Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.

Synthesis and Antitumour Evaluation of Indole-2-Carboxamides against Paediatric Brain Cancer Cells

Shahinda S. R. Alsayed[a], Amreena Suri[b], Anders W. Bailey[b], Samuel Lane[c], Eryn L Werry[c,d], Chiang-Ching Huang[e], Li-Fang Yu[f], Michael Kassiou[c,*], Simone Treiger Sredni[b,g,*], and Hendra Gunosewoyo[a,*]

[a] Curtin Medical School, Faculty of Health Sciences, Curtin University, Bentley, Perth, WA 6102, Australia

[b] Division of Pediatric Neurosurgery, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL 60611, USA

[c] School of Chemistry, The University of Sydney, NSW, 2006, Australia

[d] Faculty of Medicine and Health, The University of Sydney, NSW 2006, Australia

[e] Department of Biostatistics, Zilber School of Public Health, University of Wisconsin, Milwaukee, WI 53205, USA

[f] Shanghai Engineering Research Center of Molecular Therapeutics and New Drug Development, School of Chemistry and Molecular Engineering, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, China

[g] Department of Surgery, Northwestern University, Feinberg School of Medicine, Chicago, IL 60611, USA

* Corresponding author. Michael Kassiou: michael.kassiou@sydney.edu.au

* Corresponding author. Simone Treiger Sredni: simone.sredni@gmail.com

* Corresponding author. Hendra Gunosewoyo: Hendra.Gunosewoyo@curtin.edu.au

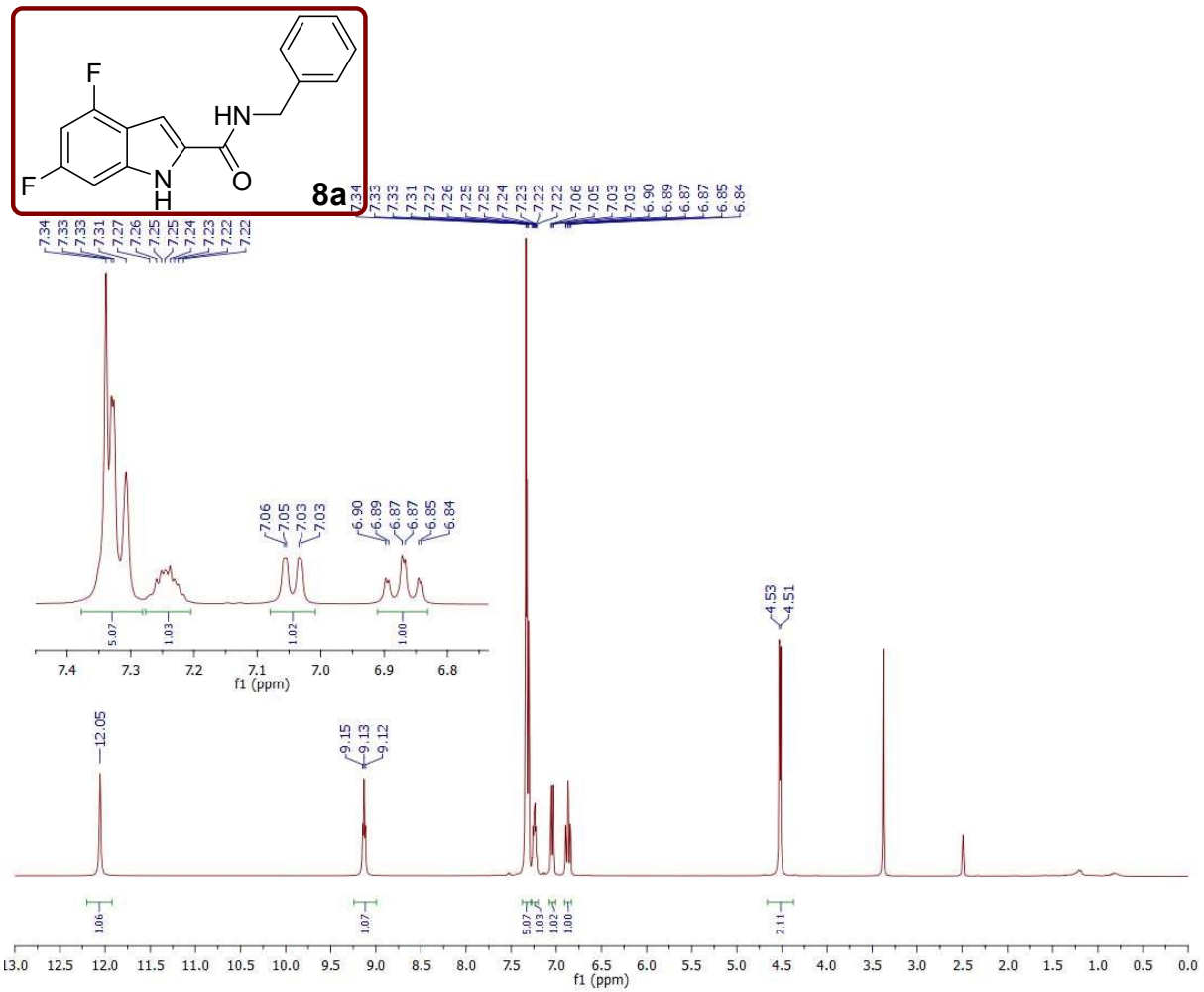
Table S1. Downregulated genes in 8a-treated KNS42 cells

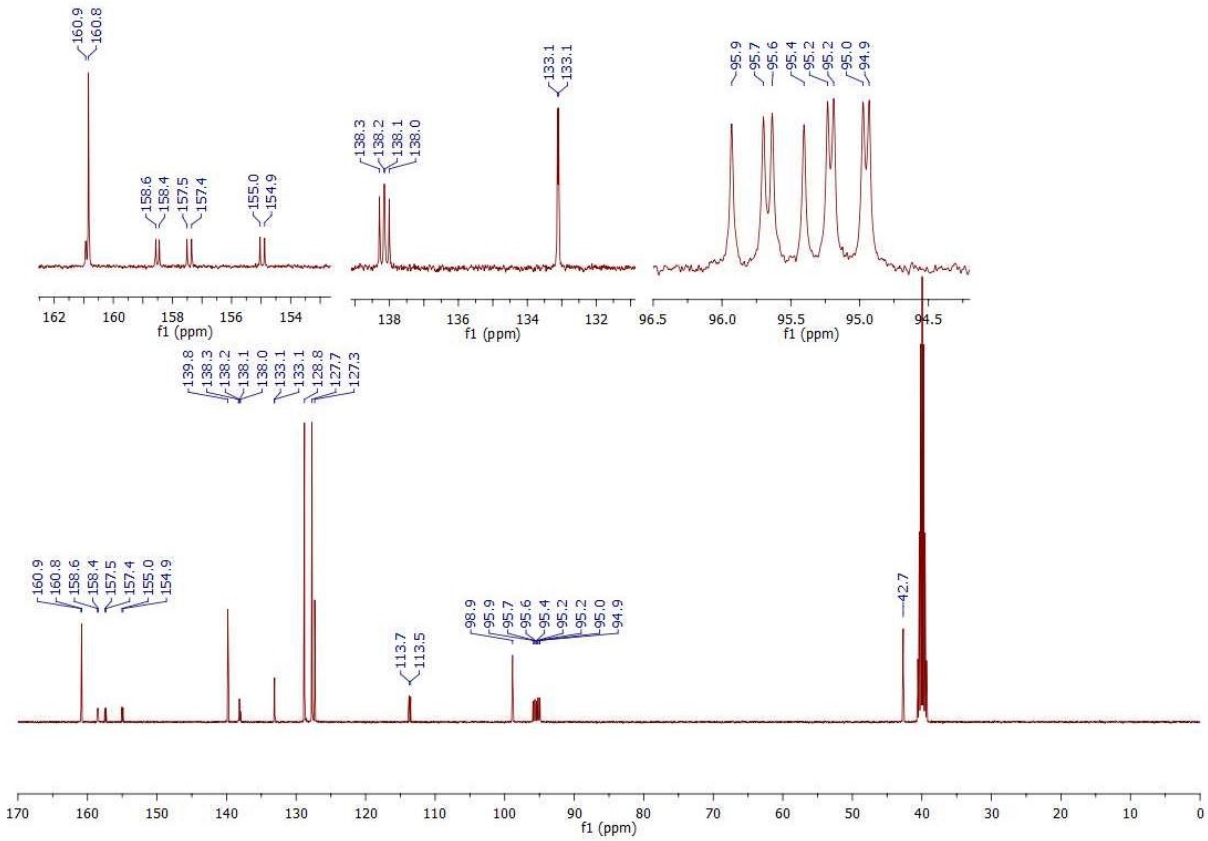
Gene Symbol	Description[a]	Fold Change	*P* value	Function[a]
PLAC1	Placenta specific protein1	30	0.0028	Placental development
CLECL1	C-type lectin-like domain family 1	19	0.0123	Immune response regulation
ETV7	ETS Variant Transcription Factor 7	19	0.0057	Transcriptional repressor
TNS1	Tensin-1	18	0.0100	Fibrillar adhesion and crosslinking actin filaments
KCNJ12	ATP-sensitive inward rectifier potassium channel 12	17	0.0060	Potassium ion transfer
NT5C1B	Cytosolic 5'-nucleotidase 1B	14	0.0124	Adenosine level regulation
TREH	Trehalase	13	0.0154	Trehalose hydrolysis
FAM186A	Family with sequence similarity 186, member A	13	0.0286	ND[b]
LOC105377622	A non-coding RNA (ncRNA) gene	13	0.0221	ND[b]
OPCML	Opioid-binding protein/cell adhesion molecule-like	13	0.0204	Cell contact regulation
DNASE2B	Deoxyribonuclease-2-beta	13	0.0254	DNA degradation
ARHGAP9	Rho GTPase-activating protein 9	12	1.23E-12	Cytoskeletal dynamics regulation[1]
APELA	Apelin receptor early endogenous ligand	11	0.0159	Cardiovascular homeostasis
MISP	Mitotic interactor and substrate of PLK1	10	0.0181	Cell division and migration
JSRP1	Junctional sarcoplasmic reticulum protein 1	10	0.0215	Modulation of Skeletal muscle excitation-contraction coupling
CCDC42	Coiled-coil domain-containing protein 42	10	0.0104	Sperm development
KNCN	Kinocilin	10	0.0374	Vacuolar trafficking
FLG	Filaggrin	9	3.05E-88	Keratinisation
ADM2	Adrenomedullin 2	8	1.08E-47	Gastrointestinal and cardiovascular homeostasis
CHAC1	Glutathione-specific gamma-glutamylcyclotransferase 1	8	2.69E-76	neuronal differentiation and Glutathione level Modulation
IRX3	Iroquois Homeobox 3	7	0.0329	Neural development
GPR45	G Protein-Coupled Receptor 45	7	0.0306	Mediation of Signalling processes
NDUFA4L2	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 4-like 2	7	0.0002	Cell survival regulation[2]
TESC	Tescalcin or Calcineurin B homologous protein 3	6	0.0009	Cell pH regulation
MAPK4	Mitogen-Activated Protein Kinase 4	6	0.0001	Phosphorylation of microtubule-associated protein 2 (MAP2)[3]
SH2D3C	SH2 domain-containing protein 3C	6	0.0237	Mediation of cell signalling pathways implicated in cell adhesion, migration, and invasion
CABP1	Calcium-binding protein 1	5	0.0254	Signal transduction
SLC7A5 (LAT1)	Large neutral amino acids transporter small subunit 1	5	5.30E-217	Amino acid exchanger
ANGPTL4	Angiopoietin-related protein 4	5	0.0106	Regulation of insulin sensitivity, glucose homeostasis, and lipid metabolism
MIOX	Myo-Inositol Oxygenase	5	4.55E-08	ND[b]
PLIN5	Perilipin-5	5	0.0017	Maintaining the balance between lipolysis and lipogenesis.
ACTN3	Actinin Alpha 3	5	0.0221	Crosslinking actin with various intracellular structures (a bundling protein)
CCKAR	Cholecystokinin receptor type A	5	0.0346	Mediator of smooth muscle contraction of stomach and gallbladder, as well as pancreatic enzyme secretion and growth. Regulation of satiety and release of dopamine and □-endorphin

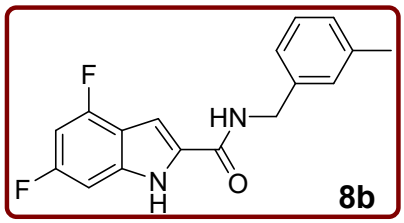
[a] All descriptions and functions were retrieved from uniprot (https://www.uniprot.org/) and/or genecards (https://www.genecards.org/) websites. In addition, other relevant references are interspersed therein. [b] ND: not determined.

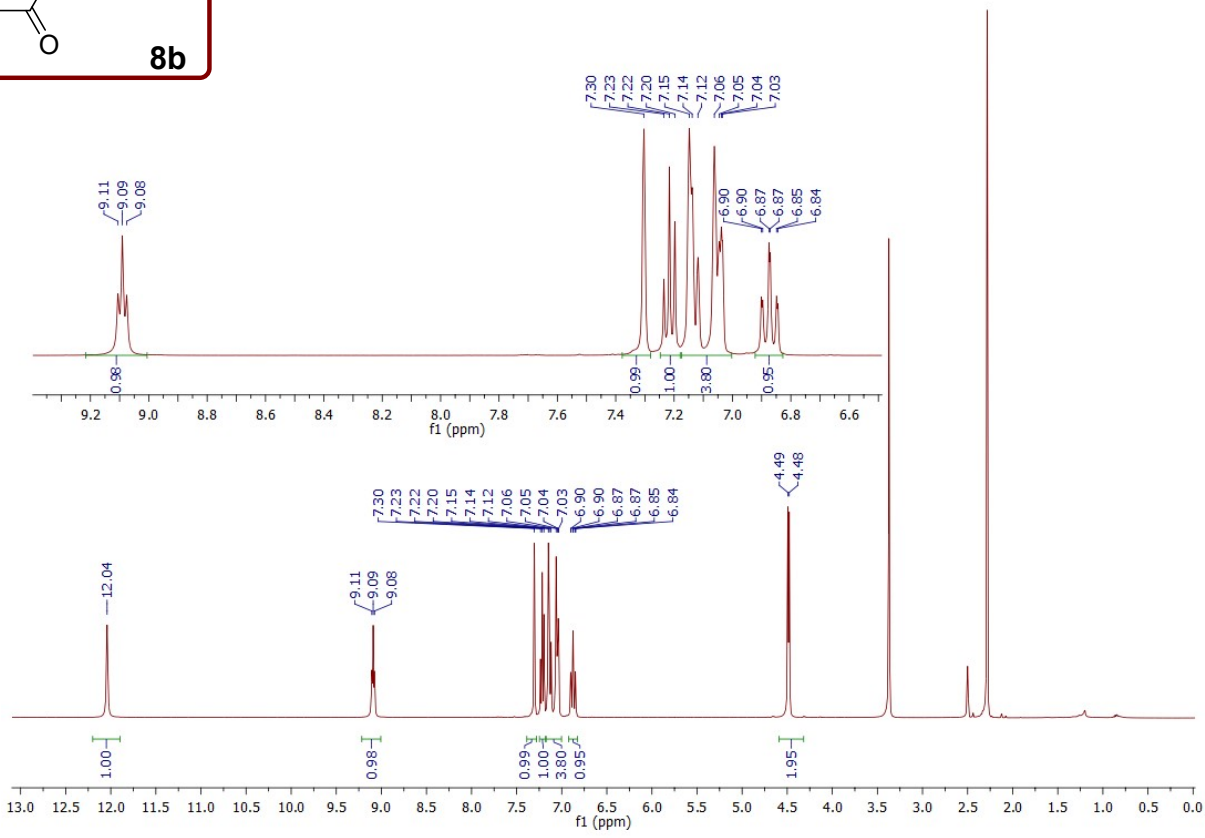
References:

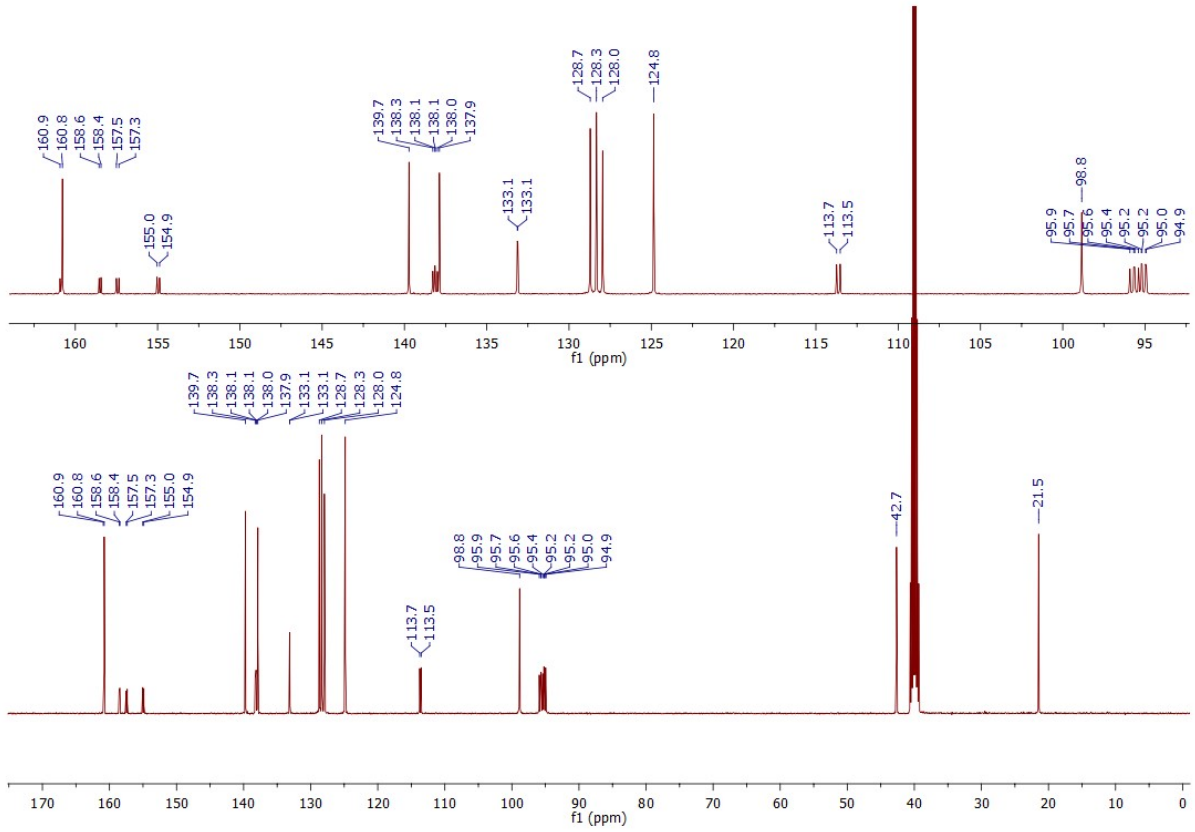
1. C. Han, S. He, R. Wang, X. Gao, H. Wang, J. Qiao, X. Meng, Y. Li and L. Yu, *J. Transl. Med.*, 2021, **19**, 65.
2. L. Meng, X. Yang, X. Xie and M. Wang, *Thorac. Cancer*, 2019, **10**, 676-685.
3. C. Sanchez, J. Diaz-Nido and J. Avila, *Prog. Neurobiol.*, 2000, **61**, 133-168.

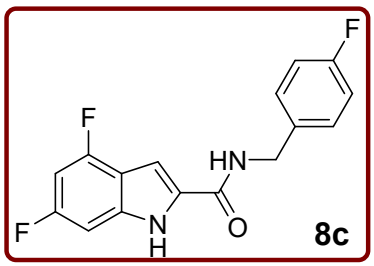


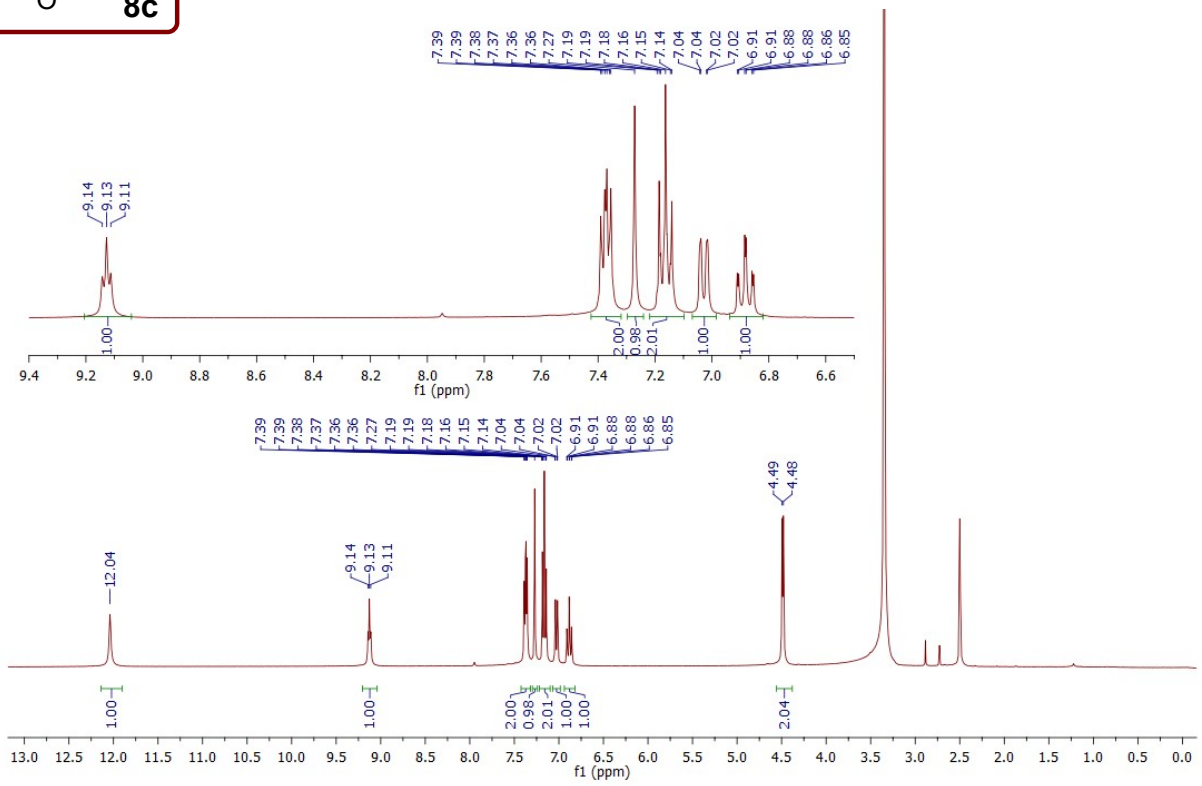

160.9
160.8
158.6
158.4
157.5
157.4
155.0
154.9
138.3
138.2
138.1
138.0
133.1
133.1
95.9
95.7
95.6
95.4
95.2
95.2
95.0
94.9
f1 (ppm)
139.8
138.3
138.2
138.1
138.0
133.1
133.1
128.8
127.7
127.3
113.7
113.5
98.9
95.9
95.7
95.6
95.4
95.2
95.2
95.0
94.9
42.7

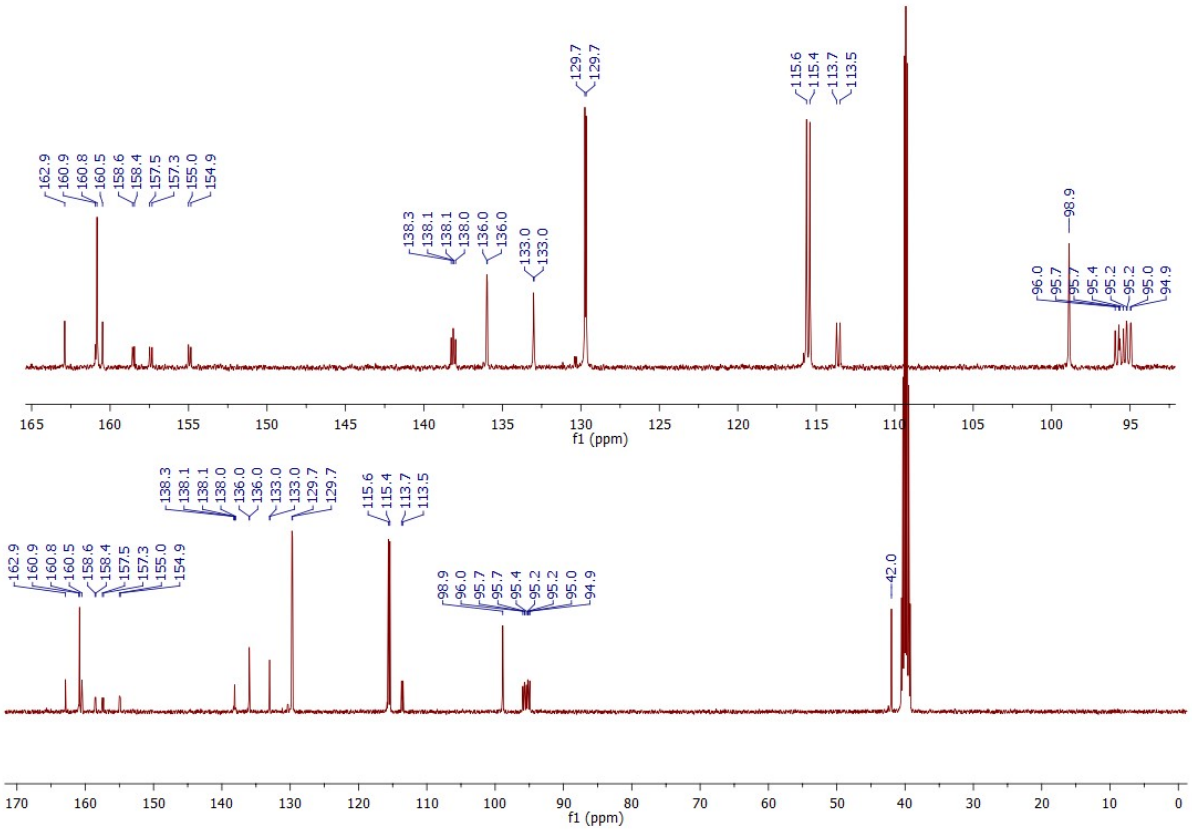

F
HN
F
N
H
O
8b

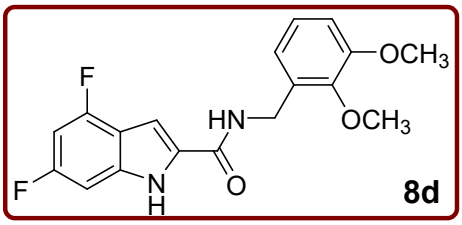

7.30
7.23
7.22
7.20
7.15
7.14
7.12
7.06
7.05
7.04
7.03
9.11
9.09
9.08
6.90
6.90
6.87
6.87
6.85
6.84
0.98
0.99
1.00
3.80
0.95
f1 (ppm)
4.49
4.48
12.04
1.00
0.98
0.99
1.00
3.80
0.95
1.95

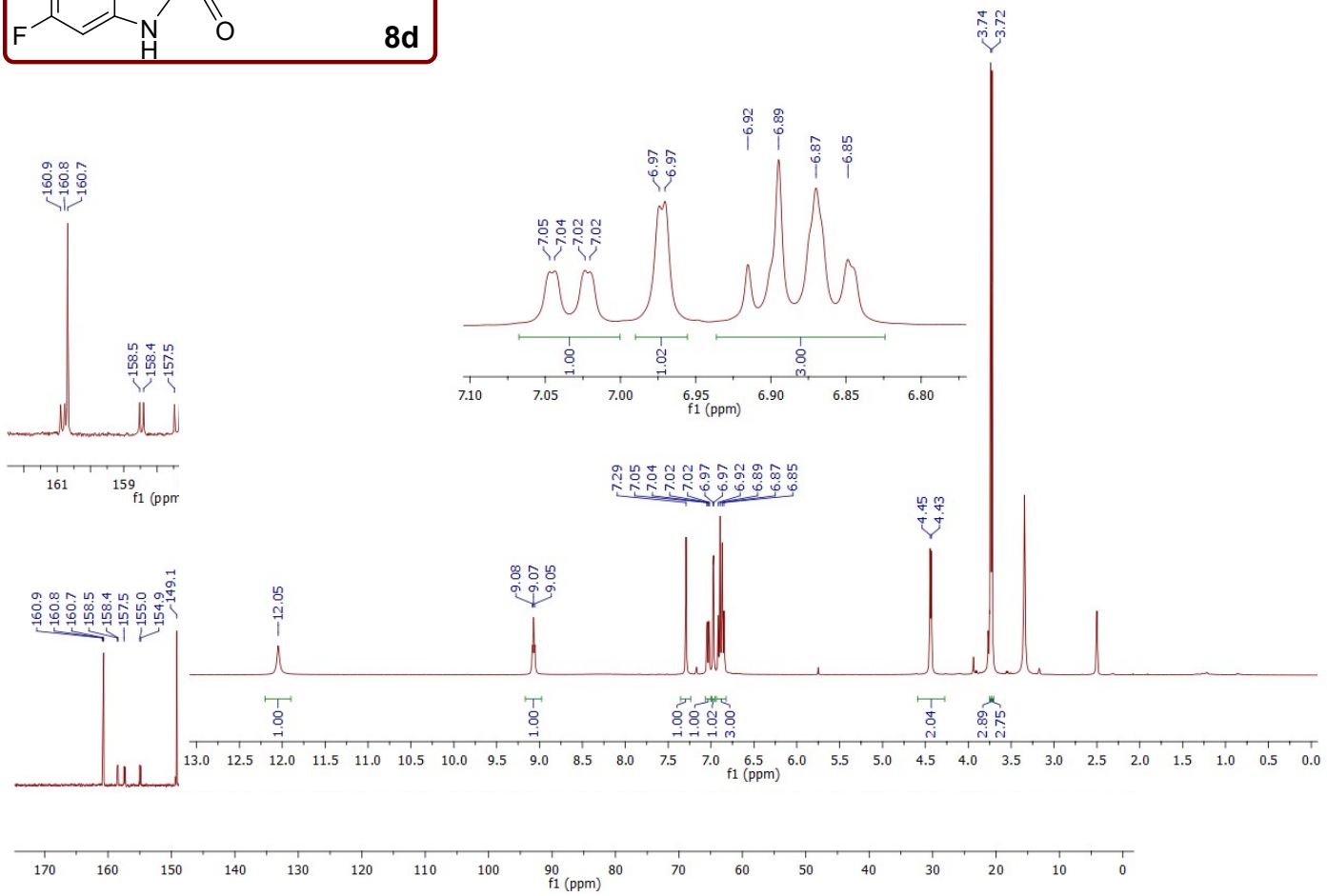

160.9
160.8
158.6
158.4
157.5
157.3
155.0
154.9
139.7
138.3
138.1
138.1
138.0
137.9
133.1
133.1
128.7
128.3
128.0
124.8
113.7
113.5
98.8
95.9
95.7
95.6
95.4
95.2
95.2
95.0
94.9
f1 (ppm)
42.7
21.5

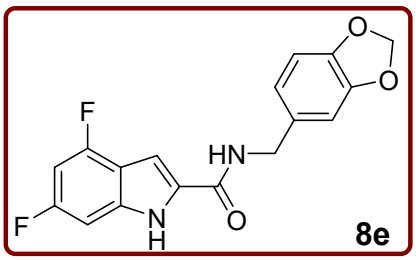

F
F
HN
F
N
H
O
8c

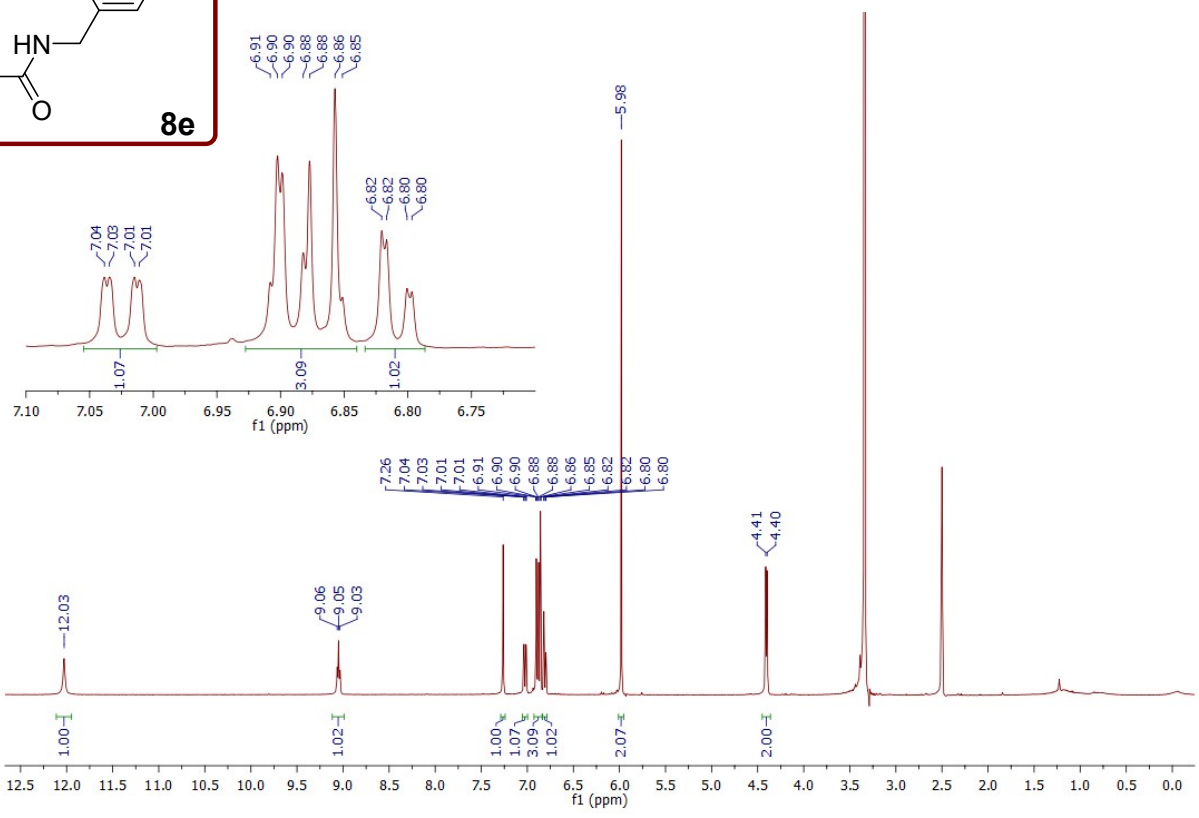

7.39
7.39
7.38
7.37
7.36
7.36
7.27
7.19
7.19
7.18
7.16
7.15
7.14
7.04
7.04
7.02
7.02
6.91
6.88
6.88
6.86
6.85
9.14
9.13
9.11
1.00
2.00
0.98
2.01
1.00
1.00
f1 (ppm)
12.04
4.49
4.48
2.04

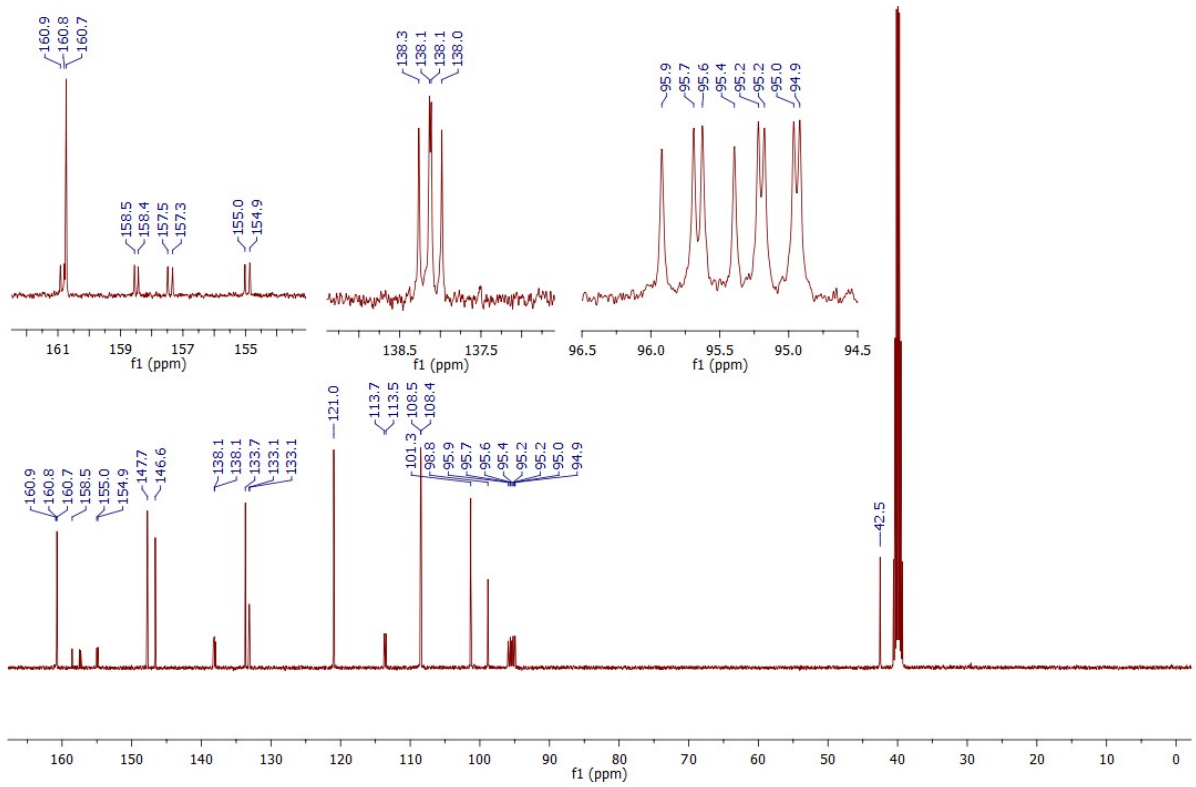

162.9
160.9
160.8
160.5
158.6
158.4
157.5
157.3
155.0
154.9
138.3
138.1
138.1
138.0
136.0
136.0
133.0
133.0
129.7
129.7
115.6
115.4
113.7
113.5
98.9
96.0
95.7
95.7
95.4
95.2
95.2
95.0
94.9
f1 (ppm)
42.0

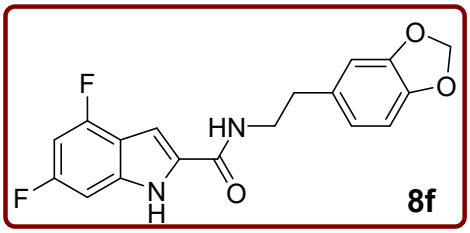

F
OCH3
HN
OCH3
F
N
H
O
8d

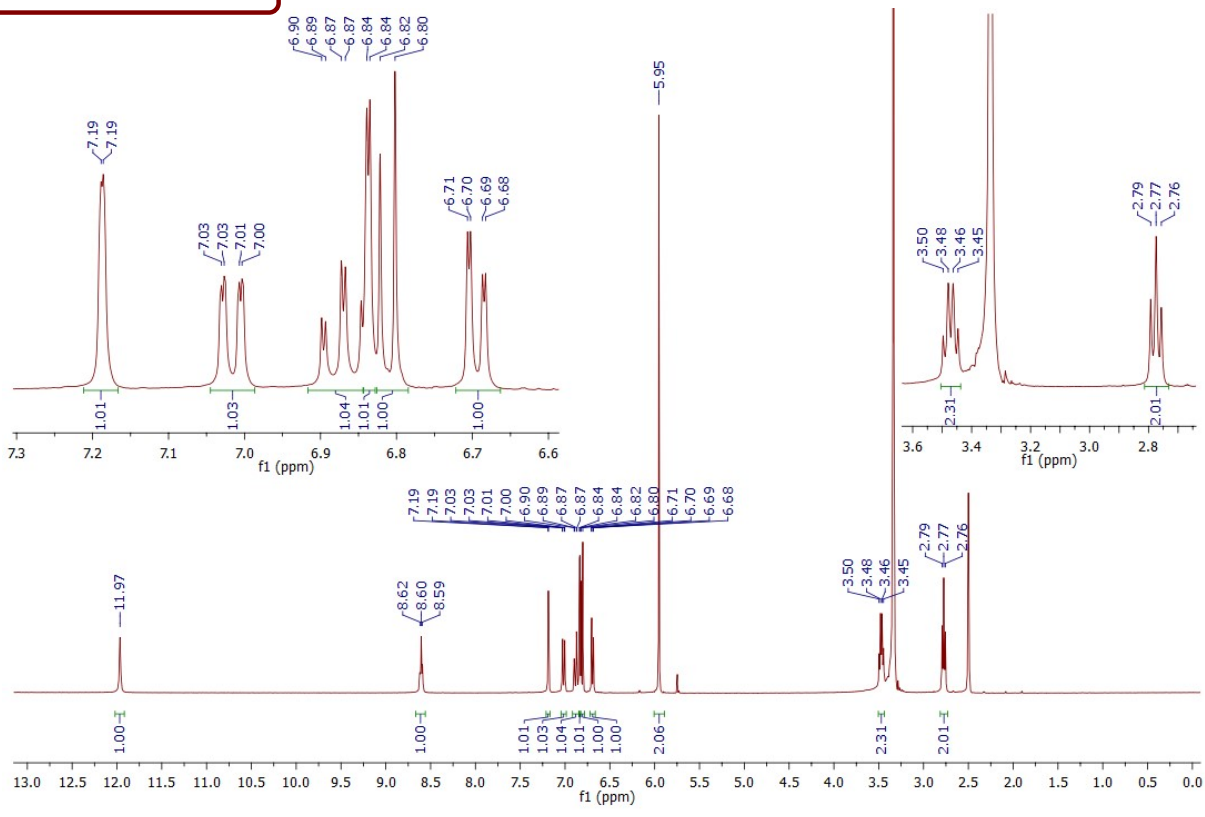

3.74
3.72
6.92
6.89
6.87
6.85
6.97
6.97
7.05
7.04
7.02
7.02
160.9
160.8
160.7
158.5
158.4
157.5
7.29
7.05
7.04
7.02
7.02
6.97
6.92
6.89
6.87
6.85
4.45
4.43
9.08
9.07
9.05
12.05
160.9
160.8
160.7
158.5
158.4
157.5
155.0
154.9
149.1
1.00
1.00
1.00
1.02
3.00
2.04
2.89
2.75
f1 (ppm)

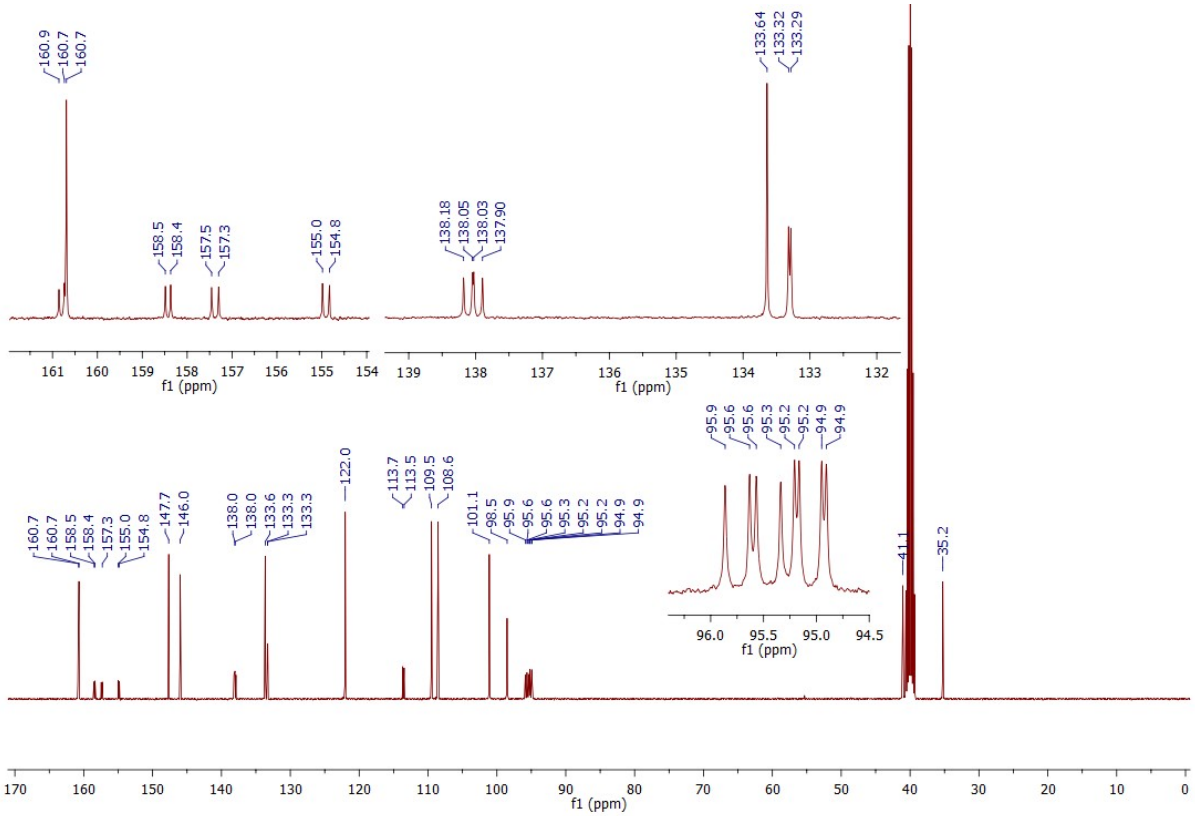

O
O
F
HN
N
H
O
F
8e

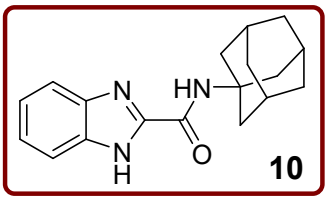

6.91
6.90
6.90
6.88
6.88
6.86
6.85
5.98
6.82
6.82
6.80
6.80
7.04
7.03
7.01
7.01
1.07
3.09
1.02
f1 (ppm)
7.26
7.04
7.03
7.01
7.01
6.91
6.90
6.90
6.88
6.88
6.86
6.85
6.82
6.80
6.80
4.41
4.40
9.06
9.05
9.03
12.03
1.00
1.02
1.00
1.07
3.09
1.02
2.07
2.00
f1 (ppm)

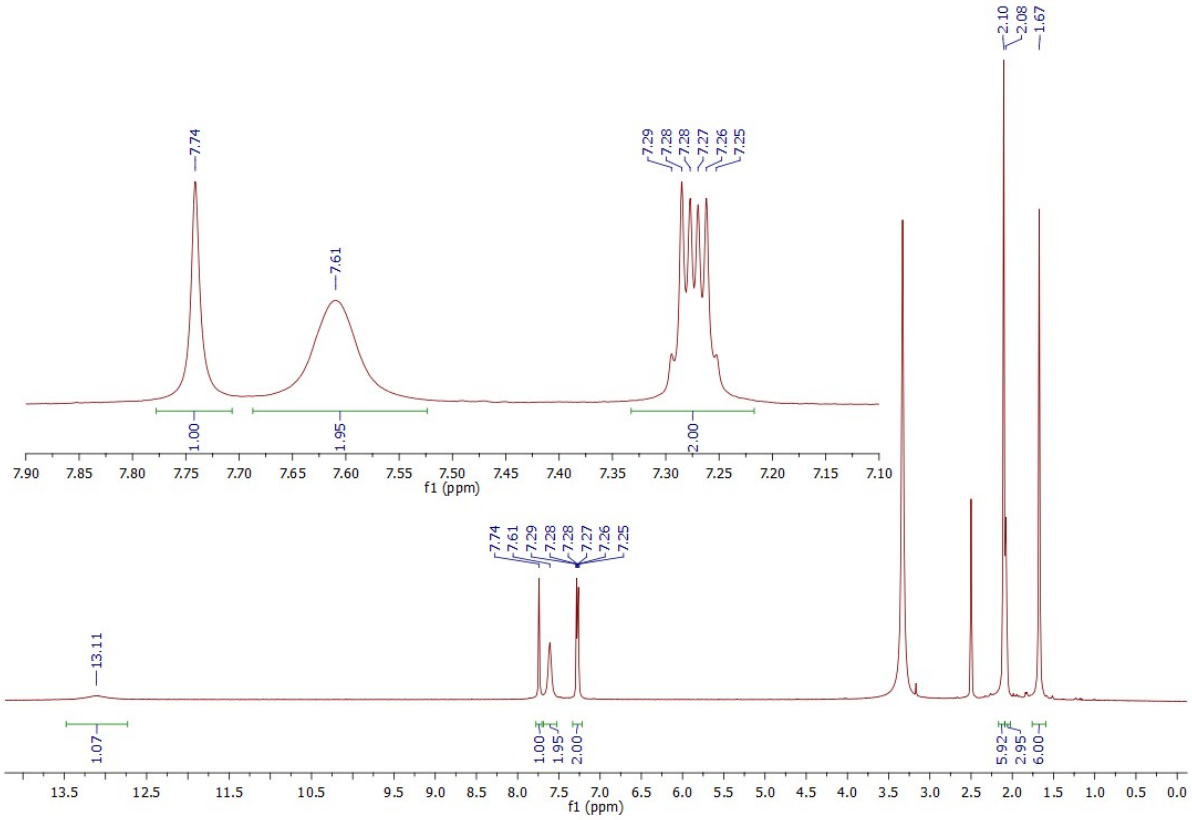

160.9
160.8
160.7
158.5
158.4
157.5
157.3
155.0
154.9
138.3
138.1
138.1
138.0
95.9
95.7
95.6
95.4
95.2
95.2
95.0
94.9
f1 (ppm)
121.0
113.7
113.5
108.5
108.4
101.3
98.8
95.9
95.7
95.6
95.4
95.2
95.2
95.0
94.9
147.7
146.6
138.1
138.1
133.7
133.1
133.1
42.5

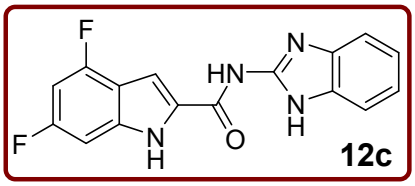

F
F
HN
O
O
O
N
H
8f

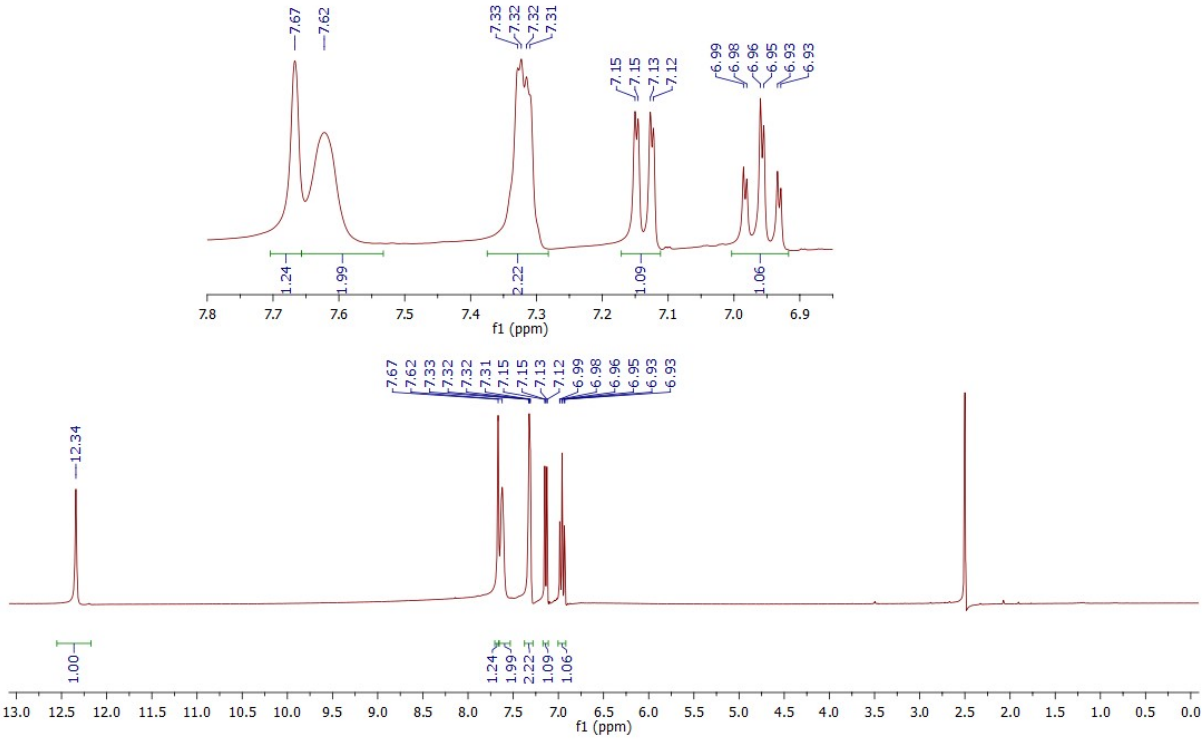

6.90
6.89
6.87
6.87
6.84
6.84
6.82
6.80
5.95
7.19
7.19
6.71
6.70
6.69
6.68
7.03
7.03
7.01
7.00
3.50
3.48
3.46
3.45
2.79
2.77
2.76
11.97
8.62
8.60
8.59
f1 (ppm)

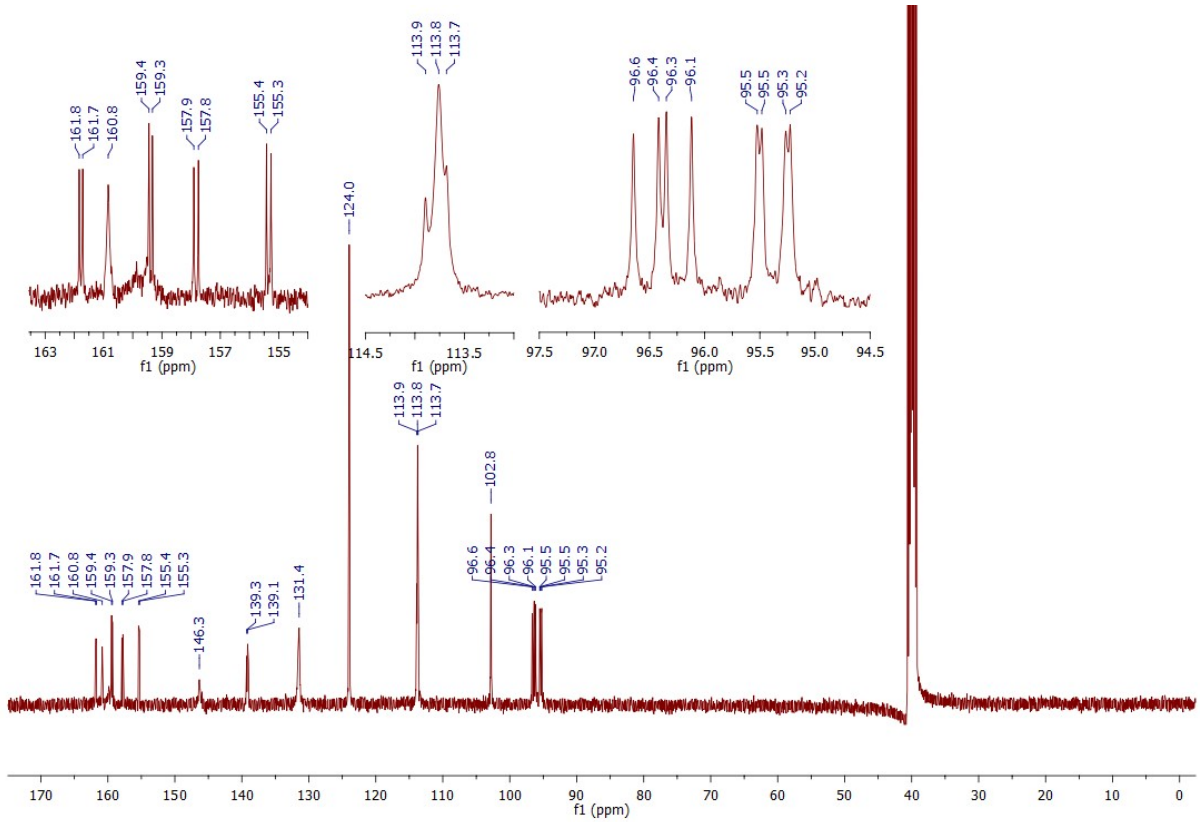

160.9
160.7
160.7
158.5
158.4
157.5
157.3
155.0
154.8
133.64
133.32
133.29
138.18
138.05
138.03
137.90
f1 (ppm)
160.7
160.7
158.5
158.4
157.3
155.0
154.8
147.7
146.0
138.0
138.0
133.6
133.3
133.3
122.0
113.7
113.5
109.5
108.6
101.1
98.5
95.9
95.6
95.6
95.3
95.2
95.2
94.9
94.9
95.9
95.6
95.6
95.3
95.2
95.2
94.9
94.9
41.1
35.2
f1 (ppm)
f1 (ppm)

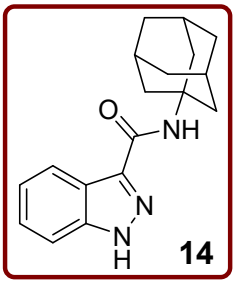

N
HN
N
H
O
10

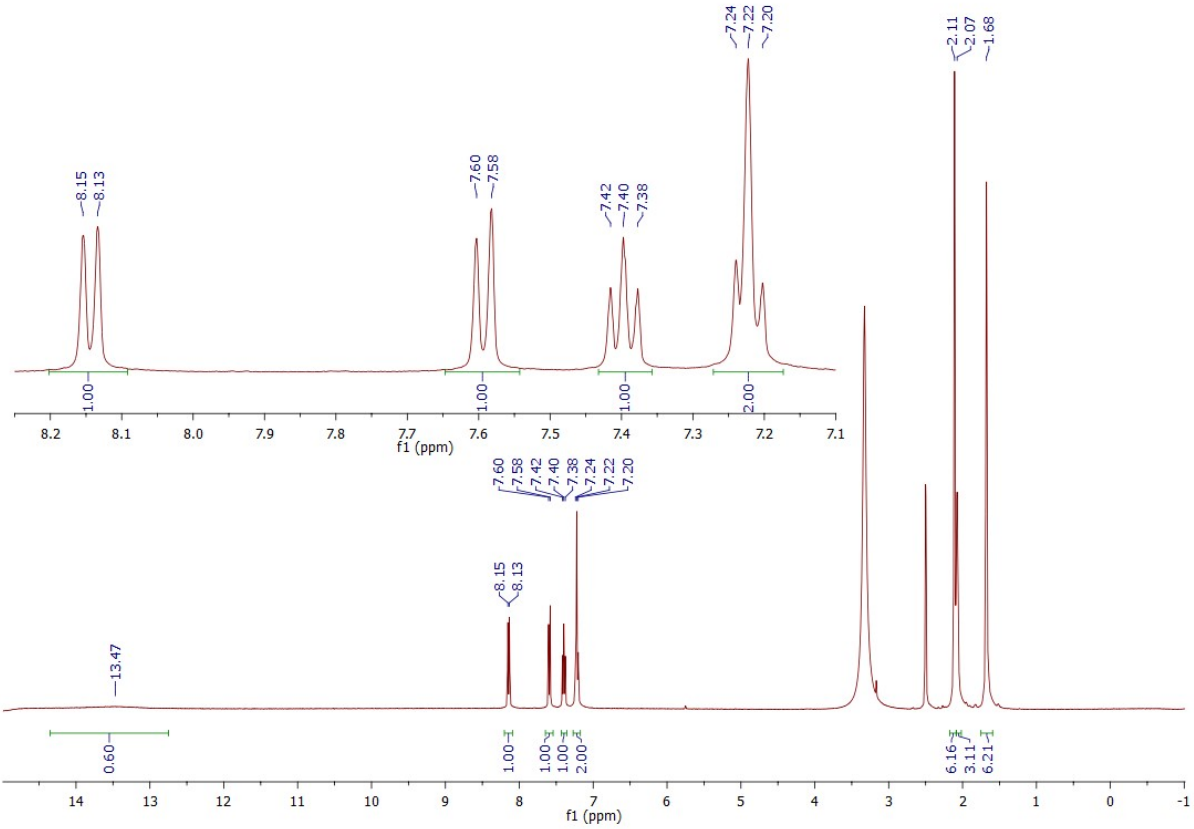

7.74
7.61
7.29
7.28
7.28
7.27
7.26
7.25
2.10
2.08
1.67
13.11
1.00
1.95
2.00
1.07
5.92
2.95
6.00
f1 (ppm)

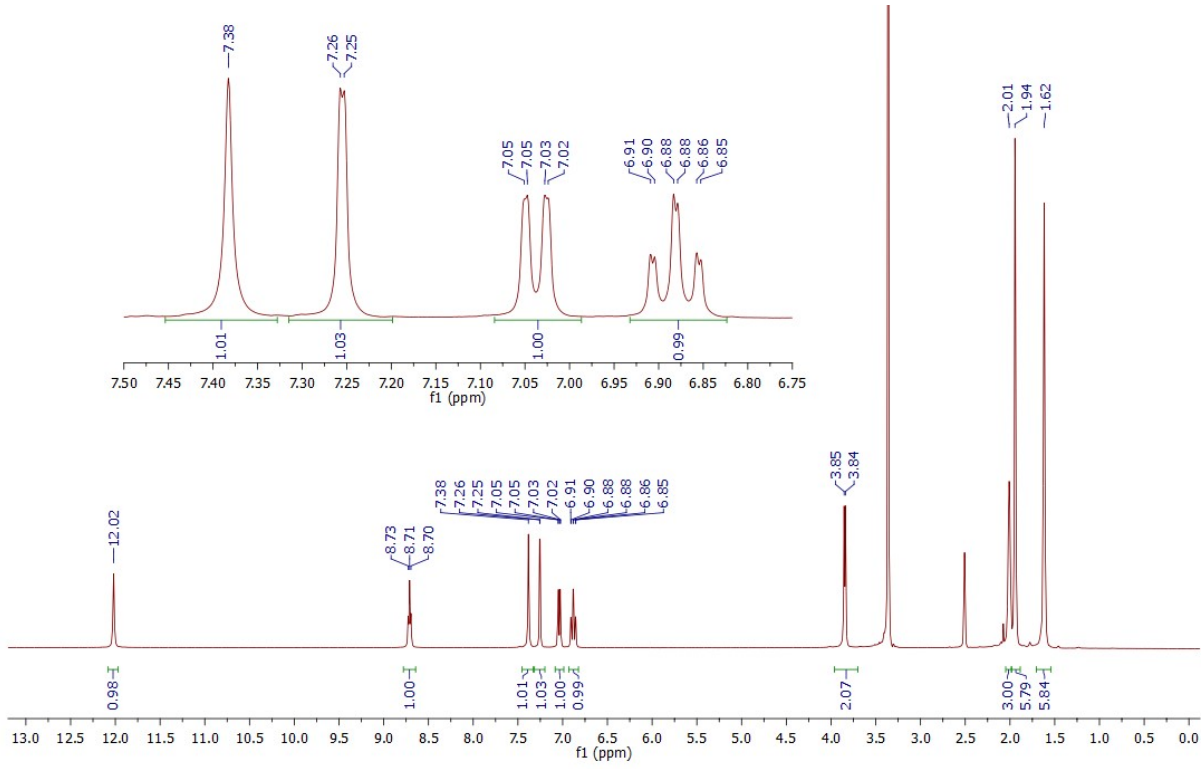

F
F
HN
N
H
N
H
O
12c

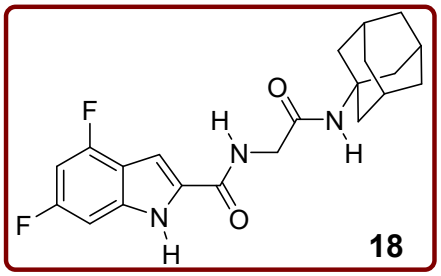

7.67
7.62
7.33
7.32
7.32
7.31
7.15
7.15
7.13
7.12
6.99
6.98
6.96
6.95
6.93
6.93
1.24
1.99
2.22
1.09
1.06
f1 (ppm)
12.34
1.00
f1 (ppm)

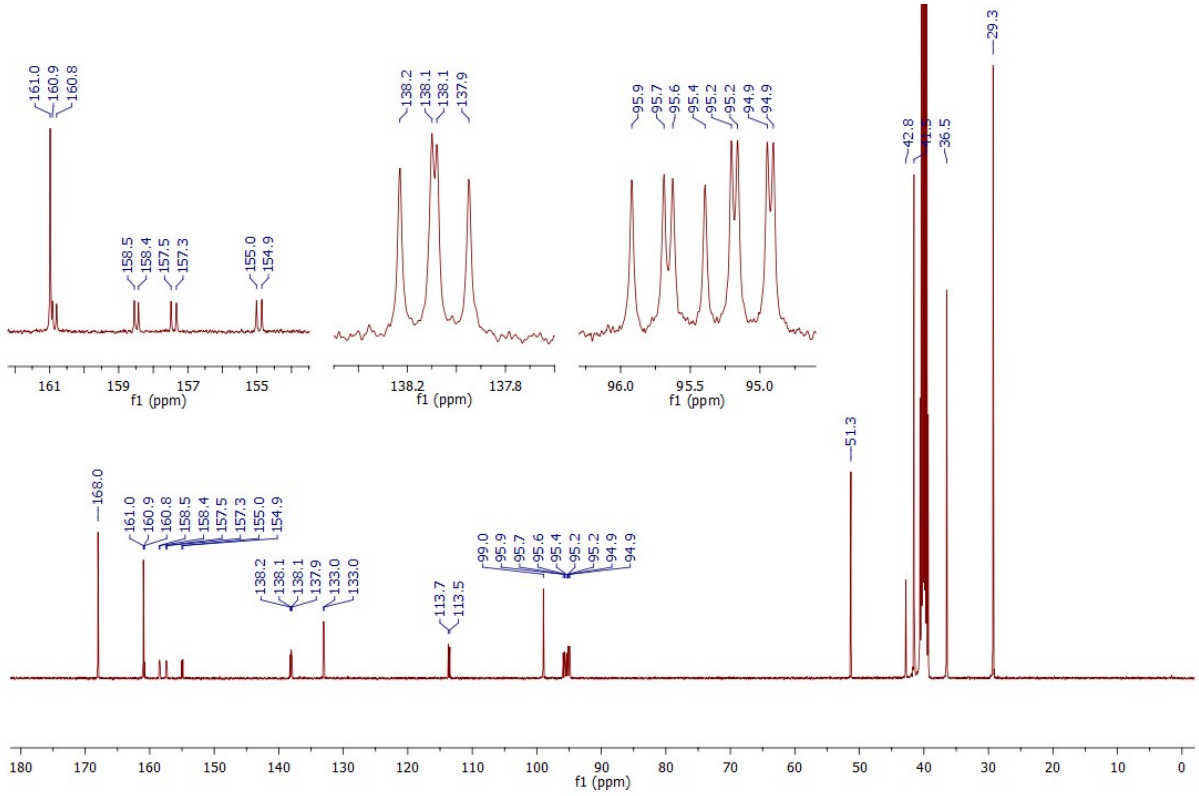

161.8
161.7
160.8
159.4
159.3
157.9
157.8
155.4
155.3
124.0
113.9
113.8
113.7
96.6
96.4
96.3
96.1
95.5
95.5
95.3
95.2
f1 (ppm)
102.8
146.3
139.3
139.1
131.4
f1 (ppm)

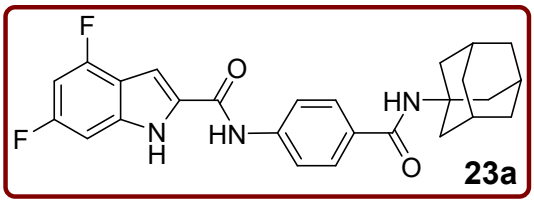

O
NH
N
N
H
14

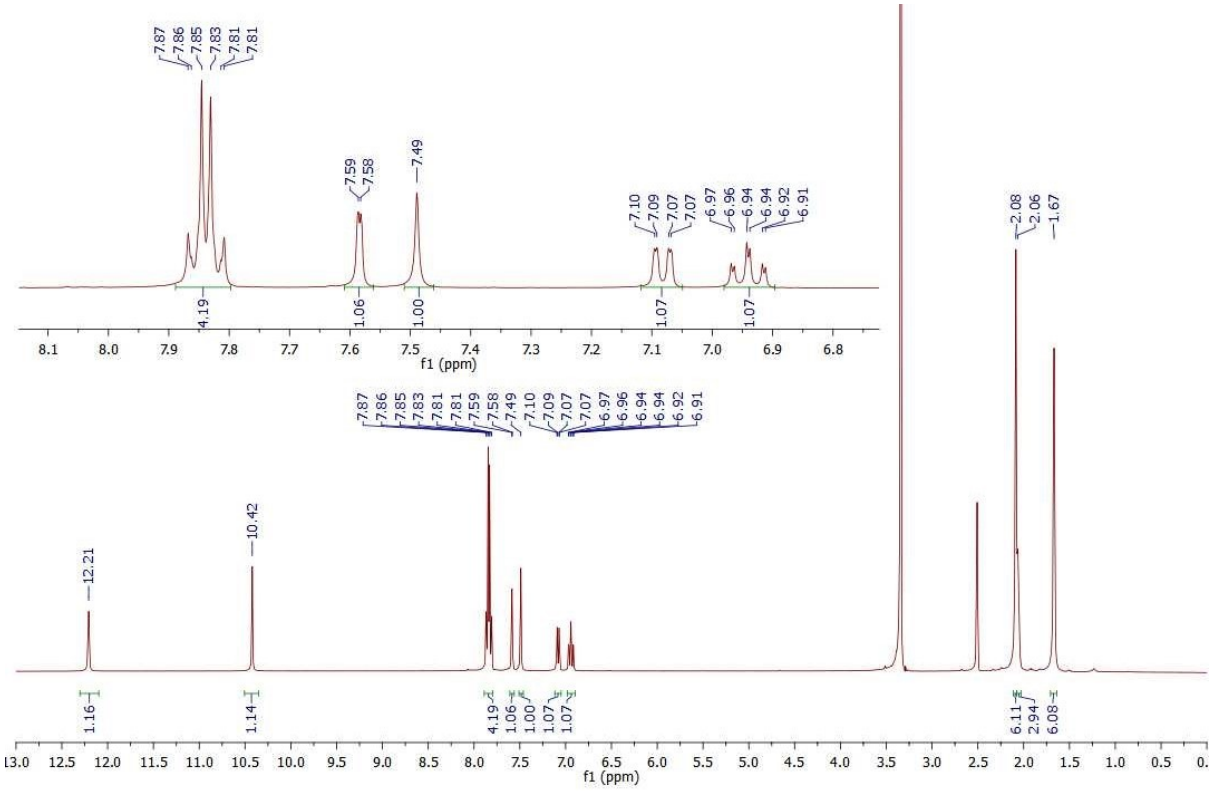

8.15
8.13
7.60
7.58
7.42
7.40
7.38
7.24
7.22
7.20
2.11
2.07
1.68
13.47
1.00
1.00
1.00
2.00
0.60
1.00
1.00
1.00
2.00
6.16
3.11
6.21
f1 (ppm)
f1 (ppm)

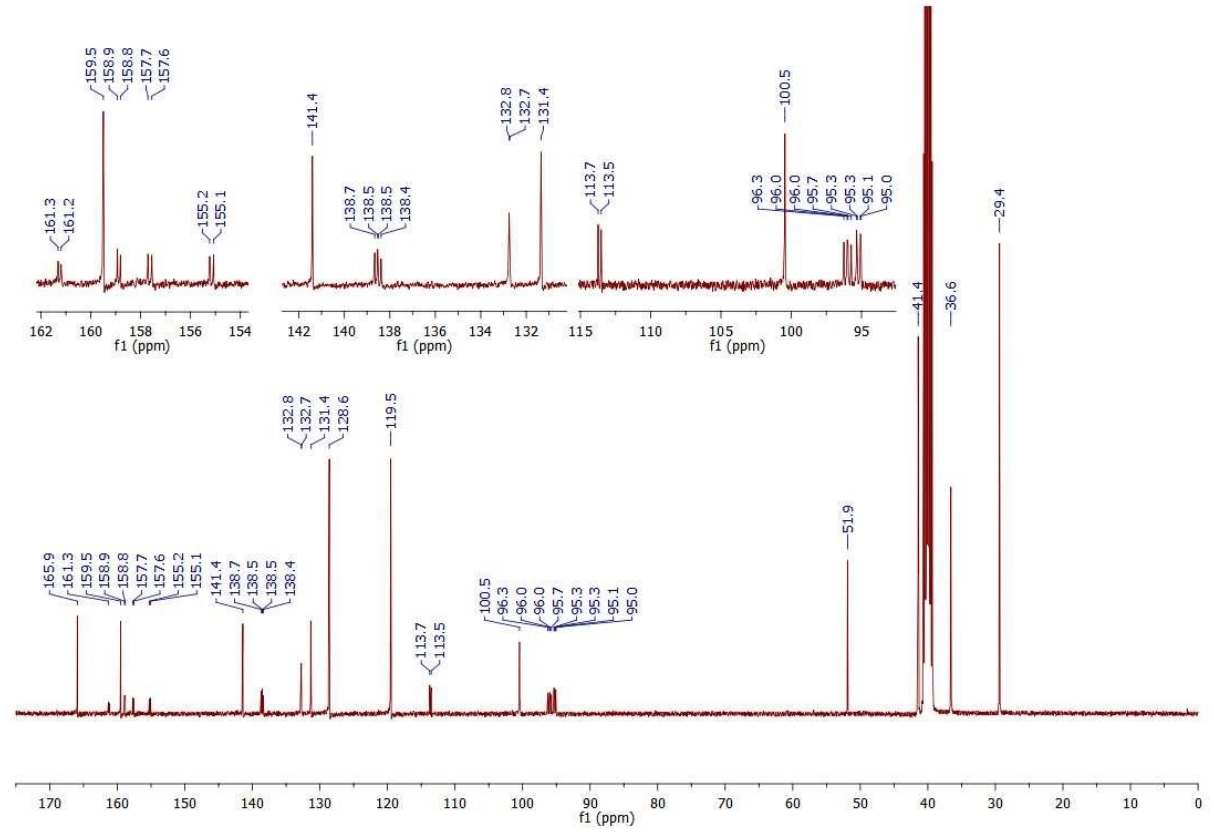

7.38
7.26
7.25
7.05
7.05
7.03
7.02
6.91
6.90
6.88
6.88
6.86
6.85
2.01
1.94
1.62
1.01
1.03
1.00
0.99
f1 (ppm)
12.02
8.73
8.71
8.70
3.85
3.84
0.98
1.00
1.01
1.03
1.00
0.99
2.07
3.00
5.79
5.84
f1 (ppm)

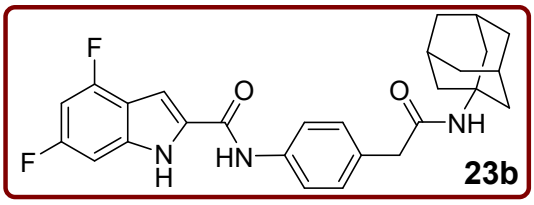

F
F
H
N
O
N
H
O
N
H
18

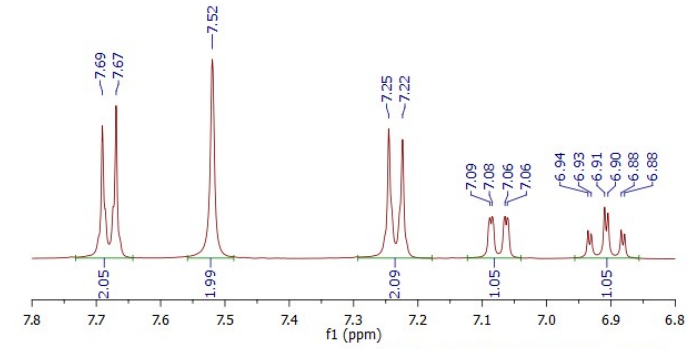

161.0
160.9
160.8
158.5
158.4
157.5
157.3
155.0
154.9
138.2
138.1
138.1
137.9
95.9
95.7
95.6
95.4
95.2
95.2
94.9
94.9
42.8
36.5
29.3
51.3
168.0
161.0
160.9
160.8
158.5
158.4
157.5
157.3
155.0
154.9
138.2
138.1
138.1
137.9
133.0
133.0
113.7
113.5
99.0
95.9
95.7
95.6
95.4
95.2
95.2
94.9
94.9
f1 (ppm)

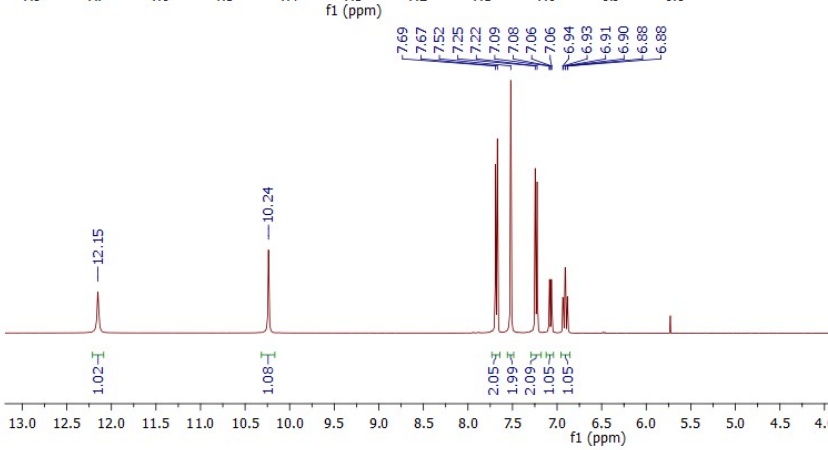

F
O
HN
F
N
H
HN
O
23a

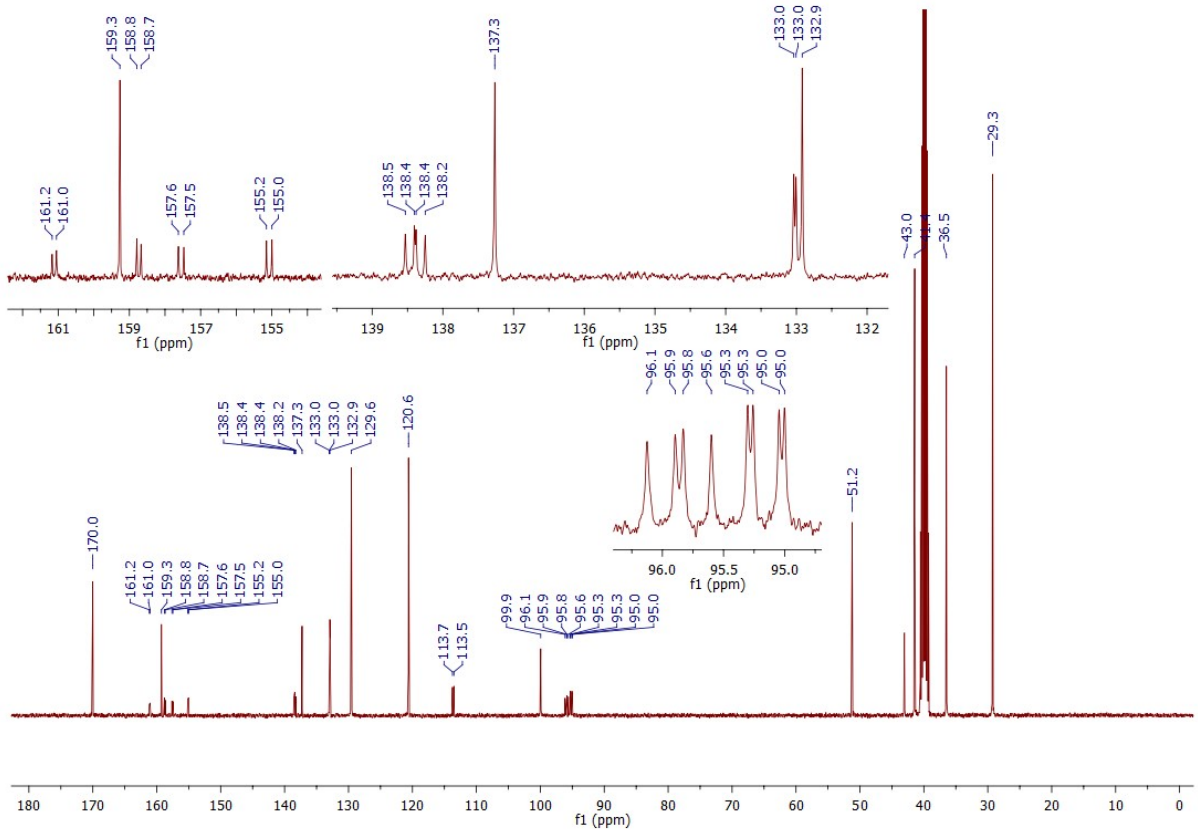

7.87
7.86
7.85
7.83
7.81
7.81
7.59
7.58
7.49
7.10
7.09
7.07
7.07
6.97
6.96
6.94
6.94
6.92
6.91
2.08
2.06
1.67
4.19
1.06
1.00
1.07
1.07
f1 (ppm)
12.21
10.42
1.16
1.14
4.19
1.06
1.00
1.07
1.07
6.11
2.94
6.08
f1 (ppm)


159.5
158.9
158.8
157.7
157.6
161.3
161.2
155.2
155.1
141.4
138.7
138.5
138.5
138.4
132.8
132.7
131.4
113.7
113.5
100.5
96.3
96.0
96.0
95.7
95.3
95.3
95.1
95.0
29.4
41.4
36.6
f1 (ppm)
132.8
132.7
131.4
128.6
119.5
165.9
161.3
159.5
158.9
158.8
157.7
157.6
155.2
155.1
141.4
138.7
138.5
138.5
138.4
113.7
113.5
100.5
96.3
96.0
96.0
95.7
95.3
95.3
95.1
95.0
51.9
f1 (ppm)


F
O
O
NH
F
N
H
HN
23b


7.69
7.67
7.52
7.25
7.22
7.09
7.08
7.06
7.06
6.94
6.93
6.91
6.90
6.88
6.88
2.05
1.99
2.09
1.05
1.05
f1 (ppm)


12.15
10.24
1.02
1.08
2.05
1.99
2.09
1.05
1.05
f1 (ppm)


159.3
158.8
158.7
137.3
133.0
133.0
132.9
161.2
161.0
157.6
157.5
155.2
155.0
138.5
138.4
138.4
138.2
43.0
36.5
29.3
f1 (ppm)
96.1
95.9
95.8
95.6
95.3
95.3
95.0
95.0
96.0
95.5
95.0
f1 (ppm)
138.5
138.4
138.4
138.2
137.3
133.0
133.0
132.9
129.6
120.6
51.2
170.0
161.2
161.0
159.3
158.8
158.7
157.6
157.5
155.2
155.0
113.7
113.5
99.9
96.1
95.9
95.8
95.6
95.3
95.3
95.0
95.0
f1 (ppm)