Electronic Supplementary Material (ESI) for ChemComm.

New methods for the synthesis of naphthyl amines; application to the synthesis of dihydrosanguinarine, sanguinarine, oxysanguinarine and maclekarpines B and C

Matthew R. Tatton, Iain Simpson[¥] and Timothy J. Donohoe*

Department of Chemistry, University of Oxford, Chemistry Research Laboratory, 12 Mansfield Road, Oxford, OX1 3TA, UK.

[¥]*AstraZeneca Pharmaceauticals, Mereside, Alderely Park, Macclesfield, Cheshire, SK10 4TG, UK.*

Electronic Supporting Information

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General methods

^1H nuclear magnetic resonance spectra (NMR) were recorded at 200 MHz, 400 MHz or 500 MHz. ^{13}C NMR spectra were recorded at 100 MHz or 125 MHz as stated. Chemical shifts are reported relative to residual solvent peaks or tetramethylsilane internal standard with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), sextet (sxt.) septet (sept.) and broad singlet (br. s). Coupling constants, *J*, are quoted to the nearest 0.1 Hz and to 1 Hz for ^1H NMR and ^{13}C NMR, respectively. ^1H and ^{13}C NMR spectra were recorded at room temperature.

Fourier transform infrared spectra (FTIR) were recorded as evaporated films. Absorption maxima are quoted in wavenumbers (cm^{-1}) for the range 3500-800 cm^{-1}. Mass spectra were recorded on a Fisons Platform II spectrometer under electrospray ionisation (ESI). Melting points (m.p.) were obtained from recrystallised samples using a Lecia VMTG heated-stage microscope and are uncorrected. The solvent systems used for recrystallisation are quoted in parentheses. Optical rotations were recorded on a Perkin Elmer 241 Polarimeter (using the sodium D line, 589 nm) and $[\alpha]_D^{20}$ are given in units of deg $dm^{-1}cm^3g^{-1}$; concentrations given in brackets are in g $(100\ mL)^{-1}$.

Flash column chromatography was performed using silica gel (60 Å, 0.040-0.063 mm, VWR). TLC analyses were performed on Merck Kiesegel 60 F254 0.25 mm precoated silica plates. Petrol refers to petroleum ether in the boiling range 40-60 °C. Product spots were visualized under UV light (λmax = 254 nm) and/or by staining with potassium permanganate or vanillin solutions as deemed appropriate. Reagents obtained from Aldrich, Alfa and TCI suppliers were used directly as supplied. All anhydrous reactions were carried out in flame-dried glassware and under an inert atmosphere of argon. THF and CH_2Cl_2 were dried by purification through activated alumina purification columns.

General Procedure 1 for palladium-catalysed α-arylation of ketones

(D*t*BPF)PdCl$_2$ (5.0 mol%) and NaO*t*Bu (250 mol%) were sealed in a dry microwave vial and the vial sealed. Aryl halide (100 mol%) was dissolved in THF (0.2 M with respect to ketone) and the resulting solution was added *via* syringe to the tube at room temperature. The ketone (200 mol%) was then added *via* syringe to the tube. The tube was then heated to 70 °C for 18 h. The reaction was then cooled to room temperature and quenched by the addition of H_2O. The aqueous layer was extracted with Et_2O and the combined organics were dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to give the crude product which was purified under the conditions noted.

General Procedure 2 for deprotection of acetal

para-Toluenesulfonic acid monohydrate (10 mol%) was added to a solution of the acetal substrate (100 mol%) in THF/H_2O (1:1, 0.1 M with respect to acetal) in a microwave vial and the vial sealed. The tube was heated to 60 °C for 18 h then cooled to room temperature. Saturated aqueous $NaHCO_3$ was added and the aqueous layer extracted with EtOAc (3x) and the combined organics dried over Na_2SO_4, filtered and the solvent removed *in vacuo* to give the crude product, which was purified as specified.

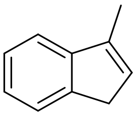
General Procedure 3 for Lewis acid cyclisation to form napthyl amine

A microwave vial fitted with a magnetic follower was charged with the corresponding 1,5-dicarbonyl (100 mol%) and $ZnCl_2$ (1.0 M in Et_2O, 100 mol%), dissolved in CH_2Cl_2 (0.10 M with respect to 1,5-dicarbonyl) and the corresponding amine (500 mol%) added. The reaction mixture was heated at 55 °C for 18 h and then cooled to room temperature. The crude mixture was concentrated and purified by flash column chromatography, under the conditions noted to afford the corresponding napthyl amine.

General Procedure 4 for acid cyclisation to form napthyl amine

A microwave vial fitted with a magnetic follower was charged with the corresponding 1,5-dicarbonyl (100 mol%), dissolved in PhMe/AcOH 3:1 (0.10 M with respect to 1,5-dicarbonyl) and the corresponding amine (500 mol%) added carefully. The reaction mixture was heated at 110 °C for 18 h and then cooled to room temperature. The crude mixture was washed with 1.0 M NaOH (20 mL/mmol) and extracted into EtOAc (3x). The organic layers were combined, dried ($MgSO_4$) and concentrated. The crude product was purified by flash column chromatography, under the conditions noted to afford the corresponding napthyl amine.

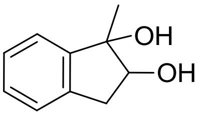
3-Methyl-1H-indene, S1



$CeCl_3$ (4.23 g, 11.4 mmol) was heated at 130 °C under a high vacuum for 2 h. THF (50 mL) was added and the reaction stirred for 90 min at rt. The reaction was cooled for −78 °C and then MeLi (7.13 mL, 1.6 M in Et_2O, 11.4 mmol) added and stirred for 30 min. A solution of indanone (1.00 g, 7.58 mmol) in THF (2 mL) was added dropwise and the resulting solution stirred for 1 h, then allowed to warm to rt. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl then the THF removed *in vacuo*. The mixture was then partitioned between Et_2O and water and the organic layer separated. The aqueous layer was washed with Et_2O (2 x 100 mL), the organic layers combined, dried ($MgSO_4$), filtered and concentrated. The residue was dissolved in CH_2Cl_2 (50 mL) and *para*-toluenesulfonic acid monohydrate (72 mg, 0.38 mmol) added. The reaction was stirred for 30 min, then concentrated and purified by flash column chromatography (petrol) to give indene **S1** (845 mg, 86%).

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.53 (1 H, d, *J*=7.3 Hz), 7.35 - 7.46 (2 H, m), 7.26 - 7.33 (1 H, m), 6.28 (1 H, s), 3.39 (2 H, s), 2.26 (3 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 146.2, 144.4, 140.0, 128.8, 126.1, 124.5, 123.7, 118.9, 37.7, 13.1; Data were consistent with those previously reported.[1]

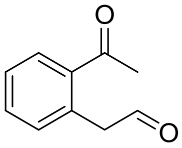
1-Methyl-2,3-dihydro-1H-indene-1,2-diol, S2



$K_2OsO_4.2H_2O$ (14 mg, 0.051 mmol) was added to a solution of indene **S1** (200 mg, 1.54 mmol), *N*-methylmorpholine *N*-oxide (360 mg, 3.08 mmol) in H_2O/THF/*t*BuOH (1:10:8, 10 mL) and the reaction stirred for 18 h. The reaction was quenched with a saturated solution of sodium sulphite (10 mL) and extracted with EtOAc (3 x 25 mL). The organic layers were combined, dried ($MgSO_4$), filtered and concentrated. Purification by flash column chromatography (petrol-EtOAc, 1:1) afforded *diol* **S2** (170 mg, 69%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.23 - 7.30 (1 H, m,), 7.14 - 7.20 (2 H, m), 7.08 - 7.14 (1 H, m), 3.94 (1 H, br. s.), 3.12 (1 H, br. s.), 3.03 (1 H, d, *J*=4.9 Hz), 2.99 (1 H, d, *J*=5.8 Hz), 2.73 (1 H, dd, *J*=16.2, 4.6 Hz), 1.37 (3 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 145.6, 139.4, 128.8, 127.3, 125.4, 123.4, 80.0, 78.7, 38.2, 24.8; **FTIR** 3231, 2940, 1480, 1368, 1321, 1224, 1170, 1107, 1088, 1061, 1021, 963, 916, 844, 804, 759, 739, 717, 648 cm^{-1}; **HRMS** m/z $[C_{10}H_{12}O_2+Na]^+$ cal. 187.0729, found 187.0729.

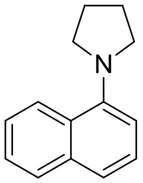
2-(2-Acetylphenyl)acetaldehyde, 1



Diol **S2** (170 mg, 1.04 mmol), was dissolved in CH_2Cl_2 (10 mL) and $NaIO_4.SiO_2$ (5.6 g, 3.6 g/mmol, 1.56 mmol) and stirred. After 1 h the reaction was filtered and washed with CH_2Cl_2. The filtrate was concentrated to give 1,5-dicarbonyl **1** (140 mg, 89% yield) which was used in the next step without further purification.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 9.76 (1 H, s), 7.84 - 7.92 (1 H, m), 7.50 (1 H, td, *J*=7.5, 1.2 Hz), 7.38 - 7.45 (1 H, m), 7.23 (1 H, d, *J*=7.6 Hz), 3.99 (2 H, s), 2.60 (3 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 200.8, 199.0, 136.6, 133.5, 133.1, 132.5, 130.5, 127.7, 49.4, 28.7; **FTIR** 1721, 1676, 1600, 1573, 1488, 1357, 1256, 1034, 959, 761 cm^{-1}; **HRMS** m/z $[C_{10}H_{10}O_2]$ cal. 162.0681, found 162.0677.

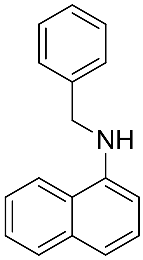
1-(Naphthalen-1-yl)pyrrolidine, 4



1,5-dicarbonyl **1** (60 mg, 0.37 mmol) and pyrrolidine were subjected to general procedure 4. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **4** (49 mg, 68%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 8.30 (1 H, s), 7.87 (1 H, s), 7.51 (3 H, s), 7.39 - 7.47 (1 H, m), 7.04 (1 H, d, *J*=7.3 Hz), 3.43 (4 H, br. s.), 2.08 (4 H, br. s.); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 147.8, 135.1, 128.4, 128.3, 126.0, 125.6, 124.9, 124.4, 121.4, 111.5, 52.8, 24.9. Data were consistent with those previously reported.[2]

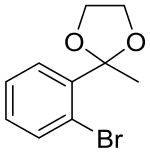
N-benzylnaphthalen-1-amine, 5



1,5-dicarbonyl **1** (60 mg, 0.368 mmol) and benzylamine were subjected to general procedure 4. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **5** (39 mg, 45%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.75 - 7.86 (2 H, m), 7.23 - 7.53 (9 H, m), 6.62 (1 H, d, *J*=7.6 Hz), 4.68 (1 H, b. s.), 4.49 (2 H, s); ^{13}C NMR (101 MHz, *CHLOROFORM-d*) δ ppm 143.2, 139.1, 134.2, 128.7, 128.7, 127.7, 127.4, 126.6, 125.7, 124.7, 123.3, 119.9, 117.6, 104.7, 48.6 **^{13}C NMR (**100 MHz, *CHLOROFORM-d*) δ ppm 142.2, 138.0, 133.2, 127.7, 127.7, 126.7, 126.4, 125.6, 124.7, 123.7, 122.3, 118.8, 116.6, 103.7, 47.6. Data were consistent with those previously reported.[2]

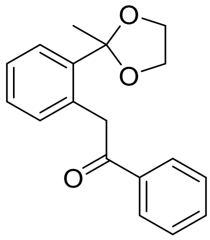
2-(2-Bromophenyl)-2-methyl-1,3-dioxolane, S3



para-Toluenesulfonic acid monohydrate (2.0 mol%) was added to a solution of 2'-bromoacetophenone **(**2.00 g, 10.1 mmol) and ethanediol (130 mol%) in toluene (100 mL). The flask was equipped with a Dean-Stark apparatus and the solution heated to reflux for 18 h. The reaction mixture was cooled to rt and quenched by the addition of saturated aqueous NH_4Cl and extracted with EtOAc (3 × 100 mL). The organic extracts were combined and extracted with brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded acetal **S3** (2.19 g, 90%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.59 (1 H, dd, *J*=7.8, 1.7 Hz, Ar*H*), 7.47 - 7.55 (1 H, m, Ar*H*), 7.15 - 7.26 (1 H, m, Ar*H*), 7.06 (1 H, td, *J*=7.6, 1.7 Hz, Ar*H*), 3.92 - 4.05 (2 H, m, OCH_2), 3.62 - 3.76 (2 H, m, OCH_2), 1.74 (3 H, s, CH_3); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 141.1, 135.0, 129.5, 127.9, 127.2, 120.6, 108.8, 64.3, 25.3. Data were consistent with those previously reported.[3]

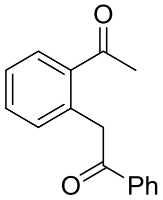
2-(2-(2-Methyl-1,3-dioxolan-2-yl)phenyl)-1-phenylethan-1-one, S4



Acetal **S3** (100 mg, 0.413 mmol) and acetophenone were subjected to general procedure 1. Purification by flash column chromatography (petrol-EtOAc, 9:1) afforded acetal **S4** (96 mg, 83%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 8.09 (2 H, d, *J*=8.3 Hz), 7.57 - 7.68 (2 H, m), 7.52 (2 H, t, *J*=7.6 Hz), 7.30 - 7.34 (2 H, m), 7.15 - 7.20 (1 H, m), 4.56 (2 H, s), 3.81 - 3.92 (2 H, m), 3.60 - 3.68 (2 H, m), 1.70 (3 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 197.8, 141.2, 137.4, 133.1, 132.8, 132.3, 128.6, 128.2, 128.1, 127.1, 126.4, 109.1, 64.2, 43.9, 27.7. Data were consistent with those previously reported.[3]

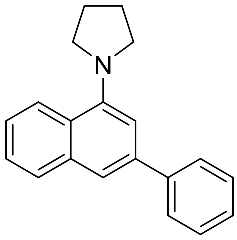
2-(2-Acetylphenyl)-1-phenylethan-1-one, 2



Acetal **S4** (90 mg, 0.319 mmol) was subjected to general procedure 2. Purification by flash column chromatography (petrol-EtOAc, 9:1) afforded 1,5-dicarbonyl **2** (61 mg, 80%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 8.07 (2 H, d, *J*=7.6 Hz), 7.88 (1 H, d, *J*=7.8 Hz), 7.55 - 7.63 (1 H, m), 7.47 - 7.54 (3 H, m), 7.39 - 7.46 (1 H, m), 7.27 (1 H, d, *J*=7.3 Hz), 4.68 (2 H, s), 2.59 (3 H, s); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 201.2, 197.4, 137.3, 137.0, 135.3, 133.1, 133.0, 132.1, 130.2, 128.6, 128.2, 127.3, 44.7, 28.7. Data were consistent with those previously reported.[4]

1-(3-Phenylnaphthalen-1-yl)pyrrolidine, 6

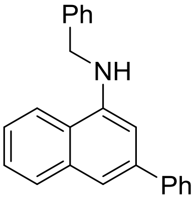


Method A 1,5-dicarbonyl **2** (22 mg, 0.092 mmol) was subjected to general procedure 3. Purification by flash column chromatography (petrol-EtOAc, 49:1 to 19:1) afforded napthyl amine **6** (16 mg, 58%) as a colourless oil.

Method B 1,5-dicarbonyl **2** (50 mg, 0.21 mmol) and pyrrolidine were subjected to general procedure 3. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **6** (39 mg, 69%) as a colourless oil.

^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 8.27 (1 H, d, *J*=8.1 Hz), 7.84 - 7.94 (1 H, m), 7.75 - 7.80 (2 H, m), 7.68 (1 H, s), 7.38 - 7.56 (5 H, m), 7.24 - 7.28 (1 H, m), 3.49 (4 H, m), 2.01 - 2.17 (4 H, m); ^{13}**C NMR** (125 MHz, *CHLOROFORM-d*) δ ppm 147.9, 141.7, 138.6, 135.2, 128.7, 128.6, 127.4, 127.2, 127.1, 126.0, 124.5, 119.6, 119.4, 111.4, 52.9, 24.9. Data were consistent with those previously reported.[5]

N-Benzyl-3-phenylnaphthalen-1-amine, 7

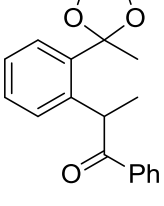


Method A 1,5-dicarbonyl **2** (22 mg, 0.092 mmol) was subjected to general procedure 3. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **7** (16 mg, 58%) as a colourless oil.

Method B 1,5-dicarbonyl **2** (50 mg, 0.21 mmol) and benzylamine were subjected to general procedure 4. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **7** (40 mg, 63%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.83 (1 H, d, *J*=8.1 Hz), 7.78 (1 H, d, *J*=8.3 Hz), 7.64 (2 H, d, *J*=7.8 Hz), 7.27 - 7.49 (11 H, m), 6.87 (1 H, s), 4.70 (1 H, br. s.), 4.53 (2 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 143.6, 142.1, 139.4, 139.0, 134.6, 129.0, 128.8, 128.7, 127.9, 127.5, 127.4, 127.2, 126.2, 124.8, 122.8, 119.8, 116.0, 104.6, 48.8; **FTIR** 3063, 1680, 1597, 1579, 1490, 1448, 1338, 1259, 1215, 1096, 1052, 999, 759, 690, 665 cm^{-1}; **HRMS** m/z $[C_{23}H_{19}N+H]^+$ cal. 310.1590, found 310.1581.

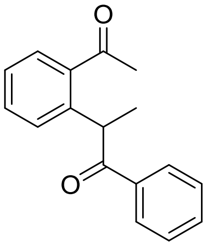
2-(2-(2-Methyl-1,3-dioxolan-2-yl)phenyl)-1-phenylpropan-1-one, S5



Acetal **S3** (250 mg, 1.04 mmol) and propiophenone were subjected to general procedure 1. Purification by flash column chromatography (petrol-EtOAc, 9:1) afforded acetal **S5** (234 mg, 76%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 8.01 - 8.08 (2 H, m, Ar*H*), 7.63 (1 H, dd, *J*=7.8, 1.5 Hz, Ar*H*), 7.52 (1 H, tt, *J*=7.4, 1.7 Hz, Ar*H*), 7.39 - 7.46 (3 H, m, Ar*H*), 7.32 (1 H, t, *J*=7.6 Hz, Ar*H*), 7.24 (1 H, t, *J*=7.8 Hz, Ar*H*), 5.51 (1 H, q, *J*=7.1 Hz, C*H*), 3.97 - 4.05 (1 H, m, CH_aH_b), 3.71 - 3.87 (2 H, m, CH_2), 3.46 - 3.54 (1 H, m, CH_aH_b), 1.78 (3 H, s, CCH_3), 1.57 (3 H, d, *J*=7.1 Hz, $CHCH_3$); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 202.2, 140.0, 138.3, 137.2, 132.4, 129.5, 128.7, 128.4 (2C), 126.7, 126.4, 109.3, 64.4, 64.1, 43.4, 28.1, 19.8. Data were consistent with those previously reported.[3]

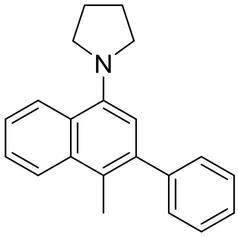
2-(2-Acetylphenyl)-1-phenylpropan-1-one, 3



Acetal **S5** (200 mg, 1.04 mmol) was subjected to general procedure 2. Purification by flash column chromatography (petrol-EtOAc, 9:1) afforded 1,5-dicarbonyl **3** (137 mg, 81%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.86 - 7.94 (2 H, m, Ar*H*), 7.66 (1 H, d, *J*=7.6 Hz, Ar*H*), 7.36 (1 H, d, *J*=7.3 Hz, Ar*H*), 7.25 - 7.33 (3 H, m, Ar*H*), 7.15 - 7.24 (2 H, m, Ar*H*), 5.60 (1 H, q, *J*=6.8 Hz, C*H*), 2.55 (3 H, s, CCH_3), 1.40 (3 H, d, *J*=6.8 Hz, $CHCH_3$); **^{13}C NMR** (100 MHz *CHLOROFORM-d*) δ ppm 202.3, 201.3, 141.3, 136.5, 136.2, 132.7, 132.3, 130.0, 129.0, 128.8, 128.5, 126.7, 43.2, 29.8, 18.9; **FTIR** 2977, 1679, 1597, 1572, 1485, 1448, 1356, 1293, 1236, 1180, 1001, 951, 759, 727, 691 cm^{-1}; **HRMS** m/z $[C_{17}H_{16}O_2+Na]^+$ cal. 275.1043, found 275.1043.

