Electronic Supplementary Material (ESI) for Faraday Discussions.

Halogen effects on the solid-state packing of phenylalanine derivatives and the resultant gelation properties

Susana M. Ramalhete,[a] Jamie S. Foster, [b] Hayley R. Green,[b] Karol P. Nartowski,[a] Margaux Heinrich,[b] Peter C. Martin,[c] Yaroslav Z. Khimyak*[a] and Gareth O. Lloyd*[b]

[a.] *Department of Pharmaceutical Science School of Pharmacy, University of East Anglia, Norwich, United Kingdom, NR4 7TJ, E-mail: Y.Khimyak@uea.ac.uk.*

[b.] *Institute of Chemical Sciences, School of Engineering and Physical Sciences, Heriot-Watt University, Edinburgh, Scotland, United Kingdom, EH14 4AS, E-mail: G.O.Lloyd@hw.ac.uk*

[c.] *Department of Chemistry, Cambridge University, Lensfield Road, Cambridge, United Kingdom, CB2 1EW.*

CCDC 1532628-1532632

Summary of Data CCDC 1532628

Compound Name:
Formula: C9 H9 F2 N1 O2,H2 O1
Unit Cell Parameters: a 13.100(3) b 5.4019(12) c 14.423(4) P21

Summary of Data CCDC 1532629

Compound Name:
Formula: C9 H10 Br1 N1 O2,H2 O1
Unit Cell Parameters: a 6.3036(4) b 5.3042(3) c 15.9161(9) P21

Summary of Data CCDC 1532630

Compound Name:
Formula: C9 H10 F1 N1 O2,H2 O1
Unit Cell Parameters: a 13.3028(14) b 5.4628(6) c 14.0151(15) P21

Summary of Data CCDC 1532631

Compound Name:
Formula: C9 H10 I1 N1 O2,H2 O1
Unit Cell Parameters: a 5.3139(3) b 6.3152(4) c 32.741(2) P212121

Summary of Data CCDC 1532632

Compound Name:
Formula: C9 H10 Cl1 N1 O2,H2 O1
Unit Cell Parameters: a 13.5539(8) b 5.4096(3) c 15.0157(9) P21

NMR

					T_1 (s)			
					Arom		$C_\alpha H$	$C_\beta H_2$
		Phe	Cl-Phe $H_{3,5}$	Cl-Phe $H_{2,6}$	F-Phe $H_{3,5}$	F-Phe $H_{2,6}$		
Hydrogel	Phe	2.45 (0.14)	-	-	-	-	2.42 (0.15)	2.41 (0.15)
	Cl-Phe	-	2.75 (0.07)	2.17 (0.06)	-	-	2.10 (0.08)	0.93 (0.04)
	F-Phe	-	-	-	2.52 (0.07)	3.66 (0.02)	2.84 (0.15)	0.87 (0.01)
Solution	Phe	2.07 (0.02)	-	-	-	-	2.20 (0.03)	0.63 (0.01)
	Cl-Phe	-	3.74 (0.06)	2.34 (0.09)	-	-	2.65 (0.05)	0.70 (0.06)
	F-Phe	-	-	-	2.75 (0.03)	3.73 (0.02)	2.90 (0.04)	0.85 (0.02)

Rheology

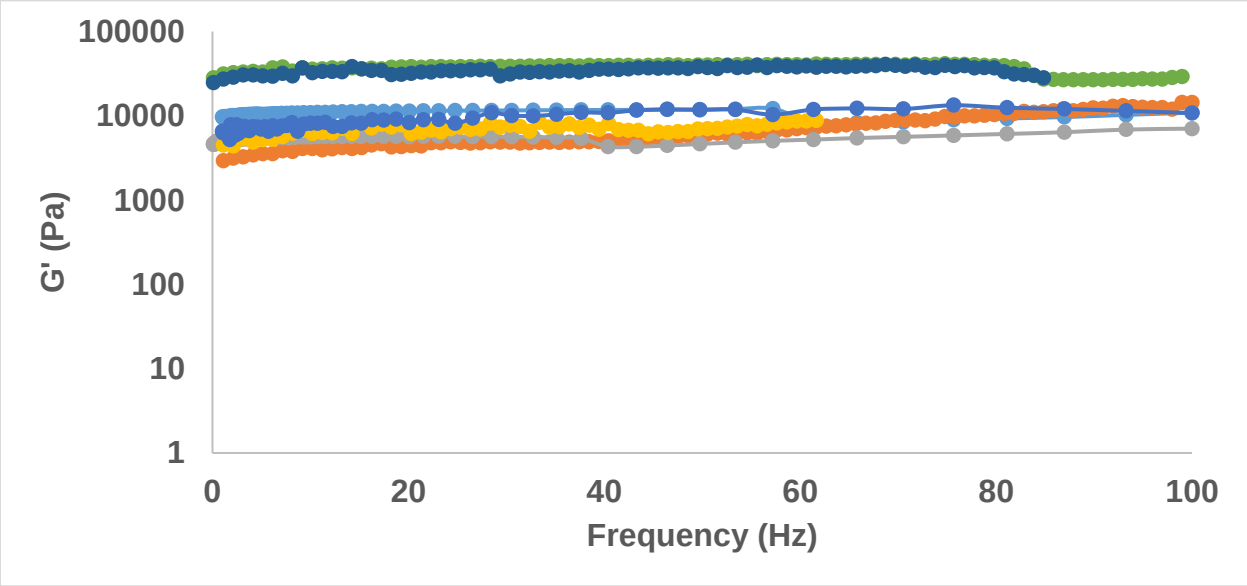

Fig. S1. Frequency sweeps of all gels in DMSO. Green, Br-Phe; Dark Blue, Phe, light blue, F-Phe; medium blue, 2Cl-Phe; light orange, Cl-Phe; grey, 5F-Phe; dark orange, 2F-Phe.

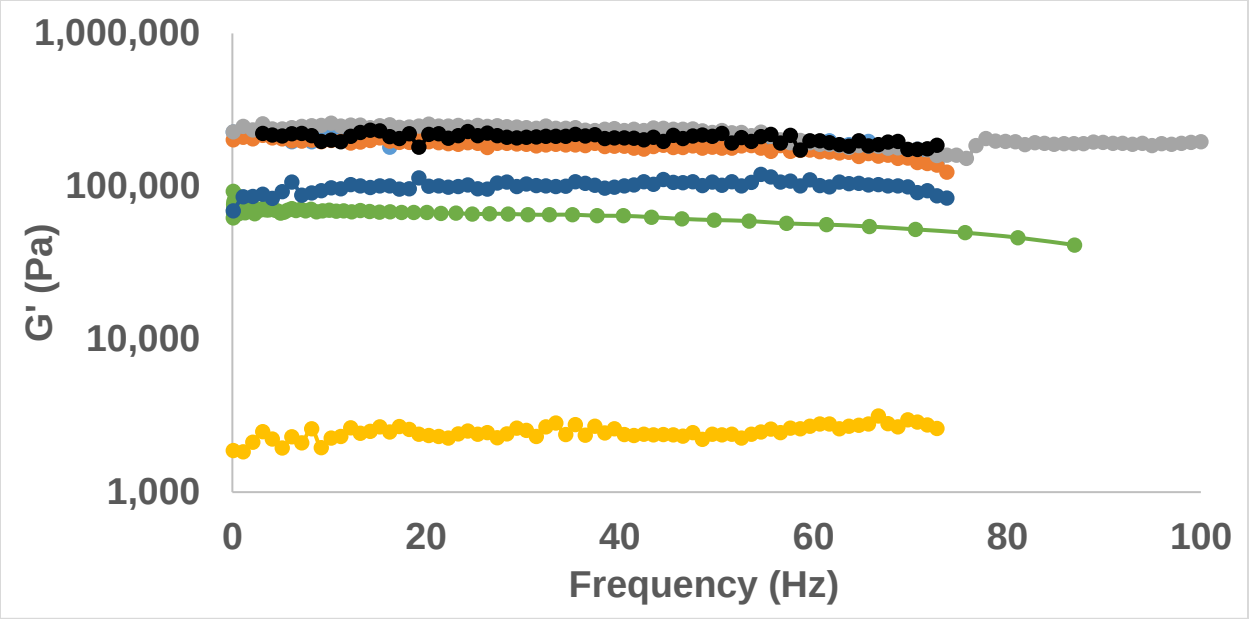

Fig. S2. Frequency sweeps of all gels in water. Green, Br-Phe; Dark Blue, Phe, light blue, F-Phe (only a few of the plotted data points are visible); medium blue, 2Cl-Phe; black, Cl-Phe; grey, 5F-Phe; dark orange, 2F-Phe.

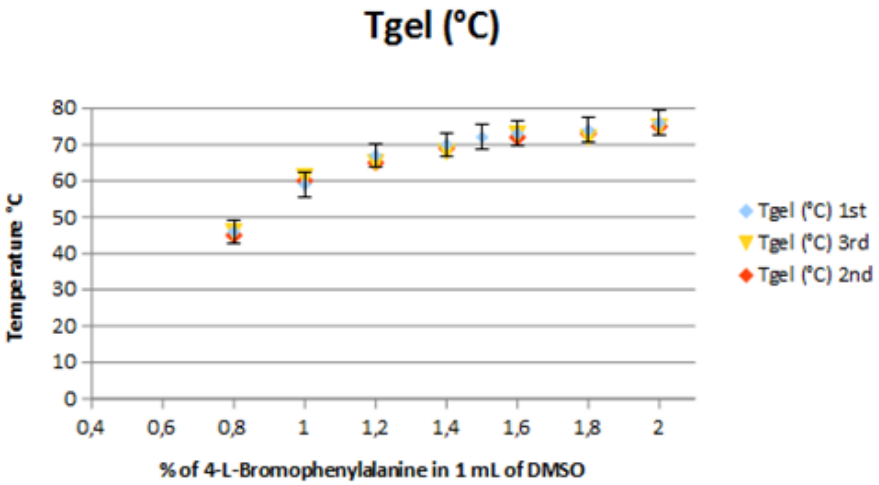

Fig. S3. T_{gel} determination of Br-Phe in DMSO.

PXRD patterns

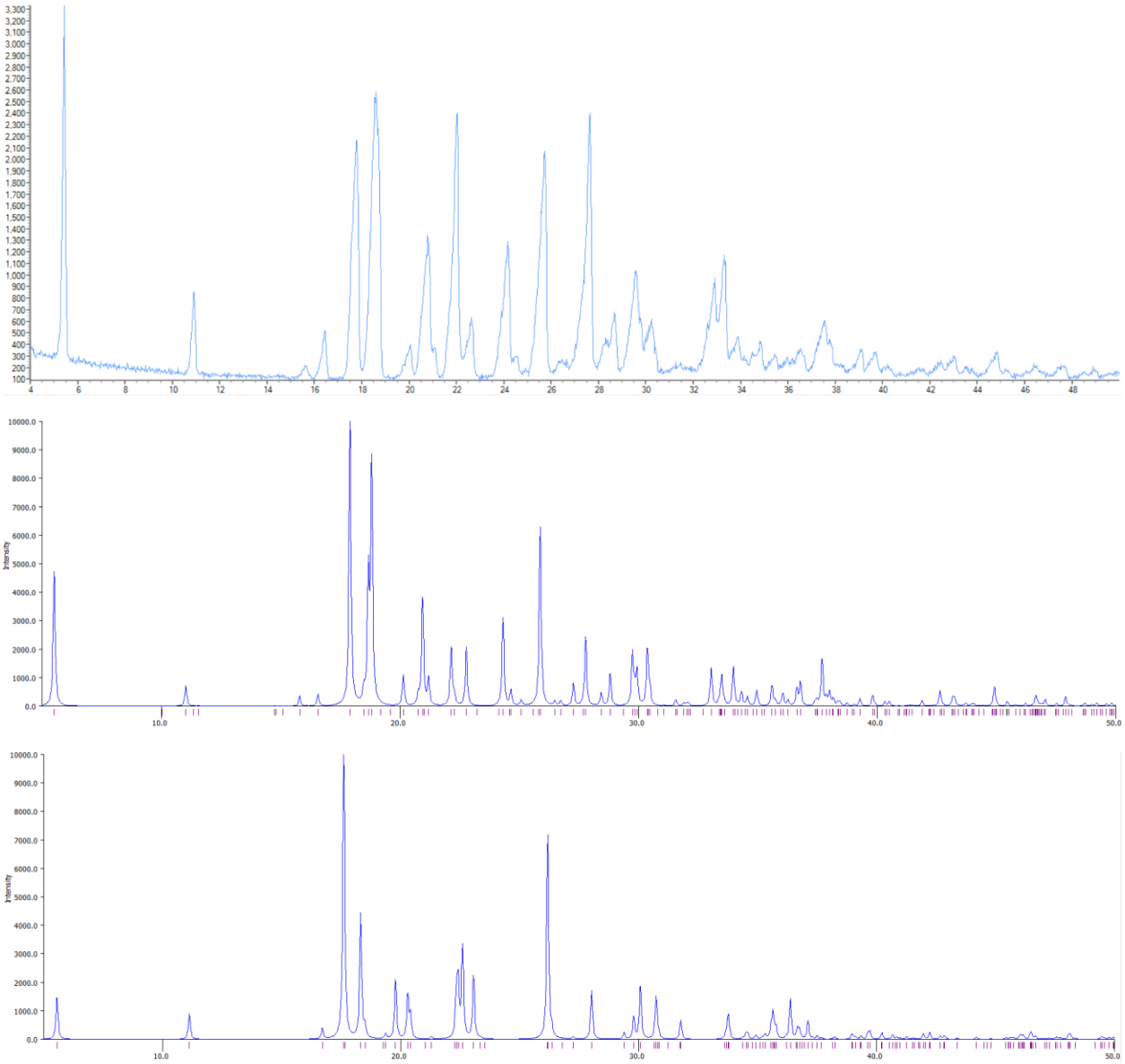

Fig. S4. F-Phe commercial sample matches the known form (EXAXEG) 2nd pattern, and not the other published form (DOMVUW).[1]

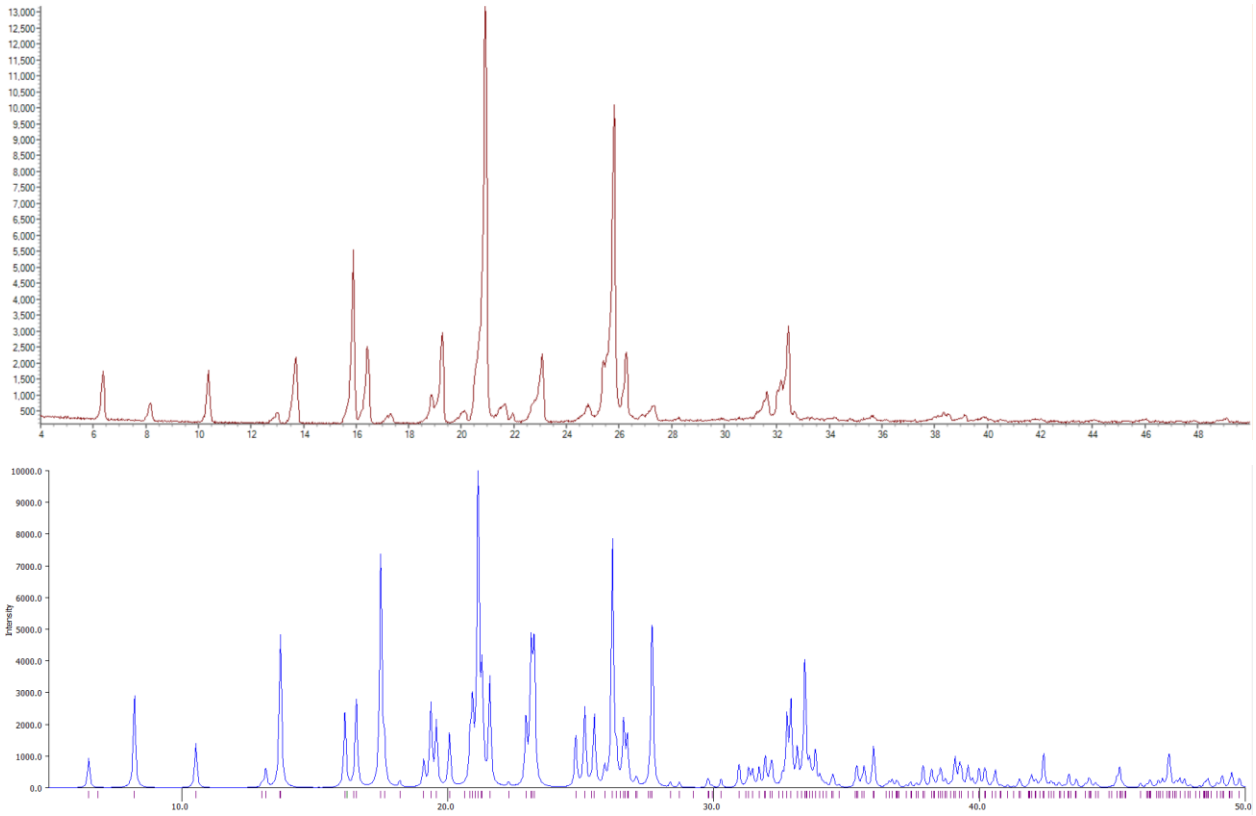

Fig. S5. F-Phe h2o gel pxrd sample top with single crystal data simulated pattern bottom.

