

Supporting Information

*Total Synthesis of Indole-3-Acetonitrile-4-Methoxy-2-C- β -D-Glucopyranoside. Proposal
for Structural Revision of the Natural Product*

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Experimental procedures and spectroscopic data for compounds:

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¹HNMR and ¹³CNMR spectra for compounds:

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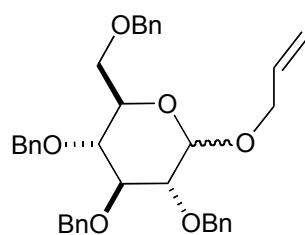
NOESY **12** p. S23

COSY, HSQC, HMBC data for **1** pp. S28-S29

IR data for **1** p. S30

COSY, NOESY data for **15** pp. S32-S33

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 (20-30mmHg). 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.



4

To a solution of dextrose (5 g, 27.7 mmol) in allyl alcohol (25 mL) was added dropwise sulfuric acid (1 mL). The mixture was heated at 85°C for 2 hours until all the solids had dissolved. Neutralization of the reaction mixture with NH₄OH (15 M), followed by evaporation of the solvent and azeotropic drying with toluene (50 mL x 5) afforded crude allyl glucopyranoside as a mixture of C.1 epimers. The crude glycoside was dissolved in DMF (150 mL) and cooled to 0°C NaH (5.54 g, 138.5 mmol, 60% dispersion in mineral oil) and imidazole (938 mg, 13.8 mmol) were added, followed by BnBr (16.4 mL, 138.5 mmol), and TBAI (1.0 g, 2.77 mmol). The mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was then quenched with a saturated solution of NaHCO₃ (20 mL) and ether (150 mL). The phases were separated and the aqueous layer was extracted with ether (2 x 100 mL). The combined organic extracts were twice washed with sat. aq. NaCl (150 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (SiO₂, 10% EtOAc in hexanes) afforded **4** (12g, 20.0 mmol, 75%) as a 4:1 mixture of anomers.

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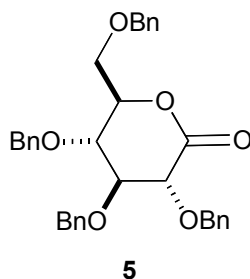
¹H NMR: (400 MHz, CDCl₃)

7.46-7.30 (m, 19H); 7.22 (m, 1H); 5.99 (m, 1H); 5.42 (d, *J*=17.2 Hz, 1H); 5.29 (d, *J*=10.4 Hz, 1H); 5.10-4.52 (m, 9H); 4.26-4.21 (m, 1H); 4.13-4.07 (m, 2H); 3.91-3.51 (m, 5H).

¹³C NMR: (100 MHz, CDCl₃)

138.9; 138.3; 138.2; 138.0; 128.5; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.8; 127.7; 127.5; 95.9; 95.6; 82.2; 82.1; 80.0; 79.8; 75.9; 75.2; 73.6; 73.5; 73.4; 73.2; 70.4; 68.5; 68.2; 65.9.

HRMS (ESI): calculated for C₃₇H₄₀NaO₆ 603.2723 found 603.2635 (M+Na)⁺



A solution of **4** (5 g, 8.62 mmol) in DMF (17 ml, 0.5 M) was treated with solid potassium *tert*-butoxide (4.8 g, 43 mmol) at 70°C. After 15 minutes, the reaction was removed from the heat bath, and aqueous HCl (50 mL, 6M) was added rapidly. The mixture was cooled to room temperature and allowed to stir for 2 hours. At this time, TLC indicated complete hydrolysis of the allyl acetal. The mixture was diluted with ether (50 mL) and the phases were separated. The aqueous layer was extracted with ether (2 x 50 mL). The combined organic extracts were washed three times with saturated aqueous NaCl (50 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give yellow crystals which were recrystallized from a 50:1 Hexanes/Et₂O solution.

Oxalyl Chloride (1.65 mL, 19.4 mmol) was dissolved in CH₂Cl₂ (86 mL) and cooled to -78°C with stirring. DMSO (2.69 mL, 38.8 mmol) was added and the reaction was stirred for 10 minutes. The alcohol obtained above dissolved in CH₂Cl₂ (20 mL) was then added dropwise and the mixture was stirred at -78°C for 15 minutes. Then NEt₃ (5.38 mL, 38.8 mmol) was added and the mixture was allowed to warm to 0°C. The reaction mixture was diluted with ether (150 mL) and quenched with saturated NH₄Cl solution (50 mL); the phases were separated. The aqueous layer was extracted with ether (2 x 50 mL). The combined organic extracts were washed three times with saturated aqueous NaCl (50 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (SiO₂, 5-15% EtOAc in hexanes) afforded **5** (3.2 g, 6 mmol, 70%) as a yellow oil.

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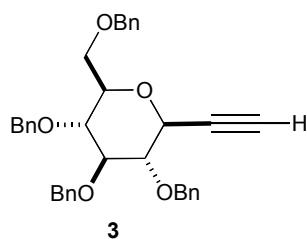
¹H NMR: (400 MHz, CDCl₃)

7.47-7.25 (m, 20H); 5.08 (d, *J*=11.2 Hz, 1H); 4.82-4.52 (m, 8H); 4.21 (d, *J*=6.4 Hz, 1H); 4.01 (m, 2H); 3.78 (qd, *J*=11.6, 3.2 Hz, 2H).

¹³C NMR: (100 MHz, CDCl₃)

169.4; 137.6; 137.0; 128.6; 128.5; 128.4; 128.2; 128.1; 128.0; 127.9; 127.8; 80.9; 78.2; 76.1; 76.0; 74.1; 73.9; 73.8; 73.7; 73.6; 73.5; 68.3.

HRMS (ESI): calculated for C₃₄H₃₄NaO₆ 561.2253 found 561.2392 (M+Na)⁺



CeCl₃•7H₂O (4.46 g, 12 mmol) was heated under vacuum at 120°C for 1h and then at 140°C for 1h. The flask was cooled to 0°C, flushed with Ar, and then anhydrous THF (42.8 mL) was added. The suspension was allowed to stir at room temperature for 2 hours and was then cooled to -78°C. Separately, a solution of TMS acetylene (2.14 mL, 15 mmol) in THF (17 mL) was cooled to -78°C and then *n*-BuLi in hexanes (6.85 mL of a 2M solution, 13.7 mmol) was added. After 45 minutes at -78°C, the CeCl₃ solution was treated with the acetylene solution. The resulting slurry was allowed to stir at -78°C for 30 minutes before lactone **5** (3.2 g, 6.0 mmol) in THF (42.8 mL) was added dropwise. After being stirred for 2 h while warming to room temperature, the reaction was diluted with EtOAc (50 mL), and then washed with 0.1 N HCl (20 mL), water (20 mL), and saturated NaCl solution (20 mL). The organic layer was dried and concentrated *in vacuo* to give a crude yellow oil.

The crude ketose (~6 mmol) was dissolved in 7:3 CH₃CN/CH₂Cl₂ (100 mL) and cooled to -10°C. A solution of Et₃SiH (6.2 mL) in 2:1 CH₃CN/CH₂Cl₂ (24 mL) was added, followed by a solution of BF₃•OEt₂ (2.4 mL) in CH₃CN (16 mL). And the reaction was allowed to stir at -10°C for 1 hour. The mixture was diluted with EtOAc (20 mL) and washed with water (15 mL) and saturated NaCl solution (15 mL). The organic layer was dried (Na₂SO₄) and concentrated *in vacuo* to yield a crude oil. The silylalkyne was purified by flash chromatography (SiO₂, 10% EtOAc in hexanes) to yield an oil.

The oil (3.05 g, 4.9 mmol) was dissolved in 5:1 CH₃OH/CH₂Cl₂ (200 mL), and 1N NaOH (11 mL) was added, and the reaction was allowed to stir for one hour before 1N HCl (11 mL) was added. The solvent was evaporated and the residue was partitioned between EtOAc (50 mL) and water (35 mL). The layers were separated and the organic layer was washed with water (35 mL) and saturated NaCl solution (35 mL). The organic layer was dried (Na₂SO₄) and concentrated *in vacuo* to yield crude **3**. The alkyne was purified by flash chromatography (SiO₂, 5-10% EtOAc in hexanes) to yield pure **3** (2.2 g, 4.0 mmol, 68% overall from **5**).

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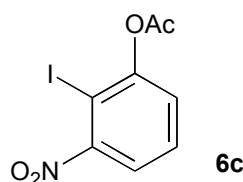
¹H NMR: (400 MHz, CDCl₃)

7.25-7.02 (m, 20H); 4.91 (d, *J*=10.4 Hz, 1H); 4.81 (d, *J*=11.2 Hz, 1H); 4.71 (m, 2H); 4.50 (t, *J*=12.0 Hz, 2H); 4.41 (t, *J*=12.4 Hz, 2H); 3.94 (d, *J*=8.0 Hz, 1H); 3.62-3.51 (m, 5H); 3.32 (m, 1H); 2.39 (s, 1H).

¹³C NMR: (100 MHz, CDCl₃)

138.6; 138.2; 138.1; 128.6; 128.5; 128.4; 128.1; 128.0; 127.9; 127.8; 86.1; 82.2; 81.2; 79.3; 75.8; 75.6; 75.2; 74.6; 73.6; 69.8; 68.9.

HRMS (ESI): calculated for C₃₆H₃₆NaO₅ 571.2460 found 571.2238 (M+Na)⁺



2-amino-3-nitrophenol (2.48 g, 16.1 mmol) was added to a mixture of DMSO (84 mL) and H₂SO₄ (84 mL of a 30% aqueous solution) and the resulting mixture was stirred at 50°C for 2 h then cooled to 0 °C. The mixture was treated, over 5 min, with a solution of sodium nitrite (3.38 g, 49 mmol) in water (8.5 mL). The reaction was stirred at 0 °C for 1 h and then treated, in one portion, with sodium iodide (7.22 g, 48 mmol) in water (8.5 mL). After a further 1 h the reaction mixture was warmed to room temperature, and another portion of sodium iodide (7.22 g, 48 mmol) in water (8.5 mL) was added and the mixture was stirred at room temperature for one hour. The solution was then extracted with EtOAc (100 mL). The separated organic phase was washed with saturated aqueous sodium thiosulfate (2 x 25 mL), water (2 x 25 mL) then brine (25 mL) before being dried (Na₂SO₄) and concentrated *in vacuo* to give crude 2-iodo-3-nitrophenol (3.46 g) as an orange-brown solid.

Crude 2-iodo-3-nitrophenol (3.46 g, ~13 mmol) was dissolved in CH₂Cl₂ (30 mL) and NEt₃ (4.6 mL, 32.5 mmol, 2.5 equiv) was added and the solution was cooled to 0°C. Acetyl chloride (1.43 mL, 20 mmol, 1.5 equiv) was added dropwise and the reaction was allowed to stir for 30 minutes. The mixture was diluted with ether (50 mL) and quenched with saturated aqueous NaHCO₃ solution (20 mL). The layers were separated and the organic layer was washed twice with water (20 mL) and saturated NaCl (20 mL). The organic layer was dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by chromatography (SiO₂, 5-15% EtOAc in hexanes) to afford **6c** (3.67g, 12 mmol, 80%) as a yellow solid.

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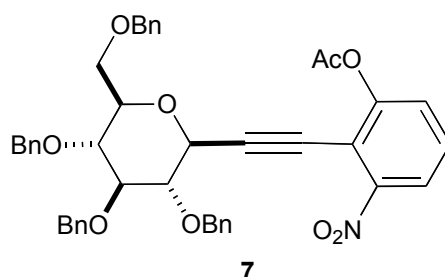
¹H NMR: (400 MHz, CDCl₃)

7.79 (d, *J*=7.6 Hz, 1H); 7.62 (t, *J*=8.0 Hz, 1H); 7.43 (d, *J*=8.0 Hz, 1H);
2.54 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

168.1; 154.9; 153.0; 129.9; 126.5; 122.5; 85.5; 21.2.

HRMS (ESI): calculated for C₈H₆NaNIO₄ 329.9239 found 329.1892 (M+Na)⁺



To a solution of **6c** (816 mg, 2.66 mmol) and **3** (2.2 g, 4 mmol, 1.5 equiv) in CH₃CN (40 mL) and *N,N*-diisopropylethylamine (2.4 mL) were added Cl₂Pd(PPh₃)₂ (186 mg, 0.26 mmol, 10 mol%) and CuI (50 mg, 0.26 mmol, 10 mol%) and the reaction was stirred at 70°C for 2 hours. The mixture was cooled to room temperature and stirred overnight. The reaction was diluted with ether (50 mL) and quenched with saturated NaHCO₃ solution (20 mL). The layers were separated and the organic layer was washed twice with water (20 mL) and saturated NaCl (20 mL). The organic layer was dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by chromatography (SiO₂, 25-35% EtOAc in hexanes) to afford **7** (1.25 g, 1.71 mmol, 66%) as a yellow oil.

