Enantioselective Synthesis of the 5-6-7 Carbocyclic Core of the Gagunin Diterpenoids

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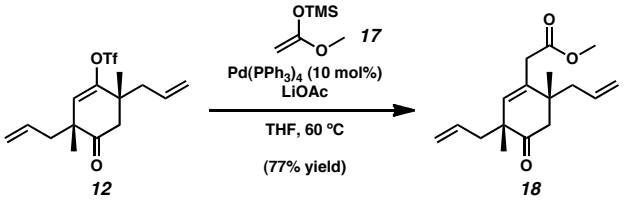
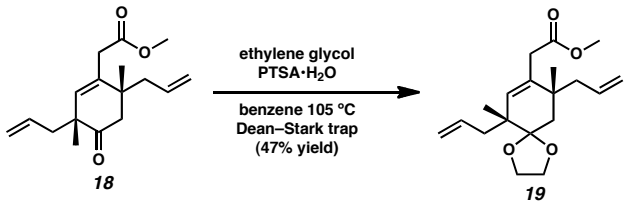
Materials and Methods. Unless stated otherwise, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents (distilled or passed over a column of activated alumina).[1] Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, anisaldehyde, or CAM staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040–0.063 mm) was used for flash chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 500 (at 500 and 125 MHz, respectively) and are reported to $CDCl_3$ (δ 7.26 and 77.16 respectively) or C_6D_6 (δ 7.16 and 128.06 respectively). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). IR spectra were recordere on a Perkin Elmer Paragon 1000 Spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) or mixed (MM) ionization mode. Preparatory HPLC was performed on an Agilent 1200 series HPLC with an Agilent Prep-SIL 30 x 250 mm, 5 μm column employing a 50 mL/min and a variable gradient of hexanes and ethyl acetate as eluent. Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm using a 100 mm path-length cell.

Experimental Procedures



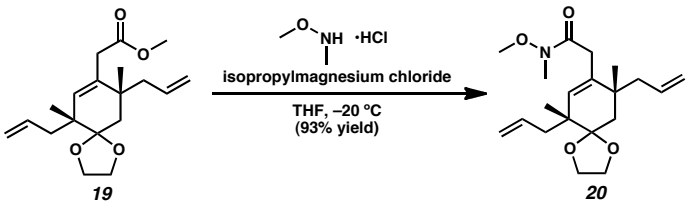
Methyl ester 18: To a flame-dried 100-mL 3-neck round bottom flask equipped with a reflux condenser was added triflate **12** (1.1 g, 3.1 mmol). The atmosphere was evacuated under vacuum for 10 min and then backfilled with N_2 gas. THF (31 mL, 0.10 M) was added followed by flame-dried LiOAc (520 mg, 7.9 mmol, 2.5 equiv) then $Pd(PPh_3)_4$ (360 mg, 0.31 mmol, 0.10 equiv). Silyl ketene acetal **17** (0.91 mg, 6.3 mmol, 2.0 equiv) was added and the flask was heated to 65 ºC for 15 min. The solution was cooled to ambient temperature and diluted with water (50 mL) and extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a yellow oil with solids. The crude product was purified by flash chromatography (92:8 hexanes:EtOAc) to afford **18** as a colorless oil (664 mg, 77%). Characterized as a 3.7:1.0 mixture of diastereomers: R_f = 0.33 (5:1 hexanes:EtOAc); ^{1}H (500 MHz, $CDCl_3$) δ 5.74–5.60 (m, 1H), 5.403 (t, *J* = 1.0, 0.22H), 5.395 (t, *J* = 1.0, 0.87H), 5.12–4.98 (m, 4H), 3.69 (s, 3H), 3.10–3.03 (m, 2H), 2.53 (d, *J* = 14.0, 0.22H), 2.52 (d, *J* = 14.0, 0.78H), 2.40–2.35 (m, 1H), 2.29 (d, *J* = 14.0, 0.87H), 2.24 (d, *J* = 14.0, 0.25H), 2.21–2.10 (m, 2H), 2.04–1.98 (m, 1H), 1.14 (s, 0.66H), 1.13 (s, 2.37H), 1.03 (s, 0.68H), 1.02 (s, 2.39H); ^{13}C (125 MHz, $CDCl_3$) δ 213.6, 172.5, 136.4, 134.1, 134.0, 133.9, 119.2, 118.4, 52.1, 49.5, 45.0, 44.4, 44.0, 43.0, 37.7, 26.1, 24.8; IR: 2965, 2928, 1740, 1714, 1435, 1164, 917 cm^{-1}; HRMS (Multimode-

ESI/APCI) *m*/*z* calc'd for $C_{17}H_{25}O_3$ $[M+H]^+$: 277.1798, found 277.1786; $[\alpha]^{25}_D$ –12.96 (*c* 0.55, $CHCl_3$).



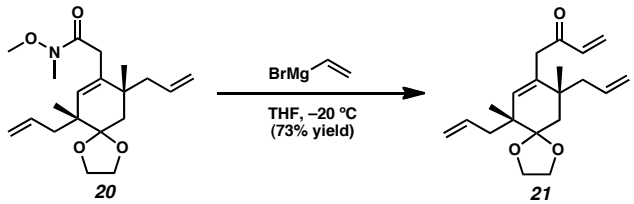
Ketal 19: To a 100-mL round bottom flask equipped with a stirbar, Dean–Stark trap, and reflux condenser was added ketoester **18** (0.76 g, 2.7 mmol) and benzene (14 mL, 0.20 M). Ethylene glycol (0.77 mL, 14 mmol, 5.0 equiv) and *p*-toluenesulfonic acid (160 mg, 0.82 mmol, 0.30 equiv) were added to the flask. The flask was heated to 105 ºC for 12 h, then additional ethylene glycol (0.77 mL, 14 mmol, 5.0 equiv) and *p*-toluenesulfonic acid (160 mg, 0.82 mmol, 0.30 equiv) were added to the solution and the reaction was stirred for 3 h. The solution was cooled to ambient temperature and diluted with water (25 mL), neutralized with aq. sat. $NaHCO_3$ (20 mL), and then extracted with EtOAc (3 x 30 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a light-yellow oil. Analysis of the crude product by ^{1}H NMR spectroscopy shows a 3.3:1 mixture of product to starting material. The crude product was purfied by silica gel chromatography (95:5 hexanes:diethyl ether) to afford **19** as a colorless oil (409 mg, 47%) and a 1.0:1.25 mixture of product **19** to starting material **18** (63 mg). Characterized as a 4.5:1.0 mixture of diastereomers: R_f = 0.27 (95:5 hexanes:diethyl ether); ^{1}H (500 MHz, $CDCl_3$) δ 5.90–5.83 (m, 1H), 5.73–5.66 (m, 1H), 5.37 (s, 0.18H), 5.32 (s, 0.81H), 5.09–4.99 (m, 4H), 3.96–3.90 (m, 4H), 3.66 (s, 3H), 3.01–2.92 (m, 2H), 2.32–2.25 (m, 1H), 2.23–2.19 (m, 2H), 2.01–1.93 (m, 2H), 1.48–1.43 (m, 1H), 1.09 (s, 3H), 1.02 (s, 0.59H), 0.98 (s, 2.45H);

^{13}C (125 MHz, $CDCl_3$) δ 173.0, 135.5, 135.0, 134.3, 134.1, 118.2, 117.2, 112.0, 65.0, 64.6, 51.9, 44.8, 43.5, 43.0, 40.3, 38.0, 36.9, 26.5, 20.3; IR (thin film) 2975, 2952, 2879, 1741, 1460, 1435, 1162, 1117, 914 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{19}H_{28}O_4$ $[M+H]^+$: 321.2060, found 231.2073; $[\alpha]^{25}_D$ –45.3 (*c* 0.72, $CHCl_3$).



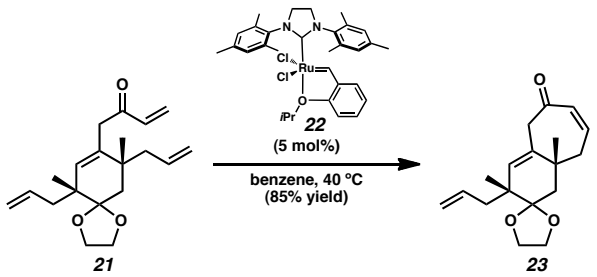
Amide 20: To a 25-mL round bottom flask containing **19** (226 mg, 0.70 mmol) was added *N*,*O*-dimethylhydroxylamine hydrochloride (110 mg, 1.1 mmol, 1.6 equiv) and the flask was evacuated under vacuum for 10 min then backfilled with an N_2 atmosphere. THF (4.7 mL, 0.15 M) was added and the resulting suspension was cooled to –20 ºC. A solution of isopropylmagnesium chloride (1.35 mL, 2.10 mmol, 3.0 equiv, 1.55 M) was added dropwise and the reaction mixture was stirred for 15 min. The reaction mixture was next quenched with sat. aq. NH_4Cl (5.0 mL), diluted with water (20 mL) and warmed to ambient temperature. The aqueous phase was extracted with diethyl ether (3 x 20 mL) and the combined organic extracts was washed with brine (5.0 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford a yellow oil. The crude product was purified by silica gel chromatography (3:1 hexanes:EtOAc) to afford **20** as a colorless oil (228 mg, 93%). Characterized as a 4.5:1.0 mixture of diastereomers:[2] R_f = 0.20 (5:1 hexanes:EtOAc); ^{1}H (500 MHz, $CDCl_3$) δ 5.91–5.82 (m, 1H), 5.78–5.67 (m, 1H), 5.23 (s, 0.18H), 5.16 (s, 0.81H), 5.09–4.97 (m, 4H), 3.96–3.87 (m, 4H), 3.67 (s, 3H), 3.20–2.98 (m, 2H), 2.36–2.27 (m, 1H), 2.25–2.18 (m, 2H), 2.02–1.97 (m, 2H), 1.45 (d, *J* = 14.5, 0.20H), 1.43 (d, *J* = 14.0, 0.80H), 1.14 (s, 0.59H), 1.12 (s, 2.36H), 1.01 (s, 0.56H), 0.96

(s, 2.38H); ^{13}C (125 MHz, $CDCl_3$, 273K) δ 173.5, 135.6, 135.1, 134.6, 132.1, 118.2, 117.2, 111.9, 64.9, 64.5, 61.5, 44.6, 43.4, 42.9, 40.1, 37.8, 34.9, 32.4, 26.4, 20.4; IR: 2974, 2934, 2879, 1668, 1378, 1118, 1012 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{20}H_{32}NO_4$ $[M+H]^+$: 350.2326, found 350.2340; $[\alpha]^{25}_D$ –32.2 (*c* 0.83, $CHCl_3$).



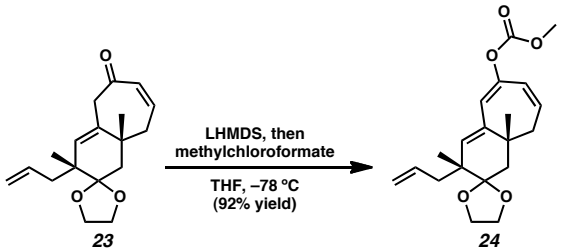
Vinylketone 21: To a cooled (–20 ºC) solution of **20** (648 mg, 1.90 mmol) in THF (18.5 mL, 0.10 M) was added a solution of vinylmagnesium bromide (2.90 mL, 2.04 mmol, 1.1 equiv, 0.70 M) dropwise. The reaction mixture was stirred at –20 ºC for 80 min then additional vinylmagnesium bromide (0.53 mL, 0.370 mmol, 0.20 equiv, 0.70 M) was added and the resulting solution was stirred for 20 min. The reaction was quenched by the addition of saturated aq. NH_4Cl (20 mL) and water (10 mL) and then warmed to ambient temperature. The phases were separated and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a yellow oil. The crude product was purified by column chromatography (95:5 hexanes:EtOAc) to afford **21** as a colorless oil (431 mg, 74% yield). Characterized as a 2.7:1.0 mixture of diastereomers: R_f = 0.54 (5:1 hexanes:EtOAc); ^{1}H (500 MHz, $CDCl_3$) δ 6.48 (dd, *J* = 10.5, 17.0, 1H), 6.26 (dd, *J* = 2.0, 17.0, 1H), 5.89–5.79 (m, 1H), 5.73 (dd, *J* = 1.5, 11.0, 1H), 5.74–5.64 (m, 1H), 5.18 (s, 0.25H), 5.11 (s, 0.70H), 5.10–4.97 (m, 4H), 3.98–3.89 (m, 4H), 3.23–3.08 (m, 2H), 2.32–2.24 (m, 1H), 2.22–2.17 (m, 2H), 2.01–1.94 (m, 2H), 1.48 (d, *J* = 14.0, 0.20H), 1.46 (d, *J* = 14.0, 0.80H), 1.11 (s, 0.85H), 1.10 (s, 2.16H), 1.01 (s, 0.85H), 0.97

(s, 2.16H); ^{13}C (125 MHz, $CDCl_3$) δ 199.2, 135.5, 135.4, 134.9, 134.8, 134.7, 128.2, 118.3, 117.3, 111.9, 64.9, 64.6, 44.8, 43.8, 43.3, 43.2, 40.4, 38.0, 26.5, 20.5; IR (thin film): 3072, 2974, 2878, 1696, 1399, 1118, 993, 914 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{20}H_{29}O_3$ $[M+H]^+$: 317.2111, found 317.2112; $[\alpha]^{25}_D$ –29.6 (*c* 1.02, $CHCl_3$).



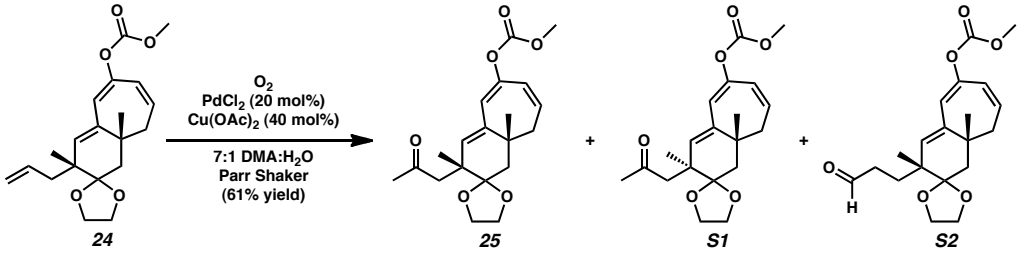
Bicyclic enone 23: To a solution of **21** (431 mg, 1.36 mmol) in sparged benzene (136 mL, 0.01 M) was added Hoveyda–Grubbs generation II catalyst **22**[3] (43 mg, 0.070 mmol, 0.05 equiv). The reaction mixture was heated to 40 ºC and stirred for 40 min. The reaction mixture was cooled to 0 ºC and ethylvinyl ether (4.0 mL) was added and the resulting solution was warmed to ambient temperature. The solution was concentrated *in vacuo* and the crude product was purified by column chromatography (SiO_2, 5:1 hexanes:EtOAc) to afford **23** as a colorless oil (351 mg, 85%). Characterized as a 2.9:1.0 mixture of diastereomers: R_f = 0.29 (5:1 hexanes:EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ6.53–6.47 (m, 1H), 5.99 (d, *J* = 11.5, 0.73H), 5.98 (td, *J* = 1.5, 11.0, 0.25H), 5.83 (ddt, *J* = 7.5, 10.4, 16.7, 0.27H), 5.70 (ddt, *J* = 7.5, 9.9, 17.0, 0.73H), 5.34 (s, 0.25H), 5.27 (s, 0.73H), 5.02–4.88 (m, 2H), 4.02–3.91 (m, 4H), 3.17–3.06 (m, 2H), 2.35–2.31 (m, 2H), 2.26 (dd, *J* = 8.7, 14.8, 0.29H), 2.19 (dd, *J* = 7.5, 13.5, 1H), 2.14 (ddd, *J* = 1.0, 7.0, 13.5, 0.27H), 2.07 (dd, *J* = 7.7, 13.1, 0.76H), 1.82 (d, *J* = 13.5, 0.77H), 1.76 (d, *J* = 13.5, 0.27H), 1.61 (d, *J* = 13.5, 1H), 1.27 (s, 3), 0.96 (s, 2.12H), 0.92 (s, 0.66H); ^{13}C NMR

($CDCl_3$, 125 MHz) δ 200.7, 143.3, 135.5, 135.0, 134.0, 133.7, 117.8, 111.6, 64.8, 64.7, 47.7, 44.1, 43.5, 41.05, 40.98, 40.3, 26.8, 19.5; IR (thin film): 2935, 2880, 1672, 1461, 1258, 1114, 914 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{18}H_{25}O_3$ $[M + H]^+$: 289.1798, found 289.1793; $[\alpha]^{25}_D$ +192.6 (*c* 0.77, $CHCl_3$).



Enol carbonate 24: To a cooled (–78 ºC) solution of LHMDS (100 mg, 0.59 mmol, 1.1 equiv) in THF (4.5 mL, 0.12 M) in a 15-mL round bottom flask was added a solution of **23** (163 mg, 0.54 mmol) in THF (1.1 mL, 0.5 M). The resulting solution was stirred at –78 ºC for 30 min then methylchloroformate (65 µL, 0.81 mmol, 1.5 equiv) was added dropwise to the flask. The reaction mixture was stirred at –78 ºC for 3 h then warmed to ambient temperature and stirred for 1 additional hour. To the solution was added sat. aq. NH_4Cl (5.0 mL) and water (10 mL) then the mixture was extracted with EtOAc (3 x 10 mL). The combined organic extract was washed with brine (5.0 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a yellow-brown oil. The crude product was purified through a silica gel plug (6:1 hexanes:EtOAc→5:1 hexanes:EtOAc) to afford **24** as a light yellow oil (172 mg, 92%, characterized as a 4.5:1 mixture of diastereomers): R_f = 0.40 (9:1 hexanes:EtOAc); ^1H NMR ($CDCl_3$, 500 MHz) δ 5.96 (s, 1H), 5.88–5.79 (m, 3H), 5.46 (s, 0.18H), 5.41 (s, 0.84H), 5.06–5.01 (m, 2H), 4.02–3.92 (m, 4H), 3.81 (s, 3H), 2.53 (m, 1H), 2.47 (m, 0.23H), 2.28–2.17 (m, 2H), 2.08

(dd, J = 17.0, 8.0, 1H), 1.81–1.73 (appar q., J = 14.0, 26.5, 2H), 1.13 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.0, 144.1, 138.0, 137.7, 135.2, 131.3, 125.1, 123.2, 117.6, 111.9, 64.9, 64.8, 55.2, 43.9, 42.8, 42.72, 42.65, 36.2, 25.1, 20.6; IR (thin film) 2957, 2929, 2880, 1759, 1440, 1257, 1037 cm^{-1}; HRMS (Multimode-ESI/APCI) m/z calc'd for $C_{20}H_{27}O_5$ $[M+H]^+$: 347.1853, found 347.1842; $[\alpha]^{25}_D$ –157.8 (c 0.75, $CHCl_3$).



Ketone 25: To a solution of **24** (82.0 mg, 0.235 mmol) in 7:1 DMA:H_2O (2.35 mL, 0.10 M) in a 10 mL Parr shaker flask was added $PdCl_2$ (8.30 mg, 0.047 mmol, 0.20 equiv) and $Cu(OAc)_2$•H_2O (19.0 mg, 0.094 mmol, 0.40 equiv). The reaction vessel was put under an atmosphere of oxygen and run in the Parr shaker for 18 h. The reaction was filtered through a plug of silica gel (2:1 hexanes:EtOAc) and concentrated *in vacuo* to afford a yellow oil. Analysis of the crude product by ^{1}H NMR showed 12% aldehyde product. The crude product was purified by column chromatography (3:1 hexanes:EtOAc) to afford **25** and **S1** as a colorless oil (206 mg, 61% yield); separation of diastereomers by HPLC (3:1 hexanes:EtOAc) afforded the major diastereomer **25** (84 mg, 25% yield), minor diastereomer **S1** (17 mg, 5% yield), and aldehyde product **S2** (8.0 mg, 9% yield)[4]:

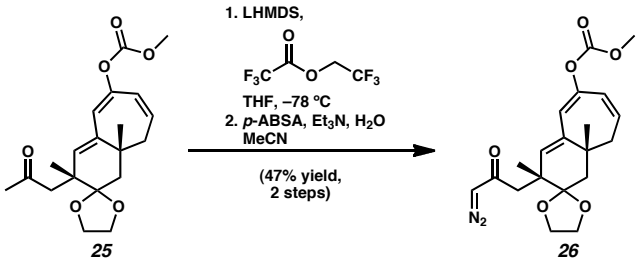
25: R_f = 0.32 (2:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, C_6D_6) δ 6.04 (s, 1H), 5.92 (ddd, J = 2.2, 3.1, 12.0, 1H), 5.69 (d, J = 0.6, 1H), 5.60 (ddd, J = 3.2, 8.7, 11.9, 1H), 3.51–3.40 (m, 3H), 3.38–3.33 (m, 1H), 3.35 (s, 3H), 2.46 (td, J = 3.1, 17.3, 1H), 2.39 (d, J = 15.1,

1H), 2.32 (d, *J* = 15.4, 1H), 1.75 (s, 3H), 1.70 (dd, *J* = 8.7, 17.0, 1H), 1.57 (d, *J* = 14.1, 1H), 1.47 (d, *J* = 14.4, 1H), 1.29 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.3, 155.1, 145.0, 137.8, 137.6, 131.2, 125.7, 123.4, 111.3, 64.8, 64.3, 54.5, 50.8, 44.5, 42.7, 42.6, 36.2, 31.4, 25.3, 21.6; IR (thin film) 2957.8, 2887.5, 1759.6, 1713.8, 1441.0, 1258.4, 1135.0, 1039.8, 1014.4, 945.0; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{20}H_{27}O_6$ $[M+H]^+$: 363.1802, found 363.1806; $[\alpha]^{25}_D$ –35.8 (*c* 0.32, $CHCl_3$).

