

Supporting Information

Concise Total Syntheses of Aspalathin and Nothofagin

Akop Yepremyan, Baback Salehani, and Thomas G. Minehan^{*}

*Department of Chemistry and Biochemistry, California State University– Northridge,
Northridge, CA 91330*

Table of Contents:

General Methods and Procedures	S2-S4
Characterization data for new compounds	S5-S12
¹ H, ¹³ C NMR spectra of compounds	S13-S40

General Methods. Distilled water was used in all of the experiments. Organic extracts were dried over Na₂SO₄, filtered, and concentrated using a rotary evaporator at aspirator pressure (20-30 mmHg). Chromatography refers to flash chromatography and was carried out on SiO₂ (silica gel 60, 230-400 mesh). ¹H and ¹³C NMR spectra were measured in CDCl₃ at 400 MHz and 100 MHz, respectively, using Me₄Si as internal standard. Chemical shifts are reported in ppm downfield (δ) from Me₄Si.

Representative procedure for the preparation of 1,2-di-*O*-acyl-3,4,6-tri-*O*-benzyl glucose, compounds 4a-4d.

3,4,6-tri-*O*-acetyl-D-glucal (3 g, 11 mmol) was dissolved in CH₃OH (5 mL) and KCN (36 mg, 0.5 mmol, 5 mol%) was added. The reaction was stirred for 2 hours, and another 36 mg KCN was added. After an additional two hours, TLC indicated that the reaction was complete, and the mixture was concentrated *in vacuo*. To the crude oil was added anhydrous DMF (11 mL) and the solution was cooled to 0 °C. Sodium hydride (1.76 g, 60% dispersion in mineral oil, 44 mmol) was added carefully, along with a catalytic amount (~20 mg) of imidazole; the mixture was stirred at 0 °C for 30 minutes. Then benzyl bromide (4.3 mL, 36.3 mmol) was added dropwise, followed by tetra-*n*-butylammonium iodide (405 mg, 1.1 mmol, 10 mol%), and the mixture was allowed to warm to room temperature overnight. The mixture was quenched dropwise by the careful addition of saturated NaHCO₃ solution (10 mL) and ether (20 mL). The phases were separated and the aqueous phase was back-extracted with ether (2 x 10 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 10:1 Hexanes:EtOAc) afforded 3,4,6-tri-*O*-benzyl-D-glucal (3.88 g, 85%)

To a solution of 3,4,6-tri-*O*-benzyl-D-glucal (3.88 g, 9.35 mmol) in 4:1 acetone:H₂O (80 mL) was added in small portions a mixture of Oxone (16.6 g, 112 mmol) and NaHCO₃ (4.58 g, 54 mmol) and the flask was stoppered and stirred at room temperature. After an hour, TLC (4:1 hexanes:ethyl acetate) indicated complete disappearance of starting material, and the acetone was evaporated. The remaining solid mass was partitioned between water (100 mL) and EtOAc (100 mL). The phases were separated and the aqueous phase was back-extracted with EtOAc (2 x 50 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*.

The crude diol was dissolved in pyridine (100 mL) and the appropriate acyl chloride (10-30 equivalents) was added, along with a catalytic amount (~100 mg) of DMAP. The reaction was stirred at 60 °C overnight, at which time TLC indicated complete conversion to the diester. The solution was concentrated *in vacuo* and the residue was partitioned between Et₂O (100 mL) and 1N HCl (100 mL). The organic layer was washed with 1N HCl (2 x 100 mL) and then with saturated aqueous NaHCO₃ (100 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 85:15 Hexanes: EtOAc) afforded 1,2-di-*O*-acyl-3,4,6-tri-*O*-benzyl-D-glucal **4a-4d** (70-90% from 3,4,6-tri-*O*-benzyl-D-glucal).

Representative procedure for C-glycosidation: Synthesis of glycosides 5a-5d.

To a stirred solution of 1,2-di-*O*-acyl-3,4,6-tri-*O*-benzyl glucose **4** (500 mg, ~0.8 mmol) in 2:1 CH₂Cl₂:THF (2.4 mL) was added tribenzylphloroglucinol **2a**^{9a} (1.26 g, 3.2 mmol, 4.0 equiv). The homogeneous solution was cooled to 0°C and TMSOTf (5-10 equiv) was added. The reaction was stirred at 0 °C for one hour and then was carefully diluted with 1:1 ether/saturated NaHCO₃ solution (15 mL). The phases were separated and the aqueous phase was back-extracted with ether (2 x 10mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂) afforded glycosides **5a-5d** in the yields indicated in table 1.

Representative procedure for formylation of 5.

To a stirred solution of **5a** (450 mg, 0.49 mmol) in DMF (3 mL) was added dropwise POCl₃ (277 μL, 2.94 mmol, 6 equiv) and the reaction was allowed to stir under an atmosphere of nitrogen overnight. At this time an additional portion (139 μL, 1.47 mmol, 3 equiv) of POCl₃ was added if TLC indicated remaining starting material. After stirring an addition four hours, the reaction mixture was carefully quenched by the addition of Et₂O (10 mL) and 1N NaOH (10 mL). The phases were separated and the aqueous phase was back-extracted with ether (2 x 50 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 85:15 Hexanes:EtOAc) afforded aldehyde **7b**.

Representative procedure for the synthesis of alkynes 10a,b from aldehydes 9a,b.

To a 0°C solution of aldehyde **9b** (1 g, 3.14 mmol) and K₂CO₃ (1.32 g, 9.43 mmol, 3 equiv) in CH₃OH (15 mL) was added dimethyl-1-diazo-2-oxopropylphosphonate²³ (1.43 g, 7.1 mmol) in CH₃OH (5 mL) dropwise. The reaction was allowed to warm to room temperature and was stirred overnight. The mixture was diluted with ether (50 mL) and quenched with water (50 mL); the volatiles were then removed *in vacuo* and the mixture was extracted with EtOAc (50 mL x 3). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 97:3 Hexanes:Ether) afforded alkyne **10b**.

Representative procedure for alkyne addition to 7b. Synthesis of alcohols 12a,b.

Alkyne **10a** (135 mg, 0.63 mmol, 3 equiv) was dissolved in THF (1 mL) and cooled to -78 °C. A 2M solution of *n*BuLi (0.29 mL, 0.58 mmol) was added dropwise and the solution was allowed to stir for 10 minutes at -78 °C. Then a solution of aldehyde **7b** (200 mg, 0.21 mmol) was added dropwise, and the reaction was allowed to stir for an additional 10 minutes. At this time, TLC indicated complete conversion of starting material. The mixture was quenched with saturated NaHCO₃ solution (5 mL) and was allowed to warm to room temperature. The reaction was diluted with EtOAc (10 mL), and H₂O (10 mL). The phases were separated and the aqueous phase was back-extracted with EtOAc (2 x 50 mL). The combined organic extracts were dried over Na₂SO₄, filtered

and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 80:20 Hexanes:EtOAc) afforded alcohols **11a,b**.

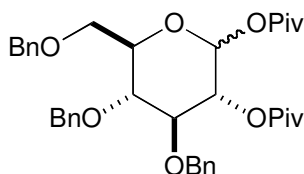
To a solution of alcohols **11a,b** (230 mg, 0.20 mmol) in Et₂O (1 mL) was added dropwise at room temperature a 3M solution of CH₃MgBr (0.4 mL, 1.2 mmol, 6 equiv). After 10 minutes, TLC indicated ~60% conversion of starting material, and an additional 0.4 mL of 3M CH₃MgBr solution was added. The reaction was then cooled to 0 °C and quenched by dropwise addition of saturated NaHCO₃ solution (3 mL). The mixture was diluted with EtOAc (10 mL) and H₂O (10 mL); the phases were separated and the aqueous phase was back-extracted with EtOAc (2 x 50 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 75:25 Hexanes:EtOAc) afforded alcohols **12a,b**.

Representative procedure for benzylic oxidation. Synthesis of ynone 13.

To a solution of alcohols **12a,b** (195 mg, 0.183 mmol) in 1:1 CH₂Cl₂: hexanes (2 mL) was added MnO₂ (200 mg, 2.29 mmol, 12.5 equiv). After 10 minutes at room temperature, TLC indicated complete conversion of the starting material. The mixture was diluted with Et₂O (25 mL) and filtered through a pad of celite; the filter cake was washed with copious amounts of Et₂O, and the filtrate was concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO₂, 75:25 Hexanes:EtOAc) afforded ynone **13**.

Representative procedure for the hydrogenolysis of ynones 13 and 16. Synthesis of Aspalathin.

To a solution of ynone **16** (89 mg, 0.07 mmol) in 1:1 EtOAc:CH₃OH (1 mL) was added 10% palladium on carbon (~50 mg) and the mixture was stirred under an atmosphere of hydrogen (1 atm, hydrogen balloon). After 2 hours, TLC indicated complete conversion of the starting material. The mixture was diluted with 10% CH₃OH/EtOAc (20 mL) and filtered through a pad of celite; the filter cake was washed with copious amounts of 10% CH₃OH/EtOAc, and the filtrate was concentrated *in vacuo* to afford synthetic aspalathin.



4a

Purification: SiO₂(15% EtOAc in hexanes) affording **4a** (90%).

See spectra and page S-13 and S-14

major diastereomer (β):

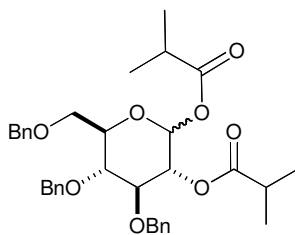
¹H NMR: (400 MHz, CDCl₃):

7.43-7.25 (m, 15H); 5.79 (d, J =8.0 Hz, 1H); 5.38 (t, J =8.4 Hz, 1H); 4.92 (d, J =11.2 Hz, 1H); 4.88 (d, J =10.8 Hz, 1H); 4.83 (d, J =11.2 Hz, 1H); 4.66 (t, J =12.4 Hz, 2H); 4.63 (d, J =12.4 Hz, 1H); 3.95-3.72 (m, 5H); 1.32 (s, 9H); 1.26 (s, 9H).

¹³C NMR: (100 MHz, CDCl₃)

176.9; 176.6; 138.1; 128.5; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.8; 127.7; 127.5; 127.4; 92.4; 83.2; 75.9; 75.0; 74.9; 73.5; 72.0; 68.0; 38.8; 27.3; 26.9.

HRMS: (ESI) Calculated for C₃₇H₄₆NaO₈ 641.3091, found m/z =641.3124 (M+Na)⁺



4b

Purification: SiO₂(15% EtOAc in hexanes) affording **4b** (87%) as a 3:1 mixture of β : α anomers.

See spectra and page S-15 and S-16

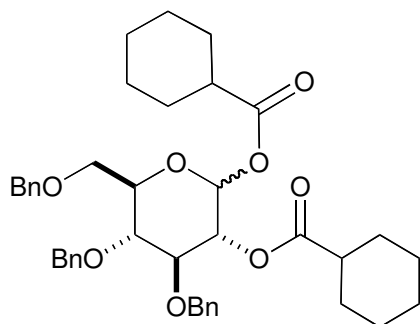
¹H NMR: (400 MHz, CDCl₃):

7.45-7.10 (m, 15H); 5.76 (d, J =8.0 Hz, 1H); 5.29 (t, J =8.8 Hz, 1H); 4.89-4.55 (m, 6H); 3.93-3.67 (m, 5H); 3.57 (d, J =4.0 Hz, 1H); 2.63 (s, J =6.8 Hz, 1H); 2.50 (s, J =6.8 Hz, 1H); 1.26 (d, J =6.8 Hz, 6H); 1.19 (d, J =6.8 Hz, 6H).

¹³C NMR: (100 MHz, CDCl₃)

175.4; 175.4; 138.1; 137.9; 130.5; 128.6; 128.5; 128.4; 128.3; 128.1; 128.0; 127.9; 127.8; 127.7; 127.6; 92.2; 82.9; 75.8; 75.0; 73.5; 71.9; 34.0; 33.9; 19.0; 18.8; 18.7; 18.4; 18.3.

HRMS: (ESI) Calculated for C₃₅H₄₆NO₈ 608.3218, found m/z =608.3227 (M+NH₄)⁺



4c

Purification: SiO₂(15% EtOAc in hexanes) affording **4c** (70%) as a 3:1 mixture of β:α anomers.

See spectra and page S-17 and S-18

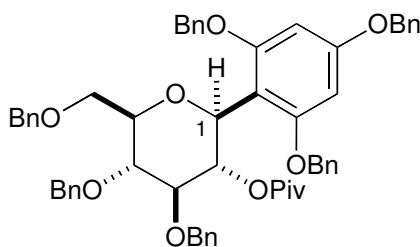
¹H NMR: (400 MHz, CDCl₃):

7.27-7.06 (m, 15H); 5.59 (d, *J*=8.4 Hz, 1H); 5.11 (t, *J*=8.4 Hz, 1H); 4.74-4.41 (m, 6H); 3.77-3.52 (m, 5H); 2.52 (tt, *J*=3.6, 11.2 Hz, 2H); 1.90-1.11 (m, 20H).

¹³C NMR: (100 MHz, CDCl₃)

182.6; 174.4; 174.3; 173.7; 138.3; 138.0; 137.9; 137.8; 128.4; 128.3; 128.2; 128.1; 127.9; 127.8; 127.7; 127.6; 92.1; 82.8; 76.8; 75.0; 73.4; 43.2; 42.9; 29.1; 28.8; 28.7; 28.6; 28.4; 25.7; 25.6; 25.4; 25.3; 25.2.

HRMS: (ESI) Calculated for C₄₁H₅₀NaO₈ 693.3398, found *m/z*=693.3406 (M+Na)⁺



5a

Purification: SiO₂(18% EtOAc in hexanes) affording **5a** (55%).

See spectra pages S19 and S20

¹H NMR: (400 MHz, CDCl₃)

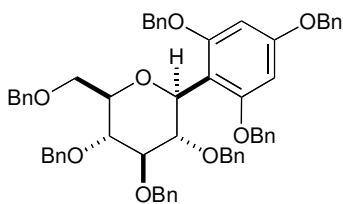
7.53-7.10 (m, 30H); 6.22 (d, *J*=2.0 Hz, 1H); 6.15 (d, *J*=2.0 Hz, 1H); 5.98 (t, *J*=9.2 Hz, 1H); 5.07-4.42 (m, 12H); 3.72-3.65 (m, 5H); 0.85 (s, 9H)

¹³C NMR: (100 MHz, CDCl₃)

176.7; 160.6; 158.7; 138.7; 138.5; 138.4; 137.4; 137.0; 136.8; 128.6; 128.5; 128.4; 128.3; 128.2; 128.0; 127.9; 127.8; 127.6; 127.4; 127.3; 127.2; 106.5; 104.4; 78.0; 76.9; 76.7; 74.9; 73.4; 72.2; 70.6; 70.0; 38.6; 26.9

HRMS: (ESI) Calculated for C₅₉H₆₀NaO₉ 935.4135, found *m/z*= 935.4867 (M+Na)⁺

¹D: -8.9° (*c* 0.02, CH₂Cl₂)



3a

Purification: SiO₂(10% EtOAc in hexanes) affording **3a** (89%) as a 3:1 (β:α) mixture of diastereomers.

