

SUPPORTING INFORMATION

Title: Total Synthesis of L-(+)-Swainsonine and Other Indolizidine Azasugars from D-Glucose

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Ref. No.: O200800649

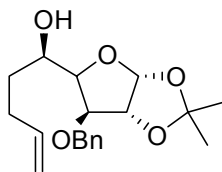
General Methods and Materials:

General: The ^1H NMR, COSY and NOE were recorded on JEOL-JNM 400 MHz and 500 MHz spectrometer. ^{13}C spectra were reported in 100 and 125 MHz spectrometer. The chemical shift values are reported in ppm using CDCl_3 as internal reference. Chemical shifts are reported in ppm downfield to tetramethyl silane. Coupling constants are reported and expressed in Hz; splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublet), q (quartet), dt (double triplet), ddd (doublet of a doublet of a doublet), m (multiplet). All reactions were carried out using freshly distilled and dry solvents. The visualization of spots on TLC plates was effected by exposure to iodine or spraying with 10% H_2SO_4 and charring. Column chromatography was performed over silica gel (100- 200 Mesh) using hexane and ethyl acetate as eluent. Rotation values were recorded on Autopol II automatic polarimeter at the wavelength of sodium D-line (589 nm) at 25 °C. Infrared spectra were recorded on Bruker Vector 22 FT-IR spectrometer and the absorption bands are reported in reciprocal centimeters (cm^{-1}). Mass spectra were obtained from high resolution ESI mass spectrometer WATERS-HAB213.

General Procedure for inhibition assay: The enzymes and all the corresponding substrate were purchased from Sigma Aldrich Chemical Co. Inhibition studies of the bicyclic aza sugars **32**, **33**, **54** and **55** were determined by measuring the residual hydrolytic activities of the glycosidases. The substrate concentration (3 mM) were prepared in 0.025 M citrate buffer with pH 4.0, and test compounds were preincubated with the enzymes for 1 h at 37 °C. The enzyme reaction was initiated by the addition of 100 μL substrate and the controls were run simultaneously in the absence of the test compound. The reaction was terminated at the end of the 10 min by the addition of 0.05 M borate buffer (pH 9.8) and the absorbance of the liberated *p*-nitrophenol was measured at 405 nm using Shimadzu spectrophotometer UV-160A. One unit of glycosidase activity is defined as the amount of enzyme that hydrolyzed 1 μM of *p*-nitrophenyl pyranoside per min at 25 °C.¹

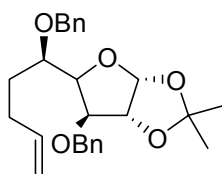
1. Y.-T. Li, S.C. Li. In *Methods in Enzymology*; Victor Ginsberg, Ed Academic, **1972**, 702.

1(1R)-1-((3aR,6S,6aR)-6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)pent-4-en-1-ol (17):



A procedure similar to that described for the synthesis of **5** was employed (4.34 g, 95%). $[\alpha]_D^{25} + 1.5$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 3410, 3066, 3031, 2984, 2931, 1640, 1497, 1454, 1382, 1311, 1217, 1092, 1023, 911, 739, 699. ^1H NMR (400 MHz, CDCl_3): δ 7.29 (m, 5 H), 5.99 (d, $J = 3.9$ Hz, 1 H), 5.74 (m, 1 H), 4.93 (m, 2 H), 4.66 (d, $J = 11.7$ Hz, 1 H), 4.56 (d, $J = 3.6$ Hz, 1 H), 4.25 (d, $J = 11.7$ Hz, 1 H), 4.41 (d, $J = 3.1$ Hz, 1 H), 4.00 (d, $J = 3.1$ Hz, 1 H), 3.88 (m, 2 H), 2.20 (m, 1 H), 2.07 (m, 1 H), 1.66 (m, 2 H), 1.41 (s, 3 H), 1.25 (s, 3 H). ^{13}C NMR (100 MHz): δ 138.3, 136.8, 128.7, 128.4, 128.0, 114.7, 111.6, 105.0, 82.0, 81.8, 71.8, 69.0, 33.4, 29.7, 26.7, 26.2. HMRS (ESI): calcd. for $\text{C}_{19}\text{H}_{26}\text{O}_5$ $[\text{M}+\text{H}]^+$ 335.1858, found 335.1821

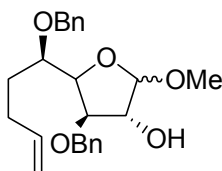
(3aR,6S,6aR)-6-(Benzyloxy)-5-((R)-1-(benzyloxy)pent-4-enyl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole (18):



A procedure similar to that described for the synthesis of **6** was employed (4.92g, 97% yield): $[\alpha]_D^{25} = -6.7$ ($c = 0.7$ CH_2Cl_2). IR (thin film, cm^{-1}): 3064, 3031, 2987, 2929, 1861, 1640, 1496, 1453, 1373, 1310, 1255, 1215, 1165, 1076, 1027, 911, 858, 736, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.33-7.24 (m, 10 H), 5.90 (d, $J = 3.6$ Hz, 1 H), 5.87 (m, 1 H), 5.03 (dd, $J = 1.7, 17.3$ Hz, 1 H), 4.94 (dd, $J = 1.7, 10.0$ Hz, 1 H), 4.65 (d, $J = 11.4$ Hz, 1 H), 4.62 (d, $J = 3.9$ Hz, 1 H), 4.57 (d, $J = 11.2$ Hz, 1 H), 4.49 (d, $J = 11.6$ Hz, 1 H), 4.42 (d, $J = 11.2$ Hz, 1 H), 4.15 (dd, $J = 2.9, 9.0$ Hz, 1 H), 4.09 (d, $J = 2.9$

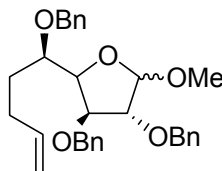
Hz, 1 H), 3.93 (m, 1 H), 2.24 (m, 2 H), 1.92 (m, 1 H), 1.79 (m, 1 H), 1.48 (s, 3 H), 1.31 (s, 3 H). ^{13}C NMR (100 MHz): δ 138.8, 137.6, 128.4, 128.3, 127.8, 127.5, 127.4, 114.3, 111.6, 104.9, 81.8, 81.1, 75.1, 71.8, 30.6, 28.5, 26.8, 26.3. HRMS (ESI): calcd. for $\text{C}_{26}\text{H}_{32}\text{O}_5$ $[\text{M}+\text{H}]^+$ 425.2328, found 425.2315.

(3R,4R)-4-(Benzyloxy)-5-((R)-1-(benzyloxy)pent-4-enyl)-2-methoxytetrahydrofuran-3-ol (19):



A procedure similar to that described for the synthesis of **7** was employed (4.22 g, 98% yield). $[\alpha]_{\text{D}}^{25} = -1.5$ ($c = 0.50$, CH_2Cl_2). IR (thin film, cm^{-1}): 3428, 3064, 3030, 2924, 1741, 1640, 1453, 1396, 1208, 1109, 1027, 931, 809, 736, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.24 (m, 10 H), 5.83 (m, 1 H), 5.05-4.99 (m, 2 H), 4.93 (m, 1 H), 4.70 (d, $J = 11.7$ Hz, 1 H), 4.52 (d, $J = 12.2$ Hz, 1 H), 4.46 (m, 2 H), 4.24 (m, 1 H), 4.18 (dd, $J = 4.6, 7.6$ Hz, 2 H), 4.03 (dd, $J = 1.9, 4.3$ Hz, 1 H), 3.86 (dd, $J = 3.6, 7.3$ Hz, 1 H), 3.46 (s, 3 H), 2.98 (m, 1 H), 2.22 (m, 2 H), 1.86 (m, 1 H), 1.74 (m, 1 H). ^{13}C NMR (100 MHz): δ 138.8, 138.6, 137.5, 130.4, 128.4, 128.3, 127.9, 127.8, 127.5, 127.4, 127.4, 127.0, 126.8, 126.3, 114.3, 111.5, 108.4, 104.8, 81.9, 81.8, 81.0, 75.0, 72.8, 71.8, 71.7, 48.8, 30.6, 29.6, 28.4, 27.7, 26.2. HRMS (ESI): calcd. for $\text{C}_{24}\text{H}_{30}\text{O}_5$ $[\text{M}+\text{H}]^+$ 399.2179, found 399.2159.

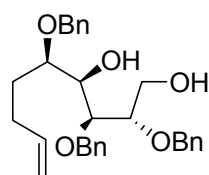
(3S,4R)-3,4-Bis(benzyloxy)-2-((R)-1-(benzyloxy)pent-4-enyl)-5-methoxytetrahydrofuran (20):



A procedure similar to that described for the synthesis of **8** was employed (4.65 g, 95% yield). $[\alpha]_{\text{D}}^{25} = +30$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 3064, 3030, 2923, 1496, 1453, 1357, 1205, 1191, 1098, 1050, 735, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.58-78.15 (m, 15 H), 5.82 (m, 1 H),

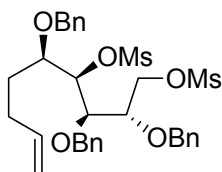
5.15 (dd, $J = 10.2, 18.8$ Hz, 1 H), 4.98 (d, $J = 17.0$ Hz, 1 H), 4.91 (m, 2 H), 4.65 (d, $J = 11.9$ Hz, 1 H), 4.58-4.45 (m, 4 H), 4.29 (t, 1 H), 4.24 (t, $J = 4.1$ Hz, 1 H), 3.79 (t, $J = 4.1$ Hz, 1 H), 3.79 (d, $J = 3.4$ Hz, 1 H), 3.41 (s, 3 H), 2.19 (m, 2 H), 1.78 (m, 2 H). ^{13}C NMR (100 MHz): δ 143.5, 141.1, 139.0, 138.7, 138.0, 137.6, 129.8, 129.4, 128.0, 127.8, 127.5, 127.3, 127.1, 114.3, 101.0, 83.8, 82.1, 76.6, 76.2, 72.6, 72.1, 71.5, 59.2, 55.3, 29.8, 29.0. HRMS (ESI): calcd. for $\text{C}_{31}\text{H}_{36}\text{O}_5$ $[\text{M}+\text{H}]^+$ 489.2641, found 489.2635.

(2S,3S,4R,5R)-2,3,5-Tris(benzyloxy)non-8-ene-1,4-diol (21):



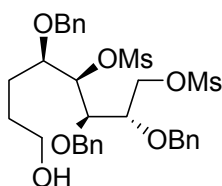
A procedure similar to that described for the synthesis of **9** was employed (2.90 g, 88% yield) as a viscous liquid. $[\alpha]_D^{25} = +2.87$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 3435, 3063, 3030, 2924, 2868, 1639, 1495, 1453, 1395, 1207, 1098, 1068, 911, 735, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.29 (m, 15 H) 5.83 (m, 1 H), 5.03 (m, 2 H), 4.57 (m, 4 H), 4.42 (d, $J = 11.4$, 1 H), 4.29 (d, $J = 11.4$ Hz, 1 H), 3.90 (d, $J = 5.6$ Hz, 1 H), 3.79 (br s, 3 H), 3.62 (m, 1 H), 3.49 (m, 1 H), 2.81 (m, 1 H), 2.63 (m, 1 H), 2.19 (m, 1 H), 1.82 (m, 2 H), 1.25 (br s, 1 H). ^{13}C NMR (100 MHz): δ 138.6, 138.4, 137.9, 137.7, 128.4, 128.3, 127.9, 127.9, 128.8, 127.6, 127.5, 114.5, 78.7, 77.9, 75.3, 73.5, 72.0, 71.1, 69.7, 60.5, 28.9, 28.5. HRMS (ESI): calcd. for $\text{C}_{30}\text{H}_{36}\text{O}_5$ $[\text{M}+\text{H}]^+$ 477.2641, found 477.2638.

(2S,3R,4R,5R)-2,3,5-Tris(benzyloxy)non-8-ene-1,4-diyl dimethanesulfonate (22):



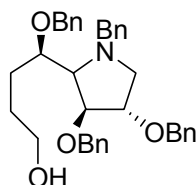
A procedure similar to that described for the synthesis of **10** was employed (3.30 g, 96% yield). $[\alpha]_D^{25} = +2.3$ ($c = 0.3$, CH_2Cl_2). IR (thin film, cm^{-1}): 3088, 3063, 3031, 2934, 2873, 1817, 1496, 1454, 1353, 1210, 1173, 1065, 936, 823, 742, 700. ^1H NMR (400 MHz, CDCl_3): δ 7.29 (m, 15 H), 5.70 (m, 1 H), 5.20 (dd, $J = 2.2, 5.1$ Hz, 1 H), 4.64 (m, 2 H), 4.82 (d, $J = 11.2$ Hz, 1 H), 4.66 (d, $J = 11.4$ Hz, 1 H), 4.60 (d, $J = 10.7$ Hz, 1 H), 4.52 (d, $J = 11.2$, 1 H), 4.47 (d, $J = 11.4$ Hz, 1 H), 4.39 (d, $J = 11.76$ Hz, 1 H), 4.34 (d, $J = 11.7$ Hz, 1 H), 4.31 (d, $J = 11.7$ Hz, 1 H), 3.77 (dd, $J = 4.4, 9.0$ Hz, 1 H), 3.69 (dd, $J = 4.4, 7.3$ Hz, 1 H), 3.61 (d, $J = 9.76$ Hz, 1 H), 3.01 (s, 3 H), 2.92 (s, 3 H), 2.48 (m, 1 H), 1.96 (m, 1 H), 1.70 (m, 1 H), 1.53 (m, 1 H). ^{13}C NMR (100 MHz): δ 138.2, 137.8, 137.5, 137.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 115.6, 82.9, 78.0, 77.6, 76.6, 75.2, 73.3, 72.3, 68.4, 39.4, 37.5, 30.0, 29.4. HRMS (ESI): calcd. for $\text{C}_{39}\text{H}_{40}\text{O}_9\text{S}_2$ $[\text{M}+\text{H}]^+$ 633.2192, found 633.2180.

(2S,3R,4R,5R)-2,3,5-Tris(benzyloxy)-8-hydroxyoctane-1,4-diyl dimethanesulfonate (24):



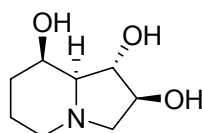
A procedure similar to that described for the synthesis of **11** was employed (1.35 g, 90% yield). $[\alpha]_D^{25} = -35$ ($c = 0.25$, CH_2Cl_2). IR (thin film, cm^{-1}): 3064, 3031, 2936, 1745, 1640, 1496, 1355, 1174, 1069, 938, 825, 747, 699. ^1H NMR (400 MHz, CDCl_3): δ 7.35-7.25 (m, 15 H), 4.92 (t, $J = 4.8$, Hz, 1 H), 4.70 (s, 3 H), 4.67 (d, $J = 6.3$ Hz, 1 H), 4.58 (d, $J = 11.4$ Hz, 1 H), 4.51 (d, $J = 11.72$ Hz, 1 H), 4.44-4.39 (m, 2 H), 4.31 (dd, $J = 4.1, 11.0$, 1 H), 3.95 (t, $J = 5.1$ Hz, 1 H), 3.86 (q, $J = 5.1, 9.0$ Hz, 1 H), 3.70 (q, $J = 5.3, 10.4$ Hz, 1 H), 3.56 (m, 2 H), 2.94 (s, 3 H), 2.91 (s, 3 H), 1.60 (m, 2 H), 1.55-1.46 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 137.2, 128.5, 128.2, 128.1, 128.0, 80.2, 76.4, 75.6, 74.5, 73.1, 71.7, 68.6, 62.3, 38.6, 37.2, 27.8, 25.7. HRMS (ESI): calcd. for $\text{C}_{31}\text{H}_{40}\text{O}_{10}\text{S}_2$ $[\text{M}+\text{H}]^+$ 637.2141, found 637.2121.

(4R)-4-((3S,4S)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)-4-(benzyloxy)butan-1-ol (25):



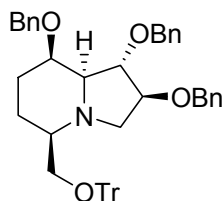
A procedure similar to that described for the synthesis of **14** was employed (1.56 g, 90% yield). $[\alpha]_D^{25} = +5.6$ ($c = 1.2$, CH_2Cl_2). IR (thin film, cm^{-1}): 3391, 3062, 3029, 2924, 1604, 1495, 1453, 1369, 1208, 1091, 1027, 736, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.30 (m, 20 H), 4.93 (d, $J = 12.3$ Hz, 1 H), 4.54–4.40 (m, 5 H), 4.31 (d, $J = 13.4$ Hz, 1 H), 4.08 (d, $J = 4.9$ Hz, 1 H), 3.93 (d, $J = 4.6$ Hz, 1 H), 3.67 (d, $J = 2.4$ Hz, 1 H), 3.57 (d, $J = 5.8$ Hz, 2 H), 3.25 (d, $J = 13.4$ Hz, 1 H), 3.10 (d, $J = 11.2$ Hz, 1 H), 2.81 (dd, $J = 2.6, 5.1$ Hz, 1 H), 2.43 (dd, $J = 5.3, 10.9$ Hz, 1 H), 1.77–1.62 (m, 5 H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.1, 138.7, 138.2, 138.1, 128.4, 128.3, 128.2, 128.1, 127.8, 127.6, 127.5, 127.4, 126.8, 85.0, 81.2, 78.1, 72.5, 72.4, 71.6, 70.7, 62.8, 59.6, 57.5, 29.6, 28.1. HRMS (ESI): calcd. for $\text{C}_{36}\text{H}_{41}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 552.3114, found 552.3108.

(1S,2S,8R,8aS)-Octahydroindolizine-1,2,8-triol (26):



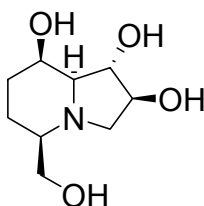
A procedure similar to that described for the synthesis of **2** was employed (149 mg, 78% yield). $[\alpha]_D^{25} = +60.0$ ($c = 1.0$, MeOH). IR (thin film, cm^{-1}): 3430, 2924, 2854, 1635, 1547, 1463, 1382, 1164, 1020. ^1H NMR (400 MHz, 50% CDCl_3 in DMSO): δ 3.85 (br s, 1 H), 3.83 (br s, 1 H), 3.76 (d, $J = 6.3$ Hz, 1 H), 2.85 (d, $J = 9.0$ Hz, 1 H), 2.75 (d, $J = 9.7$ Hz, 1 H), 2.39 (dd, $J = 6.8, 9.5$ Hz, 1 H), 1.90 (m, 1 H), 1.77 (m, 2 H), 1.38–1.17 (m, 3 H). ^{13}C NMR (100 MHz, 50% CDCl_3 in DMSO): δ 78.9, 76.1, 73.6, 62.7, 61.6, 52.7, 31.1, 19.2. HRMS (ESI): calcd. for $\text{C}_8\text{H}_{15}\text{NO}_3$ $[\text{M}+\text{H}]^+$ 174.1130, found 174.1118.

(1S,2S,5S,8R,8aS)-1,2,8-Tris(benzyloxy)-5-(trityloxymethyl)octahydroindolizine (31):



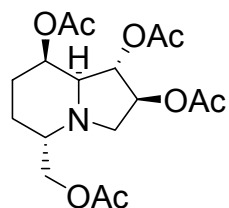
(0.43 g, 38% yield). $[\alpha]_D^{25} + 5.3$ ($c = 0.6$, CH_2Cl_2). IR (thin film, cm^{-1}): 3366, 3060, 3030, 2926, 1600, 1492, 1450, 1359, 1206, 1152, 1089, 1028, 744, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.44-7.11 (m, 30 H), 4.53 (d, $J = 12.4$ Hz, 1 H), 4.50 (d, $J = 11.9$ Hz, 1 H), 4.37-4.28 (m, 3 H), 4.21 (d, $J = 11.2$ Hz, 1 H), 4.08 (dd, $J = 2.6, 9.2$ Hz, 1 H), 3.83 (dd, $J = 2.6, 6.1$ Hz, 1 H), 3.66 (br s, 1 H), 3.28 (dd, $J = 5.4, 9.2$ Hz, 1 H), 3.17 (d, $J = 10.7$ Hz, 1 H), 3.08 (dd, $J = 6.1, 15.6$ Hz, 1 H), 2.34 (dd, $J = 6.8, 10.5$ Hz, 1 H), 2.23 (m, 1 H), 2.10-2.03 (m, 2 H), 1.70 (m, 1H), 1.57 (m, 1 H), 1.28 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3): δ 137.2, 137.0, 125.5, 128.3, 128.1, 127.9, 127.7, 127.5, 126.7, 79.4, 79.3, 76.2, 75.6, 74.4, 73.2, 72.1, 71.1, 68.8, 39.3, 38.6, 37.2, 29.6, 22.0. HRMS (ESI): calcd. for $\text{C}_{49}\text{H}_{49}\text{NO}_4$ $[\text{M}+\text{H}^+]$ 716.3740, found 716.3732.

(1S,2S,5R,8R,8aS)-5-(Hydroxymethyl)octahydroindolizine-1,2,8-triol (33):



$[\alpha]_D^{25} = + 0.82$ ($c = 0.2$ CH_2Cl_2). IR (thin film, cm^{-1}): 3384, 3060, 2933, 1678, 1492, 1453, 1266, 1204, 1057, 738, 700. HRMS (ESI): calcd. for $\text{C}_9\text{H}_{17}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 204.1236, found 204.1222.

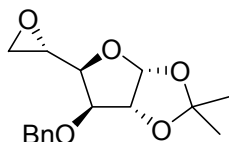
(1S,2S,5S,8R,8aS)-5-(Acetoxymethyl)octahydroindolizine-1,2,8-triyl triacetate (35):



A procedure similar to that described for the synthesis of **34** was employed (25 mg, 97 % yield). $[\alpha]_D^{25} = +0.93$ ($c = 0.3$ CH₂Cl₂). IR (thin film, cm⁻¹): 2960, 2927, 2855, 1739, 1651, 1551, 1428, 1374, 1260, 1104, 1028. ¹H NMR (400 MHz, CDCl₃): δ 5.18 (dd, $J = 3.2, 8.6$ Hz, 1 H), 5.07 (dd, $J = 3.4, 6.3$ Hz, 1 H), 5.01 (d, $J = 2.4$ Hz, 1 H), 4.10 (dt, $J = 6.1, 11.7$ Hz, 2 H), 3.29 (d, $J = 11.4$ Hz, 1 H), 2.72 (dd, $J = 7.3, 11.4$ Hz, 1 H) 2.34-2.28 (m, 2 H), 2.17 (s, 3 H), 2.10 (s, 3 H), 2.08-2.09 (m, 1 H), 2.07 (s, 3 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 1.63-1.53 (m, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 170.9, 170.8, 170.6, 170.0, 76.2, 75.7, 68.9, 66.7, 65.0, 61.6, 58.0, 27.6, 23.2, 21.2, 21.0, 20.9, 20.7. HRMS (ESI): calcd. for C₁₇H₂₅NO₇ [M+H]⁺ 372.1658, found 372.1657.

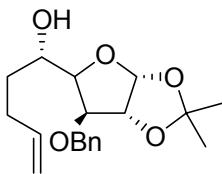
(3aR,5R,6S,6aR)-6-(Benzyloxy)-2,2-dimethyl-5-((S)-oxiran-2-yl)tetrahydrofuro[2,3-d]

[1,3]dioxole (37):



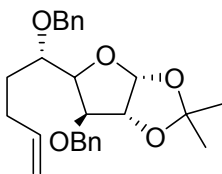
A procedure similar to that described for the synthesis of **4** was employed (5 g, 69 % yield). $[\alpha]_D^{25} = -5.2$ ($c = 0.8$, CH₂Cl₂). IR (thin film, cm⁻¹): 3061, 3030, 2988, 2933, 1603, 1455, 1375, 1216, 896, 857, 740, 699. ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.28 (m, 5 H), 5.00 (d, $J = 3.6$ Hz, 1 H), 4.74 (d, $J = 12.2$ Hz, 1 H), 4.64 (d, $J = 3.6$ Hz, 1 H), 4.52 (d, $J = 12.2$ Hz, 1 H), 3.97 (d, $J = 3.6$ Hz, 1 H), 3.80 (dd, $J = 3.6, 6.3$ Hz, 1 H), 3.27 (m, 1 H), 2.76 (t, $J = 4.3$ Hz, 1 H), 2.54 (dd, $J = 2.6, 4.8$ Hz, 1 H), 1.54 (s, 3 H), 1.32 (d, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ 137.2, 128.4, 128.0, 127.6, 111.8, 105.4, 105.3, 71.9, 71.9, 71.8, 50.1, 50.0, 43.0, 26.8, 26.2.

(1S)-1-((3aR,6S,6aR)-6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl) pent-4-en-1-ol (38):



A procedure similar to that described for the synthesis of **5** was employed (5.5 g, 95 % yield) $[\alpha]^{25}_D + 3.2$ ($c = 1.0$, CH_2Cl_2). IR (thin film, cm^{-1}): 3428, 2985, 2950, 2935, 2902, 2872, 1456, 1374, 1317, 1287, 1248, 1220, 1162, 1120, 1065, 1031, 963, 885, 847, 784. ^1H NMR (400 MHz, CDCl_3) δ 7.31-7.19 (m, 5 H), 5.92 (d, $J = 3.8$ Hz, 1 H), 5.72 (m, 1 H), 4.95 (d, $J = 17.3$ Hz, 1 H), 4.87 (d, $J = 10.2$ Hz, 1 H), 4.65 (d, $J = 11.7$ Hz, 1 H), 4.59 (d, $J = 3.8$ Hz, 1 H), 4.39 (d, $J = 11.7$ Hz, 1 H), 3.95 (dd, $J = 3.6, 5.6$ Hz, 1 H), 3.91 (m, 1 H), 3.88 (d, $J = 3.6$ Hz, 1 H), 2.20 (m, 1 H), 2.07 (m, 1 H), 1.52 (m, 1 H), 1.42 (s, 3 H), 1.35 (m, 1 H), 1.26 (s, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 138.3, 136.8, 128.7, 128.3, 128.0, 114.7, 111.5, 105.0, 82.1, 82.0, 81.9, 81.8, 71.9, 71.8, 71.7, 69.0, 33.5, 29.7, 26.7. HRMS (ESI): calcd. for $\text{C}_{19}\text{H}_{26}\text{O}_5$ $[\text{M}+\text{H}]^+$ 335.1858, found 335.1822.

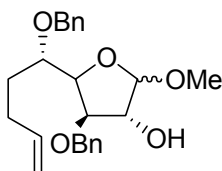
(3aR,6S,6aR)-6-(Benzyloxy)-5-((S)-1-(benzyloxy)pent-4-enyl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole (39):



A procedure similar to that described for the synthesis of **6** was employed (5 g, 97 % yield) $[\alpha]^{25}_D = -9.7$ ($c = 1.0$, CH_2Cl_2). IR (thin film, cm^{-1}): 3068, 3031, 2982, 2928, 1734, 1639, 1377, 1214, 1078, 1025, 739. ^1H NMR (400 MHz, CDCl_3): δ 7.38-7.22 (m, 10 H), 6.02 (d, $J = 3.8$ Hz, 1 H), 5.69 (m, 1 H), 3.92 (m, 3 H), 4.68 (d, $J = 11.4$ Hz, 1 H), 4.63 (d, $J = 3.9$ Hz, 1 H), 4.52 (d, $J = 11.2$ Hz, 1 H), 4.42 (d, $J = 11.7$ Hz, 1 H), 4.19 (dd, $J = 3.2, 8.3$ Hz, 1 H), 3.86 (d, $J = 3.4$ Hz, 1 H), 3.78 (m, 1 H),

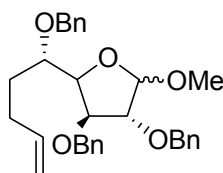
2.25 (m, 1H), 2.12 (m, 1 H), 1.49 (s, 3 H), 1.45 (m, 2 H), 1.33 (s, 3 H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.2, 138.3, 136.9, 128.5, 128.2, 128.1, 128.0, 127.3, 114.7, 111.5, 105.1, 84.3, 82.3, 81.3, 73.3, 71.6, 30.6, 29.6, 26.7, 26.3. HRMS (ESI): calcd. for $\text{C}_{26}\text{H}_{32}\text{O}_5$ $[\text{M}+\text{H}]^+$ 425.2328, found 425.2315.

(3R,4R)-4-(Benzyloxy)-5-((S)-1-(benzyloxy)pent-4-enyl)-2-methoxytetrahydrofuran-3-ol (40):



A procedure similar to that described for the synthesis of **7** was employed (4.50 mg, 98 % yield) $[\alpha]_D^{25} = -2.90$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 3428, 3064, 2924, 1640, 1496, 1453, 1358, 1208, 1109, 1052, 1027, 736, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.40-7.24 (m, 10 H), 5.72 (m, 1 H), 4.98-4.87 (m, 3 H), 4.69 (d, $J = 11.7$ Hz, 1 H), 5.99 (d, $J = 10.7$, 1 H), 4.42 (d, $J = 11.9$ Hz, 1 H), 4.27 (d, $J = 4.1$ Hz, 1 H), 4.19 (dd, $J = 4.6, 8.3$ Hz, 1 H), 3.82 (t, $J = 4.6$ Hz, 1 H), 3.78 (d, $J = 4.6$ Hz, 1 H), 3.48 (s, 3 H), 2.20 (m, 1 H), 2.15 (m, 1 H), 1.82 (d, $J = 4.3$ Hz, 1 H), 1.45 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.2, 138.5, 137.2, 128.3, 127.9, 127.3, 114.6, 110.2, 84.9, 82.6, 78.3, 78.1, 73.8, 71.7, 56.2, 30.7, 29.7. HRMS (ESI): calcd. for $\text{C}_{24}\text{H}_{30}\text{O}_5$ $[\text{M}+\text{H}]^+$ 399.2179, found 399.2156.

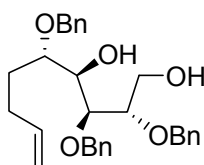
(3S,4R)-3,4-Bis(benzyloxy)-2-((S)-1-(benzyloxy)pent-4-enyl)-5-methoxytetrahydrofuran (41):



A procedure similar to that described for the synthesis of **8** was employed (4.00 mg, 95 % yield) $[\alpha]_D^{25} = -1.2$ ($c = 0.2$, CH_2Cl_2). IR (thin film, cm^{-1}): 3064, 3030, 2923, 1640, 1496, 1453, 1357, 1206, 1191, 1098, 1045, 735, 697. ^1H NMR (400 MHz, CDCl_3): δ 7.35-7.25 (m, 15 H), 5.75 (m, 1 H), 4.98 (d, $J = 17.1$ Hz, 1 H), 4.93 (d, $J = 10.2$ Hz, 1 H), 4.87 (d, $J = 3.8$ Hz, 1 H), 4.71 (d, $J = 10.6$

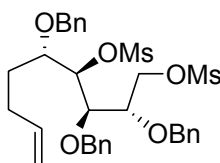
Hz, 1 H), 4.67 (dd, $J = 2.4, 11.9$ Hz, 2 H), 4.54 (d, $J = 11.9$ Hz, 1 H), 4.47 (dd, $J = 6.6, 11.7$ Hz, 2 H), 4.16 (m, 3 H), 3.63 (m, 1 H), 3.41 (s, 3 H), 2.13 (m, 2 H), 1.58 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.0, 138.4, 137.8, 128.4, 128.3, 128.1, 128.1, 127.9, 127.7, 127.3, 114.6, 100.8, 83.0, 82.0, 79.4, 73.1, 72.6, 72.2, 55.3, 30.7, 30.0. HRMS (ESI): calcd. for $\text{C}_{31}\text{H}_{36}\text{O}_5$ $[\text{M}+\text{H}]^+$ 489.2641, found 489.2635.

(2S,3S,4R,5S)-2,3,5-Tris(benzyloxy)non-8-ene-1,4-diol (42):



A procedure similar to that described for the synthesis of **9** was employed (3.8 mg, 88 % yield) $[\alpha]_D^{25} = -2.90$ ($c = 0.2$, CH_2Cl_2). IR (thin film, cm^{-1}): 3550, 3442, 3087, 3063, 3030, 2924, 2854, 1725, 1604, 1496, 1358, 1266, 1209, 1173, 1067, 1027, 959, 917, 819, 739, 699. ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.22 (m, 15 H), 5.73 (m, 1 H), 4.99-4.91 (m, 2 H), 4.69 (d, $J = 11.4$ Hz, 1 H), 4.65 (d, $J = 11.4$ Hz, 1 H), 4.57-4.58 (m, 4 H), 3.94 (s, 1 H), 3.81 (s, 1 H), 3.69 (s, 2 H), 3.49 (d, $J = 4.1$ Hz, 1 H), 2.91 (s, 1 H), 2.75 (s, 1 H), 2.14 (m, 1 H), 2.04 (m, 1 H), 1.62 (m, 1 H), 1.48 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3): δ 138.2, 138.1, 138.0, 137.7, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.7, 114.7, 79.4, 78.0, 73.3, 72.2, 72.1, 69.9, 60.4, 29.3, 29.2. HRMS (ESI): calcd. for $\text{C}_{30}\text{H}_{36}\text{O}_5$ $[\text{M}+\text{H}]^+$ 477.2641, found 477.2638.

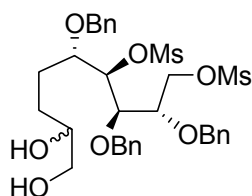
(2S,3R,4R,5S)-2,3,5-Tris(benzyloxy)non-8-ene-1,4-diyl dimethanesulfonate (43):



A procedure similar to that described for the synthesis of **10** was employed (3.50 mg, 96 % yield). $[\alpha]_D^{25} = +2.40$ ($c = 0.3$ CH_2Cl_2). IR (thin film, cm^{-1}): 3063, 3031, 2934, 2872, 1496, 1353, 1210,

1067, 962, 921, 743, 700. ^1H NMR (400 MHz, CDCl_3): δ 7.35-7.25 (m, 15 H), 5.73 (m, 1 H), 4.99-4.91 (m, 3 H), 4.69-4.62 (m, 3 H), 4.56 (d, $J = 11.4$ Hz, 1 H), 4.49 (d, $J = 11.4$ Hz, 1 H), 4.43 (d, $J = 11.4$ Hz, 1 H), 4.37 (d, $J = 5.4$ Hz, 1 H), 4.30 (dd, $J = 3.8, 10.9$ Hz, 1 H), 3.91 (t, $J = 5.1$ Hz, 1 H), 3.85 (dd, $J = 5.1, 9.2$ Hz, 1 H), 3.66 (m, 1 H), 2.94 (s, 3 H), 2.88 (s, 3 H), 2.07 (m, 2 H), 1.64 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 137.5, 137.4, 137.1, 137.0, 128.5, 128.4, 128.2, 128.0, 127.9, 115.3, 79.9, 76.2, 75.5, 74.4, 73.1, 71.8, 68.6, 38.6, 37.2, 29.1, 28.8. HRMS (ESI): calcd. for $\text{C}_{39}\text{H}_{40}\text{O}_9\text{S}_2$ $[\text{M}+\text{H}]^+$ 633.2192, found 633.2180.

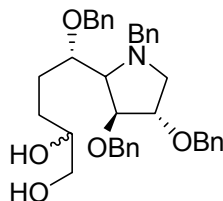
(2S,3R,4R,5S)-2,3,5-Tris(benzyloxy)-8,9-dihydroxynonane-1,4-diyl dimethanesulfonate (44):



A procedure similar to that described for the synthesis of **23** was employed (2.50 g, 98% yield). $[\alpha]_D^{25} = +2.52$ ($c = 0.4$, CH_2Cl_2). IR (thin film, cm^{-1}): 3436, 3060, 2929, 2881, 1606, 1495, 1453, 1355, 1208, 1096, 1027, 912, 798. ^1H NMR (400 MHz, CDCl_3) δ 7.36-7.25 (m, 15 H), 4.91 (m, 1 H), 4.68 (s, 2 H), 4.64 (d, $J = 11.4$ Hz, 1 H), 4.57 (dd, $J = 5.8, 11.4$ Hz, 1 H), 4.53 (d, $J = 11.4$ Hz, 1 H), 4.43-4.38 (m, 2 H), 4.30 (m, 1 H), 3.95 (dd, $J = 4.8, 10$ Hz, 1 H), 3.82 (m, 1 H), 3.67 (m, 1 H), 3.52 (m, 2 H), 3.36 (m, 1 H), 2.95 (s, 3 H), 2.91 (m, 3 H), 1.71 (m, 2 H), 1.38 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 137.4, 137.2, 128.5, 128.2, 128.0, 80.2, 76.6, 76.5, 75.7, 74.5, 73.1, 71.8, 71.7, 68.5, 66.4, 66.3, 38.6, 37.2, 28.2, 28.0, 25.2. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{42}\text{O}_{11}\text{S}_2$ $[\text{M}+\text{H}]^+$ 667.2247, found 667.2239.

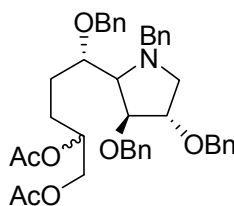
(5S)-5-((3S,4S)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)-5-(benzyloxy)pentane-1,2-diol

(45):



A procedure similar to that described for the synthesis of **14** was employed (3.00 g, 91% Yield). $[\alpha]_D^{25} = + 3.37$ ($c = 0.7$, CH_2Cl_2). IR (thin film, cm^{-1}): 3429, 3087, 3062, 3030, 2926, 2868, 1954, 1811, 1667, 1495, 1207, 1094, 1056, 737, 698. ^1H NMR (400 MHz, CDCl_3): δ 7.25-7.25 (m, 20 H), 4.91 (d, $J = 11.4$ Hz, 1 H), 4.60-4.52 (m, 4 H), 4.47 (t, $J = 7.2$ Hz, 1 H), 4.39 (d, $J = 11.4$ Hz, 1 H), 4.25 (dd, $J = 4.8, 9.7$ Hz, 1 H), 4.13 (d, $J = 4.6$ Hz, 1 H), 4.01 (dt, $J = 3.6, 6.8$ Hz, 1 H), 3.92 (br s, 1 H), 3.86 (d, $J = 9.7$ Hz, 1 H), 3.76 (t, $J = 5.6$ Hz, 1 H), 3.55-3.43 (m, 2 H), 3.31 (m, 2 H), 2.02 (m, 1 H), 1.56-1.45 (m, 4 H). ^{13}C NMR (100 MHz, CDCl_3): δ 138.9, 137.7, 137.4, 128.5, 128.2, 128.0, 127.6, 127.4, 84.4, 82.7, 81.2, 78.5, 78.0, 73.4, 71.7, 71.4, 66.7, 29.2, 28.7, 27.6, 27.2. HRMS (ESI): calcd. for $\text{C}_{37}\text{H}_{43}\text{NO}_5$ $[\text{M}+\text{H}]^+$ 582.3219, found 582.3215.

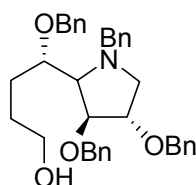
(5S)-5-((3S,4S)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)-5-(benzyloxy)pentane-1,2-diyl diacetate (46):



A procedure similar to that described for the synthesis of **15** was employed (50 mg, 98% Yield) $[\alpha]_D^{25} = + 5.20$ ($c = 0.7$, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.23 (m, 20 H), 5.06-5.00 (m, 1 H), 4.91 (t, $J = 11.4$ Hz, 1 H), 4.54 (d, $J = 2.4$ Hz, 1 H), 4.53 (s, 2 H), 4.49 (d, $J = 3.1$ Hz, 1 H), 4.46 (d, $J = 3.2$ Hz, 1 H), 4.29 (t, $J = 13.4$ Hz, 1 H), 4.18 (dt, $J = 3.4, 11.9$ Hz, 1 H), 4.11 (t, 1 H), 4.07 (d, $J = 4.8$ Hz, 1 H), 4.00-3.91 (m, 2 H), 3.67 (m, 1 H), 3.25 (d, $J = 13.4$ Hz, 1 H), 3.09 (d,

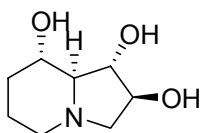
$J = 10.9$ Hz, 1 H), 2.77 (dd, $J = 4.6, 7.3$ Hz, 1 H), 2.43 (ddd, $J = 3.2, 5.3, 8.5$ Hz, 1 H), 2.02 (s, 3 H), 3.96 (s, 3 H), 1.80-1.75 (m, 2 H), 1.70-1.67 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3): δ 170.0, 170.5, 139.1, 138.8, 138.2, 128.3, 128.0, 127.8, 127.8, 127.6, 127.5, 127.4, 126.8, 85.1, 84.9, 81.1, 77.7, 72.7, 72.4, 72.2, 71.7, 71.6, 71.0, 70.7, 65.2, 68.9, 59.6, 59.5, 57.5, 27.6, 27.4, 27.0, 26.9, 21.0, 20.9, 20.7.

(4S)-4-((3S,4S)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)-4-(benzyloxy)butan-1-ol (47):



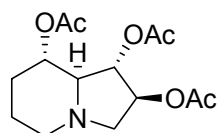
A procedure similar to that described for the synthesis of **14** was employed (2.50, 95% Yield) $[\alpha]_{\text{D}}^{25} = +9.30$ ($c = 0.3$, CH_2Cl_2). IR (thin film, cm^{-1}): 3395, 3062, 3029, 2924, 1604, 1495, 1449, 1369, 1209, 1091, 1027, 736, 700. ^1H NMR (400 MHz, CDCl_3): δ 7.35-7.21 (m, 20 H), 4.94 (d, $J = 11.4$ Hz, 1 H), 4.68 (s, 2 H), 4.53 (d, $J = 11.4$ Hz, 1 H), 4.47 (d, $J = 12.2$ Hz, 1 H), 4.44 (d, $J = 13.1$ Hz, 1 H), 4.40 (d, $J = 12.2$ Hz, 1 H), 4.30 (d, $J = 13.4$ Hz, 1 H), 4.09 (d, $J = 4.8$ Hz, 1 H), 3.93 (d, $J = 5.3$ Hz, 1 H), 3.66 (t, $J = 4.8$ Hz, 1 H), 3.55 (t, $J = 6.3$ Hz, 1 H), 3.25 (d, $J = 13.4$ Hz, 1 H), 3.10 (d, $J = 11.0$ Hz, 1 H), 2.81 (dd, $J = 2.6, 5.1$ Hz, 1 H), 2.43 (dd, $J = 5.3, 10.9$ Hz, 1 H), 1.78 (br s, 1 H), 1.72-1.66 (m, 2 H), 1.61 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 139.2, 138.8, 138.1, 128.3, 127.6, 126.8, 85.2, 81.4, 78.2, 72.4, 71.7, 70.8, 62.8, 59.7, 59.5, 29.6, 28.1. HRMS (ESI): calcd. for $\text{C}_{36}\text{H}_{41}\text{NO}_4$ $[\text{M}+\text{H}^+]$ 552.3114, found 552.3108.

Octahydro-indolizine-1,2,8-triol (48):



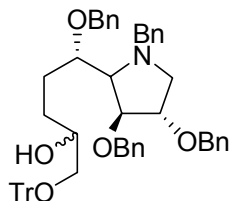
A procedure similar to that described for the synthesis of **2** was employed (149 mg, 78%) yield. $[\alpha]_D^{25} = +20.35$ ($c = 0.8$, MeOH). ^1H NMR (500 MHz, 50% d_6 DMSO in CDCl_3): δ 3.84-3.75 (m, 3 H), 2.85 (d, $J = 7.3$ Hz, 1 H), 2.75 (d, $J = 7.7$ Hz, 1 H), 2.38 (t, $J = 7.8$ Hz, 1 H), 1.92-1.88 (m, 1 H), 1.83-1.75 (m, 3 H), 1.37-1.24 (m, 2 H). HRMS calcd for $\text{C}_8\text{H}_{15}\text{NO}_3$ $[\text{M}+\text{H}]^+$ 174.1130, found 174.1122.

(1S,2S,8S,8aS)-Octahydroindolizine-1,2,8-triyl triacetate (49):



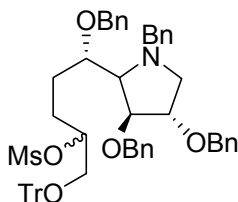
A procedure similar to that described for the synthesis of **15** was employed (84.68 mg, 98%): $[\alpha]_D^{25} = +28$ ($c = 0.25$, CH_2Cl_2). IR (thin film, cm^{-1}): 3086, 3062, 2927, 2864, 1337, 1644, 1495, 1359, 1174, 1095, 968, 738, 699. ^1H NMR (400 MHz, CDCl_3): δ 5.18 (dd, $J = 2.2, 7.5$ Hz, 1 H), 4.99 (ddd, $J = 0.7, 2.4, 3.2$ Hz, 1 H), 4.78 (ddd, $J = 4.6, 9.5, 14.1$ Hz, 1 H), 3.02 (d, $J = 11.0$ Hz, 1 H), 2.95 (dt, $J = 2.9, 10.7$ Hz, 1 H), 2.72 (dd, $J = 6.3, 11.0$ Hz, 1 H), 2.17-2.09 (m, 1 H), 2.07-1.99 (m, 2 H), 2.08 (s, 3 H), 2.06 (s, 3 H), 1.97 (s, 3 H), 1.71 (m, 2 H), 1.27-1.19 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.7, 169.9, 169.2, 80.5, 72.9, 69.7, 59.0, 51.5, 30.1, 23.3, 21.0, 20.8. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{21}\text{NO}_6$ $[\text{M}+\text{H}]^+$ 300.1147, found 300.1138.

(5S)-5-((3S,4S)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)-5-(benzyloxy)-1-(trityloxy)pentan-2-ol (50):



A procedure similar to that described for the synthesis of **28** was employed (1.60 g, 80 % yield). $[\alpha]_D^{25} = +1.40$ ($c = 0.2$, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 7.43 (d, $J = 1.4$ Hz, 3 H), 7.41 (s, 3 H), 7.29-7.19 (m, 29 H), 4.89 (d, $J = 11.4$ Hz, 1 H), 4.51 (s, 1 H), 4.48 (d, $J = 4.3$ Hz, 2 H), 4.43 (d, $J = 8.0$ Hz, 2 H), 4.27 (d, $J = 13.4$ Hz, 1 H), 4.09 (d, $J = 4.8$ Hz, 1 H), 3.91 (d, $J = 5.3$ Hz, 1 H), 3.64 (m, 2 H), 3.23 (d, $J = 15.2$ Hz, 1 H), 3.09 (m, 2 H), 3.00 (m, 1 H), 2.75 (dd, $J = 2.4, 4.8$ Hz, 1 H), 2.41 (dd, $J = 5.6, 11.4$ Hz, 2 H), 1.78 (m, 1 H), 1.65 (m, 1 H), 1.54 (m, 1 H), .88 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3): δ 144.0, 138.8, 138.2, 138.0, 128.6, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.3, 126.9, 88.4, 86.6, 82.1, 78.4, 72.8, 71.8, 71.0, 70.5, 66.6, 62.1, 55.7, 30.2, 27.9. HRMS (ESI): calcd. for $\text{C}_{56}\text{H}_{57}\text{NO}_5$ $[\text{M}+\text{H}]^+$ 824.4315, found 824.4309.

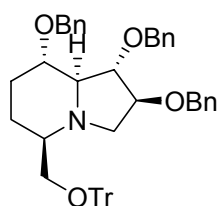
(5S)-5-((3S,4S)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)-5-(benzyloxy)-1-(trityloxy)pentan-2-yl methanesulfonate (51):



A procedure similar to that described for the synthesis of **29** was employed (1.50 g, 92% yield). $[\alpha]_D^{25} = +3.62$ ($c = 0.5$ CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.38 (m, 6 H), 7.32-7.18 (m, 29 H), 4.89 (d, $J = 11.4$ Hz, 1 H), 4.72 (br s, 1 H), 4.50 (d, $J = 11.6$ Hz, 1 H), 4.48 (s, 2 H), 4.47-4.39 (m, 3 H), 4.29 (d, $J = 13.6$ Hz, 1 H), 4.08 (m, 1 H), 3.91 (t, $J = 5.4$ Hz, 1 H), 3.52 (m, 1 H), 3.24 (m,

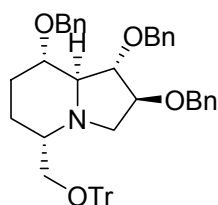
2 H), 3.08 (d, $J = 11.0$ Hz, 1 H), 2.88 (s, 3 H), 2.75 (dd, $J = 2.4, 4.8$ Hz, 1 H), 2.41 (q, $J = 5.3, 10.9$ Hz, 1 H), 1.85 (m, 1 H), 1.66 (m, 1 H), 1.27 (m, 1 H), 0.87 (m, 1 H). ^{13}C NMR (100 MHz, CDCl_3): δ 143.3, 143.3, 142.4, 139.2, 139.1, 138.8, 138.7, 138.3, 138.2, 138.1, 138.0, 128.6, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.7, 127.6, 127.5, 127.4, 127.1, 126.8, 126.7, 87.0, 85.0, 83.1, 82.1, 81.2, 77.7, 76.8, 76.6, 72.6, 72.4, 71.6, 70.7, 70.6, 65.2, 59.4, 57.5, 38.5, 28.6, 28.3, 23.8, 26.7. HRMS (ESI): calcd. for $\text{C}_{56}\text{H}_{57}\text{NO}_7\text{S}$ $[\text{M}+\text{H}]^+$ 902.4090, found 902.4076.

(1S,2S,5R,8S,8aS)-1,2,8-Tris(benzyloxy)-5-(trityloxymethyl)octahydroindolizine (52):



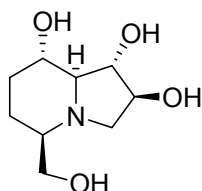
A procedure similar to that described for the synthesis of **30** was employed to synthesize **52** and **53** (0.48 g, 37% yield). $[\alpha]_{\text{D}}^{25} = +8.35$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 3086, 3061, 3030, 2924, 2855, 1747, 1599, 1493, 1451, 1369, 1223, 1075, 1028, 899, 737. ^1H NMR (400 MHz, CDCl_3): δ 7.43 (s, 3 H), 7.41 (s, 3 H), 7.25 (m, 24 H), 4.59 (d, $J = 11.7$ Hz, 1 H), 4.51 (d, $J = 11.7$ Hz, 1 H), 4.48 (d, $J = 10.5$ Hz, 1 H), 4.39 (dd, $J = 3.2, 12.2$ Hz, 3 H), 3.92 (d, $J = 1.9$ Hz, 1 H), 3.81 (d, $J = 1.4$ Hz, 1 H), 3.34 (m, 2 H), 3.10 (m, 3 H), 2.95 (m, 1 H), 2.61 (m, 1 H), 2.09-1.78 (m, 2 H), 1.25 (m, 2 H). ^{13}C NMR (100 MHz, CDCl_3): δ 144.0, 138.8, 138.2, 138.1, 128.6, 128.2, 128.0, 127.7, 127.3, 126.9, 88.5, 86.6, 82.1, 78.4, 72.8, 71.8, 71.0, 70.5, 66.6, 62.1, 55.7, 51.8, 30.3, 29.6, 27.9. HRMS (ESI): calcd. for $\text{C}_{49}\text{H}_{49}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 716.3740, found 716.3729.

(1S,2S,5S,8S,8aS)-1,2,8-Tris(benzyloxy)-5-(trityloxymethyl)octahydroindolizine (53):



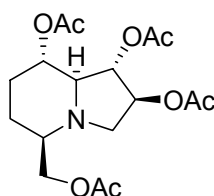
(0.50 g, 38% yield). $[\alpha]^{25}_D = + 5.80$ ($c = 1.0$, CH_2Cl_2). IR (thin film, cm^{-1}): 2928, 2857, 1650, 1455, 1071, 868. ^1H NMR (400 MHz, CDCl_3): δ 7.43 (d, $J = 7.3$ Hz, 6 H), 7.30-7.20 (m, 24 H), 4.62 (d, $J = 11.7$ Hz, 1 H), 4.51 (d, $J = 11.2$ Hz, 1 H), 4.48 (d, $J = 10.9$ Hz, 1 H), 4.42 (d, $J = 12.2$ Hz, 1 H), 4.32 (d, $J = 12.4$ Hz, 1 H), 3.83 (d, $J = 5.8$ Hz, 1 H), 3.37 (dt, $J = 4.1, 10.0$ Hz, 1 H), 3.18 (q, $J = 5.6, 9.5$ Hz, 1 H), 3.06 (m, 2 H), 2.43 (dd, $J = 5.3, 10.4$ Hz, 1 H), 2.32 (br d, $J = 5.3, 10.4$ Hz, 1 H), 2.18 (m, 2 H), 1.86 (d, $J = 5.3$ Hz, 1 H), 1.35-1.25 (m, 4H). HRMS (ESI): calcd. for $\text{C}_{49}\text{H}_{49}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 716.3740, found 716.3728.

(1S,2S,5R,8S,8aS)-5-(Hydroxymethyl)octahydroindolizine-1,2,8-triol (54):



$[\alpha]^{25}_D = + 0.75$ ($c = 0.2$ MeOH). IR (thin film, cm^{-1}): 3428, 2987, 2936, 1619, 1454, 1375, 1259, 1217, 1160, 1072, 872, 794. HRMS (ESI): calcd. for $\text{C}_9\text{H}_{17}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 204.1236, found 204.1225.

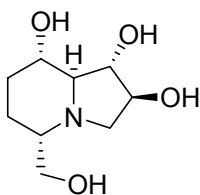
(1S,2S,5R,8S,8aS)-5-(Acetoxymethyl)octahydroindolizine-1,2,8-triyl triacetate (56):



A procedure similar to that described for the synthesis of **34** was employed (40 mg, 98 % yield). $[\alpha]^{25}_D = + 6.41$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 2924, 2853, 1745, 1454, 1372, 1248, 1040, 890, 716. ^1H NMR (400 MHz, CDCl_3) δ 5.19 (dd, $J = 2.4, 7.5$ Hz, 1 H), 5.01 (dd, $J = 2.4, 6.6$ Hz, 1 H), 4.79 (dt, $J = 4.6, 10.0$ Hz, 1 H), 4.05 (dq, $J = 4.6, 11.4, 15.8$ Hz, 2 H), 3.15 (d, $J = 11.2$ Hz, 1 H), 2.74 (dd, $J = 6.5, 10.9$ Hz, 1 H), 2.35-2.32 (m, 1 H), 2.28 (t, $J = 7.8$ Hz, 1 H), 2.18 (m, 1 H),

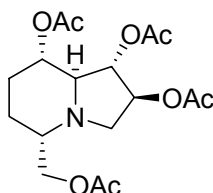
2.08 (s, 3 H), 2.07 (s, 3 H), 2.06 (s, 3 H), 1.97 (s, 3 H), 1.79-1.76 (m, 1 H), 1.45 (dd, $J = 3.9, 11.1$ Hz, 1 H), 1.34-1.35 (m, 2 H). ^1H NMR (100 MHz, CDCl_3): δ 171.3, 170.6, 169.8, 169.1, 79.9, 72.6, 69.4, 66.2, 60.4, 56.8, 29.6, 27.0, 20.8. HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{25}\text{NO}_7$ $[\text{M}+\text{H}]^+$ 372.1658, found 372.1636.

(1S,2S,5S,8S,8aS)-5-(Hydroxymethyl)octahydroindolizine-1,2,8-triol (55):

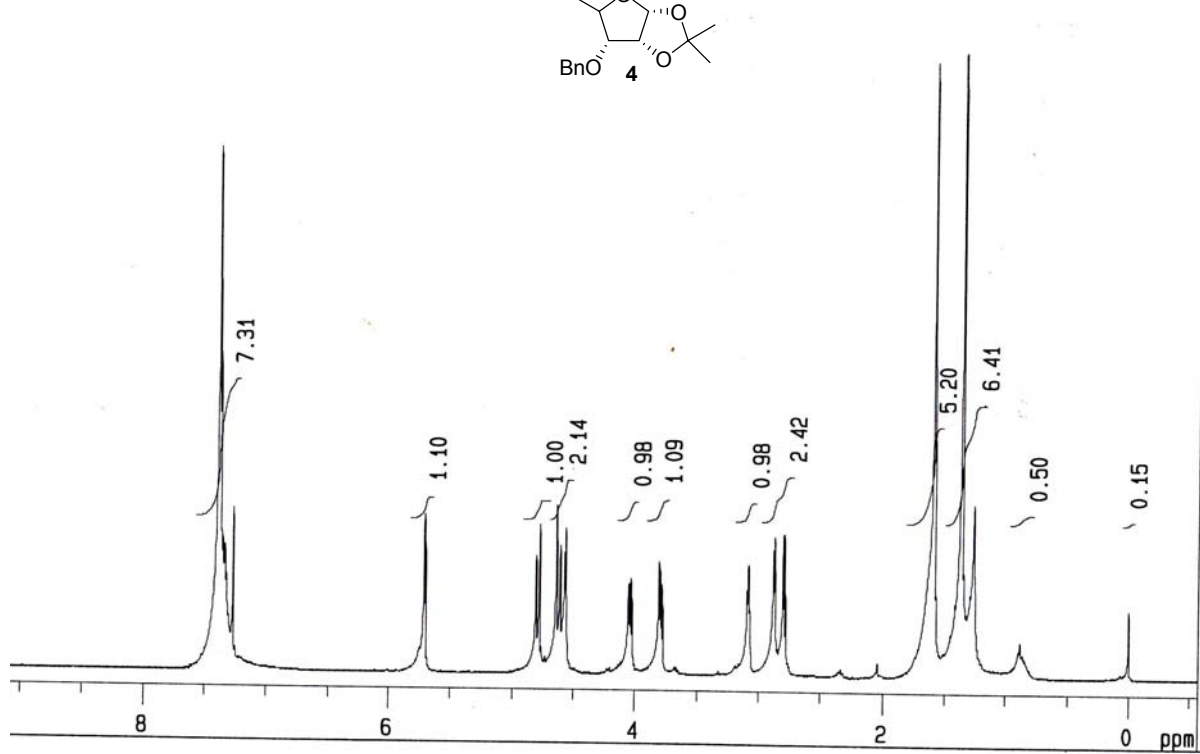
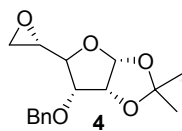


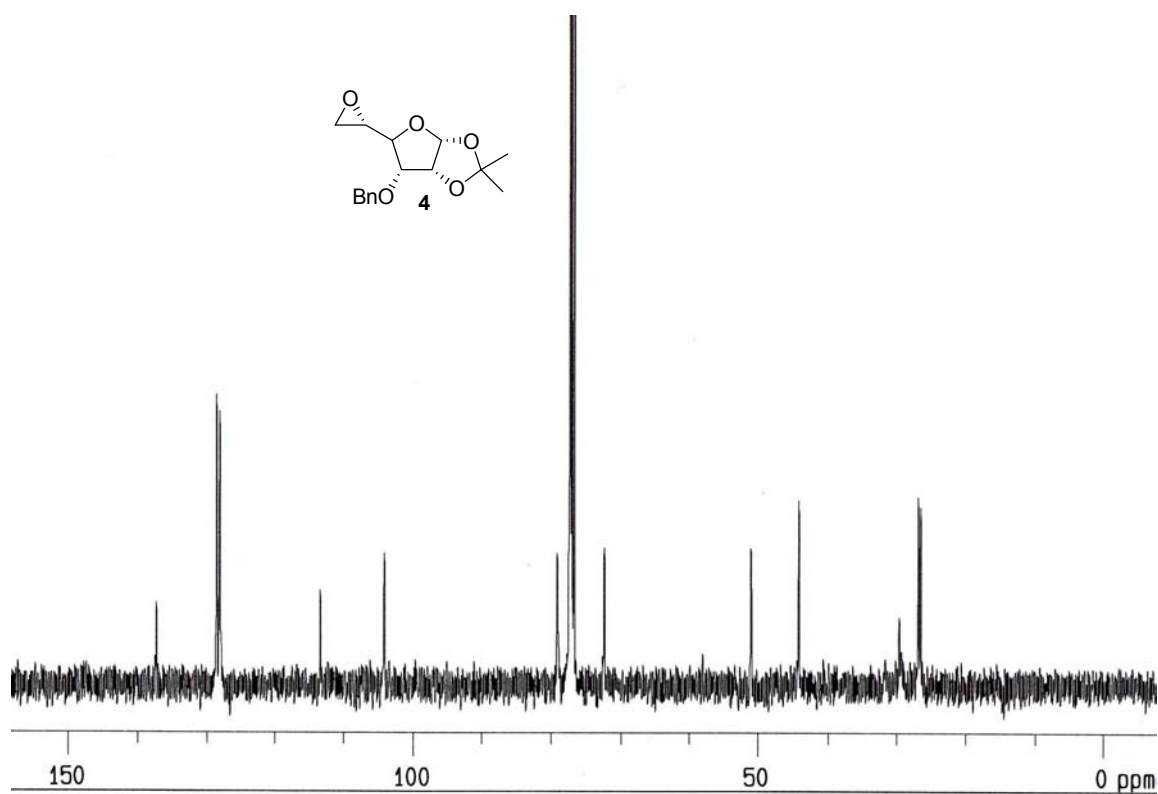
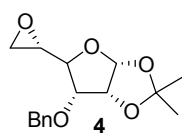
$[\alpha]^{25}_{\text{D}} = +0.92$ ($c = 0.2$ MeOH). IR (thin film, cm^{-1}): 3488, 2986, 2925, 1620, 1456, 1374, 1215, 1164, 1122, 1061, 1018, 852. HRMS (ESI): calcd. for $\text{C}_9\text{H}_{17}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 204.1236, found 204.1228.

