

Supporting Information, SI, section

CYCLOADDITION AND ONE-CARBON HOMOLOGATION STUDIES IN THE SYNTHESIS OF ADVANCED IRIDOID PRECURSORS

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General procedure for dienophile preparation

(*S*)-5-Hydroxymethylfuran-2(*5H*)-one (4–10 mmol) and imidazole (~1.2 equivalents), were dissolved in dry dichloromethane (to give ~1 M solution). The silyl chloride (~1.1 equivalents) was added and the reaction was stirred at 25 °C until the consumption of starting material was complete (TLC). Water was added and the resulting mixture was extracted with dichloromethane. The organic phase was dried (MgSO₄) and the solvent was removed under reduced pressure to give a residue which chromatographed on silica gel using ethyl acetate–hexane in varying proportions.

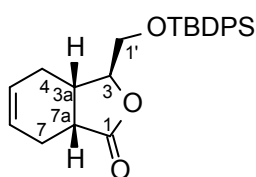
(*S*)-(5-*O*-*t*-Butyldiphenylsilyloxymethyl)furan-2(*5H*)-one 2a, (68%), mp 79–82 °C (from ether–hexane); δ_{H} (200 MHz, CDCl₃) 1.03 [s, 9H, C(CH₃)₃], 3.89 (2H, dd, *J* 4.4 and 2.1 Hz, 5-H₂), 5.03–5.10 (1H, m, 4-H), 6.16 (1H, dd, *J* 5.8 and 2.0 Hz, 2-H) and 7.20–7.70 (11H, m, Ar-H and 3-H).

(*S*)-(5-*O*-Triisopropylsilyloxymethyl)furan-2(*5H*)-one 2b, (65%) as an oil, α_{D} –133.7 (*c* 1 in CHCl₃); ν_{max} (CHCl₃)/cm^{–1} 1756 (CO); δ_{H} (400 MHz, CDCl₃) 0.98–1.08 [21H, m, 3 x CH(CH₃)₂], 3.87 (1H, dd, *J* 10.4 and 5.7 Hz, 5-H_A), 4.06 (1H, dd, *J* 10.4 and 4.6 Hz, 5-H_B), 5.05–5.10 (1H, m, 4-H), 6.16 (1H, dd, *J* 5.7 and 2.0 Hz, 2-H) and 7.54 (1H, dd, *J* 5.7 and 1.5 Hz, 3-H); δ_{C} (100 MHz, CDCl₃) 11.9 [3 x CH(CH₃)₂], 17.8 [3 x CH(CH₃)₂], 63.5 (C-5), 83.3 (C-4), 122.4 (C-2), 154.5 (C-3) and 172.8 (C-1), (Found: M⁺–C₃H₇, 227.1117. Calc. for C₁₁H₁₉O₃Si: *M*, 227.1104).

(*S*)-(5-*O*-*t*-Butyldimethylsilyloxymethyl)furan-2(*5H*)-one 2c, (96%), mp 30–32 °C; δ_{H} (300 MHz; CDCl₃) 0.05 and 0.06 (6H, 2 x s, 2 x CH₃), 0.86 (9H, s, C(CH₃)₃), 3.79 (1H, dd, *J* 10.7 and 5.4 Hz, 5-H_A), 3.92 (1H, dd, *J* 10.7 and 4.5 Hz, 5-H_B), 4.99–5.07 (1H, m, 4-H), 6.15 (1H, dd, *J* 5.7 and 1.9 Hz, 2-H) and 7.48 (1H, dd, *J* 5.7 and 1.6 Hz, 3-H).

General procedure for cycloadditions of furanones **2a**, **2b** and **2c** with butadiene (**a**) Lewis acid catalysed cycloadditions

The butenolide was dissolved in dichloromethane ($\sim 2 \text{ cm}^3/\text{mmol}$ butenolide) under nitrogen. Ethylaluminium dichloride (1.0 M solution in hexanes, ~ 0.4 equivalents) was added and the resulting mixture was added to cooled ($-78 \text{ }^\circ\text{C}$) butadiene ($\sim 2 \text{ cm}^3/\text{mmol}$ butenolide) in a pressure tube which was sealed and heated at $60 \text{ }^\circ\text{C}$ for 168 h. (CAUTION-explosion risk) The tube was cooled to $-78 \text{ }^\circ\text{C}$ and aqueous saturated sodium hydrogen carbonate was added. The mixture was extracted with dichloromethane and the organic extract was dried (MgSO_4). The solvent was removed *in vacuo* to give the cycloadduct which was purified by chromatography on silica gel using ethyl acetate–hexane.



a) The reaction of **2a** (2.00 g, 5.7 mmol) gave a solid mass (3.25 g) after work-up. Chromatography on silica gel (250 g) using ethyl acetate–hexane (1:9) as eluent afforded (3*S*, 3*aS*, 7*aR*)-3-*t*-butyldiphenylsilyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-one **6** (1.61 g, 70%); mp $71\text{--}74 \text{ }^\circ\text{C}$ (from hexane); $[\alpha]_{\text{D}} +19.0$ (*c* 9.7 in CHCl_3); $[\alpha]_{\text{D}} +19.6$; δ_{H} (400 MHz, CDCl_3) 1.07 [9H, s, $\text{C}(\text{CH}_3)_3$], 1.88–1.98 (1H, br d, 4- H_A), 2.22–2.48 (3H, m, 4- H_B , 7- H_2), 2.66–2.75 (1H, m, 3*a*-H), 3.00 (1H, td, J 2 x 10.4 and 4.4 Hz, 7*a*-H), 3.77 (1H, dd, J 11.4 and 3.8 Hz, 1'- H_A), 3.88 (1H, dd, J 11.4 and 3.8 Hz, 1'- H_B), 4.16 (1H, q, J 3 x 3.8 Hz, 3-H), 5.76–5.90 (2H, m, 5-H and 6-H), 7.30-7.49 (6H, m, Ar-H) and 7.61-7.67 (4H, m, Ar-H); δ_{C} (100 MHz, CDCl_3) 19.2 [$\text{C}(\text{CH}_3)_3$], 22.6 (C-7), 25.5 (C-4), 26.8 [$\text{C}(\text{CH}_3)_3$], 34.1 (C-3*a*), 37.4 (C-7*a*) 64.3 (C-1'), 84.8 (C-3), 125.6 and 126.5 (C-5 and C-6), 127.9, 129.9, 132.6(4) and 132.9(3), 135.5(5) and 135.6(4) (Ar-C), 179.4 (C-1).

b) The reaction of **2b** (1.40 g, 5.19 mmol) gave a residue (1.66 g) after work-up. Chromatography on silica gel (160 g) using ethyl acetate–hexane (1:19) as eluent afforded (3*S*, 3*aS*, 7*aR*)-3-triisopropylsilyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-one **7** (689 mg, 41%) as an oil, $[\alpha]_{\text{D}} +3.8$ (*c* 3.3 in CHCl_3); $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 1766 (CO); δ_{H} (400 MHz, CDCl_3) 1.06 [21H, m, 3 x $\text{CH}(\text{CH}_3)_2$], 1.92–2.02 (1H, m, 4- H_A), 2.24–2.45 (3H, m, 4- H_B , 7- H_2), 2.70 (1H, m, 3*a*-H), 3.01 (1H, td, J 2 x 8.6 and 4.4 Hz, 7*a*-H), 3.86 (1H, dd, J 11.0 and 3.3 Hz, 1'- H_A), 3.94 (1H, dd, J 11.0 and 4.0 Hz, 1'- H_B), 4.13 (1H, q, J 3 x 3.7 Hz, 3-H) and 5.65 (2H, m, 5-H and 6-H); δ_{C} (100

MHz, CDCl₃) 11.9 [3 x CH(CH₃)₂], 17.9 [3 x CH(CH₃)₂], 22.5 (C-7), 25.7 (C-4), 34.1 (C-3a), 37.4 (C-7a) 64.2 (C-1'), 85.1 (C-3), 125.7 and 126.5 (C-5 and C-6) and 179.4 (C-1) (Found: M⁺ 324.2126. Calc. for C₁₈H₃₂O₃Si: *M*, 324.2121).

c) The reaction of **2c** (1.41 g, 6.18 mmol) gave a residue (1.25 g) after work-up. Chromatography on silica gel (160 g) using ethyl acetate–hexane (1:9) as eluent afforded (3*S*, 3*aS*, 7*aR*)-3-*t*-butyldimethylsilanyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-one **8** (238 mg, 14%) as an oil, [α]_D +3.1 (*c* 1.4 in CHCl₃); ν_{max}(CHCl₃)/cm⁻¹ 1766 (CO); δ_H (400 MHz, CDCl₃) 0.07 and 0.08 (6H, 2 x s, 2 x CH₃), 0.90 [9H, s, C(CH₃)₃], 1.92–2.10 (1H, m, 4-H_A), 2.24–2.45 (3H, m, 4-H_B, 7-H₂), 2.60–2.71 (1H, m, 3*a*-H), 2.99 (1H, td, *J* 2 x 8.5 and 4.6 Hz, 7*a*-H), 3.76 (1H, dd, *J* 11.4 and 3.3 Hz, 1'-H_A), 3.85 (1H, dd, *J* 11.4 and 3.9 Hz, 1'-H_B), 4.13 (1H, q, *J* 3 x 3.9 Hz, 3-H) and 5.65 (2H, m, 5-H and 6-H); δ_C (100 MHz, CDCl₃) 5.3 and 5.4 (2 x CH₃) 18.4 [C(CH₃)₃], 22.7 (C-7), 25.8 (C-4), 25.9 [CH(CH₃)₃], 34.3 (C-3*a*), 37.6 (C-7*a*) 64.0 (C-1'), 85.1 (C-3), 125.8 and 126.6 (C-5 and C-6) and 179.6 (C-1) (Found: M⁺ 282.1640. Calc. for C₁₅H₂₆O₃Si: *M*, 282.1651).

General procedure for cycloadditions of furanones **2a**, **2b** and **2c** with butadiene (b)

Thermally induced cycloadditions

The butenolide (1-6 mmol) and hydroquinone (5 mg) were weighed into a pressure tube. Butadiene (~2.5 cm³/ mmol butenolide) was condensed into the tube which was sealed and the mixture was heated at 210 °C for 16 h. (CAUTION-explosion risk) The tube was cooled to -40 °C and opened. The mixture was warmed to 25 °C and the excess butadiene was evaporated to leave a rubbery residue which was dissolved in dichloromethane and slurried with silica gel (~5g/g residue). The solvent was evaporated to leave the adsorbed residue which was slurried in ethyl acetate–hexane (1:9) and loaded onto a column of silica gel (~20g/g residue). Elution with ethyl acetate–hexane (1:9) afforded the cycloadduct.

a) The reaction of **2a** (2.00 g, 5.7 mmol) afforded (3*S*, 3*aS*, 7*aR*)-3-*t*-butyldiphenylsilanyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-one **6** (1.45 g, 63%)

b) The reaction of **2b** (504 mg, 1.87 mmol) afforded (3*S*, 3*aS*, 7*aR*)-3-triisopropylsilanyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-one **7** (412 mg, 68%)

c) The reaction of **2c** (610 mg, 2.68 mmol) afforded (3*S*, 3*aS*, 7*aR*)-3-*t*-butyldimethylsilanyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-one **8** (492 mg, 65%)

Desilylation of cycloadduct **6**

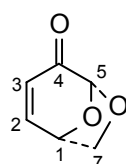
a) Acetic acid (1.0 M solution in THF, 1.1 cm³, 1.10 mmol) and tetrabutylammonium fluoride (1.0 M solution in THF, 1.1 cm³, 1.10 mmol) were added to a stirred solution of silyl ether **6** (406 mg, 1.00 mmol) was in 5 cm³ tetrahydrofuran at 0 °C. The solution was warmed to 10 °C and stirred for 1 h. Saturated aqueous ammonium chloride (10 cm³) was added and the mixture was concentrated under reduced pressure. The aqueous slurry was extracted with ethyl acetate, dried (MgSO₄) and the solvent was removed *in vacuo* to give a residue (430 mg). Column chromatography on silica gel (15 g) using ethyl acetate–hexane (3:2) as eluent afforded the alcohol **9** (131 mg, 78%).

b) Hydrogen fluoride [40% HF–MeCN (40:60), 6 cm³, 8.00 mmol] was added to a stirred solution of **6** (1.00 g, 2.50 mmol) in acetonitrile (10 cm³). The mixture was stirred at 25 °C for 24 h after which saturated aqueous sodium carbonate was added and the resulting mixture was extracted with ethyl acetate. The organic phase was dried (MgSO₄) and the solvent was removed under reduced pressure to give an oily residue (992 mg). Column chromatography on silica gel (50 g) using ethyl acetate–hexane (3:2) as eluent afforded the alcohol **9** (315 mg, 75%).

c) Tetrabutylammonium fluoride (1.0 M solution in THF, 1.2 cm³, 1.20 mmol) was added to a stirred solution of silyl ether **6** (406 mg, 1.00 mmol) was in 5 cm³ tetrahydrofuran at 0 °C. The solution was warmed to 25 °C and stirred until the consumption of starting material was complete (TLC). Saturated aqueous ammonium chloride (10 cm³) was added and the mixture was concentrated under reduced pressure. The aqueous slurry was extracted with ethyl acetate, dried (MgSO₄) and the solvent was removed *in vacuo* to give a residue (539 mg). Chromatography on silica gel (50 g) using ethyl acetate–hexane (3:2) as eluent yielded an inseparable mixture of **117** and a minor product, **119** (162 mg, 96%), δ_{H} (400 MHz; CDCl₃) *major* 2.63–2.71 (1H, m, 3a-H), 2.91–2.98 (1H, m, 7a-H), 3.90 (1H, dd, *J* 12.4 and 3.2 Hz, 1'-H_A), 4.21 (1H, dt, *J* 2 x 4.9 and 3.2 Hz, 3-H), *minor* 3.47–3.53 (1H, m, 7a-H), 3.96 (1H, dd, *J* 12.4 and 3.2 Hz, 1'-H_A), 4.25 (1H, ddd, *J* 9.9, 4.7 and 2.7 Hz, 3-H) and *mixed* 1.92–2.55, 3.65–3.75 and 5.69–5.87.

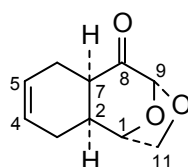
MODEL SYNTHESIS FROM LEVOGLUCOSENONE

(1*S*, 5*R*)-6,8-Dioxabicyclo[3.2.1]oct-2-en-4-one **3**



Finely shredded newspaper was soaked in 1.5% H₃PO₄ for 24 h after which the mixture was stirred with an overhead stirrer. The resulting pulp was removed from the acid solution, spread out, and dried to give a fibrous residue (1.450 kg). The dry paper were stuffed into a glass tube (50 cm x 5 cm) and placed into a tube furnace. The top of the tube was fitted with an argon inlet and the bottom was attached to a 2-necked flask fitted with an argon outlet. The flask contained chloroform–water (1:1, ~2 dm³) and was immersed in an ice bath. The tube was heated to 300 °C where the temperature was maintained until the drip rate slowed (~20 min). The pyrolysis experiment was repeated nineteen times after which the combined solvents were placed in a separating funnel and the aqueous phase was extracted with chloroform. The organic extract was dried (MgSO₄) and the solvent was removed under reduced pressure to give the crude pyrolysate (102 g). Distillation through a vigreux column gave a forerun of furfural followed by a levoglucosenone fraction (32 g, 75–85 °C/0.8 mm Hg) which was further purified by chromatography on silica gel (400 g) using ethyl acetate–hexane (3:7) as eluent to give levoglucosenone **3** (12.4 g, 0.9%), δ_{H} (200 MHz, CDCl₃), 3.99–4.09 (1H, m, 7-H_A), 4.19 (1H, d, *J* 7.6, 7-H_B), 4.50 (1H, d, *J* 5.2 Hz, 1-H), 5.13 (1H, s, 5-H), 5.87 (1H, d, *J* 11.0 Hz, 2-H) and 6.51 (1H, d, *J* 11.0 Hz, 3-H).

(1S, 2S, 7R, 9R)-10,12-Dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-8-one **4**

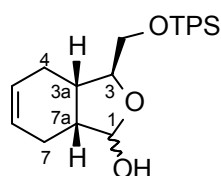


a) Butadiene (~5 cm³) was condensed into a pressure tube which held levoglucosenone (270 mg, 2.14 mmol). The tube was sealed, mildly agitated, and slowly heated to 160 °C (CAUTION-explosion risk). After 3 h the mixture was cooled to 25 °C, diluted with dichloromethane and slurried with silica gel (6 g). The solvent was evaporated and the adsorbed mixture was chromatographed on silica gel (20 g) using ethyl acetate–hexane (2:3) as eluent to give cycloadduct **4** (276 mg, 72%), mp 63–66 °C (from dichloromethane–hexane); $[\alpha]_{\text{D}}$ –55 (*c* 1.1 in CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 1737 (CO), δ_{H} (400 MHz, CDCl₃), 1.98–2.11 (2H, m, 3-H₂), 2.33–2.52 (2H, m, 6-H₂), 2.67–2.75 (1H, br.d, 2-H), 3.18 (1H, t, *J* 2 x 7.2 Hz, 7-H), 4.03 (1H, dd, *J* 7.6 and 4.8 Hz, 11-H_A), 4.19 (1H, dd, *J* 7.6 and 0.4 Hz, 11-H_B), 4.46 (1H, dd, *J* 4.8 and 1.6 Hz, 1-H), 5.13 (1H, s, 9-H) and 5.60–5.69 (2H, m, 4-H and 5-H); δ_{C} (100 MHz, CDCl₃), 20.4 (C-3), 24.2 (C-6), 38.1 (C-2), 40.7 (C-7), 67.3 (C-11), 77.3 (C-1), 101.8 (C-9), 124.1 (C-4), 124.6 (C-5) and 201.8 (C-8).

