Pyrimidine-Based Inhibitors of Dynamin I GTPase Activity: Inhibition of Dynamin I GTPase's PH Domain

Luke R. Odell, Mohammed K. Abdel-Hamid, Timothy A. Hill, Ngoc Chau, Kelly A. Young, Fiona M Deane, Jennette A. Sakoff, Sofia Andersson, James A. Daniel, Phillip J. Robinson, and Adam McCluskey

Electronic Supporting Information

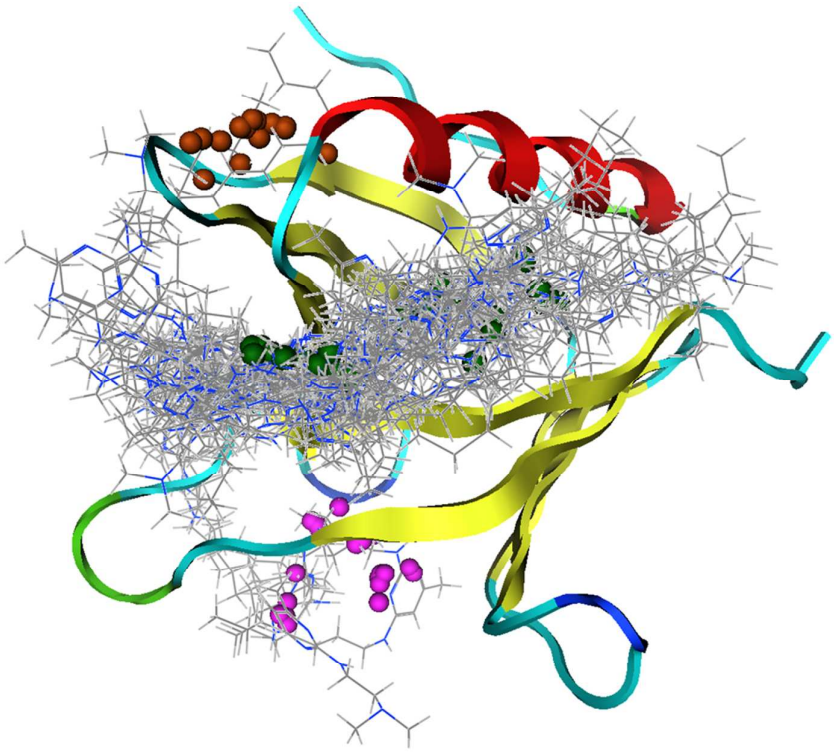


Figure S1. Ribbon representation of dynI PH domain showing potential small-molecule binding sites as colour coded spheres; pink (site 1), green (site 2) and brown (site 3). The predicted binding clusters for the docked **1** poses are rendered in line representation. Site 2 shows major clustering of docked poses (~ 96 %) followed by site 1 (3%) and site 3 (0.7%).

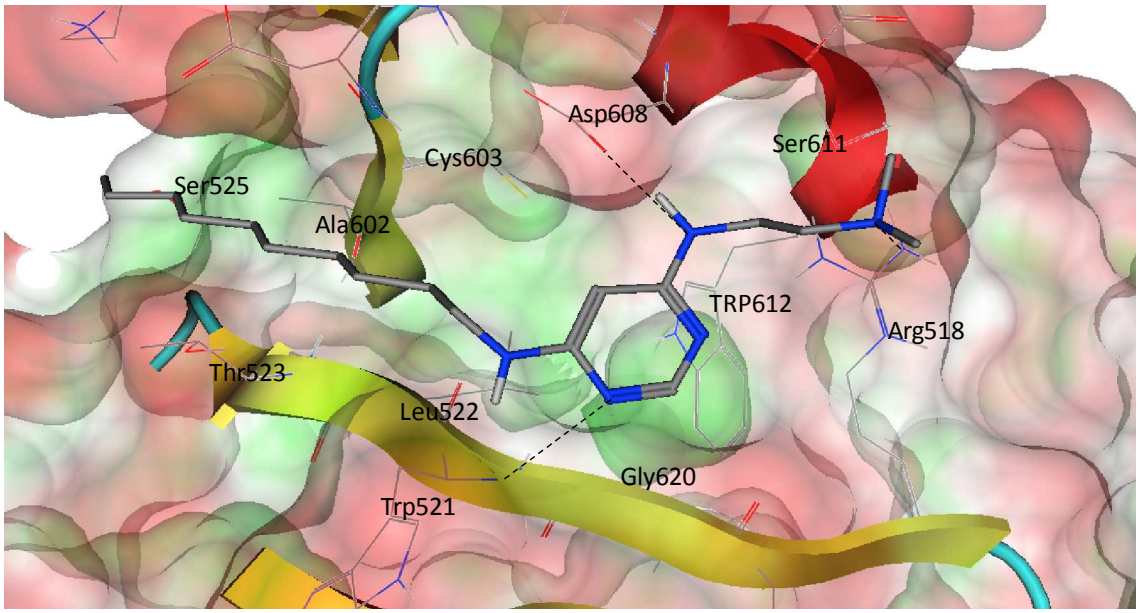
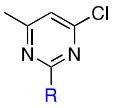
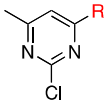
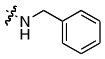
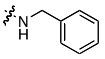
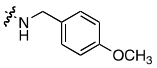
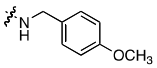
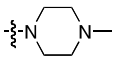
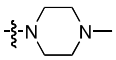


Figure S2. A representation of the predicted binding pose of 42 (stick, colour coded by atom type) within the Site-2 binding site of dynI PH domain (selected residues and backbone are shown and labelled). Surface representation; red: exposed, green: cavity. The alkyl side chain of 42 is pointed towards a hydrophobic grove while the aminopyrimidine moiety projects towards the hydrophilic region of the binding site. Potential hydrogen bond interactions are shown as dashed lines.

Table S1. Inhibition dynI GTPase activity by chloroaminopyrimidines **10a** – **26b**.





	R	Dyn I IC_{50} (μM)		R	Dyn I IC_{50} (μM)
10a	$NHCH_2CH_3$	-[a]	**10b**	$NHCH_2CH_3$	-
11a	$NHCH_2CH_2CH_3$	-	**11b**	$NHCH_2CH_2CH_3$	-
12a	$NHCH_2(CH_2)_2CH_3$	-	**12b**	$NHCH_2(CH_2)_2CH_3$	-
13a	$NHCH_2(CH_2)_4CH_3$	-	**13b**	$NHCH_2(CH_2)_4CH_3$	-
14a	$NHCH_2(CH_2)_6CH_3$	-	**14b**	$NHCH_2(CH_2)_6CH_3$	-
15a	$NHCH_2(CH_2)_8CH_3$	-	**15b**	$NHCH_2(CH_2)_8CH_3$	-
16a	$NHCH_2(CH_2)_{12}CH_3$	>>300	**16b**	$NHCH_2(CH_2)_{12}CH_3$	-
16a	$NHCH(CH_3)CH_2CH_3$	-	**17b**	$NHCH(CH_3)CH_2CH_3$	-
18a		-	**18b**		-
19a		-	**19b**		-
20a			**20b**		
21a		-	**21b**		-
22a	$N(CH_3)_2$	-	**22b**	$N(CH_3)_2$	-
23a	$NHCH_2CH_2CH_2N(CH_3)_2$	327 ± 14.0	**23b**	$NHCH_2CH_2CH_2N(CH_3)_2$	264 ± 40.8
24a	$NHCH_2CH_2NH_2$	-	**24b**	$NHCH_2CH_2NH_2$	-
25a	$NHCH_2CH_2NHBoc$	-	**25b**	$NHCH_2CH_2NHBoc$	-
26a		-	**26b**		-

[a] no activity at 300 μM drug concentration

Table S2. CEREP ExpresS Panel Screening of **1** at 10 μM drug concentration.

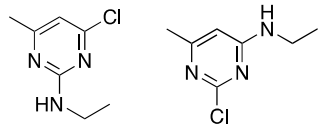
Assay		% Inhibition of Control Specific Binding	Reference Compound	IC_{50} Ref (nM)	K_i Ref (nM)
Adenosine	A_1 [a]	3	DPCPX	0.75	0.47
	A_{2A} [a]	-17	NECA	19	16
	A_3 [a]	-9	IB-MECA	0.38	0.23
Adrenergic	alpha 1 [b]	10	prazosin	0.23	0.06
	alpha 2 [b]	35	yohimbine	0.56	24
	beta 1 (h) [c]	75	atenolol	180	130
	beta 2 (h) [c]	19	ICI 118551	0.41	0.14
Angiotensin-II	AT1 (h) [a]	6	saralasin	1.0	0.51
GABA	BZD (central) [c]	-26	diazepam	11	8.8
Bradykinin	B2 (h) [c]	-11	NPC 567	11	5.5
Cannaboid	CB1 (h) [c]	31	CP 55940	0.28	0.24
Cholecystokinin	CCK1 (CCKA) (h) [c]	86	CCK-8s	0.095	0.071
Dopamine	D1 (h) [a]	80	SCH 23390	0.16	0.063
	D2S (h) [a]	99	(+)-butaclamol	0.81	0.27
Endothelin	14	14	14	0.040	0.020
GABA (non-selective) (agonist radioligand)		-4	-4	-4	28
GAL2 (h) [c]		31	31	31	0.57
CXCR2 (IL-8B) (h) [c]		48	IL-8	0.046	0.022
CCR1 (h) [c]		-2	MIP-1alpha	0.035	0.024
H1 (h) [a]		102	pyrilamine	1.9	0.71
H2 (h) [a]		106	cimetidine	500	490
MC4 (h) [c]		96	NDP-alpha -MSH	0.16	0.14
MT1 (ML1A) (h) [c]		42	melatonin	0.53	0.43
M1 (h) [a]		91	pirenzepine	27	24
M2 (h) [a]		83	methoctramine	21	15
M3 (h) [a]		104	4-DAMP	0.31	0.22
NK2 (h) [c]		93	[Nleu10]-NKA (4-10)	3.6	2.0
NK3 (h) [a]		2	SB 222200	9.3	5.0
Y1 (h) [c]		50	NPY	0.076	0.054
Y2 (h) [c]		40	NPY	0.071	0.029
NTS1 (NT1) (h) [c]		62	neurotensin	0.20	0.17
delta 2 (DOP) (h) [c]		46	DPDPE	1.2	0.69
kappa (KOP) [c]		97	U 50488	0.68	0.45
mu (MOP) (h) [c]		50	DAMGO	0.90	0.37
NOP (ORL1) (h) [c]		31	nociceptin	0.42	0.14
EP4 (h) [c]		33	PGE2	0.30	0.11

5-HT1A (h) [c]	87	8-OH-DPAT	0.47	0.29
5-HT1B [a]	87	serotonin	45	27
5-HT2A (h) [c]	93	ketanserin	0.52	0.28
5-HT2B (h) [c]	94	(±)DOI	3.2	1.6
5-HT3 (h) [a]	38	MDL 72222	5.8	4.1
5-HT5a (h) [c]	99	serotonin	260	130
5-HT6 (h) [c]	91	serotonin	130	61
5-HT7 (h) [c]	98	serotonin	0.47	0.17
sst (non-selective) (agonist radioligand)	34	somatostatin-14	0.19	0.12
VPAC1 (VIP1) [c]	-6	VIP	0.096	0.053
V1a (h) [c]	18	[d(CH2)51,Tyr(Me)2]-AVP	1.3	0.79
Ca2+ channel (L, verapamil site) (phenylalkylamine) [a]	57	D 600	21	11
KV channel [a]	7	alpha -dendrotoxin	0.65	0.52
SKCa channel [a]	1	apamin	0.021	0.011
Na+ channel (site 2) [a]	84	veratridine	7200	6500
Cl- channel (GABA-gated) [a]	0	picrotoxinin	360	300
norepinephrine transporter (h) [a]	96	protriptyline	2.9	2.1
dopamine transporter (h) [a]	105	BTCP	12	6.2
5-HT transporter (h) [a]	86	imipramine	1.6	0.72

[a] antagonist radio-ligand; [b] non-selective, antagonist radio-ligand

Chemistry

(4-Chloro-6-methylpyrimidin-2-yl)ethylamine (10a) and (2-Chloro-6-methylpyrimidin-4-yl)ethylamine (10b) [S1]

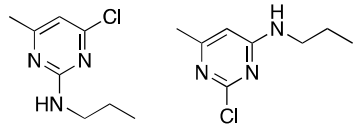


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and propylamine. The obtained residue was purified by flash chromatography using 1:9 ethyl acetate:hexanes to yield the corresponding isomers.

(10a) Yield 254 mg, 35%, mp 90-91°C; ^{1}H NMR ($CDCl_3$): δ 1.72 (t, 3H, *J* = 7.2 Hz), 2.25 (s, 3H), 3.42 (q, 2H, *J* = 7.1 Hz), 5.46 (br s, 1H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 14.2, 23.1, 35.6, 108.2, 160.5, 161.7, 168.8.

(10b) Yield 397 mg, 54%, mp 73-74°C; ^{1}H NMR ($CDCl_3$): δ 1.10 (t, 3H, *J* = 7.1 Hz), 2.18 (s, 3H), 3.24 (p, 2H, *J* = 7.0 Hz), 5.85 (br s, 1H), 5.99 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.6, 22.9, 35.6, 99.5 (br), 159.4, 163.5, 165.2 (br).

(4-Chloro-6-methylpyrimidin-2-yl)propylamine (11a) and (2-Chloro-6-methylpyrimidin-4-yl)propylamine (11b) [S2]

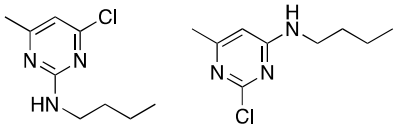


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and propylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(11a) Yield 136 mg, 25% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.96 (t, 3H, *J* = 7.4 Hz), 1.62 (m, 2H), 2.28 (s, 3H), 3.37 (q, 2H, *J* = 7.0 Hz), 5.19 (br s, 1H), 6.41 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 10.7, 22.2, 23.2, 42.7, 108.4, 160.5, 161.8, 168.9.

(11b) Yield 176 mg, 31% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.82 (t, 3H, *J* = 7.4 Hz), 1.48 (m, 2H), 2.31 (s, 3H), 3.08 (q, 2H, *J* = 7.1 Hz), 5.72 (br s, 1H), 6.10 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 11.8, 22.8, 26.1, 43.7, 97.9 (br), 159.9, 164.0, 168.4.

(4-Chloro-6-methylpyrimidin-2-yl)butylamine (12a) and (2-Chloro-6-methylpyrimidin-4-yl)butylamine (12b) [S3]

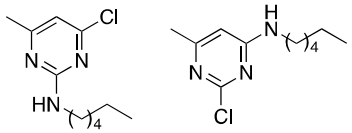


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and butylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(12a) Yield 326 mg, 38%, mp 42-43°C; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.35 (m, 2H), 1.52 (m, 2H), 2.24 (s, 3H), 3.38 (q, 2H, *J* = 7.1 Hz), 5.47 (br s, 1H), 6.35 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.0, 19.4, 23.1, 31.1, 40.5, 108.2, 160.5, 161.8, 168.8.

(12b) Yield 507 mg, 59%, mp 56-57°C; ^{1}H NMR ($CDCl_3$): δ 0.80 (t, 3H, *J* = 7.0 Hz), 1.25 (m, 2H), 1.45 (m, 2H), 2.17 (s, 3H), 3.17 (q, 2H, *J* = 7.1 Hz), 5.81 (br s, 1H), 5.98 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 12.9, 19.2, 22.9, 30.5, 40.6, 98.9 (br), 159.4, 163.7, 166.6 (br).

(4-Chloro-6-methylpyrimidin-2-yl)hexylamine (13a) and (2-Chloro-6-methylpyrimidin-4-yl)hexylamine (13b) [S2]

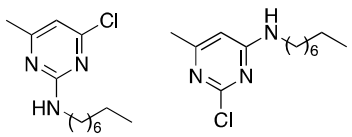


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and hexylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(13a) Yield 230 mg, 23%, mp 36-37°C; ^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3H, *J* = 7.2 Hz), 1.23 (m, 6H), 1.55 (p, 2H, *J* = 7.3 Hz), 2.25 (s, 3H), 3.37 (q, 2H, *J* = 7 Hz), 5.42 (br s, 1H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 23.1, 25.8, 28.9, 30.9, 40.8, 108.1, 160.5, 161.8, 168.8.

(13b) Yield 246 mg, 25% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.73 (t, 3H, *J* = 6.7 Hz), 1.18 (m, 6H), 1.45 (m, 2H), 2.14 (s, 3H), 3.17 (q, 2H, *J* = 6.5 Hz), 5.91 (br s, 1H), 5.97 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.8, 25.7, 28.4, 30.7, 40.9 (br), 99.4 (br), 159.4, 163.7, 166.5 (br).

(4-Chloro-6-methylpyrimidin-2-yl)octylamine (14a) and (2-Chloro-6-methylpyrimidin-4-yl)octylamine (14b) [S4]

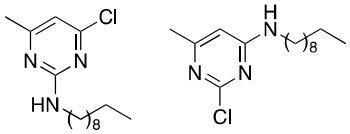


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and octylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(14a) Yield 266 mg, 22% mp 37-38°C; ^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3H, *J* = 7.3 Hz), 1.48 (m, 10H), 1.55 (m, 2H), 2.23 (s, 3H), 3.37 (q, 2H, *J* = 7.0 Hz), 5.38 (br s, 1H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 26.2, 28.6, 28.8, 28.9, 29.0, 31.2, 40.8, 108.1, 160.5, 161.8, 168.8.

(14b) Yield 176 mg, 31%, mp 36-38°C; ^{1}H NMR ($CDCl_3$):δδ 0.77 (t, 3H, *J* = 7.0 Hz), 1.15 (m, 10H), 1.48 (m, 2H), 2.19 (s, 3H), 3.17 (q, 2H, *J* = 6.5 Hz), 5.81 (br s, 1H), 5.99 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.9, 26.1, 28.4, 28.7, 28.9, 31.0, 40.9, 99.4 (br), 159.5, 163.7, 166.7 (br).

(4-Chloro-6-methylpyrimidin-2-yl)decylamine (15a) and (2-Chloro-6-methylpyrimidin-4-yl)decylamine (15b)

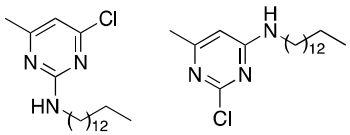


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and decylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(15a) Yield 266 mg, 32%, mp 46-48°C; ^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3H, *J* = 7.3 Hz), 1.48 (m, 14H), 1.53 (m, 2H), 2.21 (s, 3H), 3.37 (q, 2H, *J* = 6.8 Hz), 5.42 (br s, 1H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 22.0, 28.6, 28.7, 28.8 (2 x C), 28.9 (2 x C), 31.2, 40.8, 108.3, 160.5, 161.8, 168.8; HRMS calculated for $C_{15}H_{26}ClN_3$, 283.1815; found 283.1820.

(15b) Yield 231 mg, 28%, mp 29-31°C; ^{1}H NMR ($CDCl_3$): δ 0.77 (t, 3H, *J* = 6.8 Hz), 1.28 (m, 14H), 1.44 (m, 2H), 2.19 (s, 3H), 3.17 (q, 2H, *J* = 6.6 Hz), 5.75 (br s, 1H), 6.08 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.9, 28.6, 28.7, 28.8 (2 x C), 28.9 (2 x C), 31.0, 40.9, 98.8 (br), 161.1, 163.7, 165.8 (br); HRMS calculated for $C_{15}H_{26}ClN_3$, 283.1815; found 283.1818.

(4-Chloro-6-methylpyrimidin-2-yl)tetradecylamine (16a) and (2-Chloro-6-methylpyrimidin-4-yl)tetradecylamine (16b)

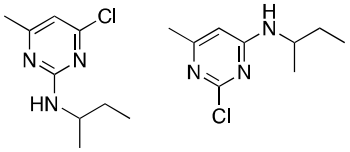


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and tetradecylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(16a) Yield 801 mg, 48%, mp 61-63°C; ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H, *J* = 6.4 Hz), 1.42 (s, 22H), 1.56 (m, 2H), 2.26 (s, 3H), 3.38 (q, 2H, *J* = 6.9 Hz), 5.33 (br s, 1H), 6.38 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 22.1, 23.4, 26.3, 28.7, 28.9 (3 x C), 29.0 (3 x C), 29.1 (2 x C's), 31.3, 40.9, 108.2, 160.5, 161.8, 168.7; HRMS calculated for $C_{19}H_{34}{}^{35}ClN_3$, 339.2441; found 339.2439.

(16b) Yield 724 mg, 44%, mp 102-104°C; ^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3H, *J* = 6.4 Hz), 1.22 (s, 22H), 1.62 (m, 2H), 2.43 (s, 3H), 3.42 (q, 2H, *J* = 6.9 Hz), 6.76 (br s, 1H), 7.59 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 19.4 (br), 21.8, 26.2, 28.1, 28.5, 28.6, 28.8 (2 x C), 28.9 (3 x C), 31.3, 41.3, 102.5 (br), 153.0 (br,) 155.6 (br), 162.4; HRMS calculated for $C_{19}H_{34}{}^{35}ClN_3$, 339.2441; found 339.2444.

***sec*-Butyl-(4-chloro-6-methylpyrimidin-2-yl)amine (17a) and *sec*-Butyl-(2-chloro-6-methylpyrimidin-4-yl)amine (17b)**

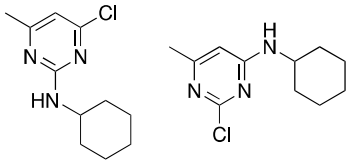


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and sec-butylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(17a) Yield 338 mg, 39% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, *J* = 7.4 Hz), 1.13 (d, 3H, *J* = 6.5 Hz), 1.52 (m, 2H), 2.23 (s, 3H), 3.98 (m, 1H), 5.07 (br s, 1H), 6.35 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.5, 19.5, 23.1, 29.0, 47.6, 108.2, 160.5, 161.3, 168.8; Analysed for: C, 54.14; H, 7.07; Cl, 17.75; N, 21.04, found C, 54.23; H, 7.15; Cl, 17.44; N, 20.74.

(17b) Yield 508 mg, 58%, mp 91-93°C; ^{1}H NMR ($CDCl_3$): δ 0.74 (t, 3H, *J* = 7.4 Hz), 1.01 (d, 3H, *J* = 6.5 Hz), 1.39 (m, 2H), 2.10 (s, 3H), 3.61 (br s, 1H), 5.28 (br s, 1H), 5.94 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.4, 19.2, 22.9, 28.7, 47.7 (br), 99.9 (br), 159.5, 163.1, 166.4 (br); Analysed for: C, 54.14; H, 7.07; Cl, 17.75; N, 21.04, found C, 54.19; H, 7.25; Cl, 17.49; N, 20.86.

(4-Chloro-6-methylpyrimidin-2-yl)cyclohexylamine (18a) and (2-Chloro-6-methylpyrimidin-4-yl)cyclohexylamine (18b) [S2]

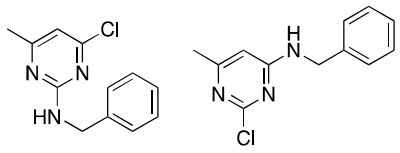


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and cyclohexylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(18a) Yield 326 mg, 42% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 1.18 (m, 3H), 1.37 (m, 2H), 1.57 (m, 1H), 1.67 (m, 2H), 1.96 (m, 2H), 2.25 (s, 3H), 3.81 (m, 1H), 5.09 (br s, 1H), 6.36 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 23.9, 24.7, 25.7, 33.0, 49.4, 108.6, 161.1, 161.3, 169.2; HRMS calculated for $C_{11}H_{16}ClN_3$, 225.1033; found 225.1021.

(18b) yield 386 mg, 49% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 1.36 (m, 3H), 1.37 (m, 2H), 1.62 (m, 1H), 1.72 (m, 2H), 1.96 (m, 2H), 2.31 (s, 3H), 3.51 (m, 1H), 5.32 (d, 1H), 6.08 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 23.7, 24.5, 25.4, 32.7, 60.3, 100.1 (br), 160.1, 162.9, 166.4; HRMS calculated for $C_{11}H_{16}ClN_3$, 225.1033; found 225.1030.

***N*-benzyl-4-chloro-6-methylpyrimidin-2-amine (19a) and *N*-benzyl-2-chloro-6-methylpyrimidin-4-amine (19b)** [S2]

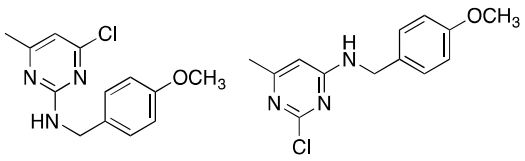


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and benzylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(19a) Yield 142 mg, 19%, mp 136-138°C; ^{1}H NMR ($CDCl_3$):δδ 2.29 (s, 3H), 4.64 (d, 2H), 5.48 (br s, 1H), 6.48 (s, 1H), 7.31 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 23.2, 44.9, 109.0, 126.7, 126.9, 128.0, 139.2, 160.7, 161.6, 169.0.

