Relay Tricyclic Pd(II)/Ag(I) Catalysis: Design of a Four-Component Reaction Driven by Nitrene-Transfer on Isocyanide Yields Inhibitors of EGFR

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Experimental Procedures

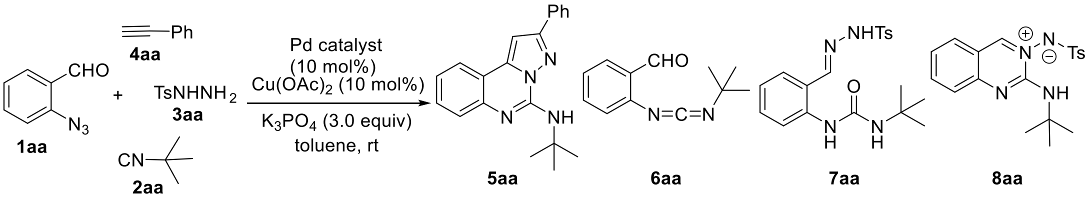
S1. General Considerations

All other reagents were purchased from Aldrich or Spectrochem used as such without purification. Analytical TLC was performed using 2.5*5cm plated coated with a 0.25mm thickness of silica gel (60F-254 Merck) and visualization was accomplished with UV light or I_2/ $KMnO_4$ staining. ^{1}H and ^{13}C NMR spectra were obtained from Bruker's Ascend 500 MHz spectrophotometer operating at 500.3 MHz for ^{1}H and 125.8 MHz for ^{13}C experiments. The chemical shifts are reported in ppm scale relative to residual $CDCl_3$ (δ 7.269 ppm) for ^{1}H and residual TMS. ^{13}C NMR spectra were reported relative to $CDCl_3$ (δ 77.00 ppm). Melting Points were recorded on BuchiM-655 Melting Point Apparatus and are uncorrected. High-resolution mass spectra (HRMS) were taken in the ESI positive ion mode. The abbreviations for multiplicities are used as: s=singlet, d=doublet, t=triplet, q=quartet, dd=doublet of doublets, m=multiplet, br s=broad singlet, dt=doublet of triplets, tt=triplet of triplets, ddd=doublet of doublet of doublets. All starting materials were prepared as reported in the literature.[1]

S2. Detailed Results of Screening

S2.1 Table S1: Initial Screening

We started our investigation using 2-azido benzaldehyde **1aa** (1 equiv), *tert.* butyl isocyanide **2aa** (1.2 equiv), tosyl hydrazide **3aa** (1 equiv) and phenylacetylene **4aa** (1.5 equiv) as a benchmark reaction using $PdCl_2$ (10 mol%), AgOTf (10 mol%), as catalytic system, in toluene with K_3PO_4 as a base, which did not lead to the formation of desired product **5aa** (Table S1, Entry 1).

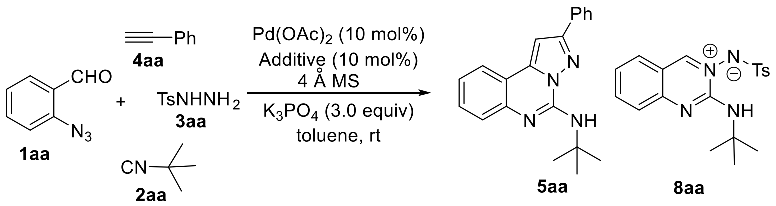


S.No.	Catalyst	Yield[a]				
		5aa	**6aa**	**7aa**	**8aa**	**1aa**
1.	$PdCl_2$	-	-	-	-	95
2.	$Pd(PPh_3)_2Cl_2$	5	45	-	-	45
3.	$Pd(PPh_3)_4$	7	25	40	-	24
4.	$Pd_2(dba)_3$	20	20	30	-	10
5.	$Pd(OAc)_2$	33	-	50	5	-
6.	$Pd(OAc)_2$	75[b]	-	-	13	-

[a]*Isolated yield,*[b]additionof 4 Å MS

On extensive screening of various Pd sources, we found that $Pd_2(dba)_3$ and $Pd(OAc)_2$ could afford the desired product **5aa** in 20% and 33% isolated yields Of these, $Pd(OAc)_2$ proved to be optimal because of complete consumption of starting material (Entry 5). We observed the formation of **7aa** as a major side product (Characterized by single–crystal X-ray diffraction analysis, refer Section 6), formed mainly due to condensation of **6aa** and **3aa** followed by nucleophilic attack of water. The origin of **7aa** could be due to the nucleophilic attack of water on carbodiimide **6aa**. Gratifyingly, a substantial improvement in the yield was observed on employing the 4 Å MS (Entry 6).

S2.2 Table S2: Additive effect

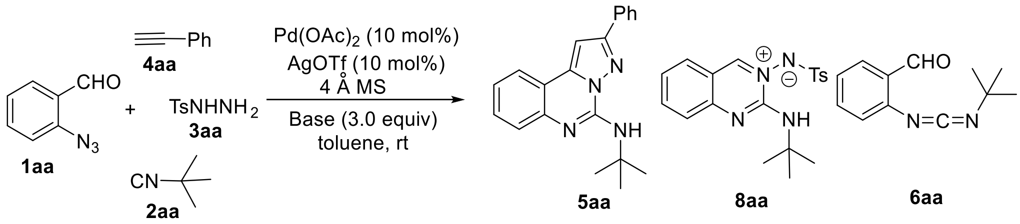


S.No.	Additive	Yield[a]	
		5aa	**8aa**
1.	$Cu(OAc)_2$	75	13
2.	CuI	63	21
3.	CuBr	55	28
4.	CuCl	59	23
5.	AgOTf	96	-
6.	AgOAc	78	15
7.	Ag_2CO_3	72	21
8.	$AgSbF_6$	15	68

[a]Isolated yield

To enhance the reactivity, we surveyed a variety of additives which revealed that both silver and copper salts facilitate this reaction. Of these, AgOTf was the most efficient additive for this strategy by overcomes the formation of a side product.

S2.3 Table S3: Base effect

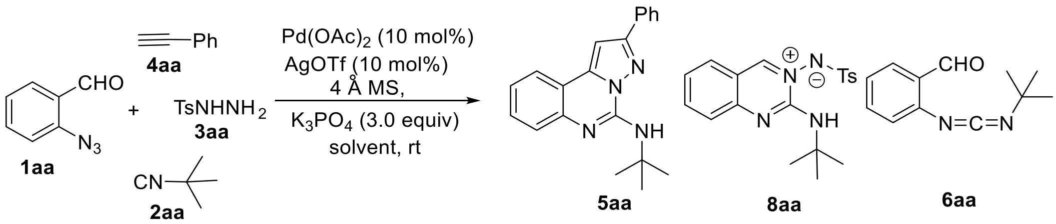


S.No.	Base	Yield[a]		
		5aa	**8aa**	**6aa**
1.	DABCO	82	-	12
2.	NaOAc	38	31	25
3.	Cs_2CO_3	35[b]	-	30
4.	KO^tBu	48	-	40
5.	DBU	64	-	26
6.	K_3PO_4	96	-	-

[a]Isolated yield, [b]1aa recovered.

The choice of base significantly affected the final outcome of this reaction. K_3PO_4 as a base produced best results among various bases screened in Table S3.

S2.4 Table S4: Solvent Effect

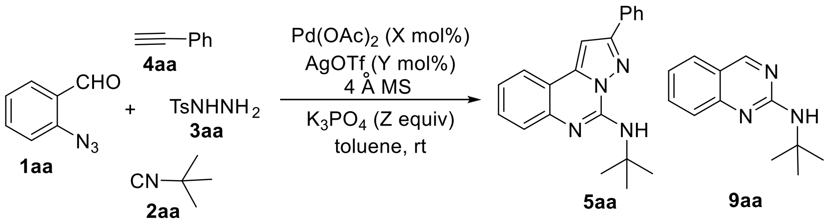


S.No.	Solvent	Yield[a]		
		5aa	**8aa**	**6aa**
1.	THF	62	20	-
2.	DCE	30	40	25
3.	DMF	-[b]	-	-
4.	DMSO	-	47[b]	-
5.	dioxane	49	15	12
6.	toluene	96	-	-

[a]Isolated yield, [b]1aa recovered

Next, we screened various solvents for 4-CR. The highest yield of **5aa** was obtained in toluene.

S2.5 Table S5: Final optimization

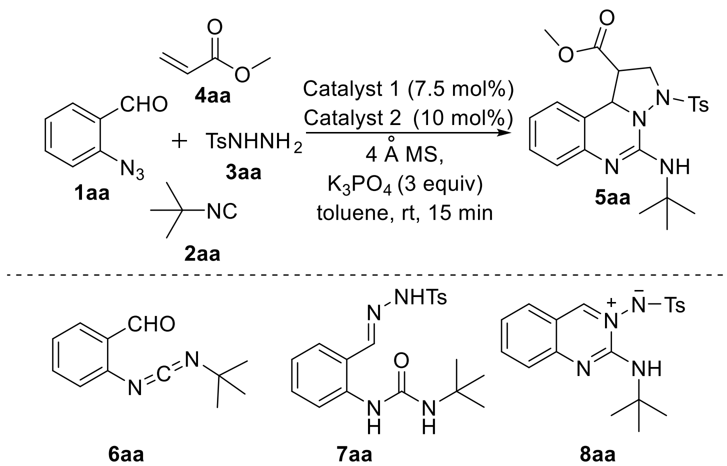


S. No	X	Y	Z	Yield[a] (%)
1.	10	10	3	96
2.	**7.5**	**10**	**3**	**95**
3.	5	10	3	61
4.	7.5	7.5	3	74
5.	7.5	5	3	43
6.	7.5	10	2	61
7.	7.5	10	1	55
8.	7.5	10	3	25[b]

[a]Isolated yield, [b]Major side product isolated at 60 °C

Next, we scrutinized the stoichiometric screening of the catalyst, additive and base and observed that decreased in the catalytic loading of $Pd(OAc)_2$ from 10 mol % to 7.5 mol % resulted the desired product **5aa** in comparable yields, but there is substantial reduction in the yield, when 5 mol % of either of the catalysts was employed (entry 3). Furthermore, decrease in the loading of additive and base lead to diminished yields. Evidently, there is a detrimental effect of increasing the temperature from rt to 60 °C, which afforded the lower yield of **5aa** with major side product **9aa** that was characterized by single-crystal X-ray diffraction analysis (refer section S8).

S2.6 Table S6: Optimization of reaction condition for alkene.



Entry	Catalyst 1	Catalyst 2	Additives	isolated yield[a] (%)				
				5aa	**6aa**	**7aa**	**8aa**	**1aa**
1.	$PdCl_2$	$Cu(OAc)_2$	-	-	-	-	-	95
2.	$Pd(PPh_3)_2Cl_2$	$Cu(OAc)_2$	-	10	40	-	-	44
3.	$Pd(PPh_3)_4$	$Cu(OAc)_2$	-	5	20	50	-	21
4.	$Pd_2(dba)_3$	$Cu(OAc)_2$	-	15	20	25	-	10
5.	$Pd(OAc)_2$	$Cu(OAc)_2$	-	30	-	45	5	-

6.	$Pd(OAc)_2$	$Cu(OAc)_2$	4 Å MS	80	-	-	10	-
7.	$Pd(OAc)_2$	CuI	4 Å MS	71	-	-	20	-
8.	$Pd(OAc)_2$	CuBr	4 Å MS	65	-	-	30	-
9.	$Pd(OAc)_2$	CuCl	4 Å MS	55	-	-	27	-
10.	$Pd(OAc)_2$	AgOTf	4 Å MS	95	-	-	-	-
11.	$Pd(OAc)_2$	AgOAc	4 Å MS	70	-	-	25	-
12.	$Pd(OAc)_2$	Ag_2CO_3	4 Å MS	65	-	-	30	-
13.	$Pd(OAc)_2$	$AgSbF_6$	4 Å MS	42	-	-	25	-
14.	-	AgOTf	4 Å MS	-	-	-	-	91
15.	$Pd(OAc)_2$	-	4Å MS	38	-	-	55	-
16.	$Pd(OAc)_2$	AgOTf,	4Å MS	93^b	-	-	-	-

[a]Reaction Condition: **1aa** (1 equiv), **2aa** (1.2 equiv), **3aa** (1 equiv), **26aa** (1 equiv). [b] 7.5 mol % of $Pd(OAc)_2$

Thorough optimisation studies for 4CR of alkene were carried out. An analogous reaction condition was required for this reaction compared to reactions involving alkynes. We observed that both palladium and co-catalyst (either Cu or Ag) were essential for this transformation.

S3. General Procedure for the synthesis of compounds 5 and 26

A mixture of 2-Azidobenzaldehyde (1.0 equiv), isocyanide (1.2 equiv), $Pd(OAc)_2$ (7.5 mol%), 4 Å MS, $TsNHNH_2$ (1.0 equiv), alkyne/alkenes (1.5 equiv), AgOTf (10 mol%) and K_3PO_4 (3.0 equiv) in toluene was added to a 20 mL Schlenk tube. The formed mixture was stirred at rt for 15 min. The reaction mixture was diluted with ethyl acetate (15 mL) and washed with water (10 mL). The organic layer was separated, dried on Na_2SO_4 and evaporated under vacuum. The crude product, so obtained, was purified by column chromatography to afford the desired product.

S4. Analytical Data for the compounds 5aa-5hb and 26aa-26ha

5aa: *N*-(*tert*-butyl)-2-phenylpyrazolo[1,5-*c*]quinazolin-5-amine
Pale yellow solid, Yield: 0.102 g (95%), m.p.: 83-85 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, 2H, aromatic C-*H*, *J* = 7.0 Hz), 7.91 (dd, 1H, aromatic C-*H*, *J* = 7.85, 1.1 Hz), 7.67 (d, 1H, aromatic C-*H*, *J* = 8.2 Hz), 7.54-7.48 (m, 3H, aromatic C-*H*), 7.44-7.42 (m, 1H, aromatic C-*H*), 7.29 (td, 1H, aromatic C-*H*, *J* = 8.0, 1.1 Hz), 7.19 (s, 1H, aromatic C-*H*), 6.50 (br s, 1H, N-*H*), 1.69 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.4, 142.2, 141.9, 140.9, 132.6, 129.7, 128.9, 128.8, 126.6, 126.1, 123.1, 122.8, 115.9, 95.5, 51.9, 29.1. HRMS (ESI) calcd for $C_{20}H_{21}N_4$ $[M+H]^+$ 317.1761, found 317.1755.

5ab: *N*-(*tert*-butyl)-2-(4-methoxyphenyl)pyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.113 g (96%), m.p.: 138-140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, 2H, aromatic C-*H*, *J* = 8.8 Hz), 7.90 (dd, 1H, aromatic C-*H*, *J* = 7.8, 1.2 Hz), 7.66 (d, 1H, aromatic C-*H*, *J* = 7.9 Hz), 7.51 (td, 1H, aromatic C-*H*, *J* = 7.2, 1.4 Hz), 7.27 (td, 1H, aromatic C-*H*, *J* = 8.0, 1.0 Hz), 7.11 (s, 1H, aromatic C-*H*), 7.02 (d, 2H, aromatic C-*H*, *J* = 8.7 Hz), 6.48 (br s, 1H, N-*H*), 3.89 (s, 3H, OMe), 1.68 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 153.2, 142.2, 141.9, 140.9, 129.6, 127.9, 126.1, 125.3, 123.1, 122.7, 115.9, 114.1, 94.9, 55.4, 51.9, 29.1. HRMS (ESI) calcd for $C_{21}H_{23}N_4O$ $[M+H]^+$ 347.1867, found 347.1865.

5ac: 2-(4-cyanophenyl)-*N*-(*tert*-butyl)pyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.093 g (80%), m.p.: 214-216 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, 2H, aromatic C-*H*, *J* = 8.4 Hz), 7.90 (dd, 1H, aromatic C-*H*, *J* = 7.8, 1.1 Hz), 7.76 (d, 2H, aromatic C-*H*, *J* = 8.3 Hz),7.68 (d, 1H, *J* = 8.0 Hz), 7.54 (td, 1H, aromatic C-*H*, *J*=7.5, 1.5 Hz), 7.30 (td, 1H, aromatic, C-*H*, *J* = 7.9, 0.9 Hz), 7.21 (s, 1H, aromatic C-*H*), 6.44 (br s, 1H, N-*H*), 1.69 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.2, 141.9, 141.8, 141.4, 137.0, 132.6, 130.0, 127.0, 126.3, 123.1, 123.0, 118.8, 115.7, 112.2, 95.9, 52.1, 29.1.

5ad: *N*-(*tert*-butyl)-2-(4-nitrophenyl)pyrazolo[1,5-*c*]quinazolin-5-amine
Yellow solid, Yield: 0.120 g (97%), m.p.: 209-211 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, 2H, aromatic C-*H*, *J* = 8.3 Hz), 8.19 (d, 2H, aromatic C-*H*, *J* = 8.1 Hz), 7.92 (d, 1H, aromatic C-*H*, *J* = 7.8 Hz), 7.69 (d, 1H, aromatic C-*H*, *J* = 8.2 Hz), 7.55 (t, 1H, aromatic C-*H*, *J* = 7.2 Hz), 7.31 (t, 1H, aromatic C-*H*, *J* = 7.4 Hz), 7.27 (s, 1H, aromatic C-*H*), 6.46 (br s, 1H, N-*H*), 1.69 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.8, 147.9, 141.8,

141.5, 138.9, 130.1, 127.2, 126.3, 124.2, 123.12, 123.13, 115.7, 96.2, 52.2, 29.1. HRMS (ESI) calcd for $C_{20}H_{20}N_5O_2$ $[M+H]^+$ 362.1612, found 362.1600.

5ae: 2-(4-bromophenyl)-*N*-(*tert*-butyl)pyrazolo[1,5-*c*]quinazolin-5-amine
Yellow solid, Yield: 0.102 g (76%), m.p.: 146-148 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90-7.88 (m, 3H, aromatic C-*H*), 7.68 (d, 1H, aromatic C-*H*, *J* = 8.2 Hz), 7.61 (d, 2H, aromatic C-*H*, *J* = 8.4 Hz), 7.53 (td, 1H, aromatic C-*H*, *J* = 8.3, 1.3 Hz),7.28 (td, 1H, aromatic C-*H*, *J* = 7.9, 0.8 Hz), 7.14 (s, 1H, aromatic C-*H*), 6.46 (br s, 1H, N-*H*), 1.69 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.2, 142.0, 141.9, 141.1, 131.9, 131.6, 129.8, 128.1, 126.2, 123.1, 122.9, 122.8, 115.8, 95.4, 52.0, 29.1. HRMS (ESI) calcd for $C_{20}H_{20}BrN_4$ $[M+H]^+$ 395.0866, found 395.0860.

5ba: 2-phenyl-*N*-(2,4,4-trimethylpentan-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.115 g (91%), m.p.: 82-83 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (d, 2H, aromatic C-*H*, *J* = 7.1 Hz), 7.92 (dd, 1H, aromatic C-*H*, *J* = 7.8, 1.2 Hz), 7.67 (d, 1H, aromatic C-*H*, *J* = 8.15 Hz), 7.54-7.49 (m, 3H, aromatic C-*H*), 7.44-7.41 (m, 1H, aromatic C-*H*), 7.28 (td, 1H, aromatic C-*H*, *J* = 8.0, 1.0 Hz), 7.19 (s, 1H,aromatic C-*H*), 6.67 (br s, 1H, N-*H*), 2.09 (s, 2H, sp^3 C-*H*), 1.76 (s, 6H, sp^3 C-*H*), 1.11 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.3, 142.1, 141.9, 140.8, 132.7, 129.6, 128.9, 128.8, 126.6, 126.2, 123.1, 122.6, 115.9, 95.4, 55.8, 52.4, 31.9, 31.7, 29.3. HRMS (ESI) calcd for $C_{24}H_{29}N_4$ $[M+H]^+$ 373.2387, found 373.2366.

5bb: 1-(4-(5-((2,4,4-trimethylpentan-2-yl)amino)pyrazolo[1,5-*c*]quinazolin-2-yl)phenyl)ethan-1-one
White solid, Yield: 0.131 g (93%), m.p.: 155-157 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, 4H, aromatic C-*H*, *J* = 8.2 Hz), 7.91 (d, 1H, aromatic C-*H*, *J* = 7.1 Hz), 7.67 (d, 1H,aromatic C-*H*, *J* = 7.9 Hz), 7.53 (t, 1H, aromatic C-*H*, *J* = 7.2 Hz), 7.29-7.25 (m, 2H, aromatic C-*H*), 6.64 (br s, 1H, N-*H*), 2.67 (s, 3H, sp^3 C-*H*), 2.08 (s, 2H, sp^3 C-*H*), 1.75 (s, 6H, sp^3 C-*H*), 1.10 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.6, 151.9, 141.9, 141.8, 141.1, 137.2, 137.1, 129.8, 128.9, 126.6, 126.2, 123.1, 122.8, 115.8, 95.9, 55.8, 52.5, 31.9, 31.6, 29.3, 26.7. HRMS (ESI) calcd for $C_{26}H_{31}N_4O$ $[M+H]^+$ 415.2493, found 415.2490.

5bc: 2-(3-nitrophenyl)-*N*-(2,4,4-trimethylpentan-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
Pale yellow solid, Yield: 0.122 g (86%), m.p.: 152-154 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.86 (t, 1H, aromatic C-*H*, *J* = 1.8 Hz), 8.33 (d, 1H, aromatic C-*H*, *J* = 7.7 Hz), 8.26 (dd, 1H, aromatic C-*H*, *J* = 8.1, 1.3 Hz), 7.92 (dd, 1H, aromatic C-*H*, *J* = 7.8, 1.0 Hz), 7.69-7.65 (m, 2H, aromatic C-*H*), 7.55 (td, 1H, aromatic C-*H*, *J* = 8.3, 1.3 Hz), 7.31 (td, 1H, aromatic C-*H*, *J* = 0.9, 7.95 Hz), 7.26 (s, 1H, aromatic C-*H*), 6.62 (br s, 1H, N-*H*), 2.09 (s, 2H, sp^3 C-*H*), 1.76 (s, 6H, sp^3 C-*H*), 1.10 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.8, 148.8, 141.9, 141.8, 141.4, 134.6, 132.3, 130.0, 129.7, 126.3, 123.3, 123.1, 122.9, 121.4, 115.7, 95.7, 55.9, 52.3, 31.9, 31.6, 29.4. HRMS (ESI) calcd for $C_{24}H_{28}N_5O_2$ $[M+H]^+$ 418.2238, found 418.2226. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^{1}H and ^{13}C NMR spectra. The isolated yield has been modified to 86 %.

5bd: 2-(2-bromophenyl)-*N*-(2,4,4-trimethylpentan-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
Yellow solid, Yield: 0.118 g (77%), m.p.: 95-96.5 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (dd, 1H, aromatic C-*H*,*J* = 7.7, 0.9 Hz), 7.82 (dd, 1H, aromatic C-*H*,*J* = 7.6, 1.5 Hz), 7.73 (dd, 1H, aromatic C-*H*, *J* = 8.0, 0.7 Hz), 7.67 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.52 (td, 1H, aromatic C-*H*, *J* = 8.3, 1.3 Hz), 7.43 (td, 1H, aromatic C-*H*, *J* = 7.5, 0.9 Hz), 7.34 (s, 1H, aromatic C-*H*), 7.28 (t, 2H, aromatic C-*H*, *J* = 7.7 Hz), 6.59 (br s, 1H, N-*H*), 2.07 (s, 2H, sp^3 C-*H*), 1.73 (s, 6H, sp^3 C-*H*), 1.08 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 141.89, 141.87, 139.9, 134.0, 133.8, 131.8, 129.9, 129.6, 127.4, 126.1, 123.2, 122.7, 122.5, 115.9, 99.4, 52.8, 52.1, 31.8, 31.6, 29.4. HRMS (ESI) calcd for $C_{24}H_{28}BrN_4$ $[M+H]^+$ 451.1492, found 451.1489.

5be: 2-(2-aminophenyl)-*N*-(2,4,4-trimethylpentan-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
Light brown solid, Yield: 0.112 g (85%), m. p.:114-116 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (dd, 1H, aromatic C-*H*,*J* = 7.8, 1.0 Hz), 7.72 (dd, 1H, aromatic C-*H*, *J* = 7.7, 1.3 Hz),7.68 (d, 1H, aromatic C-*H*,*J* = 8.1 Hz), 7.54 (td, 1H, aromatic C-H, *J* = 7.2, 1.3 Hz), 7.29 (td, 1H, aromatic C-*H*, *J* = 8.0, 1.0 Hz), 7.22 (td, 1H, aromatic C-H, *J* = 8.6, 1.4 Hz), 7.19 (s, 1H, aromatic C-*H*), 6.88-6.84 (m, 2H, aromatic C-*H*), 6.41 (br s, 1H, N-*H*), 5.38 (br s, 2H, N-*H*), 2.03 (s, 2H, sp^3 C-*H*), 1.76 (s, 6H, sp^3 C-*H*), 1.11 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.0, 145.2, 141.9, 141.8, 140.1, 129.8, 129.7, 129.6, 126.1, 123.3, 122.8, 117.8, 116.7, 115.8, 115.7, 96.6, 55.9, 53.1, 31.9, 31.7, 29.1. HRMS (ESI) calcd for $C_{24}H_{30}N_5$ $[M+H]^+$ 388.2496, found 388.2494.

5ca: *N*-(tert-butyl)-2-butylpyrazolo[1,5-*c*]quinazolin-5-amine
Pale yellow oil, Yield: 0.076 g (76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (dd, 1H, aromatic C-*H*,*J* = 7.8, 1.0 Hz), 7.65 (dd, 1H,aromatic C-*H*,*J* = 8.2, 0.5 Hz), 7.49 (td, 1H, aromatic C-*H*, *J* = 8.4, 1.4 Hz), 7.24 (td, 1H, aromatic C-*H*, *J* = 8.0, 1.1 Hz), 6.69 (s, 1H, aromatic C-*H*), 6.35 (br s, 1H, N-*H*), 2.84 (t, 2H, sp^3 C-*H*, *J* = 7.7 Hz), 1.79 (quintet, 2H, sp^3 C-*H*, *J* = 7.5 Hz), 1.67 (s, 9H, sp^3 C-*H*), 1.50-1.44 (sextet, 2H, sp^3 C-*H*, *J* = 7.4 Hz), 1.00 (t, 3H, sp^3 C-*H*,

J = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 142.2, 141.9, 140.3, 129.3, 126.0, 123.0, 122.5, 116.0, 97.1, 51.9, 31.7, 29.1, 28.4, 22.6, 13.9. HRMS (ESI) calcd for $C_{18}H_{25}N_4$ $[M+H]^+$ 297.2074, found 297.2060.

5cb: *N*-(*tert*-butyl)-2-pentylpyrazolo[1,5-*c*]quinazolin-5-amine
Yellow oil, Yield: 0.077 g (73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (dd, 1H, aromatic C-*H*, J = 7.8, 1.1 Hz), 7.65 (d, 1H, aromatic C-*H*, J = 8.1 Hz) 7.49 (td, 1H,aromatic C-*H*, J = 8.3, 1.3 Hz), 7.24 (td, 1H, aromatic C-*H*, J = 7.9, 1.0 Hz), 6.69 (s, 1H, aromatic C-*H*), 6.35 (br s, 1H, N-*H*), 2.83 (t, 2H, sp^3 C-*H*, J = 7.7 Hz), 1.81-1.77 (m, 2H, sp^3 C-*H*), 1.67 (s, 9H, sp^3 C-*H*), 1.45-1.39 (m, 4H, sp^3 C-*H*), 0.95 (t, 3H, sp^3 C-*H*, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.5, 142.2, 141.9, 140.3, 129.3, 126.0, 123.0, 122.5, 115.9, 97.1, 51.9, 31.7, 29.3, 29.1, 28.6, 22.5, 14.1. HRMS (ESI) calcd for $C_{19}H_{27}N_4$ $[M+H]^+$ 311.2230, found 311.2217.

5cc: *N*-2-di-tert-butylpyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.071 g (71%), m.p.: 99-101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (dd, 1H, aromatic C-*H*, J = 7.8, 1.1 Hz), 7.62 (d, 1H, aromatic C-*H*, J = 8.1 Hz), 7.47 (td, 1H, aromatic C-*H*, J = 8.4, 1.4 Hz), 7.23 (td, 1H, aromatic C-*H*, J= 8.0, 1.0 Hz), 6.74 (s, 1H, aromatic C-*H*), 6.38 (br s, 1H, N-*H*), 1.66 (s, 9H, sp^3 C-*H*), 1.44 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.7, 142.3, 141.8, 139.9, 129.2, 125.9, 122.9, 122.4, 116.1, 94.9, 51.7, 32.6, 30.6, 29.1.HRMS (ESI) calcd for $C_{18}H_{25}N_4$ $[M+H]^+$ 297.2074, found 297.2055.

5cd: *N*-(tert-butyl)-2-(trimethylsilyl)pyrazolo[1,5-*c*]quinazolin-5-amine
Colorless oil, Yield: 0.049 g (46%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, 1H, aromatic C-*H*, J = 7.7 Hz), 7.69 (d, 1H, aromatic C-*H*, J = 8.1 Hz), 7.52 (t, 1H, aromatic C-*H*, J = 7.3 Hz), 7.29 (d, 1H, aromatic C-*H*, J = 7.8 Hz), 7.02 (s, 1H, aromatic C-*H*), 6.57 (br s, 1H, N-*H*), 1.70 (s, 9H, sp^3 C-*H*), 0.45 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.1, 142.4, 141.8, 139.7, 129.2, 125.9, 123.1, 122.6, 116.4, 104.4, 51.8, 29.1, -1.1. HRMS (ESI) calcd for $C_{17}H_{25}N_4Si$ $[M+H]^+$ 313.1843, found 313.1836.

5cd': *N*-(tert-butyl)pyrazolo[1,5-*c*]quinazolin-5-amine
Transparent oil, Yield: 0.032 g (39%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, 1H, aromatic C-*H*, J = 2.0 Hz), 7.88 (dd, 1H, aromatic C-*H*, J = 7.8, 1.2 Hz), 7.66 (d, 1H, aromatic C-*H*, J = 8.2 Hz), 7.51 (td, 1H, aromatic C-*H*, J = 7.1, 1.4 Hz), 7.29-7.26 (m, 1H, aromatic C-*H*), 6.89 (d, 1H, aromatic C-*H*, J = 2.0 Hz), 6.40 (br s, 1H, N-*H*), 1.66 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.1, 141.7, 141.5, 139.8, 129.6, 126.1, 123.1, 122.8, 116.1, 98.3, 51.9, 29.1. HRMS (ESI) calcd for $C_{14}H_{17}N_4$ $[M+H]^+$ 241.1448, found 241.1435.

5ce: *N*-(tert-butyl)-2-(thiophen-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.079 g (72%), m.p.: 132-135 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (dd, 1H, aromatic C-*H*,J = 7.8, 1.3 Hz), 7.66 (d, 1H, aromatic C-*H*, J = 8.2 Hz),7.59 (dd, 1H, aromatic C-*H*, J = 3.5, 0.8 Hz), 7.52 (td, 1H, aromatic C-*H*, J = 8.3, 1.2 Hz), 7.38 (dd, 1H, aromatic C-*H*, J = 5.0, 0.8 Hz),7.29-7.26 (m, 1H, aromatic C-*H*),7.15 (dd, 1H, aromatic C-*H*, J = 4.9, 3.6 Hz), 7.08 (s, 1H,aromatic C-*H*), 6.41 (br s, 1H, N-*H*), 1.68 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.6, 142.0, 141.0, 135.7 129.8, 127.7, 126.16, 126.15, 125.8, 123.2, 122.8, 115.8, 95.5, 52.0, 29.1. HRMS (ESI) calcd for $C_{18}H_{19}N_4S$ $[M+H]^+$ 323.1325, found 323.1321.

5cf: *N*-(tert-butyl)-2-(pyridin-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
Pale yellow solid, Yield: 0.092 g (85%), m.p.: 81-83 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (d, 1H, aromatic C-*H*, J = 4.3 Hz), 8.19 (d, 1H, aromatic C-*H*, J = 7.8 Hz), 7.93 (d, 1H, aromatic C-H, J = 7.8 Hz), 7.81 (t, 1H, aromatic, C-*H*, J = 7.7 Hz), 7.67 (d, 1H, aromatic C-*H*, J = 8.2 Hz), 7.55 (s, 1H, aromatic C-*H*), 7.52 (t, 1H, aromatic C-*H*, J = 8.0 Hz), 7.30 (q, 2H, aromatic C-*H*, J = 6.9 Hz), 6.49 (br s, 1H, N-*H*), 1.69 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.4, 151.6, 149.7, 142.1, 141.8, 141.1, 136.7, 129.7, 126.1, 123.4, 123.2, 122.9, 121.1, 116.1, 97.1, 52.1, 29.1. HRMS (ESI) calcd for $C_{19}H_{20}N_5$ $[M+H]^+$ 318.1713, found 318.1701.

5cg: ethyl 5-(tert-butylamino)pyrazolo[1,5-*c*]quinazoline-2-carboxylate
White solid, Yield: 0.051 g (48%), m.p.: 73.3-74.9 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (dd, 1H, aromatic C-*H*, J = 7.8, 1.1 Hz), 7.67 (d, 1H, aromatic C-*H*, J = 8.1 Hz), 7.55 (td, 1H, aromatic C-*H*, J = 8.4, 1.4 Hz), 7.39 (s, 1H, aromatic C-*H*), 7.30 (td, 1H, aromatic C-*H*, J = 8.0, 1.0 Hz), 6.48 (br s, 1H, N-*H*), 4.50 (q, 2H, sp^3 C-*H*, J = 7.1 Hz), 1.66 (s, 9H, sp^3 C-*H*), 1.48 (t, 3H, sp^3 C-*H*, J = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.4, 145.0, 141.7, 141.6, 140.9, 130.2, 126.3, 123.3, 123.1, 115.8, 100.8, 61.6, 52.4, 28.9, 14.3. HRMS (ESI) calcd for $C_{17}H_{21}N_4O_2$ $[M+H]^+$ 313.1659, found 313.1640.

5cg': ethyl 5-(tert-butylamino)pyrazolo[1,5-*c*]quinazoline-1-carboxylate
Transparent oil, Yield: 0.038g (36%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.44 (dd, 1H, aromatic C-*H*, J = 8.2, 1.2 Hz), 8.37 (s, 1H,aromatic C-*H*), 7.69 (d, 1H, aromatic C-*H*, J = 7.4 Hz), 7.62 (td, 1H, aromatic C-*H*, J = 7.0, 1.3Hz), 7.35 (td, 1H, aromatic C-*H*, J = 8.2, 1.2 Hz), 6.51 (br s, 1H, N-*H*), 4.43 (q, 2H, sp^3 C-*H*, J = 7.1 Hz), 1.65 (s, 9H,

sp^3 C-*H*), 1.46 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3, 144.8, 143.5, 141.9, 140.7, 131.3, 127.3, 125.9, 123.1, 115.5, 108.9, 60.6, 52.2, 28.9, 14.4. HRMS (ESI) calcd for $C_{17}H_{21}N_4O_2$ [M+H]$^+$ 313.1659, found 313.1644.

5ch: (5-(tert-butylamino)pyrazolo[1,5-*c*]quinazolin-2-yl)methyl acetate
Pale yellow solid, Yield: 0.093 g (88%), m.p.: 93.5-95 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (dd, 1H, aromatic C-*H*, *J* = 7.8, 1.1 Hz), 7.65 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.51 (td, 1H, aromatic C-*H*, *J* = 7.3, 1.4 Hz), 7.27 (td, 1H, aromatic C-*H*, *J* = 6.9, 1.0 Hz), 6.90 (s, 1H, aromatic C-*H*), 6.34 (br s, 1H, N-*H*), 5.32 (s, 2H, sp^3 C-*H*), 2.16 (s, 3H, sp^3 C-*H*), 1.65 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 150.1, 141.9, 141.8, 140.8, 129.8, 126.1, 123.1, 122.9, 115.8, 98.1, 60.1, 52.0, 29.0, 21.0. HRMS (ESI) calcd for $C_{17}H_{21}N_4O_2$ [M+H]$^+$ 313.1659, found 313.1644.

5da: (5-((2,4,4-trimethylpentan-2-yl)amino)pyrazolo[1,5-*c*]quinazolin-2-yl)methanol
Pale yellow solid, Yield: 0.084 g (76%), m.p.: 116-117 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (dd, 1H, aromatic C-*H*, *J* = 7.8, 0.9 Hz), 7.66 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.51 (td, 1H, aromatic C-*H*, *J* = 8.3, 1.3 Hz), 7.27-7.24 (m, 1H, aromatic C-*H*), 6.85 (s, 1H, aromatic C-*H*), 6.42 (br s, 1H, N-*H*), 4.91 (s, 2H, sp^3 C-*H*), 2.08 (s, 2H, sp^3 C-*H*), 1.71 (s, 6H, sp^3 C-*H*), 1.04 (s, 9H, sp^3 C-*H*).^{13}C NMR (125 MHz, $CDCl_3$): δ 154.7, 141.8, 141.7, 140.7, 129.7, 126.1, 123.1, 122.7, 115.8, 96.4, 59.4, 55.8, 51.7, 31.7, 31.5, 29.5. HRMS (ESI) calcd for $C_{19}H_{27}N_4O$ [M+H]$^+$ 327.2180, found 327.2178. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^{1}H and ^{13}C NMR spectra. The isolated yield has been modified to 76 %.

5db: *N*-((5-((2,4,4-trimethylpentan-2-yl)amino)pyrazolo[1,5-*c*]quinazolin-2-yl)methyl)benzamide
Pale yellow solid, Yield: 0.140 g (96%), m.p.: 110-112 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86-7.82 (m, 3H, aromatic C-*H*), 7.64 (d, 1H, aromatic C-*H*, *J* = 8.0 Hz), 7.55-7.45 (m, 4H, aromatic C-*H*), 7.27-7.24 (m, 1H, aromatic C-*H*), 6.87 (s, 1H, aromatic C-*H*), 6.77 (br s, 1H, N-*H*), 6.42 (br s, 1H, N-*H*), 4.88 (d, 1H, sp^3 C-*H*, *J* = 5.3 Hz), 2.04 (s, 2H, sp^3 C-*H*), 1.71 (s, 6H, sp^3 C-*H*), 1.06 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.4, 151.8, 141.8, 141.7, 140.9, 134.3, 131.7, 129.7, 128.6, 127.0, 126.1, 123.2, 122.8, 115.7, 97.1, 55.8, 52.3, 38.3, 31.8, 31.6, 29.3. HRMS (ESI) calcd for $C_{26}H_{32}N_5O$ [M+H]$^+$ 430.2602, found 430.2601.

5dc: 2-(naphthalen-1-yl)-*N*-(2,4,4-trimethylpentan-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
Off-white solid, Yield: 0.113 g (93%), m.p.: 127-129.5 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.62-8.61 (m, 1H, aromatic C-*H*), 7.97-7.95 (m, 3H, aromatic C-*H*), 7.87 (d, 1H, aromatic C-*H*, *J* = 6.8 Hz), 7.73 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.61 (t, 1H, aromatic C-*H*, *J* = 7.6 Hz), 7.58-7.55 (m, 3H, aromatic C-*H*), 7.31 (t, 1H,aromatic C-*H*, *J* = 7.4 Hz), 7.19 (s, 1H, aromatic C-*H*), 6.71 (br s, 1H, N-*H*), 2.09 (s, 2H, sp^3 C-*H*), 1.78 (s, 6H, sp^3 C-*H*), 1.13 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.4, 142.1, 142.0, 140.3, 134.0, 131.5, 130.9, 129.7, 129.2, 128.4, 128.1, 126.6, 126.2, 126.1, 126.0, 125.4, 123.2, 122.7, 115.9, 99.5, 55.8, 52.5, 31.9, 31.6, 29.4. HRMS (ESI) calcd for $C_{28}H_{31}N_4$ [M+H]$^+$ 423.2543, found 423.2537.

5dd: 2-cyclopropyl-*N*-(2,4,4-trimethylpentan-2-yl)pyrazolo[1,5-*c*]quinazolin-5-amine
Yellow oil, Yield: 0.098 g (86%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (dd, 1H, aromatic C-*H*, *J* = 7.8, 1.2 Hz), 7.63 (d, 1H, aromatic C-*H*, *J* = 8.2 Hz), 7.48 (td, 1H, aromatic C-*H*, *J* = 7.2, 1.4 Hz), 7.23 (td, 1H, aromatic C-*H*, *J* = 8.0, 1.1Hz), 6.52 (s, 1H, aromatic C-*H*), 6.45 (br s, 1H, N-*H*), 2.14 (tt, 1H, sp^3 C-*H*, *J* = 8.4, 5.0 Hz), 2.07 (s, 2H, sp^3 C-*H*), 1.71 (s, 6H, sp^3 C-*H*), 1.09-1.08 (m, 2H, sp^3 C-*H)*, 1.07 (s, 9H, sp^3 C-*H*) 0.94 (dt, 2H, sp^3 C-*H*, *J* = 7.0, 4.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.2, 141.95, 141.92, 140.3, 129.3, 126.0, 122.9, 122.3, 115.8, 94.6, 55.6, 52.1, 31.8, 31.6, 29.4, 9.7, 9.1. HRMS (ESI) calcd for $C_{21}H_{29}N_4$ [M+H]$^+$ 337.2387, found 337.2366.

5ea: 8-bromo-*N*-(tert-butyl)-2-phenylpyrazolo[1,5-*c*]quinazolin-5-amine
Pale yellow solid, Yield: 0.057 g (65%), m.p.: 168-170 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, 2H, aromatic C-*H*, *J* = 7.0 Hz), 7.84 (d, 1H, aromatic C-*H*, *J* = 1.9 Hz), 7.74 (d, 1H, aromatic C-*H*, *J* = 8.4 Hz), 7.50 (t, 2H, aromatic C-*H*, *J* = 7.2 Hz), 7.43 (t, 1H, aromatic C-*H*, *J* = 6.2 Hz), 7.37(dd,1H, aromatic C-*H*, *J* = 8.3, 1.9 Hz), 7.15 (s, 1H, aromatic C-*H*), 6.56 (br s, 1H, N-*H*), 1.68 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.7, 143.0, 142.6, 140.4, 132.4, 129.0, 128.8, 128.7, 126.6, 125.8, 124.3, 123.3, 114.7, 95.7, 52.2, 29.1. HRMS (ESI) calcd for $C_{20}H_{20}BrN_4$ [M+H]$^+$ 395.0866, found 395.0862.

5eb: *N*-(tert-butyl)-2-phenyl-8-(trifluoromethyl)pyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.070 g (78%), m.p.: 54-56 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, 2H, aromatic C-*H*, *J* = 7.2 Hz), 7.99 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.94 (s, 1H, aromatic C-*H*), 7.52-7.43 (m, 4H, aromatic C-*H*), 7.25 (s, 1H, aromatic C-*H*), 6.60 (br s, 1H, N-*H*), 1.69 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.8, 142.7, 141.7, 140.0, 132.2, 131.4 (q, $J_{C\text{-}F}$ = 18 Hz), 129.1, 128.9, 126.7, 123.8, 123.4 (q, $J_{C\text{-}F}$ = 18 Hz), 118.7 (q, $J_{C\text{-}F}$ = 3.7 Hz), 118.2, 96.6, 52.3, 29.0. ^{19}F NMR (470 MHz, $CDCl_3$): δ -62.44. HRMS (ESI) calcd for $C_{21}H_{20}F_3N_4$

$[M+H]^+$ 385.1635, found 385.1630. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^1H and ^{13}C NMR spectra. The isolated yield has been modified to 78 %.

5ec: *N*-(tert-butyl)-8-fluoro-2-phenylpyrazolo[1,5-*c*]quinazolin-5-amine
Off white solid, Yield: 0.068 g (67%), m.p.: 107-109 ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, 2H, aromatic C-*H*, *J* = 7.1 Hz), 7.87 (dd, 1H, aromatic C-*H*, *J* = 8.7, 6.1 Hz), 7.49 (t, 2H, aromatic C-*H*, *J* = 7.2 Hz), 7.44-7.41 (m, 1H, aromatic C-*H*), 7.32 (dd, 1H, aromatic C-*H*, *J* = 10.6, 2.5 Hz),7.12 (s, 1H, aromatic C-*H*), 7.02 (td, 1H, aromatic C-*H*, *J* = 8.5, 2.5 Hz), 6.56 (br s, 1H, N-*H*), 1.68 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7 (d, J_{C-F} = 245 Hz), 153.6, 142.7, 140.6, 132.5, 128.9, 128.8, 126.3, 124.7 (d, J_{C-F} = 10.0 Hz), 112.6, 111.5, 111.3, 111.1, 95.2, 52.1, 29.1. ^{19}F NMR (470 MHz, $CDCl_3$): δ -110.9. HRMS (ESI) calcd for $C_{20}H_{20}FN_4$ $[M+H]^+$ 335.1667, found 335.1665.

5ed:*N*-(tert-butyl)-8-chloro-2-phenylpyrazolo[1,5-*c*]quinazolin-5-amine
White solid, Yield: 0.071 g (74%), m.p.: 134-136 ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.01 (d, 2H, aromatic C-*H*, *J* = 7.2 Hz), 7.79 (d, 1H, aromatic C-*H*, *J* = 8.3 Hz), 7.67 (d, 1H, aromatic C-*H*, *J* = 1.9 Hz), 7.50 (t, 2H, aromatic C-*H*, *J* = 7.2 Hz), 7.43 (t, 1H, aromatic C-*H*, *J* = 7.2 Hz), 7.23 (dd, 1H, aromatic C-*H*, *J* = 8.3, 2.0 Hz), 7.14 (s, 1H, aromatic C-*H*), 6.56 (br s, 1H, N-*H*), 1.68 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.7, 142.9, 142.7, 140.4, 135.1, 132.4, 129.0, 128.8, 126.6, 125.6, 124.2, 123.1, 114.4, 95.7, 52.2, 29.1. HRMS (ESI) calcd for $C_{20}H_{20}ClN_4$ $[M+H]^+$ 351.1371, found 351.1369.

5fa: dimethyl-5-(tert-butylamino)pyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
White solid, Yield: 0.089 g (74%), m.p.: 159-161ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.76 (dd, 1H, aromatic C-*H*, *J* = 8.1, 0.9 Hz), 7.69 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.62 (td, 1H, aromatic C-*H*, *J* = 8.3, 1.2 Hz), 7.33 (td, 1H, aromatic C-*H*, *J* = 8.1, 1.0 Hz), 6.45 (br s, 1H, N-*H*), 4.03 (s, 3H, sp^3 C-*H*), 3.99 (s, 3H, sp^3 C-*H*), 1.64 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7, 163.2, 145.8, 143.1, 141.3, 140.1, 131.5, 126.3, 125.5, 123.4, 114.9, 108.0, 52.9, 52.49, 52.48, 28.9.

5fb: dimethyl 5-(tert-butylamino)-8-chloropyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
White solid, Yield: 0.087 g (81%), m.p.: 181-182 ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.82 (d, 1H, aromatic C-*H*, *J* = 8.7 Hz), 7.69 (d, 1H, aromatic C-*H*, *J* = 2.1 Hz), 7.28 (dd, 1H, aromatic C-*H*, *J* = 8.8, 2.1 Hz), 6.52 (br s, 1H, N-*H*), 4.03 (s, 3H, sp^3 C-*H*), 3.97 (s, 3H, sp^3 C-*H*), 1.63 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4, 163.2, 146.4, 144.2, 141.8, 139.8, 137.3, 127.1, 125.7, 123.9, 113.4, 107.9, 53.0, 52.7, 52.5, 28.8. HRMS (ESI) calcd for $C_{18}H_{20}ClN_4O_4$ $[M+H]^+$ 391.1168, found 391.1165.

5ga: diethyl-5-(tert-butylamino)pyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
Off-white solid, Yield: 0.110 g (84%), m.p.: 63-65 ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.83 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.69 (d, 1H,aromatic C-*H*, *J* = 8.1 Hz), 7.61 (t, 1H, aromatic C-*H*, *J* = 8.1 Hz), 7.33 (t, 1H, aromatic C-*H*, *J* = 8.0 Hz), 6.46 (br s, 1H, N-*H*), 4.49 (q, 2H, sp^3 C-*H*, *J* = 7.1 Hz), 4.45 (q, 2H, sp^3 C-*H*, *J* = 7.1 Hz), 1.64 (s, 9H, sp^3 C-*H*), 1.45 (t, 3H, sp^3 C-*H*, *J* = 7.1Hz), 1.42 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3, 162.9, 146.3, 143.1, 141.4, 140.0, 131.4, 126.3, 125.7, 123.4, 115.0, 108.1, 62.2, 61.5, 52.5, 28.9, 14.2, 14.1.

5gb: diethyl-8-bromo-5-(tert-butylamino)pyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
Off-white solid, Yield: 0.075 g (74%), m.p.: 125-127 ºC.^1H NMR (500 MHz, $CDCl_3$): δ 8.82 (d, 1H, aromatic C-*H*, *J* = 8.8 Hz), 7.87 (d, 1H, aromatic C-*H*, *J* = 2.0 Hz), 7.42 (dd, 1H, aromatic C-*H*, *J* = 8.7, 2.0 Hz), 6.53 (br s, 1H, N-*H*), 4.49 (q, 2H, sp^3 C-*H*, *J* = 7.1 Hz), 4.43 (q, 2H, sp^3 C-*H*, *J* = 7.1 Hz), 1.63 (s, 9H, sp^3 C-*H*), 1.45 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz), 1.41 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.925, 162.920, 146.9, 144.3, 141.9, 139.8, 128.8, 127.3, 126.5, 125.6, 113.8, 108.0, 62.3, 61.5, 52.7, 28.8, 14.2, 14.1.

5ha: dimethyl-5-((2,4,4-trimethylpentan-2-yl)amino)pyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
White solid, Yield: 0.119 g (85%), m.p.: 103-105 ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.76 (dd, 1H, aromatic C-*H*, *J* = 8.2, 1.0 Hz),7.70 (dd, 1H, aromatic C-*H*, *J* = 8.2, 0.7 Hz), 7.63-7.59 (m, 1H, aromatic C-*H*), 7.35-7.32 (m, 1H, aromatic C-*H*), 6.51 (br s, 1H, N-*H*), 4.03 (s, 3H, sp^3 C-*H*), 3.99 (s, 3H, sp^3 C-*H*), 2.08 (s, 2H, sp^3 C-*H*), 1.69 (s, 6H, sp^3 C-*H*), 1.02 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8, 163.2., 145.8, 143.1, 141.2, 139.9, 131.4, 126.3, 125.5, 123.4, 114.8, 107.6, 56.2, 52.9, 52.5, 51.3, 31.8, 31.5, 29.4. HRMS (ESI) calcd for $C_{22}H_{29}N_4O_4$ $[M+H]^+$ 413.2184, found 413.2178. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^1H and ^{13}C NMR spectra. The isolated yield has been modified to 85 %.

5hb: diethyl-5-((2,4,4-trimethylpentan-2-yl)amino)pyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
White solid, Yield: 0.111 g (73%), m.p.: 176-178 ºC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.83 (dd, 1H, aromatic C-*H*, *J* = 8.2, 1.0 Hz), 7.69 (dd, 1H, aromatic C-*H*,*J* = 8.0, 0.7 Hz), 7.63-7.59 (m, 1H, aromatic C-*H*), 7.34-7.31 (m, 1H,

aromatic C-*H*), 6.53 (br s, 1H, N-*H*), 4.49 (q, 2H, sp^3 C-*H*, *J* = 7.2 Hz), 4.45 (q, 2H, sp^{3}C-*H*, *J* = 7.2 Hz), 2.08 (s, 2H, sp^3 C-*H*), 1.69 (s, 6H, sp^3 C-*H*), 1.45 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz), 1.42 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz), 1.02 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.3, 162.9, 146.3, 143.1, 141.2, 139.9, 131.3, 126.3, 125.7, 123.3, 114.9, 108.1, 62.1, 61.5, 56.2, 51.4, 31.8, 31.5, 29.4, 14.2, 14.1. HRMS (ESI) calcd for $C_{24}H_{33}N_4O_4$ $[M+H]^+$ 441.2497, found 441.2490.

26aa: Methyl 5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
White solid, Yield: 0.144 g (93%), m.p.: 137-138 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, 2H, aromatic *C-H*, *J* = 8.1 Hz), 7.36 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.12 (t, 1H, aromatic *C-H*, *J* = 7.0 Hz), 6.93 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 6.80 (t, 1H, aromatic *C-H*, *J* = 7.2 Hz), 6.76 (d, 1H, aromatic *C-H*, *J* = 6.8 Hz), 5.21 (br s, 1H, N-*H*), 4.14 (d, 1H, sp^3 C-*H*, *J* = 7.2 Hz), 3.91 (dd, 1H, sp^3 C-*H*, *J* = 12.1, 8.4 Hz), 3.79 (dd, 1H, sp^3 C-*H*, *J* = 12.1, 2.8 Hz), 3.36 (td, 1H, sp^3 C-*H*, *J* = 8.0, 2.8 Hz), 3.21 (s, 3H, sp^3 OC-*H*), 2.47 (s, 3H, sp^3 C-*H*), 1.33 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 148.9, 145.6, 142.4, 131.8, 130.1, 129.16, 129.14, 126.6, 123.7, 120.8, 117.5, 62.4, 52.6, 51.9, 51.2, 47.9, 28.9, 21.7. HRMS (ESI) calcd for $C_{23}H_{29}N_4O_4S$ $[M+H]^+$ 457.1904, found 457.1894.

26ab: Methyl 8-bromo-5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
Yellow solid, Yield: 0.101 g (85%), m.p.: 178-180 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.36 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.10 (d, 1H, aromatic *C-H*, *J* = 1.7 Hz), 6.91 (dd, 1H, aromatic *C-H*, *J* = 8.0, 1.8 Hz), 6.62 (d, 1H, aromatic *C-H*, *J* = 8.0 Hz), 5.28 (br s, 1H, N-*H*), 4.10 (d, 1H, sp^3 C-*H*, *J* = 7.2 Hz), 3.90 (dd, 1H, sp^3 C-*H*, *J* = 12.1, 8.3 Hz), 3.77 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 2.8 Hz), 3.35 (td, 1H, sp^3 C-*H*, *J* = 8.1, 2.8Hz), 3.27 (s, 3H, sp^3 OC-*H*), 2.47 (s, 3H, sp^3 C-*H*), 1.31 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 149.6, 145.8, 144.1, 131.7, 130.2, 129.1, 127.8, 126.4, 123.4, 122.6, 116.3, 61.9, 52.3, 52.1, 51.4, 47.9, 28.8, 21.7. HRMS (ESI) calcd for $C_{23}H_{28}BrN_4O_4S$ $[M+H]^+$ 535.1009, found 535.1007.

26ac: Methyl 5-(*tert*-butylamino)-8-chloro-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
Yellow solid, Yield: 0.116 g (86%), m.p.: 173-175 ºC, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.36 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 6.94 (d, 1H, aromatic C-*H*, *J* = 2.0 Hz), 6.76 (dd, 1H, aromatic *C-H*, *J* = 8.1, 2.1 Hz), 6.68 (d, 1H, aromatic C-*H*, *J* = 8.1 Hz), 5.28 (br s, 1H, N-*H*), 4.12 (d, 1H, sp^3 C-*H*, *J* = 7.2 Hz), 3.91 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 8.3 Hz), 3.78 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 2.9 Hz), 3.36 (td, 1H, sp^3 C-*H*, *J* = 8.2, 2.9 Hz), 3.27 (s, 3H, sp^3 OC-*H*), 2.47 (s, 3H, sp^3 C-*H*), 1.31 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 149.6, 145.7, 143.9, 134.5, 131.7, 130.2, 129.1, 127.5, 123.4, 120.5, 115.9, 61.8, 52.4, 52.1, 51.4, 47.9, 28.8, 21.7. HRMS (ESI) calcd for $C_{23}H_{28}ClN_4O_4S$ $[M+H]^+$ 491.1515, found 491.1510.

26ad: Methyl 5-(*tert*-butylamino)-8-fluoro-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
Colorless liquid, Yield: 0.130 g (91%), ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, 2H, aromatic *C-H*, *J* = 8.1 Hz), 7.37 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 6.71 (dd, 1H, aromatic *C-H*, *J* = 8.2, 6.4 Hz), 6.63 (d, 1H, aromatic *C-H*, *J* = 10.0 Hz), 6.51 (td, 1H, aromatic *C-H*, *J* = 8.4, 2.5 Hz), 5.29 (br s, 1H, N-*H*), 4.14, (d, 1H, sp^3 C-*H*, *J* = 7.2 Hz), 3.91 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 8.3 Hz), 3.78 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 2.8 Hz), 3.34 (td, 1H, sp^3 C-*H*, *J* = 8.0, 2.8 Hz), 3.26 (s, 3H, sp^3 OC-*H*), 2.48 (s, 3H, sp^3 C-*H*), 1.32 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 163.54 (d, J_{C-F} = 243 Hz), 149.5, 145.7, 131.8, 130.2, 129.2, 127.6 (d, J_{C-F} = 10 Hz), 113.2, 109.9 (d, J_{C-F} = 15.2 Hz), 107.6 (d, J_{C-F} = 22.5 Hz), 61.9, 52.4, 52.0, 51.4, 47.9, 28.8, 21.7. ^{19}F NMR (470 MHz, $CDCl_3$): δ -113.74. HRMS (ESI) calcd for $C_{23}H_{28}FN_4O_4S$ $[M+H]^+$ 475.1810, found.475.1798.

26ae: Methyl 5-(*tert*-butylamino)-3-tosyl-8-(trifluoromethyl)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
Pale yellow Oil, Yield: 0.106 g (87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.38 (d, 2H, aromatic *C-H*, *J* = 7.8 Hz), 7.18 (s, 1H, aromatic *C-H*), 7.03 (d, 1H, aromatic *C-H*, *J* = 7.6 Hz), 6.87 (d, 1H, aromatic *C-H*, *J* = 7.6 Hz), 5.29 (br s, 1H, N-*H*), 4.20 (d, 1H, sp^3 C-*H*, *J* = 7.1 Hz), 3.94 (dd, 1H, sp^3 C-*H*, *J* = 12.1, 8.5 Hz), 3.80 (dd, 1H, sp^3 C-*H*, *J* = 12.1, 2.4 Hz), 3.41 (t, 1H, sp^3 C-*H*, *J* = 6.0 Hz), 3.23 (s, 3H, sp^3 OC-*H*), 2.48 (s, 3H, sp^3 C-*H*), 1.32 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 149.7, 145.8, 143.2, 131.7, 131.5 (q, J_{C-F} = 31.5 Hz), 130.2, 129.2, 127.0, 124.1 (q, J_{C-F} = 270.7 Hz), 120.9, 120.3 (d, J_{C-F} = 4.6 Hz), 116.9 (d, J_{C-F} = 7.5 Hz), 61.8, 52.4, 52.0, 51.5, 47.8, 28.8, 21.7. ^{19}F NMR (470 MHz, $CDCl_3$): δ -62.88. HRMS (ESI) calcd for $C_{24}H_{28}F_3N_4O_4S$ $[M+H]^+$ 525.1778, found. 525.1764.

26ba: methyl 5-(*tert*-butylamino)-3-(phenylsulfonyl)-1,2,3,10b-tetrahydropyrazolo[1,5-c]quinazoline-1-carboxylate

Off-white solid, Yield: 0.134 g (89%), m.p.: 130-132 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (dd, 2H, aromatic *C-H, J* = 8.5, 0.8 Hz), 7.71 (t, 1H, aromatic *C-H, J* = 7.5 Hz), 7.58 (t, 2H, aromatic *C-H, J* = 8.0 Hz), 7.13 (td, 1H, aromatic *C-H, J* = 8.7, 1.3 Hz), 6.94 (d, 1H, aromatic C-*H, J* = 7.8 Hz*)*, 6.81, (td, 1H, aromatic C-*H, J* = 7.4, 1.1 Hz*)*, 6.75 (dd, 1H, aromatic C-*H, J* = 7.3, 1.1 Hz*)*, 5.19 (br s, 1H, N-*H*), 4.12 (d, 1H, sp^3 C-*H, J* = 7.3 Hz), 3.94 (dd, 1H, sp^3 C-*H, J* = 12.2, 8.3 Hz), 3.82 (dd, 1H, sp^3 C-*H, J* = 12.2, 3.0 Hz), 3.36, (td, 1H, sp^3 C-*H, J* = 8.2, 3.0 Hz), 3.22 (s, 3H, sp^3 OC-*H*), 1.32 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 148.8, 142.3, 134.9, 134.3, 129.5, 129.1, 128.1, 126.6, 123.7, 120.9, 117.4, 62.5, 52.5, 51.9, 51.2, 48.0, 28.9. HRMS (ESI) calcd for $C_{22}H_{27}N_4O_4S$ $[M+H]^+$ 443.1748, found 443.1735.

26bb: methyl 5-(*tert*-butylamino)-3-((4-iodophenyl)sulfonyl)-1,2,3,10b-tetrahydropyrazolo[1,5-c]quinazoline-1-carboxylate

White solid, Yield: 0.174 g (90%), m.p.: 147-149 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, 2H, aromatic *C-H, J* = 8.1 Hz), 7.68 (d, 2H, aromatic *C-H, J* = 8.1 Hz), 7.15 (t, 1H, aromatic *C-H, J* = 7.0 Hz), 7.95 (d, 1H, aromatic *C-H, J* = 7.8 Hz), 6.85-6.80 (m, 2H, aromatic C-*H)*, 5.12 (brs, 1H, N-*H*), 4.21 (d, 1H, sp^3 C-*H, J* = 7.1 Hz), 3.88 (dd, 1H, sp^3 C-*H, J* = 12.0, 8.5 Hz), 3.82 (dd, 1H, sp^3 C-*H, J* = 12.0, 2.2 Hz), 3.39, (td, 1H, sp^3 C-*H, J* = 7.0, 5.5 Hz), 3.22 (s, 3H, sp^3 OC-*H*), 1.33 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 148.6, 142.2, 138.8, 134.5, 130.4, 129.3, 126.7, 123.8, 121.0, 117.3, 102.5, 62.6, 52.4, 52.0, 51.3, 47.9, 28.9. HRMS (ESI) calcd for $C_{22}H_{26}IN_4O_4S$ $[M+H]^+$ 569.0714, found 569.0700.

26bc: Methyl 3-((4-bromophenyl)sulfonyl)-5-(*tert*-butylamino)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

White solid, Yield: 0.160 g (91%), m.p.: 142-144 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, 2H, aromatic *C-H, J* = 8.5 Hz), 7.72 (d, 2H, aromatic *C-H, J* = 8.2 Hz), 7.15 (t, 1H, aromatic *C-H, J* = 6.6 Hz), 6.95 (d, 1H, aromatic *C-H, J* = 7.7 Hz), 6.86-6.80 (m, 2H, aromatic *C-H)*, 5.13 (br s, 1H, N-*H*), 4.20 (d, 1H, sp^3 C-*H, J* = 7.2 Hz), 3.89 (dd, 1H, sp^3 C-*H, J* = 12.1, 8.1 Hz), 3.39 (td, 1H, sp^3 C-*H, J* = 7.6, 2.4 Hz), 3.22 (s, 3H, sp^3 OC-*H*), 1.33 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 148.6, 142.2, 133.9, 132.8, 130.6, 129.9, 129.3, 126.6, 123.8, 121.0, 117.3, 62.6, 52.4, 52.0, 51.3, 48.0, 28.9. HRMS (ESI) calcd for $C_{22}H_{26}BrN_4O_4S$ $[M+H]^+$ 521.0853, found 521.0849.

26bd: Methyl 5-(*tert*-butylamino)-3-((4-nitrophenyl)sulfonyl)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

Yellow solid, Yield: 0.147 g (89%), m.p.: 131-133 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, 2H, aromatic *C-H*, *J* = 8.6 Hz), 8.19 (d, 2H, aromatic *C-H*, *J* = 8.6 Hz), 7.16 (t, 1H, aromatic *C-H*, *J* = 7.4 Hz), 6.96 (d, 1H, aromatic *C-H*, *J* = 7.9 Hz), 6.84 (t, 1H, aromatic *C-H*, *J* = 7.4 Hz), 6.78 (d, 1H, aromatic *C-H*, *J* = 7.0 Hz), 5.13 (br s, 1H, N-*H*), 4.13 (d, 1H, sp^3 C-*H*, *J* = 7.1 Hz), 3.91-3.89 (m, 2H, sp^3 C-*H*), 3.42-3.38 (m, 1H, sp^3 C-*H*), 3.22 (s, 3H, sp^3 OC-*H*), 1.33 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 151.1, 148.2, 141.9, 140.6, 130.6, 129.4, 126.6, 124.5, 123.9, 121.3, 117.1, 62.9, 52.1, 52.0, 51.4, 48.2, 28.9. HRMS (ESI) calcd for $C_{22}H_{26}N_5O_6S$ $[M+H]^+$ 488.1599, found 488.1599.

26be: Methyl 5-(*tert*-butylamino)-3-(naphthalen-1-ylsulfonyl)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

Yellow solid, Yield: 0.149 g (89%), m.p.: 176-178 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.89 (d, 1H, aromatic *C-H*, *J* = 8.1 Hz), 8.36 (d, 1H, aromatic *C-H*, *J* = 6.8 Hz), 8.18 (d, 1H, aromatic *C-H*, *J* = 7.6 Hz), 8.02 (d, 1H, aromatic *C-H, J* = 7.7 Hz), 7.77 (t, 1H, aromatic *C-H, J* = 6.6 Hz), 7.66 (t, 1H, aromatic C-*H*, *J* = 7.0 Hz), 7.58 (t, 1H, aromatic C-*H*, *J* = 7.1 Hz), 7.12 (t, 1H, aromatic *C-H*, *J* = 6.5 Hz), 6.96 (d, 1H, aromatic *C-H*, *J* = 6.5 Hz), 6.86 (d, 2H, aromatic *C-H*, *J* = 7.4 Hz), 5.05 (d, 1H, aromatic *C-H*, *J* = 7.2 Hz), 4.46 (t, 1H, sp^3 C-*H*, *J* = 11.2 Hz), 4.32 (br s, 1H, *N-H*), 3.80 (d, 1H, sp^3 C-*H, J* = 11.7 Hz), 3.62 (s, 1H, sp^3 C-*H*), 3.19 (s, 3H, sp^3 OC-*H*), 0.72 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.5, 148.2, 142.3, 135.9, 134.3, 133.6, 130.2, 129.6, 129.5, 129.0, 128.9, 127.4, 126.9, 124.6, 124.3, 123.5, 120.9, 117.9, 63.3, 52.2, 51.9, 50.5, 46.6, 28.2. HRMS (ESI) calcd for $C_{26}H_{29}N_4O_4S$ $[M+H]^+$ 493.1904, found 493.1897.

26bf: Methyl 5-(*tert*-butylamino)-3-((4-fluorophenyl)sulfonyl)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

Off-white solid, Yield: 0.131 g (84%), m.p.: 131-133 ºC.^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03-7.99 (m, 2H, aromatic C-*H*), 7.27-7.23 (m, 2H, aromatic C-*H*), 7.14 (td, 1H, aromatic C-*H*, *J* = 8.8, 1.6 Hz), 6.96 (d, 1H, aromatic C-*H*, *J* = 7.8 Hz), 6.85-6.79 (m, 2H, aromatic C-H), 5.18 (br s, 1H, N-*H*), 4.17 (d, 1H, sp^3 C-*H, J* = 7.2 Hz), 3.90 (dd, 1H, sp^3 C-*H, J* = 12.1, 8.2 Hz), 3.83 (dd, 1H, sp^3 C-*H, J* = 12.1, 3.0 Hz), 3.39 (td, 1H, sp^3 C-*H, J* = 8.0, 3.0 Hz), 3.22

(s, 3H, sp^3 OC-*H*), 1.34 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 167.3, 165.2, 148.7, 132.0 (d, J_{C-F} = 9.6 Hz), 130.9, 129.3, 126.6, 123.7, 121.0, 117.3, 116.8 (d, J_{C-F} = 22.4 Hz), 62.6, 52.4, 52.0, 51.3, 48.0, 28.9. HRMS (ESI) calcd for $C_{22}H_{26}FN_4O_4S$ [M+H]$^+$ 461.1654, found 461.1644.

26ca: methyl 3-((4-methoxyphenyl)sulfonyl)-5-((2,4,4-trimethylpentan-2-yl)amino)-1,2,3,10b-tetrahydropyrazolo[1,5-c]quinazoline-1-carboxylate

Off-white solid, Yield: 0.159 g (89%), m.p.: 161-163 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, 2H, aromatic *C-H*, *J* = 8.8 Hz), 7.12 (t, 1H, aromatic *C-H*, *J* = 7.1 Hz), 7.00 (d, 2H, aromatic *C-H, J* = 8.8 Hz), 6.93 (d, 1H, aromatic *C-H,J* = 7.8 Hz), 6.80 (t, 1H, aromatic *C-H*, *J* = 7.3 Hz), 6.74 (d, 1H, aromatic *C-H,J* = 7.0 Hz), 5.39 (br s, 1H, N-*H*), 4.06 (d, 1H, sp^3 C-*H, J* = 7.4 Hz), 3.92-3.90 (m, 1H, sp^3 C-*H*), 3.88 (s, 3H, sp^3 OC-*H*), 3.77 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 3.1 Hz), 3.35 (td, 1H, sp^3 C-*H*, *J* = 8.0, 3.1 Hz), 3.21 (s, 3H, sp^3 C-*H*), 2.04 (d, 1H, sp^3 C-*H*, *J* = 14.7 Hz), 1.48-1.45 (m, 4H, sp^3 C-*H*), 1.45 (s, 3H, sp^3 C-*H*), 1.02 (s, 9H, sp^3 C-*H*).^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0, 164.3, 148.6, 142.4, 131.3, 129.1, 126.6, 126.0, 123.7, 120.6, 117.5, 114.7, 62.4, 55.8, 55.1, 52.7, 52.1, 51.9, 48.3, 31.6, 31.5, 28.4. HRMS (ESI) calcd for $C_{27}H_{37}N_4O_5S$ [M+H]$^+$ 529.2479, found 529.2465.

26cb: Methyl 3-((4-chlorophenyl)sulfonyl)-5-((2,4,4-trimethylpentan-2-yl)amino)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

Pale yellow solid, Yield: 0.161 g (89%), m.p.: 171-173 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, 2H, aromatic *C-H*, *J* = 5.8 Hz), 7.55 (d, 2H, aromatic *C-H*, *J* = 5.7 Hz), 7.14 (s, 1H, aromatic *C-H*), 6.95 (d, 1H, aromatic *C-H,J* = 5.8 Hz), 6.82-6.79 (m, 2H, aromatic *C-H*), 5.31 (br s, 1H, N-*H*), 4.09 (d, 1H, sp^3 C-*H, J* = 4.7 Hz), 3.90-3.81 (m, 2H, sp^3 C-*H*), 3.37 (s, 1H, sp^3 C-*H*), 3.22 (s, 3H, sp^3 OC-*H*), 2.02 (d, 1H, sp^3 C-*H, J* = 14.3 Hz), 1.49-1.40 (m, 7H, sp^3 C-*H*), 1.03 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 148.2, 142.3, 141.3, 133.3, 130.5, 129.9, 129.2, 126.6, 123.8, 120.8, 117.3, 62.6, 55.2, 52.4, 52.2, 51.9, 48.4, 31.6, 31.5, 29.7, 28.3. HRMS (ESI) calcd for $C_{26}H_{34}ClN_4O_4S$ [M+H]$^+$ 533.1984, found 533.1975.

26cc: Methyl 3-(benzylsulfonyl)-5-((2,4,4-trimethylpentan-2-yl)amino)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

White solid, Yield: 0.156 g (90%), m.p.: 143-145 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47-7.42 (m, 5H, aromatic *C-H*), 7.20 (td, 1H, aromatic *C-H*, *J* = 7.8, 1.2 Hz), 7.03 (d, 2H, aromatic *C-H*, *J* = 7.8 Hz), 7.00 (d, 2H, aromatic *C-H*, *J* = 7.3 Hz), 6.91 (t, 1H, aromatic *C-H*, *J* = 7.32 Hz), 5.53 (br s, 1H, N-*H*), 5.07 (d, 1H, sp^3 C-*H*, *J* = 7.7 Hz), 4.57 (d, 1H, sp^3 C-*H*, *J* = 13.3 Hz), 4.40 (d, 1H, sp^3 C-*H*, *J* = 13.3 Hz), 4.05 (dd, 1H, sp^3 C-*H, J* = 12.2, 8.6 Hz), 3.72 (dd, 1H, sp^3 C-*H*, *J* = 12.3, 3.6 Hz), 3.55 (td, 1H, sp^3 C-*H*, *J* = 8.1, 3.7 Hz), 3.25 (s, 3H, sp^3 OC-*H*), 2.11 (d, 1H, sp^3 C-*H, J* = 14.3 Hz), 1.59 (d, 1H, sp^3 C-*H*, *J* = 14.8 Hz), 1.53 (s, 6H, sp^3 C-*H*), 1.06 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 148.2, 142.2, 131.0, 129.3, 129.2, 129.1, 126.9, 126.4, 123.8, 121.2, 117.8, 63.4, 55.6, 54.7, 52.6, 51.99, 51.96, 47.5, 31.6, 29.6, 28.3. HRMS (ESI) calcd for $C_{27}H_{37}N_4O_4S$ [M+H]$^+$ 513.2530, found 513.2525.

26cd: Methyl 3-(octylsulfonyl)-5-((2,4,4-trimethylpentan-2-yl)amino)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

White solid, Yield: 0.167 g (92%), m.p.: 137-138 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (t, 1H, aromatic *C-H*, *J* = 7.4 Hz), 7.00 (d, 2H, aromatic *C-H*, *J* = 8.9 Hz), 6.89 (t, 1H, aromatic *C-H*, *J* = 7.3 Hz), 5.47 (br s, 1H, N-*H*), 5.03 (d, 1H, sp^3 C-*H,J* = 7.8 Hz), 4.07 (dd, 1H, sp^3 C-*H*, *J* = 12.3, 8.5 Hz), 3.64 (dd, 1H, sp^3 C-*H*, *J* = 12.3, 3.7 Hz), 3.58 (td, 1H, sp^3 C-*H,J* = 8.1, 3.8 Hz), 3.25 (s, 3H, sp^3 OC-*H*), 2.20 (d, 1H, sp^3 C-*H*, *J* = 14.8 Hz), 1.91 (quint, 2H, sp^3 C-*H*, *J* = 7.8 Hz), 1.59 (d, 1H, sp^3 C-*H*, *J* = 14.8 Hz), 1.52 (d, 6H, sp^3 C-*H*, *J* = 3.6 Hz), 1.47-1.42 (m, 2H, sp^3 C-*H*), 1.32-1.27 (m, 10H, sp^3 C-*H*), 1.07 (s, 9H, sp^3 C-*H*), 0.88 (t, 3H, sp^3 C-*H*, *J* = 6.4 Hz).^{13}C NMR (125 MHz, $CDCl_3$): δ 171.3, 148.2, 142.1, 129.2, 127.0, 123.8, 121.2, 117.9, 63.1, 55.5, 52.4, 51.9, 51.8, 49.2, 46.5, 31.7, 31.6, 29.8, 28.98, 28.94, 28.53, 28.4, 22.7, 22.6, 14.0. HRMS (ESI) calcd for $C_{28}H_{47}N_4O_4S$ [M+H]$^+$ 535.3313, found 535.3309.

26ce: Methyl 3-tosyl-5-((2,4,4-trimethylpentan-2-yl)amino)-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate

Yellow solid, Yield: 0.155 g (89%), m.p.: 132-134 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.35 (d, 2H, aromatic *C-H*, *J* = 8.1 Hz), 7.12 (td, 1H, aromatic *C-H*, *J* = 8.3, 1.2 Hz), 6.93 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 6.79 (t, 1H, aromatic *C-H*, *J* = 6.7 Hz), 6.73 (d, 1H, aromatic *C-H*, *J* = 6.7 Hz), 5.36 (br s, 1H, N-*H*), 4.06 (d, 1H, sp^3 C-*H*, *J* = 7.5 Hz), 3.93 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 8.4 Hz), 3.77 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 3.3 Hz), 3.34 (td, 1H, sp^3 C-*H*, *J* = 8.1, 3.3 Hz), 3.21 (s, 3H, sp^3 OC-*H*), 2.46 (s, 3H, sp^3 C-*H*), 2.02 (d, 1H, sp^3 C-*H*, *J* = 14.7 Hz), 1.48 (d, 1H, sp^3 C-*H*, *J* = 14.7 Hz), 1.45 (s, 3H, sp^3 C-*H*), 1.39 (s, 3H, sp^3 C-*H*), 1.02 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 148.5, 145.5, 142.4, 131.9, 130.1, 129.1, 129.0, 126.6, 123.7, 120.6, 117.5, 62.4, 55.1, 52.6, 52.1, 51.9, 48.3, 31.6, 31.5, 29.7, 28.3, 21.7. HRMS (ESI) calcd for $C_{27}H_{37}N_4O_4S$ $[M+H]^+$ 513.2530, found 513.2515.

26da: Ethyl 5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
White solid, Yield: 0.140 g (88%), m.p.: 153-155 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.35 (d, 2H, aromatic *C-H*, *J* = 8.1 Hz), 7.12 (td, 1H, aromatic *C-H*, *J* = 8.3, 2.3 Hz), 6.92 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 6.81-6.77 (m, 2H, aromatic *C-H*), 5.20 (br s, 1H, N-*H*), 3.90 (dd, 1H, sp^3 C-*H*, *J* = 8.2, 7.2 Hz), 3.81 (dd, 1H, sp^3 C-*H*, *J* = 12.1, 3.0 Hz), 3.73-3.63 (m, 2H, sp^3 C-*H*), 3.34 (td, 1H, sp^3 C-*H*, *J* = 7.9, 3.0 Hz), 2.46 (s, 3H, sp^3 C-*H*), 1.32 (s, 9H, sp^3 C-*H*), 0.74 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 148.9, 145.5, 142.7, 131.9, 130.1, 129.2, 129.1, 126.7, 123.7, 120.7, 117.7, 62.4, 61.2, 52.2, 51.2, 48.0, 28.8, 21.7, 13.3. HRMS (ESI) calcd for $C_{24}H_{31}N_4O_4S$ $[M+H]^+$ 471.2061, found 471.2059. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^{1}H and ^{13}C NMR spectra. The isolated yield has been modified to 76 %.

26db: Butyl 5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate:
White solid, Yield: 0.158 g (93%), m.p.: 137-138 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.35 (d, 2H, aromatic *C-H*, *J* = 8.1 Hz), 7.13 (m, 1H, aromatic *C-H*, *J* = 8.5, 1.6 Hz), 6.93 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz) 6.81-6.76 (m, 2H, aromatic *C-H*), 5.19 (br s, 1H, *N-H*), 4.13 (t, 1H, sp^3 C-*H*, *J* = 7.1 Hz), 4.02 (t, 2H, sp^3 C-*H*, *J* = 6.6 Hz), 3.91-3.83 (m, 3H, sp^3 C-*H*), 3.80 (d, 1H, sp^3 C-*H*, *J* = 12.1, 2.9 Hz), 3.35 (td, 1H, sp^3 C-*H*, *J* = 7.9, 2.9 Hz), 2.46 (s, 3H, sp^3 C-*H*), 2.19-2.16 (m, 1H, sp^3 C-*H)*, 1.98-1.94 (m, 1H, sp^3 C-*H)*, 1.57 (quintet, 1H, sp^3 C-*H*, *J* = 6.8 Hz), 1.31 (s, 9H, sp^3 C-*H*), 0.93 (t, 3H, sp^3 C-*H*, *J* = 7.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 148.9, 145.6, 142.6, 131.9, 130.1, 129.2, 129.1, 126.8, 123.7, 120.7, 117.7, 62.4, 60.3, 52.0, 51.3, 47.9, 30.5, 28.8, 21.7, 19.0, 13.7.

26dc: *tert*-butyl 5-(tert-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
White solid, Yield: 0.155 g (92%), m.p.: 153-155 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84, (d, 2H, aromatic *C-H*, *J* = 8.1 Hz), 7.34 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.13 (td, 1H, aromatic *C-H*, *J* = 8.3, 2.3 Hz), 6.92 (d, 1H,aromatic *C-H*, *J = 7.8* Hz), 6.82-6.78 (m, 1H, aromatic *C-H*), 5.21 (br s, 1H, N-*H*), 4.10 (d, 1H, sp^3 C-*H*, *J* = 7.2 Hz), 3.82-3.81 (m, 2H, sp^3 C-*H*), 3.22 (td, 1H, sp^3 C-*H*, *J* = 6.9, 4.3 Hz), 2.46 (s, 3H, sp^3 C-*H*), 1.31 (s, 9H, sp^3 C-*H*), 0.98 (s, 3H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5, 149.0, 145.4, 142.9, 131.9, 130.0, 129.2, 128.9, 127.0, 123.7, 120.5, 118.2, 81.5, 62.3, 52.4, 51.2, 48.0, 28.8, 27.2, 21.7. HRMS (ESI) calcd for $C_{26}H_{35}N_4O_4S$ $[M+H]^+$ 499.2374, found 499.2367.

26dd: Phenyl 5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1 carboxylate
Pale yellow solid, Yield: 0.155 g (88%), m.p.: 177-179 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.38 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.21-7.15 (m, 3H, aromatic *C-H*), 7.08 (t, 1H, aromatic *C-H*, *J* = 7.3 Hz), 7.02 (d, 1H, aromatic *C-H*, *J* = 7.4 Hz), 6.91 (d, 1H, aromatic *C-H*, *J* = 6.4 Hz), 6.83 (td, 1H, aromatic *C-H*, *J* = 7.3, 1.0 Hz), 6.43 (d, 2H, aromatic *C-H*, *J = 7.6 Hz*), 5.20 (br s, 1H, N-*H*), 4.35 (d, 1H, sp^3 C-*H*, *J* = 7.3 Hz), 4.06 (dd, 1H, sp^3 C-*H*, *J* = 12.3, 8.4 Hz), 3.92 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 3.0 Hz), 3.62 (td, 1H, sp^3 C-*H*, *J* = 8.2, 3.0 Hz), 2.48 (s, 3H, sp^3 C-*H*), 1.22 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.6, 150.0, 148.8, 145.7, 142.8, 131.9, 130.2, 129.4, 129.2, 129.1, 127.0, 125.8, 123.9, 121.2, 121.1, 117.3, 62.5, 52.3, 51.2, 48.0, 28.8, 21.7. HRMS (ESI) calcd for $C_{28}H_{31}N_4O_4S$ $[M+H]^+$ 519.2061, found 519.2059.

26de: Benzyl-5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1- carboxylate
Off-white solid, Yield: 0.159 g (88%), m.p.: 148-150 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, 2H, aromatic *C-H*, *J* = 7.9 Hz), 7.27 (d, 2H, aromatic *C-H*, *J* = 7.8 Hz), 7.18-7.17 (m, 3H, aromatic *C-H*), 7.05 (t, 1H, aromatic *C-H*, *J* = 6.1 Hz), 6.87-6.85 (m, 3H, aromatic *C-H*), 6.72-6.69 (m, 2H, aromatic *C-H*), 5.14 (br s, 1H, N-*H*), 4.60 (d, 1H, sp^3 C-*H*, *J* = 12.1 Hz), 4.40 (d, 1H, sp^3 C-*H*, *J* = 12.1 Hz), 4.07 (d, 1H, sp^3 C-*H*, *J* = 7.1 Hz), 3.83 (dd, 1H, sp^3 C-*H*, *J* = 11.9, 8.4 Hz), 3.75 (dd, 1H, sp^3 C-*H*, *J* = 11.8, 2.3 Hz), 3.31 (t, 1H, sp^3 C-*H*, *J* = 7.1 Hz), 2.38 (s, 3H, sp^3 C-*H*), 1.24 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 148.9, 145.6, 142.6, 134.9, 131.9, 130.1, 129.2, 129.1, 128.5, 128.3, 128.2, 126.7, 123.9, 120.8, 117.6, 67.1, 62.4, 52.2, 51.3, 48.2, 28.8, 21.7. HRMS (ESI) calcd for $C_{29}H_{33}N_4O_4S$ $[M+H]^+$ 533.2217, found 533.2211.

26ea: 1-(5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazolin-1-yl)ethan-1-one
Off-white solid, Yield: 0.134 g (79%), m.p.: 113-115 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.34 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.16 (td, 1H, aromatic *C-H*, *J* = 8.9, 1.6 Hz), 6.95 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 6.89 (dd, 1H, aromatic *C-H*, *J* = 7.4, 1.4 Hz), 6.84 (td, 1H, aromatic *C-H*, *J* = 7.3, 1.0 Hz), 5.22 (br s, 1H, N-*H*), 4.12 (t, 1H, sp^3 C-*H*, *J* = 7.7 Hz), 3.86 (dd, 1H, sp^3 C-*H*, *J* = 11.5, 1.9 Hz), 3.66 (dd, 1H, sp^3 C-*H*, *J* = 11.5, 7.6 Hz), 3.49 (td, 1H, sp^3 C-*H*, *J* = 7.4, 1.7 Hz), 2.46 (s, 3H, sp^3 C-*H*), 1.56 (s, 3H, sp^3 C-*H*),

1.31 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.7, 149.4, 145.4, 142.8, 131.8, 130.0, 129.6, 129.2, 126.2, 124.2, 120.9, 117.7, 62.6, 58.0, 51.3, 47.2, 30.5, 28.7, 21.7. HRMS (ESI) calcd for $C_{23}H_{29}N_4O_3S$ [M+H]$^+$ 441.1955 found 441.1951. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^{1}H and ^{13}C NMR spectra. The isolated yield has been modified to 79 %.

26fa: Diethyl 5-(*tert*-butylamino)-3-tosyl-1,2,3,10b-tetrahydropyrazolo[1,5-*c*]quinazoline-1,2-dicarboxylate
White solid, Yield: 0.156 g (70%), m.p.: 133-135 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, 2H, aromatic *C-H*, *J* = 8.2 Hz), 7.37 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.12 (td, 1H, aromatic *C-H*, *J* = 8.2, 1.2 Hz), 6.90 (d, 1H, aromatic *C-H*, *J* = 7.9 Hz), 6.85-6.79 (m, 2H, aromatic *C-H*), 5.42 (br s, 1H, N-*H*), 4.96 (d, 1H, sp^3 C-*H*, *J* = 8.8 Hz), 4.57 (d, 1H, sp^3 C-*H*, *J* = 6.8 Hz), 4.21 (q, 2H, sp^3 C-*H*, *J* = 7.1 Hz), 3.80 (dd, 1H, sp^3 C-*H*, *J* = 8.7, 7.0 Hz), 3.68-3.63 (m, 2H, sp^3 C-*H*), 2.47 (s, 3H, sp^3 C-*H*), 1.22 (s, 9H, sp^3 C-*H*), 0.87 (t, 3H, sp^3 C-*H*, *J* = 6.3 Hz), 0.67 (t, 3H, sp^3 C-*H*, *J* = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.8, 167.8, 148.9, 145.6, 143.0, 132.4, 130.1, 129.4, 129.2, 126.7, 123.8, 120.6, 117.0, 63.8, 62.0, 61.2, 60.7, 55.6, 51.0, 28.6, 21.7, 14.1, 13.3. HRMS (ESI) calcd for $C_{27}H_{35}N_4O_6S$ [M+H]$^+$ 543.2272, found 543.2265. Despite repeated drying on high vacuum, a significant solvent peak is observed in ^{1}H and ^{13}C NMR spectra. The isolated yield has been modified to 70 %.

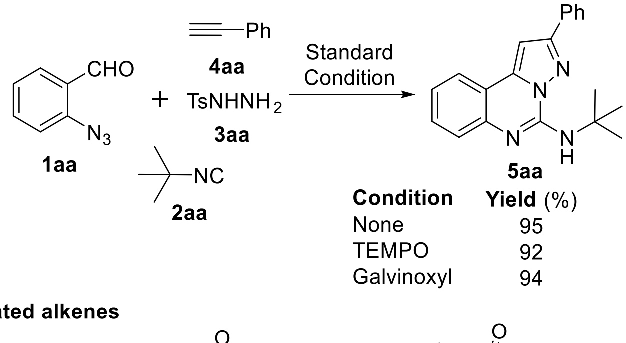
26ga: 5-(*tert*-butylamino)-3-((4-fluorophenyl)sulfonyl)-1,2,3,10b-tetrahydropyrazolo[1,5 *c*]quinazoline-1-carbonitrile
Yellow solid, Yield: 0.120 g (83%), m.p.: 179-181 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02-7.99 (m, 2H, aromatic *C-H*), 7.29-7.25 (m, 3H, aromatic *C-H*), 7.11 (d, 1H, aromatic *C-H*, *J* = 7.8 Hz), 6.91 (t, 1H, aromatic *C-H*, *J* = 7.3 Hz), 6.81 (d, 1H, aromatic *C-H*, *J* = 7.3 Hz), 5.10 (brs, 1H, N-*H*), 4.08 (d, 1H, sp^3 C-*H*, *J* = 5.0 Hz), 4.03 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 8.9 Hz), 3.77 (dd, 1H, sp^3 C-*H*, *J* = 12.2, 1.7 Hz), 3.51 (t, 1H, sp^3 C-*H*, *J* = 6.0 Hz), 1.34 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4 (d, J_{C-F} = 257.5 Hz), 147.5, 142.3, 132.1 (d, J_{C-F} = 11.25 Hz), 130.3, 125.9, 124.6, 121.8, 117.2, 116.9, 116.8, 116.2, 61.9, 51.6, 49.2, 38.9, 28.7. ^{19}F NMR (470 MHz, $CDCl_3$): δ -100.77. HRMS (ESI) calcd for $C_{21}H_{23}FN_5O_2S$ [M+H]$^+$ 428.1551, found 428.1540.

26ha: Methyl 3-benzoyl-5-(*tert*-butylamino)-1,2,3,10-b-tetrahydropyrazolo[1,5-*c*]quinazoline-1-carboxylate
Colorless oil, Yield: 0.110 g (80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, 2H, aromatic *C-H*, *J* = 7.5 Hz), 7.49-7.45 (m, 1H, aromatic *C-H*), 7.38 (t, 2H, aromatic *C-H*, *J* = 7.6 Hz), 7.16 (t, 1H, aromatic *C-H*, *J* = 7.4 Hz), 7.00 (d, 1H, aromatic *C-H*, *J* = 7.7 Hz), 6.94 (d, 1H, aromatic *C-H*, *J* = 7.2 Hz), 6.85 (t, 1H, aromatic *C-H*, *J* = 7.2 Hz), 5.09 (br s, 1H, N-*H*), 4.69 (s, 1H, sp^3 C-*H*), 4.50 (d, 1H, sp^3 C-*H*, *J* = 8.0 Hz), 3.66 (dd, 1H, sp^3 C-*H*, *J* = 11.5, 4.2 Hz), 3.53 (q, 1H, sp^3 C-*H*, *J* = 8.4 Hz), 3.23 (s, 3H, sp^3 OC-*H*), 1.47 (s, 9H, sp^3 C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.7, 171.4, 148.8, 142.6, 132.6, 131.7, 130.5, 129.2, 128.6, 128.2, 126.7, 123.9, 121.1, 63.9, 51.8, 51.2, 46.2, 30.9, 29.2. HRMS (ESI) calcd for $C_{23}H_{27}N_4O_3$ [M+H]$^+$ 407.2078, found 407.2068.

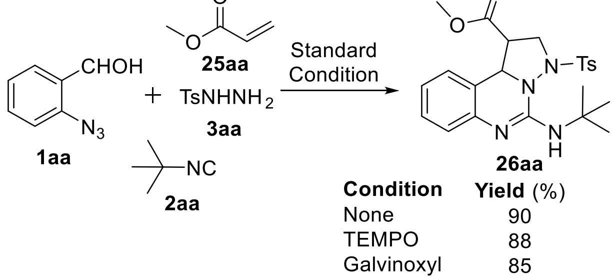
S5. Control Experiments for Elucidating Mechanism of 4-CR

S5.1. Radical Trap Experiment

A) For alkynes



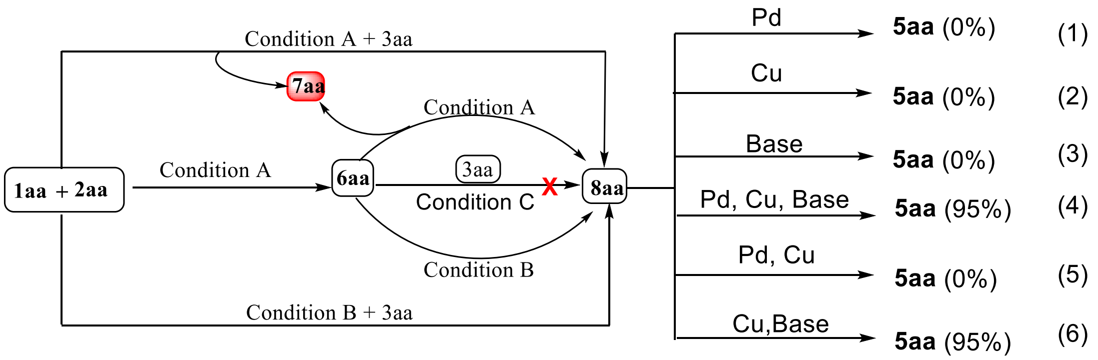
B) For activated alkenes



PROCEDURE: The reactions were been carried out as per the protocol reported in section S3 for alkynes and acrylates in the presence of either TEMPO or Galvinoxyl (free radical scavenger). The products were purified by silica-gel column chromatography (EtOAc: Hexane) to produce **5aa** and **26aa** respectively. Radical scavengers did not alter the reaction pathway suggesting the involvement of a non-radical pathway (A & B).

S5.2 Evolution of species

Initially, a mixture of **1aa** and **2aa** was reacted under condition A leading to the formation of carbodiimide **6aa** that was characterized by ^{1}H NMR. The intermediate **6aa** was highly unstable and immediately converted to the corresponding urea upon prolonged exposure to air. Hence, it was generated *in situ*. Interestingly, **6aa**, generated in situ, or a mixture of **1aa** and **2aa** produced **8aa**, characterized by X-ray crystallographic studies (refer section S8), upon reacting with **3aa**, albeit in a low yield of 38%. On careful analysis of these two reaction mixtures, we observed a side product urea **7aa**, which was characterized by X-ray crystallographic studies (section S8). However, the yield was improved substantially after using 4 Å MS (condition B). Both these steps needed Palladium as a catalyst as **6aa** failed to produce **8aa** under the condition C. The conversion of **8aa** to **5aa** was dependent on both addition of second transition metal (Either Ag and Cu) and a suitable base.



Condition A: 7.5 mol% $Pd(OAc)_2$, toluene, rt; Condition B: 7.5 mol% $Pd(OAc)_2$, 4 Å MS, toluene, rt, Condition C: 4 Å MS, toluene, rt

6aa: 2-(((*tert*-butylimino)methylene)amino)benzaldehyde
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.52 (s, 1H, aldehydic *C-H*), 7.84 (d, 1H, aromatic *C-H*, *J* = 7.7, 1.4 Hz), 7.51 (td, 1H, aromatic *C-H*, *J* = 8.0, 1.5 Hz), 7.25 (d, 1H, aromatic *C-H*, *J* = 8.0 Hz), 7.18 (t, 1H, aromatic *C-H*, *J* = 7.5 Hz), 1.45 (s, 9H, sp^{3} C-*H*).

7aa: (E)-*N*'-(2-(3-(*tert*-butyl)ureido)benzylidene)-4-methylbenzenesulfonohydrazide
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.58 (s, 1H, aldehydic *C-H*), 8.32 (d, 1H, aromatic *C-H*, *J* = 7.7 Hz), 7.73-7.71 (m, 3H, aromatic *C-H*), 7.23-7.19 (m, 3H, aromatic *C-H*), 6.98 (d, 1H, aromatic *C-H*, *J* = 7.0 Hz), 6.81 (t, 1H, aromatic *C-H*, *J* = 5.8 Hz), 5.02 (br s, 1H, N-*H*), 2.32 (s, 3H, sp^{3} C-*H*), 1.45 (s, 9H, sp^{3} C-*H*).

8aa: 2-(*tert*-butylamino)quinazolin-3-ium-3-yl)(tosyl)amide
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.40 (s, 1H, aromatic *C-H*), 7.84 (t, 1H, aromatic *C-H*, *J* = 7.3 Hz), 7.76 (d, 1H, aromatic *C-H*, *J* = 8.0 Hz), 7.60 (d, 1H, aromatic *C-H*, *J* = 8.5 Hz), 7.53 (d, 2H, aromatic *C-H*, *J* = 8.0 Hz), 7.38 (t, 1H, aromatic *C-H*, *J* = 7.4 Hz), 7.21 (s, 1H, aromatic *C-H*), 7.17 (d, 2H, aromatic *C-H*, *J* = 7.8 Hz), 2.36 (s, 3H, sp^{3} C-*H*), 1.18 (s, 9H, sp^{3} C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.8, 150.3, 148.2, 141.7, 141.1, 137.9, 129.6, 128.7, 126.1, 126.0, 124.9, 117.2, 52.2, 27.6, 21.3.

9aa: *N*-(*tert*-butyl)quinazolin-2-amine
Yellow solid, Yield: 0.037 g (55%) , m.p.: 79-81 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H, aromatic *C-H*), 7.67-7.62 (m, 2H, aromatic *C-H*), 7.57 (d, 1H, aromatic *C-H*, *J* = 8.3 Hz), 7.20 (td, 1H, aromatic *C-H*, *J* = 7.8, 0.9 Hz), 5.29 (br s, 1H, N-*H*), 1.53 (s, 9H, sp^{3} C-*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4, 159.1, 151.9, 133.9, 127.4, 125.8, 122.3, 119.8, 51.1, 28.9.

S5.3 Chemical Kinetics of 4-CR

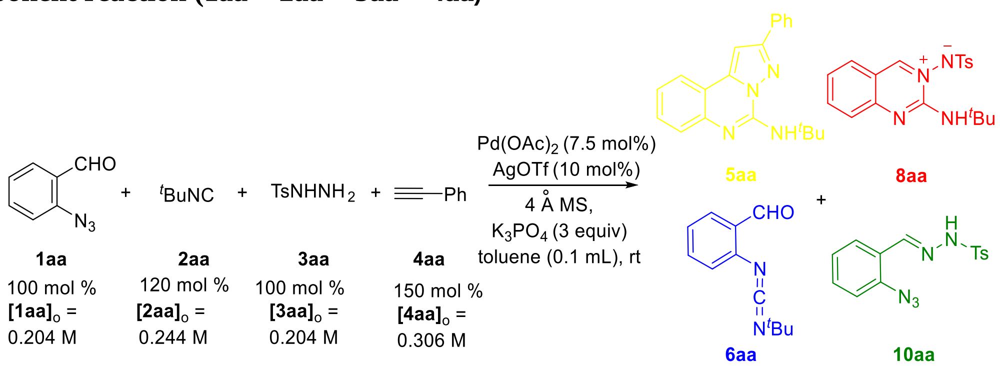
General Methods: Chemical kinetic study was performed by monitoring the reaction mixture using ^{1}H NMR (500 MHz) spectroscopy with dibenzyl ether as the internal standard. The spectra were processed and integrated with MestReNova (8.0.2) and the data was processed in Excel (2010). The graphs were plotted with OriginPro (8.6). The reported initial rates are the average of three independent experiments.

General Procedure: A reaction vial (10 mL) was charged with 2-azidobenzaldehyde (1.0 equiv), *tert*-butylisocyanide (1.2 equiv), $Pd(OAc)_2$ (7.5 mol %,), 4 Å MS, $TsNHNH_2$ (1 equiv), phenyl acetylene (1.5 equiv), AgOTf (10 mol%), K_3PO_4 (3.0 equiv) and toluene (0.5 mL). The reaction mixture was stirred at room temperature for the particular time interval. Then, the reaction mixture was filtered through a bed of Celite® and the solution so obtained was evaporated under reduced pressure. The mixture was then transferred into to a standard 5 mm bore NMR tube and subjected to ^{1}H NMR (500 MHz) spectroscopy using dibenzyl ether (25 μL) as the internal standard.

Table S6. Characteristic ^{1}H NMR resonances used for monitoring chemical species.

Species	δ
1aa	10.36
5aa	7.19
8aa	9.40
6aa	10.52
10aa	8.01

S5.3.1 Four-component reaction (1aa + 2aa + 3aa + 4aa)



Initial rate for formation of **6aa**: 5.9 mM min^{-1} (average of three experiments)
Initial rate for formation of **8aa**: 6.0 mM min^{-1} (average of three experiments)
Initial rate for formation of **10aa**: 1.43 mM min^{-1} (average of three experiments)

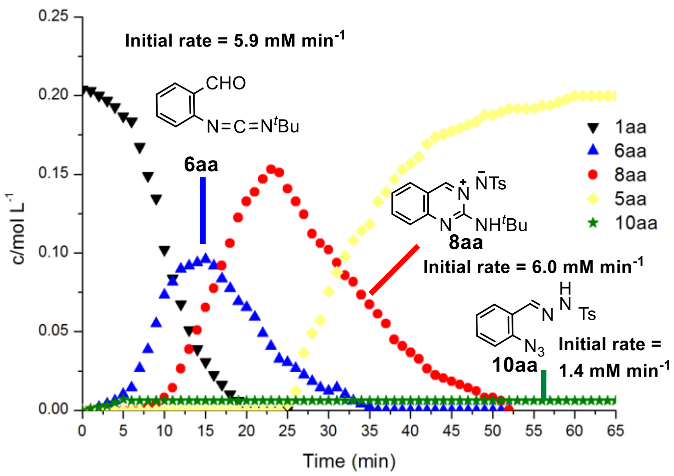
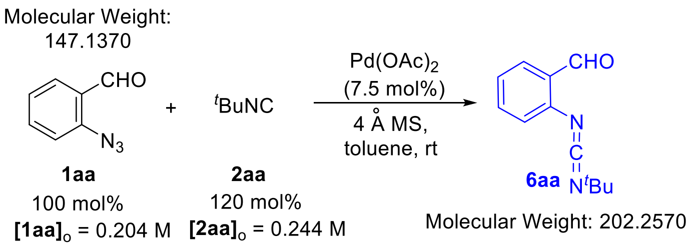


Figure S1. ^{1}H NMR spectroscopy profile of domino four CR

S5.3.2 Two-component reaction (1aa + 2aa)

Procedure: Same as section 5.3 with 2-azidobenzaldehyde (1.0 equiv), *tert*-butylisocyanide (1.2 equiv), $Pd(OAc)_2$ (7.5 mol%) and 4 Å MS in toluene.



Initial rate for formation of **6aa**: 9.8 mM min^{-1} (average of two experiments)

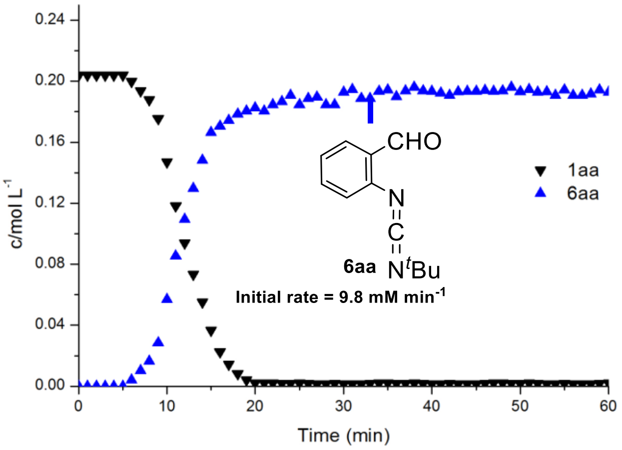
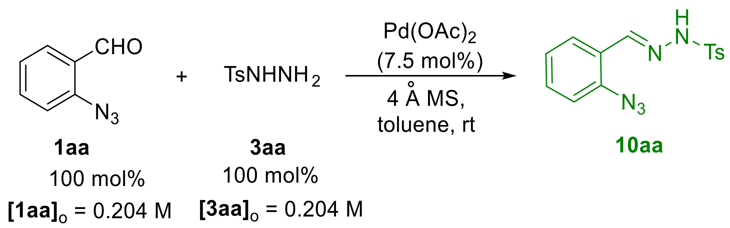


Figure S2. ^{1}H NMR spectroscopy profile of two CR (**1aa** + **2aa**)

S5.3.3 Two-component reaction (1aa + 3aa)

Procedure: Same as section 5.3 with 2-azidobenzaldehyde (1.0 equiv), tosyl hydrazide (1.0 equiv), $Pd(OAc)_2$ (7.5 mol%) and 4 Å MS in toluene.



Initial rate for formation of **10aa**: 5.9 mM min^{-1} (average of two experiments)

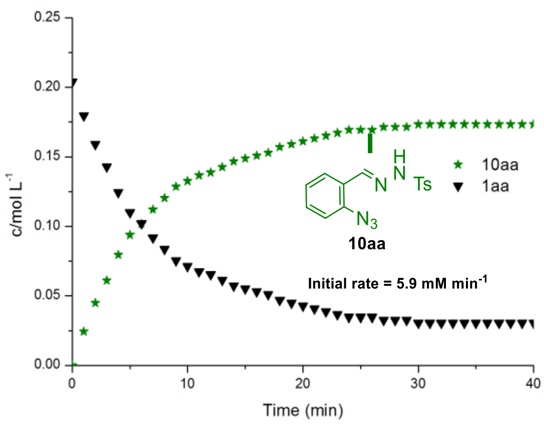
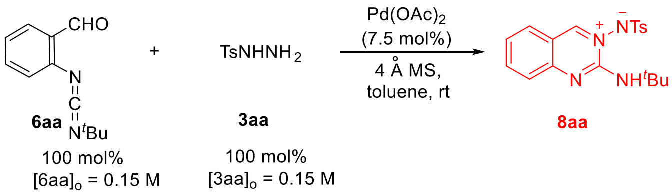


Figure S3. ^{1}H NMR spectroscopy profile of two CR (**1aa** + **3aa**)

S5.3.4 Two-component reaction (6aa + 3aa)

Procedure: Same as section 5.3 with carbodiimide (1.0 equiv), tosyl hydrazide (1 equiv), $Pd(OAc)_2$ (7.5 mol%) and 4 Å MS in toluene.



Initial rate for formation of **8aa**: 47.5 mM min^{-1} (average of two experiments)

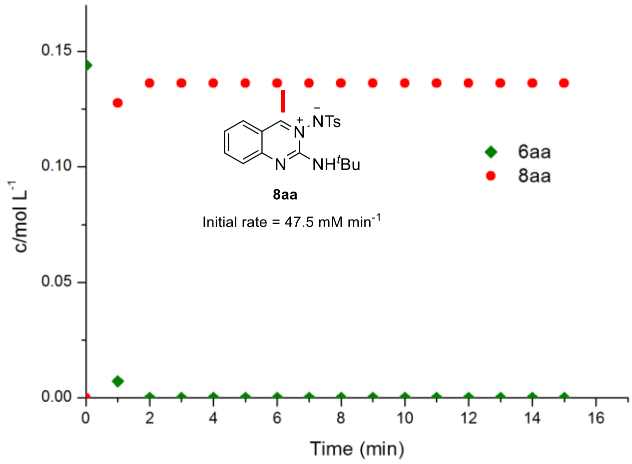
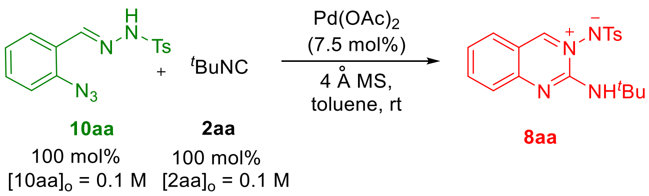


Figure S4. ^{1}H NMR spectroscopy profile of two CR (**6aa** + **3aa**)

S5.3.5. Two-component reaction (10aa + 2aa)

Procedure: Same as section 5.3 with hydrazone (1.0 equiv), *tert*.-butyl isocyanide (1 equiv), $Pd(OAc)_2$ (7.5 mol%) and 4 Å MS in toluene.



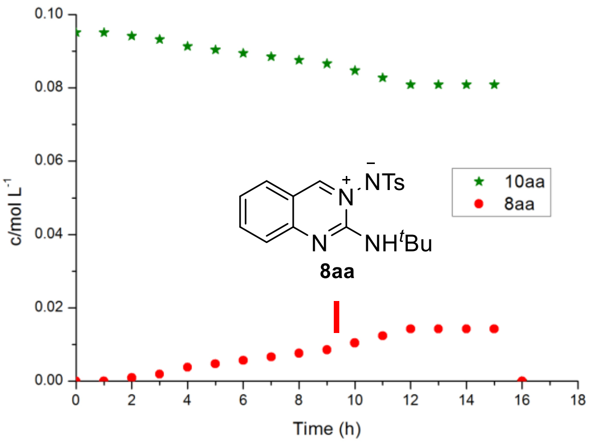


Figure S5. ^{1}H NMR spectroscopy profile of two CR (**10aa** + **2aa**)

S5.3.6. Result and discussion for kinetic studies

Two plausible routes can be drawn for the generation of the intermediate **8aa**:

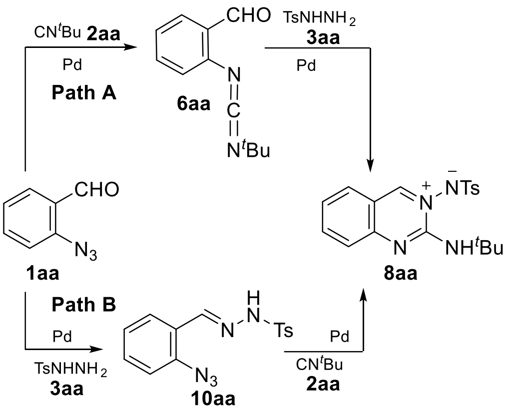
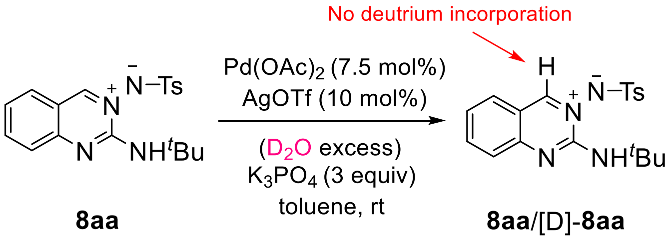


Figure S6: Proposed reaction pathways for the formation of **8aa**

To probe whether the formation of **8aa** could proceed through both path A and path B, or whether one of these pathways was dominating, kinetic studies of 4CR were carried out by monitoring the reaction progress with ^{1}H NMR spectroscopy, indicated that the formation of **6aa (1aa + 2aa)** was four times faster than the formation of **10aa (1aa + 3aa)**. Each coupling step of the process then examined individually by two-component coupling reaction of **1aa** and **2aa** *via* Pd-catalyzed azide-isocyanide denitrogenative coupling reaction for the formation of **6aa** proceeds at comparable rates in both 4-CRs (5.9 mM min^{-1}, the blue line in Fig. S1) and individual 2-CR (9.8 mM min^{-1}, Fig. S2). In contrast, condensation of **1aa** and tosyl hydrazide **3aa** for the formation of **10aa** proceeded faster in the individual 2-CR (5.9 mM min^{-1}, Fig. S3) compared that of the 4-CR (1.4 mM min^{-1}, the green line in Fig. 3a). The reaction of carbodiimide **6aa** with **3aa** exhibited a very rapid conversion to **8aa** (Fig. S4). In addition, the azide-isocyanide denitrogenative coupling of **10aa** and **2aa** was extremely sluggish and unproductive (furnished **8aa** in 15% yields even after prolonging the reaction, Fig. S5). Thus kinetic profiling and isolation of reaction intermediates unequivocally ruled out path B for the formation of **8aa**. The sluggish rate of reaction of the competing concurrent catalytic processes, such as path B, ensured the time-resolution of the relay catalytic process.

S5.4 Experiments on H/D Exchange



8aa (30 mg, 1 equiv), $Pd(OAc)_2$ (2 mg, 7.5 mol%), AgOTf (7.6 mg, 10 mol%), K_3PO_4 (51.5 mg, 3.0 equiv), D_2O (5 equiv) and toluene were added to a 20 mL Schlenk tube. The mixture was stirred at rt for 1 h. The reaction mixture was diluted with ethyl acetate (15 mL) and evaporated under vacuum. The crude product was purified by column chromatography to afford the product. These results revealed that no deuterium atom was incorporated at the C-4 position of the intermediate **8aa**. The result indicates that the reaction is not going through C-H activation.

S5.4.1 Result and discussion

For the conversion of the azomethine imine **8aa** to the title compound **5aa**, a possibility of three reaction pathways emerged as depicted in Fig. S7: (1) dipolar cycloaddition; (2) C-H activation alkynylation; (3) direct alkynylation.

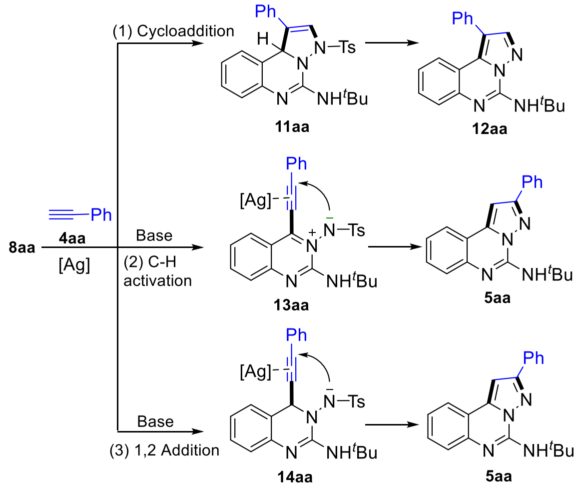
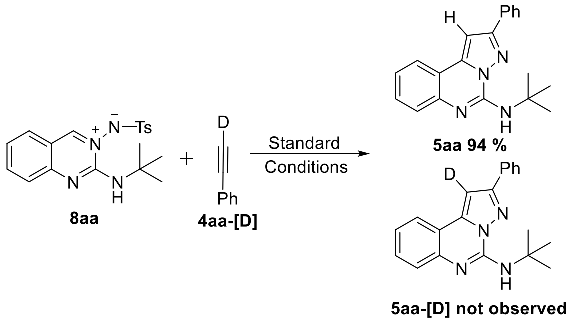


Figure S7: Three plausible pathways for the reaction of azomethine imine **8aa** and alkyne and their control experiments

The regiochemical outcome of 4-CR and H/D scrambling experiment (Section S5.4) ruled out dipolar cycloaddition and C-H activation/alkynylation routes, respectively. Hence control experiments supported a base-mediated direct alkynylation as a possible route for the conversion of the azomethine imine **8aa** to **5aa**.

