Intramolecular Noncovalent Carbon Bonding Driven Conformational Preference in Spiroisatin-based *N*-Acyl Hydrazones

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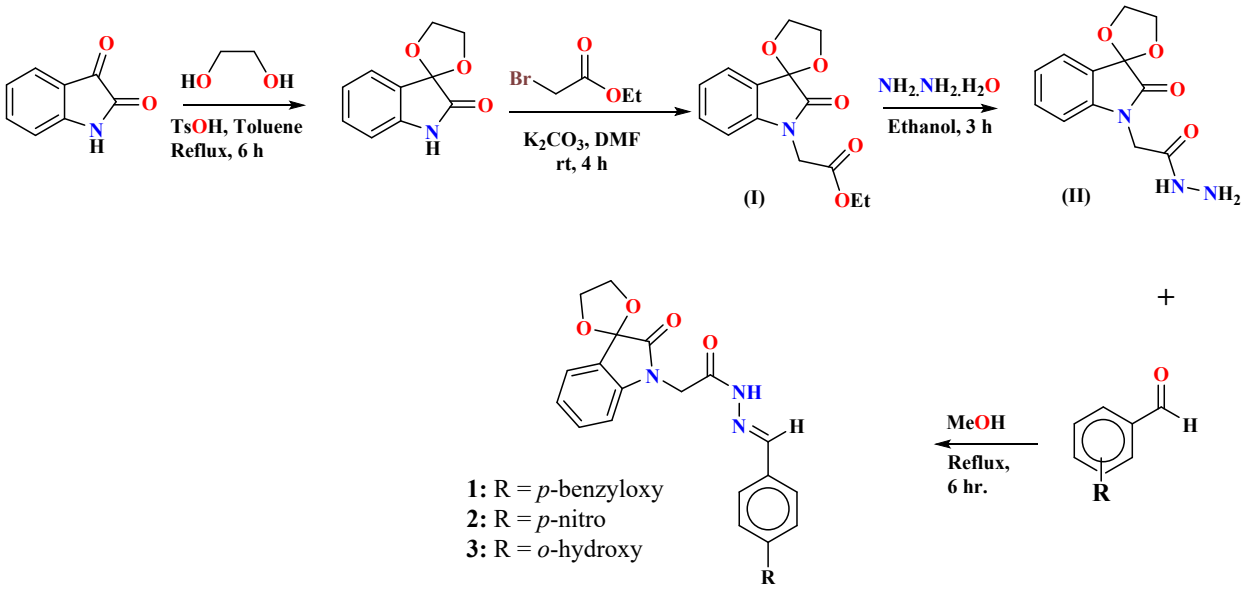
1. General Considerations

To proceed with the experiments more precisely all the reactions were performed in completely washed, rinsed, and dried apparatus. All the solvents were freshly dried in specific desiccants. To check the progress of reactions at regular intervals, thin layer chromatography was used using Merck silica gel-60 F_{254} 0.2mm pre-coated aluminium plates. 254 nm wavelength of U.V. lamp was used to visualize the U.V. active compounds. IR spectroscopy was used for the characterization of different functional groups in the synthesized compounds. IR spectra were recorded using Bruker Transor-II FT-IR spectrophotometer, and absorption frequencies were reported in per centimetres (cm^{-1}) units. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Advance 300 MHz and 75 MHz spectrophotometer, respectively. Chemical shift (δ) values were reported in ppm units and coupling constants in Hertz (Hz). Mass of all the compounds were verified using LC-MS Agilent 6310 Ion Trap in Isocrative, Negative Mode ACN. Melting points of synthesized compounds were recorded using Gallenkamp melting point instrument MPD350.BM3.5 (UK).