The combined mother liquors were concentrated to give a mixture of **4** and its *trans* epimer, (~3:2 by NMR); δ_{H} (200 MHz, CDCl_3) 3.18 (1H, t, J 2 x 7.0 Hz, 7-H), 3.99 (1H, dd, J 7.6 and 5.0 Hz, 11- H_{A}), 4.18 (1H, d, J 7.6 Hz, 11- H_{B}), 5.07 (1H, s, 9-H), *minor* 3.60—3.74 (2H, m, 11- H_2) 5.13 (1H, s, 9-H), *mixed* 1.40—2.75 (5H, m, 2-H, 3- H_2 , 6- H_2 , and *minor* 7-H) and 5.50—5.81 (2H, m, 4-H and 5-H); δ_{C} (50 MHz, CDCl_3), *major* 20.3 (C-3), 24.0 (C-6), 38.0 (C-2), 40.5 (C-7), 67.2 (C-11), 77.2 (C-1), 101.5 (C-9), 123.9 (C-4), 124.5 (C-5) and 202.0 (C-8), *minor* 24.6 (C-3), 32.6 (C-6), 38.0 (C-2), 41.1 (C-7), 70.8 (C-11), 76.7 (C-1), 98.8 (C-9), 125.9 (C-4), 126.4 (C-5) and 205.9 (C-8).

b) Ethylaluminium dichloride (1.0 M solution in hexanes, 11.9 cm^3 , 11.9 mmol) was added to a solution of levoglucosenone (5.0 g, 39.7 mmol) in dichloromethane (20 cm^3) under nitrogen. The resulting mixture was added to butadiene (~7 cm^3) in a pressure tube at $-78\text{ }^\circ\text{C}$. The tube was sealed and warmed to $0\text{ }^\circ\text{C}$. After 60 min at $0\text{ }^\circ\text{C}$ the tube was cooled to $-78\text{ }^\circ\text{C}$, opened and water (2 cm^3) and 1 M HCl (2 cm^3) were added. The mixture was warmed to $25\text{ }^\circ\text{C}$, extracted with dichloromethane and the organic extract was dried (MgSO_4). The solvent was removed *in vacuo* to give the cycloadduct (5.70 g). Chromatography on silica gel (250 g) using ethyl acetate—hexane (3:7) as eluent furnished **136** (4.59 g, 64%).

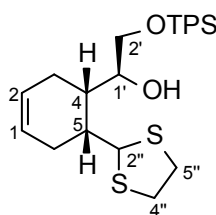
**(3*S*, 3*aS*, 7*aR*)-3-*t*-Butyldiphenylsilyloxymethyl-3*a*,4,7,7*a*-tetrahydro-3*H*-isobenzofuran-1-
o1 10**



Diisobutylaluminium hydride (1.5 M in toluene, 0.40 cm^3 , 0.60 mmol) was slowly added to a stirred solution of **6** (200 mg, 0.49 mmol) in toluene (4 cm^3) at $-78\text{ }^\circ\text{C}$. After 20 min the reaction was quenched with 1 M HCl and warmed to $25\text{ }^\circ\text{C}$. The mixture was extracted with ethyl acetate and the organic extract was dried (MgSO_4). The solvent was removed under reduced pressure to give a residue (230 mg). Chromatography on silica gel (20 g) using ethyl acetate—hexane (3:7) as eluent, afforded *lactol 10* (183 mg, 91%) as a mixture (~2:1 by NMR) of diastereomers, $[\alpha]_{\text{D}} -11.1$ (c 1.0 in CHCl_3); $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3450 (OH); δ_{H} (400 MHz, CDCl_3) *major* 1.08 [9H, s, $\text{C}(\text{CH}_3)_3$], 2.66—2.76 (1H, m, 1-H), 5.07 (1H, s, 9-H), *minor* 1.06 [9H, s, $\text{C}(\text{CH}_3)_3$], 2.42—2.53 (1H, m, 1-H), 5.05 (1H, s, 9-H), *mixed* 1.75—2.35 (5H, m, 2- H_2 , 5- H_2 and 6-H), 3.43—3.90 (3H, m, 7-H and 10- H_2), 5.52—5.75 (2H, m, 3-H and 4-H), 7.30-7.48 (6H, m, Ar-H) and 7.61-7.67 (4H, m, Ar-H); δ_{C} (100 MHz, CDCl_3) *major* 19.2 [$\text{C}(\text{CH}_3)_3$], 22.8 (C-2), 23.3 (C-5), 26.8 [$\text{C}(\text{CH}_3)_3$], 32.1 (C-

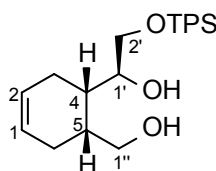
6), 41.7 (C-1) 64.5 (C-10), 83.4 (C-7), 103.0 (C-9), 123.9 and 125.2 (C-3 and C-4), *minor* 19.2 [C(CH₃)₃], 23.1 (C-2), 23.1 (C-5), 26.8 [C(CH₃)₃], 34.8 (C-6), 40.2 (C-1) 66.7 (C-10), 83.1 (C-7), 104.1 (C-9), 124.3 and 124.9 (C-3 and C-4), *mixed* 127.5(6), 127.6(0) and 127.7(1), 129.5(4), 129.5(6), 129.7(4) and 129.8(0), 132.9(5) and 133.0(7), 135.5(5), 135.5(9) and 135.6(4) (Ar-C) [Found (FAB): M⁺-OH, 391.2079. Calc. for C₂₅H₃₁O₂Si: M, 391.2085].

(4*S*, 5*R*)-4-[(*S*)-2-*t*-Butyldiphenylsilyloxy-1-hydroxyethyl]-5-(1,3-dithiolan-2-yl) cyclohexene
11



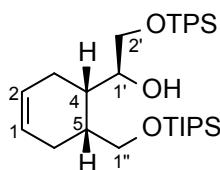
1,2-Ethandiol (0.04 cm³, 0.04 mg, 0.48 mmol) and titanium tetrachloride (1.0 M in CH₂Cl₂, 0.10 cm³, 0.10 mmol) were added sequentially to a solution of **10** (148 mg, 0.36 mmol) in dichloromethane (4 cm³) at -78 °C. After 15 min at -78 °C, aqueous saturated sodium hydrogen carbonate was added and the resulting mixture was warmed to room temperature. The mixture was extracted with dichloromethane, the organic extract was dried (MgSO₄) and the solvent was removed under reduced pressure to give a residue (178 mg). Purified by chromatography on silica gel (20 g) using ethyl acetate-hexane (1:9) as eluent gave the *thioacetal* **11** (140 mg, 80%) as a gum, [α]_D -3.6 (*c* 3.4 in CHCl₃); ν_{max}(CHCl₃)/cm⁻¹ 3557 (OH); δ_H (400 MHz, CDCl₃), 1.07 [9H, s, C(CH₃)₃], 1.57 (1H, br.s, -OH), 1.67—1.77 (1H, m, 3-H_A), 1.98—2.18 (3H, m, 3-H_B, 6-H_A and 5-H), 2.26—2.33 (1H, m, 4-H), 2.34—2.42 (1H, m, 6-H_B), 3.13—3.25 (4H, m, 4''-H₂ and 5''-H₂), 3.57 (1H, dd, *J* 10.1 and 6.4 Hz, 2'-H_A), 3.72 (1H, dd, *J* 10.1 and 2.9 Hz, 2'-H_B), 3.79—3.85 (1H, m, 1'-H), 5.00 (1H, d, *J* 9.8 Hz, 2''-H), 5.40—5.49 (1H, m, 2-H), 5.57—5.65 (1H, m, 1-H), 7.37—7.49 (6H, m, Ar-H) and 7.63—7.70 (4H, m, Ar-H); δ_C (100 MHz, CDCl₃), 19.2 [C(CH₃)₃], 26.8 [C(CH₃)₃], 28.1 (C-3), 29.4 (C-6), 38.0 (C-4'' and C-5''), 38.3 (C-5), 45.3 (C-4), 58.4 (C-2''), 66.9 (C-2'), 70.8 (C-1'), 124.7 (C-2), 126.7 (C-1), 127.8, 129.8, 133.0, 135.5(2) and 135.5(5) (Ar-C) (Found: M⁺-C₄H₉, 427.1227. Calc. for C₂₃H₃₇O₂S₂Si: M, 427.1219)

(4*S*, 5*R*)-4-[(*S*)-2-*t*-Butyldiphenylsilyloxy-1-hydroxyethyl]-5-hydroxymethylcyclohexene **12**



Lithium borohydride (62 mg, 3.4 mmol) was added to a solution of **6** (400 mg, 0.99 mmol) in tetrahydrofuran (20 cm³). The resulting mixture was stirred at 25 °C for 85 h. The reaction mixture was diluted with water, extracted with dichloromethane and the organic phase was dried (MgSO₄). The solvent was removed under reduced pressure to give a residue (440 mg) which was purified by column chromatography on silica gel (40 g) using ethyl acetate–hexane (1:4) as eluent to give the diol **12** (259 mg, 63%) as an oil, $[\alpha]_D +14.4$ (*c* 2.2 in CHCl₃); δ_H (400 MHz, CDCl₃); 1.09 [9H, s, C(CH₃)₃], 1.81–2.28 (6H, m, 3-H₂, 4-H, 5-H, 6-H₂), 3.05 (2H, br.s, 2 x OH), 3.52 (1H, dd, *J* 11.1 and 4.8 Hz, 1''-H_A), 3.62–3.69 (1H, m, 2'-H_A), 3.73–3.82 (3H, m, 1'-H, 2'-H_B, 1''-H_B), 5.50–5.65 (2H, m, 1-H, 2-H), 7.38–7.49 (6H, m, Ar-H) and 7.66–7.70 (4H, m, Ar-H); δ_C (100 MHz, CDCl₃), 19.2 [C(CH₃)₃], 25.9 (C-3 or C-6), 26.9 [C(CH₃)₃], 28.2 (C-3 or C-6), 35.7 (C-5), 37.8 (C-4), 63.3 (C-1''), 66.8 (C-2'), 72.6 (C-1'), 125.3 and 125.8 (C-1 and C-2), 127.8, 129.9, 133.1(0) and 133.1(3), 135.5(2) and 135.5(4) (Ar-C).

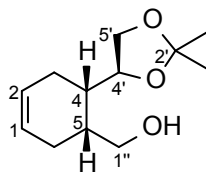
(4*S*, 5*R*)-4-[(*S*)-2-*t*-Butyldiphenylsilyloxy-1-hydroxyethyl]-5-triisopropylsilyloxymethyl-cyclohexene **13**



Triisopropylsilyl chloride (0.63 cm³, 2.95 mmol) and imidazole (219 mg, 3.21 mmol) were added to a stirred solution of **12** (1.10 g, 2.68 mmol) in acetonitrile (100 cm³). After 5 h at 25 °C, the solvent was removed under reduced pressure and water was added. The mixture was extracted with dichloromethane, the organic phase was dried (MgSO₄) and the solvent was removed under reduced pressure to give an oil (2.53 g). Chromatography on silica gel (150 g) using ethyl acetate–hexane (1:19) as eluent furnished the *1''*-triisopropylsilyl ether **13** (1.454 g, 96%) as an oil, $[\alpha]_D +1.3$ (*c* 1.7 in CHCl₃); ν_{\max} (CHCl₃)/cm⁻¹ 3329 (OH); δ_H (400 MHz, CDCl₃), 0.98–1.20 [30H, m, 3 x CH(CH₃)₂ and C(CH₃)₃], 1.63 (1H, br.s, OH), 1.78–2.15 (4H, m, 3-H₂, 4-H, 6-H_A), 2.16–2.29 (1H, m, 6-H_B), 2.29–2.40 (1H, m, 5-H), 3.52 (1H, dd, *J* 10.0 and 5.6 Hz, 1''-H_A), 3.62–3.80 (3H, m, 1'-H and 2'-H₂), 3.85 (1H, dd, *J* 10.0 and 8.1 Hz, 1''-H_B), 5.50–5.60 (2H, m, 1-H, 2-H), 7.33–7.47 (6H, m, Ar-H) and 7.64–7.72 (4H, m, Ar-H); δ_C (100 MHz, CDCl₃), 11.9 (3 x CH(CH₃)₂), 18.0 (3 x CH(CH₃)₂), 19.2 [C(CH₃)₃], 25.4 (C-3), 26.9 [C(CH₃)₃], 29.2 (C-6), 34.3 (C-5), 37.8 (C-4), 63.5 (C-1''), 66.4 (C-2'), 73.3 (C-1'), 125.3 and 126.0 (C-1 and C-2), 127.6(5) and

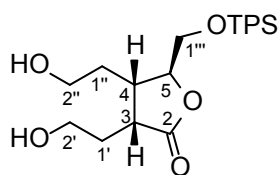
127.6(6), 129.6, 133.6 and 135.6 (Ar-C). (Found: M^+ , 566.3612. Calc. for $C_{34}H_{54}O_3Si_2$: M , 566.3627).

(4*S*, 5*R*)- 4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-5-hydroxymethyl-cyclohexene 14



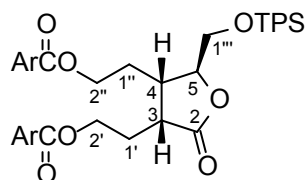
Cycloadduct **6** (408 mg, 1.00 mmol) was added to a stirred suspension of lithium aluminium hydride (160 mg, 4.20 mmol) in diethyl ether (20 cm³) and the mixture was refluxed for 60 min. Saturated aqueous sodium sulfate was added dropwise until flocculation occurred and the resulting mixture was stirred for 60 min. The mixture was filtered through layers of Celite and MgSO₄ which were rinsed with hot methanol–chloroform (50:50). The combined filtrate was evaporated under reduced pressure to give the crude triol which was dissolved in acetone (5 cm³) and toluene-*p*-sulfonic acid (10 mg) was added. After stirring for 16 h at 25 °C, anhydrous copper sulfate (200 mg) was added and the mixture refluxed for 5 h. Triethylamine (2 cm³) was added, and the mixture was filtered through a Celite pad, which was washed with ethyl acetate. Removal of the solvent under reduced pressure gave a residue (570 mg) which was loaded onto a silica column (50 g) and eluted with ethyl acetate–hexane (1:4) to give the *acetone* **14** (60 mg, 28%) as an oil, [α]_D +13.9 (*c* 3.6 in CHCl₃); ν_{\max} (CHCl₃)/cm⁻¹ 3442 (OH); δ_H (400 MHz, CDCl₃) 1.35 (3H, s, CH₃), 1.40 (3H, s, CH₃), 1.69–1.80 (1H, m, 3-H_A), 1.90–2.01 (1H, m, 4-H), 2.02–2.30 (4H, m, 3-H_B, 5-H, 6-H₂), 2.81 (1H, br.s, OH), 3.58 (1H, t, *J* 2 x 7.9 Hz, 5'-H_A), 3.50–3.83 (2H, m, 1''-H₂), 4.04 (1H, dd, *J* 7.9 and 5.9 Hz, 5'-H_B), 4.13 (1H, ddd, *J* 9.7, 7.9 and 5.9 Hz, 4'-H), 5.52–5.62 (1H, m, 1-H), 5.64–5.72 (1H, m, 2-H); δ_C (100 MHz, CDCl₃) 25.7 (CH₃), 25.9 (C-6), 26.8 (CH₃), 27.2 (C-3), 37.6 (C-5), 38.9 (C-4), 64.4 (C-1''), 69.4 (C-5'), 75.5 (C-4'), 109.0 (C-2'), 124.3 (C-2), 126.5 (C-1) (Found: M^+ , 212.1421. Calc. for C₁₂H₂₀O₃: M , 212.1412)

(3*R*, 4*S*)-5-[(*S*)-*t*-Butyldiphenylsilyloxymethyl]-3,4-bis(2-hydroxyethyl)-dihydrofuran-2-one
16



