Supporting Information

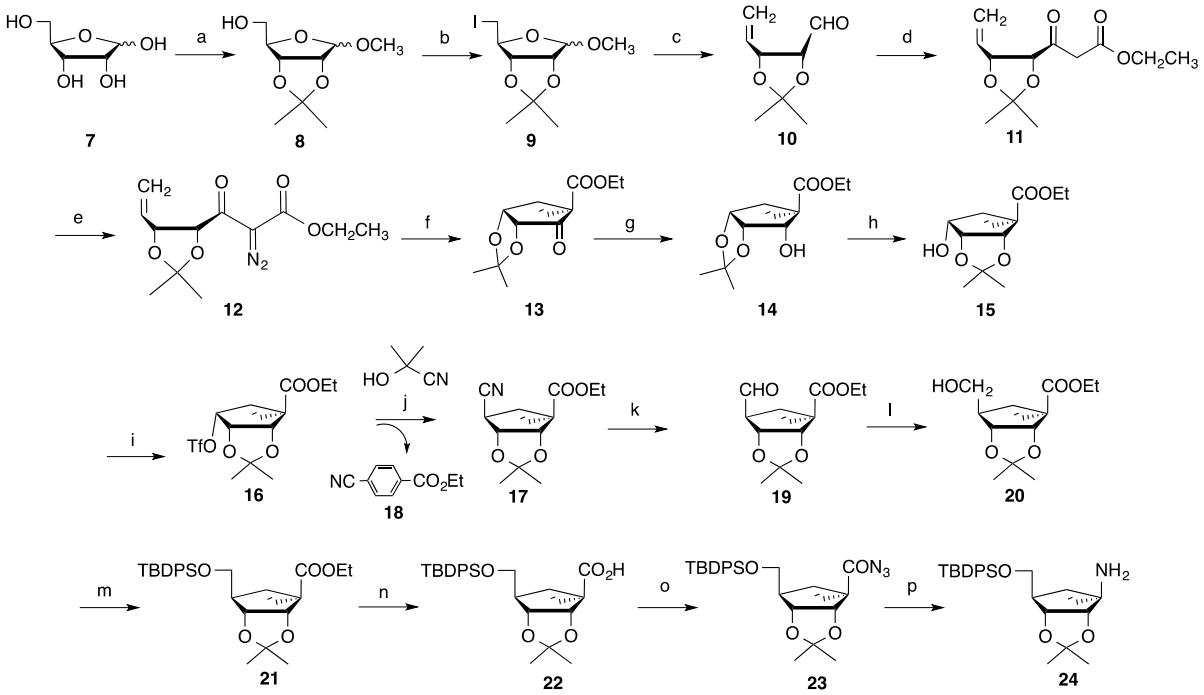
South (S)- and North (N)-Methanocarba-7-Deazaadenosine Analogues as Inhibitors of Human Adenosine Kinase

Kiran S. Toti, Danielle Osborne, Antonella Ciancetta, Detlev Boison, Kenneth A. Jacobson*

Contents:

A modification of the previously reported route[1,2] to intermediate **24** was devised in order to achieve a larger scale preparation. The major modification over the previously reported route was the use of acetone cyanohydrin/ LiH combination in place of lithium cyanide in a synthetically challenging 10th step. This led to a considerably higher ratio of product to byproduct for this step and resulted in the key intermediate **24** with 0.04% overall yield over 16 steps. The yield was largely limited by the low yield of the isopropylidene isomerization in step h, which was only 11% (barring that the total yield would be 0.34%). Other contributing low yield steps were d, f, g and n. An improvement would greatly increase the global yield and hence, further optimization may be needed before adapting this route to a production process.

Scheme S1: Synthesis of intermediate 24.



Reagents and conditions: (a) acetone, MeOH, HCl, overnight, rt, 91%; (b) PPh_3, I_2, imidazole, CH_3CN, toluene, 70 °C, 1 h, 85%; (c) Zn, MeOH, 60 °C, 20 min, 83%; (d) N_2CHCO_2Et, $SnCl_2$, CH_2Cl_2, 0 °C, 30 min, 38%; (e) TsN_3, CH_3CN, TEA, 0 °C, 30 min, 99%; (f) CuI, toluene, 80-83 °C, 36 h, 40%; (g) $NaBH_4$, EtOH, 15 °C, 1 h, 48%; (h) TFA, acetone, 22-25 °C, 40 h, 11%; (i) Tf_2O, pyridine, CH_2Cl_2, 0 °C, 30 min; (j) LiH, DMF, CH_2Cl_2, 75%, often lower yield, produces side product **18**; (k) H_2/Pd/C, MeOH, HOAc, 25 °C, 2 h, 79%; (l) $NaBH_4$, MeOH, rt, 30 min, 62%; (m) TBDPSCl, imidazole, DMF, 25 °C, overnight, 62%; (n) NaOH, 80 °C, 2 h, 48%; (o) $(PhO)_2P(O)Cl$, DIPEA, NaN_3, acetone, 22-25 °C, 30 min, 91%; (p) benzene, THF, H_2O, 30 min, rt, 74%.

[(4R,6R)-6-Methoxy-2,2-dimethyl-tetrahydro-2H-furo[3,4-d][1,3]dioxol-4-yl]methanol (8). Into a 20-L 4-necked round-bottom flask purged and maintained with an inert

atmosphere of nitrogen, was placed D-ribose **7** (2.00 kg, 13.32 mol, 1.00 equiv.), acetone (4.00 L), 2.2-dimethoxypropane (4.00 L) and methanol (4.00 L). The reaction mixture was cooled to 0 °C and added a saturated solution of hydrogen chloride in methanol (0.80 L) dropwise with stirring. The resulting solution was stirred overnight at room temperature. The *p*H was adjusted to 7 with aqueous $NaHCO_3$ and stirred for additional 40 min. The solids were removed by filtration, and the filtrate was concentrated under vacuum. The residue after concentration was dissolved in ethyl acetate (24 L) and washed with brine (24 L). The aqueous phase was extracted with ethyl acetate (12 L x 2) and the combined organic layer was dried over anhydrous sodium sulfate. The drying agent was filtered off and the filtrate concentrated under vacuum to give title compound as yellow oil. A total of 13 batches (26 kg) resulted in 32.5 kg of the title compound with 91% average yield.

(4S,6R)-4-(Iodomethyl)-6-methoxy-2,2-dimethyl-tetrahydro-2H-furo[3,4-d][1,3]dioxole (9). Into a 20-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **8** (1.60 kg, 7.83 moles, 1.00 equiv.), imidazole (0.80 kg, 11.74 moles, 1.50 equiv.), toluene (8.00 L), CH_3CN (2.00 L) and the mixture was stirred for 30 min. This was followed by the addition of PPh_3 (2157 g, 8.22 moles, 1.05 equiv.) portion wise with stirring and then at 40 °C was added I_2 (2381 g, 9.41 moles, 1.20 equiv.) in several batches with stirring. The reaction mixture was stirred at 70 °C for 1 h in an oil bath and then cooled to 0 °C with an ice/salt bath. The solids formed were removed by filtration and the filtrate was concentrated under vacuum. The residue was treated with hexane (32 L) and the solids formed were filtered off. Concentration of the filtrate under vacuum gave the title compound as yellow oil. A total of 20 batches (32.5 kg) resulted in 42.4 kg of the required product in 85% average yield.

5-Ethenyl-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (10). Into a 20-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **9** (3.28 kg, 10.44 moles, 1.00 equiv.) and methanol (8.00 L). This was followed by the addition of Zn (497 g, 7.65 moles, 1.20 equiv.) in several batches. The reaction solution was stirred at 60 °C for 20 min in a hot bath. The solids were removed by filtration, and the filtrate was concentrated under vacuum. The residue was diluted with water (12 L) and the solids were filtered off. The filtrate was extracted with ethyl acetate (12 L). The organic layer was washed with brine (15 L), dried over anhydrous sodium sulfate and concentrated under vacuum. The resulting residue was treated with 6 L of hexane and the solids were filtered off. The filtrate was concentrated under vacuum to afford title compound as brown oil. A total of 13 batches (42.4 kg) resulted in 14.77 kg of the desired product in 83% average yield.

Ethyl 3-(5-ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl)-3-oxopropanoate (11). Into a 20-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **10** (1200 g, 7.68 moles, 1.00 equiv.), dichloromethane (2.40 L), stannous chloride (175 g, 0.923 moles, 0.12 equiv.) sequentially. At 0 °C was added with stirring, a solution of ethyl 2-diazoacetate (701.5 g, 6.15 moles, 0.80 equiv.) in dichloromethane (9.60 L) dropwise over 3h. The reaction mixture was allowed to warm to room temperature in 30 min and concentrated under vacuum. The product was diluted with of hexane (4.8 L), stirred at 0 °C for 30 min, solids were removed by filtration, and the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether,

1:60→1:30). A total of 11 batches (14.77 kg) resulted in 7.81 kg (38%) of the title compound as a yellow oil.

Ethyl 2-diazo-3-(5-ethenyl-2,2-dimethyl-1,3-dioxolan-4-yl)-3-oxopropanoate (12). Into a 20-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **11** (2.00 kg, 8.26 moles, 1.00 equiv.), MeCN (10 L) and tosyl azide (1628 g, 8.26 moles, 1.00 equiv.). Followed by at 0 °C, was added TEA (1669 g, 16.49 moles, 2.00 equiv.) dropwise with stirring. The reaction mixture was stirred for 30 min at 0 °C and then allowed to attain room temperature in 30 min. The reaction mixture was concentrated under vacuum and the residue purified by silica-gel column chromatography (ethyl acetate/petroleum ether, 1:60→1:15). A total of 4 batches (7.81 kg) resulted in 8.9 kg (99%) of the title compound as a yellow oil.

Ethyl (1R,4R)-8,8-dimethyl-5-oxo-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-4-carboxylate (13). Into a 2-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **12** (200 g, 0.745 moles, 1.00 equiv.), Toluene (2 L) and cuprous iodide (7.1 g, 37.28 mmol, 0.05 equiv.). The flask was evacuated and flushed three times with hydrogen, followed by flushing with nitrogen. The resulting solution was stirred at 80-83 °C for 36 h. The reaction mixture was subjected to filtration and the filtrate concentrated under reduced pressure. The residue was applied onto a silica-gel column and eluted with ethyl acetate/petroleum ether (1:15→1:8). A total of 45 batches (8.9 kg) resulted in 3.2 kg (40%) of the title compound as a yellow oil.

Ethyl (1R,4R)-5-hydroxy-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-4-carboxylate (14). Into a 20-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **13** (1.6 kg, 6.66 mol, 1.00 equiv.), ethanol (15.00 L) and then, at 0-10 °C was added $NaBH_4$ (253 g, 6.69 mol, 1.00 equiv.) in portions. The resulting solution was stirred for 1 h at 15 °C. The reaction was then quenched by the addition of 2 L of acetone and stirred for 1 h. The solvent mixture was concentrated under vacuum and the residue was dissolved in ethyl acetate (8 L). The organic layer was washed trice with brine (8 L), dried over anhydrous sodium sulfate and concentrated under vacuum. The product was diluted with hexane (3.2 L) and the solids were collected by filtration. A total of 2 batches (3.2 kg) resulted in 1.542 kg (48%) of the title compound **14** as a white solid.

Ethyl (2R,5R)-5-hydroxy-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylate (15). Into a 10-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **14** (300 g, 1.24 mol, 1.00 equiv.), acetone (6 L), CF_3COOH (212 g, 1.86 mol, 1.50 equiv.) sequentially and stirred at 20-25 °C for 40 h. The reaction mixture was concentrated under vacuum, the residue dissolved in DCM (10 L) and treated with 10% aqueous Na_2CO_3 until the *p*H = 9. The organic layer was separated, washed with brine, dried over anhydrous sodium sulfate, filtered, and the filtrate concentrated under vacuum. The crude product was purified by re-crystallization from cyclohexane. A total of 3 batches (900 g) resulted in 100 g (11%) of the title compound **15** as a white solid.

Ethyl (2R,5R)-8,8-dimethyl-5-[(trifluoromethane)sulfonyloxy]-7,9-

dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylate (16). Into a 2-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **15** (50 g, 206.38 mmol, 1.00 equiv.), dichloromethane (500 mL), Pyridine (20 g, 252.84 mmol, 1.20 equiv.), then at 0 °C was added a solution of trifluoromethanesulfonic anhydride (70 g, 248.10 mmol, 1.20 equiv.) in dichloromethane (500 mL) dropwise with stirring. After stirred for additional 30 min at 0 °C in an ice/salt bath, hexane (500 mL) was added and the solids filtered. The solids were washed with a mixture of 3:7 ethyl acetate/ petroleum ether (200 mL). The filtrate was concentrated under vacuum and diluted with 250 ml dichloromethane. The resulting solution was used directly for the next step without further purification (The reaction was repeated for 17 times).

Ethyl (2R,5R)-5-cyano-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylate (17). Into a 3-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed LiH (2.3 g, 281.81 mmol, 1.37 equiv.), N,N-dimethylformamide (250 mL) and cooled to 0 °C. To this was added 2-hydroxy-2-methylpropanenitrile (acetone cyanohydrin, 22 g, 258.51 mmol, 1.25 equiv.) dropwise and stirred at 10-15 °C for 6 h. The suspension was filtered in to a 3-L 4-necked round-bottom flask purged and maintained under nitrogen and the solids were washed with DMF (125 mL). Into another of nitrogen, was placed the solution in the first reaction. To this filtrate at 0 °C was added a solution of **16** (77 g, 205.70 mmol, 1.00 equiv.) in dichloromethane (250 mL) dropwise with stirring. The resulting solution was stirred for 30 min at 0 °C. Ethyl acetate (1 L) was added to the reaction mixture and the organic layer was washed thrice with 700 mL of brine, dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was purified by silica gel column chromatography using ethyl acetate/petroleum ether (1:15) as eluent. A total of 18 batches (900 g of **15**) resulted in 700 g (75%) of the title compound **17** as colorless oil.

Ethyl (2R,5S)-5-formyl-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylate (19). Into a 2-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **17** (50 g, 198.98 mmol, 1.00 equiv.), methanol (600 mL), water (300 mL), acetic acid (100 mL), Palladium carbon (25 g), palladium hydroxide (25 g, 178.02 mmol, 0.89 equiv.). The flask was evacuated and flushed three times with nitrogen, followed by flushing with hydrogen. The resulting solution was stirred for 2 h at 25 °C in an oil bath. The solids were filtered out and the filtrate was concentrated under vacuum. The residue was diluted with ethyl acetate (500 mL), washed with aqueous $NaHCO_3$ (5x300 mL) and brine (3x300 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated under vacuum. A total of 11 batches (550 g) resulted in 440 g (79%) of the title compound **19** as a light yellow oil.

Ethyl (2R,5R)-5-(hydroxymethyl)-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylate (20). Into a 1-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **19** (40 g, 157.31 mmol, 1.00 equiv.) and methanol (400 mL). This was followed by the addition of $NaBH_4$ (9 g, 244.40 mmol, 1.50 equiv.) in portions at 0 °C and stirred for 30 min at room temperature. The reaction was then quenched by the addition of 80 mL of acetone. The resulting mixture was concentrated under vacuum and the residue was dissolved in 300 mL of ethyl acetate. The organic phase was washed

with brine (2x200 mL), dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column and eluted with a gradient of ethyl acetate/petroleum ether (1:6→1:3). Total of 11 batches (440 g) resulted in 176 g (40%) of the title compound **20** as a colorless oil.

Ethyl (2R,5R)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylate (21). Into a 5-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **20** (100 g, 390.18 mmol, 1.00 equiv.), N,N-dimethylformamide (2.5 L), Imidazole (13 g, 195.00 mmol, 0.50 equiv.) and *tert*-butyl(chloro)diphenylsilane (156 g, 567.56 mmol, 1.45 equiv.). The resulting mixture was stirred for 10 min and was added triethylamine (103 g, 1.02 mol, 2.60 equiv.) dropwise with stirring. The resulting solution was stirred for overnight at 25 °C. The reaction mixture was diluted with 6 L of 1:5 ethyl acetate/petroleum ether. The resulting mixture was washed with water (3 L) and brine (2x3 L). The organic layer was dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column and eluted with ethyl acetate/petroleum ether (1:100→1:30). This resulted in 120 g (62%) of the title compound **21** as a colorless oil.

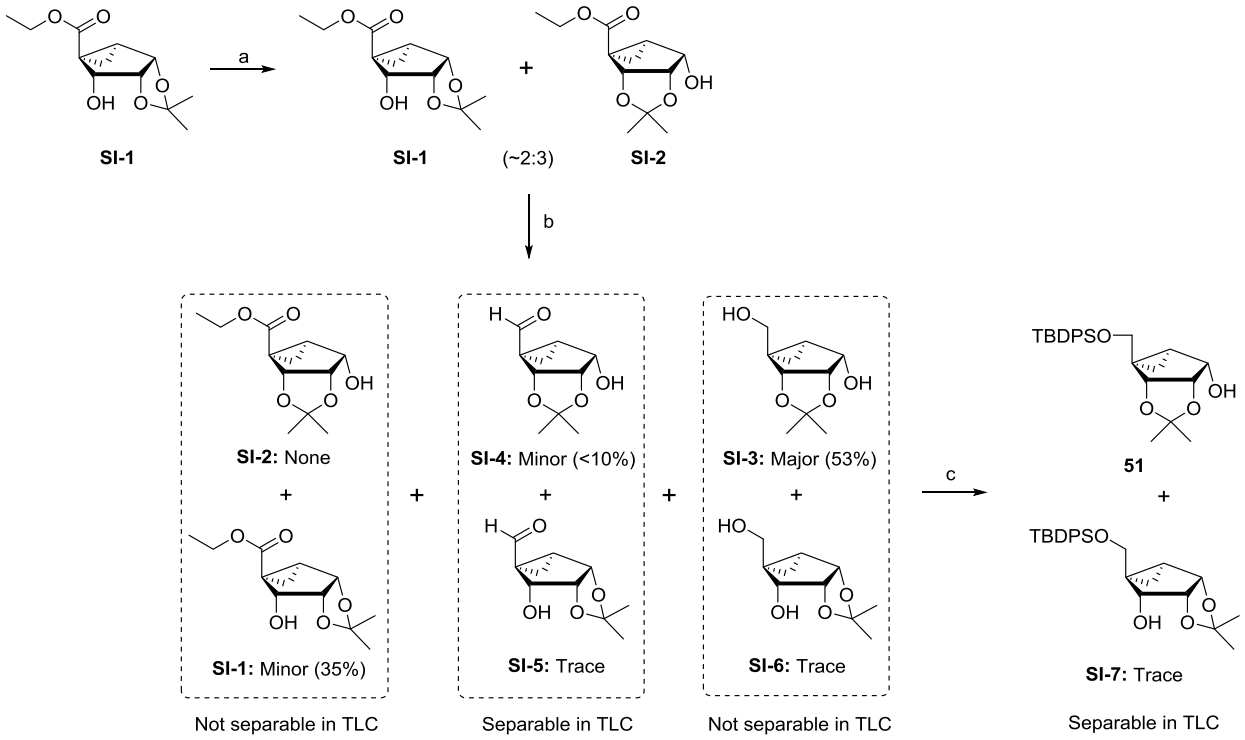
(2R,5R)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carboxylic acid (22). Into a 5-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **21** (100 g, 202.14 mmol, 1.00 equiv.) and methanol (2 L). This was followed by a solution of NaOH (16 g, 400.03 mmol, 1.98 equiv.) in water (400 mL). The resulting solution was stirred for 2 h at 80 °C in an oil bath. The resulting mixture was concentrated under vacuum. The residue was diluted with 2 L of H_2O. The *p*H was adjusted to 4-5 with HCl (5 M aqueous). The product was extracted in dichloromethane (2x2 L) and the combined organic layer was washed with water (3 L), dried over anhydrous sodium sulfate, and concentrated under vacuum. This resulted in 45 g (48%) of the title compound **22** as a brown solid.

(2R,5R)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonane-2-carbonyl azide (23). Into a 5-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **22** (104 g, 222.9 mmol, 1.00 equiv.), acetone (2.0 L) and DIPEA (35.0 g, 270.8 mmol, 1.20 equiv.). This was followed by the addition of diphenylphosphory chloride (DPCP, 72 g, 267.7 mmol, 1.20 equiv.). The resulting mixture was stirred for 30 min at room temperature. To this was added a solution of NaN_3 (19 g, 300.00 mmol, 1.33 equiv.) in water (300 mL). The resulting solution was stirred for 30 min at 20-25 °C and concentrated under vacuum. The residue was diluted with 500 mL of H_2O and the product was extracted in dichloromethane (2x300 mL). the organic layers were combined, dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column and eluted with ethyl acetate/petroleum ether (1:30). This resulted in 100 g (91%) of the title compound as a colorless oil.

(2R,5R)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-8,8-dimethyl-7,9-dioxatricyclo[4.3.0.0^[2,4]]nonan-2-amine (24). Into a 5-L 4-necked round-bottom flask purged and maintained with an inert atmosphere of nitrogen, was placed **23** (100 g, 203.40

mmol, 1.00 equiv.) and benzene (2.5 L). The resulting mixture was stirred at 80 °C for 5 h. Then the mixture was concentrated under vacuum. The residue was dissolved in oxolane (5 L) and poured in a 5-L 4-necked round-bottom flask containing a solution of NaOH (160 g, 4.00 mol, 1.00 equiv.) in water (2 L) with vigorous stirring. After stirred for 30 min at room temperature, the volatiles were removed under vacuum. The residue was diluted with 3 L of ethyl acetate and the organic phase was washed with 2x2 L of brine, dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was applied onto a silica gel column and the products eluted with ethyl acetate/petroleum ether (1:8→1:3). This resulted in 66 g (74%) of the title compound **24** as a brown oil.

Scheme S2: An alternate route to intermediate **51**.



Reagents and Conditions: (a) anhydrous CH_2Cl_2, CF_3SO_3H, rt, 5h, quantitative; (b) anhydrous THF,DIBAL-H, -78 °C, 3h, 53%; (c) anhydrous CH_2Cl_2, DMAP, imidazole TBDPS-Cl, rt, 18h, 60%.

The compound mixture **SI-1**,**2** was synthesized following the reported protocol.[3]

(3aR,3bR,4aS,5S,5aS)-3b-(hydroxymethyl)-2,2-dimethylhexahydrocyclopropa[3,4]cyclopenta[1,2-d][1,3]dioxol-5-ol (**SI-3**): The mixture of compounds **SI-1** and **SI-2** (25 mg, 0.103 mmol) was dried by chasing with anhydrous toluene (2x2mL) and desolved in anhydrous THF (1 mL). DIBAL-H (1M in toluene, 0.83 mL, 0.825 mmol) was added drop wise at -78 °C and stirred at this temperature for 3h. The reaction was

quenched by adding saturated Rochelle salt solution (2 mL) and stirred at rt for 30 min. Products were extracted in 10% isopropyl alcohol in chloroform (10x10 mL), combined , dried over anhydrous Na_2SO_4, evaporated and the residue purified by silica-gel flash chromatography to afford **SI-1** (9 mg, 35%, R_f-0.8); **SI-4** (3 mg, 9%, R_f-0.65); **SI-5** (~1 mg as a mixture with SI-4, R_f-0.60); **SI-3** (11 mg, 53%, R_f-0.2); TLC eluent = ethyl acetate. Data for **SI-3:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93 (dt, *J* = 1.2, 6.5 Hz, 1H), 4.62 – 4.47 (m, 2H), 3.68 (d, *J* = 11.5 Hz, 1H), 3.50 (d, *J* = 11.5 Hz, 1H), 2.34 (s, 2H), 1.78 (dtd, *J* = 1.2, 4.7, 9.2 Hz, 1H), 1.53 (s, 3H), 1.28 (s, 3H), 1.18 (t, *J* = 4.9 Hz, 1H), 0.65 (ddt, *J* = 1.1, 5.3, 8.9 Hz, 1H).