Scheme S1: Synthesis of spiroisatin-based *N*-acyl hydrazones **1-3**

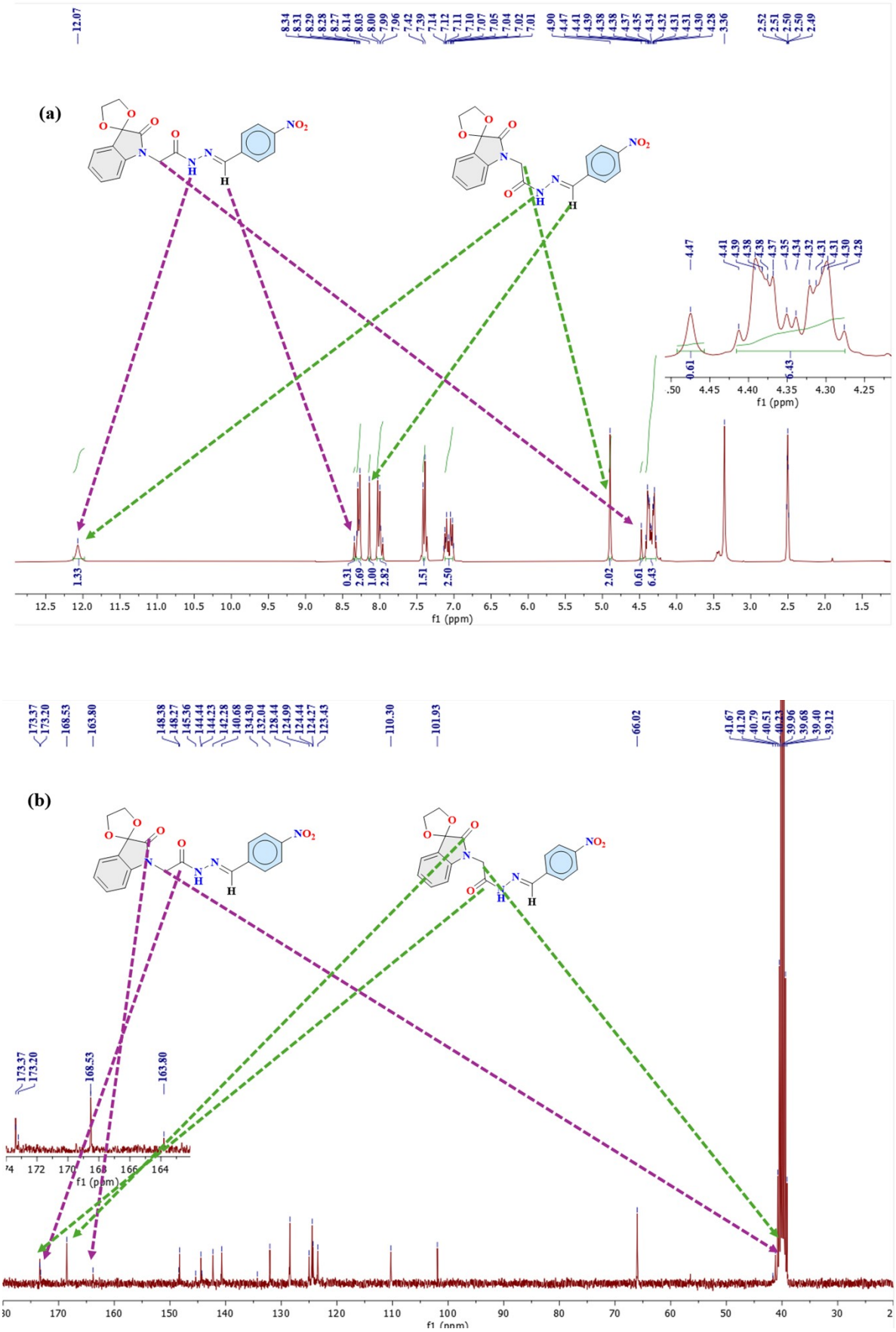


Fig. S1: ^{1}H & ^{13}C NMR spectra of compound **2**

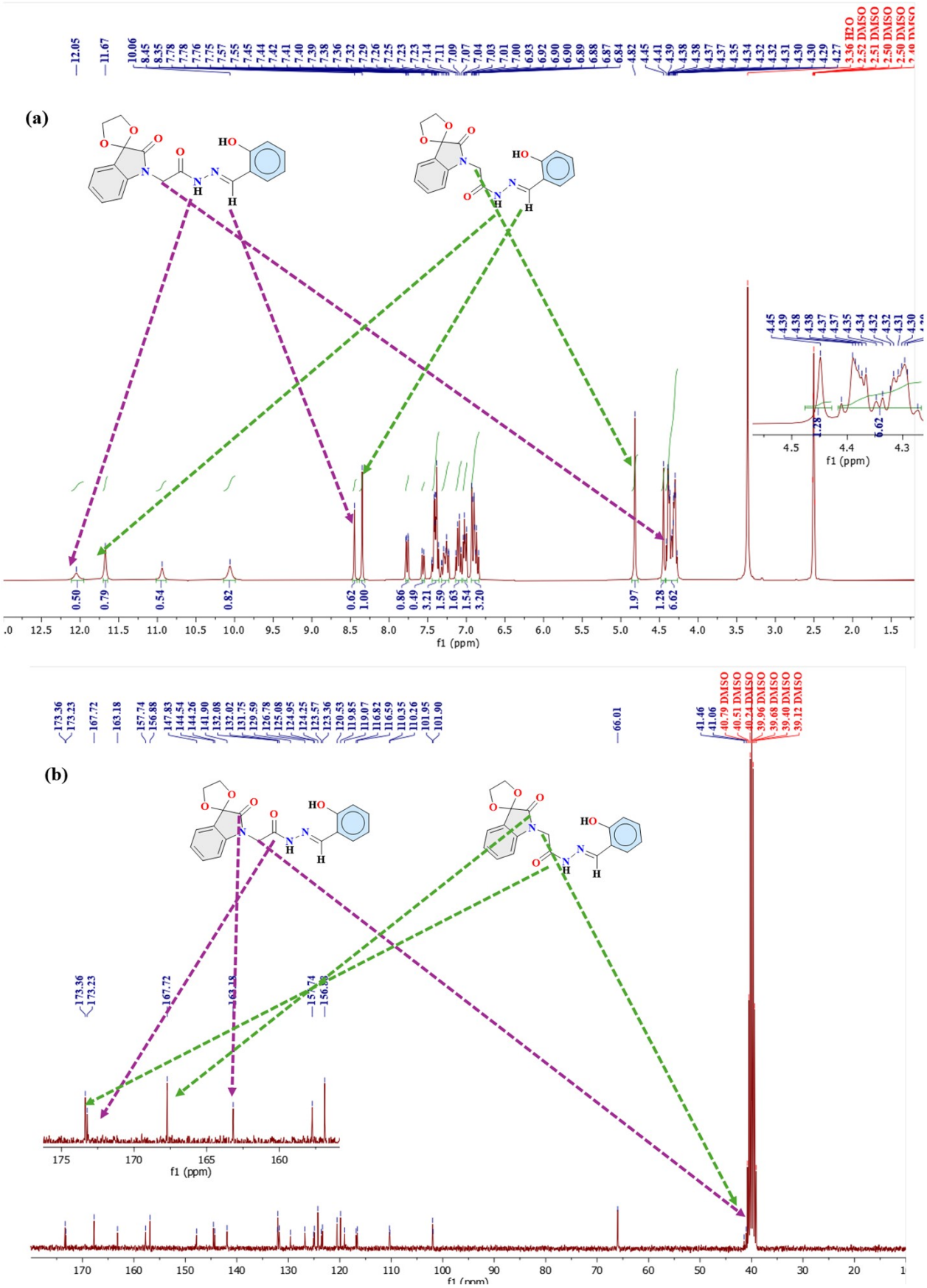


Fig. S2: ^{1}H & ^{13}C NMR spectra of compound **3**

Table S1: Single crystal XRD data collection and refinement details of compounds **1-3**