(19b) Yield 340 mg, 49%, mp 78-81°C; ^{1}H NMR ($CDCl_3$): δ 2.25 (s, 3H), 4.51 (d, 2H), 6.06 (s, 1H), 6.15 (br s, 1H), 7.29 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 23.1, 44.9, 99.9 (br), 126.7, 127.1, 128.3, 136.8, 159.6, 163.8, 171.1 (br).

4-Chloro-*N*-(4-methoxybenzyl)-6-methylpyrimidin-2-amine (20a) and 2-Chloro-*N*-(4-methoxybenzyl)-6-methylpyrimidin-4-amine (20b)

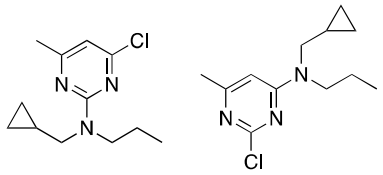


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and 4-methoxybenzylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(19a) Yield 142 mg, 23%, mp 145-147°C; ^{1}H NMR ($CDCl_3$): δ 2.27 (s, 3H), 3.72 (s, 3H), 4.54 (d, 2H), 6.28 (br s, 1H), 6.58 (s, 1H), 6.91 (d, 2H), 7.11 (d, 2H); ^{13}C NMR ($CDCl_3$): δ 22.8, 45.3, 55.7, 101.7, 118.9, 128.4, 130.2, 154.1, 160.7, 162.3, 170.4; HRMS calculated for $C_{13}H_{14}ClN_3O$, 263.0825; found 263.0833.

(19b) Yield 340 mg, 48%, mp 101-103°C; ^{1}H NMR ($CDCl_3$): δ 2.25 (s, 3H), 3.71 (s, 3H), 4.31 (d, 2H), 6.36 (s, 1H), 6.15 (br s, 1H), 6.90 (d, 2H), 7.13 (d, 2H); ^{13}C NMR ($CDCl_3$): δ 23.2, 44.9, 56.1, 100.9 (br), 119.1, 127.7, 128.1, 158.3, 160.8, 161.6, 171.1 (br); HRMS calculated for $C_{13}H_{14}ClN_3O$, 263.0825; found 263.0836.

(4-Chloro-6-methylpyrimidin-2-yl)(1-cyclopropylmethylpropyl)amine (21a) and (2-Chloro-6-methylpyrimidin-4-yl)cyclopropylmethylpropylamine (21b) [S5]

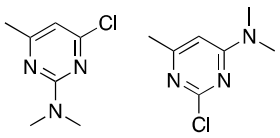


Synthesized using the general procedure as for **4a,b** from 2,4-dichloro-6-methylpyrimidine and cyclopropylmethylpropylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(21a) Yield 387 mg, 30% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.28 (q, 2H, *J* = 5.0 Hz), 0.46 (q, 2H, *J* = 6.5 Hz), 0.90 (t, 3H, *J* = 7.4 Hz), 1.06 (m, 1H), 1.62 (m, 2H), 2.25 (s, 3H), 3.48 (d, 2H, *J* = 6.7 Hz), 3.58 (t, 2H, *J* = 7.5 Hz), 6.30 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 3.5, 9.9, 11.4, 20.8, 24.0, 49.3, 51.8, 107.3, 160.7, 161.7, 168.7.

(21b) Yield 690 mg, 53% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 0.21 (q, 2H, *J* = 5.0 Hz), 0.46 (q, 2H, *J* = 6.5 Hz), 0.87 (t, 3H, *J* = 7.4 Hz), 0.97 (m, 1H), 1.56 (m, 2H), 2.29 (s, 3H), 3.34 (d, 2H, *J* = 6.7 Hz), 3.40 (t, 2H, *J* = 7.5 Hz), 6.10 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 3.6, 9.4, 11.2, 20.3, 23.8, 49.9, 52.8, 99.4, 160.0, 162.8, 166.7.

(4-Chloro-6-methylpyrimidin-2-yl)-dimethylamine (22a) and (2-Chloro-6-methylpyrimidin-4-yl)dimethylamine (22b) [S6]

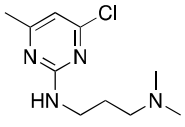
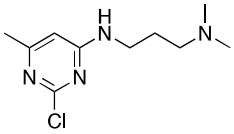


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and *N,N*-dimethylamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(22a) yield 187 mg, 29% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 2.25 (s, 3H), 3.17 (s, 6H), 6.34 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 23.3, 36.3, 106.8, 160.2, 161.6, 168.3.

(22b) yield 378 mg, 59% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 2.25 (s, 3H), 3.02 (s, 6H), 6.09 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 23.2, 36.6, 98.7, 159.4, 163.2, 166.4.

***N*^{1}-(4-Chloro-6-methylpyrimidin-2-yl)-*N*^{3},*N*^{3}-dimethylpropane-1,3-diamine (23a) and 2-Chloro-4-(2-dimethylaminopropylamine)-6-methylpyrimidine (23b)** [S7]

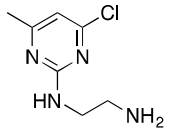
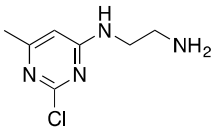



Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and N^1,N^1-dimethylpropane-1,3-diamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(23a) yield 141 mg, 17% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 1.74 (m, 2H), 2.25 (s, 6H), 2.35 (s, 3H), 2.37 (t, 2H, J = 6.2 Hz), 3.40 (q, 2H, J = 5.9 Hz), 5.84 (br s, 1H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 26.1, 29.8, 39.9, 44.8, 57.2, 108.2, 160.5, 161.8, 168.8.

(23b) yield 253 mg, 30% pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 1.57 (m, 2H), 1.92 (s, 3H), 2.12 (s, 6H), 2.36 (m, 2H), 3.12 (br m, 2H), 5.84 (br s, 1H), 5.95 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 22.9, 24.4, 38.6 (br), 43.6, 56.1, 101.2 (br), 159.1, 163.4, 165.8 (br).

N'-(4-Chloro-6-methylpyrimidin-2-yl)-ethane-1,2-diamine (24a) and N'-(2-chloro-6-methylpyrimidin-4-yl)ethane-1,2-diamine (24b)

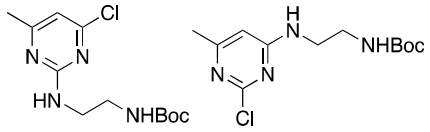



Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and ethylenediamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(24a) Yield 106 mg, 88%, mp >300°C; ^{1}H NMR ($CDCl_3$): δ 1.82 (br s, 2H), 2.21 (s, 3H), 2.83 (t, 2H, J = 5.8 Hz), 3.42 (q, 2H, J = 5.8 Hz), 5.98 (br s, 1H), 6.35 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 23.1, 40.7, 43.5, 108.9, 160.4, 161.9, 168.9; HRMS calculated for $C_7H_{11}ClN_4$, 186.0672; found 186.0677.

(24b) Yield 98 mg, 81%, mp 260-264°C; ^{1}H NMR (CD_3OD): δ 2.45 (s, 3H), 3.23 (m, 2H), 3.89 (t, 2H, J = 6.1 Hz), 6.75 (s, 1H); ^{13}C NMR (CD_3OD): δ 17.3, 37.8, 38.3, 103.3 (br), 152.6, 156.7, 163.7; HRMS calculated for $C_7H_{11}ClN_4$, 186.0672; found 186.0691.

[2-(4-Chloro-6-methylpyrimidin-2-ylamino)ethyl]carbamic acid *tert*-butyl ester (25a) and [2-(2-chloro-6-methylpyrimidin-4-ylamino)ethyl]carbamic acid *tert*-butyl ester (25b)

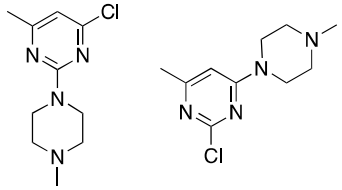


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and *N*-Boc-*N*-ethylenediamine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(25a) Yield 377 mg, 42% mp 135-138°C; ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 9H), 2.25 (s, 3H), 3.34 (q, 2H, *J* = 5.9 Hz), 3.54 (q, 2H, *J* = 5.8 Hz), 5.12 (br s, 1H), 5.69 (br s, 1H), 6.43 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 23.1, 27.8, 40.3, 41.0, 78.8, 108.9, 155.6, 160.6, 161.8, 168.9; HRMS calculated for $C_{12}H_{19}ClN_4O_2$, 286.1197; found 286.1211.

(25b) Yield 502 mg, 53% mp 116-118°C; ^{1}H NMR ($CDCl_3$): δ 1.21 (s, 9H), 2.06 (s, 3H), 3.17 (m, 2H), 3.34 (m, 2H), 5.54 (br s, 1H), 5.97 (s, 1H), 6.50 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 22.1, 27.5, 39.5, 40.9, 78.7, 102.3 (br), 156.1, 159.2, 163.7, 165.9; HRMS calculated for $C_{12}H_{19}ClN_4O_2$, 286.1197; found 286.1208.

4-Chloro-6-methyl-2-(4-methylpiperazin-1-yl)pyrimidine (26a) and 2-chloro-5-methyl-4-(4-methylpiperazin-1-yl)pyrimidine (26b)

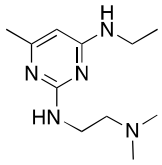


Synthesized using the general procedure as for **4a**,**b** from 2,4-dichloro-6-methylpyrimidine and *N*-methylpiperazine. Purified by flash chromatography EtOAc:Triethylamine (95:5).

(26a) Yield 278 mg, 41% mp 145-148°C; ^{1}H NMR ($CDCl_3$): δ 2.19 (s, 3H), 2.33 (s, 3H), 3.35 (t, 4H), 3.75 (t, 2H), 6.27 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 28.8, 43.7, 46.1, 54.8, 108.2, 160.9, 161.3, 169.0; HRMS calculated for $C_{10}H_{15}ClN_4$, 226.0985; found 226.1001.

(26b) Yield 312 mg, 51% mp 118-119°C; ^{1}H NMR ($CDCl_3$): δ 2.19 (s, 3H), 2.32 (s, 3H), 3.35 (t, 4H), 3.54 (t, 2H), 6.13 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 23.7, 43.9, 45.9, 54.4, 99.6, 160.2, 163.2, 167.7; HRMS calculated for $C_{10}H_{15}ClN_4$, 226.0985; found 226.0988.

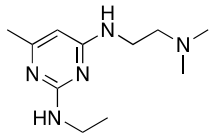
***N*^{2}-(2-(dimethylamino)ethyl)-6-methyl-*N*^{4}-propylpyrimidine-2,4-diamine (27a)**



Synthesized using the general procedure as for **5a** from 2-chloro-6-methyl-*N*-propylpyrimidin-4-amine (**10a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(27a) yield 52 mg, 51% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.92 (t, 3H, *J* = 7.4 Hz), 1.56 (m, 2H), 2.14 (s, 3H), 2.20 (s, 6H), 2.43 (t, 2H, *J* = 6.3 Hz), 3.19 (q, 2H, *J* = 6.7 Hz), 3.40 (m, 2H), 4.78 (br s, 1H), 5.21 (br s, 1H), 5.50 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 10.8, 22.2, 23.1, 38.4, 42.5, 44.6, 58.0, 91.5 (br), 161.6, 163.3, 165.0; HRMS calculated for $C_{11}H_{21}N_5$, 223.1797; found 223.1790.

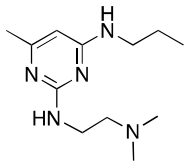
***N*^{4}-(2-Dimethylaminoethyl)-6-methyl-*N*^{2}-propylpyrimidine-2,4-diamine (27b)**



Synthesized using the general procedure as for **5b** from 4-chloro-6-methyl-*N*-propylpyrimidin-2-amine (**10b**) and *N,N*-dimethylethylenediamine. The residue was purified by short column chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(27b) yield 52 mg, 51% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.90 (t, 3H, *J* = 7.4 Hz), 1.61 (m, 2H), 2.19 (s, 6H), 2.21 (s, 3H), 2.36 (t, 2H, *J* = 6 Hz), 3.29 (m, 4H), 5.32 (br s, 1H), 5.50 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 10.8, 22.4, 34.9, 37.9, 42.5, 44.4, 57.3, 92.2 (br), 160.5, 161.1, 163.0; HRMS calculated for $C_{11}H_{21}N_5$, 223.1797; found 223.1806.

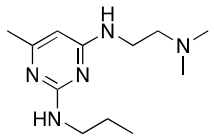
***N*^{4}-Butyl-*N*^{2}-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (28a)**



Synthesized using the general procedure as for **5a** from *N*-butyl-2-chloro-6-methylpyrimidin-4-amine (**11a**) and *N,N*-dimethylethylenediamine. The residue was purified by short column chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(28a) yield 280 mg, 82% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.73 (t, 3H, *J* = 7.3 Hz), 1.18 (m, 2H), 1.33 (q, 2H, *J* = 6.6 Hz), 1.96 (s, 3H), 2.04 (s, 6H), 2.27 (t, 2H, *J* = 6.5 Hz), 3.08 (q, 2H, *J* = 6.8 Hz), 3.25 (t, 2H, *J* = 6.4 Hz), 4.13 (br s, 1H), 5.17 (br s, 1H), 5.38 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.0, 19.3, 22.7, 35.2, 38.2, 40.1, 44.5, 57.8, 91.8 (br), 161.5, 163.1, 164.0 (br); HRMS calculated for $C_{12}H_{23}N_5$, 237.1953; found 237.1959.

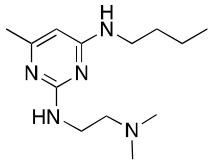
N^2-Butyl-N^4-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (28b)



Synthesized using the general procedure as for **5b** from *N*-butyl-4-chloro-6-methylpyrimidin-2-amine (**11b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(28b) yield 191 mg, 85% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.81 (t, 3H, *J* = 7.3 Hz), 1.25 (m, 2H), 1.41 (p, 2H, *J* = 6.7 Hz) 2.02 (s, 3H), 2.11 (s, 6H), 2.35 (t, 2H, *J* = 6.2 Hz), 3.24 (m, 4H), 4.08 (br s, 1H), 5.06 (br s, 1H), 5.53 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.1, 19.4, 22.7, 31.4, 37.8, 40.3, 44.5, 57.5, 92.1 (br), 161.5, 163.0, 163.9; HRMS calculated for $C_{12}H_{23}N_5$, 237.1953; found 237.1965.

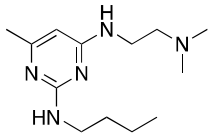
N^4-Butyl-N^2-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (29a)



Synthesized using the general procedure as for **5a** from *N*-butyl-2-chloro-6-methylpyrimidin-4-amine (**12a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(29a) yield 280 mg, 82% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.73 (t, 3H, *J* = 7.3 Hz), 1.18 (m, 2H), 1.33 (q, 2H, *J* = 6.6 Hz), 1.96 (s, 3H), 2.04 (s, 6H), 2.27 (t, 2H, *J* = 6.5 Hz), 3.08 (q, 2H, *J* = 6.8 Hz), 3.25 (t, 2H, *J* = 6.4 Hz), 4.13 (br s, 1H), 5.17 (br s, 1H), 5.38 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.0, 19.3, 22.7, 35.2, 38.2, 40.1, 44.5, 57.8, 91.8 (br), 161.5, 163.1, 164.0 (br); HRMS calculated for $C_{13}H_{25}N_5$, 251.2110; found 251.2119.

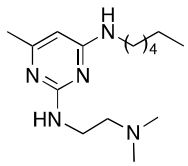
N^2-Butyl-N^4-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (29b)



Synthesized using the general procedure as for **5b** from *N*-butyl-4-chloro-6-methylpyrimidin-2-amine (**12b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(29b) yield 191 mg, 85% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.81 (t, 3H, *J* = 7.3 Hz), 1.25 (m, 2H), 1.41 (p, 2H, *J* = 6.7 Hz) 2.02 (s, 3H), 2.11 (s, 6H), 2.35 (t, 2H, *J* = 6.2 Hz), 3.24 (m, 4H), 4.08 (br s, 1H), 5.06 (br s, 1H), 5.53 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.1, 19.4, 22.7, 31.4, 37.8, 40.3, 44.5, 57.5, 92.1 (br), 161.5, 163.0, 163.9; HRMS calculated for $C_{13}H_{25}N_5$, 251.2110; found 251.2120.

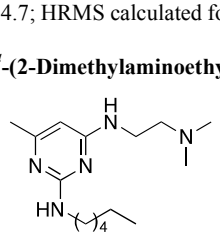
N^2-(2-Dimethylaminoethyl)-N^4-hexyl-6-methylpyrimidine-2,4-diamine (30a)



Synthesized using the general procedure as for **5a** from 2-chloro-*N*-hexyl-6-methylpyrimidin-4-amine (**13a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(30a) yield 36 mg, 15% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H), 1.28 (m, 6H), 1.53 (m, 2H), 2.17 (s, 3H), 2.26 (s, 6H), 2.46 (t, 2H, *J* = 6.3 Hz), 3.20 (q, 2H, *J* = 5.9 Hz), 3.41 (m, 2H), 4.70 (br s, 1H), 5.30 (br s, 1H), 5.55 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 23.0, 26.0, 29.0, 30.9, 38.4, 40.7, 44.6, 58.0, 91.6 (br), 161.4, 163.2, 164.7; HRMS calculated for $C_{15}H_{29}N_5$, 279.2423; found 279.2431.

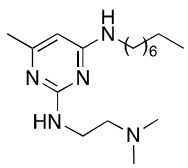
N^4-(2-Dimethylaminoethyl)-N^2-hexyl-6-methylpyrimidine-2,4-diamine (30b)



Synthesized using the general procedure as for **5b** from 4-chloro-*N*-hexyl-6-methylpyrimidin-2-amine (**13b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(30b) yield 29 mg, 43% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3H, *J* = 6.4 Hz), 1.35 (m, 6H), 1.48 (m, 2H), 2.16 (s, 3H), 2.22 (s, 6H), 2.45 (t, 2H, *J* = 6.2 Hz), 3.28-3.36 (m, 4H), 4.96 (br s, 1H), 5.19 (br s, 1H), 5.52 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.9, 26.1, 29.3, 31.0, 37.9, 40.6, 44.5, 57.5, 92.2 (br), 161.6, 163.1, 164.2; HRMS calculated for $C_{15}H_{29}N_5$, 279.2423; found 279.2429.

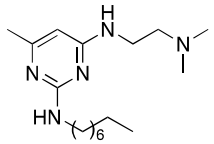
N^2-(2-Dimethylaminoethyl)-N^4-octyl-6-methylpyrimidine-2,4-diamine (31a)



Synthesized using the general procedure as for **5a** from 2-chloro-6-methyl-*N*-octylpyrimidin-4-amine (**14a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(31a) yield 203 mg, 72% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.77 (t, 3H), 1.15 (m, 10H), 1.40 (m, 2H), 2.01 (s, 3H), 2.09 (s, 6H), 2.31 (t, 2H, *J* = 6.3 Hz), 3.10 (q, 2H, *J* = 6.2 Hz) 3.31 (m, 2H), 4.97 (br s, 1H), 5.21 (br s, 1H), 5.41 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 23.0, 26.3, 28.5, 28.6, 28.9, 31.0, 38.3, 40.5, 44.5, 57.9, 91.6 (br), 161.5, 163.1, 164.6; HRMS calculated for $C_{17}H_{33}N_5$, 307.2736; found 307.2744.

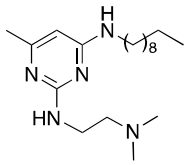
N^4-(2-Dimethylaminoethyl)-N^2-octyl-6-methylpyrimidine-2,4-diamine (31b)



Synthesized using the general procedure as for **5b** from 4-chloro-6-methyl-*N*-octylpyrimidin-2-amine (**14b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(31b) yield 57 mg, 35% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3H), 1.38 (m, 10H), 1.50 (m, 2H), 2.16 (s, 3H), 2.22 (s, 6H), 2.45 (t, 2H, *J* = 5.8 Hz), 3.33 (m, 4H), 4.91 (br s, 1H), 5.15 (br s, 1H), 5.53 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 22.0, 22.9, 26.4, 28.6, 28.7, 29.3, 31.2, 37.9, 40.7, 44.5, 57.4, 91.2 (br), 161.5, 163.0, 164.5; HRMS calculated for $C_{17}H_{33}N_5$, 307.2736; found 307.2746.

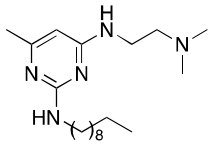
N^2-(2-Dimethylaminoethyl)-N^4-decyl-6-methylpyrimidine-2,4-diamine (32a)



Synthesized using the general procedure as for **5a** from 2-chloro-*N*-decyl-6-methylpyrimidin-4-amine (**15a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(32a) yield 230 mg, 68% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.71 (t, 3H, *J* = 6.2 Hz), 1.13 (s, 14H), 1.39 (m, 2H), 1.98 (s, 3H), 2.08 (s, 6H), 2.33 (t, 2H, *J* = 6.3 Hz), 3.16 (m, 2H) 3.29 (t, 2H, *J* = 6.3 Hz), 5.39 (br s, 1H), 5.57 (s, 1H), 6.15 (br s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.2, 21.9, 26.3, 28.5, 28.6, 28.7, 28.8 (2 x C), 28.9, 31.1, 38.2, 40.5, 44.4, 57.7, 93.0 (br), 159.0 (br), 159.8 (br), 162.9; HRMS calculated for $C_{19}H_{37}N_5$, 335.3049; found 335.3062.

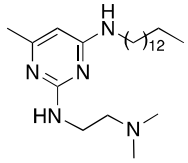
N^4-(2-Dimethylaminoethyl)-N^2-decyl-6-methylpyrimidine-2,4-diamine (32b)



Synthesized using the general procedure as for **5b** from 4-chloro-*N*-decyl-6-methylpyrimidin-2-amine (**15b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(32b) yield 217 mg, 80% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.81 (t, 3H, *J* = 7.0 Hz), 1.25 (m, 14H), 1.46 (m, 2H), 2.08 (s, 3H), 2.15 (s, 6H), 2.38 (t, 2H, *J* = 6.3 Hz), 3.16 (q, 2H, *J* = 6.3 Hz) 3.35 (t, 2H, *J* = 6.1 Hz), 4.97 (br s, 1H), 5.30 (br s, 1H), 5.47 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.8, 26.3, 28.5, 28.6, 28.7, 28.8, 28.9, 31.2, 38.3, 40.6, 44.5, 57.9, 91.7 (br), 161.3, 163.2, 164.6 (br); HRMS calculated for $C_{19}H_{37}N_5$, 335.3049; found 335.3056.

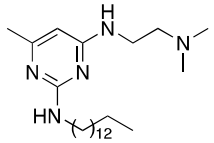
N^2-(2-Dimethylaminoethyl)-6-methyl-N^4-tetradecylpyrimidine-2,4-diamine (33a)



Synthesized using the general procedure as for **5a** from 2-chloro-6-methyl-*N*-tetradecylpyrimidin-4-amine (**16a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(33a) yield 174 mg, 51%, mp 51-53°C; ^{1}H NMR ($CDCl_3$): δ 0.84 (t, 3H, *J* = 6.2 Hz), 1.25 (s, 22H), 1.50 (m, 2H), 2.10 (s, 3H), 2.19 (s, 6H), 2.42 (t, 2H, *J* = 6.2 Hz), 3.19, (q, 2H, *J* = 6.5 Hz), 3.38 (t, 2H, *J* = 6.2 Hz), 4.36 (br s, 1H), 5.21 (br s, 1H), 5.53 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.1 (br), 26.4, 28.6, 28.7, 28.8, 28.9 (2 x C), 29.0 (4 x C), 31.3, 38.3, 40.7, 44.6, 57.9, 92.1 (br), 160.6, 162.9 (br), 163.1; HRMS calculated for $C_{23}H_{45}N_5$, 391.3675; found 391.3680.

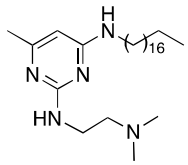
N^4-(2-Dimethylaminoethyl)-6-methyl-N^2-tetradecylpyrimidine-2,4-diamine (33b)



Synthesized using the general procedure as for **5b** from 4-chloro-6-methyl-*N*-tetradecylpyrimidin-2-amine (**16b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(33b) yield 271 mg, 87%, mp 65-66°C; ^{1}H NMR ($CDCl_3$): δ 0.84 (t, 3H, *J* = 7.0 Hz), 1.25 (s, 22H), 1.53 (m, 2H), 2.14 (s, 3H), 2.19 (s, 6H), 2.43 (t, 2H, *J* = 6.2 Hz), 3.32 (m, 4H), 4.92 (br s, 1H), 5.21 (br s, 1H), 5.50 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 22.0, 23.1, 26.4, 28.7, 28.8, 28.9 (3 x C), 29.0 (2 x C), 29.1, 29.3, 31.3, 37.9, 40.8, 44.5, 57.5, 92.1 (br), 161.7, 163.0, 164.4; HRMS calculated for $C_{23}H_{45}N_5$, 391.3675; found 391.3682.

