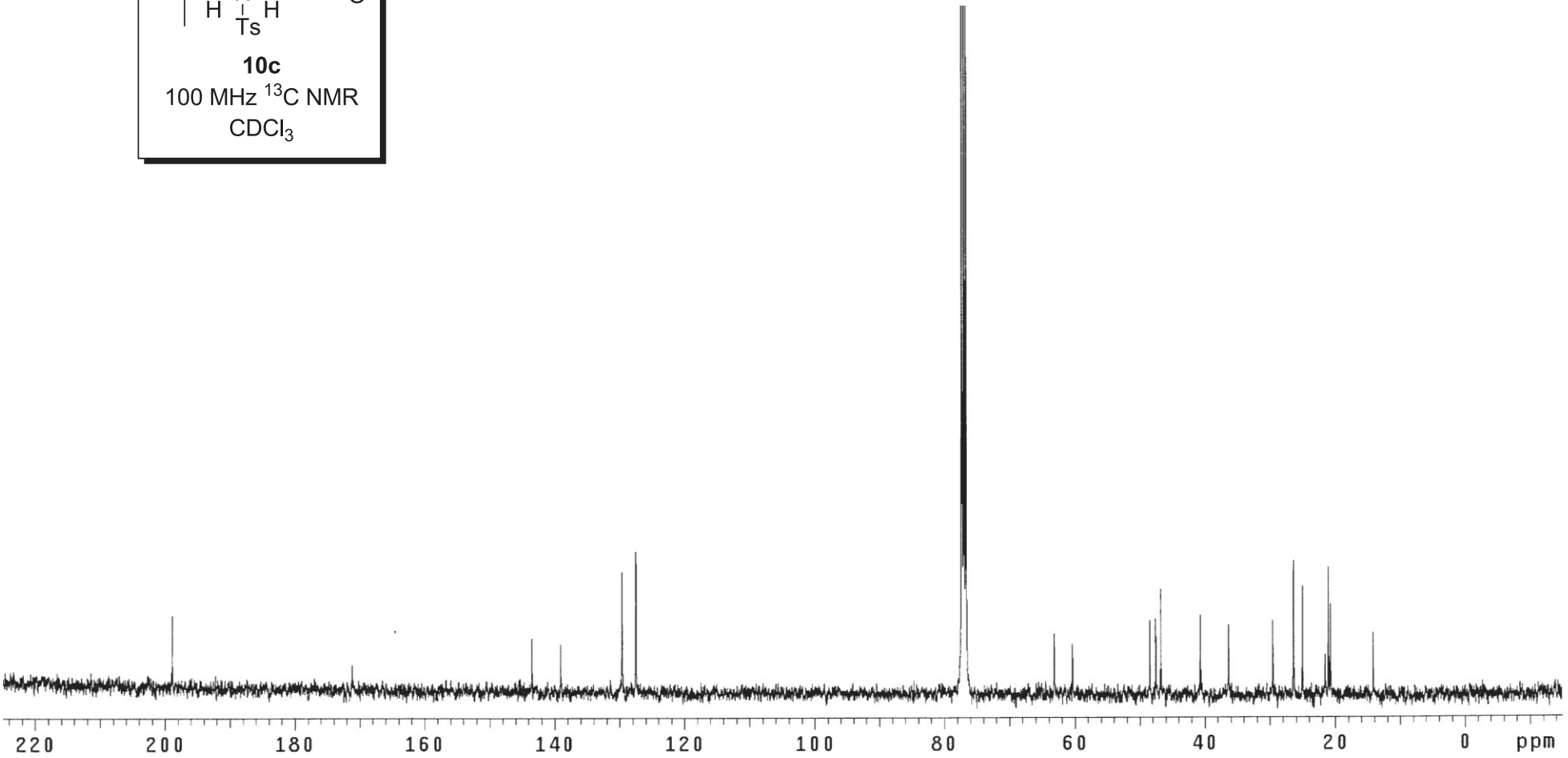


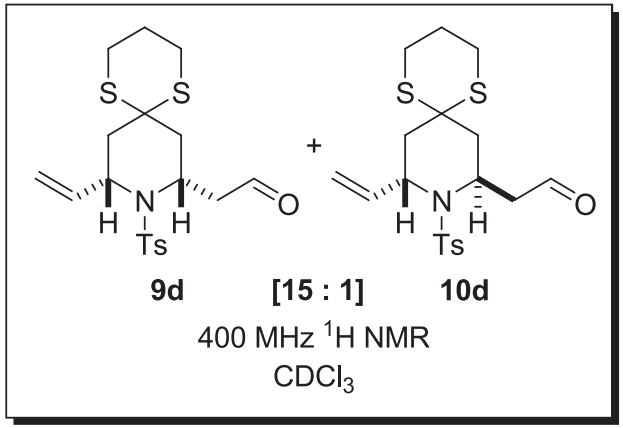
10c
400 MHz ^{1}H NMR
$CDCl_3$





10c
100 MHz ^{13}C NMR
$CDCl_3$

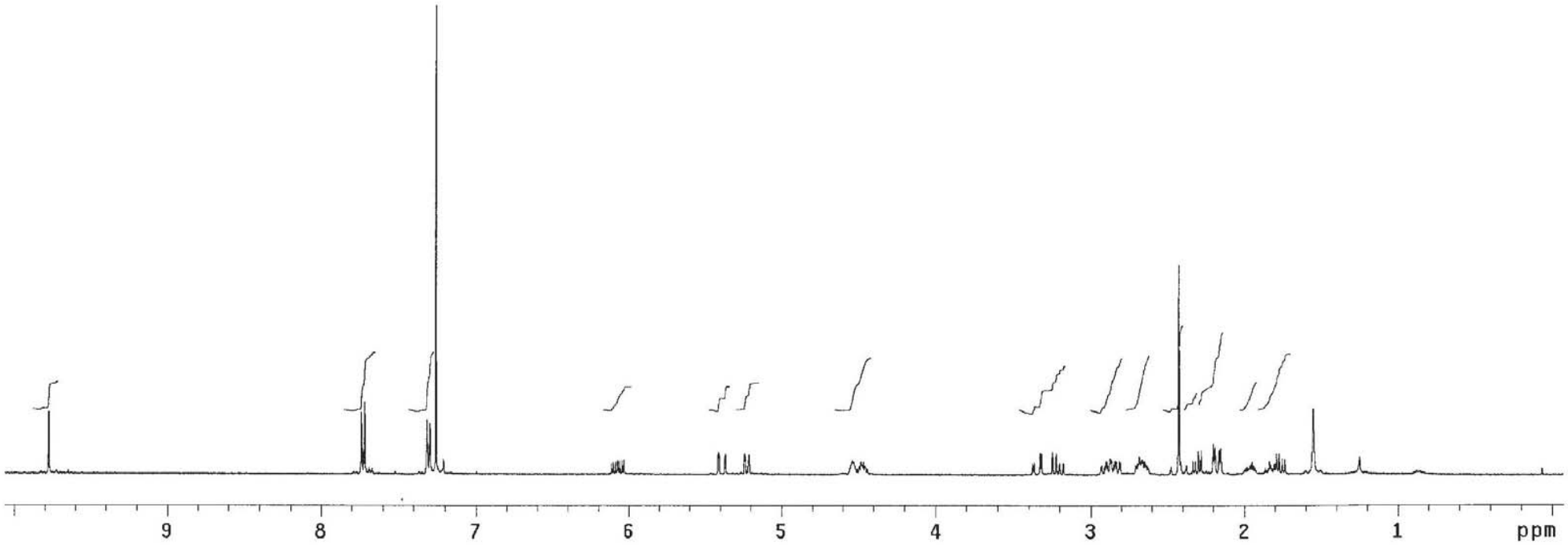


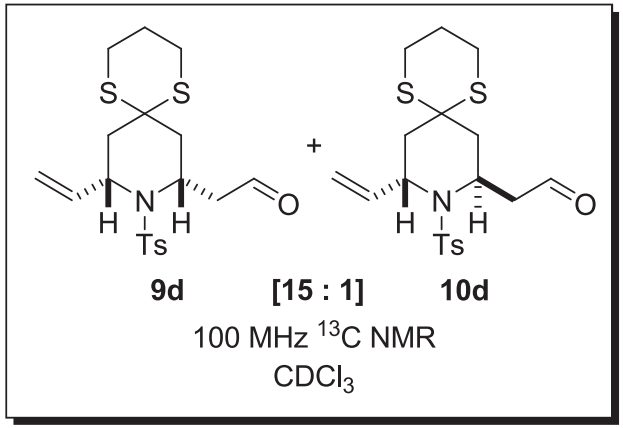


9d **[15 : 1]** **10d**

400 MHz ^{1}H NMR

$CDCl_3$

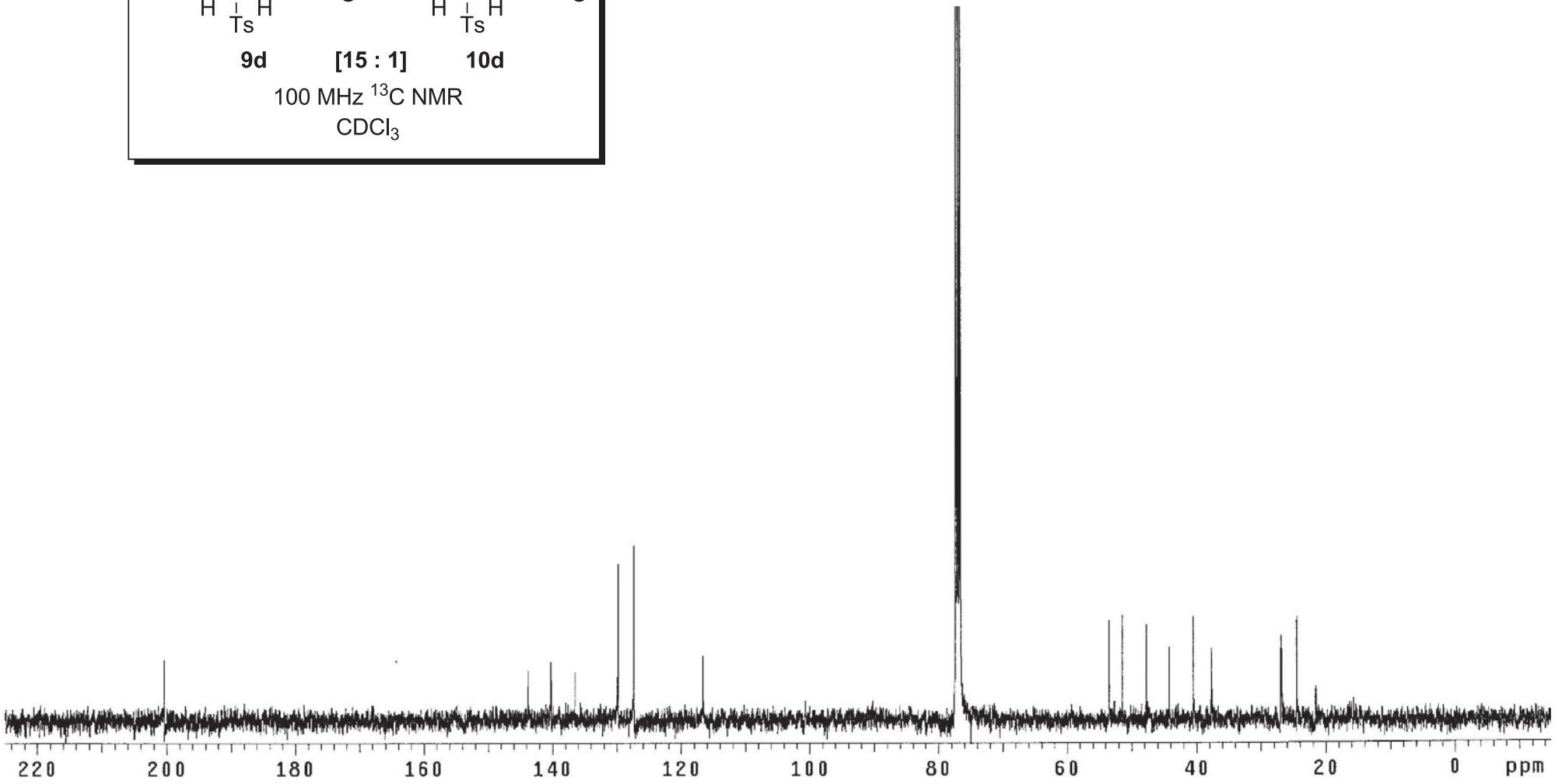


