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Identification and characterization of an imidazolium by-product formed during the synthesis of 4-methylmethcathinone (mephedrone)

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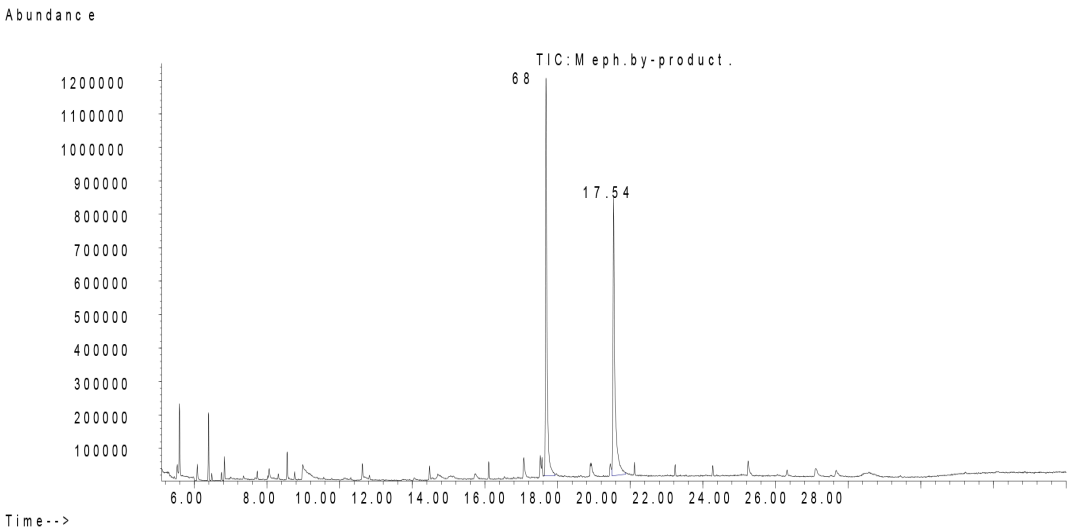
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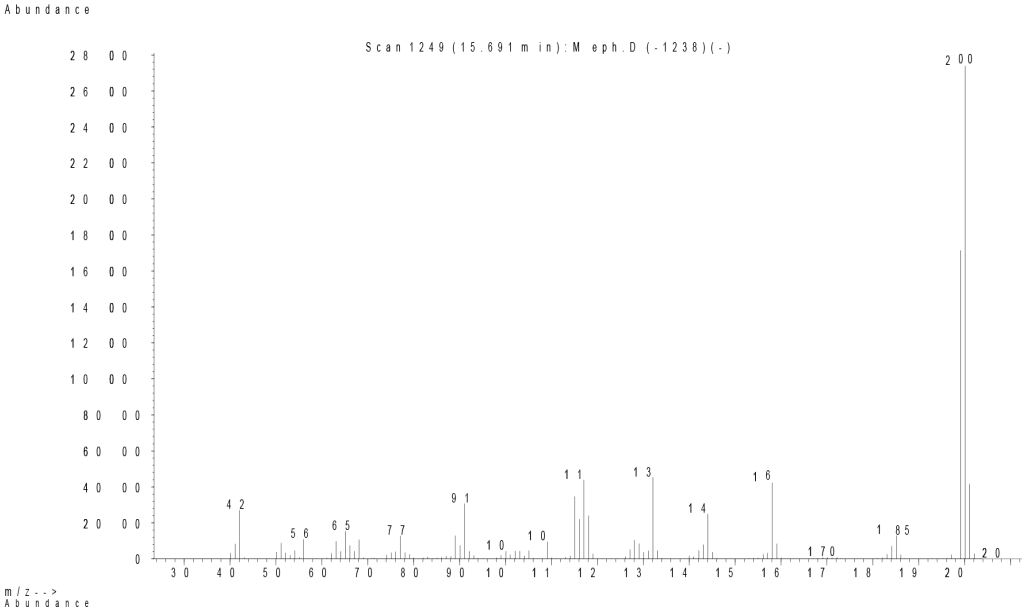
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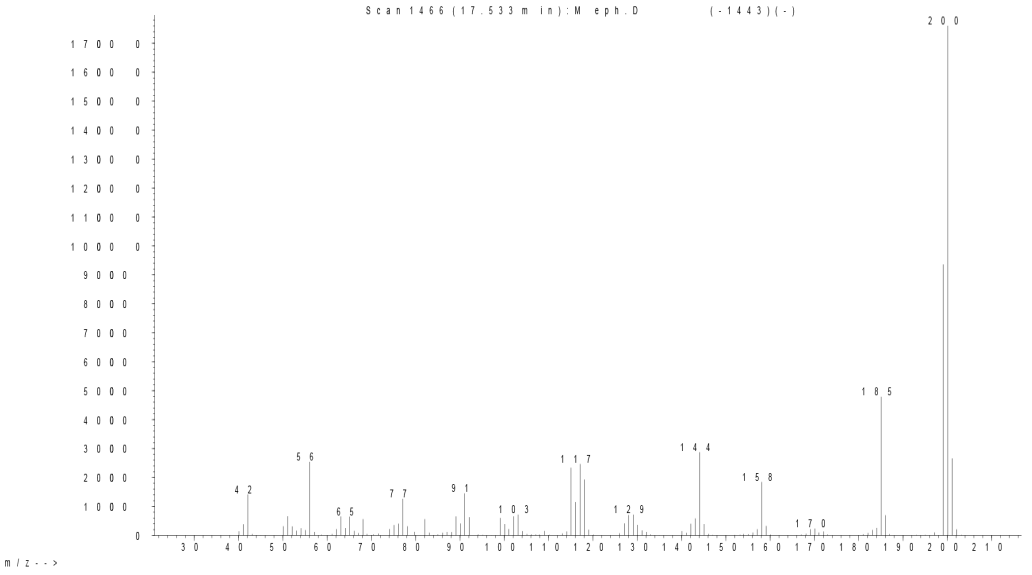
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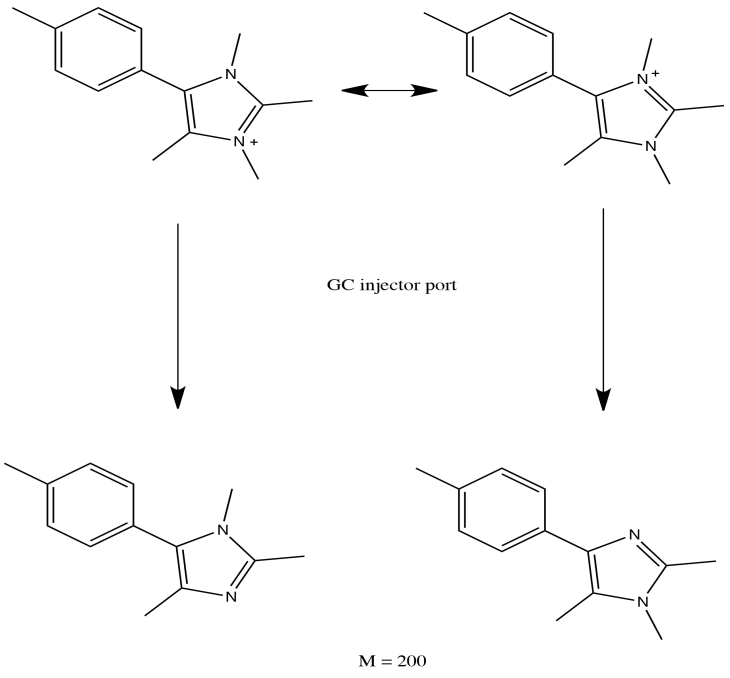
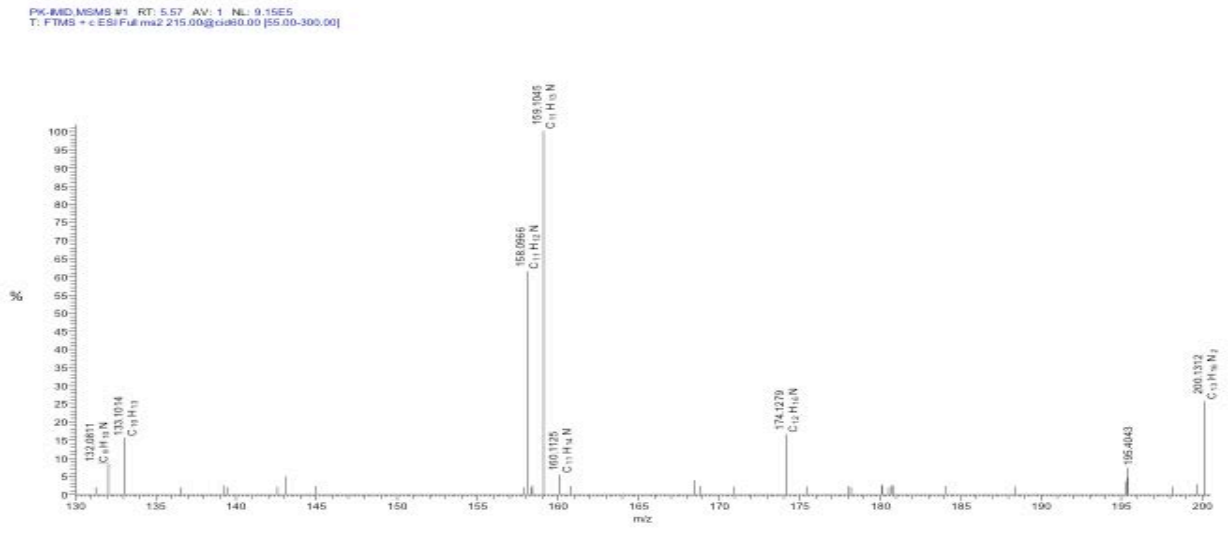


