

Supplementary Information:

Influence of the Local Chemical Environment in the Formation of Multicomponent Crystals of L- Tryptophan with N- Heterocyclic Carboxylic Acids: Unusual Formation of Double Zwitterions

Babulal Das*, Hemant Kumar Srivastava*

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781039, Assam,

India, Email: dasbld@iitg.ernet.in, hemantkrsri@gmail.com Tel: +913612582337;

+913612582302; Fax: +913612582349.

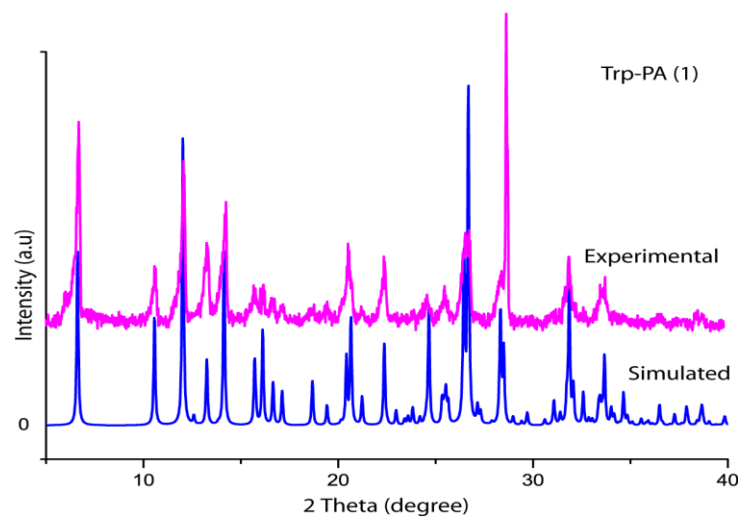


Fig. S1(a). PXRD pattern of Trp-PA (1)

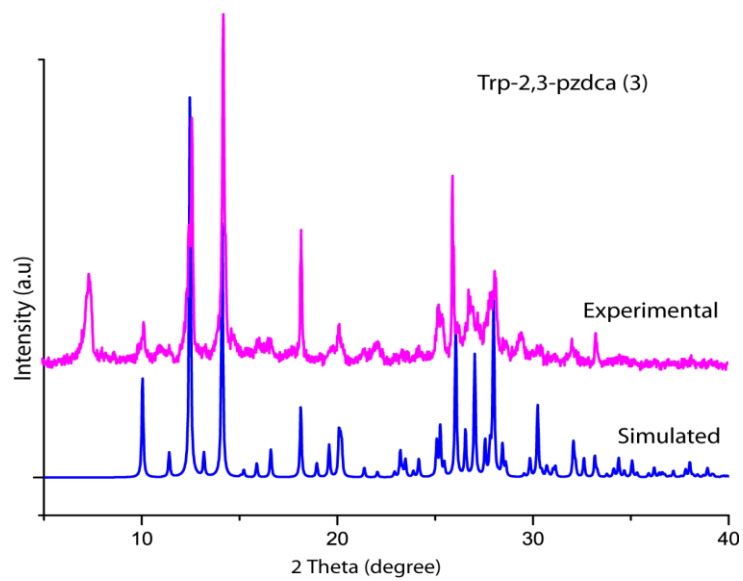


Fig. S1(b). PXRD pattern of Trp-2,3-pzdca (3)