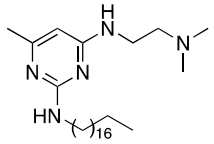
N^2-(2-Dimethylaminoethyl)-6-methyl-N^4-octadecylpyrimidine-2,4-diamine (34a)



Synthesized using the general procedure as for **5a** from 2-chloro-6-methyl-*N*-octadecylpyrimidin-4-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(34a) yield 177 mg, 71%, mp 64-66°C; ^{1}H NMR ($CDCl_3$): δ 0.84 (t, 3H, *J* = 6.8 Hz), 1.23 (s, 30H), 1.50 (m, 2H), 2.13 (s, 3H), 2.20 (s, 6H), 2.43 (t, 2H, *J* = 6.3 Hz), 3.19, (q, 2H, *J* = 6.2 Hz), 3.40 (t, 2H, *J* = 6.1 Hz), 4.98 (br s, 1H), 5.53 (br s, 2H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.1 (br), 26.4, 28.4, 28.6, 28.7, 28.8 (2 x C), 28.9 (3 x C), 29.0 (2 C's), 29.1 (2C's), 29.2, 31.2, 38.4, 40.7, 44.6, 57.9, 91.9 (br), 160.9, 163.2, 163.1 (br); HRMS calculated for $C_{27}H_{53}N_5$, 447.4301; found 447.4312.

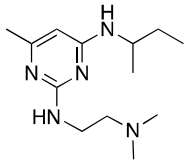
N^4-(2-Dimethylaminoethyl)-6-methyl-N^2-octadecylpyrimidine-2,4-diamine (34b)



Synthesized using the general procedure as for **5b** from 4-chloro-6-methyl-*N*-octadecylpyrimidin-2-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(**34b**) Yield 259 mg, 76%, mp 60-62°C; ^{1}H NMR ($CDCl_3$): δ 0.83 (t, 3H, *J* = 6.5 Hz), 1.22 (s, 30H), 1.48 (m, 2H), 2.11 (s, 3H), 2.19 (s, 6H), 2.43 (t, 2H, *J* = 6.1 Hz), 3.30 (m, 4H), 5.08 (br s, 1H), 5.32 (br s, 1H), 5.49 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.4, 22.0, 23.1, 26.4, 28.7 (3 x C), 28.8 (2 x C), 28.9 (3 x C), 29.0 (2 x C), 29.1, 29.2, 29.3, 31.3, 37.9, 40.7, 44.5, 57.5, 92.2 (br), 161.4, 163.0, 163.8 (br); HRMS calculated for $C_{27}H_{53}N_5$, 447.4301; found 447.34305.

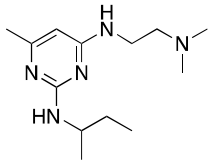
N^4-*sec*-Butyl-N^2-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (35a)



Synthesized using the general procedure as for **5a** from *N*-sec-butyl-2-chloro-6-methylpyrimidin-4-amine (**17a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(35a) yield 161 mg, 86% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.91 (t, 3H, *J* = 7.4 Hz), 1.14 (d, 3H, *J* = 6.6 Hz), 1.52 (m, 2H), 2.08 (s, 3H), 2.27 (s, 6H), 2.52 (t, 2H, *J* = 6.8 Hz), 3.45 (t, 2H, *J* = 6.8 Hz), 3.92 (m, 1H), 5.63 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.0, 18.7, 22.3, 28.7, 37.9, 43.7, 48.0, 57.9, 92.9 (br), 161.4, 163.0, 164.2; HRMS calculated for $C_{13}H_{25}N_5$, 251.2110; found 251.2124.

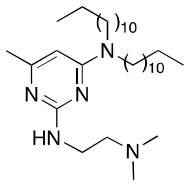
N^2-*sec*-Butyl-N^4-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (35b)



Synthesized using the general procedure as for **5b** from *N*-sec-butyl-4-chloro-6-methylpyrimidin-2-amine (**17b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(35b) yield 224 mg, 89% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.78 (t, 3H, *J* = 7.4 Hz), 1.03 (d, 3H, *J* = 6.5 Hz), 1.25 (m, 2H), 1.99 (s, 3H), 2.09 (s, 6H), 2.33 (t, 2H, *J* = 6.2 Hz), 3.22 (q, 2H, *J* = 6 Hz), 3.85 (m, 1H), 4.72 (br s, 1H), 5.32 (br s, 1H), 5.40 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 9.5, 19.8, 22.8, 29.1, 37.7, 44.5, 47.0, 57.5, 92.1 (br), 161.2, 163.0, 164.1; HRMS calculated for $C_{13}H_{25}N_5$, 251.2110; found 251.2111.

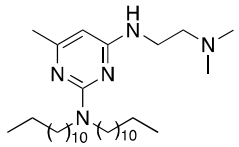
2-(2-Dimethylaminoethyl)-4-*N*-(didecylamino)-6-methylpyrimidine (36a)



Synthesized using the general procedure as for **5a** from 2-chloro-*N,N*-didecyl-6-methylpyrimidin-4-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(36a) Yield 466 mg, 72% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.76 (t, 6H, *J* = 6.5 Hz), 1.19 (s, 28H), 1.47 (m, 4H), 2.12 (s, 3H), 2.18 (s, 6H), 2.45 (t, 2H, *J* = 6.9 Hz), 3.45 (m, 6H), 5.47 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 22.1, 26.3, 27.0, 28.5, 28.7, 28.8 (2 x C), 31.2, 38.2, 44.5, 48.0, 57.4, 90.8, 156.8, 157.3, 163.4; HRMS calculated for $C_{29}H_{57}N_5$, 475.4614; found 475.4629.

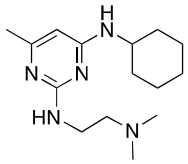
4-(2-Dimethylaminoethyl)-2-*N*-(didecylamino)-6-methylpyrimidine (36b)



Synthesized using the general procedure as for **5b** from 4-chloro-*N*,*N*-didecyl-6-methylpyrimidin-2-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(36b) Yield 150 mg, 56%, mp 66-68°C; ^{1}H NMR ($CDCl_3$): δ 0.90 (t, 6H, *J* = 6.6 Hz), 1.33 (s, 28H), 1.58 (m, 4H), 2.14 (s, 3H), 2.26 (s, 6H), 2.49 (t, 2H, *J* = 6.1 Hz), 3.38 (q, 2H, *J* = 5.5 Hz), 3.51 (t, 4H, *J* = 7 Hz), 5.49 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.4, 22.0, 23.4, 26.5, 27.5, 28.7, 28.9 (2 x C), 29.0, 31.3, 37.8, 44.6, 46.7, 57.8, 92.1, 161.0, 162.7, 164.4; HRMS calculated for $C_{29}H_{57}N_5$, 475.4614; found 475.4603.

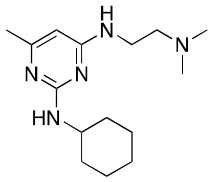
N^4-Cyclohexyl-N^2-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (37a)



Synthesized using the general procedure as for **5a** from 2-chloro-*N*-cyclohexyl-6-methylpyrimidin-4-amine (**18a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(37a) Yield 162 mg, 74% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 1.15 (m, 6H), 1.55 (m, 2H), 1.92 (m, 2H), 2.02 (s, 3H), 2.09 (s, 6H), 2.32 (t, 2H, *J* = 6.3 Hz), 3.28 (m, 2H), 3.32-3.48 (m, 1H), 4.88 (br s, 1H), 5.28 (br s, 1H), 5.43 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 22.8, 24.3, 25.1, 32.5, 38.3, 44.5, 48.9, 57.9, 92.0 (br), 161.3, 162.2, 163.9; HRMS calculated for $C_{15}H_{27}N_5$, 277.2266; found 277.2269.

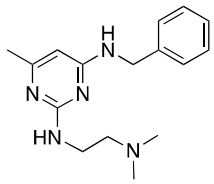
N^2-Cyclohexyl-N^4-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (37b)



Synthesized using the general procedure as for **5b** from 4-chloro-*N*-cyclohexyl-6-methylpyrimidin-2-amine (**18b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(37b) Yield 161 mg, 86% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 1.52 (m, 8H), 1.89 (m, 2H), 2.04 (s, 3H), 2.15 (s, 6H), 2.38 (t, 2H, *J* = 6.2 Hz), 3.25 (q, 2H, *J* = 6.0 Hz), 3.66 (m, 1H), 4.76 (br s, 1H), 5.25 (br s, 1H), 5.44 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 22.4, 24.3, 25.3, 32.2, 38.5, 44.8, 49.2, 58.1, 92.2 (br), 161.5, 162.5, 164.0 (br); HRMS calculated for $C_{15}H_{27}N_5$, 277.2266; found 277.2273.

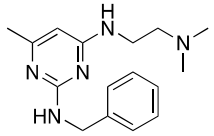
N^4-Benzyl-N^2-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (38a)



Synthesized using the general procedure as for **5a** from *N*-benzyl-2-chloro-6-methylpyrimidin-4-amine (**19a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(38a) Yield 87 mg, 37% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 2.14 (s, 3H), 2.21 (s, 6H), 2.44 (t, 2H, *J* = 6.3 Hz), 3.45 (q, 2H), 4.48 (d, 2H, *J* = 5.8 Hz), 5.08 (br s, 1H), 5.32 (br s, 1H), 5.56 (s, 1H), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 23.1, 38.4, 44.6, 57.9, 92.0 (br), 126.6, 126.7, 128.0, 138.5, 161.7, 163.1, 165.2; HRMS calculated for $C_{16}H_{23}N_5$, 285.1953; found 285.1950.

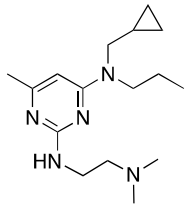
N^2-Benzyl-N^4-(2-dimethylaminoethyl)-6-methylpyrimidine-2,4-diamine (38b)



Synthesized using the general procedure as for **5b** from *N*-benzyl-4-chloro-6-methylpyrimidin-2-amine (**19b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(38b) yield 53 mg, 32% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 2.16 (s, 3H), 2.22 (s, 6H), 2.44 (t, 2H, *J* = 6.2 Hz), 3.28 (q, 2H, *J* = 6.4 Hz), 4.59 (d, 2H, *J* = 5.6 Hz), 5.19 (br s, 1H), 5.38 (br s, 1H), 5.57 (s, 1H), 7.28 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 23.0, 37.9, 44.5, 44.8, 57.5, 92.7 (br), 126.2, 126.9, 127.8, 139.6, 161.5, 163.1, 164.6 (br); HRMS calculated for $C_{16}H_{23}N_5$, 285.1953; found 285.1960.

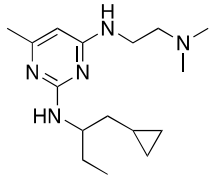
N^4-Cyclopropylmethyl-N^2-(2-dimethylaminoethyl)-6-methyl-N^4-propylpyrimidine-2,4-diamine (39a)



Synthesized using the general procedure as for **5a** from 2-chloro-*N*-(cyclopropylmethyl)-6-methyl-*N*-propylpyrimidin-4-amine (**21a**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(39a) yield 285 mg, 85% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.05 (d, 2H, *J* = 7.4 Hz), 0.30 (d, 2H, *J* = 7.8 Hz), 0.72 (t, 3H, 7.3 Hz), 0.87 (m, 1H), 1.45 (m, 2H), 1.99 (s, 3H), 2.05 (s, 6H), 2.26 (t, 2H, *J* = 6.2 Hz), 3.28 (m, 6H), 5.20 (br s, 1H), 5.47 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 2.9, 9.2, 10.6, 20.1, 23.1, 38.3, 44.5, 49.1, 51.2, 58.0, 90.8, 161.2, 162.0, 164.1; HRMS calculated for $C_{16}H_{29}N_5$, 291.2423; found 291.2431.

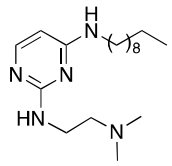
N^2-Cyclopropylmethyl-N^4-(2-dimethylamin-ethyl)-6-methyl-N^2-propylpyrimidine-2,4-diamine (39b)



Synthesized using the general procedure as for **5b** from 4-chloro-*N*-(cyclopropylmethyl)-6-methyl-*N*-propylpyrimidin-2-amine (**21b**) and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

Yield 133 mg, 48% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.22 (q, 2H, *J* = 5 Hz), 0.41 (q, 2H, *J* = 6.5 Hz), 0.86 (t, 3H, 7.4 Hz), 1.08 (m, 1H), 1.62 (m, 2H), 2.10 (s, 3H), 2.18 (s, 6H), 2.45 (t, 2H, *J* = 6.2 Hz), 3.34 (q, 2H, *J* = 5.6 Hz), 3.44 (d, 2H, *J* = 6.7 Hz), 3.54 (t, 2H, *J* = 7.5 Hz), 4.92 (br s, 1H), 5.46 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 2.9, 9.7, 10.9, 20.5, 23.5, 37.8, 44.5, 48.4, 50.7, 57.8, 91.2, 161.3, 162.7, 164.6; HRMS calculated for $C_{16}H_{29}N_5$, 291.2423; found 291.2429.

N^4-Decyl-N^2-(2-dimethylaminoethyl)pyrimidine-2,4-diamine (40a) [S8]



To a solution of 2,4-dichloro-6-methylpyrimidine (0.65 g, 4.0 mmol) in THF (5 ml) was added decylamine (1.26g, 8 mmol, 2 eq). The resulting solution was stirred at 30 °C for 18 hours, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography using 1:9 ethyl acetate:hexanes to yield a mixture of 2-chloro-N-decylpyrimidin-4-amine and 2-chloro-*N*-decylpyrimidin-4-amine. Isomers were separated by flash chromatograpghy (EtOAc:Triethylamine, 95:5).

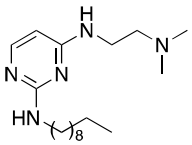
4-Chloro-*N*-decylpyrimidin-2-amine : yield 967mg, 68%, mp 80-82°C; ^{1}H NMR ($CDCl_3$): δ 0.80 (t, 3H, *J* = 6.2 Hz), 1.25 (s, 14H), 1.53 (m, 2H), 3.26 (m, 2H), 5.94 (br s, 1H), 6.18 (d, 1H, *J* = 5.9 Hz), 7.90 (d, 1H, *J* = 5.6 Hz); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 26.2, 28.4, 28.6, 28.8 (3 x C), 31.2, 40.9, 100.1 (br), 156.0 (br), 160.0, 163.3.

2-Chloro-*N*-decylpyrimidin-4-amine: yield 384mg, 27%, mp 67-68°C; ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3H, *J* = 6.6 Hz), 1.33 (s, 14H), 1.57 (m, 2H), 3.38 (q, 2H, *J* = 7 Hz), 5.59 (br s, 1H), 6.48 (d, 1H, *J* = 5.3 Hz), 8.09 (d, 1H, *J* = 5.3 Hz); ^{13}C NMR ($CDCl_3$): δ 13.4, 22.0, 26.3, 28.6, 28.7, 28.9 (3 x C), 31.2, 40.9, 108.9, 159.3, 160.7, 162.0.

The target compound **40a** was syntheszied using the general procedure as for **5a** from 4-chloro-*N*-decylpyrimidin-2-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(40a) Yield 300mg, 85% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.75 (t, 3H, *J* = 6.4 Hz), 1.17 (s, 14H), 1.41 (m, 2H), 2.10 (s, 3H), 2.33 (t, 2H, *J* = 6.3 Hz), 3.09 (q, 2H, *J* = 5.9 Hz), 3.27 (t, 2H, *J* = 6.3 Hz) 4.39 (br s, 1H), 5.29 (s, 1H), 5.53 (d, 1H, *J* = 5.9 Hz), 7.60 (d, 1H, *J* = 5.9 Hz); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 26.3, 28.5, 28.6, 28.8 (2 x C), 28.9, 31.1, 38.3, 40.5, 44.5, 57.8, 93.5 (br), 154.5 (br), 161.3, 162.6; HRMS calculated for $C_{18}H_{35}N_5$, 321.2892; found 321.2883.

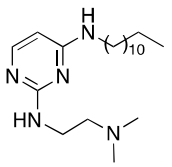
N^2-Decyl-N^4-(2-dimethylaminoethyl)pyrimidine-2,4-diamine (40b)



Synthesized using the general procedure as for **5b** from 2-chloro-*N*-decylpyrimidin-4-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(40a) Yield 238 mg, 79% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.72 (t, 3H, *J* = 7.0 Hz), 1.15 (s, 14H), 1.50 (m, 2H), 2.08 (s, 6H), 2.31 (t, 3H, *J* = 6.1 Hz), 3.21 (m, 4H), 5.48 (d, 1H, *J* = 5.8 Hz), 5.63 (br s, 1H), 7.57 (d, 1H, *J* = 5.7 Hz); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 26.3, 28.7, 28.8, 28.9 (2 x C), 29.2, 31.1, 37.6, 40.6, 44.4, 57.4, 93.7 (br), 154.3, 161.5, 162.5 (br); HRMS calculated for $C_{18}H_{35}N_5$, 321.2892; found 321.2899.

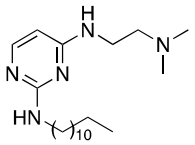
N^4-Dodecyl-N^2-(2-dimethylaminoethyl)pyrimidine-2,4-diamine (41a) [S8]



Synthesized using the general procedure as for **5a** from 4-chloro-*N*-dodecylpyrimidin-2-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(41a) Yield 226 mg, 65%, mp 36-38° C; ^{1}H NMR ($CDCl_3$): δ 0.82 (t, 3H, *J* = 6.9 Hz), 1.32 (s, 18H), 1.49 (m, 2H), 2.18 (s, 6H), 2.42 (t, 2H, *J* = 6.2 Hz), 3.19 (q, 2H, *J* = 6.1 Hz), 3.38 (t, 2H, *J* = 6.2 Hz), 5.13 (br s, 1H), 5.48 (br s, 1H), 5.63 (d, 1H, *J* = 5.9 Hz), 7.68 (d, 1H, *J* = 5.9 Hz); ^{13}C NMR ($CDCl_3$): δ 13.4, 22.0, 26.3, 28.6, 28.7, 28.9 (3 x C), 29.0, 31.2, 38.3, 40.6, 44.6, 57.9, 93.6 (br), 154.2 (br), 161.1, 162.6; HRMS calculated for $_{20}H_{39}N_5$, 349.3205; found 349.3210.

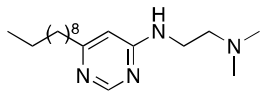
N^2-Dodecyl-N^4-(2-dimethylaminoethyl)-pyrimidine-2,4-diamine (41b)



Synthesized using the general procedure as for **5b** from 2-chloro-*N*-dodecylpyrimidin-4-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(41b) Yield 244 mg, 83% pale yellow oil; ^{1}H NMR ($CDCl_3$): δ 0.80 (t, 3H, *J* = 6.2 Hz), 1.23 (s, 18H), 1.49 (m, 2H), 2.17 (s, 6H), 2.43 (t, 2H, *J* = 6.1 Hz), 3.32 (m, 4H), 5.64 (d, 1H, *J* = 6.1 Hz), 5.78 (br s, 1H), 7.57 (d, 1H, *J* = 5.9 Hz); ^{13}C NMR ($CDCl_3$): δ 13.3, 21.9, 26.4, 28.6, 28.6, 28.7, 28.9 (3 x C), 29.1, 31.2, 37.7, 40.7, 44.4, 57.3, 94.2 (br), 151.3 (br), 160.2, 162.4 (br); HRMS calculated for $_{20}H_{39}N_5$, 349.3205; found 349.3213.

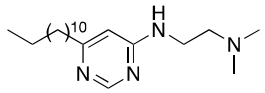
***N*-Decyl-*N′*-(2-dimethylaminoethyl)-pyrimidine-4,6-diamine (42)**



Synthesized using the general procedure as for **5a** from 6-chloro-*N*-decylpyrimidin-4-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(42) yield 289 mg, 75%, mp 61-63° C; ^{1}H NMR ($CDCl_3$): δ 0.63 (t, 3H, *J* = 6.6 Hz), 1.07 (s, 14H), 1.34 (m, 2H), 2.00 (s, 6H), 2.25 (t, 2H, *J* = 6.2 Hz), 2.88 (m, 2H), 3.16 (m, 2H), 5.01 (s, 1H), 5.67 (br s, 1H), 5.73 (br s, 1H), 7.78 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.2, 21.8, 26.3, 28.4, 28.5, 28.7, 28.8, 28.9, 31.0, 38.2, 40.9, 44.3, 57.2, 78.8 (br), 156.8, 162.2, 162.3; HRMS calculated for $C_{18}H_{35}N_5$, 321.2892; found 321.2901

***N*-Dodecyl-*N′*-(2-dimethylaminoethyl)pyrimidine-4,6-diamine (43)**



Synthesized using the general procedure as for **5** from 6-chloro-*N*-dodecylpyrimidin-4-amine and *N,N*-dimethylethylenediamine. The residue was purified by dry column flash chromatography using EtOAc followed by 1:1 $CHCl_3$:CH_3OH to yield the target compound.

(43) Yield 279 mg, 67%, mp 59-60° C; ^{1}H NMR ($CDCl_3$): δ 0.71 (t, 3H, *J* = 7.0 Hz), 1.13 (s, 18H), 1.37 (m, 2H), 2.06 (s, 6H), 2.32 (t, 2H, *J* = 6.2 Hz), 2.94 (m, 2H), 3.12 (m, 2H), 5.06 (s, 1H), 5.54 (br s, 1H), 5.60 (br s, 1H), 7.83 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 13.2, 21.8, 26.3, 28.5 (2 x C), 28.6, 28.8 (2 x C), 28.9, 31.1, 38.2, 40.9, 44.3, 57.2, 78.9 (br), 156.9, 162.2, 162.3; HRMS calculated for $C_{20}H_{39}N_5$, 349.3205; found 349.3216.

