Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# Electronical Supporting Information

# A new synthetic route towards multifunctionalized cyclic amidrazones for feeding chemical space

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**Abstract:** In the context of growing impetus to develop new molecular scaffolds as well as a variety of 3D fragments to escape from flatland, we have reintroduced the accessibility of the underexplored azaheterocyclic amidrazones as promising bioisosteres. Herein, we present an original and versatile approach to synthesize cyclic amidrazones functionalized at different positions of the scaffold in view of diversifying the substitution pattern towards multifunctionalizion, extension or fusion of the ring system and 3D-shaping of fragments.This unprecedented synthetic route represents a sweet achievement to cover further lead-like chemical space.

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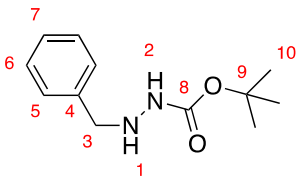
## General information

Tetrahydrofuran was distilled over sodium and benzophenone. All others solvents used were reagent grade. Solvents for water-sensible reactions were purchased in an anhydrous grade, stored on molecular sieves 4 Å and were used without further purification. All reagents were purchased from various commercial suppliers (Sigma Aldrich®, Fluka®, Alfa Aesar®, Acros®, or TCI Chemical®) and stored according to the detailed specifications. Glassware used for reaction was either flame dried under vacuum or under argon stream for several minutes. Reactions were carried out under rigorous anhydrous conditions and argon stream/positive pressure of argon. $^{1}H$ and $^{13}C$ NMR spectra were recorded on a *Bruker Avance 300* spectrometer fitted with a 5 mm i.d. BBO probe carefully tuned to the recording frequency of 300.13 MHz (for $^{1}H$) and 75.47 MHz (for $^{13}C$), the temperature of the probe was set at room temperature (around 293-294 K), on a *Bruker Avance 400* spectrometer fitted with a 5 mm i.d. BBFO+ probe carefully tuned to the recording frequency of 400.13 MHz (for $^{1}H$) and 100.61 MHz (for $^{13}C$). The spectra are referenced to the solvent in which they were run (7.26 ppm for $^{1}H$ $CDCl_3$ and 77.16 ppm for $^{13}C$ $CDCl_3$, 2.5 ppm for $^{1}H$ DMSO and 39.52 ppm for $^{13}C$ DMSO). Chemical shifts (*d*) are given in ppm, and coupling constants (*J*) are given in Hz with the following splitting abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, sx = sextuplet, sp = septuplet, m = massif and br = broad. All assignments were confirmed with the aid of two-dimensional $^{1}H$, $^{1}H$ (COSY), or $^{1}H$, $^{13}C$ (HSQC, HMBC) experiments using standard pulse programs. Reactions were monitored by TLC on commercially available precoated plates (Kieselgel 60 F254), and the compounds were visualized with cerium molybdate stain (Hanessian's Stain) or by UV (254 nm). Combi-Flash chromatography were performed on a Buchi reveleris puriflash, using 40 µm silica pre-packed cartridges. Mobile phases are reported in relative composition. Infra-Red (IR) analyses were recorded on a FTIR-ATR Bruker Vertex 70 spectrometer. The wave numbers ($\nu$) are given in cm-1 where the values represent the maximum absorption frequencies. HRMS characterizations, Electrospray (ESI)-time of flight (TOF) mass spectrometry (MS) measurements were performed by the analytical department on a Xevo G2-XS QTOF spectrometer (Waters, USA) for ESI, ESI-. An Atmospheric Solid Analysis Probe (ASAP) was also used for the direct analysis of samples by atmospheric pressure ionization (ASAP+ or ASAP-). Melting points (MP) were measured on a Tottoli Stuart™ apparatus.

## Experimental procedures

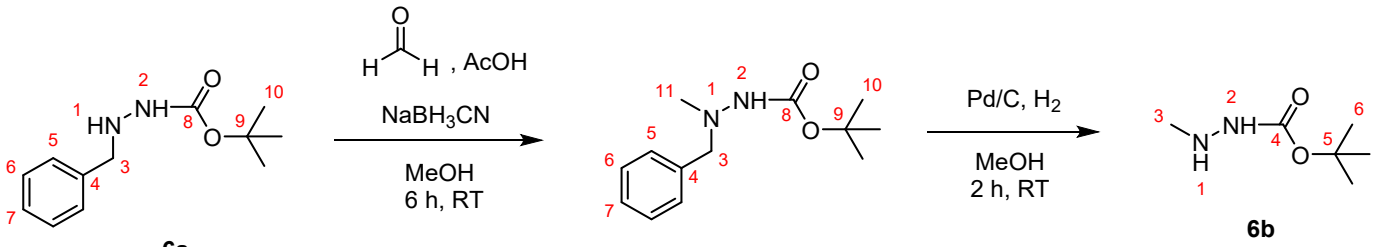
### *Synthesis of Tert-butyl 2-benzylhydrazine-1-carboxylate 6a*



$C_{12}H_{18}N_2O_2$
MW: 222,3 g.mol$^{-1}$

To a solution of *tert*-butyl hydrazinecarboxylate **5** (1.05 eq., 31.4 g, 238 mmol) in THF (0.5 M) were added benzaldehyde (1 eq., 23 mL, 227 mmol) and AcOH (2 eq., 26 mL, 454 mmol). The reaction mixture was stirred for 1 h at RT under argon atmosphere. $NaBH_3CN$ (1.6 eq., 22.8 g, 363 mmol) was added by portion (~5 g every 10 min) to the reaction mixture which was then stirred for 22 h at RT. An aqueous solution of NaOH (6.6 eq., 37 g, 1.5 mol) was added carefully in the mixture and stirred for 1 h. Then the layers were separated and the aqueous one was extracted three times with EtOAc. Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude material was purified using a puriflash device (eluent cHex/EtOAc) to afford **6a** as a colourless oil (48.85 g, 220 mmol, 97 % yield). **Rf** = 0.53 (cHex/EtOAc: 1/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 4H, H5 and H6), 7.32 – 7.27 (m, 1H, H7), 6.03 (s, 1H, NH), 4.20 (s, 1H, NH), 4.00 (s, 2H, H3), 1.47 (s, 9H, H10). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 156.8 (C8), 137.9 (C4), 129.1 (2*C5), 128.6 (2*C6), 127.6 (C7), 80.7 (C9), 56.0 (C3), 28.5 (3*C10). **HRMS (ESI)** = Calcd for $C_{12}H_{18}N_2O_2Na$ $[M+Na]^+$ 245.1266 Da, found 245.1257 Da. **IR (ATR)** ν (cm$^{-1}$) = 3304, 2976, 1700, 1453, 1149.

### *Synthesis of Tert-butyl 2-methylhydrazine-1-carboxylate 6b*




**6a**

$C_{13}H_{20}N_2O_2$
MW: 236,15 g.mol$^{-1}$

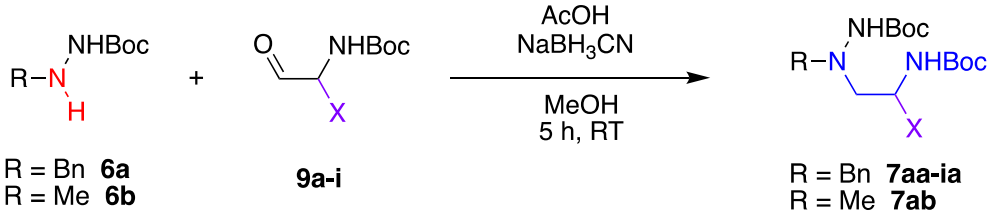
**6b**

$C_6H_{14}N_2O_2$
MW: 146,11 g.mol$^{-1}$

To a solution of *tert*-butyl 2-benzylhydrazine-1-carboxylate **6a** (1 eq., 1 g, 4.50 mmol), in MeOH (0.5 M) were added formaldehyde (37 wt. % in $H_2O$) (1.5 eq., 0.5 mL, 6.75 mmol), and AcOH (4 eq., 1.1 mL, 17.99 mmol). The reaction mixture was stirred for 3 h at RT under argon atmosphere. $NaBH_3CN$ (2 eq., 565 mg, 9.00 mmol) was added to the reaction which was then stirred for 3 h at RT. EtOAc and an aqueous solution of $K_2CO_3$ (1 M) were added to the mixture and stirred for 30 min. Then the layers were separated and the aqueous one was extracted three times with EtOAc. Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude material was purified using a puriflash device (eluent cHex/EtOAc) to afford tert-butyl 2-benzyl-2-methylhydrazine-1-carboxylate as a white solid (1.04 g, 4.40 mmol, 98 % yield). **Rf** = 0.59 (cHex/EtOAc: 7/3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 5H, H5, H6 and H7), 5.52 (s, 1H, NH), 3.90 (s, 2H, H3), 2.62 (s, 3H, H11), 1.41 (s, 9H, H10). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 154.7 (C8), 136.6 (C4), 129.5 (C5), 128.3 (C6), 127.5 (C7), 80.0 (C9), 63.0 (C3), 44.8 (C11), 28.4 (C10). **HRMS (ESI)** = Calcd for $C_{13}H_{20}N_2O_2Na$ $[M+Na]^+$ 259.1422 Da, found 259.1421 Da. **IR (ATR)** ν ($cm^{-1}$) = 3276, 3030, 2984, 2934, 1704, 1528, 1367, 1141, 735. **MP** = 86 °C

To a solution of tert-butyl 2-benzyl-2-methylhydrazine-1-carboxylate (1 eq., 3 g, 12.69 mmol) in MeOH (0.2 M), was added Pd/C (0.1 eq., 135 mg, 1.27 mmol). The reaction mixture was stirred for 2 h at RT under hydrogen atmosphere. The reaction mixture was concentrated under reduced pressure. The crude material was purified using a puriflash device (eluent cHex/EtOAc) to afford product **6b** as a white solid (1.73 g, 11.84 mmol, 93 % yield). **Rf** = 0.21 (cHex/EtOAc: 7/3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.11 (s, 1H, NH), 3.52 (s, 1H, NH), 2.62 (s, 3H, H3), 1.46 (s, H, H6). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 156.6 (C4), 80.5 (C5), 39.4 (C3), 28.4 (C6). **HRMS** = not found. **IR (ATR)** ν ($cm^{-1}$) = 3318, 3255, 3094, 2983, 2967, 1696, 1553, 14858, 1247, 1140. **MP** = 48 °C

### *General procedure for the reductive amination reaction (step two)*




R = Bn **6a**
R = Me **6b**

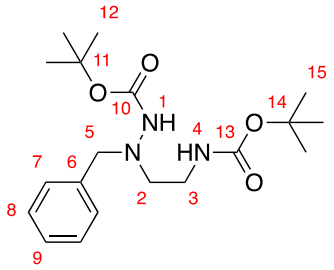
**9a-i**

R = Bn **7aa-ia**
R = Me **7ab**

To a solution of **6a-6b** (1 eq.) in MeOH (0.5 M) were added aldehyde **9a-i** (1.5 eq.) and AcOH (4 eq.) and the solution was stirred for 2 h at RT under argon atmosphere. $NaBH_3CN$ (2 eq.) was added by portion (1 or 3 times, depending on the scale, every 30 min) to the reaction mixture which was stirred for additional 3 h. EtOAc and an aqueous solution of $K_2CO_3$ (1 M) were added to the mixture and stirred for 30 min. Then the layers were separated and aqueous one was extracted with EtOAc (three times). Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered and concentrated under

reduced pressure. The crude material was purified using a puriflash device (eluent cHex/EtOAc) to afford the expected product.

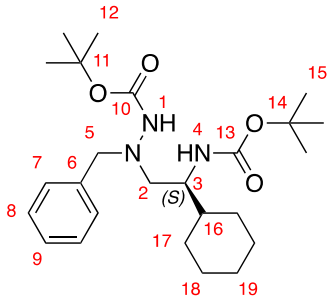
### *Synthesis of Tert-butyl 2-benzyl-2-(2-((tert-butoxycarbonyl)amino)ethyl)hydrazine-1-carboxylate 7aa*



$C_{19}H_{31}N_3O_4$
MW: 365,5 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 3.5 g scale (15.5 mmol) with N-Boc-2-aminoacetaldehyde as aldehyde to afford **7aa** as colourless oil (5.4 g, 14.8 mmol, 95 % yield). **Rf** = 0.50 (cHex/EtOAc: 1/1). **$^1$H NMR** & **$^{13}$C NMR** = unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{19}H_{32}N_3O_4$ $[M+H]^+$ 366.2393 Da, found 366.2390 Da. **IR (ATR)** $\nu$ (cm$^{-1}$) = 2976, 1691, 1502, 1158.

### *Synthesis of Tert-butyl (S)-2-benzyl-2-(2-((tert-butoxycarbonyl)amino)-3-methylbutyl)hydrazine-1-carboxylate 7ba*

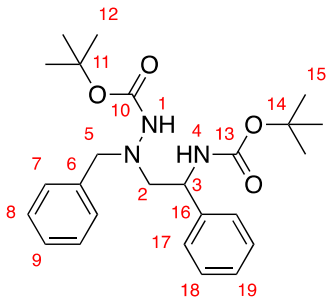


$C_{25}H_{41}N_3O_4$
MW: 447,6 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 625 mg scale (2.8 mmol) with *tert*-butyl (*S*)-(1-cyclohexyl-2-oxoethyl)carbamate as aldehyde to afford **7ba** as a white

solid (400 mg, 0.90 mmol, 32 % yield). **$^{1}$H NMR** & **$^{13}$C NMR** = unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{25}H_{42}N_3O_4$ $[M+H]^+$ 448.3175 Da, found 448.3191 Da.

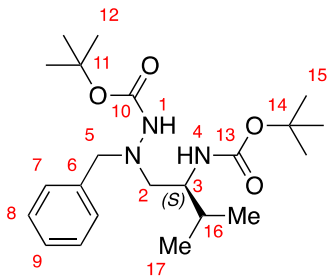
### *Synthesis of Tert-butyl 2-benzyl-2-(2-((tert-butoxycarbonyl)amino)-2-phenylethyl)hydrazine-1-carboxylate 7ca*




$C_{25}H_{35}N_3O_4$
MW: 441,6 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 470 mg scale (2.1 mmol) with *tert*-butyl (2-oxo-1-phenylethyl)carbamate as aldehyde to afford **7ca** as a white solid (mp = 121 °C) (883 mg, 2.0 mmol, 98 % yield). **Rf** = 0.50 (cHex/EtOAc: 1/1). **$^{1}$H NMR** & **$^{13}$C NMR** = Unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{25}H_{36}N_3O_4$ $[M+H]^+$ 442.2706 Da, found 442.2708 Da. **IR (ATR)** ν (cm$^{-1}$) = 3275, 2975, 1691, 1451, 1391, 1363, 1247, 1118, 1023. **MP** = 121 °C

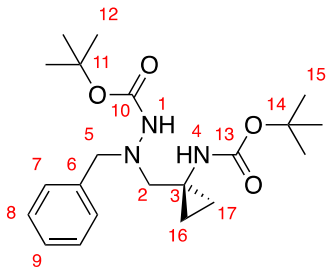
### *Synthesis of Tert-butyl (S)-2-benzyl-2-(2-((tert-butoxycarbonyl)amino)-3-methylbutyl)hydrazine-1-carboxylate 7da*




$C_{22}H_{37}N_3O_4$
MW: 407,6 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 700 mg scale (3.1 mmol) with *tert*-butyl (*S*)-(3-methyl-1-oxobutan-2-yl)carbamate as aldehyde to afford **7da** as a colourless oil (950 mg, 2.33 mmol, 74 % yield). **Rf** = 0.65 (cHex/EtOAc: 1/1). **$^{1}$H NMR** & **$^{13}$C NMR** = unclear NMR because of rotamers. **HRMS (ASAP)** = Calcd for $C_{22}H_{38}N_3O_4$ $[M+H]^+$ 408.2862 Da, found 408.2856 Da. **IR (ATR)** ν ($cm^{-1}$) = 3316, 2971, 1692, 1498, 1364, 1243, 1160, 1019.

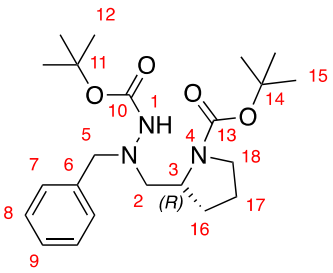
### *Synthesis of Tert-butyl 2-benzyl-2-((1-((tert-butoxycarbonyl)amino)cyclopropyl)methyl)hydrazine-1-carboxylate 7ea*



$C_{21}H_{33}N_3O_4$
MW: 391,5 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 680 mg scale (3 mmol) with *tert*-butyl (1-formylcyclopropyl)carbamate as aldehyde to afford **7ea** as a white solid, used as crude in the next step. **Rf** = 0.61 (cHex/EtOAc: 1/1). **$^{1}$H NMR** & **$^{13}$C NMR** = Unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{21}H_{34}N_3O_4$ $[M+H]^+$ 392.2549 Da, found 392.2545 Da.

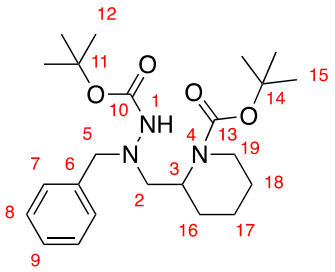
### *Synthesis of Tert-butyl (R)-2-((1-benzyl-2-(tert-butoxycarbonyl)hydrazineyl)methyl)pyrrolidine-1-carboxylate 7fa*



$C_{22}H_{35}N_3O_4$
MW: 405,5 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 1.1 g scale (5 mmol) with *tert*-butyl (*R*)-2-formylpyrrolidine-1-carboxylate as aldehyde to afford **7fa** as a colourless oil (1.15 g, 2.84 mmol, 56 % yield). **Rf** = 0.63 (cHex/EtOAc: 1/1). **$^{1}$H NMR** & **$^{13}$C NMR** = unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{22}H_{36}N_3O_4$ $[M+H]^+$ 406.2706 Da, found 406.2695 Da. **IR (ATR)** ν ($cm^{-1}$) = 3282, 2973, 2247, 1676, 1452, 1392, 1364, 1244, 1166, 1115, 909.

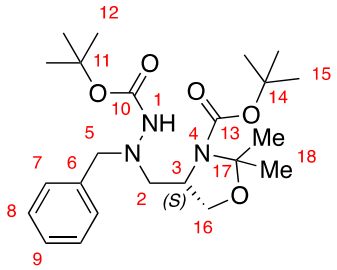
### *Synthesis of Tert-butyl 2-((1-benzyl-2-(tert-butoxycarbonyl)hydrazineyl)methyl)piperidine-1-carboxylate 7ga*




$C_{23}H_{37}N_3O_4$
MW: 419,6 $g.mol^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 500 mg scale (2.2 mmol) with *tert*-butyl 2-formylpiperidine-1-carboxylate as aldehyde to afford **7ga** as a colourless oil (843 mg, 2.0 mmol, 91 % yield). **Rf** = 0.57 (cHex/EtOAc: 1/1). **$^{1}$H NMR** & **$^{13}$C NMR** = Unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{23}H_{38}N_3O_4$ $[M+H]^+$ 420.2862 Da, found 420.2855 Da. **IR (ATR)** ν ($cm^{-1}$) = 3324, 2932, 1676, 1453, 1364, 1246, 1145, 1076.

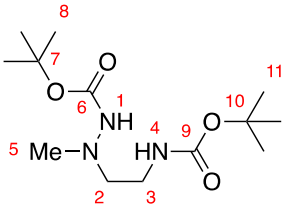
### *Synthesis of Tert-butyl (S)-4-((1-benzyl-2-(tert-butoxycarbonyl)hydrazineyl)methyl)-2,2-dimethyloxazolidine-3-carboxylate 7ha*



$C_{23}H_{37}N_3O_5$
MW: 435,6 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 650 mg scale (2.9 mmol) with *tert*-butyl (*R*)-4-formyl-2,2-dimethyloxazolidine-3-carboxylate as aldehyde to afford **7ha** as a white solid (mp = 145 °C) (955 mg, 2.20 mmol, 75 % yield). **Rf** = 0.71 (cHex/EtOAc: 1/1). **$^1$H NMR** & **$^{13}$C NMR** = Unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{23}H_{38}N_3O_5$ $[M+H]^+$ 436.2811 Da, found 436.2804 Da. **IR (ATR)** ν (cm$^{-1}$) = 3317, 2978, 1692, 1511, 1386, 1363, 1239, 1155, 1084, 1013.

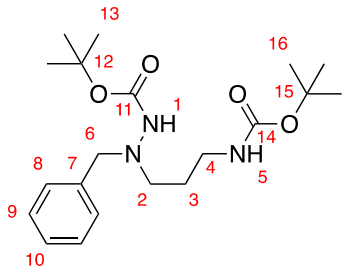
### *Synthesis of Tert-butyl 2-(2-((tert-butoxycarbonyl)amino)ethyl)-2-methylhydrazine-1-carboxylate 7ab*



$C_{13}H_{27}N_3O_4$
MW: 289,4 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 1.3 g scale (8,90 mmol) with N-Boc-2-aminoacetaldehyde as aldehyde to afford **7ab** as a white solid (2.20 g, 7.61 mmol, 86 % yield). **Rf** = 0.26 (cHex/EtOAc: 7/3). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 5.53 (s, 1H, NH), 5.34 (s, 1H, NH), 3.20 – 3.16 (m, 2H, H3), 2.67 – 2.64 (m, 2H, H2), 2.59 (s, 3H, H5), 1.44 (s, 9H, H8), 1.42 (s, 9H, H11). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 156.2 (C6), 155.5 (C9), 80.4 (C10), 79.0 (C7), 59.3 (C2), 46.9 (C5), 37.8 (C3), 28.5 (C8), 28.3 (C11). **HRMS (ASAP)** = Calcd for $C_{13}H_{28}N_3O_4$ $[M+H]^+$ 290.2080 Da, found 290.2075 Da. **IR (ATR)** ν (cm$^{-1}$) = 3396, 3306, 2979, 2935, 1705, 1692, 1513, 1151. **MP** = 95 °C

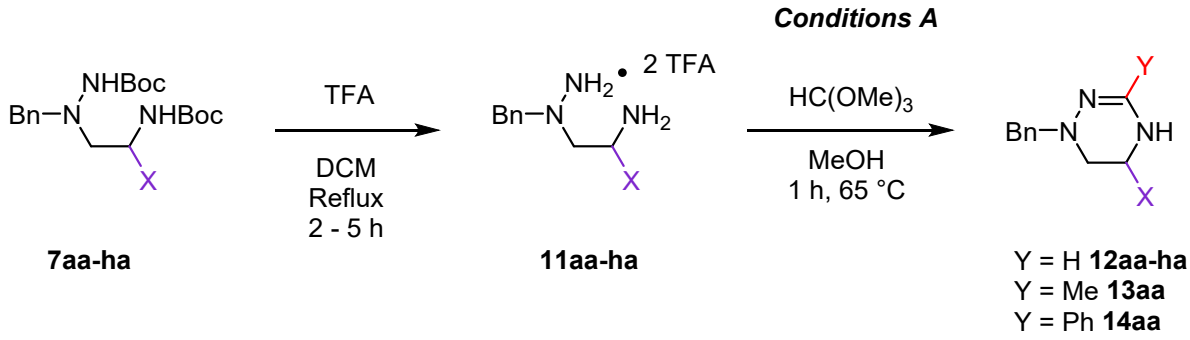
### *Synthesis of Tert-butyl 2-benzyl-2-(3-((tert-butoxycarbonyl)amino)propyl)hydrazine-1-carboxylate 7ia*



$C_{20}H_{33}N_3O_4$
MW: 379,5 g.mol$^{-1}$

**General procedure for the reductive amination reaction (step two)** was applied on 1.7 g scale (7.5 mmol) with *tert*-butyl (3-oxopropyl)carbamate as aldehyde to afford **7ia** as a colourless oil (2.7 g, 7.2 mmol, 97 % yield). **$^1$H NMR** & **$^{13}$C NMR** = Unclear NMR because of rotamers. **HRMS (ESI)** = Calcd for $C_{20}H_{34}N_3O_4$ $[M+H]^+$ 380.2549 Da, found 380.2542 Da.

### *General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure reaction*




**7aa-ha** **11aa-ha**

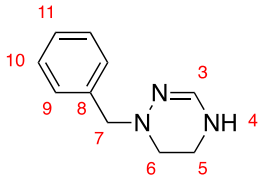
Y = H **12aa-ha**
Y = Me **13aa**
Y = Ph **14aa**

To a solution of **7aa-ia** (1 eq.) in DCM (0.4 M) was added trifluoroacetic acid (10 eq.). The reaction mixture was stirred at reflux until full deprotection of the SM ($^1$H NMR monitoring in $CD_3OD$). The reaction mixture was then concentrated under reduced pressure to afford the bistrifluoroacetate salt product **11aa-ha**, used in the next step without purification and stored carefully under argon atmosphere in the freezer.

To a solution of the diamine bistrifluoroacetate salt **11aa-ia** (1 eq.) in anhydrous MeOH (0.5 M), was added the ring closure reagent (3 eq.) at RT. The reaction mixture was stirred 1 h at reflux or 65 °C in case of sealed vial. The reaction mixture was cooled down at RT and concentrated under reduced pressure to give a residue. EtOAc and an aqueous solution of $K_2CO_3$ (1 M) were added to the residue. Phases were separated and the aqueous phase was extracted with EtOAc (x3). Combined organic phases were washed with brine, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure.

The crude material was purified using a puriflash device with the eluent DCM/DCM-MeOH (9/1) or cHex/EtOAc, according to the polarity of the product, to afford the corresponding cyclic benzylamidrazones **12aa-ia, 13aa and 14aa**.