See spectra pages S21 and S22

Major diastereomer:

¹H NMR: (400 MHz, CDCl₃)

7.69-7.12 (m, 35H); 6.45 (s, 2H); 5.28-5.02 (m, 9H); 4.83-4.66 (m, 5H); 4.62 (t, *J*=9.2 Hz, 1H); 4.39 (d, *J*=11.2 Hz, 1H); 3.99-3.90 (m, 4H); 3.77 (m, 1H).

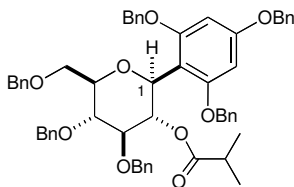
¹³C NMR: (100 MHz, CDCl₃)

160.5; 160.2; 160.1; 159.4; 139.3; 139.0; 138.7; 138.6; 137.4; 137.3; 136.9; 129.3; 128.9; 128.8; 128.7; 128.5; 128.4; 128.2; 128.1; 128.0; 127.9; 127.8; 127.7; 127.6; 127.4; 127.3; 127.2; 109.5; 109.4; 94.9; 94.3; 87.8; 79.9; 79.6; 78.5; 76.8; 75.5; 75.2; 74.2; 73.6; 73.5; 71.4; 70.8; 70.2; 69.6.

HRMS: (ESI) Calculated for C₆₁H₅₈NaO₈ 941.4029, found *m/z*= 941.5475 (M+Na)⁺

[α]_D²⁵: -19.8° (*c* 0.02, CH₂Cl₂)

Previous Preparation: Schmidt, R. R.; Effenberger, G. *Carbohydr. Res.* **1987**, 171, 59.



5b

Purification: SiO₂(18% EtOAc in hexanes) affording **5b** (65%)

See spectra pages S23 and S24

¹H NMR: (400 MHz, CDCl₃)

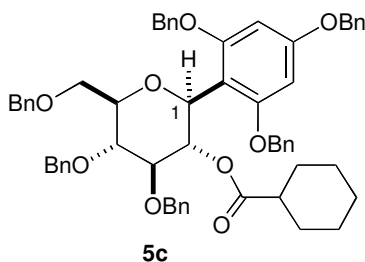
7.65-7.21 (m, 30H); 6.35 (d, *J*=2.0 Hz, 1H); 6.27 (d, *J*=2.0 Hz, 1H); 6.09 (t, *J*=9.2 Hz, 1H); 5.19-4.55 (m, 7H); 4.15 (d, *J*=6.8 Hz, 1H); 3.87-3.63 (m, 4H); 2.31 (st, *J*=6.8 Hz, 1H); 0.96 (d, *J*=6.8 Hz, 3H); 0.86 (d, *J*=7.2 Hz, 3H).

¹³C NMR: (100 MHz, CDCl₃)

175.5; 160.5; 158.7; 138.8; 138.5; 137.4; 137.1; 136.8; 128.6; 128.5; 128.4; 128.3; 128.1; 128.0; 127.9; 127.7; 127.6; 127.5; 127.4; 127.3; 127.2; 127.1; 106.6; 94.0; 93.0; 85.4; 79.7; 78.0; 75.0; 74.3; 73.4; 72.2; 71.3; 70.7; 70.6; 70.0; 34.1; 18.9; 18.5.

HRMS: (ESI) Calculated for C₅₈H₅₈NaO₉ 921.3973, found *m/z*= 921.3961 (M+Na)⁺

[α]_D²⁵: +13.4° (*c* 0.004, CH₂Cl₂)



Purification: SiO₂ (13% EtOAc in hexanes) affording **5c** (30%)

See spectra pages S25 and S26

¹H NMR: (400 MHz, CDCl₃)

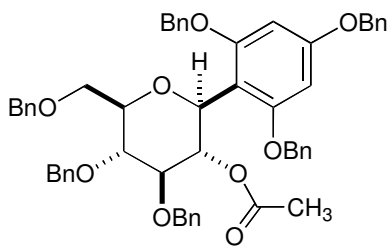
7.61-7.21 (m, 30H); 6.30 (d, *J*=2.0 Hz, 1H); 6.23 (d, *J*=2.0 Hz, 1H); 6.04 (t, *J*=10.0 Hz, 1H); 5.17 (s, 1H); 5.06-4.51 (m, 12H); 3.84-3.59 (m, 5H); 2.00 (td, *J*=7.6, 3.2 Hz, 1H); 1.62-1.09 (m, 10H).

¹³C NMR: (100 MHz, CDCl₃)

174.4; 160.5; 158.7; 138.8; 138.5; 138.4; 137.4; 137.1; 136.8; 128.6; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.8; 127.6; 127.5; 127.4; 127.3; 127.2; 127.1; 106.6; 79.6; 78.0; 76.9; 76.7; 76.6; 74.3; 71.1; 70.7; 43.3; 28.8; 28.4; 25.7; 25.4; 25.2

HRMS: (ESI) Calculated for C₆₁H₆₂NaO₉ 961.4268, found *m/z*= 961.4292 (M+Na)⁺

[α]_D²⁵: -4.25° (c 0.03, CH₂Cl₂)



Purification: SiO₂ (15% EtOAc in hexanes) affording **5d** (43%)

See spectra pages S27 and S28

¹H NMR: (400 MHz, CDCl₃)

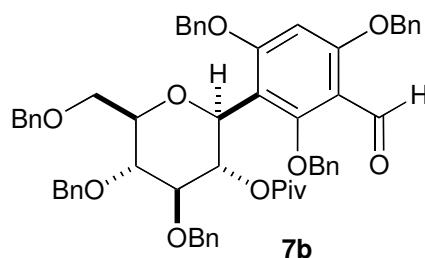
7.62-7.21 (m, 30H); 6.32 (d, *J*=2.0 Hz, 1H); 6.24 (d, *J*=2.0 Hz, 1H); 6.01 (t, *J*=9.6 Hz, 1H); 5.17-4.54 (m, 13H); 3.84-3.73 (m, 4H); 3.62 (dt, *J*=8.4, 2.0 Hz, 1H); 1.73 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

169.4; 160.5; 158.7; 138.8; 138.5; 138.4; 138.3; 137.4; 137.2; 136.7; 129.4; 129.0; 128.6; 128.5; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.8; 127.7; 127.6; 127.4; 127.3; 127.0; 120.3; 107.4; 106.8; 85.2; 79.6; 78.1; 76.7; 75.0; 74.3; 73.4; 72.2; 71.8; 70.6; 70.0; 20.7.

HRMS: (ESI) Calculated for C₅₆H₅₄NaO₉ 893.3659, found *m/z*=893.3656 (M+Na)⁺

[α]_D²⁵: -8.3 (c 0.01, CH₂Cl₂)



Purification: SiO₂(20% EtOAc in hexanes) affording **7a** (85%).

See spectra on pages S-29 and S-30

¹H NMR: (400 MHz, CDCl₃)

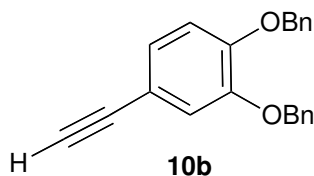
10.65 (s, 1H); 7.78-7.32 (m, 30H); 6.60 (s, 1H); 6.19 (t, *J*=9.6 Hz, 1H); 5.42-4.65 (m, 12H); 3.93-3.53 (m, 5H); 1.11 (s, 9H).

¹³C NMR: (100 MHz, CDCl₃)

187.3; 177.1; 165.2; 163.6; 162.0; 138.7; 138.4; 138.3; 136.9; 136.2; 135.9; 129.3; 129.1; 128.9; 128.7; 128.6; 128.5; 128.4; 128.2; 128.1; 128.0; 127.8; 127.6; 127.5; 127.4; 127.3; 127.2; 127.1; 126.9; 112.6; 112.2; 94.8; 85.4; 79.7; 78.8; 76.9; 75.1; 74.6; 73.5; 72.8; 71.1; 71.0; 70.9; 38.7; 27.1.

HRMS: (ESI) Calculated for C₆₀H₆₀NaO₁₀ 963.4079, found *m/z*=963.4077 (M+Na)⁺

[α]_D²⁵: -8.6° (*c* 0.23, CH₂Cl₂)



Purification: SiO₂(5% EtOAc in hexanes) affording **10b** (68%)

See spectra on pages S-31 and S-32

¹H NMR: (400 MHz, CDCl₃)

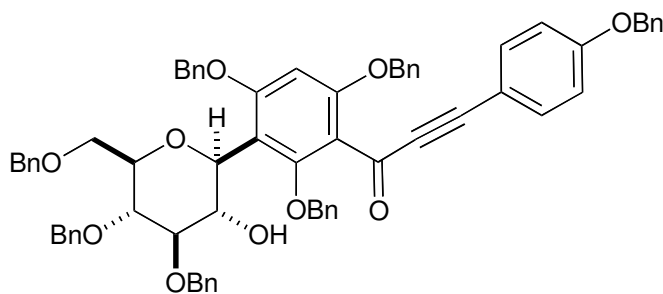
7.47-7.26 (m, 11H); 7.09 (d, *J*=8.4 Hz, 1H); 6.88 (d, *J*=8.4 Hz, 1H); 5.18 (s, 2H); 5.15 (s, 2H); 2.99 (s, 1H)

¹³C NMR: (100 MHz, CDCl₃)

149.8; 148.5; 136.9; 128.5; 127.9; 127.3; 127.2; 126.1; 118.3; 114.8; 114.5; 83.6; 75.8; 71.3; 71.0

HRMS: (ESI) Calculated for C₂₂H₁₉O₂ 315.1379, found *m/z*= 315.1382 (M+H)⁺

m.p.: 83.7°C-87.3°C



13

Purification: SiO₂(20% EtOAc in hexanes) affording **13** (75%)

See spectra on pages S-33 and S-34

¹H NMR: (400 MHz, CDCl₃)

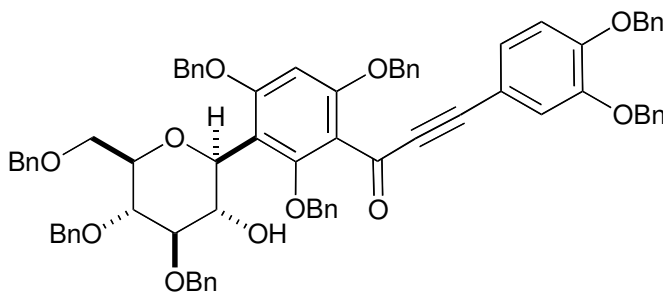
7.57-7.25 (m, 37H); 6.99 (d, *J*=8.8 Hz, 2H); 6.52 (s, 1H); 5.49 (d, *J*=10.4 Hz, 1H); 5.23-4.56 (m, 14H); 3.90-3.57 (m, 6H); 1.96 (s, 1H).

¹³C NMR: (100 MHz, CDCl₃)

178.0; 161.6; 160.6; 158.7; 139.1; 138.9; 138.3; 136.5; 136.3; 135.1; 128.7; 128.6; 128.5; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.8; 127.7; 127.6; 127.5; 127.4; 127.3; 127.2; 127.1; 127.0; 118.5; 115.1; 113.2; 112.7; 91.9; 90.7; 87.6; 76.9; 76.8; 75.0; 74.9; 70.8; 70.1.

HRMS: (ESI) Calculated for C₇₄H₆₇O₁₁ 1131.4678, found *m/z*= 1131.5032 (M-H)⁺

[α]_D²⁵: -20.9° (*c* 0.01, CH₂Cl₂)



16

Purification: SiO₂(20% EtOAc in hexanes) affording **16** (66%)

See spectra on pages S-35 and S-36

¹H NMR: (400 MHz, CDCl₃)

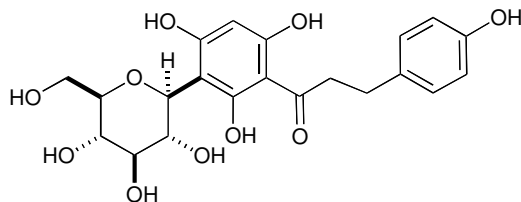
7.51-7.20 (m, 41H); 7.11 (d, *J*=7.2 Hz, 1H); 6.89 (d, *J*=8.8 Hz, 1H); 6.44 (s, 1H); 5.38 (d, *J*=10.0 Hz, 1H); 5.21-4.47 (m, 16H); 3.81-3.50 (m, 6H); 1.83 (s, 1H)

¹³C NMR: (100 MHz, CDCl₃)

177.4; 161.4; 158.7; 151.2; 148.5; 138.8; 138.3; 138.2; 136.9; 136.7; 136.6; 136.4; 136.3; 129.6; 129.3; 129.2; 128.9; 128.7; 128.6; 128.5; 128.4; 128.1; 128.0; 127.9; 127.8; 127.7; 127.6; 127.5; 127.3; 127.2; 127.0; 126.9; 126.8; 126.5; 118.7; 118.4; 114.9; 114.1; 113.1; 113.0; 91.8; 90.3; 87.5; 79.2; 76.6; 76.5; 76.4; 75.0; 74.9; 73.5; 71.1; 70.9; 70.8; 70.7.

HRMS: (ESI) Calculated for C₇₇H₆₈O₁₁Na 1191.4654, found *m/z*= 1191.4636 (M+Na)⁺

$[\alpha]_D^{25}$: +6.12° (c 0.005, CH₂Cl₂)



synthetic nothofagin

Purification: filtration through celite and concentration *in vacuo* gave **synthetic nothofagin (B)** (89%)

See spectra on pages S-37 and S-38

¹H NMR: (400 MHz, CDCl₃)

7.01 (d, *J*=8.4 Hz, 2H); 6.65 (d, *J*=8.0 Hz, 2H); 5.93 (s, 1H); 4.52 (d, *J*=10.0 Hz, 1H); 3.88 (t, *J*=8.8 Hz, 1H); 3.64 (d, *J*=11.2 Hz, 1H); 3.42 (d, *J*=11.2 Hz, 1H); 3.24 (t, *J*=8.0 Hz, 2H); 3.16 (m, 2H); 2.77 (t, *J*=7.6 Hz, 2H).

¹³C NMR: (100 MHz, CDCl₃)

204.8; 165.3; 164.2; 162.3; 155.8; 132.0; 129.1; 115.4; 104.4; 104.1; 95.3; 95.0; 94.3; 74.8; 73.3; 71.2; 70.3; 61.6; 46.0; 30.0.

