## Supporting Information

# Total Syntheses of (+)-Lyconadin A and (–)-Lyconadin B

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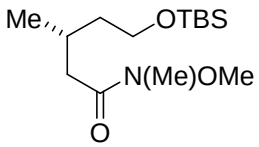
# 1. Materials and Methods

Reactions were carried out in oven- or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. All chemicals were purchased from commercial vendors and used as is, unless otherwise stated. Tetrahydrofuran was freshly distilled from sodium/benzophenone under an argon atmosphere. Dichloromethane and diethylether were filtered through activated alumina and copper solvent purification system under nitrogen (Pure SolvTM PS-400). Triethylamine, diisopropylethylamine, hexamethylphophoramide, diisopropylamine, pyridine and 2,6-lutidine were freshly distilled from calcium hydride. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates. Silica gel chromatography was performed with silica gel 60 (particle size 40-60 μm) supplied by Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. All melting points were obtained on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a Jasco Model FT/IR-480 Plus spectrometer. Proton and carbon NMR spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported relative to chloroform (δ 7.27), methanol (δ 3.30) and *N*,*N*-dimethylformamide (δ 8.03) for $^{1}$H-NMR and chloroform (δ 77.23), methanol (δ 49.00) and *N*,*N*-dimethylformamide (δ 163.15) for $^{13}$C-NMR. Optical rotations were measured on a Perkin-Elmer model 241, Jas.co P-1010 or Jas.co DIP-370 polarimeter. High resolution mass spectra were measured at the University of Pennsylvania on either a VG Micromass 70/70 H or VG ZAB-E spectrometer. Single crystal X-ray structures were determined at the University of Pennsylvania with an Enraf Nonius CAD-4 automated diffractometer.

## 2. Experimental Procedures



(–)-**10**

**Amide (–)-10**: (–)-Methyl-(*R*)-3-methylglutarate (55 g, 0.34 moles) was dissolved in dichloromethane (1 L), cooled to -20 °C and was treated with pyridine (33 mL, 0.41 moles, 1.2 equiv.). Cyanuric fluoride (62 mL, 0.69 moles, 2.0 equiv.) was added dropwise to the vigorously stirring solution over 15 minutes. The reaction mixture was stirred for 3 hours at -20 °C, treated with deionized water (400 mL), warmed to 0 °C and then stirred for an additional 30 minutes. The mixture was filtered through a pad of Celite and was washed with water (1.0 L) and dichloromethane (1.0 L). The filtrate was partitioned, the aqueous layer was extracted with chloroform (5 X 1.0 L) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The resulting acid fluoride was used without purification in the next reaction.

The above prepared acid fluoride was dissolved in chloroform (500 mL) and treated portionwise over 15 minutes with sodium borohydride (26 g, 0.69 moles, 2.0 equiv.). The mixture was cooled to 0 °C and methanol (500 mL) was added dropwise over 3 hours. After stirring for an additional 1 hour at 0 °C, the reaction mixture was diluted with hydrochloric acid (1.0 L, 1N aqueous) and extracted with chloroform (5 X 1.0 L). The combined organic extracts

were dried with sodium sulfate, filtered and concentrated *in vacuo*. The resulting alcohol was used without purification in the next reaction.

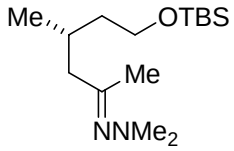
The above prepared alcohol was dissolved in chloroform (500 mL) and treated with hydrochloric acid (10 mL, 12N aqueous) and silica gel (55 g, 1 weight equiv.). The mixture was stirred vigorously for 48 hours at ambient temperature, filtered and concentrated *in vacuo* to provide the lactone as a colorless oil, which was used without purification in the next reaction. However, purification by silica gel gradient chromatography (8:2 to 1:1; hexanes:ethyl acetate) furnished the (+)-lactone as a colorless oil: $[\alpha]^{20}_{D}$ +17.6° (*c*5.62, $CHCl_3$); IR (NaCl plate, neat): 2959 (m), 2924 (m), 2872 (m), 1732 (s), 1457 (w), 1401 (m), 1341 (w), 1313 (w), 1285 (m), 1256 (s), 1228 (s), 1153 (m), 1089 (s), 1063 (m), 994 (m), 913 (w), 823 (w), 779 (w), 652 (w) $cm^{-1}$; $^{1}$H-NMR (500 MHz, $CDCl_3$) δ 4.26 (1H, ddd, *J* = 11.3, 9.7, 4.1 Hz), 4.12 (1H, td, *J* = 11.0, 3.7 Hz), 2.54–2.48 (1H, m), 1.99–1.93 (2H, m), 1.79 (1H, qd, *J* = 12.6, 4.1 Hz) 1.41–1.34 (1H, m), 0.92 (3H, d, *J* = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 171.1, 68.4, 38.0, 30.4, 26.3, 21.2 ppm; high resolution mass spectrum (ES+) *m/z* 378.1680 [$(M+Na)^+$; calculated for $C_{21}H_{25}NNaO_4$: 378.1681].

A flame-dried round bottom flask was charged with *N*,*O*-dimethylhydroxylamine hydrochloride (67 g, 0.69 mole, 2.0 equiv) and dichloromethane (500 mL). The mixture was cooled to 0 °C and trimethylaluminum (343 mL, 2.0M solution in hexanes, 2.0 equiv.) was added dropwise over 1 hour. After an additional 30 minutes at 0 °C, a dichloromethane solution (100 mL) of the above prepared lactone was added dropwise over 30 minutes to the aluminum amide and the mixture was stirred at 0 °C for an additional 1 hour. The reaction mixture was carefully quenched by the addition of sodium potassium tartrate (200 mL, aqueous saturated), which was then warmed to ambient temperature and stirred for an additional 14 hours. The

mixture was partitioned, the organic layer removed and the aqueous layer was further extracted with dichloromethane (3 X 500 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo* to provide the alcohol as a colorless oil, which required no purification: $[\alpha]^{20}_{D}$ +0.16° (*c*1.25, $CHCl_3$); IR (NaCl plate, neat): 3424 (br s), 2959 (s), 2932 (s), 2878 (s), 1731 (m), 1651 (s), 1462 (s), 1455 (s), 1418 (s), 1385 (s), 1178 (s), 1149 (m), 1119 (m), 1056 (s), 1004 (s), 967 (m), 896 (w), 855 (w), 775 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 3.61 (3H, s), 3.56 (2H, t, *J* = 6.5 Hz), 3.20 (1H, br s), 3.11 (3H, s), 2.35 (1H, dd, *J* = 15.4, 6.9 Hz), 2.25 (1H, dd, *J* = 14.9, 6.0 Hz), 2.19–2.09 (1H, m), 1.49–1.44 (2H, m), 0.91 (3H, d, *J* = 6.7 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 174.3, 61.2, 60.3, 40.0, 38.8, 32.1, 26.2, 20.7 ppm; high resolution mass spectrum (CI+) *m/z* 176.1290 [$(M+H)^+$; calculated for $C_8H_{18}NO_3$: 176.1287].

The above prepared alcohol was dissolved in dichoromethane (500 mL) and sequentially treated with *N*,*N*-dimethyl-4-aminopyridine (4.2 g, 0.034 moles, 0.1 equiv.), triethylamine (120 mL, 0.85 moles, 2.5 equiv.) and *tert*-butyldimethylchlorosilane (77 g, 0.51 moles, 1.95 equiv.). The reaction mixture was stirred at ambient temperature for 18 hours, poured into sodium bicarbonate (1 L, aqueous saturated) and the aqueous layer was extracted with dichloromethane (2 X 1L). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (9:1 to 7:3; hexanes:ethyl acetate), providing amide (–)-**10** (88 g, 88% yield) as a colorless oil: $[\alpha]^{20}_{D}$ –6.3° (*c*2.0, $CHCl_3$); IR (NaCl plate, neat): 2955 (s), 2930 (s), 2894 (m), 2857 (s), 1669 (s), 1463 (m), 1411 (m), 1384 (m), 1255 (m), 1176 (w), 1095 (s), 1006 (m), 836 (s), 775 (s) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 3.73–3.62 (2H, m), 3.68 (3H, s), 3.19 (3H, s), 2.44 (1H, dd, *J* = 14.7, 6.0 Hz), 2.30 (1H, dd, *J* = 14.5, 8.6 Hz), 2.21–2.13 (1H, m), 1.65–1.58 (1H, m), 1.48–1.41 (1H, m),

0.97 (3H, d, $J$ = 6.3 Hz), 0.90 (9H, s), 0.05 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 174.1, 61.5, 61.3, 40.0, 39.4, 32.2, 27.1, 26.1, 20.1, 18.2, -5.2 ppm; high resolution mass spectrum (ES+) *m/z* 312.1977 [$(M+Na)^+$; calculated for $C_{14}H_{32}NNaO_3Si$: 312.1970].

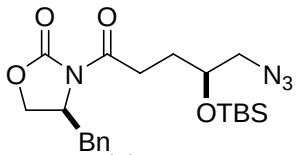



**7**

**Hydrazone 7**: Amide **10** (57 g, 0.20 moles) was dissolved in tetrahydrofuran (1 L) and cooled to -78 °C. Methyl lithium (160 mL, 1.6M in diethylether, 1.3 equiv.) was added slowly over 30 minutes. The reaction mixture was stirred for an additional 30 minutes at -78 °C, treated with sodium bicarbonate (50 mL, aqueous saturated), the cooling bath was removed and the mixture was warmed to ambient temperature. The mixture was poured into water (3 L) and the aqueous layer was extracted with ethyl acetate (2 X 1 L). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 9:1; hexanes:ethyl acetate), providing the methyl ketone (46 g, 96% yield) as a colorless oil: $[\alpha]^{20}_D$ +3.36° (*c*2.05, $CHCl_3$); IR (NaCl plate, neat): 2954 (s), 2929 (s), 2890 (m), 2855 (s), 1718 (s), 1472 (m), 1361 (m), 1256 (m), 1164 (w), 1093 (s), 1001 (w), 902 (w), 836 (s), 775 (s) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 3.68–3.60 (2H, m), 2.47 (1H, dd, $J$ = 15.6, 5.8 Hz), 2.24 (1H, dd, $J$ = 15.6, 8.2 Hz), 2.20–2.12 (1H, m), 2.12 (3H, s), 1.55–1.48 (1H, m), 1.43–1.36 (1H, m), 0.92 (3H, d, $J$ = 6.7 Hz), 0.89 (9H, s), 0.04 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 209.1, 61.2, 51.5, 39.8, 30.4, 26.5, 26.1, 20.1, 18.5, -5.1 ppm;

high resolution mass spectrum (ES+) *m/z* 267.1746 [$(M+Na)^+$; calculated for $C_{13}H_{28}NaO_2Si$: 267.1756].

The above prepared methyl ketone (3.38 g, 13.8 mmol) was dissolved in toluene (25 mL) and treated with freshly activated 4Å powdered molecular sieves (4.00 g, 1.2 weight equiv.), sodium sulfate (4.00 g, 1.2 weight equiv.), catalytic acetic acid (2 drops from 9" pipet) and *N*,*N*-dimethylhydrazine (10.5 mL, 138 mmol, 10 equiv.). The mixture was placed into an oil bath preheated to 100 °C for 1 hour. The reaction mixture was then cooled, filtered and the solid was rinsed with toluene (20 mL). The filtrate was concentrated *in vacuo* and the residue was purified by silica gel gradient chromatography (8:2 to 7:3; hexanes:ethyl acetate), providing hydrazone **7** (3.84 g, 97% yield) as a colorless oil: $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~5:1 mixture of E and Z hydrazone imine isomers, * denotes minor isomer signals) δ 3.71–3.62 (2H, m), 2.45 (6H, m), *2.39 (s), 2.22 (1H, dd, *J* = 13.0, 6.3 Hz), 2.04 (1H, dd, *J* = 12.7, 8.9 Hz), 2.03–1.95 (1H, m), 1.94 (3H, s), *1.92 (s), 1.59–1.50 (1H, m), 1.41–1.30 (1H, m), 0.91–0.90 (12H, br s), 0.91–0.90 (6H, br s) ppm; high resolution mass spectrum (ES+) *m/z* 309.2332 [$(M+Na)^+$; calculated for $C_{15}H_{34}N_2NaOSi$: 309.2338].



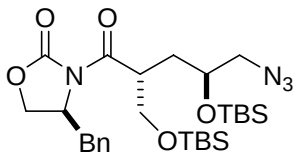
(+)-**12**

**Imide (+)-12:** Carboxylic acid **11**[1] (1.09 g, 4.00 mmol) was dissolved in tetrahydrofuran (15 mL), cooled to -78 °C and triethylamine (0.723 mL, 5.20 mmol, 1.3 equiv.) was added dropwise. After stirring for 5 minutes, 2,2,2-trimethylacetyl chloride (0.590 mL, 4.80 mmol, 1.2

equiv.) was added dropwise, the mixture was warmed to 0 °C and stirred for 1 hour. The resulting mixed anhydride was then cooled to -78 °C.

In a separate flask, L-Phe-derived oxazolidinone[2] (0.851 g, 4.80 mmol, 1.3 equiv.) was dissolved in tetrahydrofuran (7 mL), cooled to -78 °C and treated dropwise over 5 minutes with *n*-buthyl lithium (3.38 mL, 1.6M solution in hexanes, 5.40 mmol, 1.35 equiv.). The reaction mixture was stirred at -78 °C for 30 minutes and then transferred to the -78 °C mixed anhydride vessel via syringe over 5 minutes. The reaction mixture was stirred at -78 °C for 30 minutes, the dry ice/acetone bath was removed and the mixture was warmed to ambient temperature. After stirring for 30 minutes at ambient temperature, the mixture was treated with ammonium chloride (150 mL, aqueous saturated) and poured into water (200 mL). The aqueous layer was extracted with ethyl acetate (2 X 150 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (95:5 to 75:25; hexanes:ethyl acetate), providing imide (+)-**12** (1.50 g, 94% yield) as a white solid: $[\alpha]^{20}_{D}$ +32.2° (*c*1.00, $CHCl_3$); IR (NaCl plate, thin film, $CHCl_3$): 2955 (s), 2929 (s), 2885 (m), 2857 (s), 2102 (s), 1783 (s), 1700 (s), 1389 (m), 1360 (m), 1290 (m), 1259 (m), 1211 (m), 1103 (m), 1052 (w), 1012 (w), 838 (m), 809 (w), 777 (m), 748 (w), 702 (m) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 7.33 (2H, br t, *J* = 7.4 Hz), 7.29–7.27 (1H, m), 7.21 (2H, br d, *J* = 7.1 Hz), 4.81 (1H, dddd, *J* = 9.9, 7.3, 3.3, 3.3 Hz), 4.21–4.15 (2H, m), 3.94 (1H, m), 3.32 (1H, dd, *J* = 12.6, 4.5 Hz), 3.30 (1H, dd, *J* = 13.4, 3.3 Hz), 3.20 (1H, dd, *J* = 12.7, 5.6 Hz), 3.00 (2H, t, *J* = 7.6 Hz), 2.74 (1H, dd, *J* = 13.2, 9.9 Hz), 1.99–1.92 (1H, m), 1.90–1.83 (1H, m), 0.92 (9H, s), 0.13 (3H, s), 0.12 (3H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 172.8, 153.5, 135.4, 129.5, 129.1, 127.5, 70.7, 66.3, 56.7, 55.3, 38.0, 31.6, 29.2, 25.9, 18.1, -4.4, -4.6 ppm; high

resolution mass spectrum (ES+) *m/z* 455.2074 [$(M+Na)^+$; calculated for $C_{21}H_{32}N_4NaO_4Si$: 455.2091].



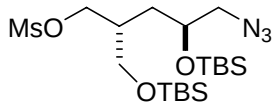
(+)-**13**

**Bissilylether (+)-13:** (Note: This reaction was run on a maximum of ~30g. On larger scale, yields dropped precipitously. Also of note, ammonium chloride (aqueous saturated) washing of the organic extracts was necessary to prevent elimination of the aldol product, which had occurred during concentration and/or column chromatography). Imide **12** (27.9 g, 64.5 mmol) was dissolved in dichloromethane (500 mL) and cooled to -10 °C. Titanium tetrachloride (7.78 mL, 70.9 mmol, 1.1 equiv.) was added dropwise to the mixture, such that the internal temperature did not rise above 0 °C. The mixture was stirred an additional 30 minutes and then *N*,*N*-diisopropylethylamine (12.9 mL, 74.2 mmol, 1.15 equiv.) was added dropwise, such that the internal temperature did not rise above 0 °C. The deep red solution was stirred an additional 45 minutes at -10 °C. *s*-Trioxane (6.97 g, 77.4 mmol, 1.2 equiv.) was added to the reaction mixture in one portion, followed by dropwise addition of titanium tetrachloride (7.78 mL, 70.9 mmol, 1.1 equiv.), such that the internal temperature did not rise above 0 °C. The reaction mixture was stirred for 3 hours at -10 °C and then quenched via dropwise addition of sodium bicarbonate (150 mL, aqueous saturated). The mixture was stirred for 30 minutes, poured into water and extracted with dichloromethane (3 X 1L). The combined organic extracts were washed once with ammonium chloride (400 mL, aqueous saturated), dried with sodium sulfate, filtered and

concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (9:1 to 7:3; hexanes:ethyl acetate), providing the aldol product (24.4 g, 82% yield) as a white solid: $[\alpha]^{20}_{D}$ +48.2° (*c*1.25, $CHCl_3$); $^1$H-NMR (500 MHz, $CDCl_3$) δ 7.34 (2H, br t, *J* = 7.3 Hz), 7.31–7.26 (1H, m), 7.24 (2H, br d, *J* = 6.7 Hz), 4.73–4.69 (1H, m), 4.24 (1H, dd, *J* = 9.1, 7.3 Hz), 4.20 (1H, dd, *J* = 8.9, 3.0 Hz), 4.11 (1H, ddd, *J* = 11.9, 6.7, 5.2 Hz), 3.93–3.88 (1H, m), 3.81 (1H, dd, *J* = 11.0, 6.9 Hz), 3.36 (1H, dd, *J* = 12.7, 4.5 Hz), 3.30 (1H, dd, *J* = 13.6, 3.5 Hz), 3.21 (1H, dd, *J* = 13.0, 5.4 Hz), 2.81 (1H, dd, *J* = 13.6, 9.5 Hz), 2.37 (1H, br s), 2.06 (1H, ddd, *J* = 13.0, 7.1, 5.5 Hz), 1.82 (1H, ddd, *J* = 14.1, 6.3, 6.0 Hz), 0.92 (9H, s), 0.14 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 175.0, 153.9, 135.3, 129.7, 129.1, 127.6, 69.7, 66.5, 64.7, 56.6, 55.8, 41.9, 38.0, 33.8, 25.9, 18.1, -4.4, -4.5 ppm.

The above prepared aldol product (27.4 g, 59.3 mmol) was dissolved in dichoromethane (200 mL) and treated with *N*,*N*-dimethyl-4-aminopyridine (0.730 g, 5.93 mmol, 0.1 equiv.) and triethylamine (14.8 mL, 107 mmol, 1.8 equiv.). The solution was cooled to 0 °C and *tert*-butyldimethylchlorosilane (13.4 g, 88.9 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred at 0 °C for 30 minutes, warmed to ambient temperature and stirred for an additional 18 hours. The reaction mixture was poured into sodium bicarbonate (300 mL, aqueous saturated) and extracted with dichloromethane (3 X 700 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 85:15; hexanes:ethyl acetate), providing bissilylether (+)-**13** (34.2 g, 99% yield) as a white amorphous solid: $[\alpha]^{20}_{D}$ +34.3° (*c*0.685, $CHCl_3$); IR (NaCl plate, thin film, $CHCl_3$): 2954 (s), 2929 (s), 2857 (s), 2120 (s), 1782 (s), 1702 (s), 1471 (m), 1389 (m), 1350 (m), 1257 (s), 1100 (s), 837 (s), 777 (s), 702 (m) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 7.33 (2H, br t, *J* = 7.3 Hz), 7.29–7.26 (1H, m), 7.22 (2H, br d, *J* = 7.1 Hz),

4.72 (1H, dddd, *J* = 9.7, 7.8, 3.3, 3.3 Hz), 4.18 (1H, dd, *J* = 8.9, 7.8 Hz), 4.14 (1H, dd, *J* = 8.9, 3.3 Hz), 4.11–4.06 (1H, m), 3.89 (1H, dd, *J* = 9.7, 4.8 Hz), 3.84 (1H, dd, *J* = 10.0, 6.3 Hz), 3.88–3.83 (1H, m), 3.33 (1H, dd, *J* = 10.1, 4.1 Hz), 3.30 (1H, dd, *J* = 10.4, 3.3 Hz), 3.16 (1H, dd, *J* = 12.3, 5.6 Hz), 2.67 (1H, dd, *J* = 13.4, 9.7 Hz), 2.08 (1H, ddd, *J* = 14.5, 7.8, 5.6 Hz), 1.78 (1H, ddd, *J* = 13.8, 6.7, 6.0 Hz), 0.91 (9H, s), 0.89 (9H, s), 0.13 (3H, s), 0.12 (3H, s), 0.06 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 174.3, 153.3, 135.6, 129.6, 129.1, 127.5, 69.9, 66.2, 64.8, 56.7, 55.4, 42.2, 38.3, 33.6, 26.0, 25.9, 18.4, 18.1, -4.5, -4.5, -5.2, -5.3 ppm; high resolution mass spectrum (ES+) *m/z* 599.3042 [$(M+Na)^+$; calculated for $C_{28}H_{48}N_4NaO_5Si_2$: 599.3061].



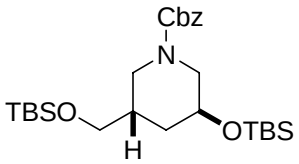

(+)-**14**

**Mesylate (+)-14:** Bissilylether **13** (34.2 g, 59.3 mmol) was dissolved in diethylether (200 mL), treated with methanol (2.65 mL, 65.2 mmol, 1.1 equiv.) and cooled to 0 °C. Lithium borohydride (1.42 g, 65.2 mmol, 1.1 equiv.) was added in one portion and the mixture was stirred for 30 minutes at 0 °C. The mixture was warmed to ambient temperature and stirred for 1 hour. The mixture was then cooled to 0 °C and sodium bicarbonate (50 mL, aqueous saturated) carefully added over 30 minutes. The biphasic mixture was stirred vigorously for 1 hour at 0 °C and then poured into water (150 mL). The aqueous layer was extracted with ethyl acetate (2 X 700 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 7:3; hexanes:ethyl acetate), providing the alcohol (22.2 g, 93% yield) as a colorless oil: $[\alpha]^{20}_D$ +2.67° (*c*1.65, $CH_2Cl_2$); IR (NaCl plate, neat): 3442 (br m), 2954 (s), 2929 (s), 2885 (m), 2857

(s), 2101 (s), 1471 (m), 1389 (w), 1361 (w), 1256 (s), 1089 (s), 1005 (w), 939 (w), 837 (s), 807 (m), 776 (s) $cm^{-1}$; $^{1}$H-NMR (500 MHz, $CDCl_3$) δ 3.91–3.87 (1H, m), 3.80 (1H, dd, *J* = 9.9, 3.9 Hz), 3.72 (1H, br dd, *J* = 10.6, 3.2 Hz), 3.63 (1H, dd, *J* = 10.4, 6.7 Hz), 3.59 (1H, dd, *J* = 9.9, 6.9 Hz), 3.31 (1H, dd, *J* = 12.5, 4.3 Hz), 3.17 (1H, dd, *J* = 12.6, 5.2 Hz), 2.69 (1H, br s), 1.86–1.79 (1H, m), 1.50 (2H, br t, *J* = 6.5 Hz), 0.91 (9H, s), 0.90 (9H, s), 0.13 (3H, s), 0.10 (3H, s), 0.08 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 70.2, 66.8, 66.6, 57.0, 38.6, 33.4, 26.1, 26.0, 26.0, 18.3, 18.2, -4.3, -4.5, -5.4, -5.4 ppm; high resolution mass spectrum (ES+) *m/z* 426.2570 [$(M+Na)^+$; calculated for $C_{18}H_{41}N_3NaO_3Si_2$: 426.2584].

The above prepared alcohol (27.6 g, 68.3 mmol) was dissolved in dichloromethane (300 mL). *N*,*N*-Dimethyl-4-aminopyridine (0.835 g, 6.83 mmol, 0.1 equiv.) and *N*,*N*-diisopropylethylamine (19.0 mL, 109 mmol, 1.6 equiv.) were added and the mixture was cooled to -78 °C. Methanesulfonyl chloride (6.88 mL, 88.9 mmol, 1.3 equiv.) was added dropwise over 3 minutes and the mixture was stirred for 45 minutes at -78 °C, then warmed to 0 °C and stirred for an additional 2 hours. The reaction mixture was then poured into sodium bicarbonate (500 mL, aqueous saturated) and extracted with dichloromethane (2 X 1 L). The combined organic extracts were washed once with ammonium chloride (400 mL, aqueous saturated), dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 75:25; hexanes:ethyl acetate), providing mesylate (+)-**14** (33.0 g, 100% yield) as a colorless oil: $[\alpha]^{20}_{D}$ +1.87° (*c*1.50, $CH_2Cl_2$); IR (NaCl plate, neat): 2929 (s), 2857 (s), 2102 (s), 1472 (m), 1360 (s), 1257 (s), 1178 (s), 1096 (s), 957 (s), 837 (s), 776 (s), 669 (m) $cm^{-1}$; $^{1}$H-NMR (500 MHz, $CDCl_3$) δ 4.24 (1H, br s), 4.23 (1H, br s), 3.92–3.87 (1H, m), 3.68 (1H, dd, *J* = 10.4, 4.1 Hz), 3.53 (1H, dd, *J* = 10.0, 6.3 Hz), 3.32 (1H, dd, *J* = 12.5, 4.7 Hz), 3.18 (1H, dd, *J* = 12.5, 5.0 Hz), 3.00 (3H, s), 2.08–2.01 (1H, m), 1.62–1.51 (2H, m), 0.91 (9H, s),

0.90 (9H, s), 0.13 (3H, s), 0.10 (3H, s), 0.07 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 70.5, 69.7, 61.6, 57.0, 37.3, 37.2, 33.1, 29.9, 26.0, 26.0, 18.2, -4.2, -4.5, -5.3, -5.4 ppm; high resolution mass spectrum (ES+) *m/z* 504.2340 [$(M+Na)^+$; calculated for $C_{19}H_{43}N_3NaO_5SSi_2$: 504.2360].



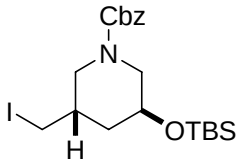
(+)-**15**

**Piperidine (+)-15:** *N,N*-Diisopropylethylamine (59.6 mL, 342 mmole, 5.0 equiv.) and Raney Nickel™ (6 spatula tips, ca. 3 g, water slurry, Aldrich 2400®) were added to *iso*-propanol (2.3 L). The mixture was mechanically stirred and sparged under an argon atmosphere. An *iso*-propanol (40 mL) solution of mesylate **14** (33.0 g, 68.3 mmol) was added to the Raney Nickel mixture via syringe pump over 10 hours. The mixture was vigorously stirred for an additional 72 hours, filtered through a pad of Celite and concentrated *in vacuo* to provide the secondary amine, which was used without purification in the following reaction. However, purification by silica gel gradient chromatography (99:1 to 90:10; dichloromethane:methanol containing 10% by volume ammonium hydroxide) furnished the secondary amine: $[\alpha]^{20}_D$ -16.4° (*c*1.075, $CH_2Cl_2$); IR (NaCl plate, neat): 2953 (s), 2928 (s), 2856 (s), 2801 (w), 2676 (w), 1574 (w), 1471 (m), 1388 (w), 1360 (w), 1254 (s), 1153 (w), 1114 (m), 1087 (s), 1063 (m), 1044 (w), 1005 (w), 938 (w), 920 (w), 836 (s), 774 (s), 687 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 5.66 (1H, br s), 3.98 (1H, s), 3.46 (1H, dd, *J* = 10.0, 5.2 Hz), 3.41 (1H, dd, *J* = 10.0, 6.0 Hz), 3.18 (1H, dd, *J* = 12.8, 2.4 Hz), 2.93 (1H, d, *J* = 13.4 Hz), 2.74 (1H, d, *J* = 12.3 Hz), 2.49 (1H, t, *J* = 12.1 Hz), 2.19–2.11 (1H, m), 1.72 (1H, d, *J* = 13.4 Hz), 1.41 (1H, ddd, *J* = 13.6, 11.5, 2.4 Hz), 0.90 (9H, s), 0.87 (9H,

s), 0.07 (3H, s), 0.06 (3H, s), 0.02 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 65.8, 64.9, 51.8, 48.1, 34.3, 33.3, 26.1, 26.0, 18.4, 18.3, -4.6, -4.7, -5.3, -5.3 ppm; high resolution mass spectrum (ES+) *m/z* 360.2769 [$(M+H)^+$; calculated for $C_{18}H_{42}NO_2Si_2$: 360.2754].

The above prepared secondary amine was dissolved in ethyl acetate (300 mL) and sodium bicarbonate (150 mL, aqueous saturated) and cooled to 0 °C with vigorous stirring. An ethyl acetate solution (40 mL) of benzyl chloroformate (15 mL, 103 mmol, 1.5 equiv.) was added slowly over 5 minutes to the vigorously stirring biphasic mixture. The mixture was warmed to ambient temperature over 2 hours and stirred for an additional 14 hours. The reaction mixture was poured into water (200 mL) and extracted with ethyl acetate (2 X 700 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 9:1; hexanes:ethyl acetate), providing piperidine (+)-**15** (30.1 g, 89% yield) as a colorless oil: $[\alpha]^{20}_D$ +5.3° (*c*3.5, $CH_2Cl_2$); IR (NaCl plate, neat): 2954 (s), 2928 (s), 2885 (m), 2856 (s), 1706 (s), 1472 (m), 1462 (m), 1430 (m), 1388 (w), 1361 (w), 1255 (s), 1225 (m), 1144 (m), 1080 (m), 1035 (w), 837 (s), 775 (s), 696 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~1:1 mixture of rotamers) δ 7.39–7.28 (m), 5.20 (br d, *J* = 12.3 Hz), 5.15 (br d, *J* = 12.7 Hz), 5.10 (br d, *J* = 12.7 Hz), 5.01 (br d, *J* = 12.6 Hz), 4.08 (br d, *J* = 11.9 Hz), 3.96–3.89 (br m), 3.85 (br d, *J* = 14.1 Hz), 3.76 (br d, *J* = 12.6 Hz), 3.51–3.39 (br m), 3.11 (br d, *J* = 13.8 Hz), 3.00 (br d, *J* = 13.4 Hz), 2.88 (br dd, *J* = 12.8, 9.9 Hz), 2.70 (br dd, *J* = 12.3, 10.8 Hz), 2.20 (br m), 1.70 (br m), 1.46 (br ddd, *J* = 13.2, 10.8, 2.4 Hz), 0.89–0.84 (br m), 0.07–-0.01 (br m) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains an ~1:1 mixture of rotamers) δ 156.1, 156.0, 137.3, 137.2, 128.6, 128.0, 128.0, 127.9, 127.8, 67.1, 67.1, 67.0, 65.4, 65.3, 65.1, 50.8, 46.8, 35.2, 35.1, 34.1, 33.3, 26.1,

26.0, 18.4, 18.3, -4.7, -4.9, -5.2, -5.3 ppm; high resolution mass spectrum (ES+) *m/z* 516.2924 [$(M+Na)^+$; calculated for $C_{26}H_{47}NNaO_4Si_2$: 516.2941].



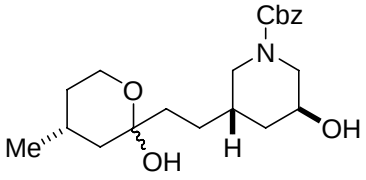
(+)-**6**

**Iodide (+)-6:** Piperidine **15** (13.0 g, 26.3 mmol) was dissolved in methanol (200 mL) and cooled to 0 °C. Hydrochloric acid (10 drops from a 9" pipet, 12N aqueous) was added and the reaction was carefully monitored by TLC. After 50 minutes at 0 °C, the reaction mixture was quenched with sodium bicarbonate (5 mL, aqueous saturated) and poured into water (1 L). The aqueous layer was extracted with ethyl acetate (3 X 800 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (1:1; hexanes:ethyl acetate), providing the primary alcohol (9.50 g, 96% yield) as a colorless oil: $[\alpha]^{20}_D$ +4.93° (*c*1.46, $CH_2Cl_2$); IR (NaCl plate, neat): 3444 (br m), 2957 (s), 2928 (s), 2882 (m), 2853 (s), 1681 (s), 1470 (s), 1433 (s), 1354 (m), 1255 (s), 1233 (s), 1142 (s), 1067 (m), 1032 (m), 975 (w), 940 (w), 865 (w), 837 (m), 778 (m), 697 (m) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~1:2 mixture of rotamers, * denotes minor rotamer signals) δ 7.38 (m), 5.20 (br d, *J* = 12.7 Hz), *5.17–5.09 (br m), 5.02 (br d, *J* = 12.3 Hz), 3.94–3.79 (br m), *3.67 (br d, *J* = 11.2 Hz), 3.57 (br dd, *J* = 12.8, 3.9 Hz), 3.52–3.46 (m), 3.46–3.38 (br m), 3.26 (br d, *J* = 13.4 Hz), *3.19 (br d, *J* = 12.6 Hz), 3.11–2.88 (br m), 2.52 (br s), *2.44 (br s), 2.20–2.07 (br m), 1.68 (br td, *J* = 13.4, 4.9 Hz), 1.49 (br ddd, *J* = 13.4, 9.3, 3.0 Hz), *0.87 (br s), 0.85 (br s), *0.07 (br s), *0.06 (br s), 0.02 (br s), 0.00 (br s) ppm; $^{13}$C-NMR

(125 MHz, $CDCl_3$; spectrum contains an ~1:2 mixture of rotamers, * denotes minor rotamer signals) δ 156.4, *155.8, *137.1, 136.8, 128.5, 128.0, 128.0, 127.8, 67.3, *67.0, 64.9, 64.6, 64.3, 51.0, *50.7, *46.4, 46.3, 35.2, 34.2, 25.8, 18.1, -4.8, -4.9 ppm; high resolution mass spectrum (ES+) *m/z* 402.2078 [$(M+Na)^+$; calculated for $C_{20}H_{33}NNaO_4Si$: 402.2077].

The above prepared alcohol (39.8 g, 105 mmol) was dissolved in tetrahydrofuran (700 mL) and treated with imidazole (17.8 g, 262 mmol, 2.5 equiv.) and triphenylphosphine (33.0 g, 126 mmol, 1.2 equiv.). The mixture was cooled to 0 °C and iodine (31.9g, 126 mmol, 1.2 equiv.) added portionwise over 10 minutes. The reaction mixture was stirred at 0 °C for 2.5 hours, warmed to ambient temperature and stirred for an additional 1 hour. The reaction mixture was quenched with sodium thiosulfate (50 mL, aqueous saturated) and water (100 mL) and then stirred for 30 minutes at ambient temperature, poured into water (500 mL) and extracted with ethyl acetate (2 X 1L). The combined organic layers were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was dissolved in hexanes (1 L) and placed in an ice bath for 1 hour. The mixture was filtered, the solid was washed with cold hexanes (500 mL) and the filtrate was concentrated *in vacuo*. The residue was again dissolved in hexanes (1L), placed in an ice bath for 1 hour. The mixture was filtered, the solid was washed with cold hexanes (500 mL) and the filtrate was concentrated *in vacuo* to provide iodide (+)-**6** (51.1 g, 99% yield) as a light yellow oil: $[\alpha]^{20}_D$ +0.28° (*c*2.90, $CH_2Cl_2$); IR (NaCl plate, neat): 2951 (s), 2927 (s), 2894 (m), 2853 (s), 1703 (s), 1458 (m), 1431 (s), 1351 (w), 1257 (s), 1231 (s), 1187 (w), 1147 (m), 1123 (m), 1084 (m), 957 (w), 934 (w), 893 (w), 837 (s), 776 (m), 696 (m) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~1:2 mixture of rotamers, * denotes minor rotamer signals) δ 7.41–7.29 (br m), 5.22 (br d, *J* = 12.3 Hz), *5.19–5.10 (br m), 5.02 (br d, *J* = 12.7 Hz), 4.18 (br d, *J* = 12.7 Hz), *3.98 (br d, *J* = 11.9 Hz), 3.95–3.89 (br m), 3.86 (br d, *J* = 13.8 Hz), *3.76 (br d,

*J* = 10.6 Hz), 3.18–3.05 (br m), 3.00 (br d, *J* = 13.0 Hz), *2.89 (br t, *J* = 10.4 Hz), 2.65 (br t, *J* = 11.5 Hz), 2.14–2.04 (br m), 1.92–1.79 (br m), *1.50 (br t, *J* = 10.4 Hz), 1.42 (br t, *J* = 12.2 Hz), 0.90–0.84 (br m), 0.11–-0.01 (br m) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains an ~1:2 mixture of rotamers, * denotes minor rotamer signals) δ 156.1, *155.7, *137.1, 137.0, 128.6, 128.1, 128.0, 67.4, *67.2, 65.1, *64.8, 50.6, 49.6, *49.4, *39.4, 39.3, *33.6, 32.5, 25.9, 18.2, 10.5, *10.1, -4.7, *-4.8 ppm; high resolution mass spectrum (ES+) *m/z* 512.1115 [$(M+Na)^+$; calculated for $C_{20}H_{32}INNaO_3Si$: 512.1094].