S1: R_f = 0.32 (2:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, C_6D_6) δ 6.10 (s, 1H), 5.97 (ddd, *J* = 2.2, 3.1, 11.7, 1H), 5.59 (ddd, *J* = 3.5, 9.0, 12.0, 1H), 5.58 (d, *J* = 0.5, 1H), 3.53–3.47 (m, 2H), 3.43–3.40 (m, 1H), 3.39–3.33 (m, 1H), 3.36 (s, 3H), 2.47 (d, *J* = 15.4, 1H), 2.15 (td, *J* = 3.2, 15.1, 1H), 2.06 (d, *J* = 15.1, 1H), 1.83 (s, 3H), 1.66 (dd, *J* = 8.8, 16.5, 1H), 1.53 (d, *J* = 14.1, 1H), 1.32 (d, *J* = 14.1, 1H), 1.17 (s, 3H), 1.14 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 205.1, 155.1, 144.8, 137.8, 137.7, 130.7, 126.2, 123.9, 111.5, 64.4, 64.3, 54.5, 50.3, 44.9, 42.6, 42.1, 36.6, 30.7, 25.1, 23.8; IR (thin film) 2916, 2848, 1758, 1697, 1441, 1261, 1135, 1040, 946, 737 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{20}H_{27}O_6$ $[M+H]^+$: 363.1802, found 363.1804.[5]

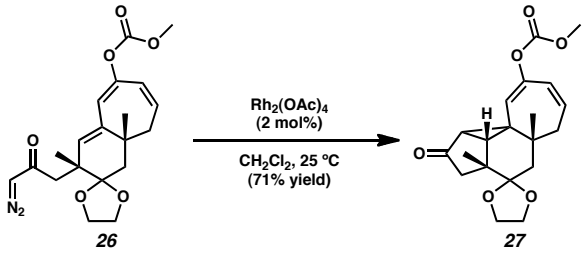
S2: R_f = 0.32 (2:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, C_6D_6) δ 9.35 (t, *J* = 1.4, 1H), 6.04 (s, 1H), 5.95 (ddd, *J* = 2.2, 3.2, 11.9, 1H), 5.59 (ddd, *J* = 3.2, 8.7, 11.9, 1H), 5.02 (d, *J* = 1.0, 1H), 3.43–3.36 (m, 4H), 3.36 (s, 3H), 2.28 (dt, *J* = 2.5, 16.7, 1H), 2.06–1.95 (m, 2H), 1.79 (ddd, *J* = 6.0, 10.0, 14.0, 1H), 1.68 (dd, *J* = 8.5, 17.0, 1H), 1.65 (ddd, *J* = 6.0, 10.0, 14.0, 1H), 1.52 (d, *J* = 14.4, 1H), 1.43 (d, *J* = 14.1, 1H), 1.23 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 200.3, 155.2, 145.0, 138.4, 137.5, 131.2, 125.8, 123.5, 112.0, 64.39, 64.37, 54.6, 42.9, 42.6, 42.5, 39.9, 36.3, 30.9, 24.7, 20.6; IR (thin film) 2922, 1760, 1722, 1441, 1259, 1118, 1040, 1015, 945 cm^{-1}; HRMS (Multimode-

ESI/APCI) *m*/*z* calc'd for $C_{20}H_{27}O_6$ $[M+H]^+$: 363.1802, found 363.1819; $[\alpha]^{25}_D = -82.4$ (*c* 0.41, $CHCl_3$).



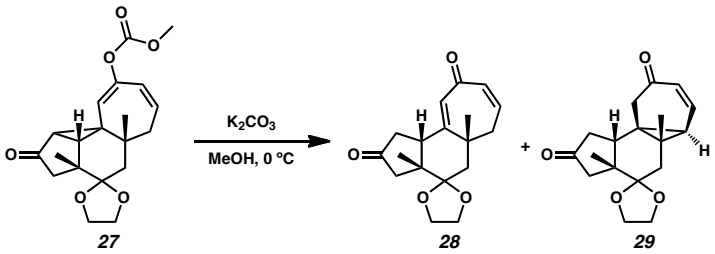
Diazoketone 26: To a –78 ºC solution of LHMDS (27 mg, 0.16 mmol, 1.5 equiv) in THF (0.40 mL, 0.40 M) was added a solution of ketone **25** (39 mg, 0.11 mmol) in THF (0.20 mL 0.50 M). The vial that previously contained **25** was next rinsed with THF (0.20 mL) and added to the reaction mixture. The solution was stirred at –78 ºC for 30 min, then 2,2,2-trifluoroethyl trifluoroacetate (46 μL, 0.34 mmol, 3.2 equiv) was added in one rapid portion and resulting reaction mixture was stirred for 30 min. The reaction mixture was poured into a separatory funnel containing diethyl ether (5.0 mL) and 1 M HCl (5.0 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (3 x 3.0 mL). The combined organic extracts were washed with brine (5.0 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was dissolved in MeCN (0.35 mL, 0.30 M). To the solution was added triethylamine (22 μL, 0.16 mmol, 1.5 equiv) and water (2.0 μL, 0.11 mmol, 1.0 equiv). A solution of *p*-acetamidobenzylsulfonyl azide (40 mg, 0.16 mmol, 1.5 equiv) in MeCN (0.27 mL, 0.40 M) was added dropwise over 25 min. The solution was stirred for 3 h then diluted with diethyl ether (15 mL) and washed with 10% NaOH (3 x 3.0 mL). The aqueous phase was extracted with diethyl ether (3.0 mL). The combined organic extract was washed with brine (3.0 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to

afford a yellow oil. The crude product was purified by column chromatography (3:1 hexanes:acetone) to afford **26** as a yellow oil (20.0 mg, 47% yield): R_f = 0.27 (3:1 hexanes:EtOAc); ^{1}H NMR (C_6D_6, 500 MHz) δ 6.03 (s, 1H), 5.95 (ddd, *J* = 2.2, 3.2, 11.9, 1H), 5.65 (s, 1H), 5.61 (ddd, *J* = 3.5, 8.8, 11.7, 1H), 4.23 (s, 1H), 3.44–3.37 (m, 4H), 3.35 (s, 3H), 2.44 (d, *J* = 13.5, 1H), 2.41 (td, *J* = 3.5, 17.0, 1H), 2.24 (d, *J* = 13.5, 1H), 1.73 (dd, *J* = 8.7, 17.0, 1H), 1.53 (d, *J* = 14.5, 1H), 1.47 (d, *J* = 14.0, 1H), 1.33 (s, 3H), 1.22 (s, 3H); ^{13}C ($CDCl_3$, 125 MHz) 193.7, 155.0, 144.6, 137.9, 136.7, 131.4, 125.2, 123.1, 111.3, 65.1, 64.9, 55.3, 44.4, 42.7, 42.5, 36.1, 25.2, 21.0; IR (thin film) 2958, 2929, 2101, 1760, 1634, 1360, 1257, 1135, 1038 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{20}H_{24}N_2O_6$ $[M + H]^+$: 389.1707, found 389.1712; $[\alpha]^{25}_D$ –334.7 (*c* 0.53, $CHCl_3$).



Cyclopropane 27: To a solution of **26** (11 mg, 0.027 mmol) in CH_2Cl_2 (1.9 mL, 0.014 M) was added a suspension of $Rh_2(OAc)_4$ (0.30 mg, 0.00050 mmol, 0.02 equiv) in CH_2Cl_2 (0.50 mL, 0.00010 M). The reaction was vigorously stirred for 3 h. The reaction was then filtered through a Celite plug and the plug was washed with CH_2Cl_2 (3 x 2.0 mL). The combined washings of CH_2Cl_2 were concentrated *in vacuo* to afford a colorless oil. The crude product was purified by column chromatography to afford **27** as a colorless oil (6.9 mg, 71% yield): R_f = 0.24 (2:1 hexanes:EtOAc); ^{1}H NMR (C_6D_6, 500 MHz) δ 5.77 (dddd, *J* =1.3, 2.2, 3.2, 12.8, 1H), 5.61 (dddd, *J* = 0.7, 3.2, 6.1, 12.8, 1H), 4.89 (d, *J* = 2.2, 1H), 3.47–3.39 (m, 1H), 3.37–3.28 (m, 3H), 3.32 (s, 3H), 2.61 (d, *J* = 17.6, 1H), 2.46 (td, *J* = 3.1, 19.6, 1H), 2.04 (d, *J* = 17.6, 1H), 1.90 (td, *J* = 1.0, 5.9, 1H), 1.82 (dd, *J*

= 6.1, 19.6, 1H), 1.60 (d, *J* = 6.1, 1H), 1.46 (s, 3H), 1.32 (d, *J* = 15.7, 1H), 1.09 (s, 3H), 0.99 (d, *J* = 15.4, 1H); ^{13}C NMR (C_6D_6, 125 MHz) δ 208.6, 154.9, 148.2, 134.2, 124.3, 123.2, 111.2, 65.1, 64.8, 55.8, 54.5, 45.4, 45.2, 44.3, 42.0, 40.9, 38.3, 36.1, 26.6, 21.4; IR (thin film) 2919, 2850, 1760, 1717, 1441, 1264, 1235, 1038, 1012 cm^{-1}; HRMS (Multimode-ESI/APCI) *m/z* calc'd for $C_{20}H_{24}O_6$ $[M + H]^+$: 361.1646, found 361.1658; $[\alpha]^{25}_D$ –51.2 (*c* 0.35, $CHCl_3$); mp 130–131 ºC.



Tricycle 28 and **Cyclopropane 29**: To a 0 ºC solution of **27** (7.2 mg, 0.020 mmol) in MeOH (1.0 mL, 0.020 M) was added K_2CO_3 (7.0 mg, 0.050 mmol, 2.5 equiv). The solution was stirred for 2 h, where upon starting material was consumed. The reaction mixture was diluted with water (1.0 mL) and extracted with diethyl ether (5 x 1.0 mL). The combined organic extracts were washed with brine (1.0 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a light-yellow residue. ^{1}H NMR analysis of the crude product showed a 1.0:1.8 mixture of **28** to **29**. The crude product was purified by column chromatography (12:1 CH_2Cl_2:EtOAc→10:1 CH_2Cl_2:EtOAc→ 5:1 CH_2Cl_2:EtOAc) to afford **28** (1.9 mg, 31% yield) and **29**. Product **29** was further purified by column chromatography (2:1 hexanes:EtOAc→1:1 hexanes:EtOAc) to afford **29** as an amorphous solid (1.8 mg, 27% yield).

28: R_f = 0.32 (5:1 CH_2Cl_2:EtOAc); ^{1}H NMR (C_6D_6), 500 MHz) δ 6.21 (ddd, *J* = 1.9, 3.1, 11.7, 1H), 6.03 (appar. t, *J* = 1.8, 1H), 5.86 (ddd, *J* = 3.2, 8.7, 11.5, 1H), 3.24–3.13 (m,

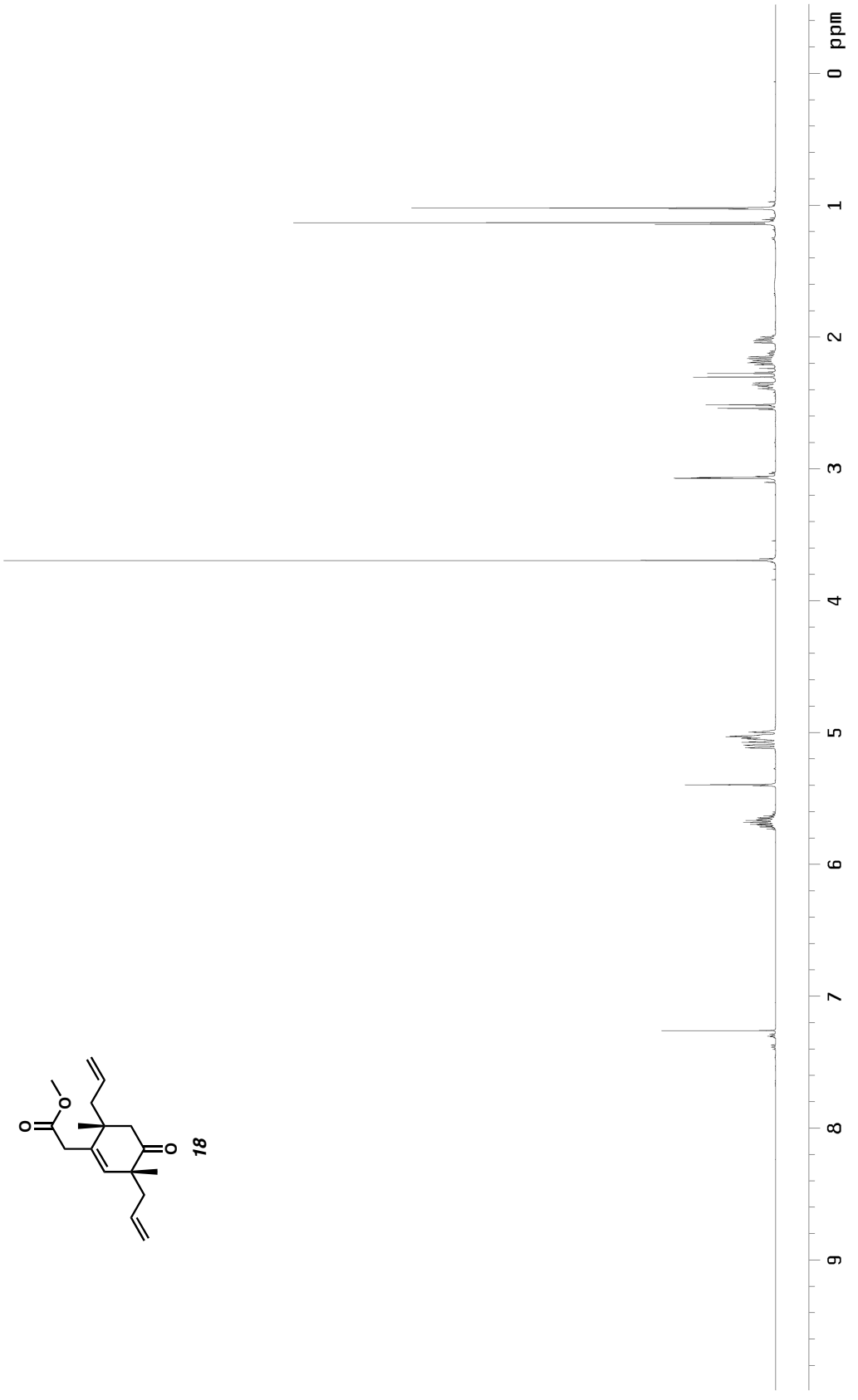
3H), 3.09–3.04 (m, 1H), 3.00 (td, *J* = 3.1, 17.0, 1H), 2.48 (d, *J* = 18.0, 1H), 2.36–2.31 (m, 2H), 2.10 (ddd, *J* = 1.1, 9.9, 19.7, 1H), 1.63 (d, *J* = 14.0, 1H), 1.62 (d, *J* = 18.0, 1H), 1.42 (dd, *J* = 8.8, 17.2, 1H), 1.08 (d, *J* = 14.4, 1H), 0.916 (s, 3H), 0.905 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) 213.2, 190.7, 158.9, 140.3, 132.9, 129.1, 110.6, 64.9, 64.1, 48.1, 47.8, 45.6, 44.5, 42.7, 41.7, 40.2, 26.4, 24.2; IR (thin film) 2958, 2918, 2849, 1742, 1738, 1652, 1605, 1173, 1069; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{18}H_{22}O_4$ [M + H]$^+$: 303.1591, found 303.1602; $[\alpha]^{25}_D$ +94.1 (*c* 0.12, $CHCl_3$).

29: R_f = 0.21 (5:1 CH_2Cl_2:EtOAc); ^{1}H NMR (C_6D_6), 500 MHz) δ 6.42 (dd, *J* = 6.3, 10.1, 1H), 5.99 (d, *J* = 9.9, 1H), 3.28–3.25 (m, 1H), 3.23–3.16 (m, 3H), 2.53 (dd, *J* = 1.8, 19.4, 1H), 2.33 (dd, *J* = 1.8, 17.8, 1H), 2.11 (ddd, *J* = 2.0, 11.0, 18.5, 1H), 2.04 (dd, *J* = 1.5, 19.0, 1H), 2.02 (dd, *J* = 10, 18.5, 1H), 1.85 (dd, *J* = 1.8, 6.3, 1H), 1.64 (t, *J* = 10.5, 1H), 1.61 (d, *J* = 14.5, 1H), 1.52 (d, *J* = 14.8, 1H), 1.46 (dd, *J* = 0.6, 18.0, 1H), 0.86 (s, 1H), 0.67 (s, 1H); ^{13}C NMR (C_6D_6, 125 MHz) δ 213.8, 194.7, 147.6, 112.4, 64.9, 64.1, 50.3, 47.5, 44.2, 43.0, 42.0, 36.0, 32.8, 29.1, 24.5, 22.9, 14.8; IR (thin film) 2918, 1741, 1661, 1396, 1248, 1182, 1140, 1061, 991 cm^{-1}; HRMS (Multimode-ESI/APCI) *m*/*z* calc'd for $C_{18}H_{22}O_4$ [M + H]$^+$: 303.1591, found 303.1603; $[\alpha]^{25}_D$ +28.5 (*c* 0.080, $CHCl_3$); decomposed at 157.1 ºC.

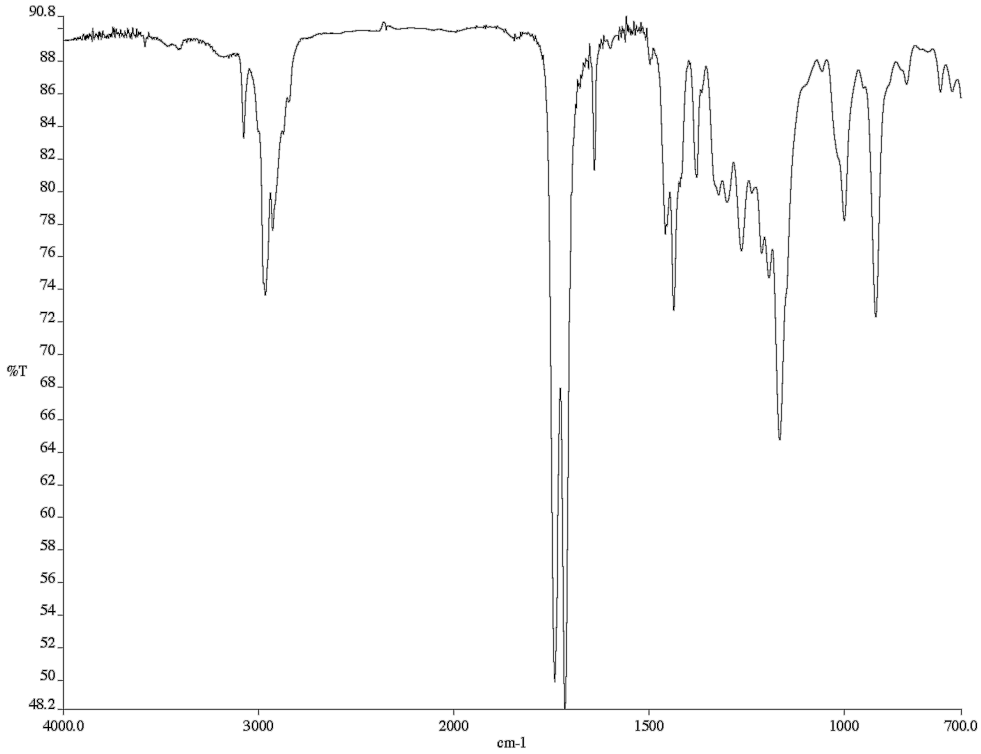
References

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15* 1518–1520.
(2) The ^{13}C NMR was taken at 273K; higher temperatures (298K and 323K) resulted in lower resolution of certain peaks due to line broadening.
(3) (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179. (b) Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 9973–9976.

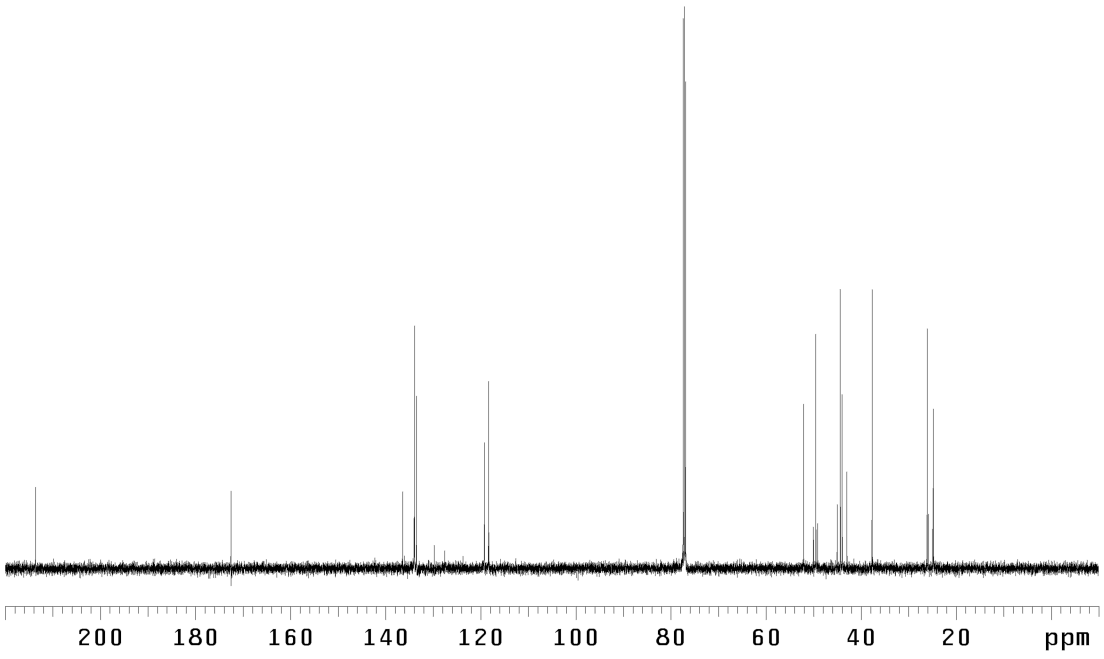
(4) An aldehyde product derived from the minor diastereomer of **24** was obtained, but was of insufficient purity to characterize.
(5) Minor diastereomer **S1** is derived from *meso*-**12** and is achiral, thus no optical rotation was obtained.



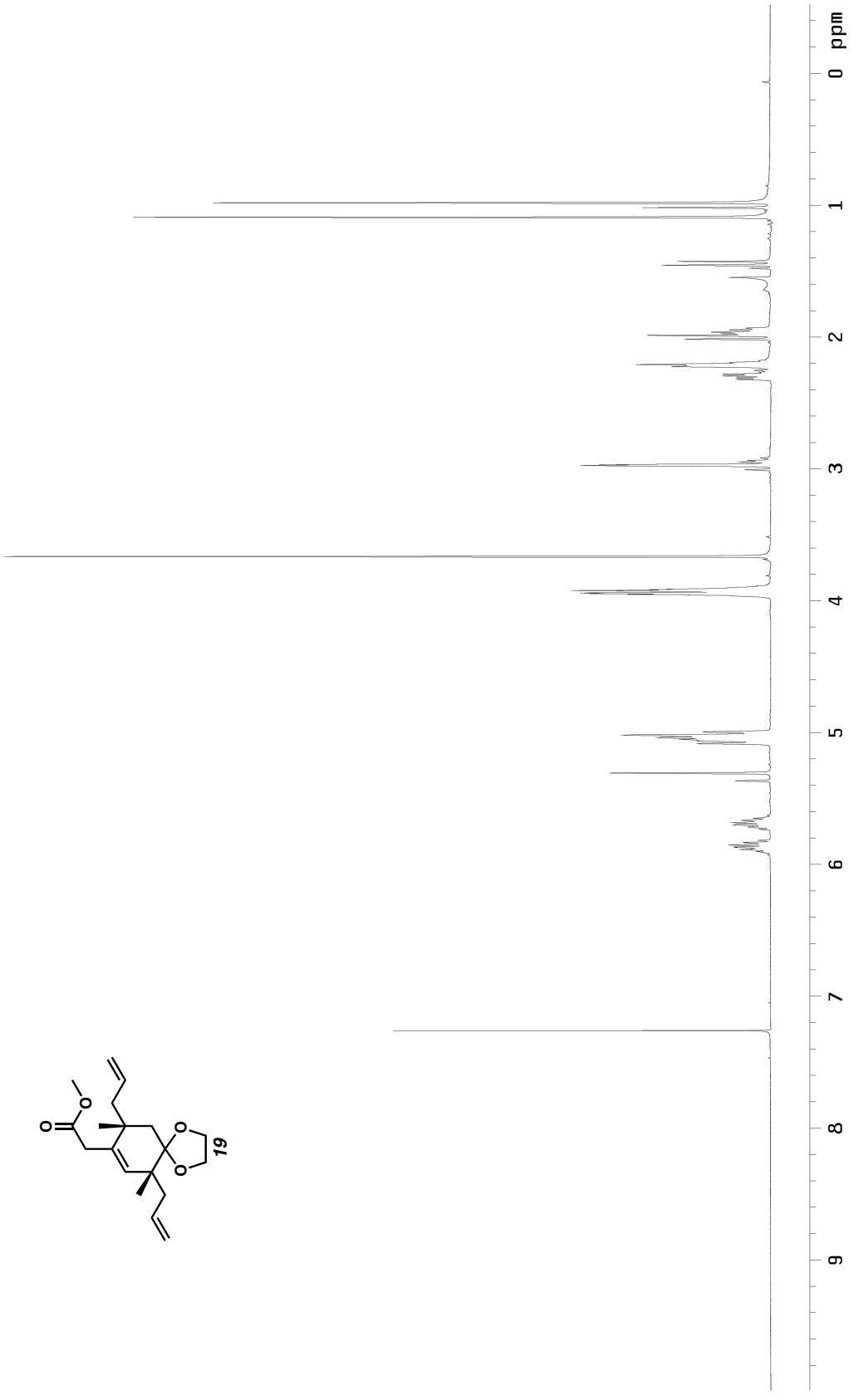
^{1}H NMR (500 MHz, $CDCl_3$) of compound **18**.



