Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Prebiotic Synthesis of 2-Deoxy-D-Ribose from Interstellar Building Blocks Promoted by Amino Esters or Amino Nitriles

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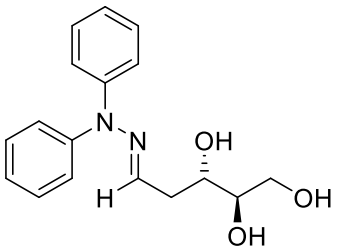
General Experimental

Unless otherwise noted all compounds were bought from commercial suppliers and used without further purification. Where a solvent is described as “dry” it was purified by PureSolv alumina columns from Innovative Technologies. Melting points were determined using a Stuart SMP3 apparatus. Optical rotations were carried out using a JASCO-DIP370 polarimeter and $[\alpha]_D$ values are given in 10^{-1}deg.cm^2.g^{-1}. Infra-red spectra were acquired on a ThermoNicolet Avatar 370 FT-IR spectrometer. Nuclear magnetic resonance spectra were recorded on a Jeol ECS-400, a Jeol 500 Avance III HD 500 or a Jeol AV500 at ambient temperature. Coupling constants (*J*) are quoted in Hertz. Mass spectrometry was performed by the University of York mass spectrometry service using electron spray ionisation (ESI) technique. Thin layer chromatography was performed on glass-backed plates coated with Merck Silica gel 60 F_{254}. The plates were developed using ultraviolet light, acidic aqueous ceric ammonium molybdate or basic aqueous potassium permanganate. Liquid chromatography was performed using forced flow (flash column) with the solvent systems indicated. The stationary

phase was silica gel 60 (220–240 mesh) supplied by Fluorochem or silica gel Merck TLC grade 11695 supplied by Sigma-Aldrich. HPLC was performed using an Agilent 1100 series instrument using a Daicel Chemical industries chiral AD column using a range of wavelengths from 210-280 nm for detection.

Synthesis of Standards

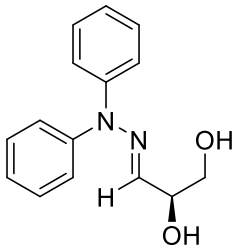
(S,R,E)-5-[N,N-diphenyl)-hydrazono]-pentane-1,2,3-triol (5)



2-Deoxy-D-ribose (50 mg, 0.37 mmol) and diphenyl hydrazine (125 mg, 0.68 mmol) were dissolved in methanol (5 mL). Two drops of acetic acid were added and the reaction stirred at room temperature for 1 hour. The reaction mixture was concentrated *in vacuo* to give a brown oil. Upon purification *via* preparative thin layer chromatography (5:95 MeOH : DCM) the pure compound, **5,** was obtained as a white crystalline solid in a 98 % yield. (100 mg 0.336 mmol); **Melting point** 114-117 ^{o}C; **IR** (ATR): 3221, 2926, 2875, 1586, 1487, 1298 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) = -5.1 (c = 0.10 g cm^{-3} in methanol); **^{1}H NMR** (500 MHz CD_3OD): δ 7.33 (4H, dd, J= 8.6 Hz, 7.4 Hz), 7.09 (2H, tt, J= 7.4 Hz, 1.2 Hz), 7.03 (4H, dd, J= 8.6, 1.2 Hz), 6.64 (1H, t, J= 5.5 Hz), 3.69 (1H, dd, J= 11.3, 3.7 Hz), 3.67 (1H, ddd, J= 10.4, 8.6, 3.7 Hz), 3.53 (1H, dd, J= 11.3, 6.5 Hz), 3.43 (1H, ddd, 10.4, 6.5, 3.8 Hz), 2.64 (1H, ddd, J= 14.9, 5.5, 3.8 Hz), 2.41 (1H, ddd, J= 14.9, 8.6, 5.5 Hz); **^{13}C NMR** (500 MHz CD_3OD): δ 145.7, 139.1, 130.7, 125.1, 123.6, 76.0, 72.0, 64.6, 37.5; **HRMS**

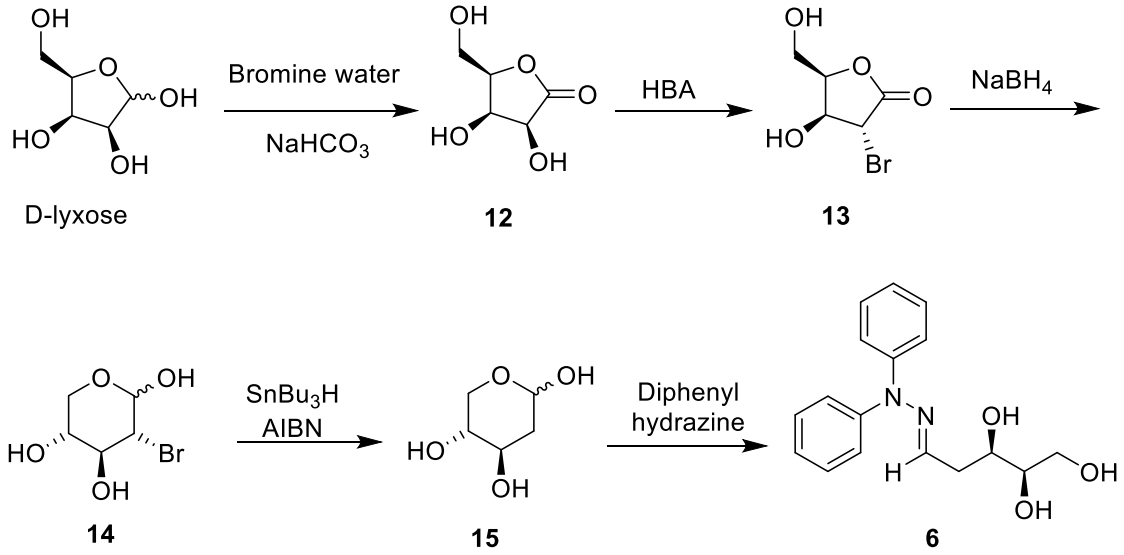
ESI (*m/z*): $[M+H]^+$ calculated for $C_{17}H_{21}N_2O_3$, 301.1547, found 301.1543. $[M+Na]^+$ calculated for $C_{17}H_{20}N_2O_3Na$, 323.1366, found 323.1360.

(1,1-Dipehnyl-hydrazono)-propane,1-2-diol (11)

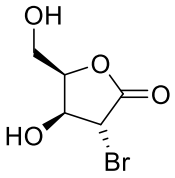


D-glyceraldehyde (51 mg, 0.56 mmol) was dissolved in methanol (8 mL). Diphenyl hydrazine (172 mg, 0.67 mmol) followed by two drops of acetic acid was added and stirred for 1 hour before concentrating *in vacuo* to give the crude product as a brown oil. Purification *via* column chromatography (10 : 90 MeOH : DCM) yielded **11** as a crystalline solid in a 95 % yield (145 mg, 0.54 mmol). **Melting point** 91-93^oC; **IR (ATR)** 3281, 2932, 1589, 1492, 1293, 1052 cm^{-1}; $\mathbf{[\alpha]_D^{25}}$ (deg cm^3 g^{-1} dm^{-1}) -0.083 (c= 1.0 g cm^{-3}, in chloroform) literature = -3.3 (c= 32.3, in chloroform)[1]; **^{1}H NMR** (500 MHz, CD_3OD): δ 7.40-7.34 (1H dd, J= 8.5, 7.4 Hz), 7.14 (2H**,** tt, J= 7.4, 1.2 Hz), 7.07-7.04 (1H dd, J= 8.5, 1.2 Hz), 6.45 (1H, d, 5.2 Hz), 4.31 (1H, ddd, 6.5, 5.2, 5.2, Hz), 3.66 (1H, dd, J= 11.3, 5.2 Hz), 3.60 (1H, dd, J= 11.3, 6.5 Hz); **^{13}C NMR** (500 MHz, CD_3OD): δ 145.1, 138.6, 130.8, 125.5, 123.5, 73.6, 65.8; **HRMS** ESI (*m/z*): $[M+H]^+$ calculated for $C_9H_{11}N_4O_6$, 257.1285, found 257.1279. $[M+Na]^+$ calculated for $C_9H_{10}N_4O_6Na$, 279.1104, found 279.1100.

Synthesis of Standard (6)



2-Bromo-2-deoxy-D-lyxono-1,4-lactone (13)

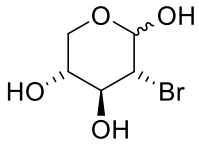


D-Lyxose (3.00 g, 22.2 mmol), and solid sodium bicarbonate (2.52 g, 30.0 mmol) were dissolved in deionised water (25 mL) and stirred at 0 ^{o}C for 5 minutes. Bromine was added dropwise to the solution every 20 minutes for 1 hour (3 x 0.38 mL) and the reaction left to stir at room temperature for 4 hours. Excess sodium thiosulfate was added to destroy the excess bromine and concentrated *in vacuo* to give an off-white precipitate. The crude material was purified by extracting with boiling methanol (3 x 50 mL). The extracts were combined and concentrated *in vacuo* to give the product as an off white solid (4.73 g). This was used in the next step without further purification.

Crude D-Lyxno-1,4-lactone **12** (1.00 g, 6.75 mmol), was added to a solution of 33 % hydrogen bromide in acetic acid (10 mL) and stirred for 2 hours at room temperature at which point TLC confirmed that all of the starting material had

been consumed. The reaction was quenched via the addition of methanol and the reaction mixture stirred for a further 24 hours. The mixture was concentrated *in vacuo*, dissolved in chloroform (10 mL) and extracted with water (7x 10 mL). The aqueous extracts were combined and concentrated *in vacuo* to give the crude product as a red oil. Purification *via* flash column chromatography over silica (50:50 cyclohexane : ethyl acetate) gave the title compound **13** as a yellow oil in a 14 % yield over 2 steps (0.20 g, 0.92 mmol): **IR** (ATR): 3315, 2991, 2967, 2949, 1763, 1464, 1372, 1329, 1182, 1145, 1023 cm^{-1}; $\mathbf{[\alpha]_D^{25}}$ (deg cm^3 g^{-1} dm^{-1}) +20.1 (0.2 g cm^{-3} in ethyl acetate) literature +26 (c= 0.025 g cm^{-3}, ethyl acetate)[2]; **^{1}H NMR** (400 MHz D_2O): δ 4.91(1H, m), 4.77 (1H, dd, J= 5.2, 4.4 Hz), 4.68 (1H, d, J= 4.4 Hz), 3.95 (2H, dd, J=5.2, 0.9 Hz); **^{13}C NMR** (400 MHz D_2O): δ 174.8, 83.3, 74.3, 59.1, 42.7; ESI (*m/z*) $[M+Na]^+$ calculated at 232.9422 for $C_5H_7Br^{79}O_4Na$ and 234.9397 for $C_5H_7Br^{81}O_4Na$ HRMS found 232.9420. An artefact of ESI MS through methanolic opening of lactone calculated for $C_6H_{11}Br^{79}NaO_5$, 264.9682, HRMS found 264.9686.

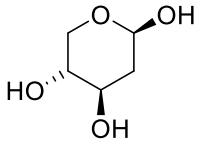
2-Bromo-2-deoxy-D-threo-pentofuranose (14)



D-lyxono-1,4-lactone **13** (435 mg, 2.06 mmol) was dissolved in water (7 mL) and stirred at 0 ^oC and amberlite IR-120-H resin was added to reduce the pH to pH 3. Sodium borohydride (39 mg, 1.03 mmol) was added in portions along with amberlite resin to keep the pH of the reaction to approximately 6. The reaction was then allowed to stir for 30 minutes at which time there was

no starting material visible by TLC. The reaction mixture was filtered to remove the resin and then concentrated *in vacuo* to give a mixture of crude product and over reduced material (367 mg). Purification *via* flash column chromatography over silica (40:60 petroleum ether : ethyl acetate) gave the pure title compound **14** as a colourless oil in a 45 % yield as a mixture of anomers (199 mg, 0.93 mmol); All data correlated with the literature.[2] **IR** (ATR): 3307, 2943, 2836, 1417, 1353, 1110, 1060, 1016 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) +64.4 (c= 1.0 g cm^{-3}, methanol) literature +51.5 (0.4 g cm^{-3} in water)[2]; **^{13}C NMR** (400 MHz D_2O): α-anomer: δ 174.8, 83.3, 74.3, 59.1, 42.8; β-anomer: 177.7, 80.4, 70.7, 69.6, 48.9, 26.5; ESI (*m/z*) $[M+Na]^+$ calculated at 232.9420 for $C_5H_9Br^{79}O_4Na$ and 234.9400 for $C_5H_9Br^{81}O_4Na$, HRMS found 232.9475.

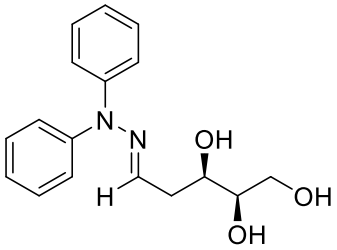
2-Deoxy-D-threo-pentofuranose (15)



To a flask containing 2-bromo-2-deoxy-D-threo-pentofuranose **14** (75 mg, 0.35 mmol) in dry THF (5 mL), tin tributyl hydride (0.11 mL, 0.43 mmol) and AIBN (9.3 mg, 0.057 mmol) were added and refluxed for 4 hours. At this point the reaction was deemed finished through TLC and the reaction mixture concentrated *in vacuo.* The crude mixture was partitioned between water (10 mL) and ethyl acetate (10 mL), extracted with water (3x 10 mL) and concentrated *in vacuo* to give the title compound **15** as a colourless oil in an 86 % yield as a mixture of anomers (47 mg, 0.30 mmol). **IR** (ATR): 3327, 2933, 2886, 1648, 1436, 1359, 1263, 1239, 1129, 1060 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3

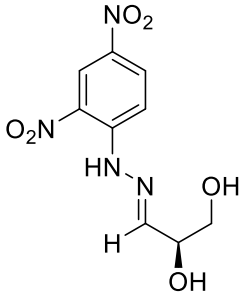
g^{-1} dm^{-1}) -10 (c= 0.5 g cm^{-3}, water) literature -1.9 (0.5 g cm^{-3})[3] ; **^{1}H NMR** as a mixture of furanose and pyanose forms and a mix of α and β anomers; **^{13}C NMR** (400 MHz CD_3OD): δ 95.7, 93.1, 72.2, 27.1, 69.7, 66.7, 63.9, 40.7, 38.7; **HRMS** ESI (*m/z*): $[M + Na]^+$ $C_5H_{10}O_5$ calculated for, 157.0471, found 157.0470.

(R,R,E)-5-[(N,N-diphenyl)-hydrazono]-pentane-1,2,3-triol (6)



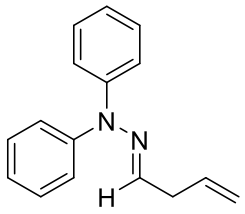
2-Deoxy-D-threopentose **15** (29 mg, 0.21 mmol) and diphenyl hydrazine (77 mg, 0.42 mmol) were dissolved in methanol (5 mL). Two drops of acetic acid were added and the reaction stirred at room temperature for 1 hour. The reaction mixture was concentrated *in vacuo* to give a brown oil. Upon purification *via* preparative thin layer chromatography (15:95 MeOH : DCM) the pure compound, **6**, was obtained as a white crystalline solid in a 84 % yield. (53 mg, 0.18 mmol); **IR** (ATR): 3351, 3059 , 2898, 1588, 1493, 1297 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) +8.0 (c = 0.10 g cm^{-3}, methanol); **^{1}H NMR** (500 MHz CD_3OD); δ 7.36 (4H, dd, 8.4, 7.4 Hz), 7.12 (2H, dt, 7.4, 1.1 Hz), 7.06 (4H, dd, 8.4, 1.1 Hz), 6.65 (1H, t, 5.5 Hz), 3.81 (1H, ddd J= 8.6, 5.4, 3.5 Hz), 3.66 (1H, dd, J= 11.1, 5.1 Hz), 3.58 (1H, dd, J= 11.1, 6.4 Hz), 3.52 (1H, ddd, J= 6.4, 5.1, 3.5 Hz), 2.58-2.48 (2H, m); **^{13}C NMR** (500 MHz CD_3OD): δ 145.6, 138.7, 130.7, 125.1, 75.1, 71.2, 64.3, 37.6; **HRMS** ESI (*m/z*): $[M+Na]^+$ calculated for $C_{17}H_{20}N_2O_3Na$, 323.1362, found 323.323.1366.

Trans-3-[(2. 4-Dinitrophenyl)-hydrazono]-2-propane-1,2-diol (16)



D-Glyceraldehyde (50 mg, 0.56 mmol) and 2,4-dinitrophenylhydrazine (132 mg, 0.67 mmol) were dissolved in water (2.5 mL) and stirred at room temperature for 24 hours. The reaction mixture was concentrated *in vacuo* to give the crude product as an orange solid. Purification *via* flash column chromotography (1:1 petroleum ether : ethyl acetate) gave the desired product, **16**, as an orange solid in a 45 % yield (67 mg, 0.25 mmol); **IR** (ATR): 3301, 3106, 3094, 2929, 1614, 1586, 1504, 1419, 1320, 1222, 1090, cm^{-1}; $\mathbf{[\alpha]_D^{25}}$ (deg cm^3 g^{-1} dm^{-1}) +32.0 (c= 0.10 in chloroform) literature +36.9 (c= 0.07, $CHCl_3$)[4]; **^{1}H NMR** (400 MHz DMSO-d^6); δ 11.40 (1H, br s), 8.84 (1H, d, 2.7 Hz), 8.36 (1H, dd, 9.6 Hz, 2.7 Hz), 7.95 (1H, d, 5.8 Hz), 7.91 (1H, d, 9.6 Hz), 4.17 (1H, q, 5.8 Hz), 3.54 (2H, d, 5.8 Hz), 3.35 (2H, br s); **^{13}C NMR** (400 MHz DMSO-d^6) δ 154.7, 144.9, 136.8, 129.8, 129.2, 123.0, 116.6, 71.7, 64.0; **HRMS** ESI (*m/z*): $[M-H]^-$ calculated for $C_9H_9N_4O_6$, 269.0528, found 269.0535.

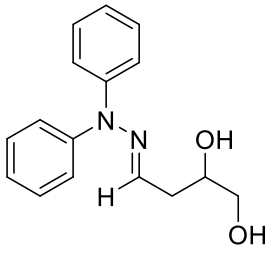
N'-But-3-enylidene-N,N-diphenylhydrazine (18)



3-Butenaldehyde (71 mg, 1.01 mmol) and *N*-*N*-diphenyl hydrazine (223 mg, 1.21 mmol) in 1 mL of DCM were stirred at room temperature for 17 hours

before concentrating *in vacuo* to give a brown solid. Purification via flash column chromatography (95:5 petroleum ether : ethyl acetate) gave the pure title compound, **18**, as a yellow oil in a 36 % yield (84 mg, 0.35 mmol). **IR (ATR):** 3061, 1589, 1494, 1298, 1208 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40-7.35 (4H, m), 7.15-7.09 (6H, m), 6.49 (1H, t, J = 5.4), 5.93-5.83 (1H, m), 5.08-5.07 (1H, m), 5.05-5.03 (1H, m), 3.07-3.04 (2H, m); **^{13}C NMR** (400 MHz, $CDCl_3$): δ 143.9, 136.9, 134.2, 129.5, 123.8, 122.2, 116.4, 36.9; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_{16}H_{17}N_2$, 237.1386, found 237.1379. $[M+Na]^+$ calculated for $C_{16}H_{16}N_2Na$, 259.1206, found 259.1196.

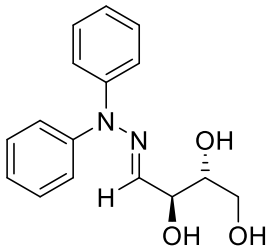
4-[(N,N-diphenyl)-hydrazono]-butane-1,2,-triol (14)



To a flask containing hydrazone **18** (20 mg, 0.085 mmol), 4-methyl morpholine-N-oxide (20 mg, 0.17 mmol) and *t*-butyl alcohol (0.25 mL) was added a solution of osmium tetroxide (0.43 mg, 0.0017 mmol) in THF (1.75 mL). The reaction was stirred for 23 hours before saturated sodium thiosulfate (2 mL) was added to quench the reaction. After 40 minutes the product was extracted with ethyl acetate (3 x 3 mL) and the combined organic extracts washed with water (1 x 5 mL) then brine (1 x 5 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Purification *via* silica filtration gave the title compound **14** as a colourless oil in an 87 % yield (20 mg, 0.074 mmol). **IR (ATR):** 3359, 2923, 1589, 1494, 1298, 1210 cm^{-1}; **^{1}H**

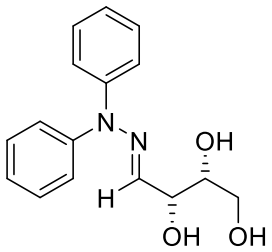
NMR (400 MHz, MeOD) δ 7.33 (4H, dd, J = 8.4, 7.6), 7.11-7.07 (2H, m), 7.02 (4H, dd, J = 8.4, 1.0), 6.59 (1H, t, J = 5.5), 3.78-3.72 (1H, m), 3.48 (1H, dd, J = 11.2, 4.7), 3.42 (1H, dd, J = 11.2, 6.2), 2.47 (1H, apparent dt, J = 14.8, 5.5), 2.36 (1H, ddd, J = 14.8, 7.7, 5.5); **^{13}C NMR** (400 MHz, MeOD): δ 145.6, 138.2, 130.7, 125.2, 123.5, 71.8, 66.9, 37.7; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_{16}H_{19}N_2O_2$, 271.1441, found 271.1431. $[M+Na]^+$ calculated for $C_{16}H_{18}N_2NaO_2$, 293.1260, found 293.1247.

(R,S,E)-4-[(N,N-diphenyl)-hydrazono]-butane-1,2,3-triol (15)



D-erythrose (20 mg, 0.16 mmol) and *N*,*N*-diphenyl hydrazine (35 mg, 0.19 mmol) were dissolved in methanol (3 mL) and stirred for 45 minutes at room temperature before concentration *in vacuo*. Purification *via* column chromatography (95:5 DCM : methanol) gave the title compound **15** as a brown oil in a 57 % yield (26 mg, 0.091 mmol). **IR (ATR):** 3352, 3061, 2925, 1590, 1494, 1297, 1212, 1040 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) -10.9 (c= 0.85 g cm^{-3}, CH_3Cl); **^{1}H NMR** (400 MHz, MeOD) δ 7.37-7.34 (4H, m), 7.12 (2H, t, J = 7.4), 7.06 (4H, m), 6.54 (1H, d, J = 6.0), 4.24 (1H, dd, J = 6.0, 5.9), 3.67-3.60 (2H, m), 3.55-3.50 (1H, m); **^{13}C NMR** (400 MHz, MeOD): δ 145.2, 139.2, 130.7, 125.4, 123.5, 75.5, 73.7, 64.3; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_{16}H_{19}N_2O_3$, 287.1390, found 287.1396. $[M+Na]^+$ calculated for $C_{16}H_{18}N_2NaO_3$, 309.1210, found 309.1212.

(S,S,E)-4-[(N,N-diphenyl)-hydrazono]-butane-1,2,3-triol (15)

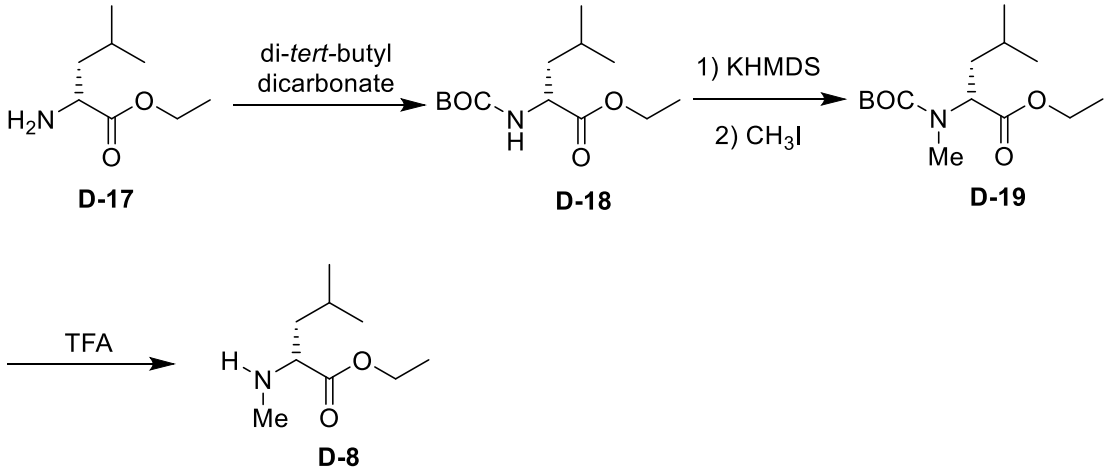


L-threose (20 mg, 0.16 mmol) and *N*,*N*-diphenyl hydrazine (35 mg, 0.19 mmol) were dissolved in methanol (3 mL) and stirred at room temperature for 1 hour before concentration *in vacuo*. Purification *via* column chromatography (95:5 DCM : methanol) gave the title compound **15** as a brown oil in a 79 % yield (36 mg, 0.13 mmol). **IR ATR** 3353, 3060, 2927, 1590, 1494, 1296, 1212, 1037 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) -5.2 (c= 1.1 g cm^{-3}, CH_3Cl); **^{1}H NMR** (400 MHz, MeOD) δ 7.35 (4H, dd, J = 8.4, 7.5), 7.18 (2H, t, J = 7.5), 7.05 (4H, dd, J = 8.4, 1.0), 6.51 (1H, d, J = 5.7), 4.27 (1H, dd, J = 5.7, 4.4 ppm), 3.65-3.60 (2H, m), 3.50 (1H, dd, J = 12.5, 8.0); **^{13}C NMR** (400 MHz, MeOD): δ 145.1, 139.0, 130.8, 125.5, 123.5, 75.2, 73.4, 64.0; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_{16}H_{19}N_2O_3$, 287.1390, found 287.1395. $[M+Na]^+$ calculated for $C_{16}H_{18}N_2NaO_3$, 309.1210, found 309.1210.