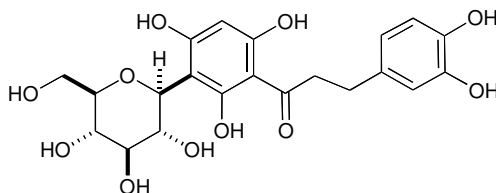
HRMS: (ESI) Calculated for C₂₁H₂₅O₁₀ 437.1442, found *m/z*= 437.1444 (M+H)⁺

$[\alpha]_D^{25}$: +36.6° (c 0.01, EtOH)

m.p. 92-110°C (decomp)(lit. 70-100°C)

UV: λ_{max}=288 (ε=14,000)(lit. λ_{max}=287.5)

IR: 3341 cm⁻¹, 2925, 1627, 1515, 1541, 1367, 1245, 1171, 1080, 1018, 911, 828.



synthetic aspalathin

Purification: filtration through celite and concentration *in vacuo* gave **synthetic aspalathin A** (77%)

See spectra on pages S-39 and S-40

¹H NMR: (400 MHz, CDCl₃)

6.63 (d, *J*=7.6 Hz, 1H); 6.61 (s, 1H); 6.47 (d, *J*=8.0 Hz, 1H); 5.93 (s, 1H); 4.54 (d, *J*=9.6 Hz, 1H); 3.87 (t, *J*=8.4 Hz, 1H); 3.66 (d, *J*=11.2 Hz, 1H); 3.42 (d, *J*=8.8 Hz, 1H); 3.21 (t, *J*=7.6 Hz, 2H); 3.14 (m, 3H) 2.70 (t, *J*=7.6 Hz, 2H).

¹³C NMR: (100 MHz, CDCl₃)

204.9; 165.5; 164.4; 162.2; 145.5; 143.8; 133.0; 119.3; 116.2; 115.9; 104.4; 104.1; 95.0; 81.7; 79.4; 74.1; 70.8; 70.5; 61.7; 45.8; 30.2

HRMS: (ESI) Calculated for C₂₁H₂₅O₁₁ 453.1391, found *m/z*= 453.1383 (M+H)⁺

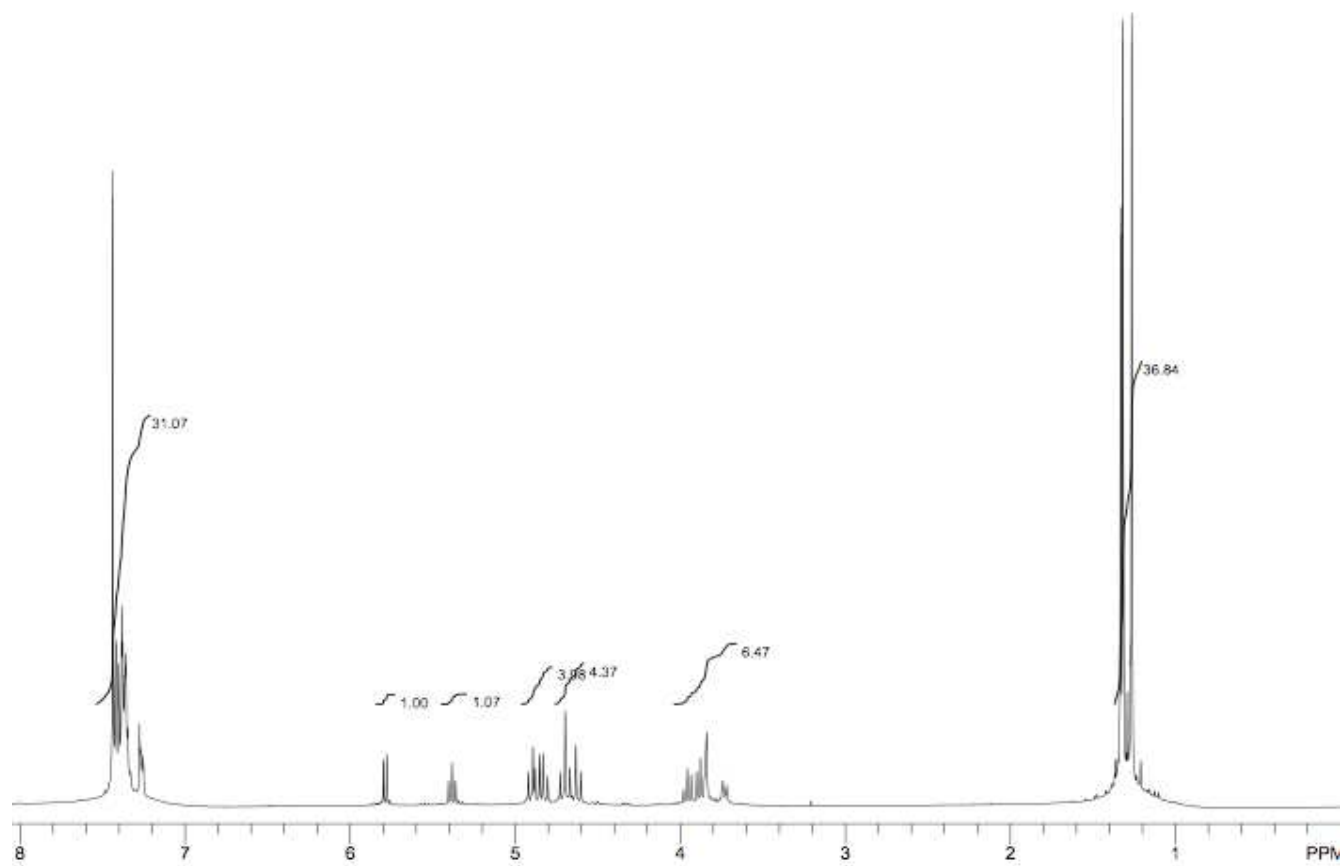
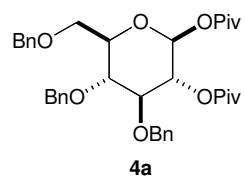
$[\alpha]_D^{25}$: +33.3° (c 0.001, EtOH) (lit. +34.7° (EtOH))

m.p. 131-165°C (lit. 140-160°C)

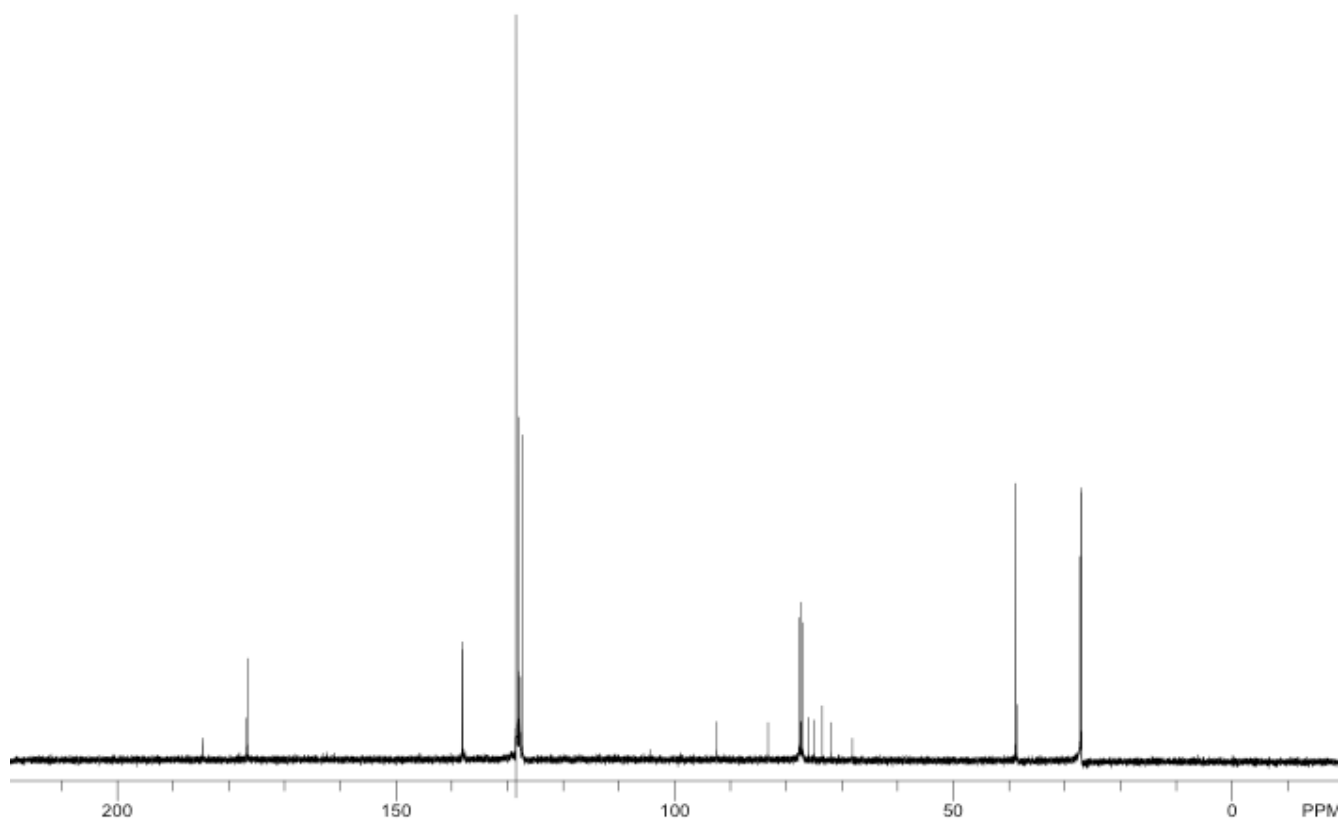
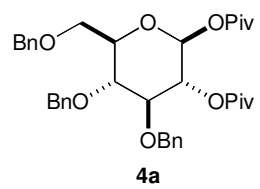
IR: 3368 cm⁻¹, 2925, 1626, 1527, 1454, 1372, 1283, 1115, 1080, 1041, 591.

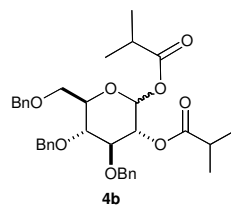
UV: λ_{max}=289 (ε=10,000) (lit. λ_{max}=287.5)

CDCl₃, 400MHz



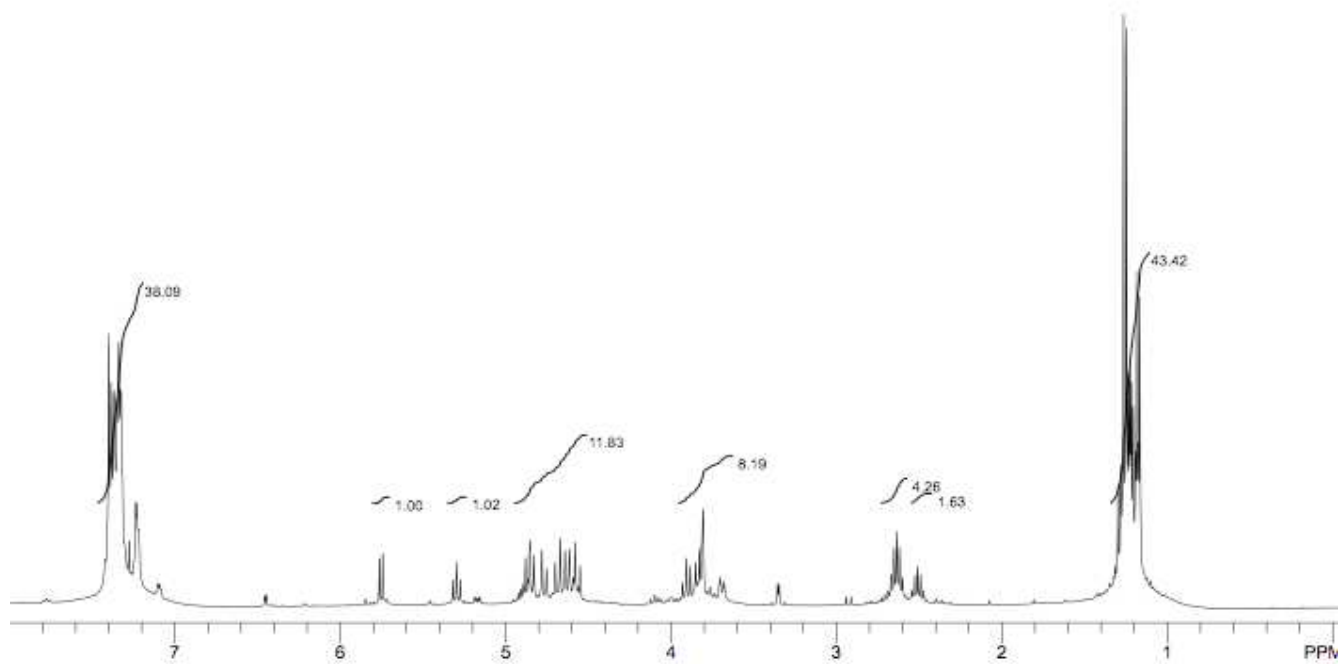
CDCl₃, 100MHz



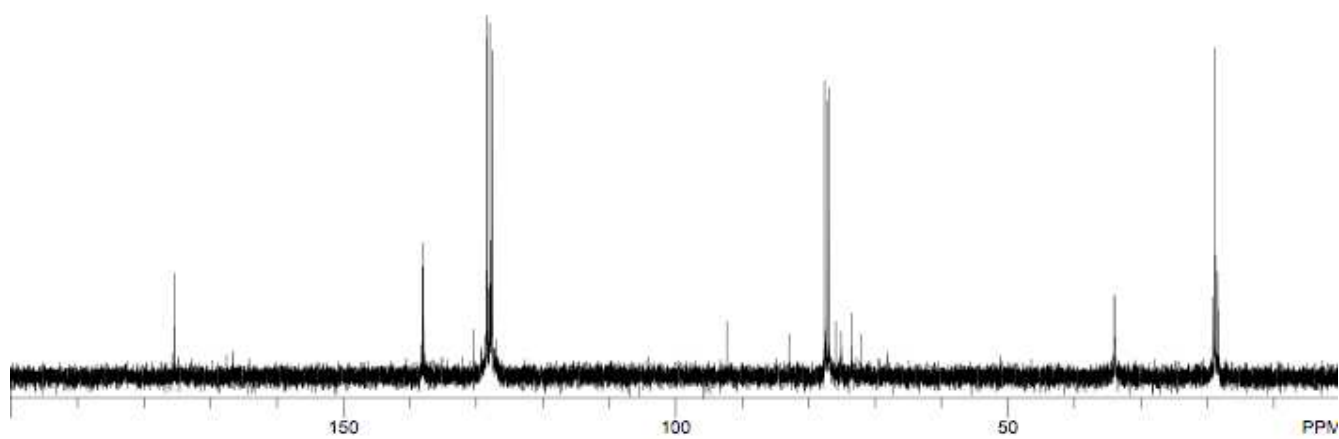
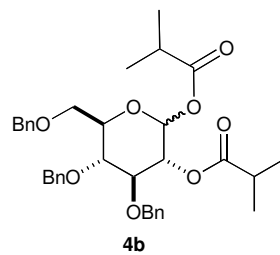