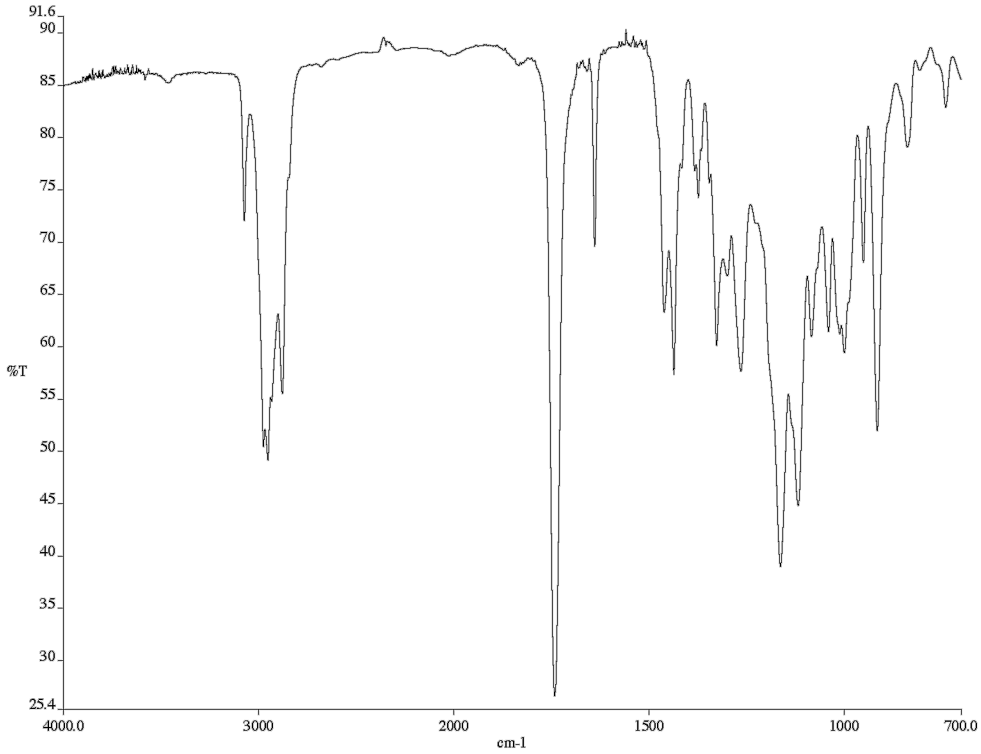
Infrared spectrum (thin film/NaCl) of compound **18**.



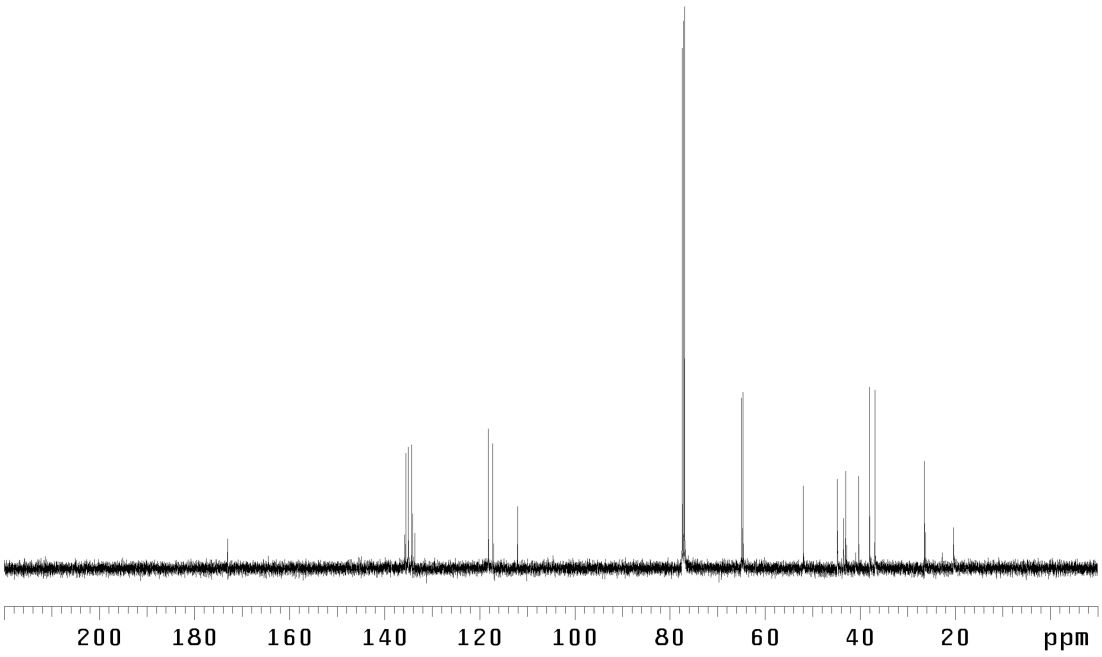
^{13}C NMR (125 MHz, $CDCl_3$) of compound **18**.



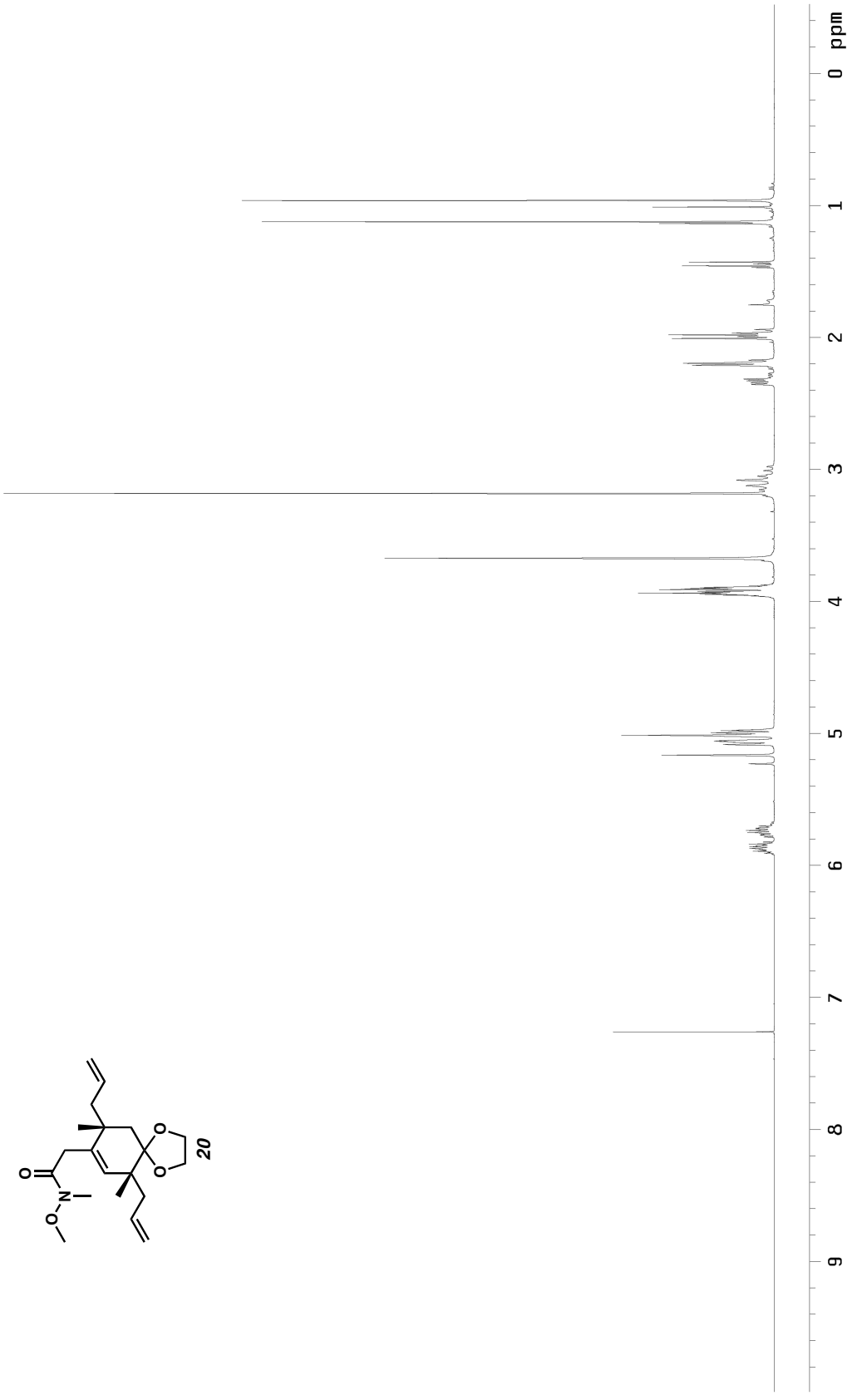
^{1}H NMR (500 MHz, $CDCl_3$) of compound **19**.



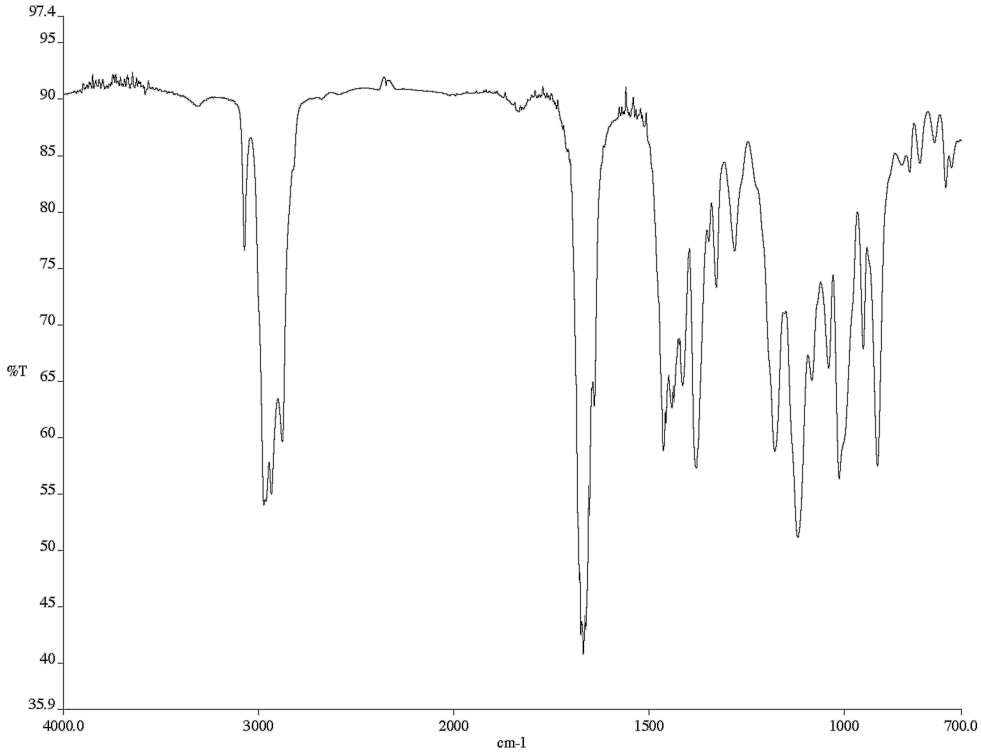
Infrared spectrum (thin film/NaCl) of compound **19**.



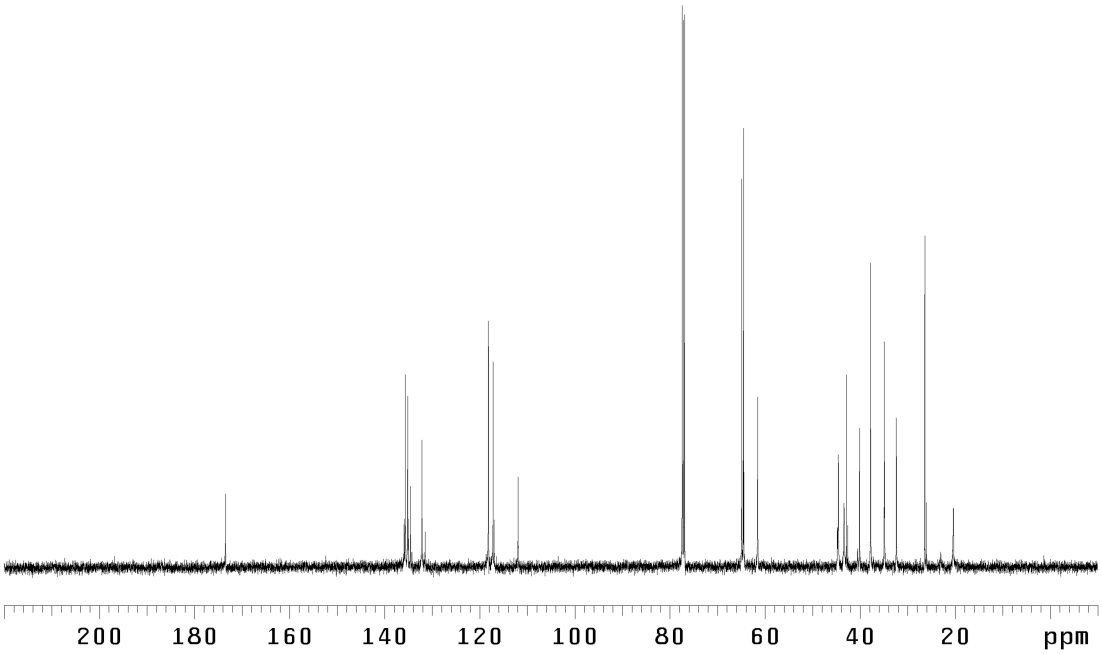
^{13}C NMR (125 MHz, $CDCl_3$) of compound **19**.



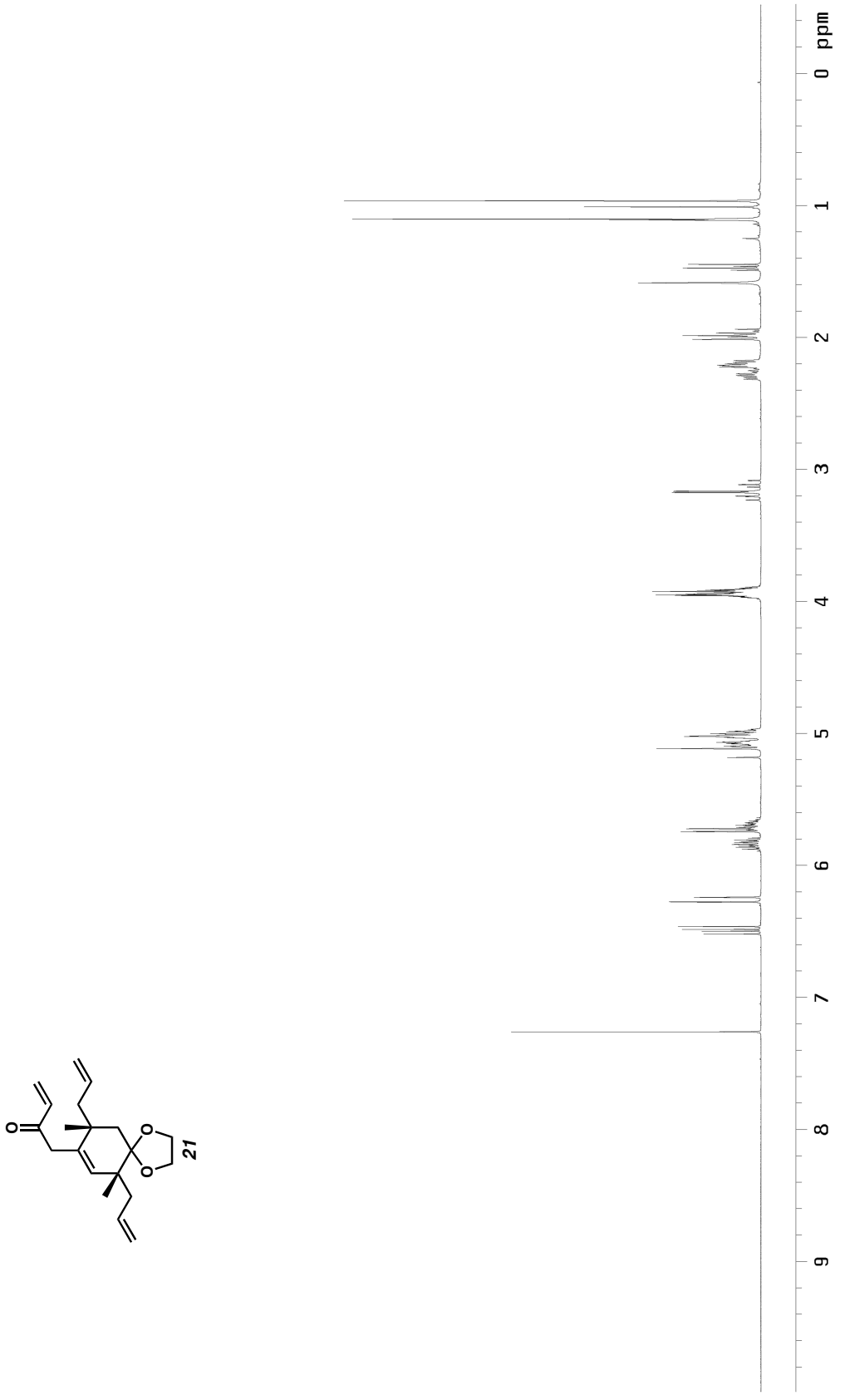
^{1}H NMR (500 MHz, $CDCl_3$) of compound **20**.



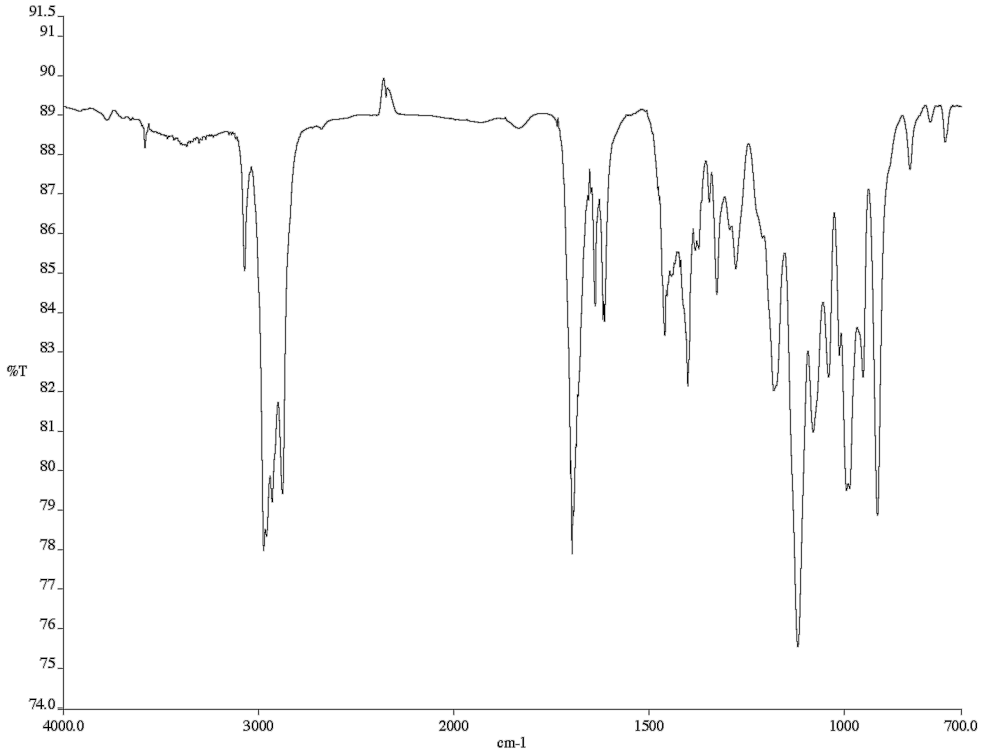
Infrared spectrum (thin film/NaCl) of compound **20**.



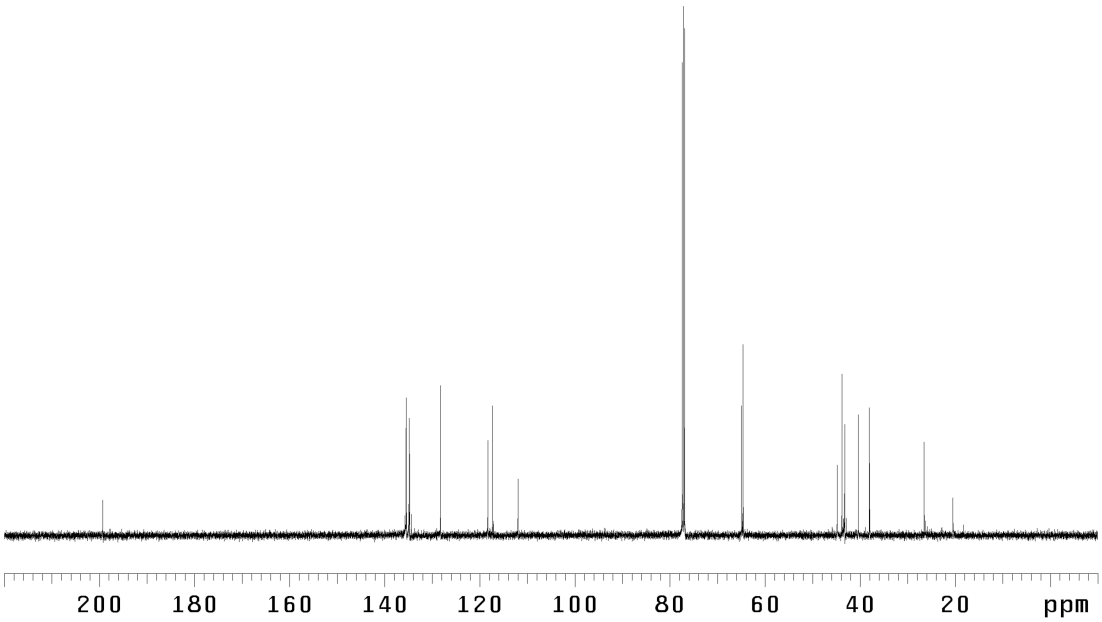
^{13}C NMR (125 MHz, $CDCl_3$) of compound **20**.