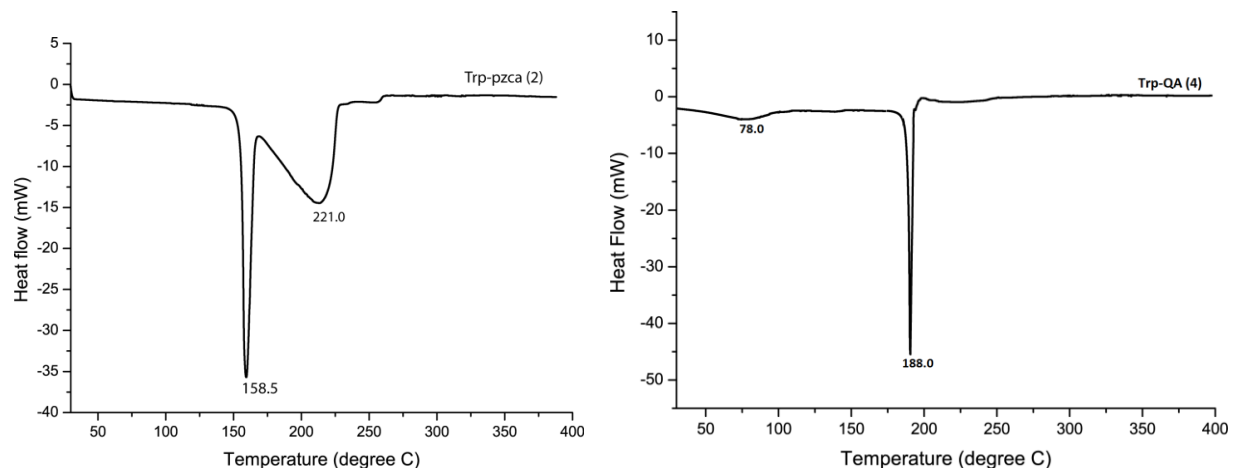


Fig. S2. DSC plots of MCCs 2 and 4

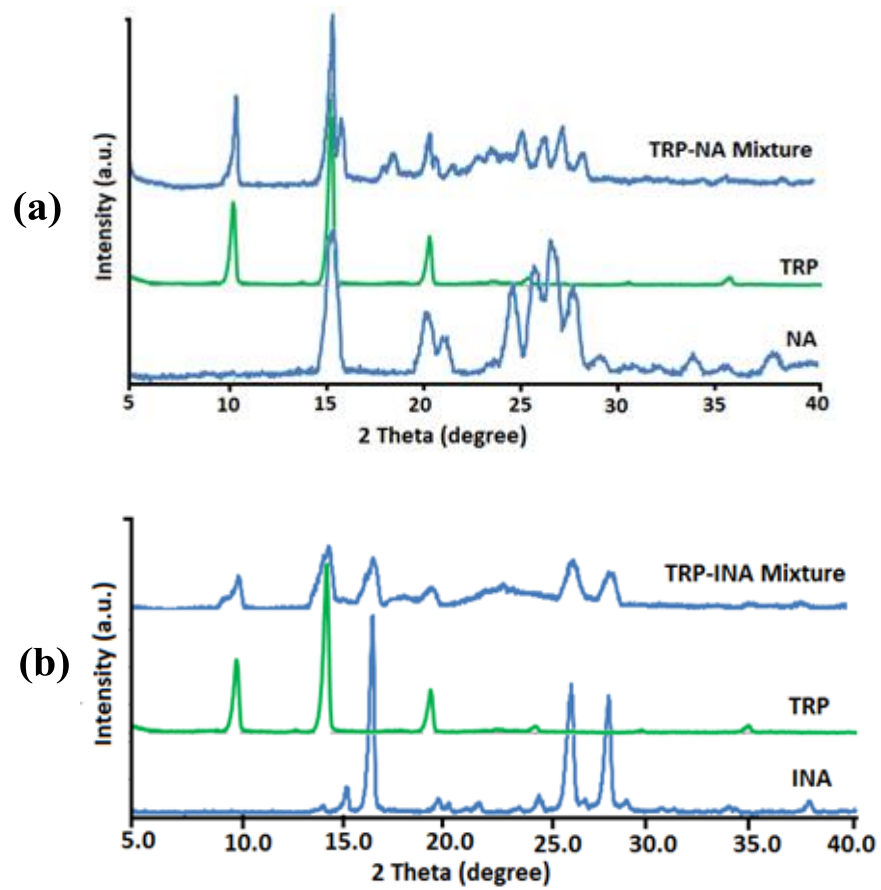


Fig. S3. PXRD pattern of TRP-NA mixture (a) and TRP-INA mixture (b)