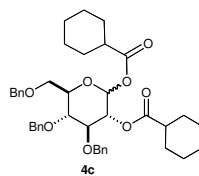
CDCl₃, 400MHz

(as a 3:1 mixture of β : α anomers)



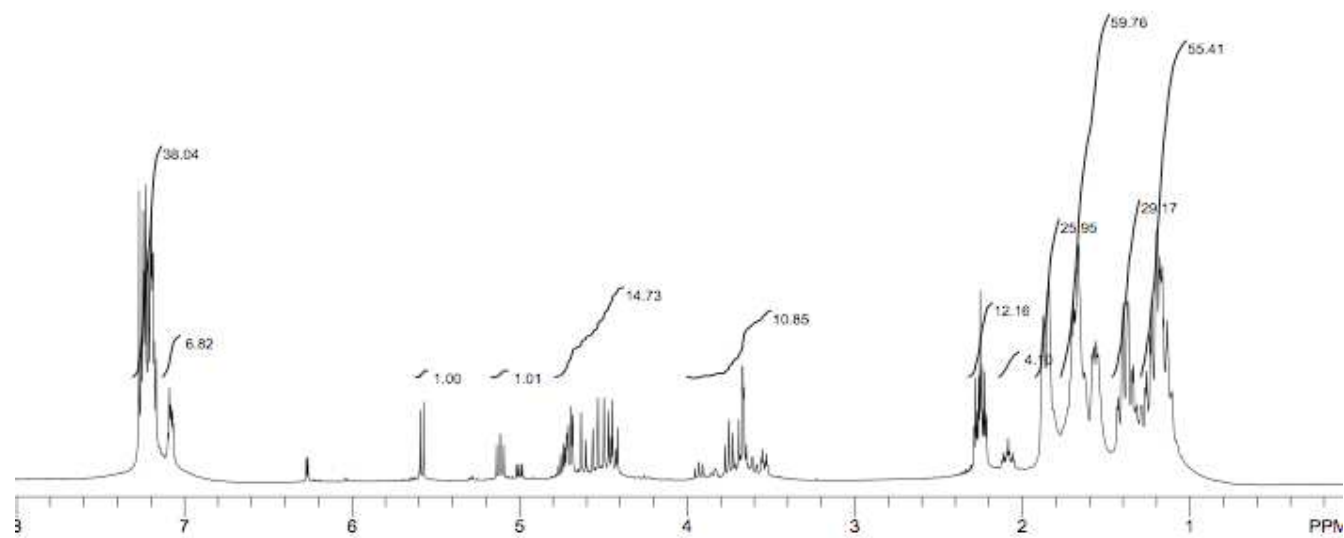
CDCl₃, 100MHz



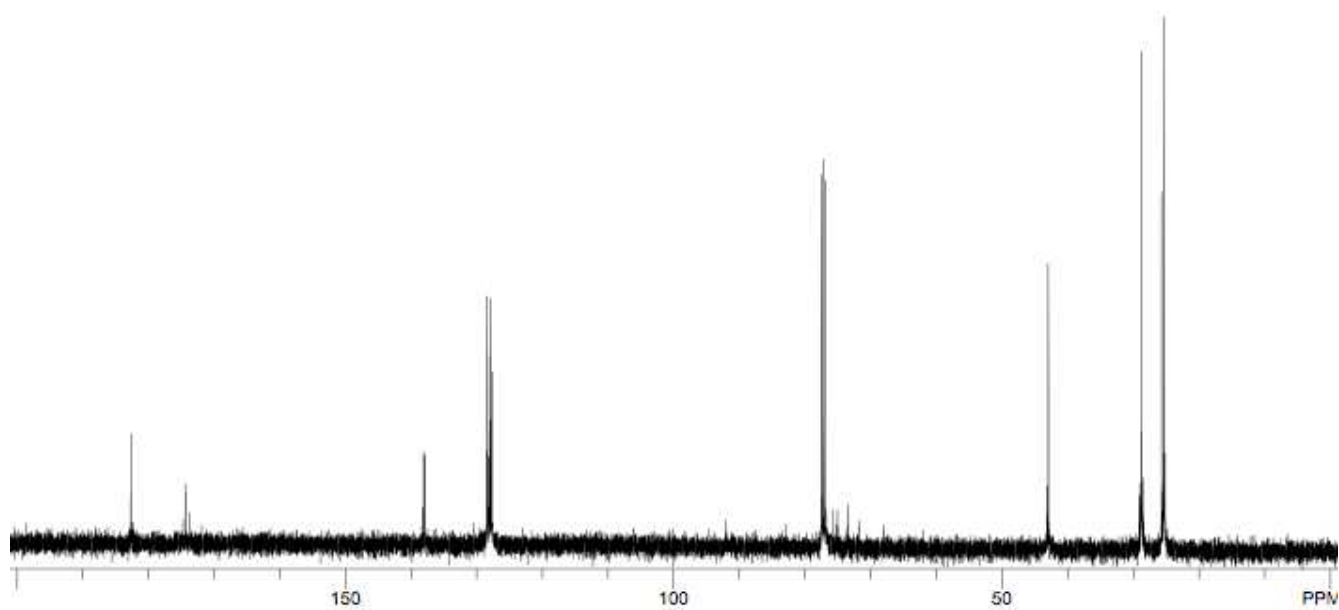
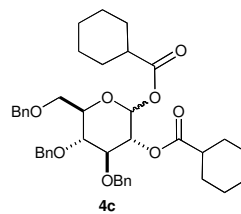


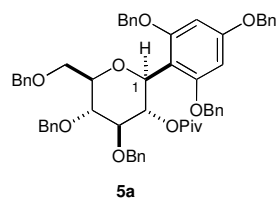
CDCl₃, 400MHz

(as a 3:1 mixture of β : α anomers)

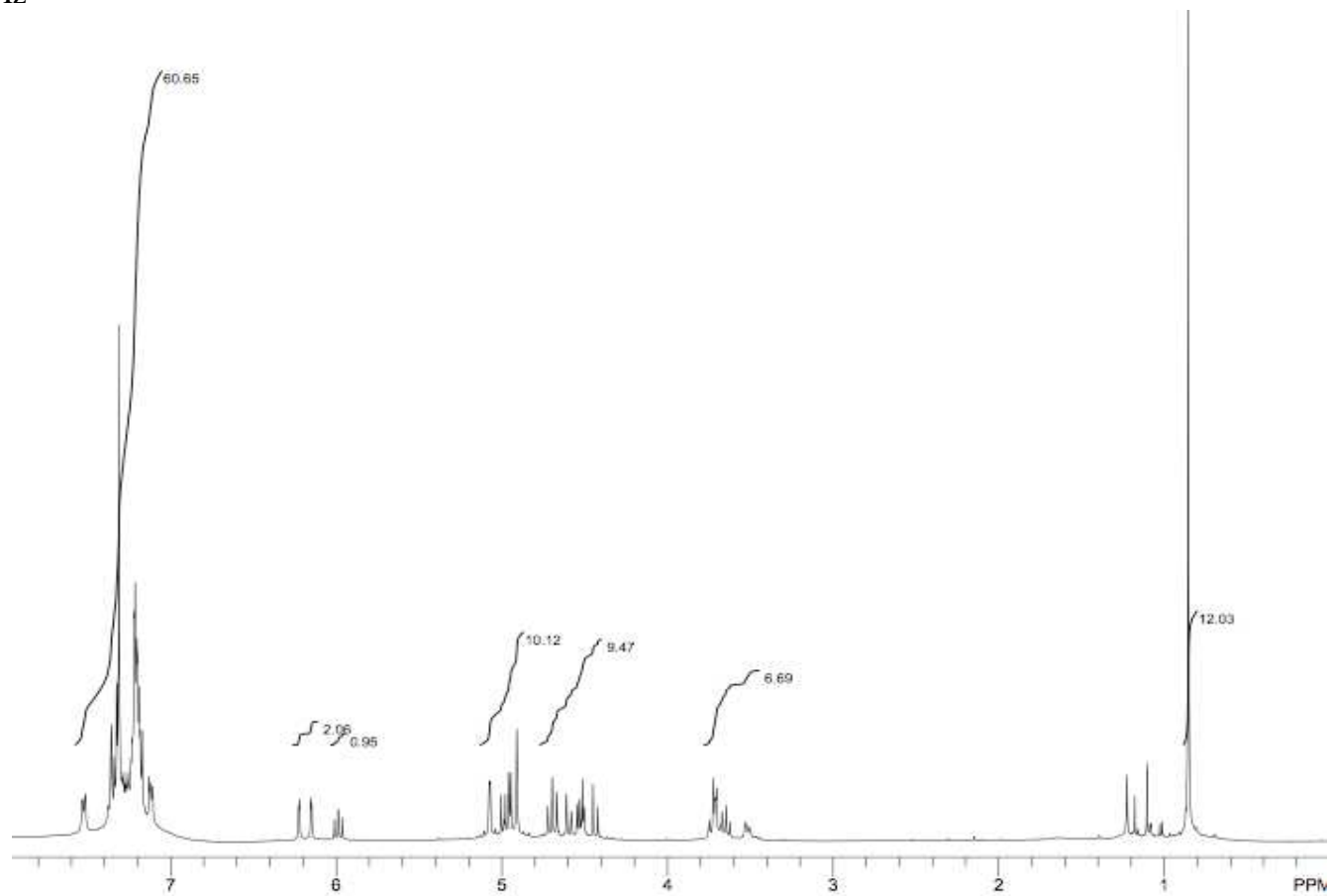


CDCl₃, 100MHz

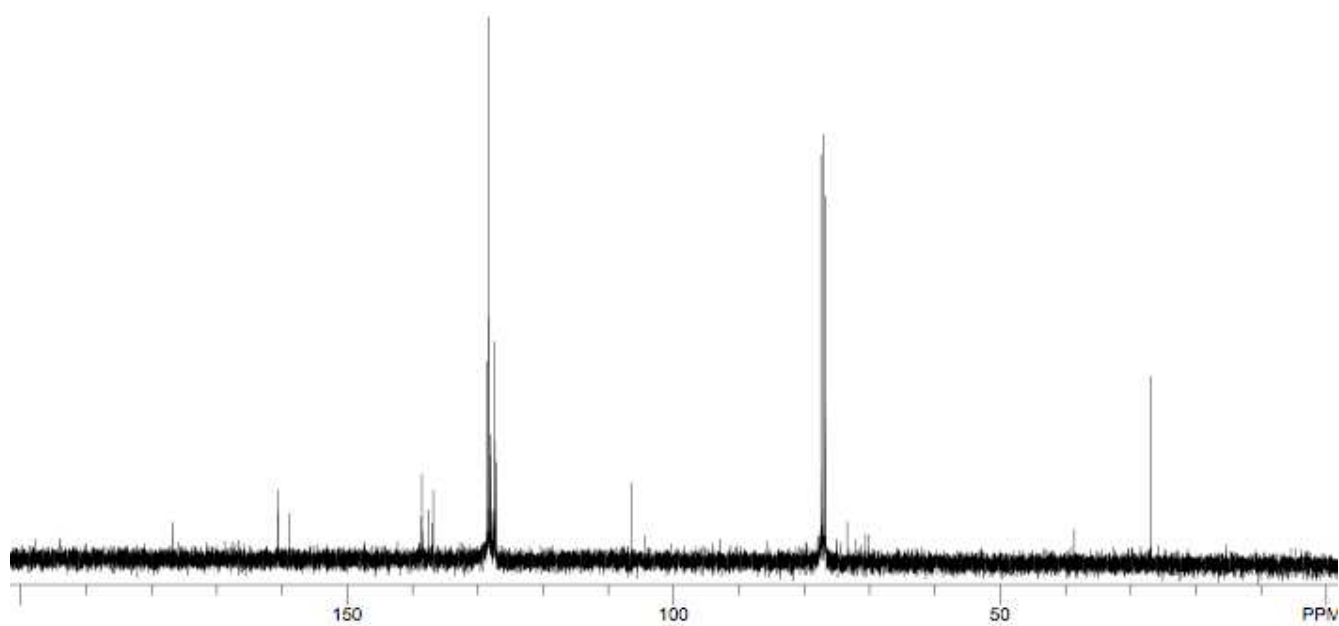
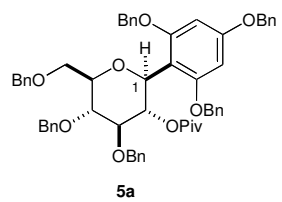


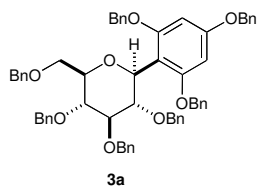


CDCl₃, 400MHz

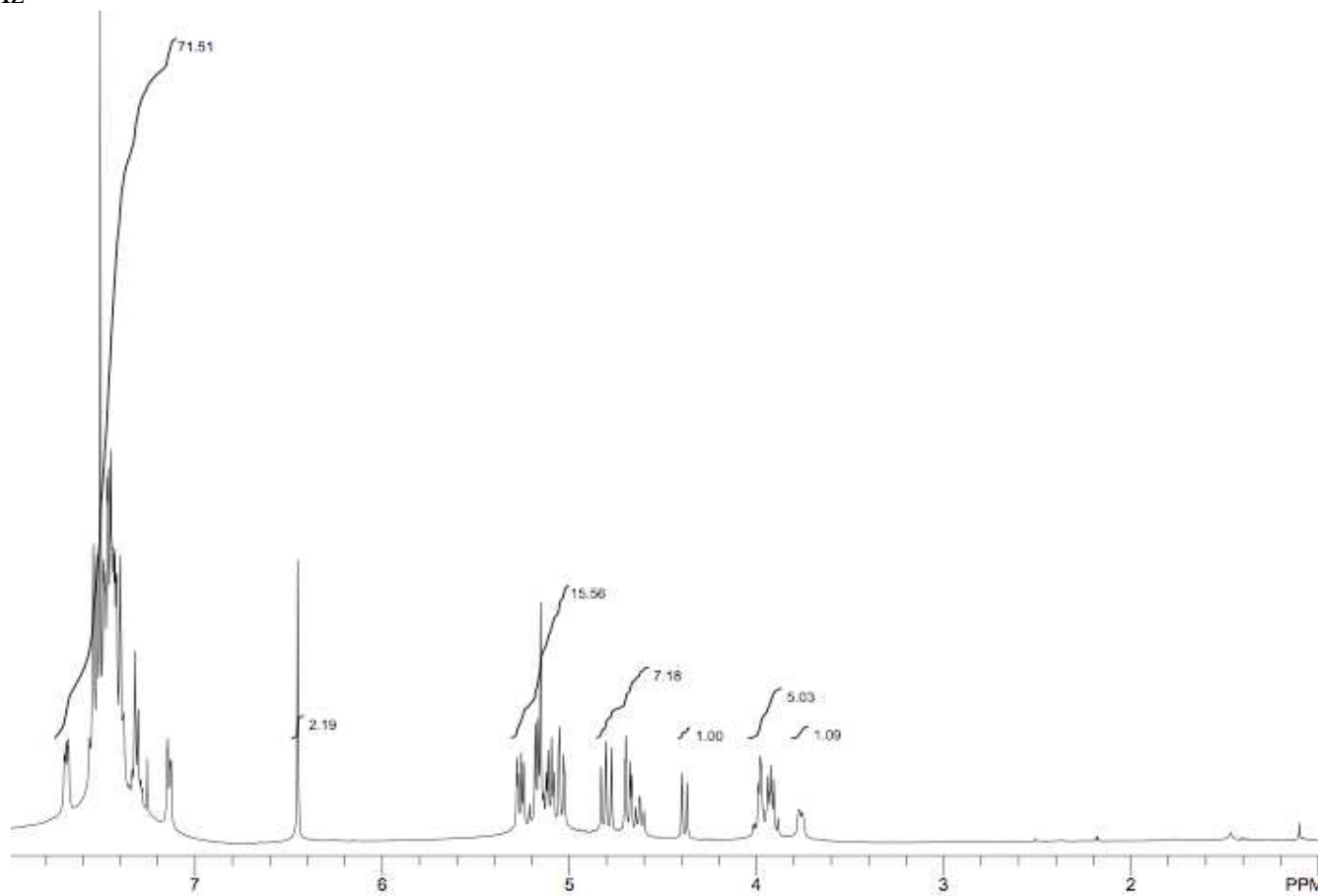


CDCl₃, 100MHz

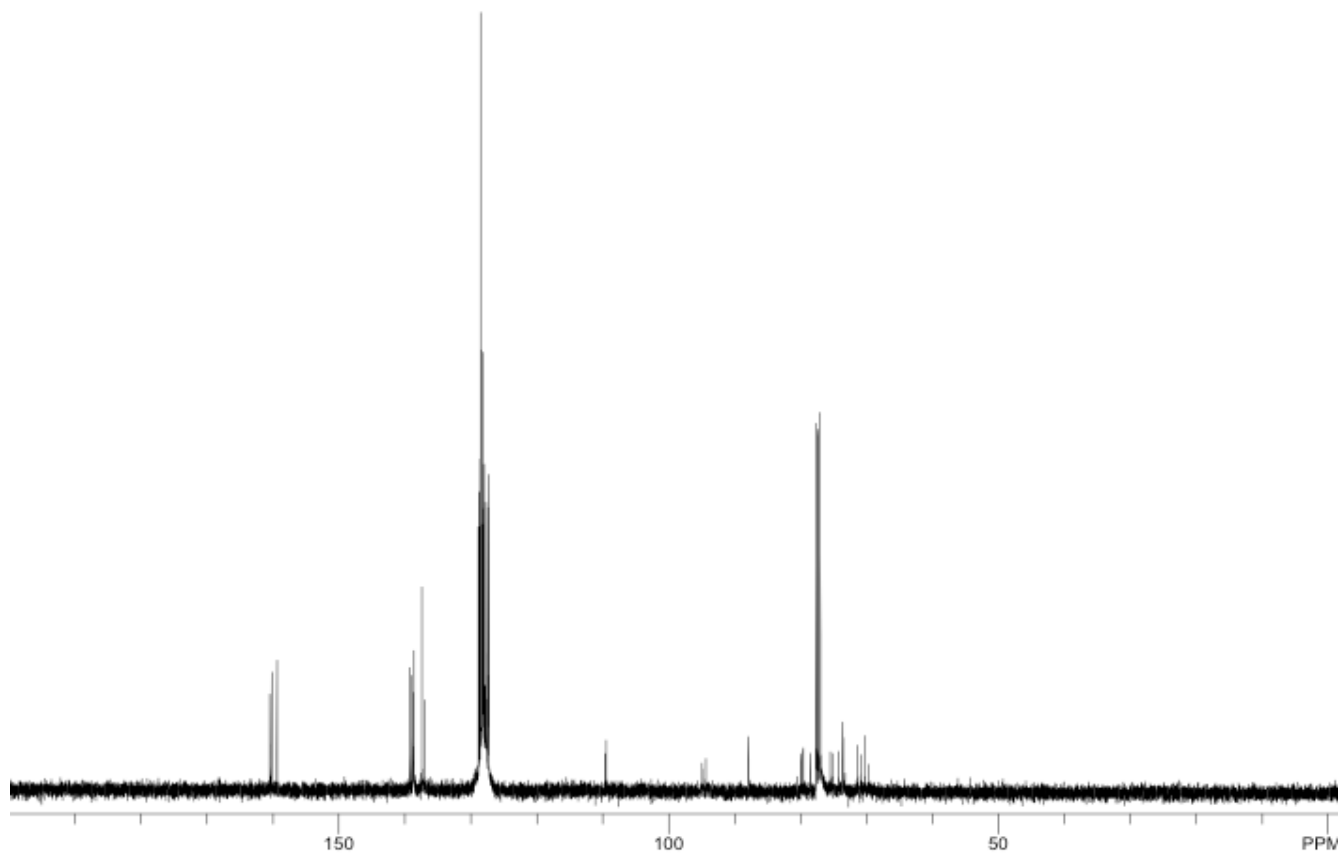
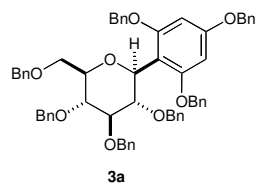




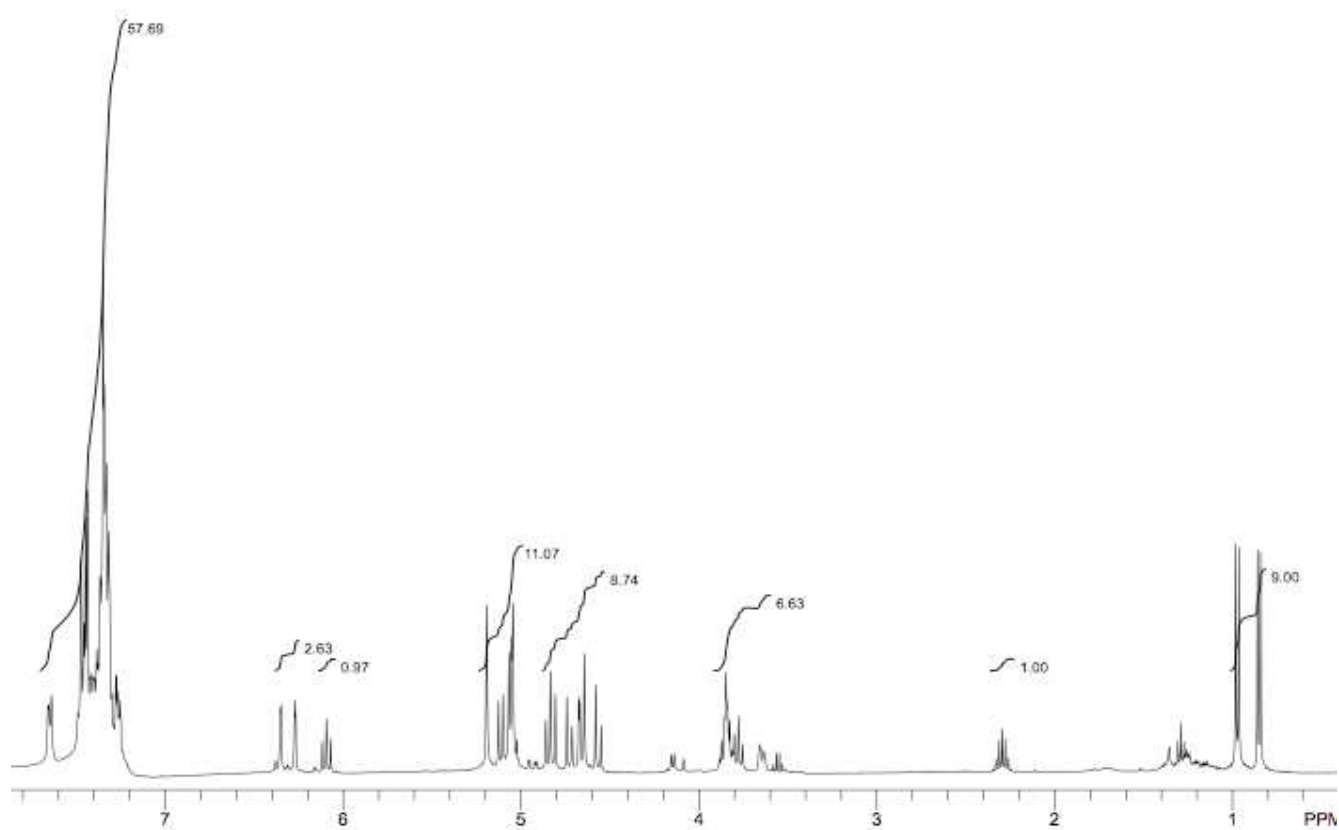
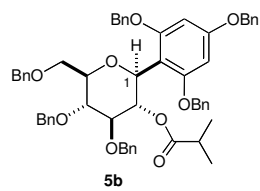
CDCl₃, 400MHz



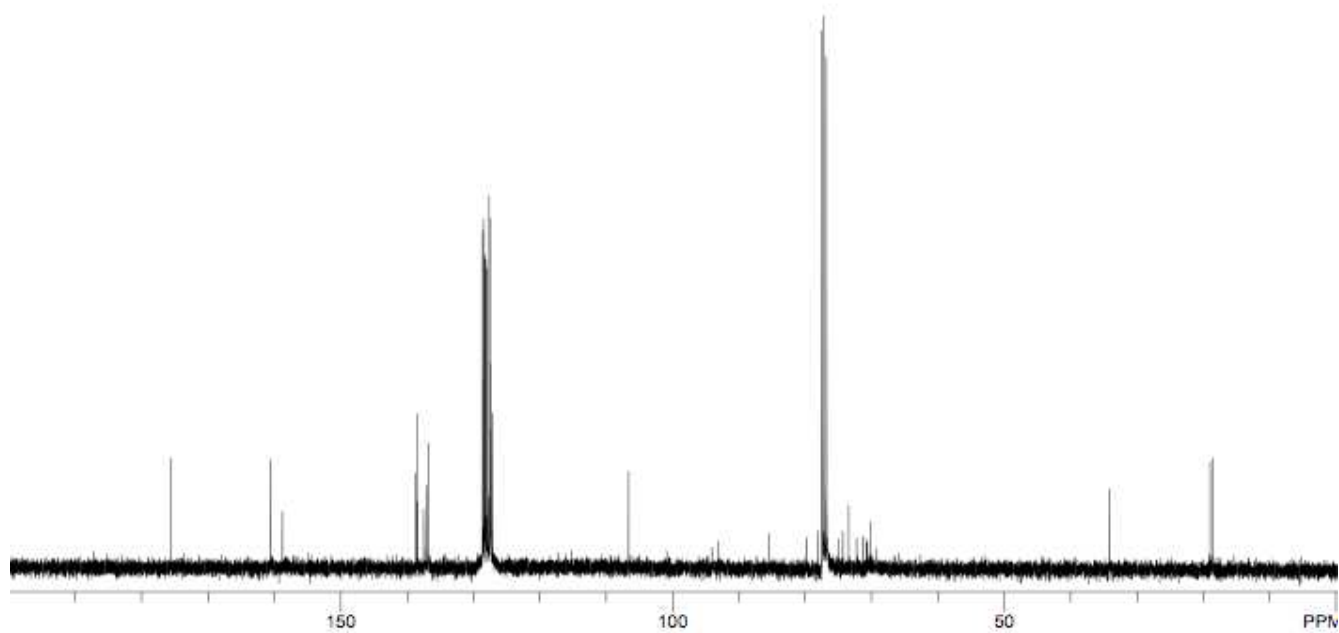
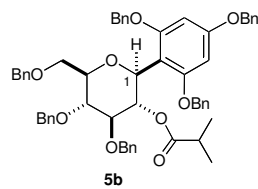
CDCl₃, 100MHz



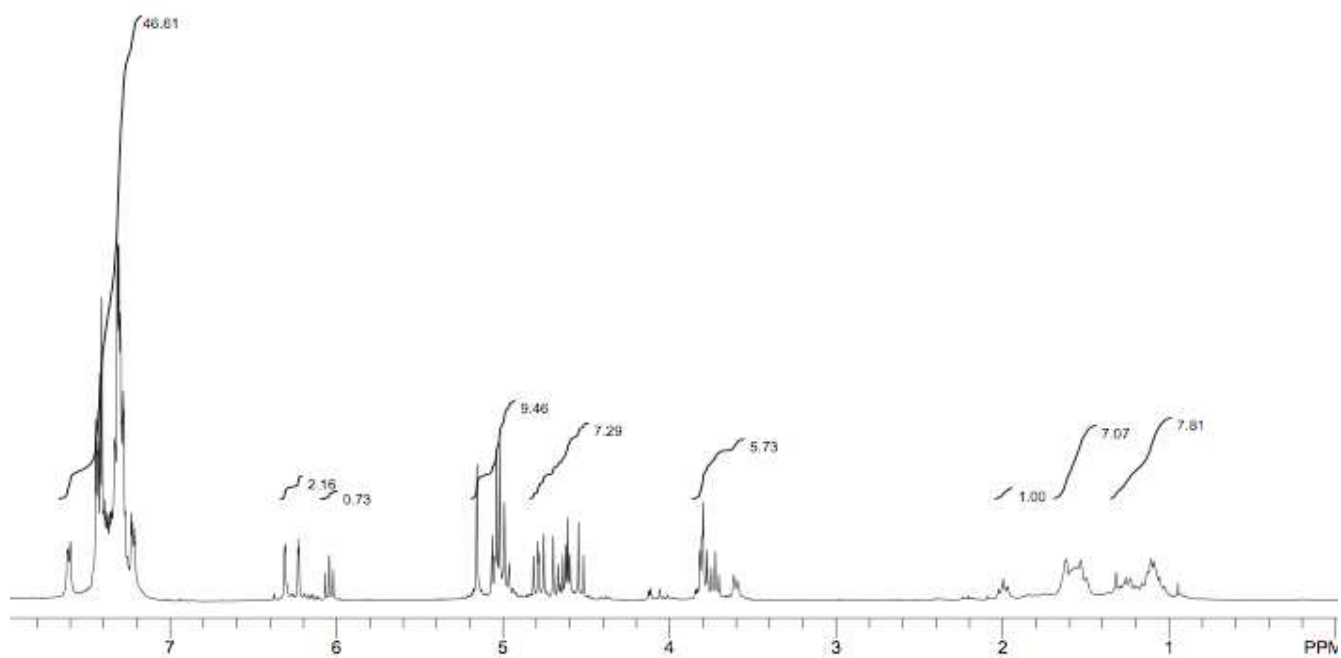
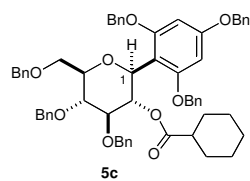
CDCl₃, 400MHz