Ozone was bubbled through a solution of **6** (1.10 g, 2.71 mmol) in methanol (100 cm³) at -78 °C until the solution turned blue. Nitrogen was then bubbled through the solution as it was warmed to 25 °C. Sodium borohydride (450 mg, 12.16 mmol) was added and the solution was stirred for 15 min. Water was added and the volatile media removed under reduced pressure. The mixture was extracted with dichloromethane, the organic phase was dried (MgSO₄) and the solvent was removed under reduced pressure to give the crude diol (1.35 g). Column chromatography on silica gel (75 g) using ethyl acetate–hexane (4:1) as eluent afforded the *diol* **16** (1.01 g, 88%) as an oil, [α]_D +17.2 (*c* 1.5 in CHCl₃); ν_{max}(CHCl₃)/cm⁻¹ 3437 (OH) and 1760 (CO); δ_H (400 MHz, CDCl₃) 1.07 [9H, s, C(CH₃)₃], 1.45–1.56 (1H, m, 1''-H_A), 1.67 (1H, br.s, OH), 1.74–1.92 (3H, m, 1'-H₂ and 1''-H_B), 2.52 (1H, br.s, OH), 2.66–2.76 (1H, m, 4-H), 3.11 (1H, td, *J* 2 x 8.6 and 6.4 Hz, 3-H), 3.61–3.92 (6H, m, 2'-H₂, 2''-H₂ and 1'''-H₂), 4.36 (1H, dd, *J* 7.5 and 3.6 Hz, 5-H), 7.38–7.48 (6H, m, Ar-H), 7.63–7.72 (4H, m, Ar-H); δ_C (100 MHz, CDCl₃) 19.2 [C(CH₃)₃], 26.8 [C(CH₃)₃], 28.4 (C-1'), 30.4 (C-1''), 37.2 (C-4), 40.6 (C-3), 60.4 (C-2''), 61.1 (C-2'), 64.5 (C-1'''), 83.0 (C-5), 127.9, 130.0, 132.5(7) and 132.8(2), 135.5(7) and 135.6(3) (Ar-C), 179.7 (C-1) (Found: M⁺-C₄H₉, 385.1477. Calc. for C₂₁H₂₅O₅Si: *M* 385.1471)

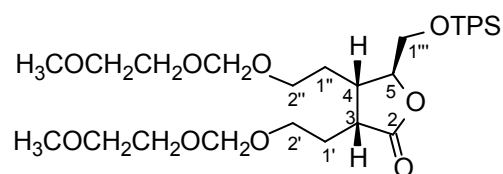
(3*R*, 4*S*)-5-[(*S*)-*t*-Butyldiphenylsilyloxymethyl]-3,4-bis[2-(3,5-dinitrobenzoyl)ethyl]-dihydrofuran-2-one **17**



4-Dimethylaminopyridine (20 mg, 0.16 mmol) and freshly prepared 3,5-dinitrobenzoyl chloride (1.54 g, 6.66 mmol) were added to a stirred solution of **16** (400 mg, 0.90 mmol) in dry pyridine (10 cm³). After stirring the mixture for 3 h at 25 °C, toluene was added and the mixture was concentrated under reduced pressure. Water was added to the remaining residue and it was extracted with ethyl acetate. The organic extract was washed with saturated aqueous ammonium chloride and brine, dried (MgSO₄) and the solvent was removed under reduced pressure to give an

oil (1.62 g). Purification by column chromatography on silica gel (750 g) using ethyl acetate–hexane (1:4) as eluent yielded the *bis(3,5-dinitrobenzoate)* **17** (604 mg, 80%) as an oil, $[\alpha]_D +7.1$ (c 1.4 in CHCl_3); $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 1734 and 1773 (CO); δ_{H} (400 MHz, CDCl_3) 1.00 [9H, s, $\text{C}(\text{CH}_3)_3$], 1.84–1.96 (1H, m, 1''-H_A), 2.07–2.22 (2H, m, 1'-H_A and 1''-H_B), 2.24 (1H, m, 1'-H_B), 2.73–2.83 (1H, m, 4-H), 3.14 (1H, dd, J 15.2 and 8.2 Hz, 3-H), 3.82 (1H, dd, J 11.5 and 3.1 Hz, 1'''-H_A), 3.95 (1H, dd, J 11.5 and 4.2 Hz, 1'''-H_B), 4.40 (1H, dd, J 7.0 and 3.2 Hz, 5-H), 4.53 (2H, t, J 2 x 6.8 Hz, 2''-H₂), 4.60–4.77 (2H, m, 2'-H₂), 7.32–7.48 (6H, m, TPS Ar-H), 7.55–7.65 (4H, m, TPS Ar-H), 9.10 (4H, t, J 2 x 2.0 Hz, DNP Ar-H) and 9.21 (2H, dt, J 8.6 and 2 x 2.0 Hz, DNP Ar-H); δ_{C} (100 MHz, CDCl_3) 19.2 [$\text{C}(\text{CH}_3)_3$], 25.0 (C-1'), 26.8 [$\text{C}(\text{CH}_3)_3$], 27.2 (C-1''), 37.0 (C-4), 39.3 (C-3), 64.1 (C-2''), 64.4 (C-1'''), 64.6 (C-2'), 81.9 (C-5), 122.5(0) and 122.6(5), 127.9(1) and 127.9(3), 129.3(6) and 129.3(9), 130.1(1) and 130.1(5), 132.1(3) and 132.5(4), 133.2(7) and 133.5(4), 135.3(5) and 135.4(9), 148.7(1) and 148.7(6) (Ar-C), 2 x 162.5 [2 x OC(O)Ar] and 177.0 (C-2) [Found (FAB): $\text{M}^+ - \text{C}_4\text{H}_9$, 773.1372. Calc. for $\text{C}_{35}\text{H}_{29}\text{N}_4\text{O}_{15}\text{Si}$: M , 773.1399]

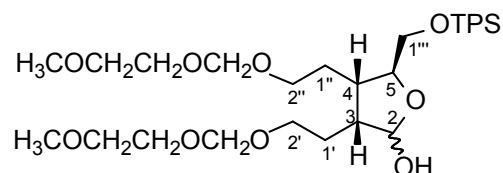
(3R, 4S)-5-[(S)-*t*-Butyldiphenylsilyloxymethyl]-3,4-bis(2-methoxyethoxymethoxyethyl)-dihydrofuran-2-one **18**



Methoxyethoxymethylchloride (0.15 cm³, 164 mg, 1.31 mmol) and diisopropylethylamine (0.24 cm³, 178 mg, 1.38 mmol) were added to diol **16** (200 mg, 0.45 mmol) in dichloromethane (3 cm³) and stirred at 25 °C for 16 h. Then saturated aqueous ammonium chloride was added and the mixture was extracted with dichloromethane. The organic extract was dried (MgSO_4) and the solvent was removed under reduced pressure to give an oil (340 mg). Chromatography on silica gel (20 g) using ethyl acetate–hexane (3:2) as eluent, afforded **18** (257 mg, 92%) as an oil, $[\alpha]_D +10.5$ (c 1.9 in CHCl_3); $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 1771 (CO); δ_{H} (400 MHz, CDCl_3) 1.05 [9H, s, $\text{C}(\text{CH}_3)_3$], 1.48–1.60 (1H, m, 1''-H_A), 1.76–1.87 (2H, m, 1'-H_A and 1''-H_B), 1.93–2.04 (1H, m, 1'-H_B), 2.63–2.73 (1H, m, 4-H), 3.15 (1H, q, J 3 x 8.0 Hz, 3-H), 3.35 (3H, s, OCH_3), 3.38 (3H, s, OCH_3), 3.47–3.76 (13H, m, 2'-H₂, 2''-H₂, 1'''-H_A, 2 x $\text{OCH}_2\text{CH}_2\text{O}$), 3.87 (1H, dd, J 11.4 and 3.5 Hz, 1'''-H_B), 4.32 (1H, q, J 3 x 3.5 Hz, 5-H), 4.64 (2H, d, J 1.5 Hz, OCH_2O), 4.69 (2H, s, OCH_2O), 7.35–7.46 (6H, m, Ar-H) and 7.62–7.65 (4H, m, Ar-H); δ_{C} (100 MHz, CDCl_3) 19.2 [$\text{C}(\text{CH}_3)_3$], 25.8 (C-1'), 26.7 [$\text{C}(\text{CH}_3)_3$], 27.9 (C-1''), 37.3 (C-4), 39.4 (C-3), 59.0 (2 x OCH_3), 64.9, 65.4 and 65.4 (C-2', C-2'' and C-1'''), 66.8, 66.9, 71.7 and 71.8 (2 x $\text{OCH}_2\text{CH}_2\text{O}$), 82.3 (C-5), 95.4 and 95.5

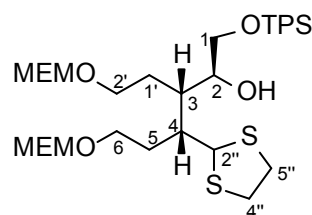
(2 x OCH₂O), 127.8, 129.9, 132.5(3) and 132.8(8), 135.5(5) and 135.6(2) (Ar-C) and 178.6 (C-2)
(Found: M⁺-C₄H₉, 561.2507. Calc. for C₂₉H₄₁O₉Si: M, 561.2520).

**(3R, 4S)-5-[(S)-*t*-Butyldiphenylsilyloxymethyl]-3,4-bis(2-methoxyethoxymethoxyethyl)-
dihydrofuran-2-ol **21****



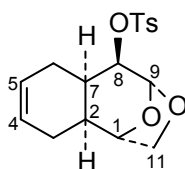
Diisobutylaluminium hydride (1.5 M in toluene, 1.30 cm³, 1.95 mmol) was added to a stirred solution of **18** (1.00 g, 1.62 mmol) in toluene (100 cm³) at -78 °C. After 10 min the solution was acidified (pH 1) with 3 M HCl and the mixture was warmed to room temperature. Water was added and the mixture extracted with ethyl acetate. The organic extract was washed with water, dried (MgSO₄) and the solvent was removed under reduced pressure to give the lactol (1.23 g) which was further purified by column chromatography on silica gel (30 g) using ethyl acetate as eluent to give the *lactol* **21** (0.94 g, 93%) as a mixture (~4:1 by NMR) of diastereomers, [α]_D +6.6 (*c* 1.4 in CHCl₃); ν_{max}(CHCl₃)/cm⁻¹ 3440 (OH); δ_H (400 MHz, CDCl₃) *major* 1.07 [9H, s, C(CH₃)₃], 2.57—2.69 (1H, m, 4-H), 3.77—3.83 (1H, m, 5-H), 5.23 (1H, d, *J* 5.1 Hz, 2-H), *minor* 1.05 [9H, s, C(CH₃)₃], 2.30—2.40 (1H, m, 4-H), 2.82 (1H, br.s, OH), 4.12—4.17 (1H, m, 5-H), 5.40 (1H, d, *J* 4.4 Hz, 2-H), *mixed* 1.33—1.45 and 1.46—1.92 (5H, m, 1''-H₂, 1'-H₂ and OH), 2.17—2.26 (1H, m, 3-H), 3.15—3.75 (20H, m, 2'-H₂, 2''-H₂, 1'''-H₂, 2 x OCH₂CH₂O and 2 x OCH₃), 4.58—4.80 (4H, m, 2 x OCH₂O), 7.33—7.46 (6H, m, Ar-H) and 7.64—7.72 (4H, m, Ar-H); δ_C (100 MHz, CDCl₃) *major* 19.4 [C(CH₃)₃], 26.1 (C-1'), 27.0 [C(CH₃)₃], 27.7 (C-1''), 36.6 (C-4), 46.3 (C-3), 59.1 (2 x OCH₃), 84.0 (C-5), *minor* 19.4 [C(CH₃)₃], 25.5 (C-1'), 27.7 [C(CH₃)₃], 30.5 (C-1'''), 38.2 (C-4), 43.7 (C-3), 59.1 (2 x OCH₃), 84.7 (C-5), *mixed* 65.2, 66.4, 66.5, 66.6 and 67.0 (C-2', C-2'' and C-1'''), 67.0(2), 67.0(4), 67.1(0), 67.1(6), 72.0(1) and 72.0(5) (2 x OCH₂CH₂O), 95.6(1), 95.6(4), and 95.6(8) (2 x OCH₂O), 99.7 and 101.7 (C-2) and 127.8, 128.0, 129.9, 130.0, 130.1, 133.1, 133.7, 133.8, 135.3, 135.5 and 135.9 (Ar-C) [Found (FAB): M⁺+⁸⁵Rb, 705. Calc. for C₃₃H₅₂O₉Si⁸⁵Rb: M, 705].

(2S, 3S, 4R)-1-*t*-Butyldiphenylsilyloxy-4-(1,3-dithiolan-2-yl)-6-methoxyethoxymethoxy-3-(methoxyethoxymethoxyethan-2-yl)hexan-2-ol 22



1,2-Ethanedithiol (0.04 cm³, 45 mg, 0.48 mmol) and titanium tetrachloride (1.0 M in CH₂Cl₂, 0.37 cm³, 0.37 mmol) were added sequentially to a stirred solution of **21** (200 mg, 0.32 mmol) in dichloromethane (5 cm³) at -84 °C. After 5 min, the reaction was quenched with saturated aqueous sodium hydrogen carbonate and the resultant mixture was extracted with dichloromethane. The organic phase was dried (MgSO₄) and the solvent was removed under reduced pressure to give a residue (320 mg) which was chromatographed on silica gel (20 g) using ethyl acetate–hexane (2:3) as eluent to give the *thioacetal* **22** (71 mg, 32%) as a glassy solid, [α]_D -34.5 (*c* 1.25 in CHCl₃); ν_{max}(CHCl₃)/cm⁻¹ 3498 (OH); δ_H (300 MHz, CDCl₃) 1.06 [9H, s, C(CH₃)₃], 1.50–1.82 (4H, m, 5-H₂ and 1'-H₂), 1.94 (1H, br.s, OH), 2.23–2.35 (1H, m, 4-H), 2.38–2.51 (1H, m, 3-H), 2.63–3.00 (4H, m, 4''-H₂ and 5''-H₂), 3.36 (3H, s, OCH₃), 3.38 (3H, s, OCH₃), 3.45–3.77 (14H, m, 1-H₂, 6-H₂, 2'-H₂, 2 x OCH₂CH₂O), 3.86–3.94 (1H, m, 2-H), 4.64 (2H, s, OCH₂O), 4.70 (2H, s, OCH₂O), 5.10 (1H, d, *J* 4.1 Hz, 2''-H), 7.34–7.46 (6H, m, Ar-H) and 7.65–7.70 (4H, m, Ar-H); δ_C (75 MHz, CDCl₃) 19.2 [C(CH₃)₃], 25.3 (C-4'' or C-5''), 26.8 [C(CH₃)₃], 27.0 and 27.4 (C-1' and C-5), 35.4 (C-4'' or C-5''), 40.0 (C-3), 45.0 (C-4), 58.9 and 59.0 (2 x OCH₃), 66.1, 66.2, 66.4, 66.7 and 66.8 (C-1, C-6, C-2' and 2 x OCH₂CH₂O), 71.7 and 71.8 (2 x OCH₂CH₂O), 84.9 (C-2), 88.5 (C-2''), 95.3 and 95.4 (2 x OCH₂O), 127.7, 129.6(3) and 129.6(5), 133.4 and 135.6 (Ar-C) [Found (FAB): M⁺+⁸⁵Rb, 781. Calc. for C₃₅H₅₆O₈S₂Si⁸⁵Rb: *M*, 781].

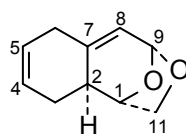
(1S, 2S, 7R, 8R, 9R)-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-8-yl-toluene-*p*-sulfone 25



Toluene-*p*-sulfonyl chloride (3.70 g, 19.40 mmol) and 4-dimethylaminopyridine (20 mg, 0.16 mmol) were added to a solution of **23** (360 mg, 1.98 mmol) in dry pyridine (25 cm³). The solution was stirred at 25 °C for 18 h after which toluene was added and the volatile material was removed under reduced pressure. Water was added to the residue and the mixture was extracted with ethyl

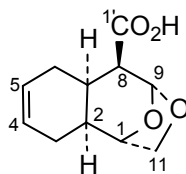
acetate, washed with saturated ammonium chloride and brine, dried (MgSO_4) and the solvent was removed under reduced pressure. The residue (872 mg) was chromatographed on silica gel (60 g) using ethyl acetate–hexane (1:4) as eluent to give the *tosylate* **25** (648 mg, 97%), mp 164–166 °C (from ethyl acetate–hexane); $[\alpha]_{\text{D}} +25.9$ (c 1.7 in CHCl_3); $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 1039, 1176 and 1362 (SO_2); δ_{H} (400 MHz, CDCl_3), 1.61 (1H, m, 6- H_A), 1.70–1.78 (1H, m, 2-H), 1.91–2.00 (1H, m, 3- H_A), 2.15–2.28 (1H, m, 6- H_B), 2.40 (1H, dd, J 8.8 and 4.4 Hz, 7-H) 2.43 (3H, s, Ar- CH_3), 2.48–2.59 (1H, m, 3- H_B), 3.80 (1H, dd, J 7.6 and 5.2 Hz, 11- H_A), 3.88 (1H, dd, J 7.6 and 0.8 Hz, 11- H_B), 4.27 (1H, dd, J 4.4 and 2.4 Hz, 8-H), 4.32 (1H, dd, J 5.2 and 2.4 Hz, 1-H), 5.31 (1H, d, J 2.4 Hz, 9-H), 5.44–5.51 (1H, m, 5-H), 5.67–5.71 (1H, m, 4-H), 7.31 (2H, br.d, Ar- m -H) and 7.77 (2H, br.d, Ar- o -H); δ_{C} (100 MHz, CDCl_3), 21.6 (Ar- CH_3), 25.1 (C-3), 25.6 (C-6), 26.3 (C-7), 34.5 (C-2), 67.2 (C-11), 76.5 (C-8), 79.0 (C-1), 100.0 (C-9), 124.0 (C-5), 125.6 (C-4), 125.6, 127.8, 129.7 and 144.7 (Ar-C) (Found: C, 60.6, H, 5.9, S, 9.4%, M^+ , 336. Calc. for $\text{C}_{17}\text{H}_{20}\text{O}_5\text{S}$: C, 60.7, H, 6.0, S, 9.5%, M , 336).