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¹H NMR: (400 MHz, CDCl₃)

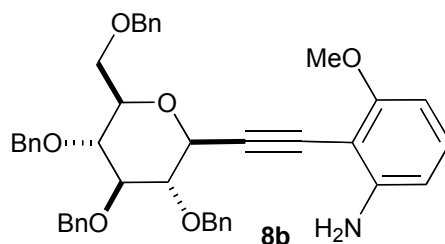
7.98 (d, *J*=8.4 Hz, 1H); 7.51-7.16 (m, 22H); 5.12 (d, *J*=10.8 Hz, 1H); 4.95 (d, *J*=10.8 Hz, 1H); 4.83 (m, 4H); 4.54 (m, 4H); 4.33 (d, *J*=9.2 Hz, 1H); 3.72 (m, 5H); 2.30 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

168.6; 153.8; 153.7; 138.4; 138.0; 137.9; 128.3; 128.2; 128.1; 127.9; 127.8; 127.7; 127.3; 122.0; 100.0; 93.0; 91.7; 76.7; 76.1; 75.7; 75.4; 75.1; 73.4; 70.3; 68.9; 63.0; 40.7; 20.6.

HRMS (ESI): calculated for C₄₄H₄₁NNaO₉ 750.2679 found 750.2817 (M+Na)⁺

[α]_D²⁵: -2.3° (c 0.003, CH₂Cl₂)



To solution of **7** (1.0 g, 1.37 mmol) in THF (20 mL) was added *n*-butylamine (0.44 mL, 4.48 mmol, 3 equiv) at room temperature. The reaction was stirred for 1 hour and was then concentrated *in vacuo*. The crude phenol was then dissolved in DMF (5 mL) and CH₃I (0.28 mL, 4.48 mmol, 3 equiv) was added. Potassium carbonate (1.0 g, 7.45 mmol, 5 equiv) was added and the reaction was stirred for 3 hours at room temperature. The reaction was diluted with ether (20 mL) and water (20 mL). The phases were separated and the aqueous layer was extracted with ether (2 x 10 mL). The combined organic layers were washed with water (2 x 10 mL) and brine (10 mL). The organic layer was dried (Na₂SO₄) and concentrated *in vacuo* to yield a crude oil. Purification by flash chromatography (SiO₂, 25 - 35 % EtOAc in hexanes) afforded a light yellow oil.

The crude methyl ether (~600 mg, 0.85 mmol) was dissolved in THF (50 mL) at 0°C and AcOH (1.44 mL) and zinc dust (3.78 g, 57.9 mmol) were added. The mixture was stirred for 1.5 hours at room temperature and then the reaction was diluted with ether (20 mL) and washed with 1N NaOH (2 x 30 mL). The combined aqueous layers were extracted with CH₂Cl₂ (30 mL). The combined organics were dried over Na₂SO₄, filtered, and concentrated *in vacuo* to yield a crude oil (560 mg, 61% overall from **7**). Compound **8b** was of sufficient purity to carry forward to the next reaction.

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¹H NMR: (400 MHz, CDCl₃)

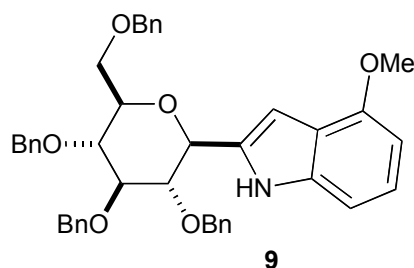
7.30-7.16 (m, 21H); 7.06 (d, *J*=8.0 Hz, 1H); 6.97 (t, *J*=8.0 Hz, 1H); 6.24 (d, *J*=8.8 Hz, 1H); 6.14 (d, *J*=8.0 Hz, 1H); 5.17 (d, *J*=10.0 Hz, 1H); 4.90 (d, *J*=11.2 Hz, 1H); 4.76 (m, 3H); 4.57 (d, *J*=12 Hz, 1H); 4.50 (d, *J*=10.8 Hz, 1H); 4.30 (d, *J*=8.4 Hz, 1H); 3.69-3.59 (m, 5H); 3.66 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

159.4; 148.0; 136.7; 136.1; 128.2; 126.5; 126.4; 126.0; 125.9; 125.8; 125.7; 105.2; 97.7; 84.1; 80.7; 77.6; 77.1; 73.7; 73.3; 73.2; 71.6; 68.8; 67.0; 53.5; 48.9.

HRMS (ESI): calculated for C₄₃H₄₃NNaO₆ 692.2988 found 692.3053 (M+Na)⁺

[α]_D²⁵: -16° (c 0.006, CH₂Cl₂)



To a solution of **8b** (500 mg, 0.74 mmol) in DMF (3 mL) was added CuI (422 mg, 2.22 mmol, 3 equiv) and the mixture was stirred at 145°C for 1-2 hours (with the addition of an additional 422 mg CuI every 30 minutes) until TLC indicated complete consumption of starting material. After cooling to room temperature, ether was added (50 mL) and the mixture was filtered over Celite (washing solids several times with more ether); the combined ethereal solution was washed with a saturated aqueous solution of NaCl (30 mL) and the combined organics were dried over Na₂SO₄. Concentration *in vacuo* provided a crude oil, which was purified by chromatography (SiO₂, 5 – 15 % EtOAc in hexanes) to provide indole **9** (321 mg, 65%).

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¹H NMR: (400 MHz, CDCl₃)

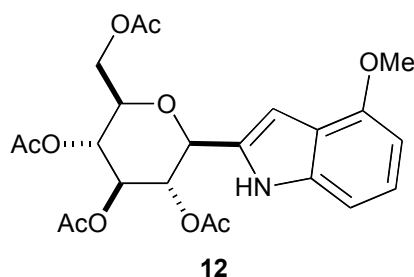
8.46 (s, 1H); 7.27-7.01 (m, 21H); 6.86 (d, *J*=8.0 Hz, 1H); 6.62 (s, 1H); 6.45 (d, *J*=7.6 Hz, 1H); 4.91 (d, *J*=10.8 Hz, 1H); 4.81 (m, 2H); 4.56-4.45 (m, 3H); 4.38 (m, 2H); 3.95 (d, *J*=10.4 Hz, 1H); 3.87 (s, 3H); 3.71 (m, 4H); 3.49 (m, 2H).

¹³C NMR: (100 MHz, CDCl₃)

153.4; 138.5; 138.1; 137.5; 134.1; 128.5; 128.4; 128.3; 127.9; 127.8; 127.7; 127.6; 122.6; 118.8; 104.4; 99.6; 98.9; 86.5; 82.6; 79.0; 75.7; 75.6; 75.1; 74.9; 73.5; 69.0; 55.3.

HRMS (ESI): calculated for C₄₃H₄₃NNaO₆ 692.2988 found 692.2541 (M+Na)⁺

[α]_D²⁵: +3.0° (c 0.007, CH₂Cl₂)



To a solution of **9** (150 mg, 0.22 mmol) in EtOAc (1 mL) and MeOH (1 mL) was added Pd(OH)₂ (20% on carbon, 50 mg) and the mixture was stirred at room temperature under an atmosphere of hydrogen for 18 hours. At this time, TLC indicated complete consumption of starting material. The mixture was diluted with 5% MeOH/EtOAc (20 mL), filtered over Celite, and concentrated *in vacuo* to yield a crude oil. The crude tetraol was dissolved in pyridine (2 mL) and acetic anhydride (2 mL) was added. The mixture was allowed to stir at room temperature for 24 hours and was then concentrated *in vacuo*. The crude oil was purified by chromatography (SiO₂, 2:1-1:1 hexanes/EtOAc) to provide indole **12** (53 mg, 50%).

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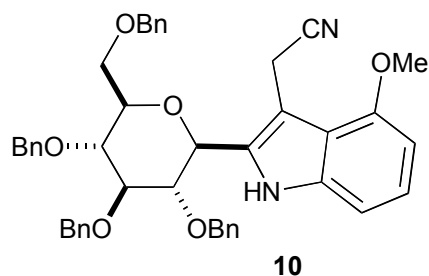
¹H NMR: (400 MHz, CDCl₃)

8.35 (s, 1H); 7.03 (t, *J*=8.0 Hz, 1H); 6.92 (d, *J*=8.4 Hz, 1H); 6.47 (d, *J*=1.6 Hz, 1H); 6.43 (d, *J*=7.6 Hz, 1H); 5.28 (t, *J*=9.2 Hz, 1H); 5.18 (t, *J*=8.0 Hz, 1H); 5.15 (t, *J*=9.6 Hz, 1H); 4.62 (d, *J*=9.6 Hz); 4.25 (dd, *J*=12.4, 5.5 Hz, 1H); 4.08 (dd, *J*=12.4, 2.4 Hz, 1H); 3.85 (s, 3H); 3.79 (m, 1H); 2.01 (s, 3H); 1.99 (s, 3H); 1.94 (s, 3H); 1.81 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

170.7; 170.3; 169.5; 169.1; 153.3; 137.6; 130.6; 123.4; 118.4; 104.6; 99.7; 98.7; 74.5; 74.0; 70.9; 68.4; 62.3; 55.2; 20.7; 20.6; 20.5.

HRMS (ESI): calculated for C₂₃H₂₇NNaO₁₀ 500.1533 found 500.1438 (M+Na)⁺



The procedure for the preparation of **14** from **13** (*vide infra*) was followed for the preparation of **10** (288 mg, 85% yield) from **9** (321 mg, 0.48 mmol).

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¹H NMR: (400 MHz, CDCl₃)

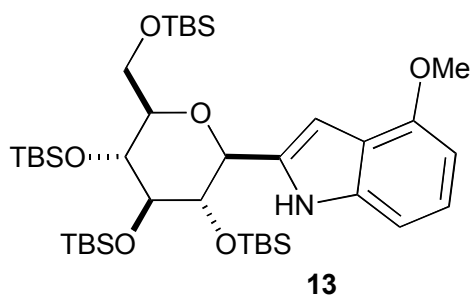
8.31 (s, 1H); 7.28-7.01 (m, 25H); 6.85 (d, *J*=7.2 Hz, 1H); 6.80 (d, *J*=8.0 Hz, 1H); 6.46 (d, *J*=8.0 Hz, 1H); 4.86 (m, 2H); 4.81 (d, *J*=10.8 Hz, 1H); 4.53-4.42 (m, 5H); 3.93 (d, *J*=10.8 Hz, 1H); 3.87 (s, 3H); 3.85-3.71 (m, 3H).

¹³C NMR: (100 MHz, CDCl₃)

154.4; 138.4; 138.0; 137.9; 137.2; 136.7; 131.4; 128.4; 128.2; 127.9; 127.8; 127.7; 123.5; 119.3; 117.1; 104.5; 102.8; 100.1; 86.5; 79.1; 75.6; 75.1; 75.0; 74.1; 73.5; 14.5.

HRMS (ESI): calculated for C₄₅H₄₄N₂NaO₆ 731.3097 found 731.3178 (M+Na)⁺

[α]_D²⁵: +6.5° (c 0.006, EtOH)



To a solution of **9** (150 mg, 0.22 mmol) in EtOAc (1 mL) and MeOH (1 mL) was added Pd(OH)₂ (20% on carbon, 50 mg) and the mixture was stirred at room temperature under an atmosphere of hydrogen for 18 hours. At this time, TLC indicated complete consumption of starting material. The mixture was diluted with 5% MeOH/EtOAc (20 mL), filtered over Celite, and concentrated *in vacuo* to yield a crude oil. The crude tetraol was dissolved in DMF (0.5 mL) and imidazole (164 mg, 2.42 mmol) and TBS-Cl (165 mg, 1.1 mmol) was added. The mixture was allowed to stir at 60°C for 12 hours and was then diluted with ether (20 mL) and a saturated solution of NaHCO₃ (10 mL). The phases were separated and the aqueous layer was extracted with ether (2 x 10 mL). The combined organic layers were washed with water (2 x 10 mL) and brine (10 mL). The organic layer was dried (Na₂SO₄) and concentrated *in vacuo* to yield a crude oil. The crude oil was purified by chromatography (SiO₂, 5-10% EtOAc in hexanes) to provide indole **13** (115 mg, 67%).