1-(4-Methyl-3-phenylnaphthalen-1-yl)pyrrolidine, 8

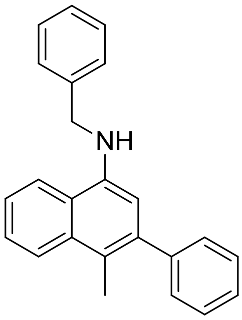


Method A 1,5-dicarbonyl 3 (25 mg, 0.11 mmol) and pyrrolidine was subjected to general procedure **3**. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **8** (17 mg, 55%) as a colourless oil.

Method B 1,5-dicarbonyl **3** (40 mg, 0.16 mmol) and pyrrolidine were subjected to general procedure 4. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **8** (34 mg, 73%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 8.32 (1 H, d, *J*=8.3 Hz), 8.10 (1 H, d, *J*=8.3 Hz), 7.39 - 7.56 (7 H, m), 6.98 (1 H, s), 3.37 (4 H, br. s.), 2.56 (3 H, s), 2.05 (4 H, br. s.); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 145.4, 143.4, 139.0, 134.2, 129.8, 128.1, 127.9, 126.7, 126.0, 125.0, 124.9, 124.2, 114.7, 53.0, 24.6, 16.0. Missing 1 C; **FTIR** 2963, 1587, 1495, 1456, 1389, 1352, 1263, 1158, 1091, 1033, 985, 907, 759, 731, 703, 645 cm^{-1}; **HRMS** m/z $[C_{21}H_{21}N+H]^+$ cal. 288.1747, found 288.1740.

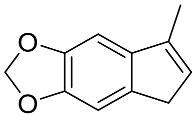
N-Benzyl-4-methyl-3-phenylnaphthalen-1-amine, 9



1,5-dicarbonyl **3** (50 mg, 0.20 mmol) and benzylamine were subjected to general procedure 4. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **9** (45 mg, 70%) as a colourless oil.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.94 (1 H, d, *J*=8.2 Hz), 7.74 (1 H, d, *J*=8.2 Hz), 7.42 (1 H, t, *J*=7.5 Hz), 7.13 - 7.36 (11 H, m), 6.48 (1 H, s), 4.42 (1 H, br. s.), 4.30 (2 H, s), 2.35 (3 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 143.6, 141.2, 139.5, 139.2, 133.7, 129.8, 128.8, 128.1, 128.0, 127.5, 126.6, 126.2, 125.5, 124.5, 123.3, 120.4, 120.1, 107.7, 48.9, 15.8; **FTIR:** 1592, 1525, 1480, 1443, 1395, 1250, 1113, 1073, 1029, 907, 841, 753, 729, 701, 648 cm^{-1}; **HRMS** m/z $[C_{24}H_{21}N+H]^+$ cal. 324.1747, found 324.1734; **m.p.** 123-126 °C (CH_2Cl_2/petrol).

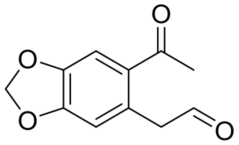
7-Methyl-5*H*-indeno[5,6-d][1,3]dioxole, 11



A suspension of $CeCl_3$ (2.80 g, 11.4 mmol) in THF (50 mL) was stirred for 30 min at rt and then cooled to −78 °C. MeLi (7.13 mL, 1.6 M in THF, 11.4 mmol) was added dropwise over 5 min. A suspension of ketone **10** (1.00 g, 5.68 mmol) was then added and the reaction stirred for 1 h then warmed to rt. The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl and the THF removed *in vacuo*. The aqueous layer was extracted with Et_2O (3 x 100 mL) and the organic layers combined, dried ($MgSO_4$) and concentrated to give crude alcohol which was dissolved in CH_2Cl_2 and pyridinium *p*-toluenesulfonate (71 mg, 0.28 mmol) added. The reaction was stirred for 30 min at rt and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (petrol-EtOAc, 19:1) to give *alkene* **11** (761 mg, 77 %) as a tan solid.

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 6.99 (1 H, s), 6.86 (1 H, s), 6.15 (1 H, s), 5.99 (2 H, s), 3.26 (2 H, br. s.), 2.15 (3 H, s); **^{13}C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 146.5, 145.6, 140.2, 139.6, 138.0, 127.6, 105.2, 100.9, 100.1, 37.6, 13.2; **FTIR** 2890, 1594, 1500, 1467, 1331, 1270, 1246, 1100, 1034, 936, 863, 812, 746 cm^{-1}; **HRMS** m/z $[C_{11}H_{10}O_2+H]^+$ cal. 175.0754, found 175.0753.

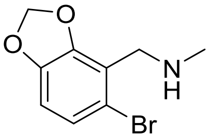
2-(6-Acetylbenzo[*d*][1,3]dioxol-5-yl)acetaldehyde, 12



To a solution of alkene **11** (320 mg, 1.84 mmol) and *N*-methylmorpholine *N*-oxide (430 mg, 3.68 mmol) in THF/*t*BuOH 10:8 (10 mL) was added a solution of $K_2OsO_4{\cdot}2H_2O$ (17 mg, 0.046 mmol) in water (1 mL). The reaction was stirred for 18 hr and then quenched by addition of a saturated solution of N_2SO_3 and extracted in to EtOAc. The organic layers were combined, dried ($MgSO_4$) and concentrated. The crude material was purified by flash column chromatography (petrol-EtOAc, 1:1) to give *diol* which was dissolved in CH_2Cl_2 (10 mL) and $NaIO_4.SiO_2$ (9.94 g, 3.6 g/mmol, 2.76 mmol) and stirred. After 1 h the reaction was filtered and washed with CH_2Cl_2. The filtrate was concentrated to give dicarbonyl **12** (280 mg, 74%) which was used in the next step without further purification.

^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 9.64 (1 H, s), 7.27 (1 H, s), 6.60 (1 H, s), 5.98 (2 H, s), 3.82 (2 H, s), 2.45 (3 H, s); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 199.0, 198.4, 150.8, 147.0, 130.1, 130.0, 113.0, 110.5, 102.2, 49.5, 28.7; **FTIR** 720, 1671, 1608, 1506, 1489, 1371, 1240, 1113, 1036, 951, 915, 869, 728, 620 cm^{-1}; **HRMS** m/z $[C_{11}H_{10}O_4+Na]^+$ cal. 229.0471, found 229.0474.

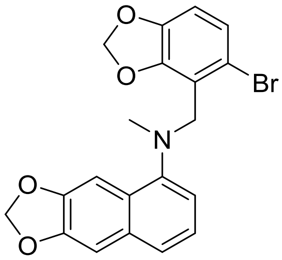
1-(5-Bromobenzo[*d*][1,3]dioxol-4-yl)-*N*-methylmethanamine, 14

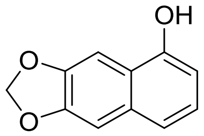


To a solution of 5-bromo-1,3-benzodioxole-4-carboxaldehyde **13** (1.00 g, 4.39 mmol) in MeOH (20 mL) was added methylamine (40% in MeOH, 6.7 mL, 74.0 mmol) and the reaction stirred at rt for 3 h. The solvent was removed *in vacuo* and the crude residue dissolved in MeOH (20 mL) and cooled to 0 °C. $NaBH_4$ (334 mg, 8.78 mmol) was added portionwise and the reaction allowed to warm to rt. After stirring for 1 hr the reaction was quenched with 1M NaOH and extracted into EtOAc. The organic layers were combined, dried ($MgSO_4$) and concentrated. The crude product was purified by flash column chromatography (CH_2Cl_2 - MeOH, 19:1) to yield *amine* **14** (1.07 g, 100%).

^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 6.94 (1 H, d, *J*=8.3 Hz), 6.54 (1 H, d, *J*=8.1 Hz), 5.91 (2 H, s), 3.76 (2 H, s), 2.35 (3 H, s), 1.65 (1 H, br. s); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 147.4, 146.7, 125.2, 121.2, 115.7, 108.5, 101.6, 49.3, 35.6; **FTIR** 2896, 1451, 1240, 1046, 927, 849, 796, 733, 644 cm^{-1}; **HRMS** m/z $[C_9H_{10}BrNO_2+H]^+$ cal. 243.9968, found 243.9971.

N-((5-Bromobenzo[*d*][1,3]dioxol-4-yl)methyl)-*N*-methylnaphtho[2,3-*d*][1,3]dioxol-5-amine, 15 and naphtho[2,3-*d*][1,3]dioxol-5-ol, S6





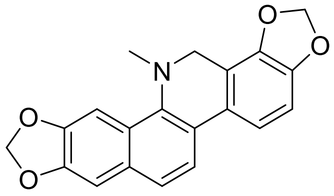
Method A Aldehyde **12 (**70 mg, 0.33 mmol) and amine **14** were subjected to general procedure 3. Purification by flash column chromatography (petrol-EtOAc, 19:1) afforded napthyl amine **15** (84 mg, 61%) as a tan solid.

Method B Amine **14** (50 mg, 0.206 mmol) and $ZnCl_2$ (1.0 M in Et_2O, 0.035 mmol) were dissolved in DCE (1.0 mL) and heated to 55 °C. To this solution, unsaturated 1,5-dicarbonyl **12** (23 mg, 0.112 mmol) was added dropwise over 12 h . The reaction mixture was stirred for 24 h, cooled and then concentrated. The crude product was purified by flash column chromatography (petrol - EtOAc, 19:1 to 5:1) to yield aryl amine **15** (20 mg, 54%) and phenol **S6** (5 mg, 24%).

Compound 15: ^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 7.70 (1 H, s), 7.31 (1 H, d, *J*=8.1 Hz), 7.17 (1 H, m), 7.05 (1 H, d, *J*=7.3 Hz), 7.00 (1 H, s), 6.94 (1 H, d, *J*=8.3 Hz), 6.52 (1 H, d, *J*=8.3 Hz,), 5.92 (2 H, s), 5.80 (2 H, s), 4.22 (2 H, s), 2.67 (3 H, s); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 149.6, 147.9, 147.5, 147.5, 146.7, 131.8, 127.2, 125.5, 124.3, 123.2, 119.9, 117.1, 115.9, 108.6, 104.1, 101.5, 101.2, 100.9, 54.2, 42.8; **FTIR** 2894, 1499, 1453, 1237, 1160, 1103, 1041, 935, 904, 850, 797, 733 cm^{-1}; **HRMS** m/z $[C_{20}H_{16}BrNO_4+H]^+$ cal. 414.0335, found 414.0326; **m.p.** 122–124 °C (petrol/CH_2Cl_2).

Compound S6: ^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 7.50 (1 H, s), 7.27 (1 H, m), 7.16 (1 H, m), 7.10 (1 H, s), 6.70 (1 H, d, *J*=7.6 Hz,), 6.04 (2 H, m), 5.28 (1 H, s,); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 151.0, 148.1, 147.2, 132.1, 124.4, 120.8, 119.9, 107.8, 103.8, 101.1, 98.6. Data were consistent with those previously reported.[6]

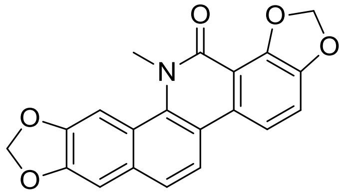
Dihydrosanguanine, 16



A Schlenk tube was charged with napthyl amine **15** (50 mg, 0.12 mmol), neocuprine (25 mg, 0.12 mmol), freshly sublimed KO^{t}Bu (81 mg, 0.72 mmol) and benzene (1 mL). The Schlenk tube was then back filled with argon and heated to 100 °C for 5 h. The reaction mixture was loaded directly onto SiO_2 and eluted with petrol:EtOAc (9:1). Fractions containing the desired product were combined and concentrated *in vacuo* to give dihydrosanguanine **(16)** (23 mg, 58%) as a tan solid.

^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 7.70 (1 H, d, *J*=8.6 Hz), 7.68 (1 H, s), 7.49 (1 H, d, *J*=8.6 Hz), 7.31 (1 H, d, *J*=8.1 Hz), 7.12 (1 H, s), 6.86 (1 H, d, *J*=8.1 Hz), 6.06 (2 H, s), 6.05 (2 H, s), 4.21 (2 H, s), 2.63 (3 H, s); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm 148.2, 147.5, 147.1, 144.7, 142.5, 130.8, 127.3, 126.5, 124.4, 124.0, 120.4, 116.2, 113.6, 107.2, 104.4, 101.4, 101.1, 100.8, 48.5, 41.6; **m.p.** 268-270 °C. Data were consistent with those previously reported.[7]

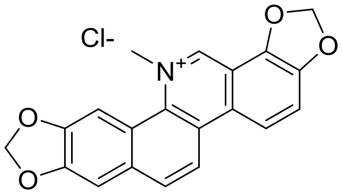
Oxysanguanine, 25



Activated MnO_2 (65 mg, 0.750 mmol) was added to a stirred solution of dihydrosanguanine **(16)** (10 mg, 0.030 mmol) in chloroform (0.7 mL) under nitrogen at room temperature. After stirring for 36 h, the mixture was filtered and the filtrate was evaporated *in vacuo* to give a brown oil which was purified by flash column chromatography (CH_2Cl_2-MeOH, 99.5:0.5) to give oxysanguanine **(25)** (4 mg, 42%).

^{1}H NMR (400 MHz, *CHLOROFORM-d*) δ ppm 7.99 (1 H, d, *J*=8.6 Hz), 7.77 (1 H, d, *J*=8.6 Hz), 7.59 (1H, s), 7.54 (1 H, d, *J*=8.8 Hz), 7.25 (1H, d, *J* =8.4 Hz), 7.17 (1 H, s), 6.28 (2 H, s), 6.11 (2 H, s), 3.92 (3 H, s). Solvent containments could not be removed even under prolonged exposure to heat and high vacuum. Data were consistent with those previously reported.[8]

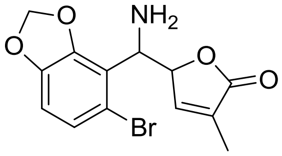
Sanguanine, 21



To a vigorously stirred solution of dihydrosanguanine **(16)** (10 mg, 0.030 mmol) in PhMe (10 mL) was added, 5% NaOH (1 mL) then DDQ (17 mg, 0.075 mmol). The reaction was stirred for 2 h at rt. Water (5 mL) was added and the mixture was extracted with EtOAc (3 x 10 mL), the organic layers combined, dried ($MgSO_4$) and concentrated. Concentrated HCl was then added to the resulting residue and the precipitate collected by filtration to yield sanguanine **(21)** (10 mg, 90%).

^{1}H NMR (200 MHz, *METHANOL-d_4*) δ ppm 9.93 (1 H, s), 8.59 (1 H, d, *J*=9.2 Hz), 8.50 (1 H, d, *J*=8.9 Hz), 8.19 (1 H, d, *J*=8.9 Hz), 8.13 (1 H, s), 7.94 (1 H, d, *J*=8.5 Hz), 7.54 (1 H, s), 6.53 (2 H, s), 6.28 (2 H, s), 4.94 (3 H, s); **^{13}C NMR** (500 MHz, *DMSO-d_6*) δ ppm 149.9, 148.7 (2 signals), 147.5, 146.3, 132.2, 131.5, 131.3, 127.2, 125.7, 120.3, 119.9, 118.9, 117.3, 109.5, 105.7, 104.9, 104.2, 102.8, 52.1. Data were consistent with those previously reported.[9]

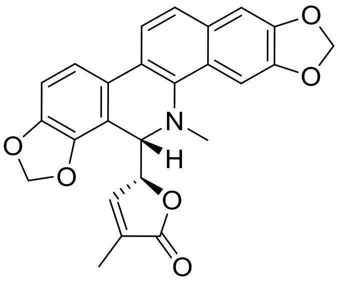
5-(Amino(5-bromobenzo[*d*][1,3]dioxol-4-yl)methyl)-3-methylfuran-2(5*H*)-one, 20

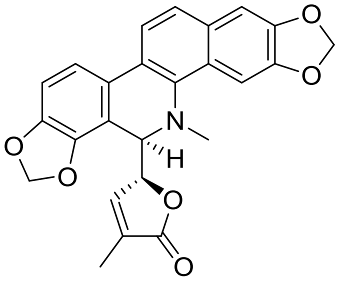


5-bromo-1,3-benzodioxole-4-carboxaldehyde (200 mg, 1.15 mmol) and o-Anisidine (141 mg, 1.15 mmol, 0.129 mL) were stirred in a round bottom flask and stirred for 15 min. Furan **22** (293 mg, 1.73 mmol) was added and the reaction stirred for a further 30 min. The crude material was filtered through a cartridge of SiO_2 (petrol - EtOAc, 7:3 to 1:1). The fractions containing the target product were combined and concentrated *in vacuo*. The crude residue was dissolved in MeOH and added over 15 min to a stirring solution of $PhI(OAc)_2$ (849 mg, 2.64 mmol) in MeOH (5 mL) cooled to 0 °C. The reaction was stirred for 30 min then 1.0 M aqueous HCl (5 mL) was added and the reaction stirred for 1 h at rt. The reaction was diluted with CH_2Cl_2, the aqueous layer washed with CH_2Cl_2, the organic layers combined and washed with 1.0 M aqueous HCl. The aqueous layers were then combined, neutralised with 1.0 M aqueous NaOH, extracted with CH_2Cl_2, dried ($NaSO_4$) and concentrated. The crude material was purified by flash column chromatography (CH_2Cl_2- MeOH, 19:1) to yield amine **20** (50 mg, 13 %, d.r. 1:0.4).

^{1}**H NMR** (400 MHz, *CHLOROFORM-d*) δ ppm 7.12 - 7.17 (0.4 H, m), 7.08 (1.0 H, d, *J*=8.3 Hz), 7.05 (0.4 H, d, *J*=8.3 Hz), 6.76 - 6.82 (1.0 H, m), 6.68 (1.0 H, d, *J*=8.3 Hz), 6.65 (0.4 H, d, *J*=8.3 Hz), 6.04 (2.0 H, d, *J*=3.9 Hz), 6.02 (0.8 H, d, *J*=5.7 Hz), 5.15 - 5.23 (1.4 H, m), 4.56 (0.4 H, d, *J*=5.9 Hz), 4.26 (1.0 H, d, *J*=7.8 Hz), 2.00 (2.8 H, br. s.), 1.89 - 1.95 (4.2 H, s); ^{13}**C NMR** (100 MHz, *CHLOROFORM-d*) δ ppm174.0,(1C missing), 147.7, 147.6, 146.7, 146.5, 146.3, 145.9, 131.7, 131.2, 126.2, 126.1, 122.0, 121.5, 114.5, 114.3, 109.5, 109.3, 101.9, 101.8, 83.8, 82.8, 57.9, 56.5, 10.8, 10.7; **FTIR:** 1755, 1452, 1240, 1092, 1049, 931, 869, 801; **HRMS** m/z $[C_{13}H_{12}BrNO_4+H]^+$ cal. 326.0022, found 326.0028.

Maclekarpine B, (23) and maclekarpine C, (24)



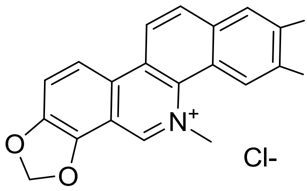


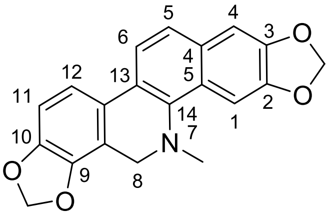
To a solution of diisopropyl amine (6 mg, 0.04 mmol) in THF (0.7 mL) at −78 °C was added *n*BuLi (0.15 mL, 0.43 mmol, 2.5 M in hexanes). The reaction was allowed to warm to rt and stirred for 10 min. The solution was then cooled to −78 °C and a suspension of sanguanine (10 mg, 0.03 mmol) **(21)** added dropwise. The solution was allowed to stir for a further 30 min then warmed to rt. The reaction was quenched by the addition of a saturated solution of NH_4Cl and extracted into EtOAc (3 x 5 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated. The crude material was purified by flash column chromatography (petrol- EtOAc, 8:2) to give maclekarpine B **(23)** and maclekarpine C **(24)** (8 mg, 73 %, d.r. 0.85:1) as an inseparable mixture.