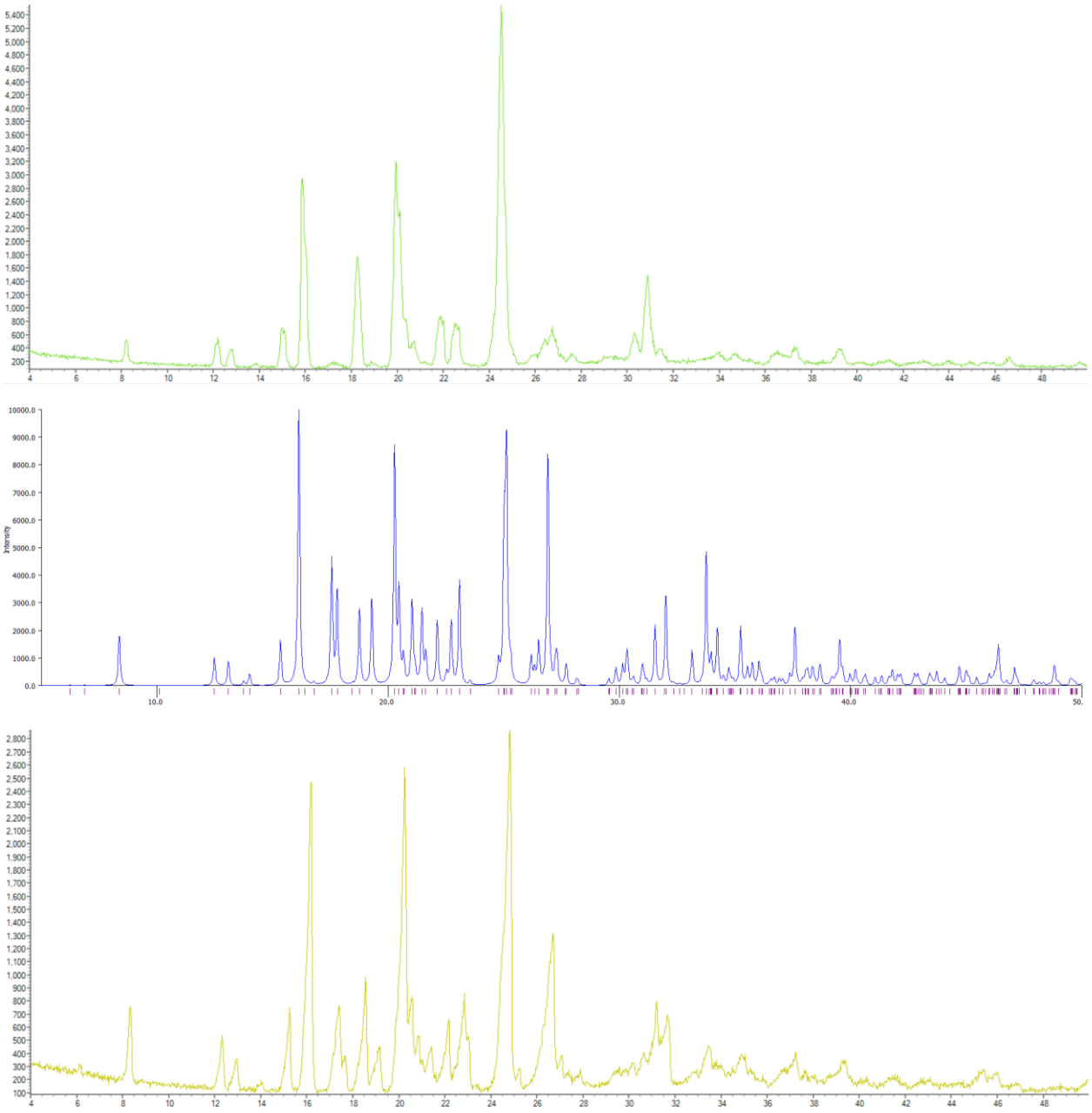

Fig. S6. 2F-Phe hydrogel PXRD sample top, simulated pattern from the single crystal data middle and commercial sample bottom (which appears to be the hydrate).

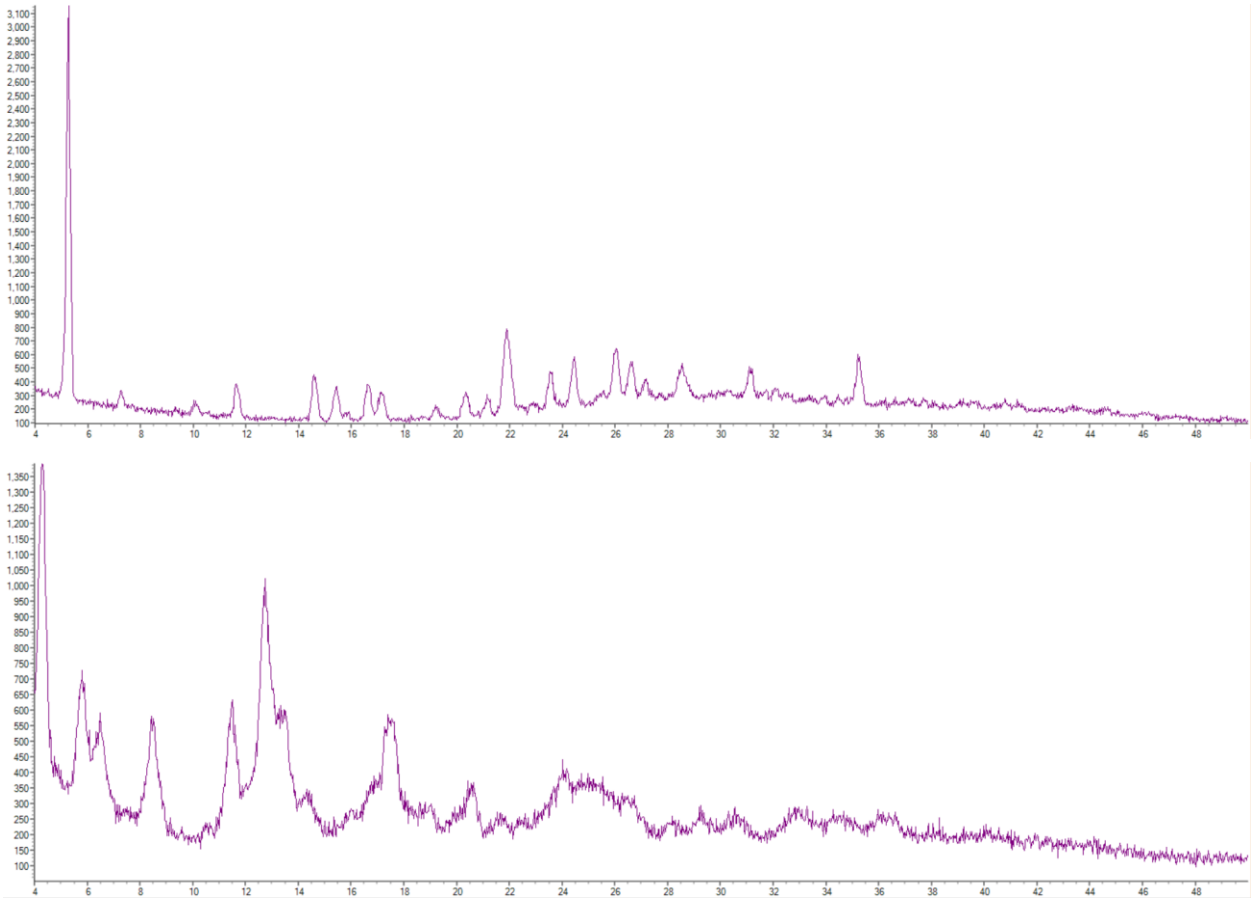

Fig. S7. 5F-Phe hydrogel PXRD sample above with commercial anhydrous form below.

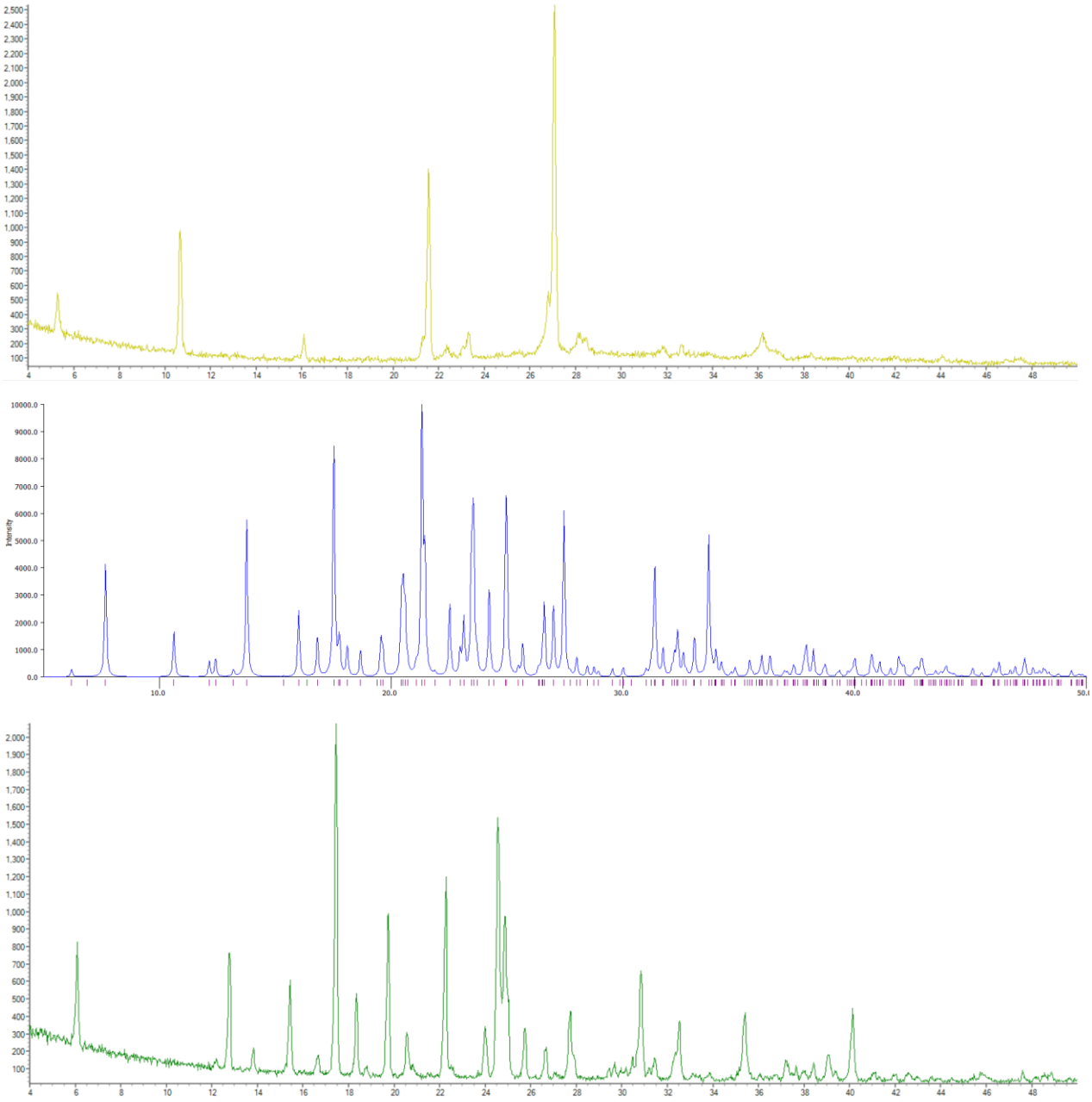

Fig. S8. Cl-Phe hydrogel PXRD sample top, with the simulated single crystal pattern middle, and the commercial sample PXRD pattern bottom. The gel sample appears to be showing signs of preferred orientation making it difficult to phase match to the single crystal data.

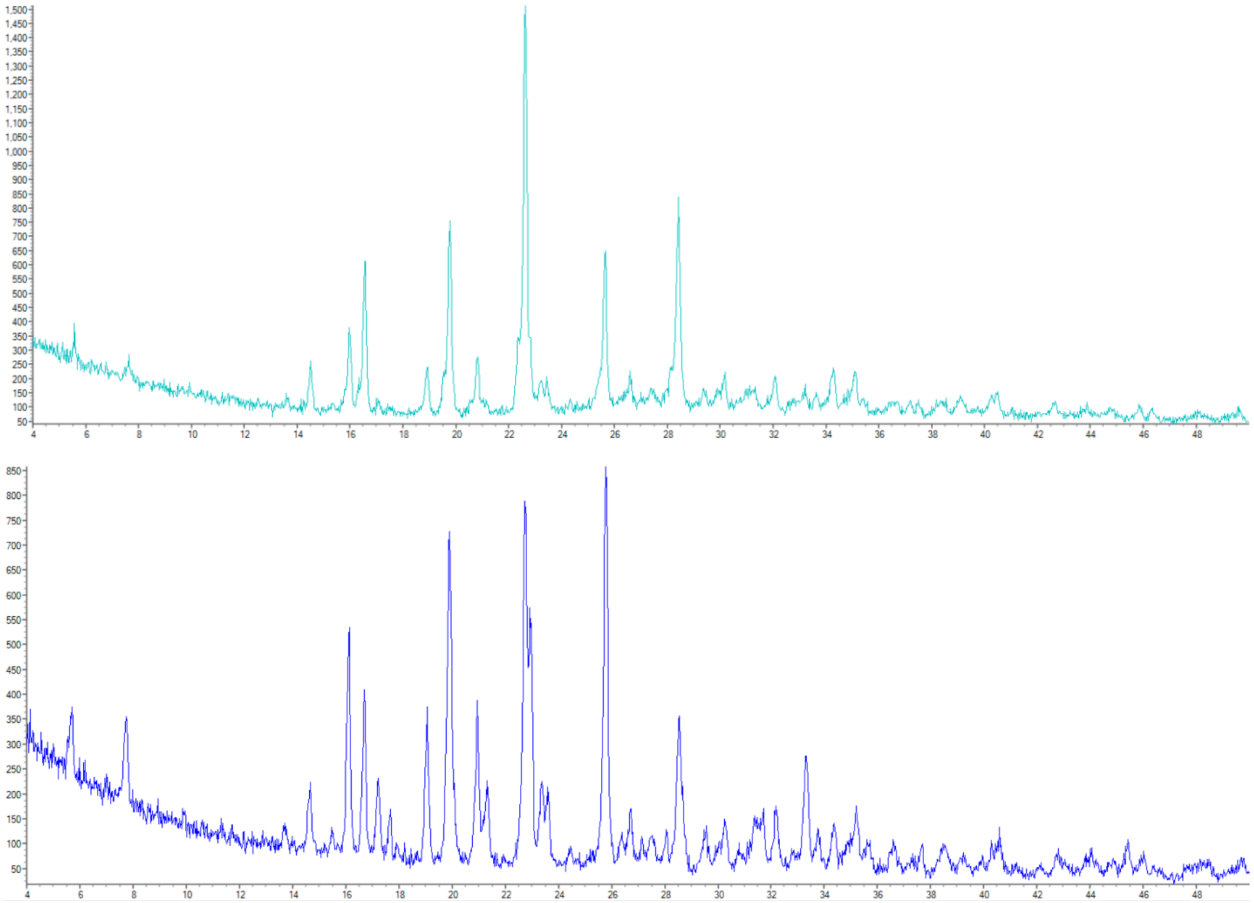

Fig. S9. 2Cl-Phe hydrogel PXRD sample top with commercial product bottom. These two phases appear to be the same.

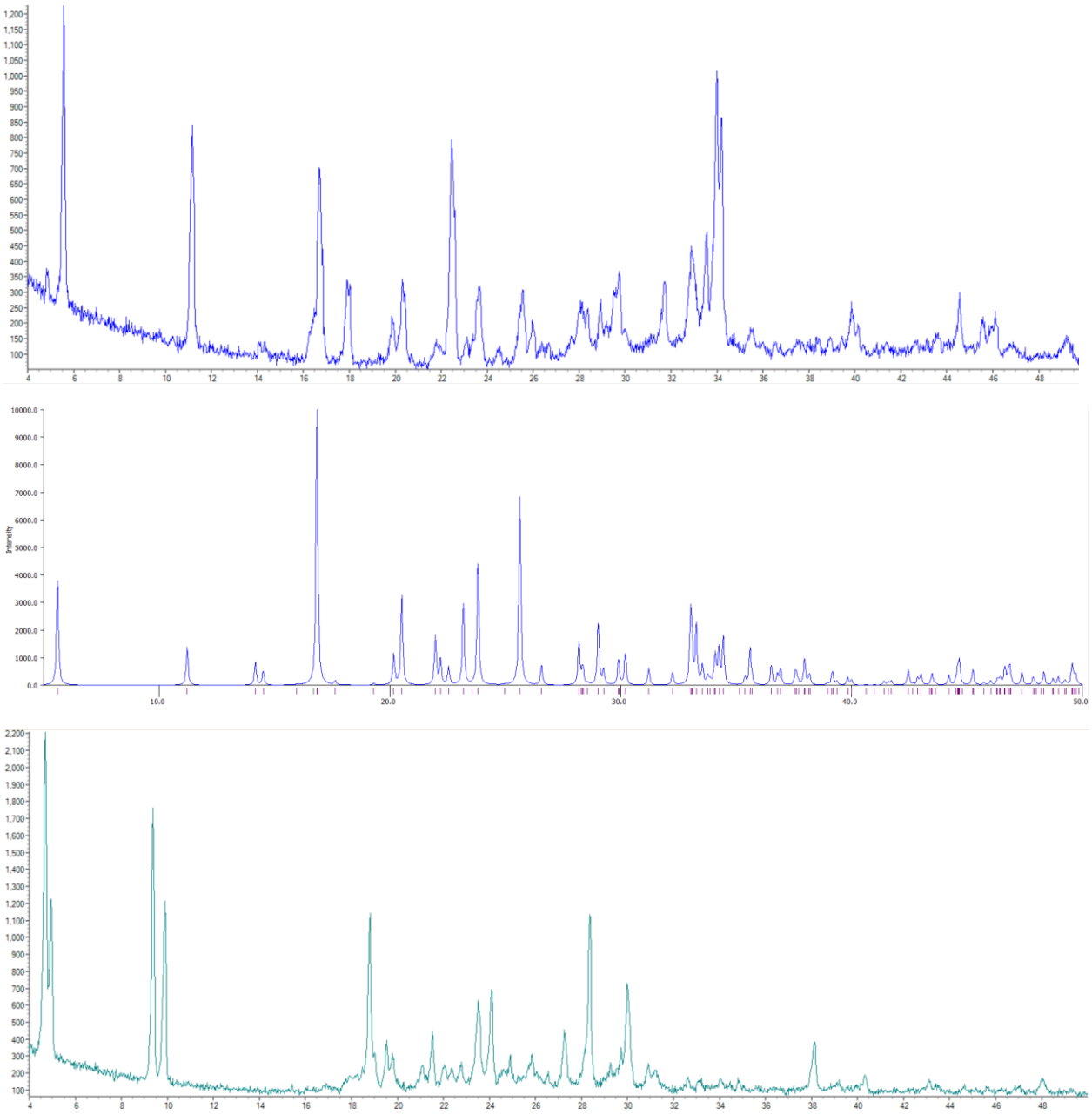

Fig. S10. Br-Phe hydrogel PXRD. Matches the single crystal data, however, there are a number of peaks that do not match. The bottom pattern is the commercial material.

Single Crystal Diagrams

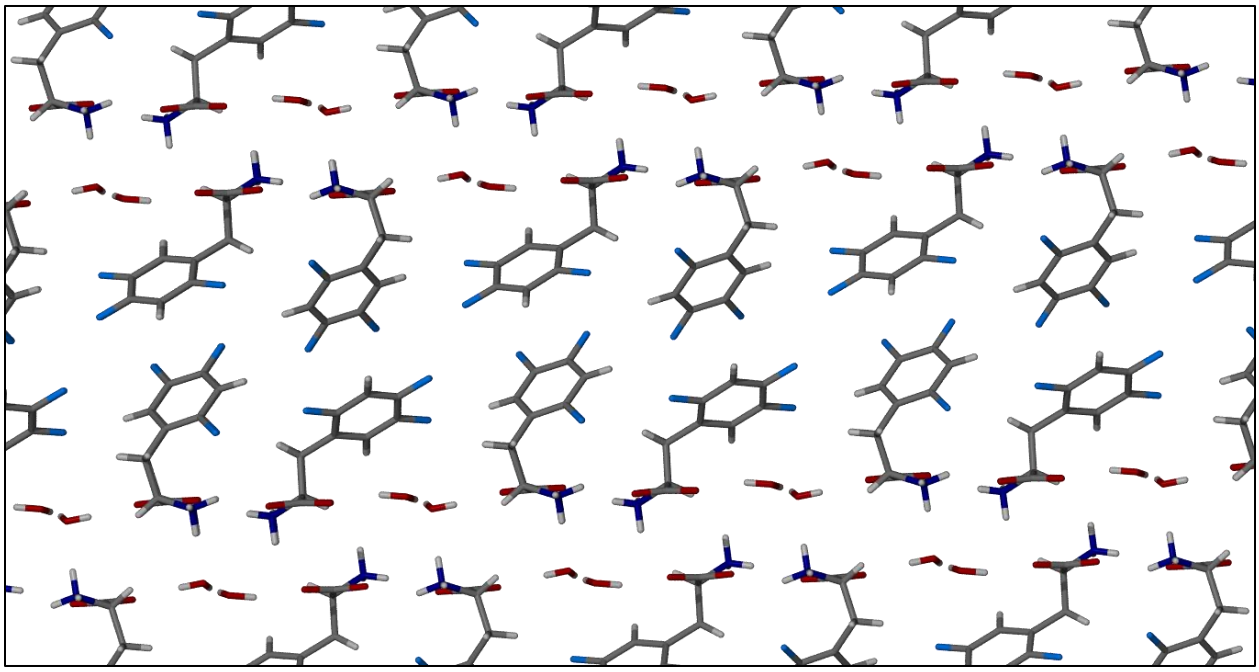

Fig. S11. 2,4,5-trifluorophenylalanine packing.

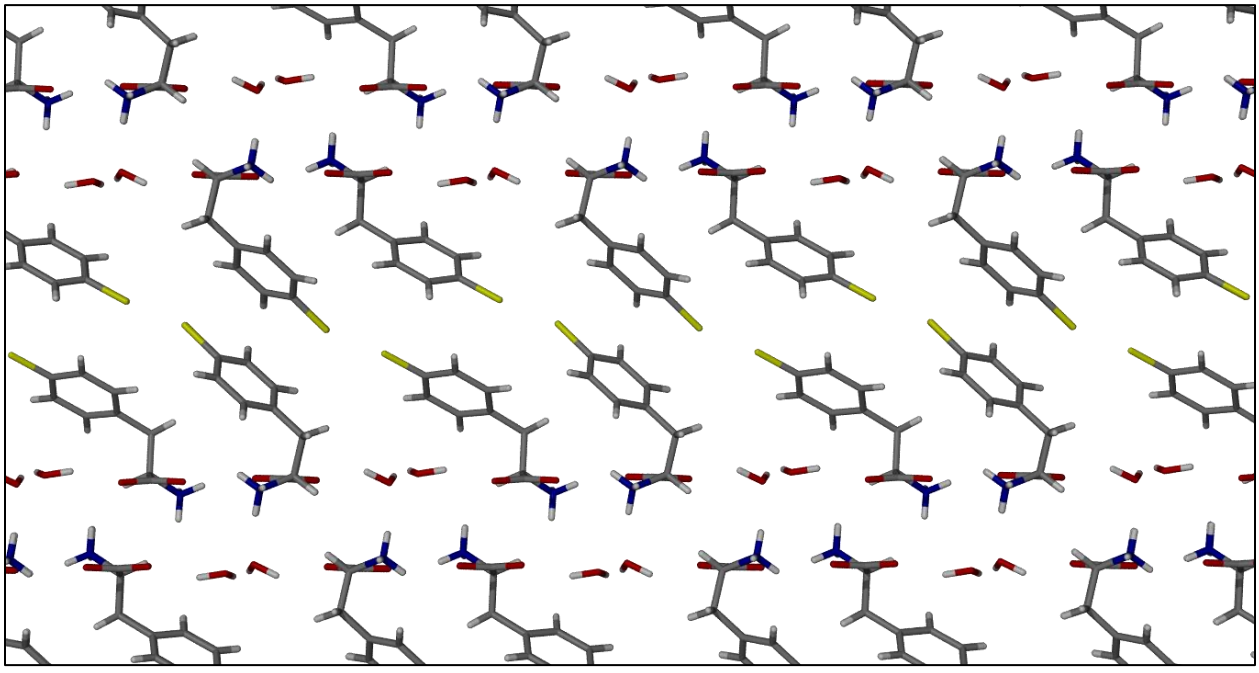

Fig. S12. Cl-Phe packing.

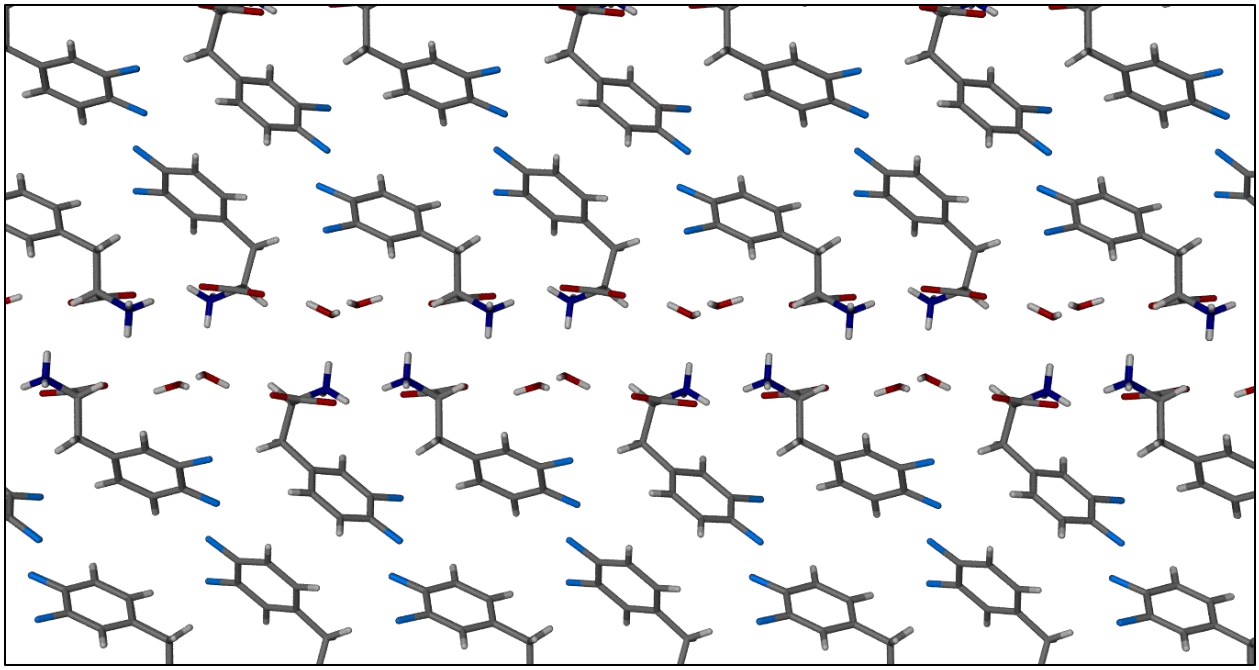

Fig. S13. 2F-Phe packing.

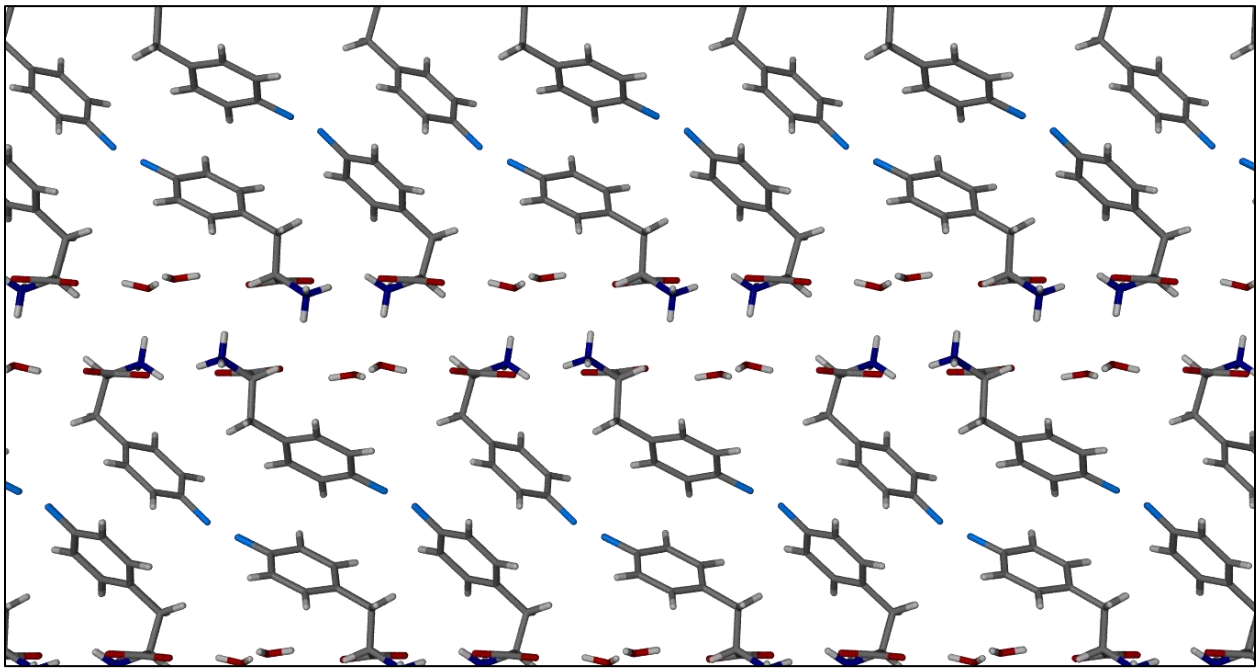

Fig. S14. F-Phe packing

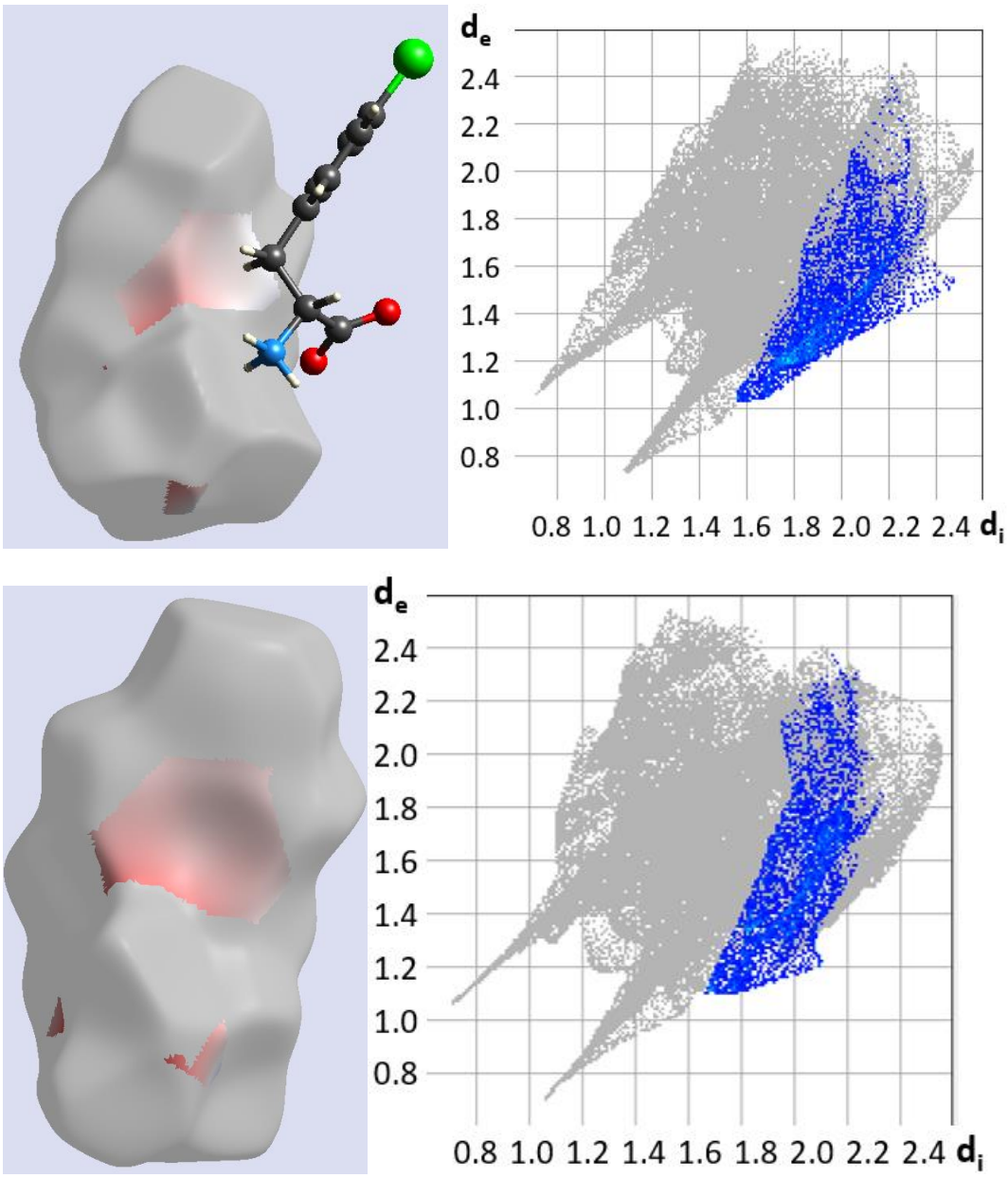

Fig. S15. C-H···π interactions/contacts within the Cl-Phe (top) and Br-Phe (bottom) monohydrate structures.

References

1. a) Y. In, S. Kishima, K. Minoura, T. Nose, Y. Shimohigashi, T. Ishida, *Chem.Pharm.Bull.*, 2003, **51**, 1258; b) Y. Hiyama, J. V. Silverton, D. A. Torchia, J. T. Gerig, S. J. Hammond, *J. Am. Chem. Soc.*, 2986, **108**, 2715.