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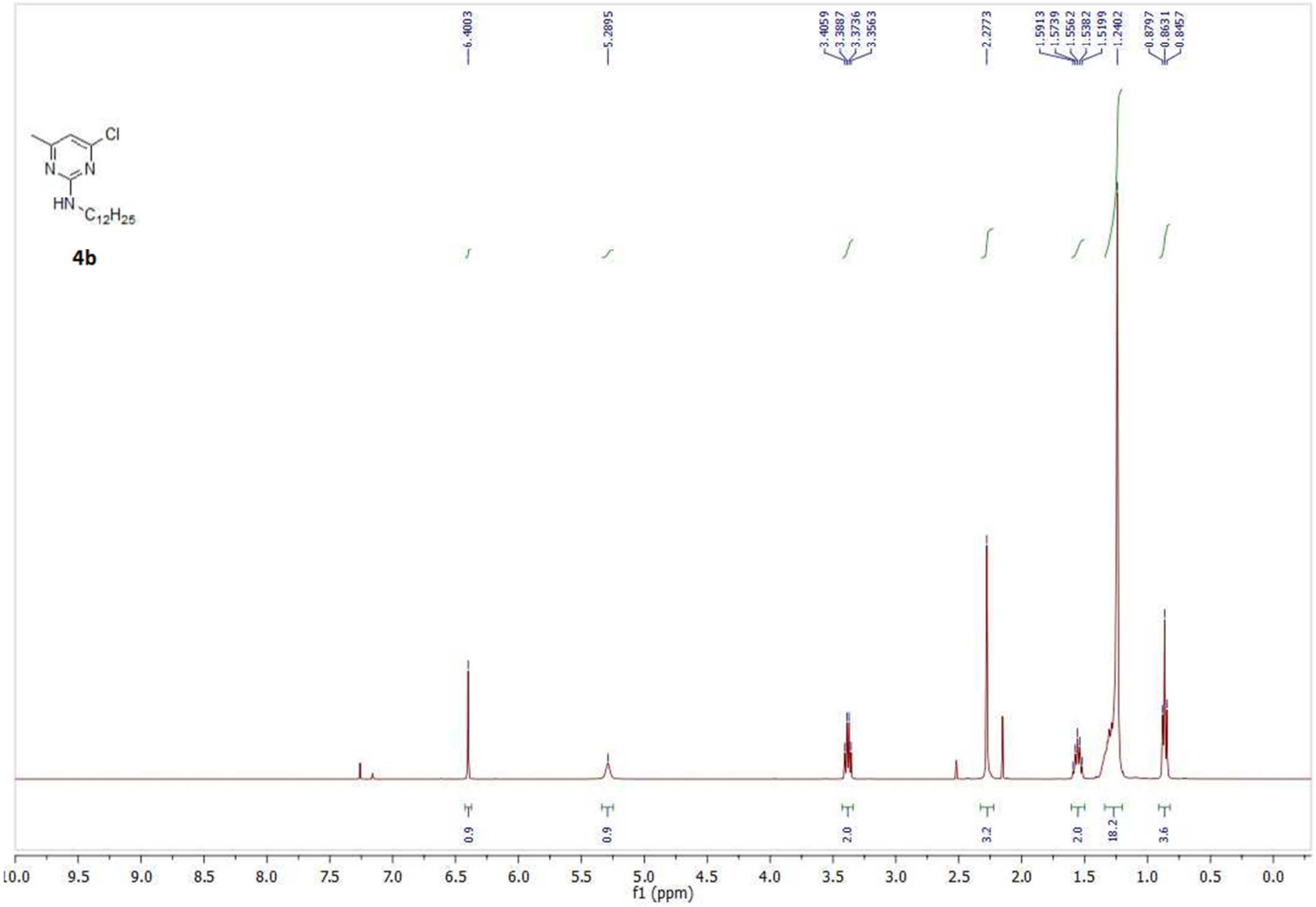
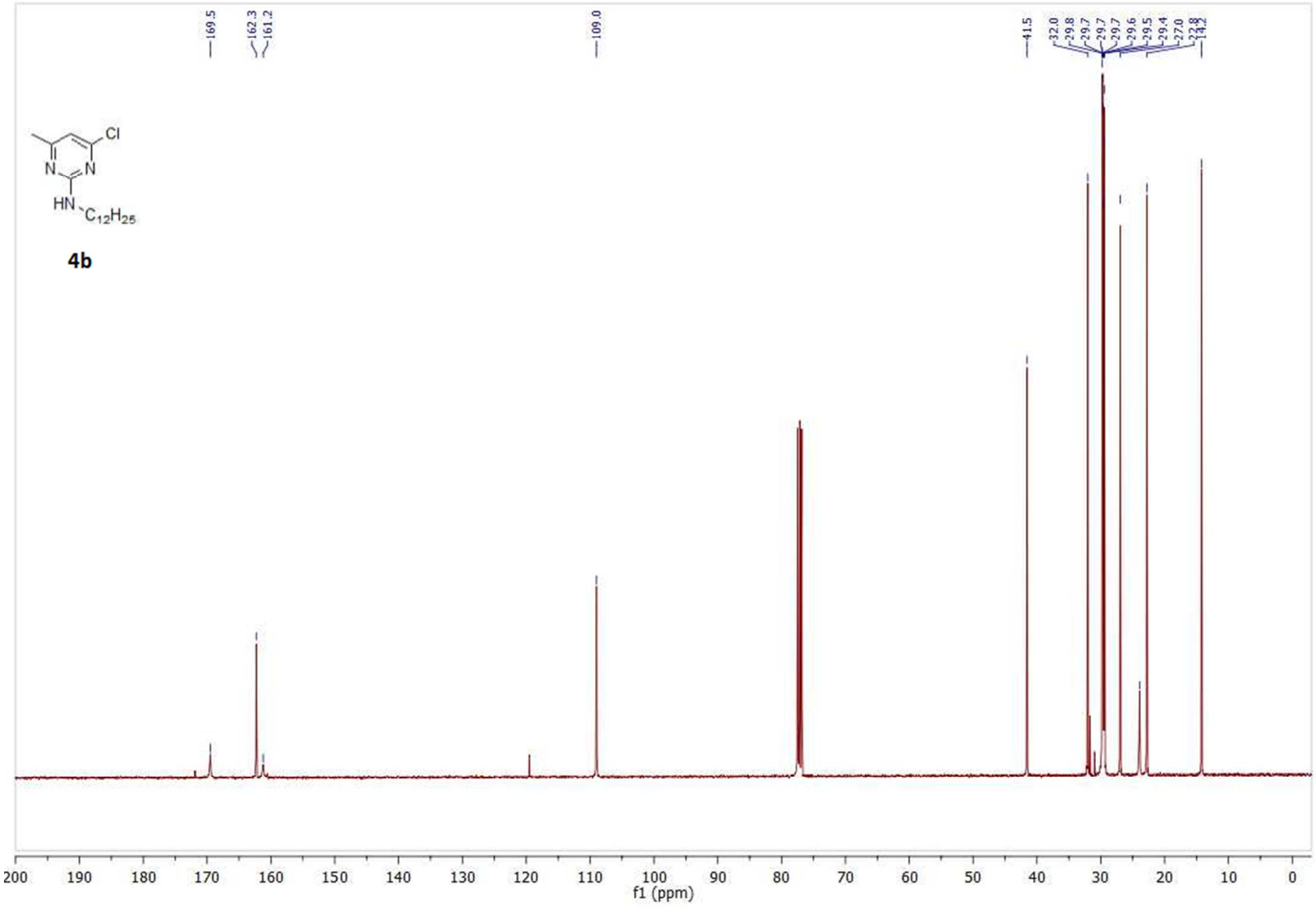
Examples for NMR spectra

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161.2
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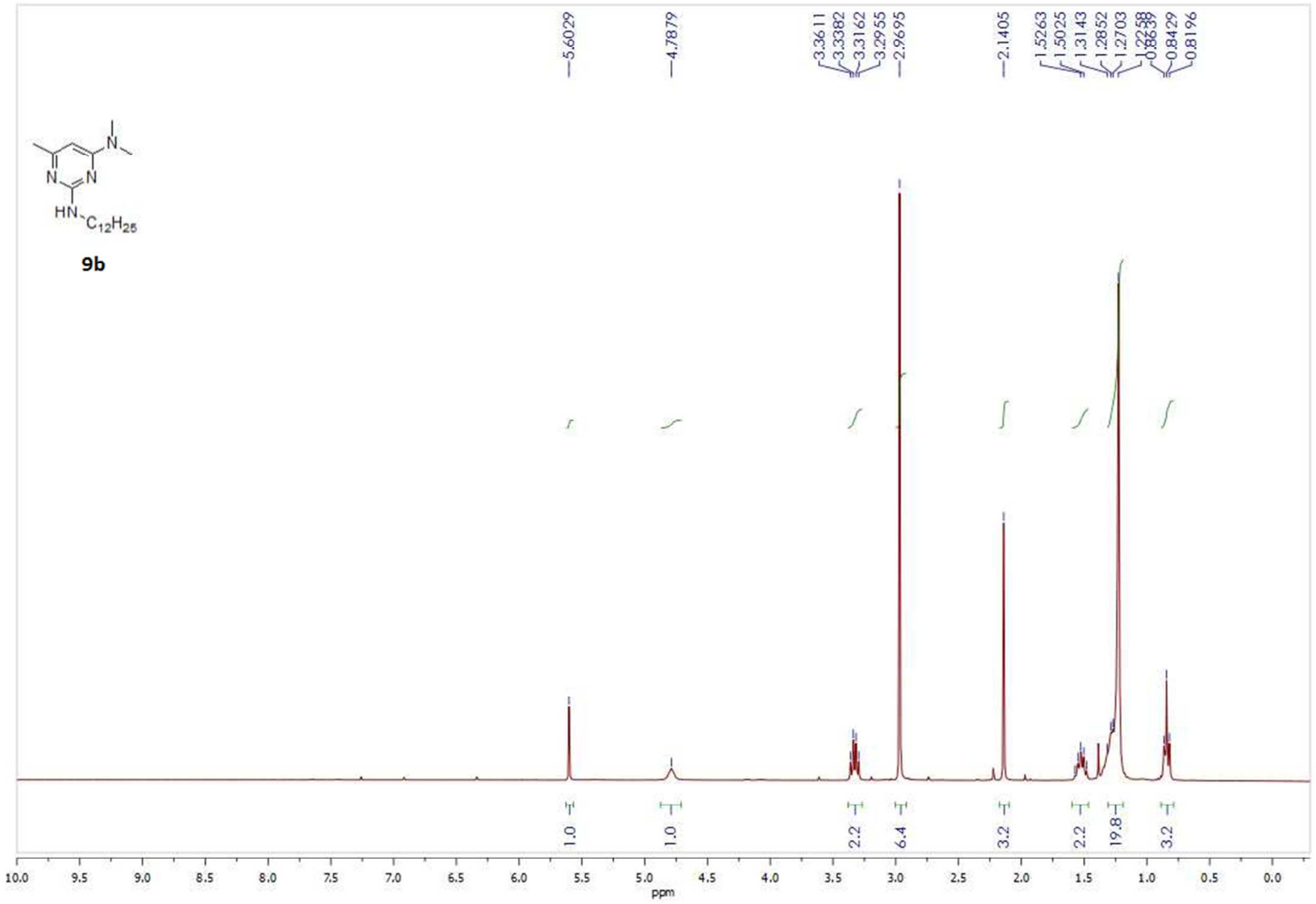
32.0
29.8
29.7
29.7
29.7
29.6
29.5
29.4
27.0
22.8
14.2
Cl
N
N
HN
C12H25
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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4.7879
3.3611
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2.9695
2.1405
1.5263
1.5025
1.3143
1.2852
1.2703
0.8639
0.8429
0.8196
1.0
1.0
2.2
6.4
3.2
2.2
19.8
3.2
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
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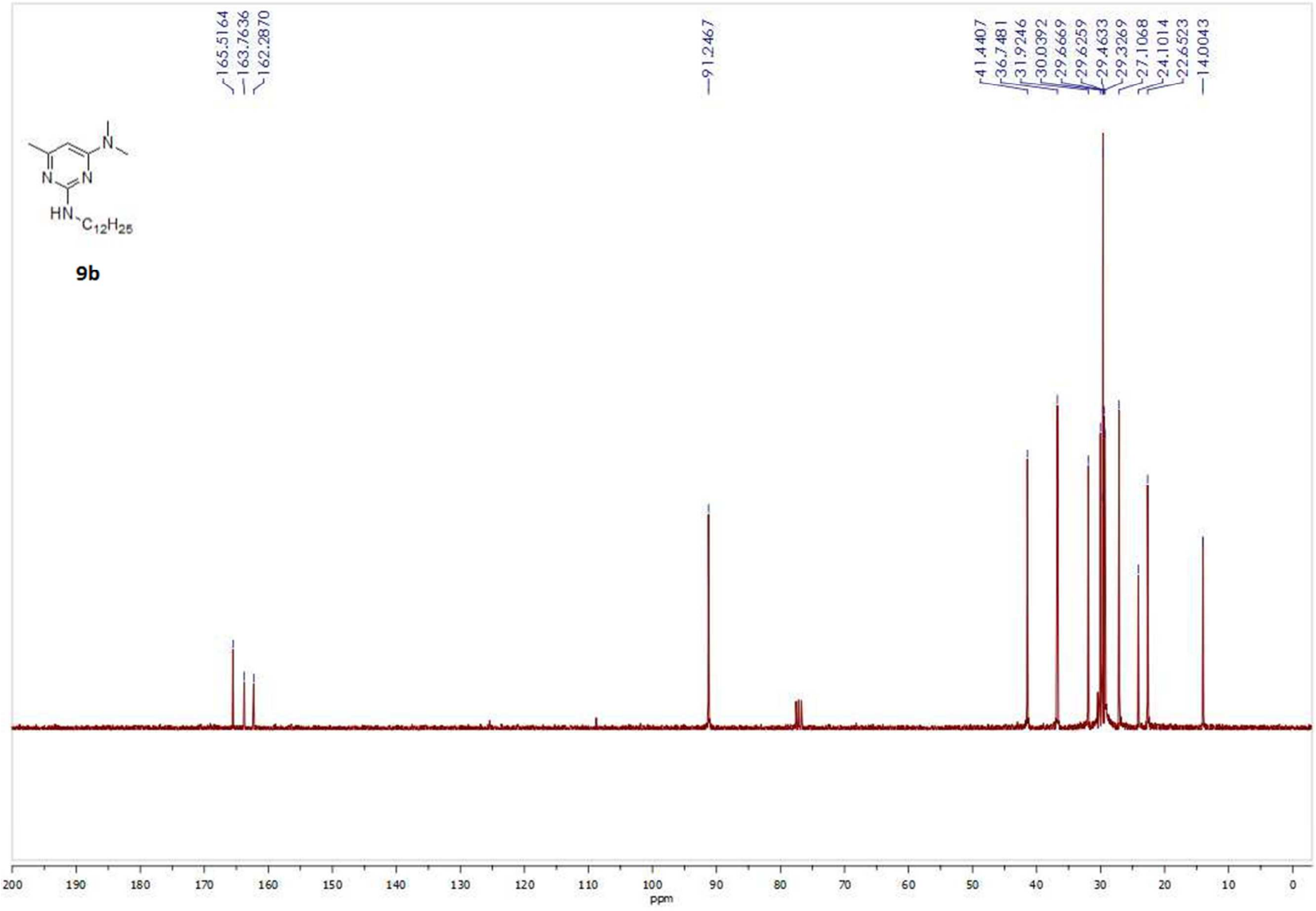
0.0
ppm

9b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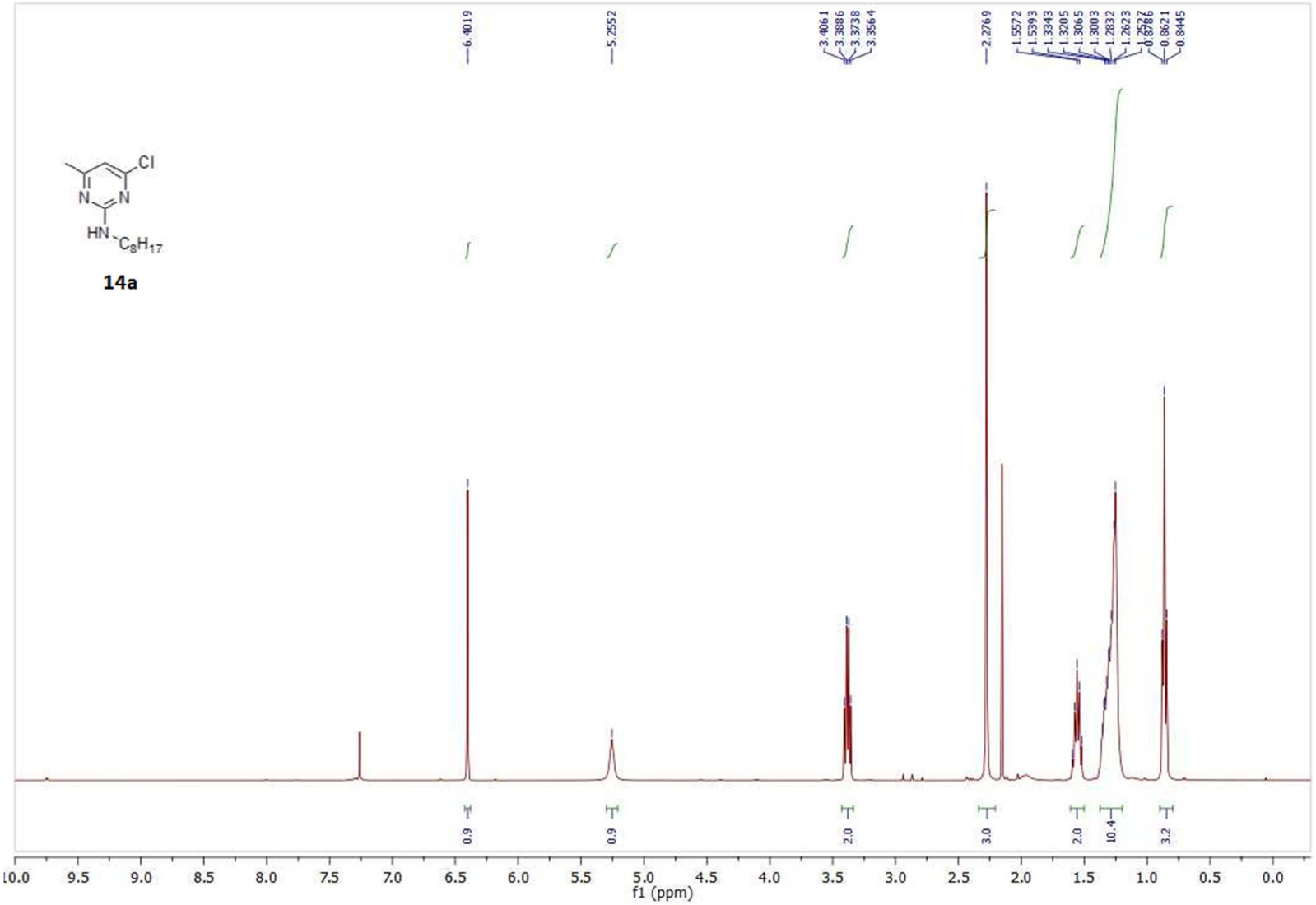
41.4407
36.7481
31.9246
30.0392
29.6669
29.6259
29.4633
29.3269
27.1068
24.1014
22.6523
14.0043
HN
$C_{12}H_{25}$
9b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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3.3738
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2.2769
1.5572
1.5393
1.3343
1.3205
1.3065
1.3003
1.2832
1.2623
1.2527
0.8786
0.8621
0.8445
Cl
N
N
HN
C8H17
14a
0.9
0.9
2.0
3.0
2.0
10.4
3.2
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
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1.0
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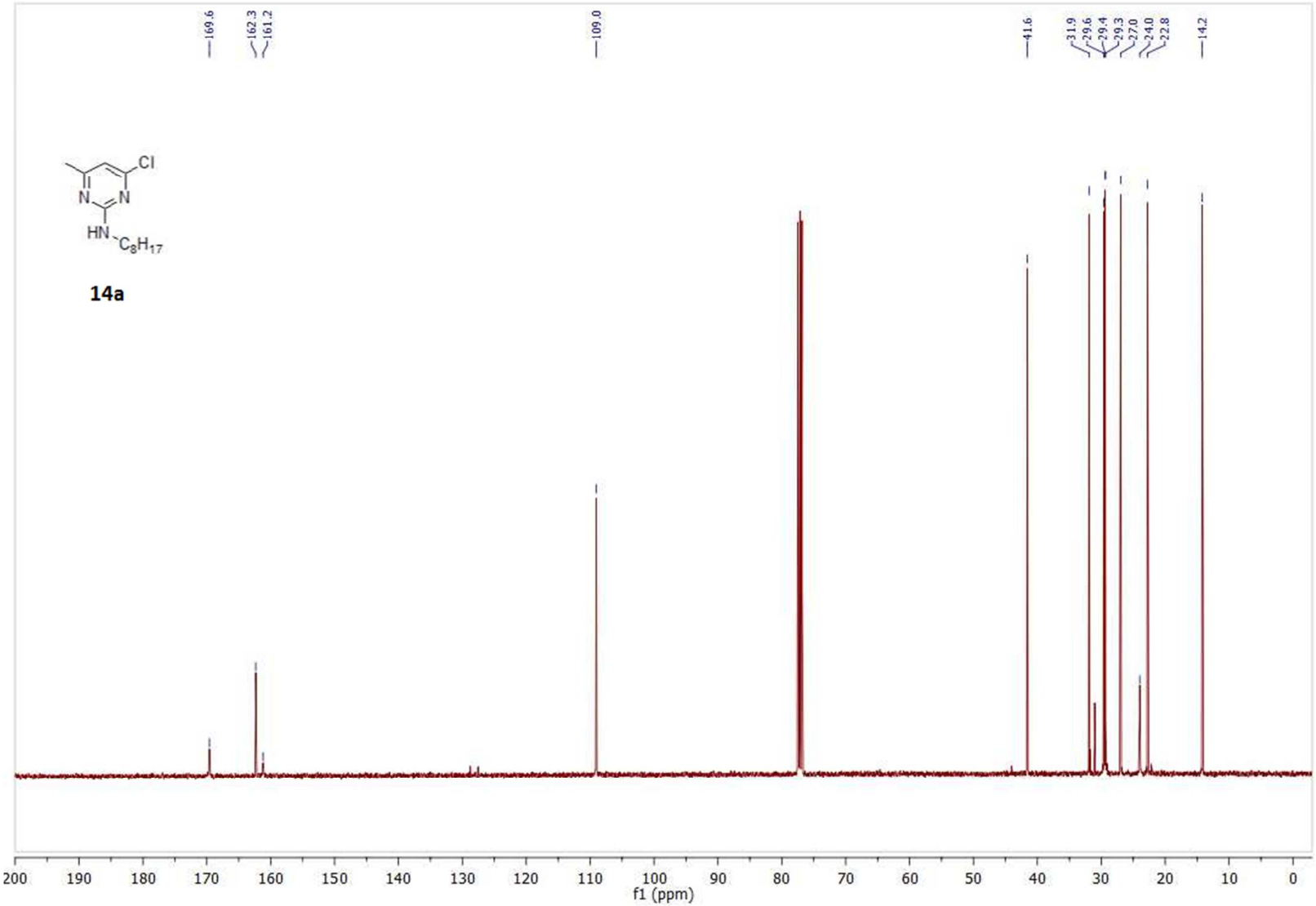
f1 (ppm)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29.6
29.4
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27.0
24.0
22.8
14.2
Cl
N
N
HN
C8H17
14a
200
190
180
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130
120
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100
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50
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30
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10
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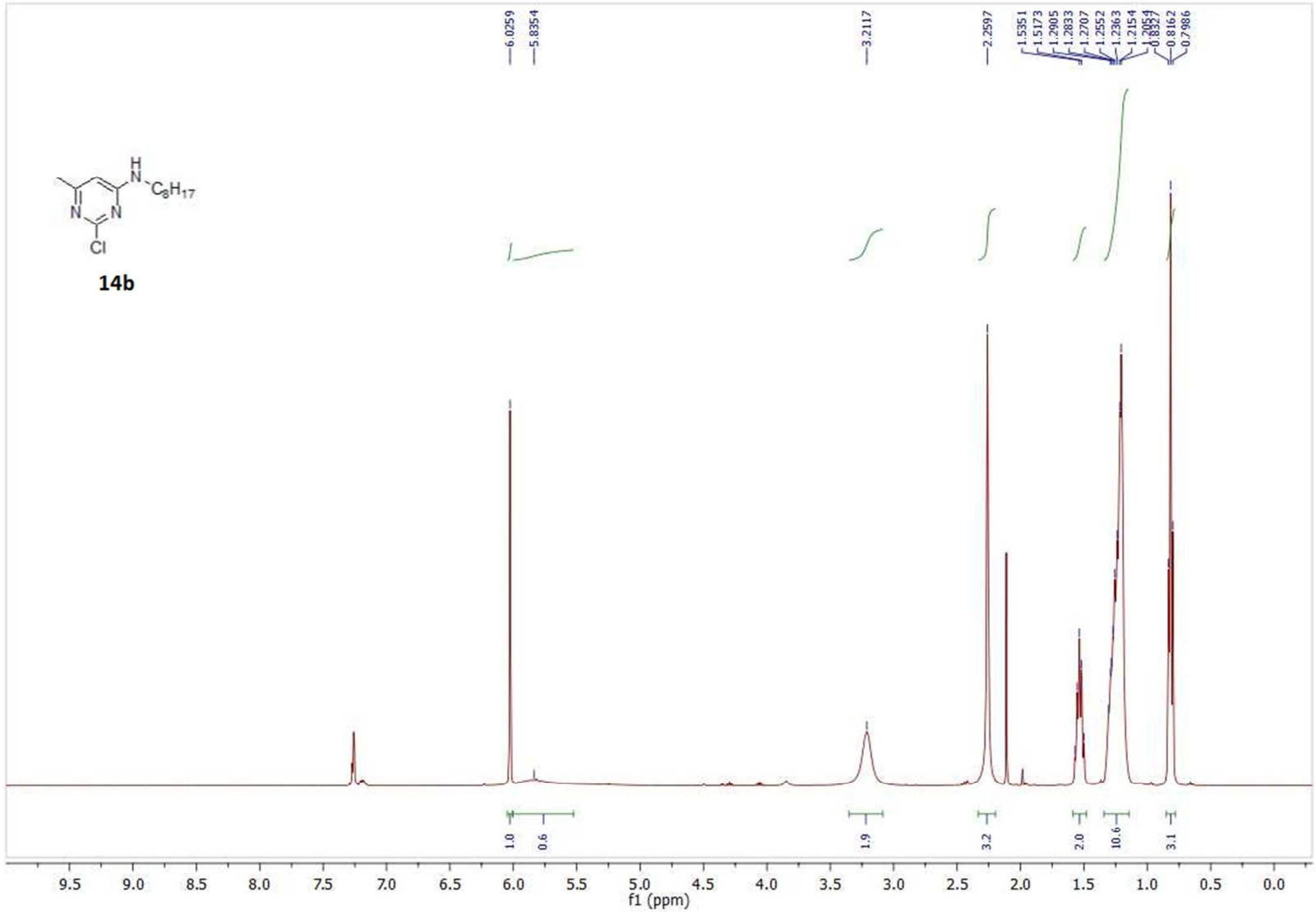
f1 (ppm)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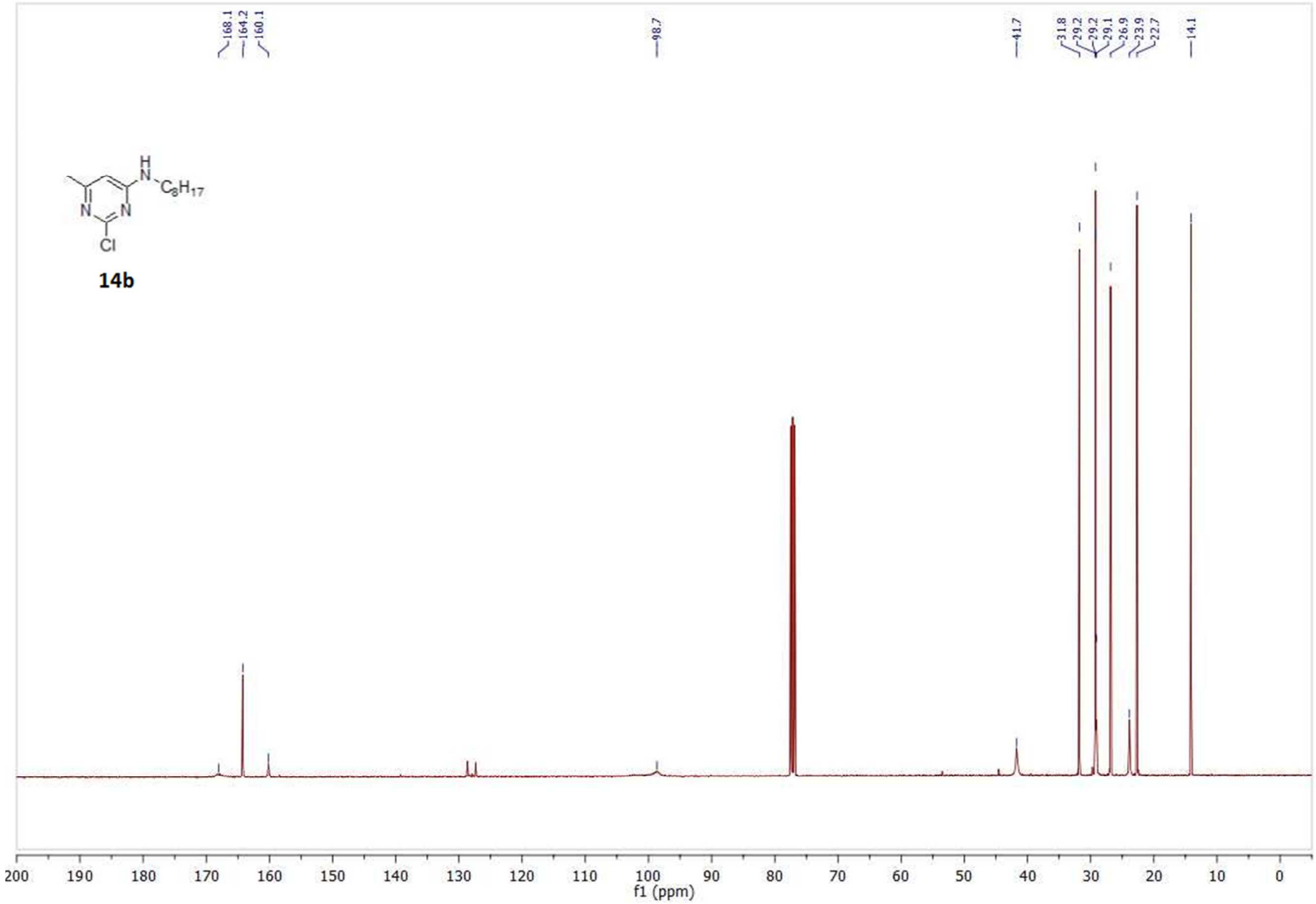
1.5173
1.2905
1.2833
1.2707
1.2552
1.2363
1.2154
1.2054
0.8327
0.8162
0.7986
1.0
0.6
1.9
3.2
2.0
10.6
3.1
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