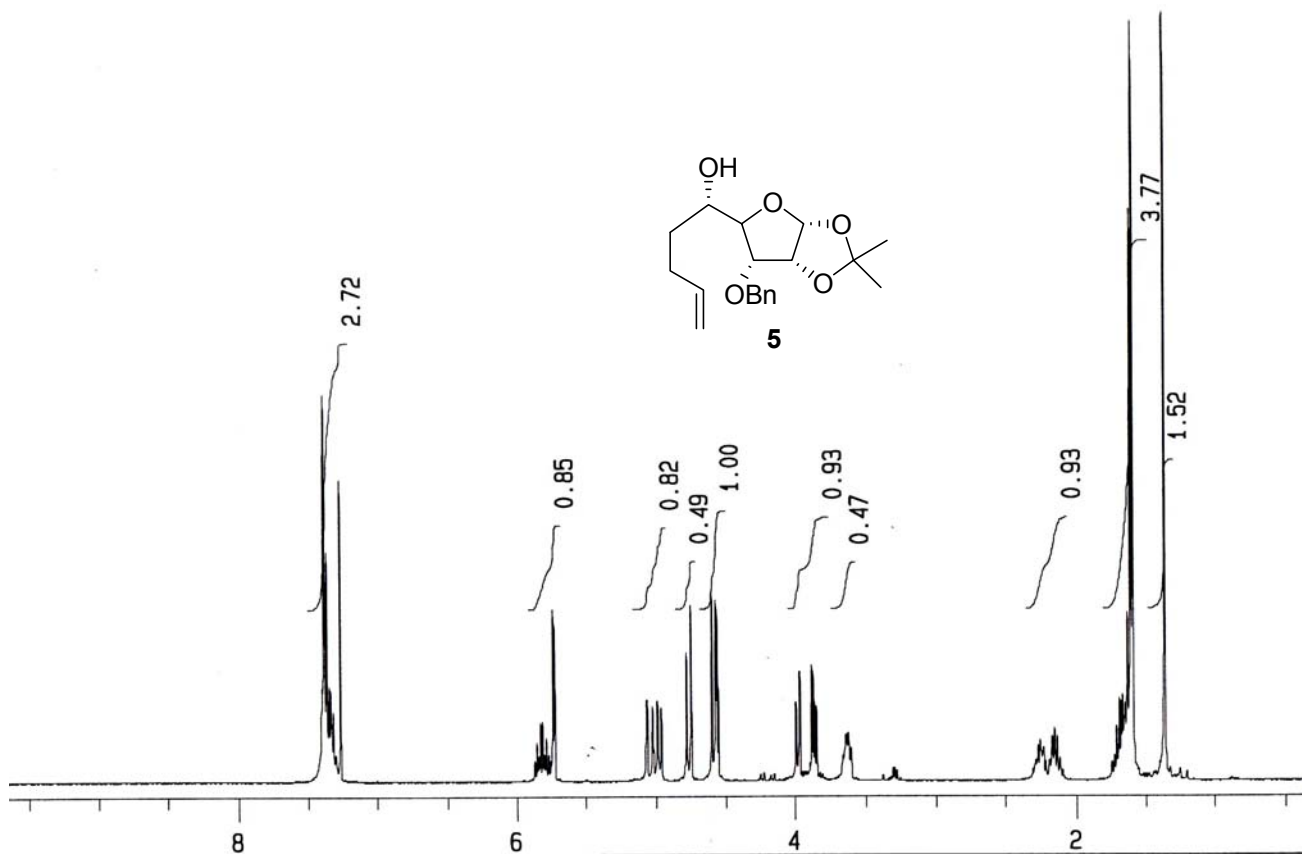
(1S,2S,5S,8S,8aS)-5-(Acetoxymethyl)octahydroindolizine-1,2,8-triyl triacetate (57):

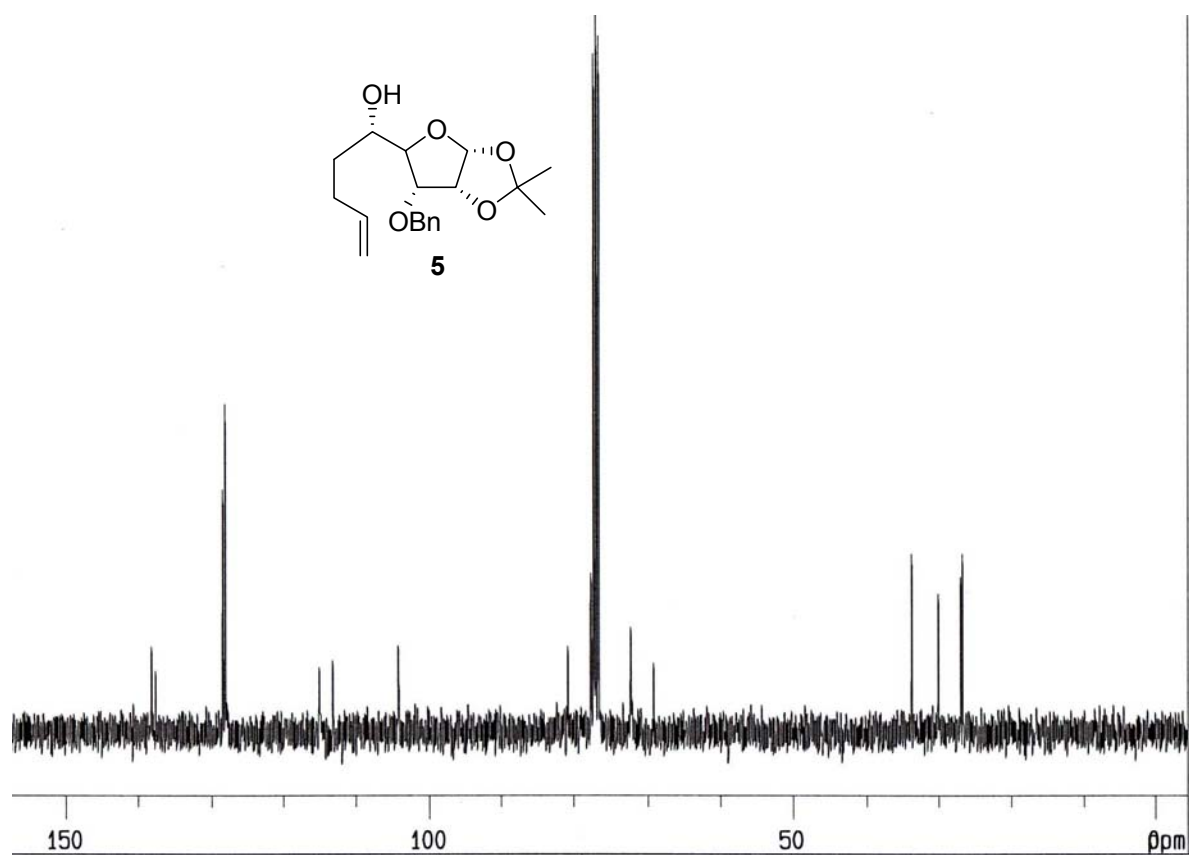
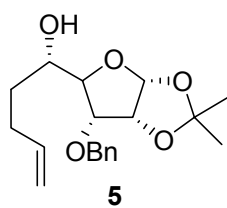


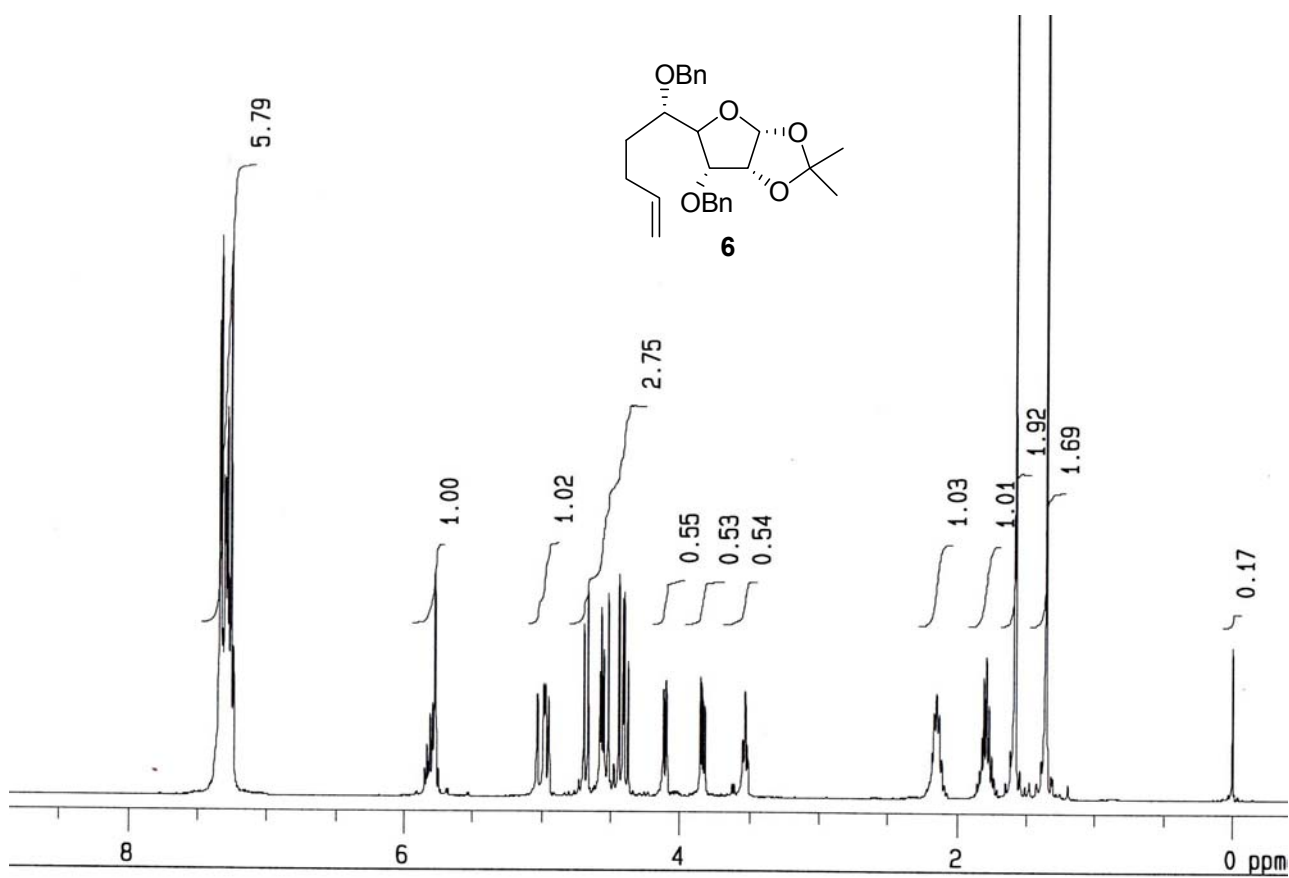
A procedure similar to that described for the synthesis of **34** was employed (40 mg, 98 % yield). $[\alpha]^{25}_{\text{D}} = +2.41$ ($c = 0.5$, CH_2Cl_2). IR (thin film, cm^{-1}): 3062, 3030, 2926, 2858, 1739, 1495, 1453, 1366, 1230, 1097, 1028, 736, 697. ^1H NMR (500 MHz, CDCl_3): δ 5.09 (dd $J = 2.0, 5.9$ Hz, 1 H), 4.96 (dt, $J = 1.8, 3.8$ Hz, 1 H), 4.78 (dt, $J = 4.6, 10.6$ Hz, 1 H), 4.32 (dd, $J = 6.6, 11.4$ Hz, 1 H), 4.11 (dd, $J = 4.0, 11.4$ Hz, 1 H), 3.33 (dd, $J = 6.3, 11.0$ Hz, 1 H), 3.19 (m, 1 H), 2.98 (dd, $J = 2.2, 11.0$ Hz, 1 H), 2.80 (dd, $J = 5.3, 9.5$ Hz, 1 H), 2.08 (s, 3 H), 2.07 (s, 3 H), 2.06 (s, 3 H), 2.01 (s, 3 H), 1.98 (m, 1 H), 1.86 (m, 1 H), 1.73 (m, 1 H), 1.44 (m, 1 H). ^1H NMR (100 MHz, CDCl_3): δ 80.2, 71.4, 63.2, 61.0, 55.1, 52.5, 25.6, 24.0, 20.8. HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{25}\text{NO}_7$ $[\text{M}+\text{H}]^+$ 372.1658, found 372.1639.

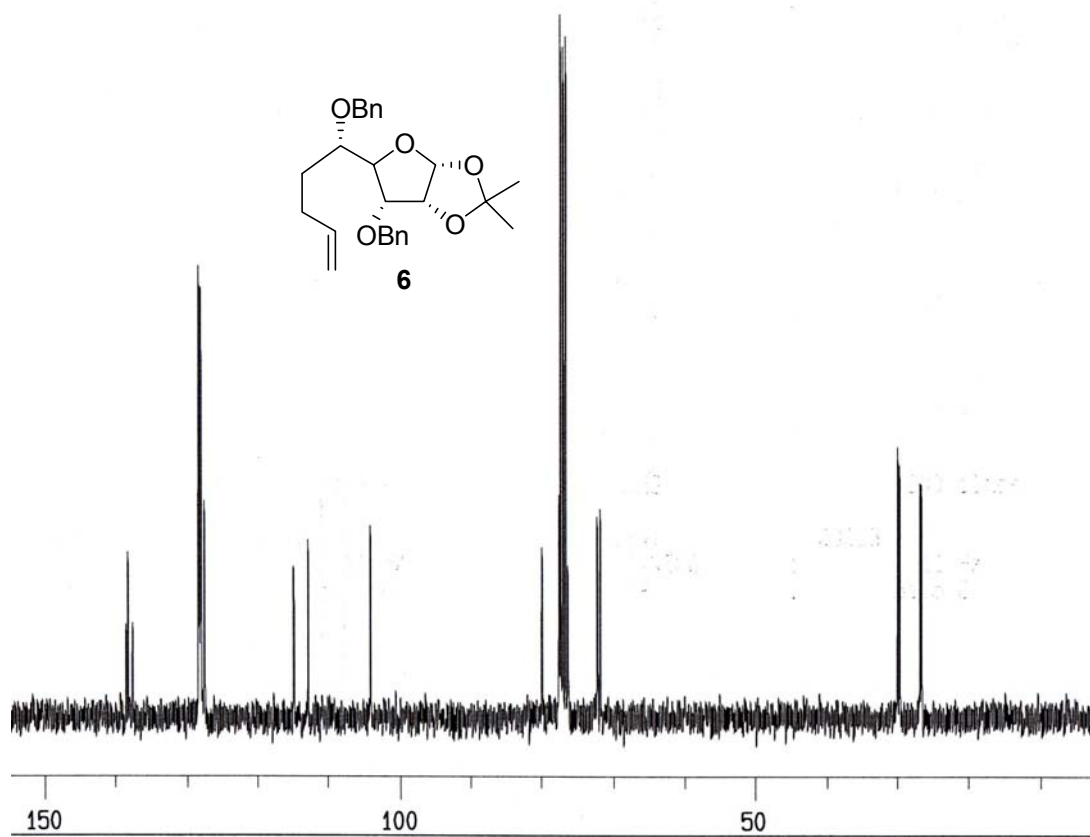
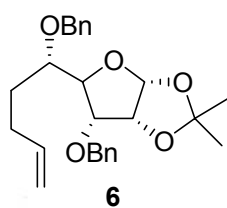


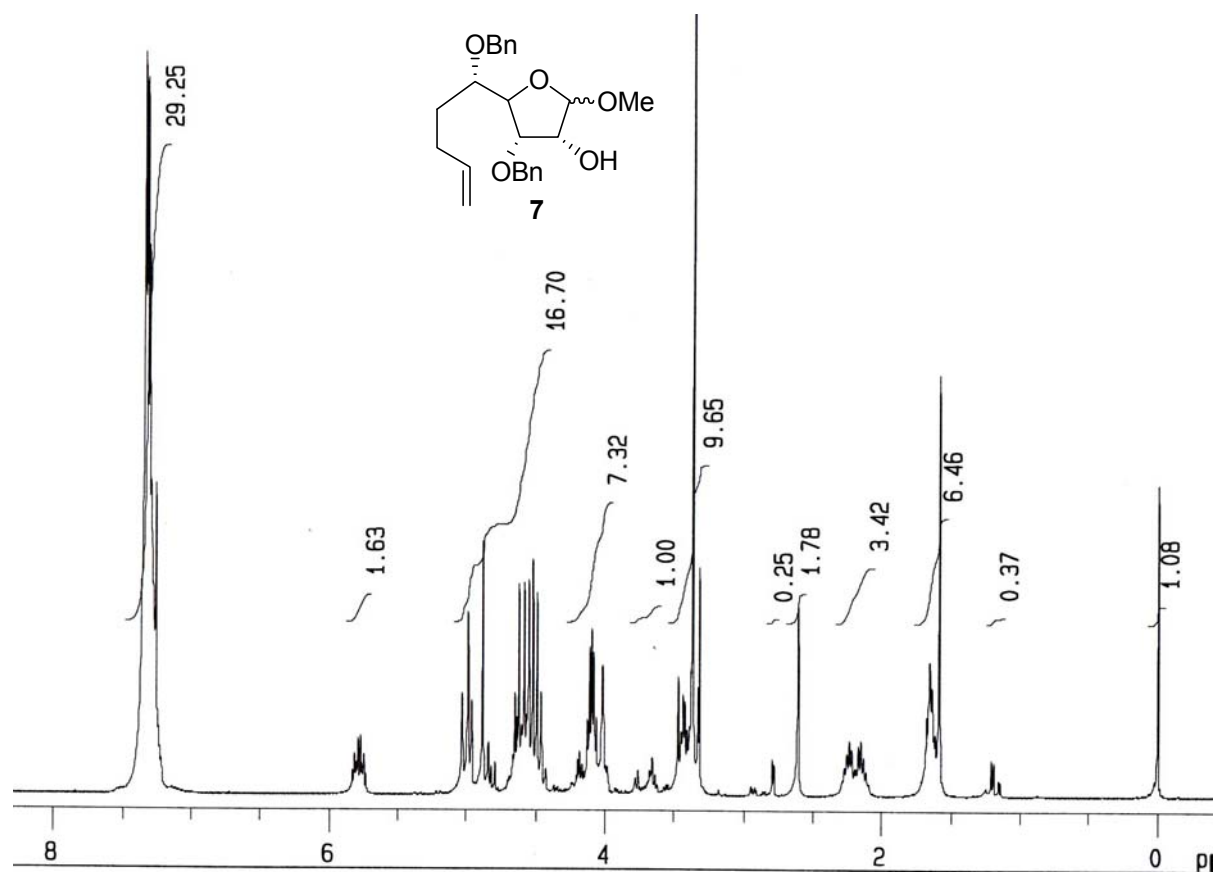


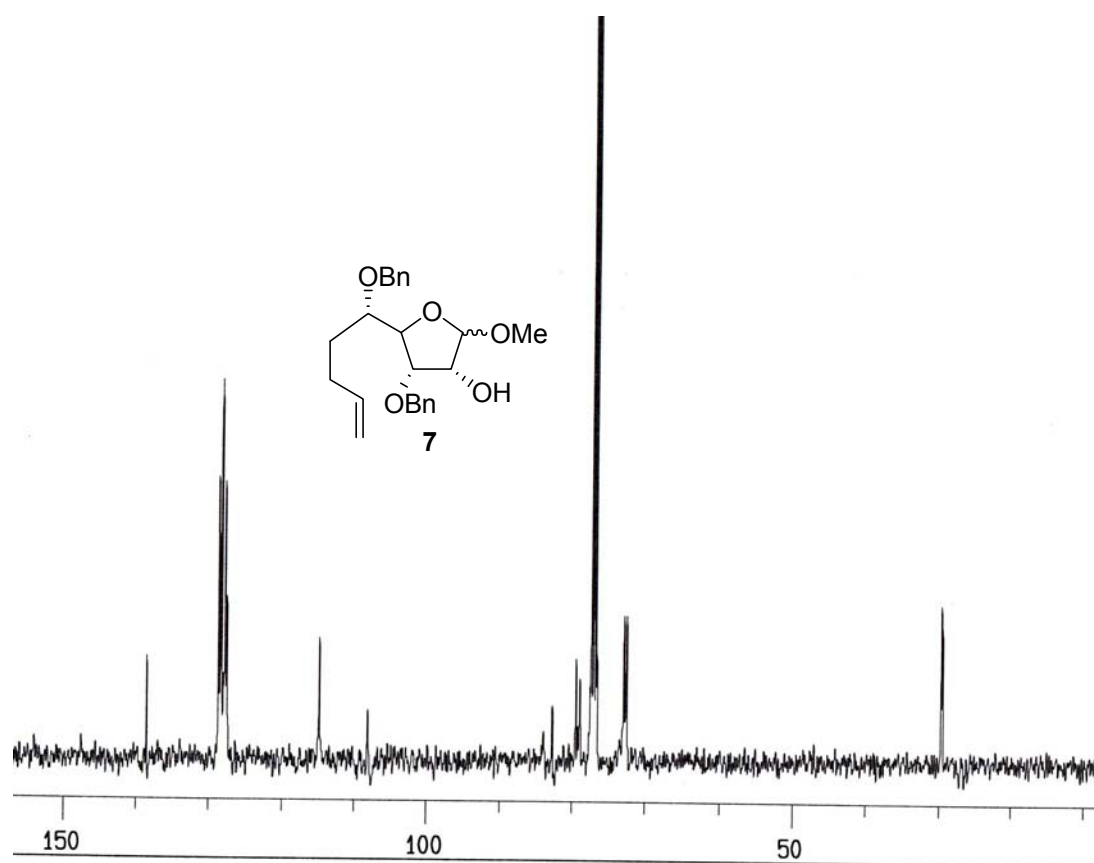


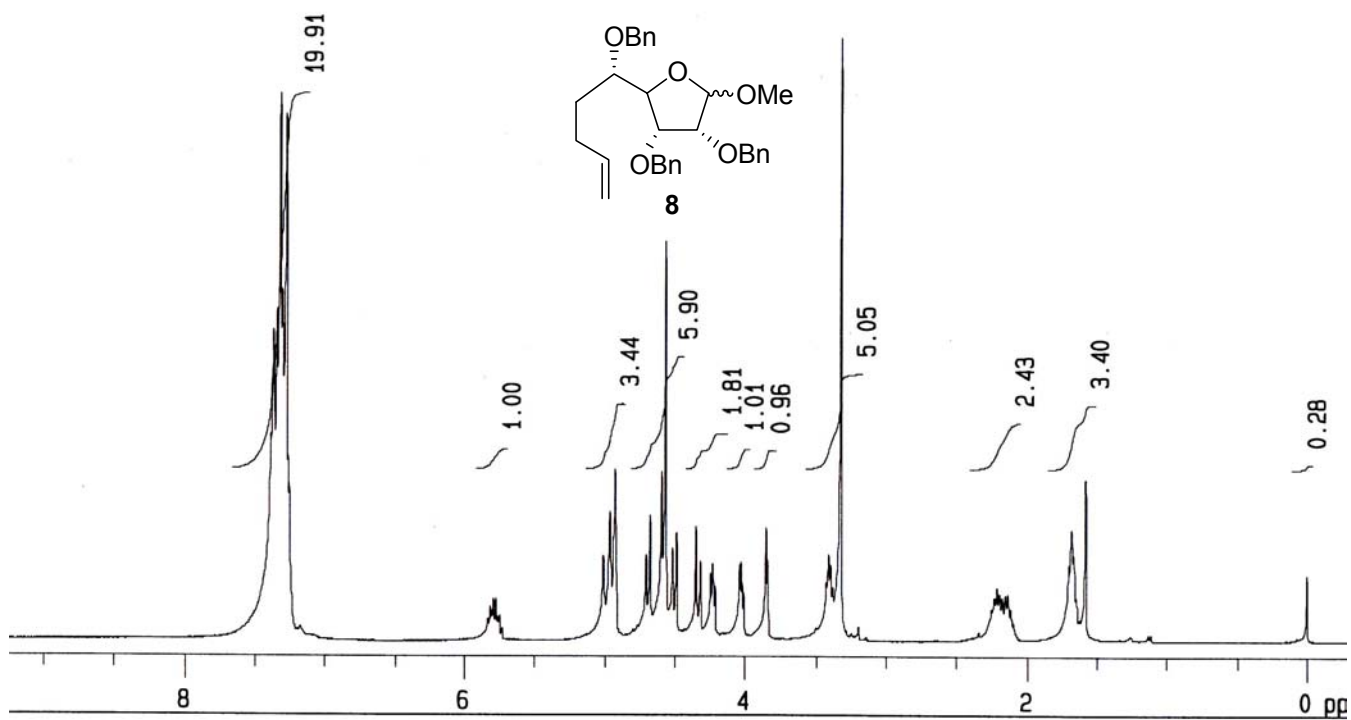


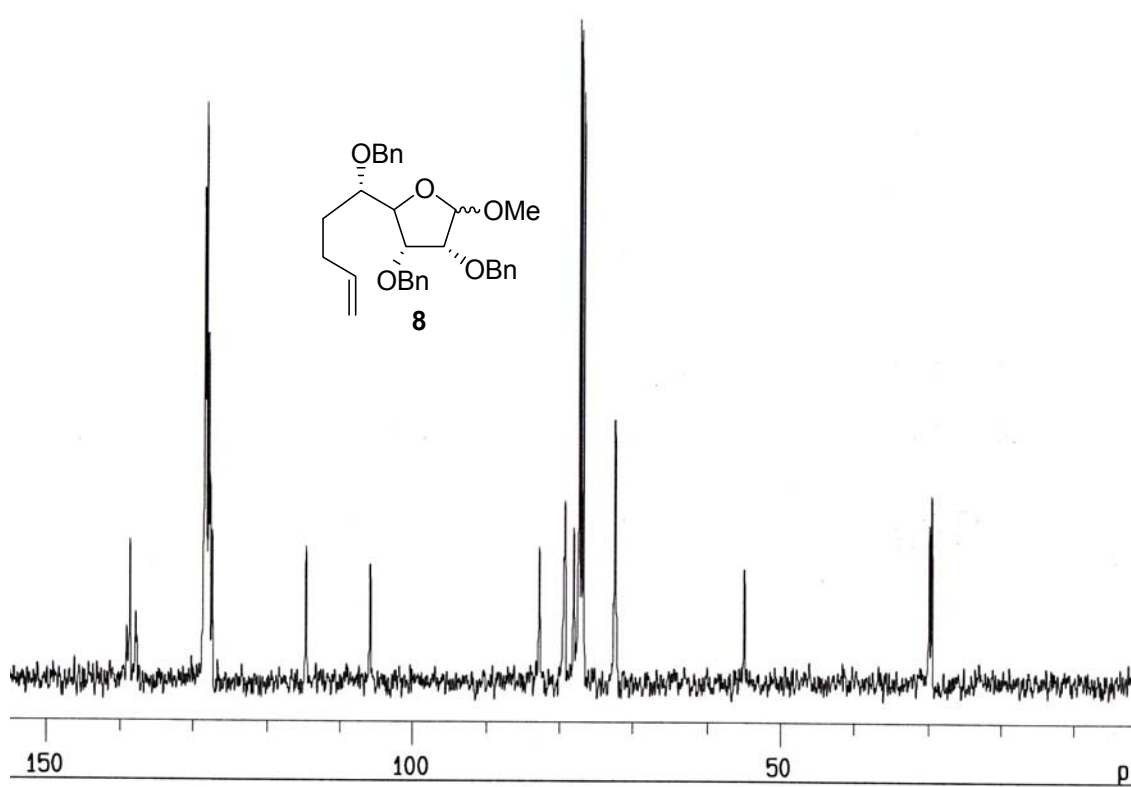


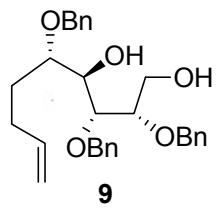
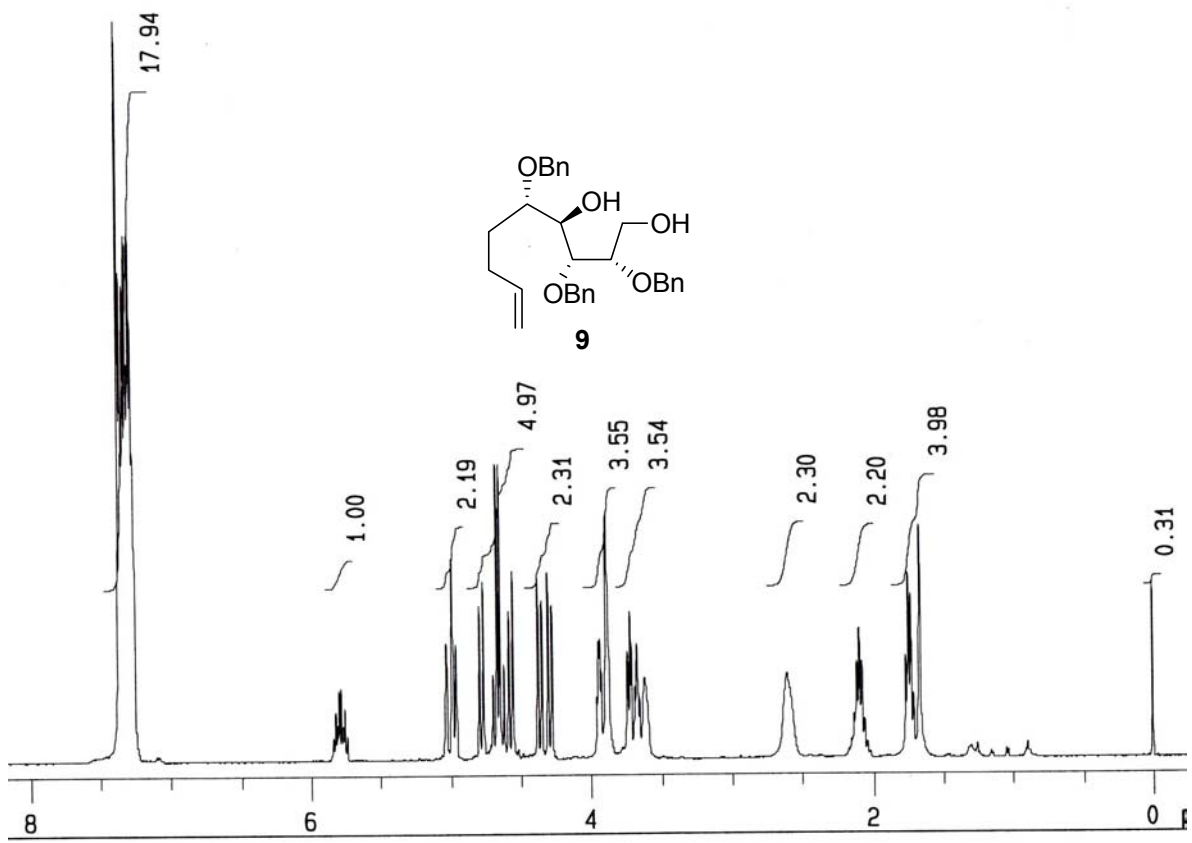


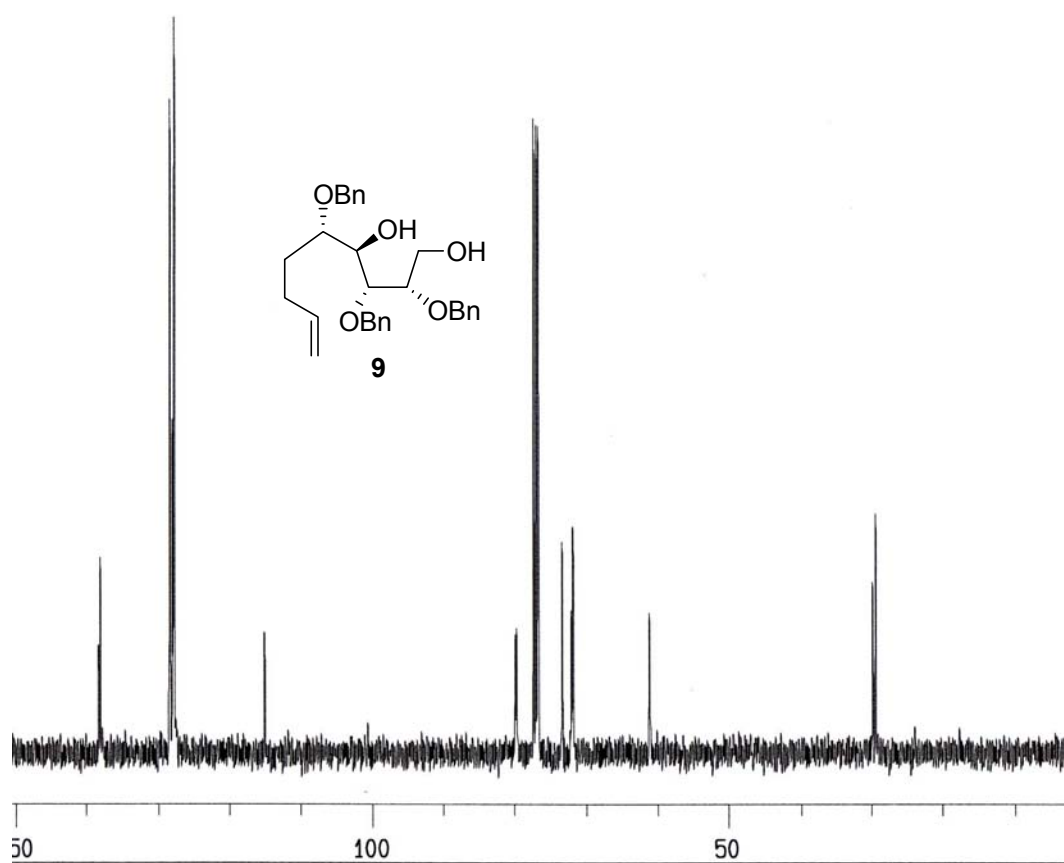


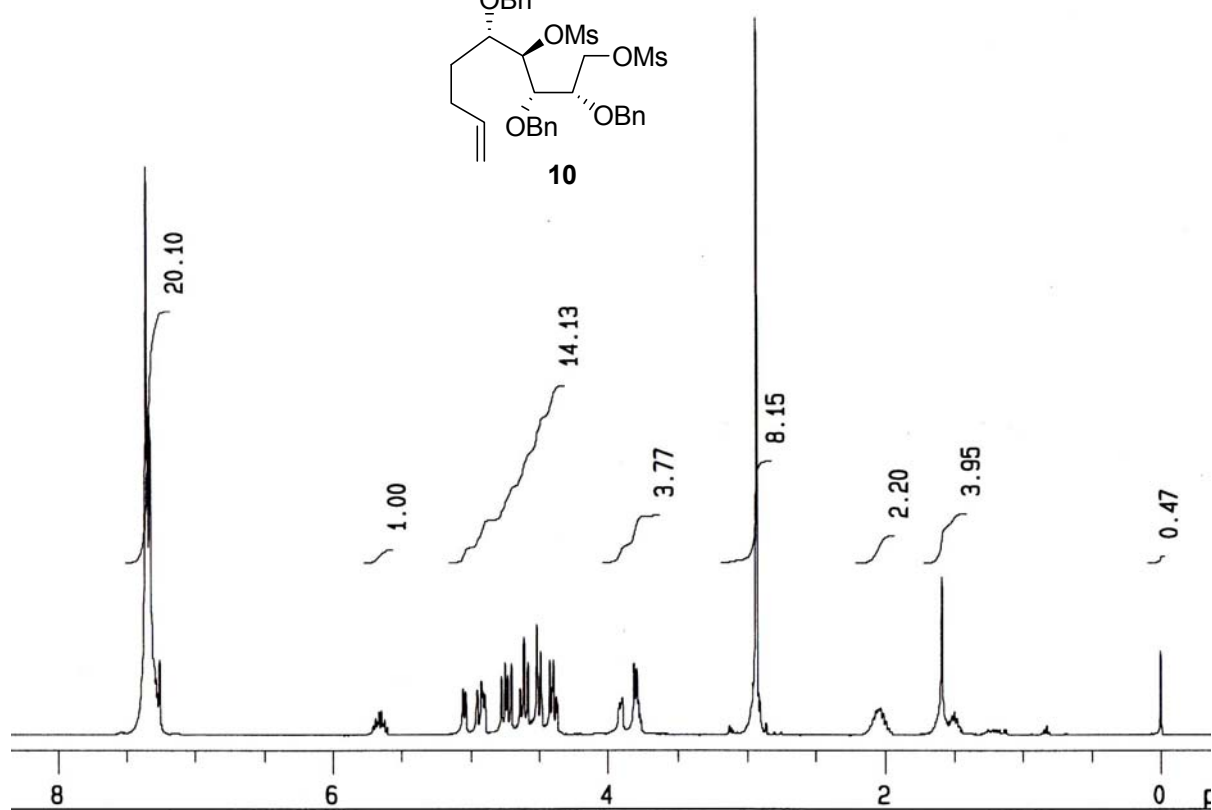
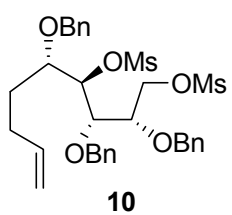


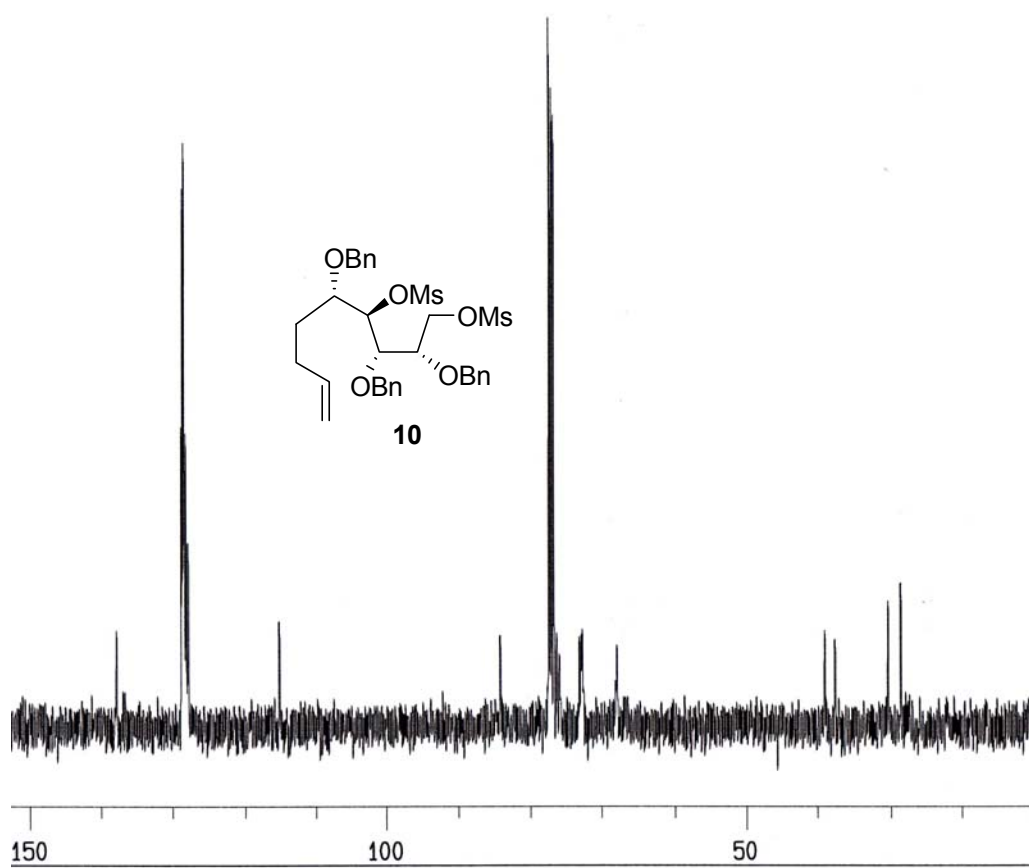


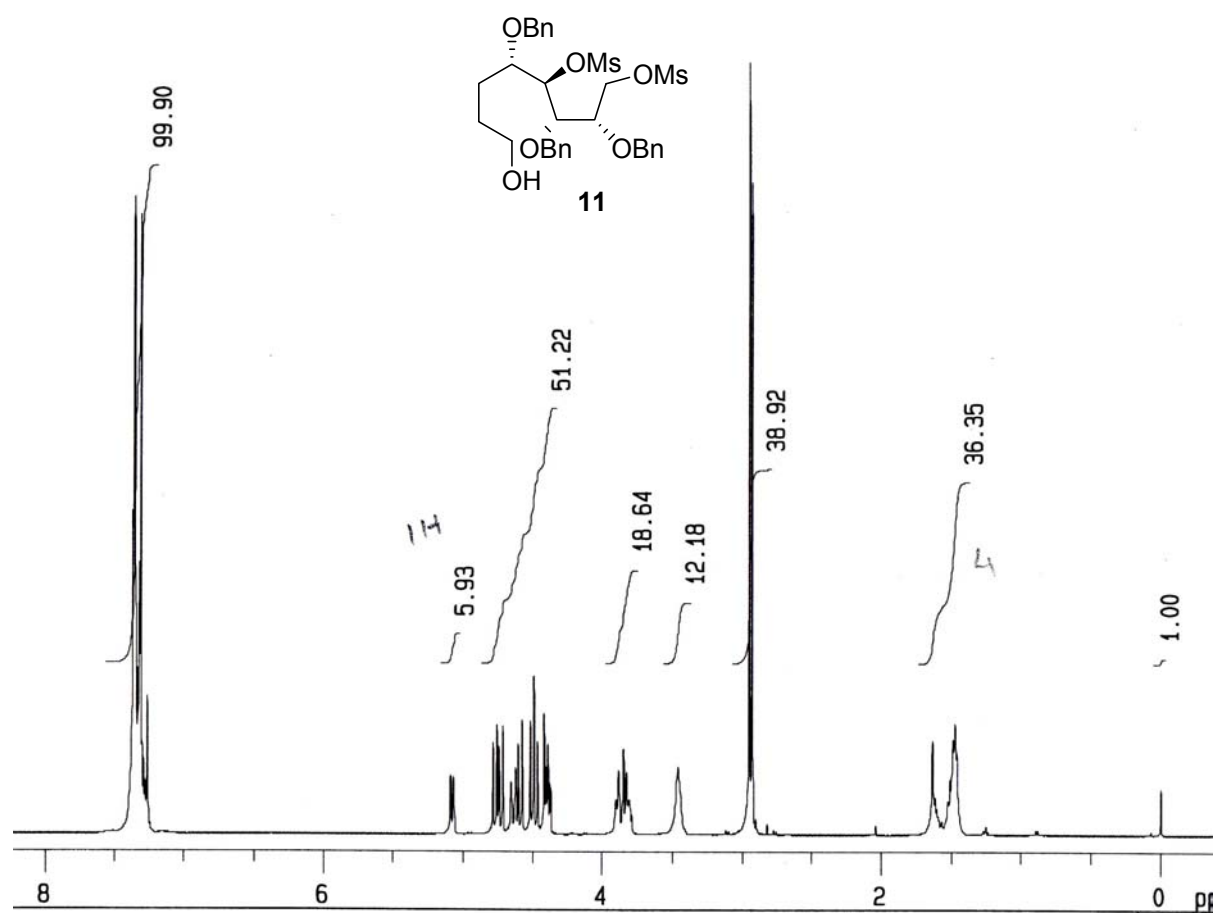


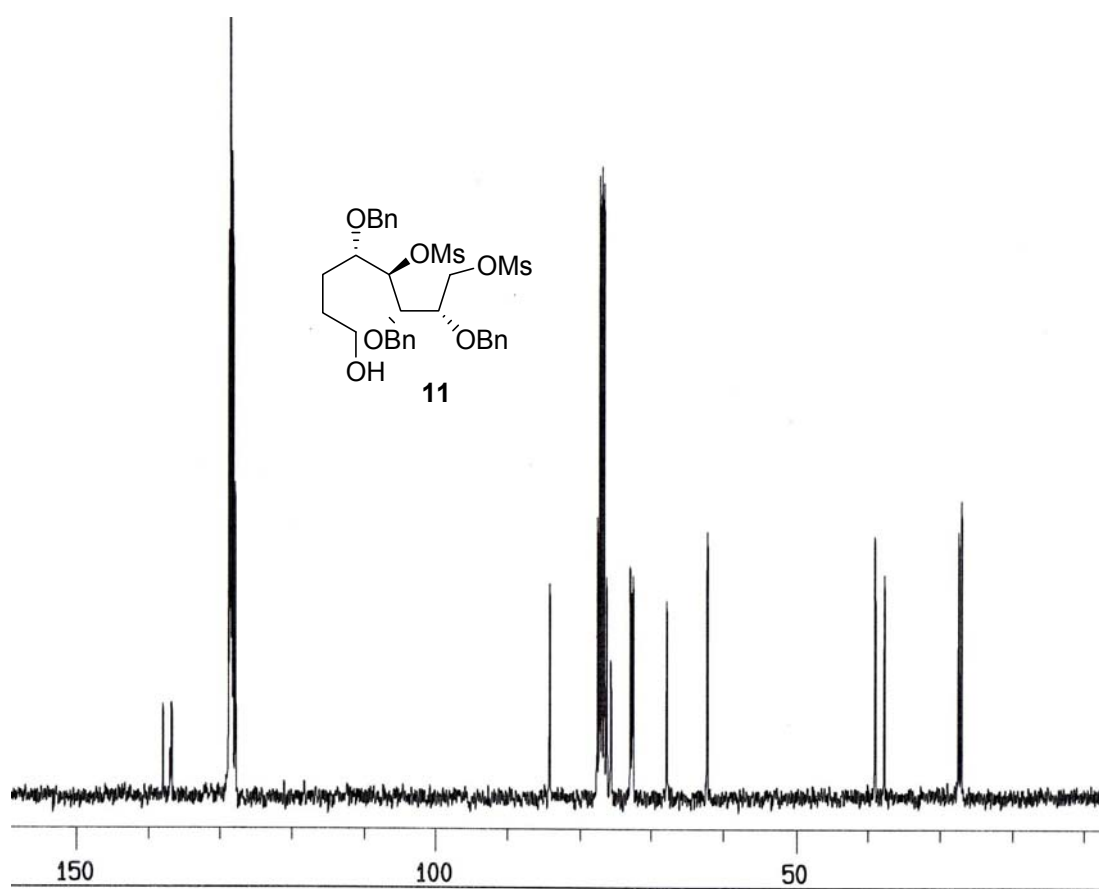


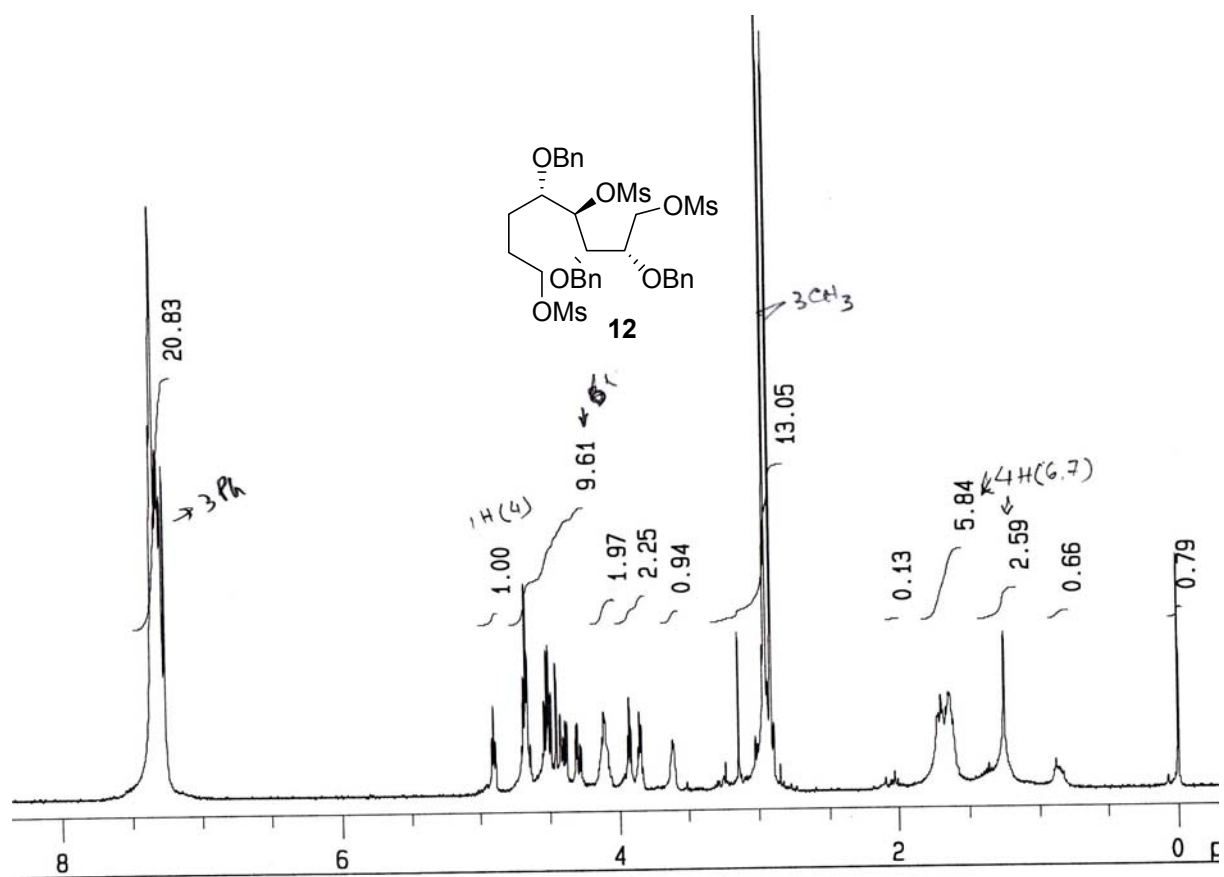


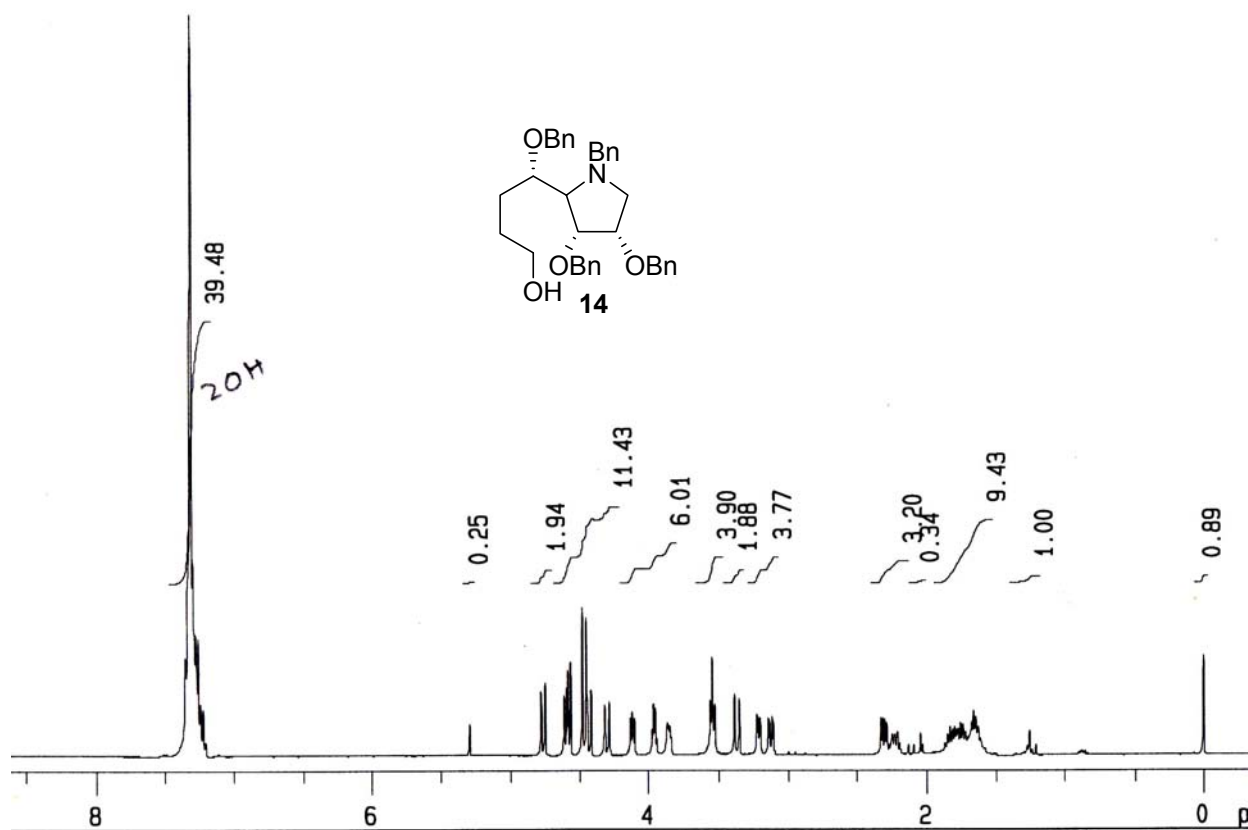


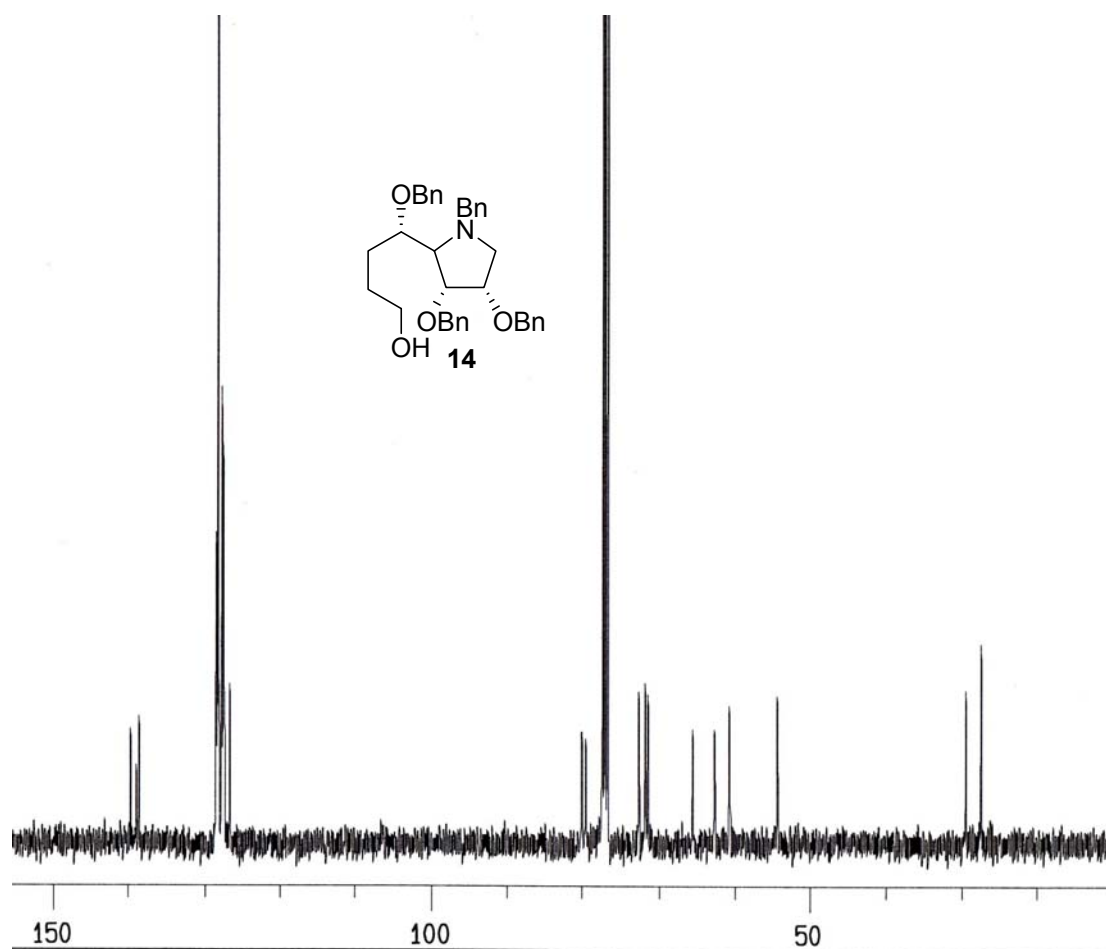
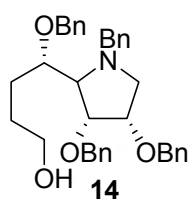


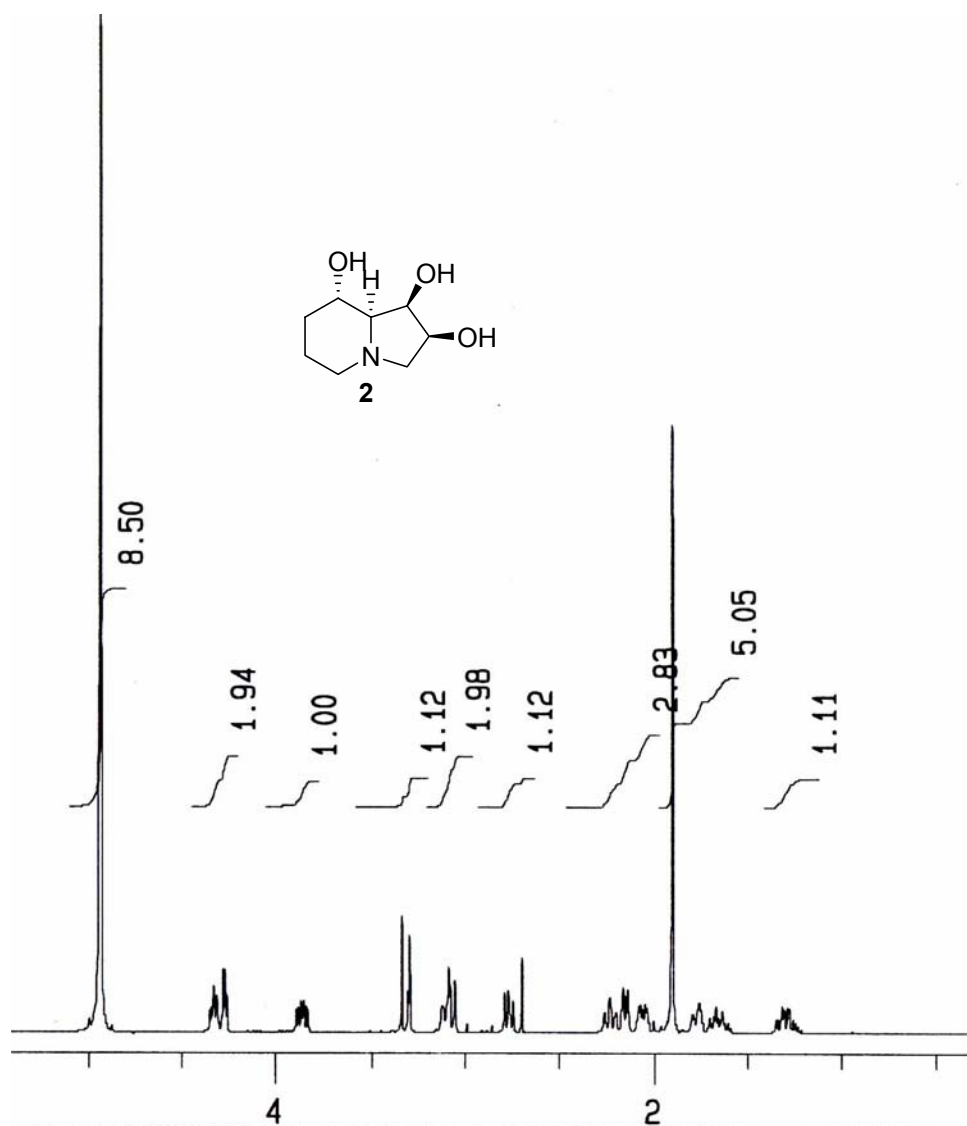
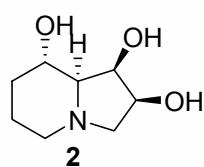