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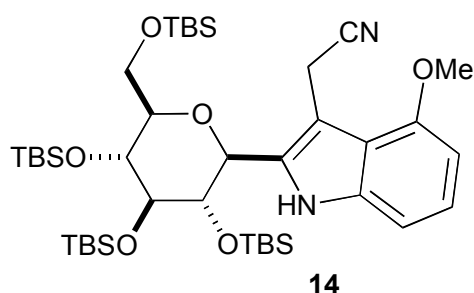
¹H NMR: (400 MHz, CDCl₃)

8.70 (s, 1H); 7.67 (t, *J*=8.0 Hz, 1H); 7.53 (d, *J*=7.6 Hz, 1H); 7.17 (s, 1H); 7.11 (d, *J*=6.4 Hz, 1H); 4.95 (d, *J*=8.4 Hz, 1H); 4.53 (s, 3H); 4.46 (s, 2H); 4.34 (t, *J*=8.0 Hz, 1H); 4.12 (m, 2H); 3.95 (d, *J*=9.6 Hz, 1H); 1.51 (m, 18H); 1.47 (s, 9H); 1.39 (s, 9H); 0.81 (s, 3H); 0.79 (s, 3H); 0.69 (s, 3H); 0.64 (s, 3H); 0.62 (m, 6H); 0.54 (s, 3H); 0.01 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

159.8; 143.0; 139.9; 128.2; 124.5; 110.0; 109.8; 105.9; 105.7; 86.9; 85.8; 80.8; 76.0; 68.1; 61.2; 35.8; 30.9; 31.9; 31.8; 31.7; 24.2; 24.1; 24.0; 2.9; 2.0; 1.8; 1.5; 1.4; 1.3; 0.5

HRMS (ESI): calculated for C₃₉H₇₆NNaO₆ 766.4750 found 766.5165 (M+Na)⁺



To a solution of **13** (115 mg, 0.15 mmol) in dioxane (0.5 mL), diethylamine (0.15 mL, 1.5 mmol) and acetic acid (0.2 mL, 3.5 mmol) were added formalin (0.15 mL, 5.4 mmol, 37% aqueous formaldehyde) and the mixture was allowed to stir at room temperature until TLC indicated disappearance of starting material (~3h). The mixture was diluted with ether (20 mL) and made alkaline with 0.1 N NaOH solution (2 mL). The phases were separated and the aqueous phase was extracted with ether (2 x 10mL) and CH₂Cl₂ (2 x 10mL). The combined organics were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude oil was dissolved in CH₂Cl₂ (1 mL) and CH₃I (0.3 mL, 4.77 mmol) was added and the mixture was stirred at room temperature for 1.5 hours. The mixture was concentrated *in vacuo* to remove all volatiles, and EtOH (1 mL) was added, along with solid NaCN (245 mg, 5 mmol). The mixture was heated to 80°C and stirred for 5 hours. The reaction was cooled to room temperature and concentrated *in vacuo*. The residue was dissolved in 1:1 EtOAc/saturated NaHCO₃ (20 mL) and the layers were partitioned. The aqueous phase was back-extracted with EtOAc (2 x 10 mL) and the combined organics were dried over Na₂SO₄ and concentrated *in vacuo*. The crude oil was purified by chromatography (SiO₂, 5-15% EtOAc in hexanes) to provide indole **14** (72 mg, 60%).

See spectra on page S26

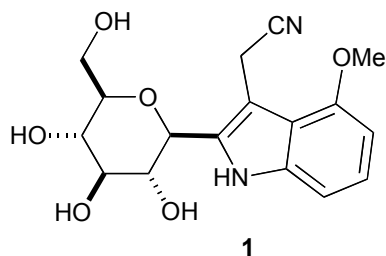
¹H NMR: (400 MHz, CDCl₃)

8.09 (s, 1H); 7.11 (t, *J*=8.0 Hz, 1H); 6.90 (d, *J*=8.0 Hz, 1H); 6.53 (d, *J*=7.6 Hz, 1H); 4.44 (d, *J*=8.4 Hz, 1H); 4.14 (d, *J*=17.6 Hz, 1H); 3.99 (d, *J*=16.8 Hz, 1H); 3.94 (s, 3H); 3.86 (s, 2H); 3.75 (t, *J*=8.4 Hz, 1H); 3.56 (m, 2H); 3.39 (d, *J*=9.6 Hz, 1H); 0.92 (m, 27H); 0.77 (s, 9H); 0.19 (s, 3H); 0.16 (s, 3H); 0.14 (s, 3H); 0.07 (s, 3H); 0.04 (s, 3H); -0.01 (s, 3H); -0.64 (s, 3H).

¹³C NMR: (100 MHz, CDCl₃)

159.9; 142.1; 137.3; 129.1; 124.5; 122.7; 109.6; 108.6; 105.7; 86.9; 85.3; 81.3; 80.6; 75.9; 67.4; 60.8; 31.4; 31.2; 23.9; 23.7; 23.4; 20.0; 1.61; 1.06; 0.68; 0.43; 0.34.

HRMS (ESI): calculated for C₄₁H₇₆N₂NaO₆Si₄ 827.4678 found 827.5047 (M+Na)⁺



To a mixture of **14** (50 mg, .06 mmol) in CH₂Cl₂ (0.1 mL) was added a solution of TBAF in THF (1M, 0.3 mL, 0.3 mmol, 5 equiv) and the solution was allowed to stir at room temperature overnight. The mixture was concentrated *in vacuo* and loaded directly onto a silica gel column with CHCl₃ (0.5 mL). Elution with 5-7% methanol in ethyl acetate provided **1** (~15 mg, 72%).

See spectra on page S27, S28, S29, S30

¹H NMR: (400 MHz, acetone-d₆)

10.23 (s, 1H); 7.01 (dd, *J*=8.0, 7.6 Hz, 1H); 6.94 (d, *J*=8.4 Hz, 1H); 6.52 (d, *J*=7.6 Hz, 1H); 4.64 (d, *J*=8.8 Hz, 1H); 4.05 (d, *J*=3.2 Hz, 2H); 3.91 (s, 3H); 3.85 (d, *J*=13.2 Hz, 1H); 3.73 (dd, *J*=12.0, 4.0 Hz, 1H); 3.60-3.49 (m, 4H); 2.83 (broad s, 5H).

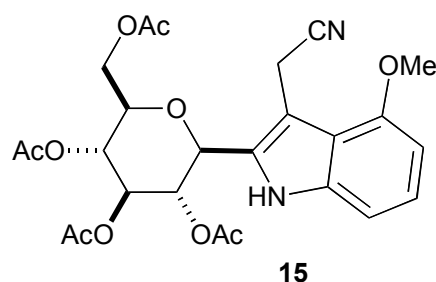
¹³C NMR: (100 MHz, acetone-d₆)

154.2; 137.2; 133.1; 122.7; 119.2; 118.0; 104.7; 102.2; 99.5; 80.7; 78.4; 74.5; 70.2; 61.8; 54.7; 13.9.

HRMS (ESI): calculated for C₁₇H₂₀N₂NaO₆ 371.1219 found 371.1248 (M+Na)⁺

[α]_D²⁵: +16.8° (c 0.002, H₃COH)

IR: 3350 cm⁻¹, 2922, 2851, 2253, 1713, 1595, 1559.



A mixture of **1** (5 mg, .01 mmol) pyridine (1.0 mL) and acetic acid (1.0 mL) was stirred at room temperature overnight and was concentrated *in vacuo*. The residue was loaded directly onto a silica gel column with benzene (1.0 mL). Elution with 2:1-1.5:1 hexanes/ethyl acetate provided **15** as a slightly yellow oil (~5 mg, 95%).

See spectra on page S31, S32, S33

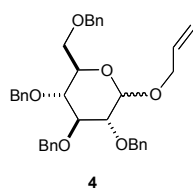
¹H NMR: (400 MHz, CDCl₃)

8.37 (s, 1H); 7.06 (dd, *J*=8.4, 7.6 Hz, 1H); 6.90 (d, *J*=8.0 Hz, 1H); 6.46 (d, *J*=8.0 Hz, 1H); 5.31 (t, dd, *J*=9.6, 8.8 Hz, 1H); 5.23 (dd, *J*=10.0, 9.2 Hz, 1H); 5.15 (dd, *J*=10.4, 9.2 Hz, 1H); 4.73 (d, *J*=10.4 Hz, 1H); 4.27 (dd, *J*=12.8, 5.6, 1H); 4.08 (d, *J*=12.4 Hz, 1H); 4.00 (d, *J*=17.2 Hz, 1H); 3.87 (s, 3H); 3.88-3.85 (m, 2H); 2.02 (s, 3H); 2.00 (s, 3H); 1.94 (s, 3H); 1.86 (s, 3H).

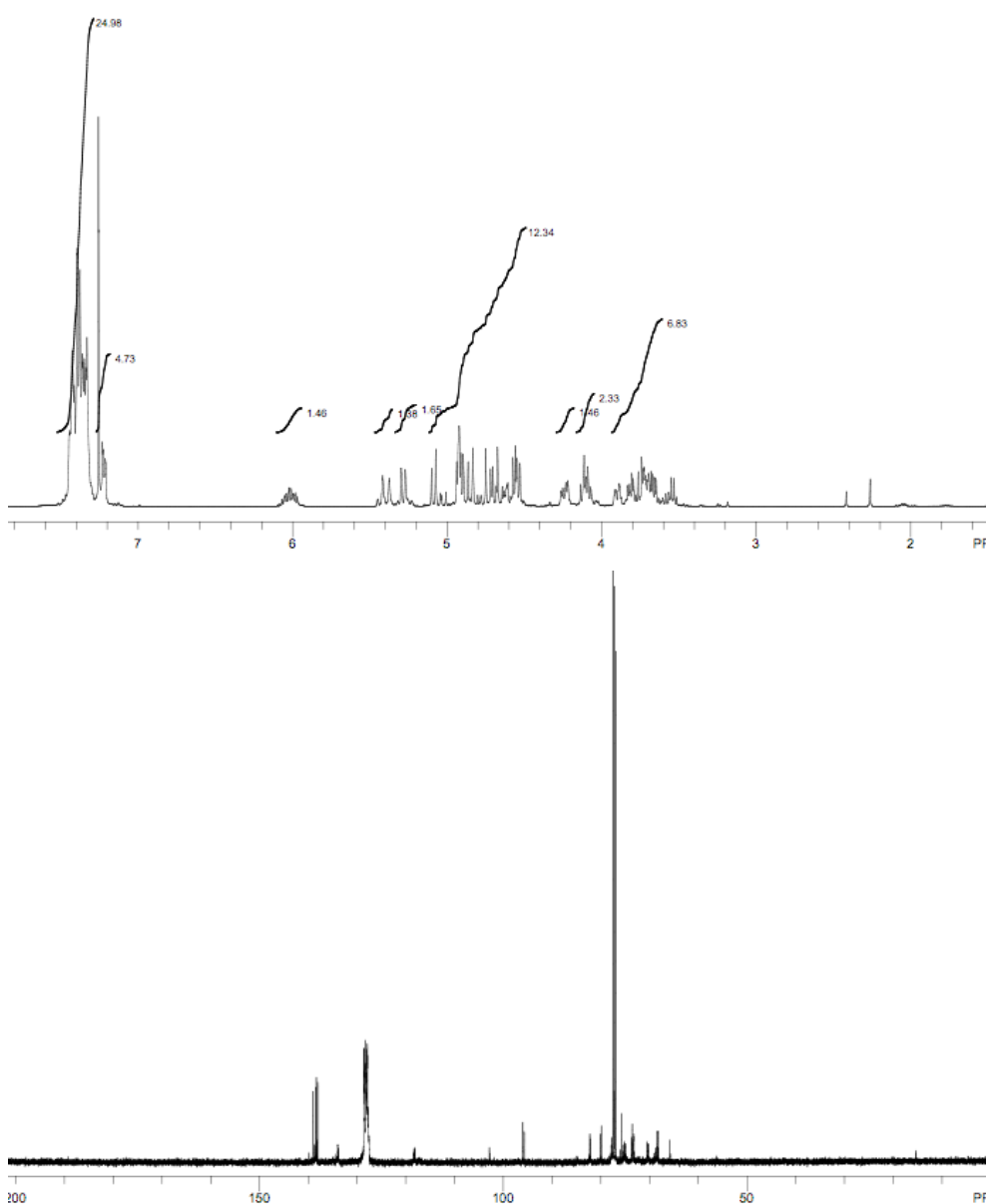
¹³C NMR: (100 MHz, CDCl₃)

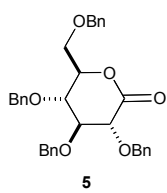
170.6; 170.2; 169.5; 169.3; 154.3; 137.0; 128.0; 124.5; 118.6; 116.7; 104.7; 104.3; 100.4; 74.0; 72.0; 71.1; 68.2; 62.2; 55.3; 55.2; 29.7; 20.7; 20.6; 20.5; 14.4.