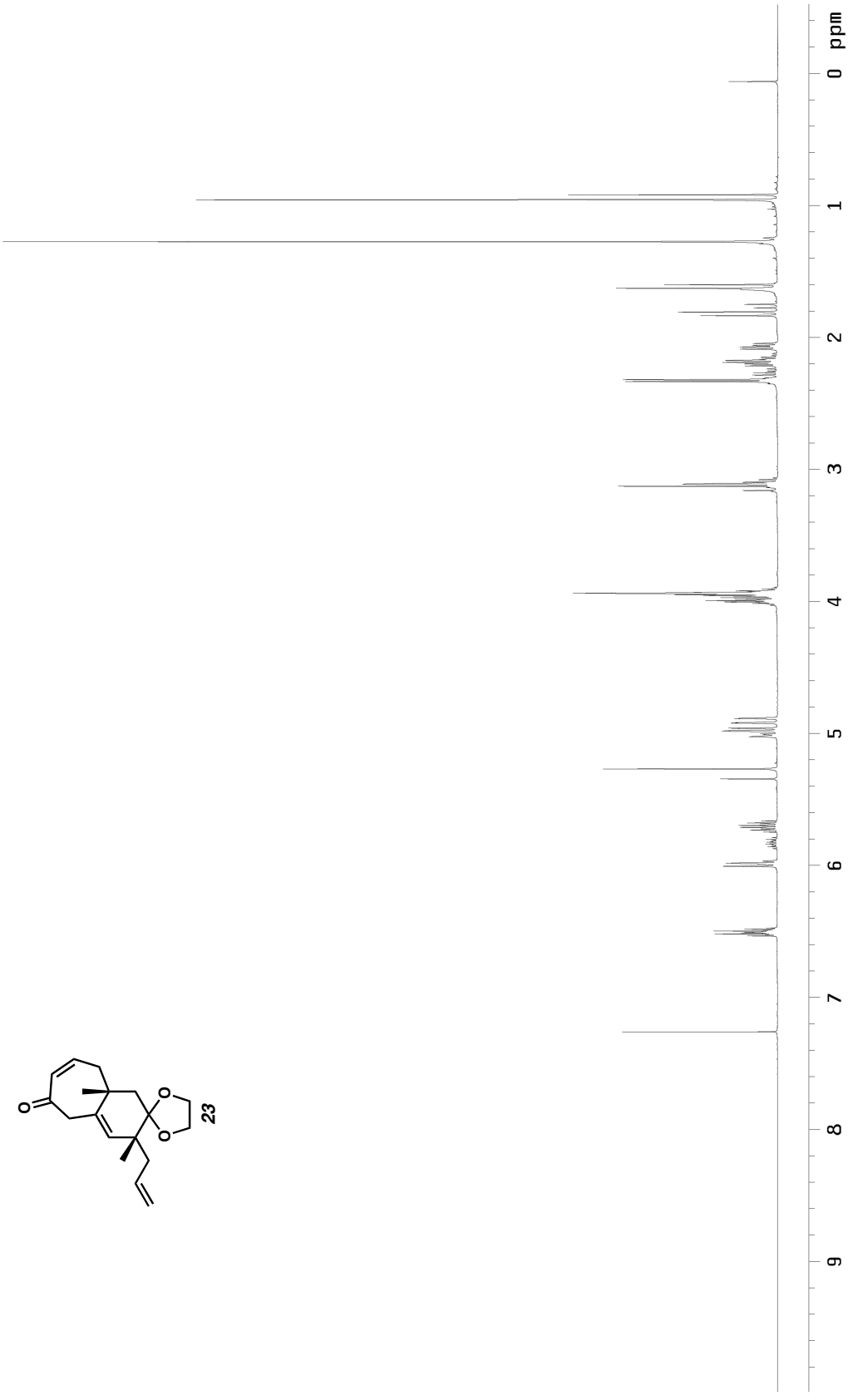
^{1}H NMR (500 MHz, $CDCl_3$) of compound **21**.



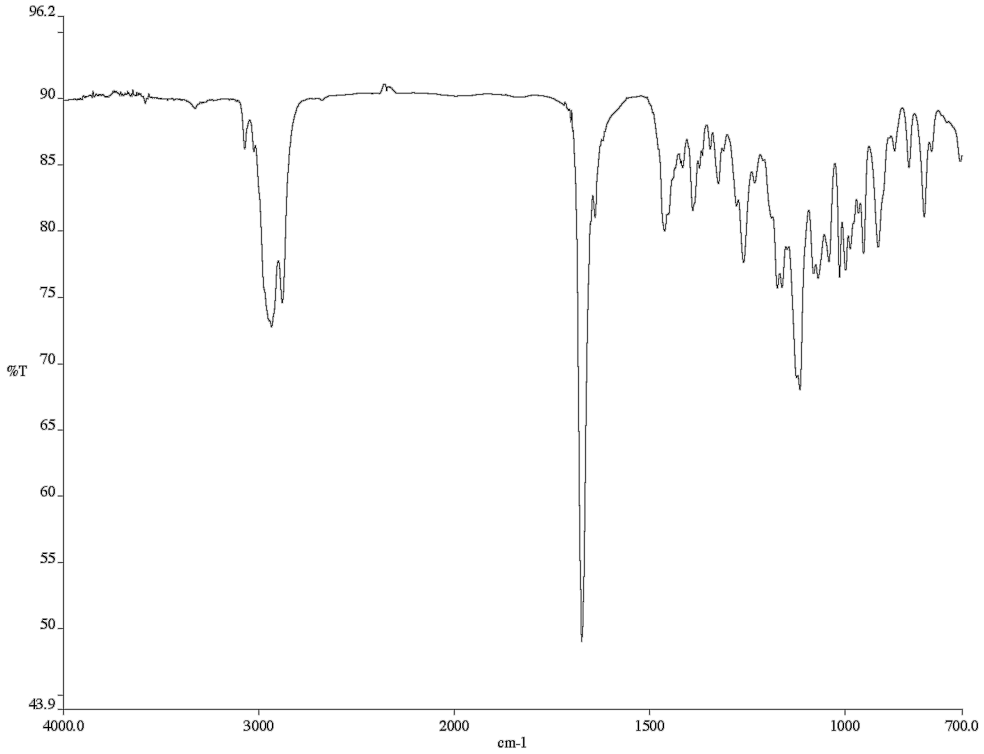
Infrared spectrum (thin film/NaCl) of compound **21**.



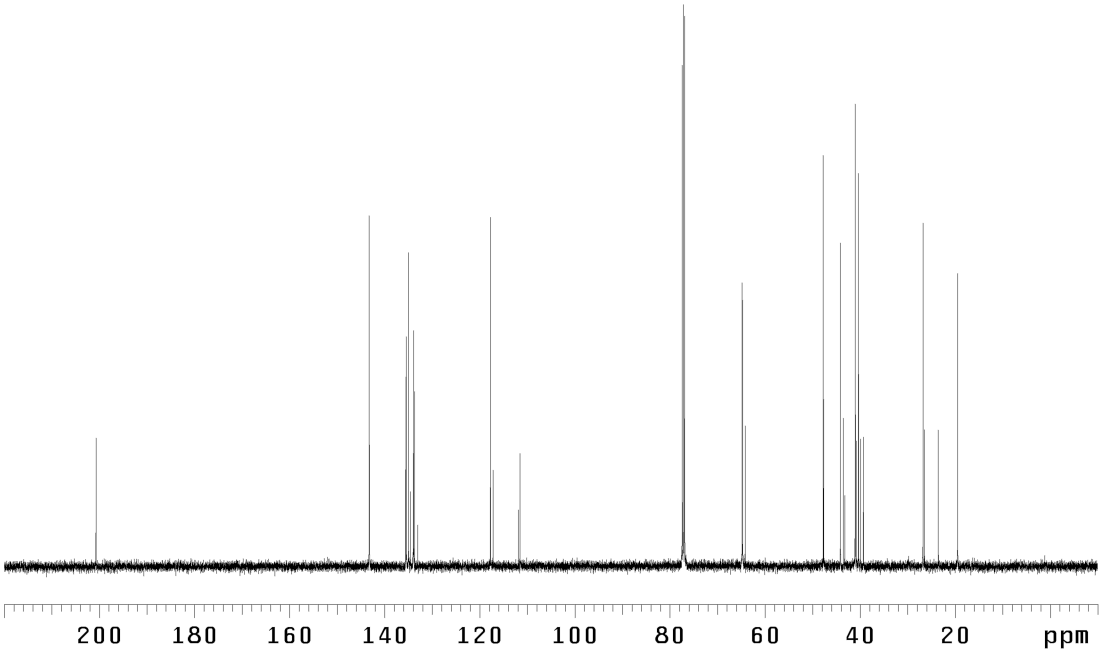
^{13}C NMR (500 MHz, $CDCl_3$) of compound **21**.



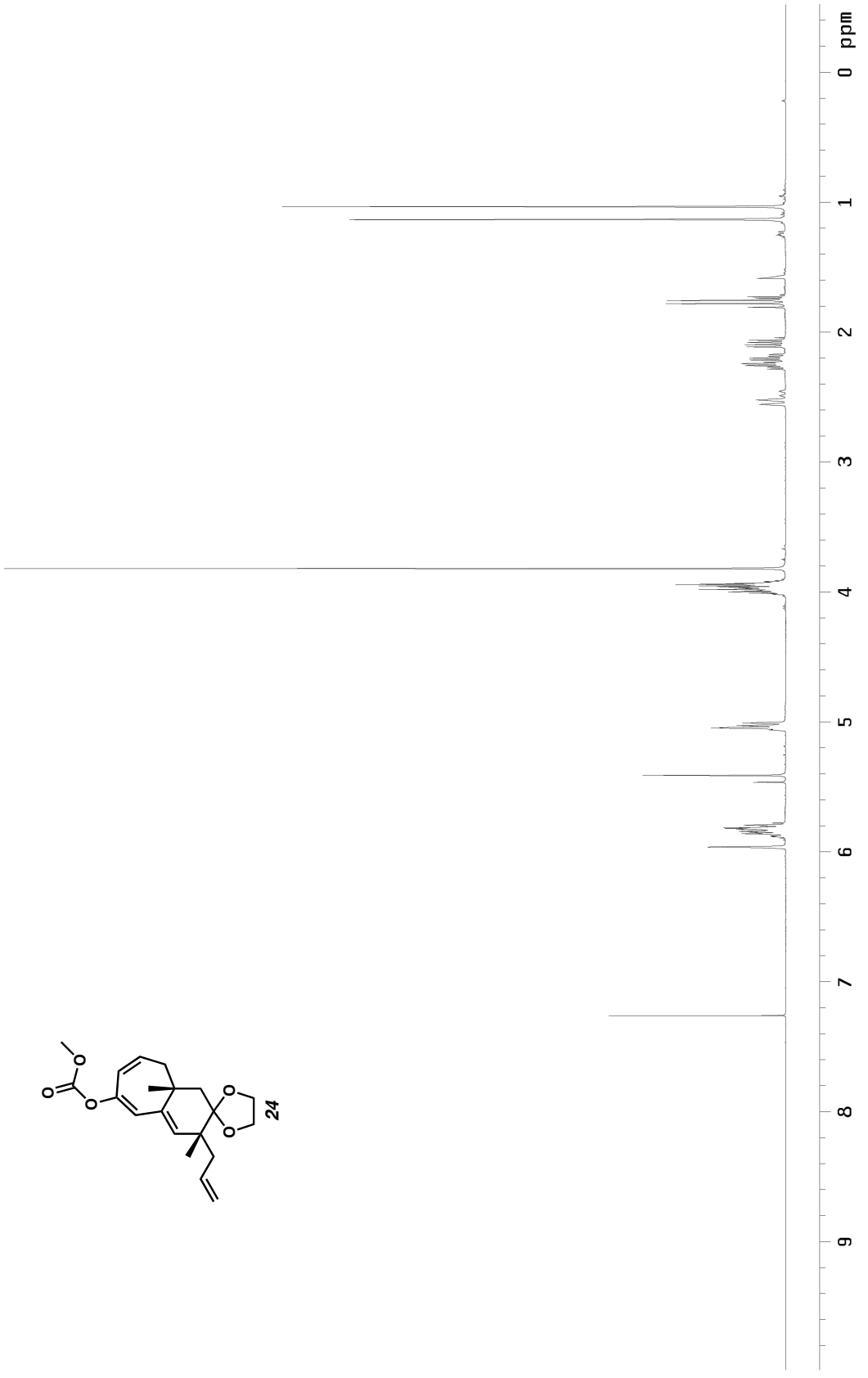
^{1}H NMR (500 MHz, $CDCl_3$) of compound **23**.



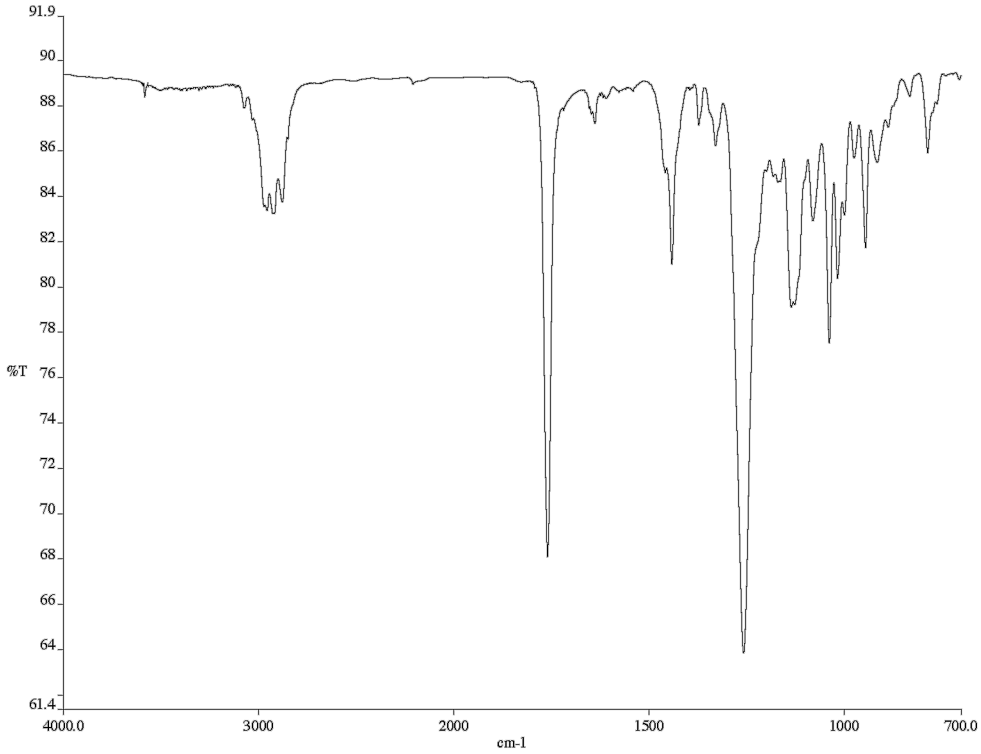
Infrared spectrum (thin film/NaCl) of compound **23**.



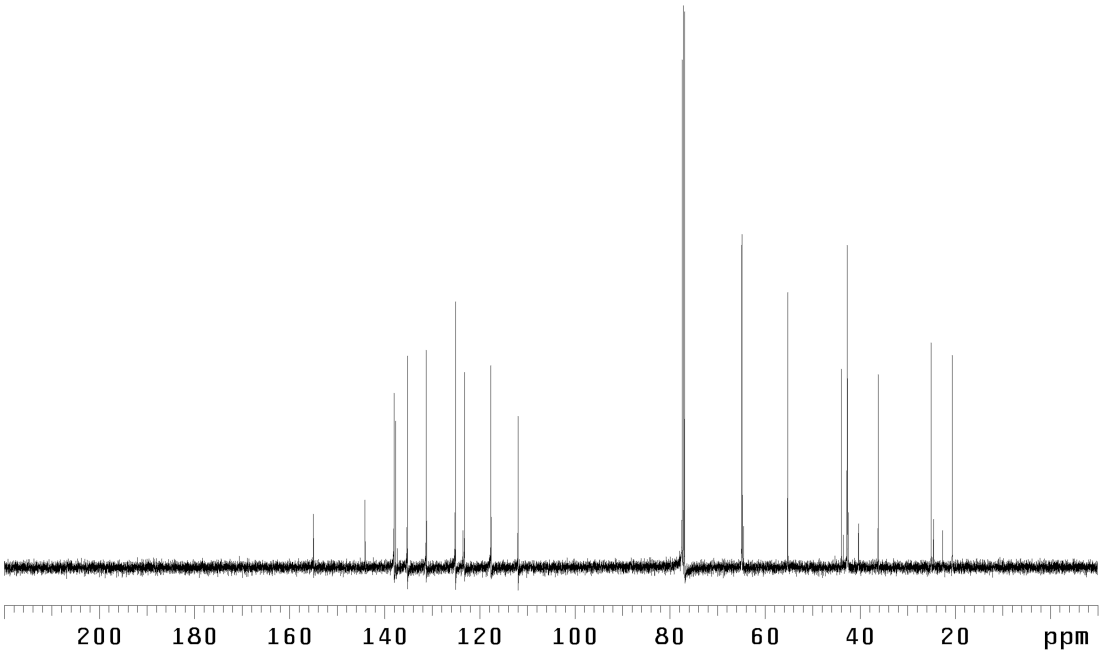
^{13}C NMR (125 MHz, $CDCl_3$) of compound **23**.



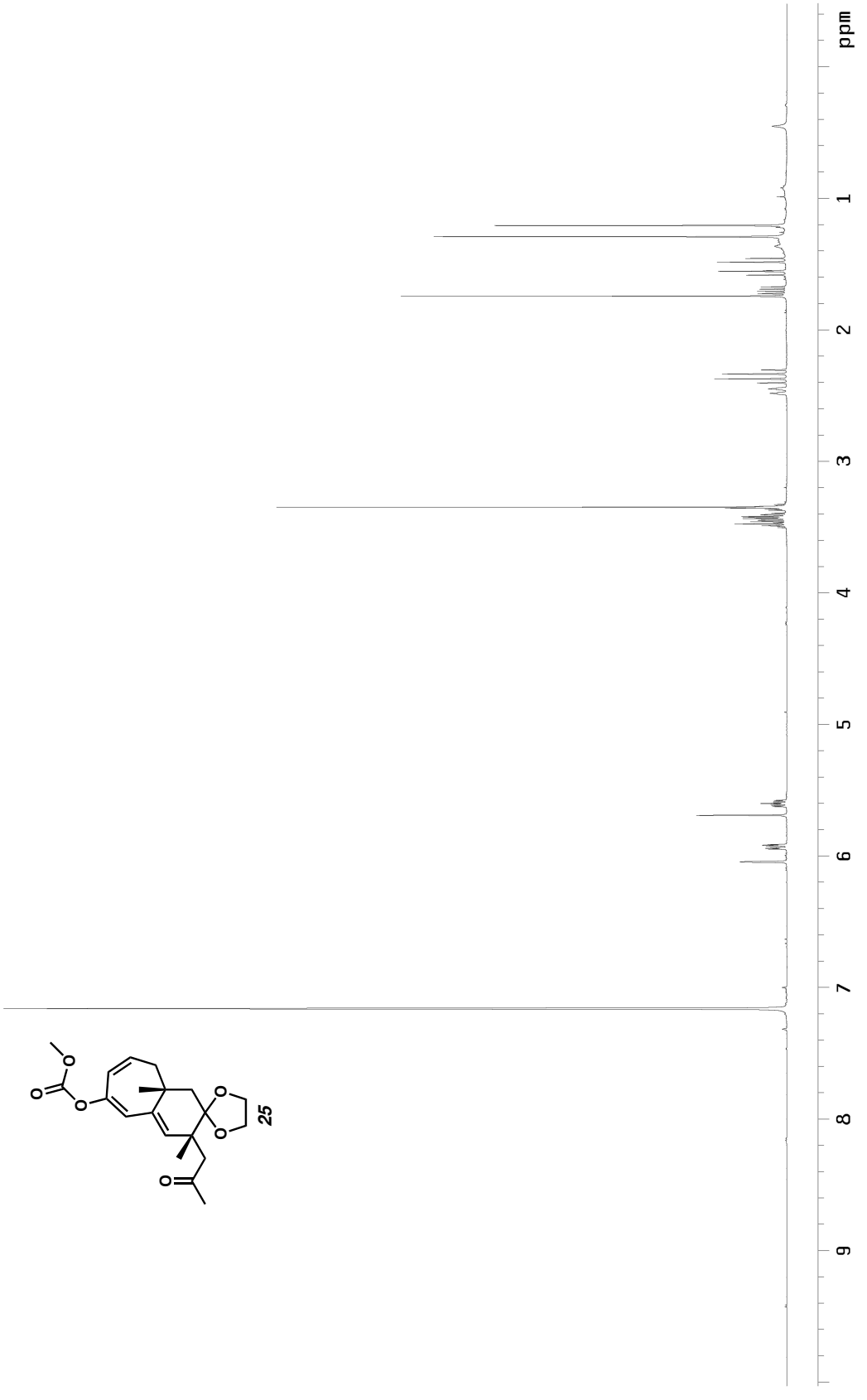
^{1}H NMR (500 MHz, $CDCl_3$) of compound **24**.



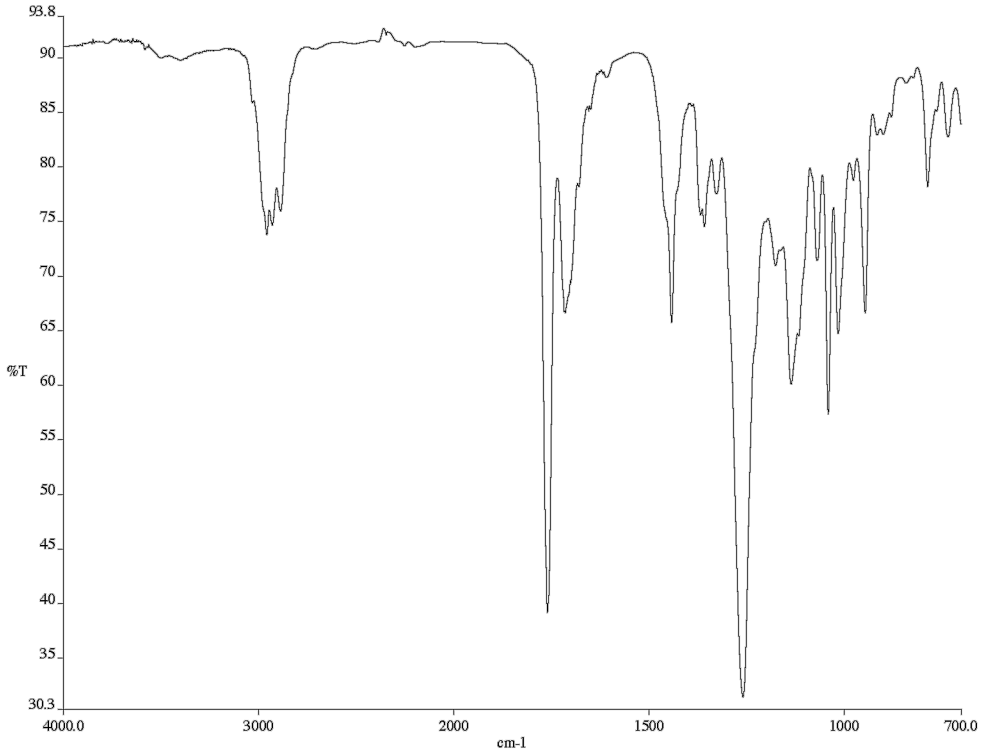
Infrared spectrum (thin film/NaCl) of compound **24**.