Parameters	Compounds		
	1	**2**	**3**
Empirical formula	$C_{26}H_{23.57}N_3O_{5.29}$	$C_{19}H_{16}N_4O_6$	$C_{19}H_{17}N_3O_5$
Formula weight	462.63	396.36	367.35
Temperature/K	296(2)	296(2)	296(2)
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1/c$	Pbca	$P2_1/c$
a/Å	6.1137 (5)	11.3756(9)	12.995(3)
b/Å	24.053 (2)	15.4485(10)	14.110(3)
c/Å	15.7613 (12)	20.4842(17)	9.660(3)
α/°	90	90	90
β/°	92.357(3)	90	101.684(17)
γ/°	90	90	90
Volume/Å^3	2315.8(3)	3599.8(5)	1734.6(8)
Z	4	8	4
ρcalcg/cm^3	1.327	1.463	1.407
μ/mm^{-1}	0.094	0.112	0.104
F(000)	971.0	1648.0	768.0
Crystal size/mm^3	0.39 × 0.337 × 0.07	? × ? × ?	? × ? × ?
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.882 to 50	5.966 to 49.526	6.404 to 50.02
Index ranges	$-7 \le h \le 6$, $-28 \le k \le 28$, $-18 \le l \le 18$	$-13 \le h \le 13$, $-16 \le k \le 18$, $-24 \le l \le 24$	$-15 \le h \le 15$, $-16 \le k \le 16$, $-11 \le l \le 11$
Reflections collected	19171	40930	30719
Independent reflections	4067 [R_{int} = 0.0427, R_{sigma} = 0.0321]	3080 [R_{int} = 0.0721, R_{sigma} = 0.0266]	3026 [R_{int} = 0.0766, R_{sigma} = 0.0338]
Data/restraints/parameters	4067/109/363	3080/1/265	3026/1/247
Goodness-of-fit on F^2	1.071	1.116	1.112
Final R indexes [I>=2σ (I)]	R_1 = 0.0452, wR_2 = 0.1015	R_1 = 0.0478, wR_2 = 0.1030	R_1 = 0.0557, wR_2 = 0.1115
Final R indexes [all data]	R_1 = 0.0692, wR_2 = 0.1165	R_1 = 0.0690, wR_2 = 0.1187	R_1 = 0.0958, wR_2 = 0.1363
Largest diff. peak/hole / e Å^{-3}	0.15/-0.19	0.20/-0.21	0.17/-0.19

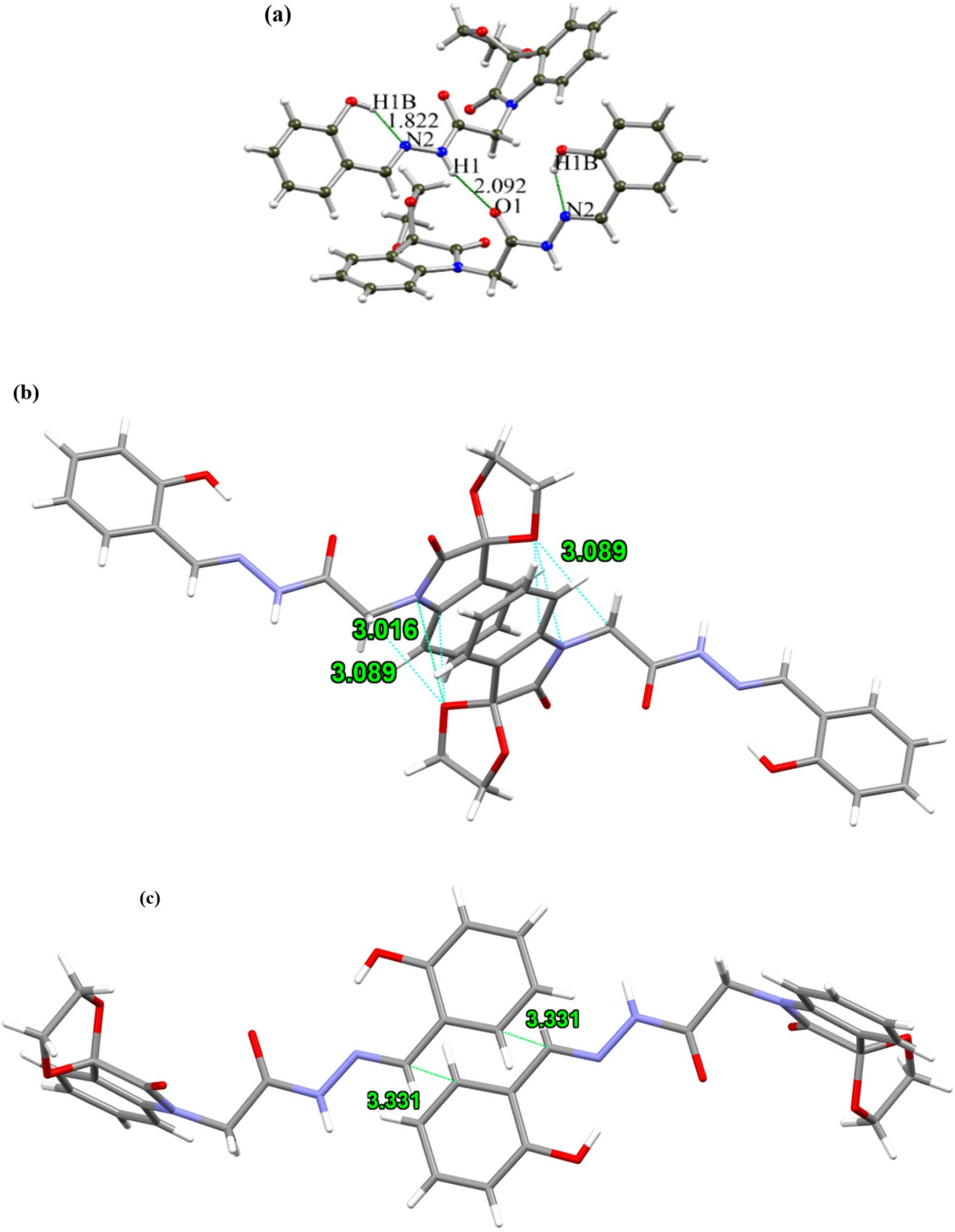
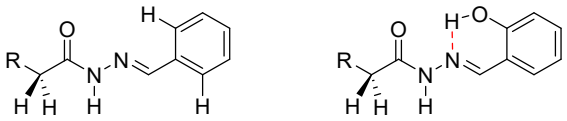