Maclekarpine B: ^{1}H NMR (500 MHz, *CHLOROFORM-d*) δ ppm 7.67 (2 H, d, *J*=8.5 Hz), 7.53 (1 H, s), 7.46 (1 H, d, *J*=8.5 Hz), 7.38 (1 H, d, *J*=8.2 Hz), 7.09 (1 H, s), 6.93 (1 H, d, *J*=7.9 Hz), 6.51 (1 H, s), 6.14 (1 H, d, *J*=1.6 Hz), 6.07 (2 H, d, *J*=1.3 Hz), 6.06 (1 H, br. s.), 4.79 - 4.84 (1 H, m), 4.62 (1 H, d, *J*=6.0 Hz), 2.72 (3 H, s), 1.34 (3 H, s); ^{13}C NMR (125 MHz, *CHLOROFORM-d*) δ ppm 174.2, 148.4, 147.7, 147.4, 145.8, 145.6, 140.0, 131.1, 129.5, 126.8, 126.0, 124.2, 123.2, 119.7, 116.3, 111.9, 108.5, 104.3, 101.8, 101.1, 100.6, 81.3, 60.2, 43.5, 10.1. Data were consistent with those previously reported.[10]

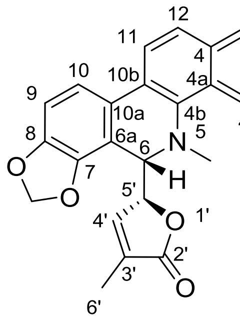
Maclekarpine C: ^{1}H NMR (500 MHz, *CHLOROFORM-d*) δ ppm 7.76 (1 H, s), 7.67 (3 H, d, *J*=8.5 Hz), 7.50 (1 H, d, *J*=8.5 Hz), 7.35 (1 H, d, *J*=8.2 Hz), 7.12 (1 H, s), 6.91 (1 H, d, *J*=8.2 Hz), 6.45 (1 H, s), 6.10 (1 H, br. s), 6.07 (6 H, br. s), 6.03 (1 H, br. s), 4.75 - 4.83 (1 H, m), 4.48 (1 H, d, *J*=7.6 Hz), 2.74 (3 H, s), 1.72 (3 H, s); ^{13}C NMR (125 MHz, *CHLOROFORM-d*) δ ppm 173.9, 148.4, 147.9, 147.3, 146.0, 145.5, 139.3, 131.0, 130.2, 127.1, 126.6, 124.3, 123.4, 119.7, 116.6, 110.9, 108.6, 104.3, 101.7, 101.2, 101.1, 81.3, 60.9, 43.2, 10.6. Data were consistent with those previously reported.[10]

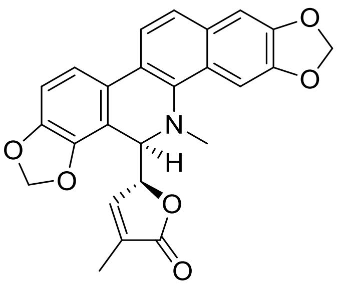
Natural product ^{1}H & ^{13}C comparison tables



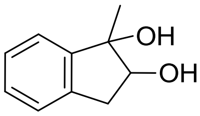


Sanguanine, **21**					Dihydrosanguanine, **16**					
δ ^{1}H lit.	δ ^{1}H	δ ^{13}C lit.	δ ^{13}C	Δ	Position	δ ^{1}H lit.	δ ^{1}H	δ ^{13}C lit.	δ^{13}C	Δ
9.95 s	9.93 s	149.8	149.9	0.1	2			148.1	148.2	0.1
8.57 d (8.9)	8.59 d (9.2)	148.6	14.7	0.1	3			147.5	147.5	0
8.48 d (8.8)	8.50 d (8.9)	148.6	148.7	0.1	8			147.1	147.1	0
8.19 d (8.9)	8.19 d (8.9)	147.4	147.5	0.1	7			144.6	144.7	0.1
8.13 s	8.13 s	146.1	146.3	0.2	4b			142.5	142.5	0
7.95 d (8.8)	7.94 d (8.5)	132.1	132.2	0.1	12a			130.8	130.8	0
7.55 s	7.54 s	131.3	131.5	0.2	10a			127.3	127.3	0
6.54 s	6.53 s	131.2	131.3	0.1	4a			126.5	126.5	0
6.30 s	6.28 s	127	127.2	0.2	10b			124.4	124.4	0
4.49 s	4.94 s	125.5	125.7	0.2	12	7.49 d (8.5)	7.49 d (8.6)	124.0	124.0	0
		120.2	120.3	0.1	11	7.69 d (8.5)	7.70 d (8.6)	120.4	120.4	0
		119.8	119.9	0.1	10	7.30 d (8.1)	7.31 d (8.1)	116.2	116.2	0
		118.7	118.9	0.2	6a			113.6	113.6	0
		117.2	117.3	0.1	9	6.85 d (8.1)	6.86 d (8.1)	107.2	107.2	0
		109.3	109.5	0.2	1	7.11 s	7.12 s	104.4	104.4	0
		105.6	105.7	0.1	OCH_2O	6.05 s	6.06 s	101.3	101.4	0.1
		104.8	104.9	0.1	OCH_2O	6.03 s	6.05 s	101.0	101.1	0.1
		104.1	104.2	0.1	4	7.68 s	7.68 s	100.8	100.8	0
		102.7	102.8	0.1	6	4.20 s	4.21 s	48.5	48.5	0
		52.0	52.1	0.1	NMe	2.62 s	2.63 s	41.6	41.6	0

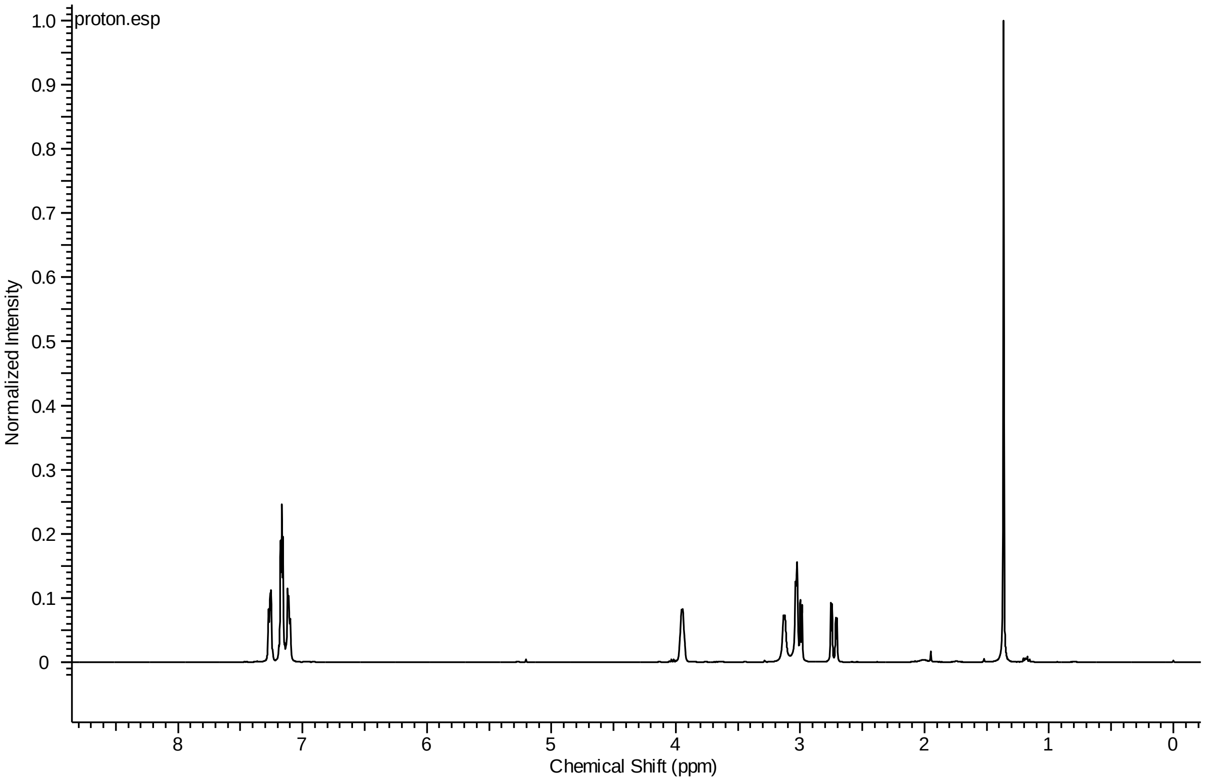




	Maclekarpine B, **23**					Maclekarpine C, **24**				
Position	δ ^{1}H lit.	δ ^{1}H	δ^{13}C lit.	δ^{13}C	Δ	δ ^{1}H lit.	δ ^{1}H	δ^{13}C lit.	δ^{13}C	Δ
1	7.08	7.09	104.3	104.3	0.0	7.11	7.12	104.3	104.3	0.0
2			147.7	147.7	0.0			147.8	147.9	0.1
3			148.4	148.4	0.0			148.4	148.4	0.0
4	7.52	7.53	100.6	100.6	0.0	7.75	7.76	101.0	101.1	0.1
4a			126.8	126.8	0.0			127.0	127.1	0.1
4b			140.0	140.0	0.0			139.3	139.3	0.0
6	4.61, d (5.5)	4.62, d (6.0)	60.2	60.2	0.0	4.46, d (7.5)	4.48, d (7.6)	60.8	60.9	0.1
6a			111.9	111.9	0.0			110.9	110.9	0.0
7			145.6	145.6	0.0			145.5	145.5	0.0
8			147.4	147.4	0.0			147.2	147.3	0.1
9	6.92, d (8.5)	6.93, d (8.2)	108.5	108.5	0.0	6.91, d(8.5)	6.92, d (8.2)	108.6	108.6	0.0
10	7.37, d (8.5)	7.38, d (8.2)	116.3	116.3	0.0	7.34, d (8.5)	7.35, d (8.2)	116.6	116.6	0.0
10a			126.0	126.0	0.0			126.6	126.6	0.0
10b			123.2	123.2	0.0			123.4	123.4	0.0
11	7.66, d (8.5)	7.67, d (8.5)	119.7	119.7	0.0	7.66, d (9.0)	7.67, d (8.6)	119.7	119.7	0.0
12	7.45, d (8.5)	7.46, d (8.5)	124.1	124.2	0.1	7.49, d (9.0)	7.50, d (8.6)	124.3	124.3	0.0
12a			131.0	131.1	0.1			131.1	131.1	0.0
1'										
2'			174.2	174.2	0.0			173.9	173.9	0.0
3'			129.5	129.5	0.0			130.2	130.2	0.0
4'	6.50, s	6.51	145.8	145.8	0.0	6.45	6.45	146.0	146.0	0.0
5'	4.80, d (6.0)	4.81, m	81.2	81.3	0.1	4.80, d (8.0)	4.80 m	81.3	81.3	0.0
6'	1.33, s	1.34	10.1	10.1	0.0	1.72, s	1.73	10.5	10.6	0.1
NMe	2.71, s	2.72	43.4	43.5	0.1	2.73, s	2.74	43.2	43.2	0.0
OCH_2O	6.07, br s	6.07, br s	101.2	101.1	0.1	6.06, br s	6.07, br s	101.2	101.2	0.0
OCH_2O	6.06, 6.14, 2 x br s	6.06, 6.14, 2 x br s	101.8	101.8	0.0	6.02, 6.10, 2 x br s	6.03, 6.10, 2 x br. s	101.6	101.7	0.1



S2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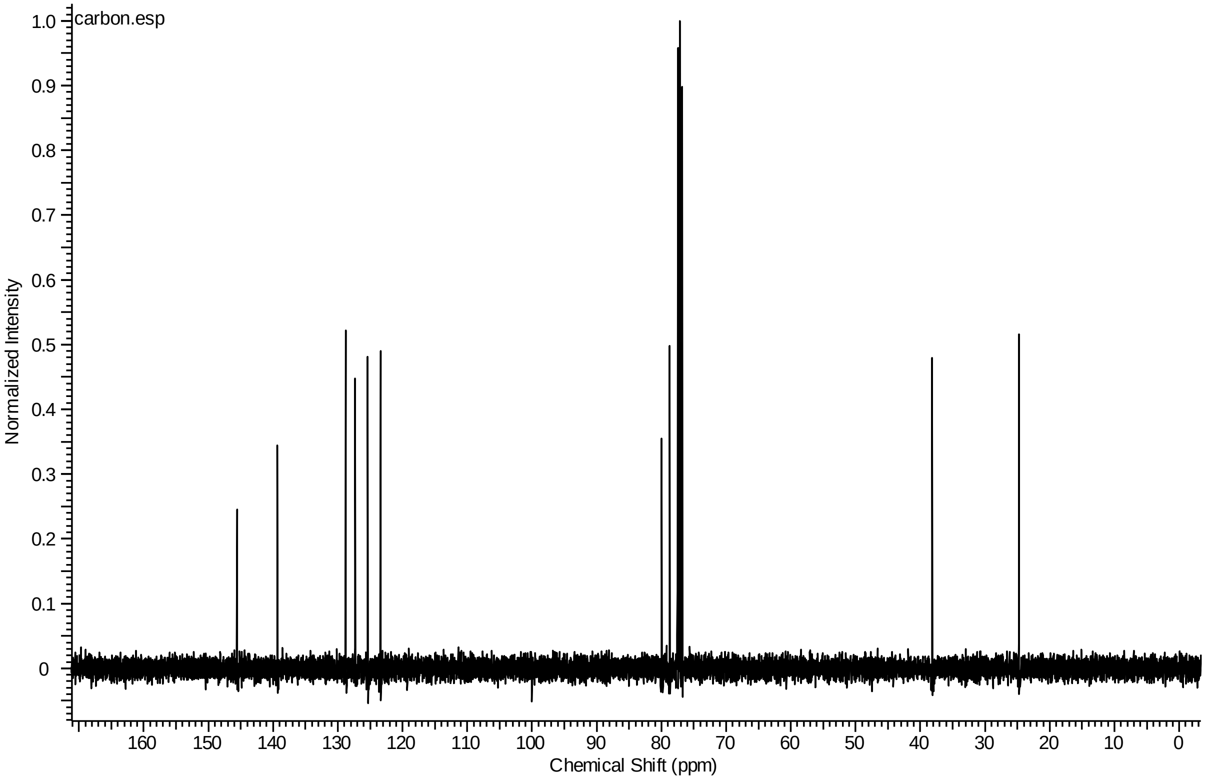
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
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0.6
0.5
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0.3
0.2
0.1
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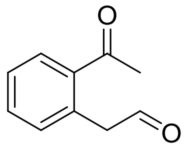
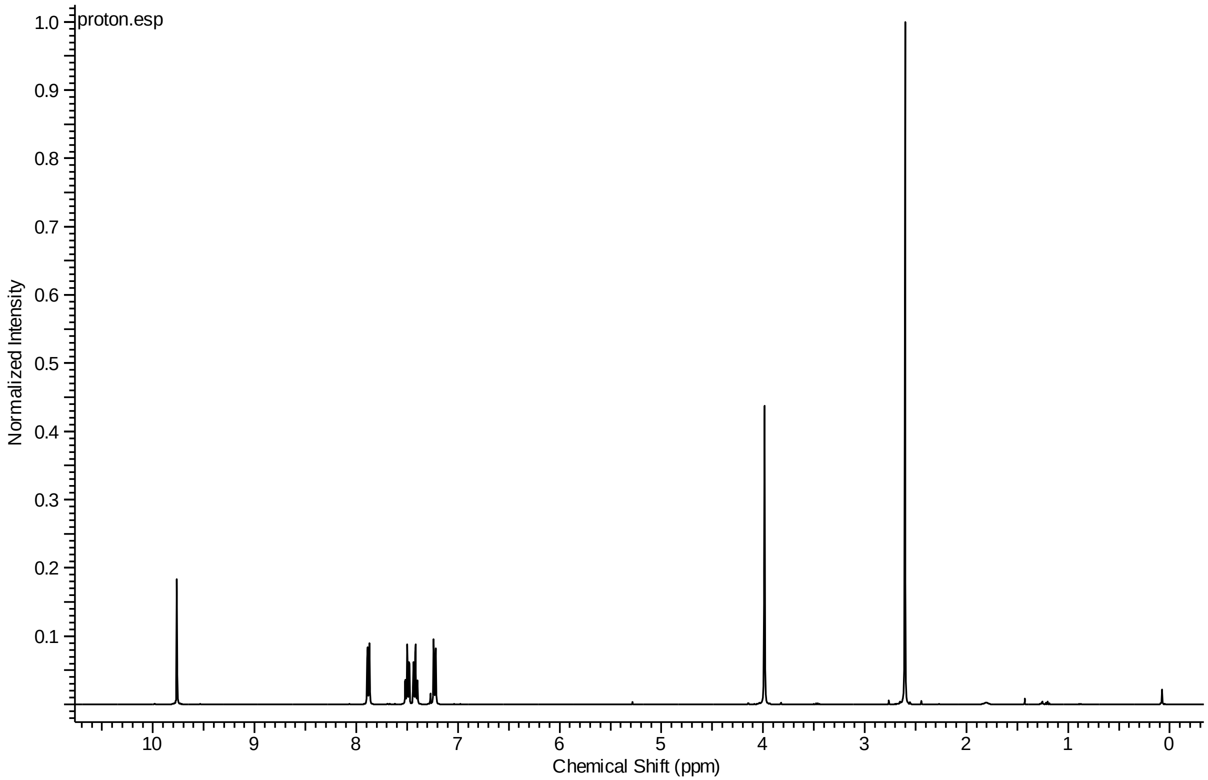
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)