HRMS (ESI): calculated for C₂₅H₂₈N₂NaO₁₀ 539.1642 found 539.1742 (M+Na)⁺

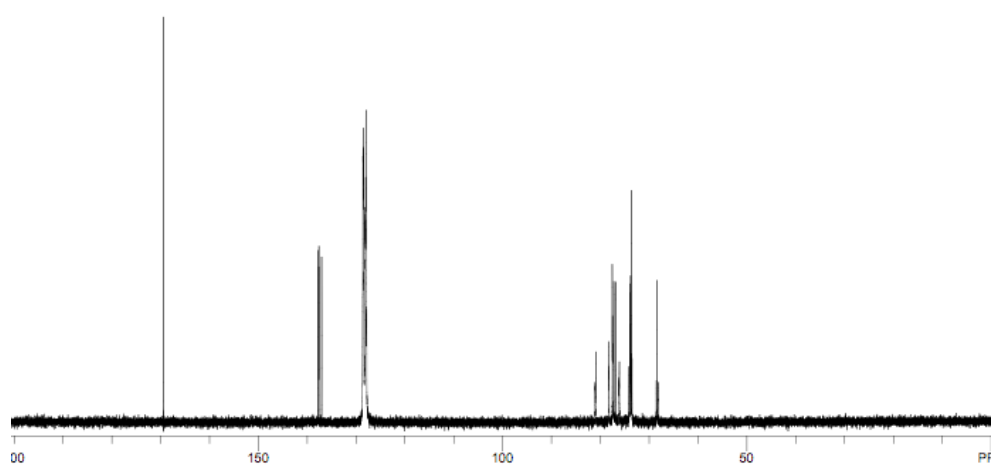
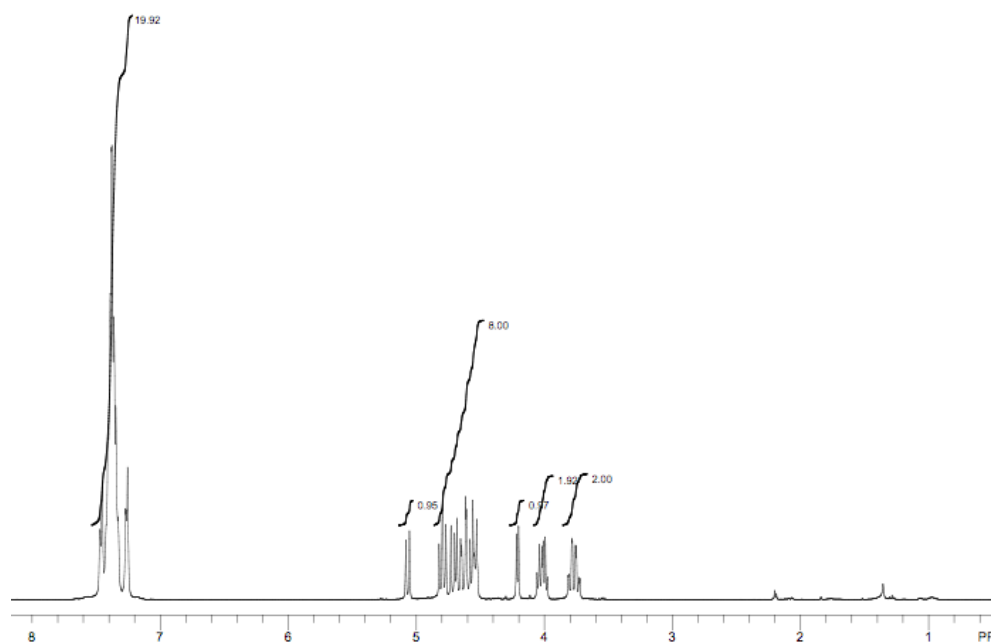


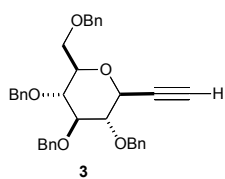
¹H (400 MHz) and ¹³C NMR (100 MHz) spectra (CDCl₃)



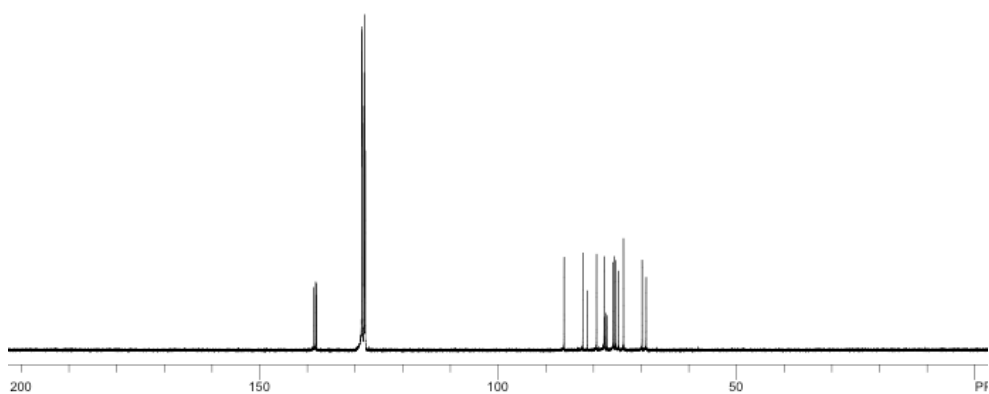
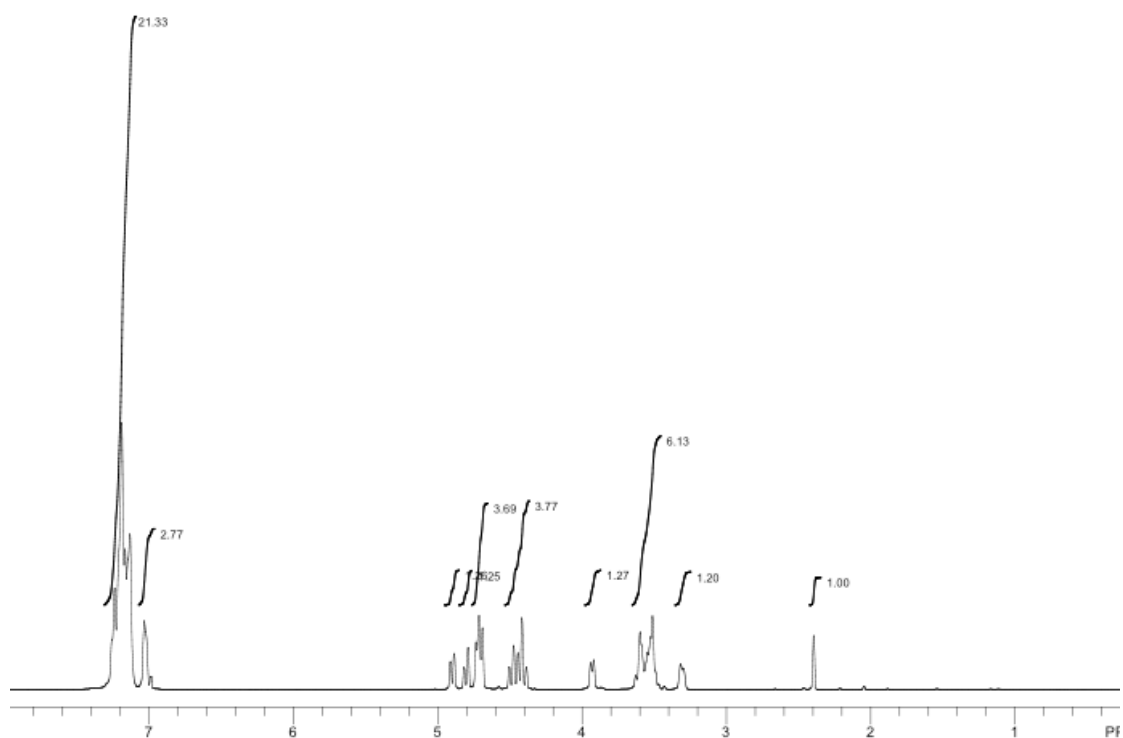


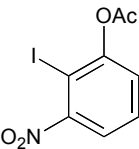
¹H (400 MHz) and ¹³C NMR (100 MHz) spectra (CDCl₃)



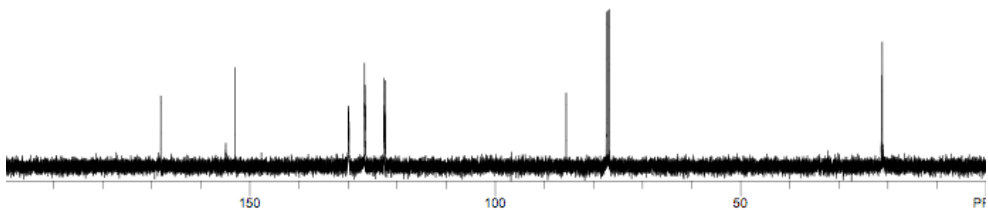
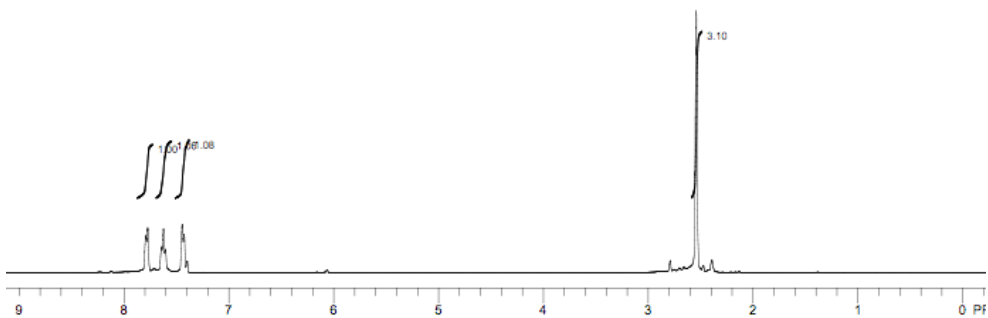


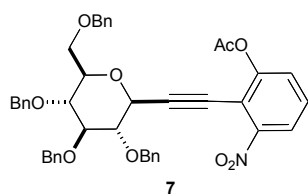
^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra (CDCl_3)



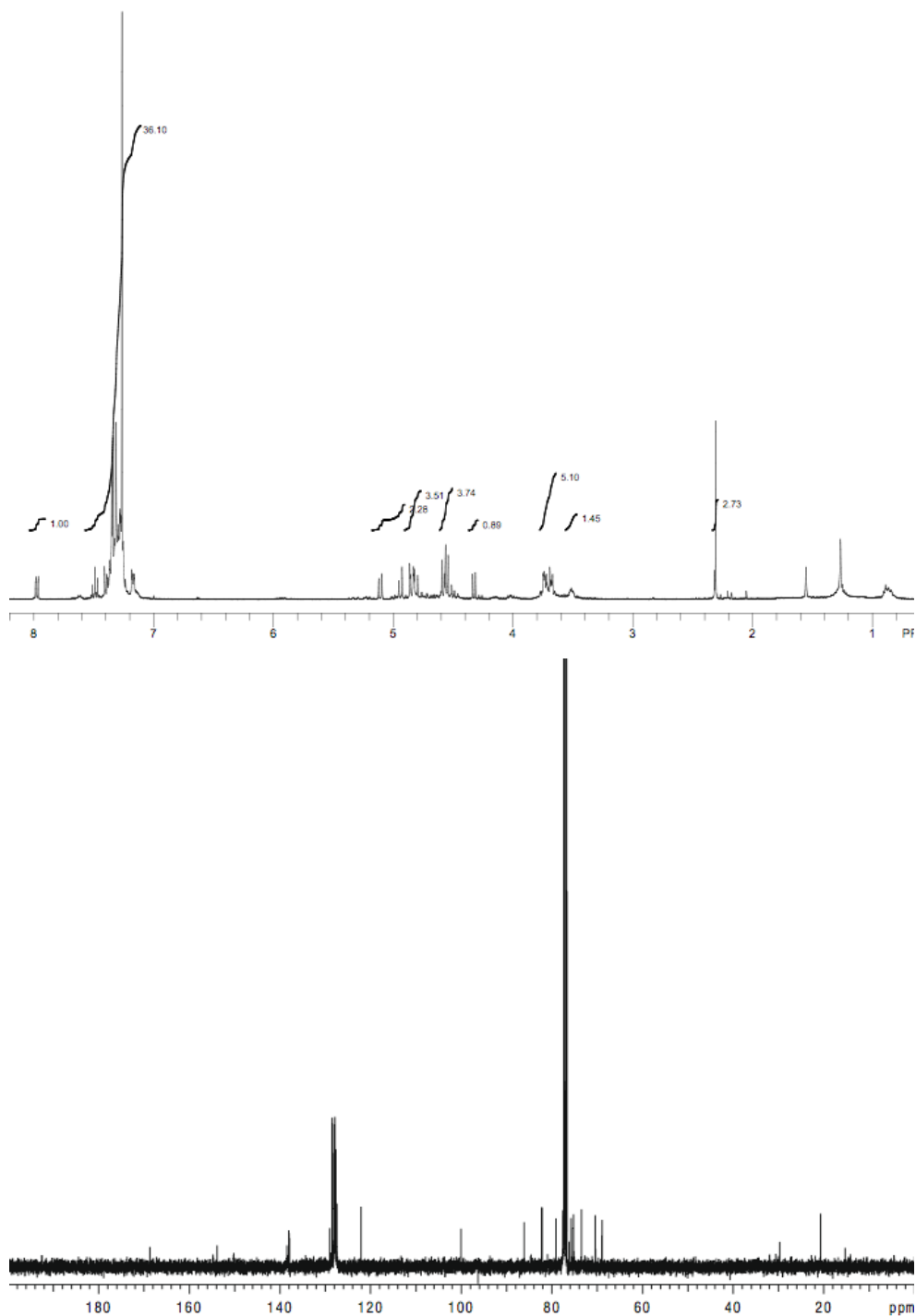


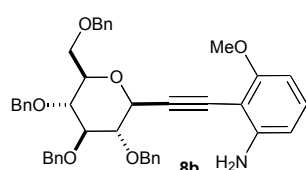
6c ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra (CDCl_3)