Fig. S3: Intermolecular interactions observed in solid state packing of compounds **3, a)** Showing NH···O [N(1)-H(1)···O(1) 2.092 Å]; **b)** showing self-complimentary intramolecular C-bond [C(9)···O(5) 3.089 Å] & O···N [C(5)···N(3) 3.089 Å] contacts; **c)** showing π···π contacts [C(2)···C(8) 3.331 Å]



Search A
20 hits
4 *trans*, 16 *cis*

Search B
20 Hits
16 *trans*, 4 *cis*

SEARCH A	SEARCH B
CIKSAR	ASOJEZ
ECESUC	IWEDIZ
EDUWEG	ABAJUK
HUYTIG	AXAFAH
MEWMUY	DOVTUF
MIHTOO	FOVYIZ
MUXTIK	HOFNEW
OFEFUB	HOFNEW01
PECVEA	KETTEJ
QAKPOJ	LAPYIM
QUYDAQ	LOFZUD
QUZCEU	MIMVIO
TUGNED	MIXXIB
VIKHAZ	PIHSOQ
XATKEK	SEDVII
XAZTAV	TICDUF
XAFWAF	UDUQIU
YAFXUA	WAKKAX
EYEKOK	YAHBIU
UZEVOM	YUPSEJ

Fig. S4. Two fragments used in the CSD searches A and B[1], and CSD search results[1]

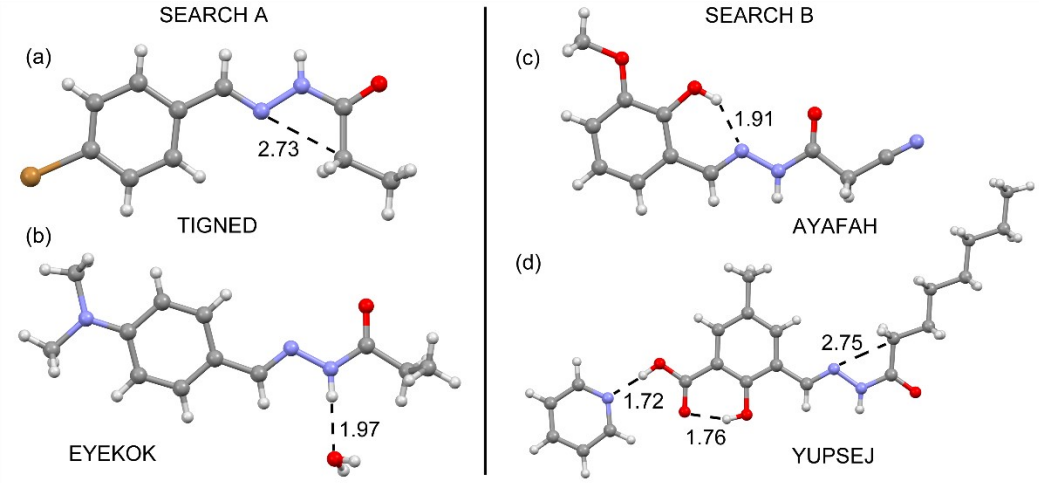


Fig. S5. Representative X-ray solid state structures retrieved from the CSD (searches A and B).[1] The CSD references codes are given. Distances in Å.

Atomic Coordinates:

Compound 1 (*cis*)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	6.017881	0.856179	-0.278951
2	6	0	4.669753	1.183170	-0.184571
3	6	0	4.258093	2.493897	-0.195662
4	6	0	5.235065	3.480630	-0.304656
5	6	0	6.577828	3.160838	-0.399314
6	6	0	6.977372	1.826920	-0.385404
7	1	0	3.224898	2.760685	-0.119958
8	1	0	4.933300	4.508878	-0.314006
9	1	0	7.309560	3.938143	-0.481808
10	1	0	8.013593	1.563795	-0.457151
11	6	0	6.150647	-0.631346	-0.231520
12	8	0	6.718443	-1.184244	-1.410656
13	6	0	7.340011	-2.453031	-1.032648
14	6	0	7.858820	-2.142001	0.376412
15	1	0	6.591716	-3.227296	-1.016862
16	1	0	8.116324	-2.666128	-1.745227
17	1	0	7.823387	-2.989605	1.037722
18	1	0	8.846363	-1.711729	0.353052
19	6	0	4.688582	-1.100825	-0.081306
20	8	0	4.304387	-2.245887	0.011367
21	6	0	2.469094	-0.053628	0.094295
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23	1	0	1.972765	0.733479	-0.449638
24	6	0	-1.338968	0.006861	1.160633
25	6	0	-2.378386	-0.041926	0.120447
26	6	0	-3.707294	-0.023430	0.498148
27	6	0	-2.050903	-0.106693	-1.231717
28	6	0	-4.682020	-0.070084	-0.476608
29	6	0	-3.041714	-0.152431	-2.192564
30	1	0	-1.019428	-0.120855	-1.515626
31	6	0	-4.372933	-0.134405	-1.817712
32	1	0	-2.783545	-0.202033	-3.229663
33	1	0	-5.156768	-0.169117	-2.540792
34	6	0	2.145782	0.036108	1.580610
35	8	0	3.001688	0.086058	2.444383
36	8	0	6.916215	-1.132025	0.861883
37	7	0	3.895773	0.011436	-0.100500
38	7	0	0.824034	0.044033	1.882580
39	1	0	0.533792	0.090967	2.841817
40	7	0	-0.114901	-0.003760	0.858921
41	1	0	-3.994168	0.026000	1.525812
42	1	0	-1.683605	0.051048	2.179838
43	6	0	-6.970926	-0.098024	-1.001763
44	1	0	-6.859079	0.744974	-1.651181
45	1	0	-6.856211	-1.000224	-1.565479
46	6	0	-8.370049	-0.068756	-0.358956
47	6	0	-9.006167	1.150866	-0.127822
48	6	0	-9.001526	-1.262353	-0.008283
49	6	0	-10.273794	1.177139	0.454332
50	1	0	-8.508658	2.091654	-0.404490
51	6	0	-10.268649	-1.236143	0.574170
52	1	0	-8.499906	-2.223841	-0.191017
53	6	0	-10.904800	-0.015959	0.805860
54	1	0	-10.774706	2.138864	0.637127
55	1	0	-10.766395	-2.176731	0.851368
56	1	0	-11.903692	0.004699	1.265299
57	8	0	-6.069571	-0.051036	-0.075074