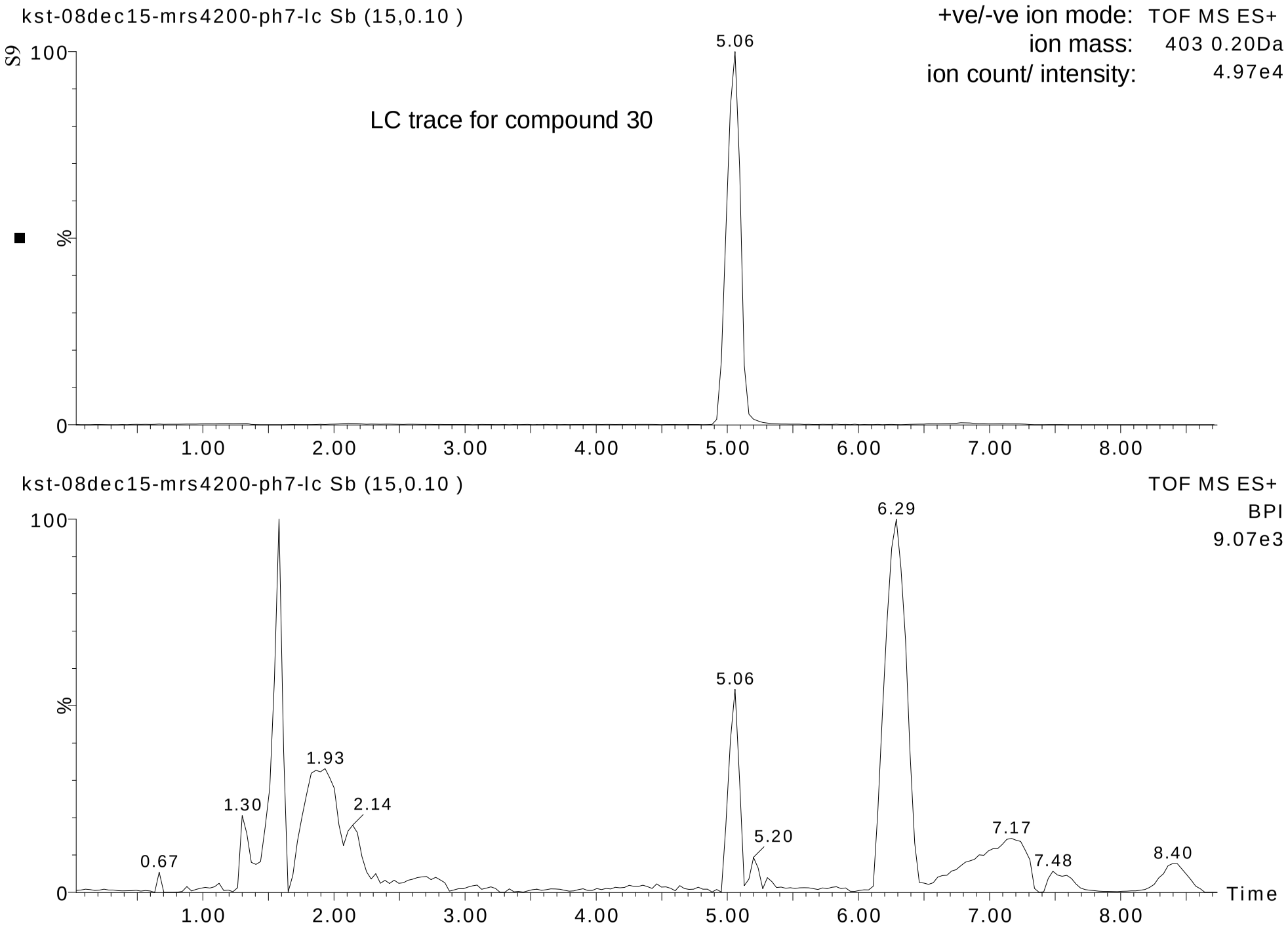
(3aR,3bR,4aS,5S,5aS)-3b-(((tert-butyldiphenylsilyl)oxy)methyl)-2,2-dimethylhexahydrocyclopropa[3,4]cyclopenta[1,2-d][1,3]dioxol-5-ol (**51**): Compound **SI-3** (37 mg, 0.185 mmol) was dissolved in anhydrous CH_2Cl_2 (1 mL). To this was added Imidazole (25 mg, 0.37 mmol), DMAP (5 mg, 0.037 mmol) and TBDPS-Cl (48 µL, 0.185 mmol) sequentially, and stirred at rt for 18h. Solvent was evaporated under reduced pressure and the residue purified by silica-gel flash column chromatography to afford desired product **51** as a white foam (50 mg, 60%, R_f-0.3; TLC eluent = 20% ethyl acetate in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.60 (m, 4H), 7.47 – 7.34 (m, 6H), 5.01 (dd, *J* = 1.2, 6.9 Hz, 1H), 4.55 (td, *J* = 0.8, 6.9 Hz, 1H), 4.50 – 4.43 (m, 1H), 4.08 (d, *J* = 11.0 Hz, 1H), 3.29 (d, *J* = 11.0 Hz, 1H), 2.19 (s, 1H), 1.65 – 1.58 (m, 1H), 1.54 (s, 3H), 1.31 (s, 3H), 1.09 (t, *J* = 4.9 Hz, 1H), 1.06 (s, 9H), 0.54 (ddt, *J* = 1.2, 5.2, 8.8 Hz, 1H).

References:

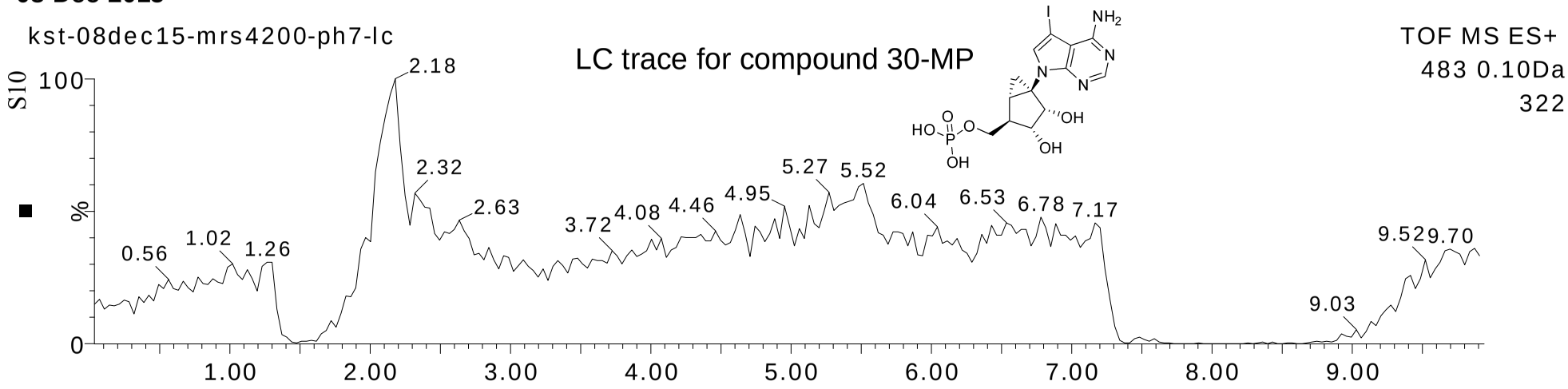
1. Joshi, B.V.; Melman, A.; Mackman, R.L.; Jacobson, K.A. Synthesis of ethyl (1*S*,2*R*,3*S*,4*S*,5*S*)-2,3-*O*-(isopropylidene)-4-hydroxy-bicyclo[3.1.0]hexane-carboxylate from L-ribose: A versatile chiral synthon for preparation of adenosine and P2 receptor ligands. *Nucleos. Nucleot. Nucleic Acids* **2008**, *27*, 279-291.
2. Melman, A.; Zhong, M.; Marquez, V.E.; Jacobson, K.A. Synthesis of enantiomerically pure (S)-methanocarbaribo uracil nucleoside derivatives for use as antiviral agents and P2Y receptor ligands. *J. Org. Chem.* **2008**, *73*, 8085-8088.
3. Santhosh Kumar, T.; Zhou, S-Y.; Joshi, B. V.; Balasubramanian, R.; Yang, T.; Liang, B. T.; Jacobson, K. A. Structure−Activity Relationship of (N)-Methanocarba Phosphonate Analogues of 5′-AMP as Cardioprotective Agents Acting Through a Cardiac P2X Receptor. *J. Med. Chem.* **2010**, *53*, 2562-2576.

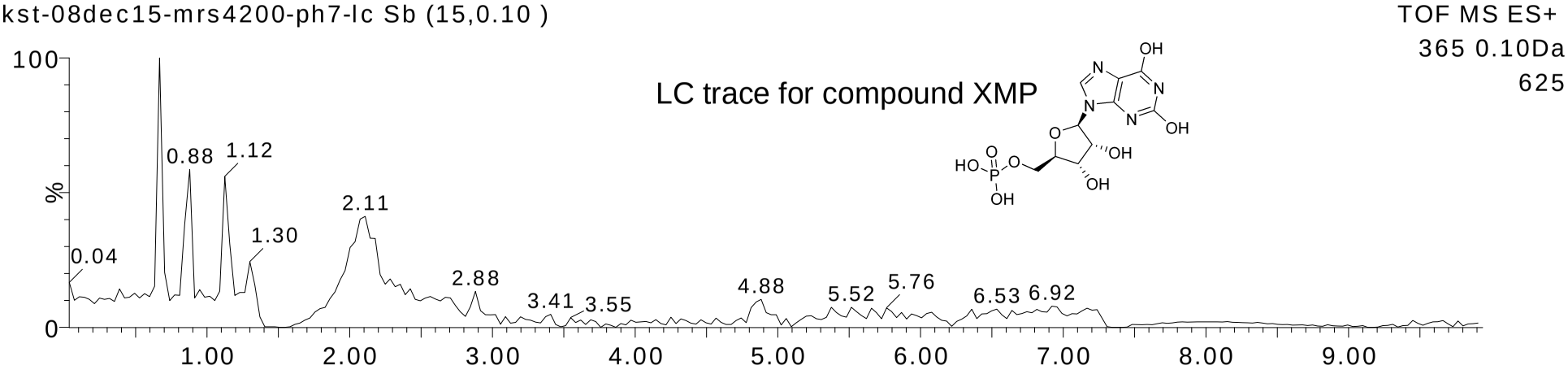
Figure S1a: Assay mix with 1.0 uM 30 and inosine

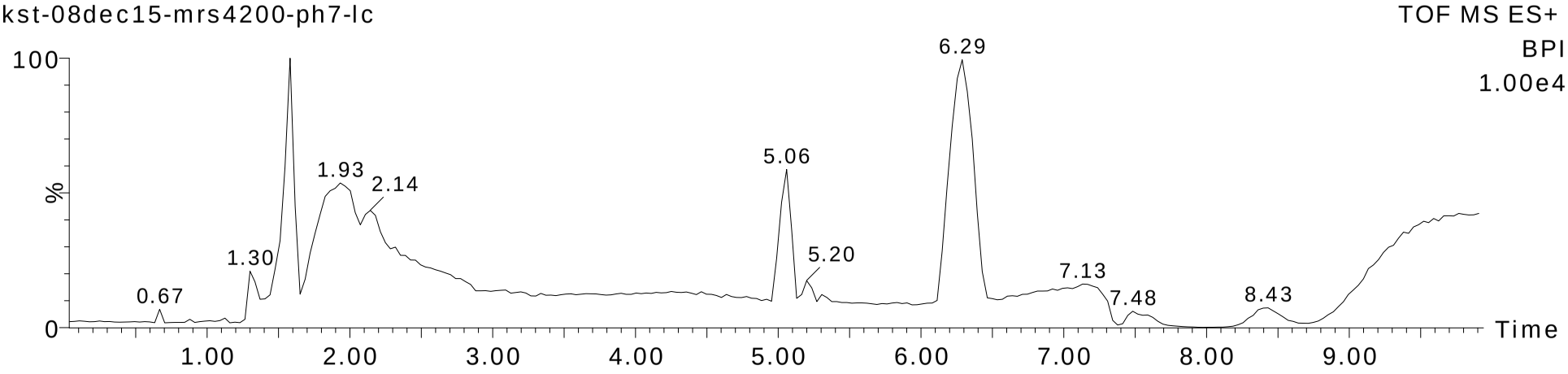
08-Dec-2015



08-Dec-2015


kst-08dec15-mrs4200-ph7-lc
LC trace for compound 30-MP
TOF MS ES+
483 0.10Da
322
S10
100
%
0
0.56
1.02
1.26
2.18
2.32
2.63
3.72
4.08
4.46
4.95
5.27
5.52
6.04
6.53
6.78
7.17
9.03
9.52
9.70
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00

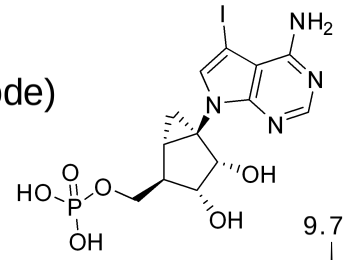

kst-08dec15-mrs4200-ph7-lc Sb (15,0.10)
LC trace for compound XMP
TOF MS ES+
365 0.10Da
625
100
%
0
0.04
0.88
1.12
1.30
2.11
2.88
3.41
3.55
4.88
5.52
5.76
6.53
6.92
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00


kst-08dec15-mrs4200-ph7-lc
TOF MS ES+
BPI
1.00e4
100
%
0
0.67
1.30
1.93
2.14
5.06
5.20
6.29
7.13
7.48
8.43
Time
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00

08-Dec-2015

kst-08dec15-mrs4200+mmrb-01

LC trace for compound 30-MP(-ve mode)



TOF MS ES-
482 0.10Da
13

S11

100

%

0

0.07
0.35
0.63
1.55
2.00
2.25
2.49
3.34
3.51
3.76
4.08
4.39
4.60
4.85
5.41
6.01
6.15
6.29
6.57
7.10
7.38
7.69
8.33
8.89
8.96
9.52
9.73
10.54
10.61
10.86
11.70

2.00 4.00 6.00 8.00 10.00

kst-08dec15-mrs4200+mmrb-01

TOF MS ES-
BPI
1.24e4

100

%

0

3.06
2.53

Time

2.00 4.00 6.00 8.00 10.00

15-Dec-2015

Figure S1b: Assay mix with inosine and without 30

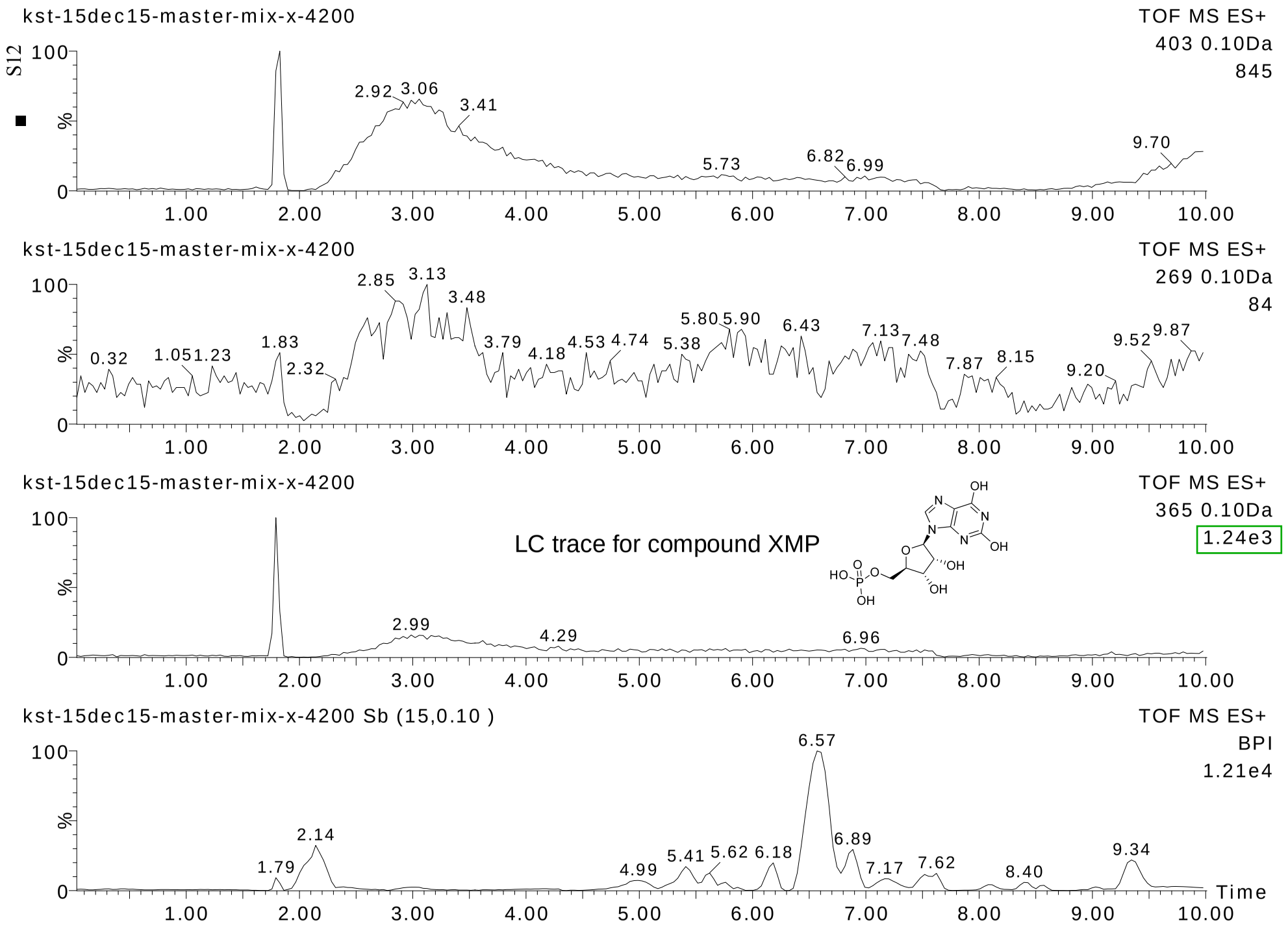


Figure S1c: Assay mix with 1.0 uM 30 without inosine

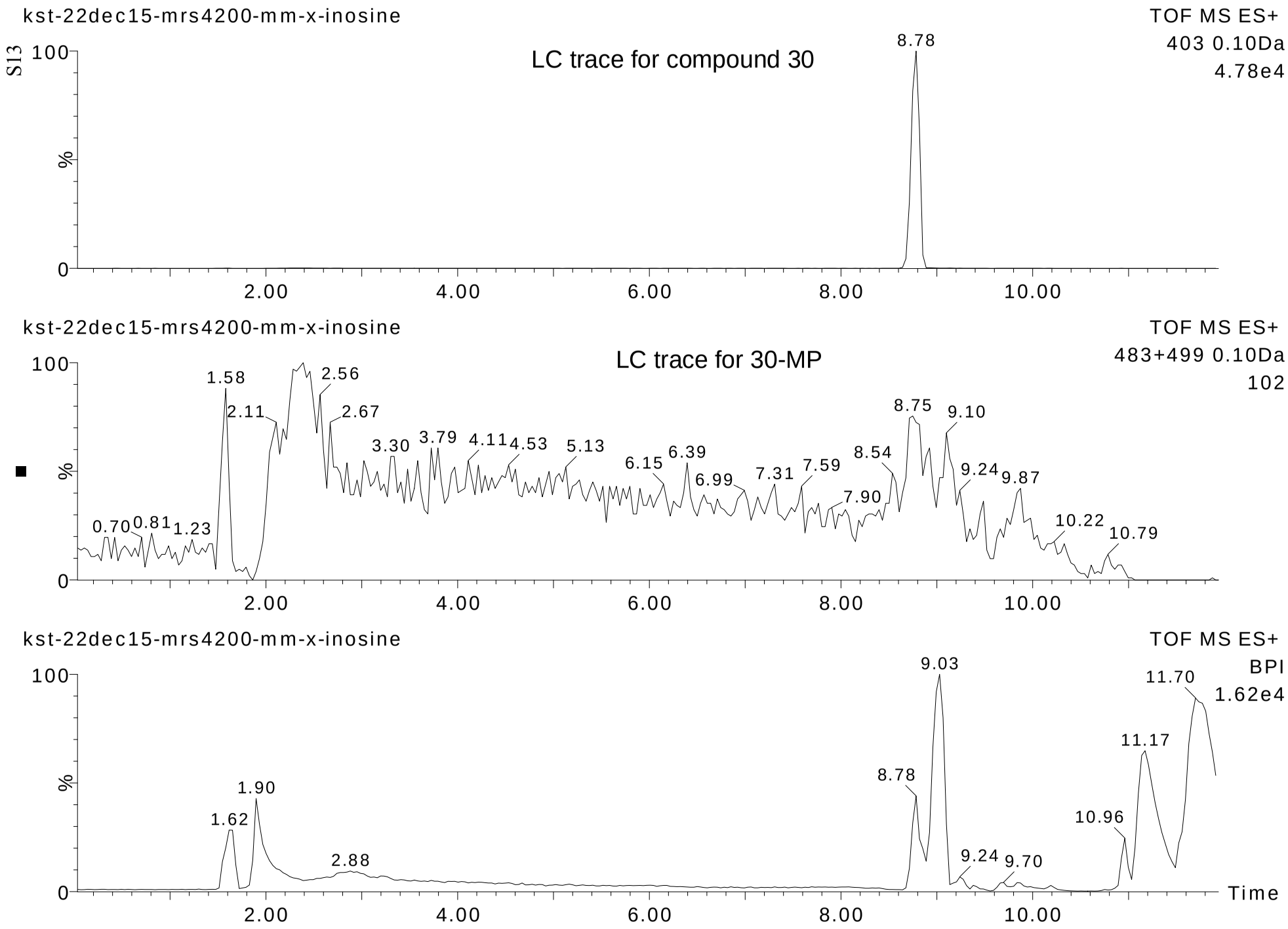
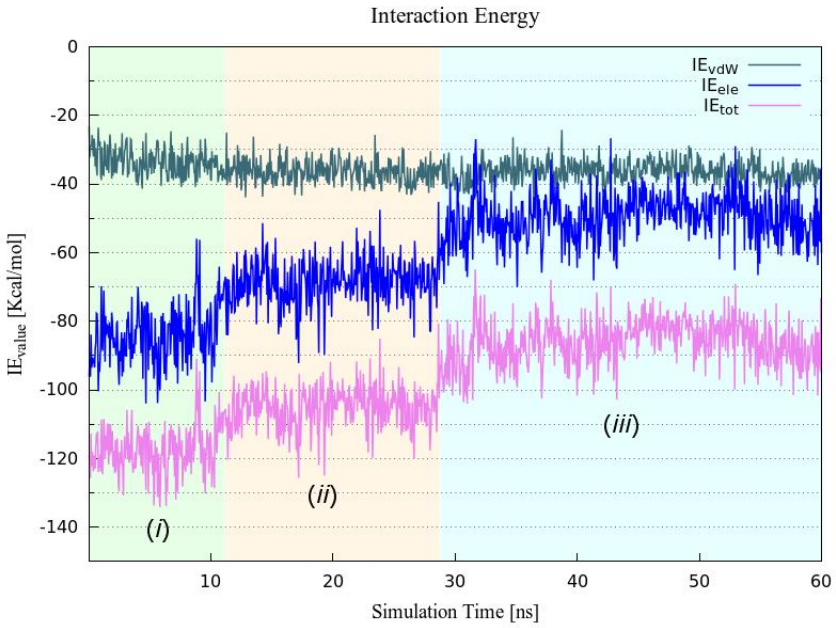


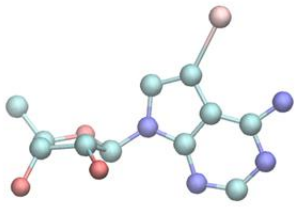
Table S1. Parameters considered for the selection of a representative trajectory among three replicas: protein alpha carbon atoms (Cα) average RMSD, ligand average RMSD/RMSF, and slope of the dynamic scoring function. RMSD and RMSF values are in Å and the $wDSF_{tot}$ is adimensional.

	1c			**30**			**57**		
	RUN1	RUN2	RUN3	RUN1	RUN2	RUN3	RUN1	RUN2	RUN3
Cα RMSD	1.90	2.01	2.81	3.95	2.37	2.21	3.78	2.19	1.74
Ligand RMSD	0.95	1.07	1.24	1.97	0.88	1.00	1.35	0.99	0.81
Ligand RMSF	0.52	0.79	0.58	1.02	0.61	0.68	0.94	0.75	0.55
$wDSF_{tot}$ (slope)	**-119.36**	-112.52	-88.37	-71.13	**-162.32**	-125.98	-102.01	-131.258	**-154.16**

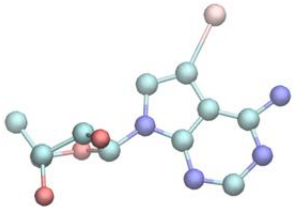
	34			**55**			**1a**		
	RUN1	RUN2	RUN3	RUN1	RUN2	RUN3	RUN1	RUN2	RUN3
Cα RMSD	2.31	1.98	3.86	1.98	1.77	2.70	4.21	2.36	3.16
Ligand RMSD	1.36	1.63	2.22	1.31	1.13	1.50	1.65	0.93	1.18
Ligand RMSF	0.68	0.81	0.97	0.85	0.68	0.93	0.87	0.89	0.75
$wDSF_{tot}$ (slope)	**-69.98**	-61.36	-42.49	-74.76	**-88.98**	-76.00	-83.61	**-163.90**	-117.76

Figure S2. Upper panel: IE profile obtained during 60 ns of MD simulations of the hAK in complex with **1c** starting from the X-Ray structure. The electrostatic (IEele) and van der Waal (IevdW) contributions and the total IE (IEtot) are represented as blue, green and pink lines, respectively. IE values are in Kcal/mol. Lower panel: selected representative ligand conformations adopted during the MD simulation: *i*) C1'-exo, *ii*) C2'-endo, and *iii*) C3'-endo conformations.

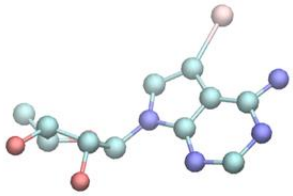




(*i*)



(*ii*)



(*iii*)

Figure S3. IE profiles during 30 ns of MD simulations of the hAdK in complex with **34** and **55** starting from the docking poses. The electrostatic (IE_{ele}) and van der Waals (IE_{vdW}) contributions and the total IE (IE_{tot}) are represented as blue, green and pink lines, respectively. IE values are in Kcal/mol.

