

Supplementary

Computer-aided studies for novel arylhydantoin 1,3,5-triazine derivatives as 5-HT₆ serotonin receptor ligands with antidepressive-like, anxiolytic and antiobesity action *in vivo*

Rafał Kurczab^{1†}, Wesam Ali^{2,6†}, Dorota Łażewska², Magdalena Kotańska³, Magdalena Jastrzębska-Więsek⁴, Grzegorz Satała¹, Małgorzata Więcek², Annamaria Lubelska², Gniewomir Latacz², Anna Partyka⁴, Małgorzata Starek⁵, Monika Dąbrowska⁵, Anna Wesołowska⁴, Claus Jacob⁶, Katarzyna Kieć-Kononowicz², Jadwiga Handzlik^{2,*}

Charcteristics of intermediates obtained before 27, 29, 50-58, 63, 65 and 68-70

Cpd	Cas number	Article
27	860787-34-4 3-(4-chlorobenzyl)-5,5-dimethyl-1H-imidazole-2,4(3H,5H)-dione	SAR-studies on the importance of aromatic ring topologies in search for selective 5-HT ₇ receptor ligands among phenylpiperazine hydantoin derivatives. By Handzlik, Jadwiga et al From European Journal of Medicinal Chemistry, 78, 324-339; 2014
29	179409-69-9, Aldlab Chemicals Building Blocks United States methyl 2-(4,4-dimethyl-2,5-dioximidazolidin-1-yl)acetate	Preparation of substituted β -keto esters as intermediates for photographic yellow couplers Yamakawa, Kazuyoshi; Sato, Tadahisa Assignee Fuji Photo Film Co Ltd, Japan 1996
50	5397-13-7 5-(4-Chloro-phenyl)-5-methyl-imidazolidine-2,4-dione	Safari J. and Javadian L., Montmorillonite K-10 as a catalyst in the synthesis of 5, 5- disubstituted hydantoins under ultrasound irradiation, J. Chem. Sci. 125 (2013) 981– 987.
51	6843-49-8 5-Methyl-5-phenylhydantoin	Safari J. and Javadian L., Montmorillonite K-10 as a catalyst in the synthesis of 5, 5- disubstituted hydantoins under ultrasound irradiation, J. Chem. Sci. 125 (2013) 981– 987.
52	6946-01-6 5-(3-chlorophenyl)-5-methyl-2,4-imidazolidinedione	Safari J. and Javadian L., Montmorillonite K-10 as a catalyst in the synthesis of 5, 5- disubstituted hydantoins under ultrasound irradiation, J. Chem. Sci. 125 (2013) 981– 987.
53	795314-76-0 5-(2,5-dichlorophenyl)-5-methylimidazolidine-2,4-dione	Werbel LM, Elslager EF, Islip PJ and Closier MD, Antischistosomal effects of 5-(2,4,5-trichlorophenyl)hydantoin and related compounds, J Med Chem. 20 (1977):1569-1572.
54	64464-19-3 5-(2,4-dichlorophenyl)-5-methyl-2,4-imidazolidinedione	Werbel LM, Elslager EF, Islip PJ and Closier MD, Antischistosomal effects of 5-(2,4,5-trichlorophenyl)hydantoin and related compounds, J Med Chem. 20 (1977):1569-1572.
55	no	(Patent) Preparation of imidazolidinedione compounds containing substituted carbinol moiety as LXR modulators for treatment and prevention of arteriosclerosis, inflammation, diabetes, etc. Matsuda, Takayuki; Okuda, Ayumu; Koura, Minoru; Yamaguchi, Yuki; Kurobuchi, Sayaka; Watanabe, Yuuichirou; Shibuya, Kimiyuki Assignee: Kowa Company, Ltd., Japan 2008

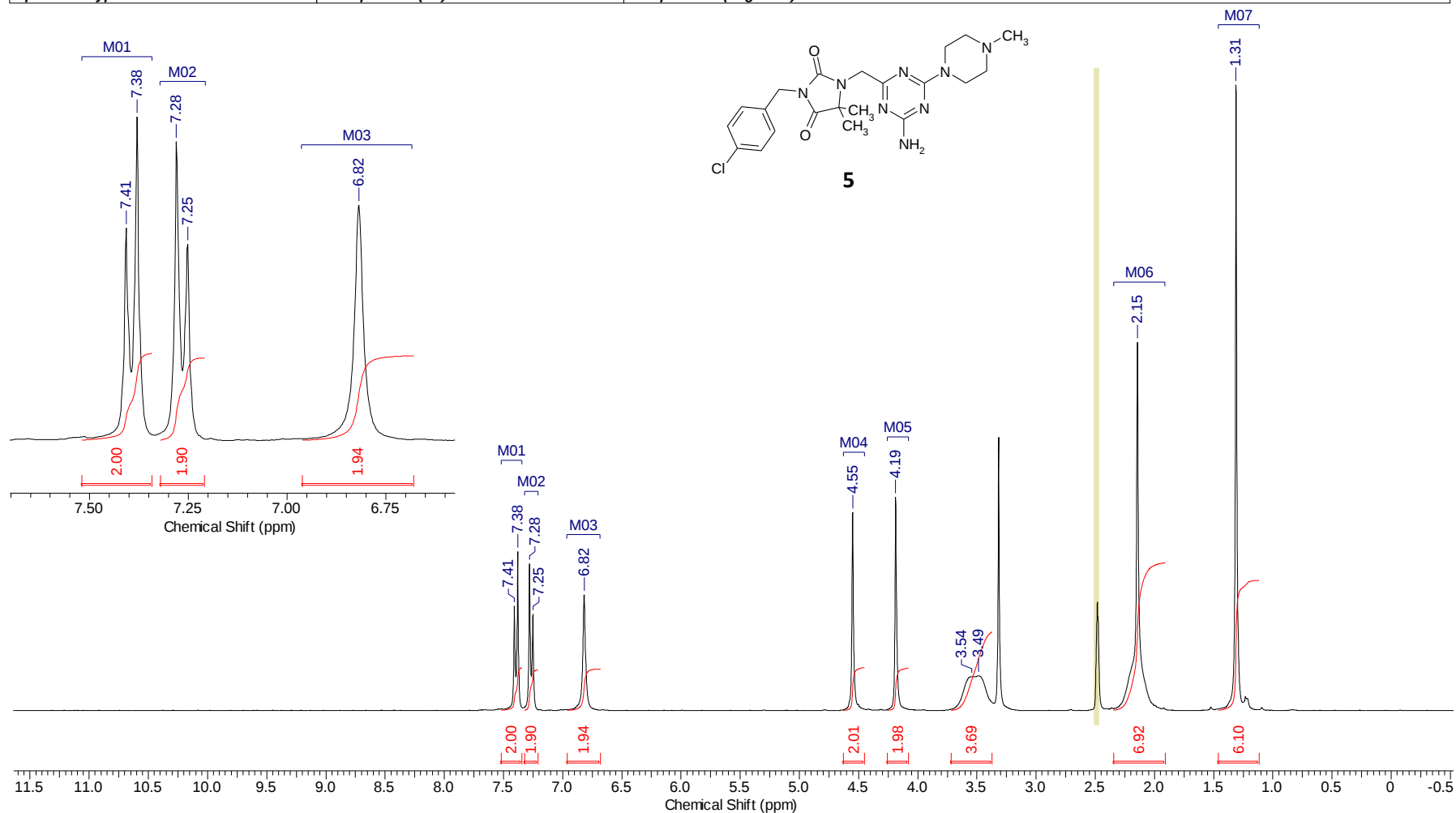
56	23186-96-1 5-methyl-5-(4-methylphenyl)-2,4-imidazolidinedione	J. Linol and G. Coquerel, Influence of high energy milling on the kinetics of the polymorphic transition from the monoclinic form to the orthorhombic form of ($\pm$)5-methyl-5-(4'-methylphenyl)hydantoin. J Therm Anal Calorim 90 (2007) 367-370.
57	82752-67-8 5-methyl-5-(1-naphthyl)-2,4-imidazolidinedione	M. L. KeshtovA. L. RusanovN. M. Belomoina and A. K. Mikitaev, Improved synthesis of bis[<i>p</i> -(phenylethynyl)phenyl]hetarylenes, Russ Chem Bull. 46 (1997) 1794-1796
58	78772-74-4 5-Methyl-5-(2-naphthyl)-2,4-imidazolidinedione	M. L. KeshtovA. L. RusanovN. M. Belomoina and A. K. Mikitaev, Improved synthesis of bis[<i>p</i> -(phenylethynyl)phenyl]hetarylenes, Russ Chem Bull. 46 (1997) 1794-1796
63	1372008-89-3, Aurora Building Blocks, United States Methyl 2-(4-(2,4-dichlorophenyl)-4-methyl-2,5-dioxoimidazolidin-1-yl)acetate	Aurora Building Blocks
65	1371767-82-6, Aurora Building Blocks, United States Methyl 2-(4-methyl-2,5-dioxo-4-p-tolylimidazolidin-1-yl)acetate	Aurora Building Blocks
68	104-88-1, 4-Chlorobenzaldehyde	sigma
69	88372-92-3 china 1,2-bis(4-chlorophenyl)ethane-1,2-dione	88372-92-3 China
70	23186-92-7, Atomax Chemicals Product List China 5,5-bis(4-chlorophenyl)imidazolidine-2,4-dione	Electrochemical characterization of phenytoin and its derivatives on bare gold electrode. Trisovic, Nemanja P.; Bozic, Bojan Dj.; Lovic, Jelena D.; Vitnik, Vesna D.; Vitnik, Zeljko J.; Petrovic, Slobodan D.; Ivic, Milka L. Avramov. Electrochimica Acta Volume 161 Pages 378-387 Journal; Online Computer File. 2015

**^1H -NMR, ^{13}C -N-NMR
for final products 5-27**

This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

1H-NMR

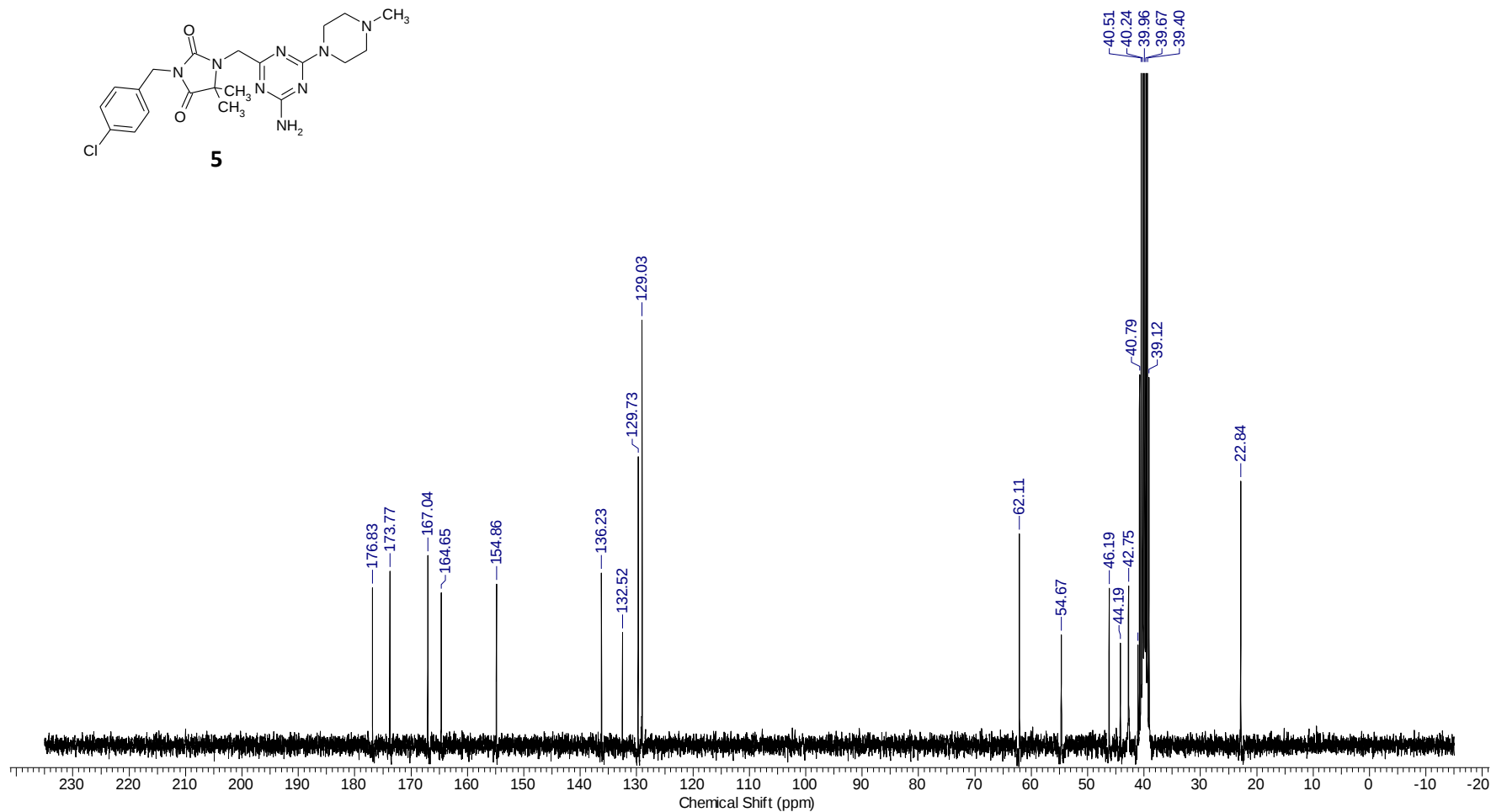
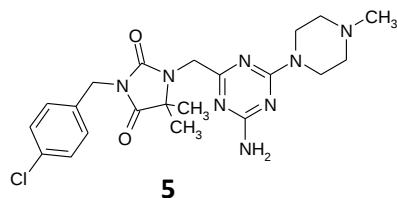
Acquisition Time (sec)	1.7064	Date	Oct 10 2017	Date Stamp	Oct 10 2017		2017-10-10 19:24:29
File Name	C:\Users\Dorota\Desktop\ANALIZY\NMR\2017\17-10-10_DJ24_dlaz\17-10-10_DJ24_dlaz_PROTON_01.fid\fid					Frequency (MHz)	300.08
Nucleus	1H	Number of Transients	32	Original Points Count	8192	Points Count	8192
Pulse Sequence	s2pul	Receiver Gain	34.00	Solvent	DMSO-d6	Spectrum Offset (Hz)	1800.4814
Spectrum Type	STANDARD	Sweep Width (Hz)	4800.77	Temperature (degree C)	AMBIENT TEMPERATURE		



This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

C13-NMR

Acquisition Time (sec)	0.8684	Date	Oct 17 2017	Date Stamp	Oct 17 2017	2017-10-18 11:39:50
File Name	C:\Users\Dorota\Desktop\ANALIZY\NMR\2017\17-10-17_DJ24_diaz\17-10-17_DJ24_diaz CARBON_01.fid\fid					
Frequency (MHz)	75.46	Nucleus	13C	Number of Transients	3000	Original Points Count 16384
Points Count	16384	Pulse Sequence	s2pul	Receiver Gain	34.00	Solvent DMSO-d6
Spectrum Offset (Hz)	8300.0879	Spectrum Type	STANDARD	Sweep Width (Hz)	18867.92	Temperature (degree C) 23.000