(1S, 2S, 9R)-10,12-Dioxatricyclo[7.2.1.0^{2,7}]dodeca-4,7-diene **26**



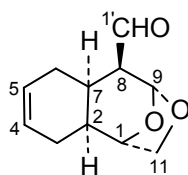
Lithium cyanide (0.5 M in N,N -dimethylformamide, 7.5 cm^3) was added to a solution of **25** (250 mg, 0.74 mmol) in N,N -dimethylformamide and heated at 80 °C for 15 h. The solution was cooled, diluted with diethyl ether, washed with water, dried (MgSO_4), and the solvent was removed under reduced pressure to give a solid residue (107 mg) which was purified by chromatography on silica gel (10 g) using ethyl acetate–hexane (1:9) as eluent to yield the *olefin* **26** (85 mg, 70%); δ_{H} (400 MHz, CDCl_3), 2.08 (1H, ddd, J 5.2, 4.8 and 1.2 Hz, 3- H_A), 2.20–2.31 (1H, m, 2-H), 2.47 (1H, ttd, J 14.2, 2 x 4.5 and 2 x 2.4 Hz, 3- H_B), 2.55–2.65 (1H, m, 6- H_A), 2.84–2.94 (1H, m, 6- H_B), 3.70 (1H, dd, J 7.2 and 2.0 Hz, 11- H_A), 3.98 (1H, dd, J 7.2 and 6.0 Hz, 11- H_B), 4.39 (1H, dt, J 6.0 and 2 x 0.8 Hz, 1-H), 5.49 (1H, d, J 3.2 Hz, 9-H), 5.59–5.67 (1H, m, 8-H) and 5.68–5.80 (2H, m, 4-H and 5-H); δ_{C} (100 MHz, CDCl_3), 30.4 (C-3), 32.9 (C-6), 42.4 (C-2), 68.0 (C-11), 75.0 (C-8), 96.3 (C-9), 120.2 (C-8), 125.4 and 126.5 (C-4 and C-5) and 137.3 (C-7) (Found M^+ 164, $\text{C}_{10}\text{H}_{12}\text{O}_2$ requires M , 164)

(1S, 2S, 7R, 8R, 9R)-10,12-Dioxatricyclo[7.2.1.0^{2,7}]dodec-4-ene-8-carboxylic acid **32**



CrO₃ (8 M, 5 cm³) was added to a solution of **30** (421 mg, 2.15 mmol) in acetone (15 cm³) at 0°C. The resulting mixture was kept at -4°C for 15 h after which excess isopropyl alcohol was added and the volume was reduced *in vacuo*. Ethyl acetate was added to the aqueous slurry and the resulting mixture was washed with water, dried (MgSO₄) and the solvent was removed under reduced pressure to give a green residue (360 mg). Chromatography on silica gel (45 g) using ethyl acetate-hexane (3:7 to 3:2 gradient), gave *acid 32* (122 mg, 27%), mp 82–85°C (from ethyl acetate), δ_H (300 MHz, CDCl₃), 1.79–1.90 (1H, m, 2-H), 1.96–2.09 (1H, m, 6-H_A), 2.19–2.42 (2H, m, 3-H₂), 2.49–2.67 (2H, m, 6-H_B and 8-H), 2.66–2.76 (1H, m, 7-H), 3.85 (1H, dd, *J* 7.1 and 5.4 Hz, 11-H_A), 4.00 (1H, dd, *J* 7.1 and 0.6 Hz, 11-H_B), 4.37–4.45 (1H, m, 1-H) and 5.62–5.66 (3H, m, 4-H, 5-H and 9-H); δ_C (75 MHz, CDCl₃), 24.6 (C-7), 25.9 and 26.5 (C-3 and C-6), 35.4 (C-2), 48.2 (C-8), 67.9 (C-11), 76.9 (C-1), 100.6 (C-9), 124.5 and 126.6 (C-4 and C-5) (Found: M⁺, 210.0892. Calc. for C₁₁H₁₄O₄: *M*, 210.0907).

(1S, 2S, 7R, 8S, 9R)-10,12-Dioxatricyclo[7.2.1.0^{2,7}]dodec-4-ene-8-carbaldehyde **31**



Dimethyl sulfoxide (0.17 cm³, 187 mg, 2.4 mmol) was added to a stirred solution of oxalyl chloride (0.11 cm³, 152 mg, 1.2 mmol) in dichloromethane (5 cm³) at -78 °C. After 10 min a solution of **30** (196 mg, 1.0 mmol) in dichloromethane (2 cm³) was added and the solution was stirred for 15 min. Triethylamine (0.5 cm³, 363 mg, 3.5 mmol) was added and the reaction was stirred at -78 °C for 30 min then warmed to 0 °C over 10 min. Cold saturated aqueous ammonium chloride was added and the mixture was extracted with dichloromethane. The organic extract was washed with cold 0.5 M HCl followed by cold aqueous saturated sodium hydrogen carbonate, dried (MgSO₄) and the solvent was removed under reduced pressure to give a residue (262 mg) which was chromatographed on silica gel (25 g) using ethyl acetate-hexane (1:9) as eluent to give the *carbaldehyde 31* (185 mg, 95%), mp 72–75 °C (from dichloromethane-hexane); [α]_D 125.4 (*c* 1.0

in CHCl_3); $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 1712 (OH); δ_{H} (400 MHz, CDCl_3), 1.89—1.97 (1H, m, 2-H), 1.98—2.07 (1H, m, 6- H_A), 2.13—2.24 (1H, m, 3- H_A), 2.29—2.40 (1H, m, 3- H_B), 2.40—2.46 (1H, m, 8-H), 2.46—2.52 (1H, m, 6- H_B), 2.75 (1H, q, J 3 x 6.5 Hz, 7-H), 3.88 (1H, dd, J 7.3 and 5.3 Hz, 11- H_A), 4.03 (1H, dd, J 7.3 and 0.7 Hz, 11- H_B), 4.43 (1H, dd, J 5.3 and 1.2 Hz, 1-H), 5.62—5.75 (3H, m, 4-H, 5-H and 9-H) and 9.71 (1H, d, J 3.3 Hz, 1'- H_A); δ_{C} (100 MHz, CDCl_3), 25.0 (C-3), 26.3 (C-7), 26.9 (C-6), 35.1 (C-2), 58.9 (C-8), 68.0 (C-11), 77.3 (C-1), 101.0 (C-9), 125.5 and 126.0 (C-4 and C-5) and 203.3 (C-1'), (Found: C, 67.8, H, 7.4%, M^+ 194. Calc. for $\text{C}_{11}\text{H}_{14}\text{O}_3$: C, 68.0, H, 7.3%, M , 194).

CRYSTAL STRUCTURE DETERMINATION OF 30

Data were collected at 295 K using a Nonius Kappa CCD with 1.5 kW graphite monochromated Mo radiation. The strategy for the data collection was evaluated using *COLLECT*. The detector to crystal distance was 40 mm. Exposure times of 40 s per frame and scan widths of 1° were used throughout the data collection. Three sets of data were collected: a 182° ϕ -scan and two ω -scans. The data were scaled and reduced using *DENZO-SMN*. Unit cell dimensions were refined on 1291 strong, well-measured reflections in the θ -range 1.02° to 27.5° (resolution between 20.00 Å and 0.77 Å). The chiral space group $P2_12_12_1$ was chosen on the basis of the systematic absences. The structure was solved and refined using *SHELX97*. Hydrogen atoms were placed in calculated positions and refined as riding atoms. Molecular graphics were generated using X-SEED.

Although the product **30** was expected to be racemic, crystallization of the specimen of the compound selected from the crystal batch for X-ray analysis in the chiral space group $P2_12_12_1$ required the molecules in the chosen crystal to be homochiral. This indicated that spontaneous resolution of the product had occurred, the batch consisting of a mixture of crystals containing exclusively left- and right-handed molecules in equimolar proportions. After solution and refinement of the structure, the Flack parameter was not definitive as regards absolute structure (an expected result for a crystal containing only C, H, O atoms) and the recommended procedure of merging the Friedel opposites was therefore followed (instruction MERG 4 in SHELX-97). The molecule shown in Fig. 2 (with configurations 1*S*, 2*S*, 7*R*, 8*S*, 9*R*) was thus chosen arbitrarily to illustrate the structure. In summary, the relative configurations in the molecule are correct but the absolute configuration of a molecule in an individual crystal could not be reliably determined from the X-ray data.

Details of the data collection and refinement are given in Table 1.

Atomic coordinates for non-hydrogen atoms are listed in Table 2.

Selected bond lengths are listed in Table 3, and bond angles in Table 4.

Table 1 Crystal data and structure refinement for **30**

Empirical formula	C ₁₁ H ₁₆ O ₃	
Formula weight	196.24	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2 ₁ 2 ₁ 2 ₁	
Unit cell dimensions	a = 7.475(1) Å	α = 90°
	b = 8.234(1) Å	β = 90°
	c = 16.061(2) Å	γ = 90°
Volume	988.5(2) Å ³	
Z	4	
Density (calculated)	1.319 Mg/m ³	
Absorption coefficient	0.095 mm ⁻¹	
F(000)	424	
Crystal size	0.45 x 0.24 x 0.17 mm ³	
θ range for data collection	1.02 to 27.48°	
Index ranges	-9 ≤ h ≤ 9, -10 ≤ k ≤ 10, -13 ≤ l ≤ 20	
Reflections collected	4919	
Independent reflections	1326 [R(int) = 0.0239]	
Completeness to θ = 27.48°	99.4%	
Max. and min. transmission	0.9841 and 0.9586	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2160 / 1 / 148	
Goodness-of-fit on F ²	1.070	
Final R indices [I > 2σ(I)]	R1 = 0.0357, wR2 = 0.0760	
R indices (all data)	R1 = 0.0496, wR2 = 0.0815	
Largest diff. peak and hole	0.166 and -0.166 e.Å ⁻³	

Table 2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **30**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor

	x	y	z	U(eq)
O(10)	3289(2)	7653(2)	834(1)	42(4)
O(12)	2030(2)	7964(2)	2105(1)	48(1)
O(2')	6850(2)	5417(2)	1781(1)	52(1)
C(7)	1795(3)	4712(2)	1508(1)	34(1)
C(1')	5276(3)	4739(3)	1412(1)	40(1)
C(2)	1147(3)	5470(2)	685(1)	36(1)
C(8)	3594(3)	5434(2)	1805(1)	35(1)
C(3)	2034(3)	4772(3)	-92(1)	47(1)
C(6)	1761(3)	2844(2)	1471(1)	48(1)
C(1)	1405(2)	7305(2)	721(1)	39(1)
C(9)	3536(3)	7270(2)	1680(1)	39(1)
C(11)	617(3)	8099(3)	1493(1)	46(1)
C(5)	2387(3)	2168(3)	663(2)	54(1)
C(4)	2496(3)	3005(3)	-25(2)	52(1)

Table 3 Selected bond lengths for **30**

Bond	Length (Å)	Bond	Length (Å)
O(10)-C(9)	1.407(2)	C(1')-C(8)	1.519(3)
O(10)-C(1)	1.449(2)	C(2)-C(1)	1.525(3)
O(12)-C(9)	1.435(2)	C(2)-C(3)	1.525(3)
O(12)-C(11)	1.447(2)	C(8)-C(9)	1.526(3)
O(2')-C(1')	1.431(2)	C(3)-C(4)	1.500(3)
C(7)-C(6)	1.540(3)	C(6)-C(5)	1.487(3)
C(7)-C(2)	1.540(2)	C(1)-C(11)	1.521(2)
C(7)-C(8)	1.545(3)	C(5)-C(4)	1.304(3)

Table 4 Selected bond angles for **30**

Bonds	Angle (°)	Bonds	Angle (°)
C(9)-O(10)-C(1)	101.8(2)	C(1')-C(8)-C(9)	110.0(2)
C(9)-O(12)-C(11)	106.2(2)	C(1')-C(8)-C(7)	116.6(2)
C(6)-C(7)-C(2)	111.5(2)	C(9)-C(8)-C(7)	108.4(2)
C(6)-C(7)-C(8)	114.2(2)	C(4)-C(3)-C(2)	114.0(2)
C(2)-C(7)-C(8)	112.6(2)	C(5)-C(6)-C(7)	113.7(2)
O(2')-C(1')-C(8)	111.2 (2)	O(10)-C(1)-C(11)	101.0(2)
C(1)-C(2)-C(3)	110.4(2)	O(10)-C(1)-C(2)	108.9(2)
C(1)-C(2)-C(7)	109.2(2)	C(11)-C(1)-C(2)	114.1(2)
C(3)-C(2)-C(7)	114.4(2)	O(10)-C(9)-O(12)	105.5(2)