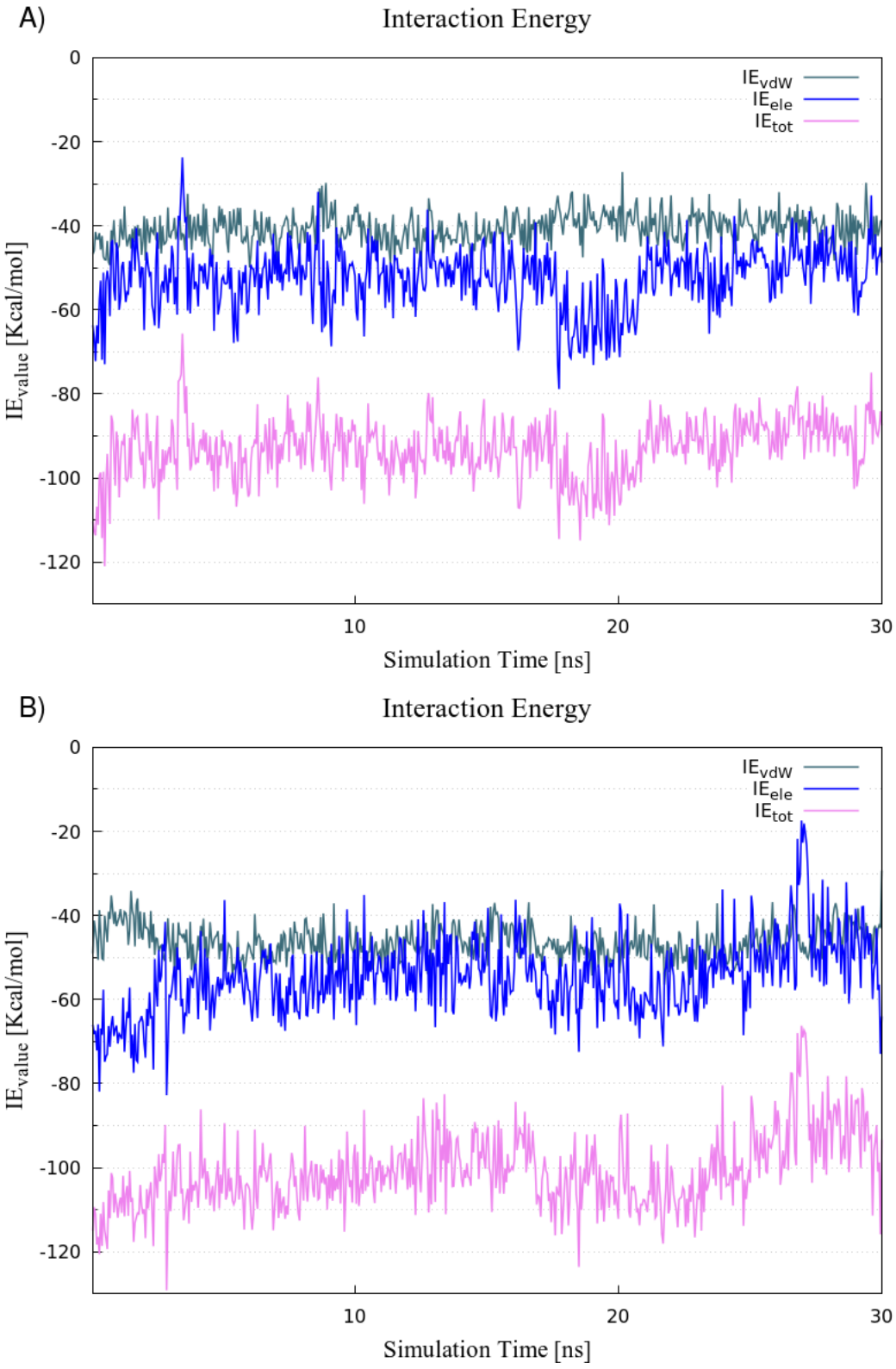


Figure S4. Panel A: Superimposition between X-Ray protein structures of the hAK in the closed (PDB ID: 2I6A, gray ribbons) and open conformation (PDB ID: 2I6B, light green ribbons). Panels B-F: superimposition of MD average protein structures obtained after 30 ns of MD simulation of hAK in complex with **1c** (B, pink ribbons), **30** (C, yellow ribbons), **57** (D, green ribbons), **34** (E, cyan ribbons), and **55** (F, orange ribbons) with the starting X-Ray protein structure in the closed conformation (PDB ID: 2I6A, gray ribbons).

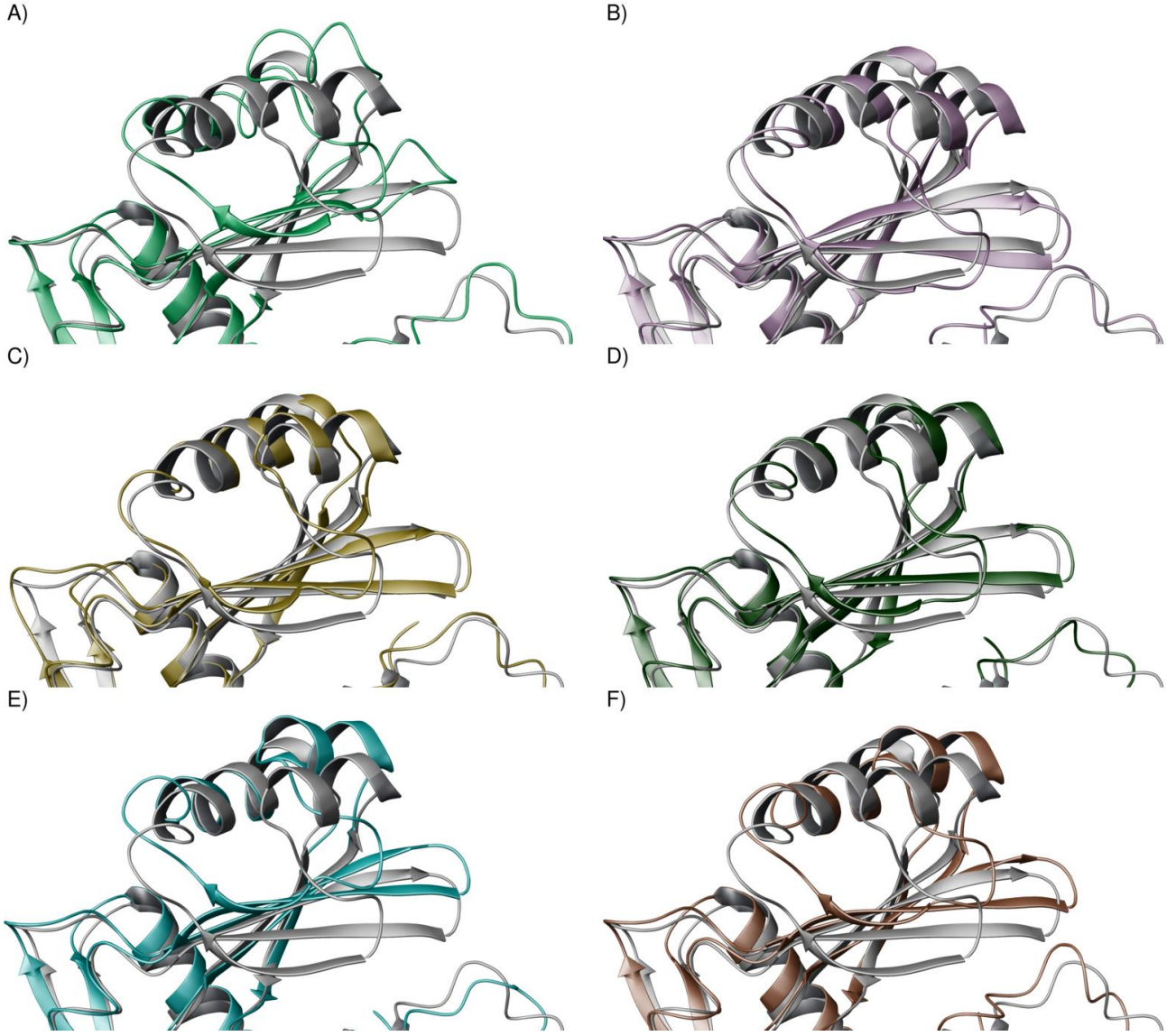


Figure S5. Panel A: Docking pose of **1a** in complex with the closed form of hAK (PDB ID: 2I6A) obtained after IFD. Ligand and side chains of residues important for ligand recognition are reported as line and sticks, respectively. H-bonds are pictured as yellow dashed lines, whereas π–π stacking interactions as blue dashed lines with the centroids of the aromatic rings displayed as cyan spheres. Nonpolar hydrogen atoms are omitted. Panel B: superimposition of the MD average protein structure obtained after 30 ns of MD simulation of hAK in complex with **1a** (magenta ribbons) with the starting X-Ray protein structure in the closed conformation (PDB ID: 2I6A, gray ribbons).

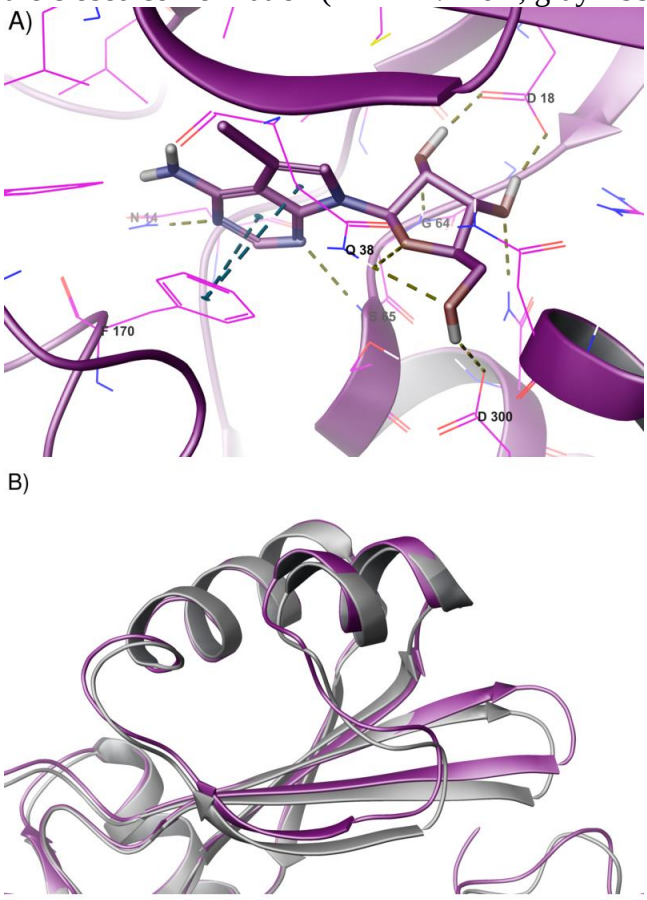


Figure S6. Endocyclic torsion υ_0-υ_4 angles used to compute the sugar pseudorotation phase angle (P).

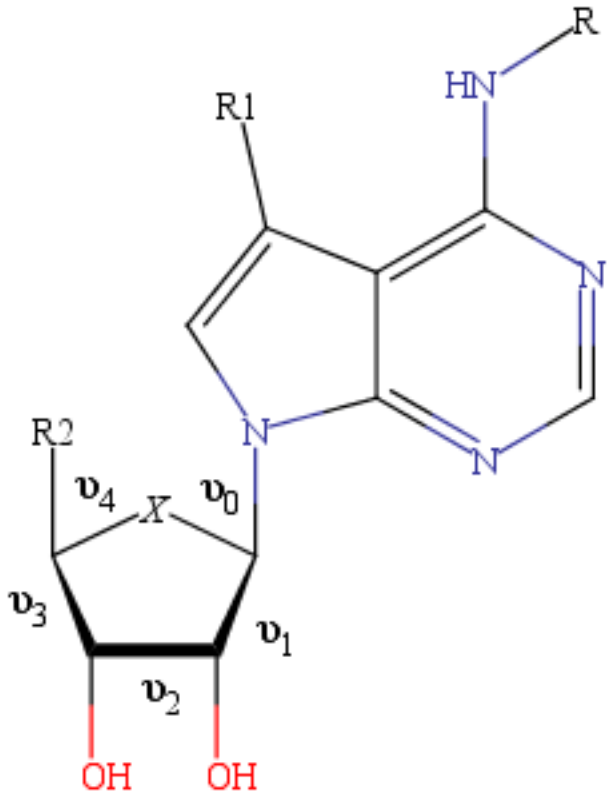
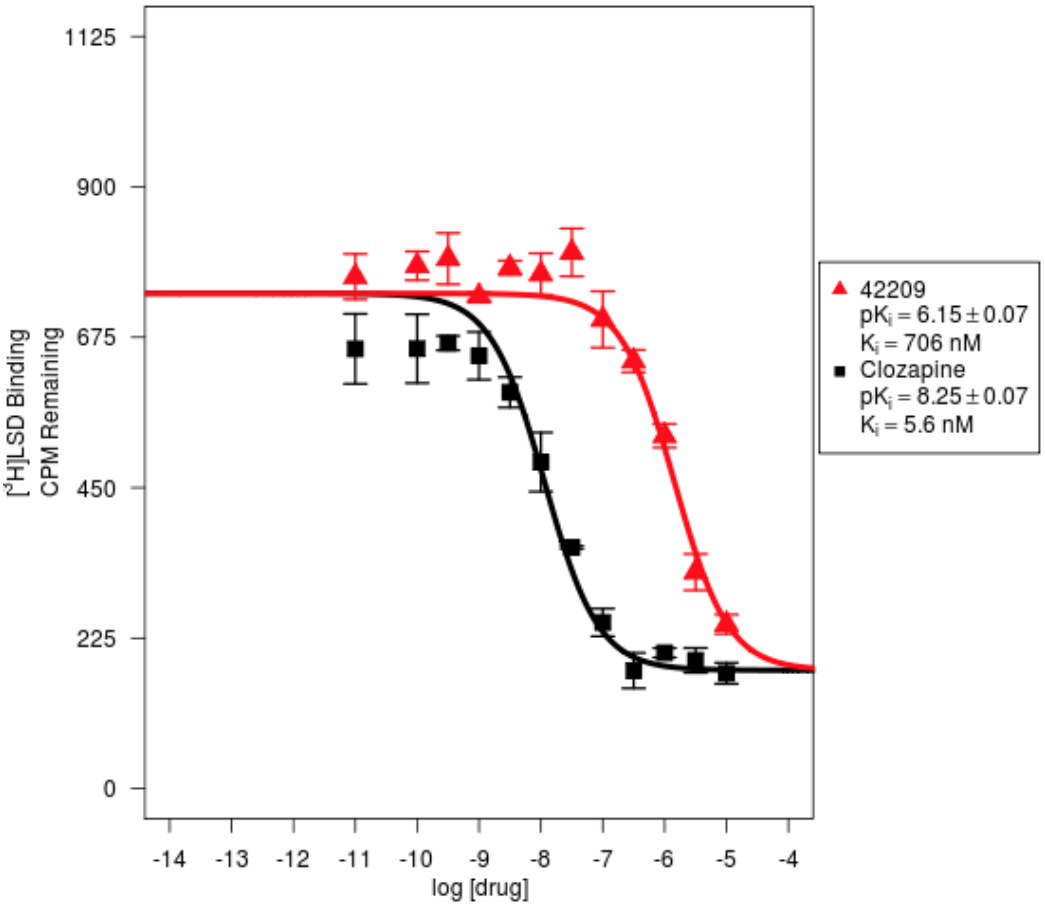


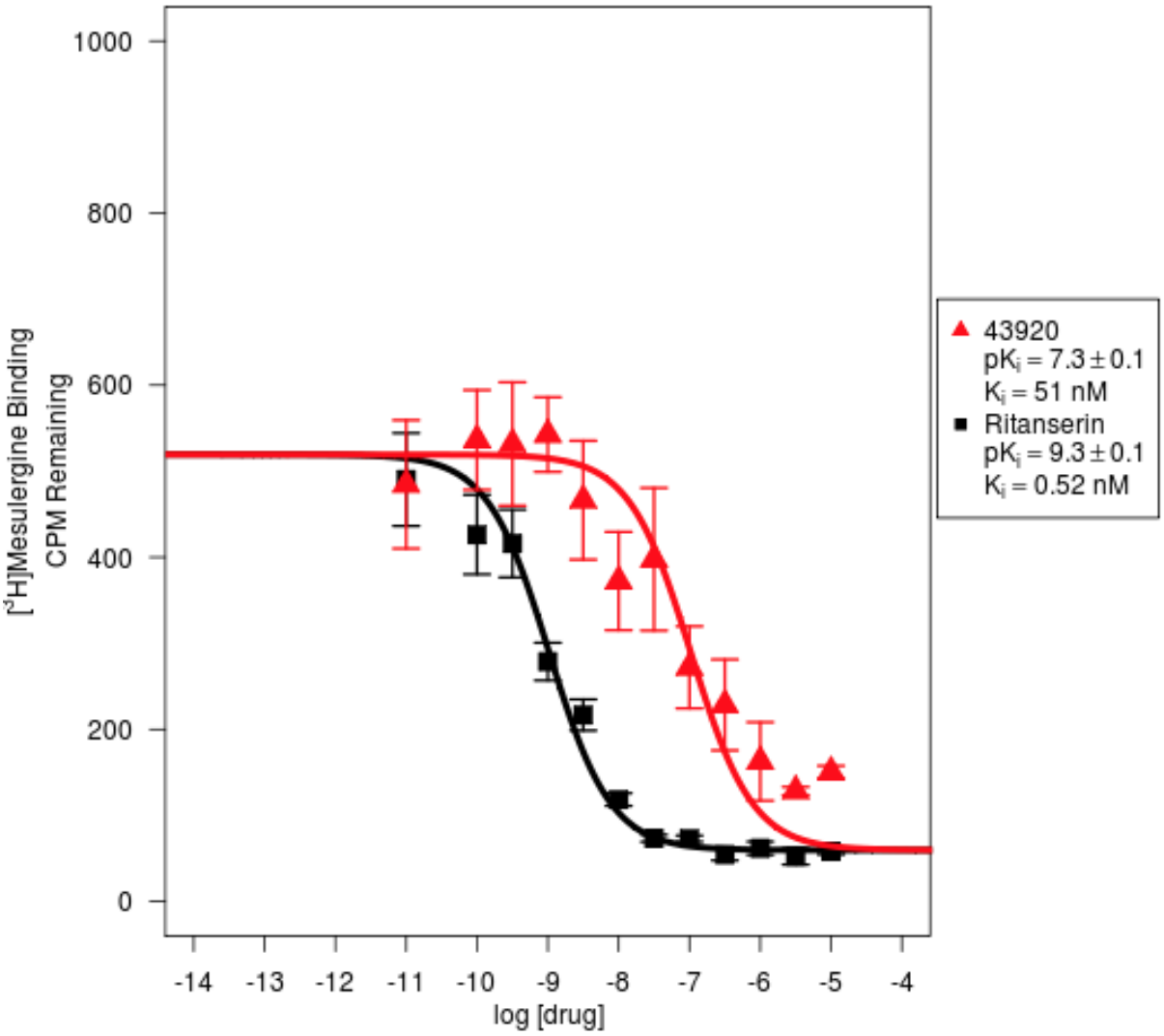
Figure S7. Off-target activities

K_i determinations and binding profiles in a broad screen of receptors and channels were generously provided by the National Institute of Mental Health's Psychoactive Drug Screening Program, Contract # HHSN-271-2008-00025-C (NIMH PDSP). The NIMH PDSP is Directed by Bryan L. Roth MD, PhD at the University of North Carolina at Chapel Hill and Project Officer Jamie Driscol at NIMH, Bethesda MD, USA. For experimental details please refer to the PDSP web site http://pdsp.med.unc.edu/ and click on "Binding Assay" or "Functional Assay" on the menu bar.

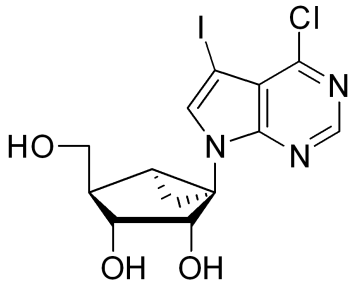
Radioligand binding inhibition by compound **38a** (MRS4203) at the $5HT_7R$:

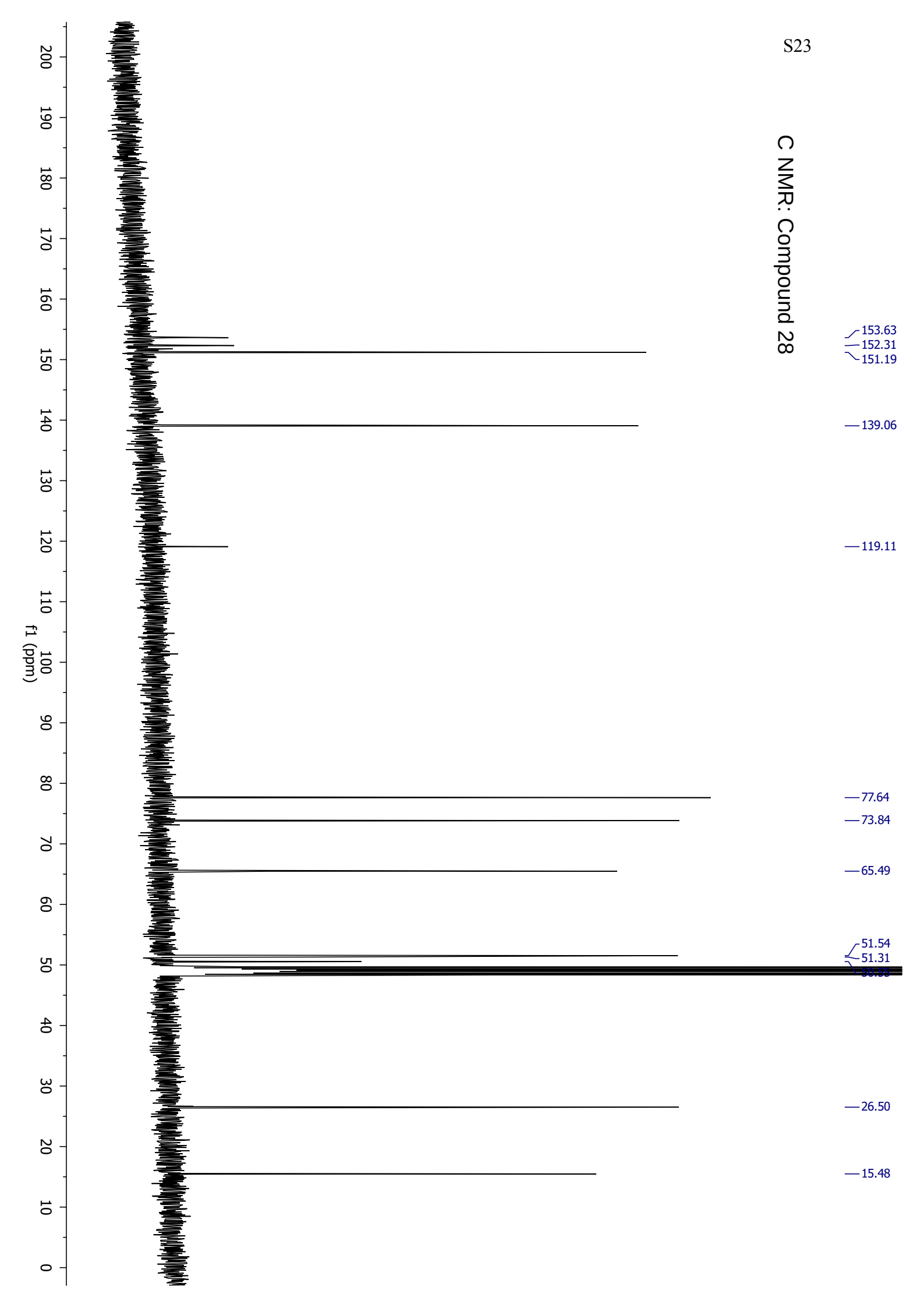


Radioligand binding inhibition by compound **55** (MRS4380) at the 5HT$_{2B}$R:



H NMR: Compound 28




C NMR: Compound 28
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
153.63
152.31
151.19
139.06
119.11
77.64
73.84
65.49
51.54
51.31
26.50
15.48

HRMS: Compound 28

Elemental Composition Report

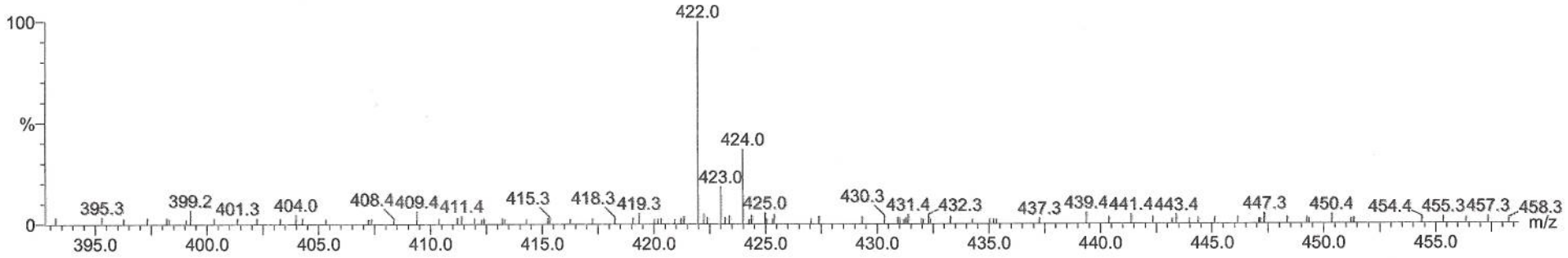
Single Mass Analysis

Tolerance = 25.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
106 formula(e) evaluated with 7 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 3-3 O: 0-12 Cl: 1-1 I: 1-1