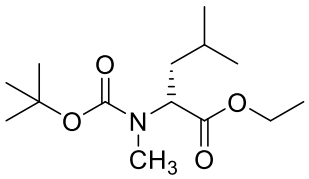
Synthesis of Catalysts

Synthesis of catalysts (D-8)

L and D *N*-methyl leucine ethyl esters were synthesised according to Burroughs *et al.*[5]



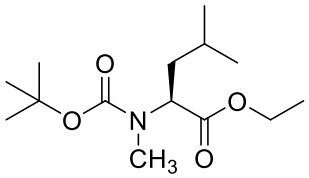
Boc-N-Methyl-D-leucine ethyl ester (D-18)



Potassium bis(trimethylsilyl)amide 0.5 M in toluene (20 mL, 9.76 mmol) was added to a stirred solution of *N*-BOC-D-Leucine ethyl ester **D-17** (2.3 g, 3.09 mmol) in dry THF (20 mL) at -78 ^{o}C. After 30 minutes methyl iodide (0.61 mL, 9.76 mmol) was added dropwise and the reaction stirred for 1 hour at -78 ^{o}C and a further 16 hours at room temperature. The solution was washed with saturated potassium carbonate solution (30 mL) followed by 1 M sodium hydroxide (30 mL) and brine (30 mL) extracting each time with dichloromethane (3x 30 mL). The combined organic extracts were dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the crude product as a yellow oil. Purification *via* column chromatography (10:90 ethyl

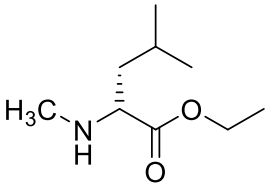
acetate : hexane) gave the title produce, **D-18**, as a colourless oil in an 83 % yield (700 mg, 2.56 mmol); **IR** (ATR): 2962, 1741, 1694, 1390, 1363, 1320, 1148, 1031 cm^{-1}; **$[\alpha]_D^{25}$,** (deg cm^3 g^{-1} dm^{-1}) +8.9 (c= 1.0 g cm^{-3}, ethanol); **^{1}H NMR** (400 MHz $CDCl_3$): Apparent rotamers δ 4.84 (1H, t, *J* = 8.0 Hz), 4.55 (1H, dd, J= 10.8, 4.7 Hz), 4.16 (4H, q, 7.1 Hz), 2.79 (3H, s), 2.76 (3H, s), 1.74-1.51 (6H, m) 1.45 (9H, s), 1.44 (9H, s), 1.27-1.23 (6H, m), 0.94 (6H, d, 6.8 Hz), 0.92 (6H, d, 6.8 Hz); **^{13}C NMR** (400 MHz $CDCl_3$): δ 172.4, 156.4, 80.3, 80.0, 61.1, 57.3, 56.1, 38.0, 28.5, 24.8, 23.4, 21.5, 21.3, 14.4; **HRMS** ESI (*m/z*): $[M+H]^+$ calculated for $C_{14}H_{28}NO_4$, 247.2013, found 274.2000. $[M+Na]^+$ calculated for $C_{14}H_{27}NO_4Na$, 296.1832, found 296.1822.

Boc-N-methyl-L-leucine ethyl ester (L-18)



Boc-*N*-methyl-L-leucine ethyl ester (**L-18**) was prepared in the same way as **D-18** from **L-17**. Spectroscopic data was in agreement with **D-18** and the literature.[5]

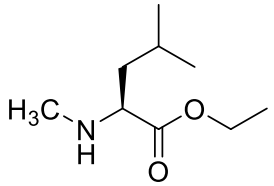
N-Methyl-D-leucine ethylester (D-8)



Trifluoroacetic acid (1.12 mL, 14.6 mmol) was added to a solution of BOC-*N*-Methyl-D-leucine ethyl ester **D-18** (200 mg, 0.73 mmol) in dichloromethane

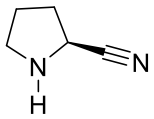
(20 mL) and stirred at 14 hours under a nitrogen atmosphere. The solution was then concentrated *in vacuo* and partitioned between dichloromethane (4 mL) and saturated sodium bicarbonate (4 mL) and extracted 2 more times with dichloromethane. The organic layers were combined, dried over magnesium sulphate and concentrated *in vaco* to give **D-8** as a colourless oil in a 90 % yield (115 mg, 0.55 mmol). **IR (ATR):** 2956 , 1731, 1469, 1368, 1178, 1026 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) -1.3 (c= 1.0 g cm^{-3}, CH_3Cl); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.29 (2H, q, 7.1 Hz), 3.81 (1H br dd, 7.6, 3.4 Hz), 2.77 (s, 3H), 1.86-1.79 (1H, m), 1.77-1.72 (2H, m), 1.31 (3H, t, 7.1 Hz), 0.96 (6H, d, 5.6 Hz,); **^{13}C NMR** (400 MHz, $CDCl_3$): δ 176.2, 62.1, 60.9, 43.1, 35.1, 25.4, 23.1, 22.9, 14.8; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_9H_{20}NO_2$, 174.1489, found 174.1491.

N-Methyl-L-leucine ethylester (L-19)



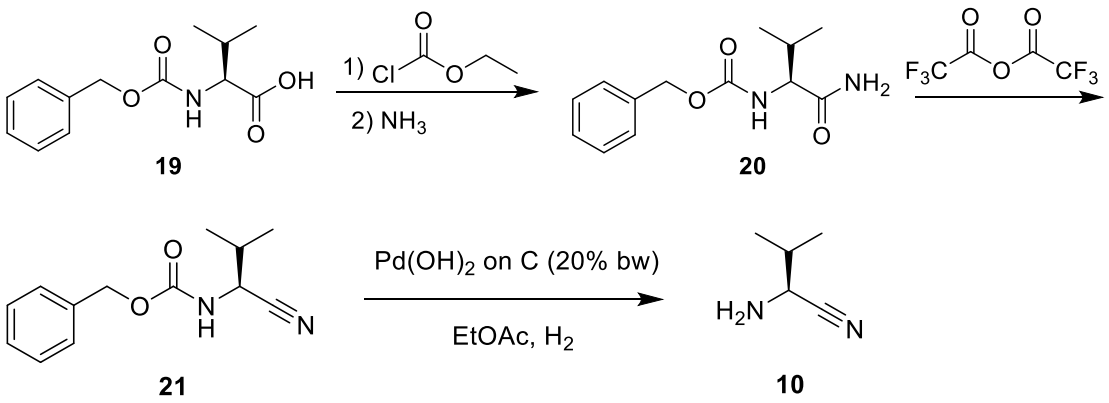
N-Methyl-L-leucine ethyl ester (12-L) was prepared in the same was as **L-8** from **L-18**. Spectroscopic data was in agreement with **D-18** and the literature.[5]

L-Pyrrolidine-2-carbonitrile (9)

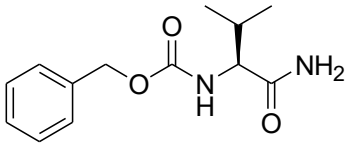


Compound **9** was synthesised according to the literature with all data in agreement.[6] **Melting point** 92-94 °C; **IR (ATR):** 2992, 2789, 2393, 1674 cm^{-1}, **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) -16.7 (c= 1.0 in methanol); **^{1}H NMR** (400 MHz, CD_3OD): δ 4.66 (1H, t, 7.4Hz), 3.34-3.50 (2H, m), 2.44-2.54 (1H, m), 2.05-2.36 (3H, m); **^{13}C NMR** (400 MHz, $CDCl_3$): δ 116.5, 116.5 , 47.9, 47.0, 31.2, 24.5; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_5H_9N_2$, 97.07602, found 97. 0757.

Synthesis of Catalyst (10)

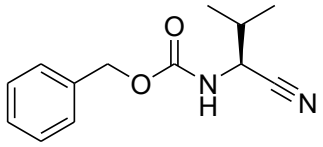


Z-L-Valine amide (20)



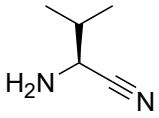
To a stirred solution of *Z*-L-valine **19** (2.0 g, 7.96 mmol) and triethylamine (1.2 mL, 1.1 eq) in dry THF (40 mL) at 0^{o}C was added ethyl chloroformate (0.76 mL, 1eq). After 30 minutes 7N ammonia in methanol (1.66 mL, 1.5 eq) was added and stirred at 0 ^{o}C for 1 hour and a further 19 hours at room temperature. The resulting white precipitate was filtered and washed with ice cold water to give the title compound **20** as a white solid in a 75 % yield (1.5 g, 6.0 mmol). **Melting point** 205-208^{o}C; **IR (ATR):** 3380, 3316, 3063, 3027, 2957, 2873, 1683, 1645, 1536, 1455, 1305, 1246, 1040 cm^{-1}; **[α]$_{D}^{25}$** (deg cm^{3} g^{-1} dm^{-1}) +25.0 (c=1.0 g cm^{-3} in dimethyl formamide) literature +24.2 (c=1.0 g cm^{-3} in dimethyl formamide)[7]; **^{1}H NMR** (400 MHz DMSO d^{6}) δ 7.37-7.30 (5H, m), 7.16 (1H, d, J= 9.0 Hz), 7.04 (1H, s), 5.03 (2H, s), 3.80 (1H, dd, J= 9.0, 6.8 Hz), 1.95 (1H, apparent oct, J= 6.8 Hz), 0.86 (3H, d, J= 6.8 Hz), 0.83 (3H, d, J= 6.8 Hz); **^{13}C NMR** (DMSO d^{6} 400 MHz) δ 173.3, 156.2, 131.2, 128.4, 127.0, 65.4, 60.1, 19.4, 18.0; **HRMS** ESI (m/z): [M+H]$^{+}$ calculated for $C_9H_{20}NO_2$, 251.1390, found 251.1387. [M+Na]$^{+}$ calculated for $C_{13}H_{18}N_2O_3Na$, 273.1210, found 273.1217.

Z-L-Valine nitrile (21)



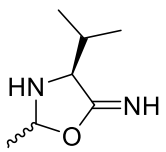
Z-L-Valine amide **20** (1.5 g, 6 mmol) and triethylamine (1.83 mL, 2.2 eq) were dissolved in dry THF (20 mL) at 0 ^{o}C. After 30 minutes trifluoroacetic anhydride (1.26 mL, 1.5 eq) was added and stirred at 0 ^{o}C for 1 hour and a further 14 hours at room temperature. The solvent was removed and the crude oil redissolved in ethyl acetate. The organic layer was washed three times with 2M HCl, then once with brine. The organic extracts were combined, dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the crude product as red translucent oil. Purification *via* column chromatography (95:5 DCM: MeOH) gave the crude product **21** as a colourless oil (1.3 g, 93 %), upon trituration a colourless crystalline compound was formed. **Melting point** 53-56 ^{o}C; **IR (ATR):** 3294, 3062, 2980, 2929, 2243, 1690, 1535, 1467, 1455, 1321, 1303, 1253, 1136, 1028, 1049 cm^{-1}; $\mathbf{[\alpha]_D^{25}}$ (deg cm^3 g^{-1} dm^{-1}) -37.3 (c = 0.97 in methanol) literature -55 (c=1.13 g cm^{-3} in chloroform)[8]; **^{1}H NMR** (400 MHz DMSO d^6): δ 8.22 (1H, br d, J= 8.2 Hz), 7.39-7.33 (5H, m), 5.09 (2H, s), 4.40 (1H, apparent t, J= 7.8 Hz), 1.98, (1H, m), 1.00 (3H, d, J= 6.8 Hz), 0.94 (3H, d, J= 6.8 Hz); **^{13}C NMR** (400 MHz $CDCl_3$): δ 155.5, 135.7, 128.8, 128.6, 128.4,117.8, 67.9, 49.1, 31.9, 18.6, 18.0; **HRMS** ESI (m/z): $[M+Na]^+$ calculated for $C_{13}H_{16}N_2O_2Na$, 255.1104, found 255.1113.

L-Valine nitrile (10)



A flask containing *Z*-L-valine nitrile **22** (400 mg, 1.72 mmol), Pearlman's reagent (20% bw, 119 mg) and ethyl acetate (15 mL) were evacuated and placed under a hydrogen atmosphere (1 atm). After 1 hour the mixture was filtered through celite washing the celite thoroughly with ethyl acetate (50 mL). 4M HCl in dioxane (1.0 mL) was added and stirred for 10 minutes turning the solution cloudy. Upon evaporation compound **10** was isolated as an off-white solid in a 75 % yield (173 mg, 1.29 mmol). The free amine was isolated by neutralisation with saturated sodium bicarbonate and subsequent extraction with dichloromethane**. IR (ATR);** 2960, 2866, 1727, 1707, 1160 cm^{-1}; **$[\alpha]_D^{25}$** (deg cm^3 g^{-1} dm^{-1}) -8.3 (c= 0.83 in dichloromethane); **^{1}H NMR** ($CDCl_3$ 400MHz): δ 3.52 (1H, d, J= 5.6 Hz), 1.93, (1H, dspt, 6.8, 5.6 Hz), 1.66 (2H, br s), 1.07 (3H, d, J= 6.8 Hz), 1.06 (3H, d, J= 6.8 Hz); **^{13}C NMR** ($CDCl_3$ 400 MHz): δ 121.4, 49.9, 33.0, 19.0, 17.7; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_5H_{11}N_2$, 99.0917, found 99.0917.

Synthesis of the cyclic by-product (17): 4-Isopropyl-2-methyl-oxazolidin-5-ylidene amine (17)

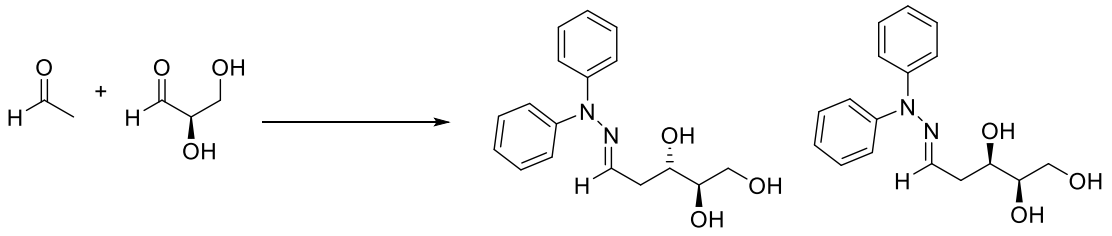


L-valine nitrile, **10** (43 mg, 0.44 mmol) was dissolved in water (1 mL) and added to a solution containing acetaldehyde (19 mg, 0.44 mmol) in water (1 mL). The solution was stirred at room temperature for 24 hours before the

solvent was removed *in vacuo*. Purification *via* column chromatography (MeOH : DCM, 5 : 95) gave the title compound **17**, as a colourless oil in a 16 % yield (10 mg, 0.07 mmol). **IR (ATR)** 3239, 2962, 2931, 2872, 1688, 1464, 1432, 1380, 1346, 1292, 1099 cm^{-1}; **^{1}H NMR** ($CDCl_3$, 400 MHz) as a mixture of diastereomers: δ 6.72 (1H, br s), 4.67 (1H, dq, J = 5.6, 1,1 Hz), 3.43 (1H, dd, J = 3.8, 1.3 Hz), 2.19-2.09 (1H, m), 1.85 (1H, br s), 1.34 (3H, d, J = 5.6 Hz), 1.05 (3H, d, J = 6.9 Hz), 0.94 (3H, d, J = 6.9 Hz); **^{13}C NMR** ($CDCl_3$ 400 MHz): As a mixture of diastereomers. Major δ 178.4, 65.6, 65.2, 29.0, 23.2, 20.0, 17.1; Minor δ 178.4, 67.1, 64.3, 30.1, 24.0, 20.0, 17.4; **HRMS** ESI (m/z): $[M+H]^+$ calculated for $C_7H_{15}N_2O$, 143.1179, found 143.1171. $[M+Na]^+$ calculated for $C_7H_{14}N_2ONa$, 165.0998, found 165.0998.

General Procedure for the Prebiotic Formation of Carbohydrates

2-Deoxy-D-ribose



Acetaldehyde (44 mg, 1 mmol) and D-glyceraldehyde (90 mg, 1 mmol) were added in 3 mL of aqueous medium to a flask containing catalyst (20 mol %) and stirred for 24 hours at room temperature. The solvent was removed *in vacuo* and redissolved in 5mL of methanol. *N*-*N*-Diphenyl hydrazine (550 mg, 3 mmol) and 2 drops of acetic acid were added and the reaction stirred for 1 hour before concentrating *in vacuo* to give a red/brown oil. The products were isolated by column chromatography (DCM : MeOH 97:3 to 90:10). Further purification *via* preparative TLC (90:10 EtOAc : Hexane) afforded the product as a mixture of diastereomers. The diastereomeric ratio was determined *via* ^{1}H NMR spectroscopy using the azomethine peaks as a reference. There are two examples shown below. The first is a ^{1}H NMR spectrum of the two sugar standards mixed together and the azomethine peak used for diasteromeric ratio determination. The second spectrum is a ^{1}H NMR spectrum of the assay after purification.

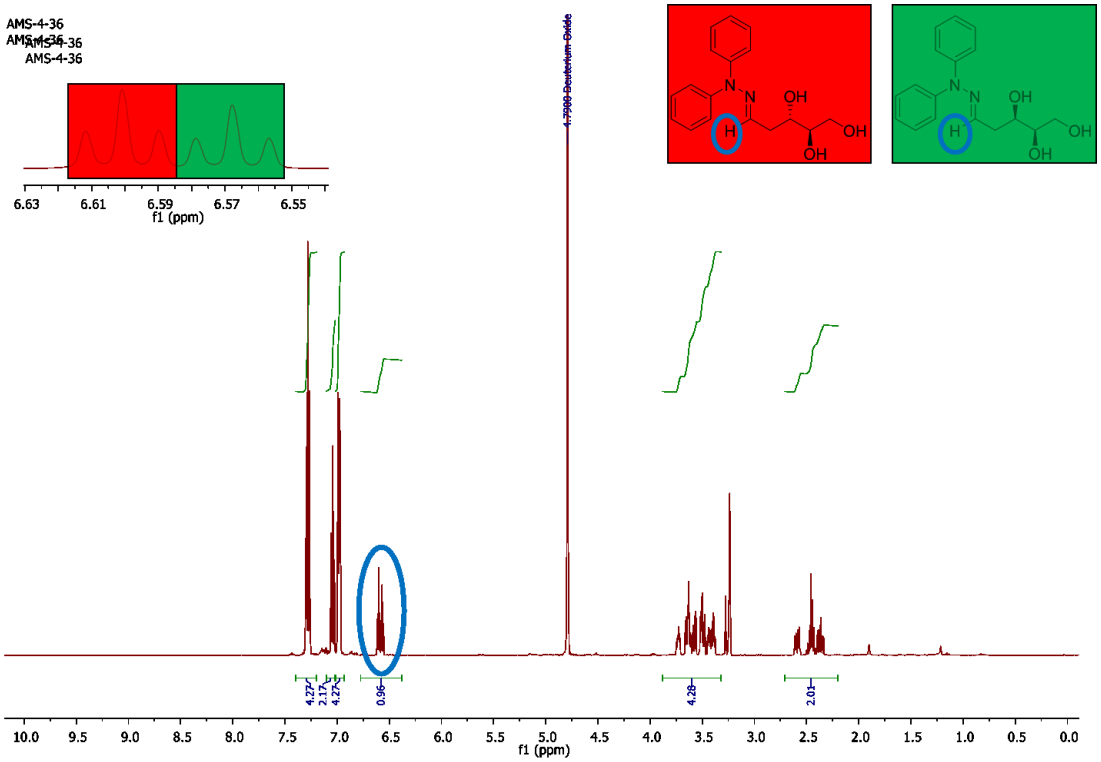


Figure 1. ^{1}H NMR spectrum of the two sugar standards.

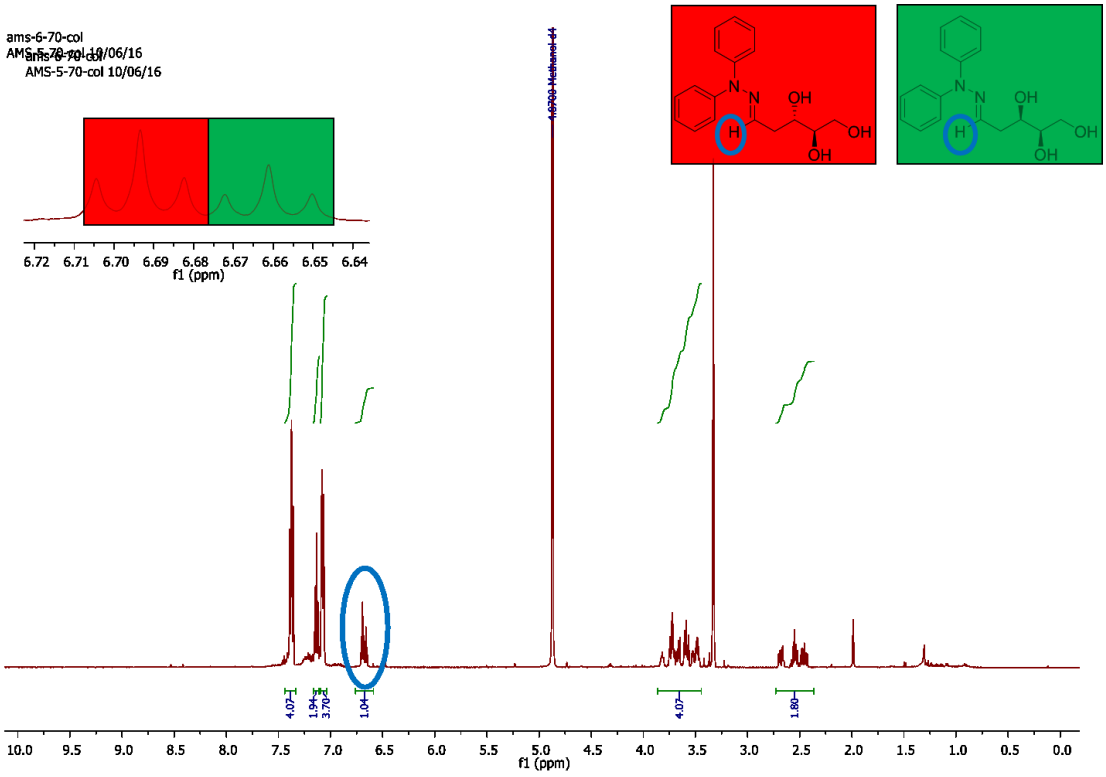
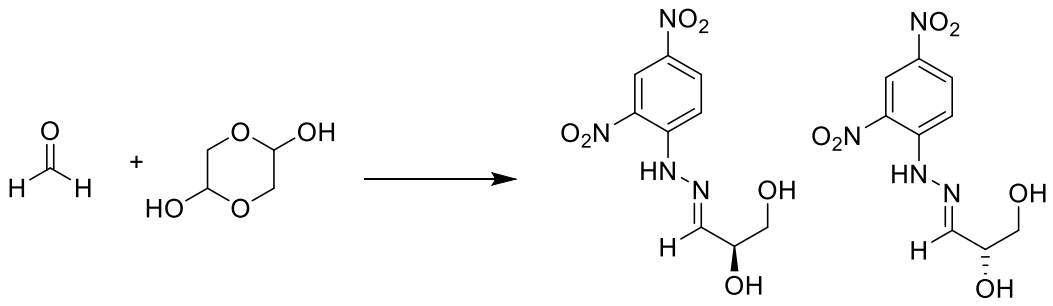


Figure 2. ^{1}H NMR spectrum of the deoxyribose forming reaction after purification.

D-Glyceraldehyde



L-Valine nitrile catalyst (20 mg, 0.20 mmol) and glycolaldehyde dimer (60 mg, 0.5 mmol) were dissolved in 1.7 mL pH 7 phosphate buffer. Paraformaldehyde (750 mg) was dissolved in water (25 mL) and heated to 60^{o}C for 2 hours. Upon cooling, 1.3 mL of the solution was added to the reaction and stirred at room temperature for 24 hours. Dinitrophenyl hydrazine (510 mg, 2.6 mmol) was added and stirred for a further 24 hours followed by concentration *in vacuo* to afford the crude mixture of hydrazones as an orange solid. Purification by column chromatography (5:95 MeOH : DCM) followed by preparative thin layer chorography (2:98 MeOH : DCM) yielded the glyceraldehyde-trapped hydrazone as a yellow solid (3 mg, 0.01 mmol). The enantiomeric excess of hydrazone product was analyzed *via* HPLC using a chiral AD column (15:85 isopropanol : hexane) at a flow rate of 1.0 mL/min.

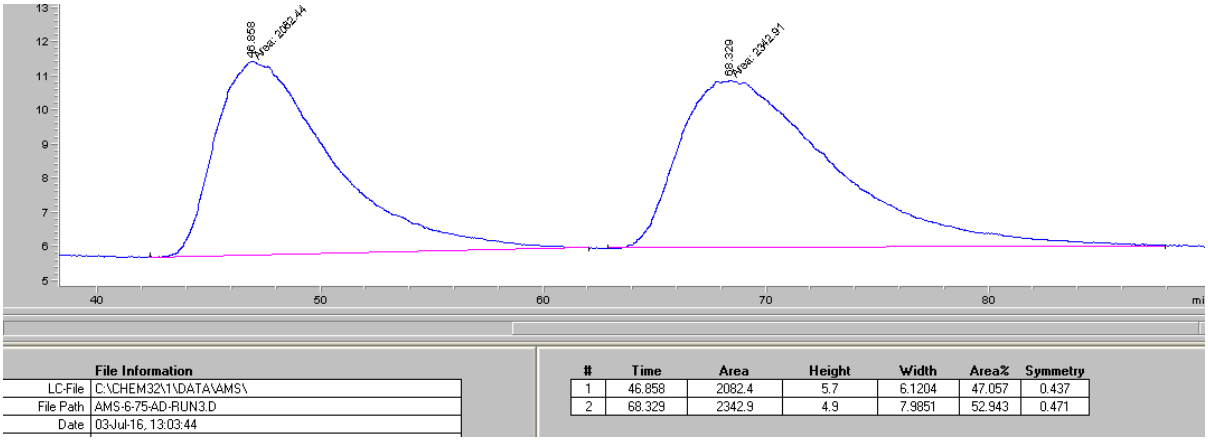


Figure 3. HPLC run of glyceraldehyde hydrazone from reaction. Each HPLC run was repeated three times and an average %ee taken. There is a 6% ee in favour of D-glyceraldehyde hydrazone. L-glyceraldehyde elutes at ~46 minutes and D-glycerladehyde at 68 minutes.