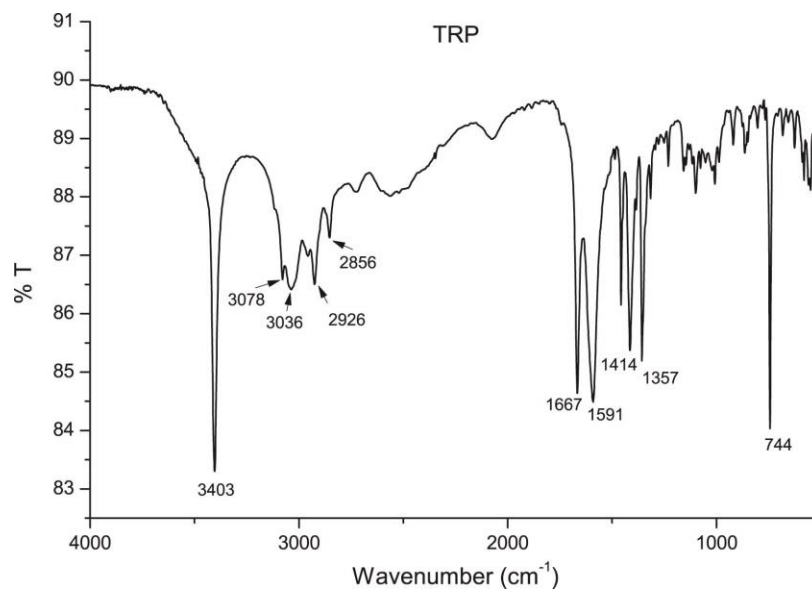


Fig. S4. FTIR spectrum of commercial TRP (Aldrich)

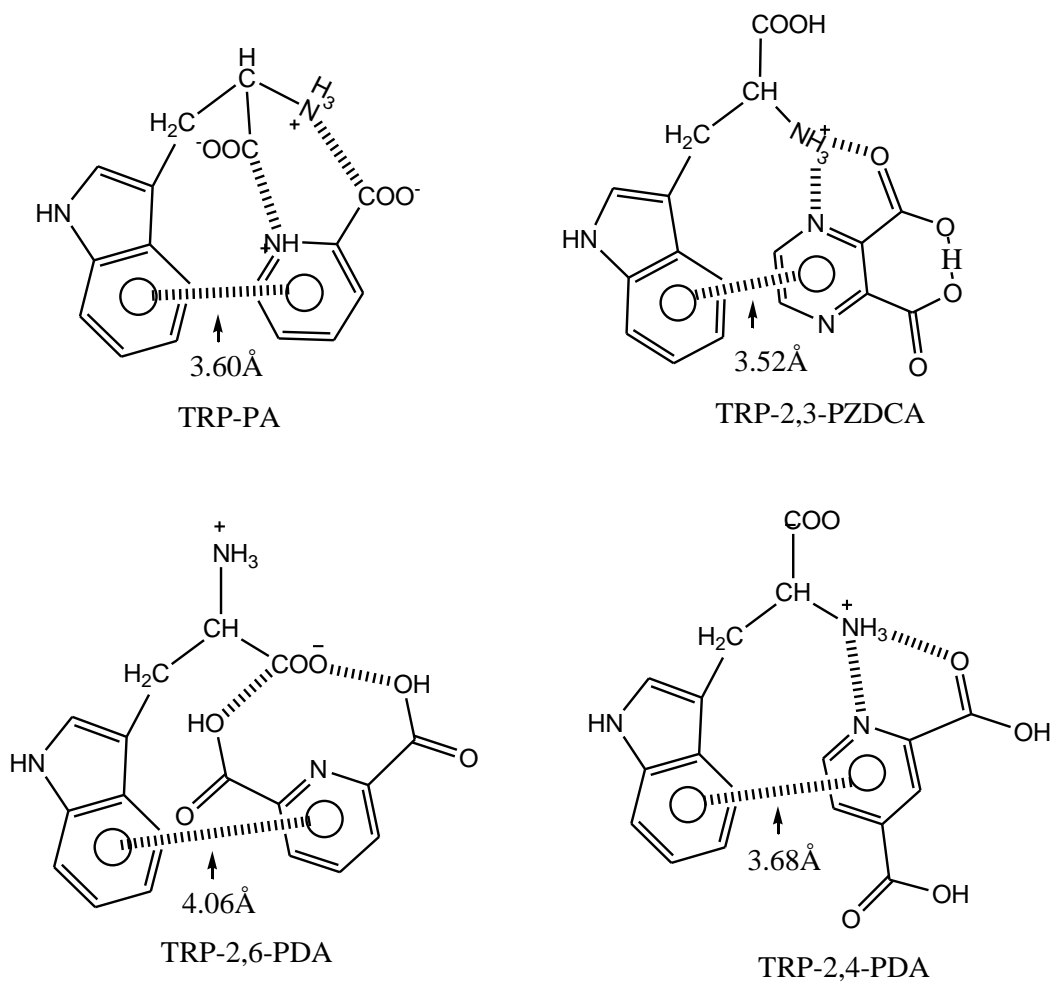


Fig. S5. Basic supramolecular synthons and π - π stacking interactions observed in TRP and N-heterocyclic acids

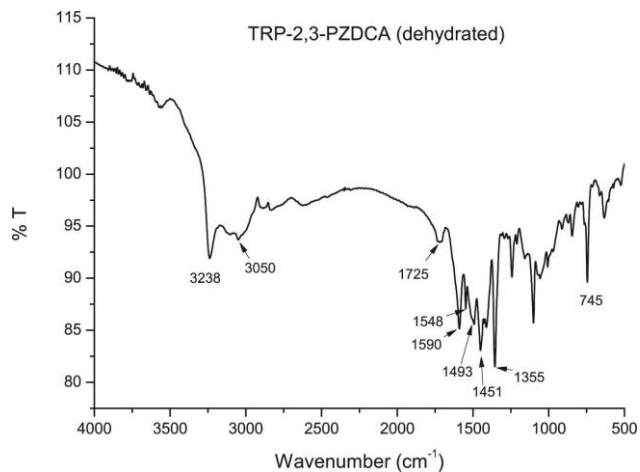
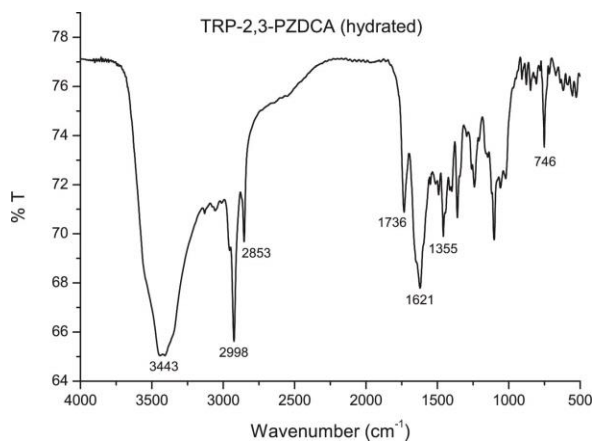
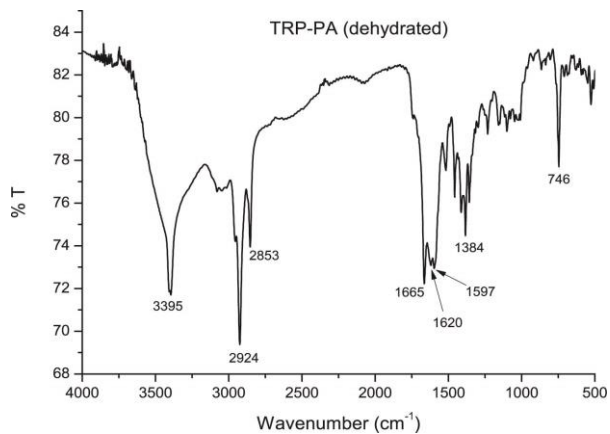
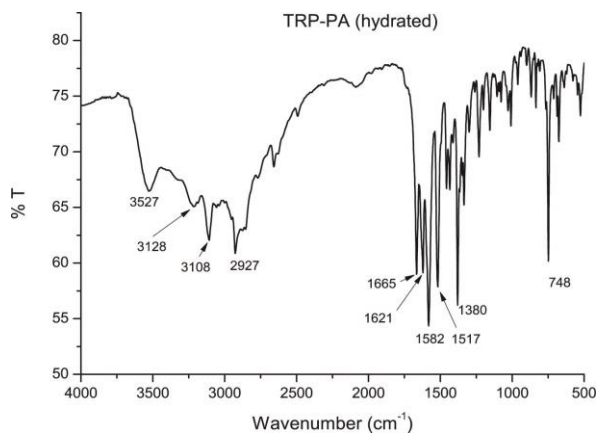


Fig. S6. FTIR spectra of TRP-PA (1) and TRP-2,3-PZDCA (3) and their dehydrated form

Table S1: The pKa value of TRP and the acids (at 25 °C)

N-heterocyclic acids	pKa	Co-crystallization
2-picolinic acid (PA)	pKa ₁ ~ 1.07; pKa ₂ ~ 5.25	Yes
Nicotinic acid (NA)	pKa ₁ ~ 2.0; pKa ₂ ~ 4.85	No
Isonicotinic acid (INA)	pKa ~ 4.96	No
Pyrazinecarboxylic acid (PZCA)	pKa ~ 2.91	Yes
2,3-Pyrazinedicarboxylic acid (2,3-PZDCA)	pKa ₁ ~ 0.8 ; pKa ₂ ~ 2.84	Yes
2-quinalidic acid (QA)	pKa ~ 1.01	Yes
3-quinolinecarboxylic acid (3-QA)	pKa ~ 2.17	No
L-tryptophan (TRP)	α – CO ₂ H ~ 2.38, α – NH ₃ ⁺ ~ 9.39	