S3


proton.esp
Normalized Intensity
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0.7
0.6
0.5
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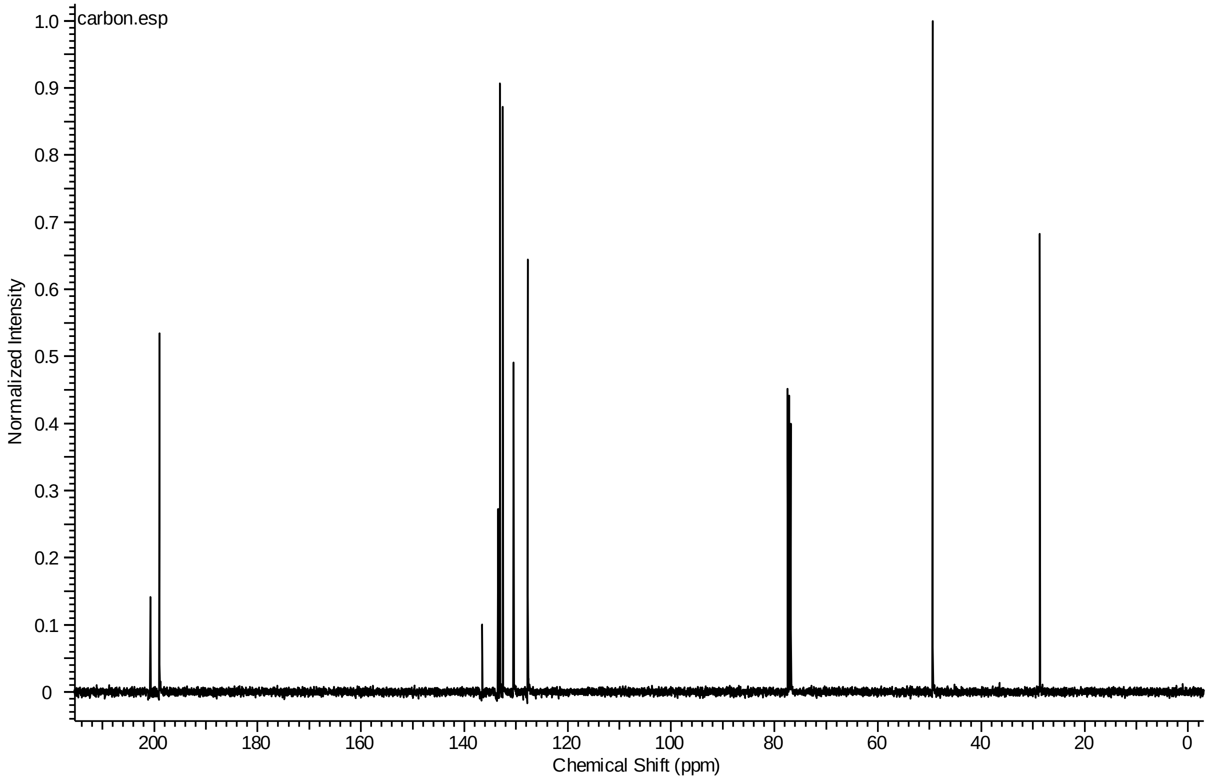
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
Normalized Intensity
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0.4
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0.1
0
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140
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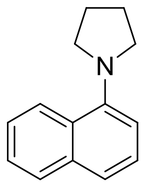
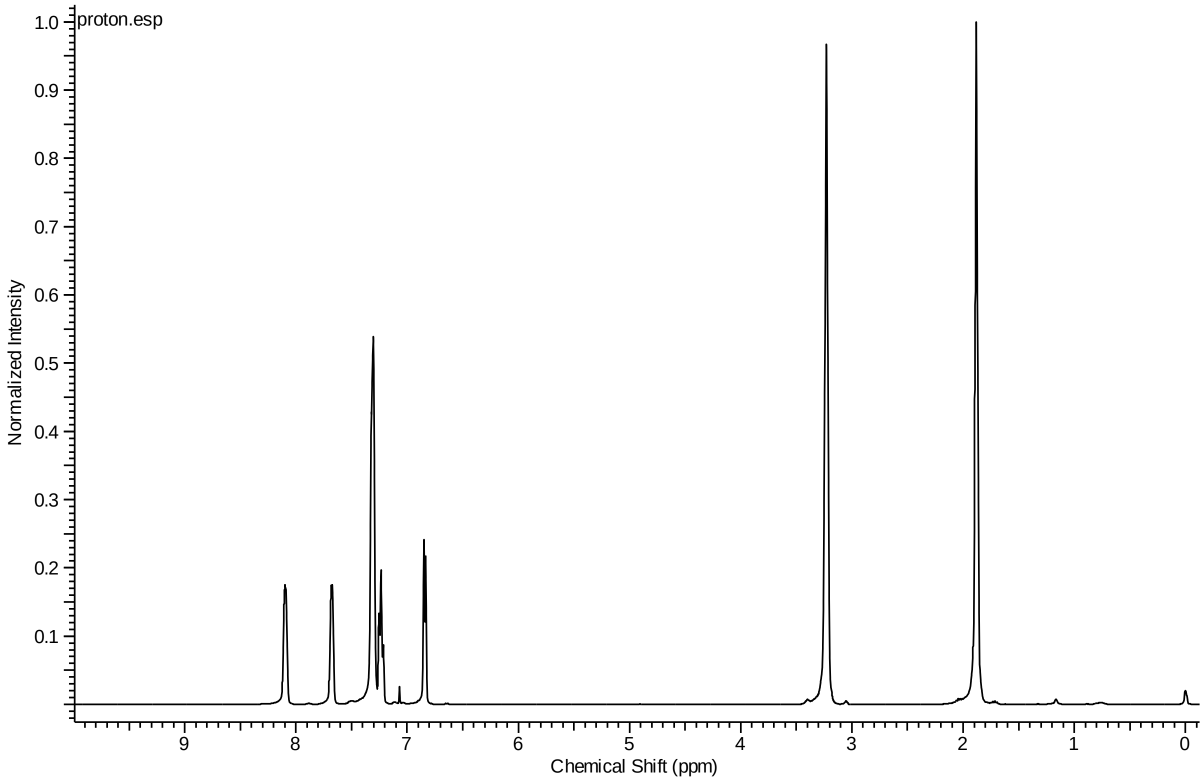
100
80
60
40
20
0
Chemical Shift (ppm)



4


proton.esp
Normalized Intensity
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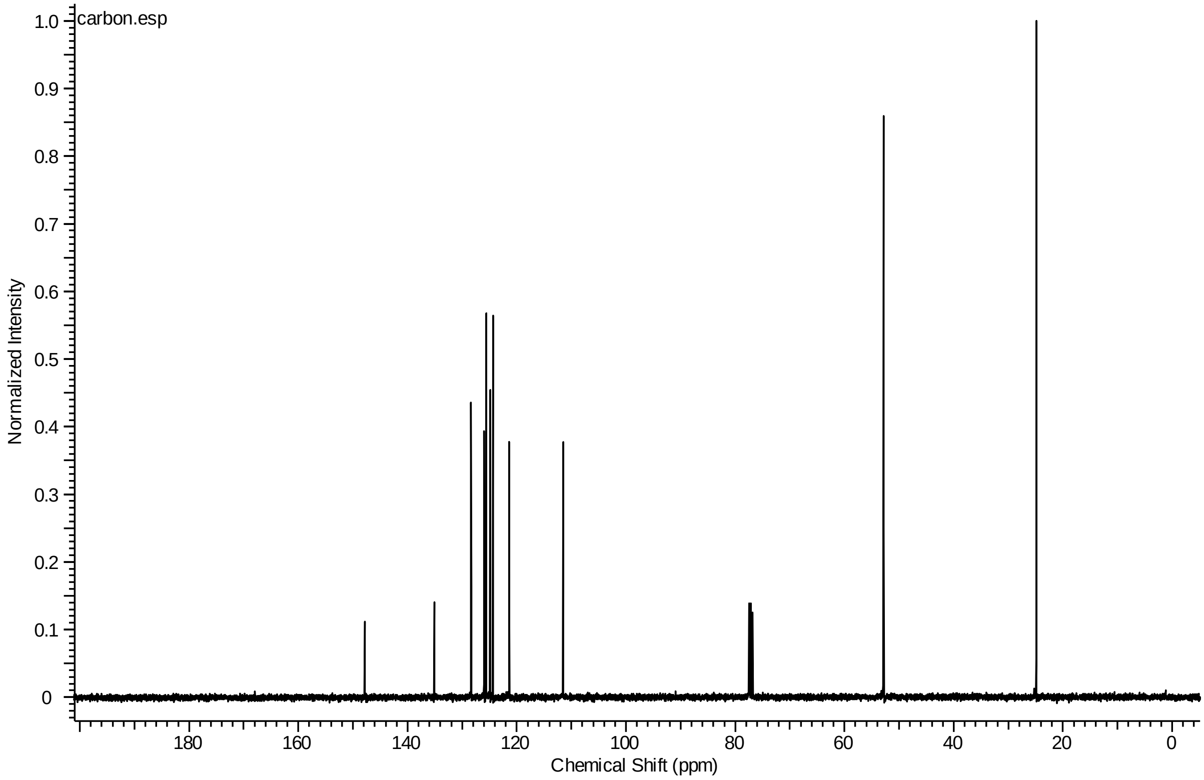
0.2
0.1
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
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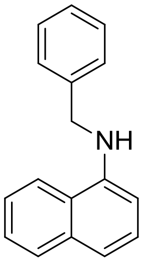
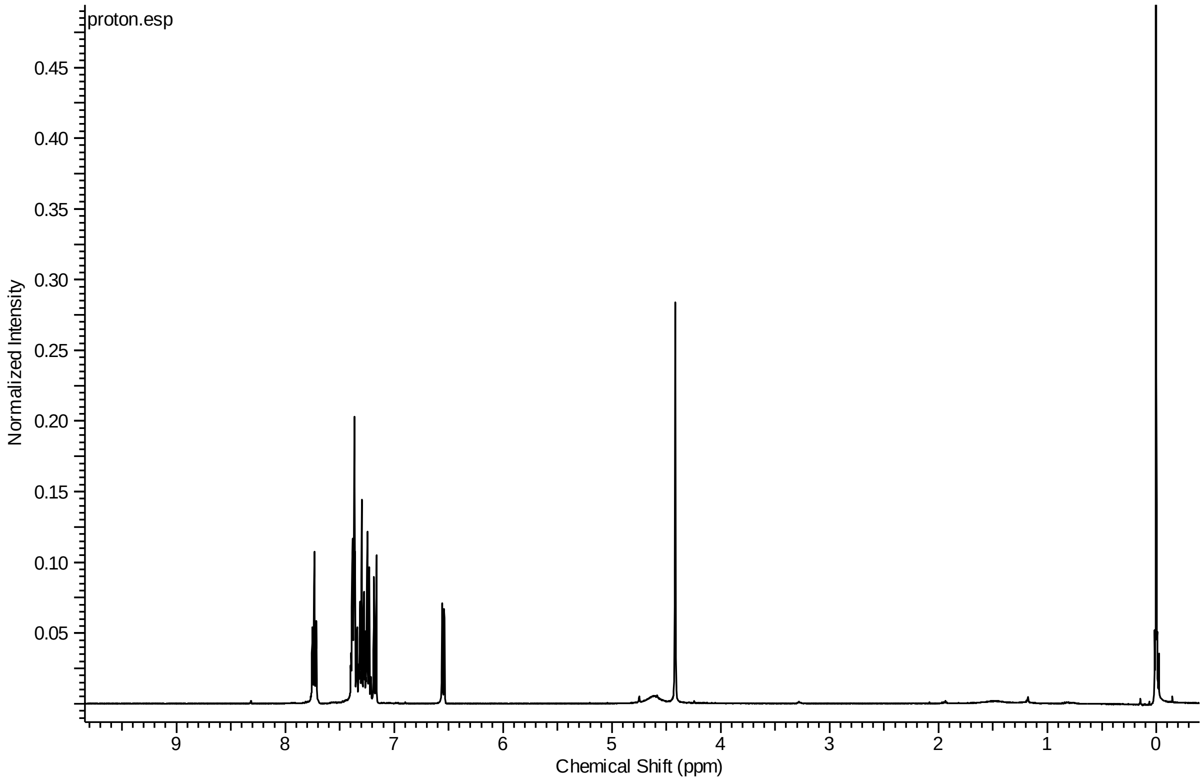
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


NH

5


proton.esp
Normalized Intensity
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0.30
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0.20
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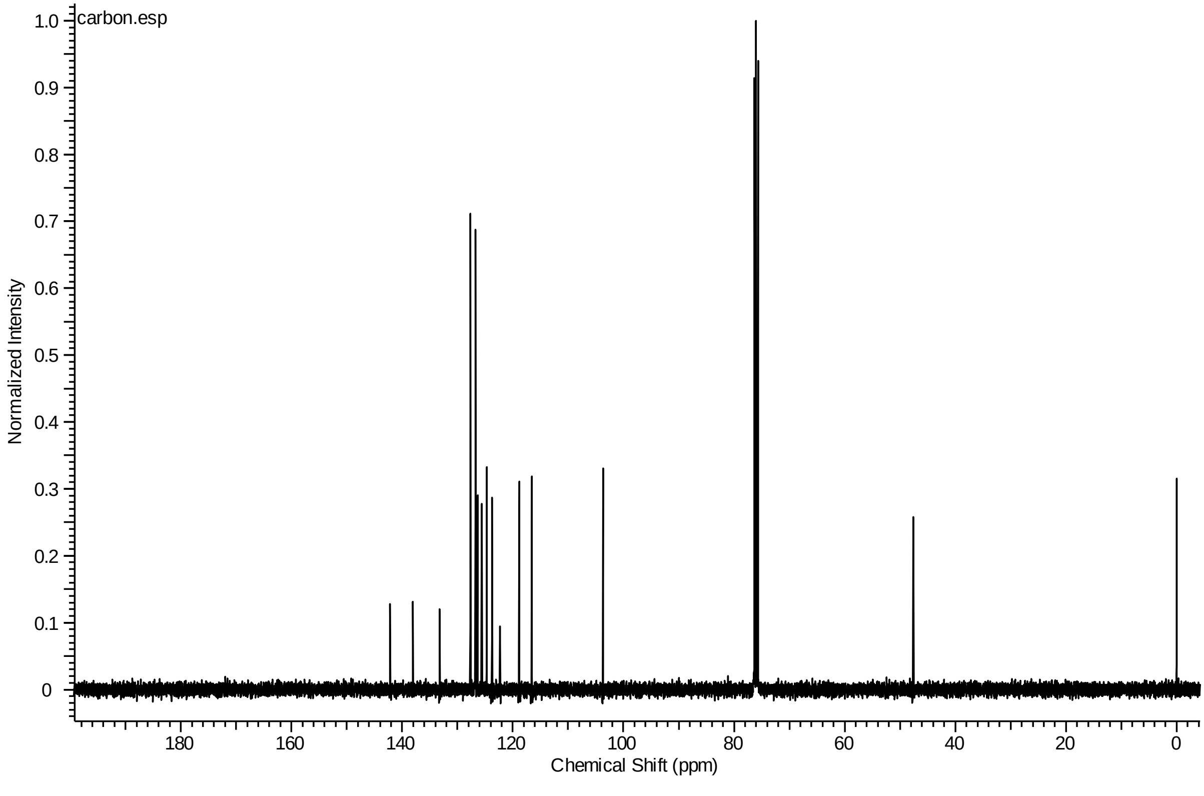
0.10
0.05
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
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0.5
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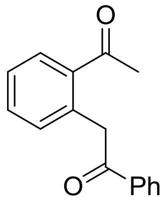
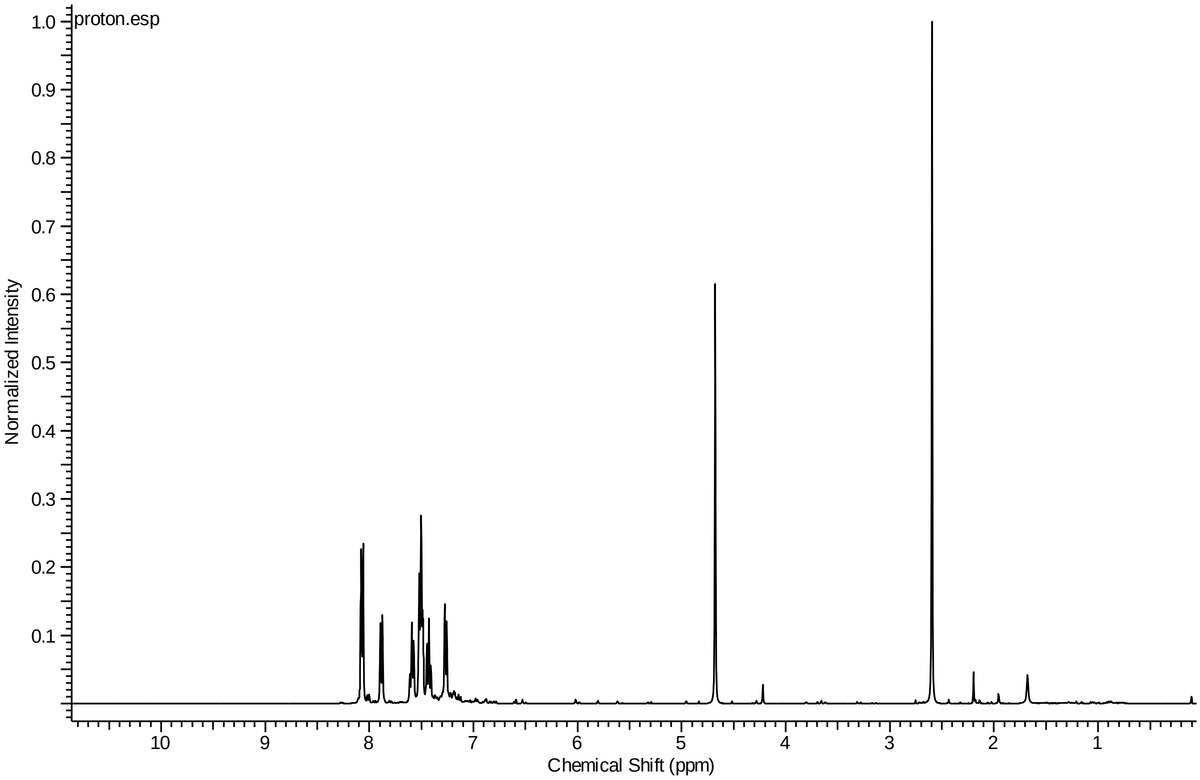
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


O
O
Ph

2


proton.esp
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0.6
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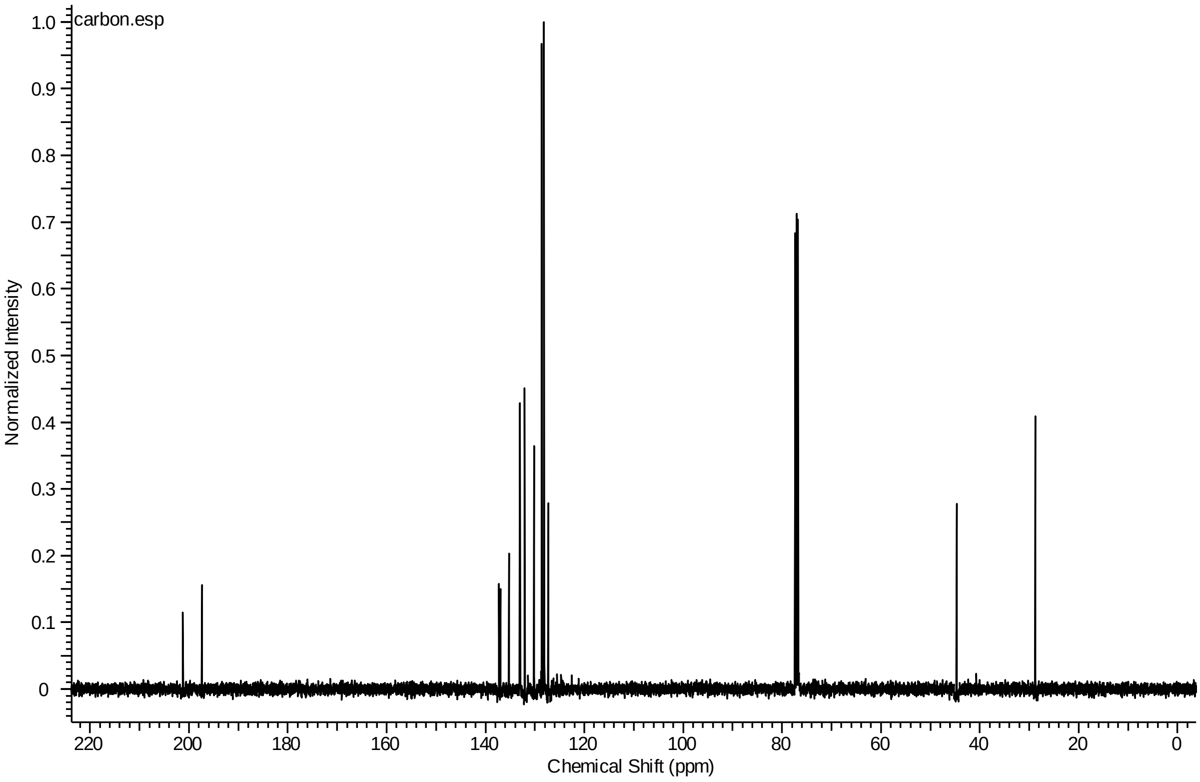
0.2
0.1
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)


carbon.esp
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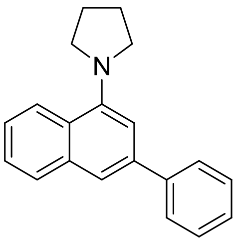
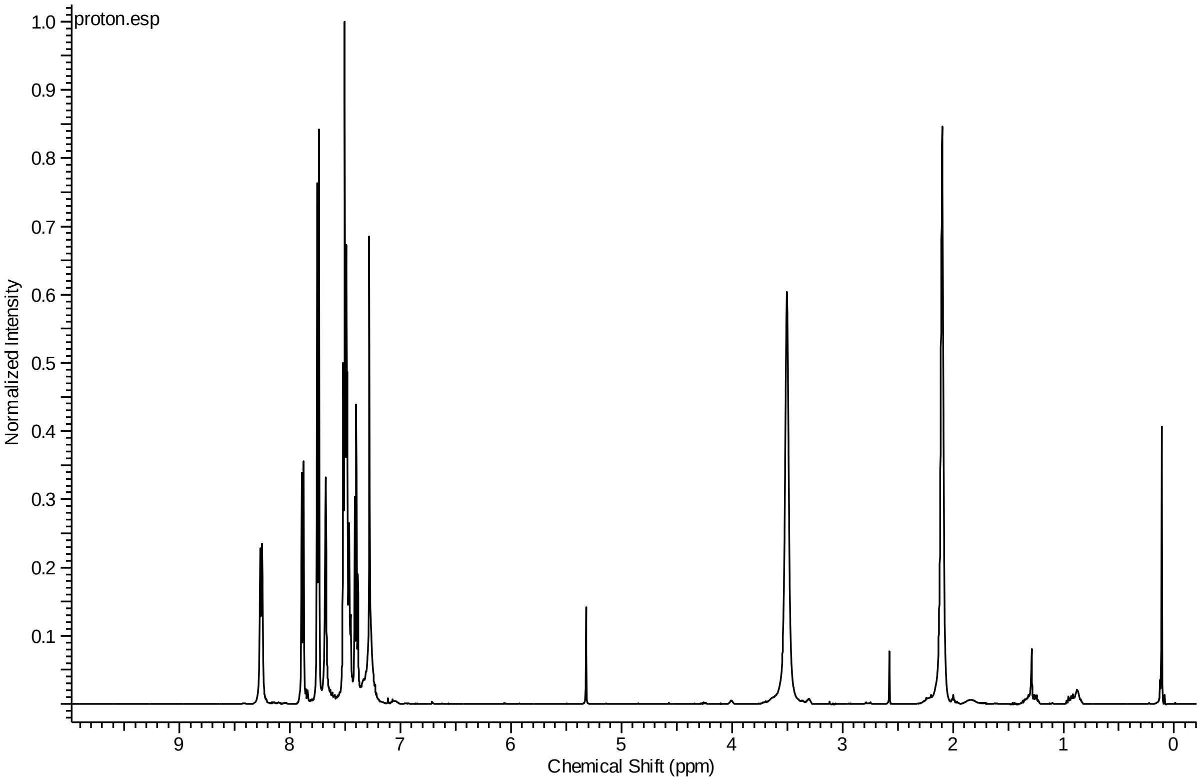
0
220
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