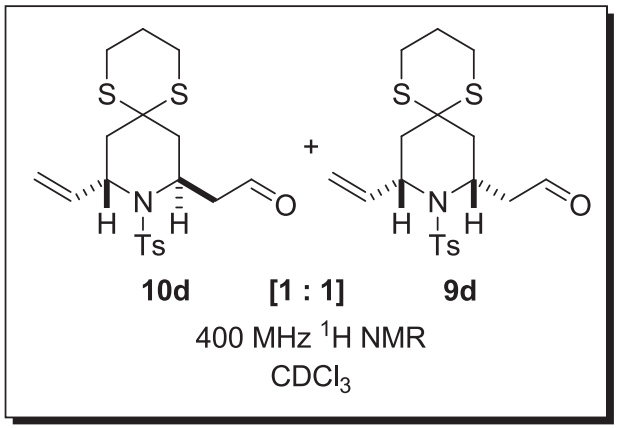


9d **[15 : 1]** **10d**

100 MHz ^{13}C NMR

$CDCl_3$

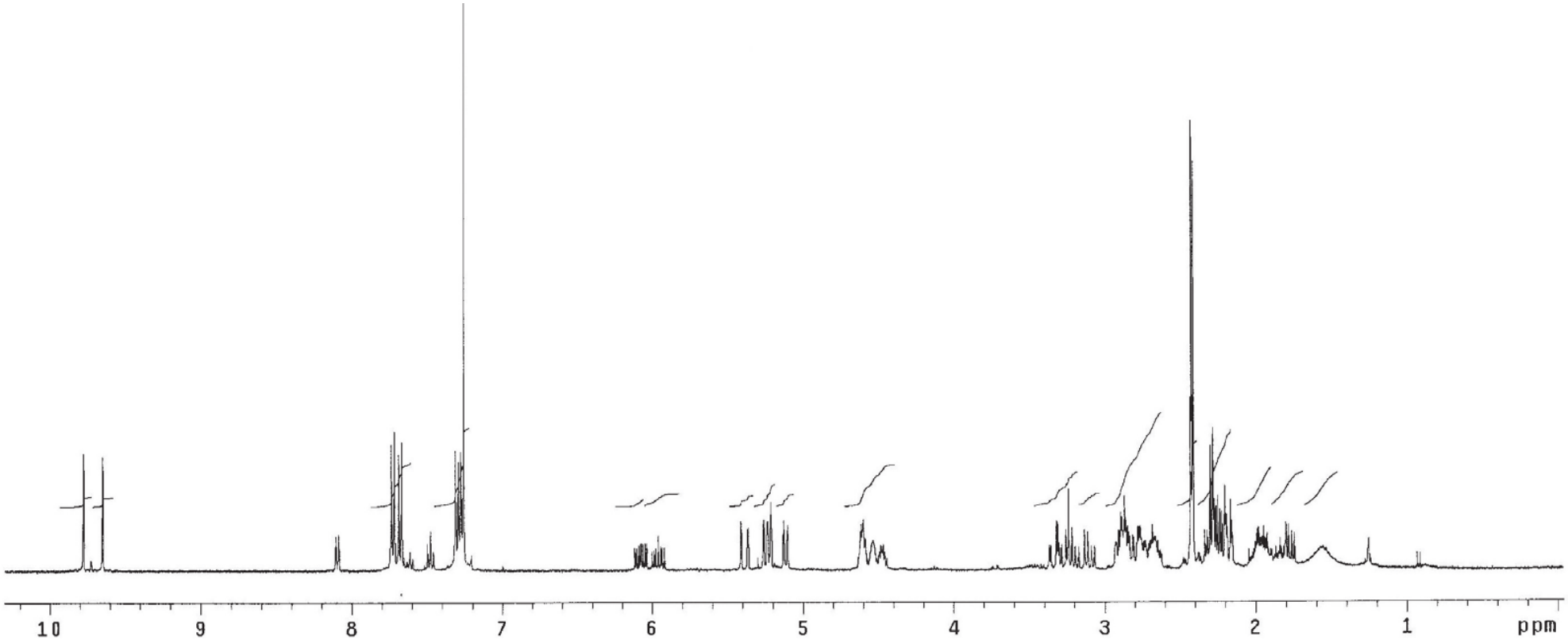


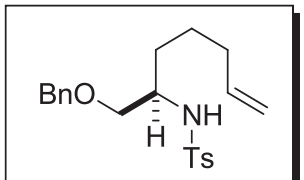


10d **[1 : 1]** **9d**

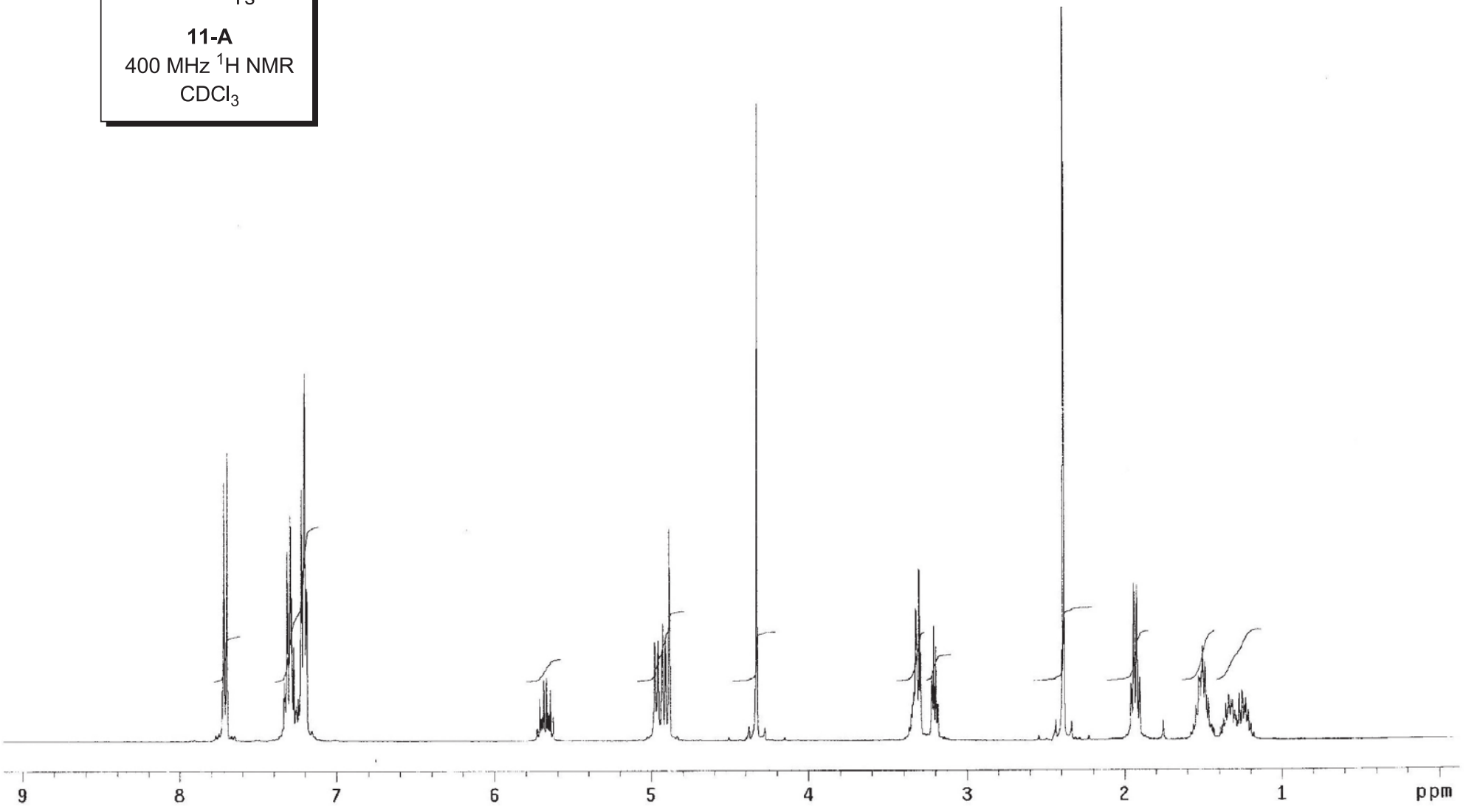
400 MHz ^{1}H NMR

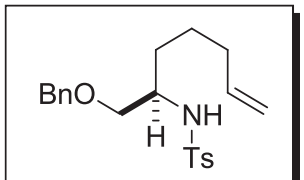
$CDCl_3$



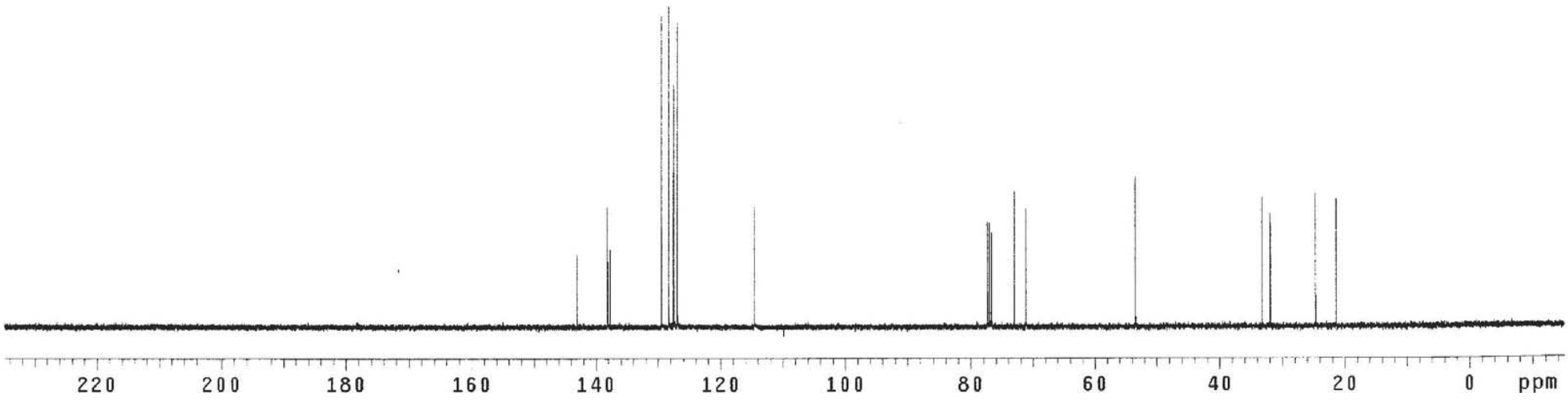