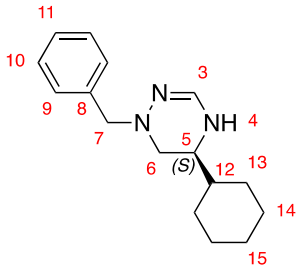
### *Synthesis of 1-benzyl-1,4,5,6-tetrahydro-1,2,4-triazine 12aa*




$C_{10}H_{13}N_3$
MW: 175,2 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 10.44 g scale (28.56 mmol) starting from *Tert*-butyl 2-benzyl-2-(2-((*tert*-butoxycarbonyl)amino)ethyl)hydrazine-1-carboxylate **7aa** with $HC(OMe)_3$ as ring closure reagent to afford **12aa** as a colourless oil (2.25 g, 18.56 mmol, 81 % yield over 2 steps). **Rf** = 0.28 (DCM/MeOH: 9/1. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 2H, H9), 7.36 – 7.29 (m, 2H, H10), 7.28 – 7.23 (m, 1H, H11), 6.80 (d, *J* = 2.5 Hz, 1H, H3), 4.13 (s, 1H, H4), 4.04 (s, 2H, H7), 3.50 – 3.36 (m, 2H, H5), 2.75 – 2.65 (m, 2H, H6). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 138.2 (C8), 137.1 (C3), 129.3 (2*C9), 128.3 (2*C10), 12, 127.3 (C11), 63.8 (C7), 46.1 (C6), 41.5 (C5). **HRMS (ESI)** = Calcd for $C_{10}H_{14}N_3$ $[M+H]^+$ 176.1188 Da, found 176.1186 Da. **IR (ATR)** ν (cm$^{-1}$) = 3262, 1632, 1350.

### *Synthesis of (S)-1-benzyl-5-cyclohexyl-1,4,5,6-tetrahydro-1,2,4-triazine 12ba*

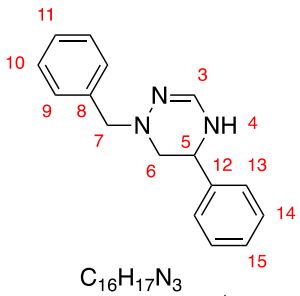



$C_{16}H_{23}N_3$
MW: 257,4 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 423 mg (0.89 mmol) scale starting from *Tert*-butyl (*S*)-2-benzyl-2-(2-((*tert*-butoxycarbonyl)amino)-3-methylbutyl)hydrazine-1-carboxylate **7ba** with $HC(OMe)_3$ as ring closure reagent to afford **12ba** as a yellow oil (120 mg, 0.47 mmol, 50 % yield over 2 steps). **Rf** = 0.33 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H, H9), 7.35 – 7.29 (m, 2H, H10), 7.28

– 7.22 (m, 1H, H11), 6.81 (d, *J* = 3.7 Hz, 1H, H3), 4.23 (s, 1H, H4), 4.04 (d, *J* = 2.3 Hz, 2H, H7), 3.25 – 3.15 (m, 1H, H5), 2.68 (dd, *J* = 3.9, 10.9 Hz, 1H, H6), 2.49 (dd, *J* = 5.8, 10.9 Hz, 1H, H6'), 1.85 – 1.50 (m, 4H, H14 and H13), 1.47 – 1.31 (m, 1H, H12), 1.31 – 1.03 (m, 4H, H14' and H13'), 0.89 (dqd, *J* = 3.5, 12.3, 24.2 Hz, 2H, H15). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 138.4 (C8), 137.0 (C3), 129.2 (2*C9), 128.3 (2*C10), 127.2 (C11), 63.7 (C7), 56.4 (C5), 49.4 (C6), 42.0 (C12), 29.1 (C15), 28.9 (C13 or C14), 26.5 (C13 or C14), 26.1 (C13' or C14'), 26.0 (C13' or C14'). **HRMS (ESI)** = Calcd for $C_{16}H_{24}N_3$ $[M+H]^+$ 258.1970 Da, found 258.1964 Da. **IR (ATR)** ν($cm^{-1}$) = 2923, 1633, 1448, 729. $[]_D^{25}$ (°.$dm^{-1}$.$g^{-1}$.$cm^3$) = +27.0 (c = 0.5357, $CHCl_3$).

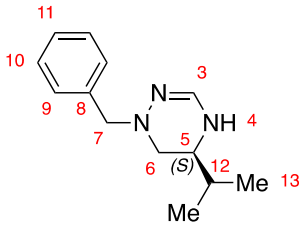
### *Synthesis of 1-benzyl-5-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine 12ca*




$C_{16}H_{17}N_3$
MW: 251,3 g.$mol^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 1 g (2.1 mmol) scale starting from *Tert*-butyl 2-benzyl-2-(2-((*tert*-butoxycarbonyl)amino)-2-phenylethyl)hydrazine-1-carboxylate **7ca** with $HC(OMe)_3$ as ring closure reagent to afford **12ca** as a light brown solid (mp = 83 °C) (279 mg, 1.1 mmol, 52 % yield over 2 steps). **Rf** = 0.56 (DCM/MeOH: 9/1). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.42 – 7.18 (m, 10H, H9, H10, H11, H13, H14 and H15), 6.99 (d, *J* = 3.1 Hz, 1H, H3), 4.66 (dd, *J* = 4.0, 6.9 Hz, 1H, H5), 4.57 (s, 1H, H4), 4.17 (d, *J* = 13.4 Hz, 1H, H7), 3.96 (d, *J* = 13.4 Hz, 1H, H7'), 3.04 (dd, *J* = 4.0, 11.0 Hz, 1H, H6), 2.51 (dd, *J* = 6.9, 11.0 Hz, 1H, H6'). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 141.3 (C12), 137.9 (C8), 137.0 (C3), 129.1 (2*C9), 128.7 (2*C14), 128.3 (2*C10), 128.1 (C11), 127.2 (C15), 126.7 (2*C13), 63.3 (C7), 55.4 (C5), 54.3 (C6). **HRMS (ASAP)** = Calcd for $C_{16}H_{18}N_3$ $[M+H]^+$ 252.1501 Da, found 252.1505. **IR (ATR)** ν ($cm^{-1}$) = 3219, 3023, 2817, 2360, 1629, 1490.

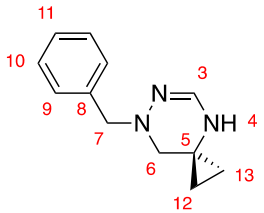
### *Synthesis of (S)-1-benzyl-5-isopropyl-1,4,5,6-tetrahydro-1,2,4-triazine 12da*




$C_{13}H_{19}N_3$
MW: 217,3 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 920 mg (2.1 mmol) scale starting from *Tert*-butyl (*S*)-2-benzyl-2-(2-((*tert*-butoxycarbonyl)amino)-3-methylbutyl)hydrazine-1-carboxylate **7da** with $HC(OMe)_3$ as ring closure reagent to afford **12da** as a light-yellow solid (mp = 47 °C) (322 mg, 1.48 mmol, 70 % yield over 2 steps). **Rf** = 0.46 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 2H, H9), 7.37 – 7.29 (m, 2H, H10), 7.31 – 7.22 (m, 1H, H11), 6.82 (s, 1H, H3), 4.39 (s, 1H, H4), 4.05 (dd, *J* = 3.3 Hz, 2H, H7), 3.21 – 3.12 (m, 1H, H5), 2.69 (dd, *J* = 4.1, 11.0 Hz, 1H, H6), 2.47 (dd, *J* = 5.9, 11.0 Hz, 1H, H6'), 1.68 (qq, *J* = 6.8 Hz, 1H, H12), 0.93 (d, *J* = 6.8 Hz, 3H, H13), 0.81 (d, *J* = 6.8 Hz, 3H, H13'). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 138.3 (C8), 137.0 (C3), 129.1 (2*C9), 128.3 (2*C10), 127.1 (C11), 63.7 (C7), 57.2 (C5), 49.6 (C6), 32.2 (C12), 18.5 (C13), 18.4 (C13'). **HRMS (ESI)** = Calcd for $C_{13}H_{20}N_3$ $[M+H]^+$ 218.1657 Da, found 218.1666. **IR (ATR)** ν (cm$^{-1}$) = 3207, 3024, 2962, 2835, 1634, 1450, 1227. $[]_D^{25}$ (°.dm$^{-1}$.g$^{-1}$.cm$^3$) = +12.2 (c = 0.5424, $CHCl_3$).

### *Synthesis of 7-benzyl-4,6,7-triazaspiro[2.5]oct-5-ene 12ea*

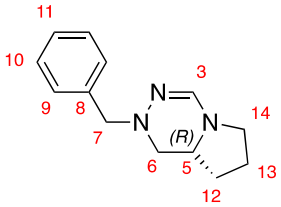



$C_{12}H_{15}N_3$
MW: 201,3 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 450 mg (1.1 mmol) scale starting from *Tert*-butyl 2-benzyl-2-((1-((*tert*-butoxycarbonyl)amino)cyclopropyl)methyl)hydrazine-1-carboxylate **7ea** with $HC(OMe)_3$ as ring closure

reagent to afford **12ea** as a brown oil (84 mg, 0.42 mmol, 39 % yield over 3 steps). **Rf** = 0.42 (DCM/MeOH: 9/1). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.35 (m, 2H, H9), 7.37 – 7.28 (m, 2H, H10), 7.29 – 7.20 (m, 1H, H11), 6.88 (s, 1H, H3), 4.11 (s, 2H, H7), 2.48 (s, 2H, H6), 0.80 – 0.67 (m, 2H, H12 and H13), 0.69 – 0.54 (m, 2H, 12' and 13'). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 137.9 (C8), 137.3 (C3), 129.1 (2*C10), 128.4 (2*C9), 127.3 (C11), 63.3 (C7), 53.7 (C6), 36.2 (C5), 13.6 (C12), 13.6 (C13). **HRMS (ASAP)** = Calcd for $C_{12}H_{16}N_3$ $[M+H]^+$ 202.1344 Da, found 202.1349. **IR (ATR)** ν ($cm^{-1}$) = 3241, 2922, 2826, 2361, 1627, 1353.

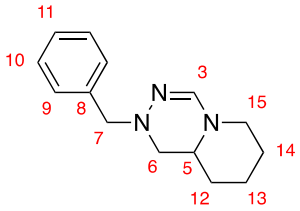
### *Synthesis of 2-benzyl-1,2,6,7,8,8a-hexahydropyrrolo[1,2-d][1,2,4]triazine 12fa*




$C_{13}H_{17}N_3$
MW: 215,3 $g.mol^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 1 g (2.3 mmol) scale starting from *Tert*-butyl (*R*)-2-((1-benzyl-2-(*tert*-butoxycarbonyl)hydrazineyl)methyl)pyrrolidine-1-carboxylate **7fa** with $HC(OMe)_3$ as ring closure reagent to afford **12fa** as a yellow oil (223 mg, 1.0 mmol, 45 % yield over 2 steps). **Rf** = 0.69 (DCM/MeOH: 9/1). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 2H, H9), 7.38 – 7.29 (m, 2H, H10), 7.33 – 7.23 (m, 1H, H11), 6.88 (d, *J* = 1.1 Hz, 1H, H3), 4.34 (d, *J* = 13.3 Hz, 1H, H7), 3.85 (d, *J* = 13.3 Hz, 1H, 7'), 3.62 (tdd, *J* = 4.5, 6.3, 9.1 Hz, 1H, H5), 3.44 (ddd, *J* = 4.5, 7.0, 9.5 Hz, 1H, H14), 3.27 – 3.23 (m, 1H, H6), 3.24 – 3.16 (m, 1H, H14'), 1.96 (dtd, *J* = 3.9, 6.3, 12.3 Hz, 1H, H12), 1.90 – 1.81 (m, 1H, H13), 1.85 – 1.73 (m, 1H, H13'), 1.66 (dd, *J* = 9.1, 10.5 Hz, 1H, H6'), 1.51 – 1.37 (m, 1H, H12'). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 139.9 (C3), 138.3 (C8), 129.3 (2*C9), 128.3 (2*C10), 127.2 (C11), 63.3 (C7), 57.4 (C5), 51.9 (C6), 49.6 (C14), 30.1 (C12), 24.2 (C13). **HRMS (ASAP)** = Calcd for $C_{13}H_{18}N_3$ $[M+H]^+$ 216.1501 Da, found 216.1509. **IR (ATR)** ν ($cm^{-1}$) = 3371, 3028, 2966, 1687, 1614, 1392. $[]_D^{25}$ ($°.dm^{-1}.g^{-1}.cm^3$) = -11.4 (c = 0.6780, $CHCl_3$)

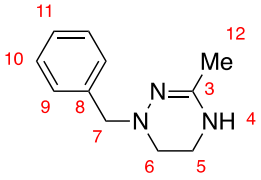
### *Synthesis of 2-benzyl-1,6,7,8,9,9a-hexahydro-2H-pyrido[1,2-d][1,2,4]triazine 12ga*




$C_{14}H_{19}N_3$
MW: 229,3 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 800 mg (1.7 mmol) scale starting from *Tert*-butyl 2-((1-benzyl-2-(*tert*-butoxycarbonyl)hydrazineyl)methyl)piperidine-1-carboxylate **7ga** with $HC(OMe)_3$ as ring closure reagent to afford **12ga** as a colourless oil (267 mg, 1.2 mmol, 68 % yield over 2 steps). **Rf** = 0.66 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H, H9), 7.30 (dd, *J* = 6.8, 8.0 Hz, 2H, H10), 7.27 – 7.19 (m, 1H, H11), 6.49 (s, 1H, H3), 4.11 (d, *J* = 13.3 Hz, 1H, H7), 3.83 (d, *J* = 13.3 Hz, 1H, H7'), 3.29 (tt, *J* = 3.6, 7.4 Hz, 1H, H5), 3.23 (ddd, *J* = 2.0, 4.3, 13.0 Hz, 1H, H15), 2.96 – 2. 93 (m, 1H, H6), 2.93 – 2.88 (m, 1H, H15'), 2.38 (dd, *J* = 7.4, 11.2 Hz, 1H, H6'), 1.83 – 1.74 (m, 1H, H13), 1.64 – 1.55 (m, 1H, H14), 1.51 (dt, *J* = 2.0, 3.6, 15.2 Hz, 1H, H12), 1.45 – 1.35 (m, 1H, H14'), 1.35 – 1.27 (m, 1H, H13'), 1.20 (dt, *J* = 3.6, 12.6 Hz, 1H, H12'). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 139.8 (C3), 138.1 (C8), 129.1 (2*C9), 128.3 (2*C10), 127.1 (C11), 63.5 (C7), 53.5 (C6), 53.1 (C5), 48.6 (C15), 29.5 (C12), 25.7 (C14), 23.4 (C13). **HRMS (ASAP)** = Calcd for $C_{14}H_{20}N_3$ $[M+H]^+$ 230.1657 Da, found 230.1660. **IR (ATR)** ν (cm$^{-1}$) = 3379, 3028, 2932, 2821, 1623.

### *Synthesis of 1-benzyl-3-methyl-1,4,5,6-tetrahydro-1,2,4-triazine 13aa*

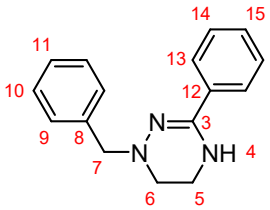



$C_{11}H_{15}N_3$
MW: 189,3 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 600 mg (1.64 mmol) scale starting from *Tert*-butyl 2-benzyl-2-(2-((*tert*-butoxycarbonyl)amino)ethyl)hydrazine-1-carboxylate **7aa** with $MeC(OMe)_3$ as ring closure reagent to afford **13aa** as a brown solid (290 mg, 1.53 mmol, 93 % yield over two steps). **Rf** = 0.19 (DCM/MeOH:

9/1). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.37 (m, 2H, H9), 7.33 – 7.22 (m, 3H, H10 and H11), 4.46 (s, 1H, NH), 4.03 (s, 2H, H7), 3.36 (m, 2H, H5), 2.57 (m, 2H, H6), 1.89 (s, 3H, H12). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 144.7 (C3), 138.1 (C8), 129.2 (2*C9), 128.2 (2*C10), 127.2 (C11), 63.9 (C7), 45.2 (C6), 41.4 (C5), 20.2 (C12). **HRMS (ESI)** = Calcd for $C_{11}H_{16}N_3$ $[M+H]^+$ 190.1344 Da, found 190.1341Da. **IR (ATR)** ν ($cm^{-1}$) = 3183, 3028, 2925, 2825, 1633, 1553, 1389, 698. **MP** = 82 °C

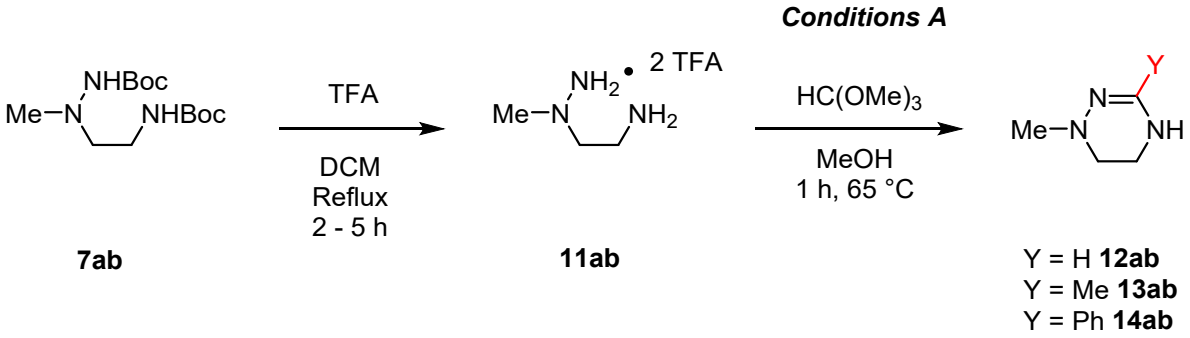
### *Synthesis of 1-benzyl-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine 14aa*




$C_{16}H_{17}N_3$
MW: 251,14 $g.mol^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 150 mg (0.41 mmol) scale starting from *Tert*-butyl 2-benzyl-2-(2-((*tert*-butoxycarbonyl)amino)ethyl)hydrazine-1-carboxylate **7aa** with $PhC(OMe)_3$ as ring closure reagent to afford **14aa** as a brown oil (75 mg, 0.30 mmol, 73 % yield over two steps). **Rf** = 0.58 (DCM/MeOH: 9/1). **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.66 -7.62 (m, 2H, H13), 7.47 – 7.45 (m, 2H, H9), 7.37 – 7.28 (m, 6H, H10, H11, H14 and H15), 4.51 (s, 1H, NH), 4.22 (s, 2H, H7), 3.59 – 3.56 (m, 2H, H5), 2.76 – 2.72 (m, 2H, H6). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 145.0 (C3), 138.0 (C8), 135.3 (C12), 129.5 (C9), 129.0 (Car), 128.4 (Car), 128.2 (Car), 127.2 (Car), 125.5 (C13), 63.9 (C7), 45.1 (C6), 41.7 (C5). **HRMS (ESI)** = Calcd for $C_{16}H_{18}N_3$ $[M+H]^+$ 252.1501 Da, found 252.1506 Da. **IR (ATR)** ν ($cm^{-1}$) = 3276, 3059, 3026, 2924, 2878, 1609, 1516, 1482, 1349, 692.

### *General procedure for the bis-Boc deprotection and the methylamidrazone ring closure reaction*



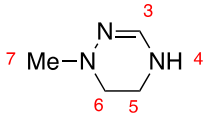

**7ab** **11ab**

Y = H **12ab**
Y = Me **13ab**
Y = Ph **14ab**

To a solution of **7ab** (1 eq.) in DCM (0.4 M) was added trifluoroacetic acid (10 eq.). The reaction mixture was stirred at reflux until full deprotection of the SM ($^1$H NMR monitoring in $CD_3OD$). The reaction mixture was then concentrated under reduced pressure to afford the bistrifluoroacetate salt product **11ab** used in the next step without purification and stored carefully under argon atmosphere in the freezer.

To a solution of the diamine bistrifluoroacetate salt **11ab** (1 eq.) in anhydrous MeOH (0.5 M), was added the ring closure reagent (3 eq.) at RT. The reaction mixture was stirred 1 h at reflux or 65 °C in case of sealed vial. The reaction mixture was cooled down at RT and concentrated under reduced pressure to give a residue. MeOH (0.5 M) and HCl (2 M in dioxane) (5 eq.) were added to the residue and stirred for 30 min. The mixture was then concentrated under reduced pressure. The residue was again diluted in MeOH (0.5 M) and solid $NaHCO_3$ (5 eq.) was added. The suspension was stirred for 30 min, then filtered and concentrated under reduced pressure. The crude material was purified using a puriflash device with the eluent DCM/DCM-MeOH (9/1), to afford the corresponding cyclic methylamidrazones **12ab-14ab.**

### *Synthesis of 1-methyl-1,4,5,6-tetrahydro-1,2,4-triazine 12ab*

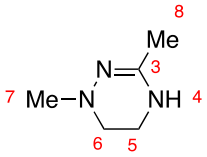



$C_4H_9N_3$
MW: 99,1 g.mol$^{-1}$

**General procedure for the bis-Boc deprotection and the methylamidrazone ring closure** was applied on 200 mg (0.69 mmol) scale starting from *Tert*-butyl 2-(2-((tert-butoxycarbonyl)amino)ethyl)-2-methylhydrazine-1-carboxylate **7ab** with $HC(OMe)_3$ as ring closure reagent to afford **12ab** as a brown oil (53 mg, 0.53 mmol, 78 % yield over two steps). **Rf** = 0.14 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.82 (s, 1H, H3), 4.38 (s, 1H, NH), 3.50 – 3.47 (m, 2H, H5), 2.78 – 2.75 (m, 2H, H6), 2.71 (s,

3H, H7). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 137.8 (C3), 49.0 (C6), 46.9 (C7), 41.0 (C5). **HRMS (ASAP)** = Calcd for $C_4H_{10}N_3$ $[M+H]^+$ 100.0875 Da, found 100.0879 Da. **IR (ATR)** ν ($cm^{-1}$) = 3231, 2952, 2930, 1630, 1352, 725.

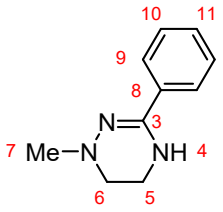
### *Synthesis of 1,3-dimethyl-1,4,5,6-tetrahydro-1,2,4-triazine 13ab*




$C_5H_{11}N_3$
MW: 113,2 $g.mol^{-1}$

**General procedure for the bis-Boc deprotection and the methylamidrazone ring closure** was applied on 200 mg (0.69 mmol) scale starting from *Tert*-butyl 2-(2-((tert-butoxycarbonyl)amino)ethyl)-2-methylhydrazine-1-carboxylate **7ab** with $HC(OMe)_3$ as ring closure reagent to afford **13ab** as a brown solid (65 mg, 0.57 mmol, 83 % yield over two steps). **Rf** = 0.08 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9,81 (s, 1H, NH), 3.49 – 3.46 (m, 2H, H5), 3.97 – 2.94 (m, 2H, H6), 2.75 (s, 3H, H7), 2.35 (s, 3H, H8). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 154.2 (C3), 47.7 (C6), 45.0 (C7), 36.2 (C5), 16.8 (C8). **HRMS (ASAP)** = Calcd for $C_5H_{12}N_3$ $[M+H]^+$ 114.1031 Da, found 114.1027 Da. **IR (ATR)** ν ($cm^{-1}$) =3251, 3048, 2962, 2830, 1666, 1622, 1448, 784. **MP** = 117 °C

### *Synthesis of 1-methyl-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine 14ab*

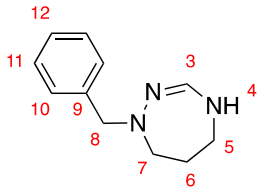



$C_{11}H_{14}N_2$
MW: 175,2 $g.mol^{-1}$

**General procedure for the bis-Boc deprotection and the methylamidrazone ring closure** was applied on 200 mg (0.69 mmol) scale starting from *Tert*-butyl 2-(2-((tert-butoxycarbonyl)amino)ethyl)-2-methylhydrazine-1-carboxylate **7ab** with $HC(OMe)_3$ as ring closure reagent to afford **14ab** as a brown solid (93 mg, 0.53 mmol, 77 % yield over two steps). **Rf** = 0.47 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.19 (s, 1H, NH), 7.84 – 7.81 (m, 2H, H9), 7.45 – 7.40 (m, 1H, H11), 7.32 – 7.27 (m, 2H, H10), 3.54 – 3.51 (m, 2H, H5), 2.96 – 2.92 (m, 2H, H6), 2.80 (s, 3H, H7). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 153.0

(C3), 132.3 (C11), 128.8 (2*C10), 127.9 (C8), 127.5 (2*C9), 47.9 (C6), 45.5 (C7), 36.6 (C5). **HRMS (ASAP)** = Calcd for $C_{10}H_{14}N_3$ $[M+H]^+$ 176.1188 Da, found 176.1183 Da. **IR (ATR)** ν ($cm^{-1}$) = 3074, 2847, 2776, 1625, 1573, 1442, 775, 687. **MP** = 130 °C

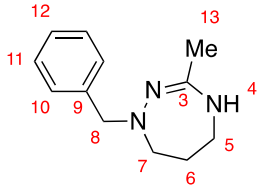
### *Synthesis of 1-benzyl-4,5,6,7-tetrahydro-1H-1,2,4-triazepine 12ia*




$C_{11}H_{15}N_3$
MW: 189,3 $g.mol^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 2 g scale (5.1 mmol) starting from *Tert*-butyl 2-benzyl-2-(3-((*tert*-butoxycarbonyl)amino)propyl)hydrazine-1-carboxylate **7ia** with $HC(OMe)_3$ as ring closure reagent to afford **12ia** as a white solid (200 mg, 1.0 mmol, 20 % yield over 2 steps). **Rf** = 0.25 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 2H, H10), 7.33 – 7.29 (m, 2H, H11), 7.27 – 7.17 (m, 1H, H12), 6.61 (s, 1H, H3), 4.25 (s, 1H, H4), 4.16 (s, 2H, H8), 3.13 – 3.09 (m, 2H, H5), 2.77 – 2.73 (m, 2H, H7), 1.78 – 1.71 (m, 2H, H6). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 139.3 (C9), 138.1 (C3), 129.0 (2*C10), 128.3 (2*C11), 127.0 (C12), 65.6 (C8), 55.4 (C7), 44.3 (C5), 29.8 (C6). **HRMS (ESI)** = Calcd for $C_{11}H_{16}N_3$ $[M+H]^+$ 190.1344 Da, found 190.1343 Da. **IR (ATR)** ν ($cm^{-1}$) = 2930, 1660.