S5.5 Experiment with labelled substrate

To the mixture of **8aa** (30 mg, 1 equiv), **4aa-[D]** (12.5 mg, 1.5 equiv), $Pd(OAc)_2$ (2 mg, 7.5 mol%), AgOTf (7.6 mg, 10 mol%) and K_3PO_4 (51.5 mg, 3.0 equiv) in a 20 mL Schlenk tube was added toluene. The mixture was stirred at rt for 1 h. The reaction mixture was diluted with ethyl acetate (15 mL) and evaporated under vacuum. The crude product, so obtained, was purified by column chromatography to afford 24 mg (94%) of the product. No deuterium incorporation was observed, which implicate that AgOTf activated alkyne by converting it to acetylide, which undergoes 1,2 addition across azomethine imine of **8aa**.



No deuterium incorporation in **5aa** was observed when the deuterated substrate (ethynyl-*d*)-benzene was reacted with **8aa**. This observation supports the formation of acetylide during the reaction.

S5.6: Proposed Reaction Mechanism

Based on experimental studies and literature precedence,[2] a plausible mechanism for the four-component reaction mediated by three independent catalytic cycles of Pd- and Ag-metals can be proposed as depicted in Fig. S8. **1aa** and **2aa** enters the catalytic cycle A of palladium metal and furnishes a coordination complex **15**. Extrusion of dinitrogen from **15** generates nitrene **16**, which triggers concerted intramolecular isocyanide-transfer on nitrene to produce the carbodiimide **6aa**. The reactive carbodiimide enters catalytical cycle B of palladium metal, where its aldehydic functional group condenses with **3aa** to furnish the hydrazone **19**[3] that further undergoes *6-exo-dig* cyclization to produce an air-stable azomethine imine **8aa**. The catalytic cycle C embarks with the formation of acetylide in the presence of base and Ag-salt. The acetylide undergoes 1,2-addition across azomethine imine **8aa** to produce **22**, which converts to **23** by an intramolecular attack of the amide on the alkyne to produce the five-membered ring. Subsequently, detosylative aromatization generates **24**. Protonolysis of the C-Ag bond upon aqueous workup generates the title compound **5aa**, explaining the lack or deuterium incorporation in the labelling studies.

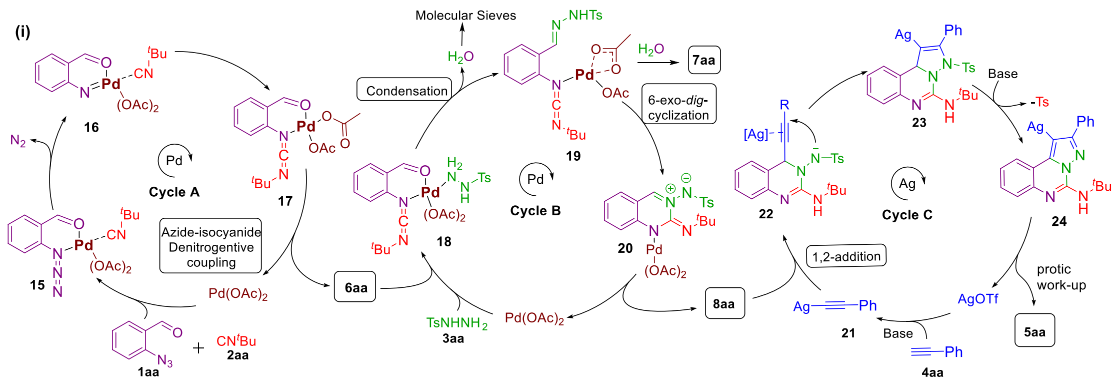


Figure S8: Plausible Reaction mechanism

S6. Experimental biology

6.1 Cell culture and reagents

Cancer cell lines A549 (Lung Cancer), HCT-116 (Colon Cancer), U-87 MG (Human Glioblastoma) were purchased from National Cell Repository at National Centre for Cell Sciences (NCCS, Pune, India). Cancer cells were maintained in Dulbecco's modified Eagle's medium (DMEM) containing 10% heat-inactivated fetal bovine serum (HI-FBS; Gibco, USA) containing penicillin and streptomycin at 100 units/ mL for each. RPMI 1640 and DMEM, Penicillin/ Streptomycin antibiotic solution, phosphate buffer saline, fetal bovine serum media and MTT dye for MTT assay were purchased from HiMedia; z-lyte kinase assay kit-tyr4 peptide for EGFR assay was procured from Invitrogen (catalogue no. PV3193); propidium iodide and RNase for cell cycle analysis were procured from Sigma Aldrich; DMSO, biological grade was purchased from SRL; JC-1 (5,5',6,6'-tetrachloro-1,1',3,3'-tetraethyl-benzimidazol-carbocyanine iodide) from Life technologies (Thermo Fisher Scientific); 2,7-dichlorofluorescein diacetate (H2DCFDA) dye from Life technologies (Thermo Fisher Scientific). Automatic cell counter (Invitrogen), incubator (Galaxy, New Brunswick), centrifuge 5430 R (Eppendorf, Germany, laminar air flow (macro scientific works) for aseptic condition, inverted microscope (Magnus, Olympus) for visualization of the cancer cell, BD accuri C6 flow cytometer for cell cycle analysis and microplate reader (BioTek) for reading absorbance in various cell based studies were used.

S6.1.1 Culturing of the cancer cell lines

Cancer cell lines were treated in the DMEM medium. Trypsin was added to detach the cancer cell lines (trypsinization). Centrifugation was done at 1200 rpm at 37 ˚C for 5 minutes for harvesting the cells. Further, supernatant was disposed and resuspension of the cell pellet was done using 2 mL of the media. The cell number was counted using an automated cell counter. The cells were transferred to fresh media every day.

S6.1.2 Maintenance and sub-culturing of cancer cell lines

The maintenance of cultured cell lines was done in 25 cm^2 or 75 cm^2 flasks containing DMEM medium supplemented with 10% Fetal Bovine serum (FBS), 1X antibiotic solution and was incubated at 37 ˚C containing 5% CO_2, 2% O_2 and 95% humid atmosphere.

S6.2 Evaluation of anticancer activity of the synthesized compounds by MTT Cytotoxicity Assay

A549 (Lung Cancer), HCT-116 (Colon Cancer) and U-87 MG (Human Glioblastoma) cancer cell lines were utilized for the biological studies. Approximately, 10000 cells were seeded in each well of the 96 well plate. The plate was incubated at 37˚C with 5% CO_2, 2% O_2 and 95% humid atmosphere for 24 h. At the end of the 24 h, treatments of investigational compounds were given to the cells in triplicate concentrations of 1 µM, 5 µM and 25 µM. The cells were further incubated for 48 h. The media was removed from each well. MTT (1 mg/ml in phosphate-buffered saline—PBS) stock solution was prepared and added as 10 µl/well. . This was subsequently incubated in the dark for 4 h. The resulting intracellular precipitate (formazan) thus formed was dissolved in DMSO solution and was subjected to mild shaking so as to dissolve all the formazan crystals. The absorbance was measured at 570 nm using an ELISA plate reader (Bio-Rad, USA). Cytotoxicity was calculated in percentage by using the formula: Cytotoxicity (%) = (OD of control – OD of test/OD of control) x 100.

Among 29 compounds of pyrazolo[1,5-*c*]quinazolines **5** analyzed, compound **5ea, 5bc, 5aa, 5hb, 5bd, 5be, 5gb, 5ec, 5fb, 5dd** and **5ba** showed activity of < 3 µM against A549 cells. Compounds **5aa, 5hb, 5be, 5gb** and **5eb** exhibited activity of < 3 µM against HCT-116 cells whereas compound 5fb and 5dd were found to possess activity of < 3 µM against U-87 MG cells. In tetrahydropyrazolo[1,5-*c*]quinazoline **26**, 18 compounds were analyzed for their antiproliferative potential. Compounds **26dd, 26dc, 26ab, 26fa, 26cc, 26be** and **26ga** exhibited low micromolar activity of < 3 μM against A549 cells. Compounds **26dd, 26cc, 26aa, 26ba, 26ca** and **26ga** were shown to be most active (< 3 μM) toward HCT-116 cells. Compounds **26ea** and **26ga** exhibited activity of < 3 μM against U-87 MG cells. The results are compiled in Table S7.

Table S7. Antiproliferative potential of the investigational compounds along with their minimal inhibitory concentrations at various cancer cell lines under study

entry	5		IC_{50} (μM)[a]		entry	5/25		IC_{50} (μM)[a]	
		A549	HCT-116	U-87MG			A549	HCT-116	U-87MG
1.	**5aa**	1.8 ± 0.7	2.9 ± 0.4	4.2 ± 0.7	24.	**5ec**	1.4 ± 0.7	4.8 ± 0.5	4.3 ± 0.2
2.	**5ab**	9.2 ± 0.3	6.5 ± 0.9	8.1 ± 0.3	25.	**5ed**	14.3 ± 0.1	17.2 ± 0.6	13.2 ± 0.4
3.	**5ac**	22.1 ± 0.6	>25	20.7 ± 0.3	26.	**5fb**	1.1 ± 0.3	2.3 ± 0.3	2.6 ± 0.3
4.	**5ad**	13.9 ± 0.5	7.7 ± 0.5	7.3 ± 0.6	27.	**5gb**	1.1 ± 0.1	1.4 ± 0.6	4.7 ± 0.7
5.	**5ae**	11.6 ± 0.9	4.9 ± 0.6	8.8 ± 0.5	28.	**5hb**	1.1 ± 0.7	2.9 ± 0.9	6.2 ± 0.5
6.	**5ba**	9.6 ± 0.7	5.3 ± 0.6	9.3 ± 0.7	29.	**26aa**	6.4 ± 0.3	1.9 ± 0.7	9.7 ± 0.9
7.	**5bb**	22.1 ± 0.6	7.3 ± 0.2	5.4 ± 0.9	30.	**26ab**	2.8 ± 0.4	7.9 ± 0.6	6.3 ± 0.8
8.	**5bc**	2.3 ± 0.9	4.7 ± 0.5	13.2 ± 0.8	31.	**26ac**	8.9 ± 0.3	6.6 ± 0.3	17.8 ± 0.3
9.	**5bd**	1.4 ± 0.3	5.3 ± 0.7	3.6 ± 0.7	32.	**26ba**	4.1 ± 0.5	2.6 ± 0.9	3.4 ± 0.8
10.	**5be**	1.6 ± 0.7	2.7 ± 0.5	3.1 ± 0.8	33.	**26bc**	1.4 ± 0.9	3.4 ± 0.8	7.6 ± 0.8
11.	**5cb**	14.3 ± 0.3	3.1 ± 0.3	<25	34.	**26be**	1.5 ± 0.9	3.7 ± 0.8	3.9 ± 0.4
12.	**5cc**	16.2 ± 0.8	22.8 ± 0.9	19.3 ± 0.5	35.	**26bf**	17.2 ± 0.7	9.2 ± 0.7	<25
13.	**5cd**	2.2 ± 0.4	7.4 ± 0.5	5.3 ± 0.9	36.	**26ca**	8.4 ± 0.8	2.3 ± 0.6	11.8 ± 0.8
14.	**5ce**	9.3 ± 0.7	6.5 ± 0.4	9.3 ± 0.8	37.	**26cb**	12.2 ± 0.4	7.6 ± 0.7	9.2 ± 0.4
15.	**5cf**	21.6 ± 0.8	16.3 ± 0.5	11.4 ± 0.4	38.	**26cc**	1.8 ± 0.3	2.2 ± 0.5	5.9 ± 0.9
16.	**5cg**	18.6 ± 0.9	11.2 ± 0.4	9.8 ± 0.3	39.	**26cd**	19.6 ± 0.6	8.7 ± 0.8	<25
17.	**5ch**	12.2 ± 0.6	7.3 ± 0.4	<25	40.	**26ce**	3.8 ± 0.7	4.2 ± 0.7	7.5 ± 0.9
18.	**5da**	2.6 ± 0.8	4.7 ± 0.9	6.7 ± 0.9	41.	**26dc**	1.8 ± 0.7	7.6 ± 0.7	8.4 ± 0.3
19.	**5db**	23.2 ± 0.9	13.4 ± 0.3	<25	42.	**26dd**	1.3 ± 0.5	1.8 ± 0.7	3.9 ± 0.9
20.	**5dc**	11.1 ± 0.7	17.2 ± 0.5	<25	43.	**26de**	17.1 ± 0.5	9.7 ± 0.8	16.7 ± 0.7
21.	**5dd**	1.4 ± 0.2	1.6 ± 0.5	2.8 ± 0.7	44.	**26ea**	1.3 ± 0.5	1.7 ± 0.5	2.3 ± 0.9
22.	**5ea**	1.4 ± 0.4	3.9 ± 0.9	6.3 ± 0.6	45.	**26fa**	1.6 ± 0.3	6.4 ± 0.3	3.9 ± 0.8
23.	**5eb**	3.1 ± 0.6	2.9 ± 0.7	7.2 ± 0.6	46.	**26ga**	1.1± 0.5	1.4 ± 0.8	2.2 ± 0.3

[a]Values are derived from averaging three independent experiments and each experiment was done in triplicate Based upon the relevant MTT data four compounds **5fb**, **5dd**, **26ea** and **26ga** were selected for further biological studies.

S6.2.1 Structure-Activity Relationship of cytotoxic activity of pyrazolo[1,5-*c*]quinazolines

1. Substitutions on C-2 of pyrazoles ring were not well tolerated
2. Substrates with electron withdrawing substituents, such as ester and cyano, on C-1 of pyrazoles were the most potent, and substrates with bulky groups on the same position were inactive
3. Substituents on benzene ring are well tolerated

S6.3 Human Peripheral Blood Mononuclear Cells (HPBMCs) culturing and treatment by investigational molecules to assess the cytotoxicity of investigational molecules

In order to perform selectivity of investigational molecules toward cancer cells, we performed HPBMCs assay. The assay was strictly performed as per the protocol no. CUPB/cc/14/IEC/4483 approved by Institutional Ethics Committee of Central University of Punjab, Bathinda. The protocol used was standard operating procedure,

provided by Institutional Ethics Committee of Central University of Punjab according to guidelines issued by Indian Council of Medical Research (ICMR), Govt. of India.
Fresh Blood was drawn from healthy individual and HPBMCs were isolated from whole blood by lysing RBCs. The cells were then suspended in RPMI media supplemented with 10% fetal bovine serum (FBS), 1% antibiotic solution and were cultured and treated as per the MTT assay procedure discussed previously. Investigational compounds **5fb, 5dd**, **26ea** and **26ga** do not cause any significant cytotoxicity towards normal HPBMCs even at the highest concentration of 25 µM, implicating a pattern of selectivity to cancer cells (Figure S9).

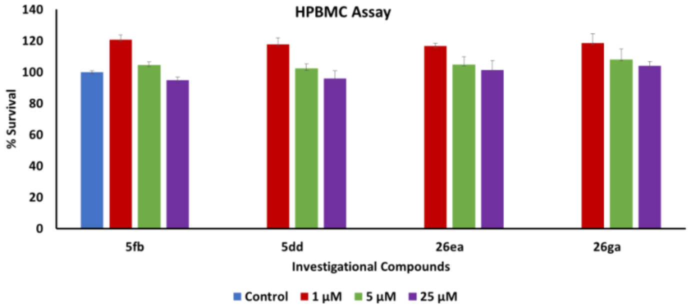


Figure S9: Graph depicting percentage survival of human peripheral blood mononuclear cells in response to treatment with selected investigational compounds for 48 h at concentrations of 1, 5 and 25 µM. Data is expressed as mean values ± S.D. of three independent experiments.

S6.4 Pyrazolo[1,5-*c*]quinazoline as EGFR inhibitors

S6.4.1. Structure Activity Relationship studies

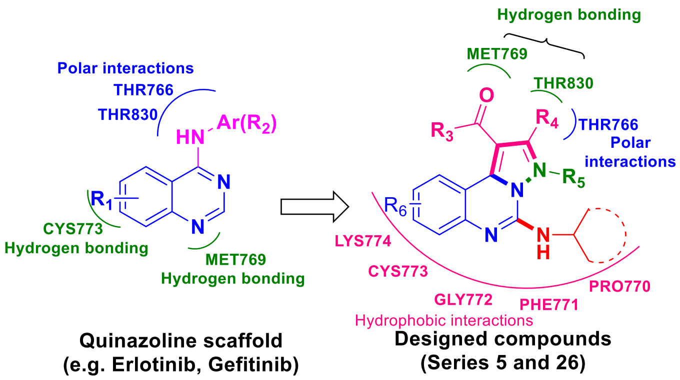


Figure S10: Design strategy for EGFR inhibitors (Series **5** and **26**, Scheme 2 and 3)

Owing to their structural resemblance to the quinazoline scaffold of gefitinib and erlotinib, the investigational compounds **5dd**, **5fb, 26ea** and **26ga** were envisaged to posses EGFR inhibitory activity. EGFR is over-expressed in almost every cancer types and is a validated drug target. Small molecules tend to occupy the ATP binding kinase domain of EGFR and thus alter the cell signalling cascade. The quinazoline-based scaffolds are found to reside in the catalytic EGFR binding pocket, where the *N*1 atom of the quinazoline ring acts as a hydrogen bond acceptor in an interaction with Met-769, the *N*3 atom interacts with Thr-830 through a bridging water molecule, and the arylamino-substituents occupies the normally empty hydrophobic pocket within the active region of EGFR receptor. The pyrazole fusion was hypothesized to occupy the extra space in ATP binding cavity available in the active site of EGFR and may be exploited for extra affinity of quinazoline based EGFR inhibitors. In addition, a bulkier alkylamino substituent at *C*2 might reduce metabolic degradation of quinazoline nucleus and could promote fitting of the bulkier group in the hydrophobic pocket, thereby enhancing the overall stability of protein-ligand complex (figure S10).

S6.4.2 EGFR inhibitory assay

The Z-LYTE® kinase assay kit-tyr4 peptide (catalogue no. PV3193) was used for the assessment of EGFR Inhibitory potential of the investigational compounds **5fb, 5dd**, **26ea** and **26ga**. The assay relies upon an enzymatic reaction through which auto phosphorylation and signalling activity of the EGFR is measured. The assay was done by our previous standardized protocol.[4] Briefly, the inhibitory effect of compounds on EGFR was measured spectrophotometrically at 400, 445 and 520 nm, respectively. Erlotinib was used as a positive control. The reagents were prepared according to catalogue no. PV3193, the assay mixture comprised of 133 µL kinase buffer, 0.5 µL kinase peptide mixtures, 0.5 µL phosphopeptide mixtures and 0.5 µL ATP test sample solution. The assay plates were prepared in triplicates. The investigational compounds **5fb, 5dd**, **26ea** and **26ga** were serially diluted at a concentration of 250 nM, 750 nM, 1 µM, 5 µM and 25 µM in DMSO (~4%), were mixed and incubated at room temperature for 1 h. After incubation, it was treated with 5 µL of development solution and kept in the dark for another 1 h. The reaction was quenched with the addition of 5 µL stop solution. The emission ratio (Coumarin Emission (445 nm)/fluorescein emission (520 nm) signifying the extent of phosphorylation was done using the given equation.

$$\%\, \boldsymbol{phosphorylation} = \mathbf{1} - \frac{(\boldsymbol{Emission\ ratio\ x\ F100\%}) - \boldsymbol{C100\%}}{(\boldsymbol{C0\%} - \boldsymbol{C100\%}) + [\boldsymbol{Emission\ ratio}\ (\boldsymbol{F100\%} - \boldsymbol{F0\%})]}$$

Where C0%= Average coumarin emission signal of the 100% Phos. Control; C100% = Average coumarin emission signal of the 0% Phos. Control; F100% = Average Fluorescein emission signal of the 100% Phos. Control; F0% = Average Fluorescein emission signal of the 0% Phos. Control

Table S8. EGFR inhibitory activity of the investigational compounds

Investigational compounds	IC_{50} [a] Cancer Cell lines (µM)			EGFR Inhibitory Activity IC_{50}[a] (nM)
	A549	HCT-116	U-87MG	
5dd	1.4 ± 0.2	1.6 ± 0.5	2.8 ± 0.7	639.4 ± 0.34
5fb	1.1 ± 0.3	2.3 ± 0.3	2.6 ± 0.3	235 ± 0.92
26ea	1.3 ± 0.5	1.7 ± 0.5	2.3 ± 0.9	3060 ± 0.65
26ga	1.1± 0.5	1.4 ± 0.8	2.2 ± 0.3	625 ± 0.74
Erlotinib	-	-	-	423± 0.89

[a]Values are derived from averaging three independent experiments and each experiment was done in triplicate

To our delight, **5fb** was found to be the most potent even with respect to the standard drug, erlotinib, while **5dd** and **26ga** showed comparable activity in the nanomolar range. To further validate these results, molecular docking studies were performed. Refer section S7 for details.

S6.5 Measurement of intracellular reactive oxygen species (ROS)

Apoptosis is linked to the increase in ROS levels and the loss of the mitochondrial membrane potential (ΔΨM).[5] The measurement of intracellular production of ROS was done using 2’,7’-dichlorofluorescein diacetate (H2DCFDA) dye, a stable non-polar compound that readily diffuses into the cell and converted to 2’,7’-dichlorofluorescin (DCF) upon cleavage of acetate groups by intracellular esterases and oxidation by peroxidase. Interestingly, the fluorescent intensity obtained is directly proportional to the amount of ROS produced by the cell. The lung cancer cell line A549 was treated with the investigational compounds **5fb, 5dd, 26ea** and **26ga** for 48 h. Then, cells were washed with PBS and incubated in H2DCFDA at 37°C for half an hour. Cells were lysed in alkaline solution and centrifuged for 10 min. The supernatant was transferred to a 96-well plate and fluorescence was measured at 5 and 25 µM concentration at Ex/Em: ~492–495/517–527 using microplate reader. Results were calculated as fluorescence intensity relative to control cells. A significant time- and dose-dependent increase in ROS level was observed with a positive control, erlotinib (Figure S11)

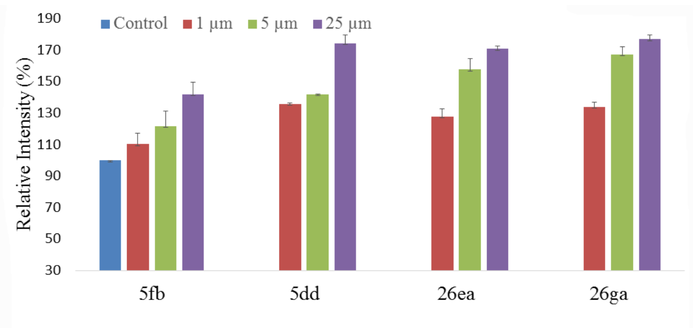


Figure S11: H2DCFDA based assay to measure intracellular ROS

S6.6 Determination of mitochondrial membrane potential (µM)

A549 cells were seeded in 96 well plated and treated with 1, 5 and 25 mM concentrations of **5fb, 5dd, 26ea** and **26ga** for 48 h. Subsequently the cells were incubated with JC-1 dye (10 mL) (5,5',6,6'-tetrachloro-1,1',3,3'tetraethylbenzimi-dazolylcarbocyanine iodide) for 30 min. Cells were washed with PBS and quantitatively analyzed under fluorescent microplate reader (emission at 527 and 590). Cells pre-treated with **5fb** were analyzed under confocal microscopy (Figure S12). JC-1 dye selectively enters mitochondria and reversibly changes colour from red to green as µM decreases (OD590/OD527 ratio). The results showed that all the compounds lead to imbalance OD590/OD527 ratios and thus altered the mitochondrial membrane (Figure S13).

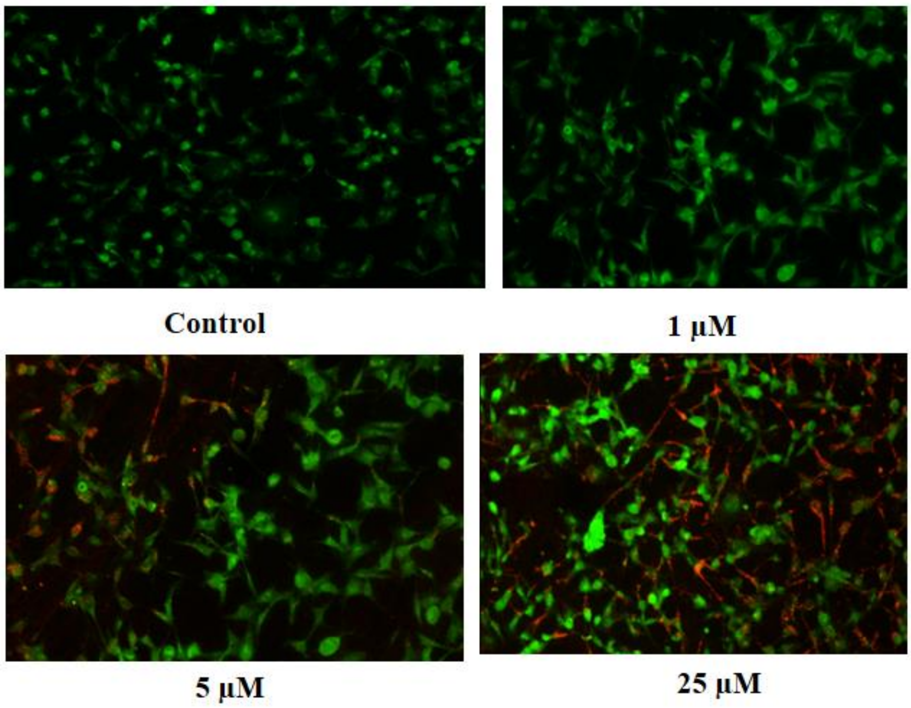


Figure S12: Confocal microscopy of cells treated with **5fb** and JC1 dye

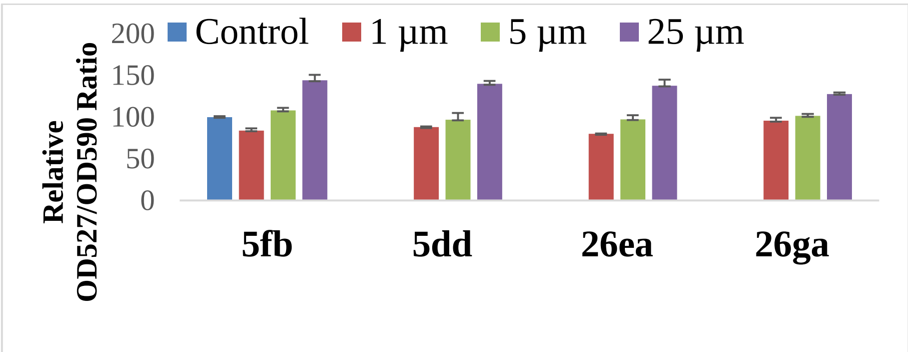


Figure S13: JC-1 dye-based assay to measure a change in mitochondrial membrane potential on A549 cancer cell line treated **5fb**, **5dd**, **26ea** and **26ga**.

S6.7 Cell apoptosis assay using Propidium Iodide

A549 cancer cells, pretreated with compound **5fb** and **26ga** at a concentration of 5 and 25 µM for 24 h, were transferred in a manner to obtain 10^6 cells per tube. The cells were further centrifuged at 1200 rpm for 5 min and washed with 1X PBS. Thereafter cells were fixed using chilled ethanol and incubated for 3 h at -20 °C. Post 3 h, cells were subjected to centrifugation at 2500 rpm and washed once with 1 X PBS. Each tube was mixed with 50 µL of propidium iodide (Sigma Aldrich) and 50 µL Ribonuclease (10 mg/mL solution in water), and incubated for 30 minutes at room temperature in the dark. The DNA content was then measured using BD Accuri C6 flow cytometer. For the cells treated with **5fb**, a substantial rise in the G1 phase of cells, 32.5% and 43.77% at concentration of 5 and 25 µM respectively, was observed compared to that of control (23.1%). Cells treated with

26ga exhibited similar results with profound G1 phase arrest at 36.32% and 40.65% at concentration of 5 and 25 µM respectively compared with the control (Figure S14-S15).

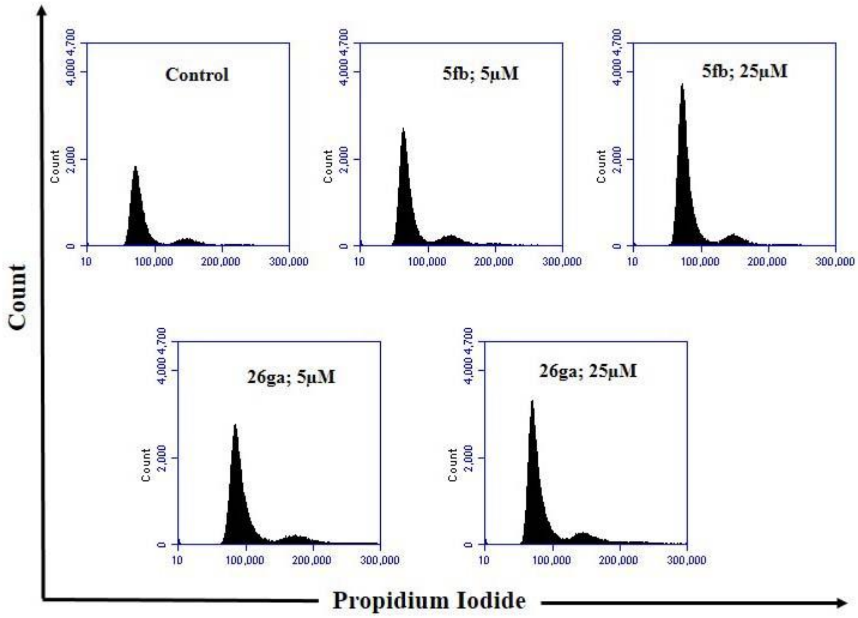


Figure S14: Cell cycle analysis using flow cytometry of A549 cancer cell line treated with **5fb** and **26ga**.

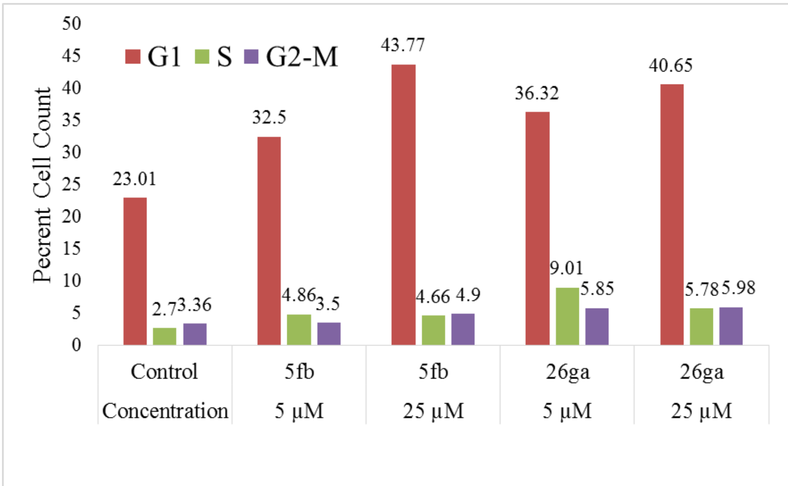
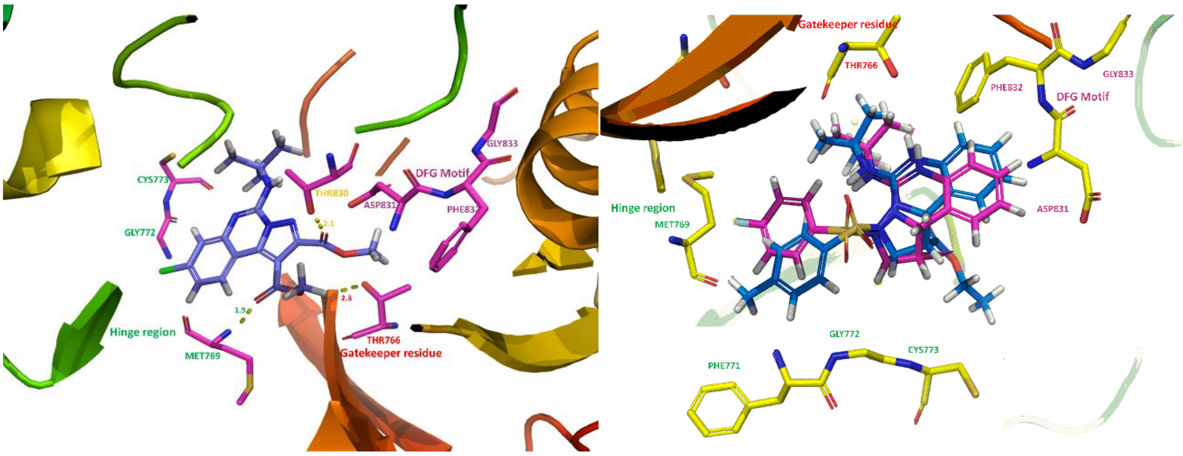


Figure S15: The bar graph represents the percent cell count (DNA) at various stages of cell cycle.

S7. Molecular Docking Studies

Molecular docking studies were performed using GLIDE module of Schrodinger Maestro Licensed software (11.1 version). The protein with PDB Id- 1M17 (2.6 Å) was retrieved from the protein data bank (https://www.rcsb.org/pdb/home/home.do). Initial protein refinement involving bond orders and addition of hydrogen to the side chains was done using protein preparation wizard. Further refinement involved optimization and minimization using OPLS3 force field. Ligands were sketched using 2D sketcher implemented in Maestro 1 and Ligprep was used for ligand optimization and minimization. Further, receptor grid generation involved defining active site in the protein structure for which co-crystallized ligand co-ordinates were used. The bound erlotinib formed the centroid of the grid box. Docking studies were performed in Xtra Precision (XP) mode. Validation of docking protocol was performed by comparing the conformation of docked erlotinib against the conformation of co-crystallized erlotinib. The RMSD of the conformations was found to be 1.27Å and the residue interaction was found to be similar to the native ligand.

In order to investigate the underlying binding pattern, potential inhibitors **5fb, 5dd, 26ea** and **26ga** showing promising biological activity (section S6.4) were docked in the generated grid along with erlotinib. The resultant docked conformations resulted in binding affinity scores and residue interaction pattern (Table S9). **5fb** exhibited comparable binding to the wild type EGFR ATP binding site, and similar to erlotinib. It was observed that compound **5fb** possessed higher affinity as compared to **5dd, 26ea** and **26ga** despite being more active in the biological evaluation. The binding pattern of the highest active compound **5fb** figuring out the important interactions are represented in Figure S16.



(a) (b)

Figure S16: Binding pattern representation of (a) the most active compound, **5fb** (blue colour), and (b) **26ea** (blue colour) and **26ga** (pink colour) with the key amino acid interactions

Table S9. Representation of selected compounds docking scores and their important interaction within the catalytic domain of EGFR

Compound	Docking score	Important interacting with the residues				
		MET769	THR766	THR830	ASP831	CYS773
5fb	-7.793	+	+	+	-	-
5dd	-4.462	-	-	-	+	-
26ga	-3.806	-	-	-	+	+
26ea	-3.509	-	-	-	+	-

Though **5dd**, **26ea** and **26ga** binds to the ATP binding site of EGFR, no hydrogen bonding interactions with MET769 and CYS773, essential amino acid residues important for the EGFR inhibitory activity, are observed. This important interaction of hinge residue MET769 is observed in **5fb**. The carbonyl group of the acetate group attached to **5fb** forms hydrogen bond with the -NH of the hinge region residue MET769 of the active site. Additionally, hydrogen bonding is observed between the THR830 and another carbonyl of acetate group and hydrogen bonding of methyl with oxygen atom of THR766. These additional interactions might have enhanced the overall affinity of **5fb** with the ATP binding domain of EGFR, exhibiting a potent activity against the kinase.

S8. Crystallographic Information

S8.1 5ad

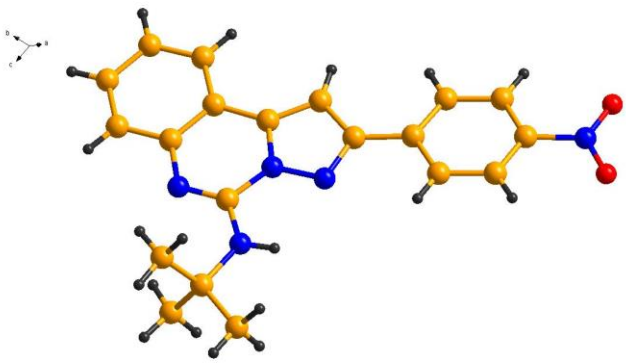


Figure S17. X-Ray crystal structure of **5ad**. (Carbon, Orange; Nitrogen, Blue; Oxygen, Red; Hydrogen, Black)

Table S10: Crystal data and structure refinement for **5ad**

Identification code	CCDC Number 1566282
Empirical formula	$C_{41}H_{40}Cl_2N_{10}O_4$
Formula weight	807.73
Temperature/K	296.15
Crystal system	Monoclinic
Space group	C2/c
a/Å	27.5324(10)
b/Å	9.3673(3)
c/Å	19.5352(7)
α/°	90.00
β/°	128.8920(10)
γ/°	90.00
Volume/Å^3	3921.4(2)
Z	4
ρ_{calc}g/cm^3	1.368
μ/mm^{-1}	0.222
F(000)	1688.0
Crystal size/mm^3	0.3 × 0.2 × 0.2
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	9.2 to 51
Index ranges	$-33 \leq h \leq 33$, $-11 \leq k \leq 11$, $-23 \leq l \leq 23$
Reflections collected	23824
Independent reflections	3307 [R_{int} = 0.0424, R_{sigma} = 0.0229]
Data/restraints/parameters	3307/0/261
Goodness-of-fit on F^2	1.325
Final R indexes [I>=2σ (I)]	R_1 = 0.0551, wR_2 = 0.1576
Final R indexes [all data]	R_1 = 0.0660, wR_2 = 0.1722
Largest diff. peak/hole / e Å^{-3}	0.56/-0.44

S8.2 8aa

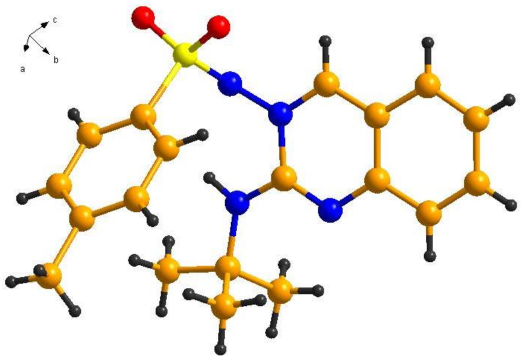


Figure S18. X-Ray crystal structure of compound **8aa**. (Carbon, Orange; Nitrogen, Blue; Oxygen, Red; Hydrogen, Black)

Table S11: Crystal data and structure refinement for **8aa**

Identification code	CCDC Number 1566284
Empirical formula	$C_{19}H_{22}N_4O_2S$
Formula weight	370.48
Temperature/K	296(2)
Crystal system	Triclinic
Space group	P-1
a/Å	7.8633(6)
b/Å	9.3267(7)
c/Å	13.5742(10)
α/°	84.166(4)
β/°	89.184(4)
γ/°	79.543(4)
Volume/Å^3	973.90(13)
Z	2
ρ_{calc}g/cm^3	1.2633
μ/mm^{-1}	0.186
F(000)	392.4
Crystal size/mm^3	0.2 × 0.2 × 0.15
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	3.02 to 51
Index ranges	$-10 \leq h \leq 11$, $-13 \leq k \leq 12$, $-19 \leq l \leq 19$
Reflections collected	22709
Independent reflections	3626 [R_{int} = 0.12, R_{sigma} = 0.1059]
Data/restraints/parameters	3626/0/238
Goodness-of-fit on F^2	1.130

Final R indexes [I>=2σ (I)]	R_1 = 0.0858, wR_2 = 0.2398
Final R indexes [all data]	R_1 = 0.1076, wR_2 = 0.2778
Largest diff. peak/hole / e Å^{-3}	0.69/-1.46

S8.3. 7aa

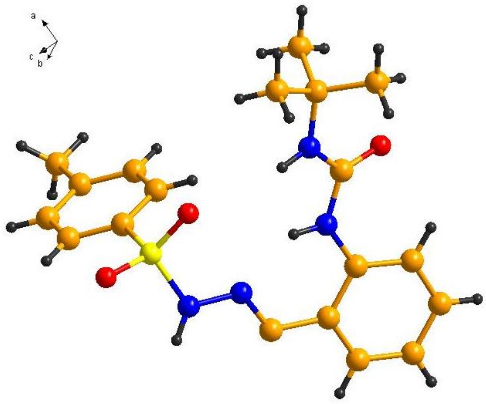


Figure S19. X-Ray crystal structure of **7aa**. (Carbon, Orange; Nitrogen, Blue; Oxygen, Red; Hydrogen, Black)

Table S12. Crystal data and structure refinement for 7aa

Identification code	CCDC Number 1566285
Empirical formula	$C_{19}H_{23}N_4O_3S$
Formula weight	387.49
Temperature/K	100(2)
Crystal system	Monoclinic
Space group	C2/c
a/Å	34.877(2)
b/Å	9.0455(6)
c/Å	12.9419(9)
α/°	90
β/°	105.171(3)
γ/°	90
Volume/Å^3	3940.7(5)
Z	8
ρ_{calc}g/cm^3	1.3061
μ/mm^{-1}	0.191
F(000)	1641.7
Crystal size/mm^3	0.2 × 0.2 × 0.2
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	2.42 to 50.98
Index ranges	-46 ≤ h ≤ 46, -10 ≤ k ≤ 12, -17 ≤ l ≤ 17

Reflections collected	29018
Independent reflections	3651 [R_{int} = 0.0418, R_{sigma} = 0.0253]
Data/restraints/parameters	3651/0/248
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.0502, wR_2 = 0.1728
Final R indexes [all data]	R_1 = 0.0623, wR_2 = 0.2088
Largest diff. peak/hole / e Å^{-3}	0.95/-0.71

S8.4. 9aa

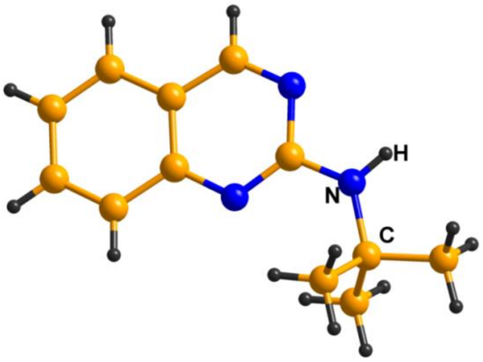


Figure S20 X-Ray crystal structure of compound **9aa**. (Carbon, Orange; Nitrogen, Blue; Oxygen, Red; Hydrogen, Black)

Table S13. Crystal data and structure refinement for **9aa**.

Identification code	CCDC number 1566113
Empirical formula	$C_{12}H_{15}N_3$
Formula weight	201.27
Temperature/K	100(2)
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	8.3134(8)
b/Å	12.5189(13)
c/Å	11.0332(12)
α/°	90
β/°	107.377(3)
γ/°	90
Volume/Å^3	1095.9(2)
Z	4
ρ_{calc}g/cm^3	1.220
μ/mm^{-1}	0.075
F(000)	432.0

Crystal size/mm^3	0.35 × 0.22 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.428 to 50.042
Index ranges	$-9 \leq h \leq 9$, $-14 \leq k \leq 14$, $-13 \leq l \leq 12$
Reflections collected	8589
Independent reflections	1924 [R_{int} = 0.0494, R_{sigma} = 0.0447]
Data/restraints/parameters	1924/0/143
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0446, wR_2 = 0.0950
Final R indexes [all data]	R_1 = 0.0705, wR_2 = 0.1060
Largest diff. peak/hole / e Å^{-3}	0.15/-0.23

S8.5. 26be

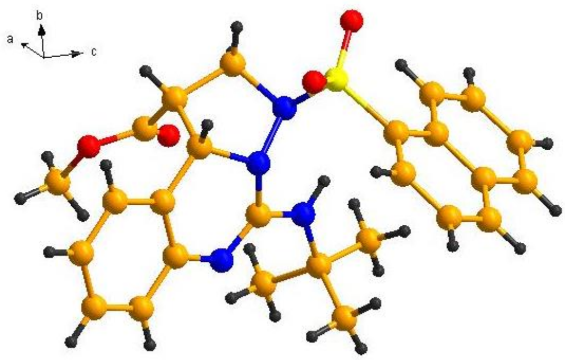


Figure S21. X-Ray crystal structure of **26be**. (Carbon, Orange; Nitrogen, Blue; Oxygen, Red; Hydrogen, Black)

Table S14. Crystal data and structure refinement for **26be**

Identification code	CCDC Number 1566283
Empirical formula	$C_{26}H_{28}N_4O_4S$
Formula weight	492.58
Temperature/K	296.15
Crystal system	Monoclinic
Space group	C2/c
a/Å	29.7473(8)
b/Å	10.1292(3)
c/Å	18.7181(5)
α/°	90.00
β/°	118.7280(10)
γ/°	90.00
Volume/Å^3	4945.8(2)

Z	8
ρ_{calc}g/cm^3	1.323
μ/mm^{-1}	0.171
F(000)	2080.0
Crystal size/mm^3	0.2 × 0.2 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	8.84 to 47.18
Index ranges	-33 ≤ h ≤ 33, -11 ≤ k ≤ 11, -21 ≤ l ≤ 21
Reflections collected	45616
Independent reflections	3519 [R_{int} = 0.0474, R_{sigma} = 0.0203]
Data/restraints/parameters	3519/0/320
Goodness-of-fit on F^2	1.282
Final R indexes [I>=2σ (I)]	R_1 = 0.0515, wR_2 = 0.1518
Final R indexes [all data]	R_1 = 0.0605, wR_2 = 0.1621
Largest diff. peak/hole / e Å^{-3}	1.04/-0.24

S9. Pharmacological activity and literature search for the synthesis of pyrazolo[1,5-*c*]quinazolines

S9.1: Pharmacological activity of pyrazolo[1,5-*c*]quinazolines reported in the literature

Asproni et al[6] have reported the synthesis and SAR studies of the pyrazolo[1,5-*c*]quinazolines as novel potent phosphodiesterase 10A(PDE10A) inhibitors. In this series, the compound **1** showed the highest affinity for PDE10A enzyme with IC_{50} = 16nm. Pae et al[7] employed structure-based virtual screening of pyrazolo quinazoline derivatives against Eg5 inhibitors. These derivatives exhibit growth inhibition in proliferation assays and induce monoastral spindles in cells with IC_{50} value of 6.3 μm (Fig.S22, 2). Kumar et al[8] have rationally designed and synthesized some 5,6-dihydropyrazolo/ pyrazolo[1,5-*c*]quinazoline derivative and evaluated these compounds for *in vitro* xanthine oxidase inhibitory activity (Fig. S22, 3-5). Cecchi et al[9] have reported the synthesis and binding activity of the 2-substituted pyrazolo[1,5-c]quinazolnes as optimal site of benzodiazepine receptor activity (Fig. S22, 6-7). Varano et al[10,11] described the binding affinity of pyrazo[1,5-c]quinzolines towards AMPA (2-amino-3-(3-hydroxy-5-methylisoxazol-4-yl)-propionic acid), Gly/ NMDA (Glycine/N-methyl-D-asparatic acid) and KA (Kainic acid) receptor and also performed their docking studies (Fig.S22, 8)

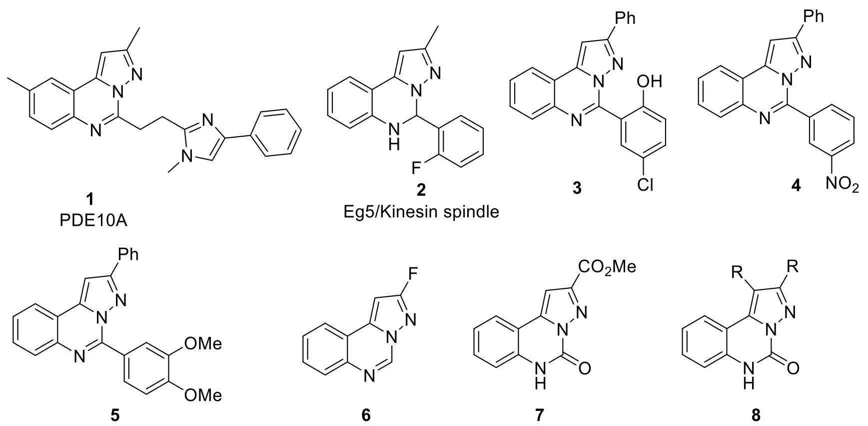


Figure S22: Pharmacological importance of pyrazolo[1,5-c]quinazoline

S9.2: Synthesis of pyrazolo[1,5-*c*]quinazolines reported in the literature

we envisaged a potential to develop a new higher-order multicomponent reaction by combining four versatile privileged synthons: 2-azidobenzaldehyde, isocyanide, sulfonyl hydrazides and alkynes. Herein, we report the realization of a four-component reaction through a Pd(II)/Ag(I) binary catalytic system for the synthesis of diverse pyrazolo[1,5-*c*]quinazolines (Fig. S23, Scheme 13) that are known to potential biological interest. Conventionally, pyrazolo[1,5-c]quinazolines are synthesized in a multi-step fashion by condensation of 2-pyrazoloanilines with triphosgene (Fig. S23, Scheme 1),[9,12] glyoxylic acid (Fig. S23, Scheme 2),[10] aldehydes (Fig. S23, Scheme 3),[13] chloroacetylchloride (Fig. S23, Scheme 4)[5] and cyanamide (Fig. S23, Scheme 5),[14] Cu-mediated cyclization of 5-(2-bromoaryl)-1H-pyrazoles with carbonyl compounds in aqueous ammonia (Fig. S23, Scheme 6),[15] reaction of 3-diazo-1,3-dihydro-2H-indol-2-one derivatives with either enaminones (Fig. S23, Scheme 7)[16] or activated alkynes (Fig. S23, Scheme 8),[17] two-component [3+2] cycloaddition reactions of *N*-aminoquinazoliumylides with olefins (Fig. S23, Scheme 9),[18] 1,3-dipolar cycloaddition of *N*-unprotected ylideneoxindoles and dimethyl diazomethylphosphonate anion generated *in situ* from Bestmann-Ohira reagent (Fig. S23, Scheme 10),[19] Au-catalysed intramolecular bicyclization of N-propargylic sulfonylhydrazones (Fig. S23, Scheme 11),[20] and Cu-catalyzed two-step reaction of 1-(2-bromophenyl)-3-alkylprop-2-yn-1-ones, hydrazines and amidines (Fig. S23, Scheme 12).[21] To the best of our knowledge, there is no report of the multicomponent assembly of pyrazolo[1,5-c]quinazolines in one-pot to date.

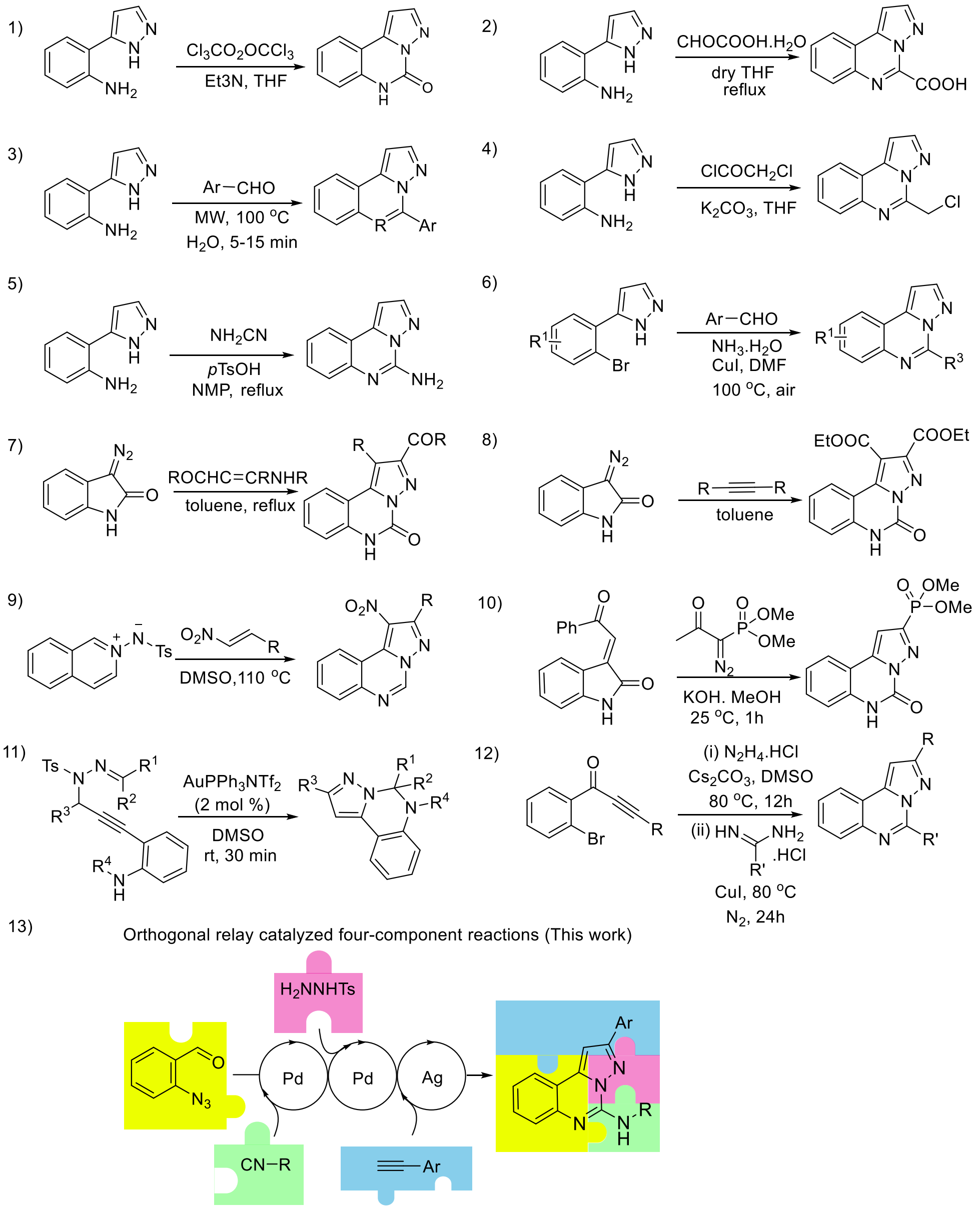
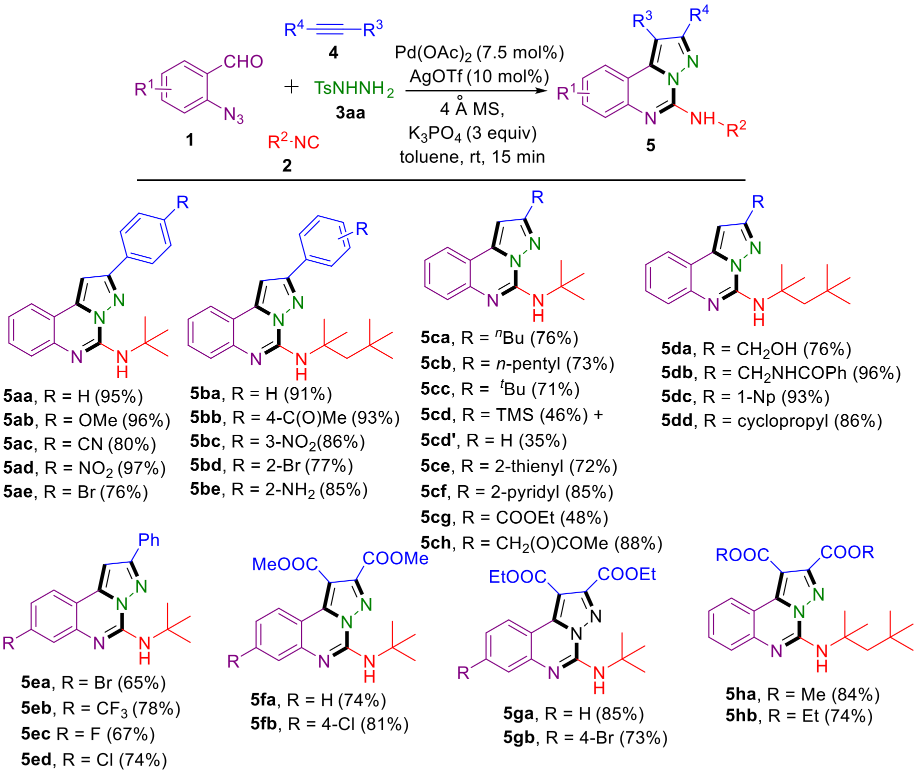


Figure S23: Various methods reported in the literature for the synthesis of pyrazolo1,5[c]quinazolines.

Results and Discussion

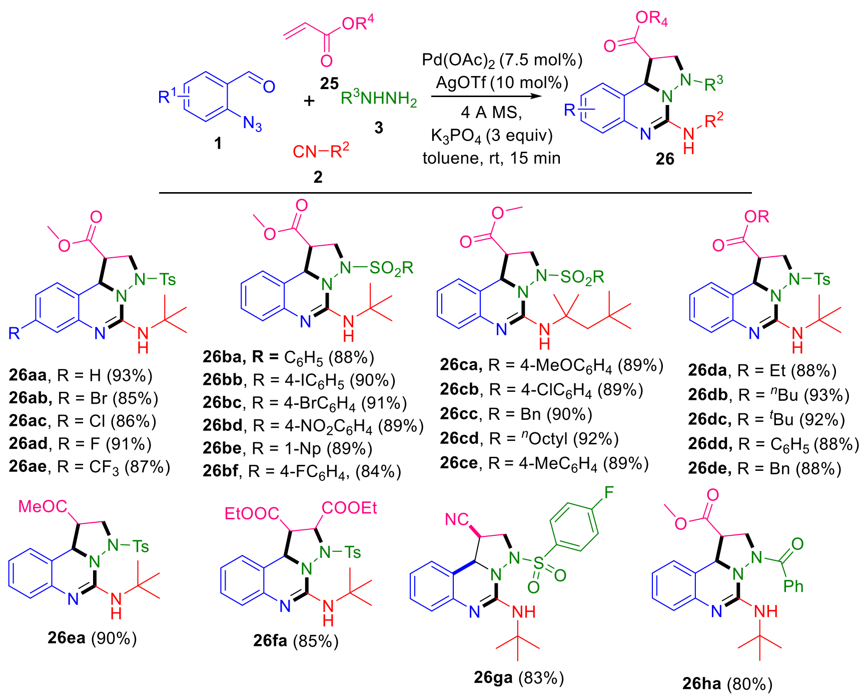
S10. Construction of the diversity-rich library of pyrazolo[1,5-c]quinazolines

The overall scope of this reaction was found to be wide (Scheme 2). Both aromatic and aliphatic terminal alkynes and electron deficient internal alkynes participated in 4CR. The chemical integrity of reactive functional groups such as cyano, ketone, ester and halides (Br and I) remained unperturbed in the standard reaction condition providing a chemical handle for further transformation. Fluorinated substitutions in **5eb**, **5ec** and **5fc** would contribute in enhancing their pharmacodynamics and pharmacokinetic properties. Interestingly, trimethylsilylacetylene participated the 4-CR to furnish **5cd** up to 46% isolated yield and a desilylated product **5cd'** was also observed with 35% isolated yield. Heteroarylalkynes such as 2-thienyl, 2-pyridyl were also subjected to the 4CR reaction to afford **5ce** and **5cf** respectively in high yields. Notably, electron deficient 2-azidobenzadehydes were compatible to deliver 4CR adduct. In contrast, electron rich 2-azidobenzadehydes did not afford desired product **5** due to low reactivity of corresponding carbodiimide intermediate **6**. The investigation underscores the high tolerance of the 4CR reaction to steric effect and excellent control over regioselectivity.



Scheme 2: Substrate Scope of Terminal and Internal Alkynes for 4CR

The 4CR could be elegantly extended to activated alkenes to furnish tetrahydropyrazolo[1,5-c]quinazolines **26** of four-point diversity exhibiting excellent atom economy (Scheme 3). Electron-deficient alkenes, such as acrylates and acrylonitrile participated efficiently in 4CR reaction to produce **26** in good to excellent yields with the formation of one diastereomer exclusively. A range of aryl and alkyl sulfonyl hydrazides were successfully incorporated. Both electron-donating and electron-withdrawing group on aryl sulfonyl hydrazides diversity were well tolerated. In all cases, the reaction proceeds with high regiochemical fidelity.



Scheme 3: Substrate Scope of alkenes for 4CR

S11. References

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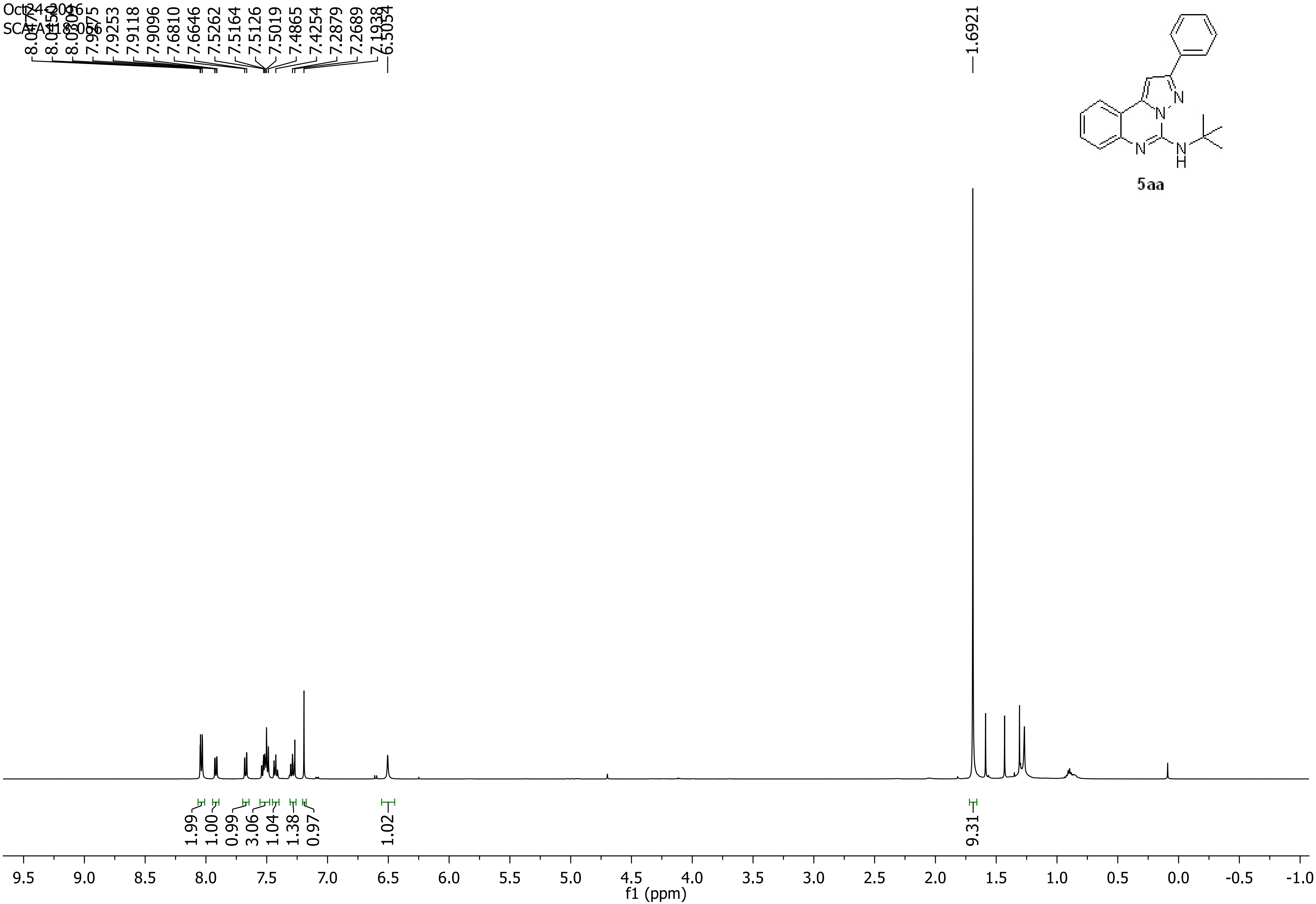
S12. Copies of ^{1}H, ^{13}C NMR and HRMS spectra



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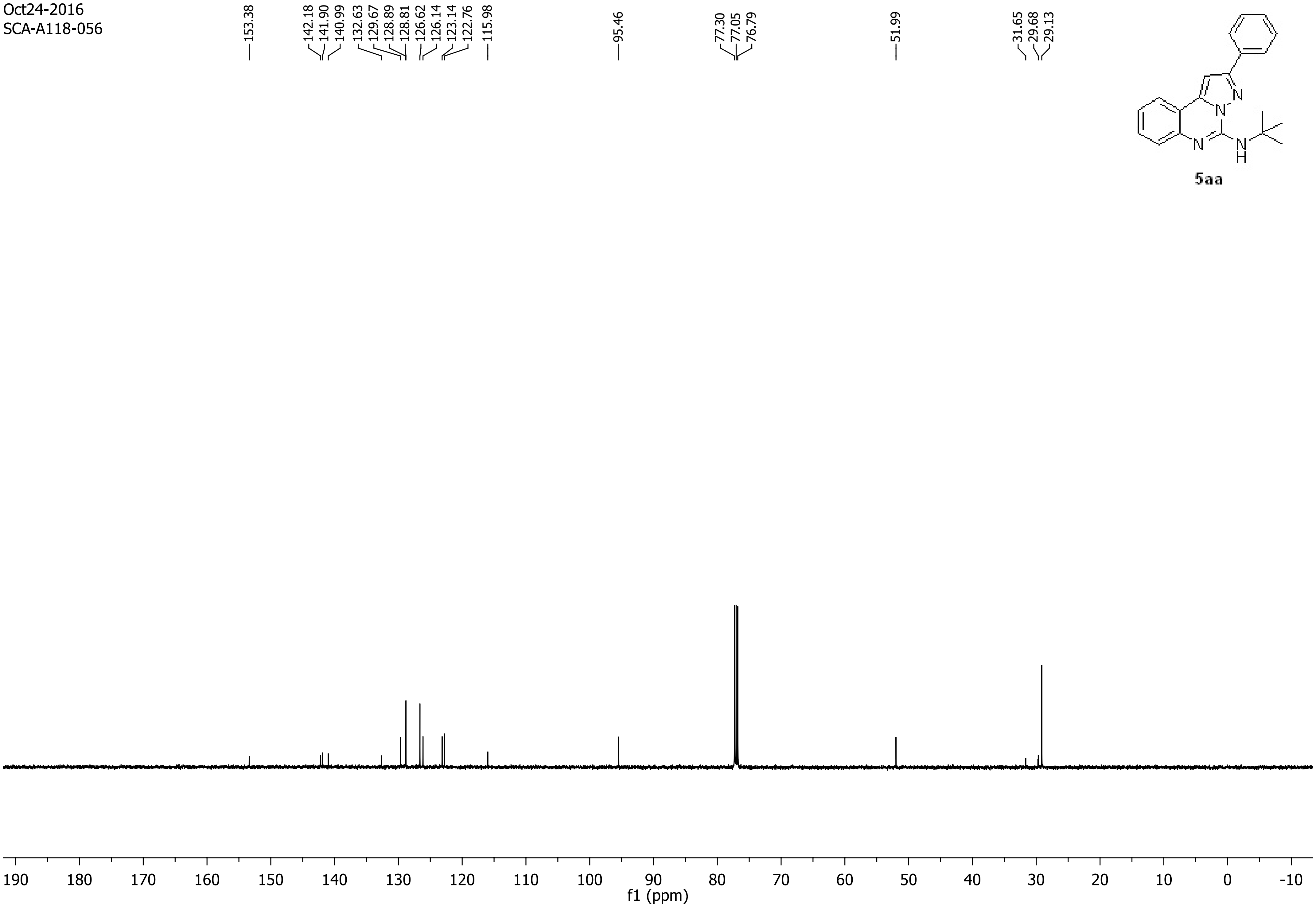
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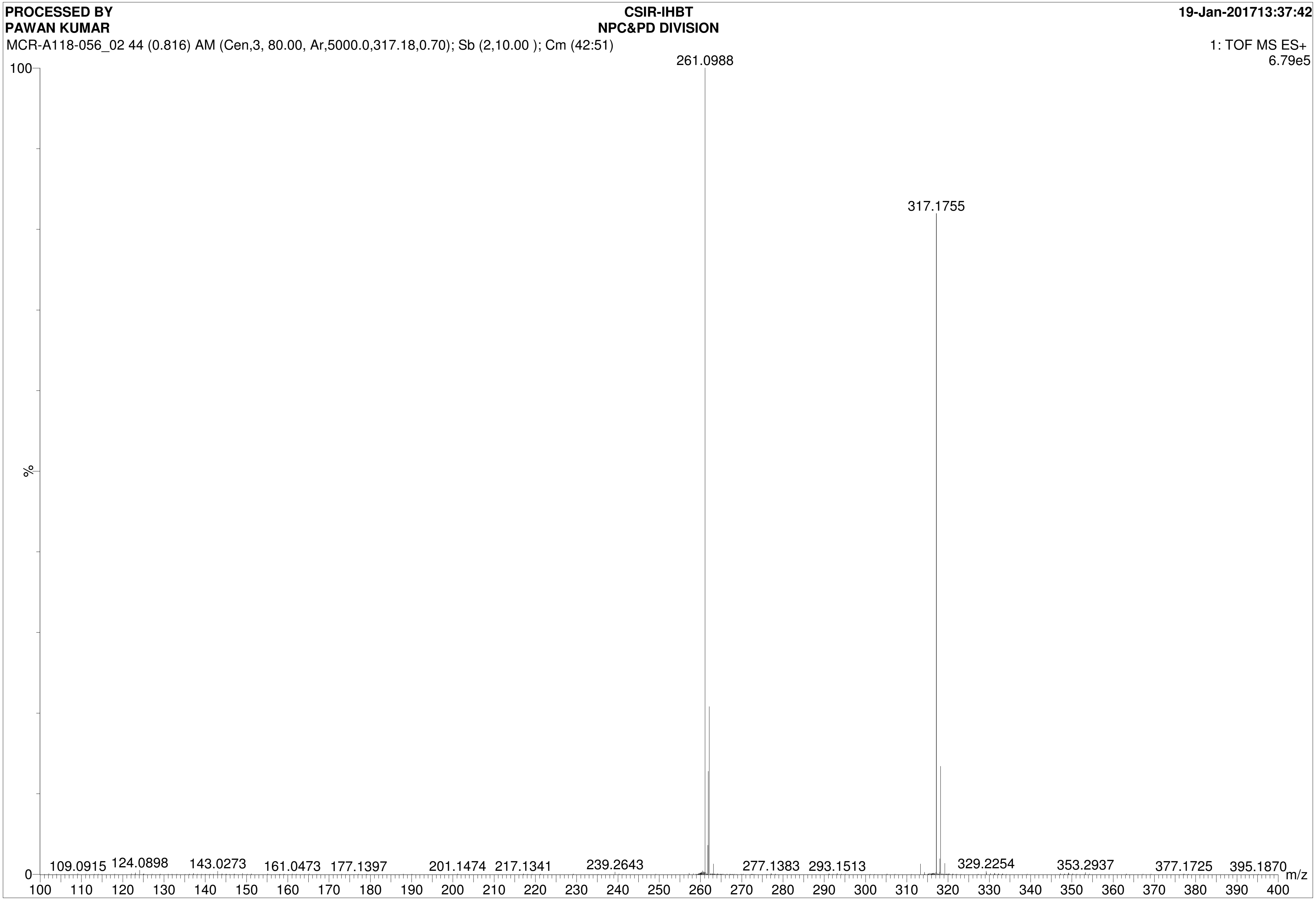
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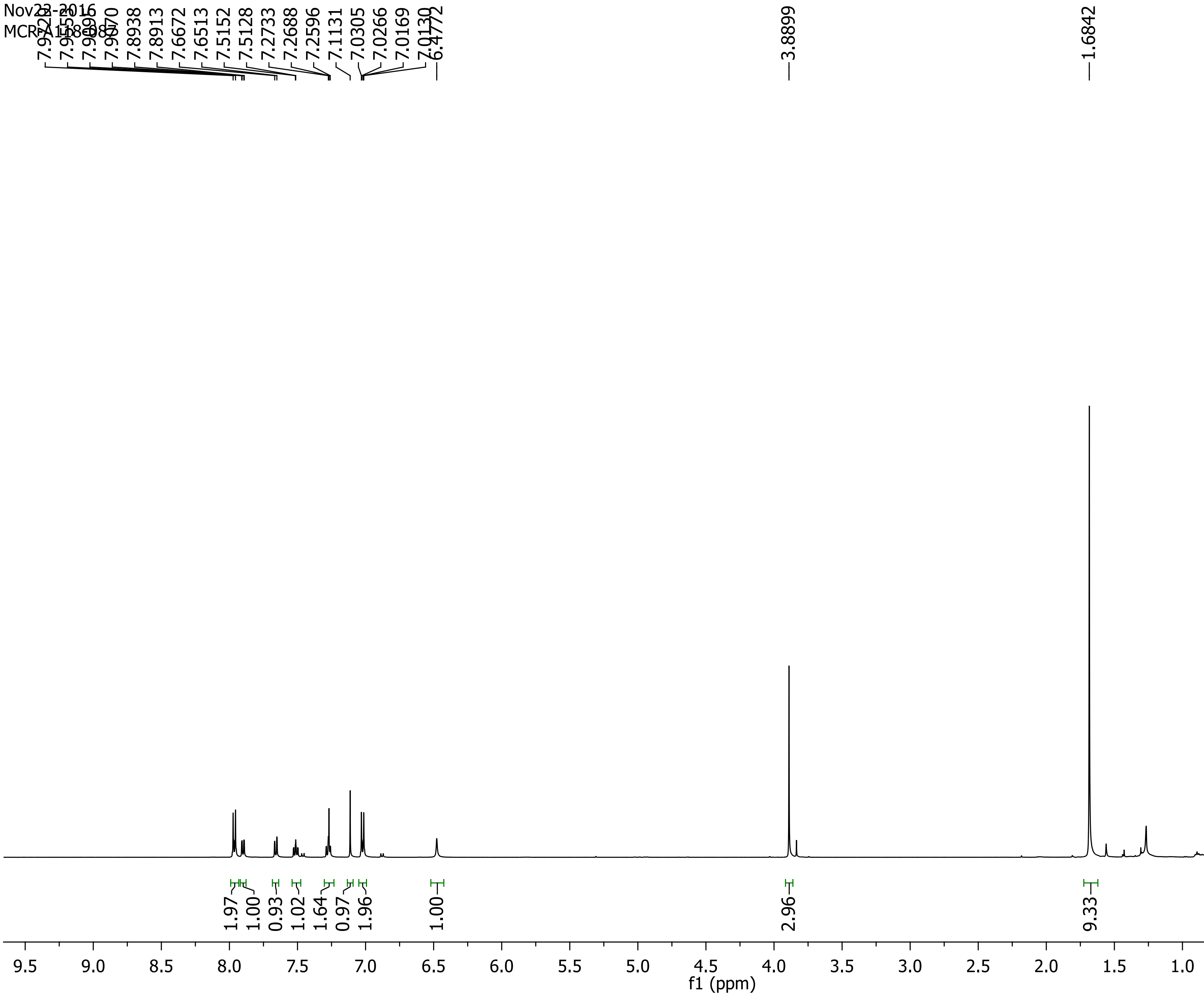

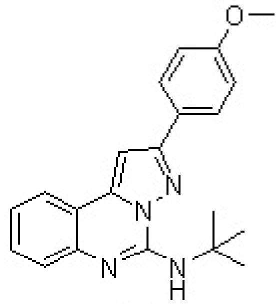

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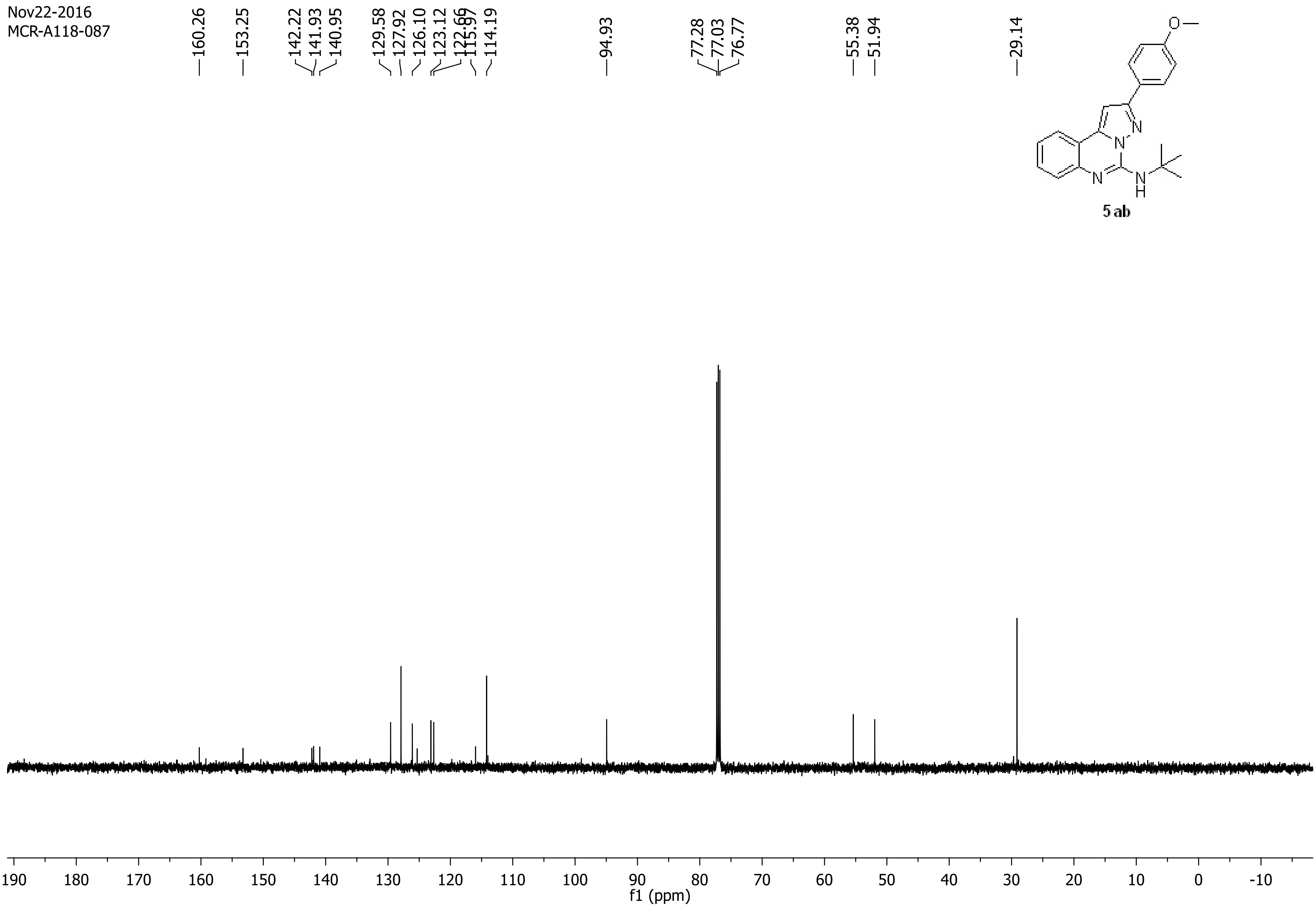

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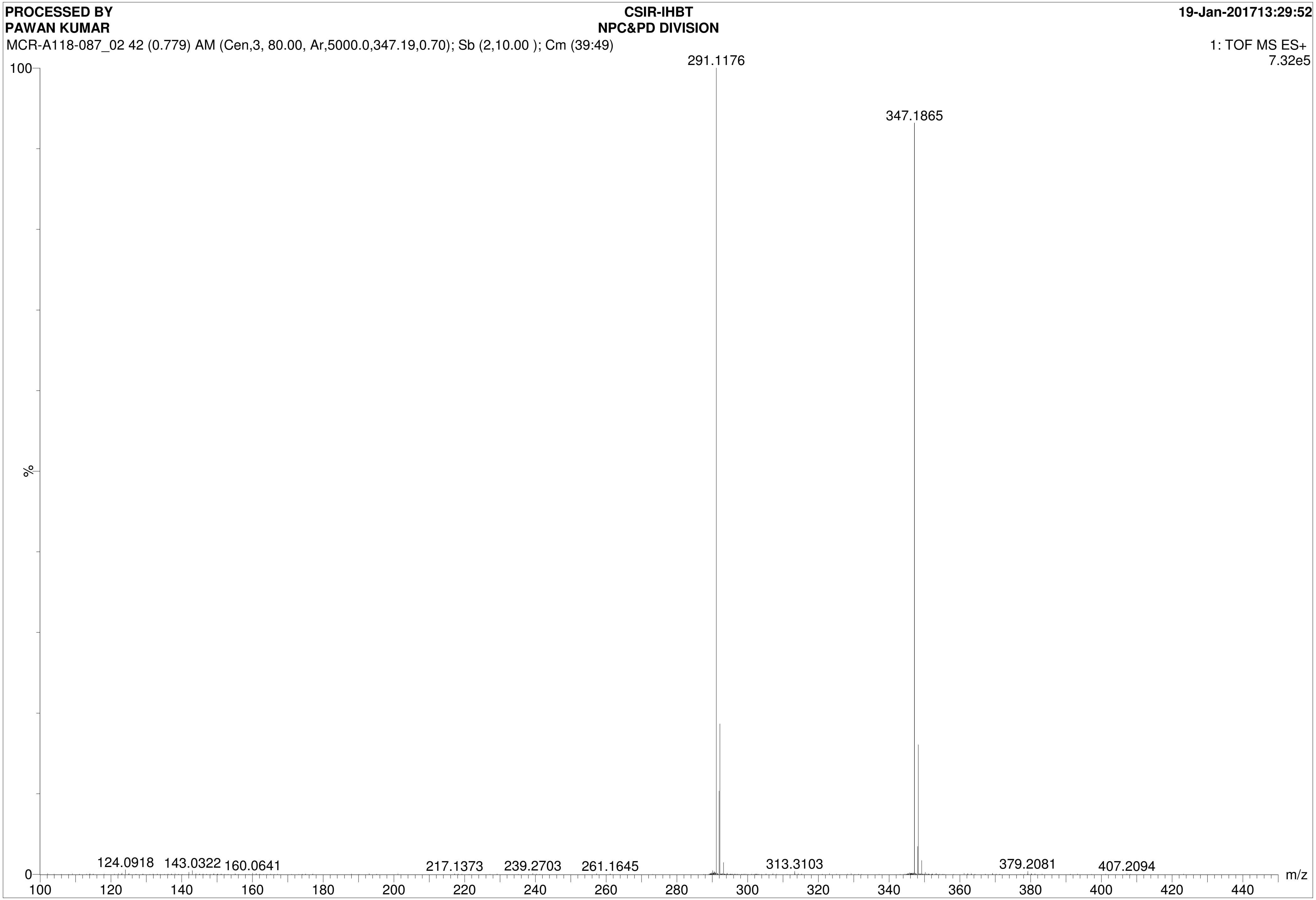
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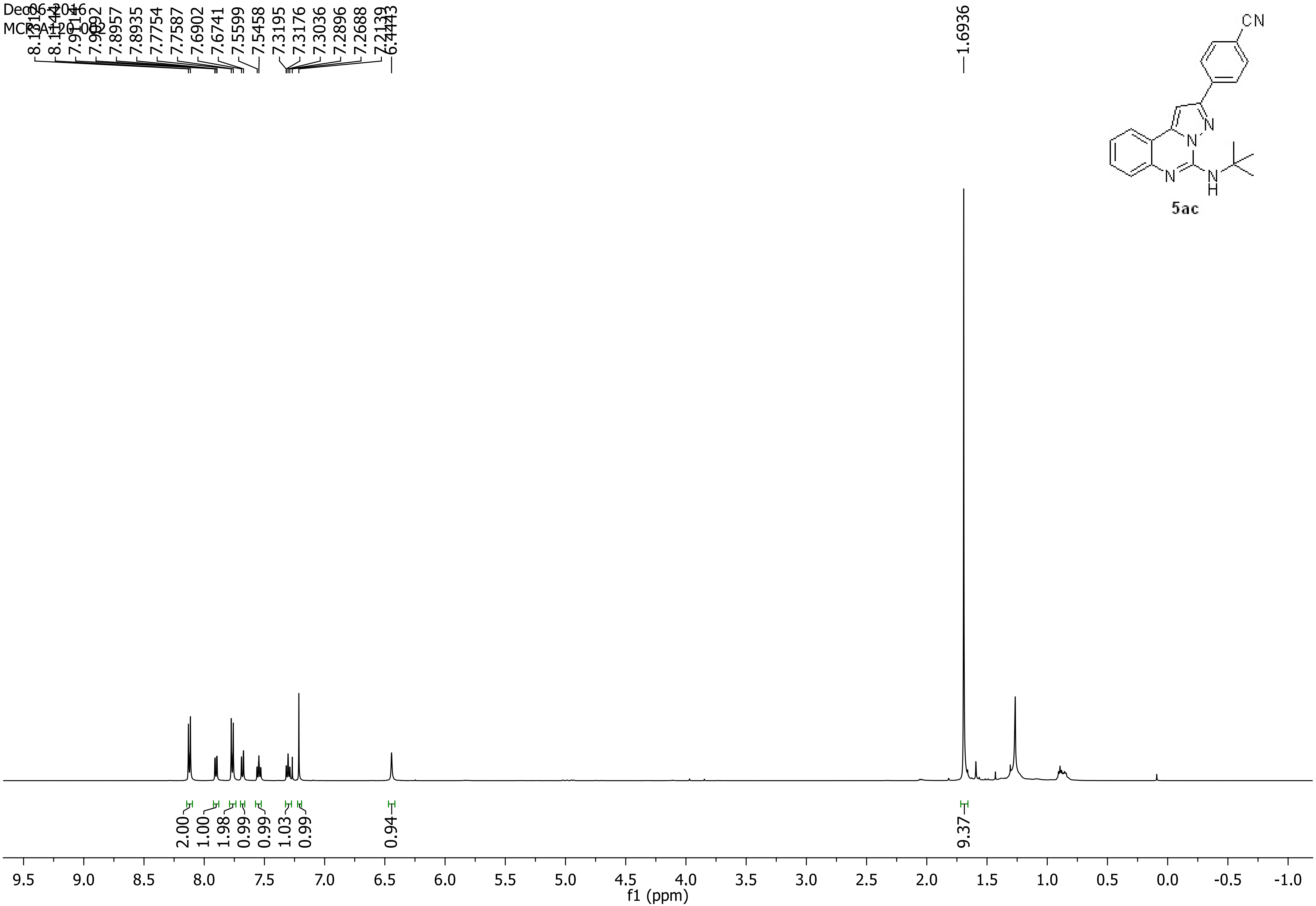
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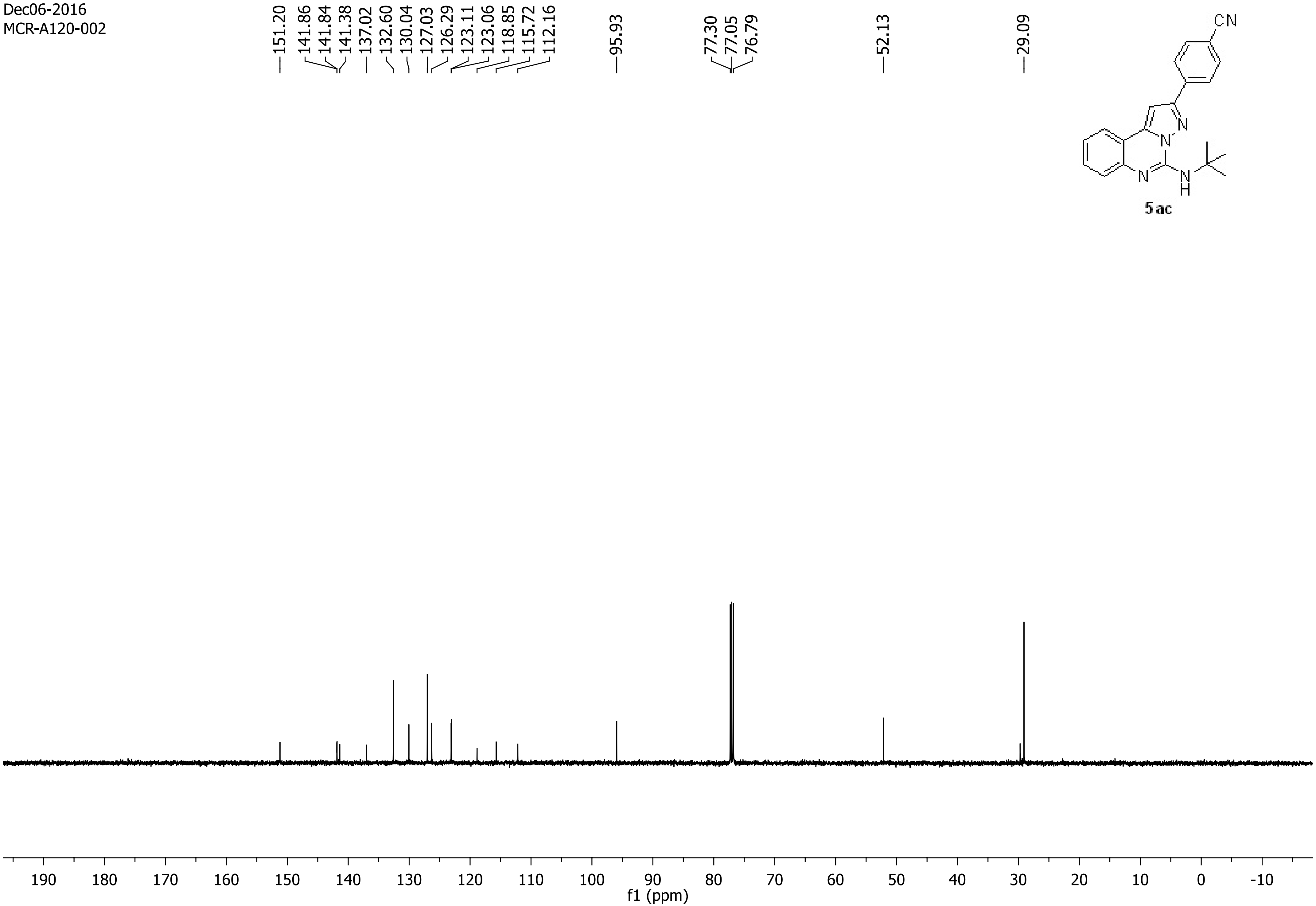
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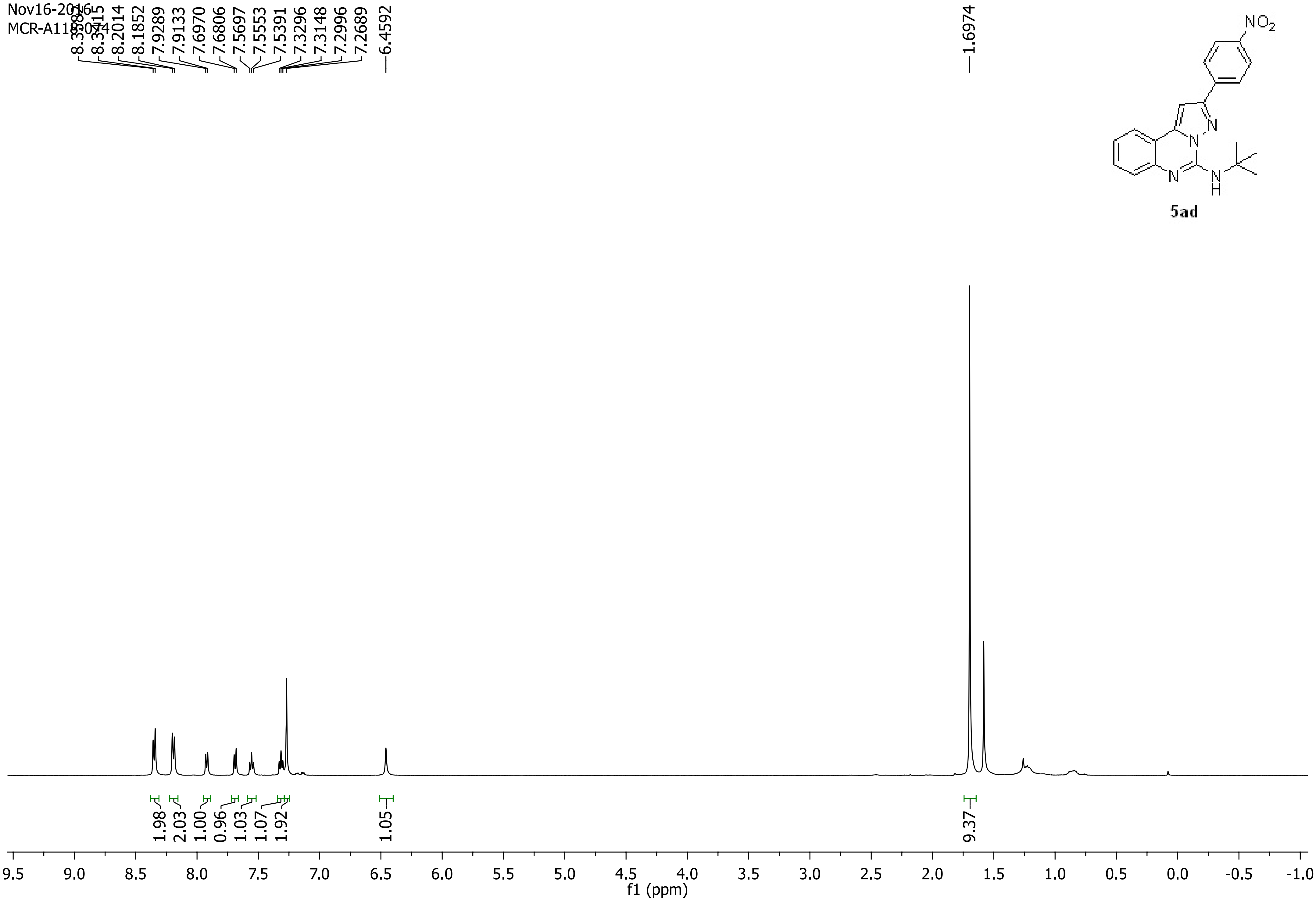
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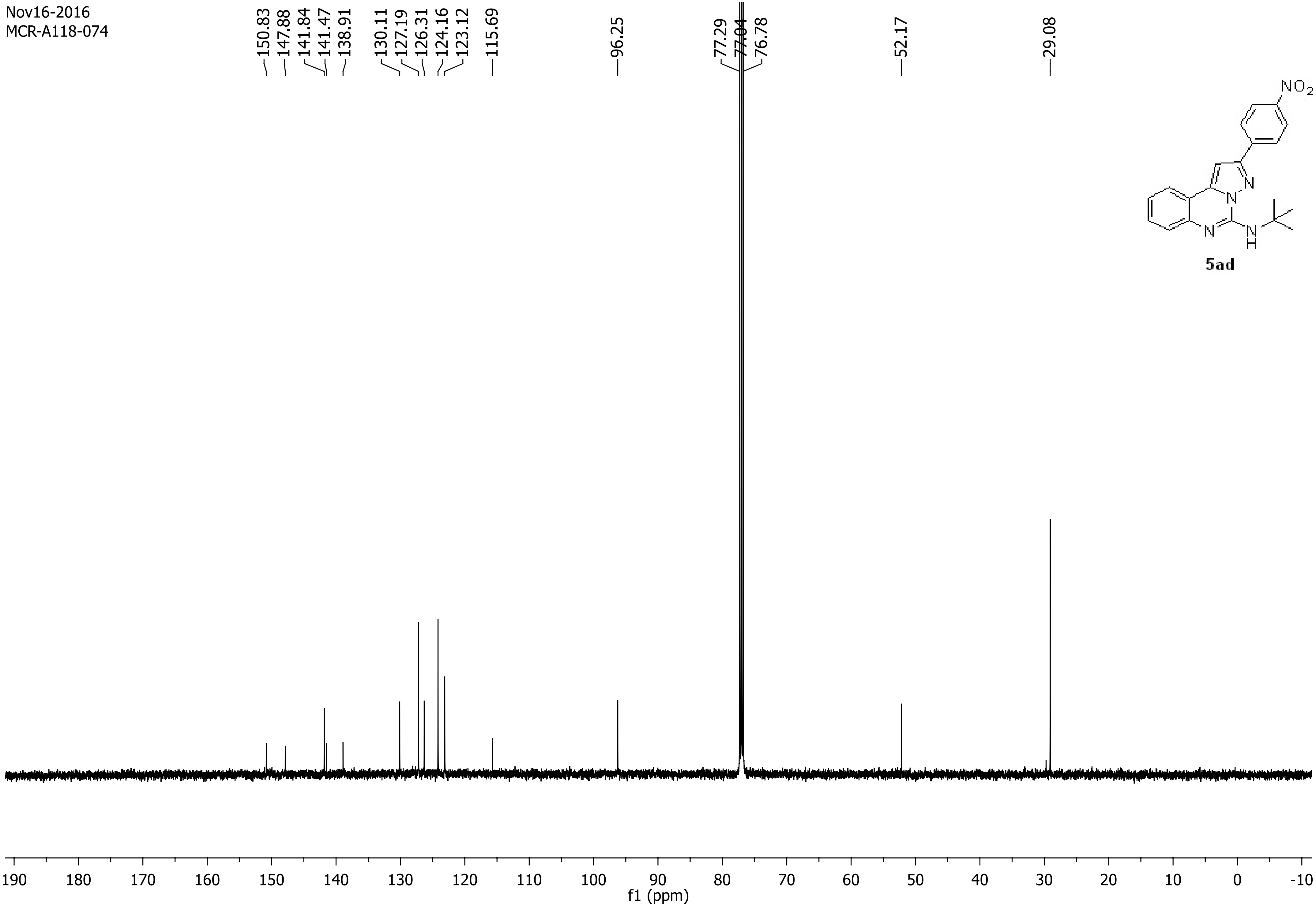
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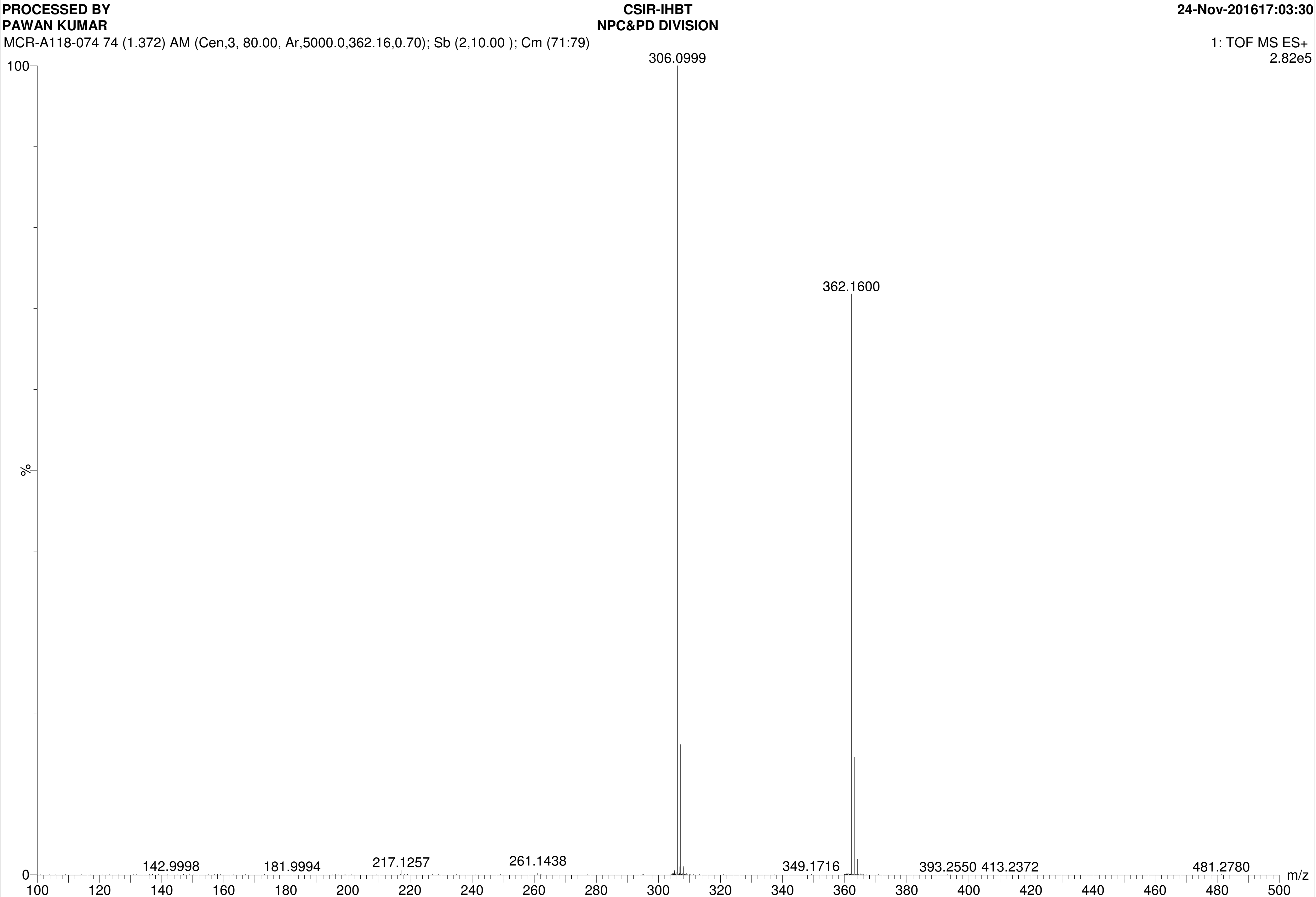
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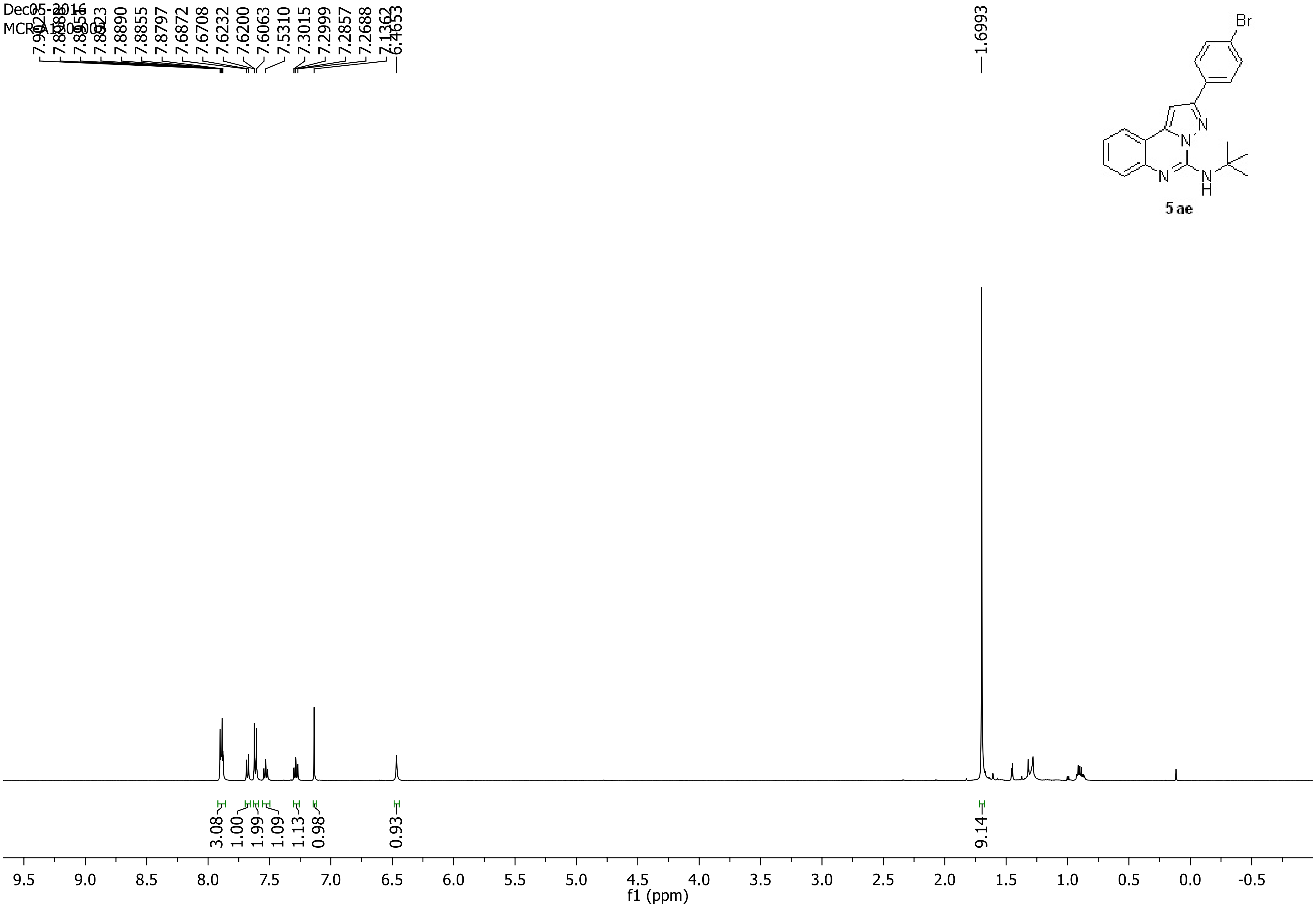
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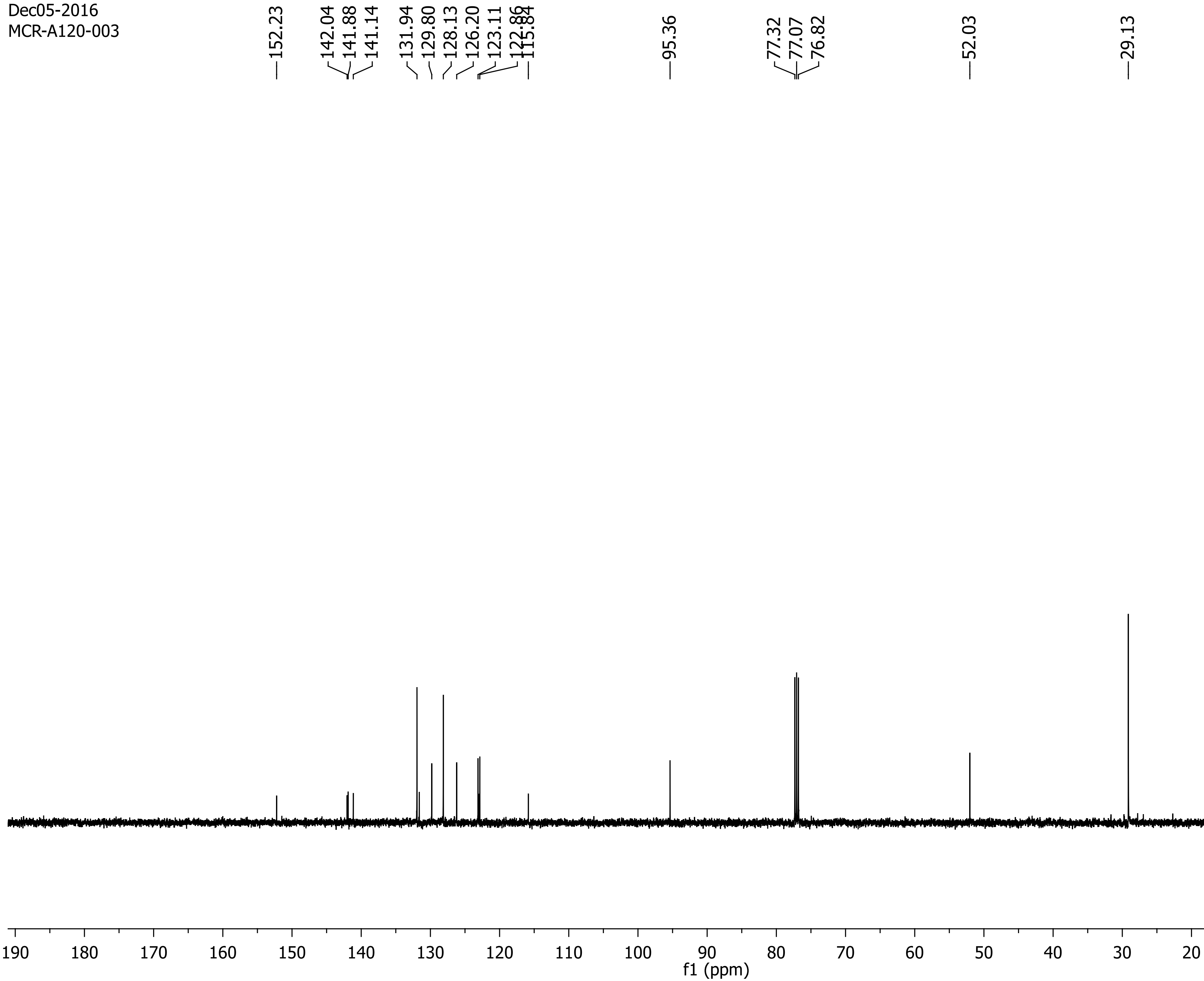
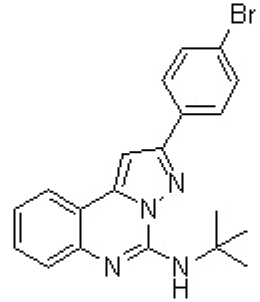
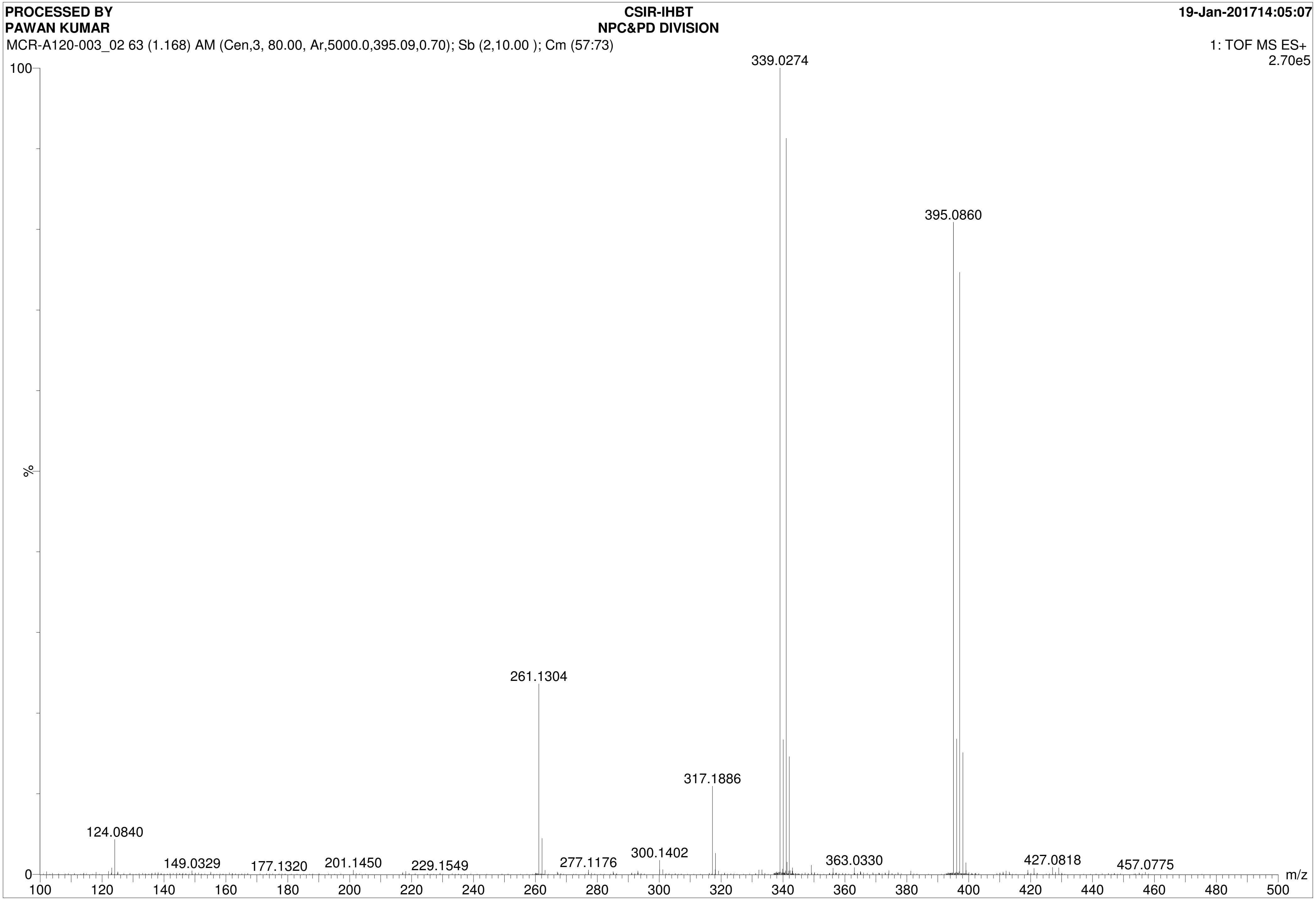
0.93
9.14
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