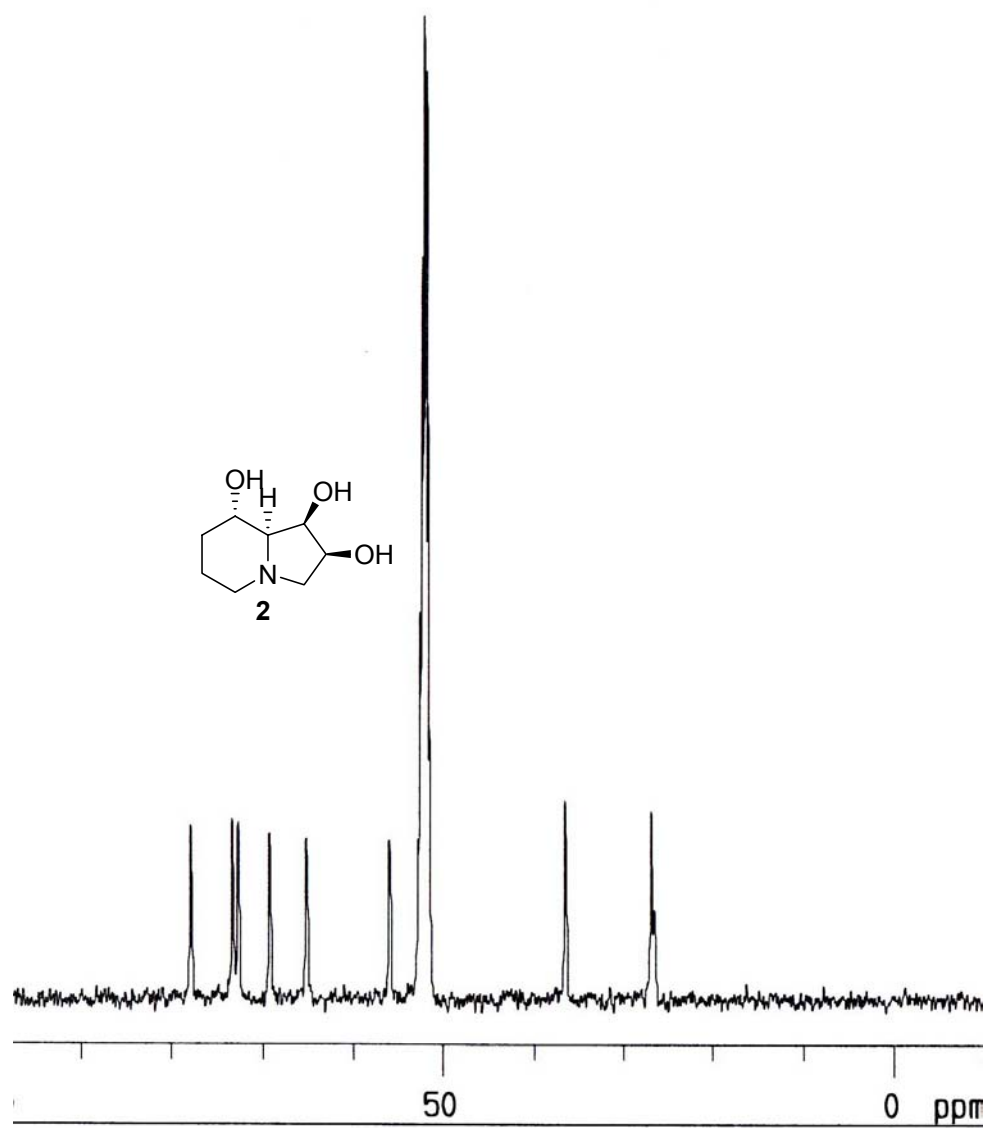


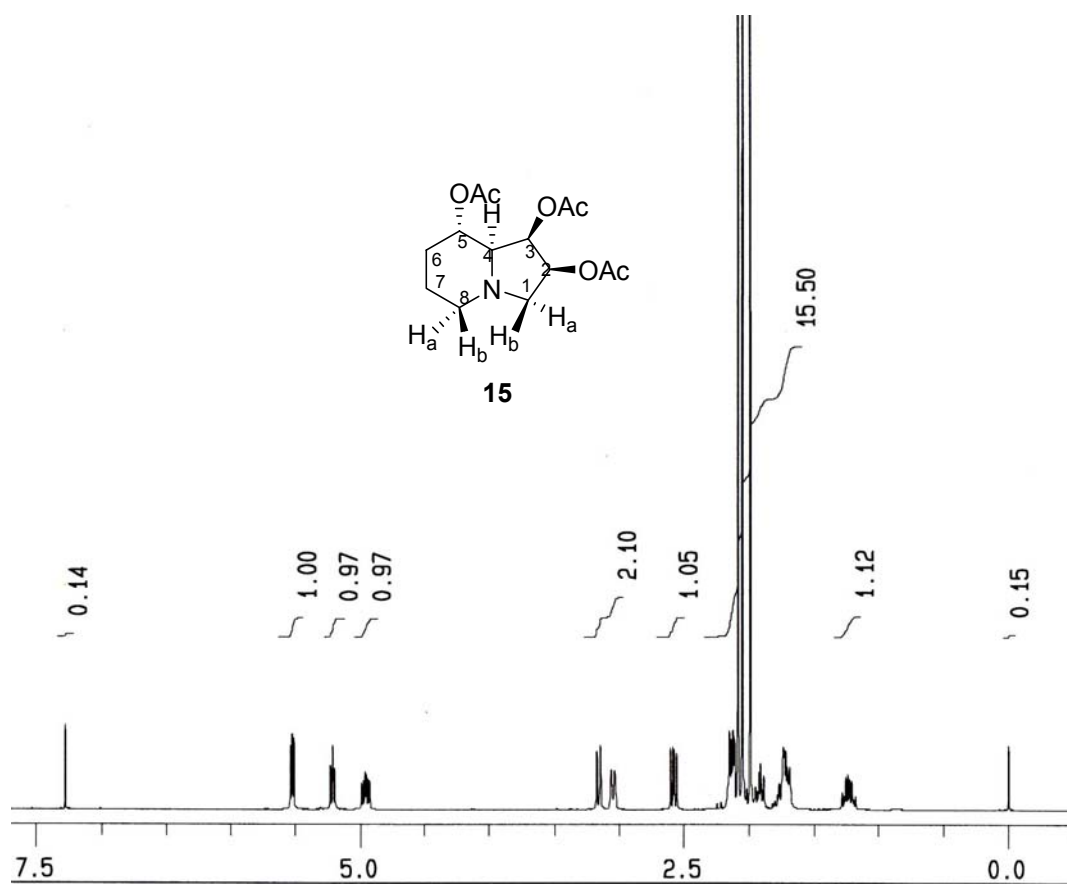


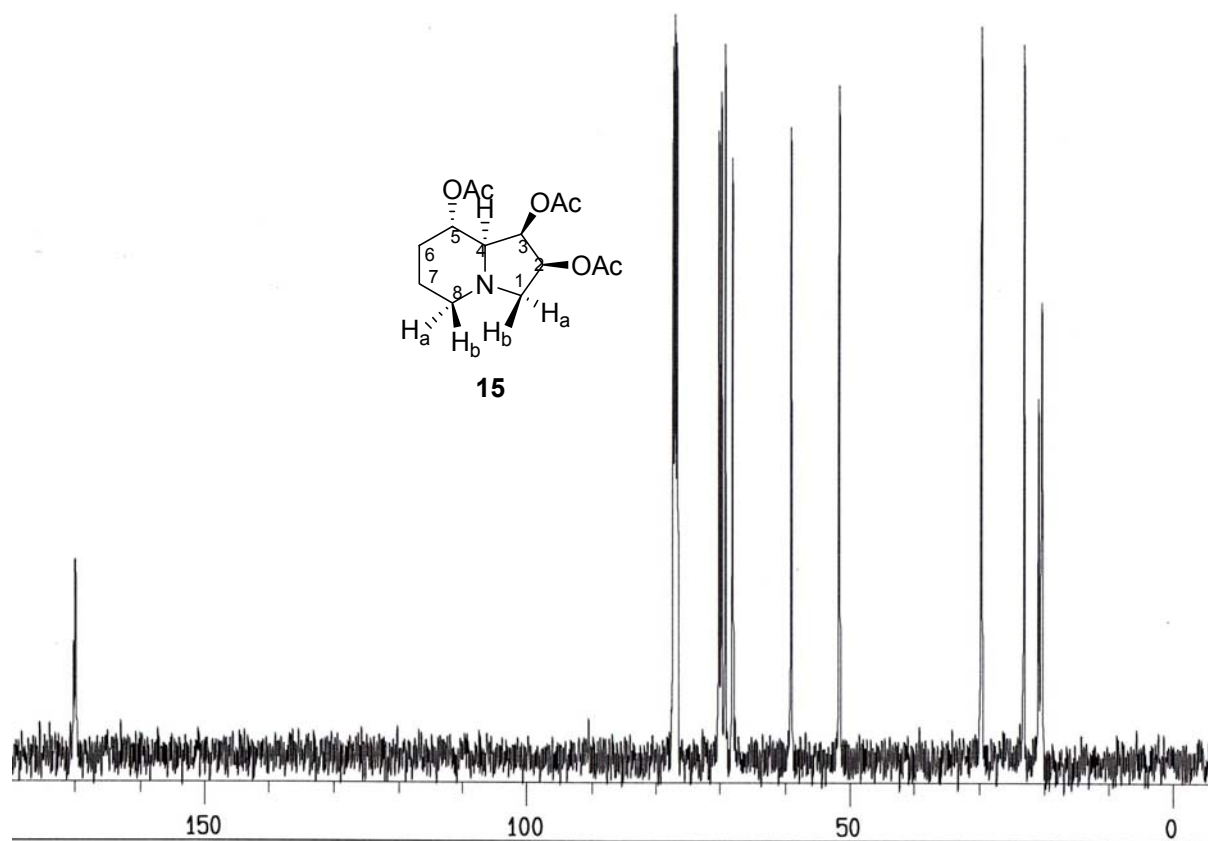
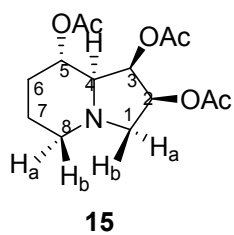




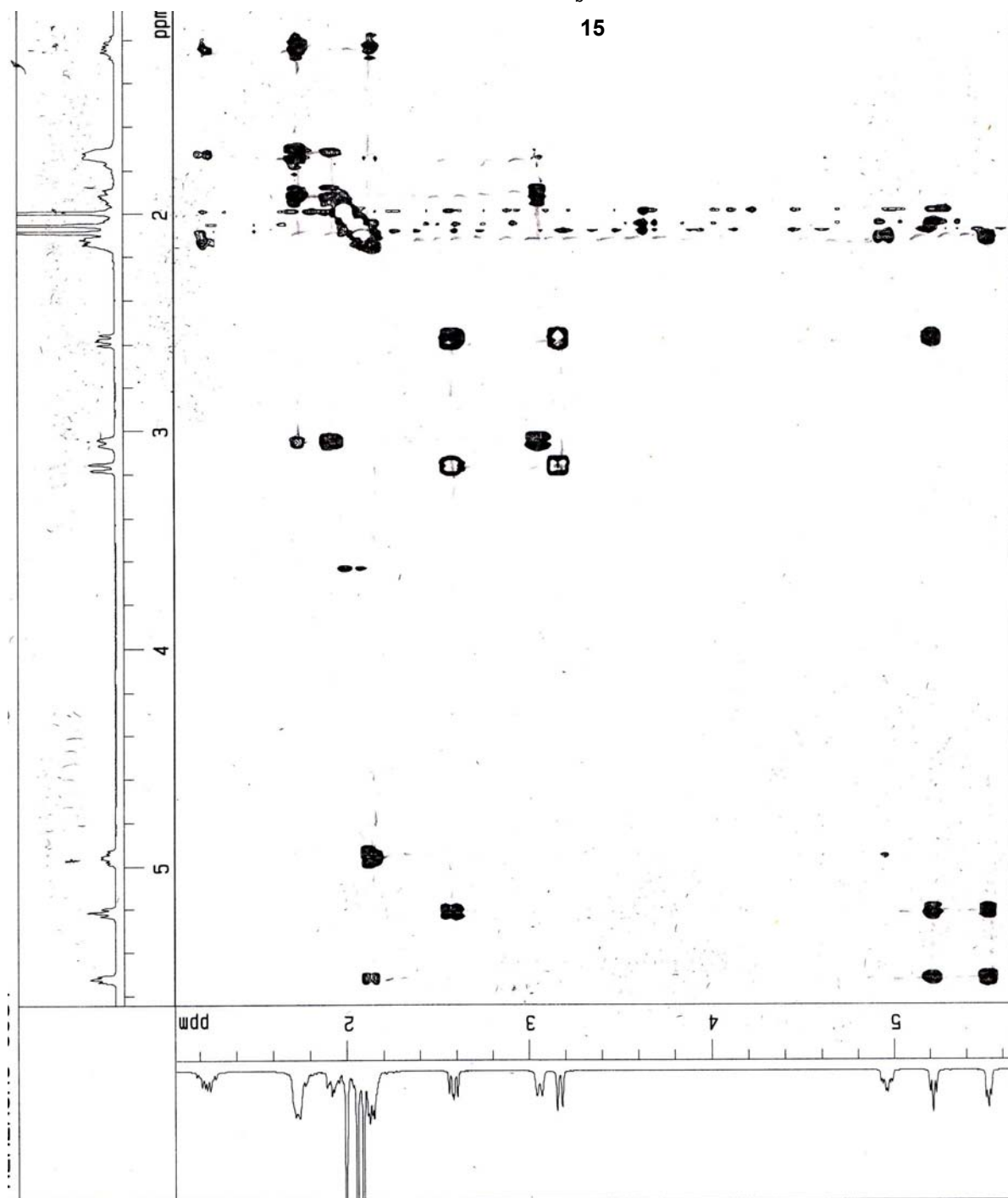
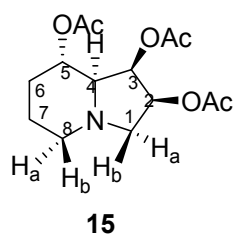




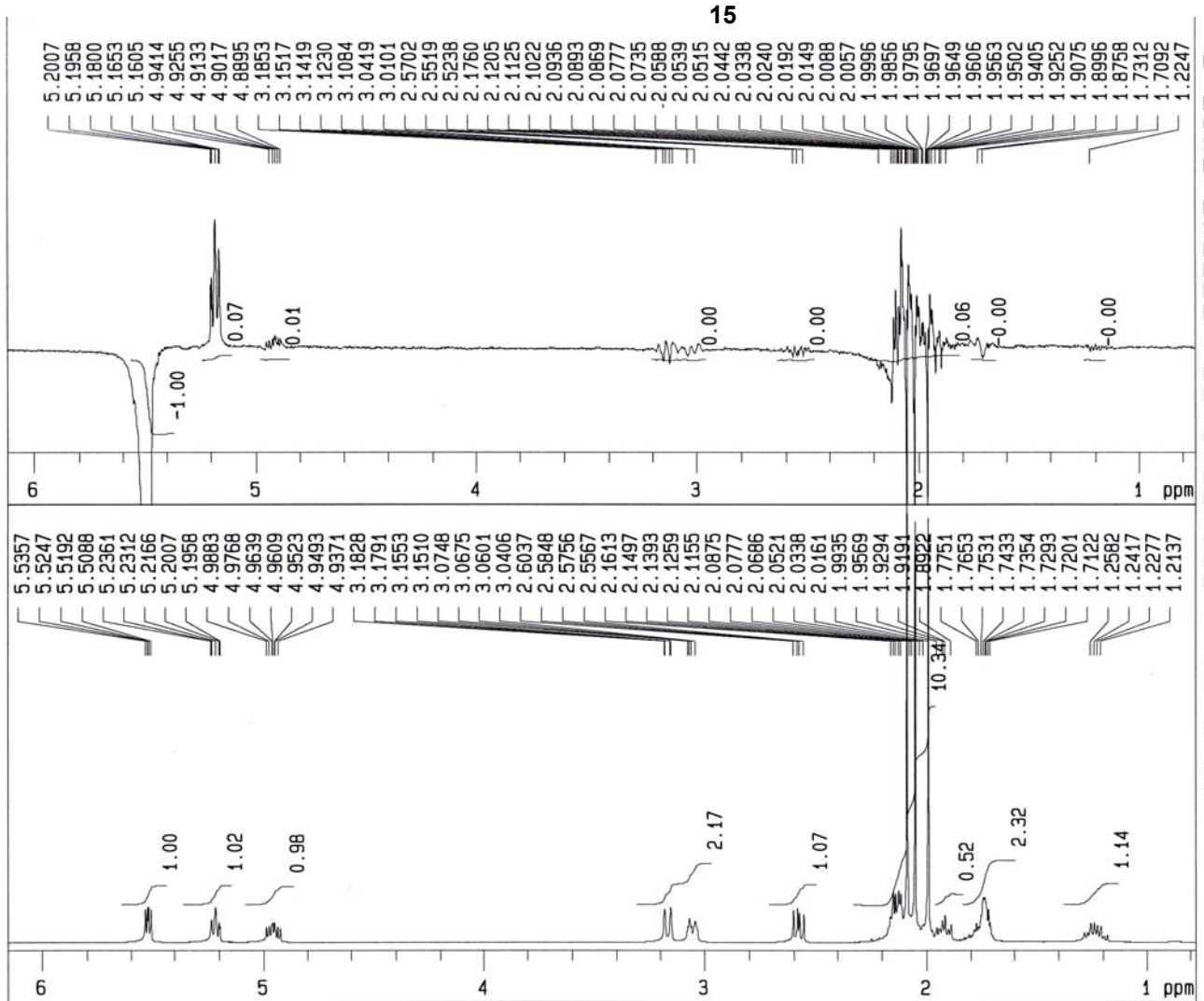
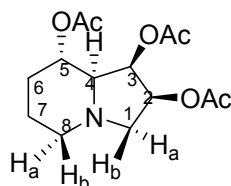




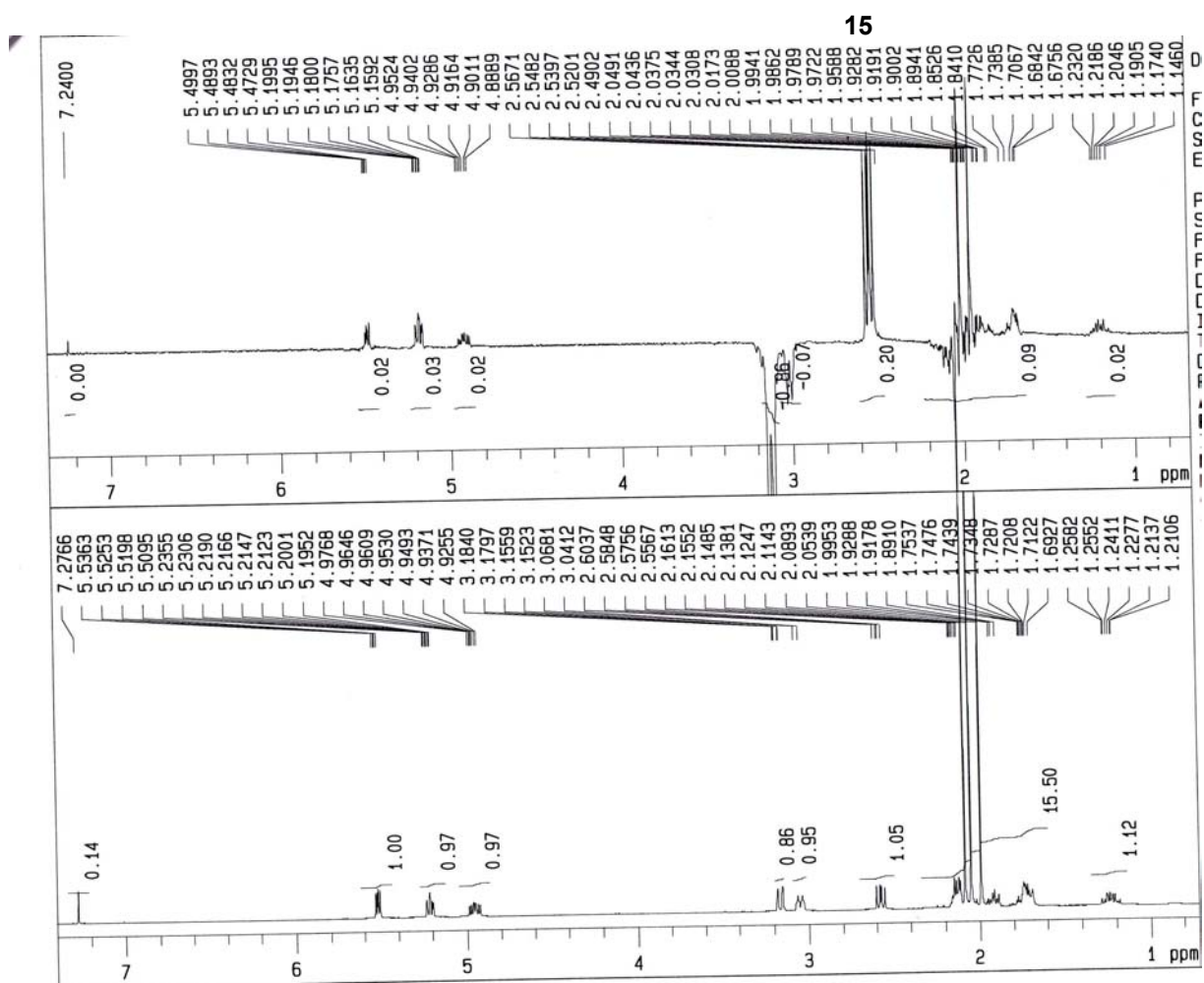
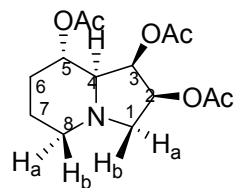
COSY spectrum of compound **15**



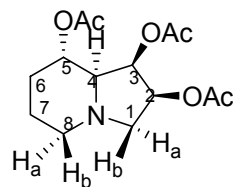
NOE spectrum of compound **15** (irradiation of H-3)



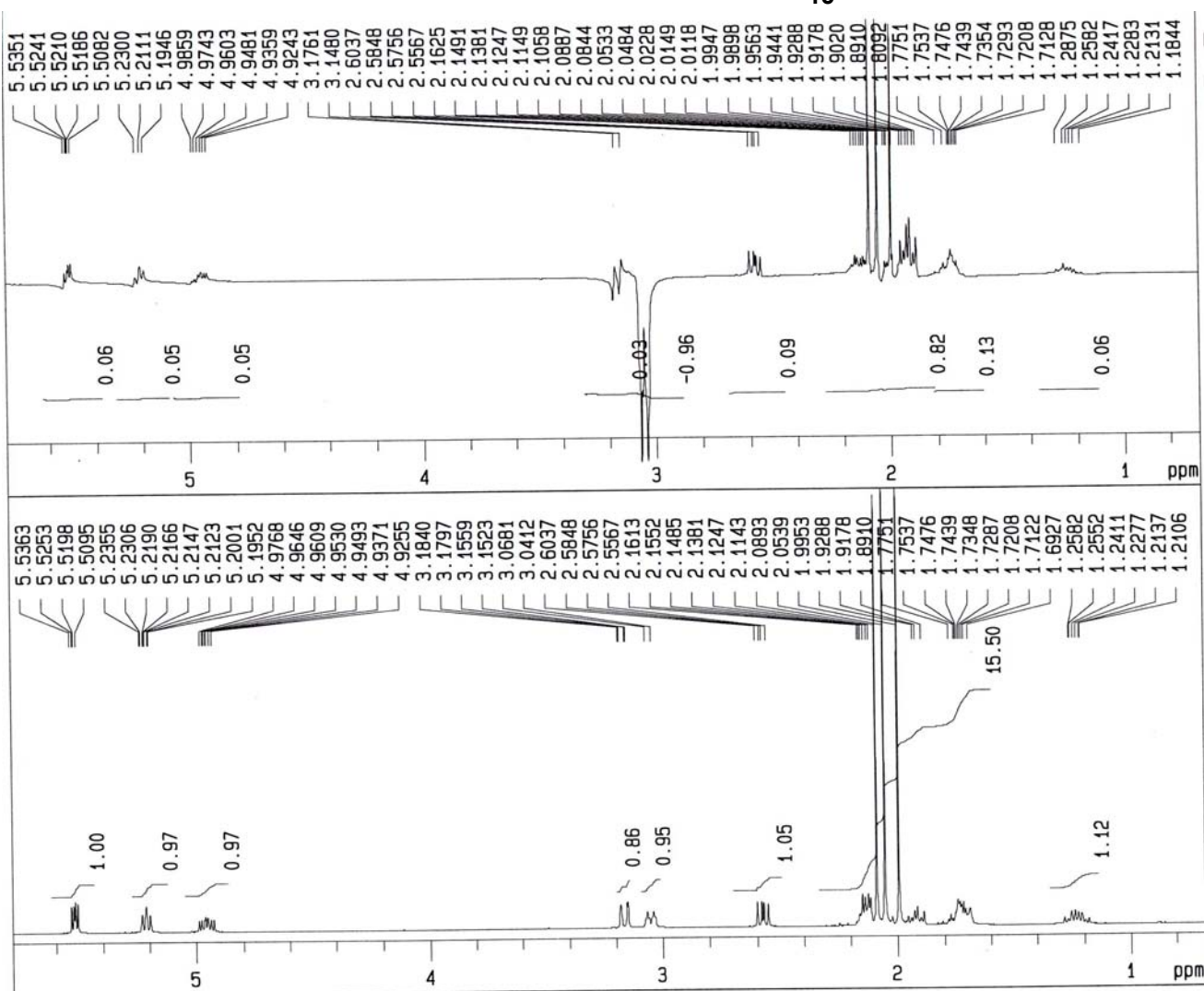
NOE spectrum of compound **15** (irradiation of H-1_a)



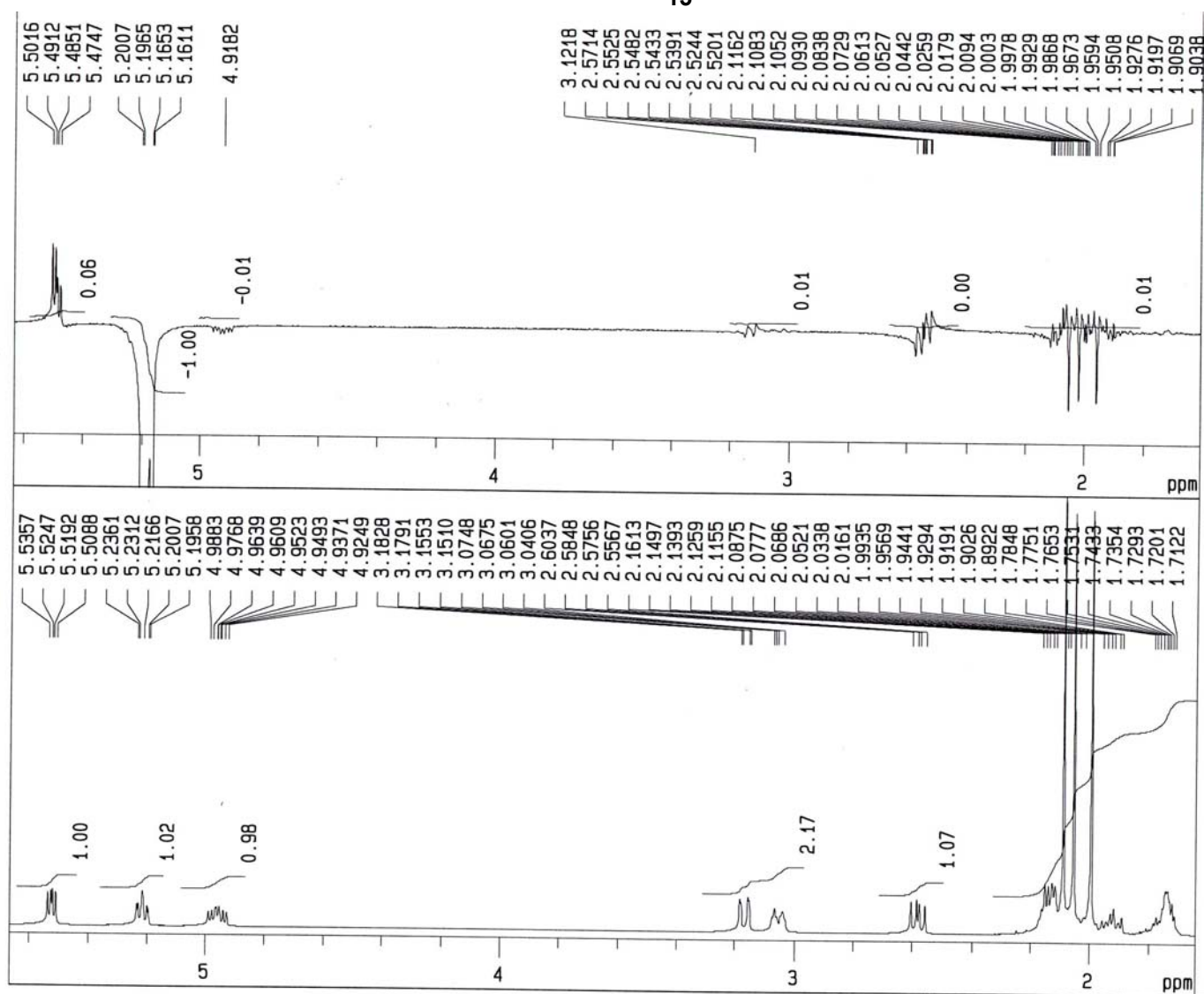
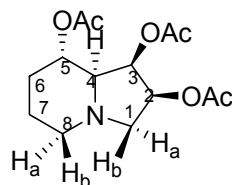
NOE spectrum of compound **15** (irradiation of H-8_b)



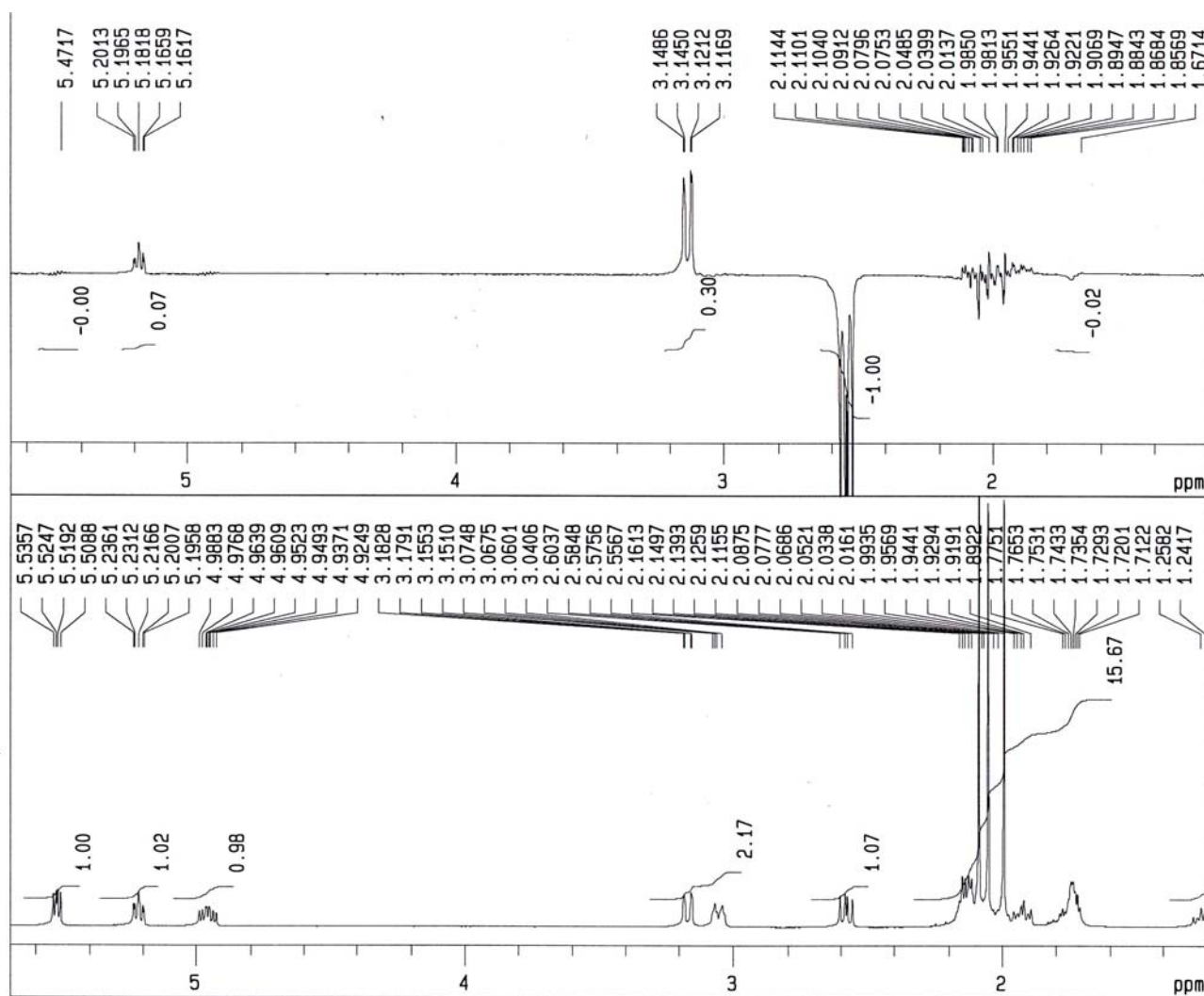
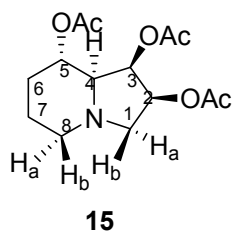
15

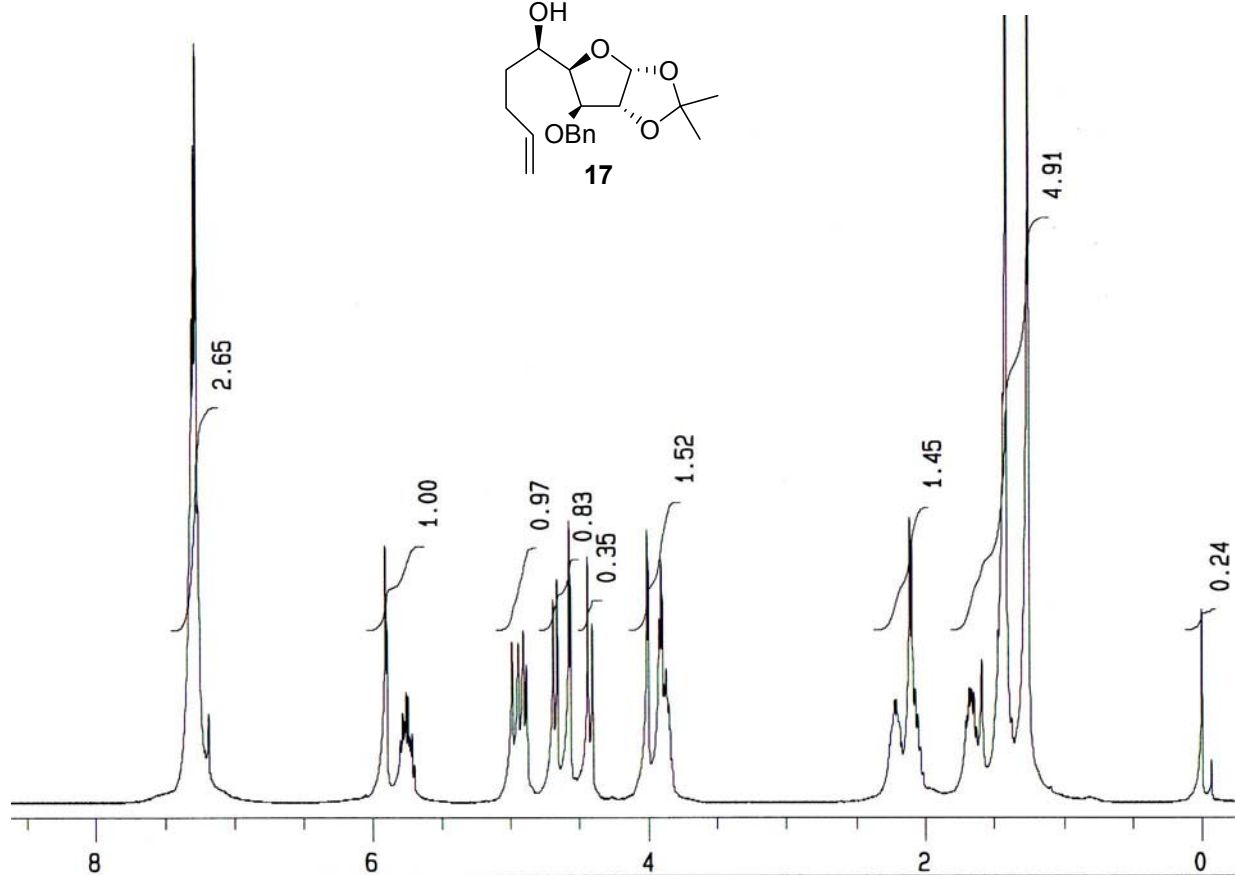
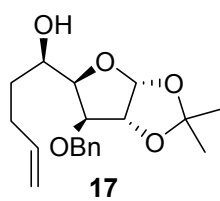


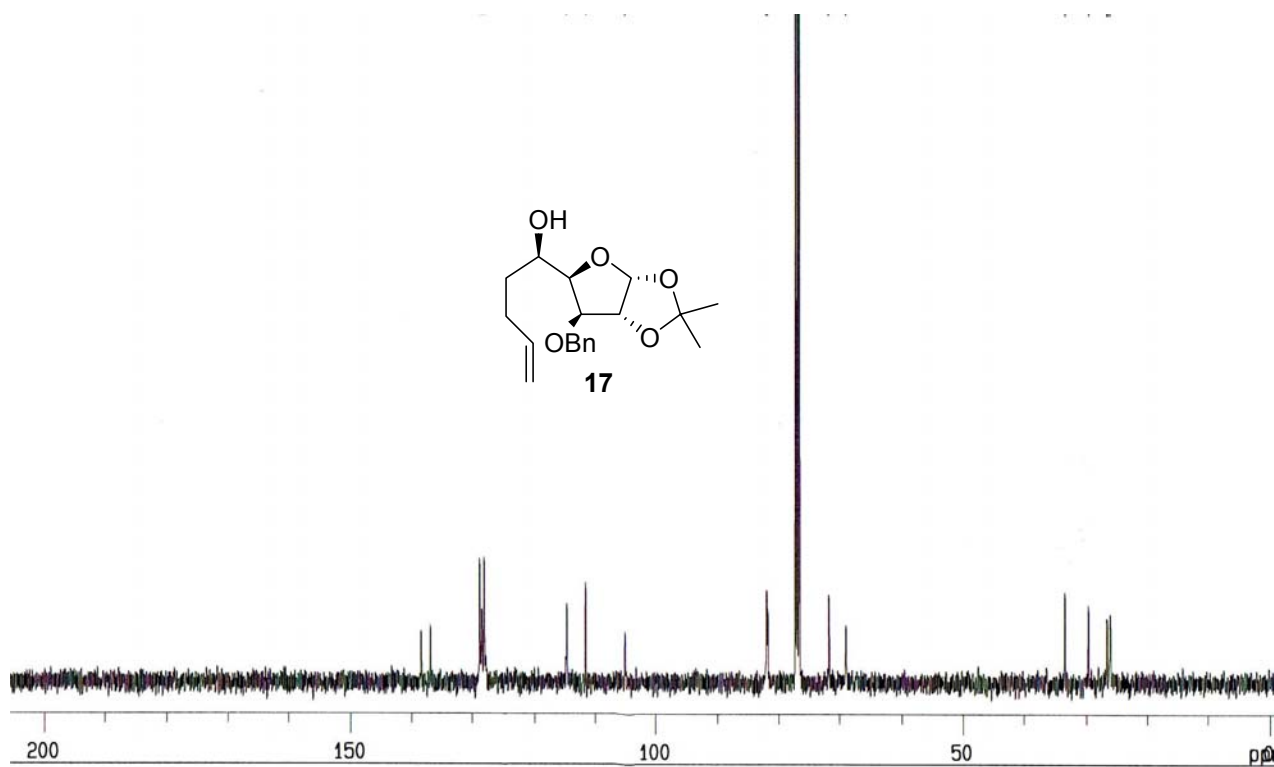
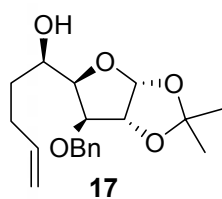
NOE spectrum of compound **15** (irradiation of H-2)

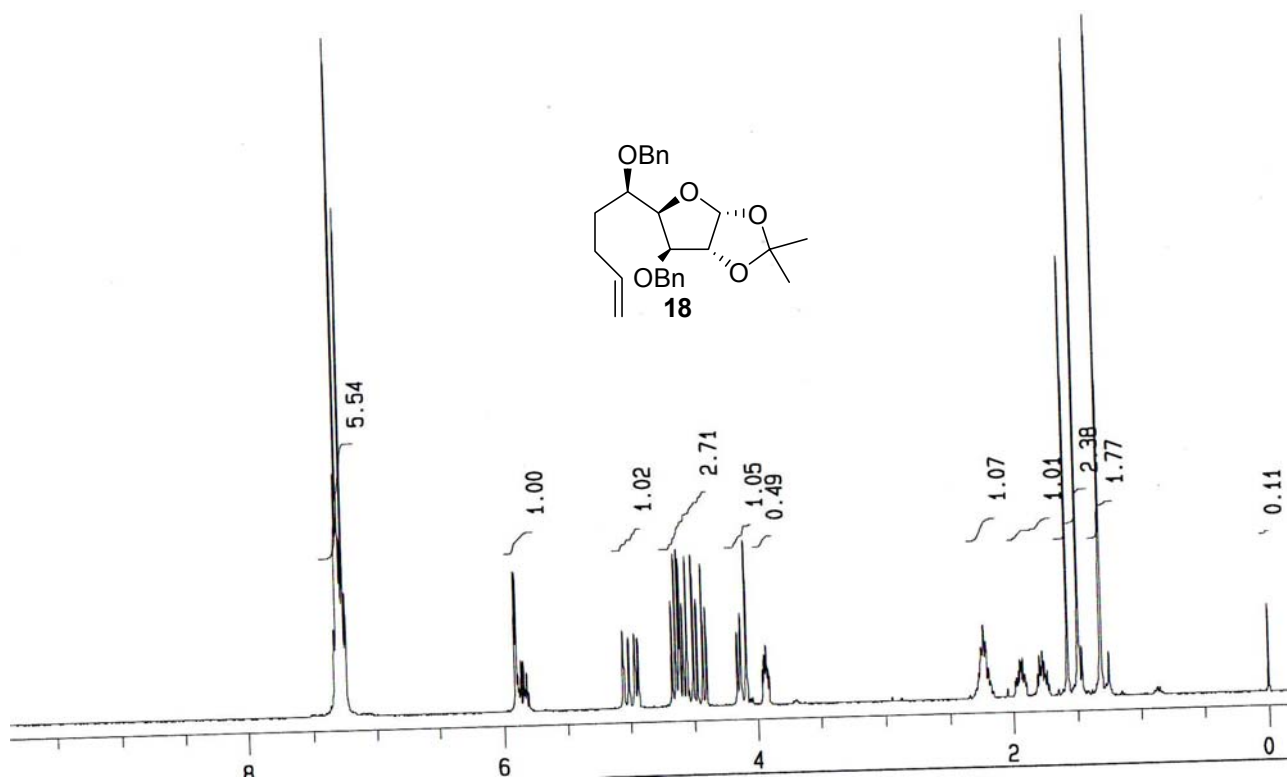
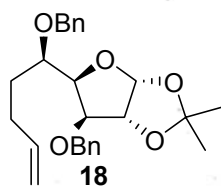


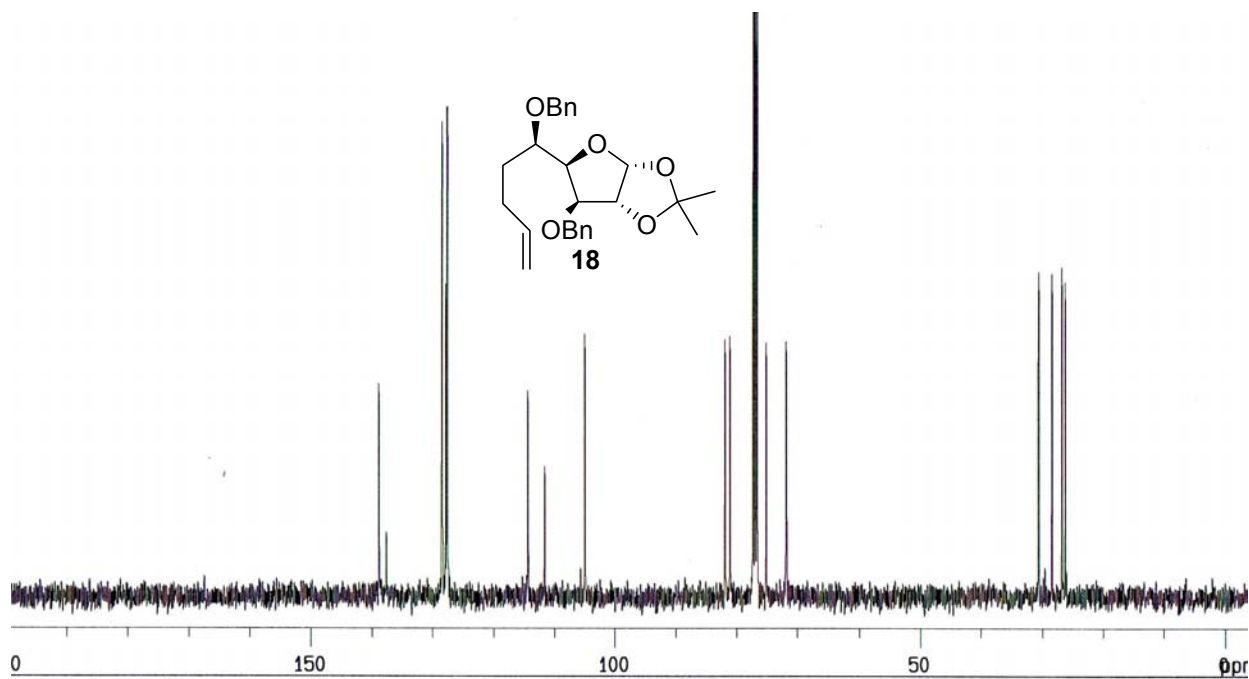
NOE spectrum of compound **15** (irradiation of H-1_b)