Supplemental 1: (a). GC-MS of imidazolium by-product, (b). structures for TMMPI degradation products (in GC injector port).



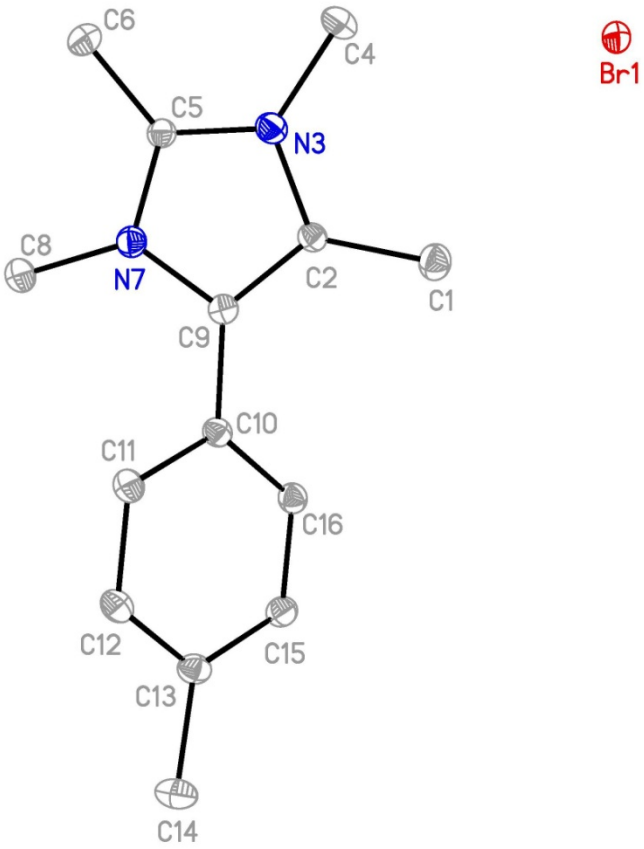
Supplemental 2: In-source CID product ion spectrum TMMPI.