N

6


proton.esp
Normalized Intensity
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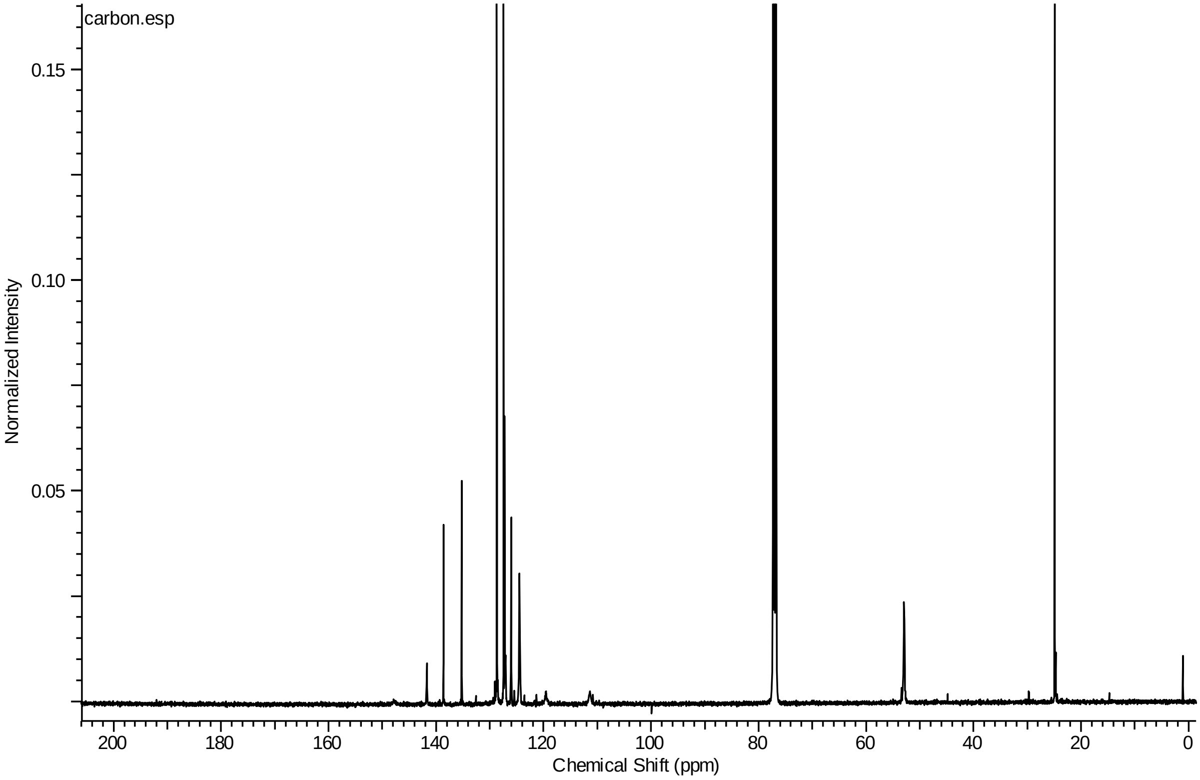
0.5
0.4
0.3
0.2
0.1
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
Normalized Intensity
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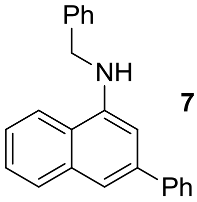
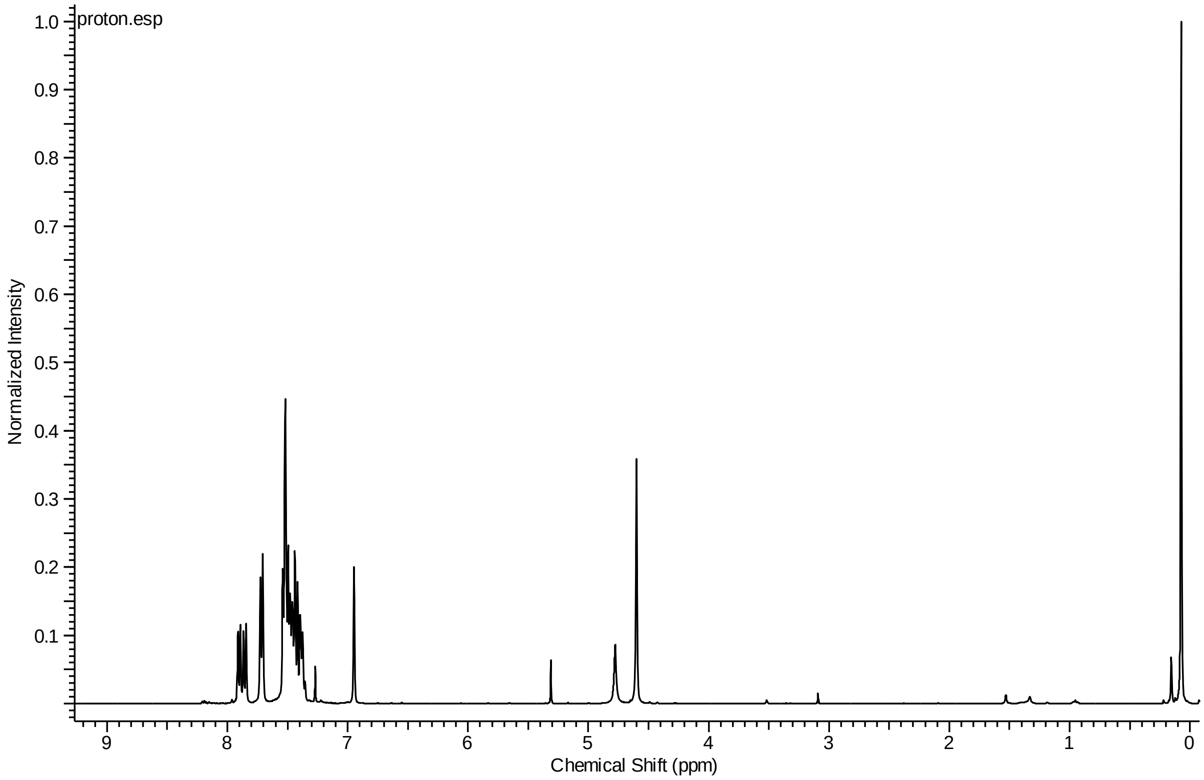
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


Ph
NH
Ph

7


proton.esp
Normalized Intensity
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0.7
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0.2
0.1
9
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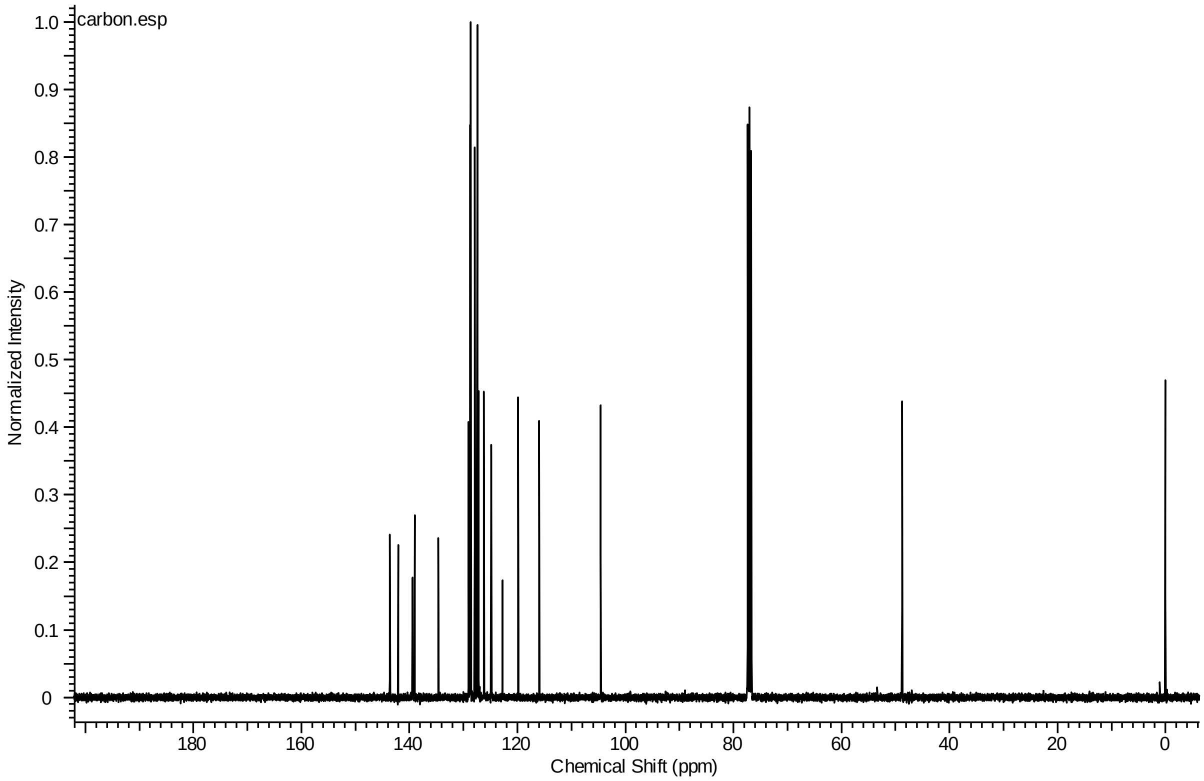
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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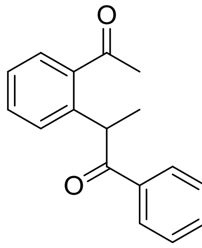
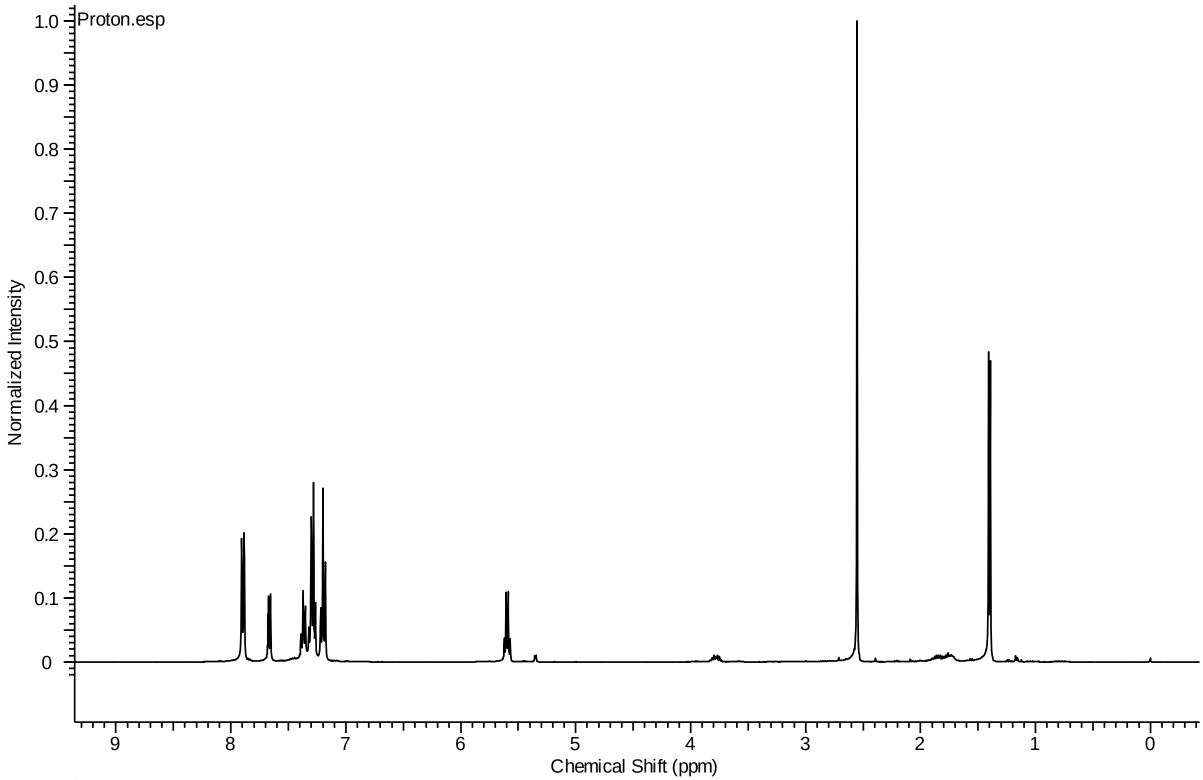
100
80
60
40
20
0
Chemical Shift (ppm)



3


Proton.esp
Normalized Intensity
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0.5
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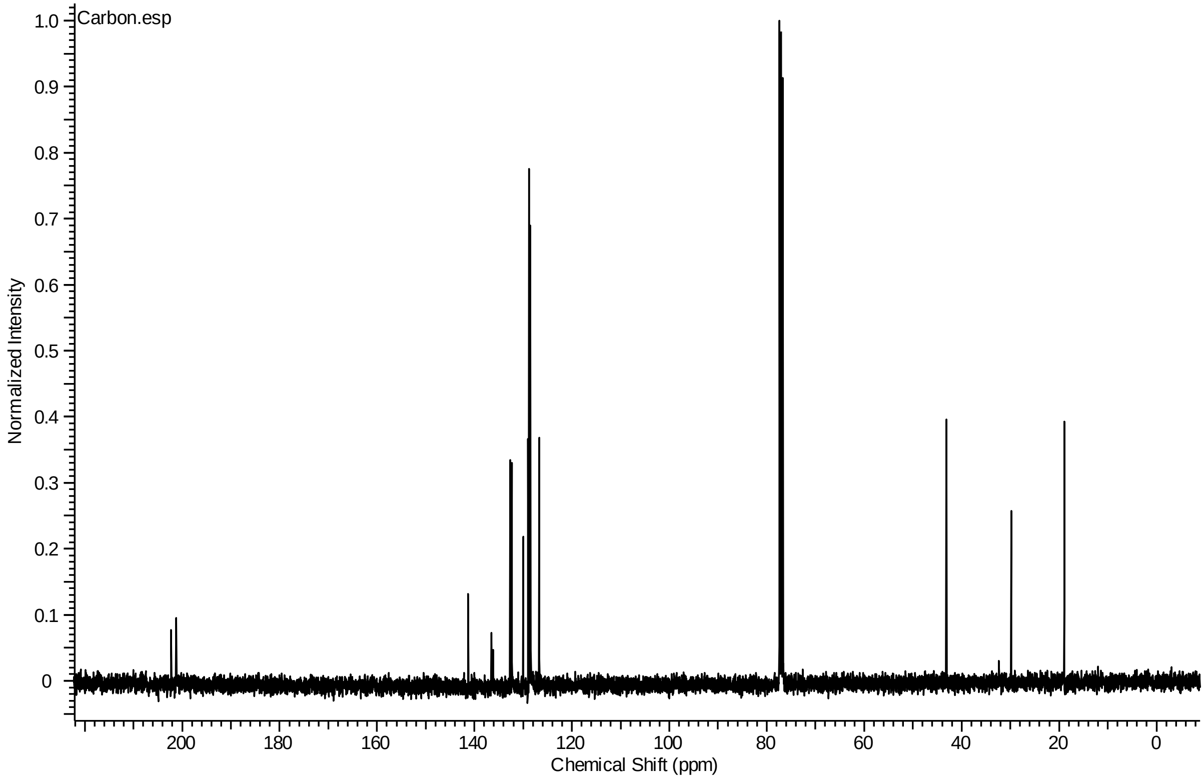
0.2
0.1
0
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Carbon.esp
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0.5
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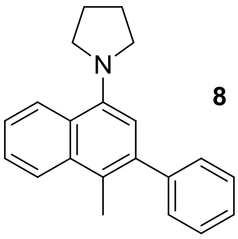
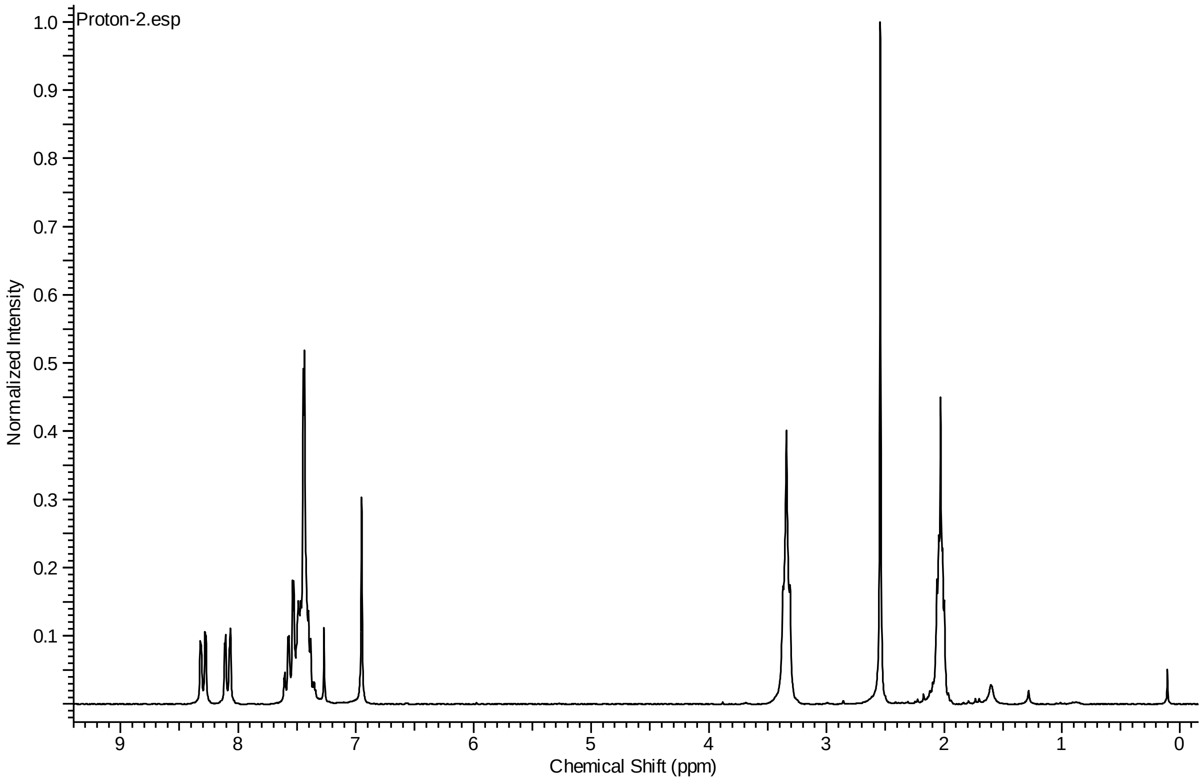
0
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