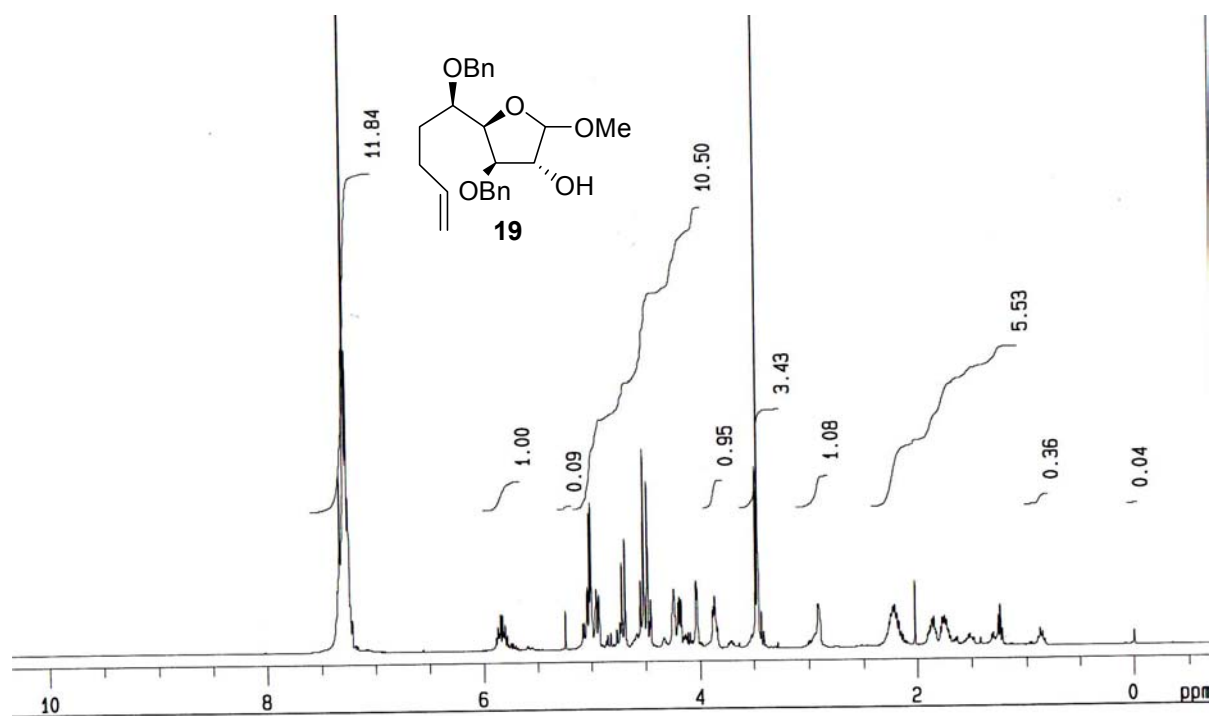


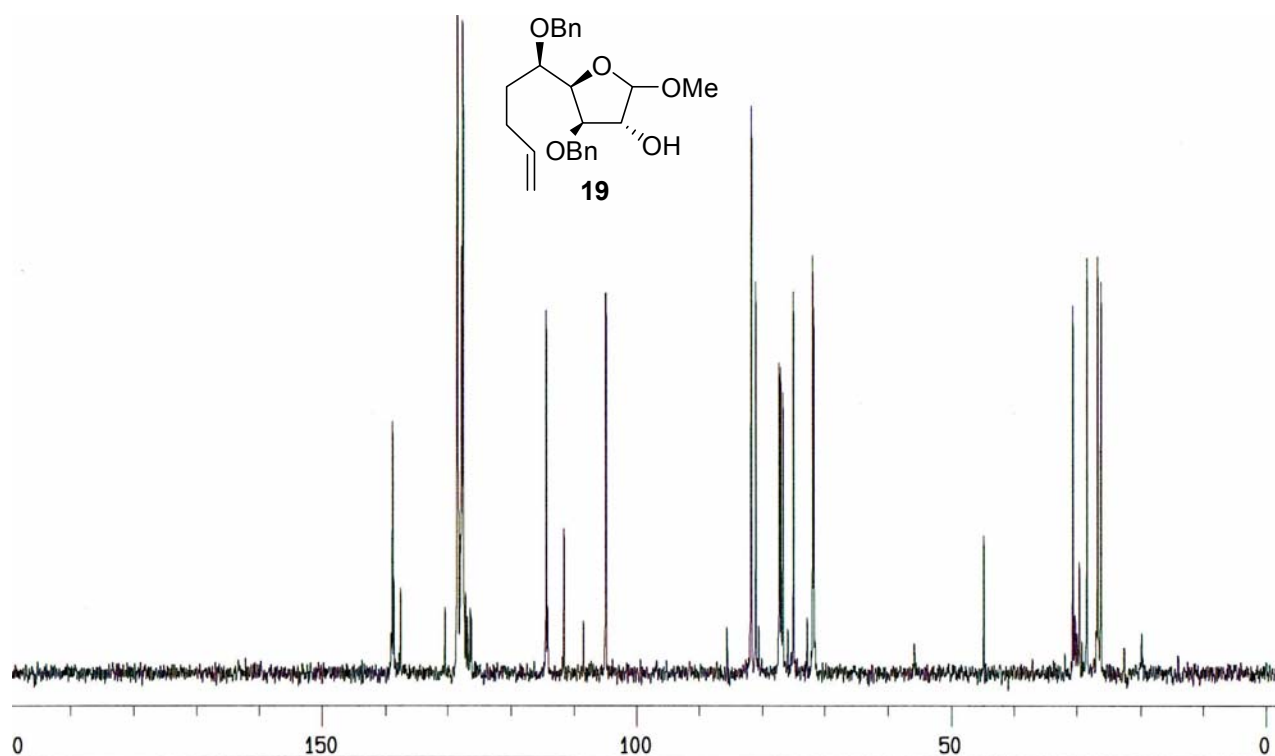


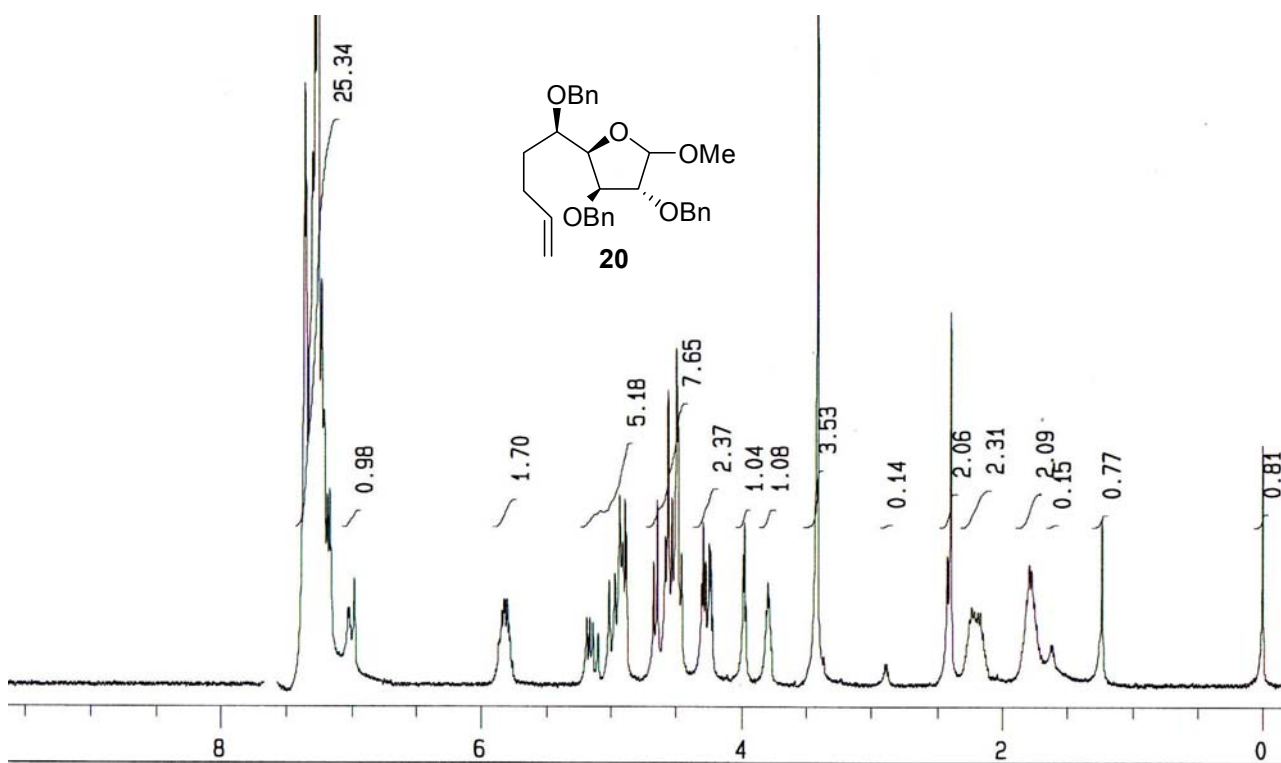


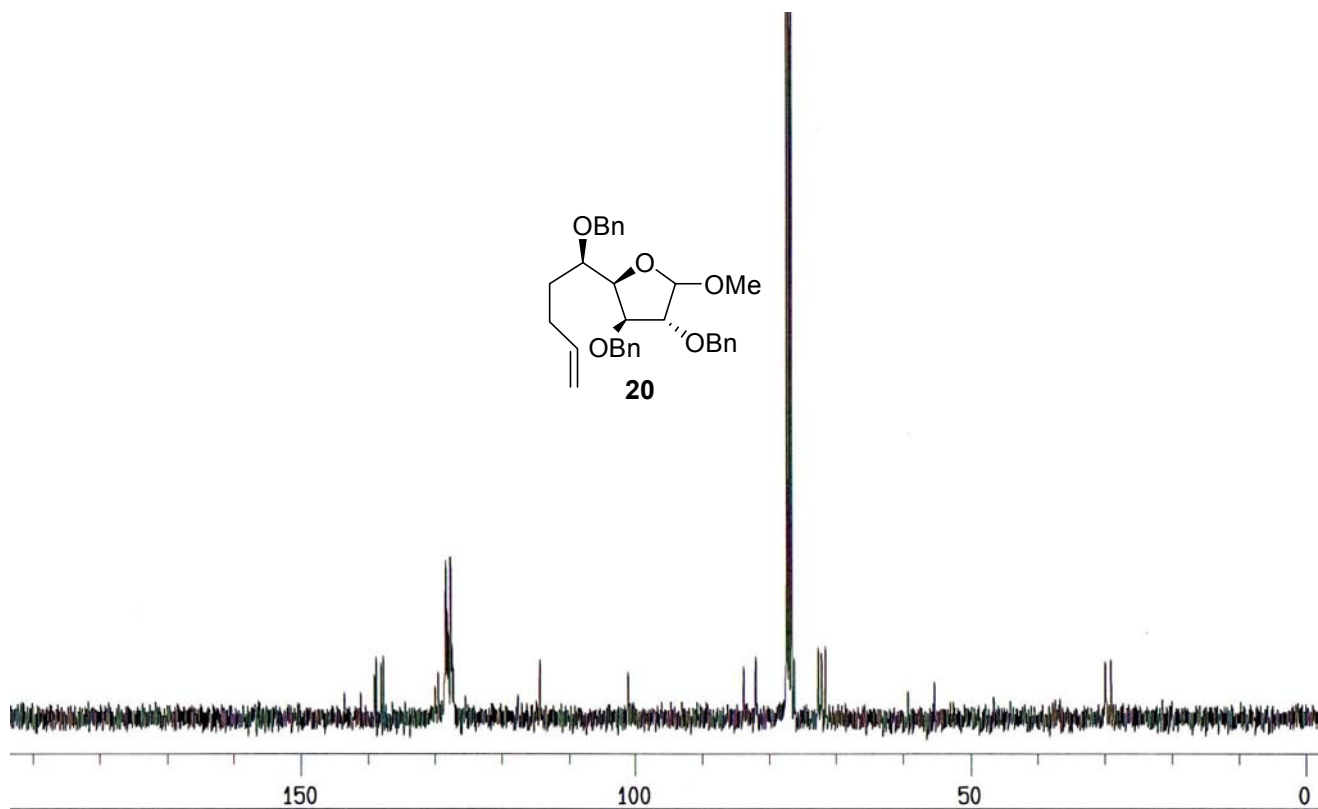


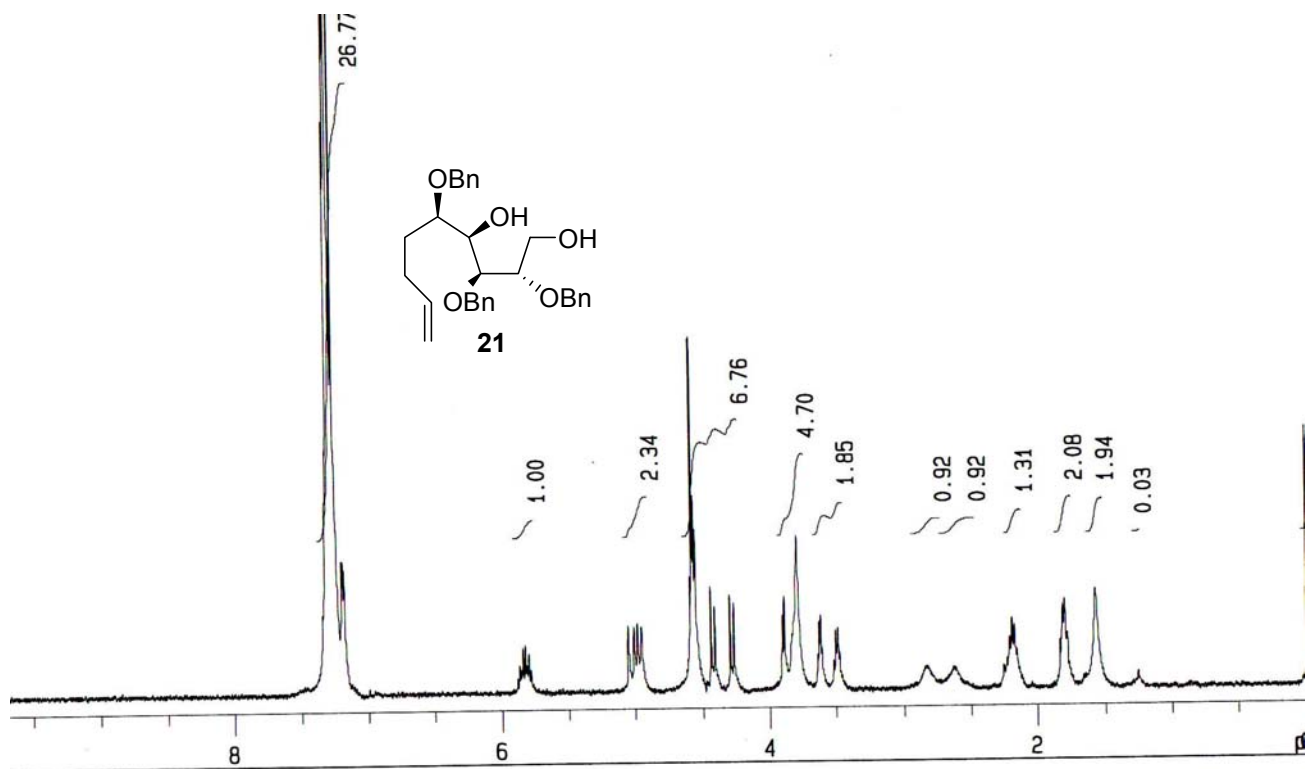


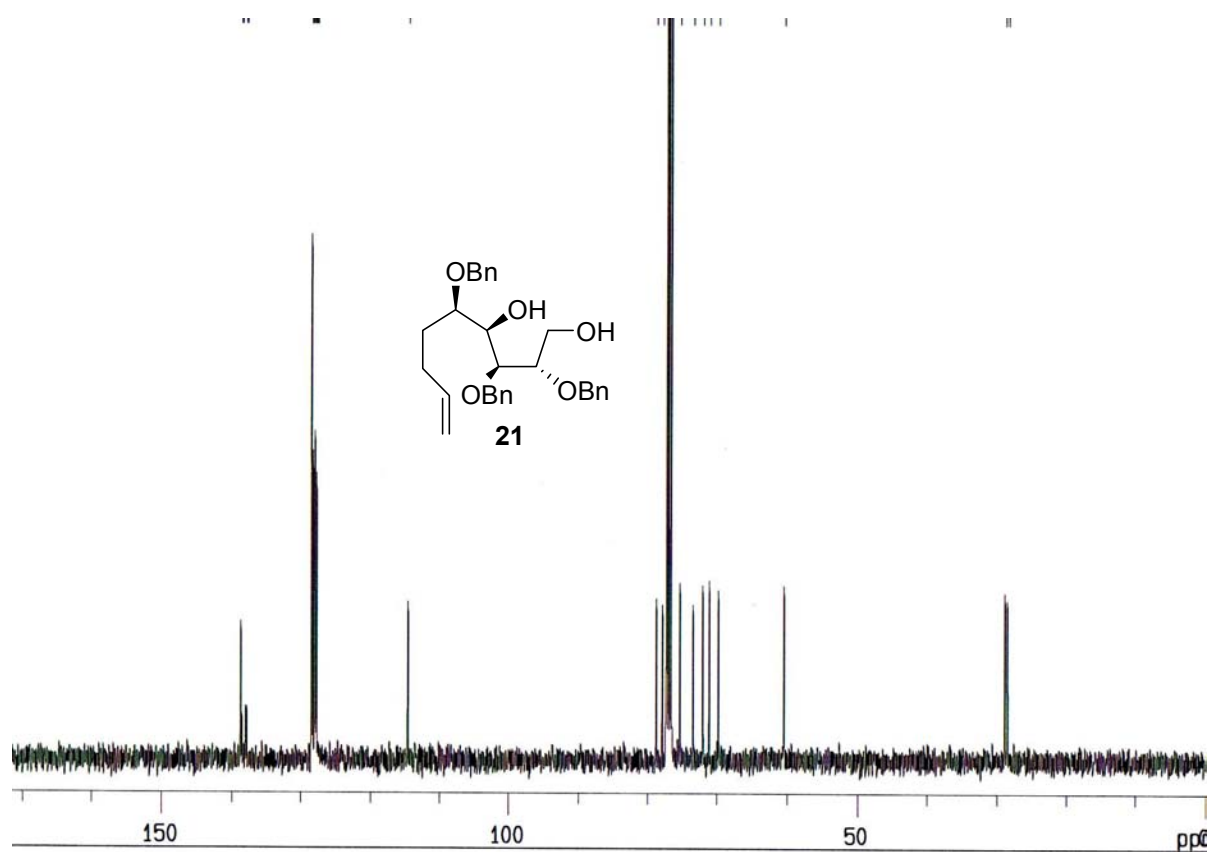


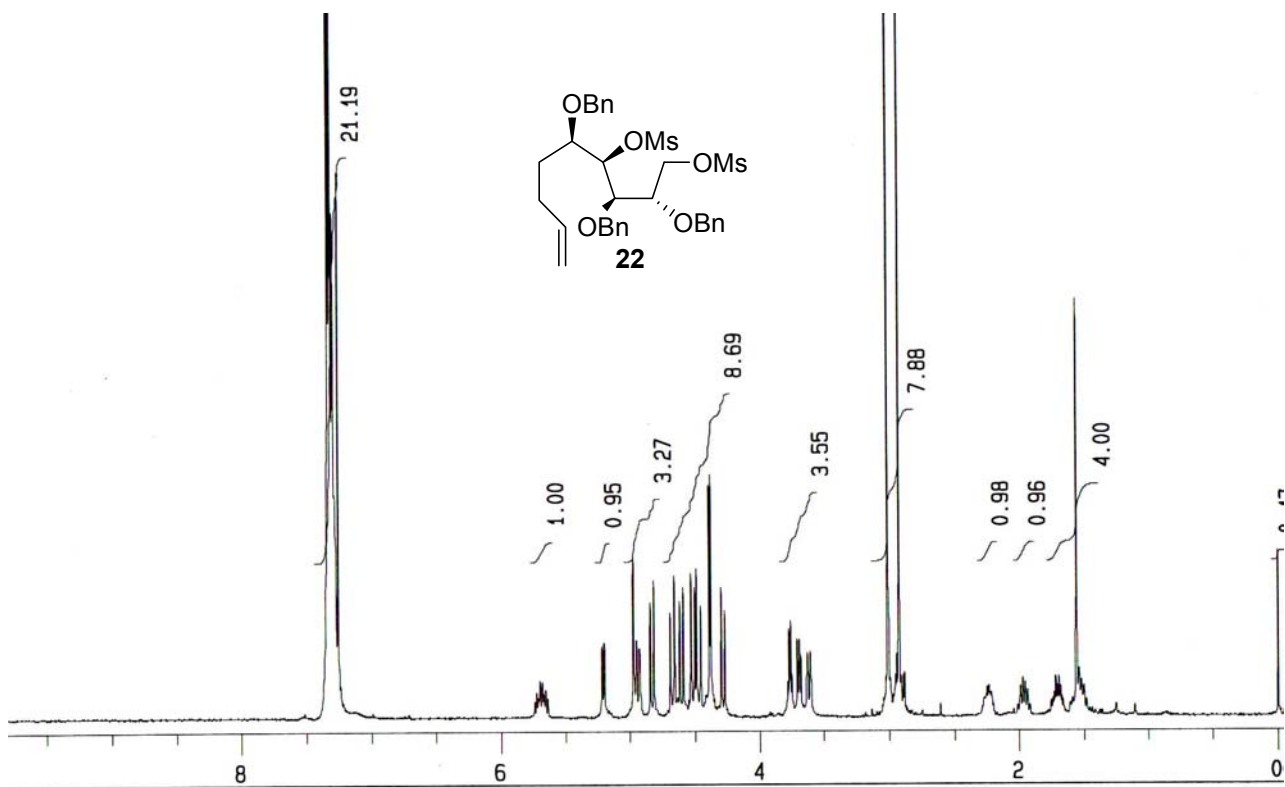


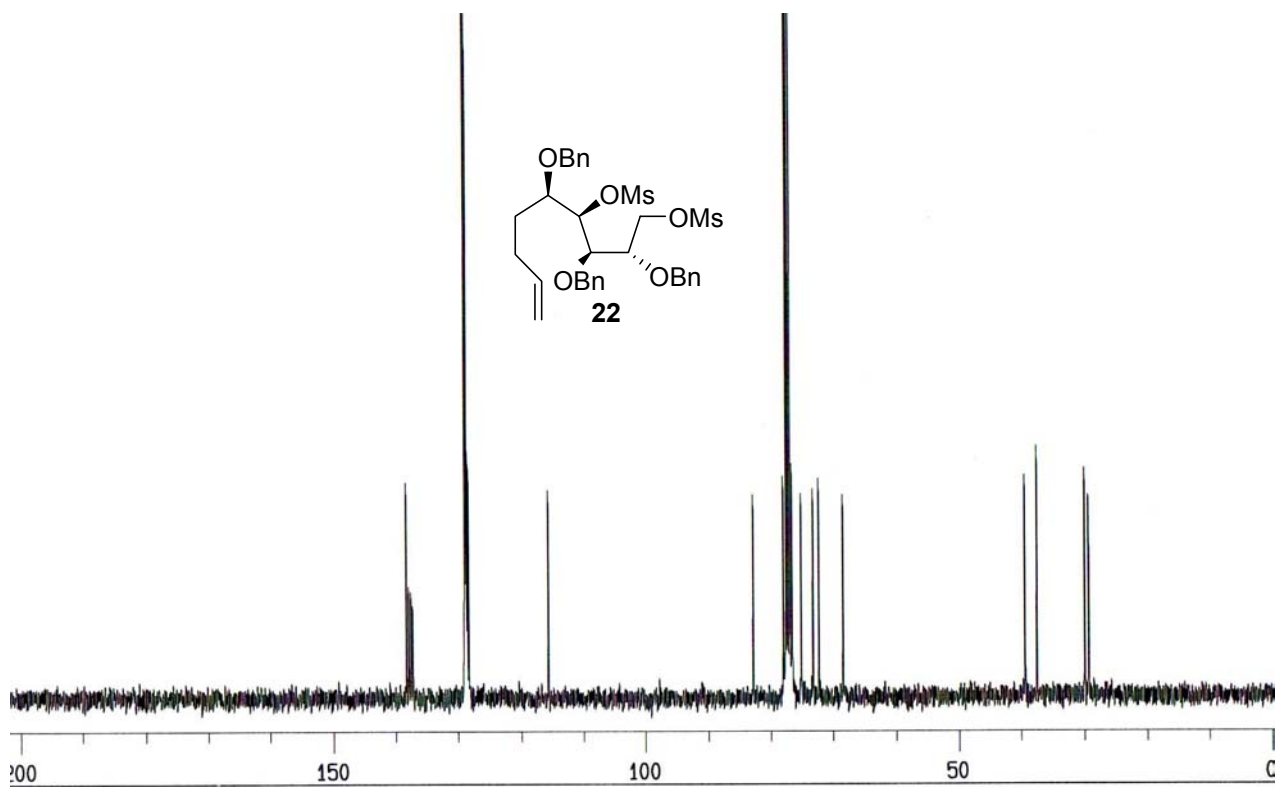


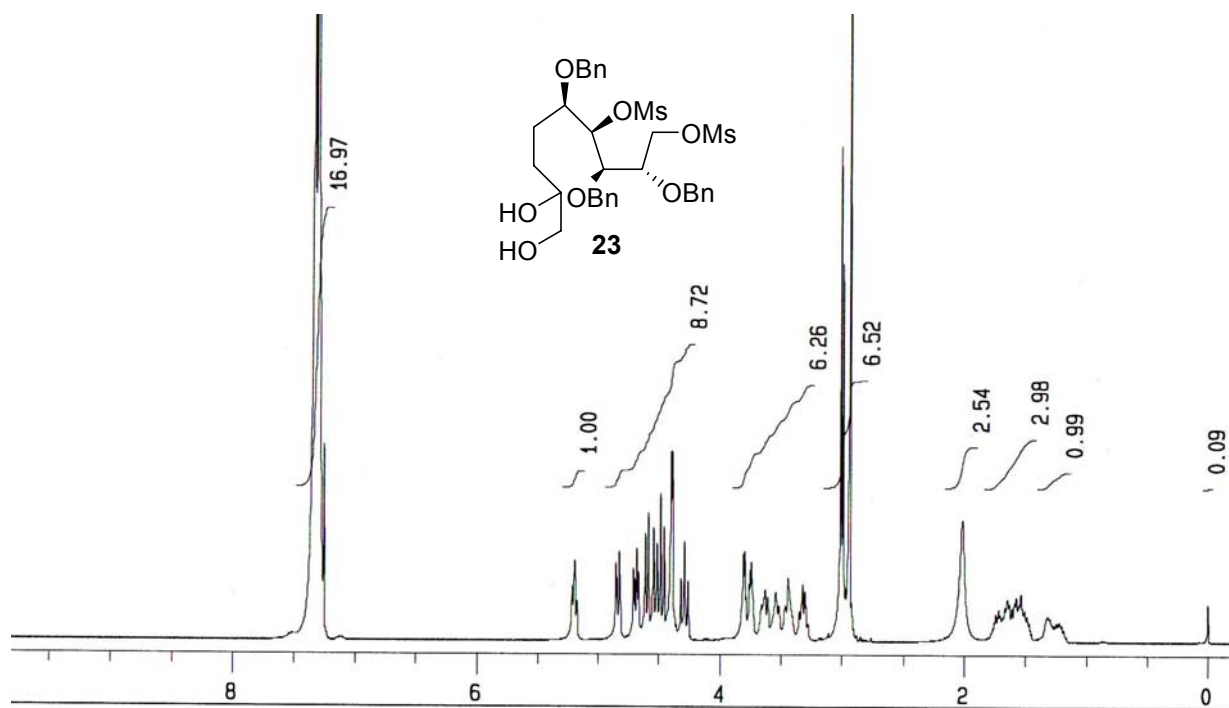


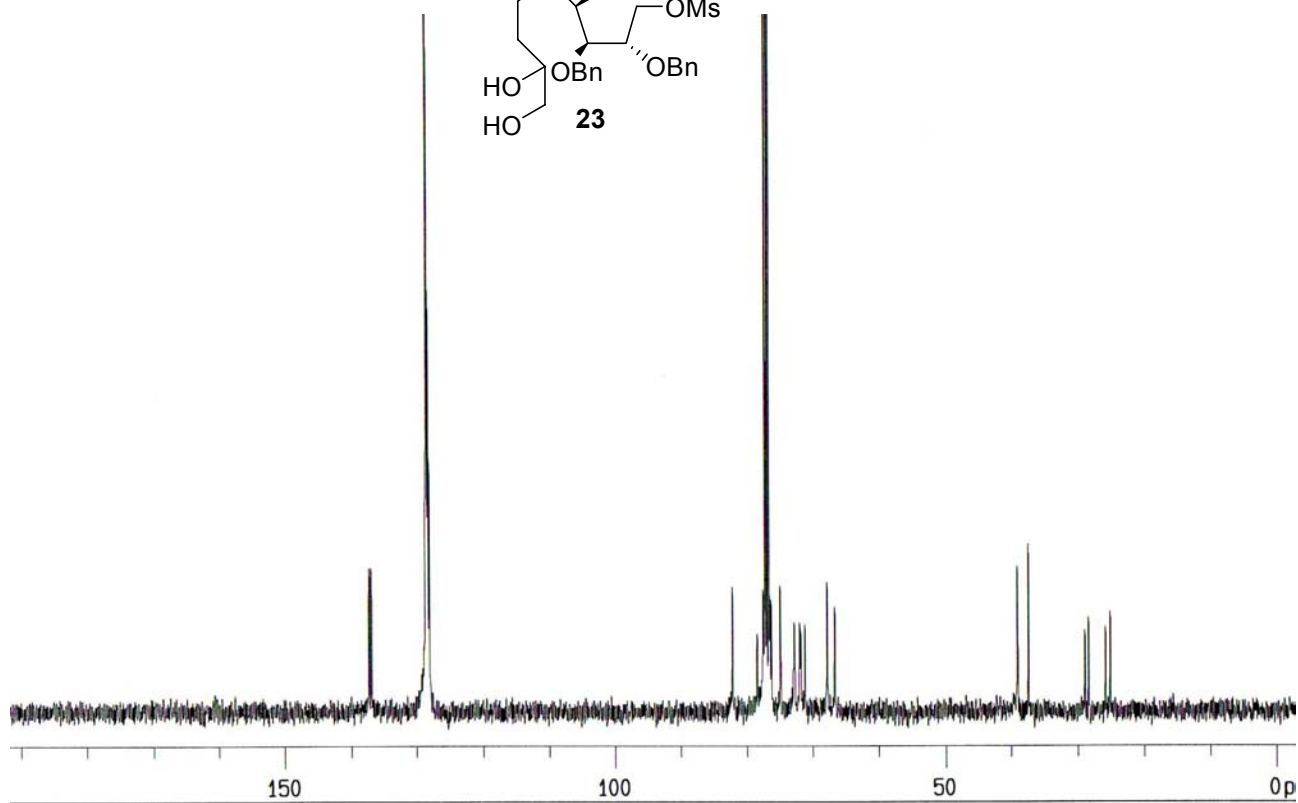
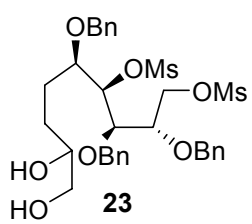


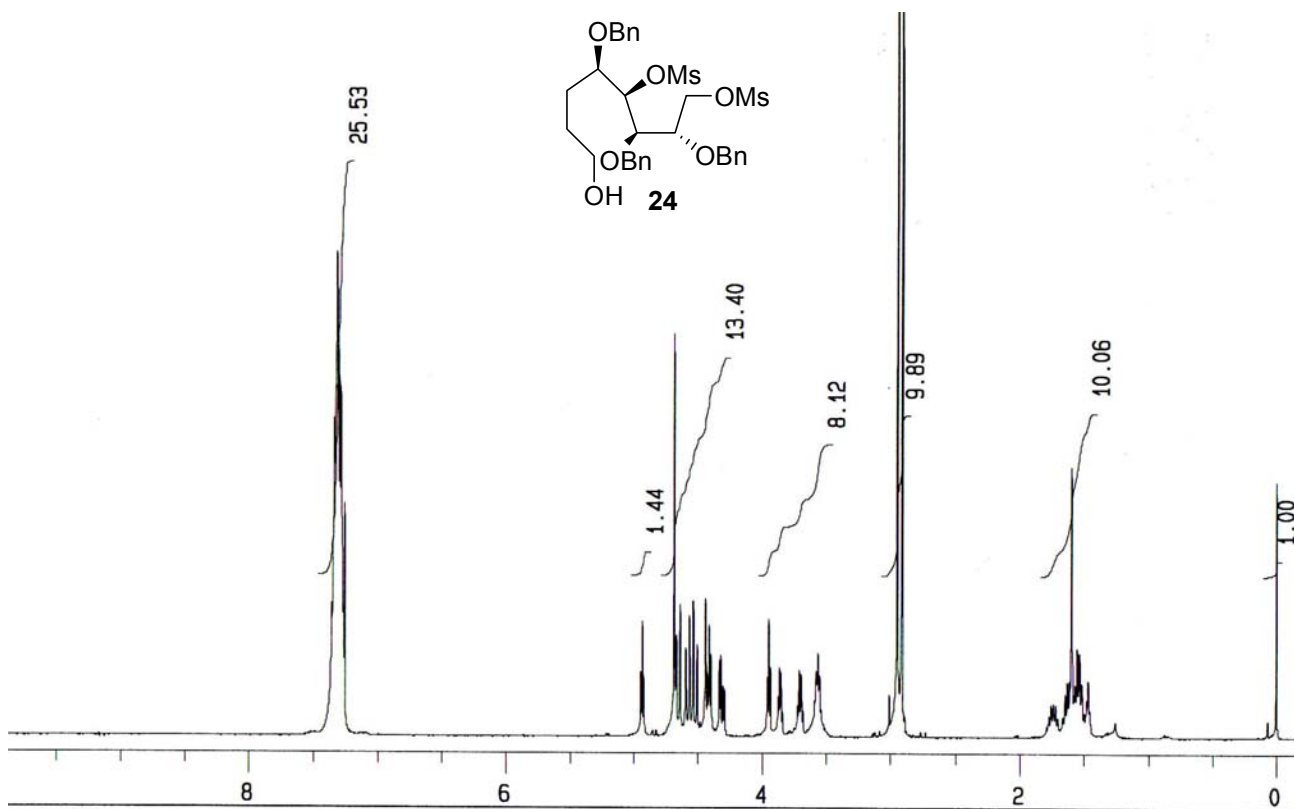


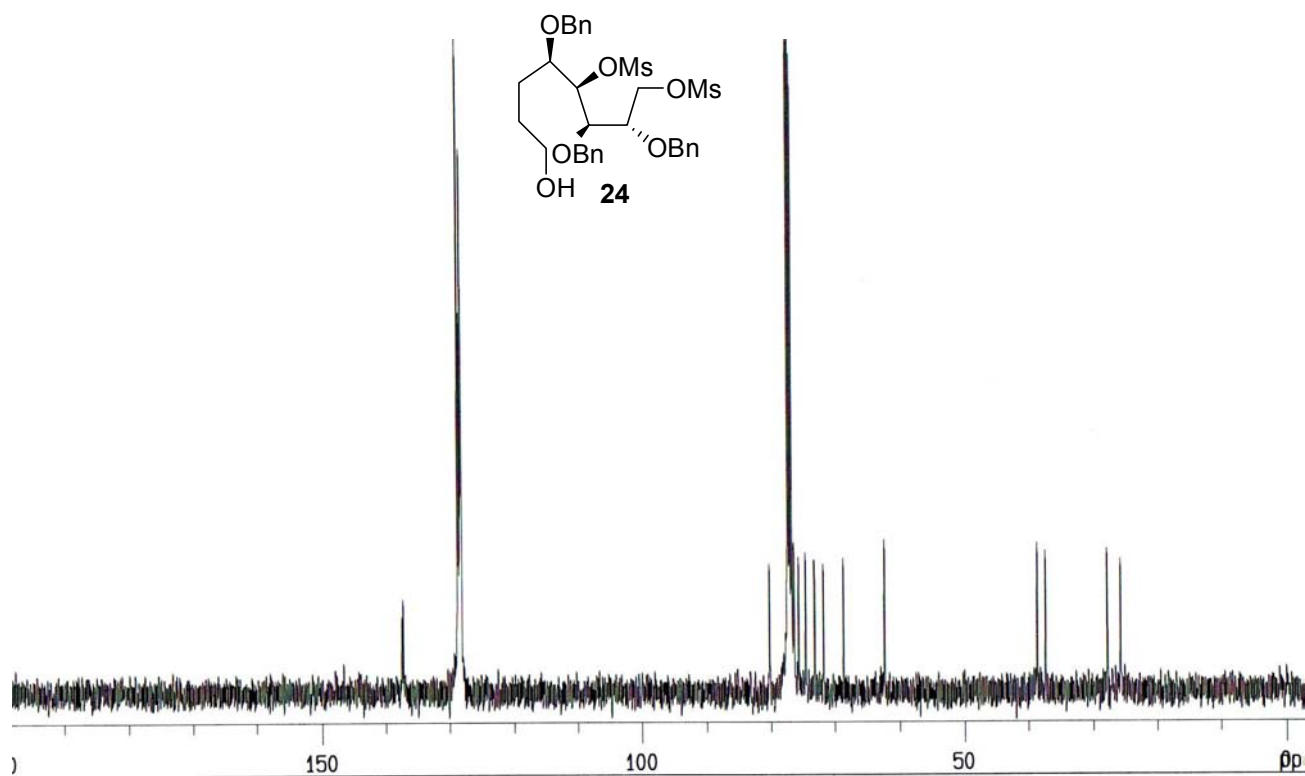


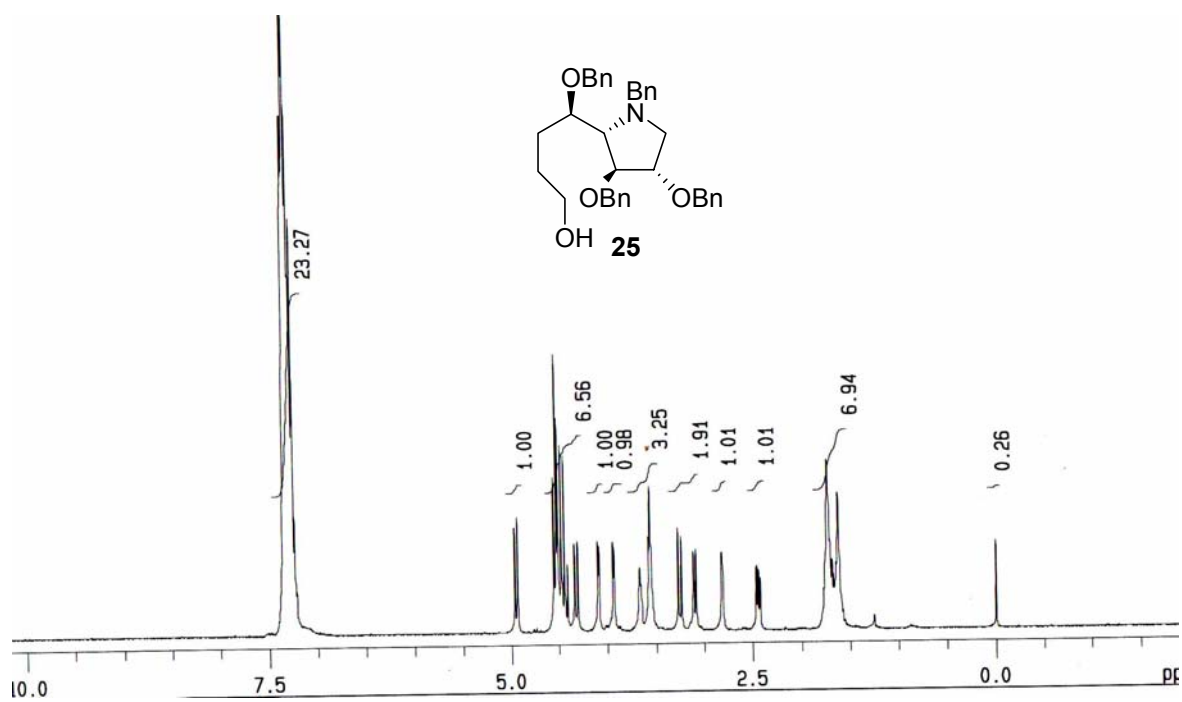


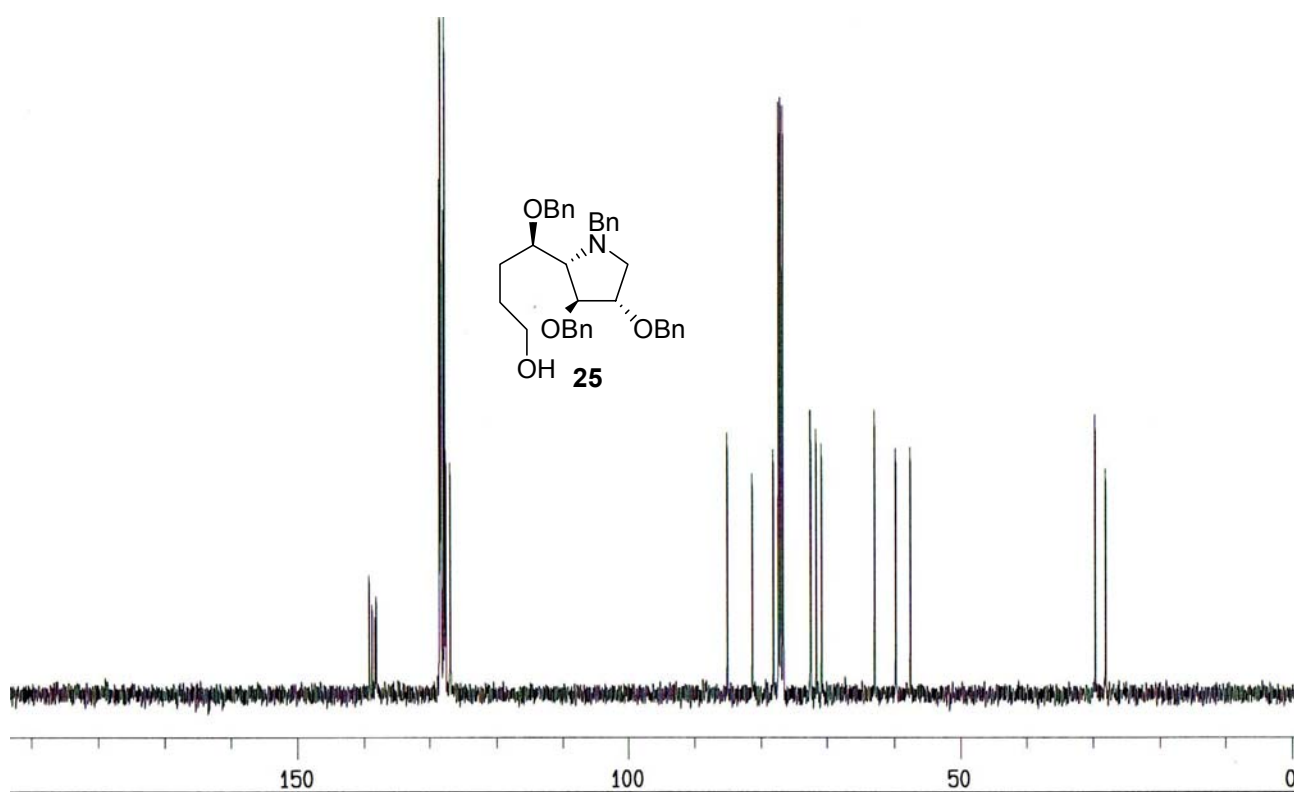




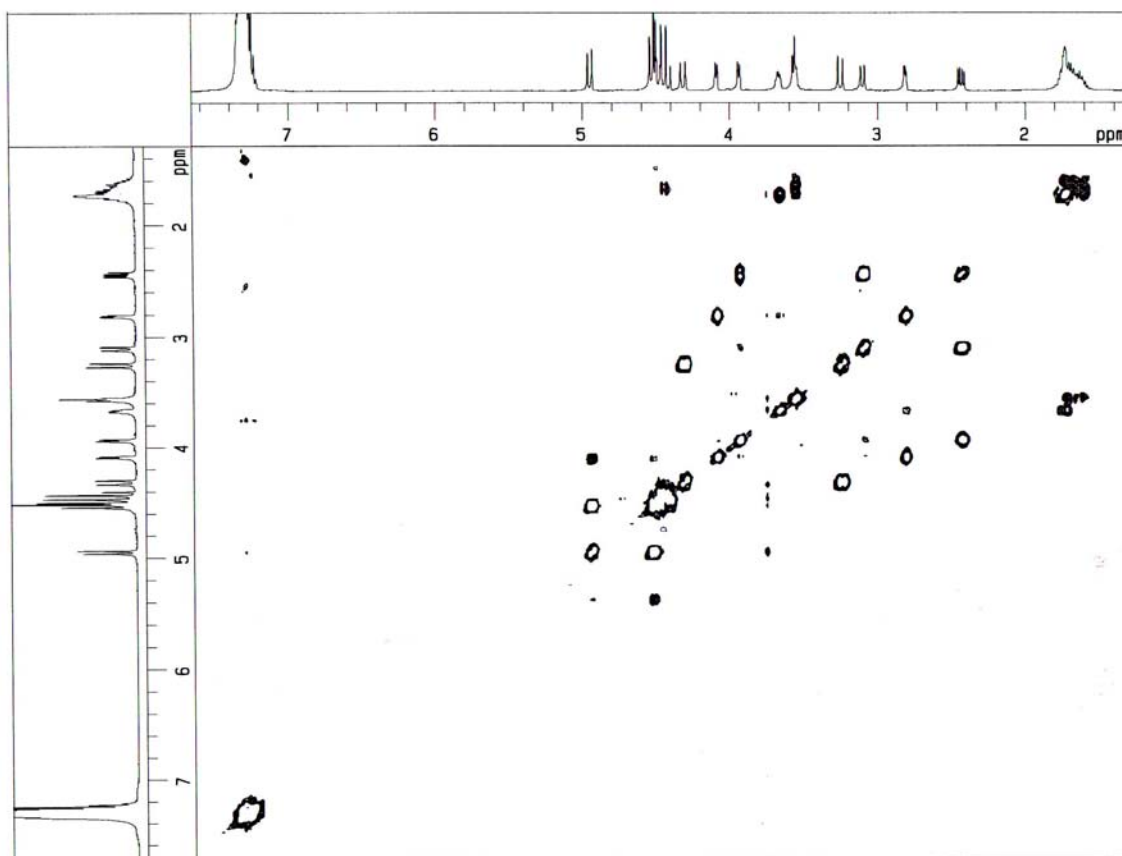
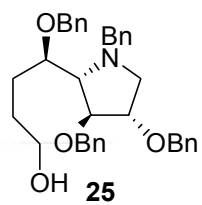


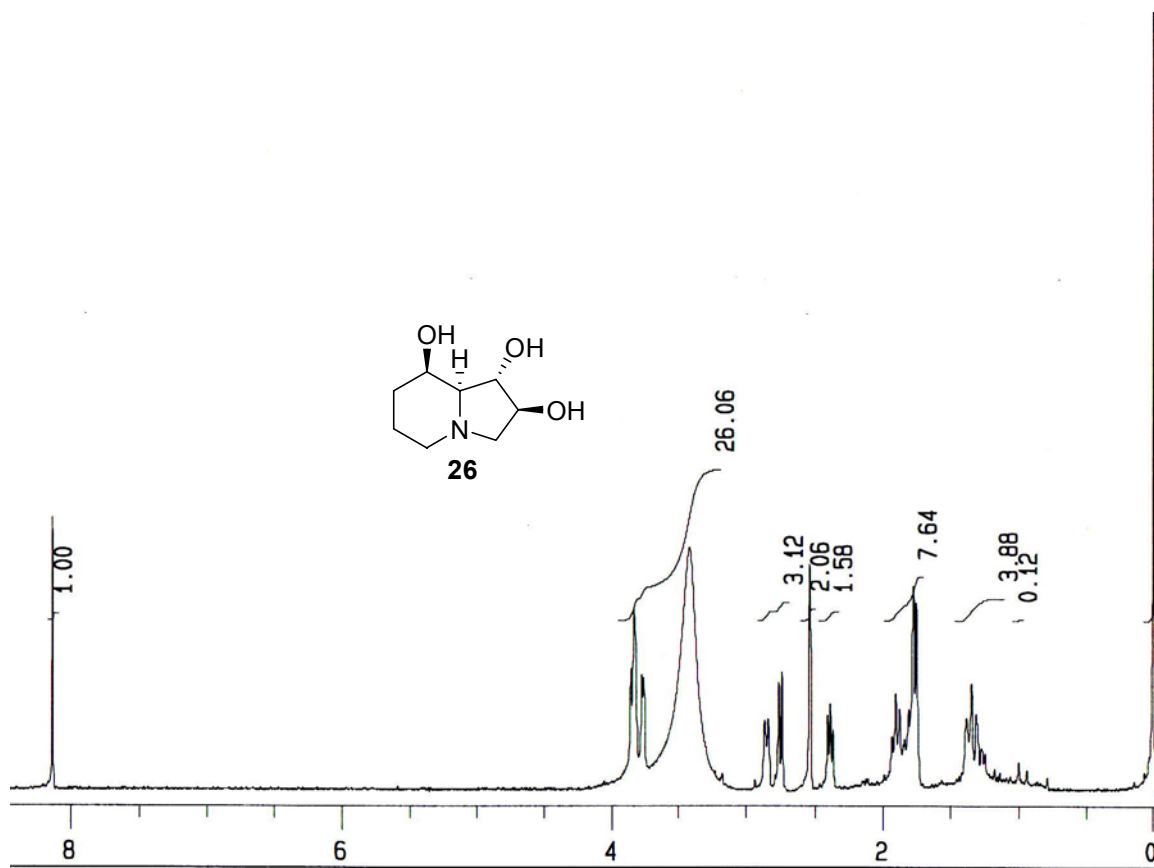
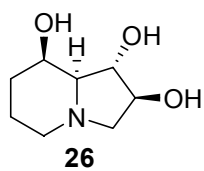


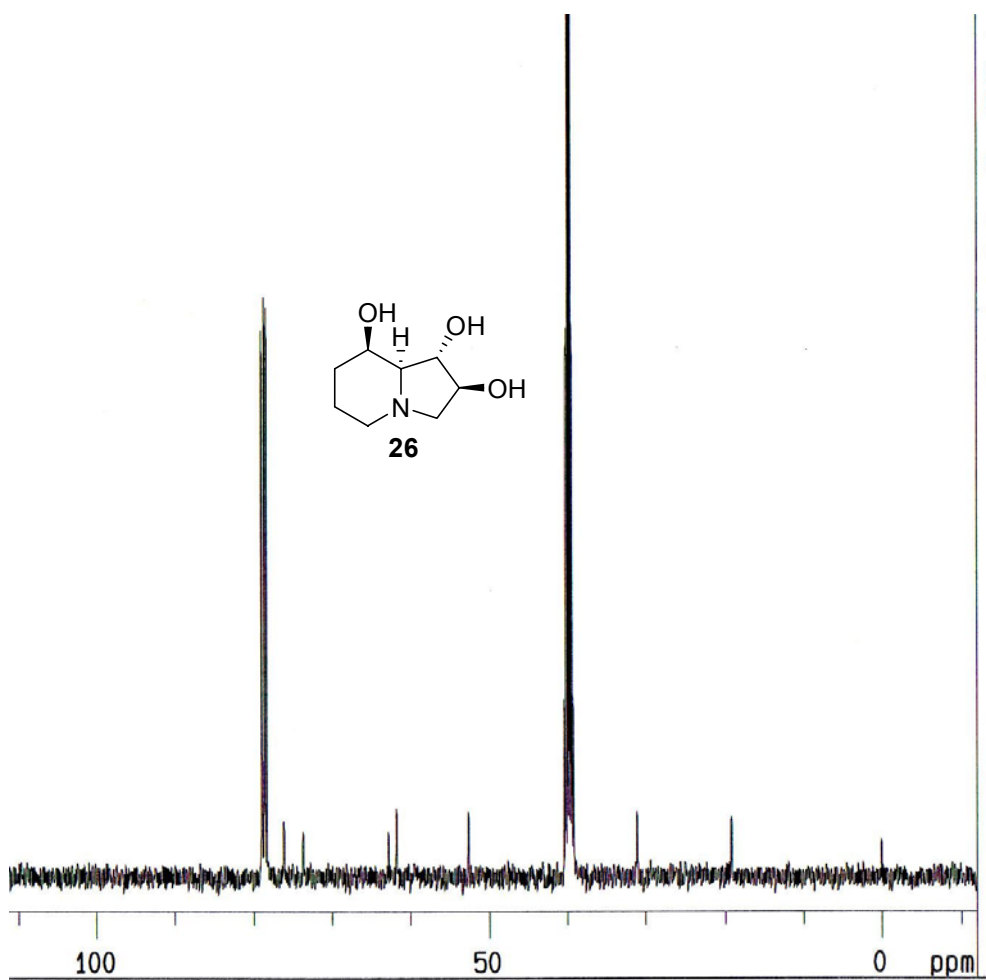




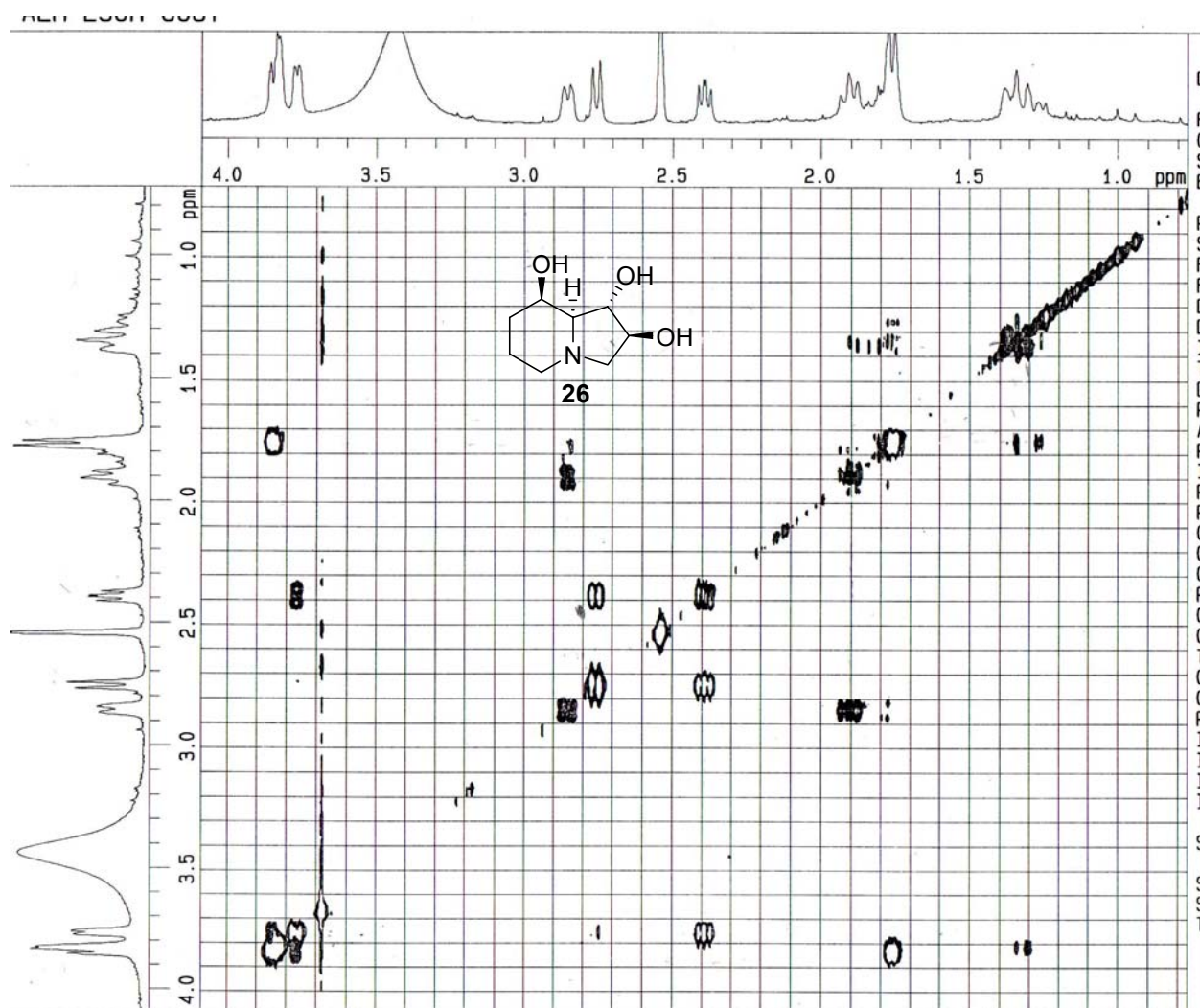
COSY spectrum of compound **25**



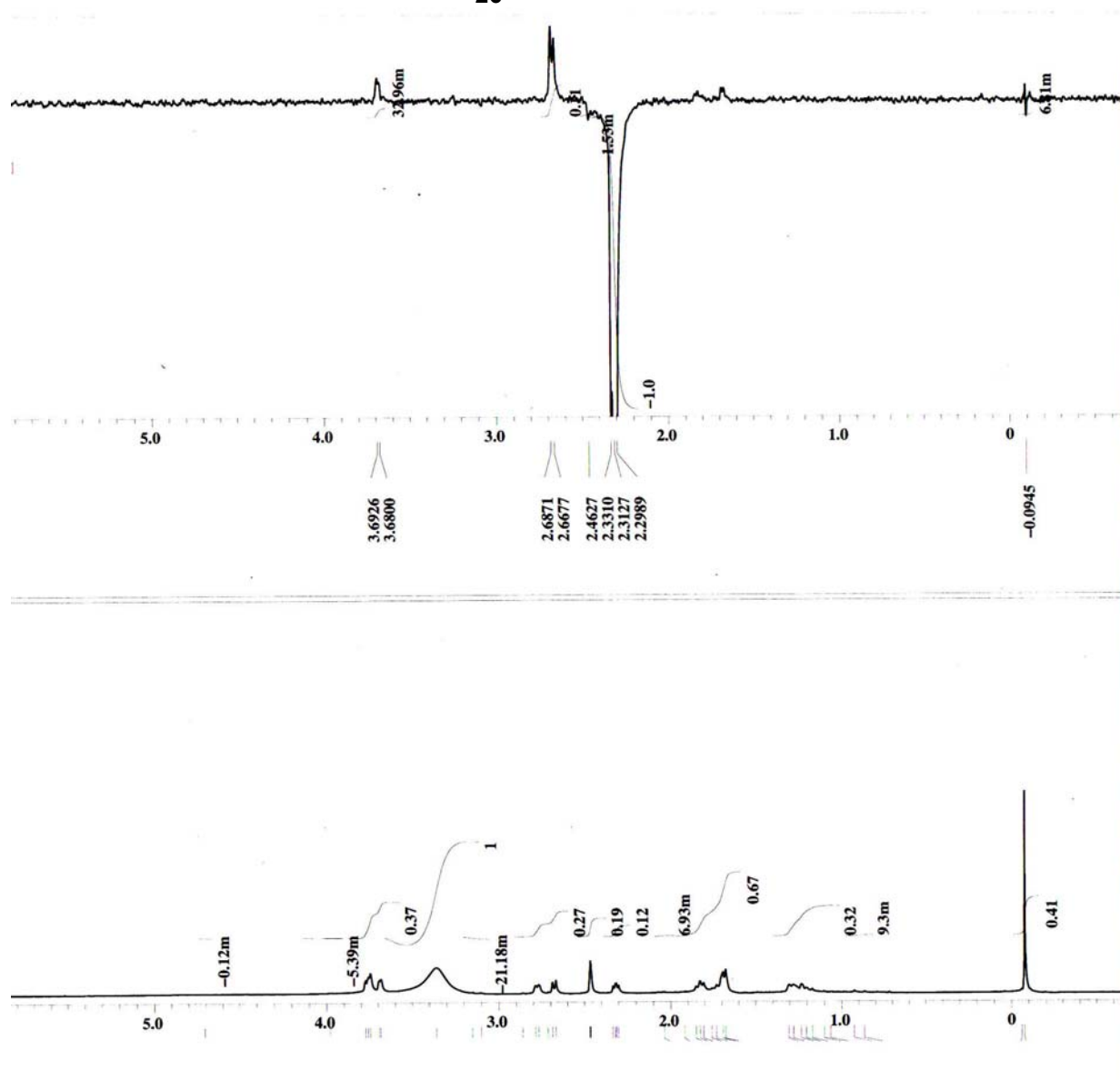
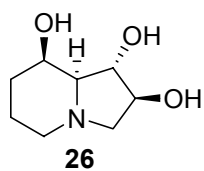




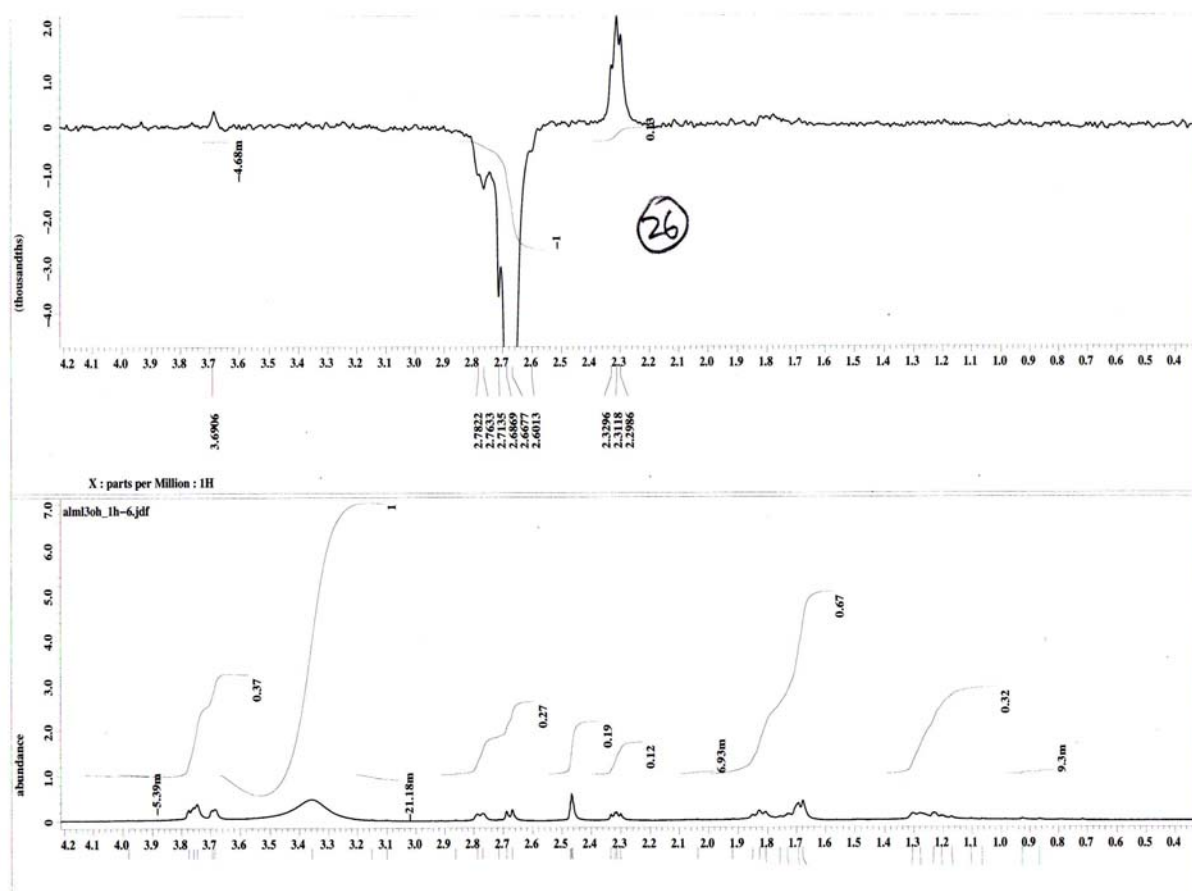
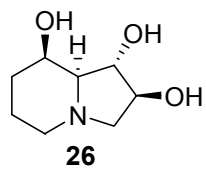
COSY spectrum of compound **26**



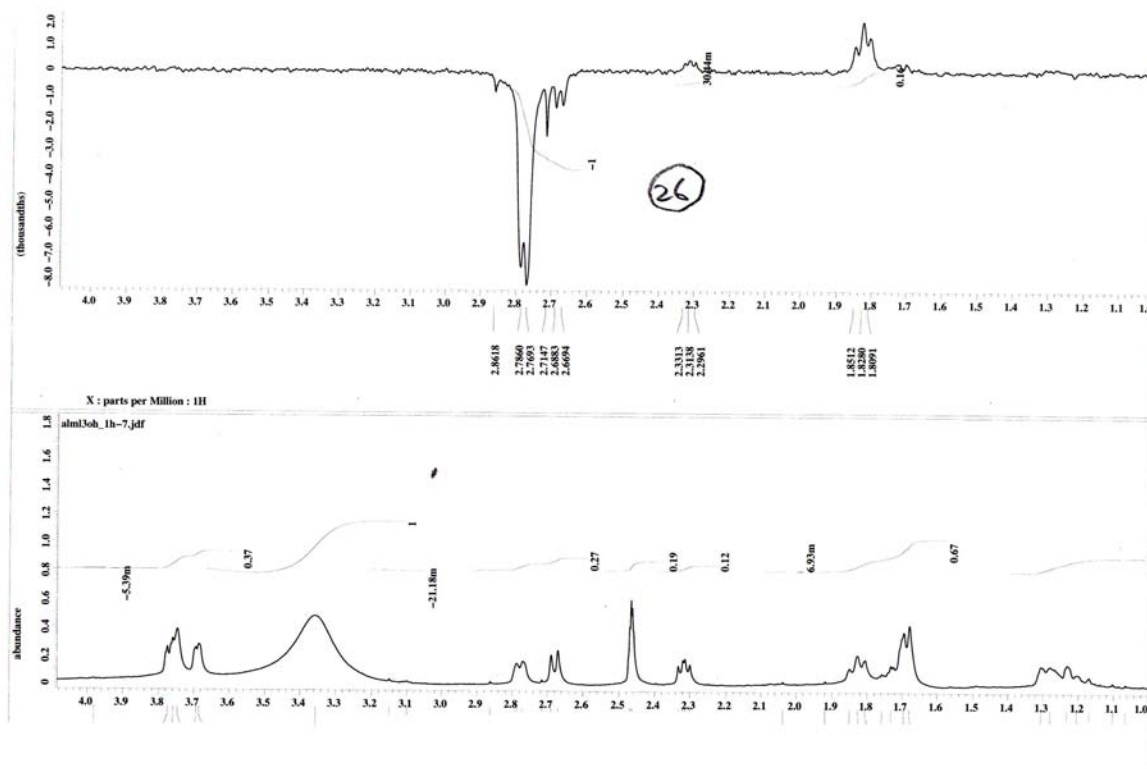
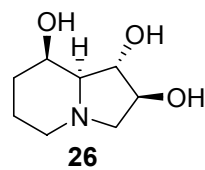
NOE spectrum of compound **26**

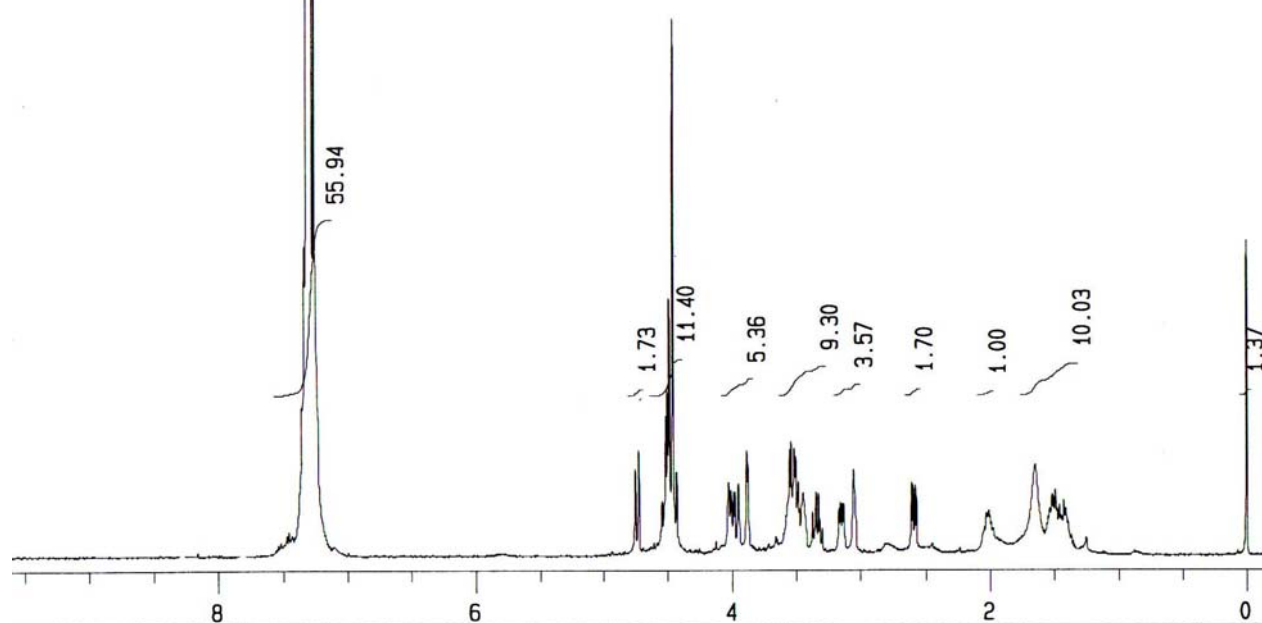
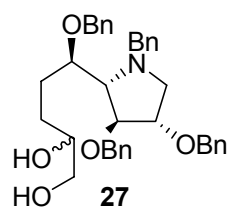


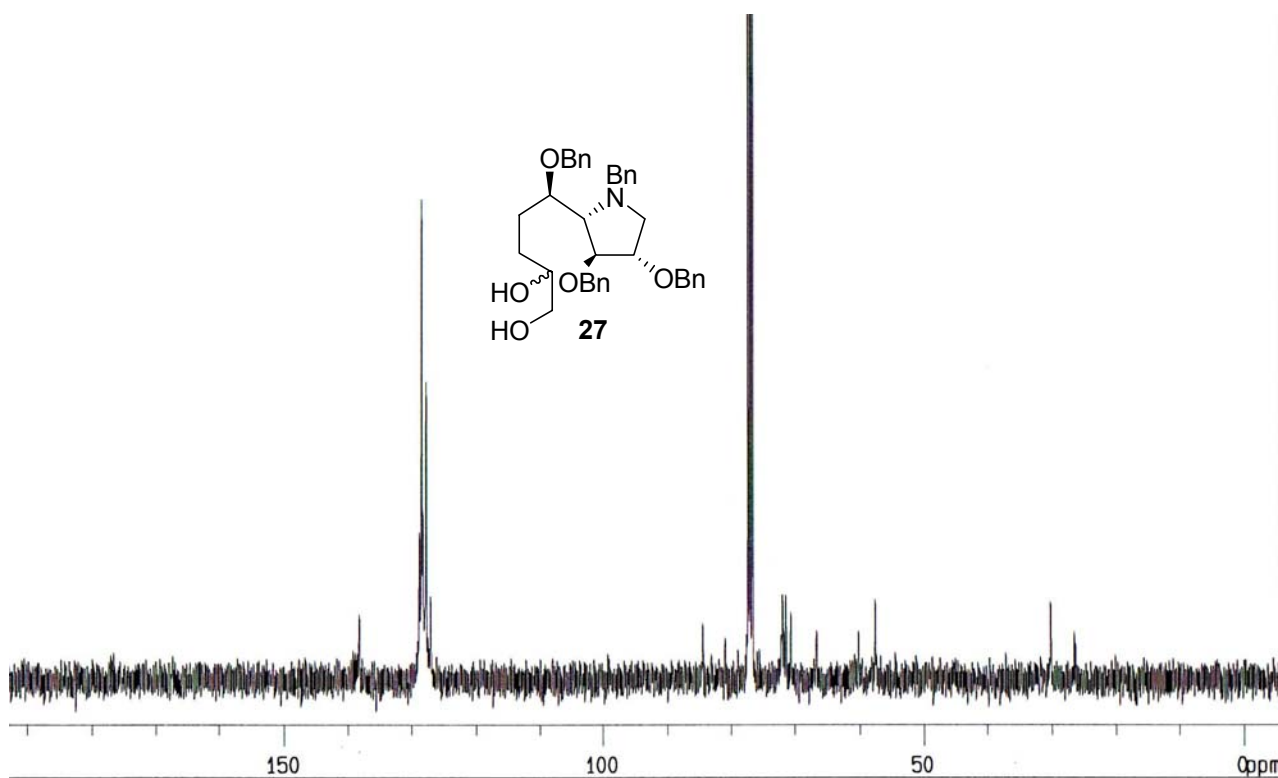
NOE spectrum of compound **26**

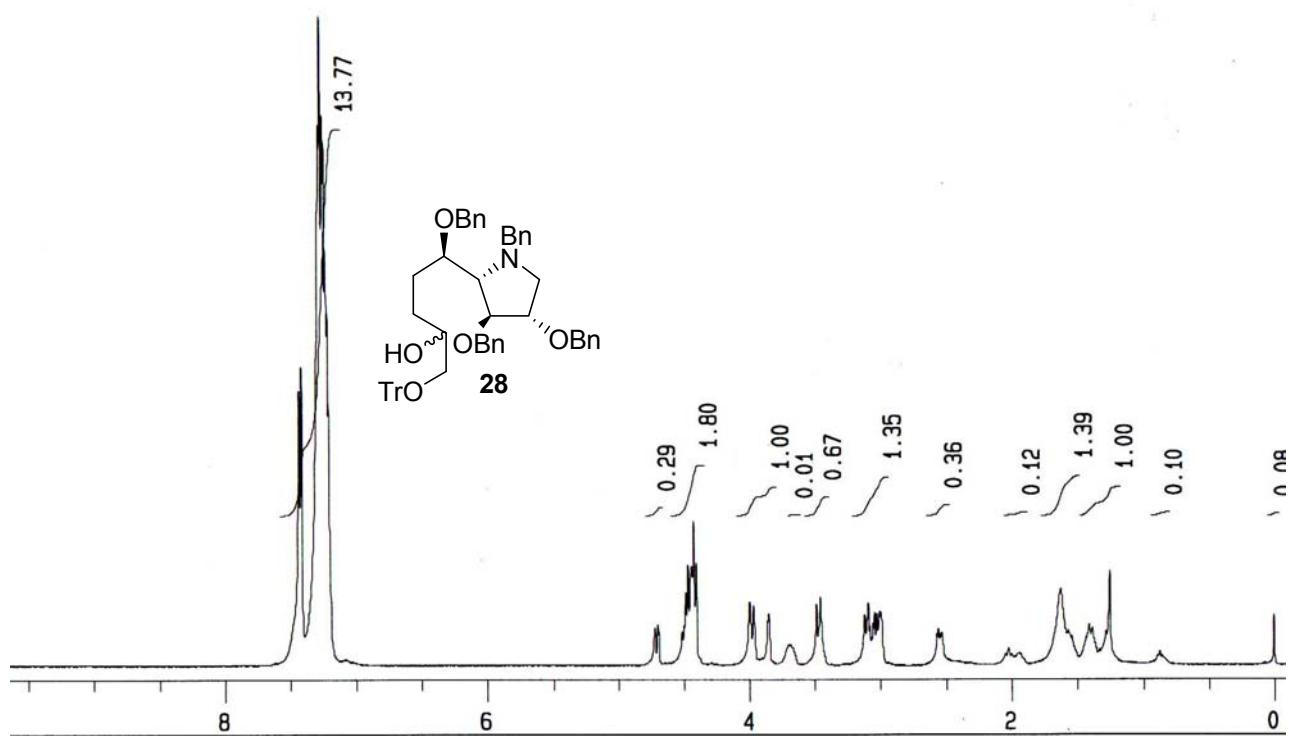


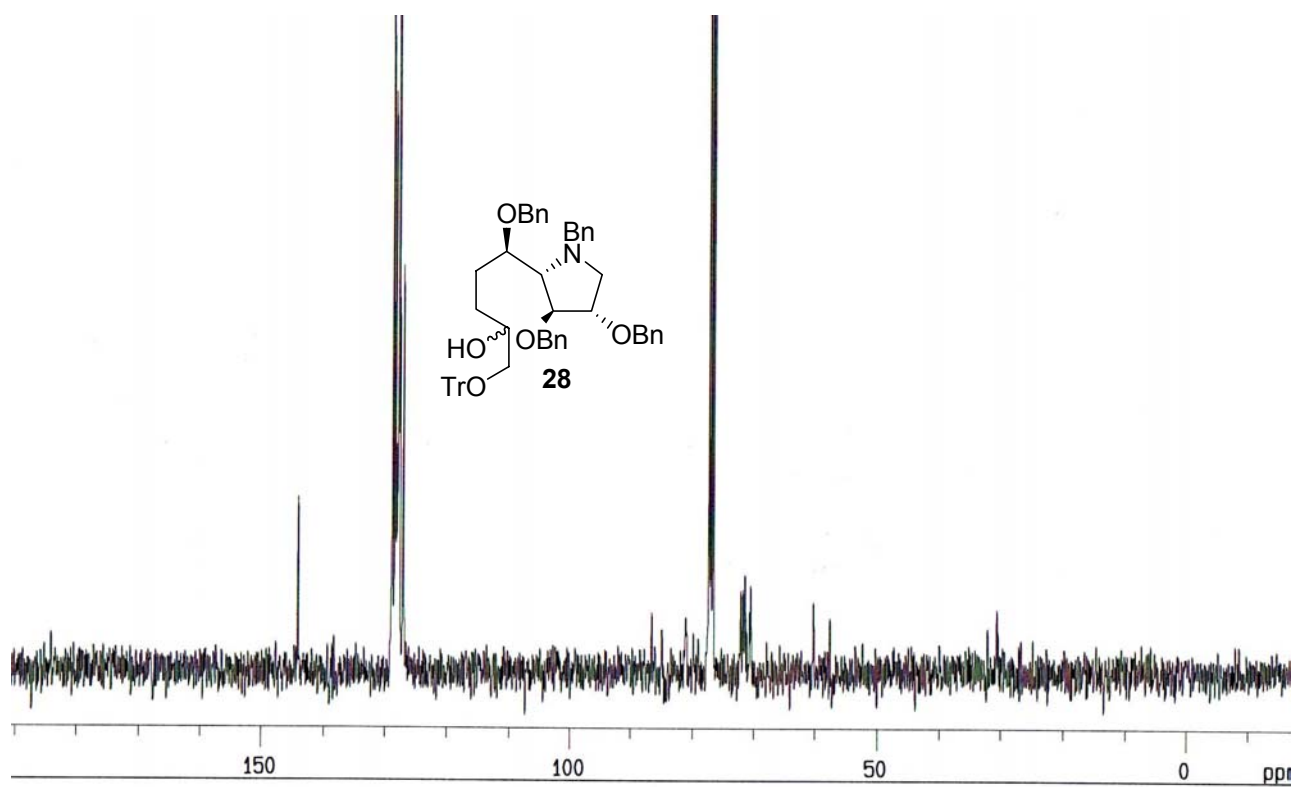
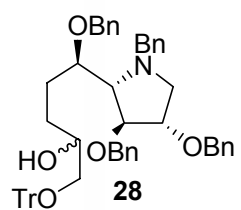
NOE spectrum of compound **26**