Compound 1 (*trans*)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	6.144361	0.925560	-0.032056
2	6	0	4.868803	1.253907	-0.476529
3	6	0	4.407285	2.546078	-0.411715
4	6	0	5.260022	3.513897	0.113758
5	6	0	6.530658	3.193219	0.557446
6	6	0	6.981407	1.877656	0.484911
7	1	0	3.426861	2.812380	-0.746974
8	1	0	4.917985	4.527679	0.173411
9	1	0	7.166947	3.955815	0.957412
10	1	0	7.962875	1.614368	0.824767
11	6	0	6.353227	-0.541597	-0.223941
12	8	0	7.416302	-0.846790	-1.115011
13	6	0	7.907146	-2.177585	-0.758023
14	6	0	7.734939	-2.178872	0.765736
15	1	0	7.289155	-2.924493	-1.226912
16	1	0	8.930172	-2.249804	-1.080491
17	1	0	7.478992	-3.145358	1.162530
18	1	0	8.597965	-1.772170	1.266307
19	6	0	5.010875	-1.002912	-0.829207
20	8	0	4.711114	-2.132347	-1.146670
21	6	0	2.866108	0.032984	-1.445328
22	1	0	2.773727	-0.852087	-2.060662
23	1	0	2.627553	0.897972	-2.047801
24	6	0	-1.608720	-0.096248	-0.098908
25	6	0	-2.715249	-0.227613	0.863409
26	6	0	-4.017696	-0.144494	0.410093
27	6	0	-2.473832	-0.431263	2.220025
28	6	0	-5.051728	-0.264722	1.315406
29	6	0	-3.522805	-0.549776	3.110282
30	1	0	-1.461827	-0.494197	2.561424
31	6	0	-4.827819	-0.466259	2.659775
32	1	0	-3.330113	-0.706147	4.151039
33	1	0	-5.655426	-0.553913	3.327433
34	6	0	1.892479	-0.089369	-0.274480
35	8	0	2.254305	-0.242343	0.872485
36	8	0	6.601248	-1.275091	0.972550
37	7	0	4.222756	0.105410	-0.971154
38	7	0	0.594774	-0.024610	-0.671003
39	1	0	0.341931	0.106964	-1.631895
40	7	0	-0.408615	-0.159029	0.283966
41	1	0	-4.240326	0.011222	-0.622919
42	1	0	-1.886172	0.055506	-1.128518
43	6	0	-6.596718	0.013270	-0.430906
44	1	0	-6.138634	0.934275	-0.725538
45	1	0	-6.158753	-0.794377	-0.979352
46	6	0	-8.107142	0.074039	-0.725057
47	6	0	-8.777628	1.296383	-0.681810
48	6	0	-8.804749	-1.093640	-1.035350
49	6	0	-10.145953	1.351240	-0.948551
50	1	0	-8.227798	2.216808	-0.437578
51	6	0	-10.172839	-1.038942	-1.301573
52	1	0	-8.275755	-2.057204	-1.069778
53	6	0	-10.843686	0.183868	-1.257798
54	1	0	-10.674412	2.314958	-0.913620
55	1	0	-10.723175	-1.959231	-1.545484
56	1	0	-11.922338	0.226938	-1.467443
57	8	0	-6.411259	-0.174823	0.835438

Compound 2 (*cis*)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	4.297339	0.861556	-0.342757
2	6	0	2.948770	1.183991	-0.239430
3	6	0	2.530804	2.492439	-0.268729
4	6	0	3.501855	3.481573	-0.405370
5	6	0	4.845022	3.166306	-0.509042
6	6	0	5.251014	1.834664	-0.476391
7	1	0	1.497231	2.755792	-0.186449
8	1	0	3.195134	4.508119	-0.429234
9	1	0	5.572129	3.945387	-0.612905
10	1	0	6.287639	1.575056	-0.554812
11	6	0	4.437660	-0.624302	-0.271042
12	8	0	4.995343	-1.194984	-1.446525
13	6	0	5.626955	-2.454177	-1.053388
14	6	0	6.159424	-2.116385	0.344370
15	1	0	4.882553	-3.231452	-1.016092
16	1	0	6.396552	-2.676068	-1.770552
17	1	0	6.135134	-2.952539	1.020590
18	1	0	7.144608	-1.682090	0.302858
19	6	0	2.979540	-1.097759	-0.096875
20	8	0	2.601800	-2.242778	0.019756
21	6	0	0.757132	-0.057793	0.084648
22	1	0	0.400502	-1.012162	-0.273400
23	1	0	0.251247	0.717489	-0.467405
24	6	0	-3.039472	0.003844	1.191027
25	6	0	-4.089787	-0.067719	0.163177
26	6	0	-5.414624	-0.048725	0.554896
27	6	0	-3.776579	-0.154445	-1.191137
28	6	0	-6.399556	-0.116724	-0.408276
29	6	0	-4.777450	-0.221360	-2.140243
30	1	0	-2.748165	-0.168832	-1.485930
31	6	0	-6.104626	-0.202896	-1.751341
32	1	0	-4.530230	-0.287773	-3.179069
33	1	0	-6.896028	-0.253719	-2.465166
34	6	0	0.449420	0.056245	1.572608
35	8	0	1.314330	0.125073	2.426052
36	8	0	5.217323	-1.102441	0.822491
37	7	0	2.181306	0.010380	-0.126709
38	7	0	-0.869023	0.063389	1.888716
39	1	0	-1.149139	0.125636	2.850089
40	7	0	-1.818688	-0.006435	0.876283
41	1	0	-5.690647	0.017222	1.584602
42	1	0	-3.373321	0.064138	2.212993
43	7	0	-7.782779	-0.097032	0.007897
44	8	0	-8.659810	-0.161689	-0.873811
45	8	0	-8.024981	-0.016471	1.227832