NMR Spectra of prepared compounds

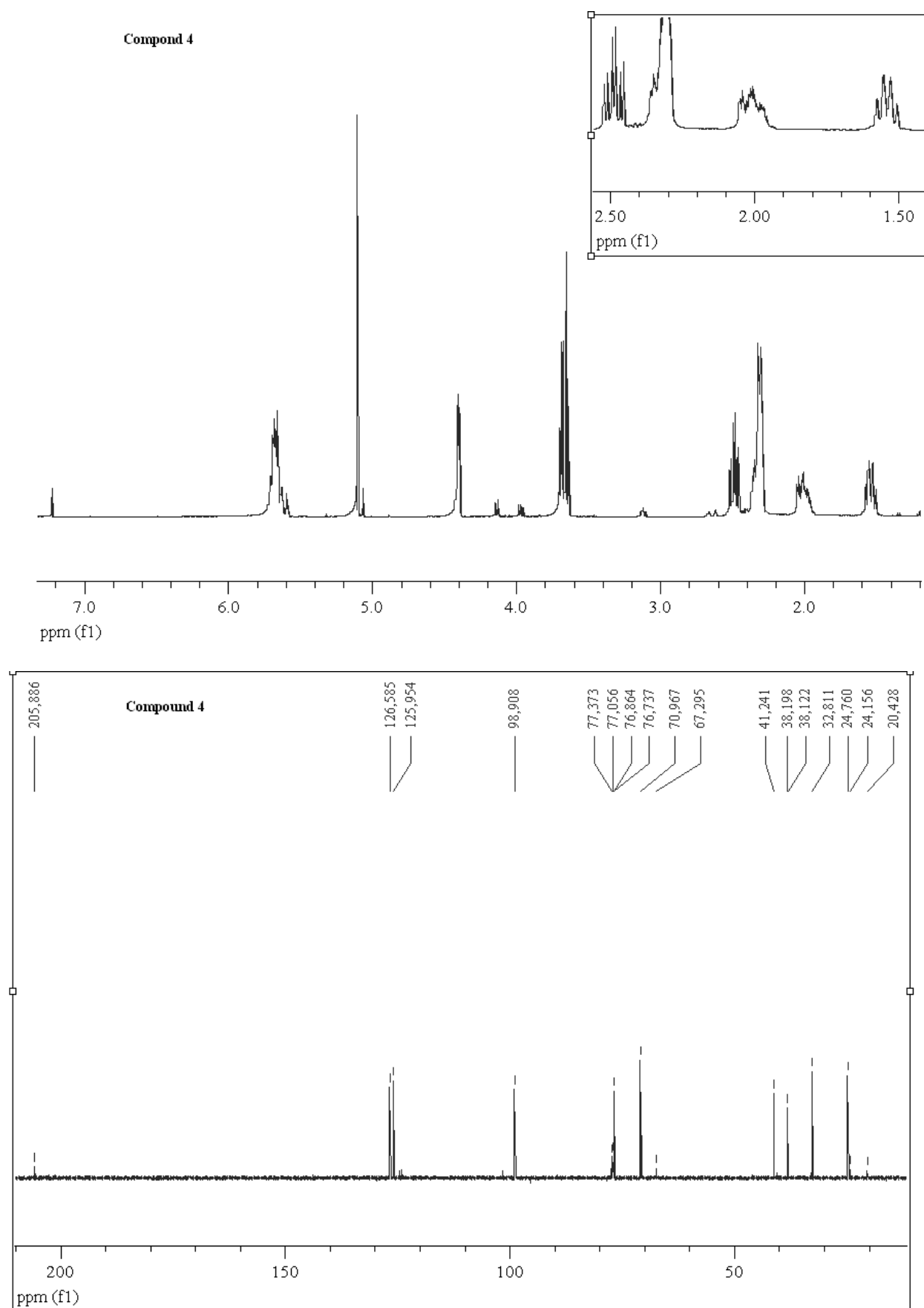


Figure S1: ^1H and ^{13}C NMR spectra of 4

Compound 6

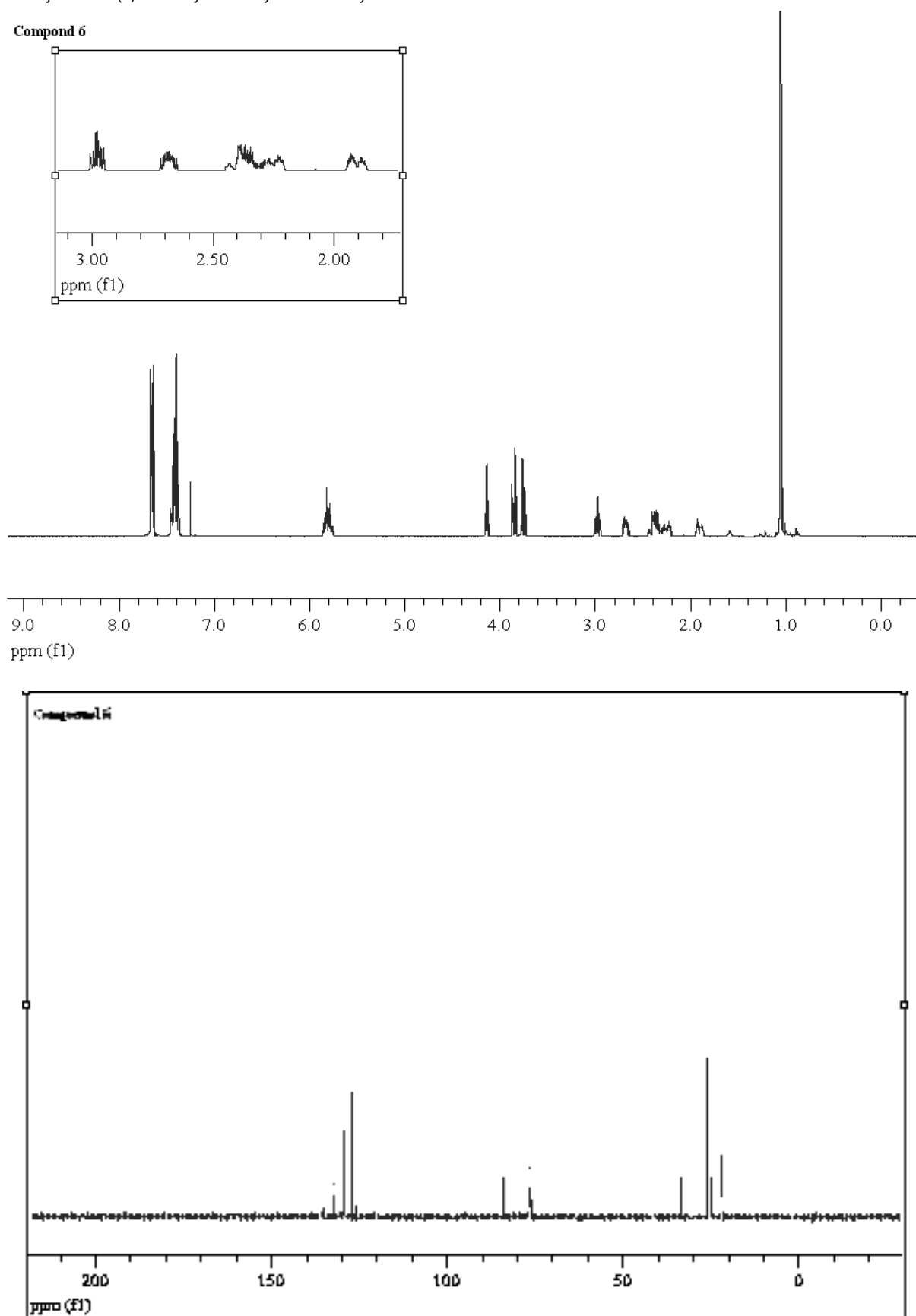


Figure S2: ^1H and ^{13}C NMR spectra of 6

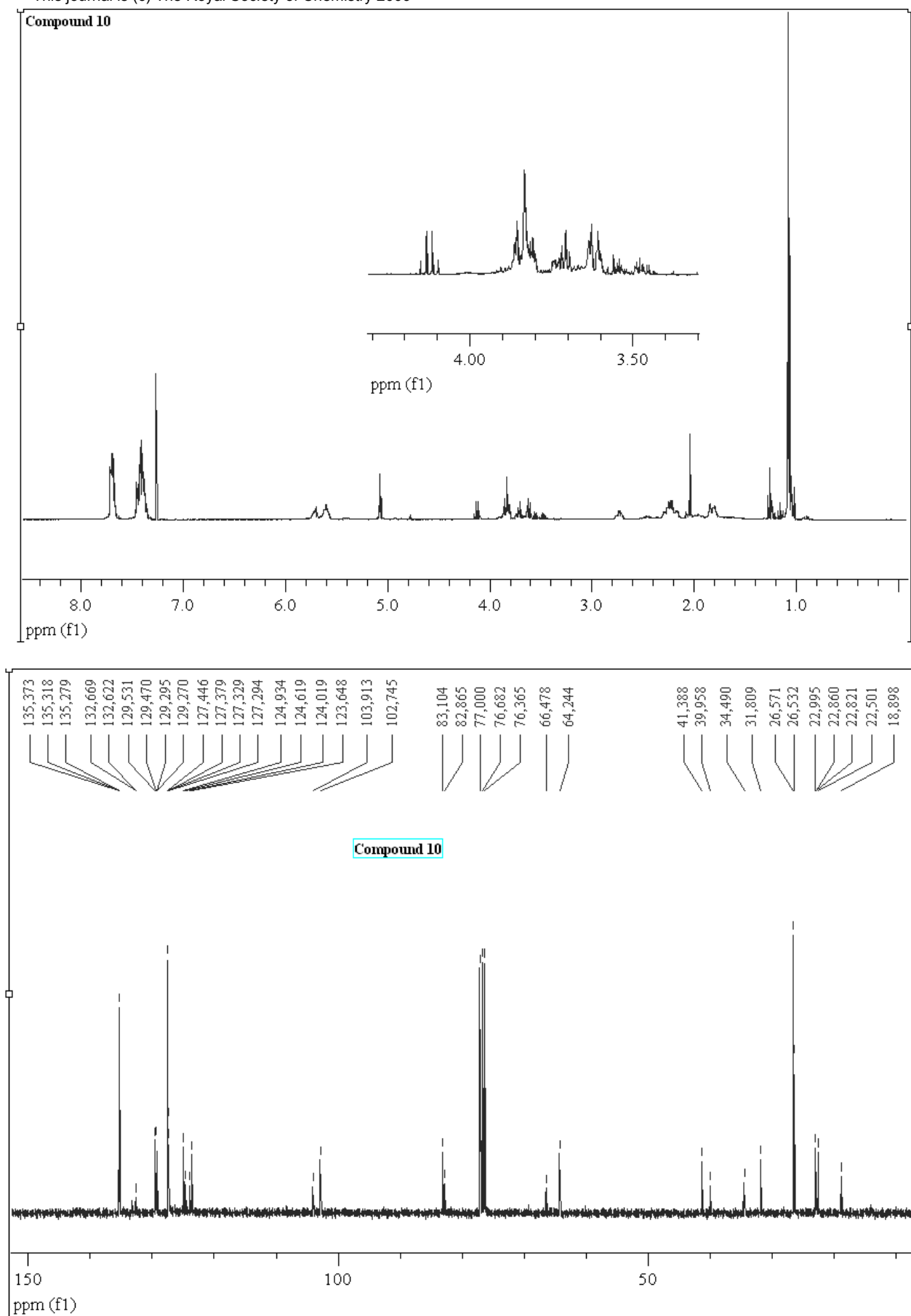


Figure S3: ^1H and ^{13}C NMR spectra of 10

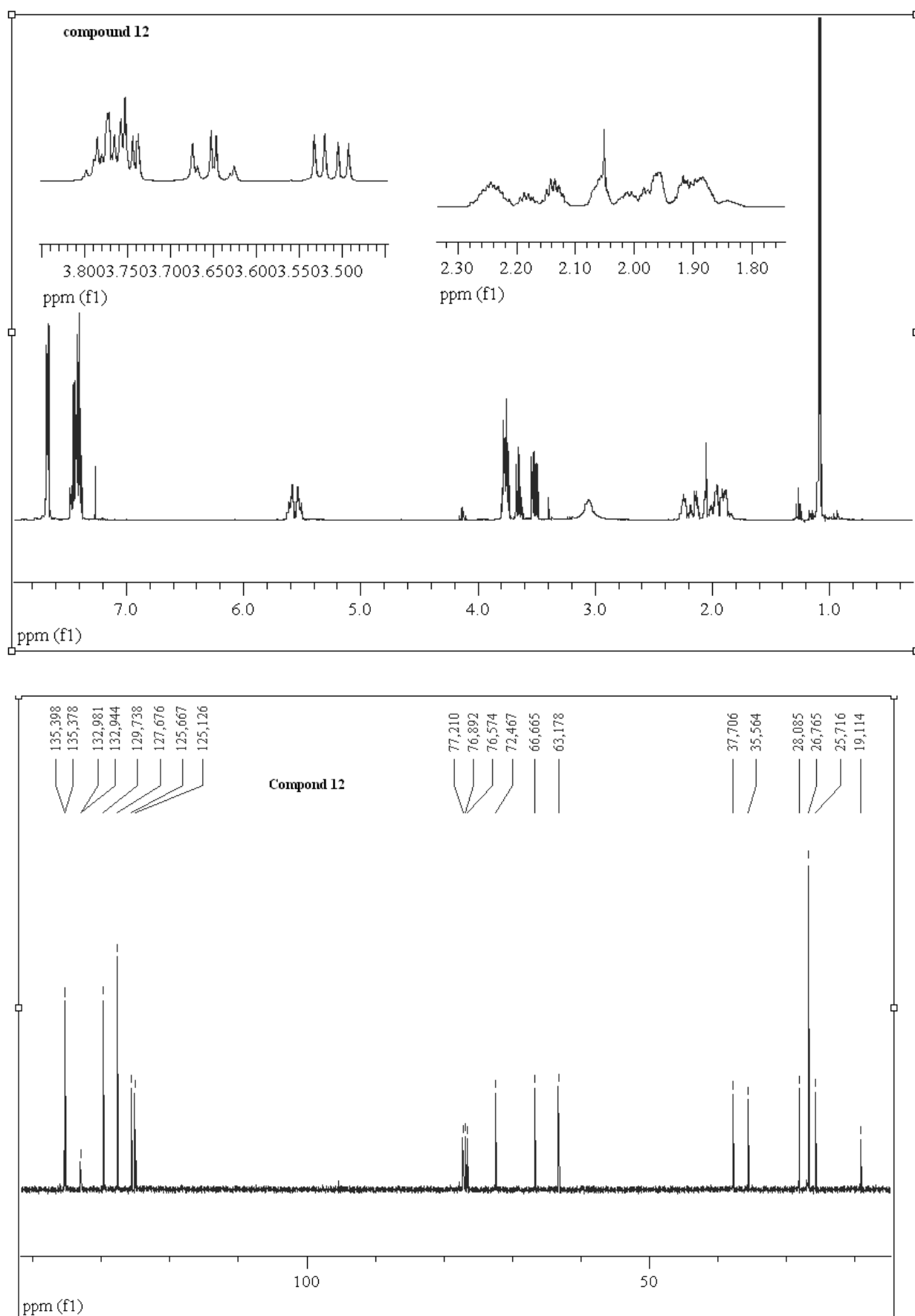


Figure S4: ^1H and ^{13}C NMR spectra of 12

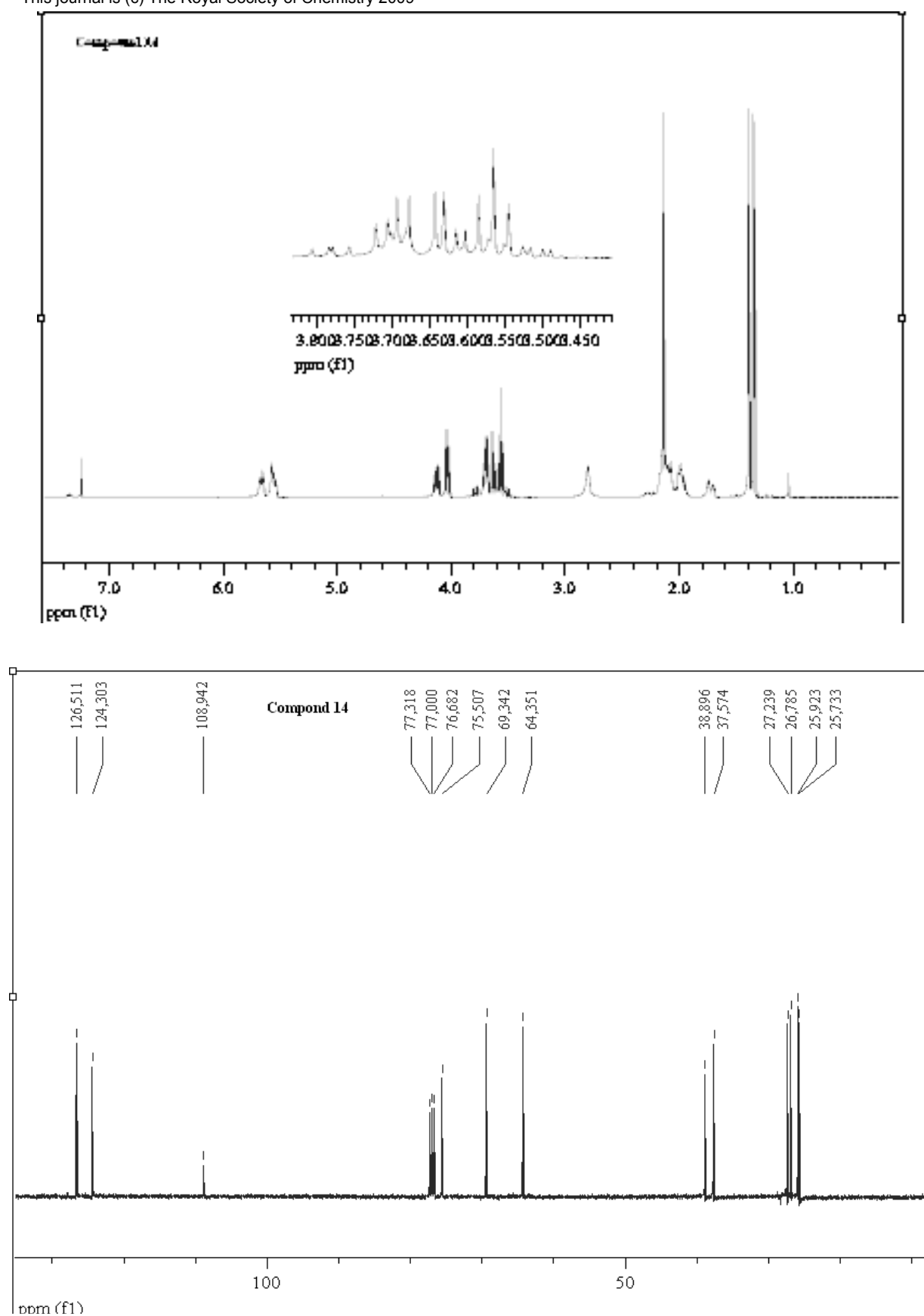