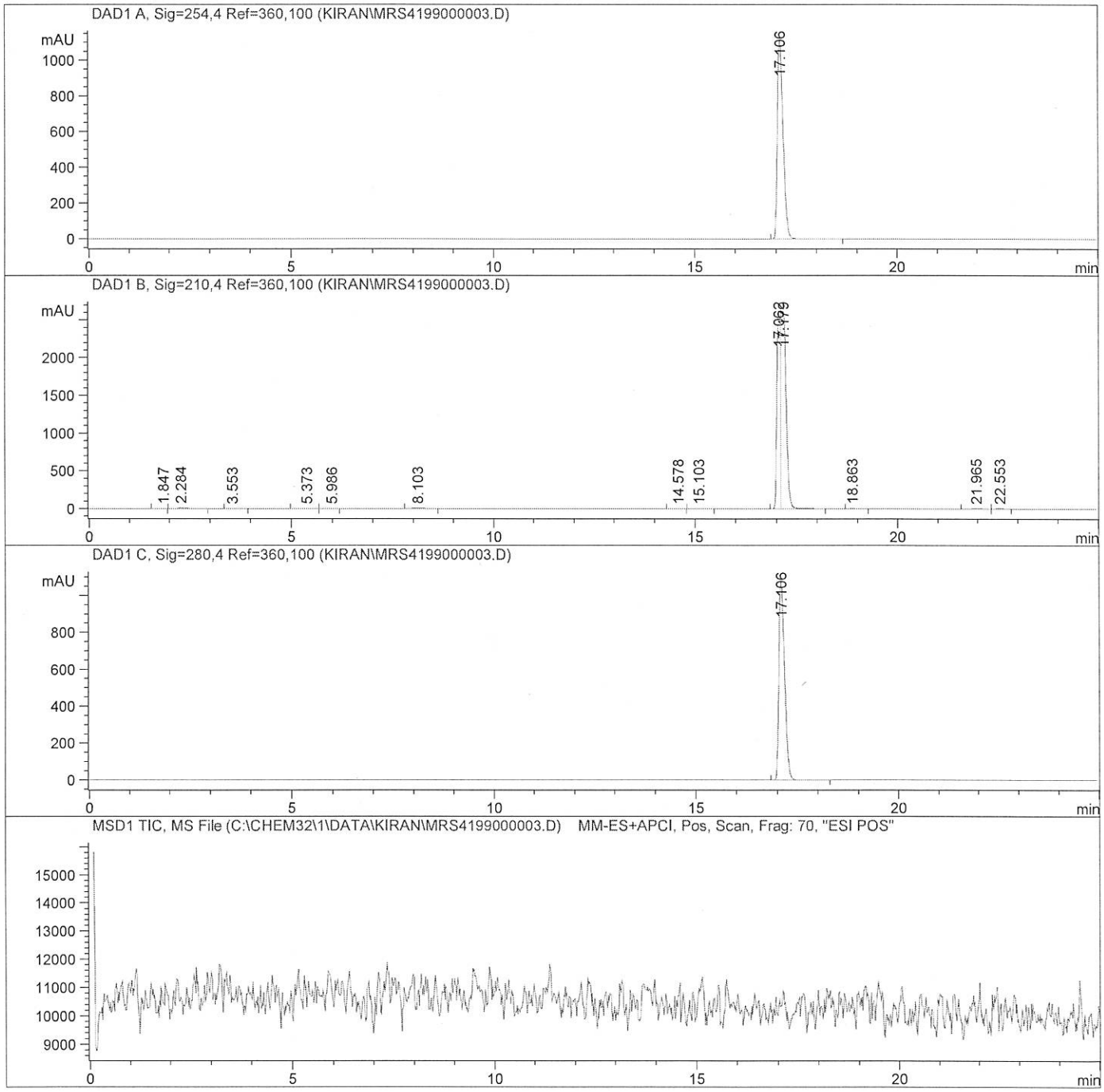
12-Dec-2014
kst-12dec14-1054 85 (1.572) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00); Sm (SG, 3x5.00)

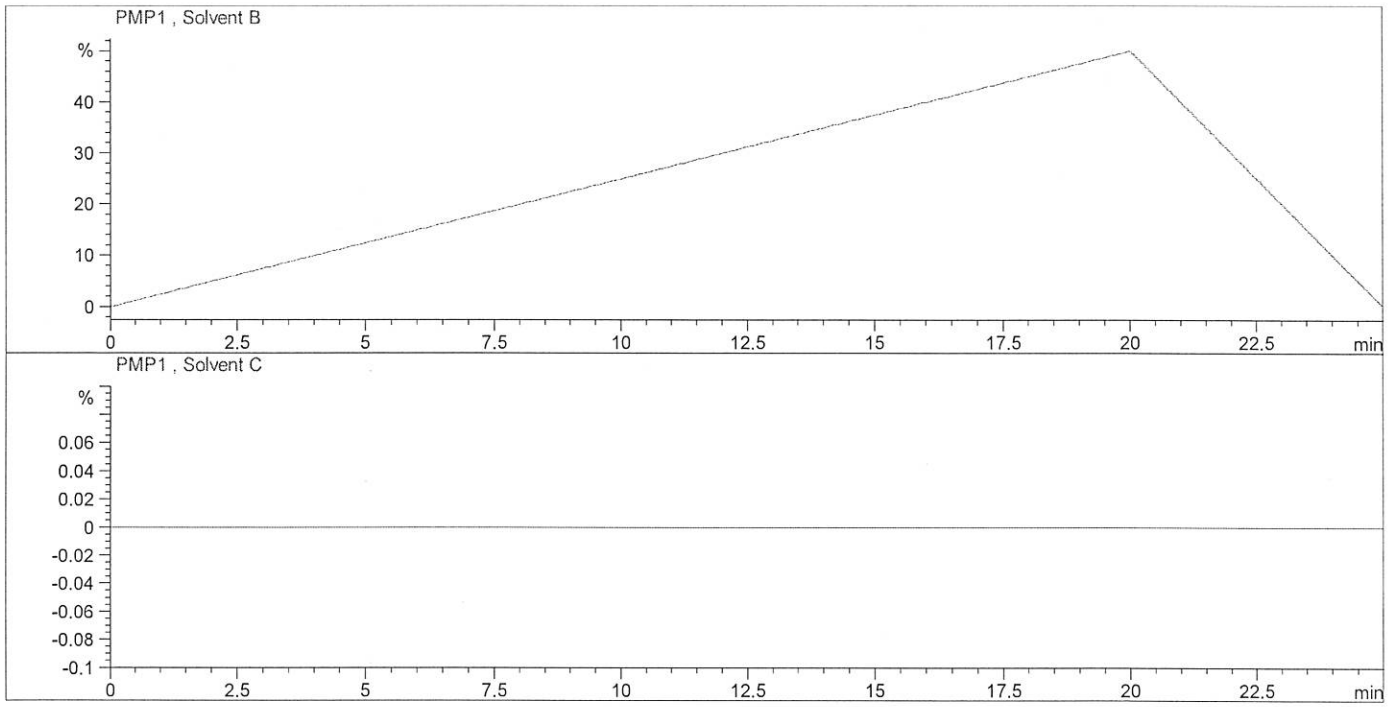
TOF MS ES+
1.23e+003



Minimum:				-50.0		
Maximum:		25.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
421.9771	421.9768	0.3	0.7	7.5	2.5	C13 H14 N3 O3 Cl I
	421.9827	-5.6	-13.3	-1.5	32.6	C6 H18 N3 O8 Cl I
	421.9675	9.6	22.8	-5.5	70.5	C2 H18 N3 O11 Cl I
	421.9921	-15.0	-35.5	11.5	9.3	C17 H14 N3 Cl I
	421.9616	15.5	36.7	3.5	21.8	C9 H14 N3 O6 Cl I
	421.9980	-20.9	-49.5	2.5	22.3	C10 H18 N3 O5 Cl I
	421.9557	21.4	50.7	12.5	15.7	C16 H10 N3 O Cl I

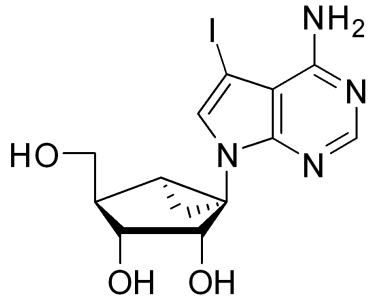
```
==========================================================================
Acq. Operator   : KIRAN
Acq. Instrument : Instrument 1                    Location : Vial 1
Injection Date  : 9/22/2015 4:19:44 PM                 Inj :   1
                                                  Inj Volume : 10.0 µl
Acq. Method     : C:\CHEM32\1\METHODS\KST0050.M
Last changed    : 9/22/2015 3:56:18 PM by KIRAN
Analysis Method : C:\CHEM32\1\METHODS\KST0050.M
Last changed    : 9/11/2015 5:21:48 PM by KIRAN
Method Info     : ESI neg
```






```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:                :     10.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.106 BB    0.1526 1.09337e4  1112.66028 100.0000

Totals :                  1.09337e4  1112.66028



Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   1.847 BB    0.0865    9.38568    1.47068   0.0239
   2   2.284 BB    0.1989  156.80090   10.45777   0.3987
   3   3.553 BB    0.2251   34.94678    2.35596   0.0889
   4   5.373 BB    0.1808   17.27020    1.37210   0.0439
   5   5.986 BB    0.1753   15.29074    1.24498   0.0389
   6   8.103 BB    0.2814   58.87189    2.91746   0.1497
   7  14.578 BB    0.1120   18.49826    2.50958   0.0470
```

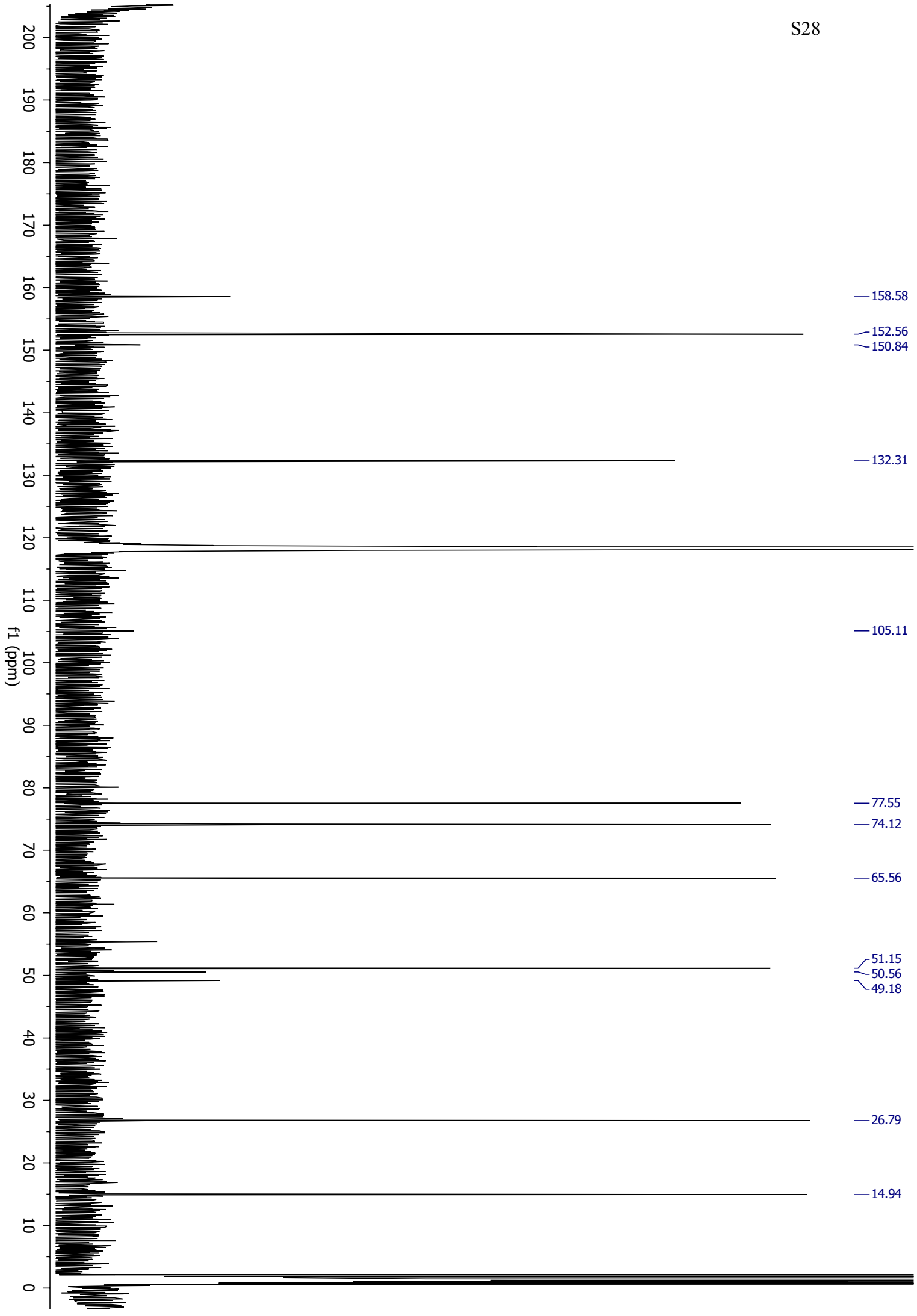
H NMR: Compound 30



G (s) 8.08
H (s) 7.35
A (dd) 4.57
C (m) 4.01
B (dd) 3.79
D (t) 2.25
E (m) 1.79
F (m) 1.14

0.53 0.65 1.00 2.27 1.24 1.06 2.27 1.21

f1 (ppm)


158.58
152.56
150.84
132.31
105.11
77.55
74.12
65.56
51.15
50.56
49.18
26.79
14.94
f1 (ppm)

S29

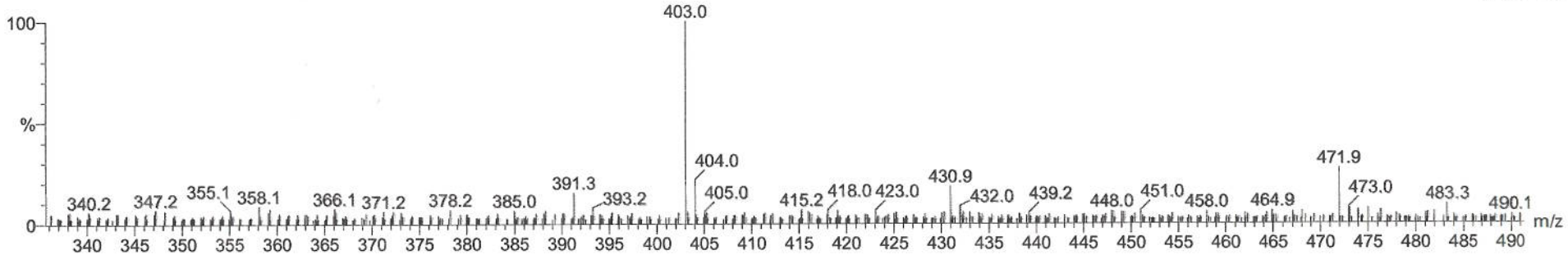
Single Mass Analysis

Tolerance = 25.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
110 formula(e) evaluated with 7 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-4 O: 0-12 I: 1-1

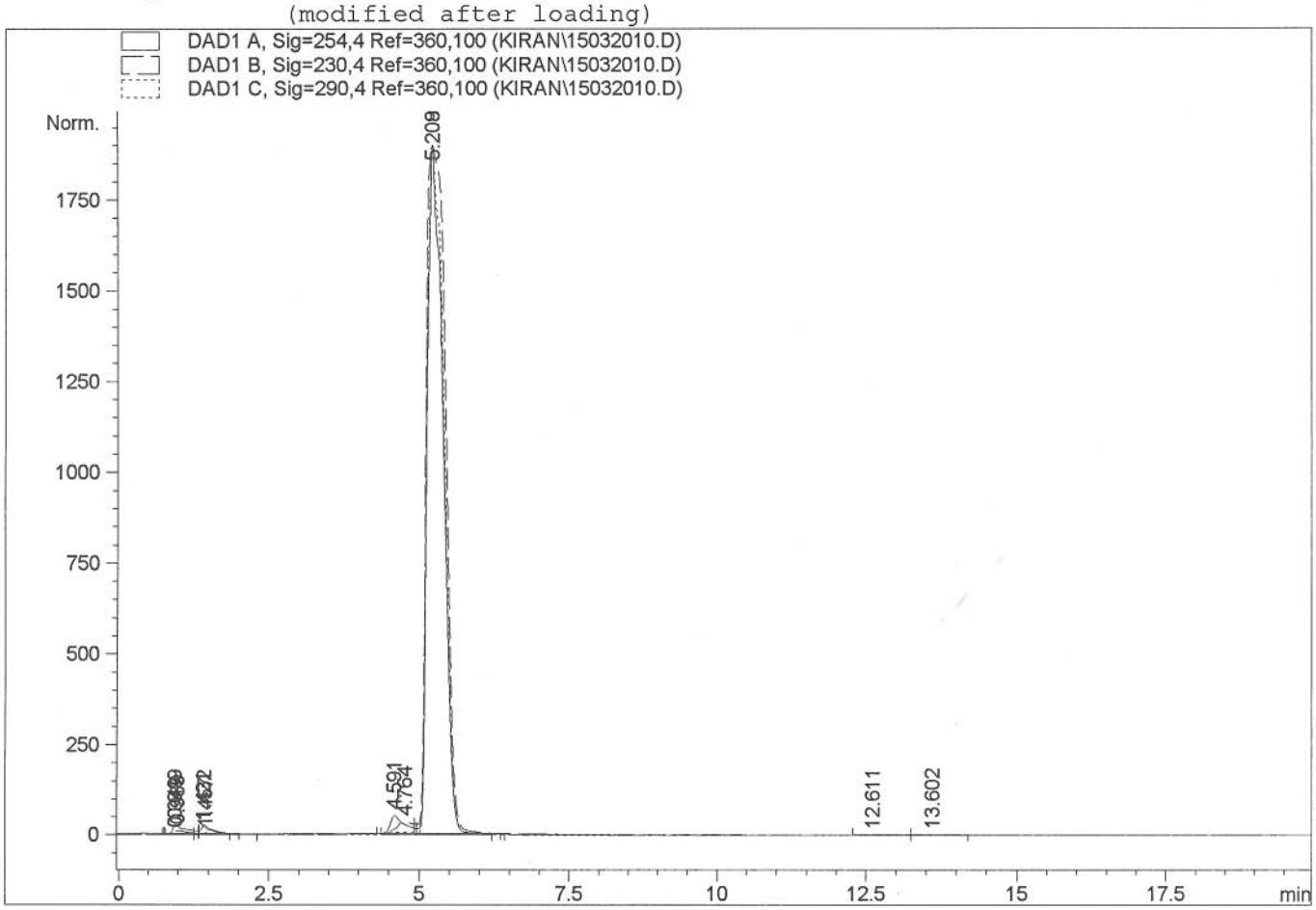
15-Dec-2014
kst-15dec14-1056 110 (2.034) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

TOF MS ES+
5.75e+002



Minimum:				-50.0		
Maximum:		25.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
403.0269	403.0267	0.2	0.5	7.5	10.1	C13 H16 N4 O3 I
	403.0326	-5.7	-14.1	-1.5	27.7	C6 H20 N4 O8 I
	403.0173	9.6	23.8	-5.5	44.7	C2 H20 N4 O11 I
	403.0420	-15.1	-37.5	11.5	9.8	C17 H16 N4 I
	403.0115	15.4	38.2	3.5	20.7	C9 H16 N4 O6 I
	403.0478	-20.9	-51.9	2.5	21.6	C10 H20 N4 O5 I
	403.0056	21.3	52.9	12.5	12.2	C16 H12 N4 O I

```
Injection Date  : 3/20/2015 4:43:53 PM
Sample Name     : MRS4200                       Location :  -
Acq. Operator   : KIRAN
Acq. Method     : C:\HPCHEM\1\METHODS\KIRANADK.M
Last changed    : 3/20/2015 4:45:20 PM by KIRAN
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\KIRANADK.M
Last changed    : 3/20/2015 5:34:44 PM by KIRAN
                  (modified after loading)
```



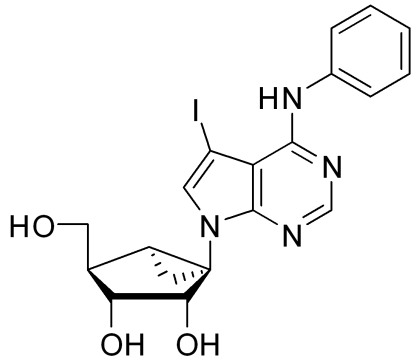
Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.949	BV	0.1927	164.42644	11.10704	1.0075
2	1.432	VP	0.1759	134.14694	10.57861	0.8219
3	4.591	BV	0.2320	386.25388	22.99147	2.3667
4	5.208	VB	0.2501	1.56248e4	867.49646	95.7367
5	12.611	PP	0.3581	5.10952	1.87425e-1	0.0313
6	13.602	VB	0.2634	5.86944	2.90903e-1	0.0360
Totals :				1.63207e4	912.65190	

H NMR: Compound 32



G (s) 8.27
H (dd) 7.74
I (s) 7.45
J (m) 7.37
K (m) 7.13
A (dd) 4.60
B (m) 4.03
C (dd) 3.81
D (m) 2.27
E (m) 1.82
F (ddp) 1.17

0.57 1.19 0.67 1.77 0.74 1.00 2.19 1.13 1.17 2.19 1.48

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)

Elemental Composition Report

Single Mass Analysis

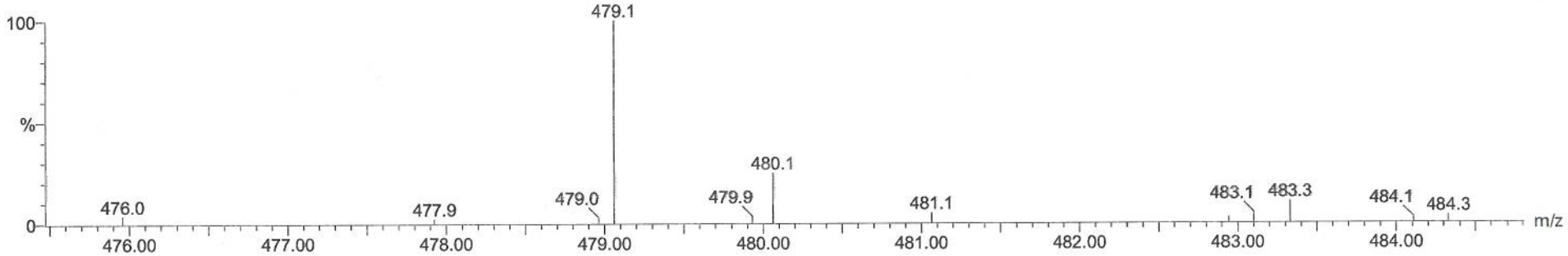
Tolerance = 10.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

S32

Monoisotopic Mass, Even Electron Ions
166 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-4 O: 0-30 I: 1-1

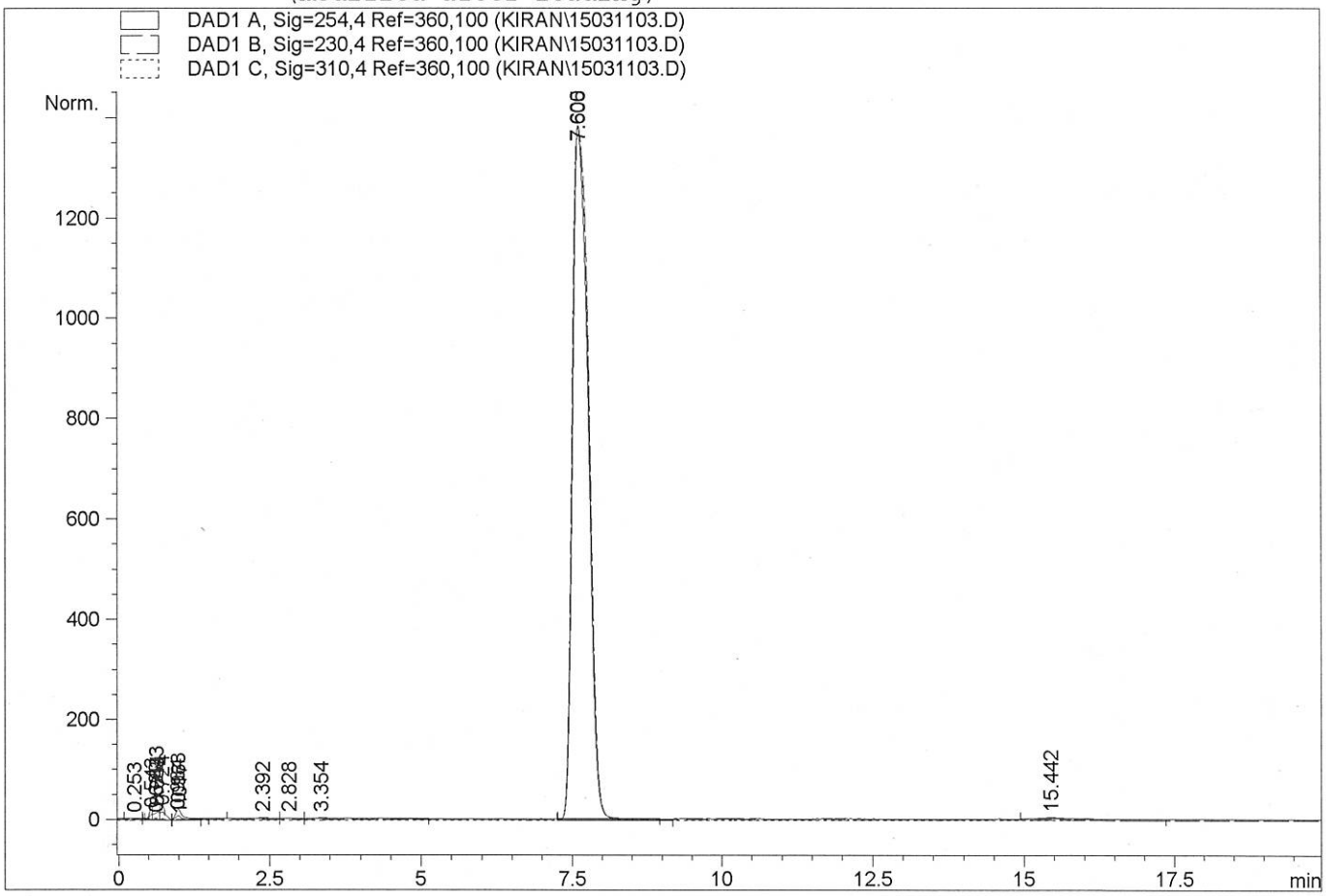
15-Jan-2015
kst-15jan15-1064 65 (1.202) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

TOF MS ES+
1.32e+003



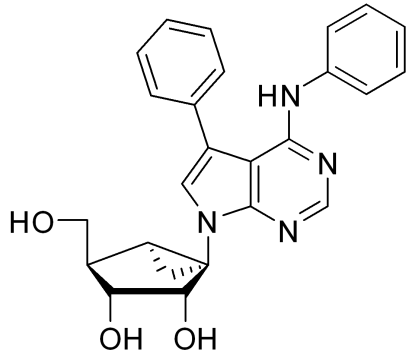
Minimum:				-50.0		
Maximum:		10.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
479.0589	479.0580	0.9	1.9	11.5	4.4	C19 H20 N4 O3 I
	479.0545	4.4	9.2	-10.5	121.6	C H28 N4 O16 I
	479.0639	-5.0	-10.4	2.5	26.4	C12 H24 N4 O8 I

```
==========================================================================
Injection Date  : 3/11/2015 2:19:19 PM
Sample Name     : MRS4201                          Location : Vial 1
Acq. Operator   : KIRAN
Method          : C:\HPCHEM\1\METHODS\KIRANADK.M
Last changed    : 3/11/2015 1:19:46 PM by KIRAN
                  (modified after loading)
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     20.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.253 BV    0.1722    3.83279 3.01671e-1   0.0510
   2   0.633 VP    0.1862  147.05983   10.32053   1.9583
   3   0.988 VB    0.1251   54.51635    6.29256   0.7259
   4   2.392 PV    0.3597    9.04957 3.38762e-1   0.1205
   5   2.828 VV    0.1889    3.53570 2.33220e-1   0.0471
   6   3.354 VP    0.3622    9.71599 3.90639e-1   0.1294
   7   7.605 BP    0.2956 7247.27979  407.25183  96.5056
   8  15.442 PP    0.5366   34.70752 9.71947e-1   0.4622

Totals :                  7509.69754  426.10115
```