### *Synthesis of 1-benzyl-3-methyl-4,5,6,7-tetrahydro-1H-1,2,4-triazepine 13ia*

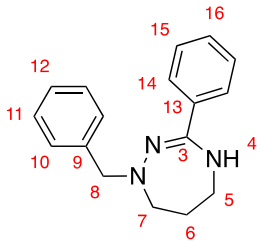



$C_{12}H_{17}N_3$
MW: 203,3 $g.mol^{-1}$

**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 300 mg scale (0.74 mmol) starting from *Tert*-butyl 2-benzyl-2-(3-((*tert*-butoxycarbonyl)amino)propyl)hydrazine-1-carboxylate **7ia** with $MeC(OMe)_3$ as ring closure reagent to afford **13ia** as a colourless oil (75 mg, 0.37 mmol, 50 % yield over 2 steps). **Rf** = 0.51 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.17 (m, 5H, H10, H11 and H12), 5.81 (s, 1H, H4), 3.66 (s, 2H, H8),

3.21 (td, *J* = 5.5, 6.7 Hz, 2H, H5), 2.66 (t, *J* = 6.7 Hz, 2H, H7), 1.78 (s, 3H, H13), 1.53 (tt, *J* = 6.7, 6.7 Hz, 2H, H6). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 170.0 (C3), 138.4 (C9), 129.9 (2*C10), 128.3 (2*C11), 127.2 (C12), 55.8 (C7), 53.5 (C8), 38.2 (C5), 27.3 (C6), 15.7 (C13). **HRMS (ASAP)** = Calcd for $C_{12}H_{18}N_3$ $[M+H]^+$ 204.1501 Da, found 204.1494 Da. **IR (ATR)** ν ($cm^{-1}$) = 1646, 1553, 1277.

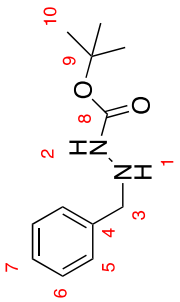
### *Synthesis of 1-benzyl-3-phenyl-4,5,6,7-tetrahydro-1H-1,2,4-triazepine 14ia*




$C_{17}H_{19}N_3$
MW: 265,4 g.mol$^{-1}$

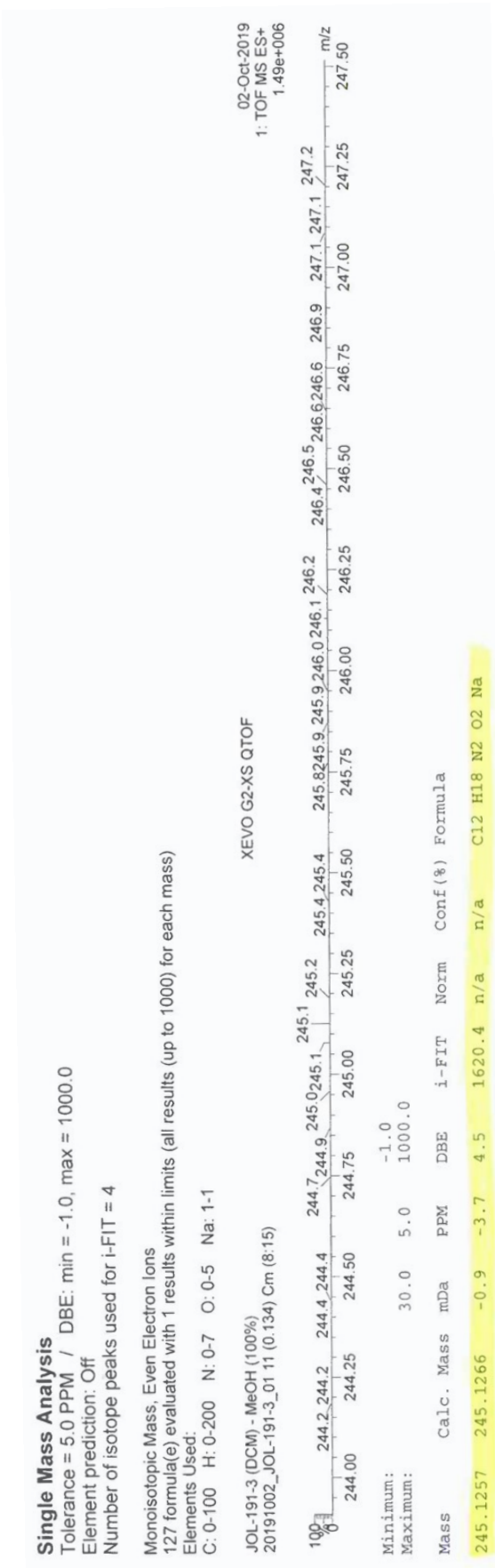
**General procedure for the bis-Boc deprotection and the benzylamidrazone ring closure** was applied on 350 mg scale (0.86 mmol) starting from *Tert*-butyl 2-benzyl-2-(3-((*tert*-butoxycarbonyl)amino)propyl)hydrazine-1-carboxylate **7ia** with $PhC(OMe)_3$ as ring closure reagent to afford **14ia** as an orange oil (20 mg, 0.07 mmol, 9 % yield over 2 steps). **Rf** = 0.31 (DCM/MeOH: 9/1). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.58 – 7.50 (m, 2H, H14), 7.50 – 7.41 (m, 2H, H10), 7.38 – 7.24 (m, 6H, H11, H12, H15 and H16), 4.23 (s, 2H, H8), 3.54 – 3.43 (m, 2H, H5), 2.96 (t, *J* = 6.2 Hz, 2H, H7), 2.01 – 1.87 (m, 2H, H6). **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 152.6 (C3), 139.1 (C9), 135.7 (C13), 130.2 (C16), 129.2 (2*C10), 128.6 (2*C11), 128.3 (2*C15), 127.5 (2*C14), 127.1 (C12), 64.9 (C8), 54.6 (C7), 44.4 (C5), 29.1 (C6). **HRMS (ASAP)** = Calcd for $C_{17}H_{20}N_3$ $[M+H]^+$ 266.1657 Da, found 266.1660 Da. **IR (ATR)** ν ($cm^{-1}$) = 2933, 1603.

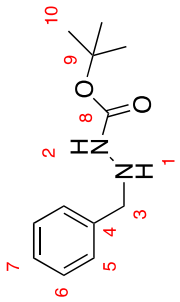
# Spectroscopy data and NMR spectra



$C_{12}H_{18}N_2O_2$
MW: 222,3 g.mol$^{-1}$

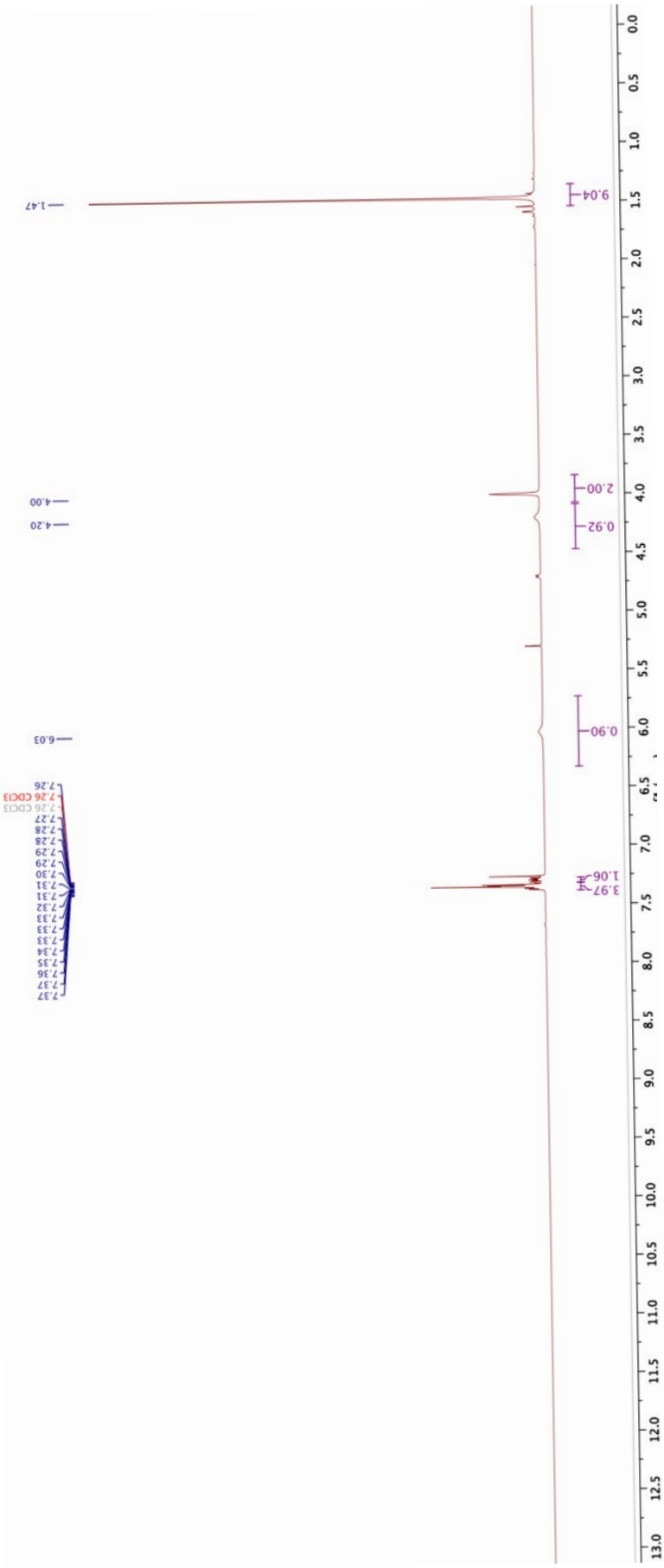
**6a**

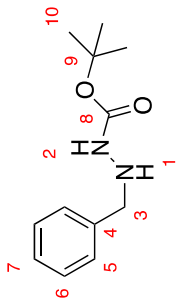




$C_{12}H_{18}N_2O_2$
MW: 222,3 g.mol$^{-1}$

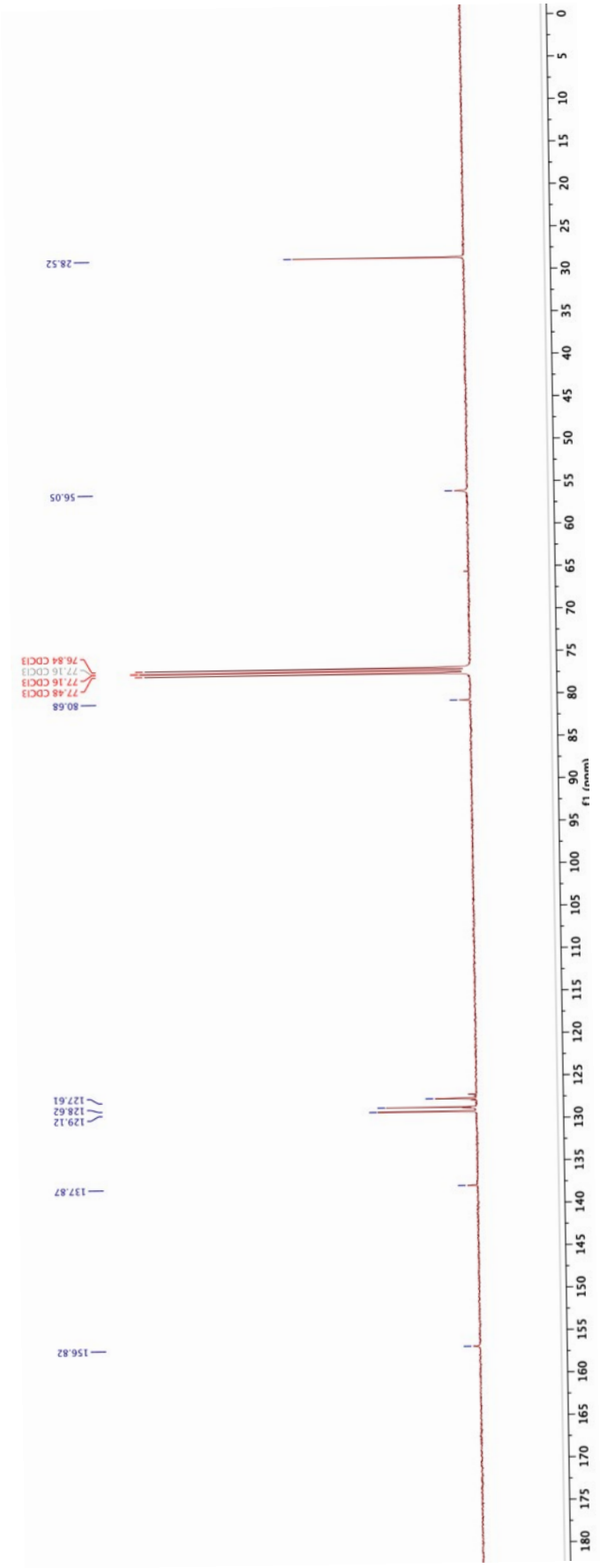
**6a**

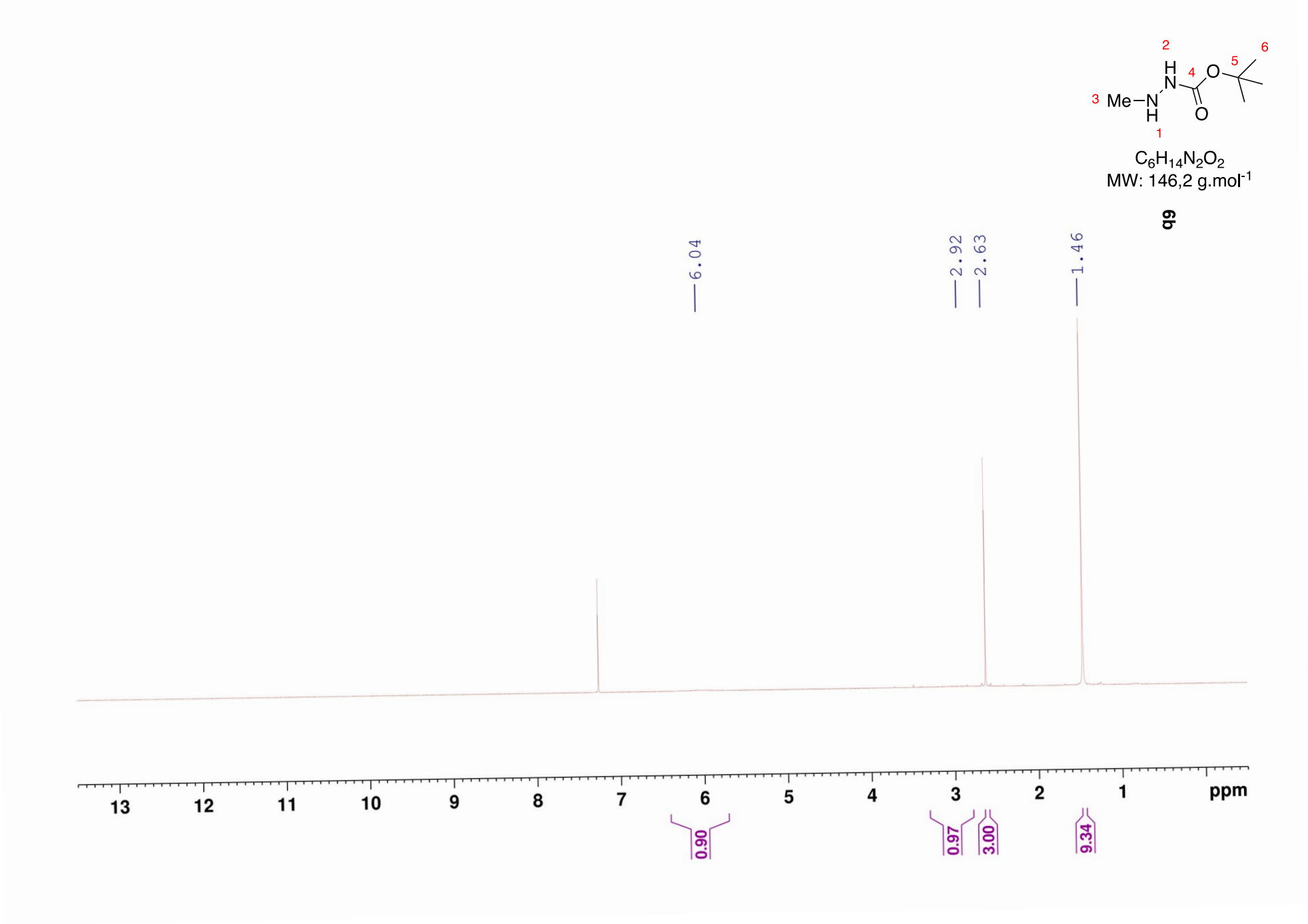


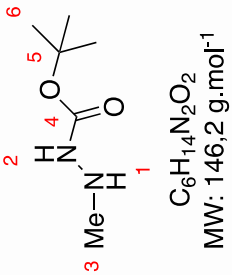


$C_{12}H_{18}N_2O_2$
MW: 222,3 g.mol$^{-1}$

**6a**

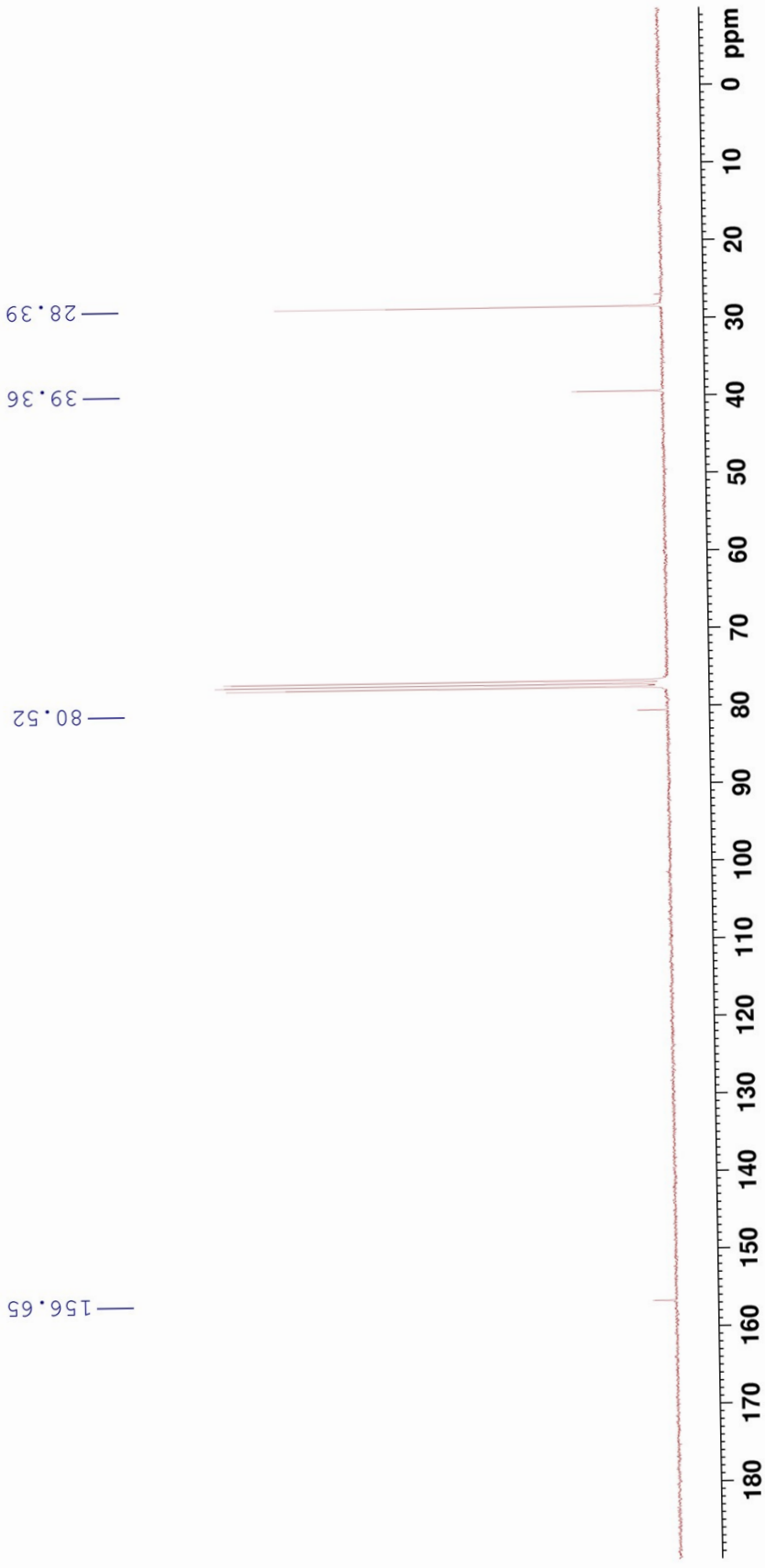



2
6
5
4
H
N
O
3 Me–N
H
O
1
$C_6H_{14}N_2O_2$
MW: 146,2 g.mol$^{-1}$
6b
6.04
2.92
2.63
1.46
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.90
0.97
3.00
9.34




$C_6H_{14}N_2O_2$
MW: 146,2 g.mol$^{-1}$

**6b**



**Elemental Composition Report** **Page 1**

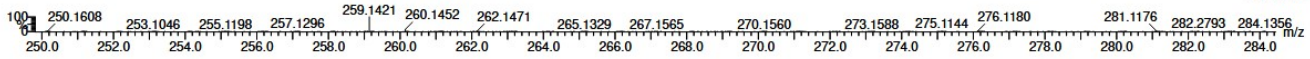
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
150 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-5 O: 0-5 Na: 1-1

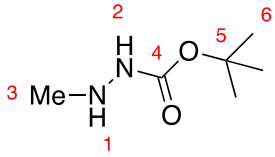
MB-234F1 (DCM) - MeOH/H2O (95/5%)
20230412_XX_MB234F1_01 57 (0.597) Cm (57:60)

XEVO G2-XS QTOF

12-Apr-2023
1: TOF MS ES+
1.35e+005

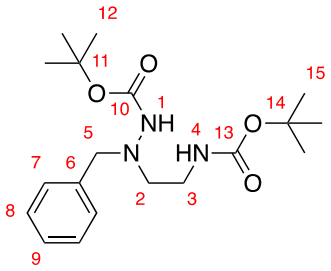



| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 259.1421 | 259.1422 | -0.1 | -0.4 | 4.5 | 453.9 | n/a | n/a | C13 H20 N2 O2 Na |




$C_6H_{14}N_2O_2$
MW: 146,2 g.mol$^{-1}$

**6b**




$C_{19}H_{31}N_3O_4$
MW: 365,5 g.mol$^{-1}$

**7aa**

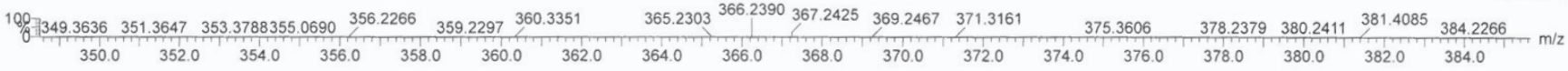
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
463 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-90 H: 0-110 N: 0-10 O: 0-10

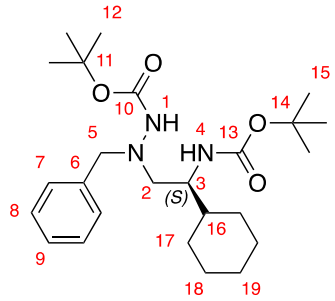
JOL-216-3 (Solide)
20191104_JOL-216-3_01 113 (1.158) Cm (111:126)

XEVO G2-XS QTOF

04-Nov-2019
1: TOF MS ASAP+
8.93e+007




| | Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
|---|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | | -1.0 | | | | |
| Maximum: | | | 30.0 | 5.0 | 1000.0 | | | | |
| | 366.2390 | 366.2393 | -0.3 | -0.8 | 5.5 | 2284.7 | 0.003 | 99.66 | C19 H32 N3 O4 |
| | | 366.2406 | -1.6 | -4.4 | 10.5 | 2290.4 | 5.696 | 0.34 | C20 H28 N7 |




$C_{25}H_{41}N_3O_4$
MW: 447,6 g.mol$^{-1}$

**7ba**



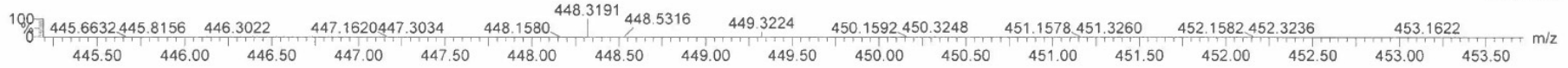
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
760 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-100 N: 0-10 O: 0-15

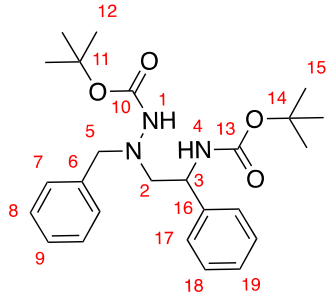
JOL-246-3 (DCM) - MeOH (100%)
20191127_JOL-246-3_01 86 (0.464) Cm (86:107)

XEVO G2-XS QTOF

27-Nov-2019
1: TOF MS ES+
2.26e+007




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 448.3191 | 448.3175 | 1.6 | 3.6 | 6.5 | 2997.7 | 0.056 | 94.58 | C25 H42 N3 O4 |
| | 448.3189 | 0.2 | 0.4 | 11.5 | 3000.5 | 2.915 | 5.42 | C26 H38 N7 |




$C_{25}H_{35}N_3O_4$
MW: 441,6 g.mol$^{-1}$

**7ca**

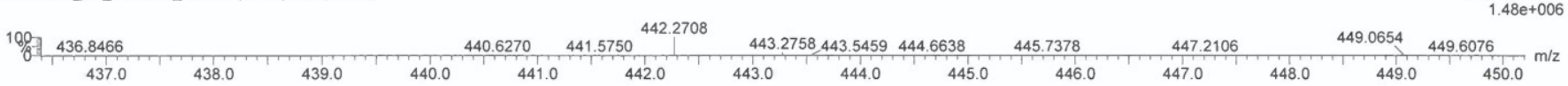
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
510 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-132 H: 0-210 N: 0-5 O: 0-10