Small Molecule X-ray Facility
School Of Chemistry

Structure Report

Filename: TCD102

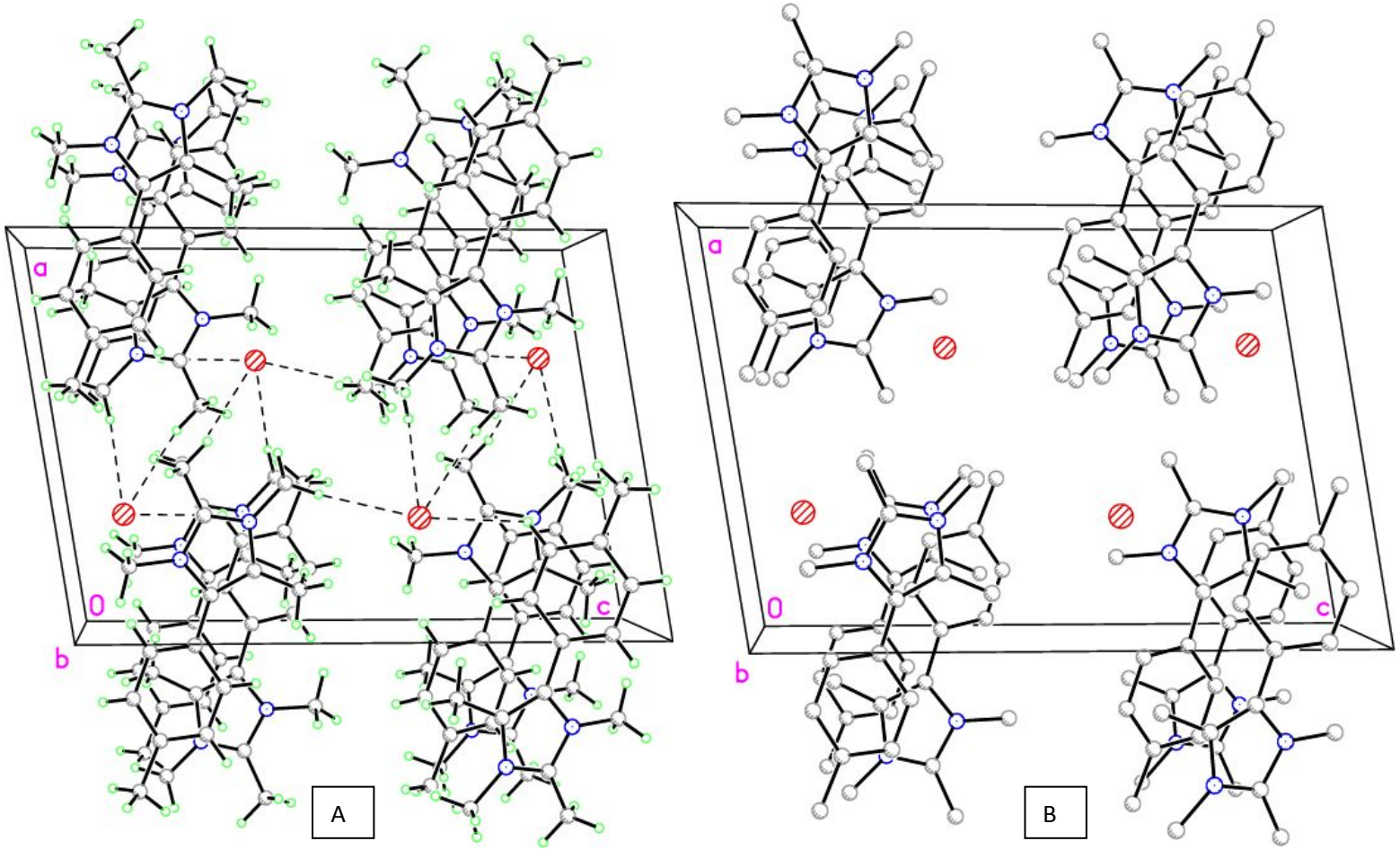
Reference: PKJDPIMID2



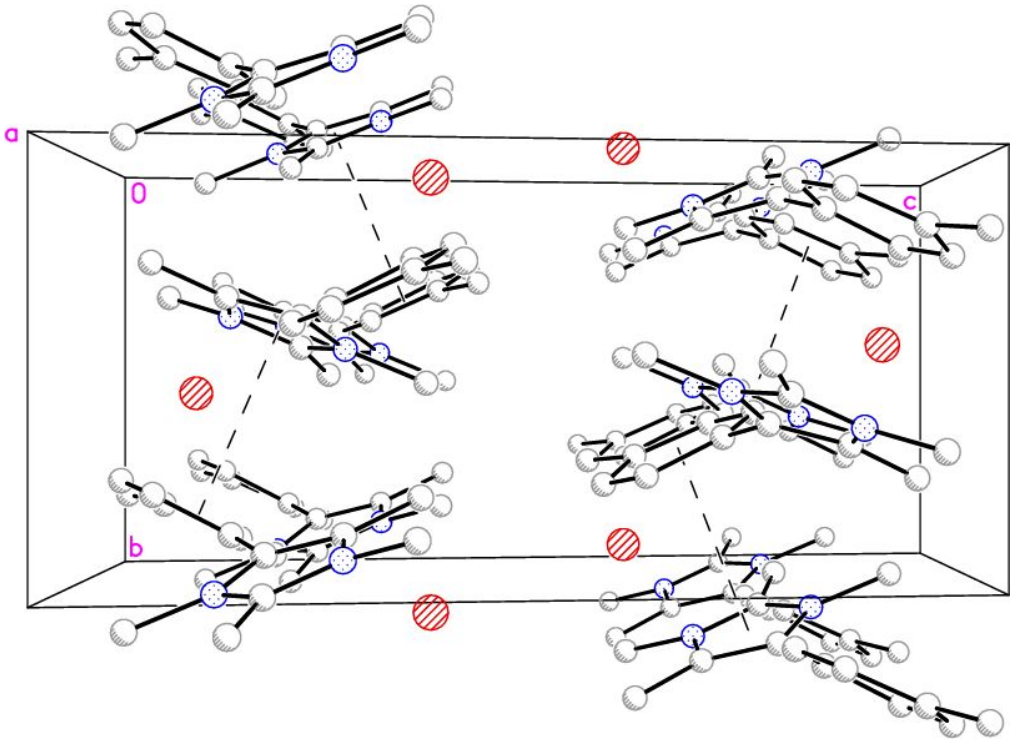
Asymmetric unit of TCD102. Displacement ellipsoids shown at 50%. Hydrogen atoms omitted for clarity.

8/8/14

Brendan Twamley



Packing Diagram of mephedrone by-product viewed down the b-axis. (A) hydrogen atoms shown with dashed lines indicating weak CH…Br interactions.(B) Hydrogen atoms removed for clarity to show the alternating head-to-tail packing assembly of the organic moiety.



Packing diagram of the mephedrone by-product viewed down the a–axis. Dashed lines indicate centroid to centroid distances between the overlapping phenyl and imidazolium ring.

Crystal Structure Report for TCD102

A specimen of $C_{14}H_{19}BrN_2$, approximate dimensions 0.060 mm x 0.090 mm x 0.220 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured at 100(2)K using an Oxford Cryosystems Cobra low temperature device using a MiTeGen micromount. See Table 1 for collection parameters and exposure time. Bruker APEX software was used to correct for Lorentz and polarization effects.

A total of 2942 frames were collected. The total exposure time was 12.26 hours. The integration of the data using a monoclinic unit cell yielded a total of 86862 reflections to a maximum θ angle of 32.68° (0.66 Å resolution), of which 4895 were independent (average redundancy 17.745, completeness = 99.9%, R_{int} = 2.63%) and 4337 (88.60%) were greater than $2\sigma(F^2)$. The final cell constants of a = 11.2256(3) Å, b = 7.4874(2) Å, c = 16.0597(5) Å, β = 99.3230(10)°, volume = 1332.00(7) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). Data were corrected for absorption effects using the multi-scan method (SADABS). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6251 and 0.7464.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_1/c$, with Z = 4 for the formula unit, $C_{14}H_{19}BrN_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 159 variables converged at R1 = 2.05%, for the observed data and wR2 = 5.37% for all data. The goodness-of-fit was 1.045. The largest peak in the final difference electron density synthesis was 0.602 $e^-/Å^3$ and the largest hole was -0.314 $e^-/Å^3$ with an RMS deviation of 0.061 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.472 g/cm^3 and F(000), 608 e^-.

References:

Bruker APEX v2012.12-0, Bruker AXS Inc., Madison, Wisconsin, USA.

SADABS (2012) Bruker AXS Inc., Madison, Wisconsin, USA; Sheldrick, G. M. University of Göttingen, Germany.

SHELXTL-2014, Bruker AXS Inc., Madison Wisconsin, USA and Sheldrick, G. M. (2014). University of Göttingen, Germany.

Acknowledgement:

Facility funded by PRTLI and ERDF.

Table 1: Data collection details for TCD102.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	45.000	32.59	24.12	135.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	33.70	280.01	93.43	51.05	1.00	124	15.00	0.71073	50	30.0	100.00
Omega	45.000	31.41	22.93	225.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	33.70	277.54	199.66	55.12	1.00	126	15.00	0.71073	50	30.0	100.00
Phi	45.000	32.59	22.93	0.00	-57.06	1.00	360	15.00	0.71073	50	30.0	100.00
Omega	45.000	33.70	323.18	63.40	76.51	1.00	75	15.00	0.71073	50	30.0	100.00
Omega	45.000	16.41	6.93	360.00	-54.74	1.00	125	15.00	0.71073	50	30.0	100.00
Phi	45.000	32.59	292.50	360.00	23.00	1.00	360	15.00	0.71073	50	30.0	100.00
Omega	45.000	31.41	22.93	180.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	31.41	22.93	0.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	1.41	351.93	0.00	-54.74	1.00	125	15.00	0.71073	50	30.0	100.00
Omega	45.000	1.41	351.93	90.00	-54.74	1.00	125	15.00	0.71073	50	30.0	100.00
Omega	45.000	1.41	351.93	270.00	-54.74	1.00	125	15.00	0.71073	50	30.0	100.00
Omega	45.000	31.41	22.93	90.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	32.59	24.12	90.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	32.59	24.12	180.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Phi	45.000	32.59	10.16	243.50	-23.00	1.00	209	15.00	0.71073	50	30.0	100.00
Omega	45.000	31.41	22.93	45.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	31.41	22.93	135.00	-54.74	1.00	123	15.00	0.71073	50	30.0	100.00
Omega	45.000	33.70	321.00	312.61	69.08	1.00	81	15.00	0.71073	50	30.0	100.00

Table 2. Crystal data and structure refinement for tcd102.

Identification code	tcd102	
Empirical formula	$C_{14}H_{19}BrN_2$	
Formula weight	295.22	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 11.2256(3) Å	α= 90°.
	b = 7.4874(2) Å	β= 99.3230(10)°.
	c = 16.0597(5) Å	γ = 90°.
Volume	1332.00(7) $Å^3$	
Z	4	
Density (calculated)	1.472 Mg/m^3	
Absorption coefficient	3.067 mm^{-1}	
F(000)	608	
Crystal size	0.220 x 0.090 x 0.060 mm^3	
Theta range for data collection	1.838 to 32.682°.	
Index ranges	$-17\leq h\leq 17$, $-11\leq k\leq 11$, $-24\leq l\leq 24$	
Reflections collected	86862	
Independent reflections	4895 [R(int) = 0.0263]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7464 and 0.6251	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4895 / 0 / 159	
Goodness-of-fit on F^2	1.045	
Final R indices [I>2sigma(I)]	R1 = 0.0205, wR2 = 0.0517	
R indices (all data)	R1 = 0.0261, wR2 = 0.0537	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.602 and -0.314 $e.Å^{-3}$	

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for tcd102. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	3012(1)	5584(1)	11094(1)	16(1)
C(1)	1194(1)	7329(2)	8909(1)	17(1)
C(2)	1697(1)	6592(1)	8181(1)	12(1)
N(3)	2907(1)	6201(1)	8227(1)	15(1)
C(4)	3839(1)	6655(2)	8947(1)	18(1)
C(5)	3089(1)	5502(1)	7489(1)	12(1)
C(6)	4233(1)	4880(2)	7249(1)	20(1)
N(7)	2022(1)	5453(1)	6969(1)	14(1)
C(8)	1896(1)	4696(2)	6115(1)	17(1)
C(9)	1133(1)	6156(1)	7384(1)	13(1)
C(10)	-117(1)	6478(1)	6975(1)	12(1)
C(11)	-327(1)	7331(1)	6186(1)	14(1)
C(12)	-1500(1)	7573(1)	5764(1)	15(1)
C(13)	-2494(1)	6986(1)	6115(1)	15(1)
C(14)	-3753(1)	7136(2)	5624(1)	20(1)
C(15)	-2278(1)	6225(2)	6921(1)	15(1)
C(16)	-1109(1)	5961(1)	7345(1)	14(1)

Table 4. Bond lengths [Å] and angles [°] for tcd102.