H NMR: Compound 34



H (m)
7.27

F (m)
7.47

C (dd)
3.84

D (s)
8.32

E (m)
7.57

I (ddt)
7.03

A (dd)
4.70

B (m)
4.08

J (m)
2.31

L (m)
1.88

K (ddd)
1.24

G (s)
7.33

0.51 3.73 2.70 0.68 1.72 0.68 1.00 2.02 1.03 1.27 2.30 0.97

f1 (ppm)

Elemental mposition Report

Single Mass Analysis

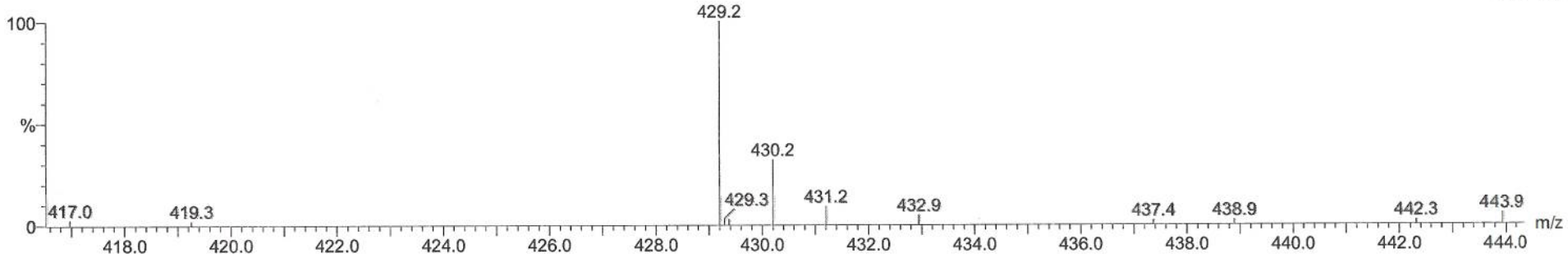
S35

Tolerance = 10.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
206 formula(e) evaluated with 3 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-4 O: 0-18

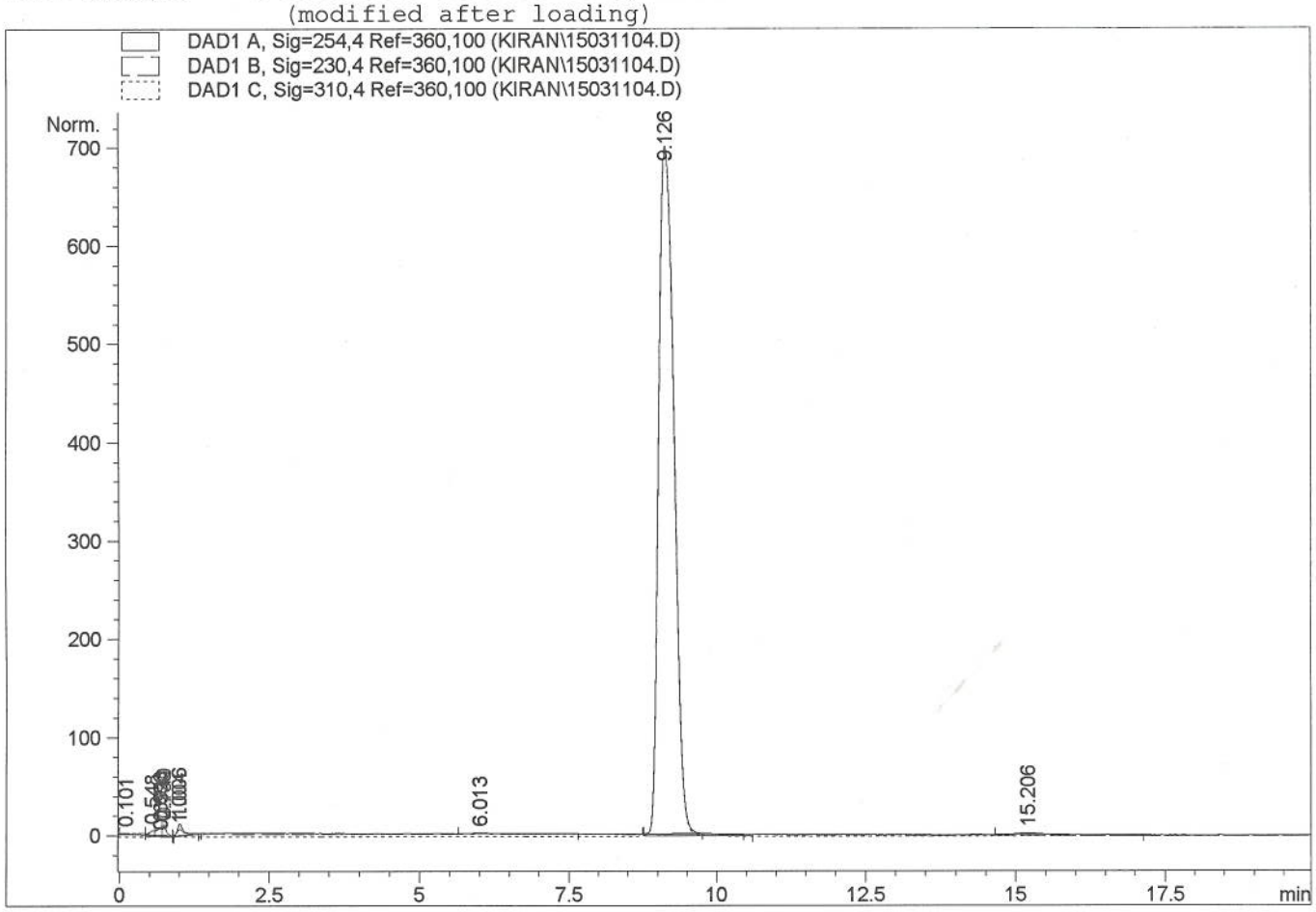
29-Jan-2015
kst-29jan15-1072 165 (3.051) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

TOF MS ES+
1.45e+003



Minimum:				-50.0		
Maximum:		10.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
429.1935	429.1927	0.8	1.9	15.5	14.4	C25 H25 N4 O3
	429.1892	4.3	10.0	-6.5	124.9	C7 H33 N4 O16
	429.1985	-5.0	-11.6	6.5	38.7	C18 H29 N4 O8

```
Injection Date  : 3/11/2015 3:06:22 PM
Sample Name     : MRS4202                          Location : Vial 1
Acq. Operator   : KIRAN
Method          : C:\HPCHEM\1\METHODS\KIRANADK.M
Last changed    : 3/11/2015 1:19:46 PM by KIRAN
                  (modified after loading)
```



Area Percent Report

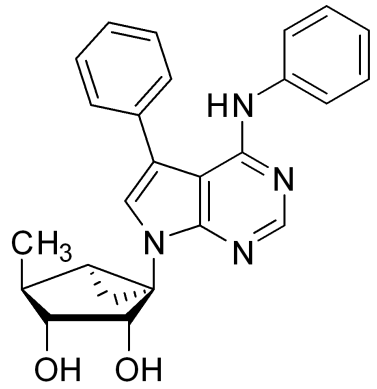
```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     20.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

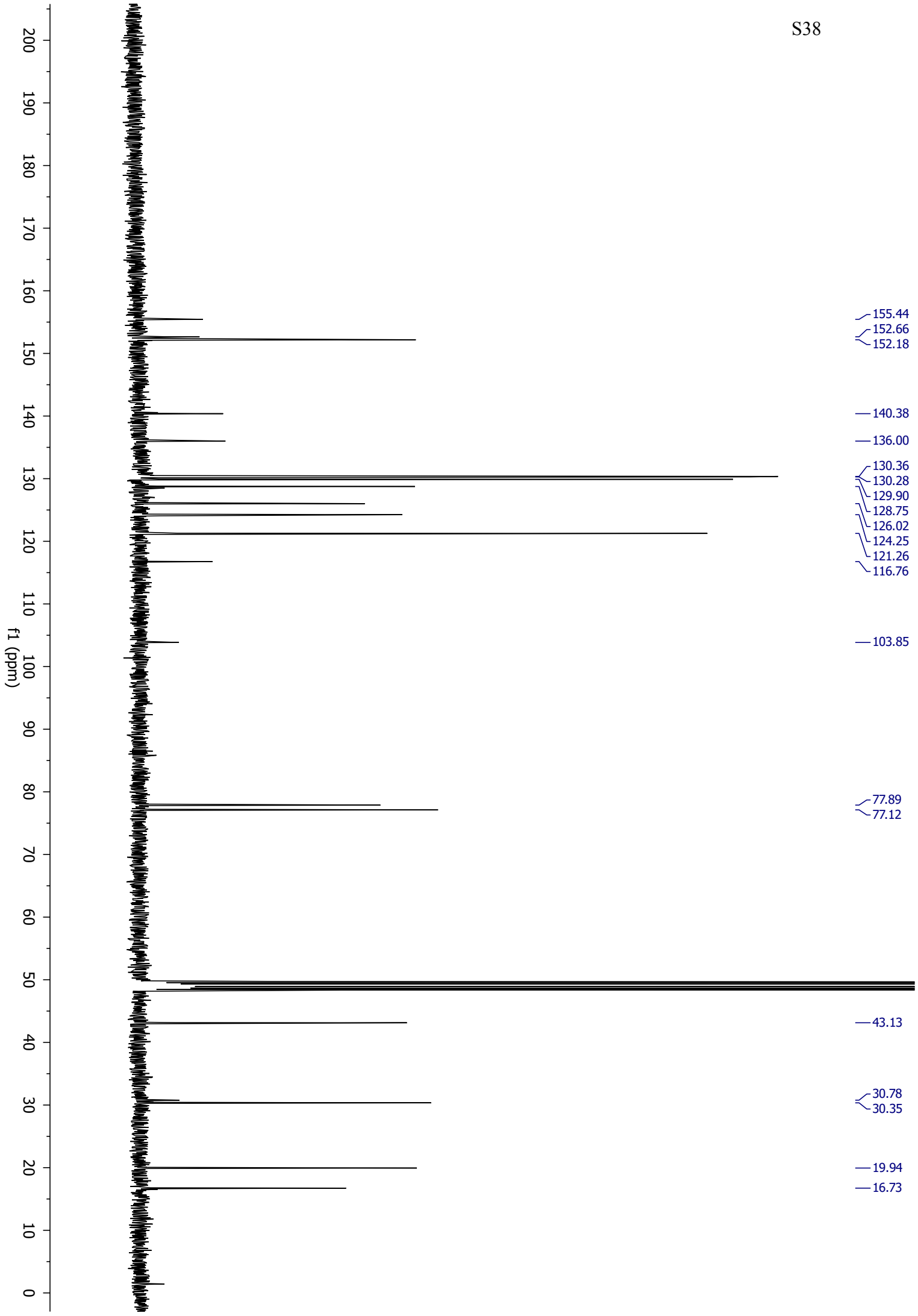
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.101	BV	0.3497	10.84599	3.72472e-1	0.2151
2	0.740	VP	0.1565	58.08654	4.68872	1.1522
3	1.006	VB	0.1197	42.08311	4.92255	0.8348
4	6.013	PP	0.3598	10.67149	3.70724e-1	0.2117
5	9.126	BP	0.2917	4895.50293	269.82489	97.1093
6	15.206	PP	0.4892	24.03884	7.93965e-1	0.4768
Totals :				5041.22889	280.97331	

Results obtained with enhanced integrator!

H NMR: Compound 38a




155.44
152.66
152.18
140.38
136.00
130.36
130.28
129.90
128.75
126.02
124.25
121.26
116.76
103.85
77.89
77.12
43.13
30.78
30.35
19.94
16.73
f1 (ppm)

Elemental Composition Report

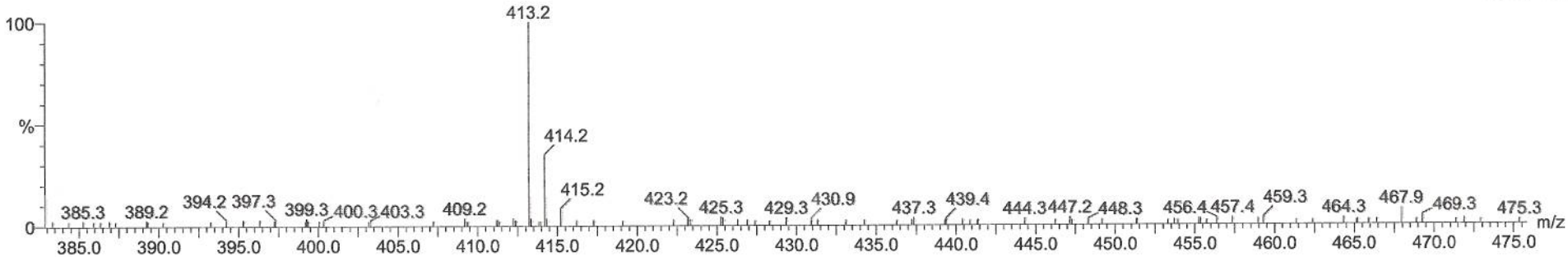
Single Mass Analysis

Tolerance = 10.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
211 formula(e) evaluated with 5 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-4 O: 0-30

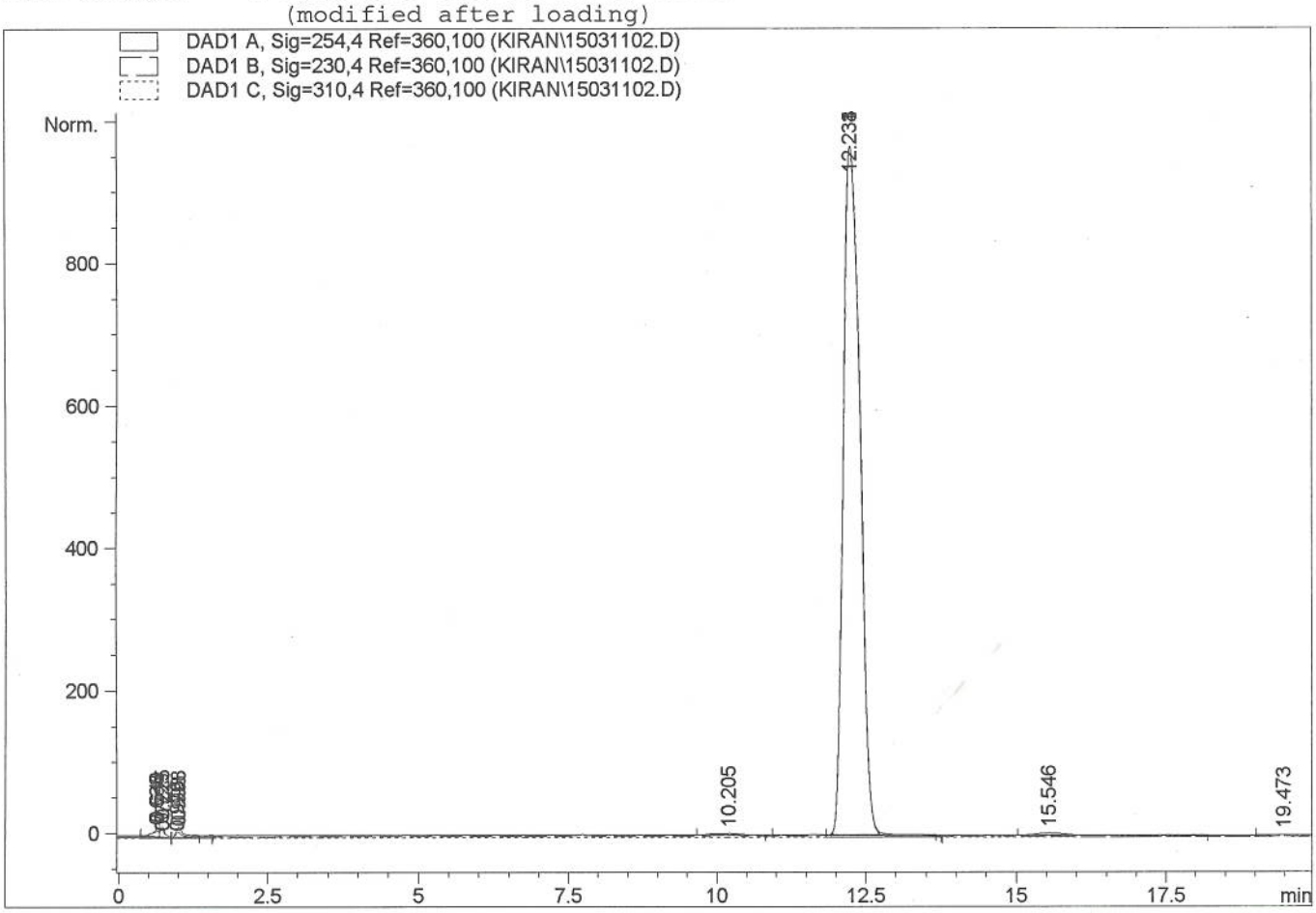
09-Mar-2015
kst-09mar15-1081 170 (3.144) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

TOF MS ES+
9.02e+002



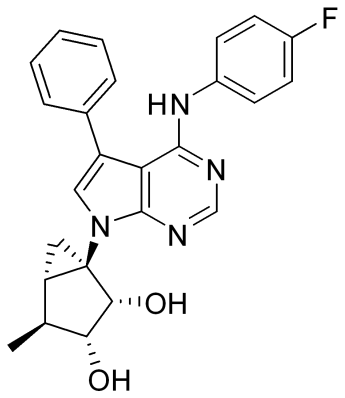
Minimum:				-50.0		
Maximum:		10.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
413.1977	413.1978	-0.1	-0.2	15.5	9.2	C25 H25 N4 O2
	413.2001	-2.4	-5.8	-15.5	141.8	H37 N4 O20
	413.1942	3.5	8.5	-6.5	87.0	C7 H33 N4 O15
	413.2036	-5.9	-14.3	6.5	28.4	C18 H29 N4 O7
	413.1884	9.3	22.5	2.5	47.4	C14 H29 N4 O10

```
Injection Date  : 3/11/2015 1:20:58 PM
Sample Name     : MRS4203                          Location : Vial 1
Acq. Operator   : KIRAN
Method          : C:\HPCHEM\1\METHODS\KIRANADK.M
Last changed    : 3/11/2015 1:19:46 PM by KIRAN
                  (modified after loading)
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount         :     20.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   0.640 BV    0.1075   39.80030    4.86134   0.5295
   2   0.725 VP    0.0775   34.21190    6.28869   0.4552
   3   0.998 VB    0.1349   59.24288    6.12125   0.7882
   4  10.205 PV    0.4124   34.24180    1.02861   0.4556
   5  12.233 PP    0.3160 7303.14941  380.42142  97.1679
   6  15.546 PP    0.5065   38.74314    1.24695   0.5155
   7  19.473 PBA   0.3487    6.62321 2.96399e-1   0.0881