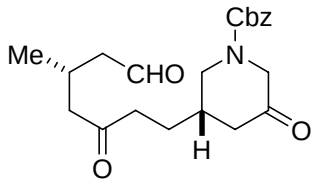



**17**

**Hemiketal 17:** Hydrazone **7** (1.12 g, 4.22 mmol, 1.1 equiv.) was dissolved in tetrahydrofuran (10 mL) and cooled to -78 °C. *n*-Butyl lithium (2.2 mL, 1.7M in tetrahydrofuran, 3.90 mmol, 1.02 equiv.) was added dropwise and the mixture stirred for 1 hour at -78 °C. Hexamethylphosphoramide (1.0 mL, 10% v/v) was added dropwise and the mixture stirred for an additional 15 minutes at -78°C, warmed to -60 °C for 15 minutes and then cooled to -78 °C. In a separate flask, iodide **6** (1.88 g, 3.84 mmol) was dissolved in tetrahydrofuran (5 mL), cooled to -78 °C and added dropwise via syringe to the hydrazone anion. After stirring for 1 hour at -78 °C, the dry ice/acetone bath was removed and the reaction mixture was warmed to ambient temperature. After stirring for 30 minutes at ambient temperature, the reaction mixture was treated with sodium bicarbonate (5 mL, aqueous saturated) and poured into a separatory funnel containing sodium bicarbonate (75 mL, aqueous saturated). The aqueous layer was

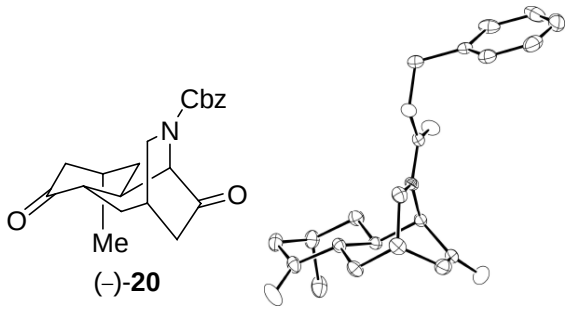
extracted with ethyl acetate (3 X 100 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The coupling product was used without purification in the next reaction. High resolution mass spectrum (ES+) *m/z* 648.4610 [$(M+H)^+$; calculated for $C_{35}H_{66}N_3O_4Si_2$: 648.4592].

The above prepared coupling product was dissolved in tetrahydrofuran (25 mL) and treated with water (10 mL) and hydrochloric acid (2 mL, 12N aqueous). The mixture was stirred vigorously for 14 hours at ambient temperature, poured into water (100mL) and extracted with ethyl acetate (3 X 100 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (1:1 to 0:1; hexanes:ethyl acetate), providing the hemiketal **17** (1.067 g, 74% yield over 2 steps) as a colorless oil: $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains a mixture of ketone and hemiketal diastereomers, which exhibit rotameric signals) δ 7.35–7.27 (5H, m), 5.19–5.05 (2H, br m), 4.06–3.81 (br m), 3.63 (br ddd, *J* = 11.2, 4.5, 1.1 Hz), 3.59 (br t, *J* = 6.3 Hz), 3.44–3.34 (br m), 3.27–3.19 (br m), 3.10 (br dd, *J* = 13.6, 2.0 Hz), 2.91–2.52 (br m), 2.52–2.31 (br m), 2.30–2.08 (br m), 1.99–1.80 (br m), 1.67 (br d, *J* = 11.2 Hz), 1.64–1.55 (br m), 1.52 (br d, *J* = 13.0 Hz), 1.45 (br dd, *J* = 13.4, 7.1 Hz), 1.32 (br tt, *J* = 11.2, 2.8 Hz), 1.14 (br dq, *J* = 12.8, 4.5 Hz), 1.01 (br t, *J* = 12.6 Hz), 0.91 (d, *J* = 6.7 Hz), 0.89 (d, *J* = 6.3 Hz), 0.86 (d, *J* = 6.7 Hz) ppm; high resolution mass spectrum (ES+) *m/z* 400.2086 [$(M+Na)^+$; calculated for $C_{21}H_{31}NaNO_5$: 400.2100].




(+)-**18**

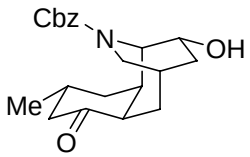
**Aldehyde (+)-18:** Hemiketal **17** (10.3 g, 27.3 mmol) was dissolved in dichloromethane (400 mL) and treated with freshly activated 4Å molecular sieves (20 g, 2 weight equiv.). To the vigorously stirring mixture was added pyridinium chlorochromate (14.7 g, 68.2 mmol, 2.5 equiv.) in several portions over 5 minutes. After stirring for 1 hour, additional pyridinium chlorochromate (14.7 g, 68.2 mmol, 2.5 equiv.) was added. The reaction mixture was stirred an additional 1 hour and diluted with diethylether (1L) and Celite (~60 g). The mixture was stirred vigorously for 1 hour and poured directly onto a silica gel column, eluting with diethyl ether (1.5 L), then ethyl acetate, providing aldehyde (+)-**18** (6.76 g, 66%) as a slightly green oil: $[\alpha]^{20}_{D}$ +10.6° (*c*1.15, $CH_2Cl_2$); IR (NaCl plate, neat): 2959 (m), 2930 (m), 2878 (m), 2721 (w), 1700 (s), 1454 (w), 1419 (m), 1367 (w), 1320 (w), 1216 (m), 1117 (m), 971 (w), 914 (w), 762 (w), 734 (w), 699 (w); $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~1:10 mixture of rotamers, * denotes minor rotamer signals) δ 9.72 (br s), *9.63 (br s), 7.40–7.29 (br m), 4.10 (br d, *J* = 17.5 Hz), 4.04–3.76 (br m), 3.27–3.14 (br m), 2.59 (br d, *J* = 4.8 Hz), 2.58 (br d, *J* = 4.1 Hz), 2.55–2.34 (br m), 2.33 (br dd, *J* = 7.1, 1.5 Hz), 2.30 (br dd, *J* = 7.1, 1.9 Hz), 2.16 (dd, *J* = 16.4, 9.7 Hz), 2.09–2.00 (br m), 1.69–1.51 (br m), *1.33 (d, *J* = 7.1 Hz), 0.98 (d, *J* = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 208.6, 204.4, 201.8, 155.3, 136.4, 128.7, 128.4, 128.2, 67.8, 54.2 br, 50.5, 49.3, 47.3 br, 45.0 br, 40.1, 34.0, 26.9, 24.2, 20.5 ppm; high resolution mass spectrum (ES+) *m/z* 396.1781 [$(M+Na)^+$; calculated for $C_{21}H_{27}NNaO_5$: 396.1787].



(–)-**20**

**Tricycle (–)-20:** Aldehyde **18** (183 mg, 0.490 mmol) was dissolved in dimethylsulfoxide (100 mL) and was sparged under an argon atmosphere. Hydrochloric acid (4 mL) was added and the vessel placed into an oil bath preheated to 70 °C for 2.5 hours. The mixture was cooled to ambient temperature, poured into water (300 mL) and extracted with ethyl acetate (3 X 200 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (1:1; hexanes:ethyl acetate), providing tricycle (–)-**20** (147 mg, 84% yield) as a white solid. X-Ray quality crystals were prepared via vapor diffusion from hexanes/dichloromethane; melting point 134–138°. See attached .cif file for details: $[\alpha]^{20}_{D}$ –83.9° (*c*2.8, $CH_2Cl_2$); IR (NaCl plate, thin film, $CH_2Cl_2$): 2954 (m), 2927 (m), 1702 (s), 1448 (w), 1409 (s), 1346 (m), 1310 (w), 1285 (s), 1233 (m), 1216 (m), 1155 (w), 1110 (m), 1079 (w), 1030 (w), 969 (w), 917 (w); $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains a mixture of rotamers) δ 7.40–7.31 (m), 5.23–5.11 (m), 4.61 (s), 4.47 (s), 3.62 (br t, *J* = 11.7 Hz), 3.53 (br dd, *J* = 12.1, 3.9 Hz), 2.68–2.62 (br m), 2.62–2.55 (br m), 2.53–2.34 (br m), 2.26–2.18 (br m), 2.16–2.09 (br m), 2.16 (s), 2.06 (br d, *J* = 4.5 Hz), 2.03 (s), 2.00 (br dd, *J* = 11.9, 2.6 Hz), 1.93 (br d, *J* = 9.3 Hz), 1.81 (br d, *J* = 12.6 Hz), 1.63 (br d, *J* = 8.6 Hz), 1.53–1.46 (m), 0.94 (d, *J* = 7.4 Hz), 0.91 (d, *J* = 7.1 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains a mixture of rotamers) δ 211.1, 210.7, 207.8, 207.6, 156.4, 155.8, 136.4, 136.1, 128.7, 128.5, 128.4, 128.2, 67.9, 67.9, 66.1, 65.5, 50.3, 50.3, 47.4, 47.3, 47.3, 47.1, 47.0,

44.0, 43.9, 43.7, 37.5, 30.5, 30.4, 30.3, 26.1, 25.7, 19.5, 19.4 ppm; high resolution mass spectrum (ES+) *m/z* 378.1686 [$(M+Na)^+$; calculated for $C_{21}H_{25}NNaO_4$: 378.1681].




(–)-**23**

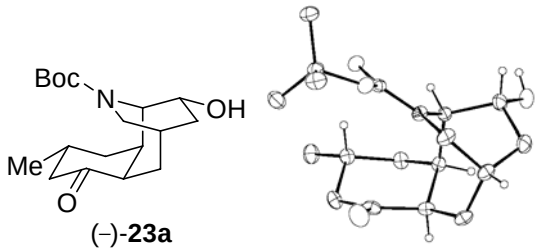
**Alcohol (–)-23:** Tricycle **20** (1.80 g, 5.1 mmol) was dissolved in a 1:1 mixture of methanol:ethyl acetate (500 mL). The solution was sparged under an argon atmosphere and then treated with $Pd(OH)_2/C$ (2 spatula tips, 20% weight Pd). The vigorously stirring mixture was sparged under an atmosphere of hydrogen (1 atm, balloon) and stirred for 90 minutes. Additional $Pd(OH)_2/C$ (1 spatula tip, 20% weight Pd) was added, the mixture was sparged under an atmosphere of hydrogen and stirred for an additional 45 minutes. The reaction mixture was sparged under an atmosphere of argon and filtered through a pad of Celite. The Celite was washed with a 1:1 mixture of methanol:ethyl acetate (500 mL) and concentrated *in vacuo* to provide compound (–)-**21**, which was used without purification in the next reaction. However, purification by silica gradient gel chromatography (99:1 to 94:6; dichloromethane:methanol containing 10% by volume ammonium hydroxide) provided (–)-**21**: $[\alpha]^{20}_D$ -163° (*c*0.90, $CH_2Cl_2$); IR (NaCl plate, neat): 3364 (br m), 2953 (m), 2921 (s), 2866 (m), 1708 (s), 1446 (w), 1403 (w), 1380 (w), 1339 (w), 1285 (w), 1232 (w), 1213 (w), 1181 (w), 1113 (w), 1032 (w), 948 (w), 915 (w), 886 (w), 770 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 3.16 (1H, d, *J* = 11.2 Hz), 3.08 (1H, dd, *J* = 11.3, 4.3 Hz), 3.04 (1H, s), 2.73 (1H, dt, *J* = 12.3, 4.2 Hz), 2.57 (1H, dd, *J* = 13.4, 5.9 Hz), 2.53–2.44 (2H, m), 2.44–2.40 (2H, m), 2.21–2.12 (3H, m), 1.96–1.81 (1H, br m), 1.87 (1H, dt, *J* = 12.3, 3.7 Hz), 1.58 (1H, d, *J* = 13.4 Hz), 1.50 (1H, dd, *J* = 14.9, 12.3 Hz), 0.95

(3H, d, $J$ = 7.1 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 212.7, 212.6, 66.7, 50.4, 47.4, 44.8, 44.3, 42.6, 37.7, 31.7, 30.7, 27.2, 19.8 ppm; high resolution mass spectrum (CI+) *m/z* 221.1411 [$(M+)^+$; calculated for $C_{13}H_{19}NO_2$: 221.1416].

Compound (–)-**21** was dissolved in an 85:15:5 mixture (1 L) of water:methanol:hydrochloric acid (12N aqueous) and placed into an oil bath preheated to 100 °C for 18 hours. The mixture was cooled to ambient temperature and the solvent was removed *in vacuo* to provide the hemiaminal salt **22**, which was used without purification in the next reaction: $^1$H-NMR (500 MHz, $d^7$-DMF) δ 4.20 (1H, ddd, $J$ = 13.0, 3.9, 2.8 Hz), 3.96 (1H, d, $J$ = 5.6 Hz), 3.03 (1H, d, $J$ = 11.9 Hz), 2.69 (1H, dd, $J$ = 14.1, 5.6 Hz), 2.65–2.60 (2H, m), 2.47 (1H, dd, $J$ = 10.0, 5.2 Hz), 2.31–2.23 (1H, m), 2.12 (1H, s), 1.89 (1H, br d, $J$ = 13.4 Hz), 1.76 (1H, d, $J$ = 14.1 Hz), 1.64 (1H, dd, $J$ = 14.0, 12.1 Hz), 1.32 (1H, t, $J$ = 11.9 Hz), 0.96 (3H, d, $J$ = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $d^7$-DMF) δ 204.9, 97.6, 69.5, 47.8, 47.3, 44.5, 43.7, 42.3, 38.2, 29.9, 26.1, 25.1, 21.6 ppm.

Hemiaminal salt **22** was dissolved in methanol (300 mL), cooled to 0 °C and treated with sodium borohydride (600 mg, 15.9 mmol, 3.15 equiv.) portionwise over 90 minutes. Hydrochloric acid (10 mL, 12N aqueous) was added and the mixture was stirred vigorously for 30 minutes. The solvent was removed *in vacuo* to provide the alcohol as a light yellow foam, which was dissolved in ethyl acetate (100 mL), treated with sodium bicarbonate (50 mL, aqueous saturated) and cooled to 0 °C with vigorous stirring. An ethyl acetate solution (20 mL) of benzyl chloroformate (2.00 mL, 11.5 mmol, 2.27 equiv.) was added slowly to the solution over 5 minutes. The reaction mixture was slowly warmed to ambient temperature over 2 hours and stirred for an additional 14 hours. The mixture was poured into water (200 mL) and extracted

with ethyl acetate (3 X 250 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 25:75; hexanes:ethyl acetate), providing alcohol (–)-**23** (919 mg, 51% yield) as a white foam: $[\alpha]^{20}_{D}$ –26.6° (*c*0.70, $CH_2Cl_2$); IR (NaCl plate, thin film, $CH_2Cl_2$): 3434 (br m), 2927 (m), 2873 (m), 1699 (s), 1452 (m), 1411 (m), 1354 (w), 1312 (m), 1255 (w), 1212 (w), 1114 (m), 1070 (w), 1015 (w), 916 (w), 734 (m), 702 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~3:1 mixture of rotamers, * denotes minor rotamer signals) δ 7.39–7.28 (m), *5.27–5.22 (br m), 5.14 (br d, *J* = 12.7 Hz), 5.08 (br d, *J* = 12.7 Hz), *4.69 (br s), 4.19 (br d, *J* = 2.6 Hz), *4.05–4.00 (br m), 3.96–3.89 (br m), 3.47 (br d, *J* = 11.2 Hz), *3.40 (br d, *J* = 17.1 Hz), *3.19–3.13 (br m), 3.07 (br d, *J* = 11.5 Hz), 2.97–2.91 (br m), *2.82–2.75 (br m), 2.68–2.59 (br m), 2.56–2.48 (br m), 2.46–2.37 (br m), 2.33 (br dd, *J* = 14.9, 4.5 Hz), 2.26–2.14 (br m), 1.86 (br dd, *J* = 14.8, 10.0 Hz), 1.79 (br d, *J* = 13.8 Hz), *1.75–1.65 (br m), 1.61 (br ddd, *J* = 13.3, 10.0, 3.5 Hz), 1.54–1.49 (br m), 1.46–1.42 (br m), 0.95 (d, *J* = 6.7 Hz), *0.86–0.81 (br m) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains an ~3:1 mixture of rotamers, only the major rotamer signals are reported) δ 211.4, 156.5, 136.9, 128.6, 128.0, 127.7, 68.1, 67.4, 58.1, 47.9, 47.7, 46.6, 38.4, 37.4, 34.7, 32.9, 29.2, 22.2 ppm; high resolution mass spectrum (CI) *m/z* 357.1943 [$(M+)^+$; calculated for $C_{21}H_{27}NO_4$: 357.1940].

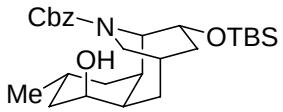



(–)-**23a**

**Alcohol (–)-23a:** Tricycle **20** (26 mg, 0.073 mmol) was dissolved in methanol (15 mL) and 12N hydrochloric acid (1 mL). The solution was sparged under an argon atmosphere and then treated with Pd/C (1 small spatula tip, 10% weight Pd). The vigorously stirring mixture was sparged under a hydrogen atmosphere (1 atm, balloon) and then heated to reflux for 14 hours. The mixture was cooled to ambient temperature, sparged under an argon atmosphere and filtered through a pad of Celite. The Celite was washed with methanol (10 mL) and the filtrate concentrated *in vacuo* to provide compound **22**, which was used without purification in the next reaction.

Compound **22** was dissolved in methanol (300 mL), cooled to 0 °C and treated with lithium borohydride (20 mg, 0.919 mmol, 12 equiv.) portionwise over 90 minutes. The solvent was removed *in vacuo*, providing the corresponding alcohol, which was suspended in acetonitrile (5 mL) and treated with di-*tert*-butyldicarbonate (30 mg, 0.141 mmol, 2 equiv.). After stirring at ambient temperature for 1 hour, the mixture was poured into sodium bicarbonate (15 mL, aqueous saturated) and extracted with ethyl acetate (2 X 50 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (98:2 to 94:6; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing alcohol (–)-**23a** (12 mg, 51% yield) as a white solid. X-Ray quality crystals were prepared via vapor diffusion from hexanes/dichloromethane; melting point 136–142°. See attached .cif file for details: $[\alpha]^{20}_{D}$ –39.8° (*c*0.60, $CH_2Cl_2$); IR (NaCl plate, thin film, $CH_2Cl_2$): 3440 (br m), 2931 (m), 2869 (m), 1693 (s), 1454 (w), 1396 (m), 1369 (m), 1319 (w), 1253 (w), 1168 (m), 1118 (w), 1068 (w), 1018 (w), 941 (w), 887 (w), 732 (w), 632 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~6:1 mixture of rotamers, * denotes minor rotamer signals) δ 4.12 (br s), *4.06–4.00 (br m), 4.00–3.90 (br s), 3.34 (br d, *J*

= 11.9 Hz), *3.11–3.04 (br m), 2.96 (br d, *J* = 11.5 Hz), 2.94–2.87 (m), *2.85–2.78 (br m), 2.67–2.51 (m), 2.51–2.45 (m), 2.39 (br d, *J* = 15.3 Hz), 2.31–2.11 (br m), 2.24 (td, *J* = 14.5, 8.4 Hz), 2.16 (br d, *J* = 13.8 Hz), *2.02–1.93 (br m), 1.90–1.85 (m), 1.79 (br d, *J* = 13.4 Hz), 1.63–1.58 (m), 1.51–1.40 (m), 0.98 (d, *J* = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains an ~6:1 mixture of rotamers, only major rotamer signals are reported) δ 210.6, 155.5, 79.8, 68.1, 57.0, 47.9, 47.6, 46.3, 38.6, 37.4, 34.6, 32.6, 29.1, 28.3, 28.0, 22.2 ppm; high resolution mass spectrum (CI) *m/z* 323.2094 [$(M+)^+$; calculated for $C_{18}H_{29}NO_4$: 323.2097].



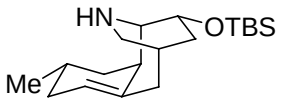

(–)-**24**

**Alcohol (–)-24:** Alcohol **23** (1.26 g, 3.52 mmol) was dissolved in dichloromethane (70 mL), treated with 2,6-di-*tert*-butyl-4-methylpyridine (1.62 g, 7.91 mmol, 2.25 equiv.) and cooled to -78 °C. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (1.01 mL, 4.39 mmol, 1.25 equiv.) was added dropwise and the reaction mixture was stirred for 1 hour at -78 °C. The reaction mixture was quenched with sodium bicarbonate (5 mL, aqueous saturated) and warmed to ambient temperature. The mixture was poured into water, extracted with dichloromethane (3 X 200 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 85:15; hexanes:ethyl acetate), providing the *O*-TBS ether (1.17 g, 70% yield) as a colorless oil: $[\alpha]^{20}_D$ –30.1° (*c*1.65, $CH_2Cl_2$); IR (NaCl plate, neat): 2951 (s), 2929 (s), 2859 (m), 1701 (s), 1453 (m), 1405 (m), 1351 (w), 1309 (m), 1258 (m), 1213 (w), 1088 (s), 941 (w), 889 (m), 862

(w), 837 (m), 777 (m), 697 (w), 668 (w) $cm^{-1}$; $^{1}$H-NMR (500 MHz, $CDCl_3$; spectrum contains an ~3:1 mixture of rotamers, * denotes minor rotamer signals) δ 7.38–7.29 (m), 5.17 (br d, *J* = 12.3 Hz), 5.08 (br d, *J* = 12.7 Hz), 4.15–4.10 (br m), *4.10–4.05 (br m), 3.94–3.84 (br m), 3.45 (br d, *J* = 11.9 Hz), *3.37 (br d, *J* = 12.3 Hz), *3.16 (br d, *J* = 12.6 Hz), 3.08 (br d, *J* = 11.5 Hz), 2.95–2.89 (m), *2.82–2.75 (br m), *2.66–2.59 (br m), 2.53 (br dd, *J* = 11.0, 5.4 Hz), 2.48–2.37 (br m), 2.33 (br dd, *J* = 14.9, 4.5 Hz), *2.27–2.21 (br m), 2.21–2.11 (br m), *1.94–1.90 (br m), 1.86 (br dd, *J* = 14.5, 9.7 Hz), 1.75–1.64 (br m), 1.60–1.43 (br m), 0.94 (br d, *J* = 6.3 Hz), 0.91–0.87 (br m), 0.80–0.03 (br m) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains an ~3:1 mixture of rotamers, * denotes minor rotamer signals) δ 211.8, 156.3, 137.1, *128.7, 128.6, *128.3, 128.0, 127.8, 68.4, 67.2, 57.8, *48.5, 47.9, 47.7, 46.9, *46.6, 37.6, 37.3, *35.3, *35.1, *33.8, 33.2, *29.9, 29.5, *29.2, *28.9, 28.5, 25.9, 22.0, *20.9, 18.1, -4.4, *-4.5, -4.6 ppm; high resolution mass spectrum (ES+) *m/z* 494.2719 [$(M+Na)^+$; calculated for $C_{27}H_{41}NNaO_4Si$: 494.2703].

The above prepared *O*-TBS ether (2.5 g, 5.3 mmol) was dissolved in tetrahydrofuran (80 mL) and cooled to -78 °C. L-Selectride® (14 mL, 1.0M in tetrahydrofuran, 2.5 equiv.) was added dropwise over 5 minutes and the reaction mixture stirred for 1 hour at -78 °C, warmed to 0 °C and then stirred for an additional 1 hour. To the reaction mixture was added additional L-Selectride (5.0 mL, 1.0M in tetrahydrofuran, 1 equiv.) and the mixture stirred for 1 hour at 0 °C. The mixture was treated with sodium bicarbonate (10 mL, aqueous saturated), stirred vigorously for 15 minutes and then poured into sodium bicarbonate (300 mL, aqueous saturated). The aqueous layer was extracted with ethyl acetate (2 X 300 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 1:1; hexanes:ethyl acetate), providing alcohol (–)-**24**

(2.5 g, 99% yield) as a colorless oil: $[\alpha]^{20}_{D}$ –47.6° (*c*0.30, $CH_2Cl_2$); IR (NaCl plate, neat): 3388 (br m), 2928 (s), 2861 (m), 1697 (m), 1458 (w), 1415 (m), 1359 (w), 1301 (m), 1255 (w), 1113 (m), 1074 (s), 891 (w), 836 (w), 769 (w), 641 (m) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$; spectrum contains a mixture of rotamers) δ 7.40–7.28 (br m), 5.21–5.10 (m), 4.71–4.47 (br m), 4.45–4.37 (br m), 4.28 (br q, *J* = 6.0 Hz), 4.16 (br q, *J* = 6.0 Hz), 4.14 (br q, *J* = 6.3 Hz), 4.13–4.00 (br m), 3.36–3.23 (br m), 2.70–1.91 (br m), 1.77–1.19 (br m), 1.10–0.84 (br m), 0.08–0.05 (br m) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectrum contains a mixture of rotamers) δ 156.6, 156.1, 137.3, 137.2, 128.7, 128.6, 128.1, 128.0, 128.0, 128.0, 127.9, 83.0, 68.3, 68.2, 68.1, 68.0, 67.9, 67.1, 67.1, 67.0, 67.0, 56.1, 55.6, 50.9, 50.5, 37.1, 36.9, 36.5, 35.4, 35.3, 34.7, 34.5, 34.3, 34.2, 34.0, 33.9, 26.1, 26.0, 25.9, 25.5, 19.0, 18.9, 18.8, 18.2, 18.1, 18.0, 15.9, 15.3, 14.7, 9.8, -4.4, -4.4, -4.5, -4.6, -4.7, -4.8 ppm; high resolution mass spectrum (ES+) *m/z* 496.2854 [$(M+Na)^+$; calculated for $C_{27}H_{43}NNaO_4Si$: 496.2859].



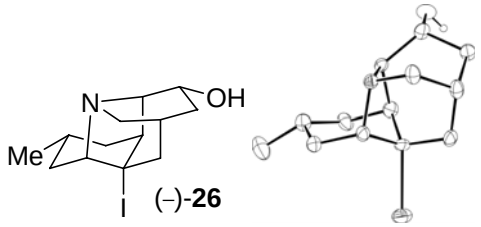

(–)-**25**

**Alkene (–)-25:** Alcohol **24** (731 mg, 1.54 mmol) was dissolved in absolute ethanol (60 mL) and was sparged under an argon atmosphere. Pd/C (200 mg, 5% Pd weight, catalytic) was added and the mixture was sparged under a hydrogen atmosphere (1 atm, balloon). The mixture was stirred vigorously for 90 minutes and then sparged under an argon atmosphere and filtered through a pad of Celite. The Celite was washed with absolute ethanol (50 mL) and the filtrate was concentrated *in vacuo*. The residue was dissolved in toluene (100 mL) and concentrated *in vacuo* two times and then placed under vacuum for 16 hours to provide the aminoalcohol (529

mg, 100% yield) as a white solid, which was used without purification in the next reaction: $[\alpha]^{20}_{D}$ −28.8° (*c*0.25, $CH_2Cl_2$); IR (NaCl plate, thin film, $CH_2Cl_2$): 3300 (br m), 3231 (br m), 2953 (s), 2927 (s), 2858 (s), 1541 (w), 1471 (m), 1461 (m), 1388 (m), 1307 (w), 1119 (m), 1093 (s), 1048 (m), 1006 (w), 909 (m), 899 (w), 867 (w), 836 (s), 776 (m), 734 (m), 668 (w), 643 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 3.98–3.94 (1H, m), 3.72 (1H, br dd, *J* = 7.6, 4.7 Hz), 2.95–2.90 (2H, br m), 2.67–2.64 (1H, br m), 2.60 (1H, dd, *J* = 9.3, 4.8 Hz), 2.17–2.11 (2H, m), 2.08–2.03 (1H, m), 1.98 (1H, ddd, *J* = 14.3, 9.3, 4.8 Hz), 1.89–1.82 (2H, m), 1.77 (1H, br d, *J* = 12.7 Hz), 1.48–1.42 (2H, m), 1.27–1.21 (2H, m), 1.16 (1H, ddd, *J* = 12.7, 10.4, 2.6 Hz), 0.89–0.88 (12H, m), 0.05 (3H, s), 0.04 (3H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$; spectra contains conformational isomers) δ 70.0, 69.9, 59.2, 45.4, 42.9, 41.4, 38.3, 36.2, 36.0, 35.9, 30.4, 29.9, 26.0, 22.9, 22.1, 18.1, -4.3, -4.6 ppm; high resolution mass spectrum (ES+) *m/z* 340.2656 [$(M+H)^+$; calculated for $C_{19}H_{38}NO_2Si$: 340.2672].

The above prepared aminoalcohol (529 mg, 1.56 mmol) was dissolved in dichloromethane (20 mL) and cooled to 0 °C. In a separate flask, a dichloromethane (10 mL) solution of Martin sulfurane reagent (2.09 g, 3.11 mmol, 2.0 equiv.), which was weighed out and stored in a glove box,[3] was prepared. From this solution, Martin sulfurane reagent (5 mL, 1.0 equiv.) was added dropwise to the aminoalcohol. After stirring for 30 minutes, additional Martin sulfurane reagent (0.5 mL, 0.10 equiv.) was added and the mixture stirred for an additional 20 minutes at 0 °C. The reaction mixture was quenched with sodium carbonate (10 mL, aqueous saturated) and poured into water (100 mL). The aqueous layer was extracted with dichloromethane (2 X 100 mL) and the combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (10:0 to 9:1; dichloromethane:methanol containing 10% by volume ammonium

hydroxide), providing alkene (–)-**25** (410 mg, 82% yield) as a light yellow oil: $[\alpha]^{20}_{D}$ –28.8° (*c*0.25, $CH_2Cl_2$); IR (NaCl plate, neat): 3360 (w), 2953 (s), 2926 (s), 2855 (s), 1649 (w), 1538 (w), 1464 (m), 1387 (m), 1253 (m), 1101 (m), 1076 (m), 873 (w), 837 (m), 777 (m), 664 (w), 567 (m) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 5.59–5.57 (1H, m), 4.15 (1H, ddd, *J* = 9.3, 6.3, 4.8 Hz), 2.95–2.82 (2H, m), 2.80 (1H, dd, *J* = 12.1, 2.0 Hz), 2.73 (1H, d, *J* = 4.5 Hz), 2.39 (1H, dd, *J* = 14.5, 6.0 Hz), 2.37–2.34 (1H, m), 2.30 (1H, ddd, *J* = 17.3, 8.2, 5.4 Hz), 2.19 (1H, d, *J* = 17.1 Hz), 1.96–1.91 (1H, m), 1.78–1.71 (1H, m), 1.65–1.59 (1H, m), 1.57 (1H, dd, *J* = 14.3, 6.5 Hz), 1.51–1.42 (2H, m), 0.94 (3H, d, *J* = 6.7 Hz), 0.90 (9H, s), 0.08 (3H, s), 0.06 (3H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 137.4, 123.2, 68.5, 62.4, 45.9, 44.2, 39.4, 38.0, 35.2, 33.5, 29.9, 26.0, 25.9, 21.1, 18.2, -4.3, -4.5 ppm; high resolution mass spectrum (ES+) *m/z* 322.2569 [$(M+H)^+$; calculated for $C_{19}H_{36}NOSi$: 322.2566].



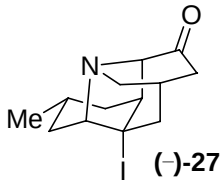
(–)-**26**

**Alcohol (–)-26:** Alkene **25** (51 mg, 0.16 mmol) was dissolved in dichloromethane (20 mL) and a dichloromethane (5 mL) suspension of *N*-iodosuccinimide (59 mg, 0.16 mmol, 1.01 equiv.) was added dropwise over 5 minutes. The reaction mixture was stirred at ambient temperature for 20 minutes and then quenched with a 1:1 mixture (5 mL) of sodium thiosulfate:sodium carbonate (aqueous saturated). After stirring vigorously for 10 minutes, the mixture was poured into water (15 mL) and extracted with dichloromethane (2 X 50 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*.

The residue was purified by silica gel gradient chromatography (100:0 to 96:4; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing the tetracycle (65 mg, 93% yield) as a light yellow solid: $[\alpha]^{20}_{D}$ –2.0° (*c*0.50, $CH_2Cl_2$); IR (NaCl plate, thin film, $CH_2Cl_2$): 2930 (s), 2855 (m), 1458 (m), 1253 (m), 1102 (s), 877 (m), 837 (m), 777 (m), 664 (w), 568 (s) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 4.20 (1H, dt, *J* = 8.6, 4.5 Hz), 3.36 (1H, d, *J* = 4.5 Hz), 3.19 (1H, d, *J* = 13.4 Hz), 3.13–3.10 (1H, m), 2.97 (1H, dd, *J* = 13.8, 5.6 Hz), 2.78–2.75 (1H, br m), 2.73 (1H, ddd, *J* = 13.4, 3.0, 1.9 Hz), 2.54 (1H, br d, *J* = 13.4 Hz), 2.24 (1H, td, *J* = 13.8, 8.9 Hz), 1.99–1.89 (2H, m), 1.86 (1H, br d, *J* = 13.4 Hz), 1.84–1.74 (3H, m), 1.46 (1H, ddd, *J* = 13.6, 8.4, 1.5 Hz), 0.96 (3H, d, *J* = 6.0 Hz), 0.89 (9H, s), 0.06 (6H, s) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 75.4, 64.7, 64.1, 56.3, 53.7, 45.0, 42.4, 39.4, 36.6, 32.4, 29.9, 25.9, 23.3, 21.8, 18.2, -4.4, -4.6 ppm; high resolution mass spectrum (ES+) *m/z* 448.1545 $[(M+H)^+$; calculated for $C_{19}H_{35}INOSi$: 448.1533].

The above prepared tetracycle (20 mg, 0.045 mmol) was dissolved in methanol (5 mL) and treated with catalytic hydrochloric acid (12N aqueous, 5 drops from a 9" pipet) and stirred for 18 hours at ambient temperature. The reaction mixture was poured into sodium hydroxide (10 mL, 5N aqueous) and extracted with dichloromethane (2 X 15 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (100:0 to 90:10; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing the alcohol (–)-**26** (15 mg, 100% yield) as an oily solid. X-Ray quality crystals were obtained via vapor diffusion from pentane/diethyl ether. Upon slow evaporation of most of the solvent, the mixture was placed into a refrigerator for 24 hours and then warmed to ambient temperature; melting point 124–126°. See attached .cif file for details: $[\alpha]^{20}_{D}$ –7.33° (*c*2.10, $CH_2Cl_2$); IR (NaCl plate, thin

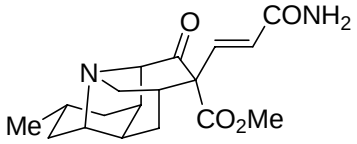
film, $CH_2Cl_2$): 2925 (s), 2967 (s), 1715 (s), 1454 (m), 1405 (w), 1378 (w), 1346 (w), 1334 (w), 1312 (w), 1281 (w), 1251 (m), 1202 (m), 1161 (m), 1117 (w), 1089 (w), 1068 (m), 1039 (w), 1000 (w), 985 (w), 969 (w), 943 (w), 925 (m), 896 (m), 866 (m), 838 (w), 821 (w), 803 (m), 791 (w), 767 (w), 749 (w), 686 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 4.19 (1H, dt, *J* = 8.9, 4.5 Hz), 3.99 (1H, br s), 3.38 (1H, d, *J* = 4.1 Hz), 3.15 (1H, dd, *J* = 13.4, 1.5 Hz), 3.10 (1H, d, *J* = 1.9 Hz), 2.97 (1H, dd, *J* = 13.6, 5.4 Hz), 2.74–2.69 (2H, m), 2.54 (1H, br d, *J* = 13.8 Hz), 2.32 (1H, td, *J* = 13.8, 8.8 Hz), 1.94–1.77 (6H, m), 1.45 (1H, ddd, *J* = 13.8, 8.9, 1.5 Hz), 0.95 (3H, d, *J* = 5.2 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 75.2, 64.3, 63.8, 60.2, 56.2, 53.7, 44.8, 42.4, 39.2, 35.2, 32.2, 23.4, 21.8 ppm; high resolution mass spectrum (ES+) *m/z* 334.0679 [$(M+H)^+$; calculated for $C_{13}H_{21}INO$: 334.0668].




**(–)-27**

**Iodoketone (–)-27:** Alcohol **26** (30 mg, 0.090 mmol) was dissolved in dichloromethane (7 mL) and sodium bicarbonate (57 mg, 0.67 mmol, 7.5 eqiuv.) and Dess-Martin periodinane (96 mg, 0.22 mmol, 2.5 equiv.) were added and the mixture stirred vigorously for 1 hour. The mixture was treated with a 1:1 mixture (3 mL) of sodium carbonate:sodium thiosulfate (aqueous saturated) and stirred for 30 minutes. The mixture was poured into water (30 mL) and the aqueous layer was extracted with dichloromethane (3 X 100 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (100:0 to 96:4; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing iodoketone (–)-**27** (27 mg, 93%

yield) as a white solid: $[\alpha]^{20}_{D}$ −2.50° (*c*1.35, $CH_2Cl_2$); IR (NaCl plate, thin film, $CH_2Cl_2$): 2925 (s), 2867 (s), 1715 (s), 1454 (m), 1405 (w), 1346 (w), 1334 (w), 1312 (w), 1281 (w), 1251 (m), 1202 (m), 1161 (m), 1099 (w), 1068 (m), 1039 (w), 987 (w), 943 (w), 925 (m), 896 (m), 866 (m), 803 (m), 749 (w), 686 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 3.67 (1H, m), 3.29–3.27 (1H, m), 3.25–3.20 (2H, m), 3.11 (1H, d, *J* = 14.1 Hz), 2.68 (1H, d, *J* = 14.5 Hz), 2.57–2.52 (3H, m), 2.14–2.08 (1H, m), 1.96–1.74 (6H, m), 0.96 (3H, d, *J* = 5.6 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 210.9, 74.4, 70.6, 58.4, 58.2, 54.1, 52.2, 44.7, 41.1, 38.9, 32.5, 23.4, 21.4 ppm; high resolution mass spectrum (ES+) *m/z* 332.0509 [$(M+H)^+$; calculated for $C_{13}H_{21}INO$: 332.0511].




(–)-**28**

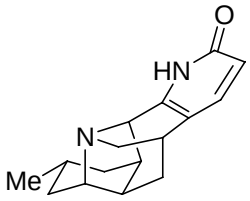
**Unsaturated amide (–)-28:** Iodoketone **27** (143 mg, 0.432 mmol) was dissolved in tetrahydrofuran (10 mL) and cooled to -78 °C. Freshly prepared lithium di-*iso*-propylamide[4] (1.4 mL, 0.39M solution in tetrahydrofuran, 1.3 equiv.) was added dropwise and the solution was stirred for 10 minutes at -78 °C. Freshly distilled hexamethylphosphoramide (1.0 mL, 10% v/v) was added dropwise to the reaction mixture over 5 minutes. The mixture was stirred for an additional 5 minutes at -78 °C, warmed to -60 °C for 10 minutes and then cooled to -78 °C. Methyl cyanoformate (55 μL, 0.691 mmol, 1.6 equiv.) was added in one portion and the reaction mixture was stirred an additional 1 hour at -78 °C. The reaction mixture was quenched with sodium bicarbonate (5 mL, aqueous saturated), warmed to ambient temperature, poured into water (50 mL) and extracted with chloroform (3 X 100 mL). The combined organic extracts

were dried with sodium sulfate, filtered and concentrated *in vacuo*. The mixture of β-ketoester diastereomers was used without purification in the next reaction. High resolution mass spectrum (ES+) *m/z* 390.0573 [$(M+H)^+$; calculated for $C_{15}H_{21}INO_3$: 390.0566].

The above prepared β-ketoester was dissolved in 2,6-lutidine (2.5 mL) and triethylsilane (2.5 mL). The mixture was stirred vigorously and palladium(II)chloride (150 mg, 0.84 mmol, 1.9 equiv.) was added in three portions over 90 minutes. The mixture was stirred an additional 30 minutes and then carefully treated with sodium bicarbonate (15 mL, aqueous saturated). The mixture was stirred for 30 minutes, poured into water (20 mL) and extracted with dichloromethane (3 X 100 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was dissolved in chloroform (50 mL) and washed twice with hydrochloric acid (20 mL, 1N aqueous). The pH was adjusted to 8 with solid sodium bicarbonate and extracted with chloroform (3 X 100 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was quickly passed through a silica gel gradient plug (100:0 to 96:4; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing a mixture of desiodo-β-ketoester diastereomers (71 mg, 74% yield). High resolution mass spectrum (ES+) *m/z* 264.1600 [$(M+H)^+$; calculated for $C_{15}H_{22}NO_3$: 264.1600].

The above prepared desiodo-β-ketoester (9.7 mg, 0.0368 mmol) was dissolved in dimethylsulfoxide (2 mL) and treated with cesium carbonate (120 mg, 0.368 mmol, 10 equiv.), followed by the addition of propiolamide (5 mg, 0.0737 mmol, 2 equiv.). The mixture was stirred for 24 hours at ambient temperature, poured into water (15 mL) and extracted with chloroform (3 X 15 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography

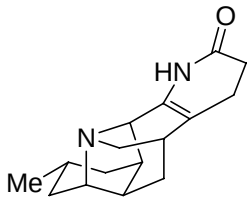
(100:0 to 92:8; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing the unsaturated amide (–)-**28** (10 mg, 82% yield) as a light yellow solid: $[\alpha]^{20}_{D}$ –80.3° (*c*0.12, $CDCl_3$); IR (NaCl plate, thin film, $CH_2Cl_2$): 3424 (br m), 3363 (br m), 3192 (br m), 2924 (s), 2849 (m), 1740 (s), 1710 (m), 1682 (s), 1455 (m), 1394 (m), 1291 (w), 1268 (w), 1230 (s), 1123 (w), 1070 (m), 1012 (w), 919 (w), 890 (w), 797 (w), 733 (w), 667 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 6.76 (1H, d, *J* = 15.6 Hz), 6.17 (1H, d, *J* = 15.6 Hz), 5.90 (1H, br s), 5.83 (1H, br s), 3.74 (3H, s), 3.64 (1H, s), 3.13 (1H, dd, *J* = 14.5, 3.7 Hz), 3.09 (1H, br t, *J* = 1.9 Hz), 3.06 (1H, dd, *J* = 14.3, 1.3 Hz), 2.75 (1H, d, *J* = 3.7 Hz), 2.24 (1H, dd, *J* = 6.3, 3.7 Hz), 2.16 (1H, ddd, *J* = 15.1, 6.5, 3.1 Hz), 1.87 (1H, br d, *J* = 13.4 Hz), 1.81 (1H, br t, *J* = 3.0 Hz), 1.79–1.76 (1H, m), 1.74 (1H, dd, *J* = 9.5, 5.0 Hz), 1.70 (1H, br d, *J* = 15.6 Hz), 1.05 (1H, t, *J* = 13.0 Hz), 1.01 (1H, ddd, *J* = 13.4, 11.9, 1.9 Hz), 0.87 (3H, d, *J* = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 206.2, 170.2, 166.7, 142.5, 126.5, 74.1, 70.9, 64.3, 55.2, 53.2, 46.3, 44.4, 40.2, 39.1, 35.4, 32.7, 24.9, 21.9 ppm; high resolution mass spectrum (ES+) *m/z* 333.1818 [$(M+H)^+$; calculated for $C_{18}H_{25}N_2O_4$: 333.1814].




(+)-**1**

**(+)-Lyconadin A (1):** Unsaturated amide **28** (2.8 mg, 0.0084 mmol) was dissolved in anhydrous acetonitrile (1.5 mL) and transferred to a screw cap vial. Tetramethylammonium acetate (11.2 mg, 0.084 mmol, 10 equiv.) was added, the vial was sealed and then placed into an oil bath preheated to 135 °C. The reaction mixture was stirred for 16 hours, cooled to ambient

temperature and poured into sodium bicarbonate (5 mL, aqueous saturated). The aqueous layer was extracted with dichloromethane (2 X 15 mL) and chloroform (1 X 15 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (100:0 to 90:10; dichloromethane:methanol containing 10% by volume ammonium hydroxide), providing (+)-lyconadin A (**1**, 1.5 mg, 71% yield) as a light yellow solid: $[\alpha]^{20}_{D}$ +33° (*c*0.13, MeOH); IR (NaCl plate, neat): 3116 (w), 2921 (s), 2855 (m), 1653 (s), 1611 (m), 1559 (w), 1457 (m), 1262 (w), 1192 (w), 1099 (m), 1065 (m), 1024 (w), 946 (w), 797 (w), 678 (m) $cm^{-1}$; $^{1}$H-NMR (600 MHz, $CD_3OD$) δ 7.42 (1H, d, *J* = 9.0 Hz), 6.36 (1H, d, *J* = 8.9 Hz), 4.27 (1H, s), 3.60 (1H, m), 3.59 (1H, m), 2.93 (1H, d, *J* = 13.2 Hz), 2.85 (1H, m), 2.27 (1H, br d, *J* = 4.2 Hz), 2.11 (1H, ddd, *J* = 14.0, 5.6, 4.0 Hz), 2.11 (1H, m), 2.08 (1H, m), 1.94 (1H, br d, *J* = 13.3 Hz), 1.86 (1H, m), 1.76 (1H, d, *J* = 13.8 Hz), 1.19 (1H, t, *J* = 12.8 Hz), 1.06 (1H, t, *J* = 13.0 Hz), 0.95 (3H, d, *J* = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $CD_3OD$) δ 165.4, 149.3, 141.8, 126.3, 116.6, 72.6, 64.0, 61.7, 50.8, 48.1, 41.0, 40.5, 34.3, 33.9, 26.2, 22.0 ppm; high resolution mass spectrum (ES+) *m/z* 257.1648 [$(M+H)^{+}$; calculated for $C_{16}H_{21}N_2O$: 257.1654].




(–)-**2**

**(–)-Lyconadin B (2):** Unsaturated amide **28** (24 mg, 0.030 mmol) was dissolved in methanol (10 mL) and the solution was sparged under an argon atmosphere. The mixture was

treated with Pd/C (5 mg, 10% weight Pd/C), sparged under a hydrogen atmosphere (1 atm, balloon) and then stirred for 3 hours. The reaction mixture was sparged under an argon atmosphere and filtered through a pad of Celite. The Celite was washed with with methanol (10 mL) and the filtrate was concentrated *in vacuo* to provide the saturated amide (24 mg, 100% yield), which was used without purification in the next reaction: $[\alpha]^{20}_{D}$ –61.3° (*c*0.14, $CH_2Cl_2$); IR (NaCl plate, neat): 3430 (br m), 3363 (br m), 3203 (br s), 2923 (s), 2849 (m), 1734 (s), 1710 (m), 1669 (s), 1453 (m), 1268 (m), 1227 (m), 1068 (m), 1024 (w), 948 (w), 919 (w), 890 (w), 803 (w) $cm^{-1}$; $^1$H-NMR (500 MHz, $CDCl_3$) δ 5.60 (1H, br s), 5.44 (1H, br s), 3.75 (3H, s), 3.55 (1H, s), 3.23 (1H, dd, *J* = 14.5, 1.9 Hz), 3.13 (1H, dd, *J* = 14.3, 3.9 Hz), 3.10–3.08 (1H, m), 2.89–2.84 (2H, m), 2.73 (1H, br d, *J* = 3.0 Hz), 2.27–2.16 (2H, m), 2.10 (1H, ddd, *J* = 14.9, 6.3, 3.0 Hz), 2.03–1.98 (1H, m), 1.96 (1H, dd, *J* = 6.0, 3.7 Hz), 1.90–1.85 (1H, m), 1.79 (1H, br t, *J* = 3.0 Hz), 1.76–1.71 (2H, m), 1.67 (1H, br d, *J* = 14.9 Hz), 1.05–0.92 (2H, m), 0.86 (3H, d, *J* = 6.3 Hz) ppm; $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 209.8, 174.6, 172.5, 74.6, 71.1, 60.6, 55.4, 52.6, 45.8, 44.7, 40.4, 39.2, 37.0, 33.8, 33.4, 31.7, 24.9, 22.0 ppm; high resolution mass spectrum (ES+) *m/z* 335.1984 [$(M+H)^+$; calculated for $C_{18}H_{27}N_2O_4$: 339.1971].

In a screw cap vial, the above prepared saturated amide (4.0 mg, 0.0120 mmol) was dissolved in freshly distilled hexamethylphosphramide (2.5 mL). Lithium chloride (5.0 mg, 0.120 mmol, 10 equiv.) was added, the vessel sealed and the mixture was placed into an oil bath preheated to 125 °C for 17.5 hours. The mixture was cooled to ambient temperature and poured into hydrochloric acid (5 mL, 1N aqueous). The aqueous layer was extracted with chloroform (2 X 15 mL) and the combined organic layers were washed with hydrochloric acid (5 mL, 1N aqueous). The organic extracts were discarded and the pH of the combined aqueous layers was carefully adjusted to 12 with sodium carbonate (15 mL, aqueous saturated) and then extracted

with chloroform (3 X 15 mL). The combined organic extracts were dried with sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by silica gel gradient chromatography (100:0 to 92:8; dichloromethane:methanol containing 10% by volume ammonium hydroxide), to provide (-)-lyconadin B (**2**; 2.1 mg, 68% yield) as a white solid: $[\alpha]^{20}_{D}$ –64.0° (*c*0.025, MeOH); IR (NaCl plate, neat): 3221 (w), 2922 (s), 2849 (m), 1671 (s), 1456 (m), 1373 (m), 1315 (w), 1233 (w), 1175 (w), 1093 (w), 1053 (w), 948 (w), 913 (w), 791 (w), 669 (w) $cm^{-1}$; $^{1}$H-NMR (600 MHz, $CD_3OD$) δ 3.50 (1H, s), 3.31 (1H, m), 3.28 (1H, m), 2.86 (1H, d, *J* = 12.1 Hz), 2.52–2.29 (4H, m), 2.27 (1H, d, *J* = 4.8 Hz), 2.13 (1H, m), 1.96 (1H, m), 1.95 (1H, s), 1.95 (1H, m), 1.85 (1H, d, *J* = 13.4 Hz), 1.74 (1H, m), 1.69 (1H, d, *J* = 13.3 Hz), 1.06 (1H, ddd, *J* = 13.4, 12.4, 2.0 Hz), 0.95 (1H, t, *J* = 13.0 Hz), 0.89 (1H, d, *J* = 6.5 Hz) ppm; $^{13}$C-NMR (125 MHz, $CD_3OD$) δ 173.3, 135.8, 120.7, 72.6, 63.7, 61.9, 49.9, 48.2, 41.1, 40.9, 34.5, 33.3, 31.5, 26.2, 25.0, 22.1 ppm; high resolution mass spectrum (ES+) *m/z* 259.1818 [$(M+H)^+$; calculated for $C_{16}H_{23}N_2O$: 259.1810].

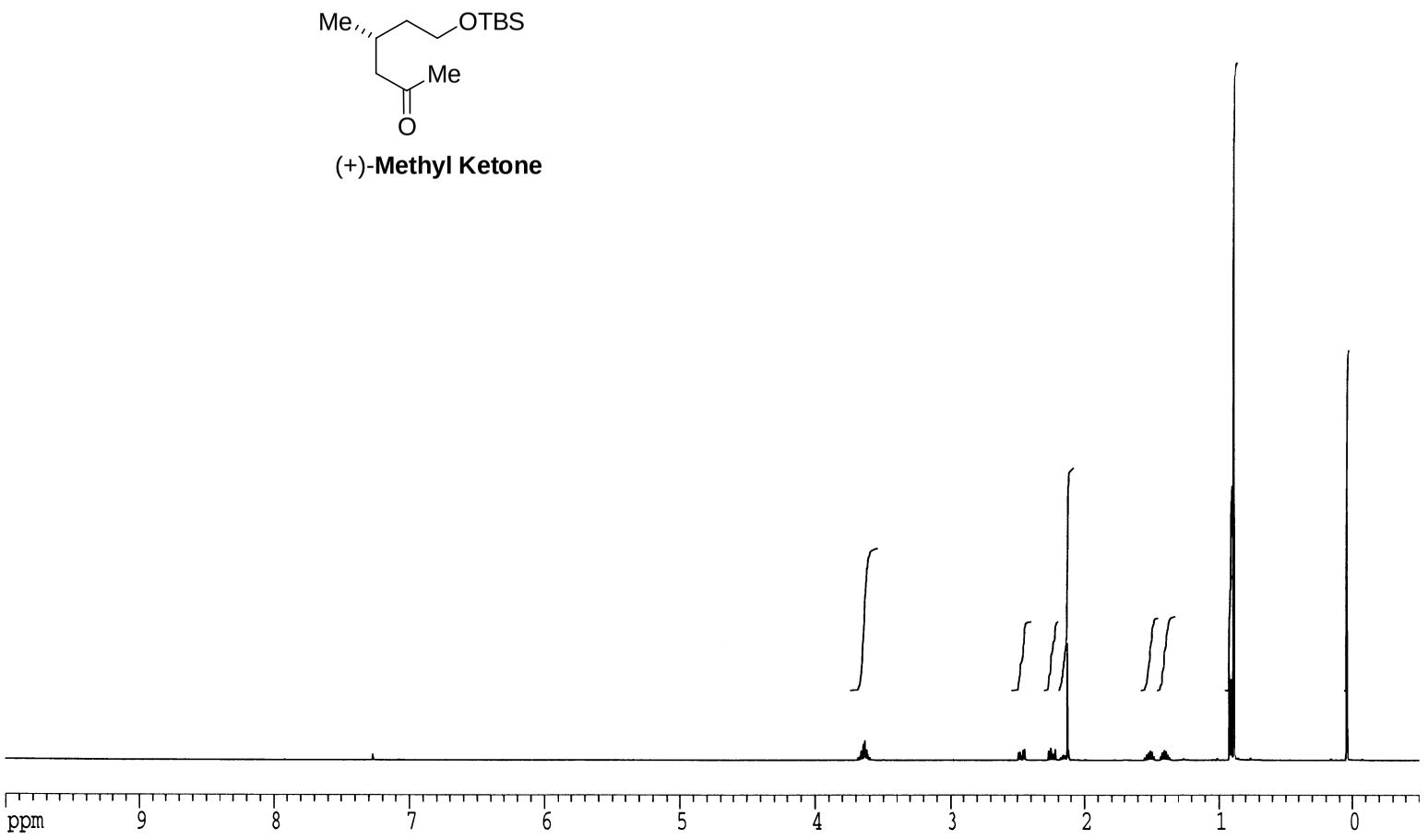
**References:**


1) Acid **11** was prepared according to the following literature procedure: Kottirsch, G.; Kottirsch, G.; Metternich, R. New Derivatives of Beta-Amino Acids with Anti-Thrombotic Activity. Eur. Patent EP 0 560 730 B1, **1996**.
2) The oxazolidinone was prepared by reduction of L-Phe, employing the iodine/sodium borohydride method reported by McKennon, M. C.; Meyers, A. I. *J. Org. Chem.* **1993**, *58*, 3568. The carbamate was prepared according to the procedure reported by Gage, J. R.; Evans, D. A. *Org. Synth* **1990**, *68*, 83.

3) Martin sulfururane was handled and stored according to the procedures described in the following paper: Arhart, R. J.; Martin, J. C. *J. Am. Chem Soc* **1972**, *94*, 5003.

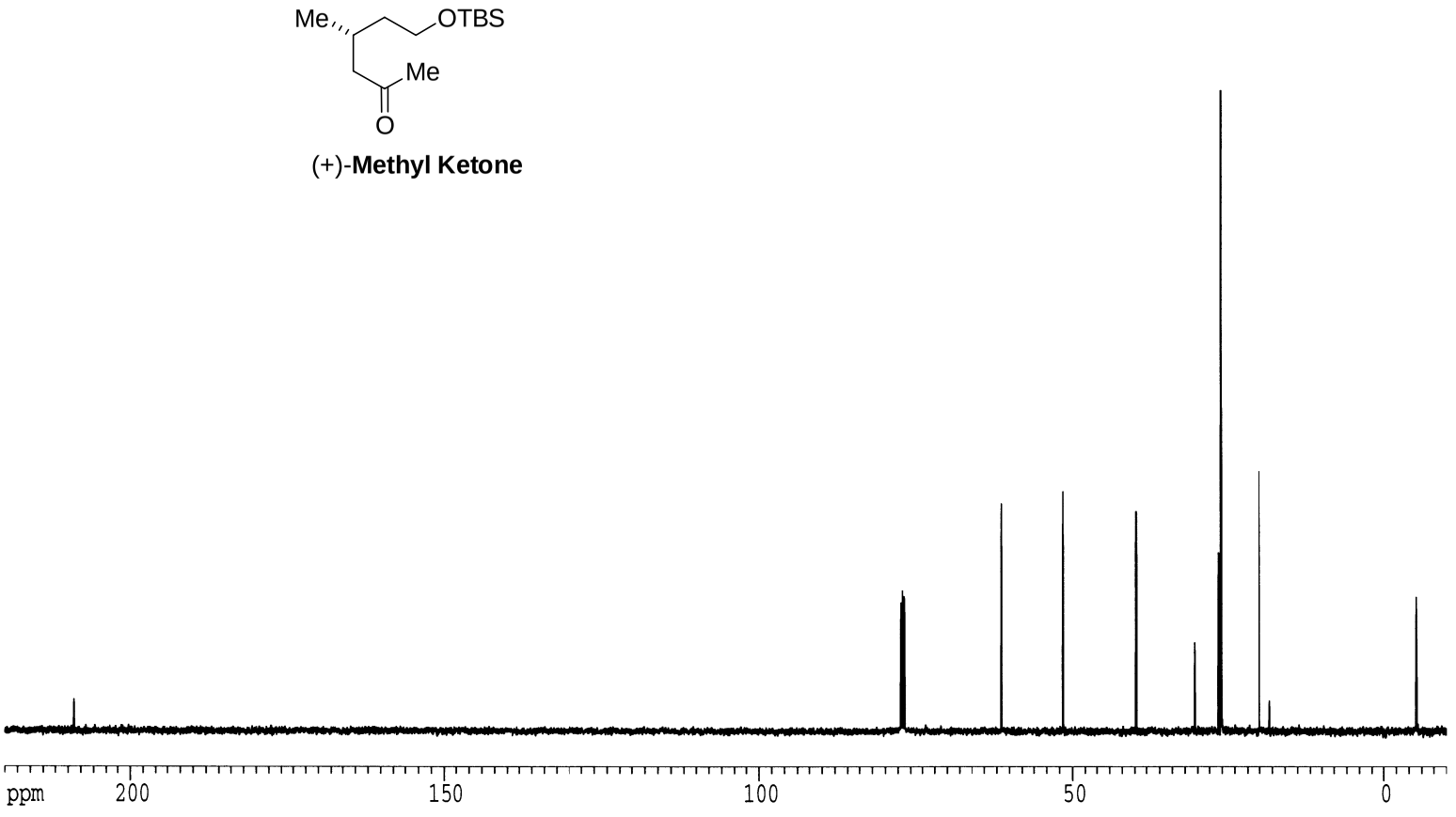
4) Lithium di-*iso*-propylamide was prepared as follows: Diisopropylamine (1.4 mL, 10 mmol, 1.1 equiv.) was dissolved in tetrahydrofuran (15 mL) and cooled to 0 °C. *n*-Butyl lithium (6.6 mL, 1.37M solution in tetrahydrofuran) was added dropwise over 5 minutes and the mixture was stirred for 1 hour at 0 °C. The resulting lithium di-*iso*-propylamide solution (0.39M) was used immediately in the reaction.

**SPECTROSCOPIC DATA**



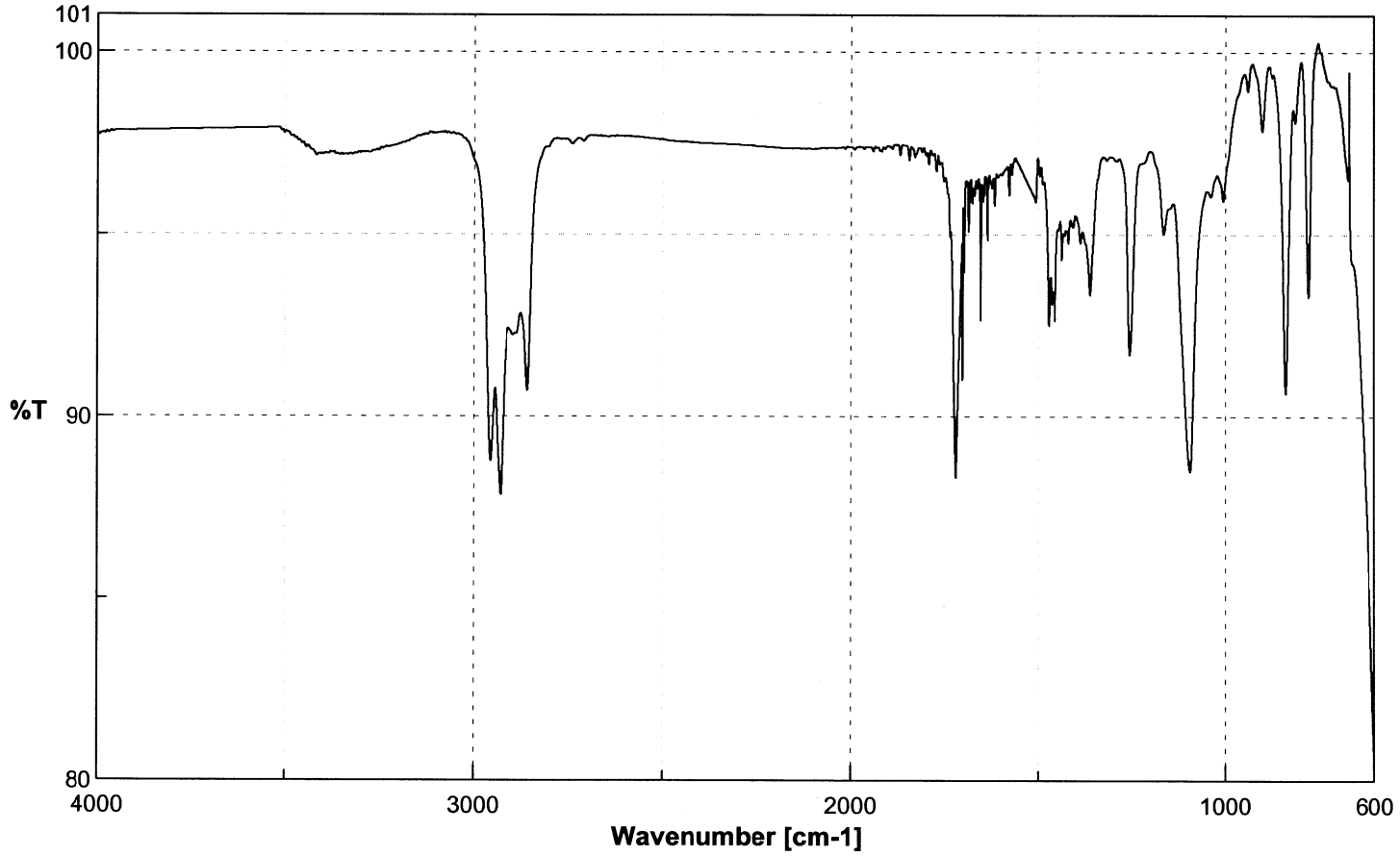

(+)-**Methyl Ketone**

The 500 MHz $^{1}$H-NMR Spectrum of (+)-**Methyl Ketone** in $CDCl_3$.

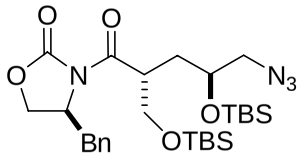



(+)-**Methyl Ketone**

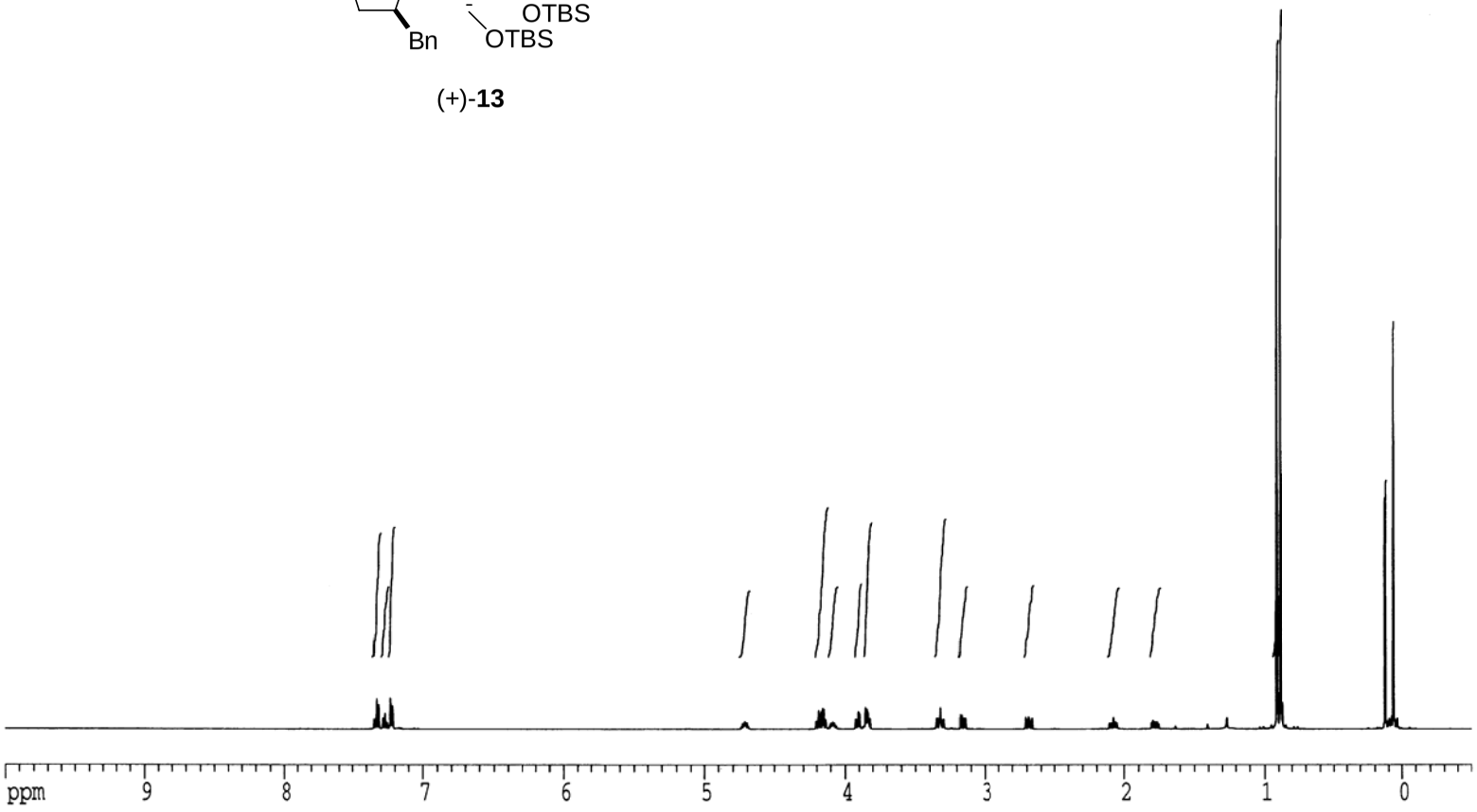
The 125 MHz $^{13}$C-NMR Spectrum of (+)-**Methyl Ketone** in $CDCl_3$.



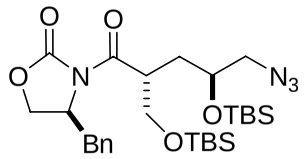

The Infrared Spectrum of (+)-**Methyl Ketone**.



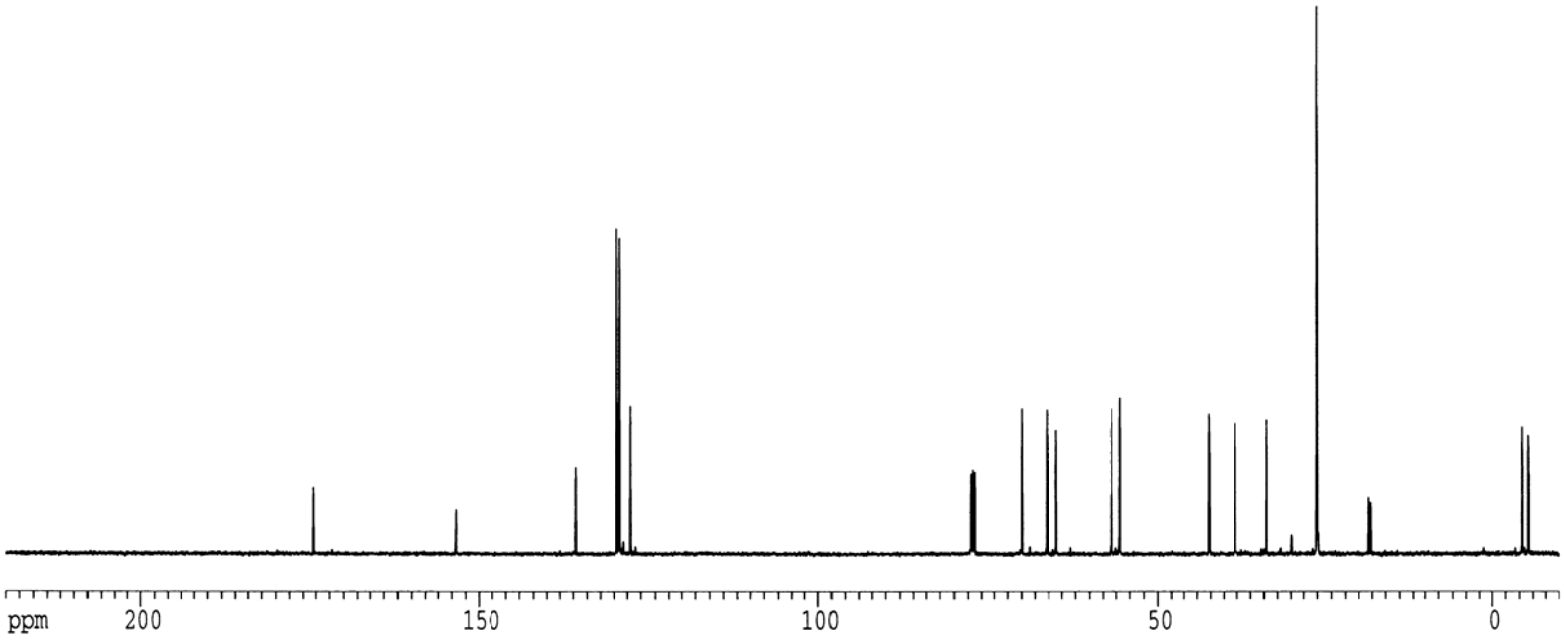

(+)-**13**



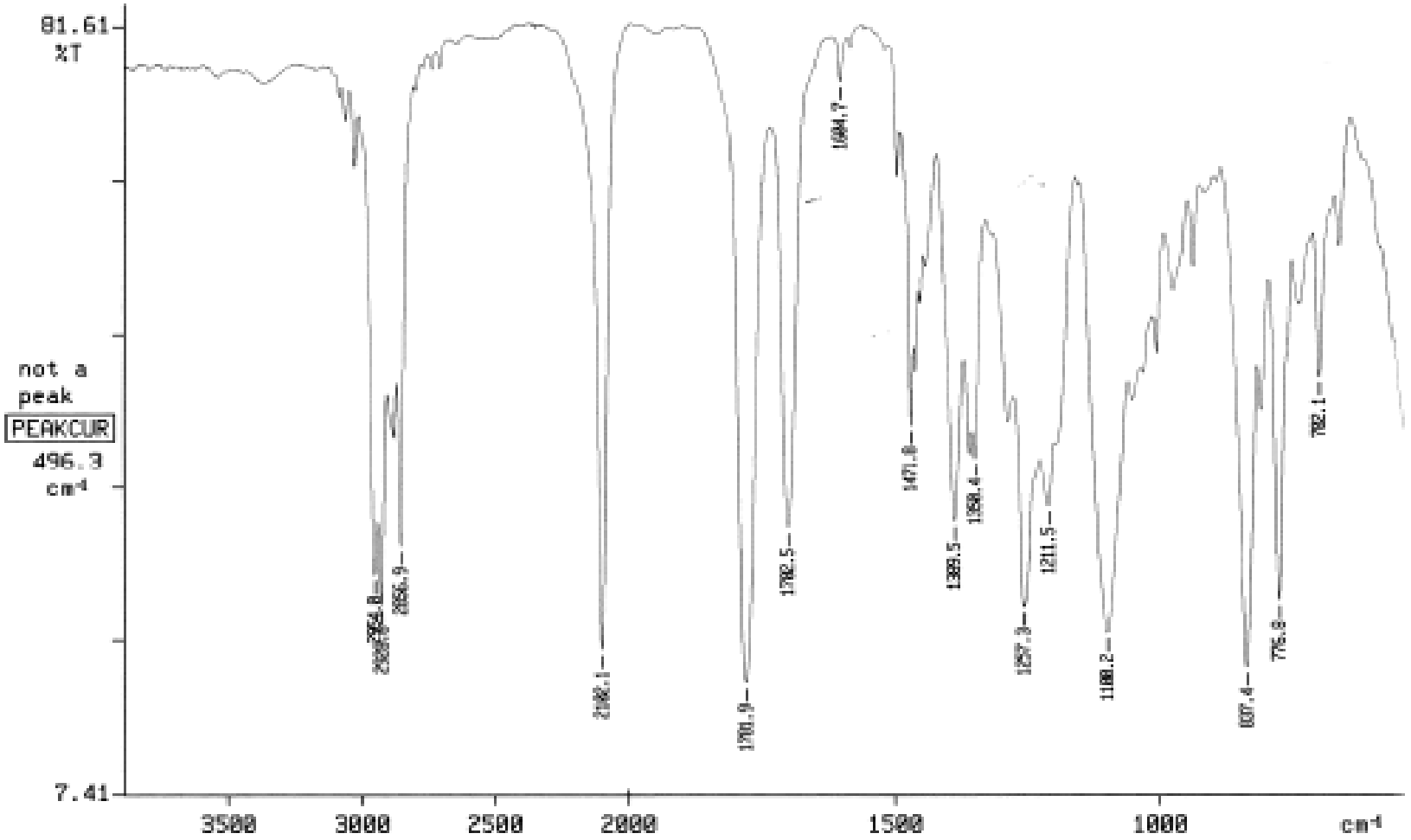

The 500 MHz $^{1}$H-NMR Spectrum of Compound (+)-**13** in $CDCl_3$.