Table S2: Details of total energy and interaction energy (IE) of the crystal systems:

Crystal system	Solvent	Gas	Stability (kJ/mol)		All	Part-1	Part-2	part1+part2	IE (kJ/mol)
			Solvent	Gas					
TRP-PA	-1123.2571	-1123.2215	0.0	0.0	-1123.2571	-686.36888	-436.85733	-1123.2262	81.17
TRP-NA	-1123.2501	-1123.2134	-17.99	-21.34	-1123.2501	-686.37130	-436.86520	-1123.2365	35.98
TRP-INA	-1123.2484	-1123.2100	-23.01	-30.54	-1123.2484	-686.37142	-436.86361	-1123.2350	35.15
TRP-QA	-1276.9028	-1276.8659	0.0	0.0	-1276.9028	-686.36842	-590.50279	-1276.8712	82.84
TRP-3-QA	-1276.8917	-1276.8552	-29.29	-28.03	-1276.8917	-686.37137	-590.50668	-1276.8781	35.98
TRP-PZCA	-1139.2800	-1139.2456	-	-	-1139.2800	-686.36837	-452.87727	-1139.2456	89.96
TRP-2,3-PZDCA	-1327.8527	-1327.8226	-	-	-1327.8527	-686.82036	-641.00269	-1327.8230	77.82

TRP-PA, TRP-QA, TRP-PZCA and TRP-2,3-PZDCA was experimentally observed. TRP-NA, TRP-INA and TRP-3-QA are hypothetical structures. Stability is the difference in total energies of experimentally observed and hypothetical structures. IE is calculated using the equation $IE = (EC) - (EP1+EP2)$. Where 'EC' is the total energy of the complex, 'EP1' is the total energy of amino acid and 'EP2' is the total energy of the cofomers. 'Solvent' indicates that the given values are obtained from calculations in water medium using IEF-PCM theory. 'Gas' indicates that the given values are obtained from gas phase calculations.

Table S3a: XYZ Coordinates of Crystal 1 (TRP-PA)

1	8	1.221860	-2.457705	-0.696908
2	8	2.376682	-1.354978	-2.304648
3	7	2.501315	-1.434628	1.307874
4	1	1.606770	-0.956866	1.563325
5	1	3.181513	-1.303353	2.061059
6	1	2.236894	-2.424064	1.244636
7	6	2.113007	-1.656333	-1.128817
8	7	0.728365	2.746340	1.426570
9	1	0.398859	3.318097	2.190384
10	6	2.049024	1.355264	0.231359
11	6	0.077783	2.556971	0.226081
12	6	0.444456	1.343763	-1.855531
13	1	1.031018	0.666163	-2.468577
14	6	0.882628	1.682194	-0.559991
15	6	3.031090	-1.026623	-0.039416
16	1	4.010770	-1.505670	-0.133941
17	6	-1.133240	3.084924	-0.238135
18	1	-1.730788	3.748390	0.380987
19	6	1.903667	2.029385	1.423416
20	1	2.567024	2.064561	2.277368
21	6	3.229361	0.498633	-0.139230
22	1	4.083002	0.776921	0.490550
23	1	3.531315	0.679050	-1.176174
24	6	-1.538402	2.730101	-1.520185
25	1	-2.473090	3.122426	-1.911902
26	6	-0.755698	1.869816	-2.320463
27	1	-1.102095	1.613415	-3.318368
28	8	-0.045885	-1.035621	2.158341
29	8	-1.948205	-0.115672	2.985100
30	7	-1.312469	-1.746236	-0.112332
31	6	-1.265576	-0.709910	2.133049
32	6	-2.018787	-1.135558	0.860162
33	6	-1.848317	-2.167855	-1.272083
34	1	-1.154757	-2.630886	-1.962346
35	6	-3.379632	-0.932609	0.659436
36	1	-3.940663	-0.439729	1.443287
37	6	-3.975478	-1.363383	-0.525769
38	1	-5.037944	-1.211150	-0.687292
39	6	-3.201589	-1.990407	-1.507937
40	1	-3.636106	-2.332717	-2.439339
41	1	-0.286360	-1.899338	0.010041

Table S3b: XYZ Coordinates of Crystal 2 (TRP-PZCA)