Totals :                  7516.01264  400.26464
```

H NMR: Compound 38b

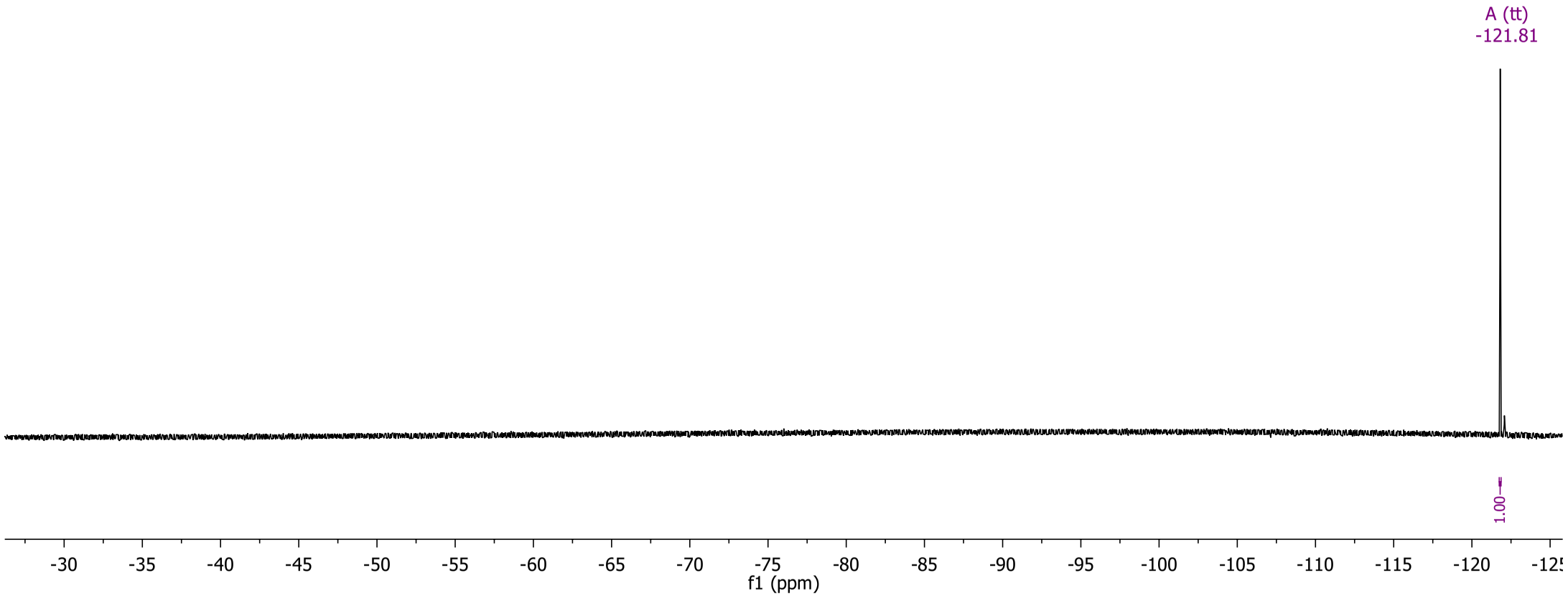


L (s) 8.32
J (m) 7.45
K (m) 7.54
I (s) 7.24
H (m) 7.01
G (m) 4.84
F (dt) 3.80
E (m) 2.19
C (ddd) 1.81
D (m) 1.92
B (d) 1.43
A (ddd) 1.21

0.52 3.24 2.39 0.77 1.71 0.84 0.96 1.00 0.80 0.93 3.03 1.00

f1 (ppm)

F NMR: Compound 38b



S43

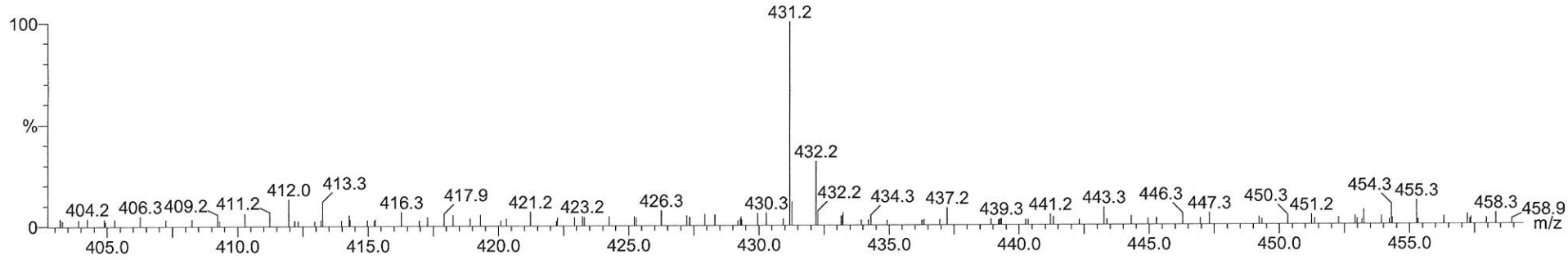
Single Mass Analysis

Tolerance = 10.0 mDa / DBE: min = -2.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
79 formula(e) evaluated with 3 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-120 H: 0-200 N: 4-4 O: 0-29 F: 1-1

28-Mar-2016
kst-28mar16-2-020 132 (2.442) Cn (Cen,5, 50.00, Ar); Sm (SG, 1x2.00); Sb (12,5.00)

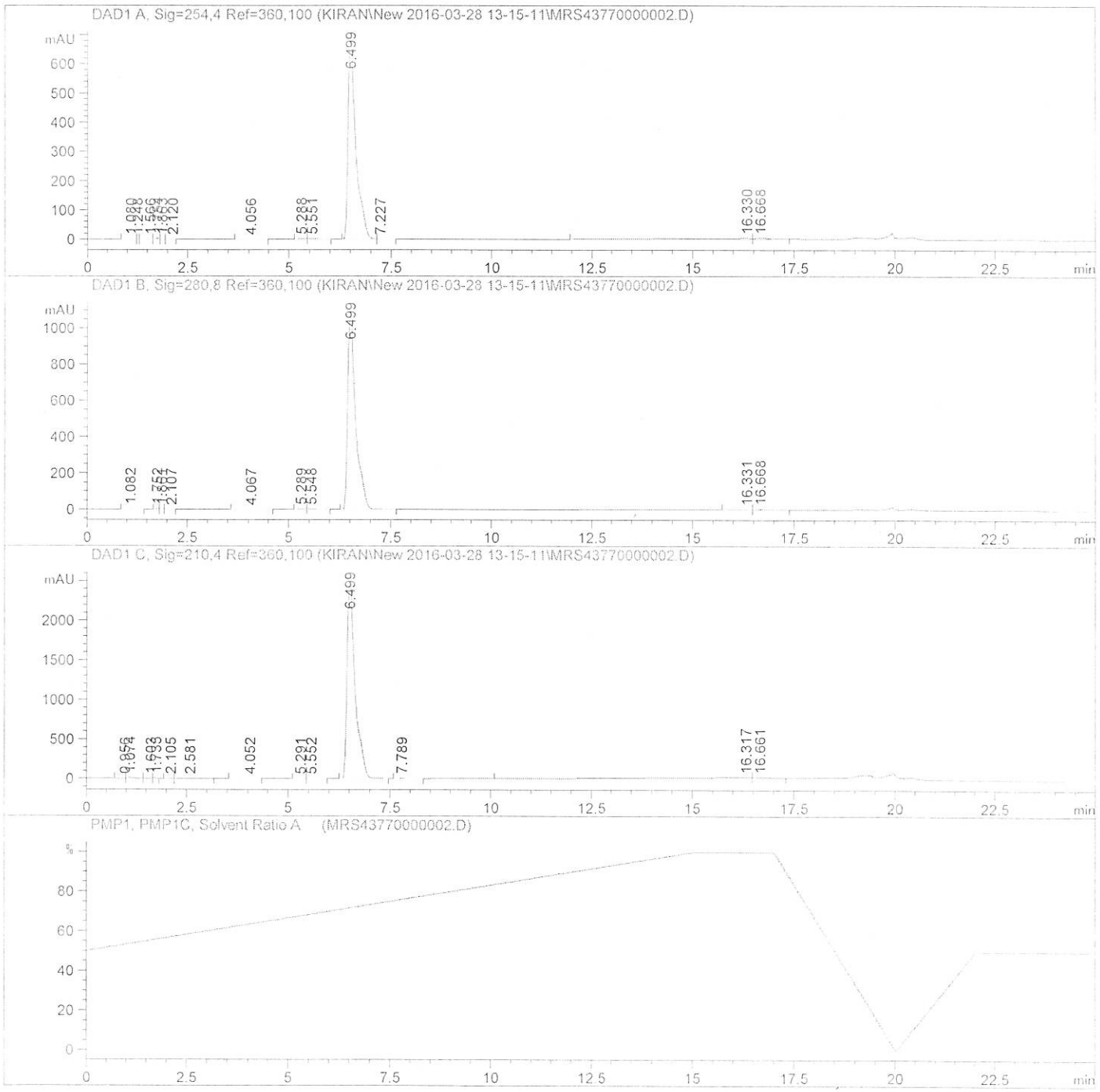
TOF MS ES+
2.81e+003



Minimum:				-2.0		
Maximum:		10.0	10.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
431.1881	431.1883	-0.2	-0.5	15.5	1.3	C25 H24 N4 O2 F
	431.1942	-6.1	-14.1	6.5	33.9	C18 H28 N4 O7 F
	431.1789	9.2	21.3	2.5	81.1	C14 H28 N4 O10 F

Data File D:\Chem32\1\Data\KIRAN\New 2016-03-28 13-15-11\MRS43770000002.D
Sample Name: MRS4377

Acq. Operator	: SYSTEM	Seq. Line	: 2
Acq. Instrument	: HPLC-001	Location	: 2
Injection Date	: 3/28/2016 1:42:29 PM	Inj	: 1
		Inj Volume	: 10.000 µl
Acq. Method	: D:\Chem32\1\Data\KIRAN\New 2016-03-28 13-15-11\ANAL_A50-100_D50-00_15MIN.M		
Last changed	: 3/28/2016 1:15:11 PM by SYSTEM		
Analysis Method	: D:\Chem32\1\Data\KIRAN\New 2016-03-28 13-15-11\ANAL_A50-100_D50-00_15MIN.M (Sequence Method)		
Last changed	: 3/28/2016 2:31:40 PM by SYSTEM (modified after loading)		
Additional Info	: Peak(s) manually integrated		



Data File D:\Chem32\1\Data\KIRAN\New 2016-03-28 13-15-11\MRS43770000002.D
Sample Name: MRS4377

Acq. Operator : SYSTEM Seq. Line : 2
Acq. Instrument : HPLC-001 Location : 2
Injection Date : 3/28/2016 1:42:29 PM Inj : 1
Inj Volume : 10.000 µl
Acq. Method : D:\Chem32\1\Data\KIRAN\New 2016-03-28 13-15-11\ANAL_A50-100_D50-00_15MIN.M
Last changed : 3/28/2016 1:15:11 PM by SYSTEM
Analysis Method : D:\Chem32\1\Data\KIRAN\New 2016-03-28 13-15-11\ANAL_A50-100_D50-00_15MIN.M
(Sequence Method)
Last changed : 3/28/2016 2:31:40 PM by SYSTEM
(modified after loading)
Additional Info : Peak(s) manually integrated

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.080	BV	0.1362	12.33841	1.21812	0.1285
2	1.248	VV	0.0579	1.97356	4.80871e-1	0.0205
3	1.566	VV	0.2206	11.94476	7.01729e-1	0.1244
4	1.754	VV	0.0722	18.90858	3.79072	0.1969
5	1.863	VV	0.0712	4.34669	9.90358e-1	0.0453
6	2.120	VV	0.1468	5.59086	5.49127e-1	0.0582
7	4.056	BB	0.2552	7.72690	3.96821e-1	0.0804
8	5.288	BV	0.1516	25.61704	2.54201	0.2667
9	5.551	VB	0.1979	32.00481	2.36415	0.3332
10	6.499	BV	0.1975	9152.18652	677.97644	95.2846
11	7.227	VB	0.2075	9.54675	6.42037e-1	0.0994
12	16.330	BV	1.5241	255.09123	1.97341	2.6558
13	16.668	VB	0.2987	67.82568	2.94471	0.7061

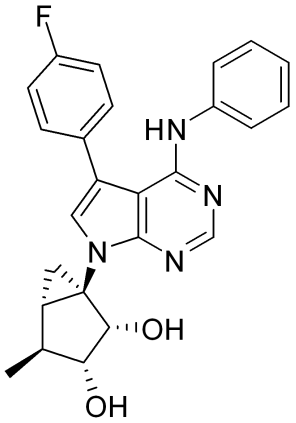
Totals : 9605.10179 696.57050

Signal 2: DAD1 B, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.082	BB	0.1488	7.34831	6.76310e-1	0.0493
2	1.752	BV	0.0617	7.58111	1.85446	0.0508
3	1.861	VV	0.0673	1.71600	4.23582e-1	0.0115
4	2.107	VV	0.1276	3.04192	3.06993e-1	0.0204
5	4.067	BB	0.2550	7.81479	4.05261e-1	0.0524
6	5.289	BV	0.1546	21.79816	2.14364	0.1461
7	5.548	VB	0.1933	21.23089	1.59540	0.1423
8	6.499	BB	0.1979	1.47441e4	1089.60168	98.8435
9	16.331	BV	0.4889	54.32557	1.36326	0.3642
10	16.668	VB	0.3060	47.65012	2.01392	0.3194

Totals : 1.49166e4 1100.38452

H NMR: Compound 38c

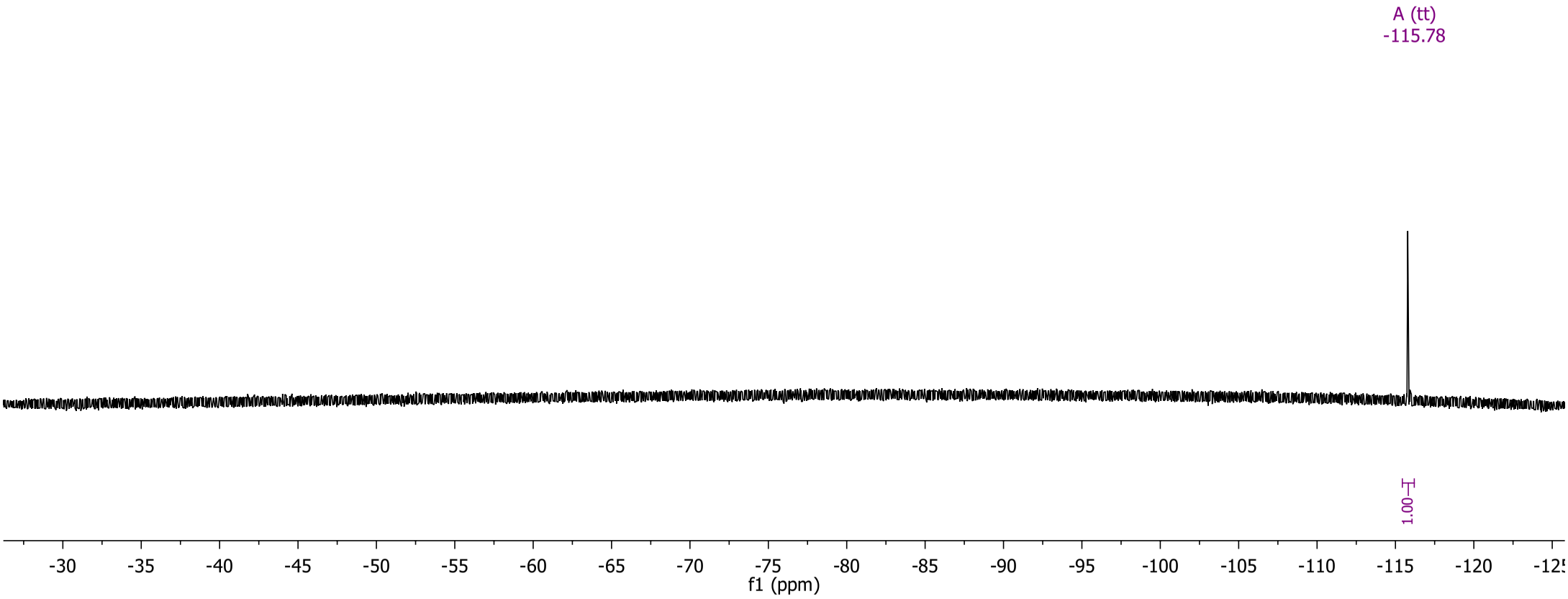


K (s) 8.37
J (m) 7.55
I (m) 7.30
H (tt) 6.98
G (m) 4.75
F (d) 3.63
C (m) 2.05
B (m) 1.65
A (t) 1.72
E (m) 1.19
D (d) 1.37

0.54 5.04 4.90 0.88 0.89 1.01 1.11 1.00 0.99 2.85 1.78

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)

F NMR: Compound 38c



S48

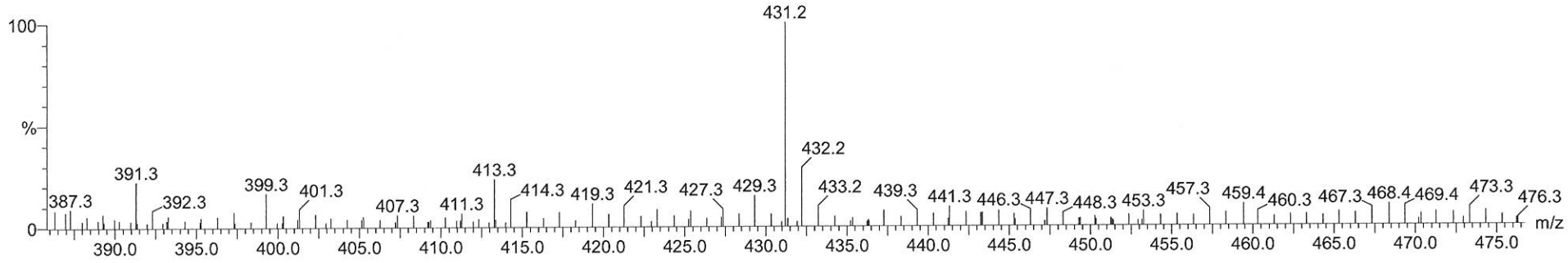
Single Mass Analysis

Tolerance = 10.0 mDa / DBE: min = -2.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
79 formula(e) evaluated with 3 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-4 O: 0-30 F: 1-1

22-Mar-2016
kst-22mar16-2-022-a 134 (2.478) Cn (Cen,5, 50.00, Ar); Sm (SG, 1x2.00); Sb (12,5.00)

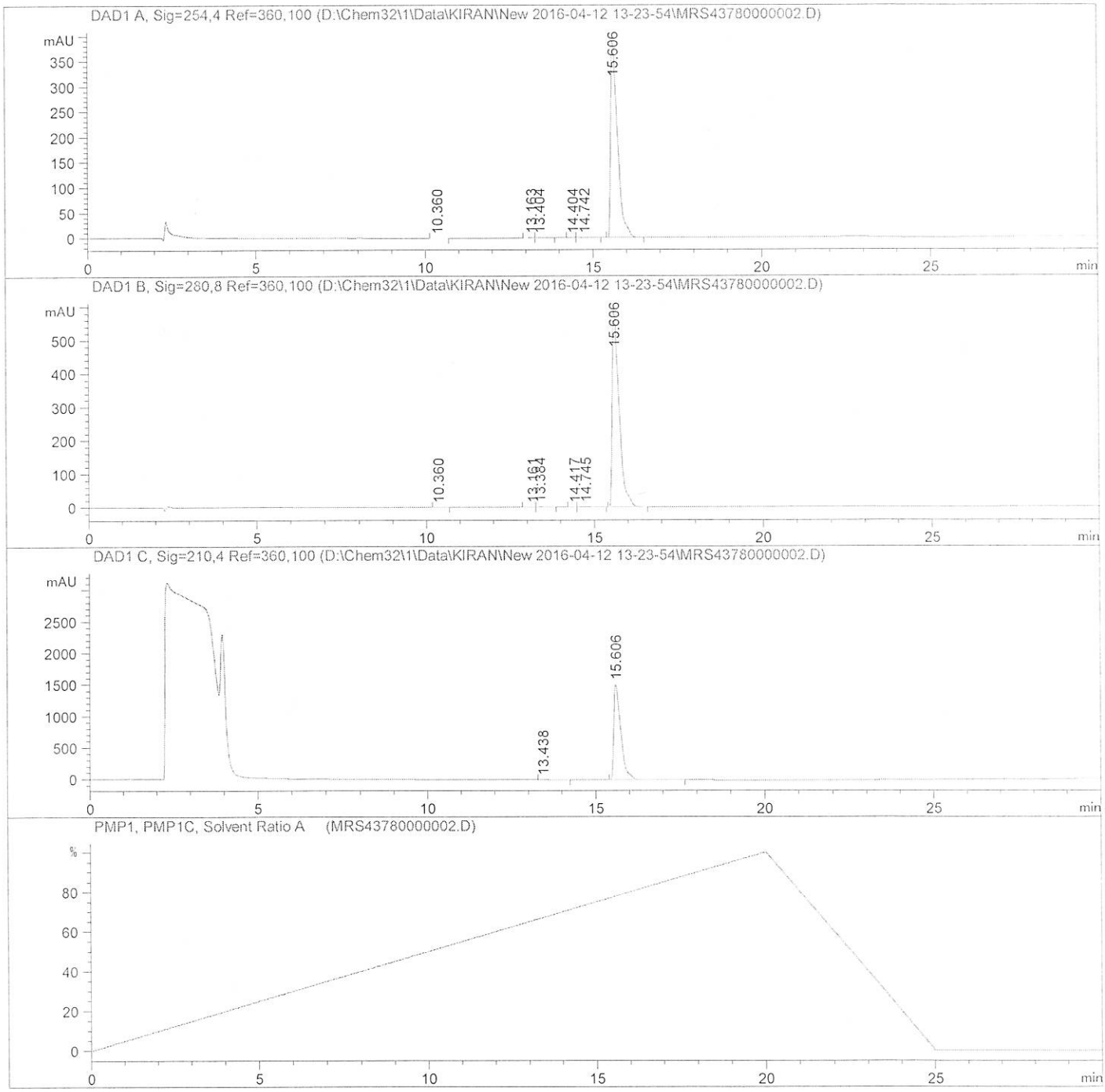
TOF MS ES+
4.83e+003



Minimum:				-2.0		
Maximum:		10.0	10.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
431.1887	431.1883	0.4	0.9	15.5	72.6	C25 H24 N4 O2 F
	431.1942	-5.5	-12.8	6.5	117.2	C18 H28 N4 O7 F
	431.1789	9.8	22.7	2.5	201.9	C14 H28 N4 O10 F

Data File D:\Chem32\1\Data\KIRAN\New 2016-04-12 13-23-54\MRS43780000002.D
Sample Name: MRS4378

```
==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : HPLC-001                        Location :   2
Injection Date  : 4/12/2016 1:55:53 PM                 Inj :   1
                                                 Inj Volume : 10.000 µl
Acq. Method     : D:\Chem32\1\Data\KIRAN\New 2016-04-12 13-23-54\WASH_00_100_30min.M
Last changed    : 4/12/2016 1:23:54 PM by SYSTEM
Analysis Method : D:\Chem32\1\Data\KIRAN\New 2016-04-12 13-23-54\WASH_00_100_30min.M (
                  Sequence Method)
Last changed    : 4/12/2016 2:38:47 PM by SYSTEM
                  (modified after loading)
Additional Info : Peak(s) manually integrated
==========================================================================
```



Data File D:\Chem32\1\Data\KIRAN\New 2016-04-12 13-23-54\MRS43780000002.D
Sample Name: MRS4378

Acq. Operator : SYSTEM Seq. Line : 2
Acq. Instrument : HPLC-001 Location : 2
Injection Date : 4/12/2016 1:55:53 PM Inj : 1
Inj Volume : 10.000 µl
Acq. Method : D:\Chem32\1\Data\KIRAN\New 2016-04-12 13-23-54\WASH_00_100_30min.M
Last changed : 4/12/2016 1:23:54 PM by SYSTEM
Analysis Method : D:\Chem32\1\Data\KIRAN\New 2016-04-12 13-23-54\WASH_00_100_30min.M (Sequence Method)
Last changed : 4/12/2016 2:38:47 PM by SYSTEM (modified after loading)
Additional Info : Peak(s) manually integrated

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.360	BB	0.2613	3.02682	1.67091e-1	0.0536
2	13.163	BV	0.1737	2.59097	2.22715e-1	0.0459
3	13.404	VB	0.2569	8.46525	4.59634e-1	0.1500
4	14.404	BV	0.1536	3.41462	3.38668e-1	0.0605
5	14.742	VB	0.2678	17.57603	8.84509e-1	0.3115
6	15.606	BB	0.2095	5607.11035	390.65805	99.3784
Totals :				5642.18405	392.73067	

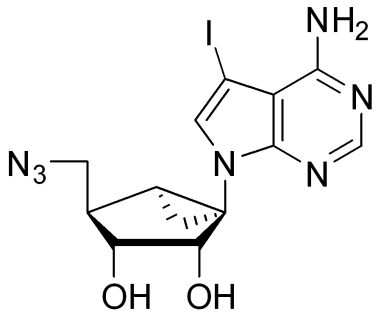
Signal 2: DAD1 B, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.360	BB	0.1989	7.48898e-1	4.93802e-2	8.896e-3
2	13.161	BV	0.1784	3.14890	2.58025e-1	0.0374
3	13.384	VB	0.2254	8.71139	5.42391e-1	0.1035
4	14.417	BV	0.1416	9.39508e-1	9.82482e-2	0.0112
5	14.745	VB	0.2548	13.31102	7.09791e-1	0.1581
6	15.606	BB	0.2096	8391.75293	584.11365	99.6809
Totals :				8418.61265	585.77148	

Signal 3: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.438	VV	0.2752	21.35071	1.20201	0.0976
2	15.606	VB	0.2106	2.18547e4	1512.45642	99.9024
Totals :				2.18760e4	1513.65843	

H NMR: Compound 43



G (s) 8.11
H (s) 7.31
A (dd) 4.66
B (m) 3.89
C (dd) 3.73
D (m) 2.26
E (m) 1.85
F (m) 1.20

0.60 0.66 1.00 1.97 1.17 0.98 2.17 1.18

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)

Single Mass Analysis

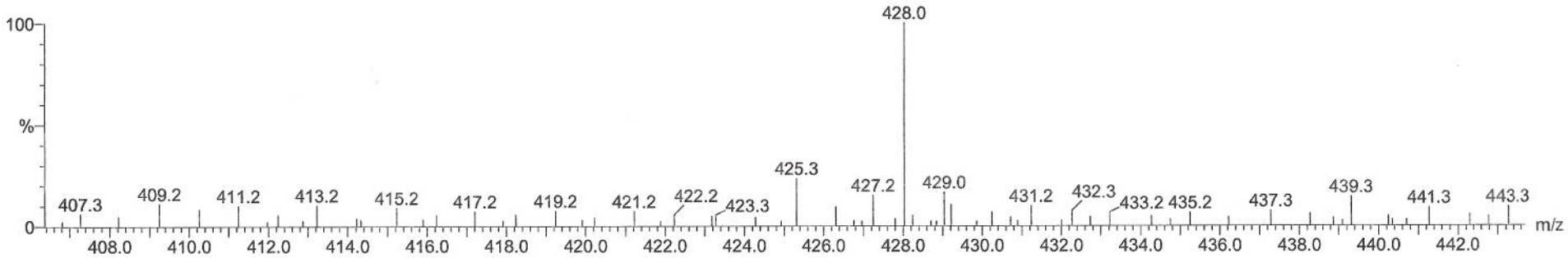
Tolerance = 10.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

S52

Monoisotopic Mass, Even Electron Ions
103 formula(e) evaluated with 3 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 7-7 O: 0-30 I: 1-1

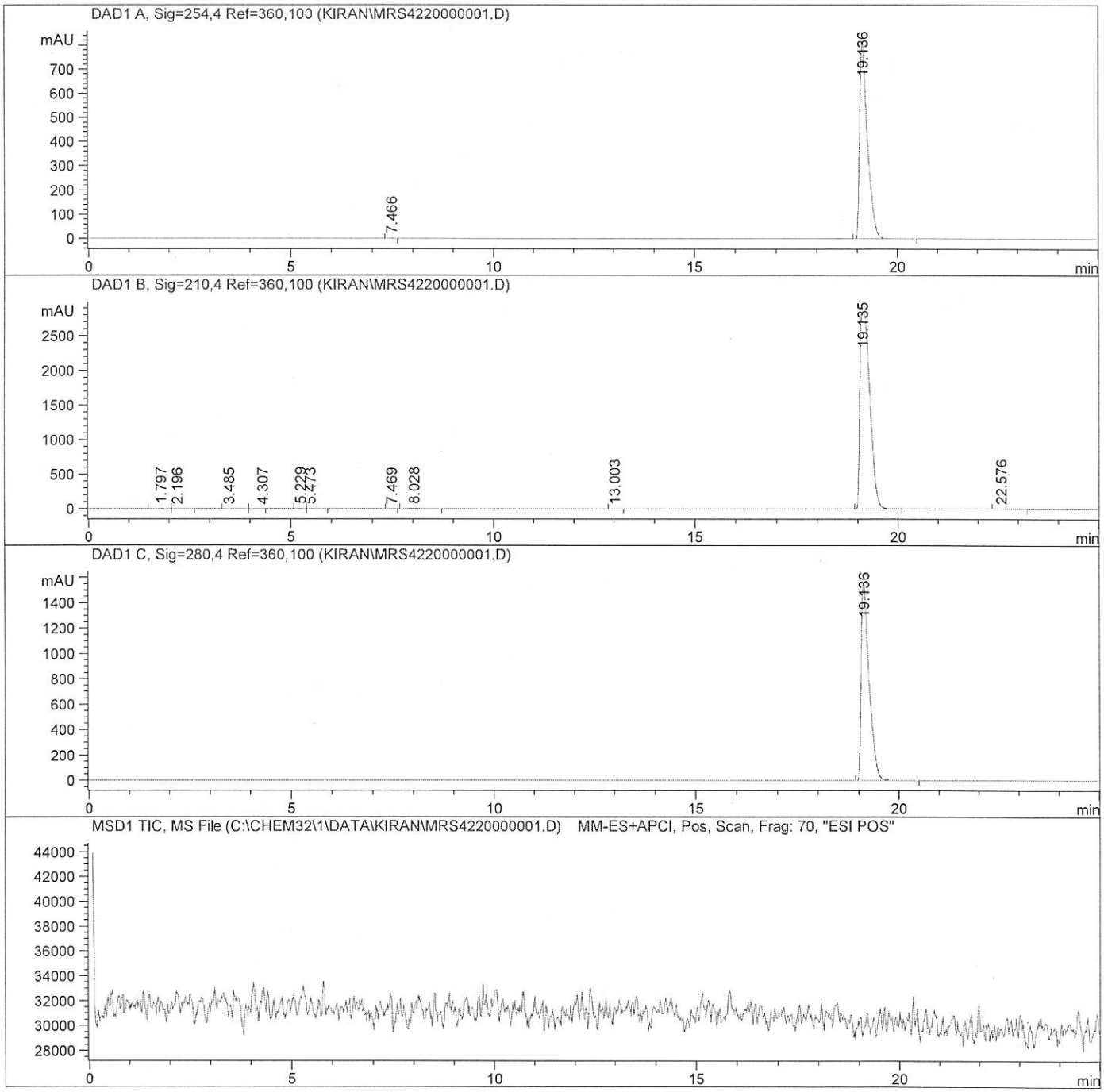
16-Apr-2015
kst-16apr15-1096 145 (2.681) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

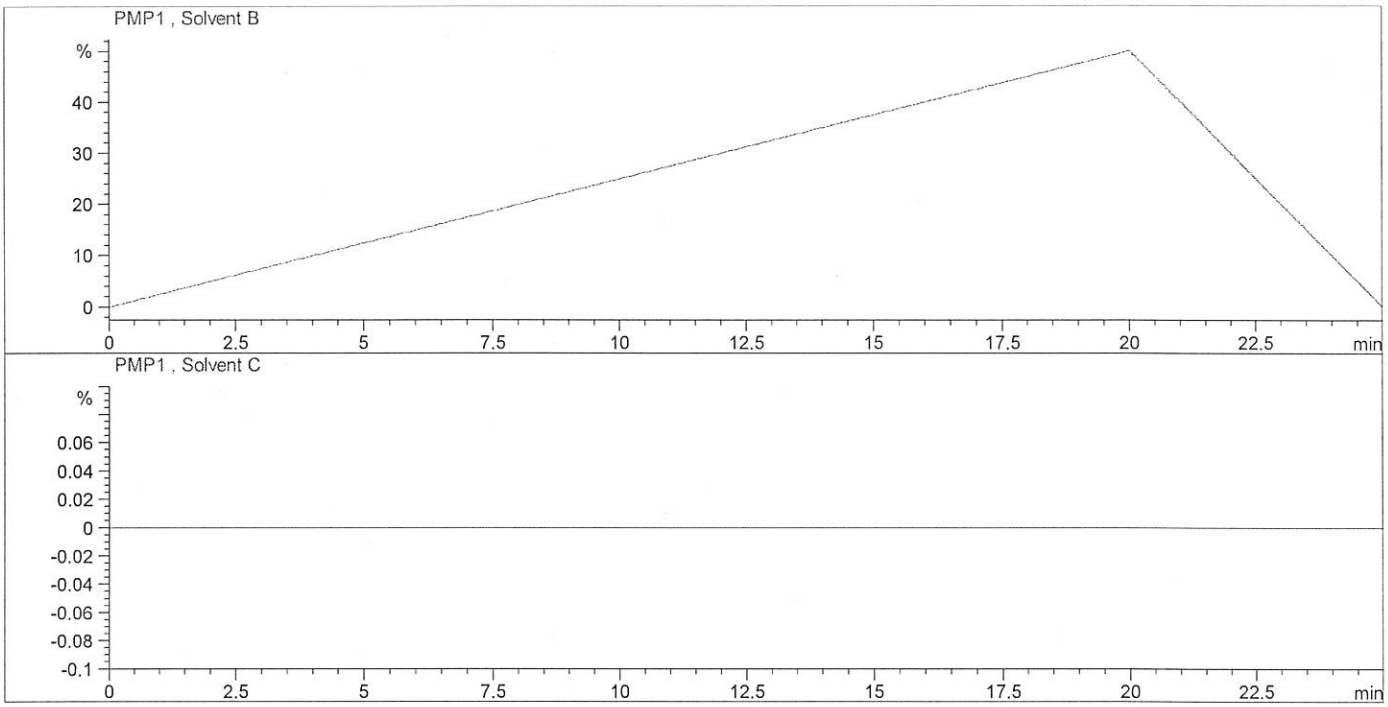
TOF MS ES+
1.17e+003



Minimum:				-50.0		
Maximum:		10.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
428.0336	428.0332	0.4	0.9	9.5	11.7	C13 H15 N7 O2 I
	428.0391	-5.5	-12.8	0.5	26.9	C6 H19 N7 O7 I
	428.0238	9.8	22.9	-3.5	54.6	C2 H19 N7 O10 I