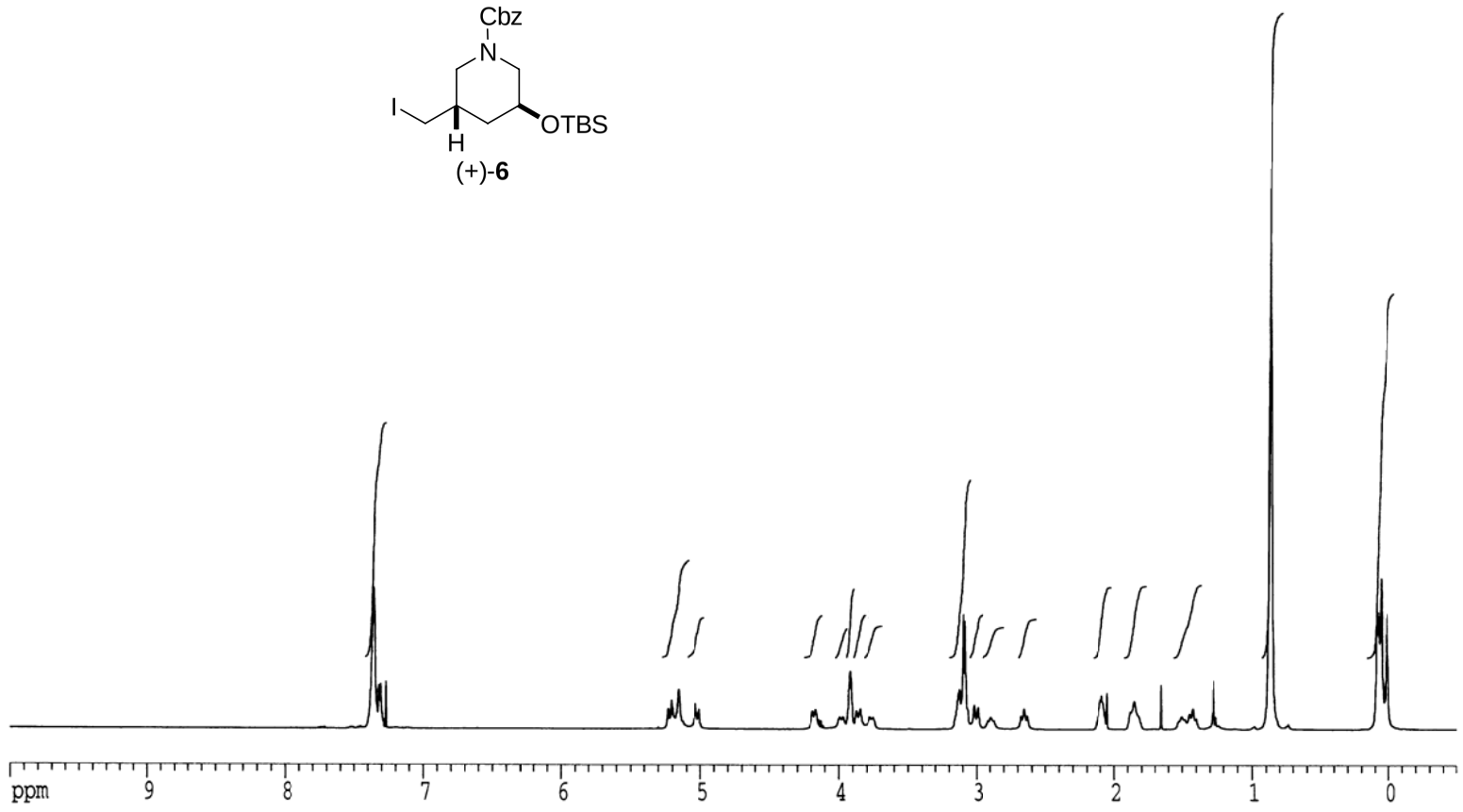

(+)-**13**



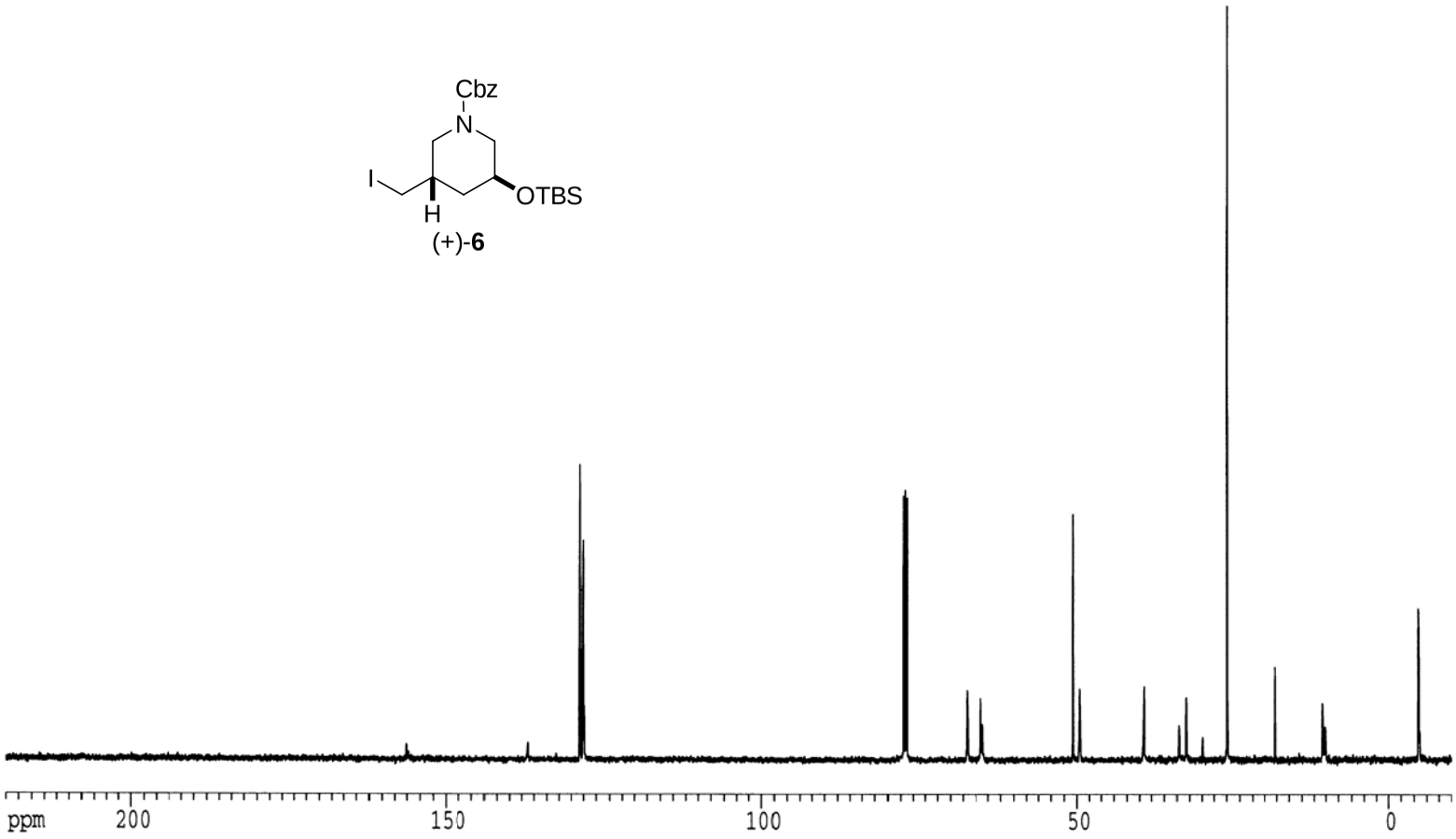

The 125 MHz $^{13}$C-NMR Spectrum of Compound (+)-**13** in $CDCl_3$.



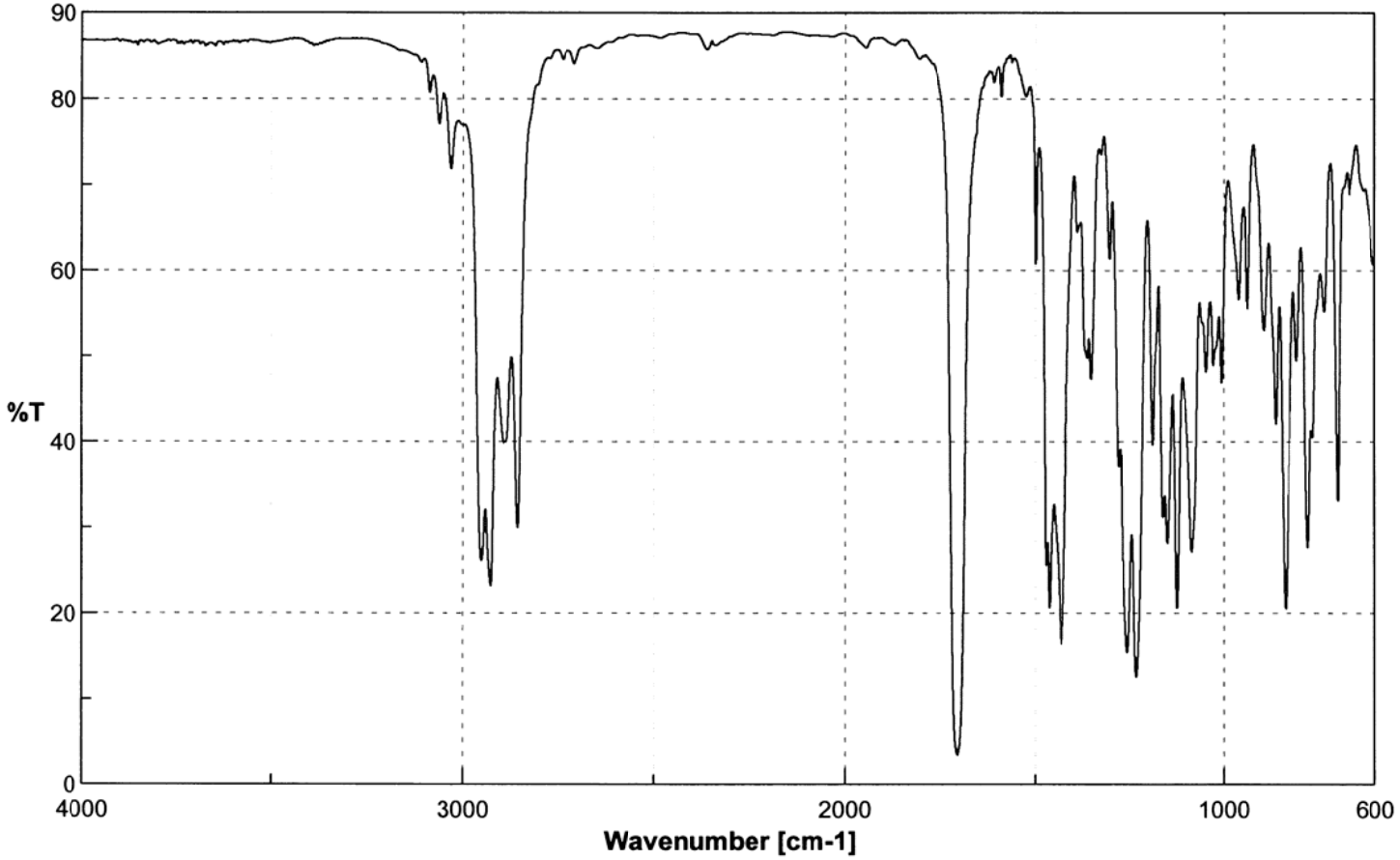

The Infrared Spectrum of Compound (+)-**13**.



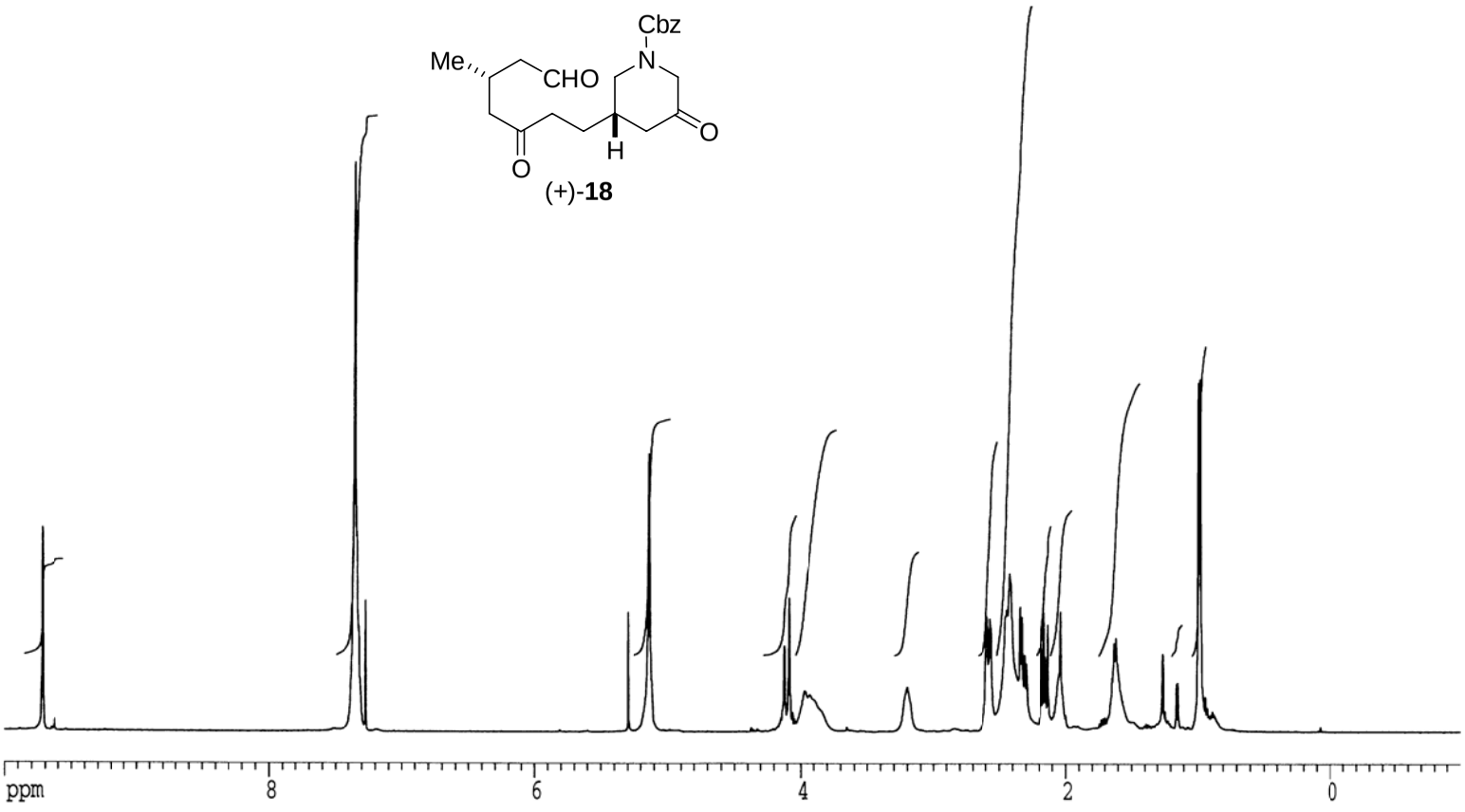

The 500 MHz $^{1}$H-NMR Spectrum of Compound (+)-**6** in $CDCl_3$.



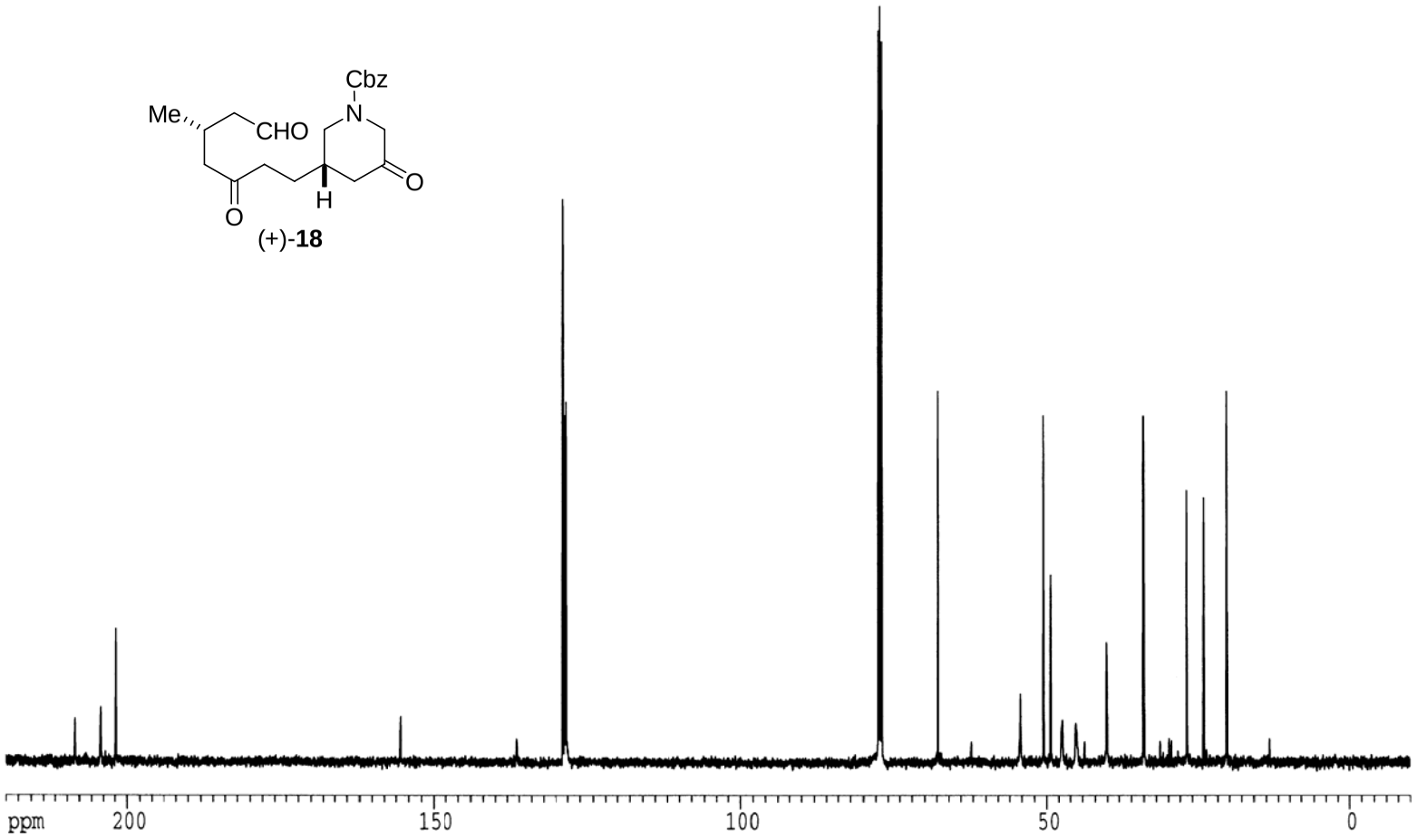

The 125 MHz $^{13}$C-NMR Spectrum of Compound (+)-**6** in $CDCl_3$.



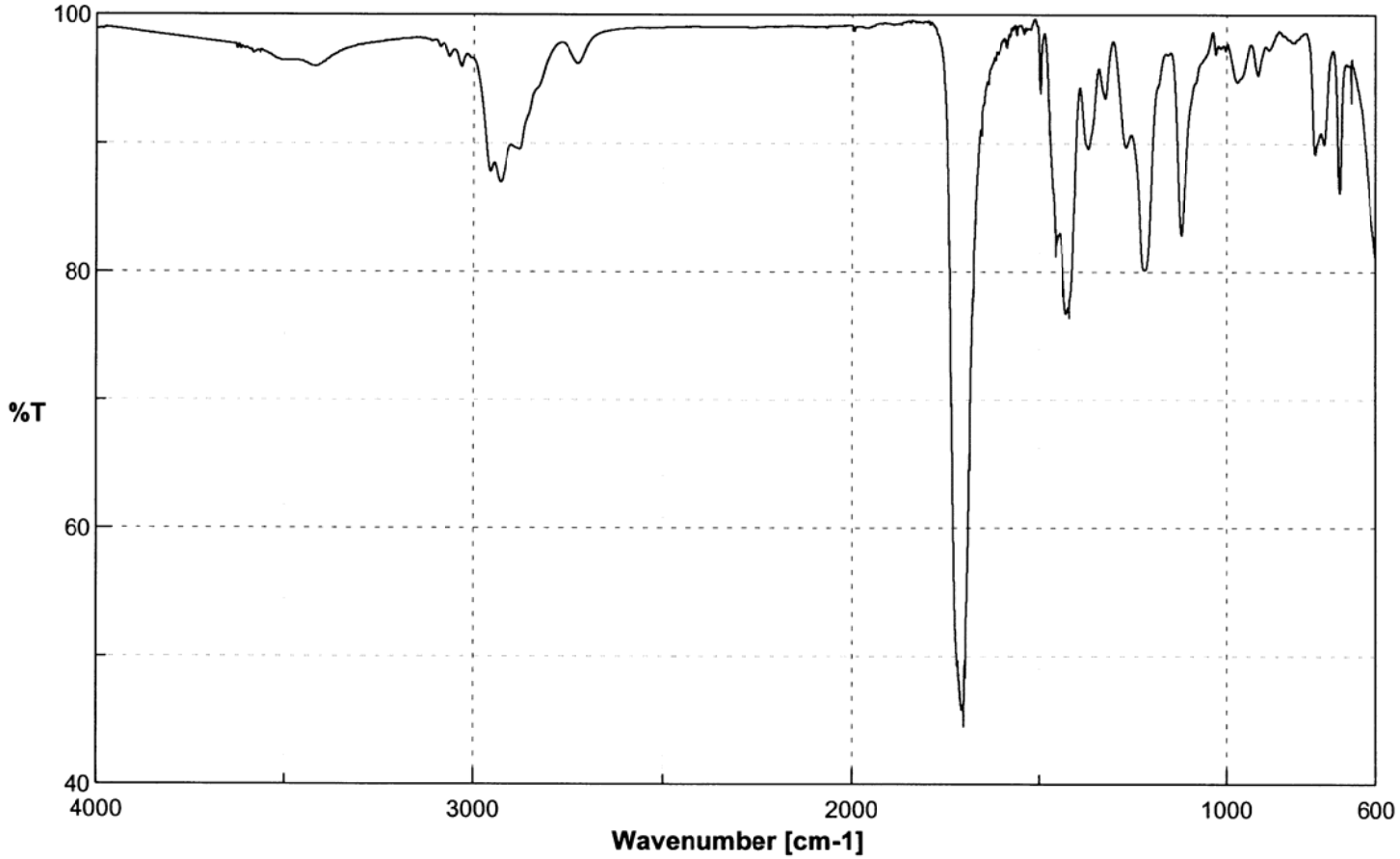

The Infrared Spectrum of Compound (+)-**6**.



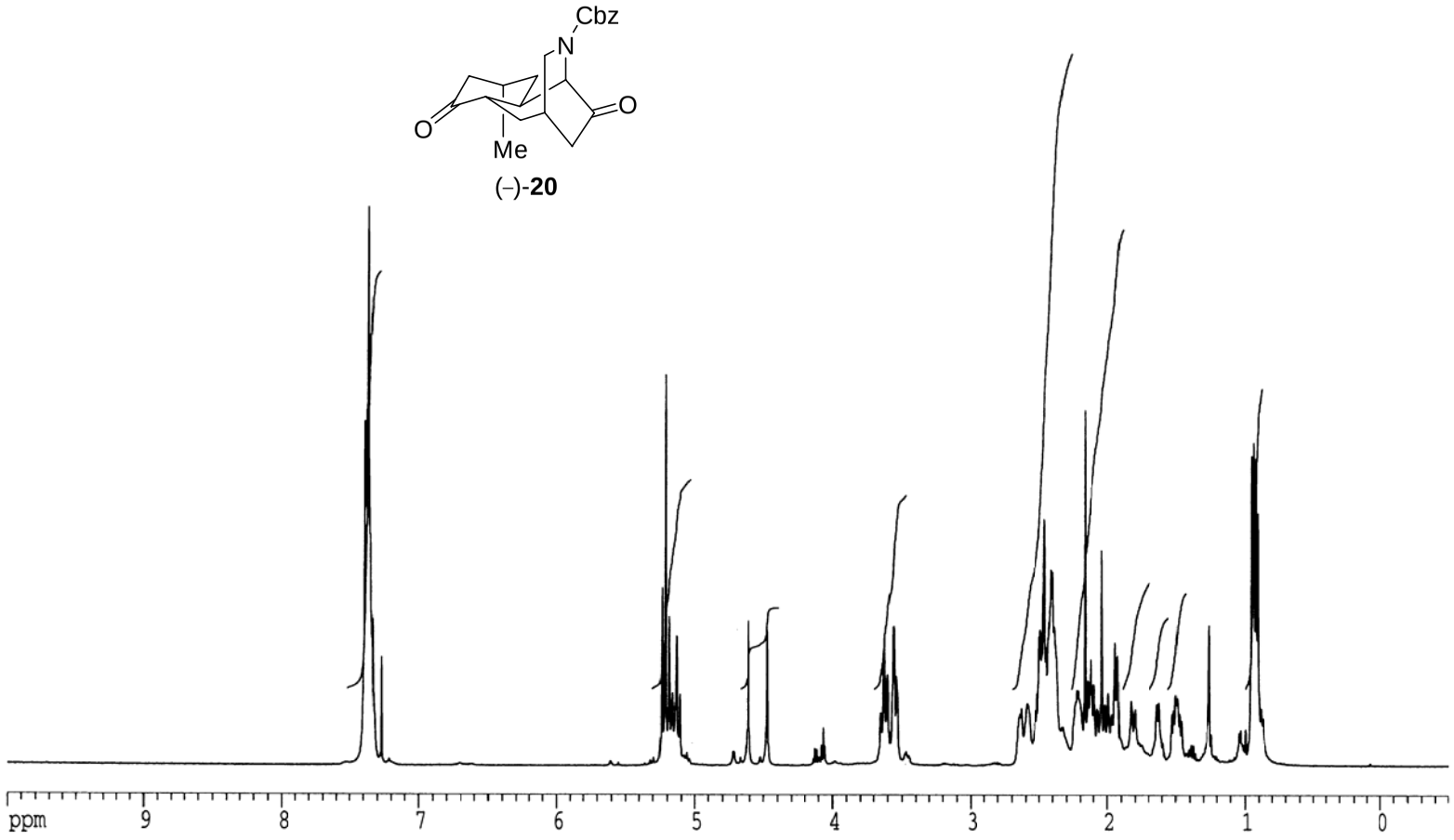

The 500 MHz $^{1}$H-NMR Spectrum of Compound (+)-**18** in $CDCl_3$.



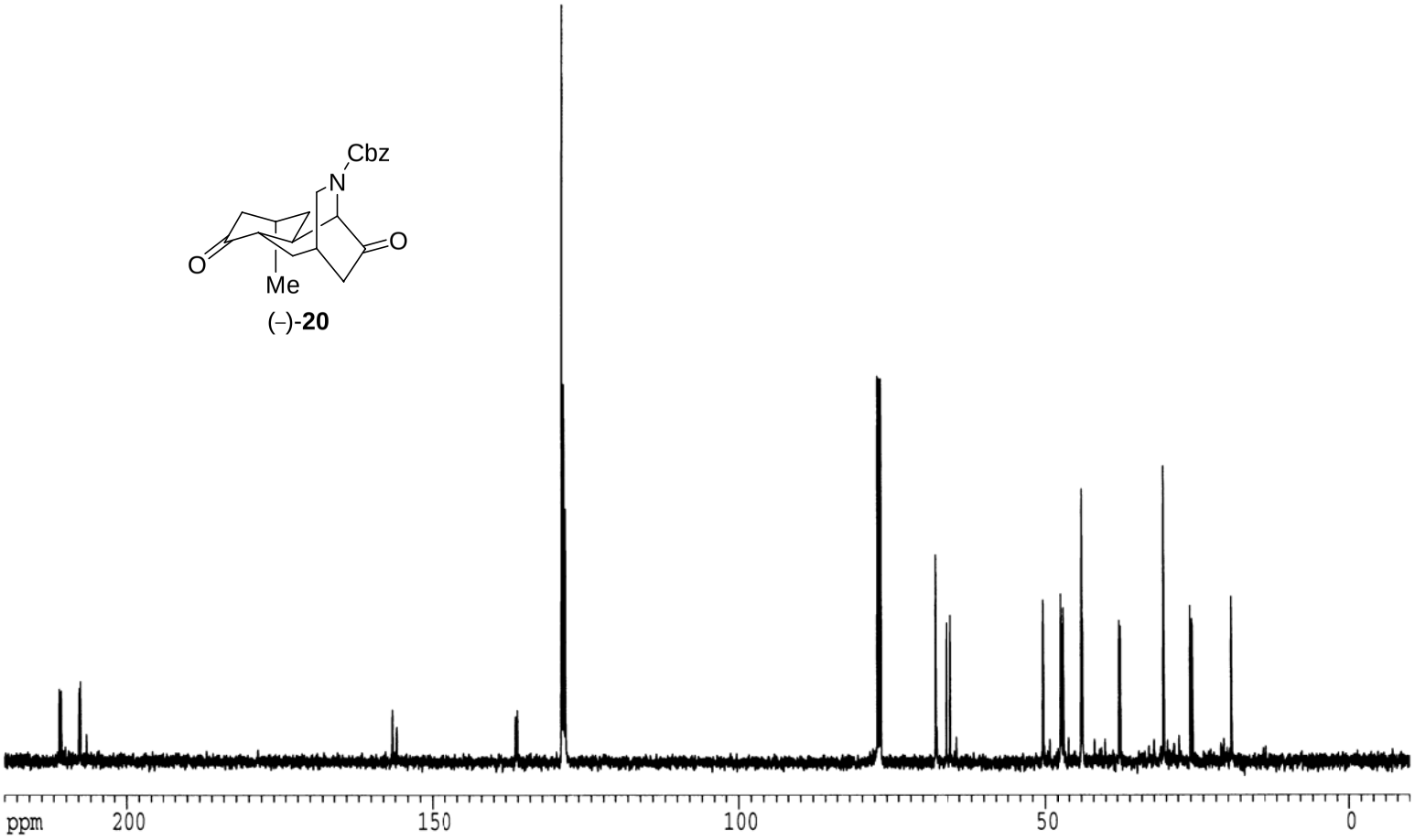

The 125 MHz $^{13}$C-NMR Spectrum of Compound (+)-**18** in $CDCl_3$.




**T**he Infrared Spectrum of Compound (+)-**18**.

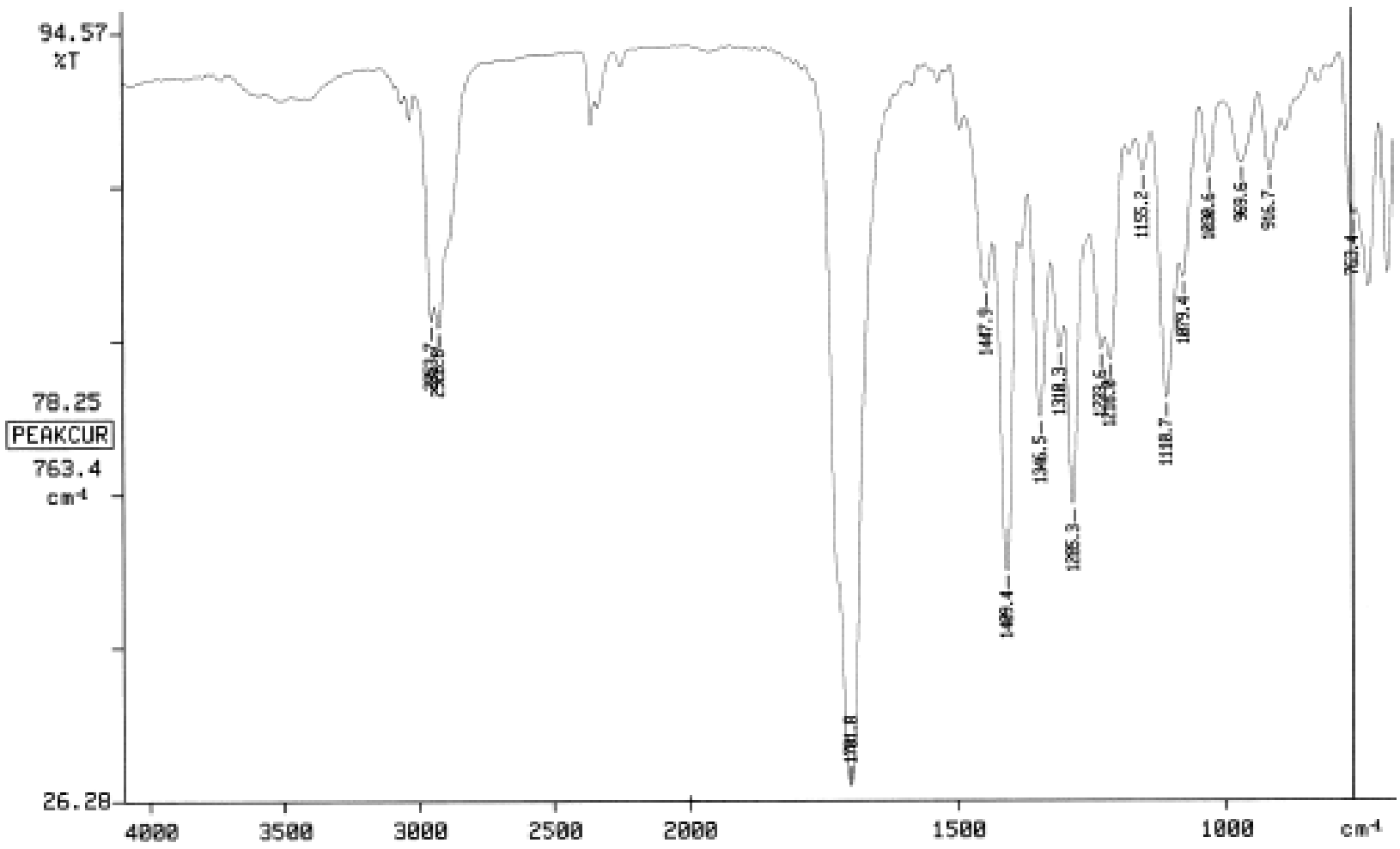



The 500 MHz $^{1}$H-NMR Spectrum of Compound (–)-**20** in $CDCl_3$.

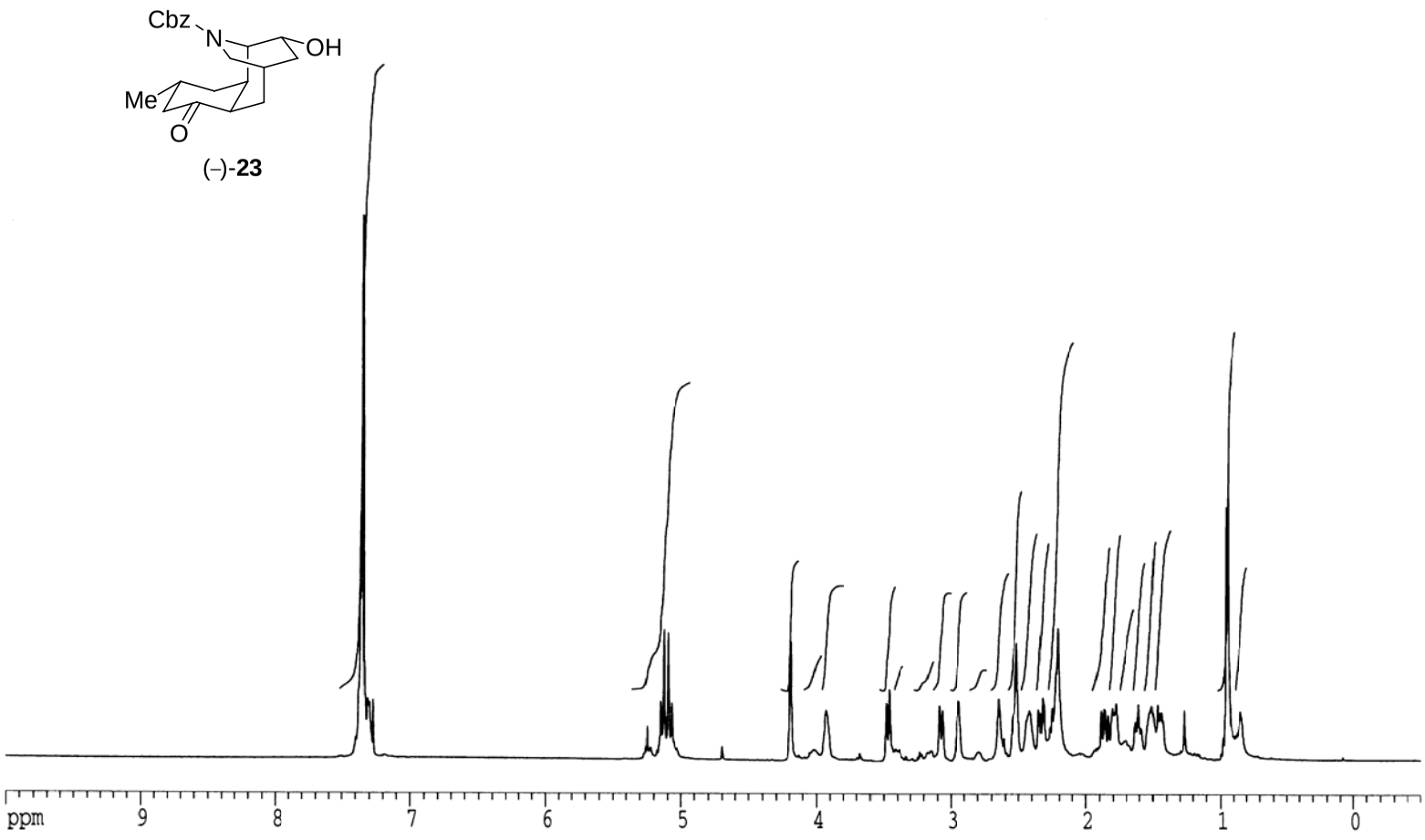



(–)-**20**

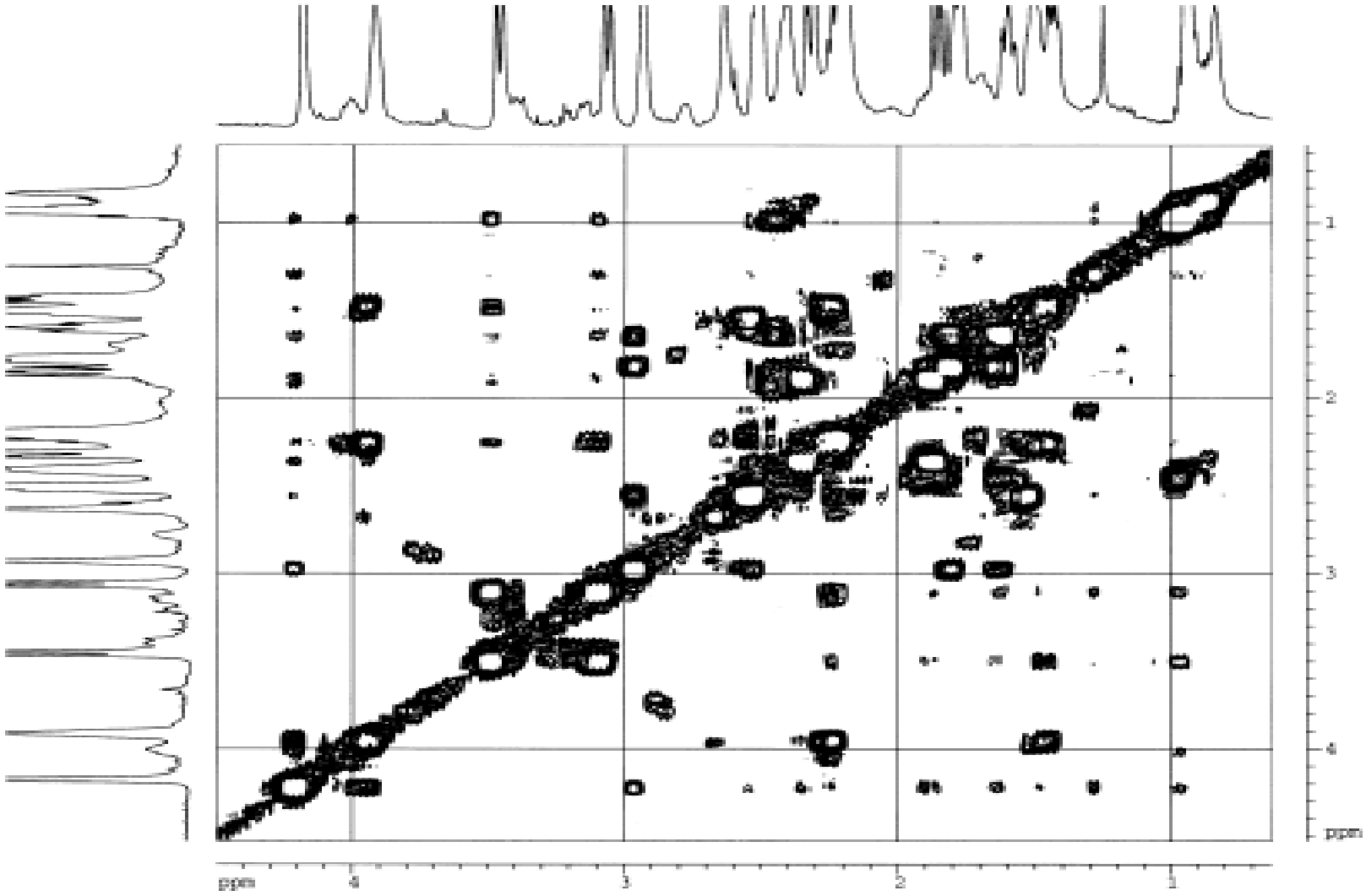
The 125 MHz $^{13}$C-NMR Spectrum of Compound (–)-**20** in $CDCl_3$.