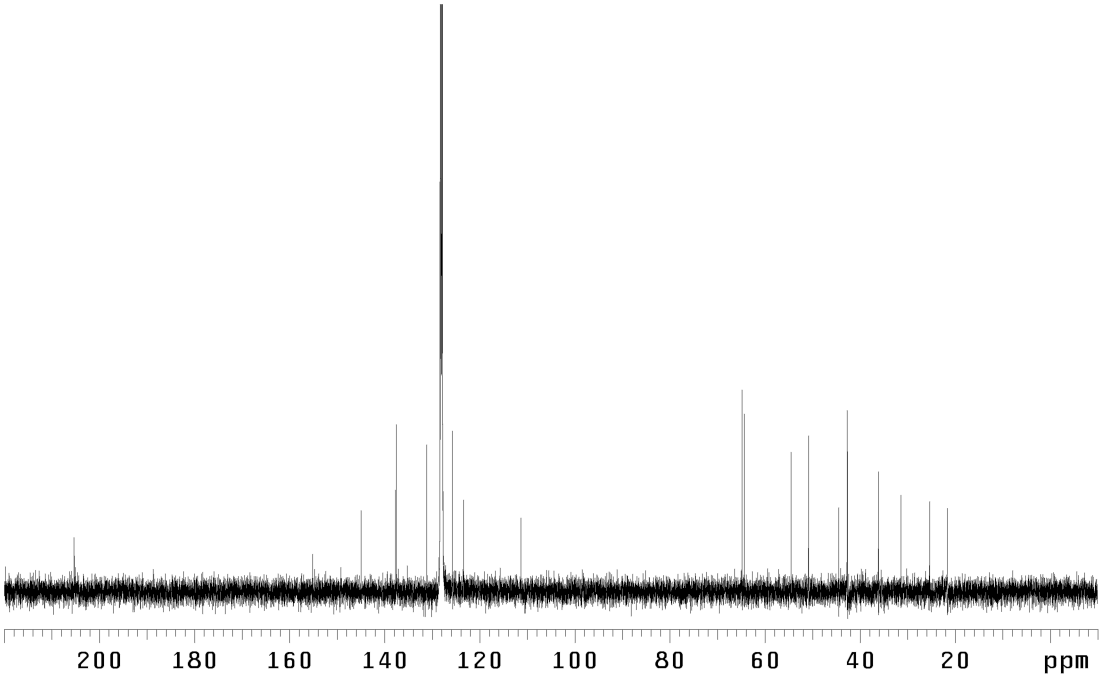
^{13}C NMR (125 MHz, $CDCl_3$) of compound **24**.



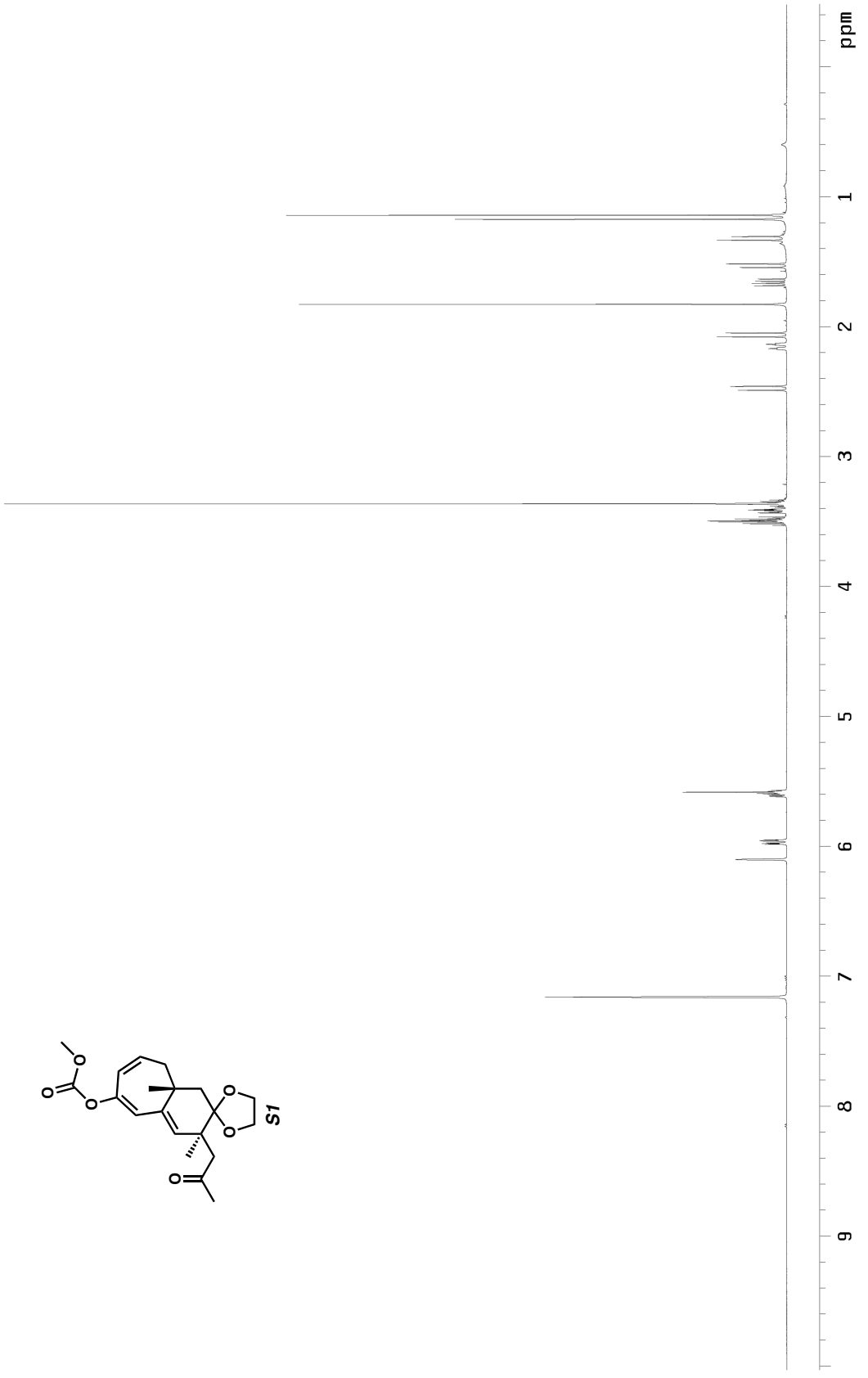
^{1}H NMR (500 MHz, C_6D_6) of compound **25**.



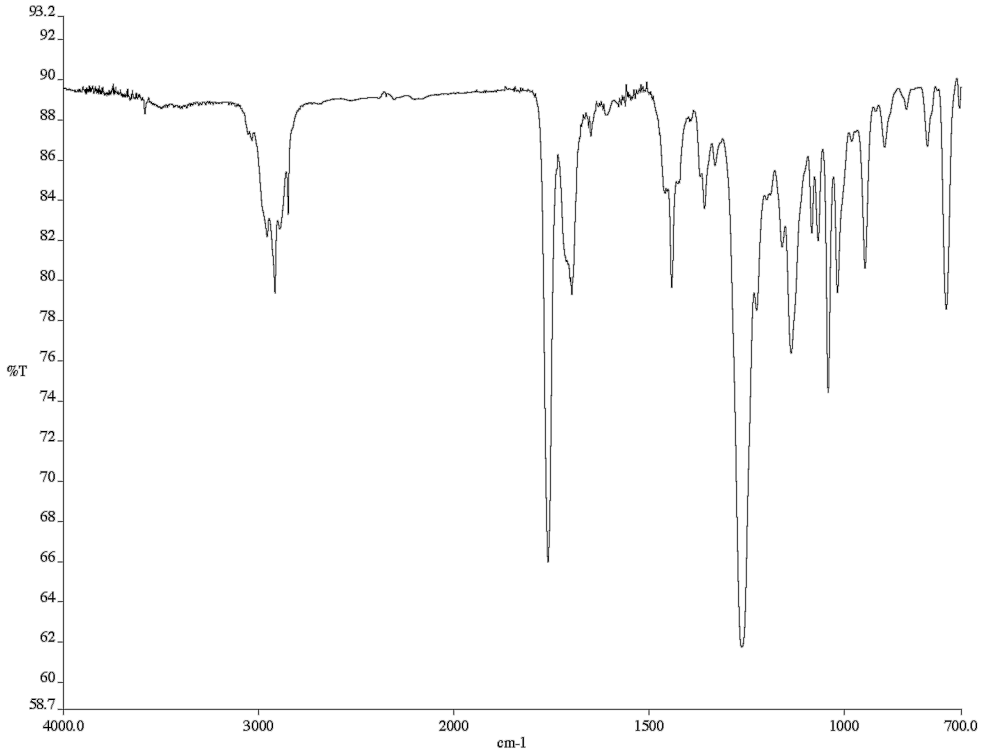
Infrared spectrum (thin film/NaCl) of compound **25**.



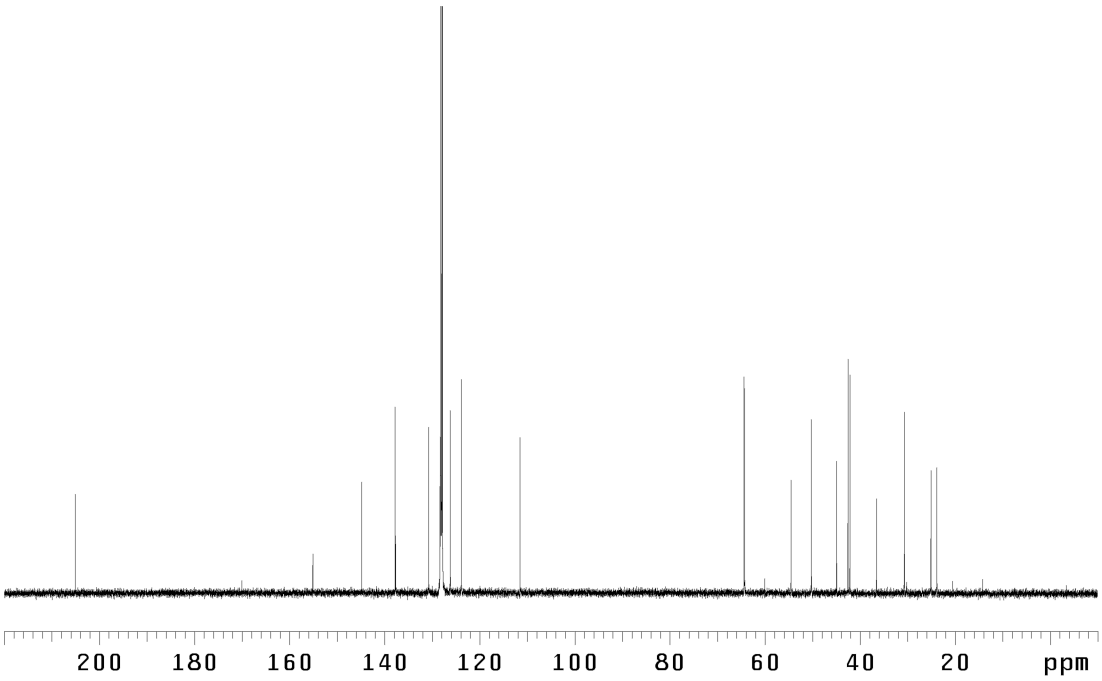
^{13}C NMR (125 MHz, C_6D_6) of compound **25**.



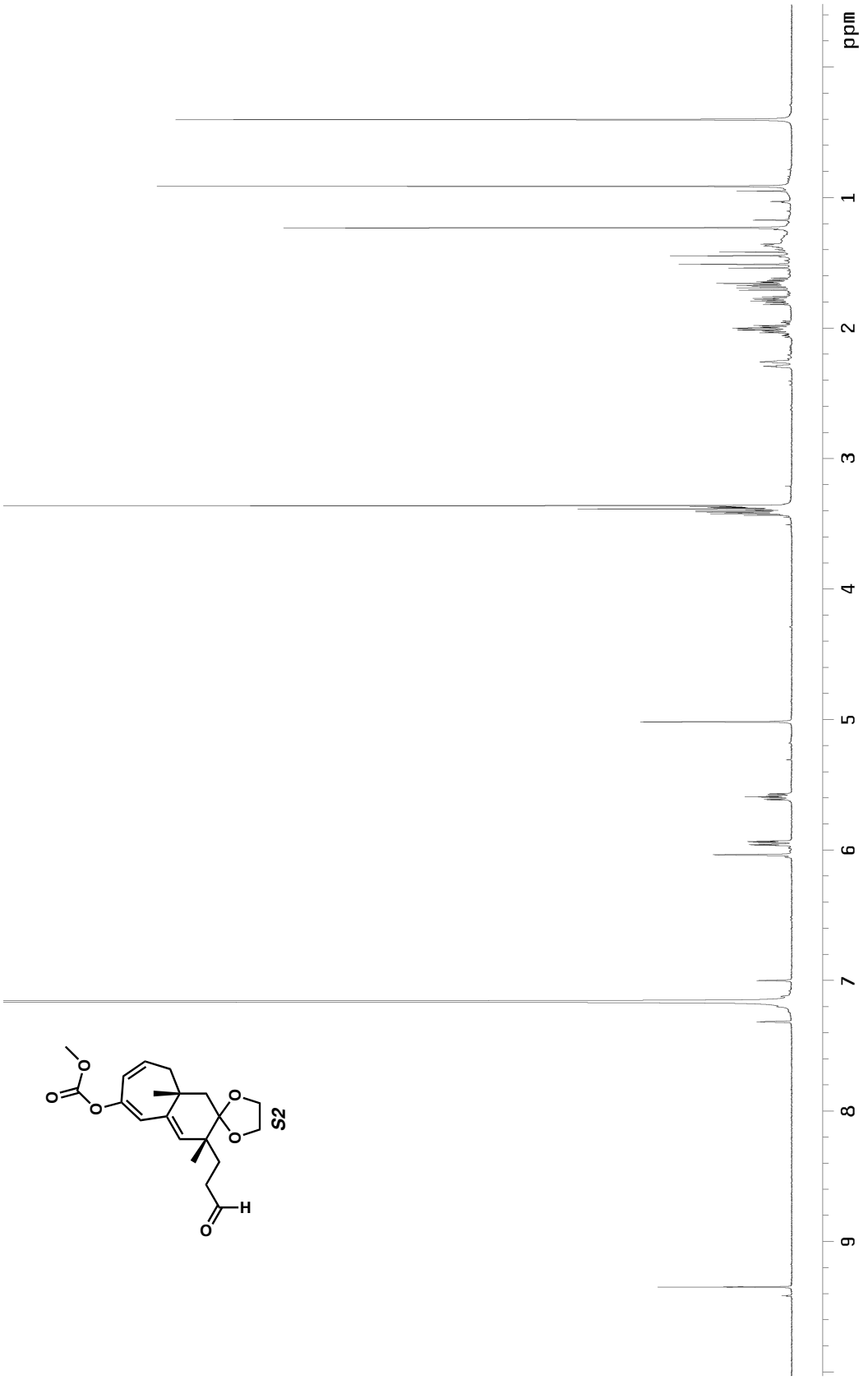
^{1}H NMR (500 MHz, C_6D_6) of compound **S1**.



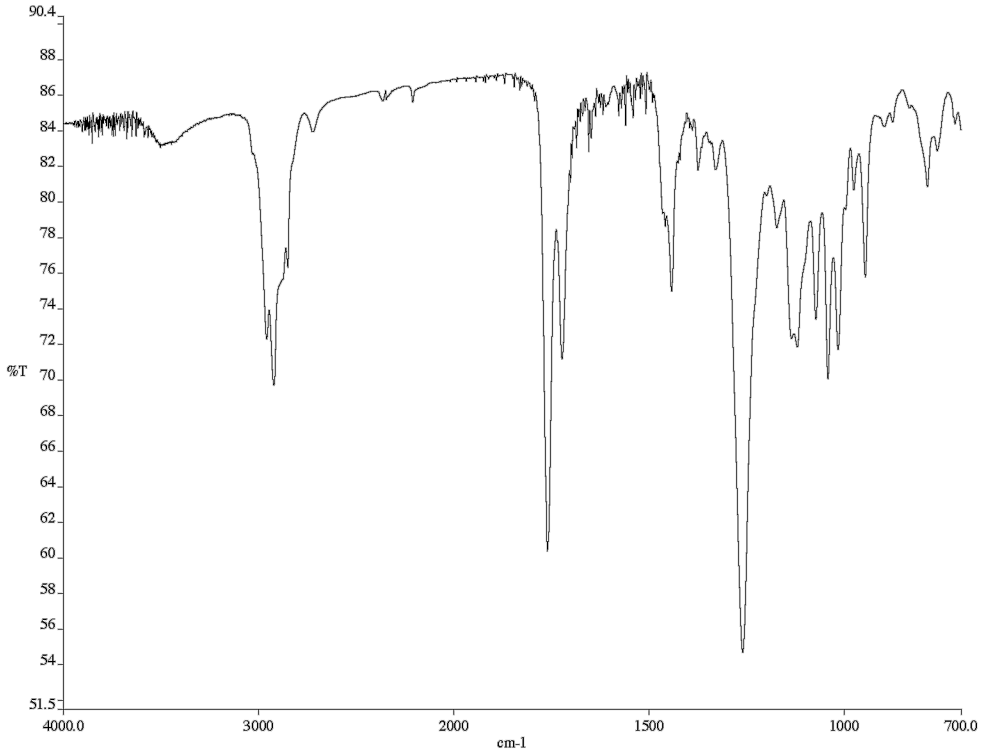
Infrared spectrum (thin film/NaCl) of compound **S1**.



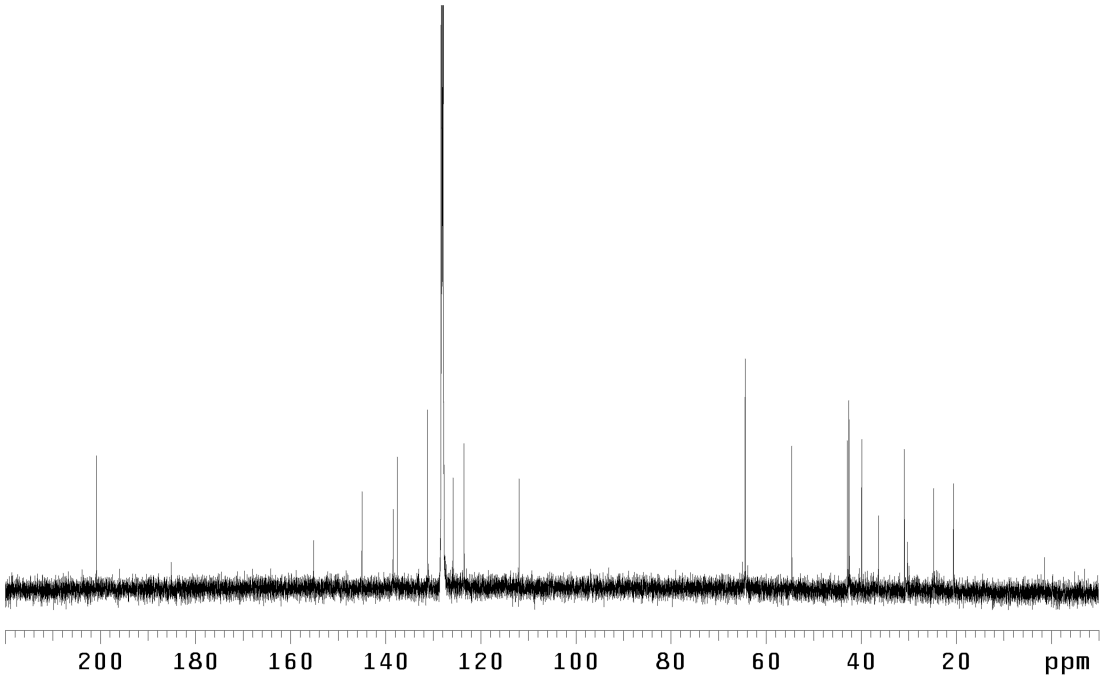
^{13}C NMR (125 MHz, C_6D_6) of compound **S1**.



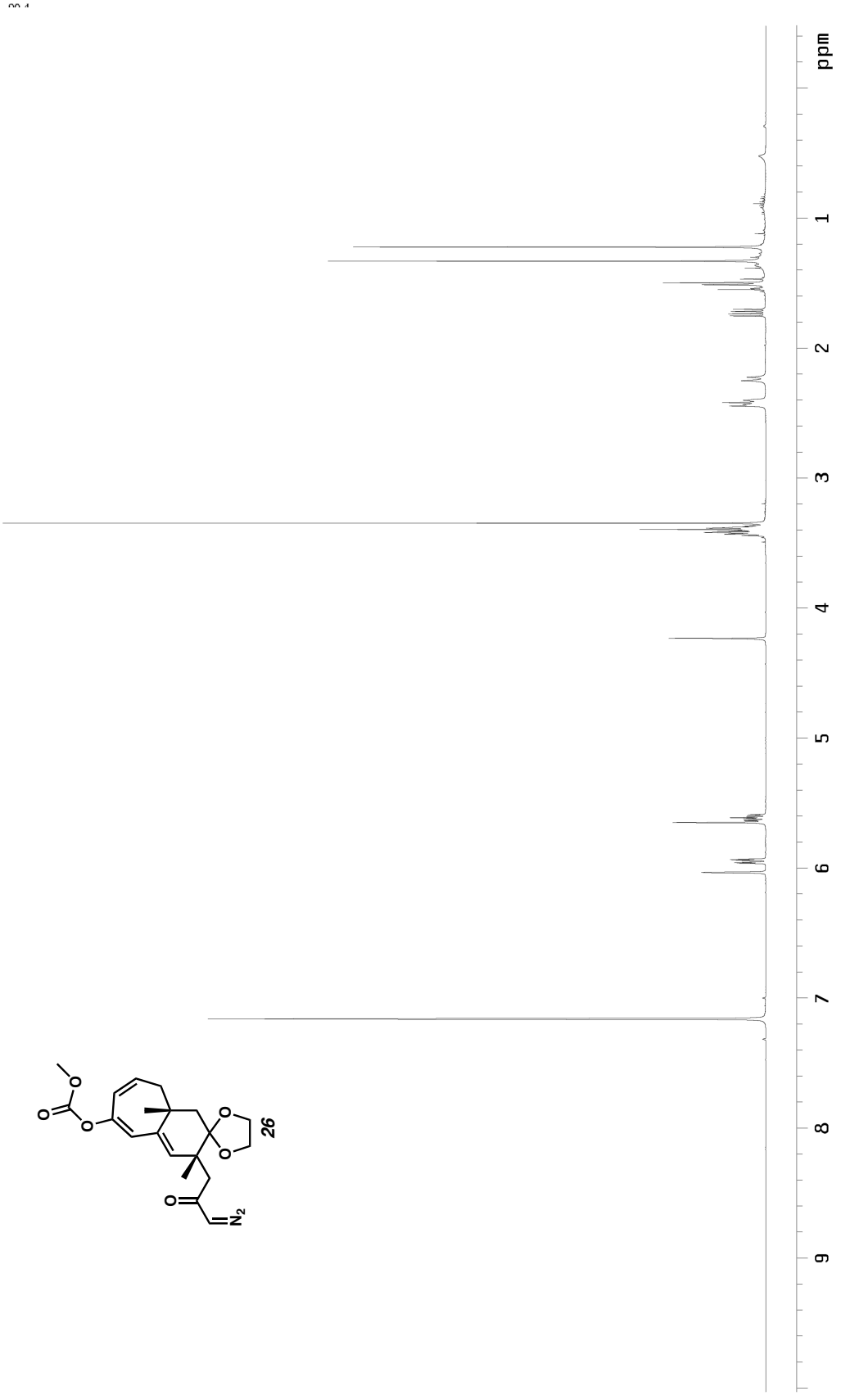
^{1}H NMR (500 MHz, C_6D_6) of compound **S2**.