```
==========================================================================
Acq. Operator    : KIRAN
Acq. Instrument  : Instrument 1                    Location : Vial 1
Injection Date   : 9/15/2015 5:14:08 PM                 Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method      : C:\CHEM32\1\METHODS\KST0050.M
Last changed     : 9/15/2015 5:11:59 PM by KIRAN
                   (modified after loading)
Analysis Method  : C:\CHEM32\1\METHODS\KST0050.M
Last changed     : 9/11/2015 5:21:48 PM by KIRAN
Method Info      : ESI neg
```





==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 10.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

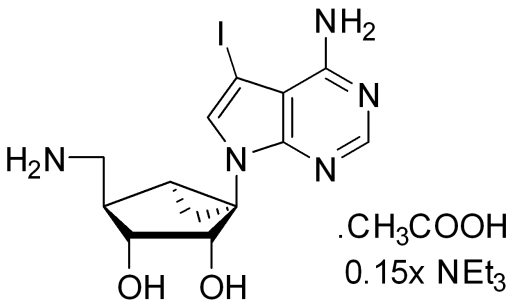
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.466	BB	0.1251	8.11424	1.03880	0.0741
2	19.136	BB	0.1956	1.09376e4	819.89508	99.9259
Totals :				1.09457e4	820.93388	

Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.797	BV	0.1537	58.13491	5.66764	0.1186
2	2.196	VB	0.2647	59.57635	2.98658	0.1216
3	3.485	BB	0.2350	58.25634	3.38218	0.1189
4	4.307	BB	0.1250	10.46638	1.12038	0.0214
5	5.229	BV	0.1386	27.83371	3.16424	0.0568
6	5.473	VB	0.1771	15.56353	1.25137	0.0318

H NMR: Compound 45



.CH_3COOH
0.15x NEt_3

H (s) 8.11
I (s) 7.34
B (d) 4.56
A (d) 4.00
G (t) 3.38
C (t) 2.43
E (d) 1.89
D (t) 1.27

0.88 0.70 1.17 1.00 1.85 1.02 5.91 3.08

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)

Single Mass Analysis

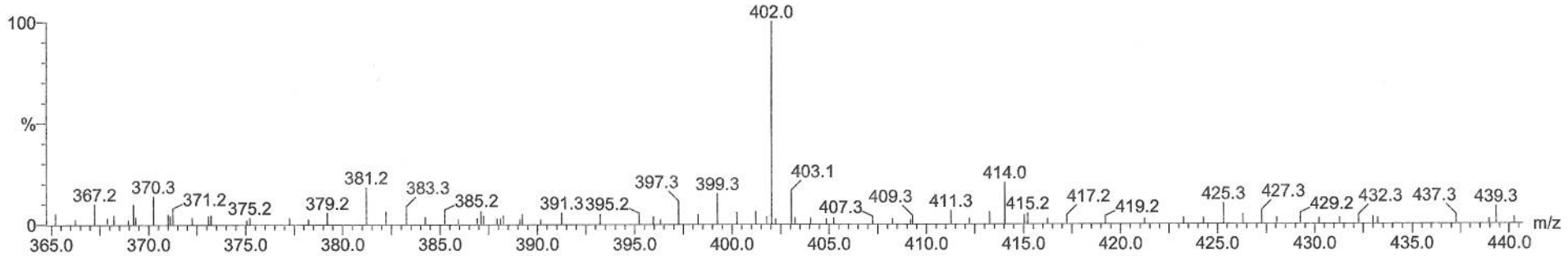
Tolerance = 10.0 mDa / DBE: min = -50.0, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

S56

Monoisotopic Mass, Even Electron Ions
101 formula(e) evaluated with 3 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 5-5 O: 0-30 I: 1-1

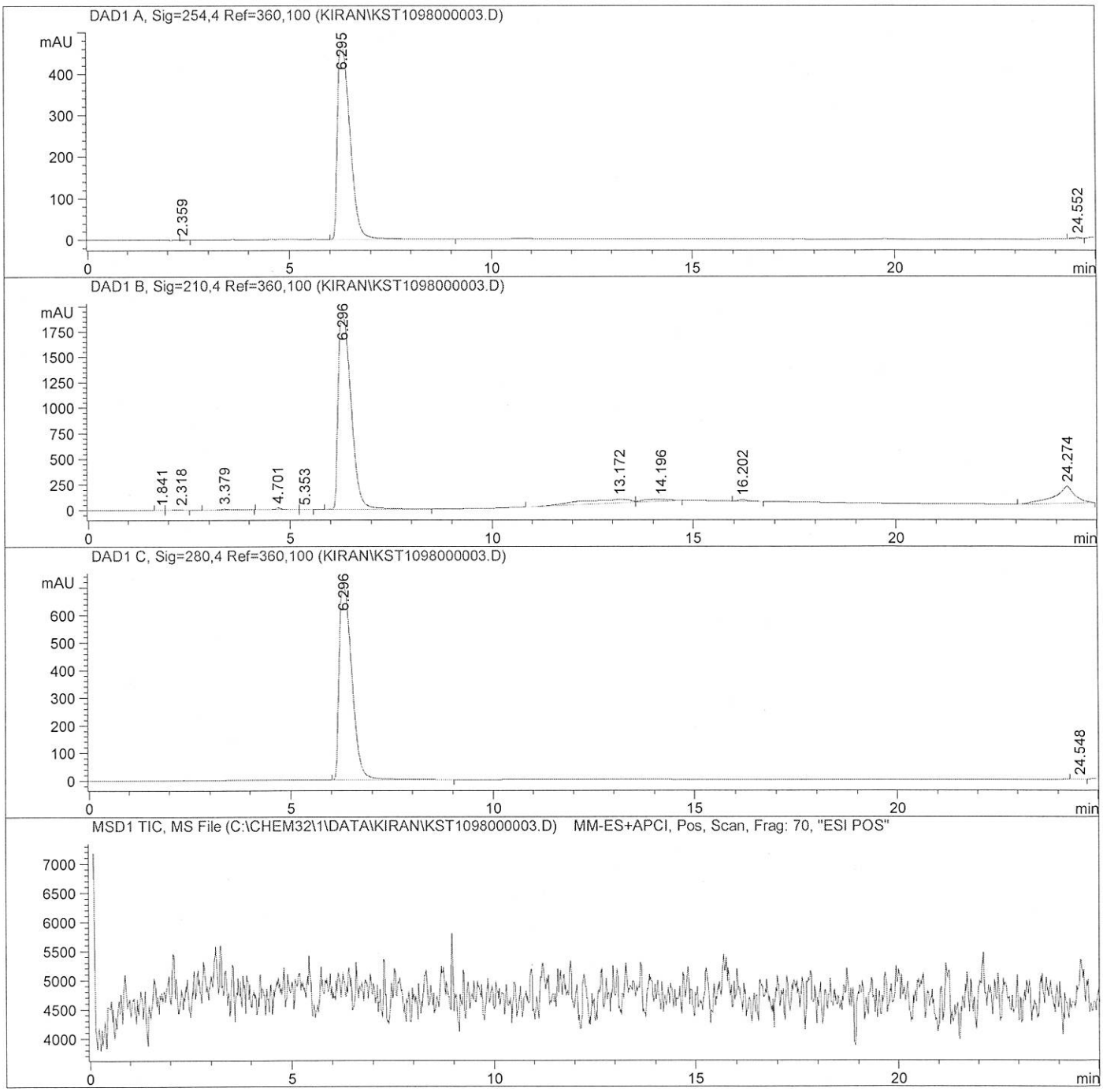
17-Apr-2015
kst-17apr15-1098 382 (7.063) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

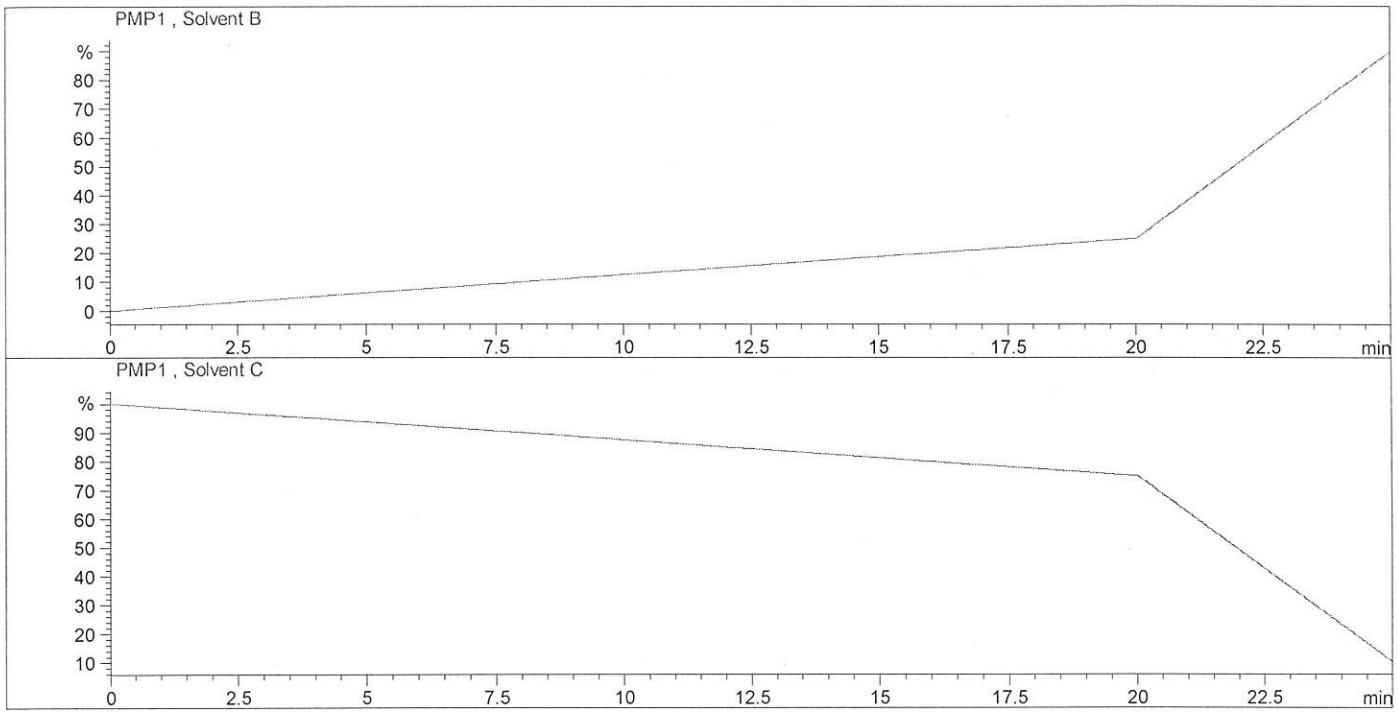
TOF MS ES+
2.37e+003



Minimum:				-50.0		
Maximum:		10.0	10.0	500.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
402.0421	402.0427	-0.6	-1.5	7.5	6.1	C13 H17 N5 O2 I
	402.0486	-6.5	-16.2	-1.5	42.4	C6 H21 N5 O7 I
	402.0333	8.8	21.9	-5.5	103.2	C2 H21 N5 O10 I

```
==========================================================================
Acq. Operator    : KIRAN
Acq. Instrument  : Instrument 1                    Location : Vial 1
Injection Date   : 9/23/2015 1:35:01 PM                 Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method      : C:\CHEM32\1\METHODS\KST0025.M
Last changed     : 9/23/2015 1:33:24 PM by KIRAN
                   (modified after loading)
Analysis Method  : C:\CHEM32\1\METHODS\KST0050.M
Last changed     : 9/11/2015 5:21:48 PM by KIRAN
Method Info      : ESI neg
```





==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 10.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

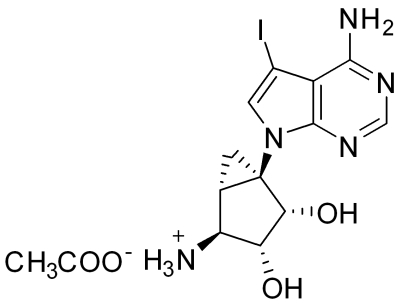
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.359	VB	0.0765	6.81629	1.23308	0.0676
2	6.295	BB	0.3405	1.00561e4	476.01416	99.6912
3	24.552	BB	0.1584	24.32964	2.35719	0.2412
Totals :				1.00873e4	479.60444	

Signal 2: DAD1 B, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.841	BB	0.0744	5.47732	1.05818	0.0104
2	2.318	BB	0.2105	102.97813	6.30528	0.1946
3	3.379	BB	0.1995	158.96597	10.68953	0.3004
4	4.701	BV	0.1768	252.66029	19.04232	0.4775
5	5.353	VB	0.1646	15.05430	1.34460	0.0285

H NMR: Compound 49



H (s) 8.13
G (s) 7.33
F (dd) 4.81
E (dd) 3.90
C (m) 1.84
A (t) 1.95
D (m) 1.29

0.72 0.63 0.89 1.02 1.00 0.86 1.75

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)

S60

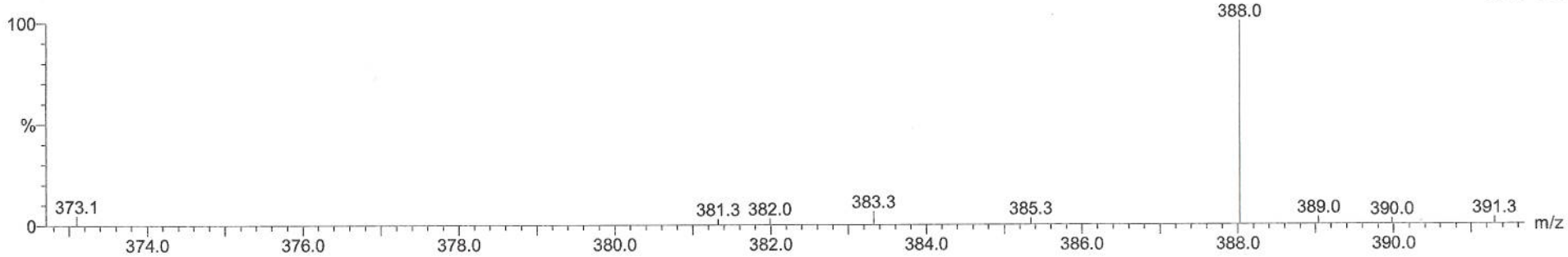
Single Mass Analysis

Tolerance = 30.0 mDa / DBE: min = -2.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
32 formula(e) evaluated with 5 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-120 H: 0-200 N: 5-5 O: 0-35 I: 1-1

29-Dec-2015
kst-29dec15--1-172c 26 (0.914) Cn (Cen,2, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

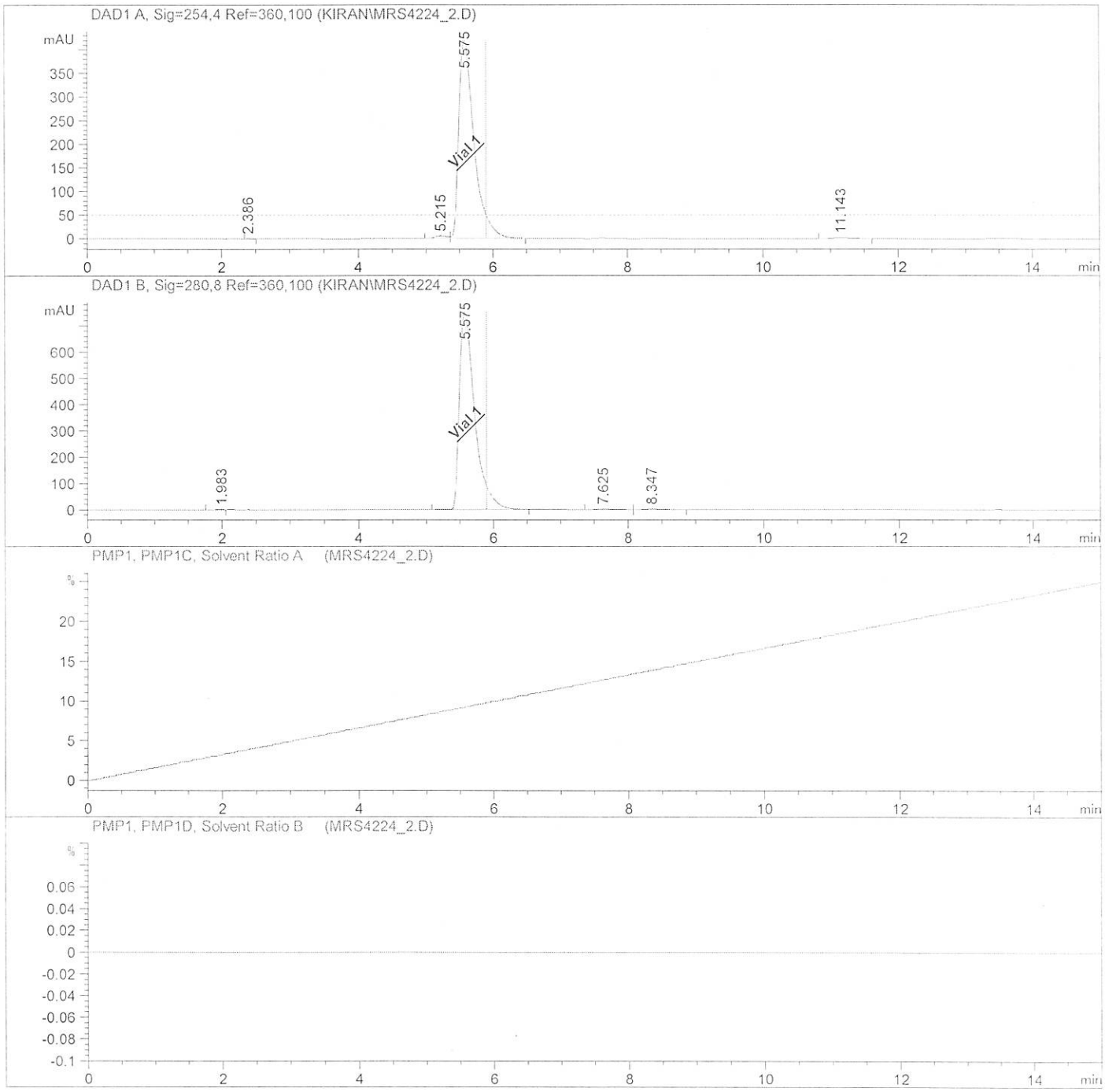
TOF MS ES+
5.77e+003



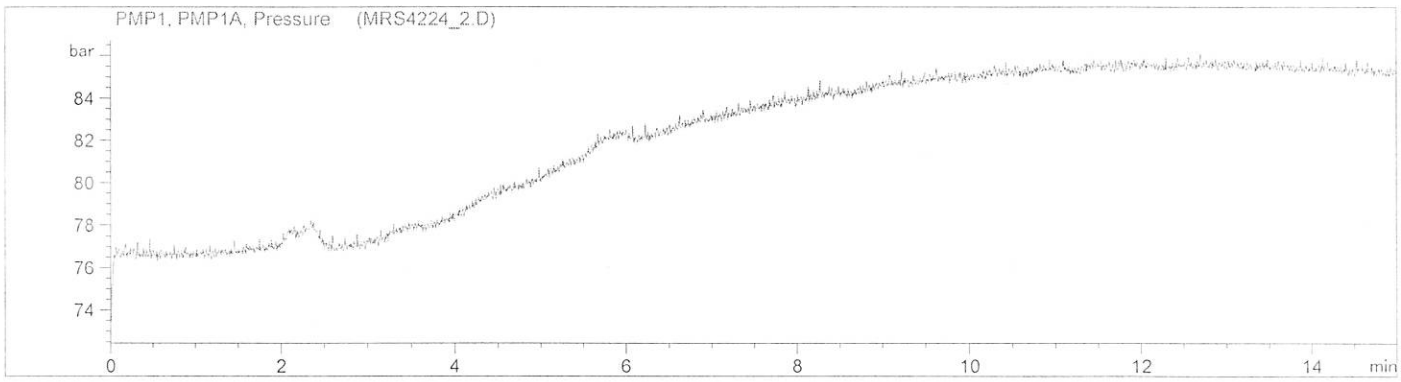
Minimum:				-2.0		
Maximum:		30.0	10.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
388.0268	388.0271	-0.3	-0.8	7.5	792.0	C12 H15 N5 O2 I
	388.0329	-6.1	-15.7	-1.5	183.5	C5 H19 N5 O7 I
	388.0118	15.0	38.7	3.5	443.3	C8 H15 N5 O5 I
	388.0059	20.9	53.9	12.5	1094.9	C15 H11 N5 I
	388.0482	-21.4	-55.2	2.5	572.5	C9 H19 N5 O4 I

Data File D:\Chem32\1\Data\KIRAN\MRS4224_2.D
Sample Name: MRS4224_

Acq. Operator : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC-001 Location : 1
Injection Date : 1/8/2016 1:13:07 PM
Inj Volume : 10.000 µl
Method : C:\CHEM32\1\METHODS\ANAL_00_25_15min.M
Last changed : 1/8/2016 1:11:33 PM by SYSTEM
(modified after loading)

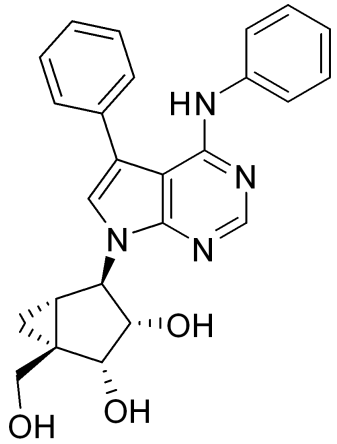


```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : HPLC-001                      Location :   1
Injection Date  : 1/8/2016 1:13:07 PM
                                                Inj Volume : 10.000 µl
Method          : C:\CHEM32\1\METHODS\ANAL_00_25_15min.M
Last changed    : 1/8/2016 1:11:33 PM by SYSTEM
                  (modified after loading)
==========================================================================
```




```
================================================================================
                          Fraction Information
================================================================================
Fraction collection peak controlled
Maximum peak duration 4 min.
Fractions are collected, when at least one peak detector detects a peak
================================================================================
Frac  Well  Location   Volume    BeginTime  EndTime    Reason        Mass
  #     #              [µl]      [min]      [min]
-----|-----|----------|----------|----------|----------|-------------|------------
  1     1    Vial 1        475.42     5.4389     5.8993  DAD1
================================================================================
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Sample Amount:                :     10.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   2.386 BB    0.0714    6.44840    1.26606   0.0946
   2   5.215 BV    0.2003   75.92068    5.81609   1.1136
   3   5.575 VB    0.2486 6695.78955  418.54694  98.2108
   4  11.143 BB    0.2997   39.61779    2.01193   0.5811