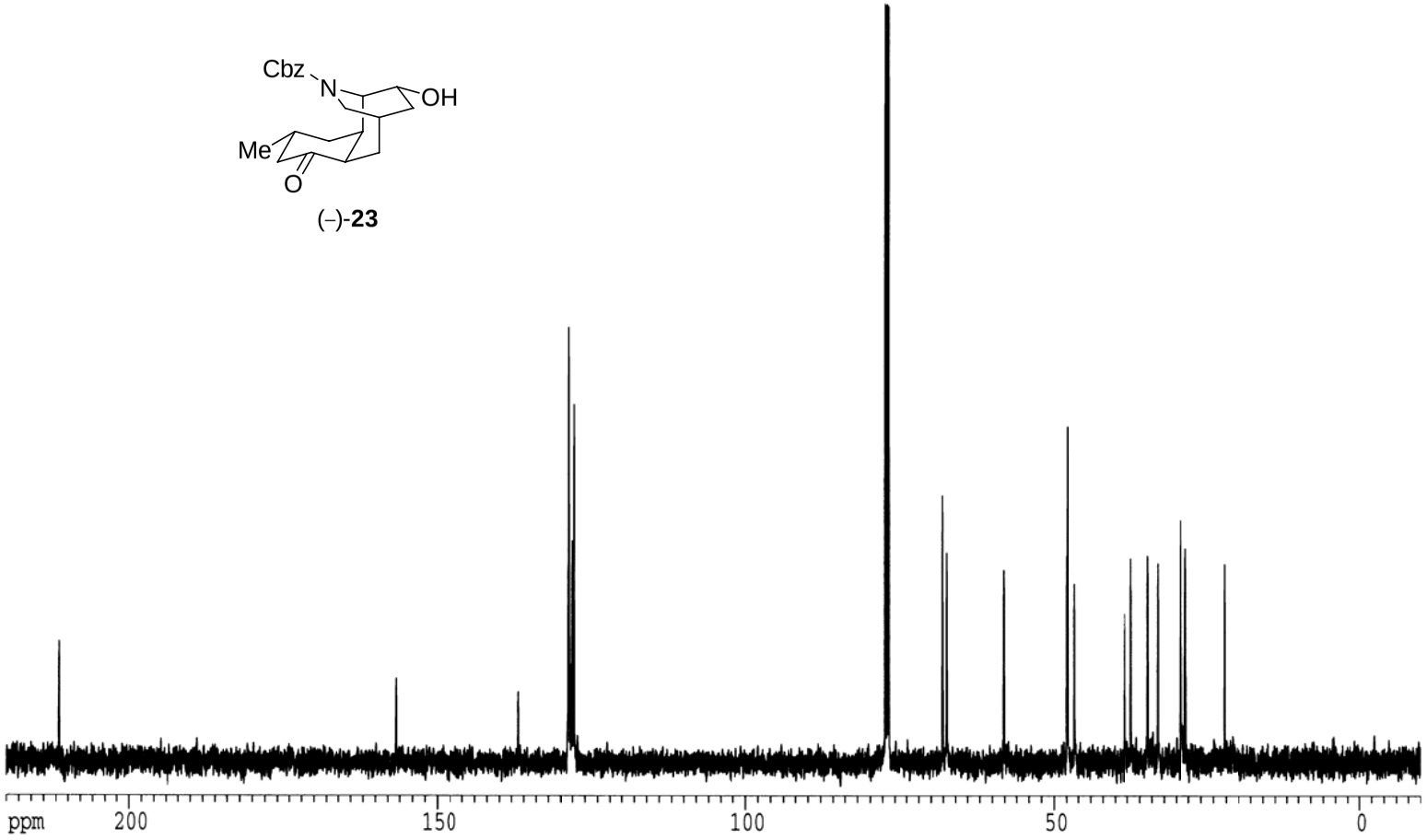

The Infrared Spectrum of Compound (−)-**20**.




The 500 MHz $^{1}$H-NMR Spectrum of Compound (–)-**23** in $CDCl_3$.

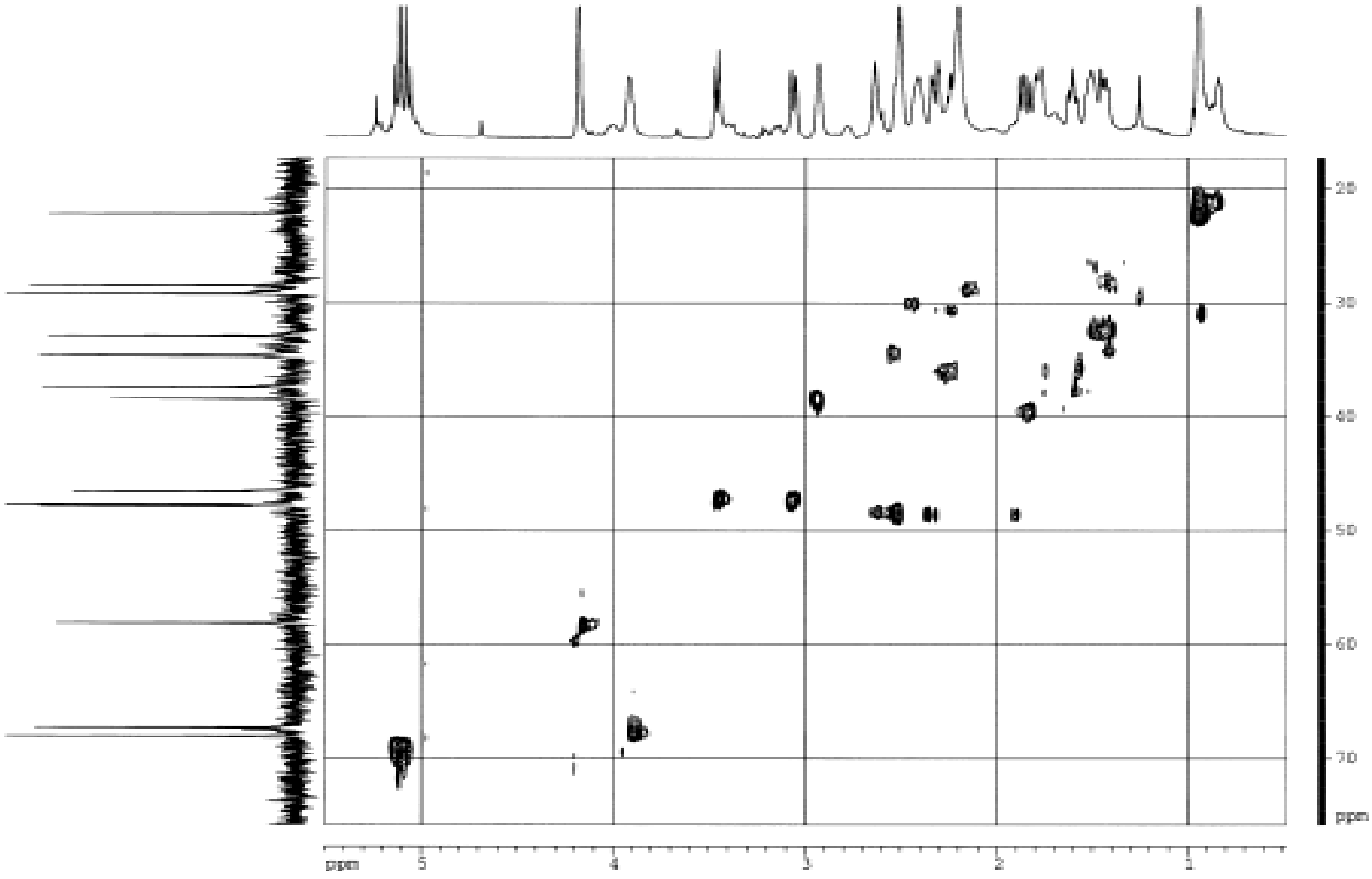



The 500 MHz $^{1}H$-$^{1}H$ COSY Spectrum of Compound (–)-**23** in $CDCl_3$.

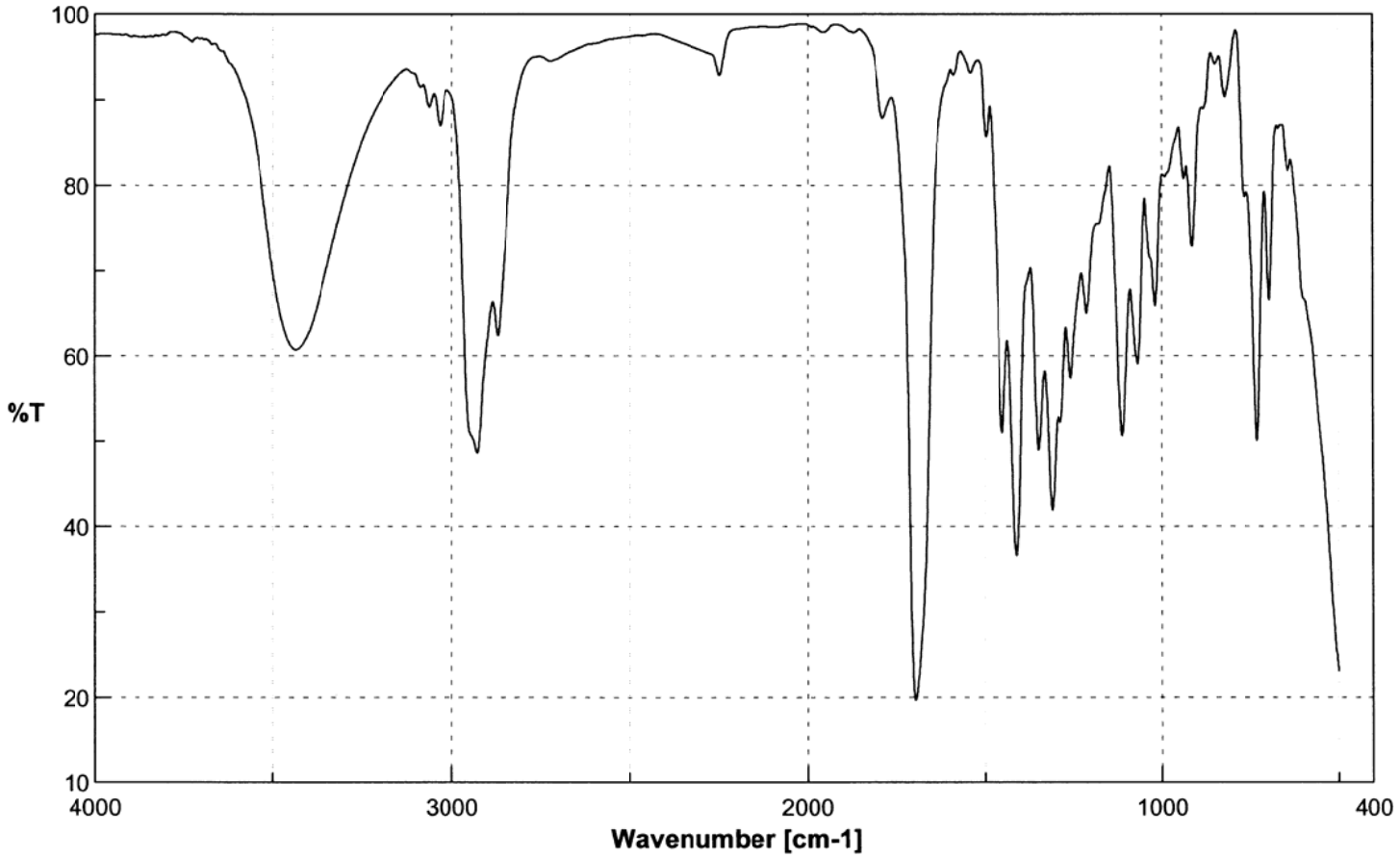



(–)-**23**

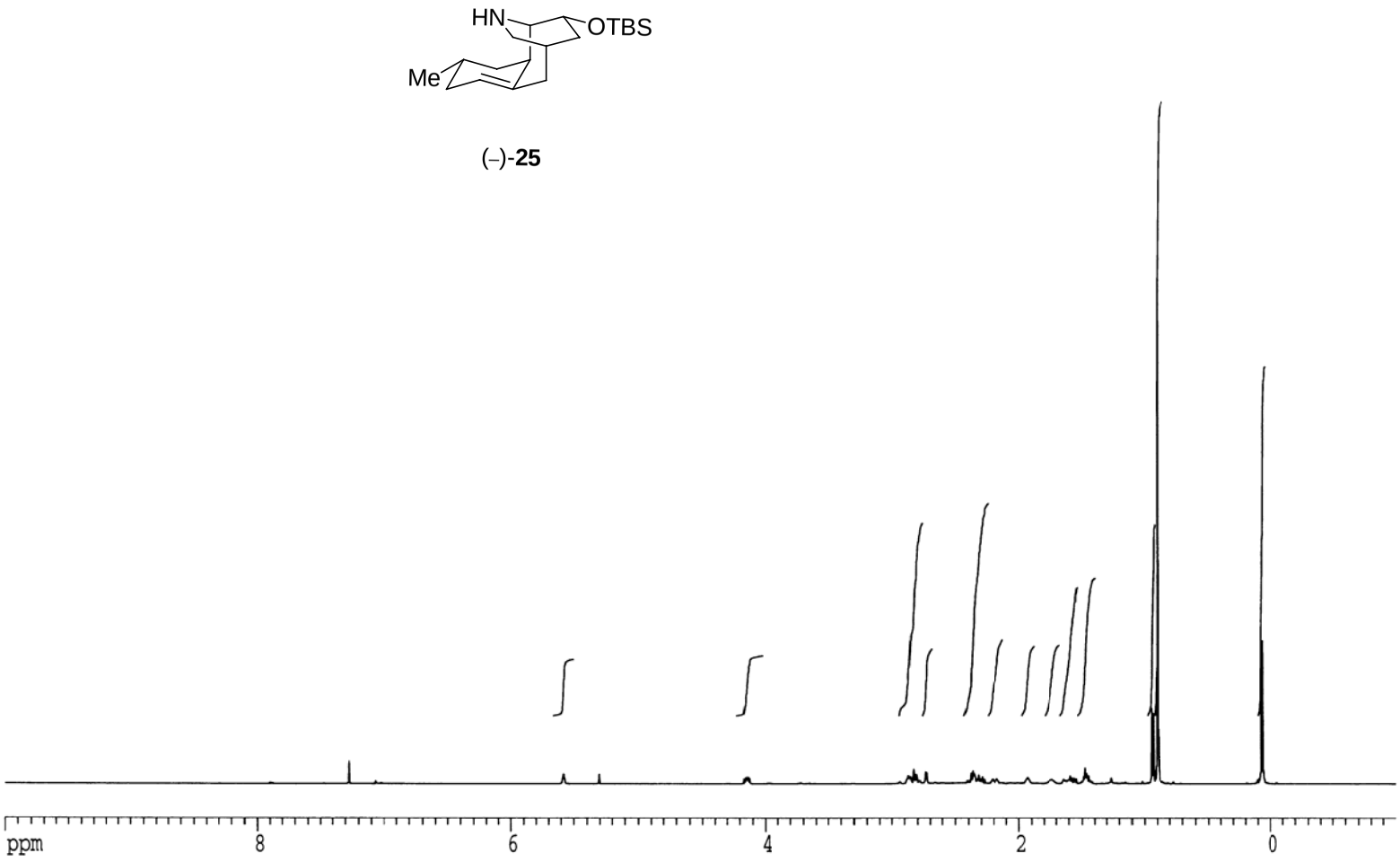
The 125 MHz $^{13}$C-NMR Spectrum of Compound (–)-**23** in $CDCl_3$.




The 500 MHz $^{1}H$-$^{13}C$ HMQC Spectrum of Compound (–)-**23** in $CDCl_3$.

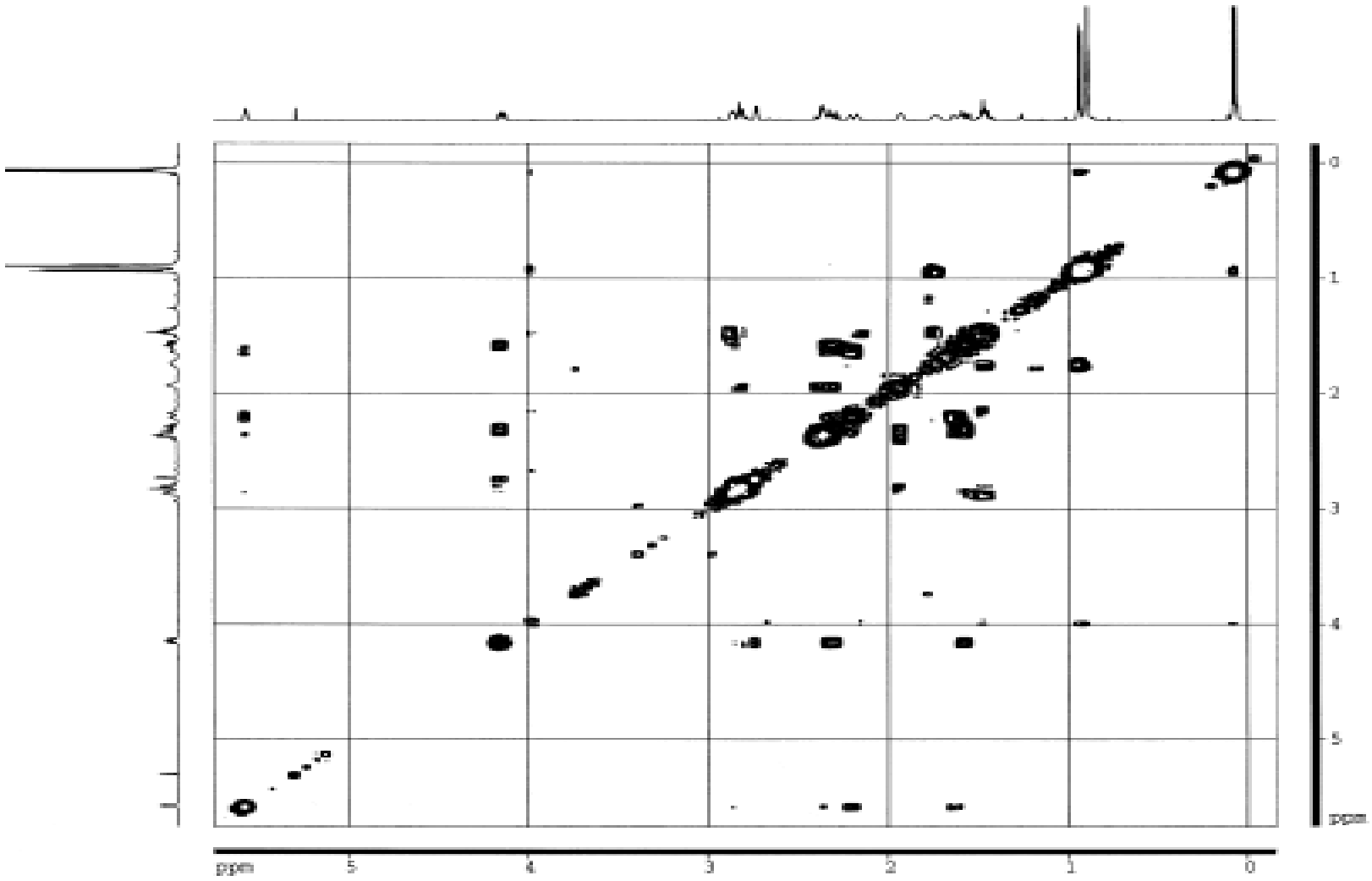



The Infrared Spectrum of Compound (–)-**23**.

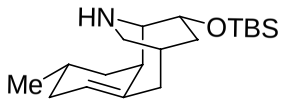



(–)-**25**

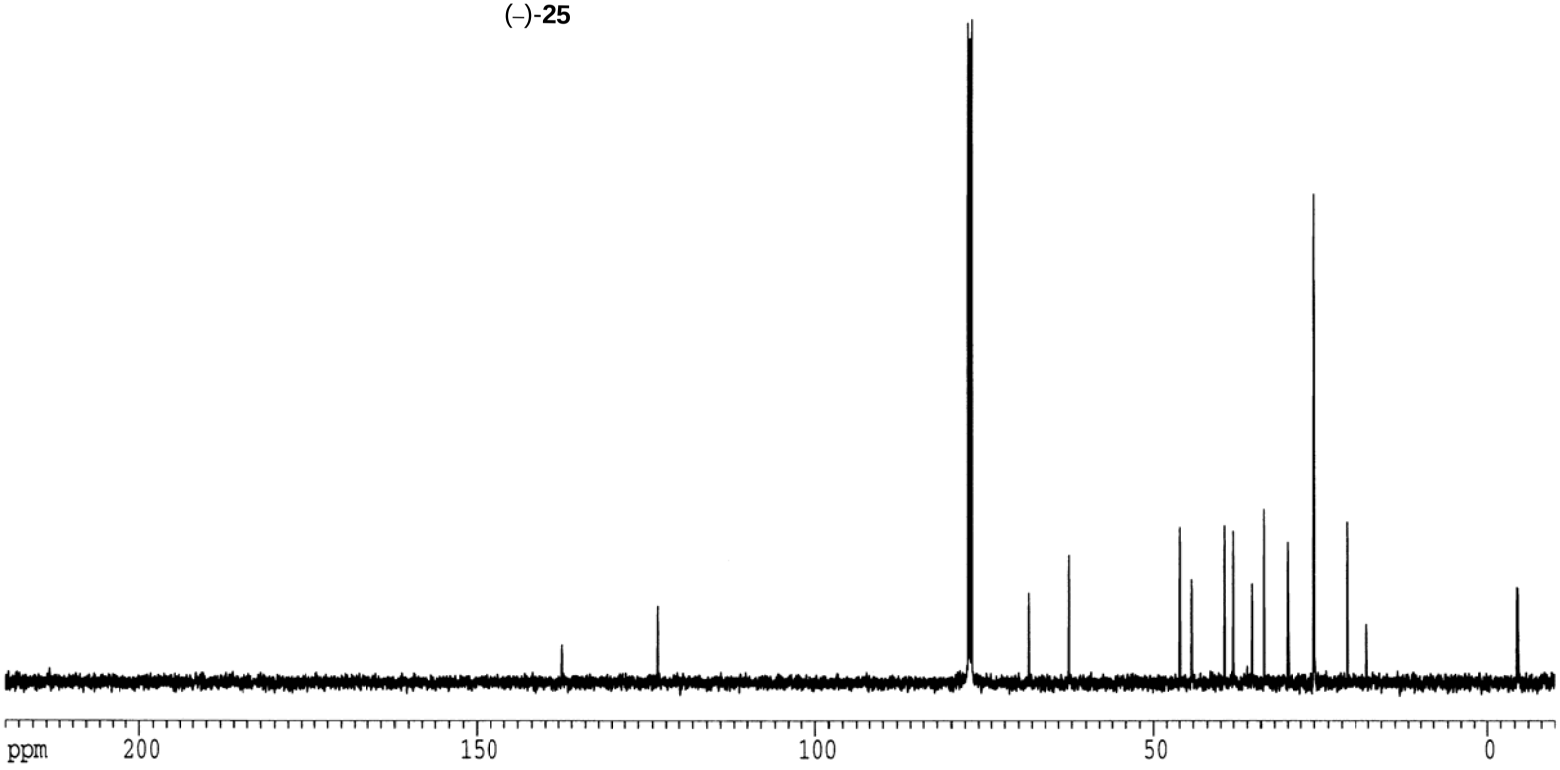
The 500 MHz $^{1}$H-NMR Spectrum of Compound (–)-**25** in $CDCl_3$.



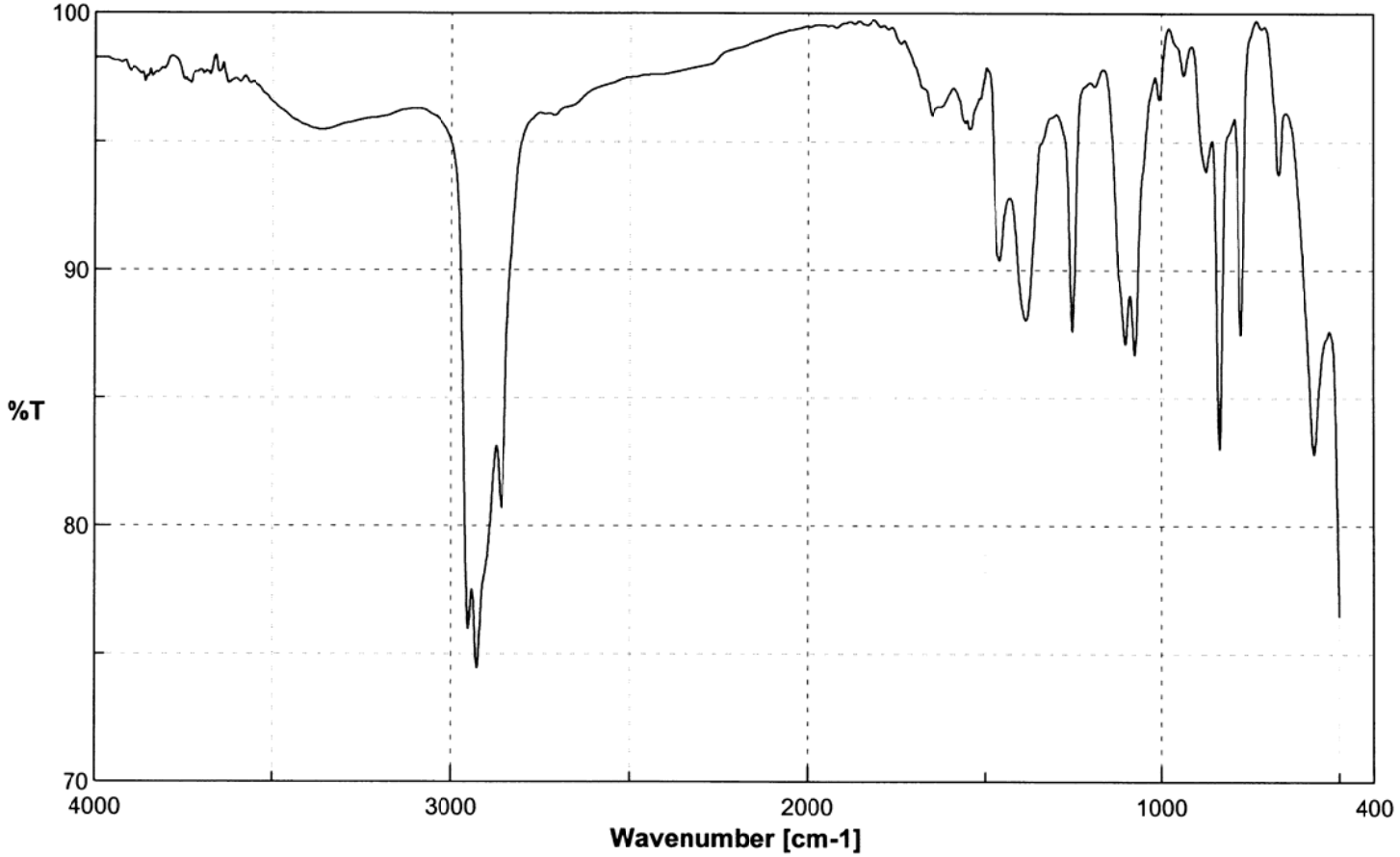

The 500 MHz $^{1}H$-$^{1}H$ COSY Spectrum of Compound (–)-**25** in $CDCl_3$.



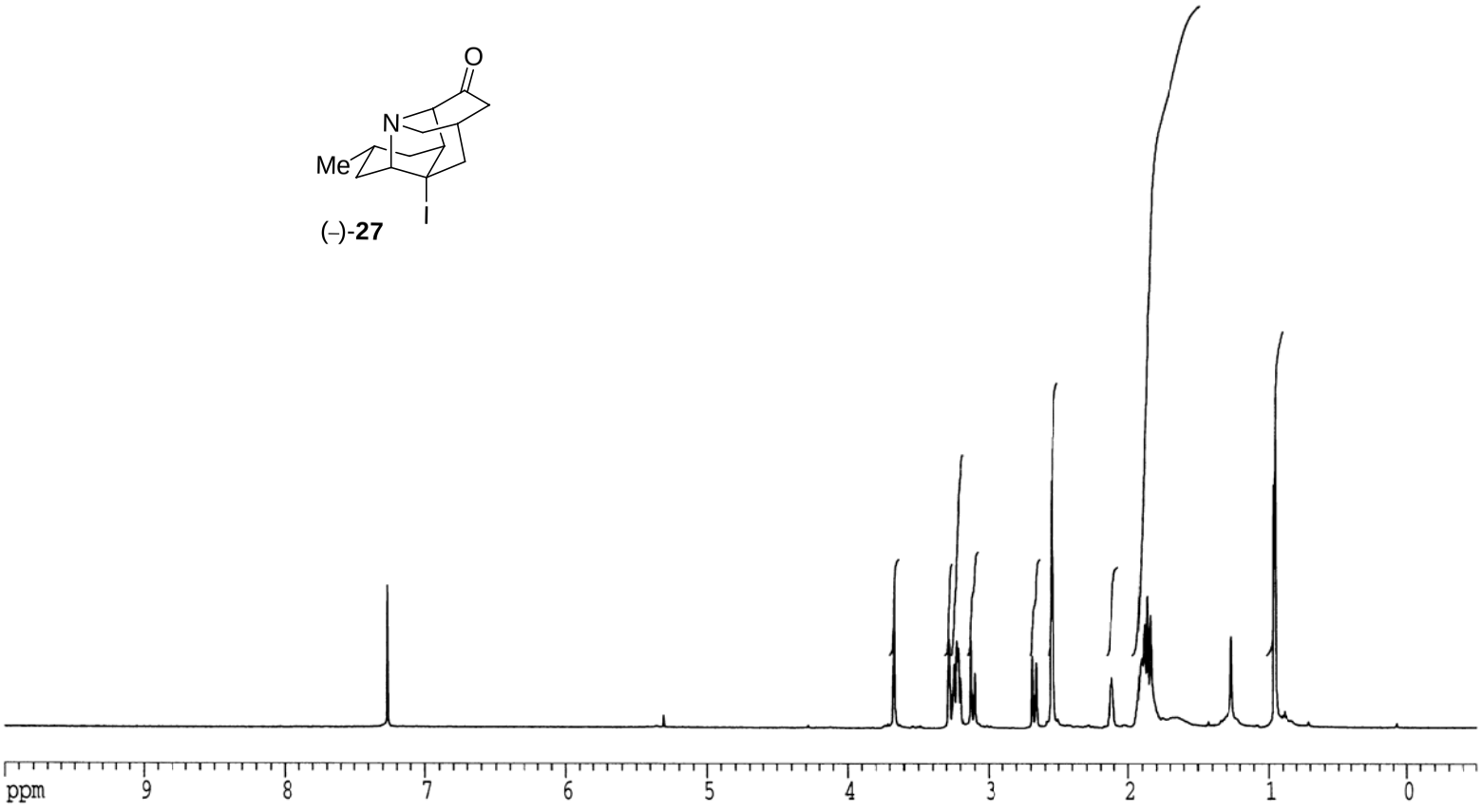

(–)-**25**



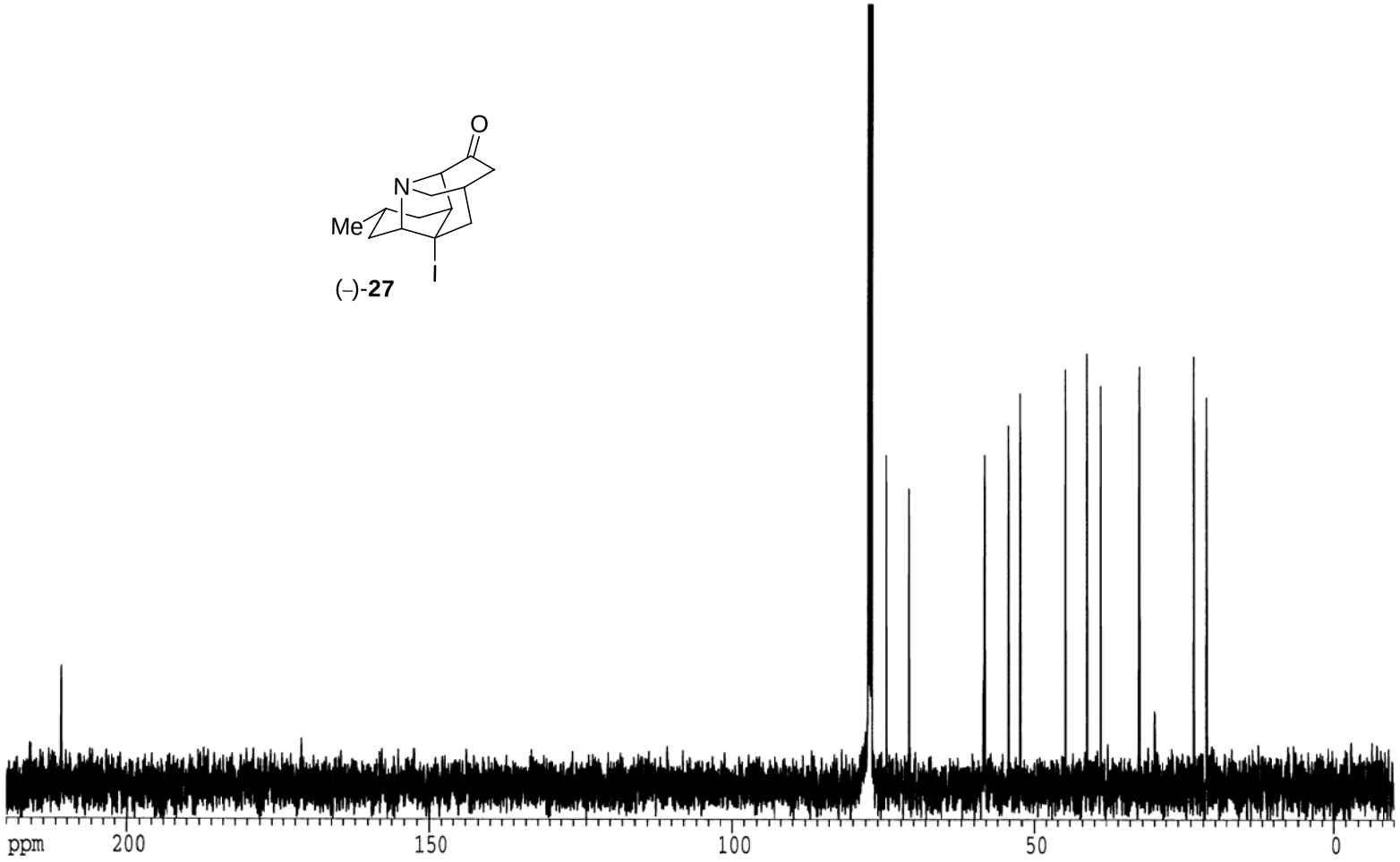

The 125 MHz $^{13}$C-NMR Spectrum of Compound (–)-**25** in $CDCl_3$.