Compound 2 (*trans*)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	4.523378	0.892755	0.216674
2	6	0	3.316237	1.222715	-0.388596
3	6	0	2.872438	2.522290	-0.421027
4	6	0	3.672316	3.495933	0.172411
5	6	0	4.874798	3.173676	0.776065
6	6	0	5.308435	1.850606	0.800280
7	1	0	1.944073	2.790036	-0.880371
8	1	0	3.342975	4.515557	0.158119
9	1	0	5.471390	3.940857	1.225397
10	1	0	6.237334	1.586012	1.264215
11	6	0	4.728660	-0.582643	0.098121
12	8	0	5.885684	-0.931571	-0.648085
13	6	0	6.307273	-2.255950	-0.192381
14	6	0	5.953312	-2.203743	1.298755
15	1	0	5.737388	-3.010010	-0.708390
16	1	0	7.360237	-2.352413	-0.386661
17	1	0	5.635074	-3.152894	1.692311
18	1	0	6.756799	-1.791823	1.886565
19	6	0	3.461028	-1.046359	-0.649636
20	8	0	3.182295	-2.181789	-0.964863
21	6	0	1.423809	-0.003654	-1.552532
22	1	0	1.390879	-0.907621	-2.146065
23	1	0	1.274164	0.843651	-2.206571
24	6	0	-3.181885	-0.028705	-0.752167
25	6	0	-4.398062	-0.113083	0.073369
26	6	0	-5.635025	-0.028136	-0.536121
27	6	0	-4.324840	-0.274165	1.454982
28	6	0	-6.772204	-0.104254	0.241245
29	6	0	-5.475013	-0.348880	2.215553
30	1	0	-3.362388	-0.338885	1.917761
31	6	0	-6.714854	-0.263406	1.608527
32	1	0	-5.411412	-0.472691	3.276393
33	1	0	-7.618033	-0.317676	2.173953
34	6	0	0.314660	-0.073764	-0.504353
35	8	0	0.533447	-0.192834	0.682155
36	8	0	4.818609	-1.278694	1.338500
37	7	0	2.714728	0.066830	-0.920756
38	7	0	-0.924731	-0.005317	-1.056338
39	1	0	-1.058054	0.097191	-2.044403
40	7	0	-2.037699	-0.094351	-0.225558
41	1	0	-5.729284	0.095675	-1.592866
42	1	0	-3.331036	0.091982	-1.812022
43	7	0	-8.062512	-0.012677	-0.401789
44	8	0	-9.079209	-0.080594	0.314339
45	8	0	-8.090247	0.129762	-1.639708

Compound 3 (*cis*)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	3.507185	0.867477	-0.335994
2	6	0	2.157621	1.187537	-0.240057
3	6	0	1.735630	2.493975	-0.289615
4	6	0	2.703944	3.483930	-0.438990
5	6	0	4.048234	3.171170	-0.535321
6	6	0	4.458184	1.841445	-0.482190
7	1	0	0.701154	2.755546	-0.213024
8	1	0	2.394162	4.509049	-0.478612
9	1	0	4.773207	3.950817	-0.649263
10	1	0	5.495720	1.583847	-0.554769
11	6	0	3.652356	-0.616730	-0.242022
12	8	0	4.214453	-1.202780	-1.407668
13	6	0	4.850179	-2.453586	-0.994639
14	6	0	5.377949	-2.093323	0.399287
15	1	0	4.108813	-3.233259	-0.947855
16	1	0	5.622371	-2.682754	-1.706690
17	1	0	5.354999	-2.919528	1.087666
18	1	0	6.361553	-1.655895	0.353859
19	6	0	2.195539	-1.092527	-0.063954
20	8	0	1.820080	-2.236257	0.069577
21	6	0	-0.029463	-0.057389	0.099360
22	1	0	-0.376837	-1.023268	-0.237860
23	1	0	-0.532547	0.708218	-0.470058
24	6	0	-3.852389	0.013954	1.284998
25	6	0	-4.970896	-0.082139	0.347067
26	6	0	-6.268782	-0.030244	0.853069
27	6	0	-4.780846	-0.224143	-1.028049
28	6	0	-7.361288	-0.115988	0.019909
29	6	0	-5.883535	-0.310577	-1.865272
30	6	0	-7.159413	-0.257076	-1.348390
31	1	0	-5.712618	-0.419142	-2.915770
32	6	0	-0.341824	0.090210	1.582511
33	8	0	0.524050	0.202042	2.431572
34	8	0	4.430834	-1.075969	0.860243
35	7	0	1.393720	0.012908	-0.112124
36	7	0	-1.656117	0.082147	1.905772
37	1	0	-1.924277	0.172360	2.868312
38	7	0	-2.640170	-0.014553	0.918411
39	1	0	-4.121434	0.112210	2.323647
40	1	0	-8.000199	-0.325181	-2.009316
41	1	0	-8.352800	-0.074562	0.421296
42	1	0	-6.410071	0.078943	1.910779
43	8	0	-3.546218	-0.284121	-1.599243
44	1	0	-2.839134	-0.220101	-0.932841

