Supporting Information

The Impact of Side-Chain Fluorination on Proton-Bound Phenylalanine Dimers: A Cryogenic Infrared Spectroscopic Study

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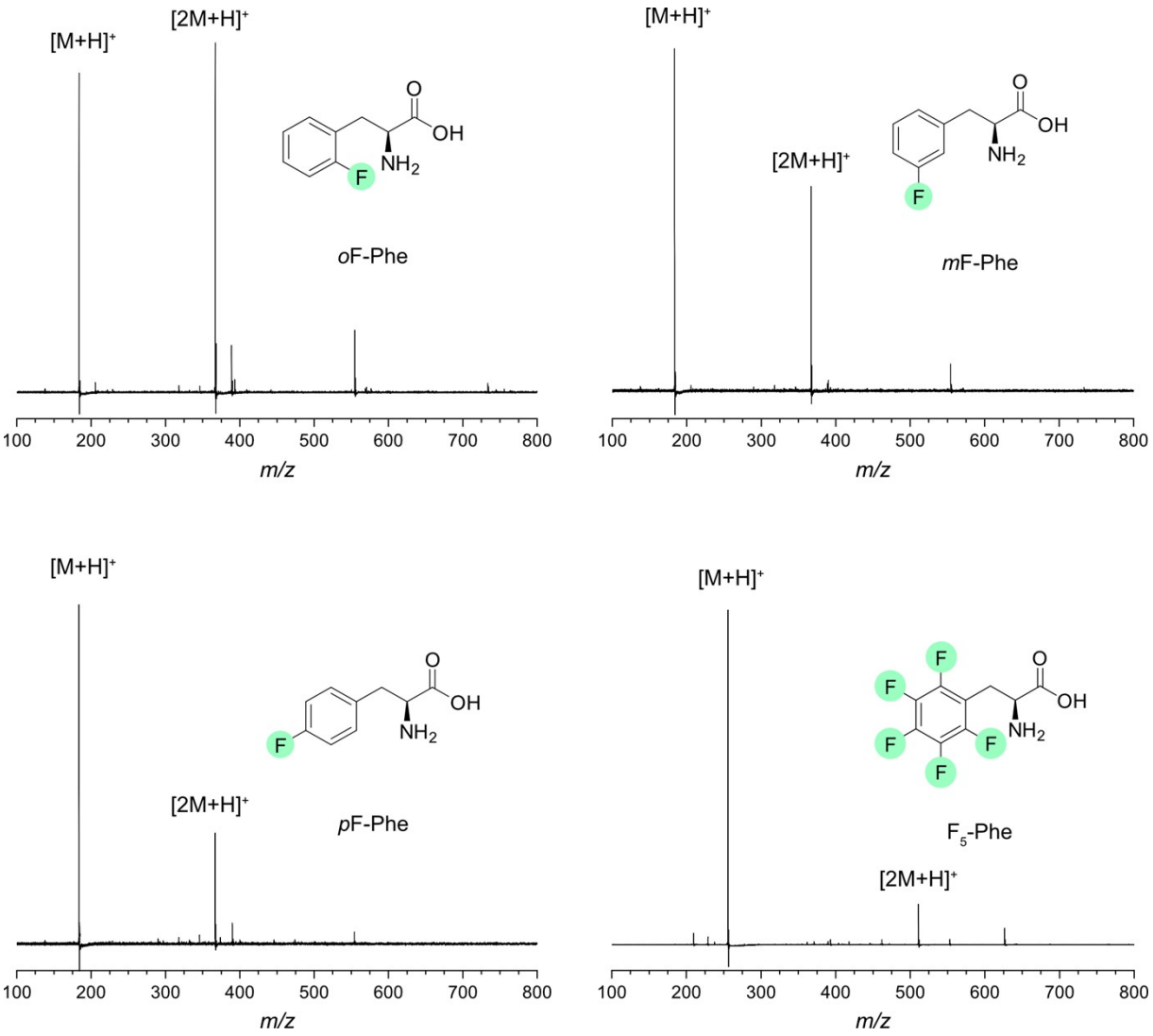


Fig. S1: Mass spectra of *ortho*- (*o*F-Phe), *meta*- (*m*F-Phe), *para*- (*p*F-Phe) and pentafluorophenylalanine (F_5-Phe) recorded on the helium droplet instrument. The proton-bound dimers $[2M+H]^+$ of the monofluorinated (*m/z* 367) and pentafluorinated phenylalanines (*m/z* 511) are generated by nESI.

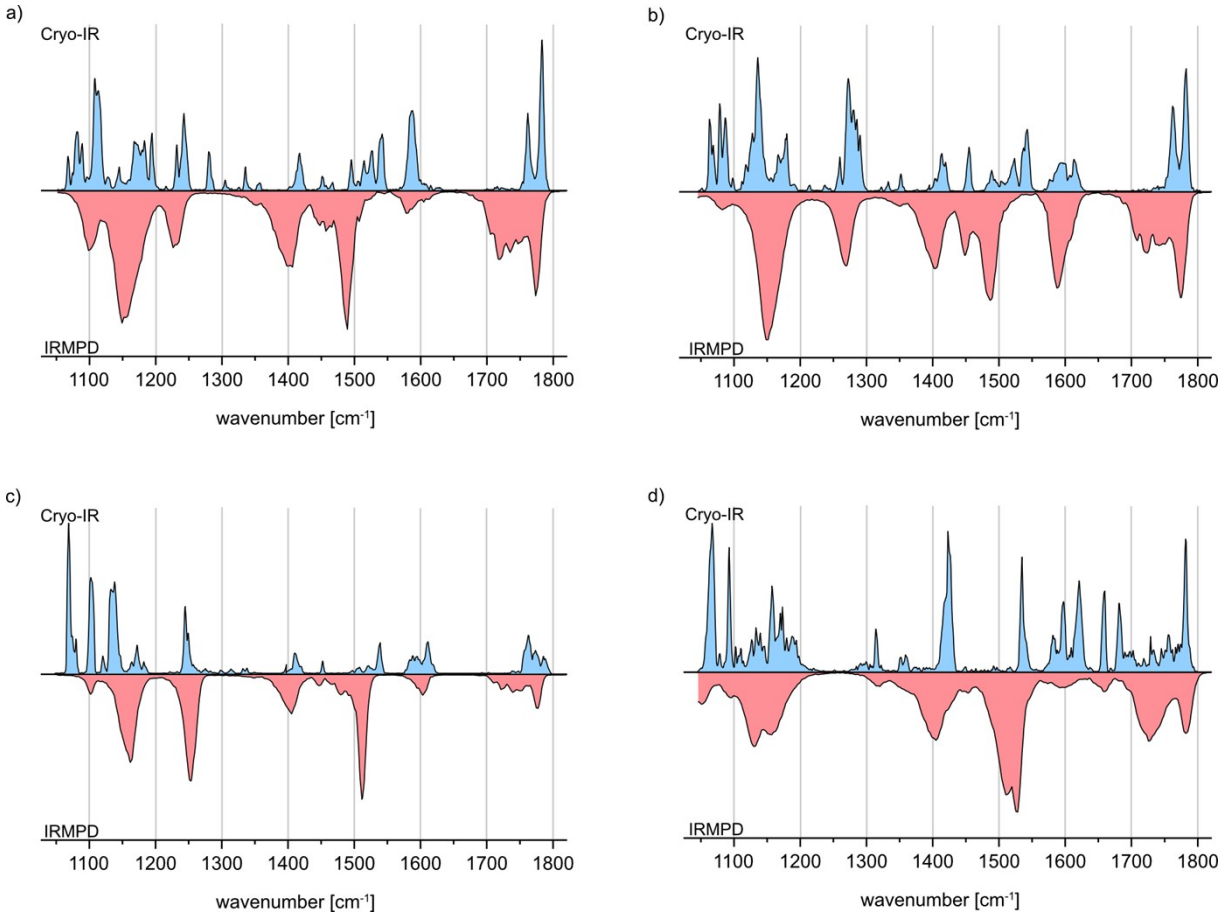


Fig. S2: Comparison of experimental IRMPD and cryogenic IR spectra of a) **(*o*F-Phe)$_2$H$^+$**, b) **(*m*F-Phe)$_2$H$^+$**, c) **(*p*F-Phe)$_2$H$^+$**, and d) **(F$_5$-Phe)$_2$H$^+$**.

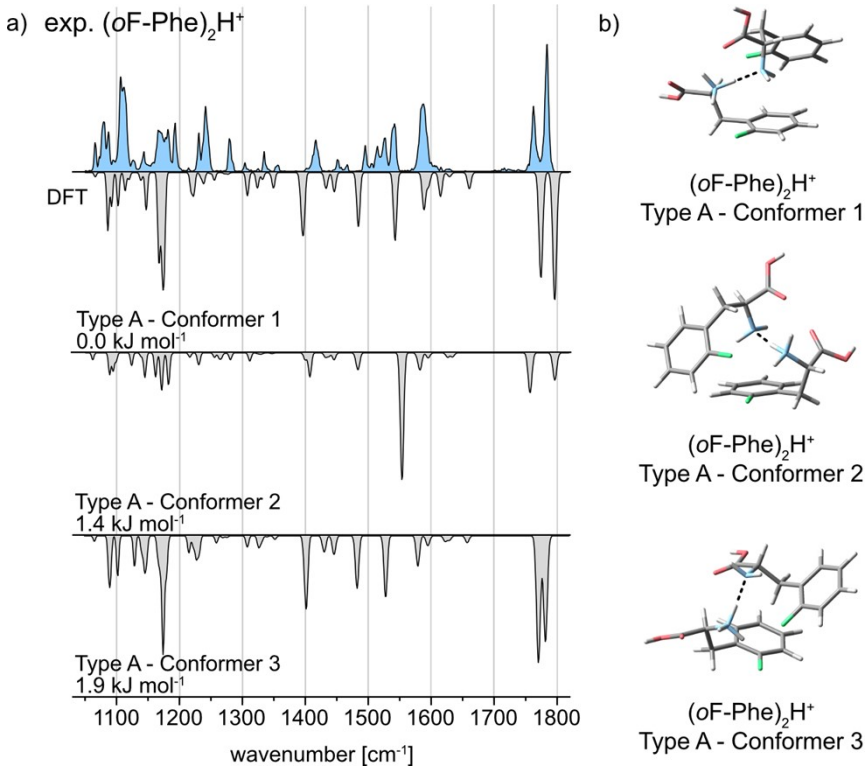


Fig. S3: a) Infrared spectra of the proton-bound homodimer of *ortho*-fluorophenylalanine. Experimental IR spectra are depicted as light blue traces. Computed spectra of the low-energy conformers are shown as gray inverted traces. Relative free energies at 90 K are indicated. b) Low-energy structures of the A type interaction for **(*o*F-Phe)$_2$H$^+$**.

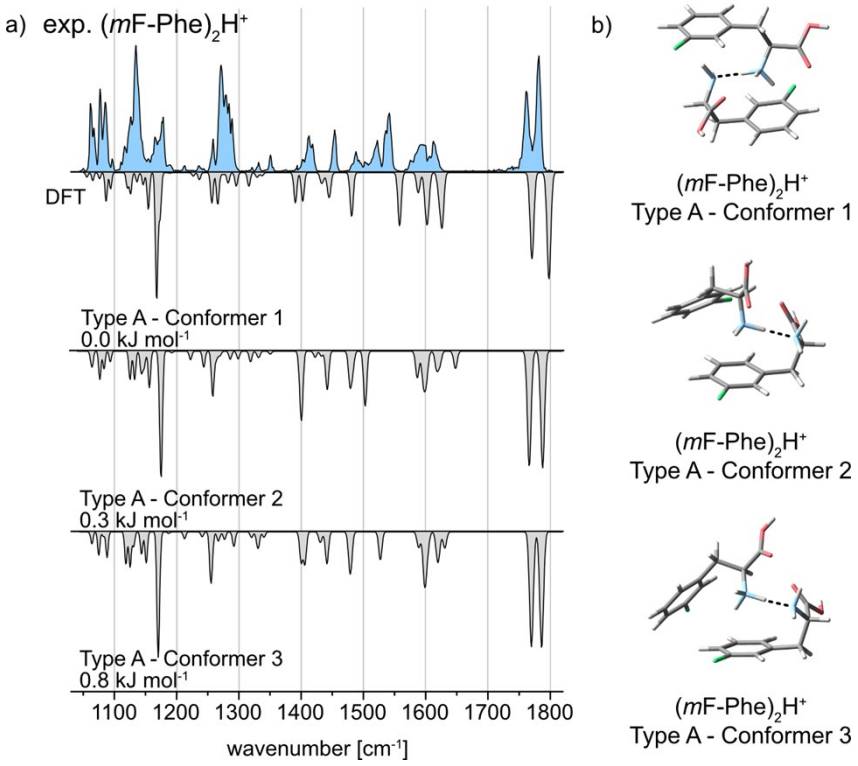


Fig. S4: a) Infrared spectra of the proton-bound homodimer of *meta*-fluorophenylalanine. Experimental IR spectra are depicted as light blue traces. Computed spectra of the low-energy conformers are shown as gray inverted traces. Relative free energies at 90 K are indicated. b) Low-energy structures of the A type interaction for **(*m*F-Phe)$_2$H$^+$**.

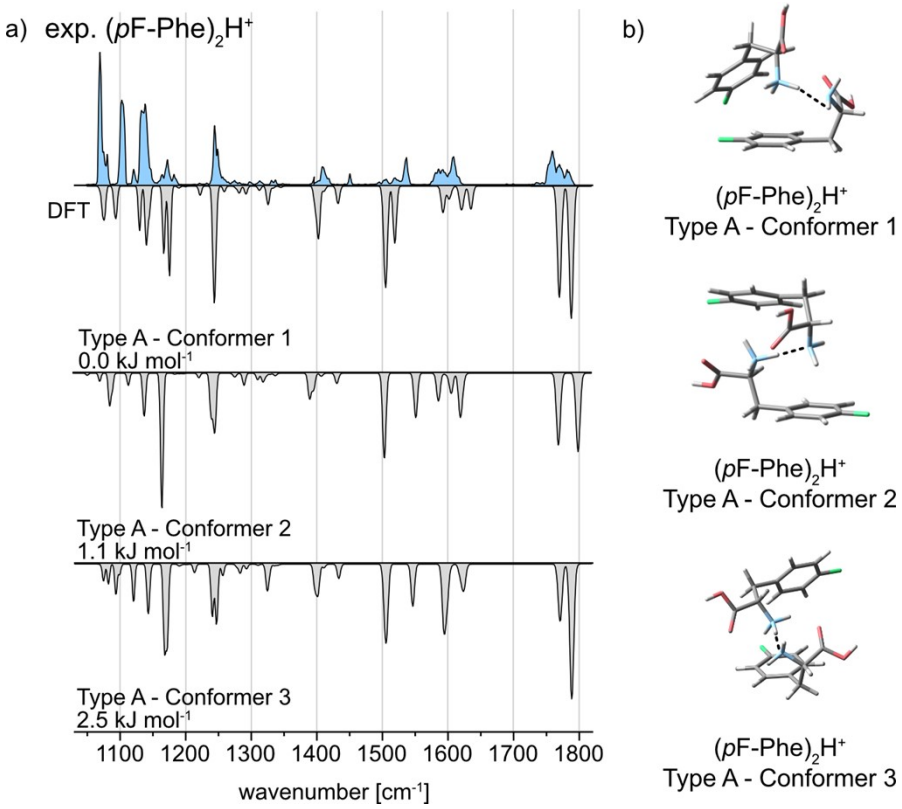
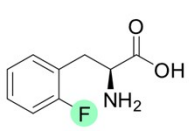
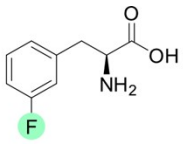


Fig. S5: a) Infrared spectra of the proton-bound homodimer of *para*-fluorophenylalanine. Experimental IR spectra are depicted as light blue traces. Computed spectra of the low-energy conformers are shown as gray inverted traces. Relative free energies at 90 K are indicated. b) Low-energy structures of the A type interaction for **(*p*F-Phe)$_2$H$^+$**.



*o*F-Phe



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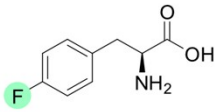
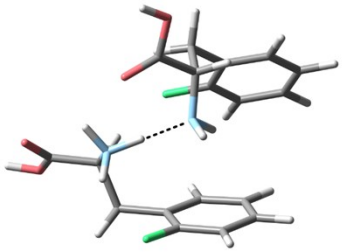
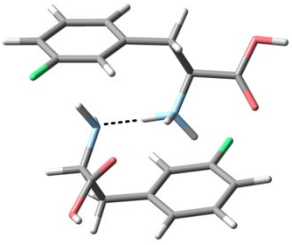


*p*F-Phe



$(oF\text{-Phe})_2H^+$
Type A



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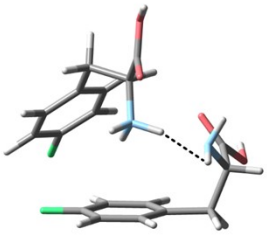
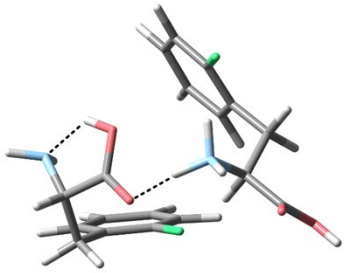


$(pF\text{-Phe})_2H^+$
Type A



$(oF\text{-Phe})_2H^+$
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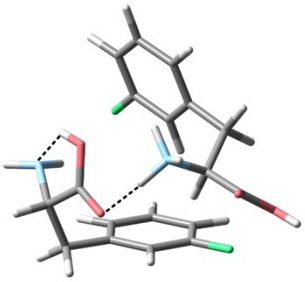

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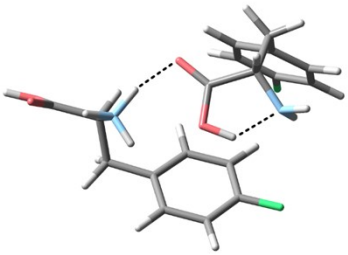
Type B



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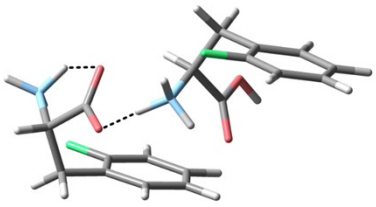
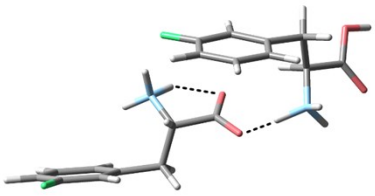
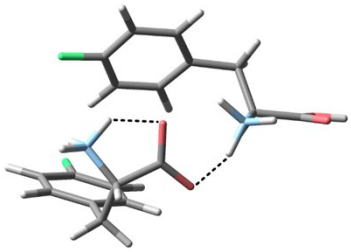
Type B



$(oF\text{-Phe})_2H^+$
Type Z



$(mF\text{-Phe})_2H^+$
Type Z



$(pF\text{-Phe})_2H^+$
Type Z

Fig. S6: Computed lowest-energy structures of the proton-bound monofluorinated dimers.

Table S1: Relative zero-point corrected total energies (ΔE) and free energies (ΔF) of selected conformers.

derivative	type	conformer	ΔE	ΔF
(*o*F-Phe)$_2$H$^+$	A	1	0.0 kJ mol^{-1}	0.0 kJ mol-1
(*o*F-Phe)$_2$H$^+$	A	2	0.5 kJ mol^{-1}	1.4 kJ mol^{-1}
(*o*F-Phe)$_2$H$^+$	A	3	1.3 kJ mol^{-1}	1.9 kJ mol^{-1}
(*o*F-Phe)$_2$H$^+$	B	1	3.2 kJ mol^{-1}	2.4 kJ mol-1
(*o*F-Phe)$_2$H$^+$	Z	1	3.6 kJ mol^{-1}	3.1 kJ mol-1
(*m*F-Phe)$_2$H$^+$	A	1	0.3 kJ mol^{-1}	0.0 kJ mol-1
(*m*F-Phe)$_2$H$^+$	A	2	0.0 kJ mol^{-1}	0.3 kJ mol-1
(*m*F-Phe)$_2$H$^+$	A	3	0.2 kJ mol^{-1}	0.8 kJ mol-1
(*m*F-Phe)$_2$H$^+$	B	1	3.4 kJ mol^{-1}	4.9 kJ mol-1
(*m*F-Phe)$_2$H$^+$	Z	1	9.4 kJ mol^{-1}	9.3 kJ mol^{-1}
(*p*F-Phe)$_2$H$^+$	A	1	0.0 kJ mol^{-1}	0.0 kJ mol^{-1}
(*p*F-Phe)$_2$H$^+$	A	2	3.0 kJ mol^{-1}	1.1 kJ mol^{-1}
(*p*F-Phe)$_2$H$^+$	A	3	4.3 kJ mol^{-1}	2.5 kJ mol^{-1}
(*p*F-Phe)$_2$H$^+$	B	1	12.5 kJ mol^{-1}	13.4 kJ mol^{-1}
(*p*F-Phe)$_2$H$^+$	Z	1	16.7 kJ mol^{-1}	18.2 kJ mol^{-1}
(F_5-Phe)$_2$H$^+$	A	1	0.0 kJ mol^{-1}	0.0 kJ mol^{-1}
(F_5-Phe)$_2$H$^+$	B	1	4.8 kJ mol^{-1}	2.5 kJ mol^{-1}
(F_5-Phe)$_2$H$^+$	Z	1	3.2 kJ mol^{-1}	2.8 kJ mol^{-1}

xyz-coordinates of reoptimized structures

xyz-Coordinates of all reoptimized geometries at the PBE0+D3BJ/6-311+G(d,p) level of theory can be found in a separate document “coordinates.xyz”.

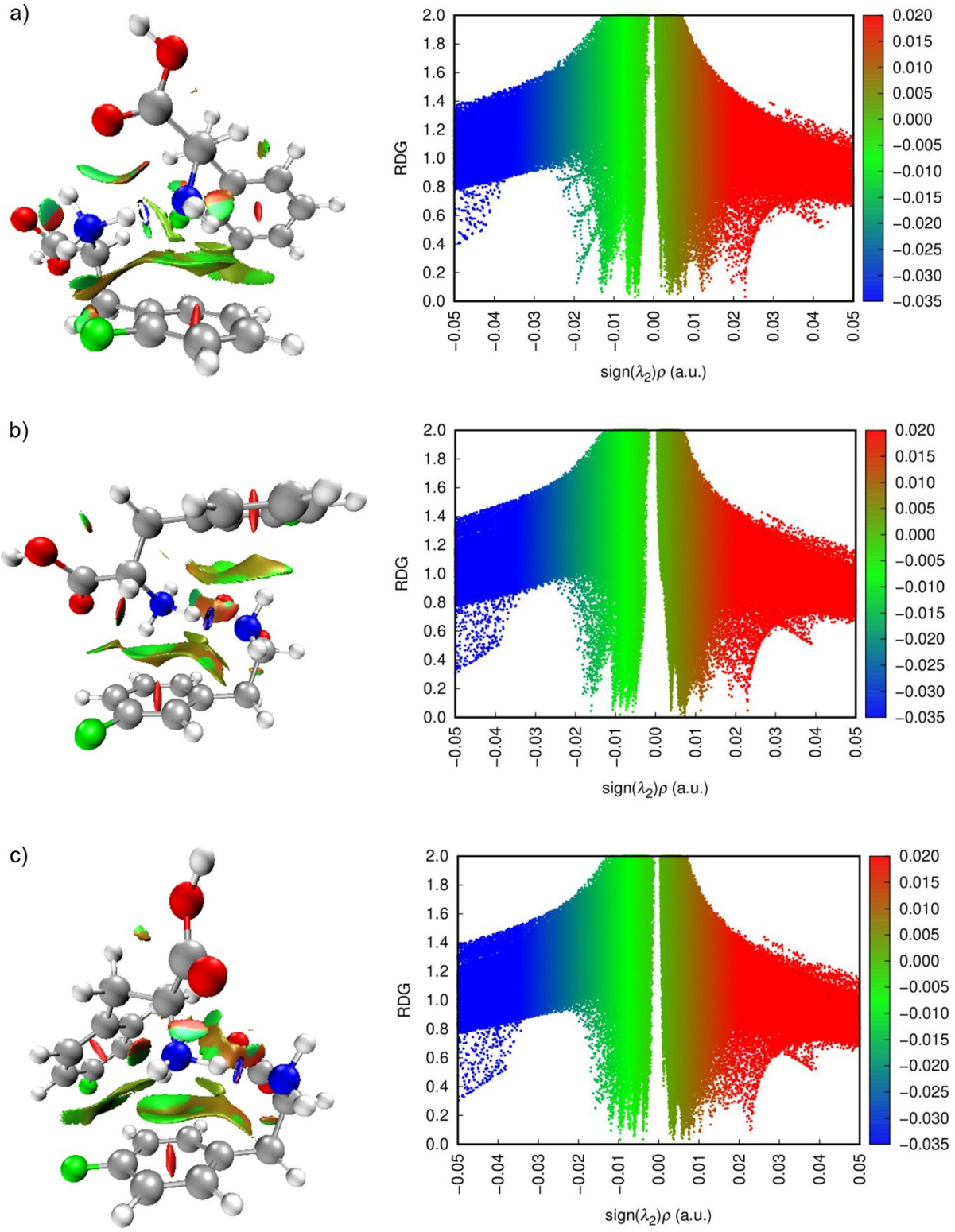


Fig. S7: Non-covalent interaction (NCI) analysis of lowest-energy type A conformers for monofluorinated phenylalalanine dimers. Reduced density gradient isosurface map (left) and scatter plot (right) for a) **(*o*F-Phe)$_2$H$^+$**, b) **(*m*F-Phe)$_2$H$^+$**, and c) **(*p*F-Phe)$_2$H$^+$**.

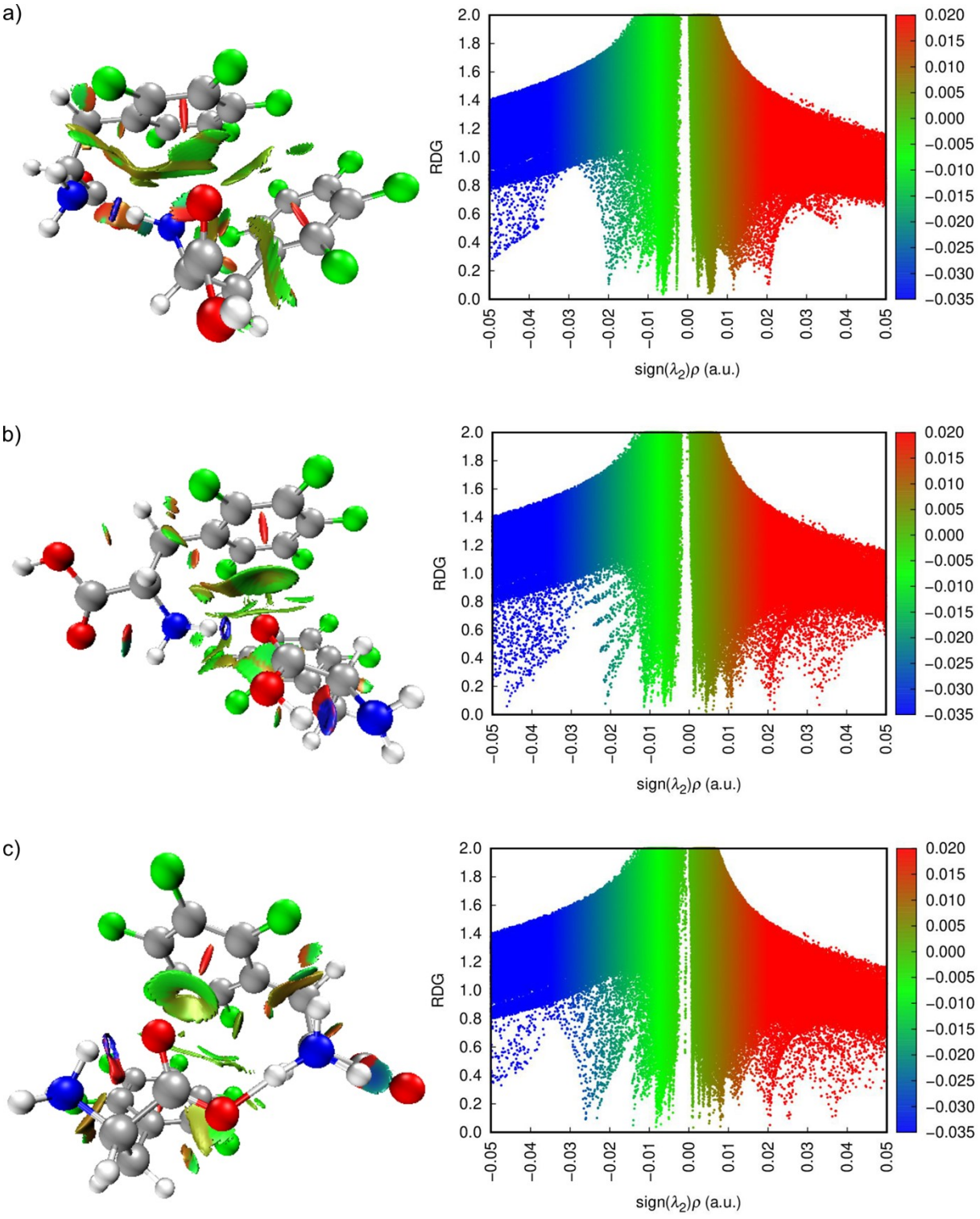


Fig. S8: Non-covalent interaction (NCI) analysis of **$(F_5$-Phe$)_2H^+$** conformers. Reduced density gradient isosurface map (left) and scatter plot (right) for the lowest-energy conformers of a) type A, b) type B, and c) type Z interaction.