Dec05-2016
MCR-A120-003

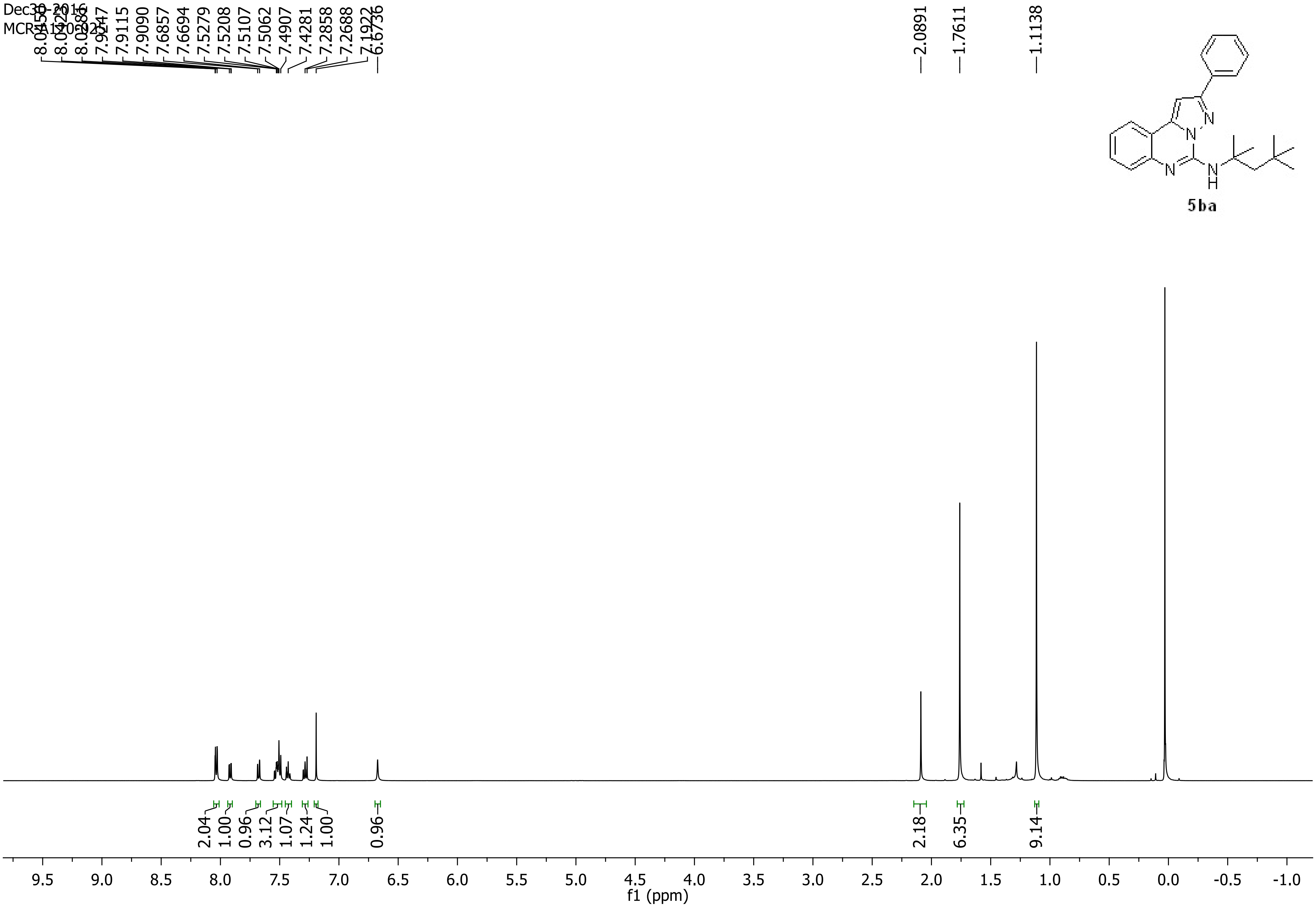




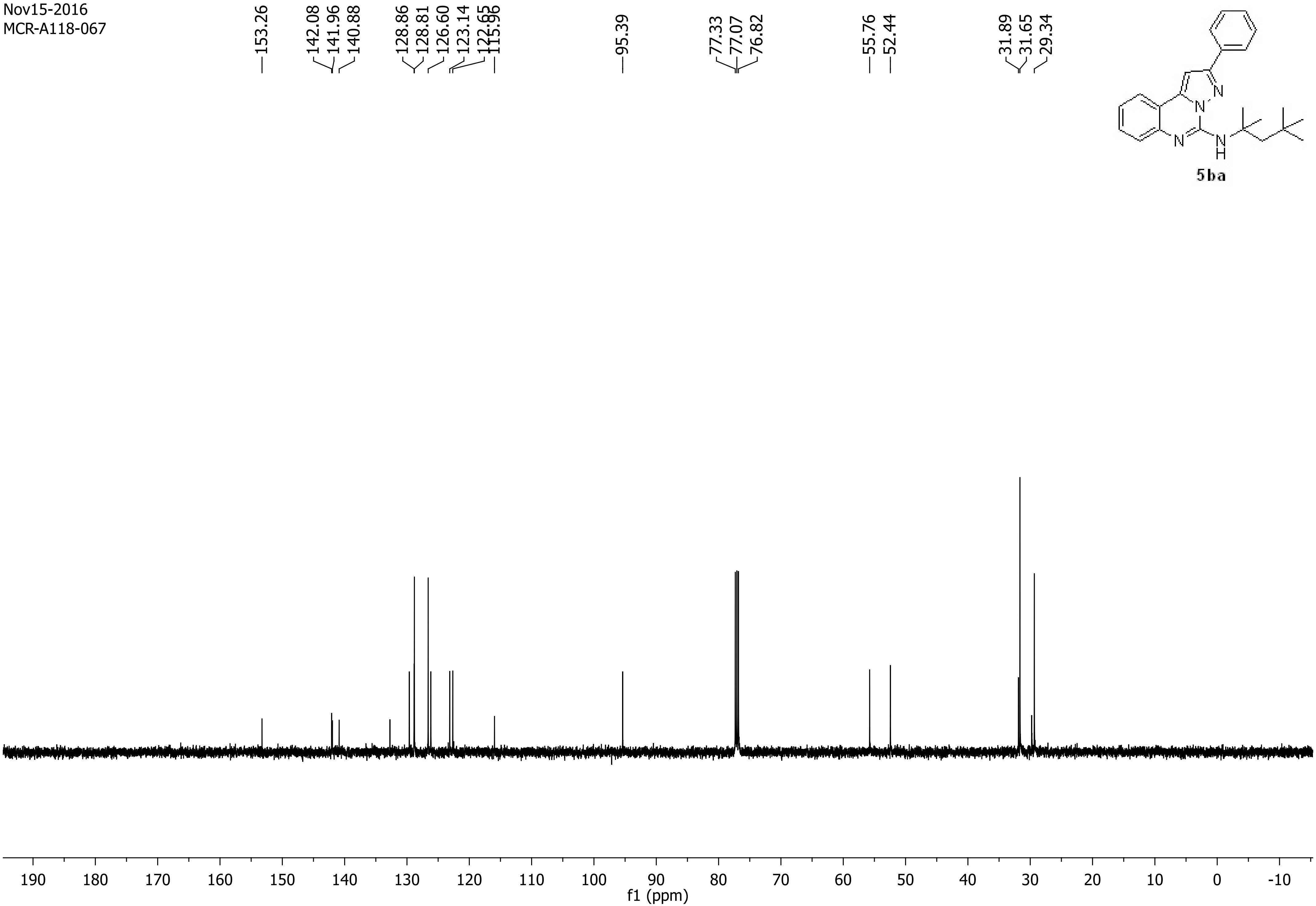
5 ae

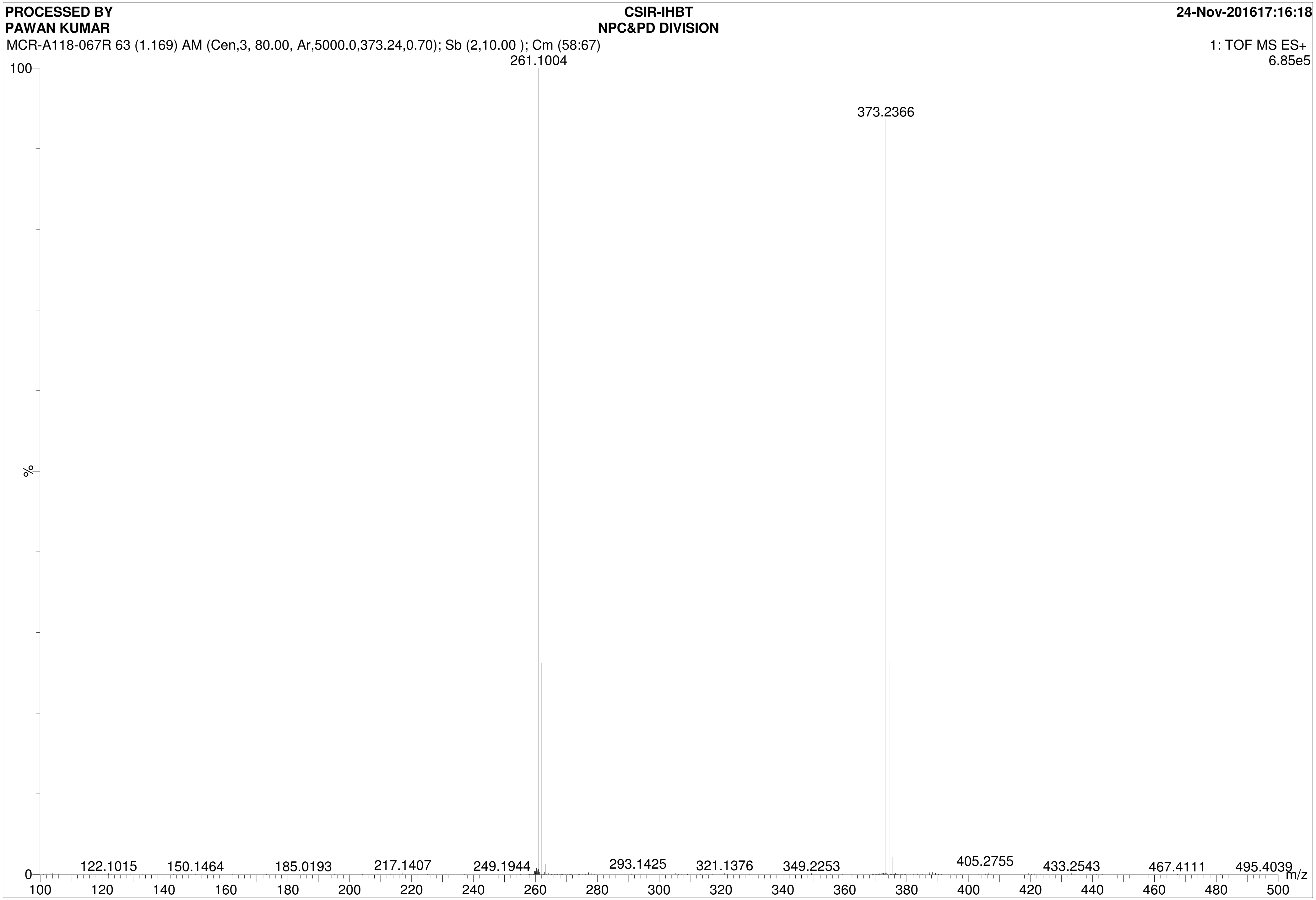


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:05:07
MCR-A120-003_02 63 (1.168) AM (Cen,3, 80.00, Ar,5000.0,395.09,0.70); Sb (2,10.00); Cm (57:73)
1: TOF MS ES+
2.70e5
339.0274
395.0860
261.1304
317.1886
124.0840
149.0329
177.1320
201.1450
229.1549
277.1176
300.1402
363.0330
427.0818
457.0775
%
m/z

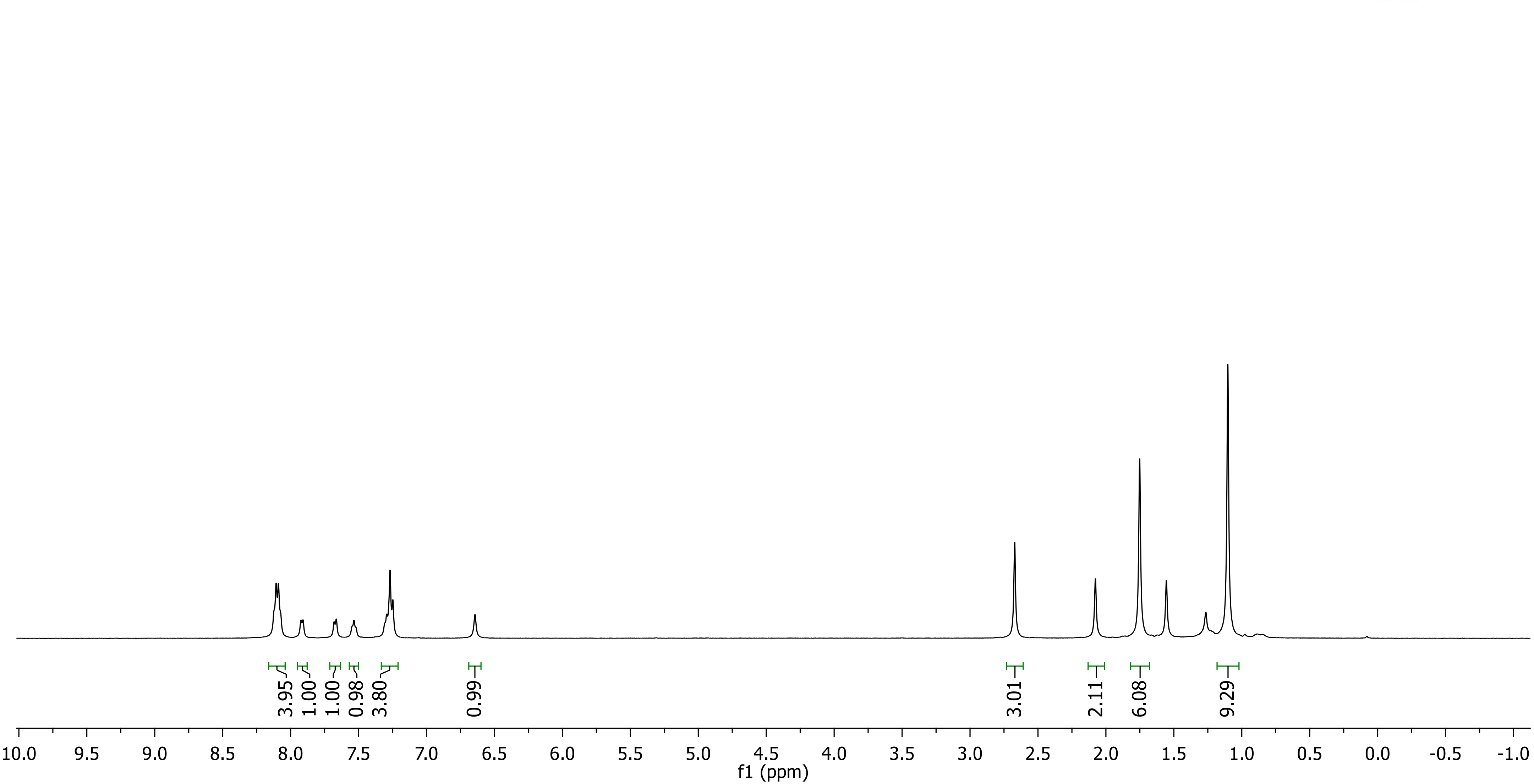

Dec30-2016
MCR-A120-021
8.0450
8.0329
8.0288
7.9247
7.9115
7.9090
7.6857
7.6694
7.5279
7.5208
7.5107
7.5062
7.4907
7.4281
7.2858
7.2688
7.1922
6.6736
2.0891
1.7611
1.1138
2.04
1.00
0.96
3.12
1.07
1.24
1.00
0.96
2.18
6.35
9.14
f1 (ppm)

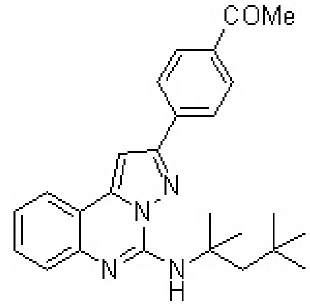
5ba


Nov15-2016
MCR-A118-067
153.26
142.08
141.96
140.88
128.86
128.81
126.60
123.14
122.65
115.96
95.39
77.33
77.07
76.82
55.76
52.44
31.89
31.65
29.34
N
N
N
N
H
5ba
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

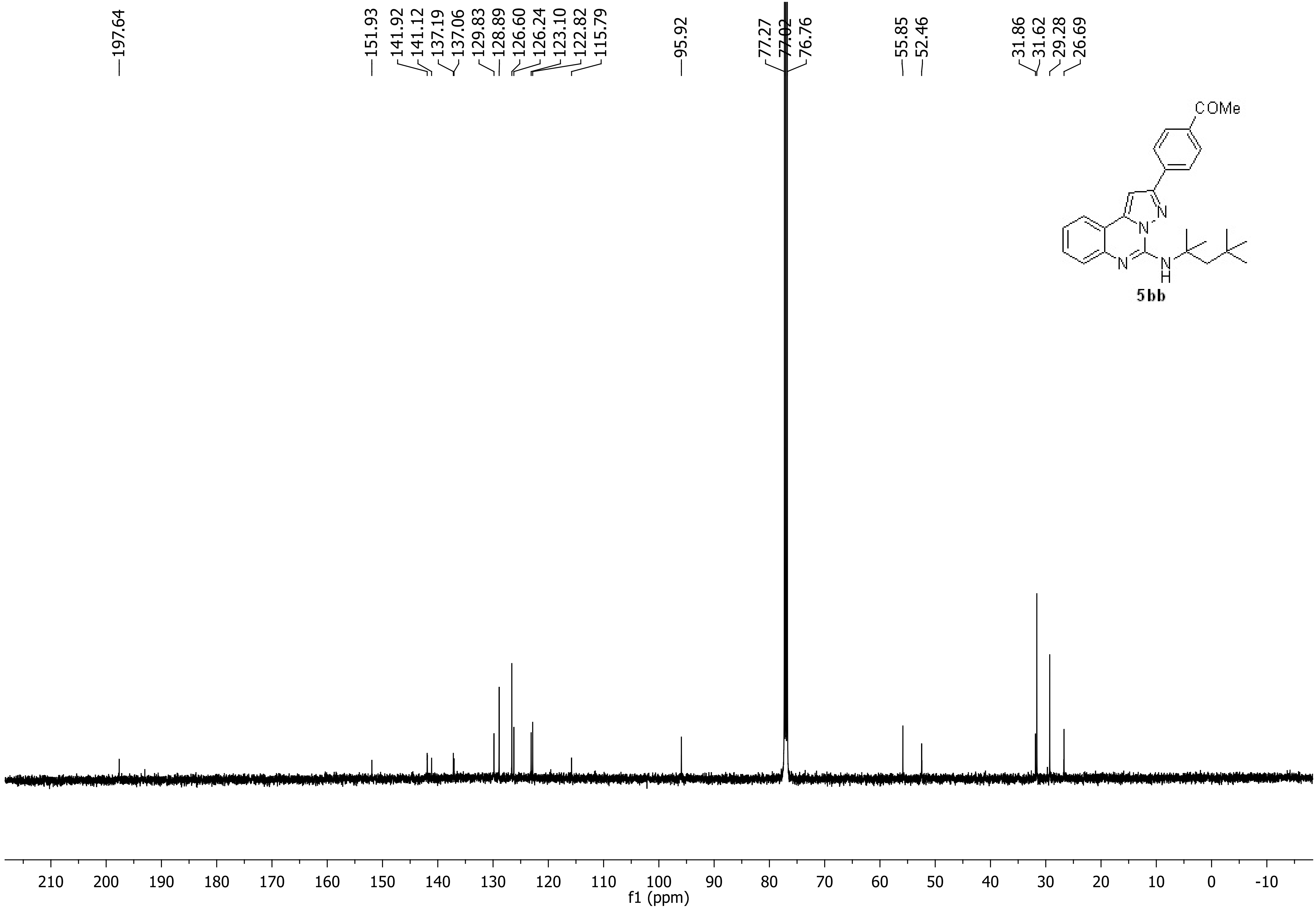

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201617:16:18
MCR-A118-067R 63 (1.169) AM (Cen,3, 80.00, Ar,5000.0,373.24,0.70); Sb (2,10.00); Cm (58:67)
1: TOF MS ES+
6.85e5
261.1004
373.2366
122.1015
150.1464
185.0193
217.1407
249.1944
293.1425
321.1376
349.2253
405.2755
433.2543
467.4111
495.4039
%
m/z

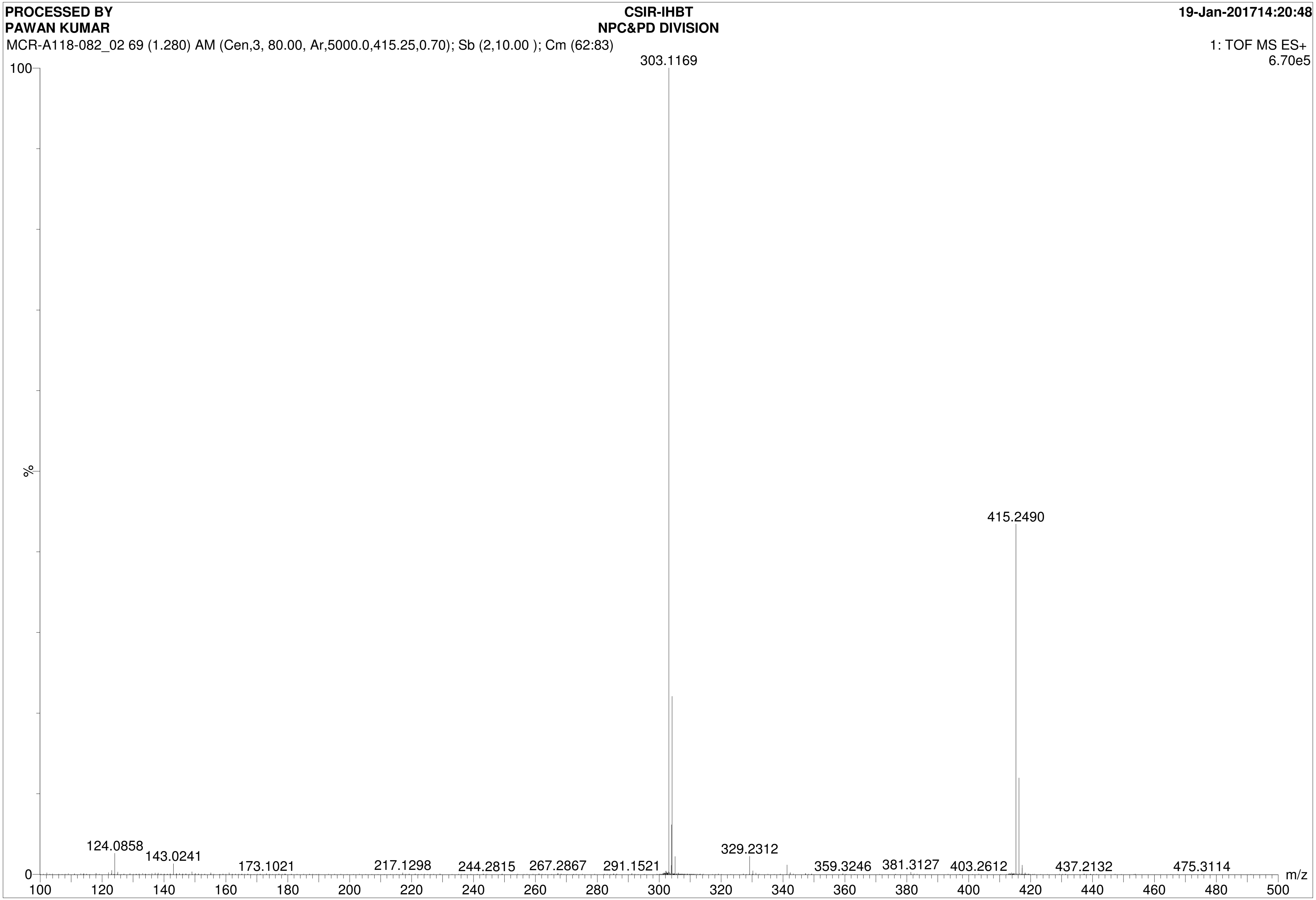
May30-2017
MCR-A118-082



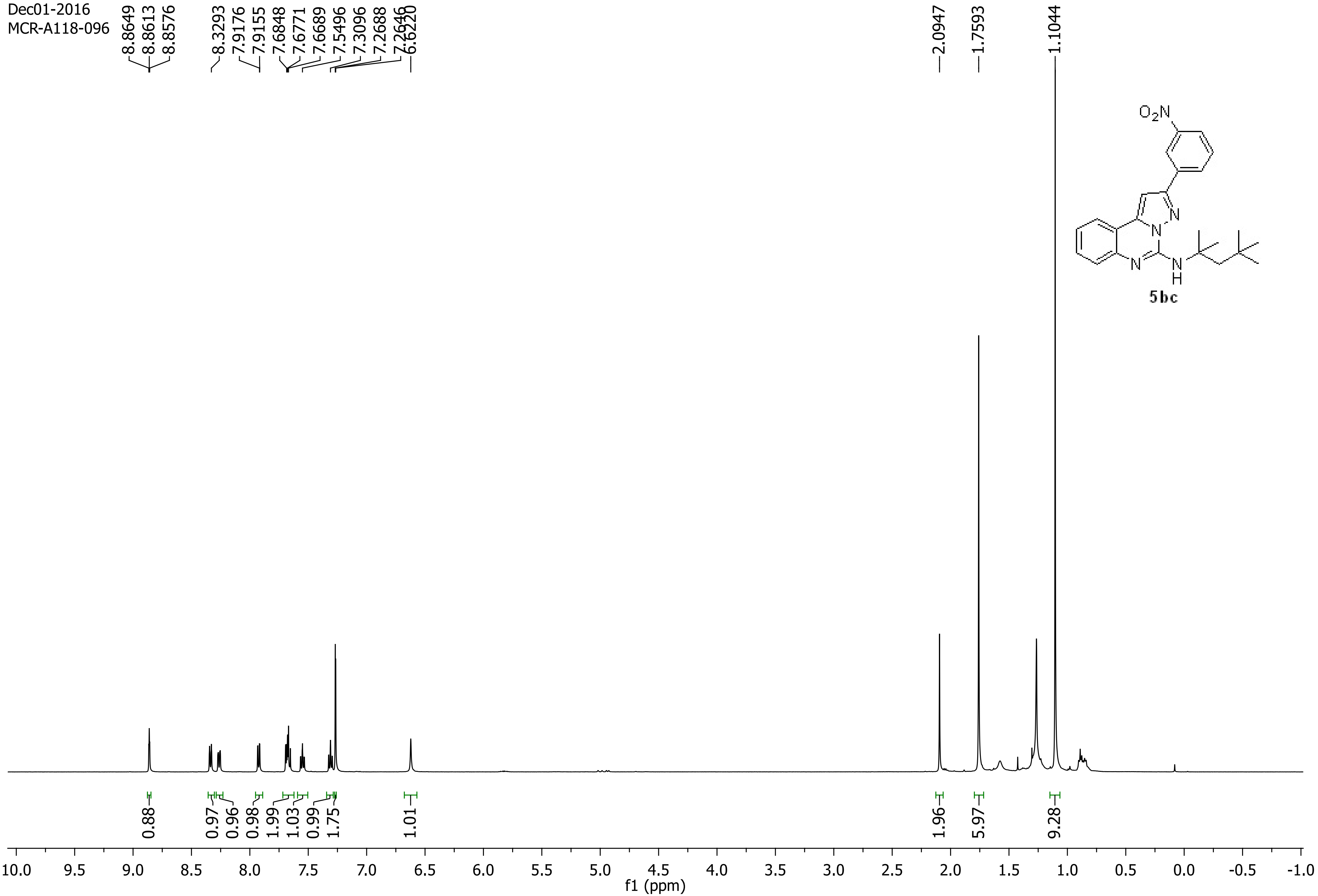


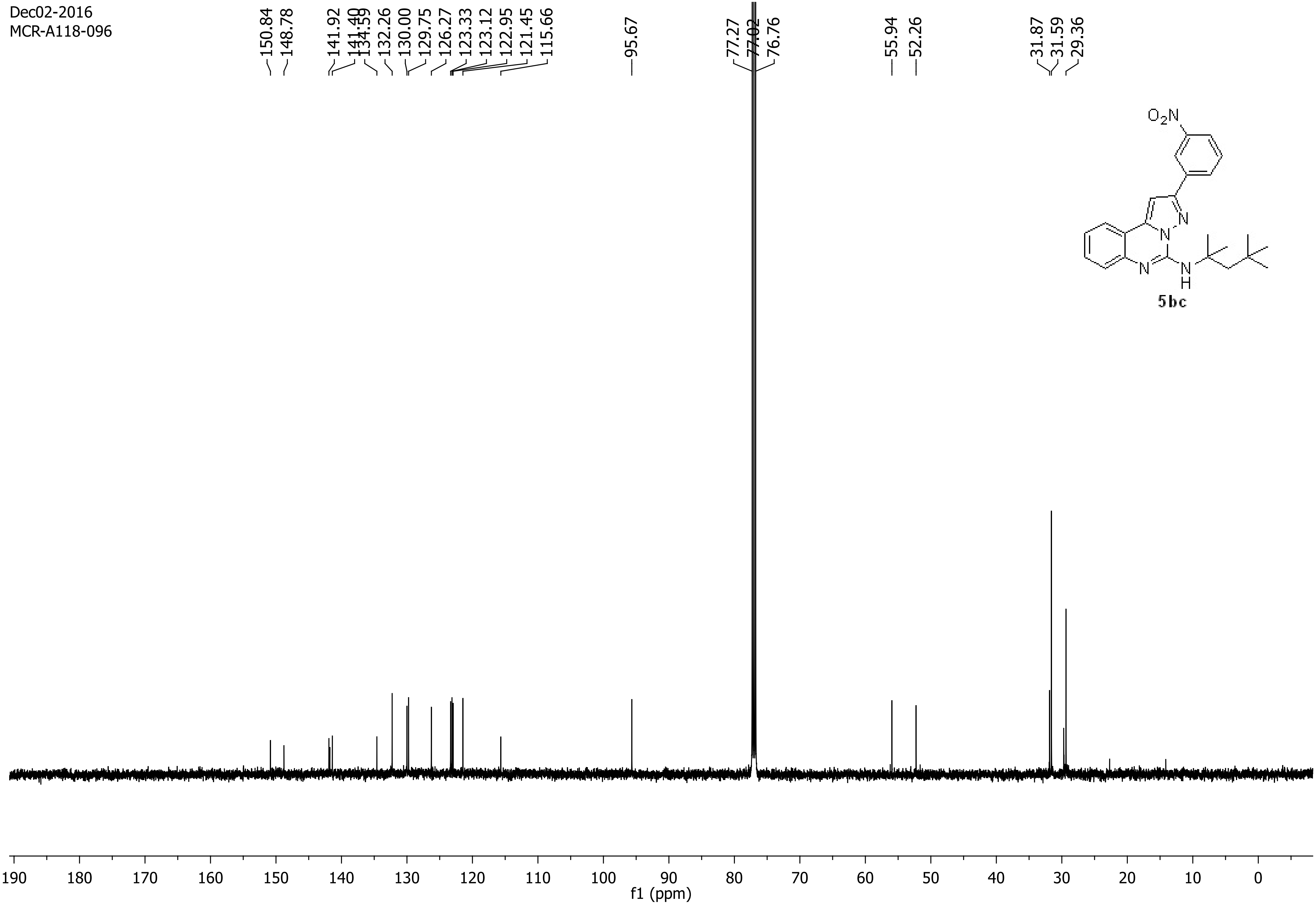
5bb

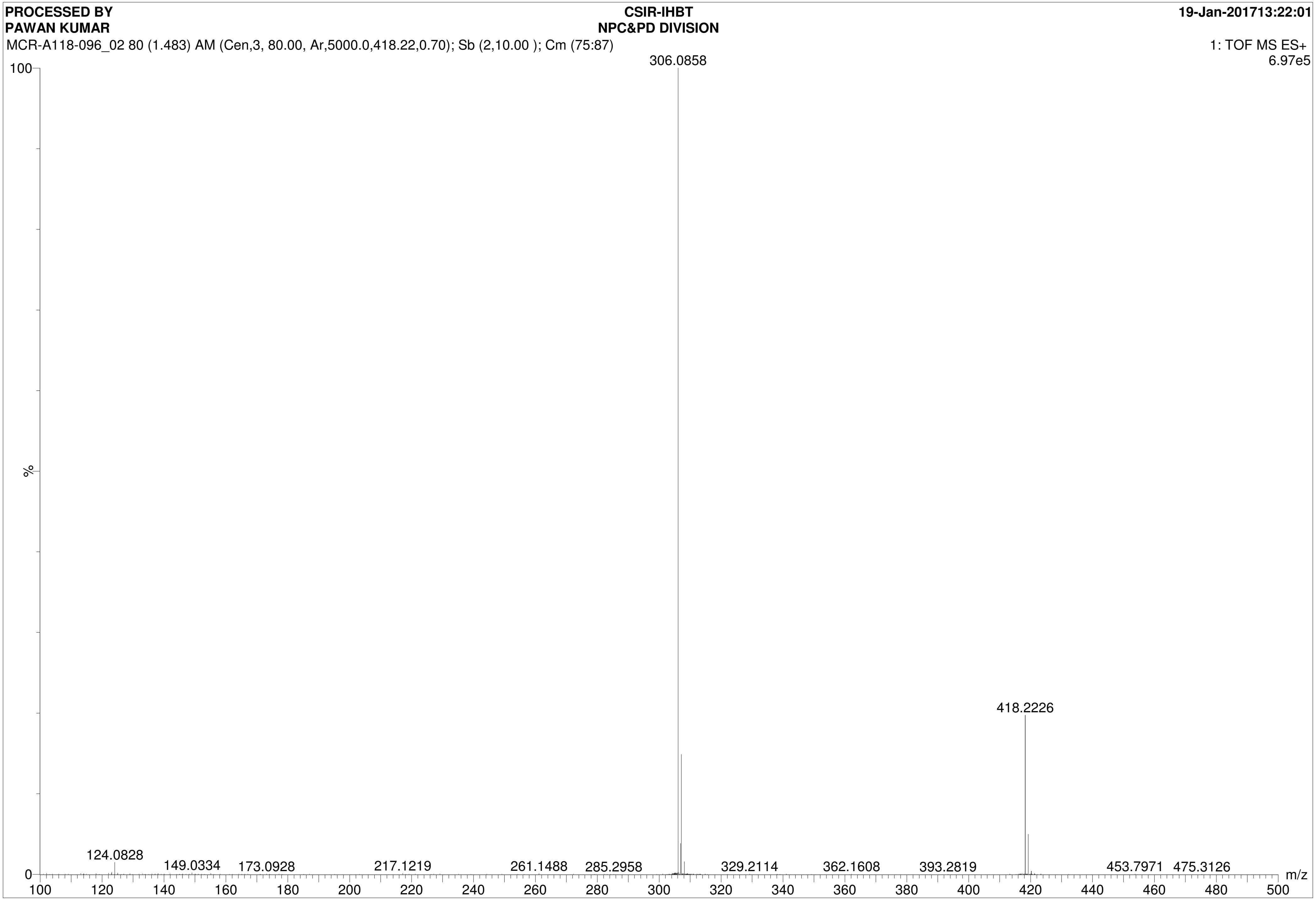

197.64
151.93
141.92
141.12
137.19
137.06
129.83
128.89
126.60
126.24
123.10
122.82
115.79
95.92
77.27
77.02
76.76
55.85
52.46
31.86
31.62
29.28
26.69
COMe
N
N
N
N
H
5bb
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

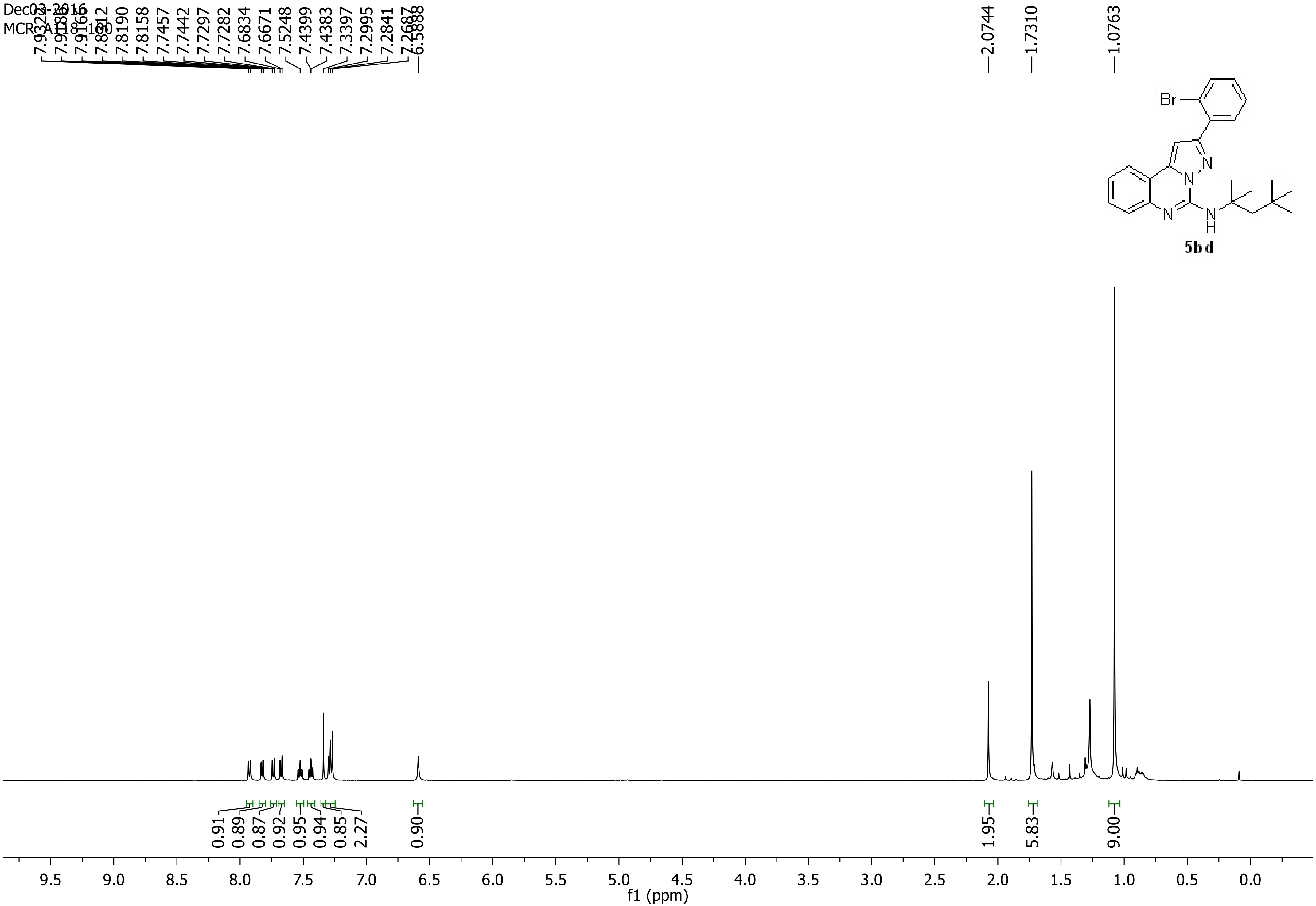


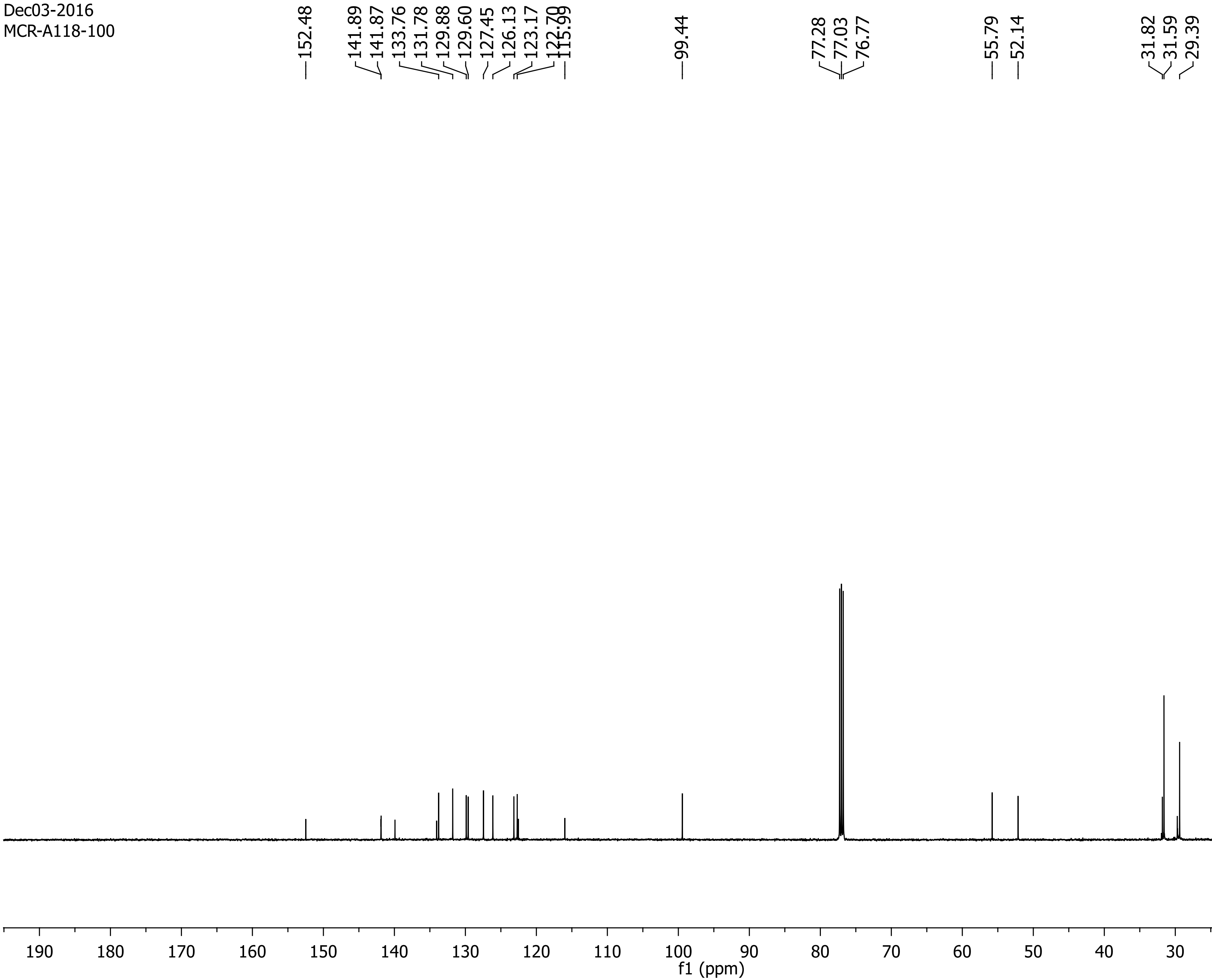
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:20:48
MCR-A118-082_02 69 (1.280) AM (Cen,3, 80.00, Ar,5000.0,415.25,0.70); Sb (2,10.00); Cm (62:83)
1: TOF MS ES+
6.70e5
303.1169
415.2490
124.0858
143.0241
173.1021
217.1298
244.2815
267.2867
291.1521
329.2312
359.3246
381.3127
403.2612
437.2132
475.3114
%
m/z

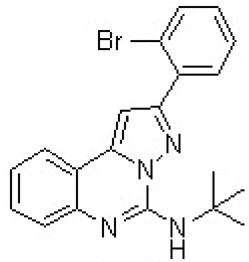

Dec01-2016
MCR-A118-096
8.8649
8.8613
8.8576
8.3293
7.9176
7.9155
7.6848
7.6771
7.6689
7.5496
7.3096
7.2688
7.2646
6.6220
2.0947
1.7593
1.1044
O_2N
N
N
N
N
H
5bc
0.88
0.97
0.96
0.98
1.99
1.03
0.99
1.75
1.01
1.96
5.97
9.28
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


Dec02-2016
MCR-A118-096
150.84
148.78
141.92
141.40
134.59
132.26
130.00
129.75
126.27
123.33
123.12
122.95
121.45
115.66
95.67
77.27
77.02
76.76
55.94
52.26
31.87
31.59
29.36
O2N
N
N
N
N
H
5bc
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

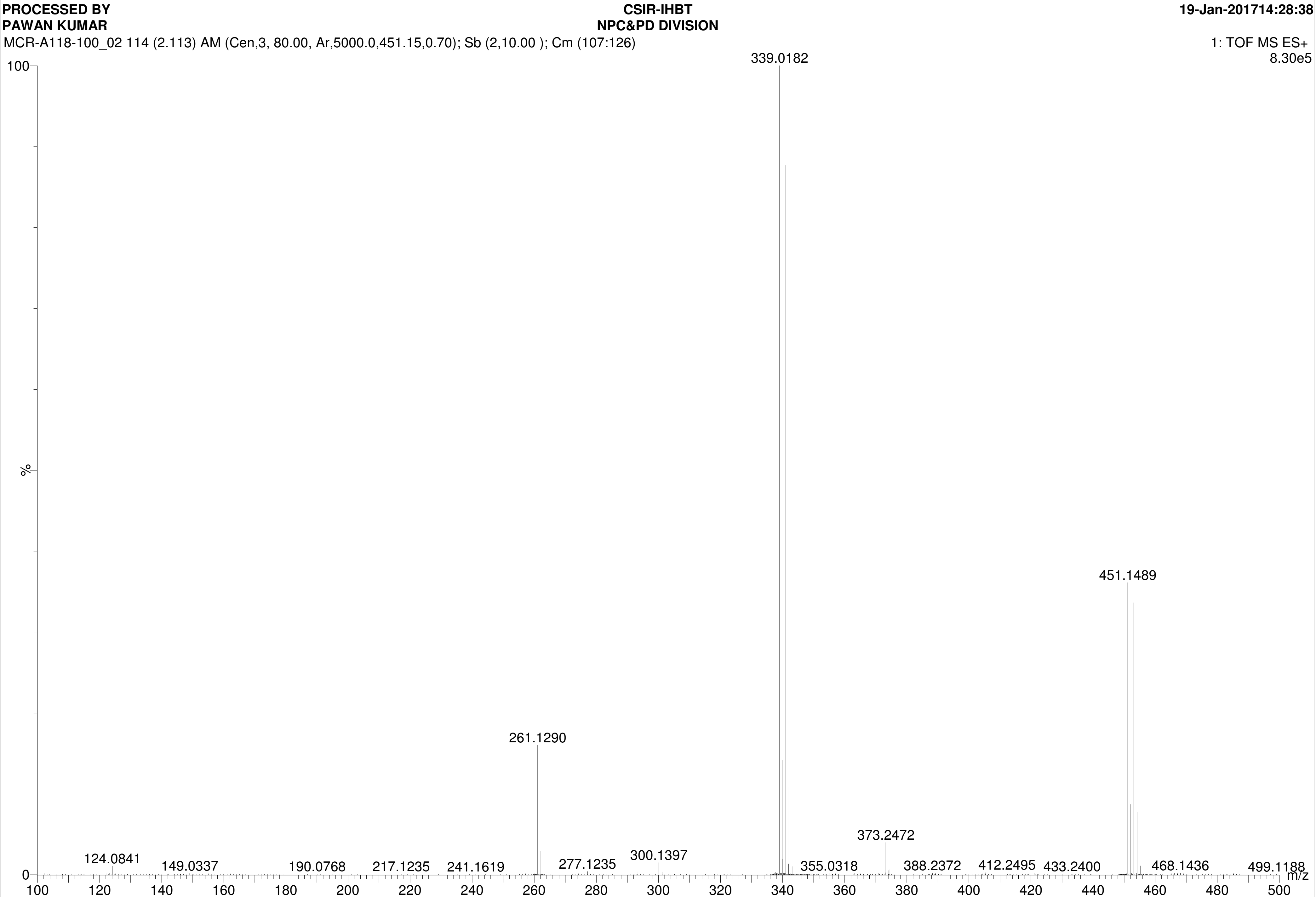

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:22:01
MCR-A118-096_02 80 (1.483) AM (Cen,3, 80.00, Ar,5000.0,418.22,0.70); Sb (2,10.00); Cm (75:87)
1: TOF MS ES+
6.97e5
306.0858
418.2226
124.0828
149.0334
173.0928
217.1219
261.1488
285.2958
329.2114
362.1608
393.2819
453.7971
475.3126
%
m/z

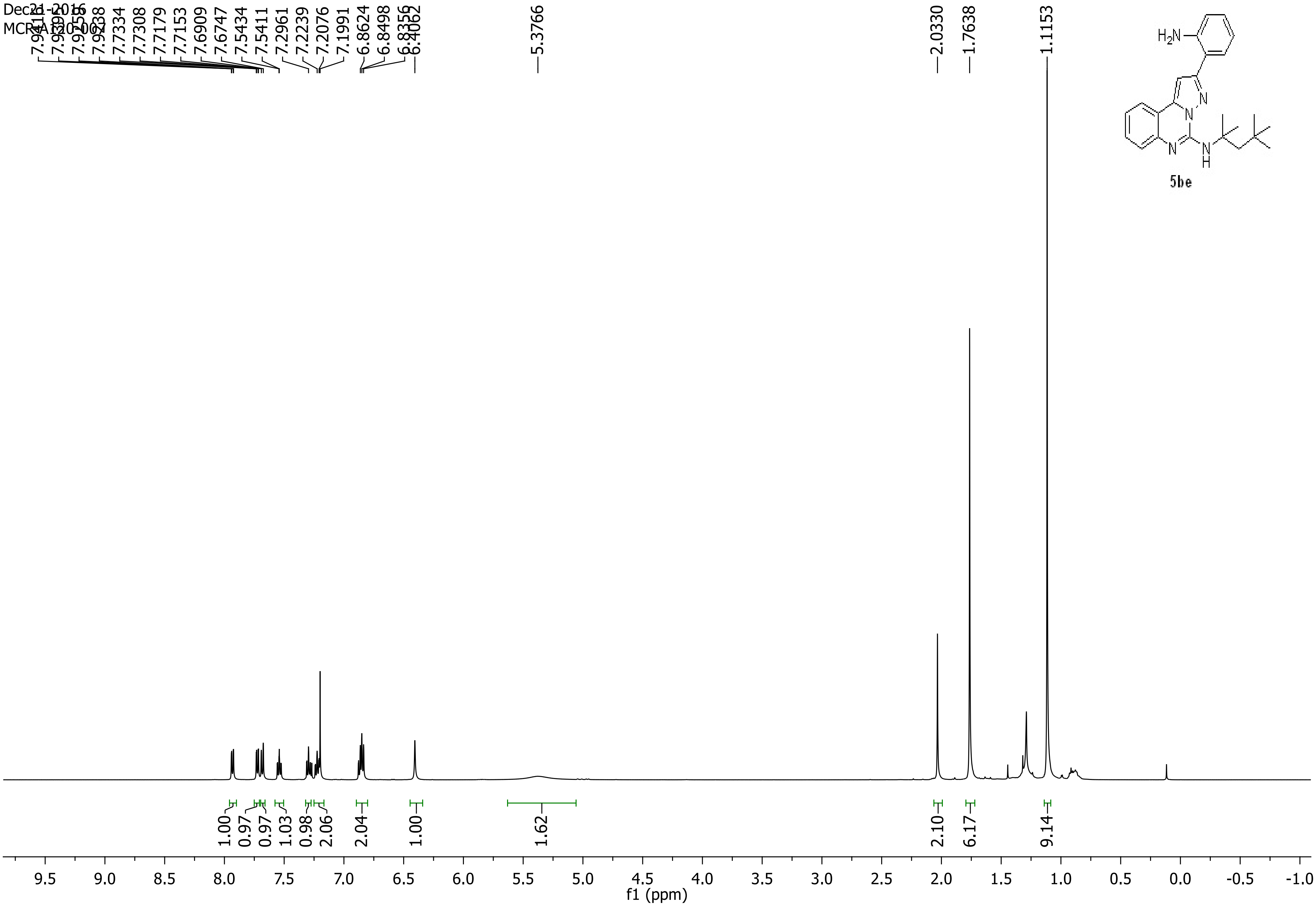

Dec03-2016
MCR-A118_100
7.9324
7.9161
7.8312
7.8190
7.8158
7.7457
7.7442
7.7297
7.7282
7.6834
7.6671
7.5248
7.4399
7.4383
7.3397
7.2995
7.2841
7.2687
6.5888
2.0744
1.7310
1.0763
Br
N
N
N
N
H
5bd
0.91
0.89
0.87
0.92
0.95
0.94
0.85
2.27
0.90
1.95
5.83
9.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Dec03-2016
MCR-A118-100
152.48
141.89
141.87
133.76
131.78
129.88
129.60
127.45
126.13
123.17
122.70
115.99
99.44
77.28
77.03
76.77
55.79
52.14
31.82
31.59
29.39
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

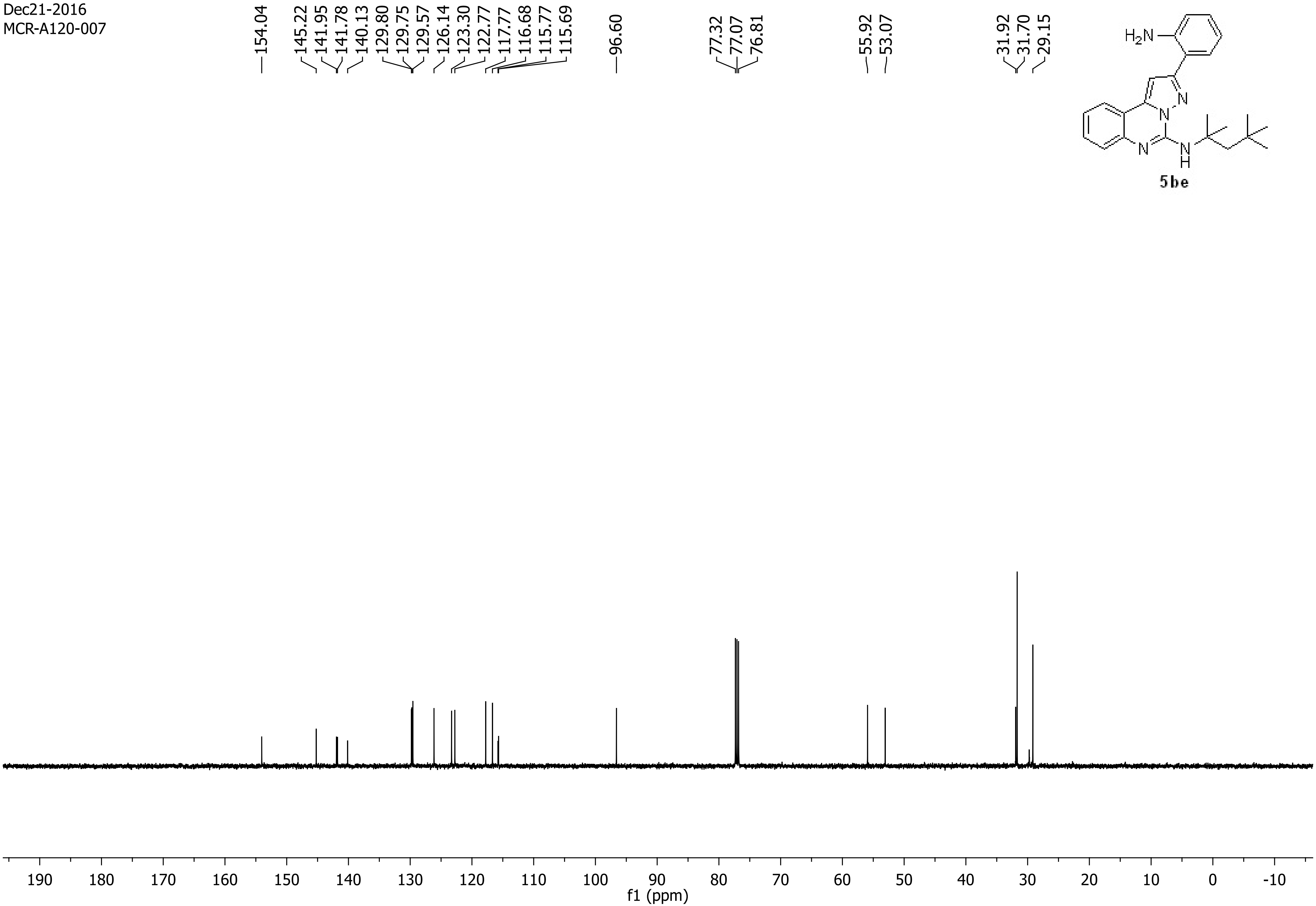

Br
N
N
N
N
H

5bd

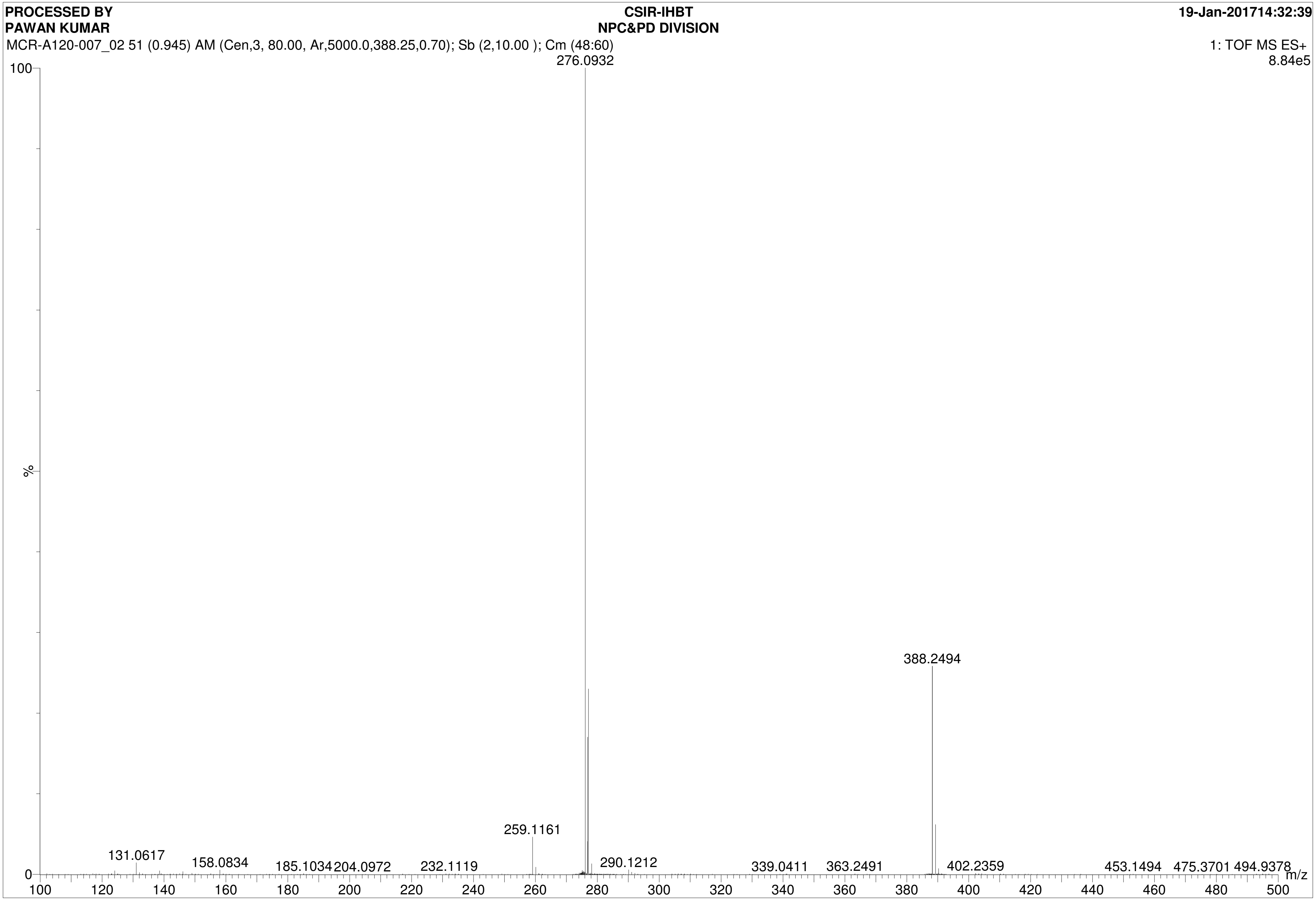

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:28:38
MCR-A118-100_02 114 (2.113) AM (Cen,3, 80.00, Ar,5000.0,451.15,0.70); Sb (2,10.00); Cm (107:126)
1: TOF MS ES+
8.30e5
339.0182
451.1489
261.1290
373.2472
124.0841
149.0337
190.0768
217.1235
241.1619
277.1235
300.1397
355.0318
388.2372
412.2495
433.2400
468.1436
499.1188
m/z
%
100
0
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500

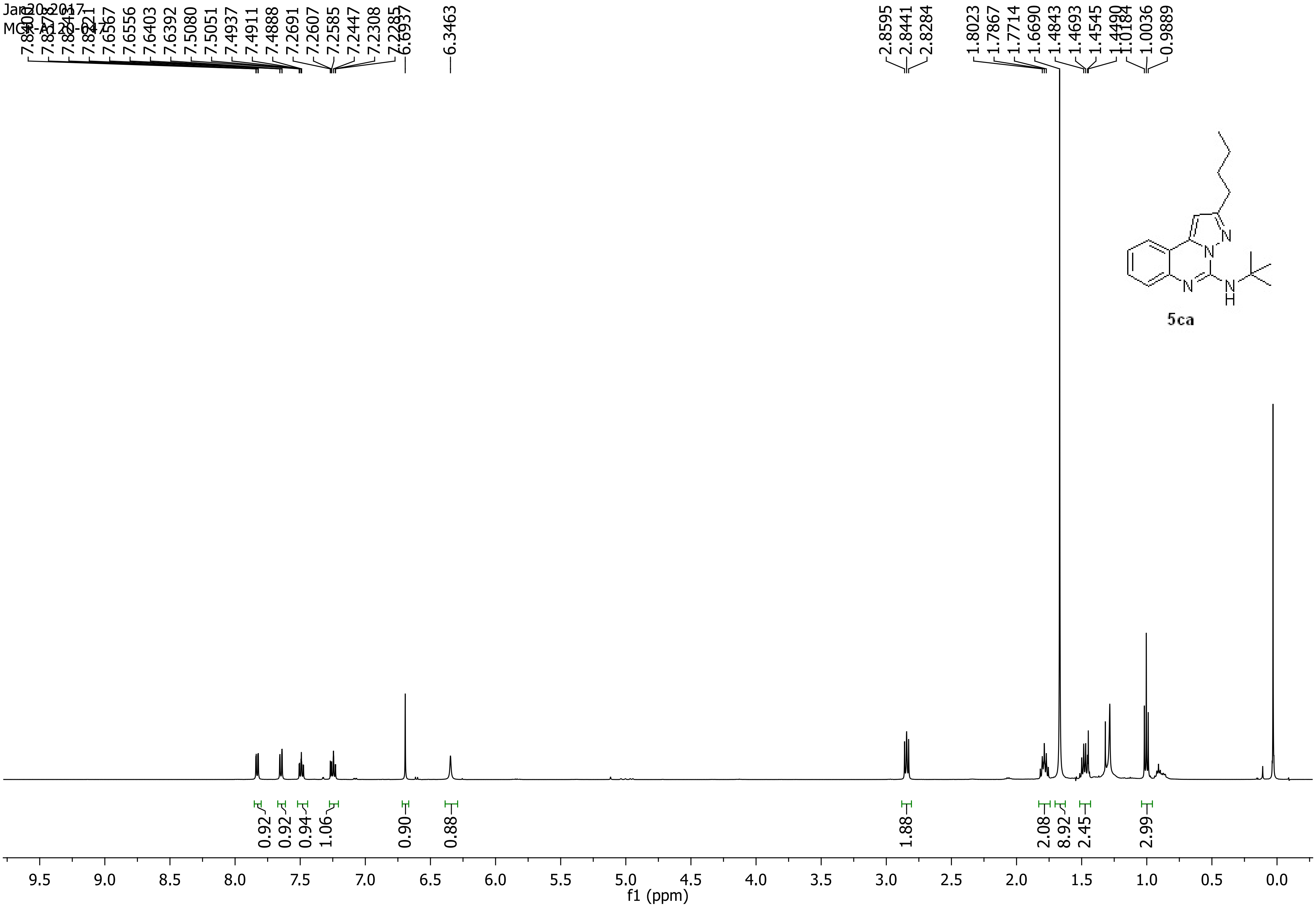


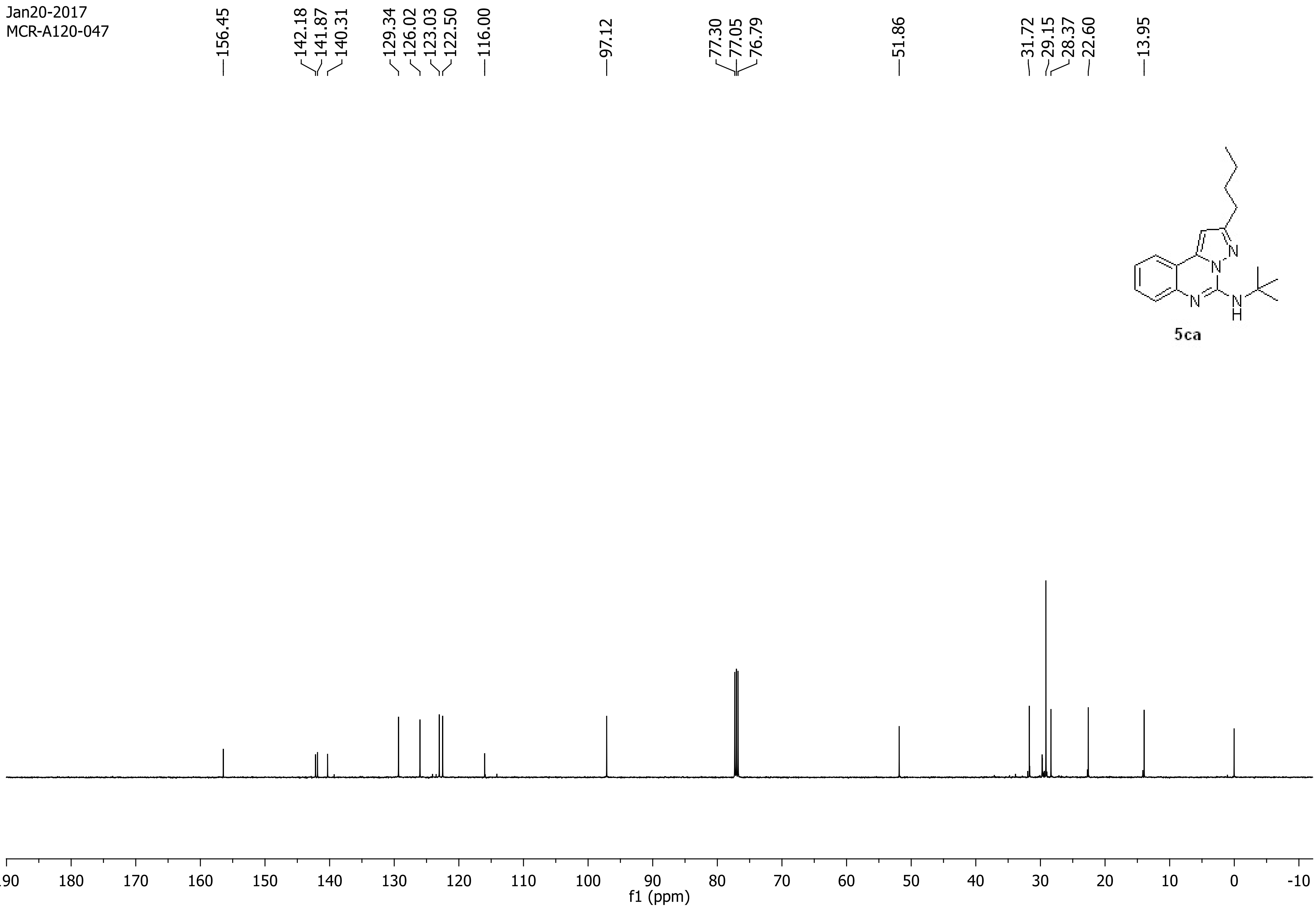
7.7334
7.7308
7.7179
7.7153
7.6909
7.6747
7.5434
7.5411
7.2961
7.2239
7.2076
7.1991
6.8624
6.8498
6.8356
6.4062
5.3766
2.0330
1.7638
1.1153
H2N
N
N
N
N
H
5be
1.00
0.97
0.97
1.03
0.98
2.06
2.04
1.00
1.62
2.10
6.17
9.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

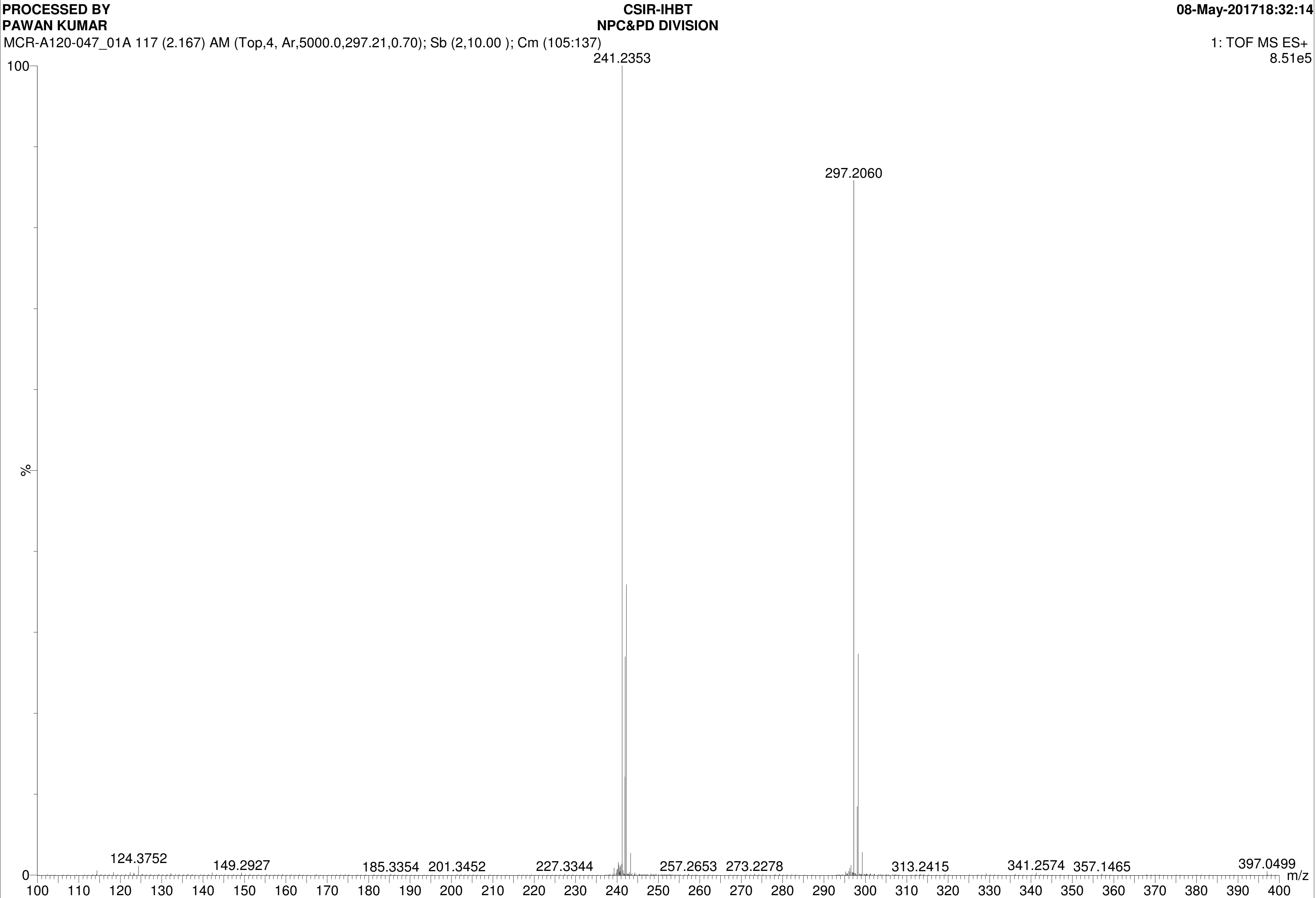

Dec21-2016
MCR-A120-007
154.04
145.22
141.95
141.78
140.13
129.80
129.75
129.57
126.14
123.30
122.77
117.77
116.68
115.77
115.69
96.60
77.32
77.07
76.81
55.92
53.07
31.92
31.70
29.15
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
H2N
N
N
N
N
H

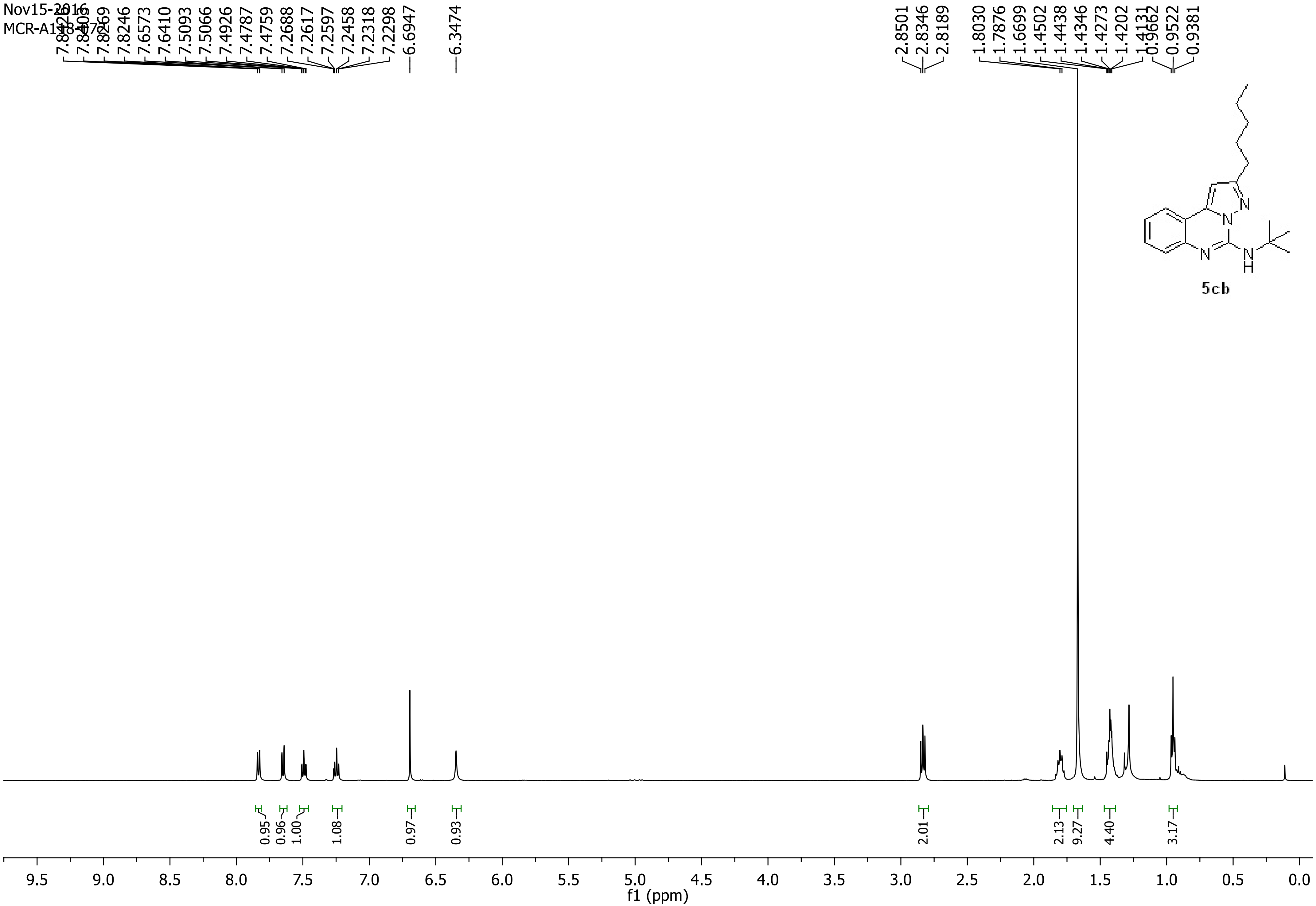
5be


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:32:39
MCR-A120-007_02 51 (0.945) AM (Cen,3, 80.00, Ar,5000.0,388.25,0.70); Sb (2,10.00); Cm (48:60)
1: TOF MS ES+
8.84e5
276.0932
388.2494
259.1161
131.0617
158.0834
185.1034
204.0972
232.1119
290.1212
339.0411
363.2491
402.2359
453.1494
475.3701
494.9378
%
m/z


Jan20-2017
MCR-A120-047
7.8303
7.8279
7.8245
7.8221
7.6567
7.6556
7.6403
7.6392
7.5080
7.5051
7.4937
7.4911
7.4888
7.2691
7.2607
7.2585
7.2447
7.2308
7.2285
6.6937
6.3463
2.8595
2.8441
2.8284
1.8023
1.7867
1.7714
1.6690
1.4843
1.4693
1.4545
1.4490
1.0184
1.0036
0.9889
N
N
N
N
H
5ca
0.92
0.92
0.94
1.06
0.90
0.88
1.88
2.08
8.92
2.45
2.99
f1 (ppm)

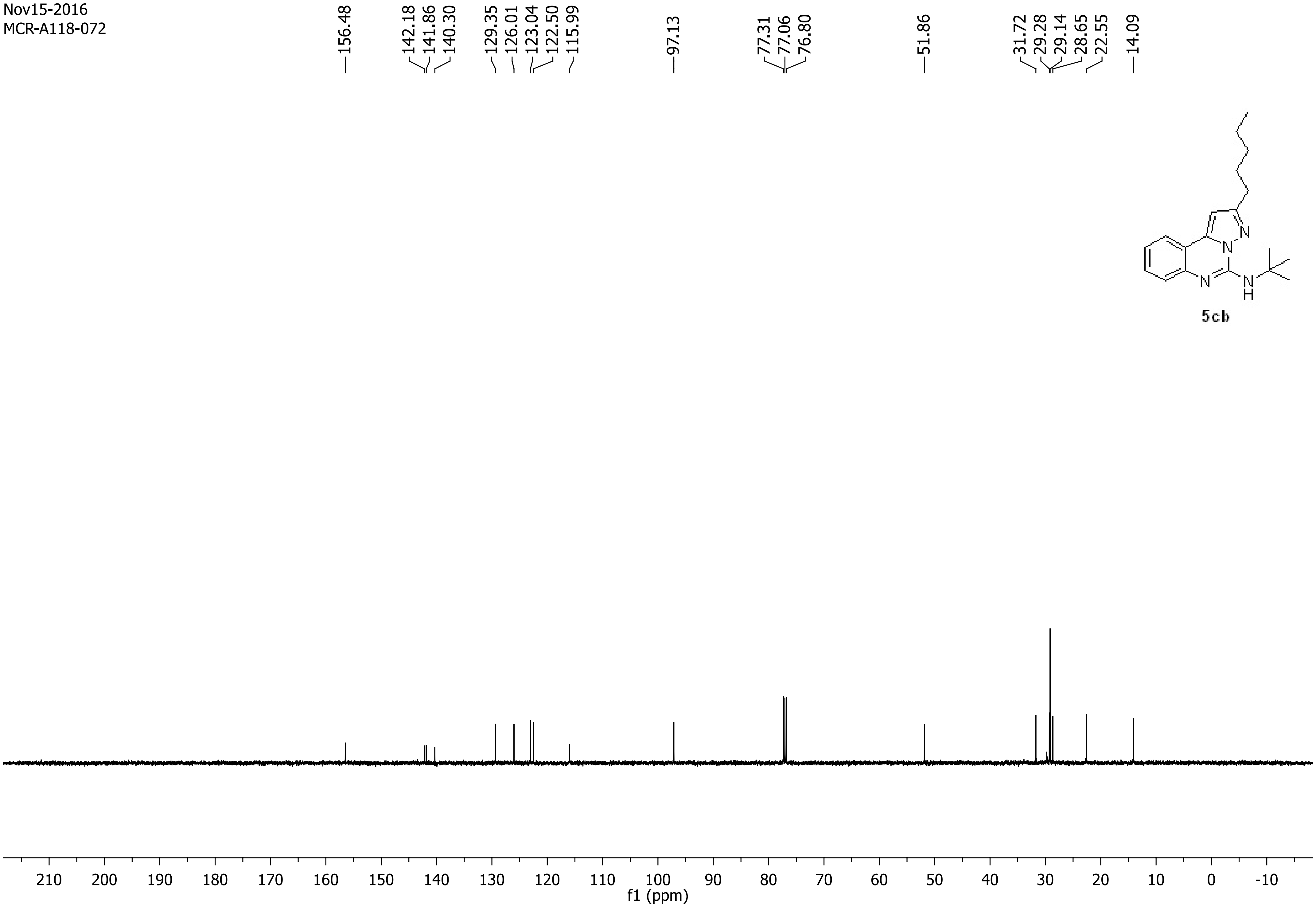

Jan20-2017
MCR-A120-047
156.45
142.18
141.87
140.31
129.34
126.02
123.03
122.50
116.00
97.12
77.30
77.05
76.79
51.86
31.72
29.15
28.37
22.60
13.95
N
N
N
N
H
5ca
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
08-May-201718:32:14
MCR-A120-047_01A 117 (2.167) AM (Top,4, Ar,5000.0,297.21,0.70); Sb (2,10.00); Cm (105:137)
1: TOF MS ES+
8.51e5
241.2353
297.2060
124.3752
149.2927
185.3354
201.3452
227.3344
257.2653
273.2278
313.2415
341.2574
357.1465
397.0499
%
m/z

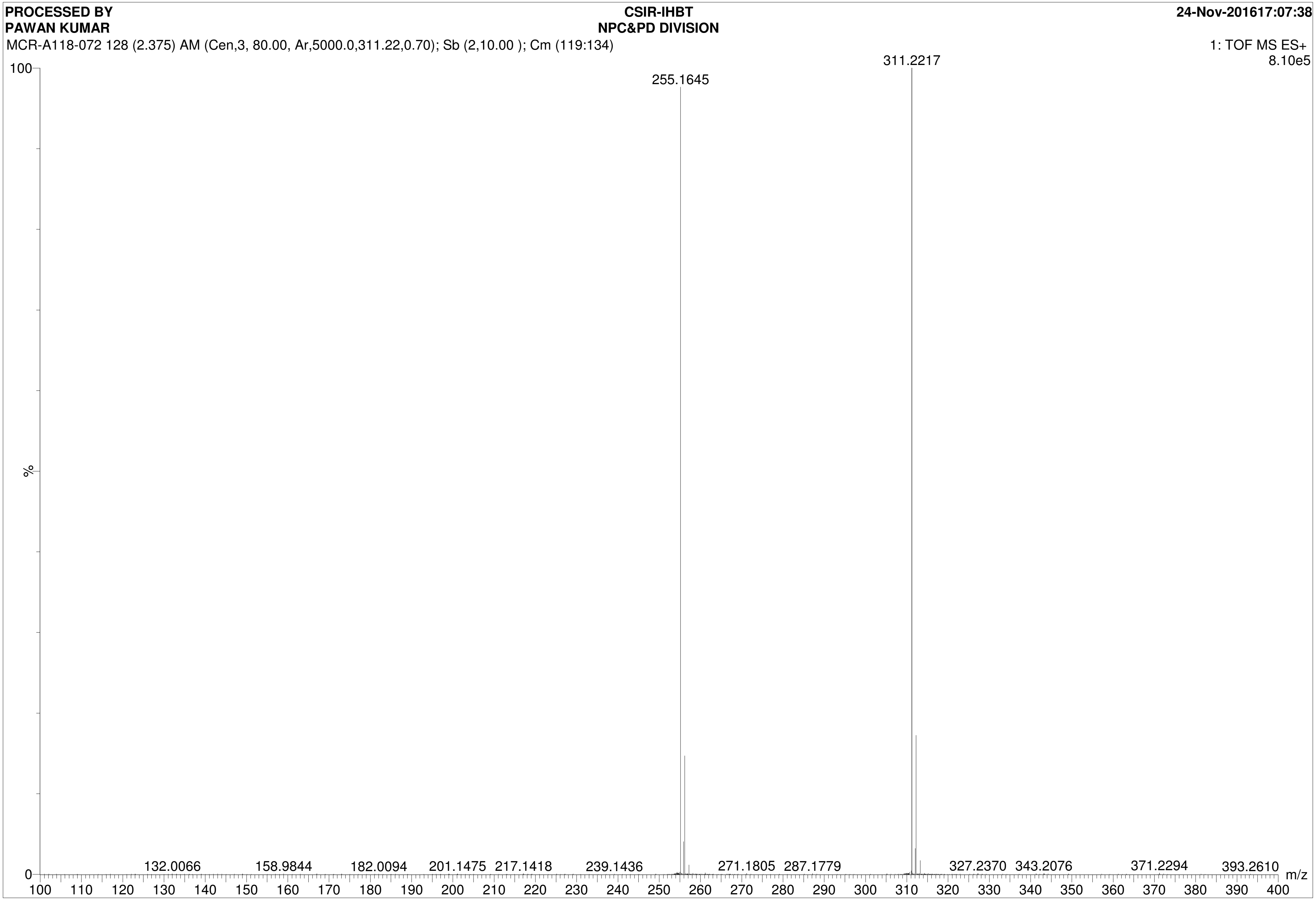


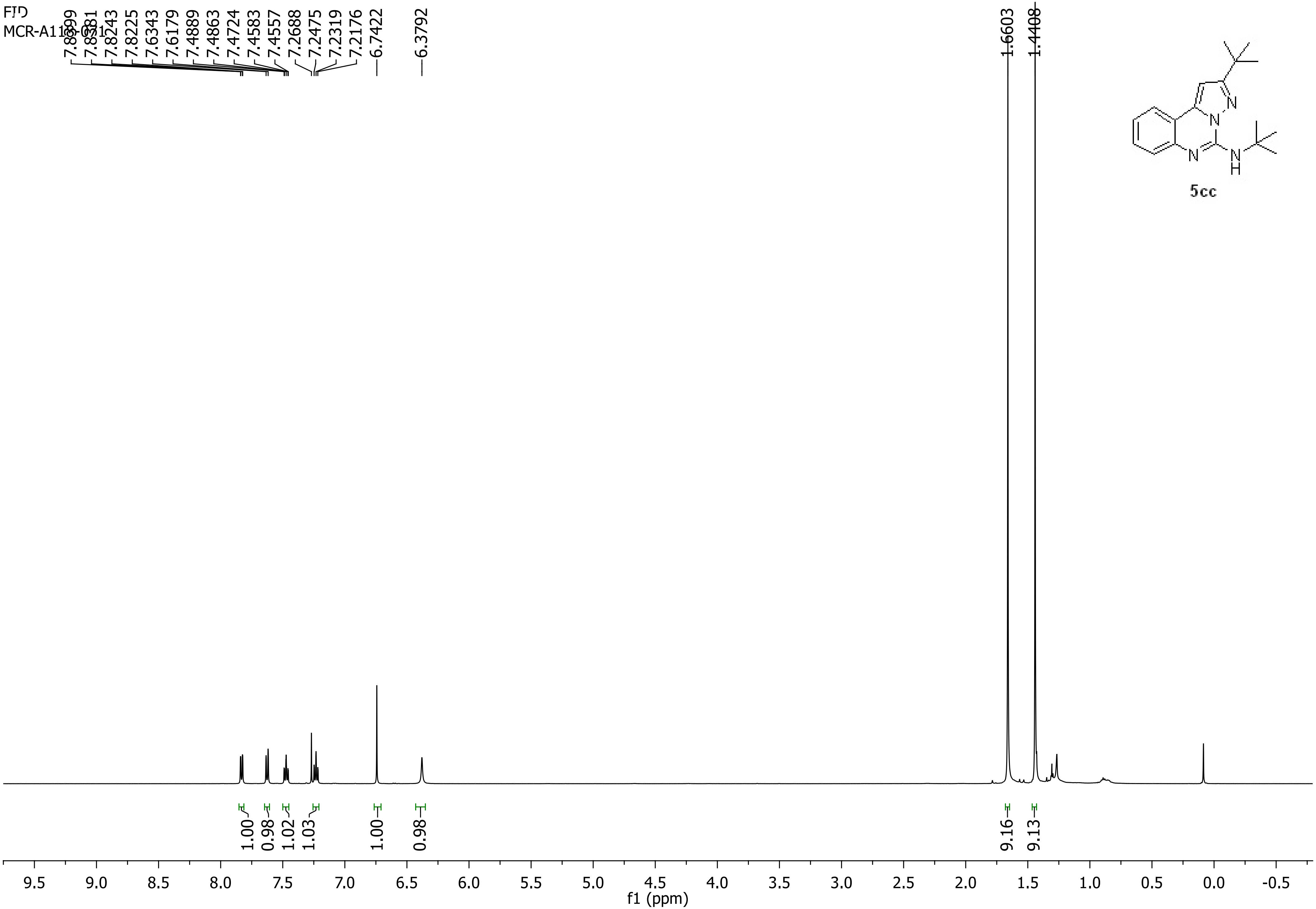
Nov15-2016
7.8529
7.8409
7.8269
7.8246
7.6573
7.6410
7.5093
7.5066
7.4926
7.4787
7.4759
7.2688
7.2617
7.2597
7.2458
7.2318
7.2298
6.6947
6.3474
2.8501
2.8346
2.8189
1.8030
1.7876
1.6699
1.4502
1.4438
1.4346
1.4273
1.4202
1.4131
0.9662
0.9522
0.9381
N
N
N
N
H
5cb
0.95
0.96
1.00
1.08
0.97
0.93
2.01
2.13
9.27
4.40
3.17
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

Nov15-2016
MCR-A118-072

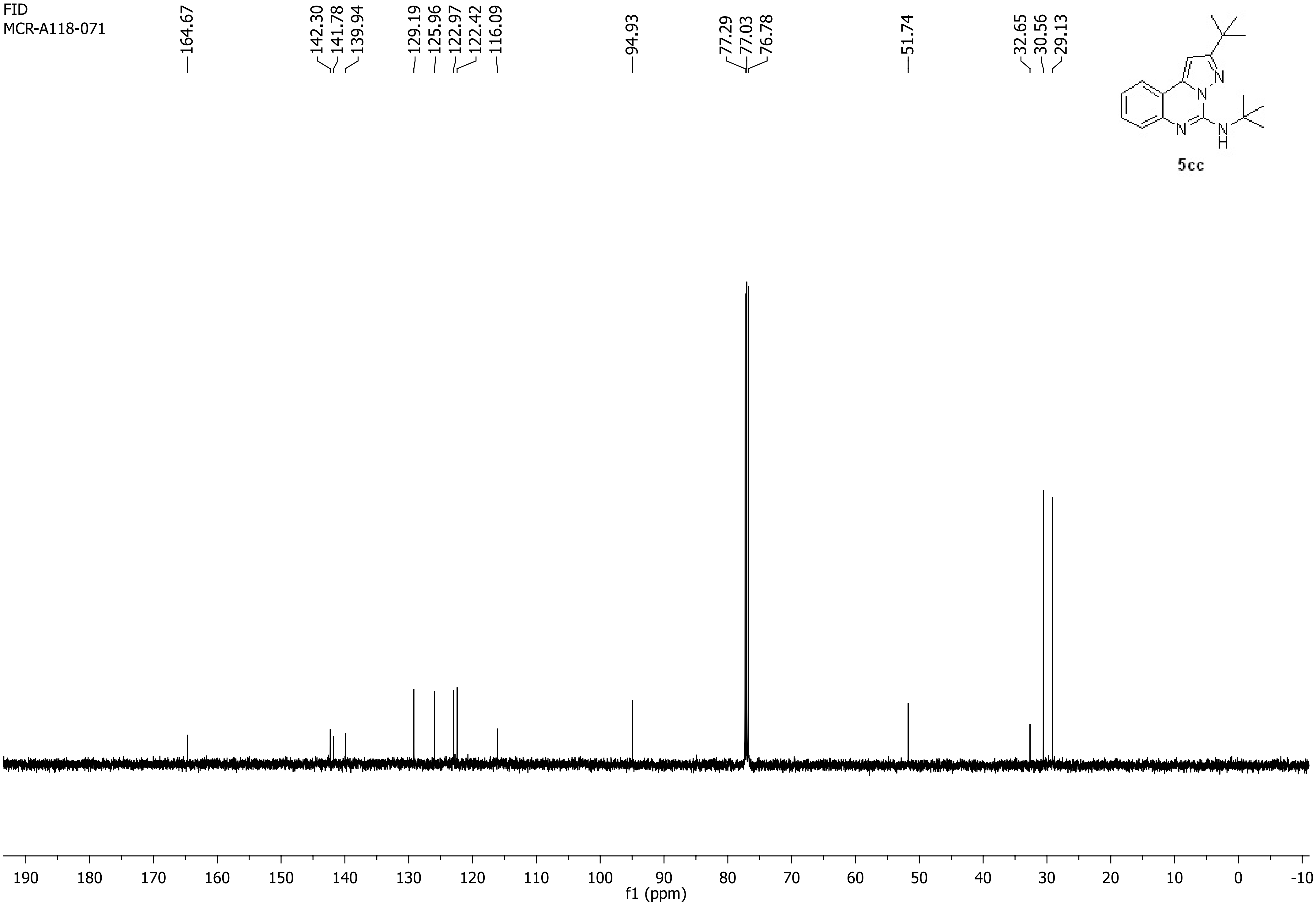


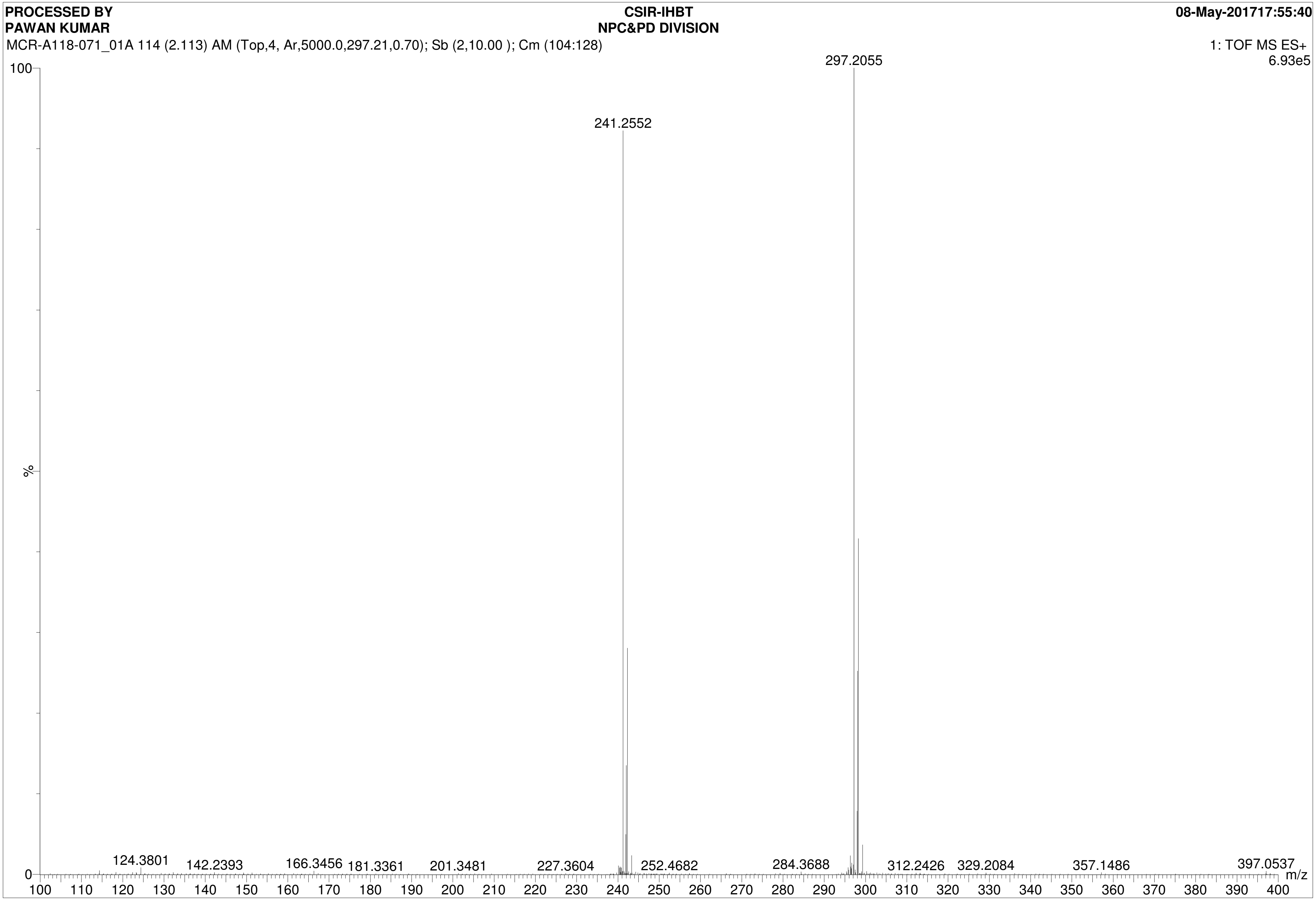
5cb

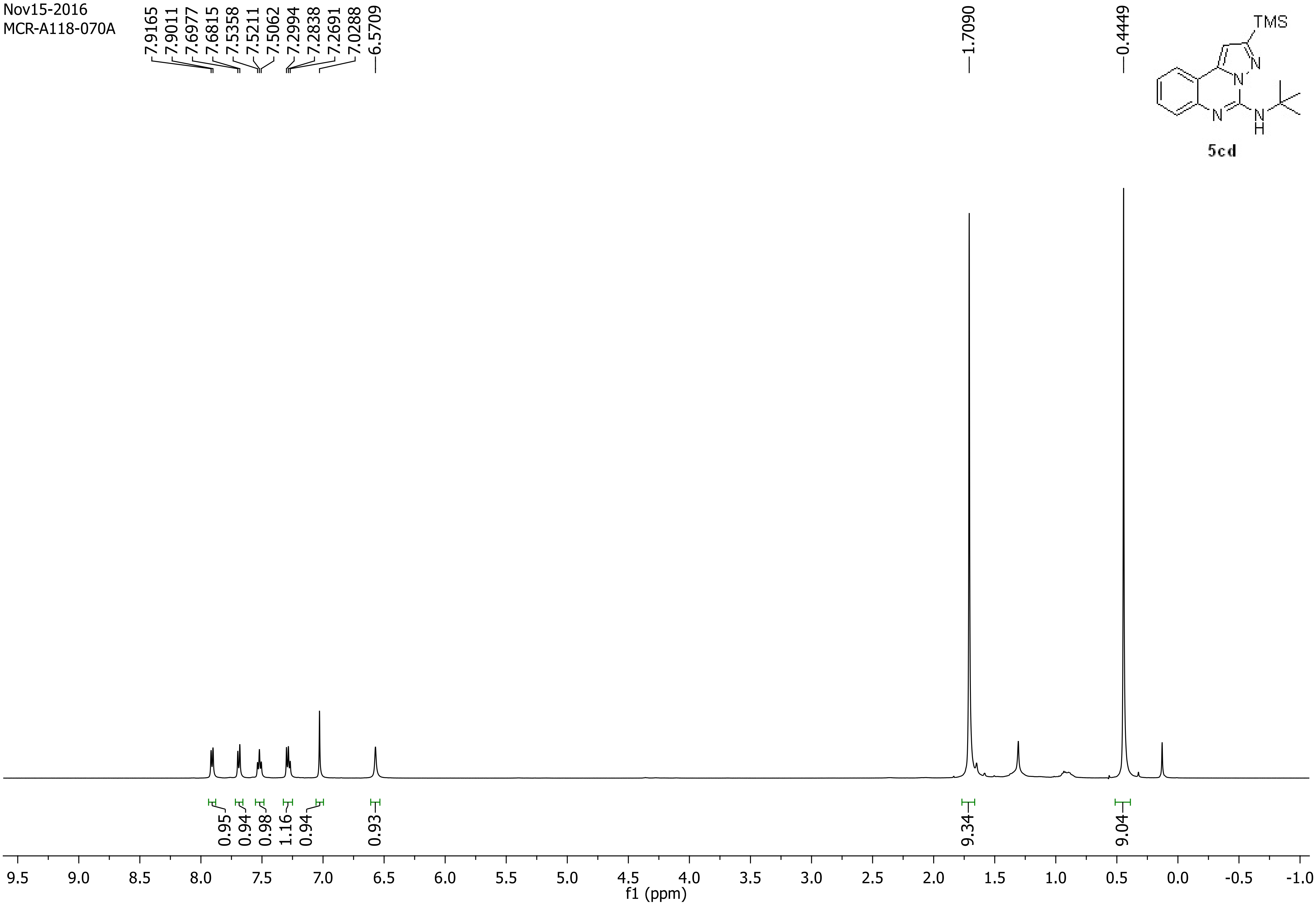

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201617:07:38
MCR-A118-072 128 (2.375) AM (Cen,3, 80.00, Ar,5000.0,311.22,0.70); Sb (2,10.00); Cm (119:134)
1: TOF MS ES+
8.10e5
311.2217
255.1645
132.0066
158.9844
182.0094
201.1475
217.1418
239.1436
271.1805
287.1779
327.2370
343.2076
371.2294
393.2610
%
m/z



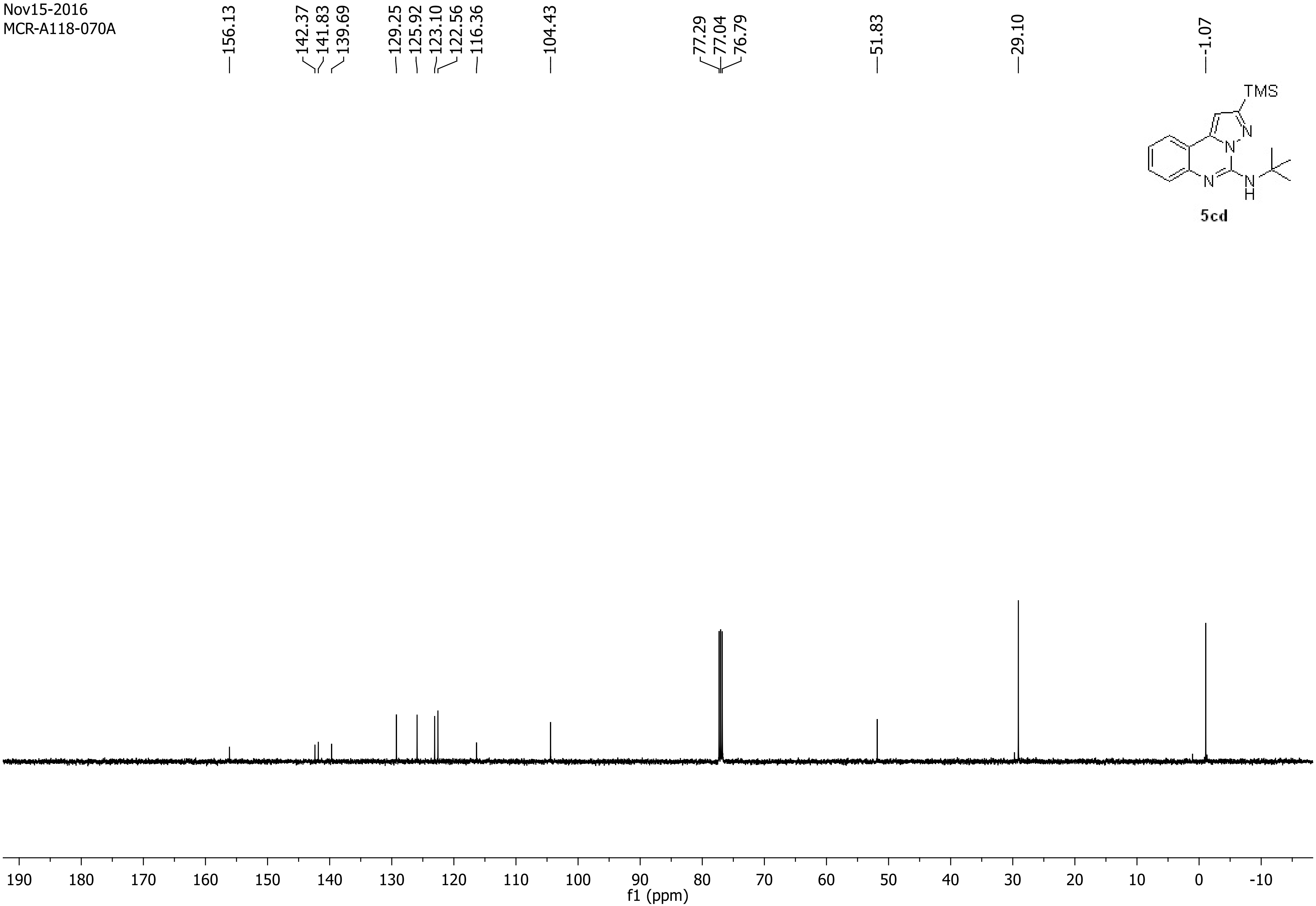
FID
MCR-A118-031
7.8399
7.8381
7.8243
7.8225
7.6343
7.6179
7.4889
7.4863
7.4724
7.4583
7.4557
7.2688
7.2475
7.2319
7.2176
6.7422
6.3792
1.6603
1.4408
N
N
N
N
H
5cc
1.00
0.98
1.02
1.03
1.00
0.98
9.16
9.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


FID
MCR-A118-071
164.67
142.30
141.78
139.94
129.19
125.96
122.97
122.42
116.09
94.93
77.29
77.03
76.78
51.74
32.65
30.56
29.13
N
N
N
N
H
5cc
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

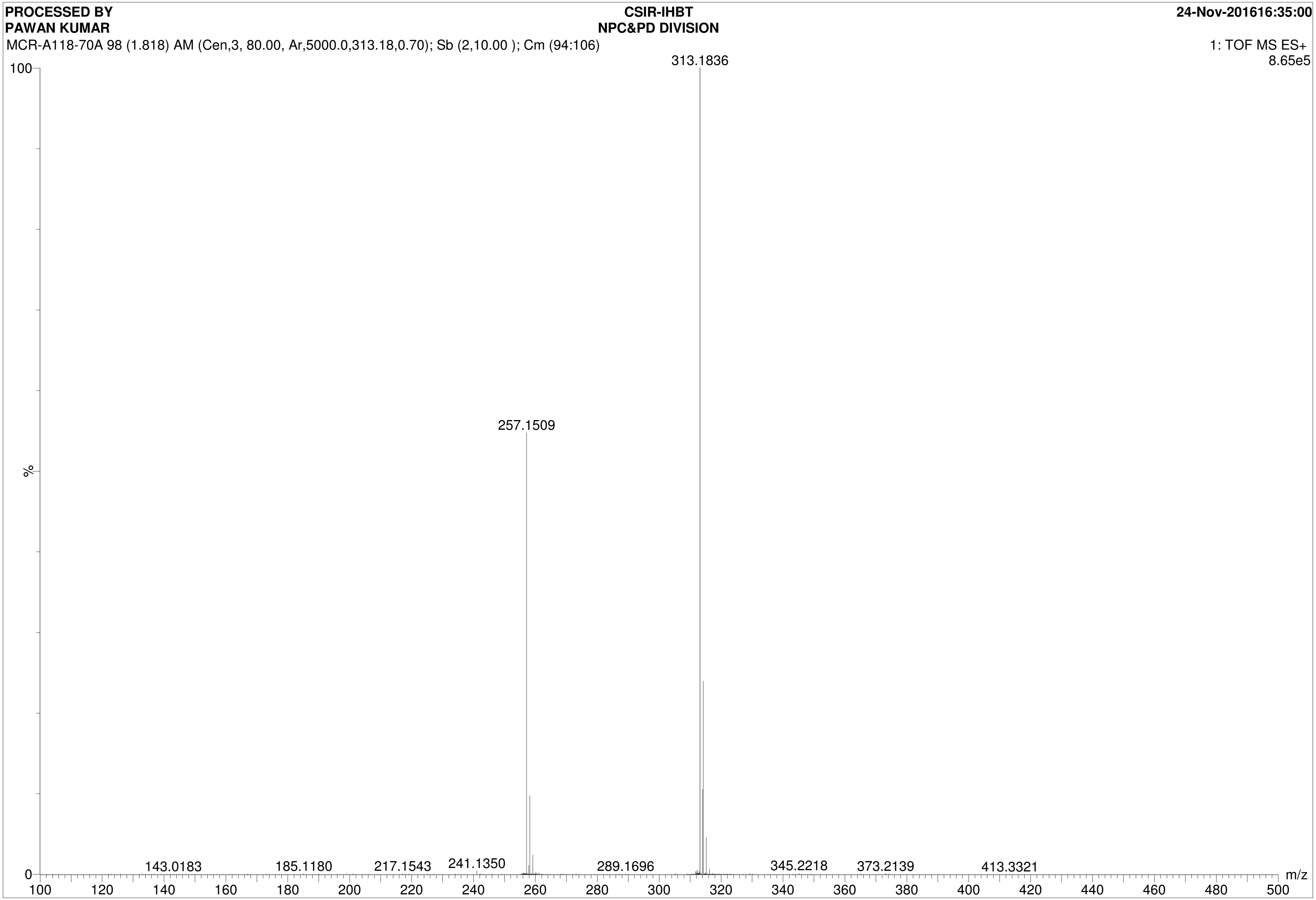

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
08-May-201717:55:40
MCR-A118-071_01A 114 (2.113) AM (Top,4, Ar,5000.0,297.21,0.70); Sb (2,10.00); Cm (104:128)
1: TOF MS ES+
6.93e5
297.2055
241.2552
124.3801
142.2393
166.3456
181.3361
201.3481
227.3604
252.4682
284.3688
312.2426
329.2084
357.1486
397.0537
100
%
0
m/z
100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 390 400

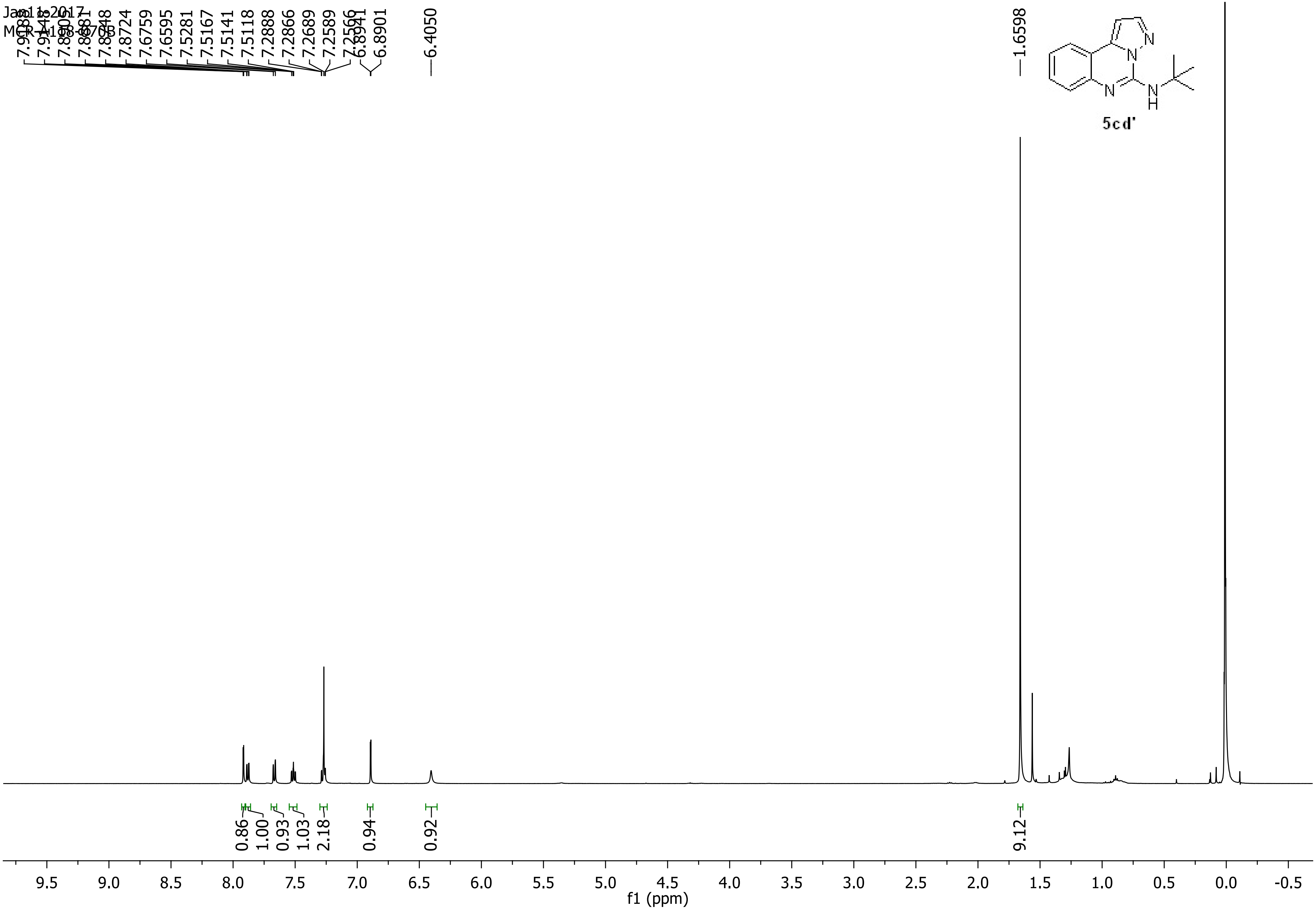

Nov15-2016
MCR-A118-070A
7.9165
7.9011
7.6977
7.6815
7.5358
7.5211
7.5062
7.2994
7.2838
7.2691
7.0288
6.5709
1.7090
0.4449
TMS
N
N
N
N
H
5cd
0.95
0.94
0.98
1.16
0.94
0.93
9.34
9.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