1	8	2.151400	-1.553378	-2.134580
2	8	3.663816	-0.110570	-1.328634
3	7	1.510657	-2.618568	0.082884
4	1	0.636731	-2.153734	0.336735
5	1	1.609151	-3.442805	0.669427
6	1	1.625844	-2.272815	-1.668230
7	6	2.880134	-1.022761	-1.144814
8	7	-0.597277	0.797243	2.278309
9	1	-1.471575	0.808653	2.782668
10	6	1.436345	0.107035	1.568499
11	6	-0.132056	1.800583	1.455205
12	6	1.854435	2.267146	0.125057
13	1	2.826399	1.979453	-0.263307
14	6	1.151011	1.398927	0.982042
15	6	2.668762	-1.727289	0.210305
16	1	3.556588	-2.363218	0.323625
17	6	-0.717447	3.020871	1.096788
18	1	-1.697597	3.305092	1.470249
19	6	0.346007	-0.205831	2.348137
20	1	0.167441	-1.078875	2.960377
21	6	2.667994	-0.741891	1.409369
22	1	2.806259	-1.345365	2.313875
23	1	3.557855	-0.109875	1.314011
24	6	0.003833	3.854981	0.249068
25	1	-0.421123	4.810098	-0.047960
26	6	1.277830	3.481589	-0.230542
27	1	1.814321	4.156533	-0.892459
28	8	-1.625990	-2.572969	0.994392
29	8	-3.695452	-1.690029	1.148196
30	7	-1.125128	-0.958535	-1.216925
31	6	-2.479150	-1.812089	0.583698
32	6	-2.313308	-0.903239	-0.597679
33	6	-0.963080	-0.155995	-2.268255
34	1	-0.001328	-0.192363	-2.772468
35	6	-3.332102	-0.048839	-1.035492
36	1	-4.290083	-0.013989	-0.526693
37	6	-1.983716	0.697782	-2.705232
38	1	-1.834175	1.344796	-3.566113
39	7	-3.170903	0.756191	-2.093899
40	1	-3.731522	-2.307489	1.903997

Table S3c: XYZ Coordinates of Crystal **3** (TRP-2,3-PZDCA)

1	8	2.782098	9.355596	-0.925766
2	8	4.285785	4.600781	1.401916
3	8	4.429693	7.911934	-1.360217
4	8	4.879207	5.668915	-0.452638
5	1	4.827929	6.636052	-0.843157
6	7	3.503956	9.245672	1.742060
7	7	4.376092	6.865940	2.836349
8	6	3.631296	8.513473	-0.576112
9	6	4.453914	5.644202	0.793468
10	6	3.784460	8.206108	0.931450
11	6	4.207467	6.980616	1.507574
12	6	3.695927	9.127667	3.054535
13	1	3.467730	9.993659	3.669238
14	6	4.156877	7.930839	3.601031
15	1	4.333232	7.828921	4.668841
16	8	2.272543	12.387282	3.120886
17	8	0.149971	13.162239	3.182188
18	1	0.440614	13.492645	4.055292
19	7	2.033803	11.402223	0.640967
20	1	2.698682	12.141416	0.397178
21	1	1.894106	10.819662	-0.204485
22	1	2.553597	10.721920	1.256770
23	7	0.050122	8.379091	3.952438
24	6	1.178350	12.521199	2.614360
25	6	0.795136	11.971693	1.244274
26	1	0.481045	12.808553	0.614155
27	6	0.038203	8.371869	1.696373
28	6	0.098954	7.761879	0.428969
29	1	0.019354	8.355179	-0.477099
30	6	-0.149995	9.728706	2.155449
31	6	-0.145272	9.674566	3.532915
32	1	-0.286265	10.464062	4.258114
33	6	0.277880	6.386130	0.349737
34	1	0.325352	5.907157	-0.624521
35	6	0.158896	7.552513	2.854691
36	6	0.344319	6.166358	2.779698
37	1	0.436214	5.562141	3.677876
38	6	-0.369270	10.951283	1.304703
39	1	-1.236995	11.519329	1.656423
40	1	-0.599576	10.657371	0.275178
41	6	0.402108	5.595641	1.513475
42	1	0.544365	4.522795	1.417696
43	1	0.085094	8.082520	4.916928

Table S3d: XYZ Coordinates of Crystal **4** (TRP-QA)