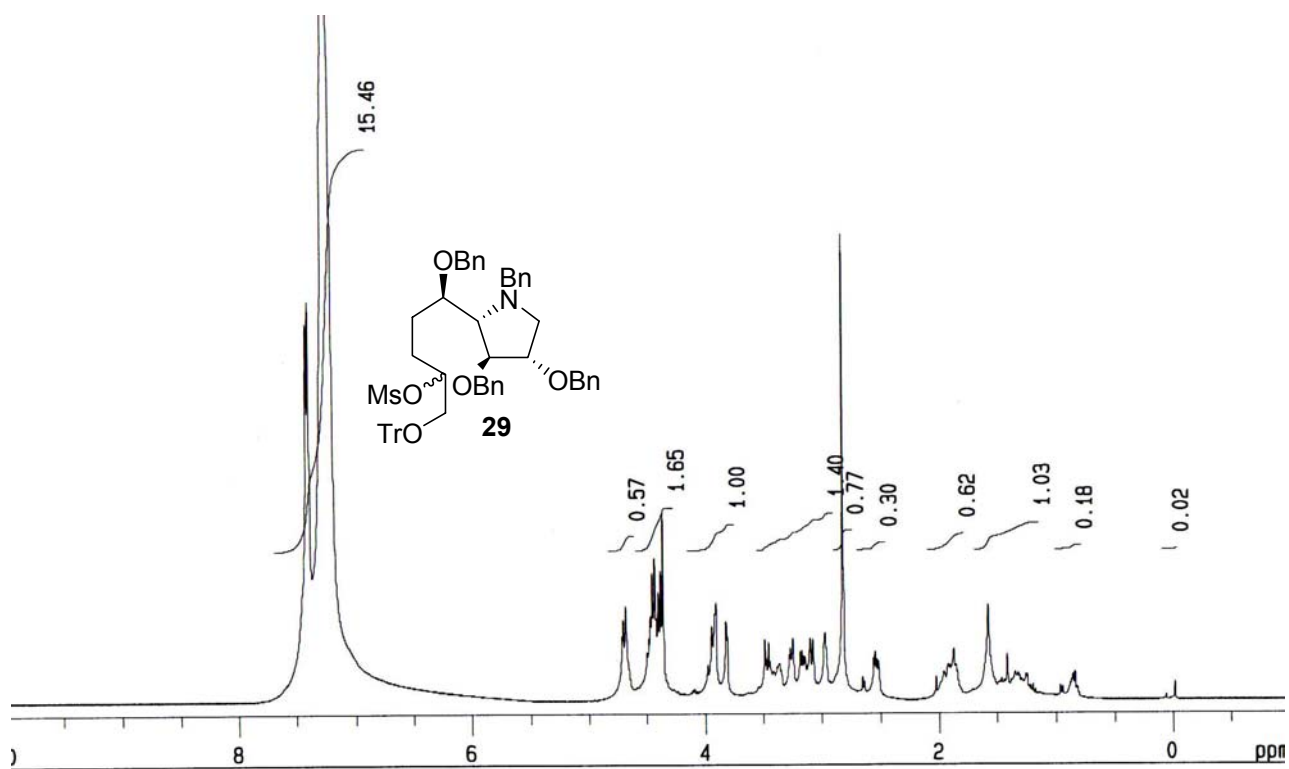


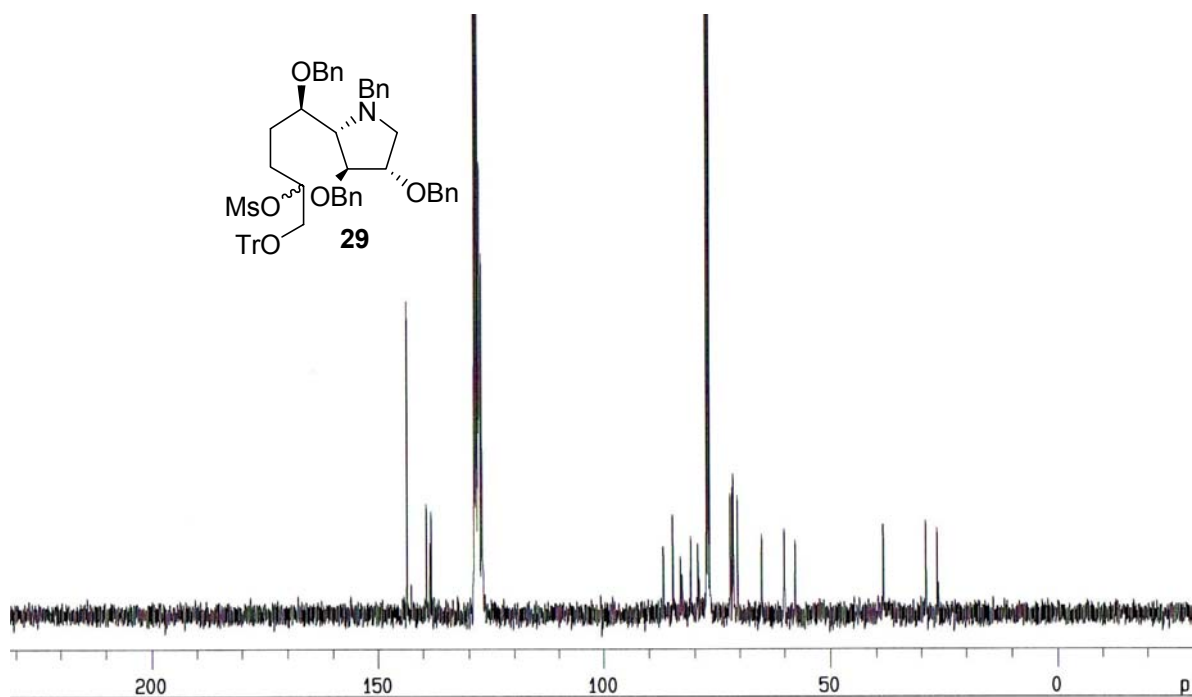




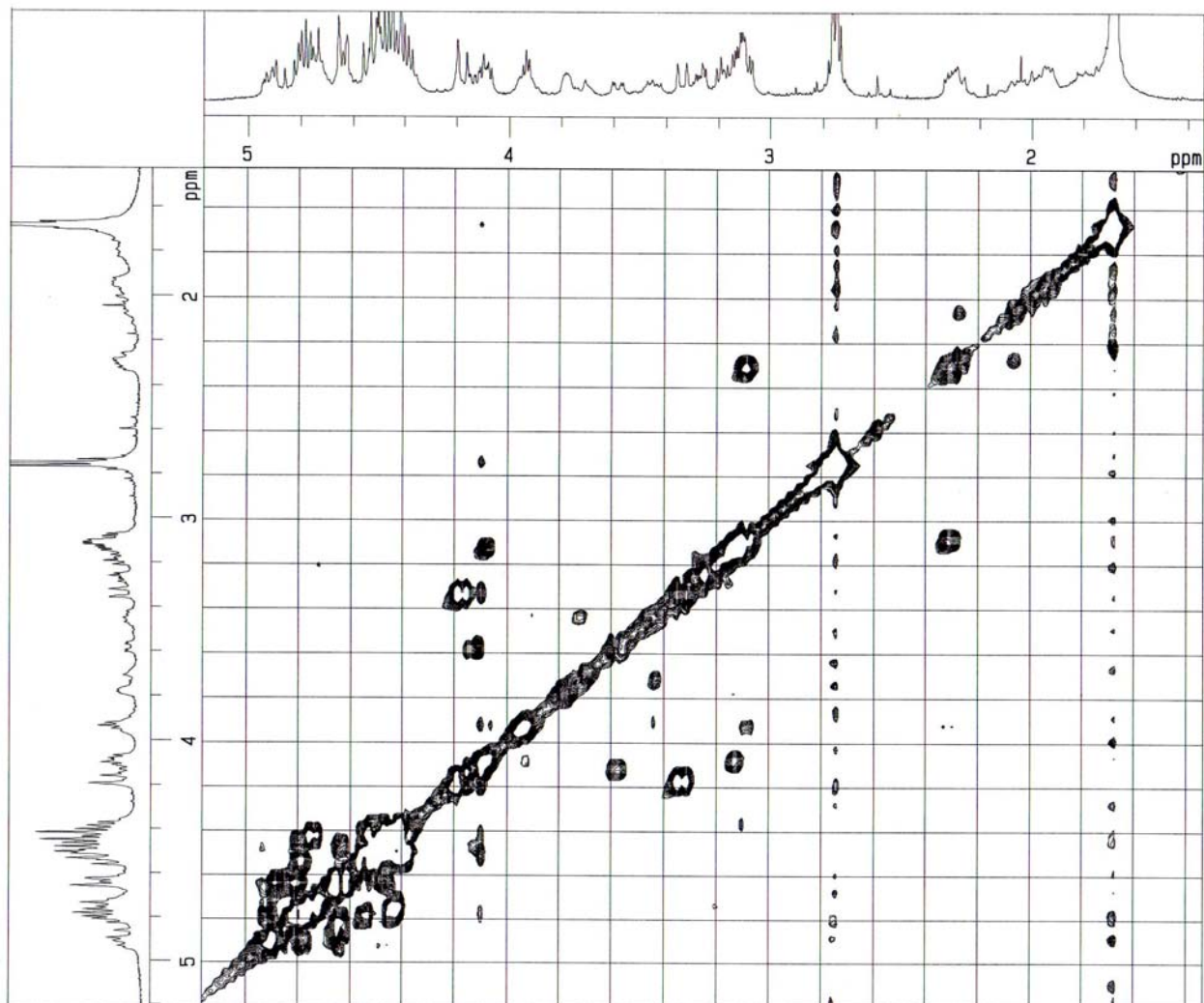
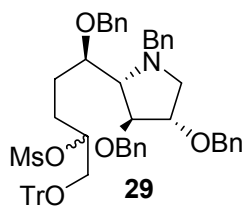


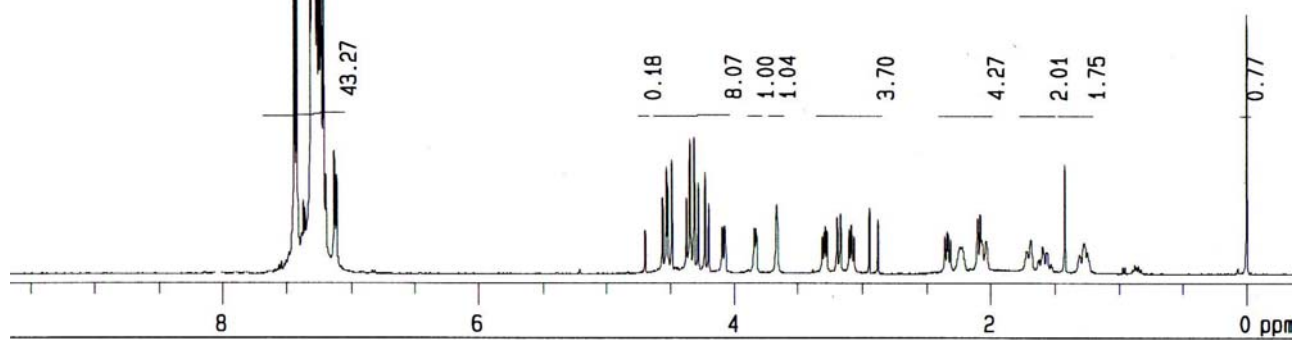
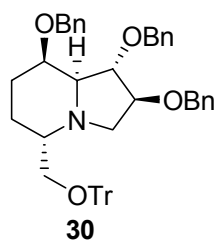


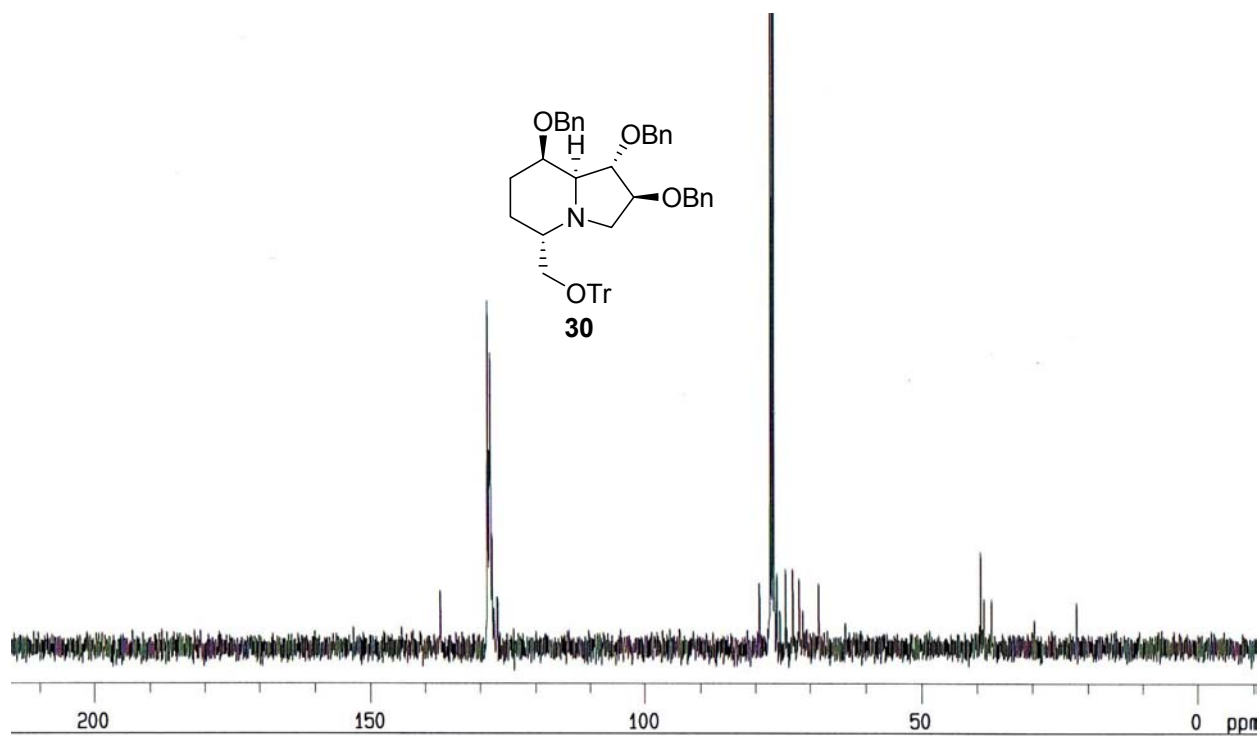




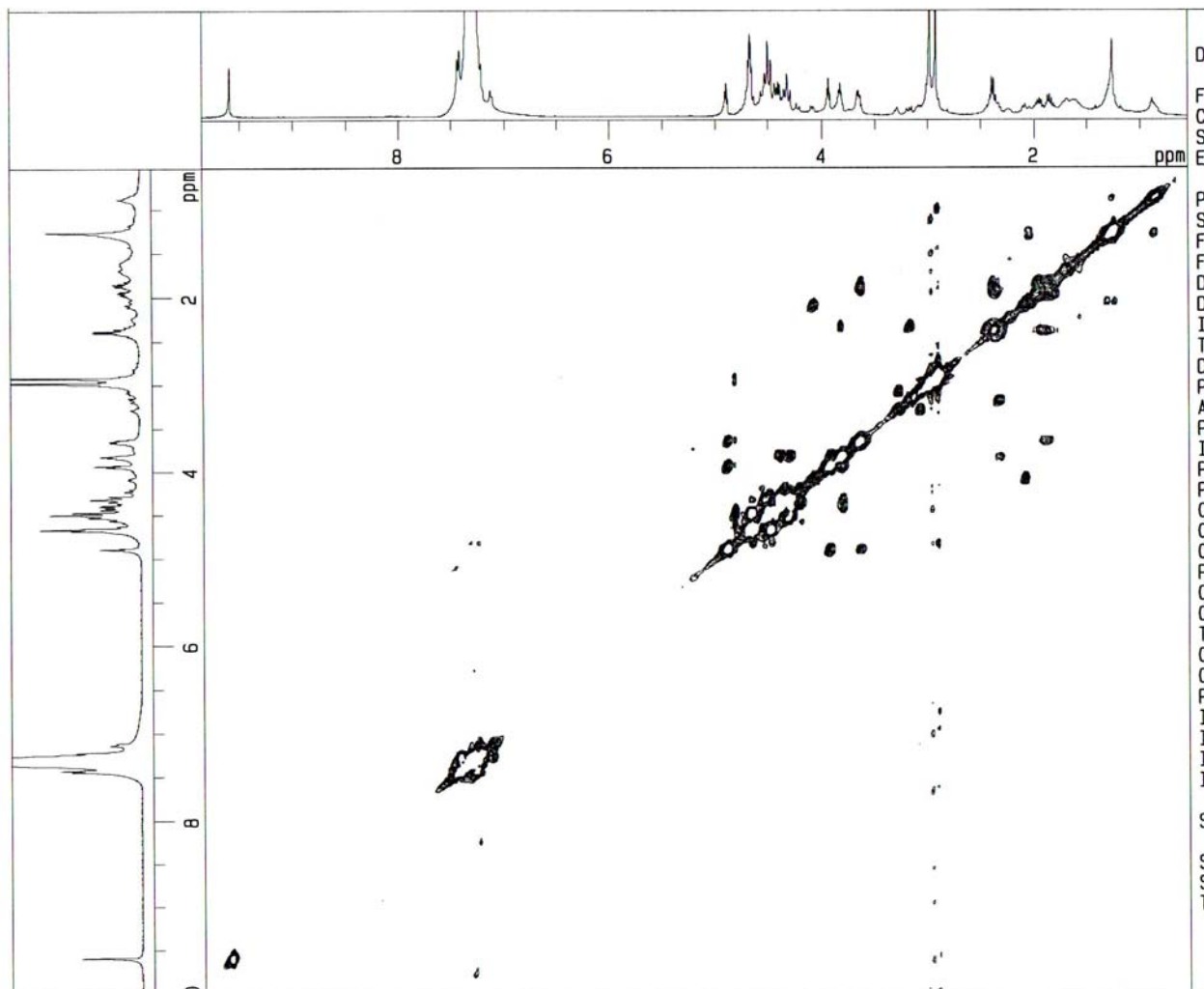
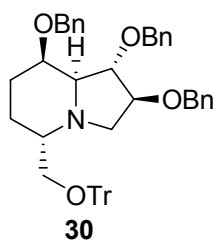
COSY spectrum of compound **29**

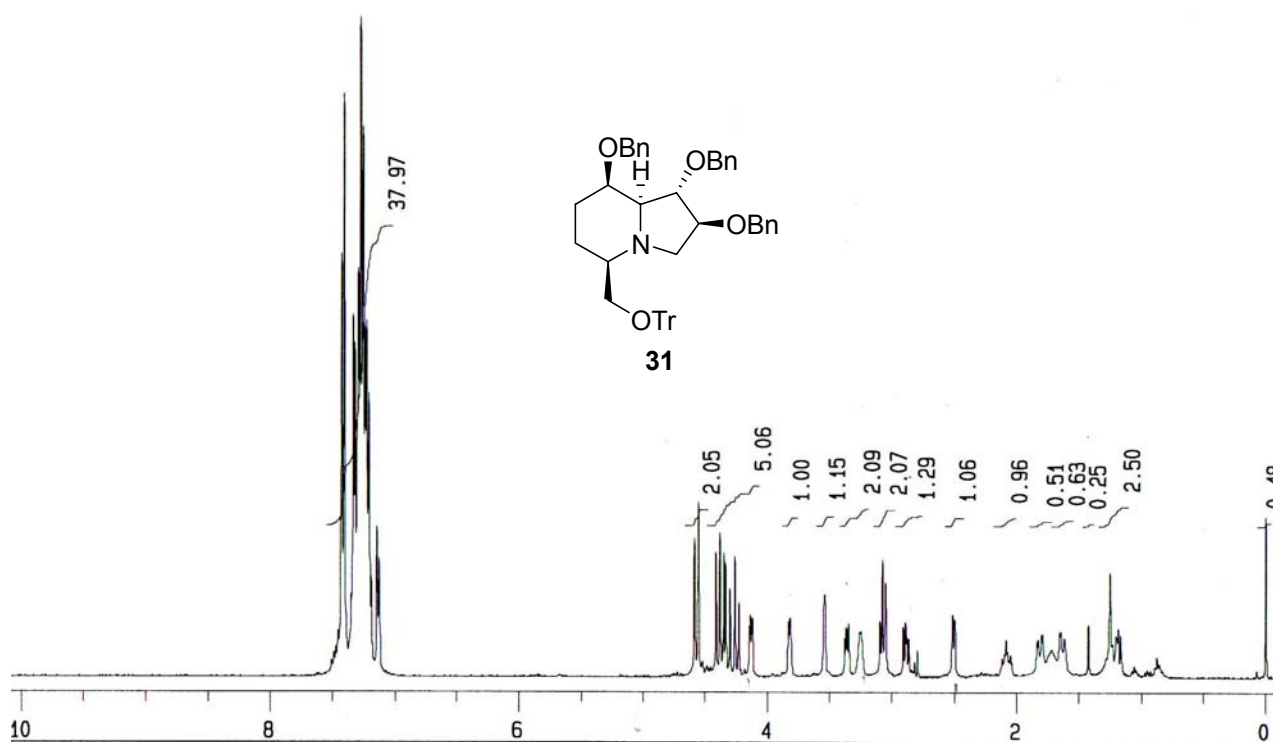


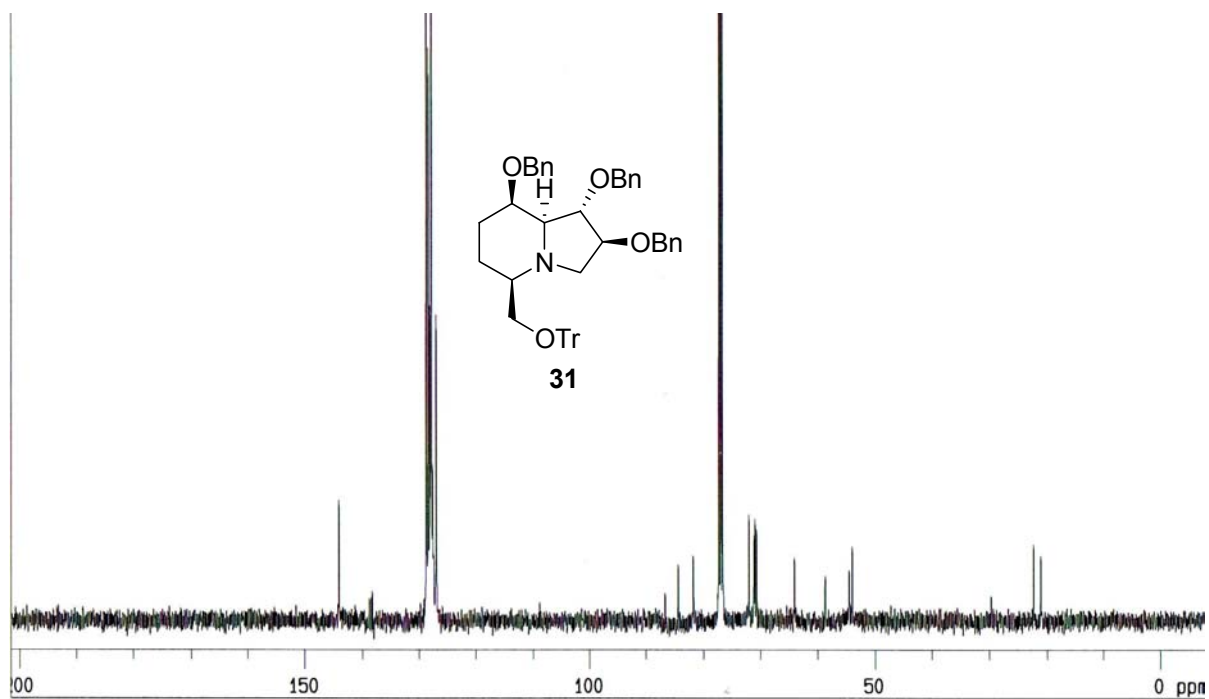




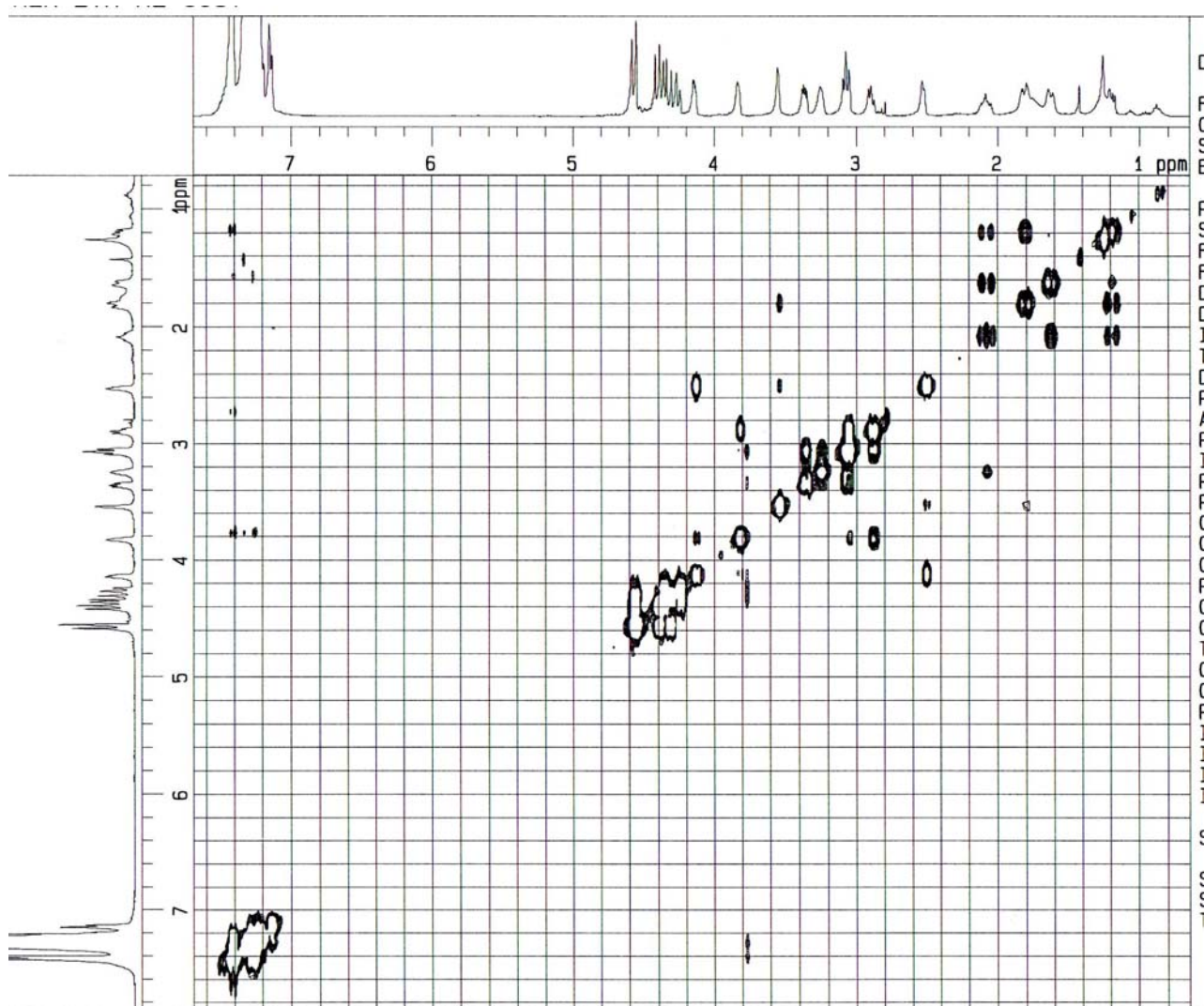
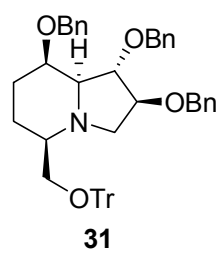
COSY spectrum of compound **30**

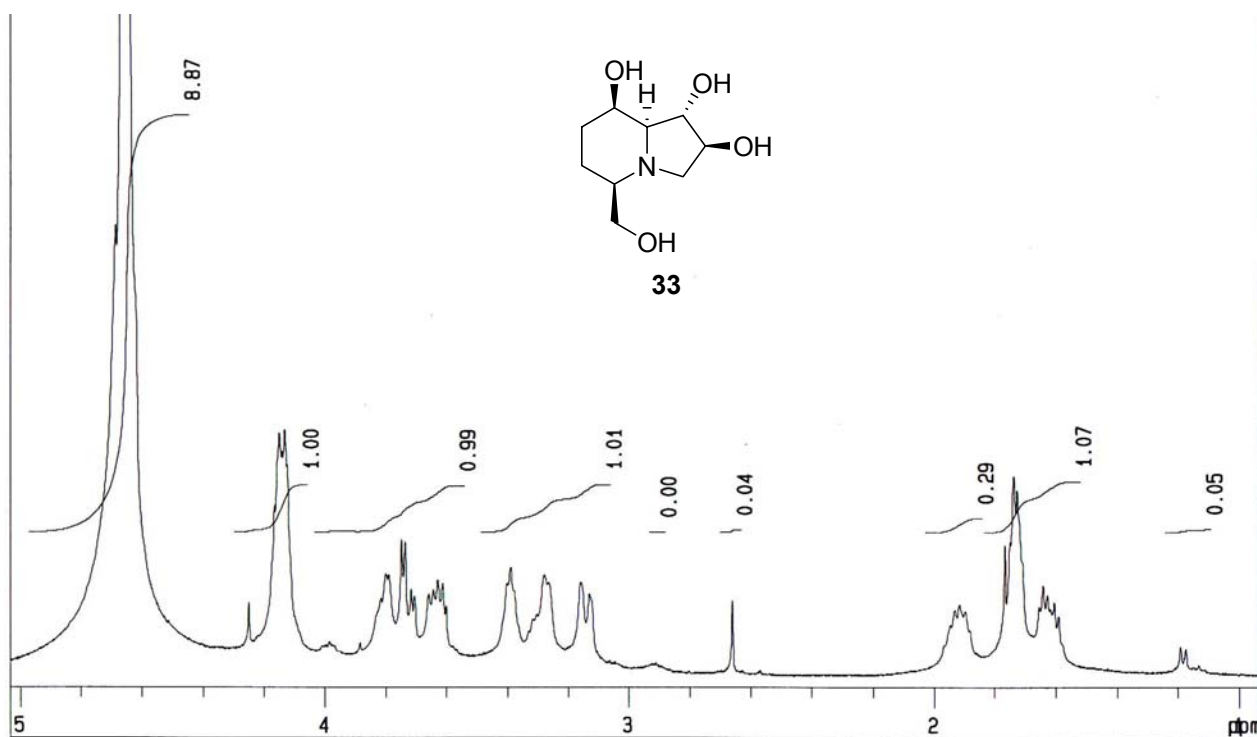


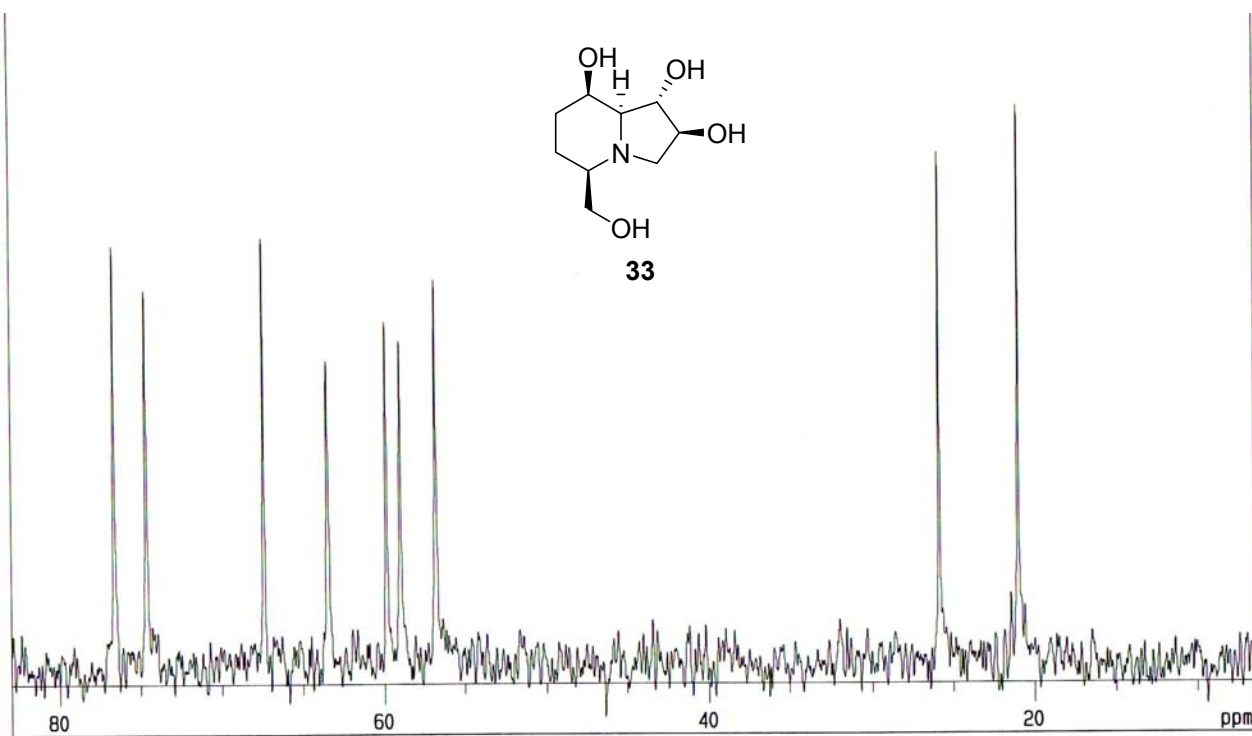
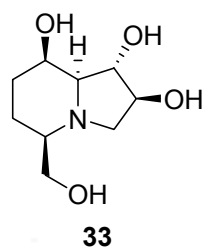


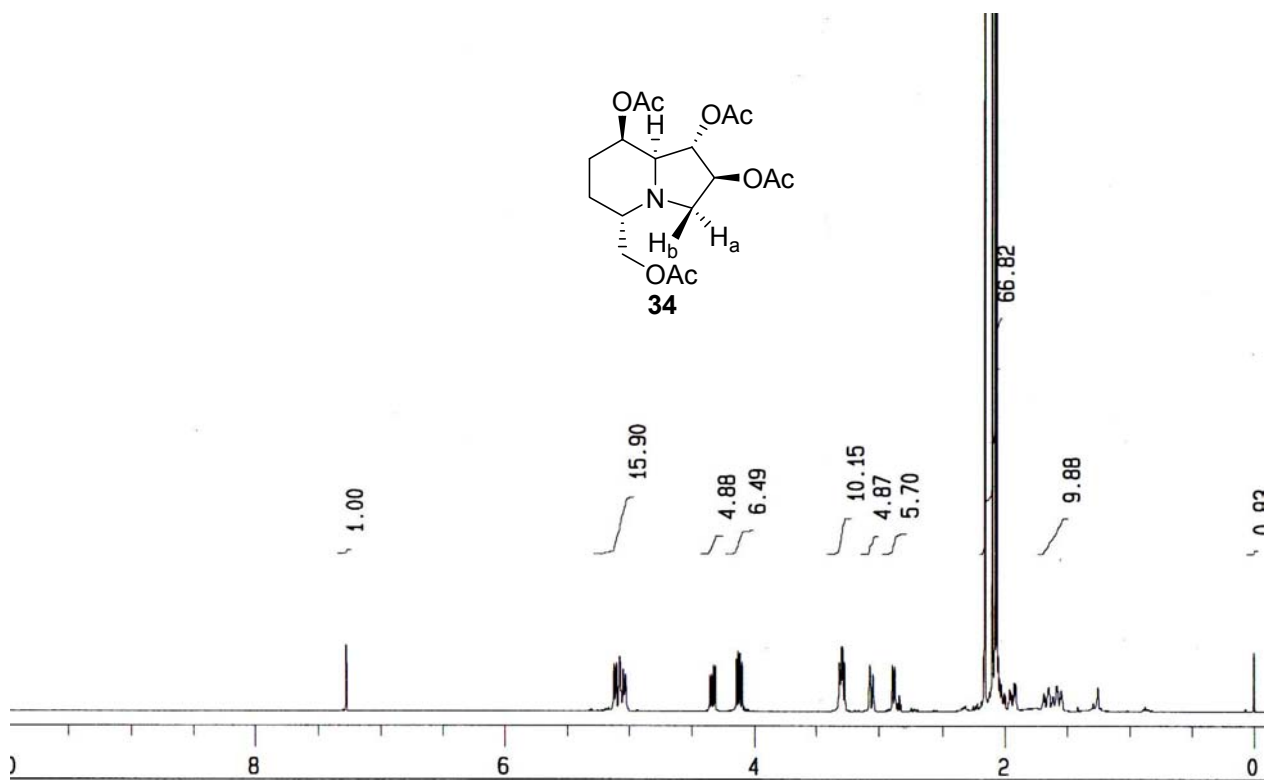
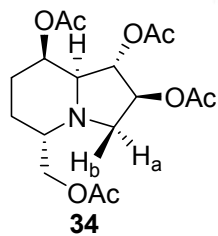


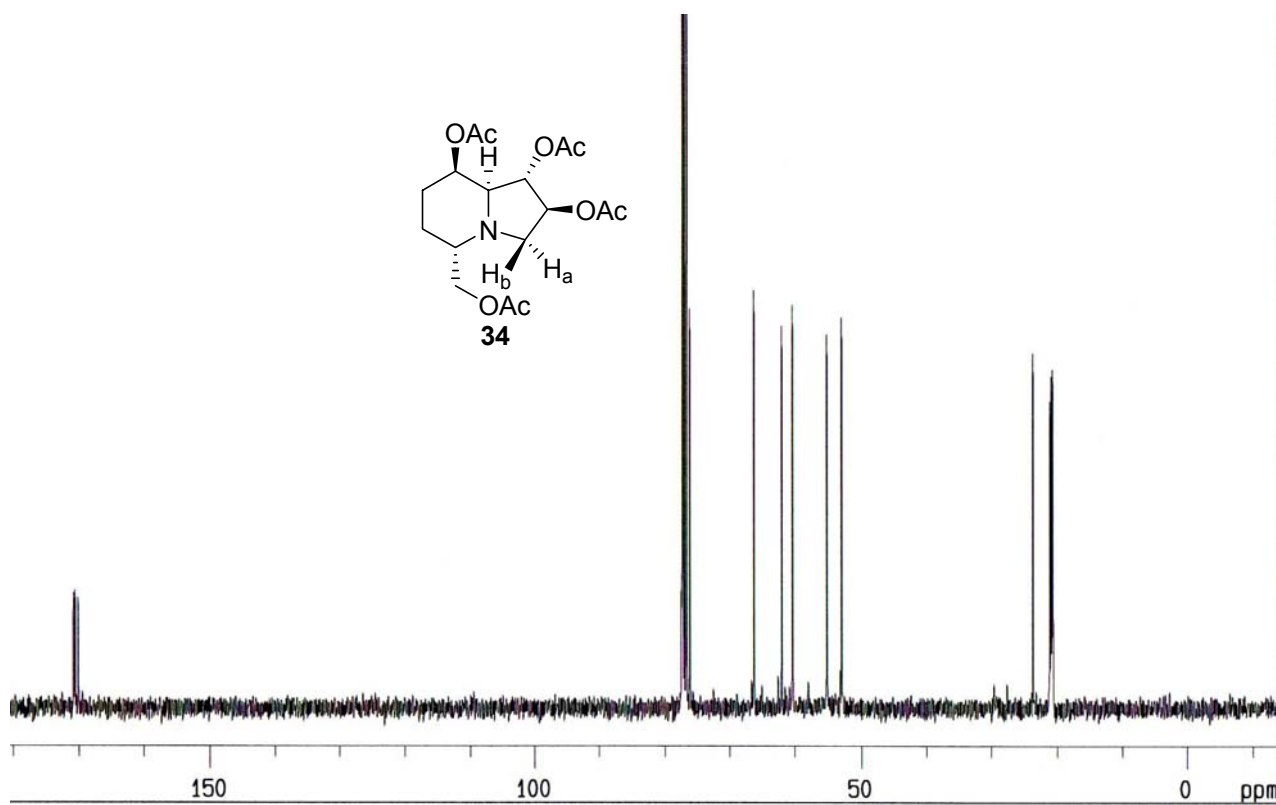
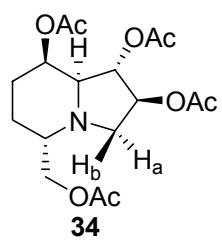
COSY spectrum of compound **31**



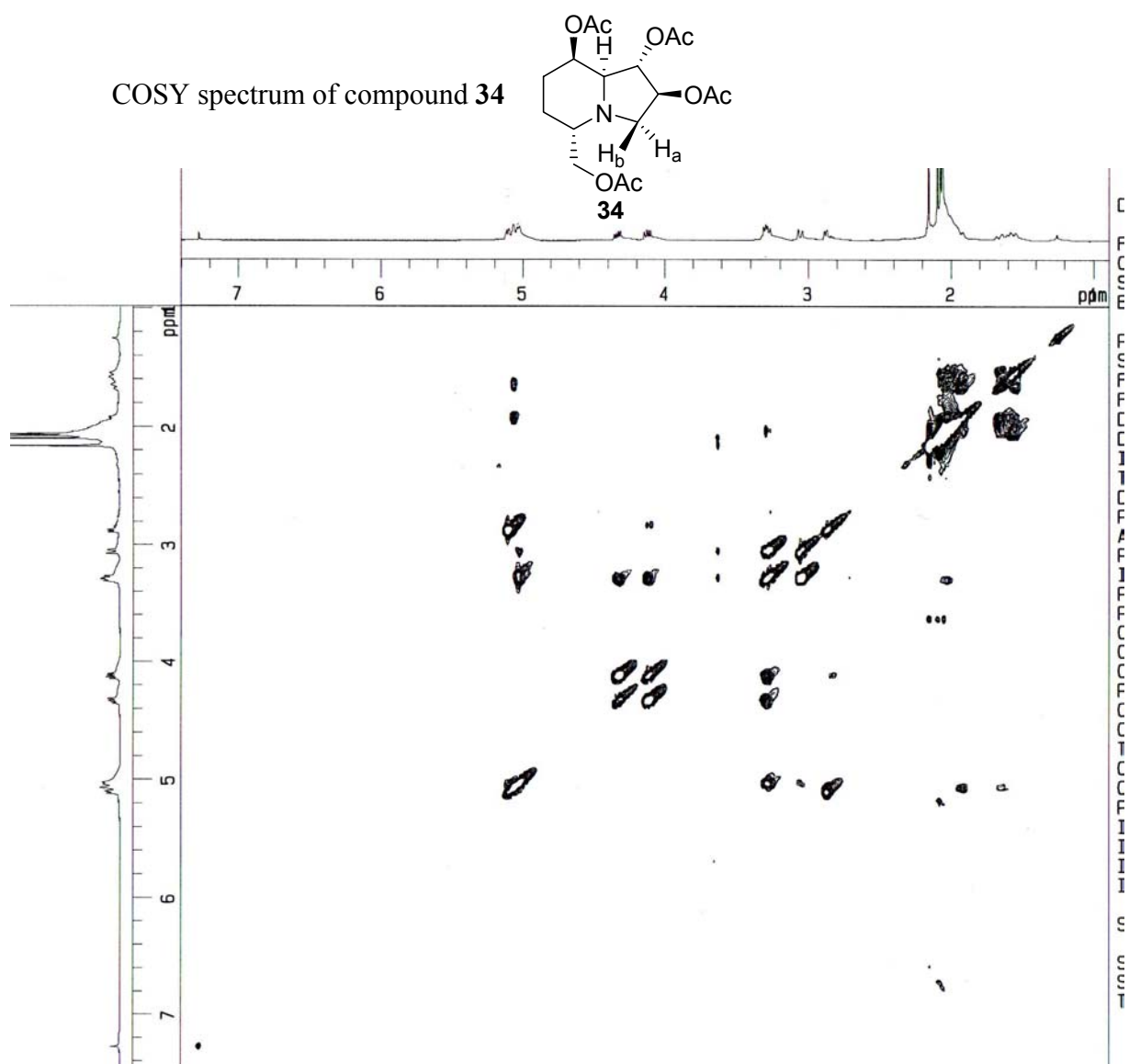




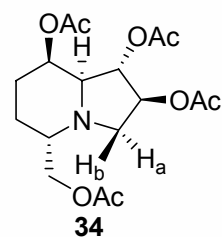
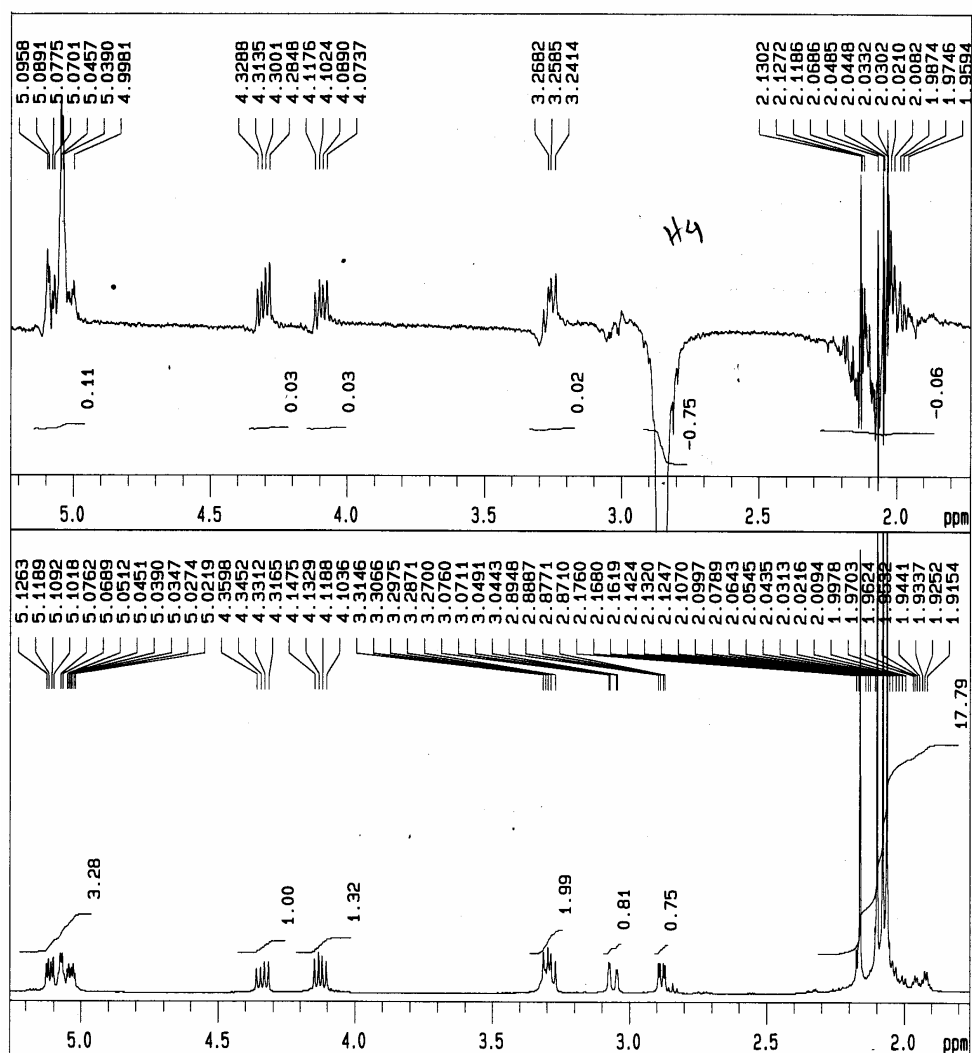




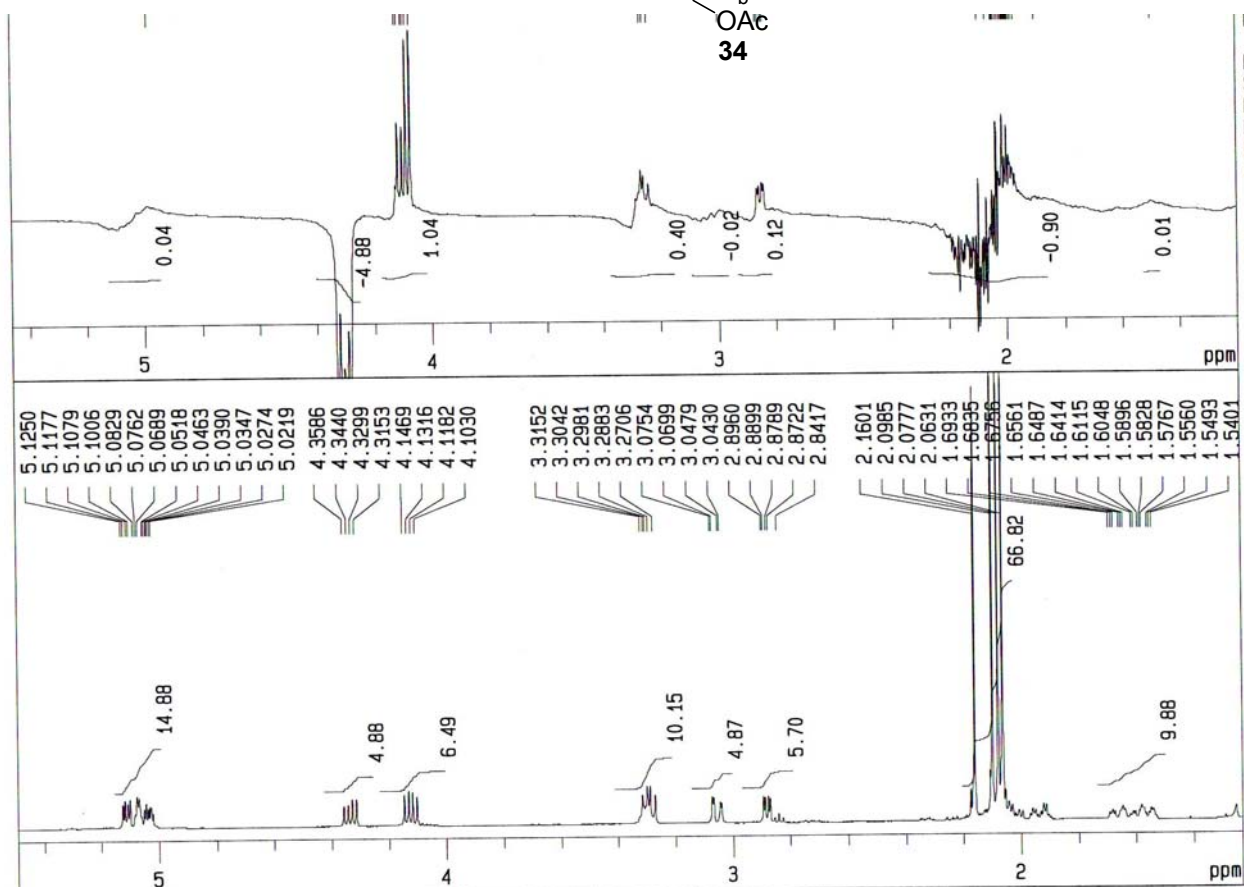
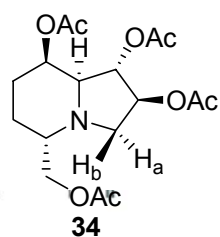
COSY spectrum of compound **34**



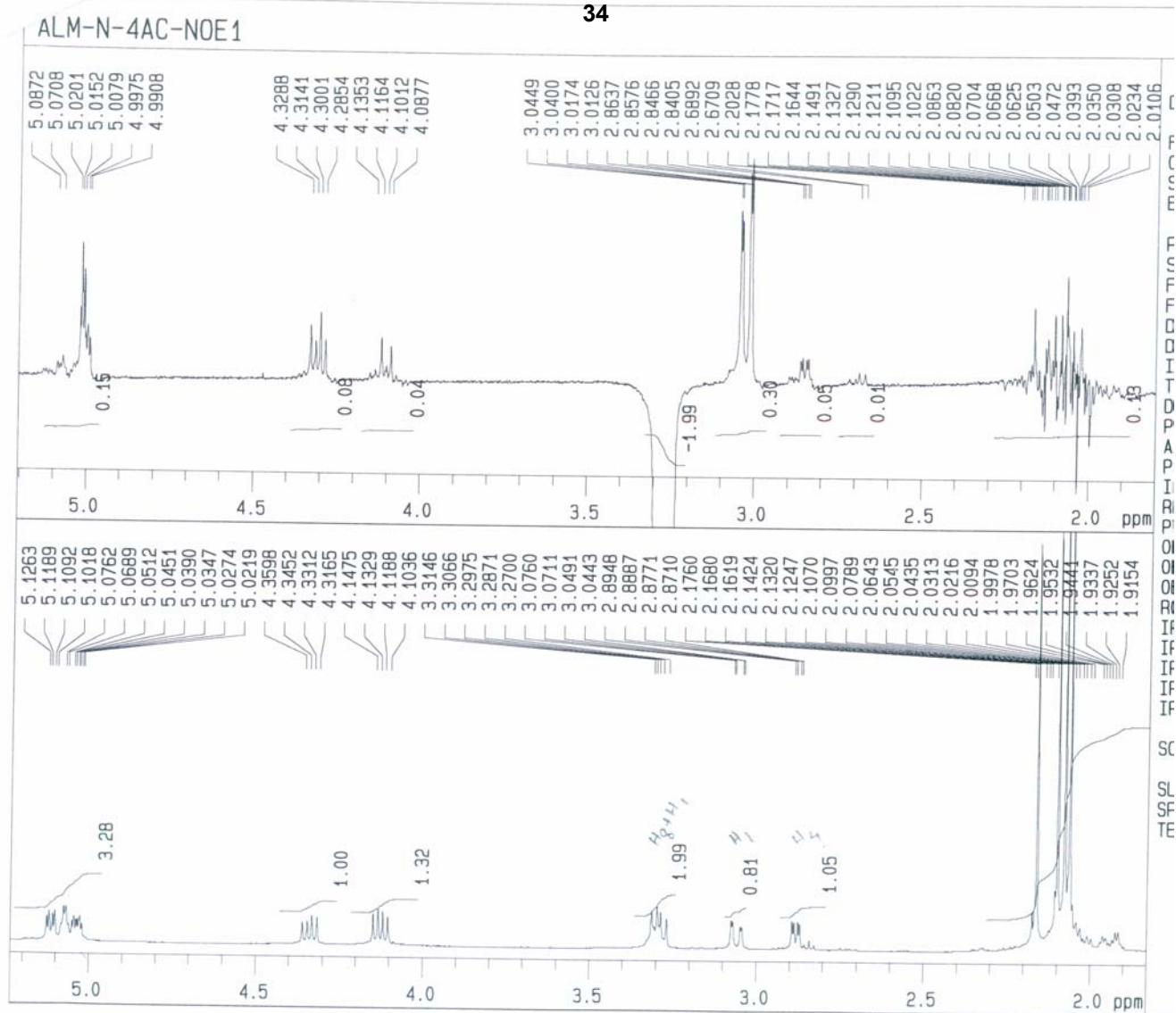
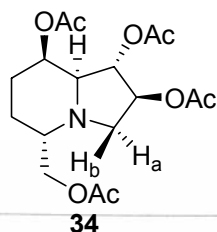
NOE spectrum of compound **34** (irradiation of H-4)



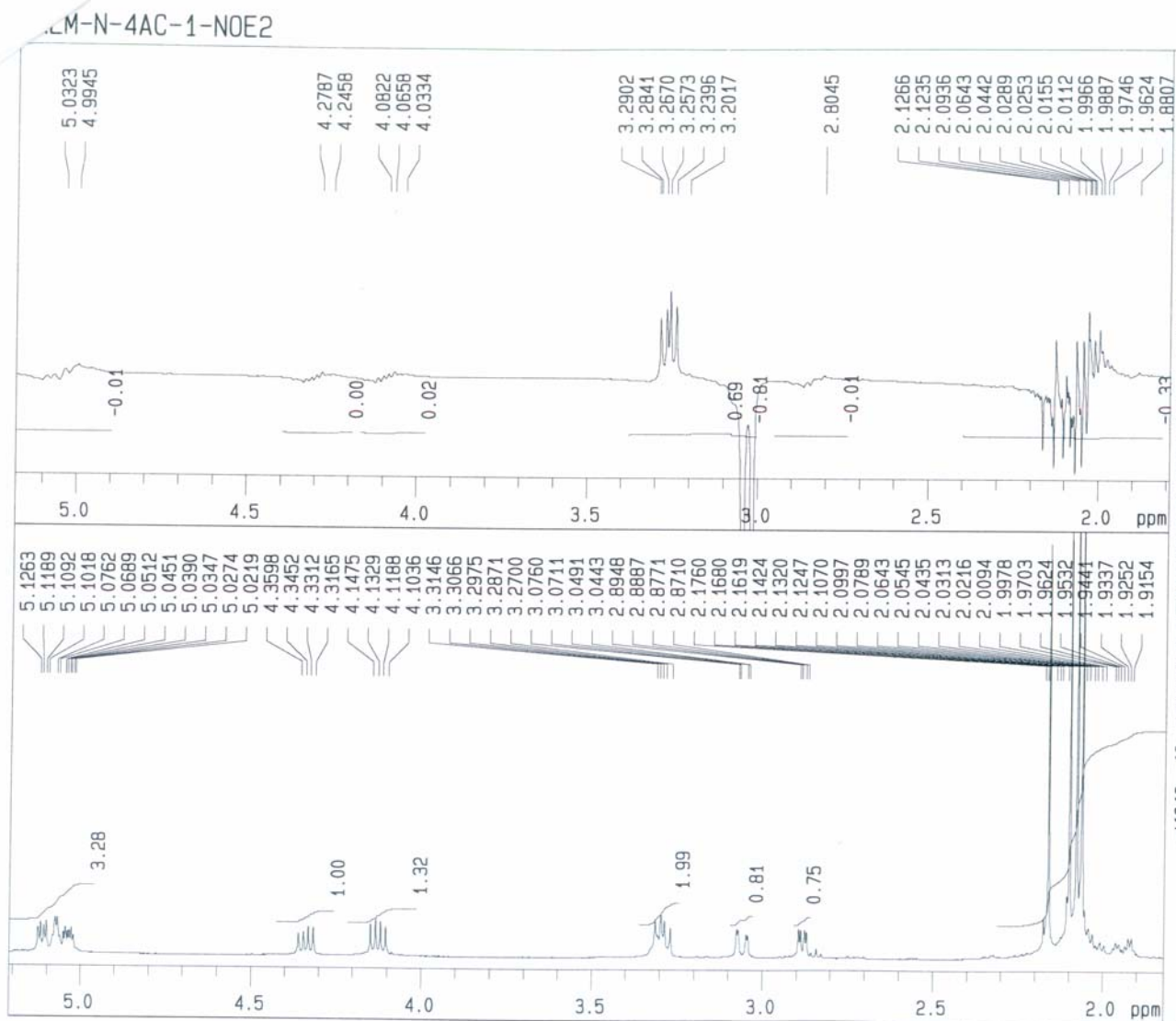
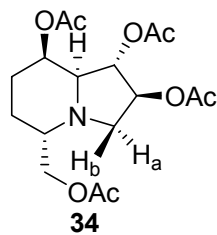
NOE spectrum of compound **34** (irradiation of H-9)

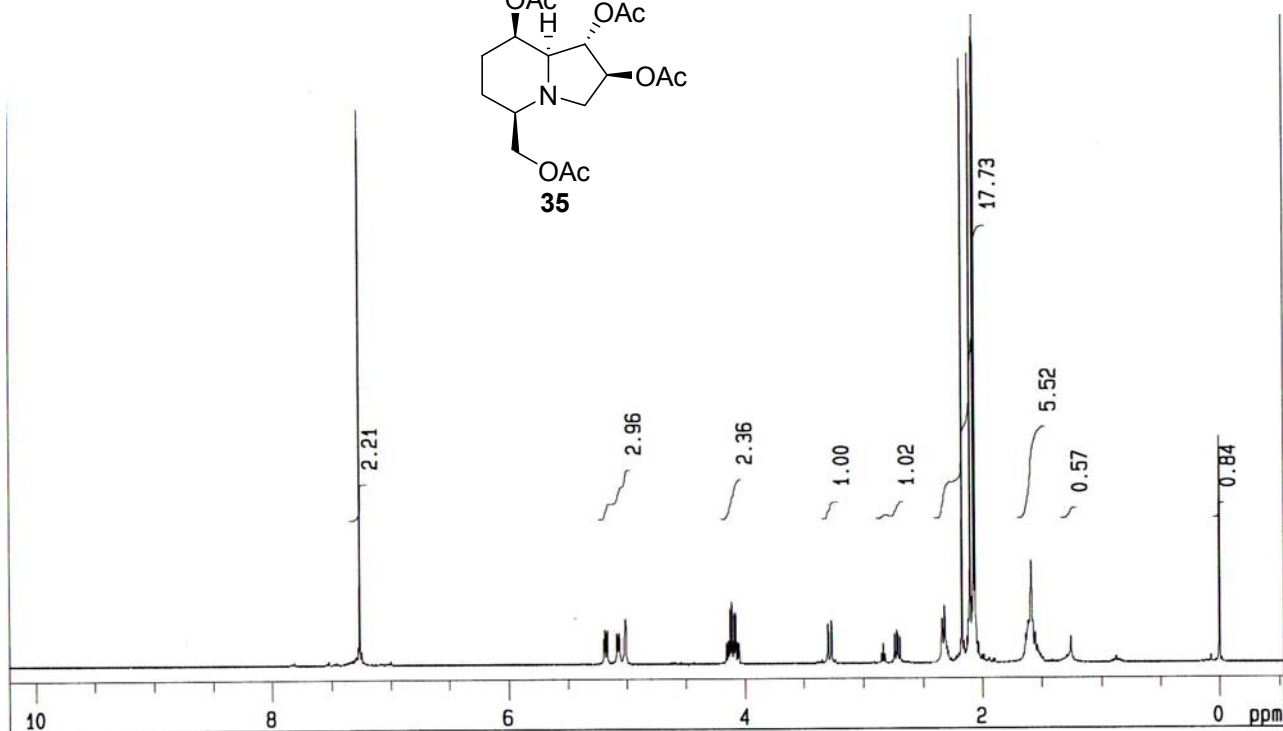
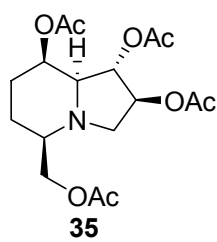


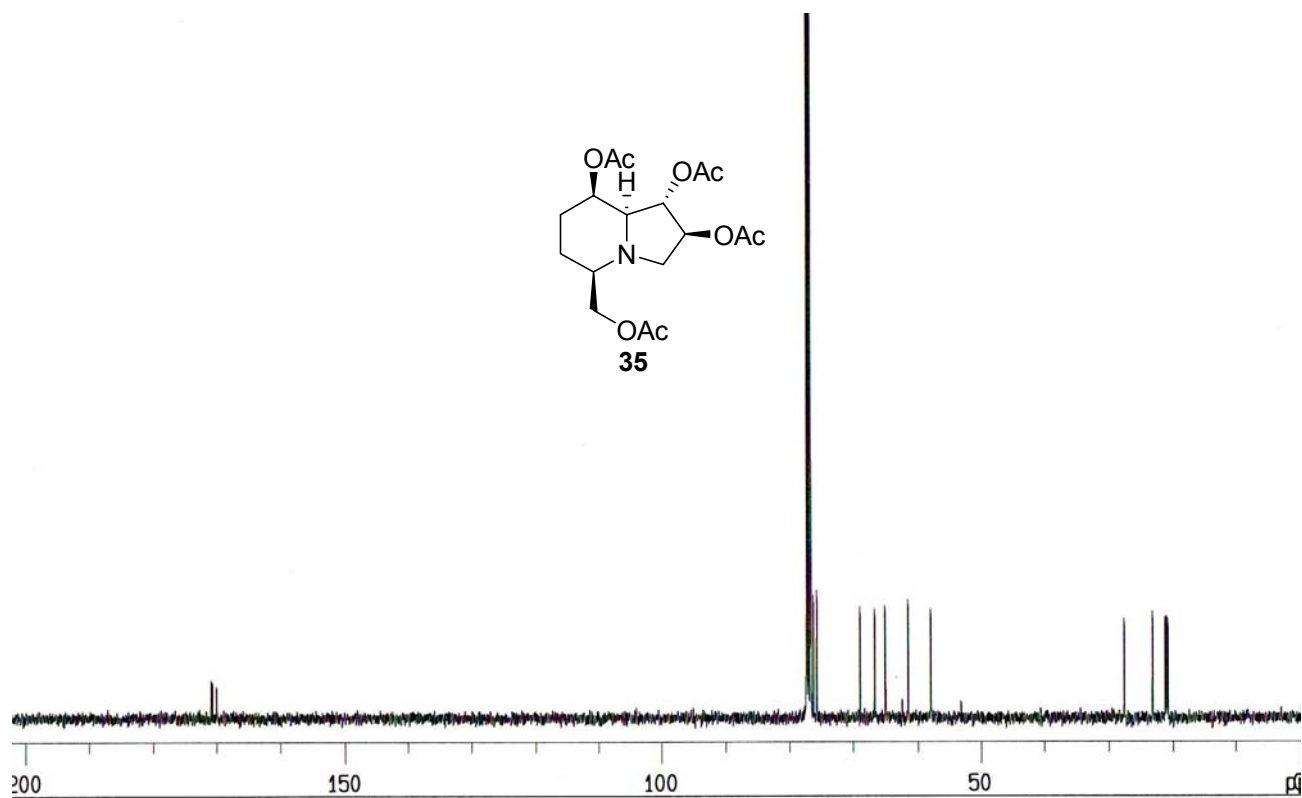
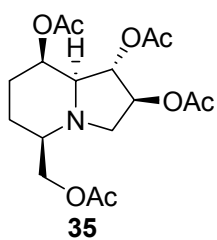
NOE spectrum of compound **34** (irradiation of H-8 and H-1b)