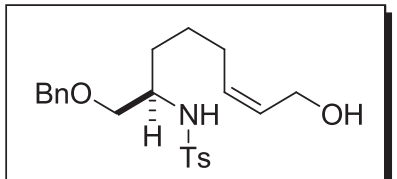
11-A
400 MHz ^{1}H NMR
$CDCl_3$



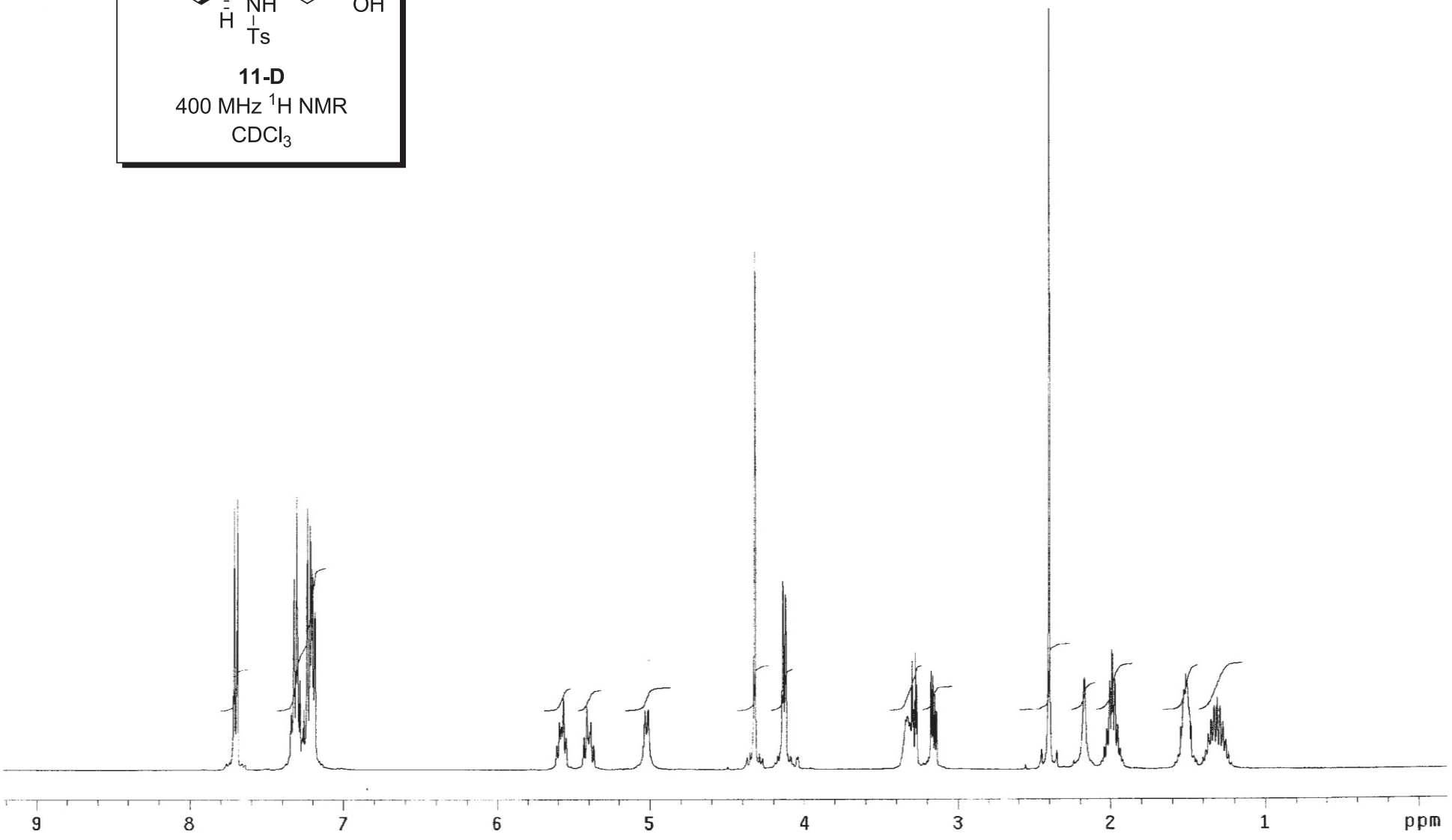


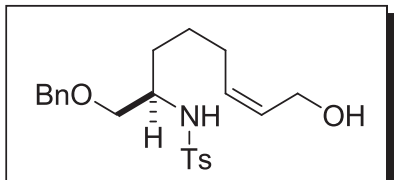
11-A
100 MHz ^{13}C NMR
$CDCl_3$



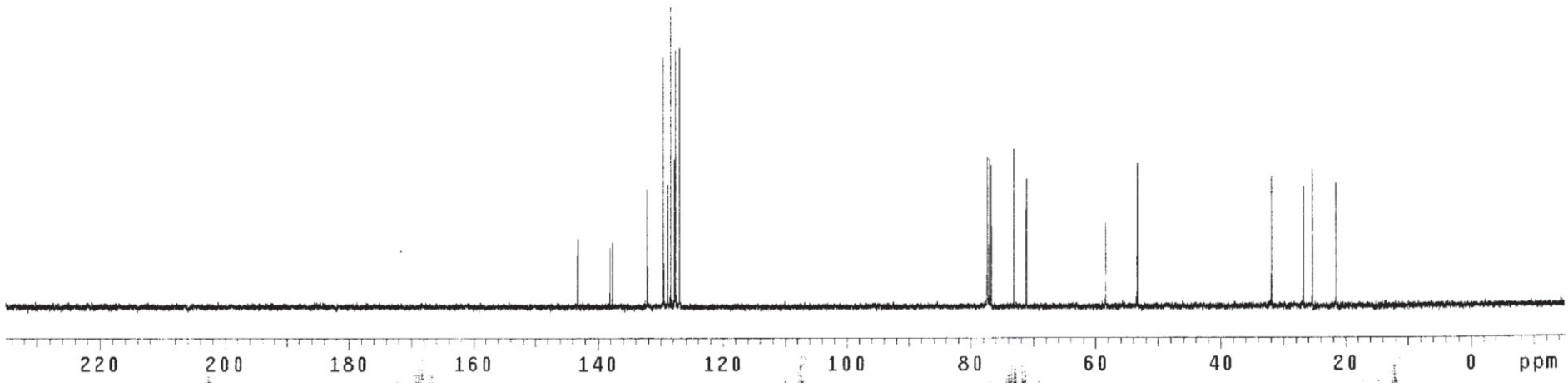


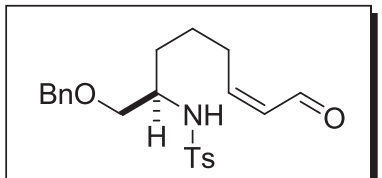
11-D
400 MHz ^{1}H NMR
$CDCl_3$