8


Proton-2.esp
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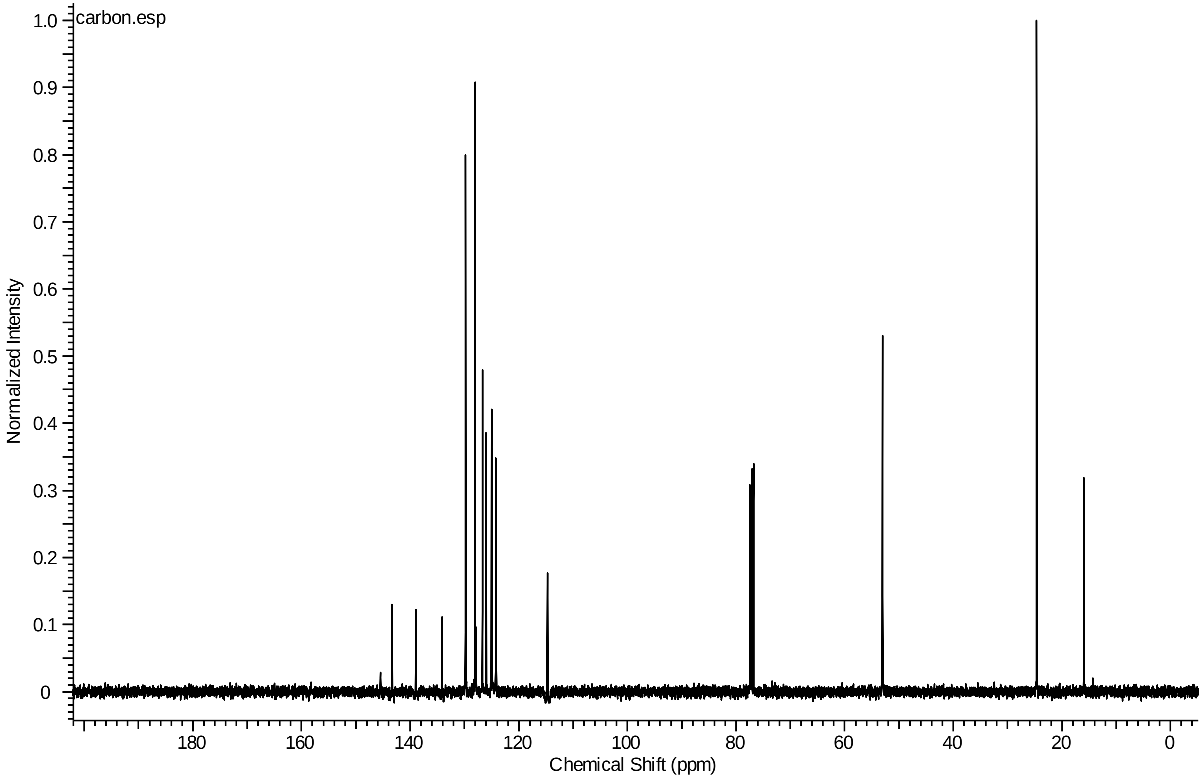
0.2
0.1
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
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0.6
0.5
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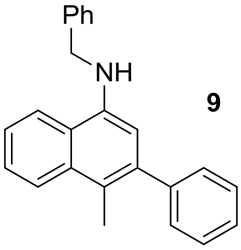
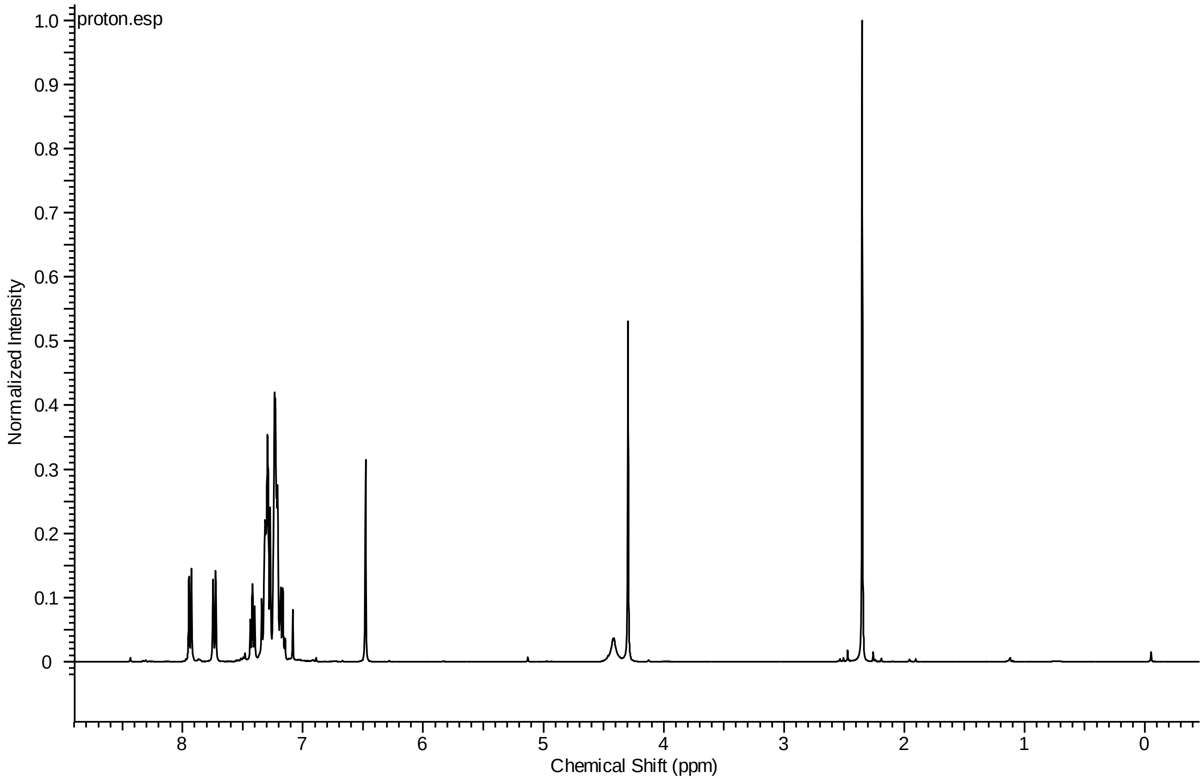
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


Ph
NH

9


proton.esp
Normalized Intensity
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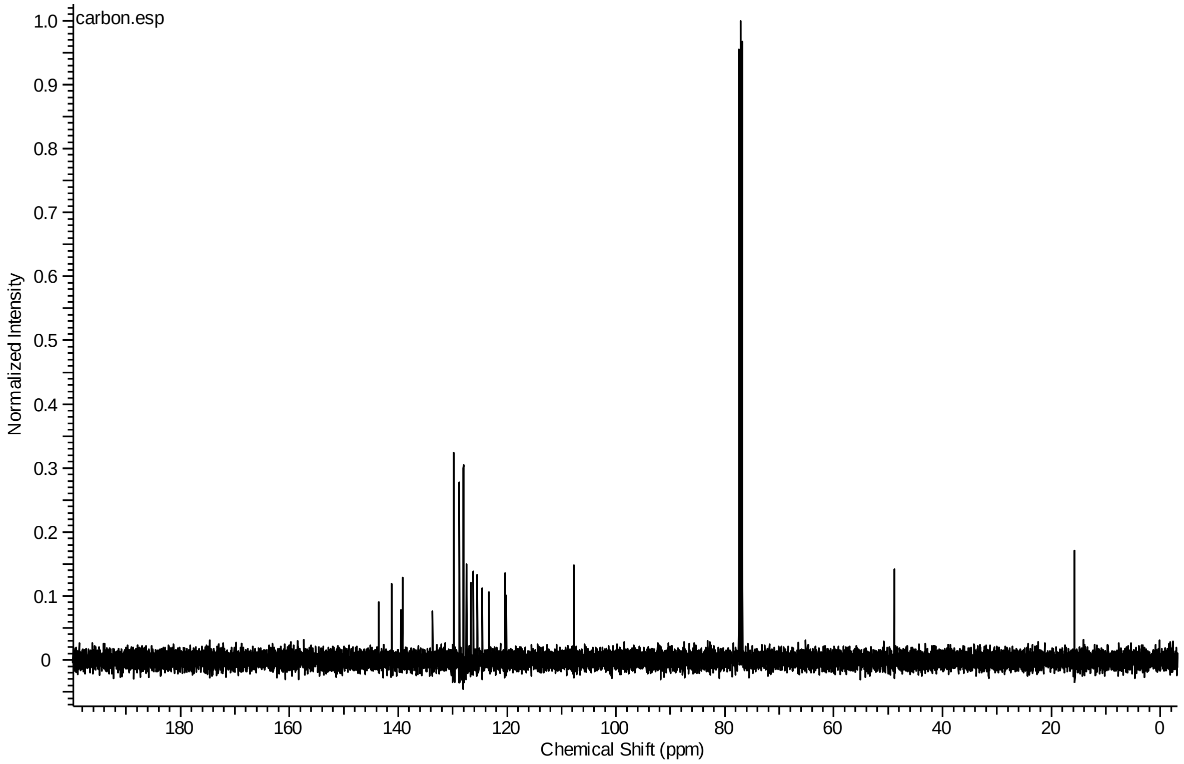
0.1
0
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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100
80
60
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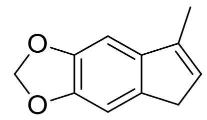
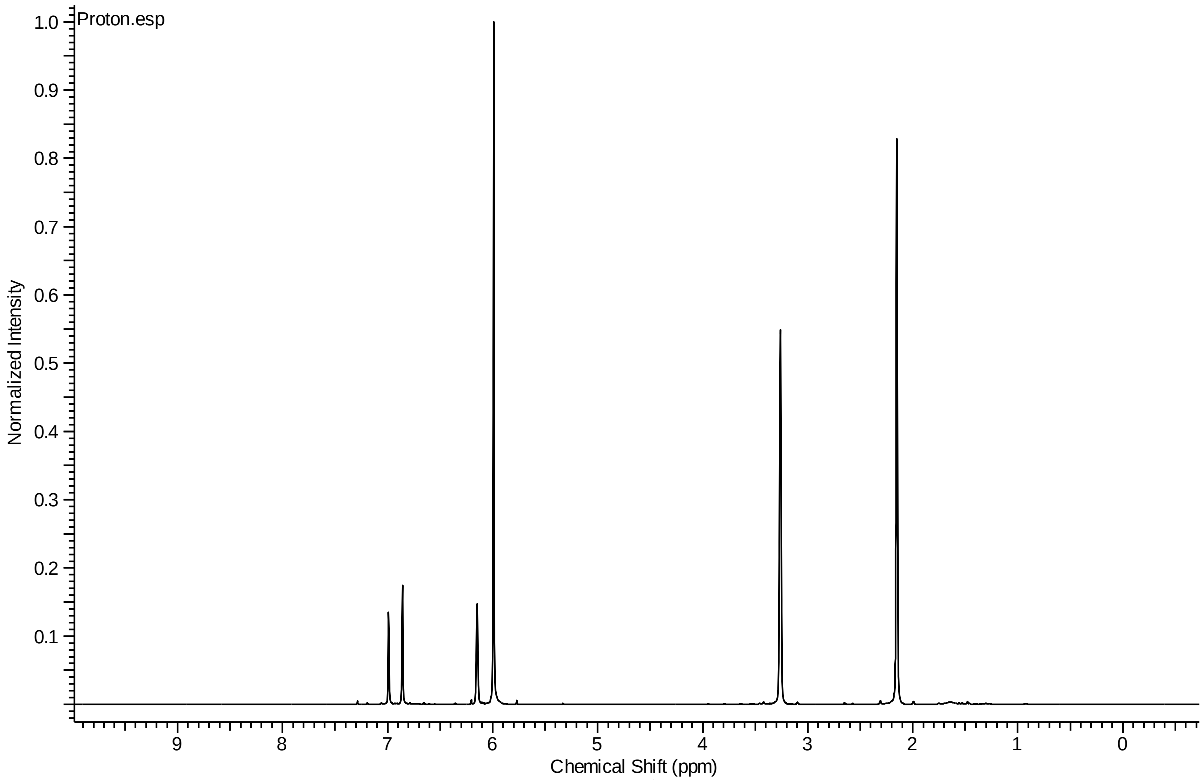
20
0
Chemical Shift (ppm)



11


Proton.esp
Normalized Intensity
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0.1
9
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7
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5
4
3
2
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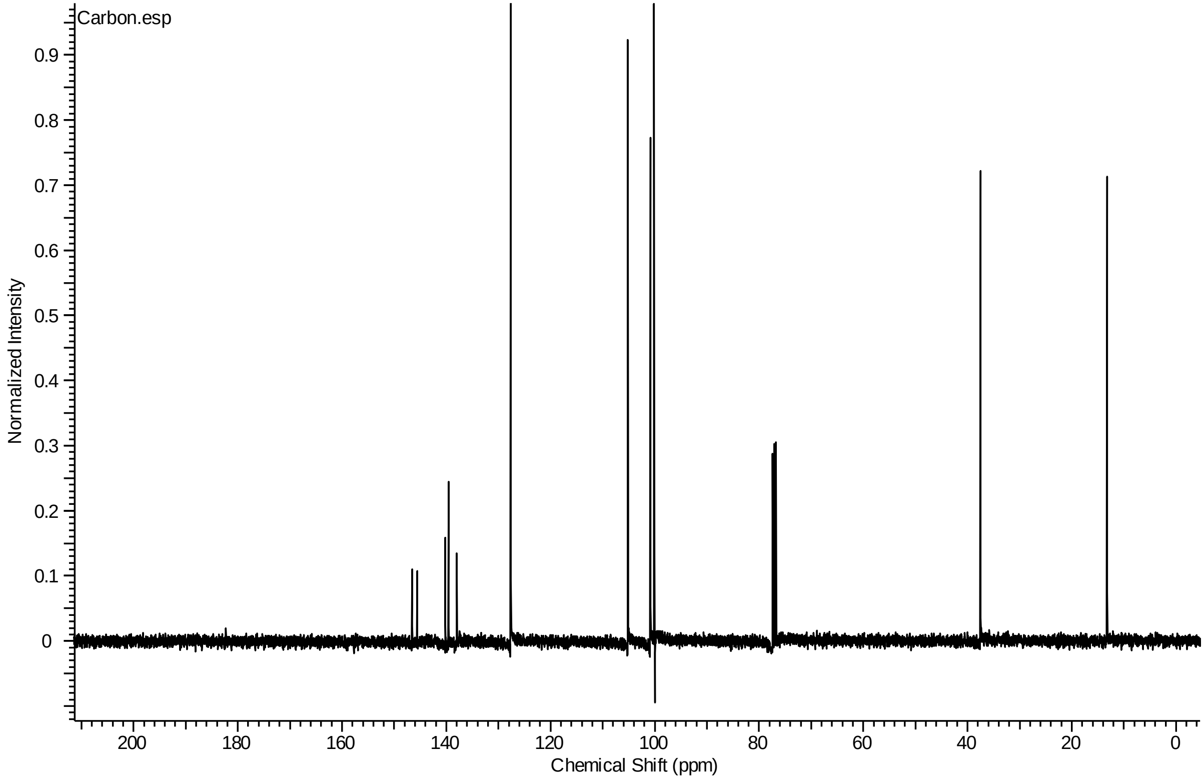
0
Chemical Shift (ppm)


Carbon.esp
Normalized Intensity
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0.4
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200
180
160
140
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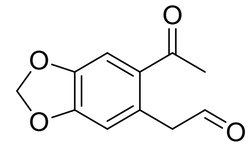
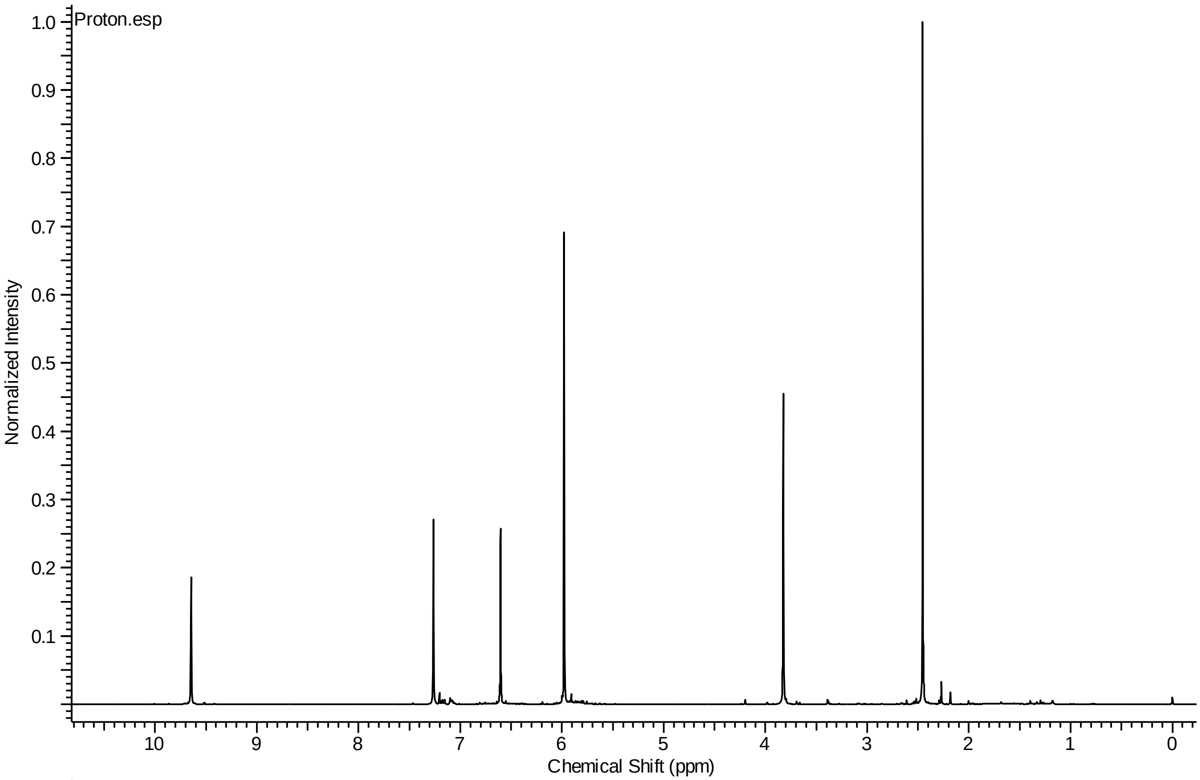
100
80
60
40
20
0
Chemical Shift (ppm)