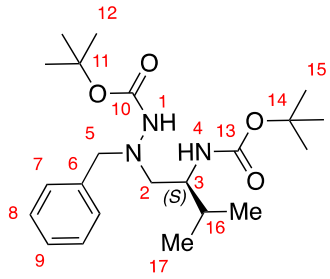
CVG-80-3 (DCM) - MeOH (100%)
20210707_XX_CVG803_01A 44 (0.463) Cm (44:48)

XEVO G2-XS QTOF

07-Jul-2021
TOF MS ES+
1.48e+006




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 442.2708 | 442.2706 | 0.2 | 0.5 | 9.5 | 91.9 | n/a | n/a | C25 H36 N3 O4 |




$C_{22}H_{37}N_3O_4$
MW: 407,6 g.mol$^{-1}$

**7da**

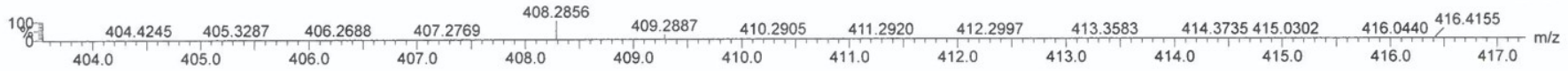
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
188 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-126 H: 0-200 N: 0-3 O: 0-5

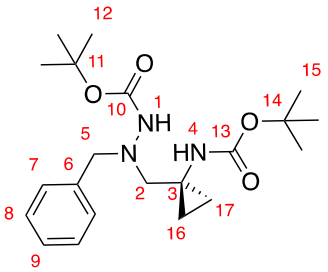
CVG-59-3 (Solide)
20210611_XX_CVG593_01 57 (0.597) Cm (57:66)

XEVO G2-XS QTOF

11-Jun-2021
1: TOF MS ASAP+
1.19e+006




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 408.2856 | 408.2862 | -0.6 | -1.5 | 5.5 | 1053.2 | n/a | n/a | C22 H38 N3 O4 |




$C_{21}H_{33}N_3O_4$
MW: 391,5 g.mol$^{-1}$

**7ea**



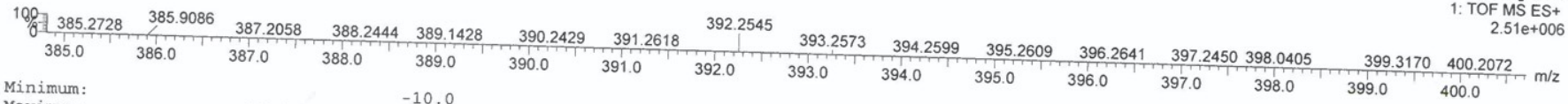


**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

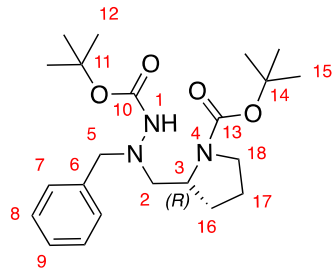
Monoisotopic Mass, Even Electron Ions
400 formula(e) evaluated with 1 results within limits (up to 5 best isotopic matches for each mass)
Elements Used:
C: 0-46 H: 0-100 N: 0-5 O: 0-11
CVG-88-2 (DCM) - MeOH (100%)
20210824_XX_CVG882_01 65 (0.677) Cm (59:65)

XEVO G2-XS QTOF

24-Aug-2021
1: TOF MS ES+
2.51e+006




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 392.2545 | 392.2549 | -0.4 | -1.0 | 6.5 | 1623.9 | n/a | n/a | C21 H34 N3 O4 |




$C_{22}H_{35}N_3O_4$
MW: 405,5 g.mol$^{-1}$

**7fa**



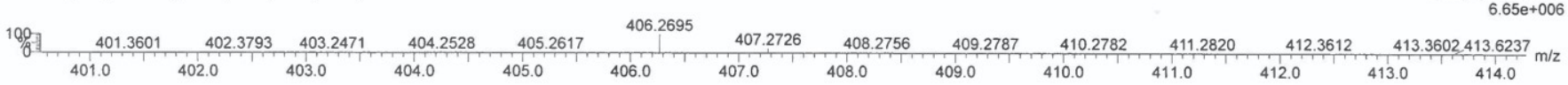
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
188 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-126 H: 0-200 N: 0-3 O: 0-5

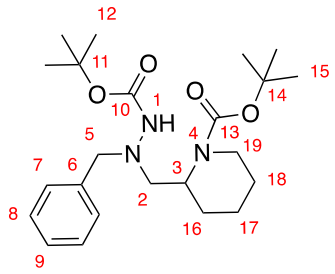
CVG-60-3 (Solide)
20210611_XX_CVG603_01 41 (0.437) Cm (40:48)

XEVO G2-XS QTOF

11-Jun-2021
1: TOF MS ASAP+
6.65e+006




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 406.2695 | 406.2706 | -1.1 | -2.7 | 6.5 | 1754.3 | n/a | n/a | C22 H36 N3 O4 |




$C_{23}H_{37}N_3O_4$
MW: 419,6 g.mol$^{-1}$

**7ga**

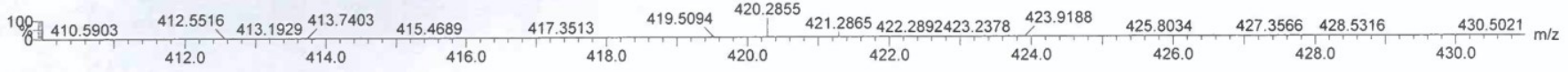


**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

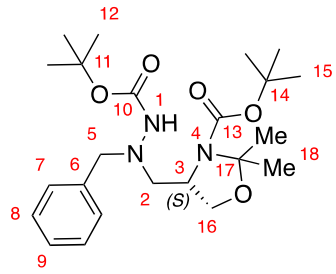
Monoisotopic Mass, Even Electron Ions
806 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-132 H: 0-210 N: 0-5 O: 0-20
CVG-81-3 (DCM) - MeOH (100%)
20210707_XX_CVG813_01 57 (0.597) Cm (54:78-2:20x5.000)

XEVO G2-XS QTOF

07-Jul-2021
1: TOF MS ES+
1.25e+006




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 420.2855 | 420.2862 | -0.7 | -1.7 | 6.5 | 176.9 | 0.373 | 68.86 | C23 H38 N3 O4 |
| | 420.2867 | -1.2 | -2.9 | -11.5 | 177.7 | 1.167 | 31.14 | C10 H46 N O15 |




$C_{23}H_{37}N_3O_5$
MW: 435,6 g.mol$^{-1}$

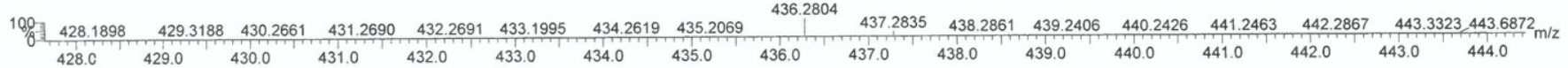
**7ha**

**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

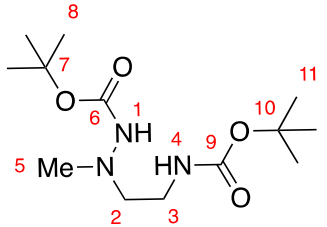
Monoisotopic Mass, Even Electron Ions
338 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-126 H: 0-200 N: 0-6 O: 0-5
CVG-65-3 (DCM) - MeOH (100%)
20210615_XX_CVG653_01 57 (0.597) Cm (50:62)

XEVO G2-XS QTOF

15-Jun-2021
1: TOF MS ES+
1.27e+007




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 436.2804 | 436.2811 | -0.7 | -1.6 | 6.5 | 2176.8 | n/a | n/a | C23 H38 N3 O5 |




$C_{13}H_{27}N_3O_4$

MW: 289,4 g.mol$^{-1}$

**7ab**





## Elemental Composition Report

### Single Mass Analysis

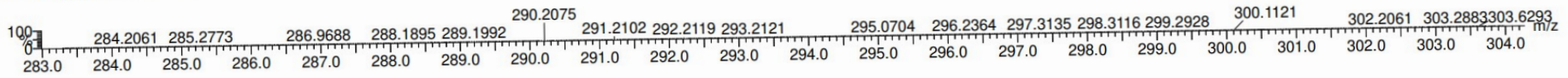
Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
295 formula(e) evaluated with 1 results within limits (up to 5 best isotopic matches for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-8 O: 0-6

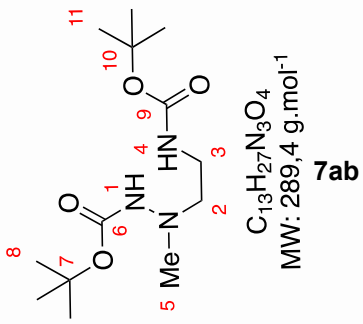
MB-222F1 (Solide)
20230130_XX_MB222F1_01 60 (0.623) Cm (53:61)

XEVO G2-XS QTOF

30-Jan-2023
1: TOF MS ASAP+
8.05e+006

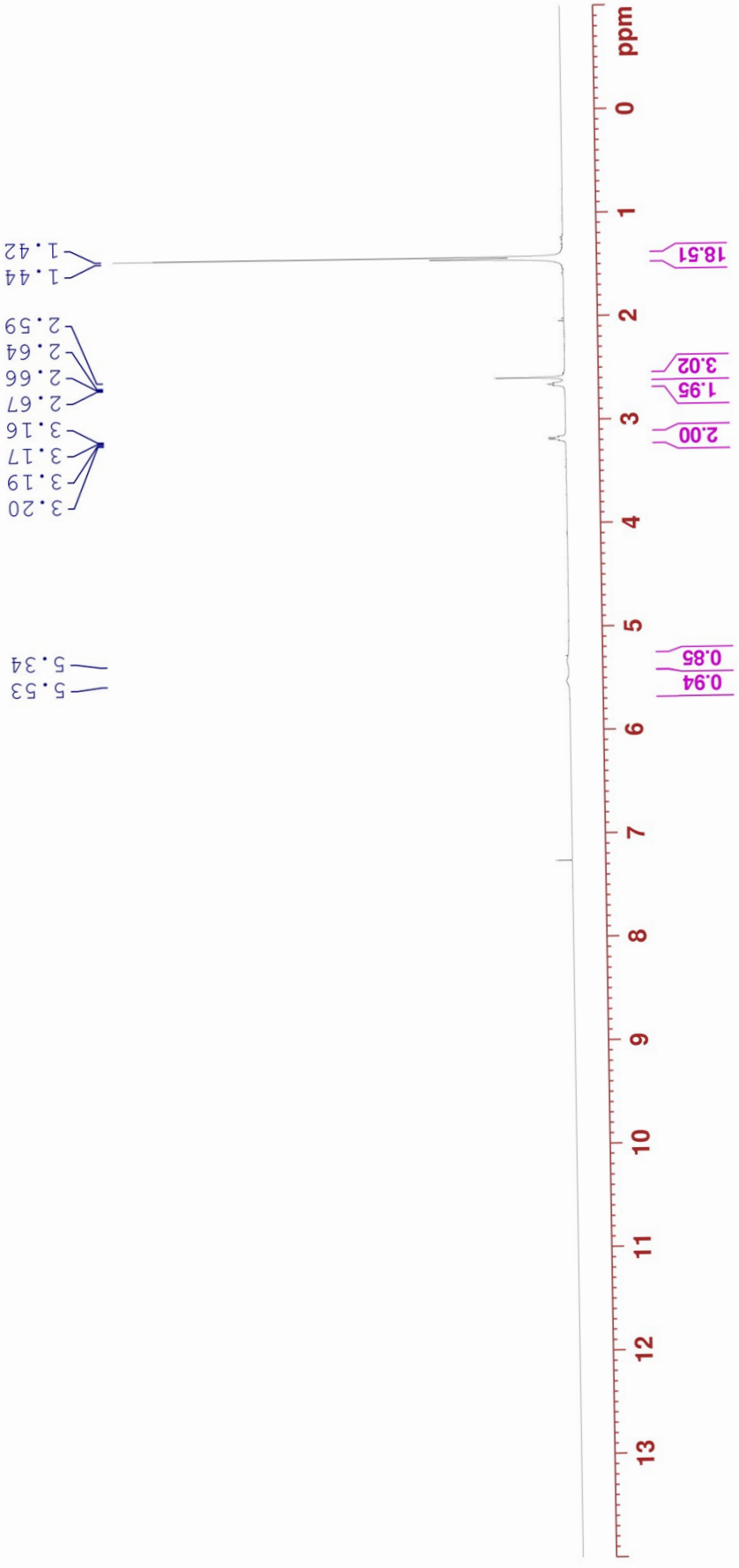


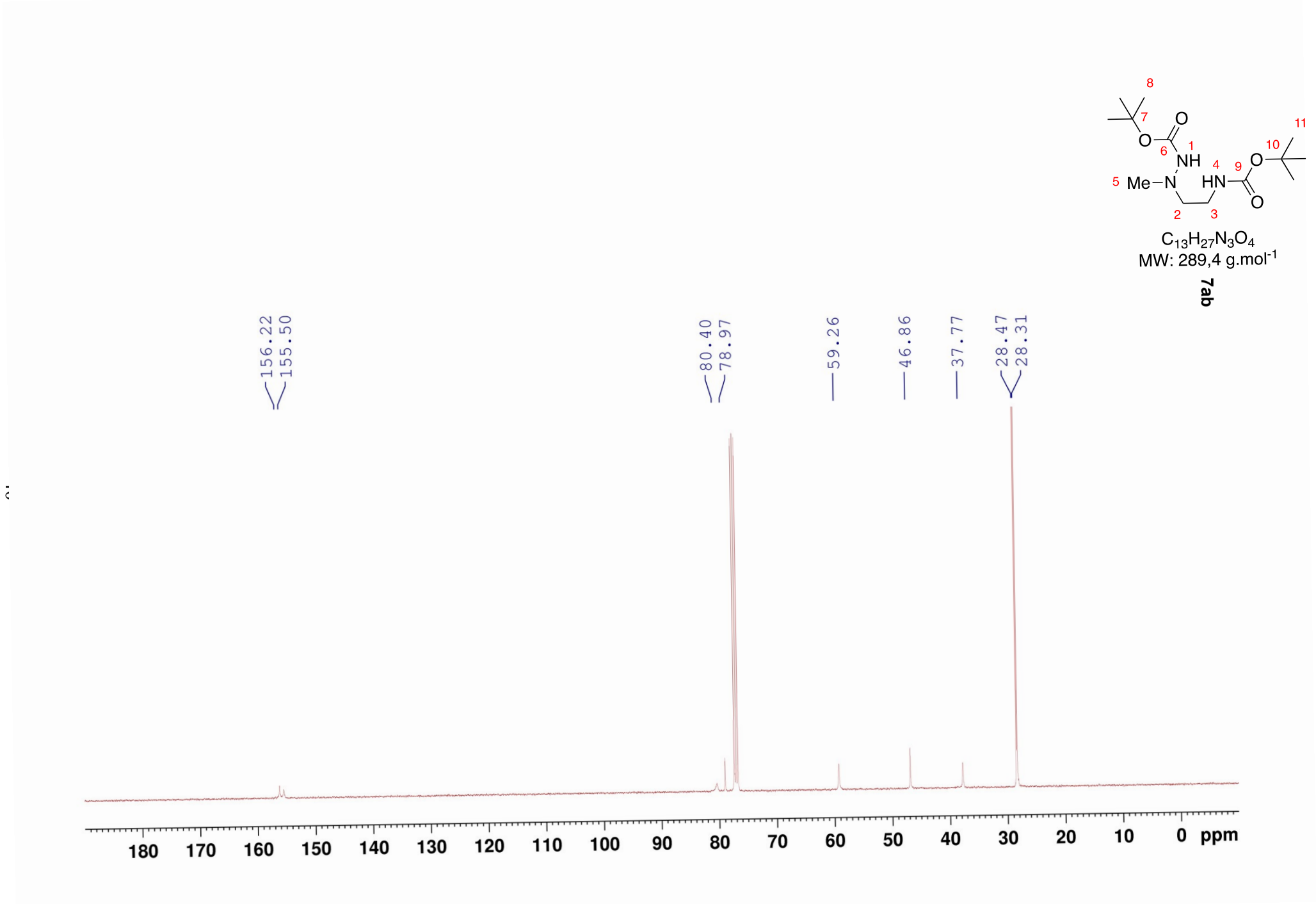

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 290.2075 | 290.2080 | -0.5 | -1.7 | 1.5 | 2422.3 | n/a | n/a | C13 H28 N3 O4 |

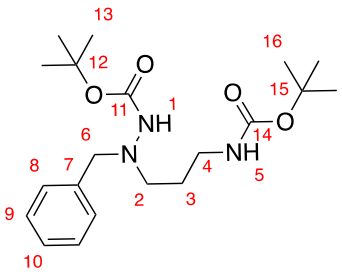



$C_{13}H_{27}N_3O_4$
MW: 289,4 g.mol$^{-1}$

**7ab**




8
7
O
O
6
1
NH
4
9
O
10
11
5
Me–N
HN
O
2
3
C13H27N3O4
MW: 289,4 g.mol-1
7ab
156.22
155.50
80.40
78.97
59.26
46.86
37.77
28.47
28.31
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm




$C_{20}H_{33}N_3O_4$
MW: 379,5 g.mol$^{-1}$

**7ia**



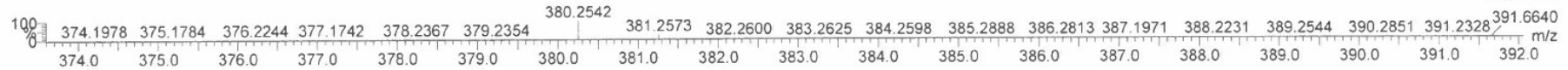
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
364 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-106 H: 0-110 N: 0-6 O: 0-12

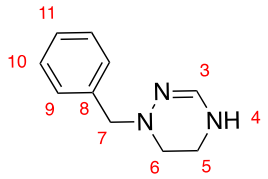
JOL-237-3 (DCM) - MeOH (100%)
20191113_JOL-237-3_01 49 (0.517) Cm (47:49)

XEVO G2-XS QTOF

13-Nov-2019
1: TOF MS ES+
2.24e+006




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 380.2542 | 380.2549 | -0.7 | -1.8 | 5.5 | 1263.4 | n/a | n/a | C20 H34 N3 O4 |




$C_{10}H_{13}N_3$
MW: 175,2 g.mol$^{-1}$

**12aa**

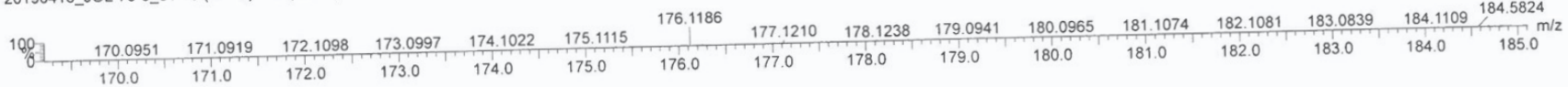
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
151 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-92 H: 0-100 N: 0-10 O: 0-10

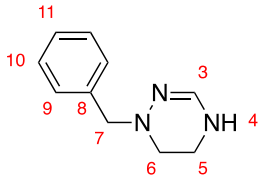
JOL-75-3 (Solide)
20190416_JOL-75-3_01 16 (0.177) Cm (12:21)

XEVO G2-XS QTOF

16-Apr-2019
1: TOF MS ASAP+
3.52e+007

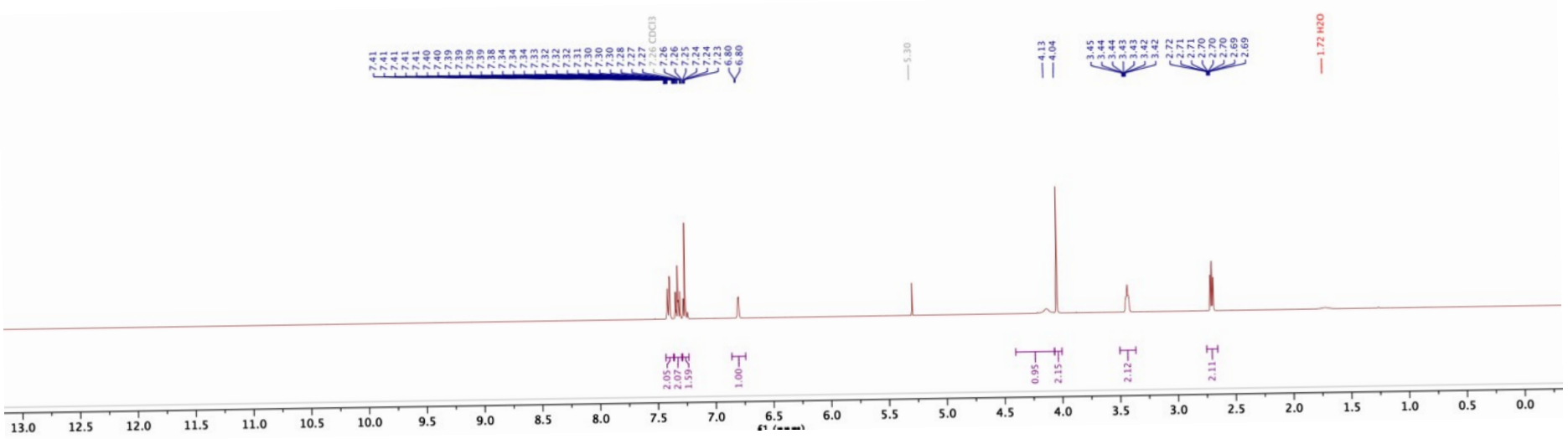


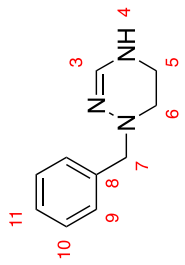

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 176.1186 | 176.1188 | -0.2 | -1.1 | 5.5 | 3077.3 | n/a | n/a | C10 H14 N3 |




$C_{10}H_{13}N_3$
MW: 175,2 g.mol$^{-1}$

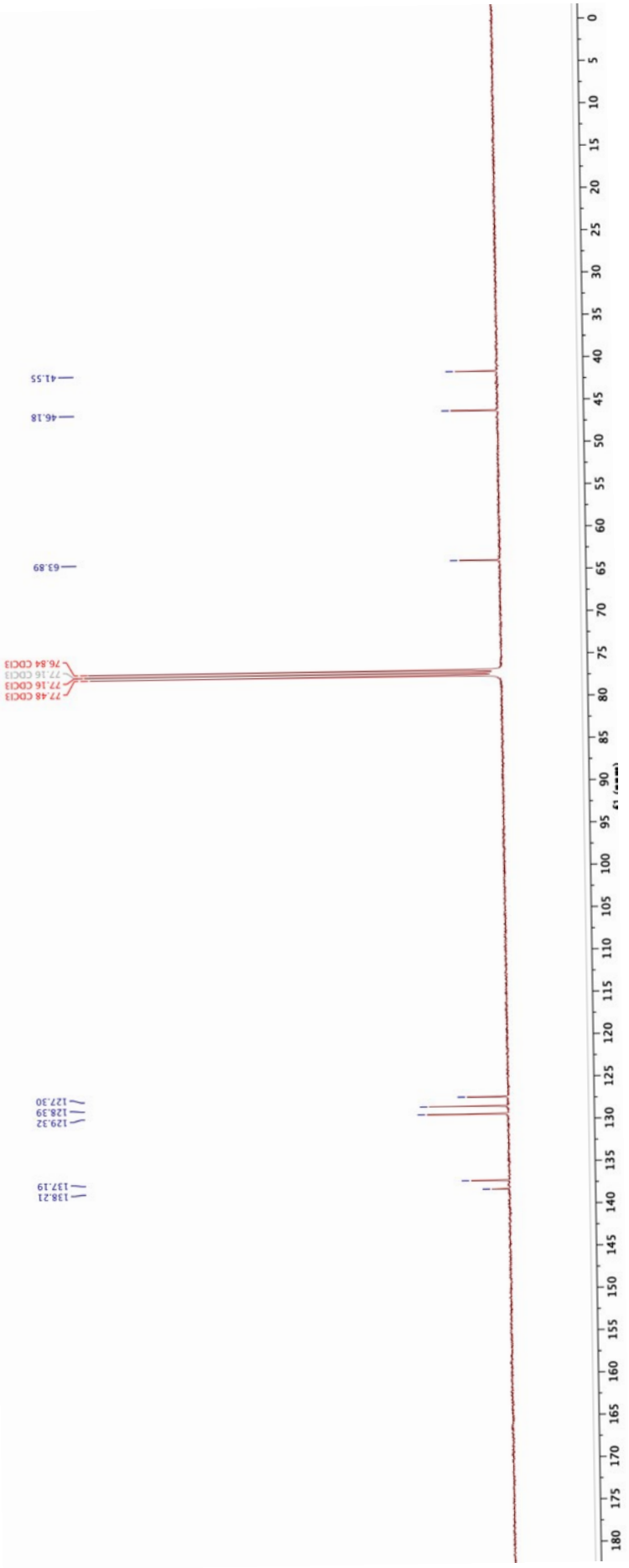
**12aa**

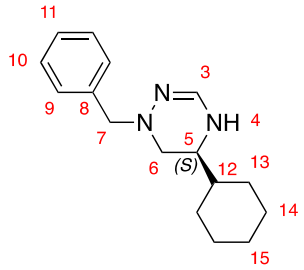





$C_{10}H_{13}N_3$
MW: 175,2 g.mol$^{-1}$

**12aa**






$C_{16}H_{23}N_3$
MW: 257,4 g.mol$^{-1}$

**12ba**



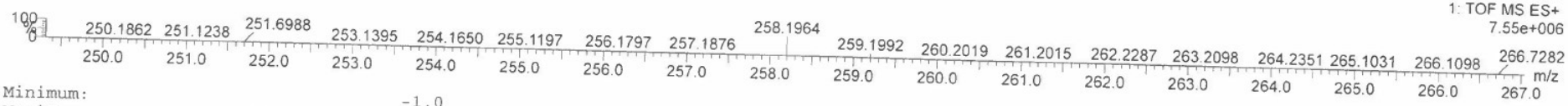
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
250 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-123 H: 0-150 N: 0-4 O: 0-10 79Br: 0-1

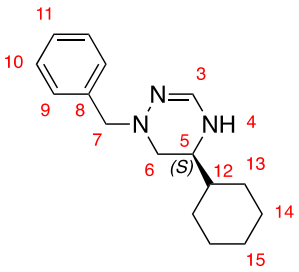
JOL-249-3 (DCM) - MeOH (100%)
20200106_JOL-249-3_01 31 (0.328) Cm (25:34)

XEVO G2-XS QTOF

06-Jan-2020
1: TOF MS ES+
7.55e+006

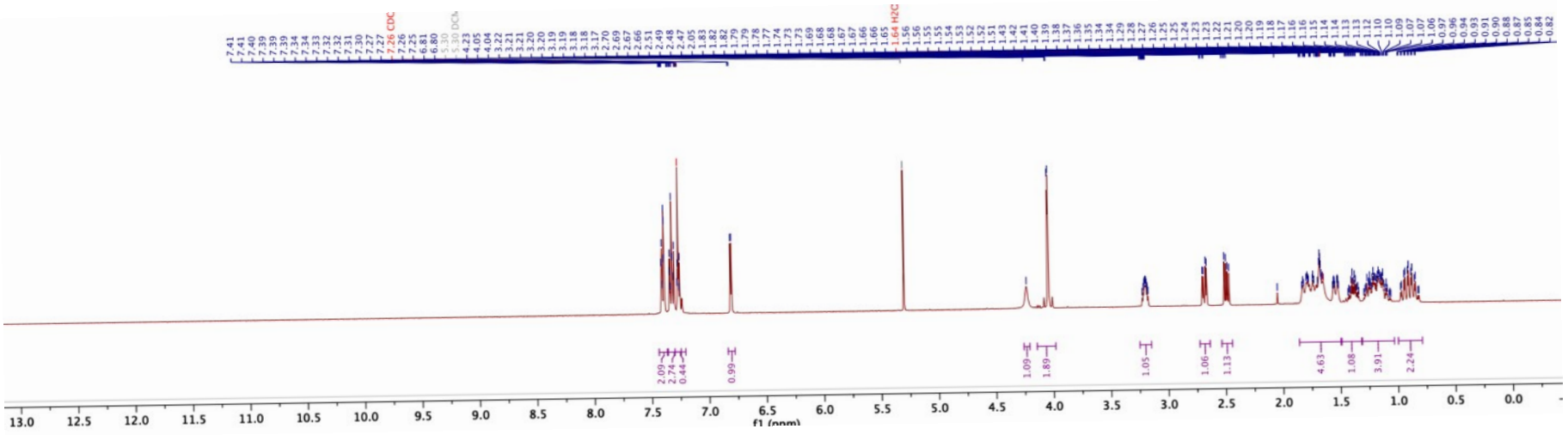


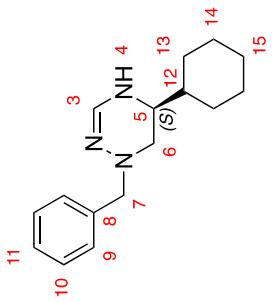

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 258.1964 | 258.1970 | -0.6 | -2.3 | 6.5 | 2187.6 | n/a | n/a | C16 H24 N3 |




$C_{16}H_{23}N_3$
MW: 257,4 g.mol$^{-1}$

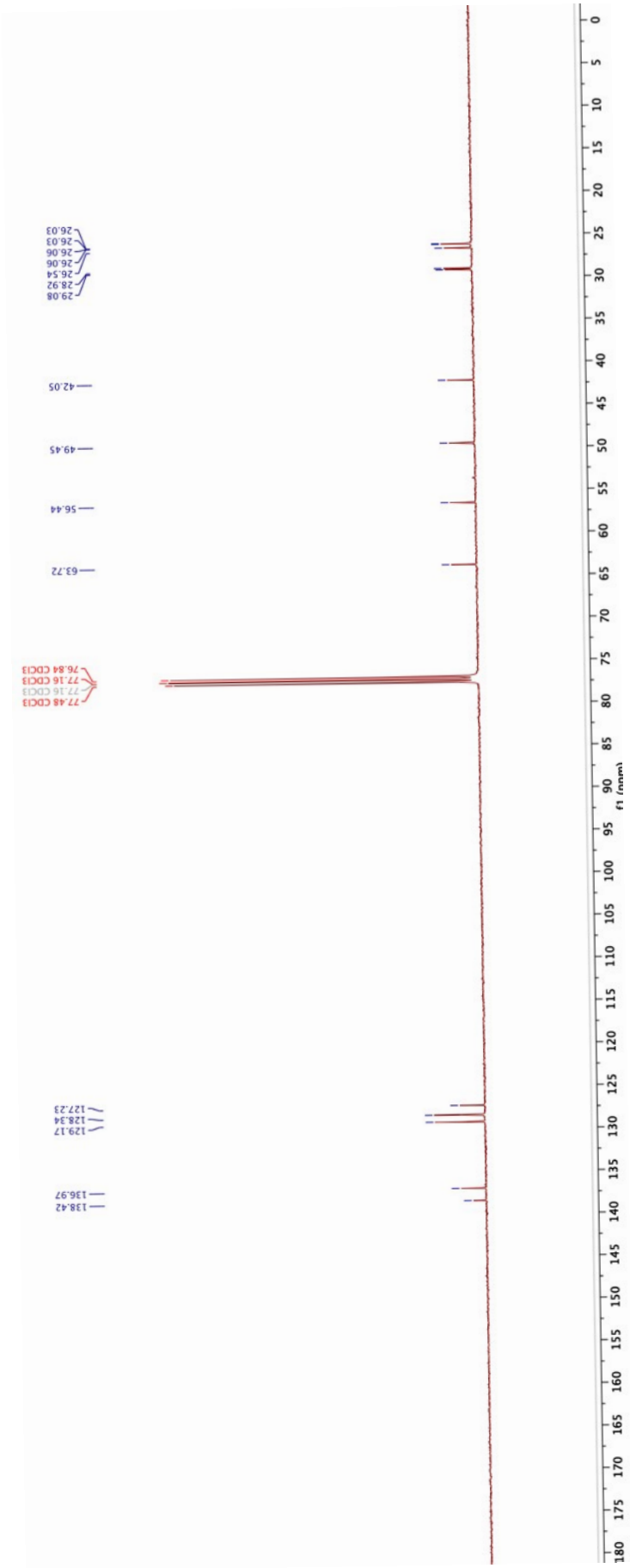
**12ba**

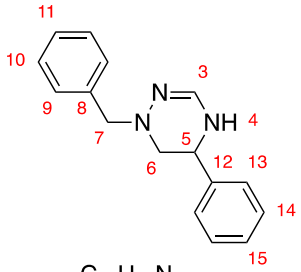




$C_{16}H_{23}N_3$
MW: 257,4 g.mol$^{-1}$

**12ba**






$C_{16}H_{17}N_3$
MW: 251,3 g.mol$^{-1}$

**12ca**



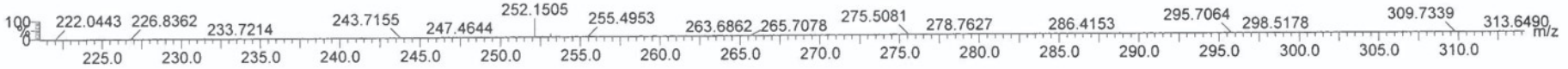
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
404 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-132 H: 0-210 N: 0-6 O: 0-10

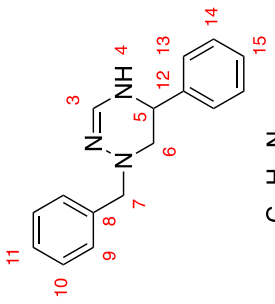
CVG-84-3 (Solide)
20210713_XX_CVG843_01A 57 (0.597) Cm (52:57)

XEVO G2-XS QTOF

13-Jul-2021
TOF MS ASAP+
5.95e+006

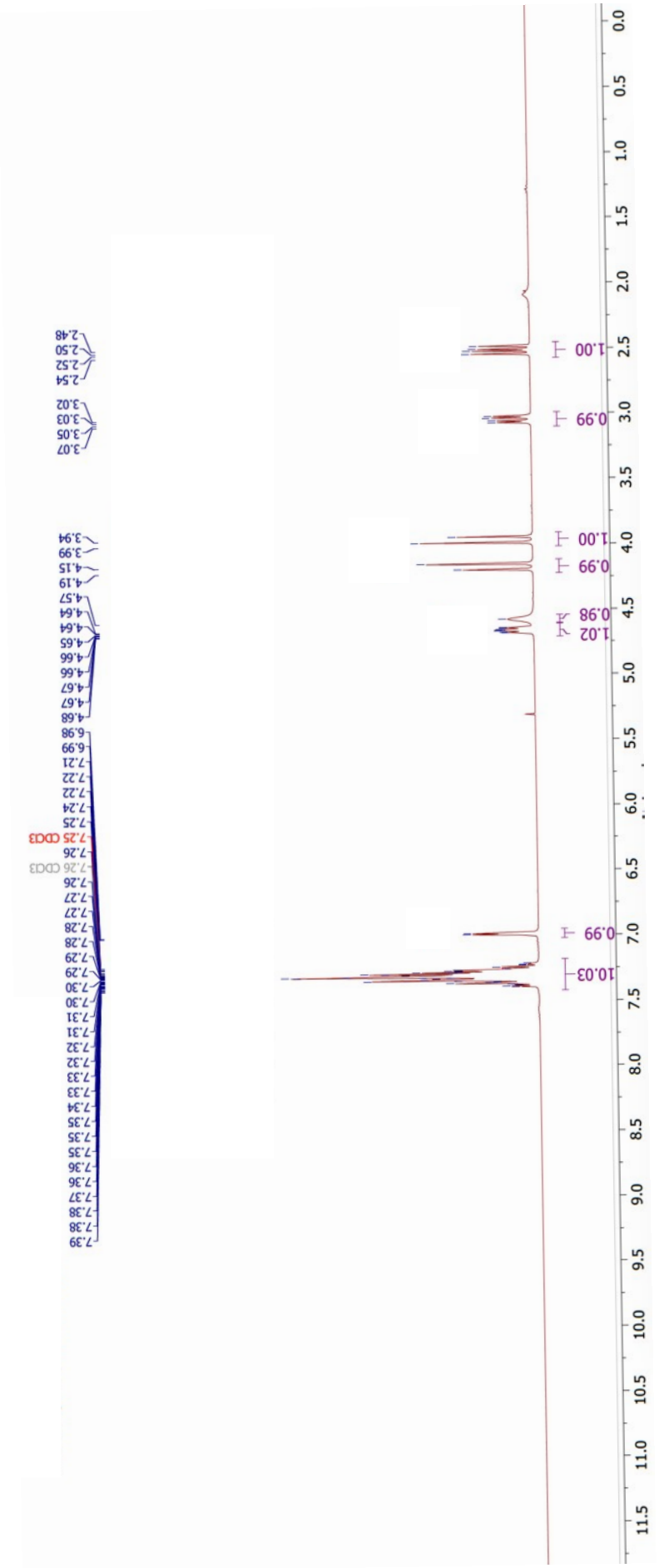


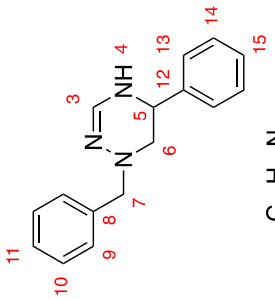

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 252.1505 | 252.1501 | 0.4 | 1.6 | 9.5 | 424.0 | n/a | n/a | C16 H18 N3 |




$C_{16}H_{17}N_3$
MW: 251,3 g.mol$^{-1}$

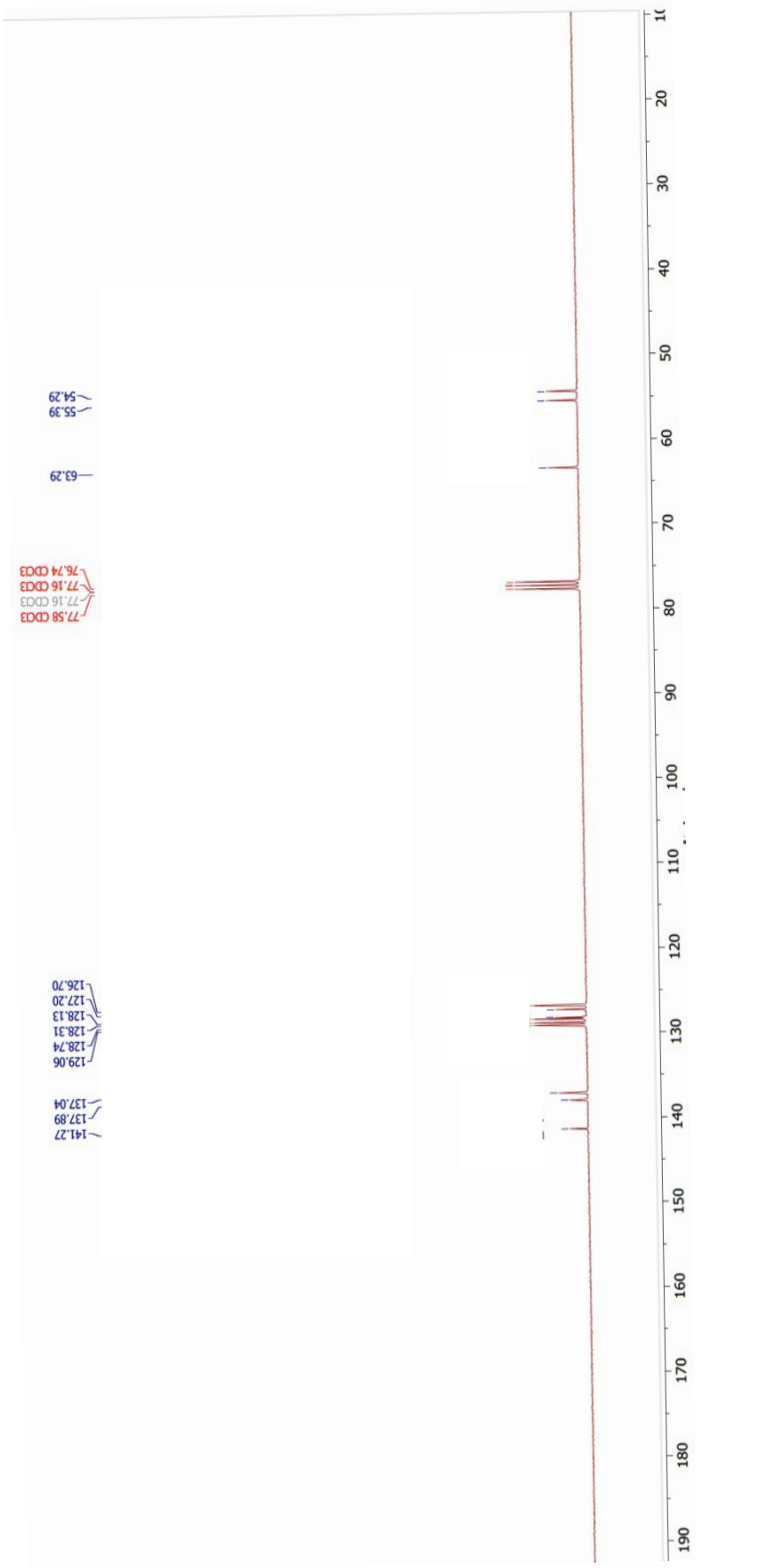
**12ca**

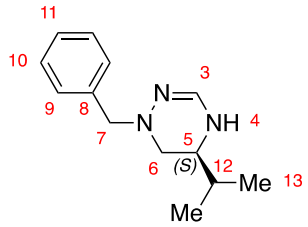





$C_{16}H_{17}N_3$
MW: 251,3 g.mol$^{-1}$

**12ca**






$C_{13}H_{19}N_3$
MW: 217,3 g.mol$^{-1}$

**12da**

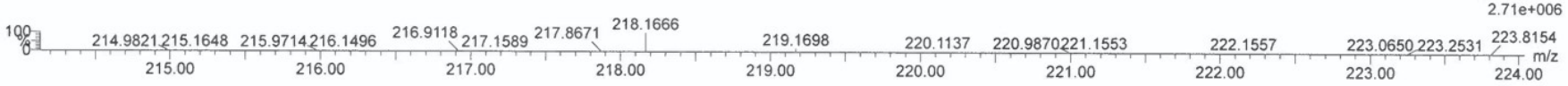
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
95 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-126 H: 0-200 N: 0-3 O: 0-3

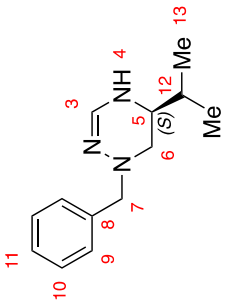
CVG-63-3 (Solide)
20210611_XX_CVG633_01 33 (0.357) Cm (28:34)

XEVO G2-XS QTOF

11-Jun-2021
1: TOF MS ASAP+
2.71e+006

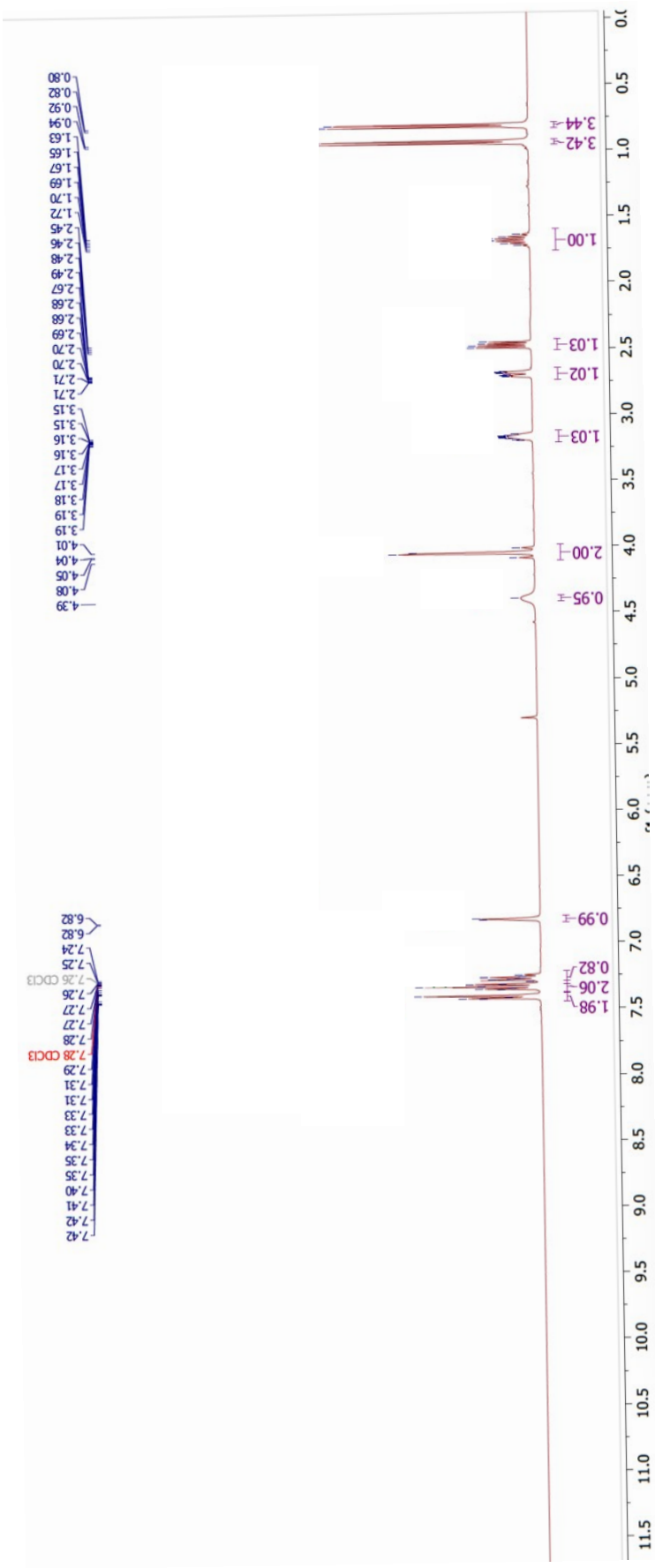


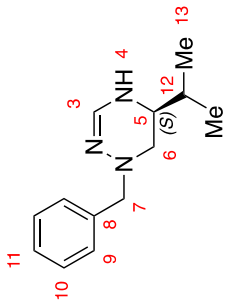

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 218.1666 | 218.1657 | 0.9 | 4.1 | 5.5 | 1589.5 | n/a | n/a | C13 H20 N3 |




$C_{13}H_{19}N_3$
MW: 217,3 g.mol$^{-1}$

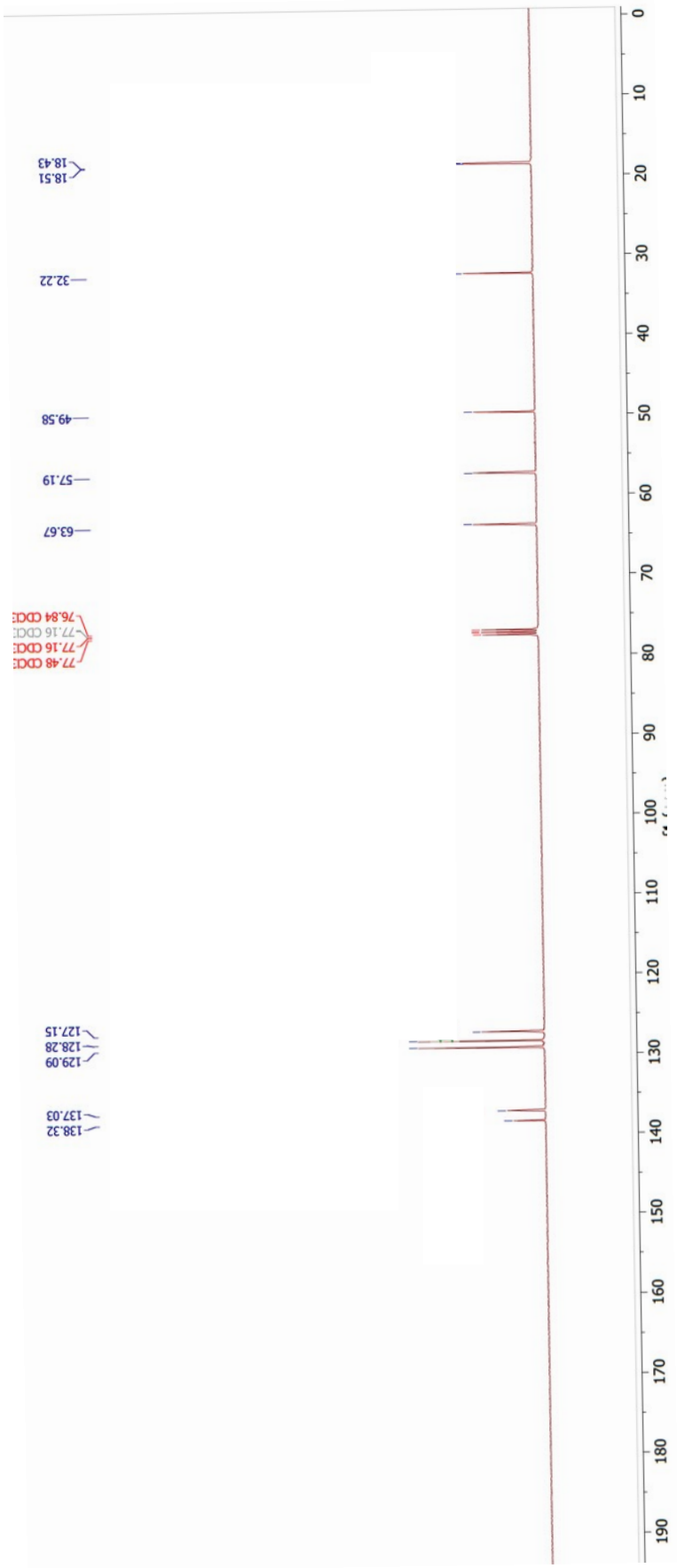
**12da**

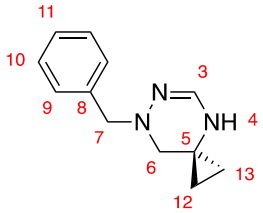





$C_{13}H_{19}N_3$
MW: 217,3 g.mol$^{-1}$

**12da**






$C_{12}H_{15}N_3$
MW: 201,3 g.mol$^{-1}$

**12ea**



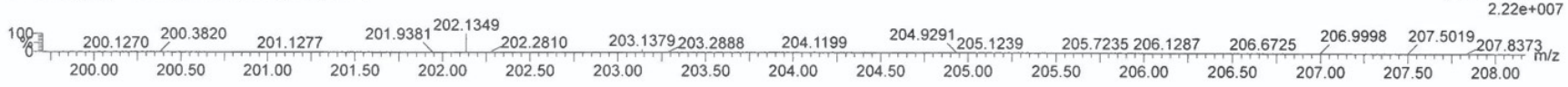
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
311 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-11 O: 0-5

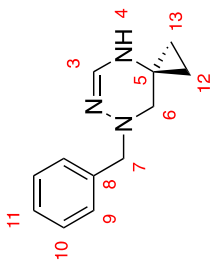
CVG-90-3 (Solide)
20210719_XX_CVG903_01A 64 (0.657) Cm (64:72)

XEVO G2-XS QTOF

19-Jul-2021
TOF MS ASAP+
2.22e+007

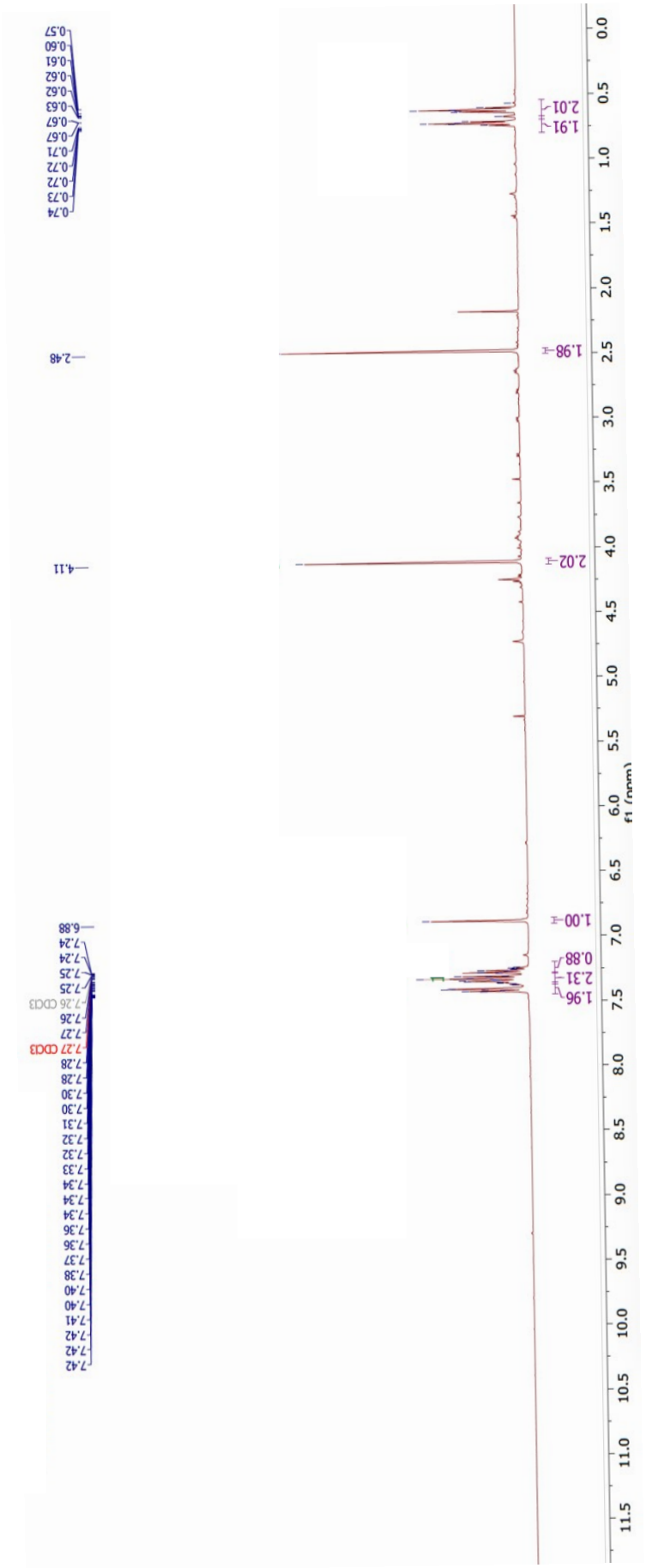


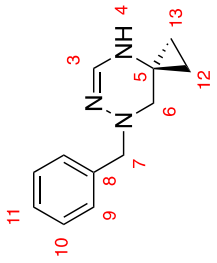

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 202.1349 | 202.1344 | 0.5 | 2.5 | 6.5 | 1073.6 | n/a | n/a | C12 H16 N3 |




$C_{12}H_{15}N_3$
MW: 201,3 g.mol$^{-1}$

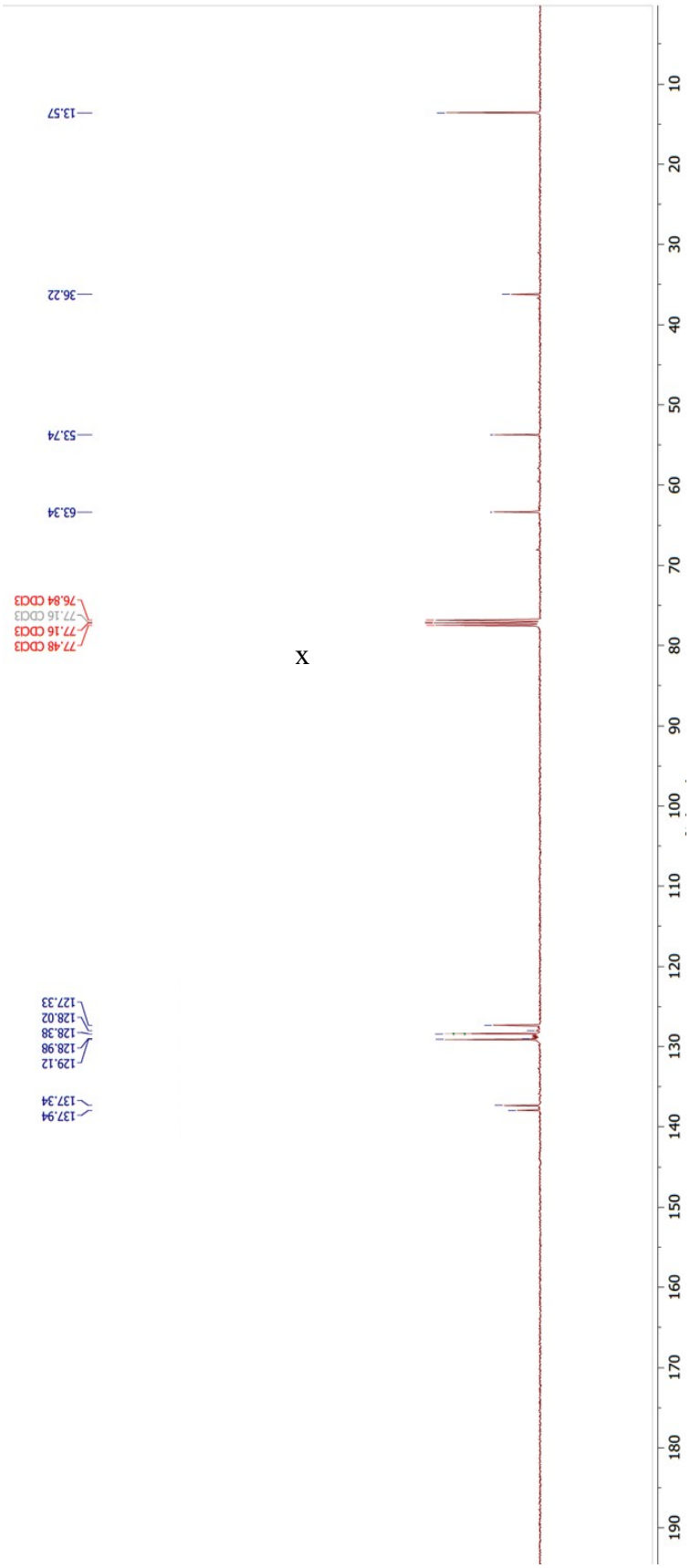
**12ea**

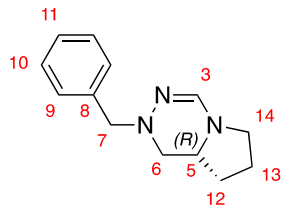





$C_{12}H_{15}N_3$
MW: 201,3 g.mol$^{-1}$

**12ea**






$C_{13}H_{17}N_3$
MW: 215,3 g.mol$^{-1}$

**12fa**



***Single* Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

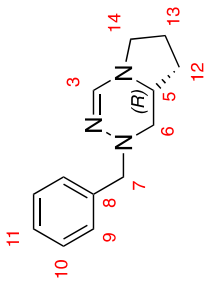
Monoisotopic Mass, Even Electron Ions
93 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 2-126 H: 0-200 N: 0-3 O: 0-3

CVG-64-3 (Solide)
20210611_XX_CVG643_01 9 (0.117) Cm (9:16)

XEVO G2-XS QTOF

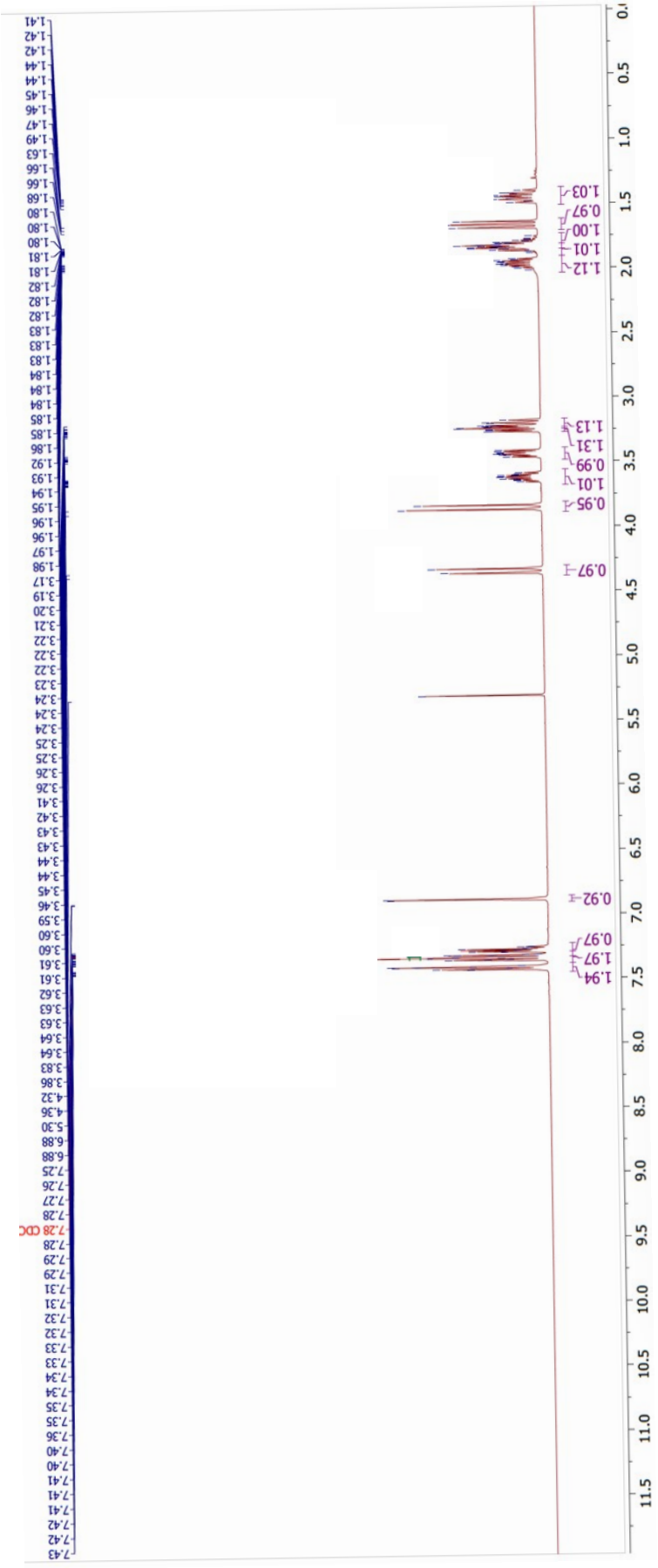
11-Jun-2021
1: TOF MS ASAP+
1.74e+007

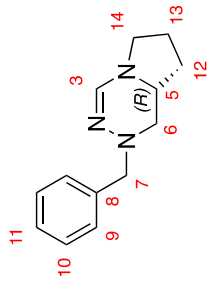

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 216.1509 | 216.1501 | 0.8 | 3.7 | 6.5 | 2351.3 | n/a | n/a | C13 H18 N3 |




$C_{13}H_{17}N_3$
MW: 215,3 g.mol$^{-1}$

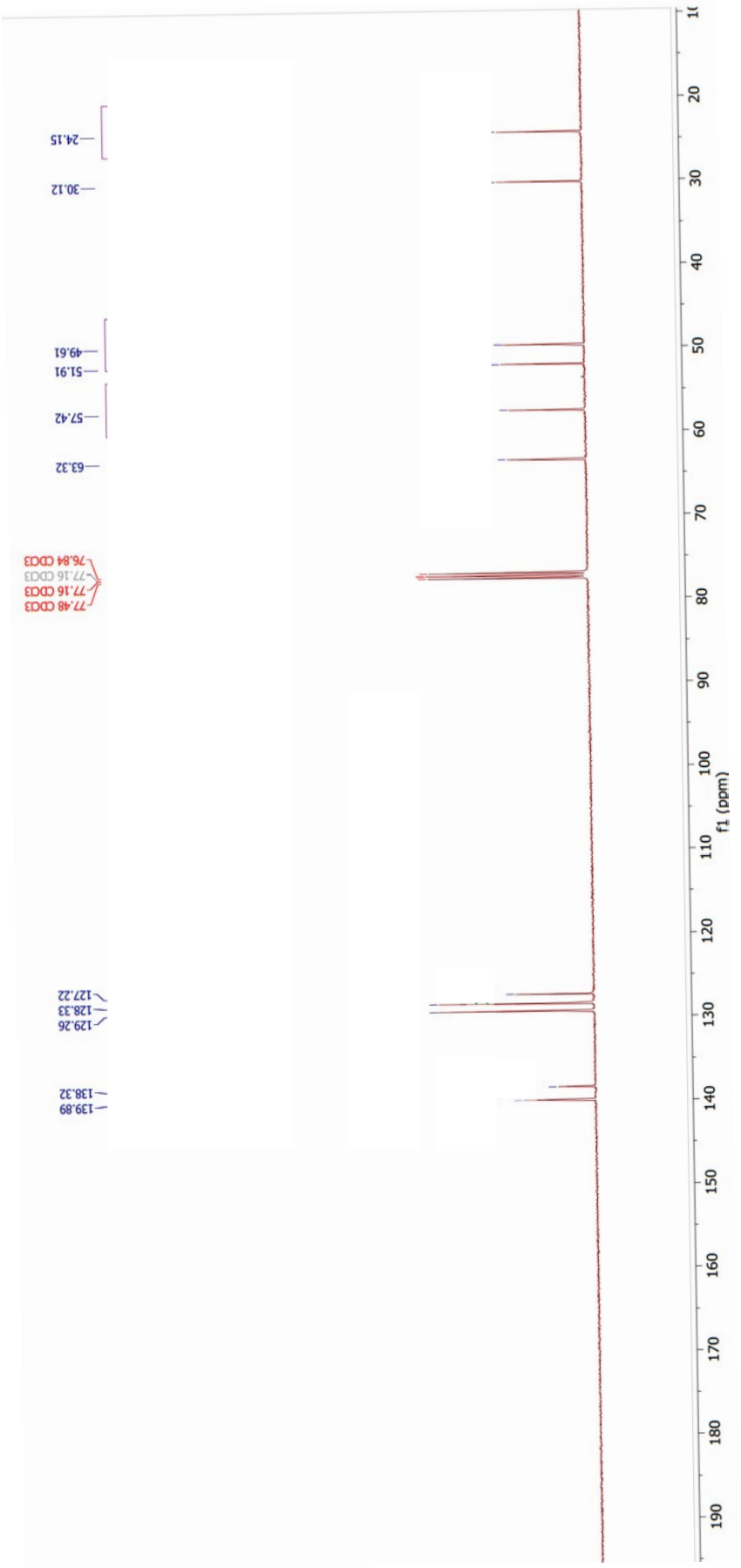
**12fa**

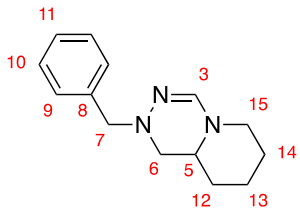





$C_{13}H_{17}N_3$
MW: 215,3 g.mol$^{-1}$

**12fa**






$C_{14}H_{19}N_3$
MW: 229,3 g.mol$^{-1}$

**12ga**

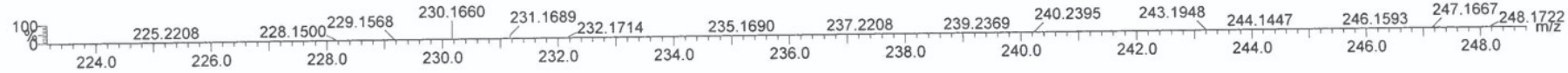
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -20.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
373 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-132 H: 0-210 N: 0-6 O: 0-10

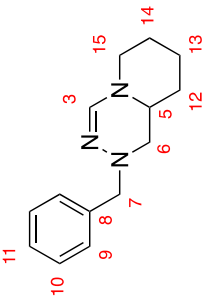
CVG-85-3 (Solide)
20210713_XX_CVG853_01 30 (0.320) Cm (29:44)

XEVO G2-XS QTOF

13-Jul-2021
1: TOF MS ASAP+
3.22e+007

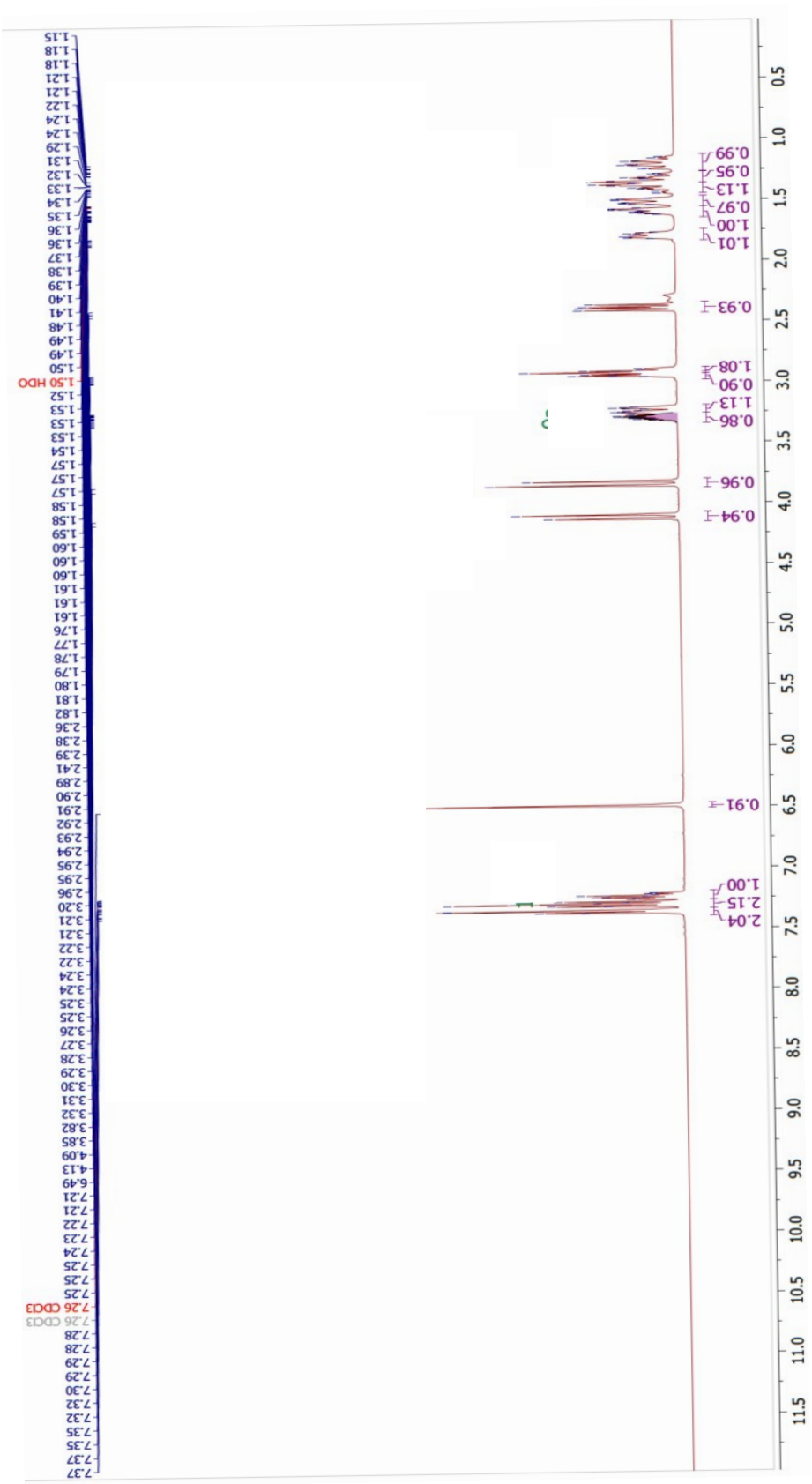


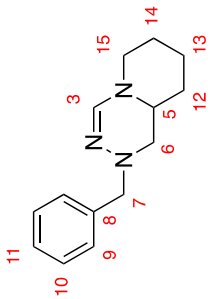

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -20.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 230.1660 | 230.1657 | 0.3 | 1.3 | 6.5 | 2824.7 | n/a | n/a | C14 H20 N3 |




$C_{14}H_{19}N_3$
MW: 229,3 g.mol$^{-1}$

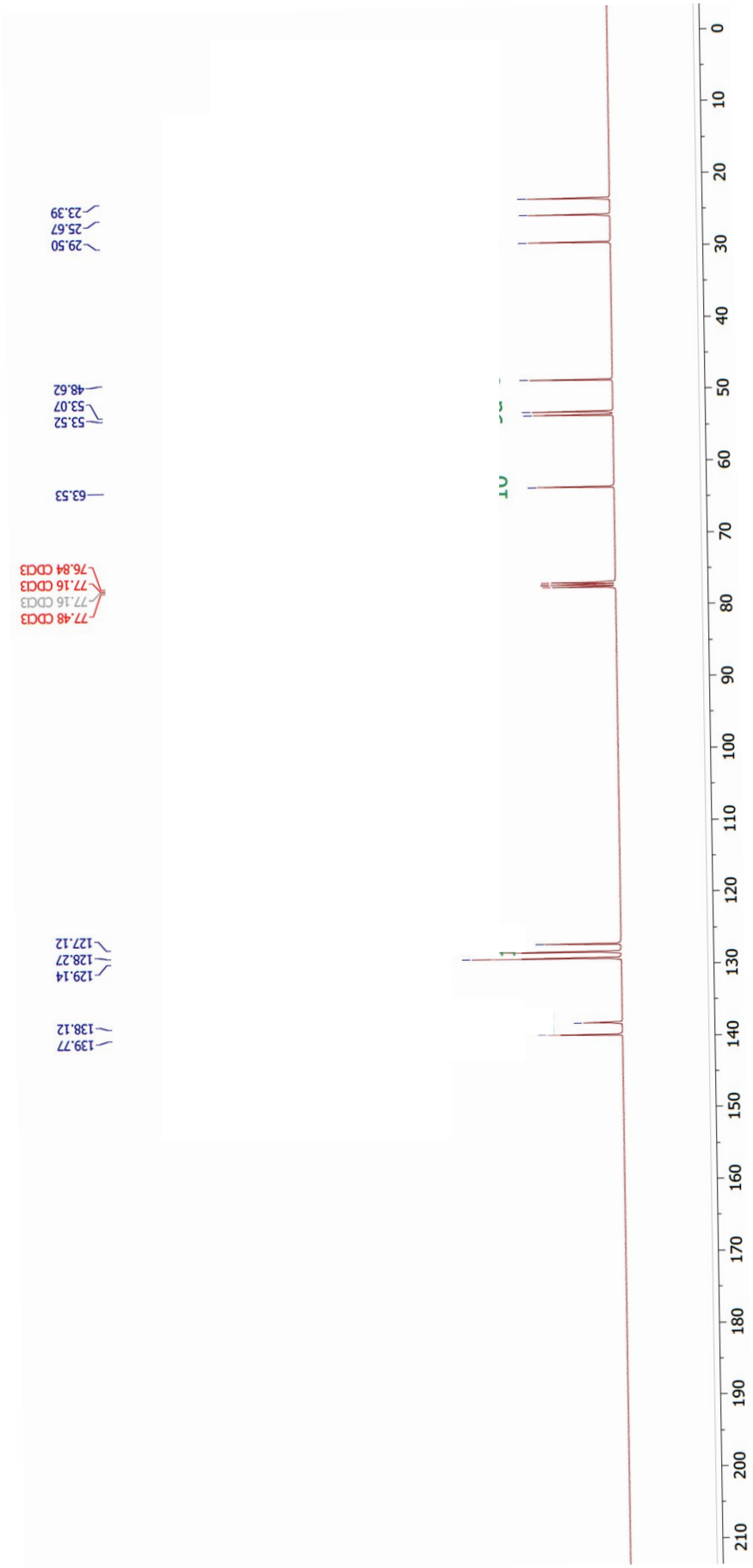
**12ga**

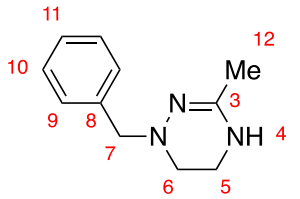





$C_{14}H_{19}N_3$
MW: 229,3 g.mol$^{-1}$

**12ga**






$C_{11}H_{15}N_3$
MW: 189,3 g.mol$^{-1}$

**13aa**

## Elemental Composition Report



### Single Mass Analysis

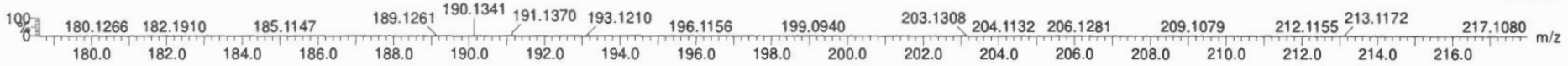
Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
698 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-4 O: 0-10 S: 0-2 Na: 0-1

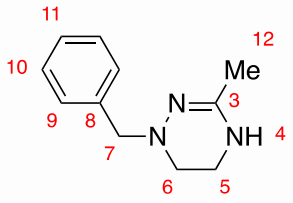
MB-203F1 (DCM) - MeOH/H2O (95/5%)
20230411_XX_MB203F1_01 41 (0.437) Cm (37:42)

XEVO G2-XS QTOF

11-Apr-2023
1: TOF MS ES+
1.26e+007



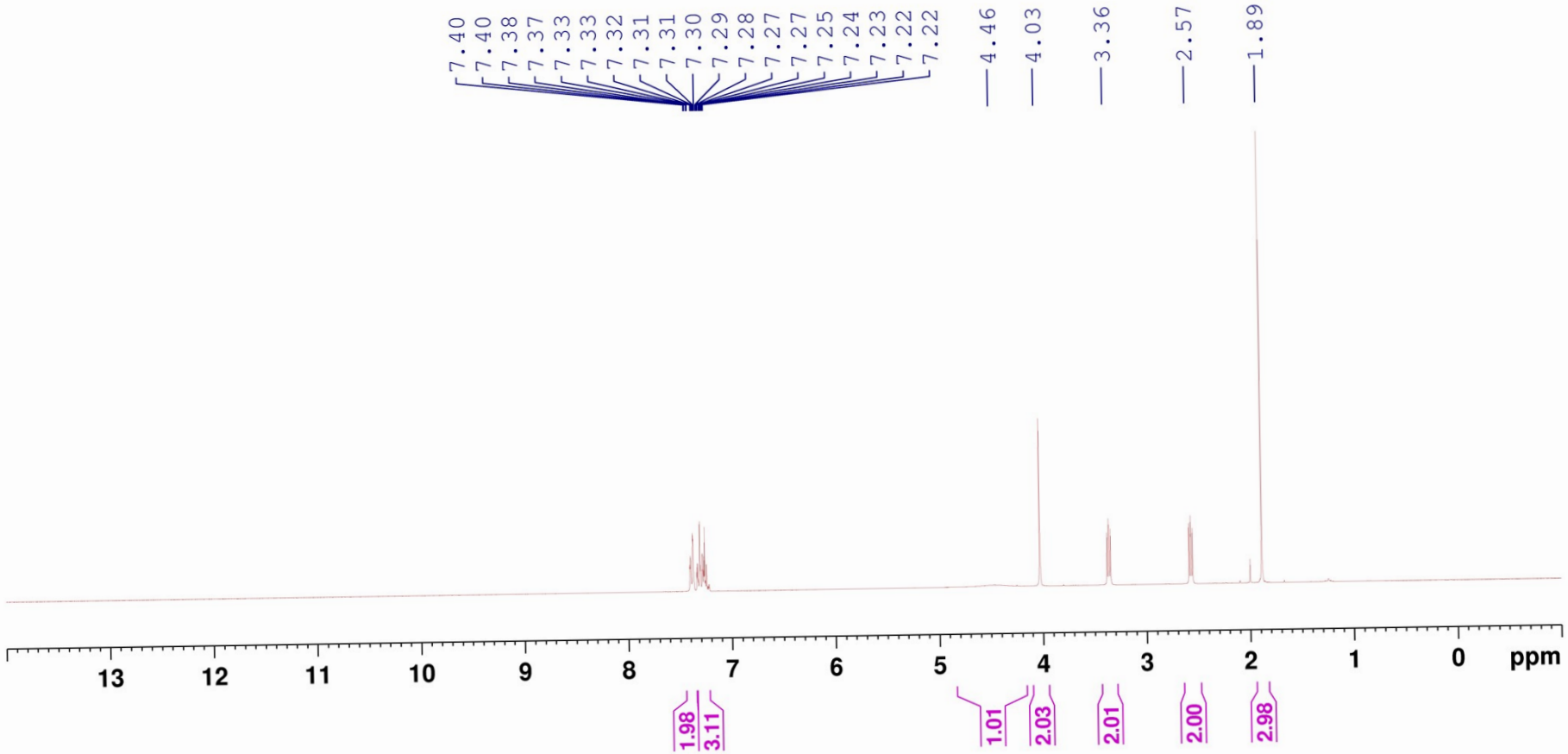

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 190.1341 | 190.1344 | -0.3 | -1.6 | 5.5 | 2087.4 | n/a | n/a | C11 H16 N3 |

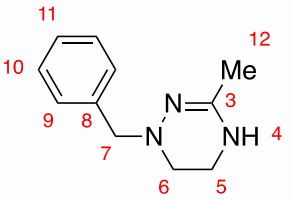



$C_{11}H_{15}N_3$

MW: 189,3 g.mol$^{-1}$

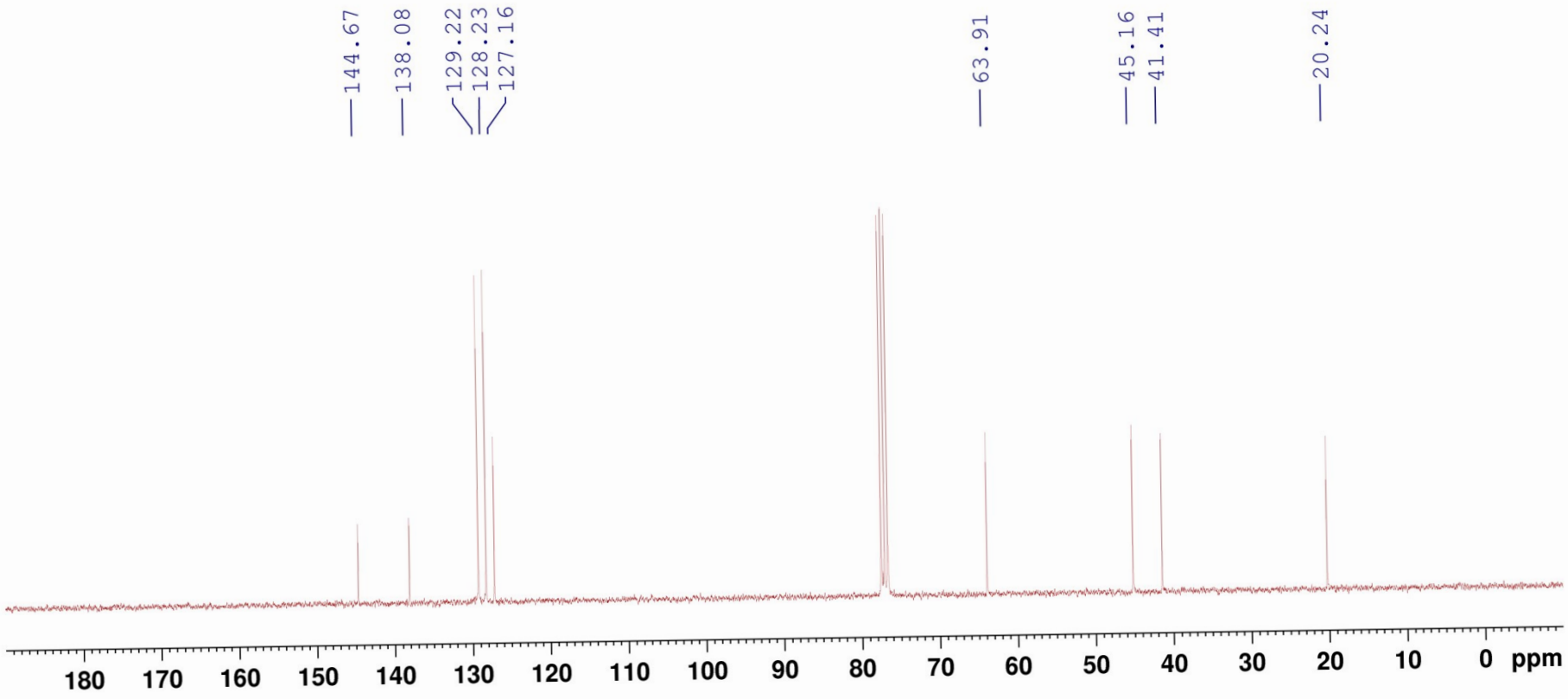
**13aa**

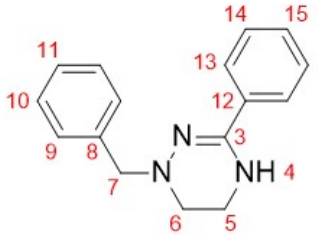





$C_{11}H_{15}N_3$
MW: 189,3 g.mol$^{-1}$

**13aa**






$C_{16}H_{17}N_3$

MW: 251,14 g.mol$^{-1}$

**14aa**



## Elemental Composition Report

### Single Mass Analysis

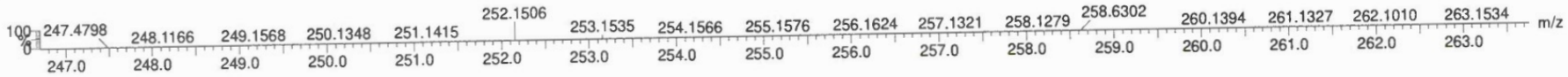
Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
1108 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-4 O: 0-10 S: 0-2 Na: 0-1

MB-204F1 (DCM) - MeOH/H2O (95/5%)
20230411_XX_MB204F1_01 65 (0.677) Cm (62:65)

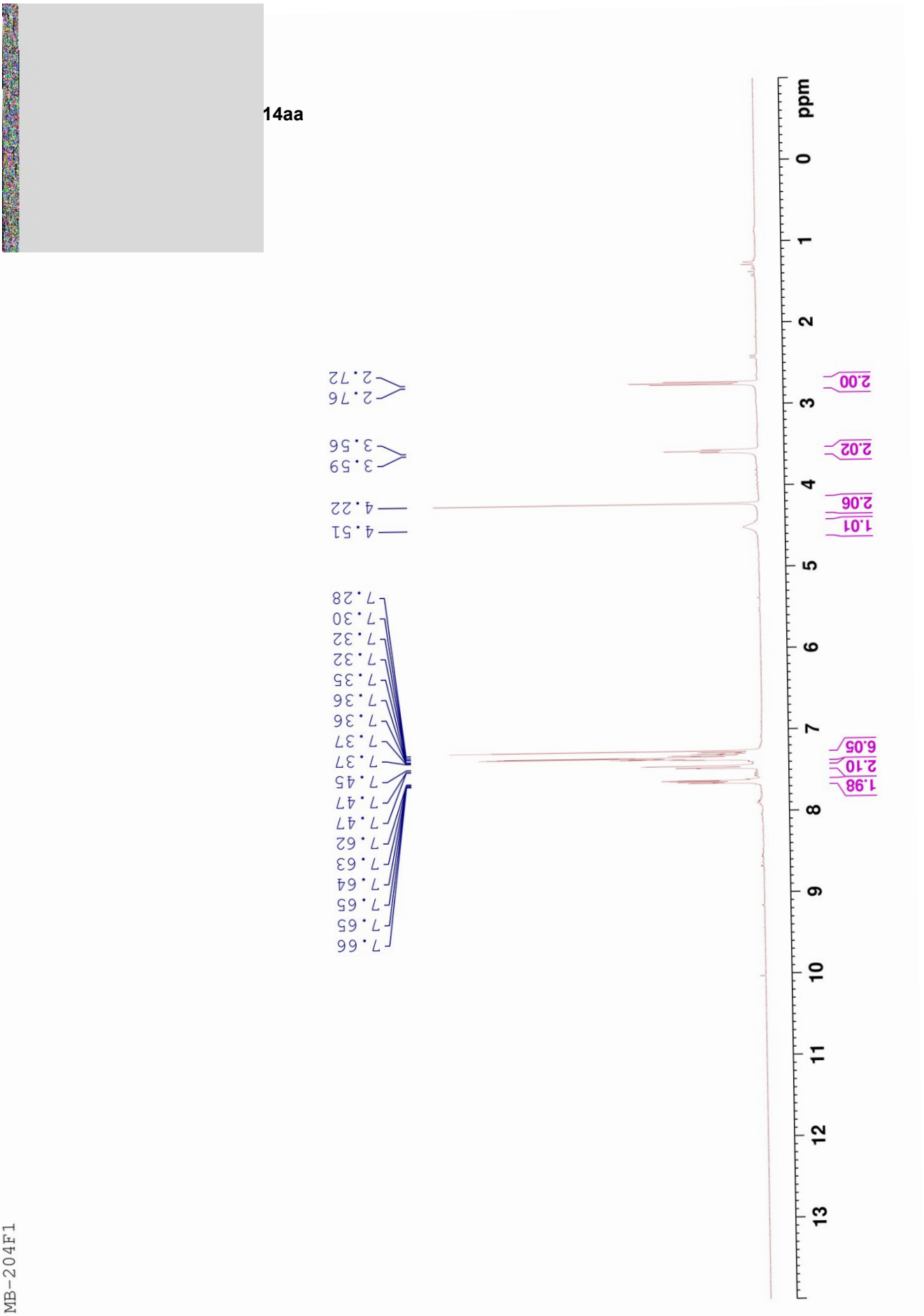
XEVO G2-XS QTOF

11-Apr-2023
1: TOF MS ES+
4.55e+006

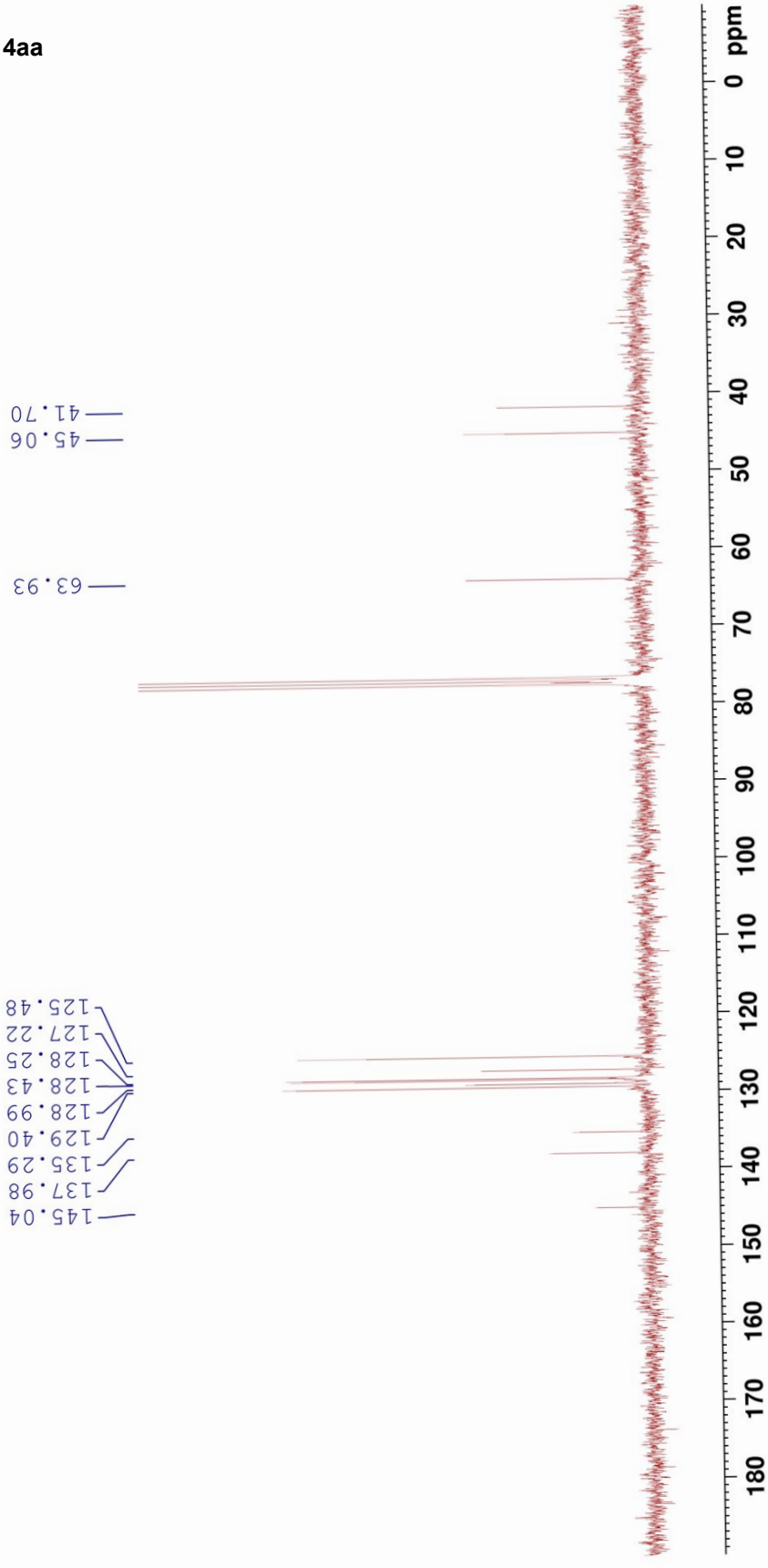


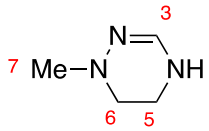

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 252.1506 | 252.1501 | 0.5 | 2.0 | 9.5 | 1609.4 | 0.000 | 100.00 | C16 H18 N3 |
| | 252.1510 | -0.4 | -1.6 | 1.5 | 1630.8 | 21.365 | 0.00 | C11 H23 N3 S Na |
| | 252.1515 | -0.9 | -3.6 | -9.5 | 1633.9 | 24.444 | 0.00 | C4 H30 N O6 S2 |

14aa


MB-204F1
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
2.00
2.02
2.06
1.01
6.05
2.10
1.98
7.66
7.65
7.65
7.64
7.63
7.62
7.47
7.47
7.45
7.37
7.37
7.36
7.36
7.35
7.32
7.32
7.30
7.28
4.51
4.22
3.59
3.56
2.76
2.72

**14aa**


41.70
45.06
63.93
125.48
127.22
128.25
128.43
128.99
129.40
135.29
137.98
145.04
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180




$C_4H_9N_3$

MW: 99,1 g.mol$^{-1}$

**12ab**

**Elemental Composition Report** **Page 1**

**Single Mass Analysis**

Tolerance = 20.0 PPM / DBE: min = -10.0, max = 1000.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

20 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-100 H: 0-200 N: 0-5

MB-232F1 (Solide)

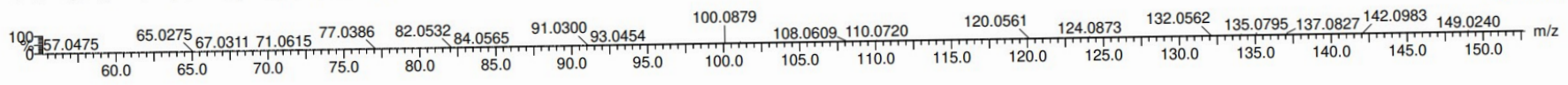
20230215_XX_MB232F1_02 175 (1.769) Cm (165:182)

XEVO G2-XS QTOF

15-Feb-2023

1: TOF MS ASAP+

1.39e+007



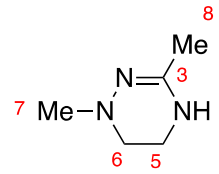

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 20.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 100.0879 | 100.0875 | 0.4 | 4.0 | 1.5 | 2513.4 | n/a | n/a | C4 H10 N3 |

$C_4H_9N_3$
MW: 99,1 g.mol$^{-1}$

**12ab**

$C_4H_9N_3$
MW: 99,1 g.mol$^{-1}$

**12ab**




$C_5H_{11}N_3$
MW: 113,2 g.mol$^{-1}$

**13ab**



**Elemental Composition Report** **Page 1**

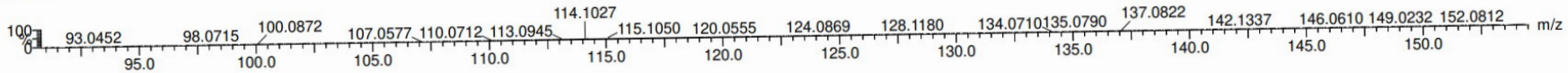
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
90 formula(e) evaluated with 1 results within limits (up to 5 best isotopic matches for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-6 O: 0-5

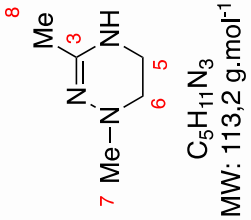
MB-243F1 (Solide)
20230227_XX_MB243F1_02 5 (0.071) Cm (5:7)

XEVO G2-XS QTOF

27-Feb-2023
1: TOF MS ASAP+
9.97e+006

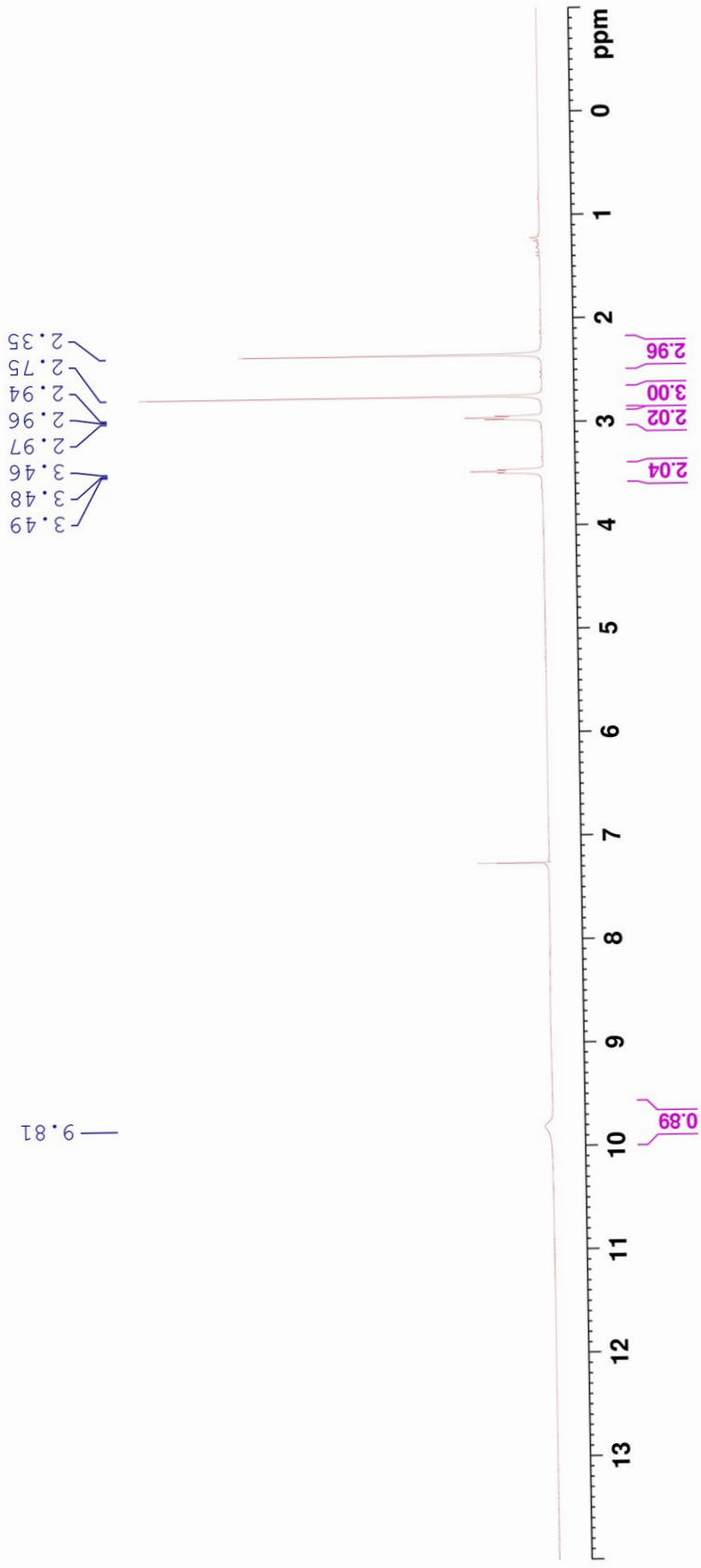


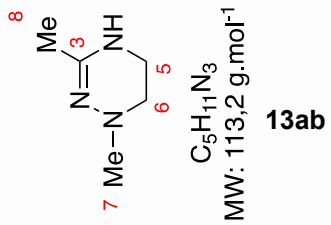

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 114.1027 | 114.1031 | -0.4 | -3.5 | 1.5 | 2429.5 | n/a | n/a | C5 H12 N3 |




$C_5H_{11}N_3$
MW: 113,2 g.mol$^{-1}$

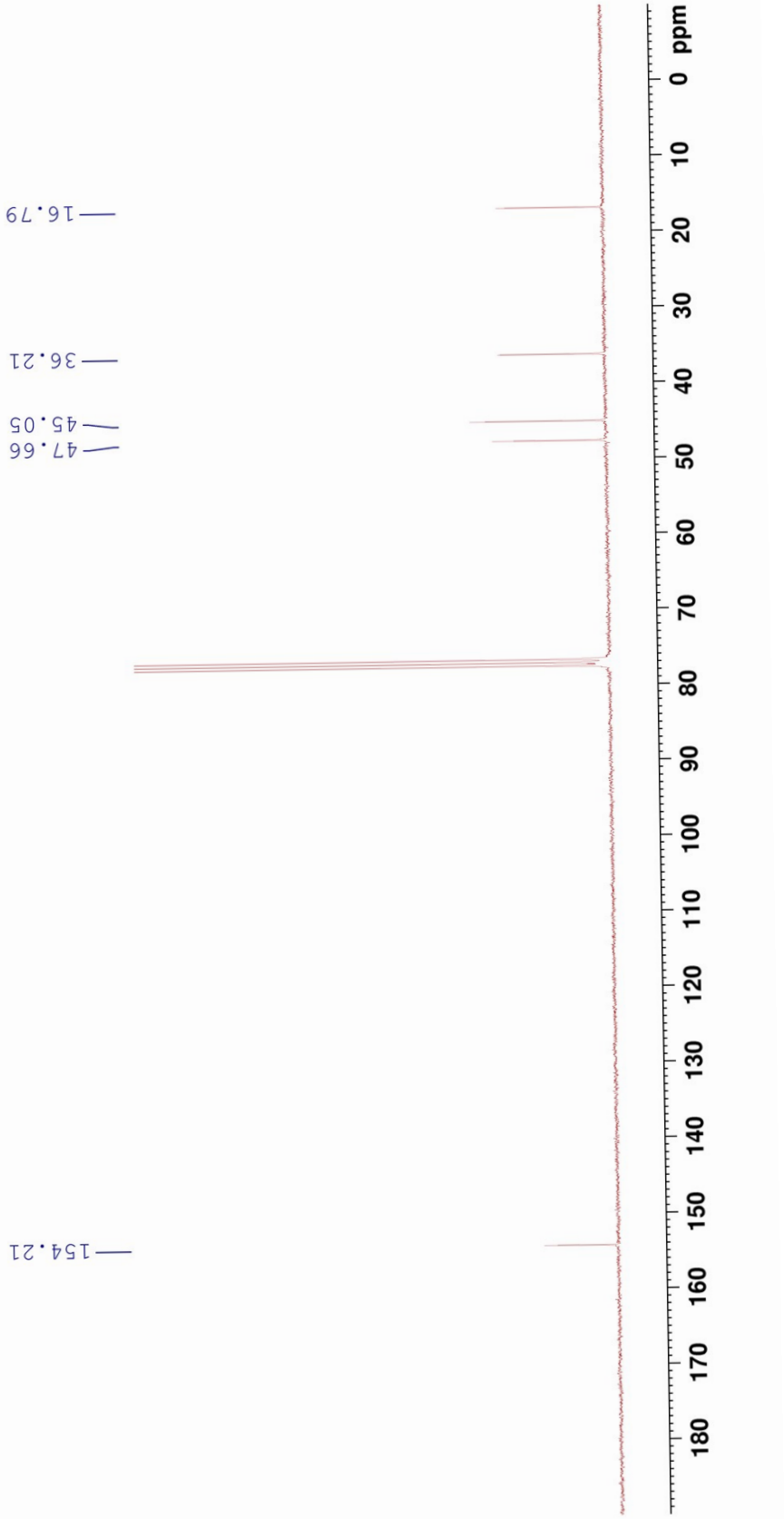
**13ab**

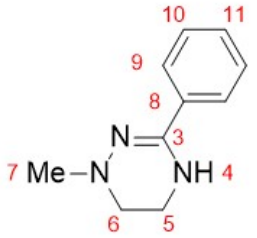





$C_5H_{11}N_3$
MW: 113,2 g.mol$^{-1}$

**13ab**






$C_{11}H_{14}N_2$

MW: 175,2 g.mol$^{-1}$

**14ab**



**Elemental Composition Report**



**Single Mass Analysis**

Tolerance = 5.0 PPM / DBE: min = -10.0, max = 1000.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

148 formula(e) evaluated with 1 results within limits (up to 5 best isotopic matches for each mass)

Elements Used:

C: 0-100 H: 0-200 N: 0-6 O: 0-5

MB-244F1 (Solide)

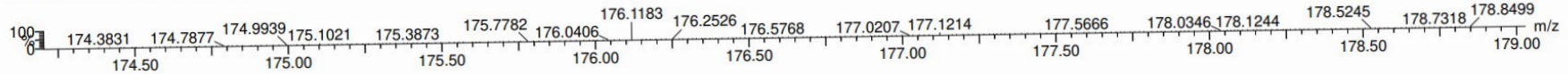
20230227_XX_MB244F1_01 54 (0.560) Cm (48:54)

XEVO G2-XS QTOF

27-Feb-2023

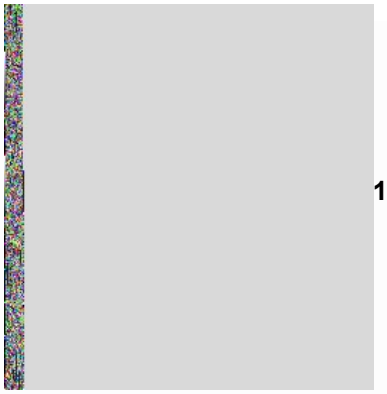
1: TOF MS ASAP+

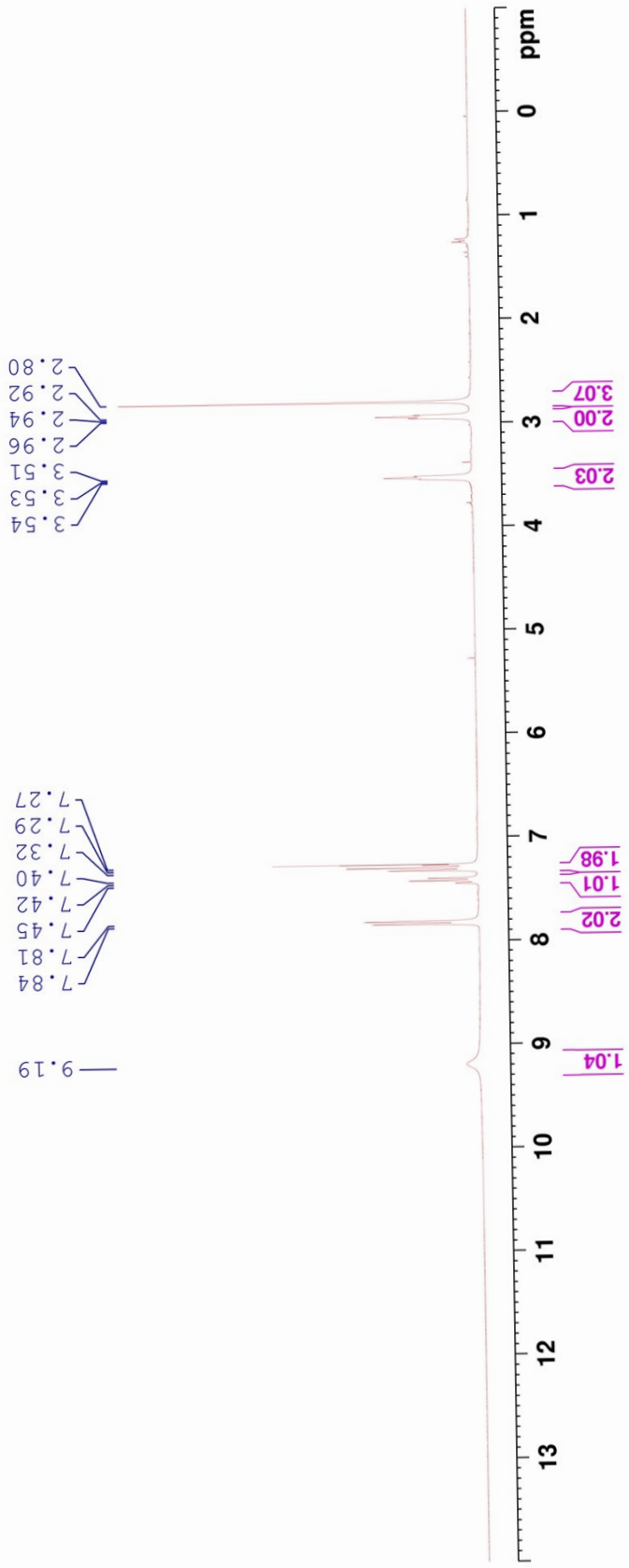
7.99e+006

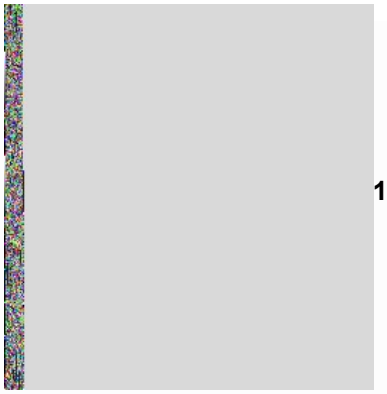



| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -10.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 176.1183 | 176.1188 | -0.5 | -2.8 | 5.5 | 1921.2 | n/a | n/a | C10 H14 N3 |

**14ab**

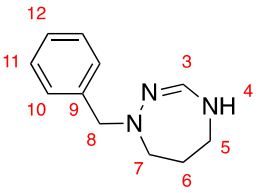



ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
3.07
2.00
2.03
1.98
1.01
2.02
1.04
2.80
2.92
2.94
2.96
3.51
3.53
3.54
7.27
7.29
7.32
7.40
7.42
7.45
7.81
7.84
9.19



**14ab**


153.01
132.31
128.76
127.95
127.50
47.87
45.53
36.56
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180




$C_{11}H_{15}N_3$
MW: 189,3 g.mol$^{-1}$

**12ia**



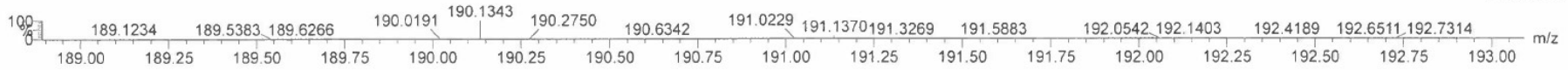
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
136 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-106 H: 0-110 N: 0-6 O: 0-12

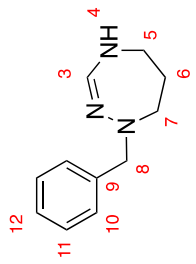
JOL-243-4 (DCM) - MeOH (100%)
20191113_JOL-243-4_01 35 (0.205) Cm (21:51)

XEVO G2-XS QTOF

13-Nov-2019
1: TOF MS ES+
2.62e+006

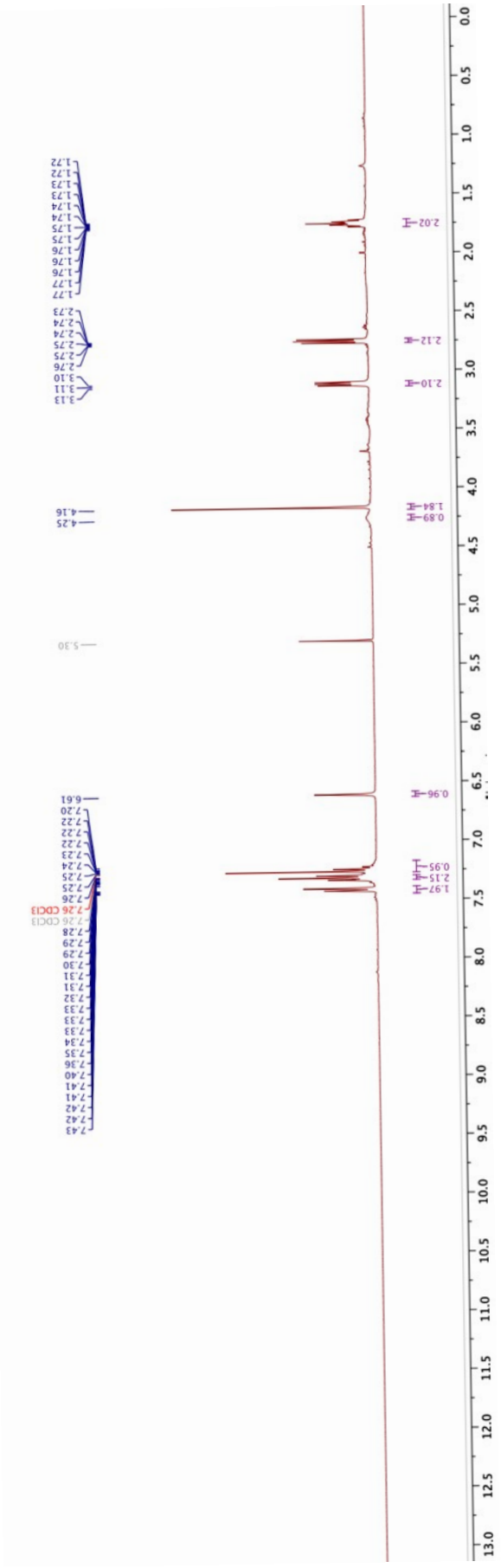


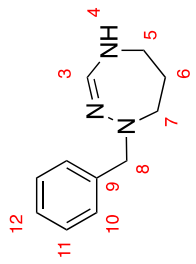

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 190.1343 | 190.1344 | -0.1 | -0.5 | 5.5 | 2086.6 | n/a | n/a | C11 H16 N3 |




$C_{11}H_{15}N_3$
MW: 189,3 g.mol$^{-1}$

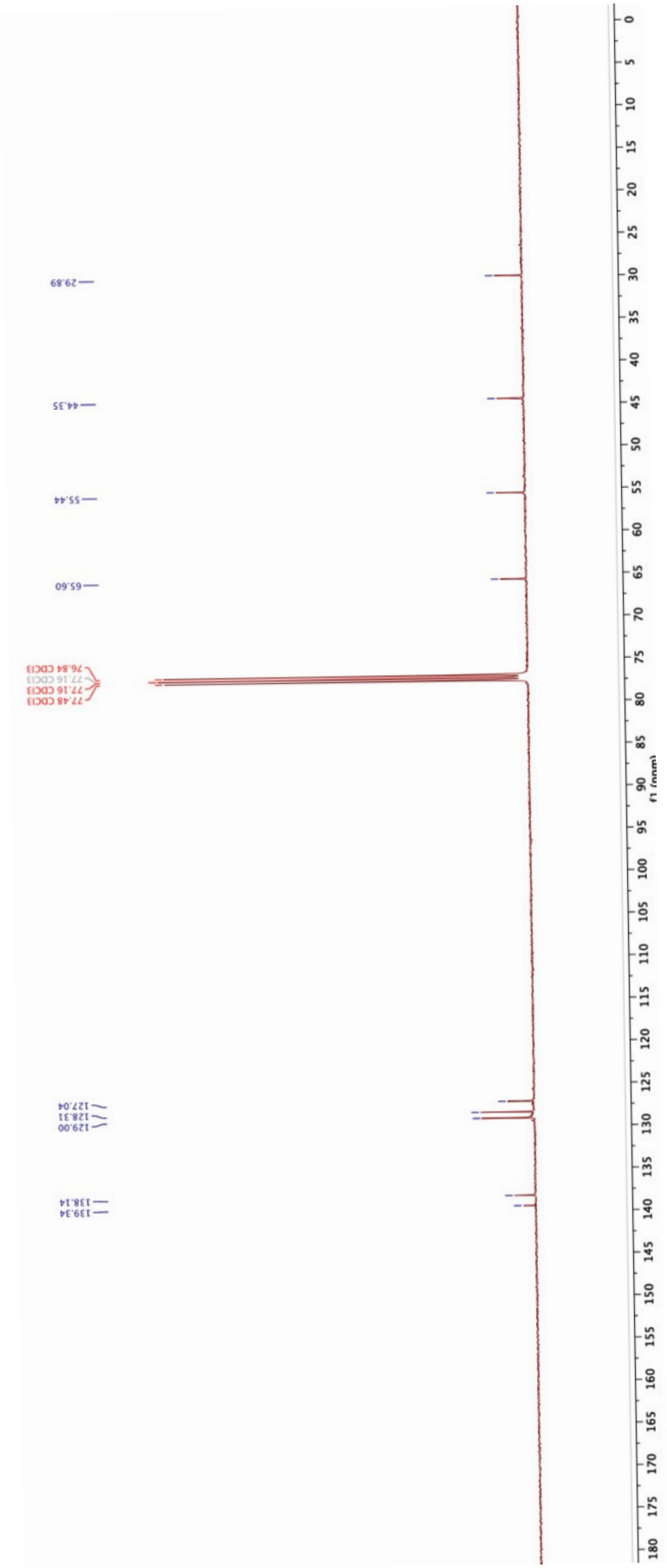
**12ia**

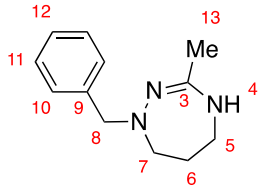





$C_{11}H_{15}N_3$
MW: 189,3 g.mol$^{-1}$

**12ia**






$C_{12}H_{17}N_3$
MW: 203,3 g.mol$^{-1}$

**13ia**

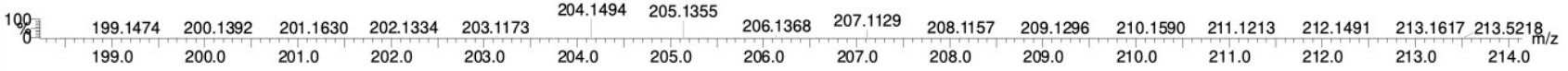
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
155 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-6 O: 0-12

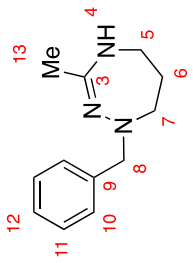
JOL-425-3 (solide)
20200729_XX_JOL4253_01 137 (1.397) Cm (134:149)

XEVO G2-XS QTOF

29-Jul-2020
1: TOF MS ASAP+
1.73e+007

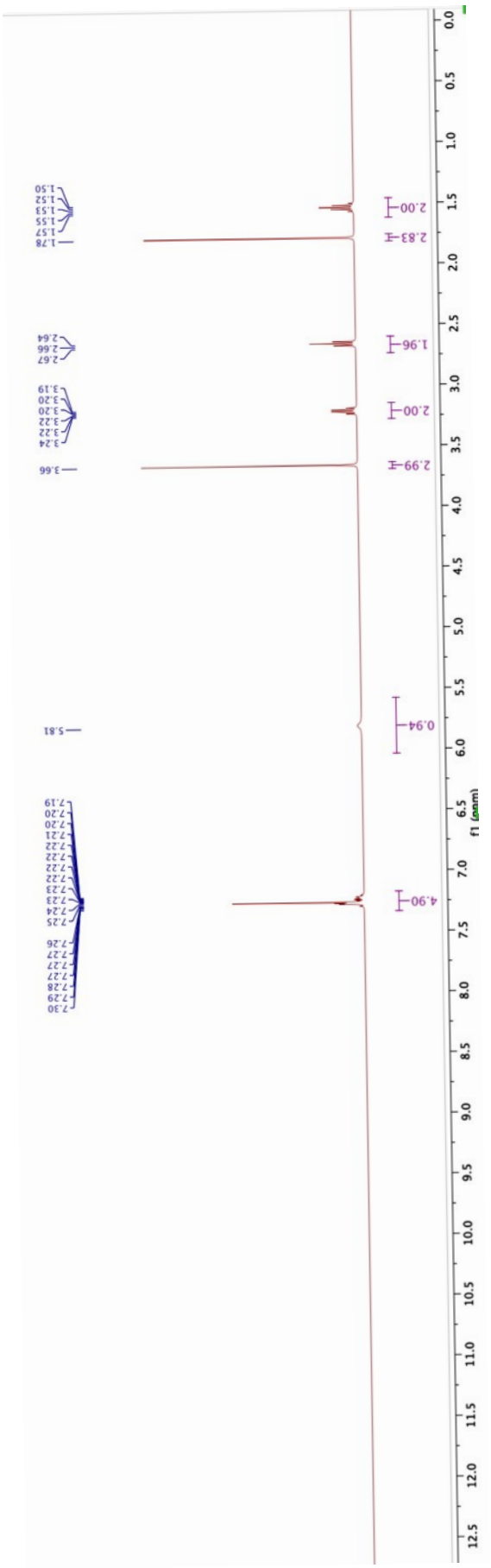


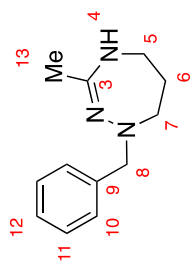

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 204.1494 | 204.1501 | -0.7 | -3.4 | 5.5 | 3407.6 | n/a | n/a | C12 H18 N3 |




$C_{12}H_{17}N_3$
MW: 203,3 g.mol$^{-1}$

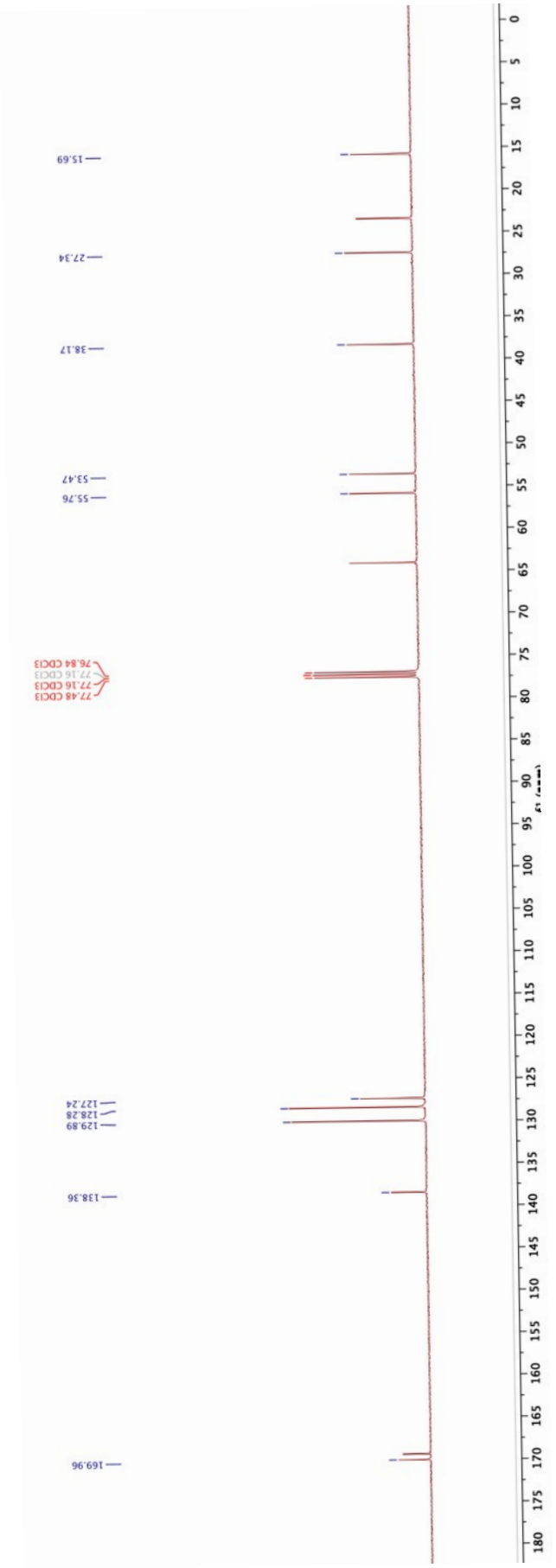
**13ia**

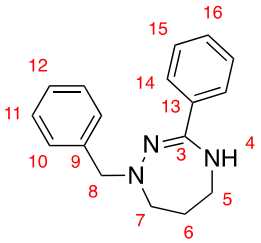





$C_{12}H_{17}N_3$
MW: 203,3 g.mol$^{-1}$

**13ia**






$C_{17}H_{19}N_3$
MW: 265,4 g.mol$^{-1}$

**14ia**

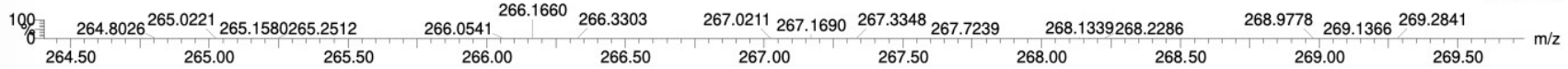
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.0, max = 1000.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
236 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-100 H: 0-200 N: 0-6 O: 0-12

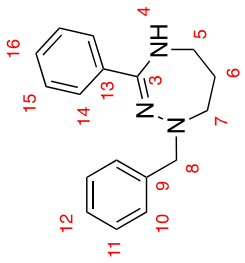
JOL-424-T10 (solide)
20200729_XX_JOL424T10_01 57 (0.597) Cm (53:62)

XEVO G2-XS QTOF

29-Jul-2020
1: TOF MS ASAP+
1.57e+007

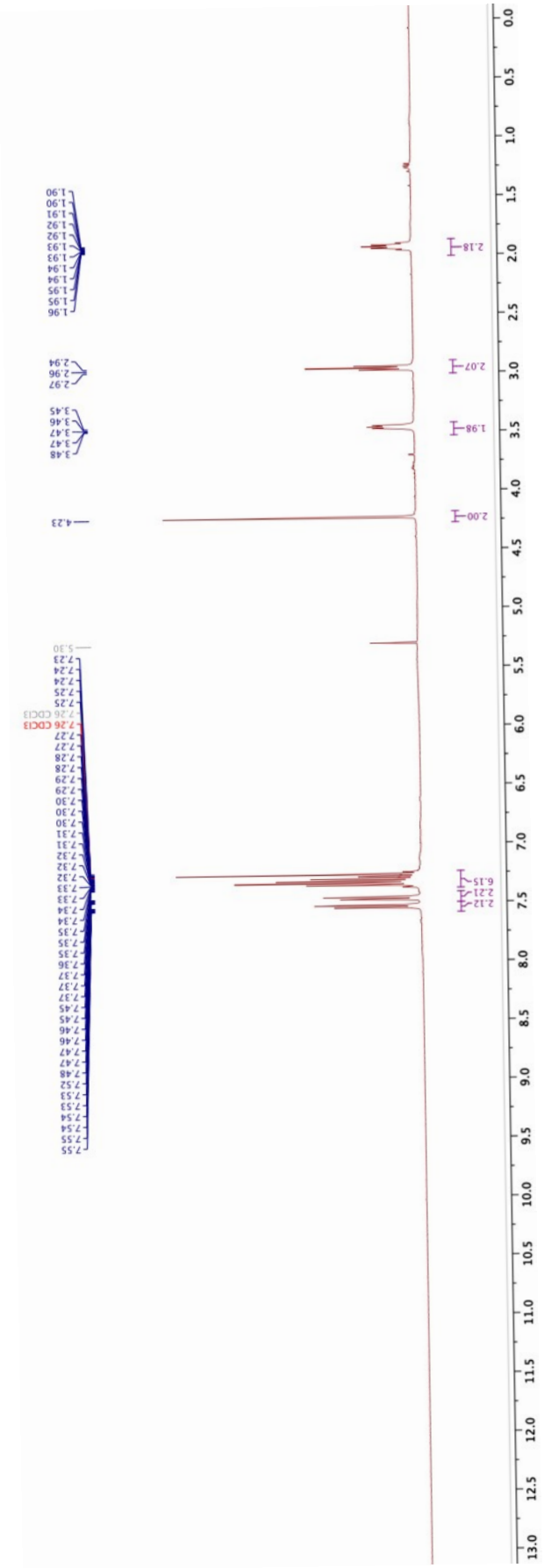


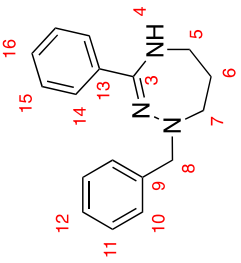

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Minimum: | | | | -1.0 | | | | |
| Maximum: | | 30.0 | 5.0 | 1000.0 | | | | |
| Mass | Calc. Mass | mDa | PPM | DBE | i-FIT | Norm | Conf(%) | Formula |
| 266.1660 | 266.1657 | 0.3 | 1.1 | 9.5 | 2603.6 | n/a | n/a | C17 H20 N3 |




$C_{17}H_{19}N_3$
MW: 265,4 g.mol$^{-1}$

**14ia**






$C_{17}H_{19}N_3$
MW: 265,4 g.mol$^{-1}$

**14ia**