1	8	-1.203003	-2.682609	-0.326579
2	8	-2.132728	-2.674404	1.739705
3	7	-3.141624	-1.426904	-1.502132
4	1	-2.435304	-0.668407	-1.654394
5	1	-3.999706	-1.193705	-2.008765
6	1	-2.705940	-2.253405	-1.924287
7	6	-2.111521	-2.416026	0.524543
8	7	-2.364936	2.807138	-0.057787
9	1	-2.358793	3.692578	-0.542533
10	6	-3.031959	0.750058	0.598868
11	6	-1.420811	2.383834	0.852991
12	6	-1.008815	0.431320	2.252291
13	1	-1.272901	-0.566389	2.590013
14	6	-1.807424	1.084643	1.292979
15	6	-3.387391	-1.732885	-0.049985
16	1	-4.186159	-2.481333	-0.032607
17	6	-0.274699	3.029851	1.332583
18	1	0.001170	4.019811	0.979725
19	6	-3.324283	1.830322	-0.203576
20	1	-4.163896	1.984924	-0.868139
21	6	-3.875075	-0.490595	0.721246
22	1	-4.896570	-0.260738	0.395079
23	1	-3.943107	-0.813826	1.765358
24	6	0.493372	2.357222	2.276622
25	1	1.389398	2.829879	2.669954
26	6	0.127931	1.071965	2.732637
27	1	0.750849	0.575118	3.471990
28	8	-1.050407	0.006898	-2.466361
29	8	0.333795	1.658738	-3.166551
30	7	0.868822	-1.052306	-0.900026
31	6	0.042231	0.643744	-2.509275
32	6	1.162808	0.063213	-1.639171
33	6	1.734638	-1.659762	-0.099718
34	1	1.358021	-2.526454	0.431071
35	6	2.429414	0.584301	-1.557696
36	1	2.655909	1.466822	-2.144578
37	6	3.412723	-0.014324	-0.728516
38	6	3.049683	-1.178716	0.028114
39	1	-0.090855	-1.458631	-0.941966
40	6	4.003494	-1.806830	0.872602
41	6	4.734467	0.486141	-0.612300
42	6	5.276562	-1.293232	0.960959
43	6	5.640533	-0.142294	0.214527
44	1	3.714310	-2.687195	1.438560
45	1	6.011483	-1.766981	1.603897
46	1	6.651017	0.245997	0.299640
47	1	5.018245	1.366405	-1.180952

Table S3e: XYZ Coordinates of TRP-NA

1	8	2.806884	-2.024066	-1.482783
2	8	4.258600	-0.316607	-1.122176
3	7	1.980504	-2.210656	0.921208
4	1	1.057653	-1.724589	0.805606
5	1	1.972182	-2.748678	1.790337
6	1	2.048433	-2.827706	0.089101
7	6	3.429666	-1.180466	-0.772522
8	7	-0.253661	1.675710	1.911327
9	1	-1.091670	1.887467	2.432512
10	6	1.761393	0.787149	1.399382
11	6	0.070938	2.181495	0.670805
12	6	1.908368	2.016894	-0.922266
13	1	2.864398	1.600296	-1.225397
14	6	1.339006	1.640349	0.309882
15	6	3.169786	-1.304157	0.768811
16	1	4.021160	-1.859463	1.177154
17	6	-0.629225	3.070226	-0.154291
18	1	-1.595528	3.469365	0.141931
19	6	0.760356	0.848679	2.342323
20	1	0.699715	0.369465	3.310429
21	6	3.042038	0.012201	1.555154
22	1	3.190327	-0.205360	2.619574
23	1	3.899240	0.613357	1.233289
24	6	-0.039744	3.422937	-1.363601
25	1	-0.556008	4.111107	-2.027770
26	6	1.216222	2.901375	-1.742359
27	1	1.646568	3.196675	-2.695982
28	7	-0.645690	-1.451961	-0.039784
29	6	-1.840944	-1.293432	0.535490
30	6	-0.574642	-1.393979	-1.381710
31	1	0.419246	-1.523474	-1.805632
32	6	-3.016708	-1.075861	-0.192207
33	6	-2.934540	-1.020558	-1.588916
34	1	-3.825452	-0.853955	-2.184047
35	6	-1.690123	-1.182166	-2.191609
36	1	-1.581931	-1.145317	-3.270264
37	1	-1.878259	-1.339288	1.619640
38	6	-4.291051	-0.914180	0.556489
39	8	-4.385413	-0.954471	1.769793
40	8	-5.350270	-0.714904	-0.254210
41	1	-6.136909	-0.619555	0.316243