Nov15-2016
MCR-A118-070A

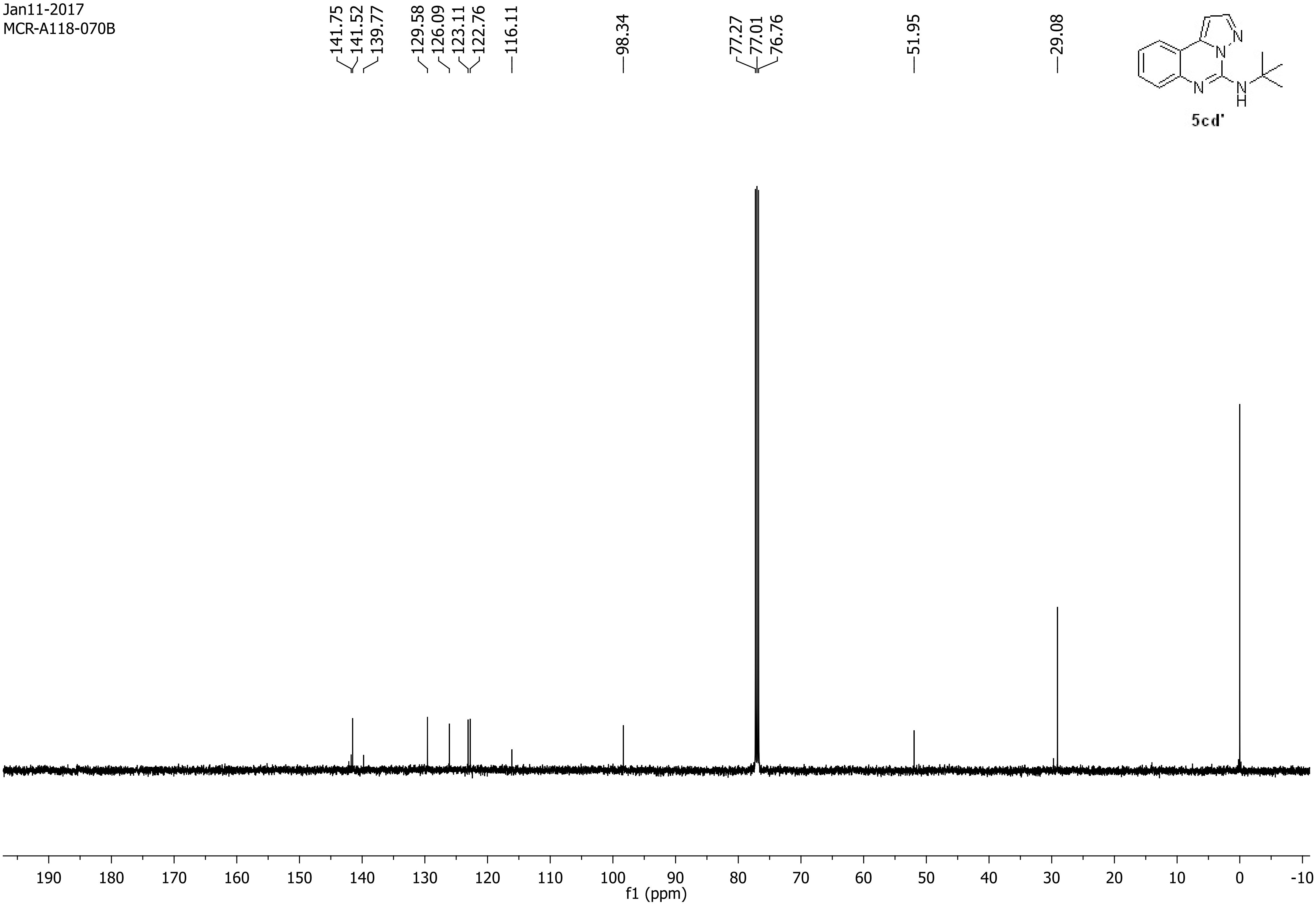


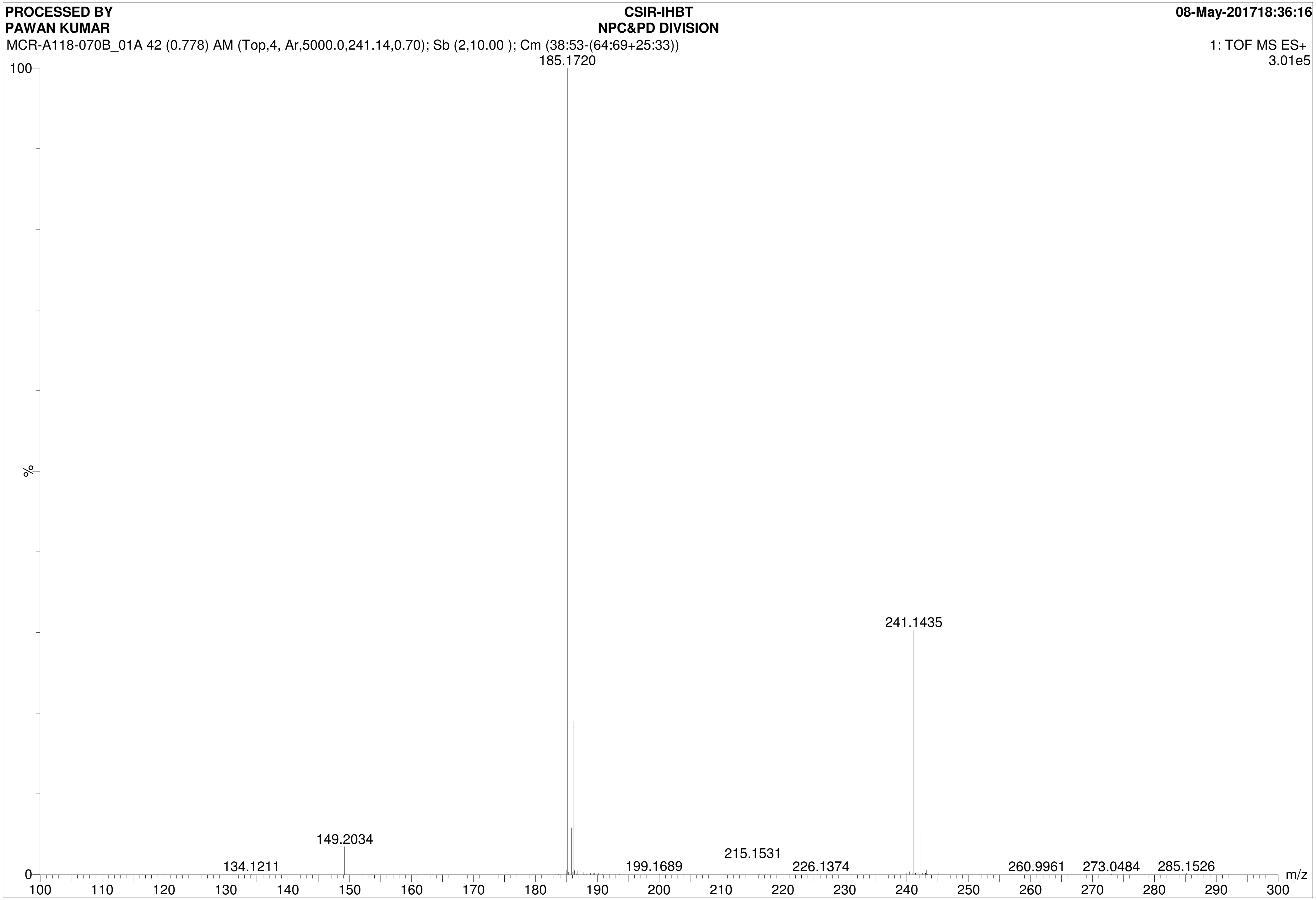
5cd

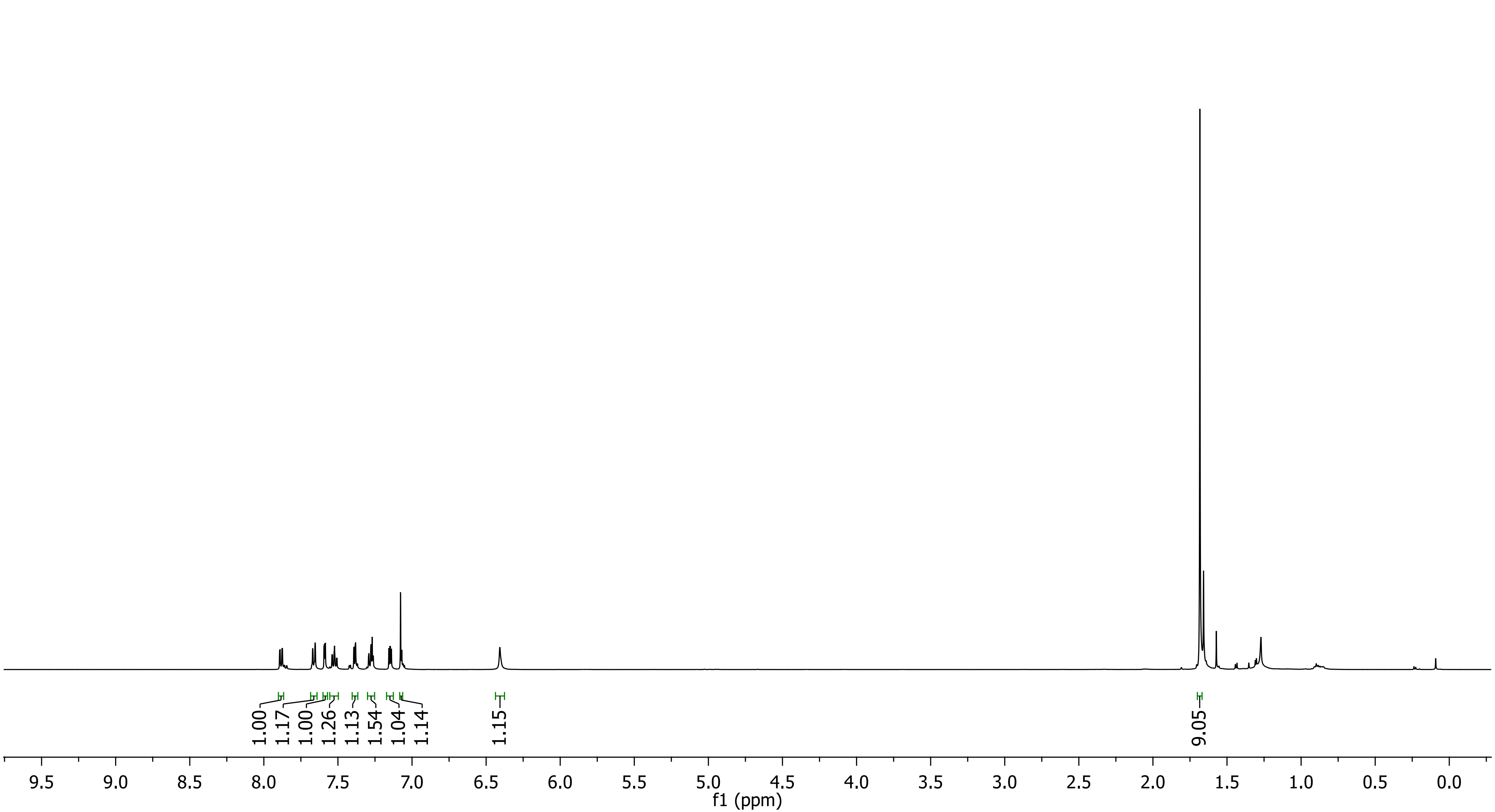

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:35:00
MCR-A118-70A 98 (1.818) AM (Cen,3, 80.00, Ar,5000.0,313.18,0.70); Sb (2,10.00); Cm (94:106)
1: TOF MS ES+
8.65e5
313.1836
257.1509
143.0183
185.1180
217.1543
241.1350
289.1696
345.2218
373.2139
413.3321
%
100
0
m/z
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500

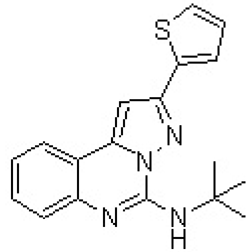

7.8724
7.6759
7.6595
7.5281
7.5167
7.5141
7.5118
7.2888
7.2866
7.2689
7.2589
6.8901
6.4050
1.6598
N
N
N
N
H
5cd'
0.86
1.00
0.93
1.03
2.18
0.94
0.92
9.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

Jan11-2017
MCR-A118-070B



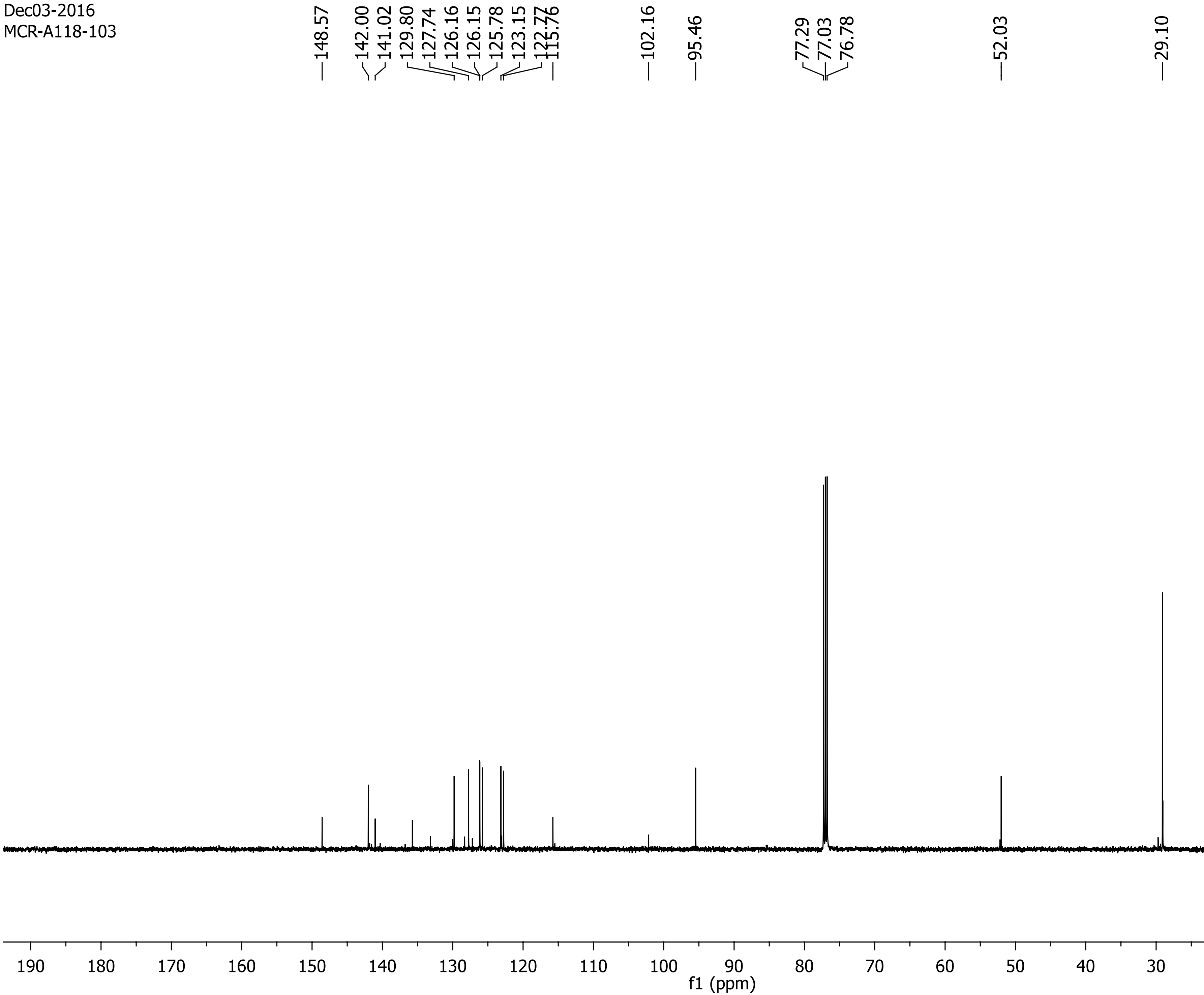

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
08-May-201718:36:16
MCR-A118-070B_01A 42 (0.778) AM (Top,4, Ar,5000.0,241.14,0.70); Sb (2,10.00); Cm (38:53-(64:69+25:33))
1: TOF MS ES+
3.01e5
185.1720
241.1435
149.2034
134.1211
199.1689
215.1531
226.1374
260.9961
273.0484
285.1526
%
m/z

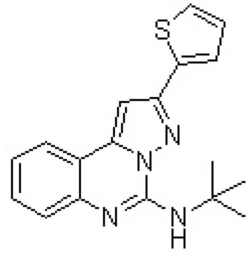

Dec03-2016
MCR-A118-103
7.8770
7.8640
7.6700
7.6536
7.5936
7.5920
7.5866
7.5849
7.5232
7.3927
7.3911
7.3826
7.3809
7.2772
7.2689
7.1565
7.1493
7.1466
7.1393
7.0774
6.4074
1.6831
1.00
1.17
1.00
1.26
1.13
1.54
1.04
1.14
1.15
9.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


S
N
N
N
N
H

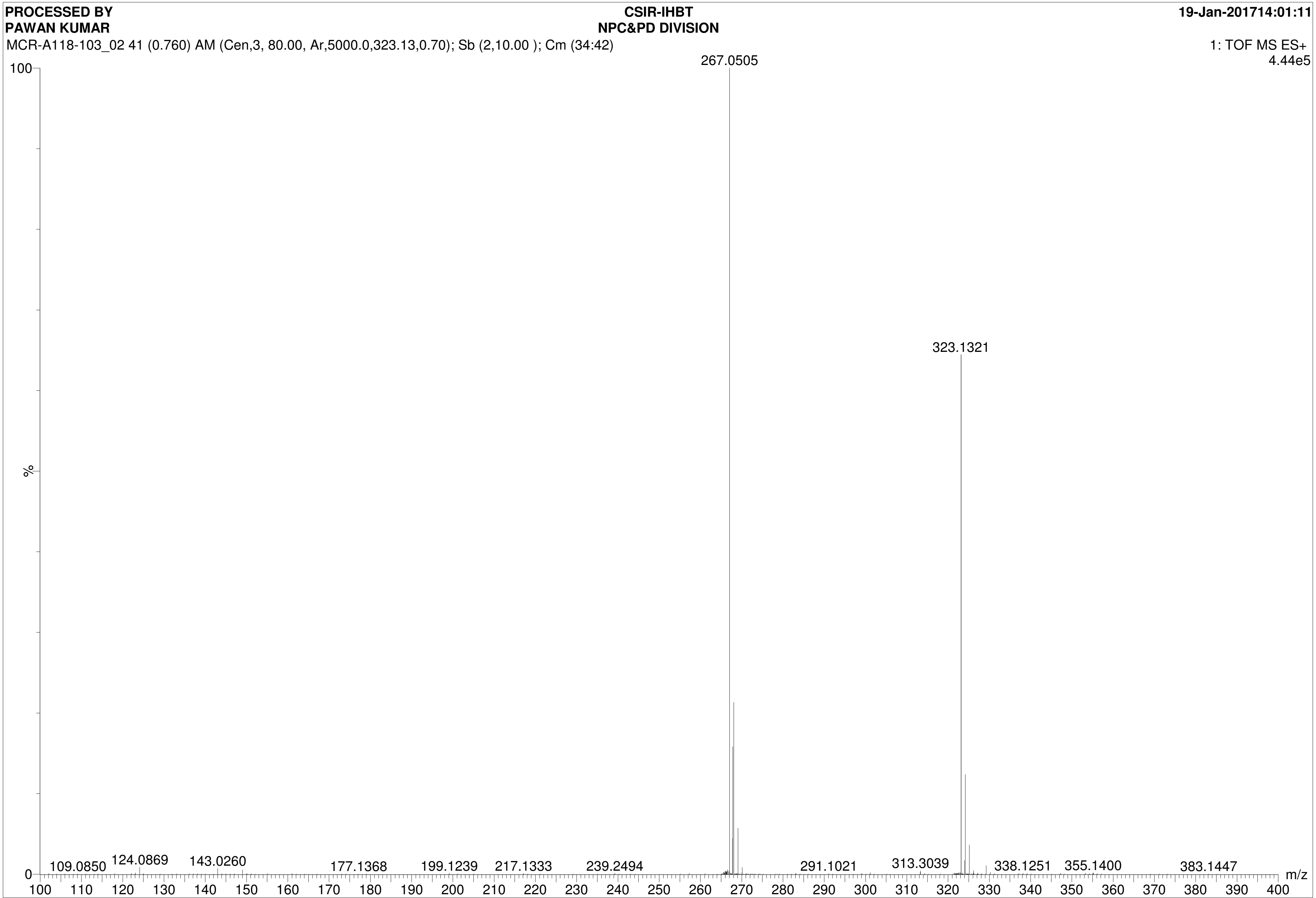
5ce

Dec03-2016
MCR-A118-103

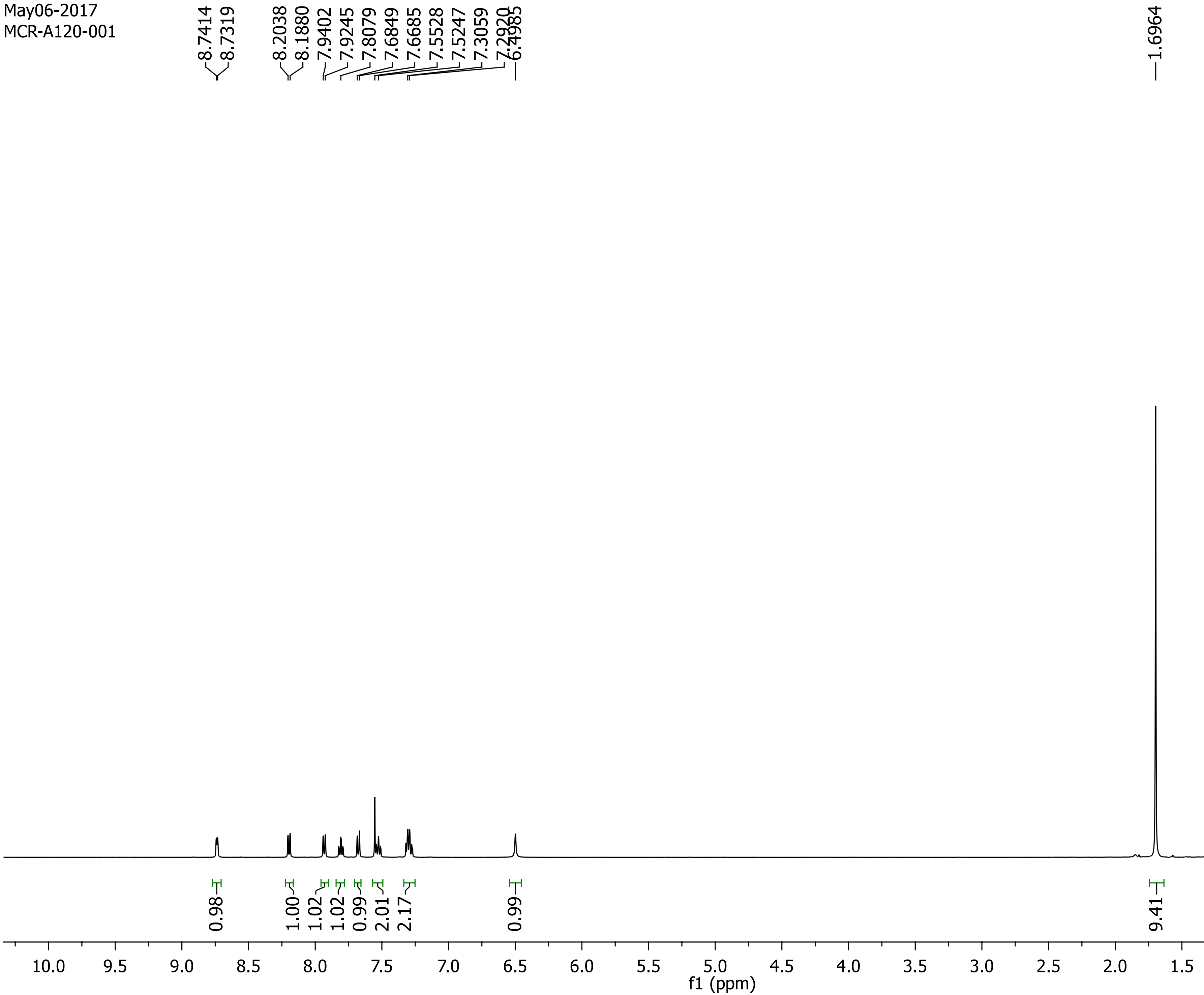


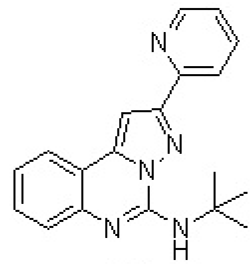


5ce

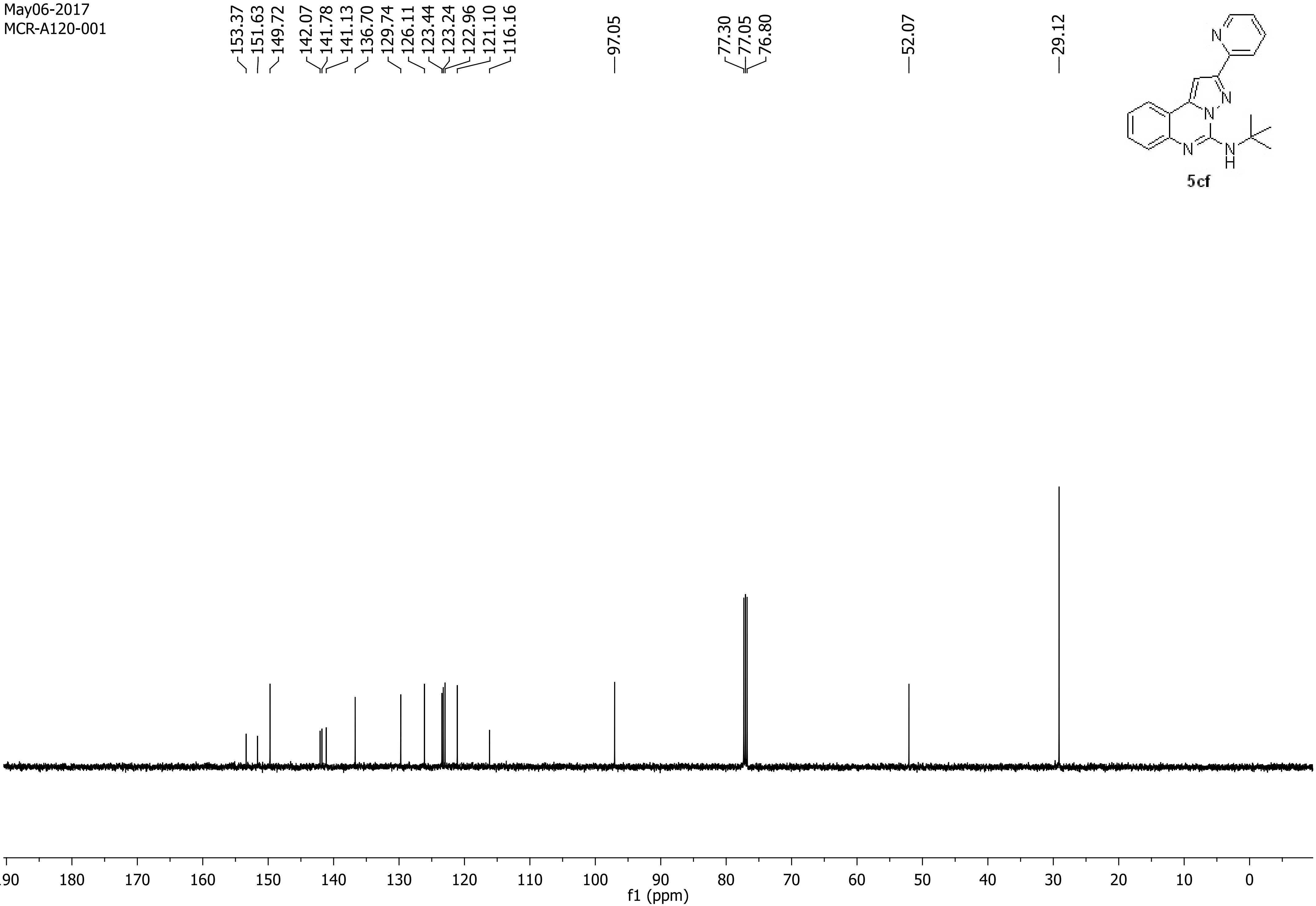

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:01:11
MCR-A118-103_02 41 (0.760) AM (Cen,3, 80.00, Ar,5000.0,323.13,0.70); Sb (2,10.00); Cm (34:42)
1: TOF MS ES+
4.44e5
267.0505
323.1321
109.0850
124.0869
143.0260
177.1368
199.1239
217.1333
239.2494
291.1021
313.3039
338.1251
355.1400
383.1447
%
m/z
100
0
100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 390 400

May06-2017
MCR-A120-001

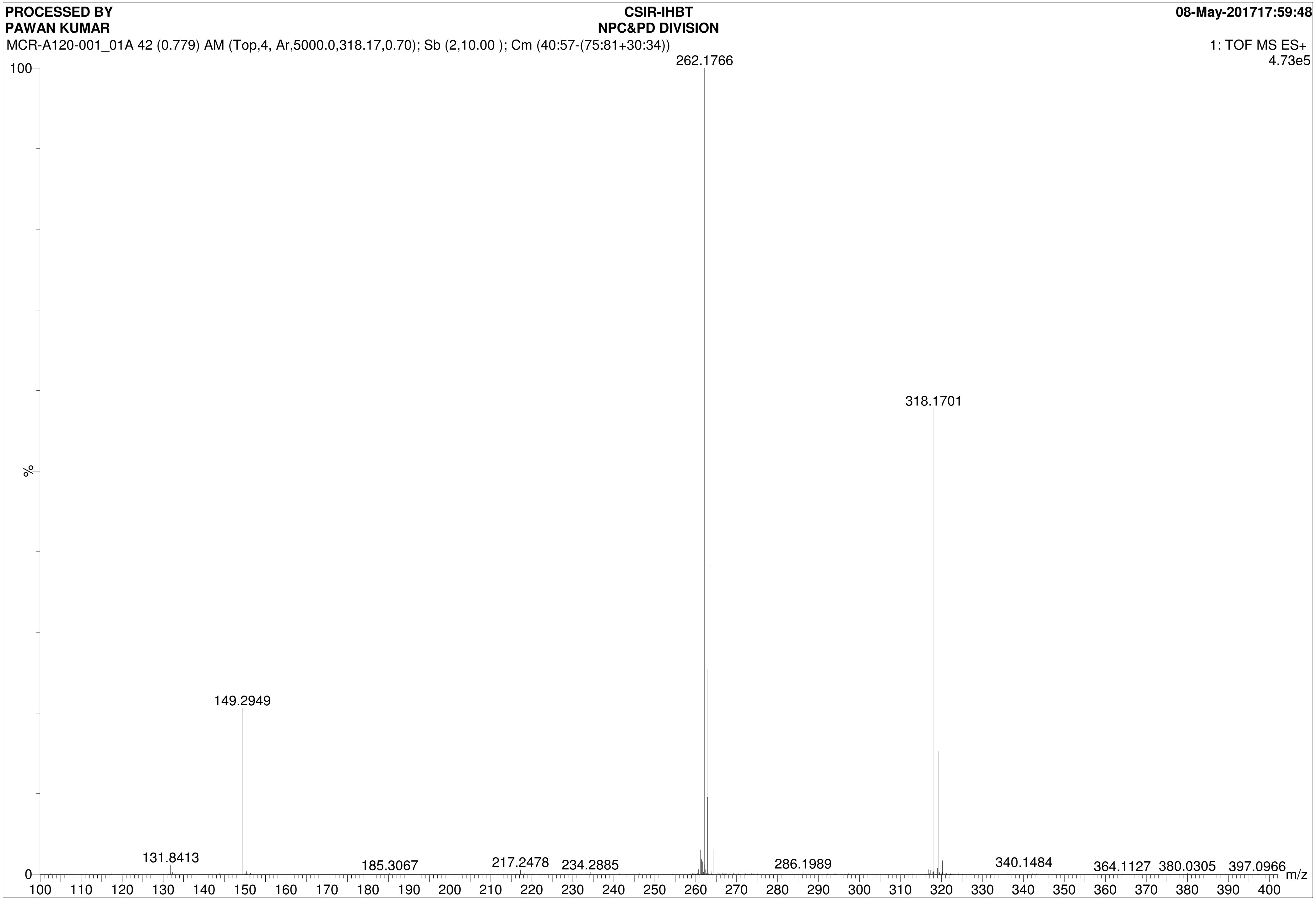




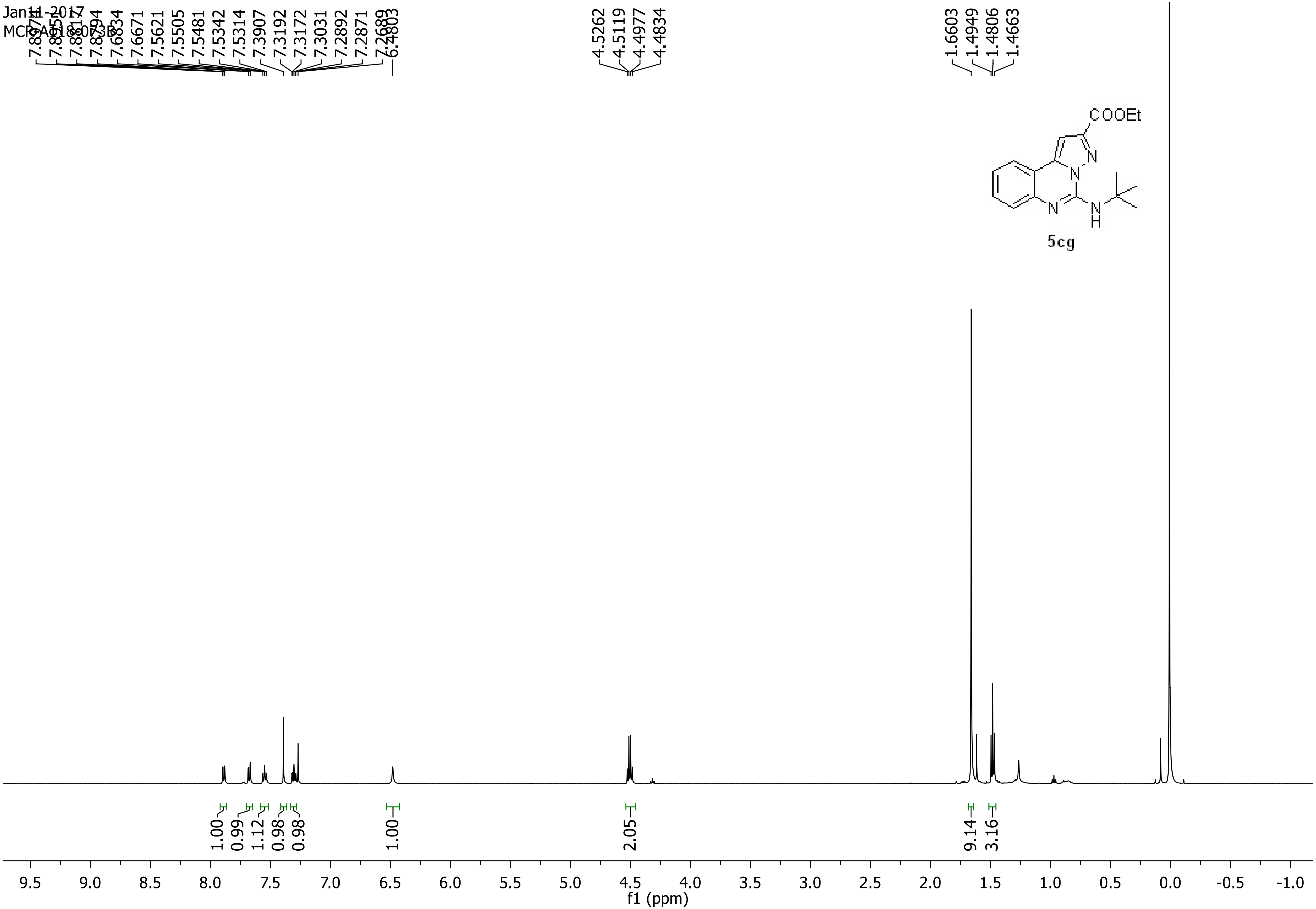
5cf


May06-2017
MCR-A120-001
153.37
151.63
149.72
142.07
141.78
141.13
136.70
129.74
126.11
123.44
123.24
122.96
121.10
116.16
97.05
77.30
77.05
76.80
52.07
29.12
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
N
N
N
N
N
H

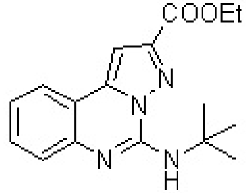
5cf



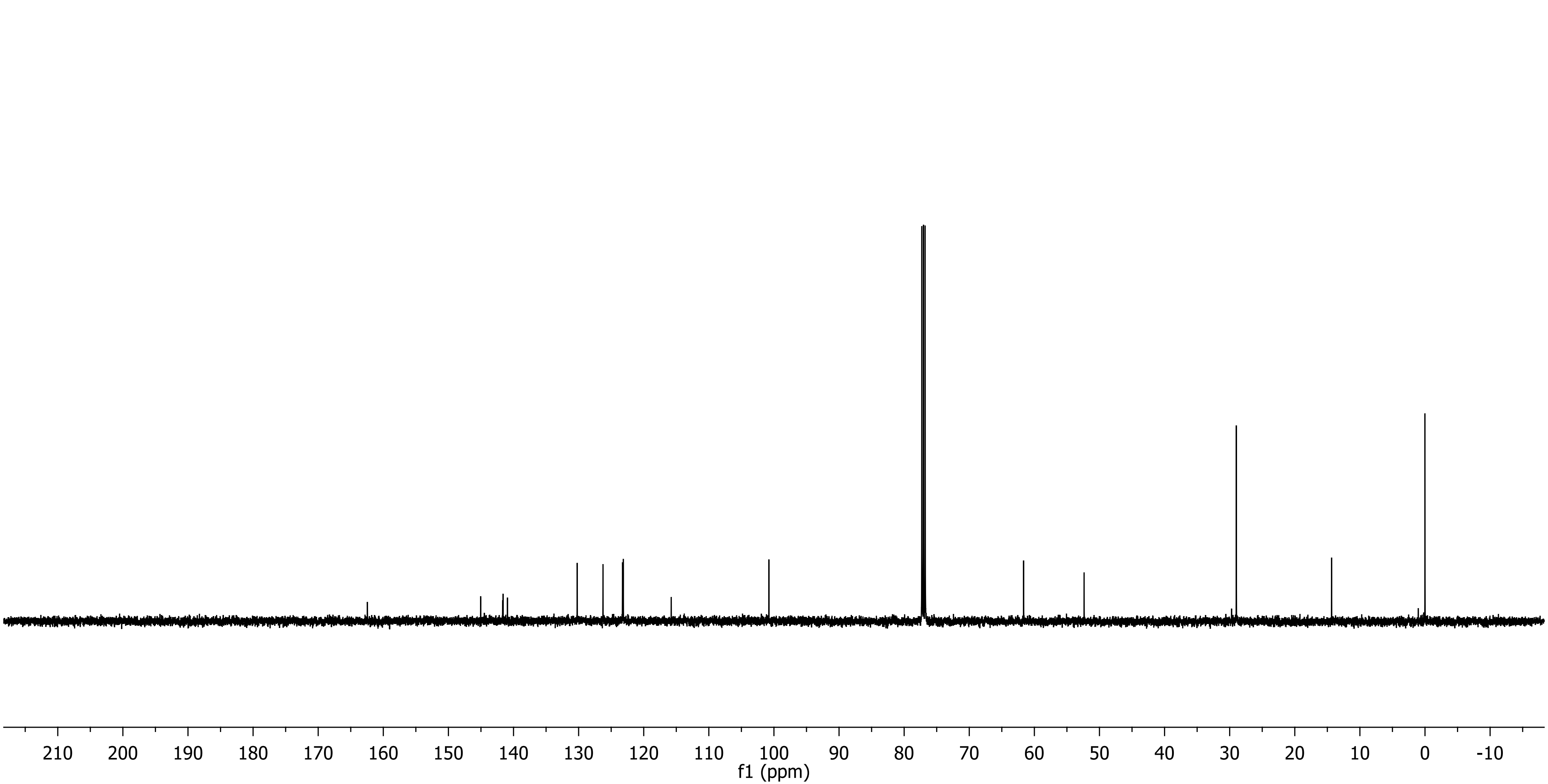
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
08-May-201717:59:48
MCR-A120-001_01A 42 (0.779) AM (Top,4, Ar,5000.0,318.17,0.70); Sb (2,10.00); Cm (40:57-(75:81+30:34))
1: TOF MS ES+
4.73e5
262.1766
318.1701
149.2949
131.8413
185.3067
217.2478
234.2885
286.1989
340.1484
364.1127
380.0305
397.0966
%
m/z

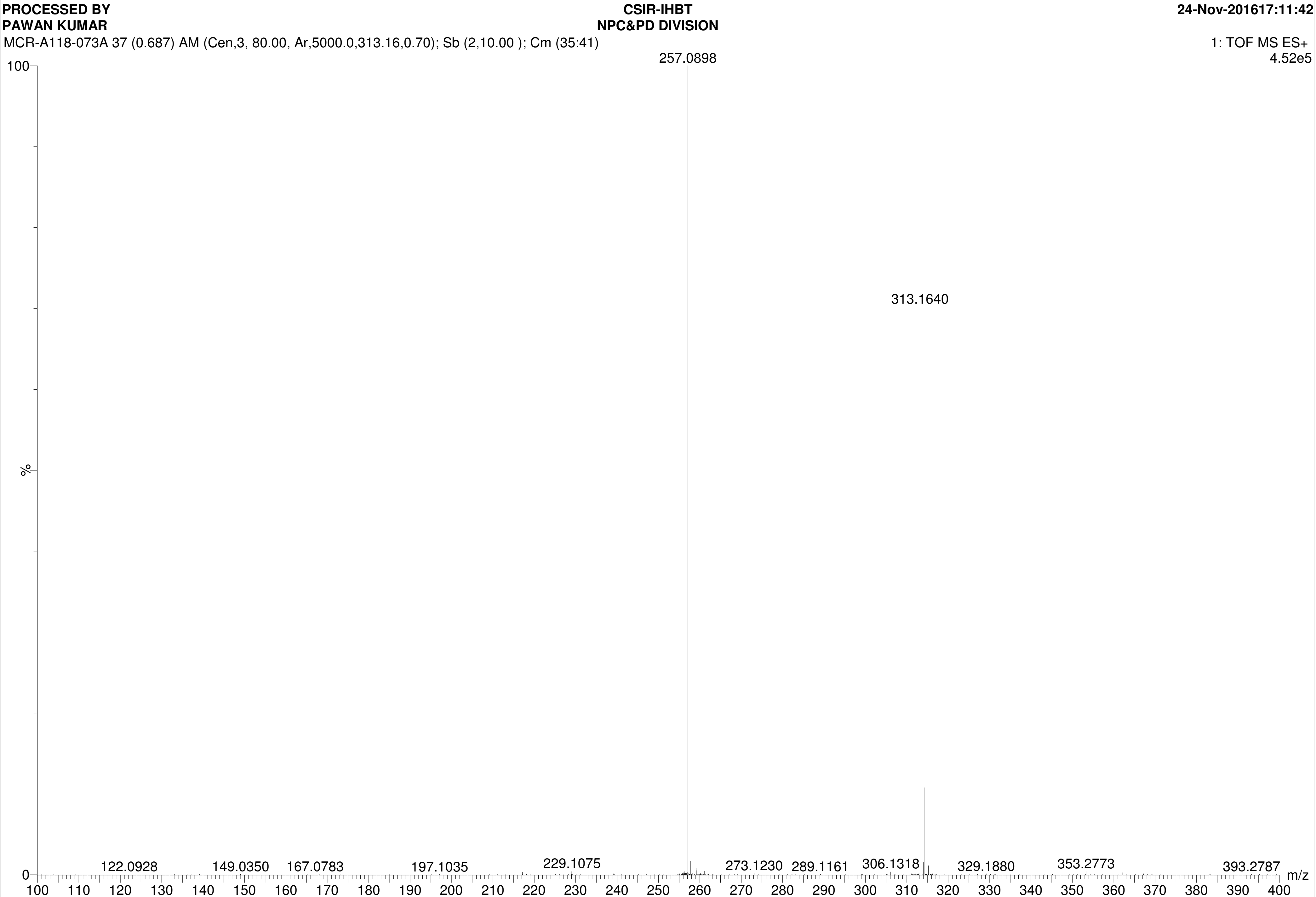

Jan11-2017
7.8794
7.6834
7.6671
7.5621
7.5505
7.5481
7.5342
7.5314
7.3907
7.3192
7.3172
7.3031
7.2892
7.2871
7.2689
6.4803
4.5262
4.5119
4.4977
4.4834
1.6603
1.4949
1.4806
1.4663
COOEt
N
N
N
N
H
5cg
1.00
0.99
1.12
0.98
0.98
1.00
2.05
9.14
3.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

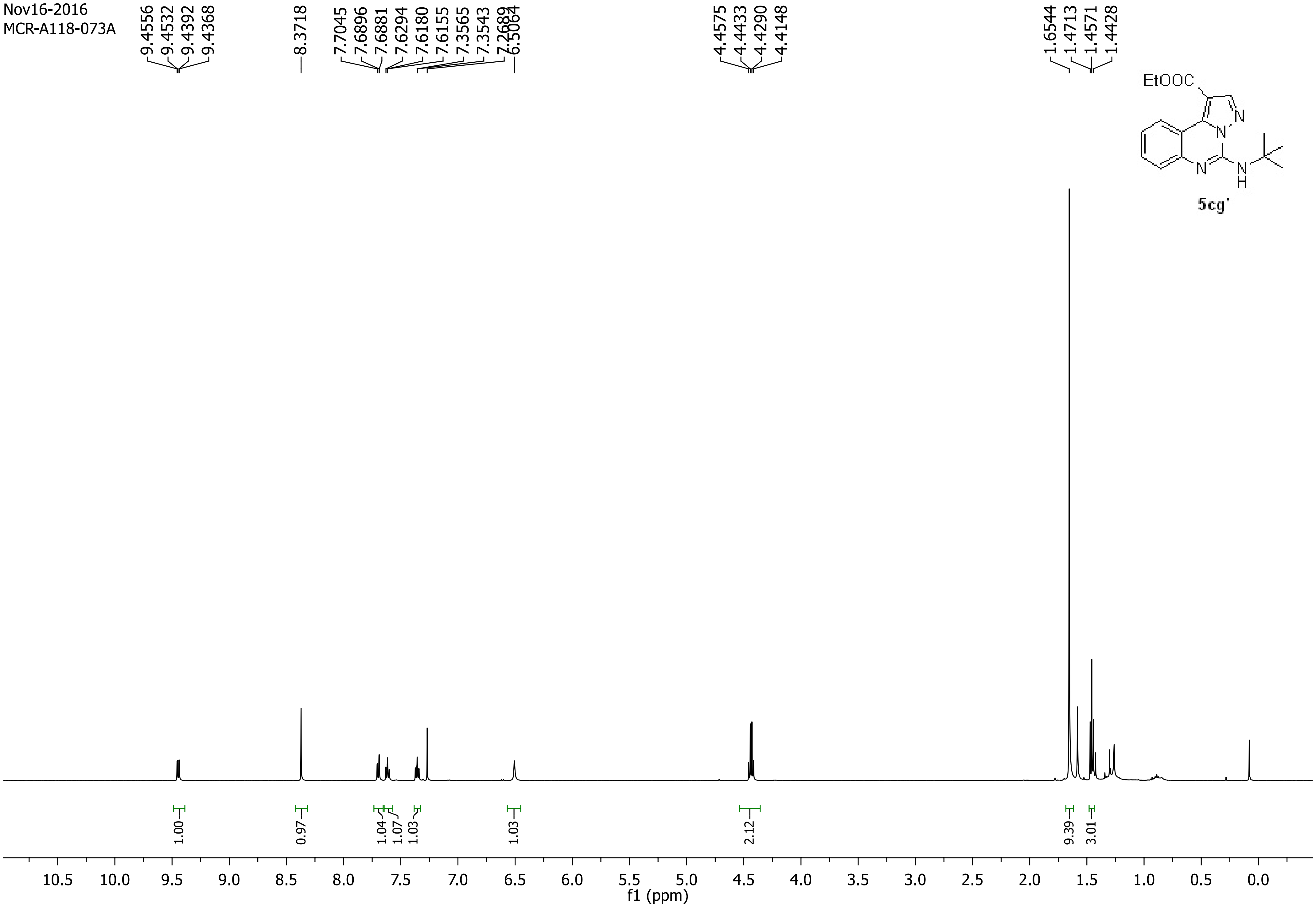
Jan11-2017
MCR-A118-073B



5cg



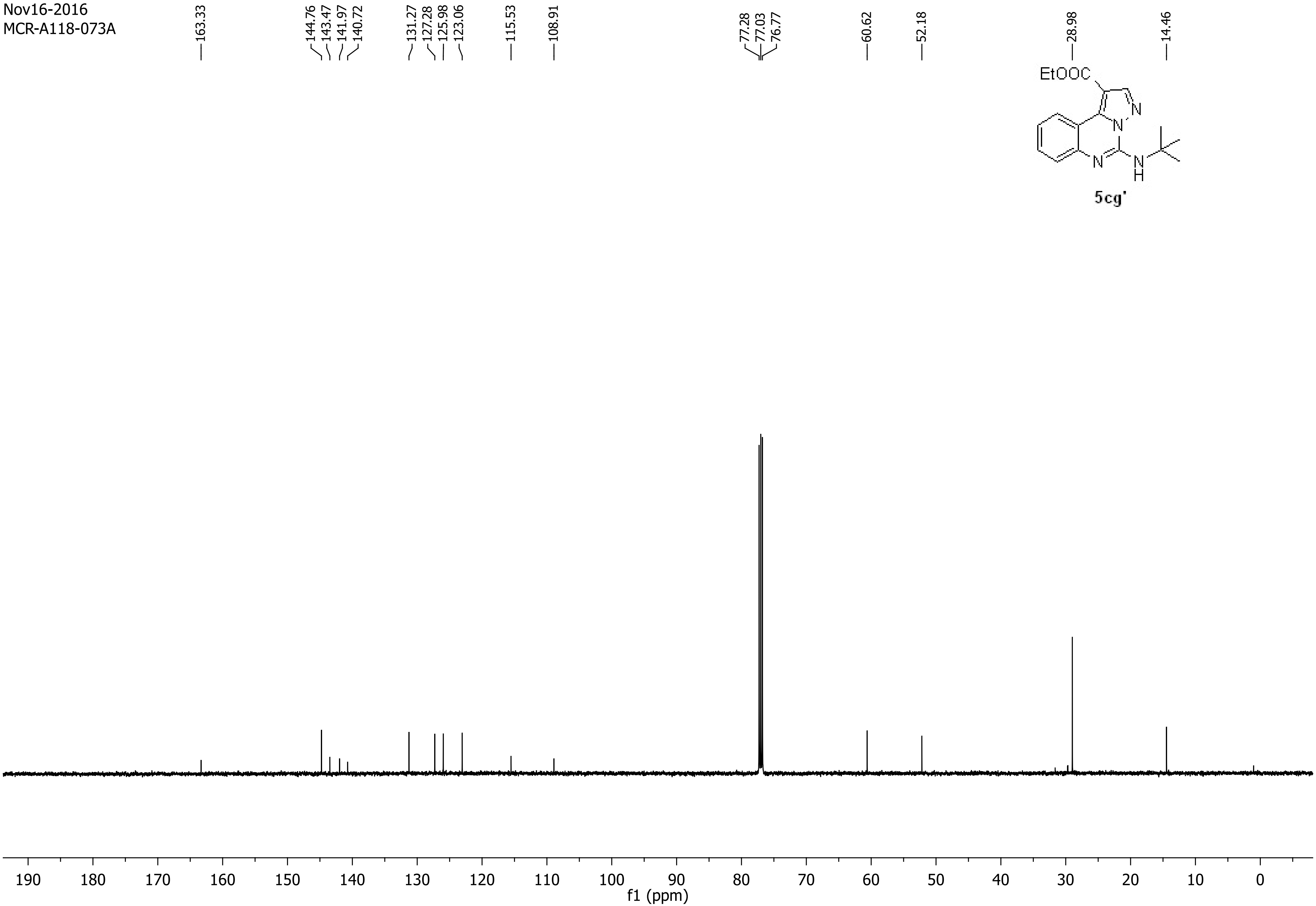

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201617:11:42
MCR-A118-073A 37 (0.687) AM (Cen,3, 80.00, Ar,5000.0,313.16,0.70); Sb (2,10.00); Cm (35:41)
1: TOF MS ES+
4.52e5
257.0898
313.1640
122.0928
149.0350
167.0783
197.1035
229.1075
273.1230
289.1161
306.1318
329.1880
353.2773
393.2787
%
m/z

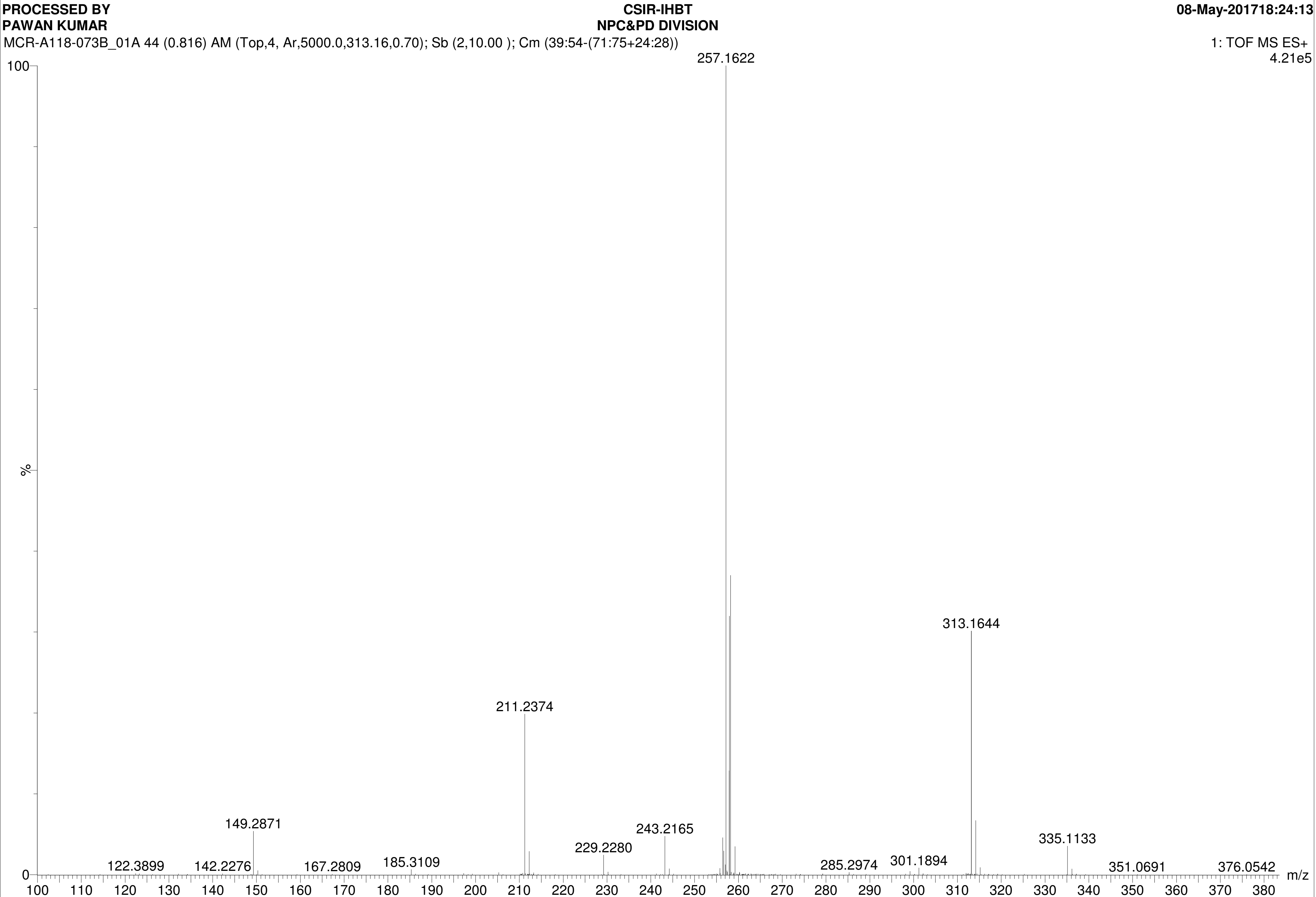


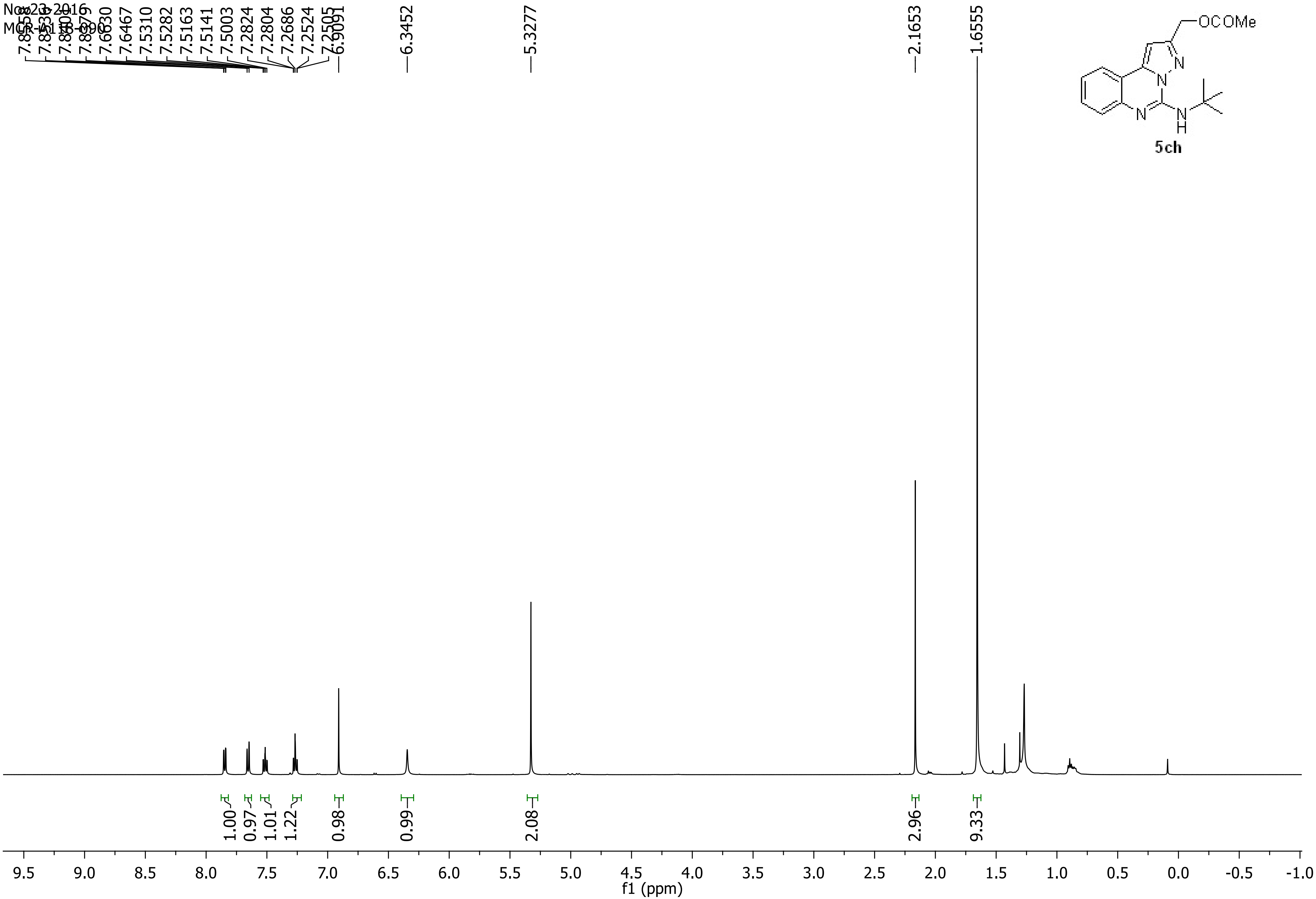
Nov16-2016
MCR-A118-073A
9.4556
9.4532
9.4392
9.4368
8.3718
7.7045
7.6896
7.6881
7.6294
7.6180
7.6155
7.3565
7.3543
7.2689
6.5064
4.4575
4.4433
4.4290
4.4148
1.6544
1.4713
1.4571
1.4428
1.00
0.97
1.04
1.07
1.03
1.03
2.12
9.39
3.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
EtOOC
N
N
N
N
H

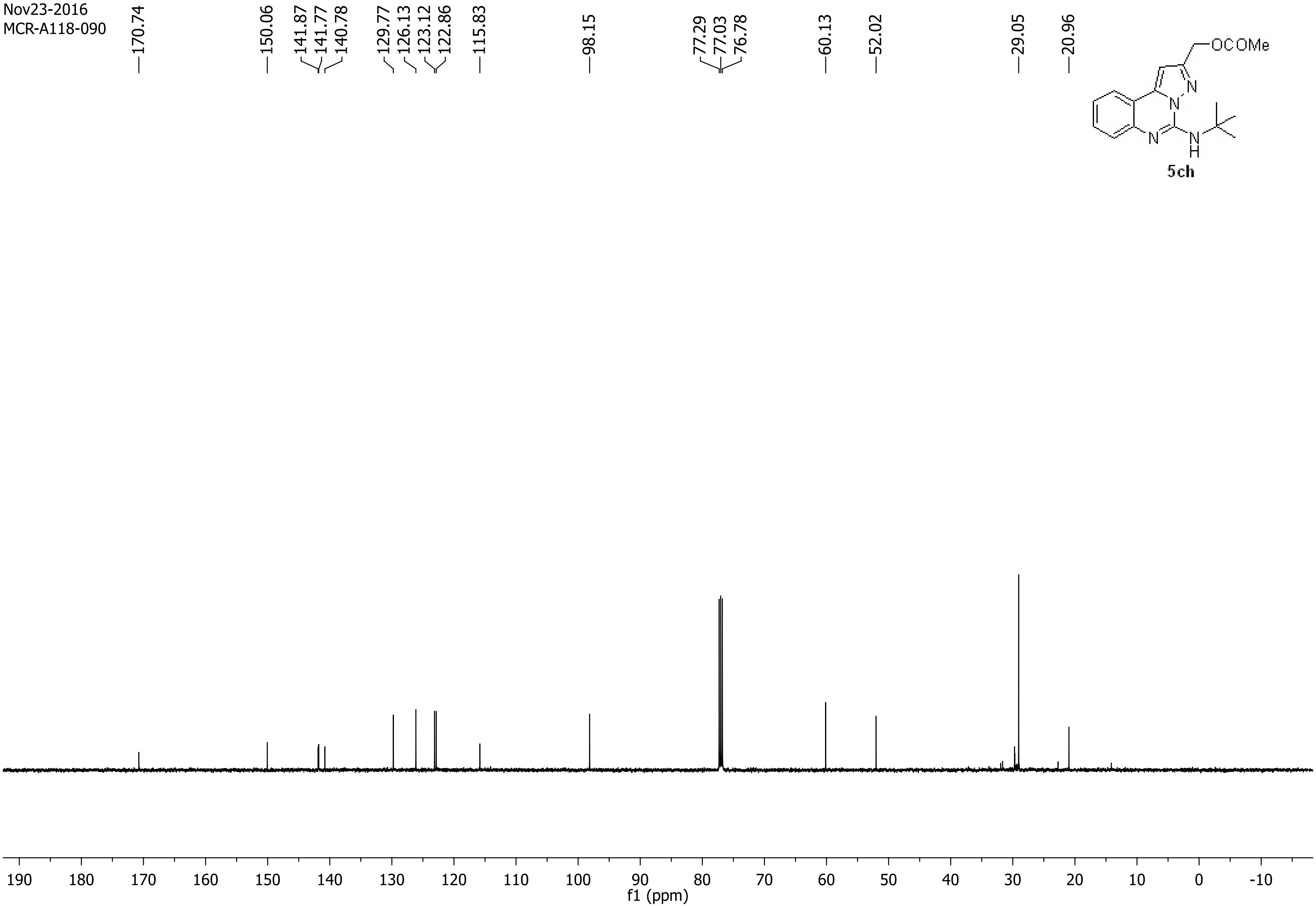
5cg'

Nov16-2016
MCR-A118-073A

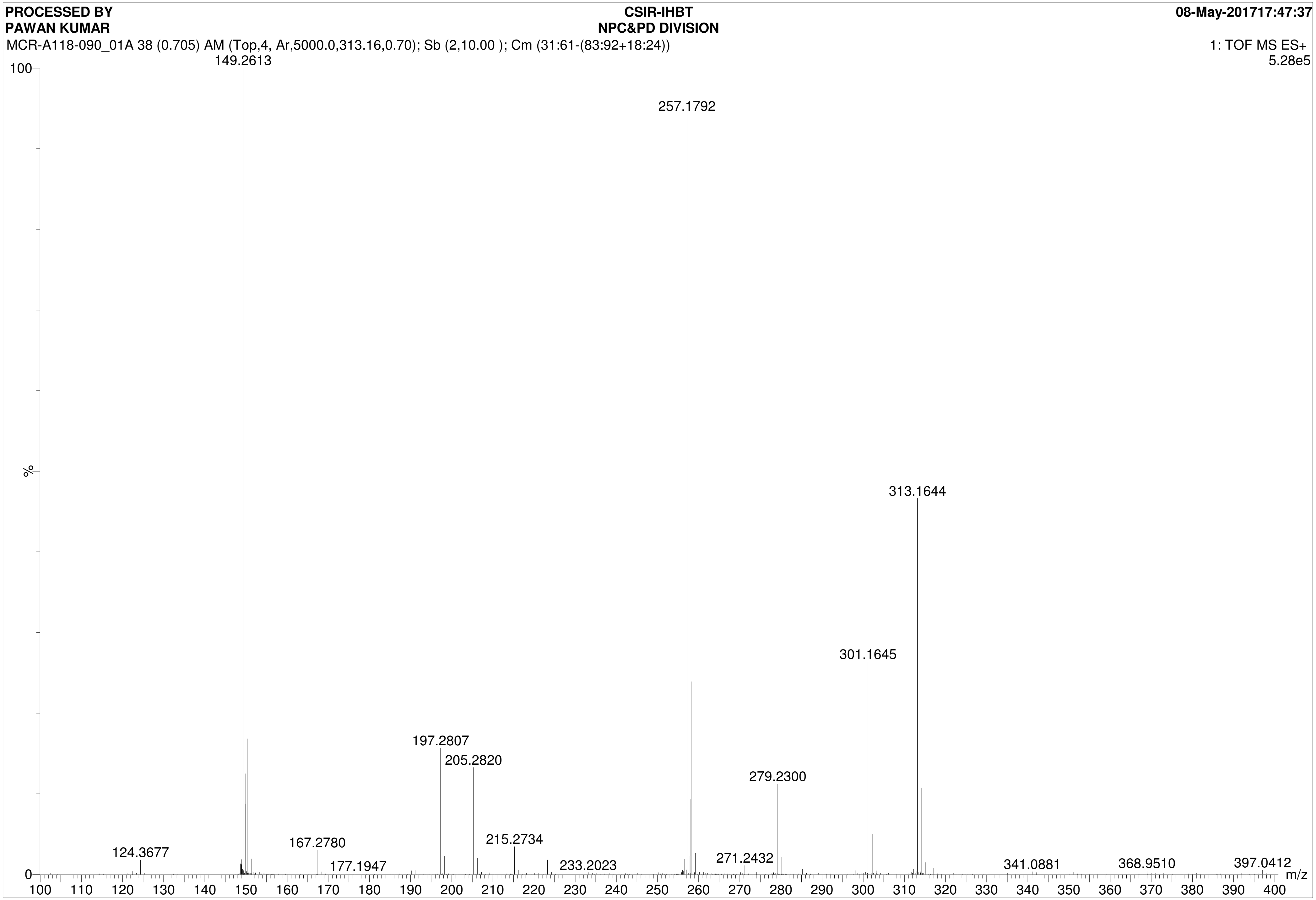



PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
08-May-201718:24:13
MCR-A118-073B_01A 44 (0.816) AM (Top,4, Ar,5000.0,313.16,0.70); Sb (2,10.00); Cm (39:54-(71:75+24:28))
1: TOF MS ES+
4.21e5
257.1622
313.1644
211.2374
149.2871
243.2165
229.2280
335.1133
122.3899
142.2276
167.2809
185.3109
285.2974
301.1894
351.0691
376.0542
%
m/z

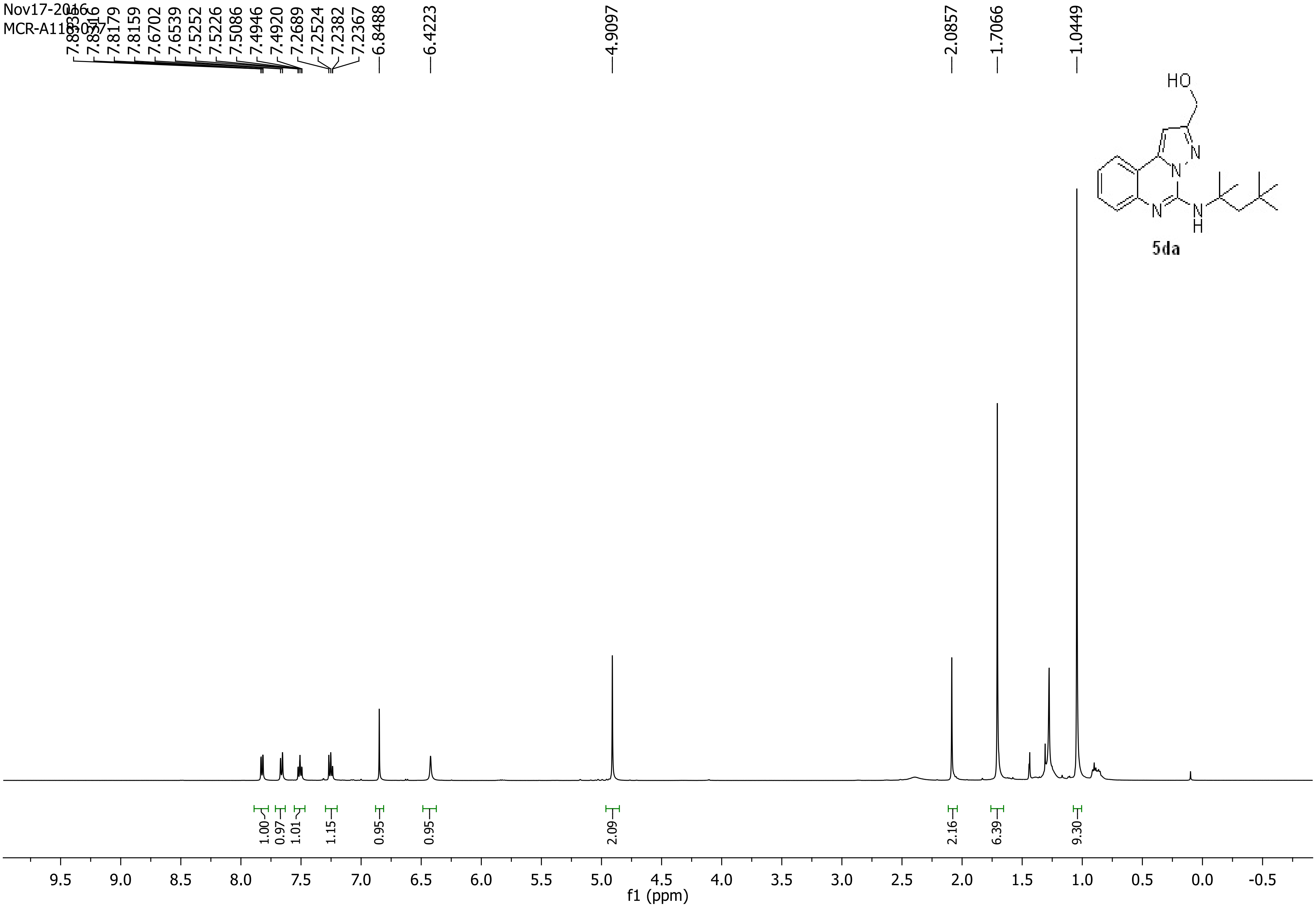

7.6630
7.6467
7.5310
7.5282
7.5163
7.5141
7.5003
7.2824
7.2804
7.2686
7.2524
6.9091
6.3452
5.3277
2.1653
1.6555
OCOMe
N
N
N
N
H
5ch
1.00
0.97
1.01
1.22
0.98
0.99
2.08
2.96
9.33
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


Nov23-2016
MCR-A118-090
170.74
150.06
141.87
141.77
140.78
129.77
126.13
123.12
122.86
115.83
98.15
77.29
77.03
76.78
60.13
52.02
29.05
20.96
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
OCOMe
N
N
N
N
H

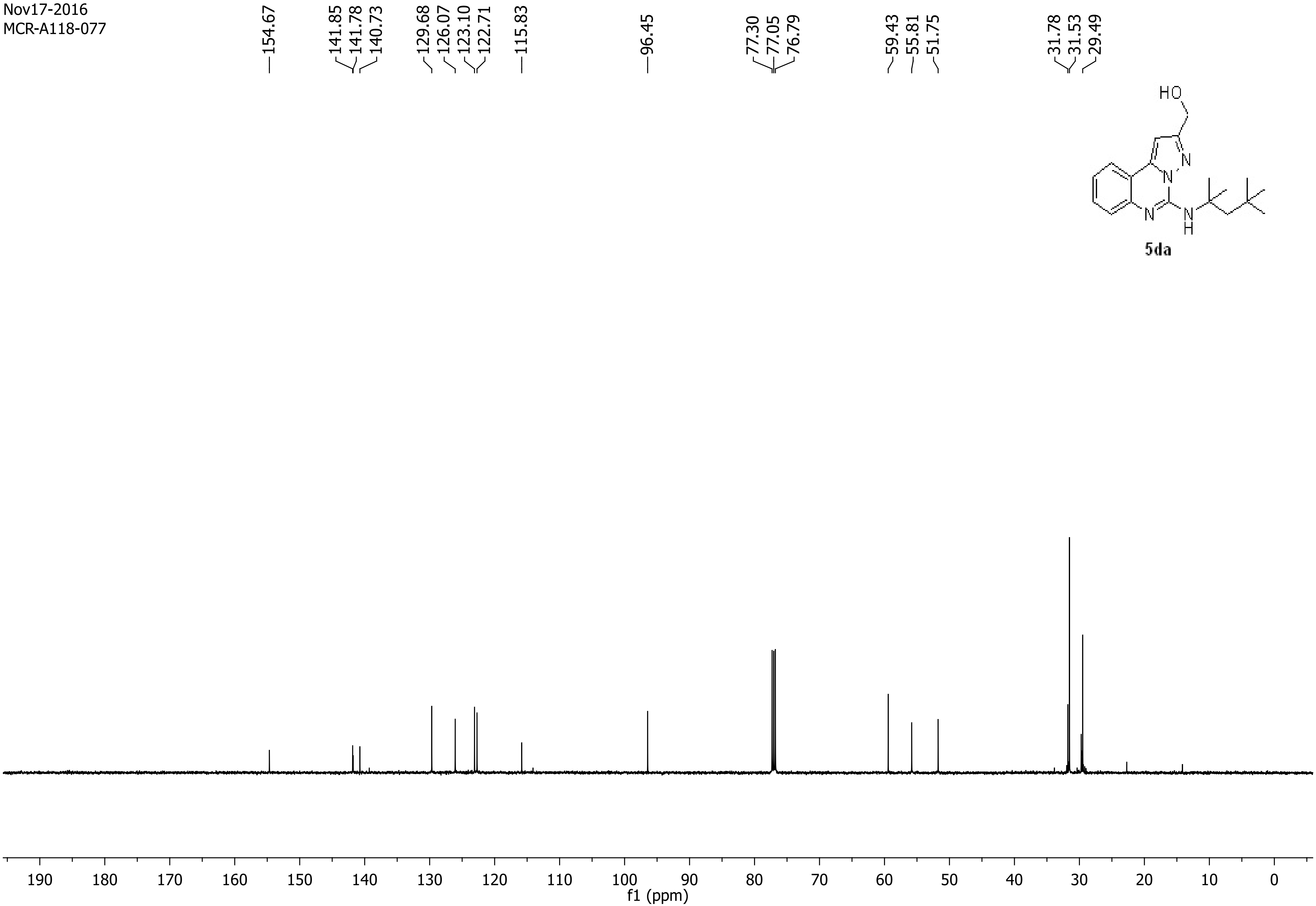
5ch



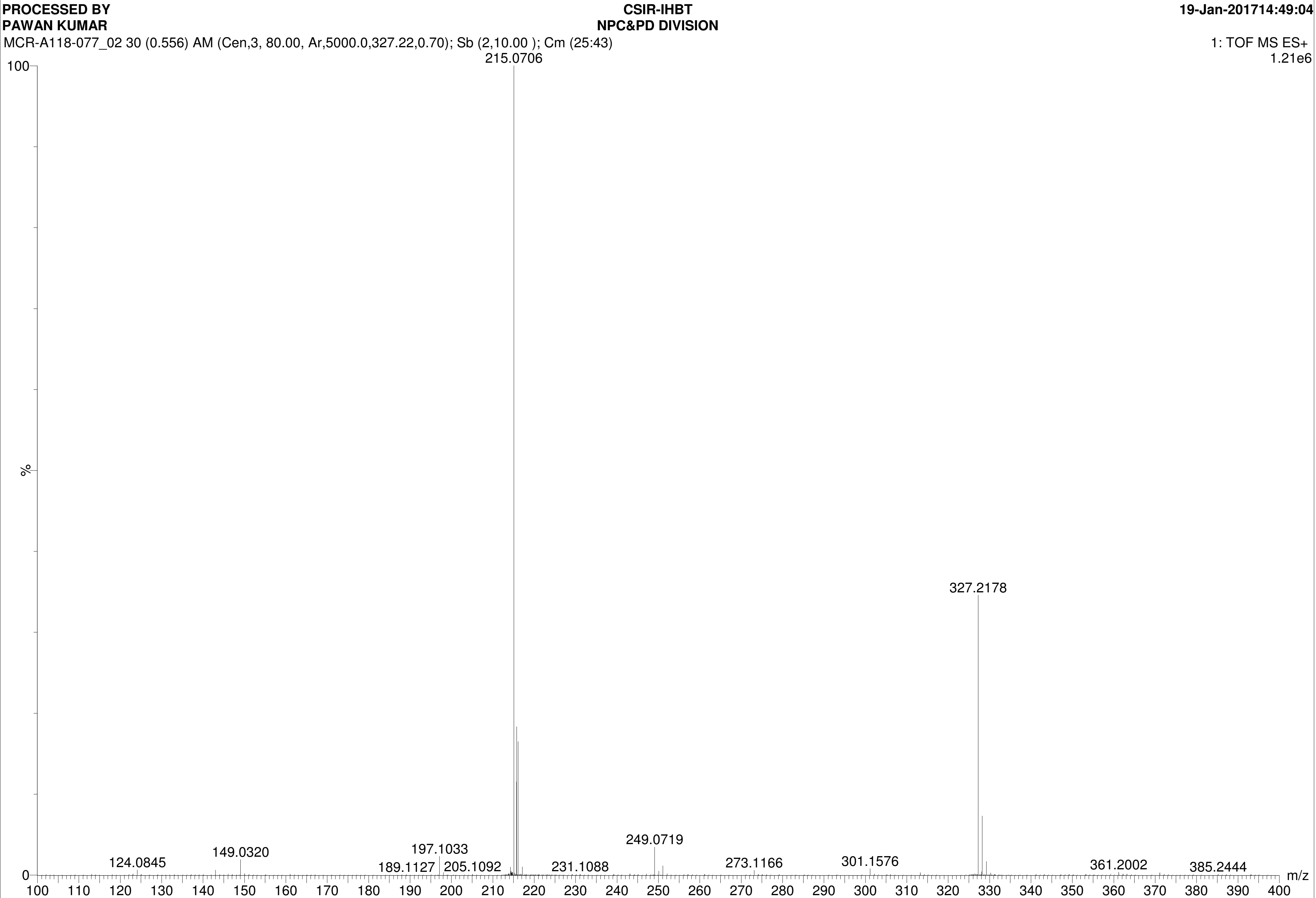
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
08-May-201717:47:37
MCR-A118-090_01A 38 (0.705) AM (Top,4, Ar,5000.0,313.16,0.70); Sb (2,10.00); Cm (31:61-(83:92+18:24))
1: TOF MS ES+
5.28e5
149.2613
257.1792
313.1644
301.1645
197.2807
205.2820
279.2300
124.3677
167.2780
177.1947
215.2734
233.2023
271.2432
341.0881
368.9510
397.0412
%
m/z


Nov17-2016
MCR-A118-077
7.8179
7.8159
7.6702
7.6539
7.5252
7.5226
7.5086
7.4946
7.4920
7.2689
7.2524
7.2382
7.2367
6.8488
6.4223
4.9097
2.0857
1.7066
1.0449
HO
N
N
N
N
H
5da
1.00
0.97
1.01
1.15
0.95
0.95
2.09
2.16
6.39
9.30
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

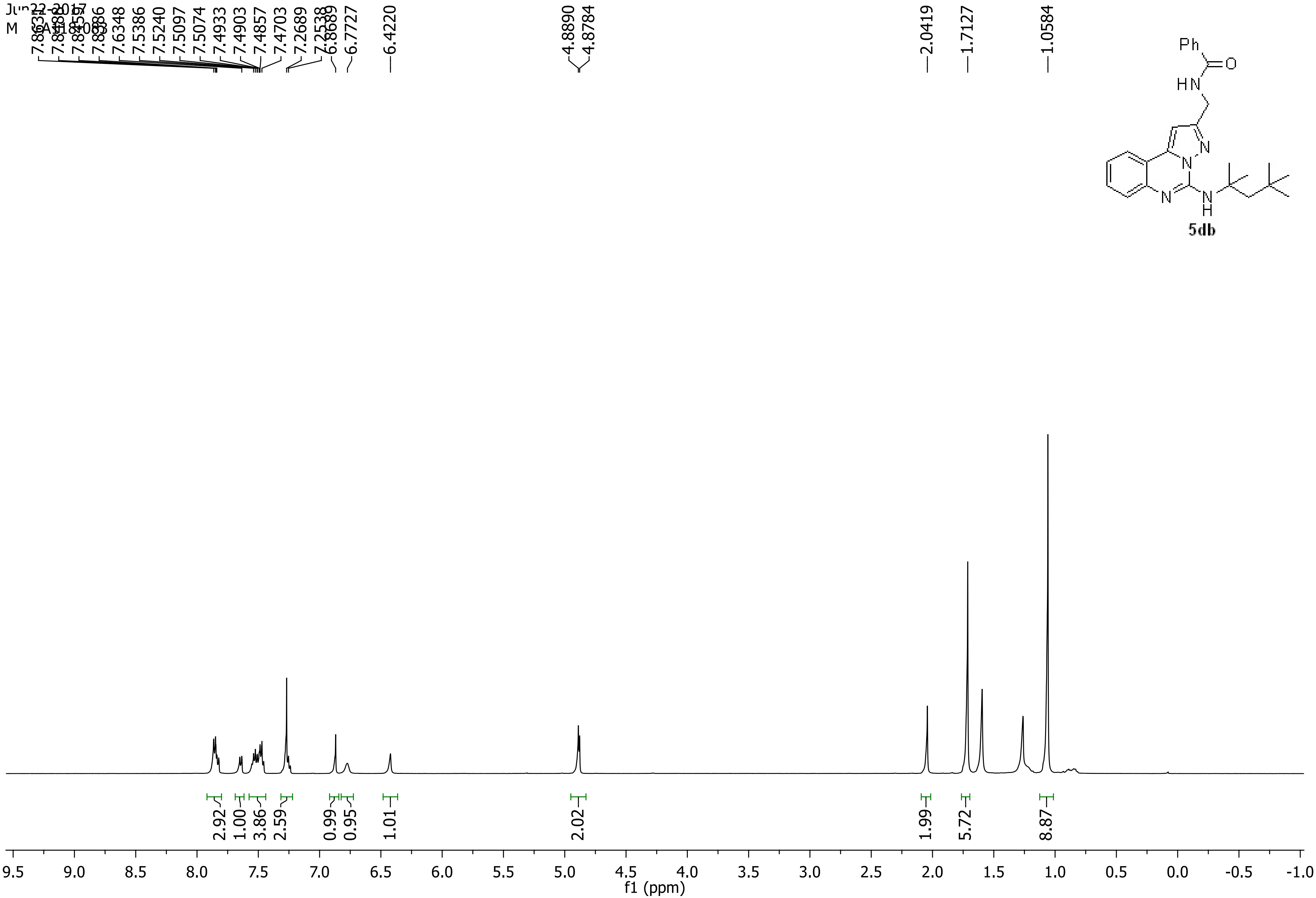
Nov17-2016
MCR-A118-077



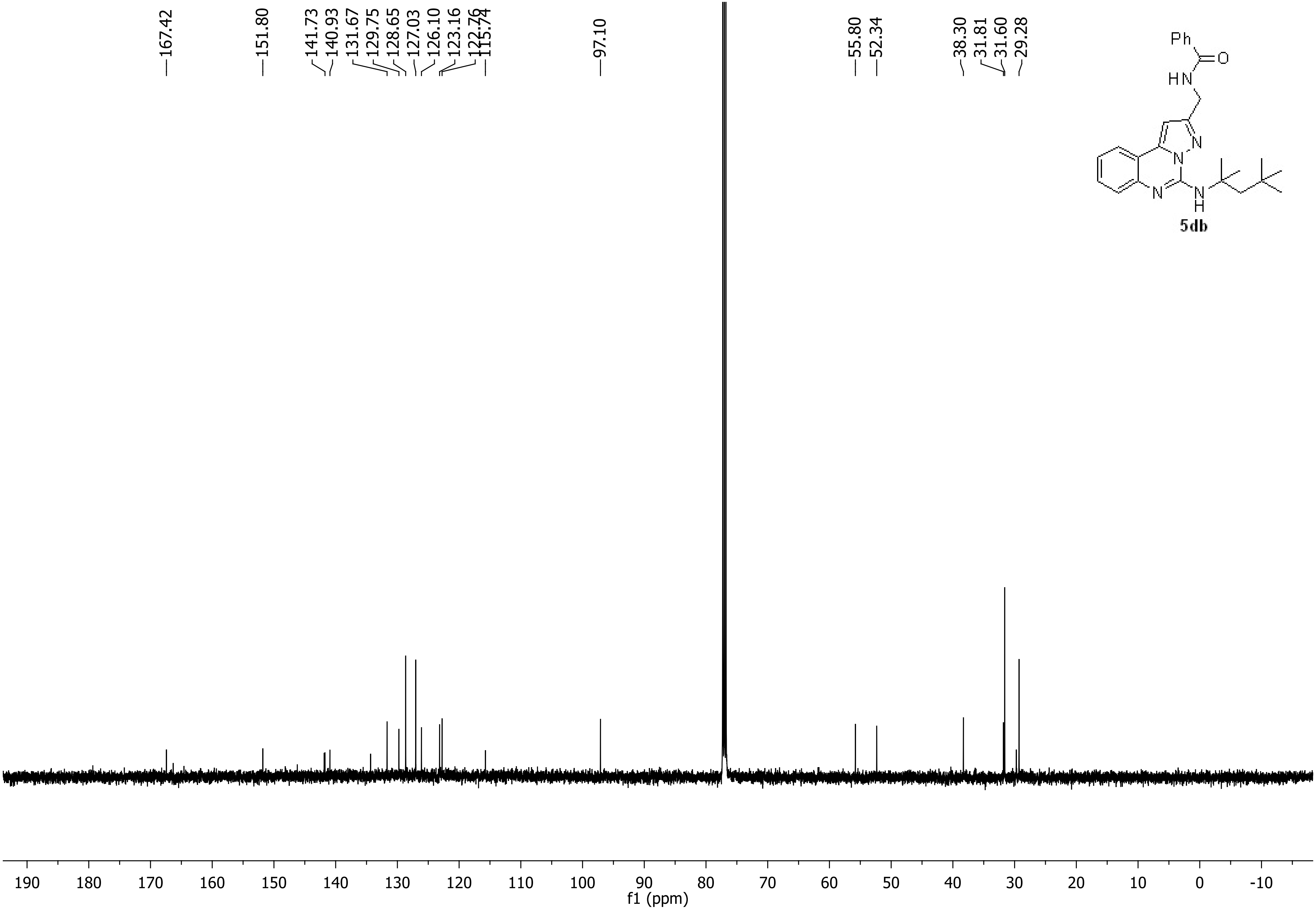
5da



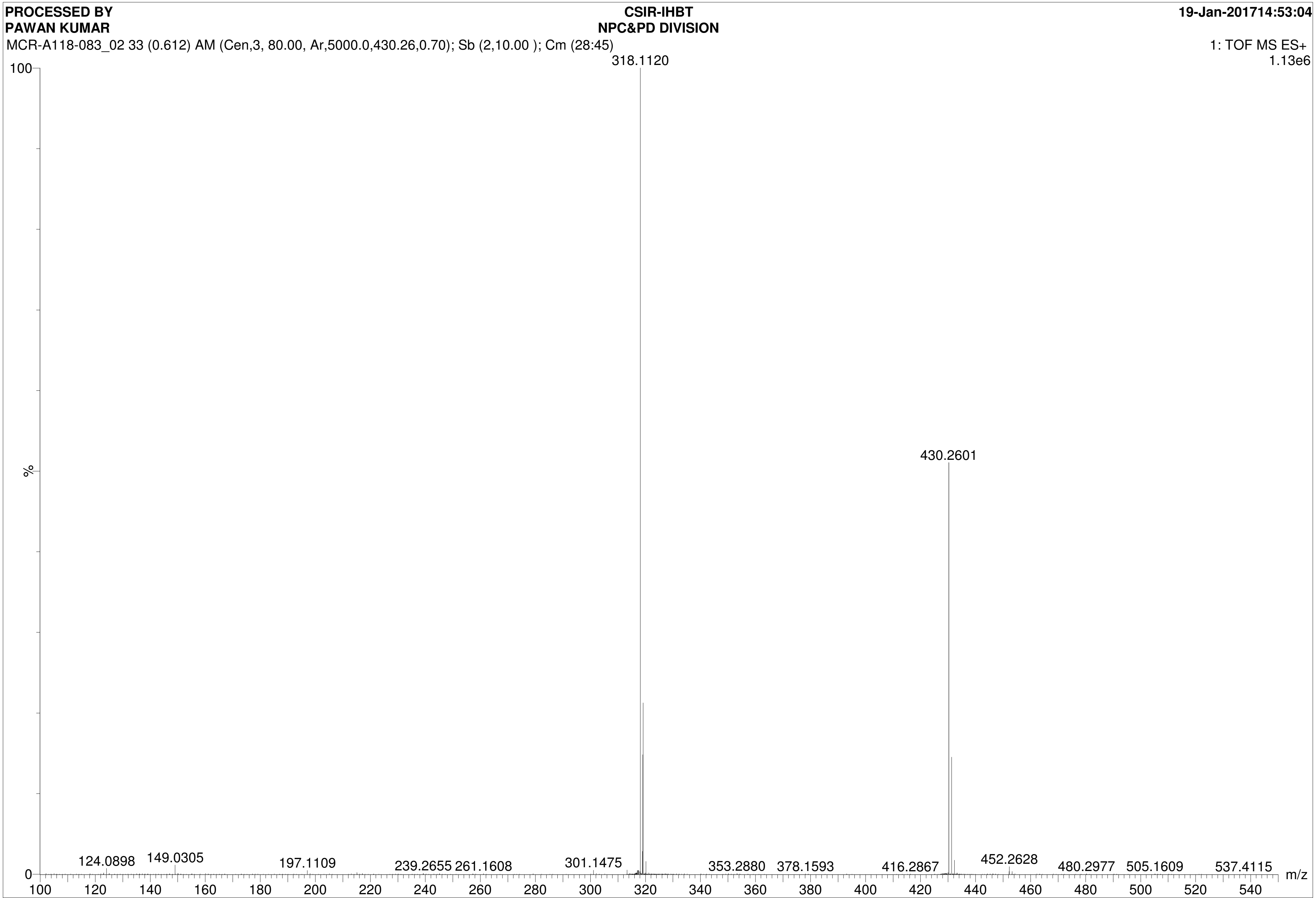
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:49:04
MCR-A118-077_02 30 (0.556) AM (Cen,3, 80.00, Ar,5000.0,327.22,0.70); Sb (2,10.00); Cm (25:43)
1: TOF MS ES+
1.21e6
215.0706
327.2178
249.0719
197.1033
149.0320
124.0845
189.1127
205.1092
231.1088
273.1166
301.1576
361.2002
385.2444
%
m/z

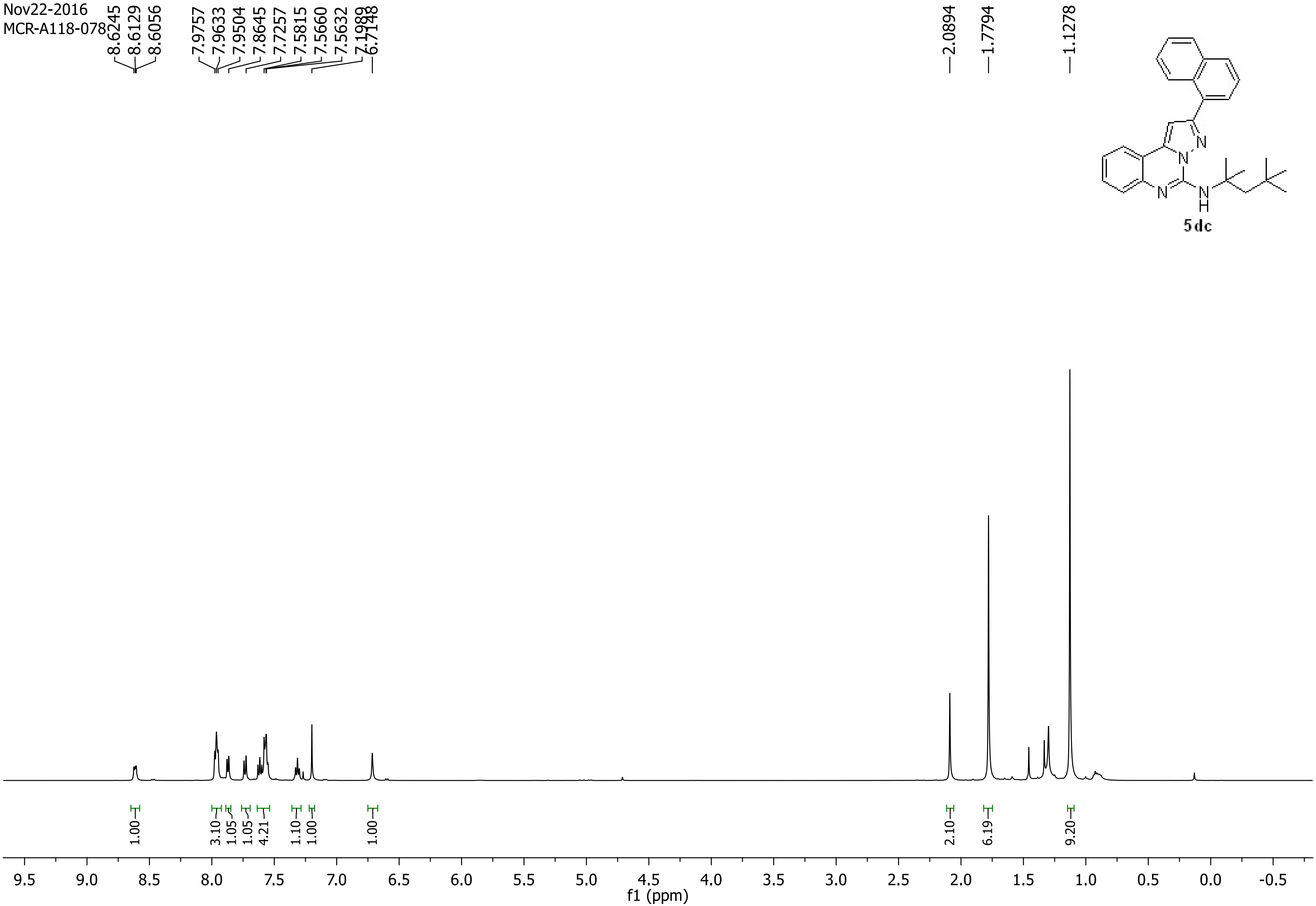


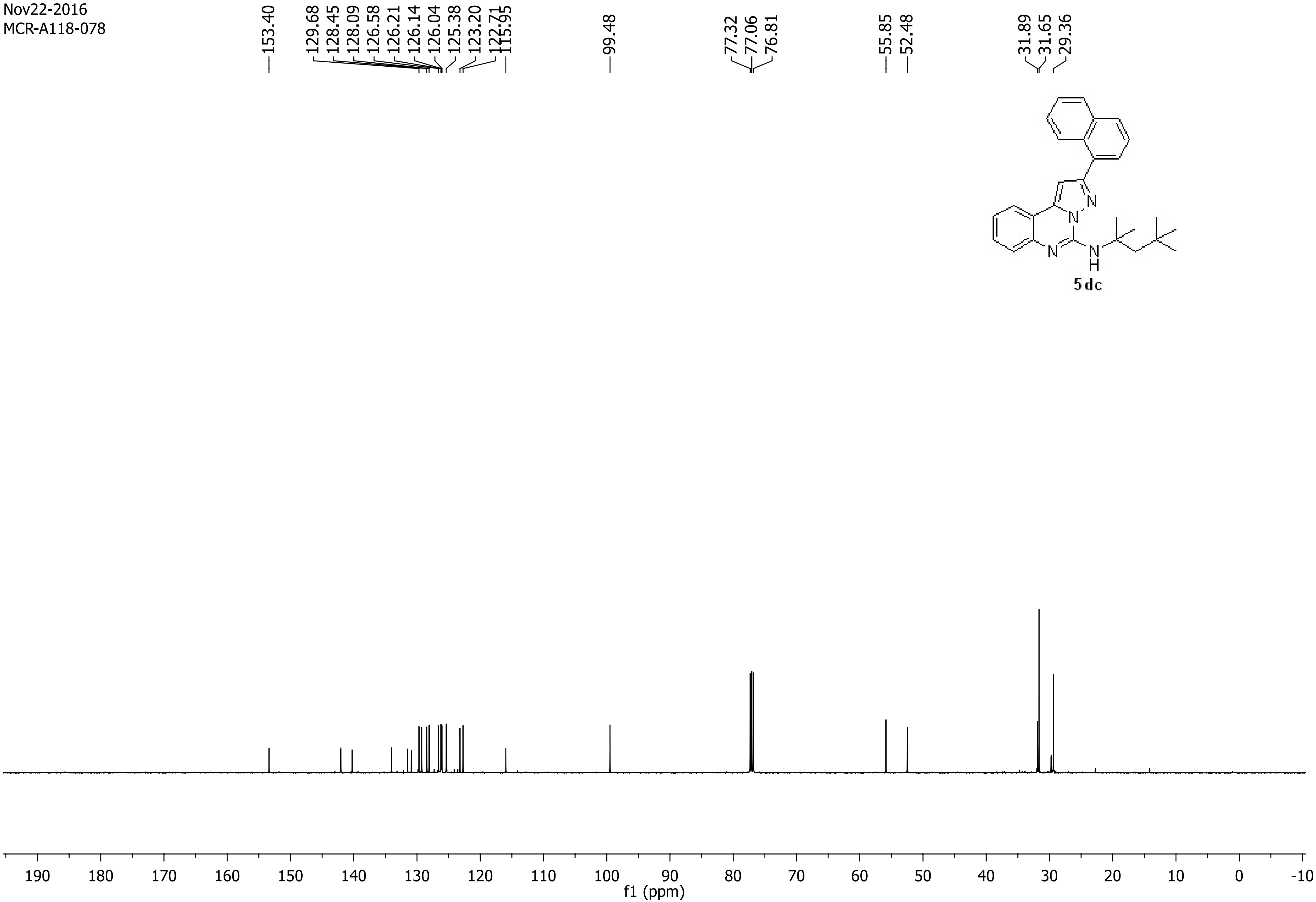
7.5386
7.5240
7.5097
7.5074
7.4933
7.4903
7.4857
7.4703
7.2689
7.2538
6.8689
6.7727
6.4220
4.8890
4.8784
2.0419
1.7127
1.0584
Ph
O
HN
N
N
N
N
H
5db
2.92
1.00
3.86
2.59
0.99
0.95
1.01
2.02
1.99
5.72
8.87
f1 (ppm)

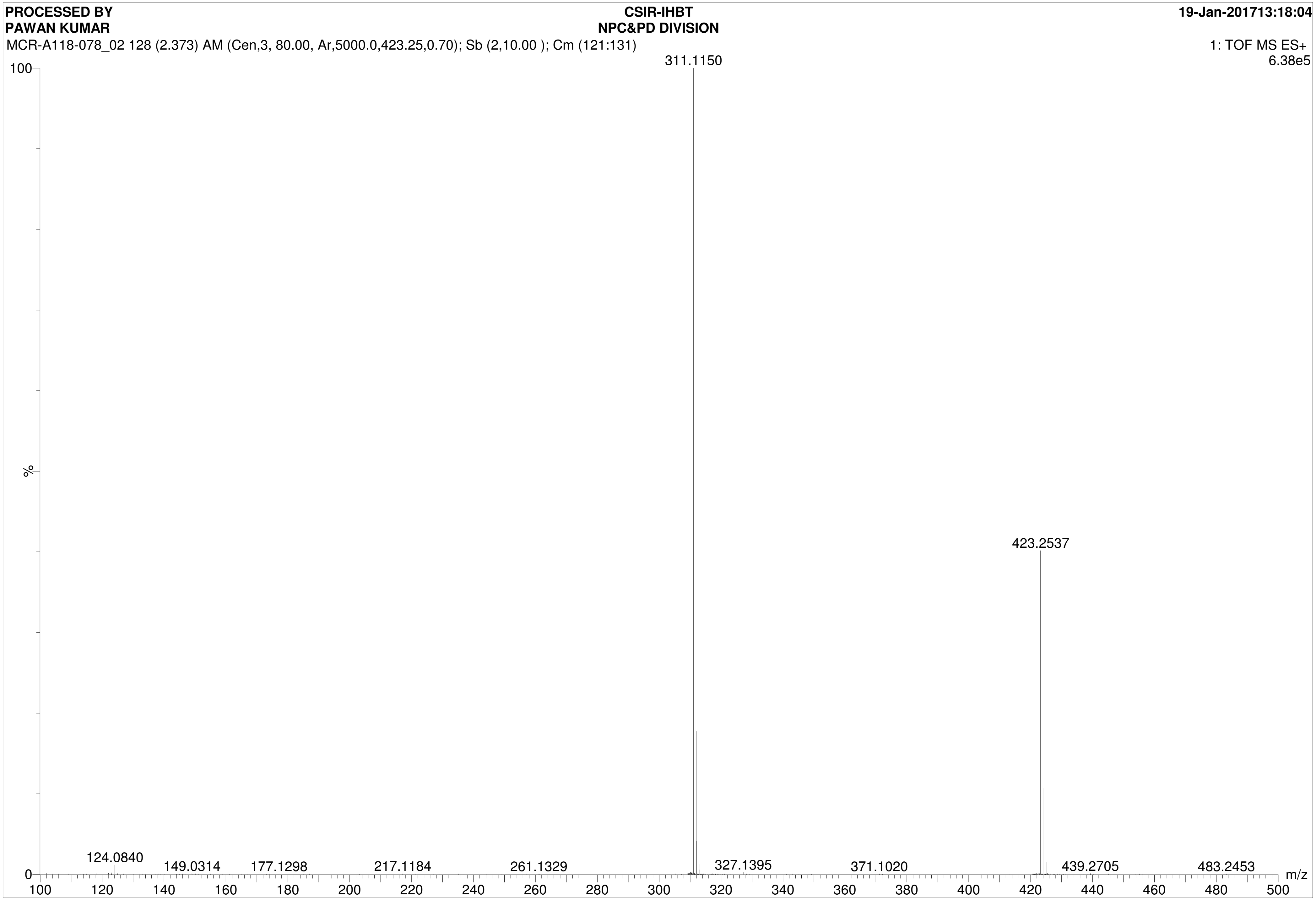

167.42
151.80
141.73
140.93
131.67
129.75
128.65
127.03
126.10
123.16
122.76
115.74
97.10
55.80
52.34
38.30
31.81
31.60
29.28
Ph
O
HN
N
N
N
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

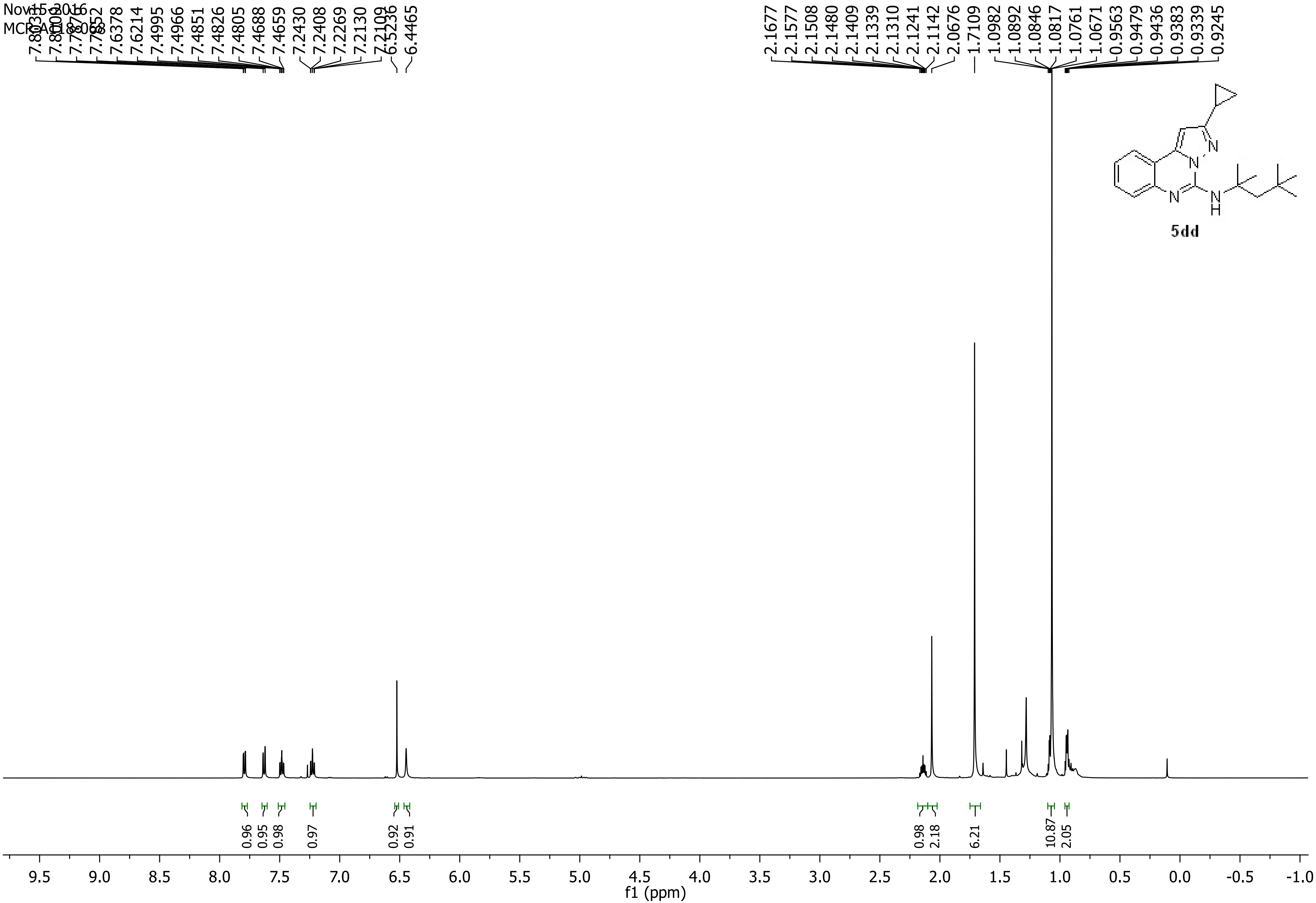
5db

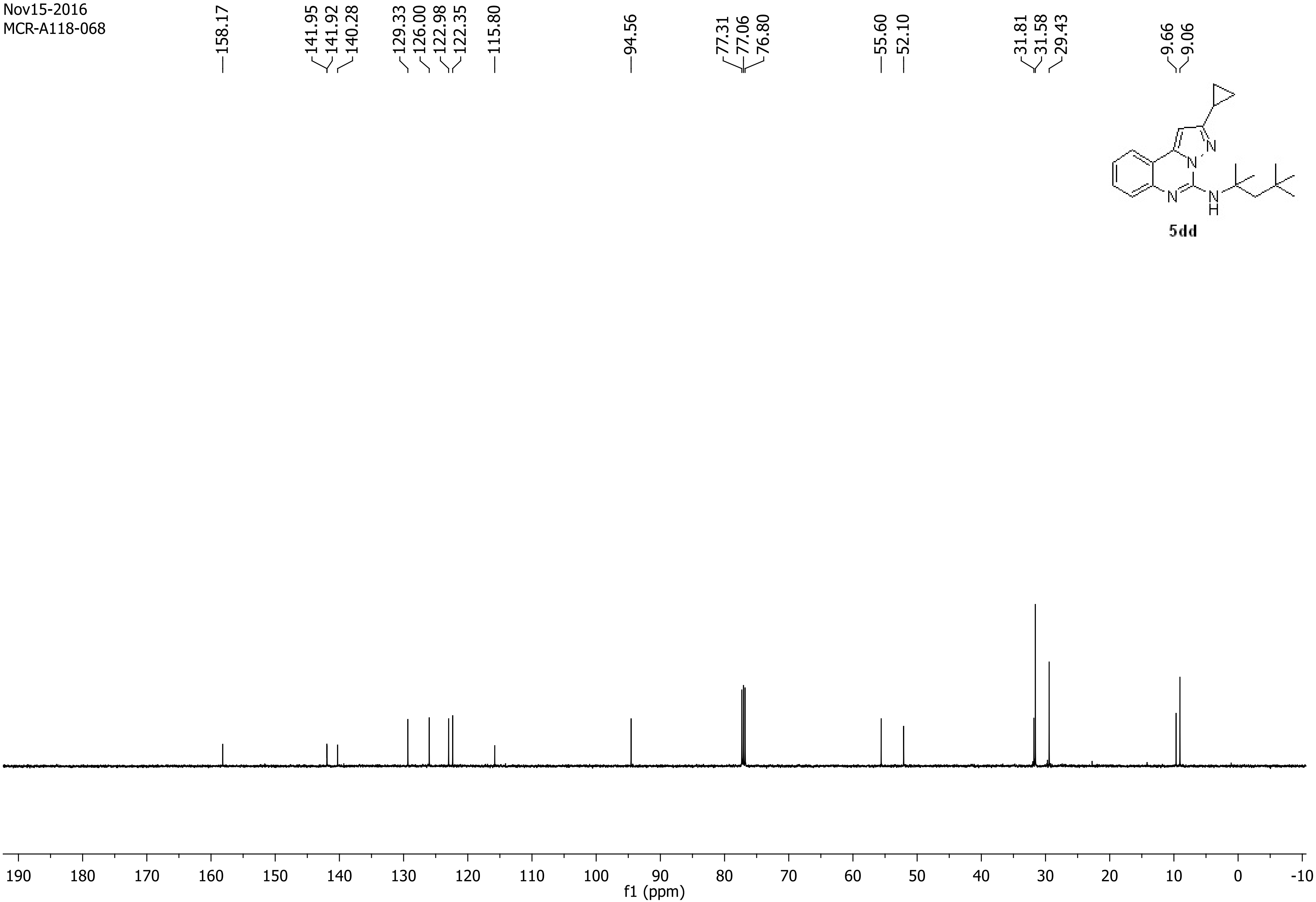

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:53:04
MCR-A118-083_02 33 (0.612) AM (Cen,3, 80.00, Ar,5000.0,430.26,0.70); Sb (2,10.00); Cm (28:45)
1: TOF MS ES+
1.13e6
318.1120
430.2601
124.0898
149.0305
197.1109
239.2655
261.1608
301.1475
353.2880
378.1593
416.2867
452.2628
480.2977
505.1609
537.4115
%
m/z


Nov22-2016
MCR-A118-078
8.6245
8.6129
8.6056
7.9757
7.9633
7.9504
7.8645
7.7257
7.5815
7.5660
7.5632
7.1989
6.7148
2.0894
1.7794
1.1278
5dc
1.00
3.10
1.05
1.05
4.21
1.10
1.00
1.00
2.10
6.19
9.20
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