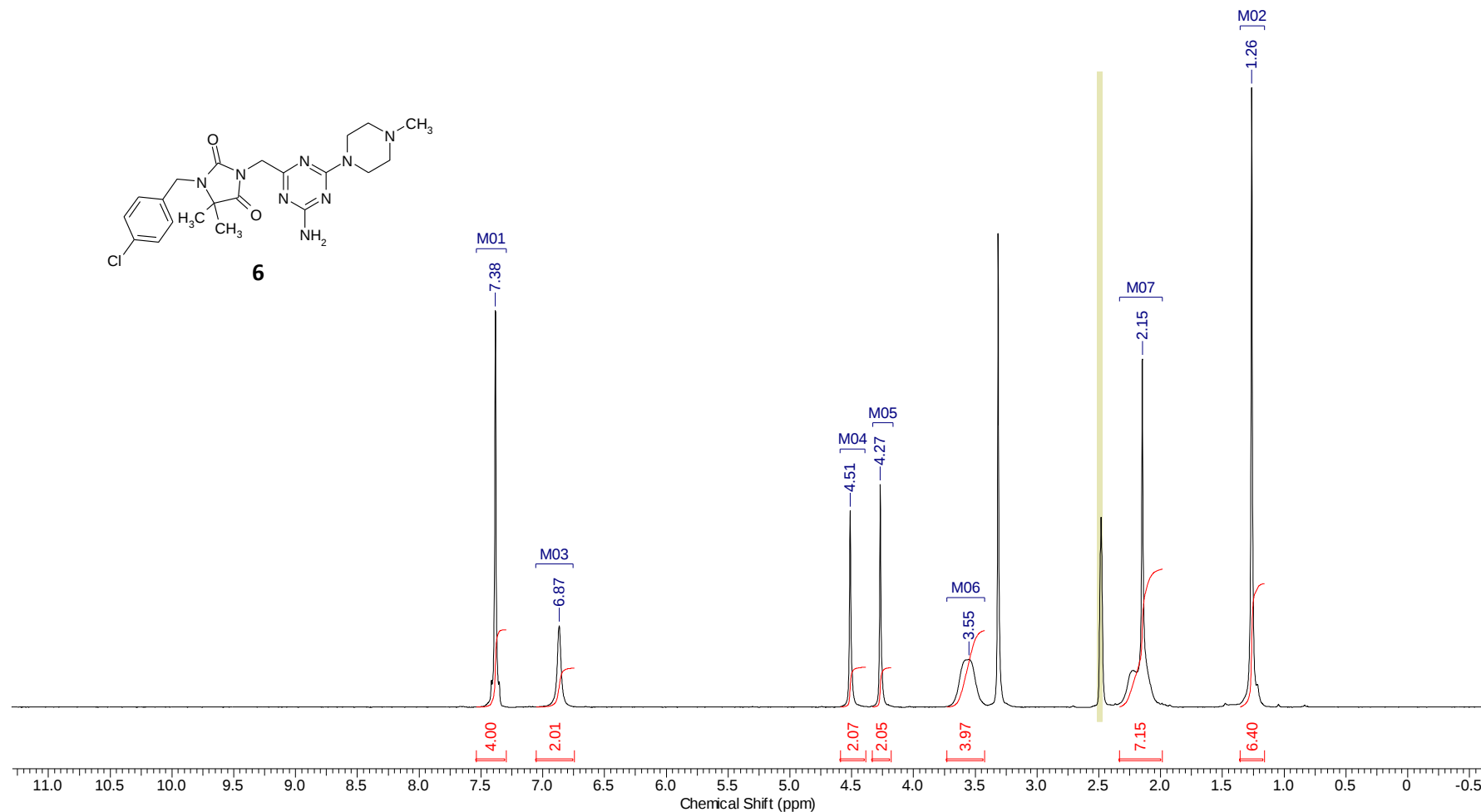


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

1H-NMR

2017-10-10 18:46:57

Acquisition Time (sec)	1.7064	Date	Oct 10 2017	Date Stamp	Oct 10 2017		
File Name	C:\Users\Dorota\Desktop\ANALIZY\NMR\2017-10-10_DJ18_dlaz\17-10-10_DJ18_dlaz_PROTON_01.fid\fid				Frequency (MHz)	300.08	
Nucleus	1H	Number of Transients	32	Original Points Count	8192	Points Count	8192
Pulse Sequence	s2pul	Receiver Gain	38.00	Solvent	DMSO-d6	Spectrum Offset (Hz)	1800.4814
Spectrum Type	STANDARD	Sweep Width (Hz)	4800.77	Temperature (degree C) AMBIENT TEMPERATURE			

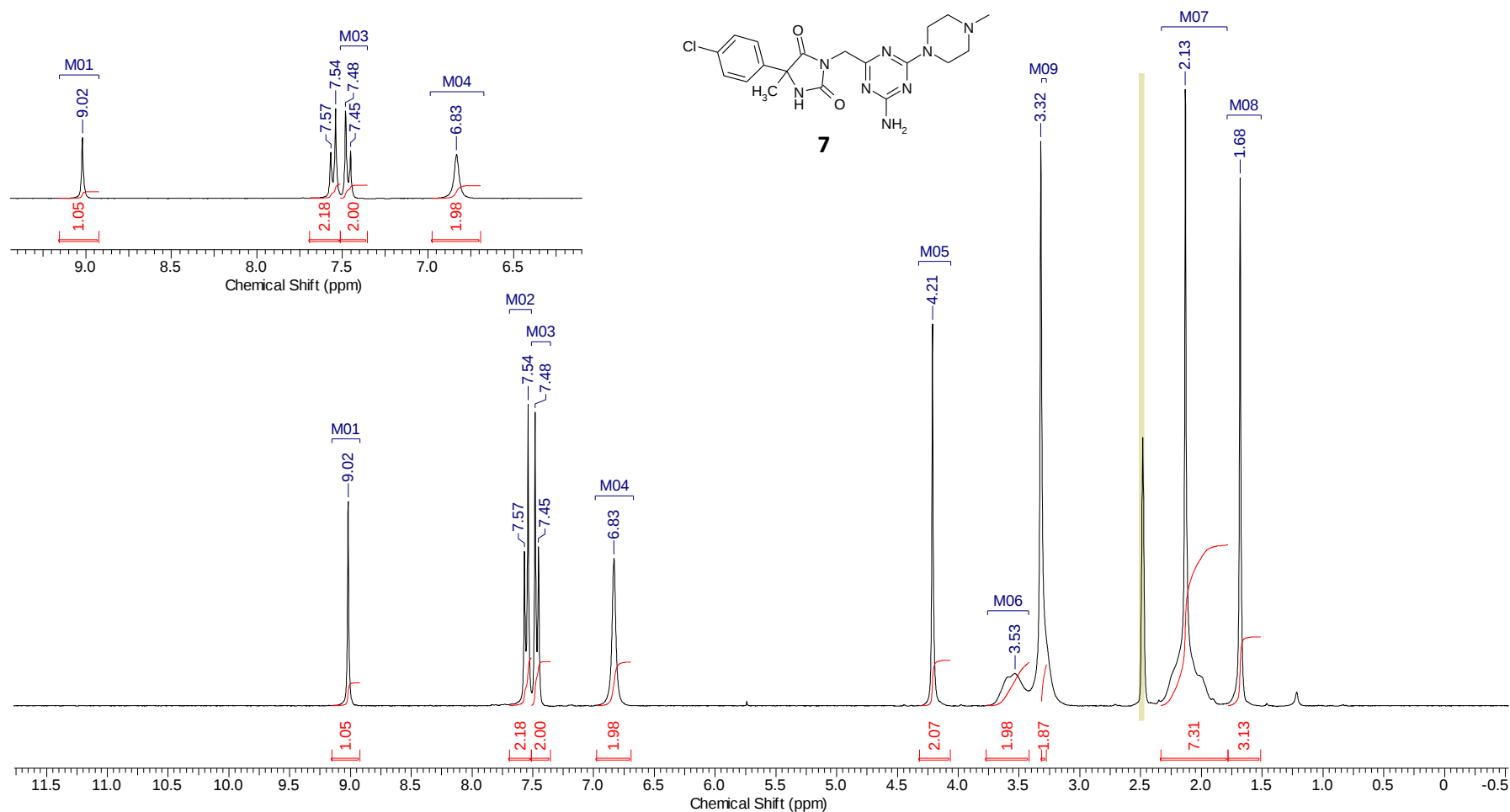


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

1H-NMR

2017-10-10 13:03:40

Acquisition Time (sec)	1.7064	Date	Oct 10 2017	Date Stamp	Oct 10 2017		
File Name	C:\Users\Dorota\Desktop\ANALIZY\NMR\2017\17-10-10_DJ2_dlaz\17-10-10_DJ2_dlaz_PROTON_01.fid\fid				Frequency (MHz)	300.08	
Nucleus	1H	Number of Transients	32	Original Points Count	8192	Points Count	8192
Pulse Sequence	s2pul	Receiver Gain	38.00	Solvent	DMSO-d6	Spectrum Offset (Hz)	1800.4814
Spectrum Type	STANDARD	Sweep Width (Hz)	4800.77	Temperature (degree C) AMBIENT TEMPERATURE			

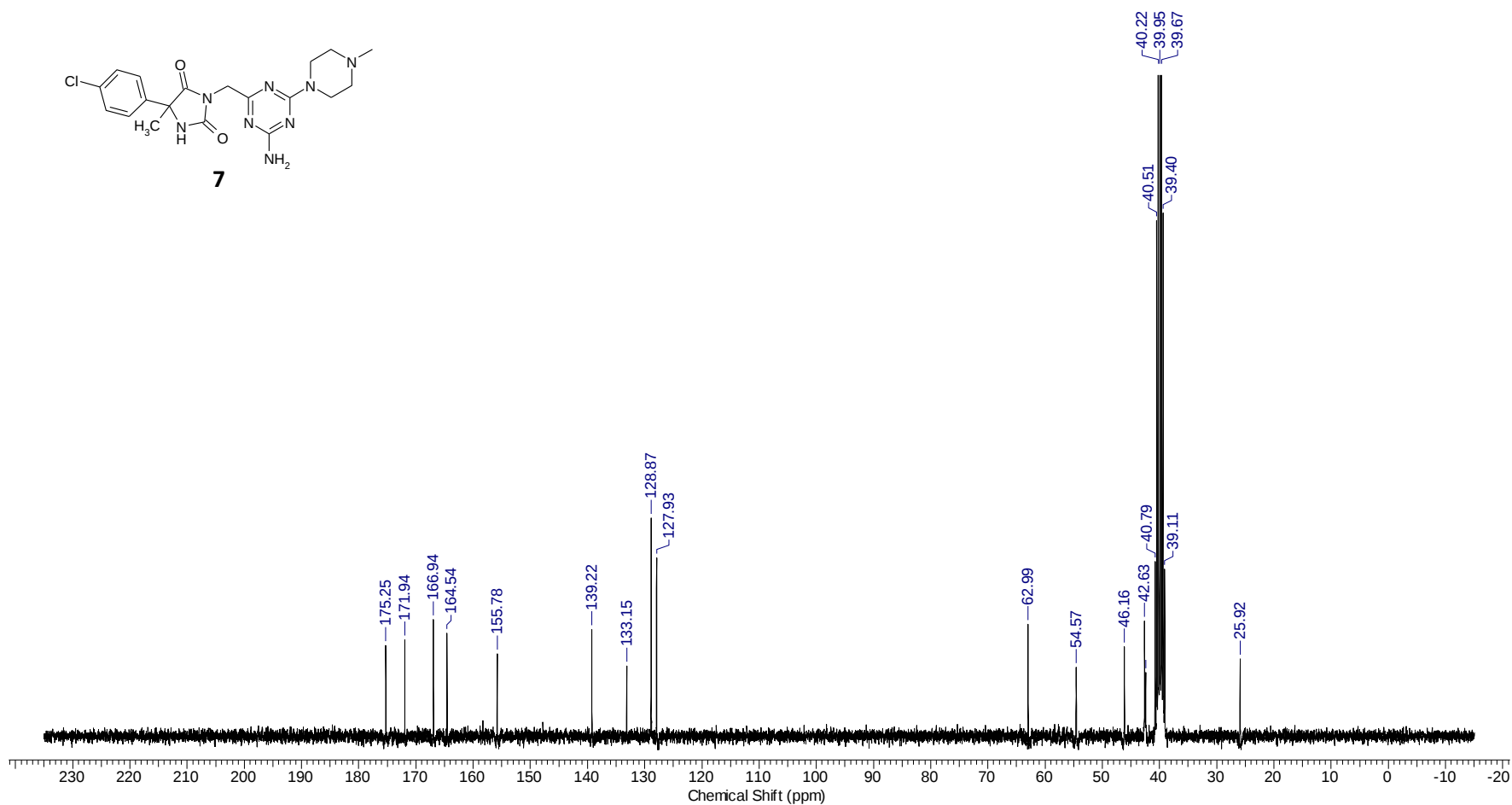
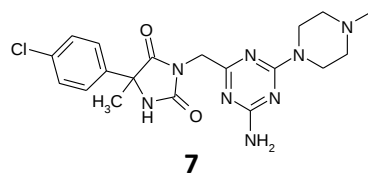


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

C13-NMR

2017-10-18 11:19:51

Acquisition Time (sec)	0.8684	Date	Oct 17 2017	Date Stamp	Oct 17 2017		
File Name	C:\Users\Dorota\Desktop\ANALIZYNMR\2017\17-10-17_DJ2_dlaz\17-10-17_DJ2_dlaz_CARBON_01.fid\fid					Frequency (MHz)	75.46
Nucleus	13C	Number of Transients	1536	Original Points Count	16384	Points Count	16384
Pulse Sequence	s2pul	Receiver Gain	34.00	Solvent	DMSO-d6	Spectrum Offset (Hz)	8300.0879
Spectrum Type	STANDARD	Sweep Width (Hz)	18867.92	Temperature (degree C)	23.000		

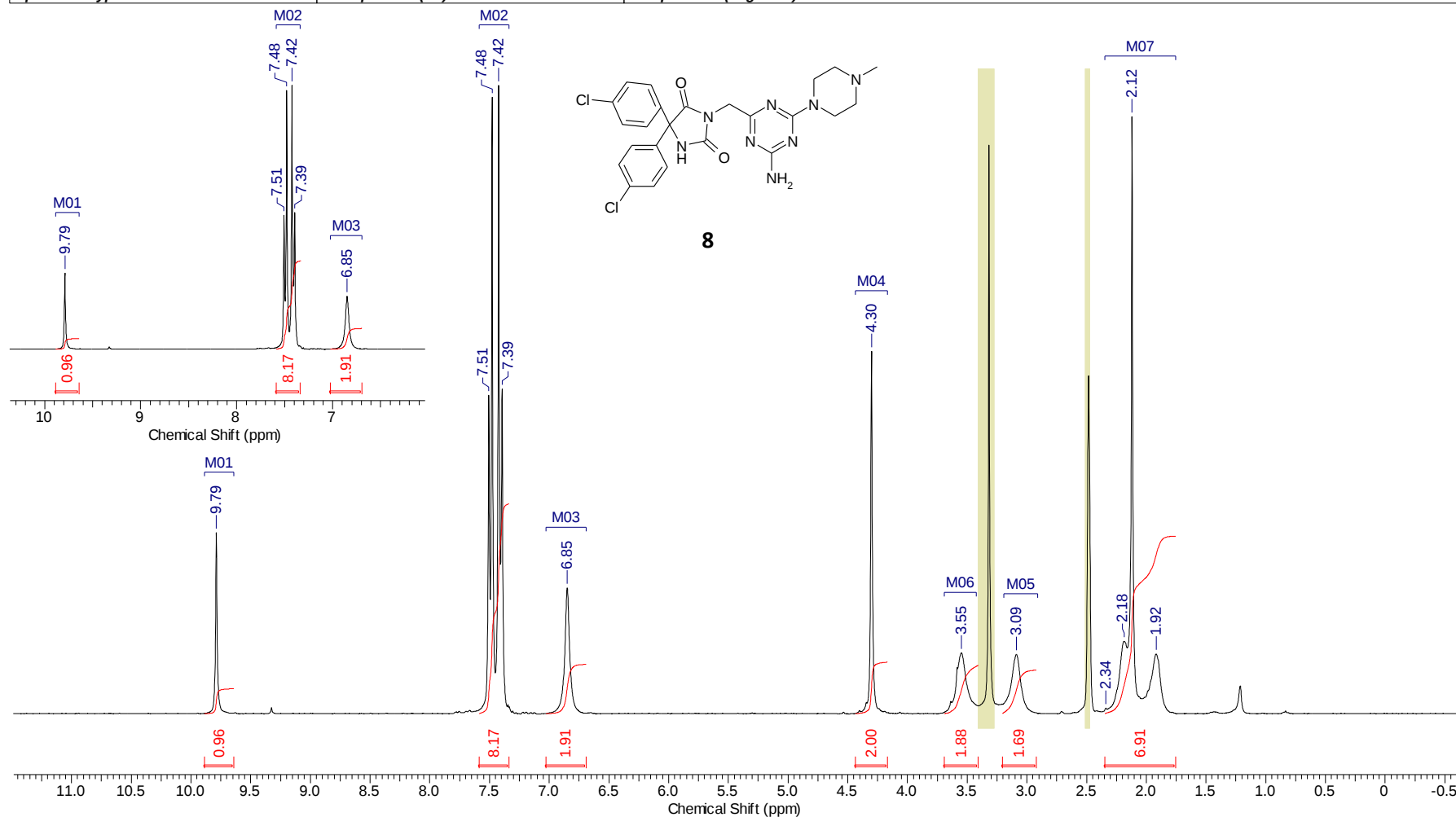


This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

1H-NMR

2017-10-10 13:19:36

Acquisition Time (sec)	1.7064	Date	Oct 10 2017	Date Stamp	Oct 10 2017	2017-10-10 13:19:32	
File Name	C:\Users\Dorota\Desktop\ANALIZY\NMR\2017\17-10-10_DJ6_dlaz\17-10-10_DJ6_dlaz_PROTON_01.fid\fid					Frequency (MHz)	300.08
Nucleus	1H	Number of Transients	32	Original Points Count	8192	Points Count	8192
Pulse Sequence	s2pul	Receiver Gain	38.00	Solvent	DMSO-d6	Spectrum Offset (Hz)	1800.4814
Spectrum Type	STANDARD	Sweep Width (Hz)	4800.77	Temperature (degree C) AMBIENT TEMPERATURE			