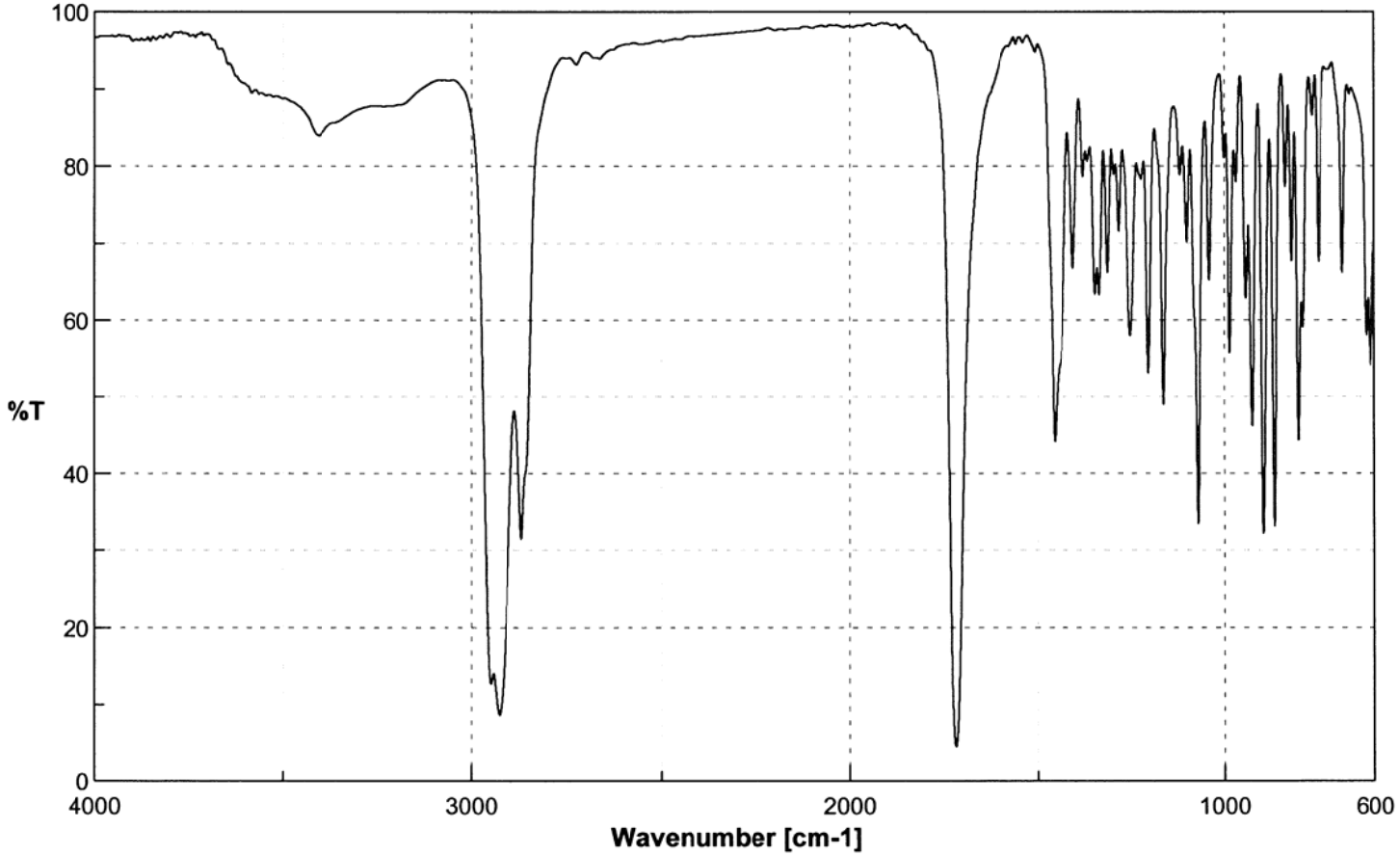

The Infrared Spectrum of Compound (–)-**25**.



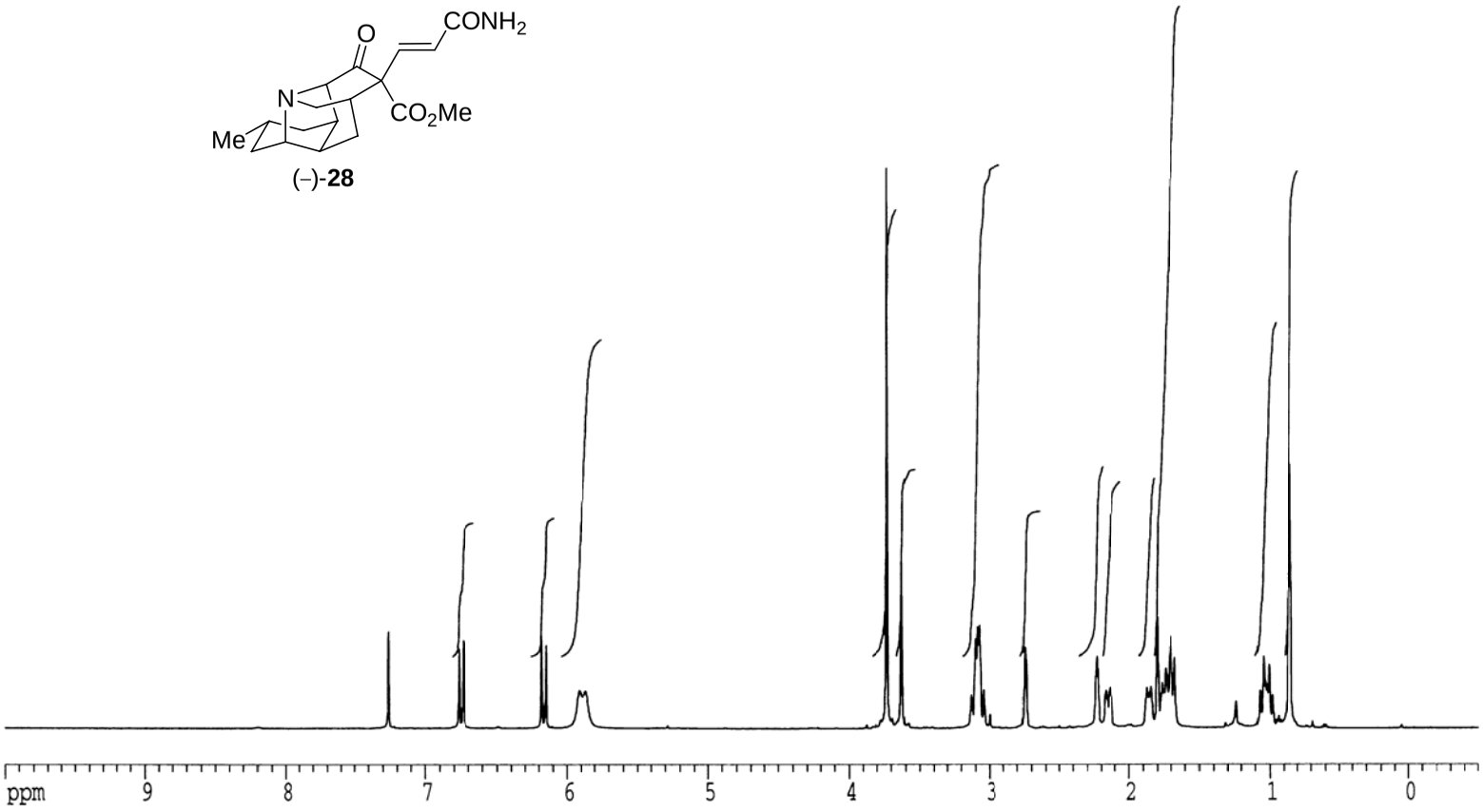

The 500 MHz $^{1}$H-NMR Spectrum of Compound (–)-**27** in $CDCl_3$.




The 125 MHz $^{13}$C-NMR Spectrum of Compound (–)-**27** in $CDCl_3$.

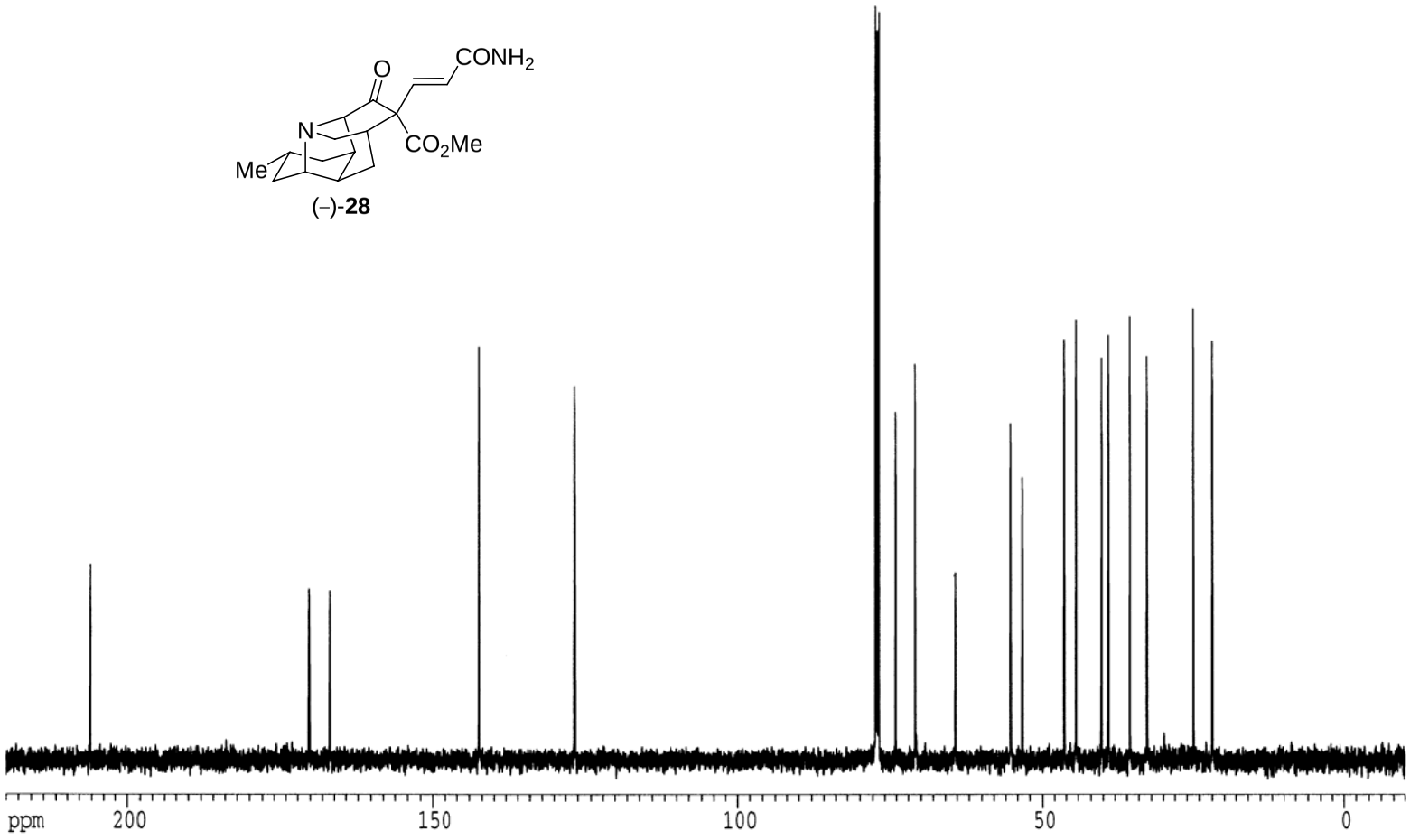



The Infrared Spectrum of Compound (–)-**27**.

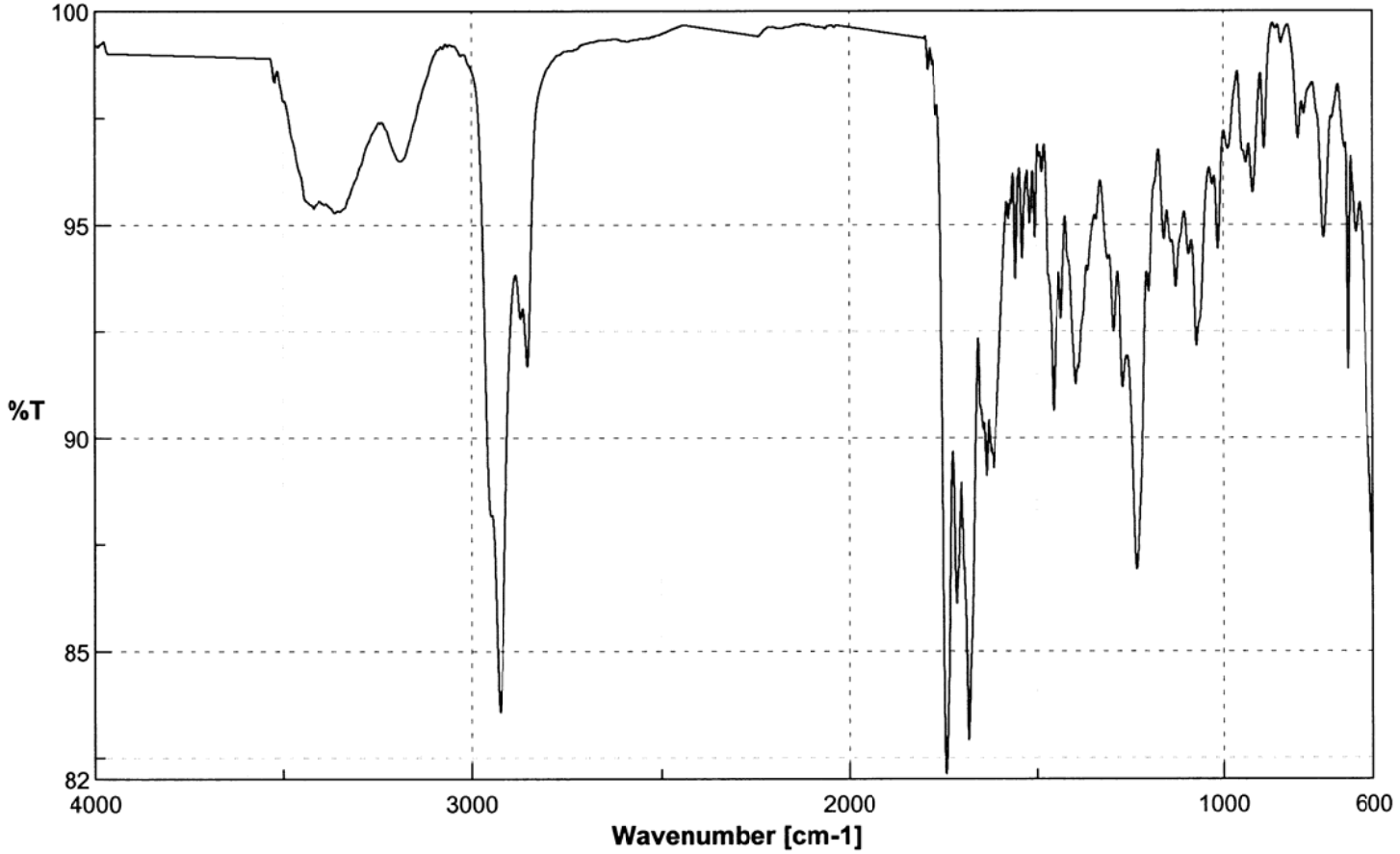



(–)-**28**

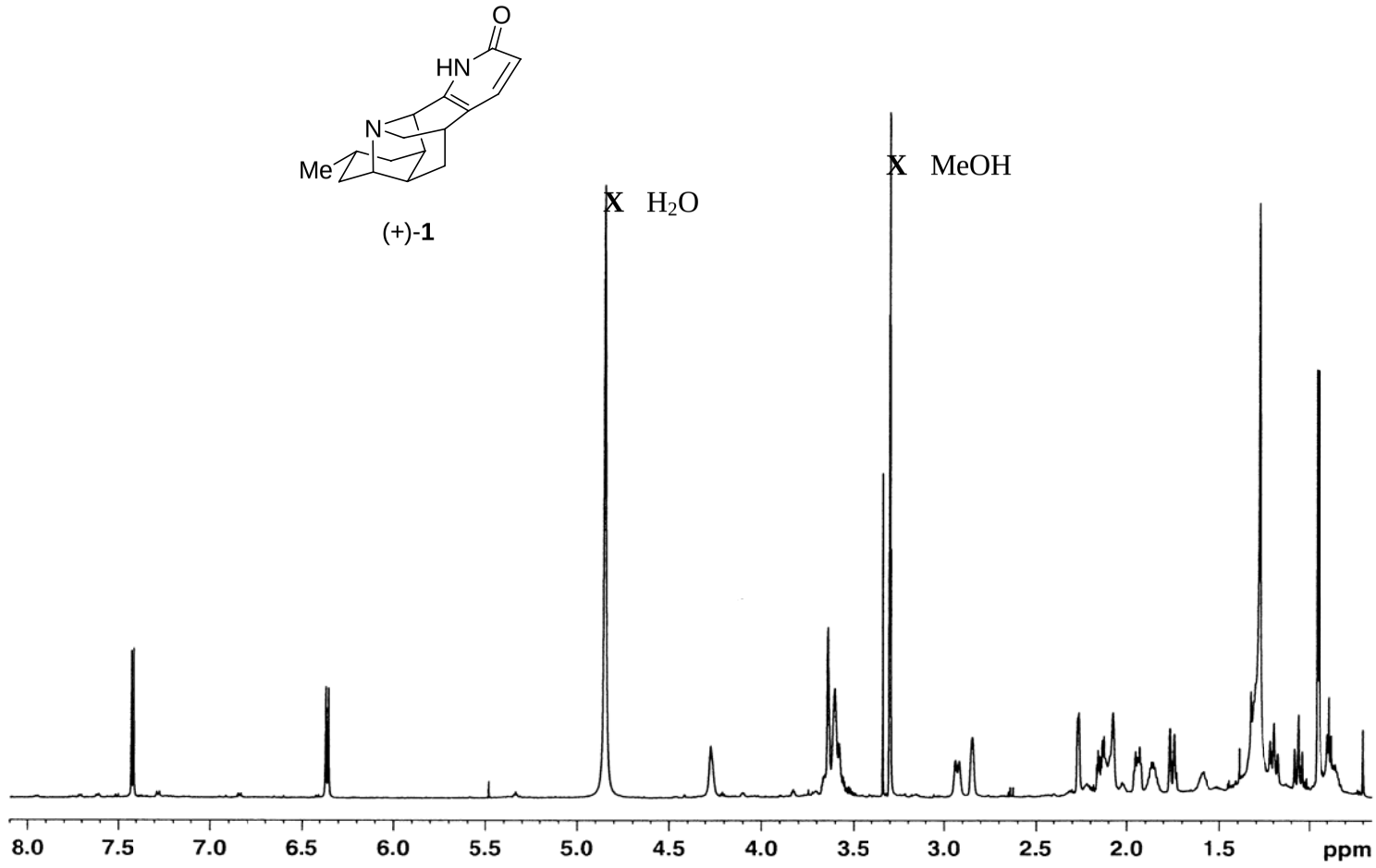
The 500 MHz $^{1}$H-NMR Spectrum of Compound (–)-**28** in $CDCl_3$.



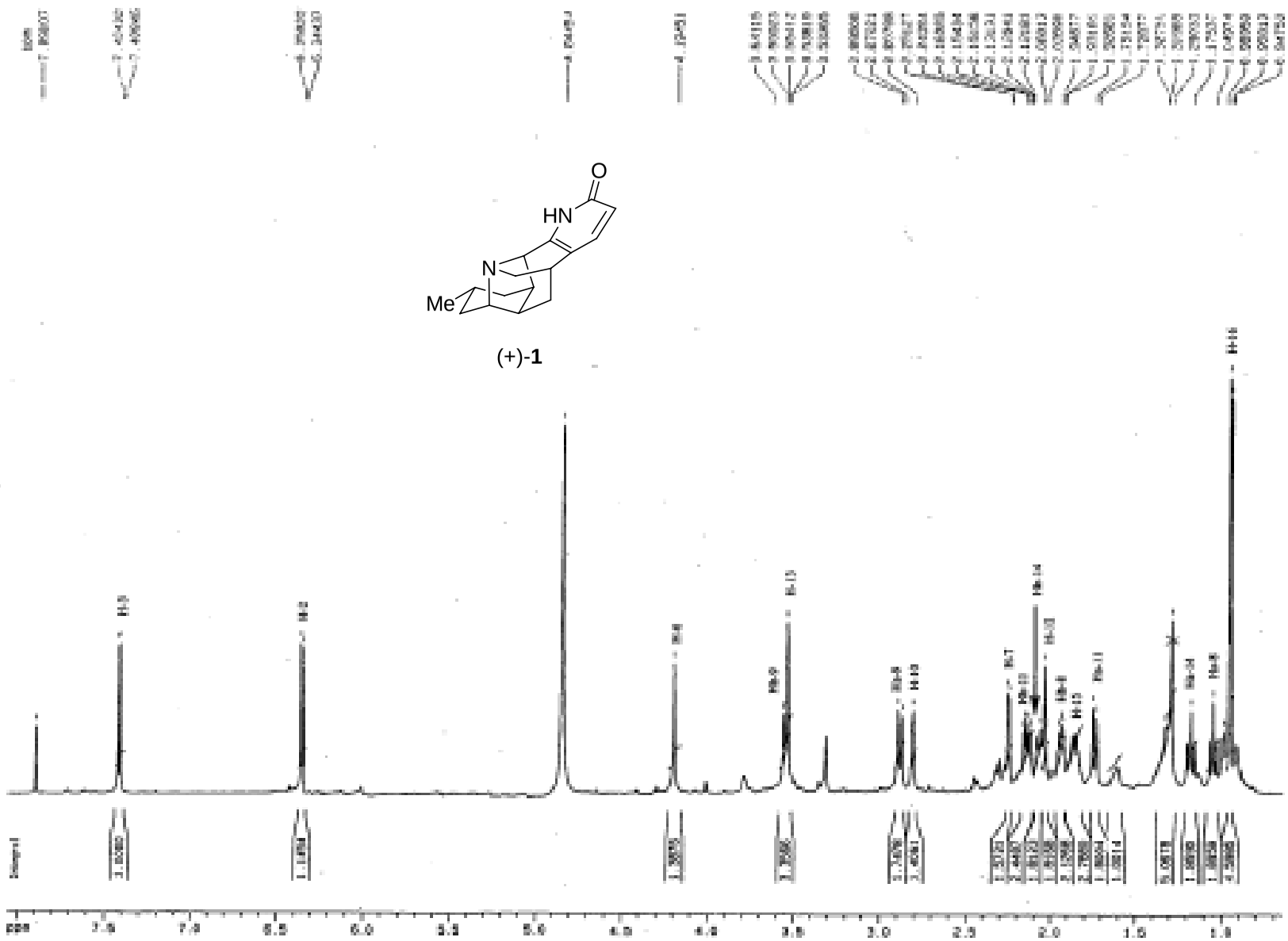

The 125 MHz $^{13}$C-NMR Spectrum of Compound (–)-**28** in $CDCl_3$.



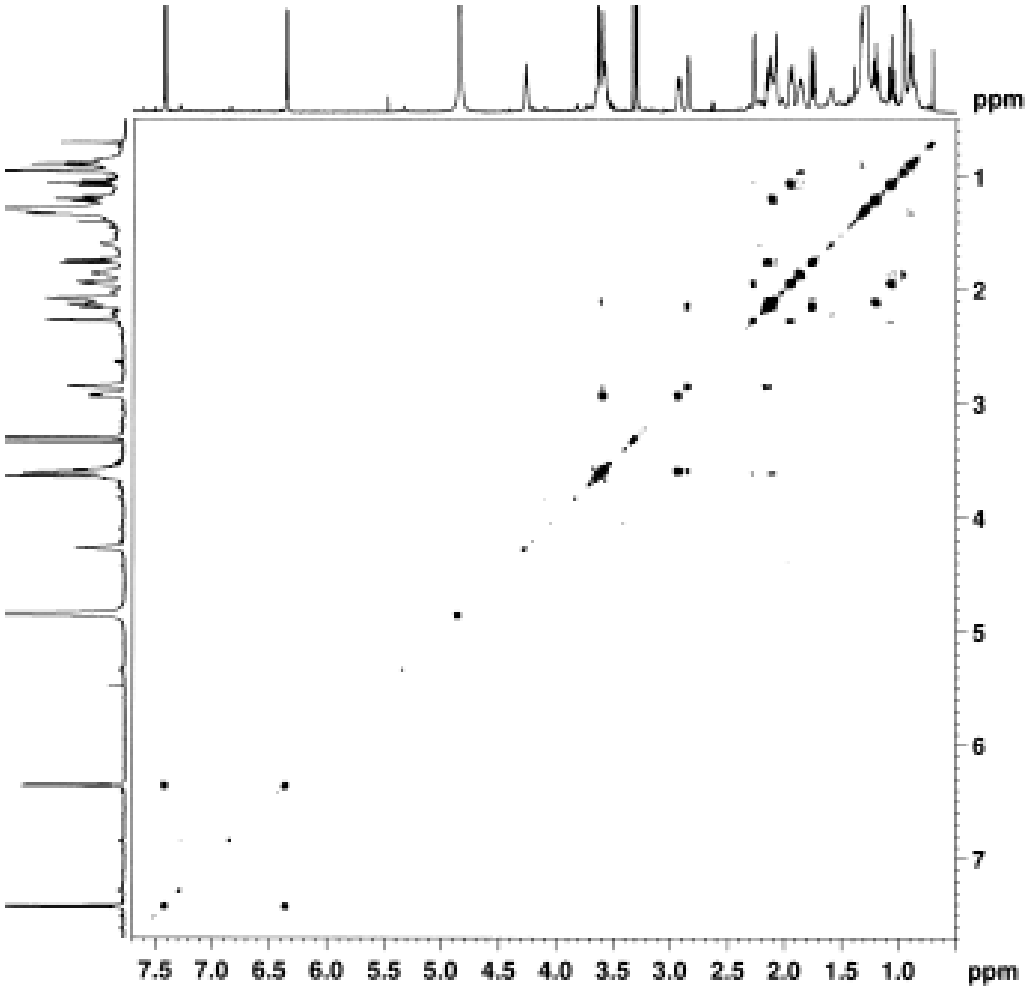

The Infrared Spectrum of Compound (–)-**28**.



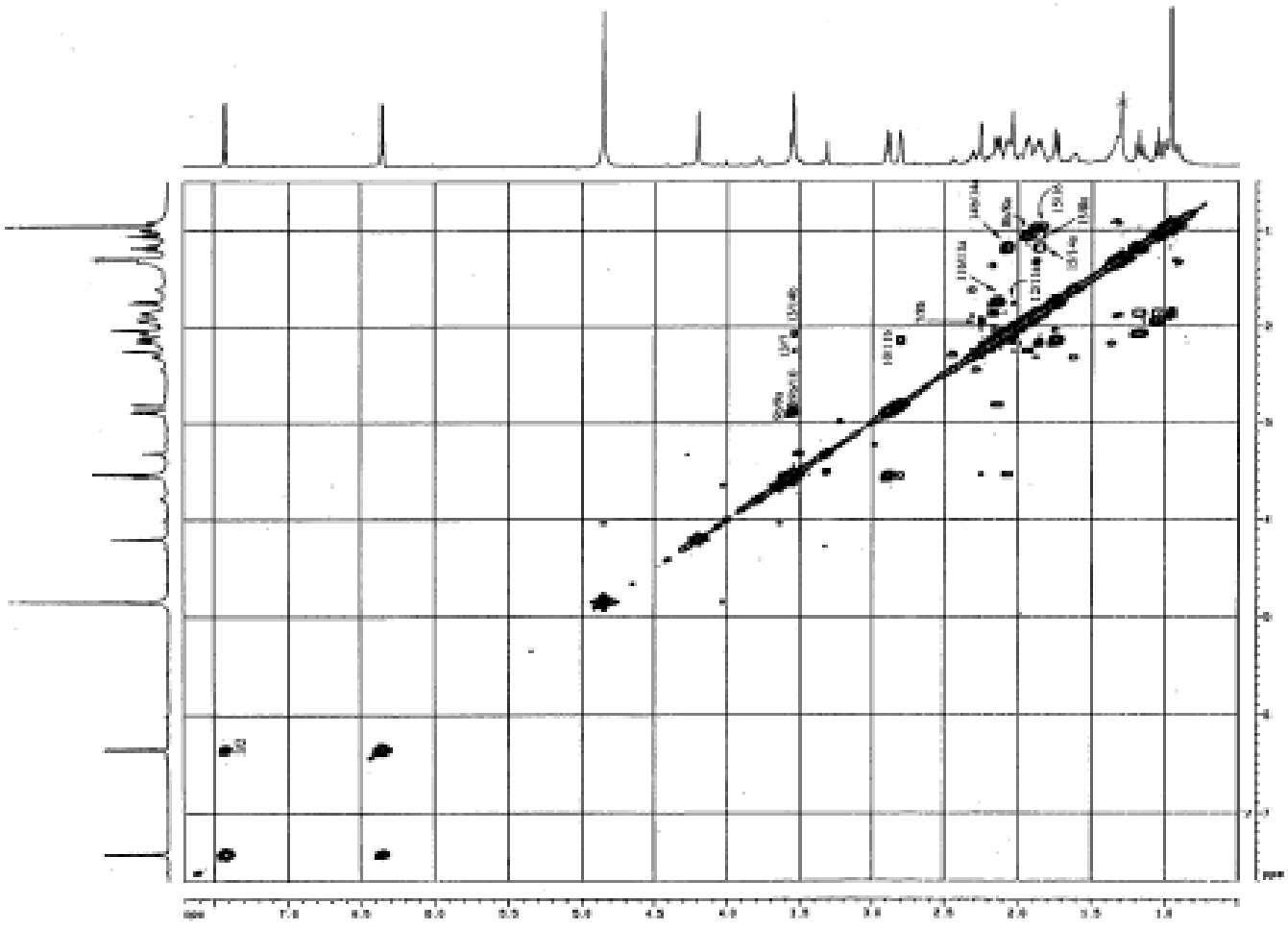

The 600 MHz $^{1}$H-NMR Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.



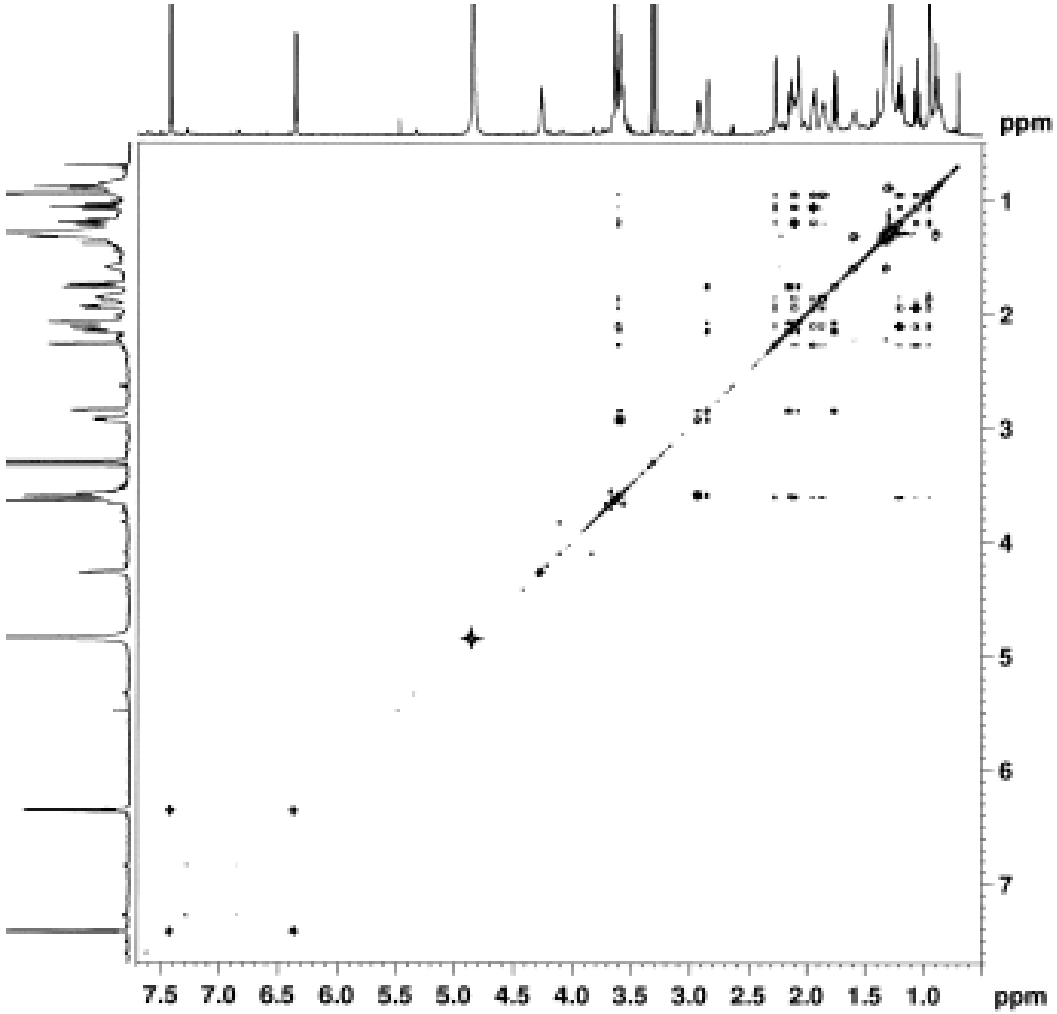

The 600 MHz $^{1}$H-NMR Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.



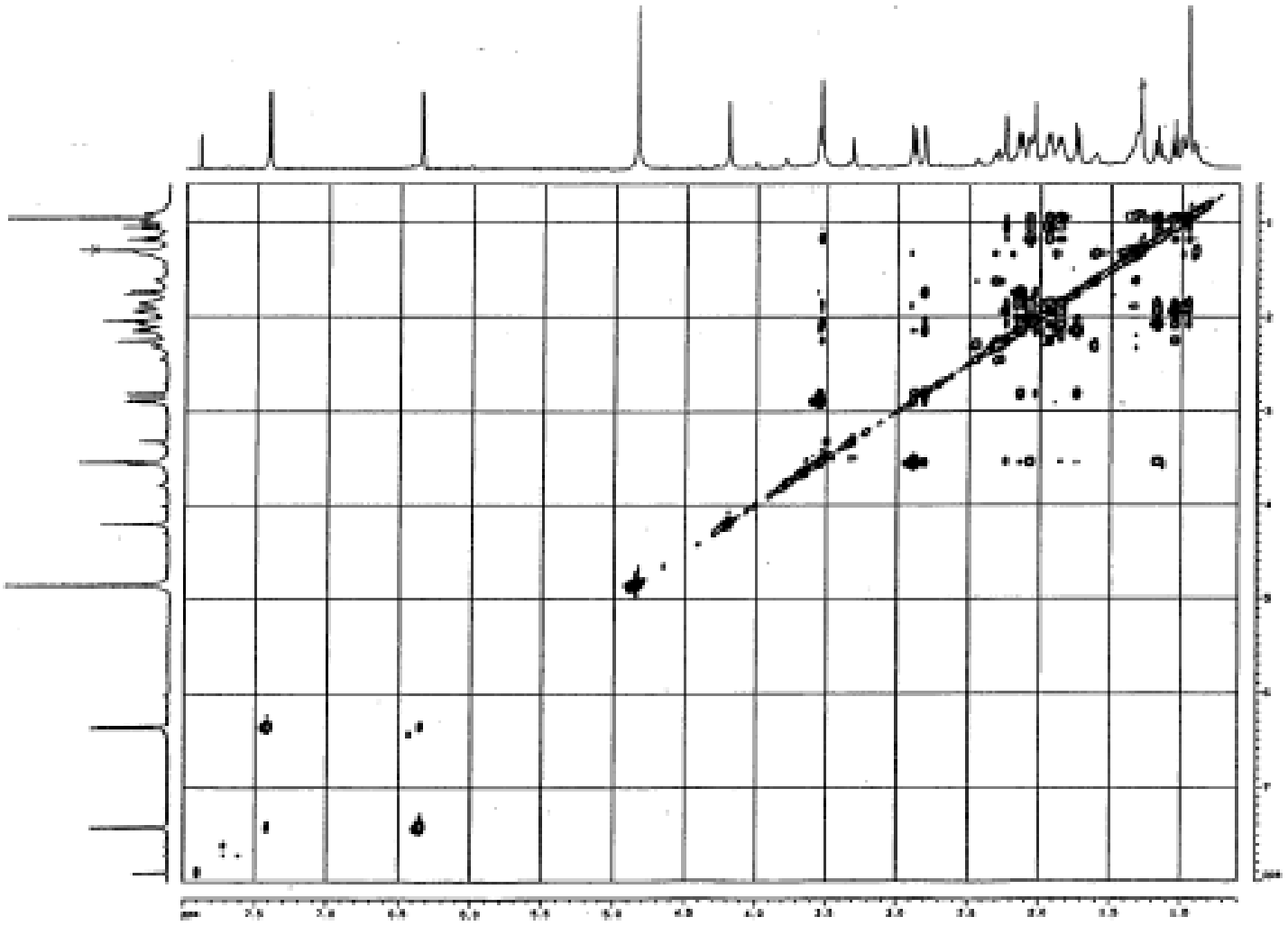

The 600 MHz $^{1}$H-$^{1}$H COSY Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.



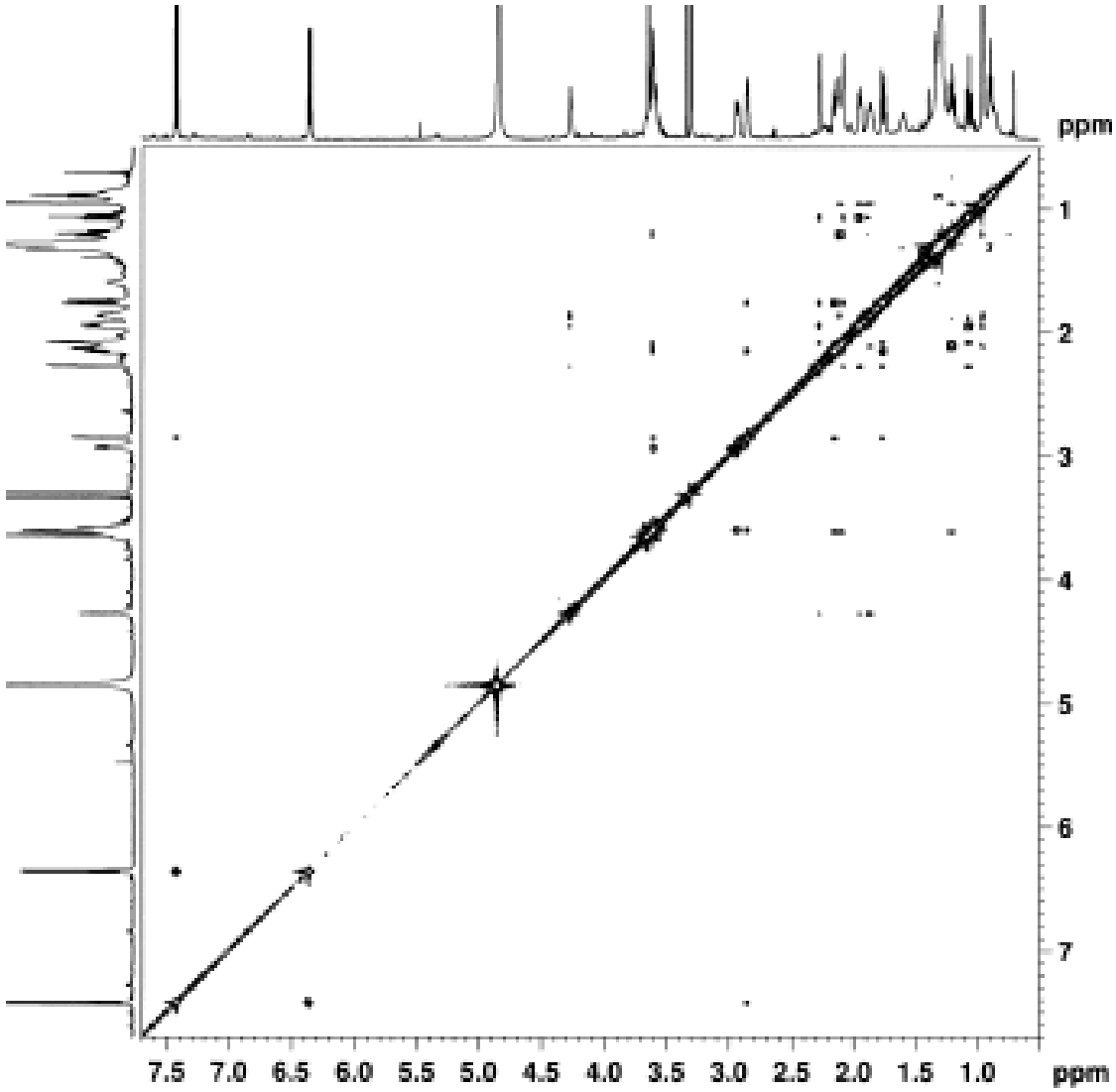
The 600 MHz $^{1}H$-$^{1}H$ COSY Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.