12


Proton.esp
Normalized Intensity
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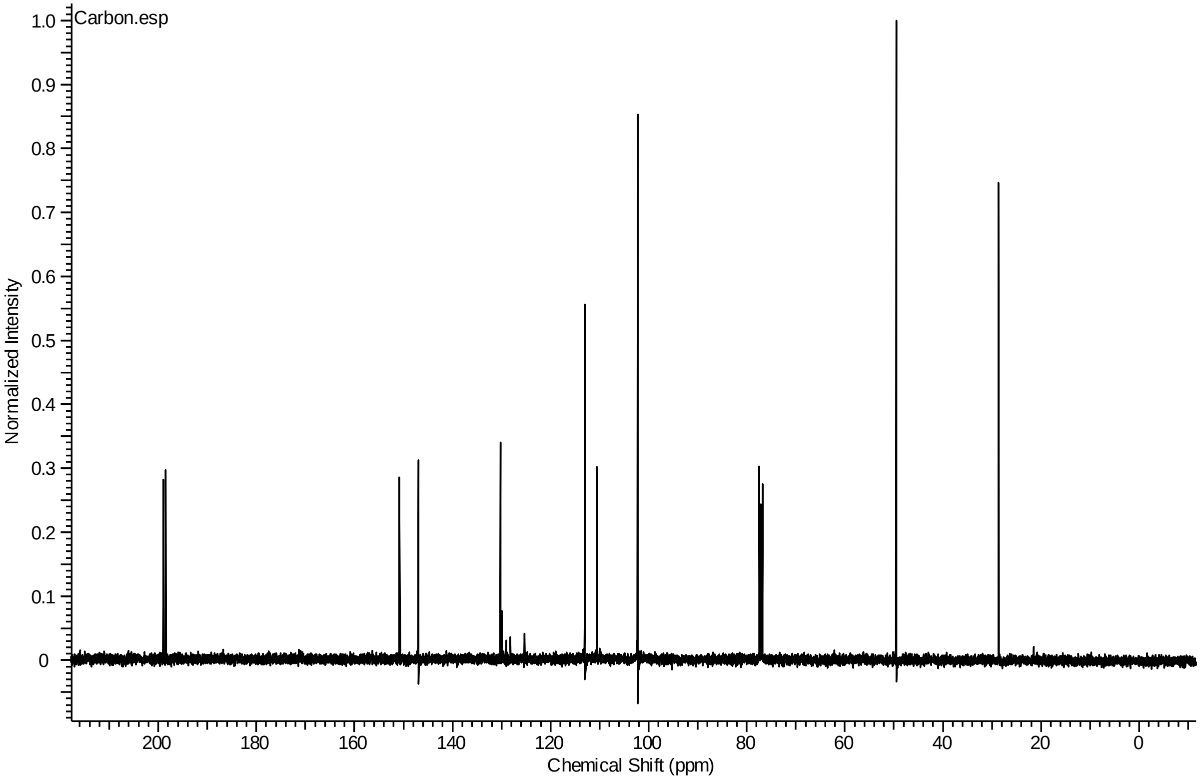
0.7
0.6
0.5
0.4
0.3
0.2
0.1
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Carbon.esp
Normalized Intensity
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0.7
0.6
0.5
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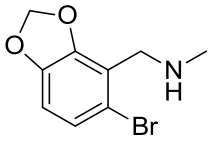
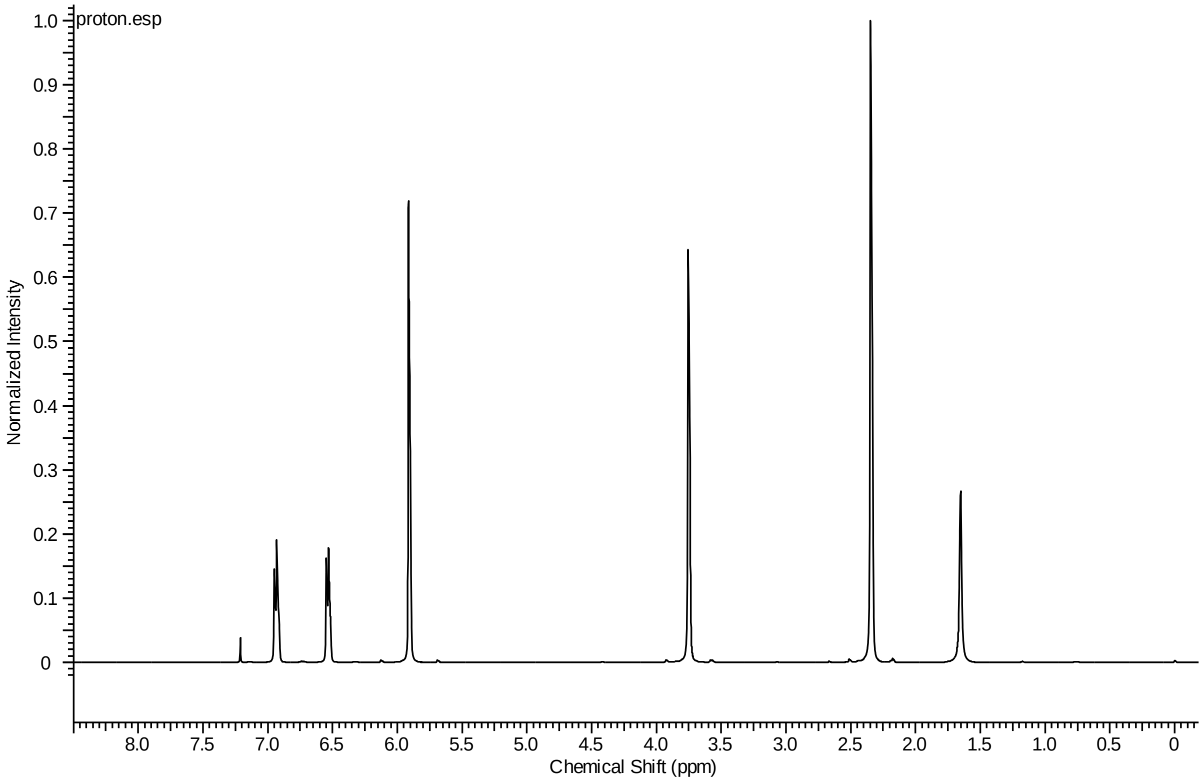
0.2
0.1
0
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)



14


proton.esp
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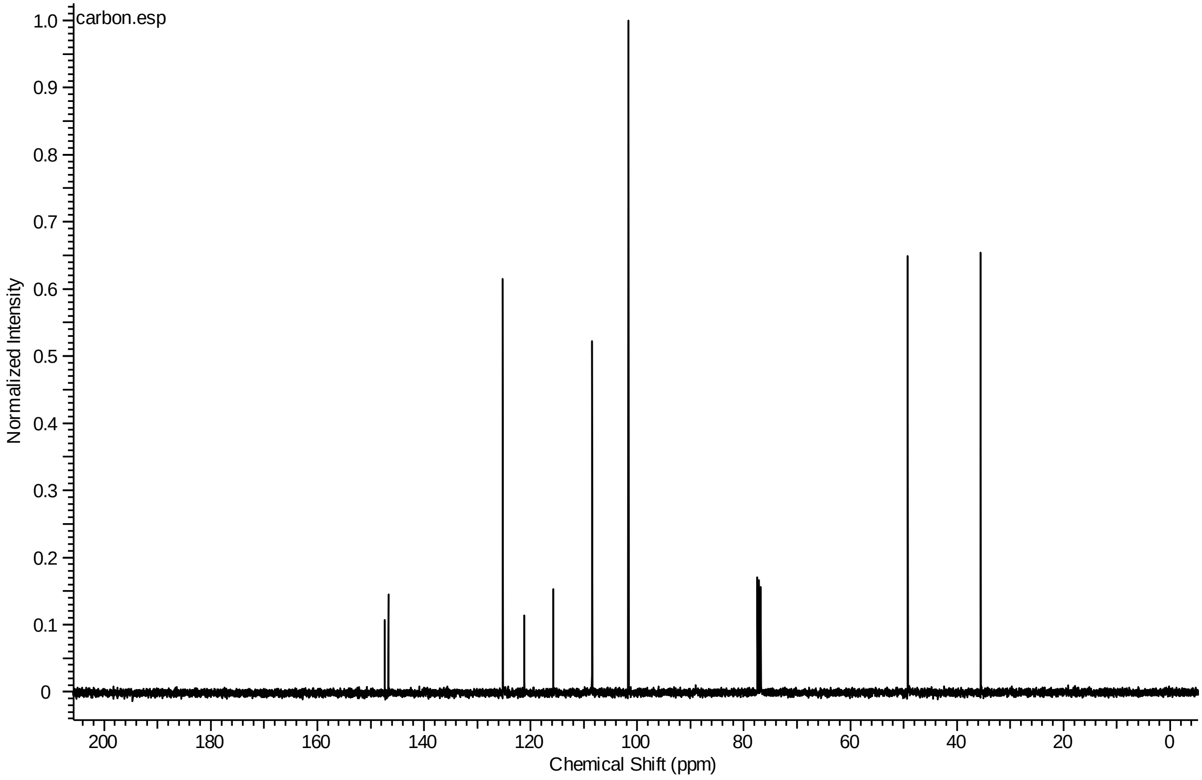
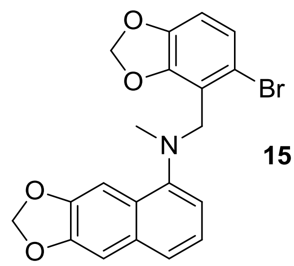
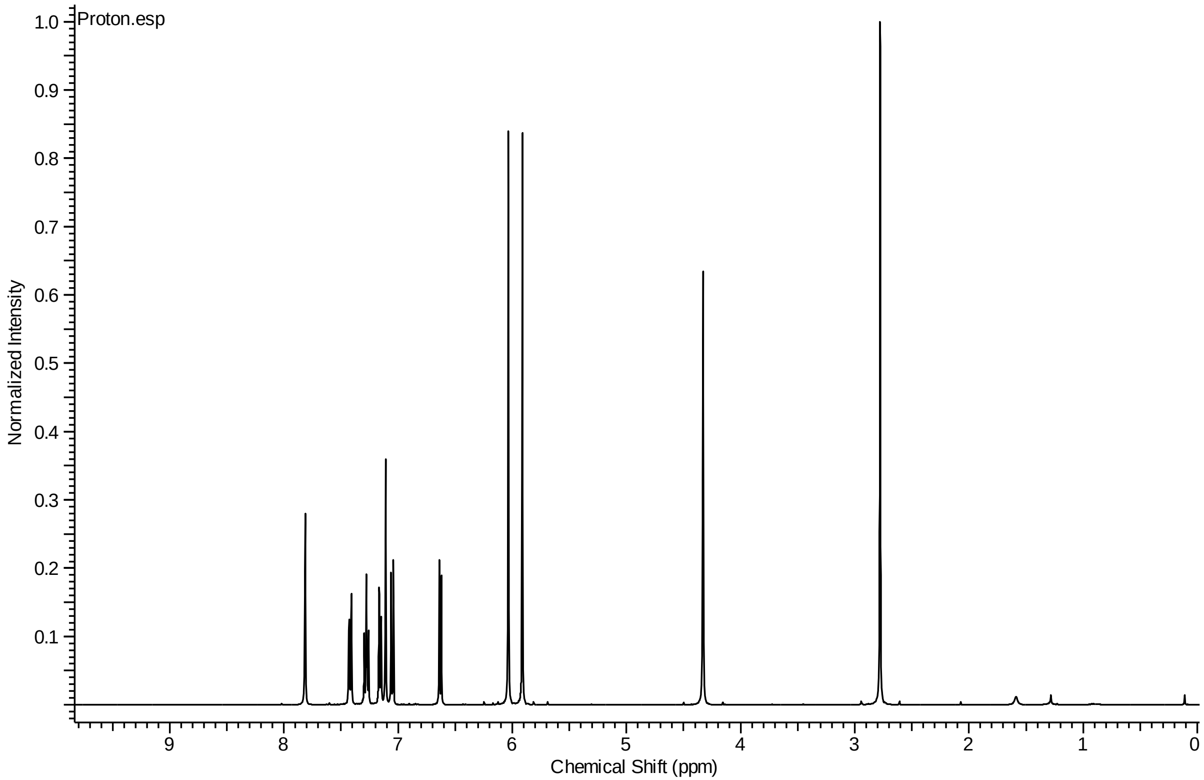
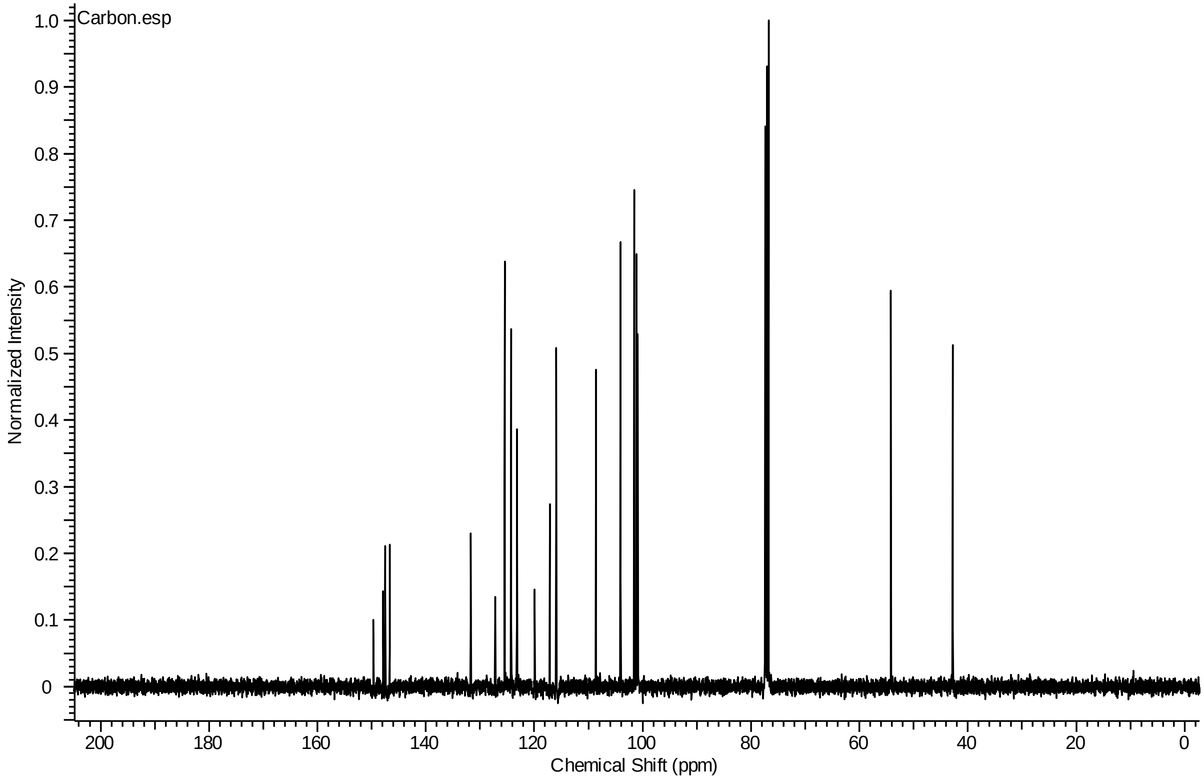
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

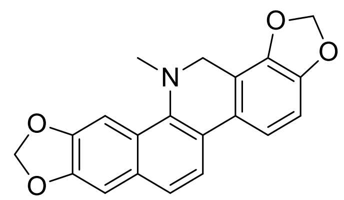

carbon.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
200 180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)