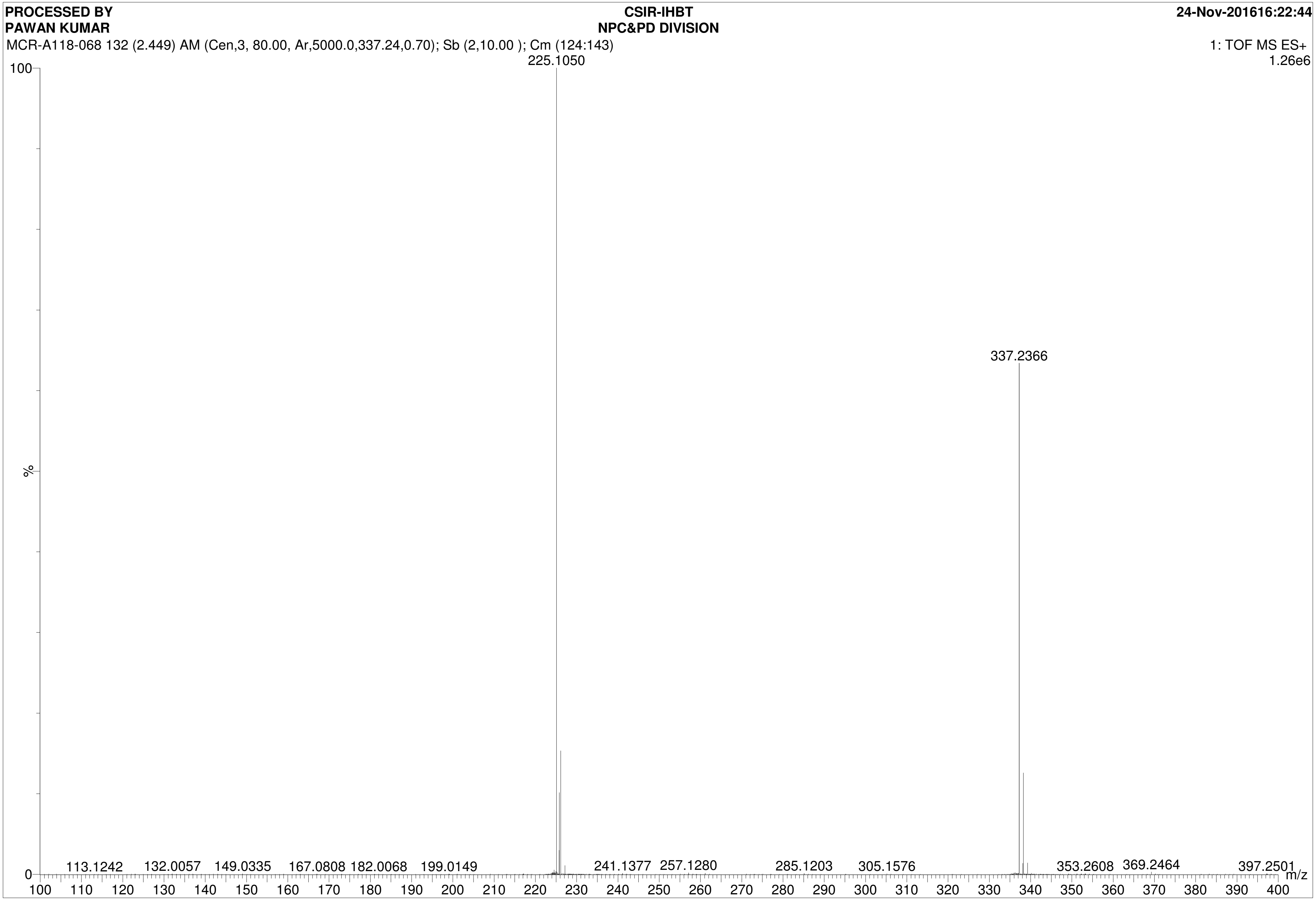

Nov22-2016
MCR-A118-078
153.40
129.68
128.45
128.09
126.58
126.21
126.14
126.04
125.38
123.20
122.71
115.95
99.48
77.32
77.06
76.81
55.85
52.48
31.89
31.65
29.36
N
N
N
N
H
5dc
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

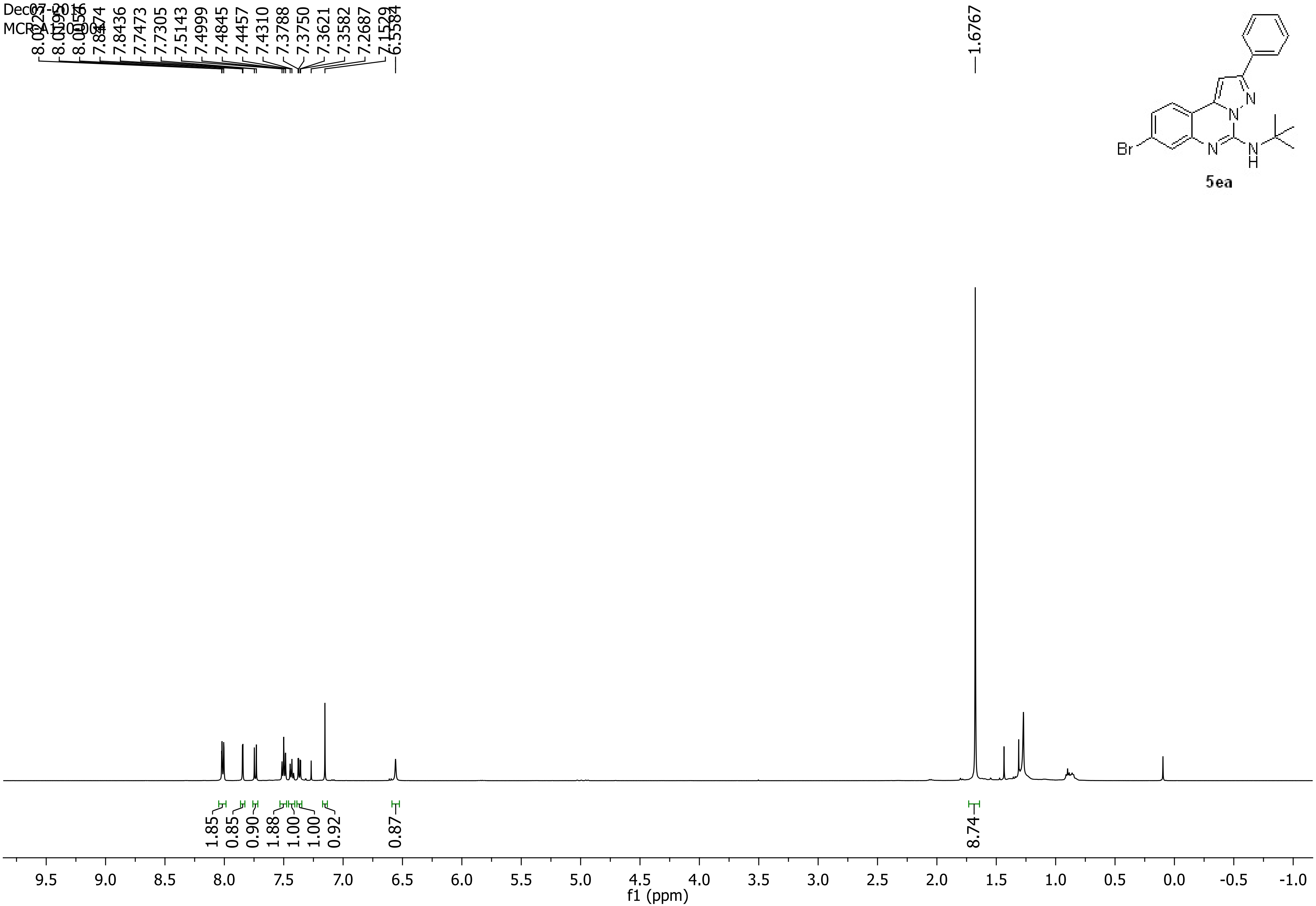

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:18:04
MCR-A118-078_02 128 (2.373) AM (Cen,3, 80.00, Ar,5000.0,423.25,0.70); Sb (2,10.00); Cm (121:131)
1: TOF MS ES+
6.38e5
311.1150
423.2537
124.0840
149.0314
177.1298
217.1184
261.1329
327.1395
371.1020
439.2705
483.2453
%
m/z
100
0
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500

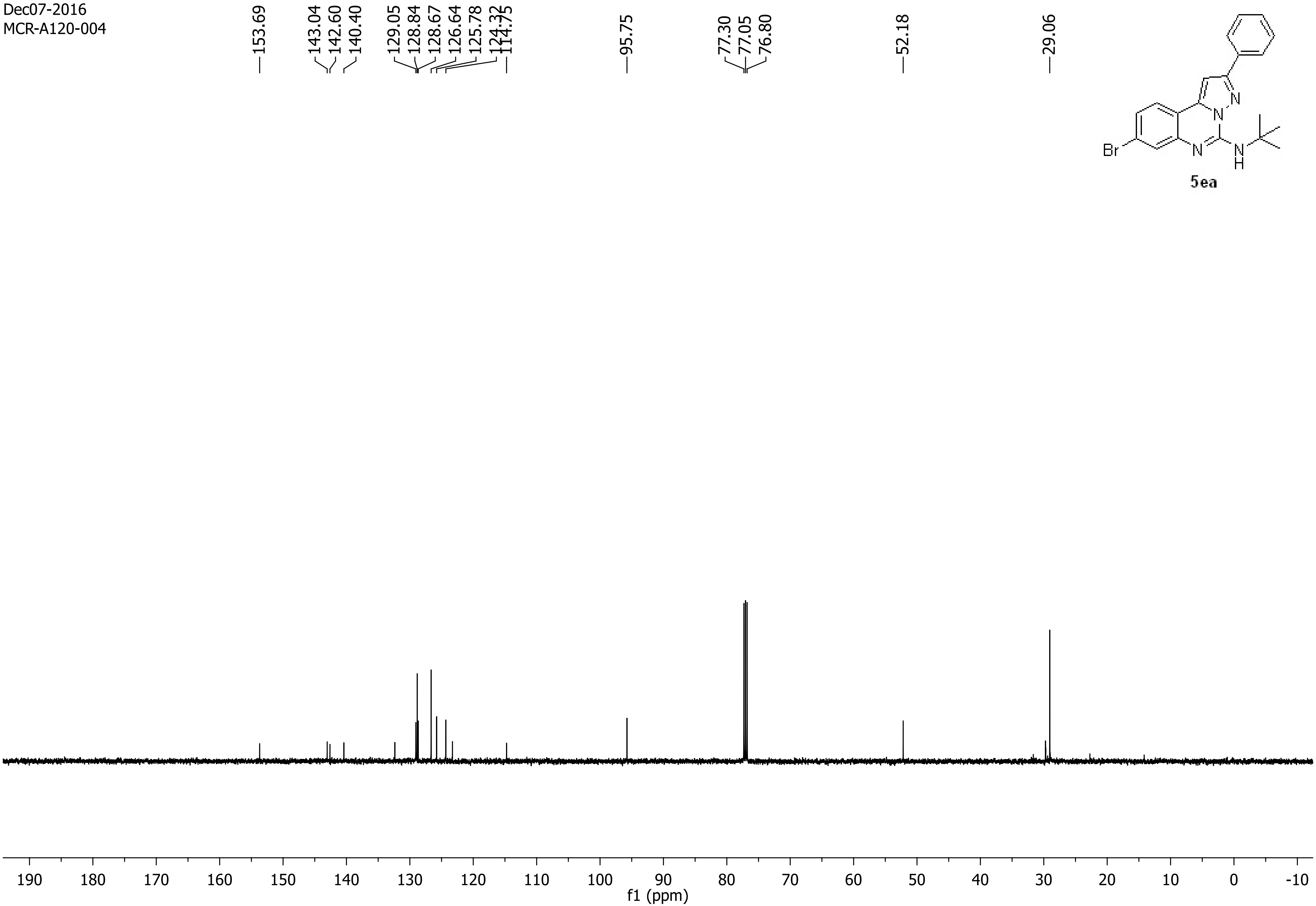

Nov15-2016
7.6378
7.6214
7.4995
7.4966
7.4851
7.4826
7.4805
7.4688
7.4659
7.2430
7.2408
7.2269
7.2130
6.5236
6.4465
2.1677
2.1577
2.1508
2.1480
2.1409
2.1339
2.1310
2.1241
2.1142
2.0676
1.7109
1.0982
1.0892
1.0846
1.0817
1.0761
1.0671
0.9563
0.9479
0.9436
0.9383
0.9339
0.9245
N
N
N
N
H
5dd
0.96
0.95
0.98
0.97
0.92
0.91
0.98
2.18
6.21
10.87
2.05
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


Nov15-2016
MCR-A118-068
158.17
141.95
141.92
140.28
129.33
126.00
122.98
122.35
115.80
94.56
77.31
77.06
76.80
55.60
52.10
31.81
31.58
29.43
9.66
9.06
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
N
N
N
N
H

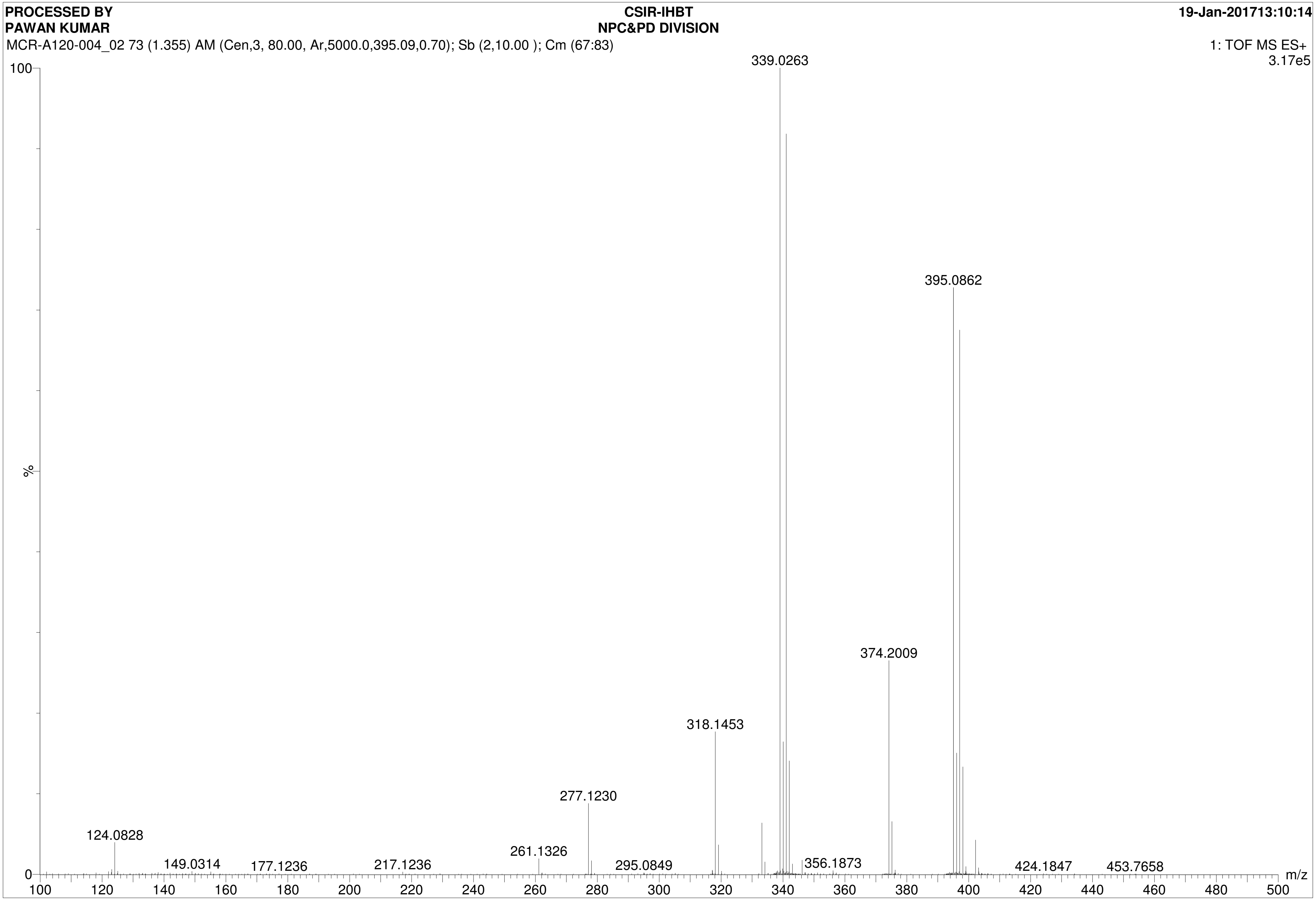
5dd

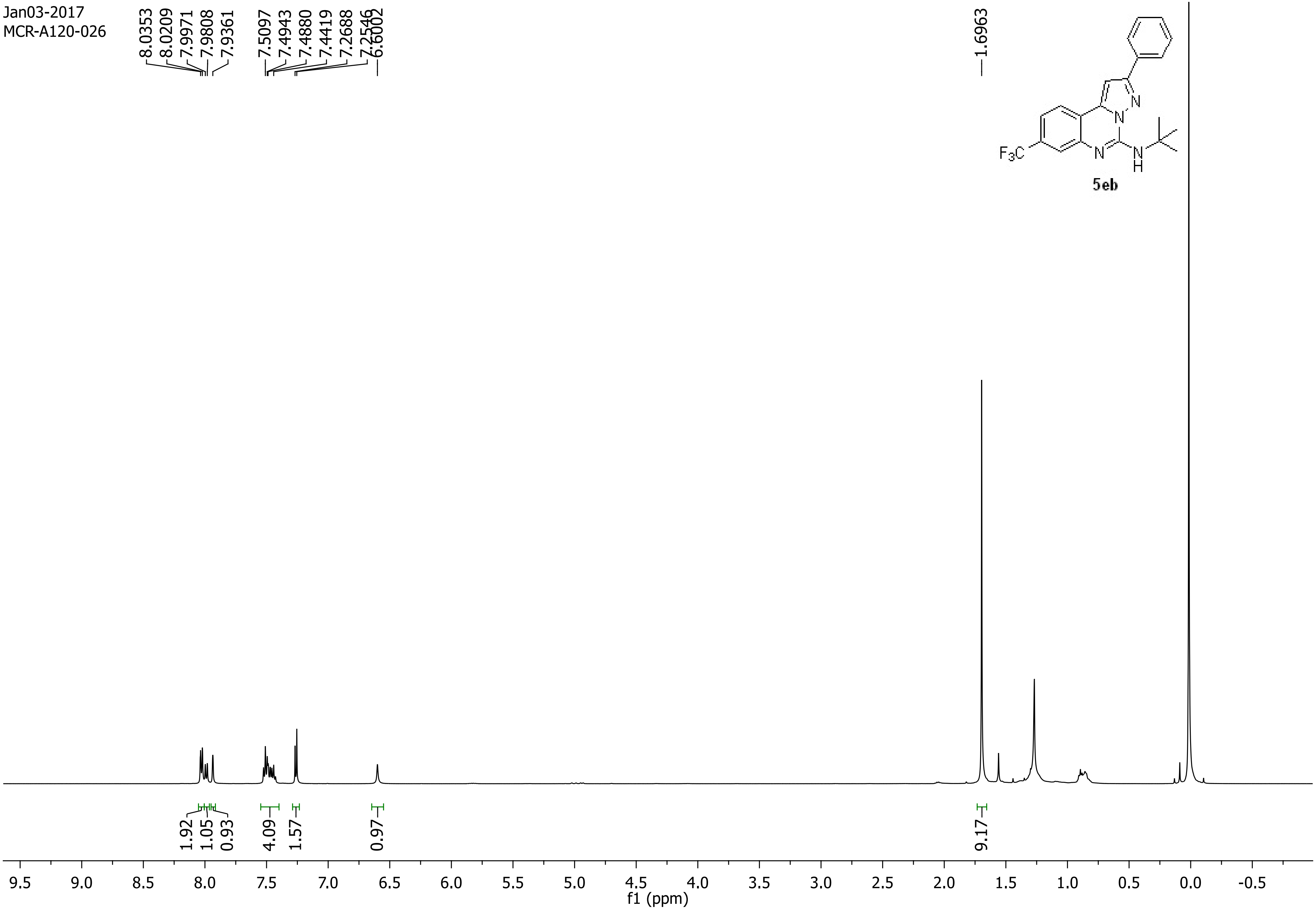

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:22:44
MCR-A118-068 132 (2.449) AM (Cen,3, 80.00, Ar,5000.0,337.24,0.70); Sb (2,10.00); Cm (124:143)
1: TOF MS ES+
1.26e6
225.1050
337.2366
113.1242
132.0057
149.0335
167.0808
182.0068
199.0149
241.1377
257.1280
285.1203
305.1576
353.2608
369.2464
397.2501
%
m/z

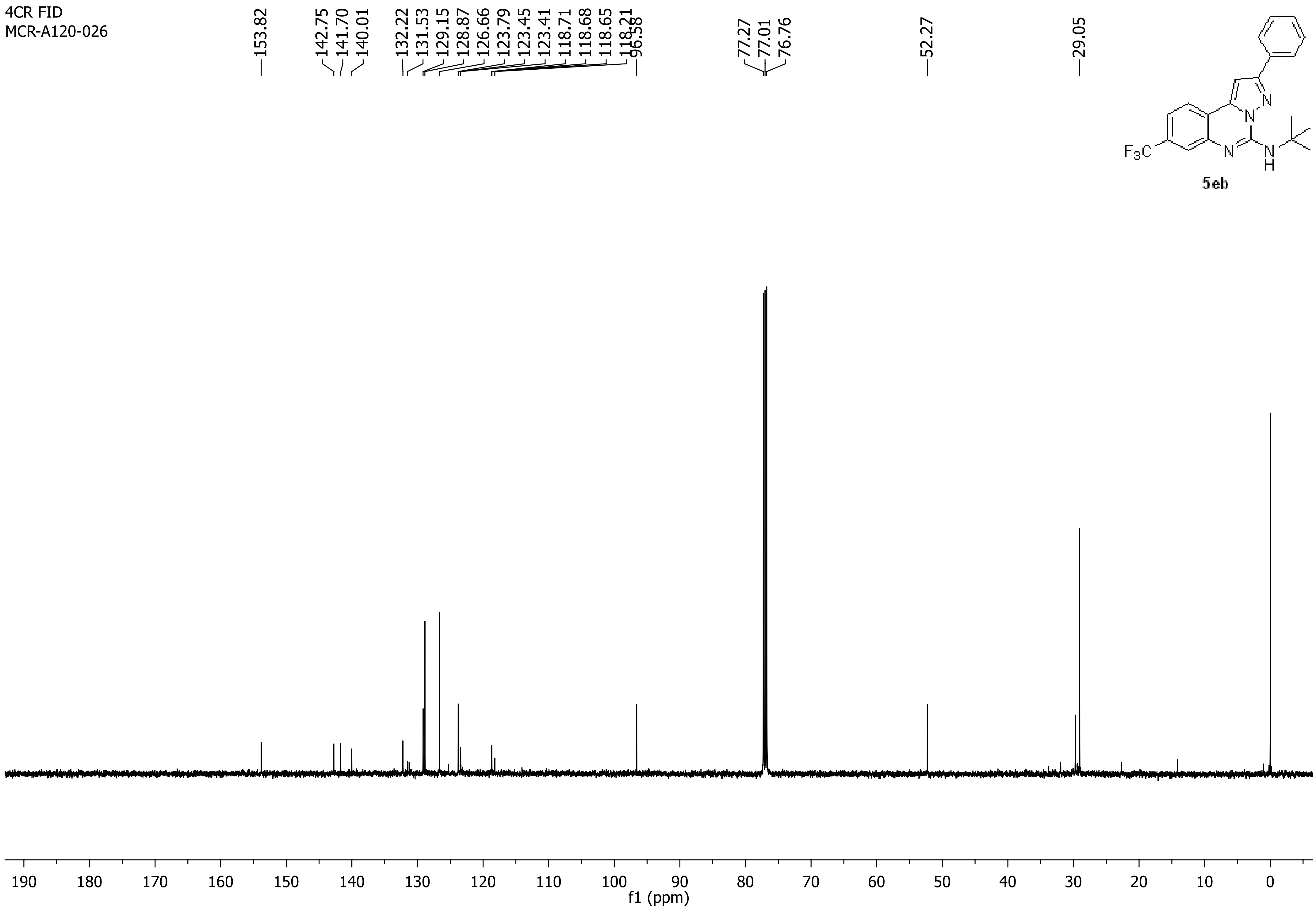

Dec07-2016
MCR-A120-004
8.0229 8.0191 8.0057 7.8474 7.8436 7.7473 7.7305 7.5143 7.4999 7.4845 7.4457 7.4310 7.3788 7.3750 7.3621 7.3582 7.2687 7.1529 6.5584
1.6767
1.85 0.85 0.90 1.88 1.00 1.00 0.92 0.87
8.74
f1 (ppm)
Br
N
N
N
N
H
5ea

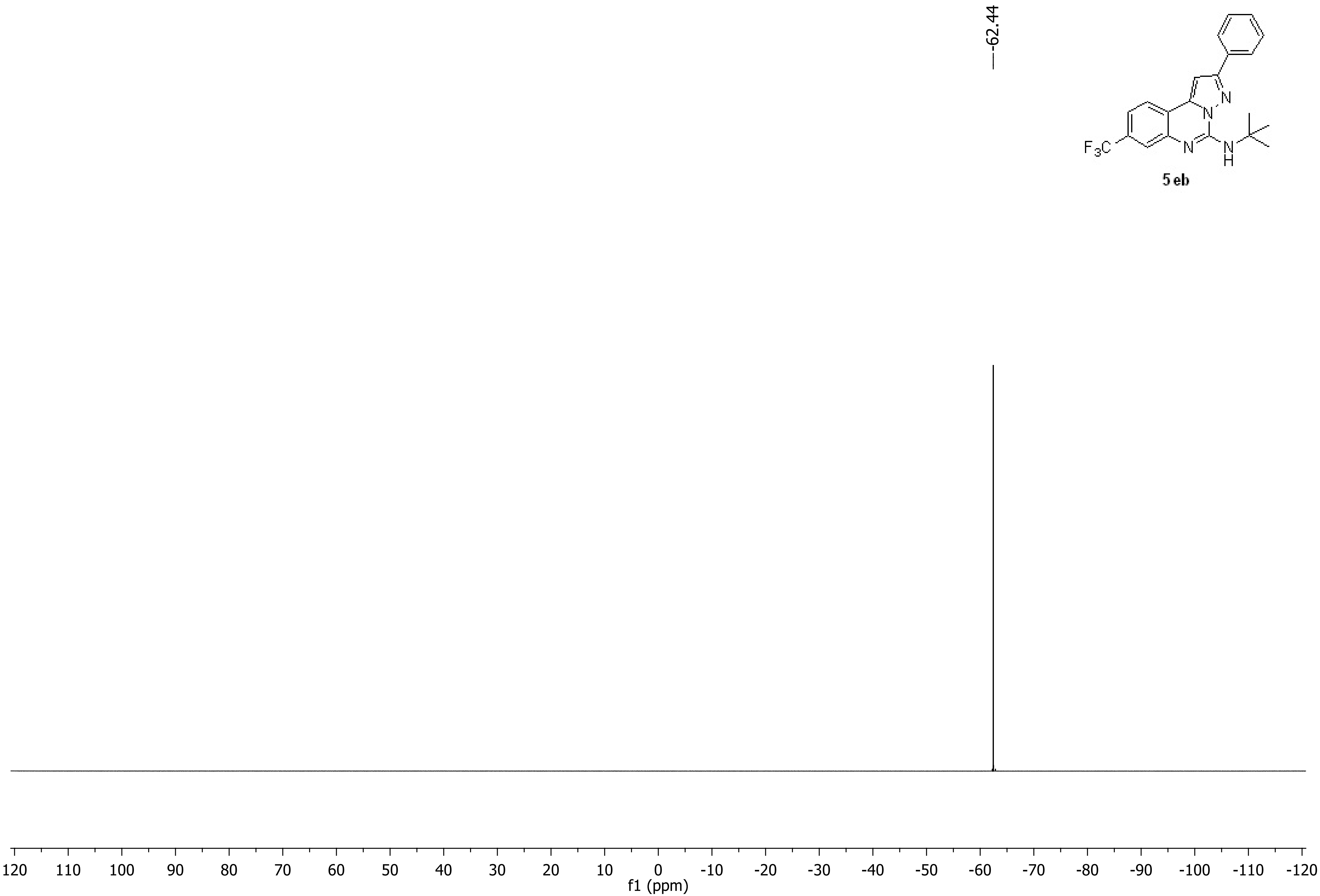

Dec07-2016
MCR-A120-004
153.69
143.04
142.60
140.40
129.05
128.84
128.67
126.64
125.78
124.32
114.75
95.75
77.30
77.05
76.80
52.18
29.06
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
Br
N
N
N
N
H

5ea


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:10:14
MCR-A120-004_02 73 (1.355) AM (Cen,3, 80.00, Ar,5000.0,395.09,0.70); Sb (2,10.00); Cm (67:83)
1: TOF MS ES+
3.17e5
339.0263
395.0862
374.2009
318.1453
277.1230
124.0828
261.1326
149.0314
177.1236
217.1236
295.0849
356.1873
424.1847
453.7658
%
m/z
100
0
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500

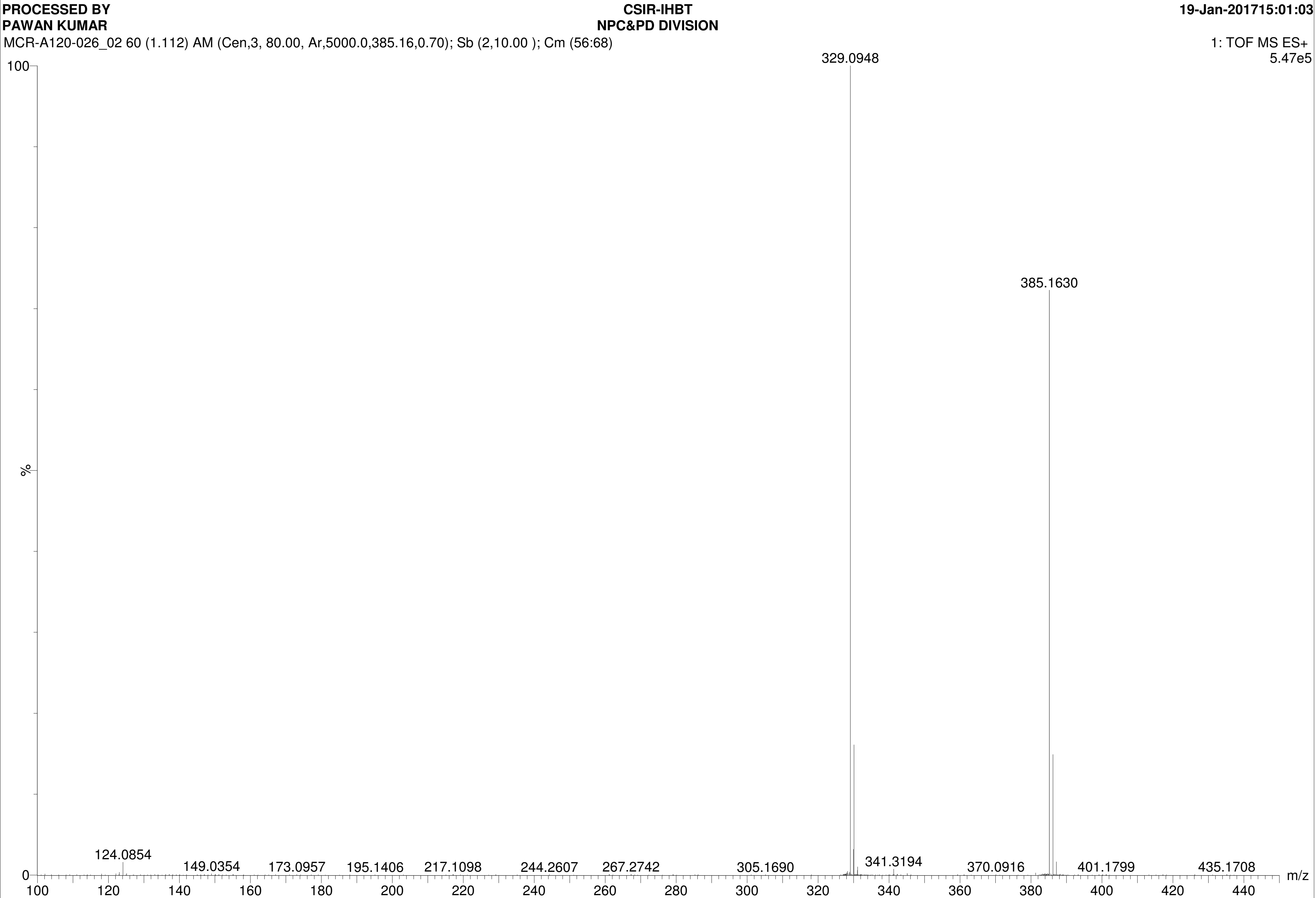

Jan03-2017
MCR-A120-026
8.0353
8.0209
7.9971
7.9808
7.9361
7.5097
7.4943
7.4880
7.4419
7.2688
7.2546
6.6002
1.6963
F_3C
N
N
N
N
H
5eb
1.92
1.05
0.93
4.09
1.57
0.97
9.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


4CR FID
MCR-A120-026
153.82
142.75
141.70
140.01
132.22
131.53
129.15
128.87
126.66
123.79
123.45
123.41
118.71
118.68
118.65
118.21
96.58
77.27
77.01
76.76
52.27
29.05
F3C
N
N
N
N
H
5eb
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

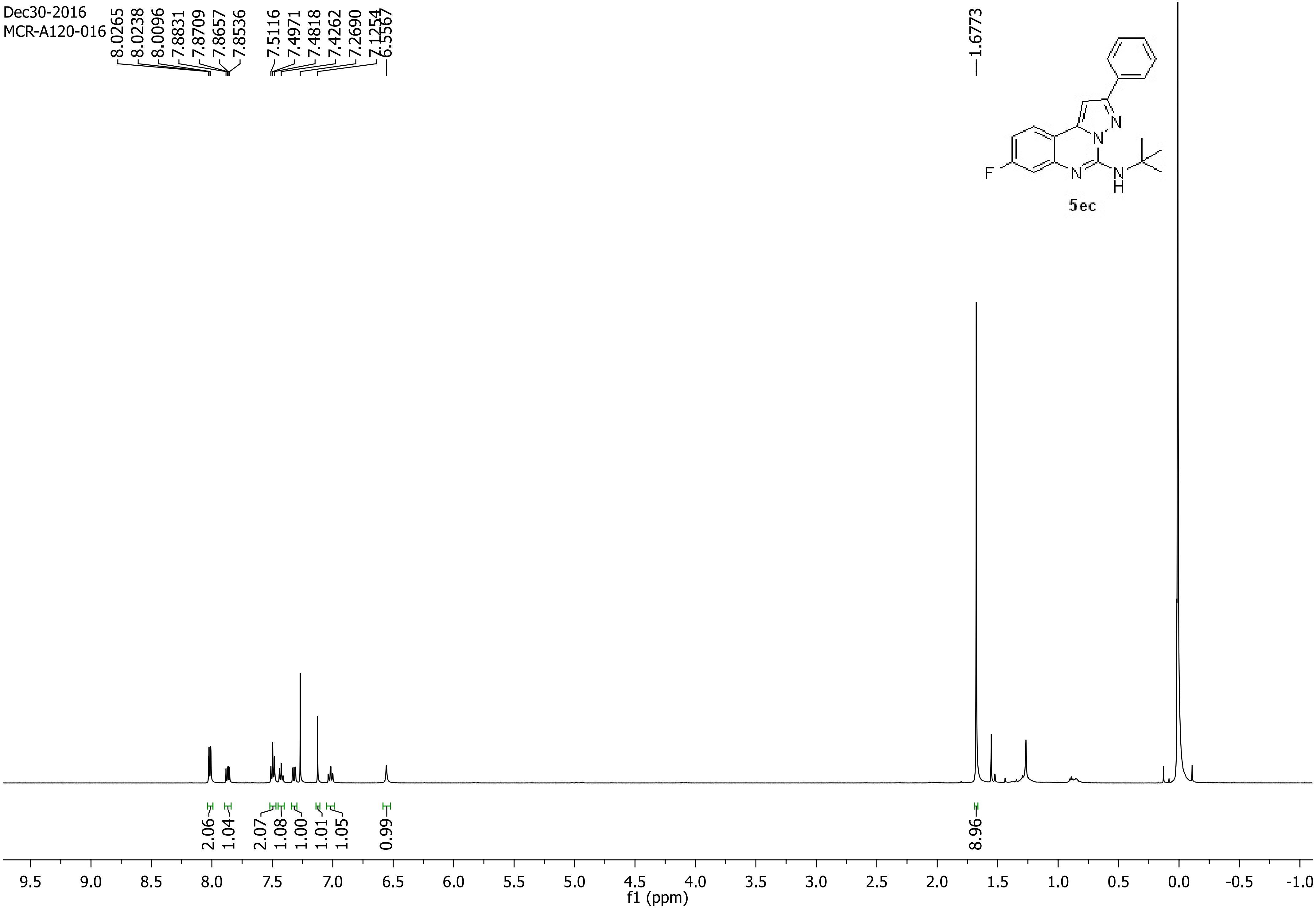


-62.44
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120
f1 (ppm)
F3C
N
N
N
N
H

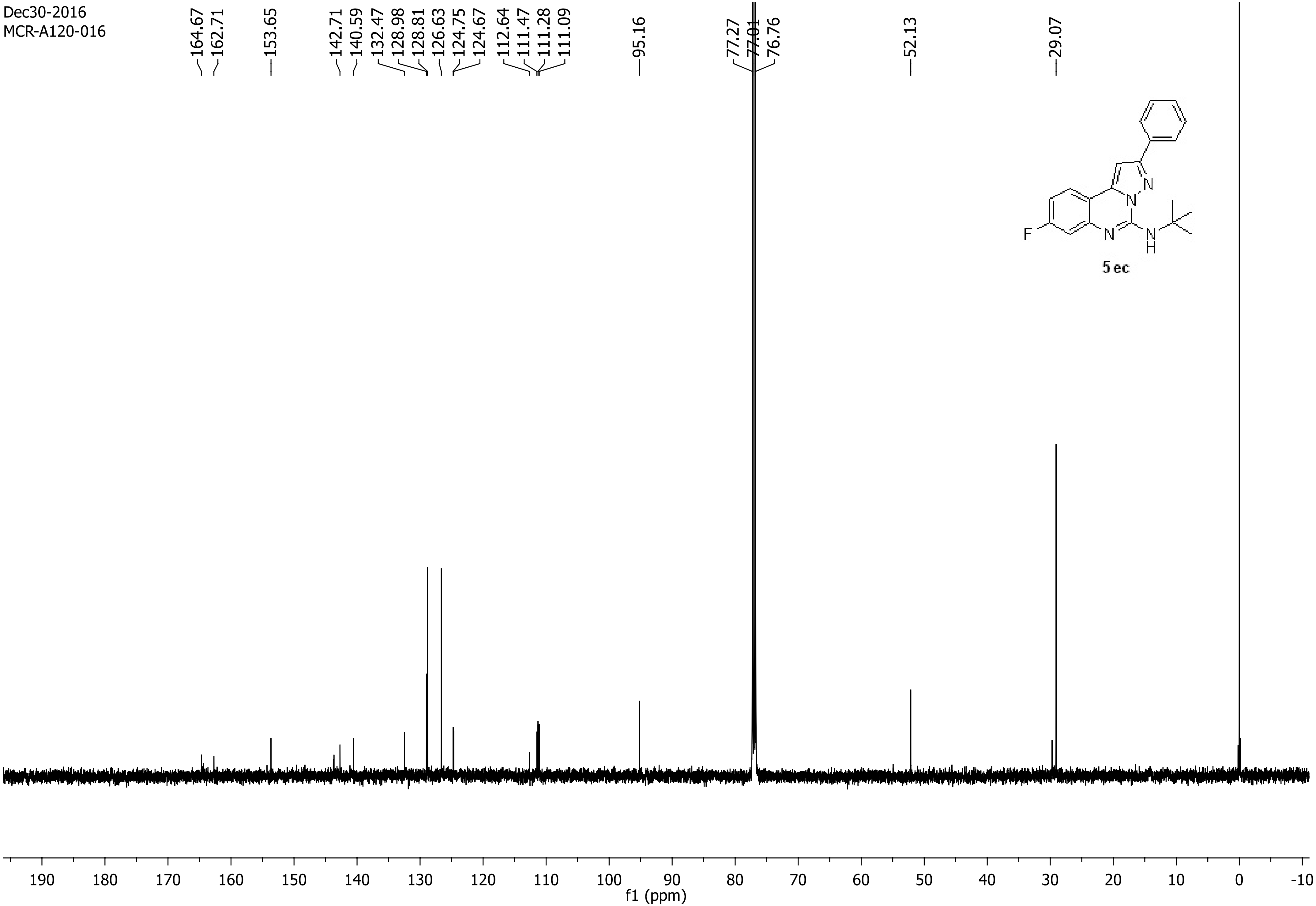
5eb



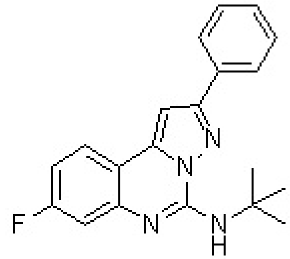
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:01:03
MCR-A120-026_02 60 (1.112) AM (Cen,3, 80.00, Ar,5000.0,385.16,0.70); Sb (2,10.00); Cm (56:68)
1: TOF MS ES+
5.47e5
329.0948
385.1630
124.0854
149.0354
173.0957
195.1406
217.1098
244.2607
267.2742
305.1690
341.3194
370.0916
401.1799
435.1708
%
m/z


Dec30-2016
MCR-A120-016
8.0265
8.0238
8.0096
7.8831
7.8709
7.8657
7.8536
7.5116
7.4971
7.4818
7.4262
7.2690
7.1254
6.5567
1.6773
F
N
N
N
N
H
5ec
2.06
1.04
2.07
1.08
1.00
1.01
1.05
0.99
8.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

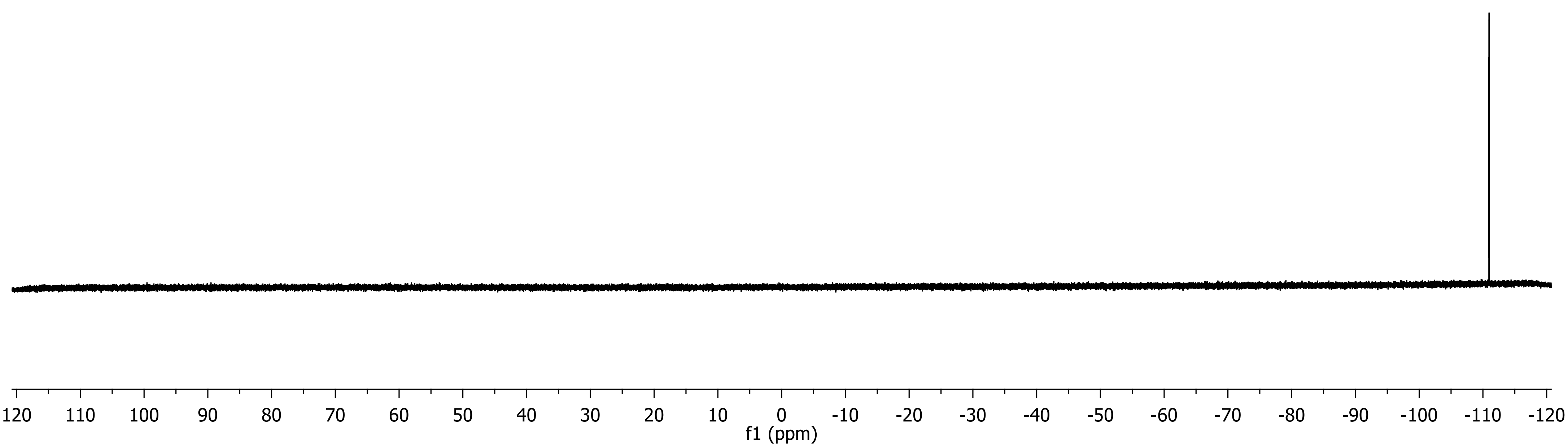
Dec30-2016
MCR-A120-016

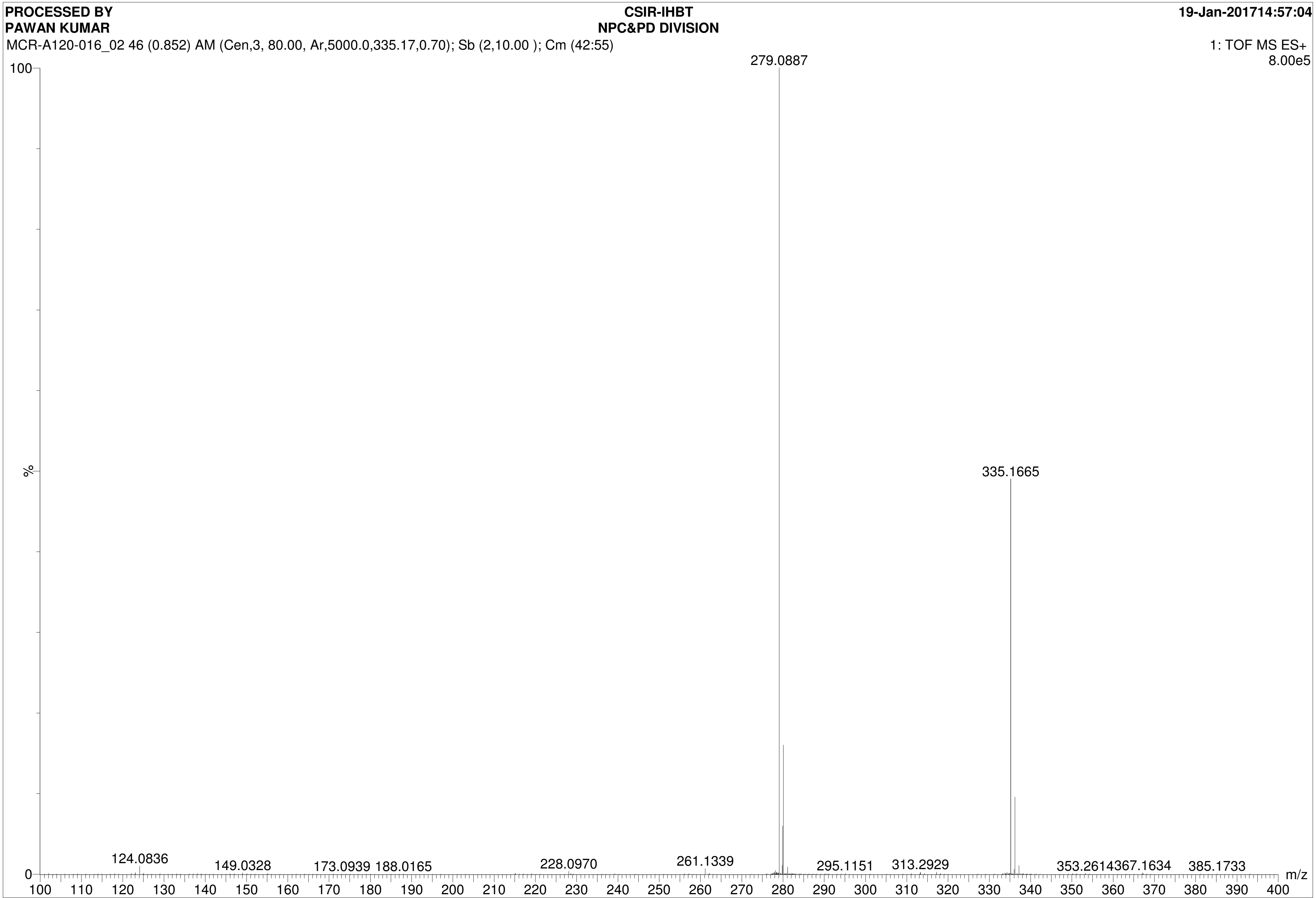


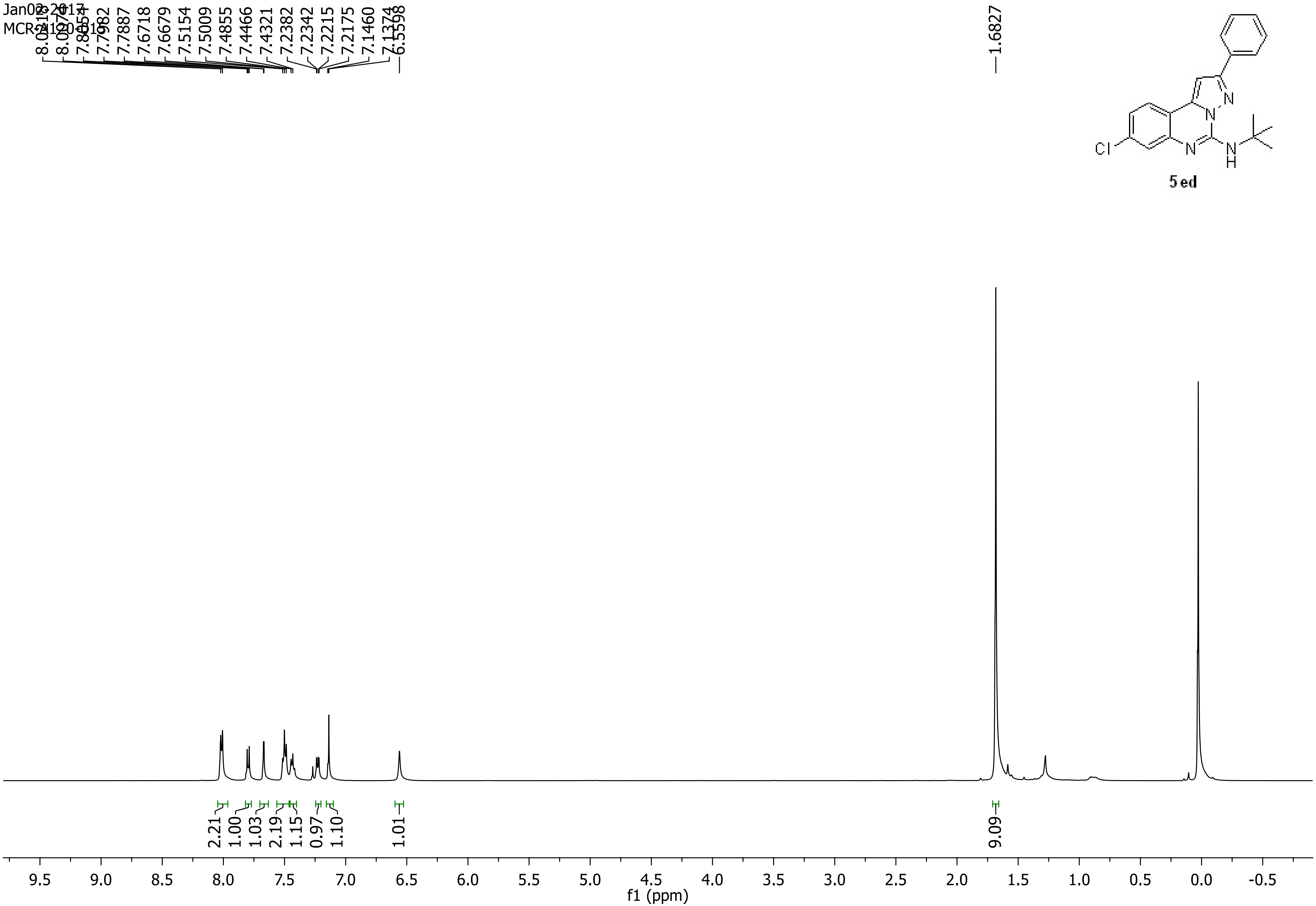
Dec31-2016
MCR-A120-016

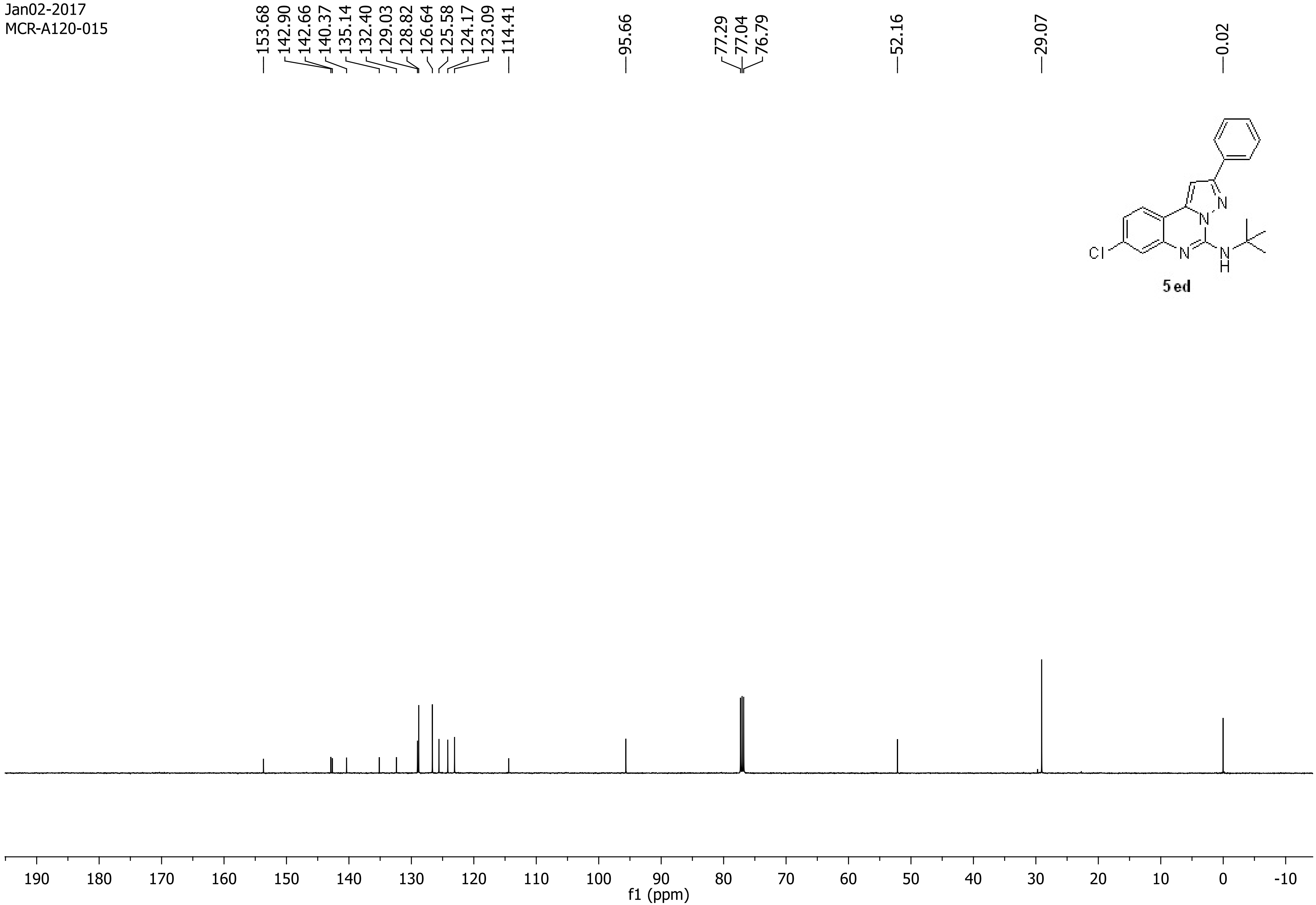


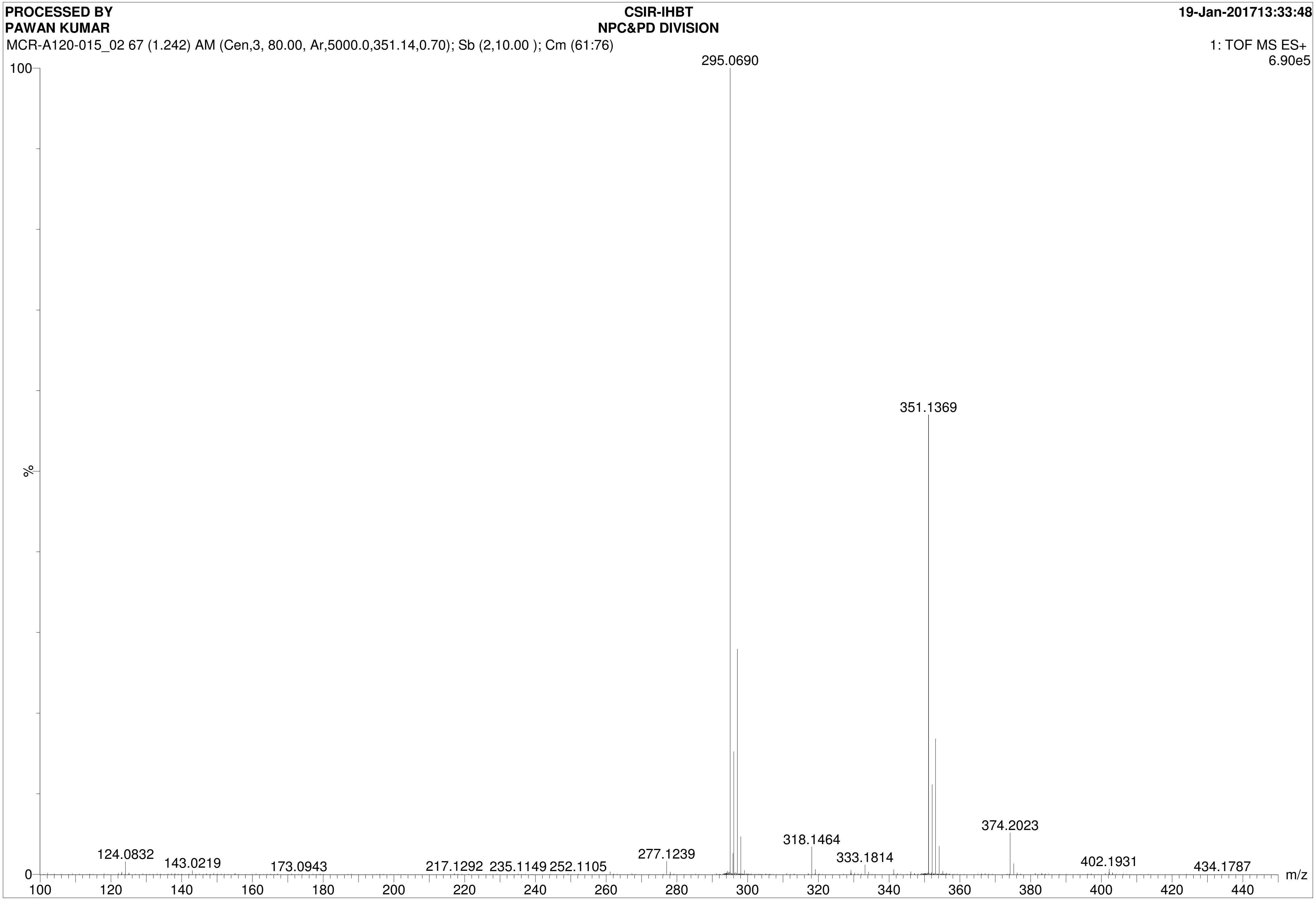
5ec



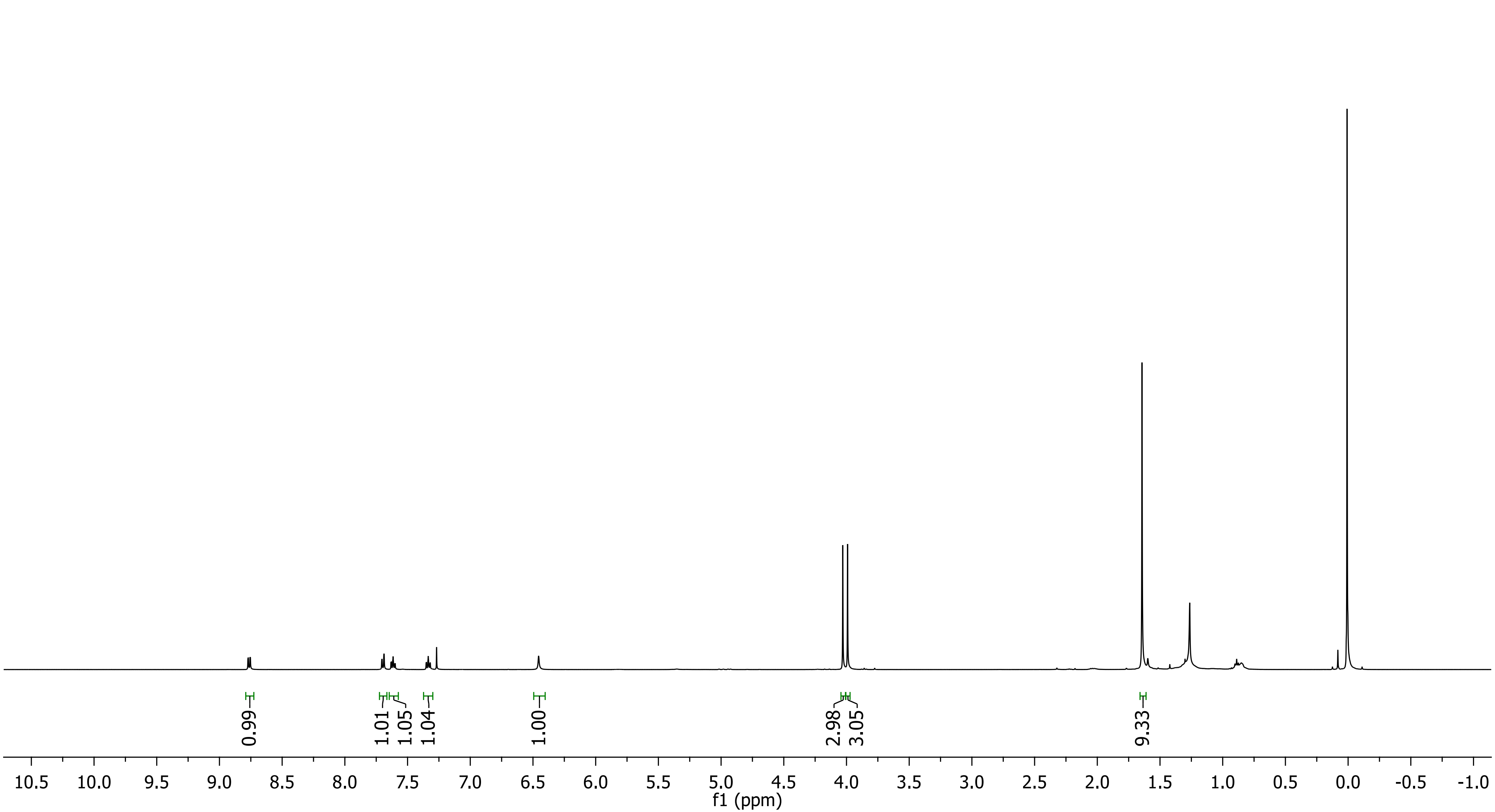

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:57:04
MCR-A120-016_02 46 (0.852) AM (Cen,3, 80.00, Ar,5000.0,335.17,0.70); Sb (2,10.00); Cm (42:55)
1: TOF MS ES+
8.00e5
279.0887
335.1665
124.0836
149.0328
173.0939
188.0165
228.0970
261.1339
295.1151
313.2929
353.2614
367.1634
385.1733
%
m/z

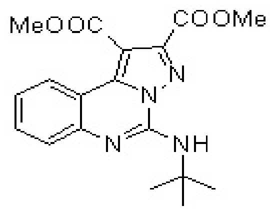

7.7982
7.7887
7.6718
7.6679
7.5154
7.5009
7.4855
7.4466
7.4321
7.2382
7.2342
7.2215
7.2175
7.1460
7.1374
1.6827
Cl
N
N
N
H
5ed
2.21
1.00
1.03
2.19
1.15
0.97
1.10
1.01
9.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Jan02-2017
MCR-A120-015
153.68
142.90
142.66
140.37
135.14
132.40
129.03
128.82
126.64
125.58
124.17
123.09
114.41
95.66
77.29
77.04
76.79
52.16
29.07
0.02
Cl
N
N
N
N
H
5ed
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

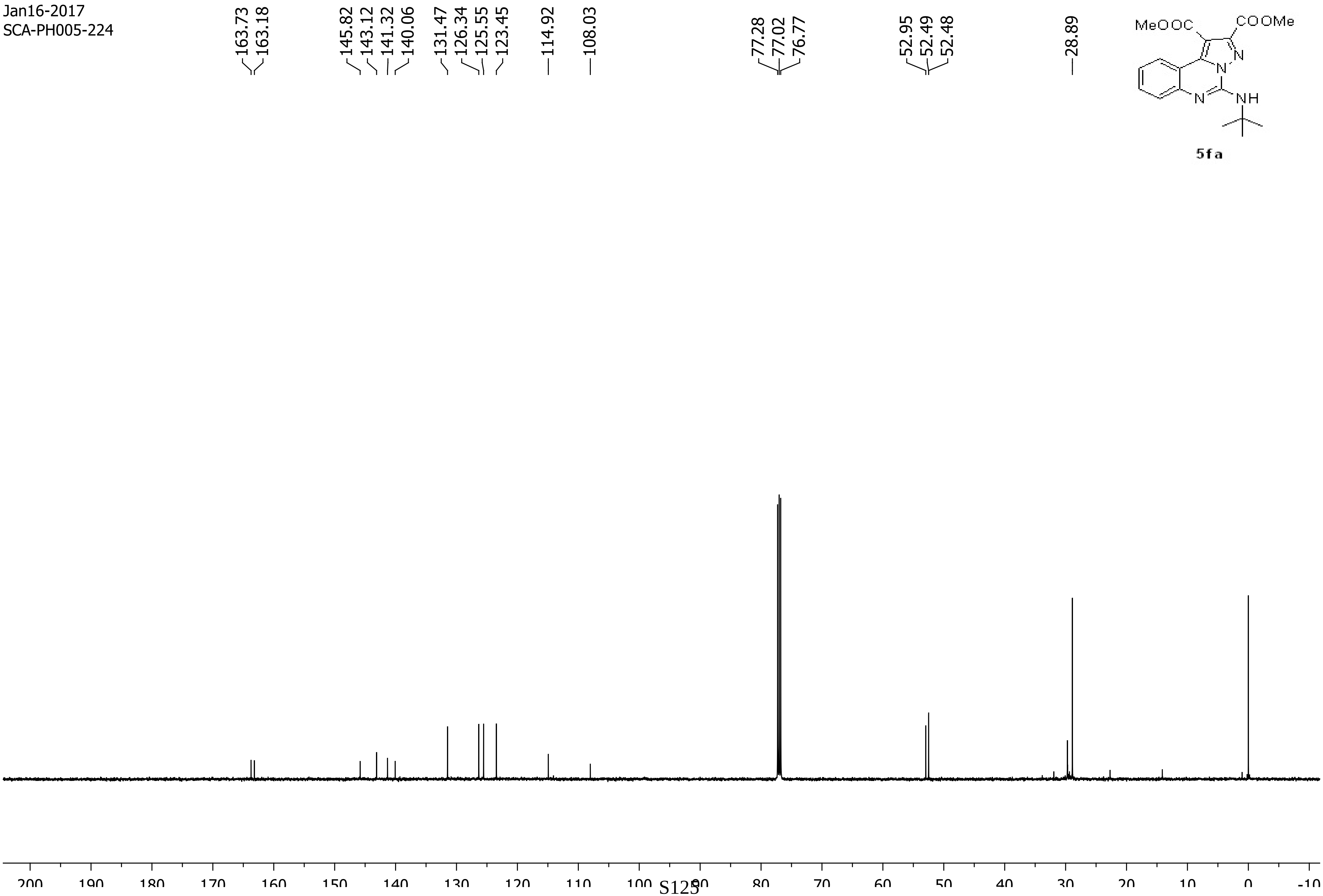

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:33:48
MCR-A120-015_02 67 (1.242) AM (Cen,3, 80.00, Ar,5000.0,351.14,0.70); Sb (2,10.00); Cm (61:76)
1: TOF MS ES+
6.90e5
295.0690
351.1369
374.2023
318.1464
333.1814
277.1239
124.0832
143.0219
173.0943
217.1292
235.1149
252.1105
402.1931
434.1787
%
m/z

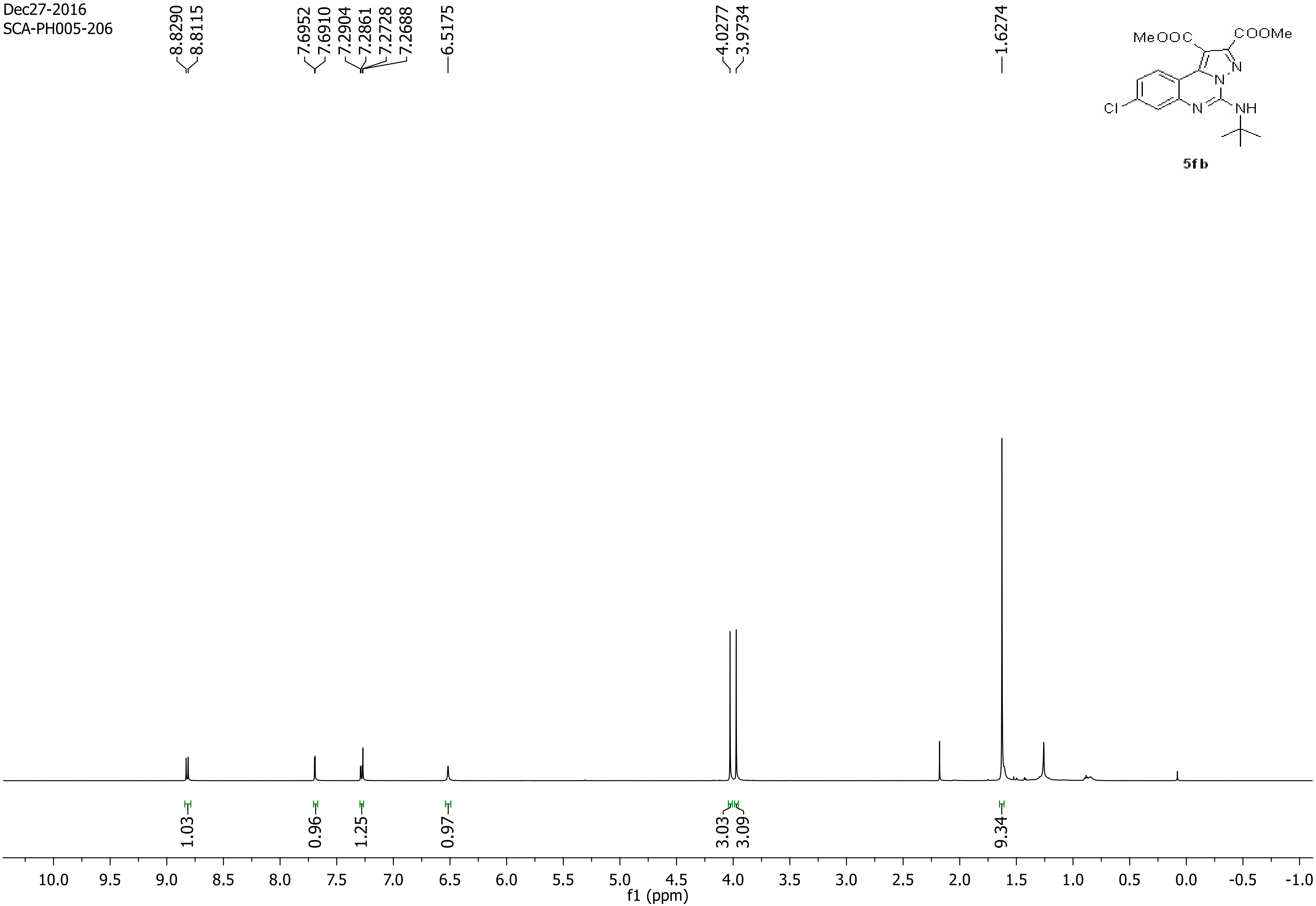
Jan16-2017
SCA-PH005-224



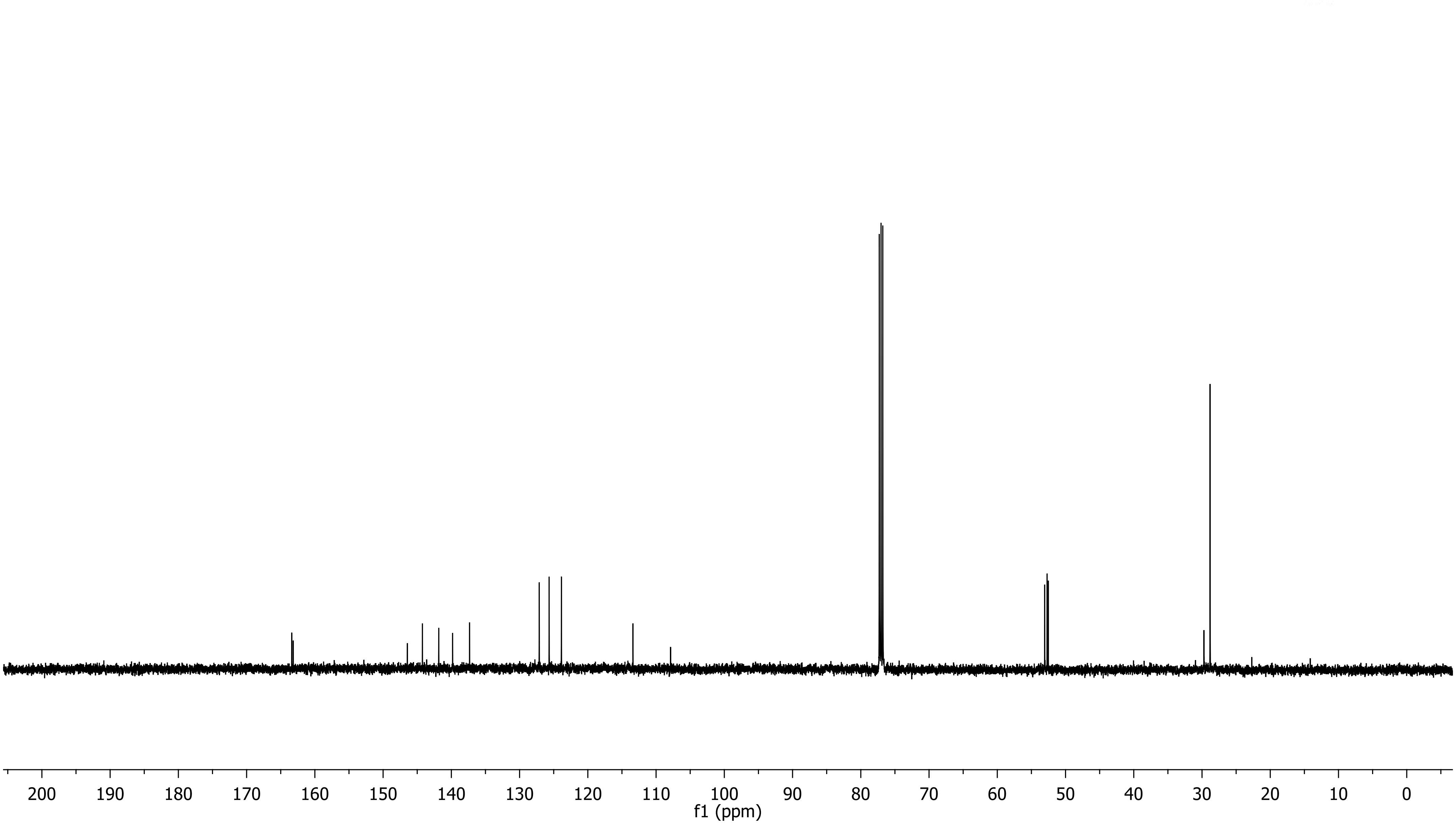


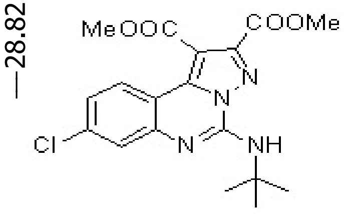
5fa


Jan16-2017
SCA-PH005-224
163.73
163.18
145.82
143.12
141.32
140.06
131.47
126.34
125.55
123.45
114.92
108.03
77.28
77.02
76.77
52.95
52.49
52.48
28.89
MeOOC
COOMe
N
N
N
NH
5fa
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

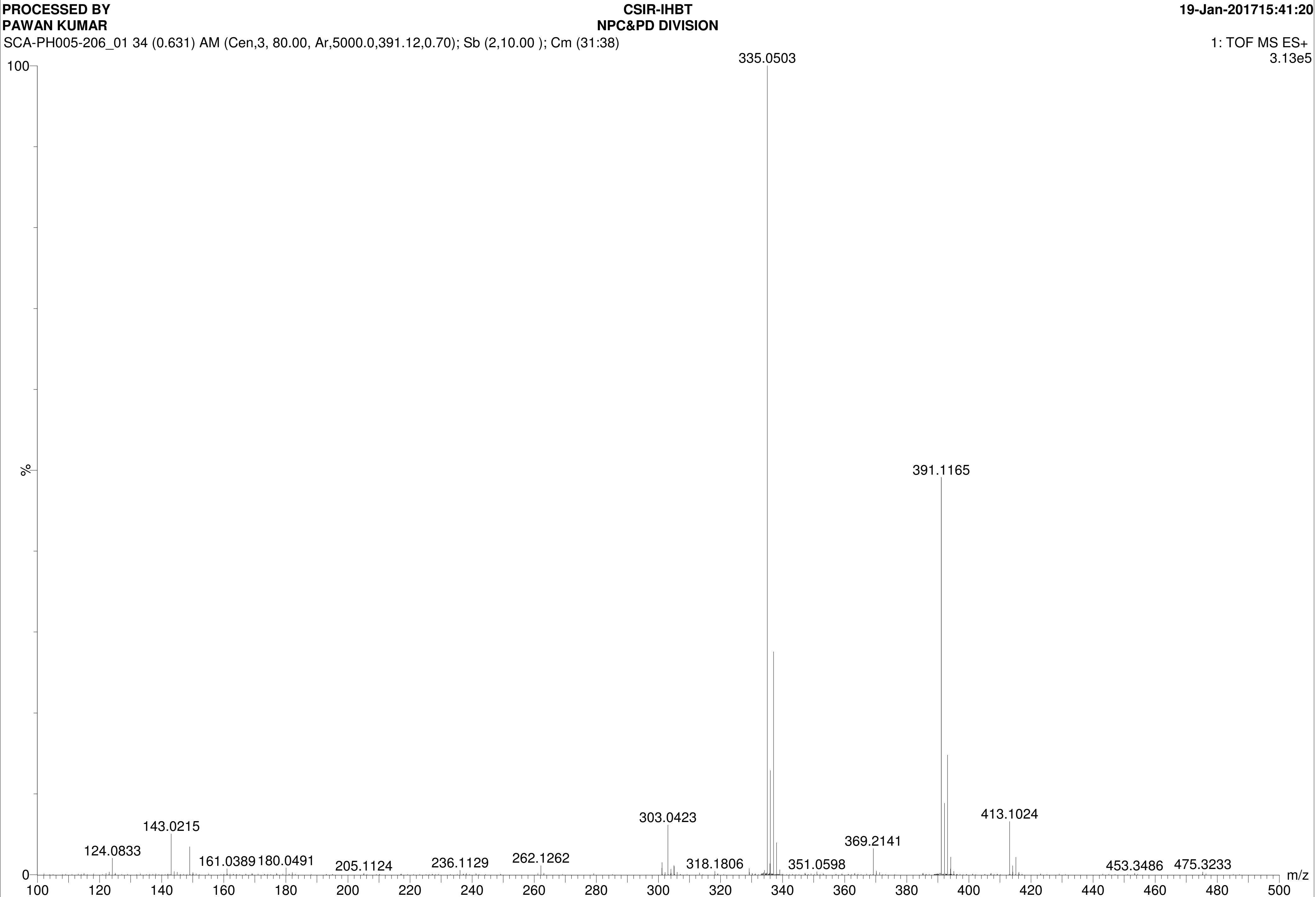

Dec27-2016
SCA-PH005-206
8.8290
8.8115
7.6952
7.6910
7.2904
7.2861
7.2728
7.2688
6.5175
4.0277
3.9734
1.6274
MeOOC
COOMe
N
N
Cl
N
NH
5fb
1.03
0.96
1.25
0.97
3.03
3.09
9.34
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

Dec27-2016
SCA-PH005-206



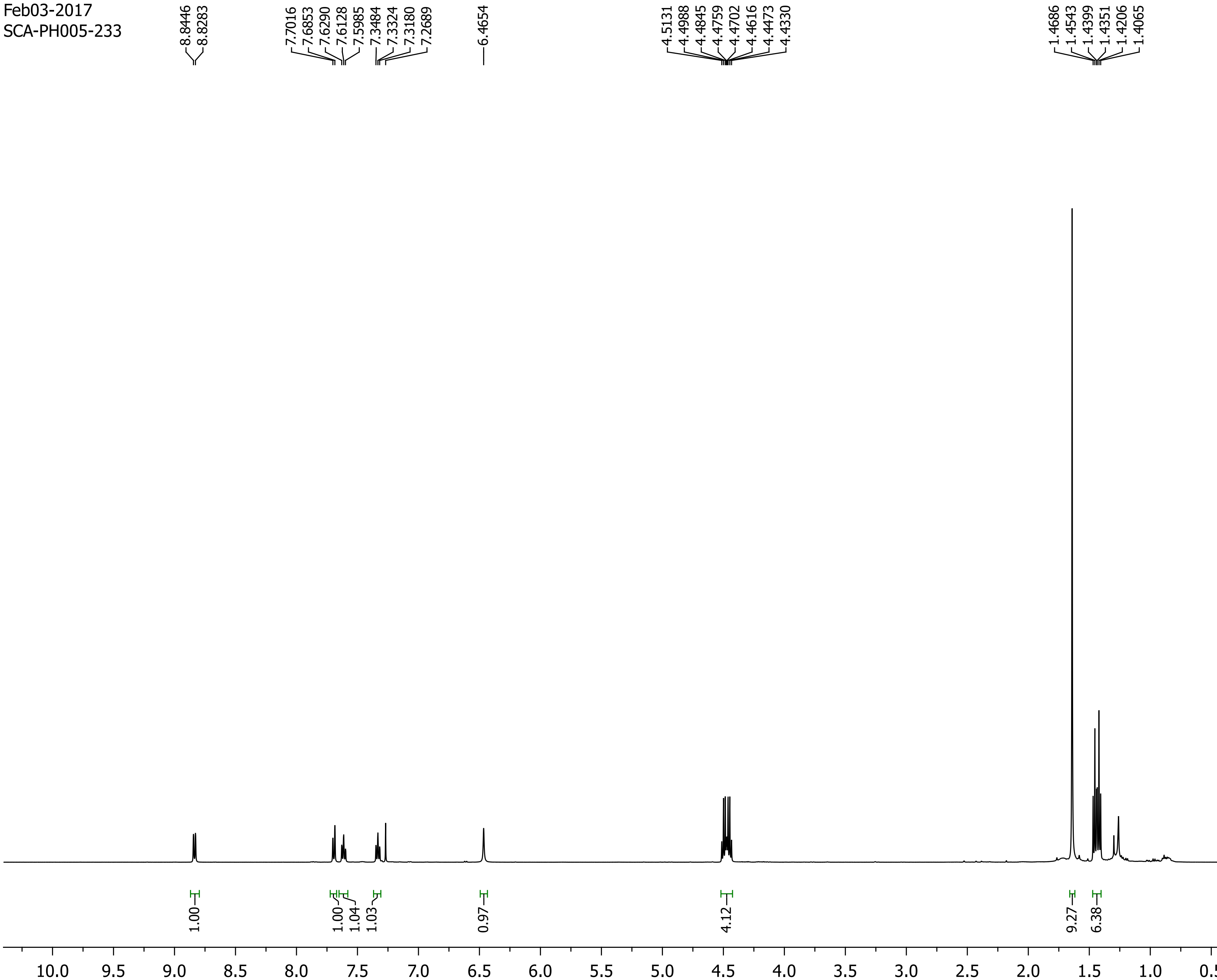


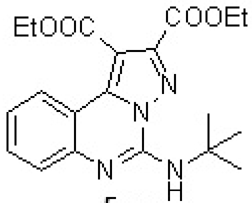
5fb



PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:41:20
SCA-PH005-206_01 34 (0.631) AM (Cen,3, 80.00, Ar,5000.0,391.12,0.70); Sb (2,10.00); Cm (31:38)
1: TOF MS ES+
3.13e5
335.0503
391.1165
413.1024
303.0423
143.0215
124.0833
161.0389
180.0491
205.1124
236.1129
262.1262
318.1806
351.0598
369.2141
453.3486
475.3233
%
m/z

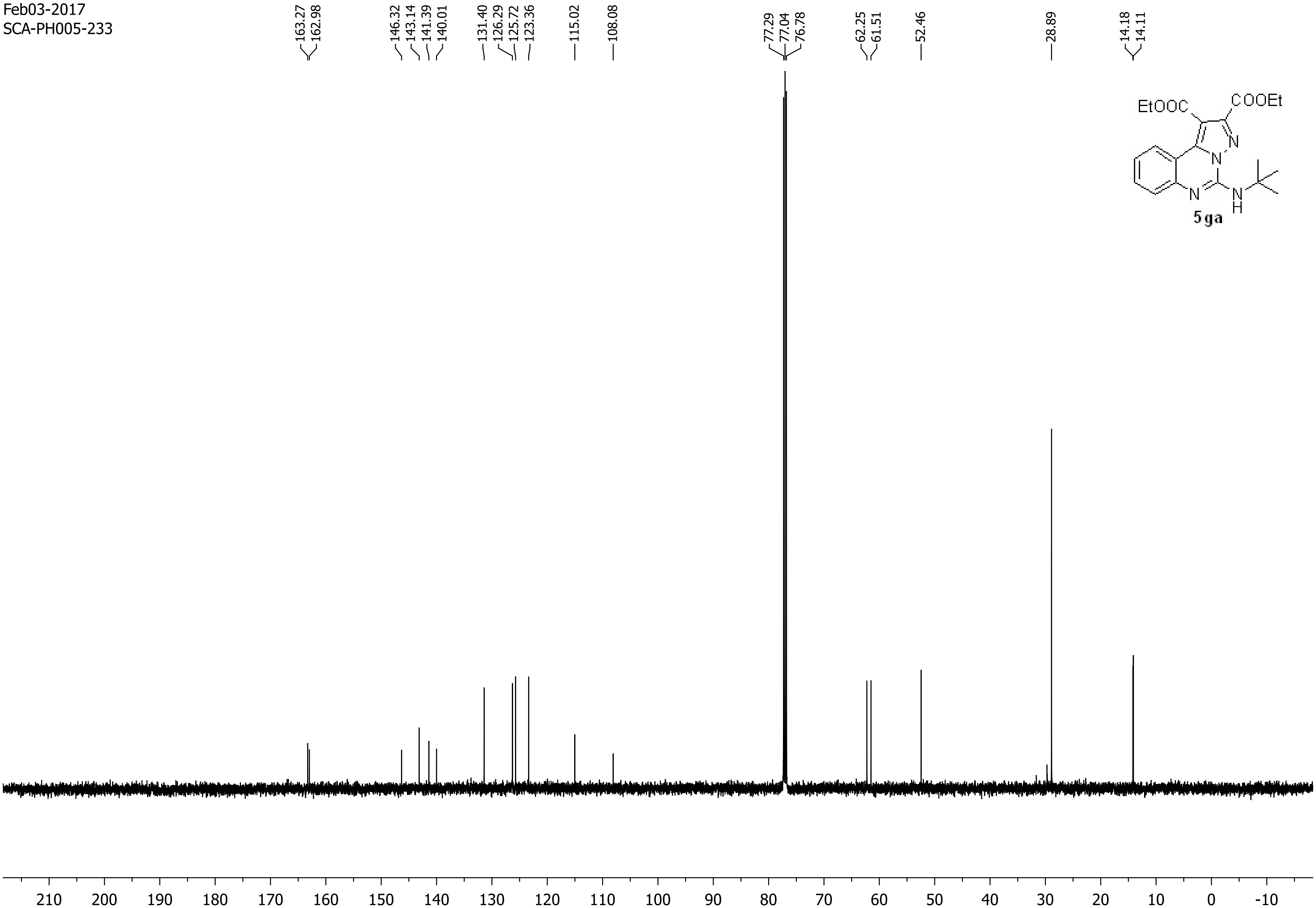
Feb03-2017
SCA-PH005-233

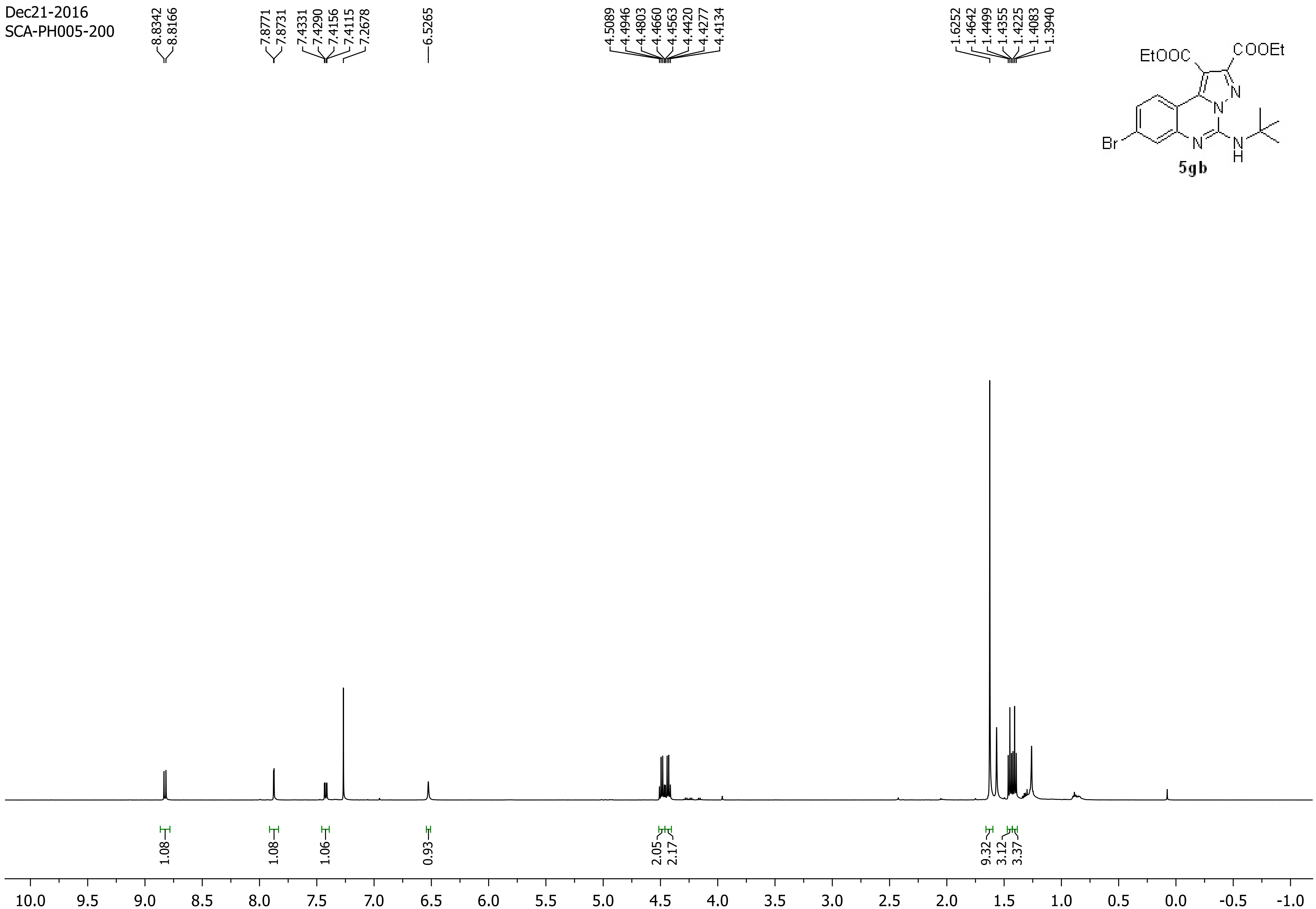


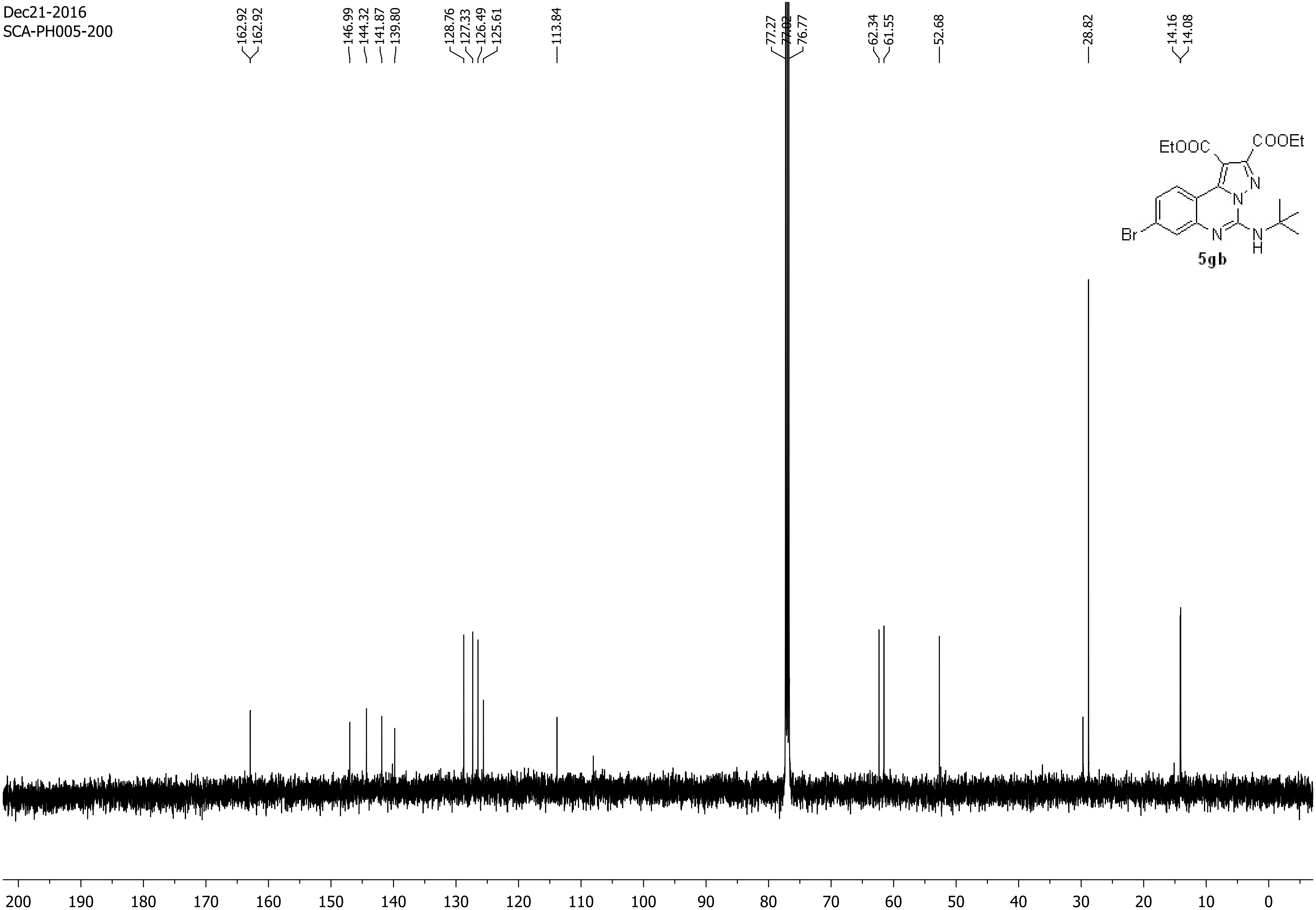


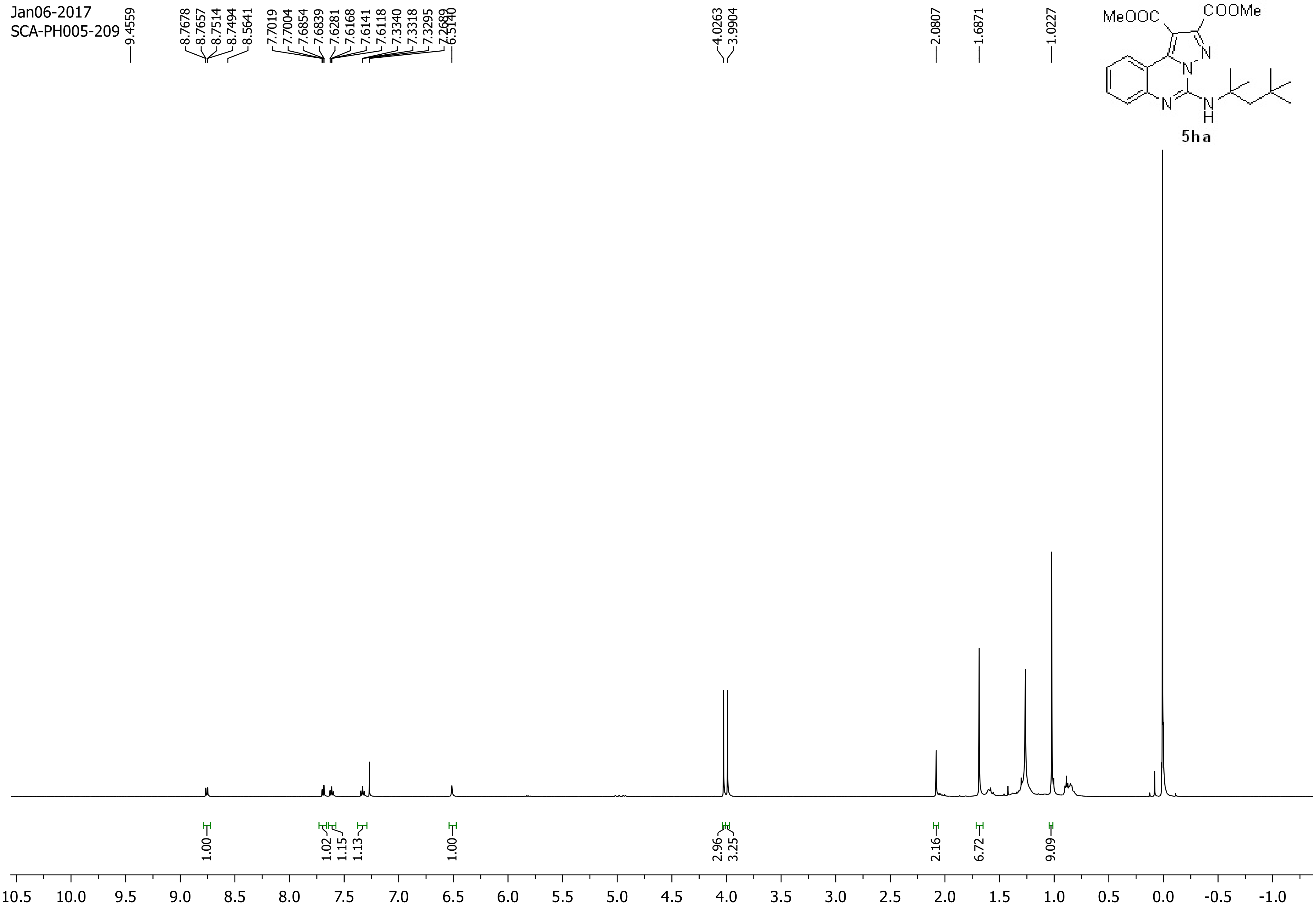
5ga

Feb03-2017
SCA-PH005-233

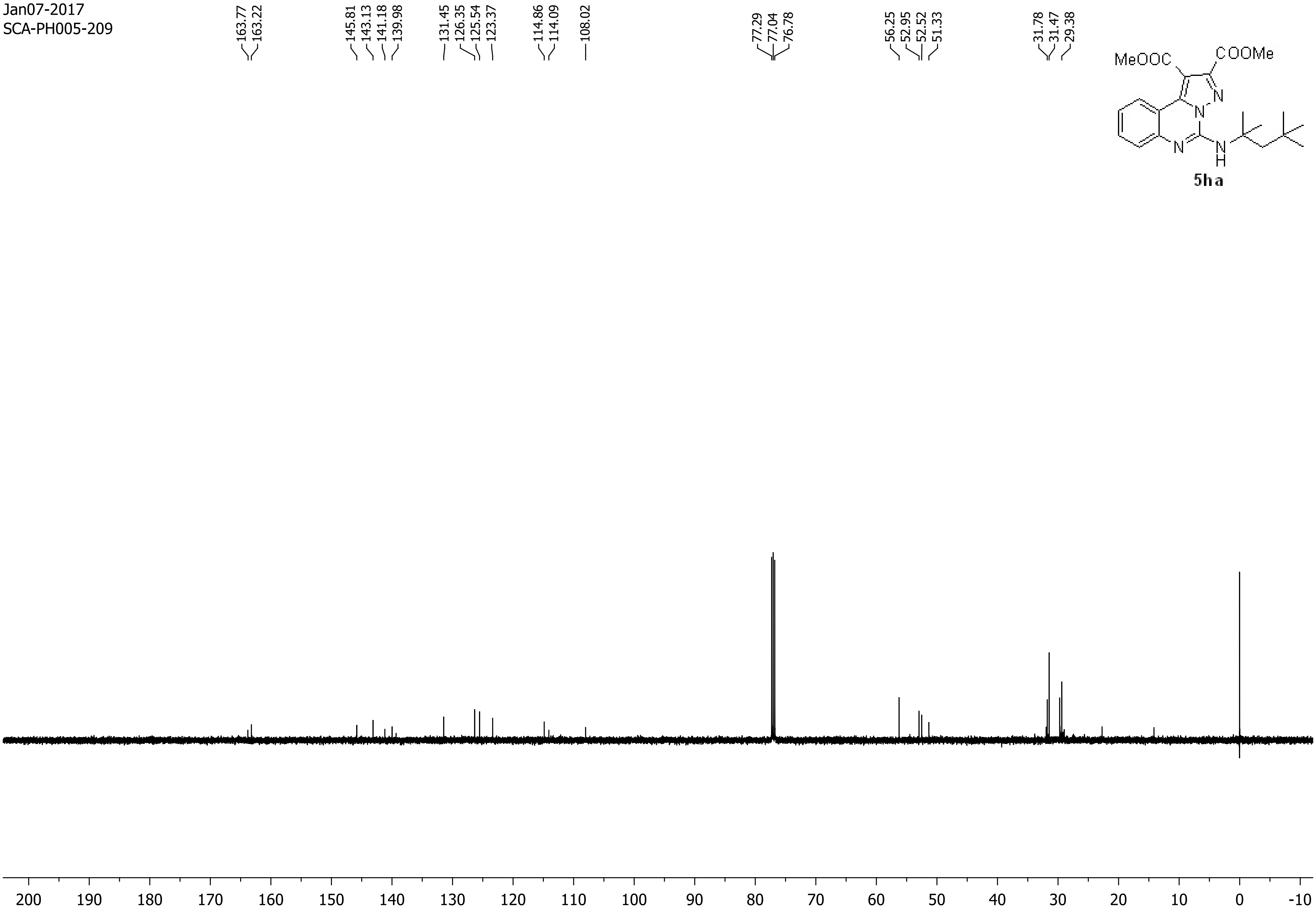


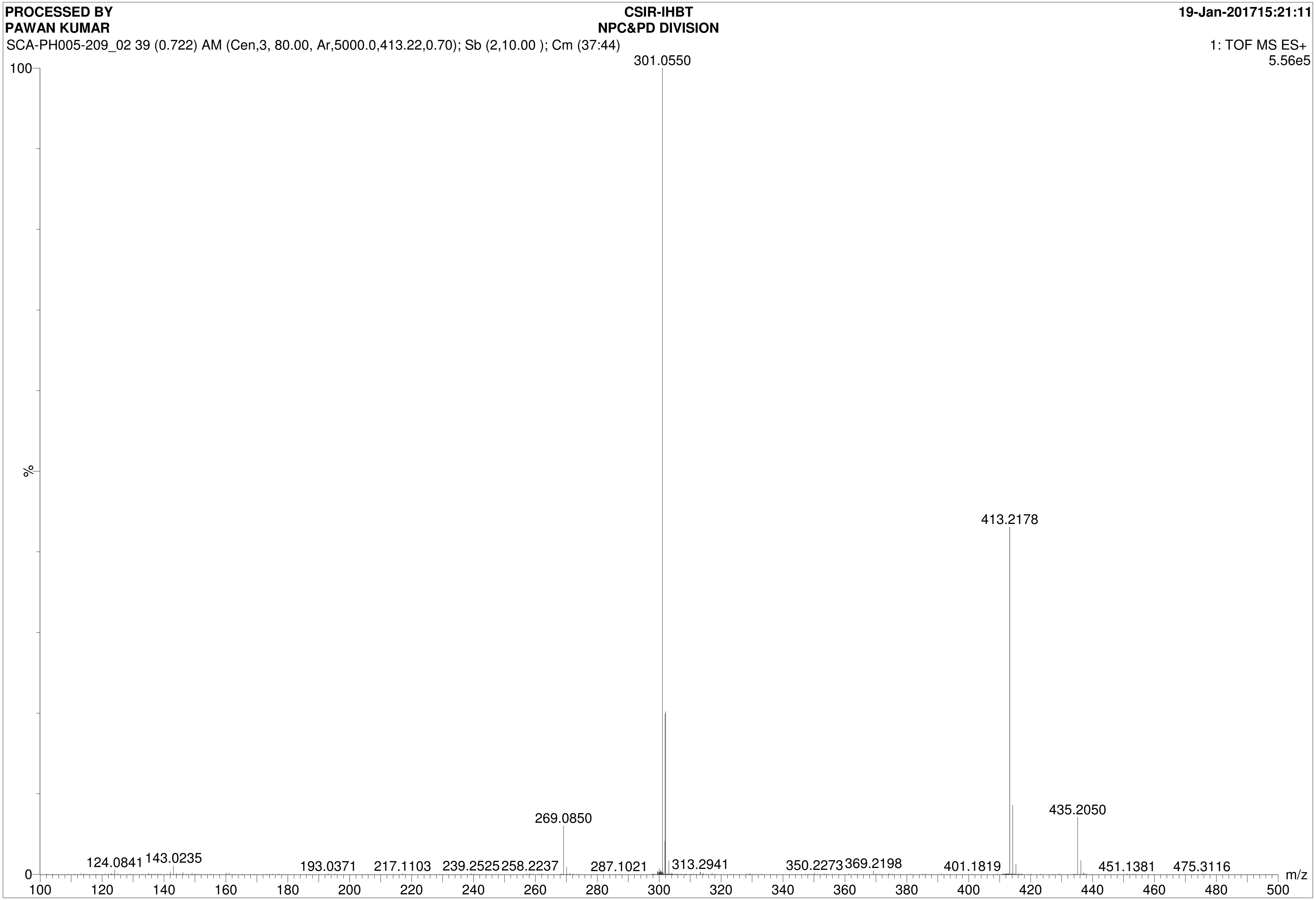

Dec21-2016
SCA-PH005-200
8.8342
8.8166
7.8771
7.8731
7.4331
7.4290
7.4156
7.4115
7.2678
6.5265
4.5089
4.4946
4.4803
4.4660
4.4563
4.4420
4.4277
4.4134
1.6252
1.4642
1.4499
1.4355
1.4225
1.4083
1.3940
EtOOC
COOEt
N
N
Br
N
N
H
5gb
1.08
1.08
1.06
0.93
2.05
2.17
9.32
3.12
3.37
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0

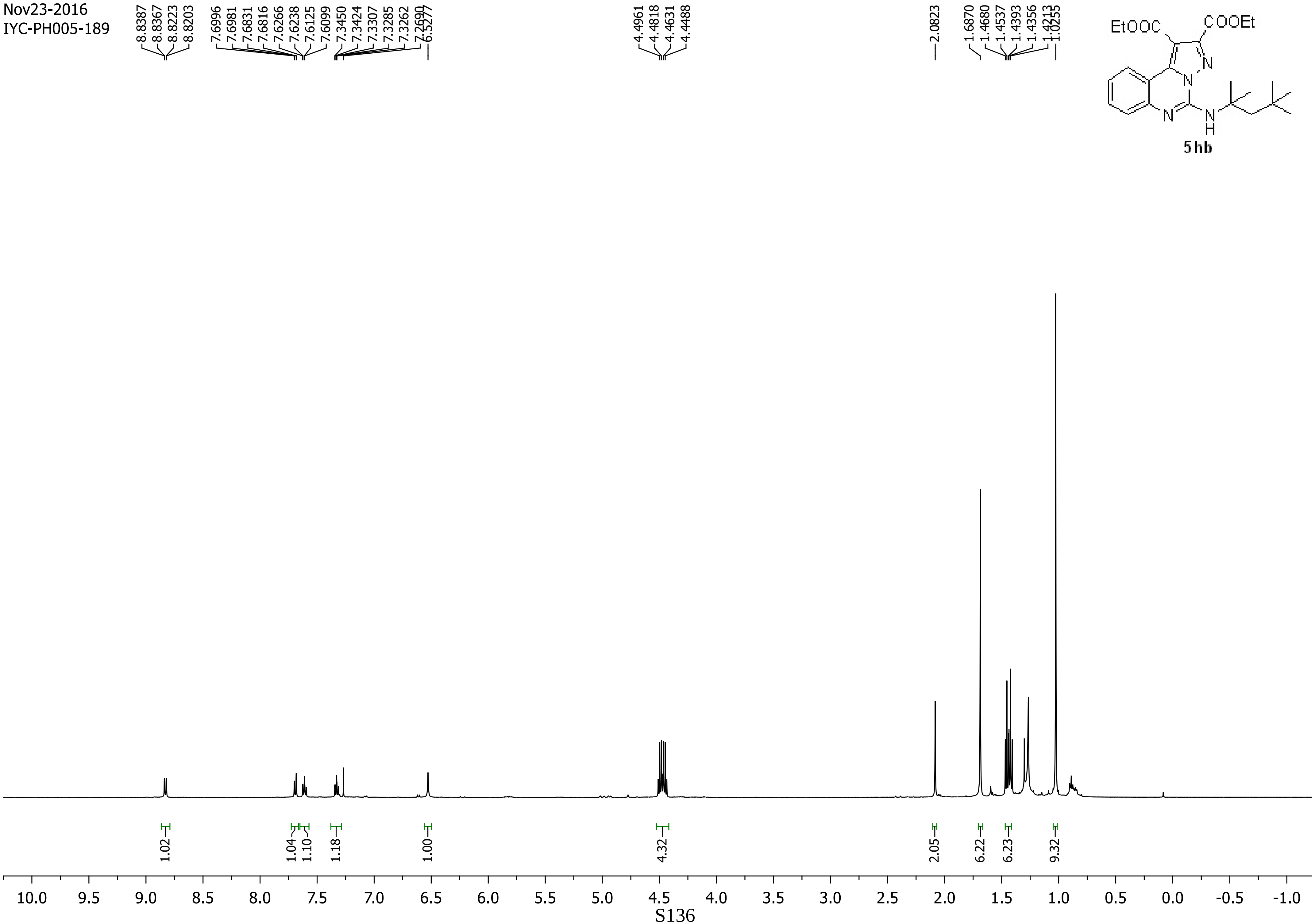

Dec21-2016
SCA-PH005-200
162.92
162.92
146.99
144.32
141.87
139.80
128.76
127.33
126.49
125.61
113.84
77.27
77.02
76.77
62.34
61.55
52.68
28.82
14.16
14.08
EtOOC
COOEt
N
N
Br
N
N
H
5gb
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



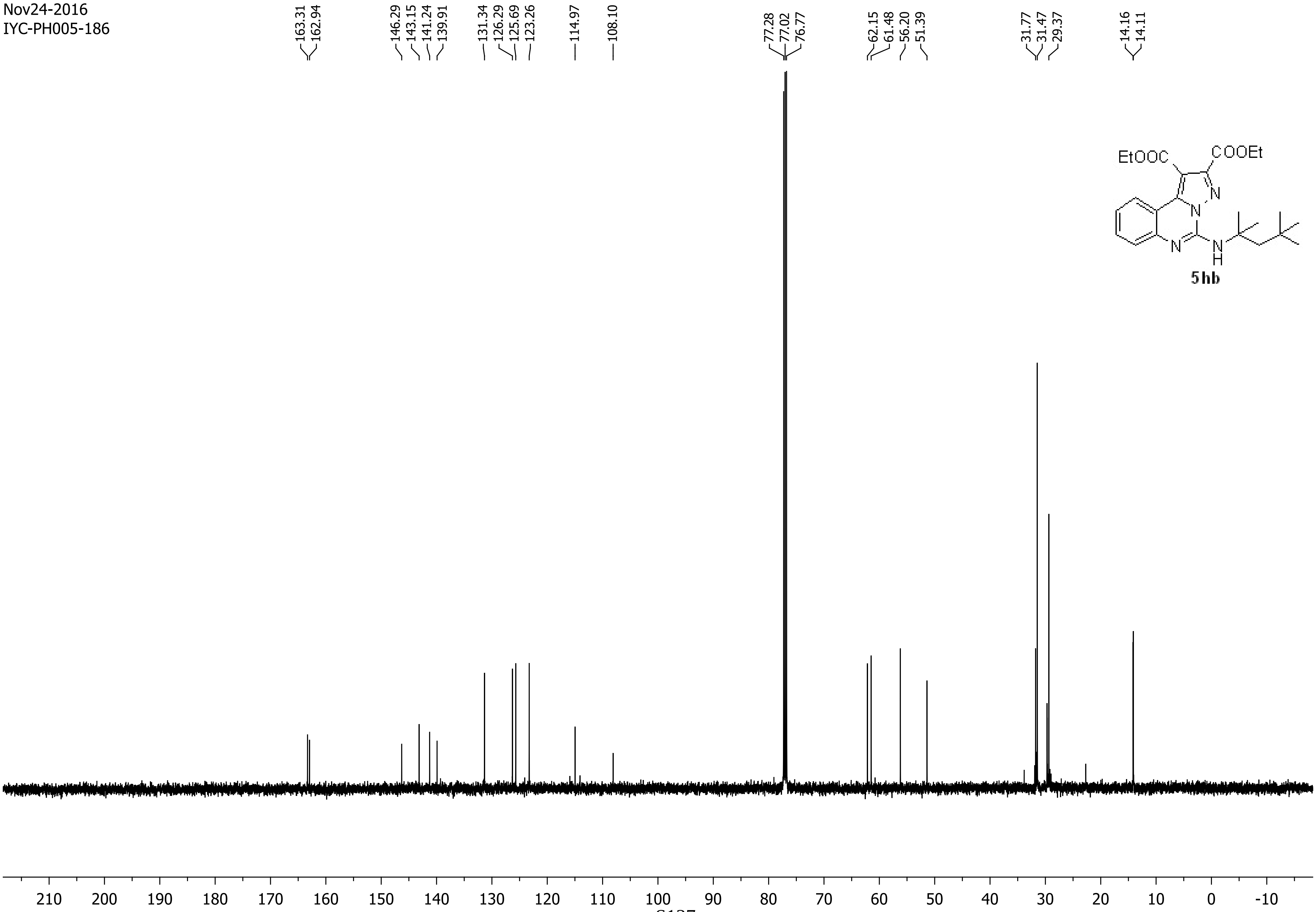
Jan06-2017
SCA-PH005-209
9.4559
8.7678
8.7657
8.7514
8.7494
8.5641
7.7019
7.7004
7.6854
7.6839
7.6281
7.6168
7.6141
7.6118
7.3340
7.3318
7.3295
7.2689
6.5140
4.0263
3.9904
2.0807
1.6871
1.0227
MeOOC
COOMe
N
N
N
N
H
5ha
1.00
1.02
1.15
1.13
1.00
2.96
3.25
2.16
6.72
9.09
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0