Compound 3 (*trans*)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	3.535873	-0.205127	-0.604223
2	6	0	2.829985	-1.248012	-0.015891
3	6	0	3.086841	-2.555312	-0.344956
4	6	0	4.085459	-2.801139	-1.285192
5	6	0	4.794474	-1.768708	-1.871991
6	6	0	4.515406	-0.447987	-1.529111
7	1	0	2.540612	-3.364951	0.091118
8	1	0	4.302051	-3.814686	-1.556893
9	1	0	5.556412	-1.984209	-2.592585
10	1	0	5.055521	0.361450	-1.977310
11	6	0	3.022224	1.090190	-0.061429
12	8	0	4.002526	1.844769	0.631302
13	6	0	3.592913	3.248547	0.562766
14	6	0	2.941426	3.321358	-0.823903
15	1	0	2.882370	3.451644	1.346071
16	1	0	4.475591	3.853995	0.661373
17	1	0	2.107556	3.999336	-0.864841
18	1	0	3.660581	3.545392	-1.593906
19	6	0	1.919108	0.631034	0.913607
20	8	0	1.186924	1.344201	1.577404
21	6	0	1.044203	-1.501987	1.804243
22	1	0	1.002324	-0.989678	2.755451
23	1	0	1.466689	-2.481163	1.943945
24	6	0	-2.970371	0.563303	0.497285
25	6	0	-4.326744	0.547539	-0.055539
26	6	0	-5.023511	1.746891	-0.175616
27	6	0	-4.935097	-0.643867	-0.462684
28	6	0	-6.301610	1.779846	-0.688560
29	6	0	-6.223095	-0.604620	-0.978634
30	6	0	-6.898844	0.591135	-1.090678
31	1	0	-6.671805	-1.526560	-1.284564
32	6	0	-0.368648	-1.662913	1.251696
33	8	0	-0.850792	-2.741848	0.965185
34	8	0	2.443547	1.958234	-1.029824
35	7	0	1.889078	-0.727693	0.903239
36	7	0	-1.025095	-0.481714	1.142502
37	1	0	-0.593883	0.387647	1.407022
38	7	0	-2.308732	-0.507492	0.615577
39	1	0	-2.577221	1.521805	0.792758
40	1	0	-7.892764	0.600146	-1.491671
41	1	0	-6.826796	2.708740	-0.775773
42	1	0	-4.549453	2.656539	0.139240
43	8	0	-4.322914	-1.856363	-0.378216
44	1	0	-3.418806	-1.780117	-0.002597

