Supporting information

Quantum chemical calculations on the model compound CBS-C(O)-NH$_2$ were performed at the B3LYP/6-311++G(d,p) level of theory, employing the polarizable continuum model (PCM) with water in order to simulate the aqueous environment. Figure S1 shows four selected eigenvectors of conformer B (Figure 6), which are assigned to the Raman bands (A)-(D) in Figure 3. Figure S1-A exhibits an amide I-like vibration at 1704 cm$^{-1}$, which has C=O stretching components predominantly located at the guanidino carbonyl part of the CBS. The excellent agreement between theory (DFT/PCM with water: 1704 cm$^{-1}$) and experiment (4 mM in water: 1702 cm$^{-1}$) is noted; in the calculated gas phase spectrum, this normal mode occurs at 1719 cm$^{-1}$.

The normal mode in Figure S1-B comprises of N-H bending motions of both the guanidino unit and the pyrrole ring and this mode occurs at 1474 cm$^{-1}$ (region B in Figure 5); it is expected to be sensitive to hydrogen bonding and substrate complexation. In contrast, the symmetrical half ring vibration of pyrrole at 1414 cm$^{-1}$ shown in Figure S1-C should not be very sensitive to hydrogen bonding or substrate binding. It was for this reason that this band was used for normalization of the experimental Raman spectra as discussed above (band C in Figure 5). Figure S1-D depicts a normal mode occurring in region labeled as D in Figure 5; it also comprises of N-H deformations, which are predominantly located at the guanidino carbonyl unit and should therefore be sensitive to substrate binding.