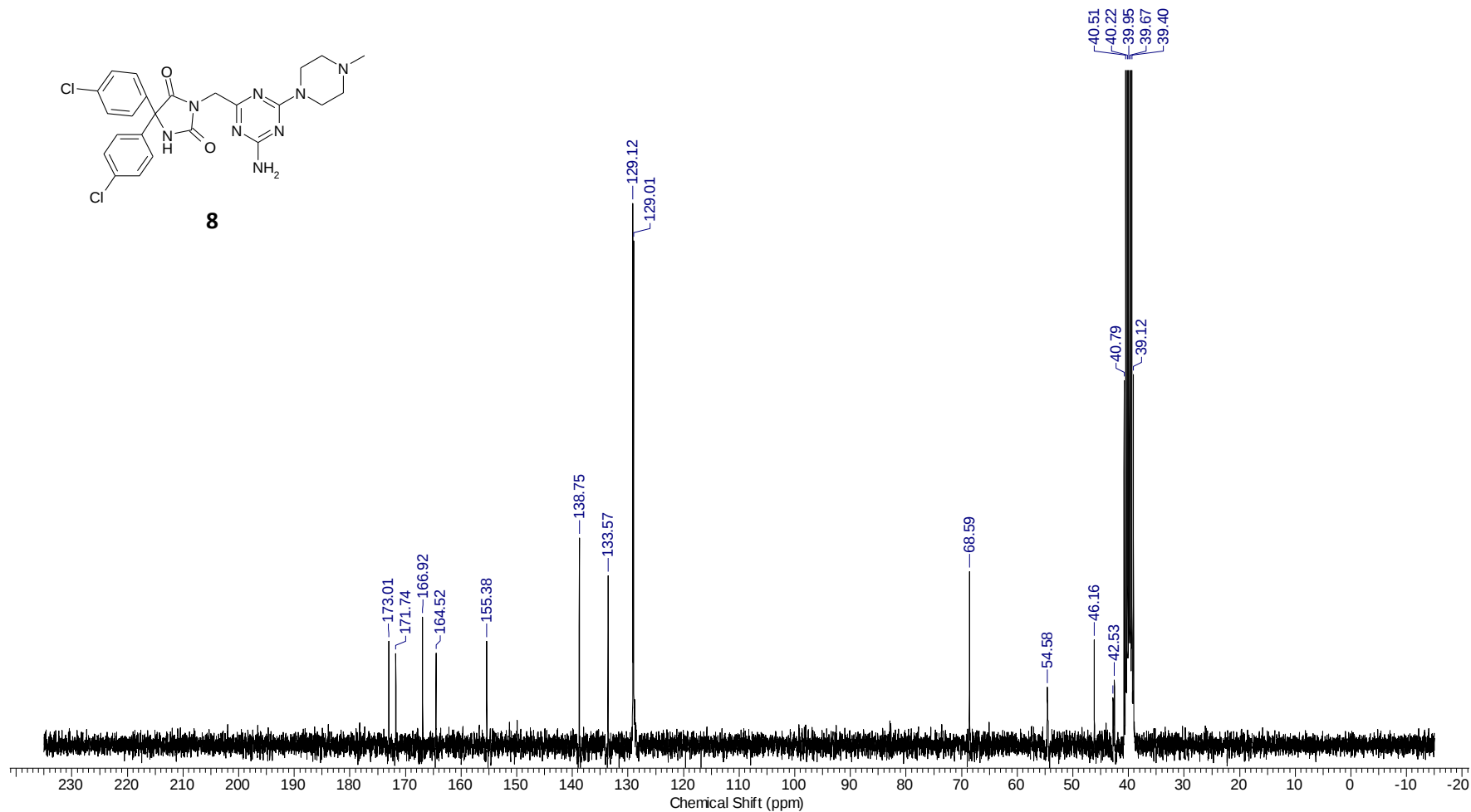
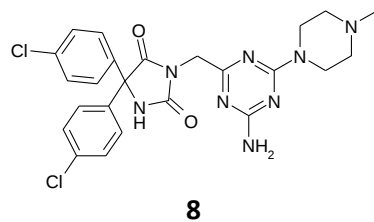


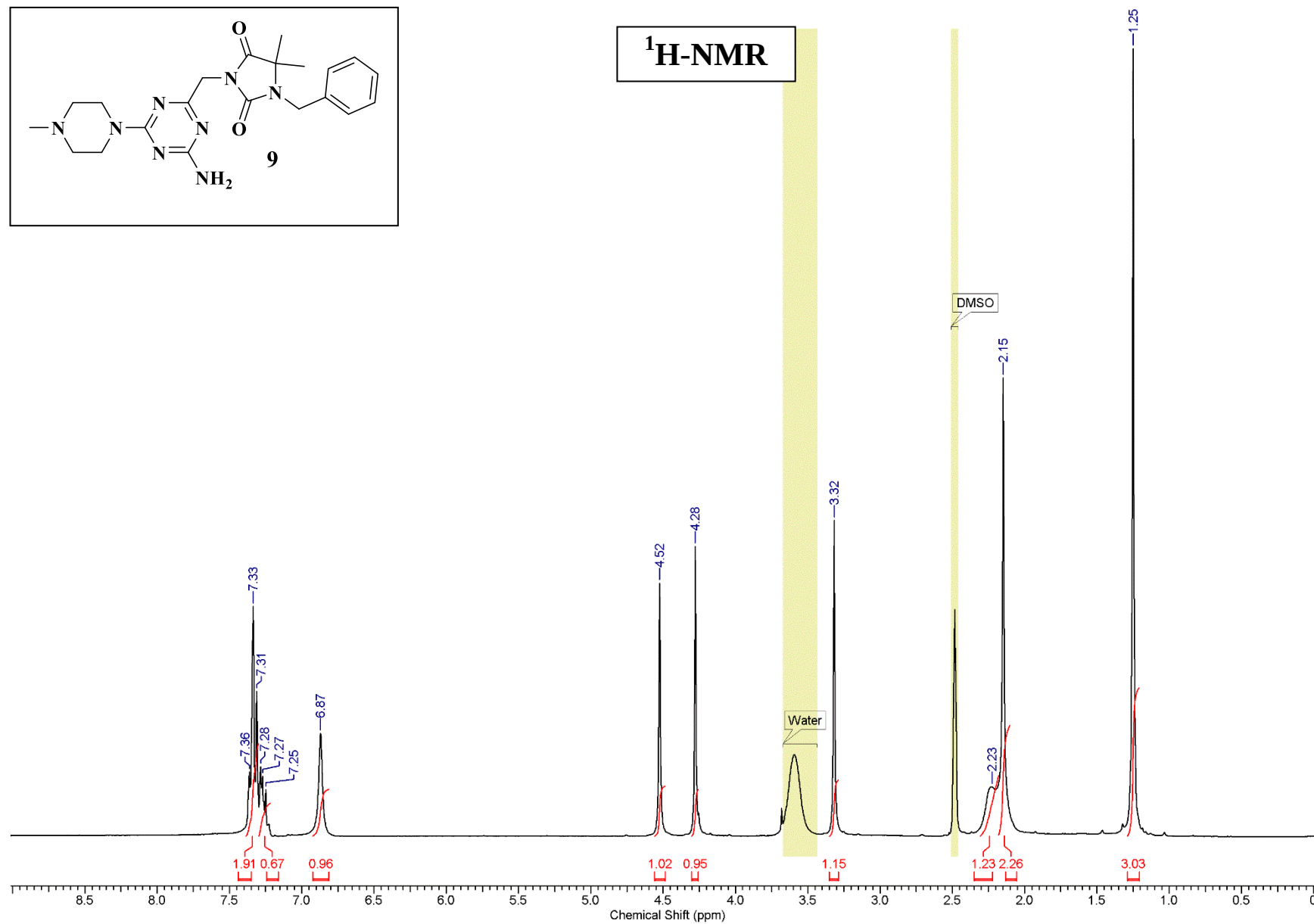
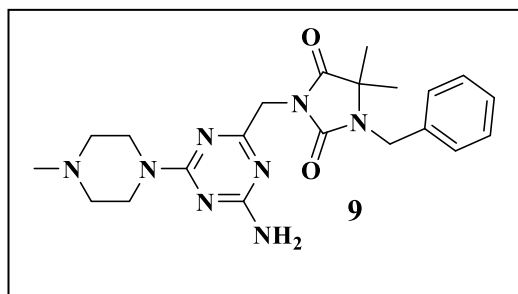
This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/

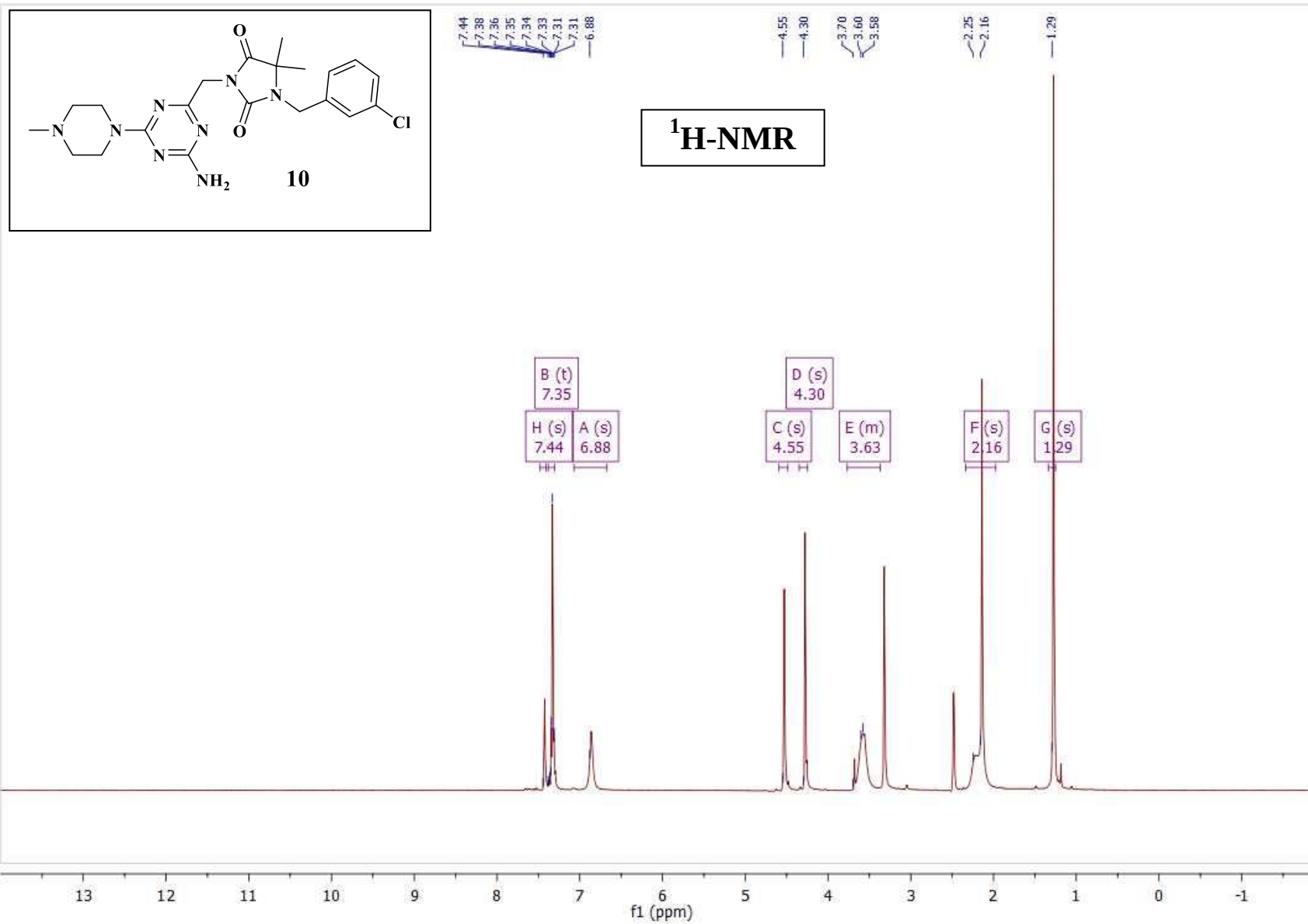
C13-NMR

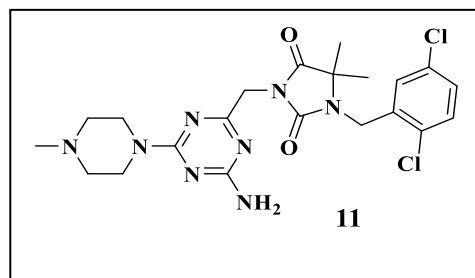
2017-10-18 11:33:03

Acquisition Time (sec)	0.8684	Date	Oct 16 2017	Date Stamp	Oct 16 2017		
File Name	C:\Users\Dorota\Desktop\ANALIZYNMR\2017\17-10-16_DJ6_dlaz\17-10-16_DJ6_dlaz_CARBON_01.fid\fid				Frequency (MHz)	75.46	
Nucleus	13C	Number of Transients	2224	Original Points Count	16384	Points Count	16384
Pulse Sequence	s2pul	Receiver Gain	34.00	Solvent	DMSO-d6	Spectrum Offset (Hz)	8300.0879
Spectrum Type	STANDARD	Sweep Width (Hz)	18867.92	Temperature (degree C)	23.000		