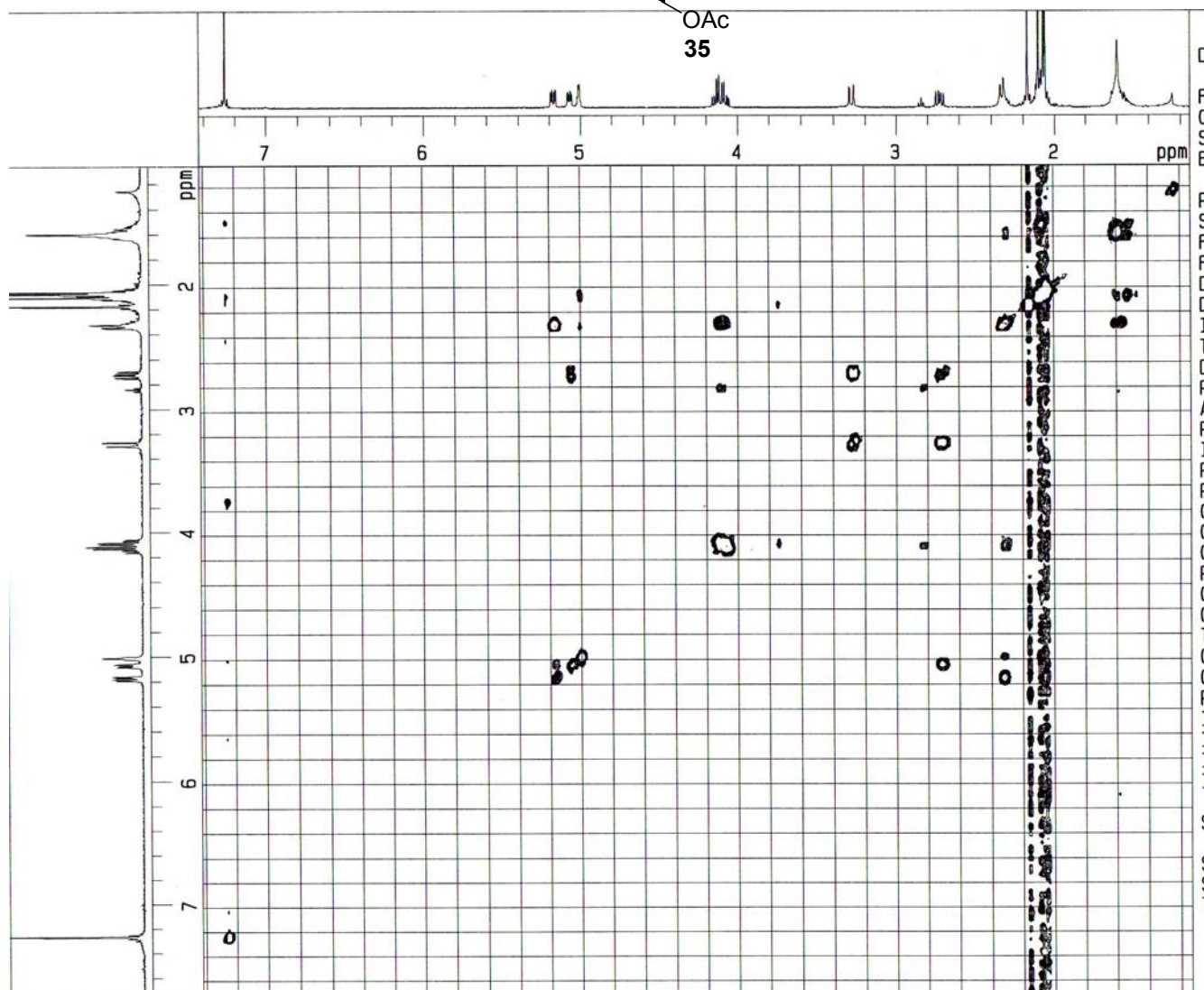
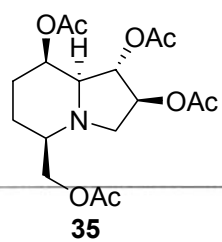
NOE spectrum of compound **34** (irradiation of H-1_b)



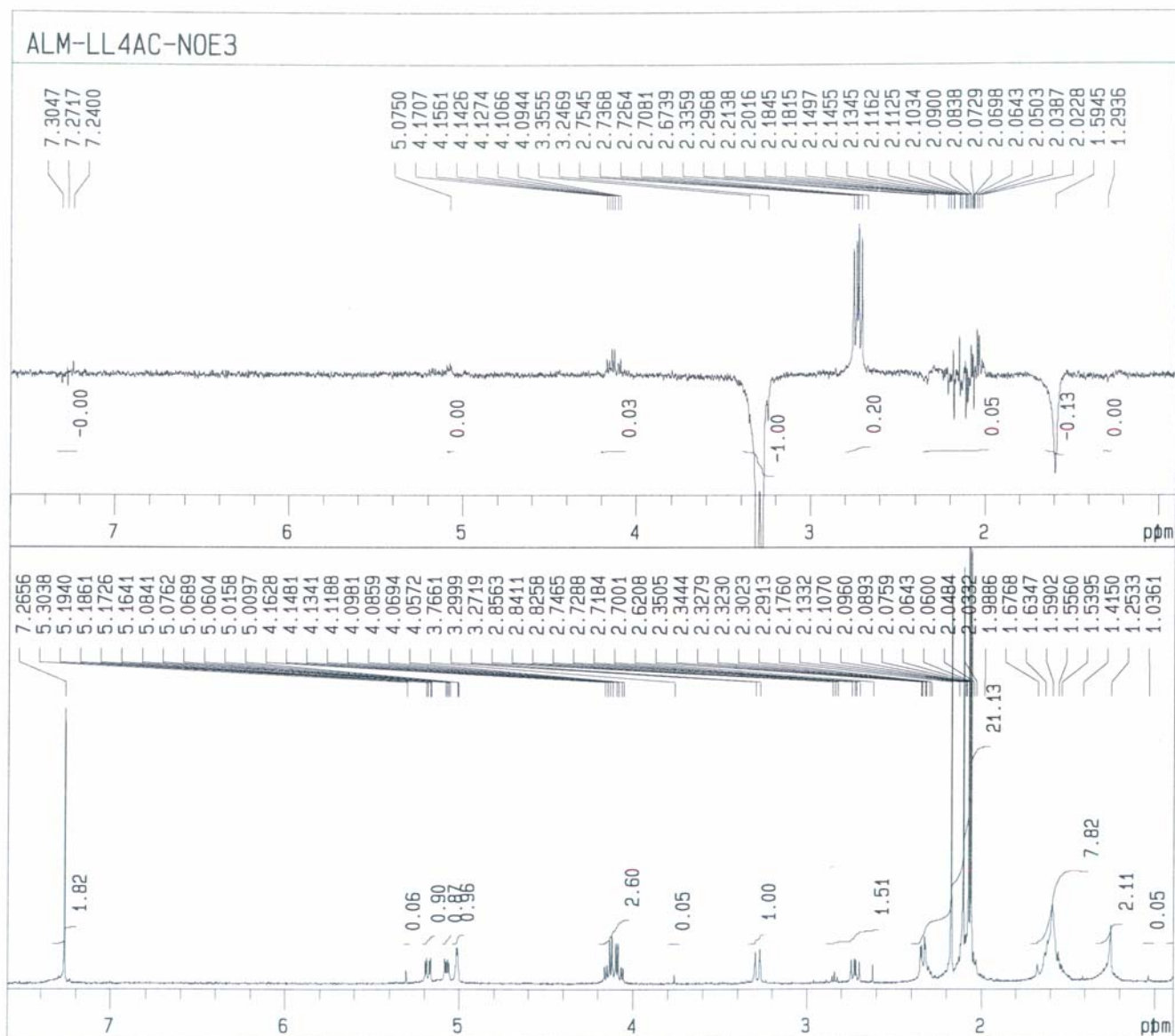
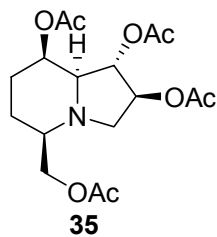




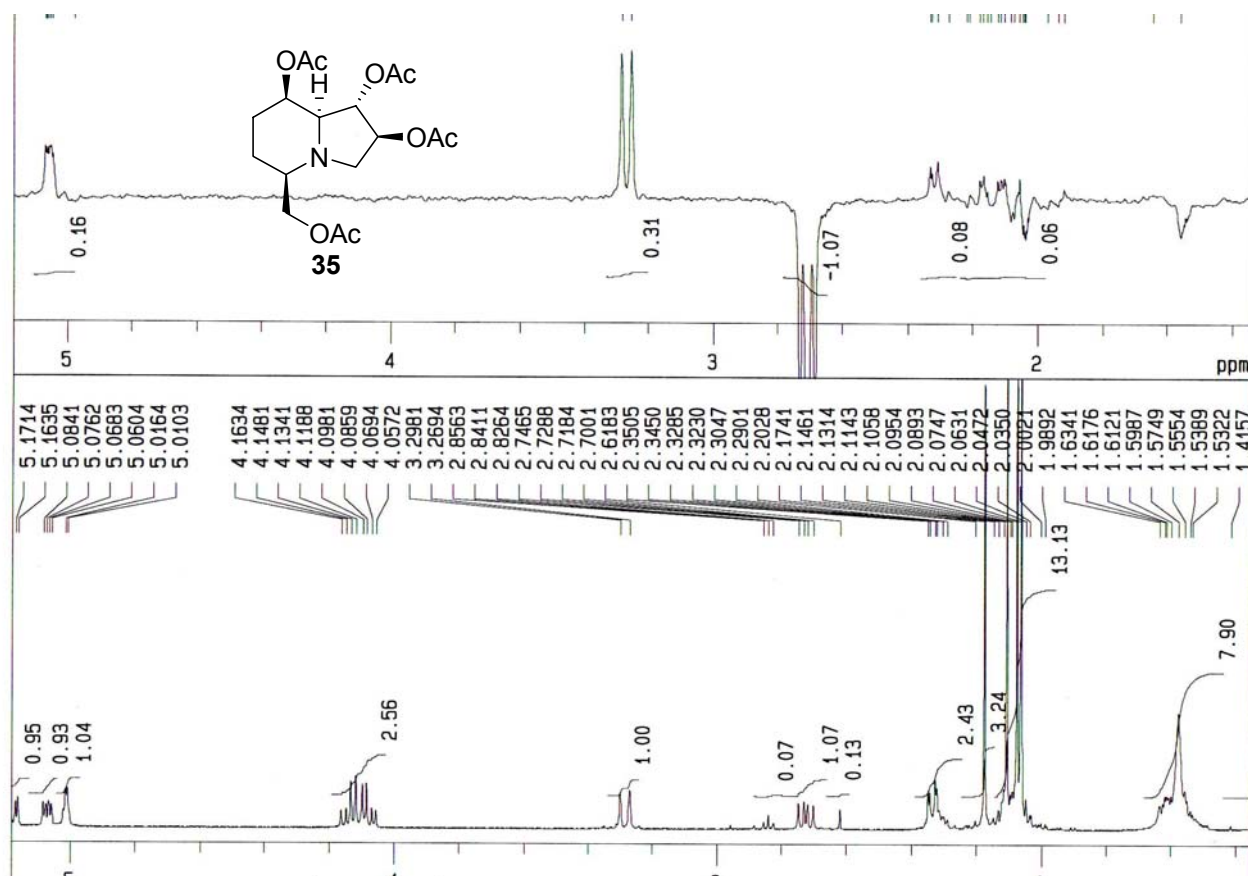
COSY spectrum of compound **35**



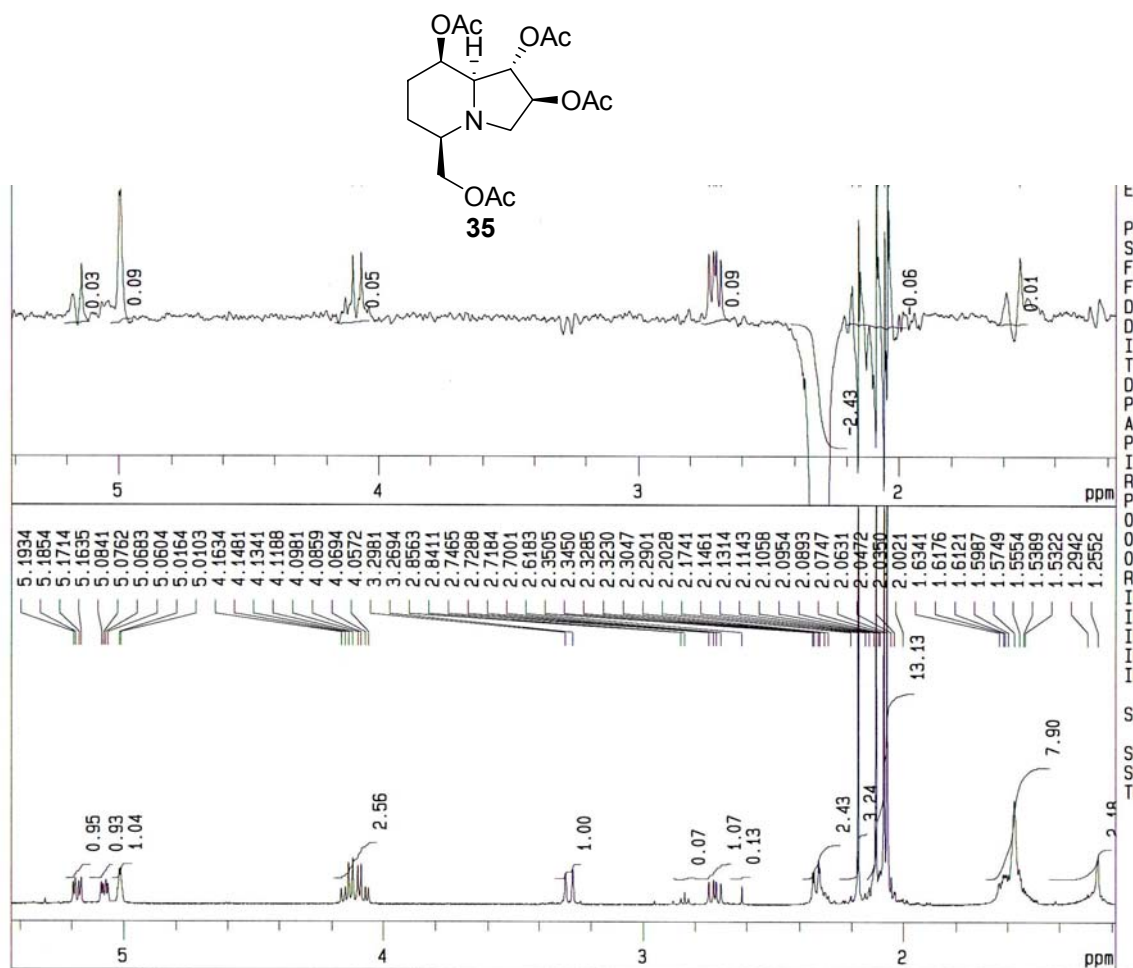
NOE spectrum of compound **35**

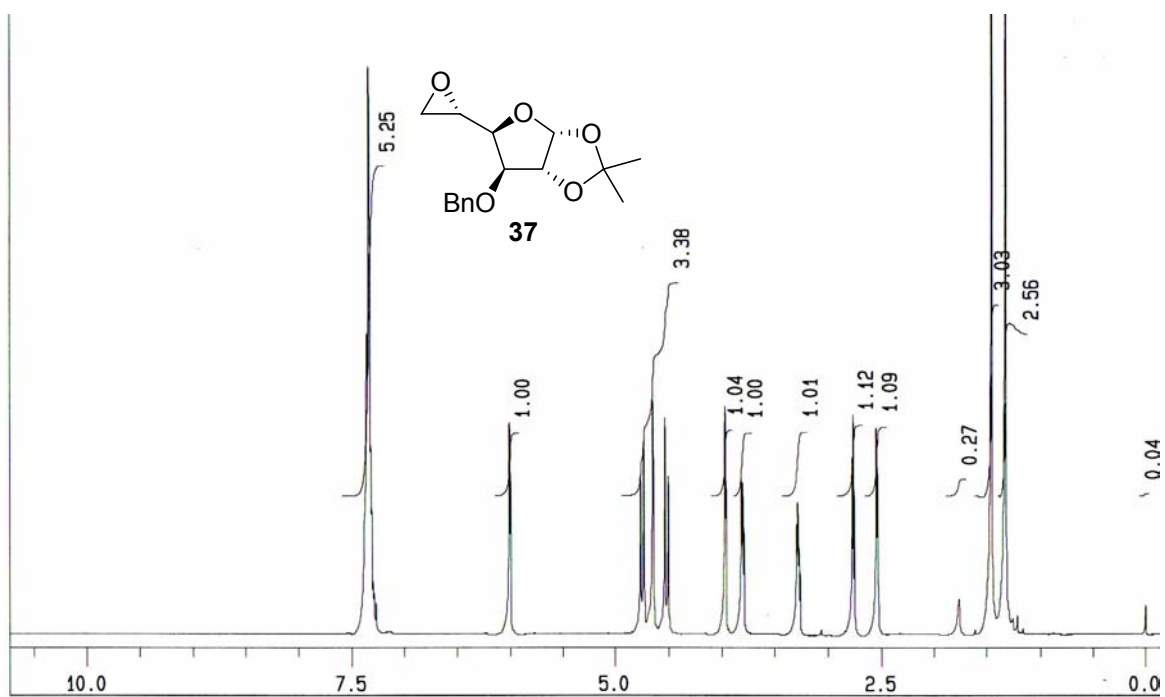


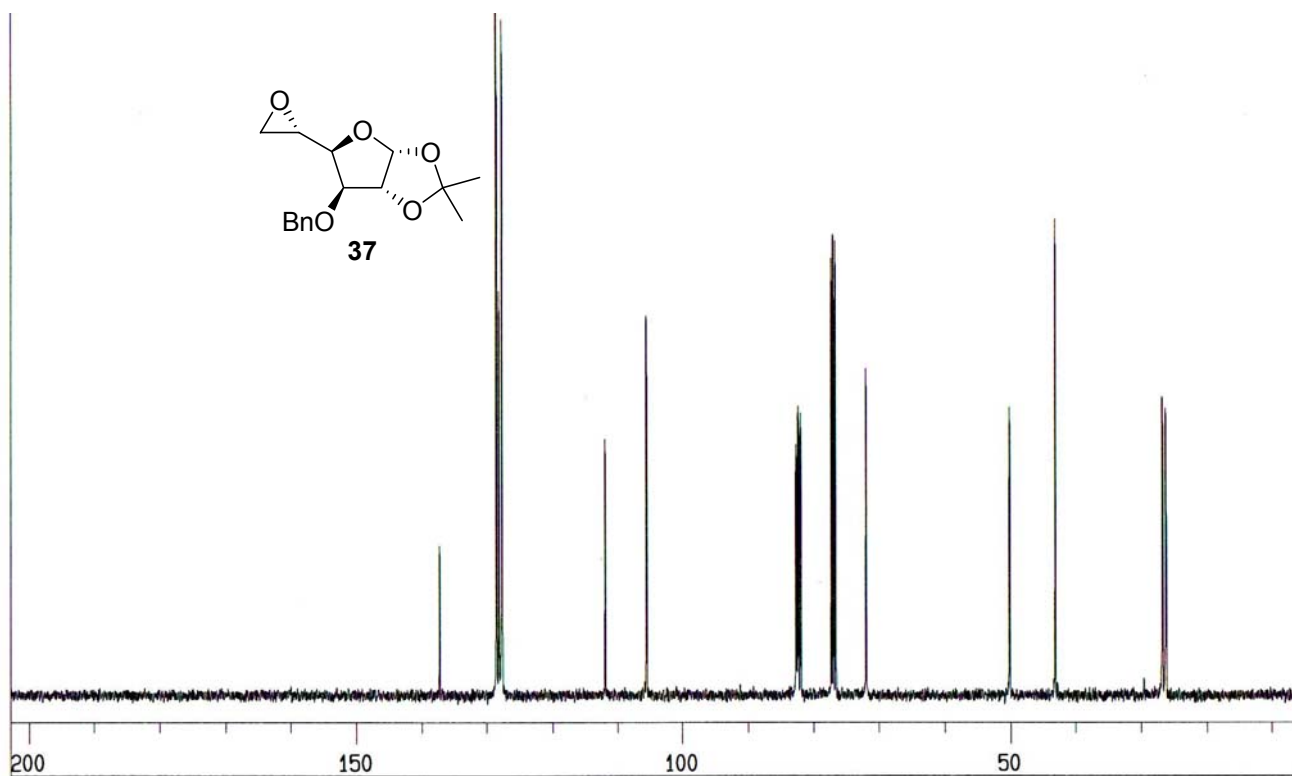
NOE spectrum of compound **35**

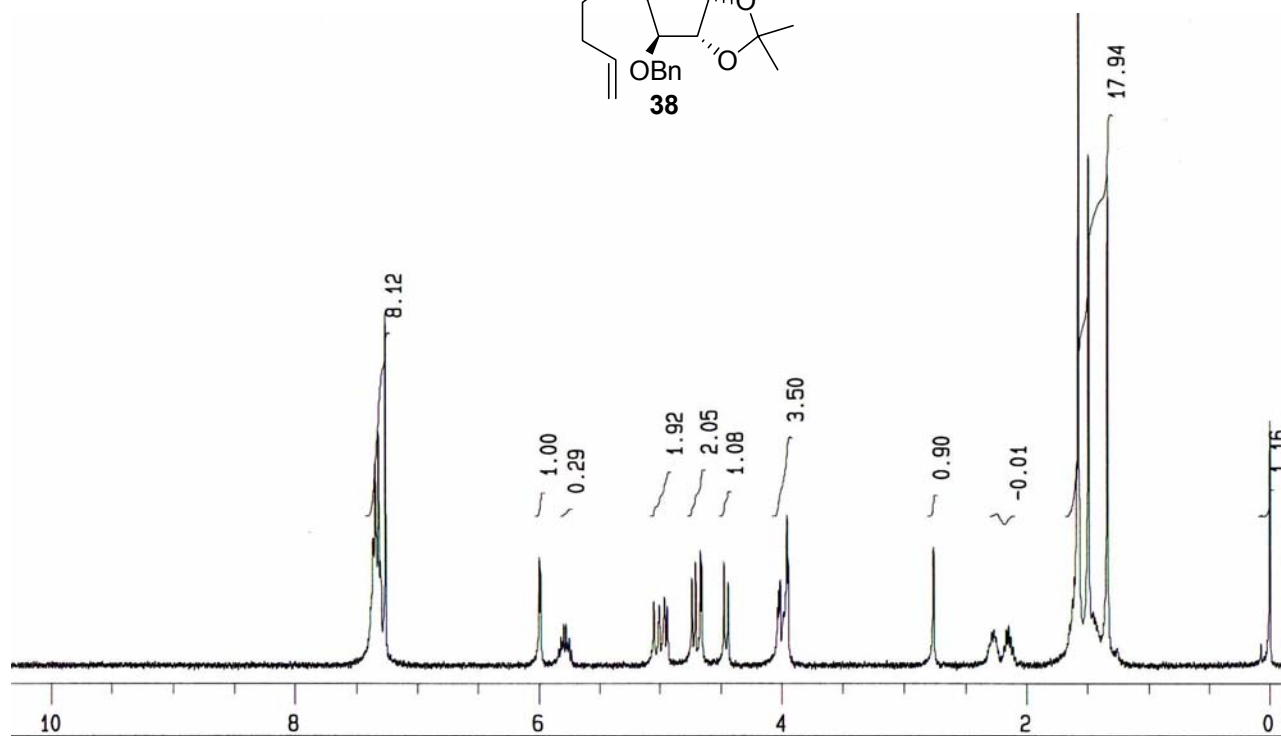
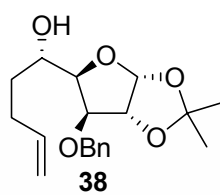


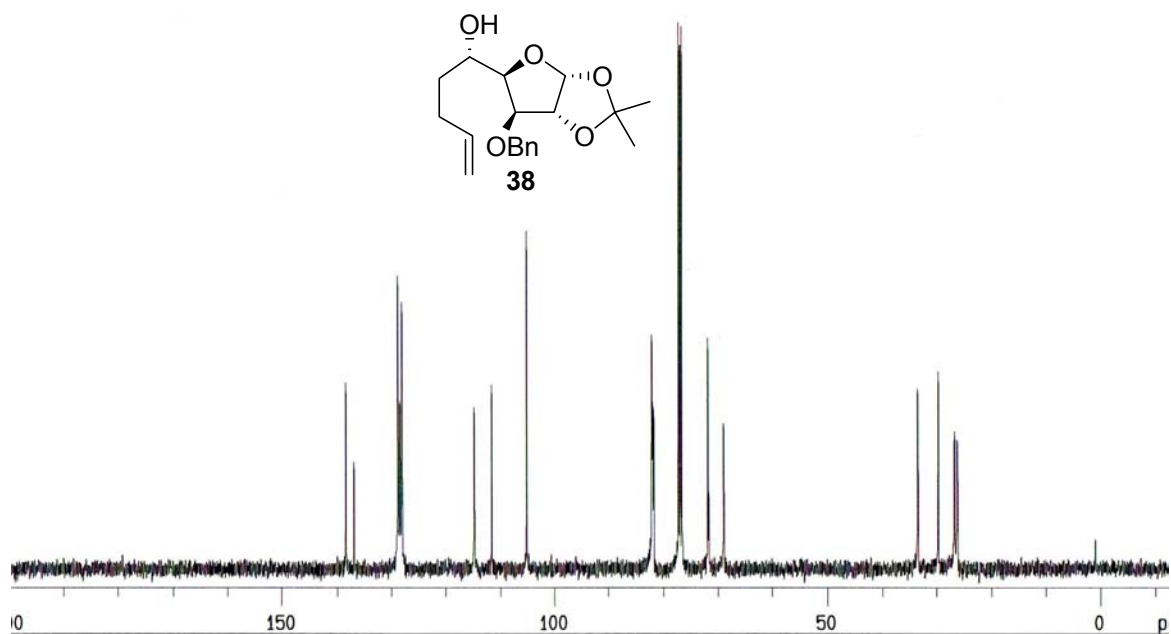
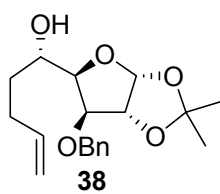
NOE spectrum of compound **35**

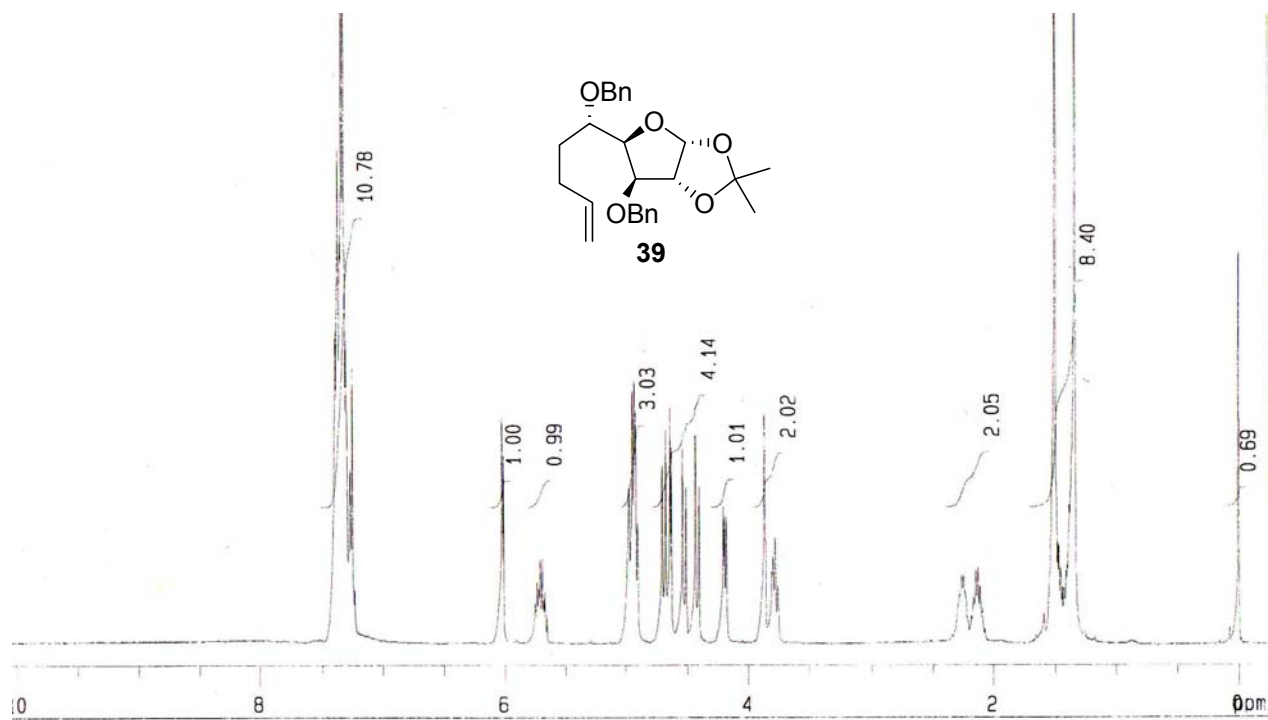


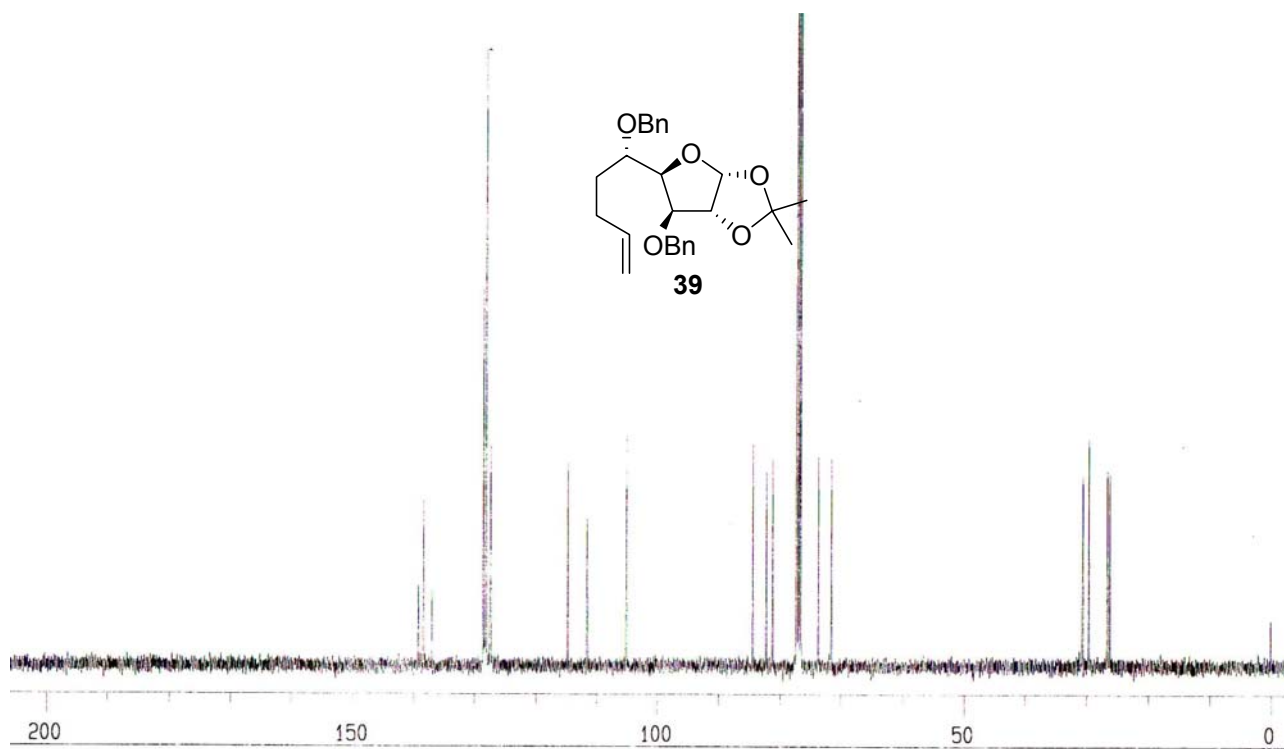
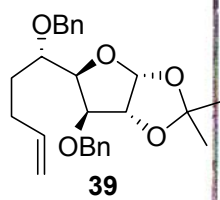


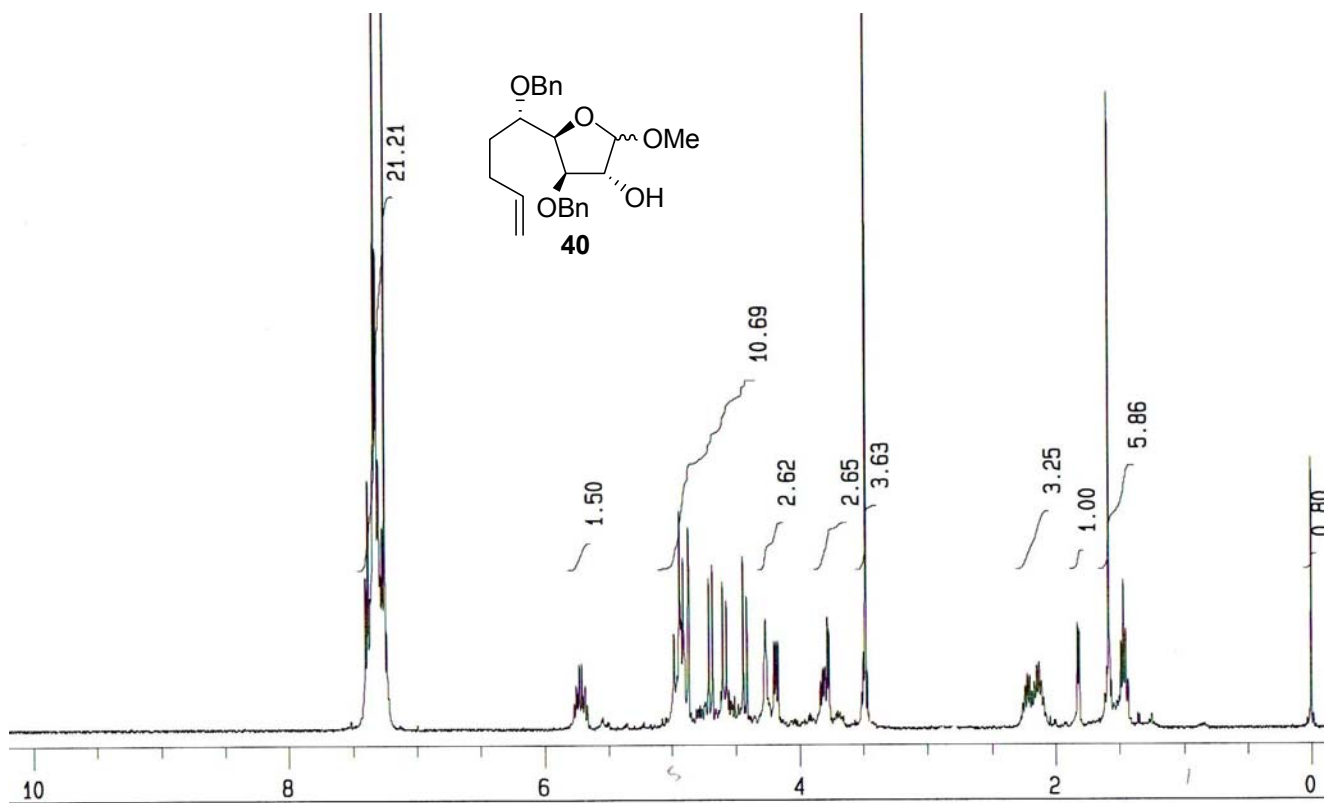


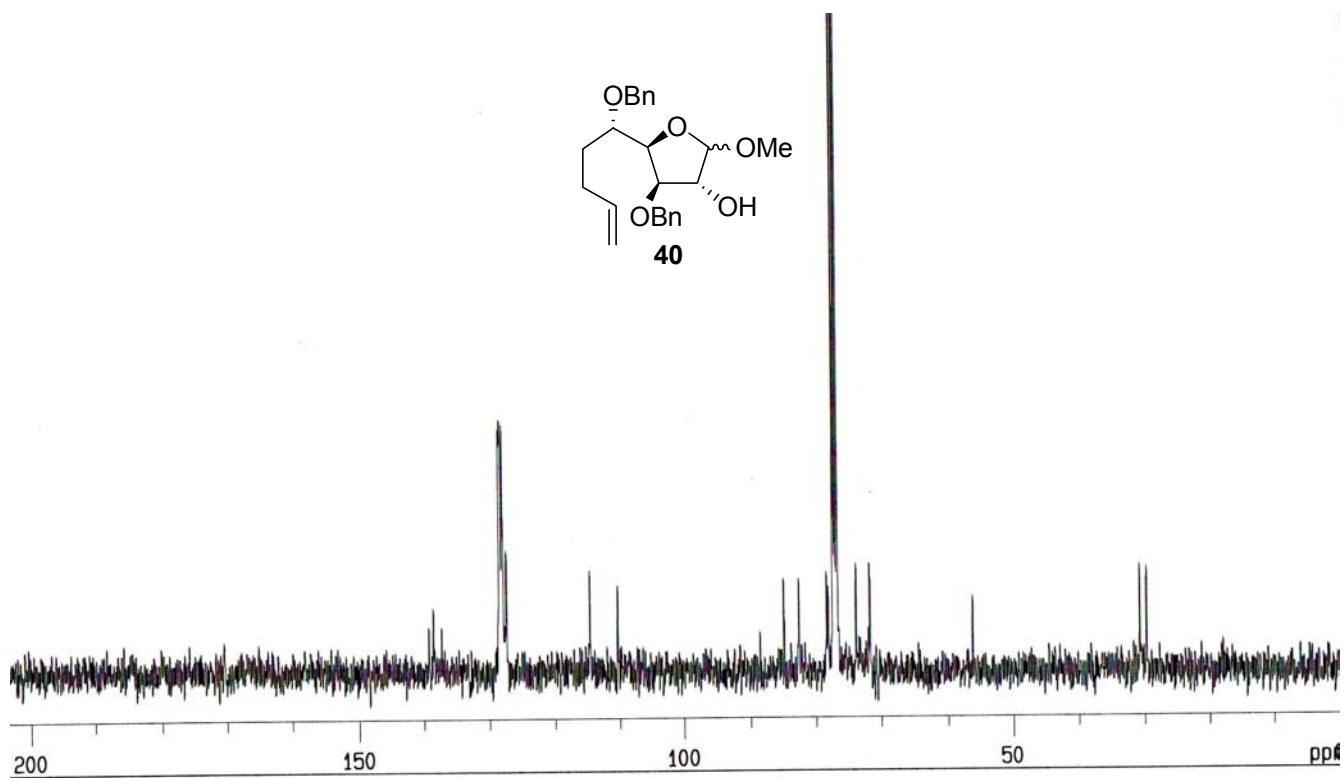
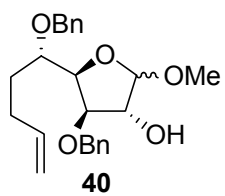


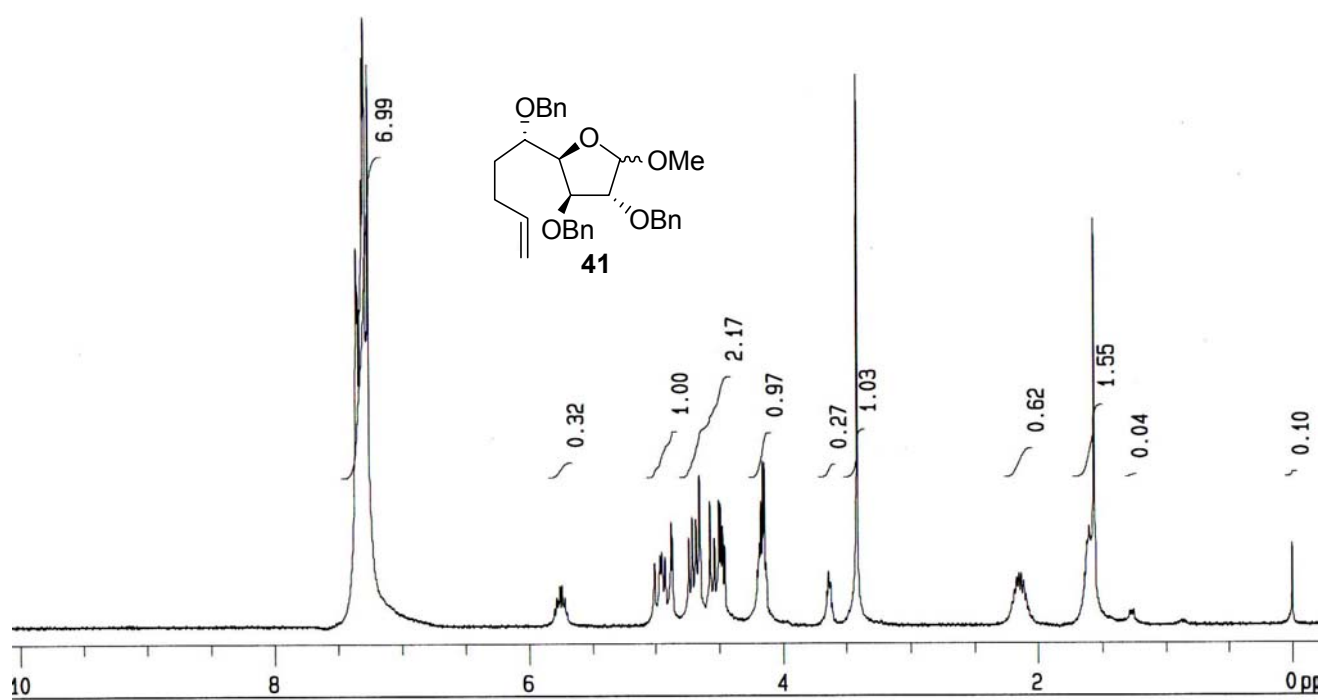


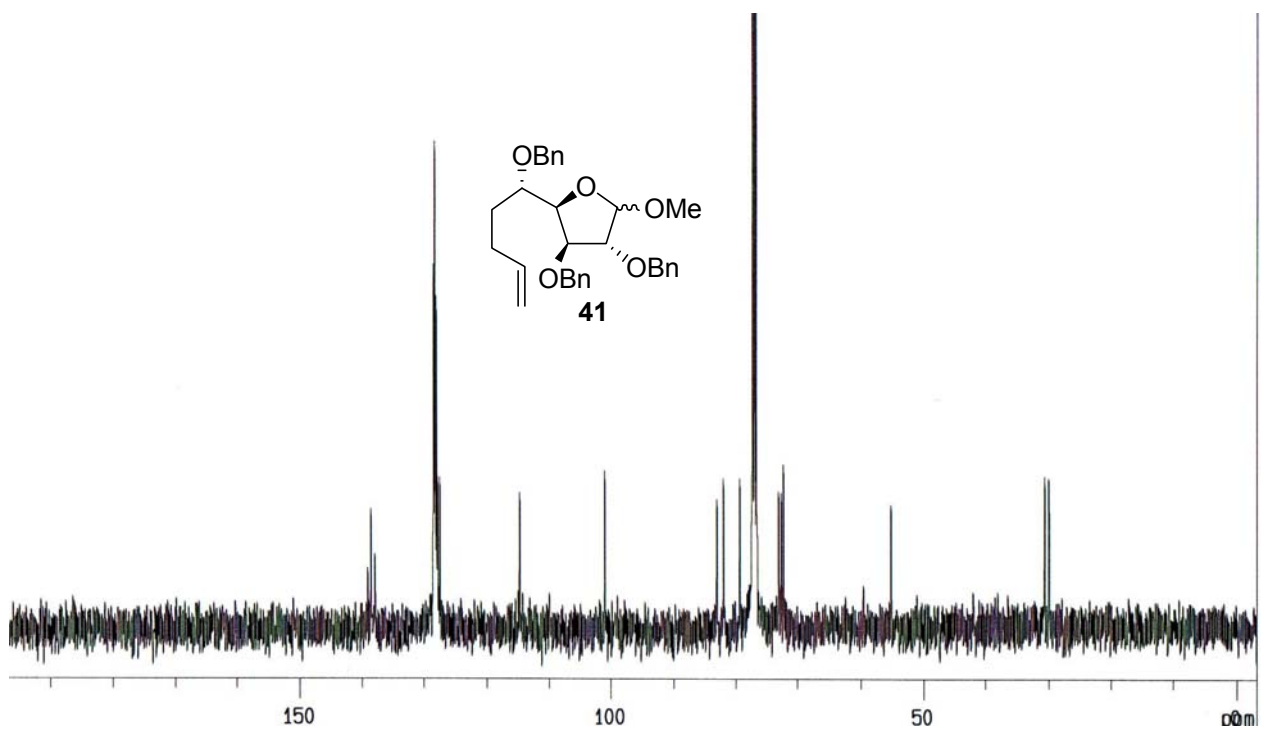


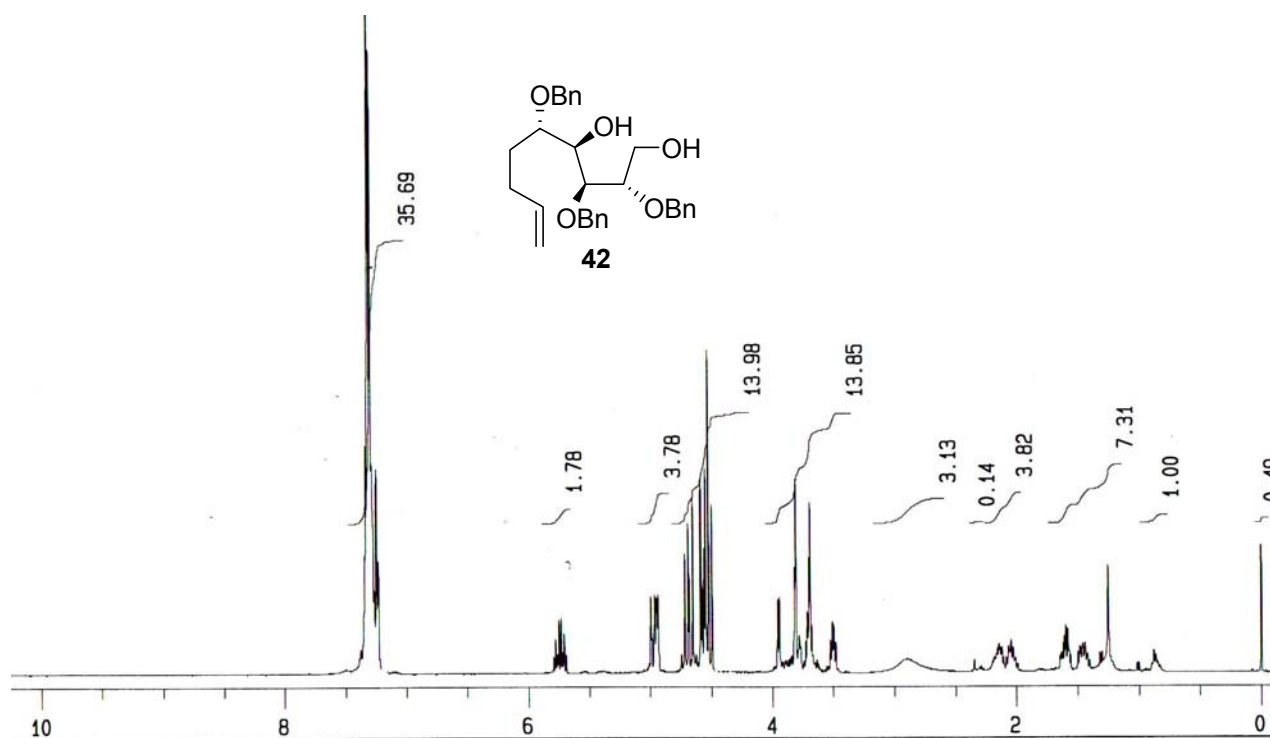


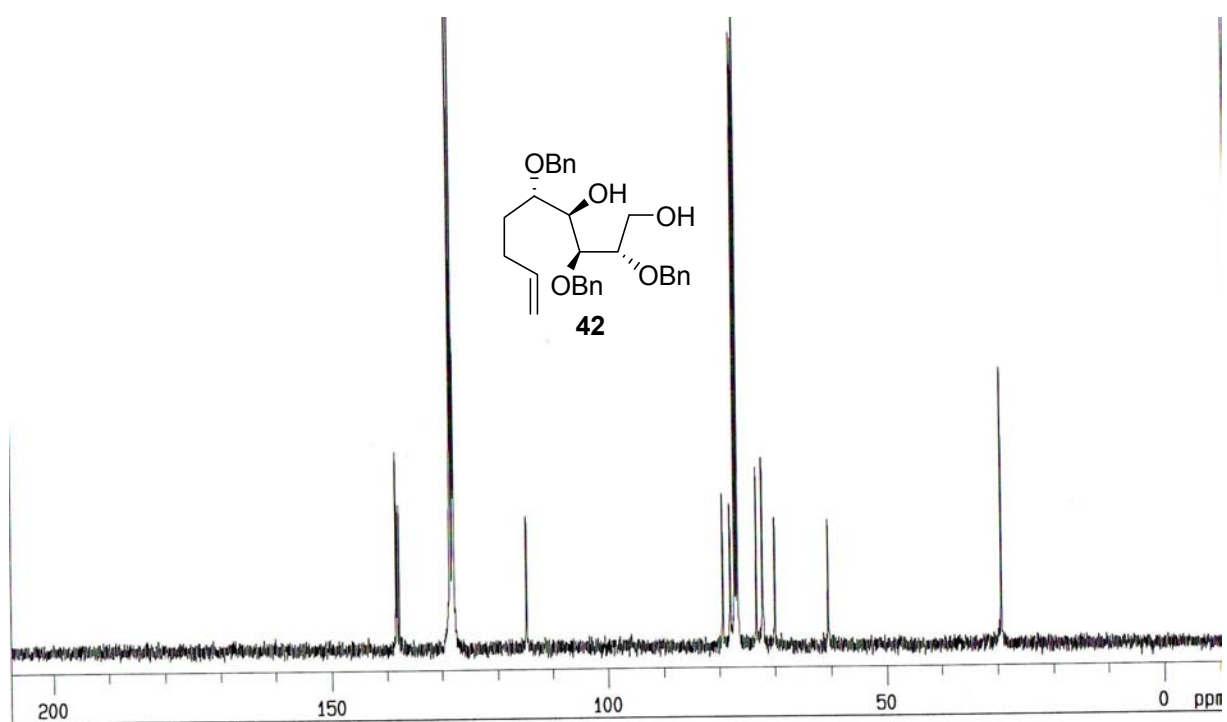


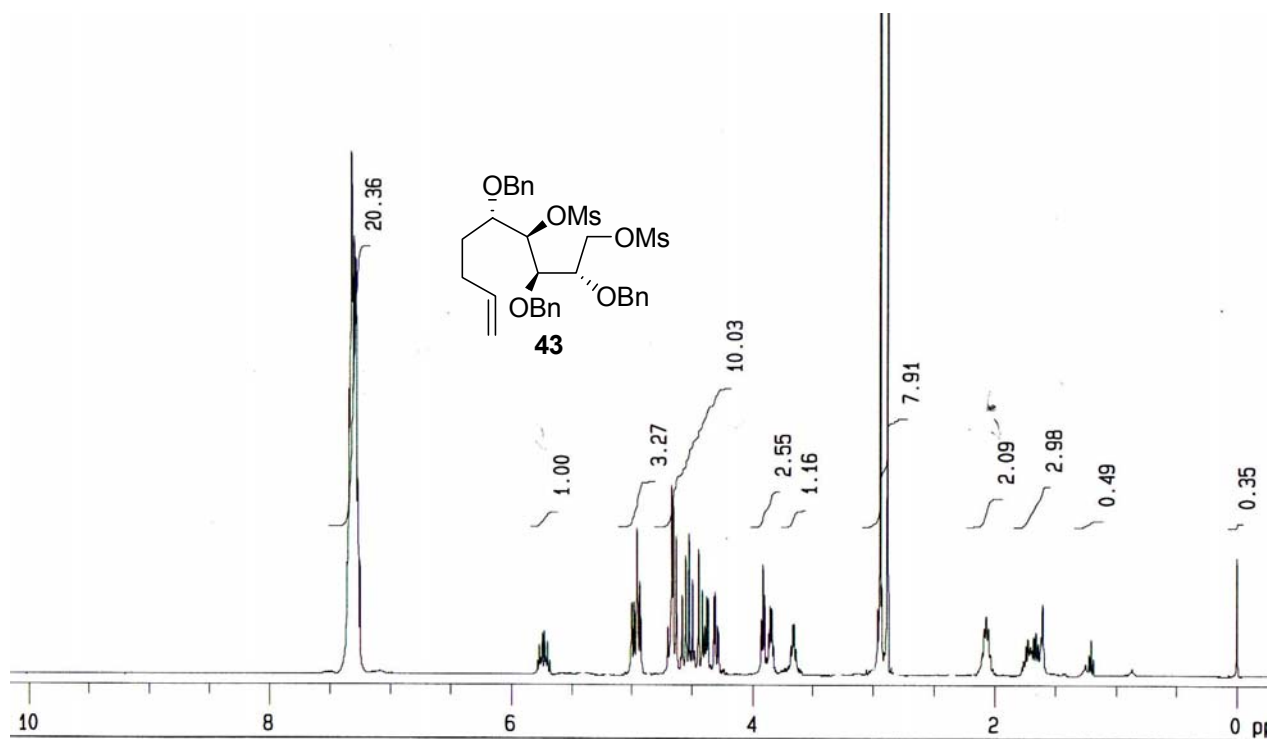


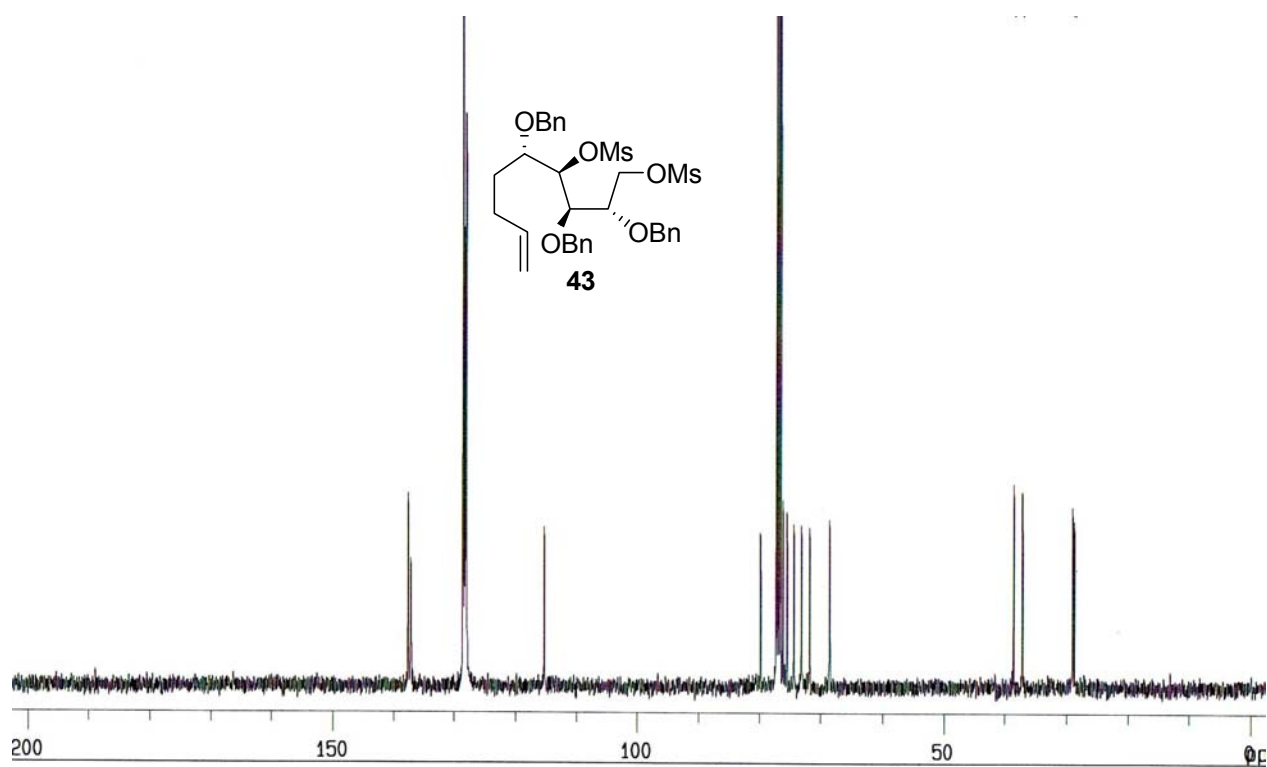


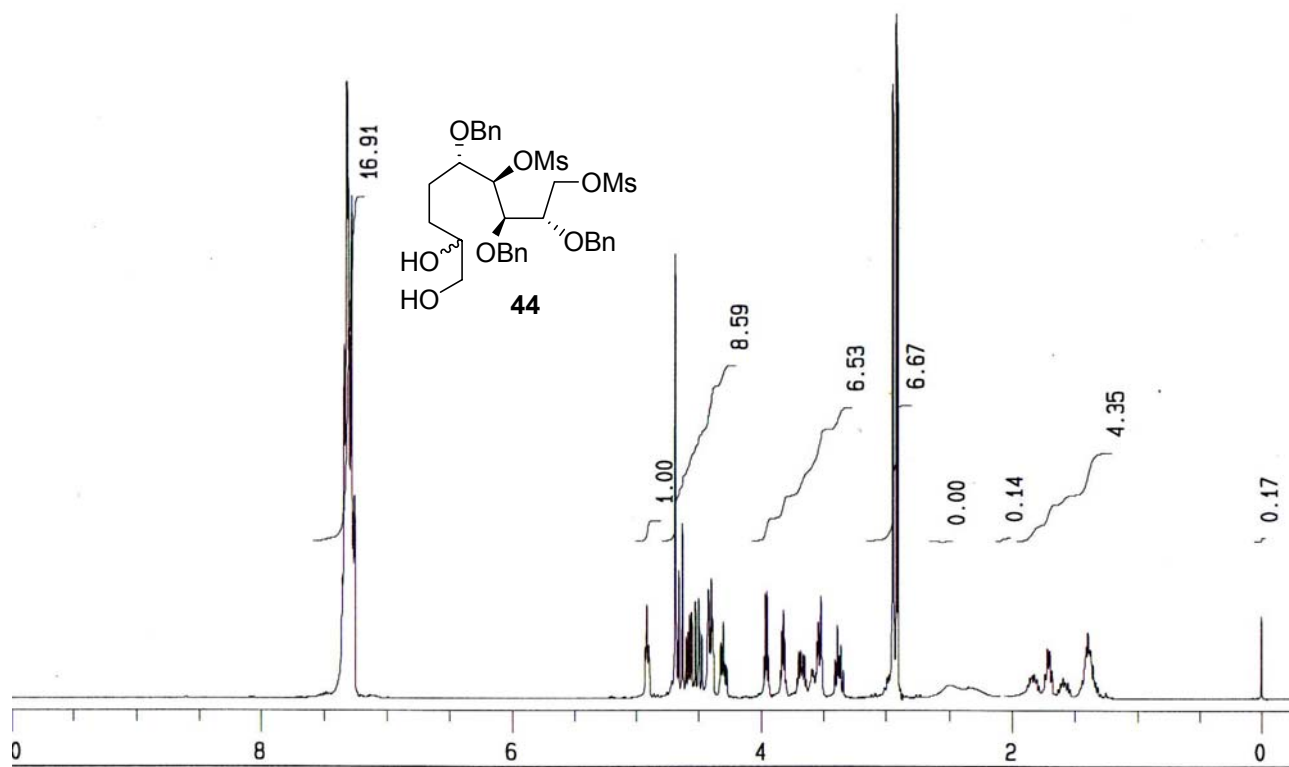


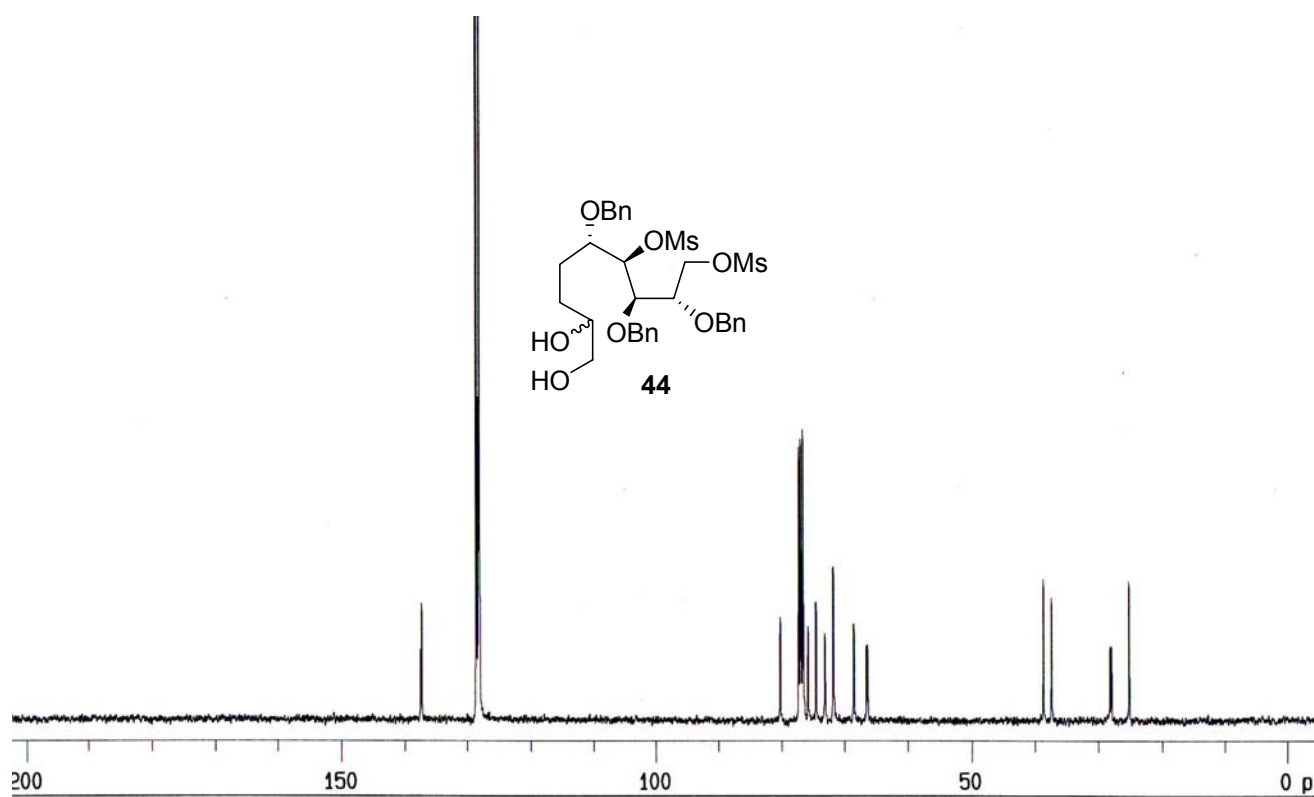




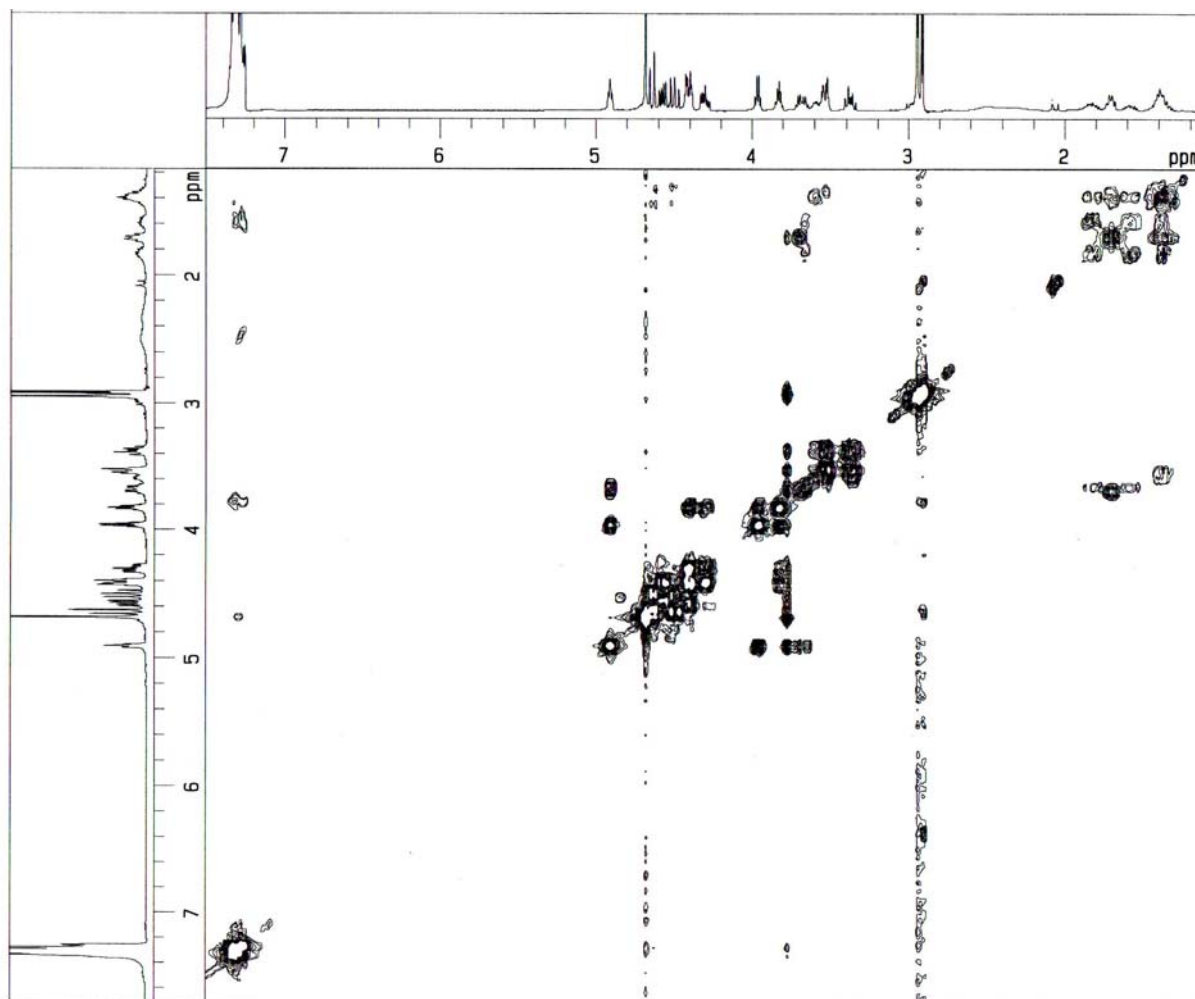
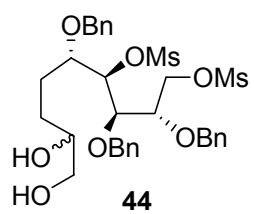


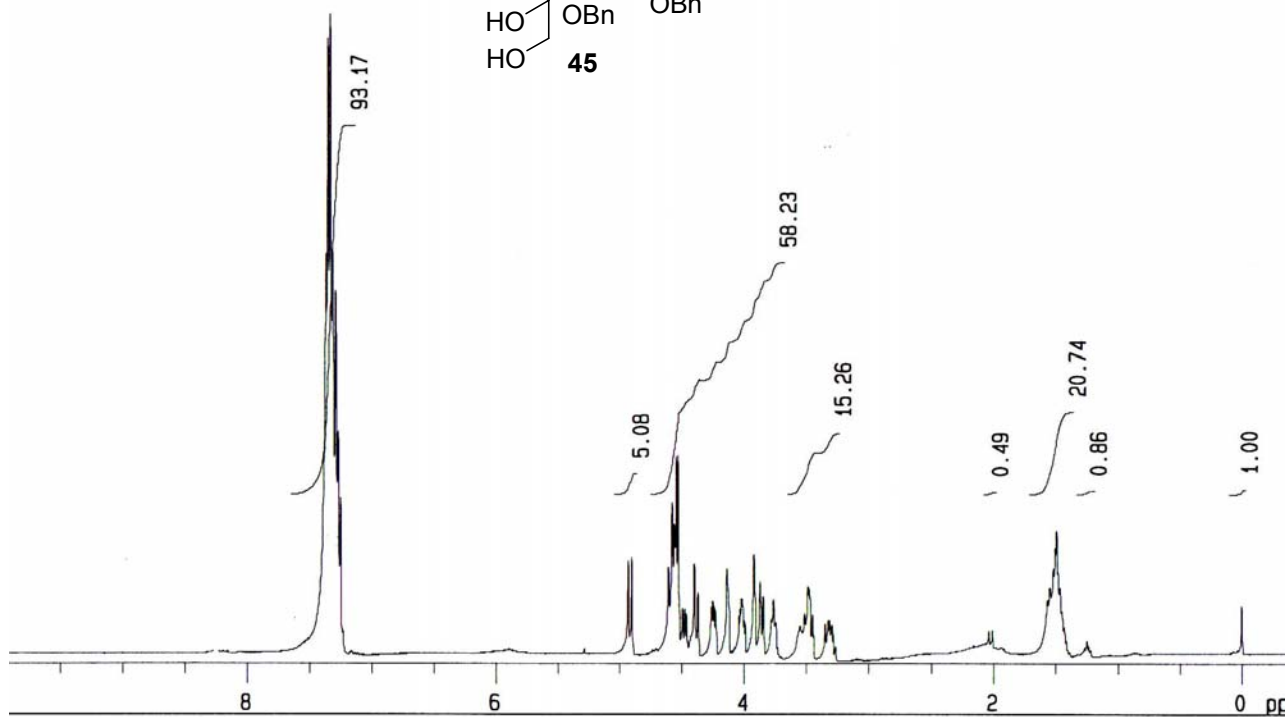
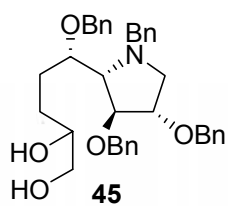


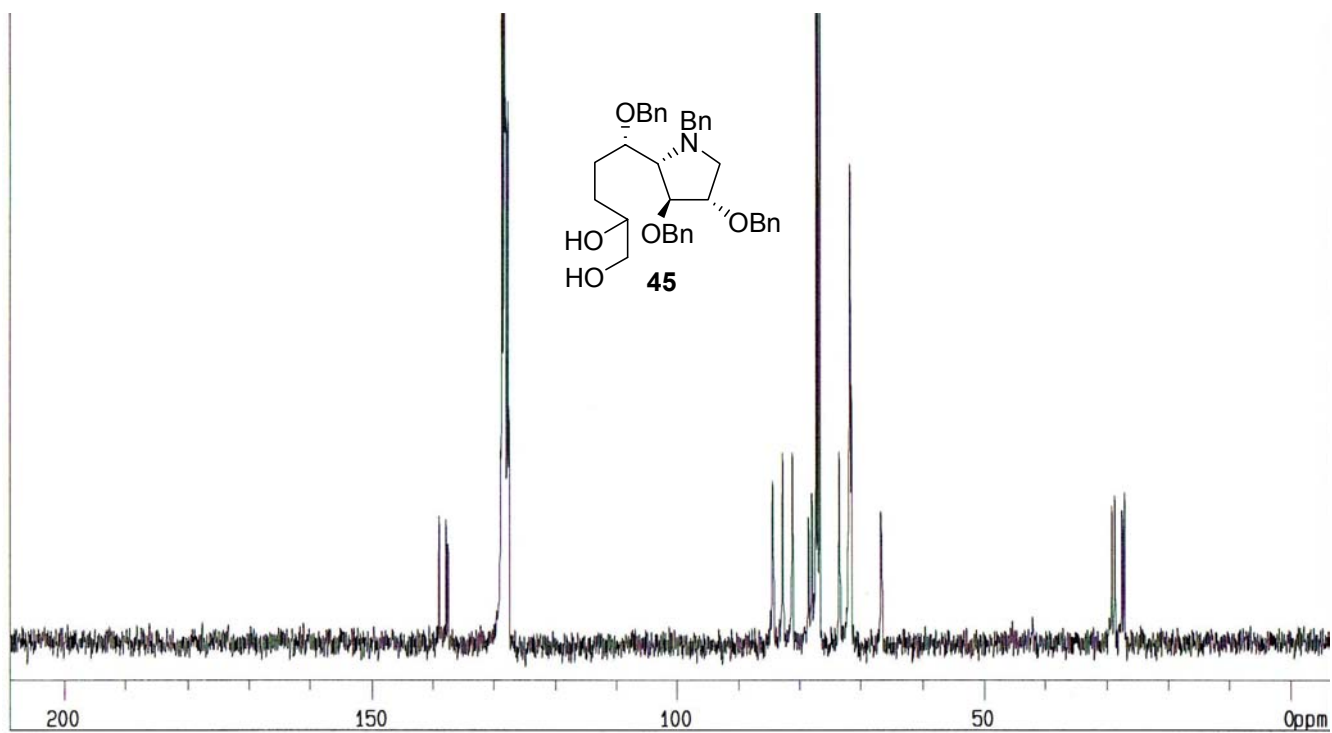




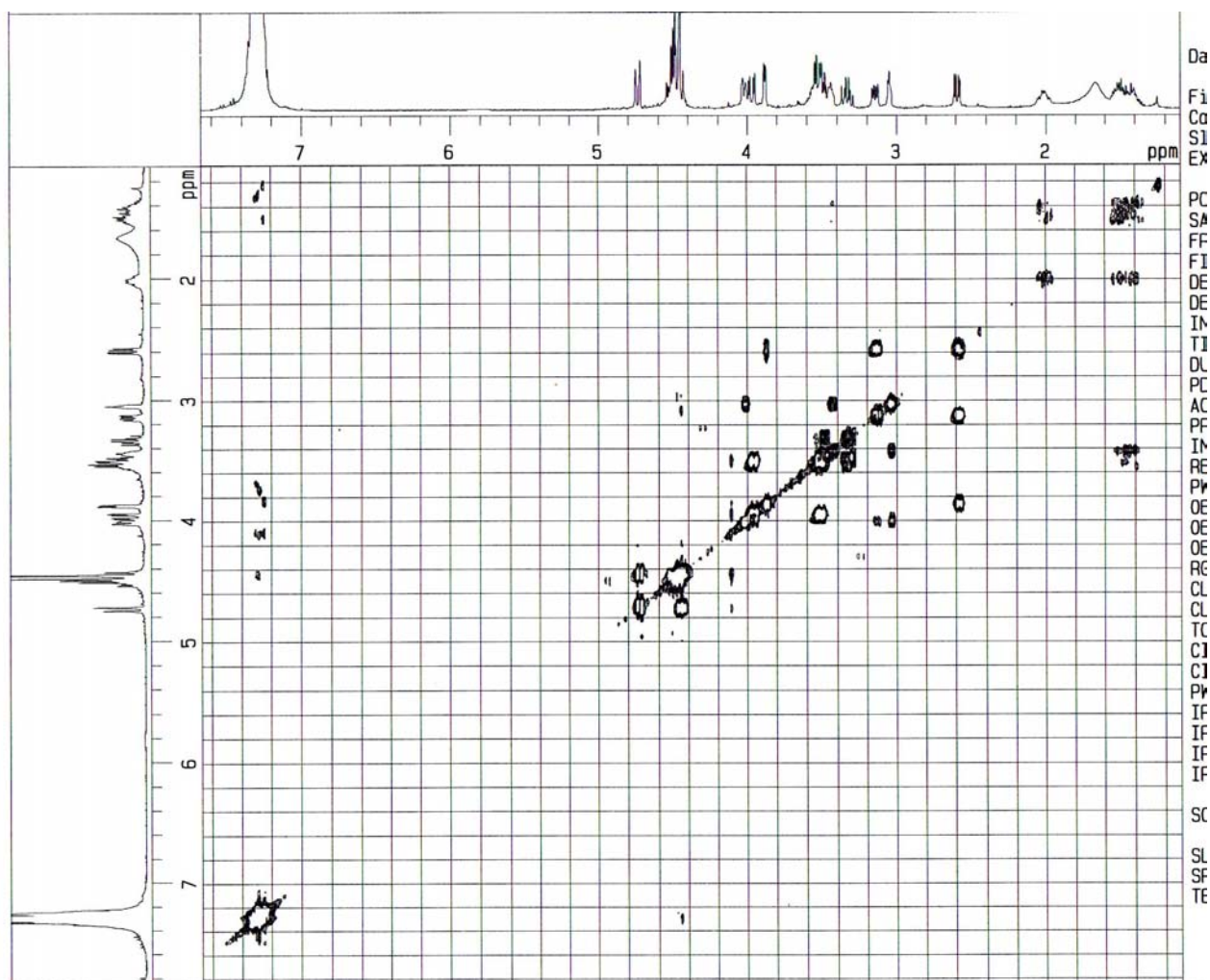
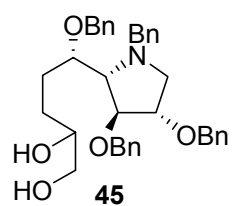
COSY spectrum of compound **44**

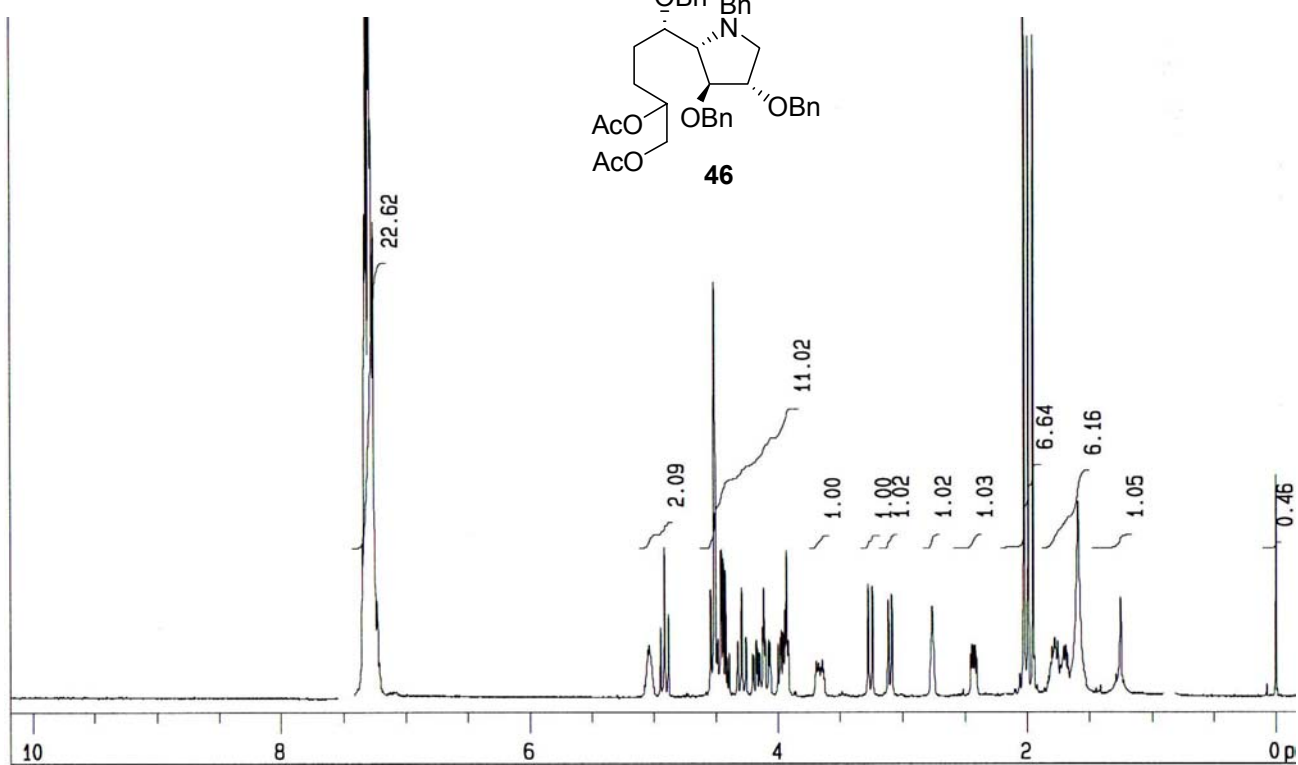
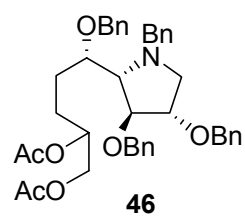


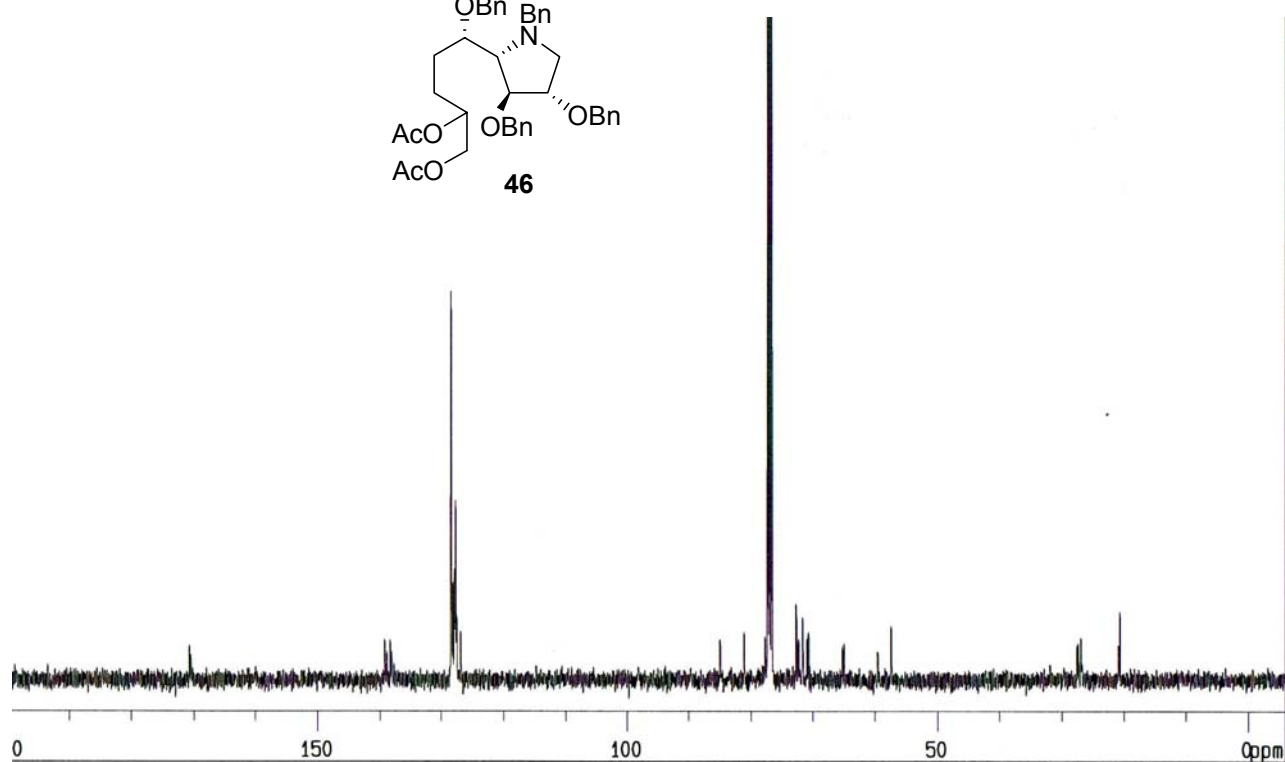
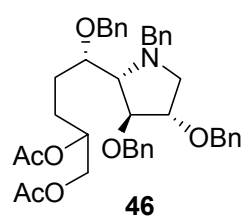


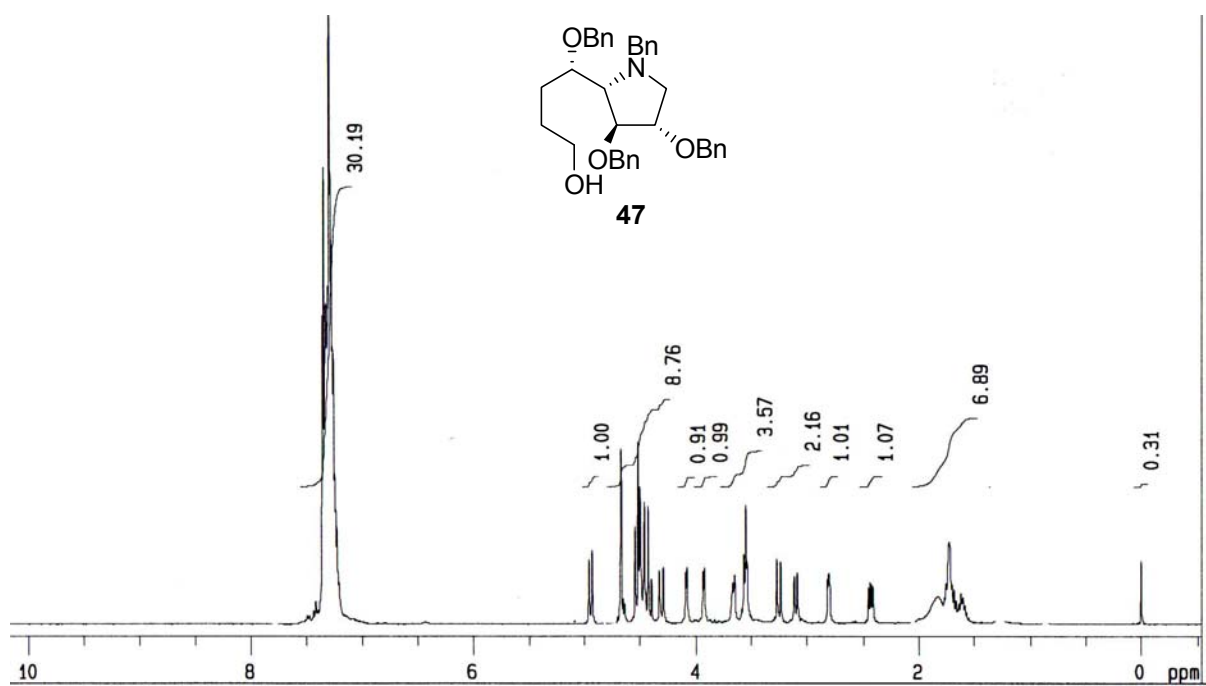


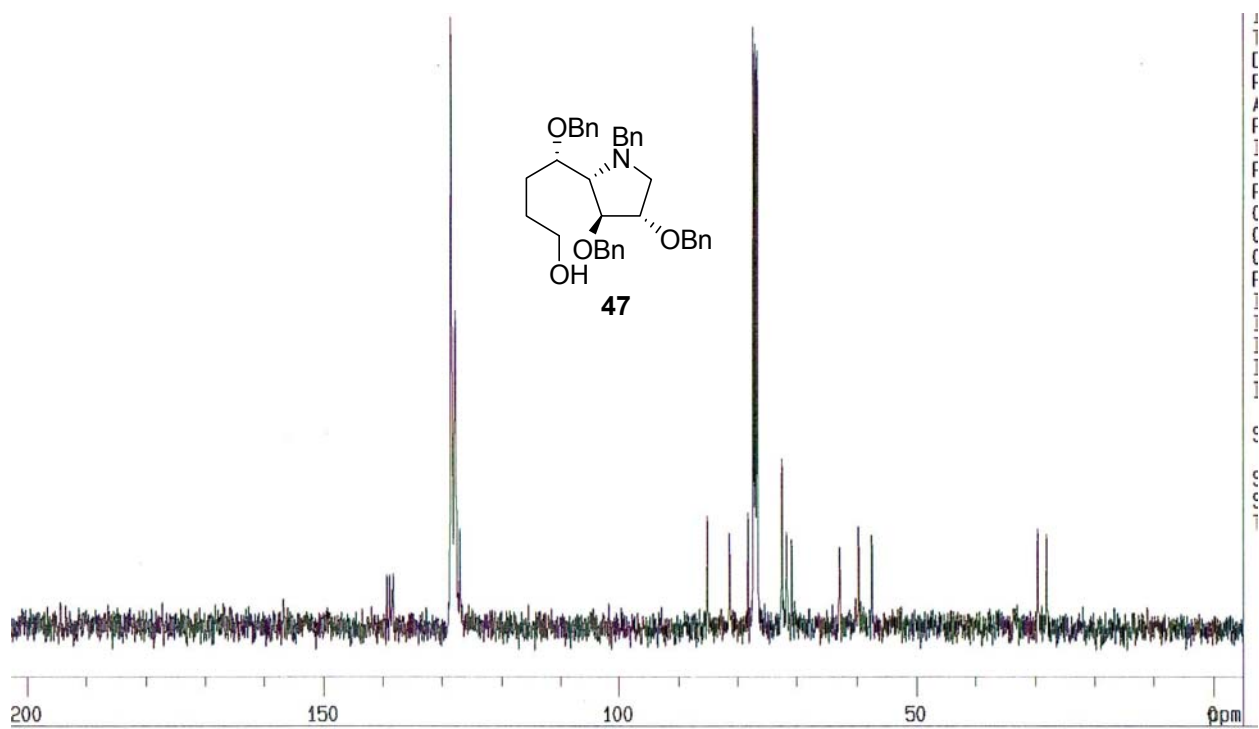
COSY spectrum of compound **45**

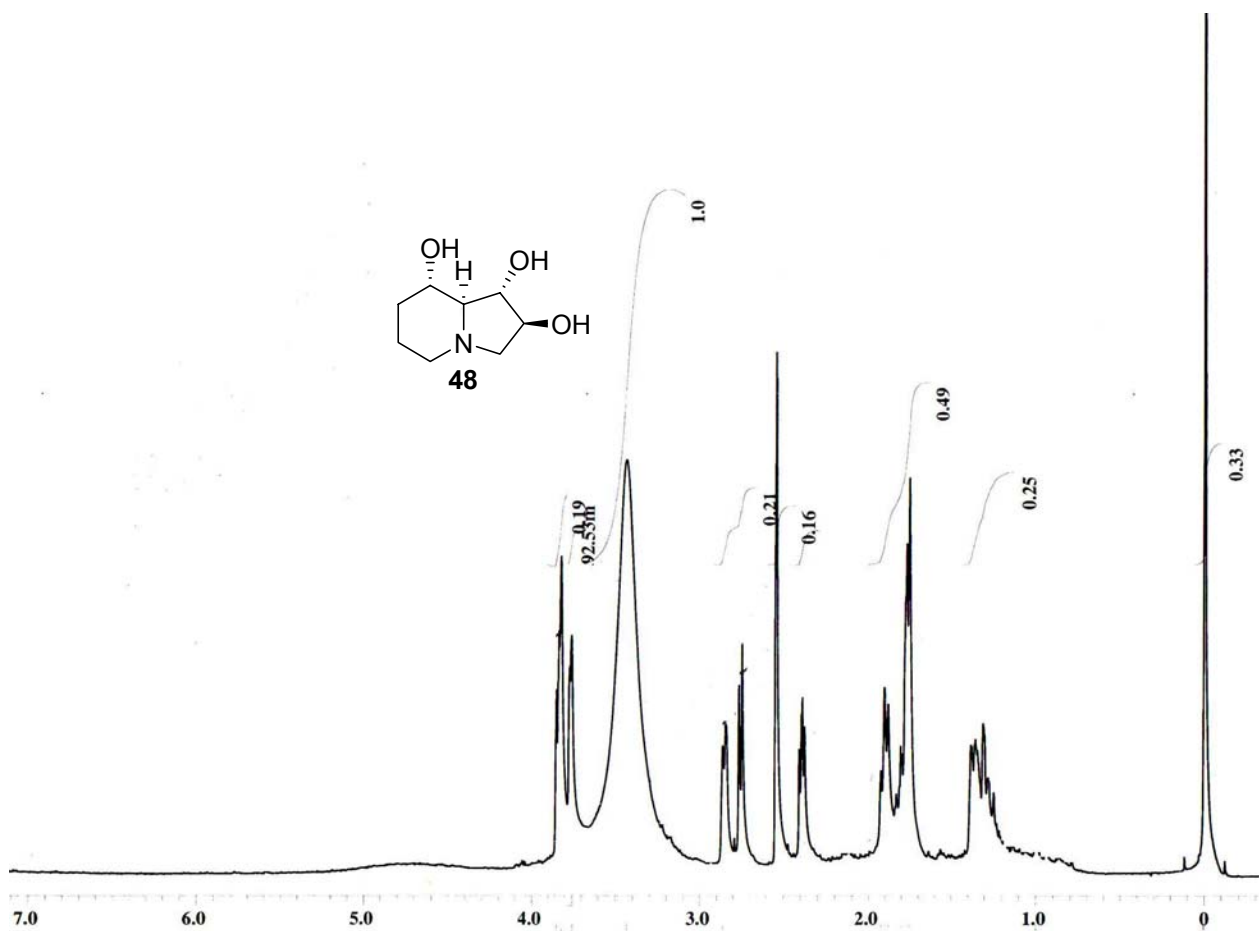
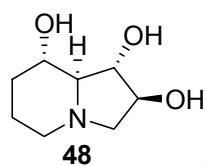


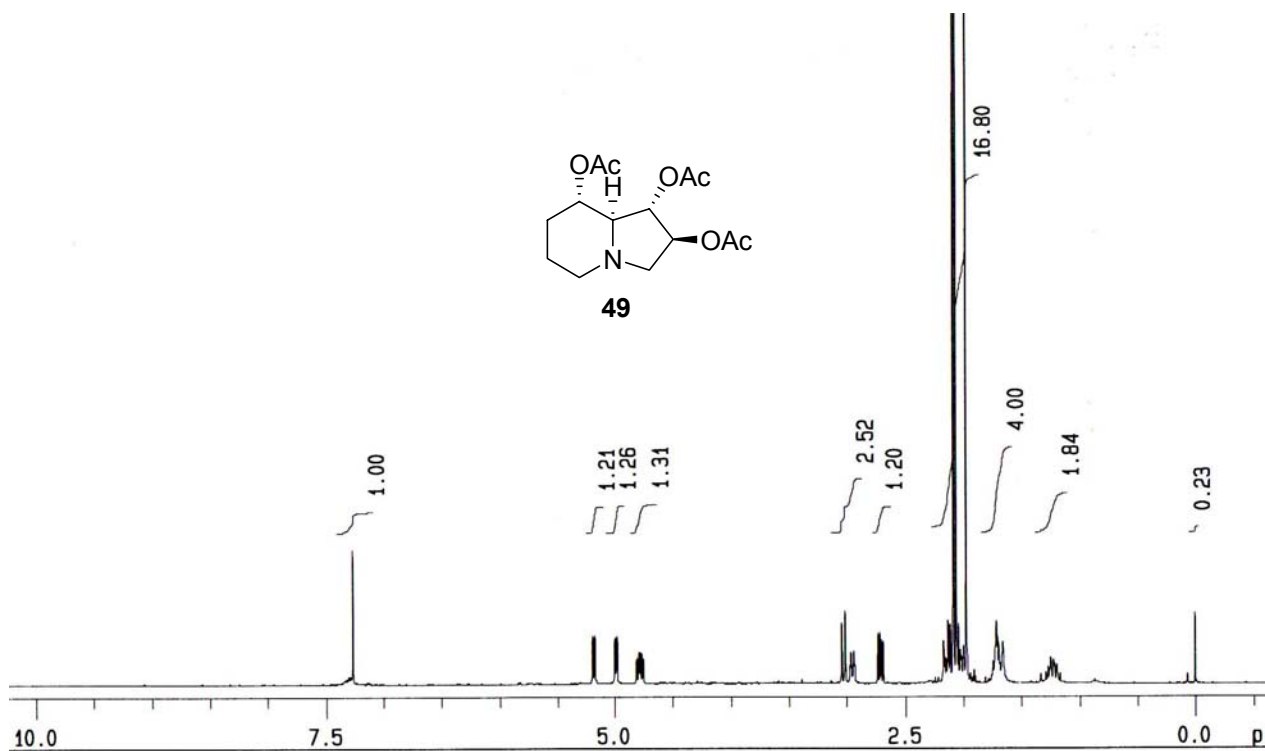
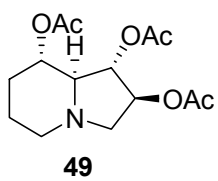


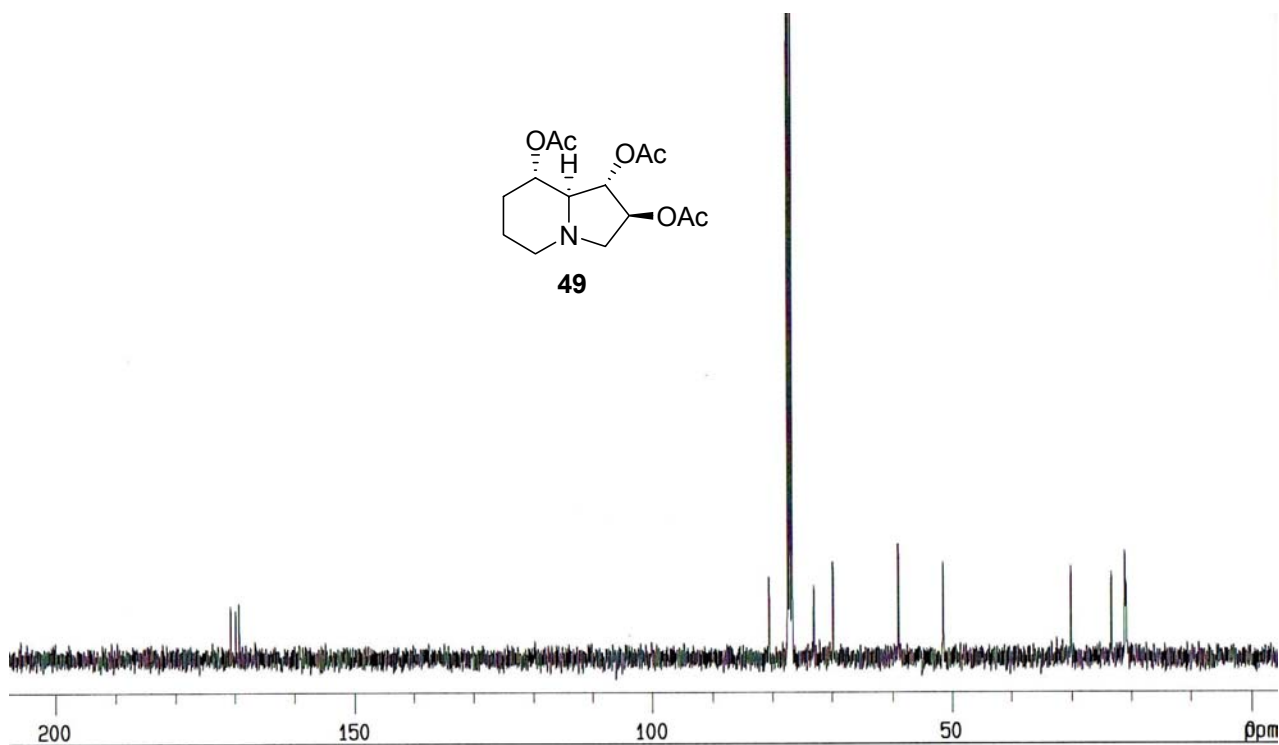
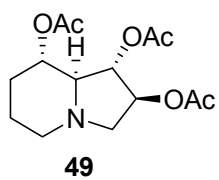




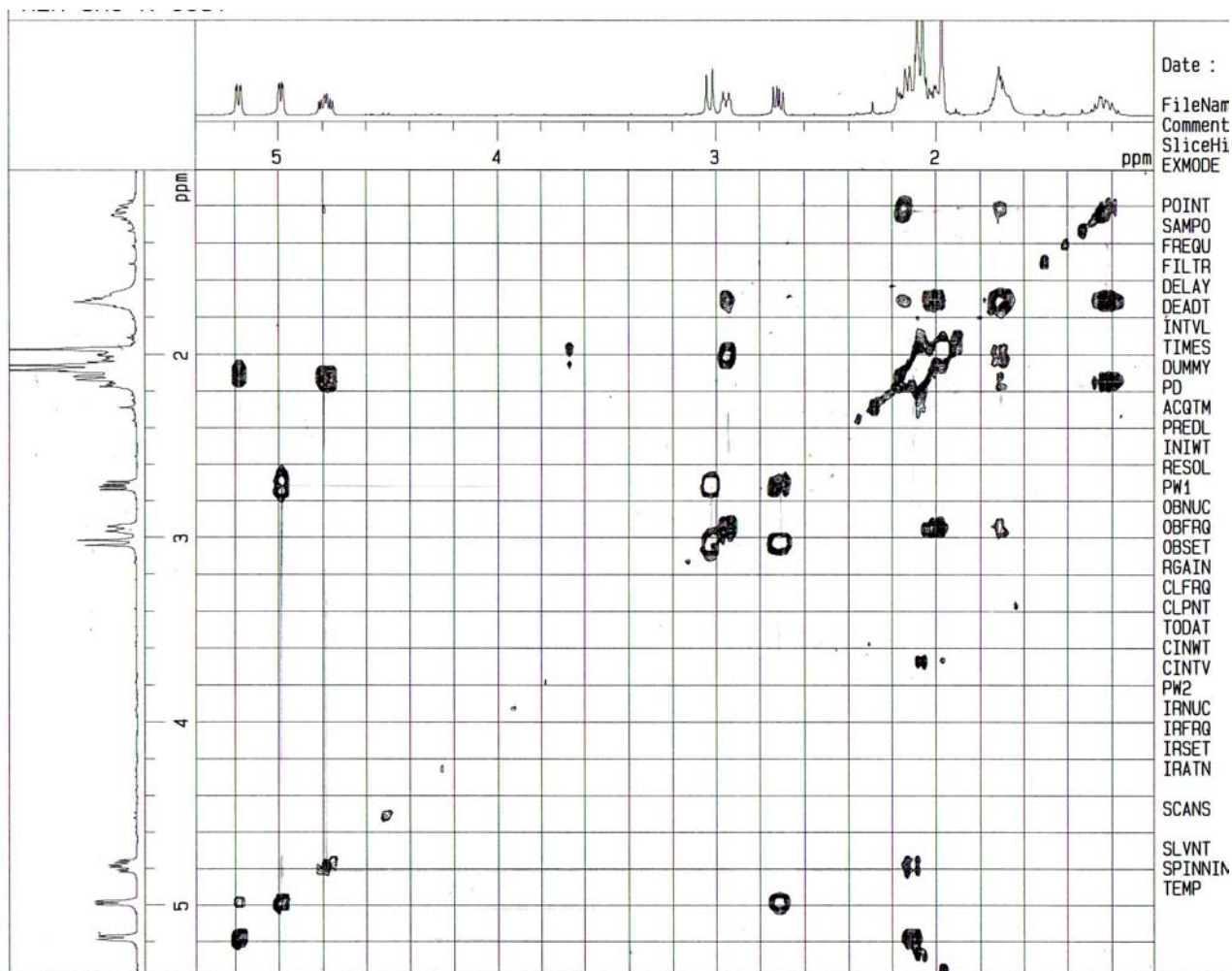
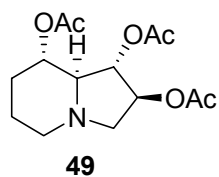




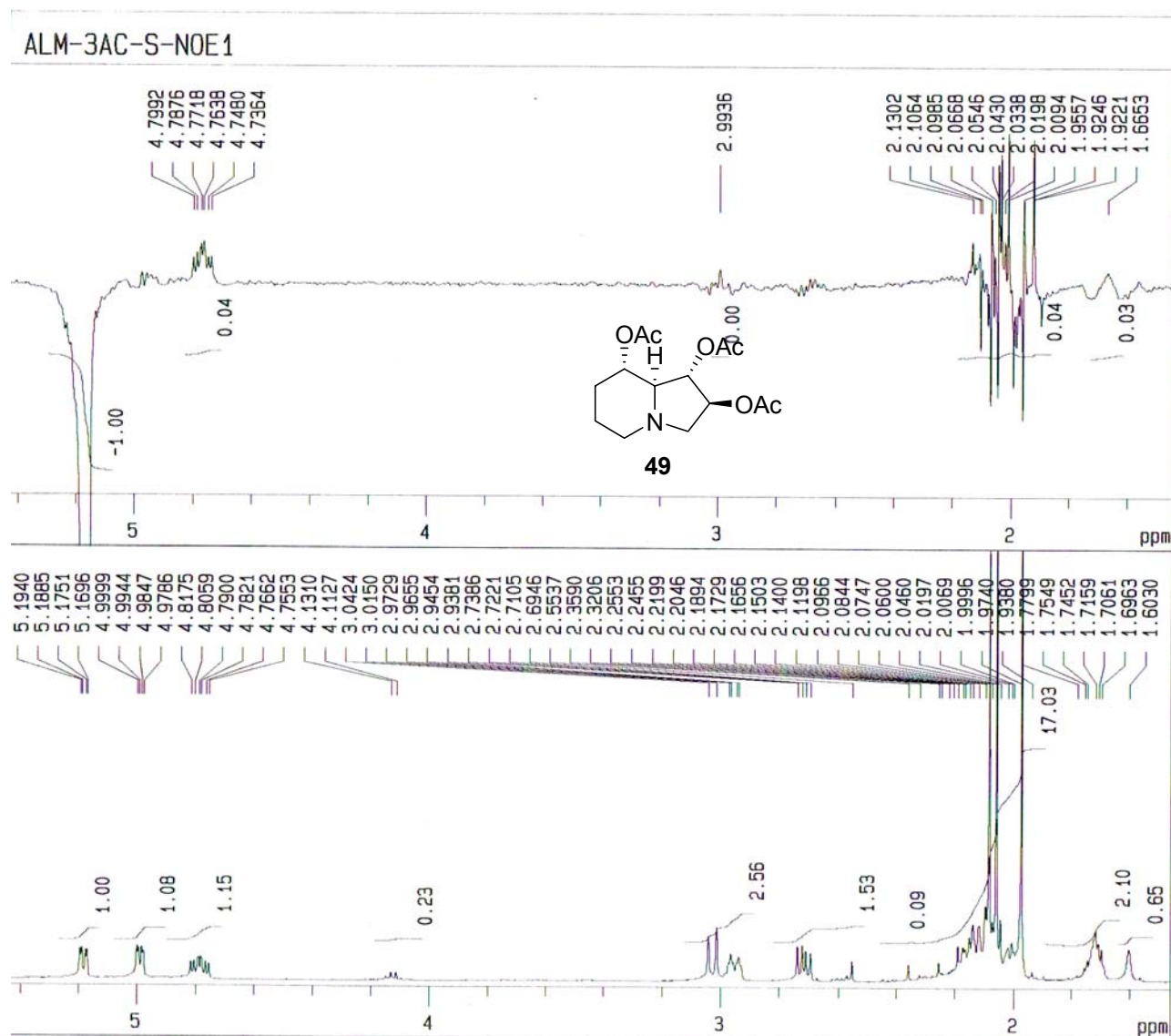




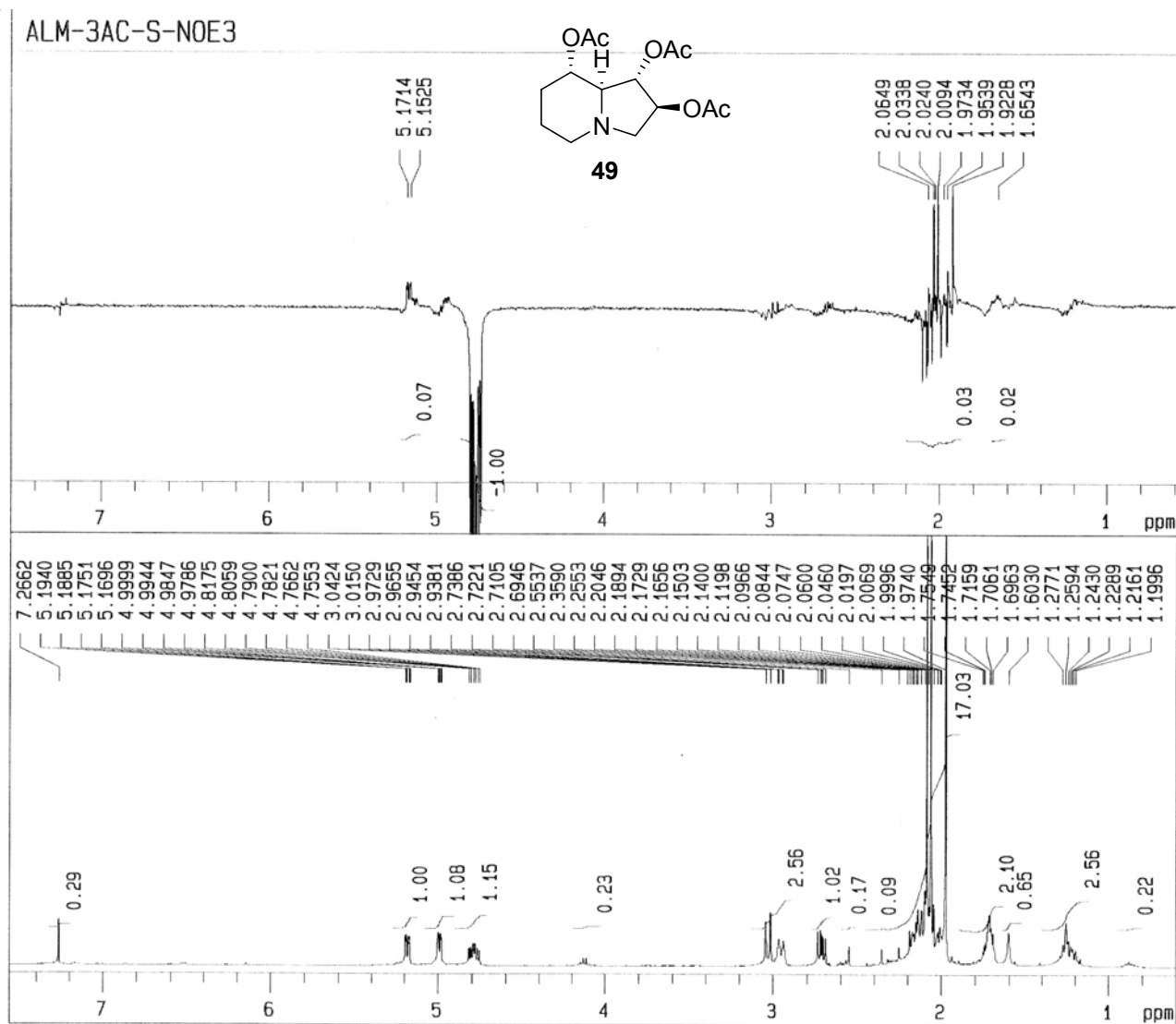
COSY spectrum of compound **49**

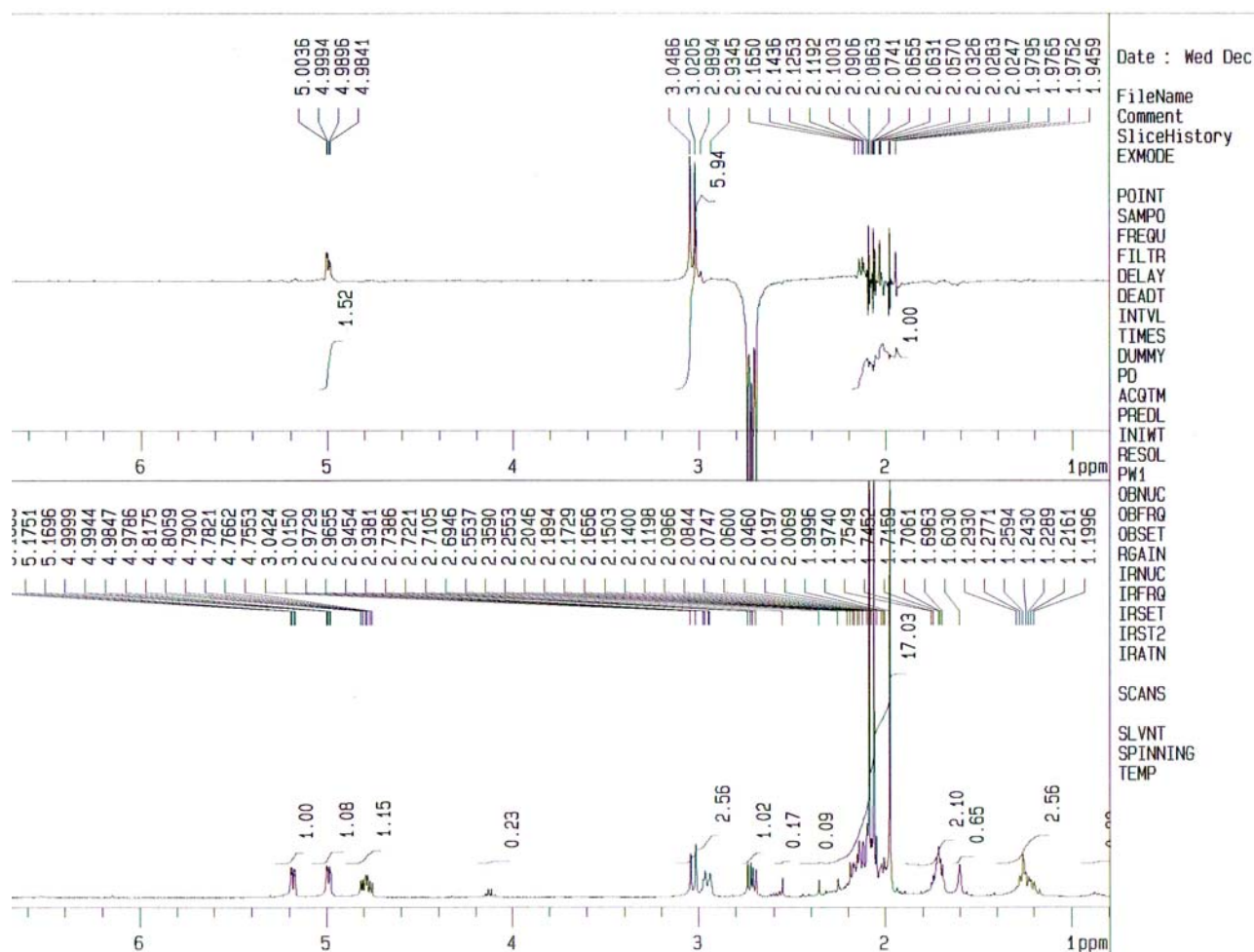
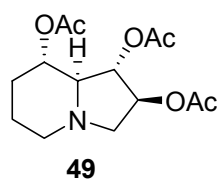


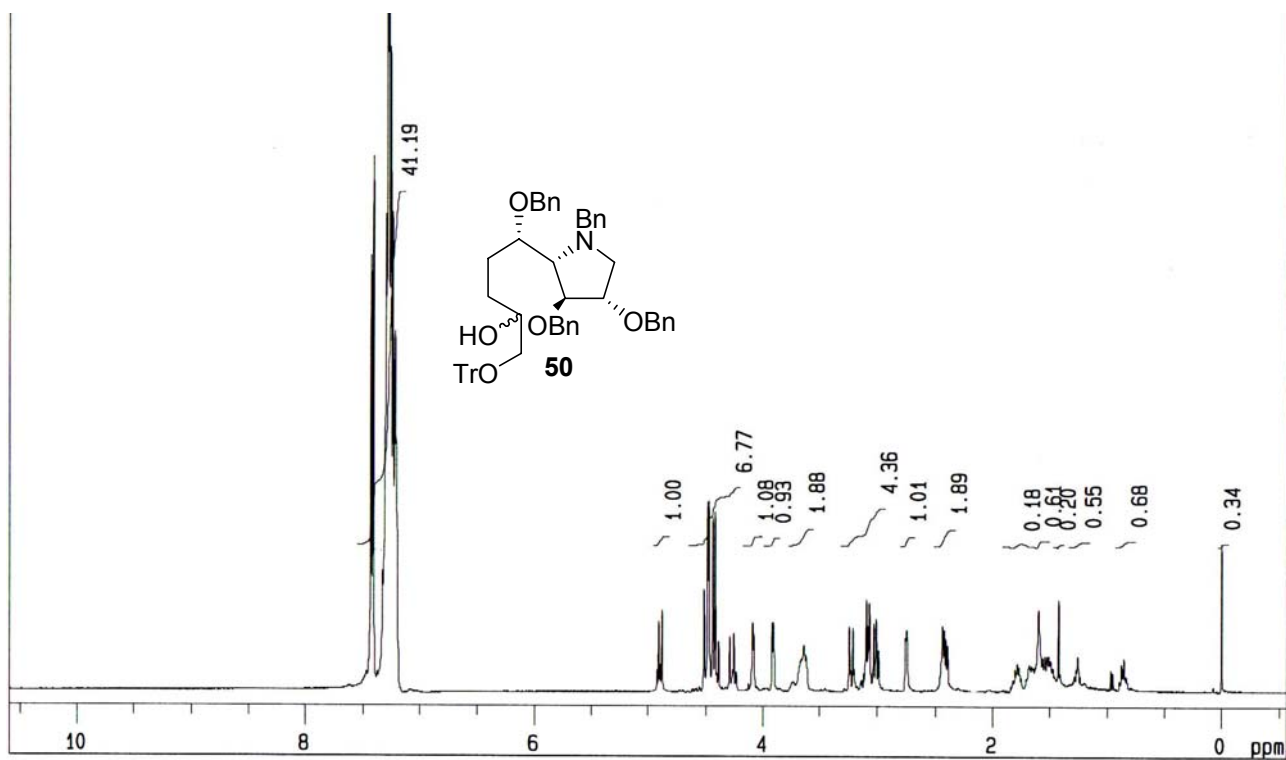
NOE spectrum of compound **49**

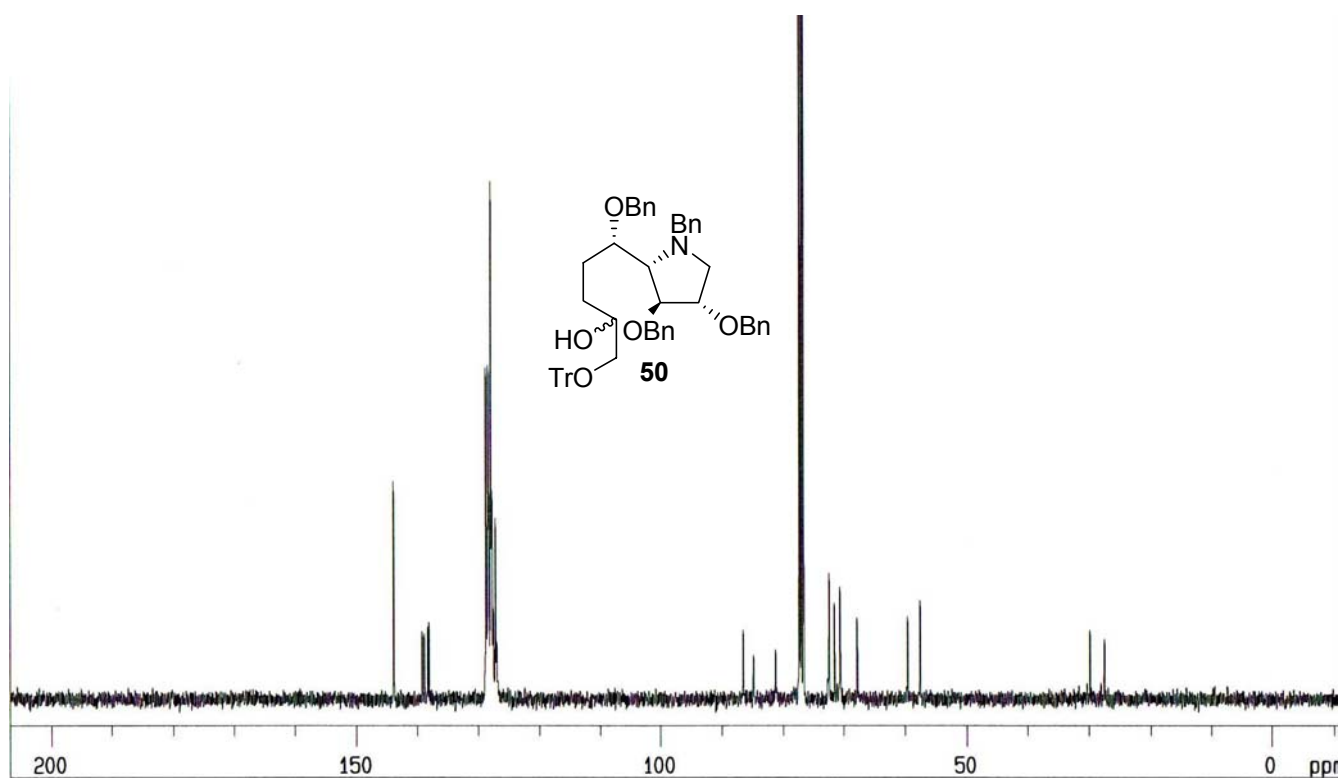


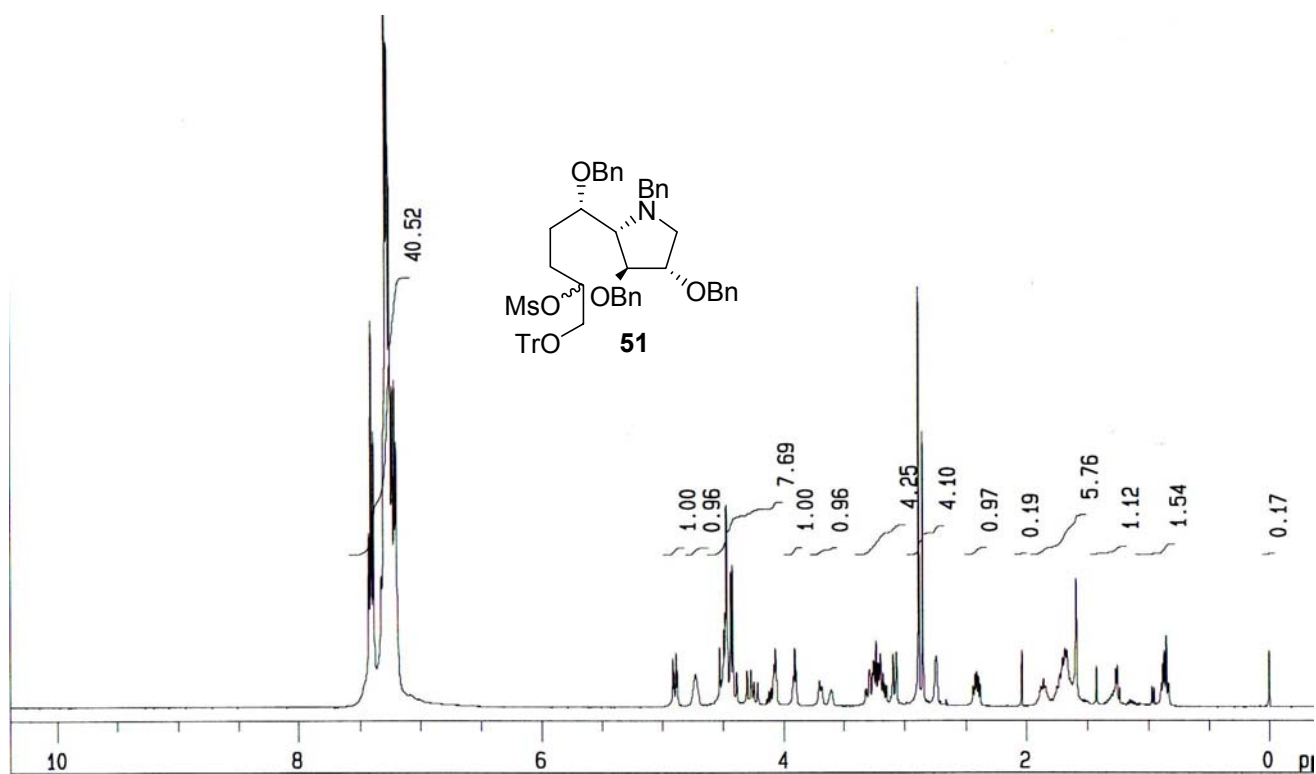
NOE spectrum of compound **49**

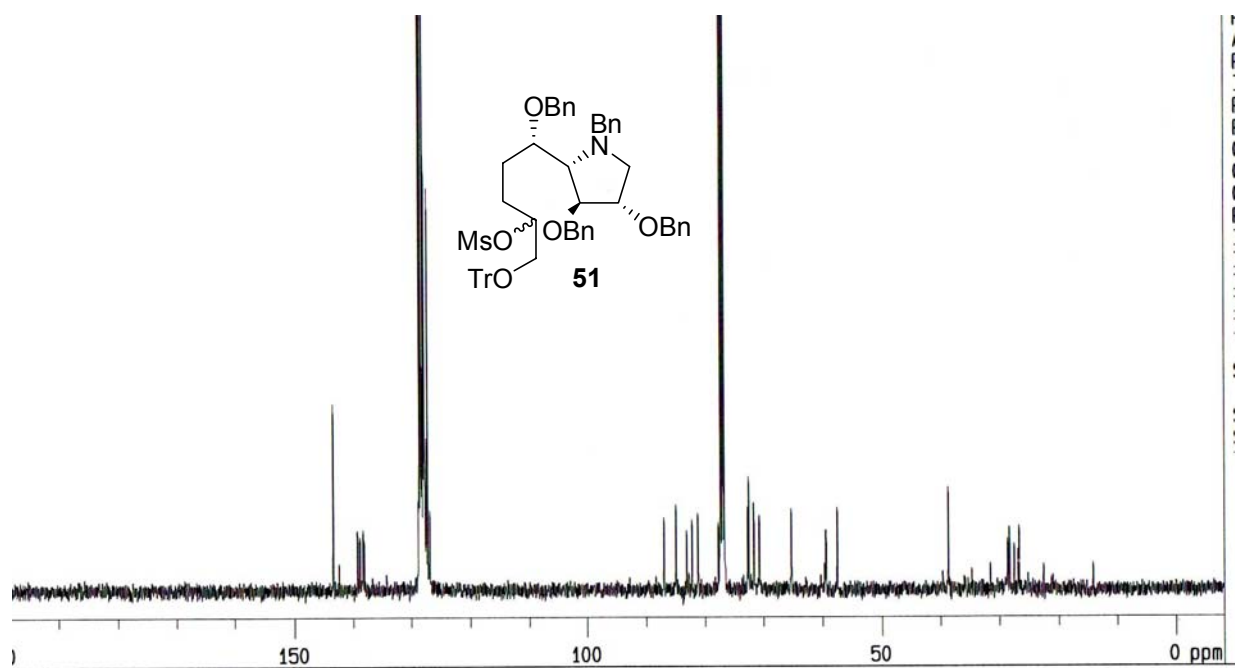


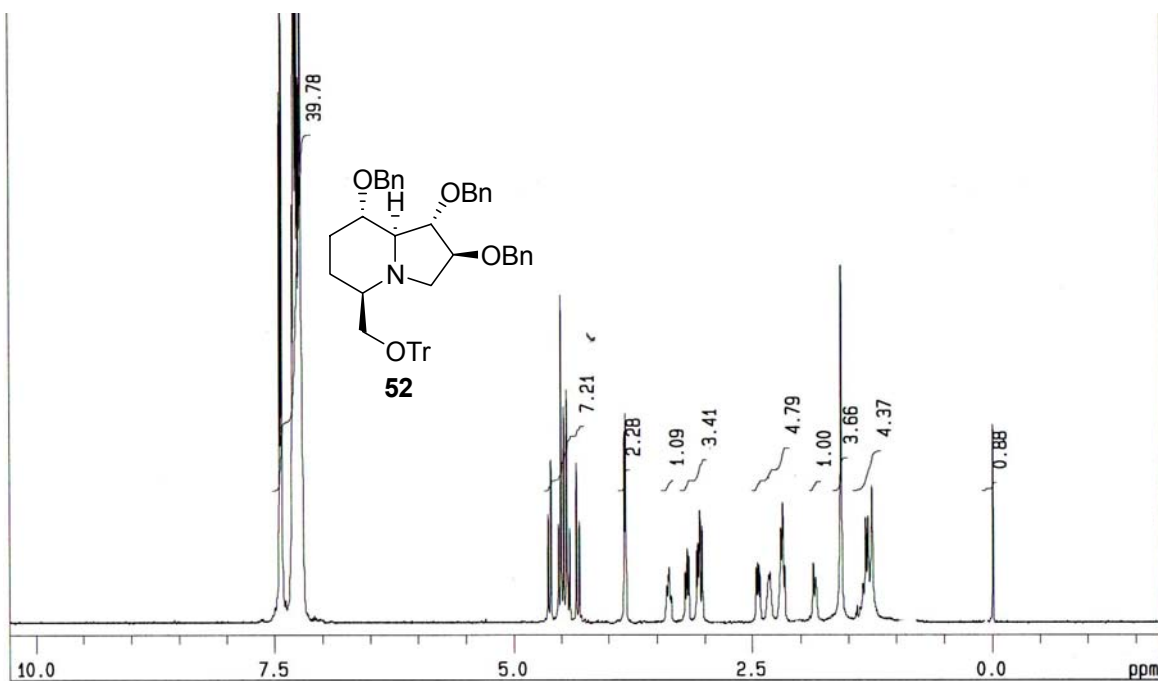
NOE spectrum of compound **49**

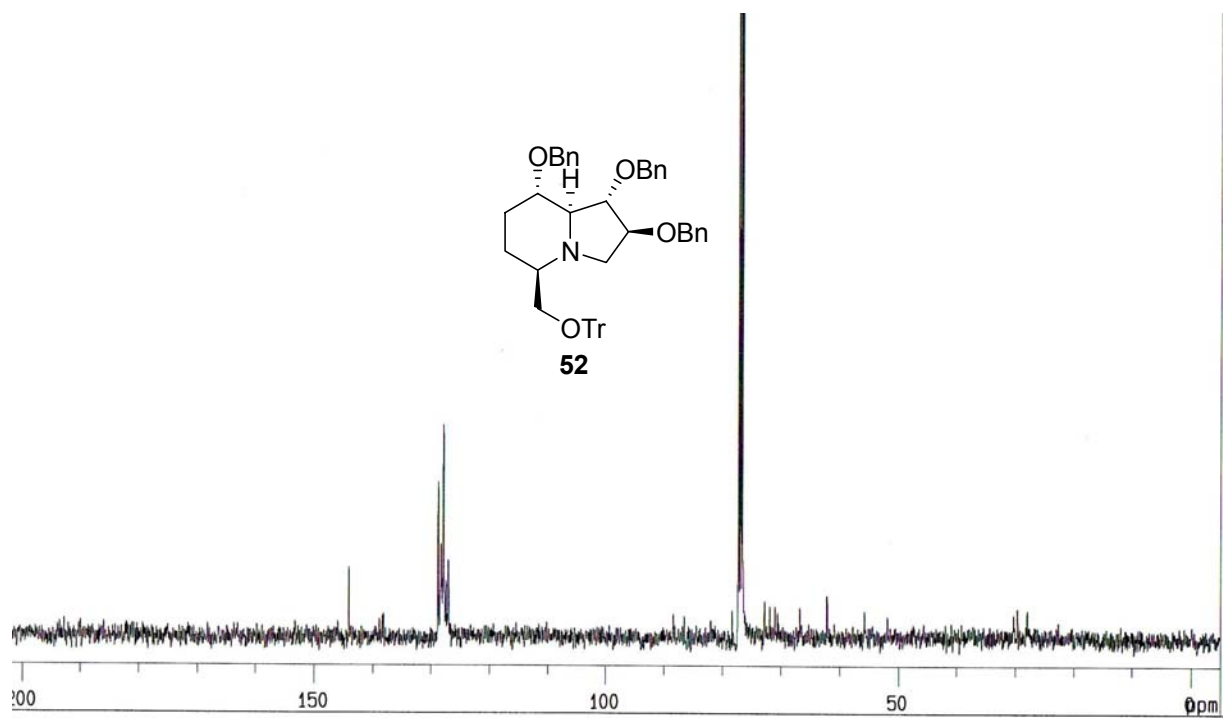
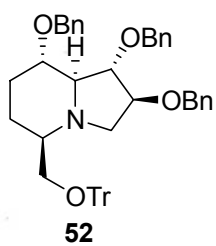


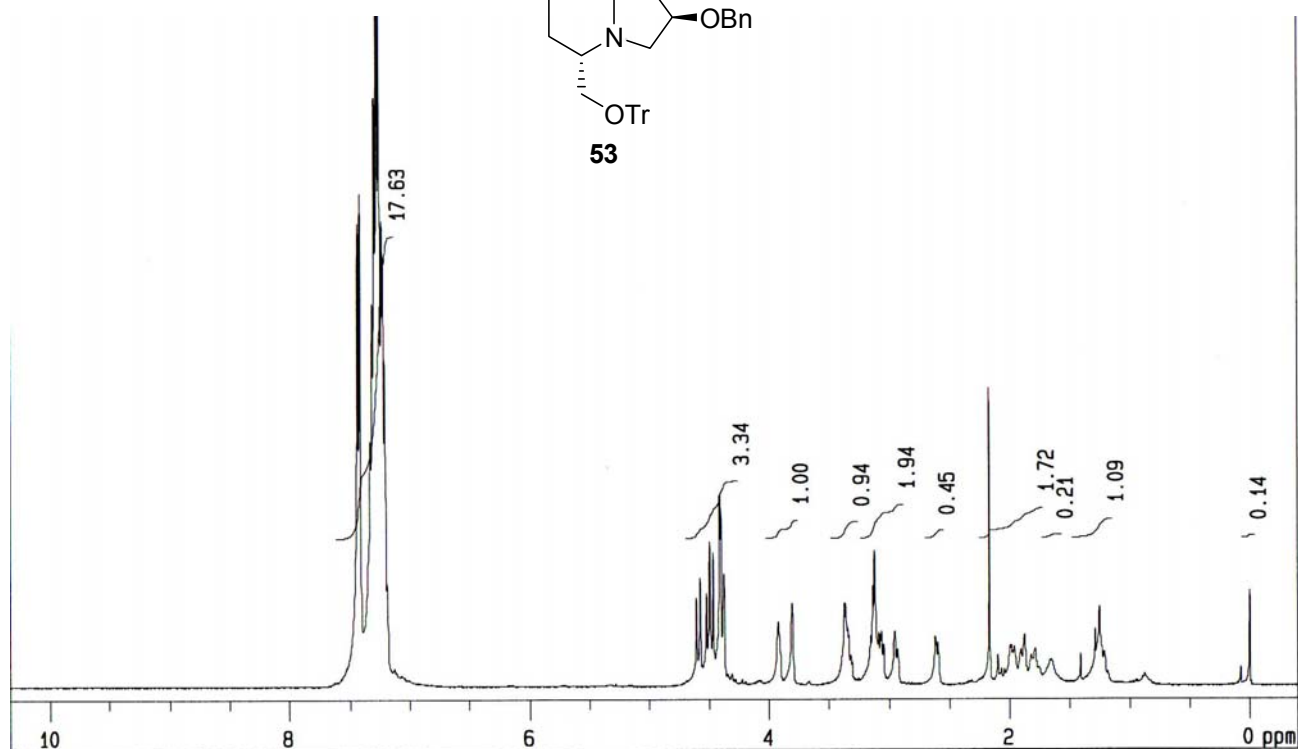
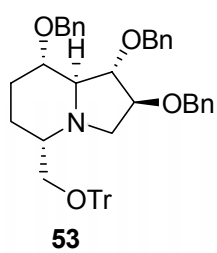


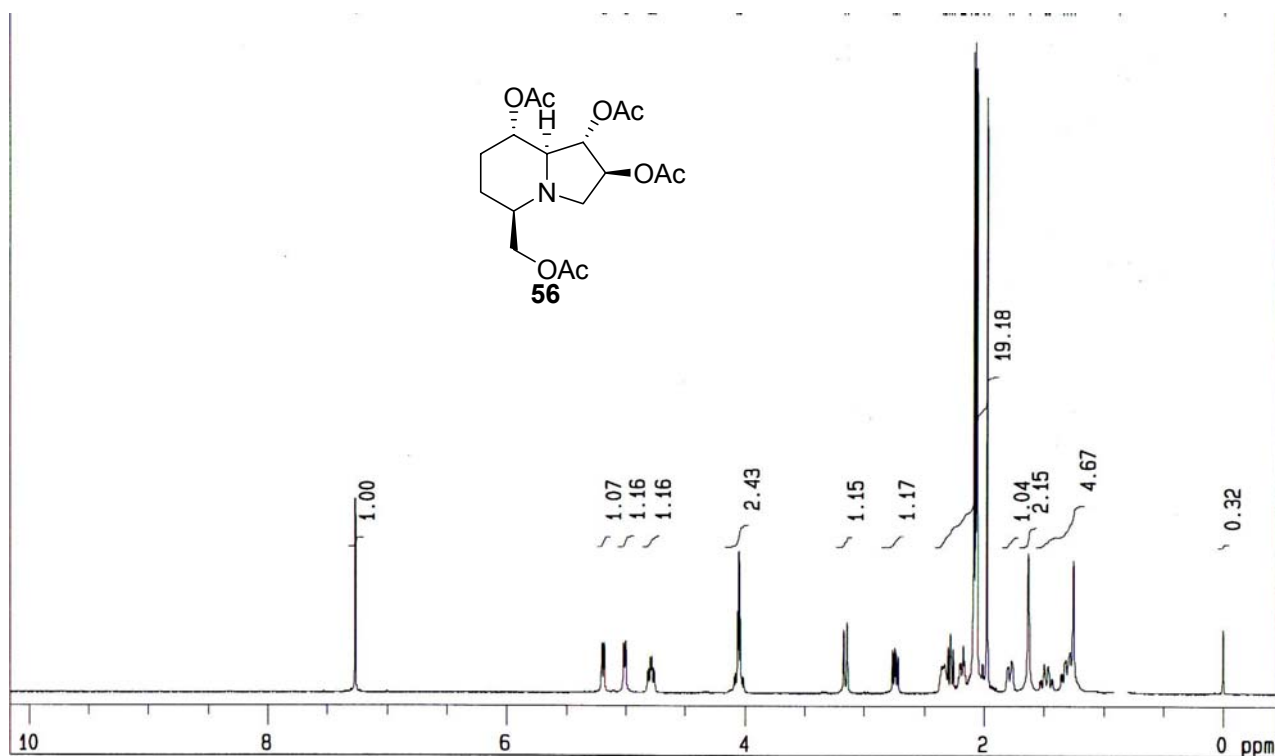
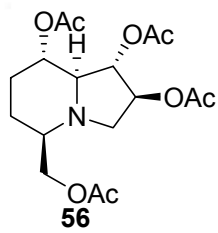


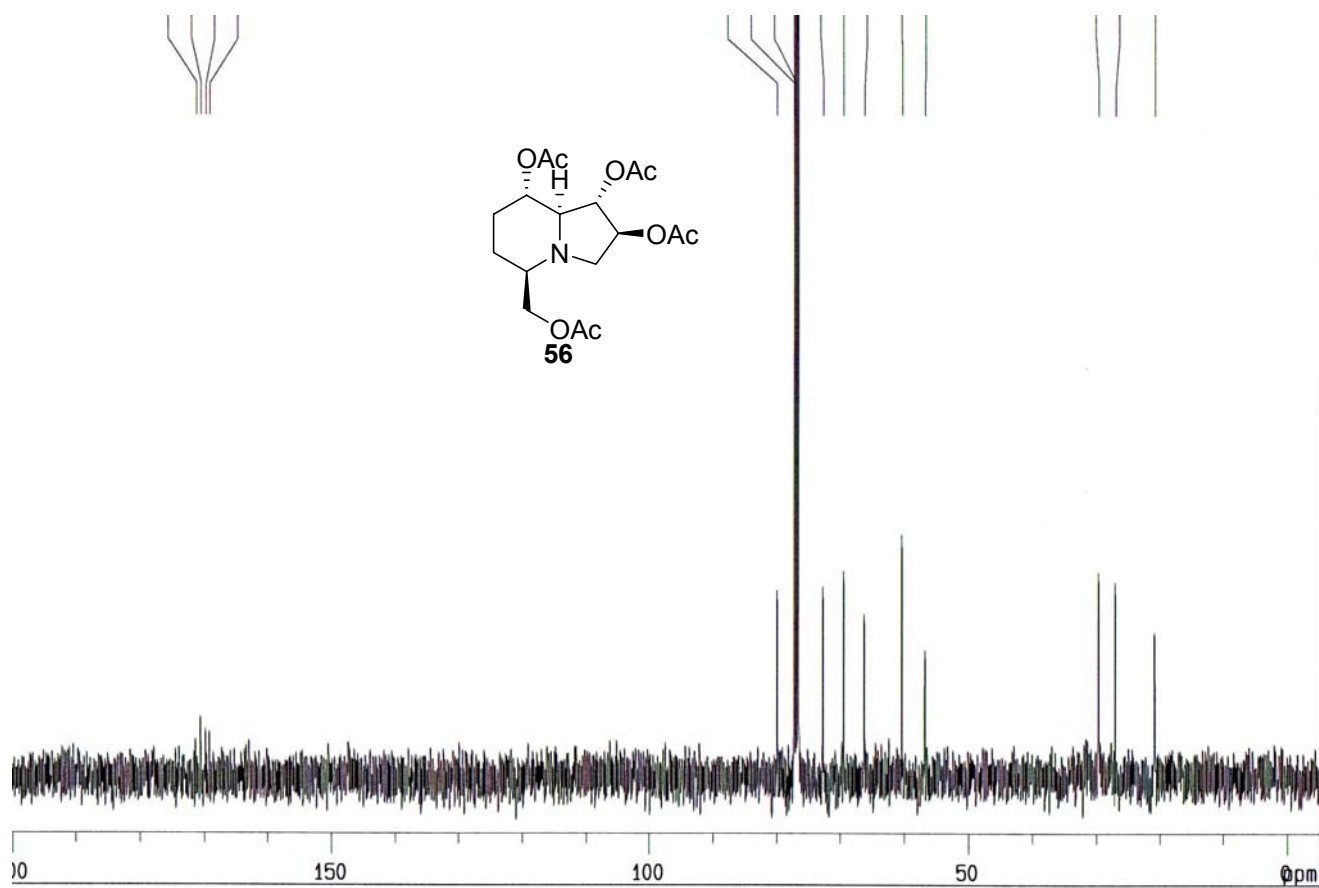


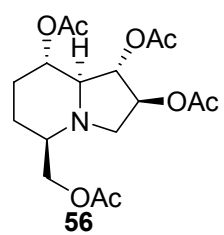




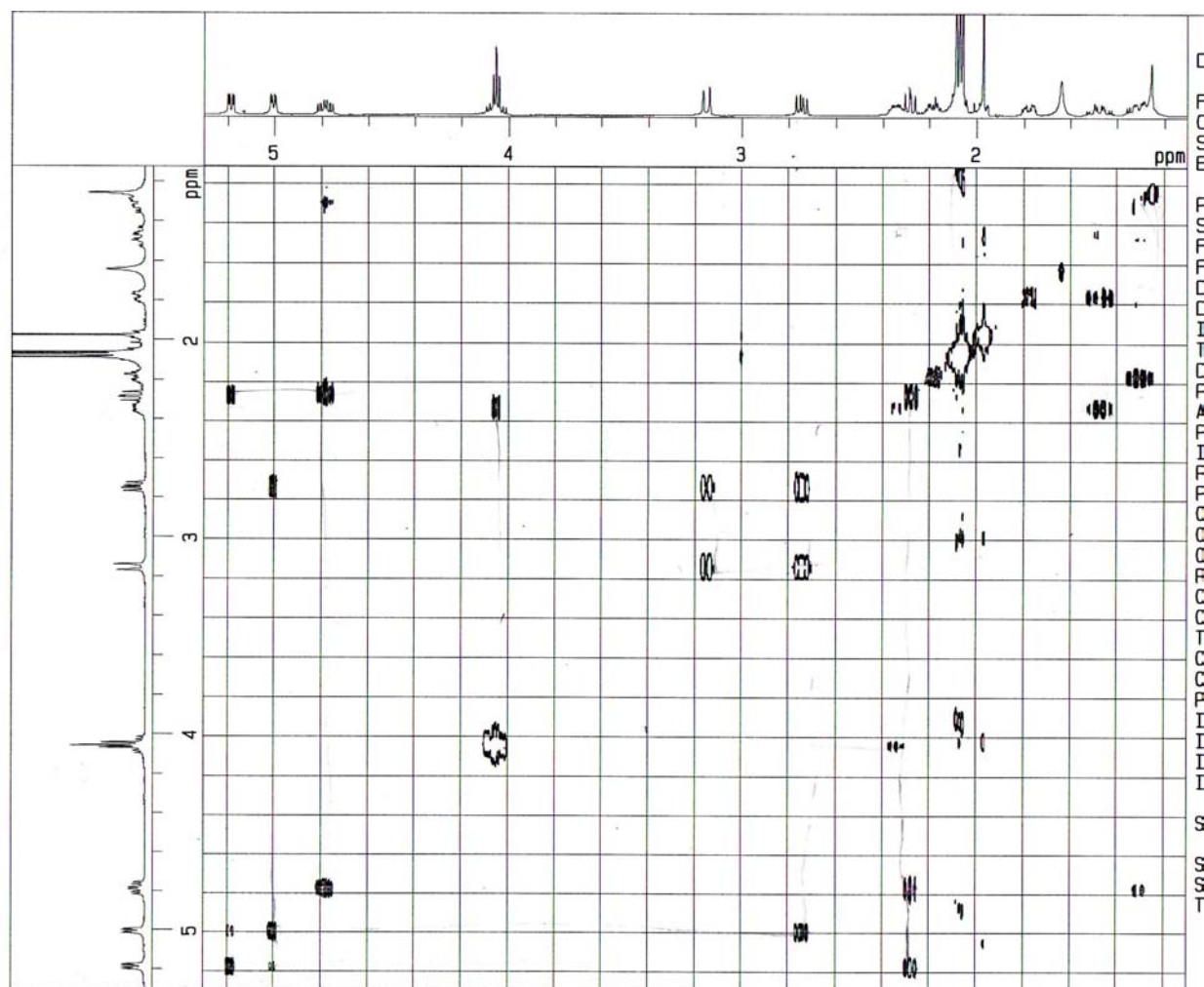




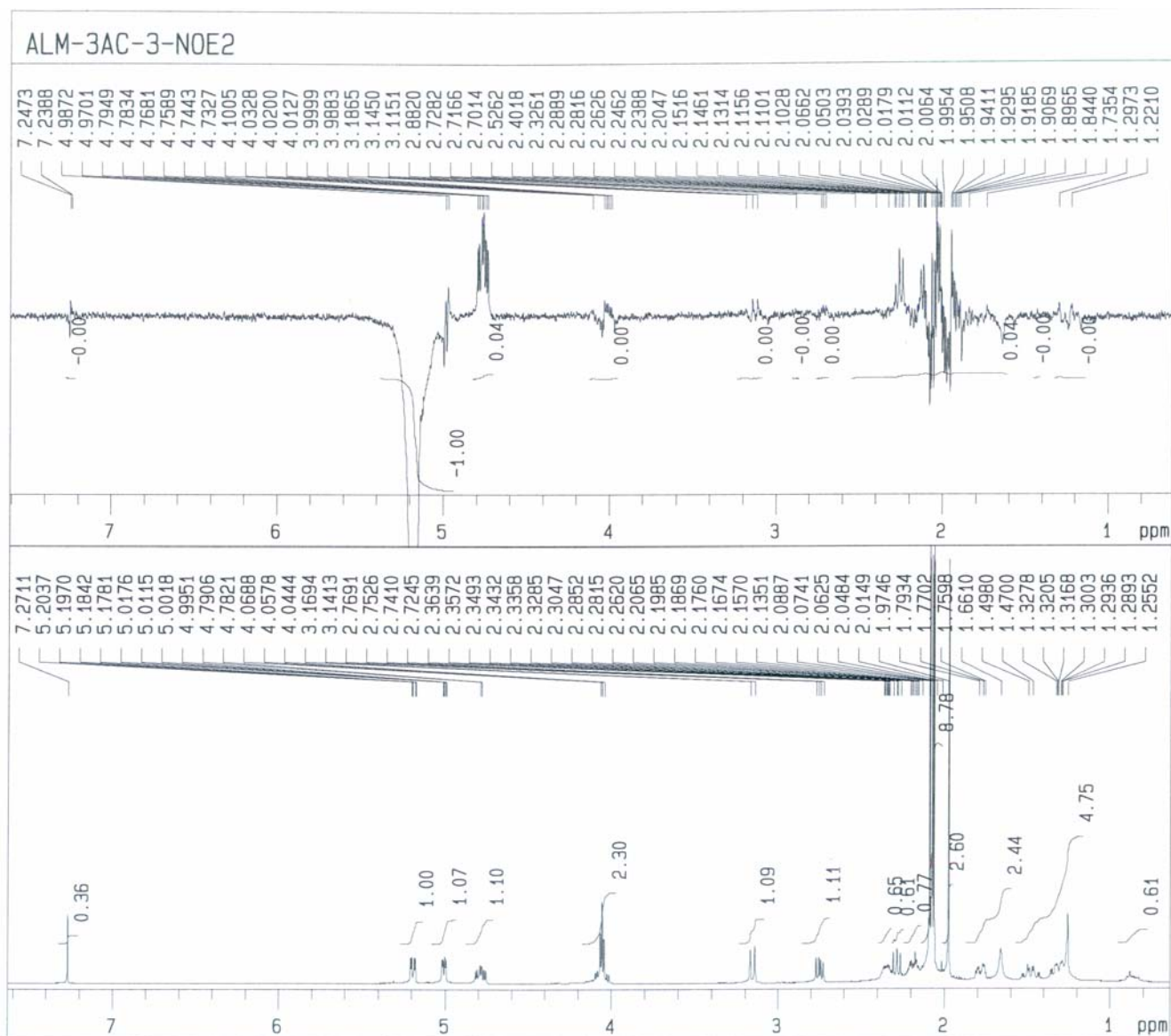
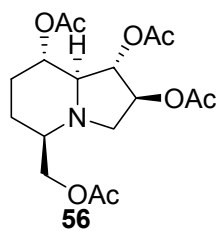




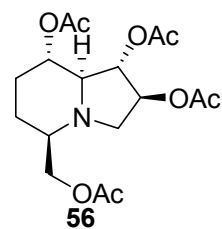
COSY spectrum of compound **56**

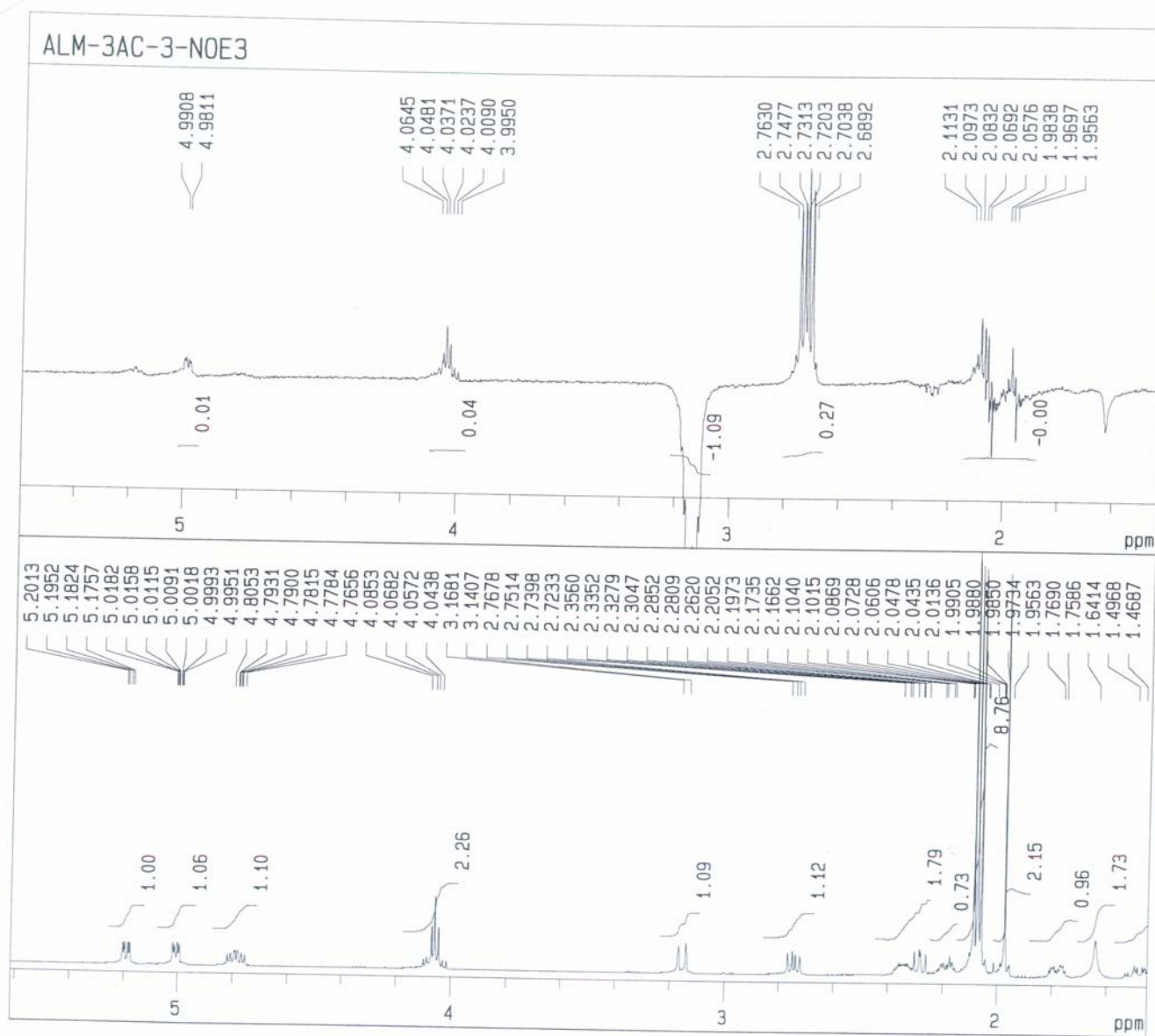


NOE spectrum of compound **56**

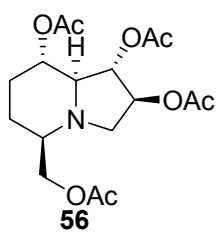


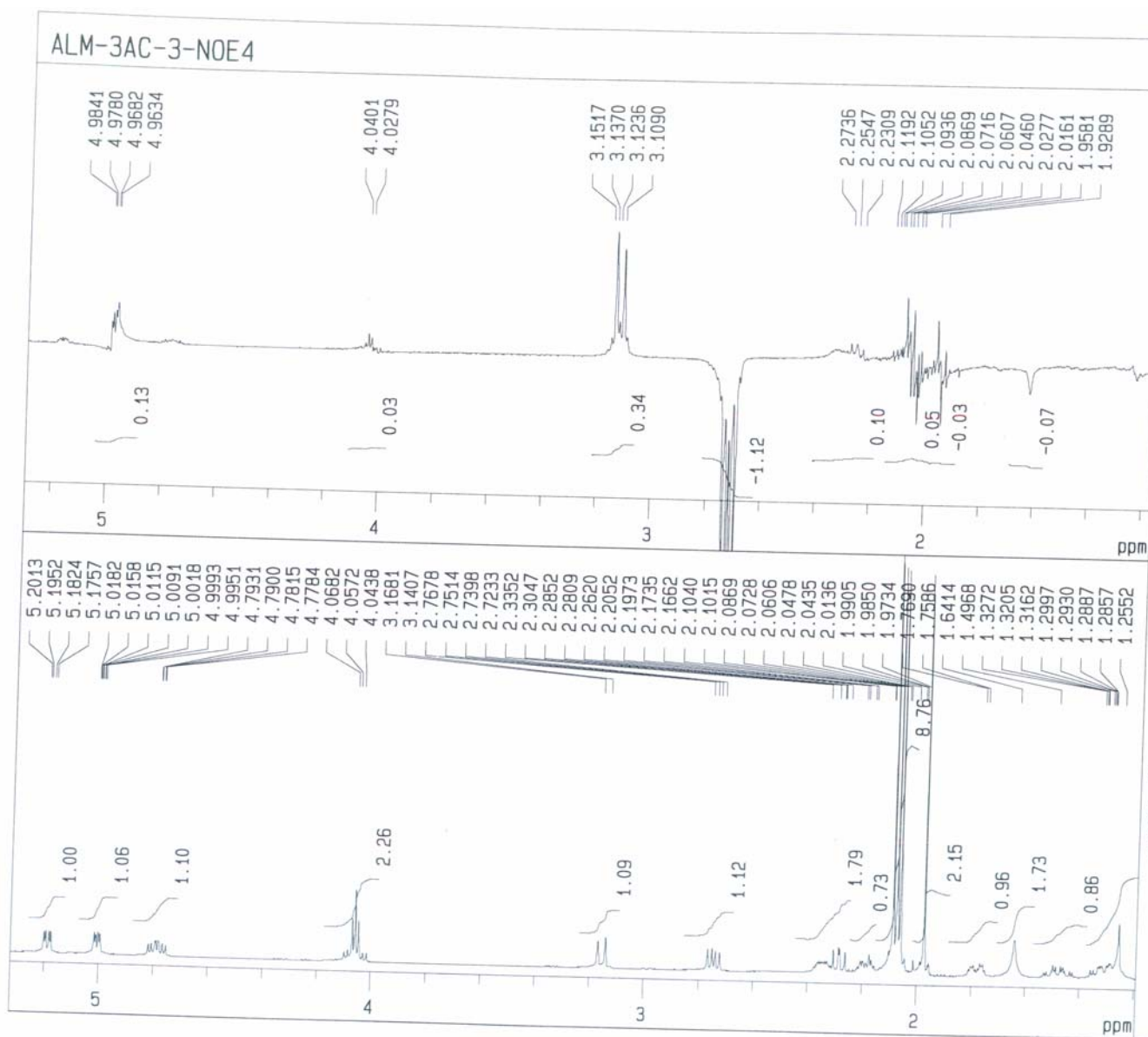
NOE spectrum of compound **56**



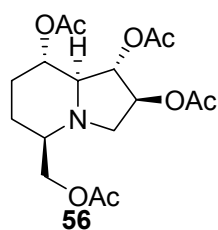


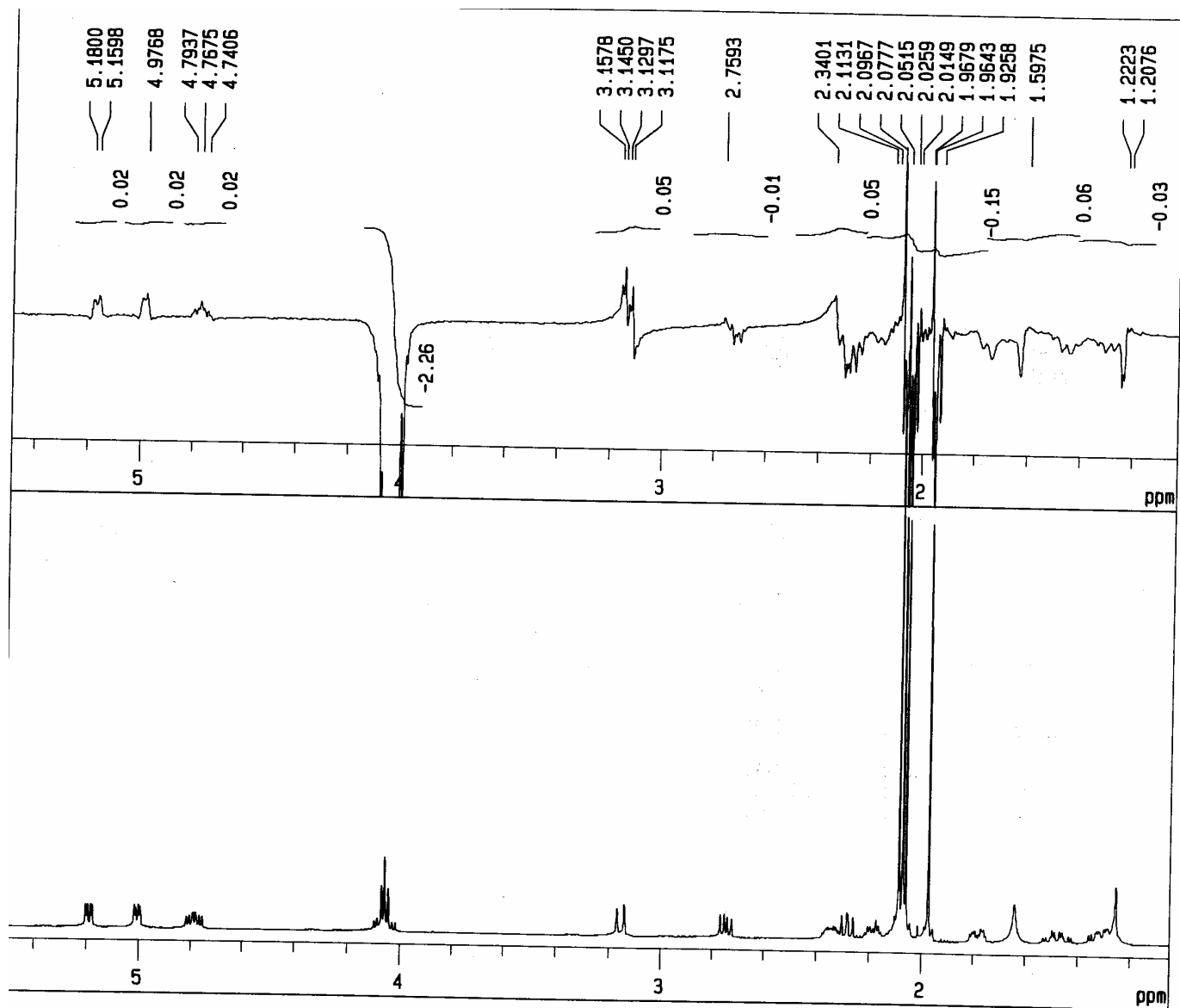
NOE spectrum of compound **56**

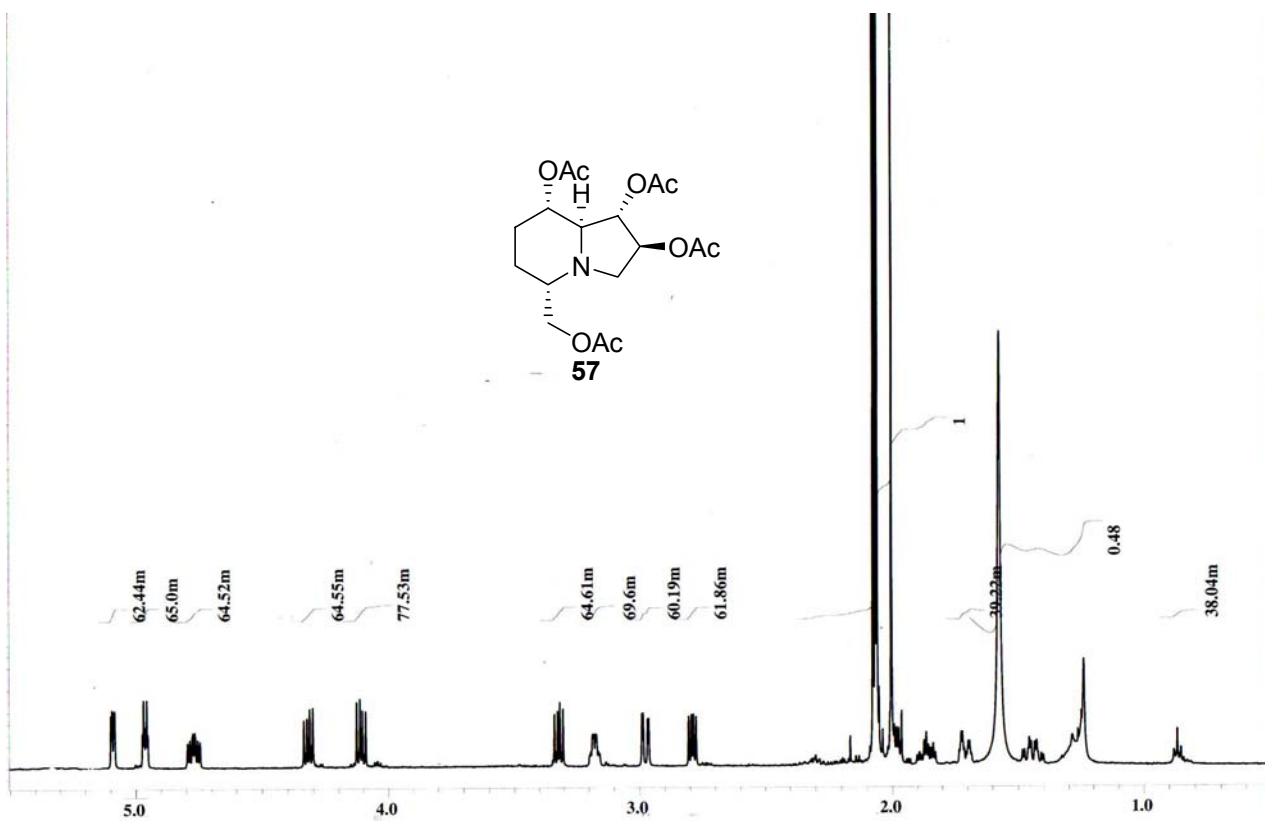
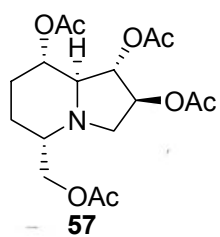


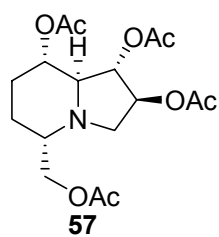
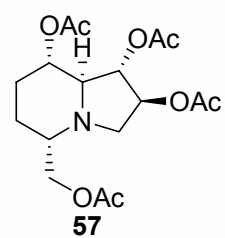
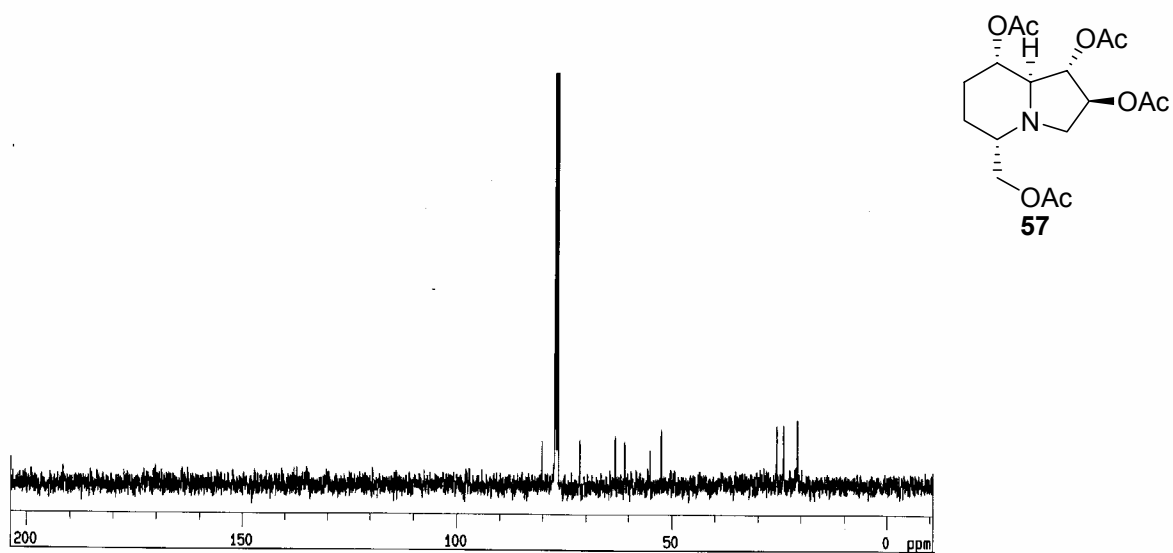


NOE spectrum of compound **56**

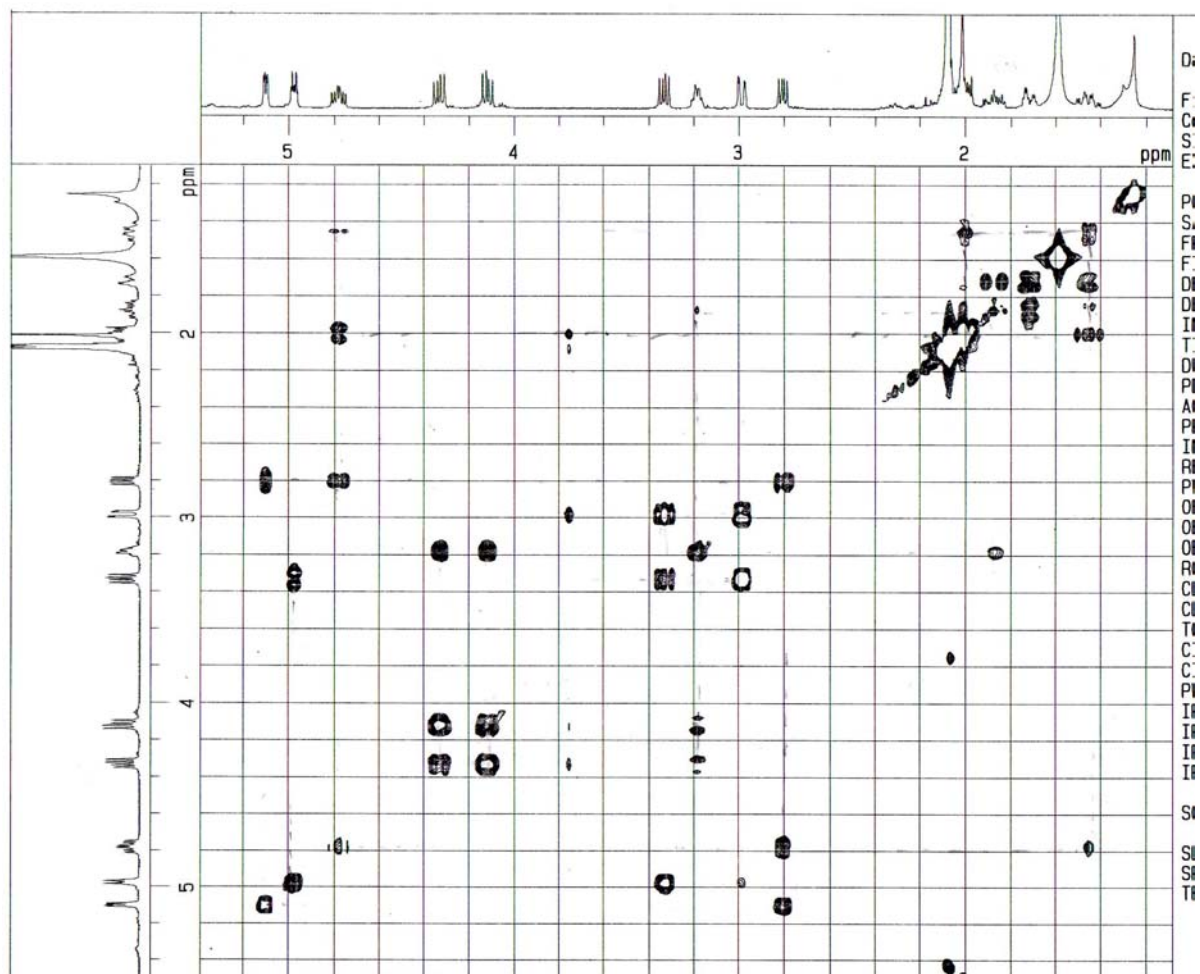




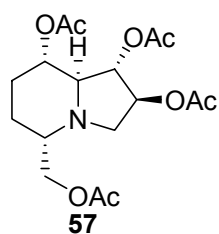




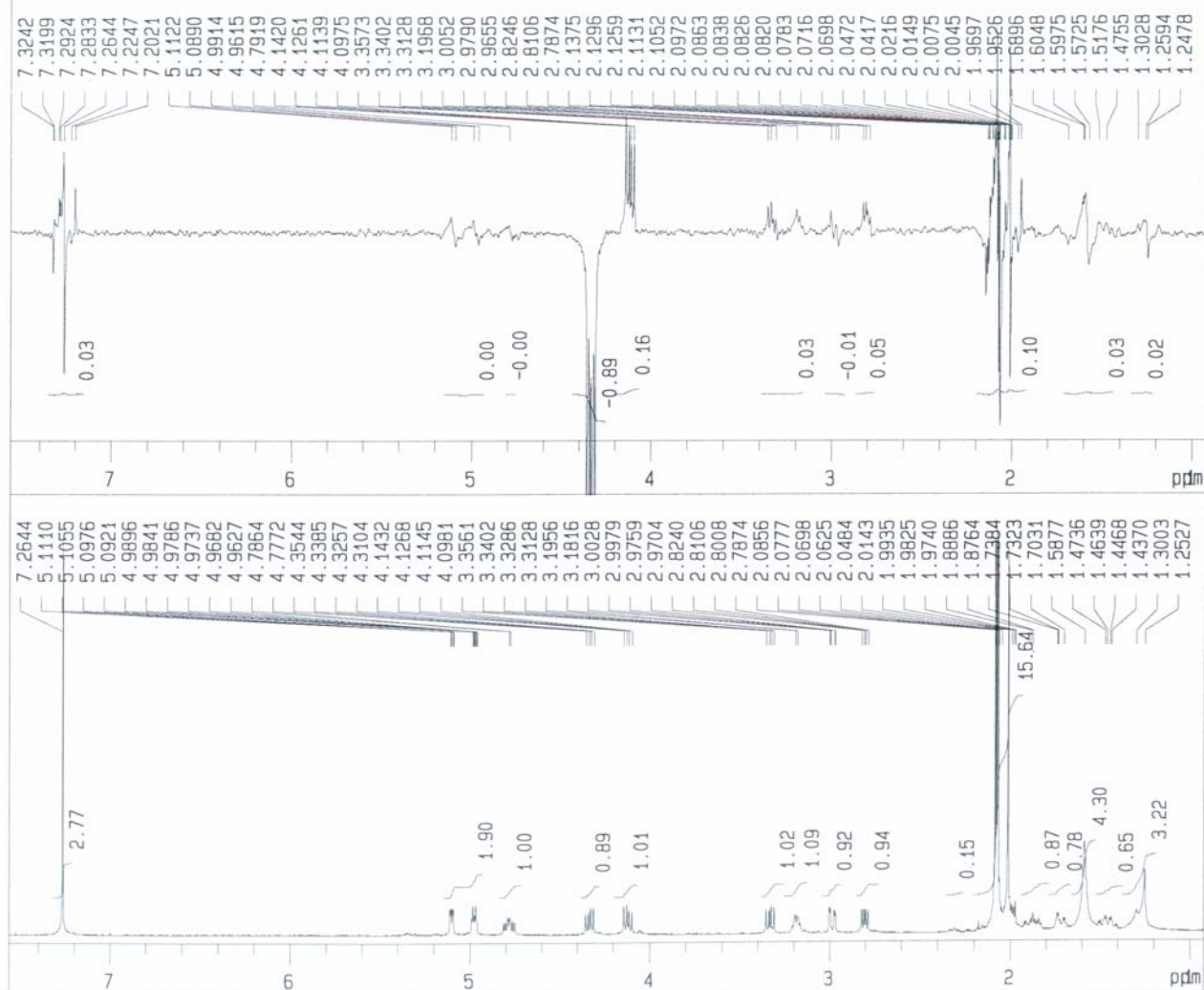
COSY spectrum of compound **57**



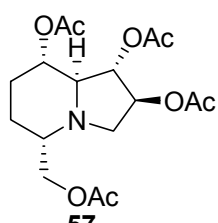
NOE spectrum of compound **57**

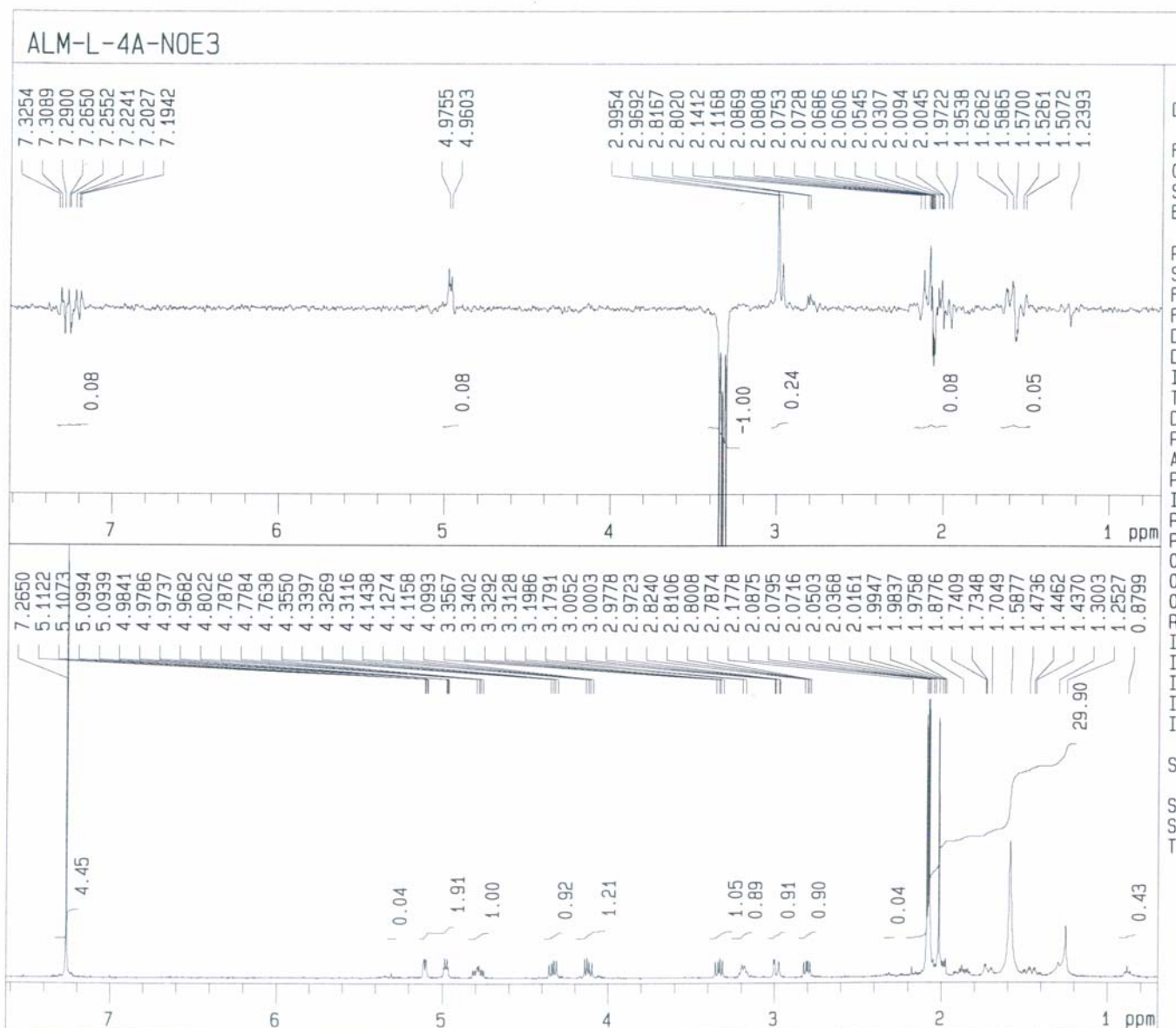


ALM-L4AC-NOE1

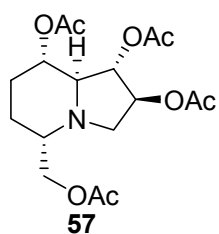


NOE spectrum of compound **57**

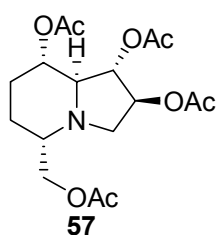
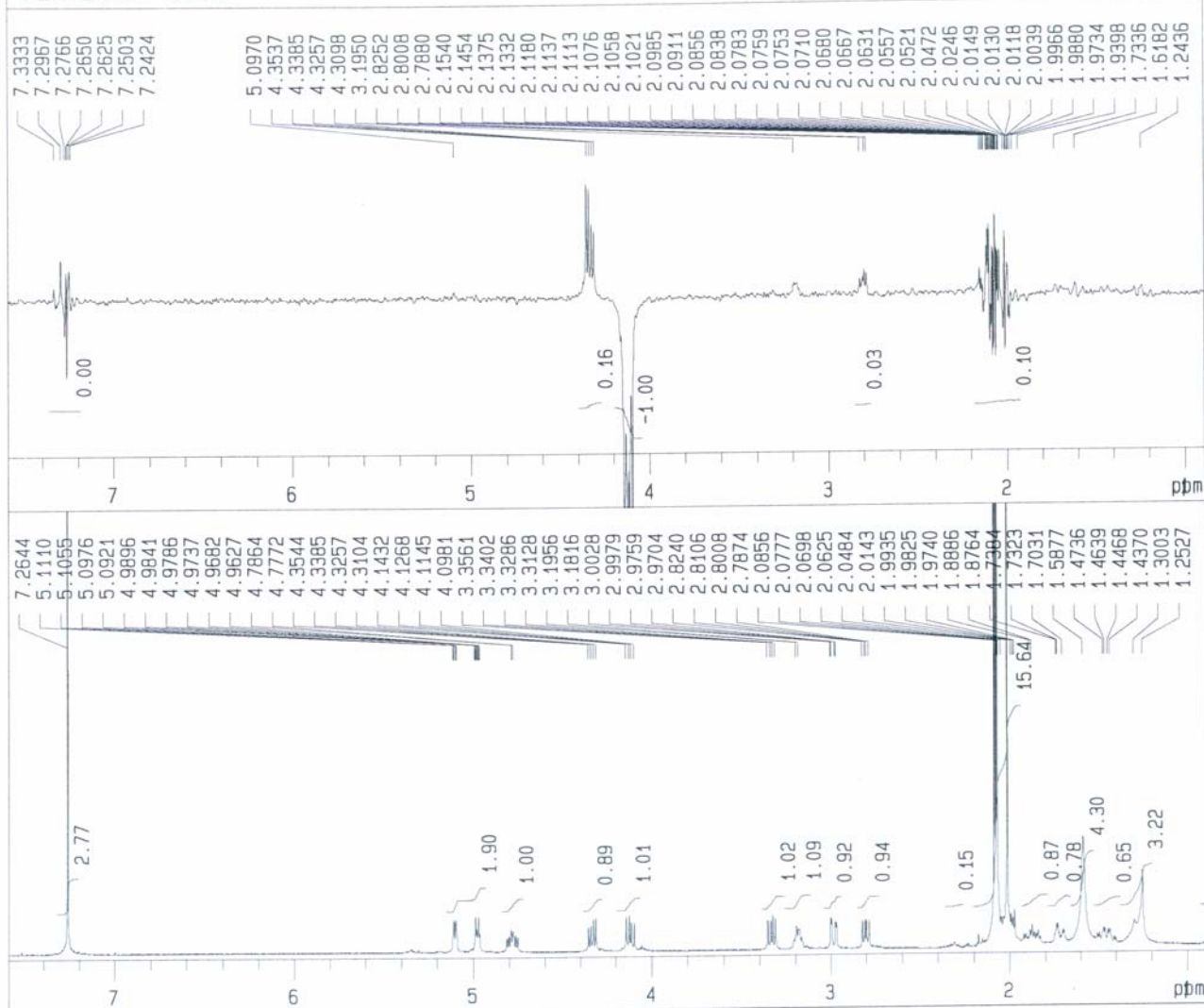




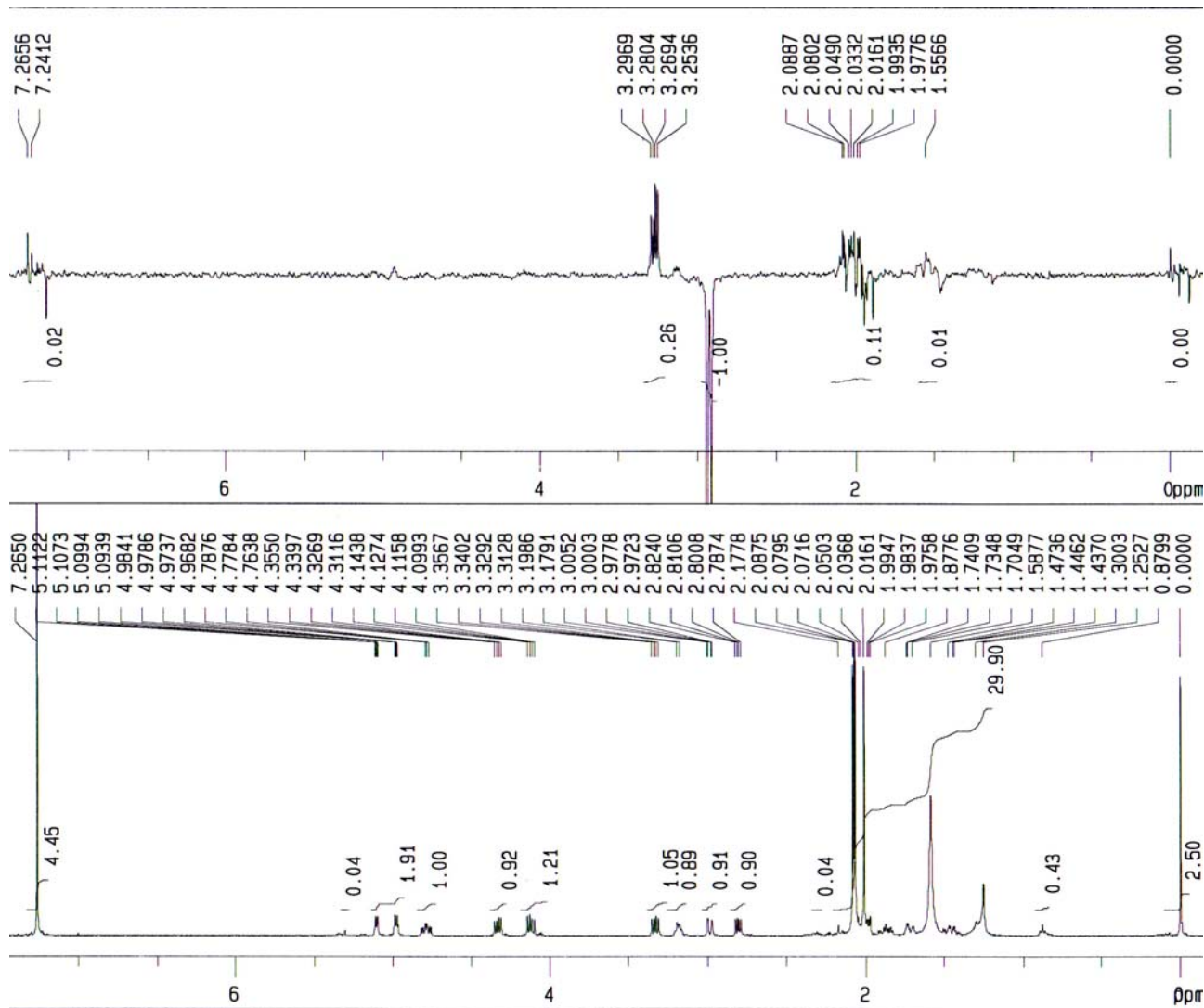
NOE spectrum of compound **57**



ALM-L4AC-NOE2



NOE spectrum of compound 57



NOE spectrum of compound **57**