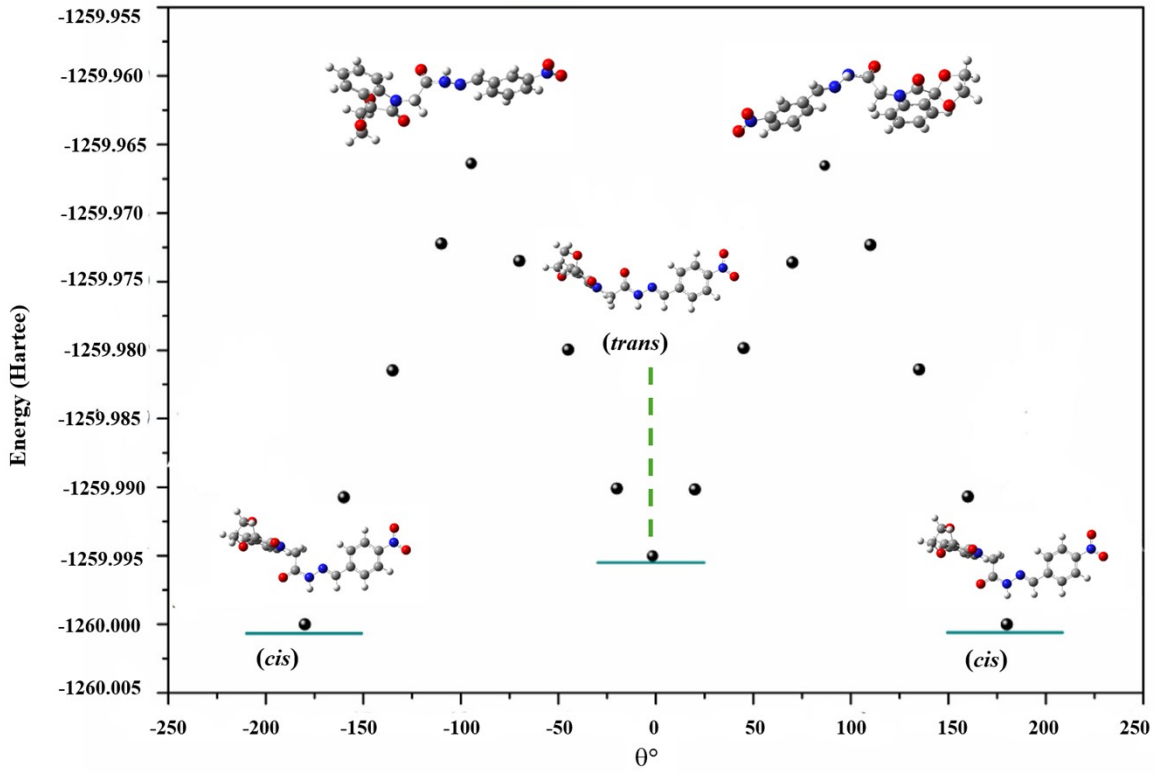

Fig. S6: PES scan of compound **2**

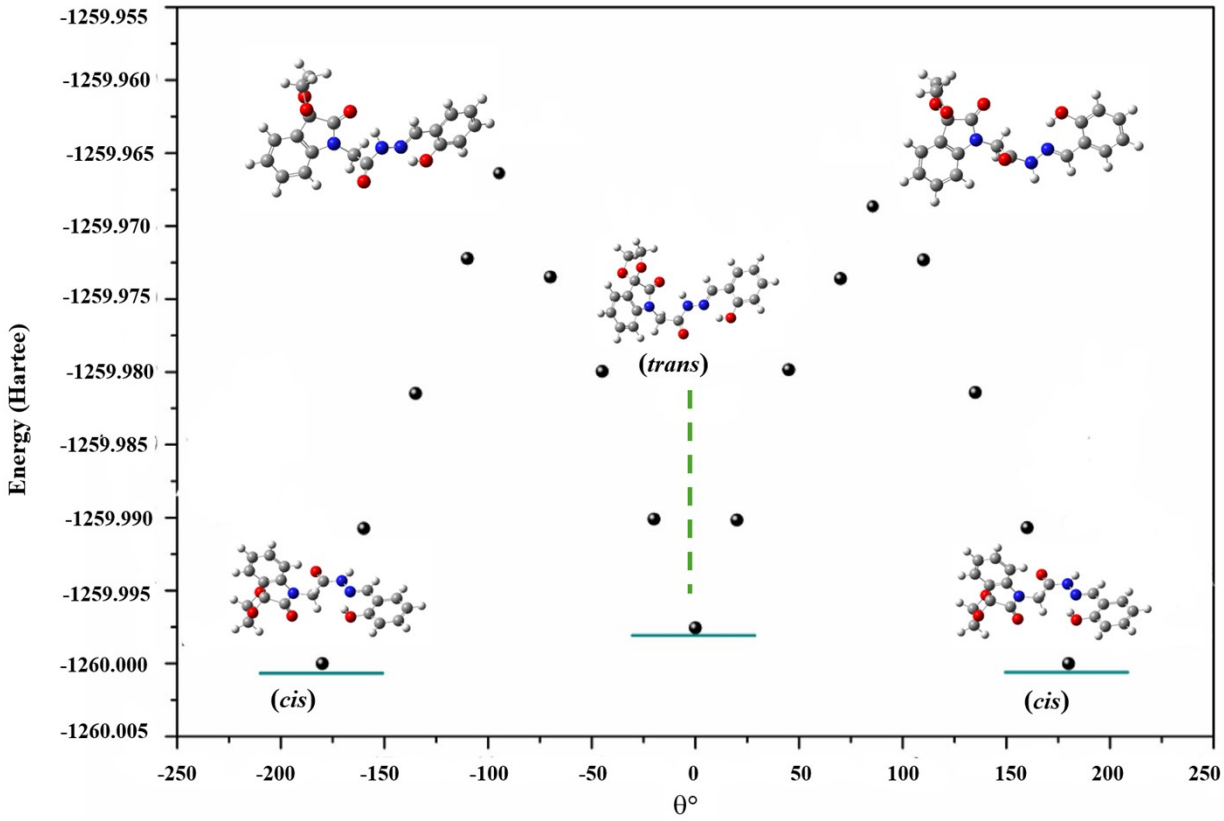

Fig. S7: PES scan of compound **3**

References:

1. M. M. Naseer, M. Hussain, A. Bauzá, K. M. Lo and A. Frontera, Intramolecular noncovalent carbon bonding interaction stabilizes the *cis* conformation in acylhydrazones, *ChemPlusChem*, 2018, **83**, 881-885.

Copies of LC-MS Spectra (1-3)

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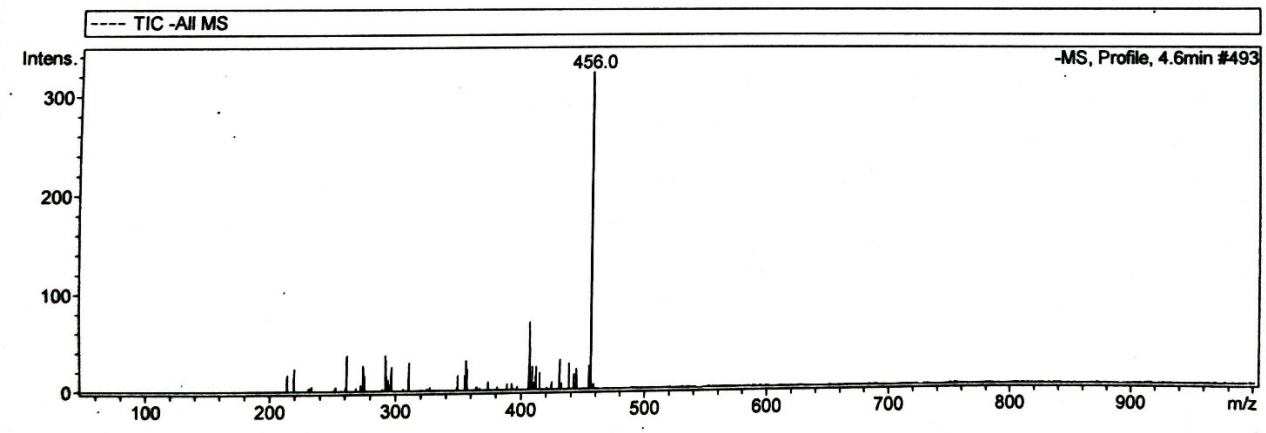

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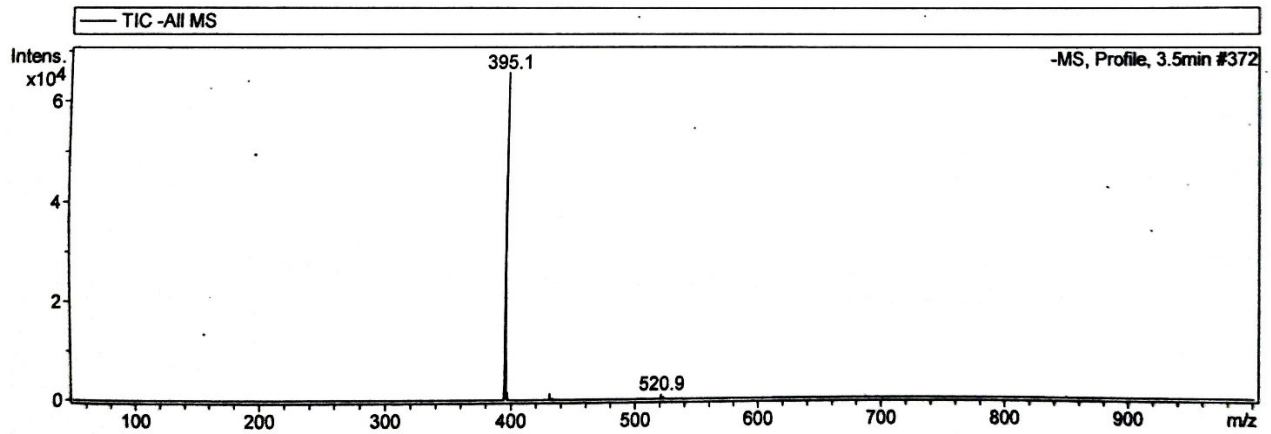

3: