Electronic supporting information for:

Resistance to tyrosine kinase inhibitors can be mediated by changes to the conformation space of the kinase

1 Supplemental Tables

Table S1: Differences in energy between the preferred ion position (Fig. 1A in the main text) and the conformation with the ion binds to the carboxylate oxygens (Fig. 1B in the main text). Energy values are in kcal/mol and calculated with ωB97-3c/SMD.

Ion	ΔΔ G
Mg^{2+}	12.3
Ca^{2+}	10.1
Mn^{2+}	131.5
Fe^{3+}	17.2
Zn^{2+}	21.6

Table S2: Binding energies for the 1:1 ciprofloxacin:ion complexes in implicit solvent, with and without ZPE corrections. Energy values are in kcal/mol and calculated as reported in the main text

Ion	Δ G^b with ZPE	Δ G^b without ZPE
Mg^{2+}	−5.6	−6.5
Ca^{2+}	6.5	6.8
Mn^{2+}	−1.5	0.1
Fe^{3+}	−0.7	1.3
Zn^{2+}	17.1	16.9

Table S3: Binding energies for the 2:1 ciprofloxacin:ion complexes in implicit solvent, with and without ZPE corrections. Energy values are in kcal/mol and calculated as reported in the main text

Ion	Δ G^b with ZPE	Δ G^b without ZPE
Mg^{2+}	−42.4	−59.7
Ca^{2+}	−24.9	−41.0
Mn^{2+}	−45.2	−90.5
Fe^{3+}	−73.4	−60.4
Zn^{2+}	−45.0	−62.1

2 Supplemental Figures

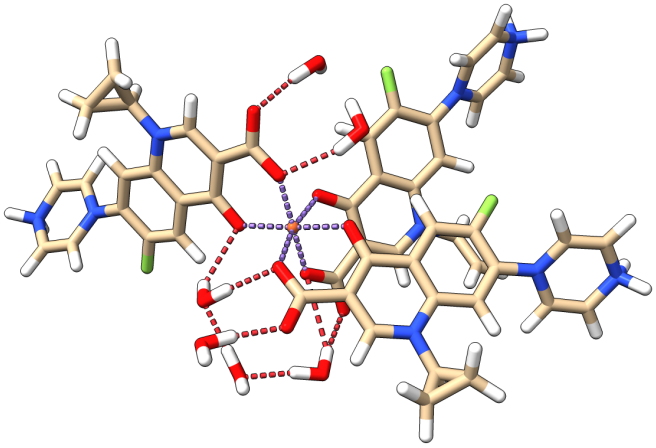

Figure S1: The optimised structures of the complexes between three ciprofloxacin molecules and Fe^{3+}, optimised with six water molecules at the ion binding site. The structures of such complexes were similar for all ions.