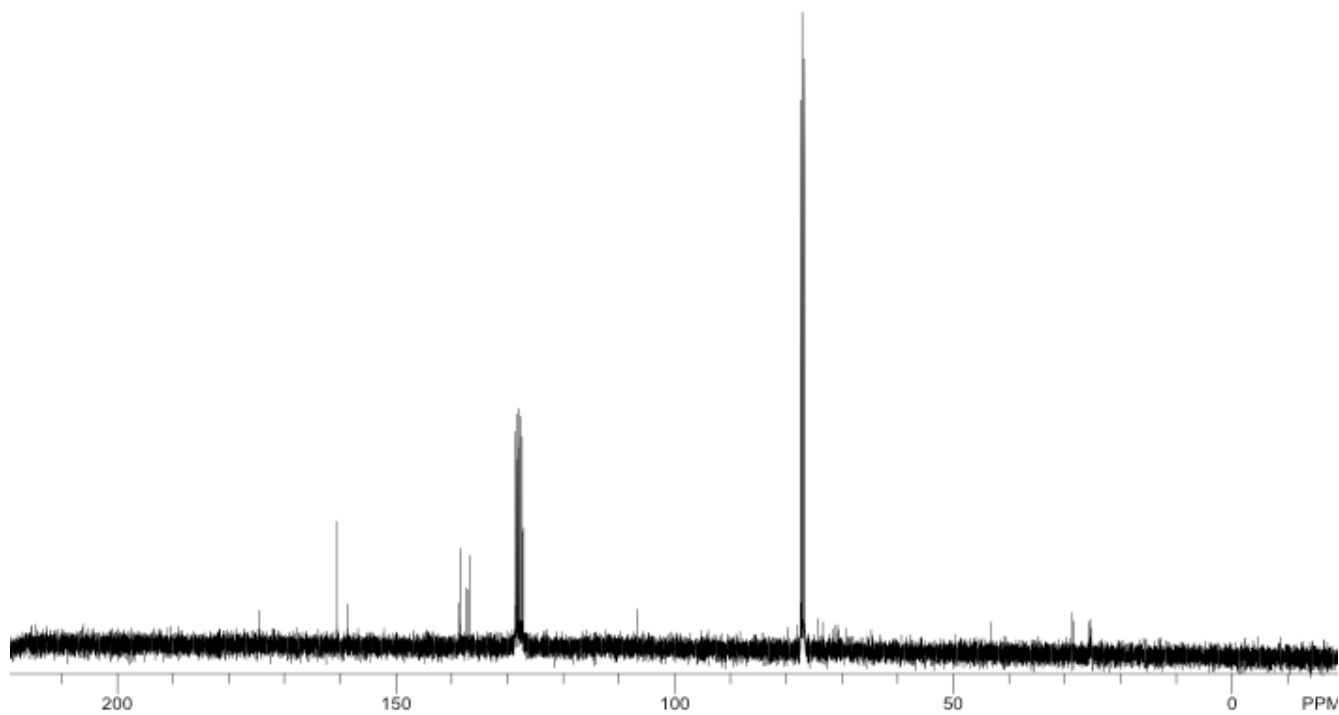
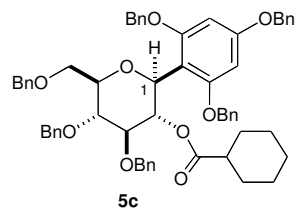
CDCl₃, 100MHz



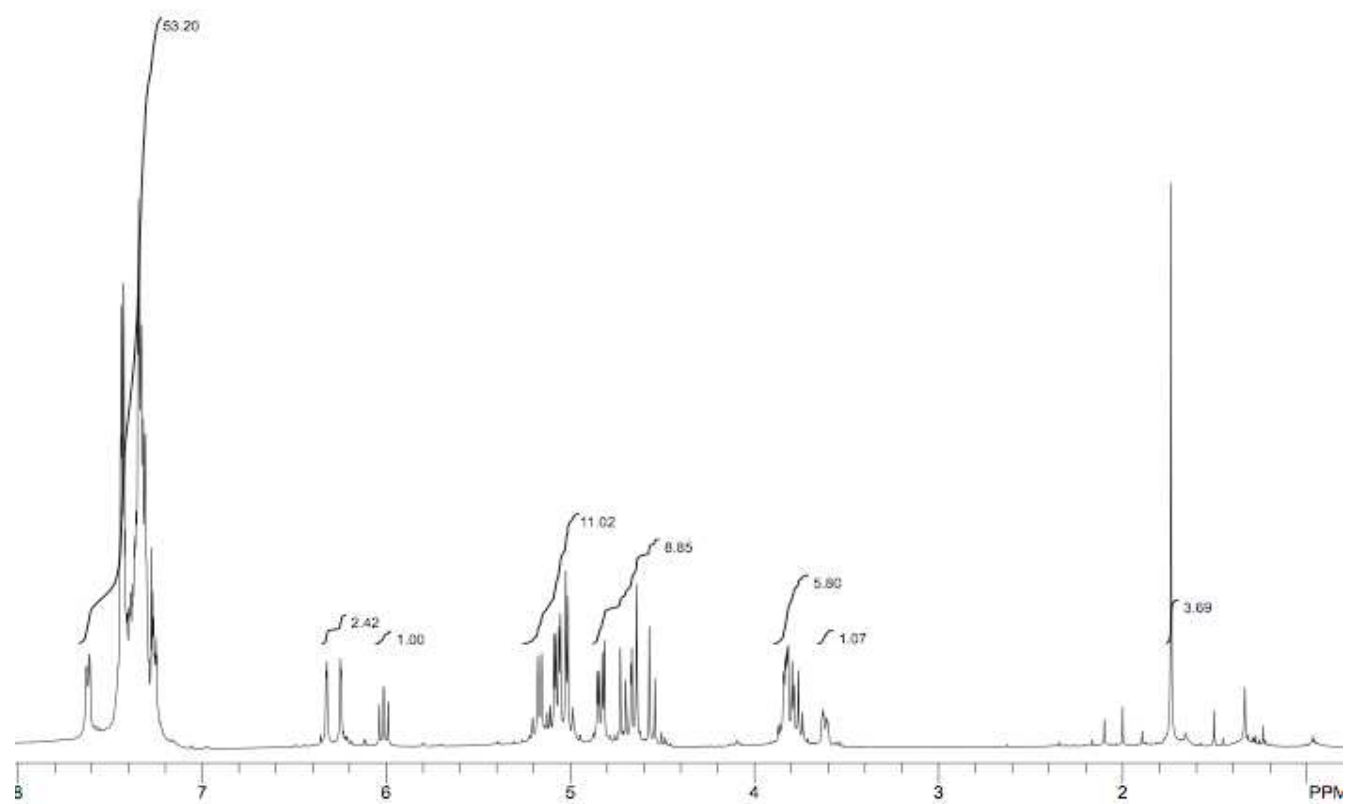
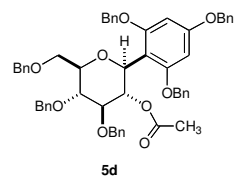
CDCl₃, 400MHz



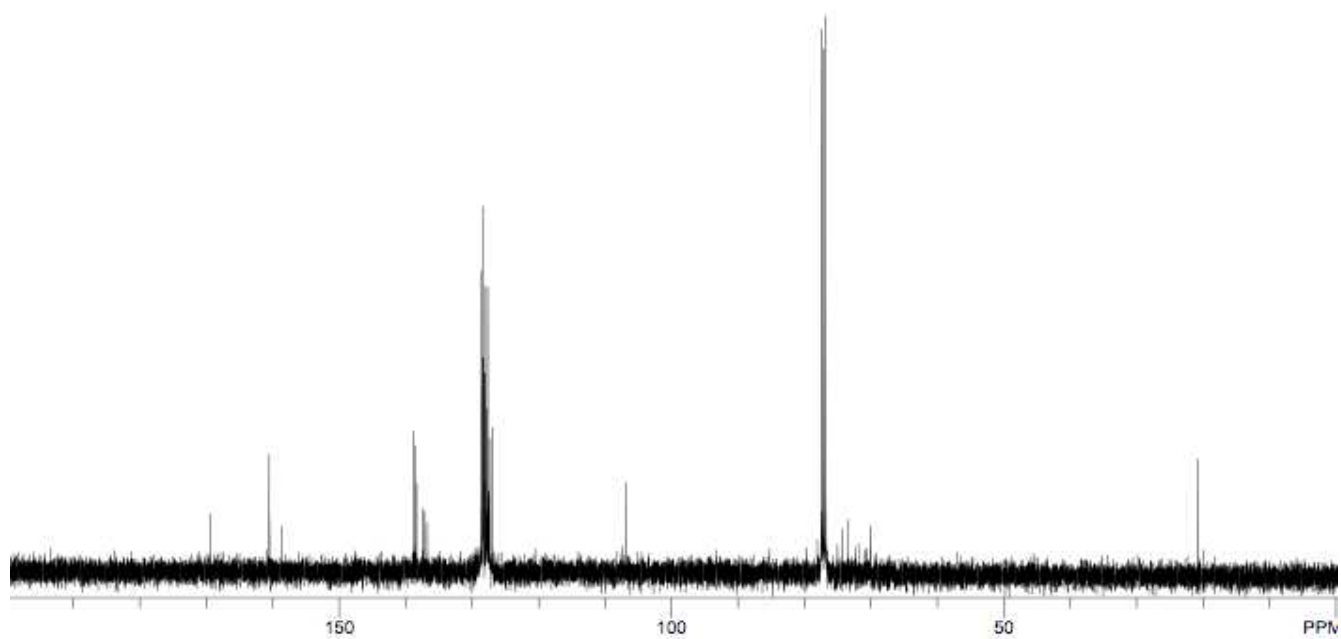
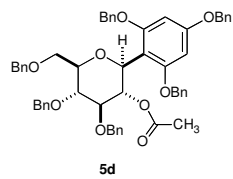
CDCl₃, 100MHz



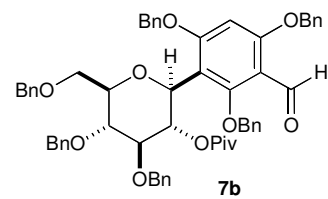
CDCl₃, 400MHz



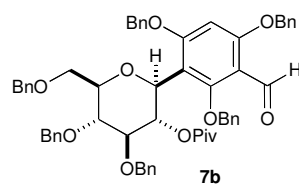
CDCl₃, 100MHz



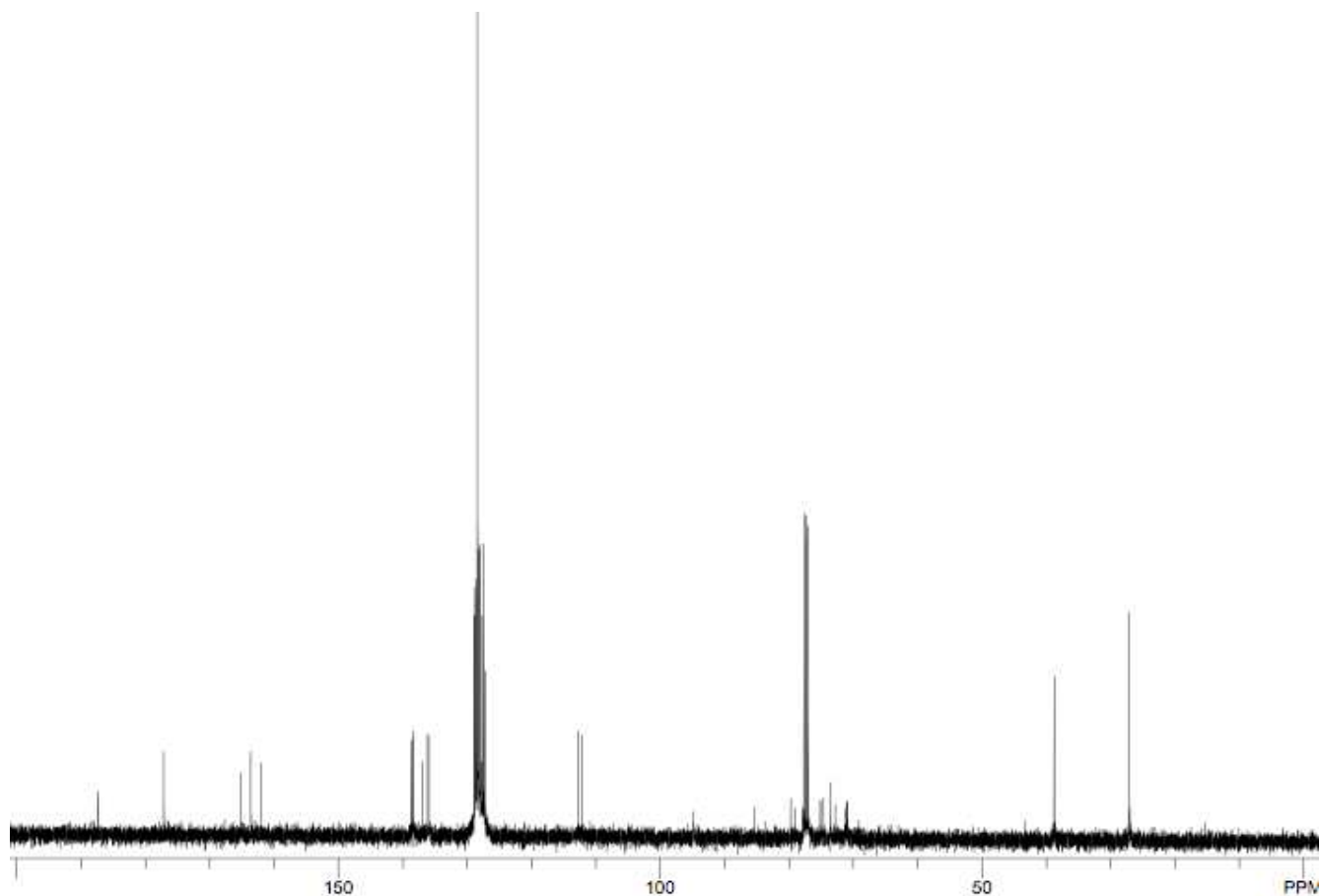
CDCl₃, 400MHz



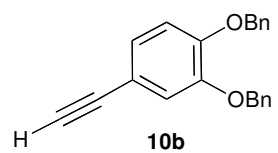
(10:1 mixture of β : α anomers)

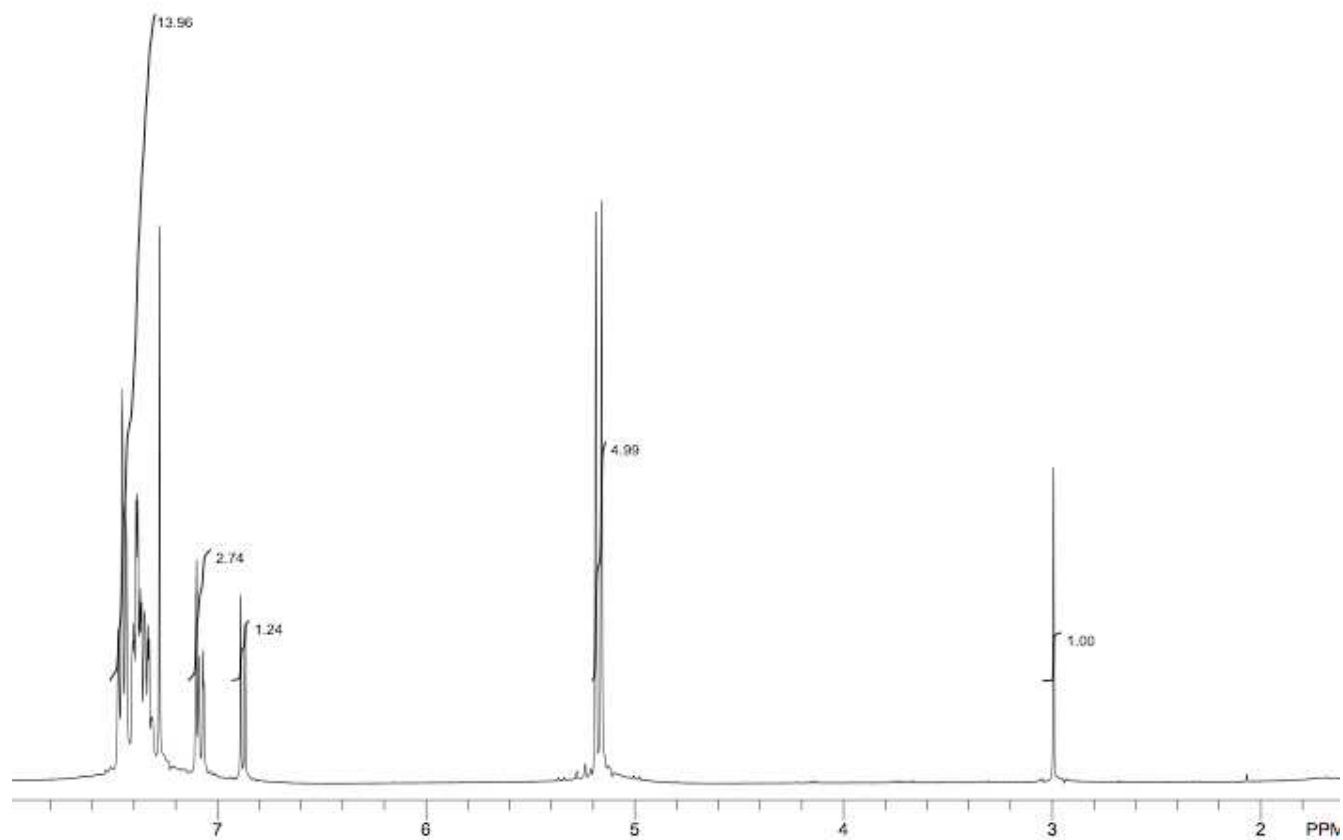


30

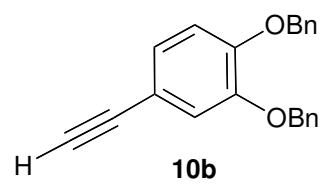


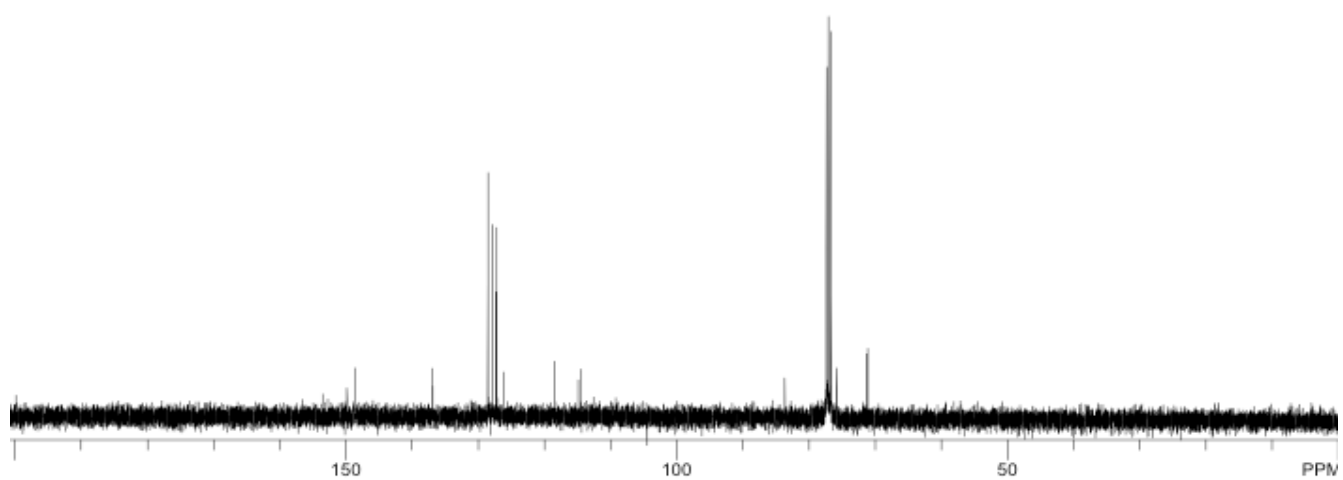
CDCl₃, 400MHz

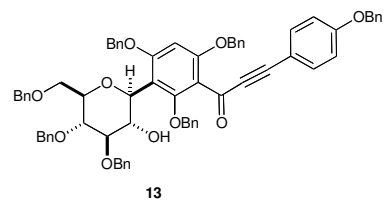




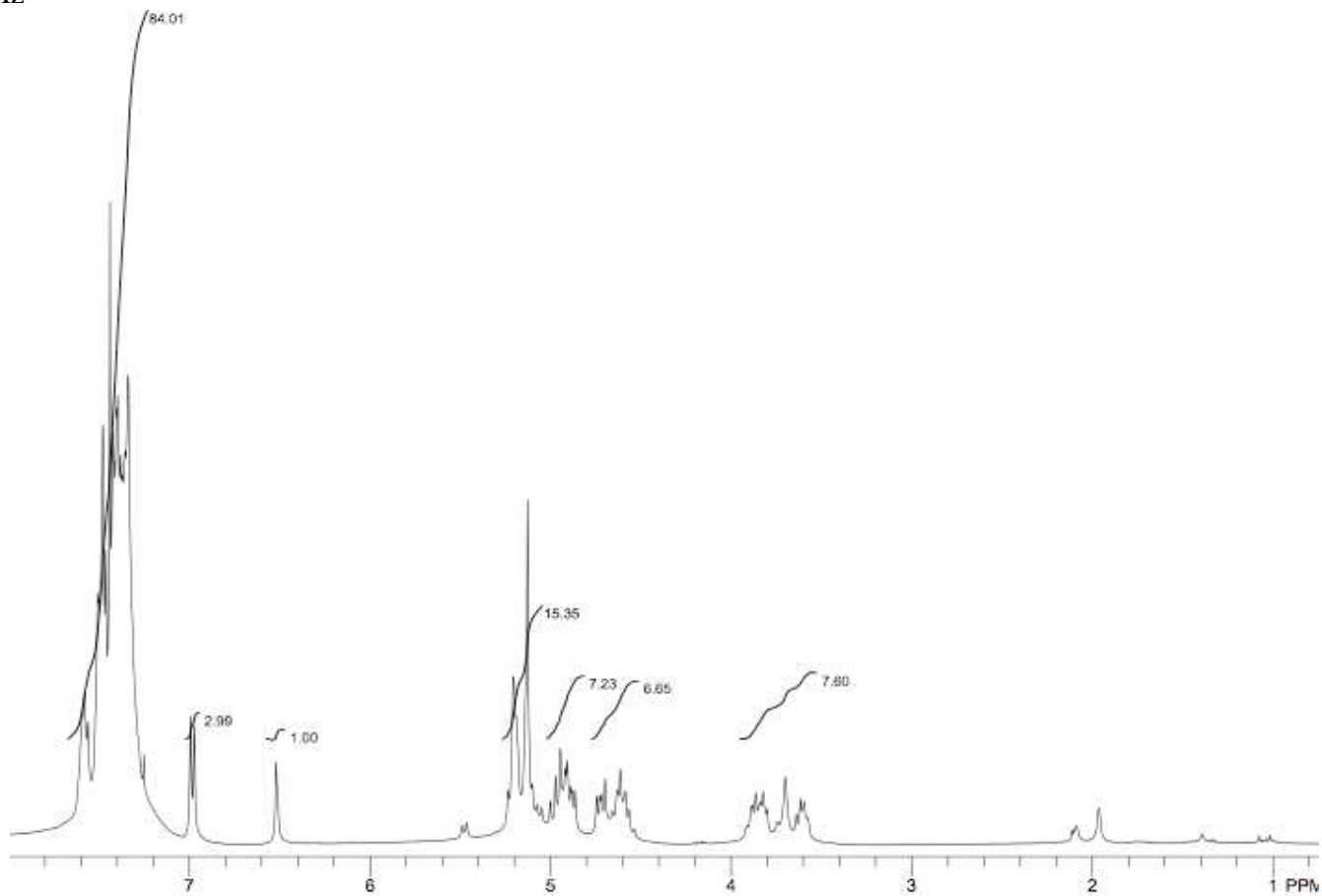
CDCl₃, 100MHz

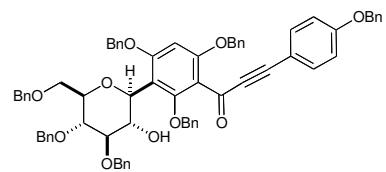






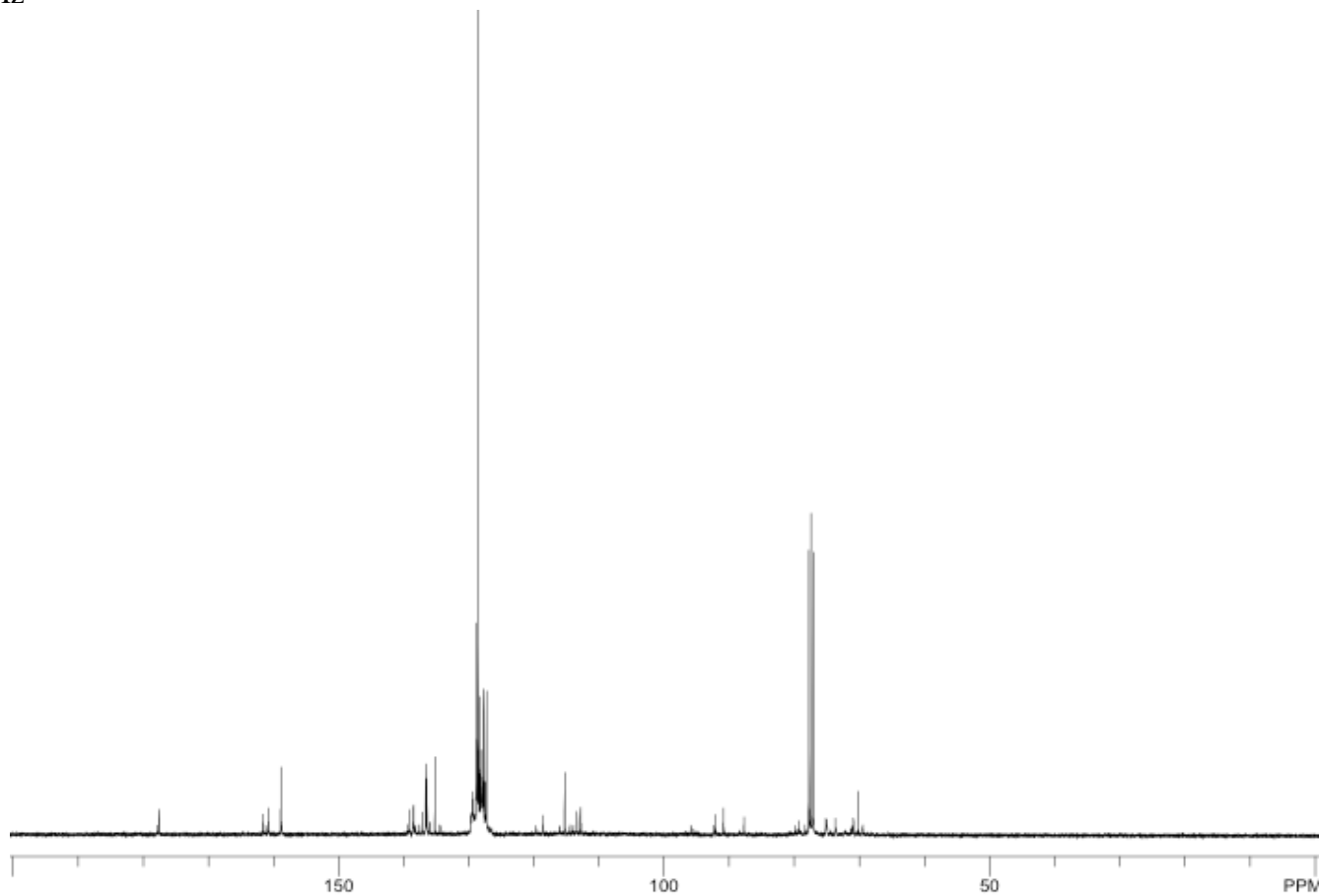
CDCl₃, 400MHz



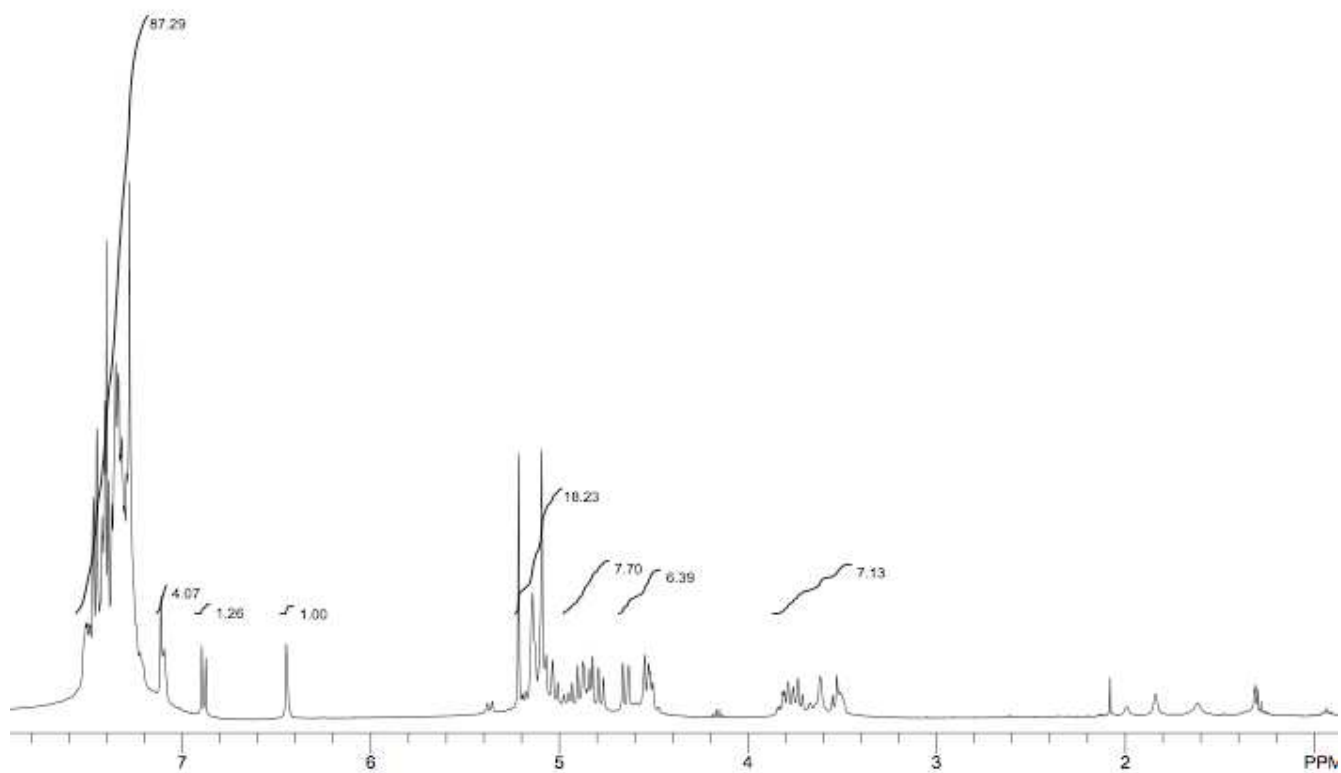
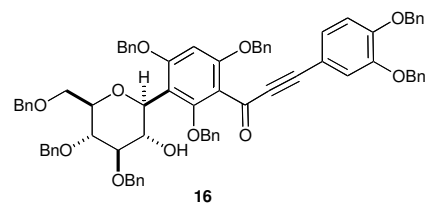


13