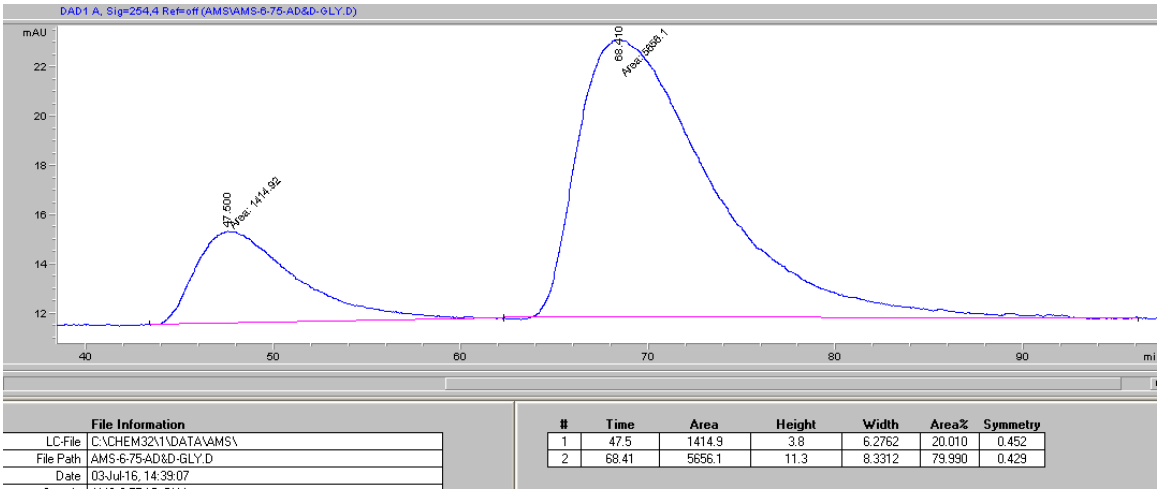
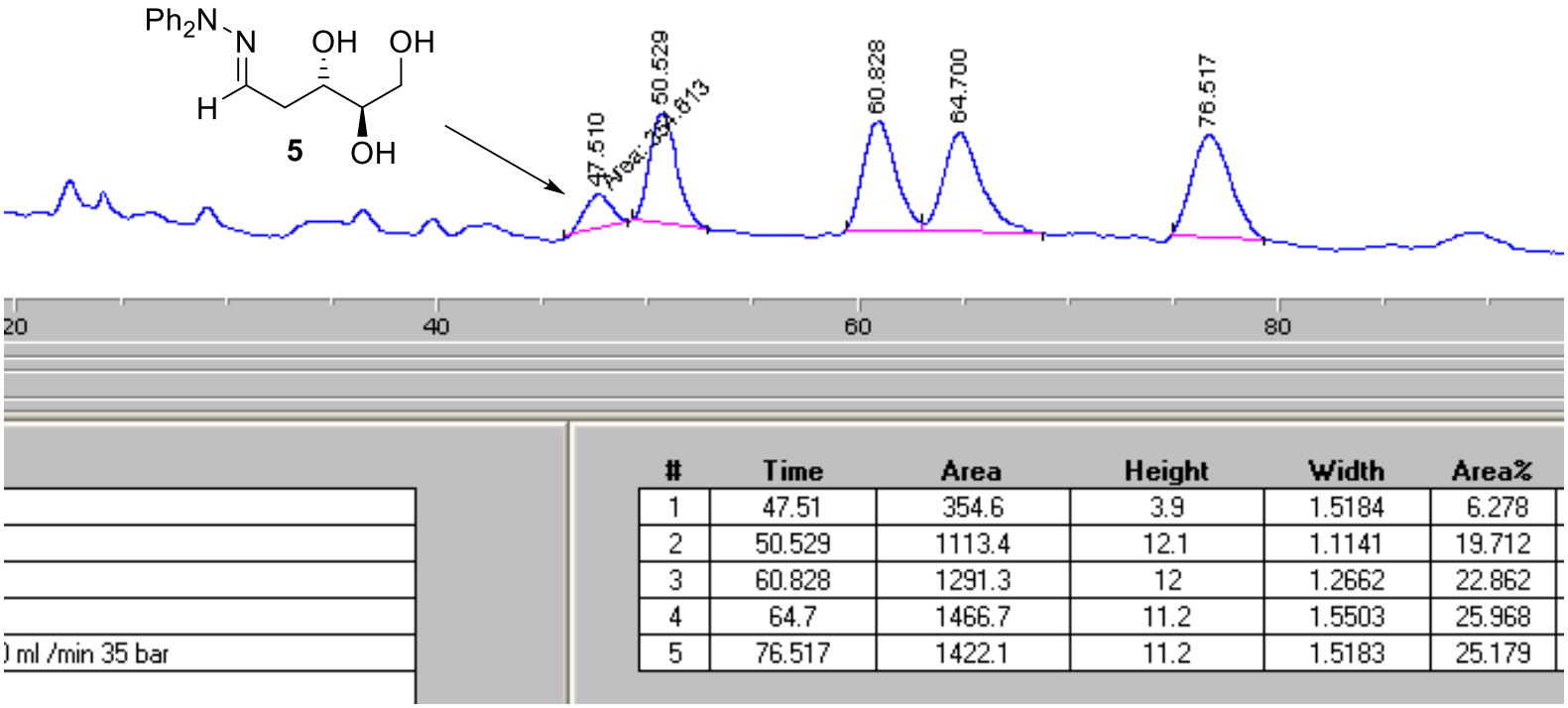


Figure 4. HPLC run of glyceraldehyde hydrazone from spiked with authentic D-glyceraldehyde hydrazone.

Procedure for one-pot synthesis of sugar molecules from interstellar starting material.

L-Proline benzylester.HCl was washed with a saturated solution of sodium bicarbonate and extracted with DCM. The organic layer was dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the free amino ester. Paraformaldehyde (750 mg) was dissolved in water (25 mL) and heated to 60^{o}C for 2 hours. 1.3 mL of the solution was added to a flask containing a solution of L-proline benzyl ester (53 mg, 0.26 mmol), glycolaldehyde dimer (77.5 mg, 0.65 mmol) and acetaldehyde (56 mg, 1.29 mmol) in 3 mL pH 7 phosphate buffer. The solution was stirred for 7 days at room temperature before concentrating *in vacuo* to give a yellow/orange oil. The mixture of products was redissolved in methanol (5 mL) to which *N, N*-diphenyl hydrazine (720 mg, 3.9 mmol) and 2 drops of acetic acid were added and stirred at room temperature for 1 hour. Concentration *in vacuo* gave the crude mixture of hydrazones as a brown oil. The products were isolated by column chromatography (5 : 95 EtOAc : hexane to 100 % EtOAc). Further separation of some compounds was achieved by PTLC. Figure 5 shows the mass spectrum of the crude reaction mixture and the fraction containing the tetrose and pentose products. The mass of deoxyribose is highlighted on the spectra.

HPLC trace of one-pot reaction. The fraction containing tetrose and pentose products trapped with diphenylhydrazine.



#	Time	Area	Height	Width	Area%
1	47.51	354.6	3.9	1.5184	6.278
2	50.529	1113.4	12.1	1.1141	19.712
3	60.828	1291.3	12	1.2662	22.862
4	64.7	1466.7	11.2	1.5503	25.968
5	76.517	1422.1	11.2	1.5183	25.179

Mass spectrum of one-pot reaction. The fraction containing tetrose and pentose products trapped with diphenylhydrazine.

ams-7-70 fr6

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

Acquisition Date 17/11/2016 12:28:00

Analysis Filename	pac61942as_P1-F-6_01_1224.d
Method	400p_acn1260_2c1s.m
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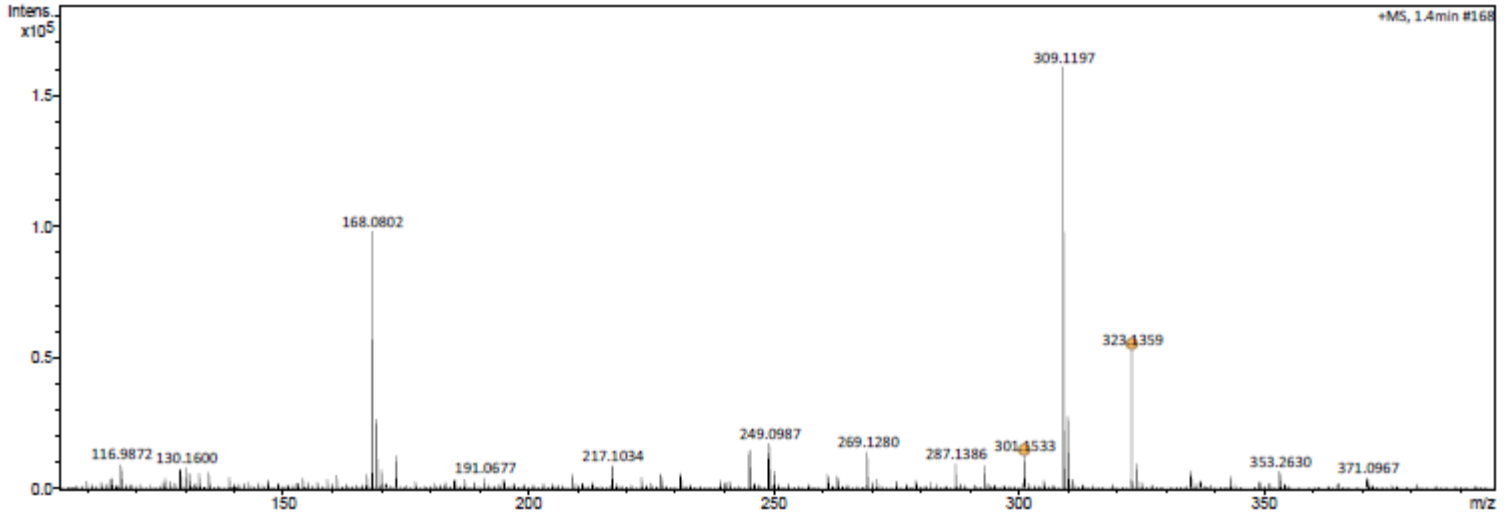
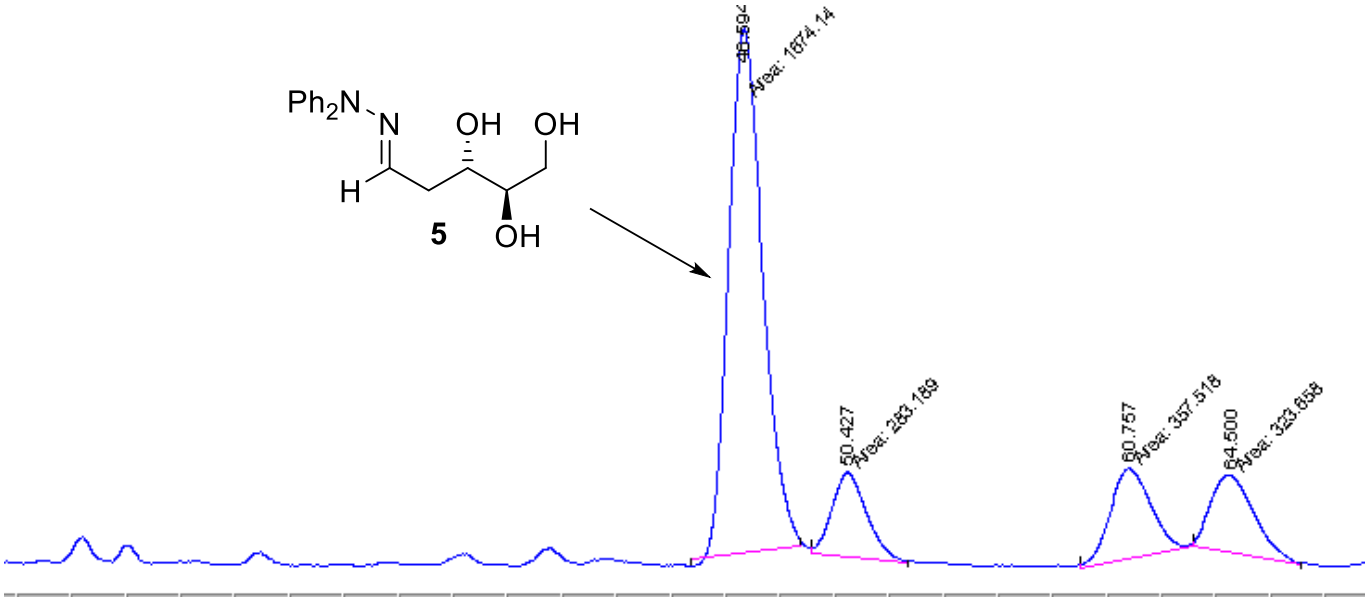
ESI	Positive



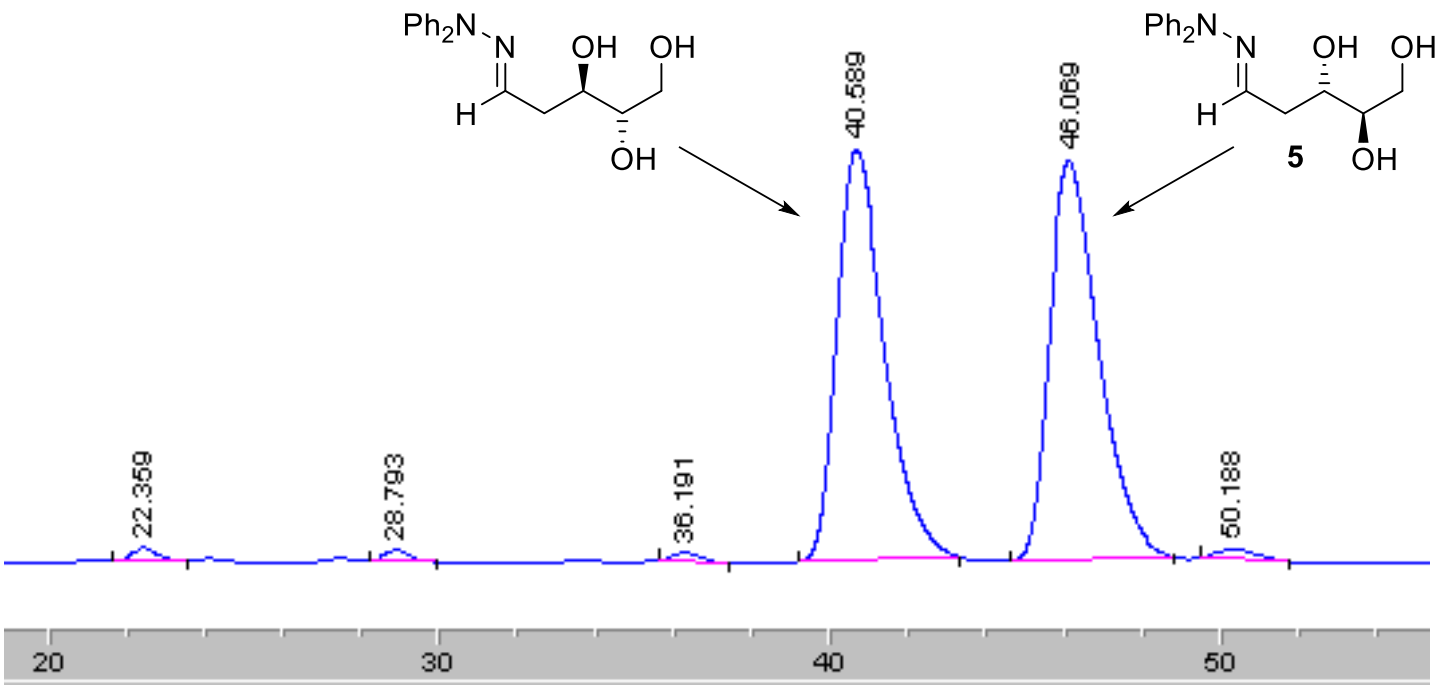
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
301.1533	1	C17H21N2O3	301.1547	-4.5	-1.3	14.1	5.0
323.1359	1	C17H20N2NaO3	323.1366	2.3	0.7	17.7	6.5

HPLC trace of one-pot reaction. The fraction containing tetrose and pentose products spiked with authentic hydrazone-trapped 2-deoxy-D-ribose.

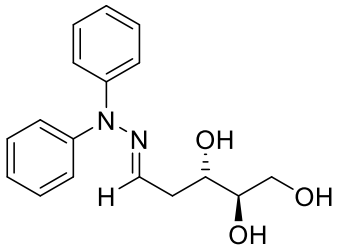


#	Time	Area	Height	Width	Area%	Symmetry
1	46.594	1674.1	19.1	1.4619	63.450	0.74
2	50.427	283.2	3.1	1.5171	10.733	0.772
3	60.757	357.5	3.3	1.7834	13.550	0.877
4	64.5	323.7	2.9	1.8818	12.267	0.604

HPLC trace of one-pot reaction. The fraction containing tetrose and pentose products spiked with authentic hydrazone-trapped 2-deoxy-D-ribose and 2-deoxy-L-ribose.

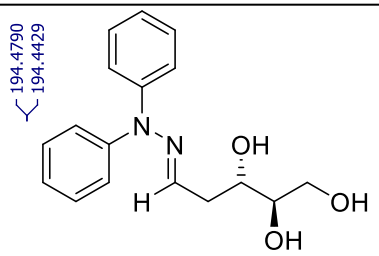


Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

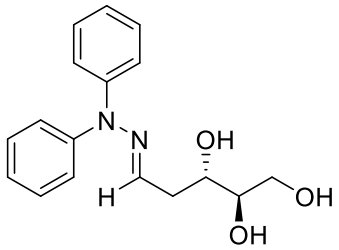


Compound **5**

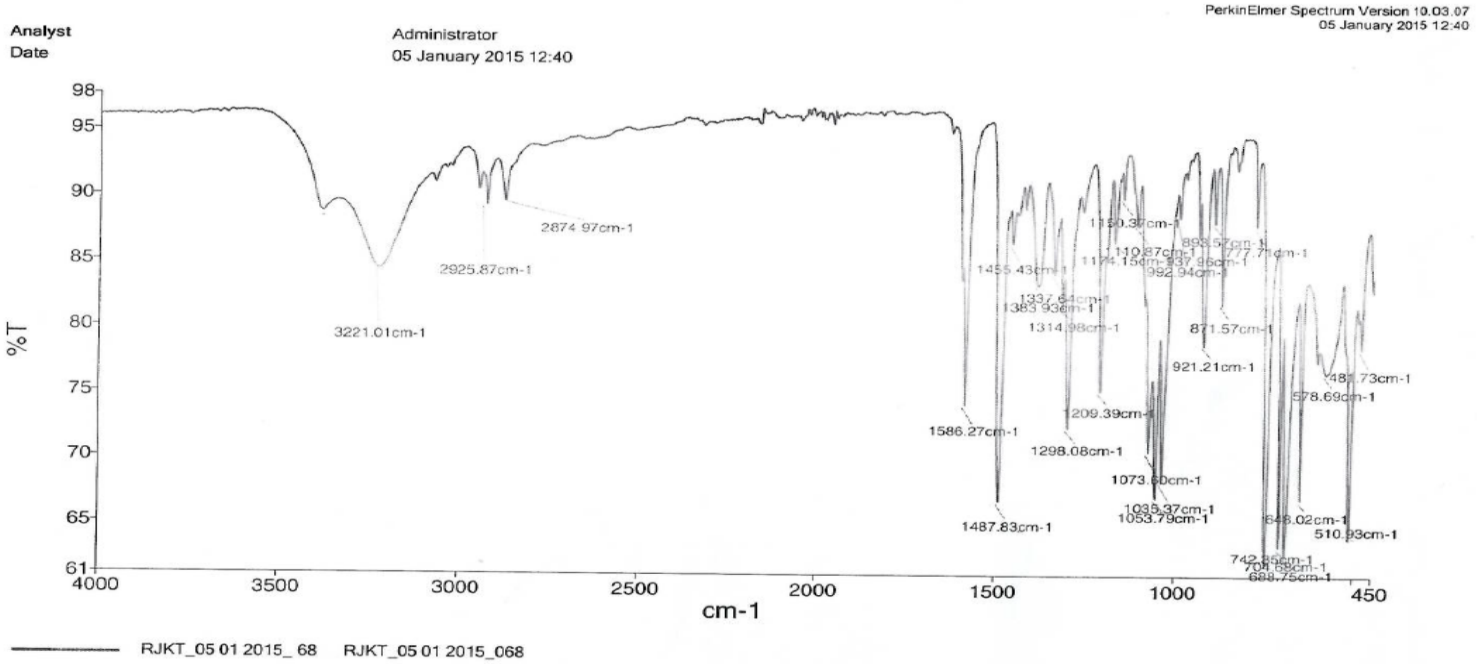
Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C



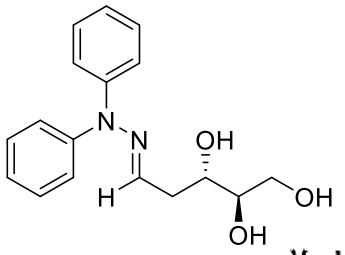
Compound **5**



Compound **5**



Page 1



Compound **5**

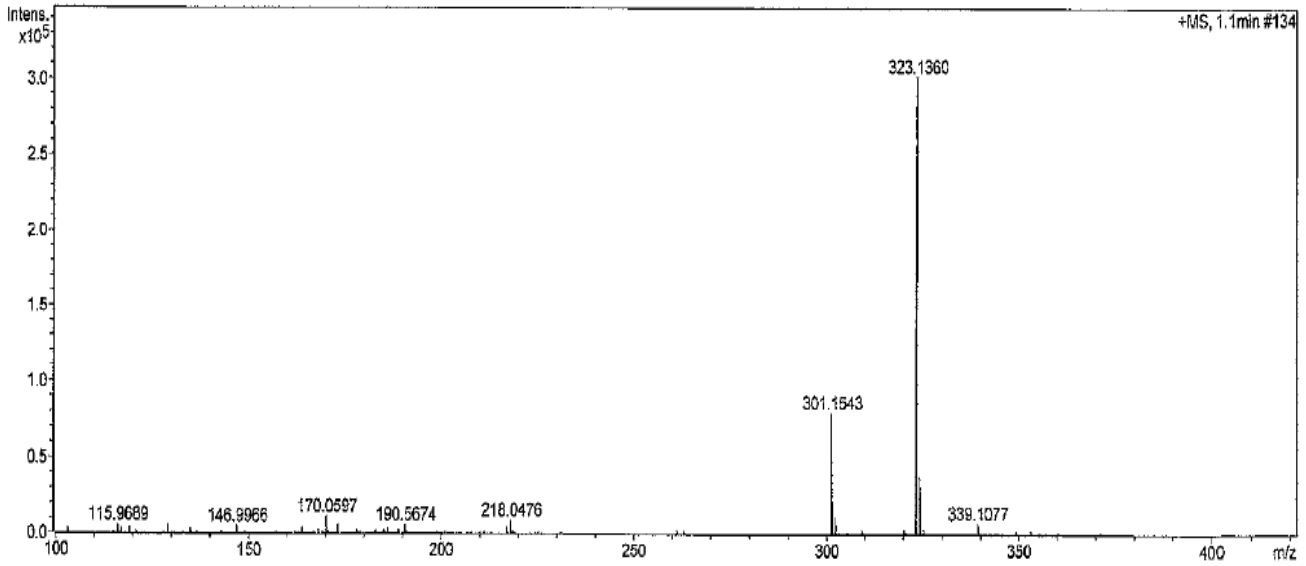
ams-3-3

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

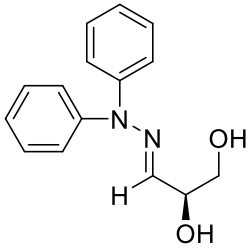
Acquisition Date 17/10/2014 12:25:09

Analysis Filename	pac48802as_P1-B-7_01_54122.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac48802as
Instrument	micrOTOF
ESI	Positive



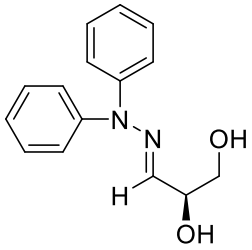
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
301.1543	1	C 17 H 21 N 2 O 3	301.1547	1.1	0.3	28.2	1.4
323.1360	1	C 17 H 20 N 2 Na O 3	323.1366	1.9	0.6	37.7	1.5

Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

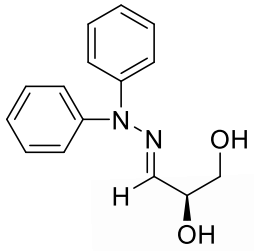


Compound **11**

Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13} C



Compound **11**

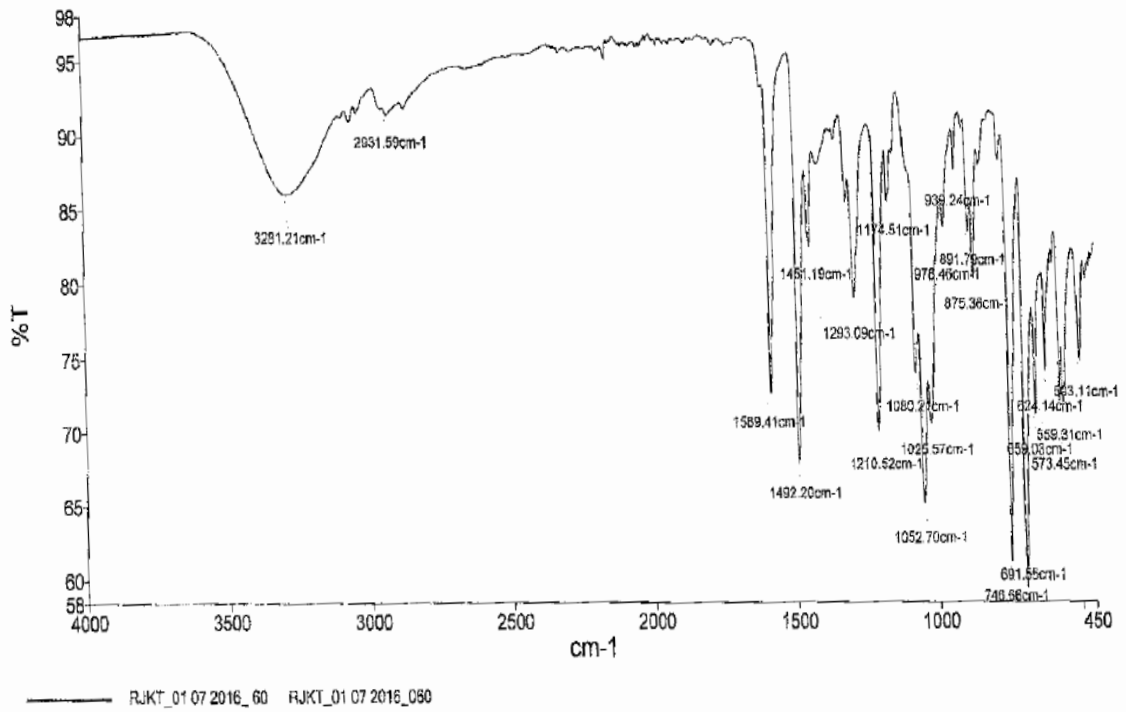


Compound **11**

PerkinElmer Spectrum Version 10.03.07
03 July 2016 15:01

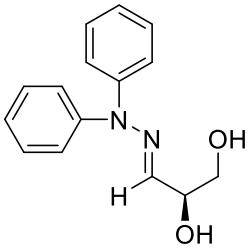
Analyst
Date

Administrator
03 July 2016 15:01



RJKT_01 07 2016_60 RJKT_01 07 2016_060

Page 1



Compound **11**

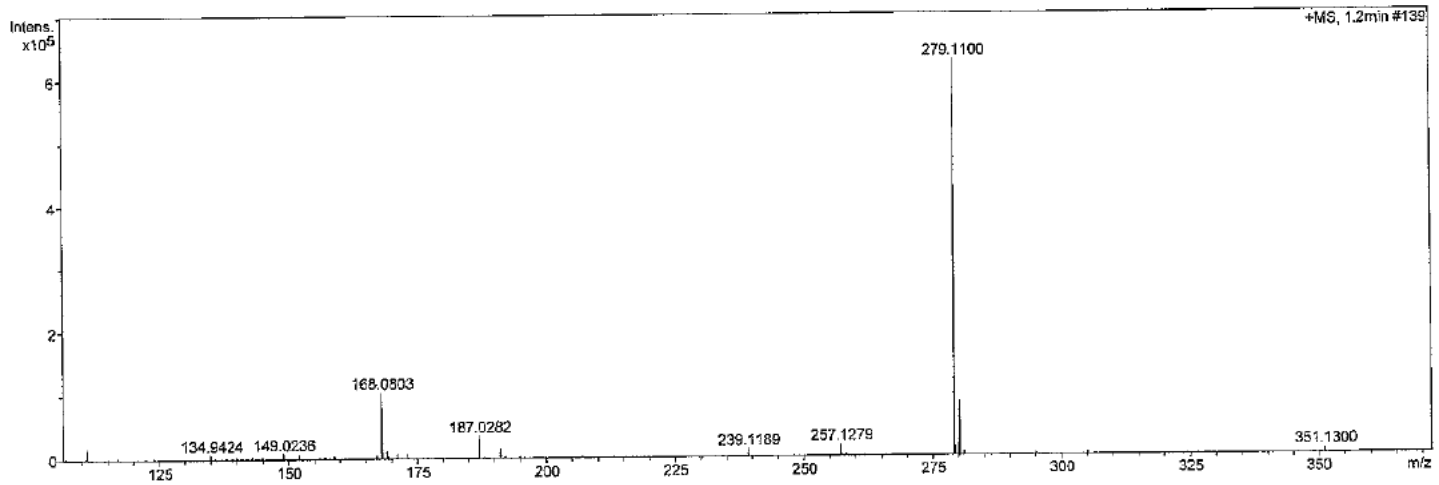
ams-3-43

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

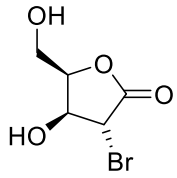
Acquisition Date 22/01/2015 09:39:10

Analysis Filename	pac50483as_P1-F-3_01_56220.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac50483as
Instrument	micrOTOF
ESI	Positive



Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
257.1279	1	C 15 H 17 N 2 O 2	257.1285	2.3	0.6	18.8	2.2
279.1100	1	C 15 H 16 N 2 Na O 2	279.1104	1.6	0.4	19.0	1.8

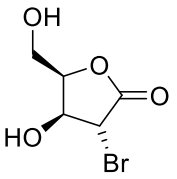
Parameter	Value
1) Solvent	D_2O
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H



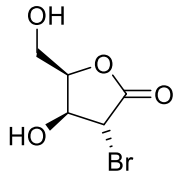
Compound **13**

Parameter	Value
1) Solvent	D_2O
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

m5090ams
A Steer ams-1-77



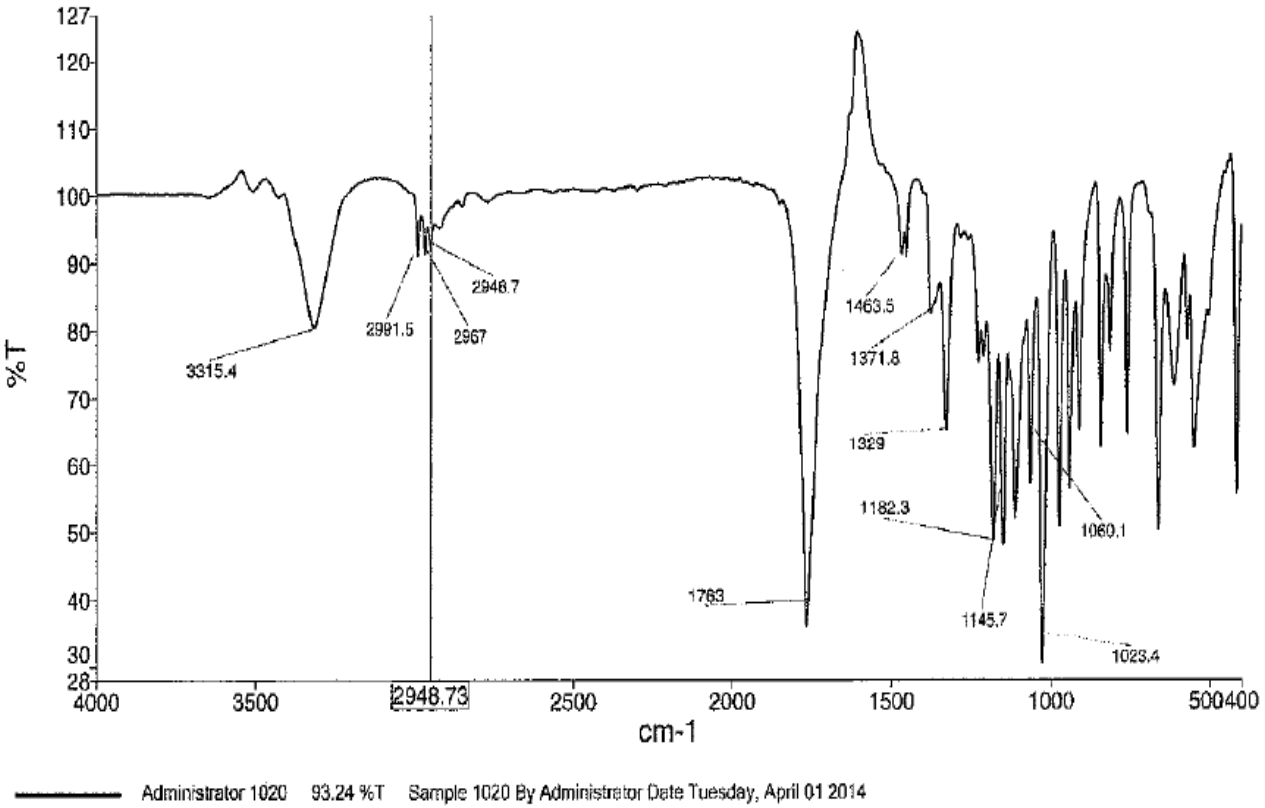
Compound **13**



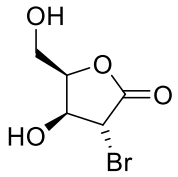
Compound **13**

PerkinElmer Spectrum Version 10.03.09
Wednesday, April 02, 2014 9:36 AM

Analyst Administrator
Date Wednesday, April 02, 2014 9:36 AM



Administrator 1020 93.24 %T Sample 1020 By Administrator Date Tuesday, April 01 2014



Compound **13**

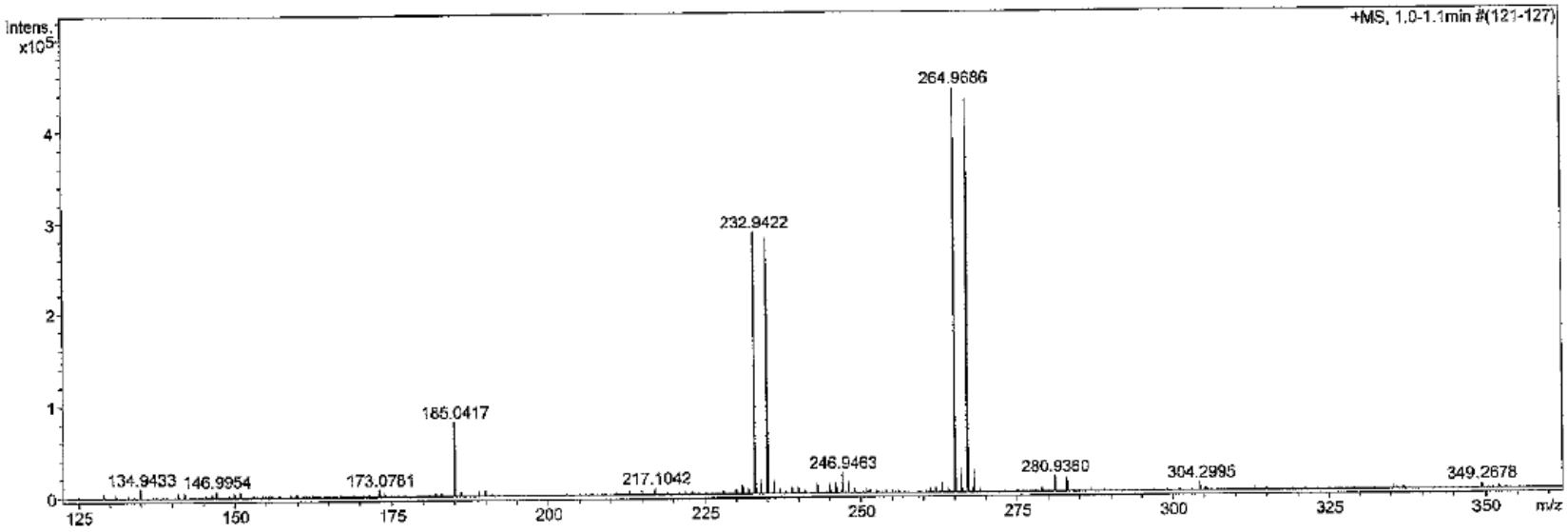
ams-1-71 col

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

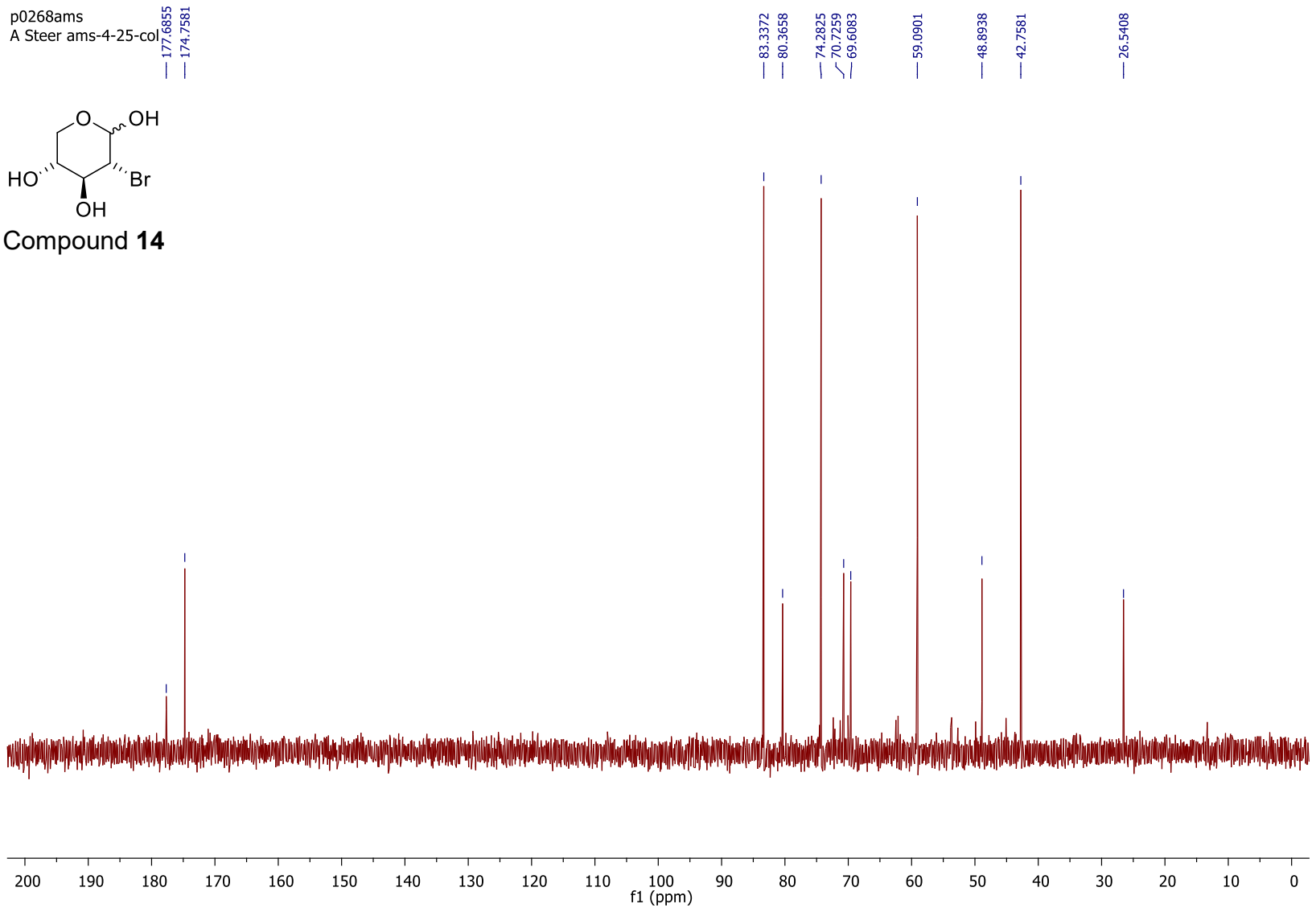
Acquisition Date 04/04/2014 11:32:11

Analysis Filename	pac45982as_1-e,7_01_50833.d
Method	400p_meoh.m
Submission Name	pac45982as
Instrument	micrOTOF
ESI	Positive

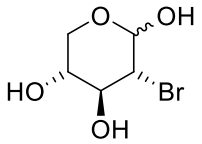


Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
232.9422	1	C 5 H 7 Br Na O 4	232.9420	-1.0	-0.2	5.8	-2.1

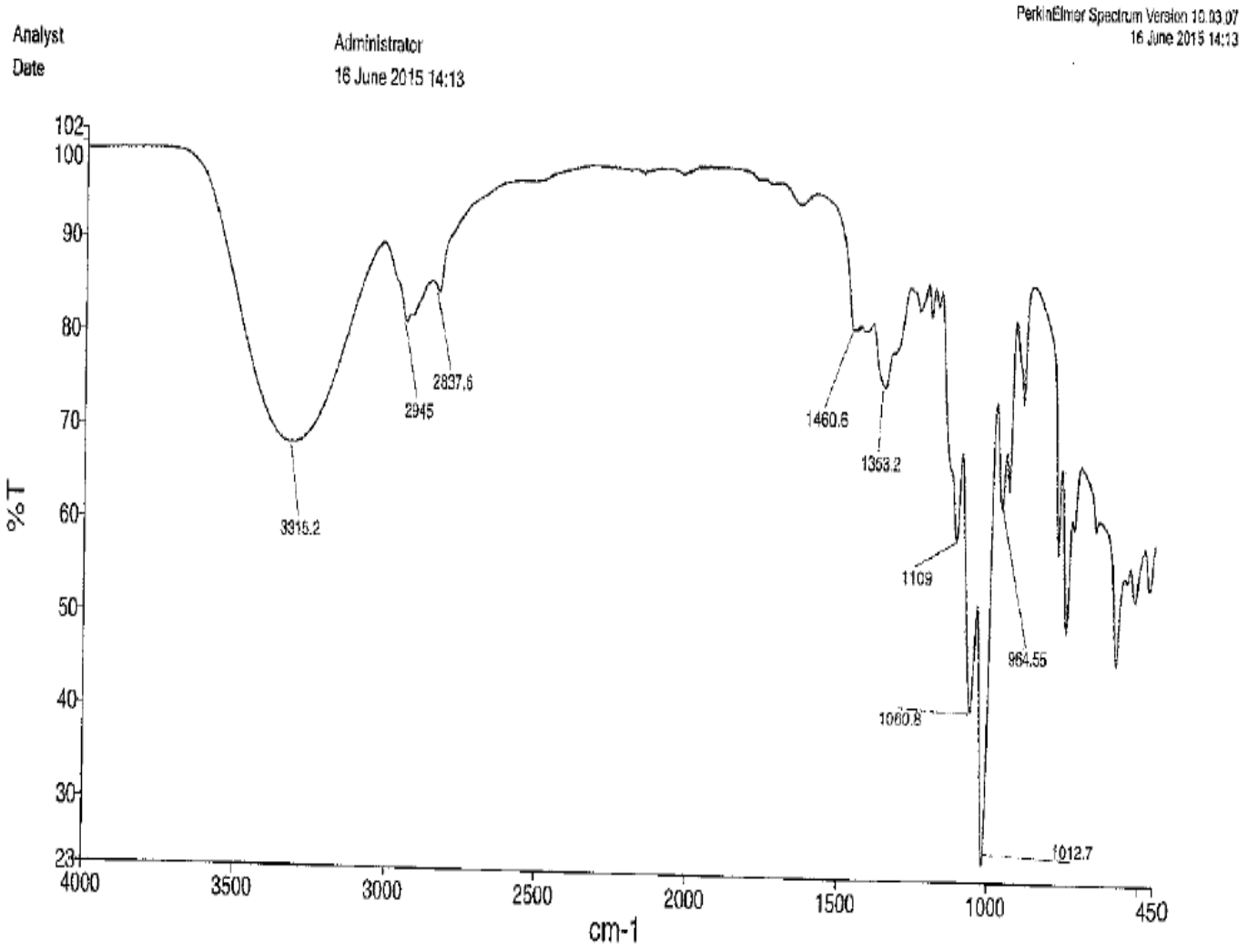
Parameter	Value
1) Solvent	D_2O
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

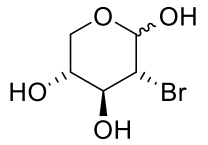


Compound **14**


O
OH
HO
Br
OH

Compound **14**


Analyst
Date
Administrator
16 June 2015 14:13
PerkinElmer Spectrum Version 10.03.07
16 June 2015 14:13
%T
cm-1
3315.2
2945
2837.6
1460.6
1353.2
1109
1060.8
964.55
1012.7
4000
3500
3000
2500
2000
1500
1000
450



Compound **14**

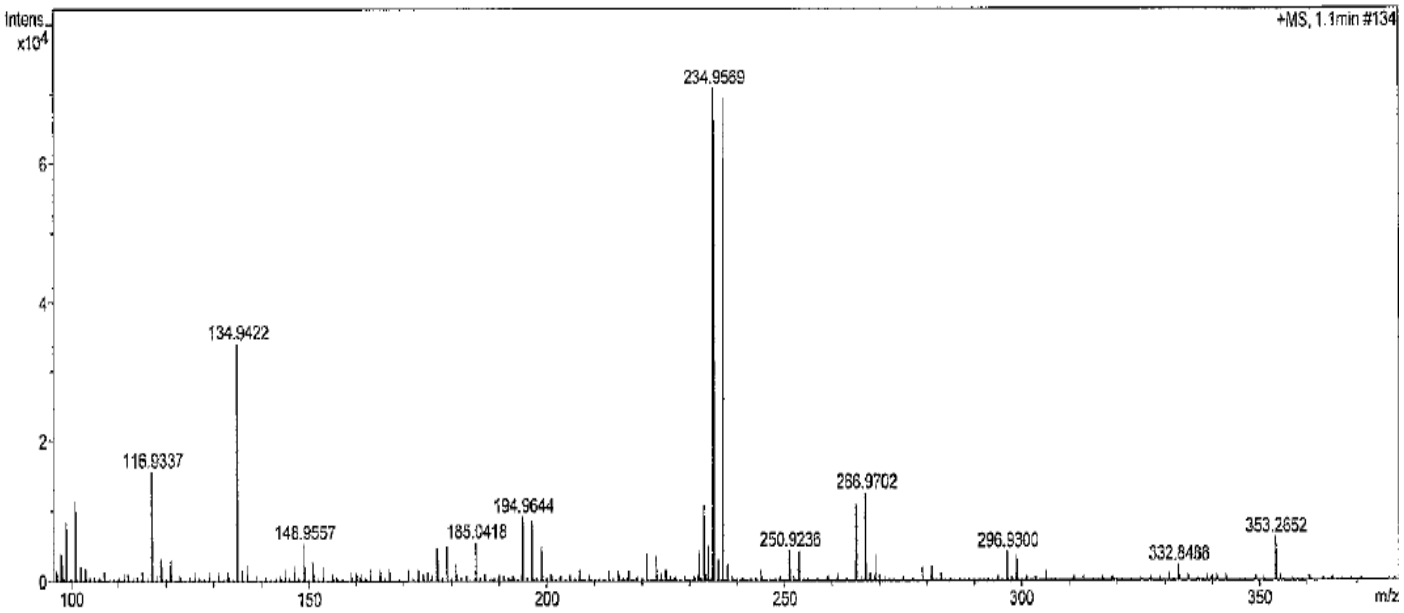
ams-4-25

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

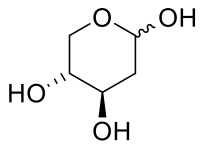
Acquisition Date 16/06/2015 12:06:16

Analysis Filename	pac53103as_P1-B-3_01_59272.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac53103as
Instrument	micrOTOF
ESI	Positive



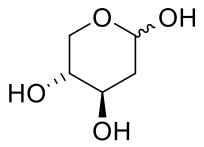
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
234.9569	1	C 5 H 9 Br Na O 4	234.9576	3.1	0.7	10.6	2.5

Parameter	Value
1) Solvent	D_2O
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

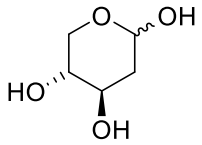


Compound **15**

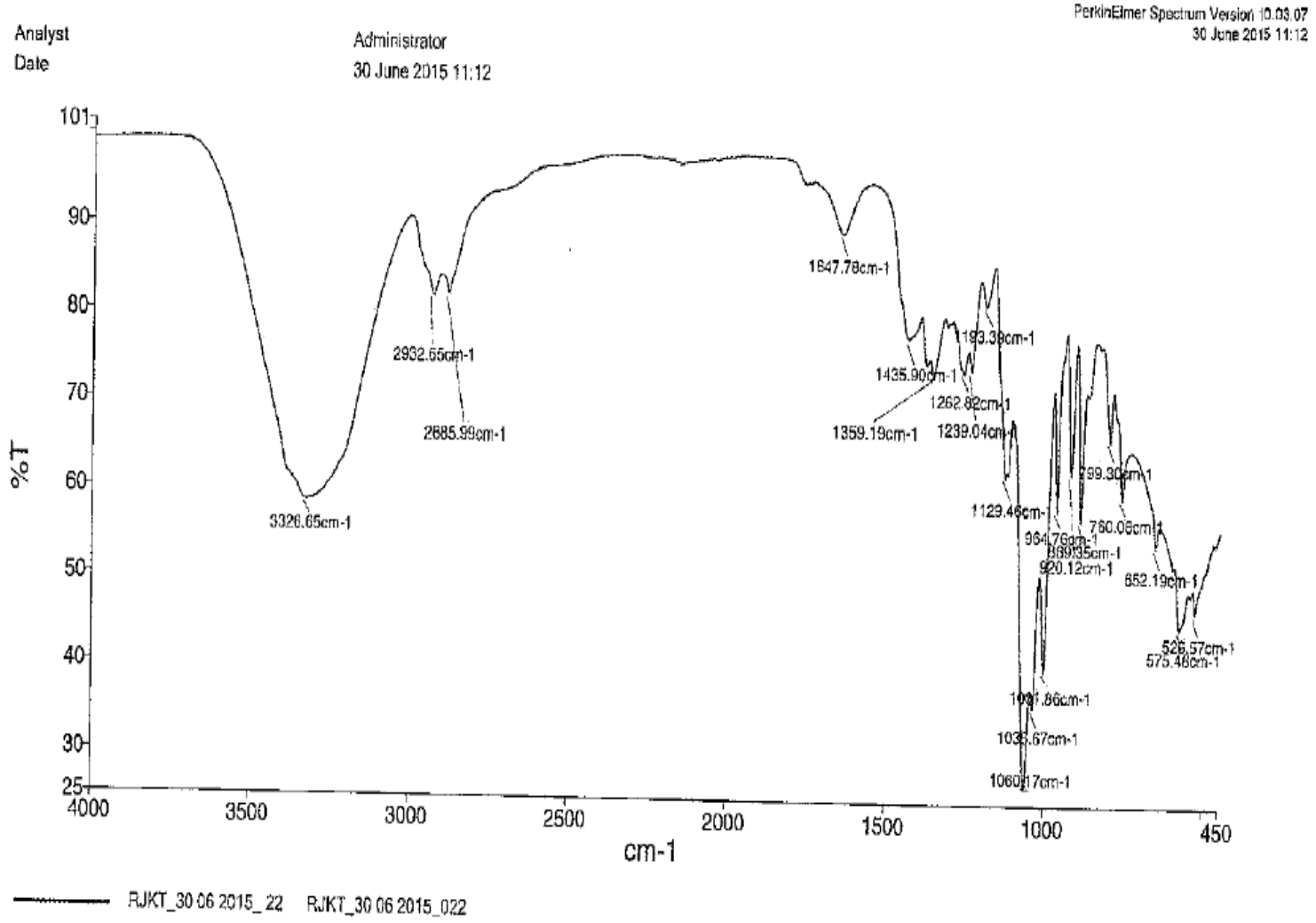
Parameter	Value
1) Solvent	D_2O
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

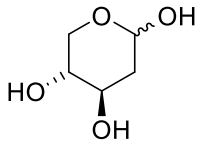


Compound **15**


O
OH
HO
OH

Compound **15**


Analyst
Date
Administrator
30 June 2015 11:12
PerkinElmer Spectrum Version 10.03.07
30 June 2015 11:12
%T
cm-1
3326.65cm-1
2932.65cm-1
2885.99cm-1
1647.78cm-1
1435.90cm-1
1359.19cm-1
1262.82cm-1
1239.04cm-1
1193.39cm-1
1129.46cm-1
964.76cm-1
920.12cm-1
760.06cm-1
652.19cm-1
575.48cm-1
526.57cm-1
1060.17cm-1
RJKT_30 06 2015_22
RJKT_30 06 2015_022



Compound **15**

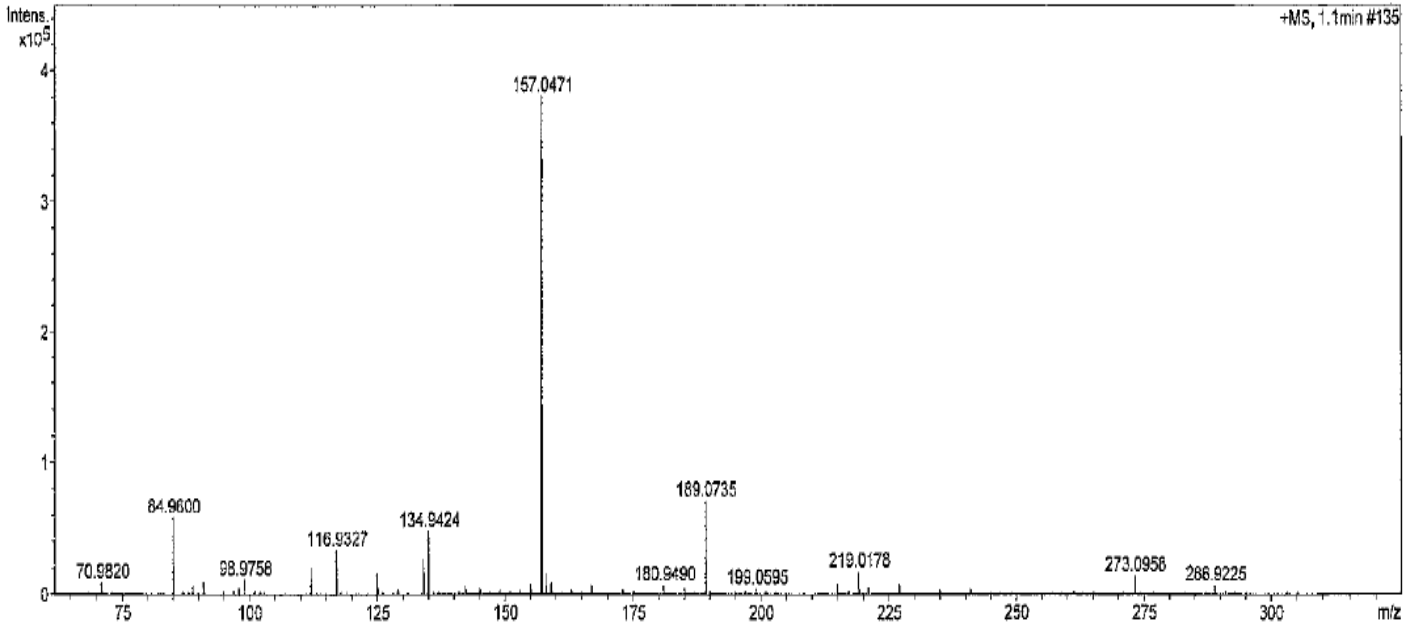
ams-4-26

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

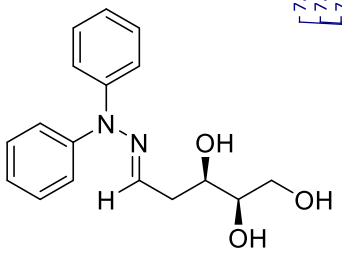
Acquisition Date 29/06/2015 09:34:42

Analysis Filename	pac53319as_P1-D-1_01_59507.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac53319as
Instrument	micrOTOF
ESI	Positive