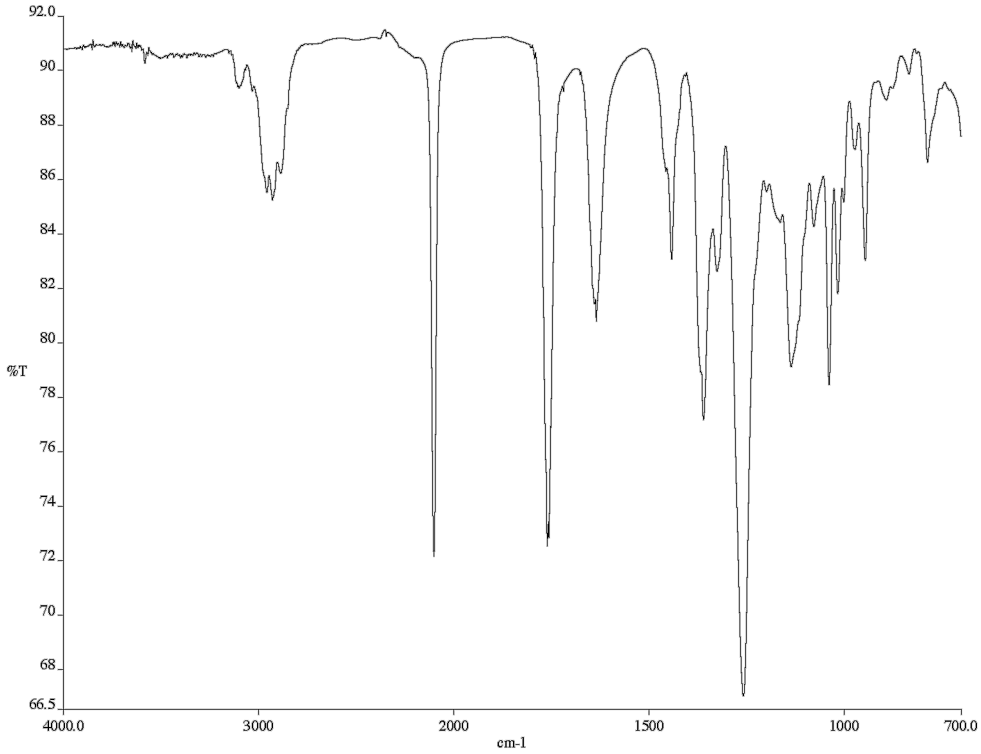
Infrared spectrum (thin film/NaCl) of compound **S2**.



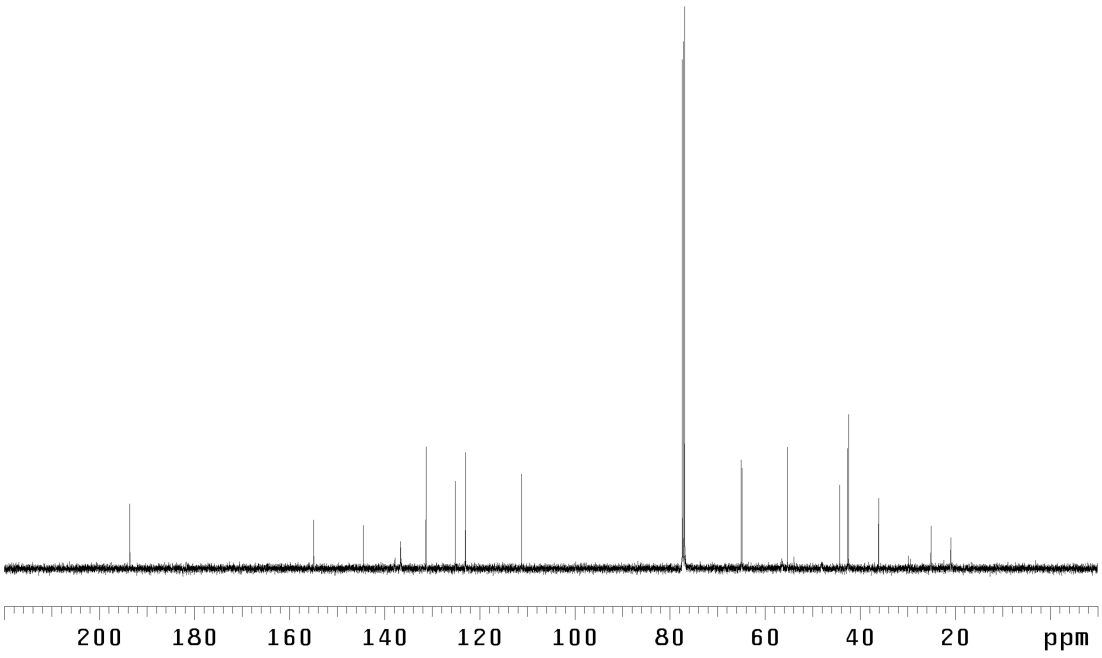
^{13}C NMR (125 MHz, $CDCl_3$) of compound **26**.



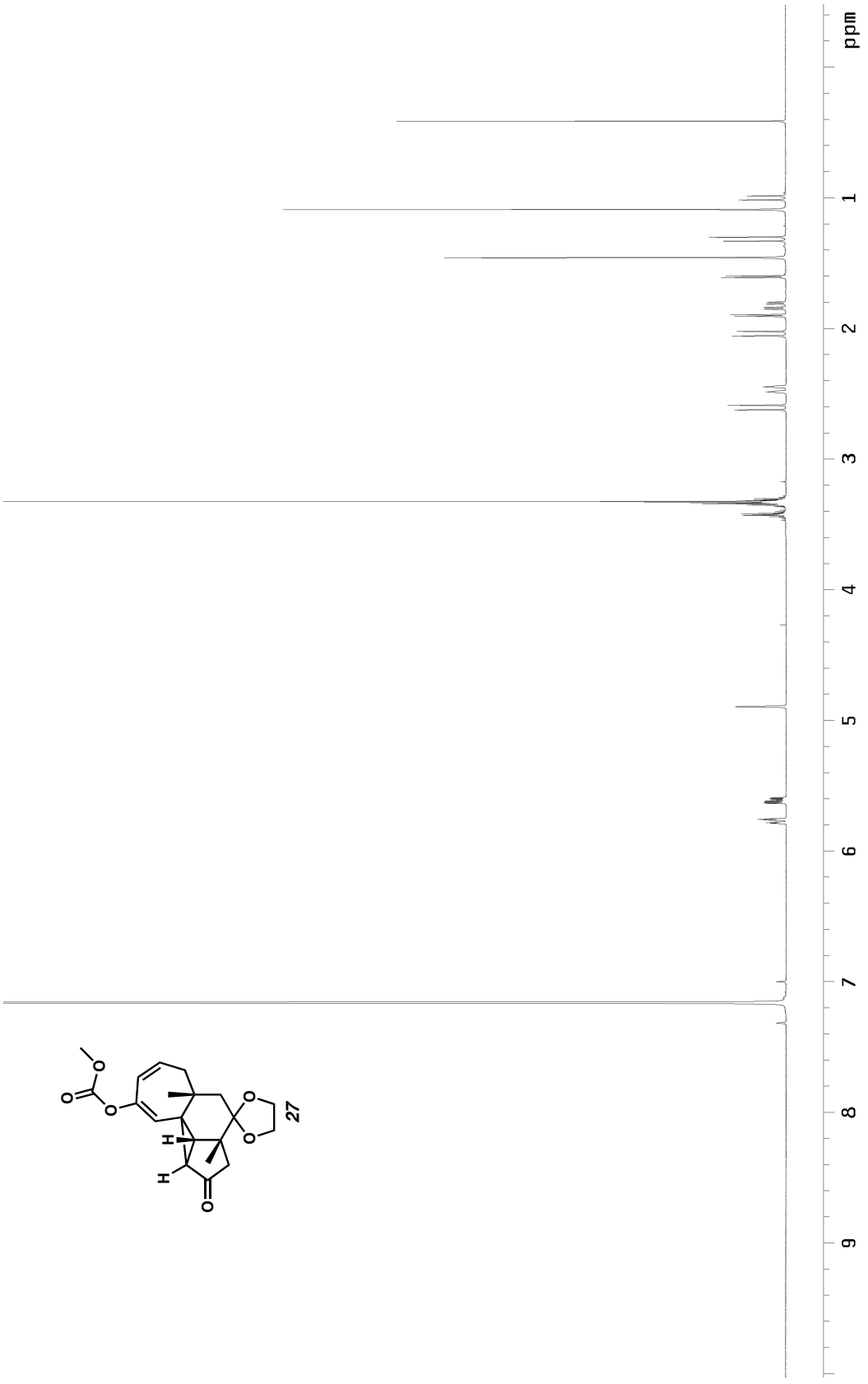
^{1}H NMR (500 MHz, C_6D_6) of compound **26**.



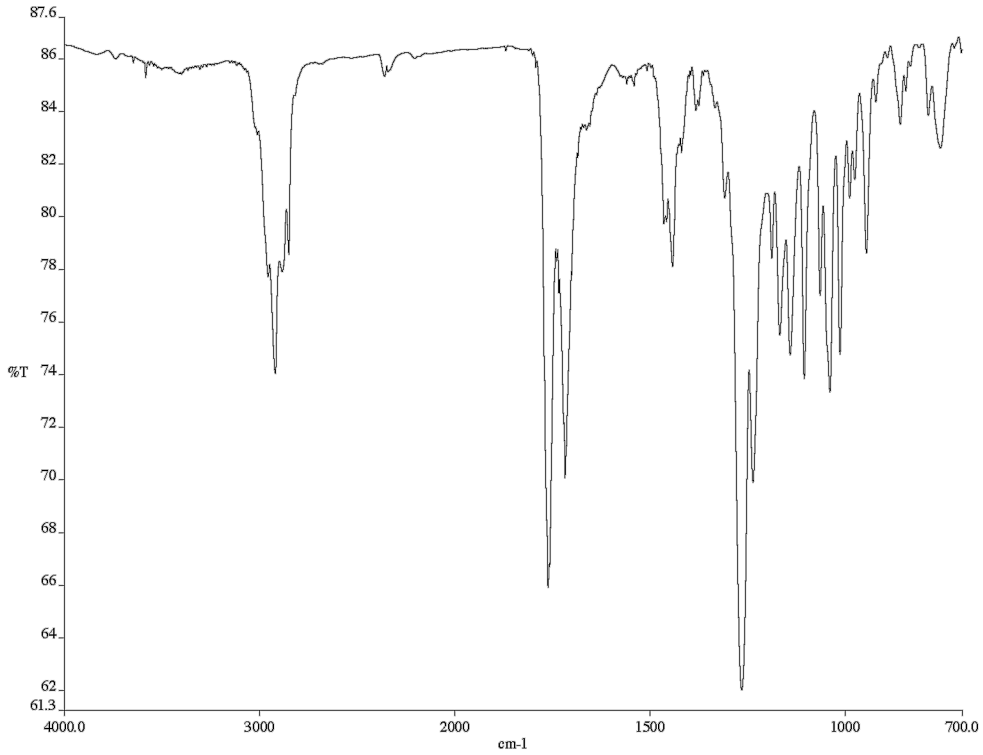
Infrared spectrum (thin film/NaCl) of compound **26**.



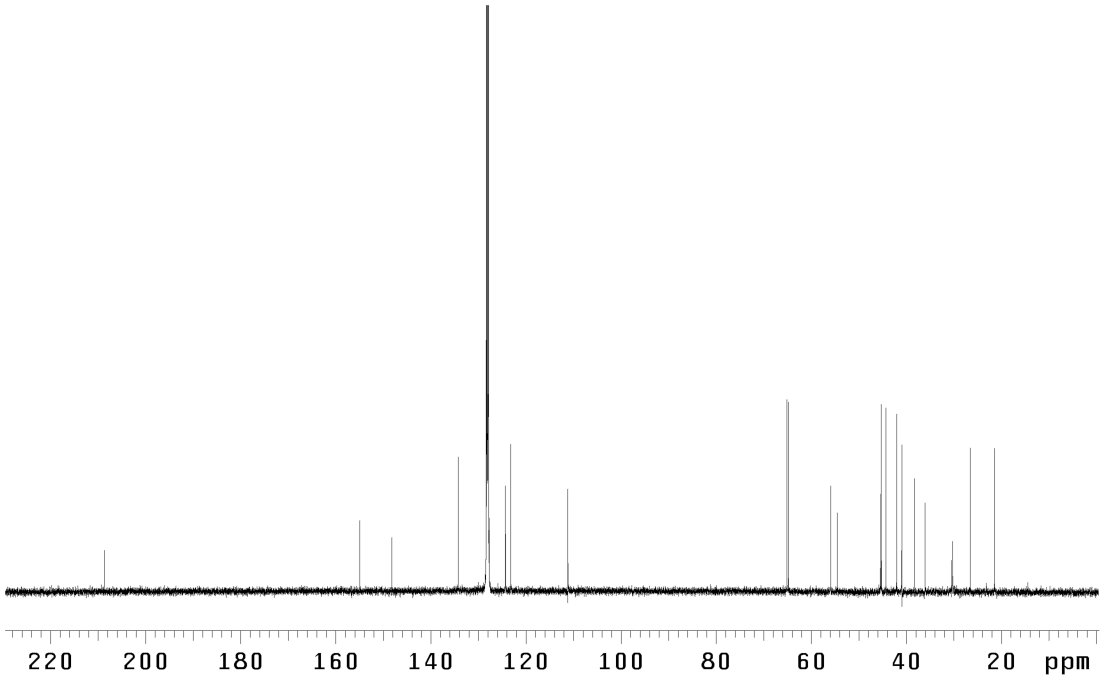
^{13}C NMR (125 MHz, $CDCl_3$) of compound **26**.



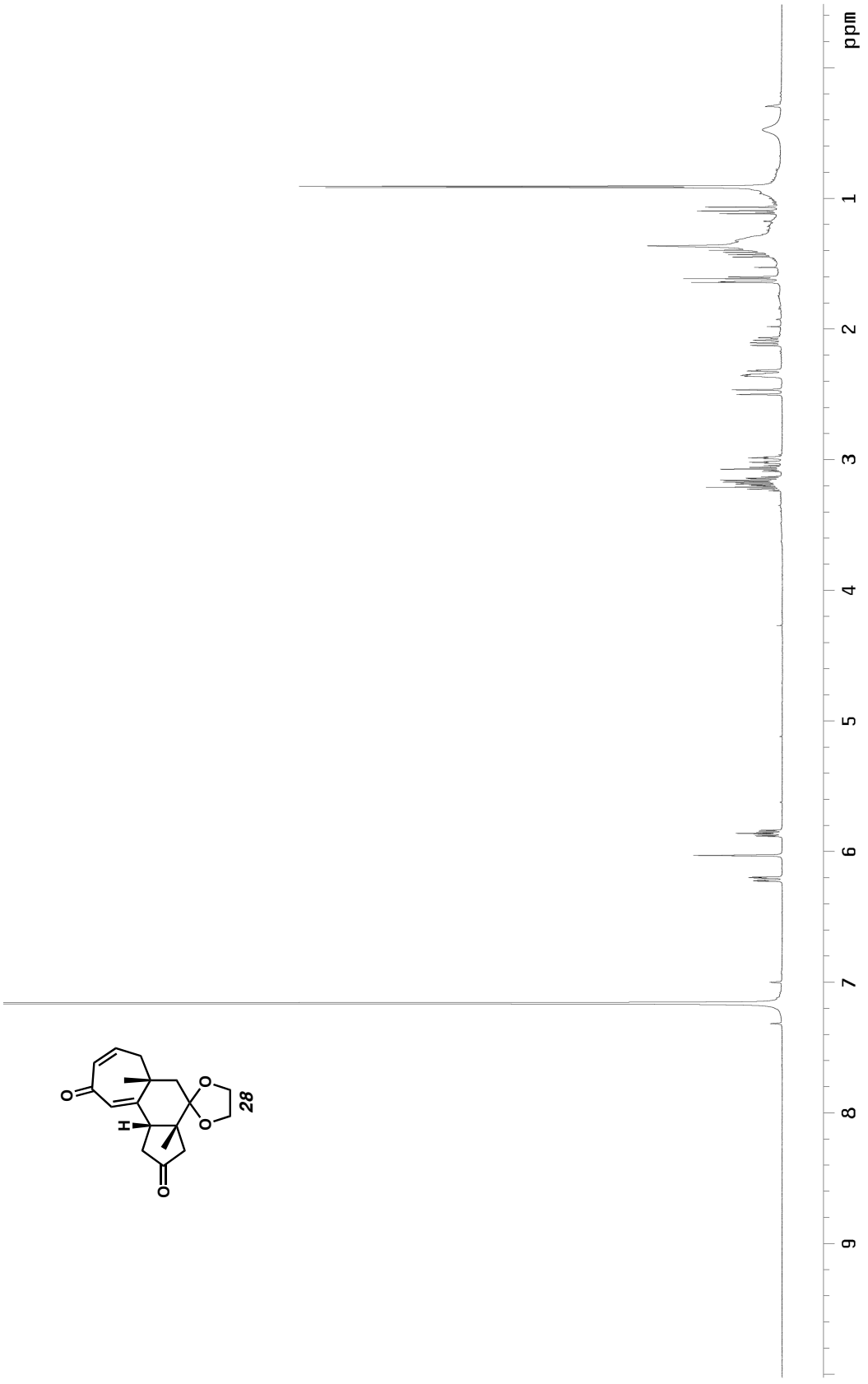
^{1}H NMR (500 MHz, C_6D_6) of compound **27**.



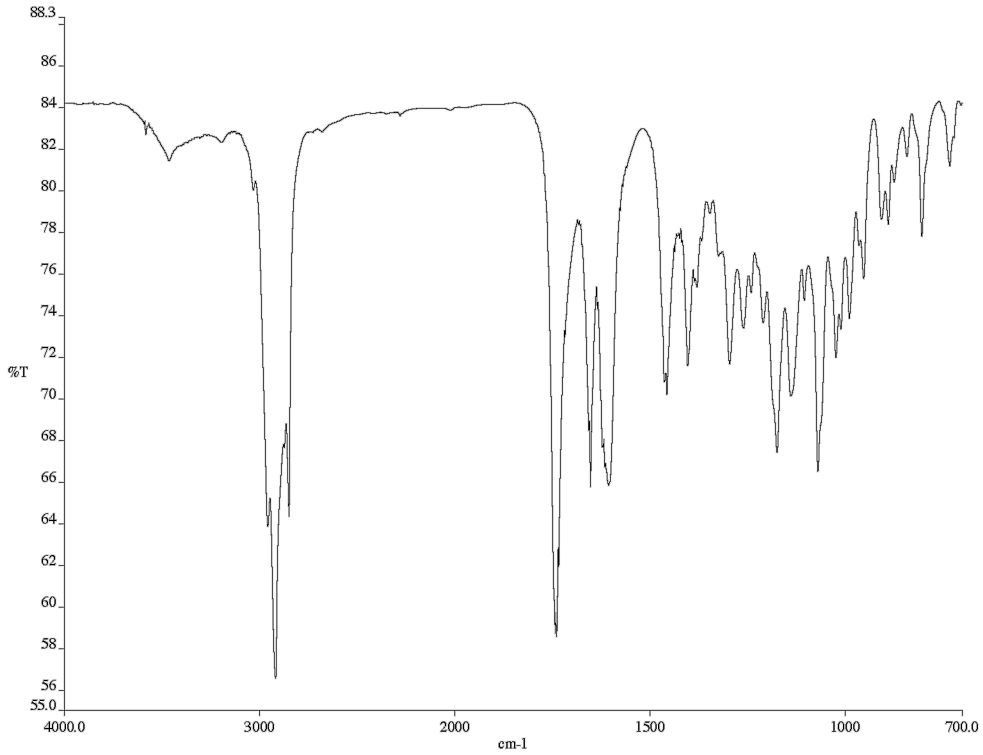
Infrared spectrum (thin film/NaCl) of compound **27**.



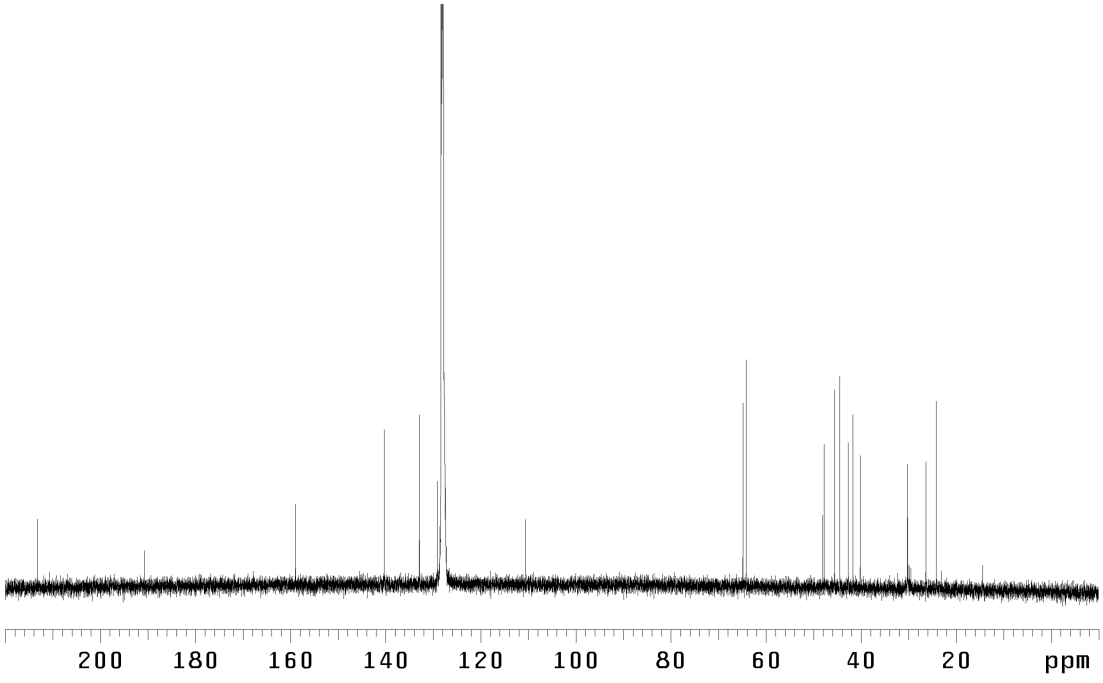
^{13}C NMR (125 MHz, C_6D_6) of compound **27**.



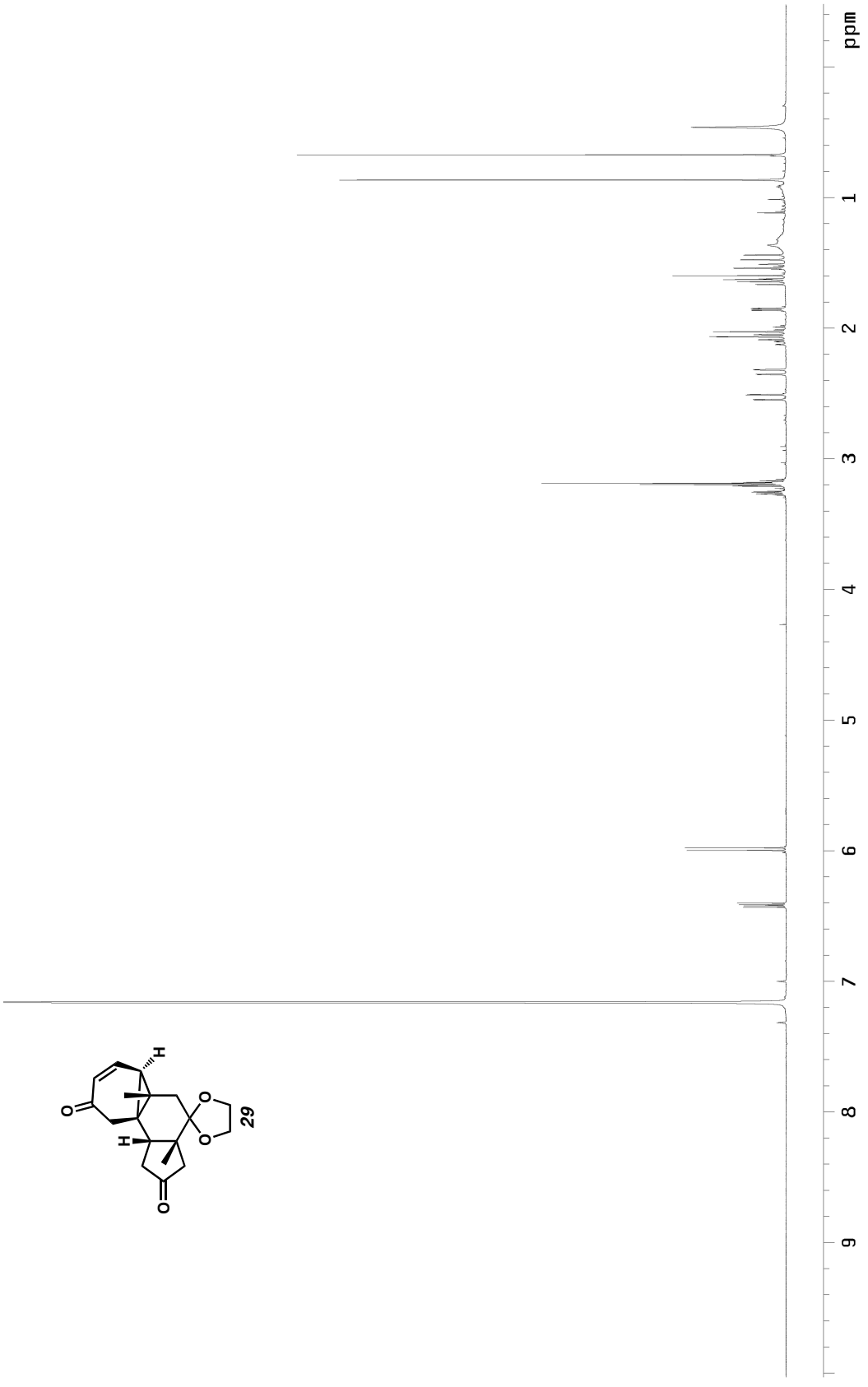
^{1}H NMR (500 MHz, C_6D_6) of compound **28**.



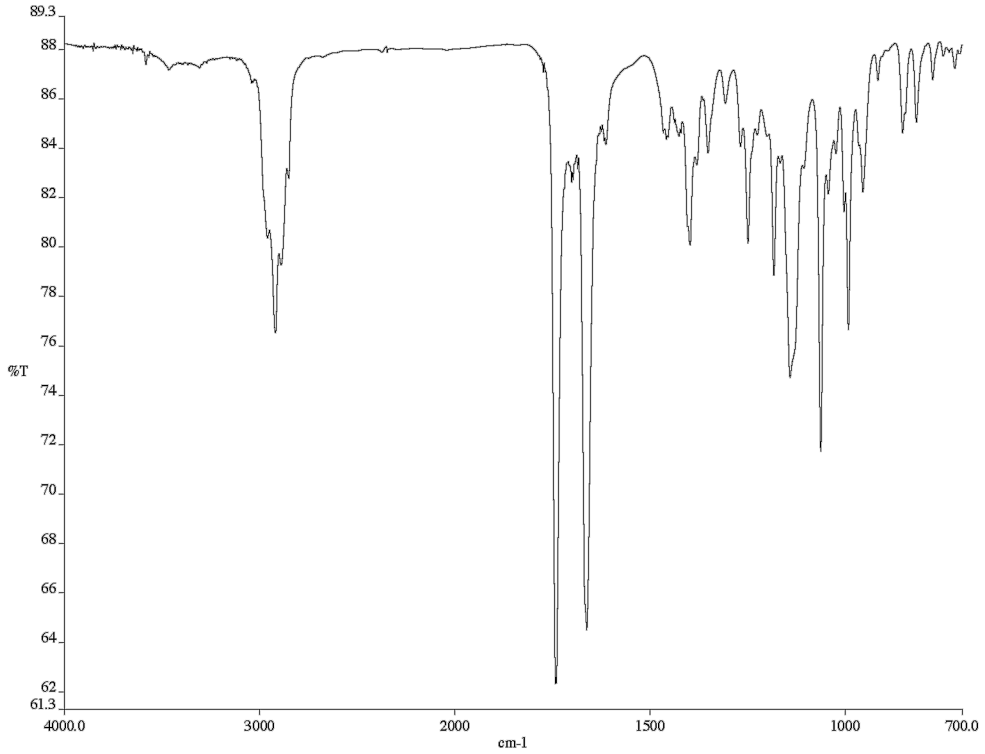
Infrared spectrum (thin film/NaCl) of compound **28**.



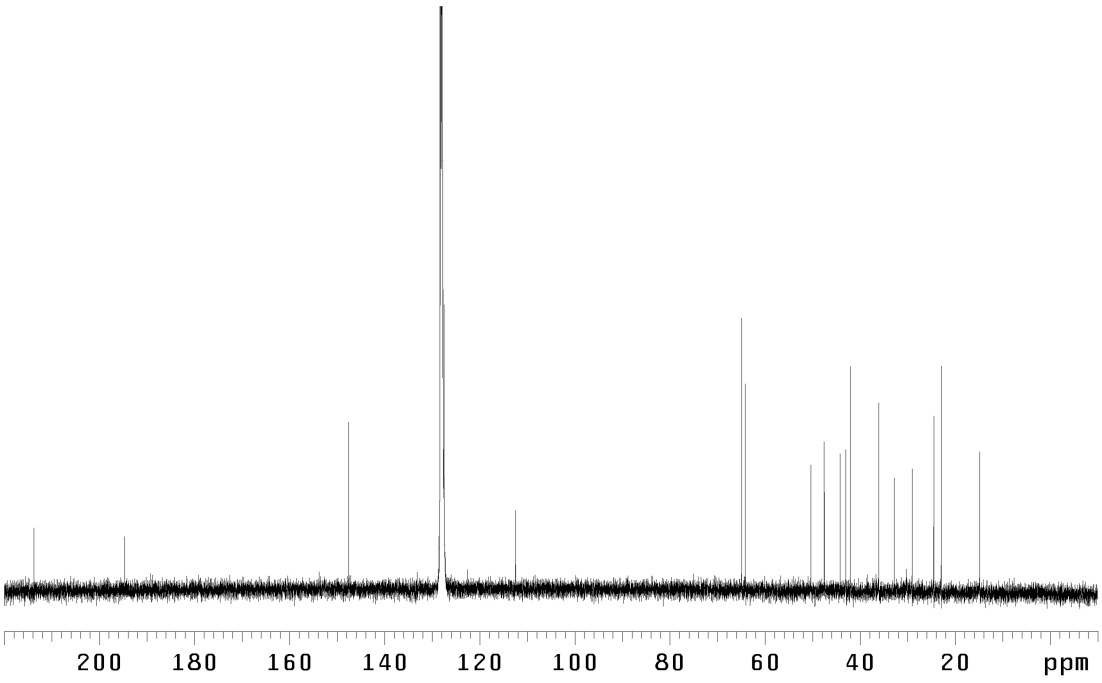
^{13}C NMR (500 MHz, C_6D_6) of compound **28**.



^{1}H NMR (125 MHz, C_6D_6) of compound **29**.



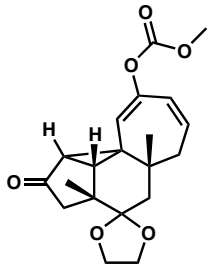
Infrared spectrum (thin film/NaCl) of compound **29**.



^{13}C NMR (125 MHz, C_6D_6) of compound **29**.

Crystal Structure Analysis of:

Compound **27**



(gms01, CCDC 936539)

By Lawrence Henling 110 Beckman Institute 626-395-2735

Email: xray@caltech.edu

Table 1. Crystal Data and Structure Analysis Details for gms01 (CCDC 936539).

Empirical formula	C20 H24 O6
Formula weight	360.39
Crystallization solvent	90:10 hexanes/DCM
Crystal shape	irregular
Crystal color	colourless
Crystal size	0.42 x 0.47 x 0.49 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK
Data collection temperature	100 K
Theta range for 9913 reflections used in lattice determination	2.61 to 41.71°

Unit cell dimensions	a = 7.3454(3) Å	α= 90°
	b = 10.9165(5) Å	β= 90°
	c = 22.3527(9) Å	γ = 90°
Volume	1792.37(13) $Å^3$	
Z	4	
Crystal system	orthorhombic	
Space group	P 21 21 21 (# 19)	
Density (calculated)	1.336 g/cm^3	
F(000)	768	
Theta range for data collection	2.1 to 43.7°	
Completeness to theta = 25.00°	99.8%	
Index ranges	$-14 \le h \le 11$, $-20 \le k \le 20$, $-43 \le l \le 43$	
Data collection scan type	and scans	
Reflections collected	63249	
Independent reflections	12908 [R_{int}= 0.0432]	
Reflections > 2σ(I)	11049	
Average σ(I)/(net I)	0.0360	
Absorption coefficient	0.10 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9276	

Structure Solution and Refinement

Primary solution method	dual
Secondary solution method	difmap
Hydrogen placement	geom
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12908 / 0 / 344
Treatment of hydrogen atoms	refall
Goodness-of-fit on F^2	2.22
Final R indices [I>2σ(I), 11049 reflections]	R1 = 0.0424, wR2 = 0.0761
R indices (all data)	R1 = 0.0551, wR2 = 0.0771
Type of weighting scheme used	calc
Weighting scheme used	calc w=1/[^2^(Fo^2^)]
Max shift/error	0.002
Average shift/error	0.000
Absolute structure parameter	-0.1(3)

Largest diff. peak and hole	0.47 and -0.32 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.18C (Bruker-AXS, 2007)
Data collection	APEX2 2012.2-0 (Bruker-AXS, 2007)
Data reduction	SAINT V8.18C (Bruker-AXS, 2007)
Structure solution	SHELXS-97 (Sheldrick, 1990)
Structure refinement	SHELXL-97 (Sheldrick, 1997)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

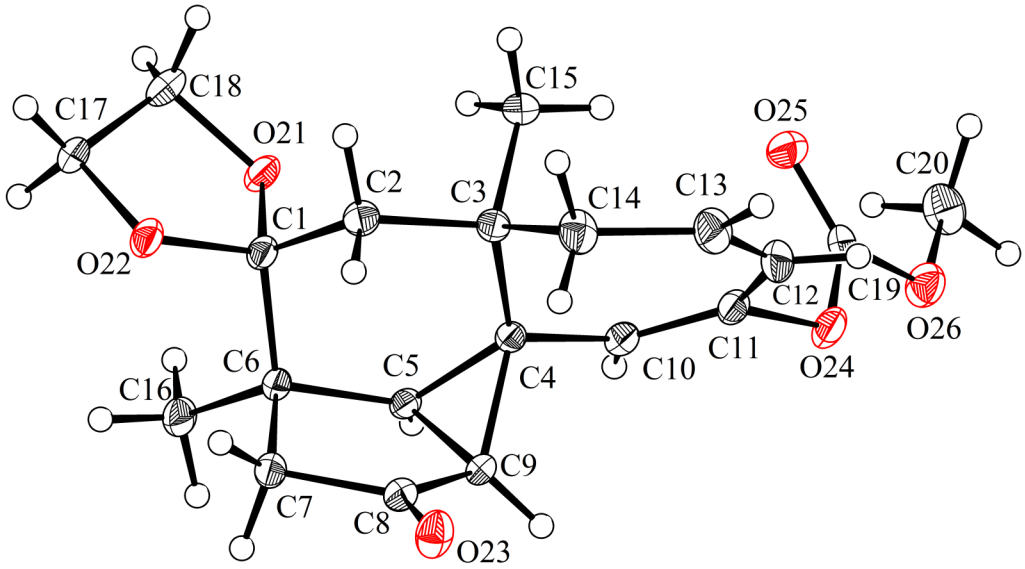


Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for gms01 (CCDC 936539). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

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	x	y	z	U_{eq}
C(1)	6733(1)	2153(1)	7625(1)	14(1)
C(2)	7984(1)	1772(1)	7112(1)	16(1)
C(3)	8076(1)	2683(1)	6580(1)	15(1)
C(4)	6193(1)	3226(1)	6441(1)	13(1)
C(5)	4647(1)	3197(1)	6885(1)	13(1)
C(6)	4750(1)	2288(1)	7416(1)	14(1)
C(7)	4101(1)	1056(1)	7154(1)	17(1)
C(8)	4386(1)	1130(1)	6484(1)	16(1)
C(9)	4465(1)	2454(1)	6314(1)	14(1)
C(10)	6146(1)	4333(1)	6051(1)	15(1)
C(11)	7128(1)	4498(1)	5554(1)	16(1)
C(12)	8479(1)	3719(1)	5270(1)	21(1)
C(13)	9176(1)	2659(1)	5469(1)	23(1)
C(14)	8824(1)	1967(1)	6038(1)	21(1)
C(15)	9405(1)	3724(1)	6740(1)	20(1)
C(16)	3519(1)	2705(1)	7927(1)	20(1)
C(17)	7369(1)	1835(1)	8641(1)	18(1)
C(17A)	8272(5)	1531(3)	8447(2)	20(1)
C(18)	8251(1)	2979(1)	8434(1)	20(1)
C(19)	7504(1)	6612(1)	5410(1)	16(1)
C(20)	7403(1)	8726(1)	5263(1)	25(1)
O(21)	7307(1)	3269(1)	7892(1)	18(1)
O(22)	6845(1)	1230(1)	8082(1)	19(1)
O(23)	4440(1)	275(1)	6136(1)	22(1)
O(24)	6741(1)	5566(1)	5214(1)	22(1)
O(25)	8576(1)	6698(1)	5812(1)	23(1)
O(26)	6824(1)	7516(1)	5082(1)	23(1)

Table 3. Bond lengths [Å] and angles [°] for gms01 (CCDC 936539).

C(1)-C(2)	1.5285(9)
C(1)-C(6)	1.5373(9)
C(1)-O(21)	1.4206(8)
C(1)-O(22)	1.4354(7)
C(2)-H(2A)	0.988(9)
C(2)-H(2B)	0.958(10)
C(2)-C(3)	1.5512(9)
C(3)-C(4)	1.5362(9)
C(3)-C(14)	1.5440(9)
C(3)-C(15)	1.5399(10)
C(4)-C(5)	1.5086(8)
C(4)-C(9)	1.5499(9)
C(4)-C(10)	1.4913(9)
C(5)-H(5)	0.968(8)
C(5)-C(6)	1.5473(8)
C(5)-C(9)	1.5186(8)
C(6)-C(7)	1.5419(9)
C(6)-C(16)	1.5273(9)
C(7)-H(7A)	0.953(10)
C(7)-H(7B)	0.963(10)
C(7)-C(8)	1.5153(9)
C(8)-C(9)	1.4962(9)
C(8)-O(23)	1.2156(8)
C(9)-H(9)	0.932(10)
C(10)-H(10)	0.929(10)
C(10)-C(11)	1.3354(9)
C(11)-C(12)	1.4522(10)
C(11)-O(24)	1.4219(8)
C(12)-H(12)	0.893(10)
C(12)-C(13)	1.3412(11)
C(13)-H(13)	0.948(11)
C(13)-C(14)	1.5014(10)
C(14)-H(14A)	0.972(11)
C(14)-H(14B)	0.957(11)
C(15)-H(15A)	0.929(10)
C(15)-H(15B)	0.949(11)
C(15)-H(15C)	0.944(11)
C(16)-H(16A)	0.958(10)
C(16)-H(16B)	0.989(9)
C(16)-H(16C)	0.953(10)
C(17)-H(17A)	0.986(10)
C(17)-H(17B)	0.971(14)
C(17)-C(18)	1.4808(12)
C(17)-O(22)	1.4650(9)
C(17A)-H(17A)	0.952(9)
C(17A)-H(17C)	1.00(5)
C(17A)-C(18)	1.582(4)
C(17A)-O(22)	1.369(3)
C(18)-H(18A)	0.847(11)
C(18)-H(18B)	0.948(12)
C(18)-O(21)	1.4312(8)

C(19)-O(24)	1.3449(8)
C(19)-O(25)	1.1973(8)
C(19)-O(26)	1.3277(8)
C(20)-H(20A)	0.928(11)
C(20)-H(20B)	0.978(11)
C(20)-H(20C)	0.984(12)
C(20)-O(26)	1.4458(10)

C(2)-C(1)-C(6)	111.48(5)
O(21)-C(1)-C(2)	111.75(5)
O(21)-C(1)-C(6)	109.06(5)
O(21)-C(1)-O(22)	106.66(4)
O(22)-C(1)-C(2)	107.99(5)
O(22)-C(1)-C(6)	109.78(5)
C(1)-C(2)-H(2A)	108.6(5)
C(1)-C(2)-H(2B)	106.4(6)
C(1)-C(2)-C(3)	115.30(5)
H(2A)-C(2)-H(2B)	108.6(8)
C(3)-C(2)-H(2A)	109.0(5)
C(3)-C(2)-H(2B)	108.7(6)
C(4)-C(3)-C(2)	111.27(5)
C(4)-C(3)-C(14)	110.91(5)
C(4)-C(3)-C(15)	109.48(5)
C(14)-C(3)-C(2)	106.98(5)
C(15)-C(3)-C(2)	108.80(5)
C(15)-C(3)-C(14)	109.34(5)
C(3)-C(4)-C(9)	124.40(5)
C(5)-C(4)-C(3)	122.44(5)
C(5)-C(4)-C(9)	59.52(4)
C(10)-C(4)-C(3)	116.85(5)
C(10)-C(4)-C(5)	112.63(5)
C(10)-C(4)-C(9)	108.30(5)
C(4)-C(5)-H(5)	117.2(5)
C(4)-C(5)-C(6)	118.74(5)
C(4)-C(5)-C(9)	61.59(4)
C(6)-C(5)-H(5)	117.6(5)
C(9)-C(5)-H(5)	121.5(5)
C(9)-C(5)-C(6)	107.87(5)
C(1)-C(6)-C(5)	109.99(5)
C(1)-C(6)-C(7)	108.94(5)
C(7)-C(6)-C(5)	104.71(5)
C(16)-C(6)-C(1)	111.18(5)
C(16)-C(6)-C(5)	110.70(5)
C(16)-C(6)-C(7)	111.12(6)
C(6)-C(7)-H(7A)	115.2(6)
C(6)-C(7)-H(7B)	108.0(6)
H(7A)-C(7)-H(7B)	109.4(8)
C(8)-C(7)-C(6)	106.58(5)
C(8)-C(7)-H(7A)	113.1(6)
C(8)-C(7)-H(7B)	103.8(5)
C(9)-C(8)-C(7)	107.95(5)
O(23)-C(8)-C(7)	126.65(6)
O(23)-C(8)-C(9)	125.28(5)
C(4)-C(9)-H(9)	114.6(6)

C(5)-C(9)-C(4)	58.89(4)
C(5)-C(9)-H(9)	124.1(6)
C(8)-C(9)-C(4)	120.68(5)
C(8)-C(9)-C(5)	107.77(5)
C(8)-C(9)-H(9)	117.9(6)
C(4)-C(10)-H(10)	118.0(6)
C(11)-C(10)-C(4)	125.62(6)
C(11)-C(10)-H(10)	116.3(6)
C(10)-C(11)-C(12)	130.82(6)
C(10)-C(11)-O(24)	116.55(6)
O(24)-C(11)-C(12)	112.49(6)
C(11)-C(12)-H(12)	114.9(7)
C(13)-C(12)-C(11)	128.40(6)
C(13)-C(12)-H(12)	116.6(7)
C(12)-C(13)-H(13)	113.9(6)
C(12)-C(13)-C(14)	130.43(7)
C(14)-C(13)-H(13)	115.7(6)
C(3)-C(14)-H(14A)	106.2(6)
C(3)-C(14)-H(14B)	110.9(6)
C(13)-C(14)-C(3)	118.11(6)
C(13)-C(14)-H(14A)	108.4(6)
C(13)-C(14)-H(14B)	107.6(6)
H(14A)-C(14)-H(14B)	104.8(9)
C(3)-C(15)-H(15A)	111.3(6)
C(3)-C(15)-H(15B)	109.8(7)
C(3)-C(15)-H(15C)	109.7(7)
H(15A)-C(15)-H(15B)	107.0(9)
H(15A)-C(15)-H(15C)	110.0(9)
H(15B)-C(15)-H(15C)	108.9(9)
C(6)-C(16)-H(16A)	109.0(6)
C(6)-C(16)-H(16B)	114.6(5)
C(6)-C(16)-H(16C)	111.7(6)
H(16A)-C(16)-H(16B)	106.8(8)
H(16A)-C(16)-H(16C)	108.0(8)
H(16B)-C(16)-H(16C)	106.4(8)
H(17A)-C(17)-H(17B)	109.5(9)
C(18)-C(17)-H(17A)	116.5(6)
C(18)-C(17)-H(17B)	109.1(8)
O(22)-C(17)-H(17A)	104.7(5)
O(22)-C(17)-H(17B)	113.7(7)
O(22)-C(17)-C(18)	103.23(6)
H(17A)-C(17A)-H(17C)	113(3)
C(18)-C(17A)-H(17A)	110.6(6)
C(18)-C(17A)-H(17C)	90(3)
O(22)-C(17A)-H(17A)	114.3(7)
O(22)-C(17A)-H(17C)	122(3)
O(22)-C(17A)-C(18)	102.7(2)
C(17)-C(18)-C(17A)	32.37(15)
C(17)-C(18)-H(18A)	117.7(8)
C(17)-C(18)-H(18B)	114.5(7)
C(17A)-C(18)-H(18A)	140.8(8)
C(17A)-C(18)-H(18B)	84.5(7)
H(18A)-C(18)-H(18B)	102.2(11)
O(21)-C(18)-C(17)	103.81(6)

O(21)-C(18)-C(17A)	103.98(13)
O(21)-C(18)-H(18A)	110.1(8)
O(21)-C(18)-H(18B)	108.5(6)
O(25)-C(19)-O(24)	125.81(6)
O(25)-C(19)-O(26)	127.11(6)
O(26)-C(19)-O(24)	107.07(5)
H(20A)-C(20)-H(20B)	112.8(10)
H(20A)-C(20)-H(20C)	108.8(10)
H(20B)-C(20)-H(20C)	112.1(9)
O(26)-C(20)-H(20A)	109.0(8)
O(26)-C(20)-H(20B)	101.7(6)
O(26)-C(20)-H(20C)	112.2(7)
C(1)-O(21)-C(18)	108.01(5)
C(1)-O(22)-C(17)	107.76(5)
C(17A)-O(22)-C(1)	107.45(15)
C(17A)-O(22)-C(17)	35.08(16)
C(19)-O(24)-C(11)	116.00(5)
C(19)-O(26)-C(20)	114.43(6)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for gms01 (CCDC 936539). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

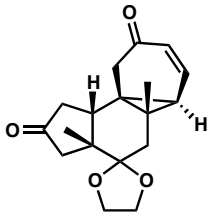
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	159(3)	145(2)	122(2)	22(2)	-22(2)	0(2)
C(2)	137(3)	177(3)	177(2)	23(2)	-6(2)	35(2)
C(3)	116(2)	182(3)	147(2)	12(2)	7(2)	18(2)
C(4)	119(2)	142(2)	115(2)	-2(2)	-2(2)	3(2)
C(5)	115(2)	156(2)	111(2)	-5(2)	-11(2)	12(2)
C(6)	132(2)	176(3)	101(2)	8(2)	-2(2)	-2(2)
C(7)	190(3)	180(3)	128(2)	14(2)	-11(2)	-41(2)
C(8)	161(3)	179(3)	137(2)	1(2)	-18(2)	-23(2)
C(9)	140(2)	170(3)	105(2)	5(2)	-22(2)	-11(2)
C(10)	154(3)	157(3)	142(2)	5(2)	-22(2)	6(2)
C(11)	193(3)	174(3)	124(2)	17(2)	-32(2)	-35(2)
C(12)	234(3)	274(3)	133(2)	4(2)	31(2)	-33(3)
C(13)	219(3)	295(4)	177(3)	-22(3)	64(2)	30(3)
C(14)	192(3)	236(3)	199(3)	3(2)	51(2)	62(3)
C(15)	136(3)	269(3)	186(3)	33(2)	-25(2)	-30(3)
C(16)	177(3)	287(3)	124(2)	-4(2)	22(2)	16(3)
C(17)	186(5)	250(4)	109(3)	16(3)	-28(3)	-18(3)
C(17A)	208(19)	198(16)	183(15)	14(11)	-55(13)	31(12)
C(18)	216(3)	243(3)	146(2)	-8(2)	-70(2)	22(3)
C(19)	160(3)	195(3)	118(2)	18(2)	35(2)	-18(2)
C(20)	306(4)	185(3)	267(3)	7(3)	51(3)	-1(3)
O(21)	223(2)	177(2)	135(2)	13(2)	-68(2)	-29(2)
O(22)	225(2)	186(2)	146(2)	51(2)	-42(2)	-14(2)
O(23)	340(3)	179(2)	156(2)	-25(2)	-4(2)	-33(2)
O(24)	303(3)	198(2)	147(2)	48(2)	-80(2)	-64(2)
O(25)	234(3)	257(3)	210(2)	26(2)	-61(2)	-69(2)
O(26)	284(3)	199(2)	215(2)	50(2)	-43(2)	-14(2)

Table 5. Hydrogen coordinates (x 10^3) and isotropic displacement parameters ($Å^2$x 10^3) for gms01 (CCDC 936539).

	x	y	z	U_{iso}
H(2A)	758(1)	96(1)	696(1)	18(2)
H(2B)	918(1)	169(1)	728(1)	24(2)
H(5)	397(1)	395(1)	694(1)	8(2)
H(7A)	464(1)	35(1)	733(1)	20(2)
H(7B)	280(1)	102(1)	720(1)	21(2)
H(9)	380(1)	271(1)	598(1)	24(2)
H(10)	535(1)	496(1)	615(1)	24(2)
H(12)	885(2)	397(1)	491(1)	27(2)
H(13)	1001(1)	229(1)	520(1)	32(3)
H(14A)	996(2)	160(1)	617(1)	32(3)
H(14B)	805(2)	129(1)	594(1)	28(2)
H(15A)	956(1)	426(1)	642(1)	22(2)
H(15B)	1057(2)	339(1)	683(1)	34(3)
H(15C)	897(2)	415(1)	708(1)	31(3)
H(16A)	233(1)	288(1)	777(1)	25(2)
H(16B)	394(1)	345(1)	814(1)	20(2)
H(16C)	340(1)	209(1)	823(1)	26(2)
H(17A)	816(1)	124(1)	885(1)	19(2)
H(17B)	634(2)	204(1)	890(1)	28(3)
H(17C)	956(7)	153(4)	830(2)	24
H(18A)	824(2)	359(1)	867(1)	38(3)
H(18B)	951(2)	290(1)	835(1)	35(3)
H(20A)	700(2)	887(1)	565(1)	39(3)
H(20B)	679(2)	924(1)	497(1)	32(3)
H(20C)	873(2)	882(1)	525(1)	33(3)

Crystal Structure Analysis of:

Compound **29**



(gms02, CCDC 936540)

By Lawrence Henling 110 Beckman Institute 626-395-2735
Email: xray@caltech.edu

Table 1. Crystal Data
Figures Minimum overlap
Table 2. Atomic coordinates
Table 3. Bond Lengths
Table 4. Anisotropic displacement parameters
Table 5. Hydrogen coordinates

Table 1. Crystal Data and Structure Analysis Details for gms02 (CCDC 936540).

Empirical formula	C18 H22 O4
Formula weight	302.36
Crystallization solvent	EtOAc in hexanes, vapor diffusion
Crystal shape	twig
Crystal color	colourless
Crystal size	0.10 x 0.12 x 0.41 mm

Data Collection

Preliminary photograph(s)	rotation
Type of diffractometer	Bruker APEX-II CCD
Wavelength	0.71073 Å MoK
Data collection temperature	100 K
Theta range for 7790 reflections used in lattice determination	2.59 to 32.49°

Unit cell dimensions	a = 7.1115(3) Å	α= 90°
	b = 8.2413(4) Å	β= 90°
	c = 26.0740(11) Å	γ = 90°
Volume	1528.15(12) $Å^3$	
Z	4	
Crystal system	orthorhombic	
Space group	P 21 21 21 (# 19)	
Density (calculated)	1.314 g/cm^3	
F(000)	648	
Theta range for data collection	2.6 to 35.2°	
Completeness to theta = 25.00°	99.9%	
Index ranges	$-11 \le h \le 11, -12 \le k \le 13, -41 \le l \le 40$	
Data collection scan type	and scans	
Reflections collected	31815	
Independent reflections	6394 [R_{int}= 0.0468]	
Reflections > 2σ(I)	5522	
Average σ(I)/(net I)	0.0412	
Absorption coefficient	0.09 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9211	

Structure Solution and Refinement

Primary solution method	dual
Secondary solution method	difmap
Hydrogen placement	geom
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6394 / 0 / 287
Treatment of hydrogen atoms	refall
Goodness-of-fit on F^2	2.07
Final R indices [I>2σ(I), 5522 reflections]	R1 = 0.0487, wR2 = 0.0732
R indices (all data)	R1 = 0.0605, wR2 = 0.0743
Type of weighting scheme used	calc
Weighting scheme used	calc w=1/[^2^(Fo^2^)]
Max shift/error	0.000
Average shift/error	0.000
Absolute structure parameter	-0.3(6)

Largest diff. peak and hole	0.58 and -0.43 e·Å^{-3}

Programs Used

Cell refinement	SAINT V8.18C (Bruker-AXS, 2007)
Data collection	APEX2 2012.2-0 (Bruker-AXS, 2007)
Data reduction	SAINT V8.18C (Bruker-AXS, 2007)
Structure solution	SHELXS-97 (Sheldrick, 1990)
Structure refinement	SHELXL-97 (Sheldrick, 1997)
Graphics	DIAMOND 3 (Crystal Impact, 1999)

References

Special Refinement Details

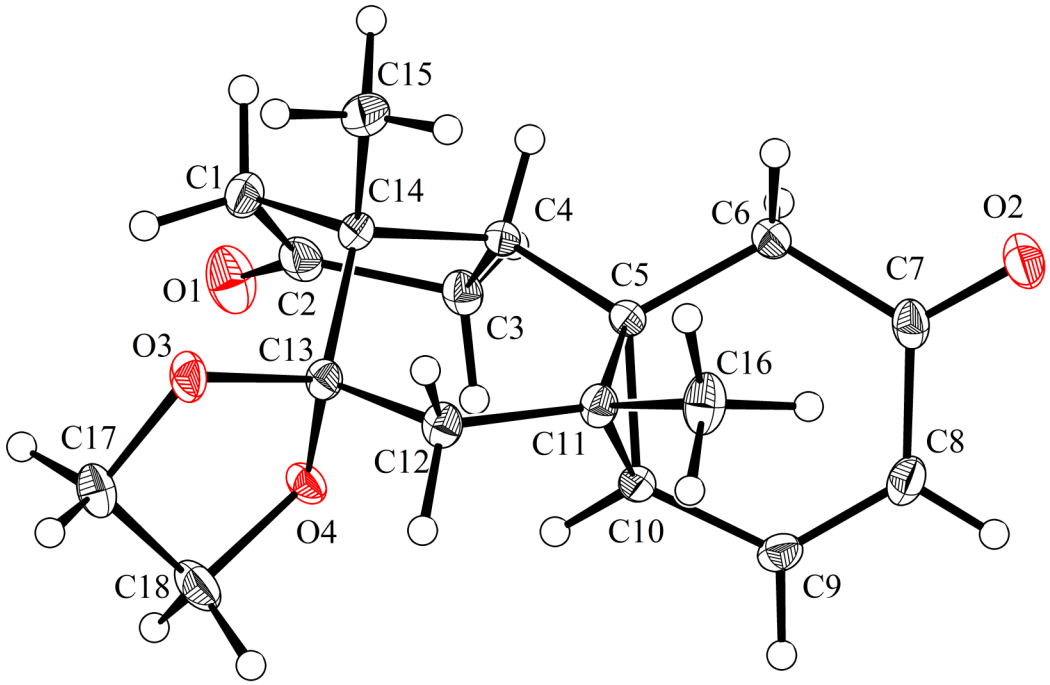


Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for gms02. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

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	x	y	z	U_{eq}
O(1)	-365(1)	2950(1)	2424(1)	28(1)
O(2)	7542(1)	7642(1)	739(1)	26(1)
O(3)	3248(1)	-828(1)	1427(1)	18(1)
O(4)	1373(1)	1338(1)	1248(1)	15(1)
C(1)	2577(2)	1570(2)	2263(1)	18(1)
C(2)	1144(2)	2908(1)	2214(1)	18(1)
C(3)	1911(2)	4222(1)	1862(1)	16(1)
C(4)	3906(2)	3663(1)	1723(1)	13(1)
C(5)	4655(2)	4220(1)	1202(1)	12(1)
C(6)	5879(2)	5721(1)	1246(1)	15(1)
C(7)	6164(2)	6755(1)	774(1)	17(1)
C(8)	4721(2)	6701(1)	376(1)	18(1)
C(9)	3452(2)	5512(1)	362(1)	16(1)
C(10)	3395(2)	4159(1)	729(1)	13(1)
C(11)	5064(2)	2981(1)	785(1)	14(1)
C(12)	4527(2)	1216(1)	878(1)	15(1)
C(13)	3276(2)	886(1)	1340(1)	13(1)
C(14)	3958(2)	1788(1)	1819(1)	14(1)
C(15)	5948(2)	1242(2)	1953(1)	22(1)
C(16)	6774(2)	3134(2)	446(1)	22(1)
C(17)	1398(2)	-1434(1)	1321(1)	20(1)
C(18)	449(2)	-72(2)	1041(1)	23(1)

Table 3. Bond lengths [Å] and angles [°] for gms02 (CCDC 936540).

O(1)-C(2)	1.2050(15)
O(2)-C(7)	1.2261(14)
O(3)-C(13)	1.4308(12)
O(3)-C(17)	1.4337(15)
O(4)-C(13)	1.4242(13)
O(4)-C(18)	1.4398(14)
C(1)-H(1A)	0.985(14)
C(1)-H(1B)	0.969(13)
C(1)-C(2)	1.5064(18)
C(1)-C(14)	1.5292(16)
C(2)-C(3)	1.5218(16)
C(3)-H(3A)	0.953(13)
C(3)-H(3B)	0.993(12)
C(3)-C(4)	1.5350(17)
C(4)-H(4)	0.945(12)
C(4)-C(5)	1.5308(15)
C(4)-C(14)	1.5656(15)
C(5)-C(6)	1.5172(15)
C(5)-C(10)	1.5236(15)
C(5)-C(11)	1.5193(15)
C(6)-H(6A)	0.960(13)
C(6)-H(6B)	0.969(12)
C(6)-C(7)	1.5110(15)
C(7)-C(8)	1.4590(17)
C(8)-H(8)	0.948(13)
C(8)-C(9)	1.3327(16)
C(9)-H(9)	0.952(12)
C(9)-C(10)	1.4691(15)
C(10)-H(10)	0.947(11)
C(10)-C(11)	1.5404(16)
C(11)-C(12)	1.5234(15)
C(11)-C(16)	1.5072(16)
C(12)-H(12A)	1.028(12)
C(12)-H(12B)	0.912(13)
C(12)-C(13)	1.5230(15)
C(13)-C(14)	1.5301(15)
C(14)-C(15)	1.5257(17)
C(15)-H(15A)	0.983(13)
C(15)-H(15B)	0.946(14)
C(15)-H(15C)	0.924(14)
C(16)-H(16A)	0.964(15)
C(16)-H(16B)	0.996(13)
C(16)-H(16C)	0.992(14)
C(17)-H(17A)	0.977(14)
C(17)-H(17B)	0.914(13)
C(17)-C(18)	1.4996(17)
C(18)-H(18A)	1.091(14)
C(18)-H(18B)	0.995(13)
C(13)-O(3)-C(17)	109.04(9)
C(13)-O(4)-C(18)	106.63(8)

H(1A)-C(1)-H(1B)	107.8(11)
C(2)-C(1)-H(1A)	113.7(8)
C(2)-C(1)-H(1B)	107.2(8)
C(2)-C(1)-C(14)	106.59(9)
C(14)-C(1)-H(1A)	113.7(8)
C(14)-C(1)-H(1B)	107.5(8)
O(1)-C(2)-C(1)	125.82(11)
O(1)-C(2)-C(3)	124.99(11)
C(1)-C(2)-C(3)	109.18(10)
C(2)-C(3)-H(3A)	108.3(8)
C(2)-C(3)-H(3B)	107.2(7)
C(2)-C(3)-C(4)	105.09(9)
H(3A)-C(3)-H(3B)	108.9(10)
C(4)-C(3)-H(3A)	114.0(8)
C(4)-C(3)-H(3B)	113.0(7)
C(3)-C(4)-H(4)	107.7(7)
C(3)-C(4)-C(14)	106.28(9)
C(5)-C(4)-C(3)	116.14(9)
C(5)-C(4)-H(4)	107.0(7)
C(5)-C(4)-C(14)	115.42(9)
C(14)-C(4)-H(4)	103.3(7)
C(6)-C(5)-C(4)	112.11(9)
C(6)-C(5)-C(10)	115.20(9)
C(6)-C(5)-C(11)	119.51(9)
C(10)-C(5)-C(4)	120.25(10)
C(11)-C(5)-C(4)	120.03(9)
C(11)-C(5)-C(10)	60.83(7)
C(5)-C(6)-H(6A)	109.1(7)
C(5)-C(6)-H(6B)	110.8(7)
H(6A)-C(6)-H(6B)	105.9(11)
C(7)-C(6)-C(5)	118.33(9)
C(7)-C(6)-H(6A)	103.3(7)
C(7)-C(6)-H(6B)	108.5(7)
O(2)-C(7)-C(6)	120.23(10)
O(2)-C(7)-C(8)	121.89(10)
C(8)-C(7)-C(6)	117.84(10)
C(7)-C(8)-H(8)	119.9(8)
C(9)-C(8)-C(7)	121.22(10)
C(9)-C(8)-H(8)	118.8(8)
C(8)-C(9)-H(9)	118.7(7)
C(8)-C(9)-C(10)	123.95(11)
C(10)-C(9)-H(9)	117.4(7)
C(5)-C(10)-H(10)	115.5(7)
C(5)-C(10)-C(11)	59.45(7)
C(9)-C(10)-C(5)	119.03(9)
C(9)-C(10)-H(10)	117.4(7)
C(9)-C(10)-C(11)	121.20(10)
C(11)-C(10)-H(10)	111.5(7)
C(5)-C(11)-C(10)	59.72(7)
C(5)-C(11)-C(12)	118.65(9)
C(12)-C(11)-C(10)	115.04(9)
C(16)-C(11)-C(5)	121.14(10)
C(16)-C(11)-C(10)	120.93(10)
C(16)-C(11)-C(12)	112.05(9)

C(11)-C(12)-H(12A)	111.4(6)
C(11)-C(12)-H(12B)	110.3(7)
H(12A)-C(12)-H(12B)	104.2(10)
C(13)-C(12)-C(11)	116.32(9)
C(13)-C(12)-H(12A)	108.8(7)
C(13)-C(12)-H(12B)	105.0(8)
O(3)-C(13)-C(12)	108.01(8)
O(3)-C(13)-C(14)	110.83(8)
O(4)-C(13)-O(3)	105.77(9)
O(4)-C(13)-C(12)	111.94(9)
O(4)-C(13)-C(14)	108.20(9)
C(12)-C(13)-C(14)	111.93(9)
C(1)-C(14)-C(4)	102.77(9)
C(1)-C(14)-C(13)	110.90(9)
C(13)-C(14)-C(4)	110.01(8)
C(15)-C(14)-C(1)	112.77(9)
C(15)-C(14)-C(4)	110.44(10)
C(15)-C(14)-C(13)	109.77(10)
C(14)-C(15)-H(15A)	110.4(9)
C(14)-C(15)-H(15B)	110.9(8)
C(14)-C(15)-H(15C)	109.9(8)
H(15A)-C(15)-H(15B)	105.0(11)
H(15A)-C(15)-H(15C)	112.3(12)
H(15B)-C(15)-H(15C)	108.3(12)
C(11)-C(16)-H(16A)	109.6(9)
C(11)-C(16)-H(16B)	113.4(8)
C(11)-C(16)-H(16C)	110.2(8)
H(16A)-C(16)-H(16B)	109.9(11)
H(16A)-C(16)-H(16C)	107.6(12)
H(16B)-C(16)-H(16C)	105.9(11)
O(3)-C(17)-H(17A)	108.5(8)
O(3)-C(17)-H(17B)	108.1(9)
O(3)-C(17)-C(18)	104.24(9)
H(17A)-C(17)-H(17B)	107.1(11)
C(18)-C(17)-H(17A)	111.5(8)
C(18)-C(17)-H(17B)	117.1(8)
O(4)-C(18)-C(17)	102.49(9)
O(4)-C(18)-H(18A)	108.0(7)
O(4)-C(18)-H(18B)	105.7(7)
C(17)-C(18)-H(18A)	110.9(7)
C(17)-C(18)-H(18B)	114.8(7)
H(18A)-C(18)-H(18B)	113.9(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for gms02 (CCDC 936540). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	274(5)	247(5)	311(5)	-47(4)	129(4)	-48(4)
O(2)	302(5)	242(5)	246(4)	16(4)	15(4)	-133(4)
O(3)	191(4)	98(4)	262(4)	37(3)	-11(4)	-6(3)
O(4)	145(4)	97(3)	209(4)	-18(3)	-36(3)	-10(3)
C(1)	244(7)	170(6)	141(5)	20(4)	8(5)	-40(5)
C(2)	231(6)	183(6)	137(5)	-48(4)	19(5)	-57(5)
C(3)	189(6)	126(5)	154(5)	-29(4)	23(4)	-12(5)
C(4)	155(5)	128(5)	107(4)	0(4)	-13(4)	-30(4)
C(5)	141(5)	111(5)	120(5)	-9(4)	-10(4)	-15(4)
C(6)	167(6)	149(5)	146(5)	-6(4)	-9(5)	-34(5)
C(7)	221(6)	110(5)	170(5)	-17(4)	41(5)	-26(4)
C(8)	271(7)	128(5)	147(5)	23(4)	21(5)	0(5)
C(9)	207(6)	151(5)	120(5)	-10(4)	-24(5)	16(5)
C(10)	148(5)	117(5)	120(5)	-2(4)	-14(4)	-11(4)
C(11)	177(6)	110(5)	138(5)	-8(4)	20(4)	3(4)
C(12)	182(6)	104(5)	168(5)	-10(4)	13(4)	22(5)
C(13)	140(5)	88(5)	166(5)	12(4)	-13(4)	17(4)
C(14)	153(5)	134(5)	133(5)	31(4)	-19(4)	-12(4)
C(15)	200(6)	231(6)	219(6)	56(5)	-56(5)	0(5)
C(16)	257(7)	166(6)	236(6)	10(5)	102(6)	15(6)
C(17)	218(6)	123(5)	254(6)	-11(5)	23(5)	-33(5)
C(18)	220(6)	151(5)	315(7)	-34(5)	-47(6)	-59(5)

Table 5. Hydrogen coordinates (x 10^3) and isotropic displacement parameters ($Å^2$x 10^3) for gms02 (CCDC 936540).

	x	y	z	U_{iso}
H(1A)	202(2)	48(2)	228(1)	28(4)
H(1B)	326(2)	176(2)	258(1)	22(3)
H(3A)	187(2)	523(2)	204(1)	24(4)
H(3B)	106(2)	428(1)	156(1)	13(3)
H(4)	473(2)	407(1)	198(1)	13(3)
H(6A)	532(2)	646(1)	149(1)	20(3)
H(6B)	710(2)	545(1)	139(1)	14(3)
H(8)	472(2)	748(2)	11(1)	23(4)
H(9)	254(2)	551(2)	10(1)	15(3)
H(10)	223(2)	362(1)	77(1)	3(3)
H(12A)	391(2)	71(1)	56(1)	18(3)
H(12B)	558(2)	60(1)	93(1)	18(3)
H(15A)	599(2)	6(2)	200(1)	31(4)
H(15B)	632(2)	167(2)	227(1)	25(4)
H(15C)	678(2)	160(2)	171(1)	25(4)
H(16A)	785(2)	270(2)	62(1)	35(4)
H(16B)	703(2)	427(2)	34(1)	25(4)
H(16C)	660(2)	250(2)	13(1)	31(4)
H(17A)	78(2)	-167(2)	165(1)	30(4)
H(17B)	152(2)	-240(2)	115(1)	23(3)
H(18A)	75(2)	-13(2)	63(1)	38(4)
H(18B)	-91(2)	7(1)	112(1)	19(3)