Supporting information

Discovery and Exploration of New Solid Forms of Dipeptide: L-Alanyl-L-Glutamine

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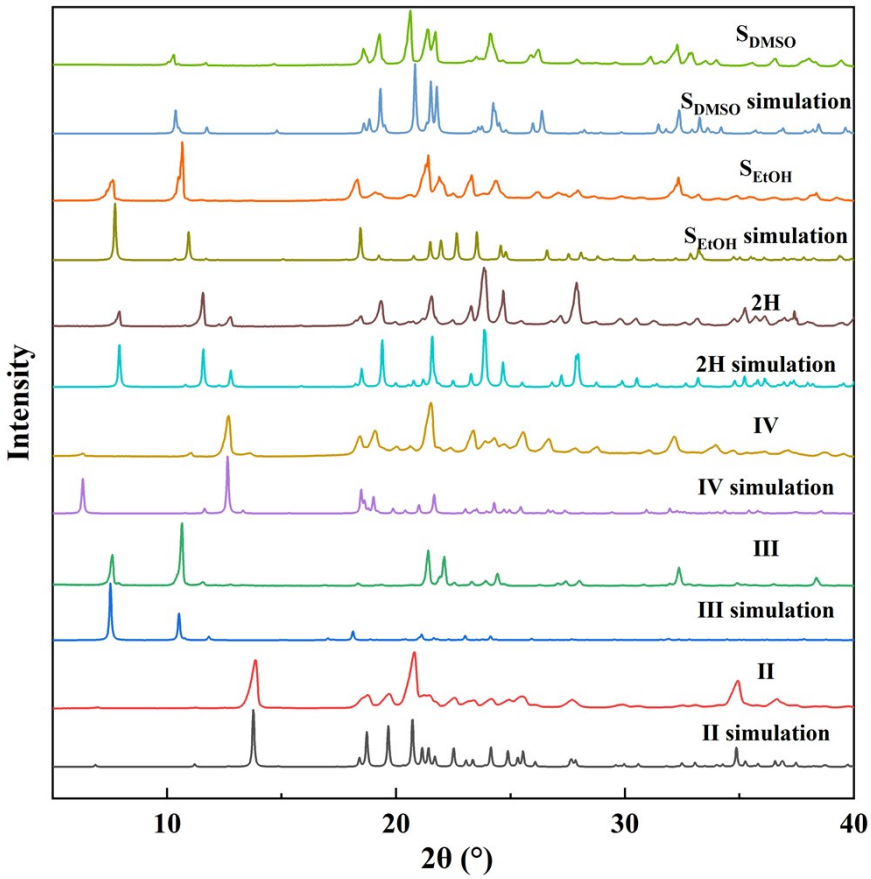

Figure S1. Powder X-ray Diffraction of different Ala-Gln solid forms.

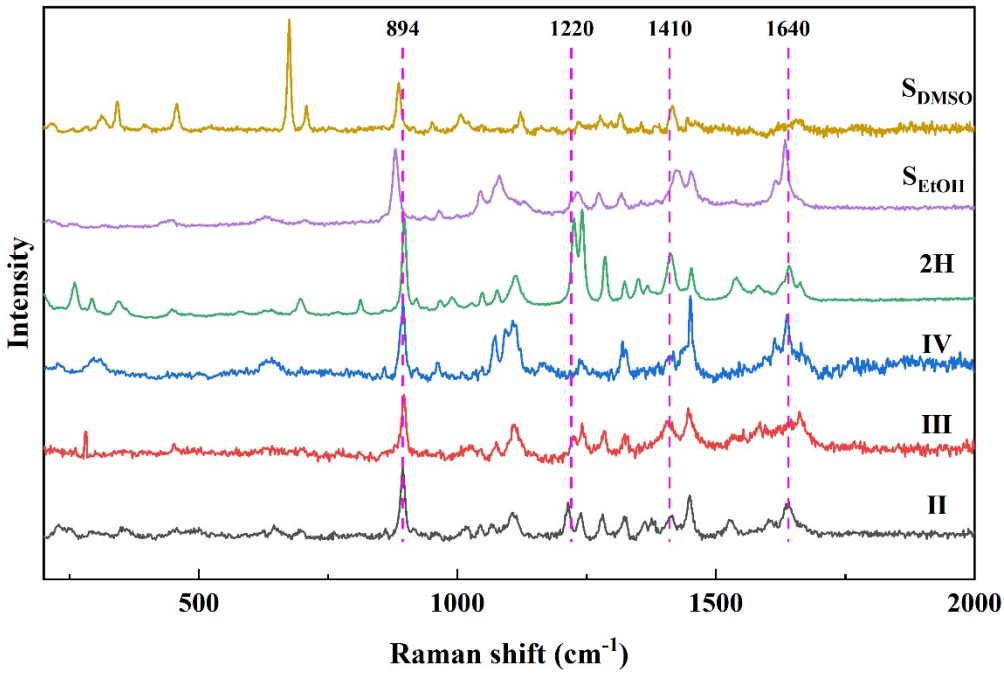

Figure S2. Raman spectroscopy analysis of different Ala-Gln solid forms.

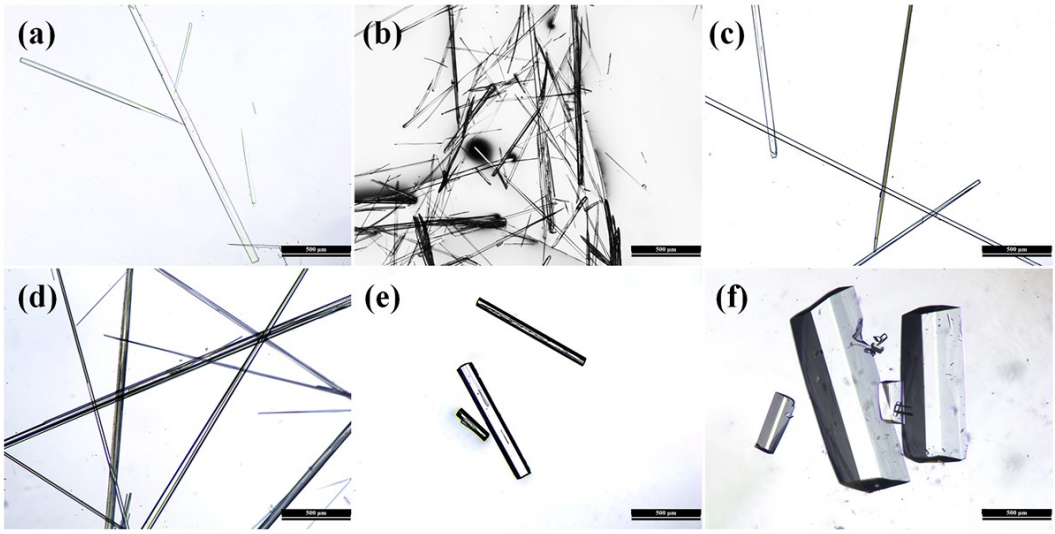

Figure S3. Microscopy images of Ala-Gln form (a) II, (b) III, (c) IV, (d) 2H, (e) S_{EtOH} and (f) S_{DMSO}.

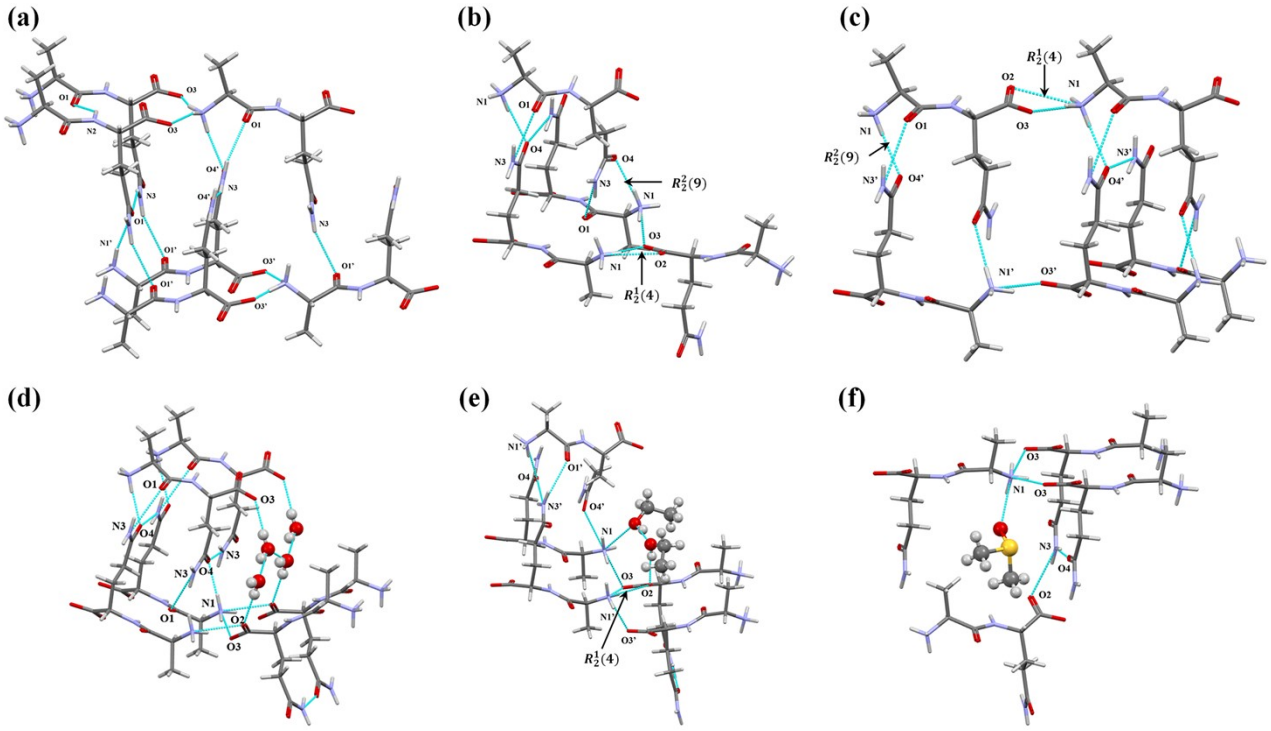

Figure S4. The crystal structure of Ala-Gln crystals form (a) II, (b) III, (c) IV, (d) 2H, (e) S_{EtOH} and (f) S_{DMSO}. The blue dot lines are intermolecular hydrogen bonding between molecules.

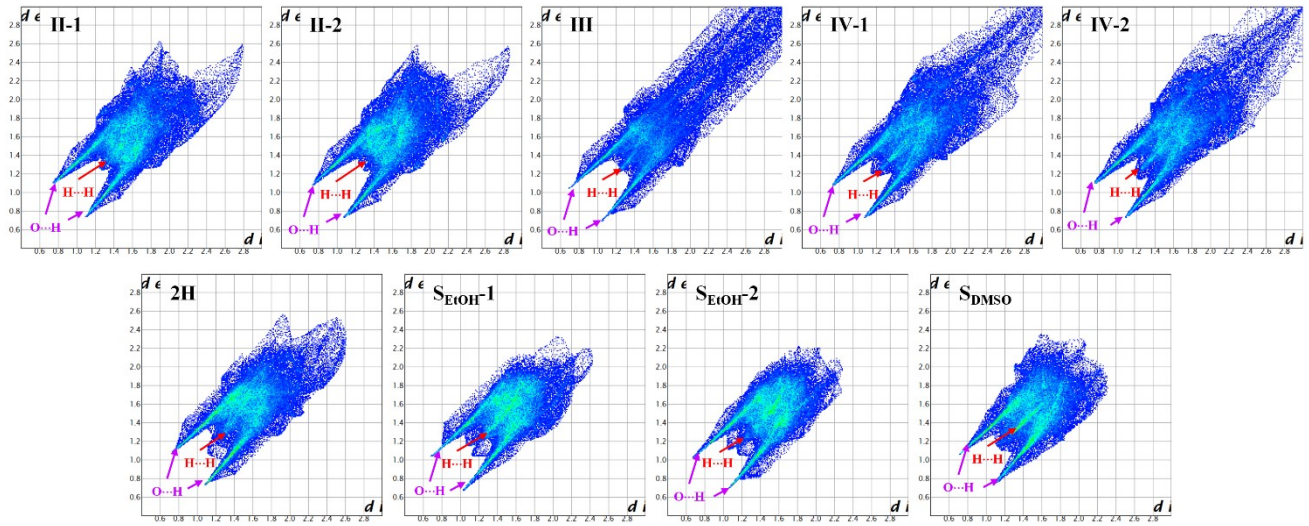

Figure S5. 2D fingerprint plots of different Ala-Gln solid forms.

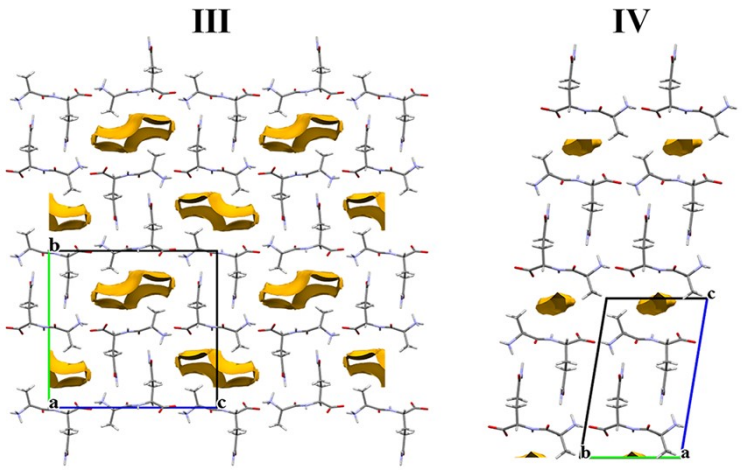

Figure S6. Voids of Ala-Gln crystals form III and IV.

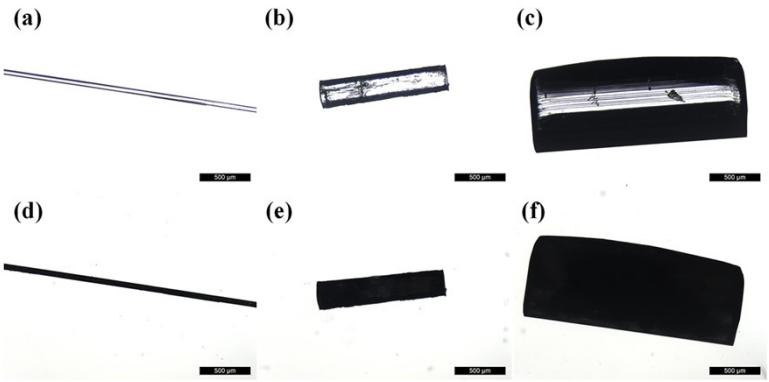

Figure S7. Microscopy images of Ala-Gln solvates before ((a) 2H, (b) S_{EtOH} and (c) S_{DMSO}) and after heating ((d)2H, (e) S_{EtOH} and (f) S_{DMSO}).

Table S1. Torsion angles of different Ala-Gln solid forms.

Torsion	C5-C4-C6-C7	C6-C7-C8-N3	C6-C7-C8-O4	N2-C4-C6-C7
II-1	-56.94	8.36	-174.36	61.27
II-2	-56.37	-169.33	7.53	63.95
III	-55.84	3.78	-177.44	65.91
IV-1	-58.38	174.28	-5.43	62.23
IV-2	-57.68	1.50	-177.79	63.51
2H	-56.04	1.84	-179.40	66.28
S_{EtOH}-1	-53.51	169.95	-9.50	68.11
S_{EtOH}-2	-53.54	-178.23	2.29	67.44
S_{DMSO}	-57.63	-179.69	-0.58	65.42

Table S2. Hydrogen bonds with H···A < r(A) + 2.000 Å and <DHA > 110° of different Ala-Gln solid forms.

Form	D-H	d (D-H)	d (H···A)	< DHA	d (D···A)
II	N1-H1A···O3	0.89	1.93	149.5	2.735
	N1'-H1'C···O4	0.89	1.99	169.2	2.864
	N1'-H1'A···O3	0.89	2.04	139.6	2.776
	N1-H1C···O4'A	0.89	1.87	168.4	2.75
	N3A_b-H3AB_b···O4A	0.86	2.12	134.2	2.79
	N1'-H1'C···O4A	0.89	1.89	167.0	2.76
	N1-H1B···O3	0.89	2.01	163.0	2.876
	N1-H1C···O4	0.89	2.04	171.5	2.92
	N1-H1C···N3'A	0.89	2.91	124.7	3.49
	N2-H2···O1	0.86	2.71	145.7	3.452
	N3_a-H3B_a···O4	0.86	2.15	133.2	2.813
	N3_a-H3A_a···O1'	0.86	2.32	152.9	3.114
	N3A_b-H3AA_b···O3'	0.86	2.32	170	3.17
	N1'-H1'B···O3'	0.89	1.97	160.5	2.825
	N2'-H2'···O1'	0.88	2.72	138	3.432
	N3'_a-H3'A_a···O1	0.86	2.11	164.2	2.952
	N3'_a-H3'B_a···O4'	0.86	2.09	147.7	2.85
III	N1-H1A···O4	0.91	1.957	171.06	2.859
	N1-H1B···O3	0.91	2.249	138.57	2.993
	N1-H1B···O2	0.91	2.015	159.19	2.883
	N1-H1C···O3	0.91	1.829	167.96	2.726
	N2-H2···O1	0.899	2.51	138.47	3.239

Form	D-H	d (D-H)	d (H···A)	< DHA	d (D···A)
	N3-H3A···O1	0.88	2.128	152.71	2.938
	N3-H3B···O4	0.88	2.059	144.77	2.824
	C4-H4···O2	1	2.35	169.89	3.339
	C2-H2···O3	1	2.635	111.11	3.137
	C2-H2···O1	1	2.506	156.63	3.447
IV	N1-H1A···O4’	0.89	1.954	174.44	2.841
	N1-H1B···O3	0.89	1.994	170.09	2.874
	N1-H1B···O2	0.89	2.502	118.62	3.031
	N1-H1C···O3	0.89	1.929	149.5	2.734
	N1’-H1A’···O4	0.89	2.002	176.66	2.891
	N1’-H1B’···O3’	0.89	1.997	169.13	2.876
	N1’-H1B’···O2’	0.89	2.557	113.12	3.02
	N1’-H1C’···O3’	0.89	1.983	144.2	2.754
	N2-H2···O2	0.902	2.141	111.2	2.607
	N3-H3A···O1’	0.86	2.175	150.32	2.953
	N3-H3B···O4	0.86	2.083	145.81	2.836
	N3’-H3A’···O1	0.86	2.204	154.58	3.003
	N3’-H3B’···O4’	0.86	2.135	134.11	2.802
	C4-H4···O2	0.98	2.345	157.77	3.273
	C4’-H4’···O2’	0.98	2.34	159.44	3.276
	C6-H6···O1	0.97	2.652	115.83	3.196
	C6’-H6’···O1’	0.97	2.63	116.52	3.183
	C2-H2···O1	0.98	2.378	158.85	3.311
	C2’-H2’···O1’	0.98	2.411	155.88	3.33
2H	N1-H1A···O2	0.89	2.033	146.33	2.818
	N1-H1A···O3	0.89	2.324	152.44	3.14
	N1-H1B···O3	0.89	1.947	166.05	2.819
	N1-H1C···O4	0.89	1.952	175.09	2.839
	N2-H2···O1	0.888	2.465	147.15	3.246
	N3-H3A···O1	0.86	2.196	151.93	2.983
	N3-H3B···O4	0.86	2.053	144.62	2.799
	C1-H1F···O5	0.96	2.65	156.69	3.552
	C2-H2A···O1	0.98	2.515	155.73	3.432
	C4-H4···O2	0.98	2.38	170.07	3.349
S_{EtOH}	N1-H1A···O2’	0.91	1.81	171.89	2.714
	N1’-H1A’···O3	0.91	2.176	145.93	2.974
	N1-H1A···O3’	0.91	2.606	130.77	3.274
	N1-H1B···O2	0.91	1.919	160.91	2.794
	N1-H1C···O4’	0.91	2.112	149.17	2.931
	N1-H1C···O5	0.91	2.427	119.21	2.979
	N2’-H2’···O1	0.889	2.495	148.89	3.289
	N2-H2···O1’	0.895	2.349	156.76	3.191
	N3’-H3A’···O1’	0.88	2.27	150.99	3.07

Form	D-H	d (D-H)	d (H···A)	< DHA	d (D···A)
	N3-H3A···O1	0.88	2.179	148.59	2.966
	N3'-H3A'···O2	0.91	2.069	149.9	2.892
	N3'-H3B'···O3'	0.91	1.823	165.13	2.713
	N3'-H3B'···O4	0.88	2.104	133.98	2.788
	N3-H3B···O4'	0.88	2.143	134.92	2.833
	N3'-H3C'···O4	0.91	1.916	169.5	2.816
	C2'-H2'···O1	1	2.501	155.87	3.438
	C2-H2···O1'	1	2.534	152.9	3.454
	C2-H2···O3'	1	2.64	113.63	3.176
	C4'-H4'···O2	1	2.387	173.72	3.383
	C4-H4···O2'	1	2.383	166.37	3.364
	O5'-H10C···O2	0.84	1.916	169.34	2.745
	O5-H5···O5'	0.84	1.96	158.96	2.761
S_{DMSO}	N1-H1A···O5	0.91	1.9	161.75	2.779
	N1-H1B···O3	0.91	1.984	154.54	2.833
	N1-H1B···O2	0.91	2.641	112.02	3.099
	N1-H1C···O3	0.91	1.995	144.76	2.788
	N1-H1A···S1	0.91	2.946	135.24	3.649
	N2-H2···O1	0.88	2.499	149.85	3.29
	N3-H3A···O2	0.88	2.15	157.55	2.983
	N3-H3B···O4	0.88	1.946	169.54	2.816
	C1-H1A···O4	0.98	2.633	130.22	3.35
	C2-H2···O1	1	2.189	157.99	3.138
	C4-H4···O2	1	2.352	151.24	3.264
	C9-H9A···O1	0.98	2.558	153.34	3.462
	C9-H10B···O5	0.98	2.422	129.77	3.14
	C10-H10A···O4	0.98	2.537	126.56	3.219

Crystal exploring experiments

Firstly, 4 g Al-Gln of form II was dissolved in 20 g water. After fully dissolved, the clarified solution was filtered through a 0.45μm filter. Secondly, 1 mL of 0.1 g/g Al-Gln aqueous solution was placed in 10 mL sample bottles and 0.056 mol organic solvents were added in. Organic solvents were methanol, ethanol, isopropanol, n-propanol, DMSO, tetrahydrofuran, acetonitrile, DMF, dioxane. Finally, after crystal for a week at the temperature of 298 K, the crystal in sample bottles were filtered.

The sample battles which added tetrahydrofuran, acetonitrile had no crystals. The crystals were direct measured without grinding and the PXRD results was shown as Figure S8. The results showed the crystals crystallized in isopropanol and DMF were form II, and the crystals in dioxane were form

III. The crystals in n-propanol were form 2H, and the crystals in DMSO were solvate form S_{DMSO}. The crystals crystallized in methanol were a mixture of form II and IV, and crystals in ethanol were form S_{EtOH}.

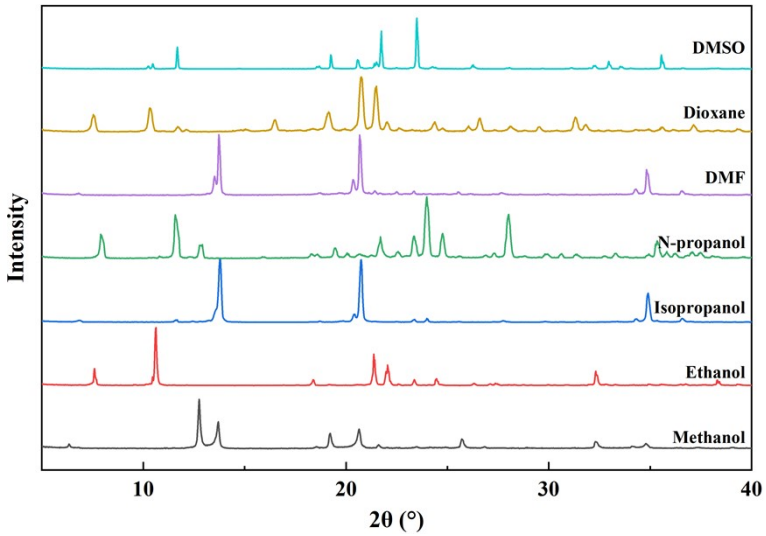

Figure S8. Powder X-ray Diffraction of crystal exploring experiments.