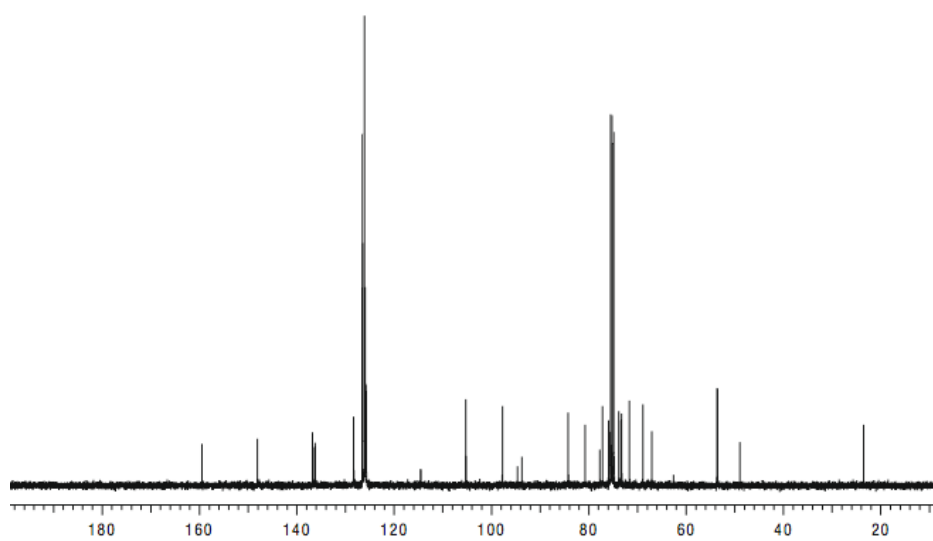
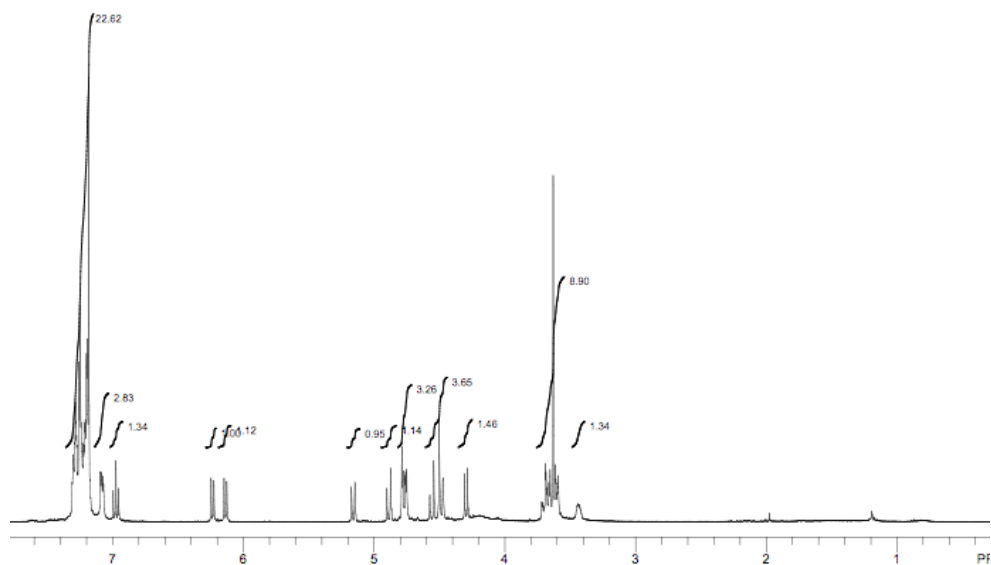


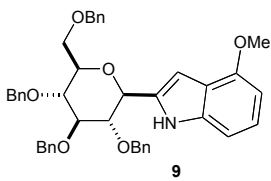
7 ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra (CDCl_3)



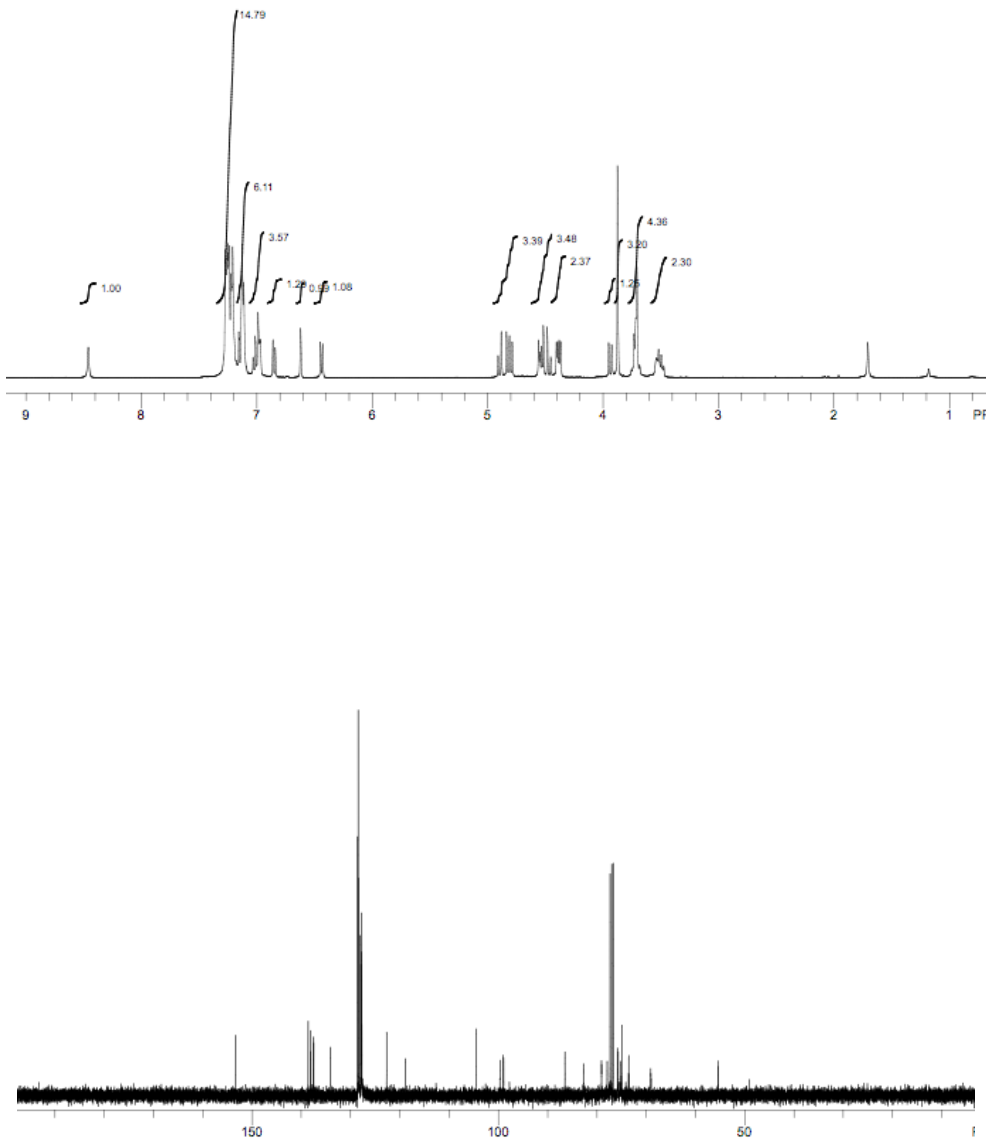


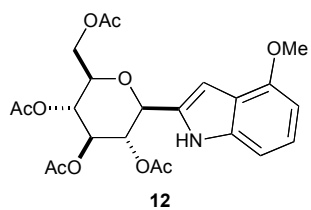
^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra (CDCl_3)



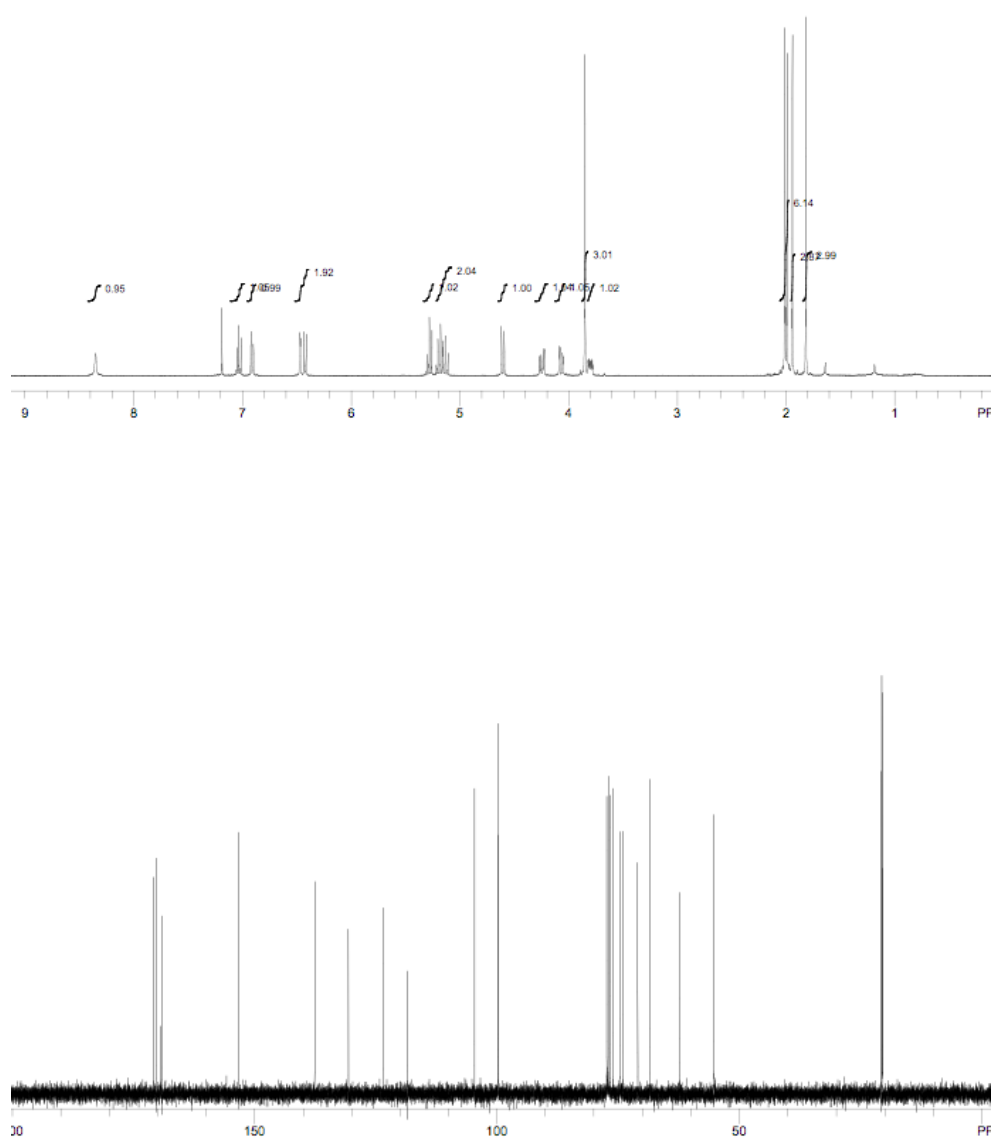


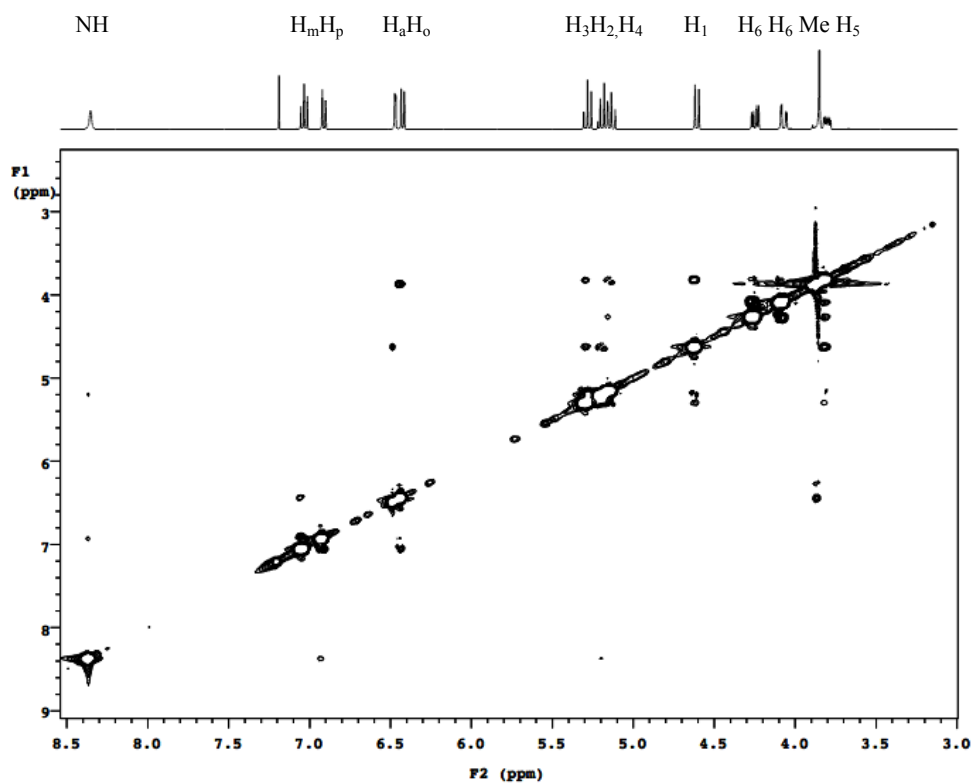
^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra (CDCl_3)



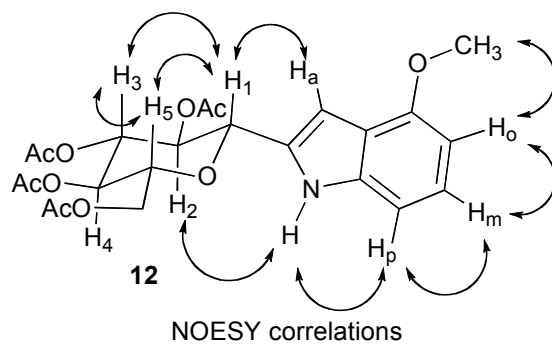


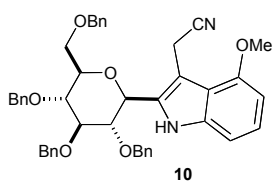
¹H (400 MHz) and ¹³C NMR (100 MHz) spectra (CDCl₃)



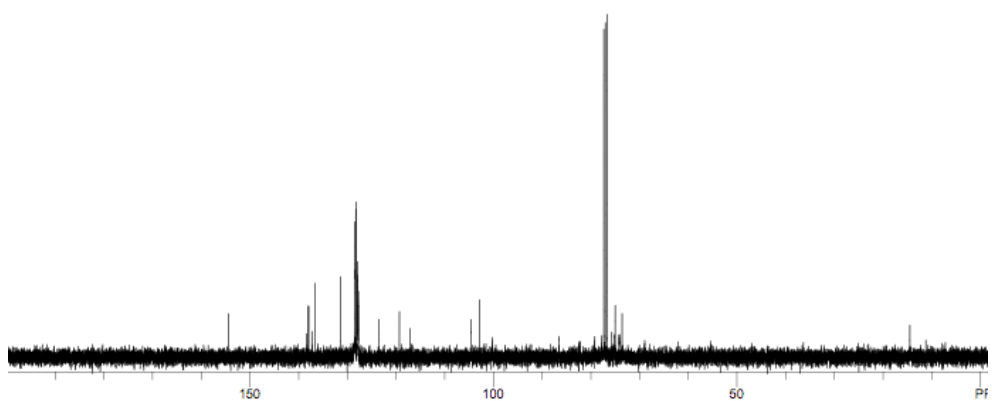
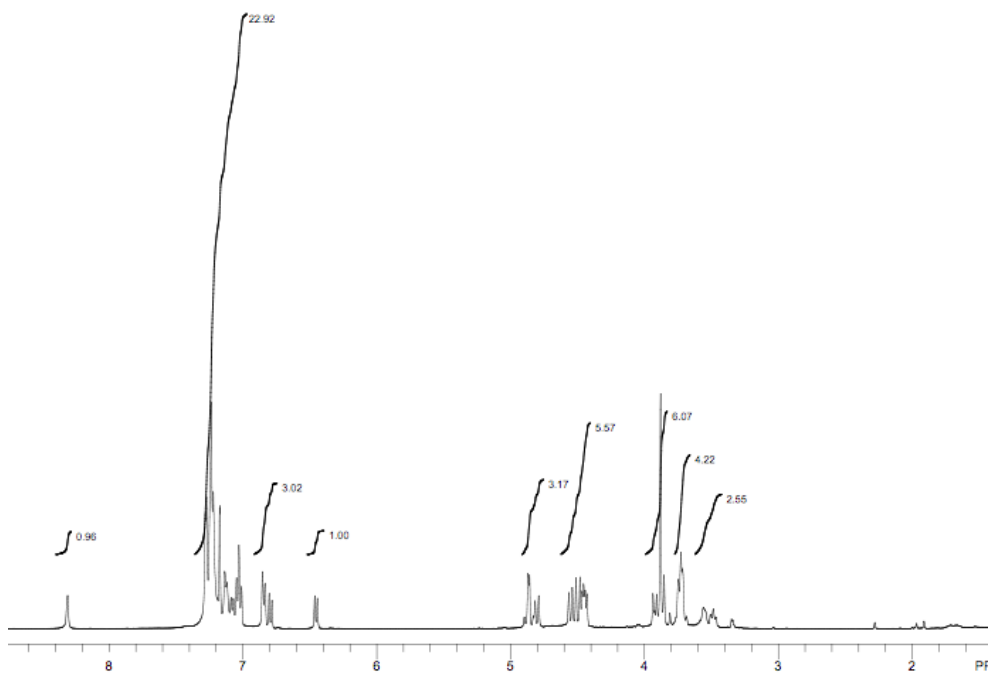


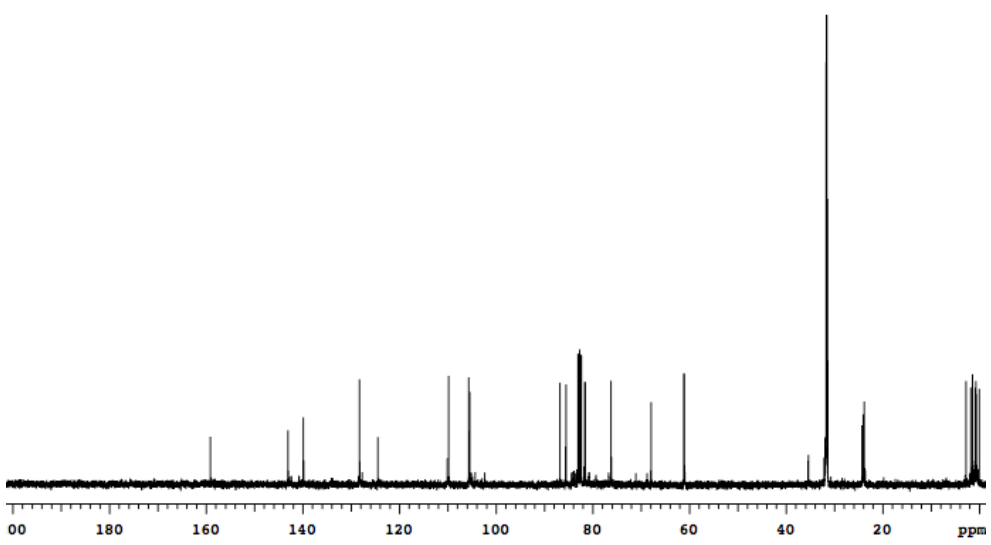
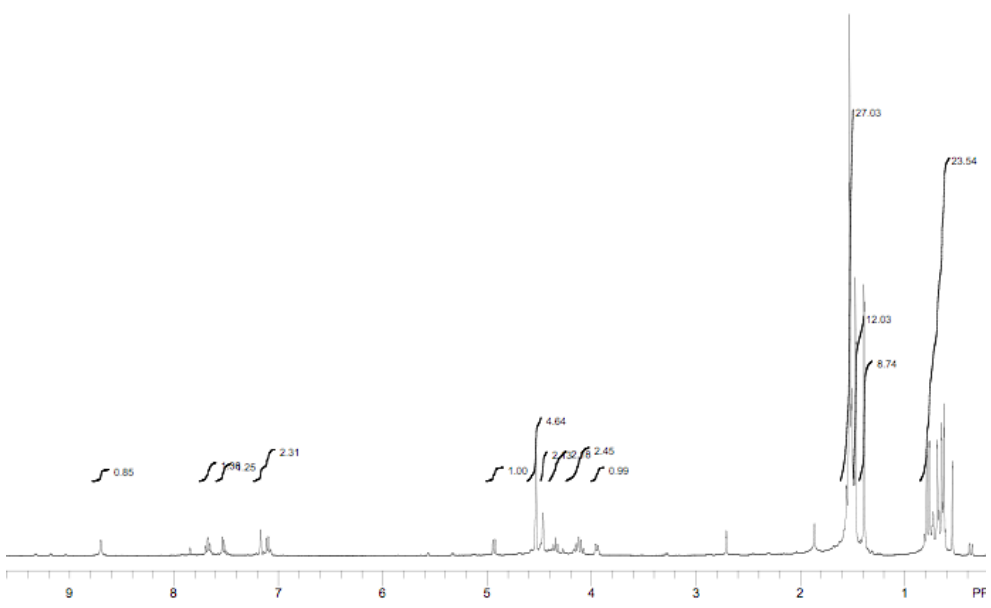
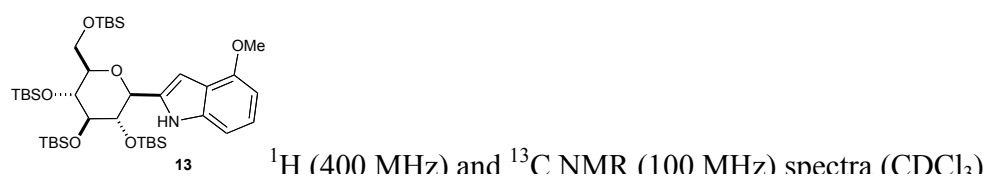
NOESY spectrum of **12** (CDCl_3)

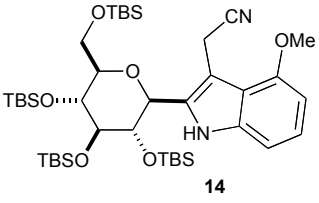




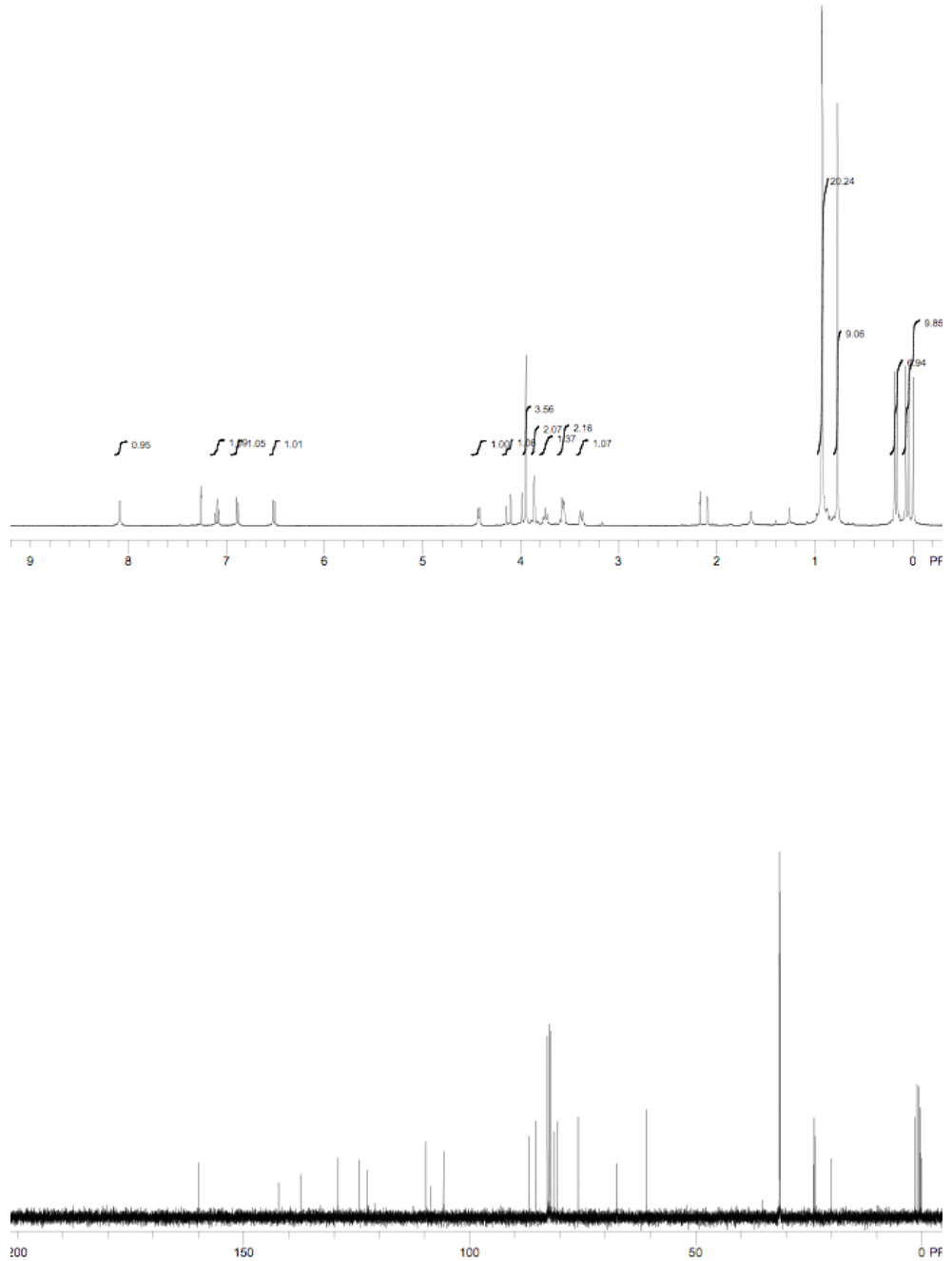
^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra (CDCl_3)