Figure S5: ^1H and ^{13}C NMR spectra of 14

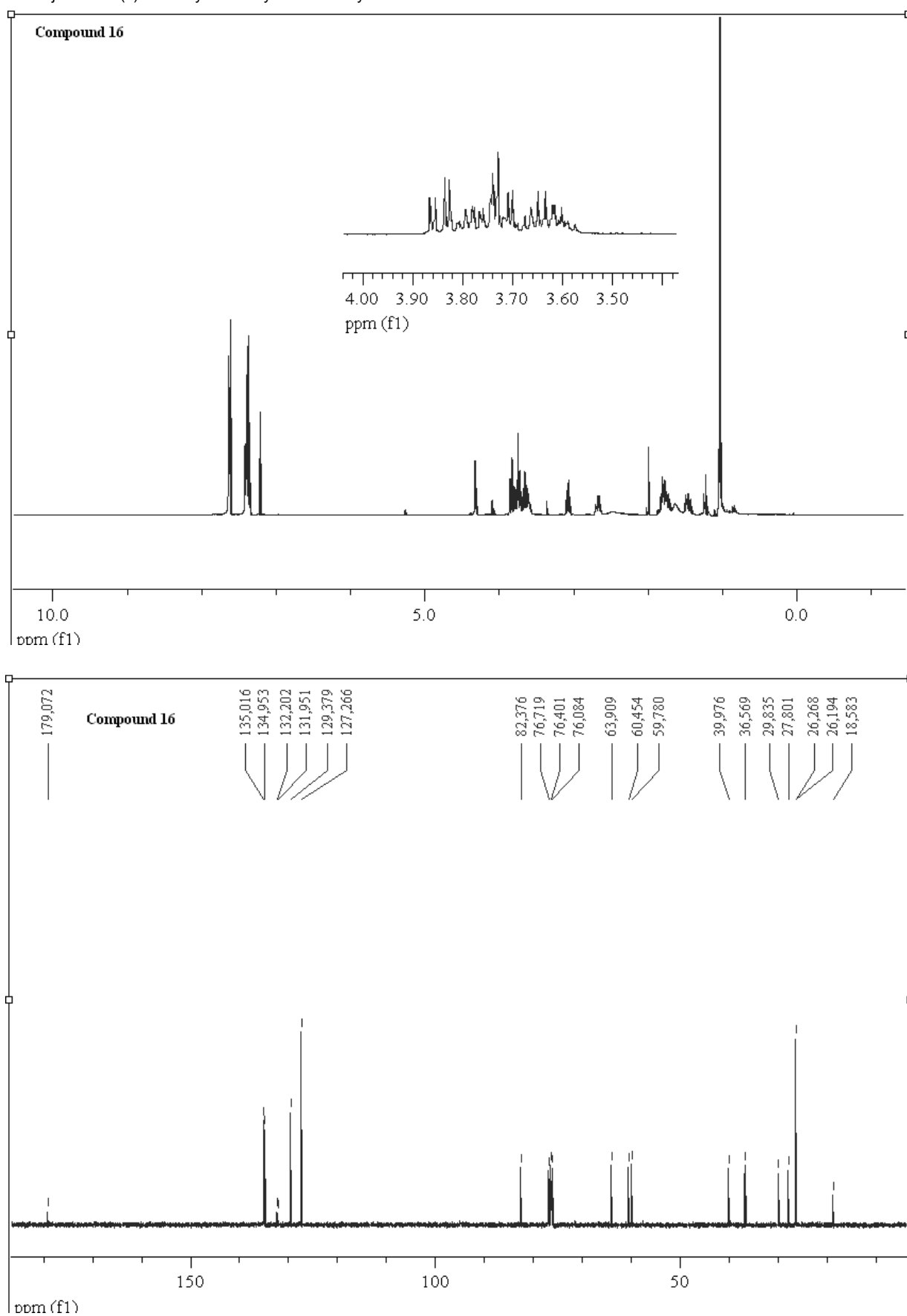


Figure S6: ^1H and ^{13}C NMR spectra of **16**

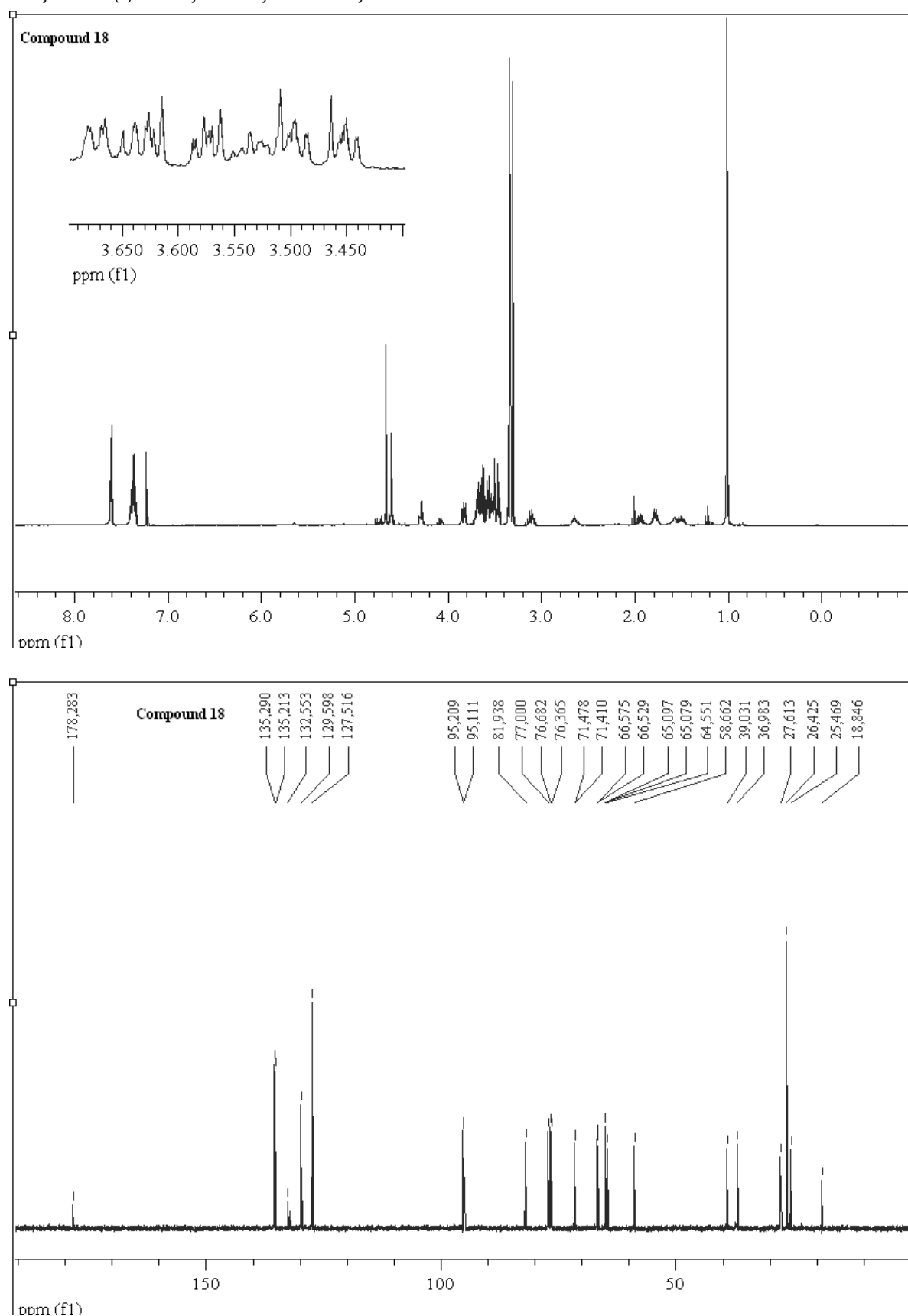


Figure S7: ^1H and ^{13}C NMR spectra of 18

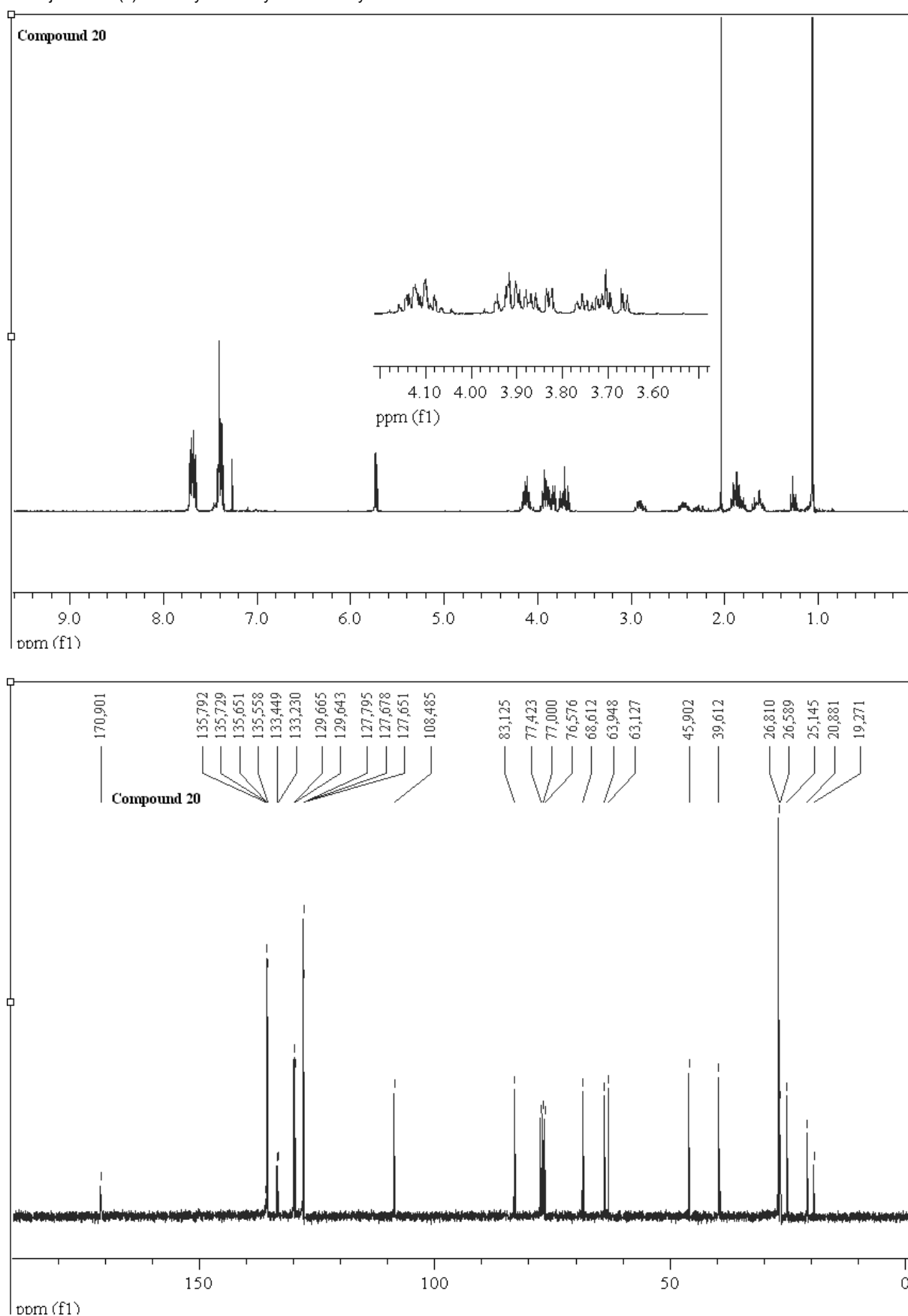


Figure S8: ^1H and ^{13}C NMR spectra of 20

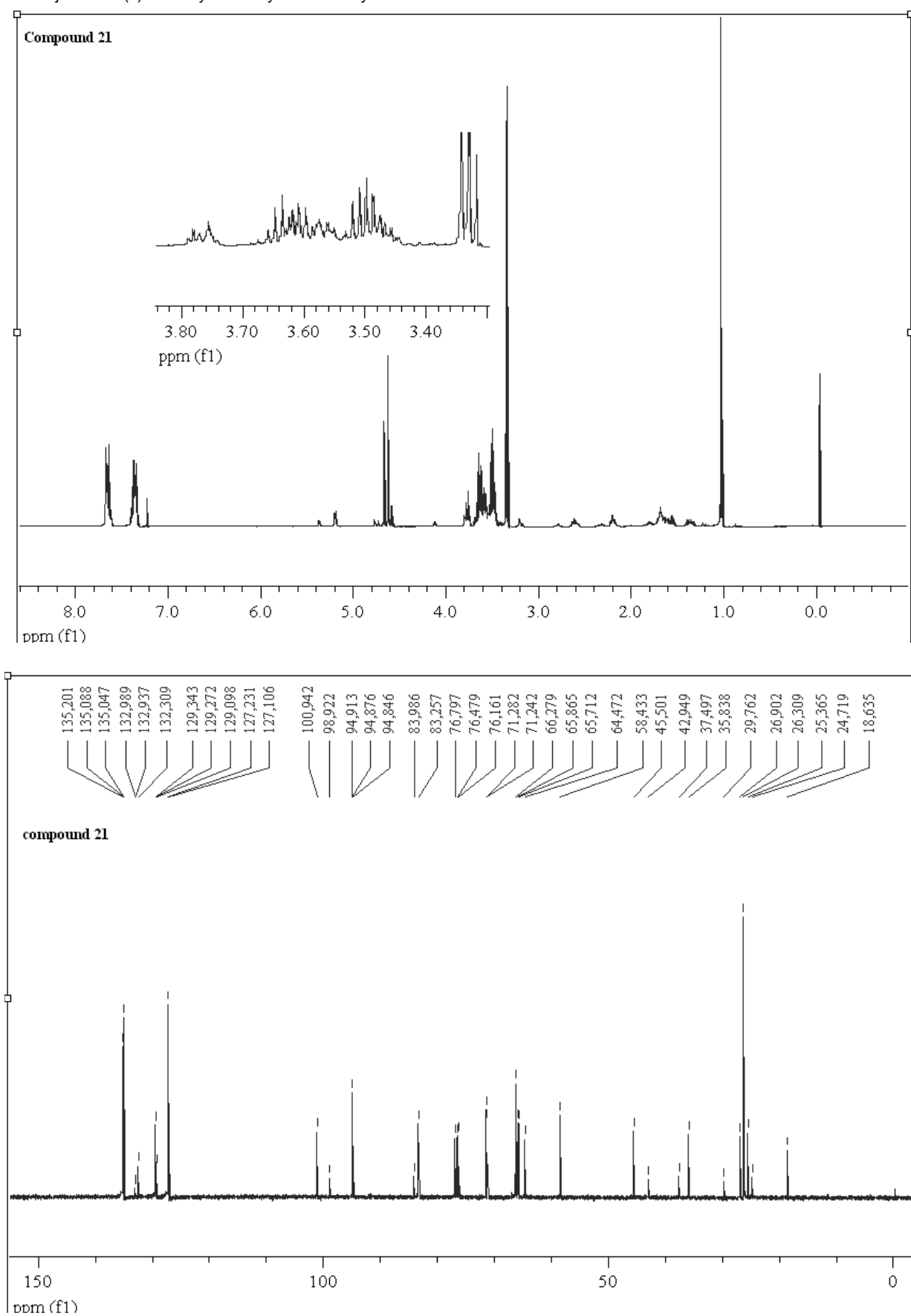


Figure S9: ^1H and ^{13}C NMR spectra of 21

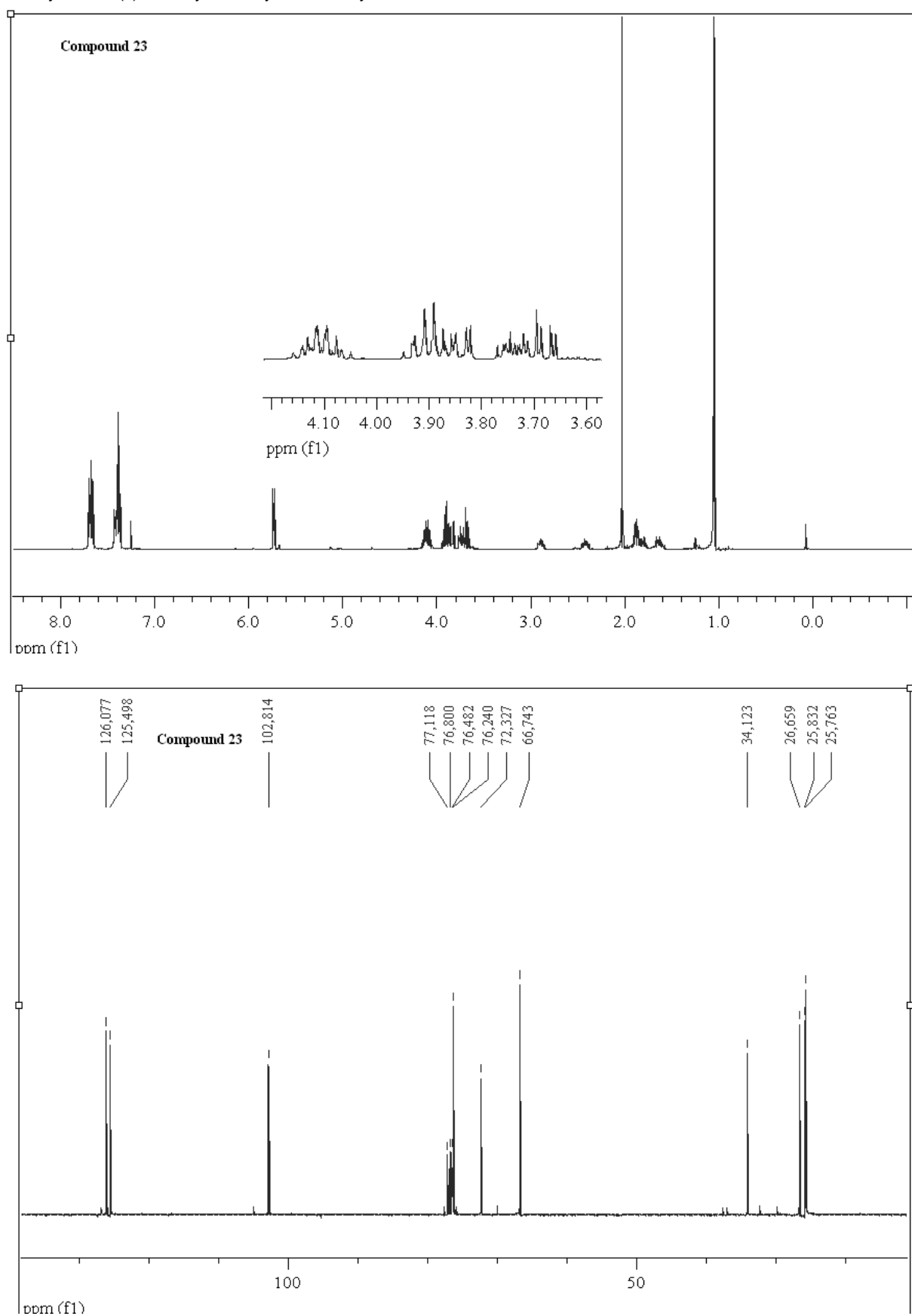


Figure S10: ^1H and ^{13}C NMR spectra of 23

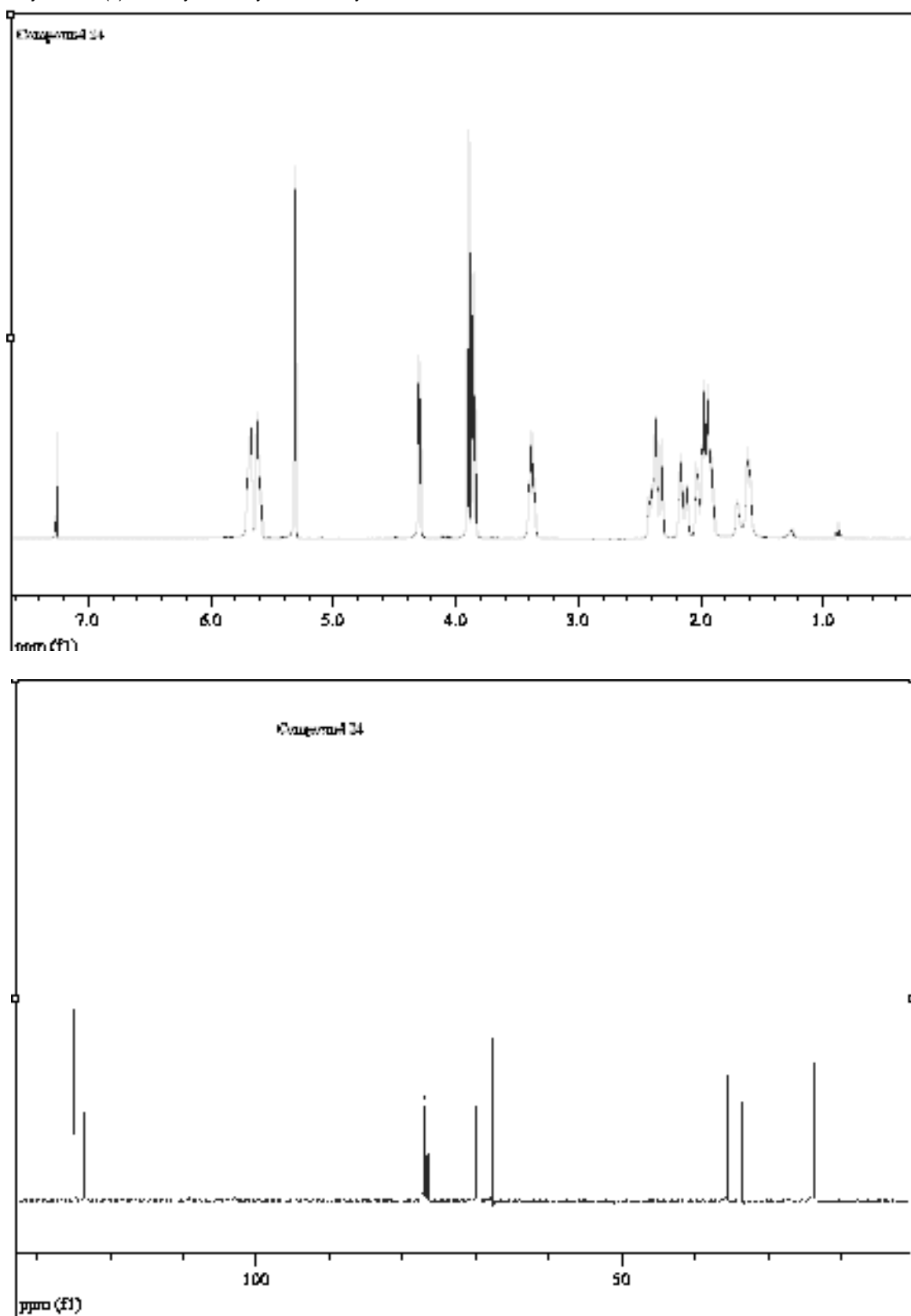


Figure S11: ^1H and ^{13}C NMR spectra of 24

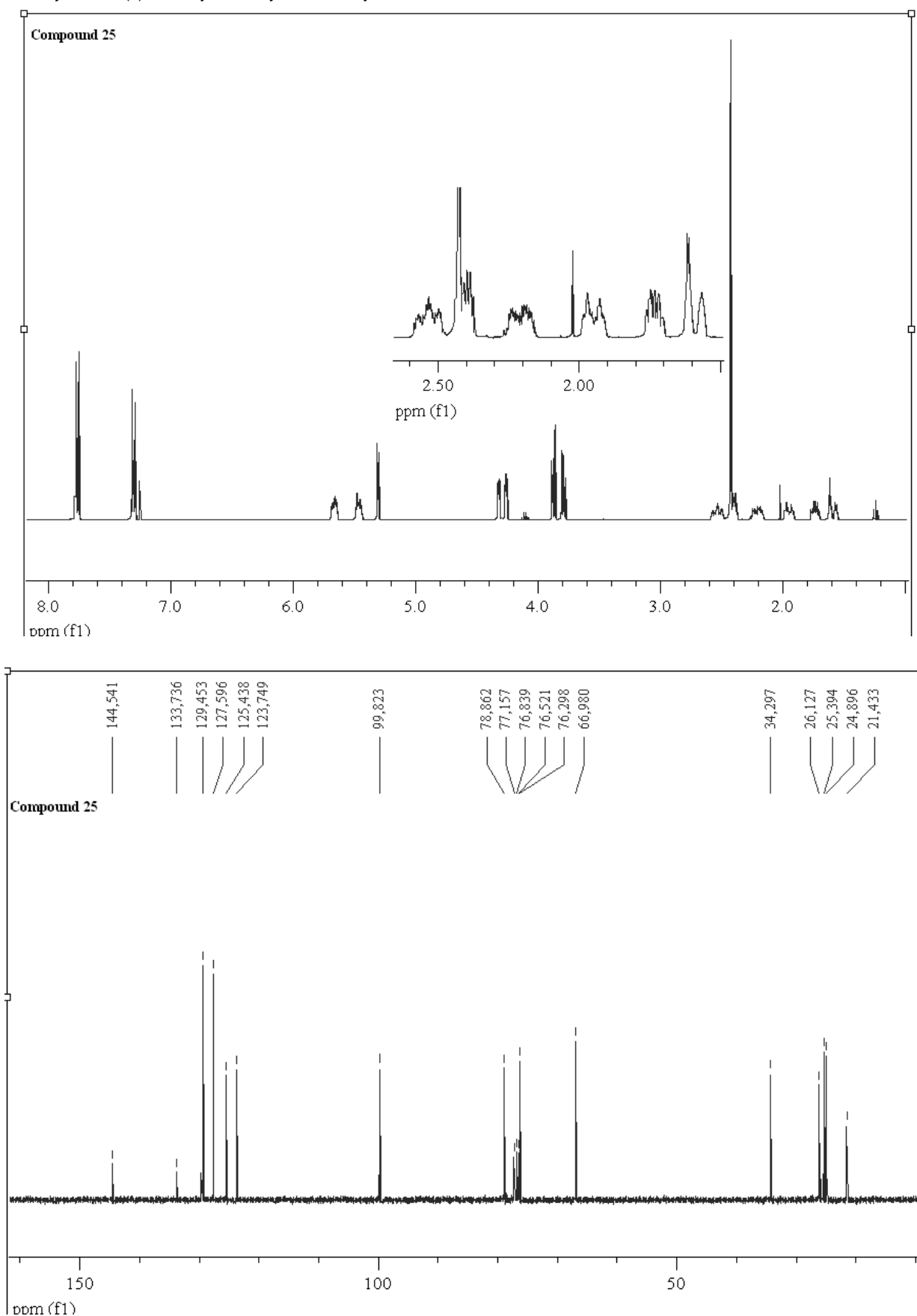


Figure S12: ^1H and ^{13}C NMR spectra of 25

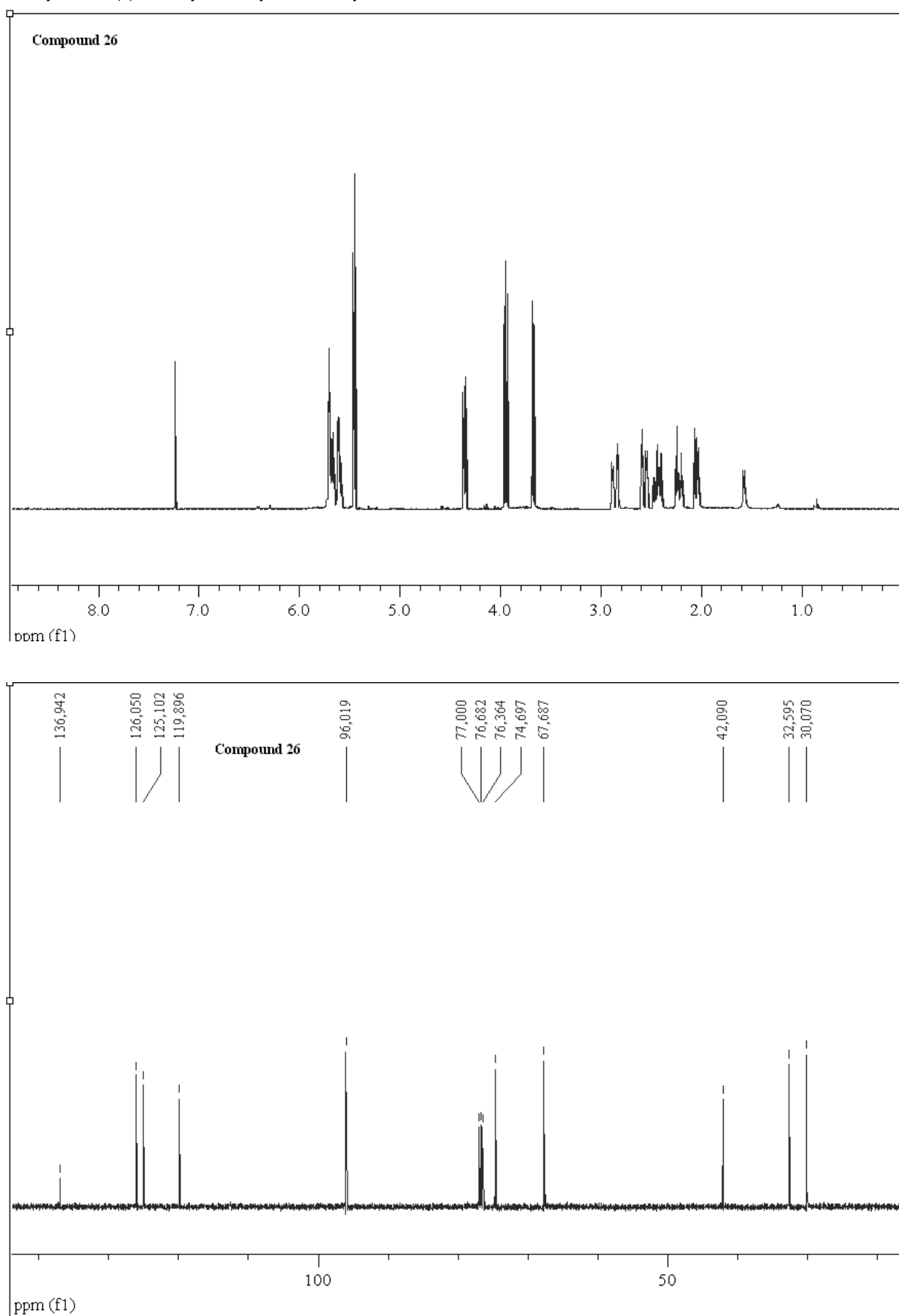


Figure S13: ^1H and ^{13}C NMR spectra of 26

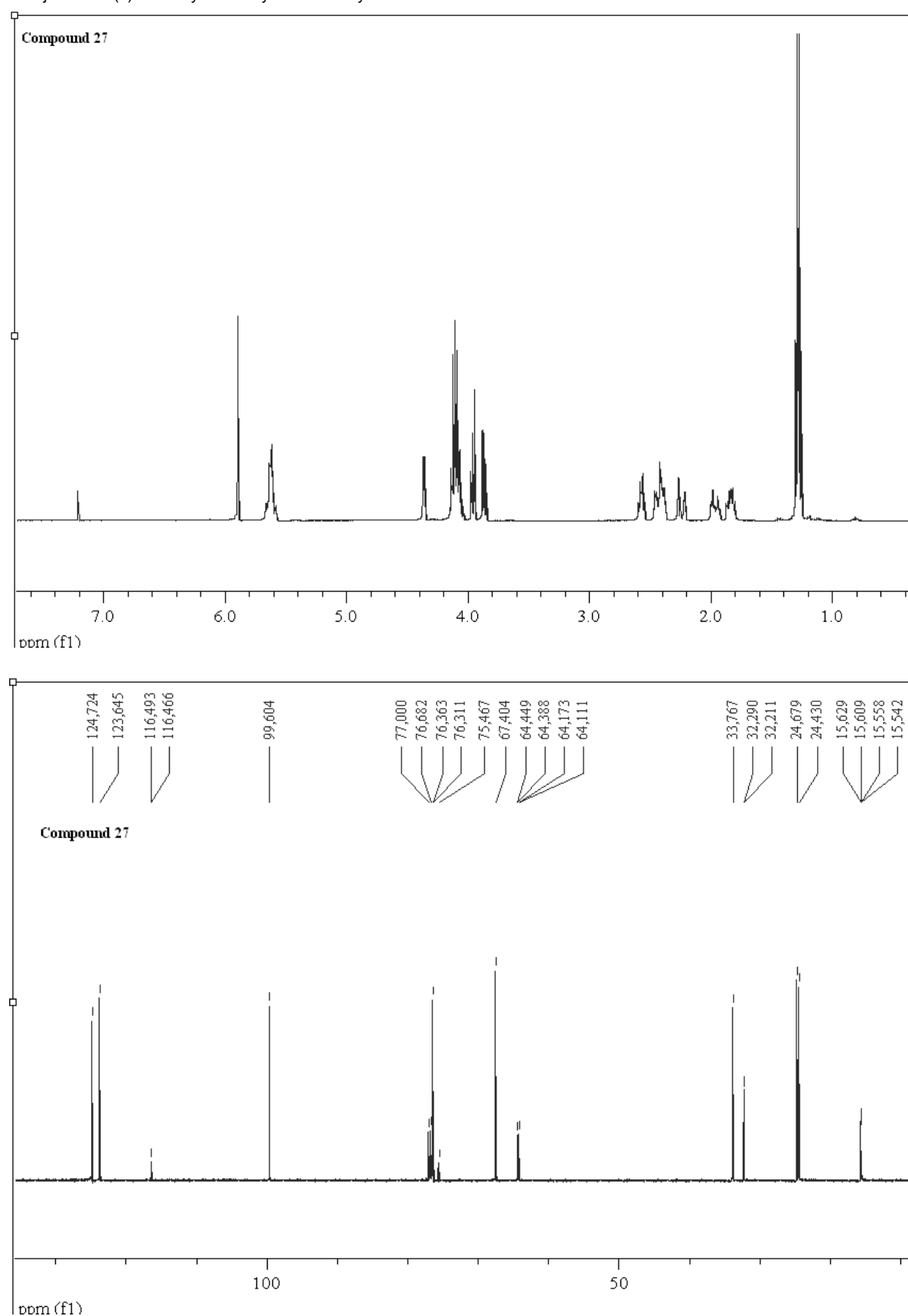


Figure S14: ^1H and ^{13}C NMR spectra of **27**

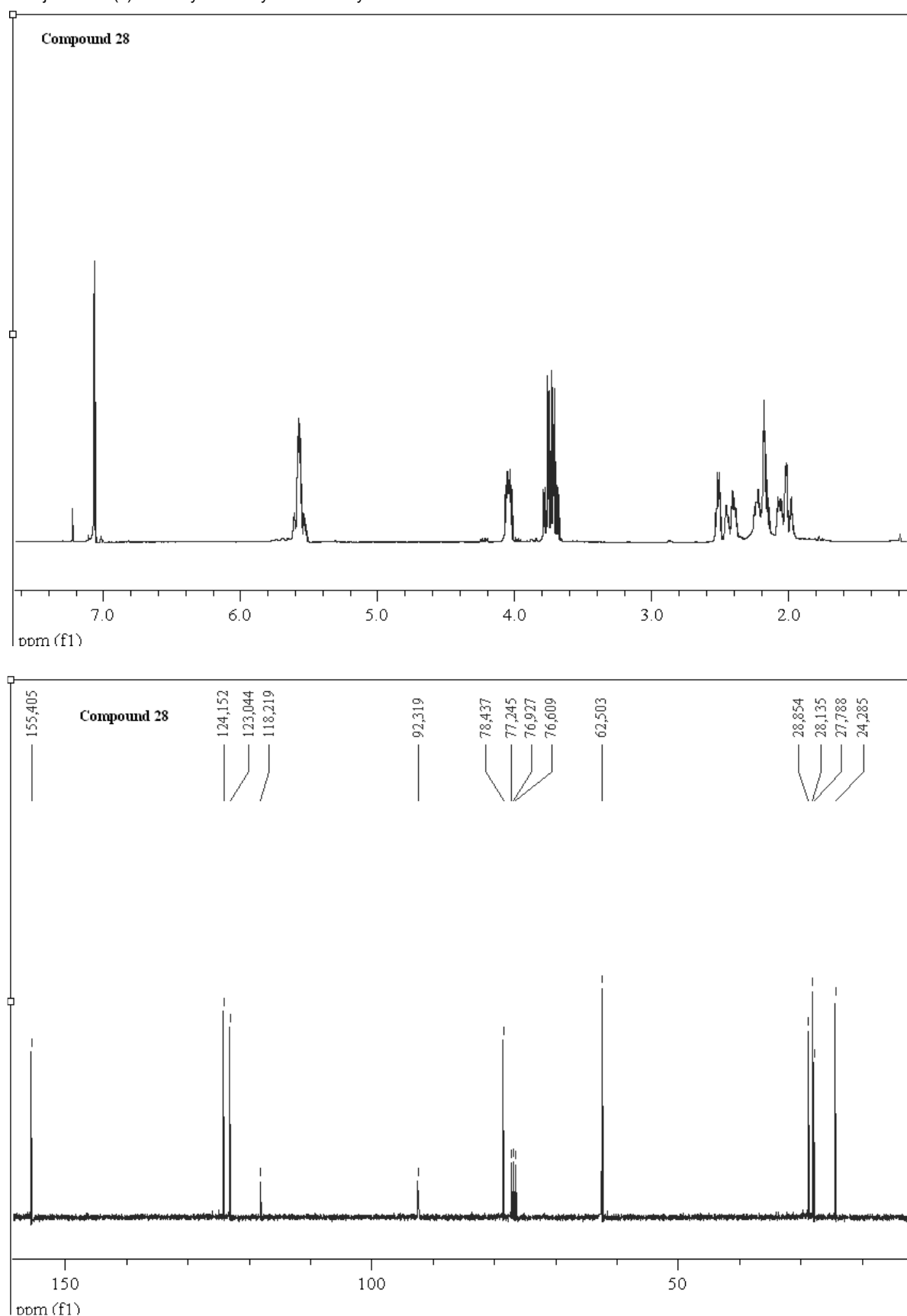


Figure S15: ^1H and ^{13}C NMR spectra of 28

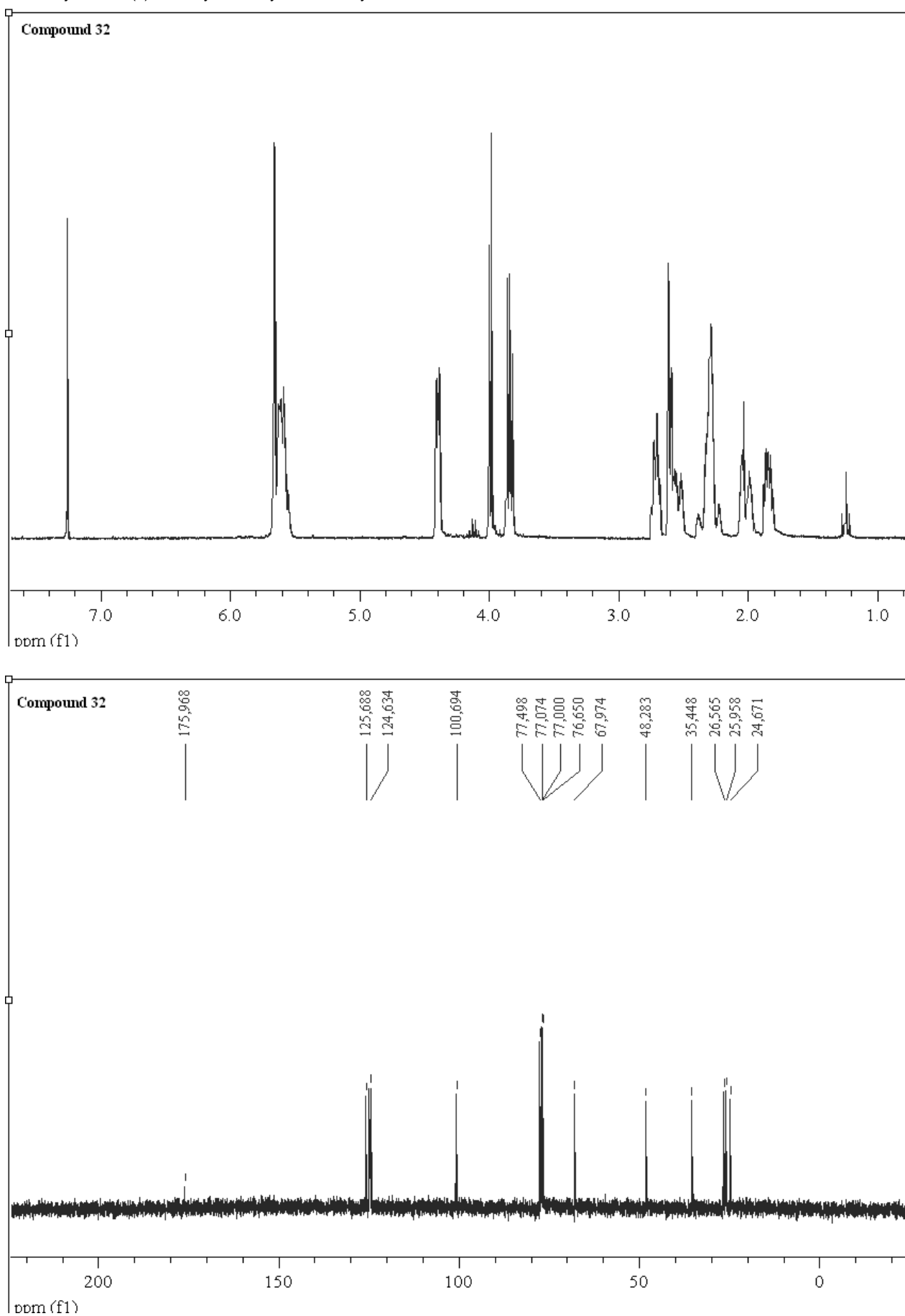


Figure S16: ^1H and ^{13}C NMR spectra of **32**

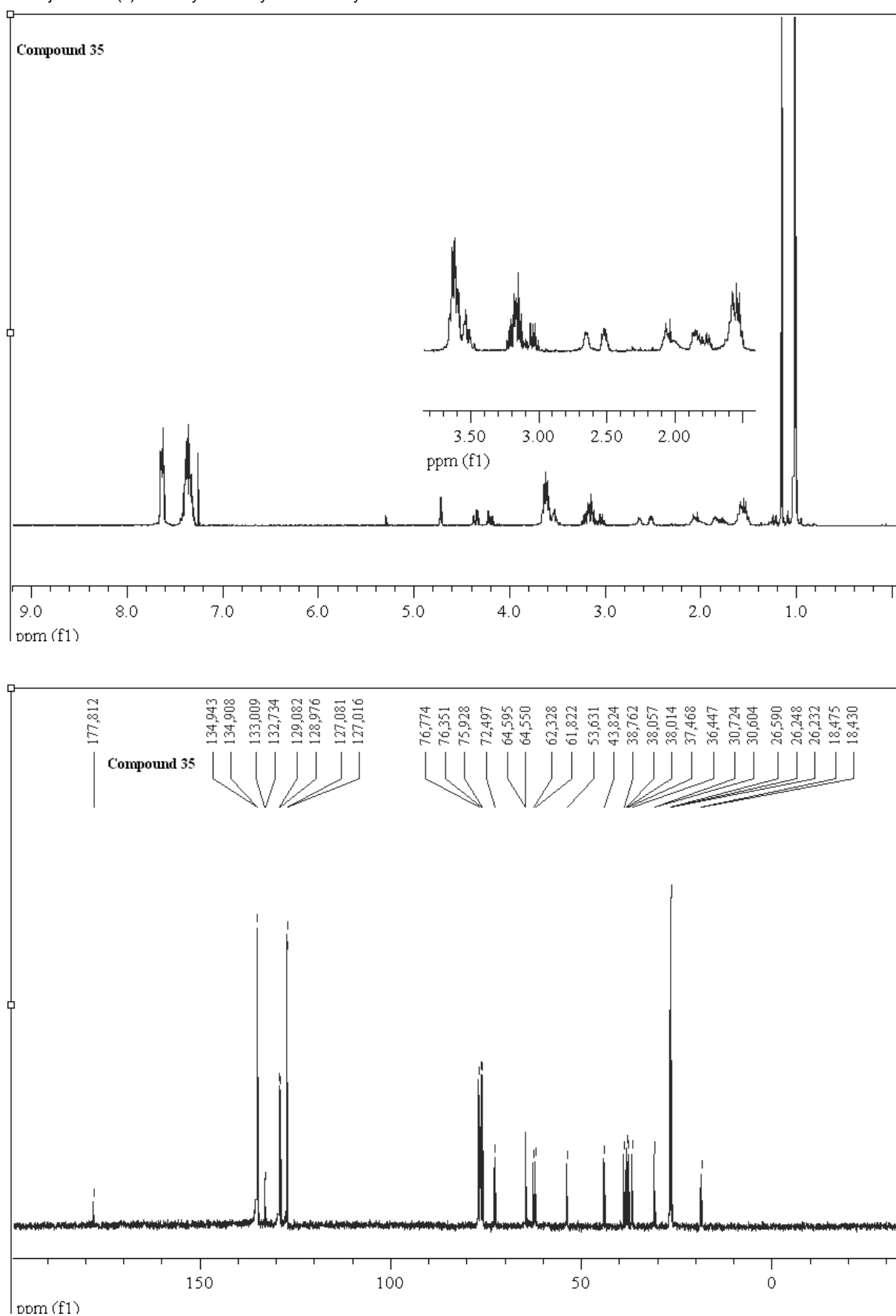


Figure S18: ^1H and ^{13}C NMR spectra of **35**

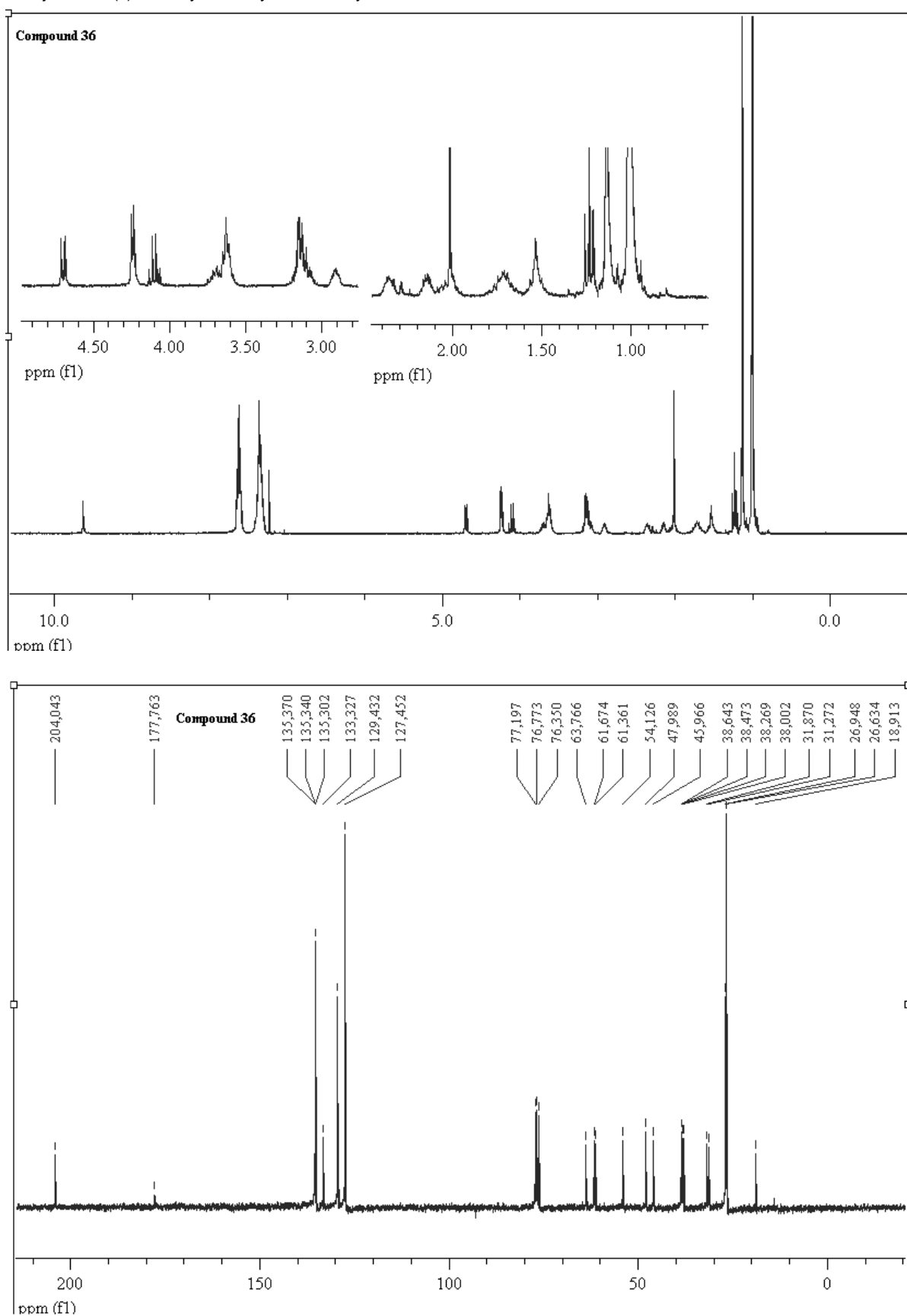


Figure S19: ^1H and ^{13}C NMR spectra of 36

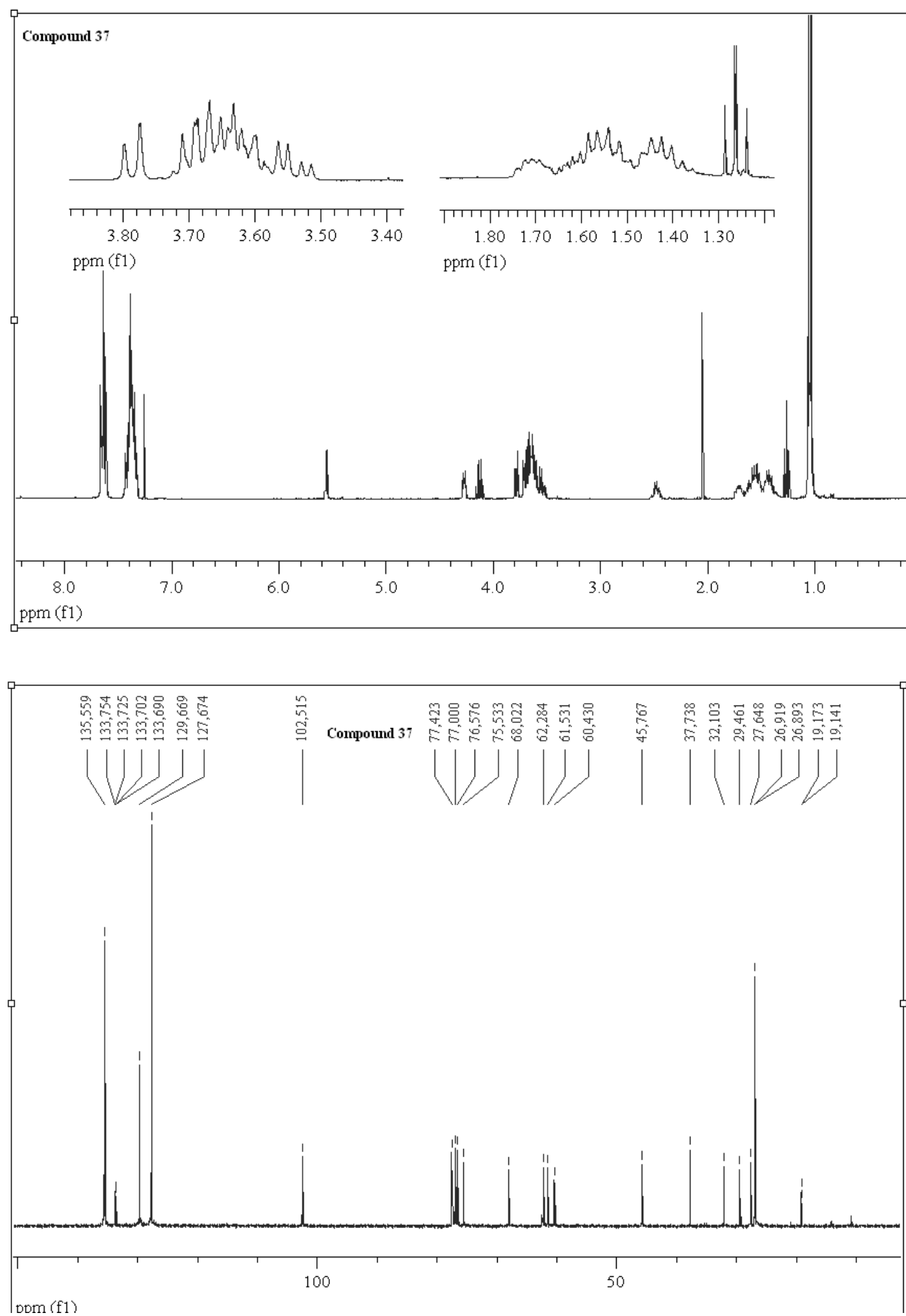


Figure S20: ^1H and ^{13}C NMR spectra of 37