pharmaceutics

MDPI

Supplementary Materials: Mechanochemical Synthesis and Physicochemical Characterization of Previously Unreported Praziquantel Solvates with 2-Pyrrolidone and Acetic Acid

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Supplementary information

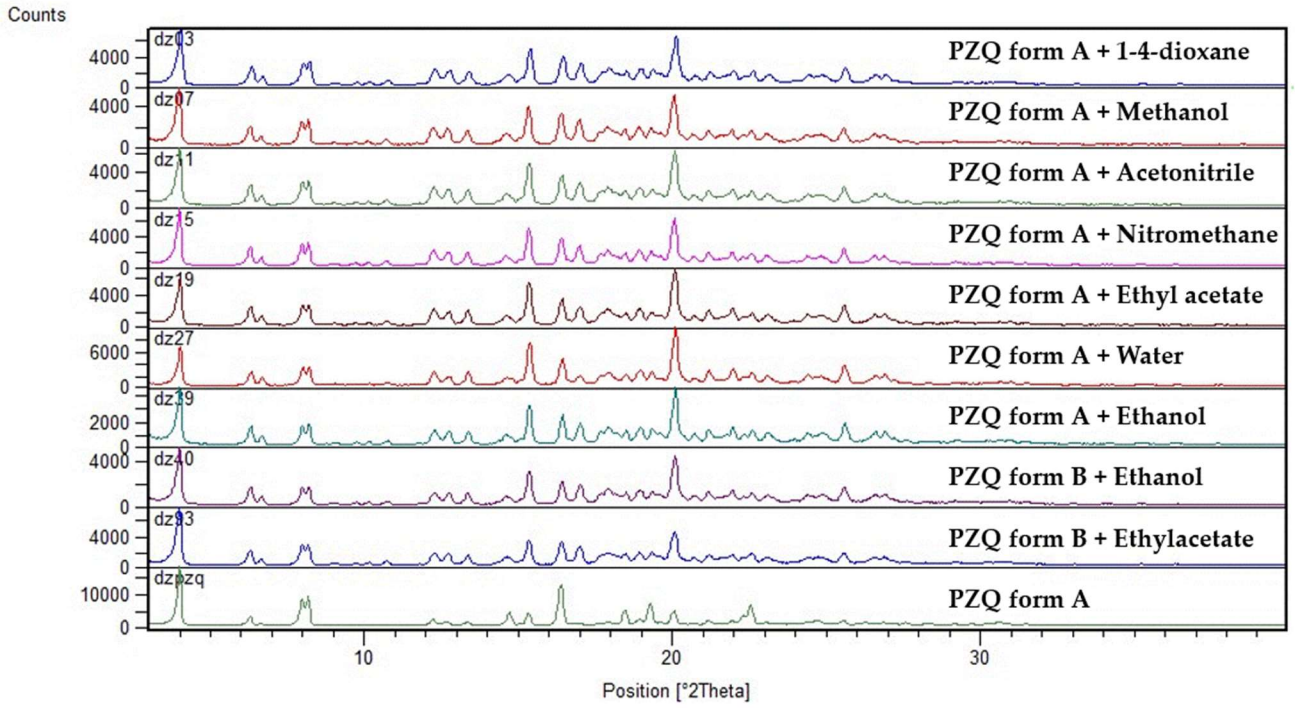


Figure S1. PXRD pattern of the solids retrieved after grinding PZQ A and B in presence of different liquid additives and PZQ A as a reference.