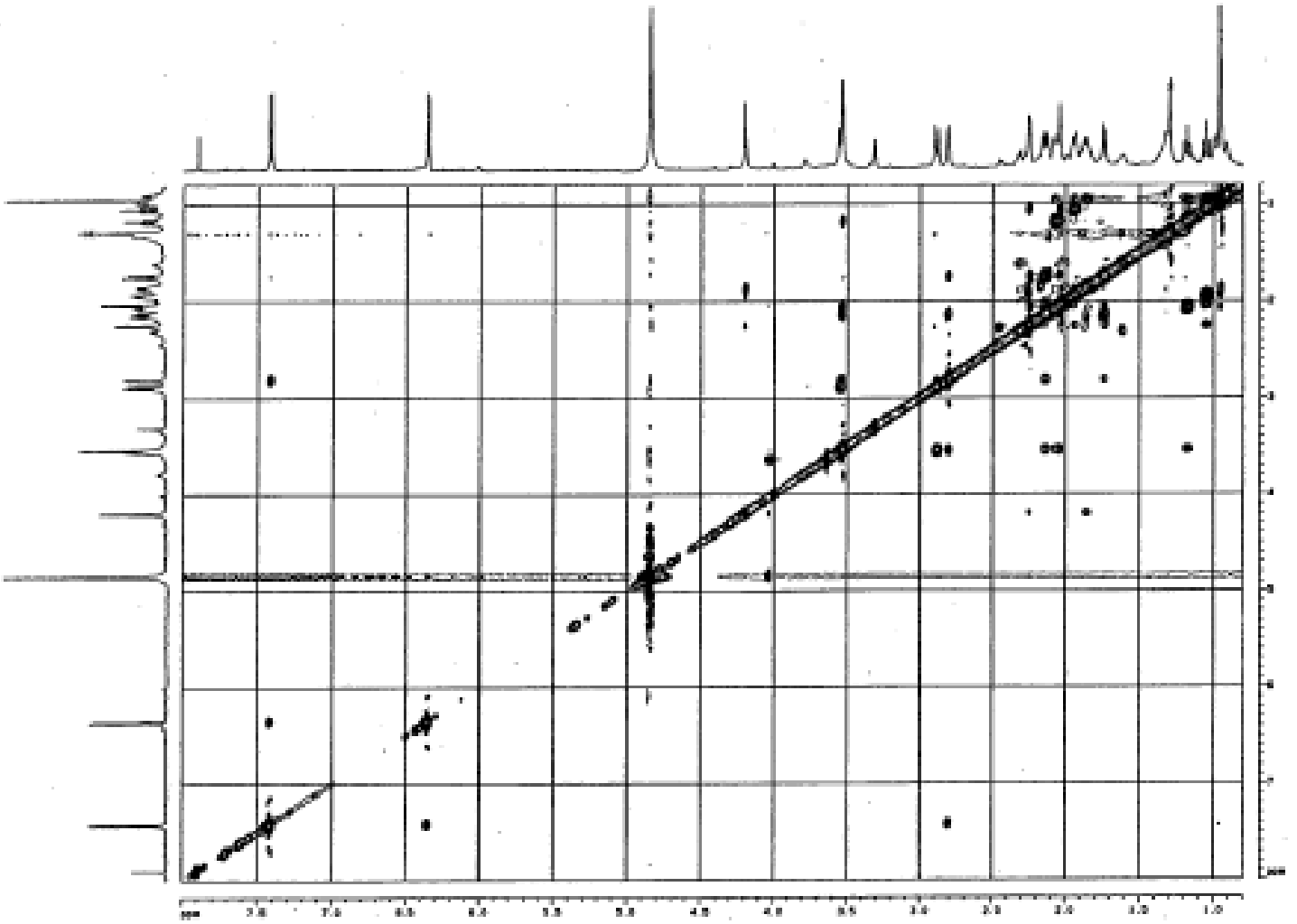

The 600 MHz $^{1}H$-$^{1}H$ TOCSY Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.



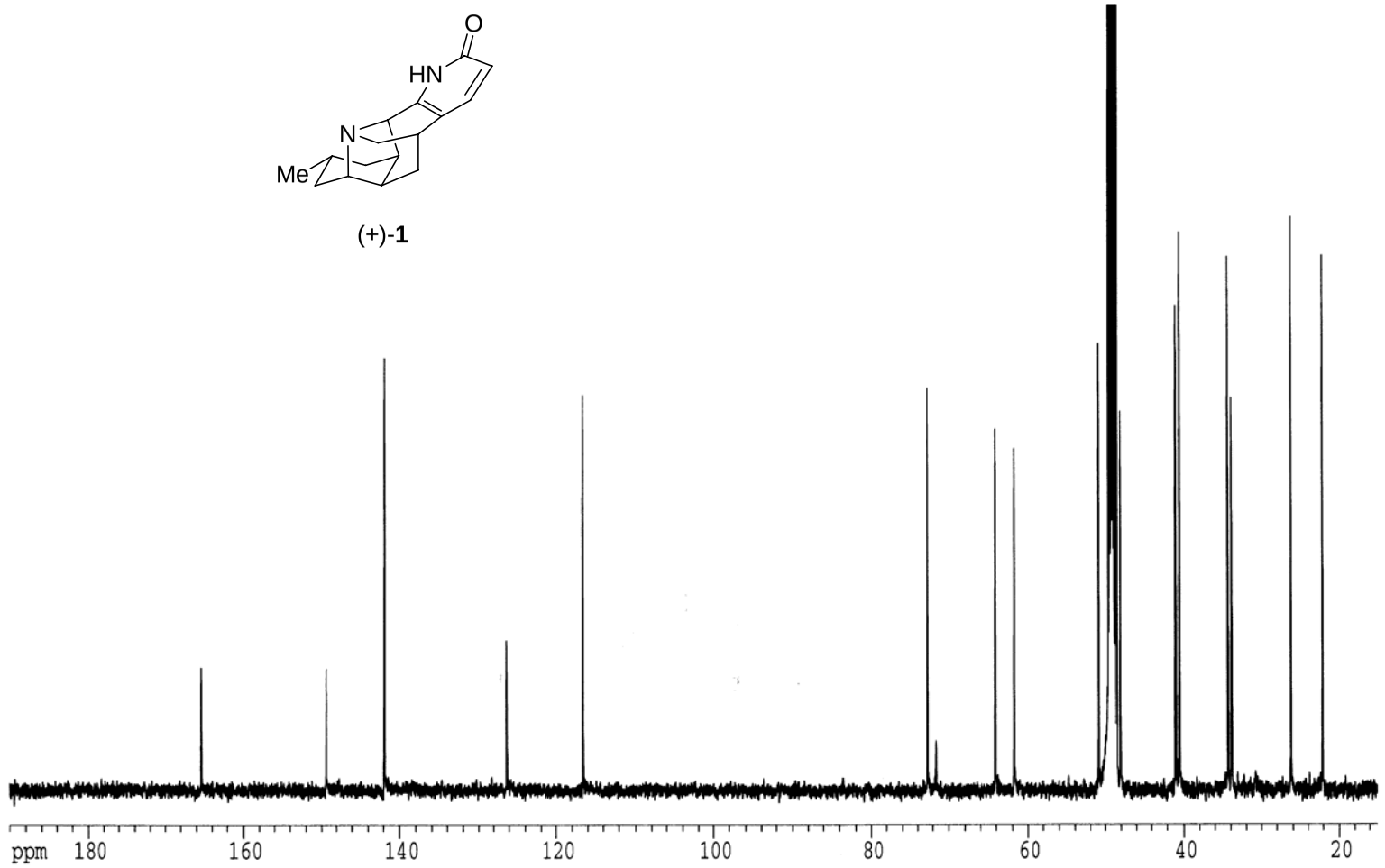
The 600 MHz $^{1}H$-$^{1}H$ TOCSY Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.




The 600 MHz NOESY Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.

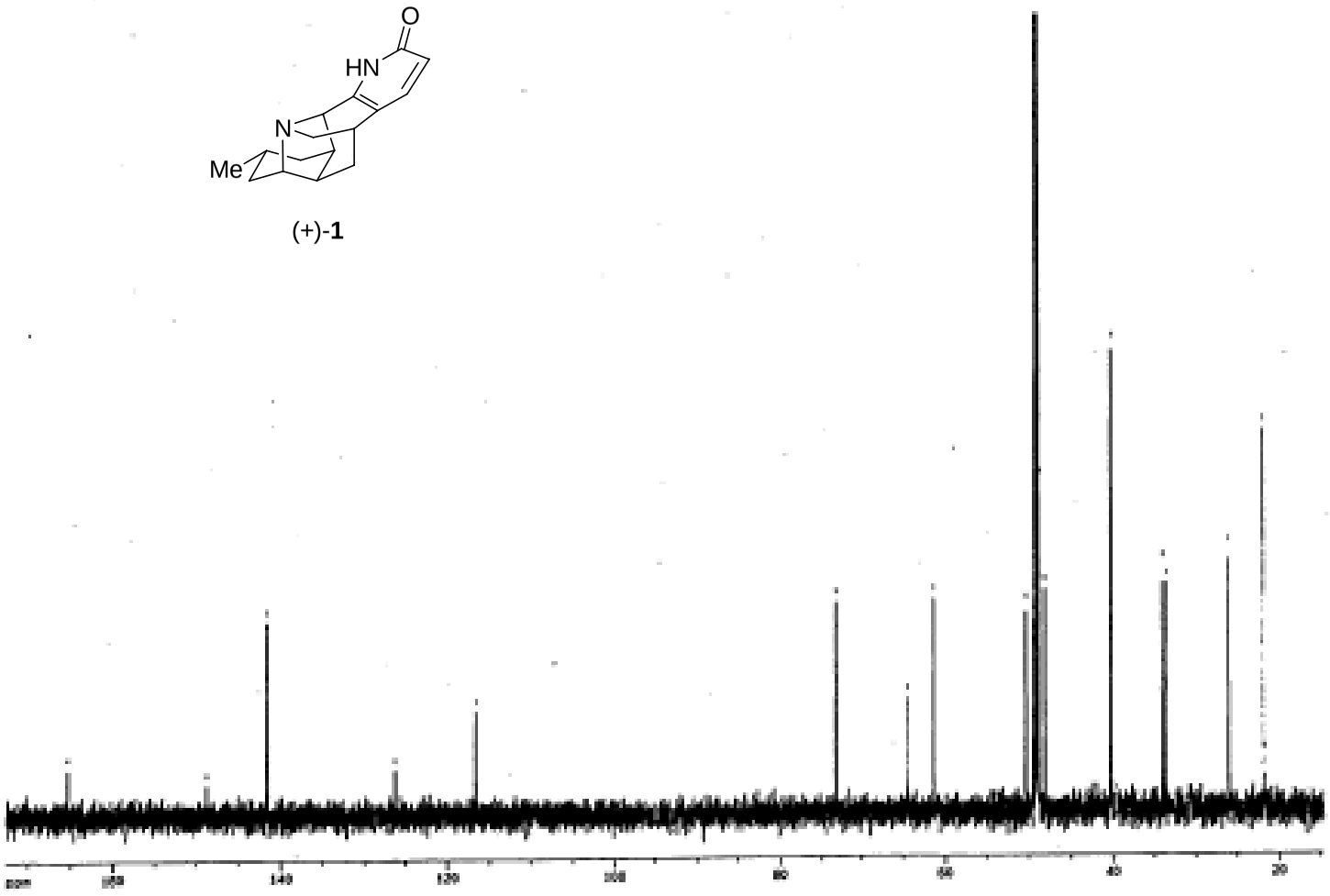


The 600 MHz NOESY Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.



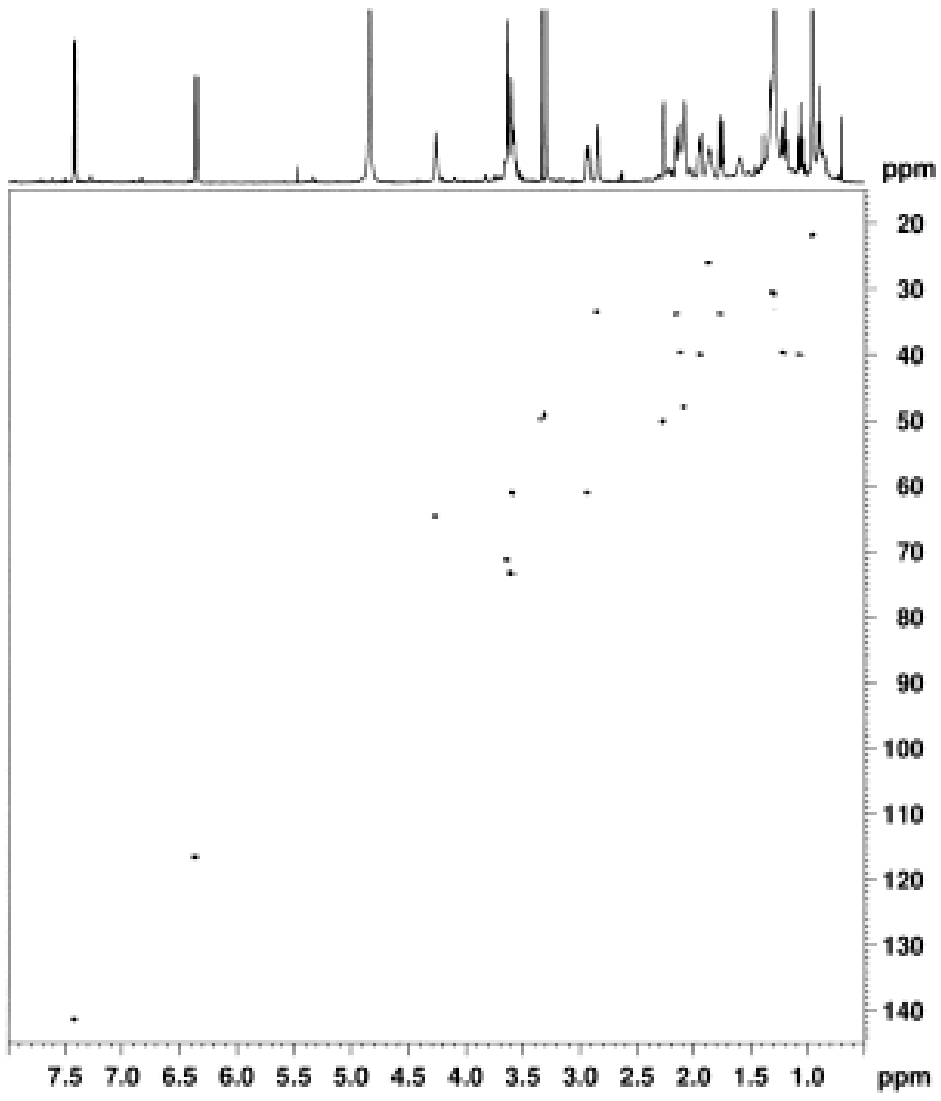

(+)-**1**

The 125 MHz $^{13}$C-NMR Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.

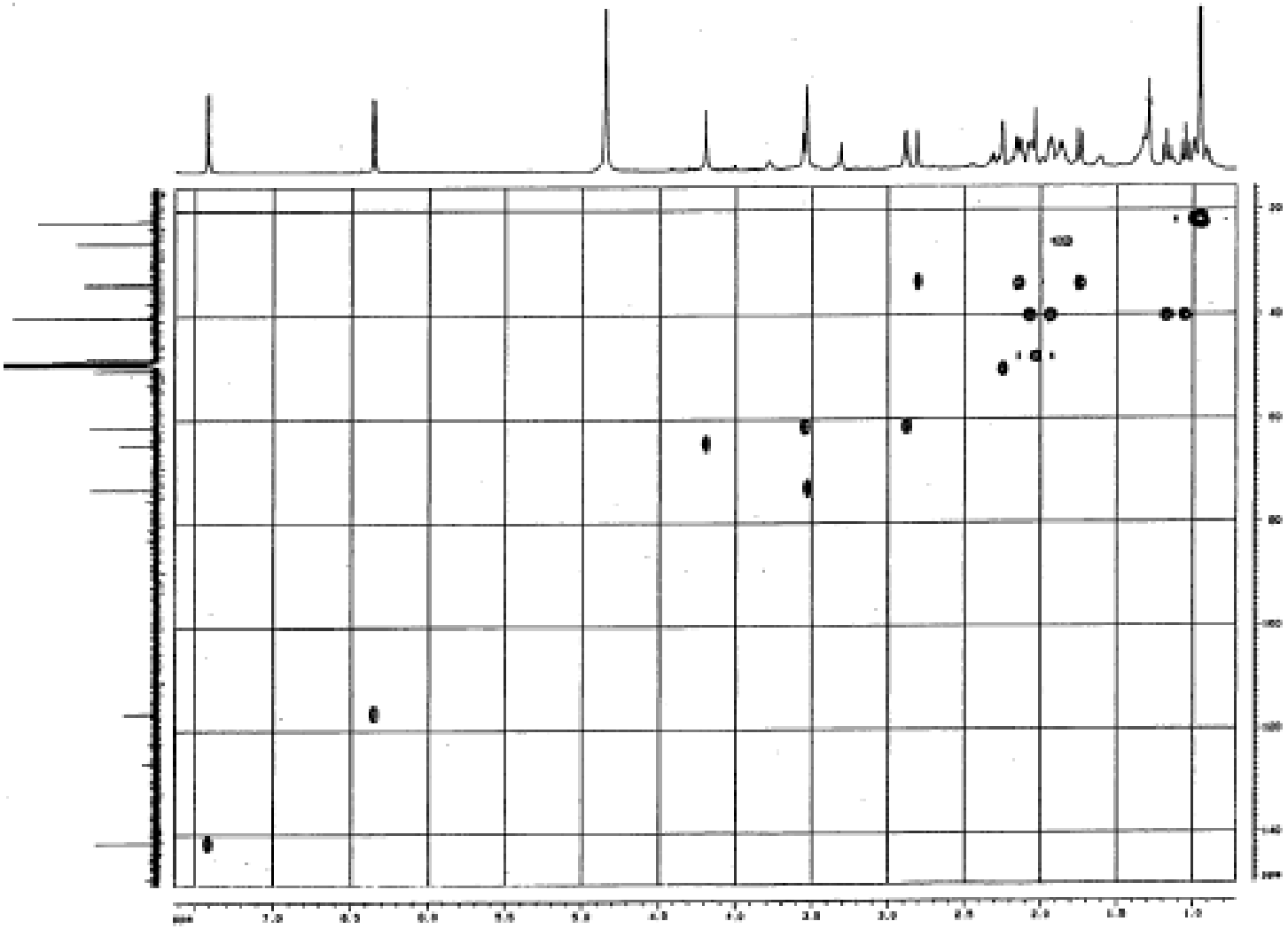



(+)-**1**

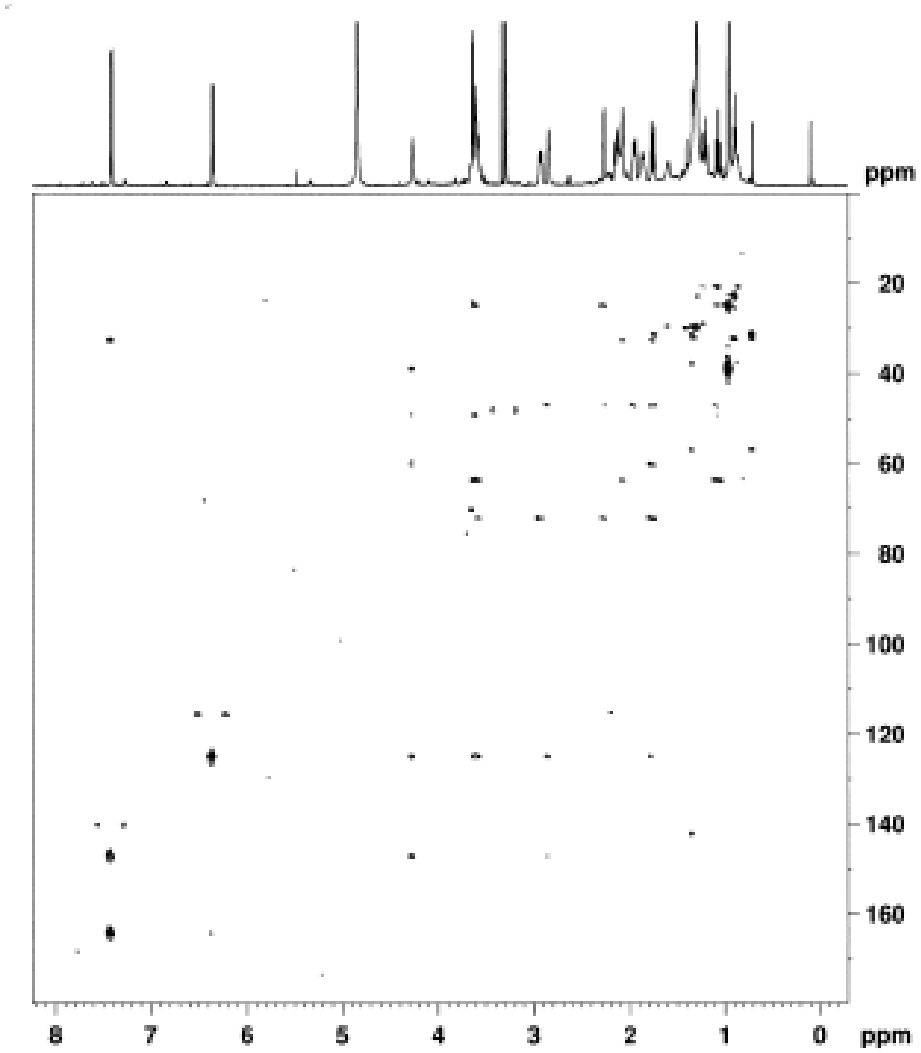
The 150 MHz $^{13}$C-NMR Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.



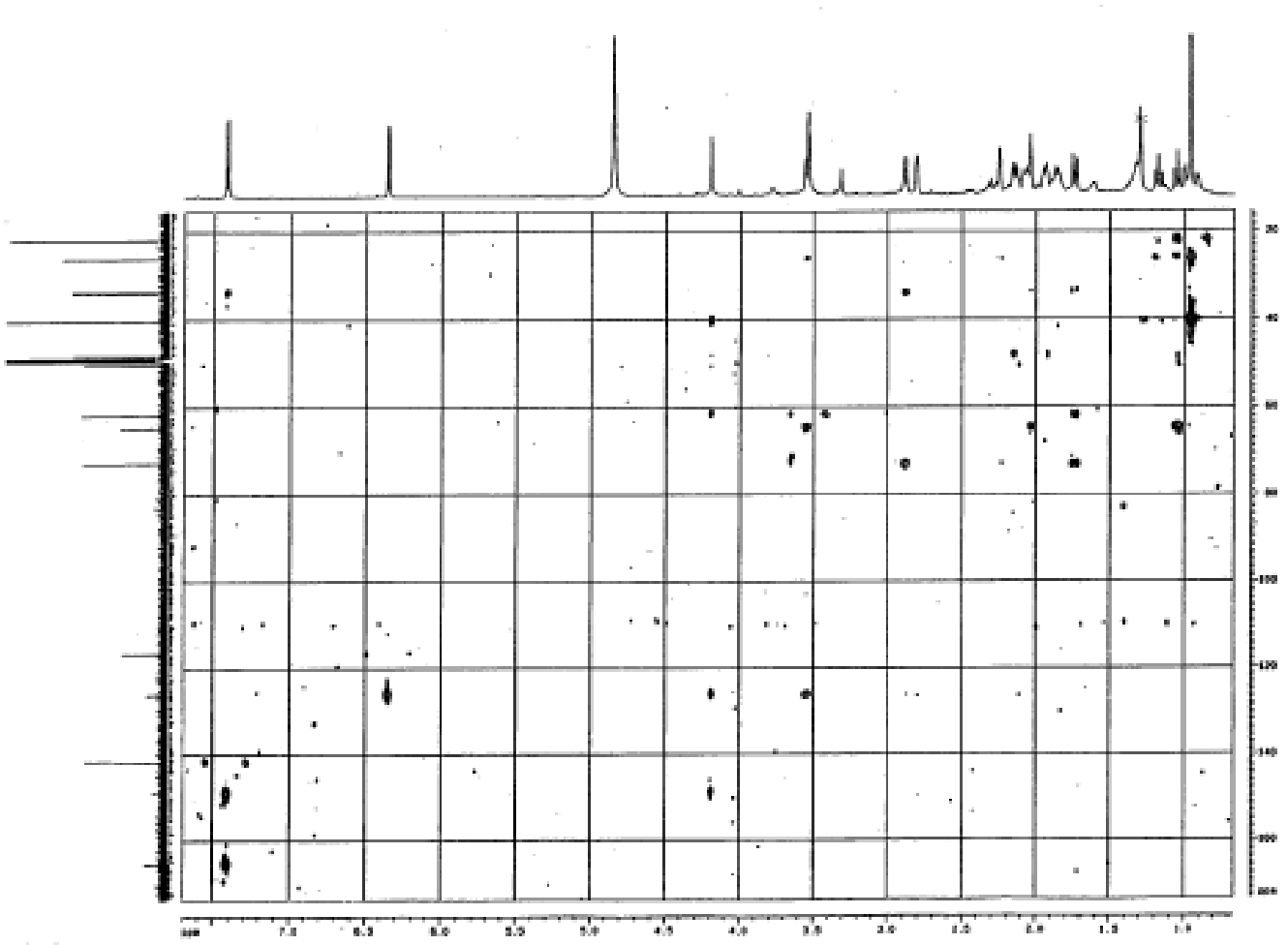

The 600 MHz $^{1}H$-$^{13}C$ HSQC Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.



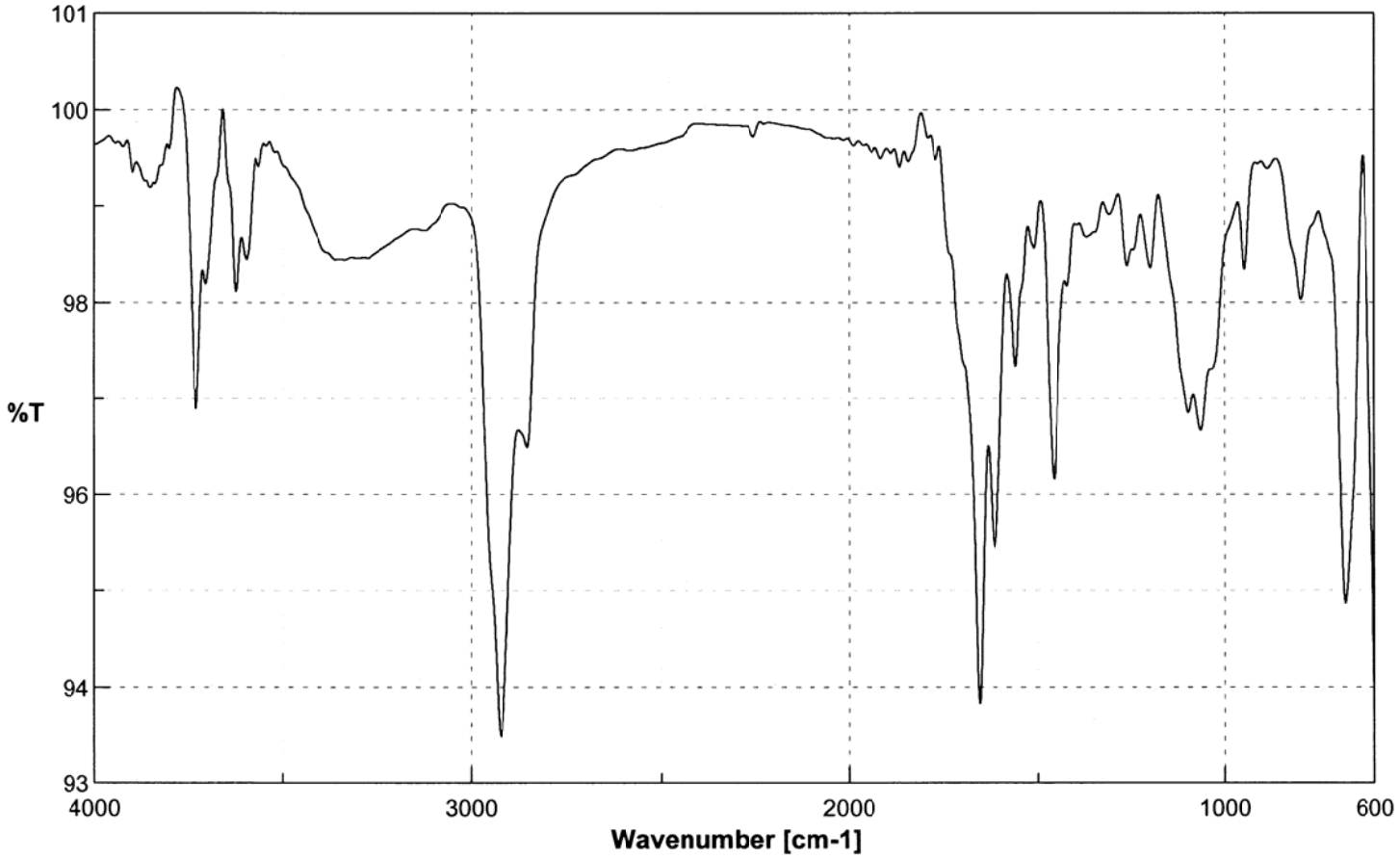
The 600 MHz $^{1}H$-$^{13}C$ HMQC Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.



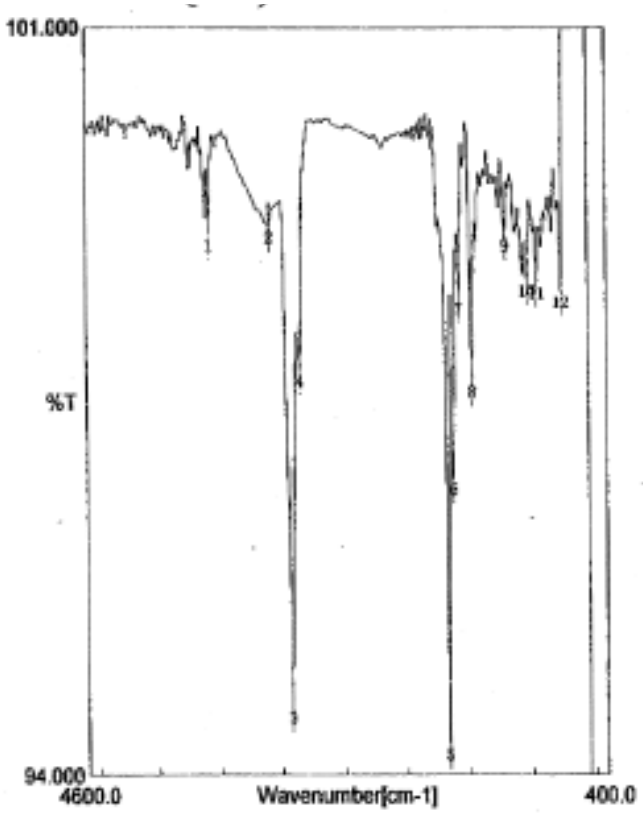

The 600 MHz $^{1}H$-$^{13}C$ HMBC Spectrum of Synthetic Lyconadin A (+)-**1** in $CD_3OD$.



The 600 MHz $^{1}H$-$^{13}C$ HMBC Spectrum of Natural Lyconadin A (+)-**1** in $CD_3OD$.




The Infrared Spectrum of Synthetic Lyconadin A (+)-**1**.




測定条件

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| サンプル名 | |
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| ゲイン | 1 |
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| ゼロフィリング | x2 |
| スピード | 2.0 xx/sec |
| 待ち時間 | 0 sec |
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| 光源 | Standard |
| 検出器 | 1 |
| ビームスプリッター | xxx |
| コメント | |

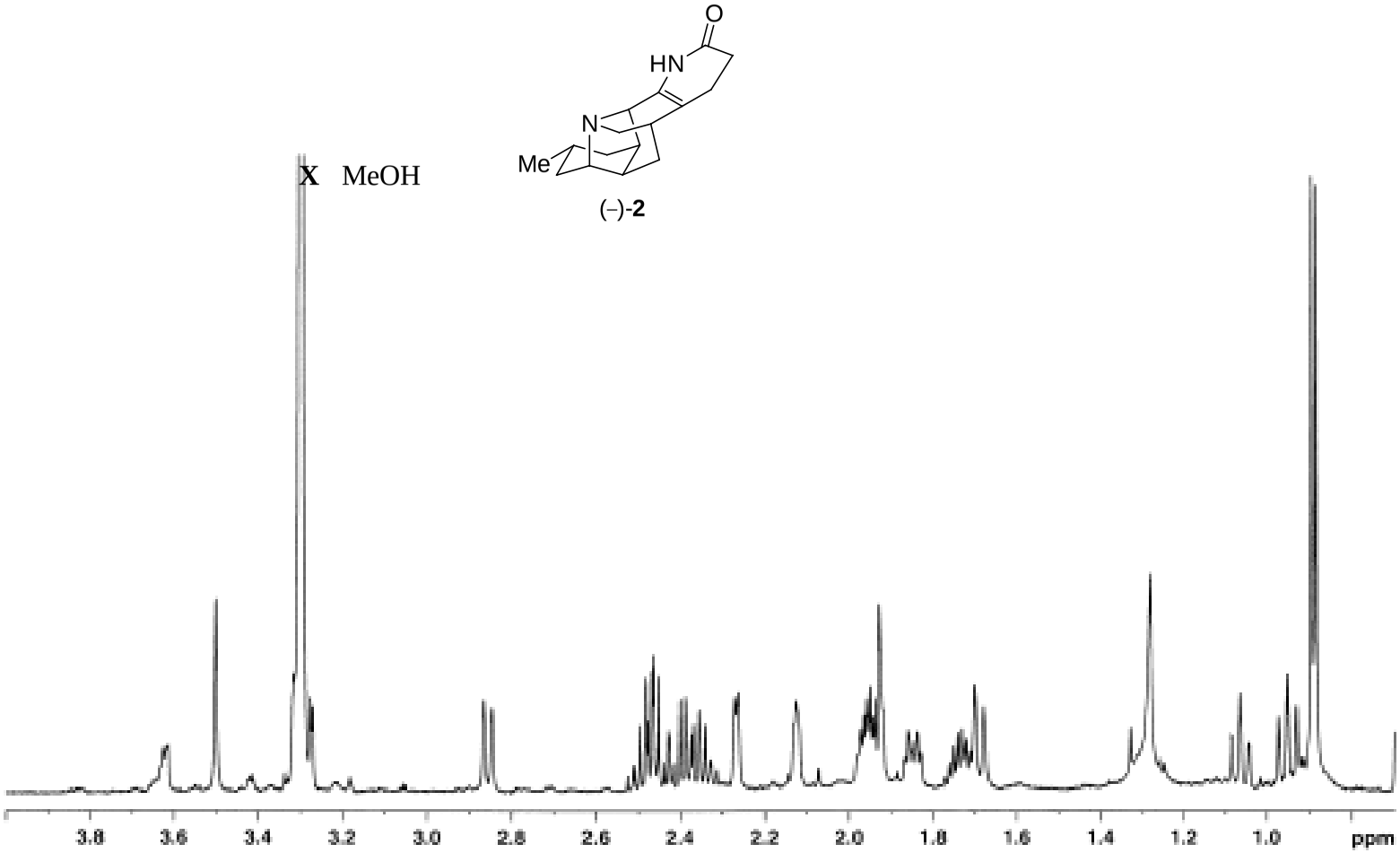
コピーライト

オペレーター

ピーク情報

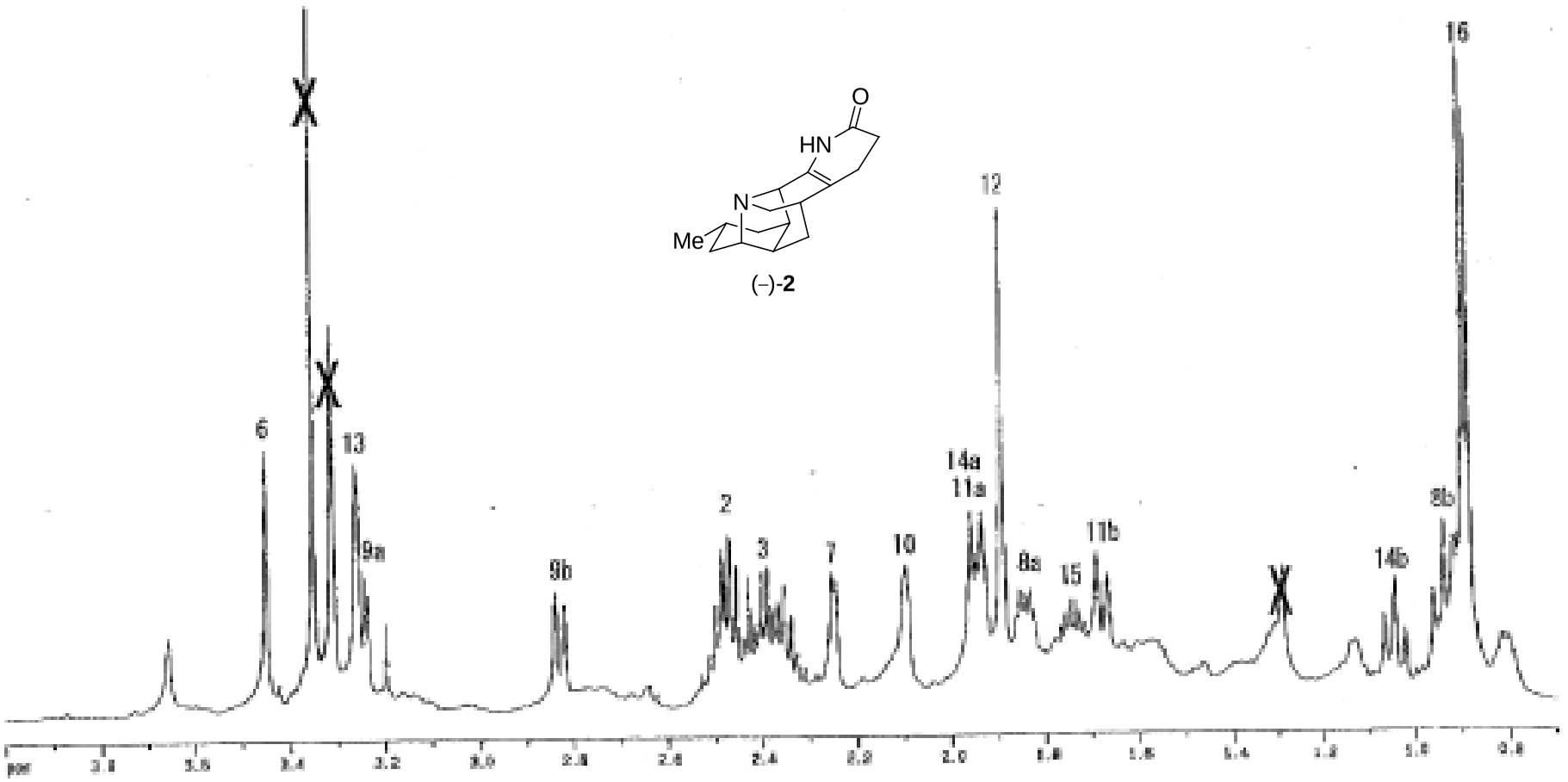
| | | | | | |
|---|---|---|---|---|---|
| 1 | 3384.06 | 99.1% | 2 | 3091.33 | 99.1% |
| 3 | 2921.63 | 94.6% | 4 | 2852.20 | 97.8% |
| 5 | 1657.52 | 94.3% | 6 | 1615.09 | 96.8% |
| 7 | 1562.06 | 98.5% | 8 | 1438.89 | 97.7% |
| 9 | 1191.79 | 99.1% | 10 | 1021.12 | 98.6% |
| 11 | 946.88 | 98.6% | 12 | 759.82 | 98.9% |

The Infrared Spectrum of Natural Lyconadin A (+)-**1**.

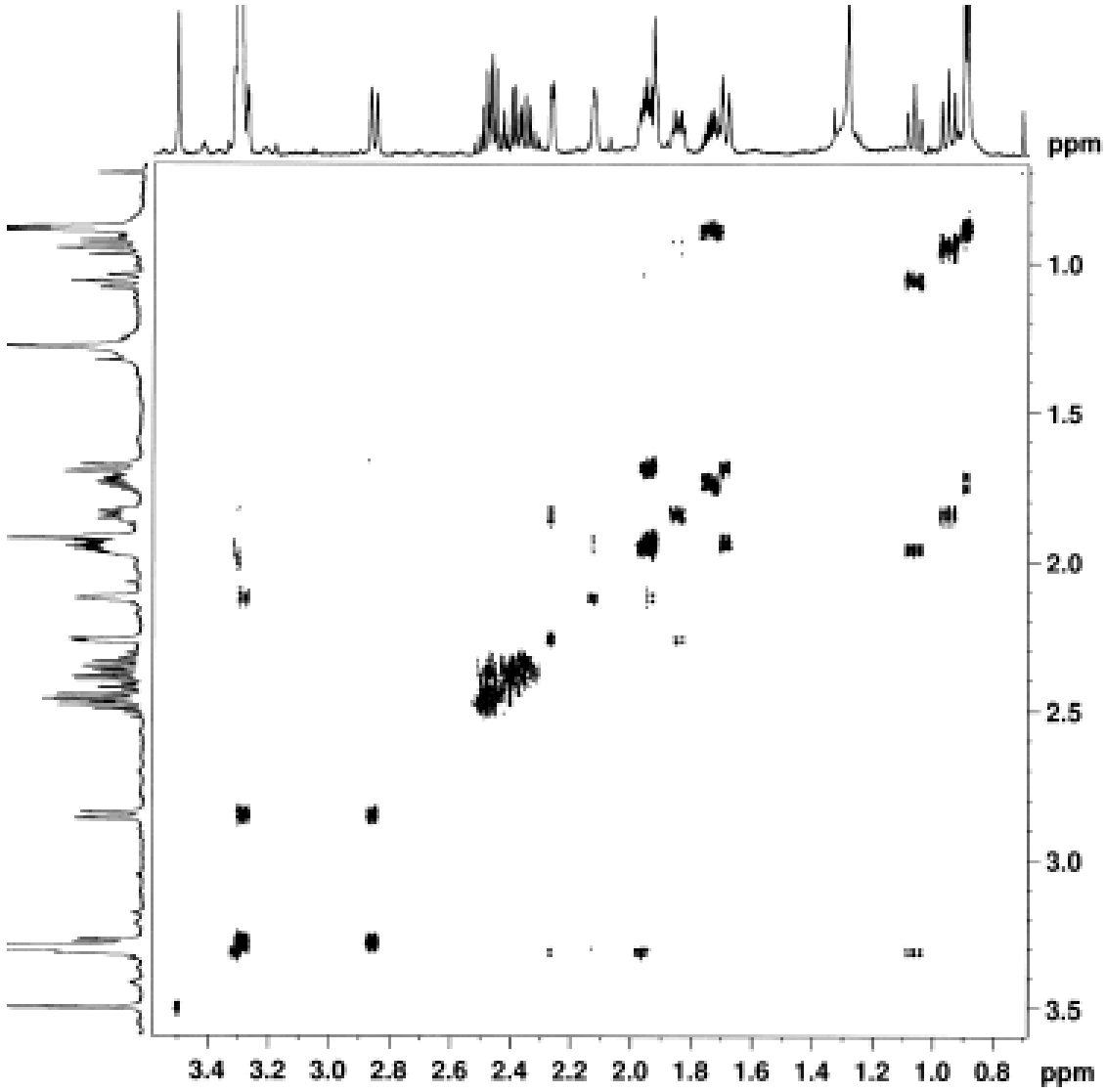



The 600 MHz $^{1}$H-NMR Spectrum of Synthetic Lyconadin B (–)-**2** in $CD_3OD$.

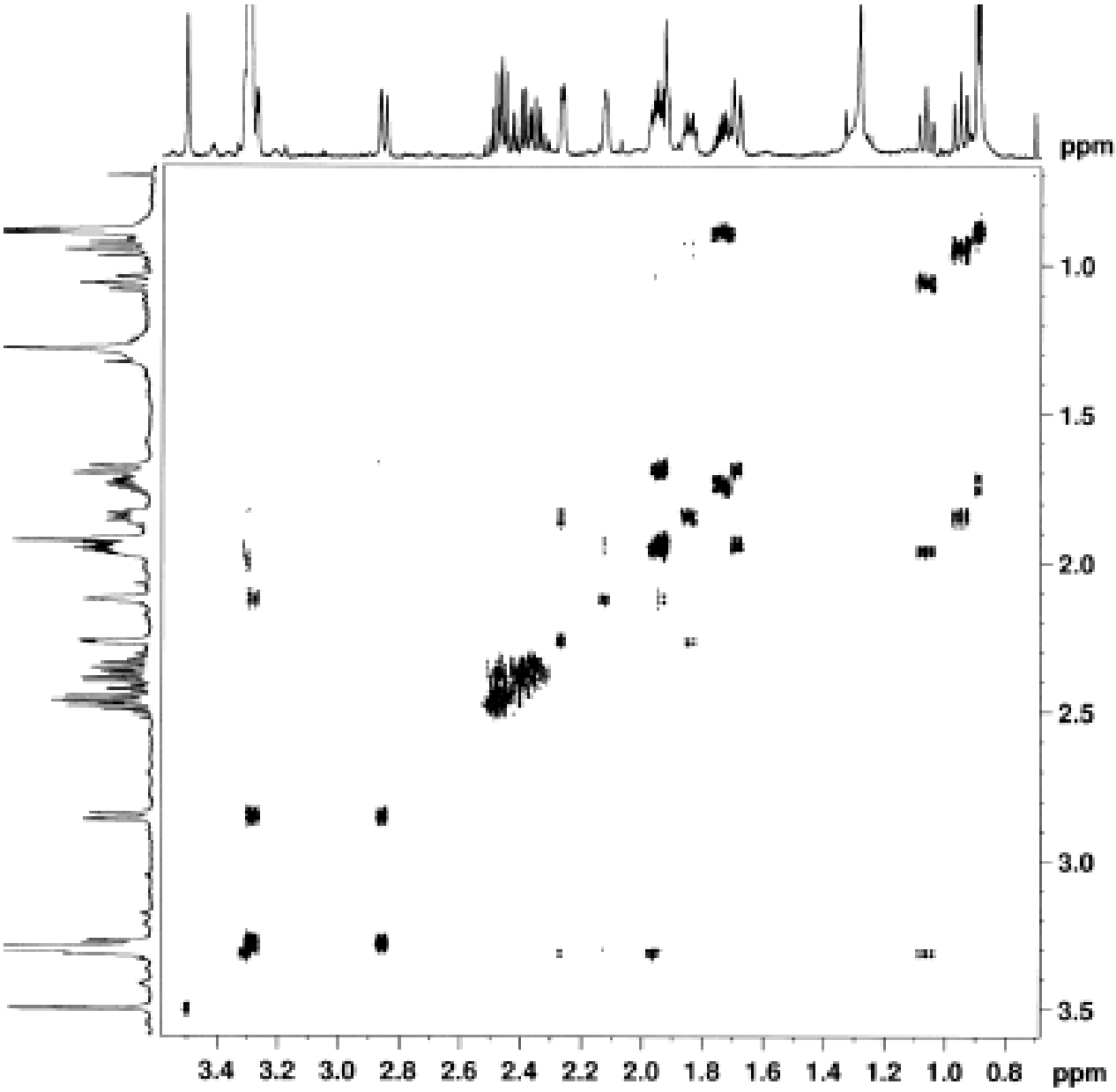
$^1$H NMR spectrum of lyconadin B in $CD_3OD$ / 600 MHz



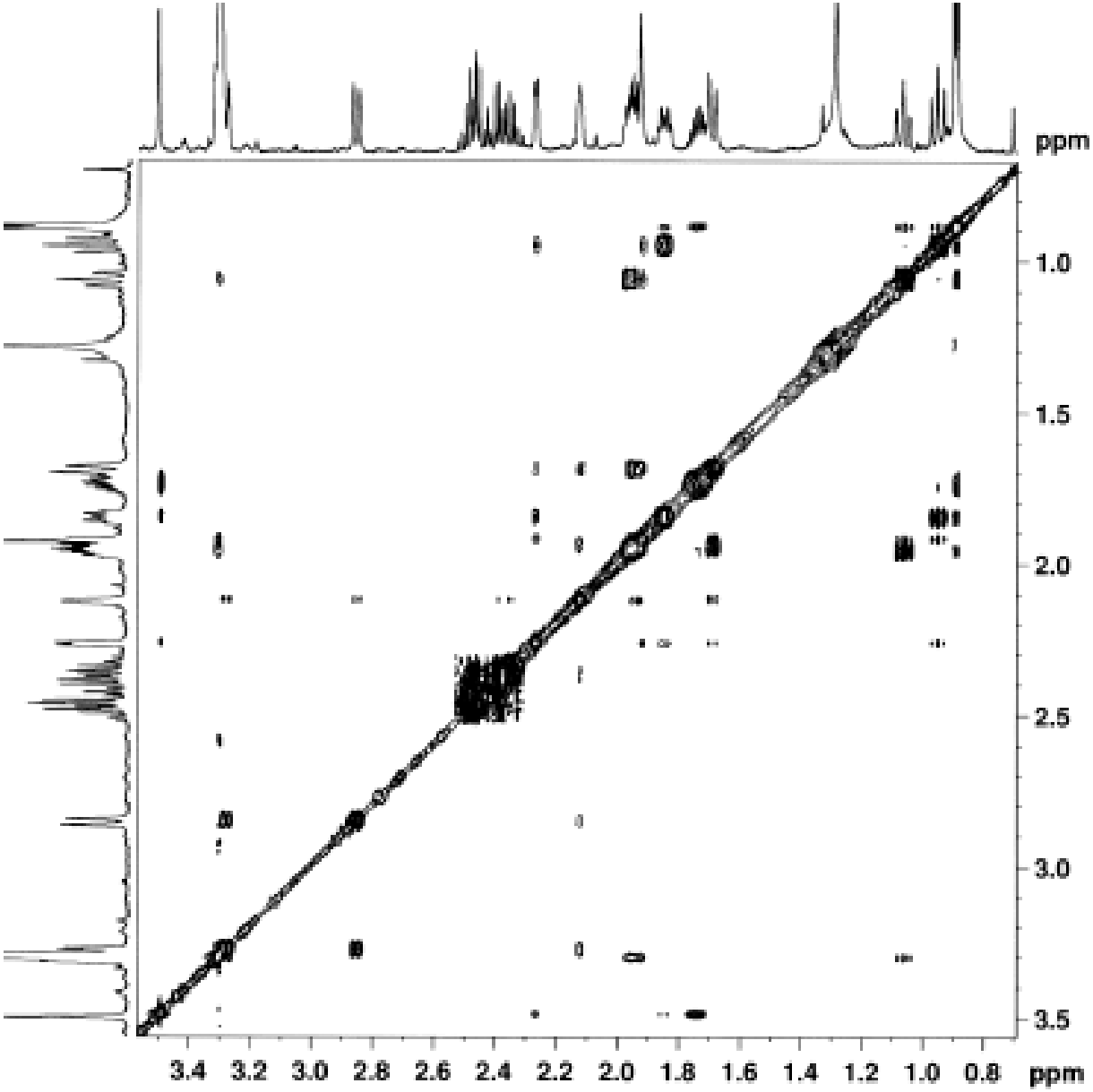

The 600 MHz $^1$H-NMR Spectrum of Natural Lyconadin B (–)-**2** in $CD_3OD$.



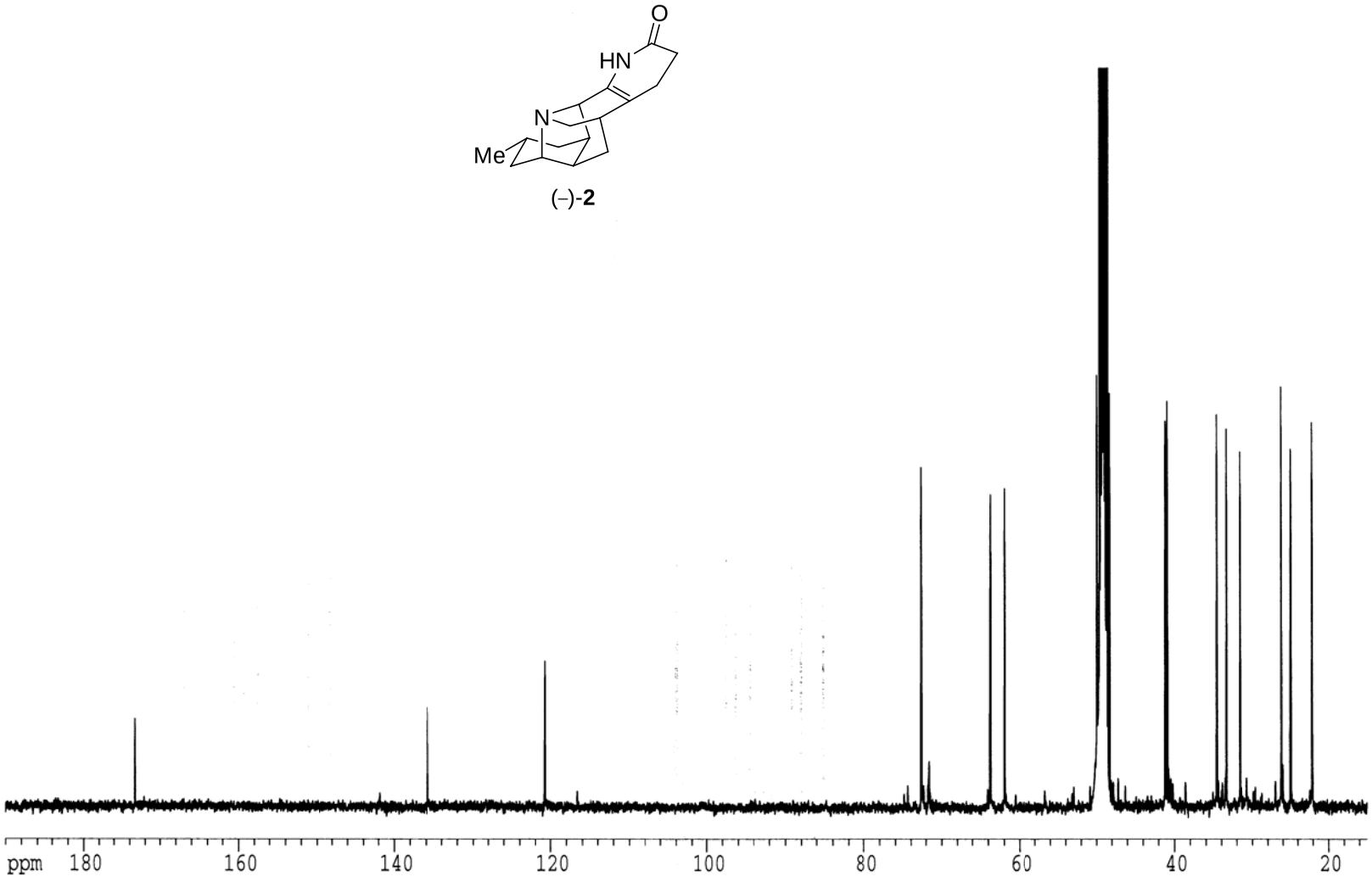

The 600 MHz $^{1}$H-$^{1}$H COSY Spectrum of Synthetic Lyconadin B (−)-**2** in $CD_3OD$.



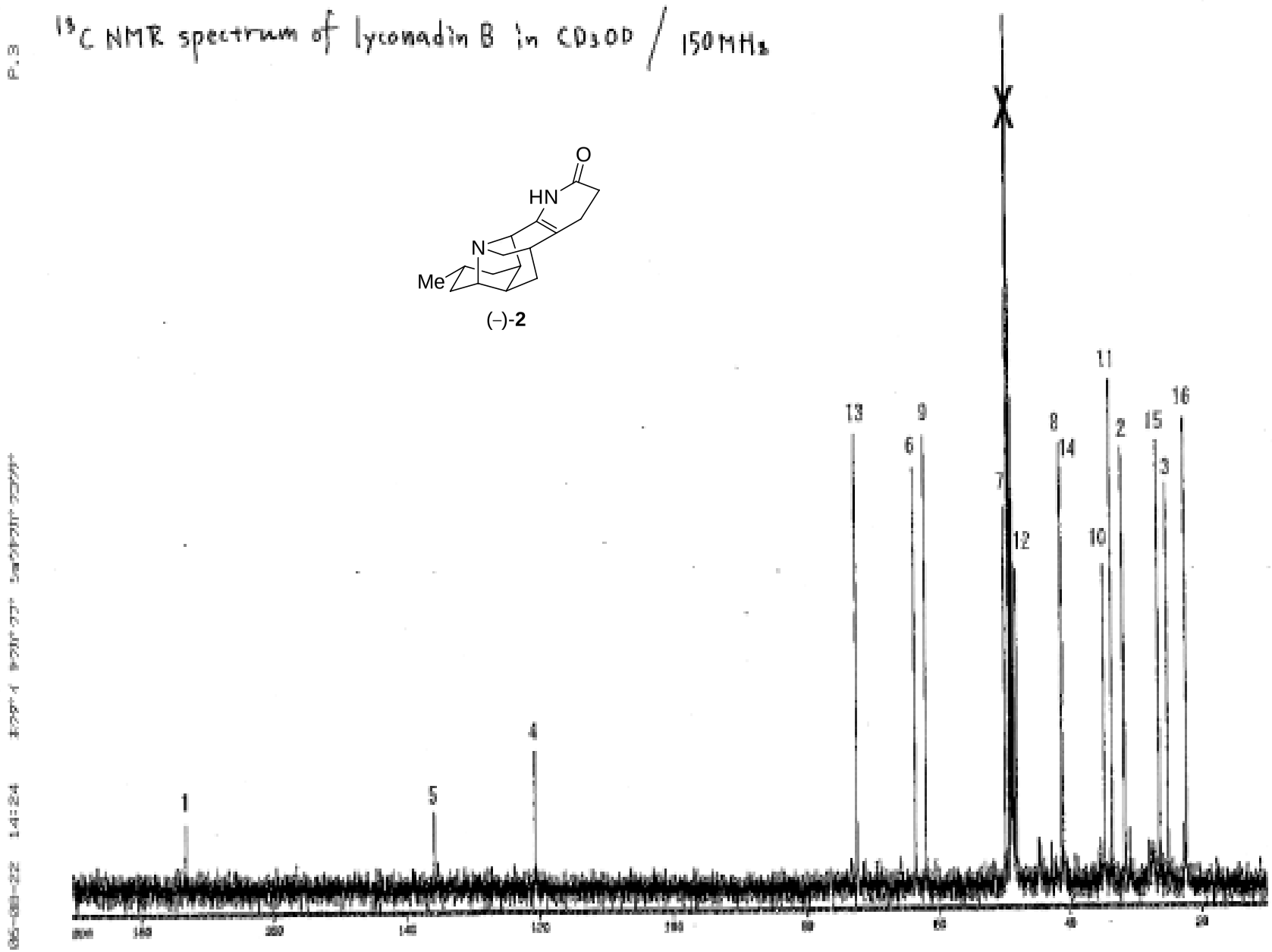

The 600 MHz $^{1}H$-$^{1}H$ TOCSY Spectrum of Synthetic Lyconadin B (–)-**2** in $CD_3OD$.



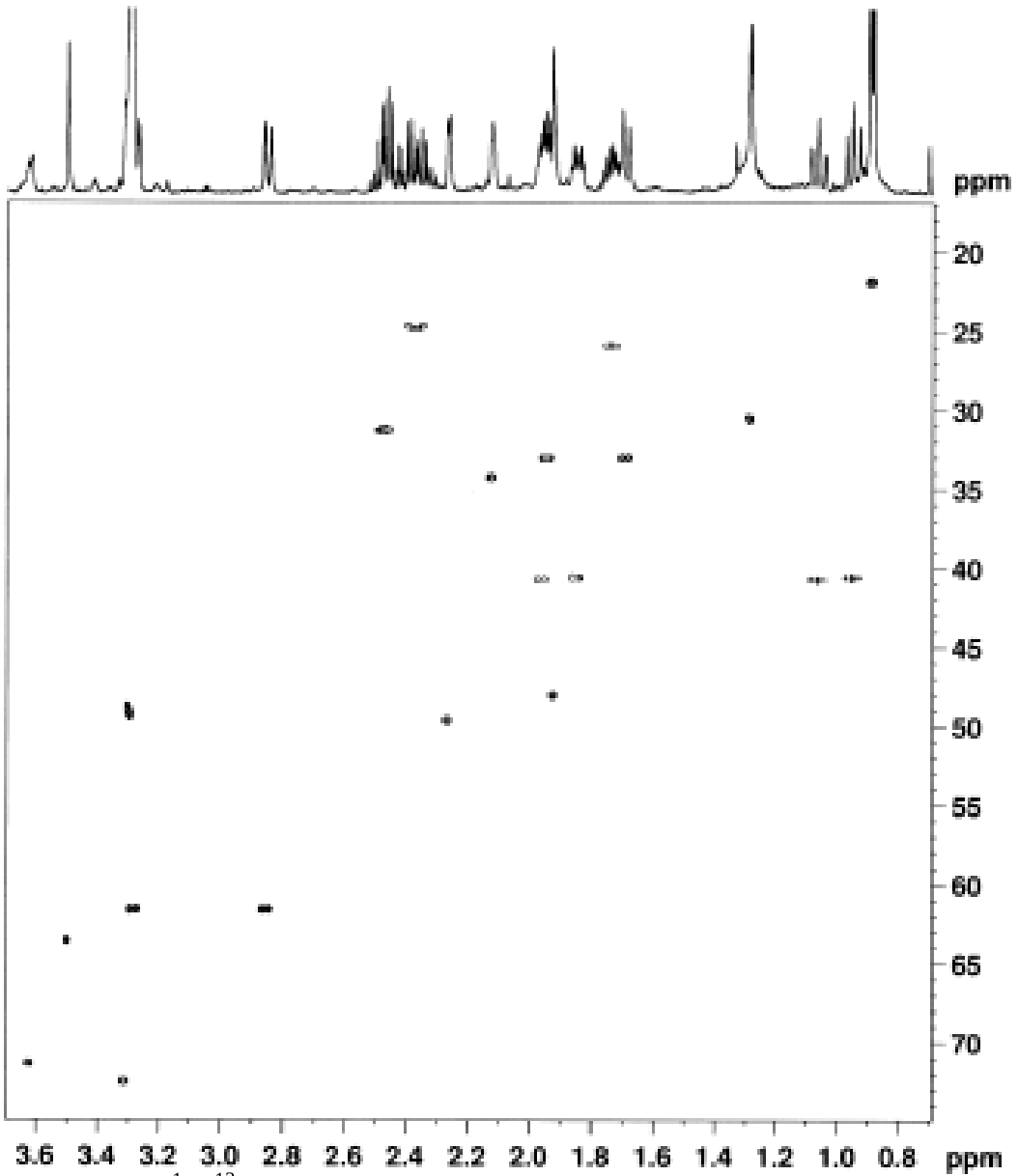

The 600 MHz NOESY Spectrum of Synthetic Lyconadin B (−)-**2** in $CD_3OD$.



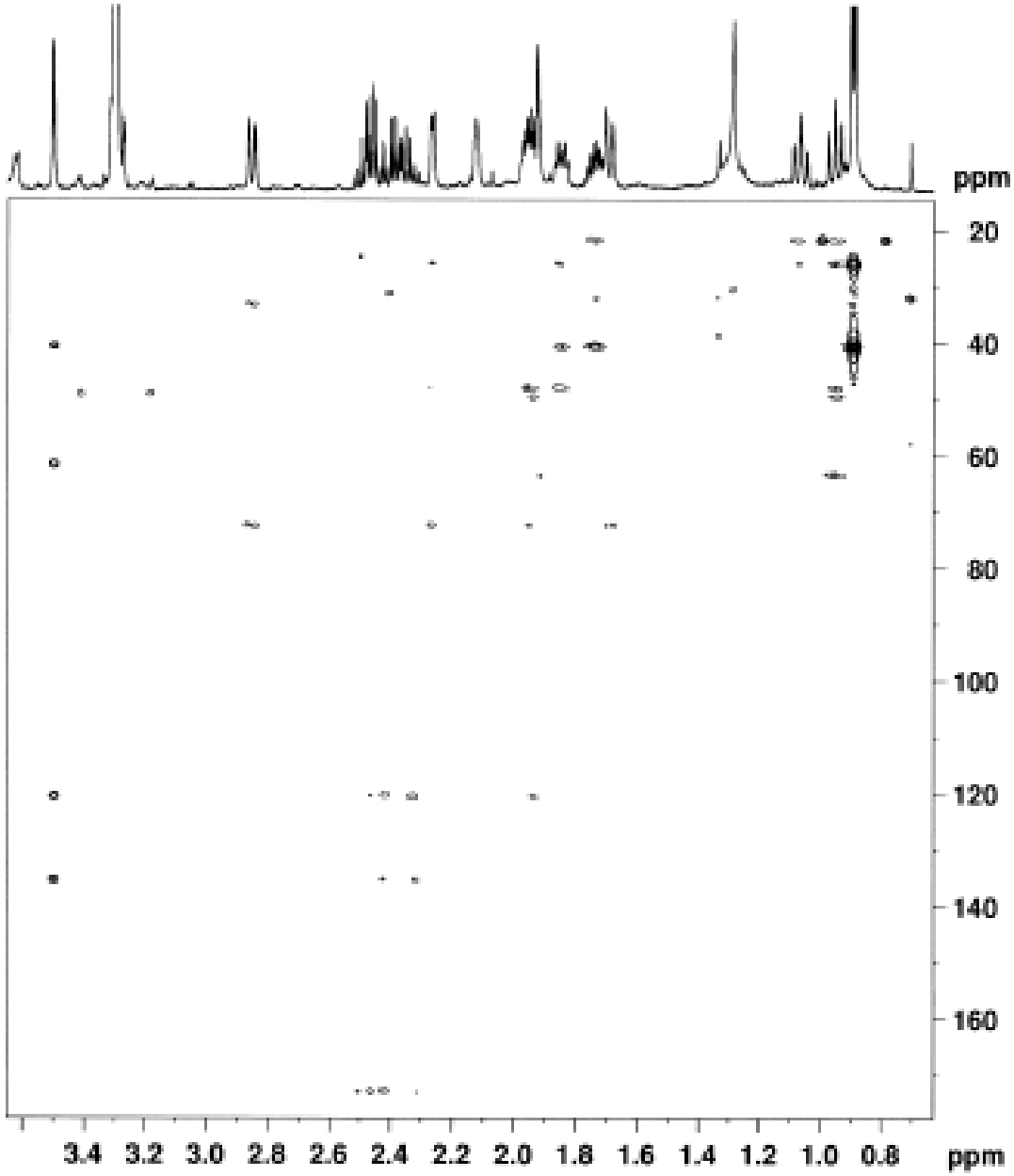

The 125 MHz $^{13}$C-NMR Spectrum of Synthetic Lyconadin B (–)-**2** in $CD_3OD$.



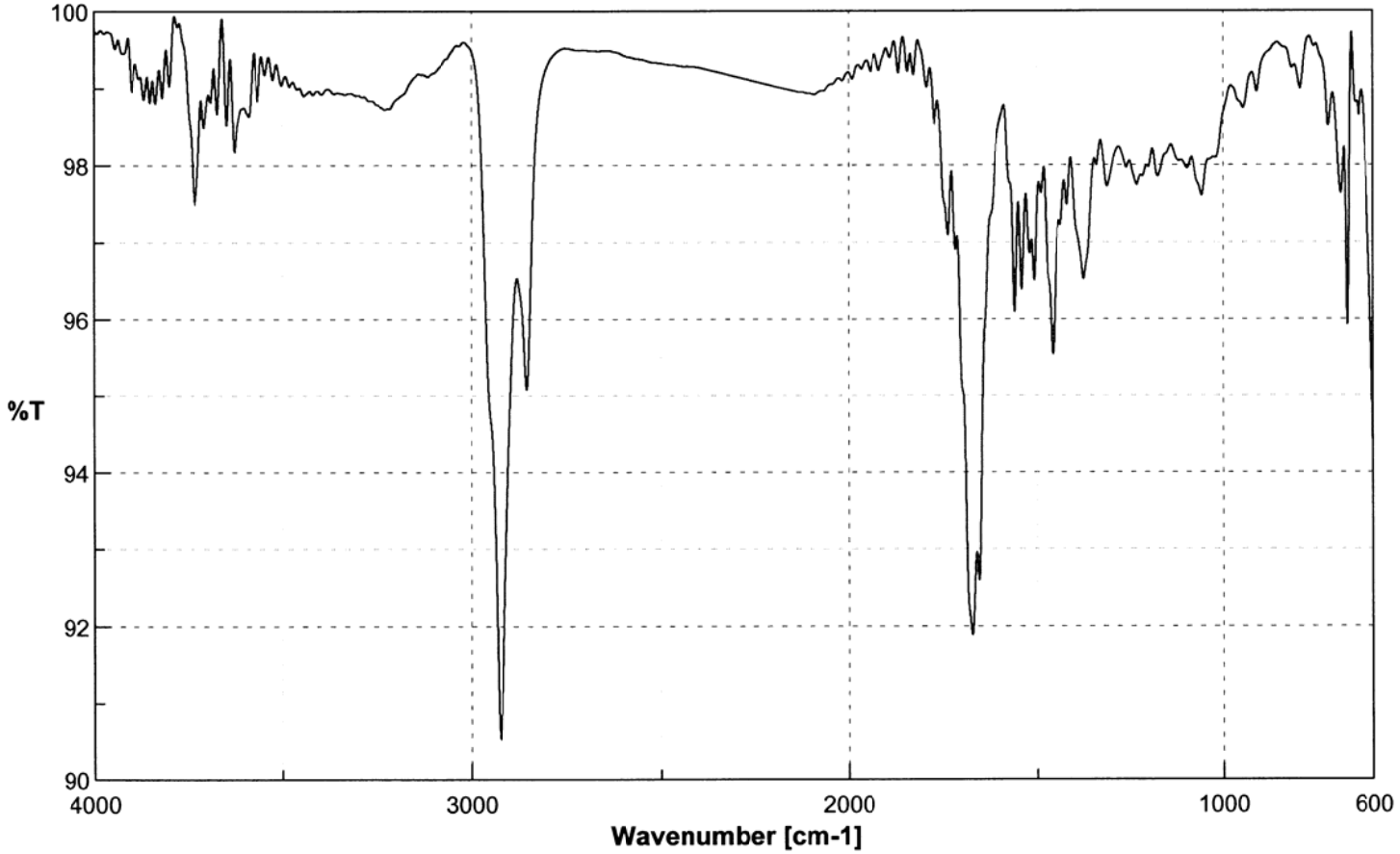

The 150 MHz $^{13}$C-NMR Spectrum of Natural Lyconadin B (–)-**2** in $CD_3OD$.



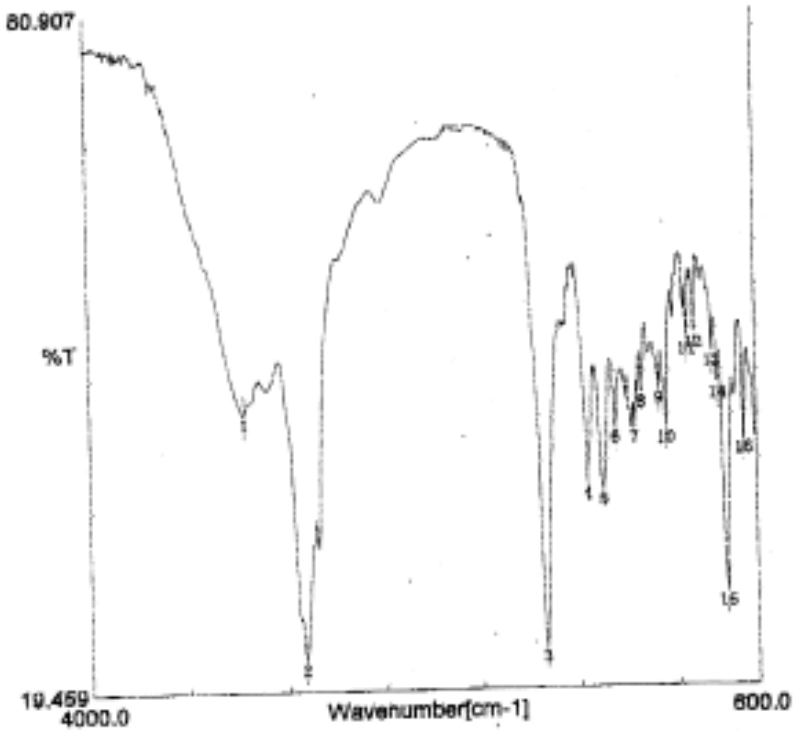

The 600 MHz $^{1}H$-$^{13}C$ HSQC Spectrum of Synthetic Lyconadin B (–)-**2** in $CD_3OD$.




The 600 MHz $^{1}H$-$^{13}C$ HMBC Spectrum of Synthetic Lyconadin B (–)-**2** in $CD_3OD$.




The Infrared Spectrum of Synthetic Lyconadin B (–)-**2**.




測定条件
積算回数 36 times
分解 4 cm-1
サンプル名 Lcc'b7-9
アポダイゼーション Cosine
日付 106/02/03 23:20

ゲイン 2
アパーチャー 100
ゼロフィリング x2
スピード 2.0 mm/sec
待ち時間 0 sec
コメント
コピーライト
オペレーター
ピーク情報

ファイル名 KONAMI78.J10
光源 Standard
検出器 1
ビームスプリッター

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 1 | 3218.61 | 44.3% | 2 | 2930.65 | 29.3% | 5 | 1672.94 | 23.1% |
| 4 | 1458.03 | 37.7% | 5 | 1374.03 | 37.1% | 9 | 1311.36 | 42.6% |
| 7 | 1214.93 | 42.6% | 8 | 1178.29 | 48.7% | 12 | 1091.81 | 46.0% |
| 10 | 1058.84 | 42.8% | 11 | 947.84 | 50.0% | 15 | 908.31 | 51.0% |
| 13 | 817.67 | 49.3% | 14 | 791.64 | 48.4% | | 758.10 | 27.8% |
| 16 | 665.39 | 41.8% | | | | | | |

The Infrared Spectrum of Natural Lyconadin B (–)-**2**.