Table S3f: XYZ Coordinates of TRP-INA

1	8	-2.200637	-2.545904	1.306504
2	8	-3.683567	-0.958478	1.964836
3	7	-2.276395	-1.994124	-1.180639
4	1	-1.381591	-1.452807	-1.256618
5	1	-2.575769	-2.287020	-2.113003
6	1	-2.032806	-2.807953	-0.582924
7	6	-3.034824	-1.610633	1.122896
8	7	-0.597746	2.236577	-1.754274
9	1	-0.008124	2.666313	-2.451695
10	6	-2.278249	1.027154	-0.846087
11	6	-0.455292	2.368710	-0.389676
12	6	-1.585229	1.597725	1.627517
13	1	-2.360349	1.013224	2.114256
14	6	-1.498506	1.614465	0.221687
15	6	-3.342826	-1.297678	-0.382496
16	1	-4.276742	-1.820176	-0.615675
17	6	0.485600	3.090778	0.354698
18	1	1.272504	3.659012	-0.133950
19	6	-1.689024	1.439091	-2.020186
20	1	-1.979407	1.233636	-3.041998
21	6	-3.521469	0.183734	-0.759496
22	1	-4.044423	0.234738	-1.722025
23	1	-4.207921	0.583140	-0.005176
24	6	0.371798	3.055169	1.740326
25	1	1.085109	3.605341	2.348343
26	6	-0.653637	2.316142	2.368976
27	1	-0.711702	2.308328	3.454500
28	7	0.523777	-1.235426	-0.983165
29	6	1.447251	-0.794293	-1.848870
30	6	0.919723	-1.561084	0.258837
31	1	0.137418	-1.909747	0.929540
32	6	2.795724	-0.661705	-1.522572
33	6	3.202643	-1.004054	-0.229319
34	6	2.243681	-1.462449	0.678222
35	1	2.532022	-1.733683	1.687327
36	1	1.092463	-0.536433	-2.842907
37	6	4.623656	-0.898813	0.222526
38	8	5.006886	-1.192043	1.338684
39	8	5.443968	-0.441295	-0.742400
40	1	6.344351	-0.403850	-0.366140
41	1	3.505244	-0.301849	-2.257837

Table S3g: XYZ Coordinates of TRP-3-QA

1	8	-2.576726	-2.517095	-1.355240
2	8	-4.231319	-2.016743	0.116124
3	7	-2.451527	-0.213675	-2.441225
4	1	-1.584419	0.135393	-1.964885
5	1	-2.640477	0.361386	-3.264997
6	1	-2.220643	-1.191438	-2.702110
7	6	-3.454176	-1.771149	-0.827691
8	7	-0.944505	2.701236	0.756448
9	1	-0.297718	3.476015	0.737329
10	6	-2.653787	1.346168	0.161406
11	6	-0.968976	1.697536	1.700835
12	6	-2.284573	-0.296454	2.183880
13	1	-3.078595	-0.992098	1.929043
14	6	-2.035755	0.816995	1.357573
15	6	-3.629280	-0.375698	-1.520792
16	1	-4.505270	-0.466659	-2.171786
17	6	-0.160149	1.495714	2.825972
18	1	0.647653	2.181002	3.068097
19	6	-1.954095	2.488470	-0.156344
20	1	-2.111275	3.185850	-0.968513
21	6	-3.849744	0.833005	-0.593904
22	1	-4.265561	1.654099	-1.190026
23	1	-4.637470	0.515564	0.097787
24	6	-0.432584	0.388318	3.621985
25	1	0.175472	0.202398	4.503382
26	6	-1.484254	-0.497769	3.303110
27	1	-1.667690	-1.355235	3.945701
28	7	0.259082	-0.035000	-1.422256
29	6	1.259574	0.877062	-1.501243
30	6	0.527188	-1.198555	-0.854557
31	1	-0.297402	-1.909742	-0.799243
32	6	2.547254	0.667775	-1.035192
33	6	2.864622	-0.592798	-0.419916
34	6	1.797836	-1.545900	-0.333671
35	6	2.012902	-2.815114	0.264293
36	6	4.129487	-0.961874	0.111535
37	6	3.250509	-3.141192	0.768158
38	6	4.307494	-2.203470	0.687689
39	1	1.184850	-3.516622	0.315995
40	1	3.420709	-4.110327	1.227019
41	1	5.282150	-2.466898	1.089052
42	1	4.949001	-0.259554	0.056478
43	1	0.997628	1.818121	-1.969720
44	6	3.551482	1.754502	-1.200491
45	8	4.743753	1.674496	-0.958050
46	8	3.005777	2.900412	-1.670566
47	1	3.737538	3.539914	-1.761853