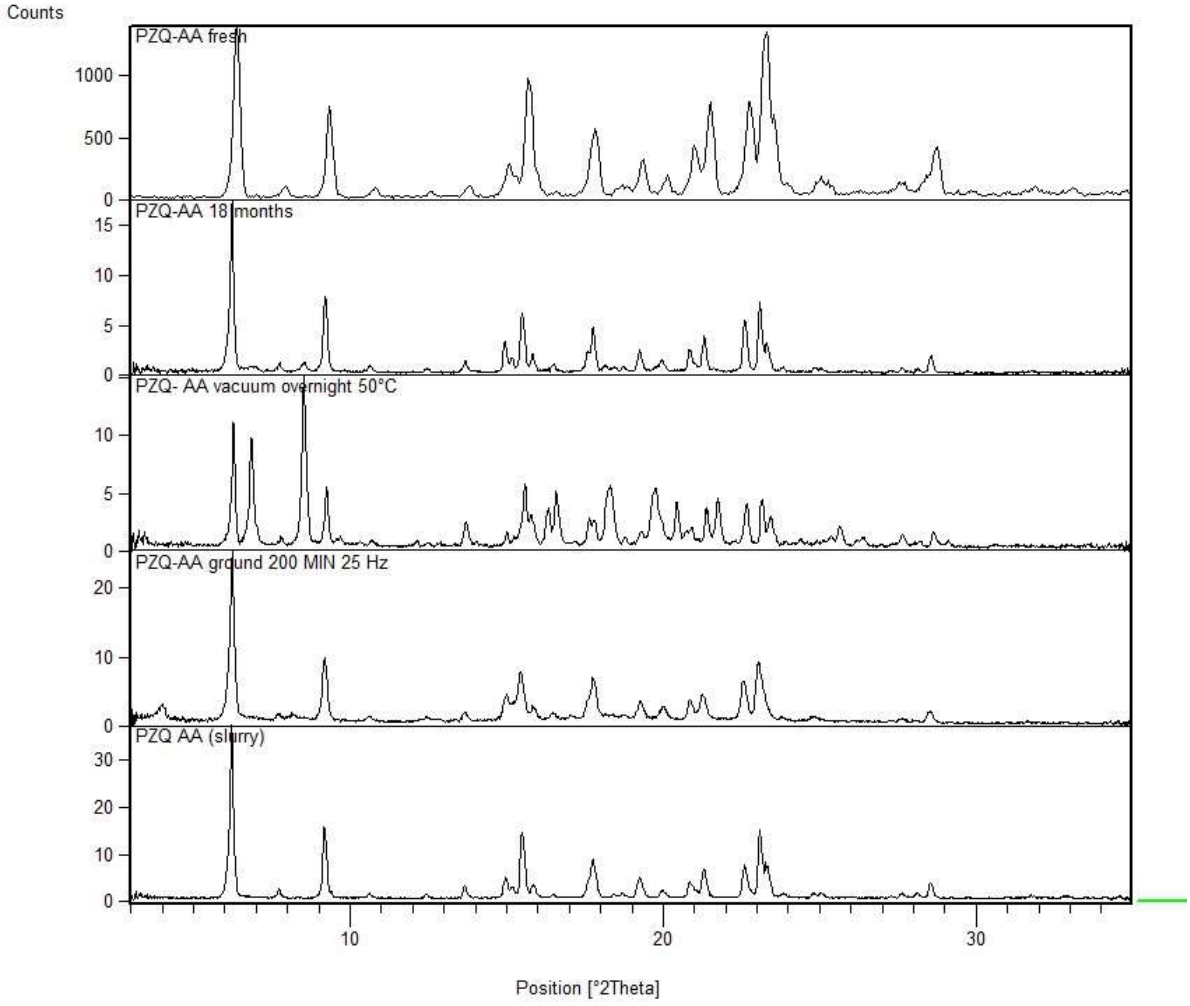


Figure S2. PZQ-AA: fresh sample, after 18 months at room temperature*, under vacuum overnight at 50°C*, ground for 200 minutes at 25 Hz* and PZQ-AA prepared by slurry method*.(*=PXRD pattern were collected using a D2 Phaser(Bruker), using a zero background (Sylicon) sample holder, from 3 to 35° of 2θ, 0.02° step, time/step 0.6 sec, at 30 V, 10 mA).

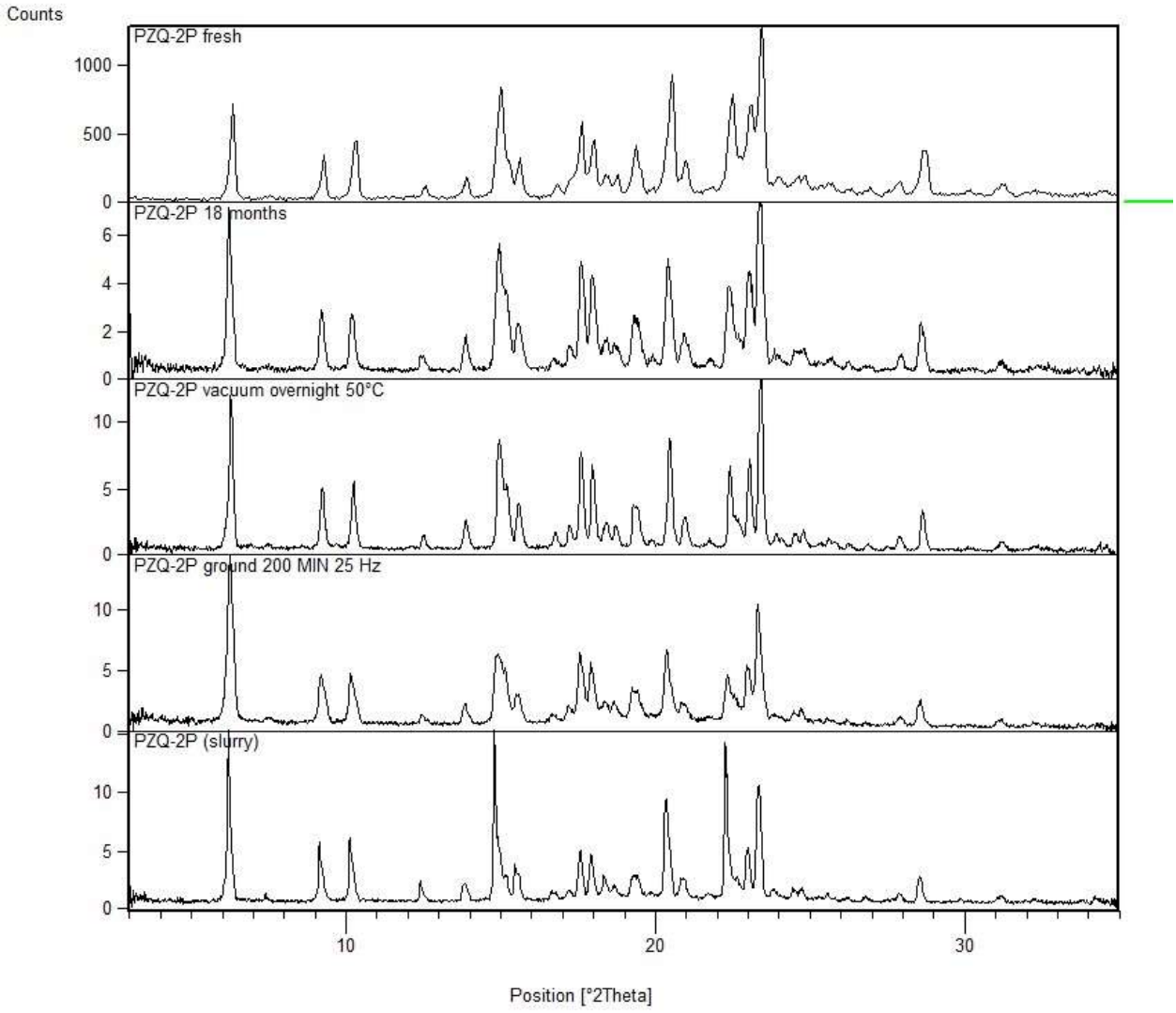
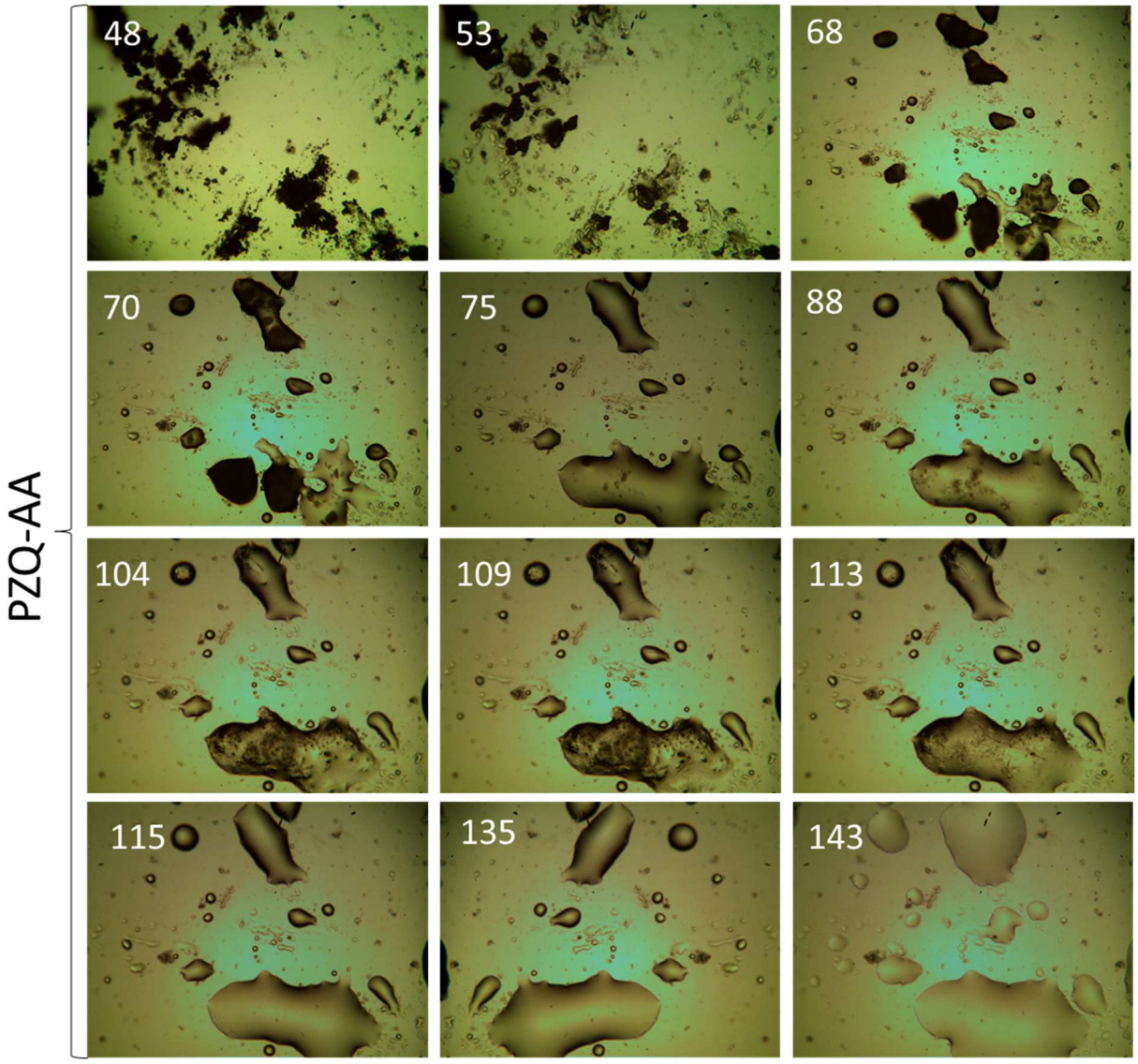


Figure S3. PZQ-2P: fresh sample, after 18 months at room temperature*, under vacuum overnight at 50°C*, ground for 200 minutes at 25 Hz* and PZQ-AA prepared by slurry method*.(*=PXRD pattern were collected using a D2 Phaser (Bruker), using a zero background (Sylicon) sample holder, from 3 to 35° of 2θ, 0.02° step, time/step 0.6 sec, at 30 V, 10 mA)


PZQ-AA
48
53
68
70
75
88
104
109
113
115
135
143

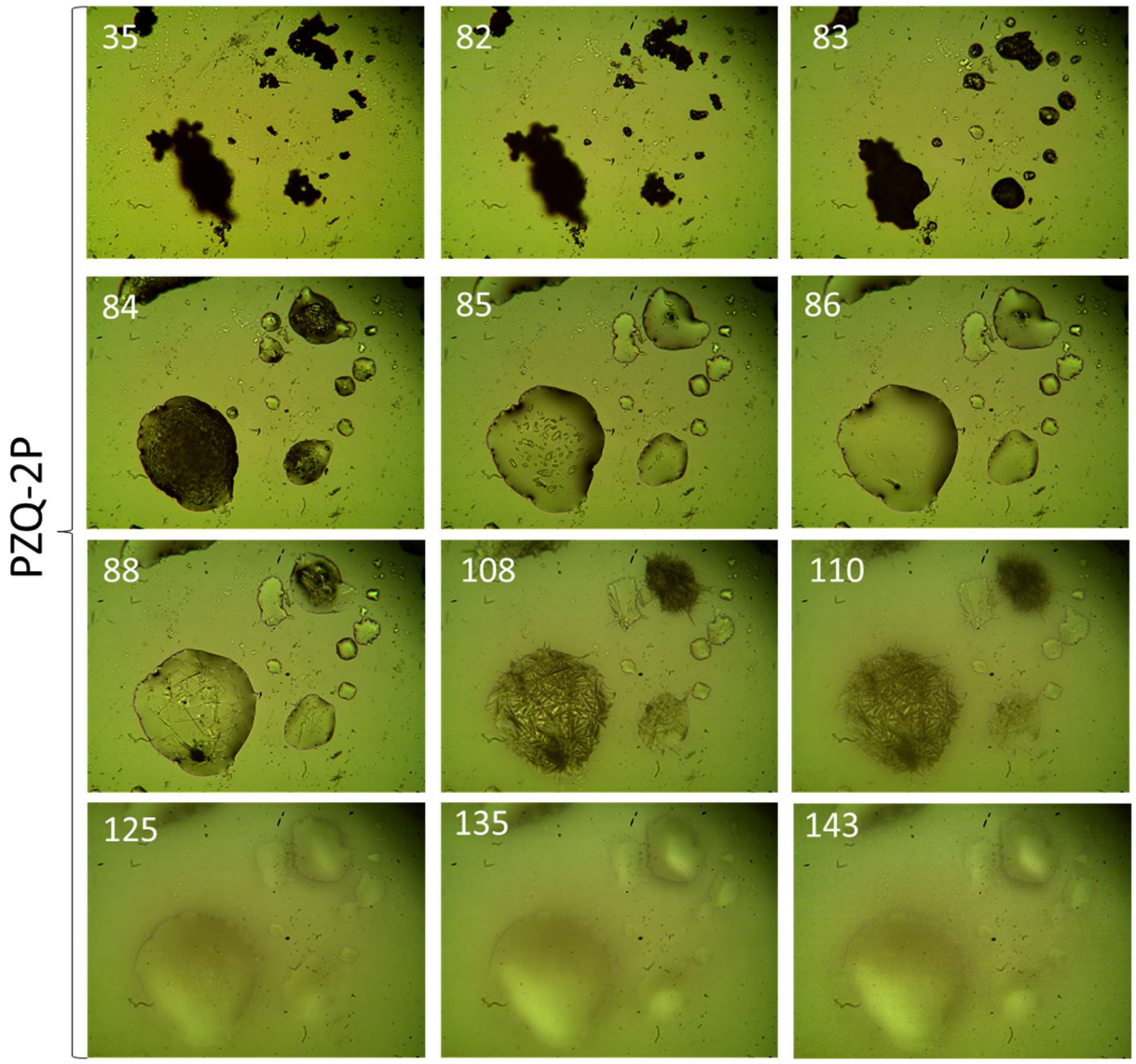


Figure S4. Optical microscopy images of PZQ-AA and PZQ-2P upon heating (with indication of operating temperature in each image). (Magnification 100x).

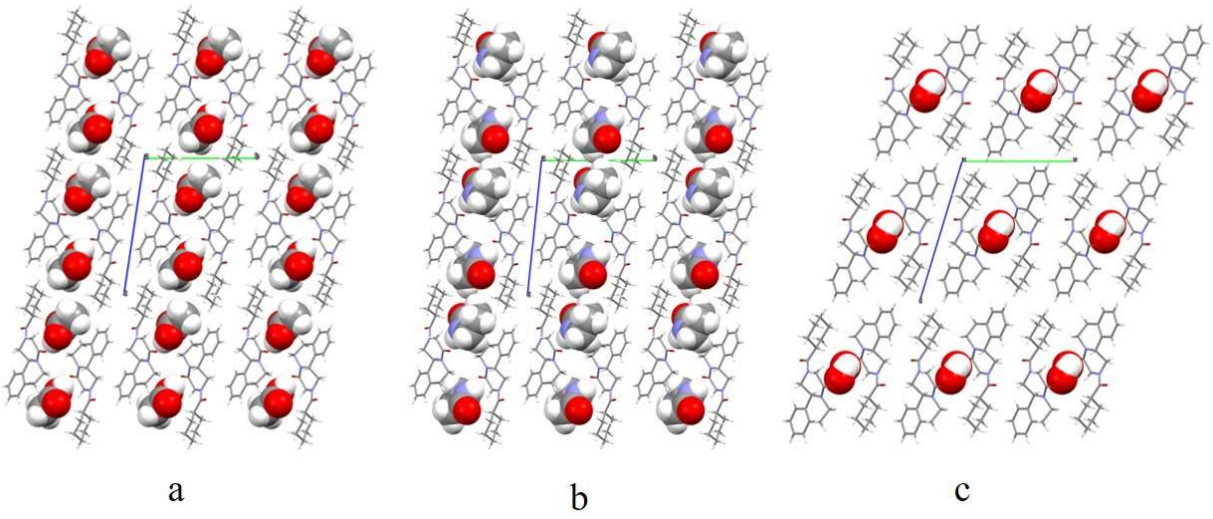


Figure S5. Crystal packing comparison along a axis of a) PZQ-AA , b) PZQ-2P and c) PZQ hemihydrate form.

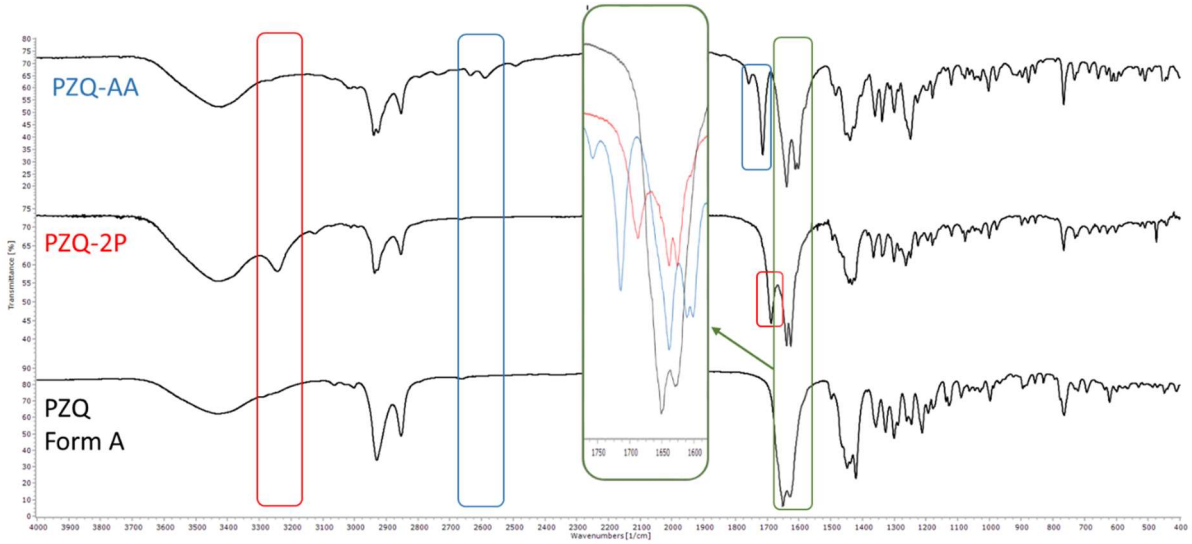


Figure S6. FT-IR spectra of PZQ-AA (blue), PZQ-2P (red) ad raw PZQ form A (green). Frames highlight with above-mentioned different colors diagnostic regions

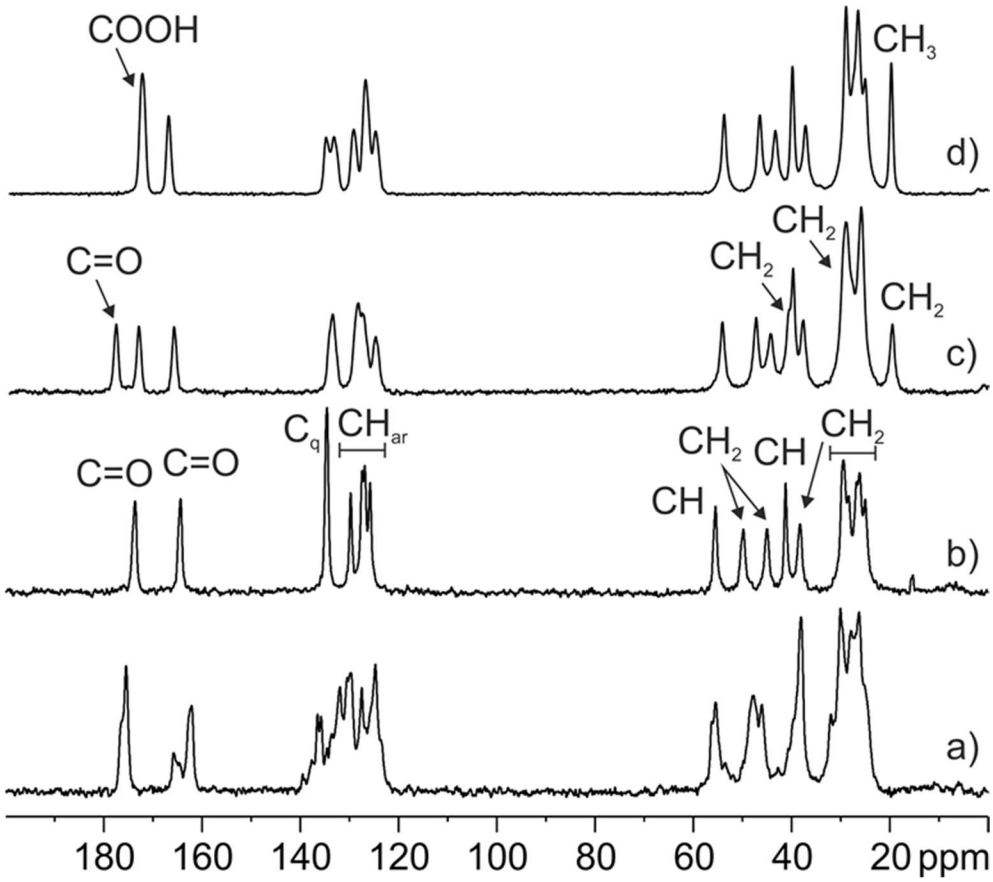
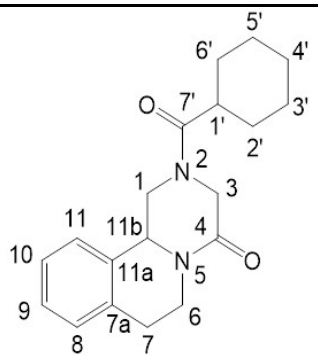


Figure S7. 13C (100.65 MHz) CPMAS SSNMR spectra of (a) PZQ form A, (b) PZQ form B, (c) PZQ-2P, and (d) PZQ-AA acquired at 12 kHz. Relevant assignments are reported for the PZQ molecule (b) and for the solvent molecules (c and d) resonances.

Table S1. Calculated shift / ppm and calculate shielding / ppm (for atom numbering please refer to Scheme).



	Acetic Acid solvate		2-Pyrrolidone solvate	
Atom	Calculate shielding / ppm	Calculated shift / ppm	Calculate shielding / ppm	Calculated shift / ppm
7'	−1,68	172,68	−2,2248	173,22
4	3,08	167,92	4,342	166,66
11a	35,04	135,96	35,2514	135,75
7a	32,97	138,03	33,8638	137,14
8	38,70	132,30	39,8349	131,17
11	44,17	126,84	44,1118	126,89
9	42,34	128,66	40,1189	130,88
10	42,09	128,91	40,9029	130,10
11b	117,58	53,42	116,1831	54,82
3	125,49	45,51	124,7734	46,23
1	129,93	41,07	128,1975	42,80
1'	131,94	39,06	131,3745	39,63
6	136,29	34,71	136,1598	34,84
6'	143,32	27,68	143,7767	27,22
2'	143,62	27,38	142,5896	28,41
7	145,70	25,30	144,7837	26,22
4'	145,39	25,61	145,9471	25,05
3'	145,54	25,46	146,6308	24,37
5'	147,40	23,60	146,4202	24,58
AA COOH	−6,13	177,13		
AA CH_3	152,97	18,03		
2P CH_2			151,9089	19,09
2P CH_2			142,8449	28,16
2P CH_2			129,5215	41,48
2P CONH			−7,9436	178,94

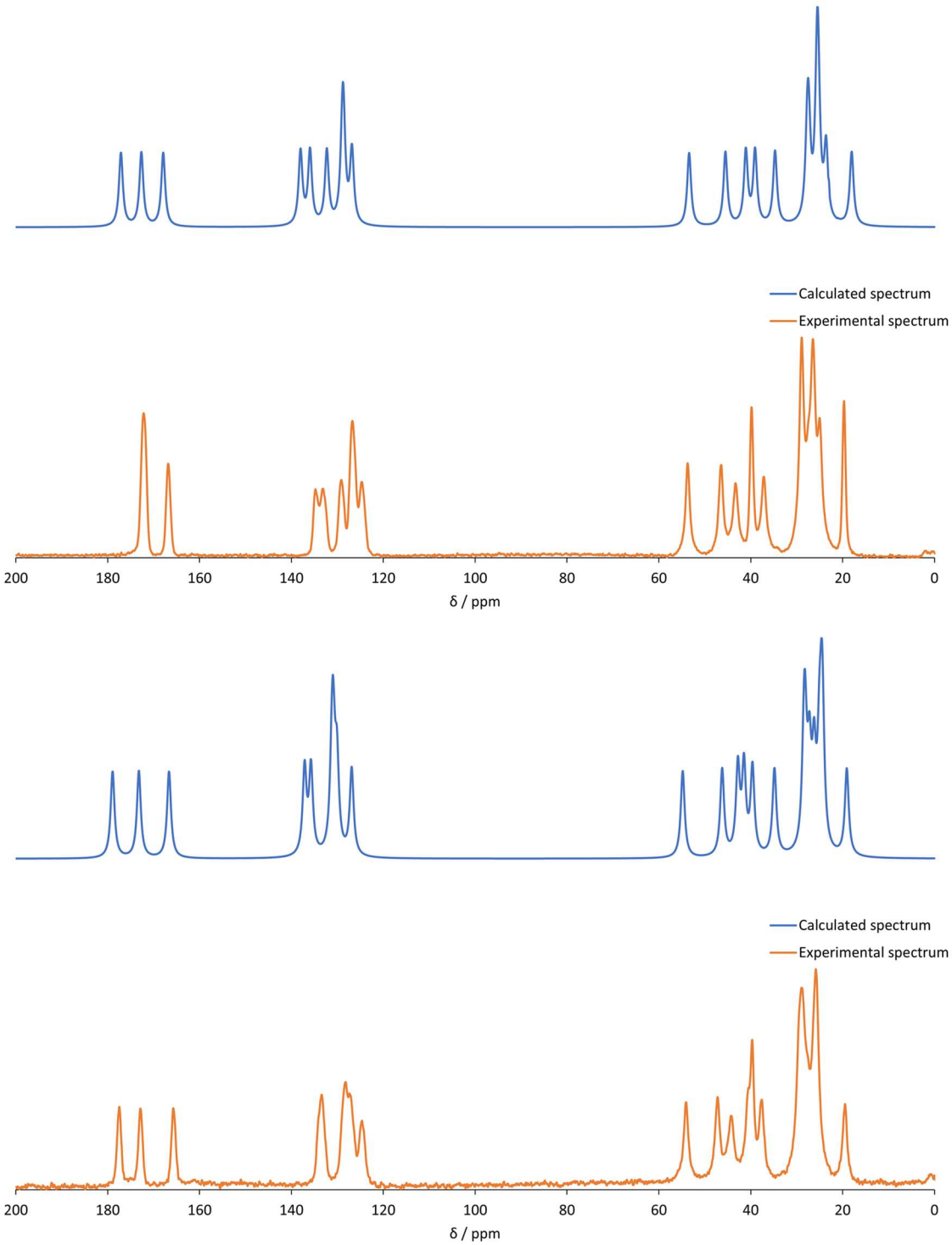


Figure S8. Comparison of experimental and calculated 13C SSNMR spectra of PZQ-AA (top) and PZQ-2P (bottom). The only significant disagreement is found for the COOH signal, at 177.1 and 172.1 ppm in the PZQ-AA calculated and experimental spectrum, respectively. The 5 ppm difference may be attributed to the difficulty in modelling the electronic environment around an acidic ionizable proton.

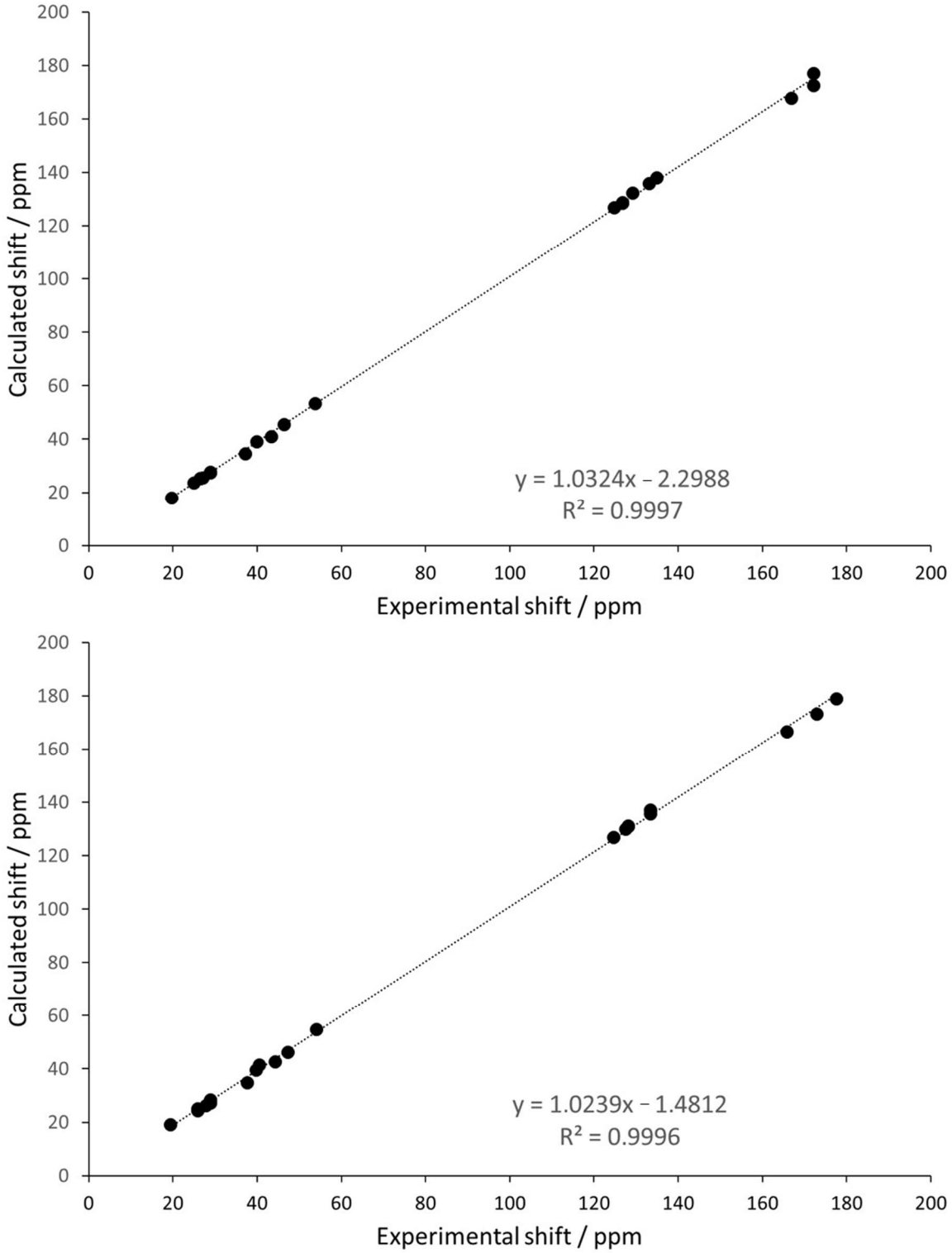


Figure S9. Quantitative comparison of experimental and calculated 13C SSNMR spectra of PZQ-AA (top) and PZQ-2P (bottom).