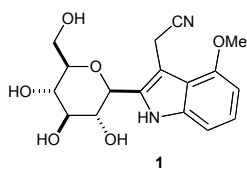




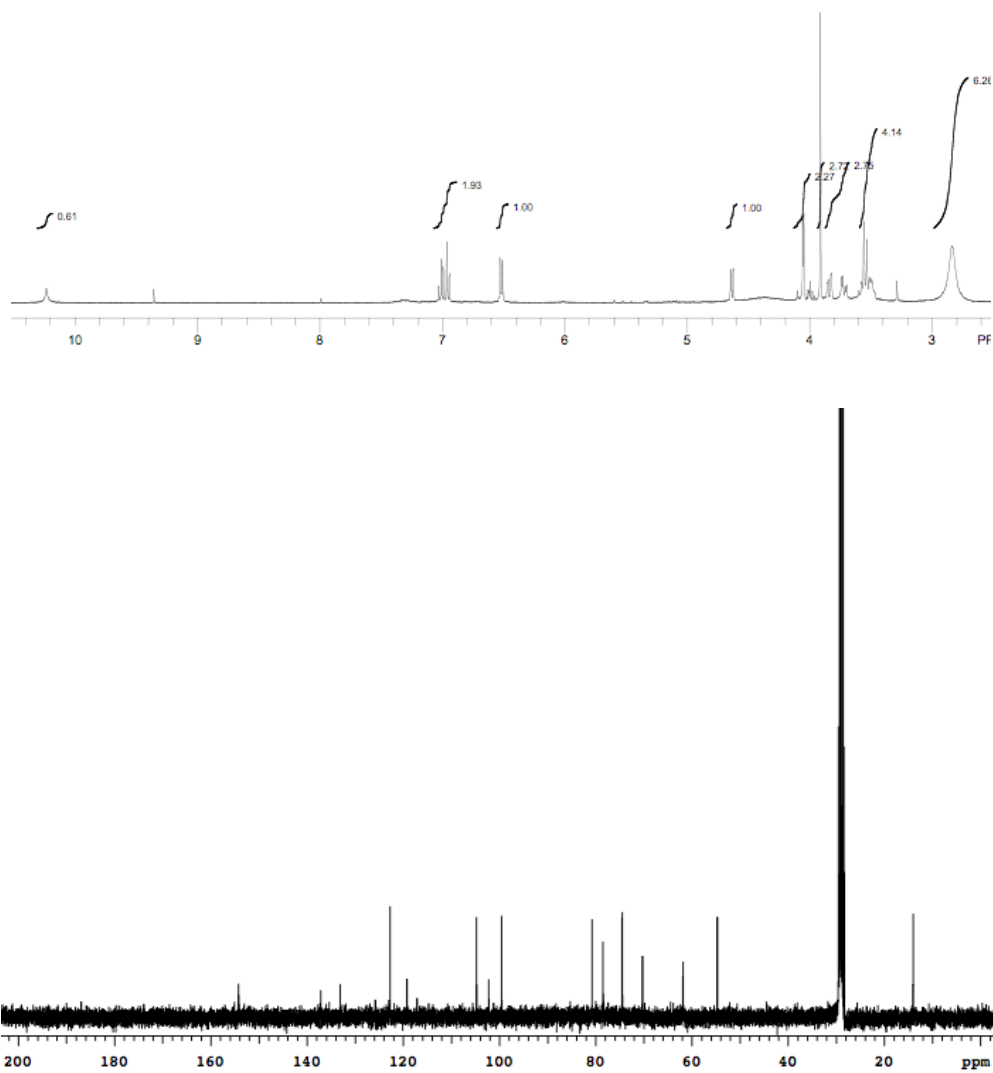


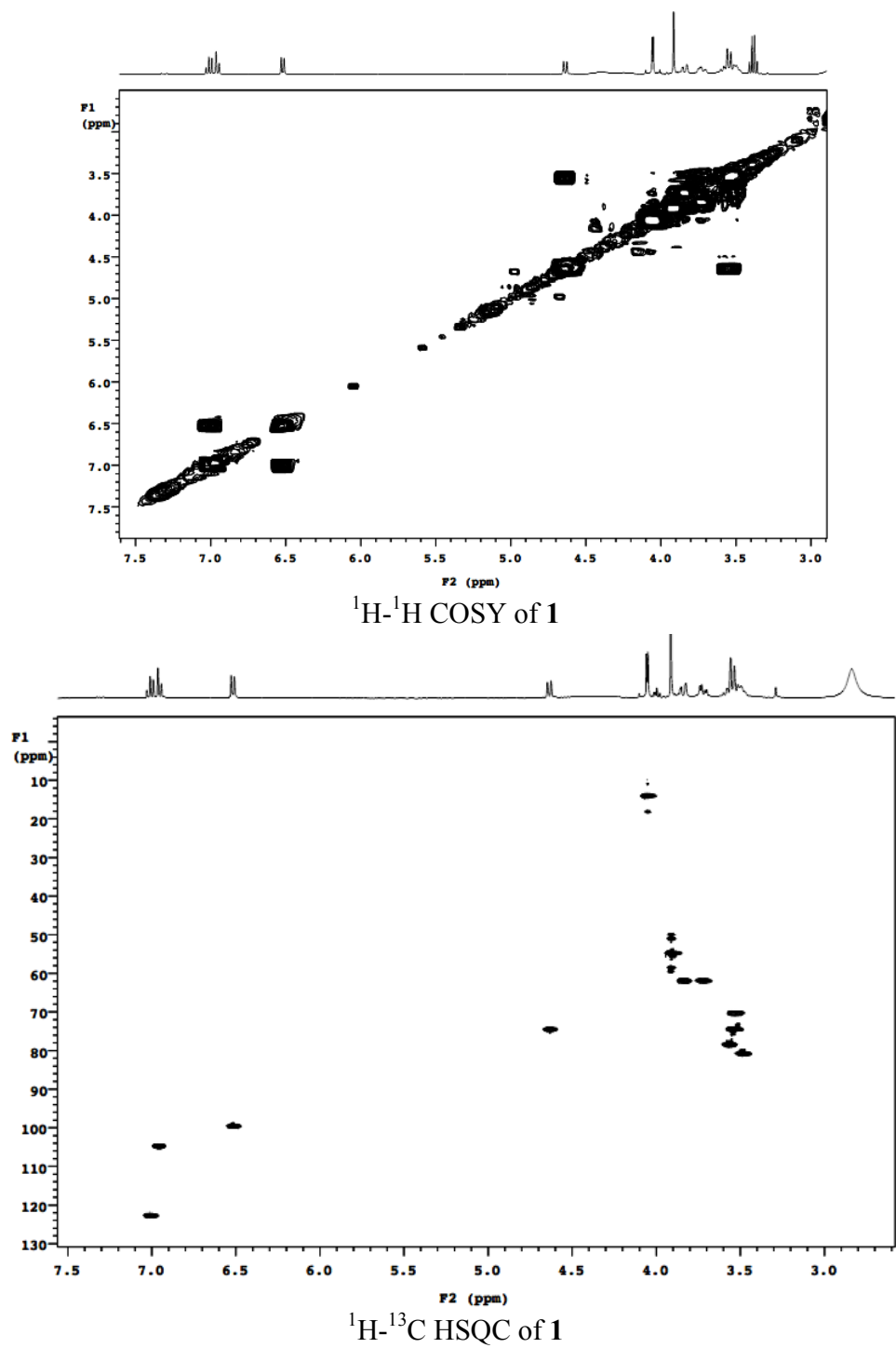
¹H (400 MHz) and ¹³C NMR (100 MHz) spectra (CDCl₃)

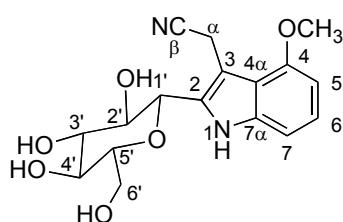
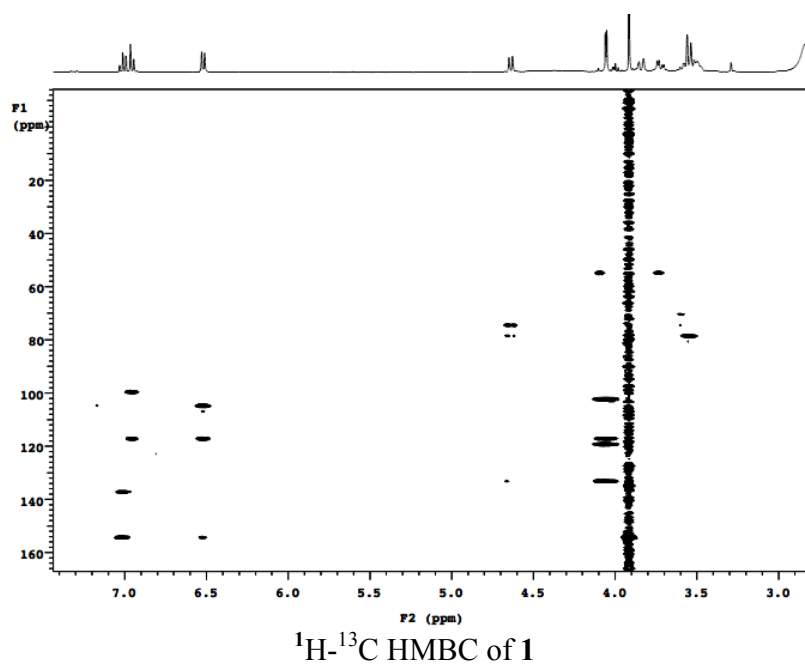




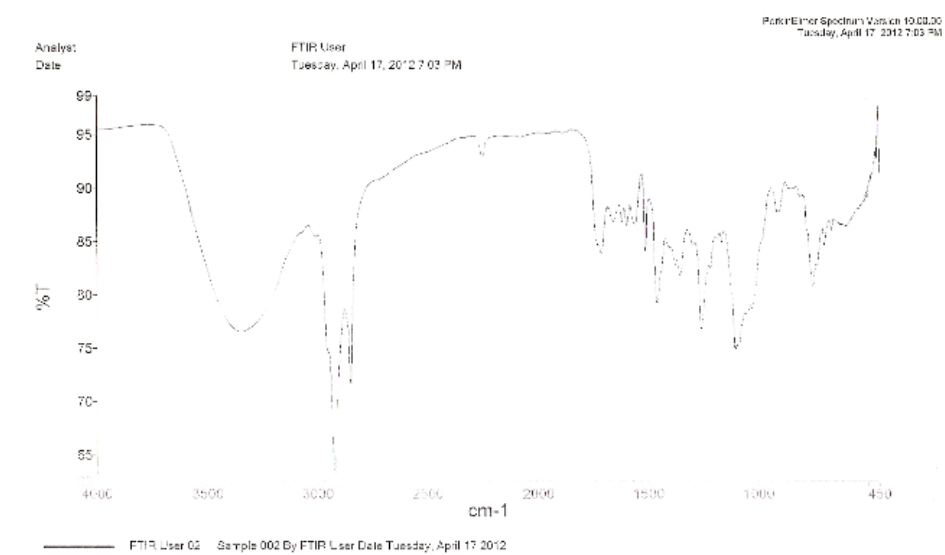
¹H (400 MHz) and ¹³C NMR (100 MHz) spectra (acetone-d₆)





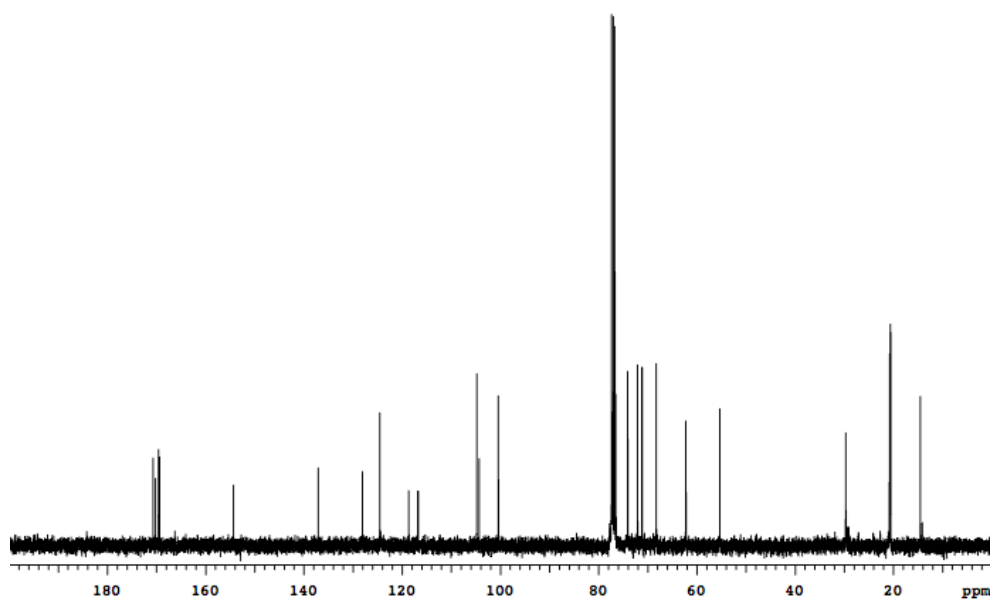
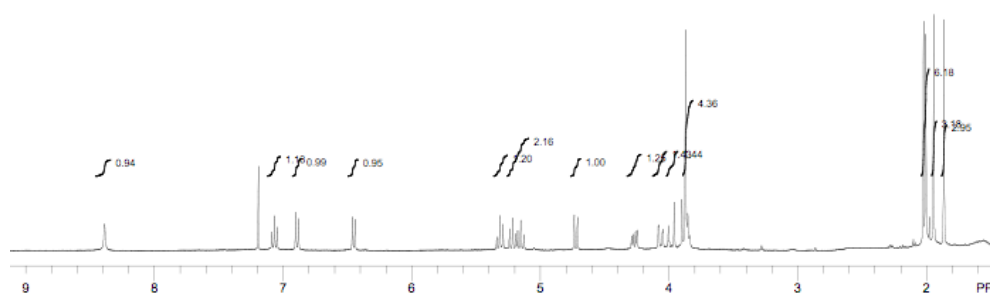
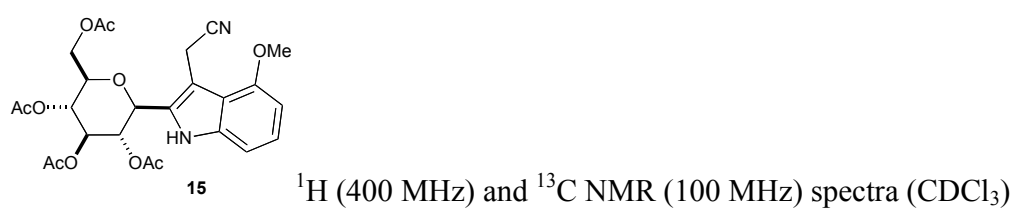


Position	1 natural		1 synthetic	
	δ_{C}	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)
1		11.26 (s)		10.23 (s)
2	121.8		133.1	
3	110.8		102.2	
4	153.2		154.2	
4 α	116.0		118.0	
5	99.7	6.54 (d, 7.8)	99.5	6.52 (d, 7.6)
6	123.9	7.09 (dd, 8.2, 7.8)	122.7	7.01 (dd, 8.0, 7.6)
7	104.7	6.95 (d, 8.2)	104.7	6.94 (d, 8.4)
7 α	137.9		137.2	
α	14.9	4.10 (s)	13.9	4.05 (s)
β	119.5		119.2	
1'	87.5	4.33 (d, 9.1)	74.5	4.64 (d, 8.8)
2'	72.2	2.76 (m)	74.5	3.60-3.49 (m)
3'	77.8	3.13 (m)	78.4	3.60-3.49 (m)
4'	69.5	2.96 (m)	70.2	3.60-3.49 (m)
5'	81.0	3.13 (m)	80.7	3.60-3.49 (m)
6'	61.0	3.67 (m)	61.8	3.85 (d, 13.3)
		3.43 (m)		3.73 (dd, 12.0, 4.0)
OCH ₃	69.6	3.88 (s)	54.7	3.91 (s)

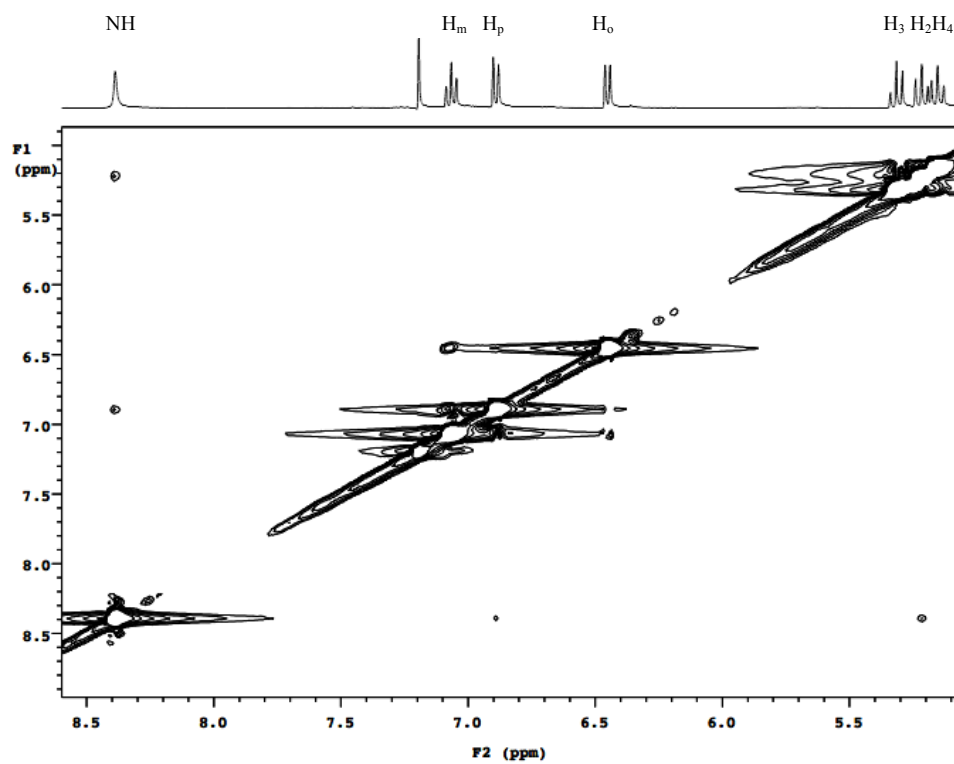
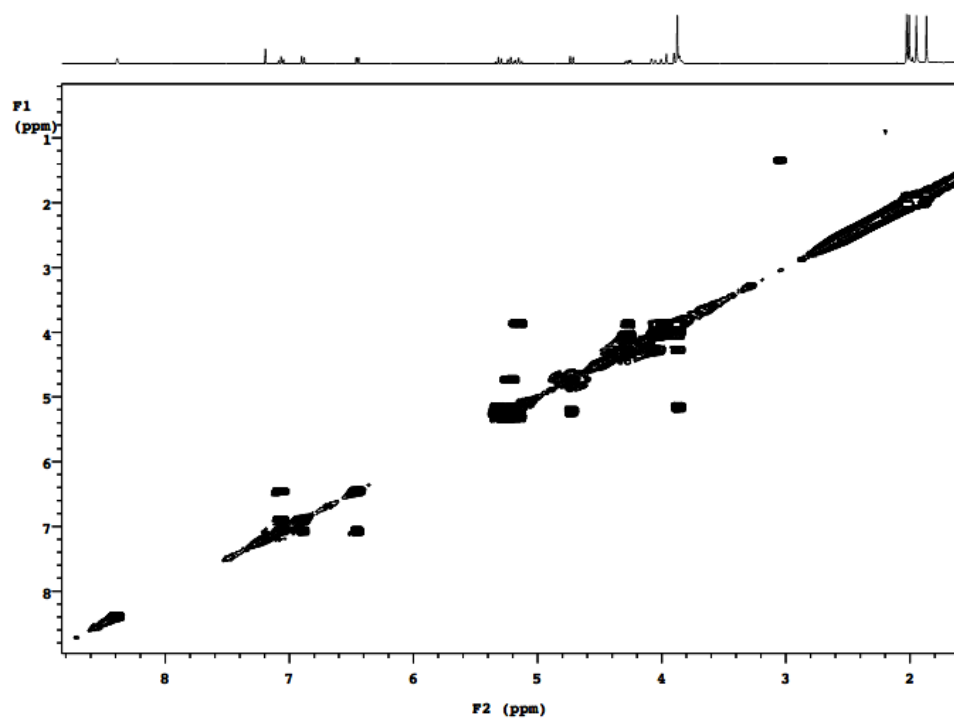


Page 1

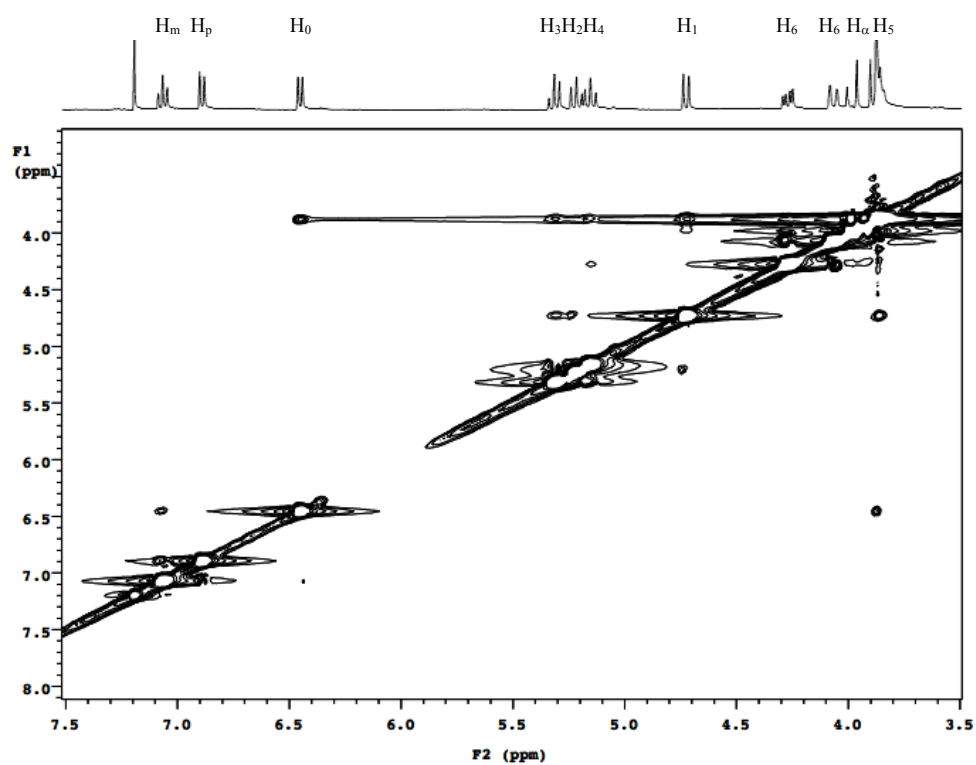
IR spectrum of synthetic **1**



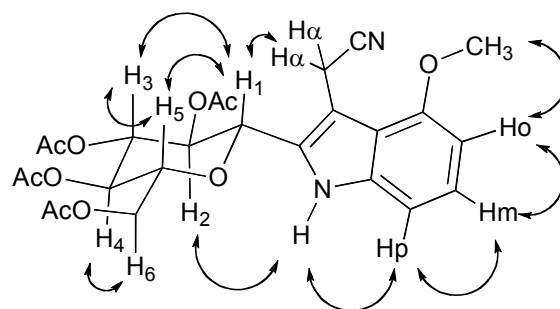
^1H - ^1H COSY of **15**



^1H - ^1H NOESY of **15**, region 5.0-8.5ppm



^1H - ^1H NOESY of **15**, region 3.4-7.5 ppm



15
NOESY correlations