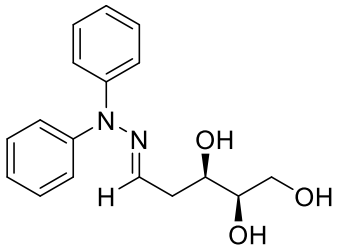
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
157.0471	1	C 5 H 10 Na O 4	157.0471	-0.0	-0.0	12.5	-1.4

Parameter	Value
1) Solvent	d[4]methanol
2) Spectrometer Frequency	500 MHz
3) Nucleus	[1]H

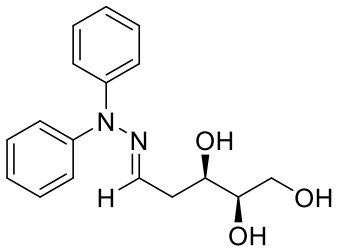


Compound **6**

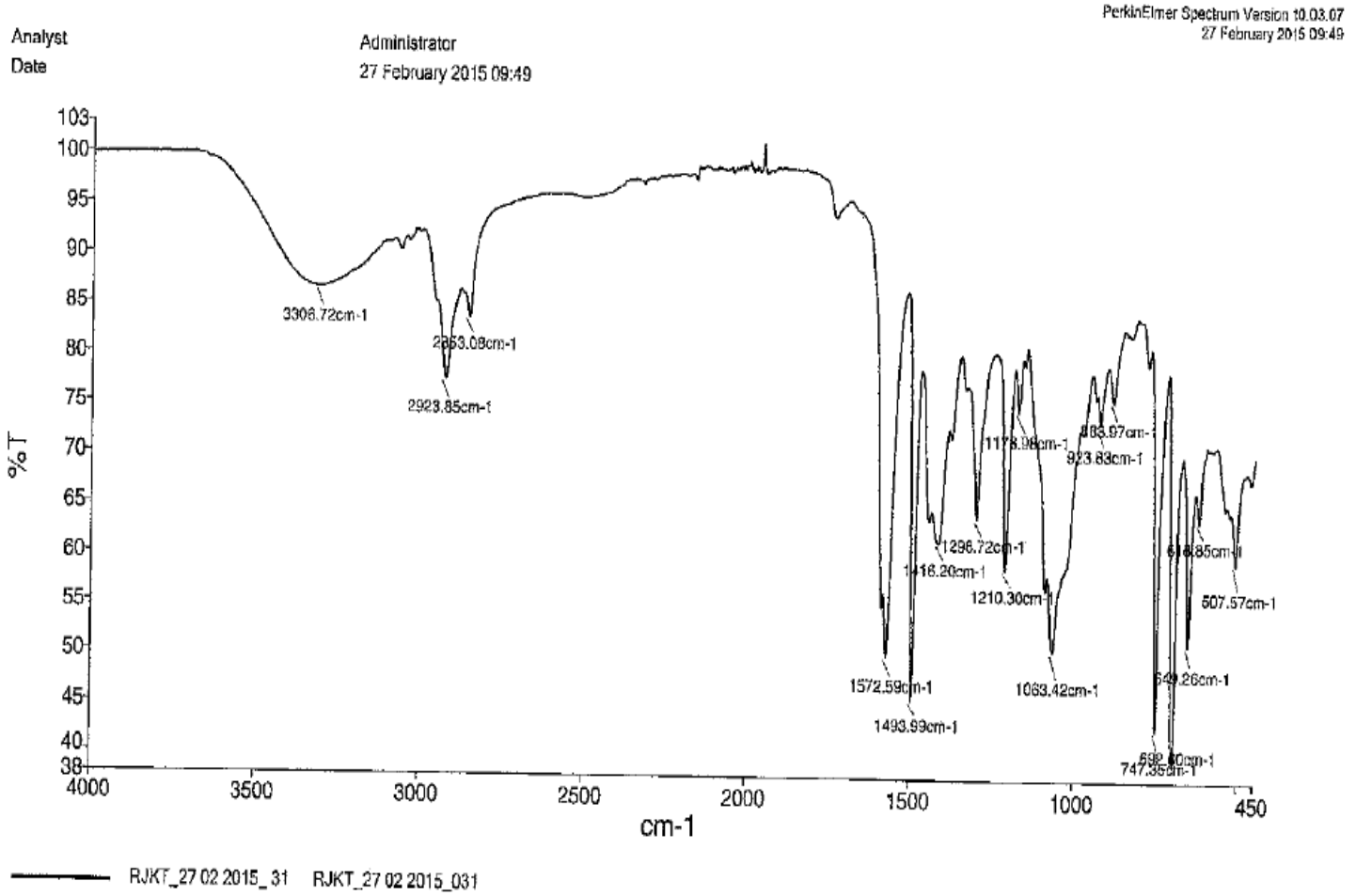
Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

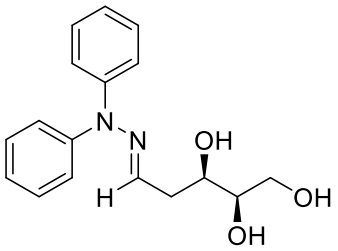


Compound **6**


N
N
OH
H
OH
OH

Compound **6**


Analyst
Administrator
Date
27 February 2015 09:49
PerkinElmer Spectrum Version 10.03.07
27 February 2015 09:49
%T
cm-1
3306.72cm-1
2923.85cm-1
1572.59cm-1
1493.99cm-1
1296.72cm-1
1210.30cm-1
1063.42cm-1
923.83cm-1
507.57cm-1
747.35cm-1
RJKT_27 02 2015_31
RJKT_27 02 2015_031



Compound **6**

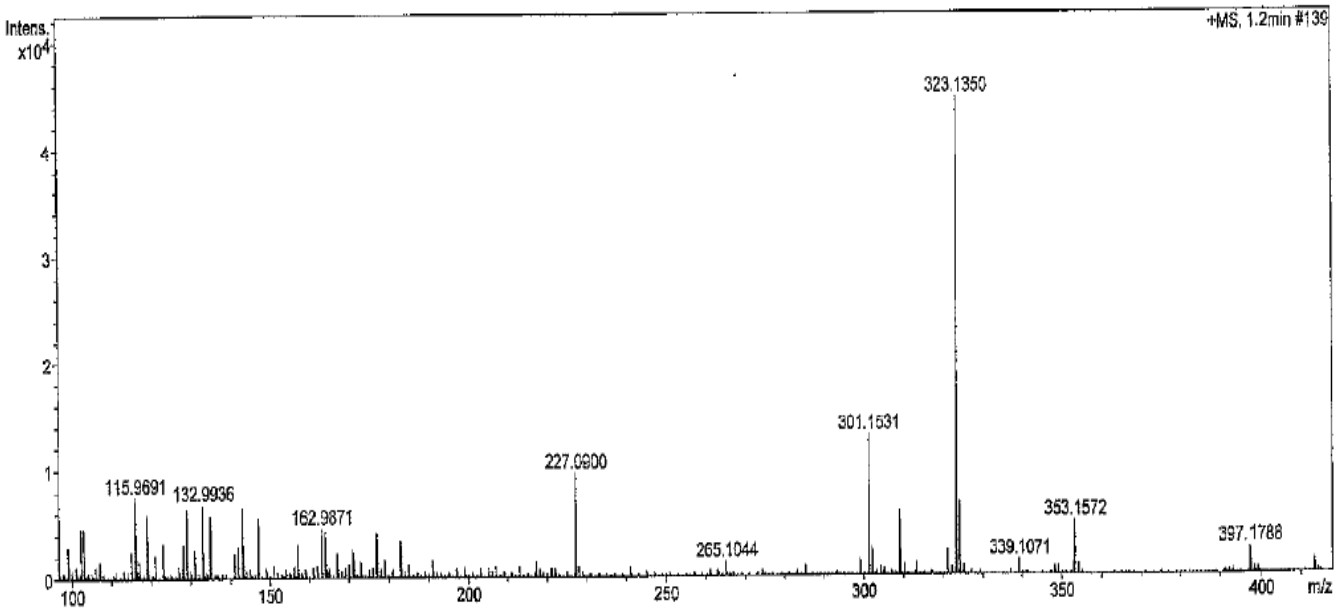
ams-3-11-1

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

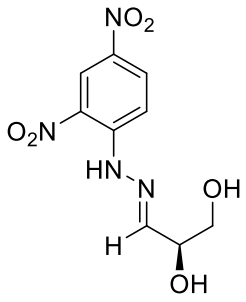
Acquisition Date 06/11/2014 09:59:57

Analysis Filename	pac49223as_P1-E-8_01_54680.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac49223as
Instrument	micrOTOF
ESI	Positive



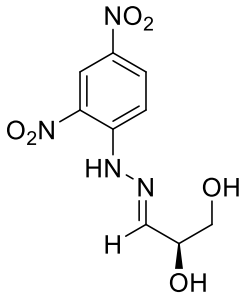
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
301.1531	1	C 17 H 21 N 2 O 3	301.1547	5.1	1.5	14.8	4.0
323.1350	1	C 17 H 20 N 2 Na O 3	323.1366	4.9	1.6	27.3	4.4

Parameter	Value
1) Solvent	d^6 DMSO
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

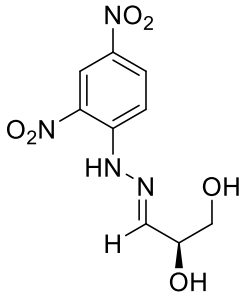


Compound **16**

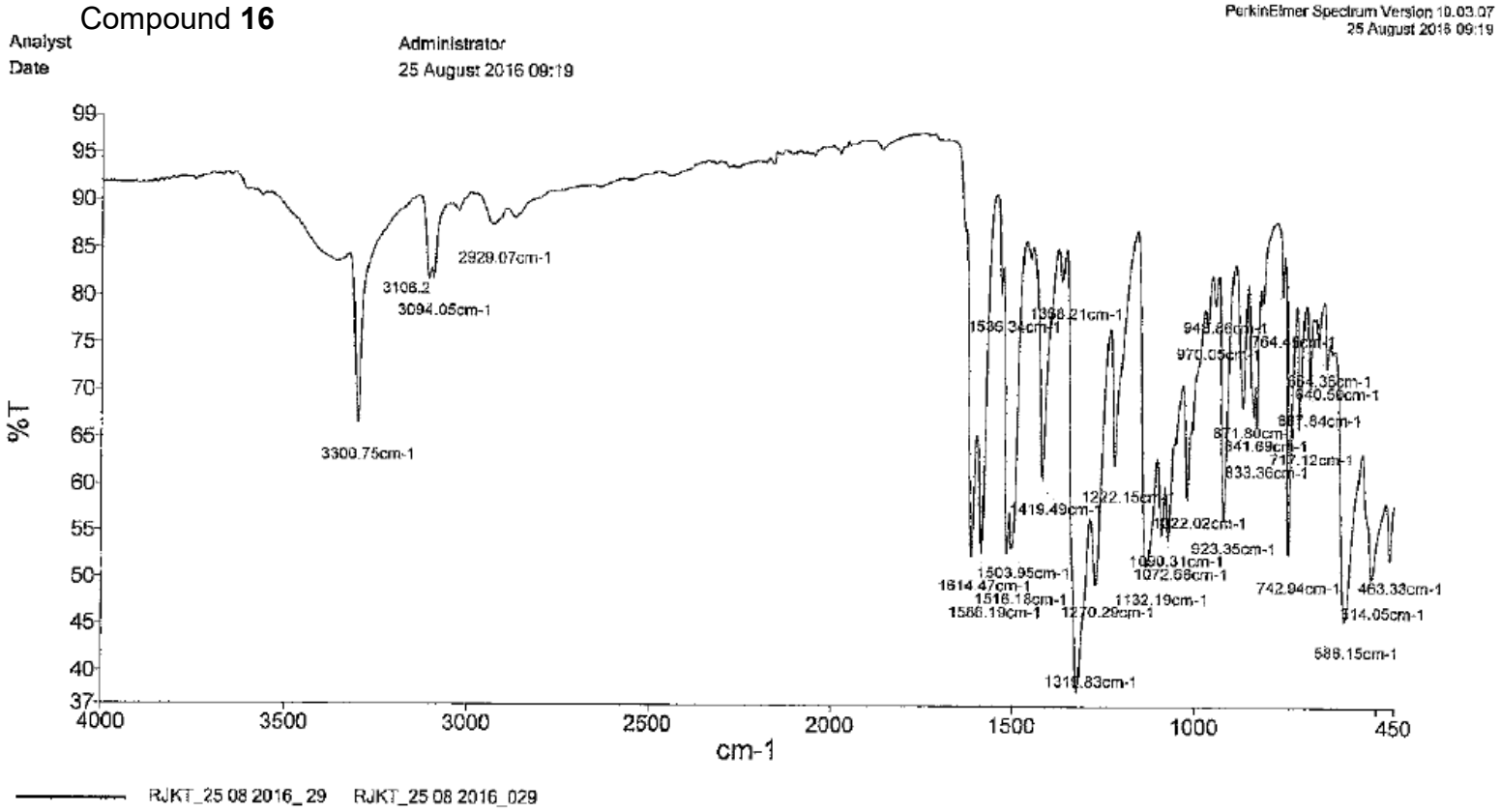
Parameter	Value
1) Solvent	d^6 DMSO
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

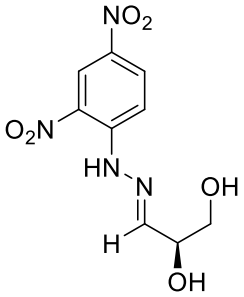


Compound **16**


NO2
O2N
HN
N
OH
H
OH

Compound **16**


Analyst
Administrator
Date
25 August 2016 09:19
PerkinElmer Spectrum Version 10.03.07
25 August 2016 09:19
%T
cm-1
3309.75cm-1
3106.2
3094.05cm-1
2929.07cm-1
1503.95cm-1
1516.18cm-1
1270.29cm-1
1132.19cm-1
1072.68cm-1
1050.31cm-1
923.35cm-1
742.94cm-1
463.33cm-1
588.15cm-1
RJKT_25 08 2016_ 29
RJKT_25 08 2016_029



Compound **16**

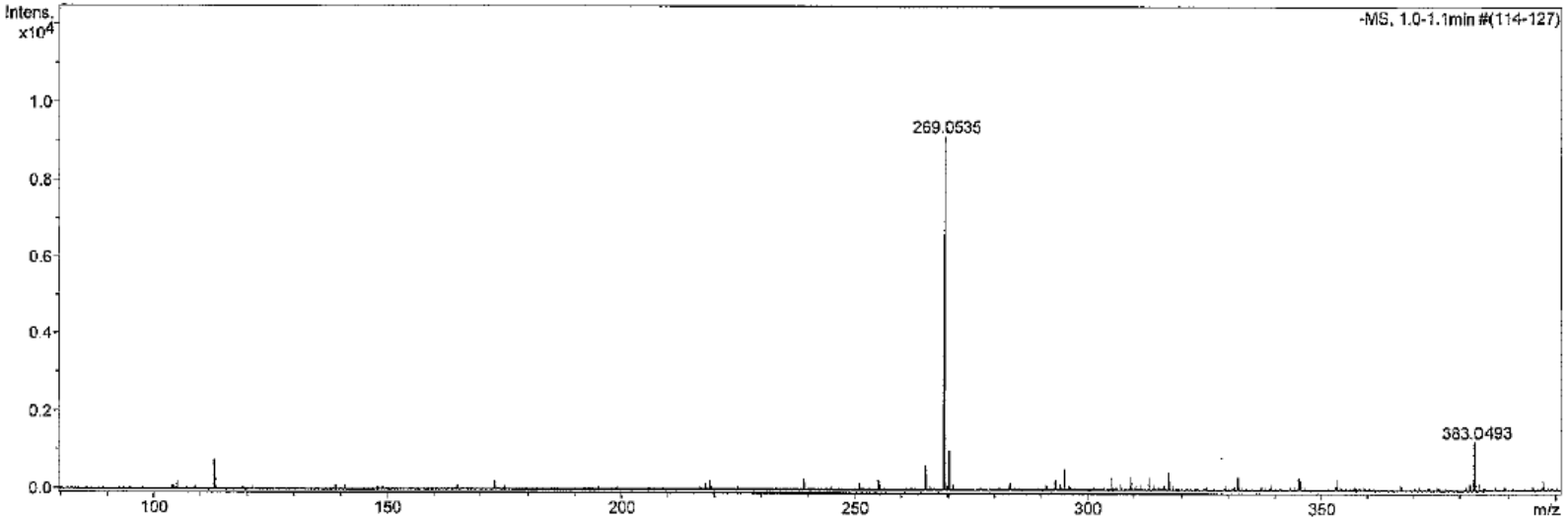
ams-2-16-b

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

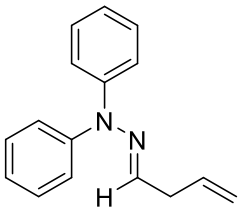
Acquisition Date 12/06/2014 15:57:35

Analysis Filename	pac46965as_1-f,1_01_51717.d
Method	400n_meoh.m
Submission Name	pac46965as
Instrument	micrOTOF
ESI	Negative



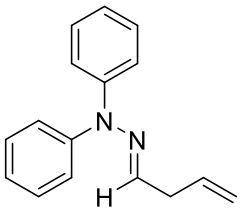
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
269.0535	1	C 9 H 9 N 4 O 6	269.0528	-2.9	-0.8	10.4	-2.4

Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

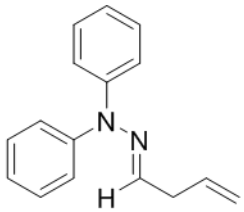


Compound **18**

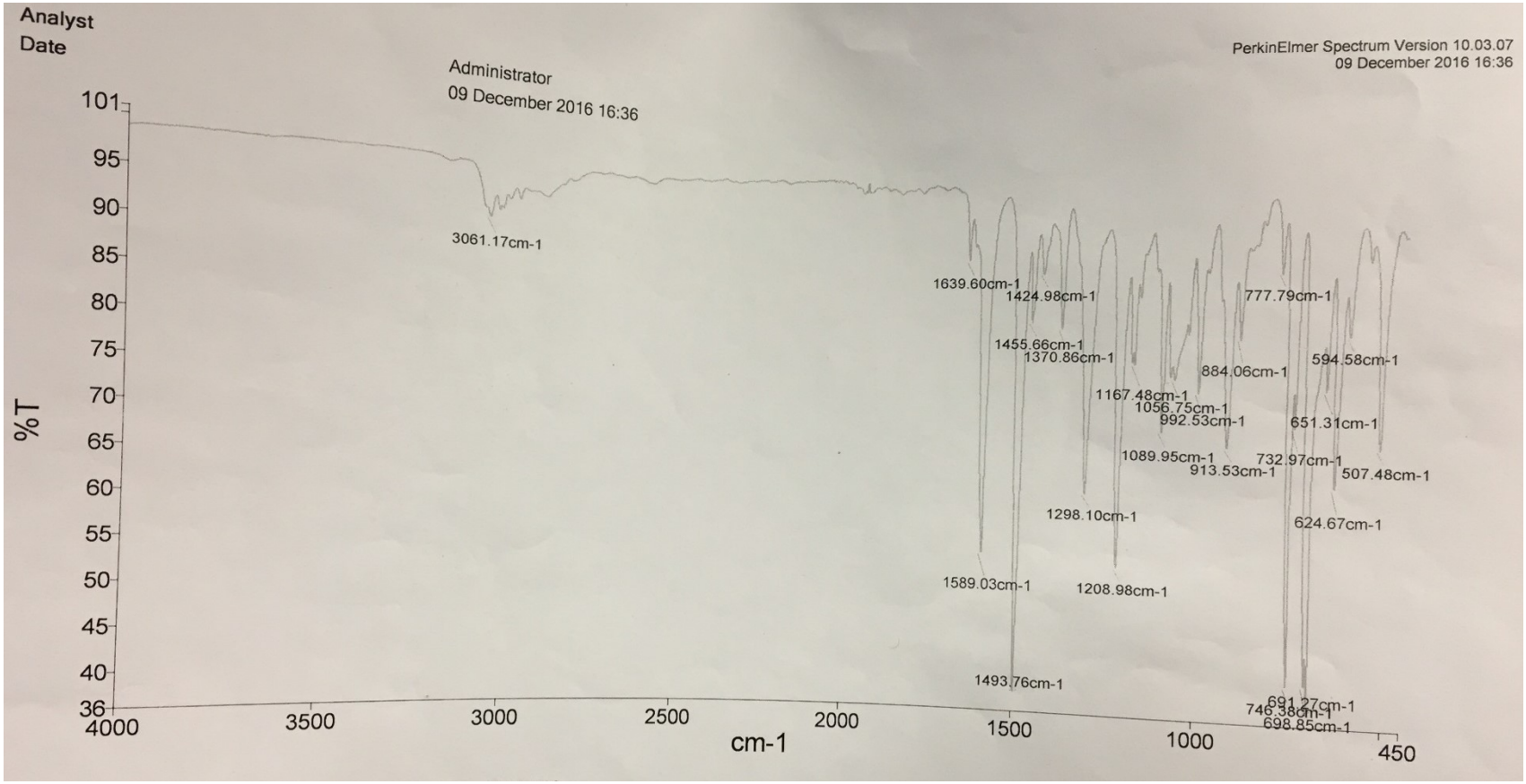
Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^{13}C



Compound **18**



Compound 18


Analyst
Date
Administrator
09 December 2016 16:36
PerkinElmer Spectrum Version 10.03.07
09 December 2016 16:36
%T
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1639.60cm-1
1424.98cm-1
777.79cm-1
1455.66cm-1
1370.86cm-1
884.06cm-1
594.58cm-1
1167.48cm-1
1056.75cm-1
992.53cm-1
651.31cm-1
1089.95cm-1
913.53cm-1
732.97cm-1
507.48cm-1
1298.10cm-1
624.67cm-1
1589.03cm-1
1208.98cm-1
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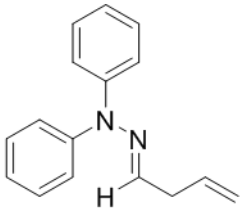
691.27cm-1
746.38cm-1
698.85cm-1



Compound 18

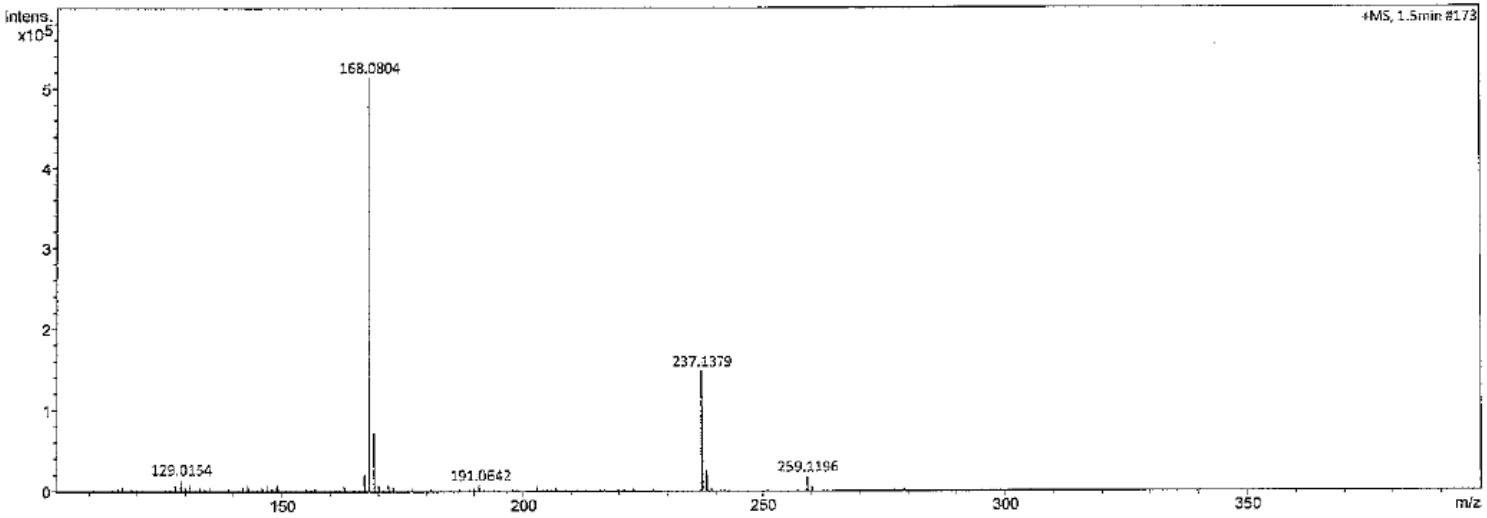
ams-7-80

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

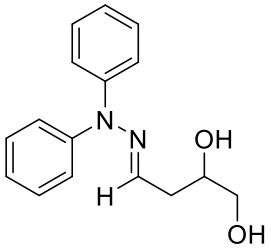
Acquisition Date 12/12/2016 09:54:50

Analysis Filename	pac62310as_P1-B-9_01_1739.d
Method	400p_acn1260_2c1s.m
Submission Name	pac62310as
Instrument	micrOTOF
ESI	Positive



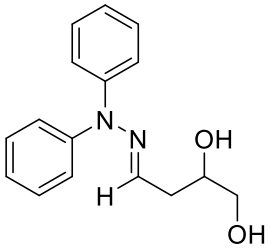
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
237.1379	1	C16H17N2	237.1386	-3.1	-0.7	7.5	2.9
259.1196	1	C16H16N2Na	259.1206	-3.7	-1.0	10.1	4.8

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

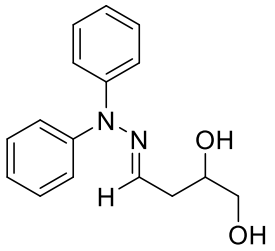


Compound **14**

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^{13}C



Compound **14**



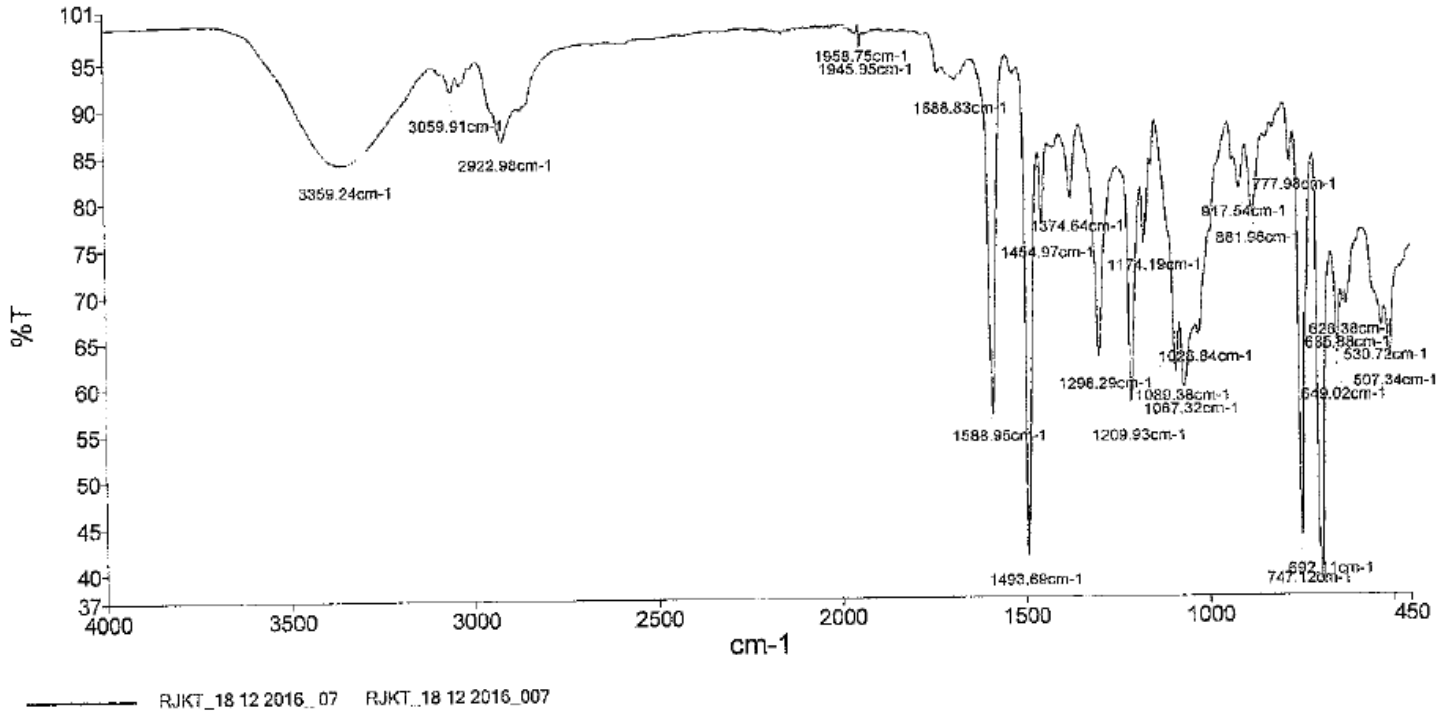
AMS-7-86

Compound **14**

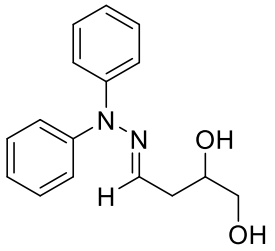
PerkinElmer Spectrum Version 10.03.07
18 December 2016 15:58

Analyst
Date

Administrator
18 December 2016 15:58



Page 1



Compound **14**

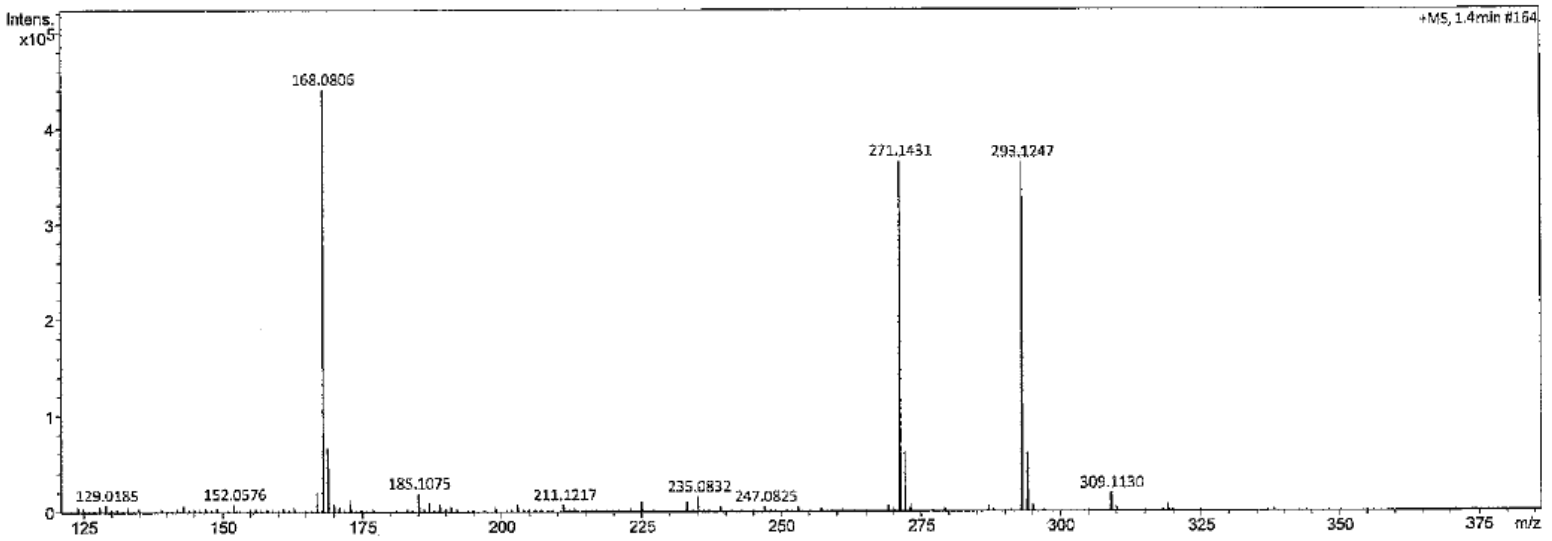
ams-7-86 cr

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

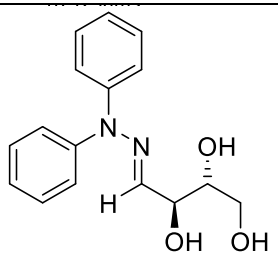
Acquisition Date 14/12/2016 13:57:53

Analysis Filename	pac62374as_P1-C-5_01_1816.d
Method	400p_lcms_2c1s.m
Submission Name	pac62374as
Instrument	micrOTOF
ESI	Positive



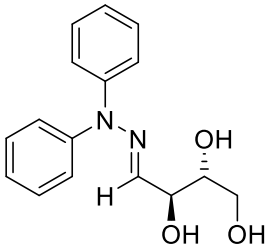
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
271.1431	1	C16H19N2O2	271.1441	-3.5	-1.0	7.6	3.2
293.1247	1	C16H18N2NaO2	293.1260	-4.7	-1.4	10.0	4.5

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

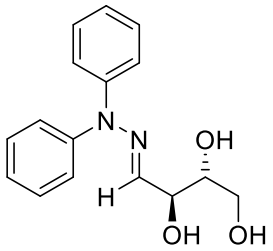


Compound **15 A**

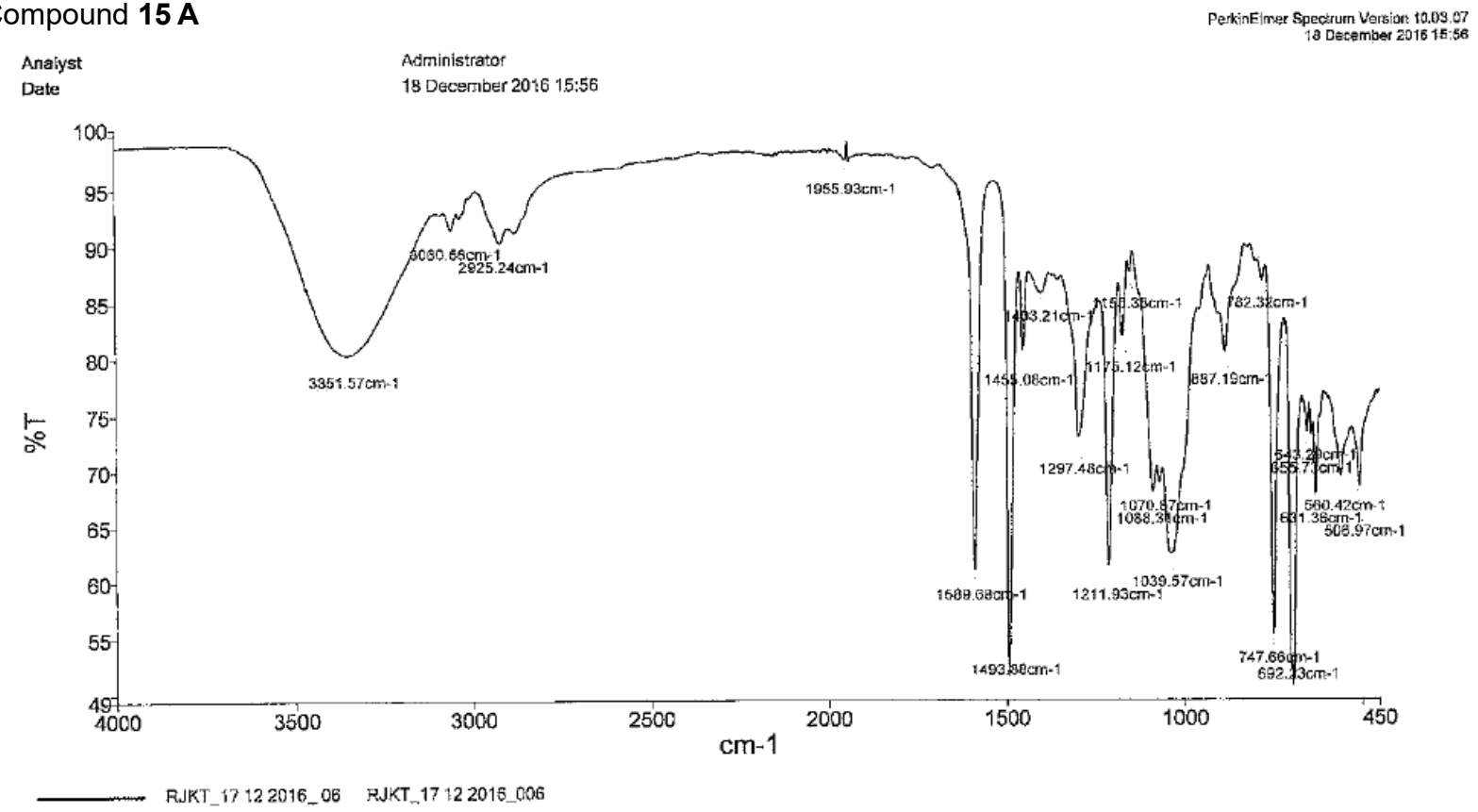
Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^{13}C

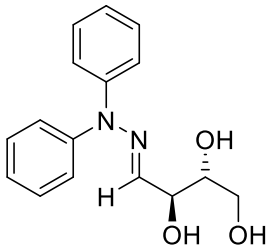


Compound **15 A**



Compound **15 A**





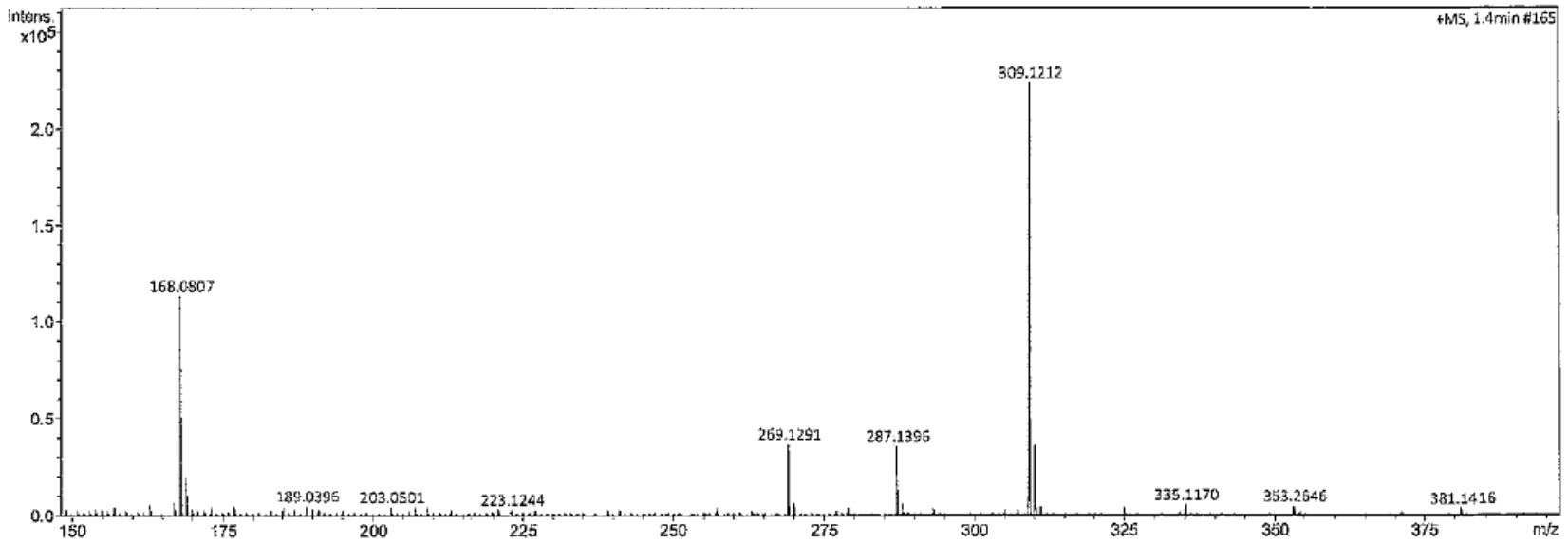
Compound **15 A**

ams-7-81

York - Chemistry - Mass Spectrometry Service Report

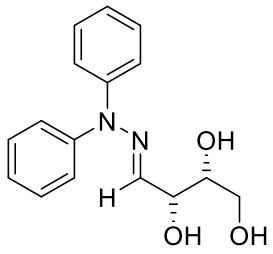
Analysis Information

Analysis Filename	pac62317as_P1-C-6_01_1745.d	Acquisition Date	12/12/2016 14:15:59
Method	400p_acn1260_2c1s.m		
Submission Name	pac62317as		
Instrument	micrOTOF		
ESI	Positive		



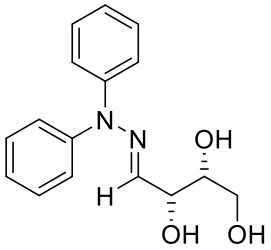
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
287.1396	1	C16H19N2O3	287.1390	1.9	0.5	10.2	-2.0
309.1212	1	C16H18N2NaO3	309.1210	0.7	0.2	12.4	-0.8

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

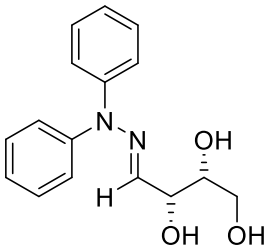


Compound **15 B**

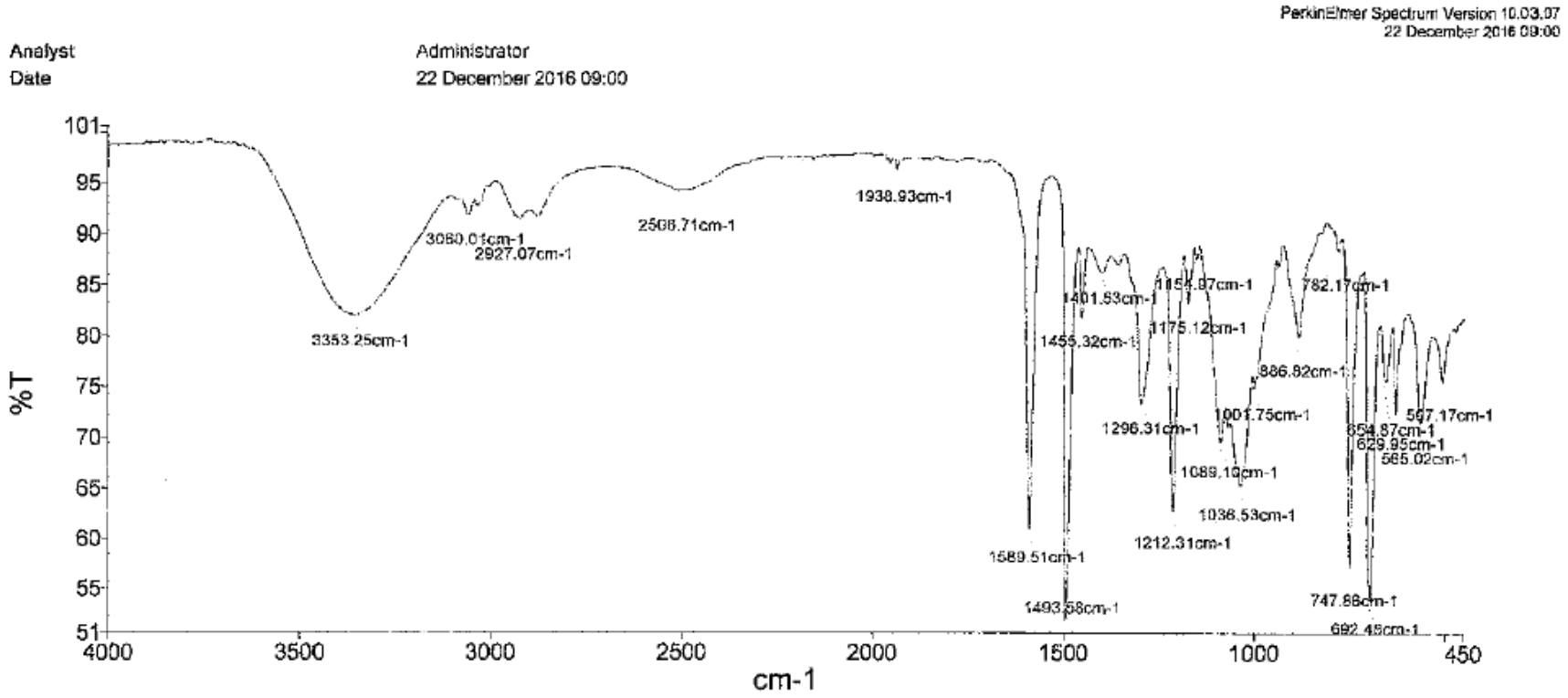
Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^{13}C

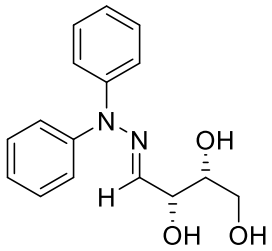


Compound **15 B**



Compound **15 B**





Compound **15 B**

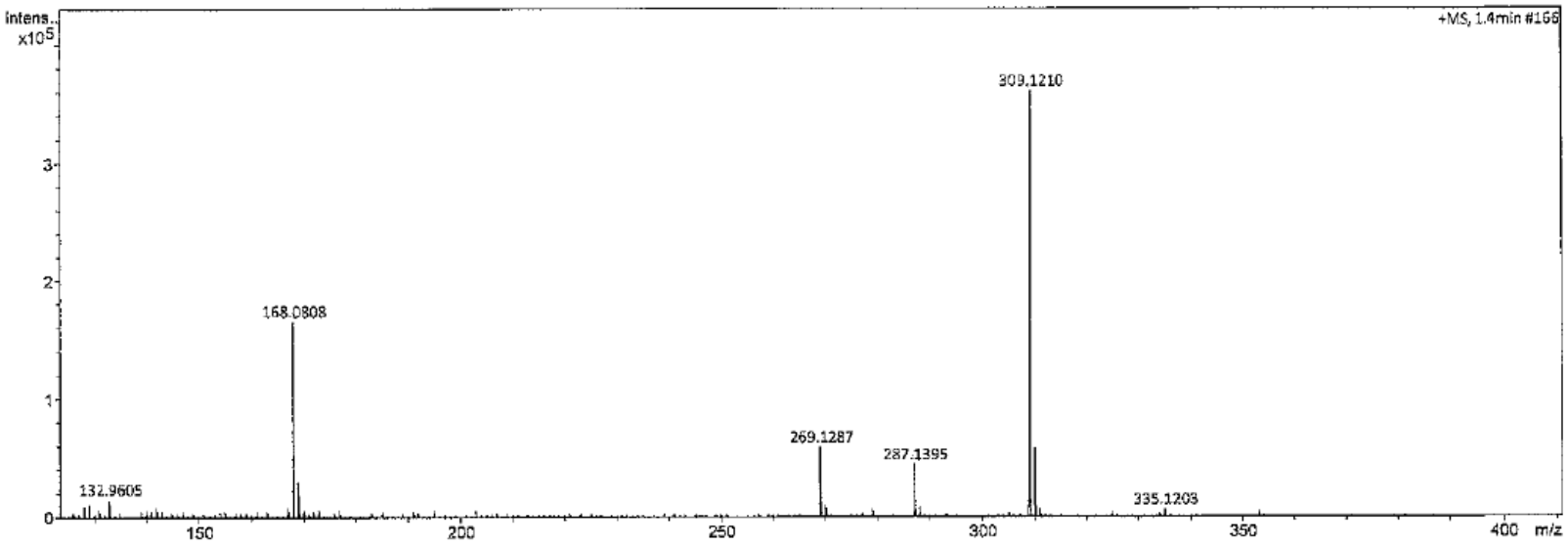
ams-7-87

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

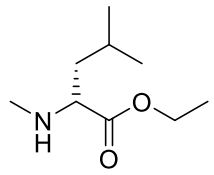
Analysis Filename	pac62368as_P1-B-8_01_1810.d
Method	400p_lcms_2c1s.m
Submission Name	pac62368as
Instrument	micrOTOF
ESI	Positive

Acquisition Date 14/12/2016 11:49:11



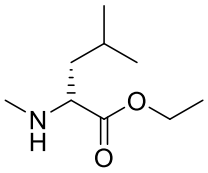
Meas. m/z	#	Ion Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
287.1395	1	C16H19N2O3	287.1390	1.5	0.4	2.4	-1.0
309.1210	1	C16H18N2NaO3	309.1210	-0.1	-0.0	13.4	-0.4

Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

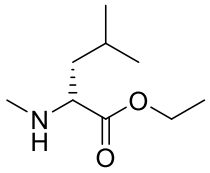


Compound **D-8**

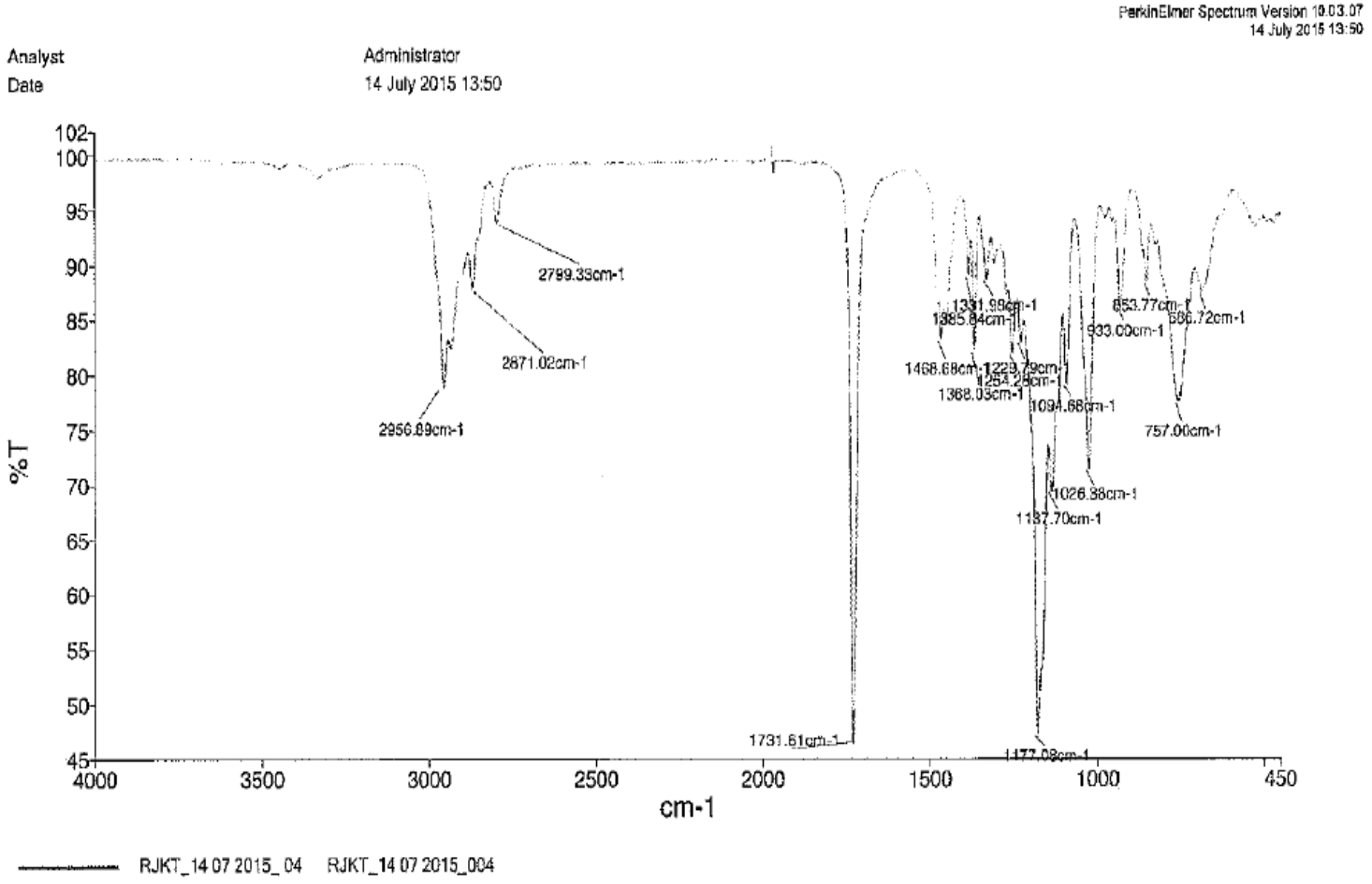
Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C



Compound **D-8**



Compound **D-8**


PerkinElmer Spectrum Version 10.03.07
14 July 2015 13:50
Analyst
Administrator
Date
14 July 2015 13:50
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2799.33cm-1
1731.61cm-1
1468.68cm-1
1385.84cm-1
1368.03cm-1
1254.25cm-1
1177.08cm-1
1137.70cm-1
1094.68cm-1
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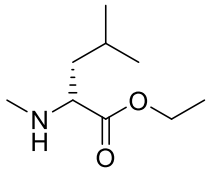
757.00cm-1
RJKT_14 07 2015_04
RJKT_14 07 2015_004