14b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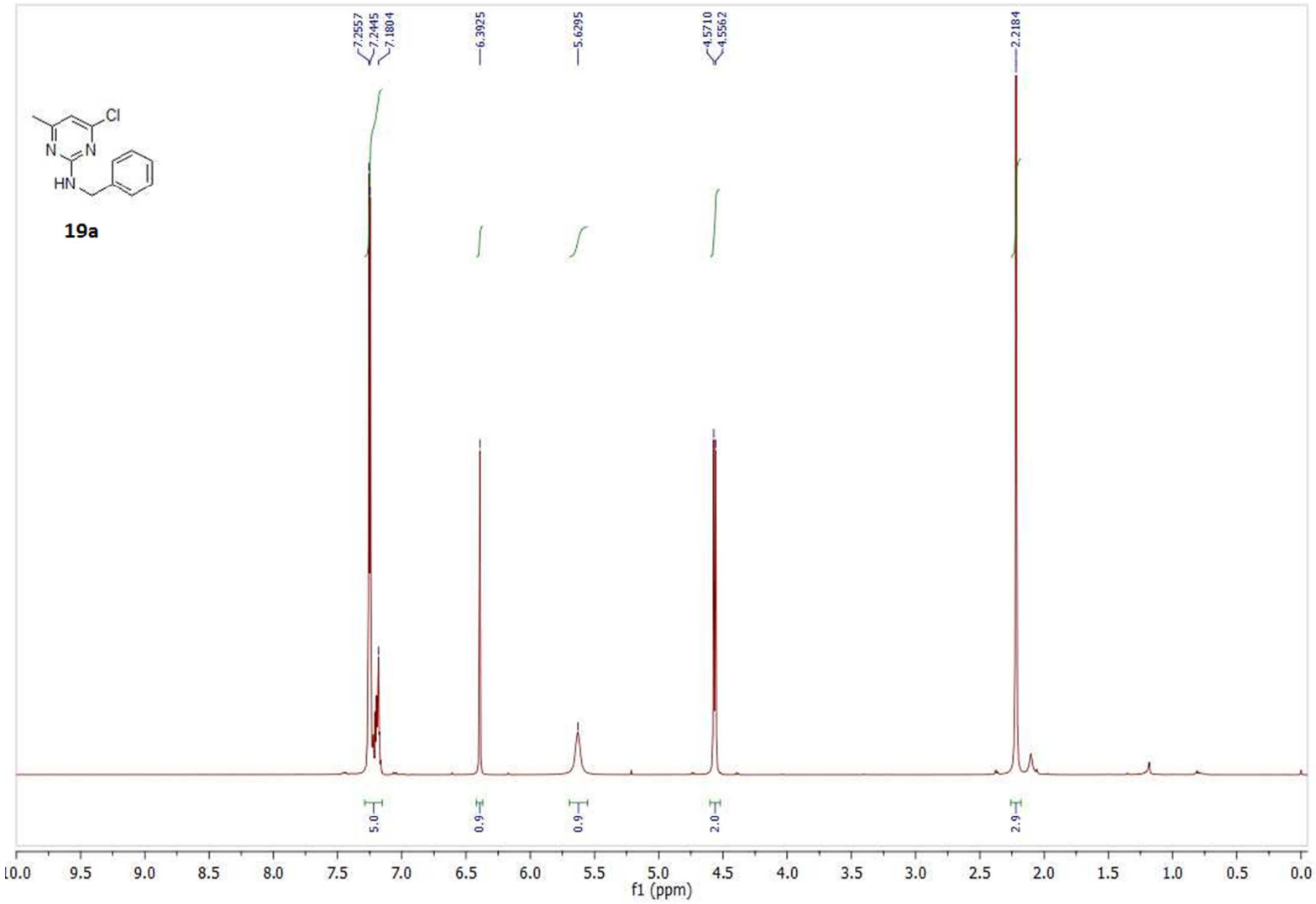
164.2
160.1
98.7
41.7
31.8
29.2
29.2
29.1
26.9
23.9
22.7
14.1
H
N
C8H17
N
N
Cl
14b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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4.5710
4.5562
2.2184
Cl
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N
HN
19a
5.0
0.9
0.9
2.0
2.9
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
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1.5
1.0
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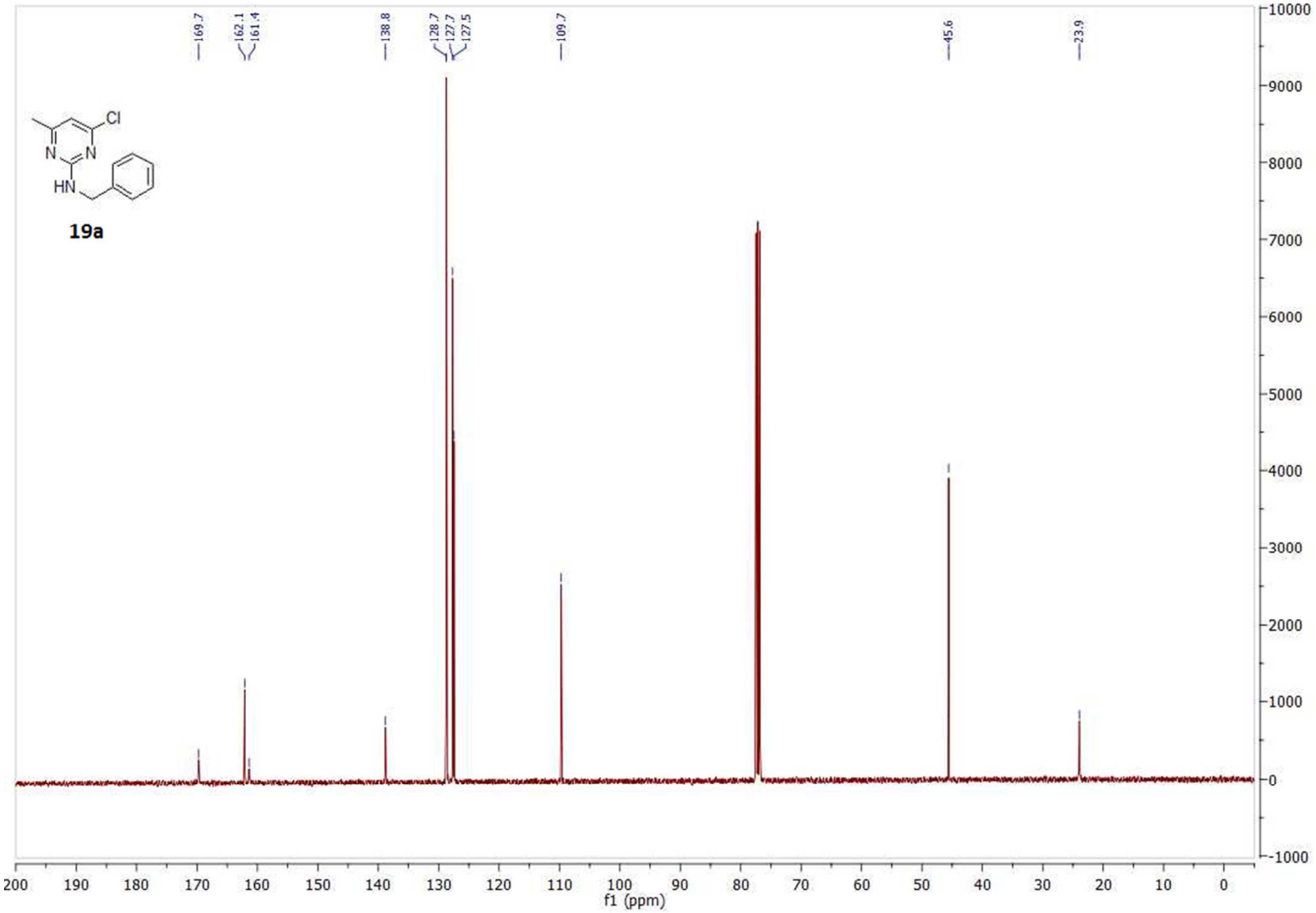
0.0
f1 (ppm)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109.7
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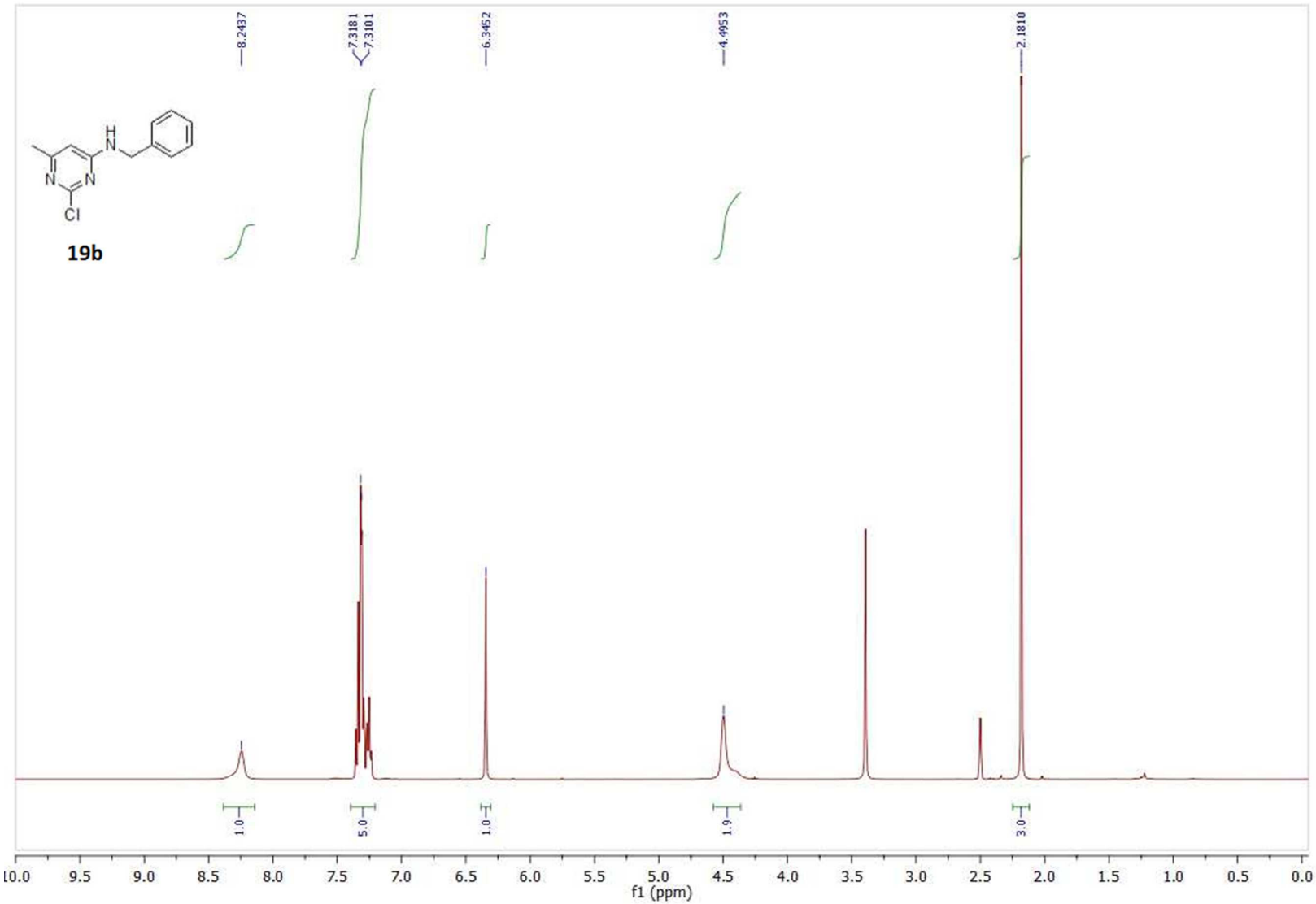
Cl
N
N
HN
19a
f1 (ppm)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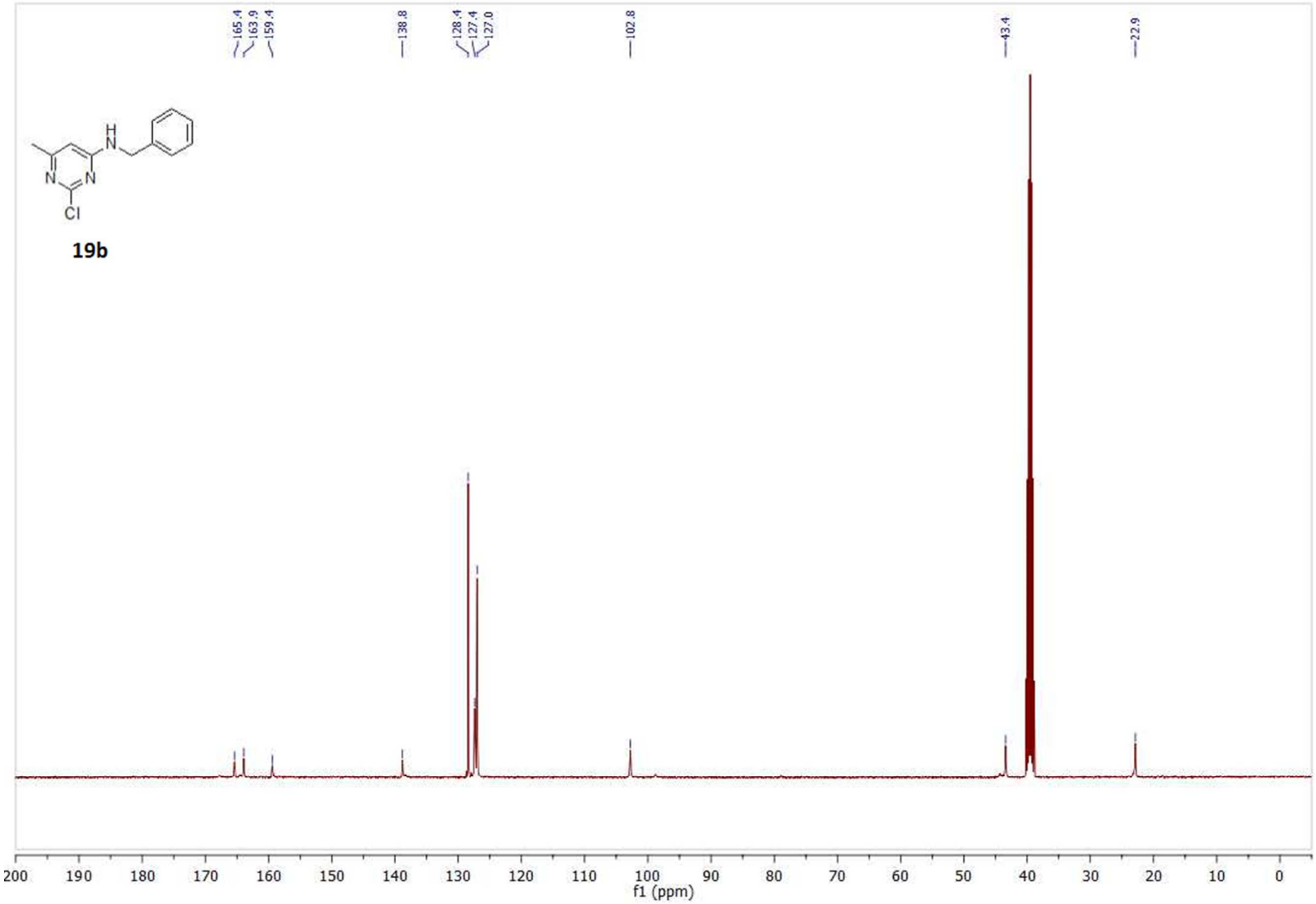
3.0
f1 (ppm)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127.4
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102.8
43.4
22.9
H
N
N
N
Cl
19b
200
190
180
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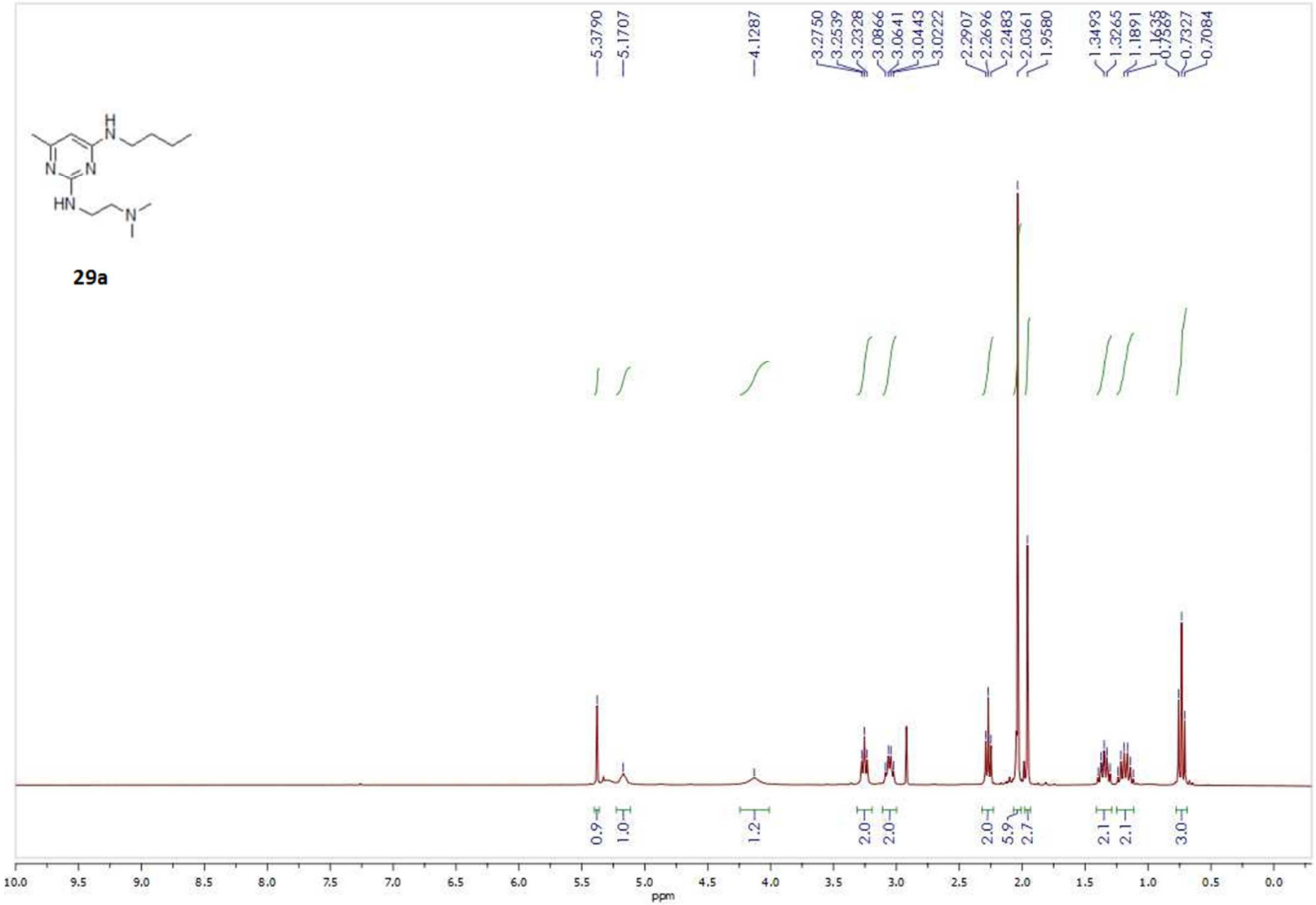
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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3.0222
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2.2696
2.2483
2.0361
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1.3493
1.3265
1.1891
1.1635
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0.7327
0.7084
0.9
1.0
1.2
2.0
2.0
2.0
5.9
2.7
2.1
2.1
3.0
10.0
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
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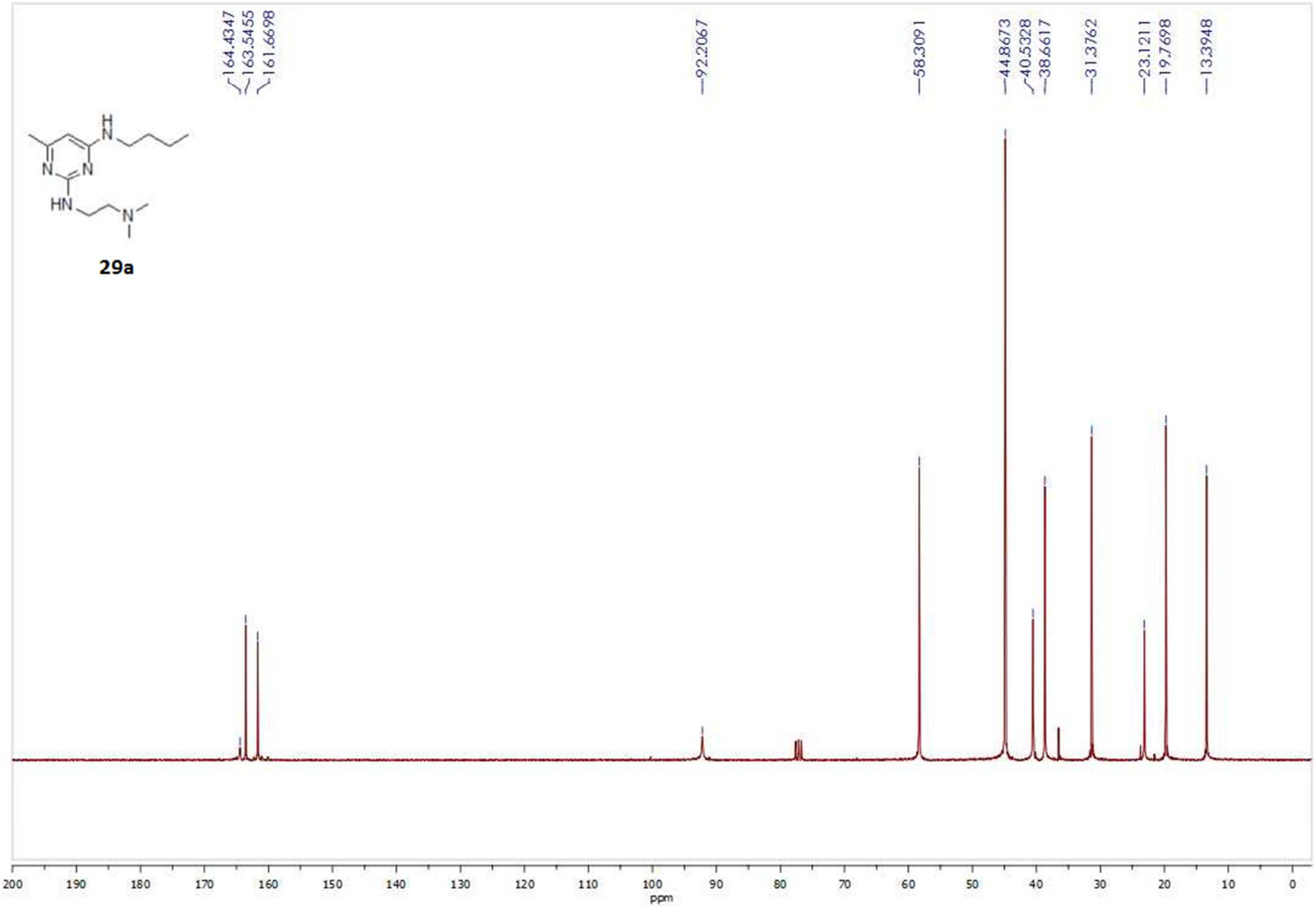
2.0
1.5
1.0
0.5
0.0
ppm

29a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29a
200
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150
140
130
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60
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20
10
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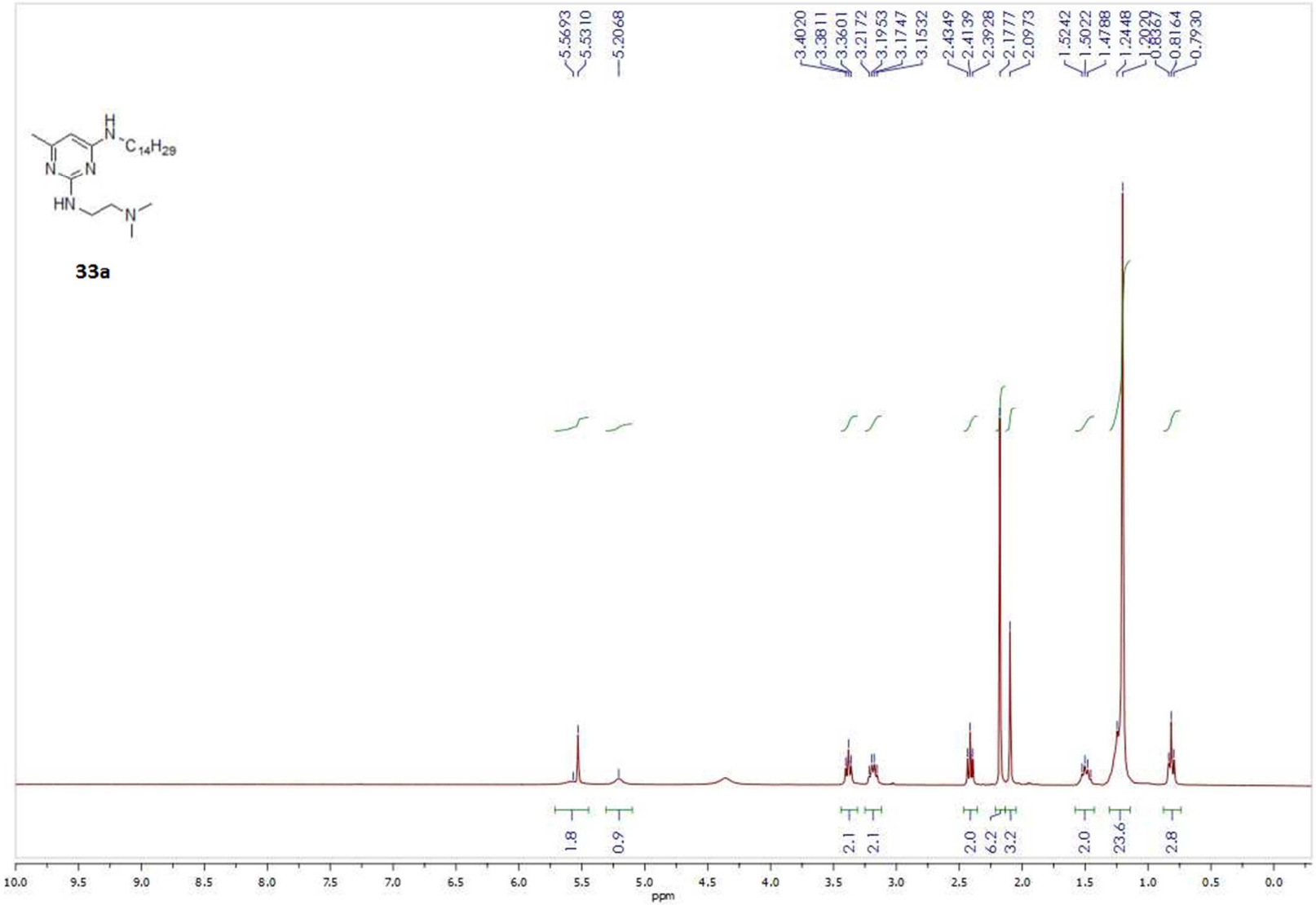
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2.4139
2.3928
2.1777
2.0973
1.5242
1.5022
1.4788
1.2448
1.2020
0.8367
0.8164
0.7930
1.8
0.9
2.1
2.1
2.0
6.2
3.2
2.0
23.6
2.8
10.0
9.5
9.0
8.5
8.0
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6.5
6.0
5.5
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2.5
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1.5
1.0
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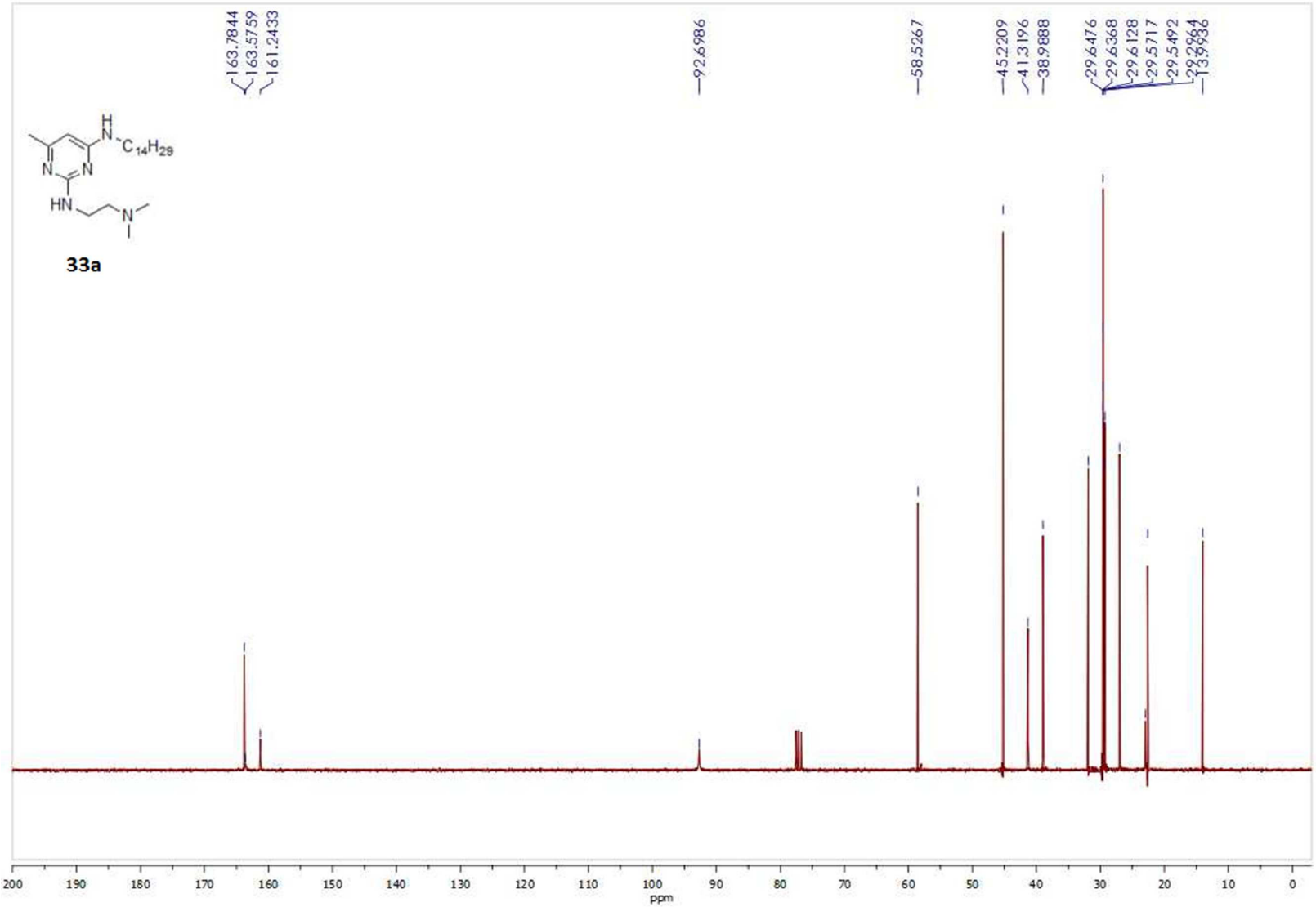
0.0
ppm

33a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29.6128
29.5717
29.5492
29.2964
13.9938
33a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
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30
20
10
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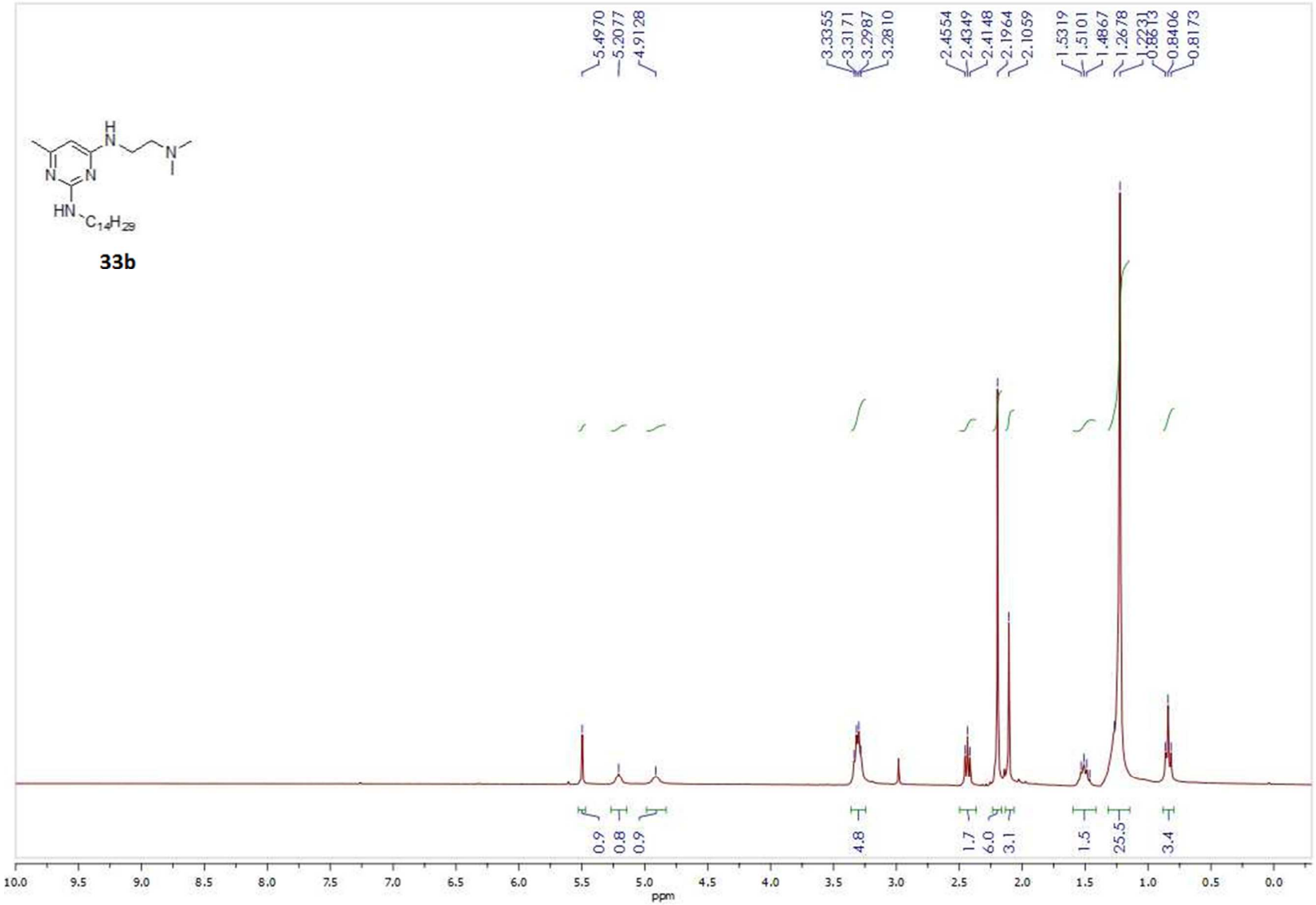
ppm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2.1964
2.1059
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1.4867
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0.8
0.9
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1.7
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3.1
1.5
25.5
3.4
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
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1.5
1.0
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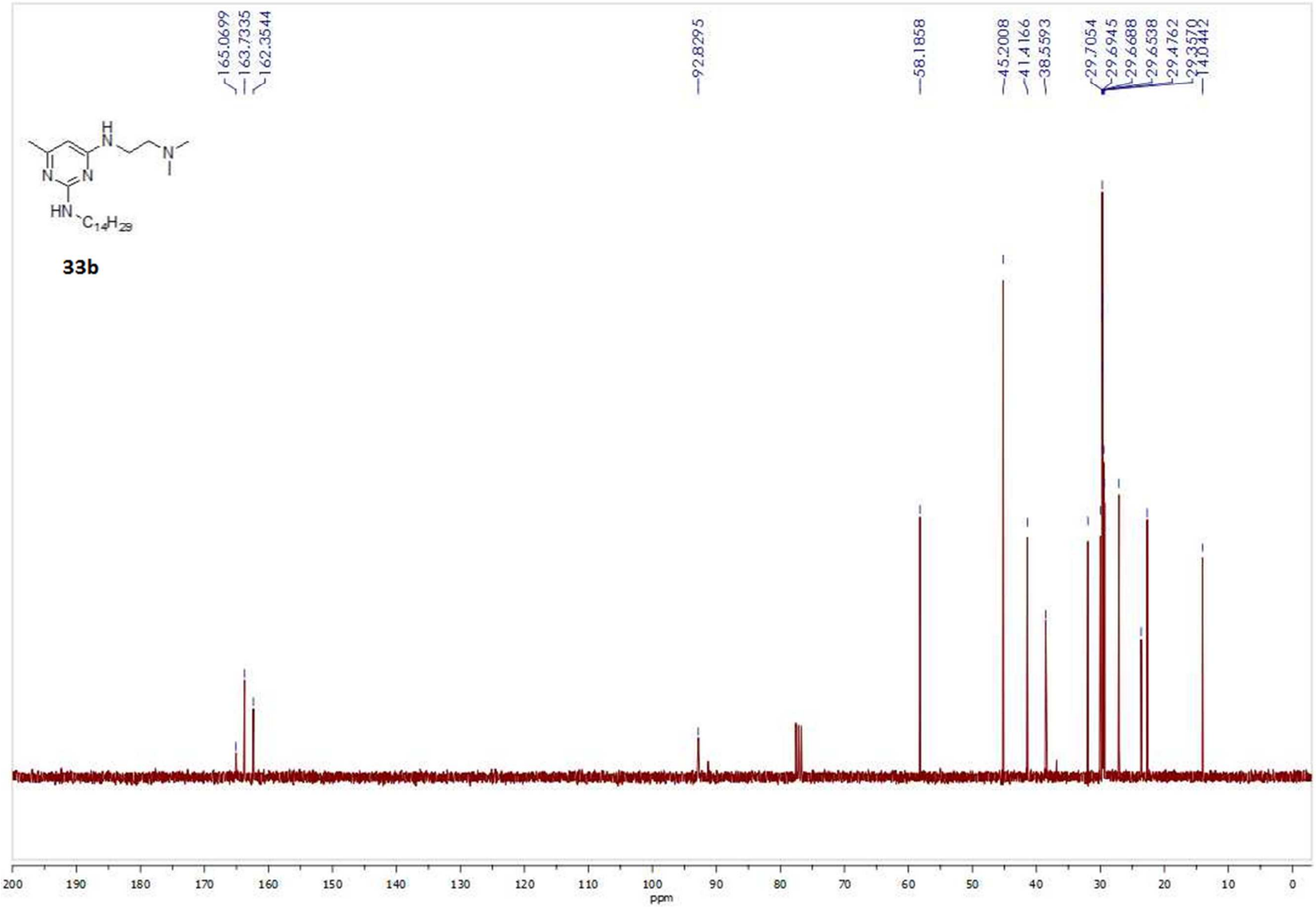
0.0
ppm

33b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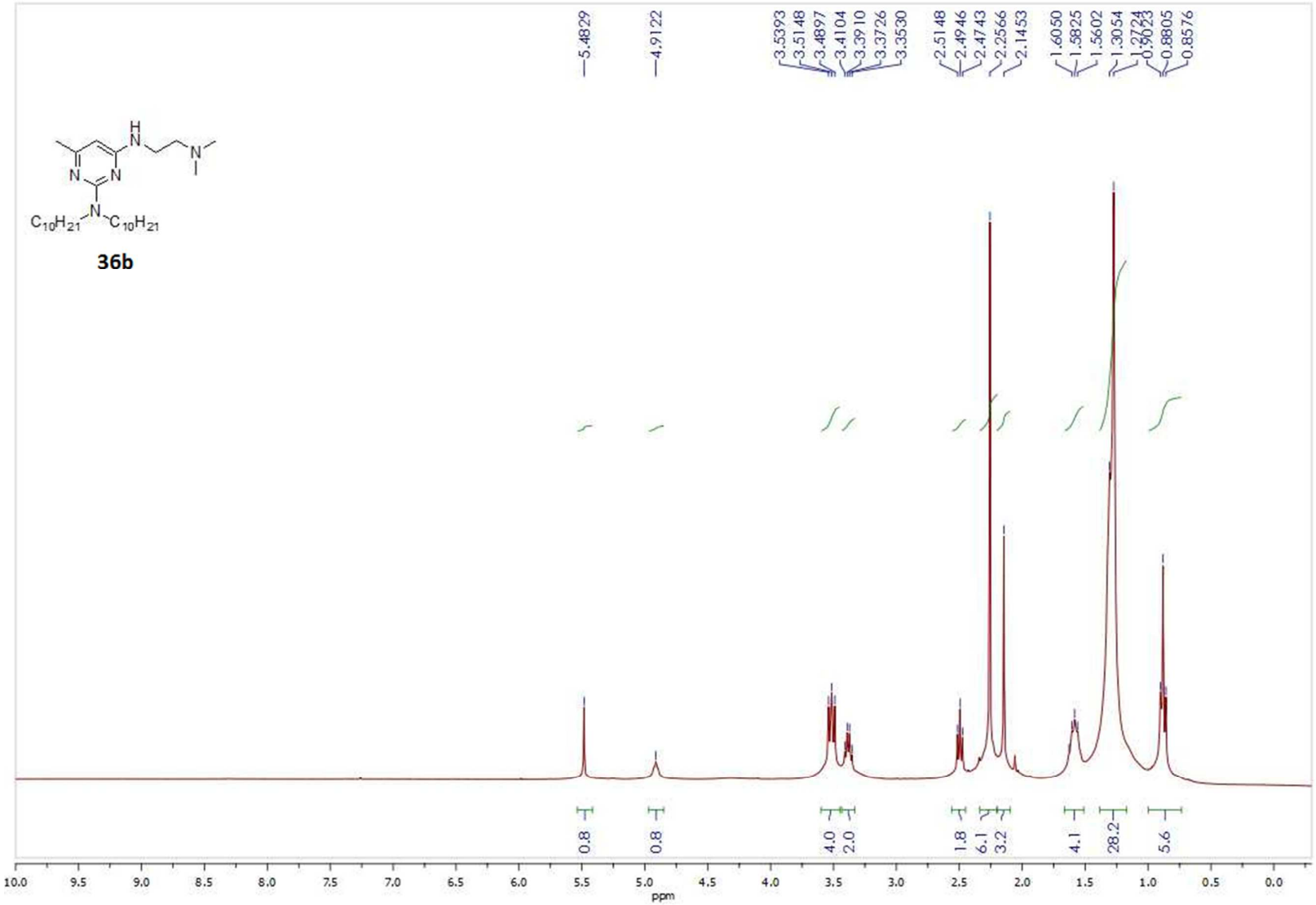
29.6688
29.6538
29.4762
29.3570
14.0442
33b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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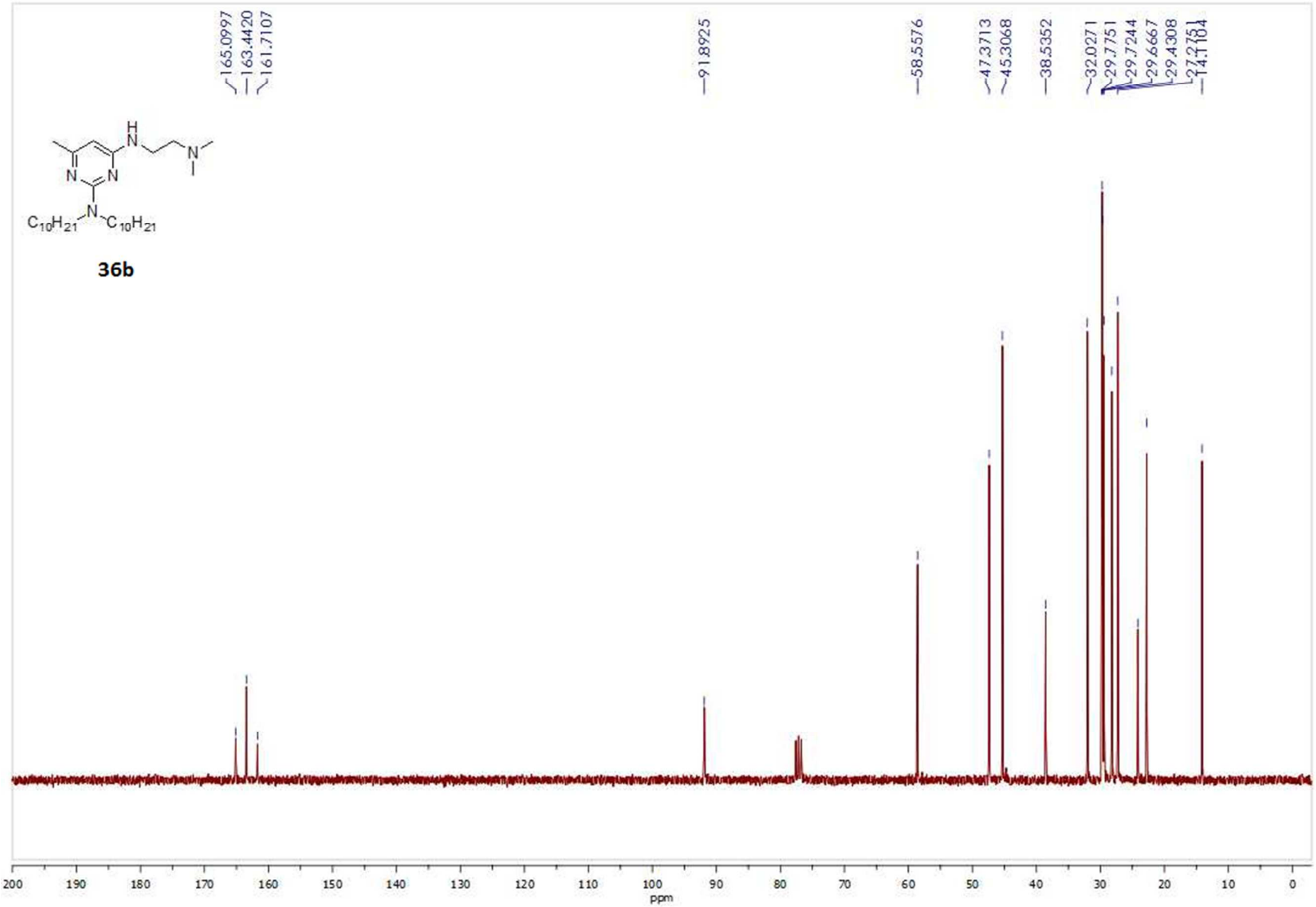
2.4743
2.2566
2.1453
1.6050
1.5825
1.5602
1.3054
1.2724
0.9023
0.8805
0.8576
0.8
0.8
4.0
2.0
1.8
6.1
3.2
4.1
28.2
5.6
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

36b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29.4308
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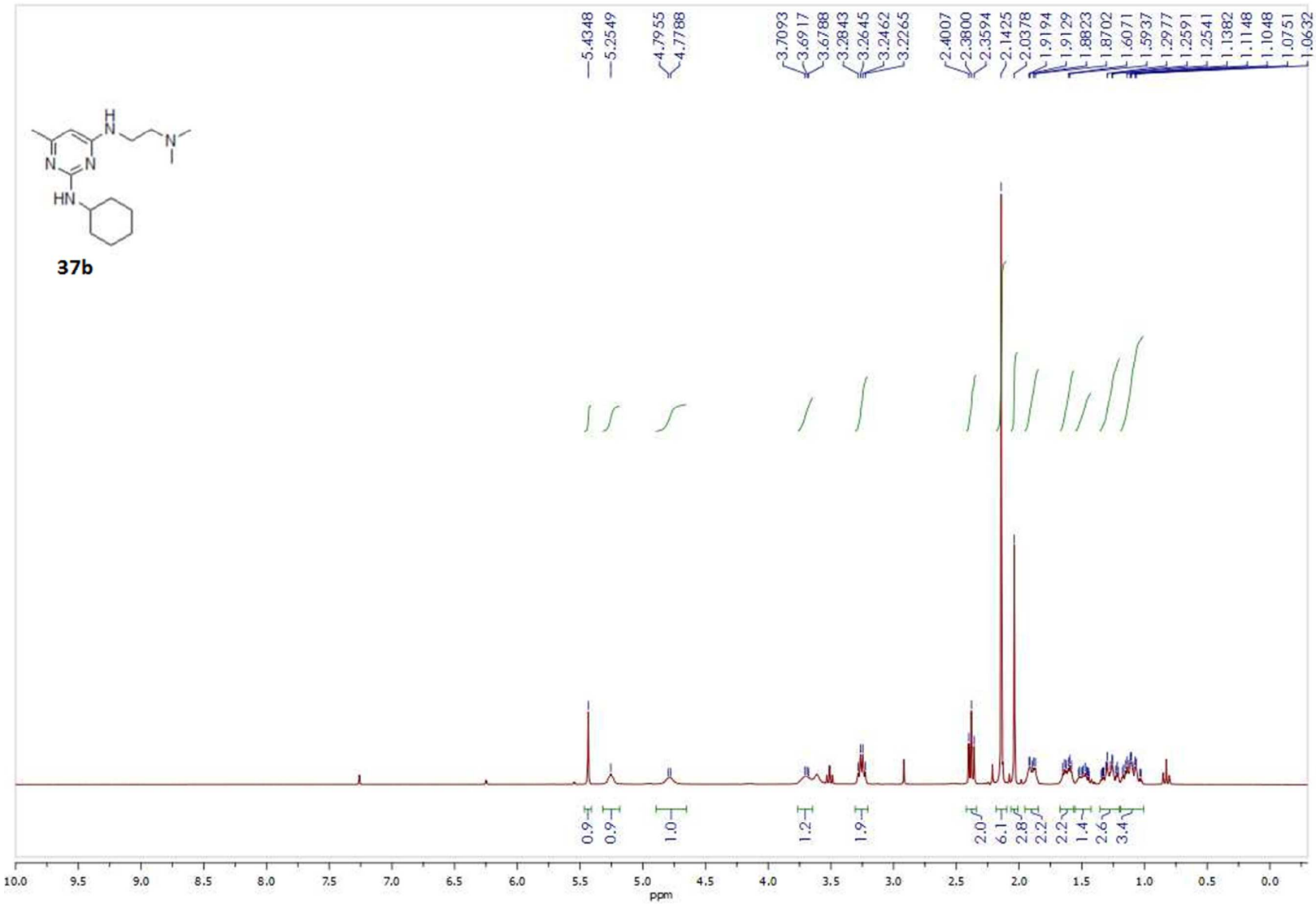
14.1184
36b
ppm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3.2462
3.2265
2.4007
2.3800
2.3594
2.1425
2.0378
1.9194
1.9129
1.8823
1.8702
1.6071
1.5937
1.2977
1.2591
1.2541
1.1382
1.1148
1.1048
1.0751
1.0632
0.9
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2.2
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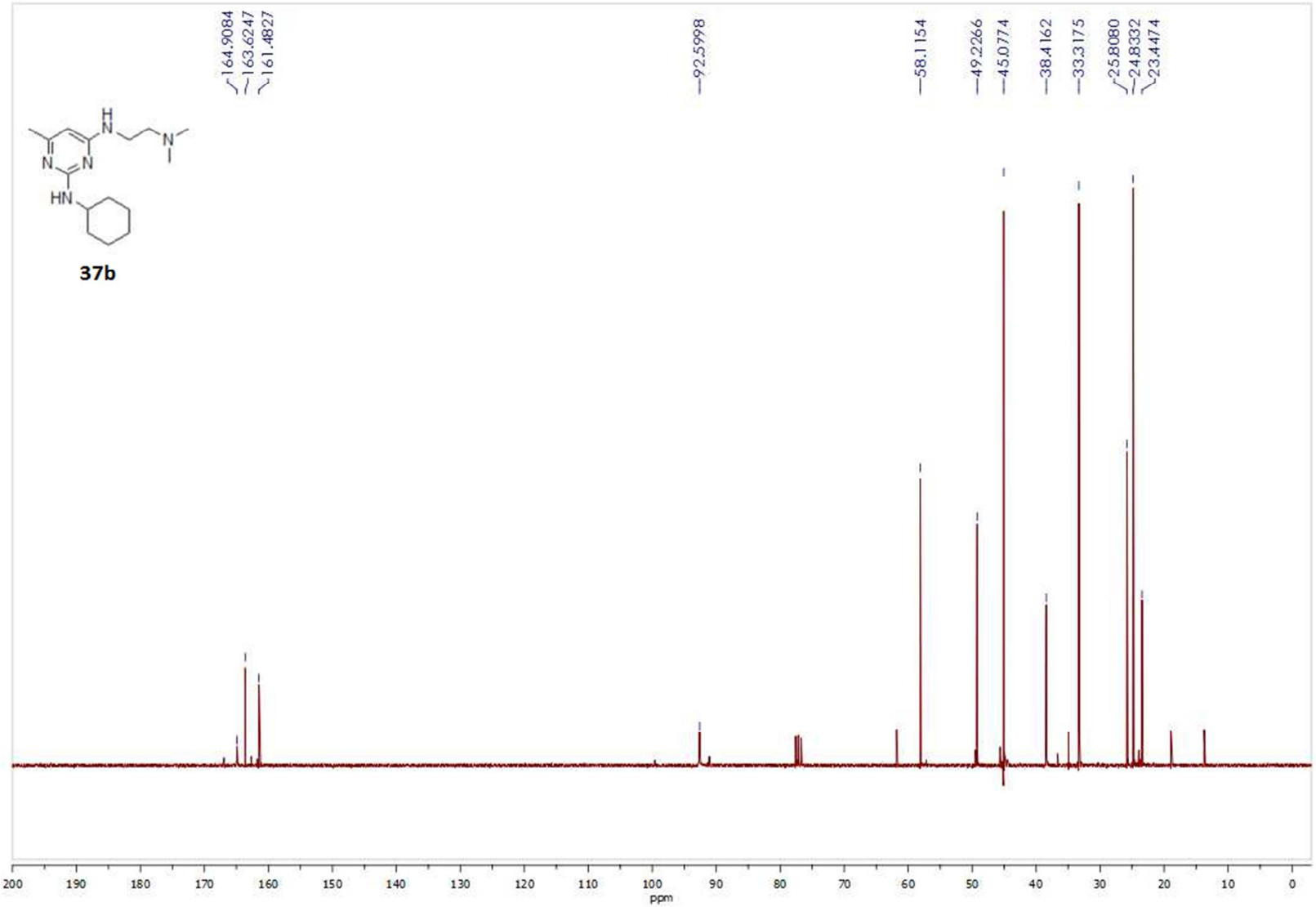
2.6
3.4
ppm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24.8332
23.4474
37b
200
190
180
170
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140
130
120
110
100
90
80
70
60
50
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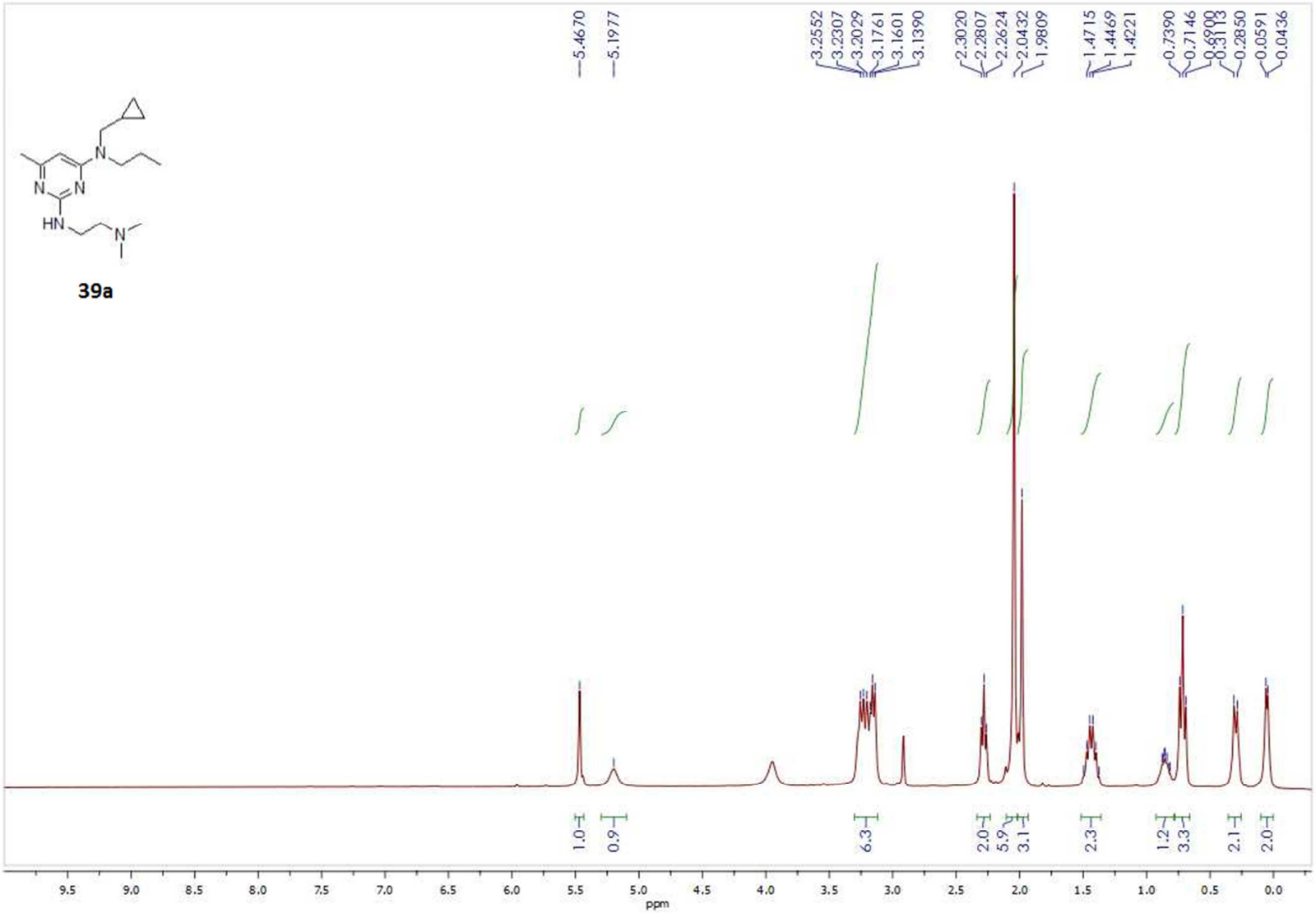
30
20
10
0
ppm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3.1390
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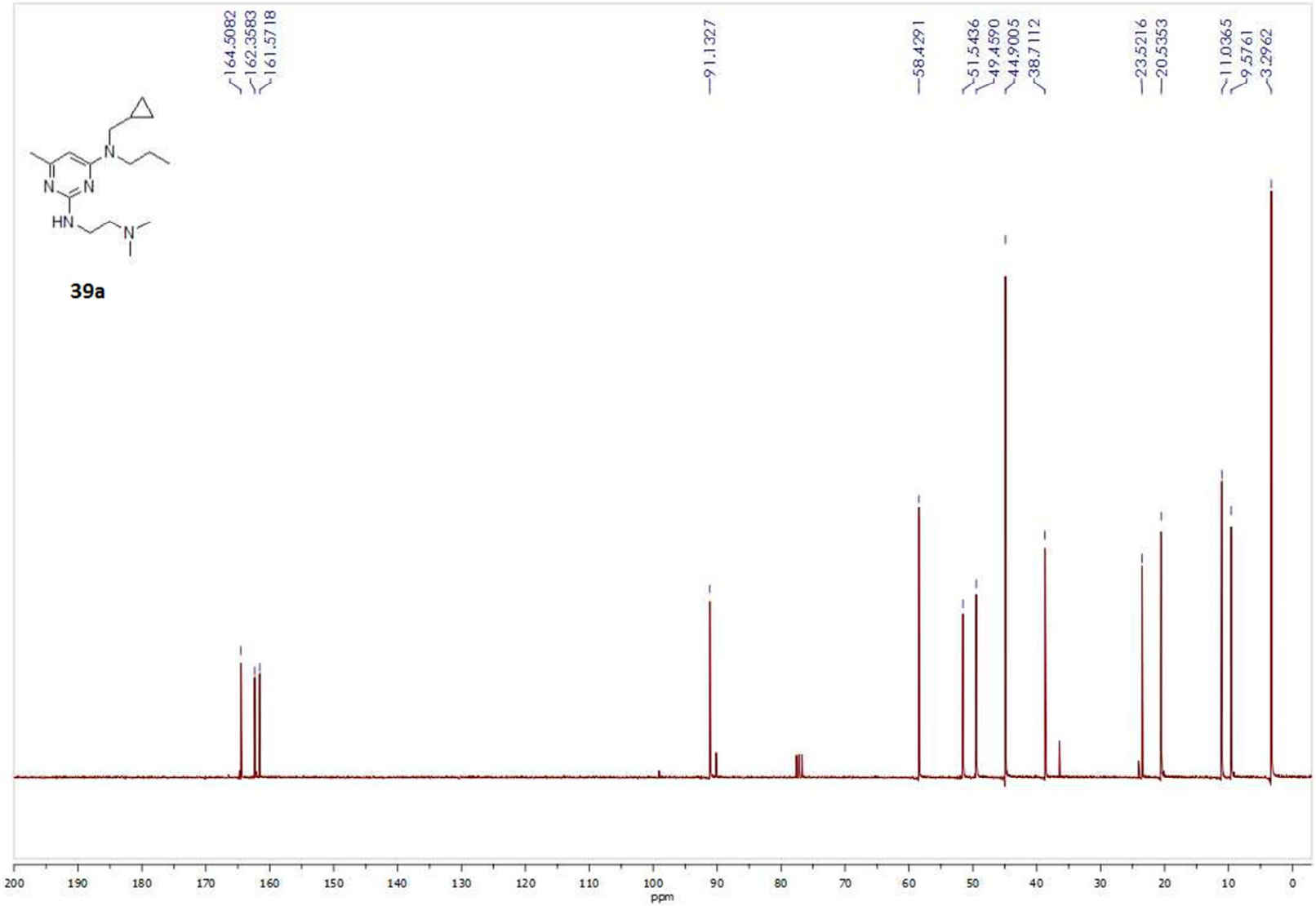
2.2624
2.0432
1.9809
1.4715
1.4469
1.4221
0.7390
0.7146
0.6900
0.3113
0.2850
0.0591
0.0436
1.0
0.9
6.3
2.0
5.9
3.1
2.3
1.2
3.3
2.1
2.0
ppm

39a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20.5353
11.0365
9.5761
3.2962
39a
200
190
180
170
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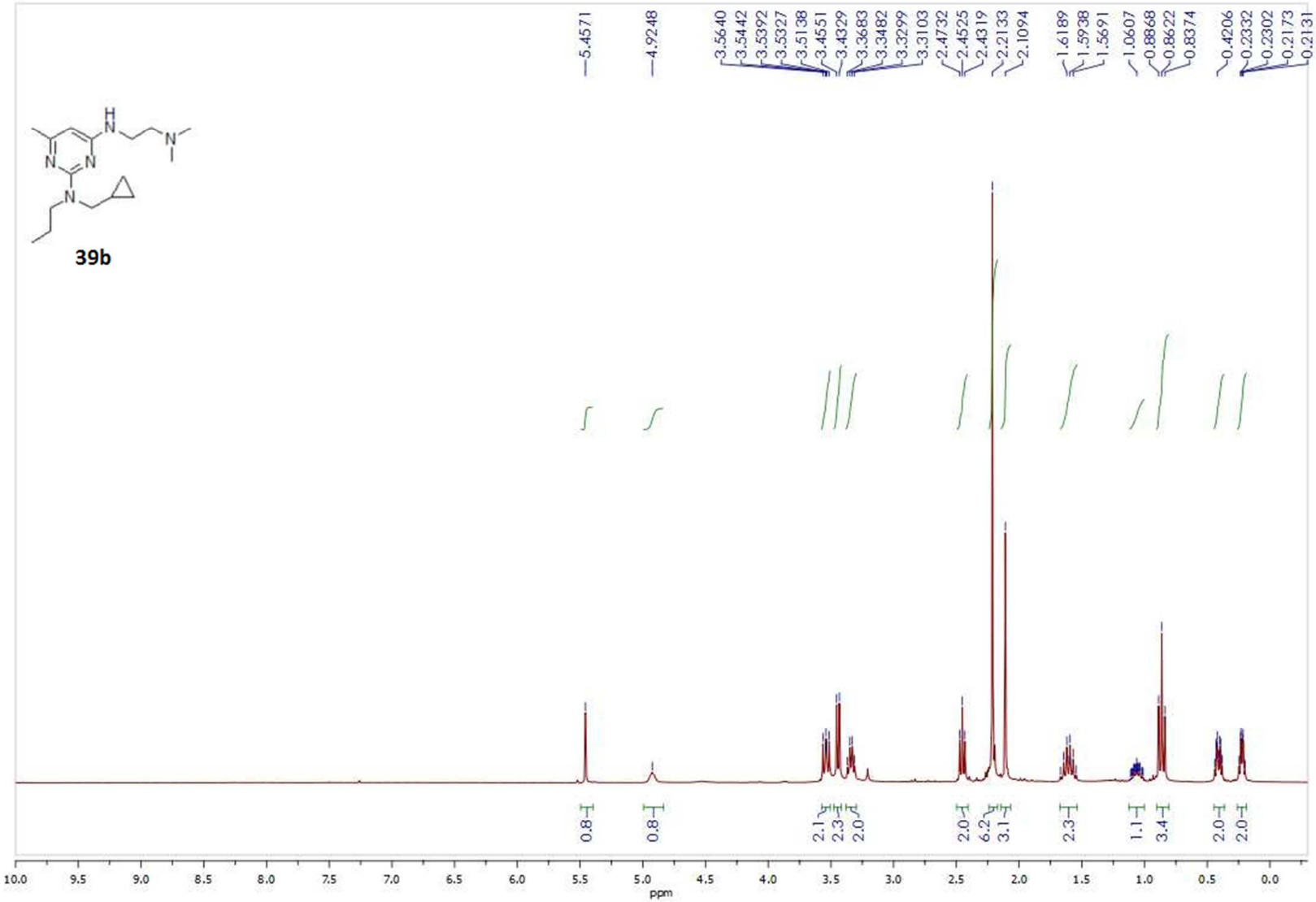
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


39b
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4.9248
3.5640
3.5442
3.5392
3.5327
3.5138
3.4551
3.4329
3.3683
3.3482
3.3299
3.3103
2.4732
2.4525
2.4319
2.2133
2.1094
1.6189
1.5938
1.5691
1.0607
0.8868
0.8622
0.8374
0.4206
0.2332
0.2302
0.2173
0.2131
0.8
0.8
2.1
2.3
2.0
2.0
6.2
3.1
2.3
1.1
3.4
2.0
2.0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
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2.0
1.5
1.0
0.5
0.0
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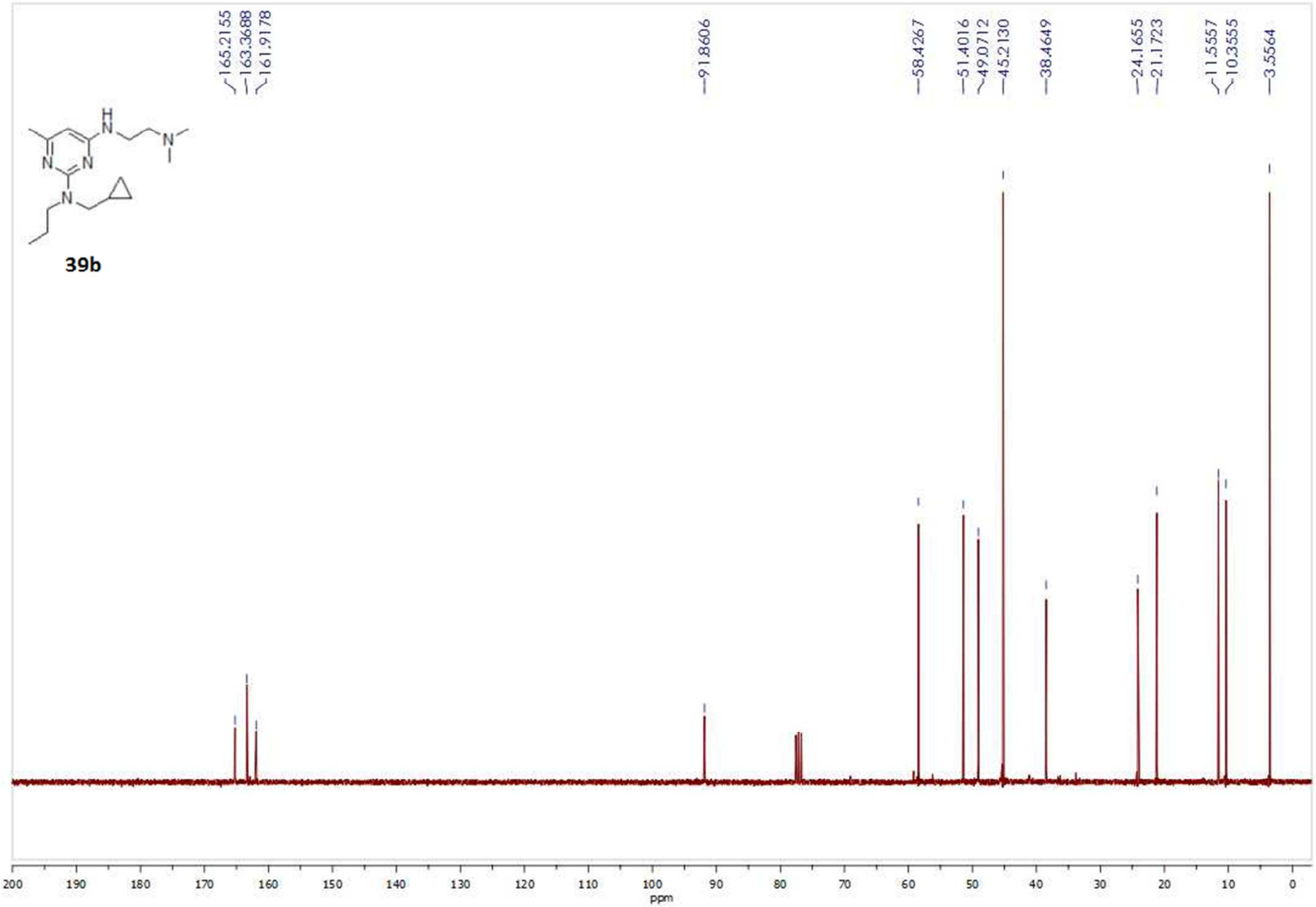
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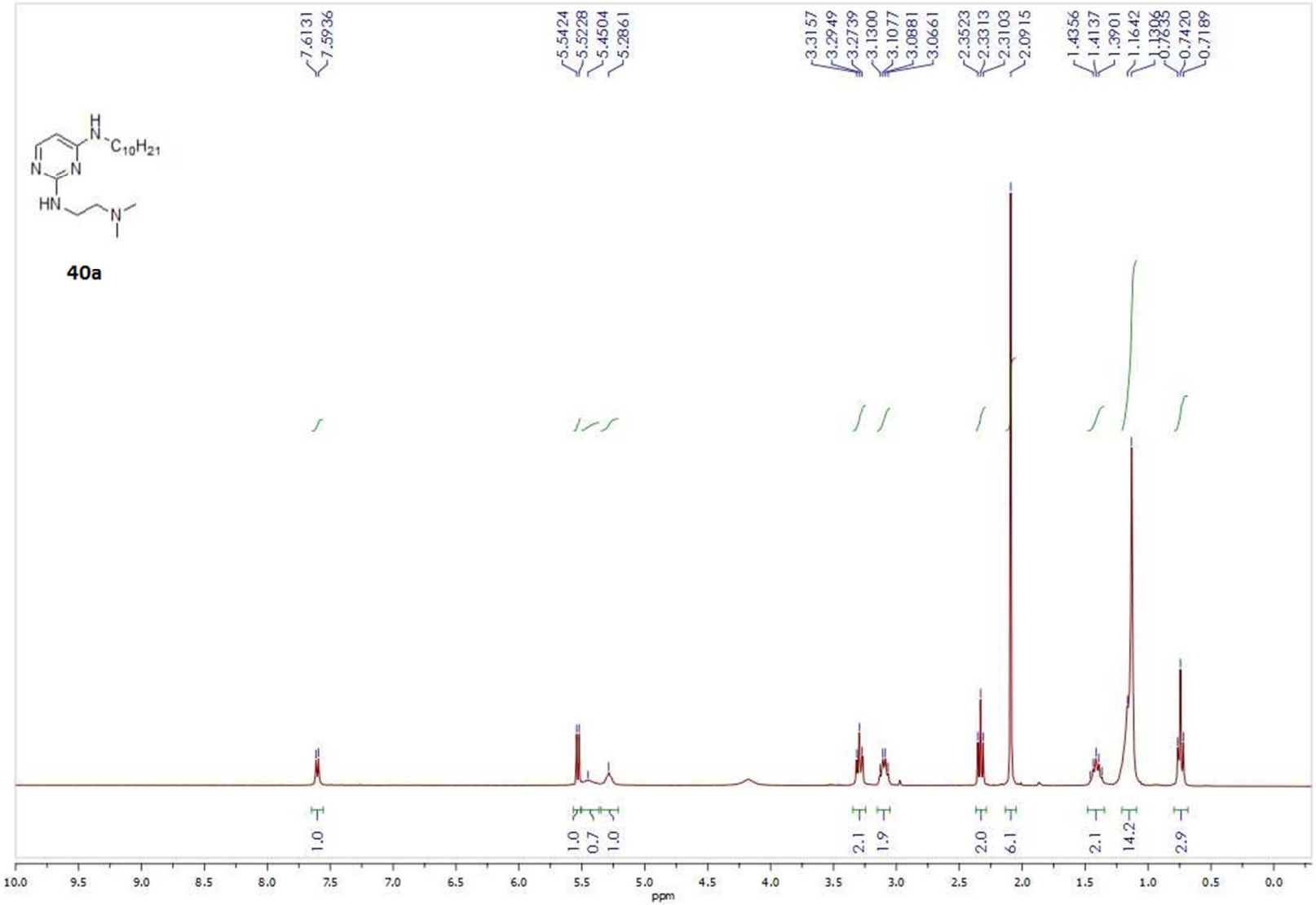
163.3688
161.9178
91.8606
58.4267
51.4016
49.0712
45.2130
38.4649
24.1655
21.1723
11.5557
10.3555
3.5564
39b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.5936
5.5424
5.5228
5.4504
5.2861
3.3157
3.2949
3.2739
3.1300
3.1077
3.0881
3.0661
2.3523
2.3313
2.3103
2.0915
1.4356
1.4137
1.3901
1.1642
1.1306
0.7635
0.7420
0.7189
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1.0
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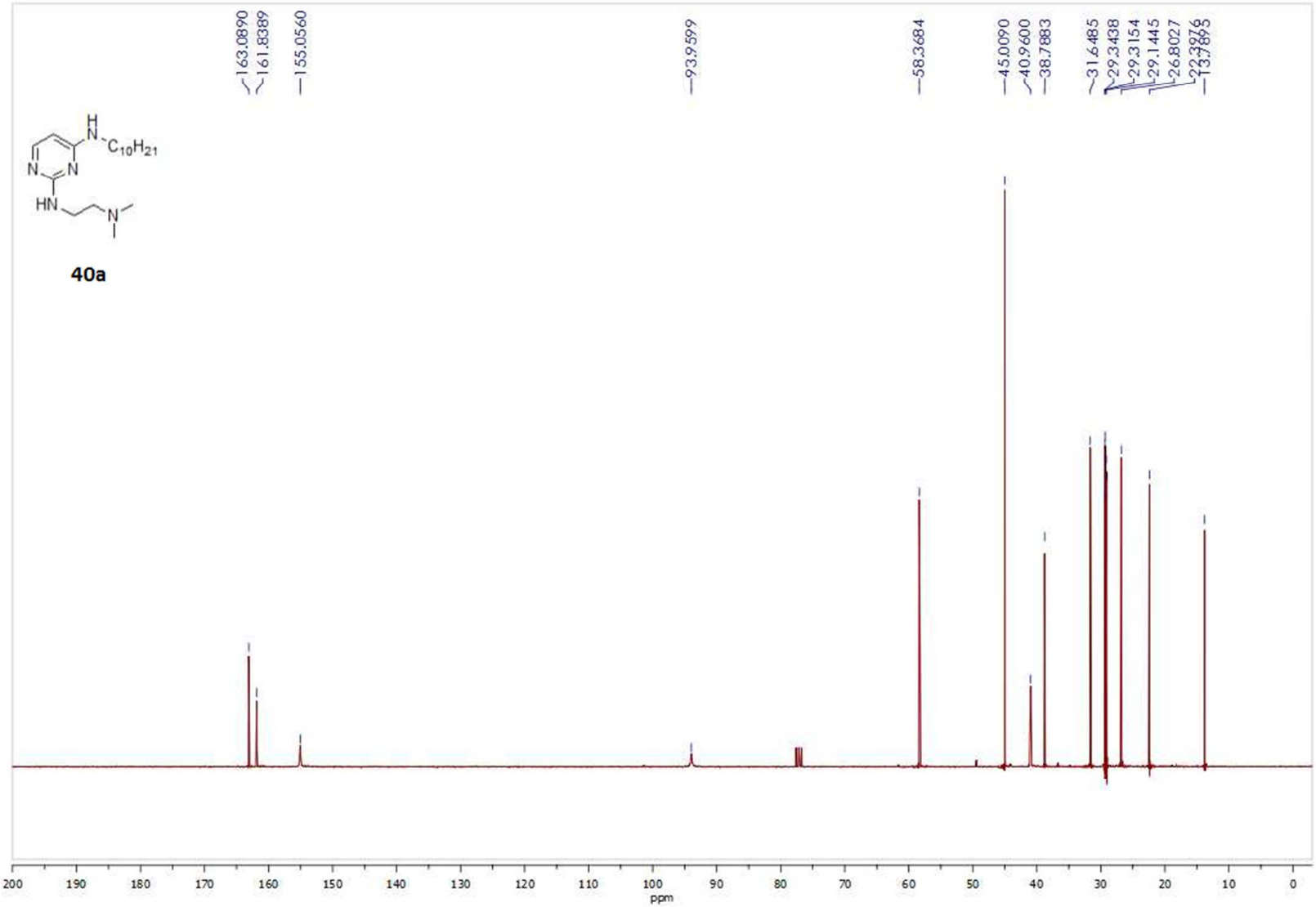
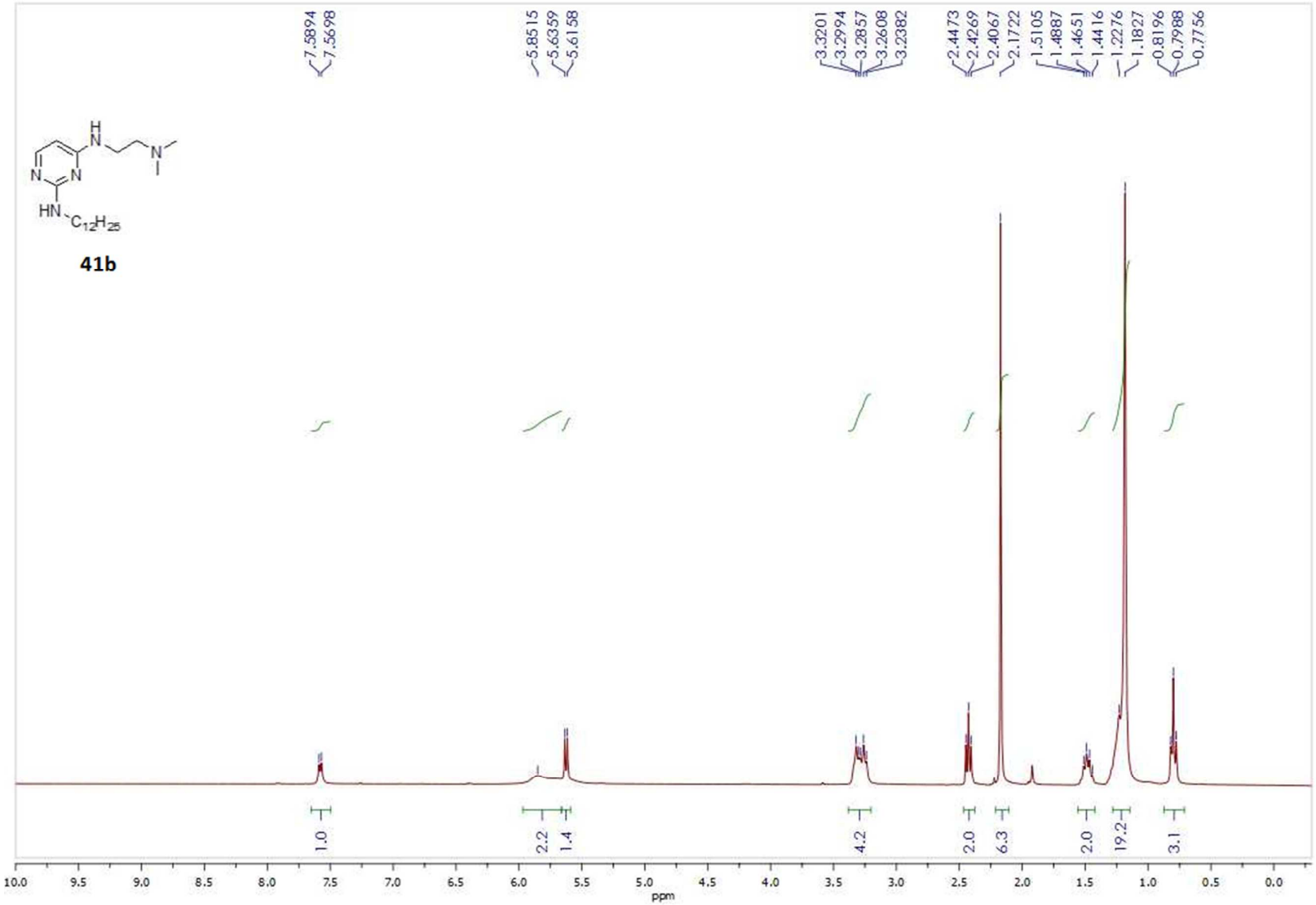
1.0
2.1
1.9
2.0
6.1
2.1
14.2
2.9
ppm

40a


163.0890
161.8389
155.0560
93.9599
58.3684
45.0090
40.9600
38.7883
31.6485
29.3438
29.3154
29.1445
26.8027
22.3876
13.7895
HN
$C_{10}H_{21}$
N
N
HN
N
40a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.5894
7.5698
5.8515
5.6359
5.6158
3.3201
3.2994
3.2857
3.2608
3.2382
2.4473
2.4269
2.4067
2.1722
1.5105
1.4887
1.4651
1.4416
1.2276
1.1827
0.8196
0.7988
0.7756
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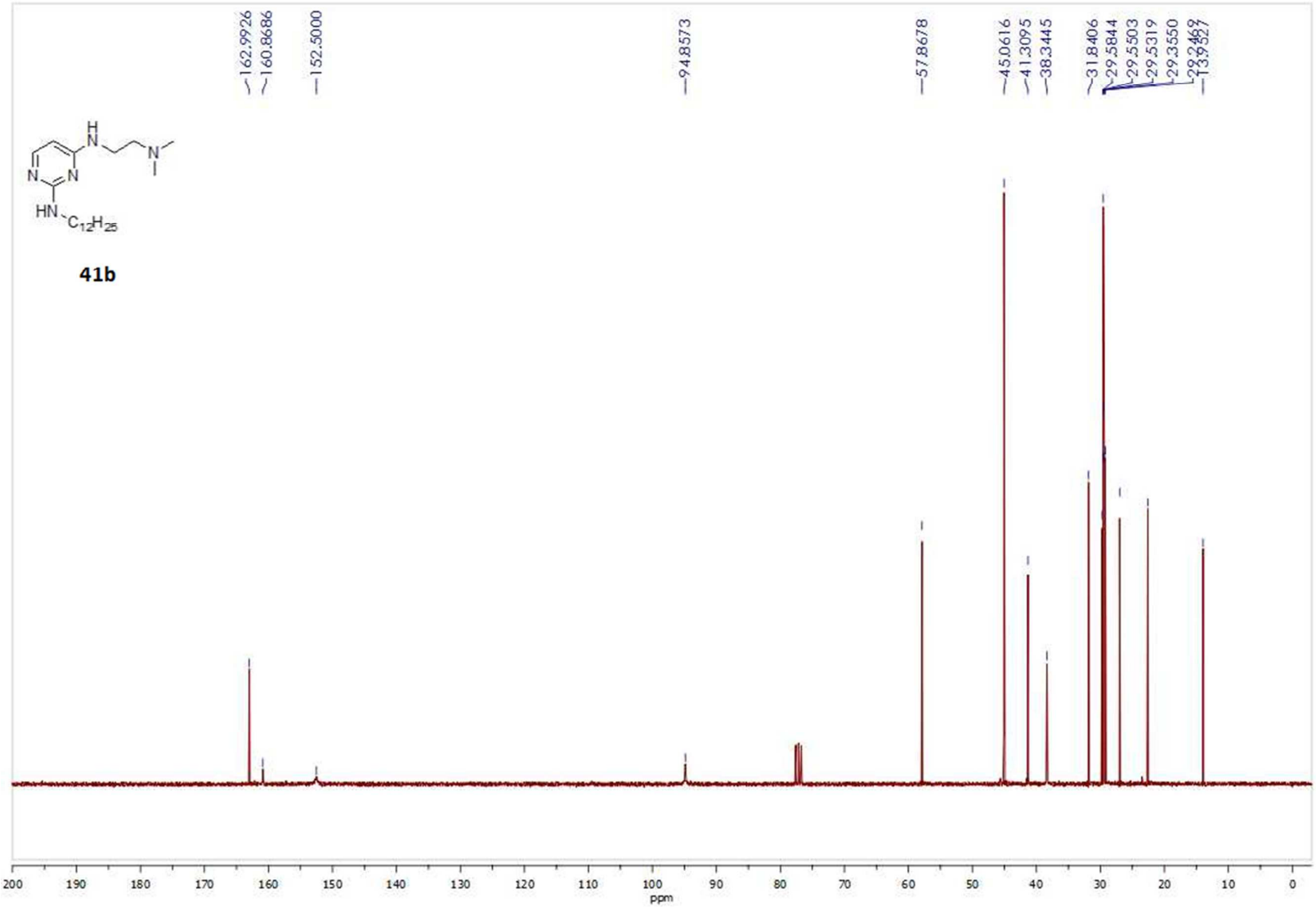
2.2
1.4
4.2
2.0
6.3
2.0
19.2
3.1
ppm

41b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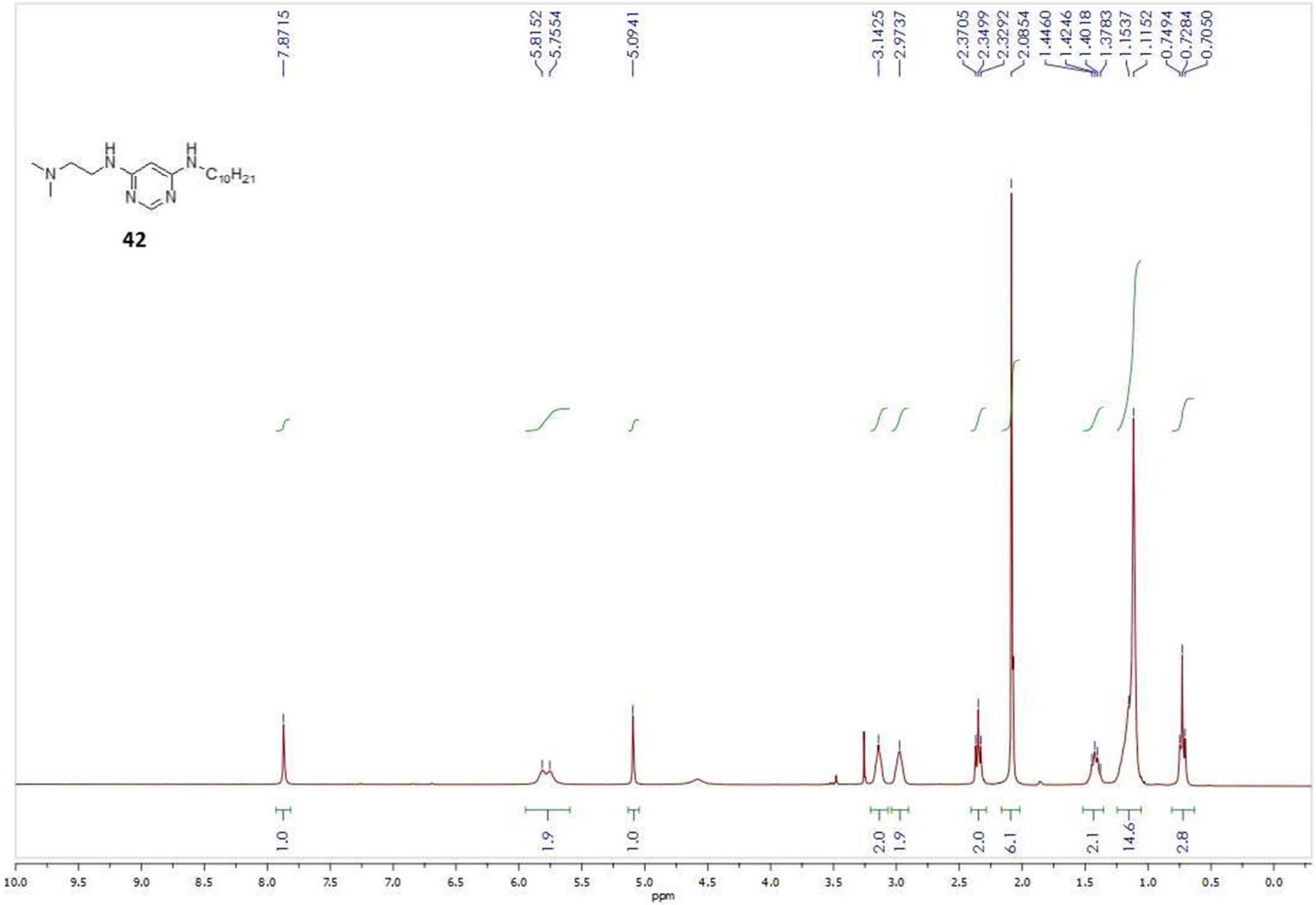
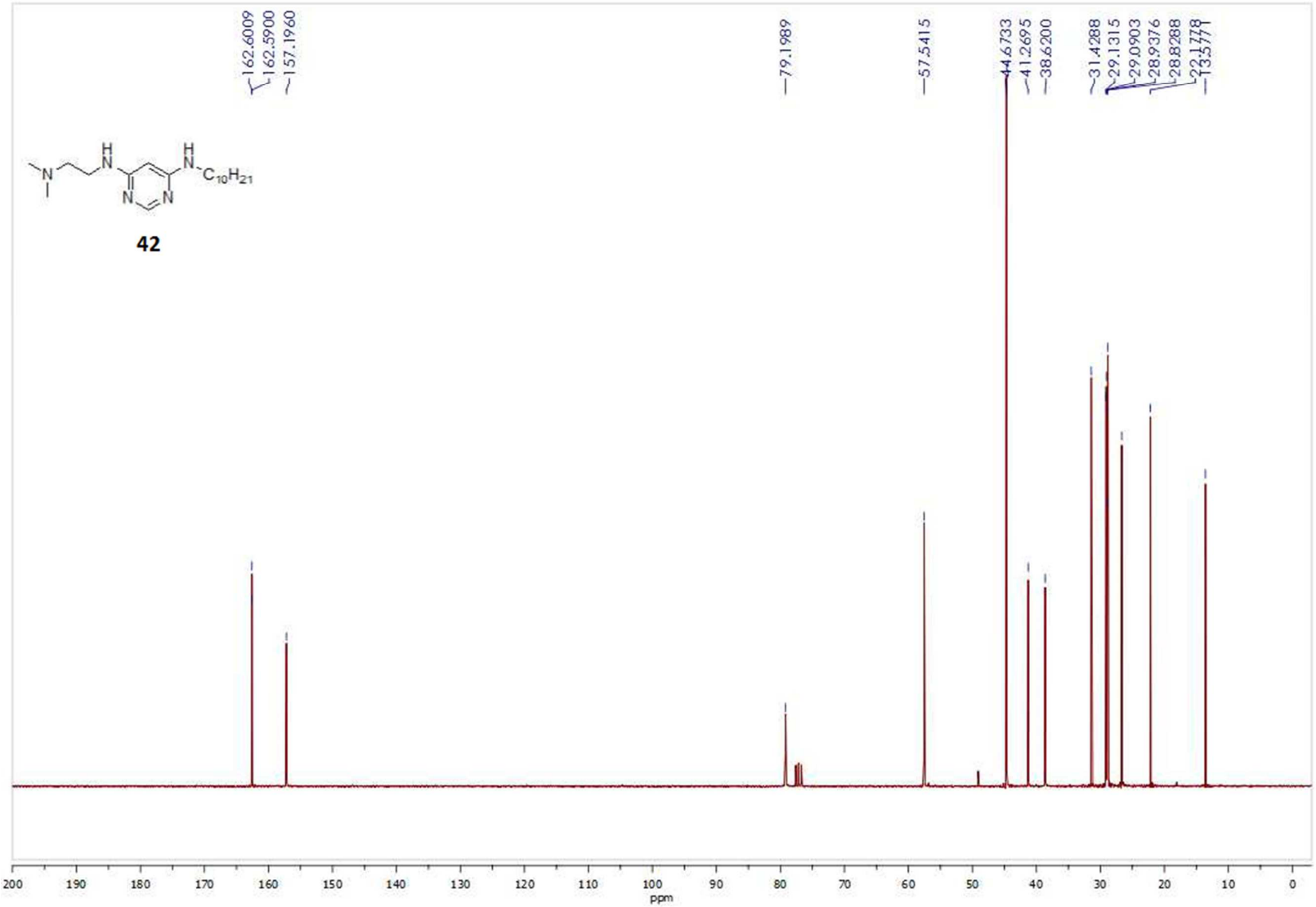
94.8573
57.8678
45.0616
41.3095
38.3445
31.8406
29.5844
29.5503
29.5319
29.3550
13.9527
41b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.8715
5.8152
5.7554
5.0941
3.1425
2.9737
2.3705
2.3499
2.3292
2.0854
1.4460
1.4246
1.4018
1.3783
1.1537
1.1152
0.7494
0.7284
0.7050
42
1.0
1.9
1.0
2.0
1.9
2.0
6.1
2.1
14.6
2.8
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
ppm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162.5900
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79.1989
57.5415
44.6733
41.2695
38.6200
31.4288
29.1315
29.0903
28.9376
28.8288
22.1778
13.5771
42
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm