

Supplementary data

Synthesis, and Molecular Structure Investigations of a New *s*-Triazine Derivatives Incorporating Pyrazole/Piperidine/Aniline Moieties

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Crystal structure determination

The crystals of **5a** and **5b** were immersed in cryo-oil, mounted in a loop, and measured at a temperature of 120 K. The X-ray diffraction data were collected on a Rigaku Oxford Diffraction Supernova diffractometer using Cu K α radiation. The *CrysAlisPro* [1] software package was used for cell refinements and data reductions. A gaussian (**5a**) or multi-scan (**5b**) absorption correction (*CrysAlisPro*) [1] was applied to the intensities before structure solution. Structures were solved by intrinsic phasing (*SHELXT*) [2] method. Structural refinement was carried out using *SHELXL* [3] software with *SHELXLE* [4] graphical user interface. The NH hydrogen atoms were located from the difference Fourier map and refined isotropically. All other hydrogen atoms were positioned geometrically and constrained to ride on their parent atoms, with C-H = 0.95-0.99 Å and $U_{iso} = 1.2-1.5 \cdot U_{eq}(\text{parent atom})$.

Hirshfeld surface analysis

The topology analyses were performed using Crystal Explorer 17.5 program [5].

Computational methods

All DFT calculations were performed using Gaussian 09 software package [6,7] utilizing B3LYP/6-31G(d,p) method. Natural bond orbital analyses were performed using NBO 3.1 program as implemented in the Gaussian 09W package [8]. The self-consistent reaction field (SCRF) method [9,10] was used to model the solvent effects when calculated the optimized geometries in solution. Then the NMR chemical shifts for the protons and carbons were computed using GIAO method [11].

Table S1 The calculated geometric parameters of **5a** and **5b** ^a.

Parameter	Calc	Exp	Parameter
	5a		5b
R(1-19)	1.404	R(1-13)	1.913
R(1-20)	1.37	R(2-18)	1.401
R(3-20)	1.354	R(2-19)	1.371
R(3-21)	1.332	R(3-19)	1.334
R(4-21)	1.326	R(3-20)	1.352
R(4-22)	1.349	R(4-20)	1.36
R(5-20)	1.332	R(4-21)	1.464
R(5-22)	1.355	R(4-33)	1.463
R(6-7)	1.373	R(5-20)	1.352
R(6-21)	1.408	R(5-36)	1.334
R(6-23)	1.391	R(6-19)	1.349
R(7-30)	1.321	R(6-36)	1.327
R(8-22)	1.358	R(7-8)	1.374
R(8-35)	1.466	R(7-36)	1.407
R(8-47)	1.462	R(7-37)	1.392
R(9-11)	1.391	R(8-44)	1.32
R(9-19)	1.406	R(9-11)	1.39
R(11-13)	1.396	R(9-18)	1.406
R(13-15)	1.395	R(11-13)	1.393
R(15-17)	1.395	R(13-14)	1.392
R(17-19)	1.403	R(14-16)	1.394
R(23-24)	1.495	R(16-18)	1.404
R(23-28)	1.373	R(21-24)	1.535
R(28-30)	1.424	R(24-27)	1.535

R(30-31)	1.497	R(27-30)	1.535
R(35-38)	1.534	R(30-33)	1.535
R(38-41)	1.536	R(37-38)	1.495
R(41-44)	1.536	R(37-42)	1.372
R(44-47)	1.536	R(42-44)	1.424
		R(44-45)	1.497
A(2-1-19)	115.696	A(1-13-11)	119.688
A(2-1-20)	111.314	A(1-13-14)	119.848
A(19-1-20)	132.957	A(18-2-19)	132.58
A(1-19-9)	116.541	A(18-2-49)	116.399
A(1-19-17)	124.418	A(2-18-9)	116.93
A(1-20-3)	112.857	A(2-18-16)	124.262
A(1-20-5)	120.998	A(19-2-49)	110.998
A(20-3-21)	113.503	A(2-19-3)	120.851
A(3-20-5)	126.145	A(2-19-6)	112.702
A(3-21-4)	126.791	A(19-3-20)	114.221
A(3-21-6)	116.625	A(3-19-6)	126.446
A(21-4-22)	114.587	A(3-20-4)	117.741
A(4-21-6)	116.583	A(3-20-5)	124.583
A(4-22-5)	124.797	A(20-4-21)	122.769
A(4-22-8)	117.016	A(20-4-33)	122.6
A(20-5-22)	114.172	A(4-20-5)	117.676
A(5-22-8)	118.187	A(21-4-33)	114.62
A(7-6-21)	118.808	A(4-21-22)	108.515
A(7-6-23)	111.793	A(4-21-23)	108.24
A(6-7-30)	105.281	A(4-21-24)	110.795
A(21-6-23)	129.399	A(4-33-30)	110.691
A(6-23-24)	126.833	A(4-33-34)	108.462
A(6-23-28)	105.395	A(4-33-35)	108.39
A(7-30-28)	111.25	A(20-5-36)	114.468
A(7-30-31)	120.399	A(5-36-6)	126.796
A(22-8-35)	121.922	A(5-36-7)	116.731
A(22-8-47)	123.1	A(19-6-36)	113.474
A(35-8-47)	114.976	A(6-36-7)	116.473
A(8-35-36)	108.196	A(8-7-36)	118.6
A(8-35-37)	108.18	A(8-7-37)	111.724
A(8-35-38)	110.576	A(7-8-44)	105.32
A(8-47-44)	110.7	A(36-7-37)	129.676
A(8-47-48)	108.577	A(7-37-38)	126.903
A(8-47-49)	108.384	A(7-37-42)	105.43
A(10-9-11)	119.87	A(8-44-42)	111.239
A(10-9-19)	119.449	A(8-44-45)	120.435
A(11-9-19)	120.681	A(10-9-11)	119.299
A(9-11-12)	119.334	A(10-9-18)	119.645
A(9-11-13)	120.355	A(11-9-18)	121.056
A(9-19-17)	119.037	A(9-11-12)	120.262

A(12-11-13)	120.311	A(9-11-13)	119.35
A(11-13-14)	120.477	A(9-18-16)	118.796
A(11-13-15)	118.965	A(12-11-13)	120.387
A(14-13-15)	120.559	A(11-13-14)	120.464
A(13-15-16)	119.861	A(13-14-15)	120.001
A(13-15-17)	121.385	A(13-14-16)	120.235
A(16-15-17)	118.754	A(15-14-16)	119.764
A(15-17-18)	121.205	A(14-16-17)	120.558
A(15-17-19)	119.577	A(14-16-18)	120.098
A(18-17-19)	119.217	A(17-16-18)	119.344
A(24-23-28)	127.772	A(22-21-23)	107.778
A(23-24-25)	111.905	A(22-21-24)	111.906
A(23-24-26)	108.403	A(23-21-24)	109.49
A(23-24-27)	111.903	A(21-24-25)	108.83
A(23-28-29)	125.907	A(21-24-26)	109.117
A(23-28-30)	106.281	A(21-24-27)	111.023
A(25-24-26)	108.931	A(25-24-26)	107.18
A(25-24-27)	106.719	A(25-24-27)	109.873
A(26-24-27)	108.908	A(26-24-27)	110.718
A(29-28-30)	127.811	A(24-27-28)	110.515
A(28-30-31)	128.351	A(24-27-29)	109.18
A(30-31-32)	111.269	A(24-27-30)	110.741
A(30-31-33)	111.284	A(28-27-29)	106.607
A(30-31-34)	109.828	A(28-27-30)	110.483
A(32-31-33)	107.257	A(29-27-30)	109.21
A(32-31-34)	108.557	A(27-30-31)	110.711
A(33-31-34)	108.545	A(27-30-32)	109.782
A(36-35-37)	108.264	A(27-30-33)	111.288
A(36-35-38)	109.625	A(31-30-32)	107.139
A(37-35-38)	111.896	A(31-30-33)	109.068
A(35-38-39)	109.07	A(32-30-33)	108.741
A(35-38-40)	108.748	A(30-33-34)	109.591
A(35-38-41)	111.286	A(30-33-35)	111.604
A(39-38-40)	107.079	A(34-33-35)	108.009
A(39-38-41)	110.696	A(38-37-42)	127.667
A(40-38-41)	109.849	A(37-38-39)	111.934
A(38-41-42)	110.572	A(37-38-40)	108.444
A(38-41-43)	109.203	A(37-38-41)	111.851
A(38-41-44)	110.781	A(37-42-43)	125.905
A(42-41-43)	106.591	A(37-42-44)	106.287
A(42-41-44)	110.436	A(39-38-40)	108.802
A(43-41-44)	109.15	A(39-38-41)	107.016
A(41-44-45)	109.826	A(40-38-41)	108.711
A(41-44-46)	110.746	A(43-42-44)	127.808
A(41-44-47)	111.154	A(42-44-45)	128.326
A(45-44-46)	107.158	A(44-45-46)	111.25

A(45-44-47)	108.746	A(44-45-47)	111.243
A(46-44-47)	109.104	A(44-45-48)	109.845
A(44-47-48)	111.707	A(46-45-47)	107.269
A(44-47-49)	109.534	A(46-45-48)	108.566
A(48-47-49)	107.838	A(47-45-48)	108.569

^aAtom numbering refer to **Fig. 5**

Table S2 The calculated natural charges of **5a** and **5b** ^a.

Atom	Charge	Atom	Charge
5a		5b	
N1	-0.5905	Br1	0.0475
H2	0.4343	N2	-0.5907
N3	-0.6247	N3	-0.6294
N4	-0.5823	N4	-0.4357
N5	-0.6272	N5	-0.6244
N6	-0.2154	N6	-0.5727
N7	-0.2777	N7	-0.2158
N8	-0.4324	N8	-0.2750
C9	-0.2677	C9	-0.2533
H10	0.2313	H10	0.2409
C11	-0.2265	C11	-0.2400
H12	0.2407	H12	0.2583
C13	-0.2603	C13	-0.1284
H14	0.2392	C14	-0.2375
C15	-0.2227	H15	0.2559
H16	0.2392	C16	-0.2511
C17	-0.2633	H17	0.2665
H18	0.2620	C18	0.1616
C19	0.1616	C19	0.6417
C20	0.6455	C20	0.6541
C21	0.6488	C21	-0.2634
C22	0.6501	H22	0.2676
C23	0.1888	H23	0.2256
C24	-0.7134	C24	-0.4771
H25	0.2598	H25	0.2384
H26	0.2443	H26	0.2471
H27	0.2594	C27	-0.4716
C28	-0.3386	H28	0.2474
H29	0.2455	H29	0.2296
C30	0.1738	C30	-0.4769
C31	-0.7137	H31	0.2466
H32	0.2451	H32	0.2379
H33	0.2450	C33	-0.2646
H34	0.2567	H34	0.2244
C35	-0.2708	H35	0.2698
H36	0.2227	C36	0.6487

H37	0.2883	C37	0.1877
C38	-0.4773	C38	-0.7129
H39	0.2467	H39	0.2587
H40	0.2386	H40	0.2460
C41	-0.4714	H41	0.2568
H42	0.2457	C42	-0.3368
H43	0.2285	H43	0.2460
C44	-0.4762	C44	0.1749
H45	0.2378	C45	-0.7142
H46	0.2451	H46	0.2455
C47	-0.2624	H47	0.2455
H48	0.2651	H48	0.2576
H49	0.2250	H49	0.4431

^aAtom numbering refer to **Fig. 5**

Table S3 The calculated and experimental chemical shifts (C.S) for **5a^a**.

Atom	(C.S) _{calc.}	(C.S) _{exp.}	Atom	(C.S) _{calc.}	(C.S) _{exp.}
C9	105.169	119.910	H2	6.518	-
C11	115.983	128.900	H10	7.002	7.572
C13	109.025	122.855	H12	7.656	7.331
C15	116.622	128.900	H14	7.349	7.052
C17	105.431	119.910	H16	7.719	7.340
C19	127.359	138.970	H18	9.106	7.593
C20	150.901	164.780	H25	3.027	2.663
C21	151.212	165.041	H26	2.560	2.663
C22	152.106	172.190	H27	3.059	2.663
C23	134.117	151.310	H29	6.385	6.007
C24	10.831	17.051	H32	2.416	2.331
C28	99.251	110.590	H33	2.420	2.331
C30	138.726	143.341	H34	2.342	2.331
C31	7.394	14.100	H36	3.050	3.806
C35	36.630	45.040	H37	5.490	3.808
C38	20.050	25.830	H39	1.838	1.660
C41	18.774	24.810	H40	1.826	1.660
C44	20.152	25.830	H42	2.052	1.707
C47	36.624	45.040	H43	1.825	1.707
			H45	1.807	1.660
			H46	1.879	1.660
			H48	5.211	3.839
			H49	3.167	3.837

^aAtom numbering refer to **Fig. 5**

Table S4 The calculated and experimental chemical shifts for **5b**^a.

Atom	(C.S)_{calc.}	(C.S)_{exp.}	Atom	(C.S)_{calc.}	(C.S)_{exp.}
C9	106.997	121.575	H10	7.009	7.440
C11	119.086	131.899	H12	7.559	7.460
C13	120.660	115.560	H15	7.597	7.460
C14	119.555	131.899	H17	9.054	7.440
C16	106.921	121.575	H22	5.175	3.810
C18	127.005	138.050	H23	3.108	3.810
C19	151.670	164.460	H25	1.906	1.645
C20	151.510	164.830	H26	1.919	1.645
C21	37.386	44.980	H28	2.084	1.710
C24	20.069	25.807	H29	1.858	1.710
C27	18.853	24.736	H31	1.832	1.645
C30	20.061	25.807	H32	1.836	1.645
C33	37.410	44.980	H34	3.056	3.810
C36	151.419	164.85	H35	5.070	3.810
C37	133.694	151.599	H39	3.048	2.650
C38	11.076	16.300	H40	2.604	2.650
C42	99.279	110.900	H41	3.053	2.650
C44	138.907	143.400	H43	6.397	6.000
C45	7.415	13.700	H46	2.418	2.310
			H47	2.417	2.310
			H48	2.357	2.310
			H49	6.664	-

^aAtom numbering refer to **Fig. 5**

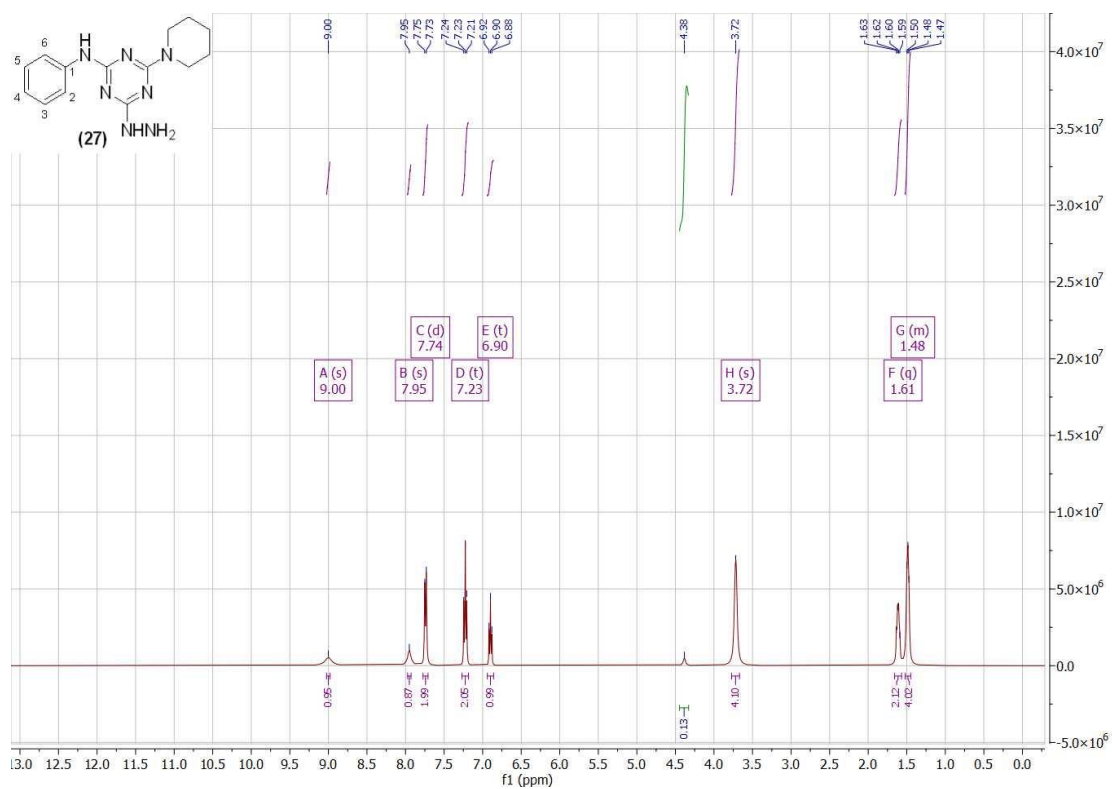


Figure S1: ¹H NMR spectrum for compound 4a.

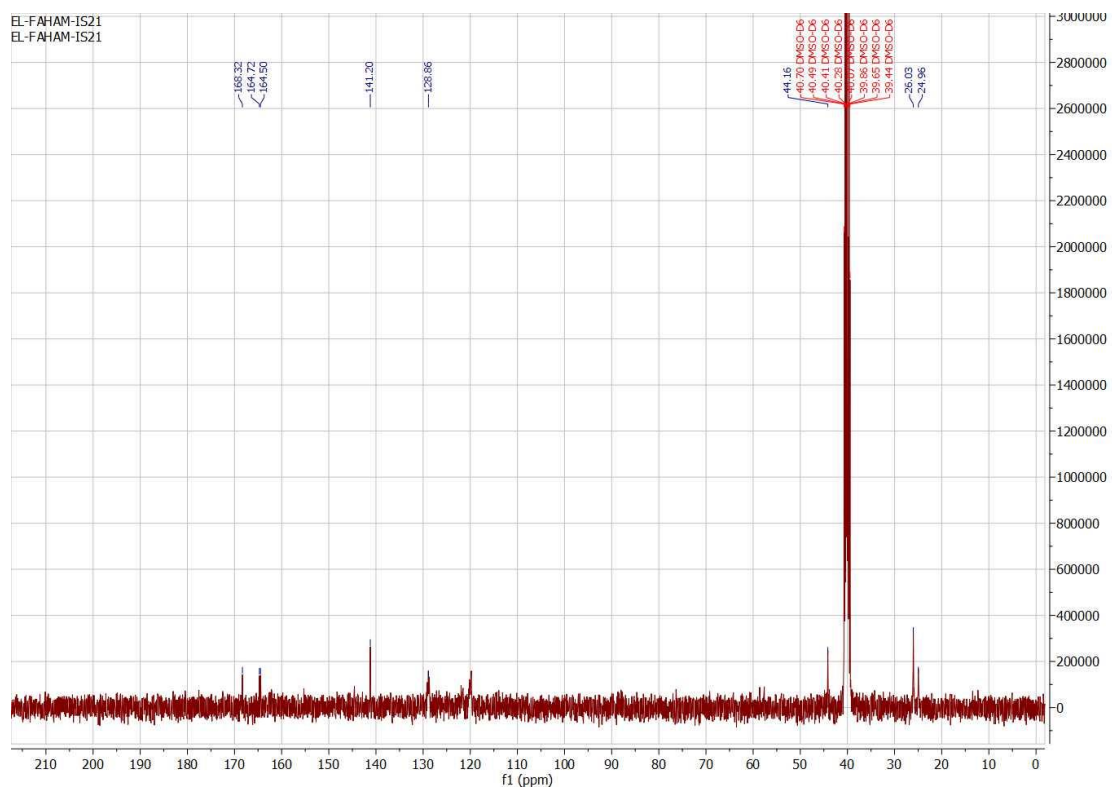


Figure S2: ¹³C NMR spectrum for compound 4a.

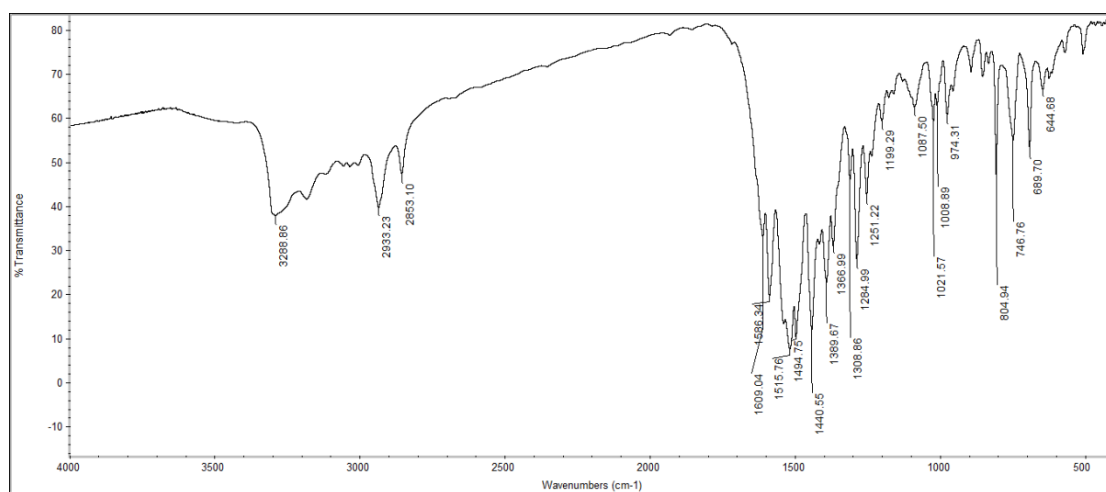


Figure S3: IR spectrum for compound **4a**.

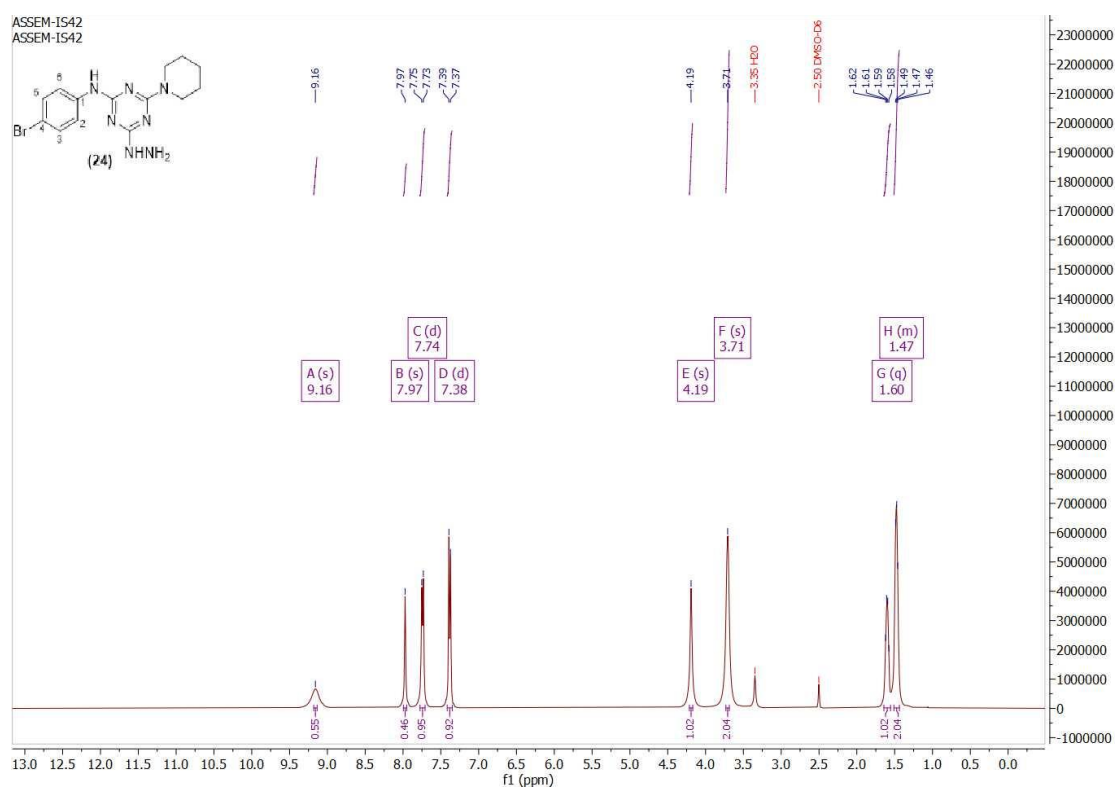


Figure S4: ^1H NMR spectrum for compound **4b**.

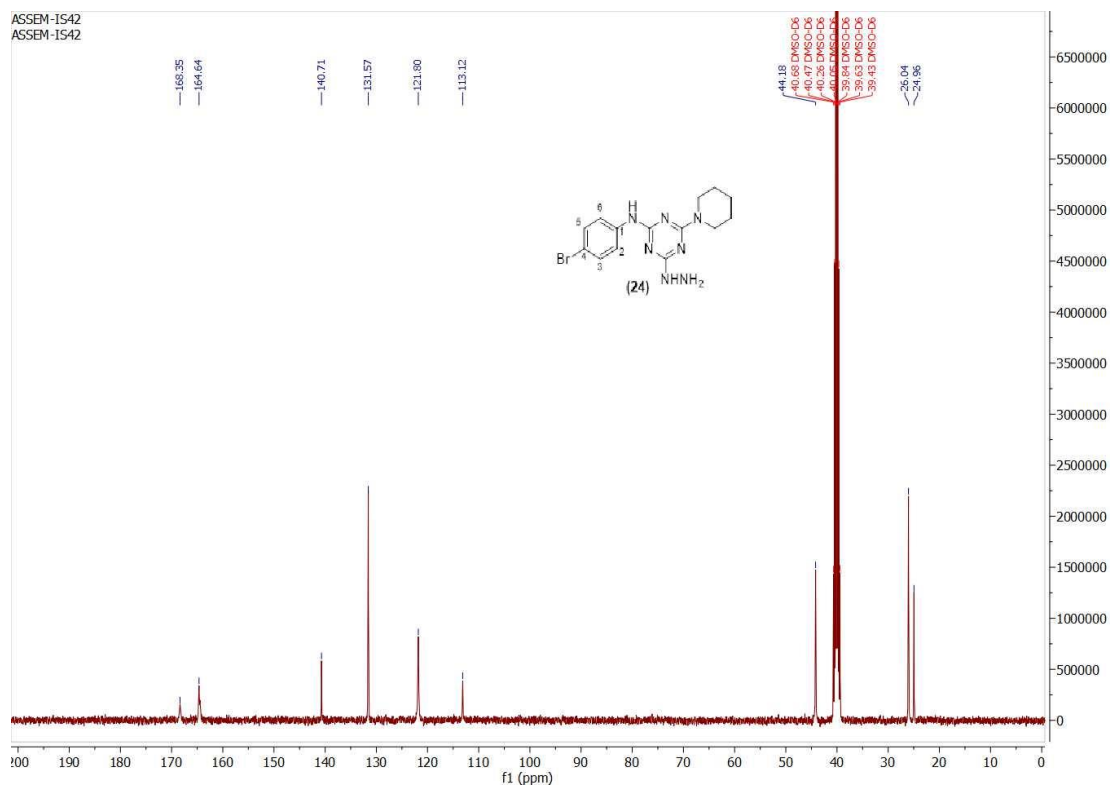


Figure S5: ^{13}C NMR spectrum for compound **4b**.

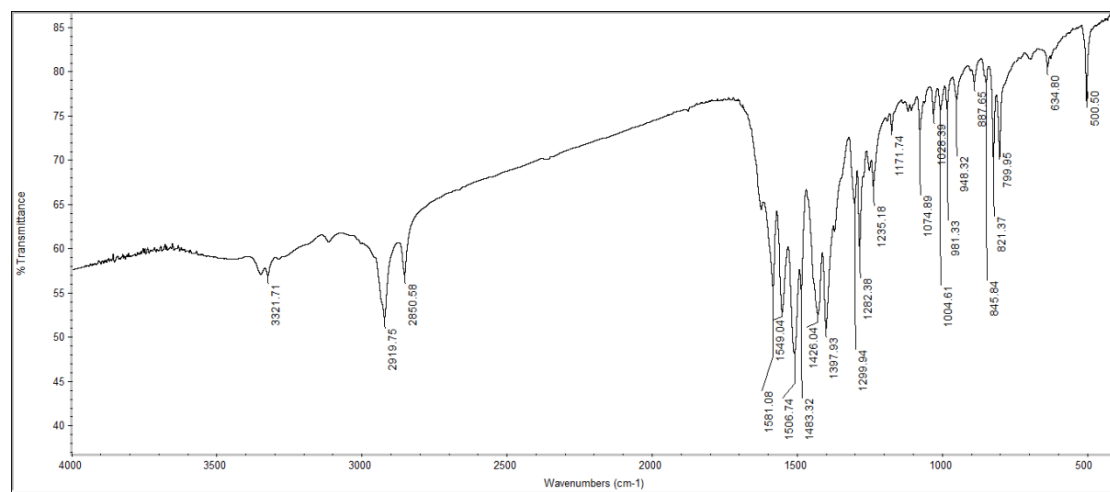


Figure S6: IR spectrum for compound **4b**.

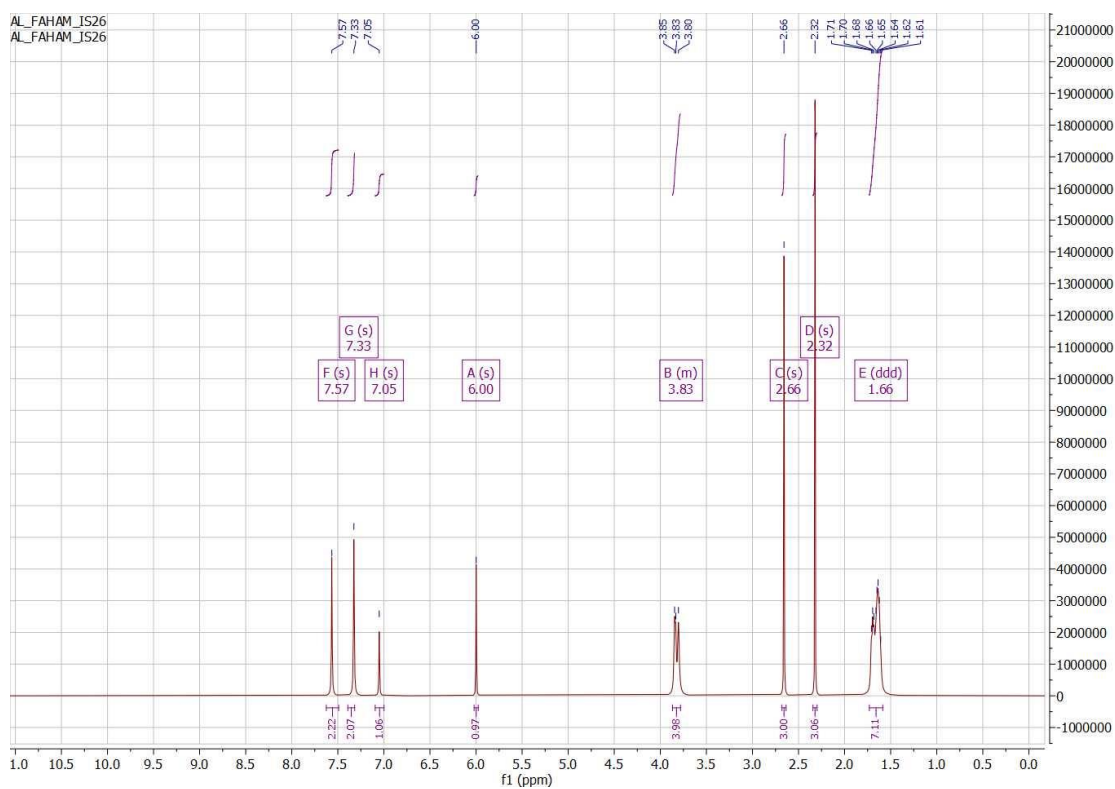


Figure S7: ^1H NMR spectrum for compound **5a**.

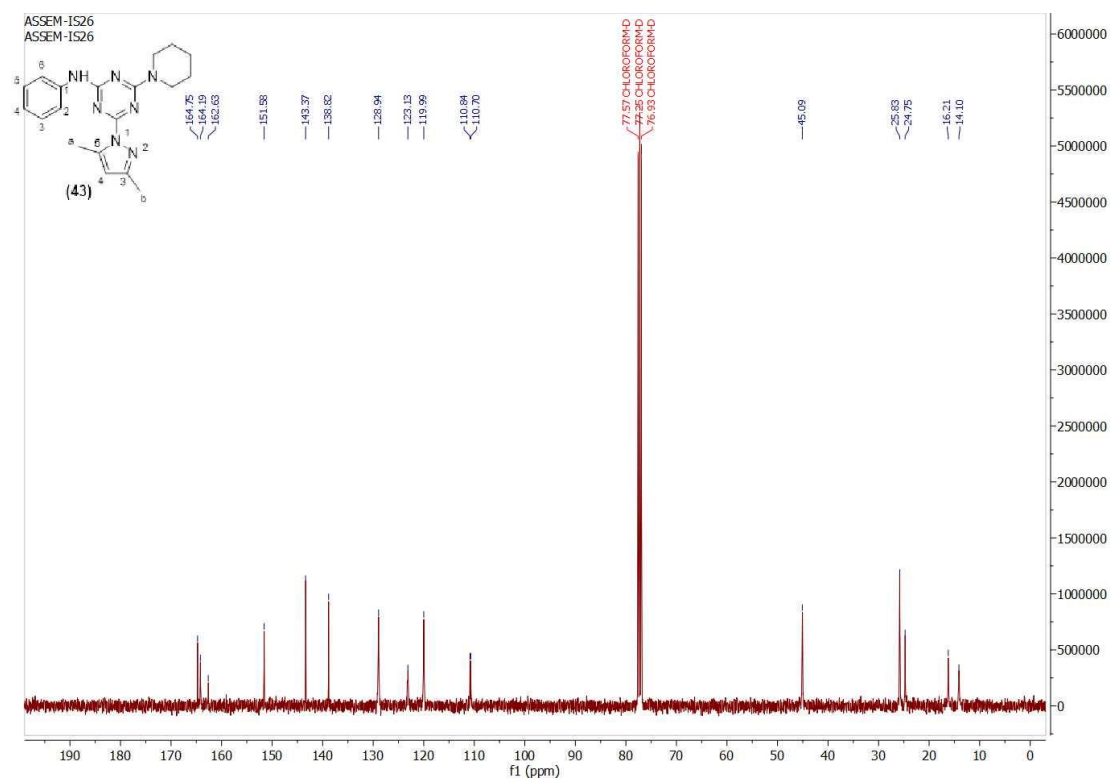


Figure S8: ^{13}C NMR spectrum for compound **5a**.

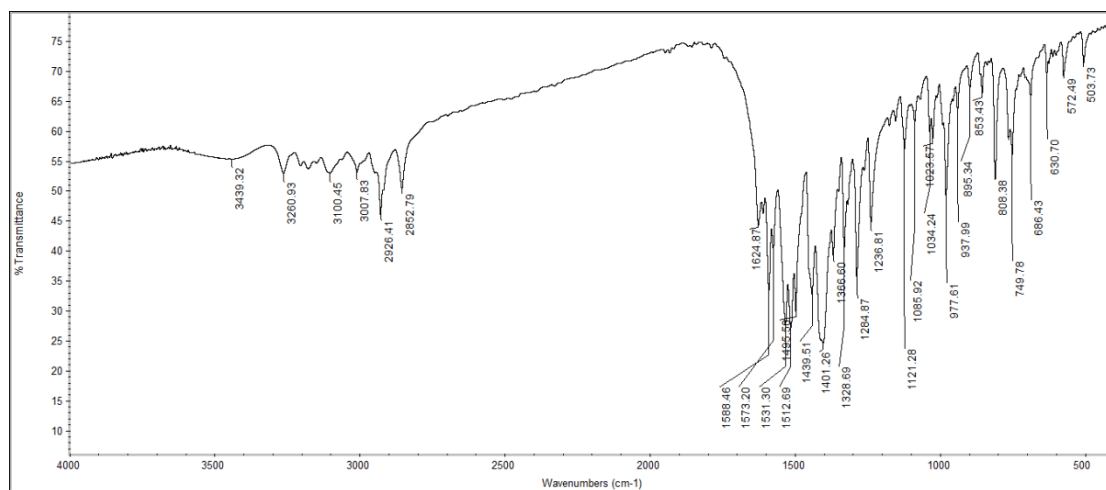


Figure S9: IR spectrum for compound 5a.

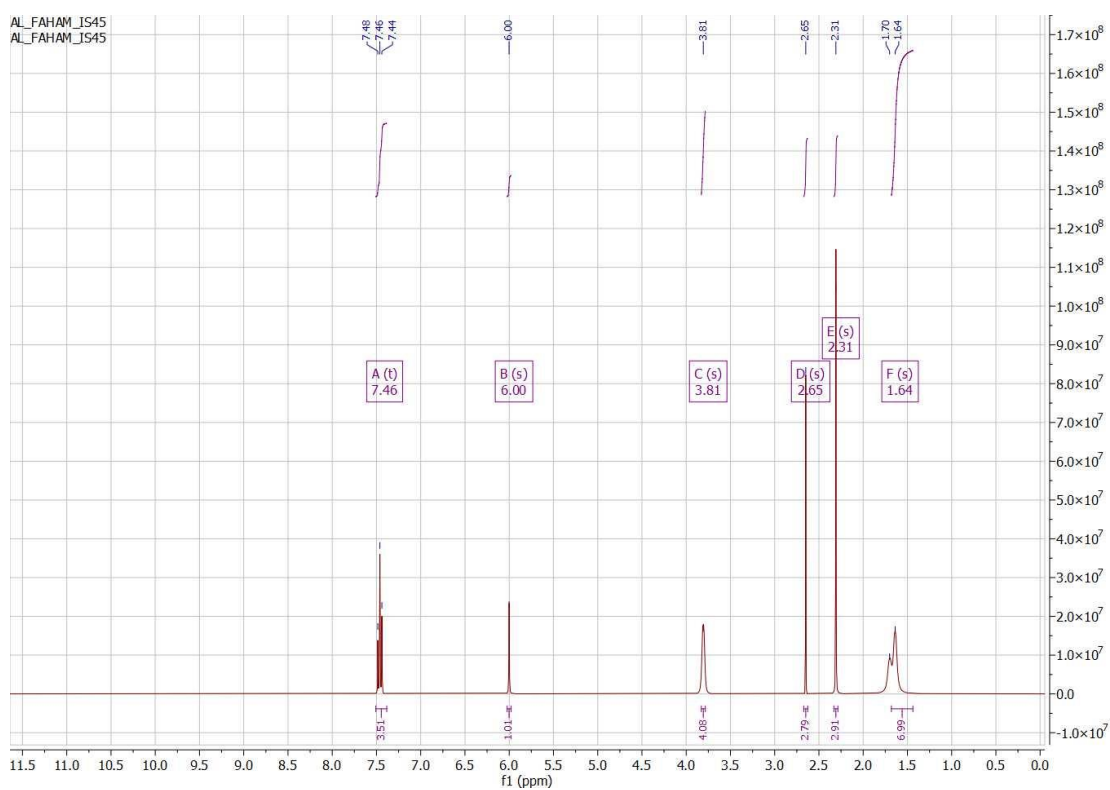


Figure S10: ¹H NMR spectrum for compound 5b.

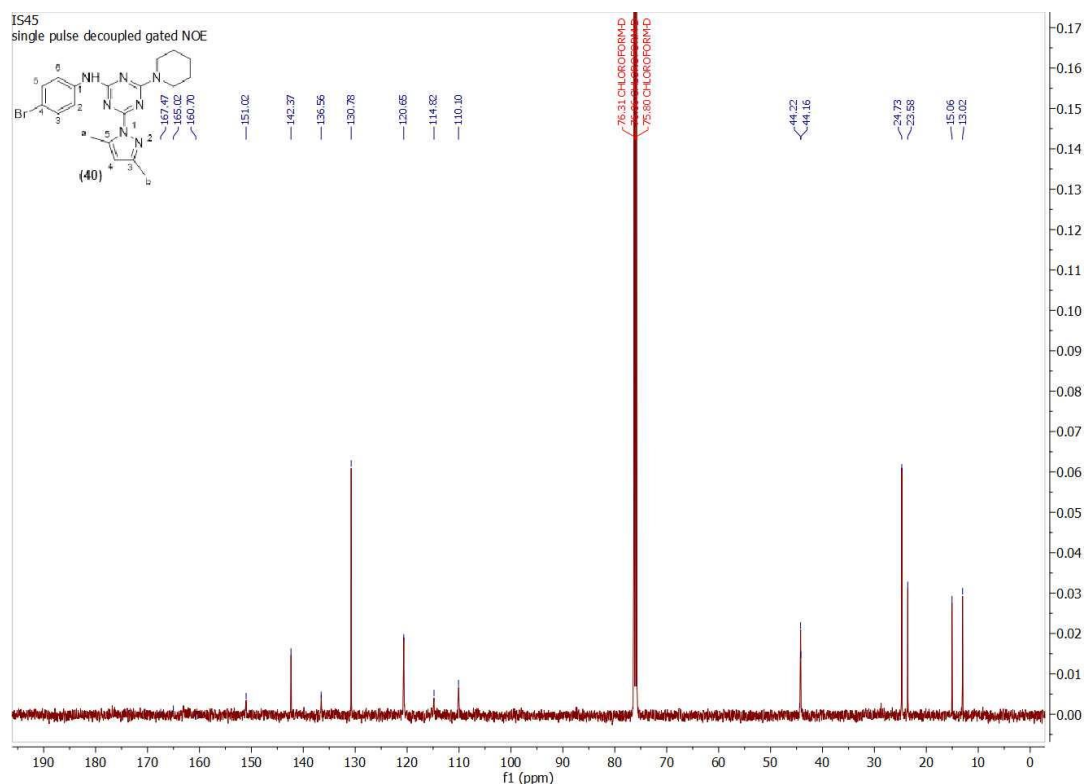


Figure S11: ¹³CNMR spectrum for compound **5b**.

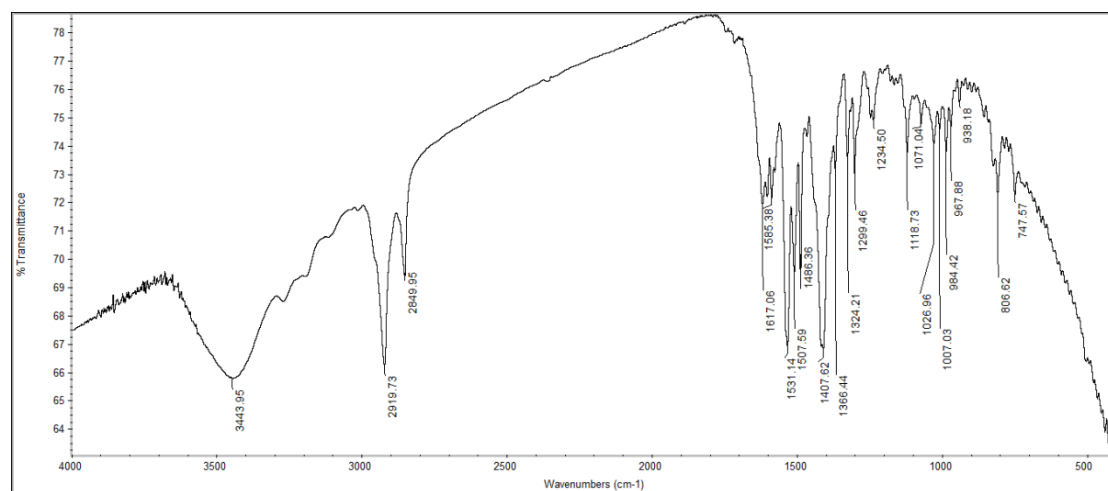


Figure S12: IR spectrum for compound **5b**.

References

1. Rikagu Oxford Diffraction, *CrysAlisPro*, Agilent Technologies inc., Yarnton, Oxfordshire, England, 2020.
2. Sheldrick, G. M. SHELXT – Integrated space-group and crystal-structure determination. *Acta Cryst.* **2015**, A71, 3-8.
3. Sheldrick, G. M. Crystal structure refinement with SHELXL. *Acta Cryst.* **2015**, C71, 3-8.

4. Hübschle, C. B.; Sheldrick, G. M.; Dittrich. ShelXle: a Qt graphical user interface for SHELXL. *B. J. Appl. Cryst.* **2011**, *44*, 1281-1284.
5. Turner, M. J.; McKinnon, J. J.; Wolff, S. K.; Grimwood, D. J.; Spackman, P. R.; Jayatilaka, D.; Spackman, M. A. Crystal Explorer17, University of Western Australia, 2017, <http://hirshfeldsurface.net>.
6. Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G.A.; *et al.* GAUSSIAN 09; Revision A02; Gaussian Inc.: Wallingford, CT, USA, 2009.
7. GaussView; Version 4.1; Dennington II, R., Keith, T., Millam, J., Eds.; Semichem Inc.: Shawnee Mission, KS, USA, 2007.
8. Reed, A.E.; Curtiss, L.A.; Weinhold, F. Intermolecular interactions from a natural bond orbital, donor-acceptor viewpoint. *Chem. Rev.* **1988**, *88*, 899–926.
9. Cheeseman, J.R.; Trucks, G.W.; Keith, T.A.; Frisch, M.J. A Comparison of Models for Calculating Nuclear Magnetic Resonance Shielding Tensors. *J. Chem. Phys.* **1996**, *104*, 5497–5509.
10. Marten, B.; Kim K.; Cortis, C.; Friesner, R. A.; Murphy, R. B.; Ringnalda, M. N.; Sitkoff, D.; Honig, B. New Model for Calculation of Solvation Free Energies: Correction of Self-Consistent Reaction Field Continuum Dielectric Theory for Short-Range Hydrogen-Bonding Effects, *J. Phys. Chem.* 1996, *100*, 11775-11765.
11. Tannor, D.J.; Marten, B.; Murphy, R.; Friesner, R.A.; Sitkoff, D.; Nicholls, A.; Ringnalda, M.; Goddard, W.A.; Honig, B. Accurate first principles calculation of molecular charge distributions and solvation energies from ab initio quantum mechanics and continuum dielectric theory. *J. Am. Chem. Soc.* **1994**, *116*, 11875–11882.