Compound **D-8**

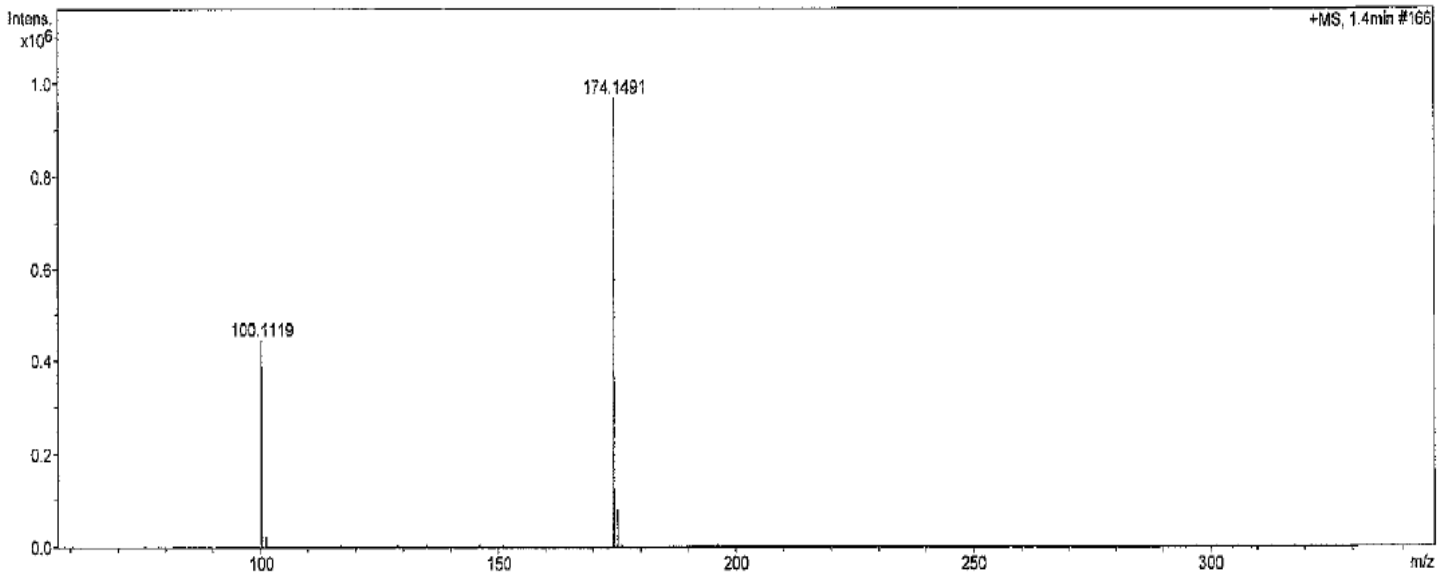
ams-4-37 cr

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

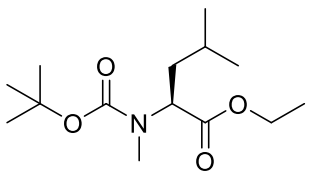
Acquisition Date 14/07/2015 12:27:44

Analysis Filename	pac53551as_P1-D-4_01_59783.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac53551as
Instrument	micrOTOF
ESI	Positive



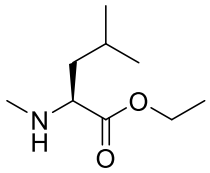
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
174.1491	1	C 9 H 20 N O 2	174.1489	-1.6	-0.3	10.9	-1.5

Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H



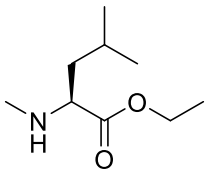
Compound **L-18**

Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

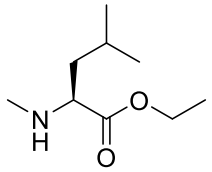


Compound **L-8**

Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C



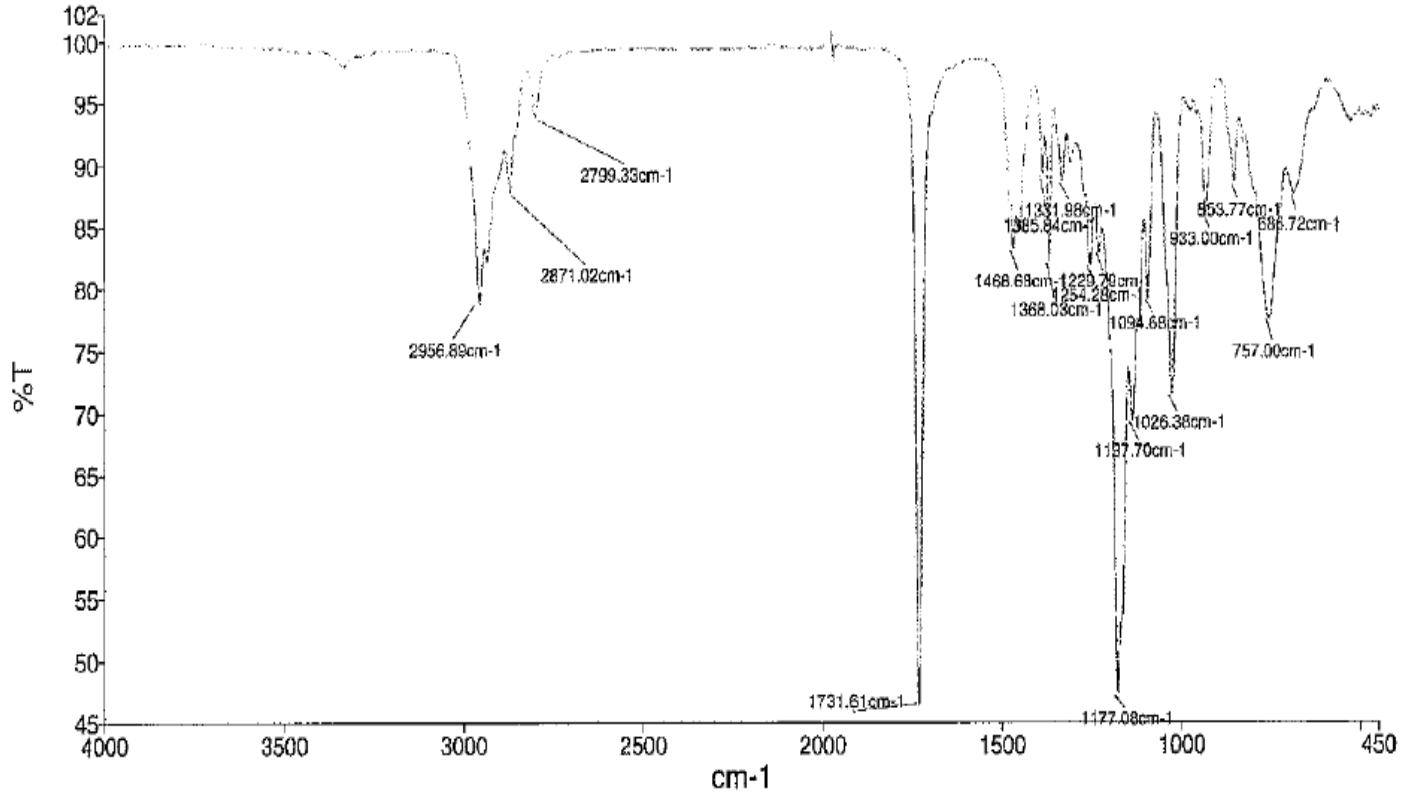
Compound **L-8**



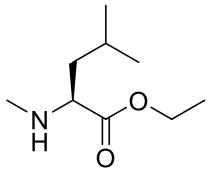
Compound **L-8**

PerkinElmer Spectrum Version 10.03.07
14 July 2015 13:49

Analyst Administrator
Date 14 July 2015 13:49



RJKT_14 07 2015_04 RJKT_14 07 2015_004



Compound **L-8**

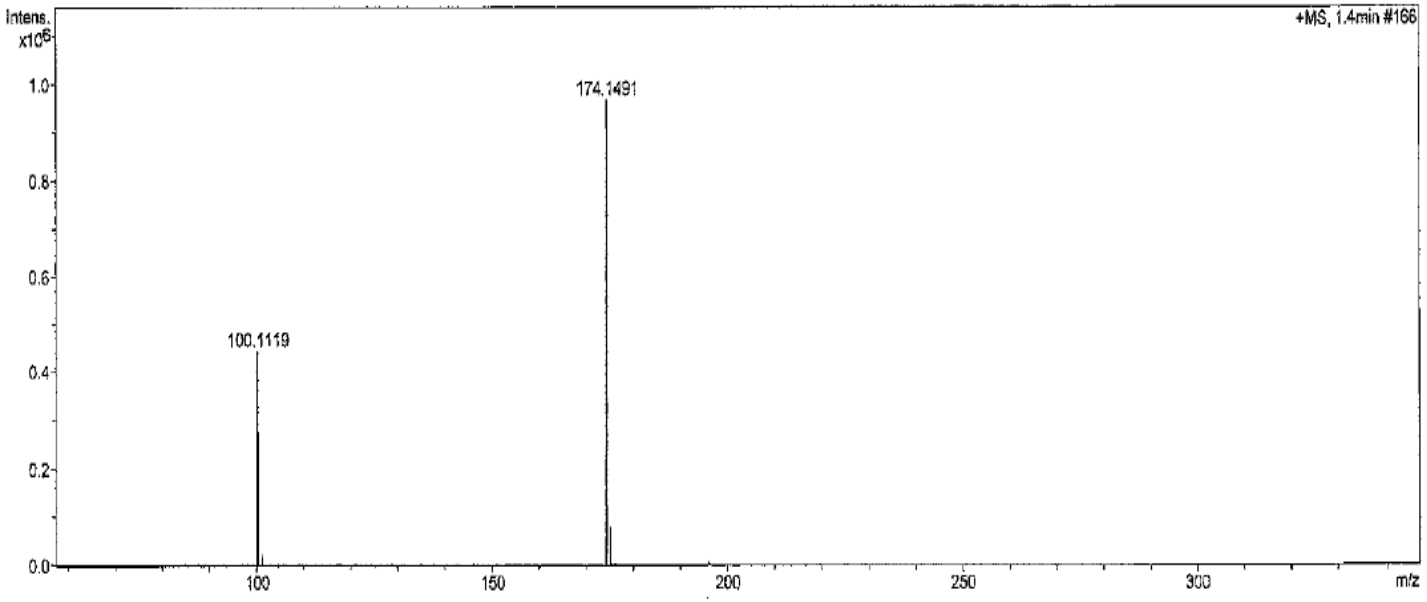
ams-4-37 cr

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

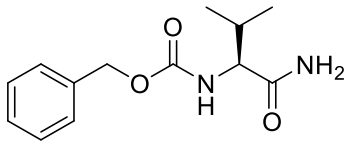
Acquisition Date 14/07/2015 12:27:44

Analysis Filename	pac53551as_P1-D-4_01_59783.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac53551as
Instrument	micrOTOF
ESI	Positive



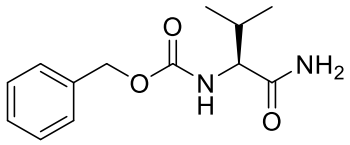
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
174.1491	1	C 9 H 20 N O 2	174.1489	-1.6	-0.3	10.9	-1.5

Parameter	Value
1) Solvent	d^6 DMSO
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

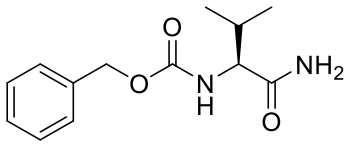


Compound **21**

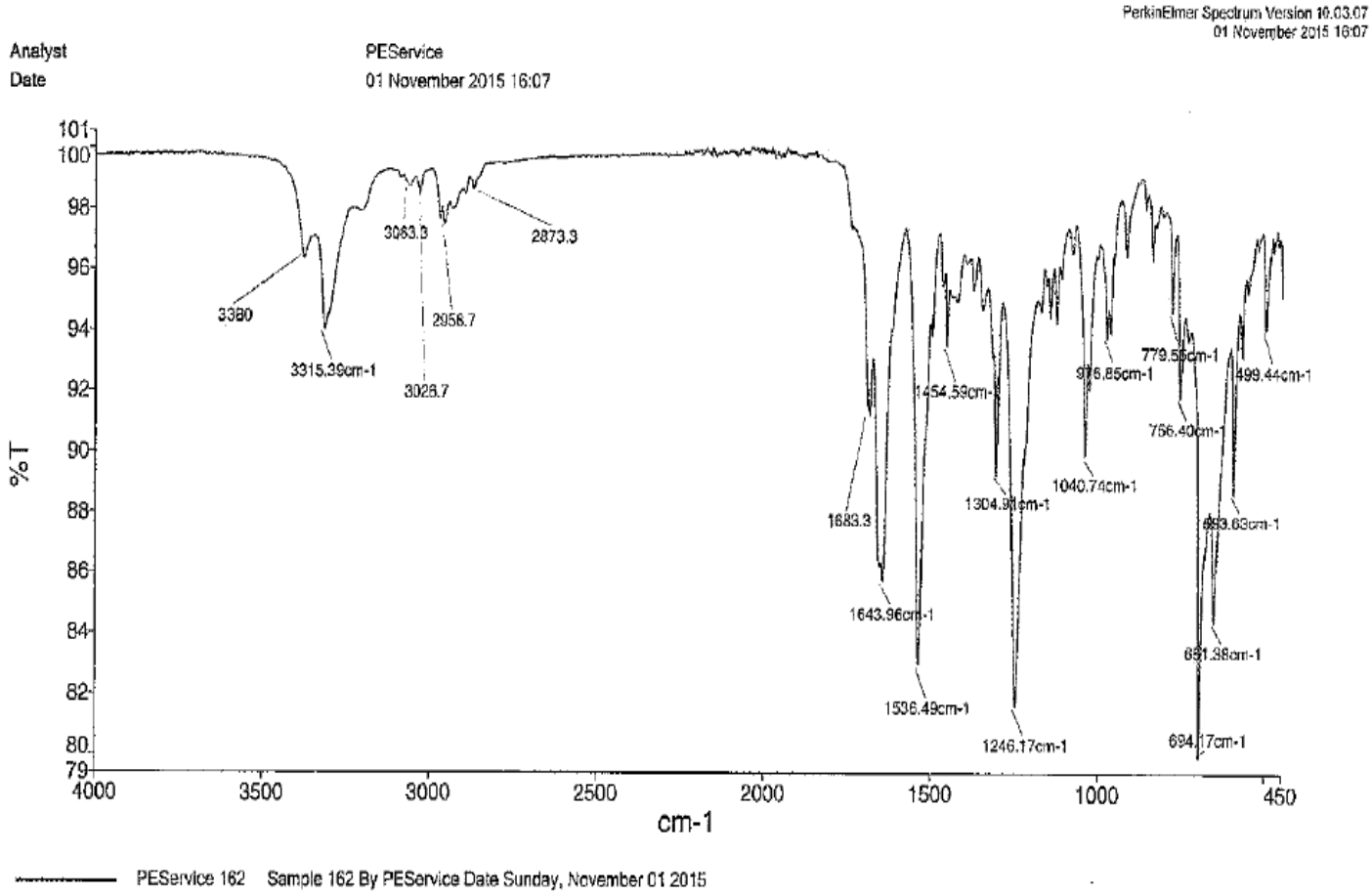
Parameter	Value
1) Solvent	d^6 DMSO
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C



Compound **21**


O
O
N
H
NH2
O

Compound **21**


PerkinElmer Spectrum Version 10.03.07
01 November 2015 16:07
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PEService
Date
01 November 2015 16:07
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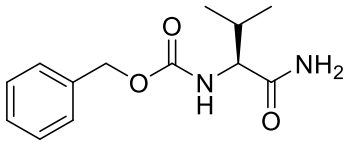
1643.96cm-1
1536.49cm-1
1454.59cm-1
1304.91cm-1
1246.17cm-1
1040.74cm-1
976.85cm-1
779.55cm-1
756.40cm-1
694.17cm-1
499.44cm-1
PEService 162 Sample 162 By PEService Date Sunday, November 01 2015



Compound **21**

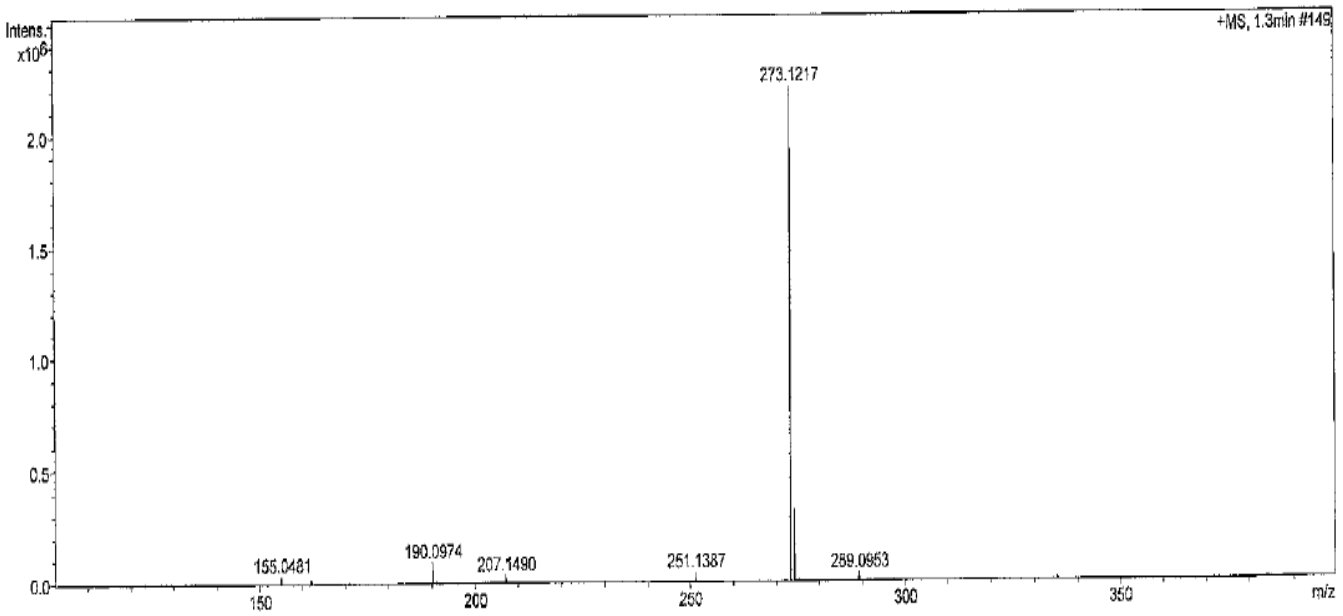
ams-5-16-separation

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

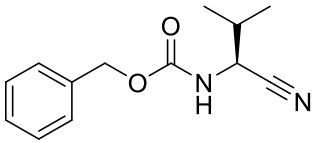
Acquisition Date 14/10/2015 09:41:57

Analysis Filename	pac55038as_P1-D-3_01_61494.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac55038as
Instrument	micrOTOF
ESI	Positive



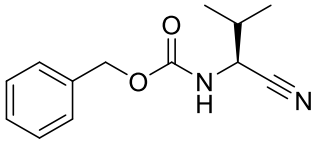
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
251.1387	1	C 13 H 19 N 2 O 3	251.1390	1.3	0.3	27.9	1.4
273.1217	1	C 13 H 18 N 2 Na O 3	273.1210	-2.6	-0.7	5.3	-2.0

Parameter	Value
1) Solvent	d^6 DMSO
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

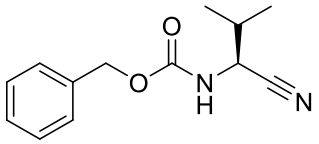


Compound **22**

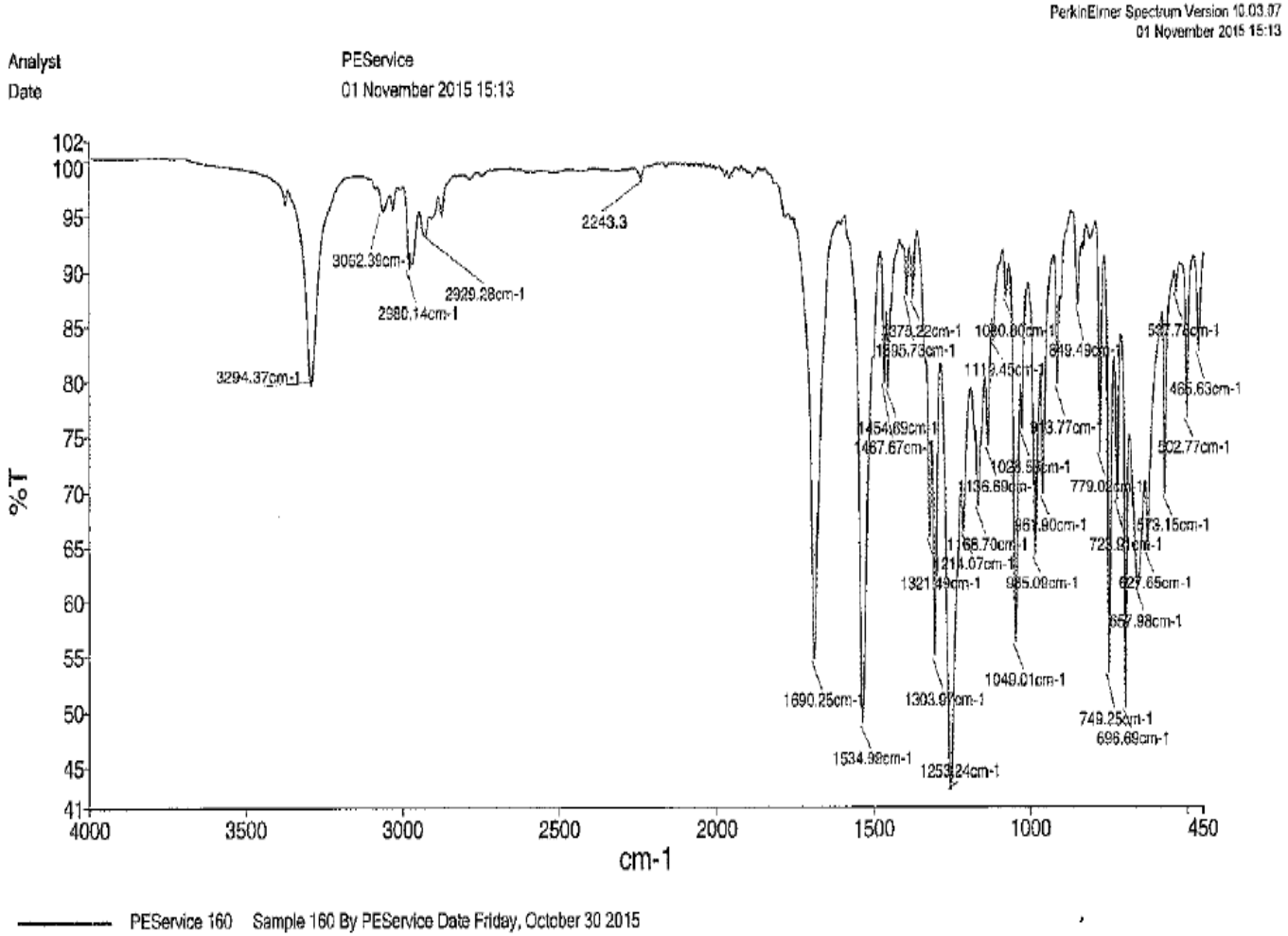
Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

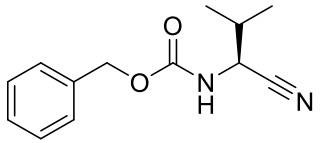


Compound **22**



Compound **22**


PerkinElmer Spectrum Version 10.03.07
01 November 2015 15:13
Analyst
PEService
Date
01 November 2015 15:13
%T
cm-1
3294.37cm-1
3052.39cm-1
2980.14cm-1
2929.28cm-1
2243.3
1690.25cm-1
1534.98cm-1
1303.97cm-1
1253.24cm-1
1049.01cm-1
985.09cm-1
749.25cm-1
698.69cm-1
PEService 160 Sample 160 By PEService Date Friday, October 30 2015



Compound **22**

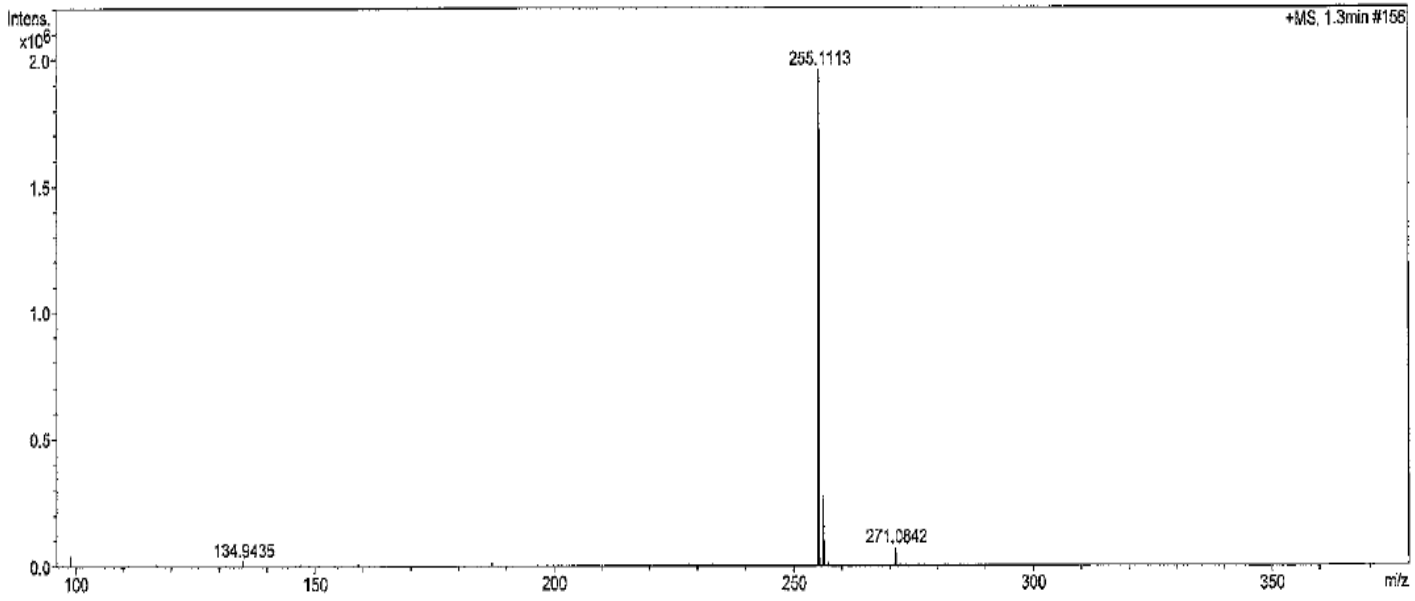
AMS-5-22

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

Acquisition Date 21/10/2015 11:14:41

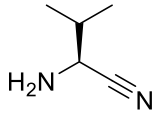
Analysis Filename	Pac55159as_P1-D-1_01_61641.d
Method	400p_meoh1260_2c1s.m
Submission Name	Pac55159as
Instrument	micrOTOF
ESI	Positive



Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
255.1113	1	C 13 H 16 N 2 Na O 2	255.1104	-3.6	-0.9	5.7	-3.1

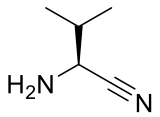
Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

r7180ams
A Steer ams-6-68-base wash

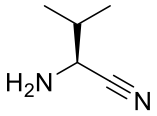


Compound **10**

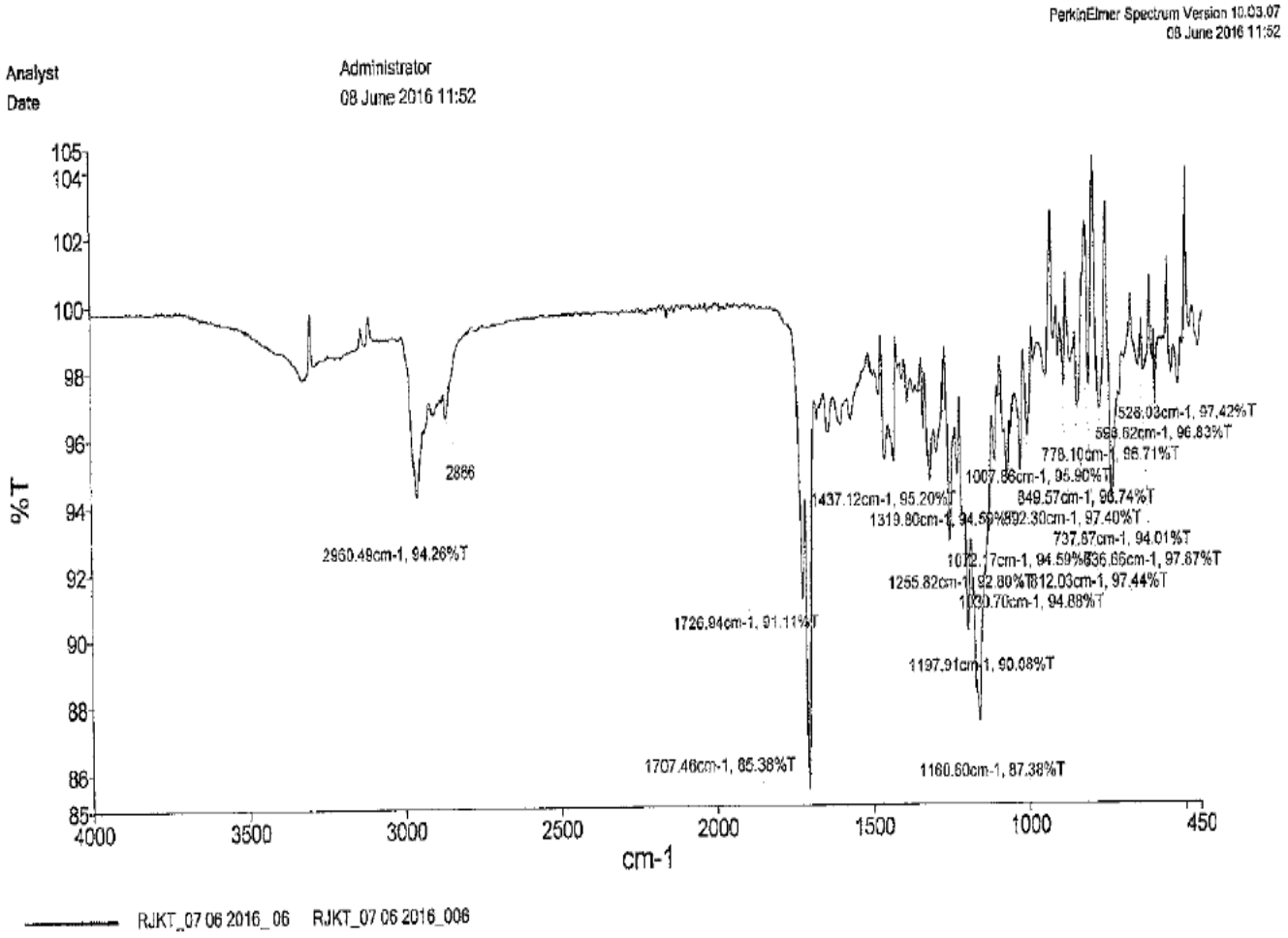
Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C

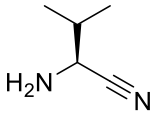


Compound **10**



Compound **10**


PerkinElmer Spectrum Version 10.03.07
08 June 2016 11:52
Analyst
Date
Administrator
08 June 2016 11:52
%T
cm-1
2960.49cm-1, 94.26%T
2886
1726.94cm-1, 91.11%T
1707.46cm-1, 85.38%T
1437.12cm-1, 95.20%T
1319.80cm-1, 94.59%T
1255.82cm-1, 92.80%T
1197.91cm-1, 90.08%T
1160.60cm-1, 87.38%T
1007.86cm-1, 95.90%T
892.30cm-1, 97.40%T
849.57cm-1, 96.74%T
778.10cm-1, 96.71%T
737.87cm-1, 94.01%T
636.66cm-1, 97.87%T
612.03cm-1, 97.44%T
528.03cm-1, 97.42%T
RJKT_07 06 2016_06
RJKT_07 06 2016_006



Compound **10**

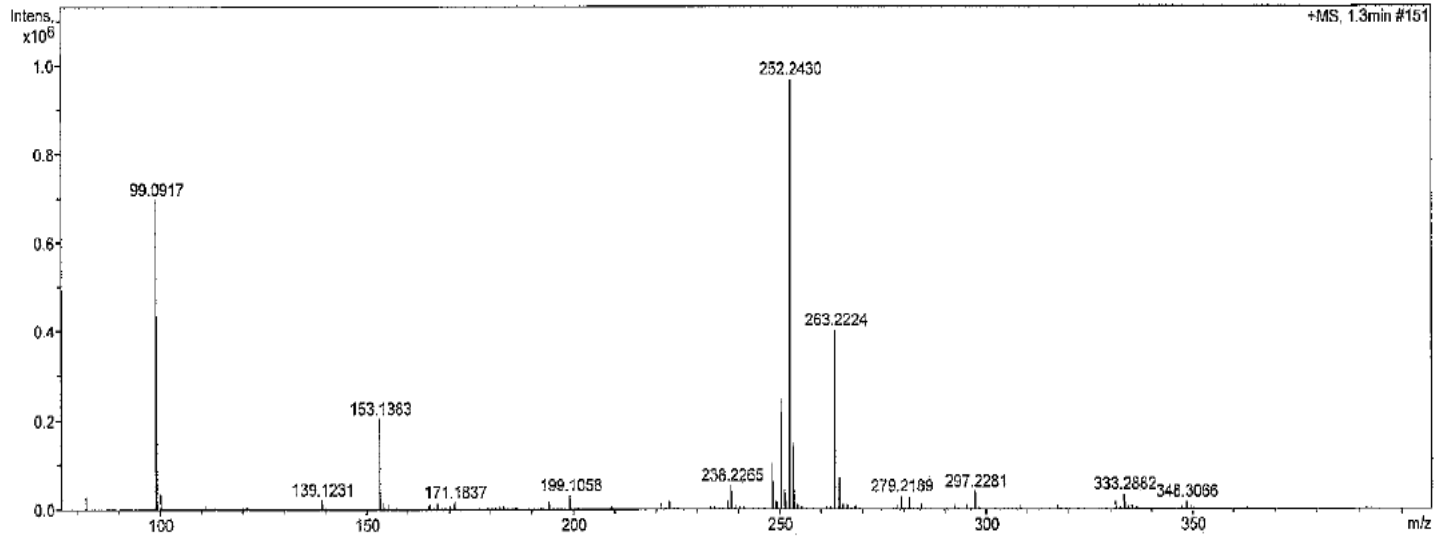
ams-5-32

York - Chemistry - Mass Spectrometry Service Report

Analysis Information

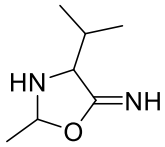
Acquisition Date 04/11/2015 16:15:46

Analysis Filename	pac55488as_P1-E-2_01_61998.d
Method	200p_meoh1260_2c1s.m
Submission Name	pac55488as
Instrument	micrOTOF
ESI	Positive



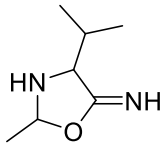
Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
99.0917	1	C 5 H 11 N 2	99.0917	0.1	0.0	7.0	0.3

Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

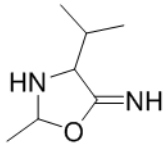


Compound **17**

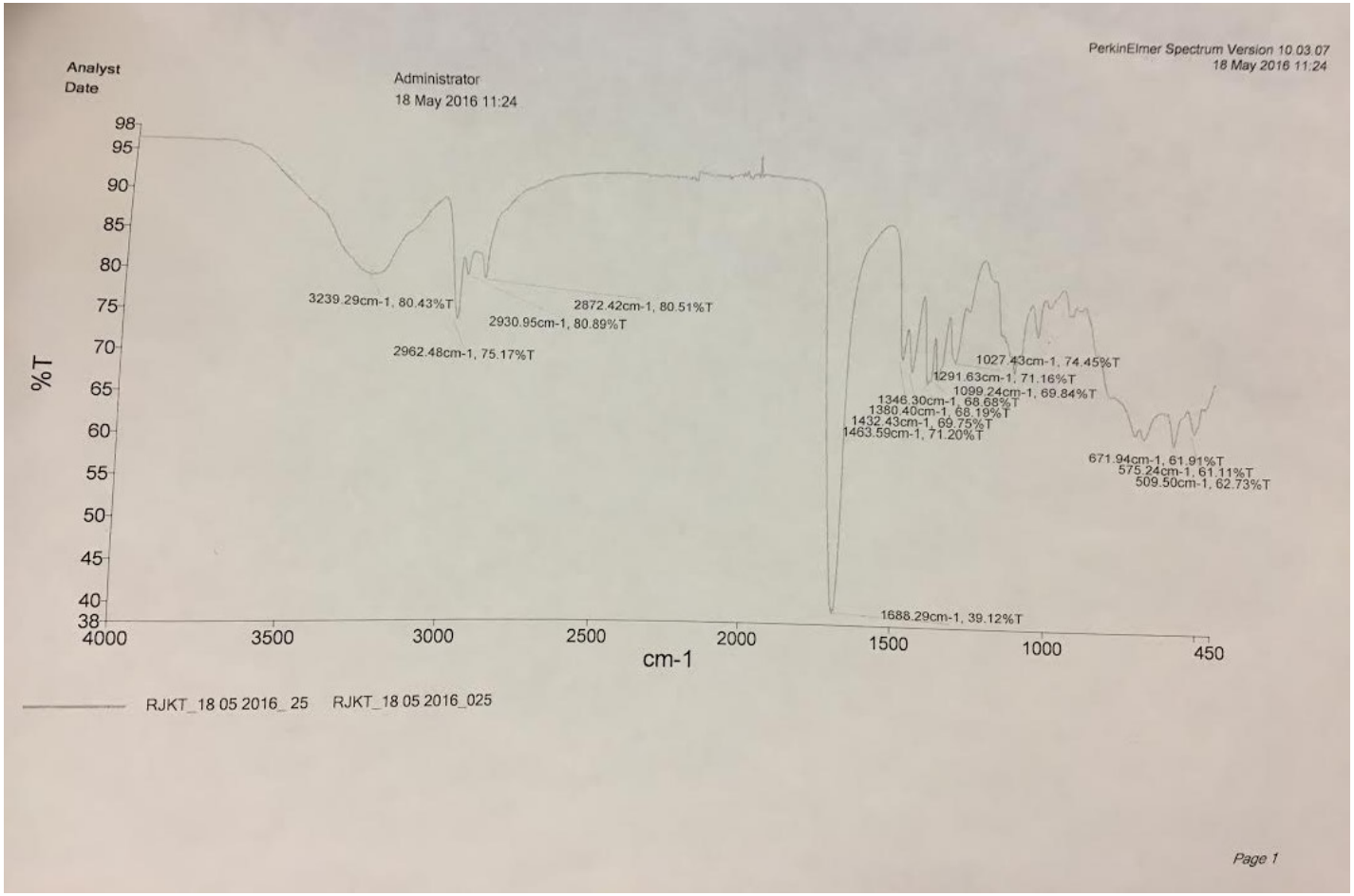
Parameter	Value
1) Solvent	$CDCl_3$
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

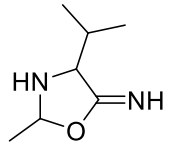


Compound **17**


HN
NH
O

Compound 17


PerkinElmer Spectrum Version 10.03.07
18 May 2016 11:24
Analyst
Date
Administrator
18 May 2016 11:24
%T
cm-1
3239.29cm-1, 80.43%T
2962.48cm-1, 75.17%T
2930.95cm-1, 80.89%T
2872.42cm-1, 80.51%T
1688.29cm-1, 39.12%T
1463.59cm-1, 71.20%T
1432.43cm-1, 69.75%T
1380.40cm-1, 68.19%T
1346.30cm-1, 68.68%T
1291.63cm-1, 71.16%T
1099.24cm-1, 69.84%T
1027.43cm-1, 74.45%T
671.94cm-1, 61.91%T
575.24cm-1, 61.11%T
509.50cm-1, 62.73%T
RJKT_18 05 2016_ 25
RJKT_18 05 2016_025
Page 1



Compound **17**

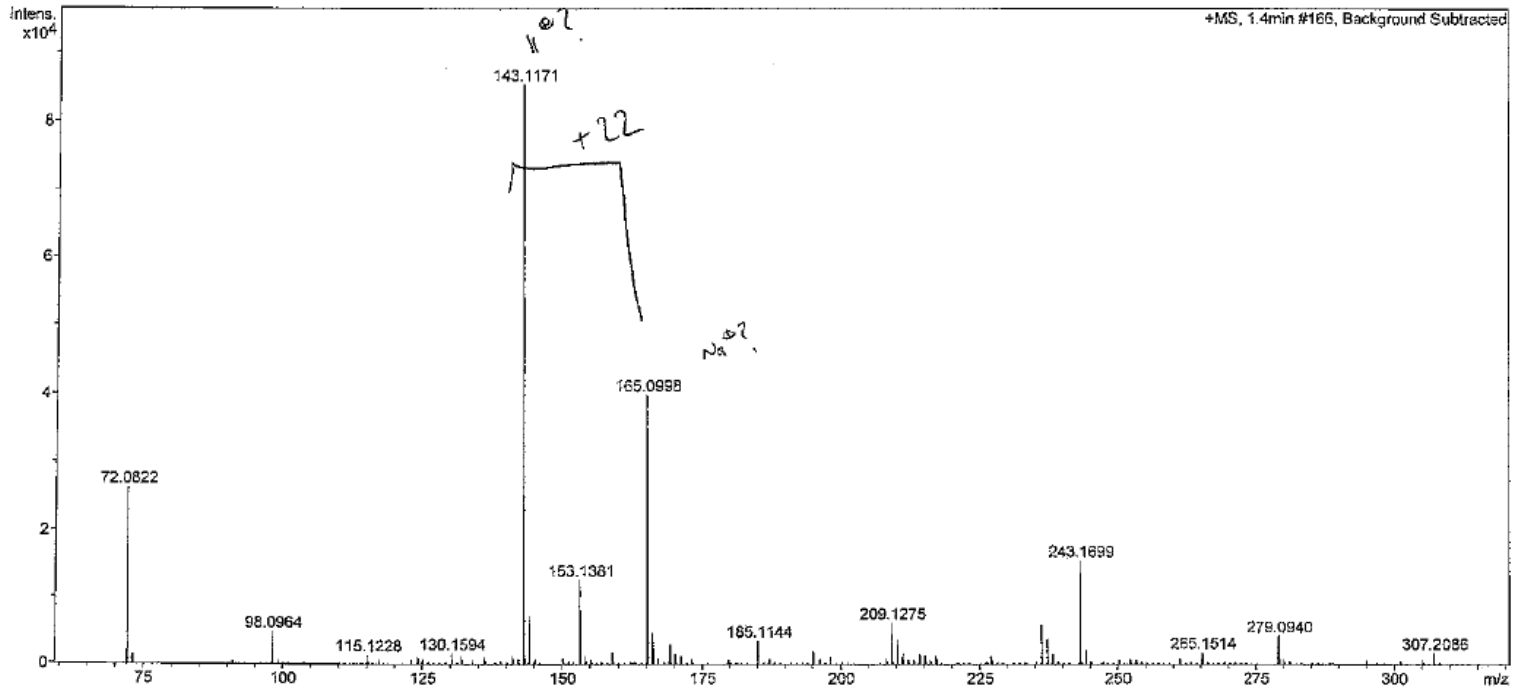
AMS-6-49-A

York - Chemistry - Mass Spectrometry Service Report

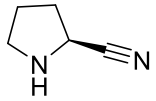
Analysis Information

Acquisition Date 18/05/2016 10:03:46

Analysis Filename	pac59036as_P1-B-7_01_66524.d
Method	400p_acn1260_2c1s.m
Submission Name	pac59036as
Instrument	micrOTOF
ESI	Positive

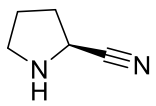


Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H

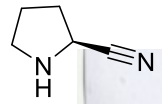


Compound **9**

Parameter	Value
1) Solvent	d^4 methanol
2) Spectrometer Frequency	100 MHz
3) Nucleus	^{13}C



Compound **9**

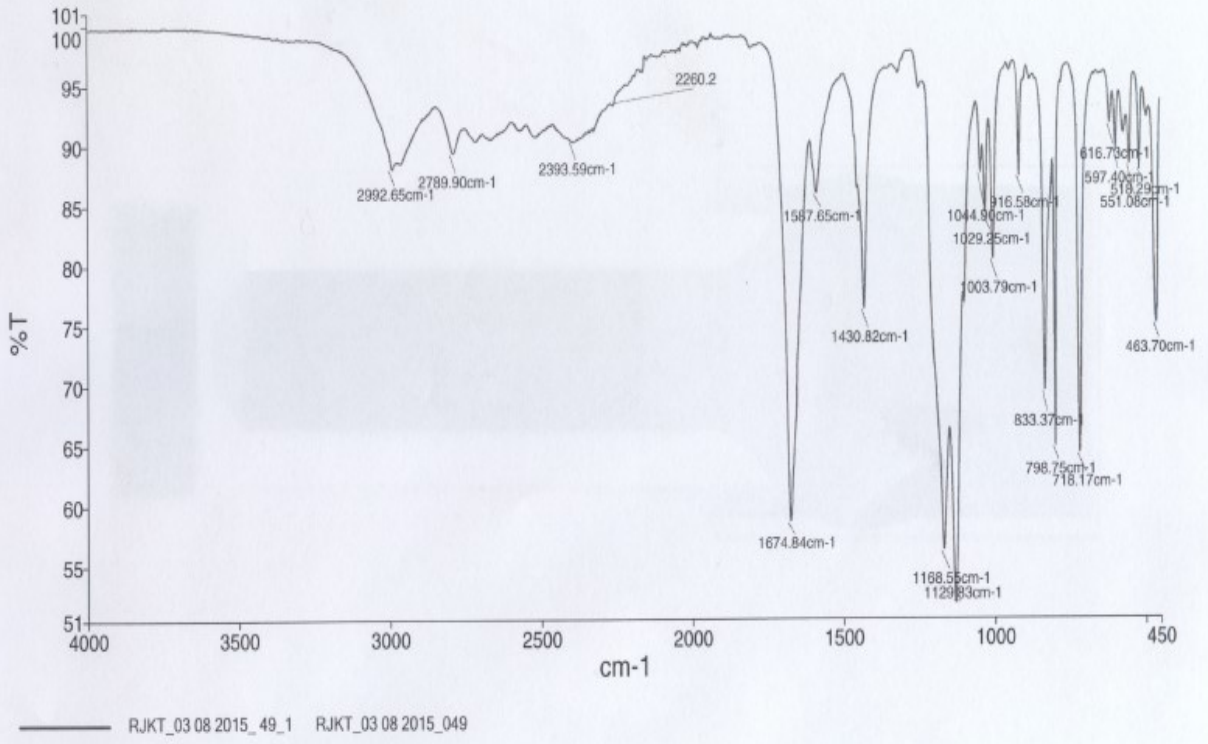


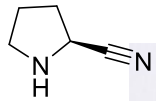
Compound **9**

PerkinElmer Spectrum Version 10.03.07
04 August 2015 10:11

Analyst
Date

Administrator
04 August 2015 10:11





Compound **9**

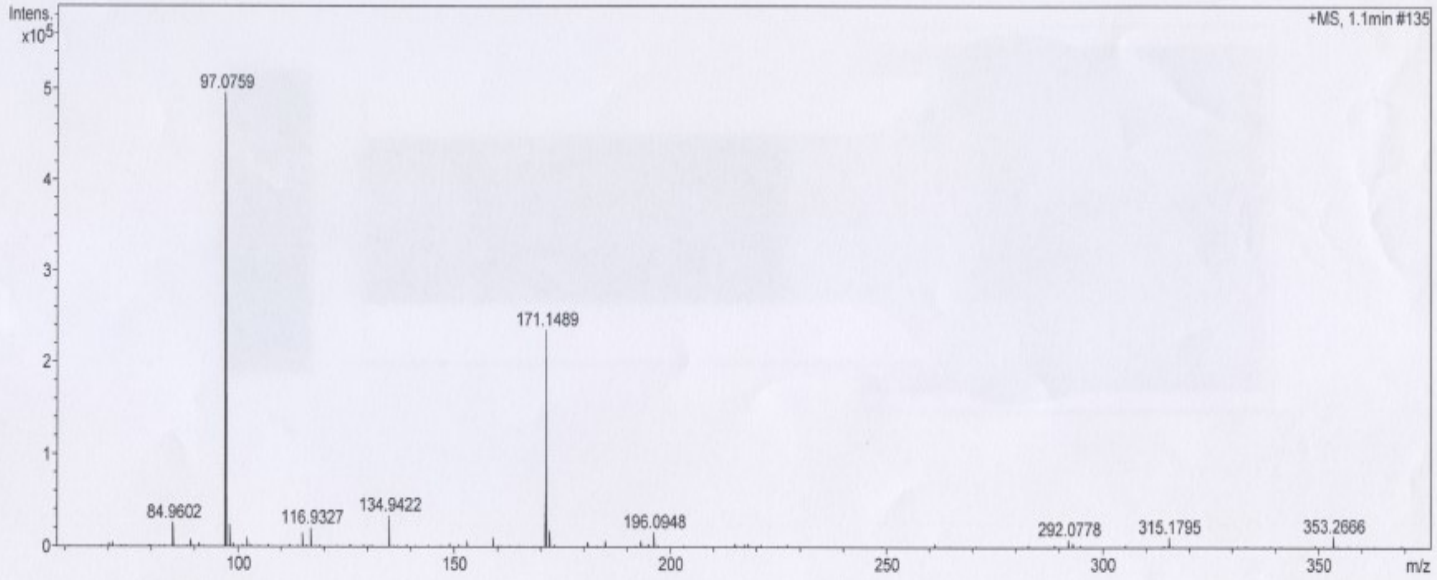
nb-01-32

York - Chemistry - Mass Spectrometry Service Report

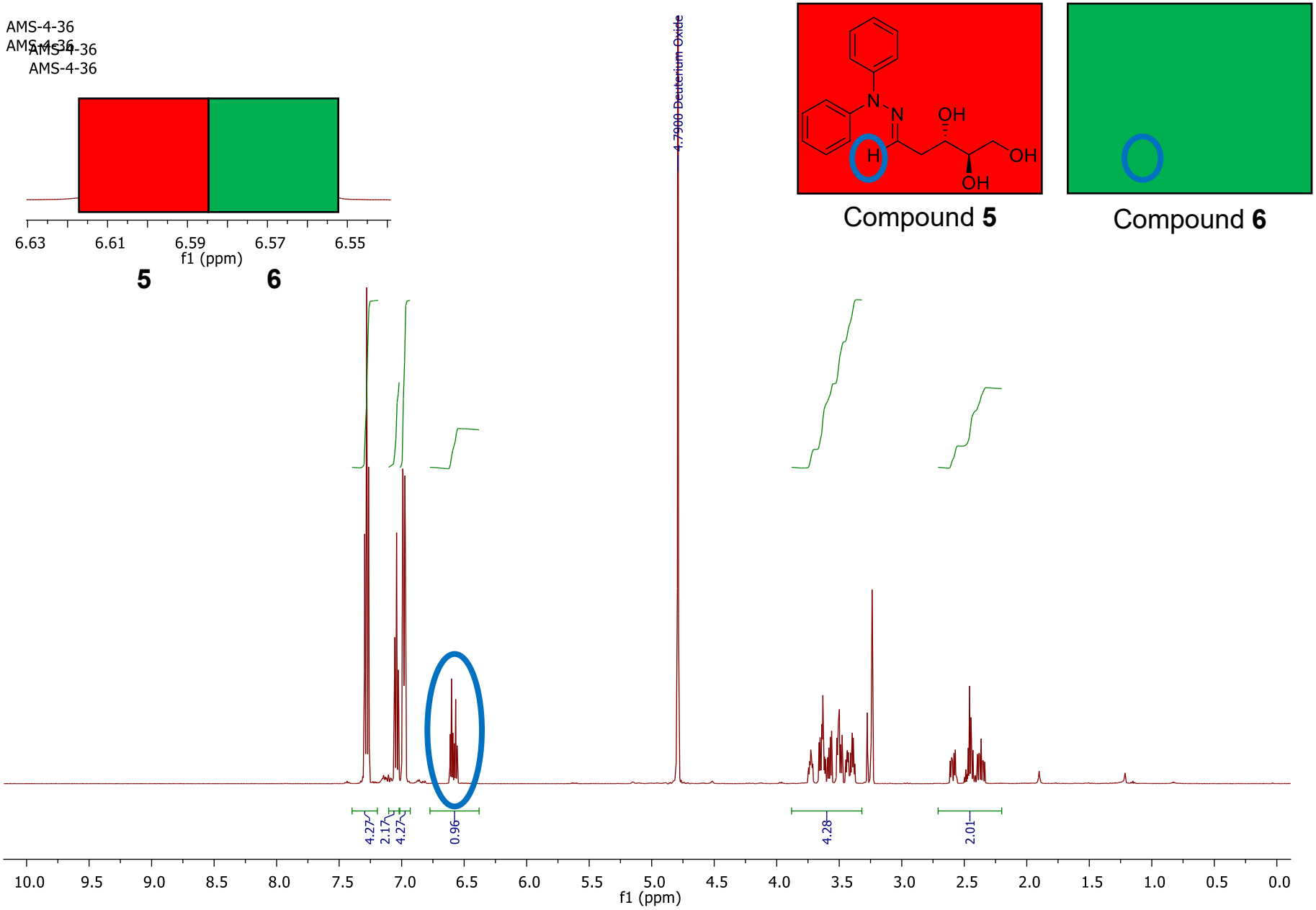
Analysis Information

Acquisition Date 11/06/2015 11:03:21

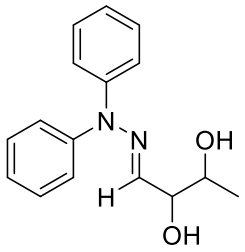
Analysis Filename	pac52991nb_P1-E-2_01_59169.d
Method	400p_meoh1260_2c1s.m
Submission Name	pac52991nb
Instrument	micrOTOF
ESI	Positive



Meas. m/z	#	Formula	m/z	err [ppm]	err [mDa]	mSigma	Mean err [ppm]
97.0759	1	C 5 H 9 N 2	97.0760	0.9	0.1	7.0	1.1

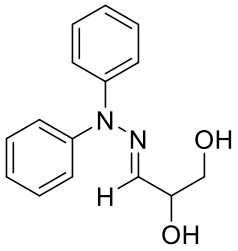

AMS-4-36
AMS-4-36
AMS-4-36
AMS-4-36
6.63
6.61
6.59
6.57
6.55
f1 (ppm)
5
6
4.7980 Deuterium Oxide
N
N
OH
OH
OH
H
Compound 5
Compound 6
4.27
2.17
4.27
0.96
4.28
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H



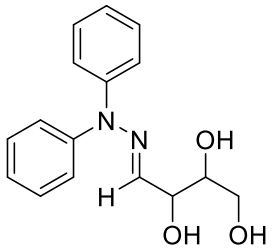
Compound **12** from one pot synthesis

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H



Compound **13** from one pot synthesis

Parameter	Value
1) Solvent	methanol d^4
2) Spectrometer Frequency	400 MHz
3) Nucleus	^1H



Compound **15** from one pot synthesis