C(1)-C(2)	1.4846(14)		
C(1)-H(1A)	0.9800	C(2)-C(1)-H(1A)	109.5
C(1)-H(1B)	0.9800	C(2)-C(1)-H(1B)	109.5
C(1)-H(1C)	0.9800	H(1A)-C(1)-H(1B)	109.5
C(2)-C(9)	1.3726(14)	C(2)-C(1)-H(1C)	109.5
C(2)-N(3)	1.3796(13)	H(1A)-C(1)-H(1C)	109.5
N(3)-C(5)	1.3401(13)	H(1B)-C(1)-H(1C)	109.5
N(3)-C(4)	1.4695(14)	C(9)-C(2)-N(3)	107.47(9)
C(4)-H(4A)	0.9800	C(9)-C(2)-C(1)	130.25(9)
C(4)-H(4B)	0.9800	N(3)-C(2)-C(1)	122.27(9)
C(4)-H(4C)	0.9800	C(5)-N(3)-C(2)	109.02(9)
C(5)-N(7)	1.3453(13)	C(5)-N(3)-C(4)	126.52(9)
C(5)-C(6)	1.4753(15)	C(2)-N(3)-C(4)	124.21(9)
C(6)-H(6A)	0.9800	N(3)-C(4)-H(4A)	109.5
C(6)-H(6B)	0.9800	N(3)-C(4)-H(4B)	109.5
C(6)-H(6C)	0.9800	H(4A)-C(4)-H(4B)	109.5
N(7)-C(9)	1.3898(13)	N(3)-C(4)-H(4C)	109.5
N(7)-C(8)	1.4698(14)	H(4A)-C(4)-H(4C)	109.5
C(8)-H(8A)	0.9800	H(4B)-C(4)-H(4C)	109.5
C(8)-H(8B)	0.9800	N(3)-C(5)-N(7)	108.14(9)
C(8)-H(8C)	0.9800	N(3)-C(5)-C(6)	128.22(10)
C(9)-C(10)	1.4696(14)	N(7)-C(5)-C(6)	123.64(9)
C(10)-C(16)	1.3997(14)	C(5)-C(6)-H(6A)	109.5
C(10)-C(11)	1.4035(14)	C(5)-C(6)-H(6B)	109.5
C(11)-C(12)	1.3918(14)	H(6A)-C(6)-H(6B)	109.5
C(11)-H(11A)	0.9500	C(5)-C(6)-H(6C)	109.5
C(12)-C(13)	1.4002(15)	H(6A)-C(6)-H(6C)	109.5
C(12)-H(12A)	0.9500	H(6B)-C(6)-H(6C)	109.5
C(13)-C(15)	1.3989(15)	C(5)-N(7)-C(9)	109.15(9)
C(13)-C(14)	1.5070(15)	C(5)-N(7)-C(8)	122.11(9)
C(14)-H(14A)	0.9800	C(9)-N(7)-C(8)	128.71(9)
C(14)-H(14B)	0.9800	N(7)-C(8)-H(8A)	109.5
C(14)-H(14C)	0.9800	N(7)-C(8)-H(8B)	109.5
C(15)-C(16)	1.3917(15)	H(8A)-C(8)-H(8B)	109.5
C(15)-H(15A)	0.9500	N(7)-C(8)-H(8C)	109.5
C(16)-H(16A)	0.9500	H(8A)-C(8)-H(8C)	109.5

H(8B)-C(8)-H(8C)	109.5	C(15)-C(13)-C(14)	121.41(10)
C(2)-C(9)-N(7)	106.19(9)	C(12)-C(13)-C(14)	120.49(9)
C(2)-C(9)-C(10)	129.82(9)	C(13)-C(14)-H(14A)	109.5
N(7)-C(9)-C(10)	123.76(9)	C(13)-C(14)-H(14B)	109.5
C(16)-C(10)-C(11)	118.71(9)	H(14A)-C(14)-H(14B)	109.5
C(16)-C(10)-C(9)	122.19(9)	C(13)-C(14)-H(14C)	109.5
C(11)-C(10)-C(9)	119.10(9)	H(14A)-C(14)-H(14C)	109.5
C(12)-C(11)-C(10)	120.44(9)	H(14B)-C(14)-H(14C)	109.5
C(12)-C(11)-H(11A)	119.8	C(16)-C(15)-C(13)	121.27(10)
C(10)-C(11)-H(11A)	119.8	C(16)-C(15)-H(15A)	119.4
C(11)-C(12)-C(13)	121.02(10)	C(13)-C(15)-H(15A)	119.4
C(11)-C(12)-H(12A)	119.5	C(15)-C(16)-C(10)	120.31(9)
C(13)-C(12)-H(12A)	119.5	C(15)-C(16)-H(16A)	119.8
C(15)-C(13)-C(12)	118.09(9)	C(10)-C(16)-H(16A)	119.8

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for tcd102. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	16(1)	20(1)	13(1)	-1(1)	3(1)	2(1)
C(1)	20(1)	16(1)	16(1)	0(1)	4(1)	3(1)
C(2)	12(1)	11(1)	12(1)	0(1)	1(1)	1(1)
N(3)	14(1)	16(1)	13(1)	1(1)	1(1)	0(1)
C(4)	17(1)	22(1)	14(1)	-1(1)	-2(1)	-1(1)
C(5)	12(1)	13(1)	12(1)	1(1)	2(1)	0(1)
C(6)	14(1)	28(1)	18(1)	1(1)	4(1)	3(1)
N(7)	14(1)	14(1)	14(1)	-1(1)	3(1)	0(1)
C(8)	18(1)	20(1)	14(1)	-3(1)	2(1)	0(1)
C(9)	13(1)	12(1)	13(1)	1(1)	2(1)	0(1)
C(10)	13(1)	12(1)	12(1)	0(1)	1(1)	0(1)
C(11)	15(1)	13(1)	13(1)	0(1)	2(1)	-1(1)
C(12)	17(1)	13(1)	13(1)	1(1)	0(1)	0(1)
C(13)	14(1)	13(1)	16(1)	0(1)	1(1)	1(1)
C(14)	15(1)	21(1)	23(1)	4(1)	-2(1)	0(1)
C(15)	14(1)	16(1)	16(1)	1(1)	3(1)	1(1)
C(16)	15(1)	13(1)	13(1)	1(1)	2(1)	1(1)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for tcd102.

	x	y	z	U(eq)
H(1A)	1561	8495	9064	26
H(1B)	1371	6511	9389	26
H(1C)	318	7468	8754	26
H(4A)	3569	6290	9473	27
H(4B)	3980	7947	8957	27
H(4C)	4590	6030	8894	27
H(6A)	4135	3653	7036	30
H(6B)	4872	4915	7743	30
H(6C)	4453	5658	6807	30
H(8A)	1039	4620	5872	26
H(8B)	2253	3498	6143	26
H(8C)	2313	5464	5760	26
H(11A)	336	7746	5940	16
H(12A)	-1627	8144	5228	17
H(14A)	-3755	7981	5158	30
H(14B)	-4301	7563	5997	30
H(14C)	-4022	5962	5398	30
H(15A)	-2943	5883	7183	18
H(16A)	-984	5426	7889	16

Table 7. Torsion angles [°] for tcd102.

C(9)-C(2)-N(3)-C(5)	-1.43(12)	C(8)-N(7)-C(9)-C(2)	176.65(10)
C(1)-C(2)-N(3)-C(5)	177.89(10)	C(5)-N(7)-C(9)-C(10)	173.47(10)
C(9)-C(2)-N(3)-C(4)	173.15(10)	C(8)-N(7)-C(9)-C(10)	-8.46(17)
C(1)-C(2)-N(3)-C(4)	-7.53(16)	C(2)-C(9)-C(10)-C(16)	-52.77(16)
C(2)-N(3)-C(5)-N(7)	0.54(12)	N(7)-C(9)-C(10)-C(16)	133.61(11)
C(4)-N(3)-C(5)-N(7)	-173.88(10)	C(2)-C(9)-C(10)-C(11)	127.28(12)
C(2)-N(3)-C(5)-C(6)	-179.70(11)	N(7)-C(9)-C(10)-C(11)	-46.33(15)
C(4)-N(3)-C(5)-C(6)	5.88(18)	C(16)-C(10)-C(11)-C(12)	-3.25(15)
N(3)-C(5)-N(7)-C(9)	0.56(12)	C(9)-C(10)-C(11)-C(12)	176.69(10)
C(6)-C(5)-N(7)-C(9)	-179.21(10)	C(10)-C(11)-C(12)-C(13)	0.47(16)
N(3)-C(5)-N(7)-C(8)	-177.66(9)	C(11)-C(12)-C(13)-C(15)	2.94(16)
C(6)-C(5)-N(7)-C(8)	2.56(16)	C(11)-C(12)-C(13)-C(14)	-175.60(10)
N(3)-C(2)-C(9)-N(7)	1.72(11)	C(12)-C(13)-C(15)-C(16)	-3.63(16)
C(1)-C(2)-C(9)-N(7)	-177.53(10)	C(14)-C(13)-C(15)-C(16)	174.90(10)
N(3)-C(2)-C(9)-C(10)	-172.76(10)	C(13)-C(15)-C(16)-C(10)	0.88(16)
C(1)-C(2)-C(9)-C(10)	7.99(19)	C(11)-C(10)-C(16)-C(15)	2.59(15)
C(5)-N(7)-C(9)-C(2)	-1.43(12)	C(9)-C(10)-C(16)-C(15)	-177.36(10)

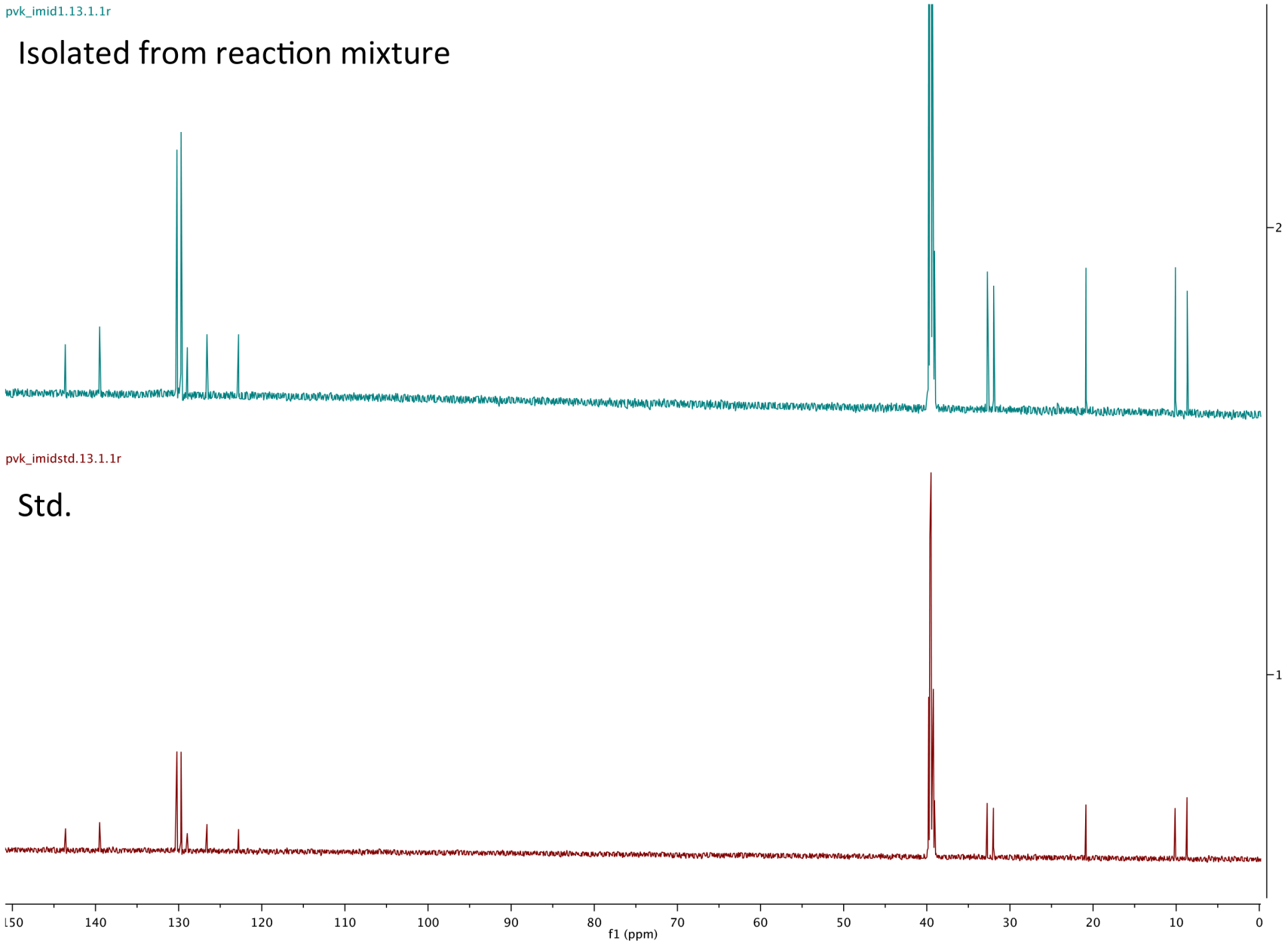
Table 8. Hydrogen bonds for tcd102 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(1)-H(1B)...Br(1)	0.98	3.12	3.9831(11)	148
C(4)-H(4A)...Br(1)	0.98	2.82	3.7976(11)	172
C(4)-H(4C)...Br(1)#1	0.98	2.95	3.9218(11)	173
C(6)-H(6B)...Br(1)#1	0.98	2.80	3.7555(12)	165
C(8)-H(8C)...Br(1)#2	0.98	3.09	3.7517(12)	126

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+2 #2 x,-y+3/2,z-1/2

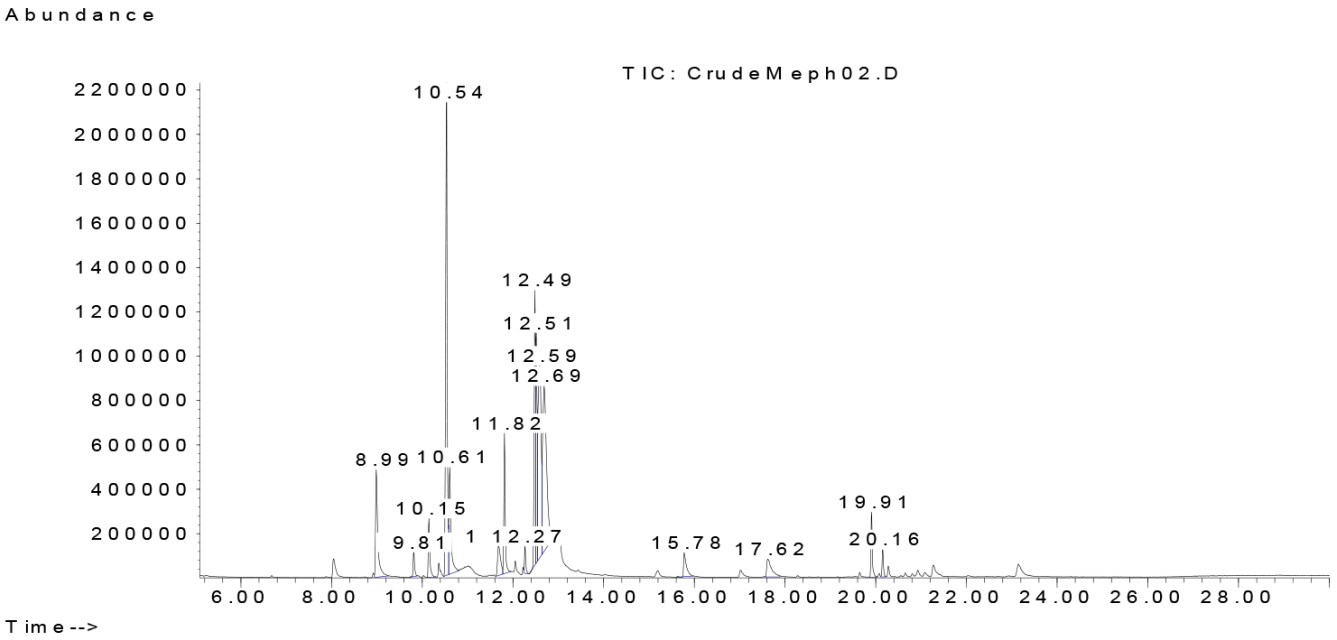
Supplemental 3: X-Ray crystallography supplemental data.

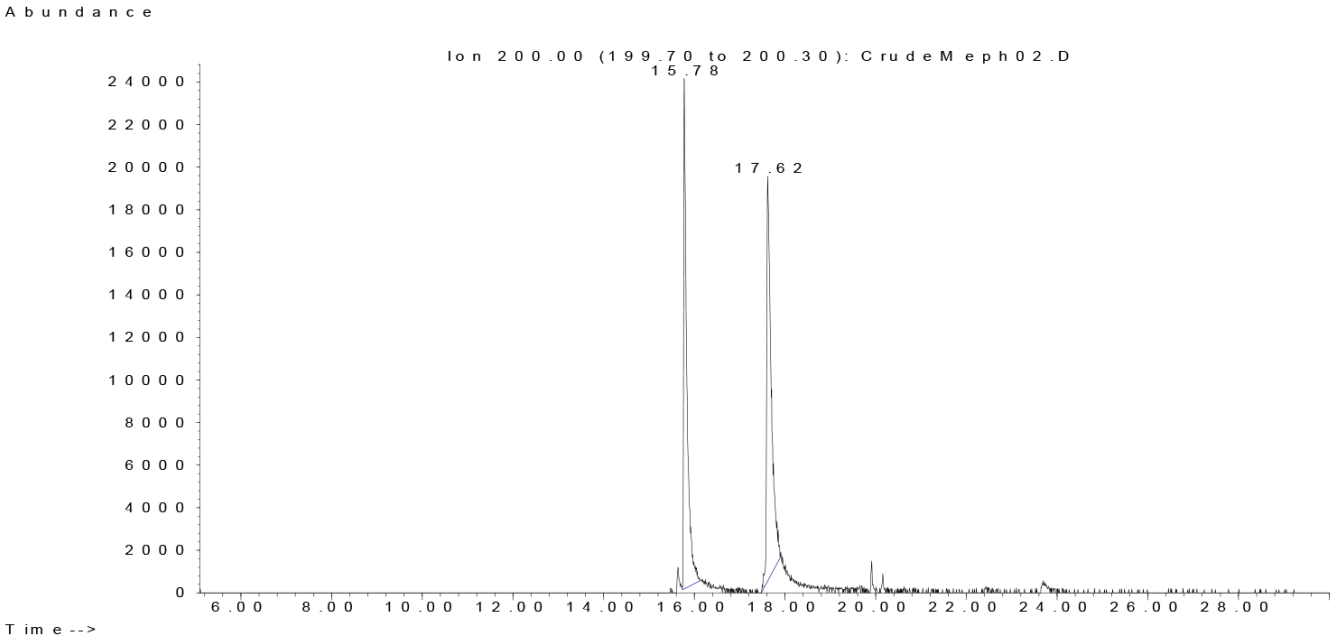


Supplemental 4: Synthesized TMPPI and the mephedrone byy product NMR

(a).

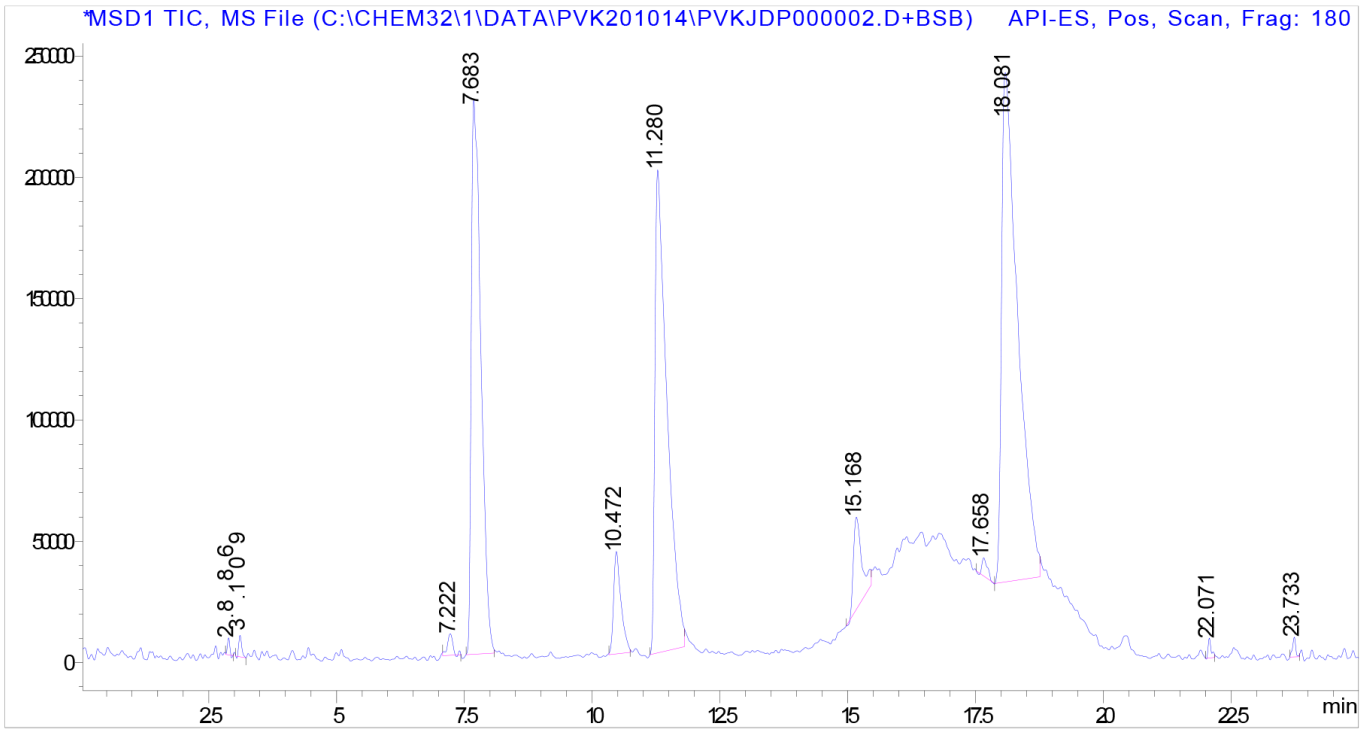
Crude Meph. HCl

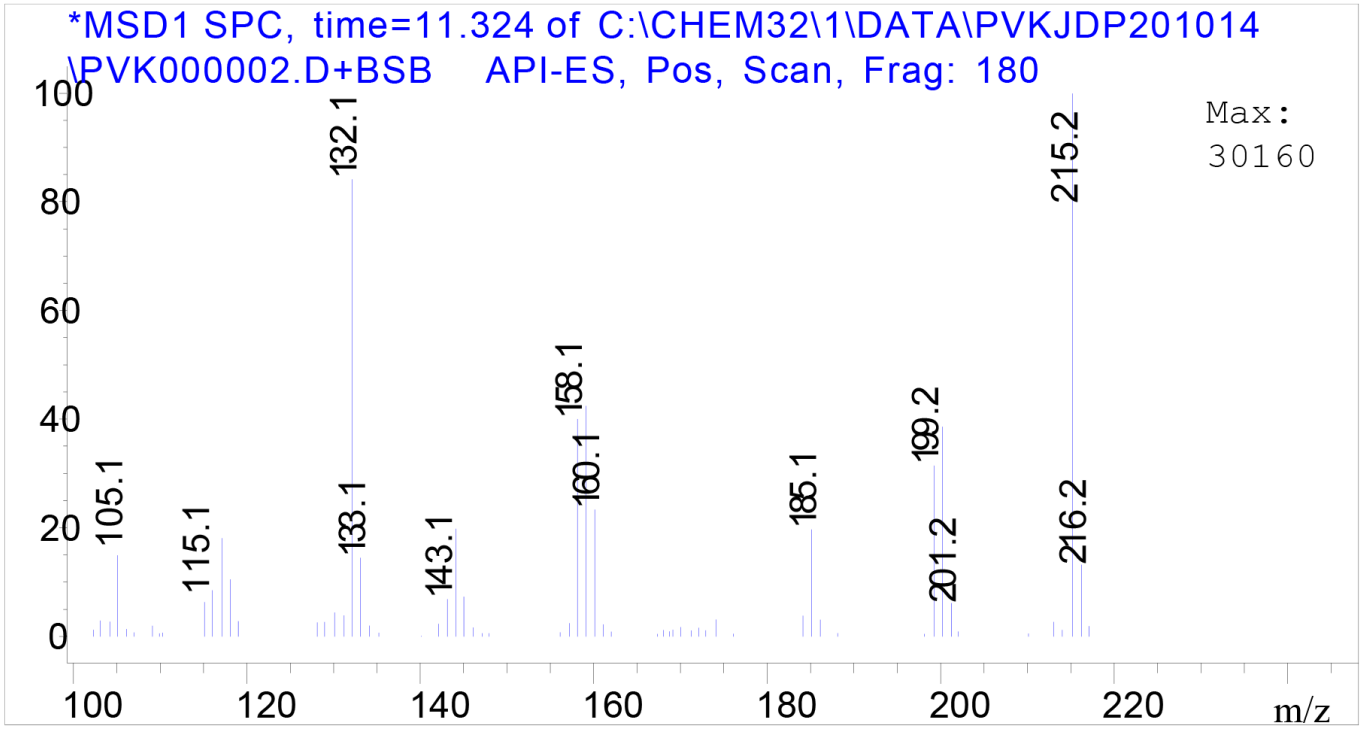




(b).

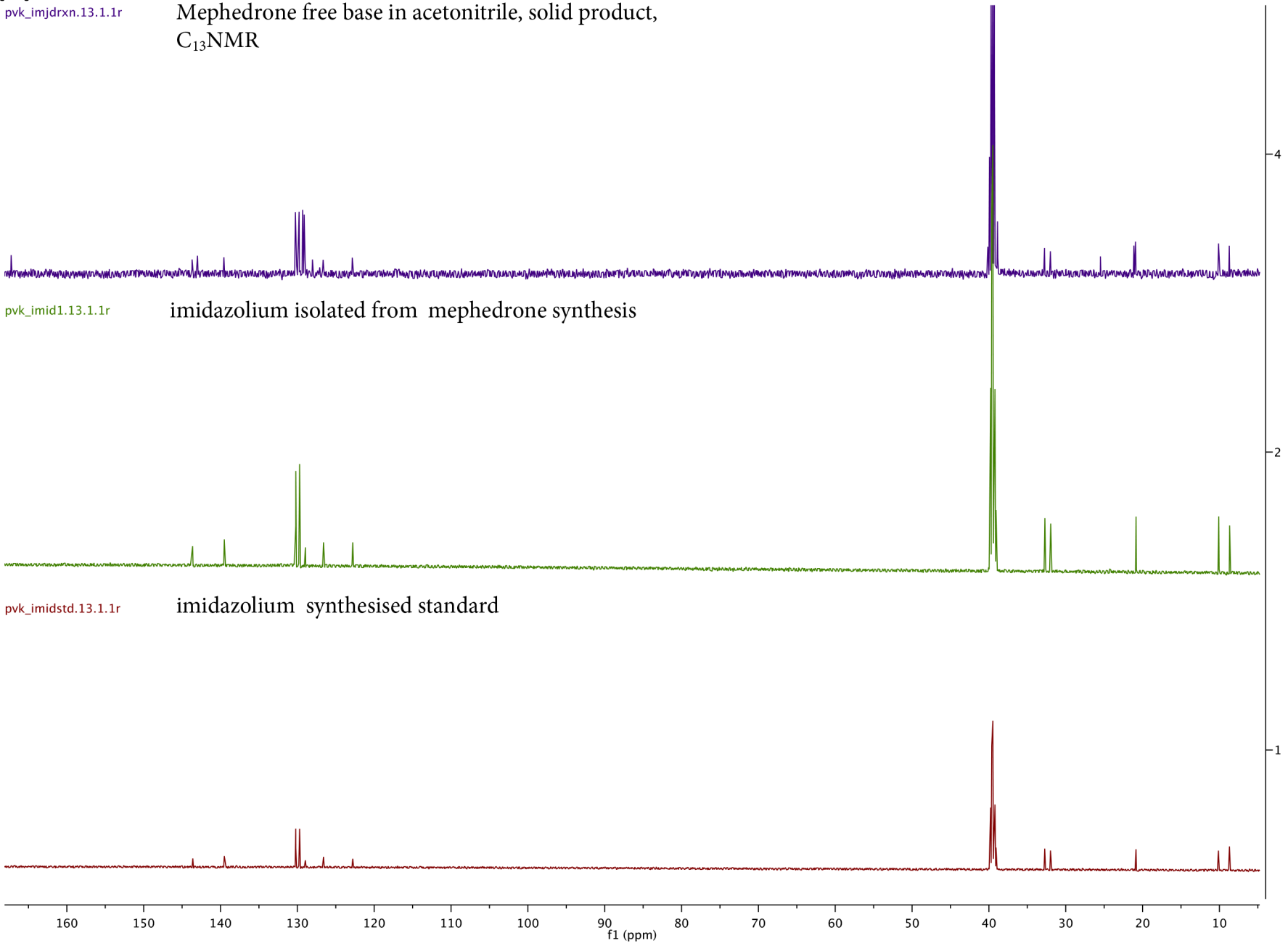
Crude Meph. HCl



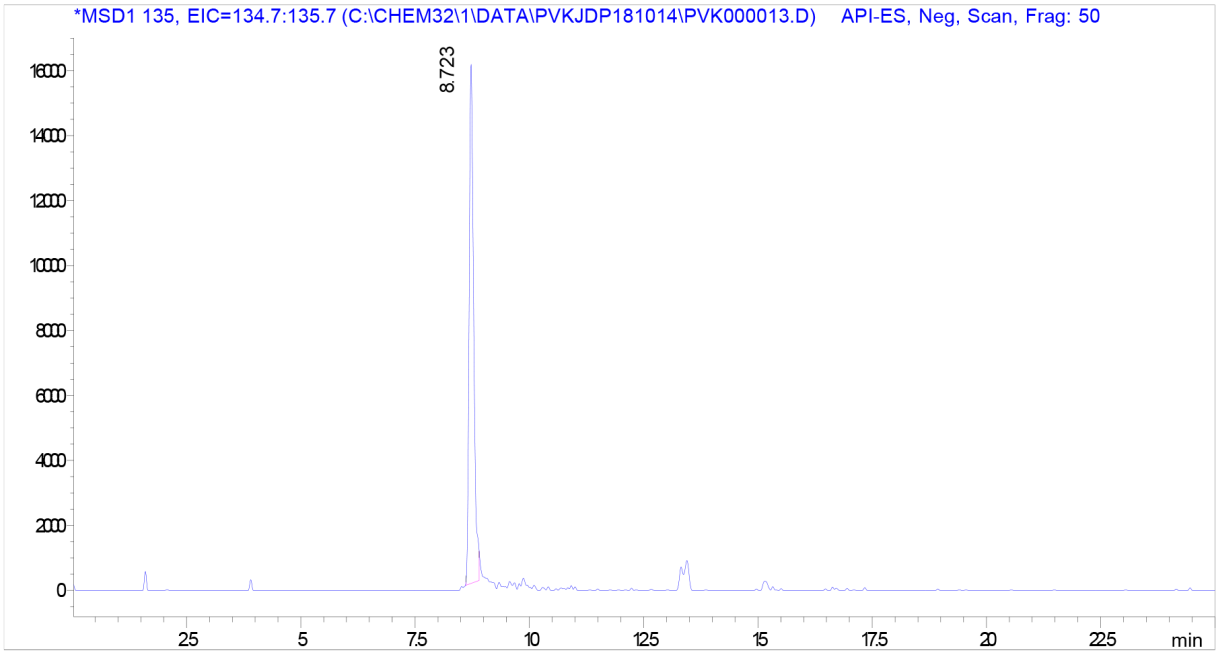


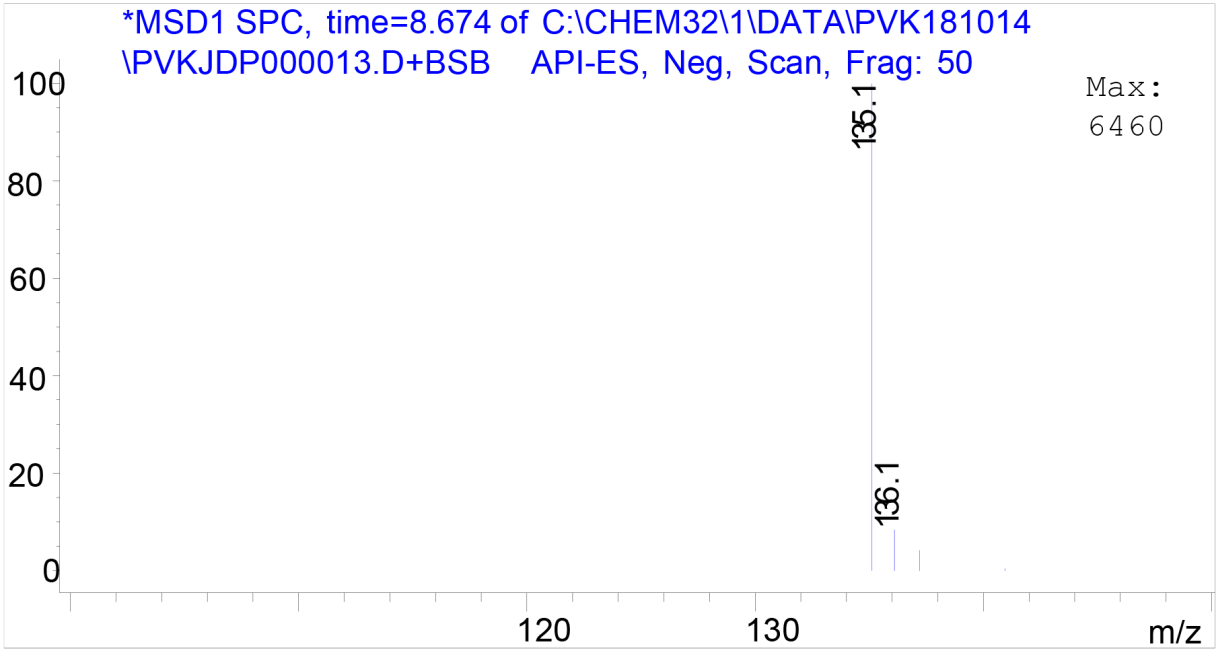
Supplemental 4: Crude mephedrone mixture analysis by (a). GC-MS, (b). LC-MS.

(a).


pvk_imjdrxn.13.1.1r
Mephedrone free base in acetonitrile, solid product,
C_{13}NMR
pvk_imid1.13.1.1r
imidazolium isolated from mephedrone synthesis
pvk_imidstd.13.1.1r
imidazolium synthesised standard
4
2
1
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

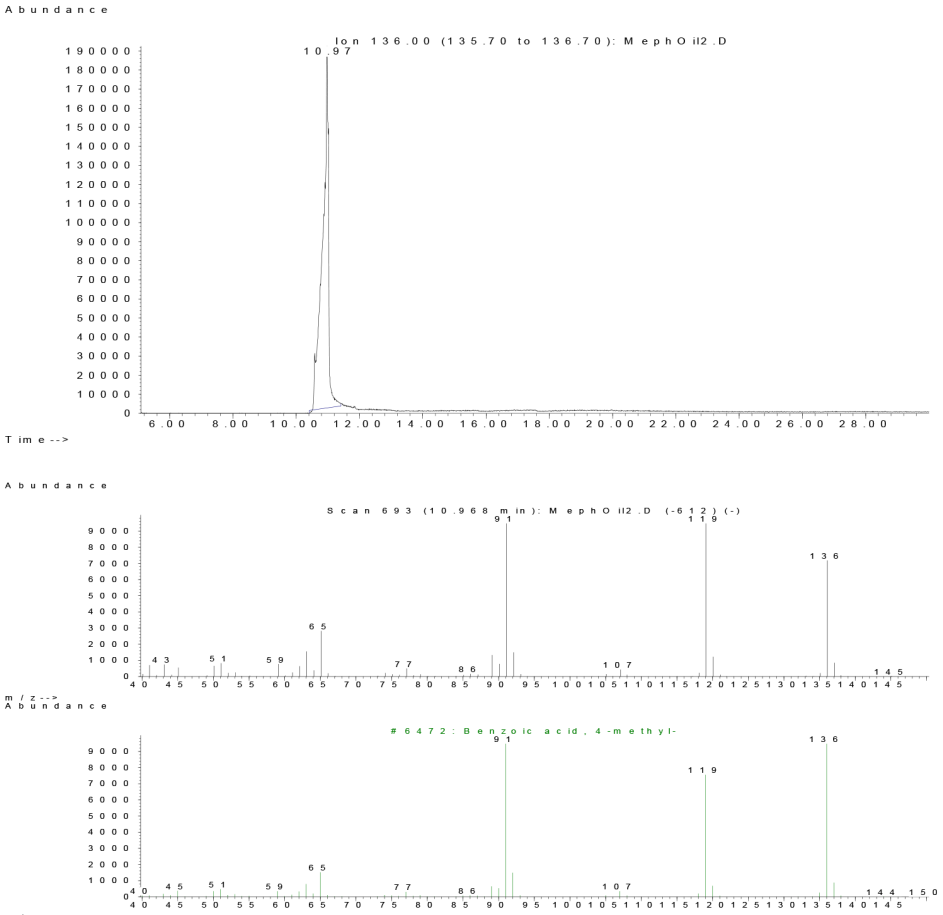
(b). Oil


*MSD1 135, EIC=134.7:135.7 (C:\CHEM32\1\DATA\PVKJDP181014\PVK000013.D) API-ES, Neg, Scan, Frag: 50
8.723
16000
14000
12000
10000
8000
6000
4000
2000
0
2.5
5
7.5
10
12.5
15
17.5
20
22.5
min


*MSD1 SPC, time=8.674 of C:\CHEM32\1\DATA\PVK181014
\PVKJDP000013.D+BSB API-ES, Neg, Scan, Frag: 50
Max:
6460
135.1
136.1
100
80
60
40
20
0
120
130
m/z

(c).

Oil - EIC m/z 136



Scan 693 (10.968 min): MephOil2.D (-612)

Modified:subtracted

1	Benzoic acid, 4-methyl-			136	C8H8O2		90	*	000099-94-5
	6472	74	18	0	98	9	59	30	76	9704

Supplemental 6: Mephedrone freebase mixture analysis by (a). NMR, (b). LC-MS and (c)GC-MS.