Totals :                  6817.77643  427.64101
```

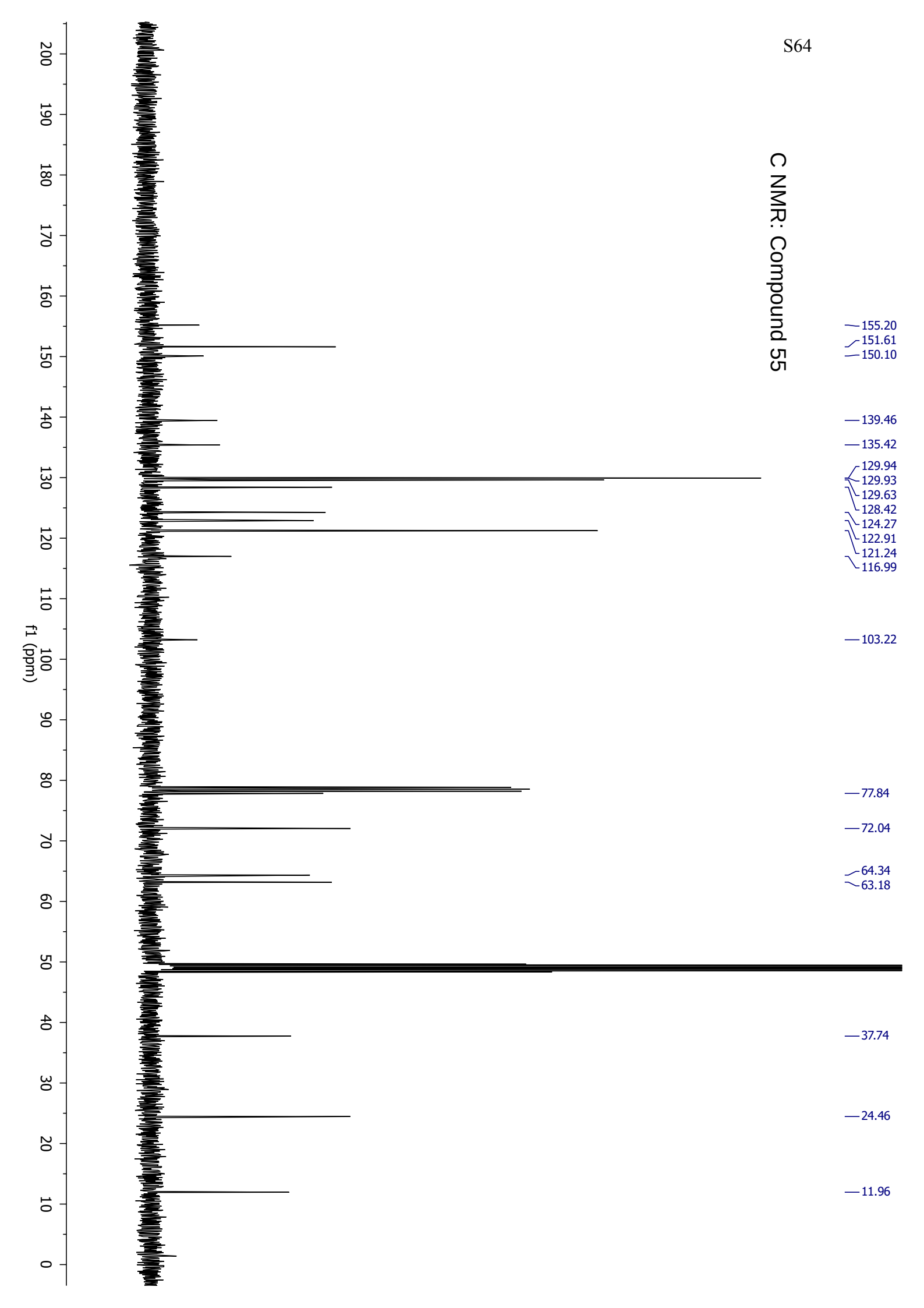
H NMR: Compound 55



M (s) 8.34
L (d) 7.75
K (m) 7.52
J (t) 7.28
I (td) 7.03
H (s) 5.11
G (dd) 4.80
F (d) 4.28
E (dd) 3.87
D (d) 3.28
C (dd) 1.63
B (t) 1.54
A (m) 0.72

0.36 0.82 5.75 1.61 0.66 0.71 1.02 0.94 0.88 0.37 0.93 0.88 1.00

f1 (ppm)


C NMR: Compound 55
155.20
151.61
150.10
139.46
135.42
129.94
129.93
129.63
128.42
124.27
122.91
121.24
116.99
103.22
77.84
72.04
64.34
63.18
37.74
24.46
11.96
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

S65

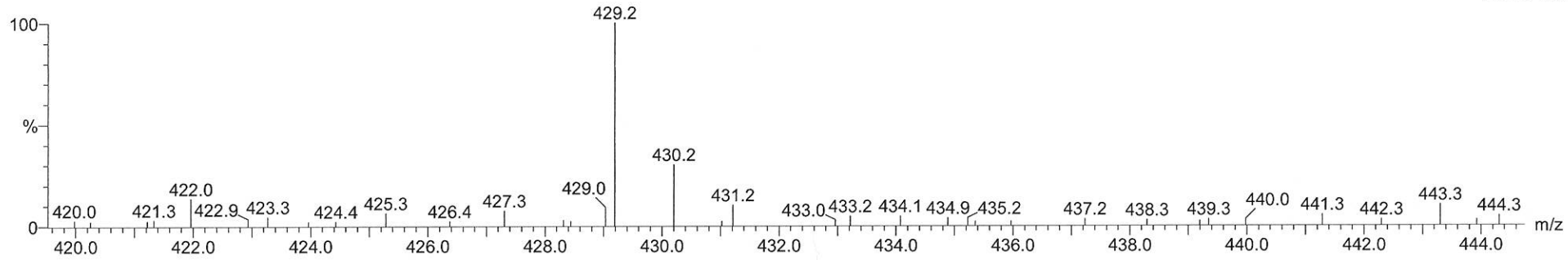
Single Mass Analysis

Tolerance = 10.0 mDa / DBE: min = -2.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
85 formula(e) evaluated with 3 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-109 H: 0-200 N: 4-4 O: 0-32

05-Apr-2016
kst-05apr16-2-038 144 (2.663) Cn (Cen,5, 50.00, Ar); Sm (SG, 3x5.00); Sb (12,5.00)

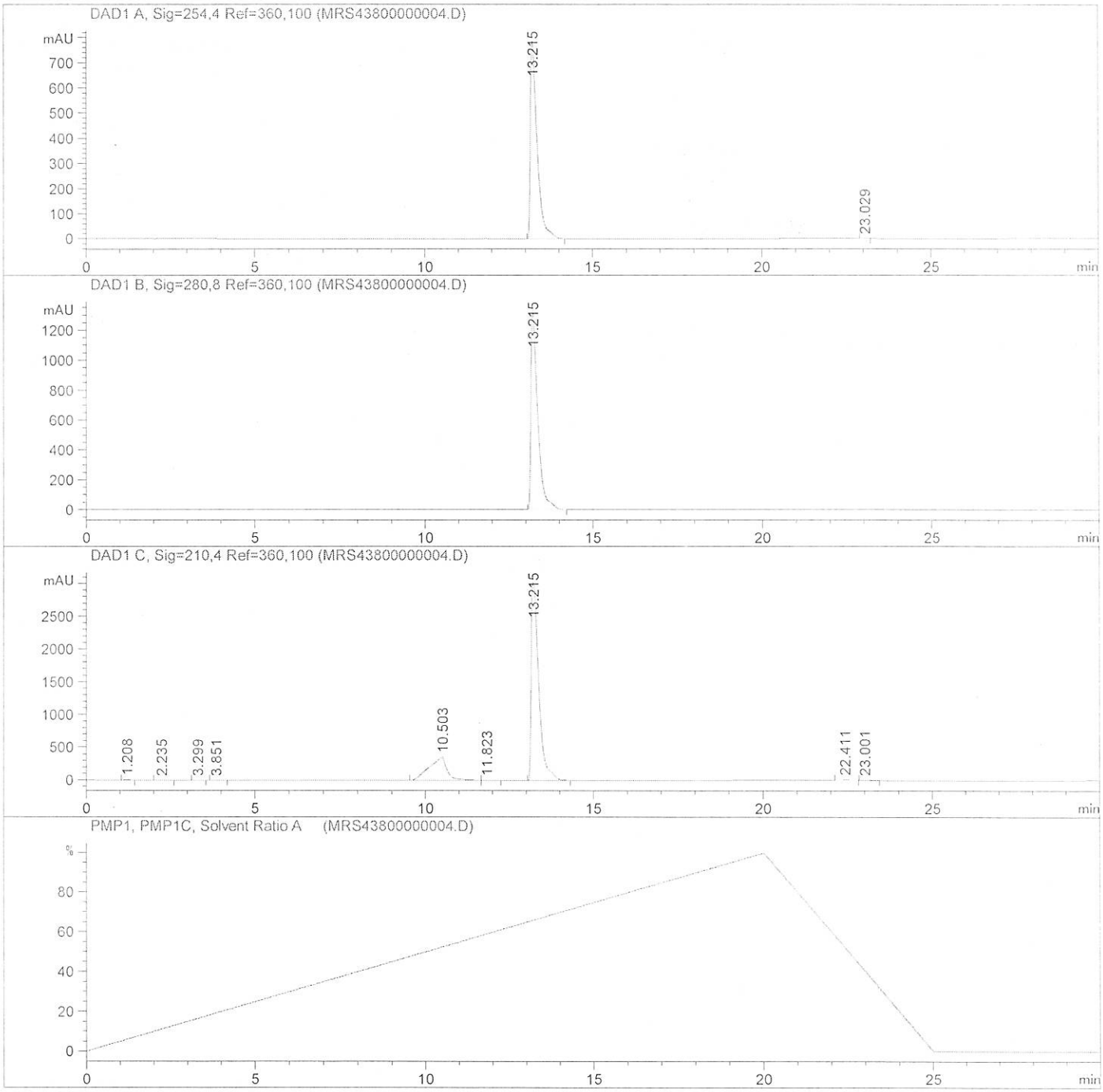
TOF MS ES+
2.82e+003



Minimum:				-2.0					
Maximum:		10.0	10.0	1000.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula			
429.1924	429.1927	-0.3	-0.7	15.5	38.6	C25	H25	N4	O3
	429.1985	-6.1	-14.2	6.5	76.4	C18	H29	N4	O8
	429.1833	9.1	21.2	2.5	124.1	C14	H29	N4	O11

Data File D:\Chem32\1\Data\KIRAN\New 2016-04-08 12-49-37\MRS43800000004.D
Sample Name: MRS4380

```
==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : HPLC-001                        Location :   2
Injection Date  : 4/8/2016 1:21:40 PM                 Inj :   1
                                                 Inj Volume : 10.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 5.000 µl
Sequence File   : D:\Chem32\1\Data\KIRAN\New 2016-04-08 12-49-37\New.S
Method          : D:\Chem32\1\Data\KIRAN\New 2016-04-08 12-49-37\WASH_00_100_30min.M (
                  Sequence Method)
Last changed    : 4/8/2016 12:49:37 PM by SYSTEM
==========================================================================
```



Acq. Operator : SYSTEM Seq. Line : 2
Acq. Instrument : HPLC-001 Location : 2
Injection Date : 4/8/2016 1:21:40 PM Inj : 1
Inj Volume : 10.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 5.000 µl
Sequence File : D:\Chem32\1\Data\KIRAN\New 2016-04-08 12-49-37\New.S
Method : D:\Chem32\1\Data\KIRAN\New 2016-04-08 12-49-37\WASH_00_100_30min.M (Sequence Method)
Last changed : 4/8/2016 12:49:37 PM by SYSTEM

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.215	BB	0.2027	1.10084e4	789.17358	99.8893
2	23.029	BB	0.1302	12.20231	1.36629	0.1107
Totals :				1.10206e4	790.53987	

Signal 2: DAD1 B, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.215	BB	0.2037	1.85816e4	1324.40186	100.0000
Totals :				1.85816e4	1324.40186	

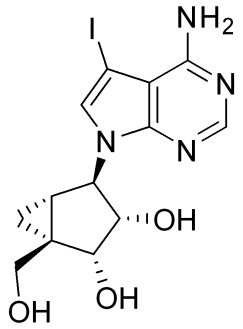
Signal 3: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.208	BB	0.1183	72.38586	8.41594	0.1208
2	2.235	BB	0.1386	15.27225	1.45315	0.0255
3	3.299	BB	0.1755	12.96953	1.06964	0.0216
4	3.851	BB	0.1740	26.95727	2.04216	0.0450
5	10.503	BB	0.4517	1.28312e4	353.28436	21.4106
6	11.823	BB	0.2644	34.32301	1.86786	0.0573
7	13.215	BB	0.2259	4.66755e4	3026.15576	77.8843
8	22.411	BB	0.2640	171.03448	8.31488	0.2854
9	23.001	BB	0.2140	89.58032	5.17464	0.1495
Totals :				5.99293e4	3407.77840	

Summed Peaks Report

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

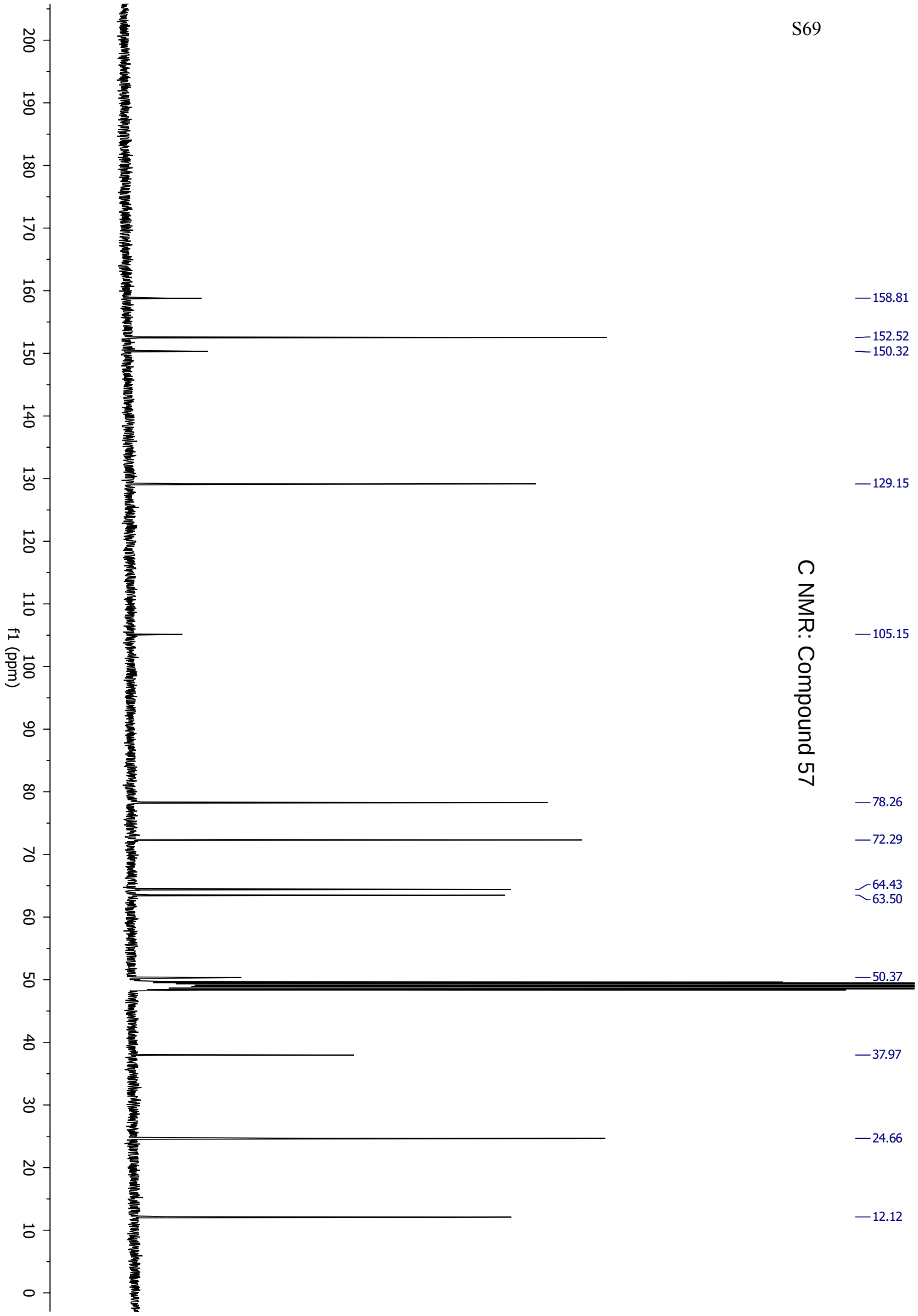
H NMR: Compound 57



I (s) 8.11
J (s) 7.79
H (s) 4.99
G (dd) 4.72
F (dd) 4.26
D (dt) 3.74
E (d) 3.33
C (d) 3.27
B (m) 1.50
A (ddd) 0.70

0.50 0.80 0.87 0.99 1.02 0.94 0.83 1.06 2.10 1.00

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
f1 (ppm)


C NMR: Compound 57
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
158.81
152.52
150.32
129.15
105.15
78.26
72.29
64.43
63.50
50.37
37.97
24.66
12.12

S70

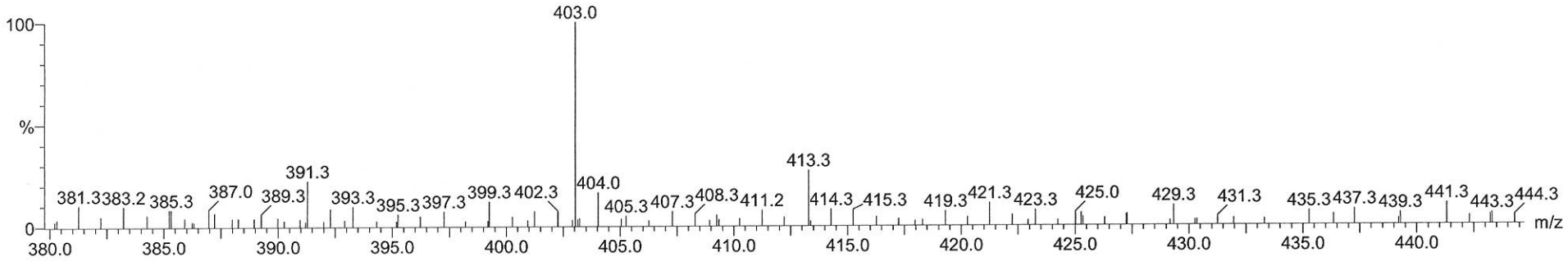
Single Mass Analysis

Tolerance = 30.0 mDa / DBE: min = -2.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
38 formula(e) evaluated with 6 results within limits (up to 19 closest results for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 4-4 O: 0-30 I: 1-1

24-Mar-2016
kst-24mar16-2-032 108 (1.997) Cn (Cen,5, 50.00, Ar); Sm (SG, 1x2.00); Sb (12,5.00)

TOF MS ES+
4.32e+003

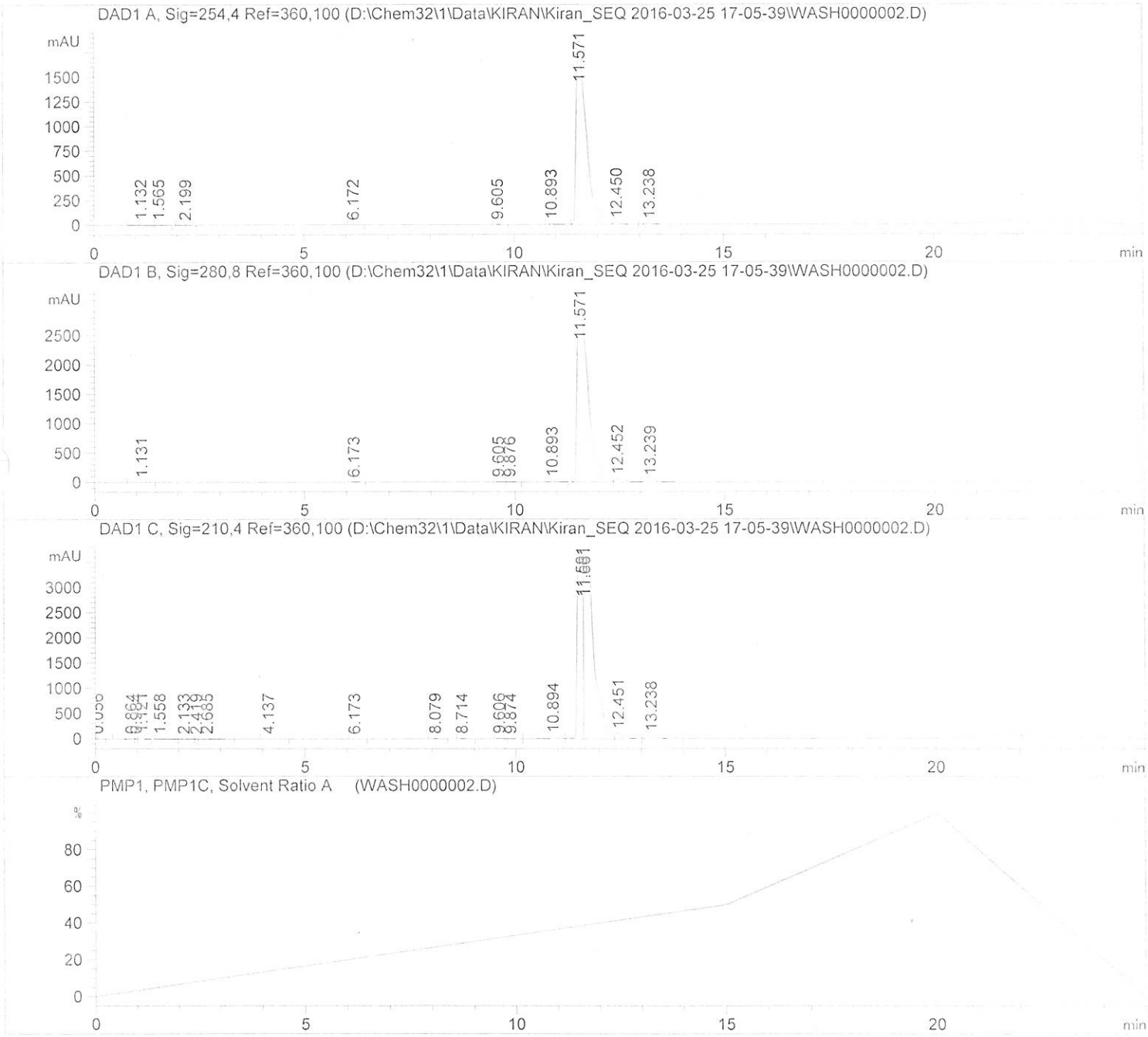


Minimum:				-2.0		
Maximum:		30.0	10.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
403.0271	403.0267	0.4	1.0	7.5	14.8	C13 H16 N4 O3 I
	403.0326	-5.5	-13.6	-1.5	87.5	C6 H20 N4 O8 I
	403.0420	-14.9	-37.0	11.5	49.6	C17 H16 N4 I
	403.0115	15.6	38.7	3.5	60.7	C9 H16 N4 O6 I
	403.0478	-20.7	-51.4	2.5	64.2	C10 H20 N4 O5 I
	403.0056	21.5	53.3	12.5	65.8	C16 H12 N4 O I

Data File D:\Chem32\1\Data\KIRAN\Kiran_SEQ 2016-03-25 17-05-39\WASH0000002.D
Sample Name: MRS4379

Acq. Operator	: SYSTEM	Seq. Line	: 2
Acq. Instrument	: HPLC-001	Location	: 1
Injection Date	: 3/25/2016 5:32:55 PM	Inj	: 1
		Inj Volume	: 10.000 µl

Different Inj Volume from Sample Entry! Actual Inj Volume : 5.000 µl
Method : D:\Chem32\1\Data\KIRAN\Kiran_SEQ 2016-03-25 17-05-39\ANAL_A00-50_D100-50_15min.M (Sequence Method)
Last changed : 3/25/2016 5:05:39 PM by SYSTEM
Additional Info : Peak(s) manually integrated



Data File D:\Chem32\1\Data\KIRAN\Kiran_SEQ 2016-03-25 17-05-39\WASH0000002.D
Sample Name: MRS4379

Acq. Operator : SYSTEM Seq. Line : 2
Acq. Instrument : HPLC-001 Location : 1
Injection Date : 3/25/2016 5:32:55 PM Inj : 1
Inj Volume : 10.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 5.000 µl
Method : D:\Chem32\1\Data\KIRAN\Kiran_SEQ 2016-03-25 17-05-39\ANAL_A00-50_D100-50_15min.M (Sequence Method)
Last changed : 3/25/2016 5:05:39 PM by SYSTEM
Additional Info : Peak(s) manually integrated

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
4	6.172	BB	0.1511	12.17699	1.19286	0.0382
5	9.605	BB	0.1440	23.32392	2.34553	0.0731
6	10.893	BB	0.2087	66.84351	4.51630	0.2096
7	11.571	BV	0.2401	3.10133e4	1863.80017	97.2628
8	12.450	VB	0.1799	223.03877	17.83738	0.6995
9	13.238	BB	0.2343	170.27087	10.01568	0.5340
Totals :				3.18861e4	1914.76489	

Signal 2: DAD1 B, Sig=280,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.131	BB	0.1702	23.39786	1.74712	0.0406
2	6.173	BB	0.1609	14.53150	1.40202	0.0252
3	9.605	BV	0.1437	17.18949	1.82830	0.0298
4	9.876	VB	0.1481	12.95157	1.25818	0.0225
5	10.893	BB	0.2250	145.65126	8.99155	0.2529
6	11.571	BV	0.2629	5.63016e4	3114.66797	97.7638
7	12.452	VV	0.1815	613.07935	48.48050	1.0646
8	13.239	VB	0.2372	460.98810	26.72404	0.8005
Totals :				5.75894e4	3205.09968	

Signal 3: DAD1 C, Sig=210,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.056	BB	0.0644	13.41560	3.10585	0.0133
2	0.864	BV	0.1867	151.84935	10.37706	0.1500
3	0.984	VV	0.0559	38.85734	9.87189	0.0384
4	1.121	VB	0.1244	237.18567	28.12972	0.2343
5	1.558	BV	0.3957	209.88603	6.69503	0.2074
6	2.133	VV	0.2731	181.43816	8.29697	0.1793
7	2.419	VV	0.0653	34.35464	8.77335	0.0339
8	2.685	VB	0.3872	273.55505	8.83481	0.2703
9	4.137	BB	0.2267	51.29127	3.17124	0.0507
10	6.173	BB	0.1526	19.17609	1.95195	0.0189
11	8.079	BB	0.1771	21.87146	1.83408	0.0216