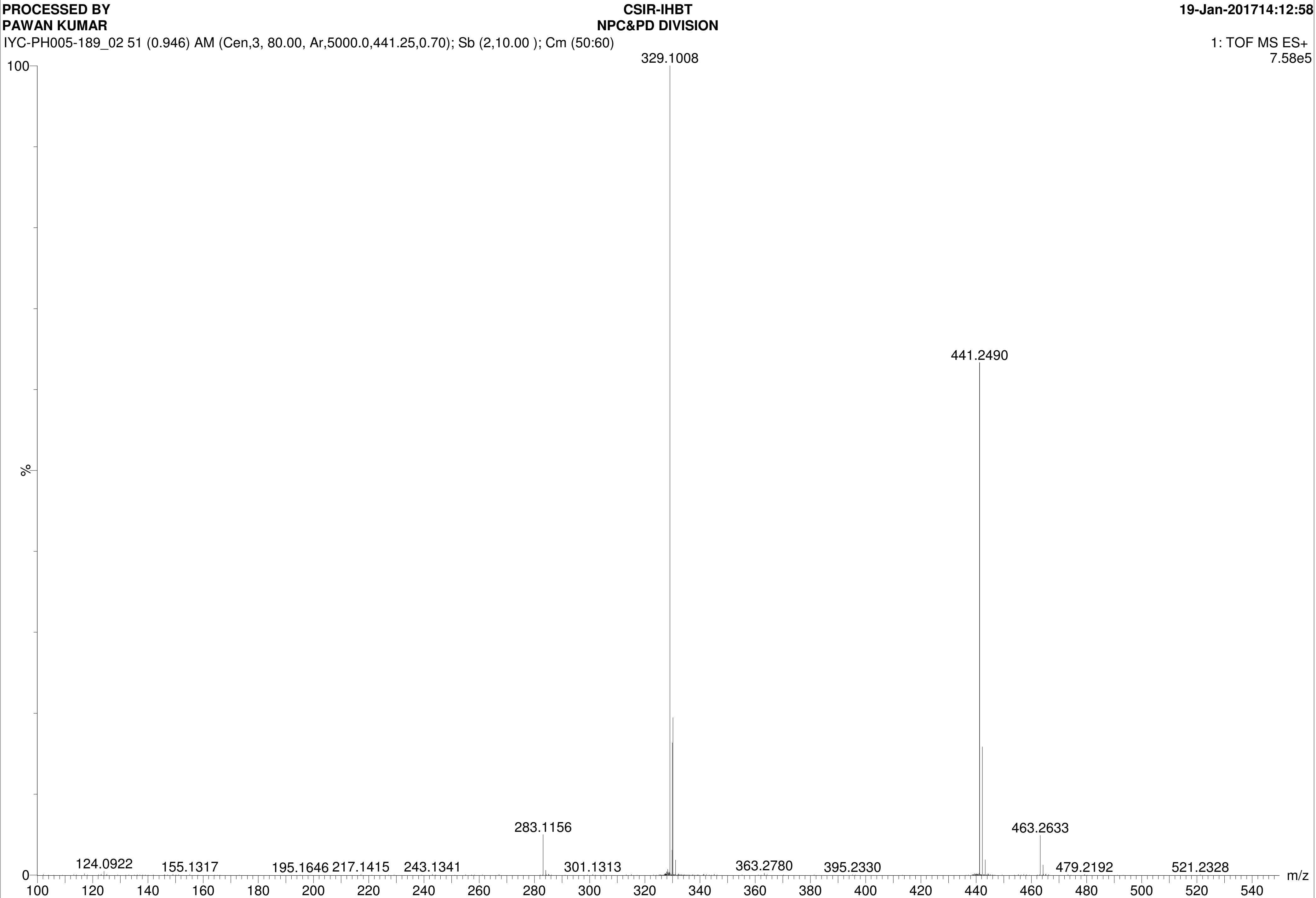

Jan07-2017
SCA-PH005-209
163.77
163.22
145.81
143.13
141.18
139.98
131.45
126.35
125.54
123.37
114.86
114.09
108.02
77.29
77.04
76.78
56.25
52.95
52.52
51.33
31.78
31.47
29.38
MeOOC
COOMe
N
N
N
N
H
5ha
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

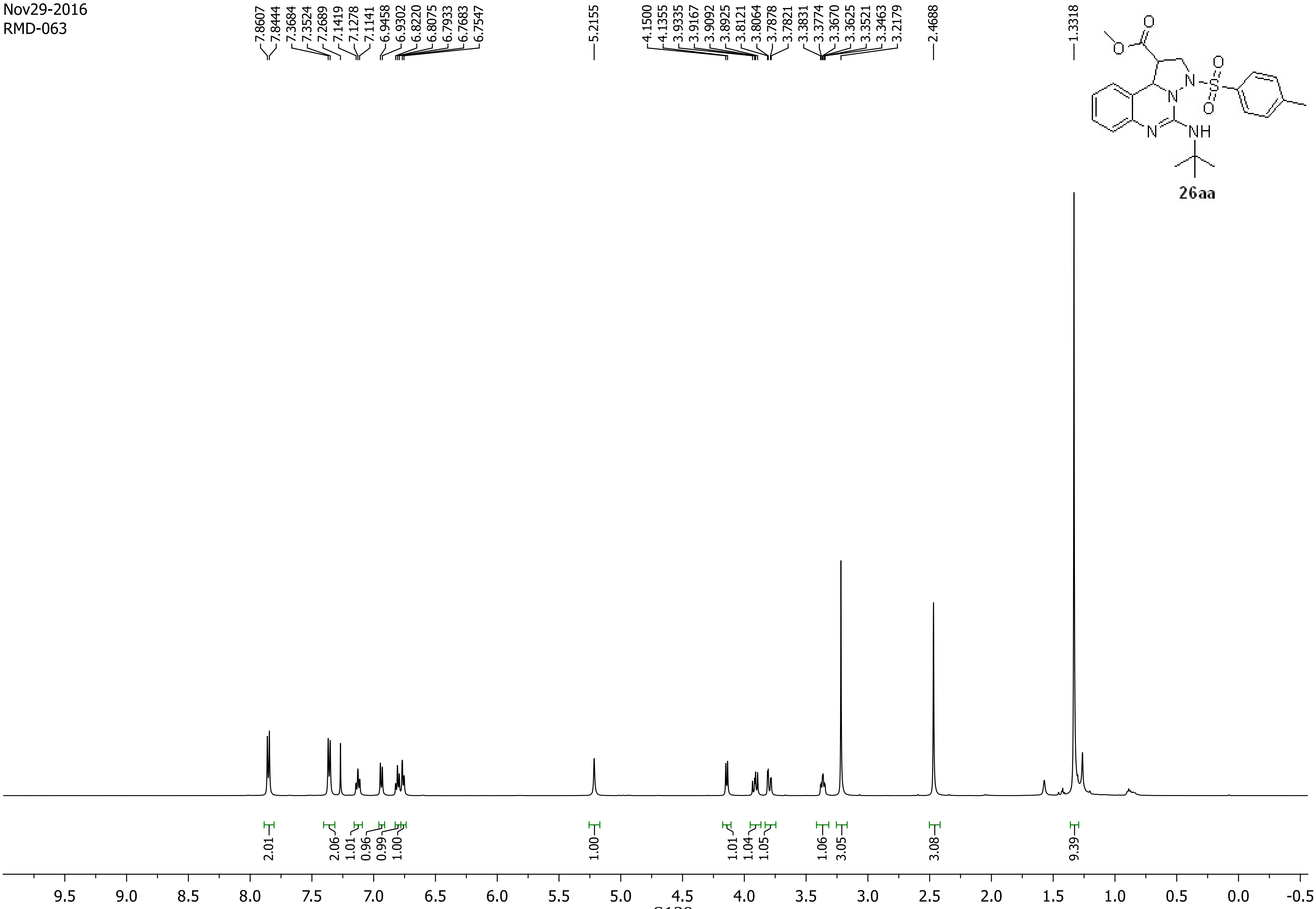

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:21:11
SCA-PH005-209_02 39 (0.722) AM (Cen,3, 80.00, Ar,5000.0,413.22,0.70); Sb (2,10.00); Cm (37:44)
1: TOF MS ES+
5.56e5
301.0550
413.2178
435.2050
269.0850
124.0841
143.0235
193.0371
217.1103
239.2525
258.2237
287.1021
313.2941
350.2273
369.2198
401.1819
451.1381
475.3116
100
%
0
m/z
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500


Nov23-2016
IYC-PH005-189
8.8387
8.8367
8.8223
8.8203
7.6996
7.6981
7.6831
7.6816
7.6266
7.6238
7.6125
7.6099
7.3450
7.3424
7.3307
7.3285
7.3262
7.2690
6.5277
4.4961
4.4818
4.4631
4.4488
2.0823
1.6870
1.4680
1.4537
1.4393
1.4356
1.4213
1.0255
EtOOC
COOEt
N
N
N
N
H
5hb
1.02
1.04
1.10
1.18
1.00
4.32
2.05
6.22
6.23
9.32
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0

Nov24-2016
IYC-PH005-186

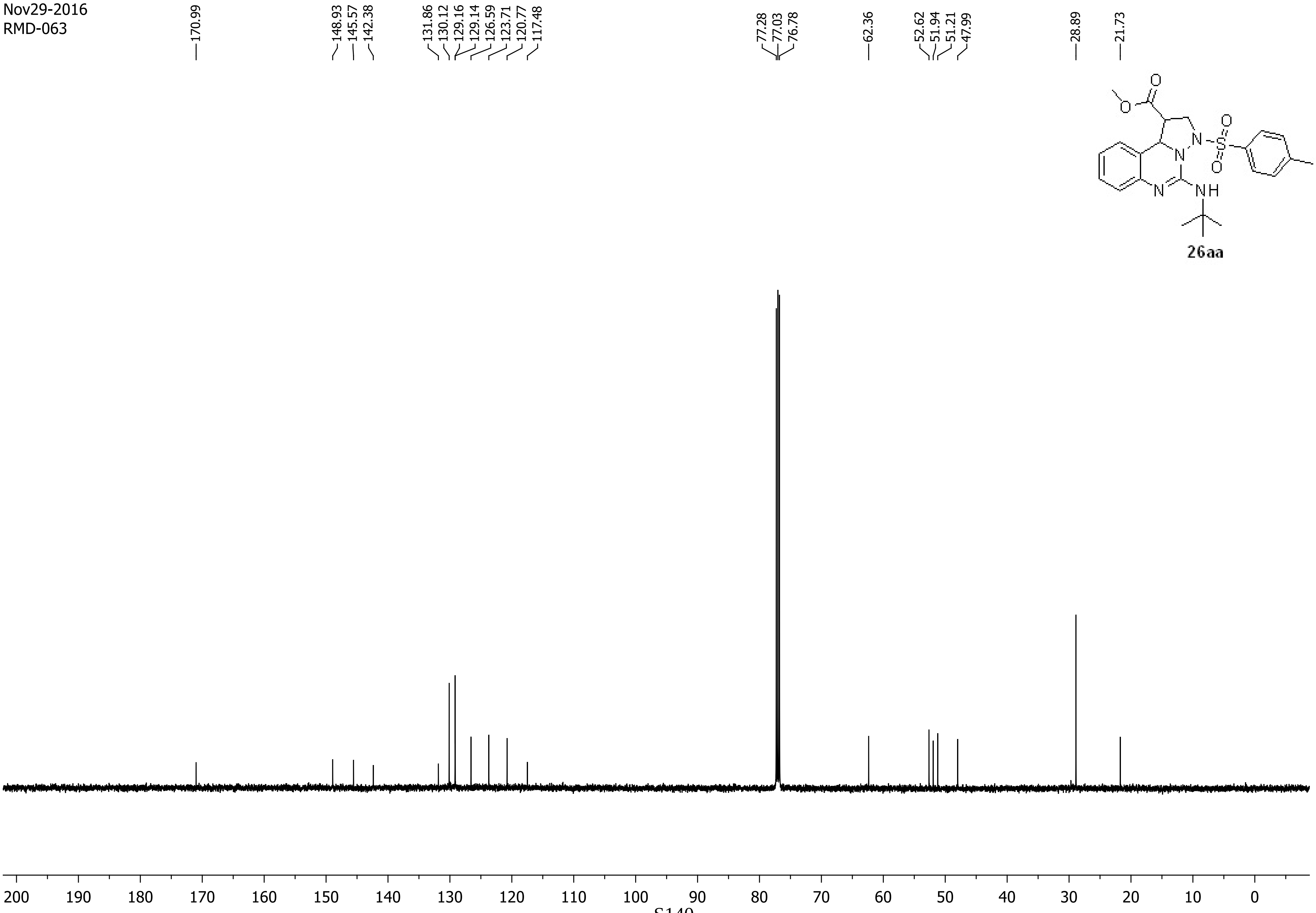


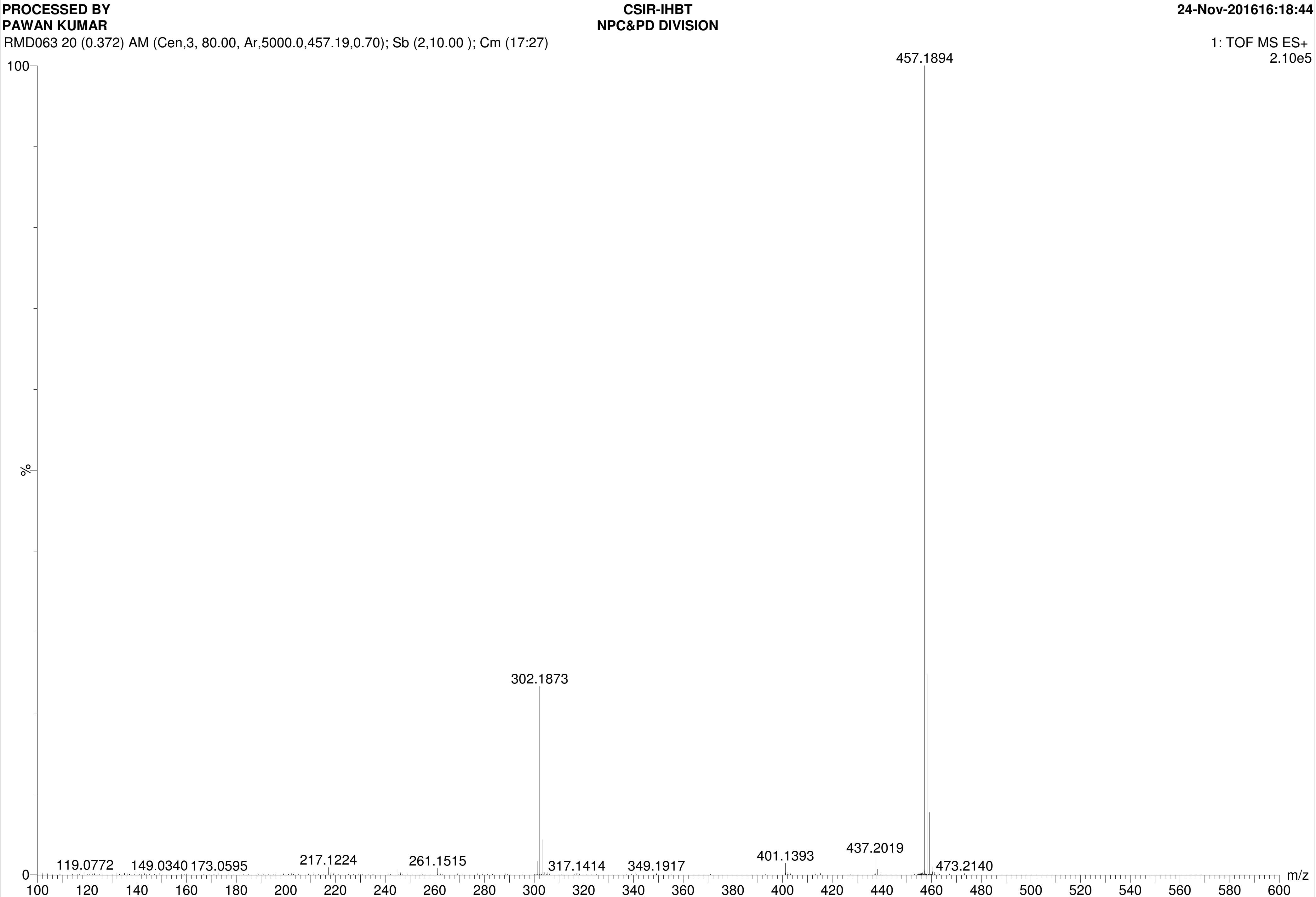

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:12:58
IYC-PH005-189_02 51 (0.946) AM (Cen,3, 80.00, Ar,5000.0,441.25,0.70); Sb (2,10.00); Cm (50:60)
1: TOF MS ES+
7.58e5
329.1008
441.2490
283.1156
463.2633
124.0922
155.1317
195.1646
217.1415
243.1341
301.1313
363.2780
395.2330
479.2192
521.2328
%
m/z



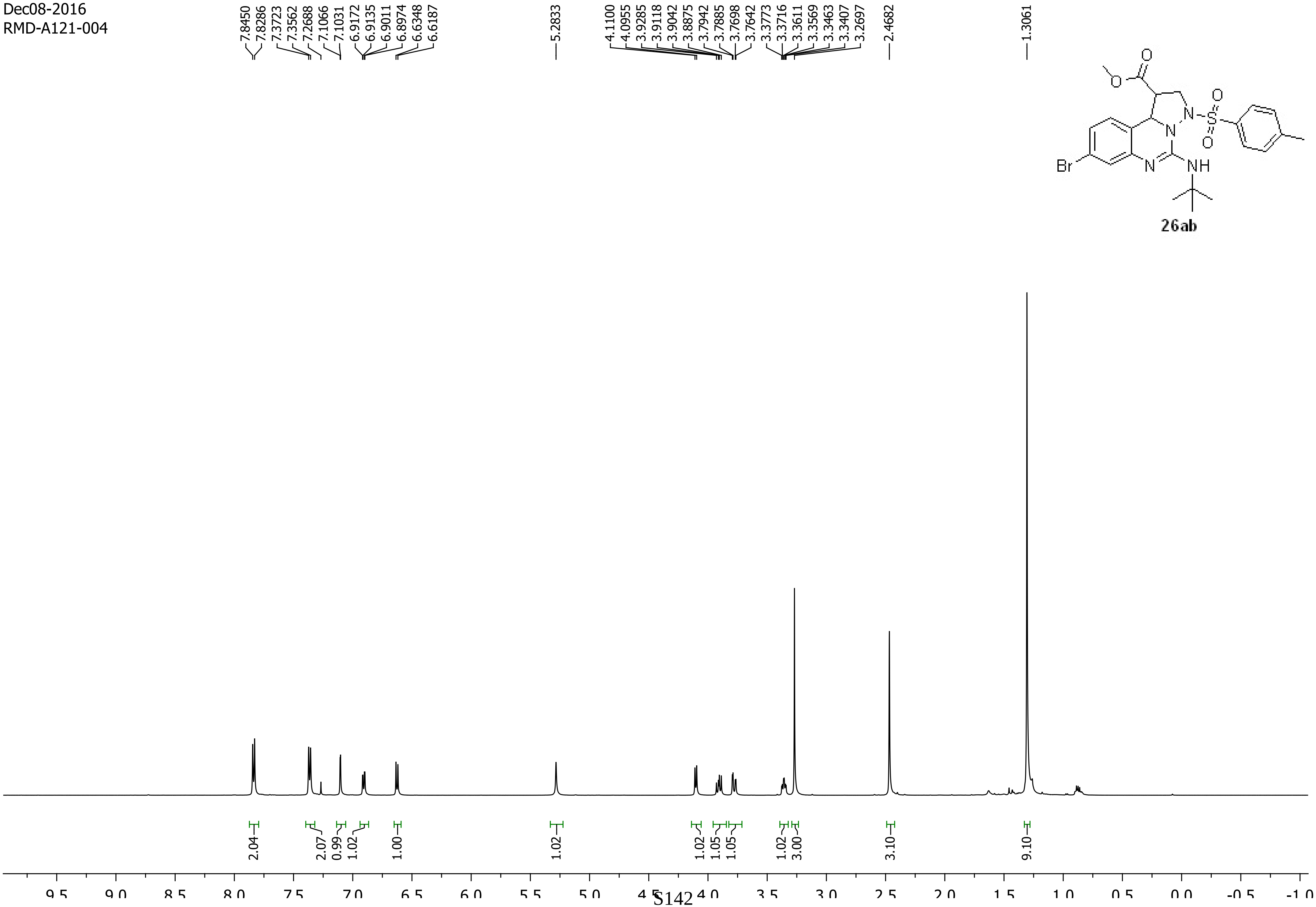
Nov29-2016
RMD-063
7.8607
7.8444
7.3684
7.3524
7.2689
7.1419
7.1278
7.1141
6.9458
6.9302
6.8220
6.8075
6.7933
6.7683
6.7547
5.2155
4.1500
4.1355
3.9335
3.9167
3.9092
3.8925
3.8121
3.8064
3.7878
3.7821
3.3831
3.3774
3.3670
3.3625
3.3521
3.3463
3.2179
2.4688
1.3318
O
O
N
N
S
O
O
N
NH
26aa
2.01
2.06
1.01
0.96
0.99
1.00
1.00
1.01
1.04
1.05
1.06
3.05
3.08
9.39
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

Nov29-2016
RMD-063

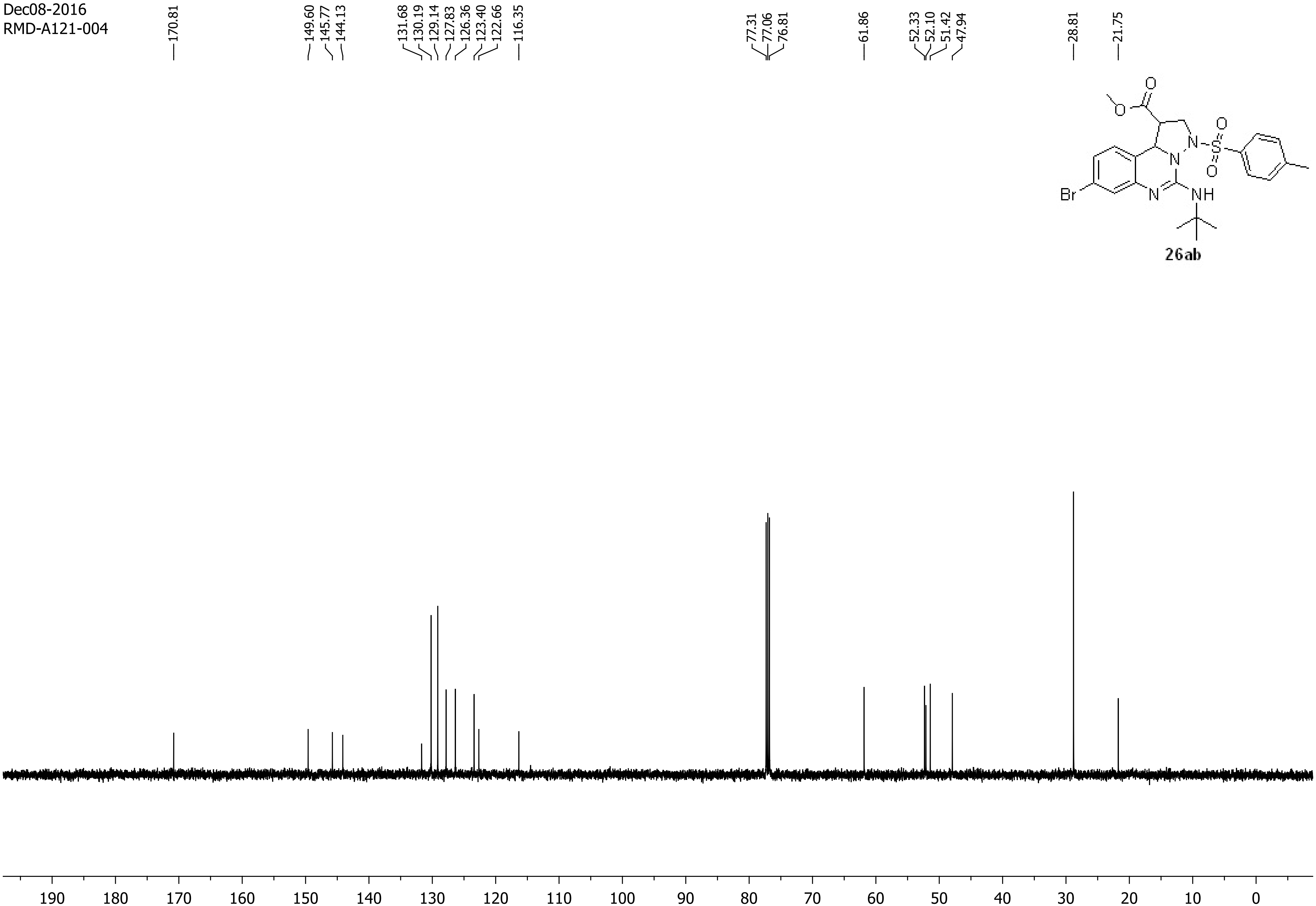


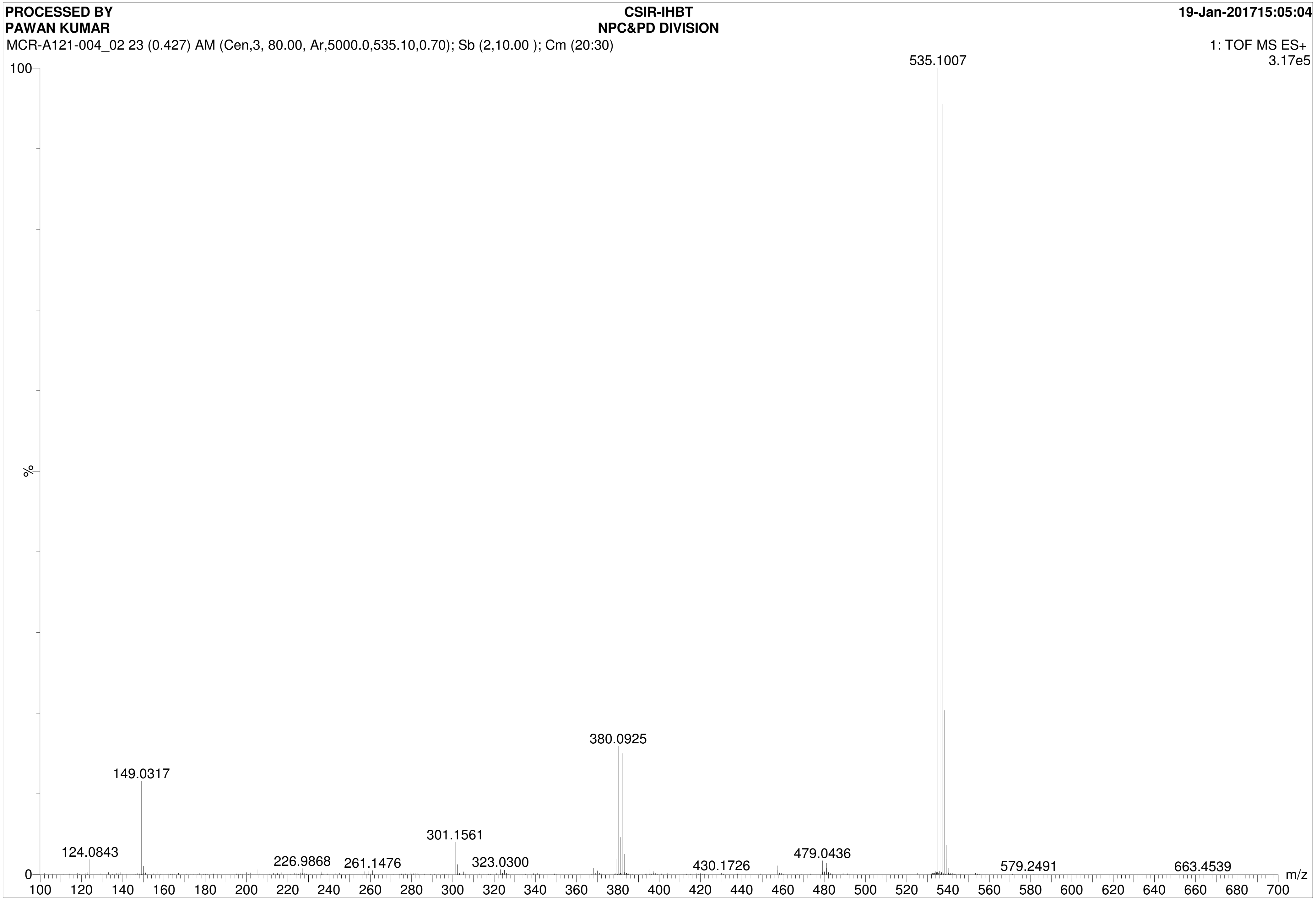

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:18:44
RMD063 20 (0.372) AM (Cen,3, 80.00, Ar,5000.0,457.19,0.70); Sb (2,10.00); Cm (17:27)
1: TOF MS ES+
2.10e5
457.1894
302.1873
119.0772
149.0340
173.0595
217.1224
261.1515
317.1414
349.1917
401.1393
437.2019
473.2140
%
m/z
100
0
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600

Dec08-2016
RMD-A121-004

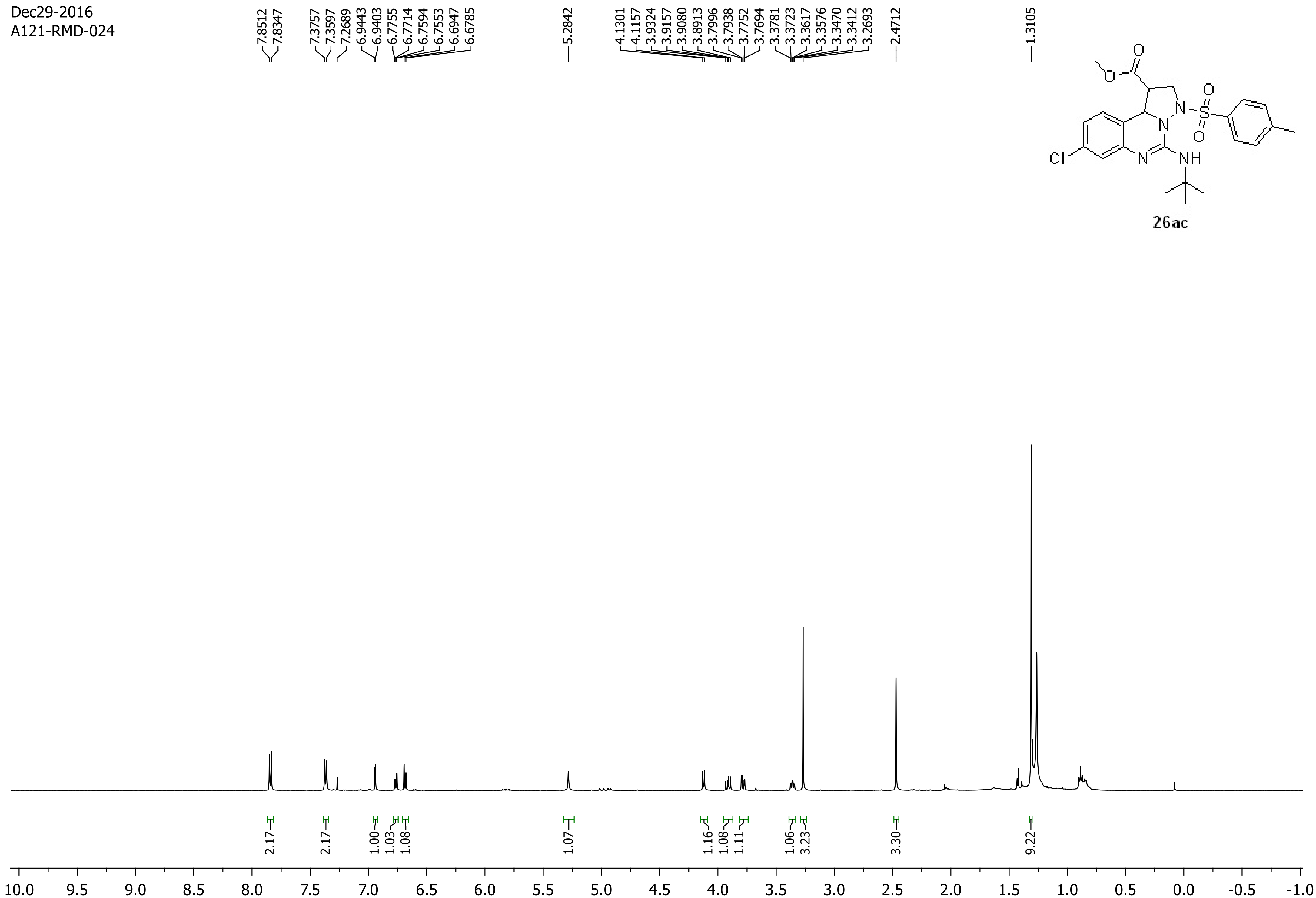


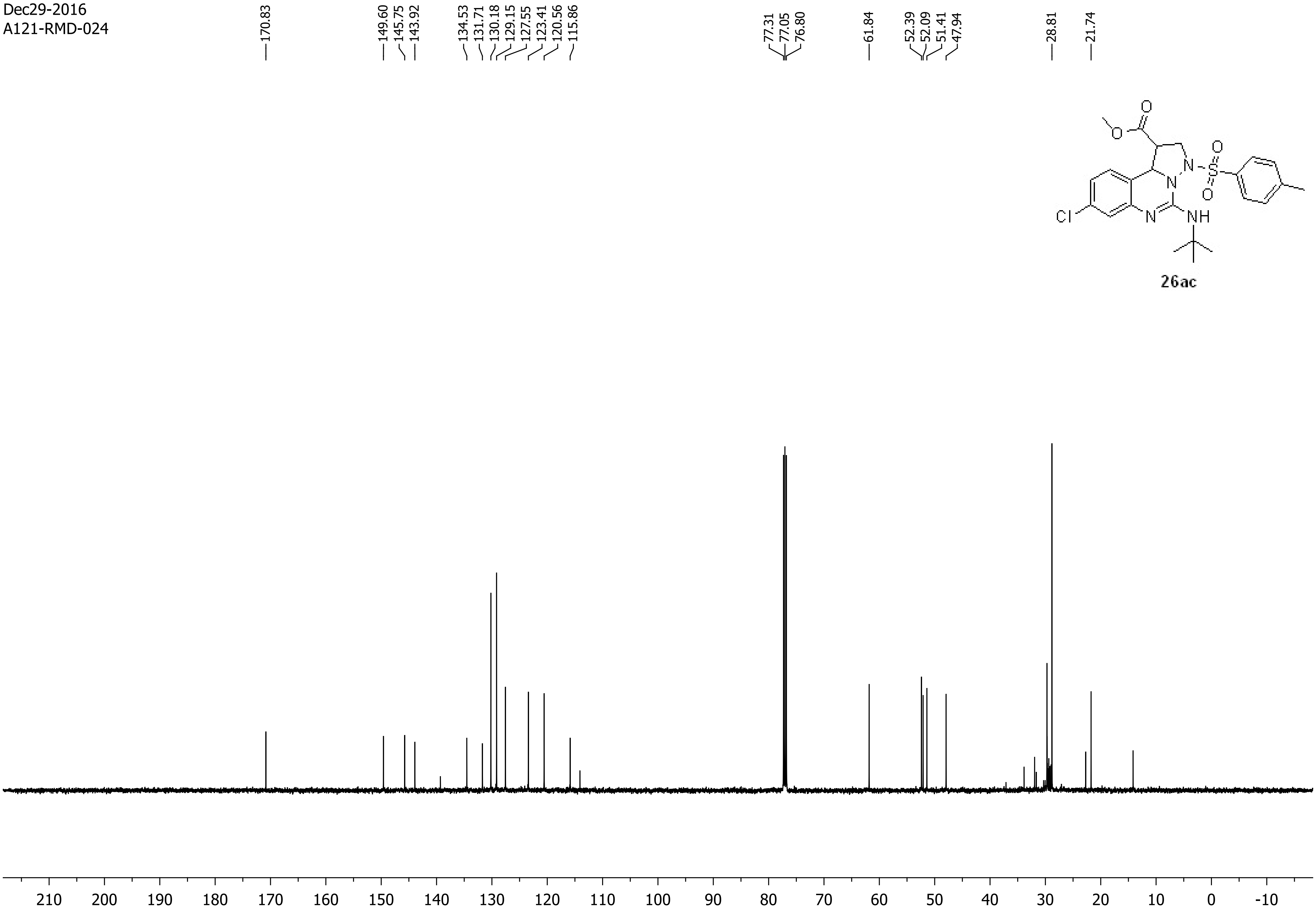
26ab


Dec08-2016
RMD-A121-004
170.81
149.60
145.77
144.13
131.68
130.19
129.14
127.83
126.36
123.40
122.66
116.35
77.31
77.06
76.81
61.86
52.33
52.10
51.42
47.94
28.81
21.75
26ab
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0



PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:05:04
MCR-A121-004_02 23 (0.427) AM (Cen,3, 80.00, Ar,5000.0,535.10,0.70); Sb (2,10.00); Cm (20:30)
1: TOF MS ES+
3.17e5
535.1007
380.0925
149.0317
301.1561
124.0843
226.9868
261.1476
323.0300
430.1726
479.0436
579.2491
663.4539
%
100
0
m/z
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700


Dec29-2016
A121-RMD-024
7.8512
7.8347
7.3757
7.3597
7.2689
6.9443
6.9403
6.7755
6.7714
6.7594
6.7553
6.6947
6.6785
5.2842
4.1301
4.1157
3.9324
3.9157
3.9080
3.8913
3.7996
3.7938
3.7752
3.7694
3.3781
3.3723
3.3617
3.3576
3.3470
3.3412
3.2693
2.4712
1.3105
O
O
N
S
O
O
N
Cl
N
NH
26ac
2.17
2.17
1.00
1.03
1.08
1.07
1.16
1.08
1.11
1.06
3.23
3.30
9.22
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0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A121-RMD-024
170.83
149.60
145.75
143.92
134.53
131.71
130.18
129.15
127.55
123.41
120.56
115.86
77.31
77.05
76.80
61.84
52.39
52.09
51.41
47.94
28.81
21.74
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
O
O
N
S
O
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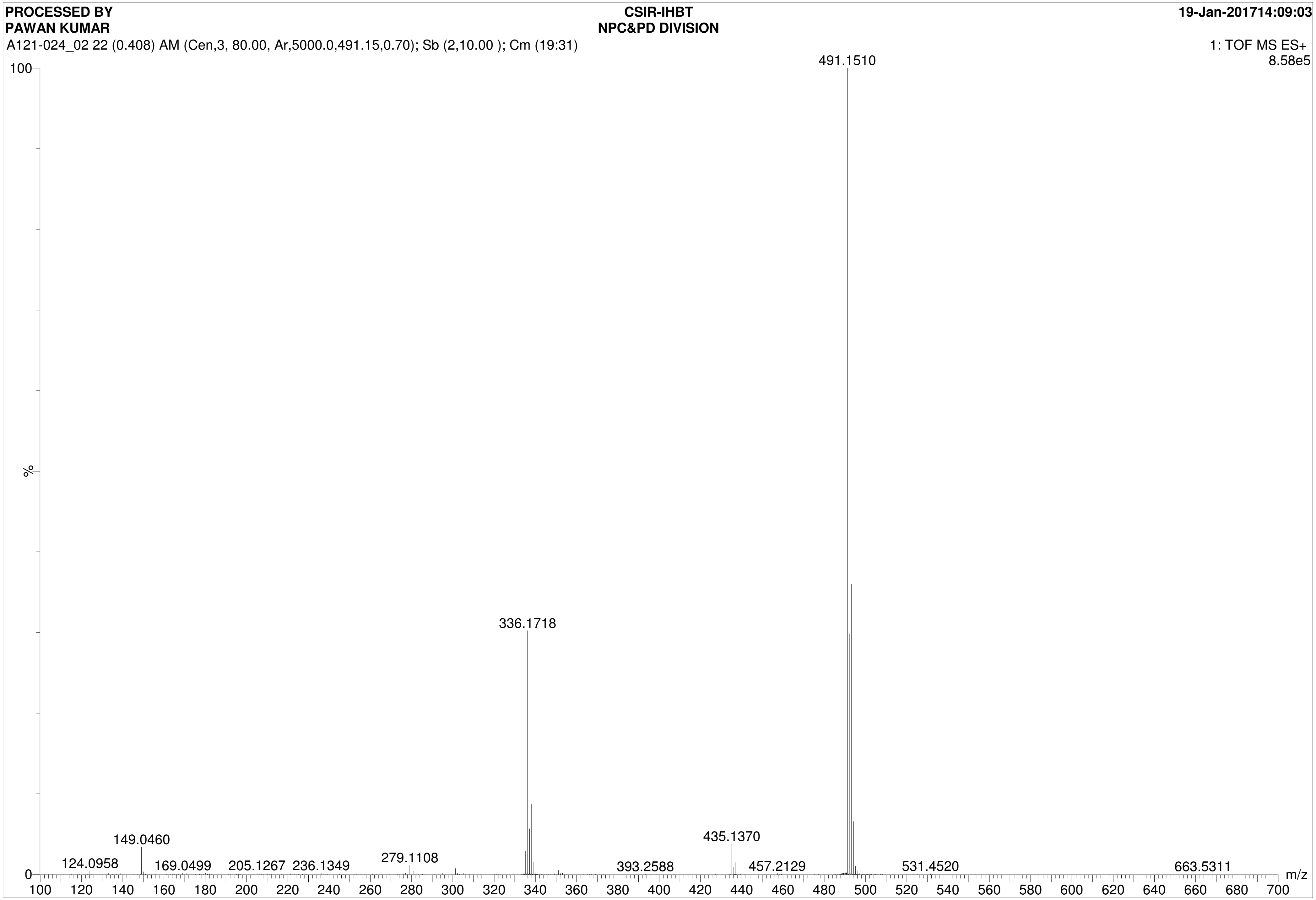
N
Cl
N
NH

26ac


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:09:03
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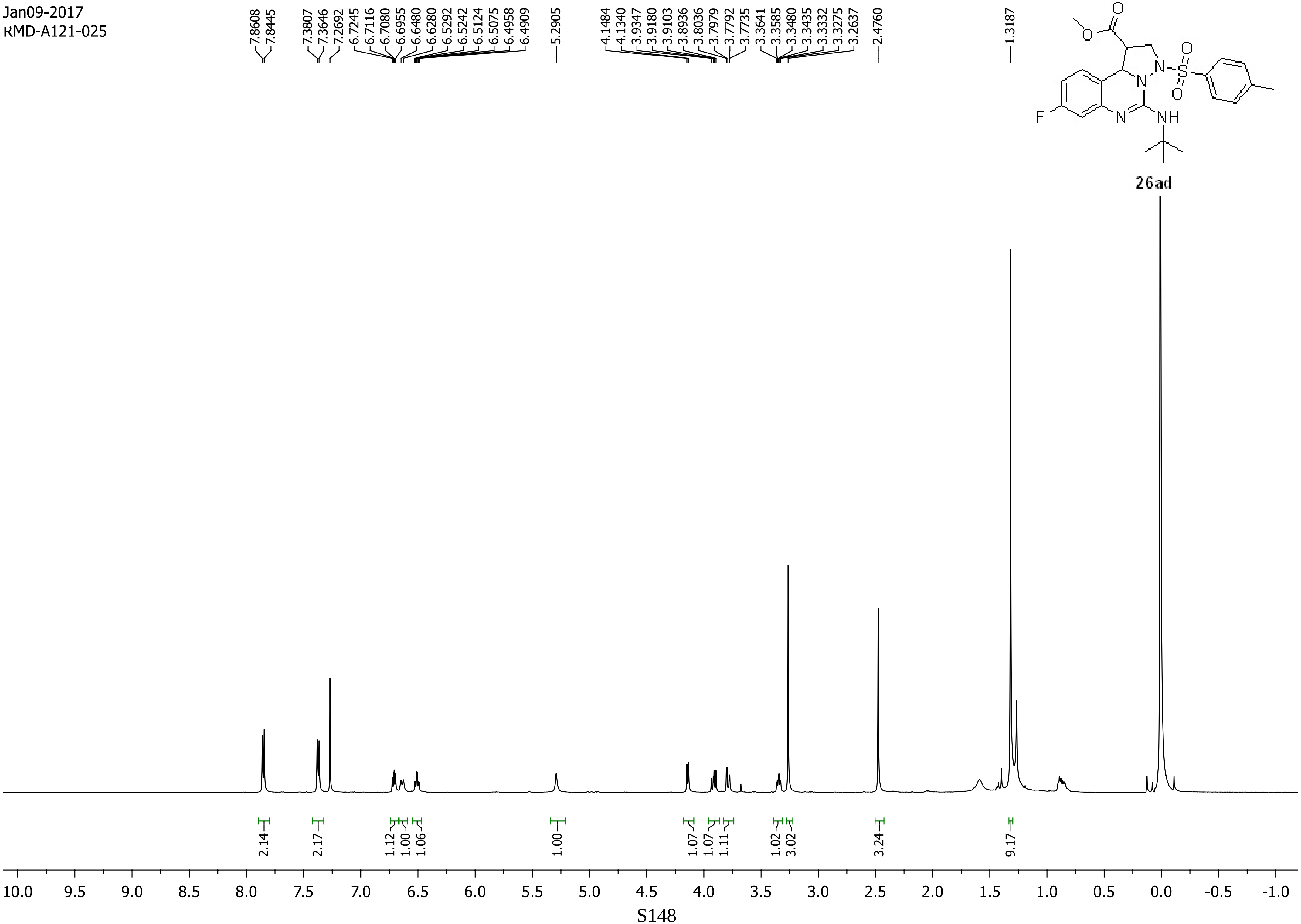
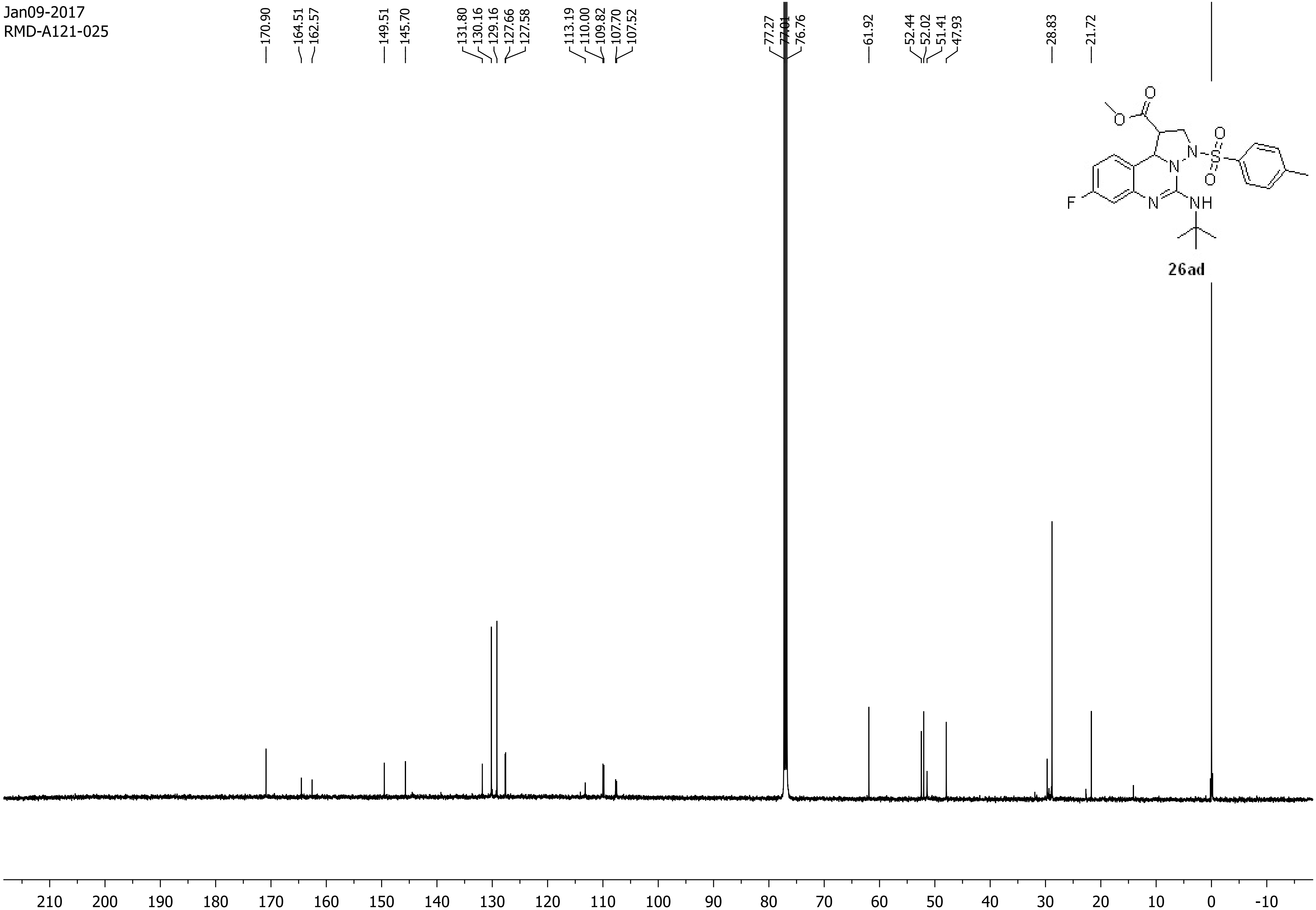
1: TOF MS ES+
8.58e5
491.1510
336.1718
149.0460
124.0958
169.0499
205.1267
236.1349
279.1108
393.2588
435.1370
457.2129
531.4520
663.5311
%
m/z

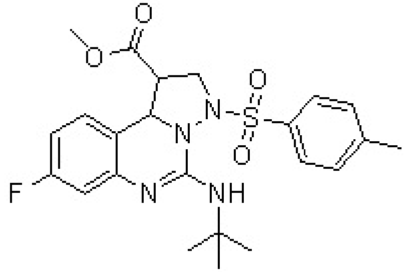
Jan09-2017
RMD-A121-025



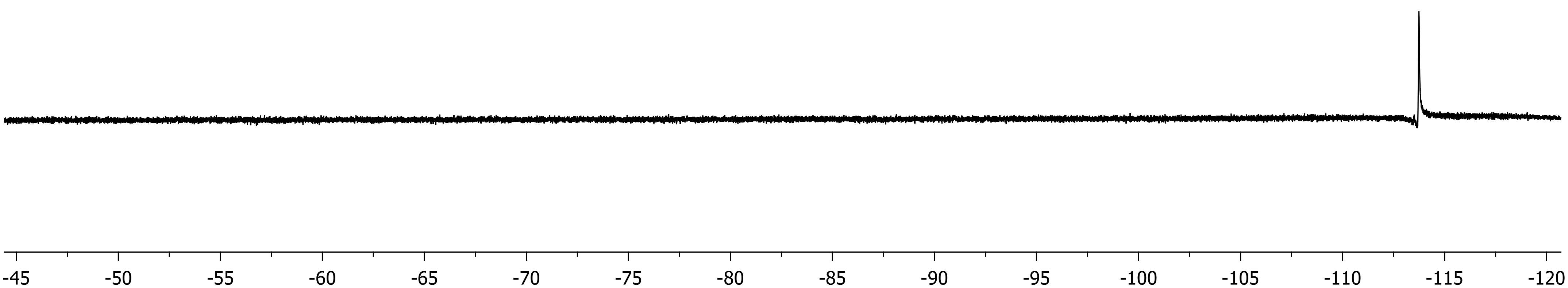
26ad

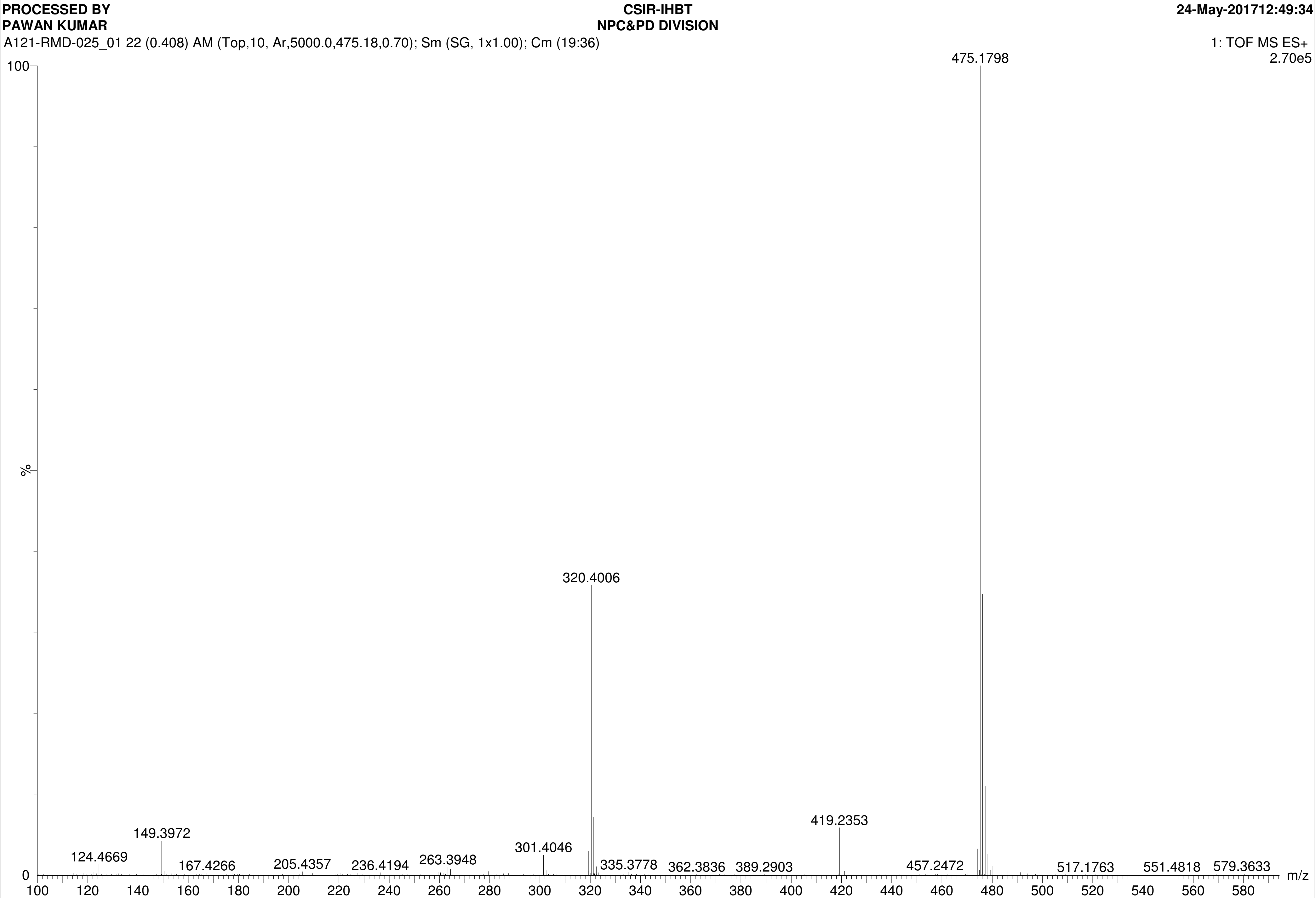

Jan09-2017
RMD-A121-025
170.90
164.51
162.57
149.51
145.70
131.80
130.16
129.16
127.66
127.58
113.19
110.00
109.82
107.70
107.52
77.27
77.01
76.76
61.92
52.44
52.02
51.41
47.93
28.83
21.72
26ad
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

Jan09-2017
RMD-A121-025

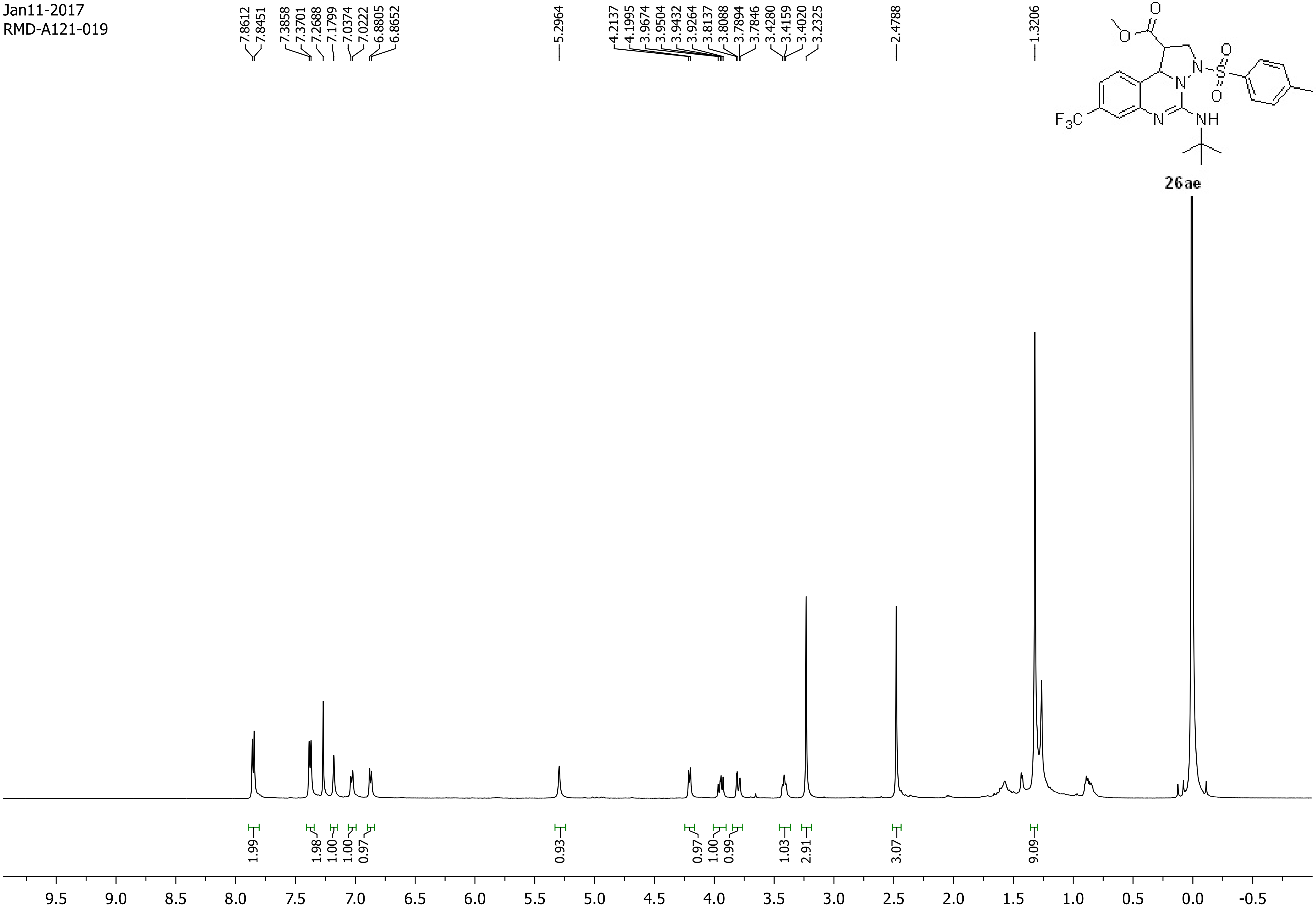


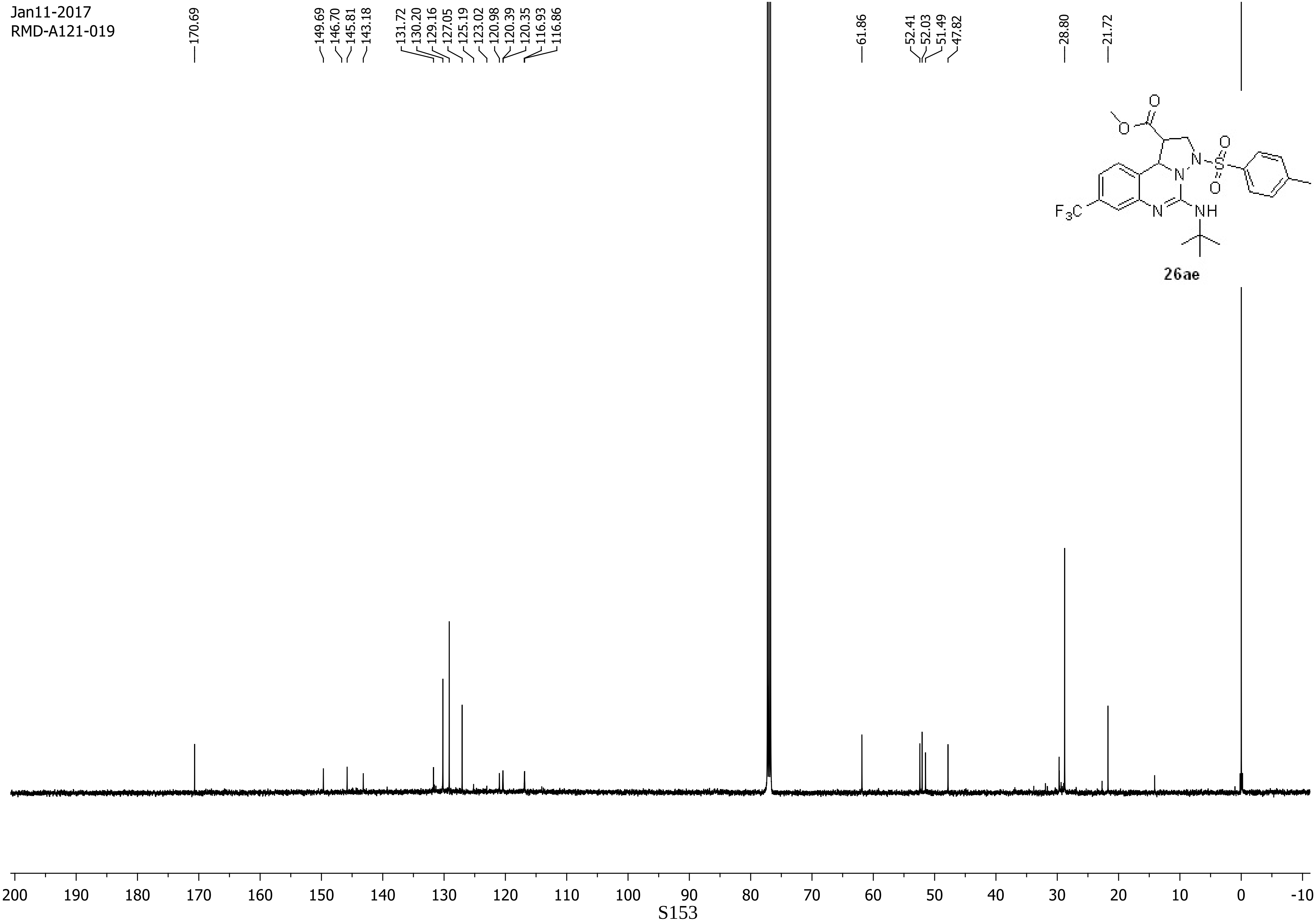
26ad



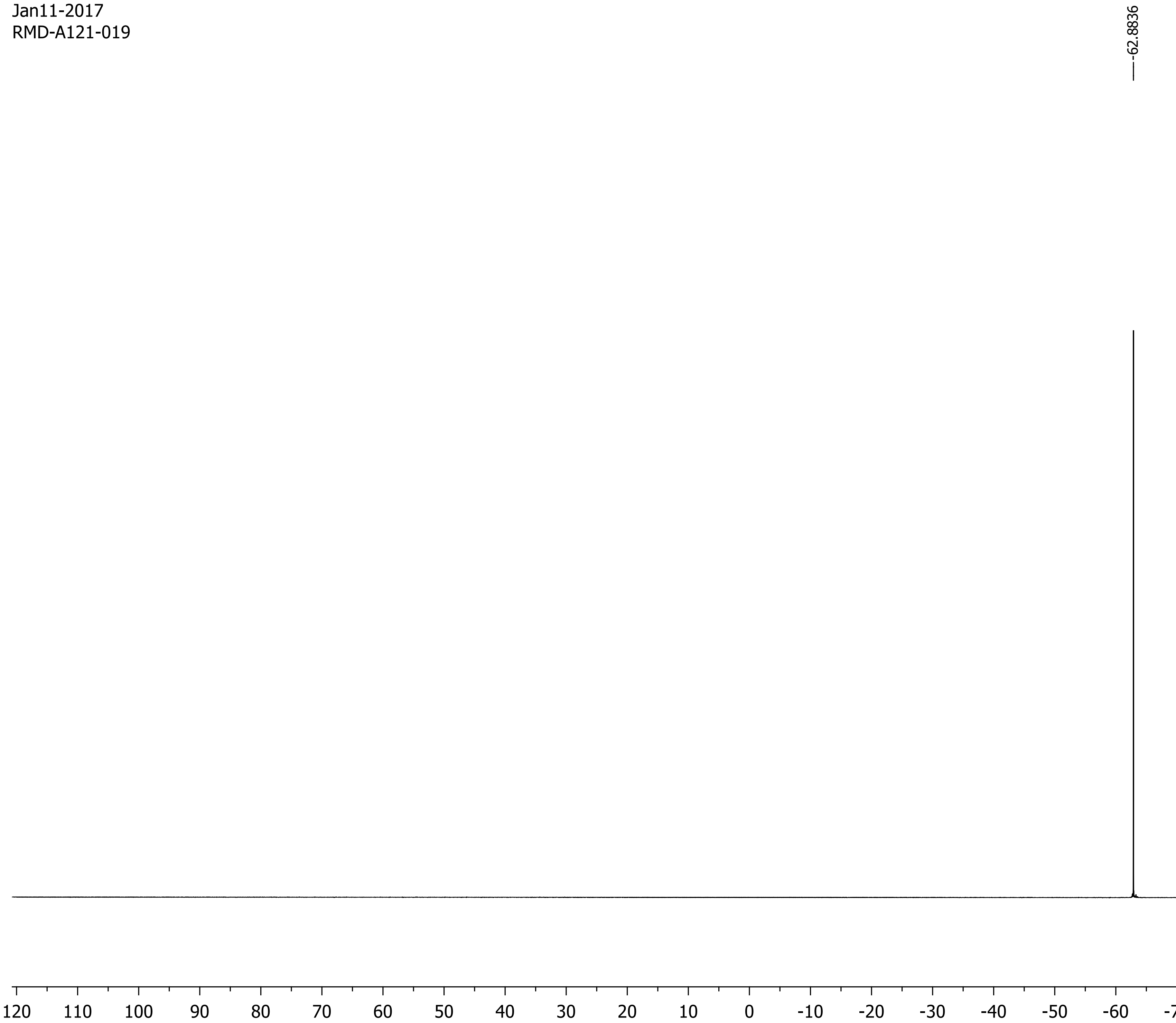

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-May-201712:49:34
A121-RMD-025_01 22 (0.408) AM (Top,10, Ar,5000.0,475.18,0.70); Sm (SG, 1x1.00); Cm (19:36)
1: TOF MS ES+
2.70e5
475.1798
320.4006
419.2353
149.3972
124.4669
167.4266
205.4357
236.4194
263.3948
301.4046
335.3778
362.3836
389.2903
457.2472
517.1763
551.4818
579.3633
%
m/z

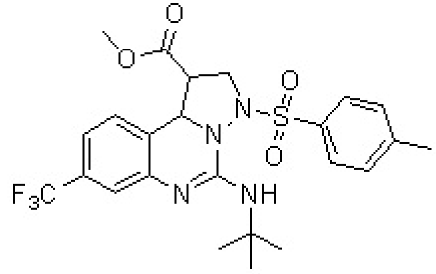
Jan11-2017
RMD-A121-019



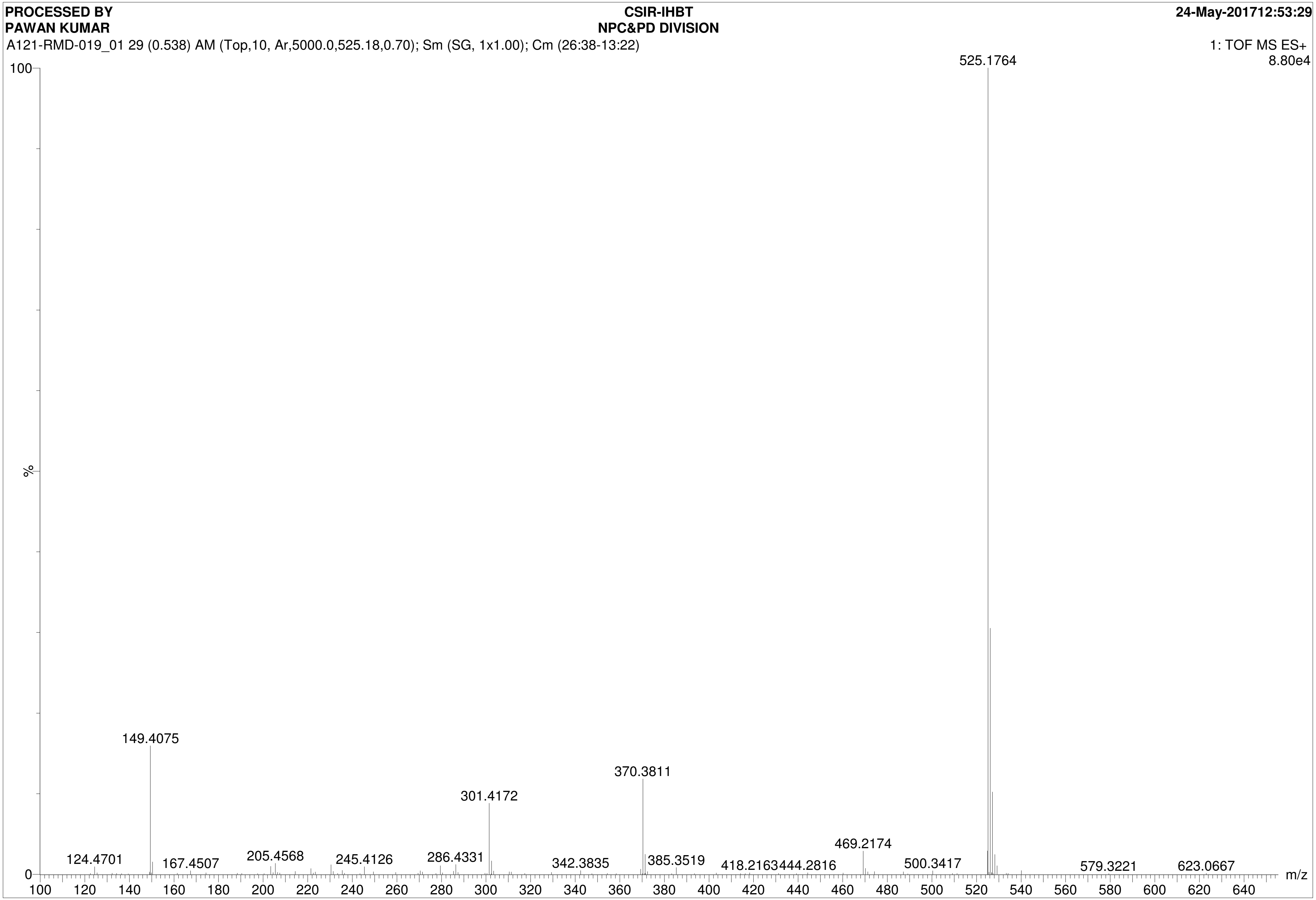

Jan11-2017
RMD-A121-019
170.69
149.69
146.70
145.81
143.18
131.72
130.20
129.16
127.05
125.19
123.02
120.98
120.39
120.35
116.93
116.86
61.86
52.41
52.03
51.49
47.82
28.80
21.72
26ae
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

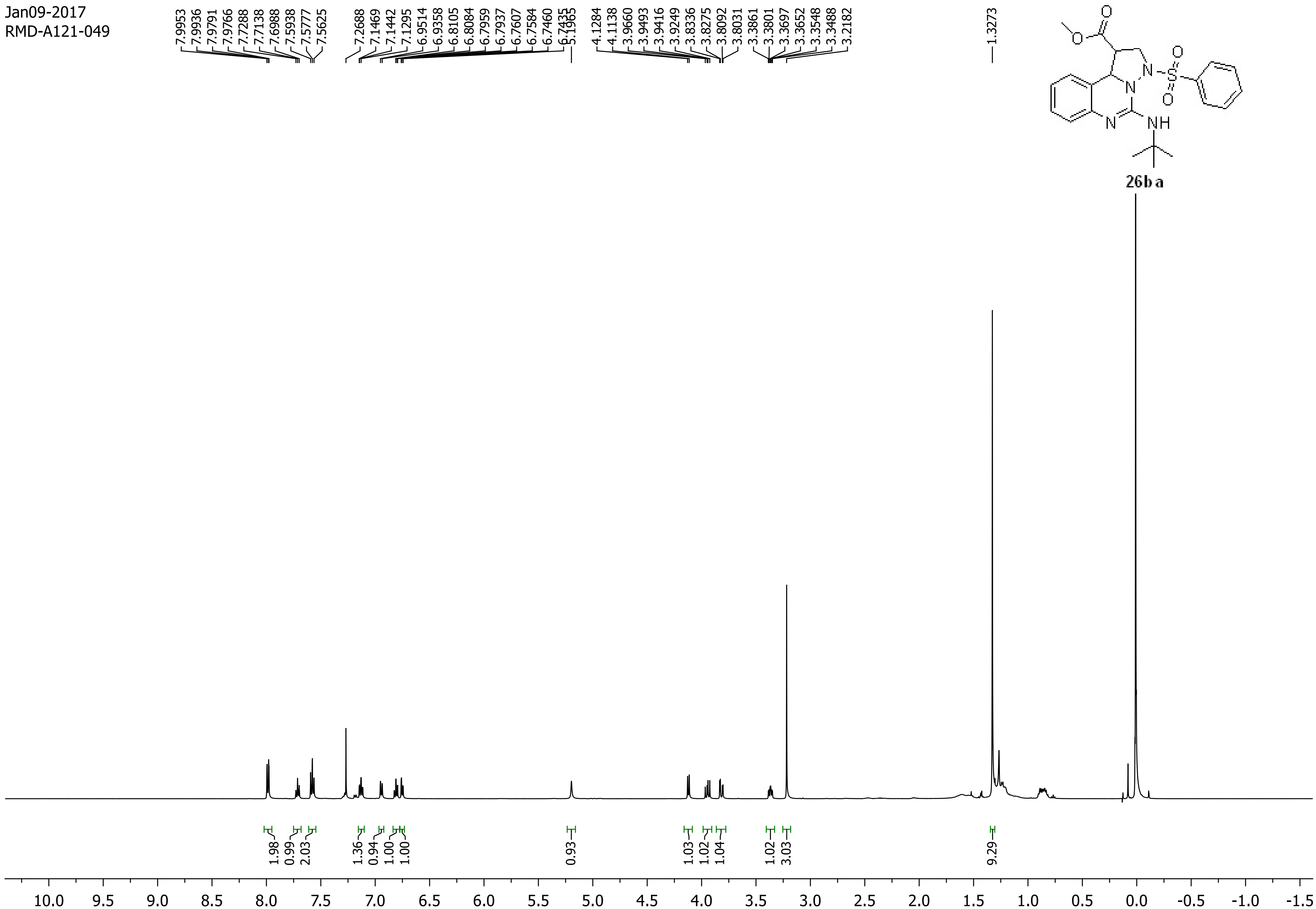
Jan11-2017
RMD-A121-019





26ae


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-May-201712:53:29
A121-RMD-019_01 29 (0.538) AM (Top,10, Ar,5000.0,525.18,0.70); Sm (SG, 1x1.00); Cm (26:38-13:22)
1: TOF MS ES+
8.80e4
100
%
0
525.1764
149.4075
370.3811
301.4172
469.2174
124.4701
167.4507
205.4568
245.4126
286.4331
342.3835
385.3519
418.2163
444.2816
500.3417
579.3221
623.0667
m/z
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640



Jan09-2017
RMD-A121-049
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7.9791
7.9766
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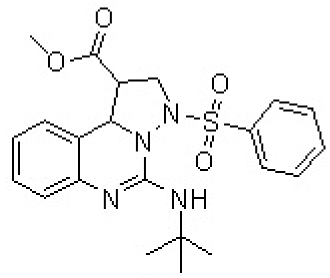
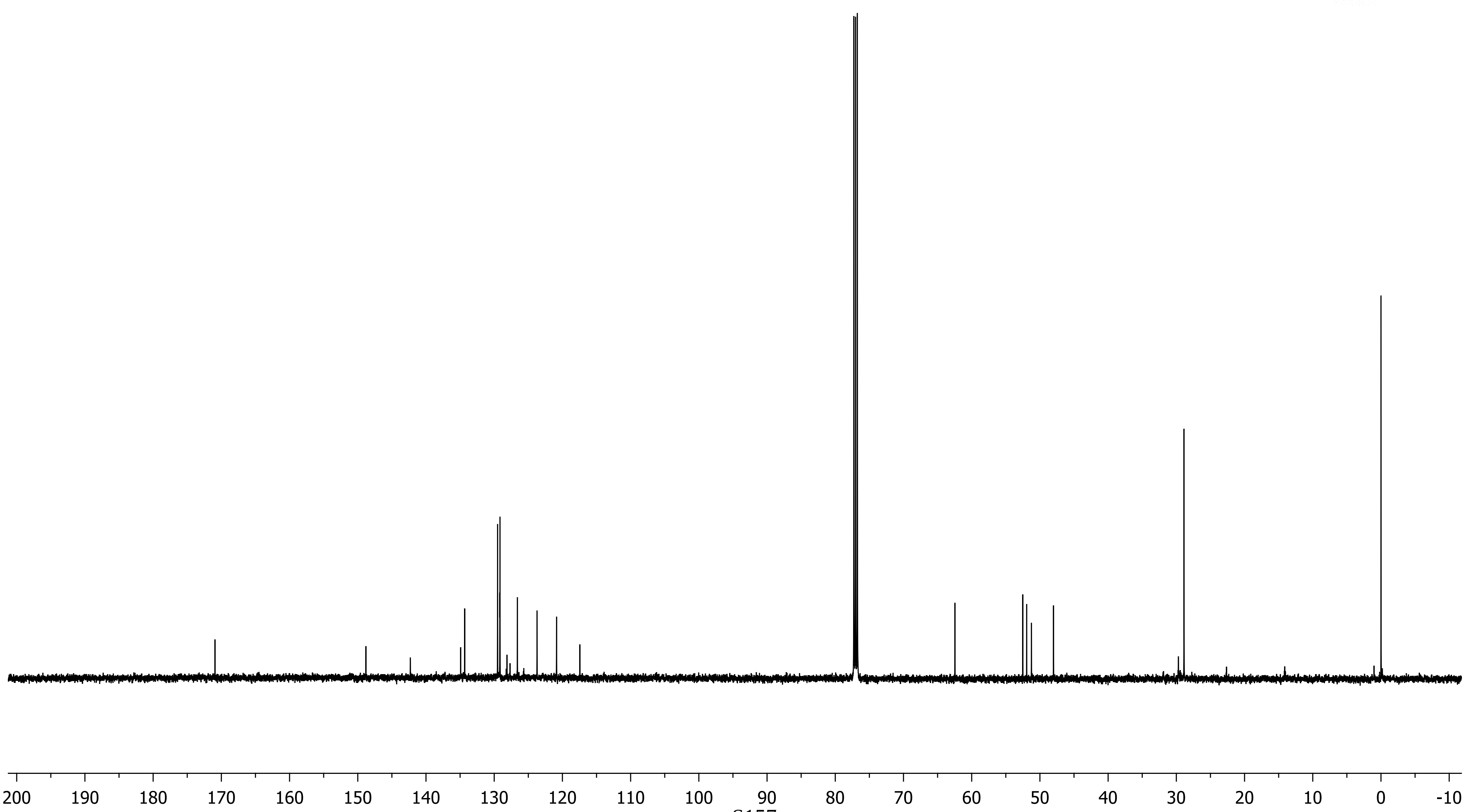
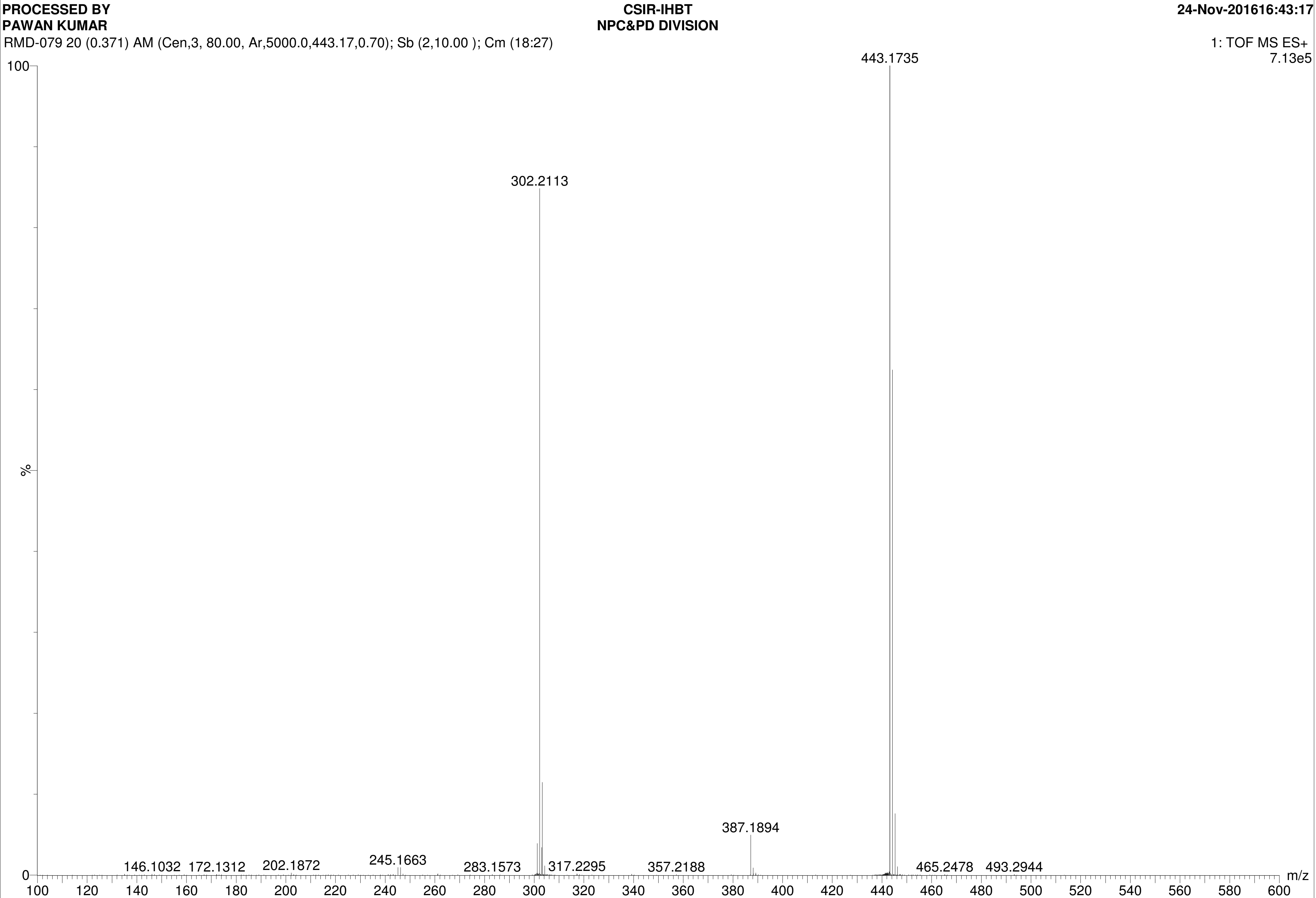
7.7138
7.6988
7.5938
7.5777
7.5625
7.2688
7.1469
7.1442
7.1295
6.9514
6.9358
6.8105
6.8084
6.7959
6.7937
6.7607
6.7584
6.7460
6.7435
5.1965
4.1284
4.1138
3.9660
3.9493
3.9416
3.9249
3.8336
3.8275
3.8092
3.8031
3.3861
3.3801
3.3697
3.3652
3.3548
3.3488
3.2182
1.3273
O
O
N
N
S
O
O
N
NH
26ba
1.98
0.99
2.03
1.36
0.94
1.00
1.00
0.93
1.03
1.02
1.04
1.02
3.03
9.29
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5

Jan09-2017
RMD-A121-049

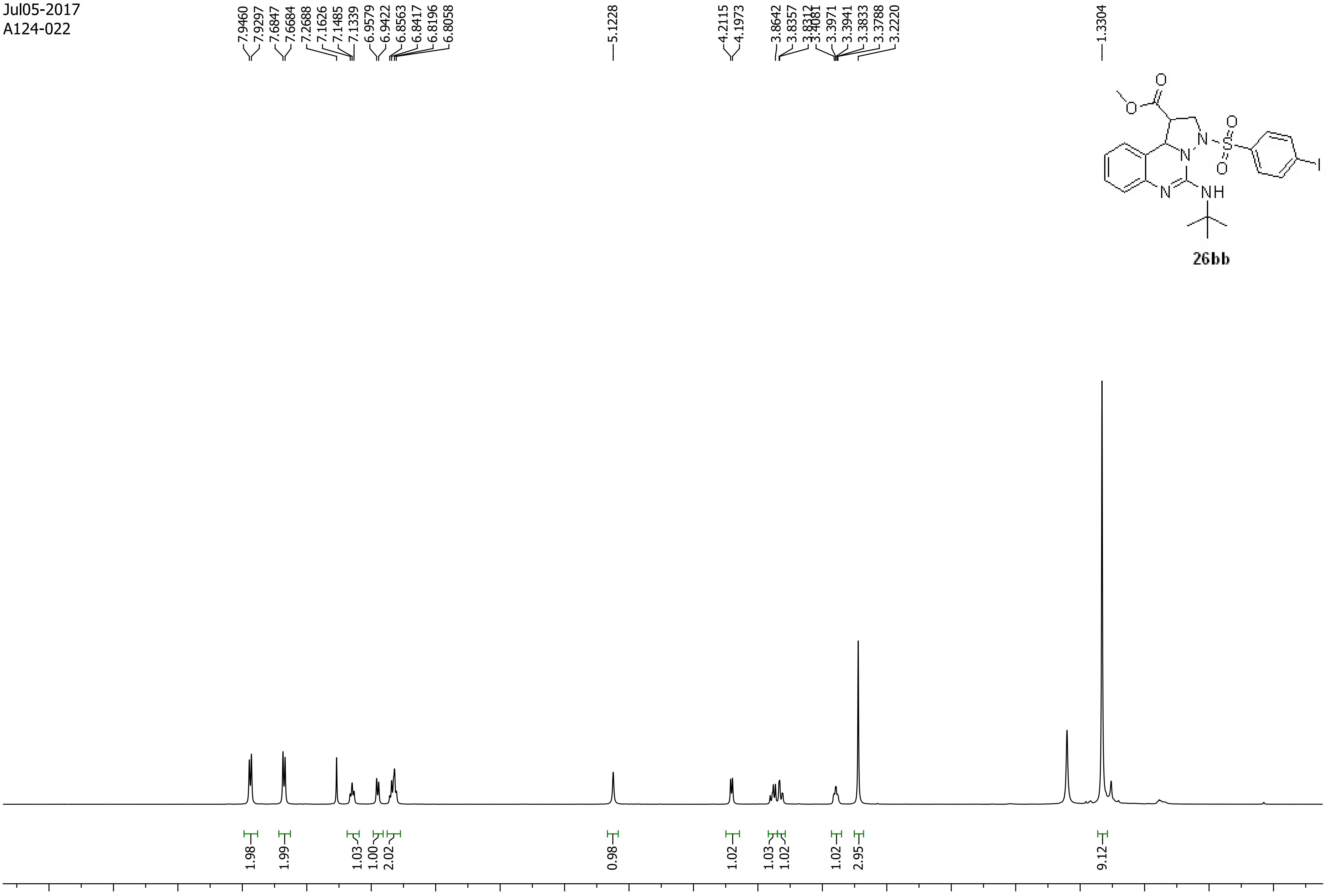


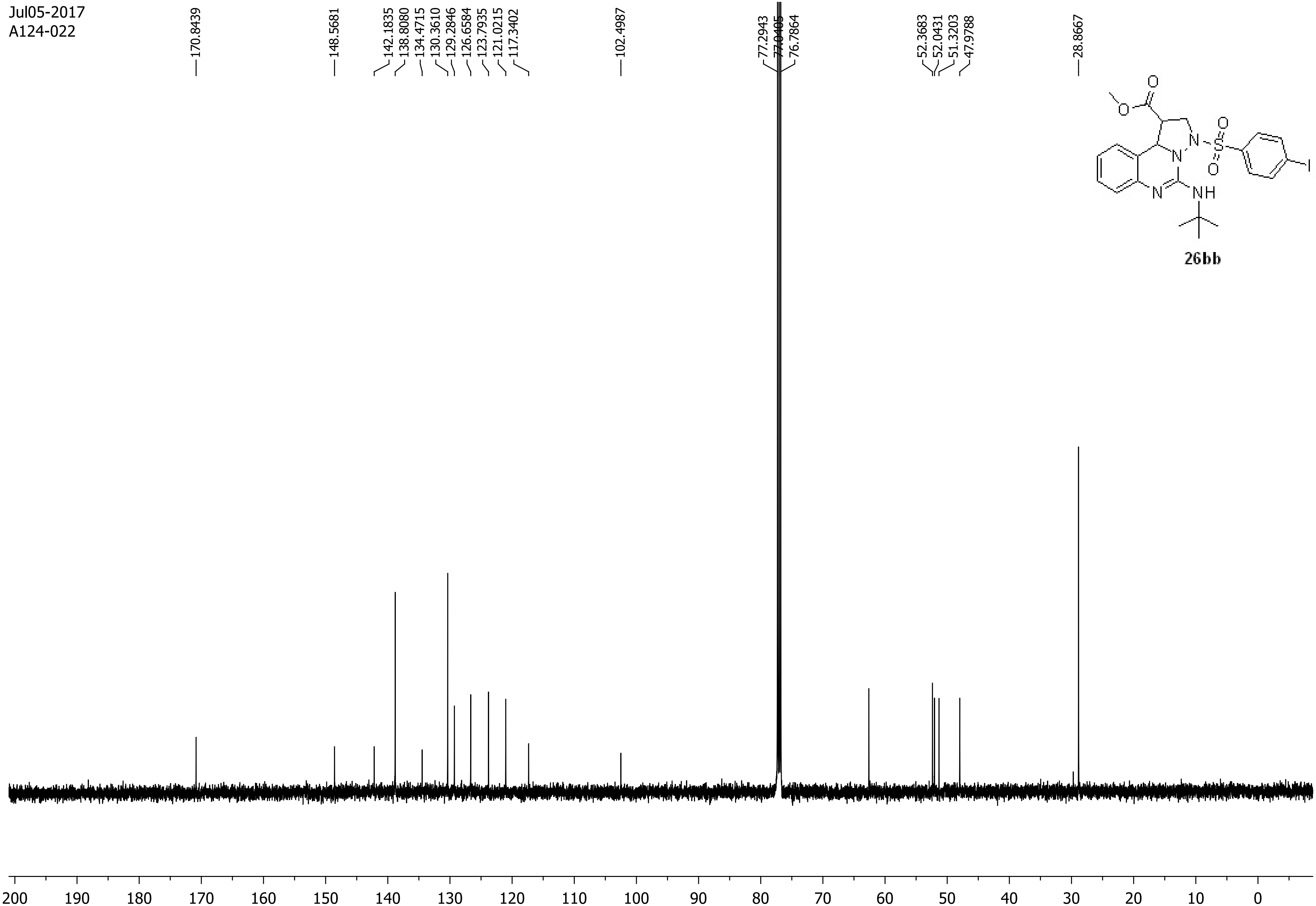
26ba





PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:43:17
RMD-079 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,443.17,0.70); Sb (2,10.00); Cm (18:27)
1: TOF MS ES+
7.13e5
443.1735
302.2113
387.1894
146.1032
172.1312
202.1872
245.1663
283.1573
317.2295
357.2188
465.2478
493.2944
%
m/z


Jul05-2017
A124-022
7.9460 7.9297 7.6847 7.6684 7.2688 7.1626 7.1485 7.1339 6.9579 6.9422 6.8563 6.8417 6.8196 6.8058
5.1228
4.2115 4.1973
3.8642 3.8357 3.8312 3.4081 3.3971 3.3941 3.3833 3.3788 3.2220
1.3304
1.98 1.99 1.03 1.00 2.02 0.98 1.02 1.03 1.02 1.02 2.95 9.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
26bb



Jul05-2017
A124-022
170.8439
148.5681
142.1835
138.8080
134.4715
130.3610
129.2846
126.6584
123.7935
121.0215
117.3402
102.4987
77.2943
77.0405
76.7864
52.3683
52.0431
51.3203
47.9788
28.8667
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
O
O
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S
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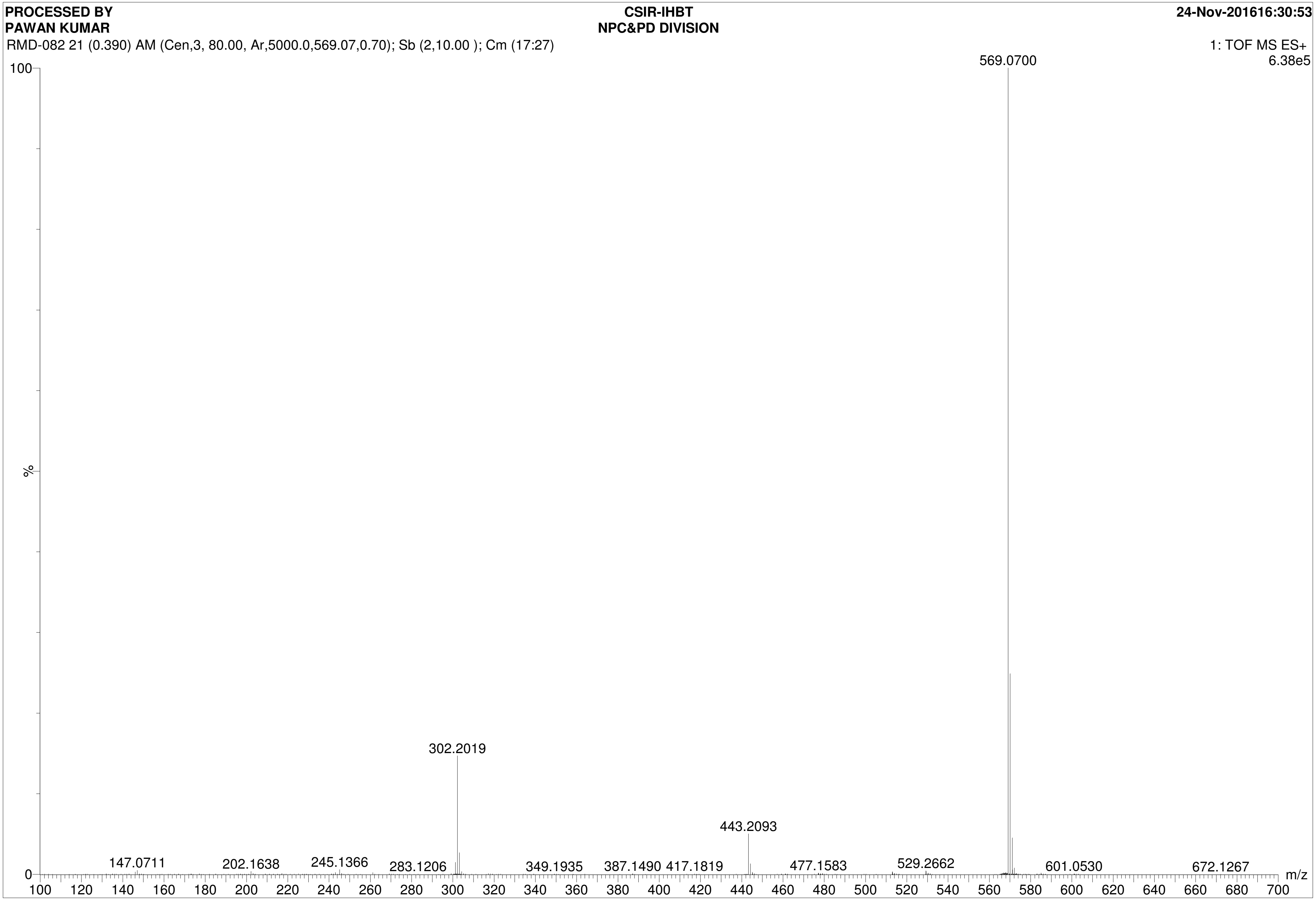
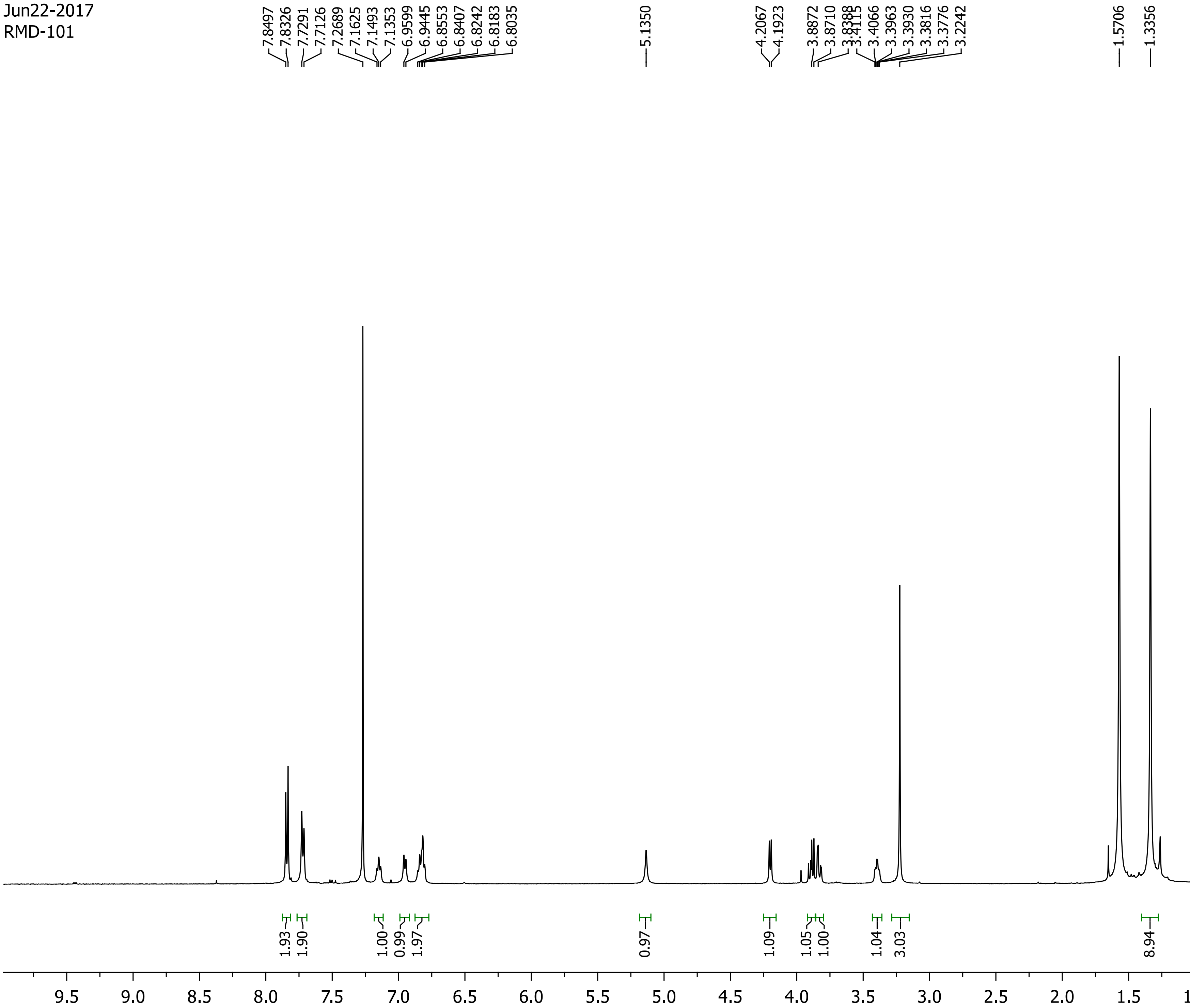
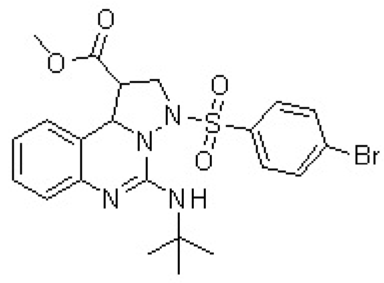
N
I
N
NH

26bb

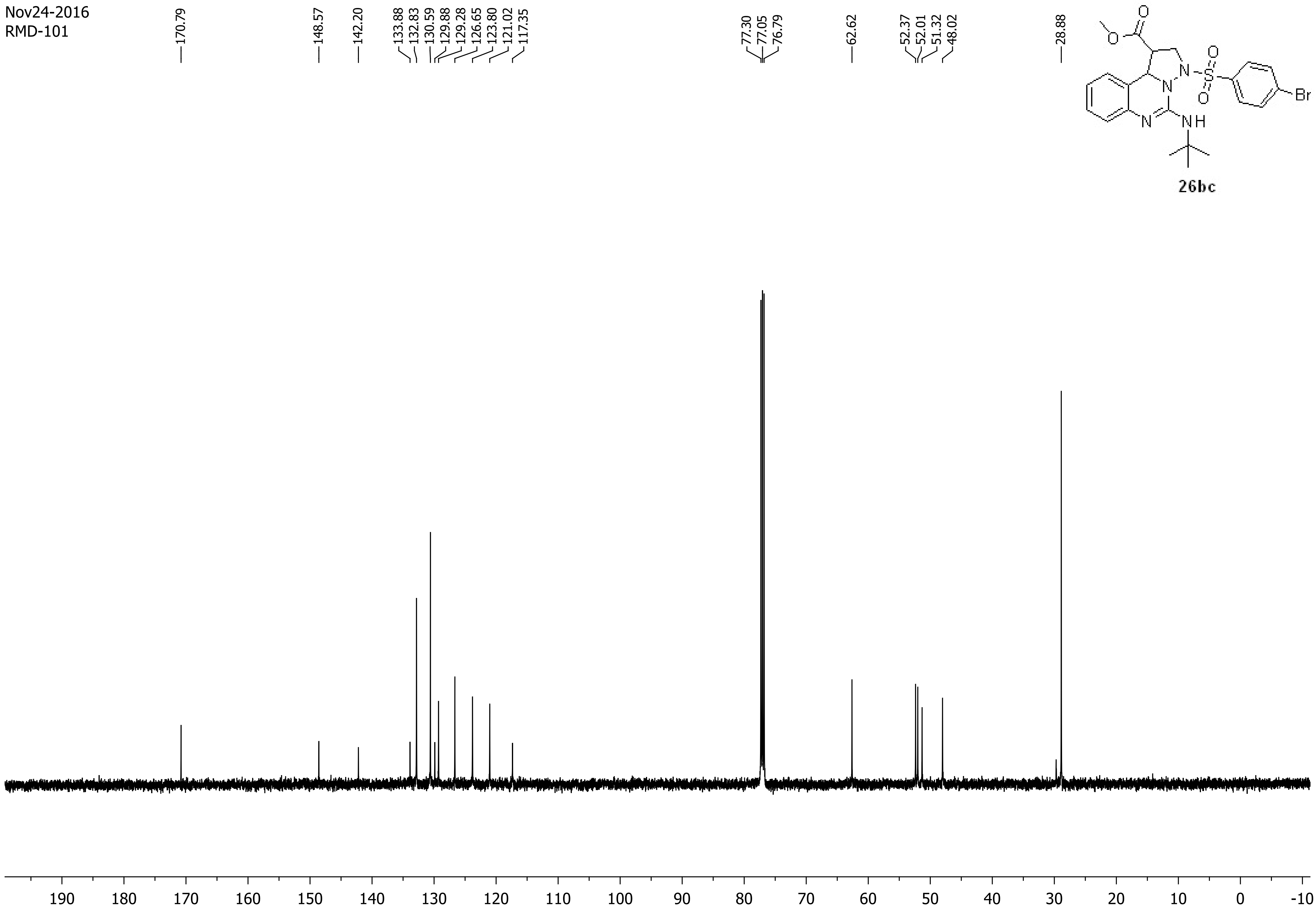

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:30:53
RMD-082 21 (0.390) AM (Cen,3, 80.00, Ar,5000.0,569.07,0.70); Sb (2,10.00); Cm (17:27)
1: TOF MS ES+
6.38e5
569.0700
302.2019
443.2093
147.0711
202.1638
245.1366
283.1206
349.1935
387.1490
417.1819
477.1583
529.2662
601.0530
672.1267
%
m/z

Jun22-2017
RMD-101

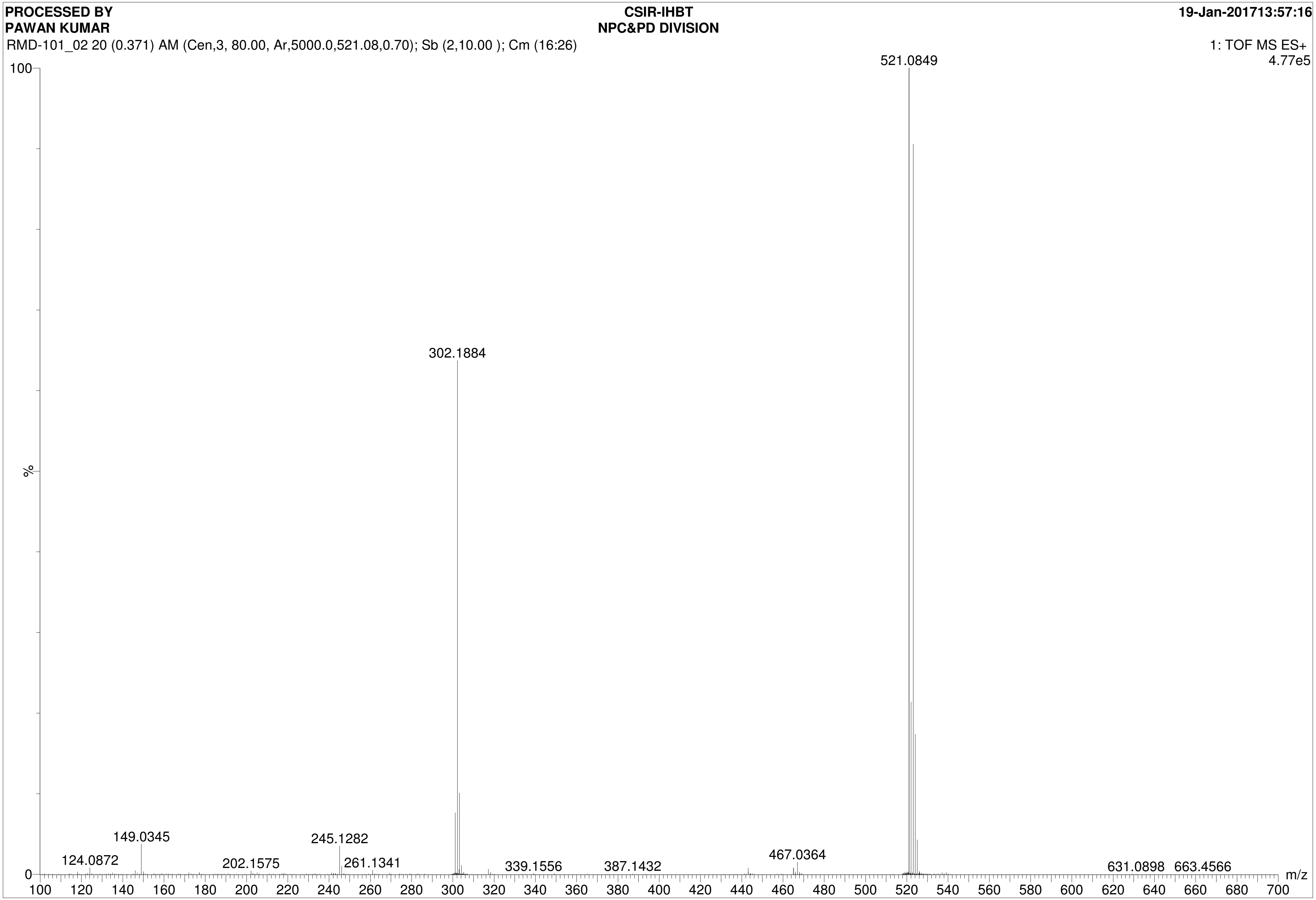




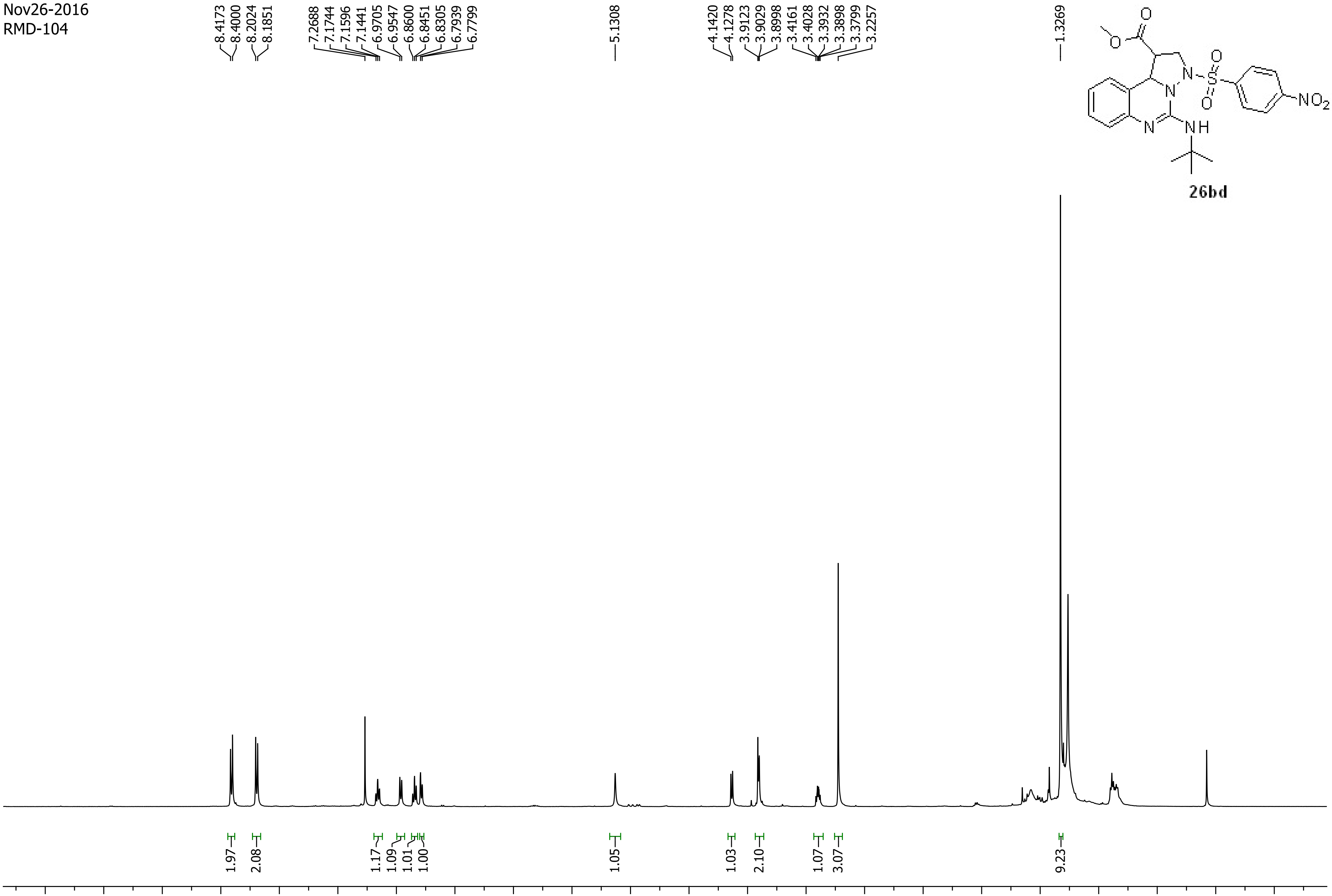
26bc


Nov24-2016
RMD-101
170.79
148.57
142.20
133.88
132.83
130.59
129.88
129.28
126.65
123.80
121.02
117.35
77.30
77.05
76.79
62.62
52.37
52.01
51.32
48.02
28.88
Br
NH
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

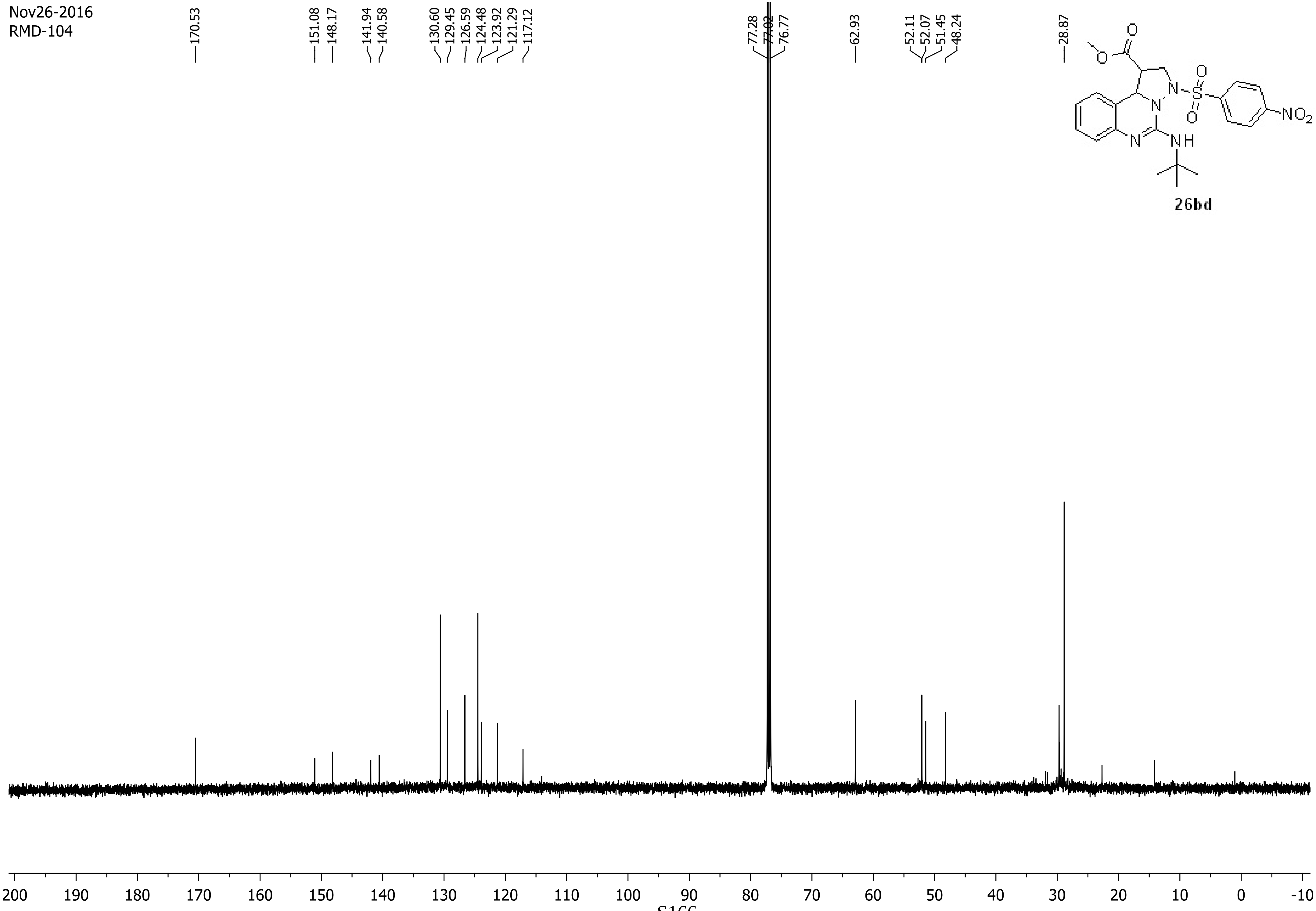
26bc


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:57:16
RMD-101_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,521.08,0.70); Sb (2,10.00); Cm (16:26)
1: TOF MS ES+
4.77e5
521.0849
302.1884
149.0345
124.0872
202.1575
245.1282
261.1341
339.1556
387.1432
467.0364
631.0898
663.4566
%
m/z

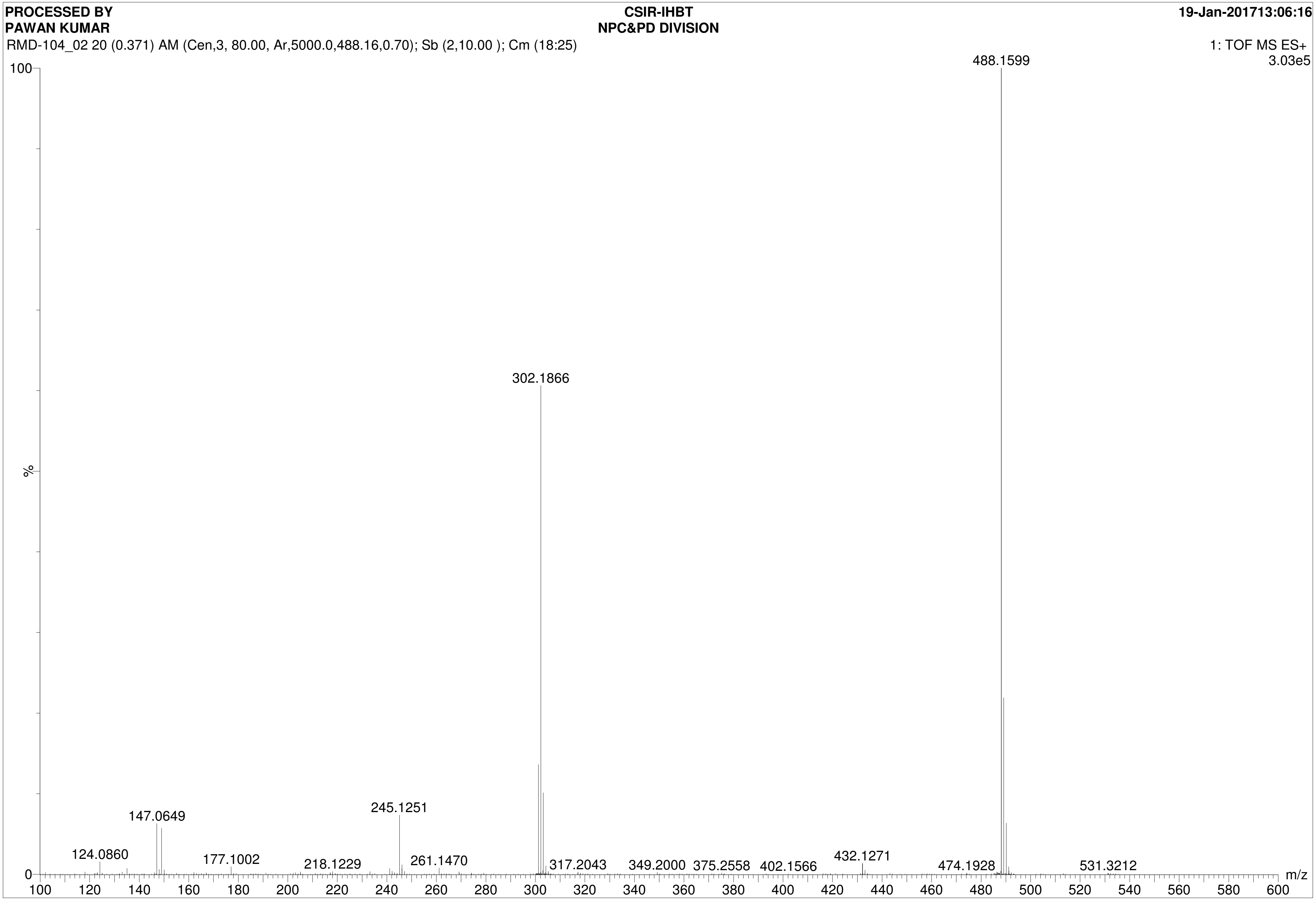
Nov26-2016
RMD-104



Nov26-2016
RMD-104

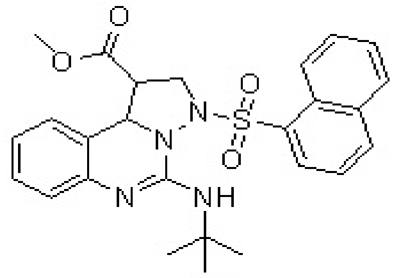


26bd

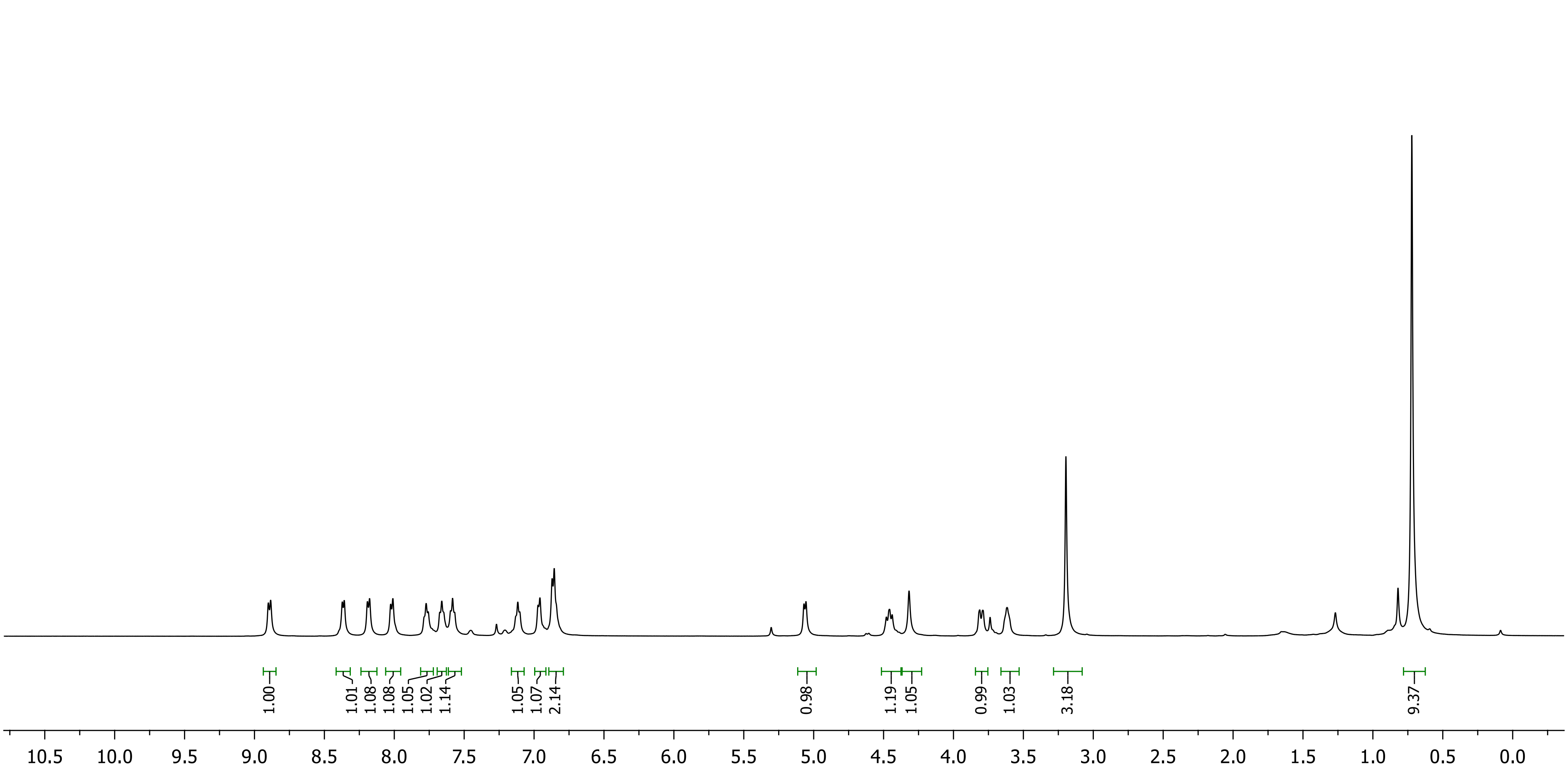


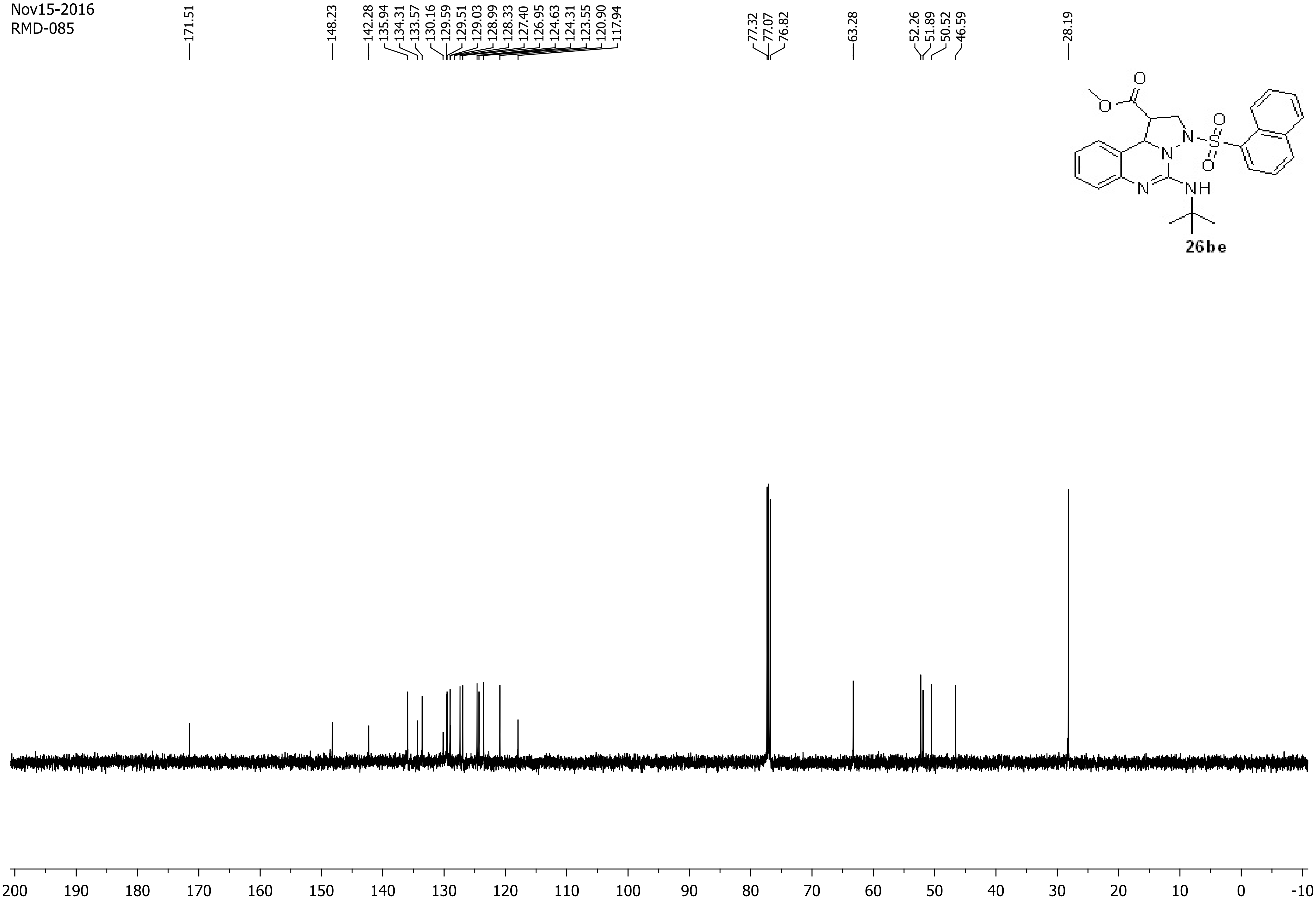
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:06:16
RMD-104_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,488.16,0.70); Sb (2,10.00); Cm (18:25)
1: TOF MS ES+
3.03e5
488.1599
302.1866
147.0649
245.1251
124.0860
177.1002
218.1229
261.1470
317.2043
349.2000
375.2558
402.1566
432.1271
474.1928
531.3212
%
m/z

Nov15-2016
RMD-085



26be




Nov15-2016
RMD-085
171.51
148.23
142.28
135.94
134.31
133.57
130.16
129.59
129.51
129.03
128.99
128.33
127.40
126.95
124.63
124.31
123.55
120.90
117.94
77.32
77.07
76.82
63.28
52.26
51.89
50.52
46.59
28.19
O
O
N
S
O
O
N
N
NH
26be
200
190
180
170
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120
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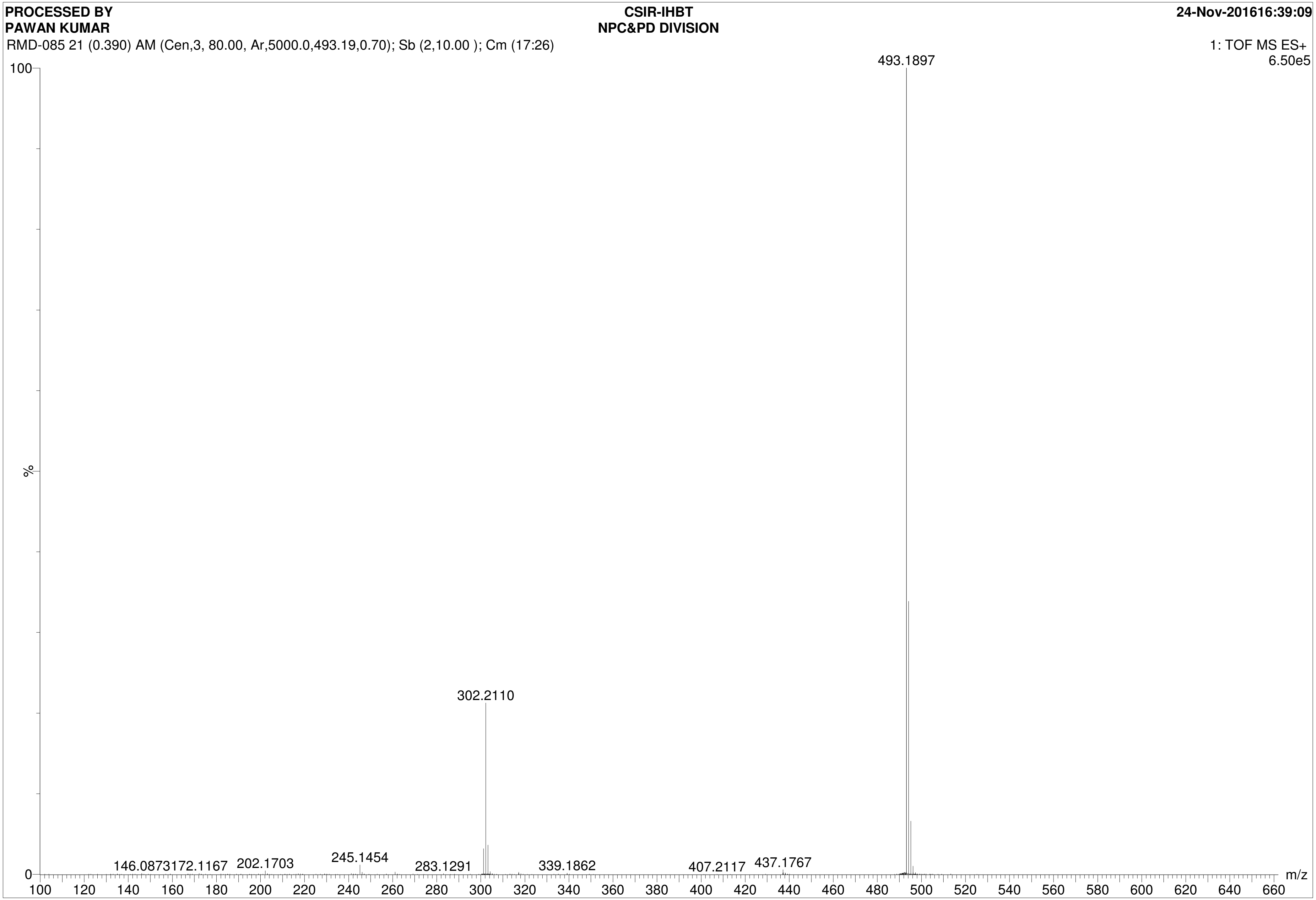
80
70
60
50
40
30
20
10
0
-10


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:39:09
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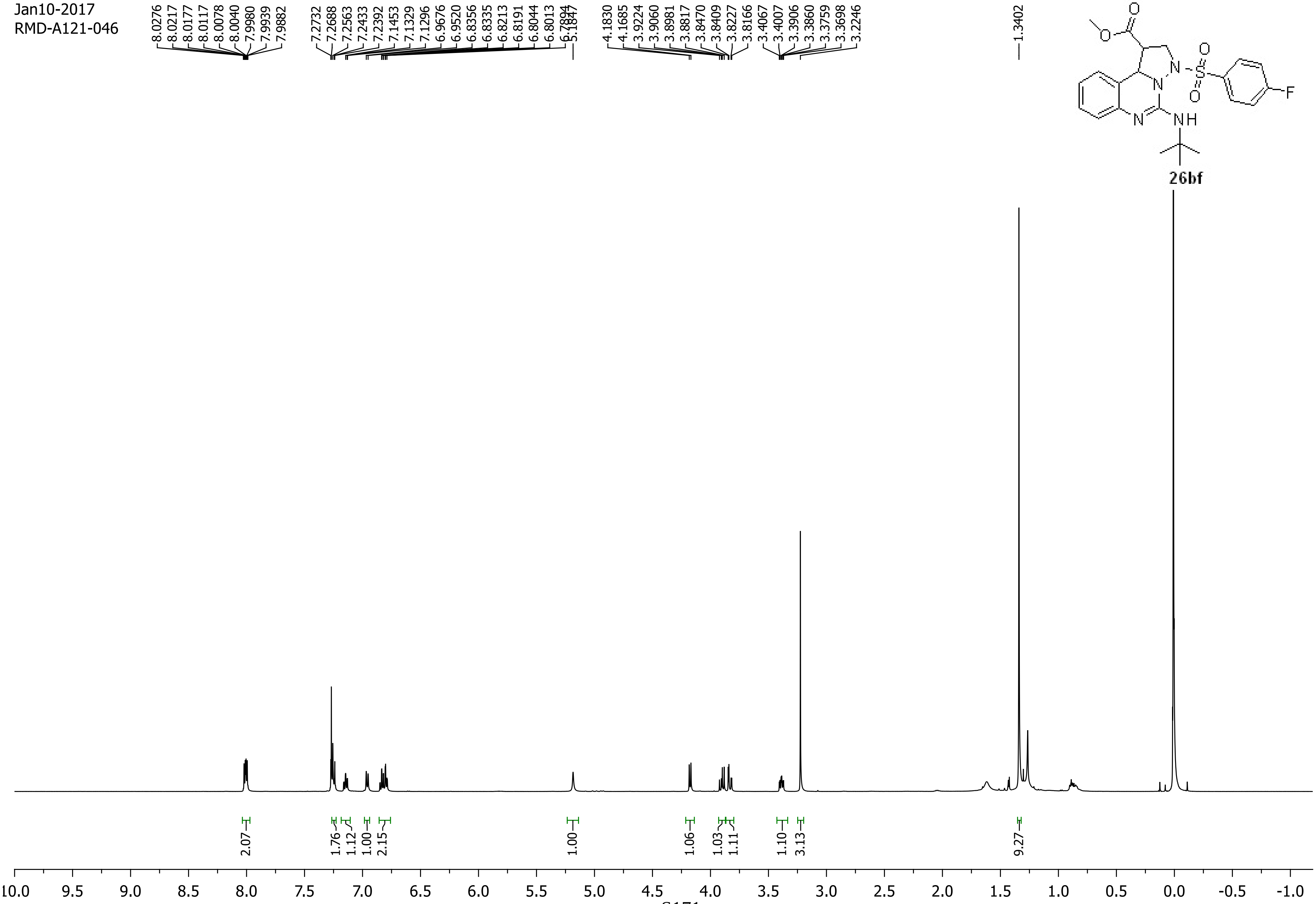
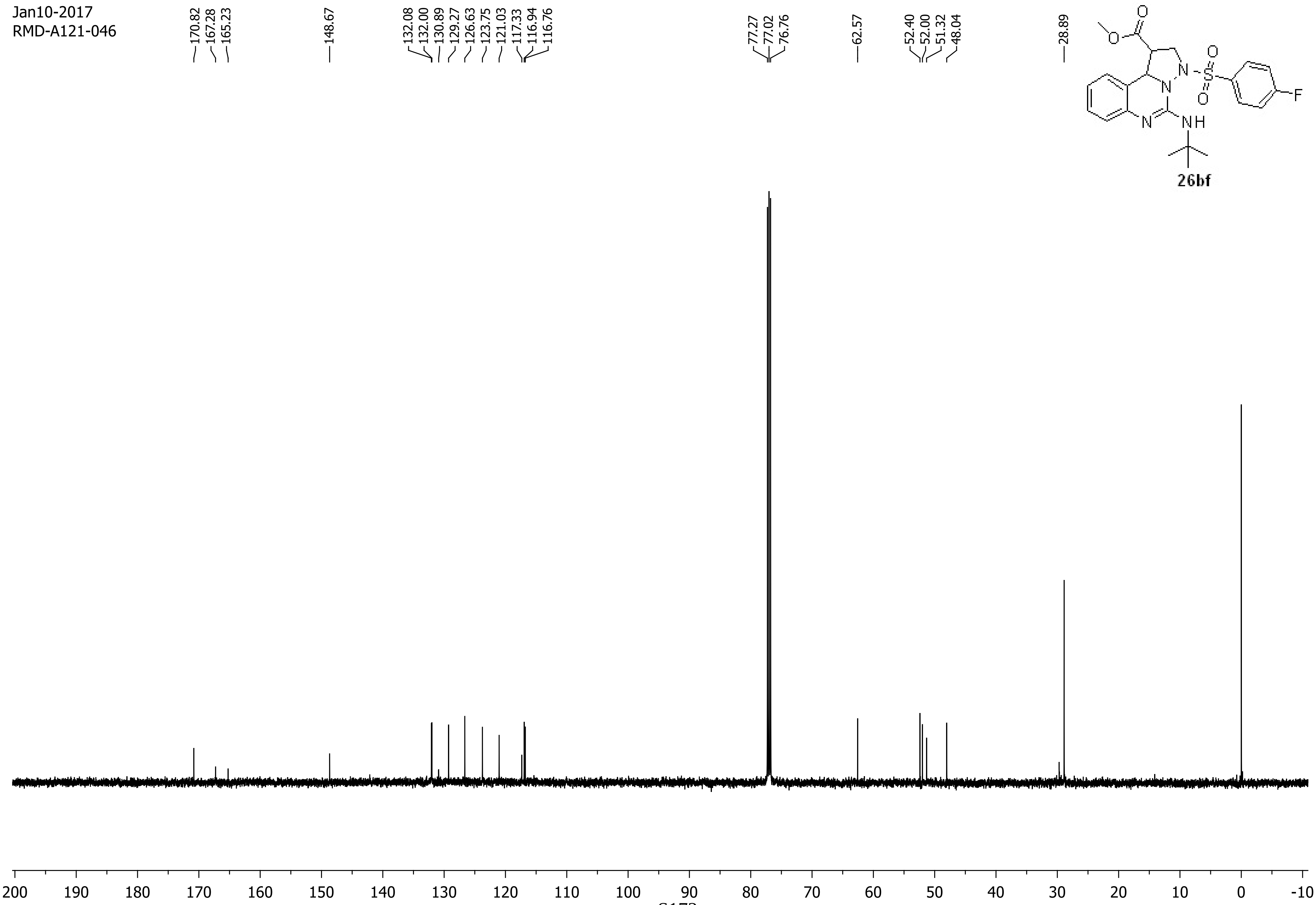
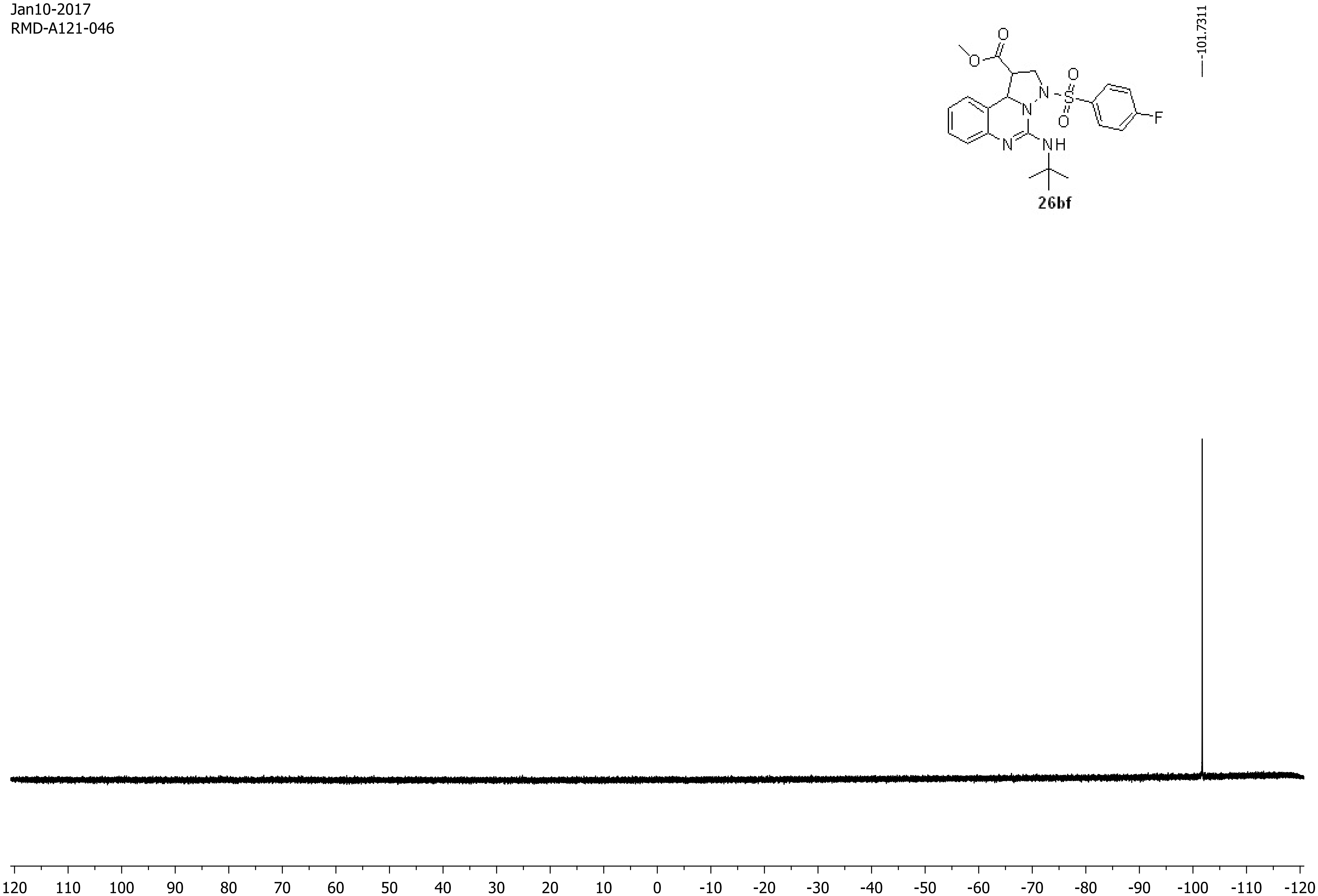
1: TOF MS ES+
6.50e5
493.1897
302.2110
146.0873172.1167
202.1703
245.1454
283.1291
339.1862
407.2117
437.1767
100
%
0
m/z
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660

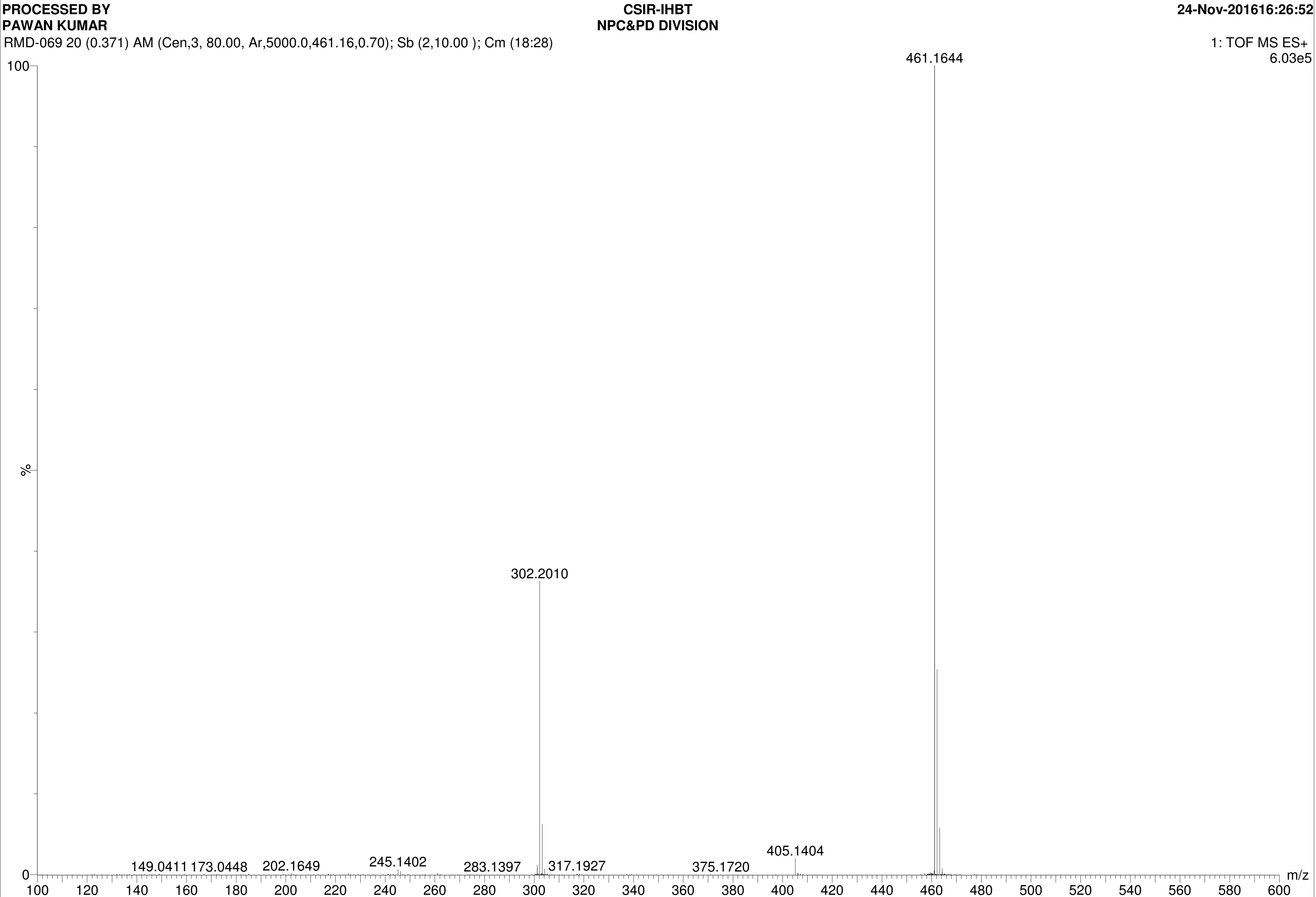
Jan10-2017
RMD-A121-046



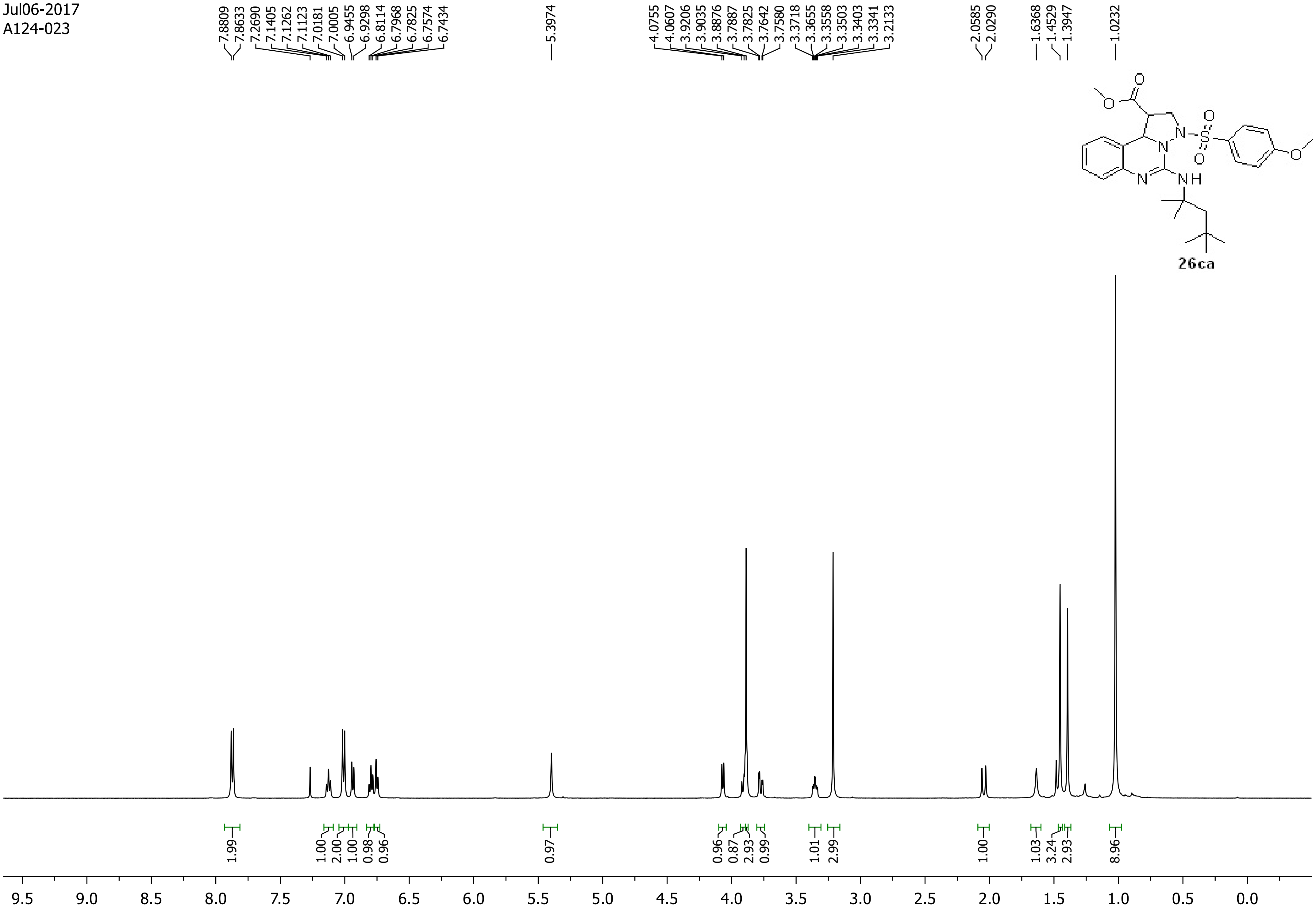

Jan10-2017
RMD-A121-046
170.82
167.28
165.23
148.67
132.08
132.00
130.89
129.27
126.63
123.75
121.03
117.33
116.94
116.76
77.27
77.02
76.76
62.57
52.40
52.00
51.32
48.04
28.89
O
O
N
N
N
S
O
O
F
NH
26bf
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


Jan10-2017
RMD-A121-046
-101.7311
O
O
N
S
O
O
F
N
N
NH
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120

26bf



PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:26:52
RMD-069 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,461.16,0.70); Sb (2,10.00); Cm (18:28)
1: TOF MS ES+
6.03e5
461.1644
302.2010
405.1404
149.0411
173.0448
202.1649
245.1402
283.1397
317.1927
375.1720
%
m/z


Jul06-2017
A124-023
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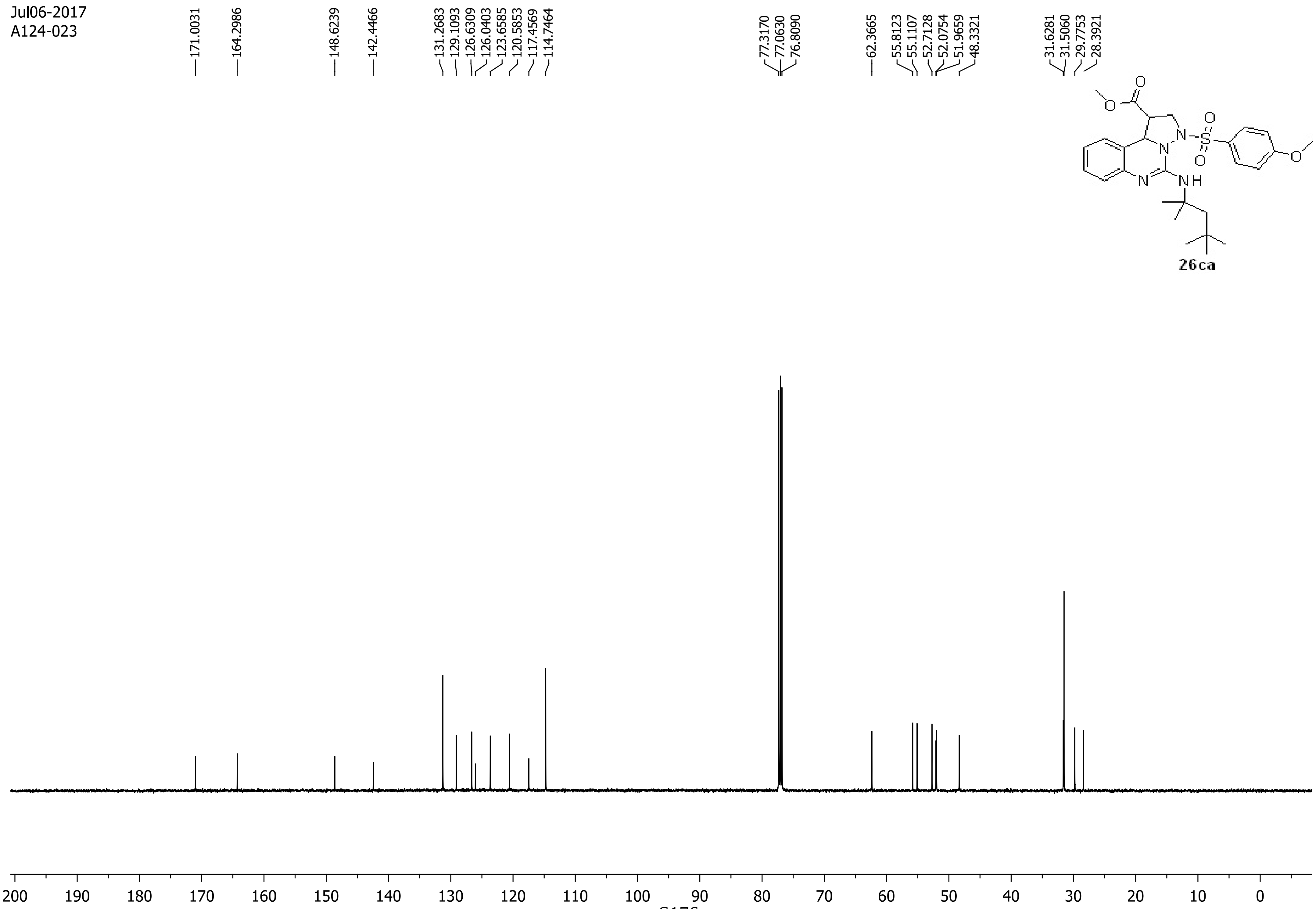
7.8633
7.2690
7.1405
7.1262
7.1123
7.0181
7.0005
6.9455
6.9298
6.8114
6.7968
6.7825
6.7574
6.7434
5.3974
4.0755
4.0607
3.9206
3.9035
3.8876
3.7887
3.7825
3.7642
3.7580
3.3718
3.3655
3.3558
3.3503
3.3403
3.3341
3.2133
2.0585
2.0290
1.6368
1.4529
1.3947
1.0232
26ca
1.99
1.00
2.00
1.00
0.98
0.96
0.97
0.96
0.87
2.93
0.99
1.01
2.99
1.00
1.03
3.24
2.93
8.96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


Jul06-2017
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142.4466
131.2683
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126.6309
126.0403
123.6585
120.5853
117.4569
114.7464
77.3170
77.0630
76.8090
62.3665
55.8123
55.1107
52.7128
52.0754
51.9659
48.3321
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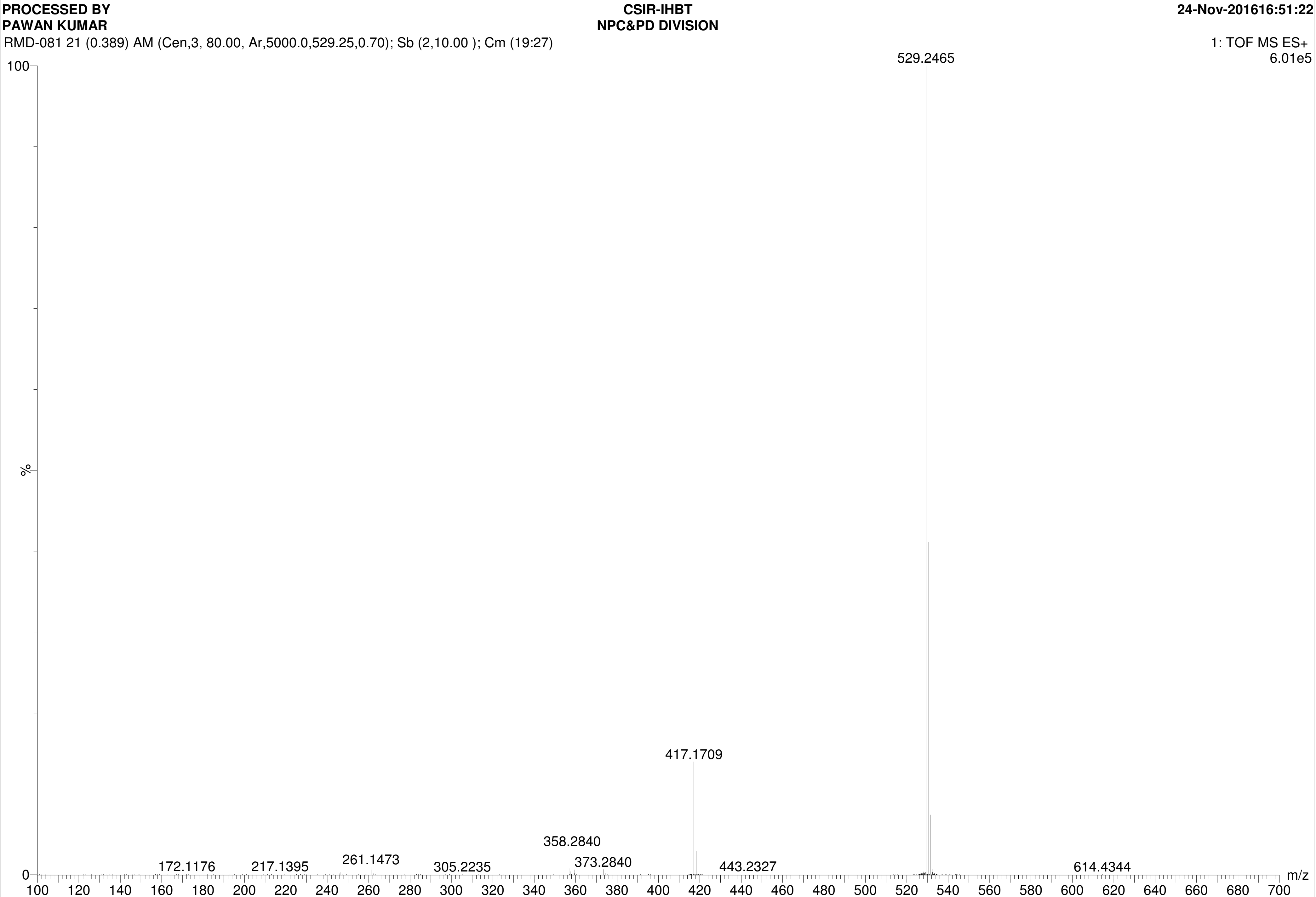
31.5060
29.7753
28.3921
26ca
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201616:51:22
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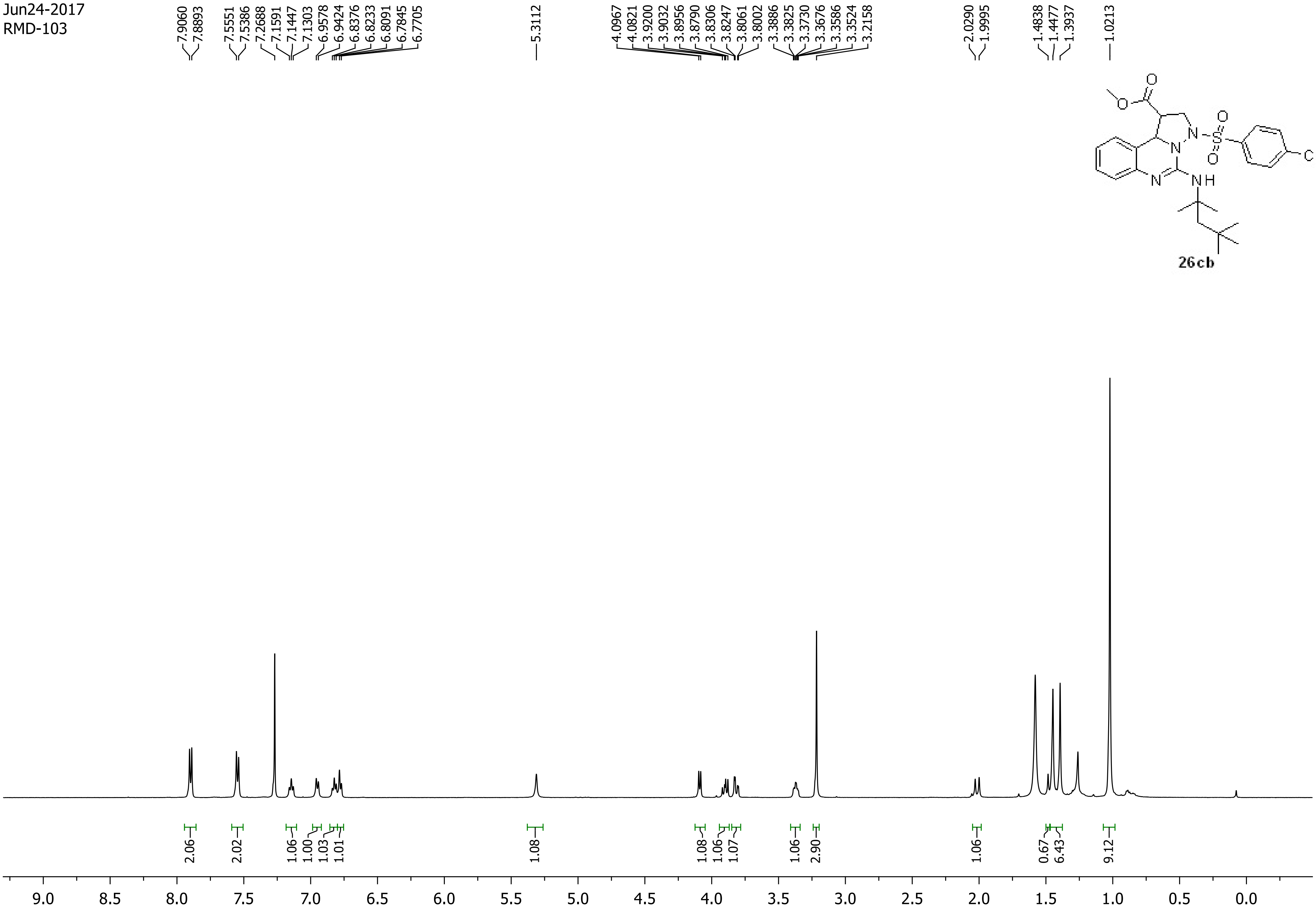
1: TOF MS ES+
6.01e5
529.2465
417.1709
358.2840
373.2840
443.2327
261.1473
305.2235
217.1395
172.1176
614.4344
%
m/z
100
0



Jun24-2017
RMD-103
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7.5551
7.5386
7.2688
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7.1447
7.1303
6.9578
6.9424
6.8376
6.8233
6.8091
6.7845
6.7705
5.3112
4.0967
4.0821
3.9200
3.9032
3.8956
3.8790
3.8306
3.8247
3.8061
3.8002
3.3886
3.3825
3.3730
3.3676
3.3586
3.3524
3.2158
2.0290
1.9995
1.4838
1.4477
1.3937
1.0213
O
O
N
S
O
O
Cl
N
N
NH
26cb
2.06
2.02
1.06
1.00
1.03
1.01
1.08
1.08
1.06
1.07
1.06
2.90
1.06
0.67
6.43
9.12
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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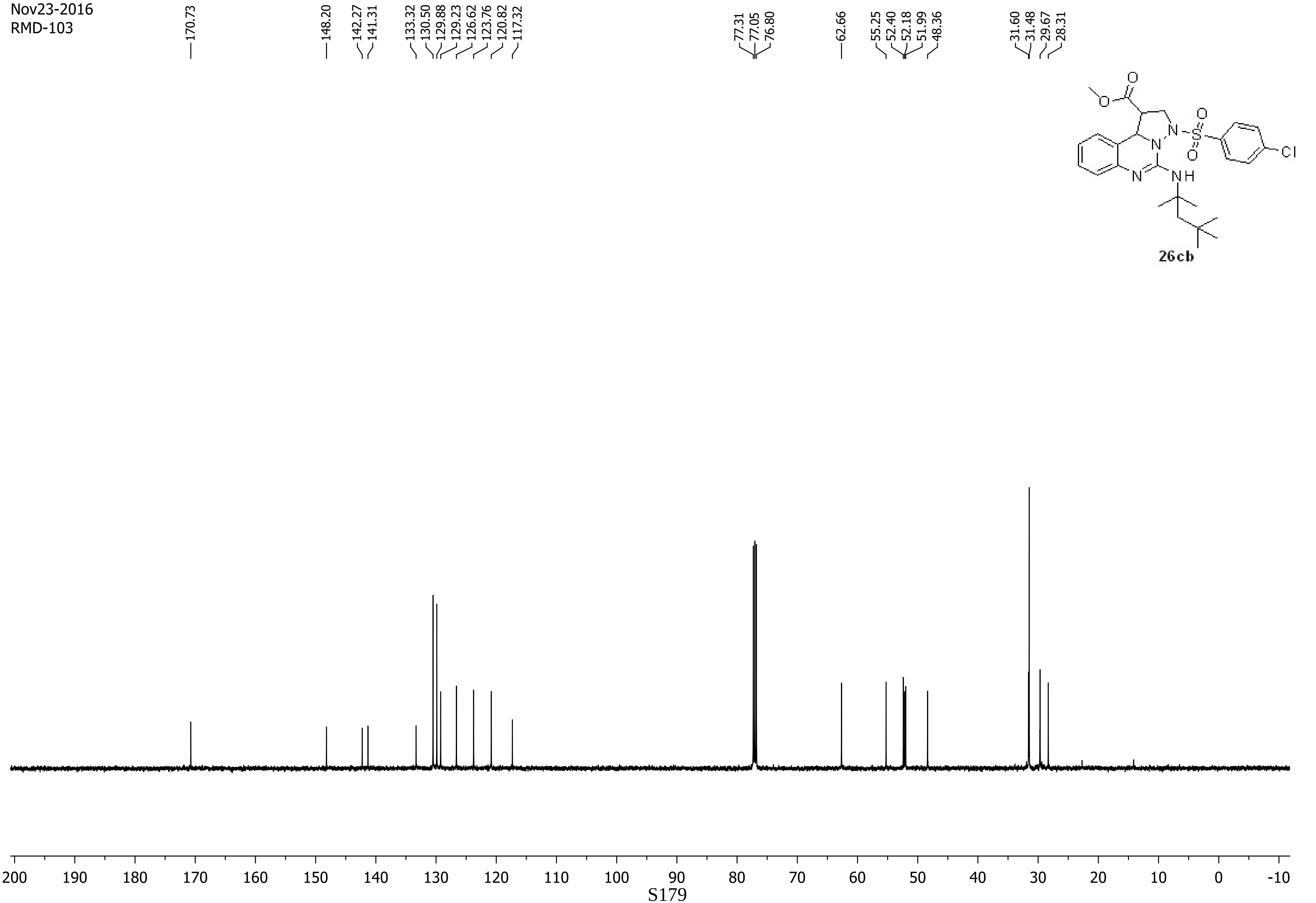
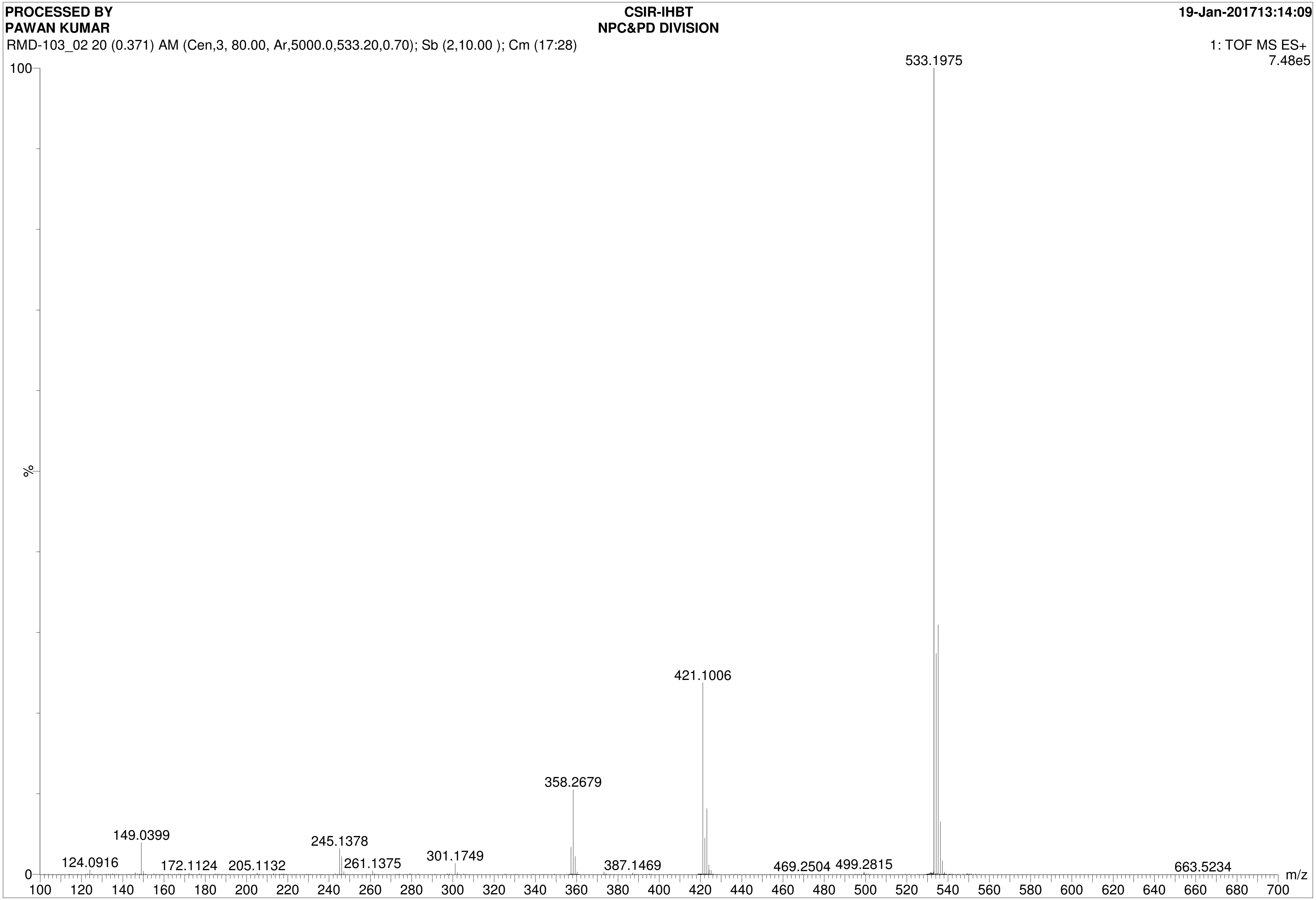
3.0
2.5
2.0
1.5
1.0
0.5
0.0

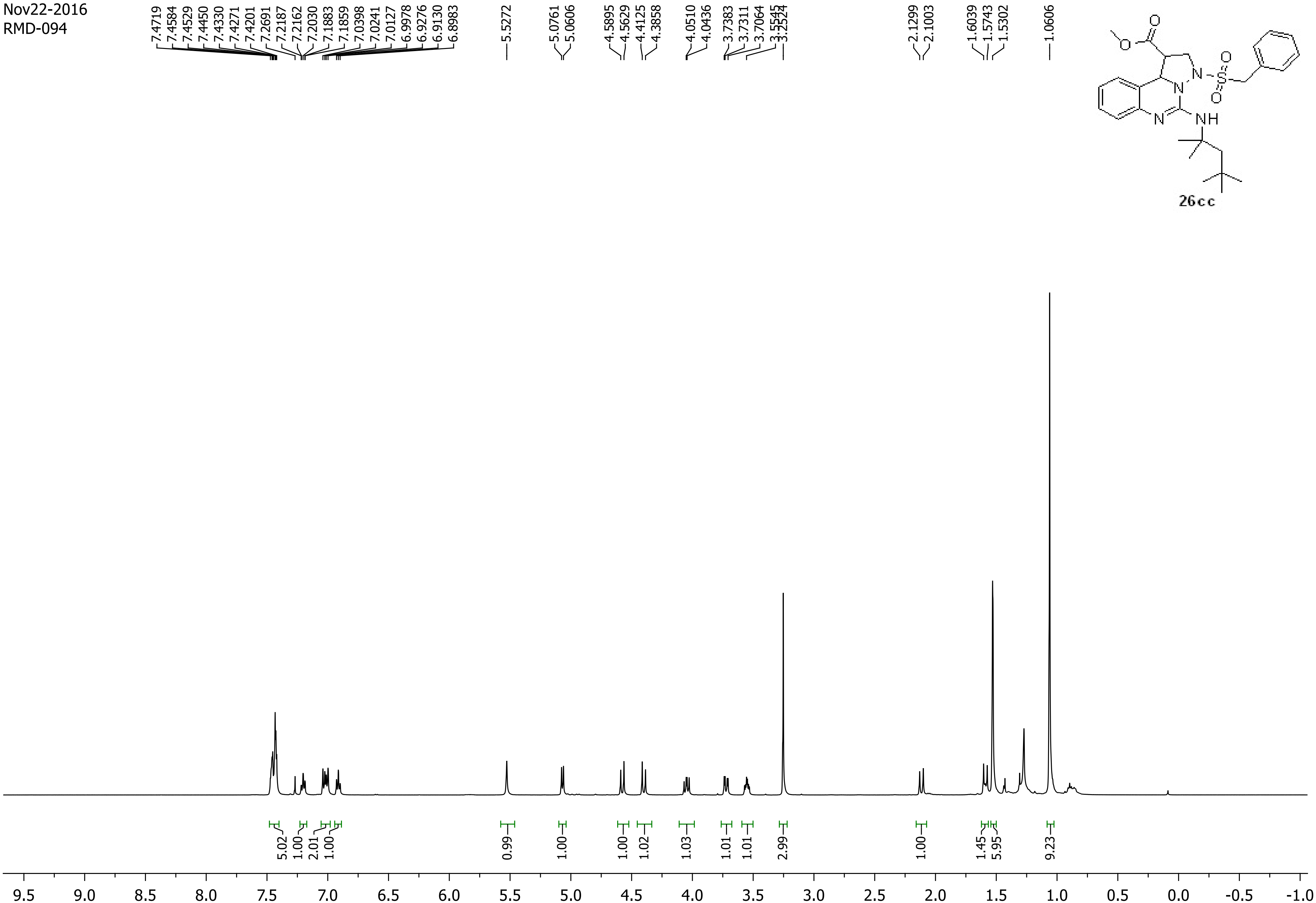
Nov23-2016
RMD-103





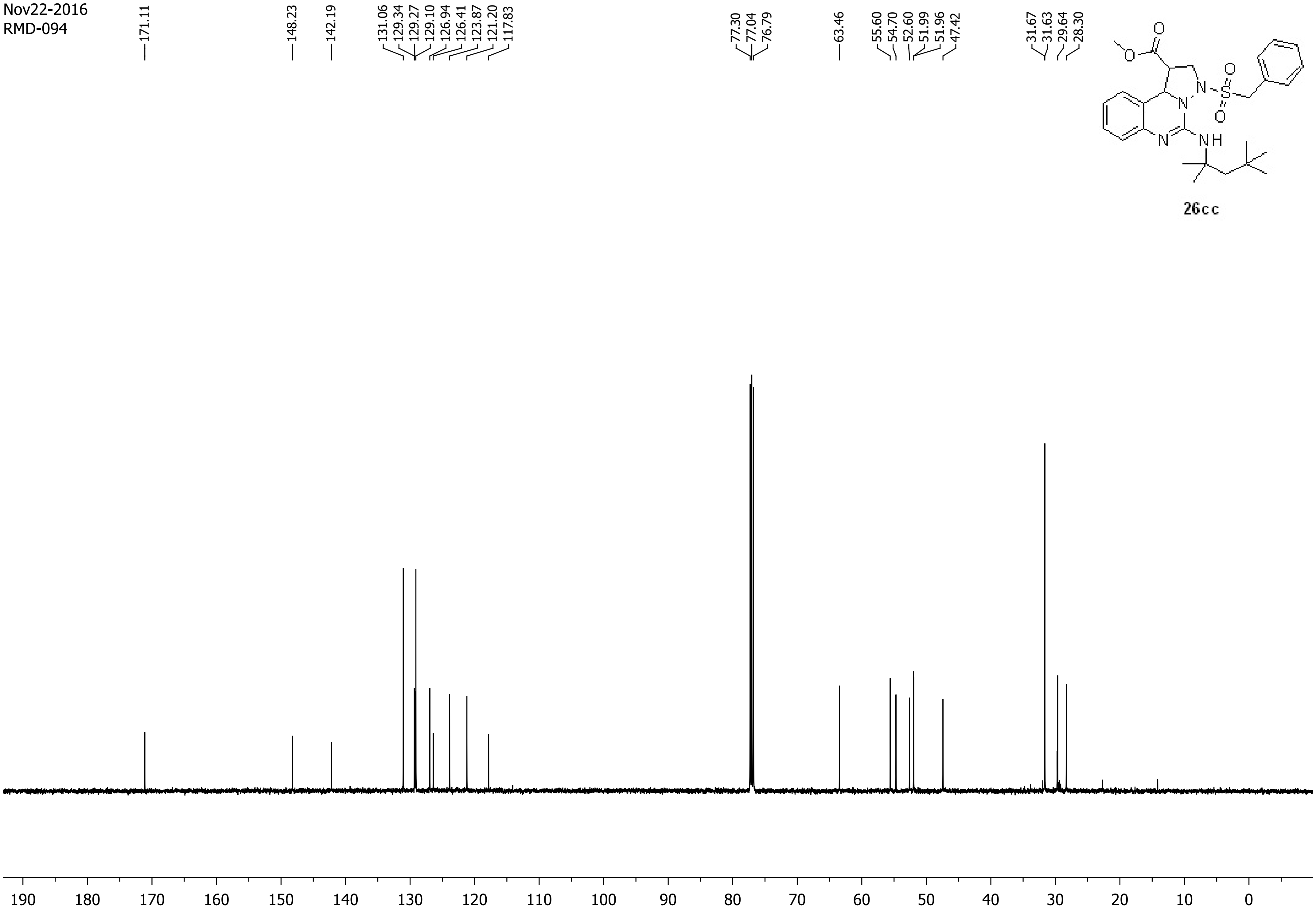
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:14:09
RMD-103_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,533.20,0.70); Sb (2,10.00); Cm (17:28)
1: TOF MS ES+
7.48e5
533.1975
421.1006
358.2679
149.0399
245.1378
301.1749
124.0916
172.1124
205.1132
261.1375
387.1469
469.2504
499.2815
663.5234
%
m/z

Nov22-2016
RMD-094

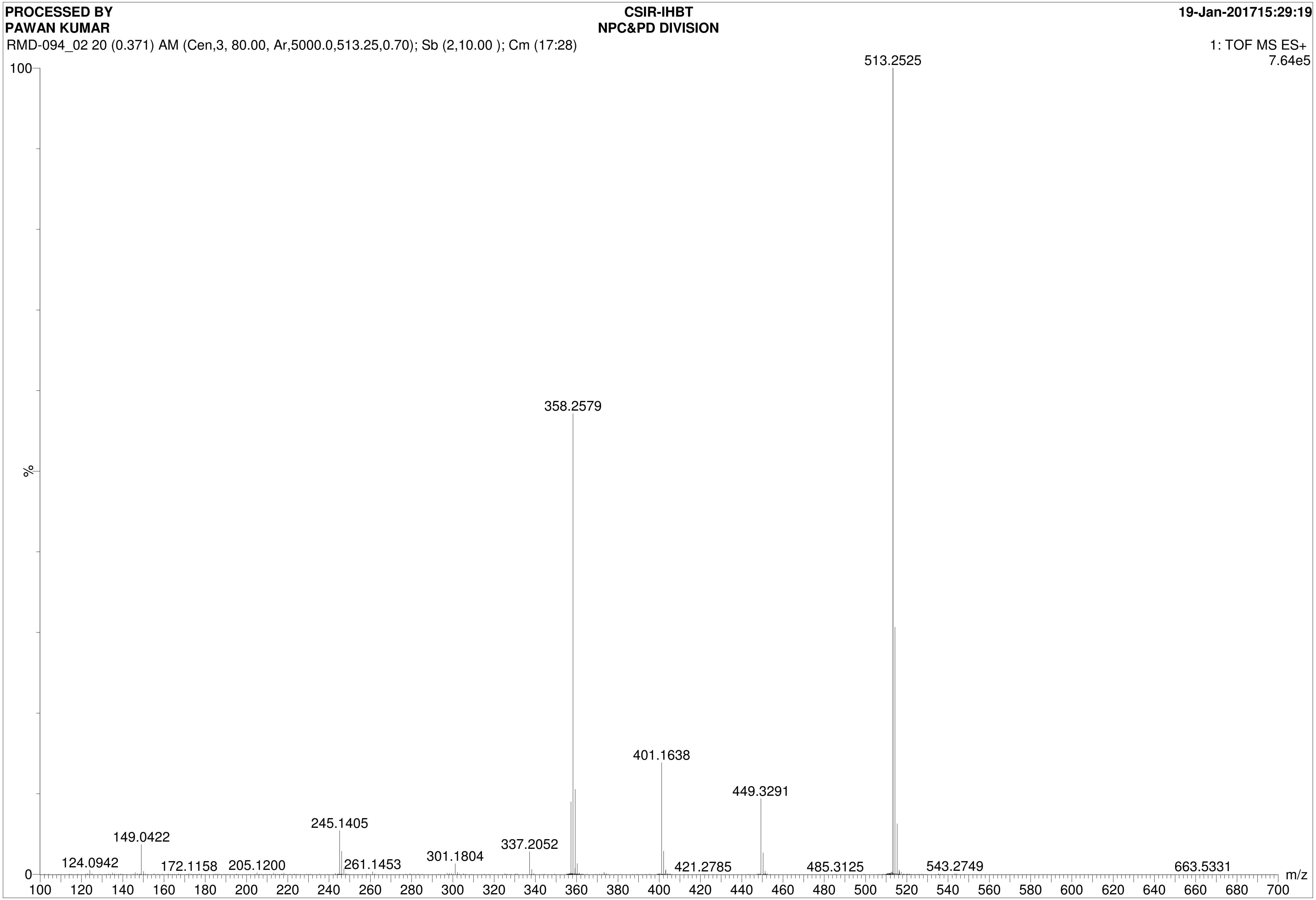


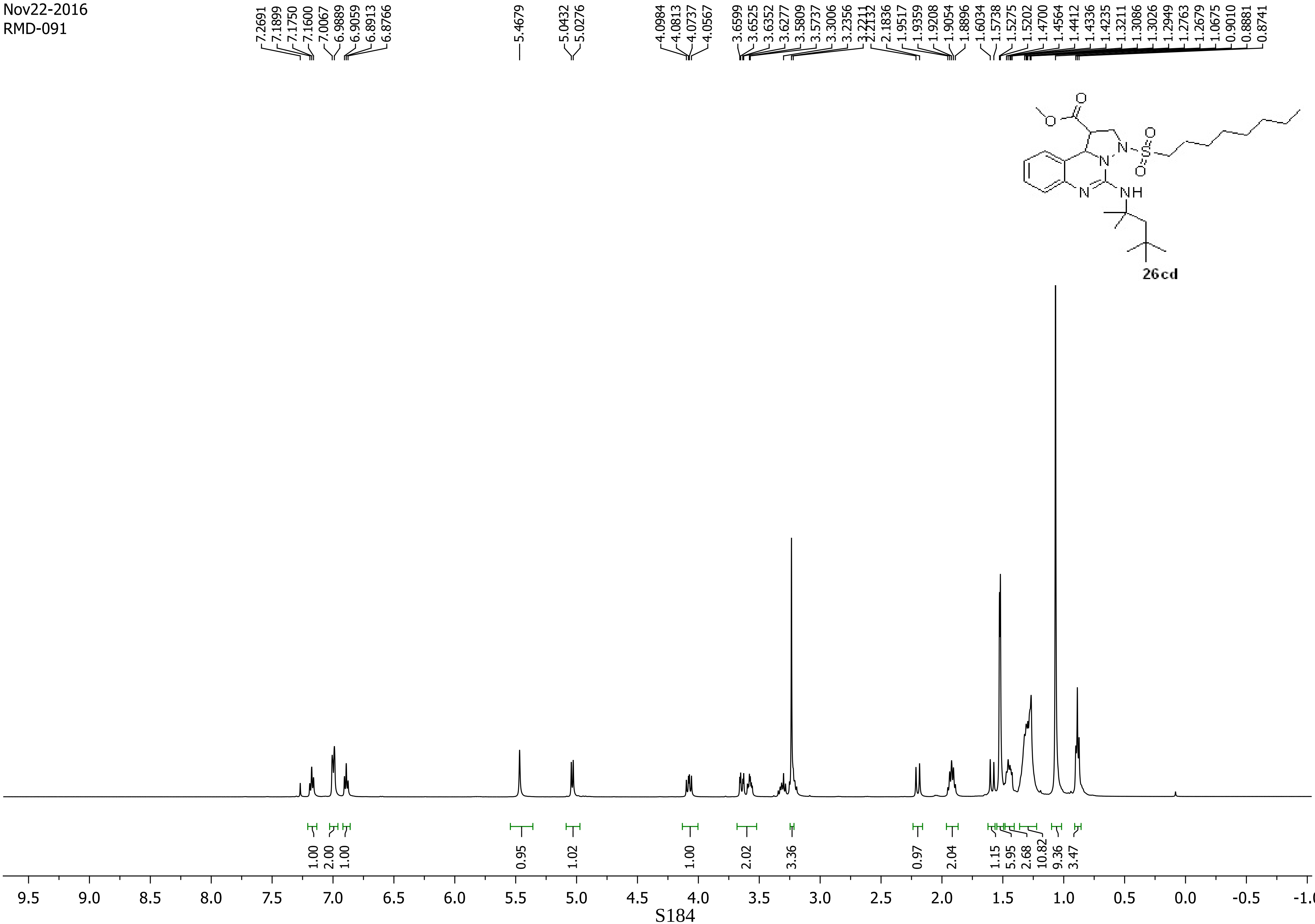
26cc

Nov22-2016
RMD-094



26cc


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:29:19
RMD-094_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,513.25,0.70); Sb (2,10.00); Cm (17:28)
1: TOF MS ES+
7.64e5
100
%
0
513.2525
358.2579
401.1638
449.3291
245.1405
149.0422
337.2052
301.1804
124.0942
172.1158
205.1200
261.1453
421.2785
485.3125
543.2749
663.5331
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500
520
540
560
580
600
620
640
660
680
700
m/z


Nov22-2016
RMD-091
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7.1899
7.1750
7.1600
7.0067
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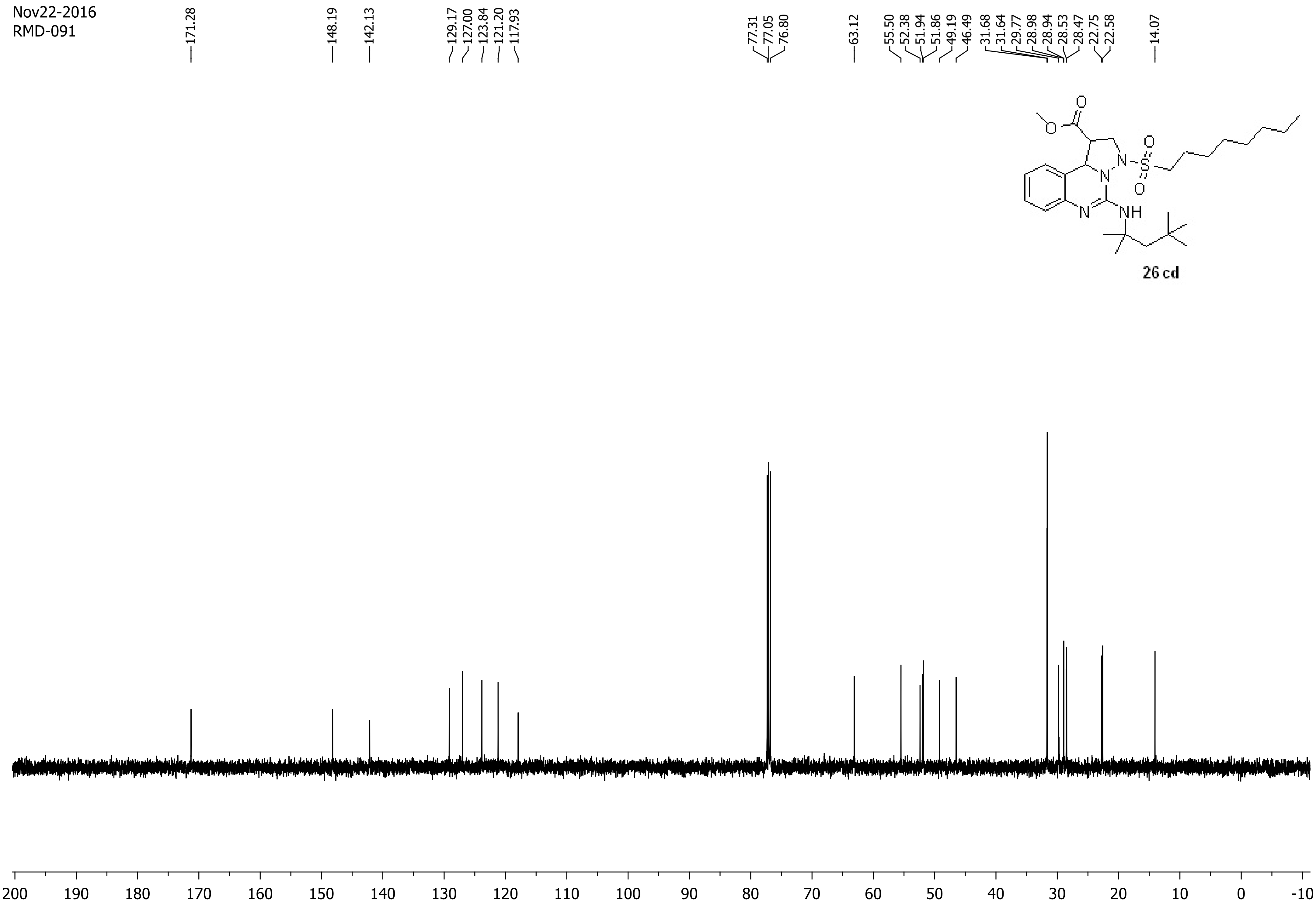
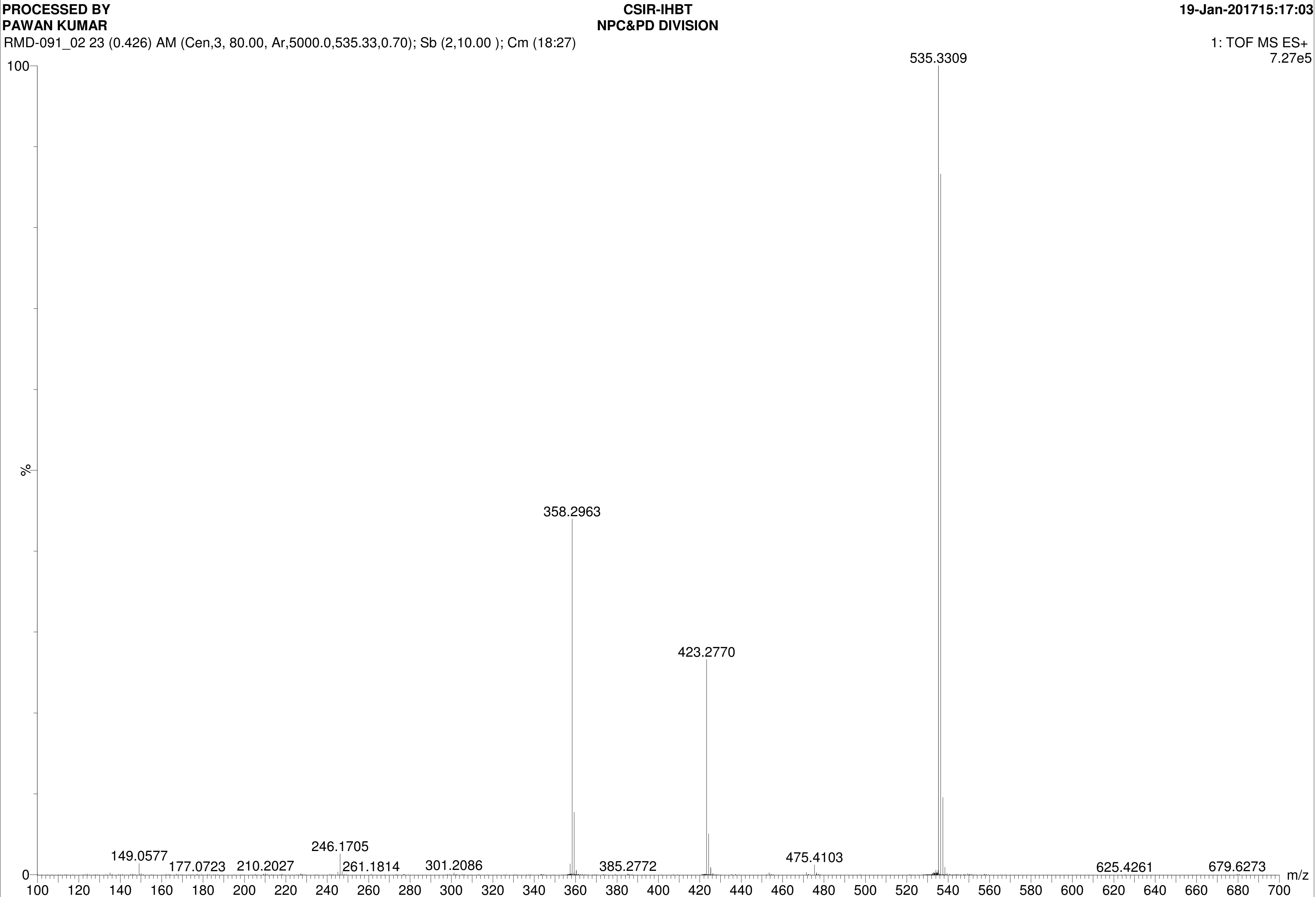
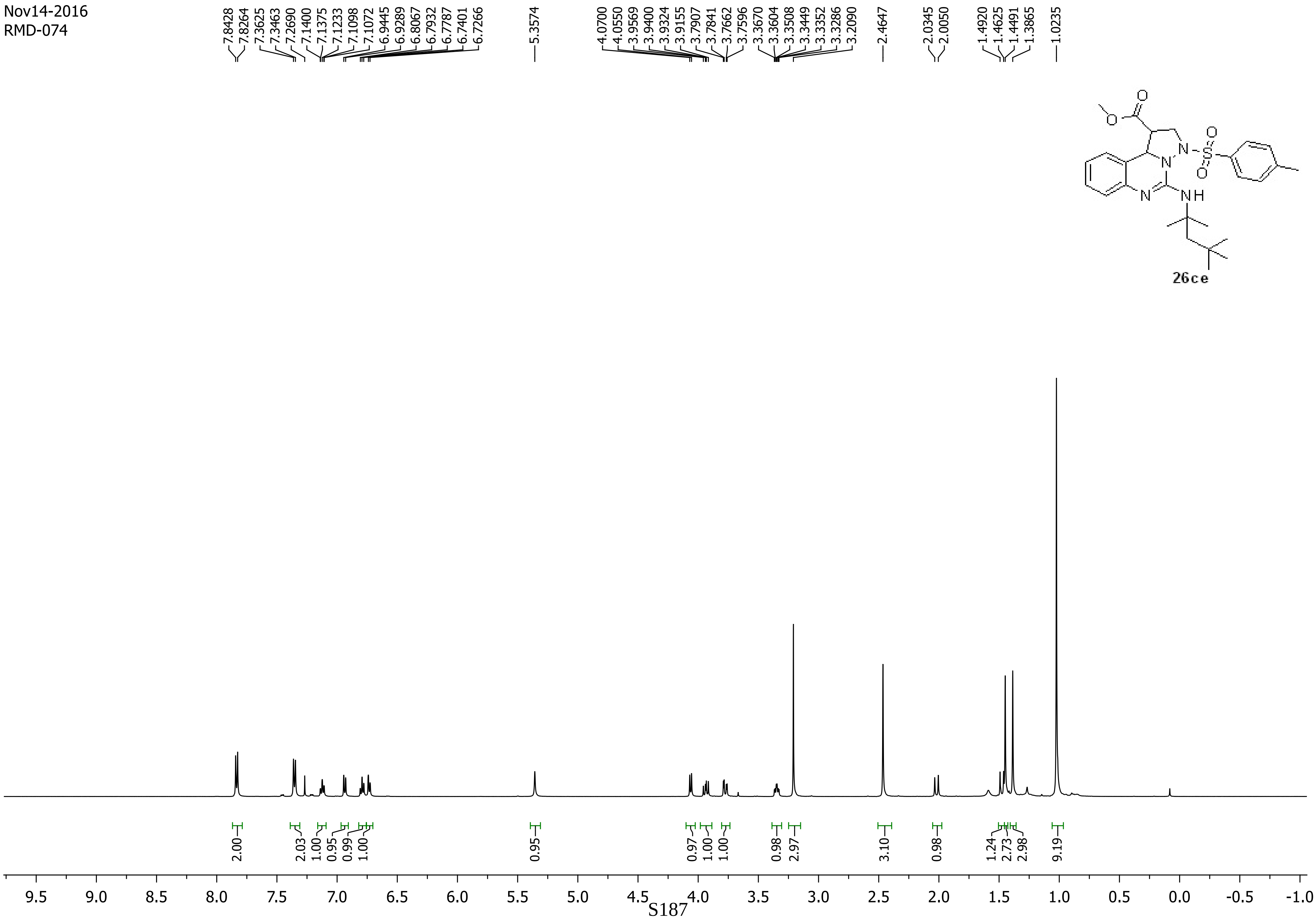
6.9059
6.8913
6.8766
5.4679
5.0432
5.0276
4.0984
4.0813
4.0737
4.0567
3.6599
3.6525
3.6352
3.6277
3.5809
3.5737
3.3006
3.2356
3.2211
3.2132
2.1836
1.9517
1.9359
1.9208
1.9054
1.8896
1.6034
1.5738
1.5275
1.5202
1.4700
1.4564
1.4412
1.4336
1.4235
1.3211
1.3086
1.3026
1.2949
1.2763
1.2679
1.0675
0.9010
0.8881
0.8741
O
O
N
S
O
O
N
N
NH
26cd
1.00
2.00
1.00
0.95
1.02
1.00
2.02
3.36
0.97
2.04
1.15
5.95
2.68
10.82
9.36
3.47
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0

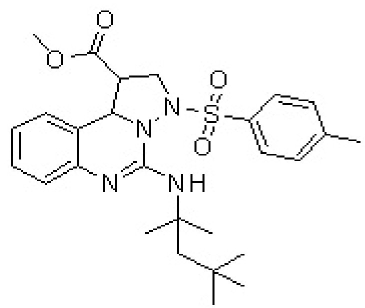

Nov22-2016
RMD-091
171.28
148.19
142.13
129.17
127.00
123.84
121.20
117.93
77.31
77.05
76.80
63.12
55.50
52.38
51.94
51.86
49.19
46.49
31.68
31.64
29.77
28.98
28.94
28.53
28.47
22.75
22.58
14.07
26cd
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:17:03
RMD-091_02 23 (0.426) AM (Cen,3, 80.00, Ar,5000.0,535.33,0.70); Sb (2,10.00); Cm (18:27)
1: TOF MS ES+
7.27e5
535.3309
358.2963
423.2770
149.0577
177.0723
210.2027
246.1705
261.1814
301.2086
385.2772
475.4103
625.4261
679.6273
%
m/z

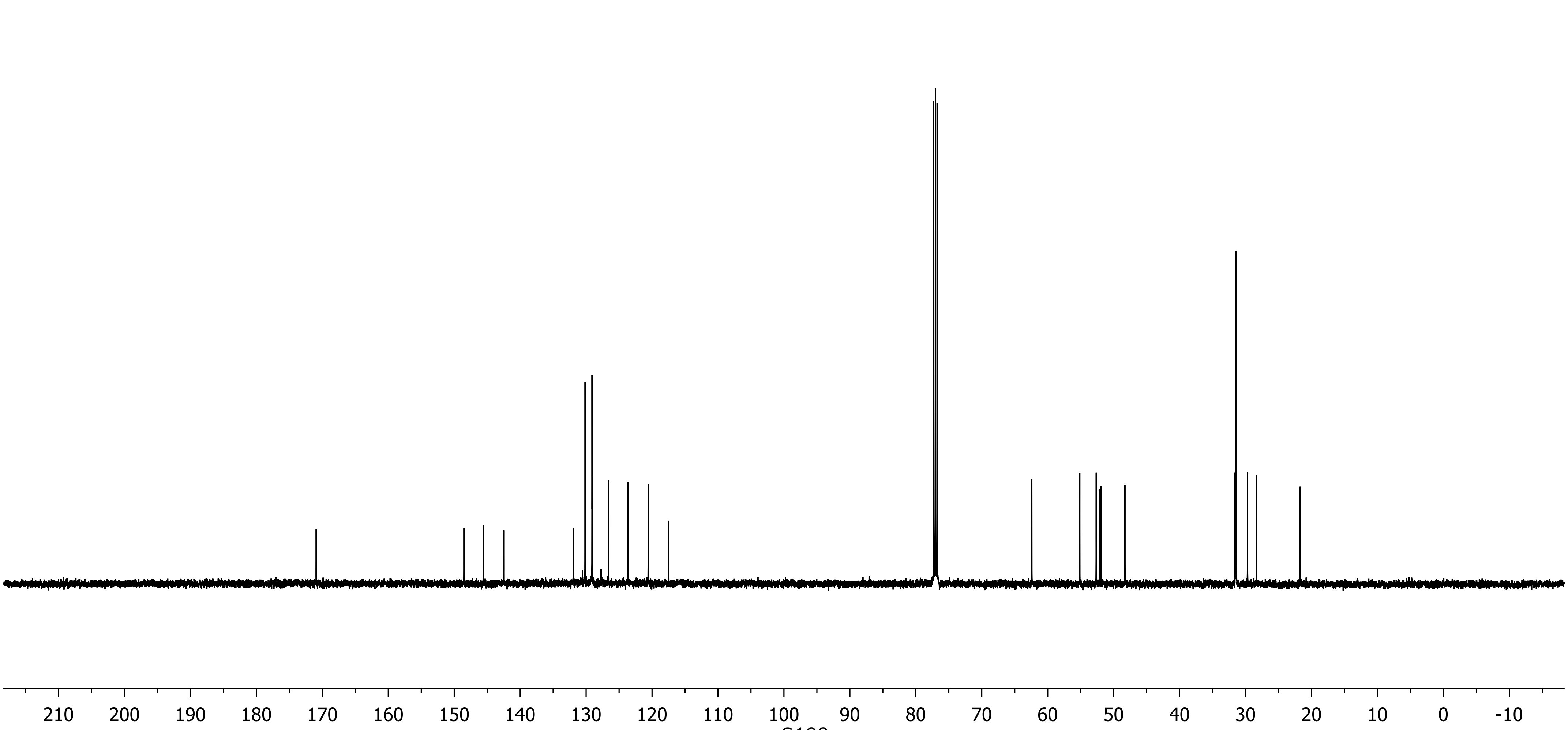
Nov14-2016
RMD-074

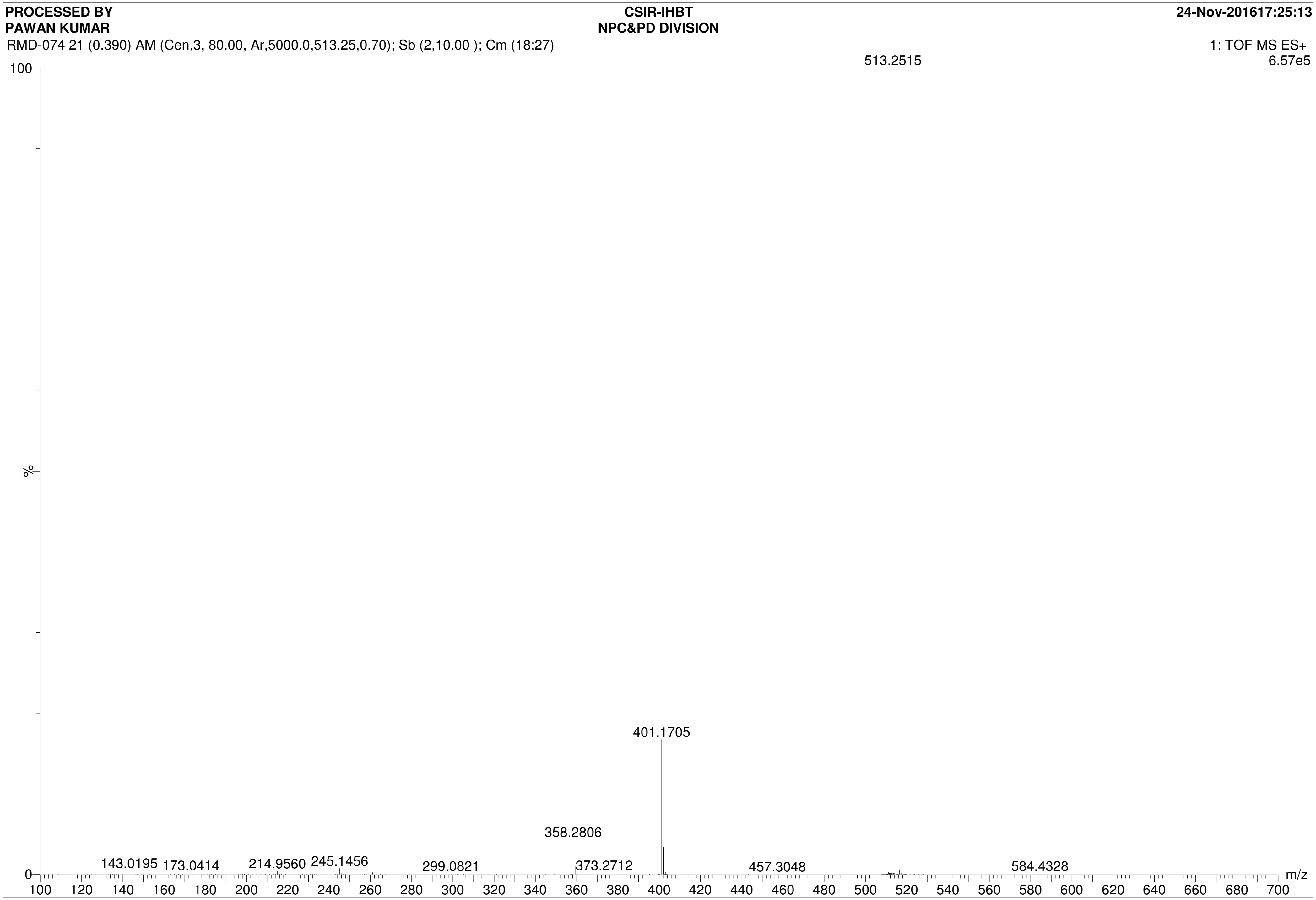


Nov14-2016
RMD-074

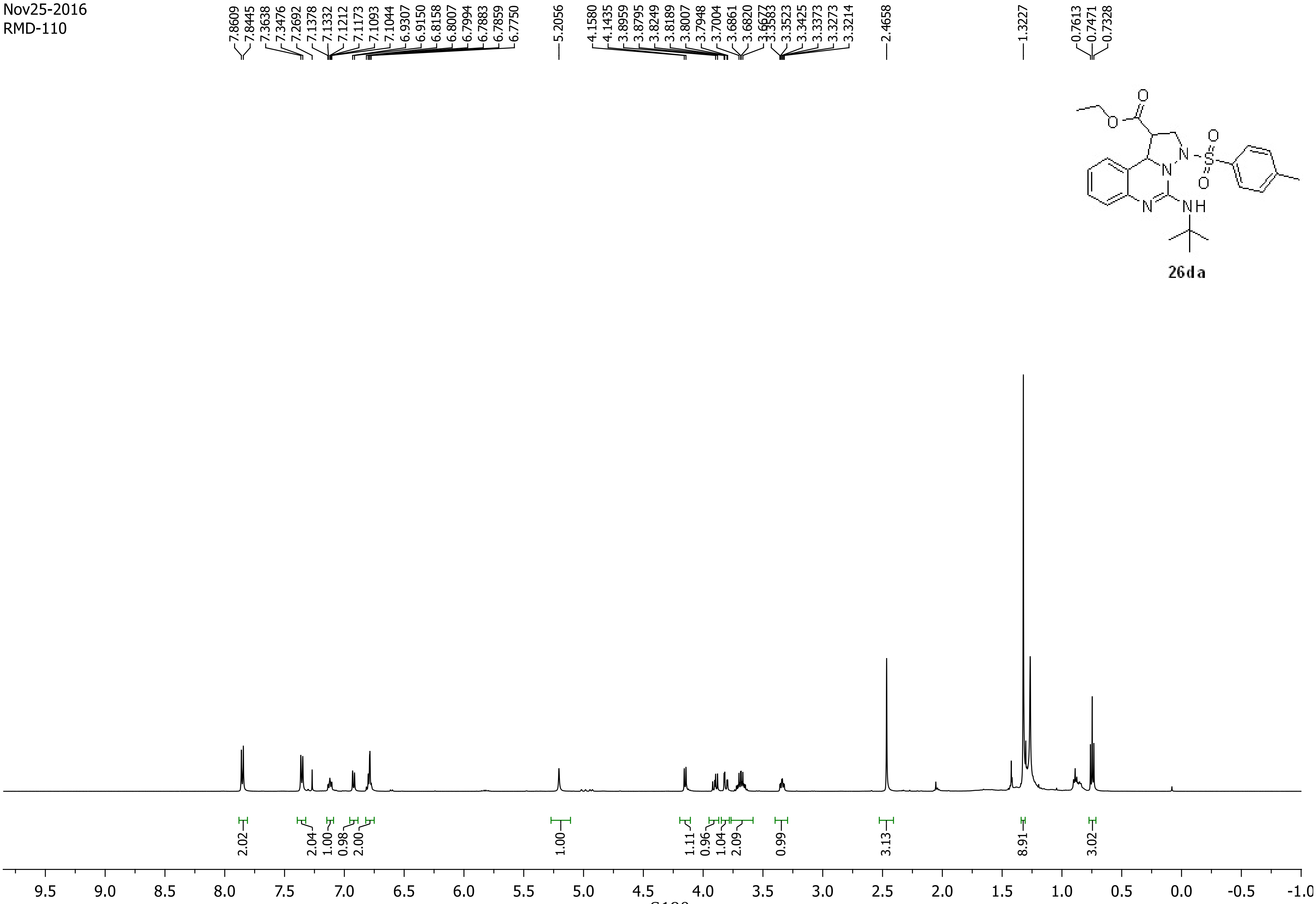


26ce



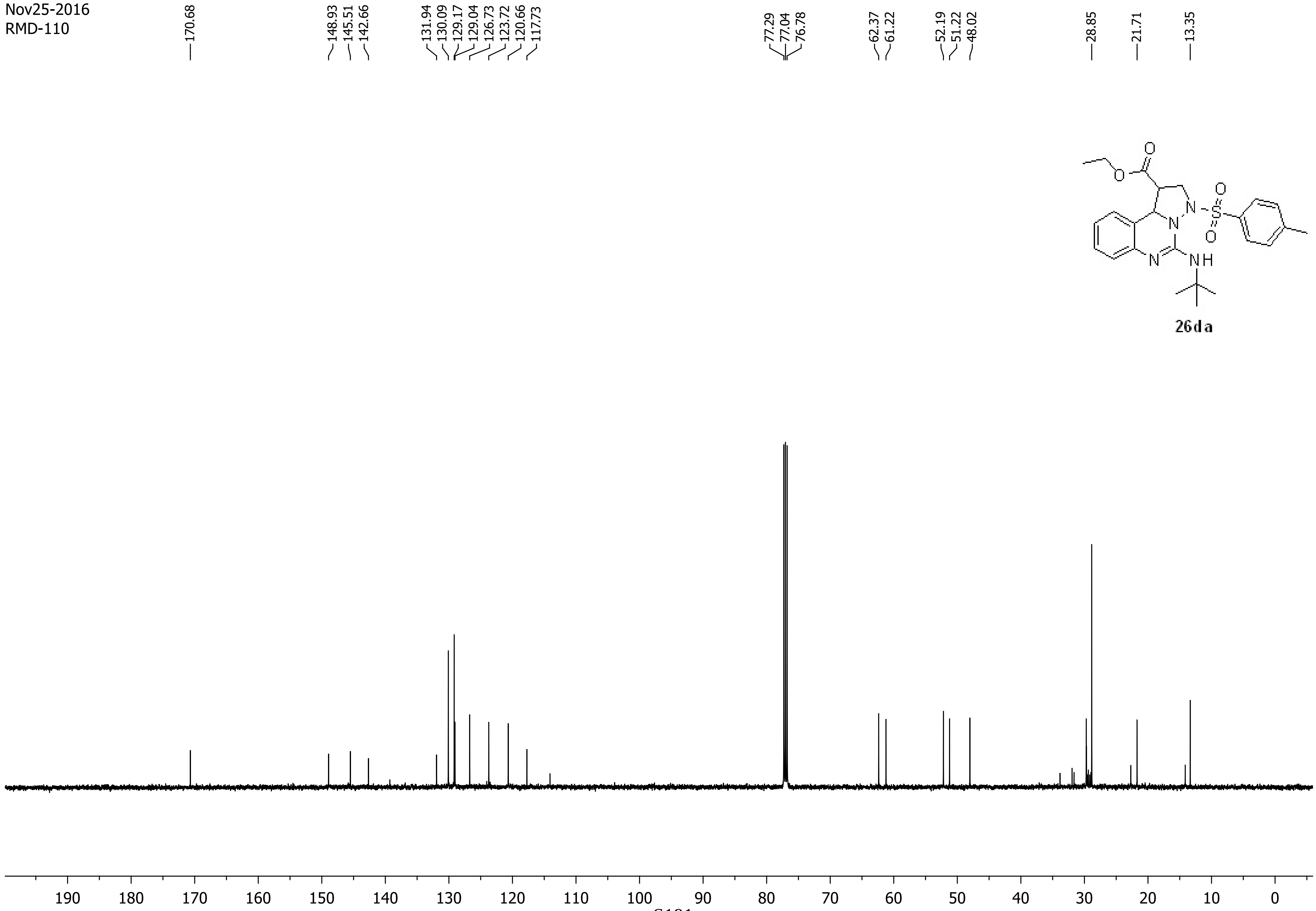

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-Nov-201617:25:13
RMD-074 21 (0.390) AM (Cen,3, 80.00, Ar,5000.0,513.25,0.70); Sb (2,10.00); Cm (18:27)
1: TOF MS ES+
6.57e5
513.2515
401.1705
358.2806
373.2712
143.0195
173.0414
214.9560
245.1456
299.0821
457.3048
584.4328
%
m/z
100
0
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700

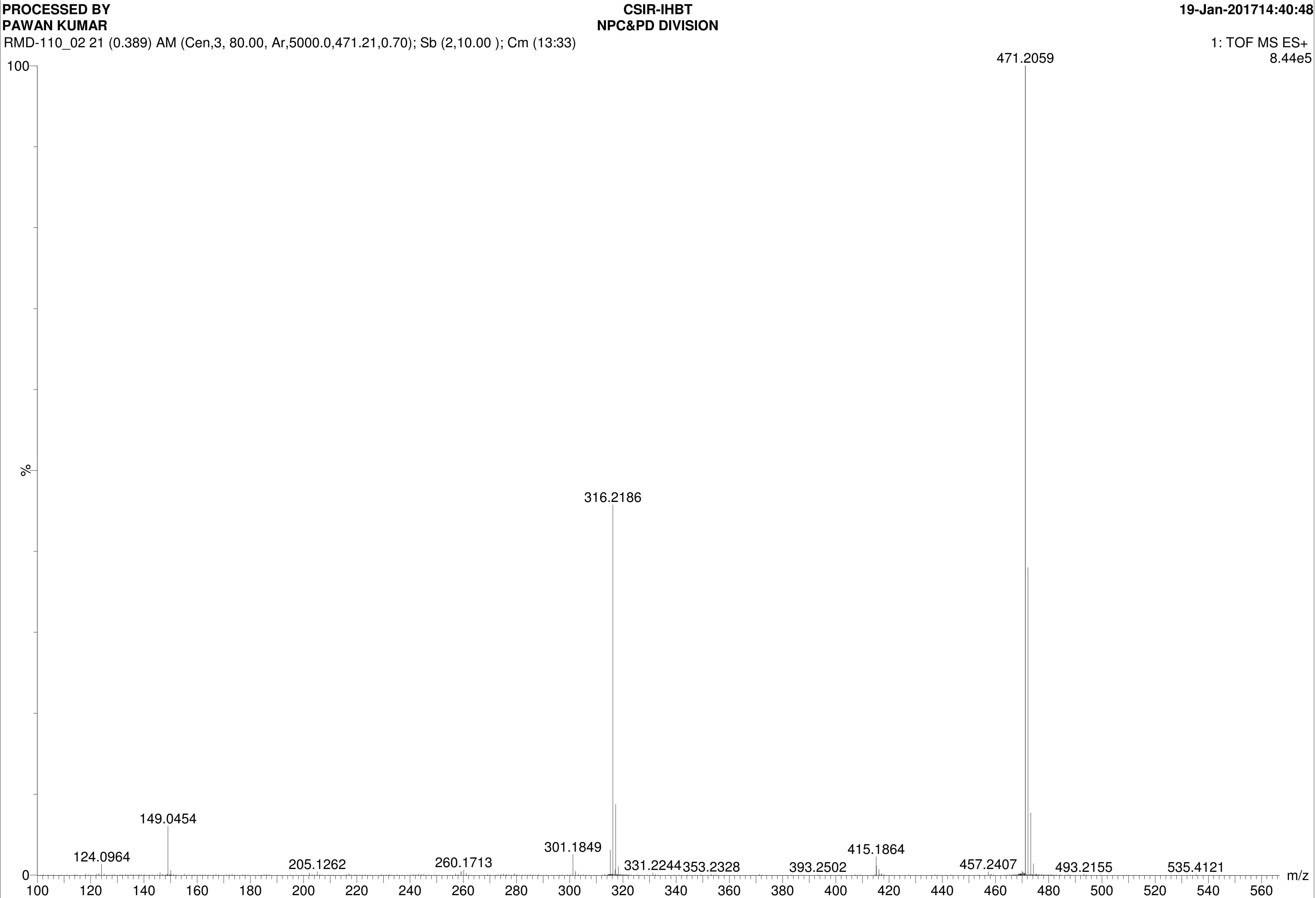
Nov25-2016
RMD-110

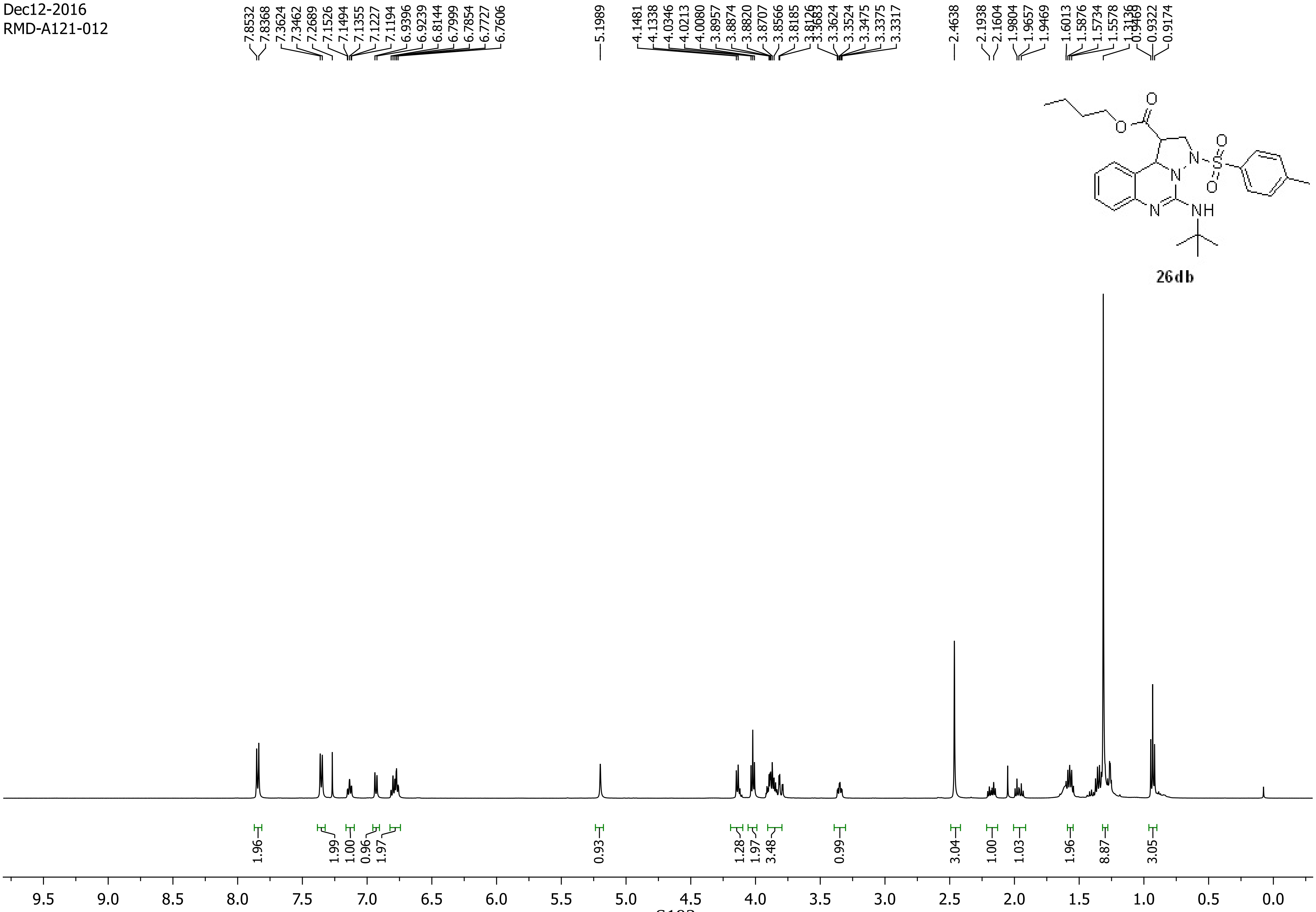


26da

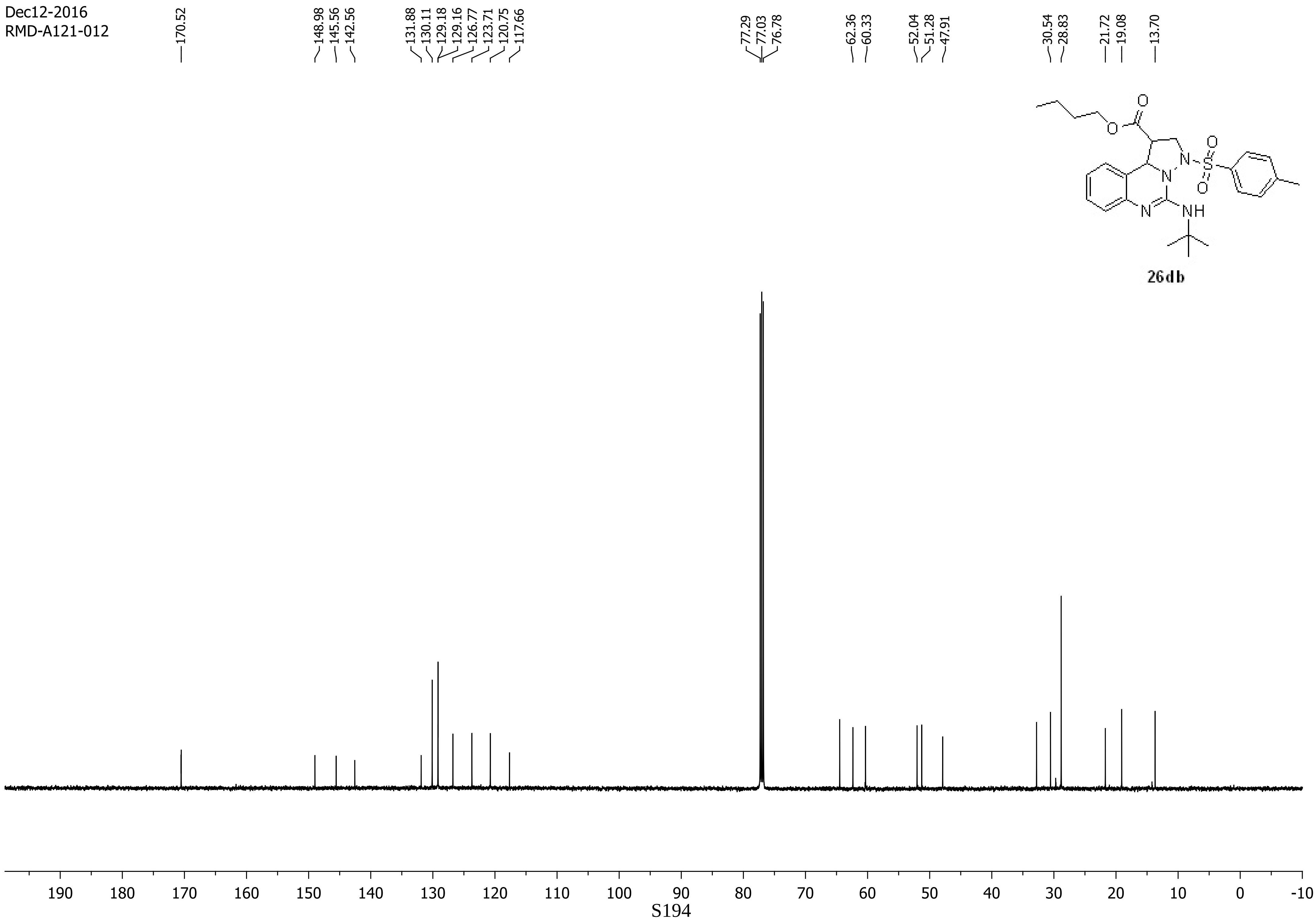
Nov25-2016
RMD-110



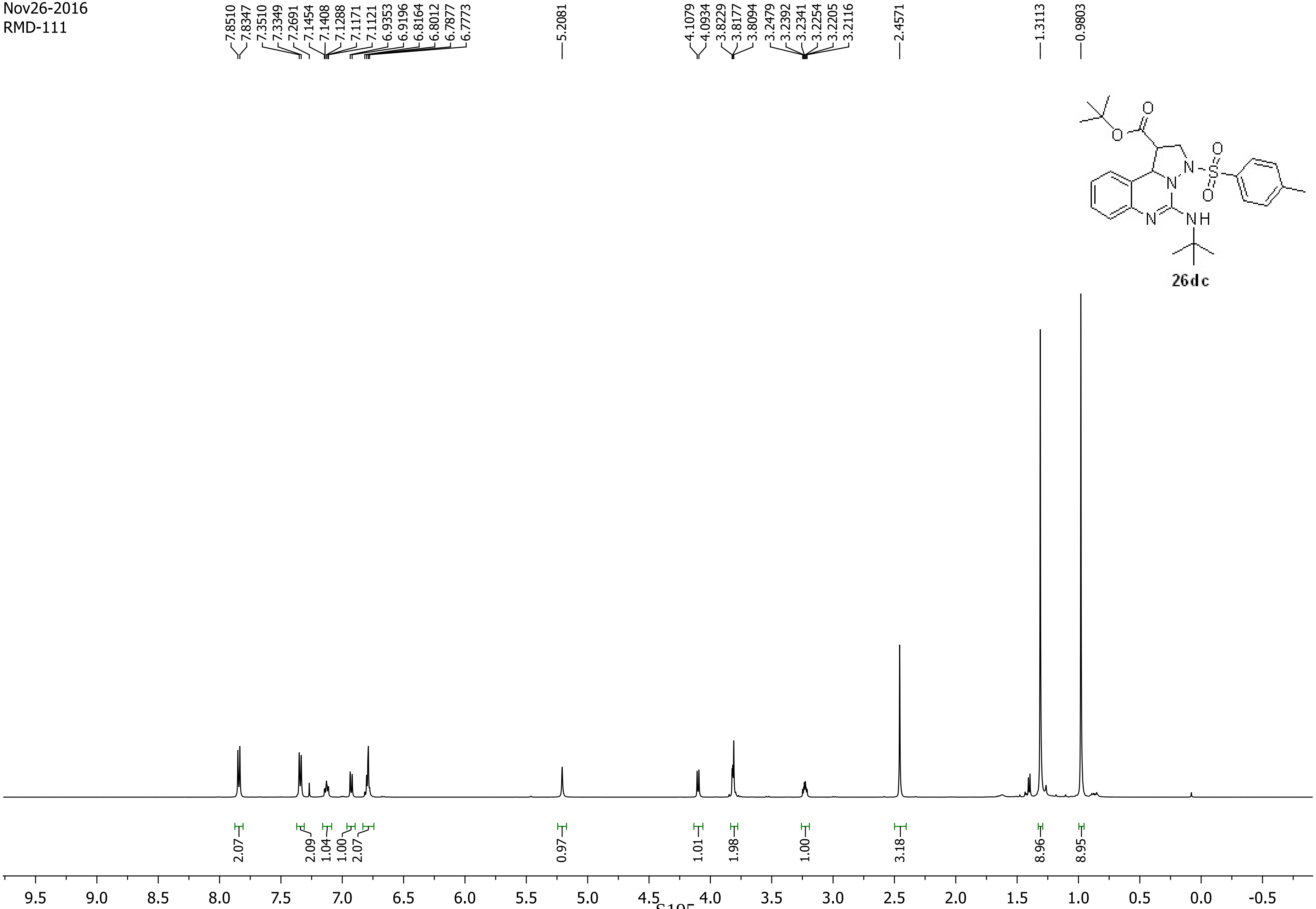

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:40:48
RMD-110_02 21 (0.389) AM (Cen,3, 80.00, Ar,5000.0,471.21,0.70); Sb (2,10.00); Cm (13:33)
1: TOF MS ES+
8.44e5
471.2059
316.2186
149.0454
124.0964
205.1262
260.1713
301.1849
331.2244
353.2328
393.2502
415.1864
457.2407
493.2155
535.4121
%
m/z


Dec12-2016
RMD-A121-012
7.8532 7.8368 7.3624 7.3462 7.2689 7.1526 7.1494 7.1355 7.1227 7.1194 6.9396 6.9239 6.8144 6.7999 6.7854 6.7727 6.7606
5.1989
4.1481 4.1338 4.0346 4.0213 4.0080 3.8957 3.8874 3.8820 3.8707 3.8566 3.8185 3.8126 3.3683 3.3624 3.3524 3.3475 3.3375 3.3317
2.4638
2.1938 2.1604 1.9804 1.9657 1.9469 1.6013 1.5876 1.5734 1.5578 1.3136 0.9469 0.9322 0.9174
1.96 1.99 1.00 0.96 1.97 0.93 1.28 1.97 3.48 0.99 3.04 1.00 1.03 1.96 8.87 3.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

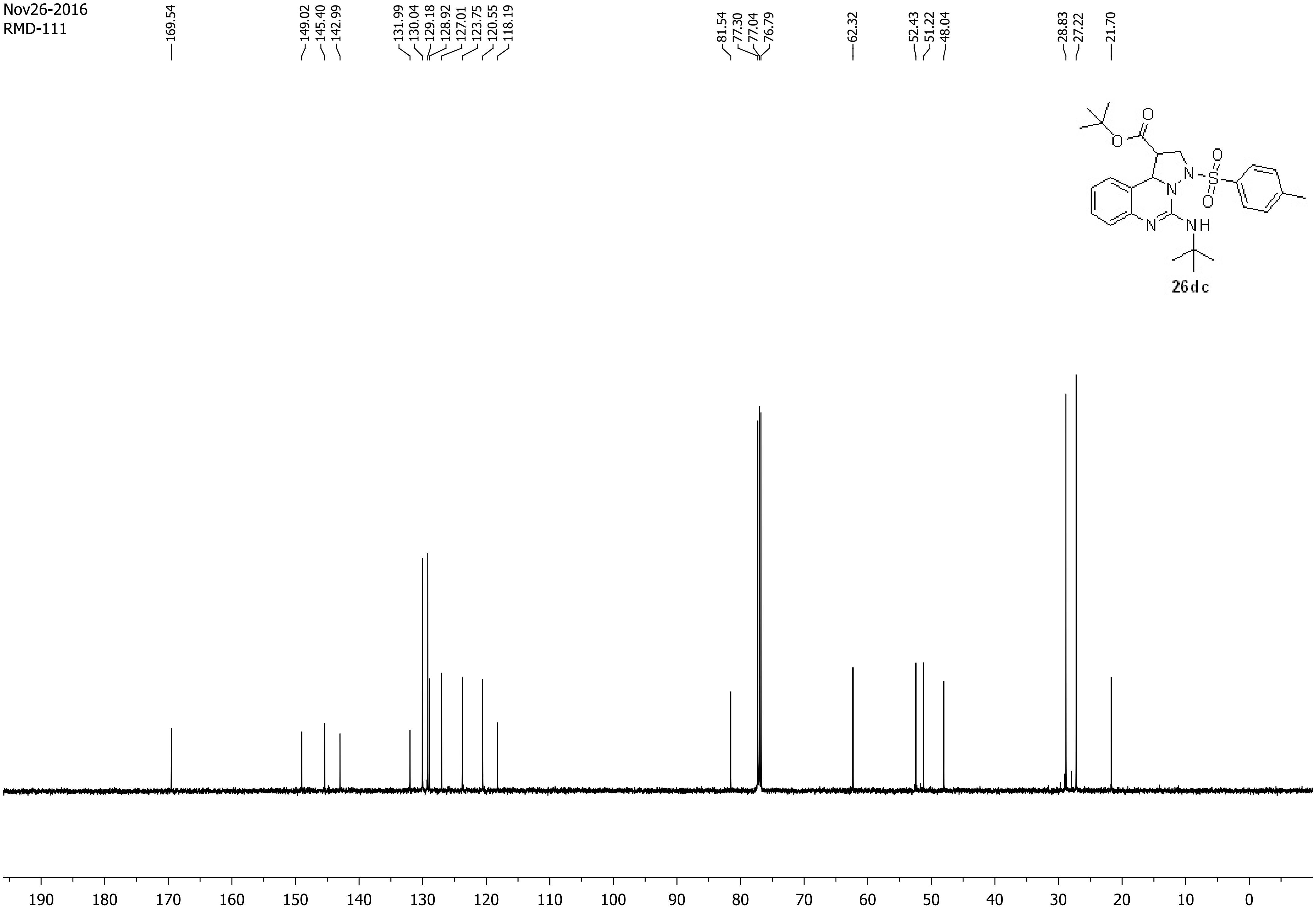
26db


Dec12-2016
RMD-A121-012
170.52
148.98
145.56
142.56
131.88
130.11
129.18
129.16
126.77
123.71
120.75
117.66
77.29
77.03
76.78
62.36
60.33
52.04
51.28
47.91
30.54
28.83
21.72
19.08
13.70
O
O
N
S
O
O
N
N
N
NH
26db
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

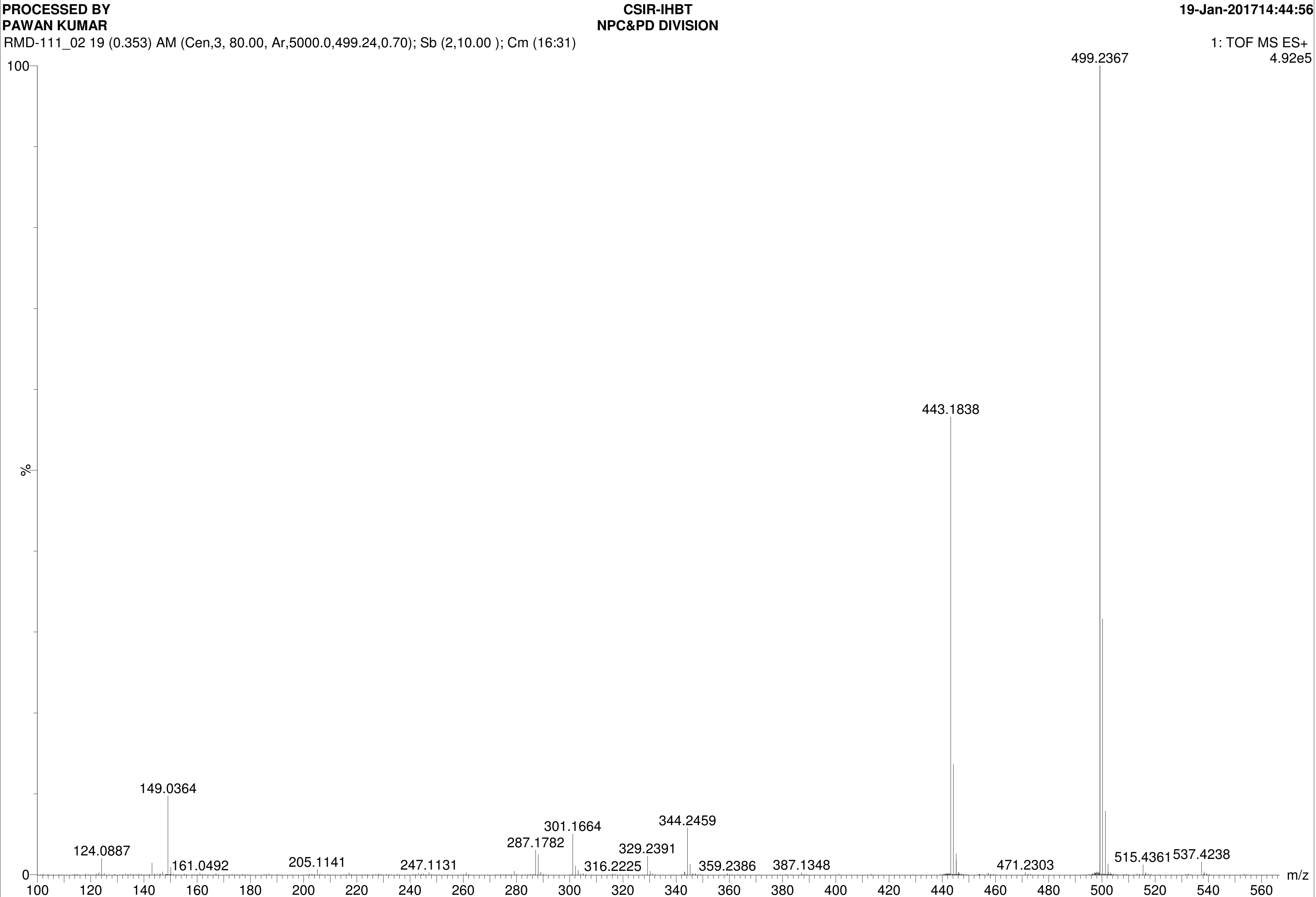
Nov26-2016
RMD-111



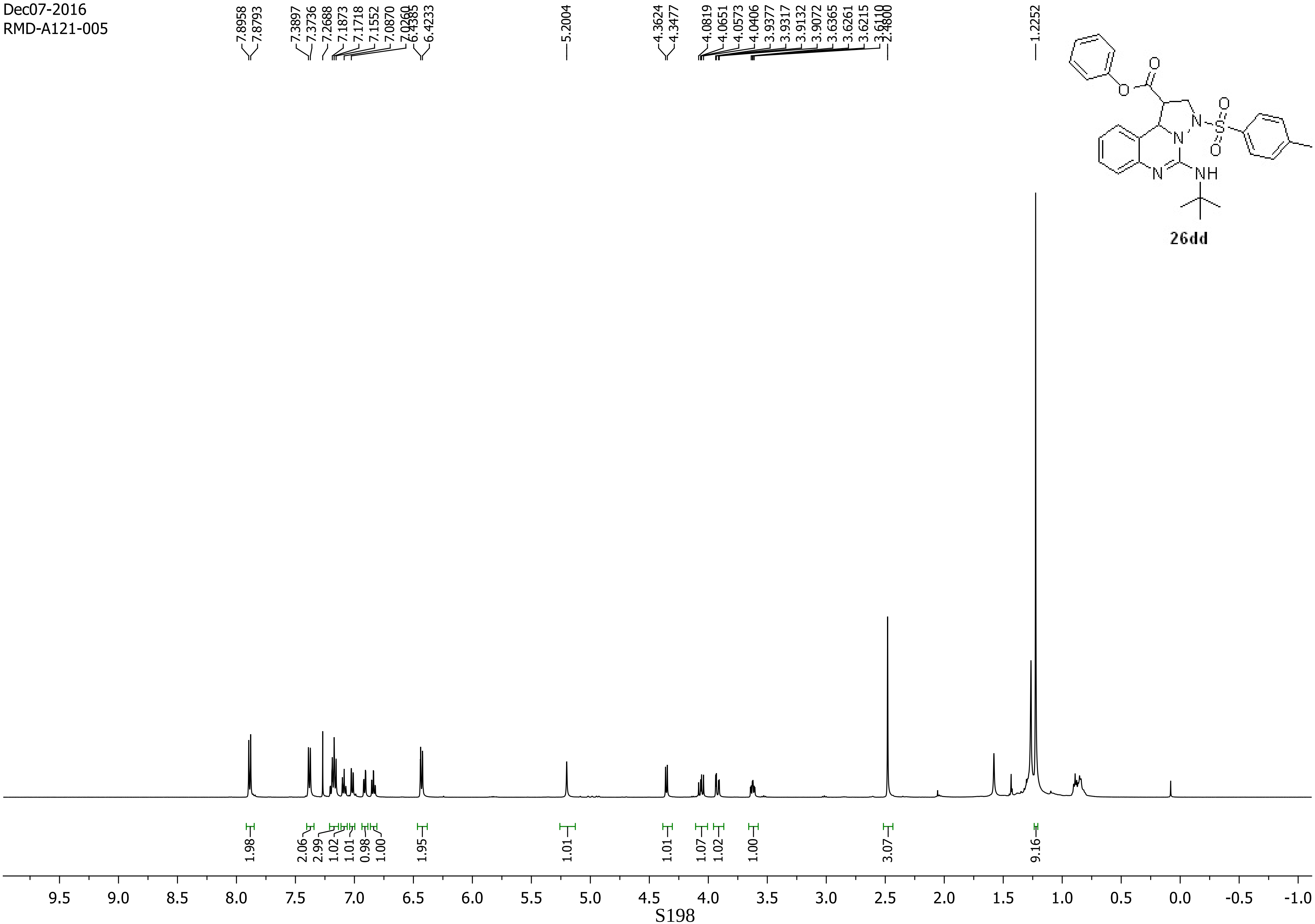
Nov26-2016
RMD-111



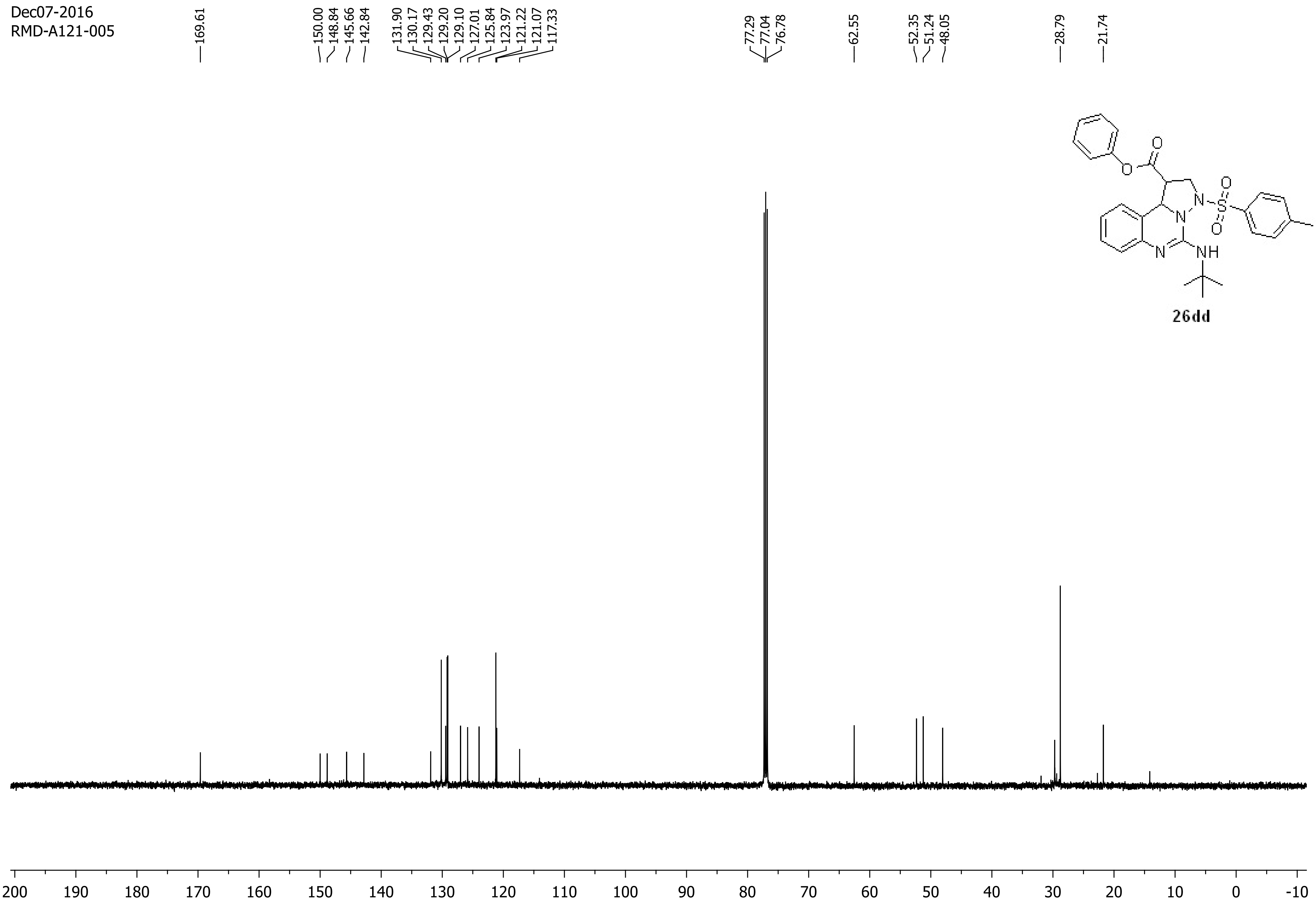
26dc

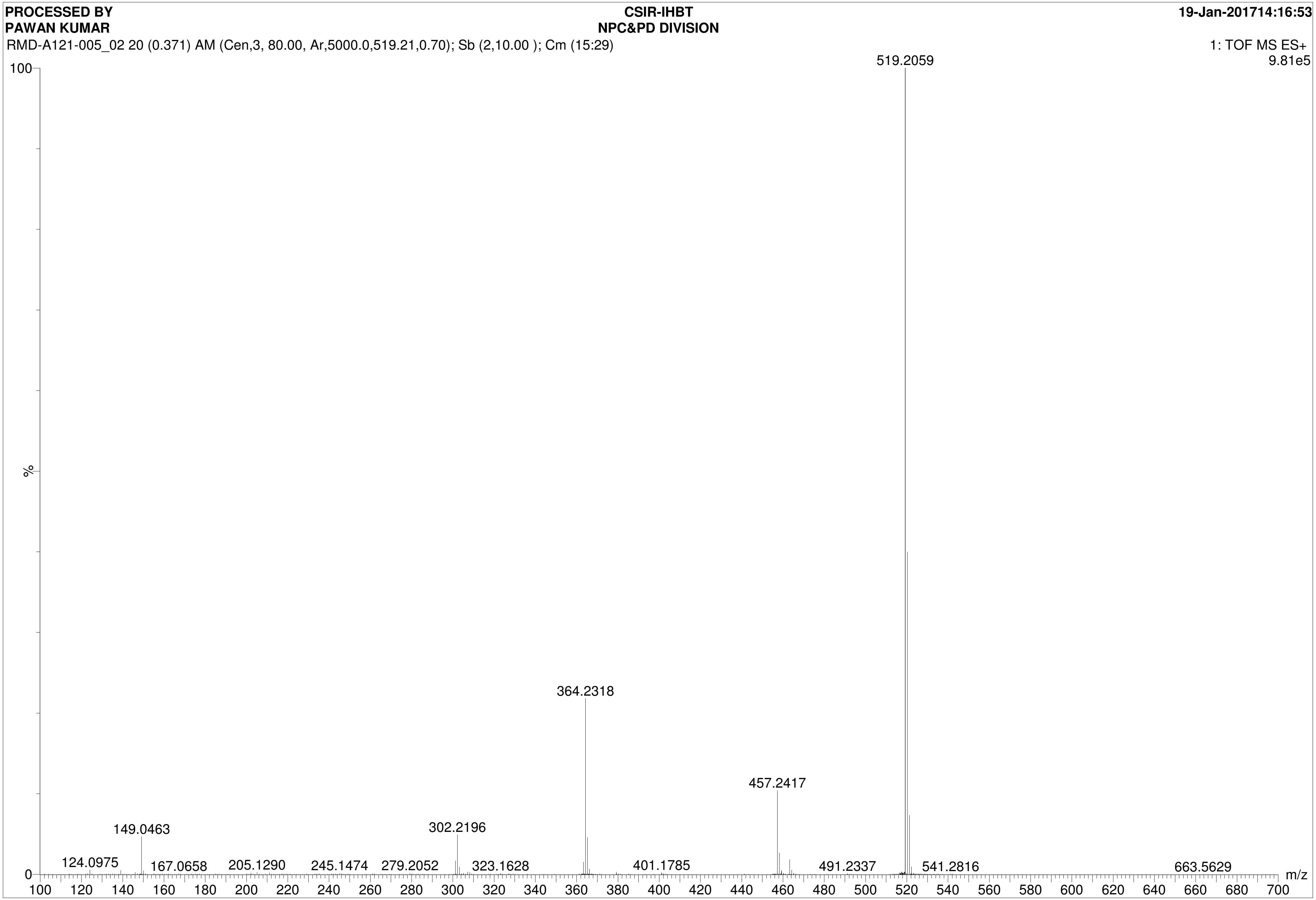

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:44:56
RMD-111_02 19 (0.353) AM (Cen,3, 80.00, Ar,5000.0,499.24,0.70); Sb (2,10.00); Cm (16:31)
1: TOF MS ES+
4.92e5
499.2367
443.1838
149.0364
124.0887
161.0492
205.1141
247.1131
287.1782
301.1664
316.2225
329.2391
344.2459
359.2386
387.1348
471.2303
515.4361
537.4238
%
m/z

Dec07-2016
RMD-A121-005

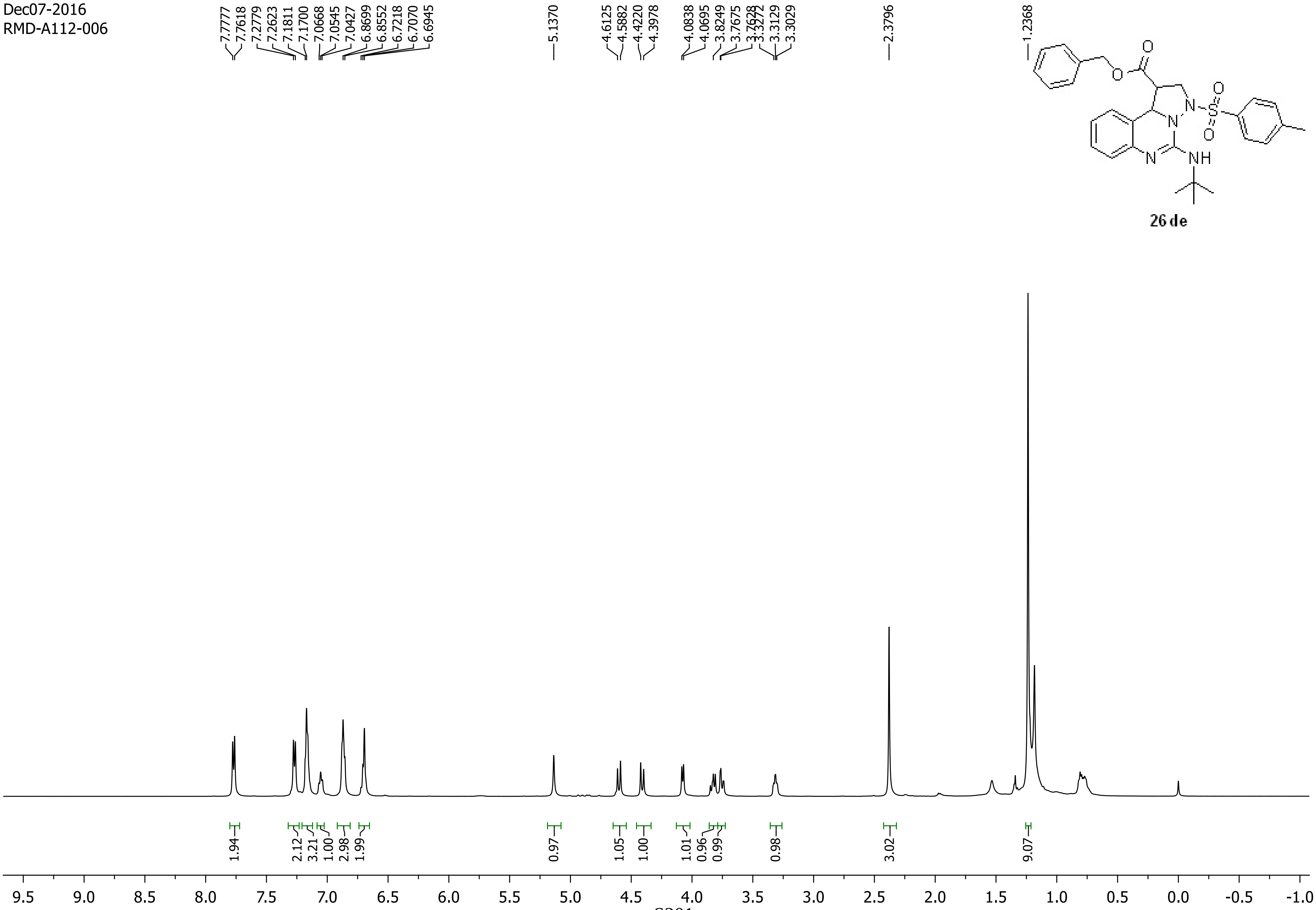


26dd

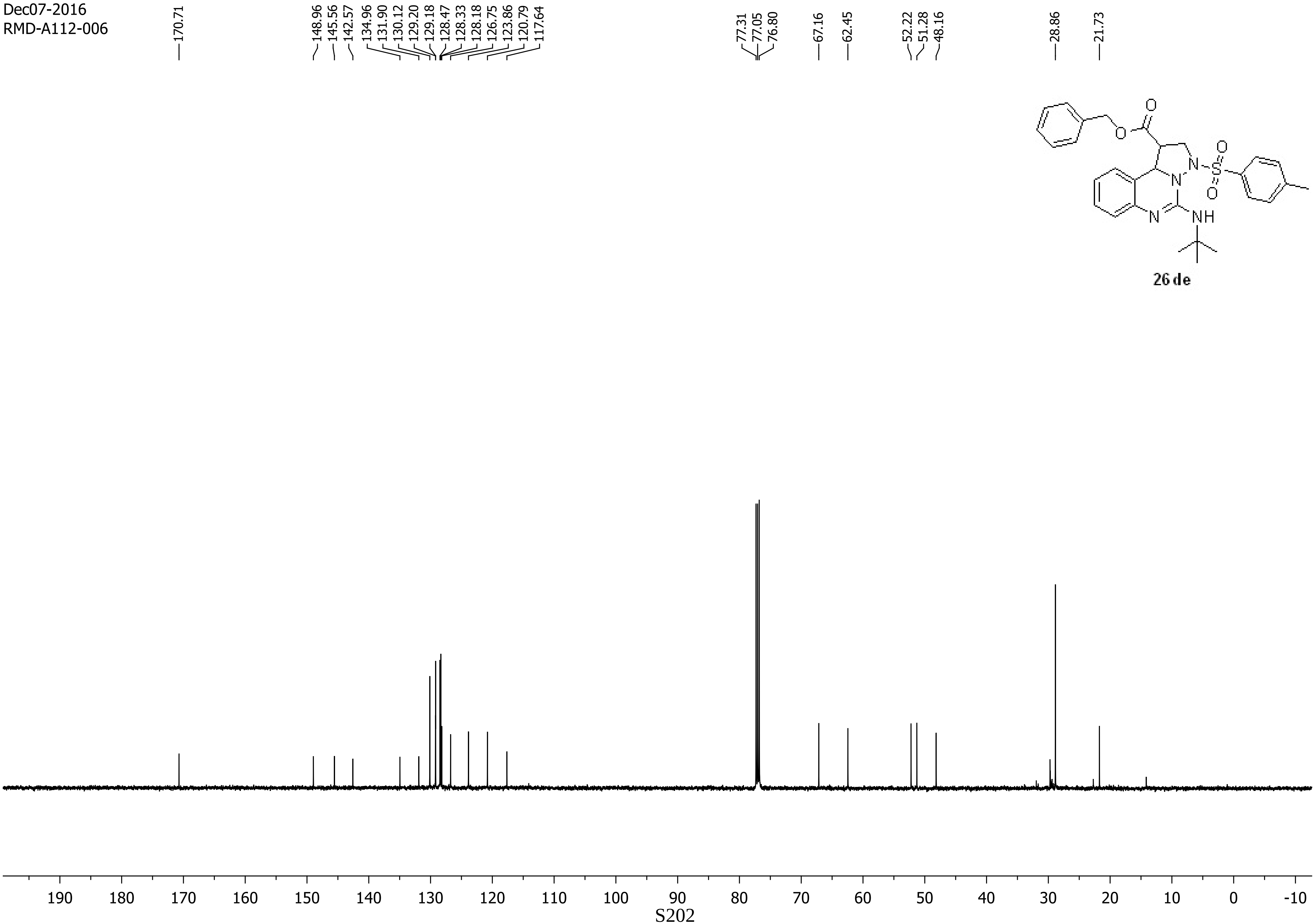

Dec07-2016
RMD-A121-005
169.61
150.00
148.84
145.66
142.84
131.90
130.17
129.43
129.20
129.10
127.01
125.84
123.97
121.22
121.07
117.33
77.29
77.04
76.78
62.55
52.35
51.24
48.05
28.79
21.74
26dd
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201714:16:53
RMD-A121-005_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,519.21,0.70); Sb (2,10.00); Cm (15:29)
1: TOF MS ES+
9.81e5
519.2059
364.2318
457.2417
149.0463
302.2196
124.0975
167.0658
205.1290
245.1474
279.2052
323.1628
401.1785
491.2337
541.2816
663.5629
%
m/z

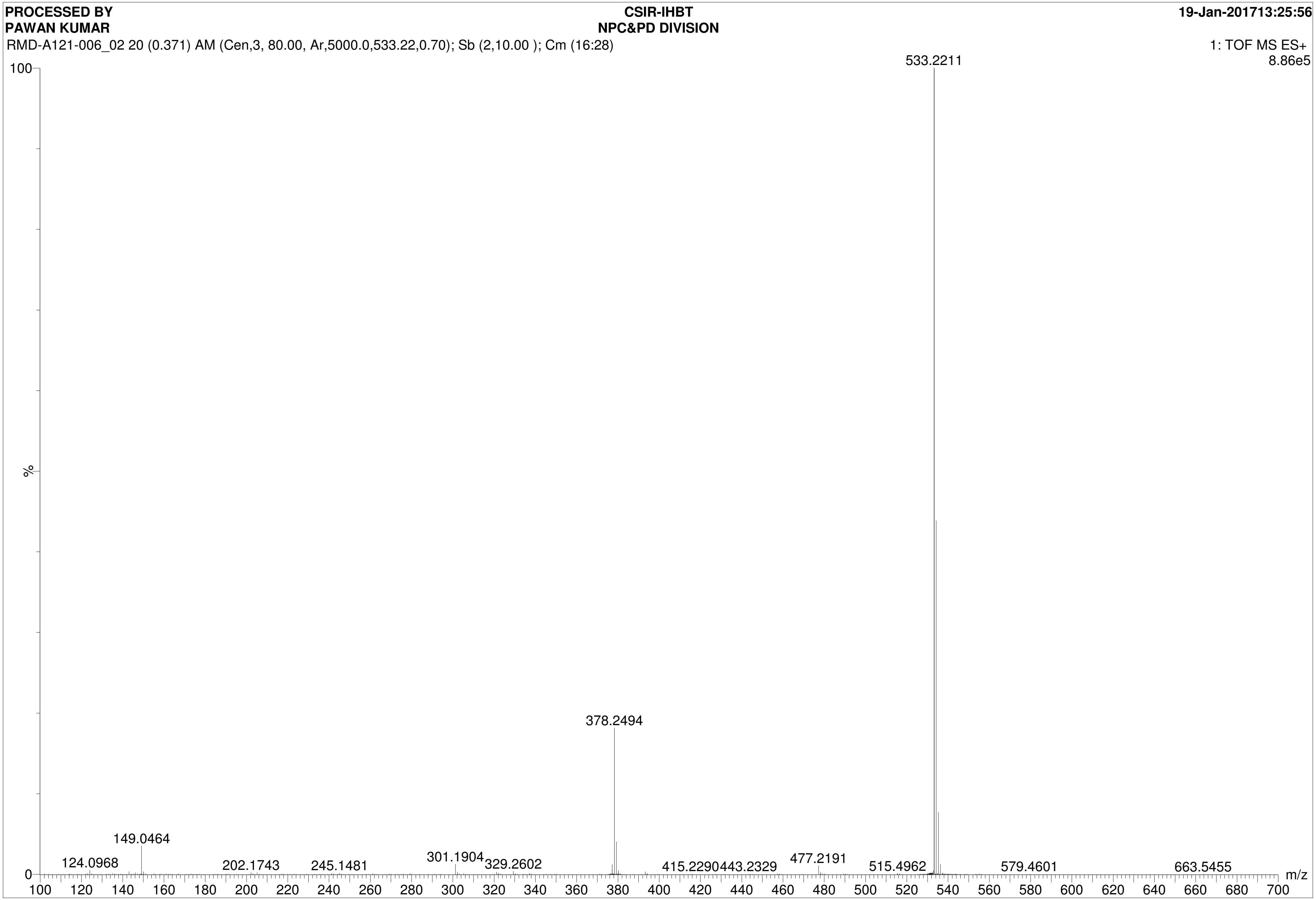
Dec07-2016
RMD-A112-006



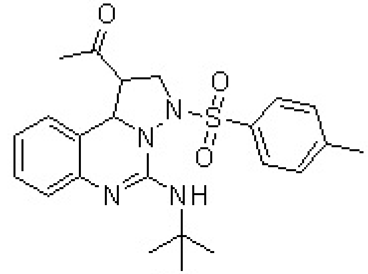
Dec07-2016
RMD-A112-006



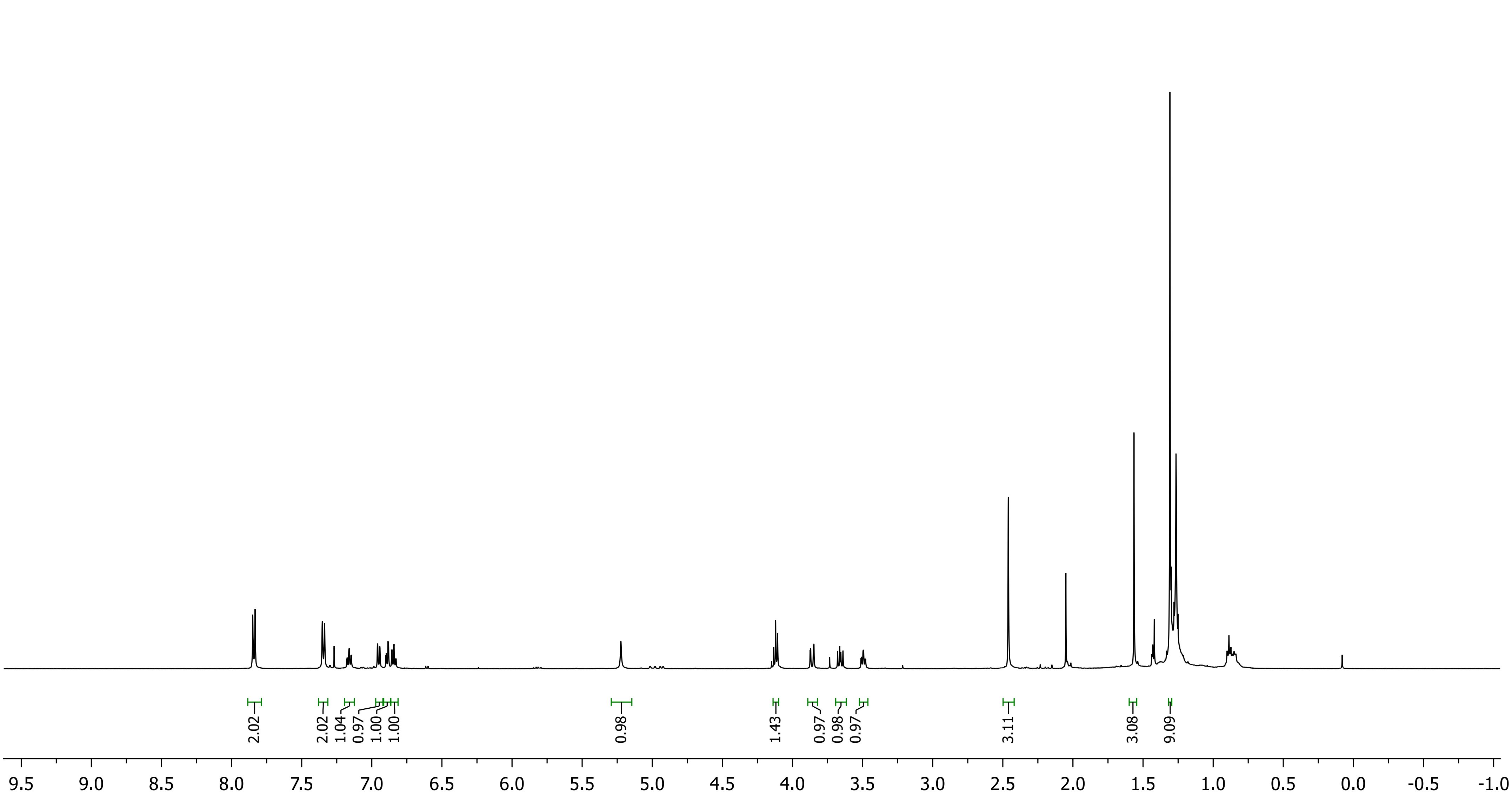
26de

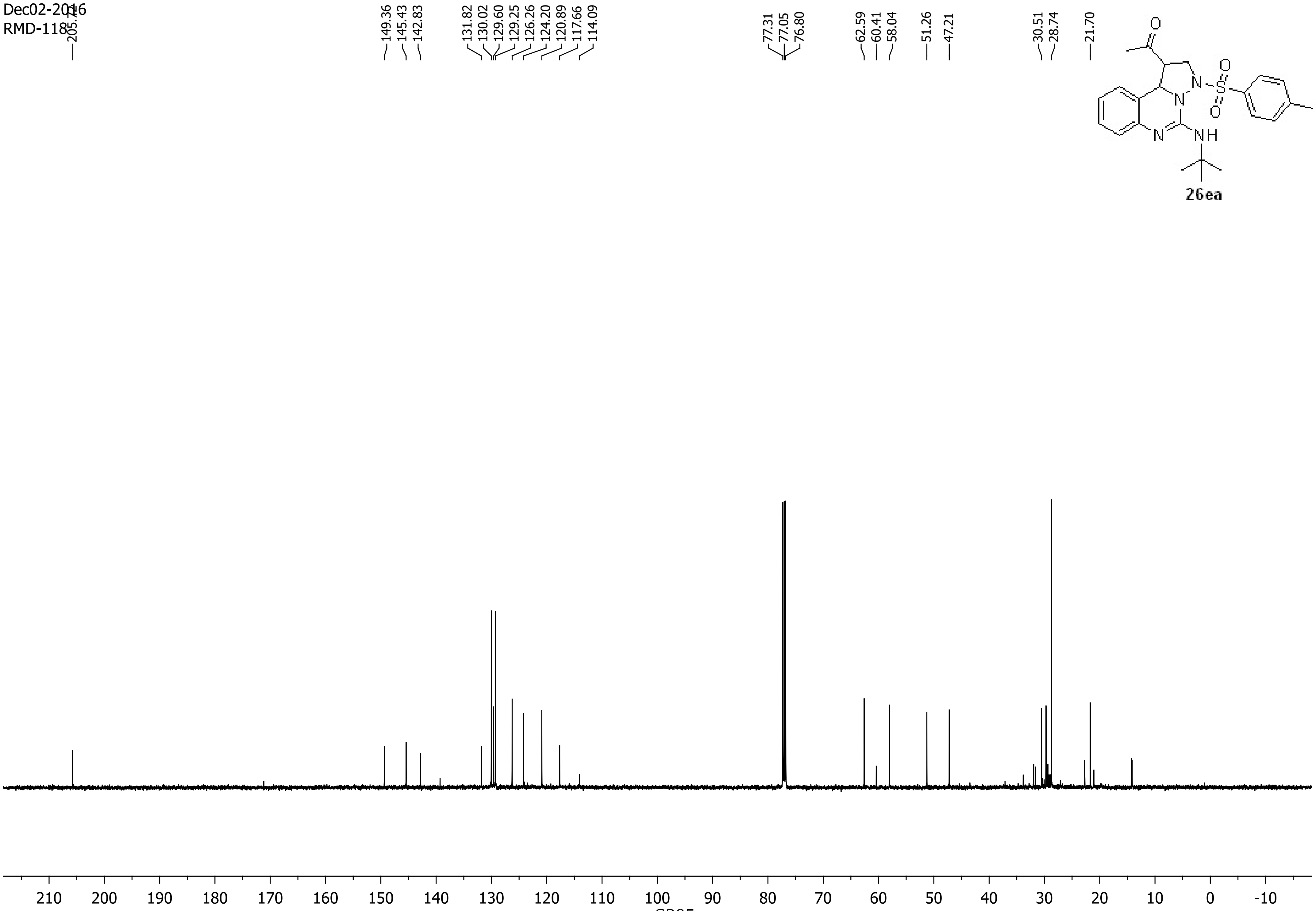

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:25:56
RMD-A121-006_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,533.22,0.70); Sb (2,10.00); Cm (16:28)
1: TOF MS ES+
8.86e5
533.2211
378.2494
149.0464
124.0968
202.1743
245.1481
301.1904
329.2602
415.2290
443.2329
477.2191
515.4962
579.4601
663.5455
%
m/z

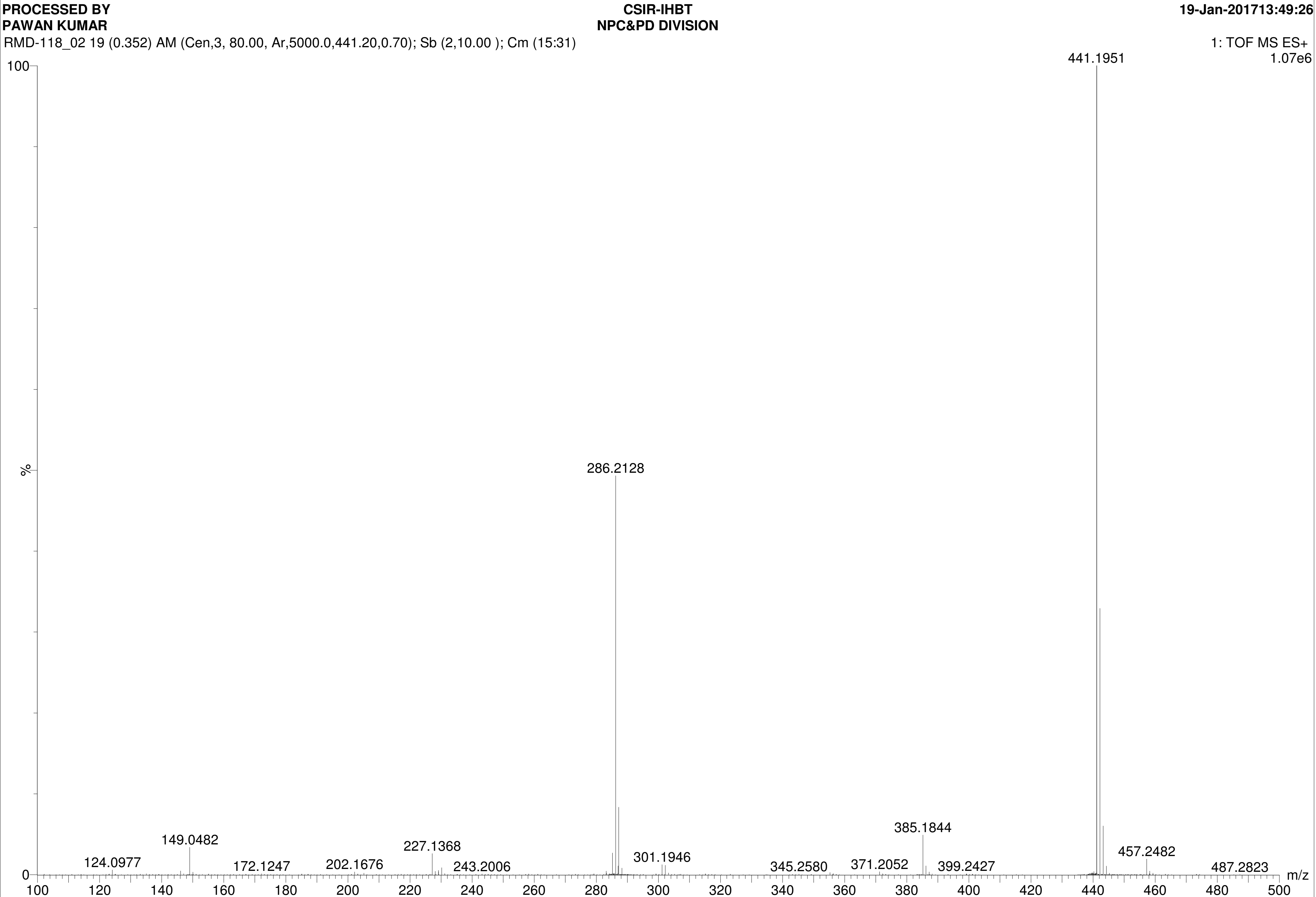
Dec02-2016
RMD-118



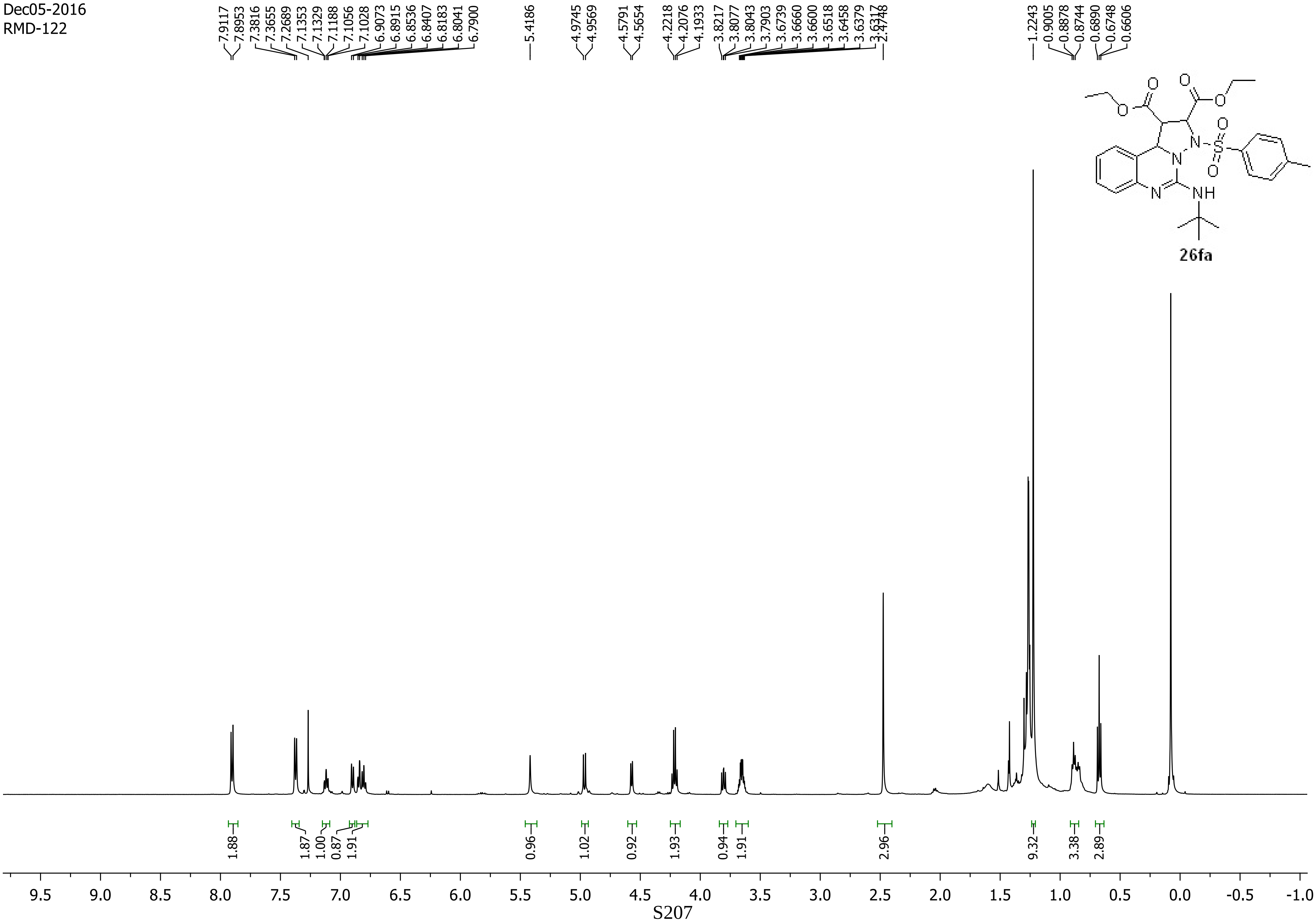
26ea

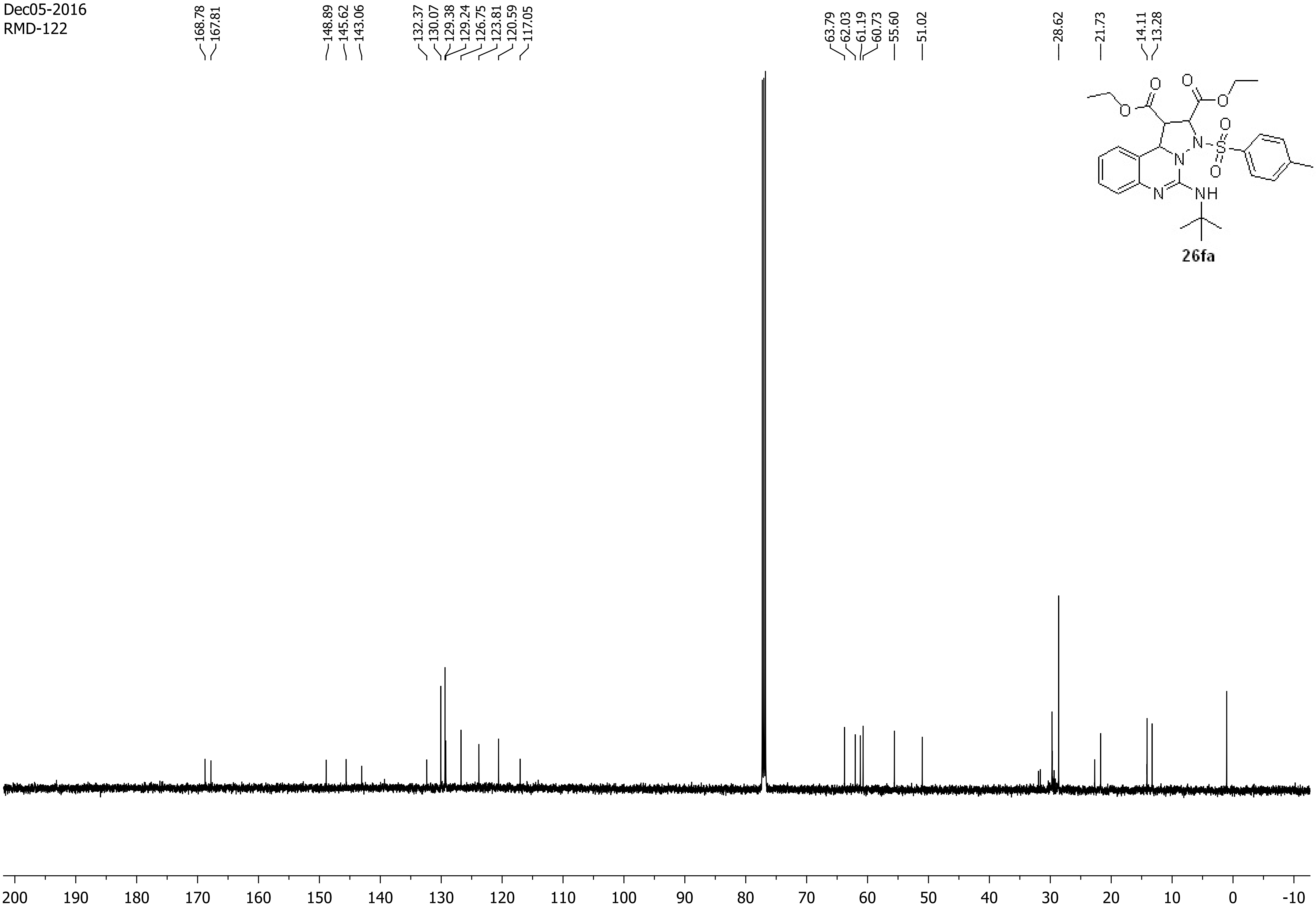


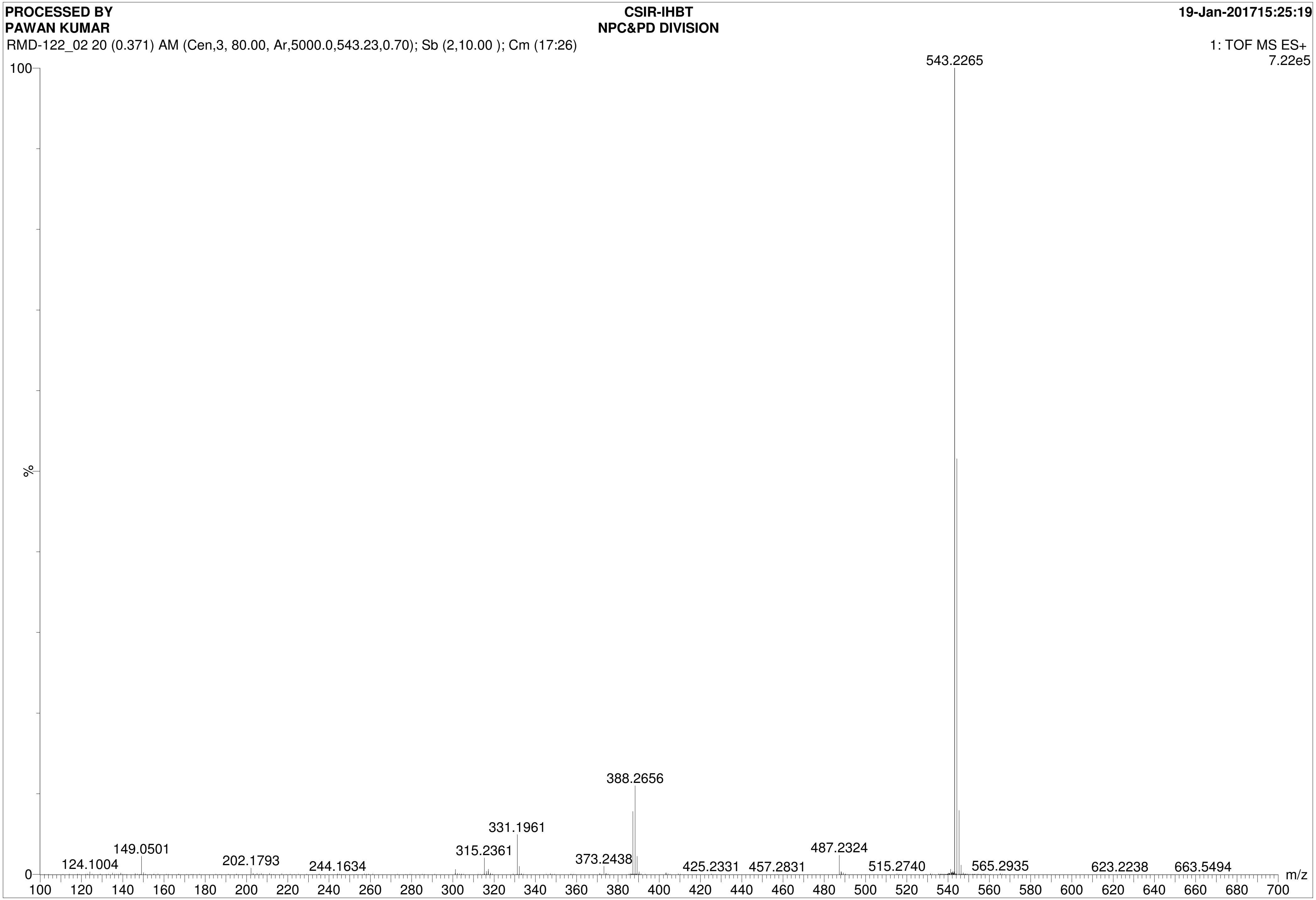

Dec02-2016
RMD-118
205.7
149.36
145.43
142.83
131.82
130.02
129.60
129.25
126.26
124.20
120.89
117.66
114.09
77.31
77.05
76.80
62.59
60.41
58.04
51.26
47.21
30.51
28.74
21.70
O
N
S
O
O
N
N
NH
26ea
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

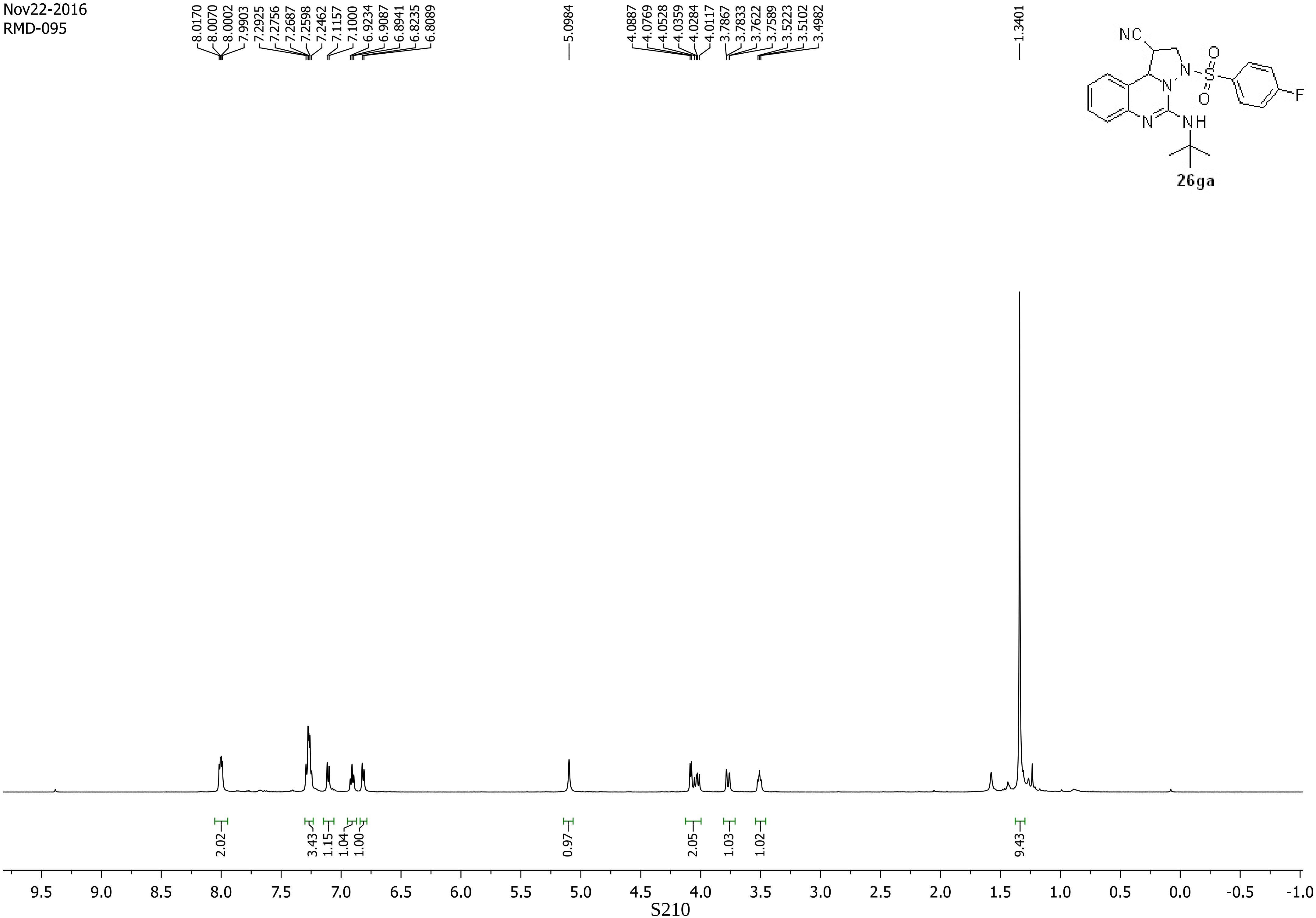


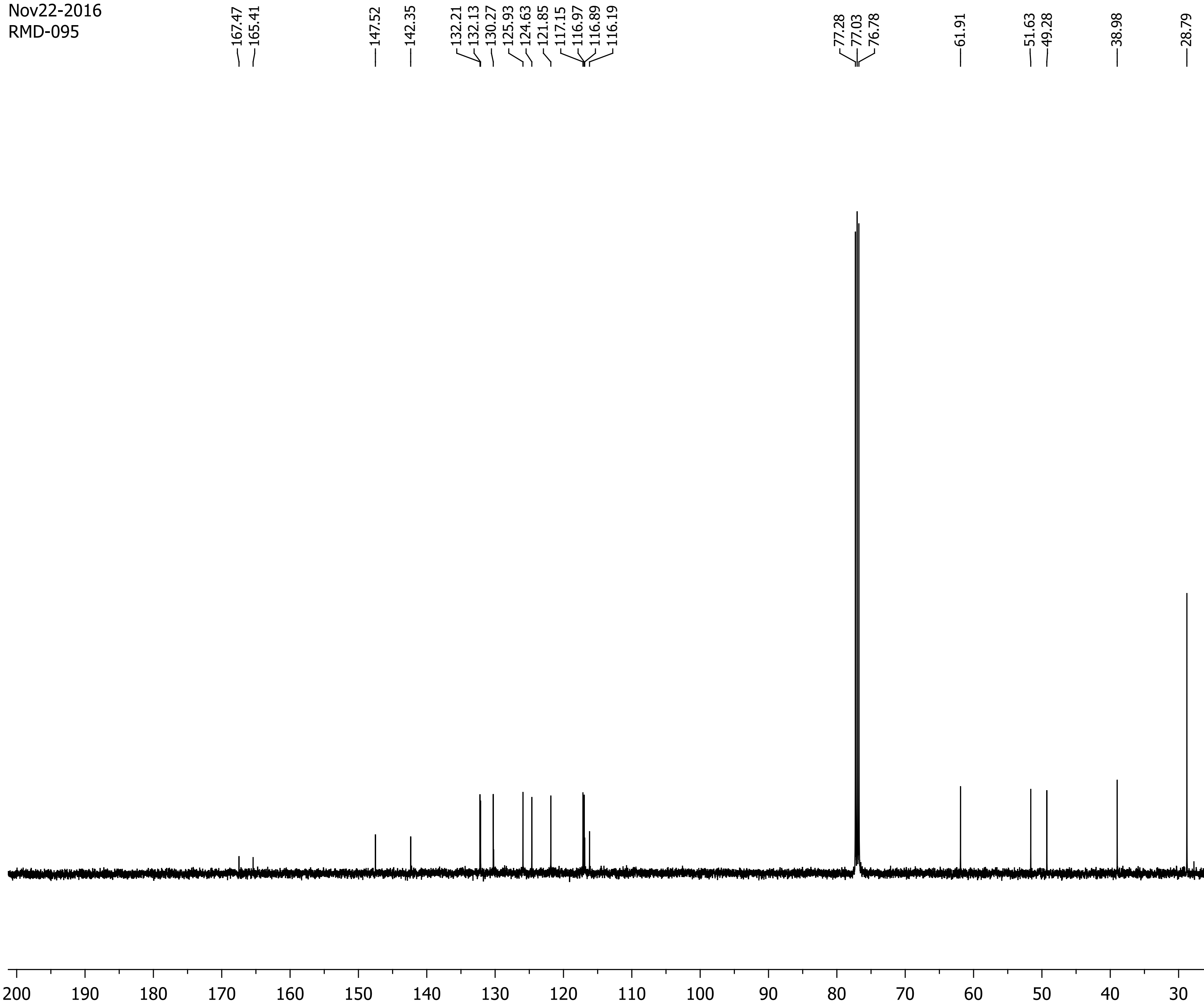
PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201713:49:26
RMD-118_02 19 (0.352) AM (Cen,3, 80.00, Ar,5000.0,441.20,0.70); Sb (2,10.00); Cm (15:31)
1: TOF MS ES+
1.07e6
441.1951
286.2128
149.0482
124.0977
172.1247
202.1676
227.1368
243.2006
301.1946
345.2580
371.2052
385.1844
399.2427
457.2482
487.2823
%
m/z

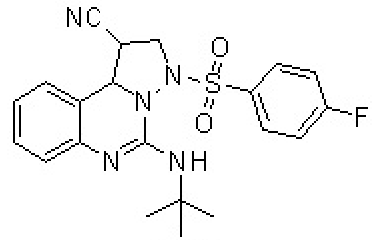

Dec05-2016
RMD-122
7.9117
7.8953
7.3816
7.3655
7.2689
7.1353
7.1329
7.1188
7.1056
7.1028
6.9073
6.8915
6.8536
6.8407
6.8183
6.8041
6.7900
5.4186
4.9745
4.9569
4.5791
4.5654
4.2218
4.2076
4.1933
3.8217
3.8077
3.8043
3.7903
3.6739
3.6660
3.6600
3.6518
3.6458
3.6379
3.6317
2.4748
1.2243
0.9005
0.8878
0.8744
0.6890
0.6748
0.6606
26fa
1.88
1.87
1.00
0.87
1.91
0.96
1.02
0.92
1.93
0.94
1.91
2.96
9.32
3.38
2.89
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0


Dec05-2016
RMD-122
168.78
167.81
148.89
145.62
143.06
132.37
130.07
129.38
129.24
126.75
123.81
120.59
117.05
63.79
62.03
61.19
60.73
55.60
51.02
28.62
21.73
14.11
13.28
26fa
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
19-Jan-201715:25:19
RMD-122_02 20 (0.371) AM (Cen,3, 80.00, Ar,5000.0,543.23,0.70); Sb (2,10.00); Cm (17:26)
1: TOF MS ES+
7.22e5
543.2265
388.2656
331.1961
149.0501
315.2361
487.2324
202.1793
373.2438
124.1004
244.1634
425.2331
457.2831
515.2740
565.2935
623.2238
663.5494
100
%
0
m/z
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700

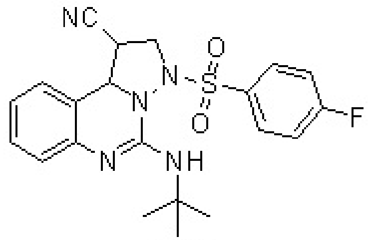

Nov22-2016
RMD-095
8.0170
8.0070
8.0002
7.9903
7.2925
7.2756
7.2687
7.2598
7.2462
7.1157
7.1000
6.9234
6.9087
6.8941
6.8235
6.8089
5.0984
4.0887
4.0769
4.0528
4.0359
4.0284
4.0117
3.7867
3.7833
3.7622
3.7589
3.5223
3.5102
3.4982
1.3401
NC
N
S
O
O
F
N
N
NH
26ga
2.02
3.43
1.15
1.04
1.00
0.97
2.05
1.03
1.02
9.43
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0


Nov22-2016
RMD-095
167.47
165.41
147.52
142.35
132.21
132.13
130.27
125.93
124.63
121.85
117.15
116.97
116.89
116.19
77.28
77.03
76.78
61.91
51.63
49.28
38.98
28.79
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

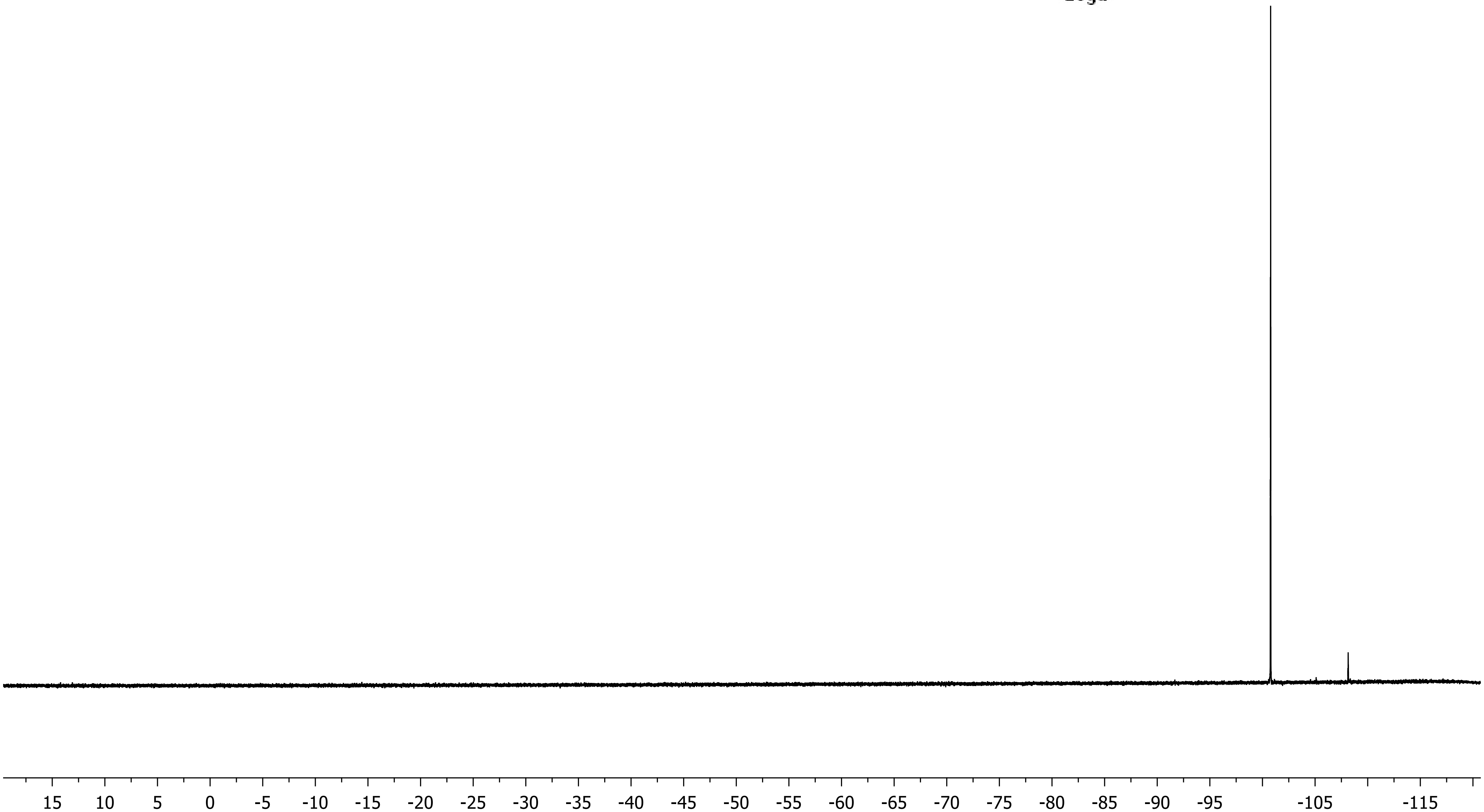

NC
N
N
N
S
O
O
F
NH

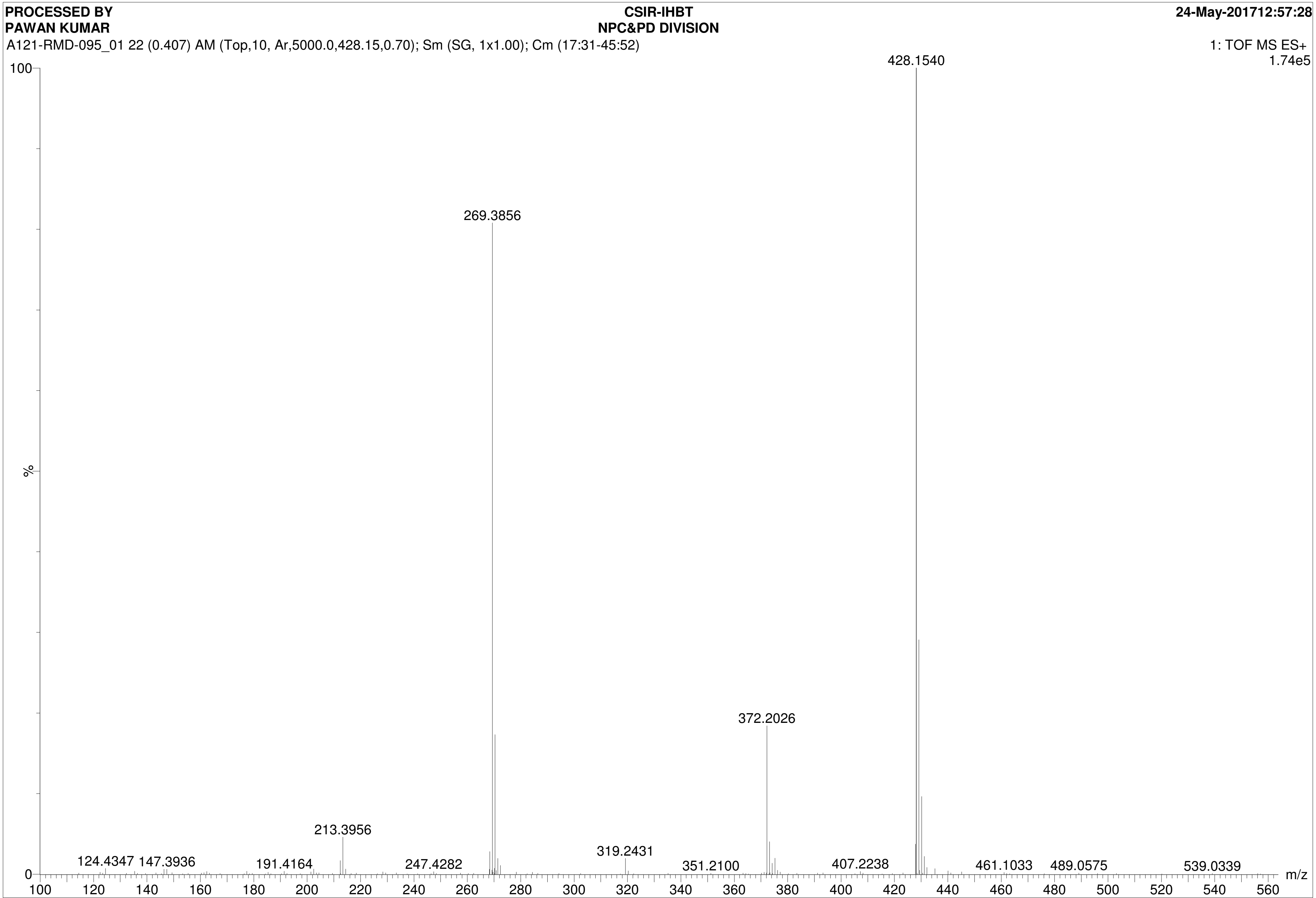
26ga

Nov24-2016
RMD-095

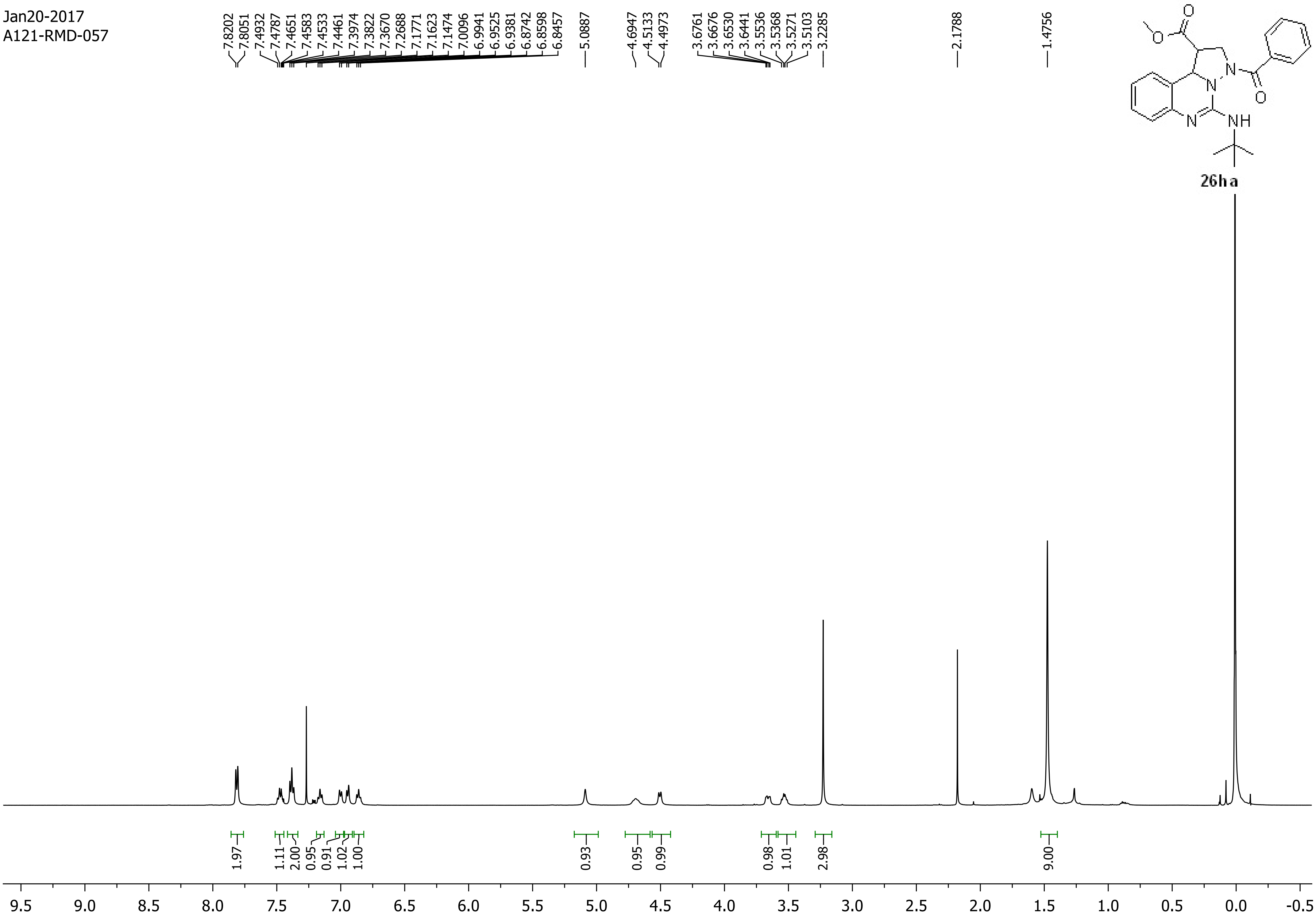


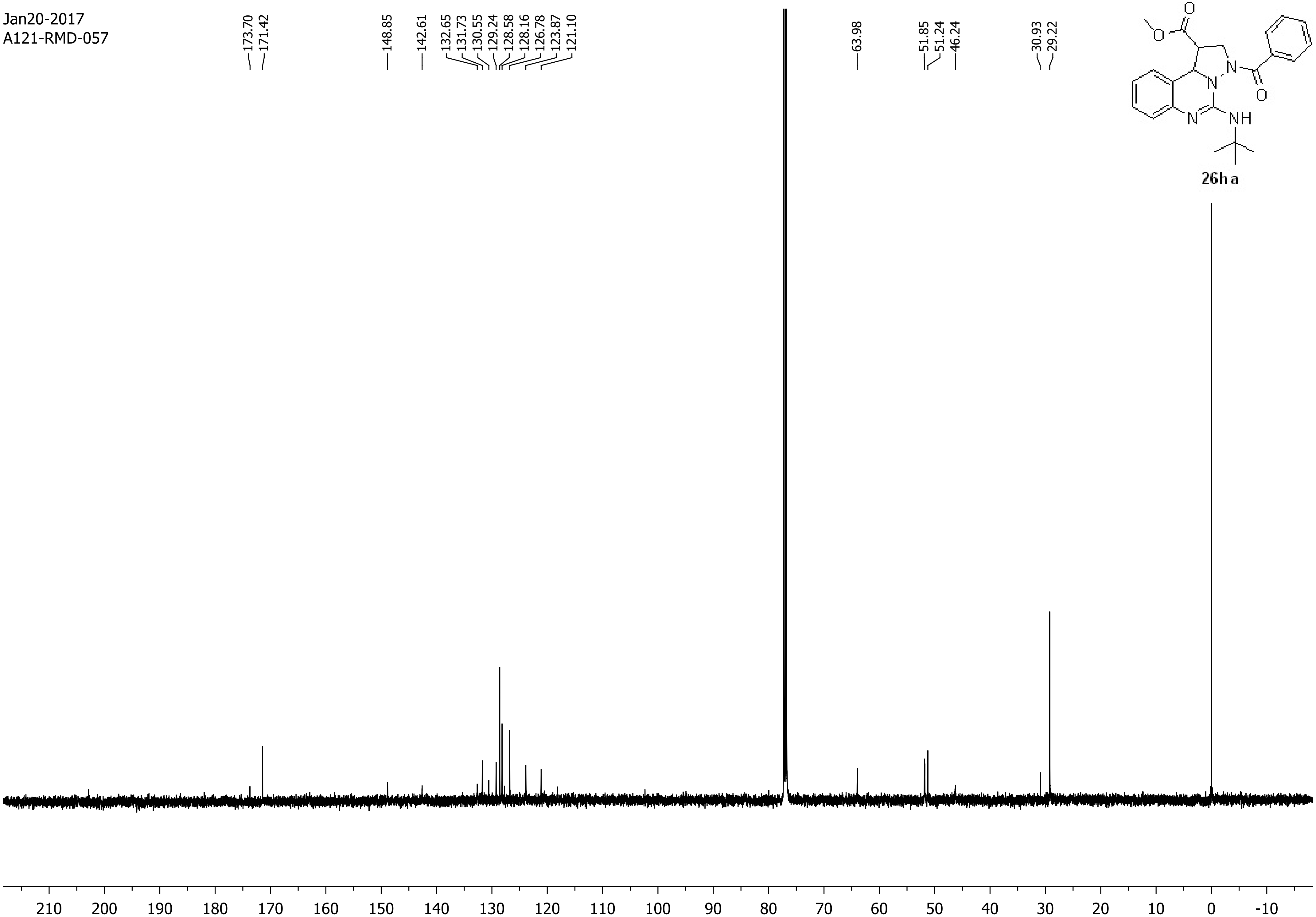
26ga



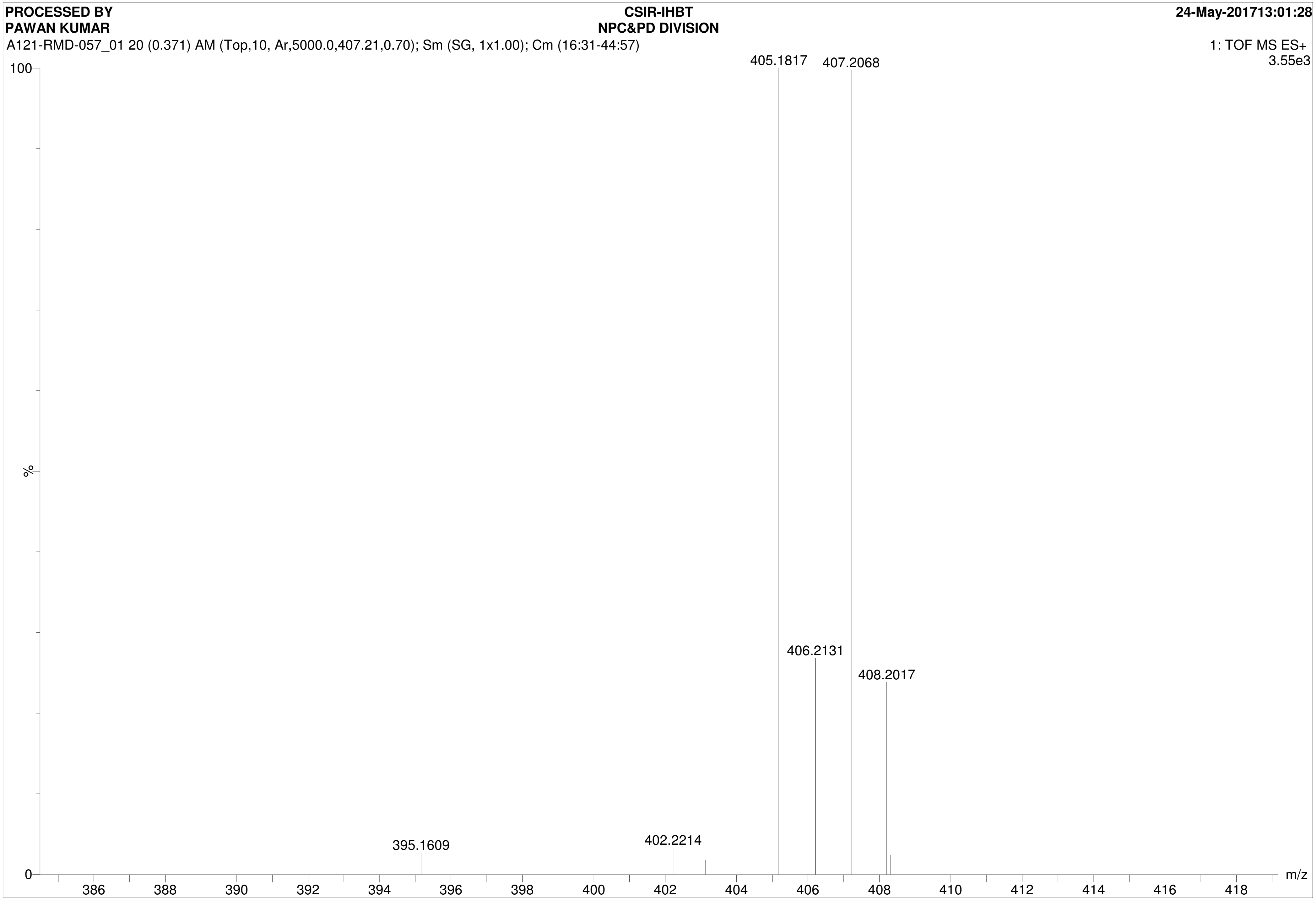

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-May-201712:57:28
A121-RMD-095_01 22 (0.407) AM (Top,10, Ar,5000.0,428.15,0.70); Sm (SG, 1x1.00); Cm (17:31-45:52)
1: TOF MS ES+
1.74e5
428.1540
269.3856
372.2026
213.3956
319.2431
124.4347
147.3936
191.4164
247.4282
351.2100
407.2238
461.1033
489.0575
539.0339
%
m/z

Jan20-2017
A121-RMD-057

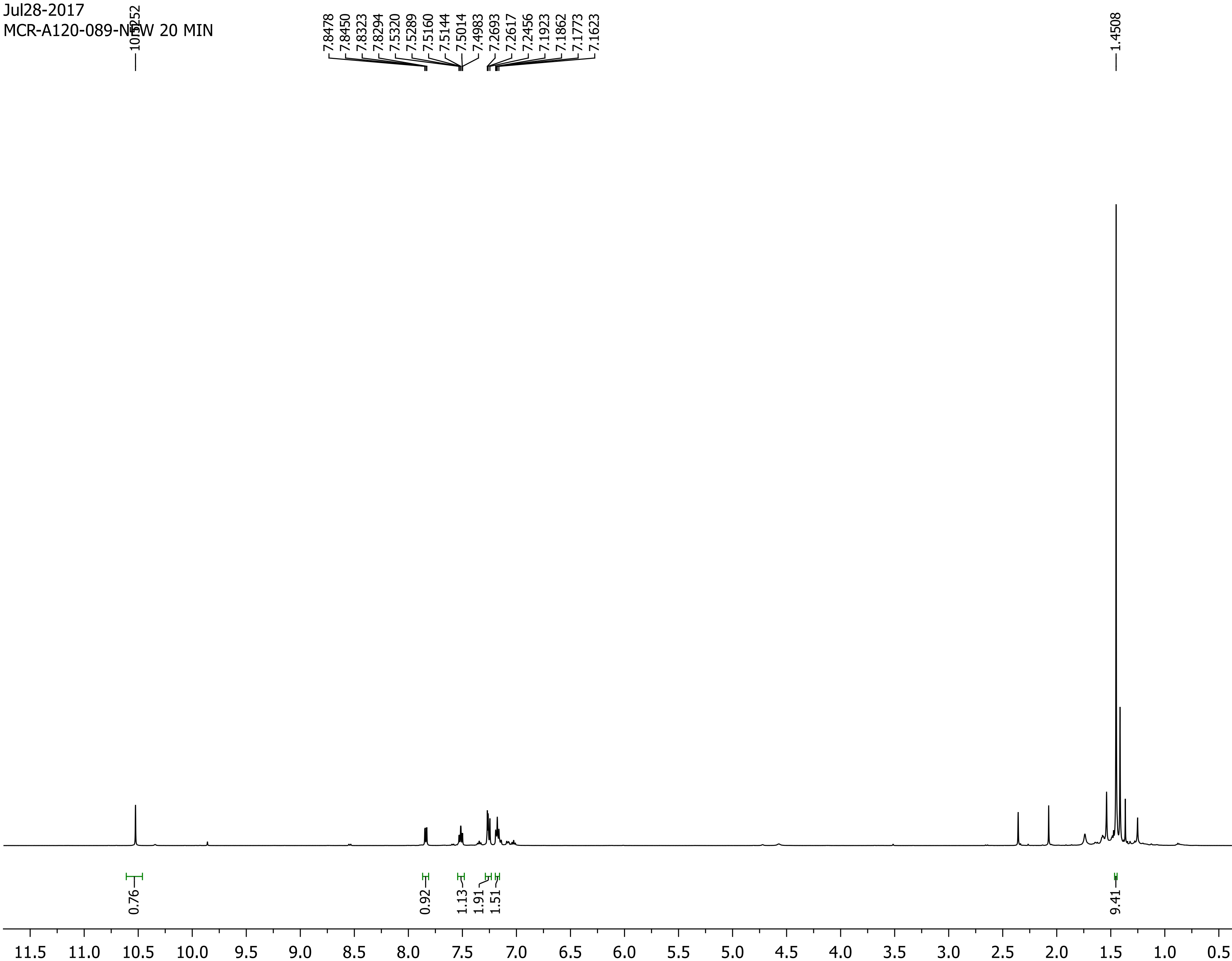


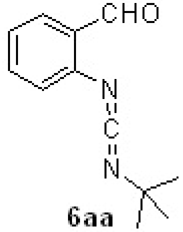


Jan20-2017
A121-RMD-057
173.70
171.42
148.85
142.61
132.65
131.73
130.55
129.24
128.58
128.16
126.78
123.87
121.10
63.98
51.85
51.24
46.24
30.93
29.22
26ha
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

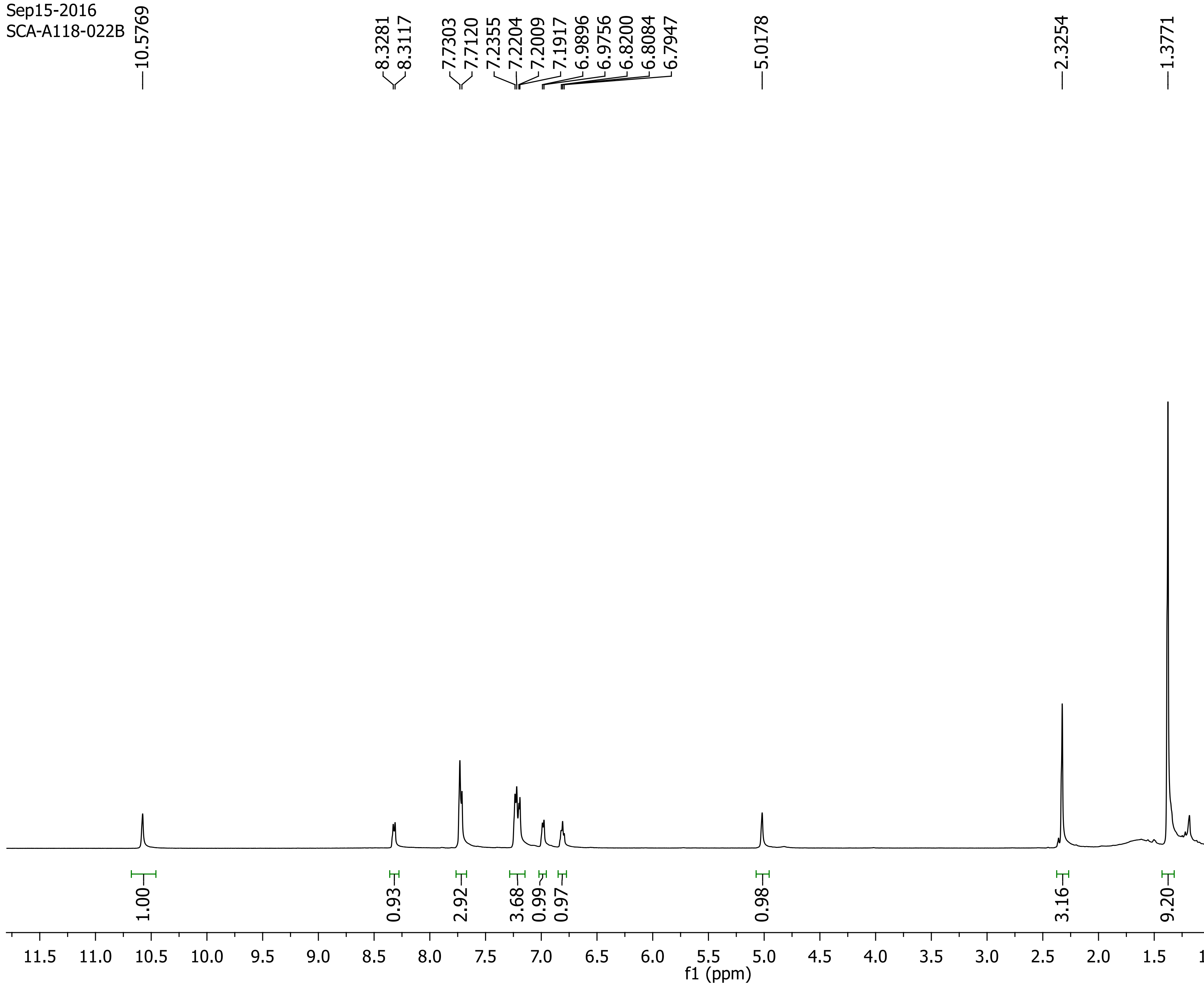

PROCESSED BY
PAWAN KUMAR
CSIR-IHBT
NPC&PD DIVISION
24-May-201713:01:28
A121-RMD-057_01 20 (0.371) AM (Top,10, Ar,5000.0,407.21,0.70); Sm (SG, 1x1.00); Cm (16:31-44:57)
1: TOF MS ES+
3.55e3
405.1817
407.2068
406.2131
408.2017
395.1609
402.2214
%
m/z

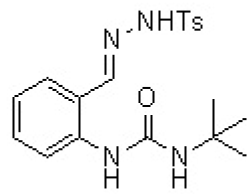
Jul28-2017
MCR-A120-089-NEW 20 MIN



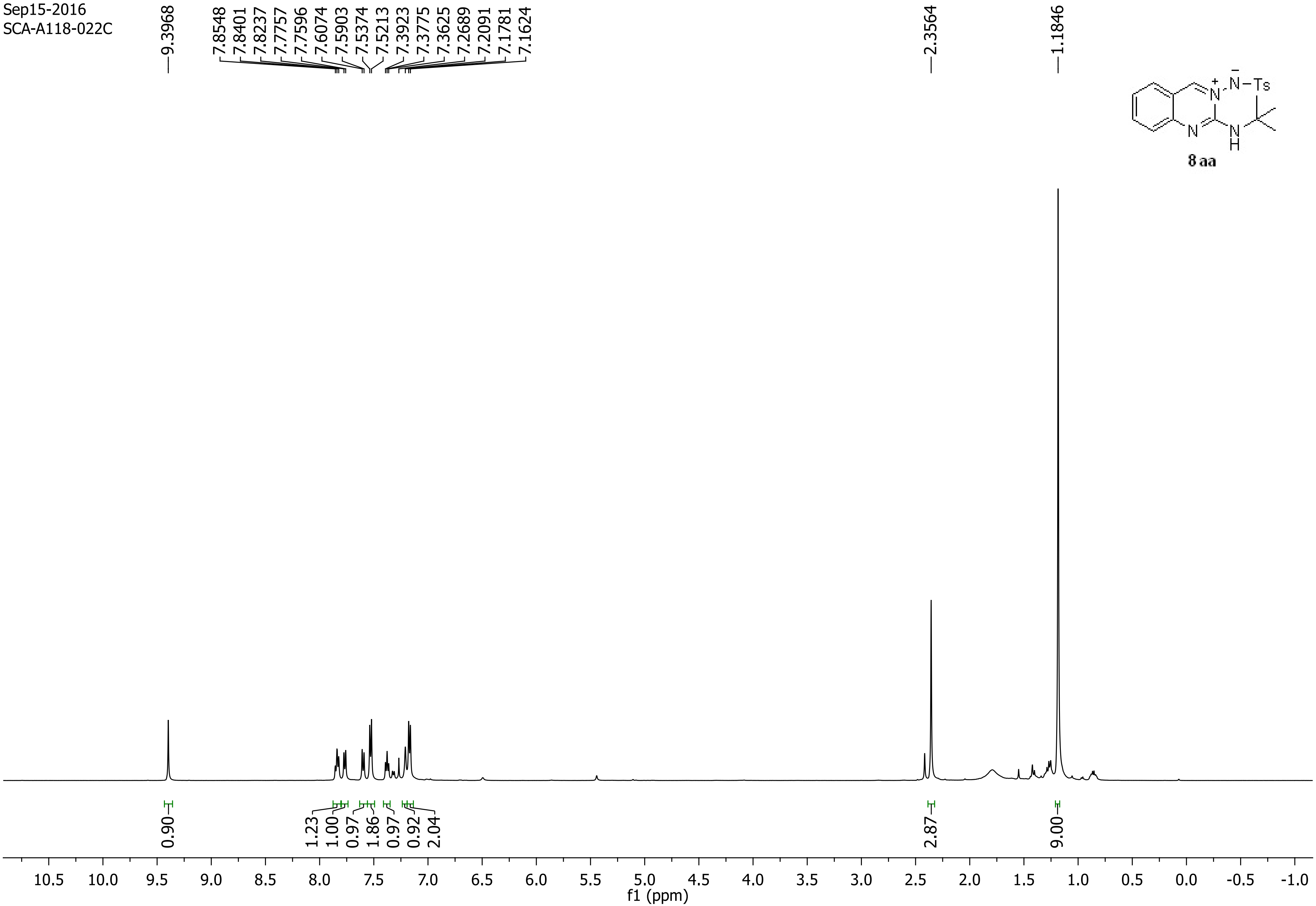


6aa


Sep15-2016
SCA-A118-022B
10.5769
8.3281
8.3117
7.7303
7.7120
7.2355
7.2204
7.2009
7.1917
6.9896
6.9756
6.8200
6.8084
6.7947
5.0178
2.3254
1.3771
1.00
0.93
2.92
3.68
0.99
0.97
0.98
3.16
9.20
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

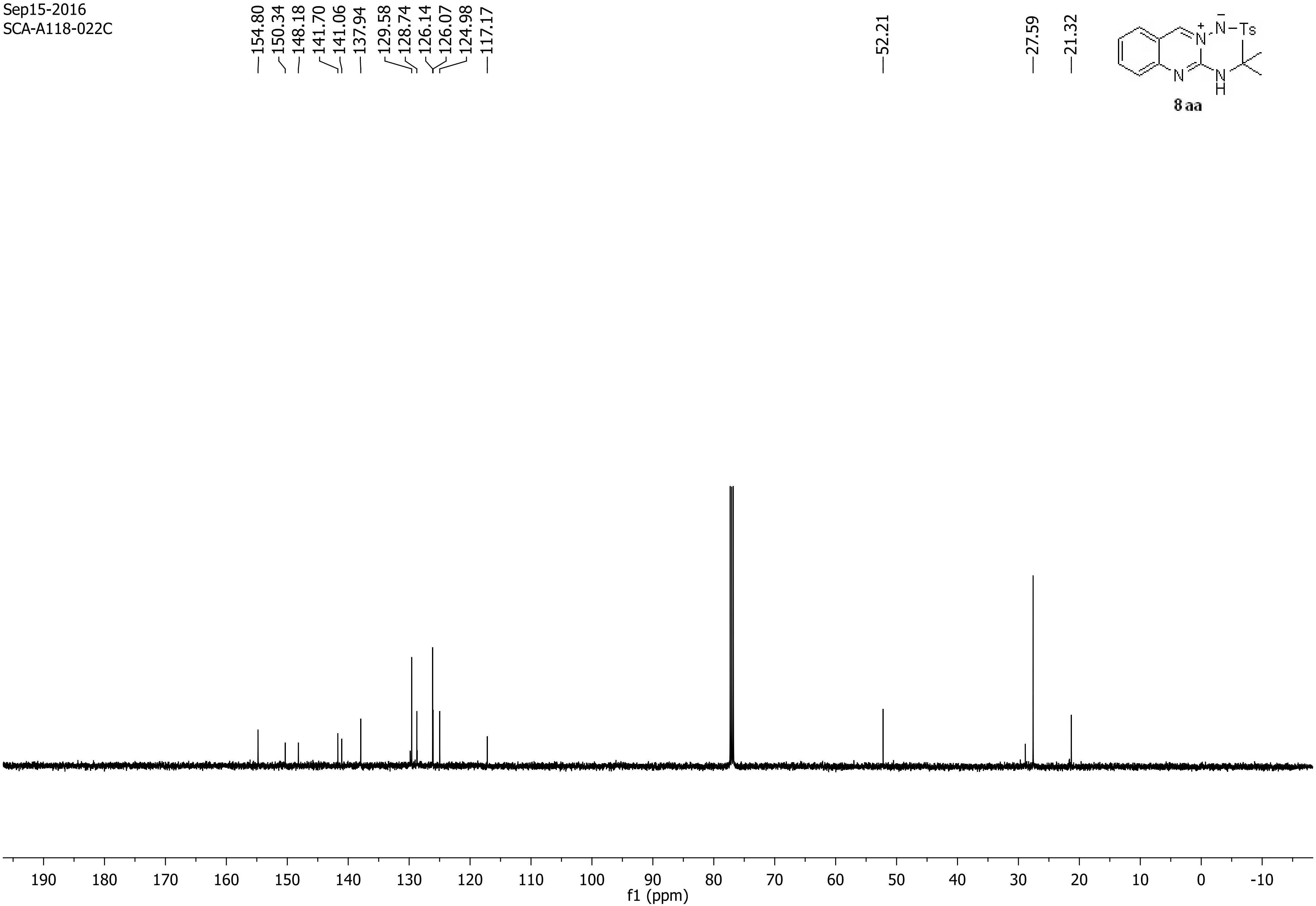

NHTs
N
O
N
H
N
H

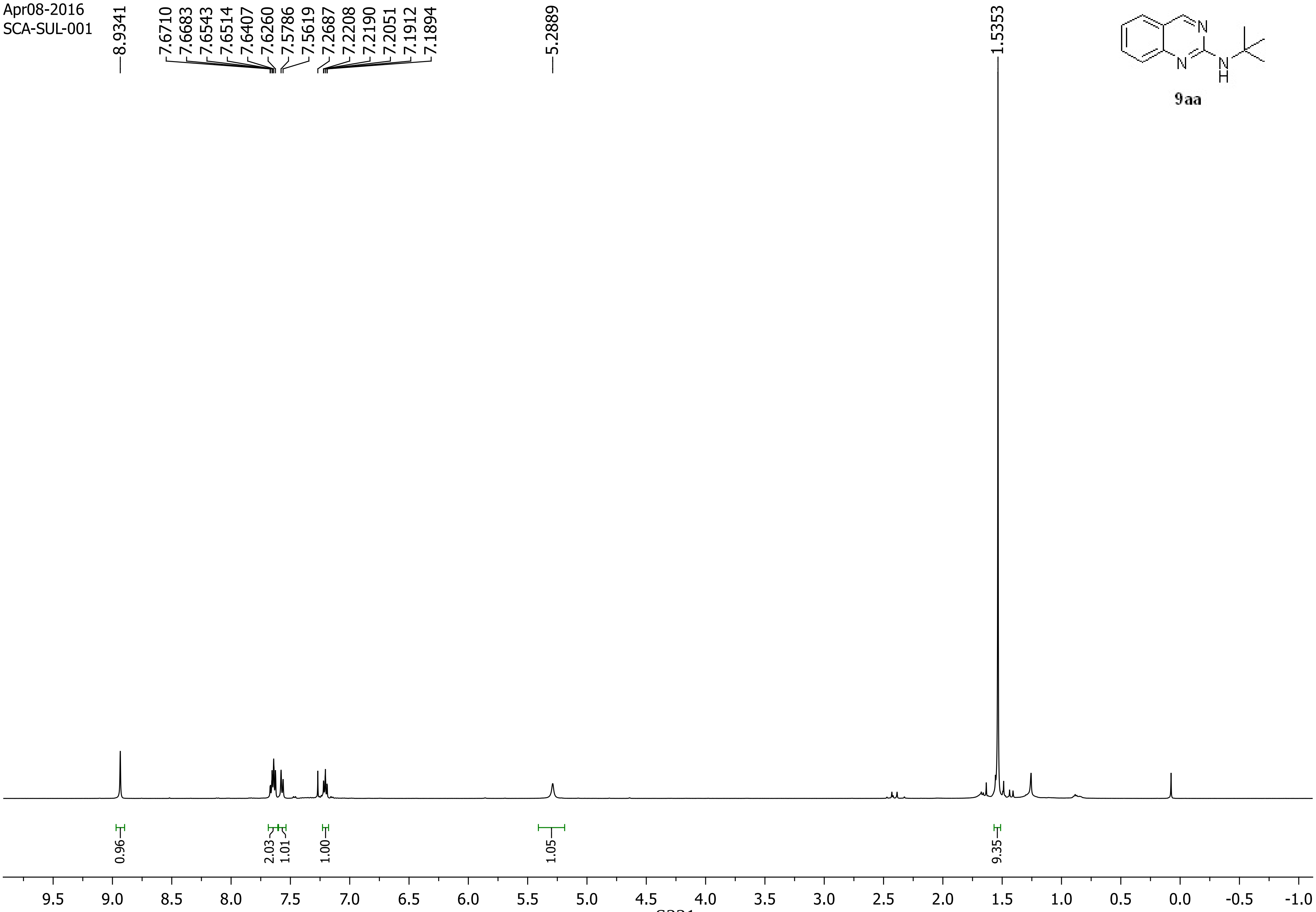
7aa

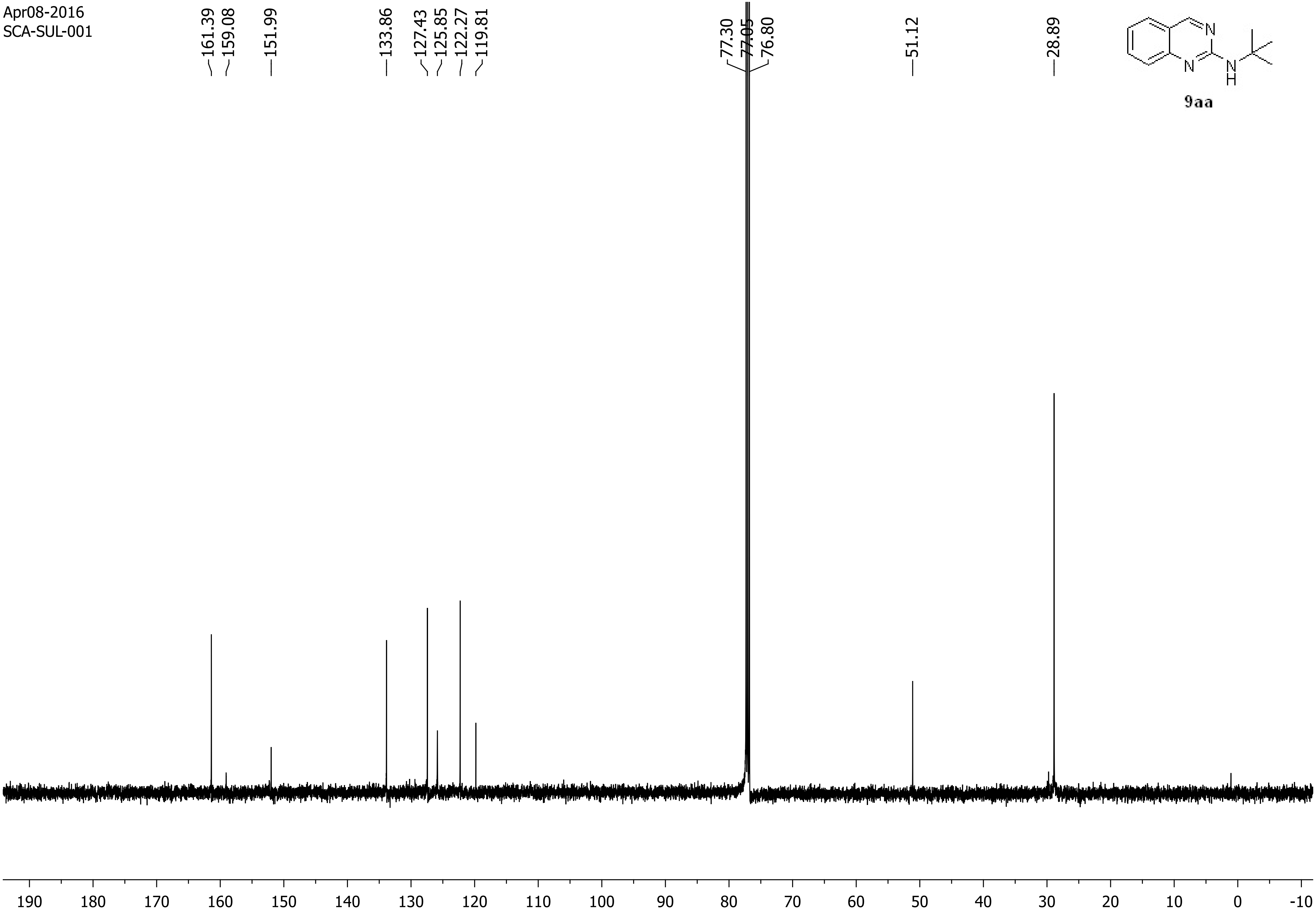

Sep15-2016
SCA-A118-022C
9.3968
7.8548
7.8401
7.8237
7.7757
7.7596
7.6074
7.5903
7.5374
7.5213
7.3923
7.3775
7.3625
7.2689
7.2091
7.1781
7.1624
2.3564
1.1846
0.90
1.23
1.00
0.97
1.86
0.97
0.92
2.04
2.87
9.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)
N
N
Ts
N
H
N

8aa

Sep15-2016
SCA-A118-022C




Apr08-2016
SCA-SUL-001
8.9341
7.6710
7.6683
7.6543
7.6514
7.6407
7.6260
7.5786
7.5619
7.2687
7.2208
7.2190
7.2051
7.1912
7.1894
5.2889
1.5353
9aa
0.96
2.03
1.01
1.00
1.05
9.35
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0


Apr08-2016
SCA-SUL-001
161.39
159.08
151.99
133.86
127.43
125.85
122.27
119.81
77.30
77.05
76.80
51.12
28.89
N
N
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

9aa