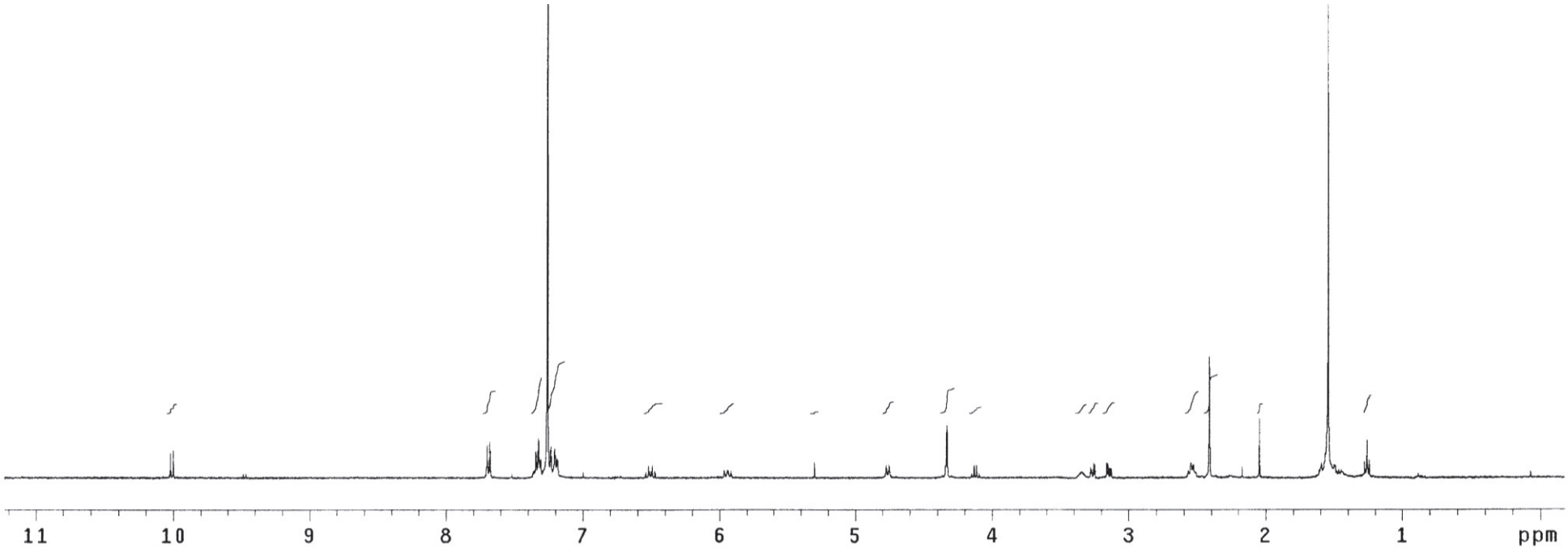


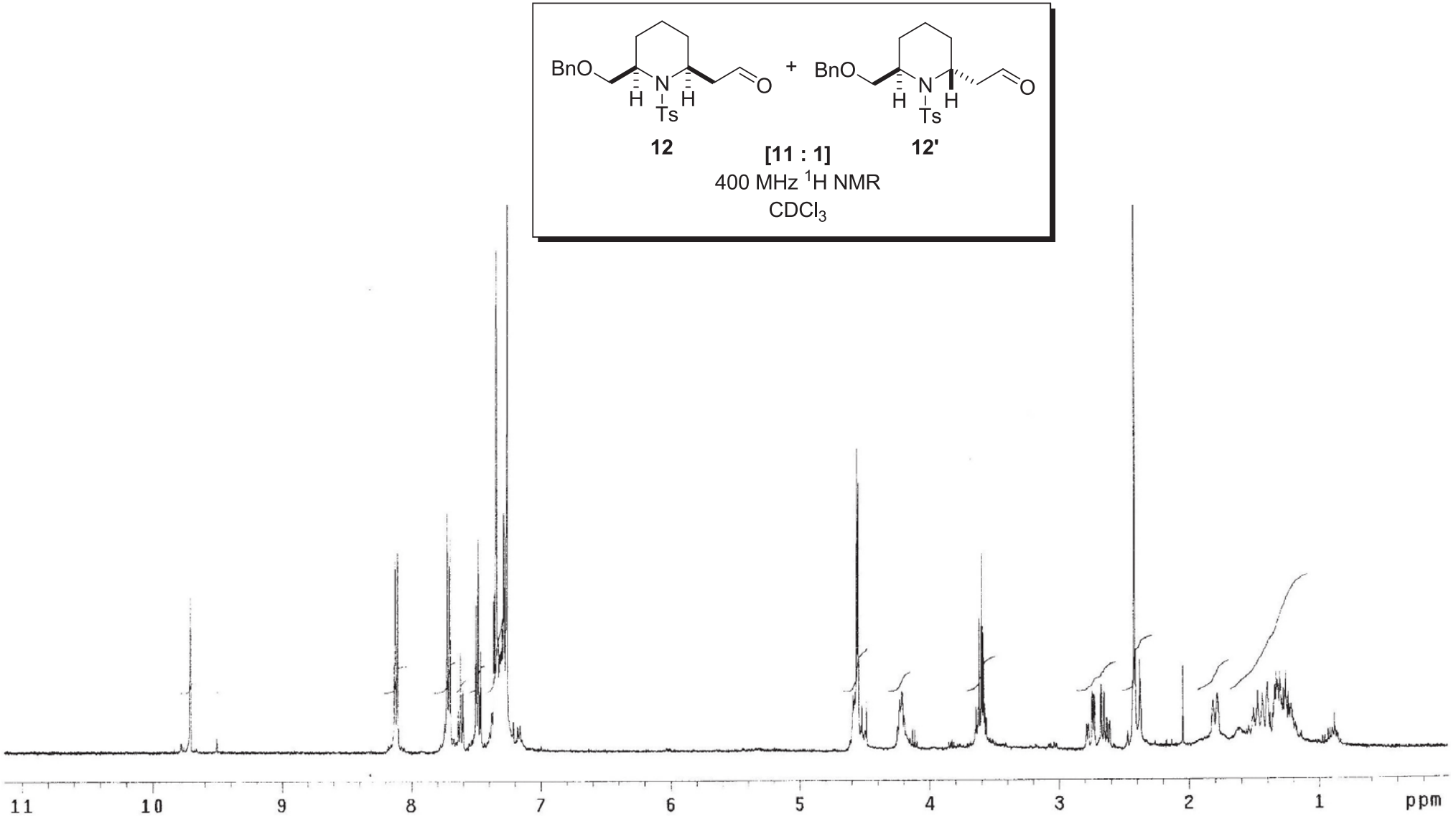
11-D
100 MHz ^{13}C NMR
$CDCl_3$

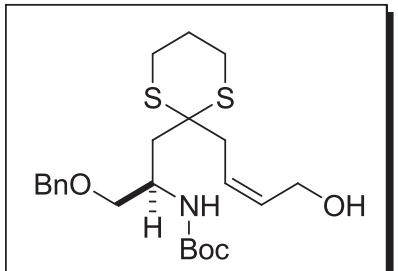




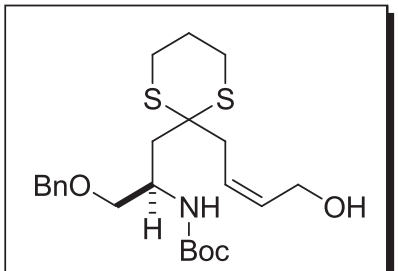
11
400 MHz ^{1}H NMR
$CDCl_3$



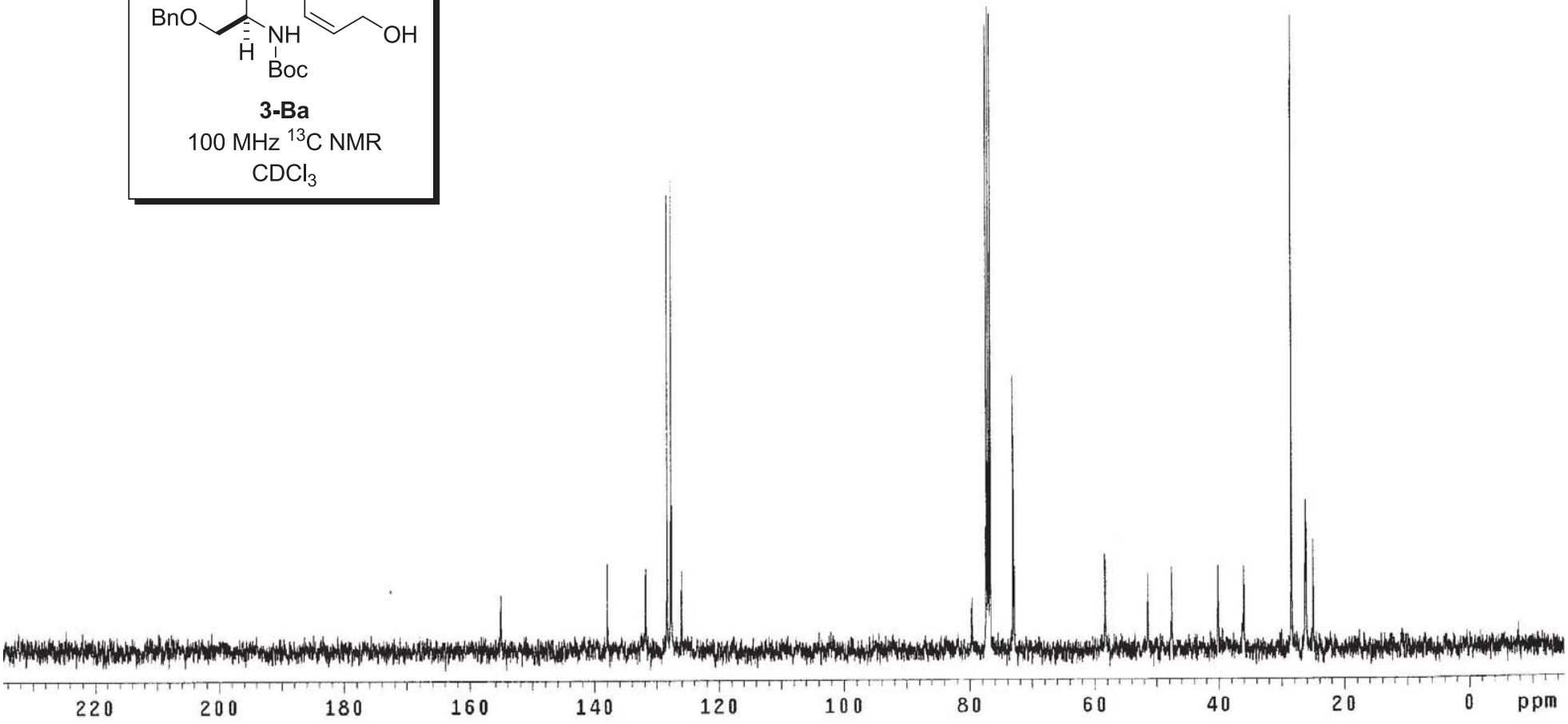

BnO
N
H
Ts
O
+
12
[11 : 1]
400 MHz ^{1}H NMR
$CDCl_3$
12'
11
10
9
8
7
6
5
4
3
2
1
ppm

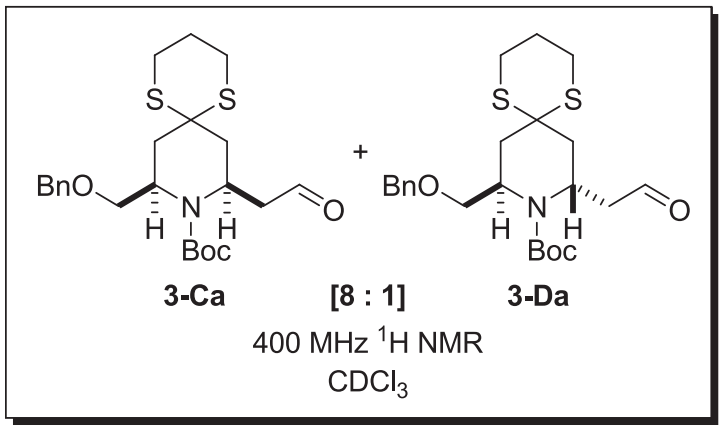


3-Ba
400 MHz ^{1}H NMR
$CDCl_3$



3-Ba
100 MHz ^{13}C NMR
$CDCl_3$

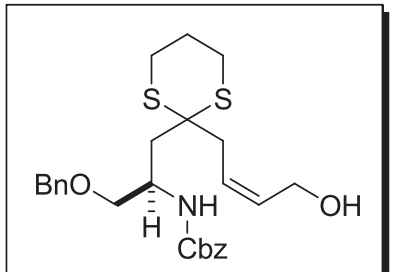




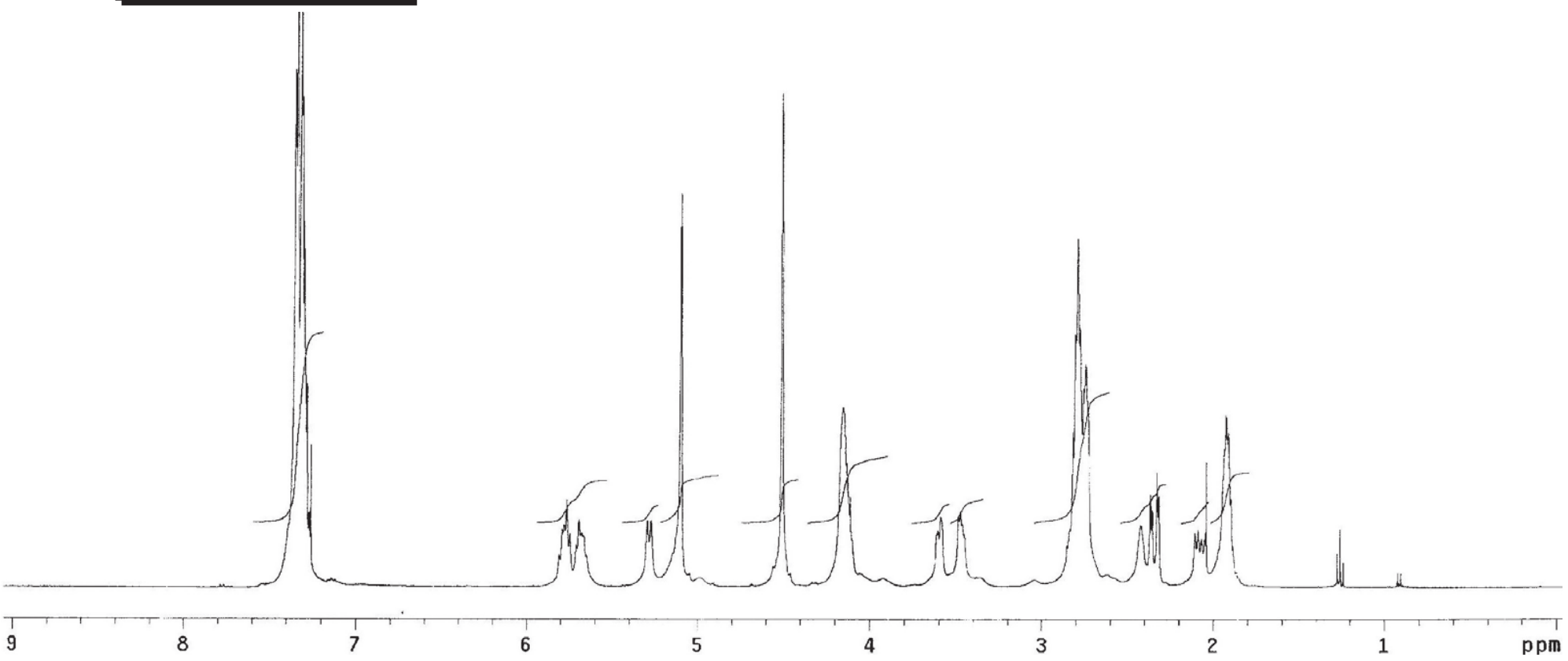
3-Ca **[8 : 1]** **3-Da**

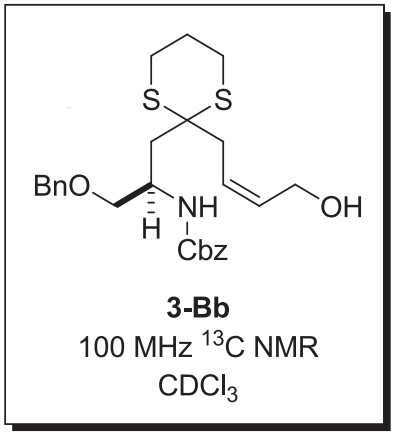
400 MHz ^{1}H NMR

$CDCl_3$

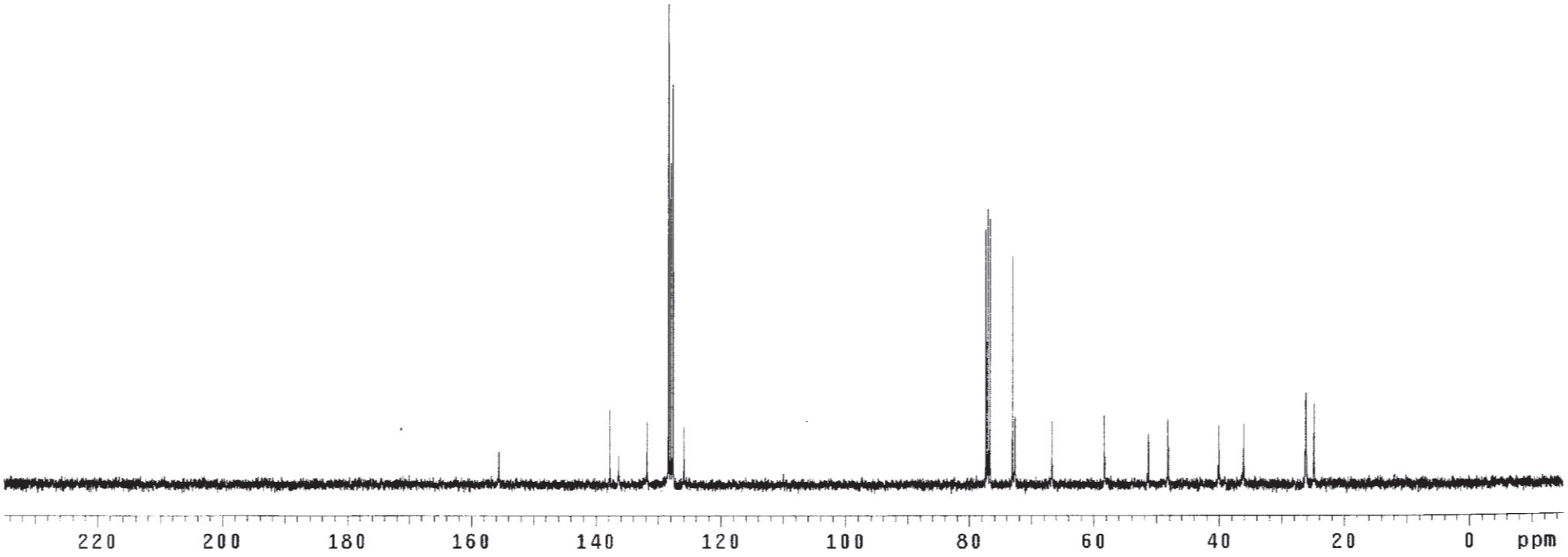


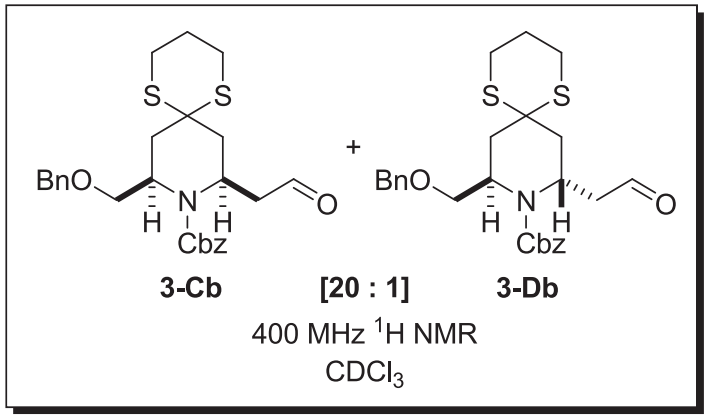
3-Bb
400 MHz ^{1}H NMR
$CDCl_3$





3-Bb
100 MHz ^{13}C NMR
$CDCl_3$

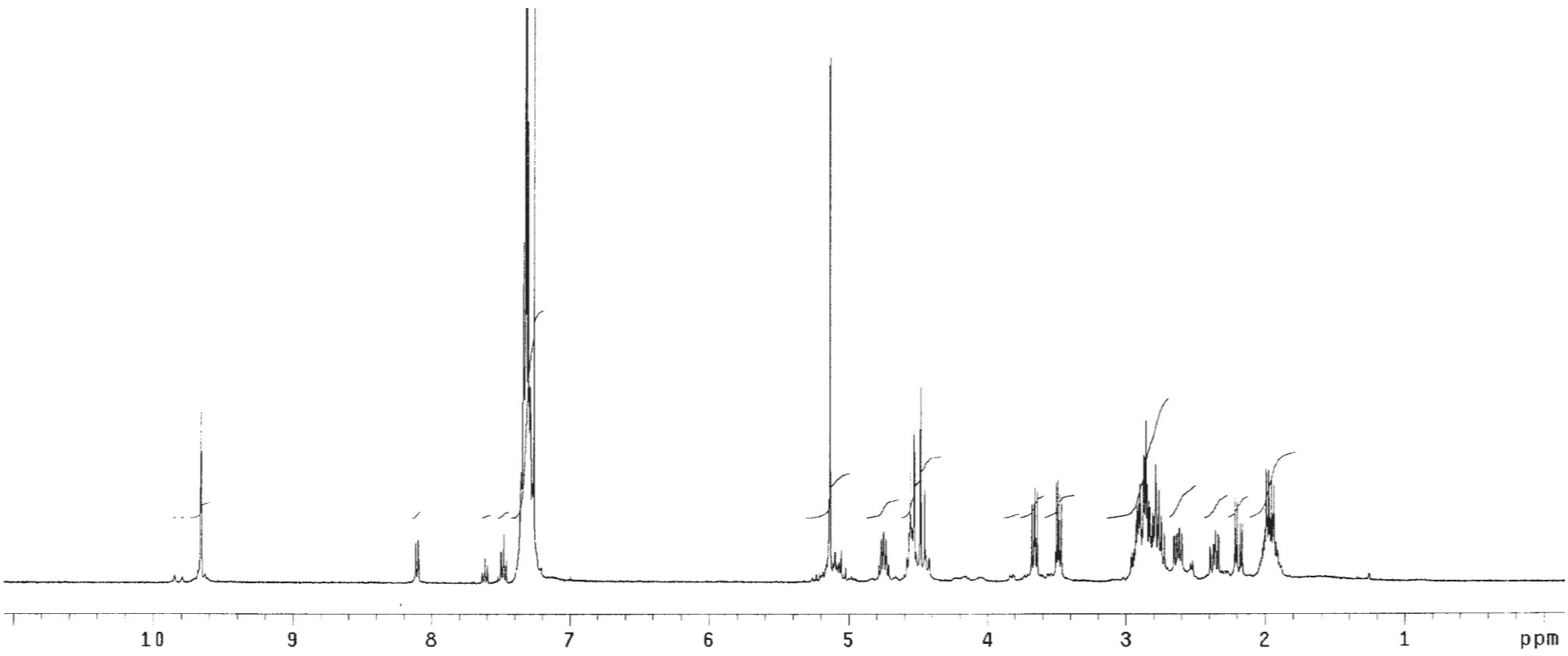


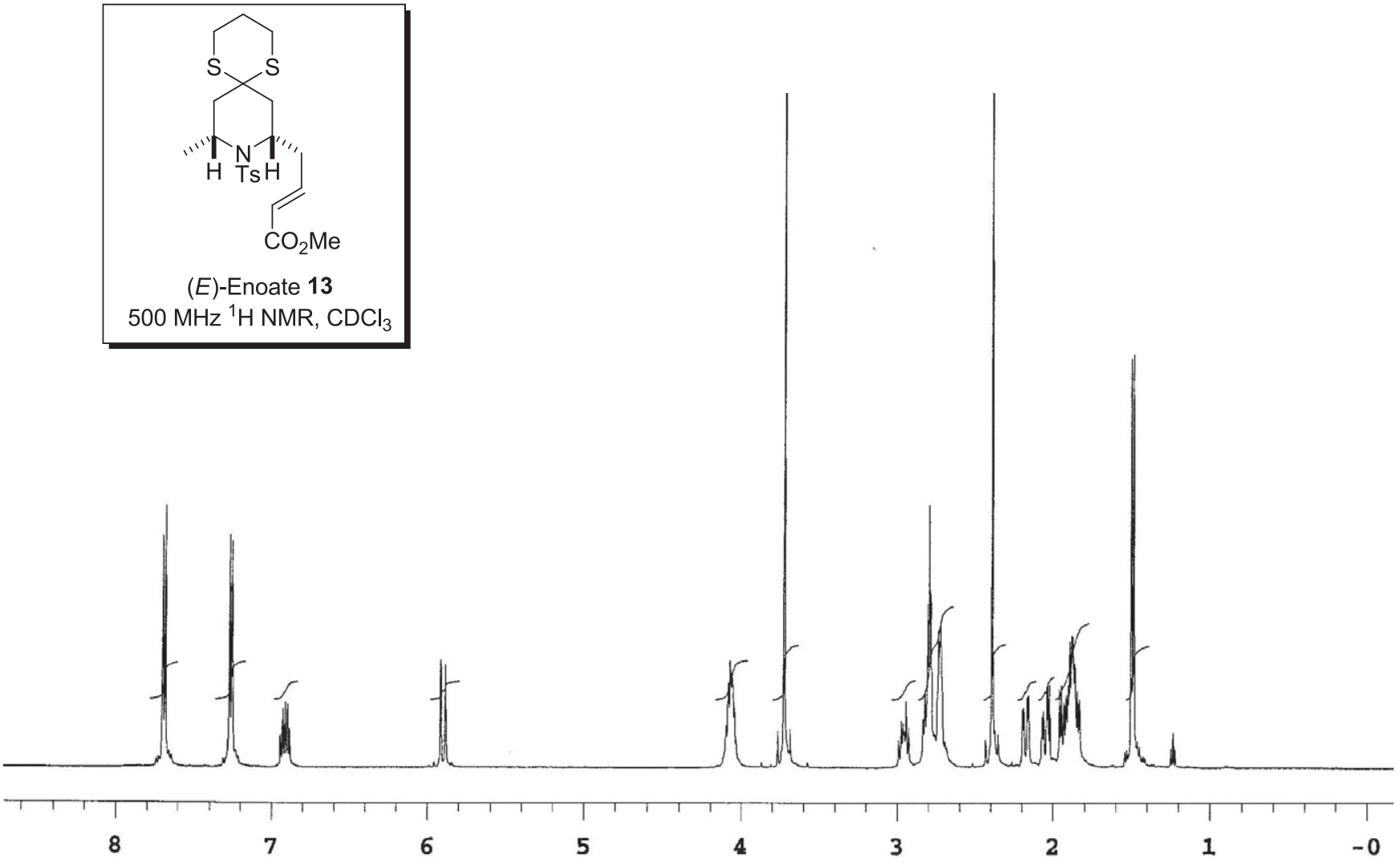


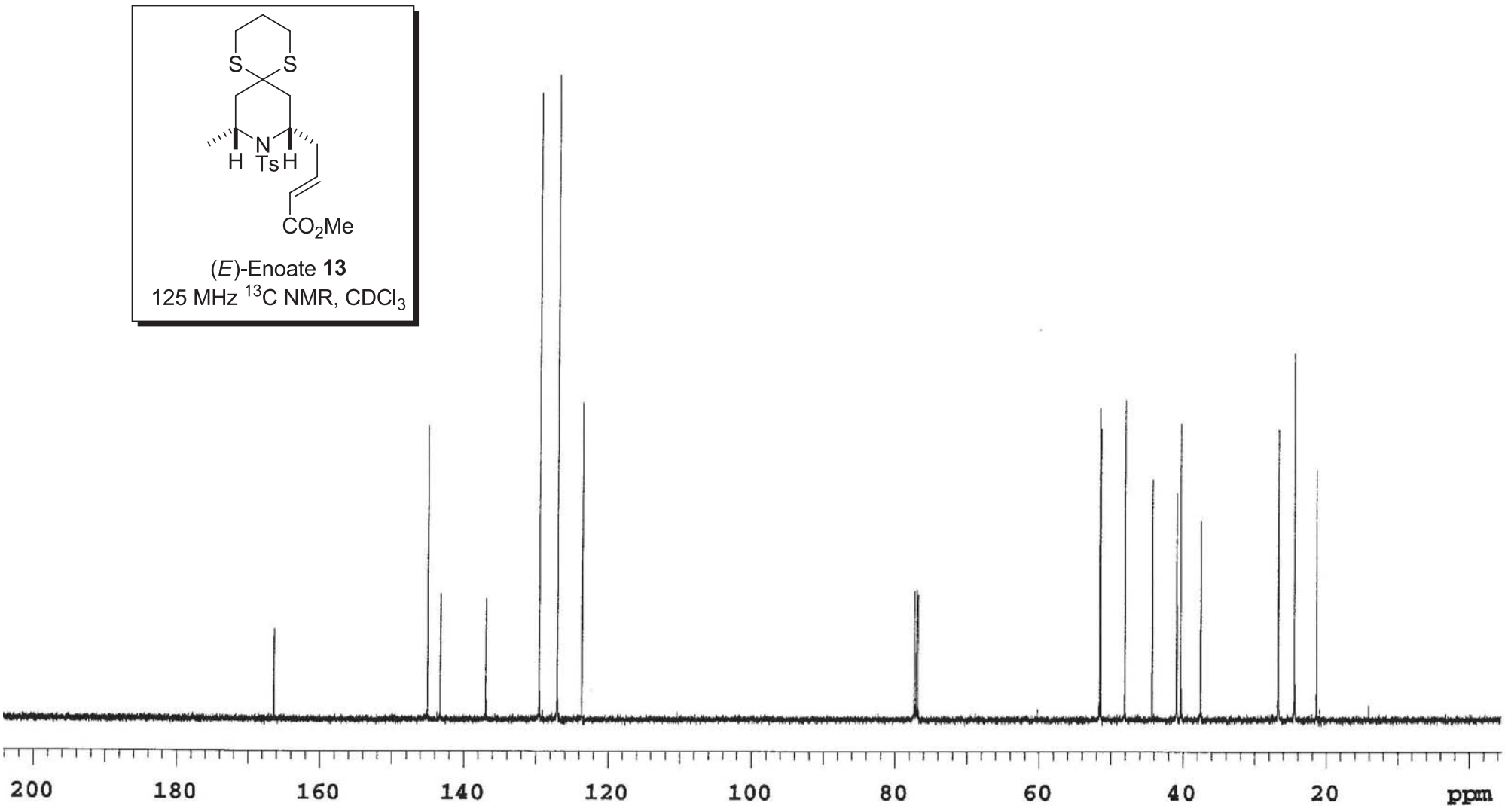
3-Cb **[20 : 1]** **3-Db**

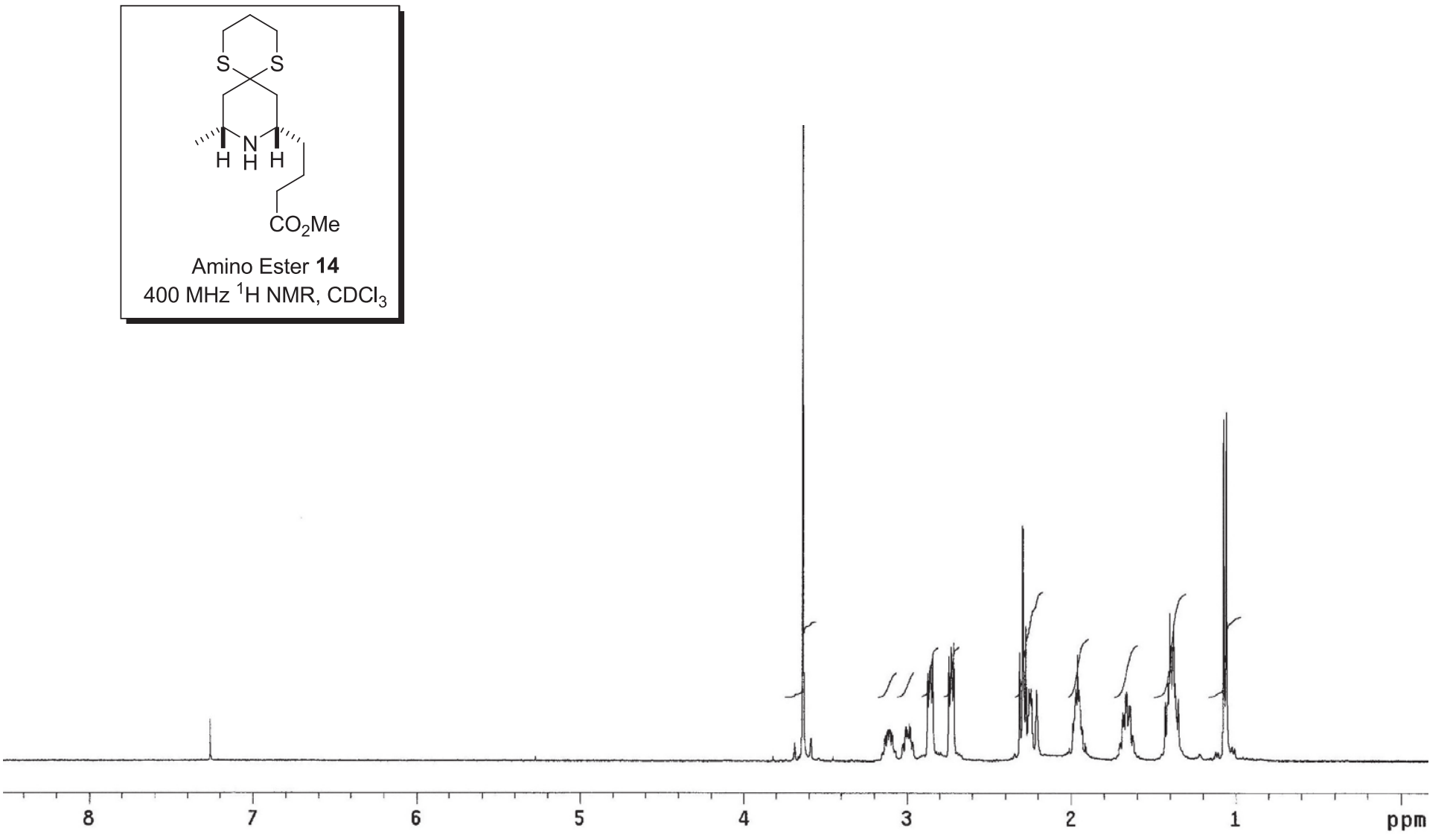
400 MHz ^{1}H NMR

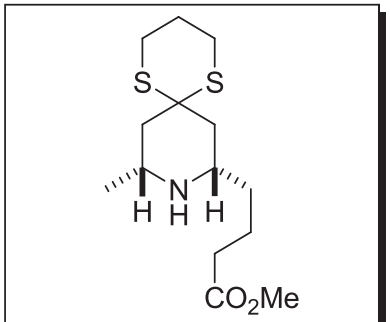
$CDCl_3$



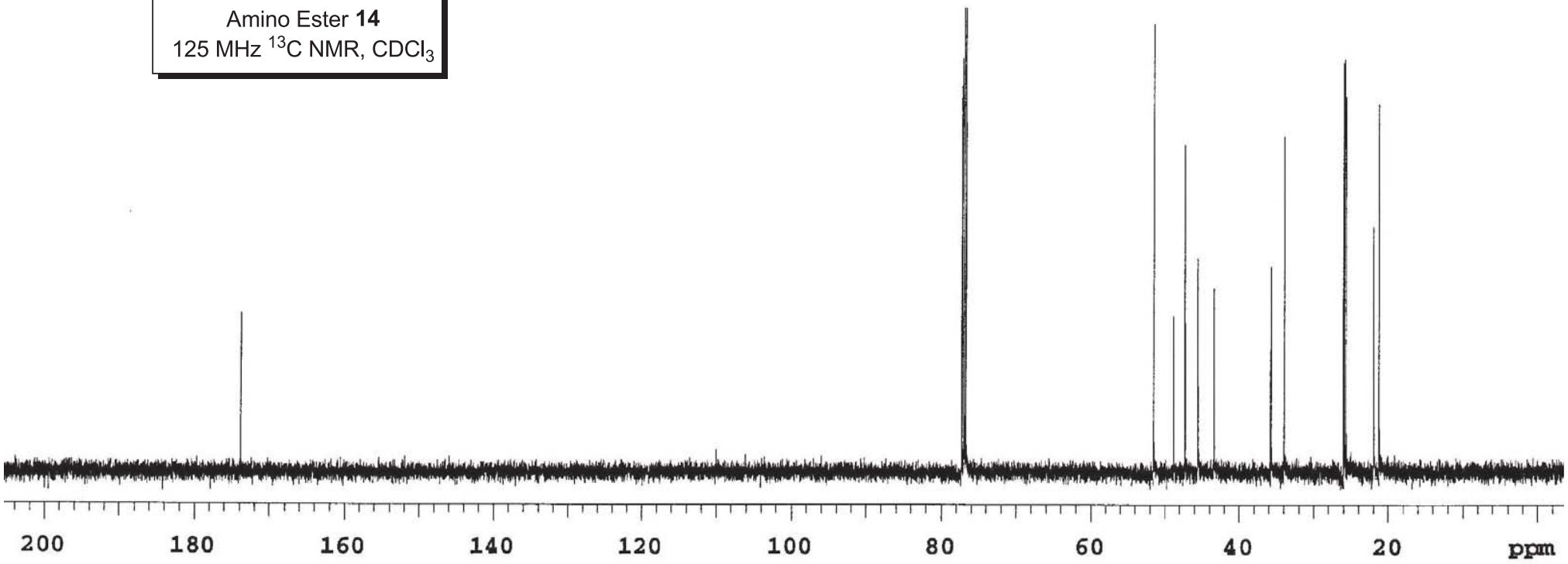

S
S
N
H
Ts
H
CO2Me
(E)-Enoate 13
500 MHz 1H NMR, CDCl3
8
7
6
5
4
3
2
1
-0

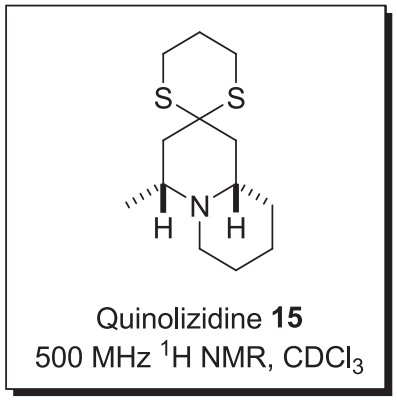

S
S
N
H
Ts
H
CO2Me
(E)-Enoate 13
125 MHz 13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm


S
S
N
H H H
CO2Me
Amino Ester 14
400 MHz 1H NMR, CDCl3
8
7
6
5
4
3
2
1
ppm

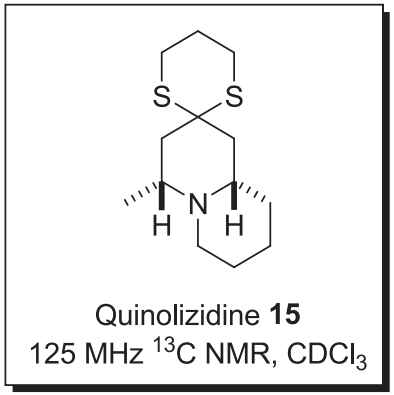


Amino Ester **14**
125 MHz ^{13}C NMR, $CDCl_3$

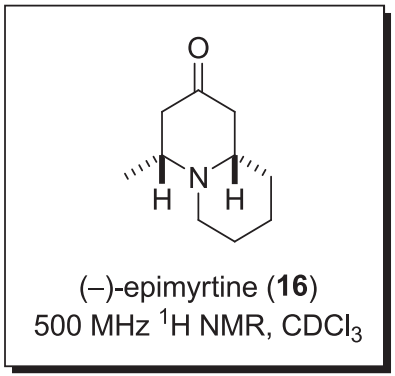




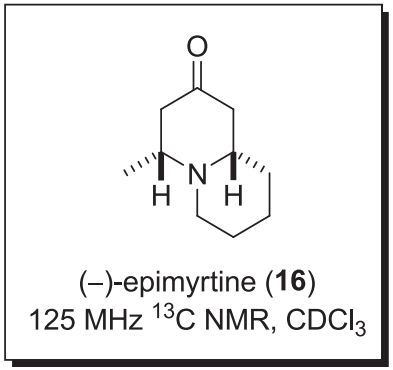
Quinolizidine **15**
500 MHz ^{1}H NMR, $CDCl_3$



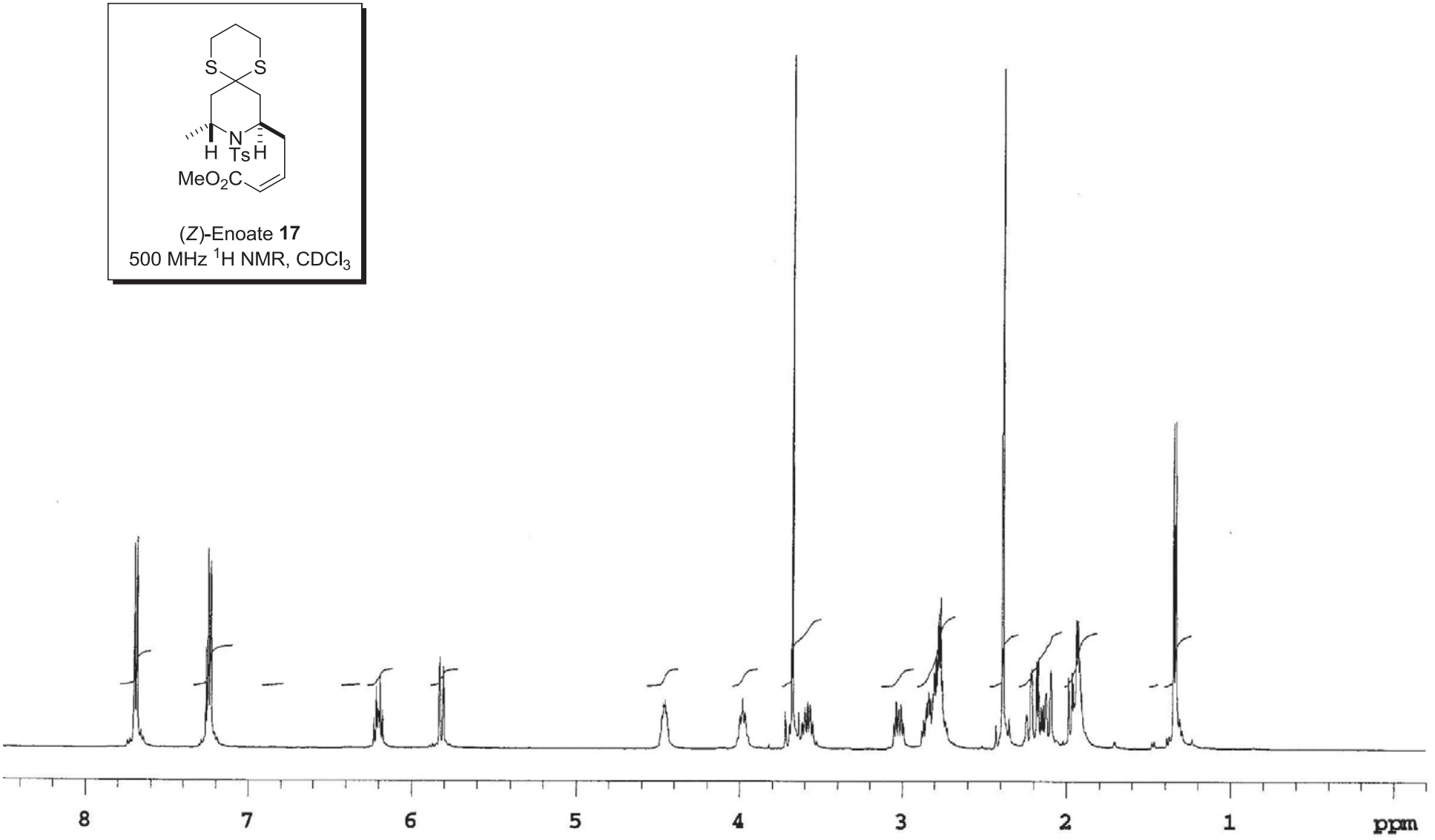
Quinolizidine **15**
125 MHz ^{13}C NMR, $CDCl_3$

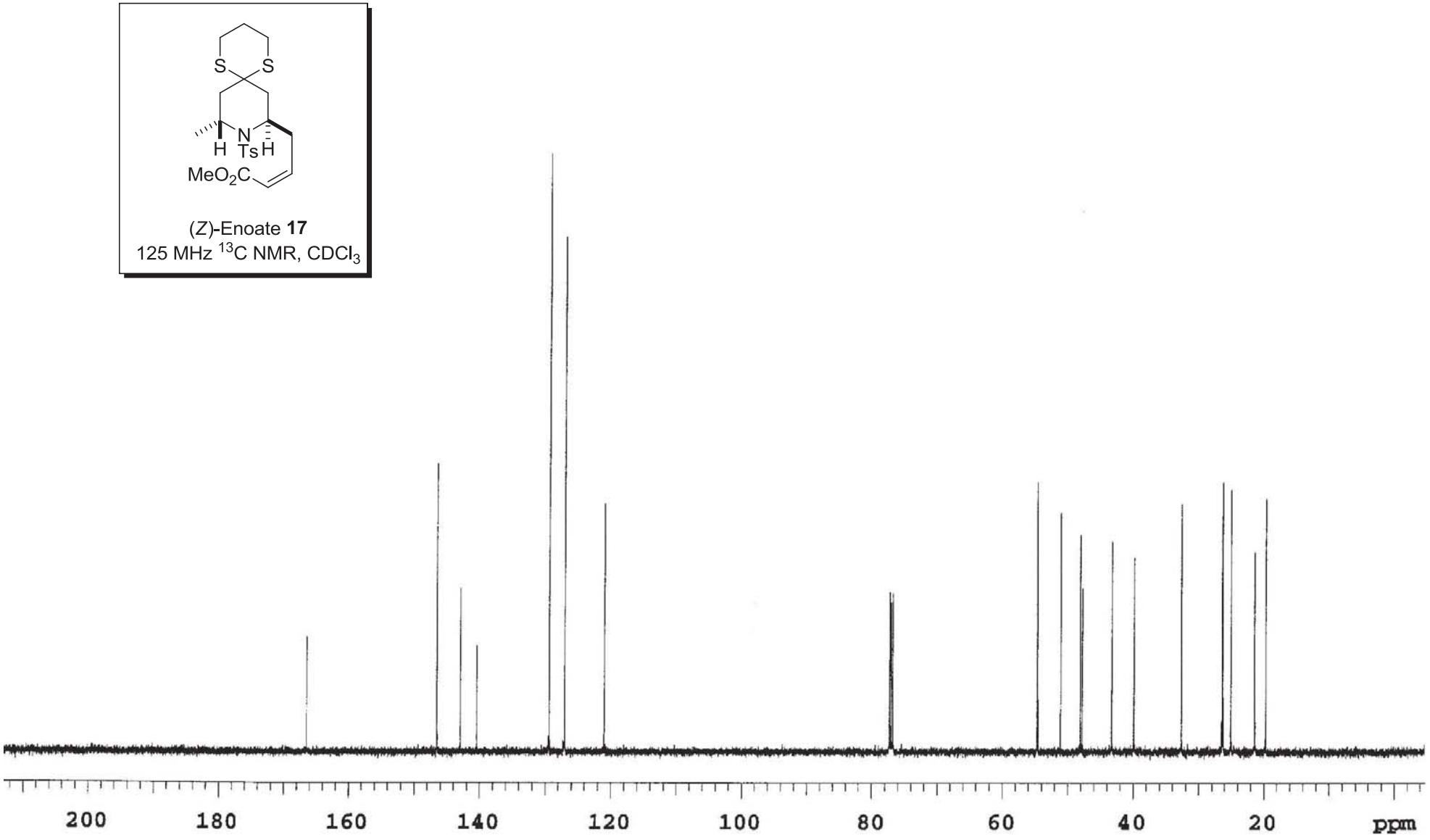


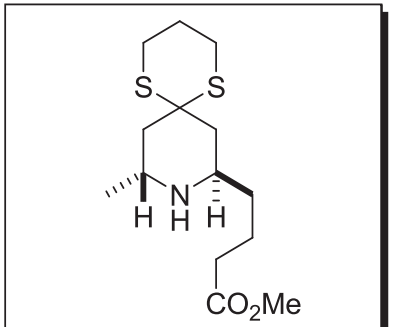
(–)-epimyrtine (**16**)
500 MHz ^{1}H NMR, $CDCl_3$



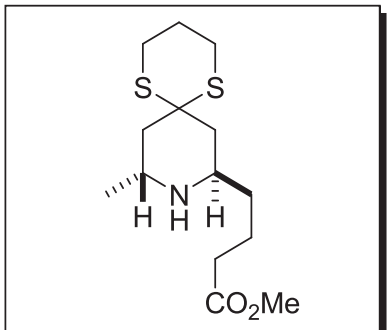
(–)-epimyrtine (**16**)
125 MHz ^{13}C NMR, $CDCl_3$


S
S
N
H
Ts
H
MeO2C
(Z)-Enoate 17
500 MHz 1H NMR, CDCl3
8
7
6
5
4
3
2
1
ppm

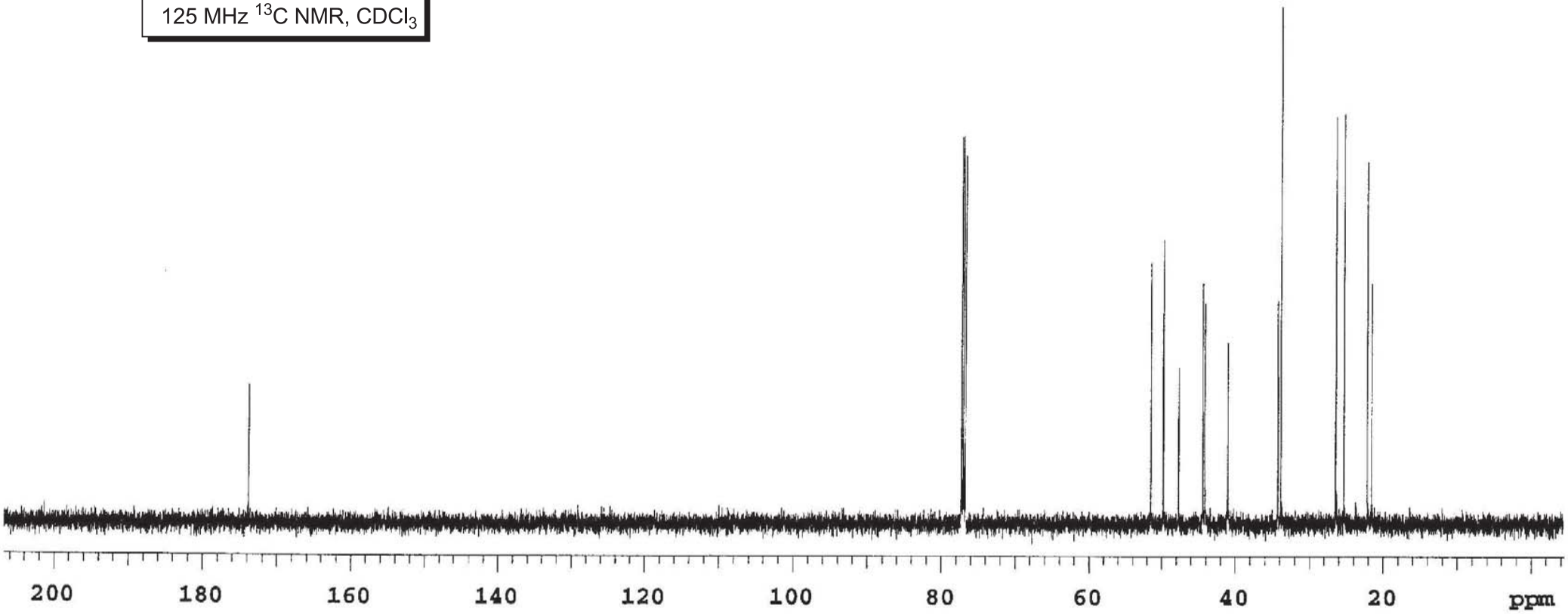

S
S
N
H
Ts
H
MeO2C
(Z)-Enoate 17
125 MHz 13C NMR, CDCl3
200
180
160
140
120
100
80
60
40
20
ppm

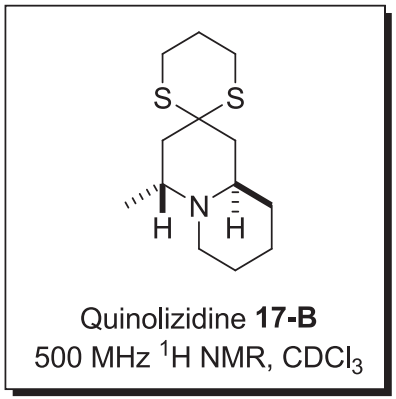


Amino Ester **17-A**
400 MHz ^{1}H NMR, $CDCl_3$

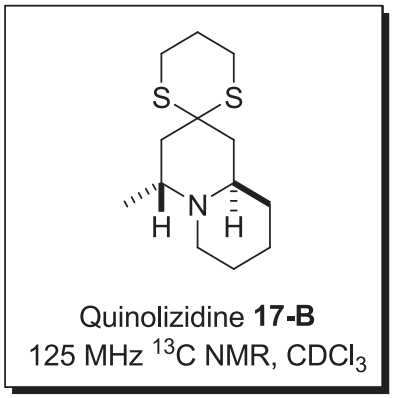


Amino Ester **17-A**
125 MHz ^{13}C NMR, $CDCl_3$

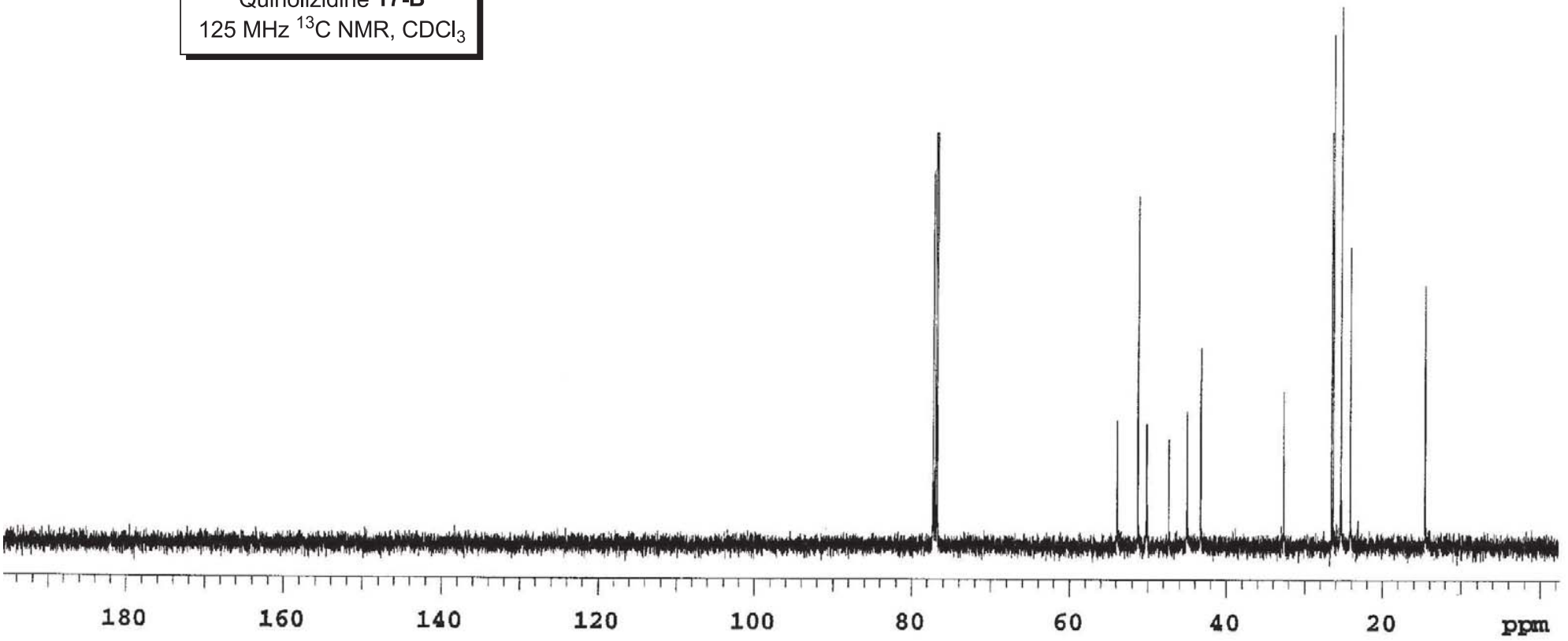


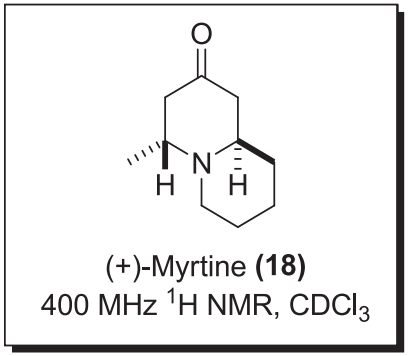


Quinolizidine **17-B**
500 MHz ^{1}H NMR, $CDCl_3$

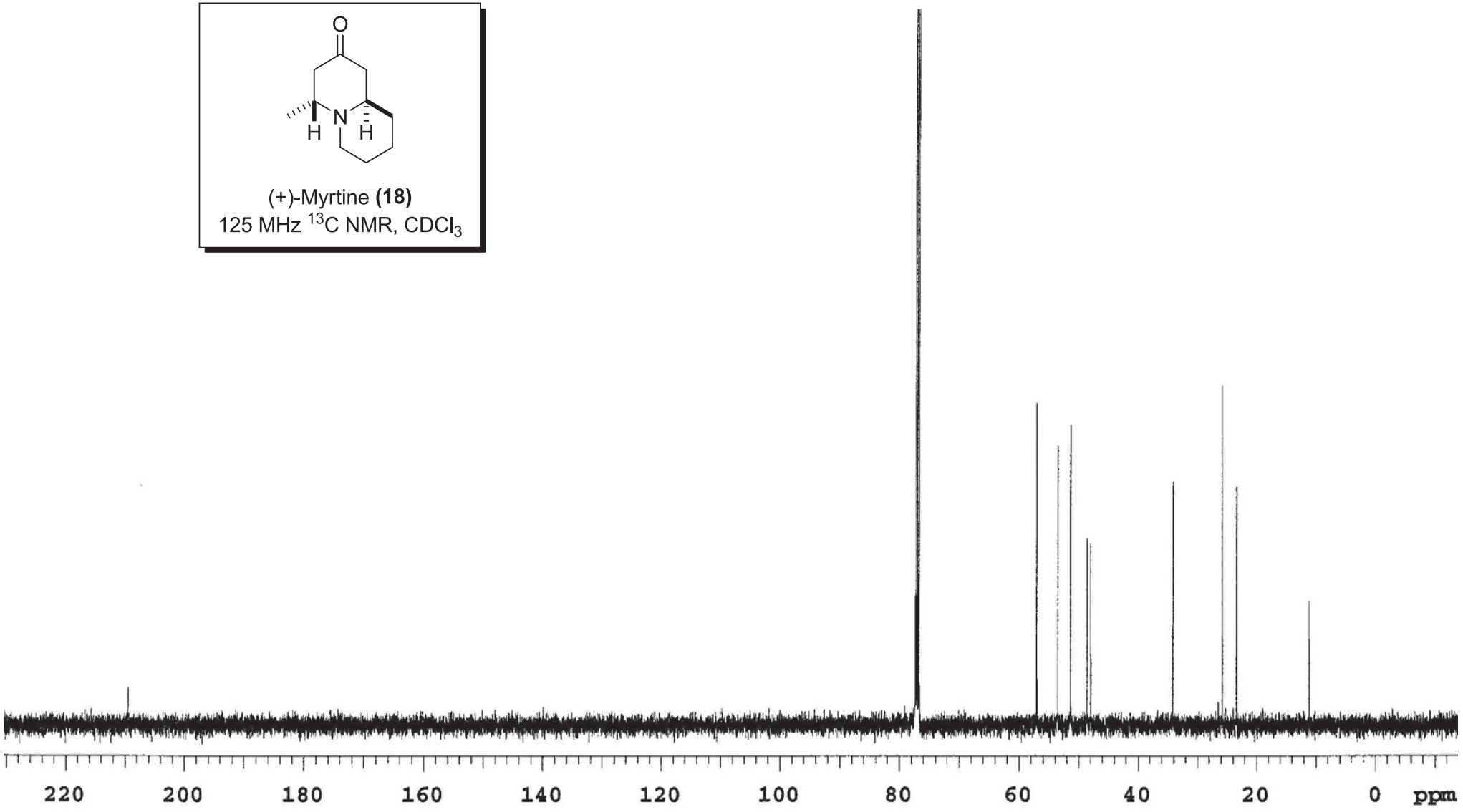


Quinolizidine **17-B**
125 MHz ^{13}C NMR, $CDCl_3$





(+)-Myrtine **(18)**
400 MHz ^{1}H NMR, $CDCl_3$


O
N
H
H
(+)-Myrtine **(18)**
125 MHz ^{13}C NMR, $CDCl_3$
220
200
180
160
140
120
100
80
60
40
20
0
ppm