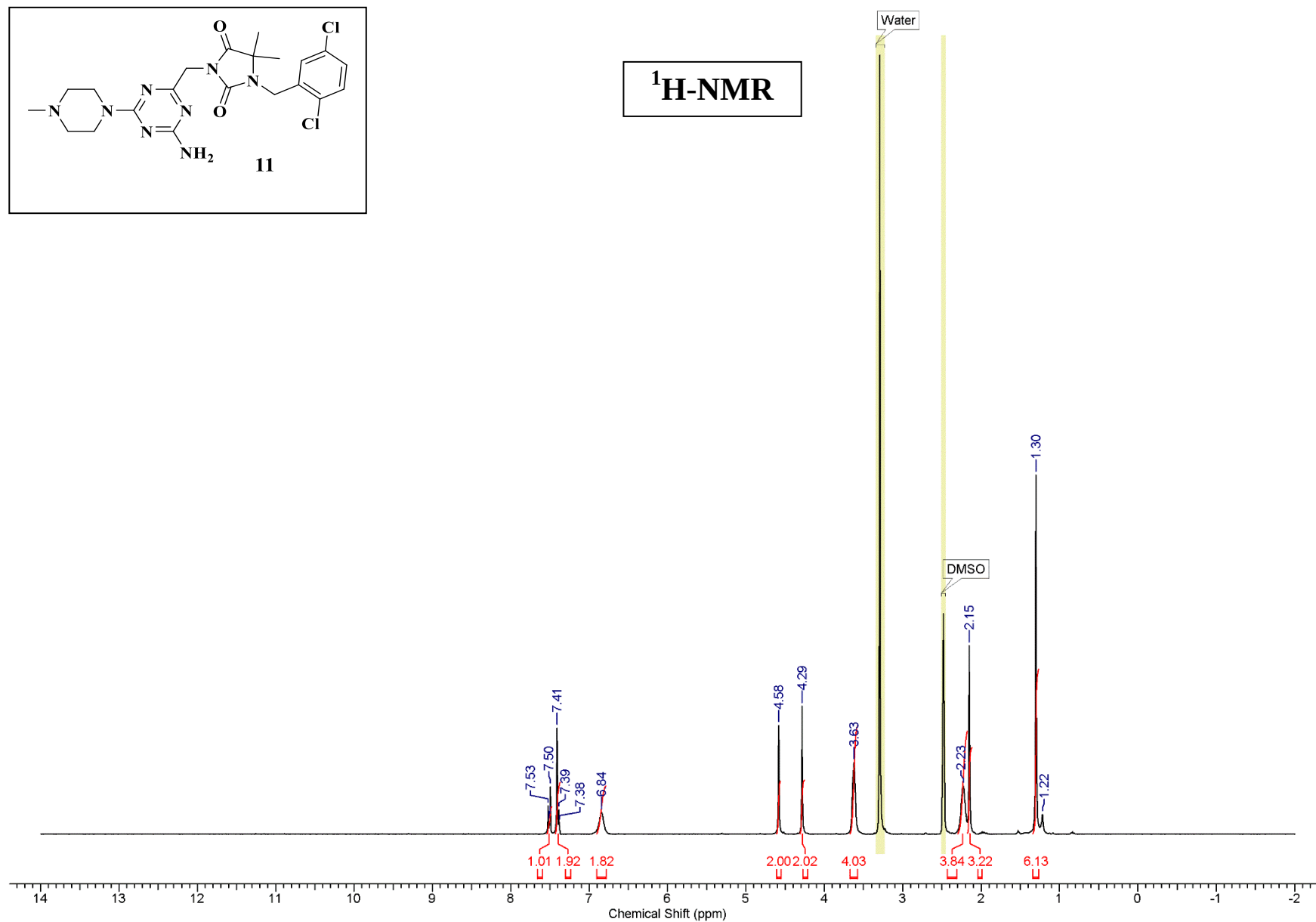


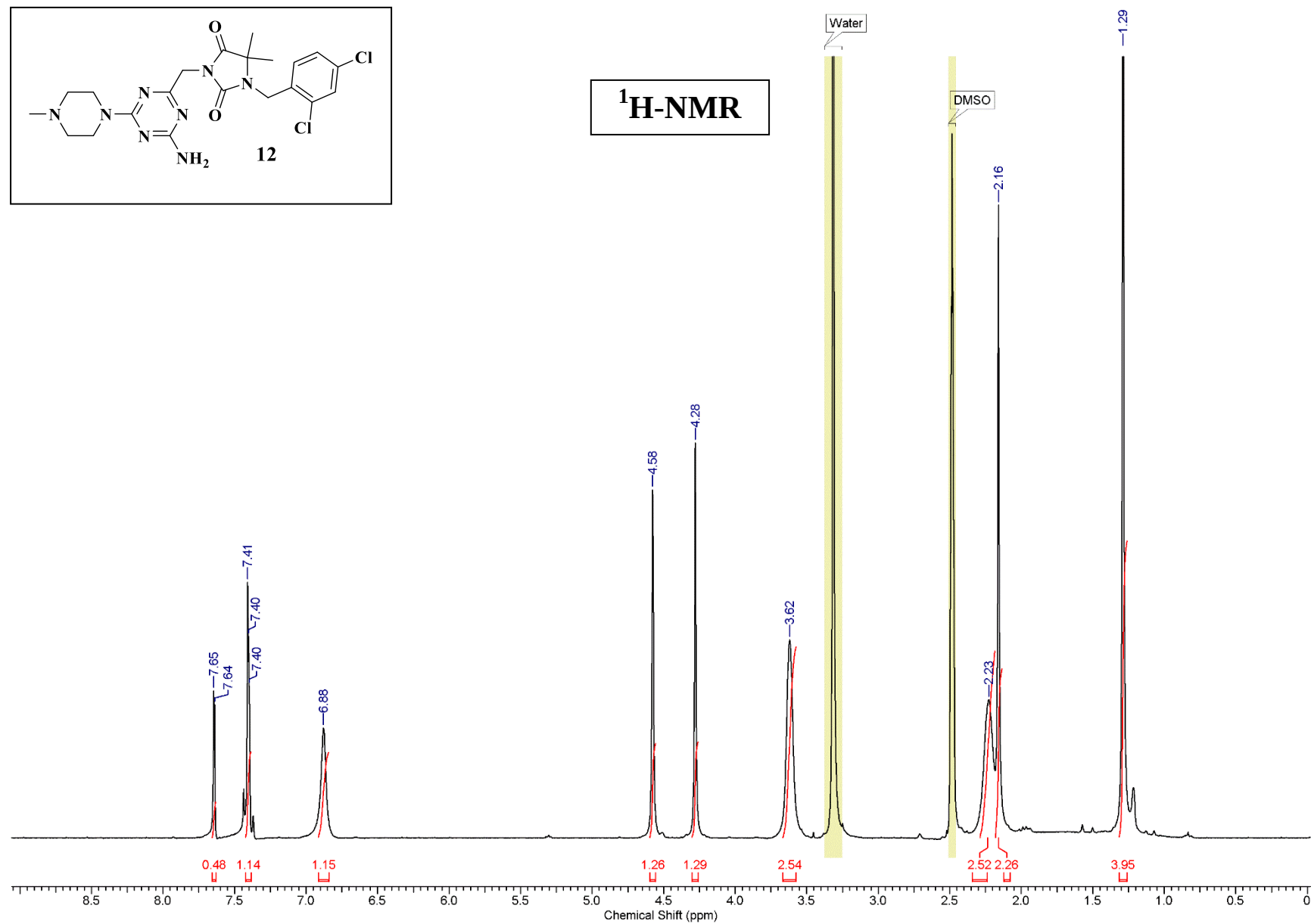


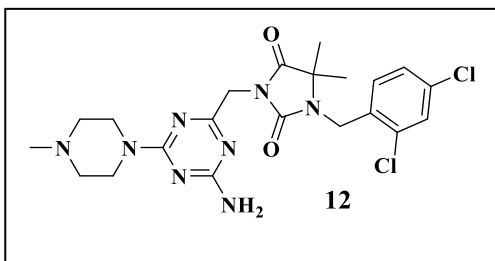




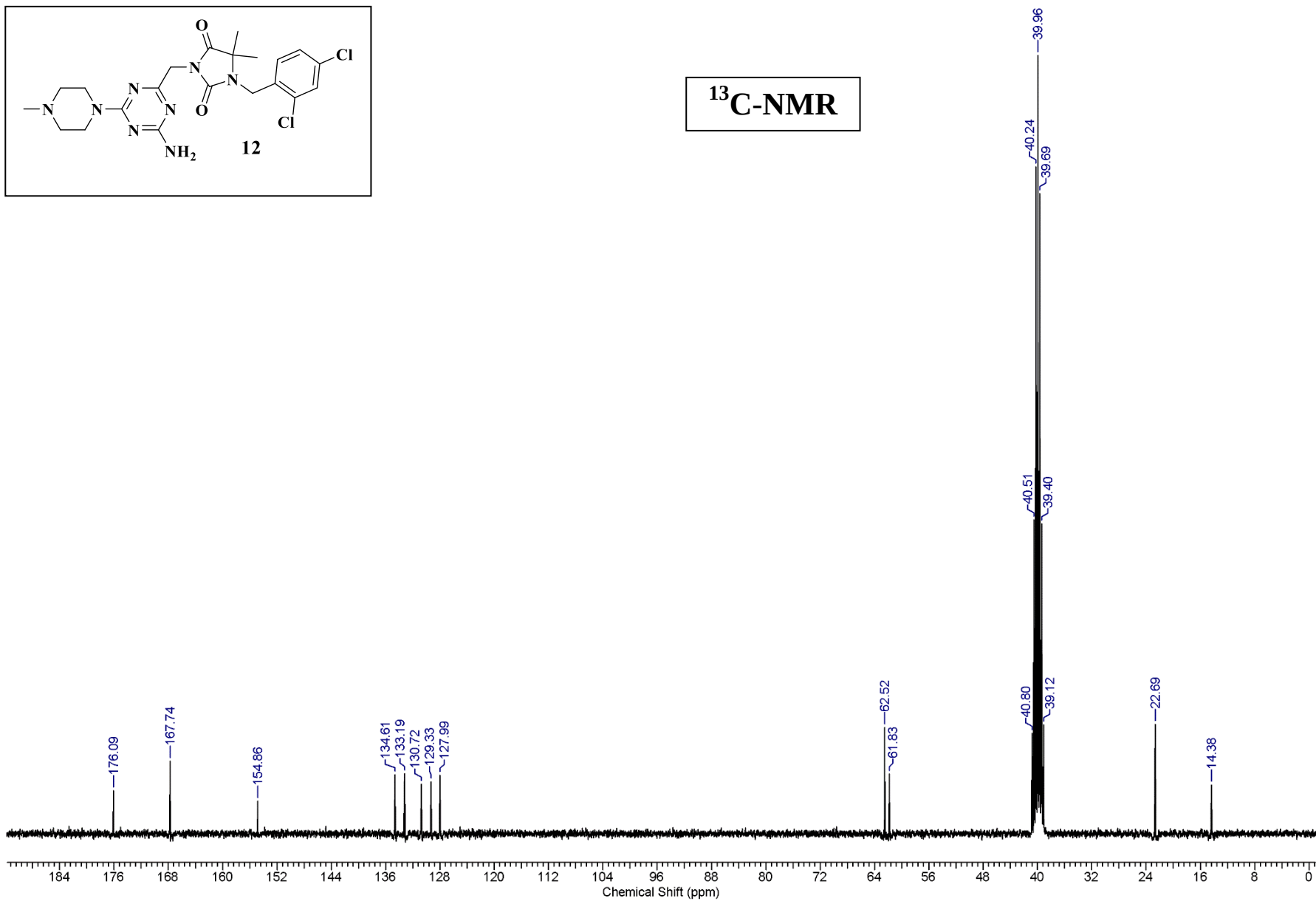
¹H-NMR

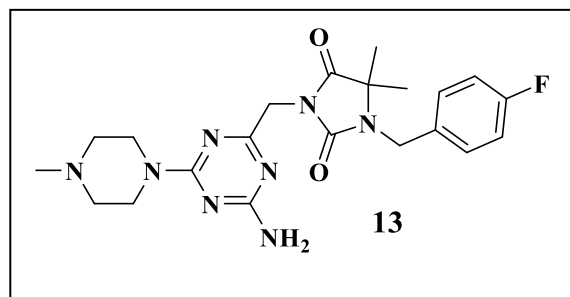




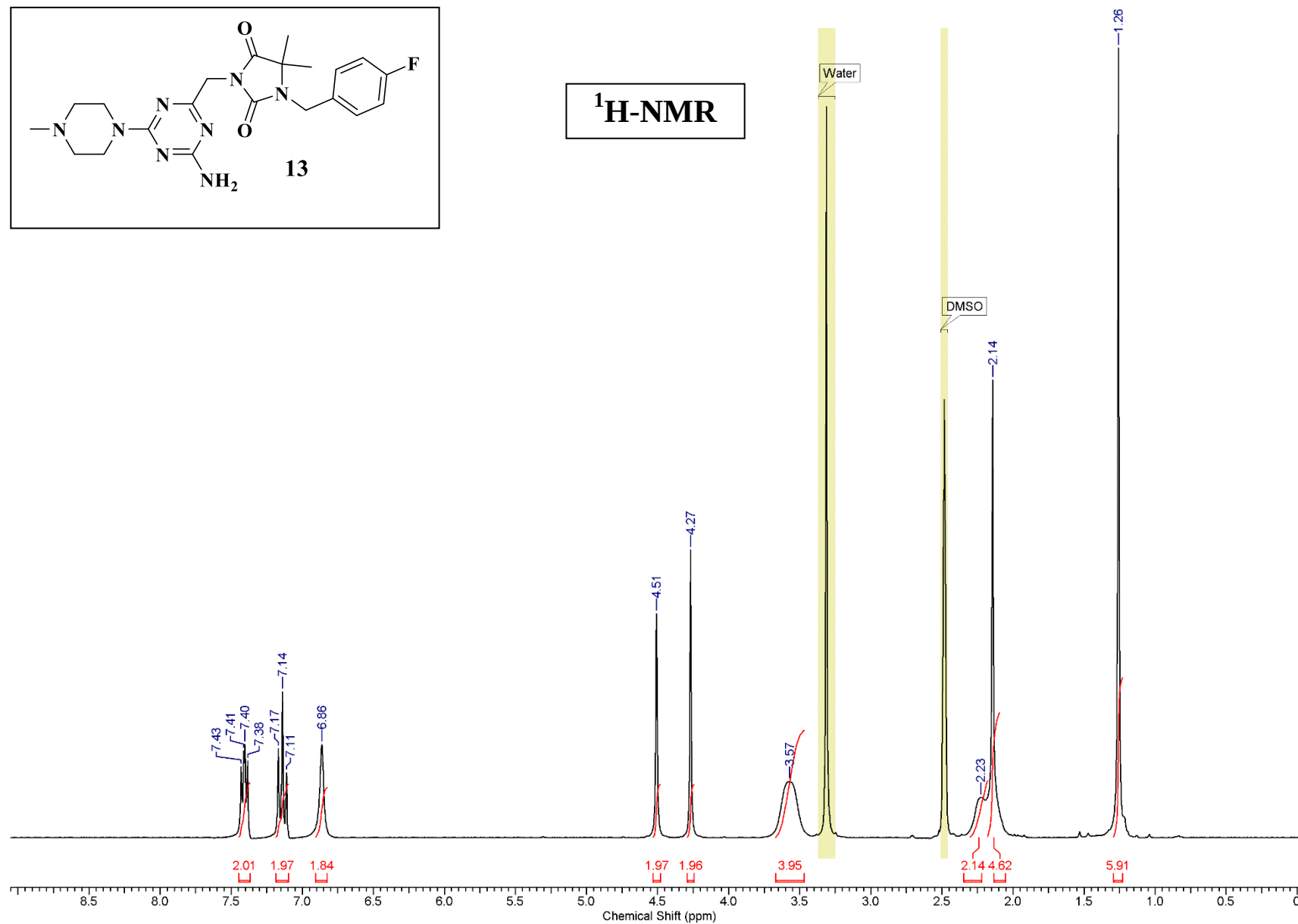


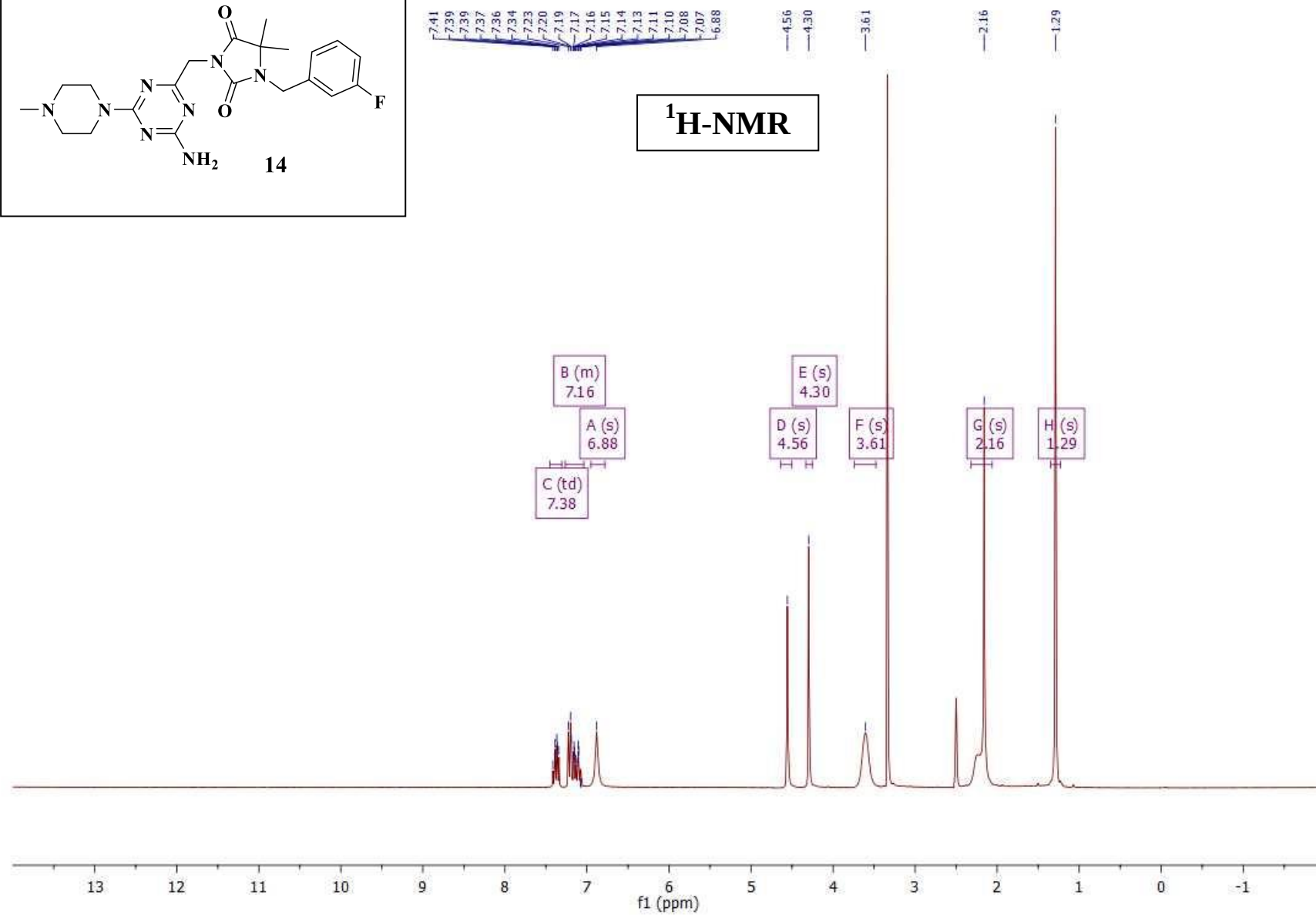
¹³C-NMR

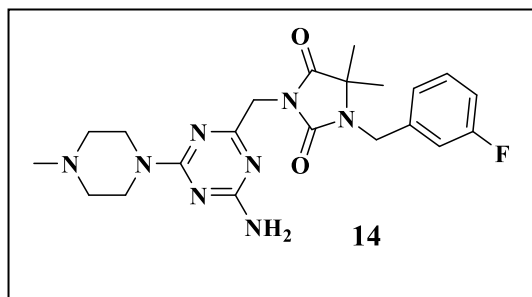




¹H-NMR







176.07
171.63