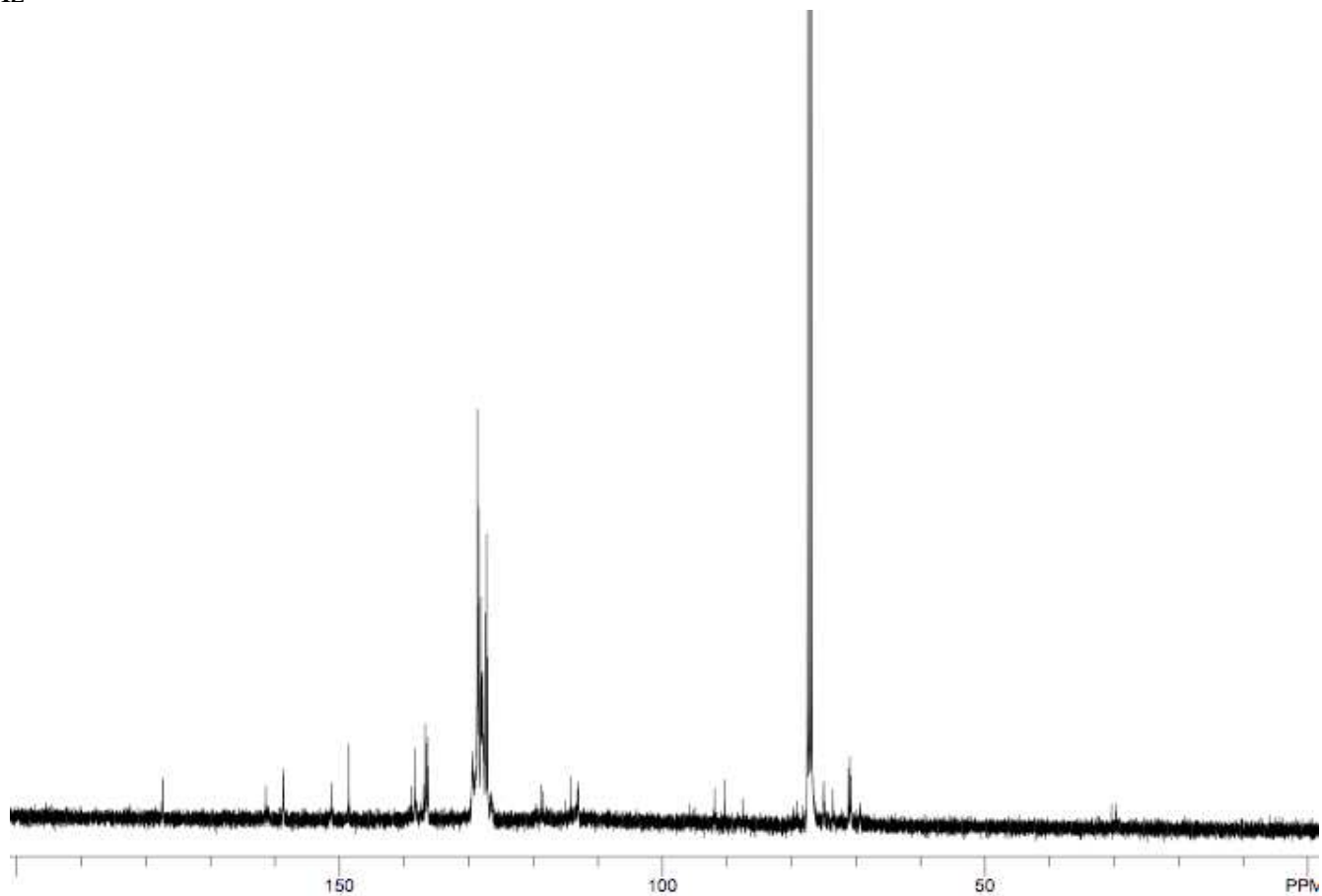
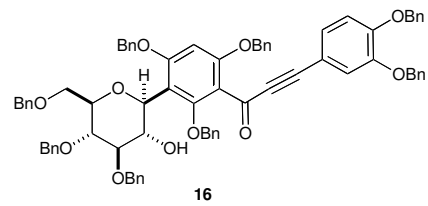
CDCl₃, 100MHz



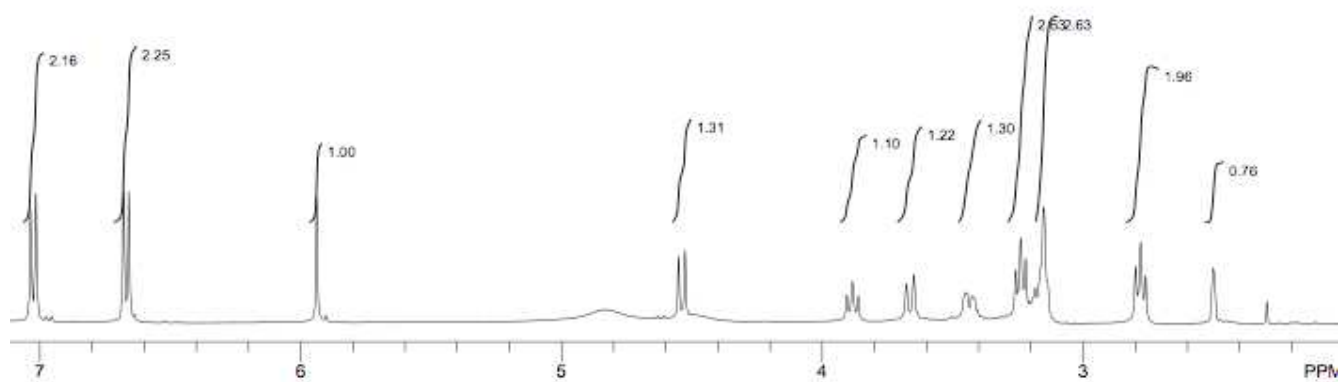
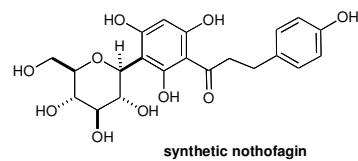
CDCl₃, 400MHz



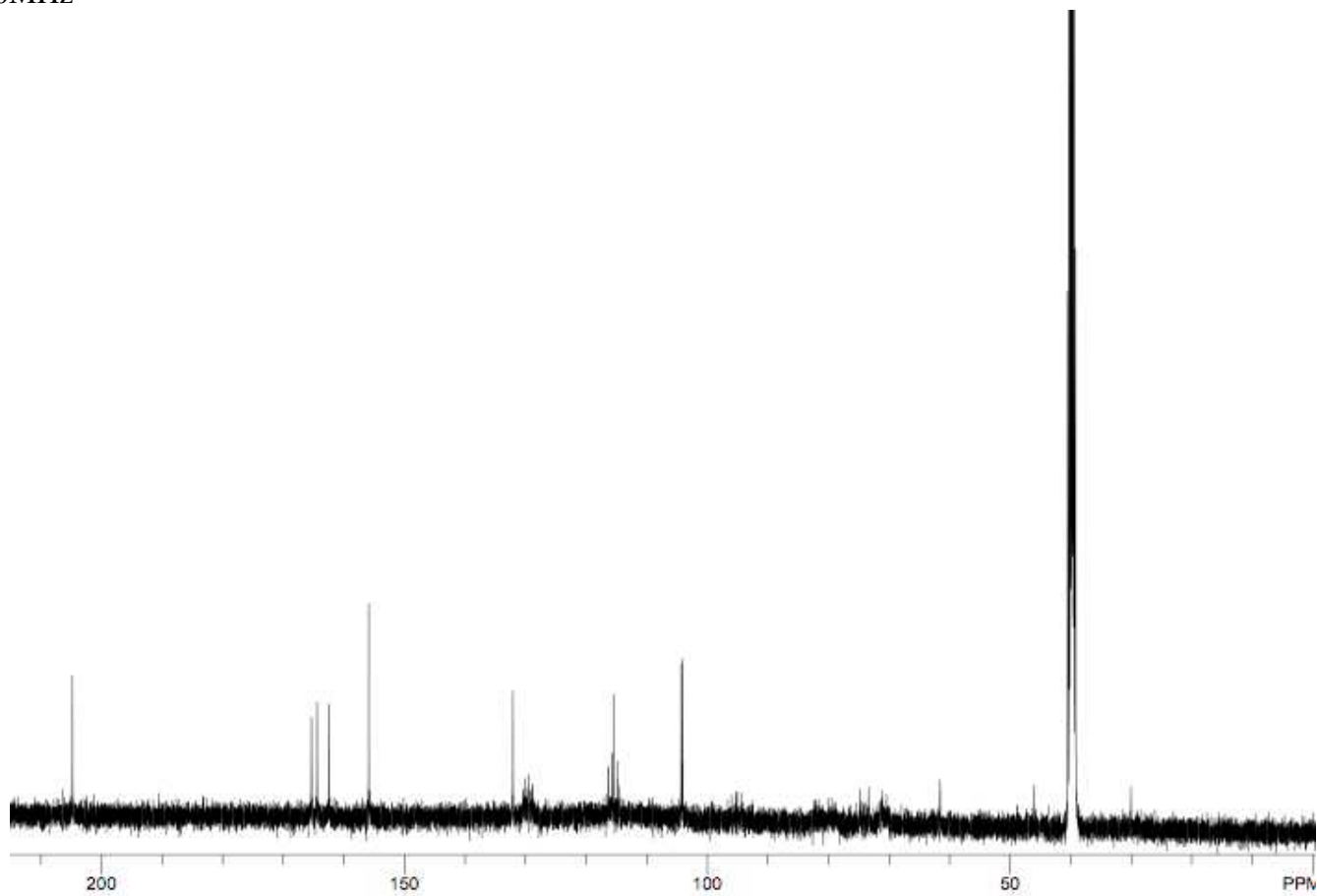
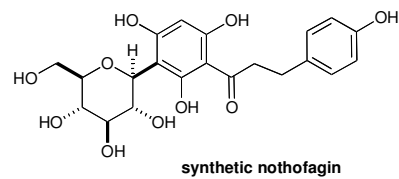
CDCl₃, 100MHz



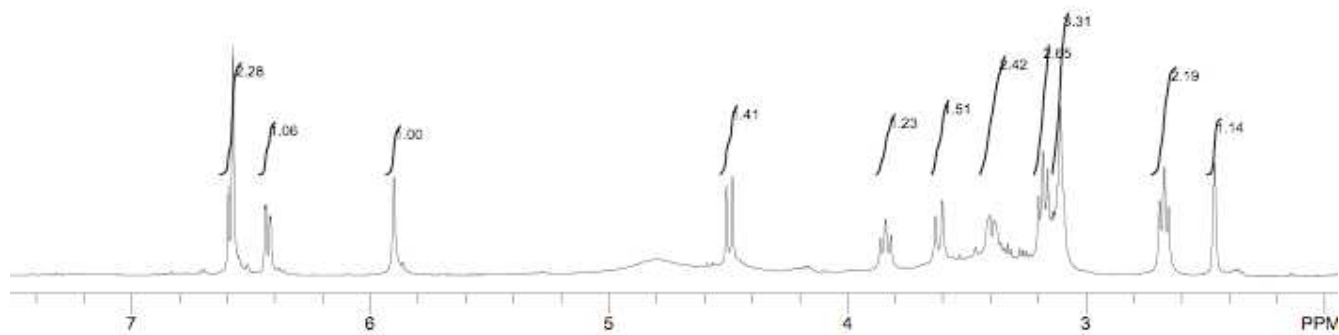
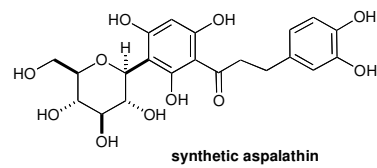
DMSO-d6, 400MHz



DMSO-d6, 100MHz



DMSO-d₆, 400MHz



DMSO-d₆, 100MHz