O
O
Br
N
O
O

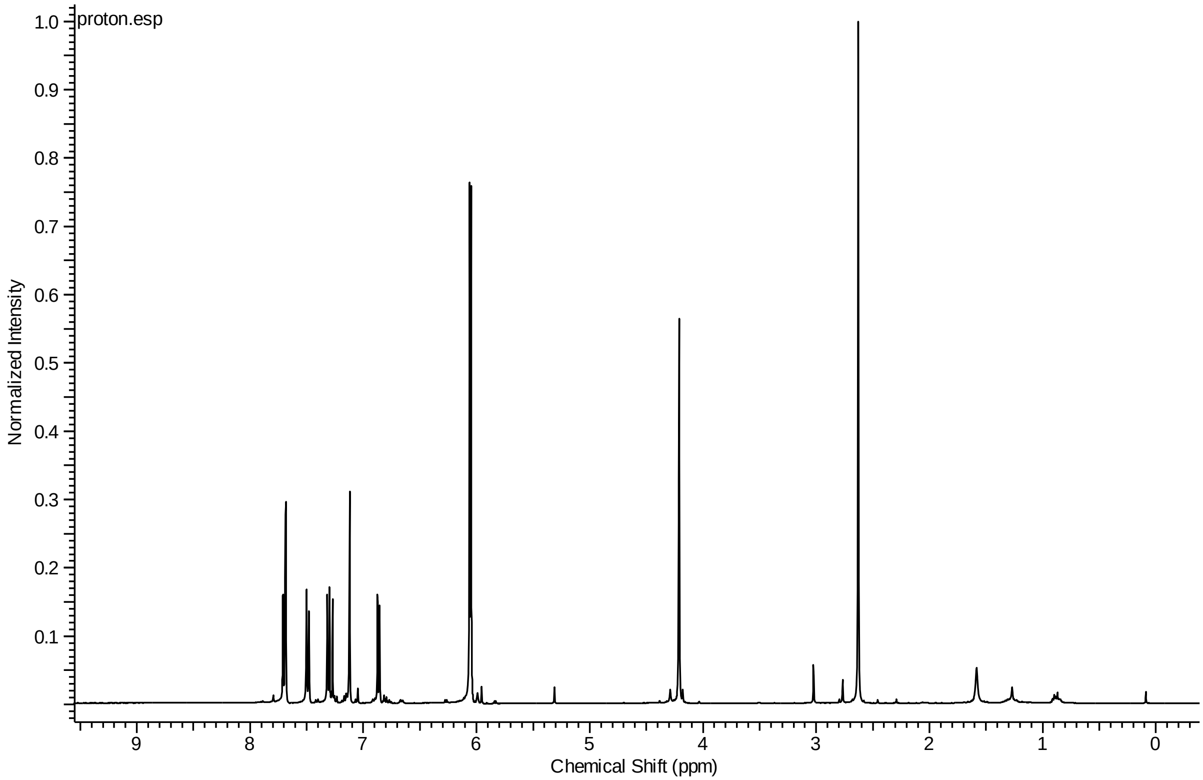
15

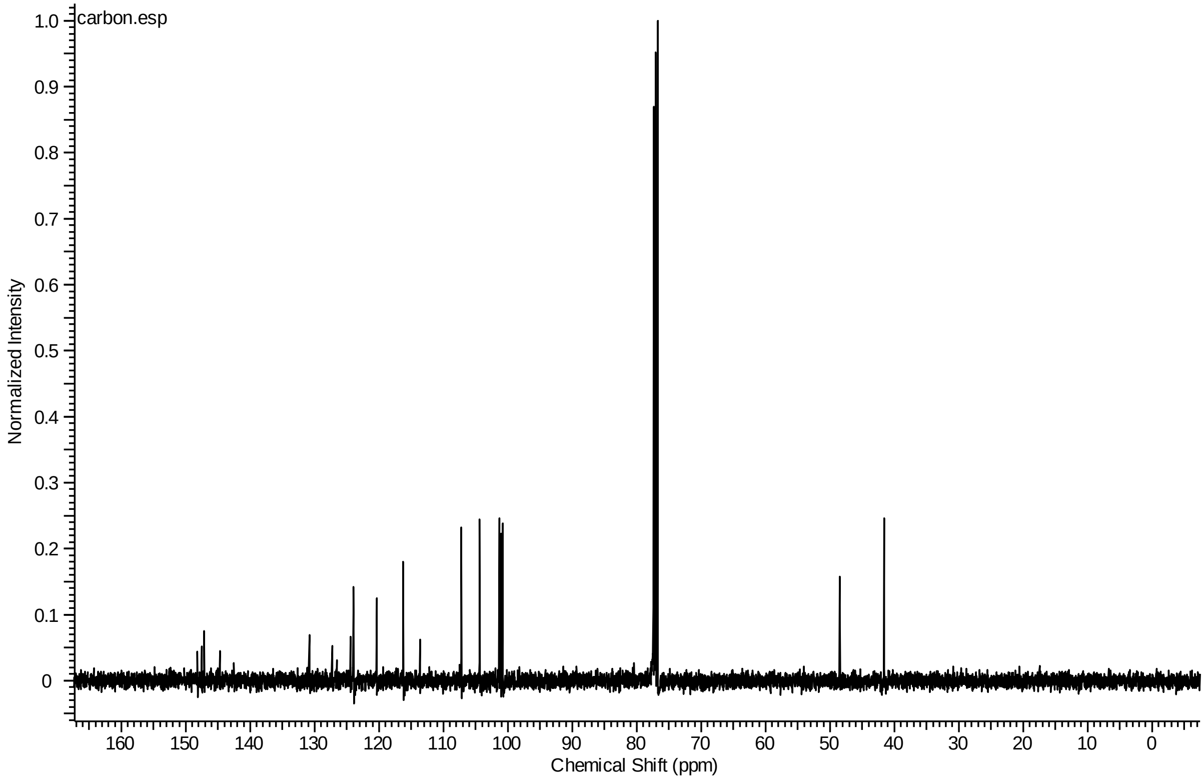

Proton.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

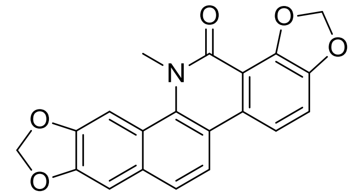

Carbon.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


N
O
O
O
O

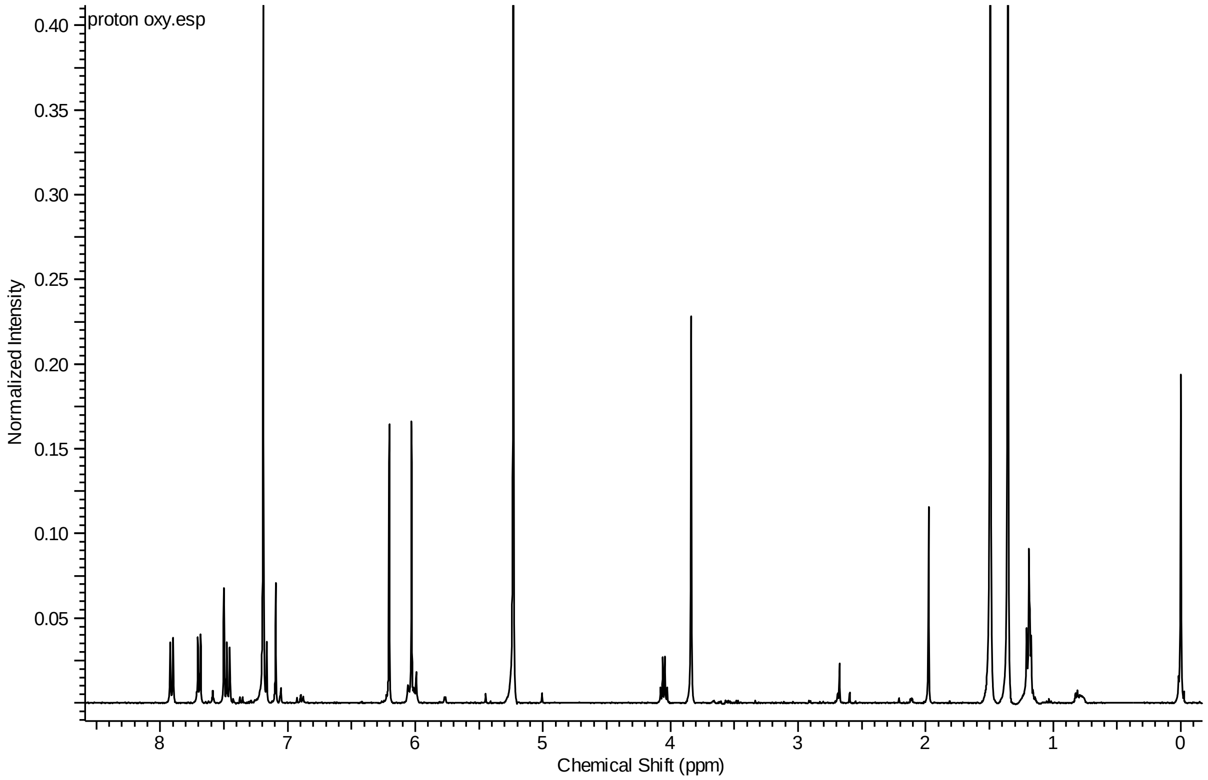
16

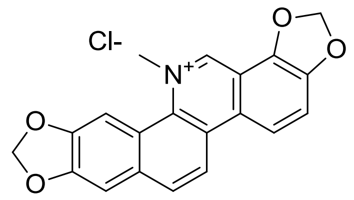

proton.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


carbon.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

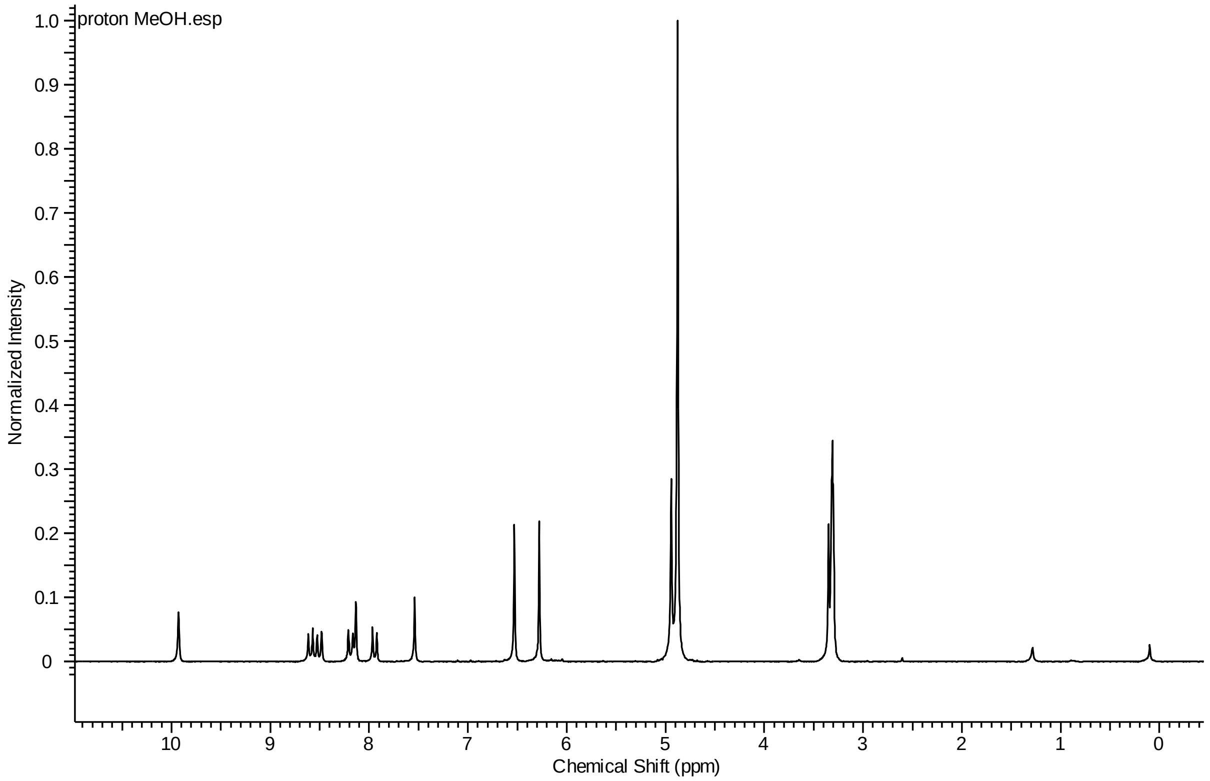

O
O
O
N
O
O

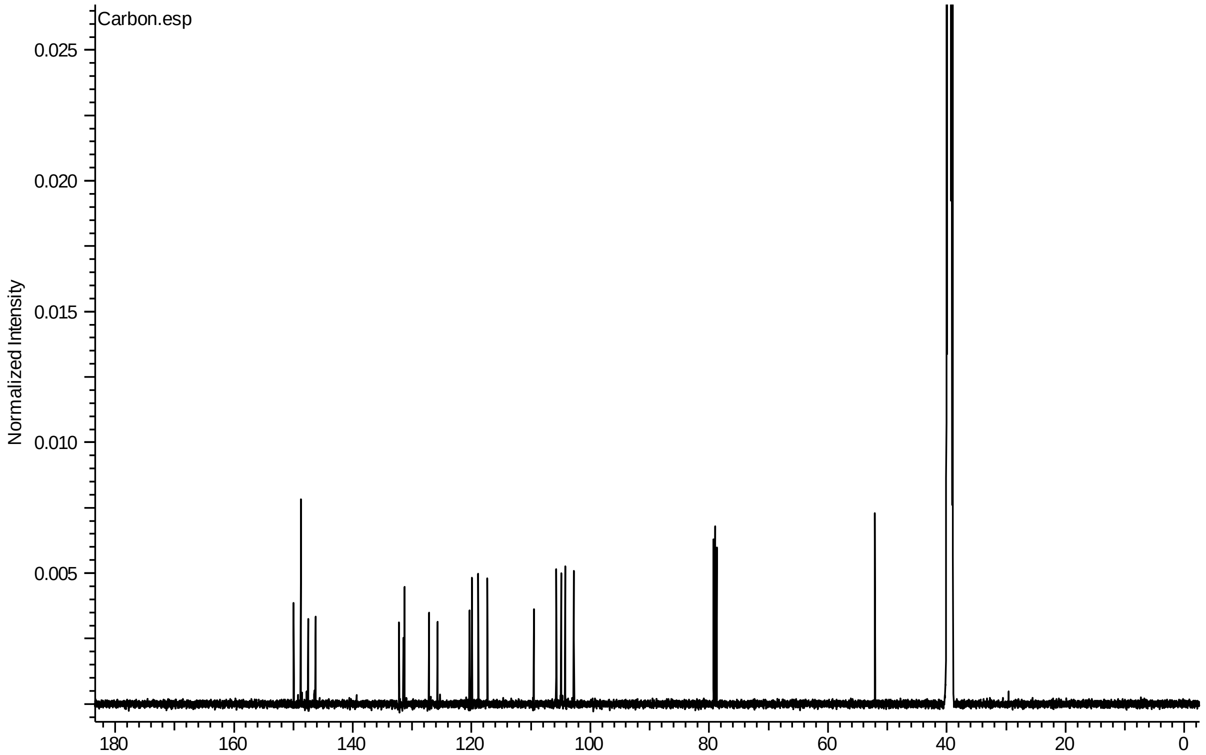
25

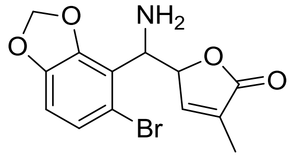

proton oxy.esp
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


Cl-
N+
O
O
O
O

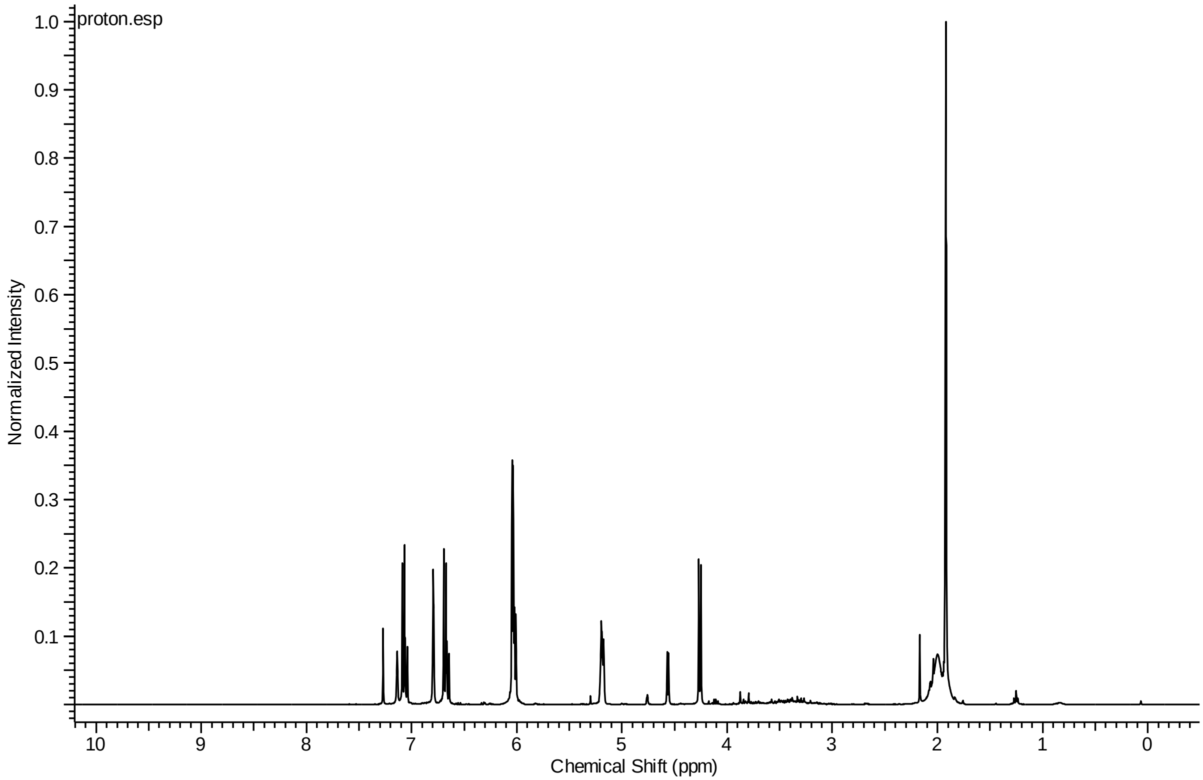
21

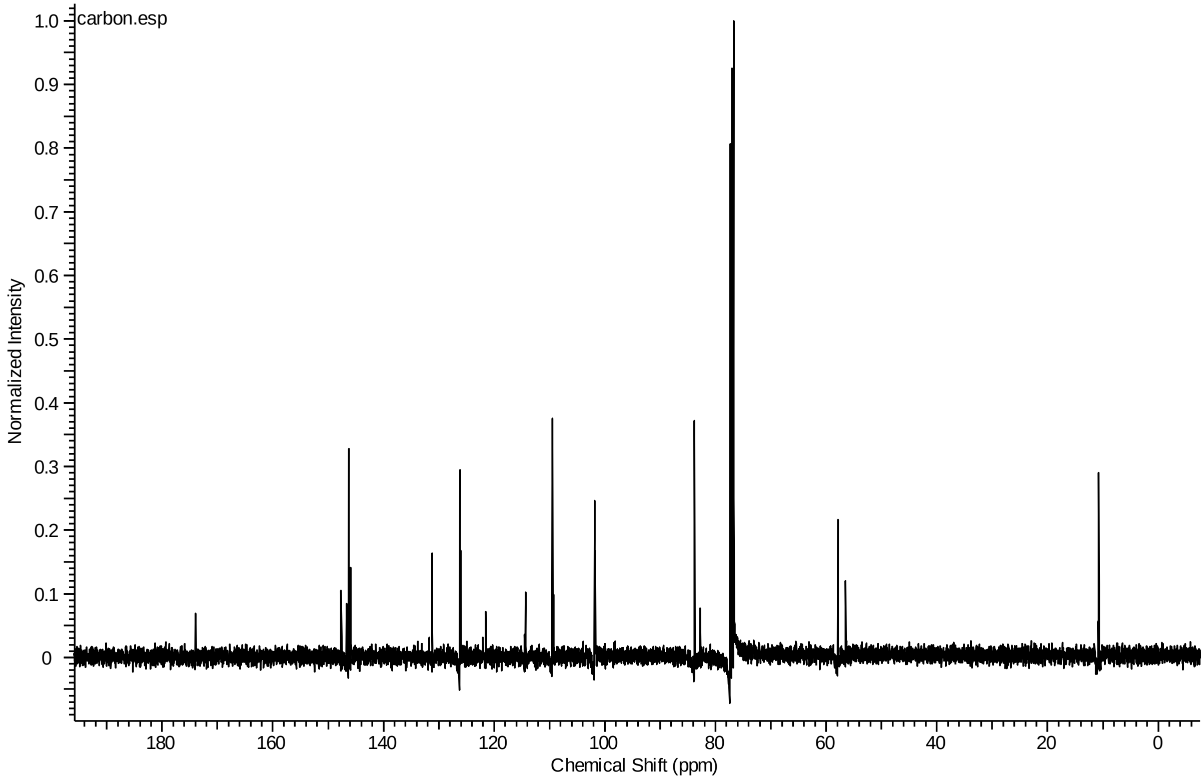

proton MeOH.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

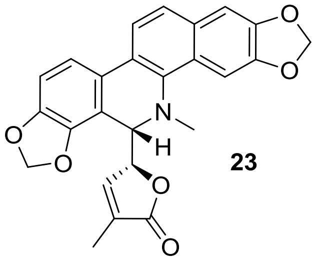

Carbon.esp
Normalized Intensity
0.025
0.020
0.015
0.010
0.005
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


O
O
NH2
O
O
Br

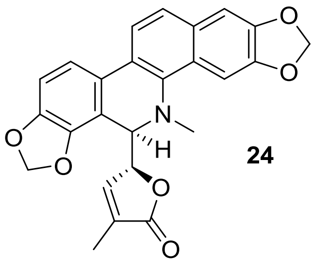
20


proton.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

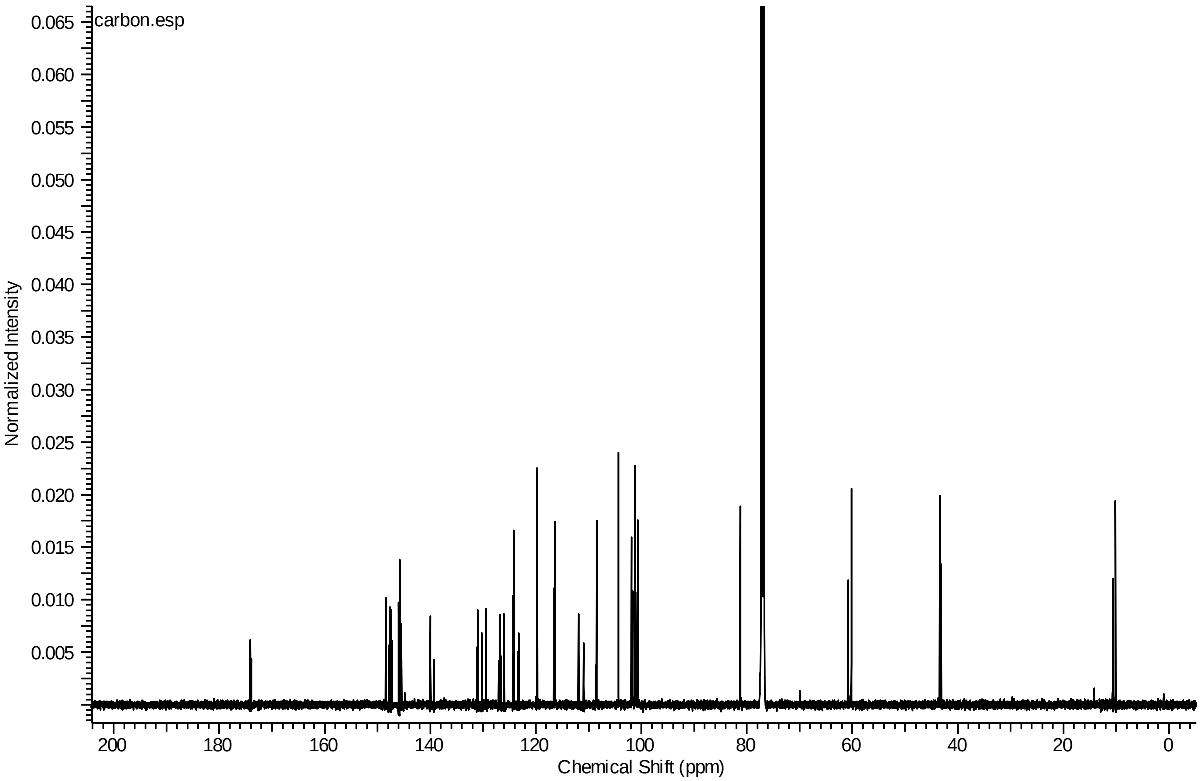

carbon.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

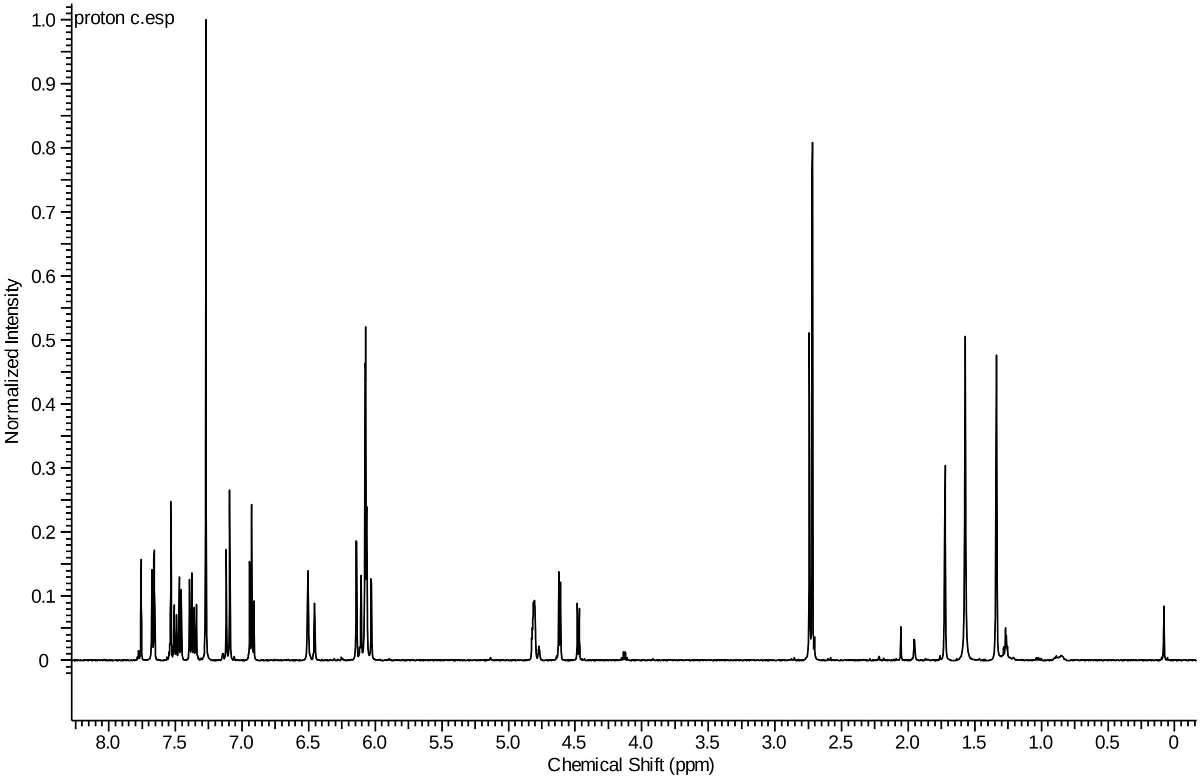


23



24


carbon.esp
Normalized Intensity
0.065
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


proton c.esp
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

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