166.58
164.18
163.75
160.53
155.20

141.72
141.62

130.44
130.33

123.57

114.38
114.16
114.09
113.87

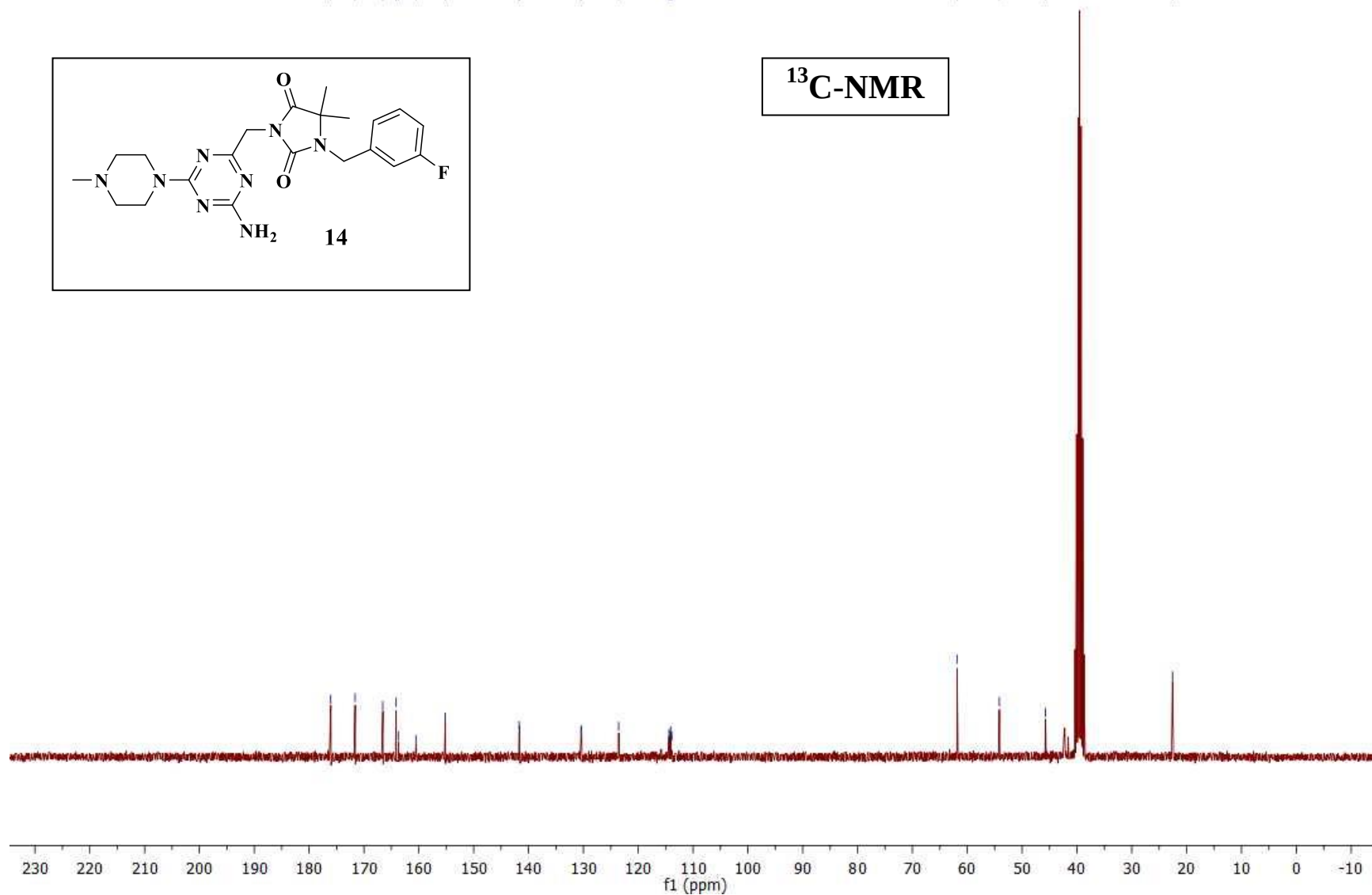
61.87

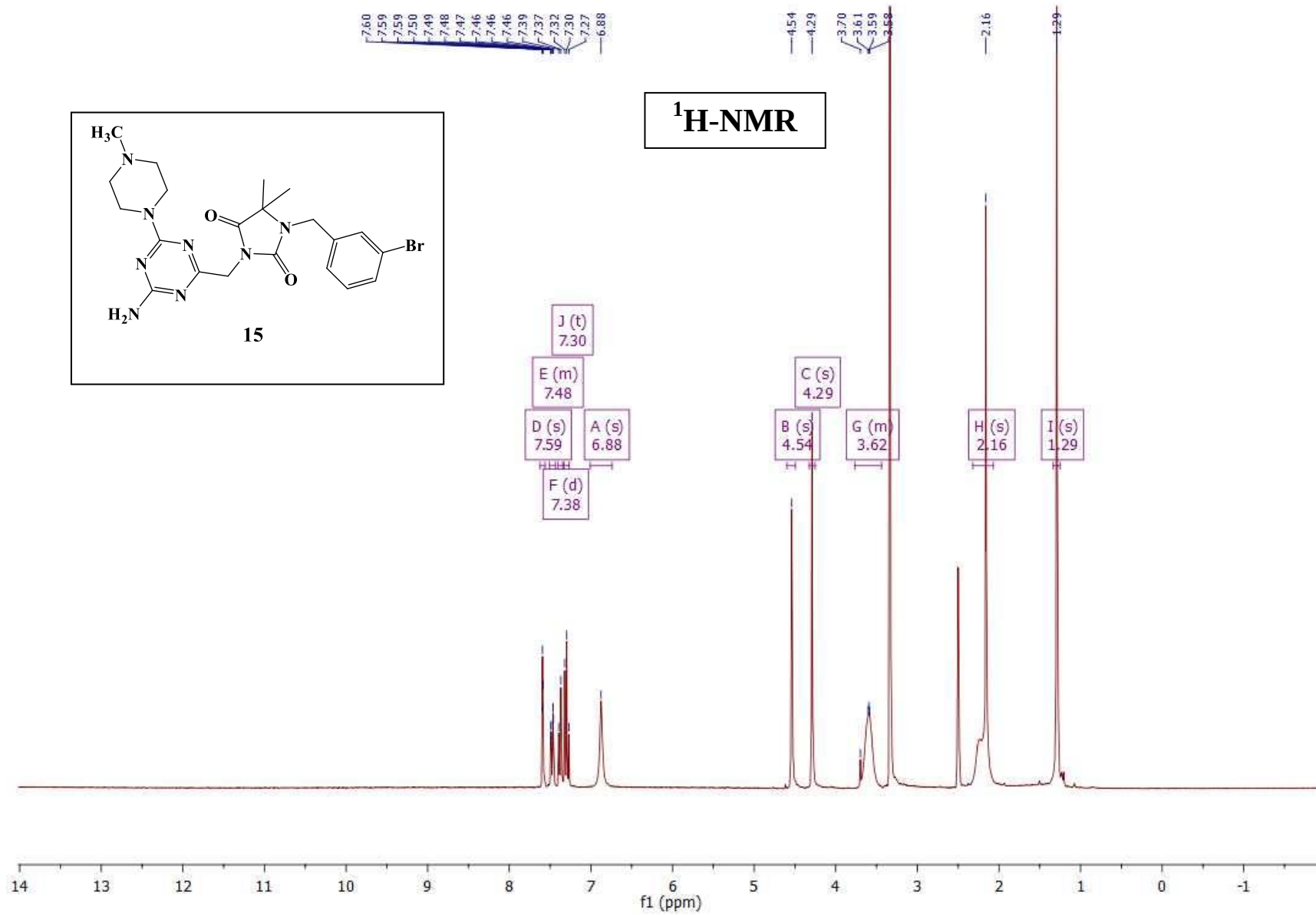
54.15

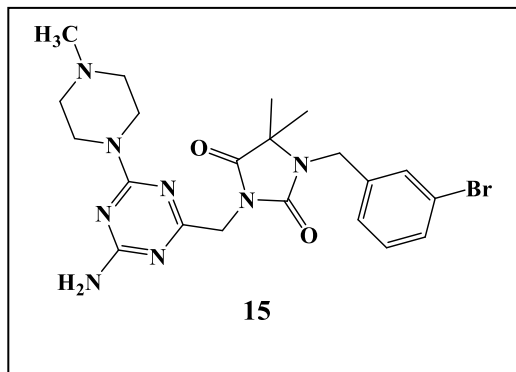
45.73

22.57

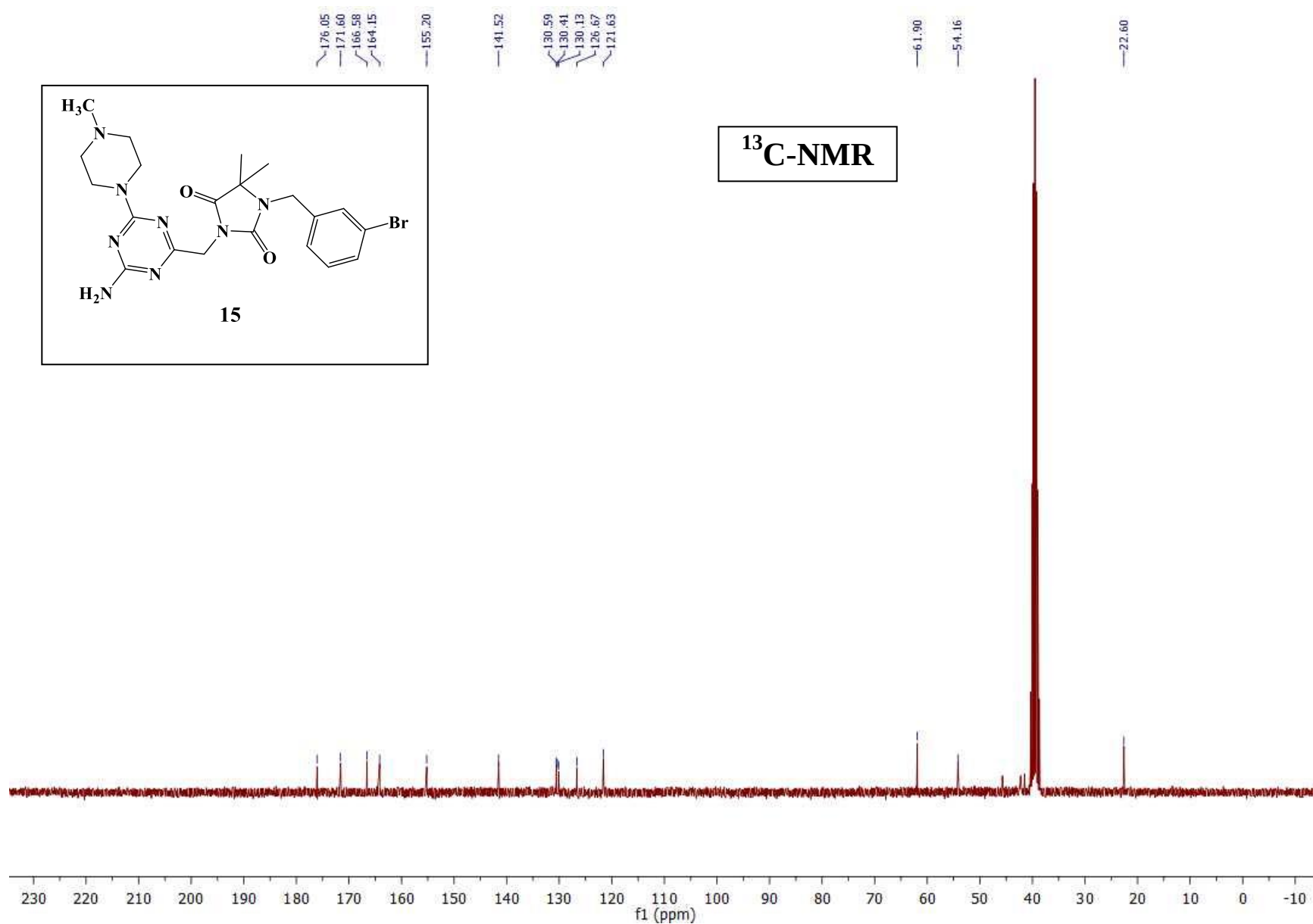
^{13}C -NMR

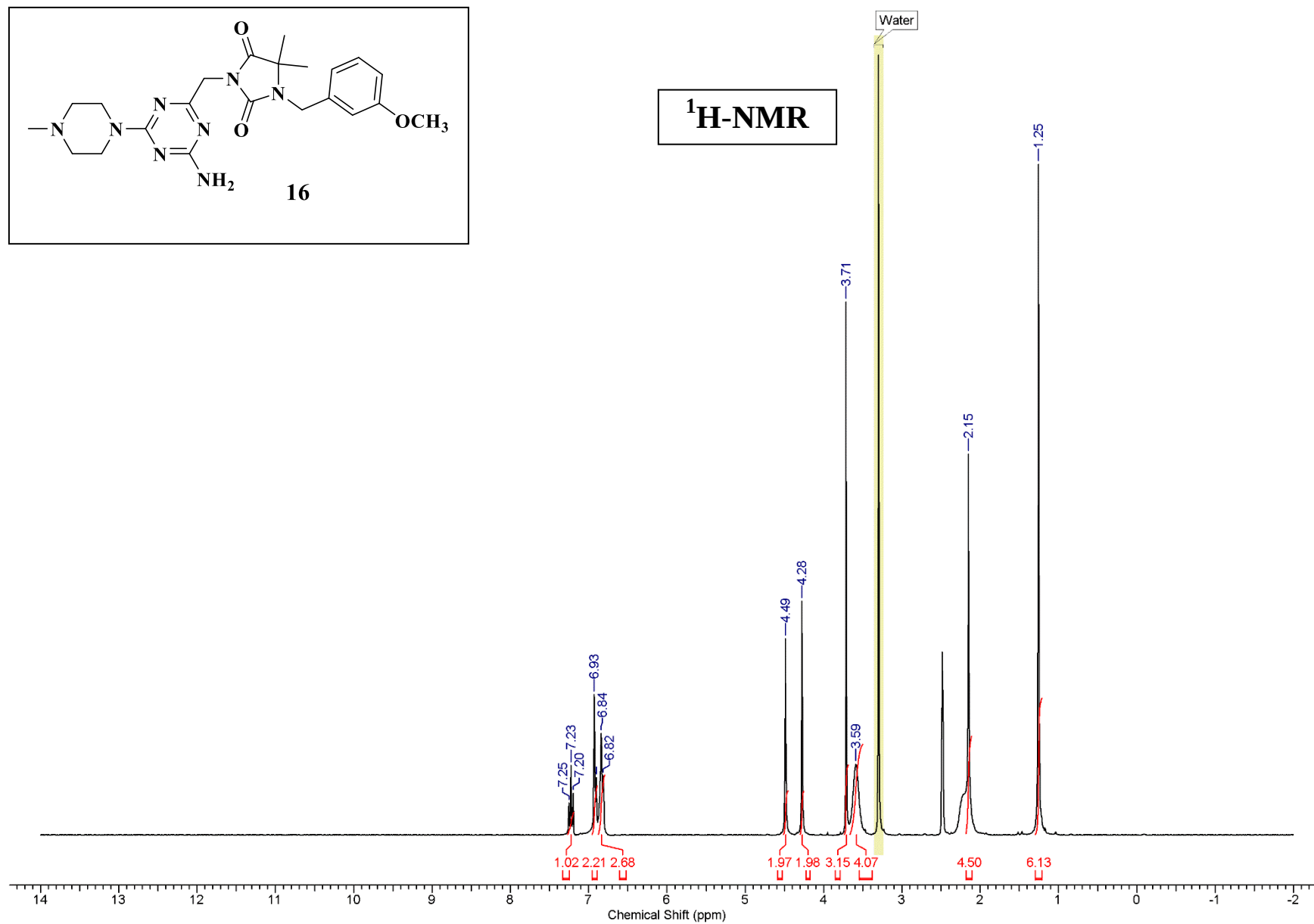
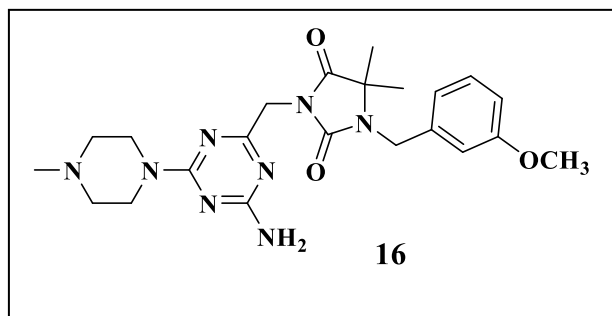


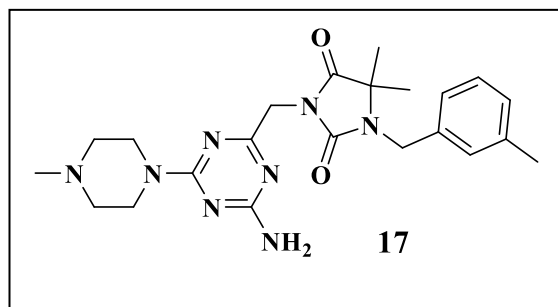




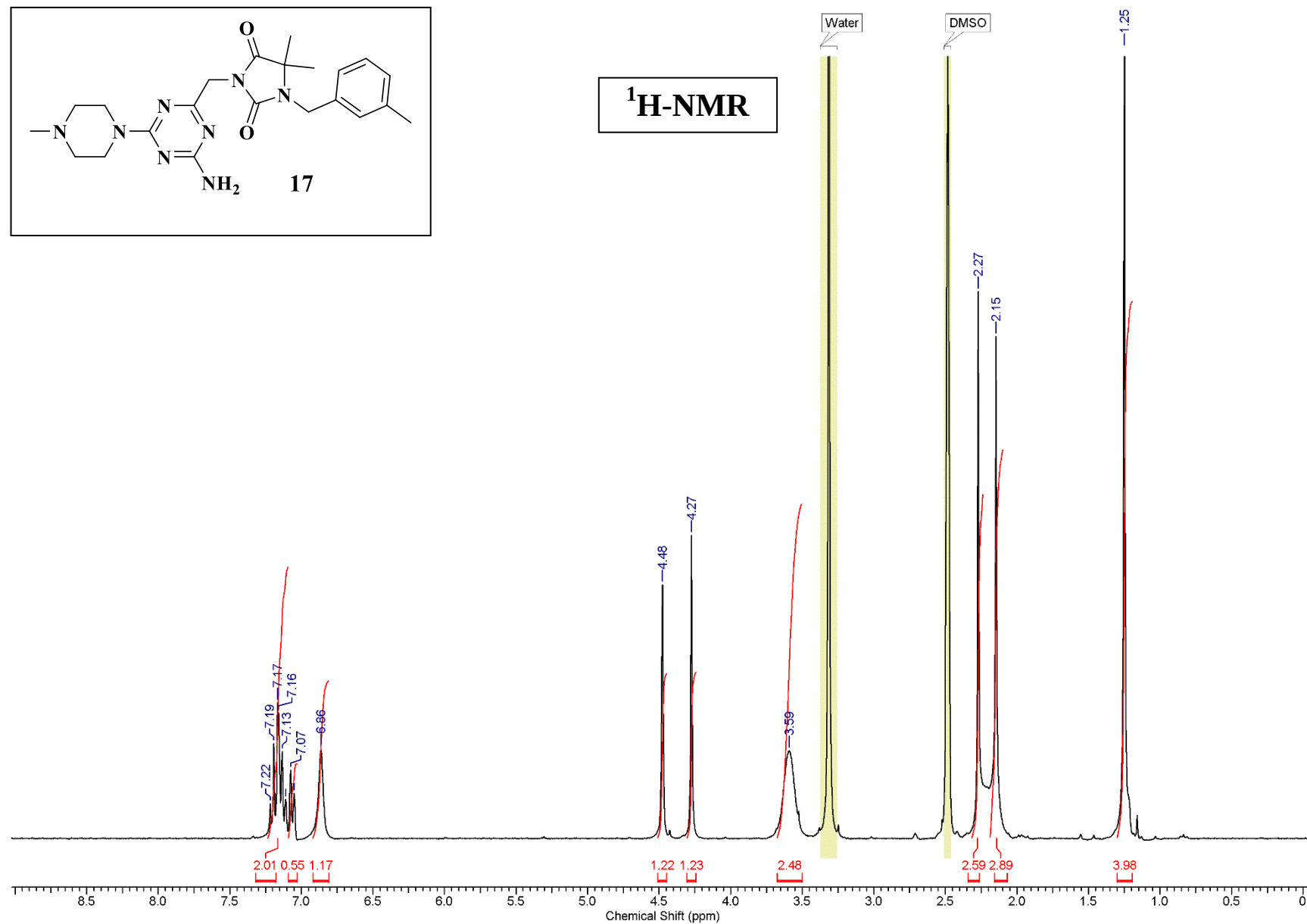
^{13}C -NMR

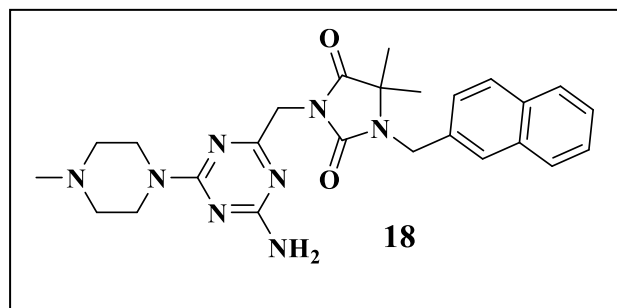




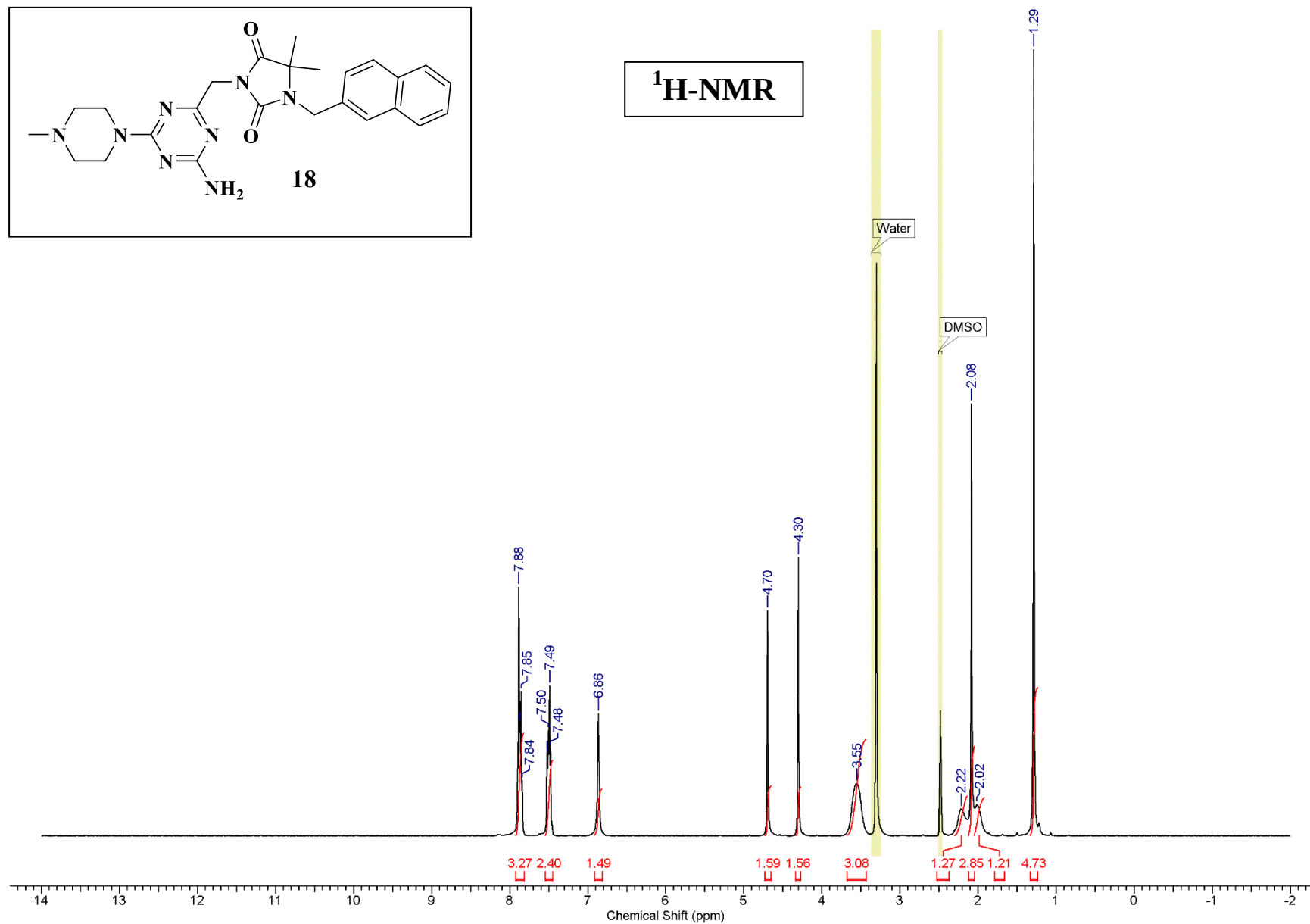


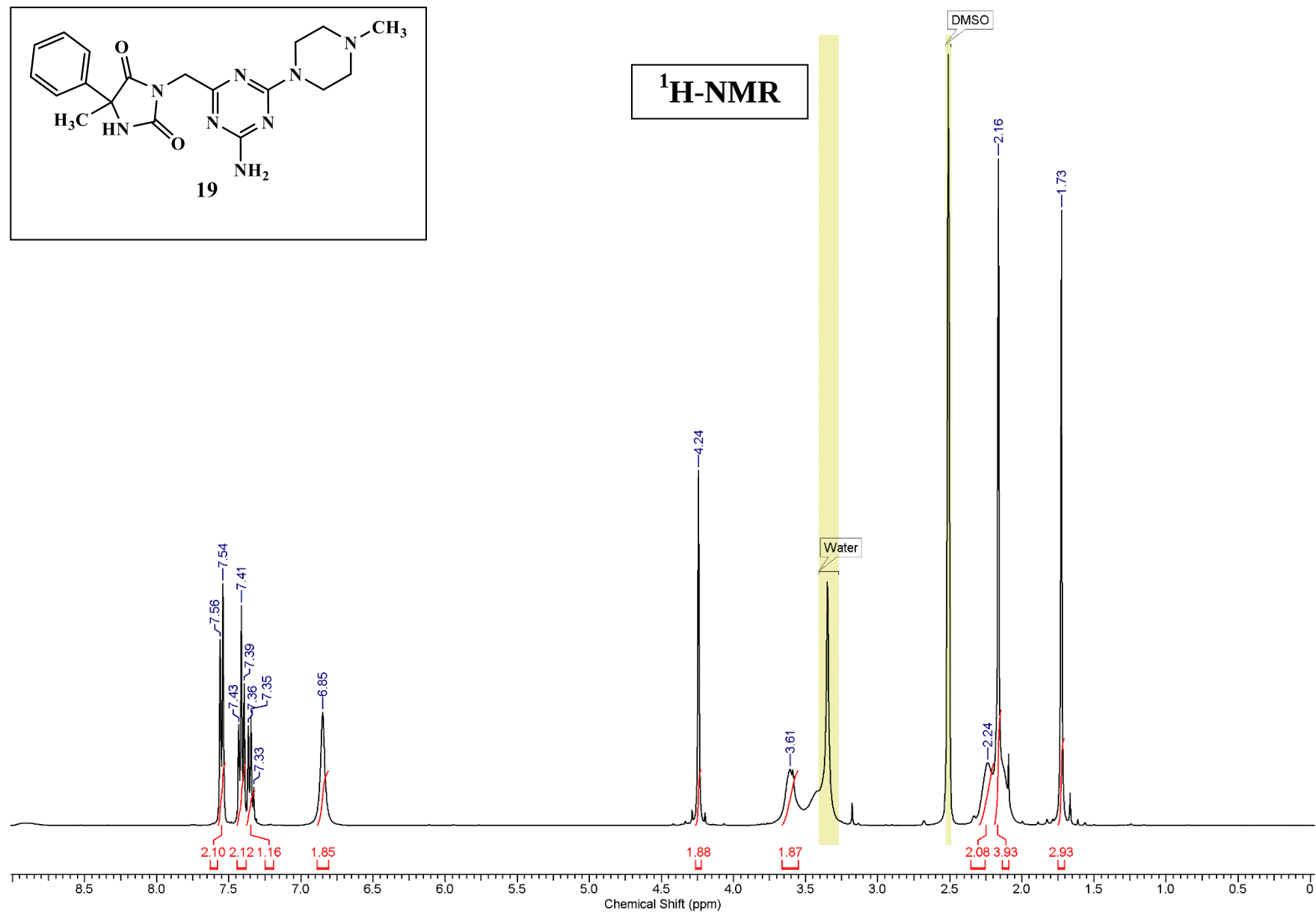
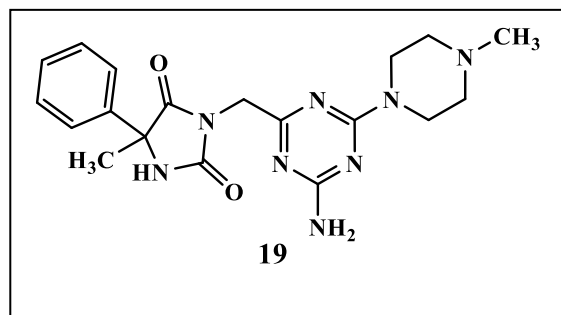
¹H-NMR

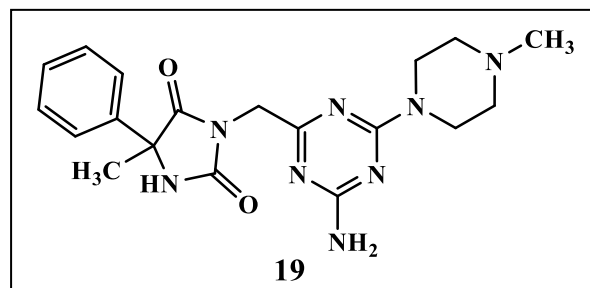




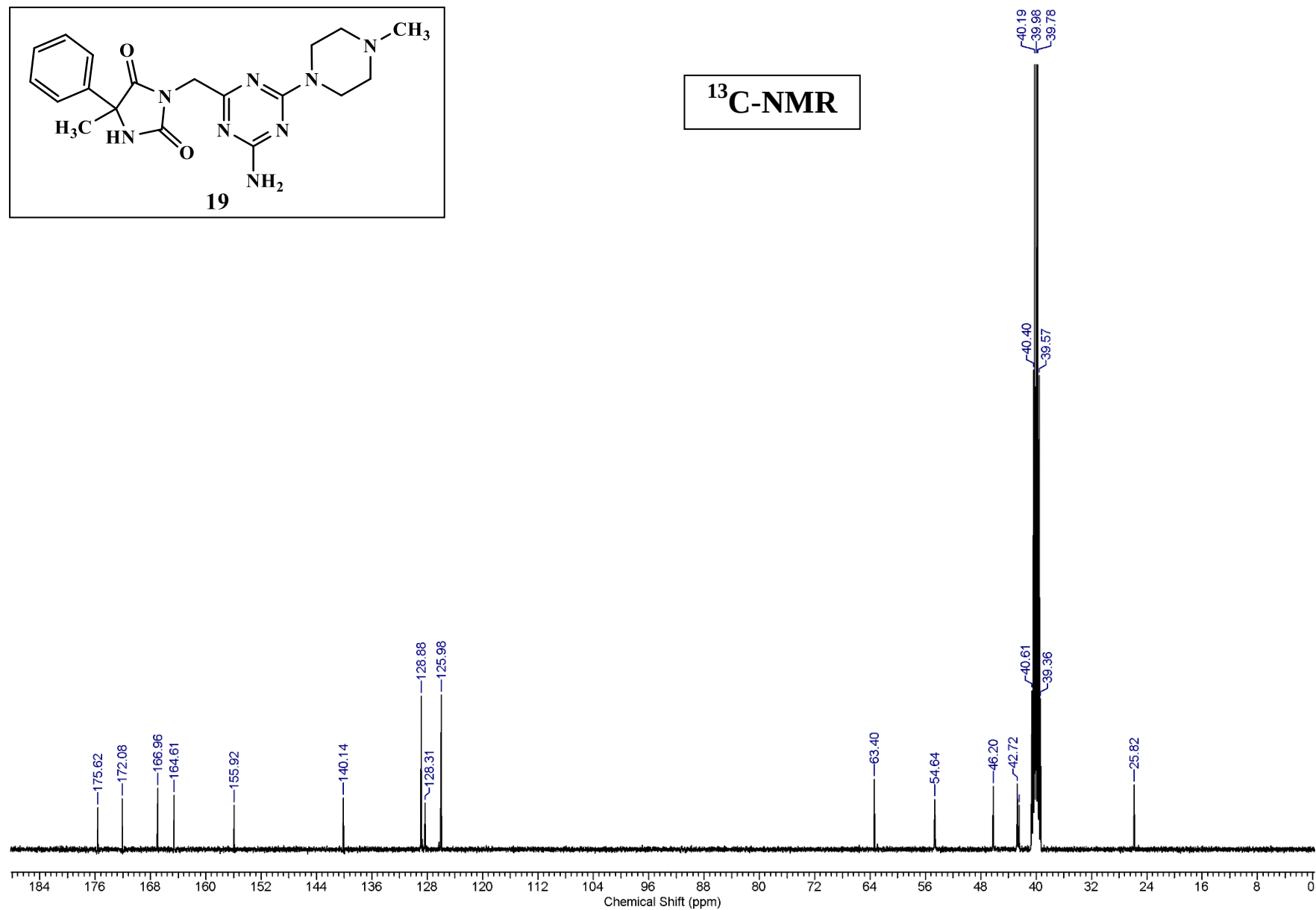
¹H-NMR

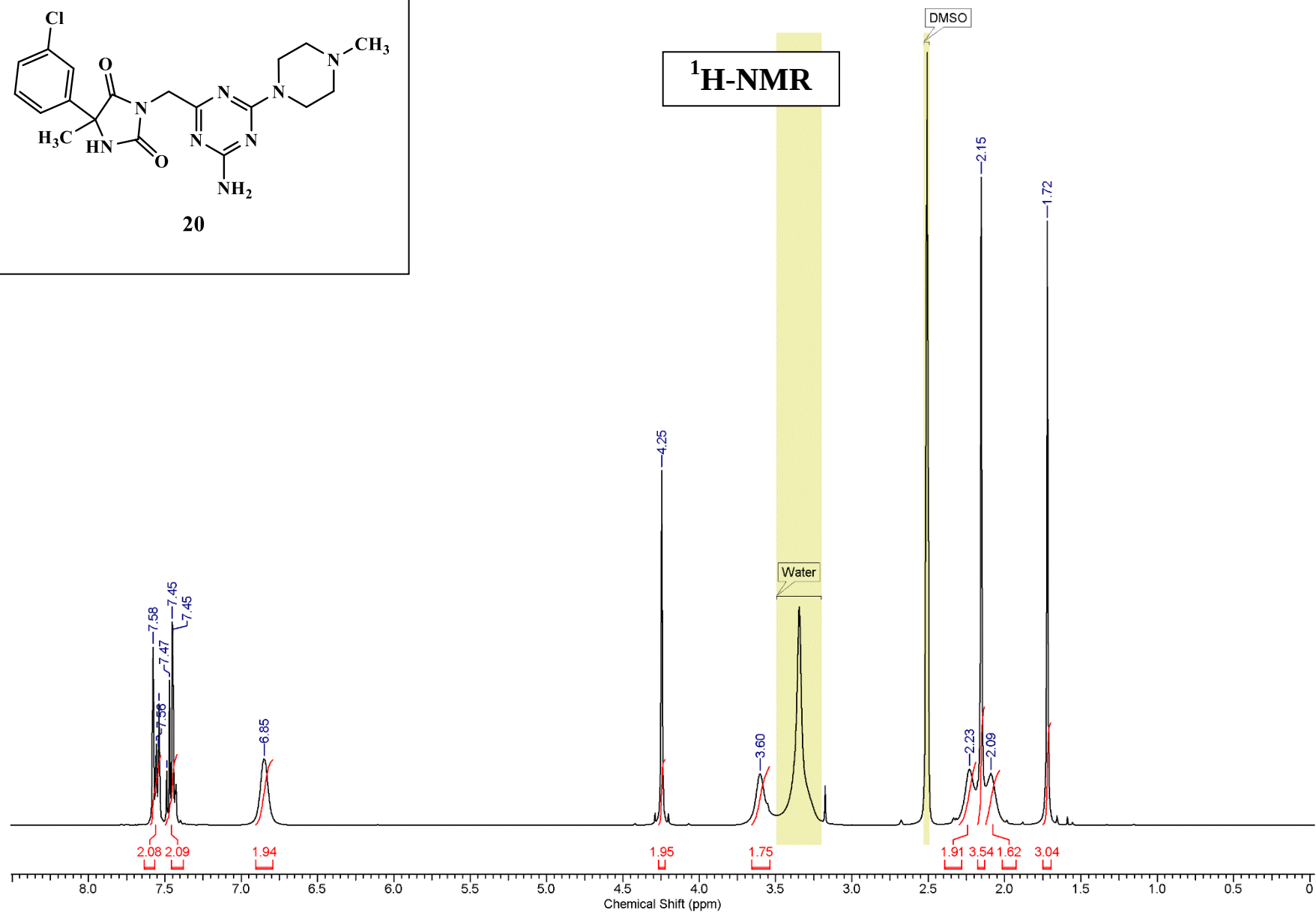
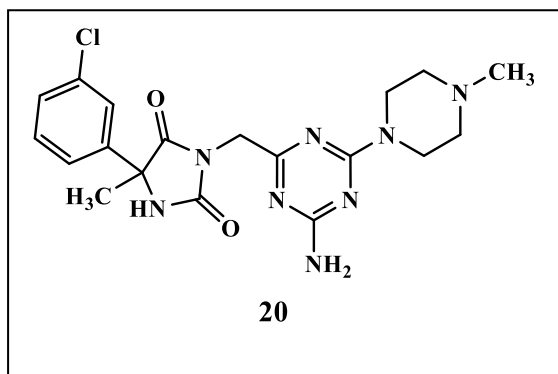


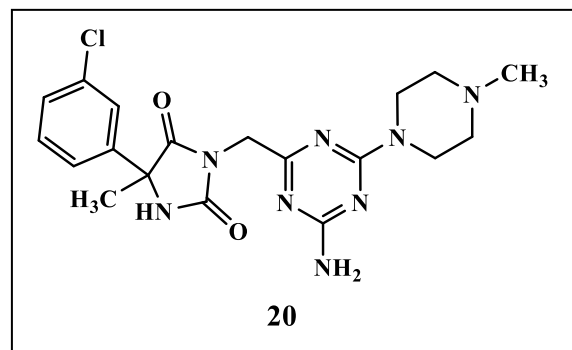




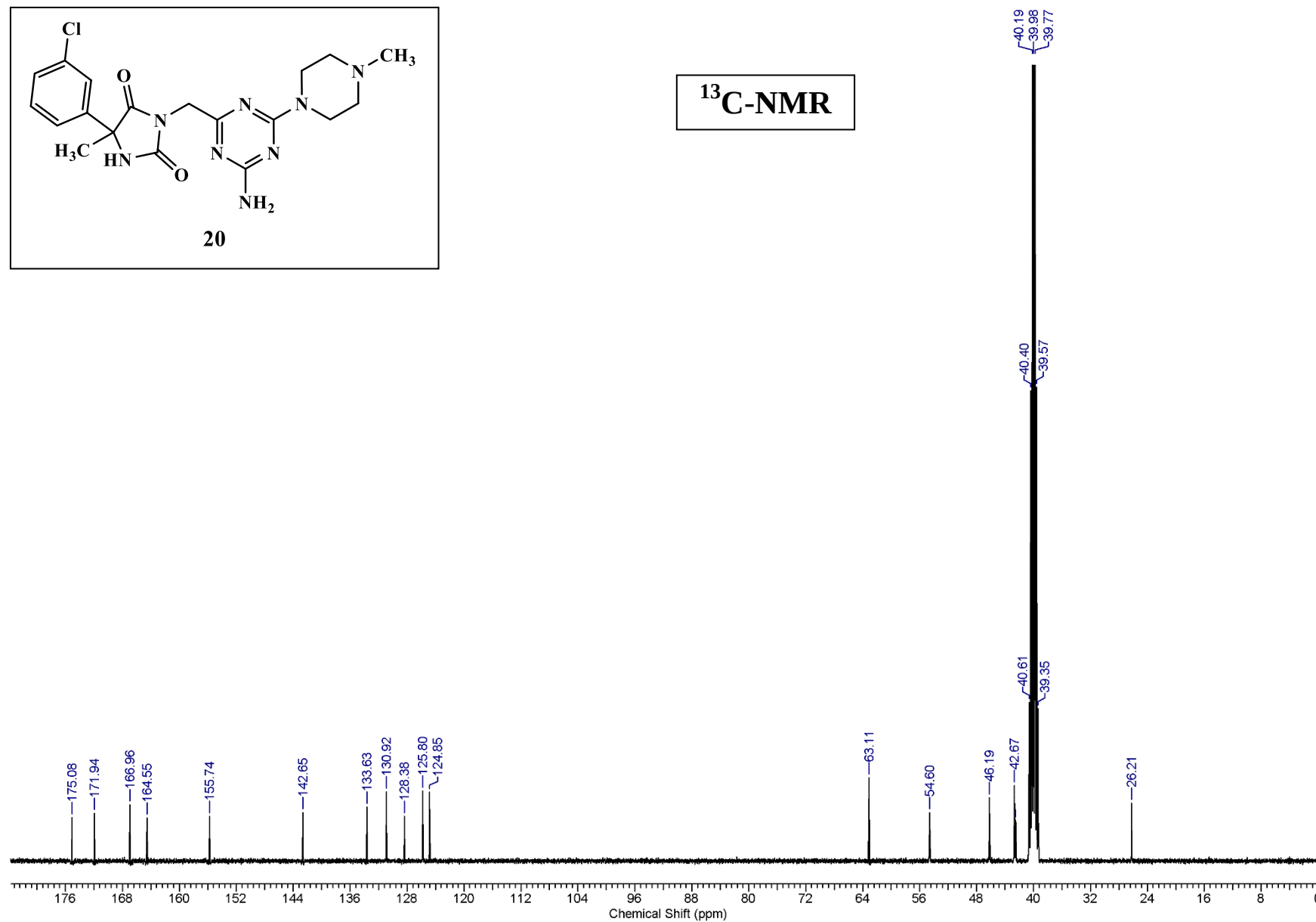
^{13}C -NMR

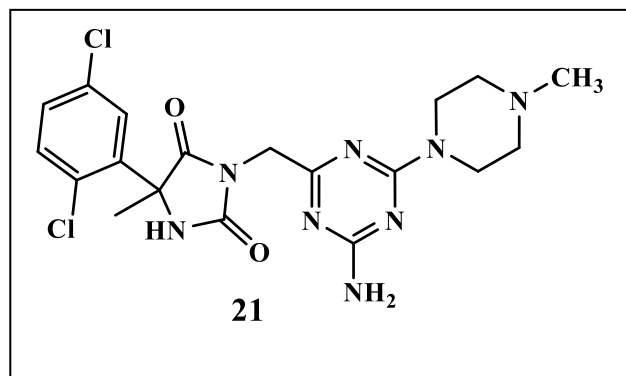




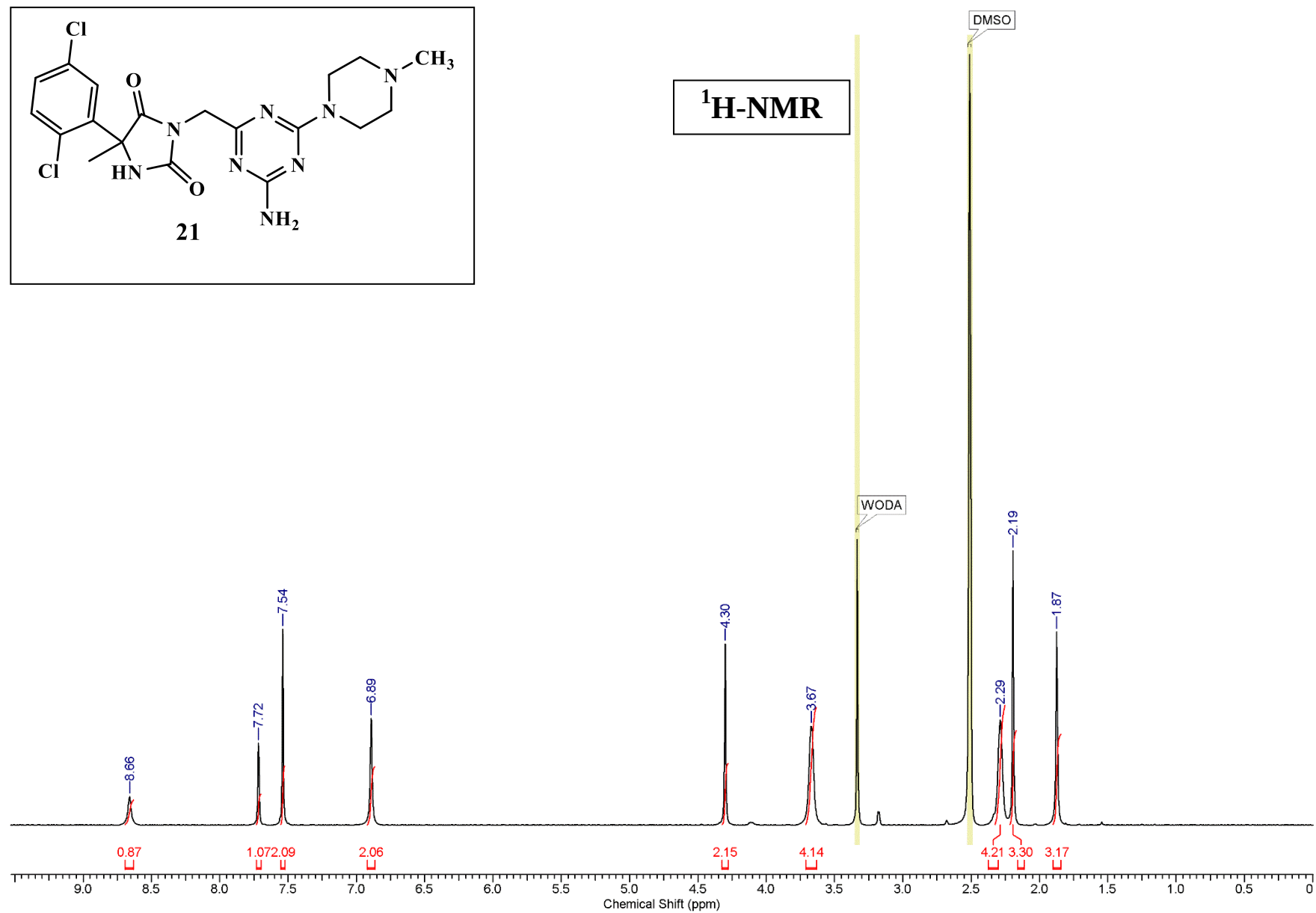


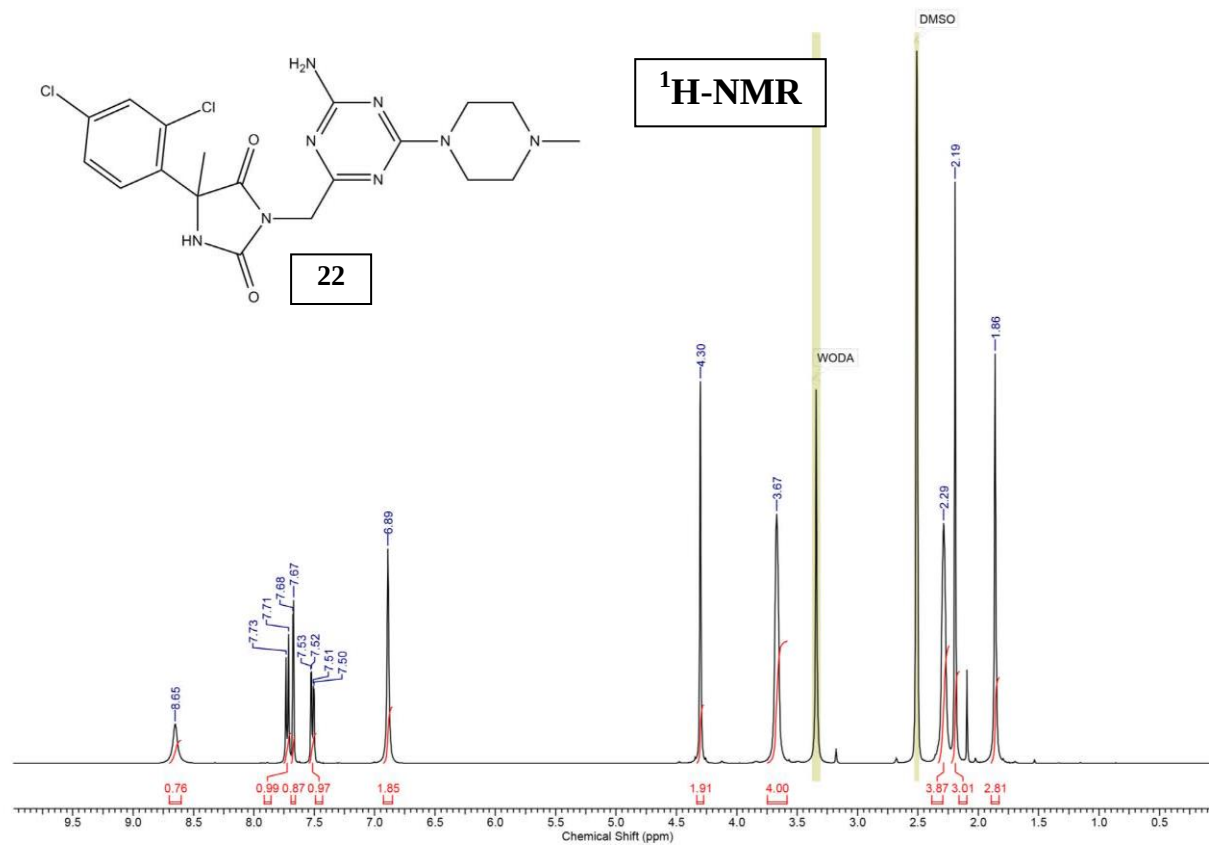
^{13}C -NMR

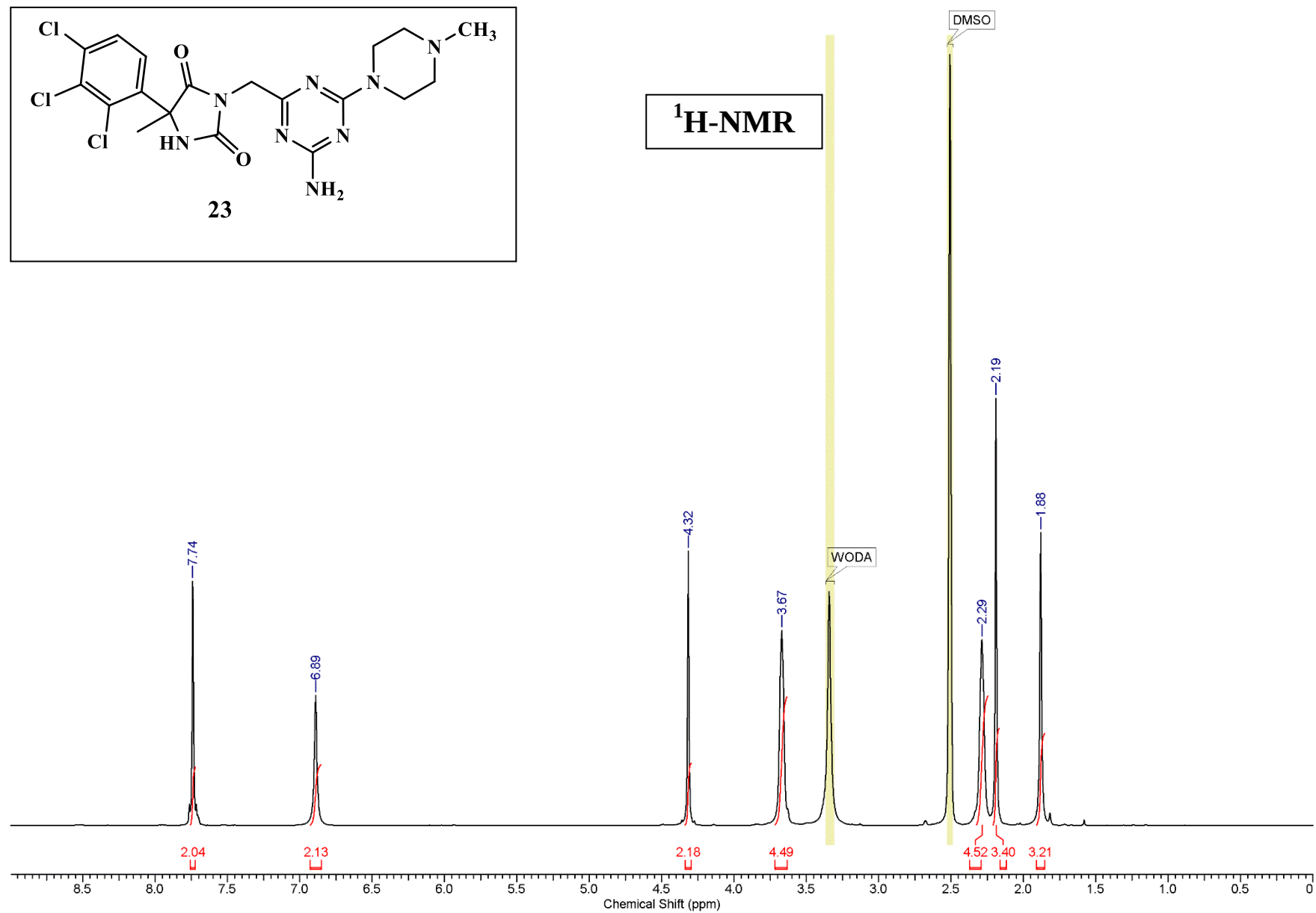
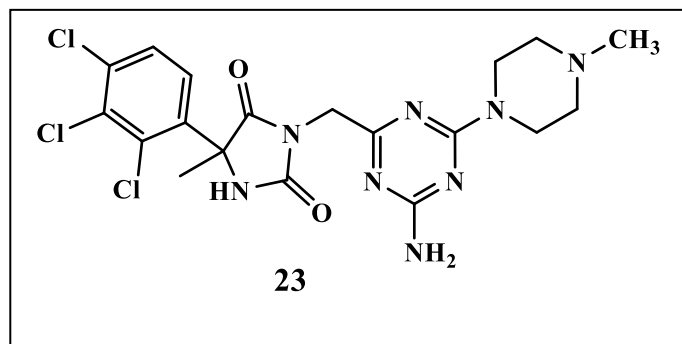


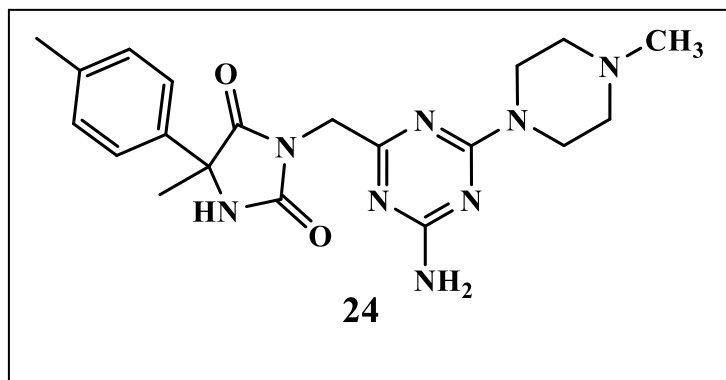


¹H-NMR

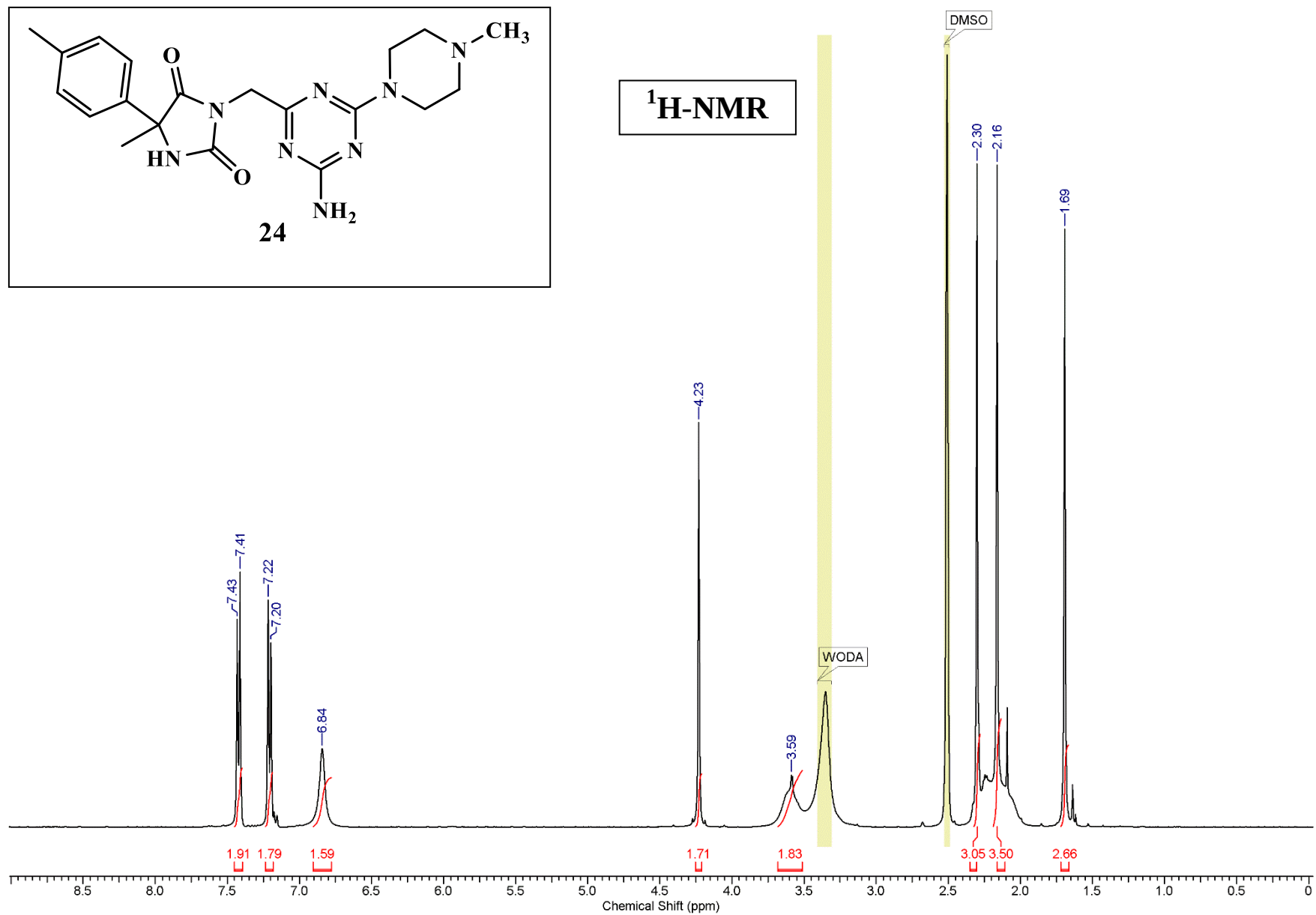


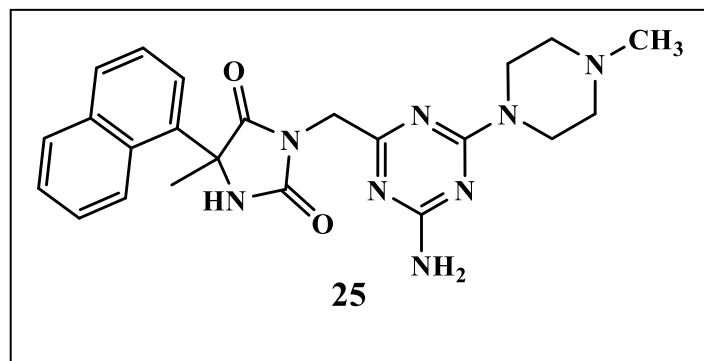




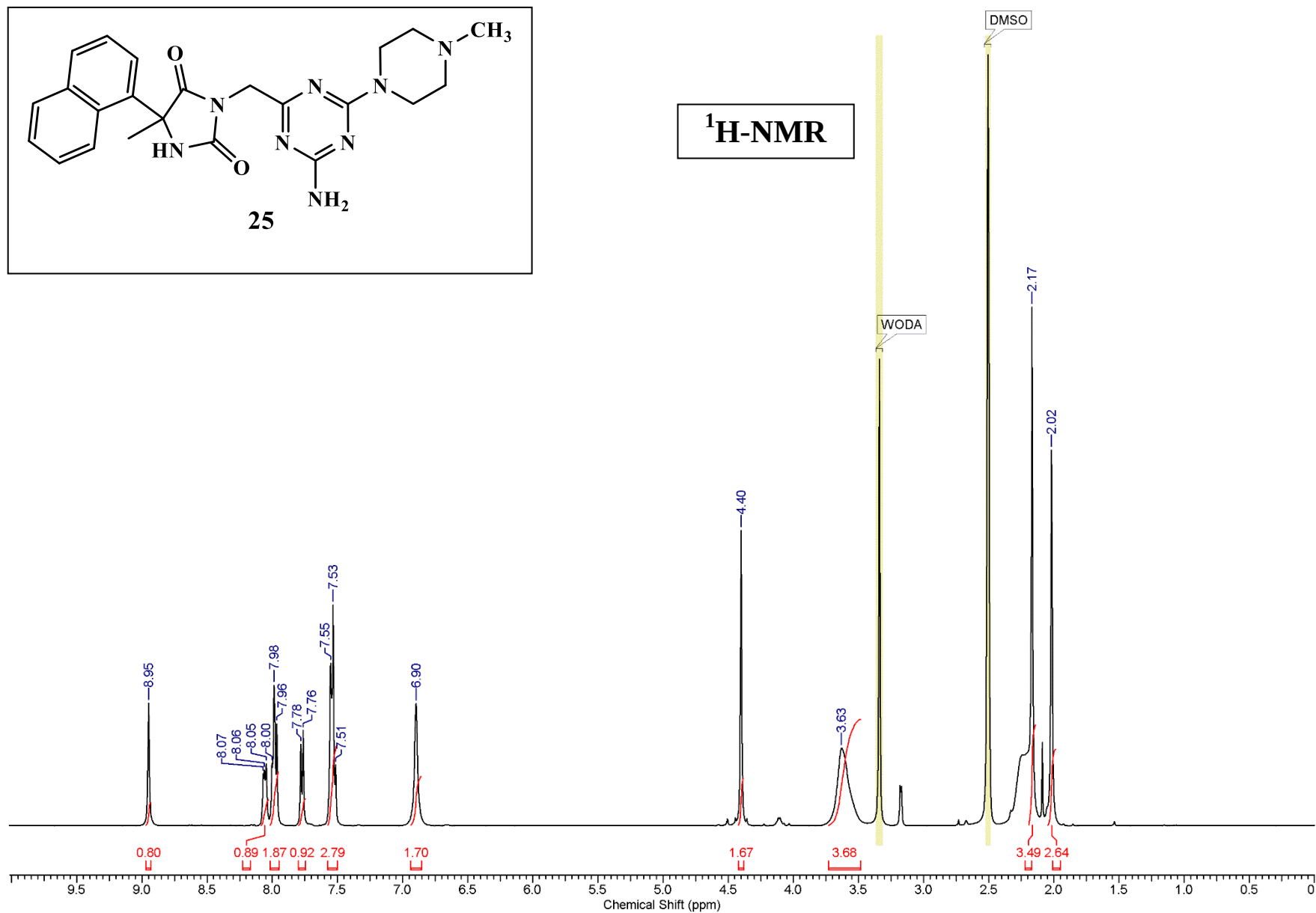


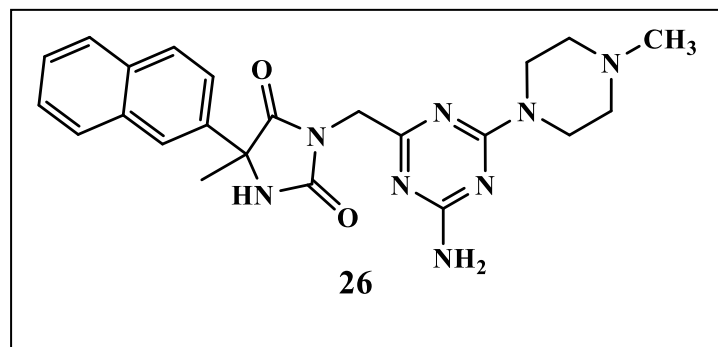
¹H-NMR



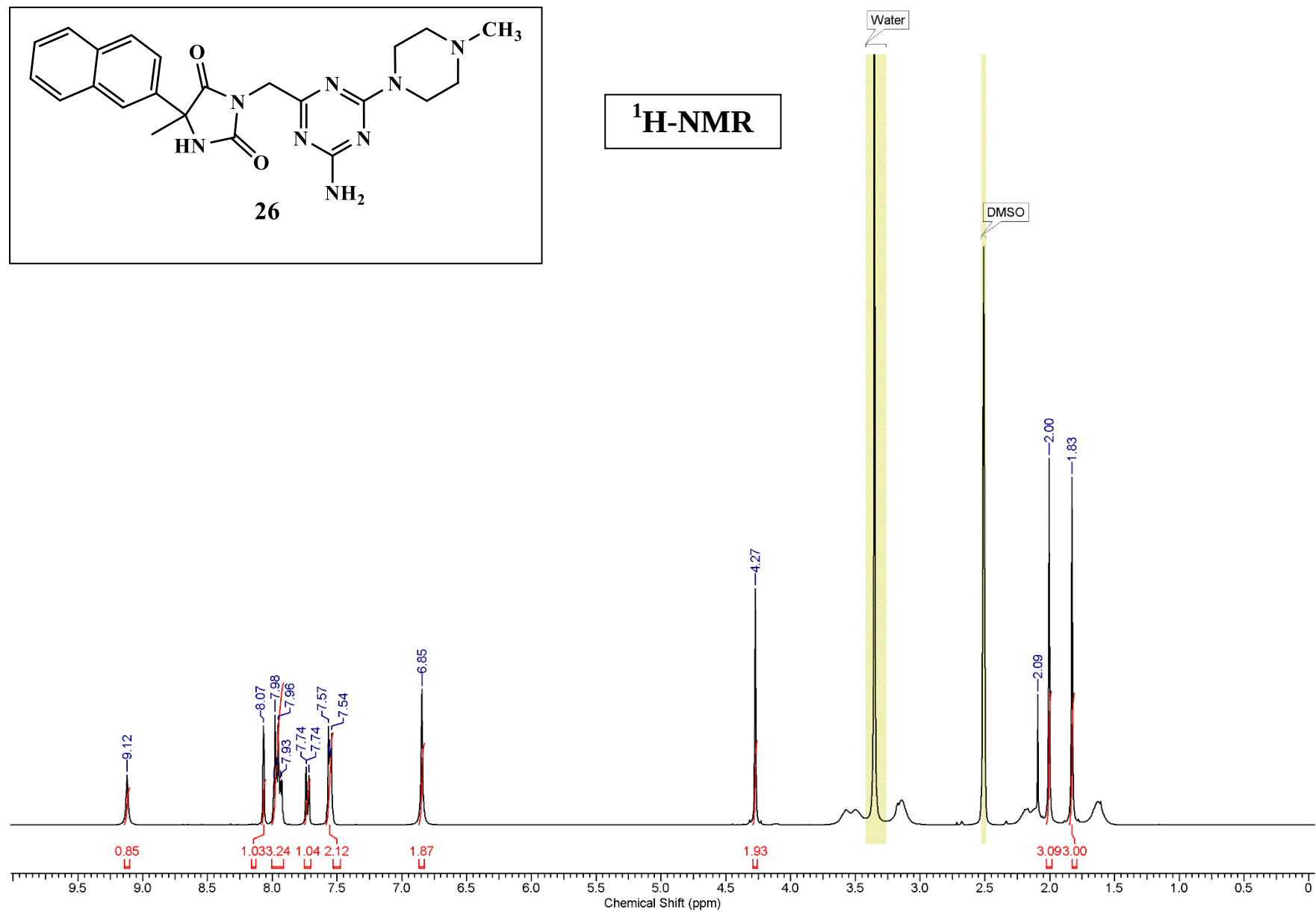


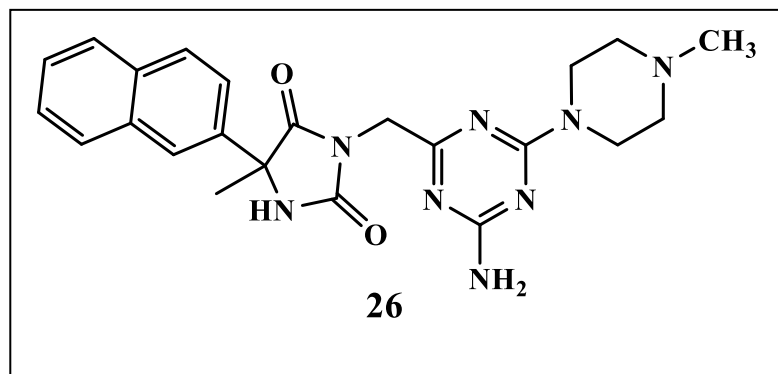
^1H -NMR





^1H -NMR





¹³C-NMR

