Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Role of Hydrogen Bonding in Bulk Aqueous Phase Decomposition, Complexation, and Covalent Hydration of Pyruvic Acid

Supplementary Material-B (NBO Analysis)

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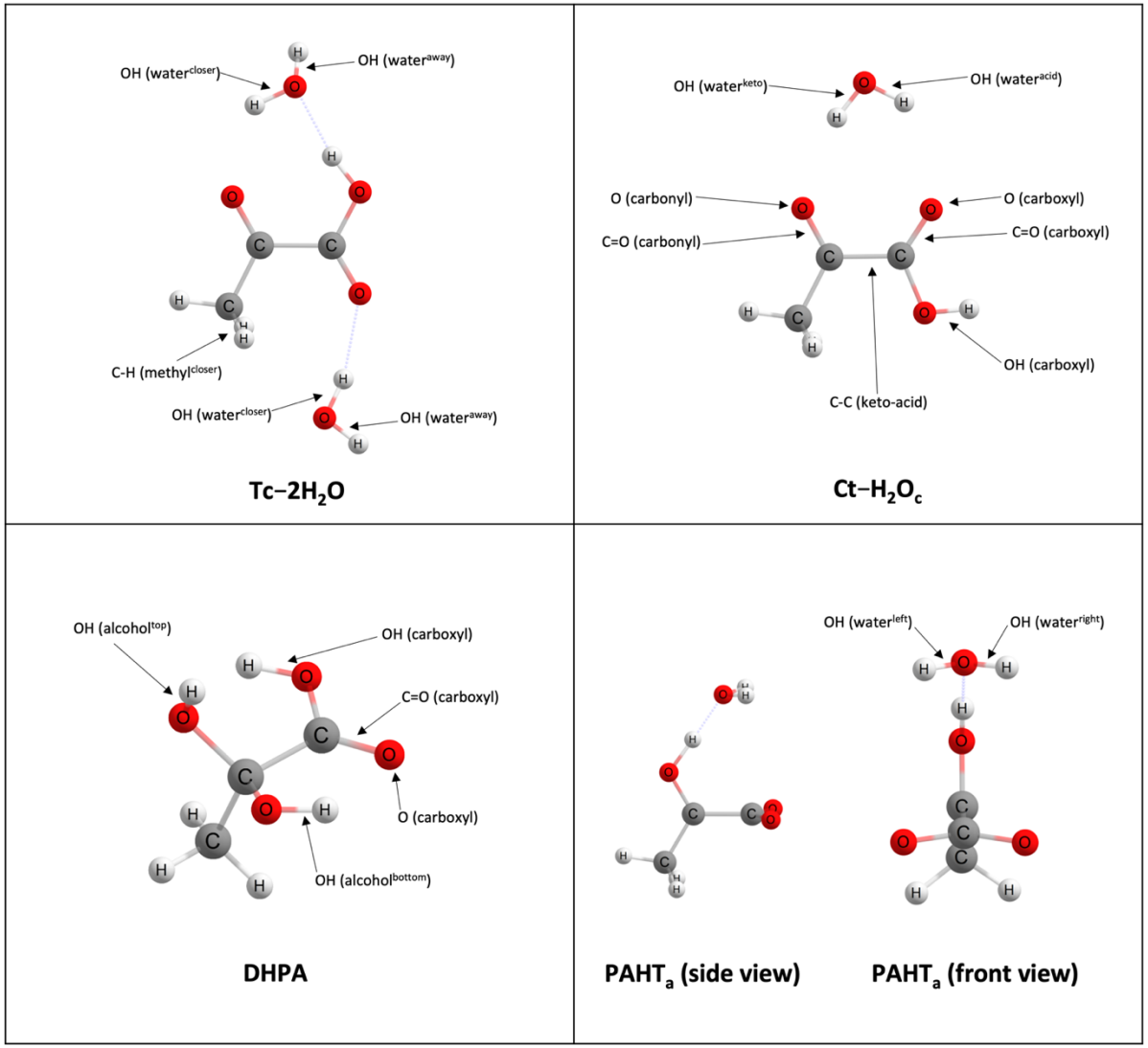

Fig. S1B Labeling used for atoms and functional groups of pyruvic acid (PA)–water complexes, 2,2-dyhydroxypropanoic acid (DHPA) and DHPA–H_2O, and PA hydrogen-transferred (PAHT) tautomer–H_2O complexes in Table S1B to S20B

Table S1B Important orbital interactions of Tc–H_2O_a calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tc–H_2O_a	Gas	--- From PA to H_2O ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.44
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.44
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.28
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	20.67
		σ Bond	O-H (water)	π antibond	C=O (carboxyl)	σ to π*	0.18
		σ Bond	O-H (water)	σ antibond	O-H (carboxyl)	σ to σ*	0.95
	Aqueous	--- From within PA ---					
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	0.78
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.06
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.09
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.41
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	30.56
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.26
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.61

Table S2B Important orbital interactions of Tc–H_2O_b calculated by NBO analysis at SMD-B2PLYP-D3BJ/aug-cc-pVTZ.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tc–H_2O_b	Aqueous	--- From within PA ---					
		Lone Pair	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	2.60
		--- From PA to H_2O ---					
		π Bond	C-C (keto-acid)	Rydberg (2)	O (water)	π to Ry	0.13
		π Bond	C-C (keto-acid)	Rydberg (4)	H (water)	π to Ry	0.07
		π Bond	C=O (carbonyl)	σ antibond	O-H ($water^{closer}$)	π to σ*	0.05
		π Bond	C=O (carboxyl)	Rydberg (2)	O (water)	π to Ry	0.06
		--- From H_2O to PA ---					
		Lone pair (1)	O (water)	π antibond	C=O (carbonyl)	p to π*	0.37
		Lone pair (2)	O (water)	π antibond	C=O (carbonyl)	p to π*	2.62
		Lone pair (2)	O (water)	π antibond	C=O (carboxyl)	p to π*	1.59
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.08
		σ Bond	O-H ($water^{away}$)	π antibond	C=O (carboxyl)	σ to π*	0.06

Table S3B Important orbital interactions of Tc–H_2O_b' calculated by NBO analysis at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tc–H_2O_b'	Gas	--- From within PA ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	0.59
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	4.03
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	2.82
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	2.92
		π Bond	C=O (carboxyl)	σ antibond	O-H ($water^{closer}$)	π to σ*	0.32
		σ Bond	C-H ($methyl^{closer}$)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.18
		--- From H_2O to PA ---					
		Lone pair (1)	O (water)	π antibond	C=O (carboxyl)	p to π*	0.05
		Lone pair (1)	O (water)	σ antibond	C-H ($methyl^{closer}$)	p to σ*	0.15
		Lone pair (2)	O (water)	σ antibond	C-H ($methyl^{closer}$)	p to σ*	0.74
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carboxyl)	σ to π*	0.13
		σ Bond	O-H ($water^{closer}$)	π antibond (2)	C=O (carboxyl)	σ to π*	0.09
		σ Bond	O-H ($water^{closer}$)	σ antibond	C-H ($methyl^{away}$)	σ to σ*	0.05
	Aqueous	--- From within PA ---					
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	2.50
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	3.71
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	4.04
		π Bond	C=O (carboxyl)	σ antibond	O-H ($water^{away}$)	π to σ*	0.09
		--- From H_2O to PA ---					
		Lone pair (1)	O (water)	π antibond	C=O (carboxyl)	p to π*	0.11
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carboxyl)	σ to π*	0.16

Table S4B Important orbital interactions of Ct–H_2O_a calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Ct–H_2O_a	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	1.05
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.25
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	4.03
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.19
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.24
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	20.30
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.91
	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	1.07
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.47
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	38.17
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.47
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.39

Table S5B Important orbital interactions of Ct–H_2O_b calculated by NBO analysis at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Ct–H_2O_b	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	1.19
		--- From PA to H_2O ---					
		π Bond (1)	C=O (carbonyl)	σ antibond	O-H ($water^{closer}$)	π to σ*	0.08
		π Bond (2)	C=O (carbonyl)	σ antibond	O-H ($water^{away}$)	π to σ*	0.17
		π Bond (2)	C=O (carbonyl)	σ antibond	O-H ($water^{closer}$)	π to σ*	0.07
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	π antibond	C=O (carbonyl)	p to π*	0.21
		Lone Pair (2)	O (water)	π antibond	C=O (carbonyl)	p to π*	1.50
		Lone Pair (2)	O (water)	π antibond	C=O (carboxyl)	p to π*	0.71
		σ Bond	O-H ($water^{closer}$)	σ antibond (1)	C (carbonyl)	σ to σ*	0.08
		σ Bond	O-H ($water^{closer}$)	σ antibond (2)	C (carbonyl)	σ to σ*	0.18
	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	1.26
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	π antibond	C=O (carbonyl)	p to π*	0.31
		Lone Pair (2)	O (water)	π antibond	C=O (carbonyl)	p to π*	2.29
		Lone Pair (2)	O (water)	π antibond	C=O (carboxyl)	p to π*	1.59
		σ Bond	O-H ($water^{away}$)	π antibond	C=O (carboxyl)	σ to π*	0.10
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carbonyl)	σ to π*	0.07

Table S6B Important orbital interactions of Ct–H_2O_c calculated by NBO analysis at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Ct–H_2O_c	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.22
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{acid}$)	p to σ*	0.07
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{acid}$)	p to σ*	0.22
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{keto}$)	p to σ*	0.92
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{keto}$)	p to σ*	1.55
		--- From H_2O to PA ---					
		Lone Pair	O (water)	π antibond	C=O (carbonyl)	p to π*	0.06
		σ Bond	O-H ($water^{keto}$)	π antibond	C=O (carbonyl)	σ to π*	0.10
	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.26
		--- From PA to H_2O ---					
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{keto}$)	p to σ*	0.28
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{keto}$)	p to σ*	2.60
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{keto}$)	p to σ*	5.37
		--- From H_2O to PA ---					
		σ Bond	O-H ($water^{keto}$)	π antibond	C=O (carbonyl)	σ to π*	0.14

Table S7B Important orbital interactions of Tt–H_2O_a calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tt–H_2O_a	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.22
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.14
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.08
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	3.59
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.18
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.22
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	19.51
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.07
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.86
	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.14
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.46
		Lone Pair (2)	O (water)	π antibond	C=O (carboxyl)	p to π*	0.10
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	37.48
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.44
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.40

Table S8B Important orbital interactions of Tt–H_2O_b calculated by NBO analysis at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tt–H_2O_b	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.34
		--- From PA to H_2O ---					
		π Bond (1)	C=O (carbonyl)	σ antibond	O-H ($water^{away}$)	π to σ*	0.08
		π Bond (2)	C=O (carbonyl)	σ antibond	O-H ($water^{closer}$)	π to σ*	0.17
		π Bond (2)	C=O (carbonyl)	σ antibond	O-H ($water^{away}$)	π to σ*	0.07
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	π antibond	C=O (carbonyl)	p to π*	0.27
		Lone Pair (2)	O (water)	π antibond	C=O (carbonyl)	p to π*	1.52
		Lone Pair (2)	O (water)	π antibond	C=O (carboxyl)	p to π*	0.71
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carbonyl)	σ to π*	0.08
		σ Bond	O-H ($water^{closer}$)	π antibond (2)	C=O (carbonyl)	σ to π*	0.14
	Aqueous	--- From H_2O to PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.34
		--- From H_2O to PA ---					
		Lone Pair (1)	O (water)	π antibond	C=O (carbonyl)	p to π*	0.33
		Lone Pair (2)	O (water)	π antibond	C=O (carbonyl)	p to π*	2.37
		Lone Pair (2)	O (water)	π antibond	C=O (carboxyl)	p to π*	1.54
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carboxyl)	σ to π*	0.10
		σ Bond	O-H ($water^{closer}$)	π antibond (2)	C=O (carboxyl)	σ to π*	0.06

Table S9B Orbital interactions of Tt–H_2O_c calculated by NBO analysis at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tt–H_2O_c	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.26
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.08
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.11
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.00
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	2.17
		--- From H_2O to PA ---					
		Lone Pair	O (water)	π antibond (1)	C=O (carbonyl)	p to π*	0.09
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carbonyl)	σ to π*	0.09
	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.33
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.08
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.10
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	2.67
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	4.37
		--- From H_2O to PA ---					
		Lone Pair	O (water)	π antibond (1)	C=O (carbonyl)	p to π*	0.11
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carbonyl)	σ to π*	0.15

Table S10B Orbital interactions of Tt–H_2O_d calculated by NBO analysis at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for aqueous phase.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tt–H_2O_d	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.36
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.93
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	4.54
		--- From H_2O to PA ---					
		Lone Pair	O (water)	σ antibond	C-H ($methyl^{closer}$)	p to σ*	0.52
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carbonyl)	σ to π*	0.57
	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.35
		--- From PA to H_2O ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	3.00
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	5.88
		--- From H_2O to PA ---					
		Lone Pair	O (water)	π antibond	C=O (carbonyl)	p to π*	0.08
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carbonyl)	σ to π*	0.15

Table S11B Orbital interactions of Tc–2H_2O in gas phase calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tc–2H_2O	Gas	--- From within PA ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	0.56
		--- From PA (carboxyl oxygen and methyl group) to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	3.58
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	3.02
		π Bond	C=O (carboxyl)	σ antibond	O-H ($water^{closer}$)	π to σ*	0.29
		σ Bond	C-H ($methyl^{closer}$)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.14
		--- From PA (carboxyl hydrogen and carbonyl oxygen) to H_2O ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.24
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.05
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.13
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.10
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.11
		--- From H_2O to PA (carboxyl oxygen and methyl group) ---					
		Lone Pair (1)	O (water)	π antibond	C=O (carboxyl)	p to π*	0.07
		Lone Pair (1)	O (water)	σ antibond	C-H ($methyl^{closer}$)	p to σ*	0.13
		Lone Pair (2)	O (water)	σ antibond	C-H ($methyl^{closer}$)	p to σ*	0.52
		σ Bond	O-H ($water^{closer}$)	π antibond (1)	C=O (carboxyl)	σ to π*	0.16
		σ Bond	O-H ($water^{closer}$)	π antibond (2)	C=O (carboxyl)	σ to π*	0.08
		σ Bond	O-H ($water^{closer}$)	σ antibond	C-H ($methyl^{closer}$)	σ to σ*	0.06
		--- From H_2O to PA (carboxyl hydrogen and carbonyl oxygen) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.30
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	22.37
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carbonyl)	σ to π*	0.18
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.99

Table S12B Orbital interactions of Tc–2H_2O in aqueous phase calculated by NBO at SMD-B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tc–2H_2O	Aqueous	--- From within PA ---					
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H (carboxyl)	p to σ*	0.75
		--- From PA (carboxyl oxygen and methyl group) to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	4.37
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	4.18
		--- From PA (carboxyl hydrogen and carbonyl oxygen) to H_2O ---					
		Lone Pair	O (carbonyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.08
		--- From H_2O to PA (carboxyl oxygen and methyl group) ---					
		Lone Pair	O (water)	π antibond	C=O (carboxyl)	p to π*	0.12
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.17
		--- From H_2O to PA (carboxyl hydrogen and carbonyl oxygen) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.45
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	32.86
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.67
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.32

Table S13B Orbital interactions of Ct–2H_2O in gas phase calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Ct–2H_2O	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.12
		--- From PA (carboxyl group) to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.68
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.09
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	2.28
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.09
		--- From PA (carboxyl oxygen and carbonyl oxygen) to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.71
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	3.06
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.05
		--- From H_2O to PA (carboxyl group) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.27
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	23.46
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.07
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.88
		--- From H_2O to PA (carboxyl oxygen and carbonyl oxygen) ---					
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.09

Table S14B Orbital interactions of Ct–2H_2O in aqueous phase calculated by NBO at SMD-B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Ct–2H_2O	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	1.15
		--- From PA (carboxyl oxygen and carbonyl oxygen) to H_2O ---					
		Lone Pair (1)	O (carboxyl)	σ antibond	O-H (water^{closer})	p to σ*	3.46
		Lone Pair (2)	O (carboxyl)	σ antibond	O-H (water^{closer})	p to σ*	6.80
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H (water^{closer})	p to σ*	0.20
		--- From H_2O to PA (carboxyl group) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.51
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	40.92
		σ Bond	O-H (water^{closer})	σ antibond	O-H (carboxyl)	σ to σ*	0.52
		σ Bond	O-H (water^{closer})	σ antibond	O-H (carboxyl)	σ to σ*	0.43
		--- From H_2O to PA (carboxyl oxygen and carbonyl oxygen) ---					
		σ Bond	O-H (water^{closer})	π antibond	C=O (carboxyl)	σ to π*	0.12

Table S15B Orbital interactions of Tt–2H_2O in gas phase calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tt–2H_2O	Gas	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	3.05
		--- From PA (carboxyl hydrogen and carbonyl oxygen) to H_2O ---					
		Lone Pair	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.13
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	1.50
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	4.68
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{closer}$)	σ to σ*	0.43
		--- From H_2O to PA (carboxyl group) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.35
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	25.96
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.77
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.24
		--- From H_2O to PA (carboxyl oxygen and carbonyl oxygen) ---					
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.08
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.10
		--- From H_2O (near carboxyl group) to H_2O (near carbonyl group) ---					
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H ($water^{away}$)	σ to σ*	0.18
		--- From H_2O (near carbonyl group) to H_2O (near carboxyl group) ---					
		Lone Pair	O (water)	σ antibond	O-H ($water^{away}$)	p to σ*	9.10

Table S16B Orbital interactions of Tt–2H_2O in aqueous phase calculated by NBO at SMD-B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
Tt–2H_2O	Aqueous	--- From within PA ---					
		σ Bond	O-H (carboxyl)	π antibond	C=O (carboxyl)	σ to π*	3.11
		--- From PA (carboxyl group) to H_2O ---					
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{closer}$)	σ to σ*	0.06
		--- From PA (carboxyl hydrogen and carbonyl oxygen) to H_2O ---					
		Lone Pair	O (carboxyl)	σ antibond	O-H ($water^{away}$)	p to σ*	0.06
		Lone Pair (1)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.77
		Lone Pair (2)	O (carbonyl)	σ antibond	O-H ($water^{closer}$)	p to σ*	2.81
		σ Bond	O-H (carboxyl)	σ antibond	O-H ($water^{closer}$)	σ to σ*	0.08
		--- From H_2O to PA (carboxyl group) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.34
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	27.73
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.92
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.17
		--- From H_2O to PA (carboxyl oxygen and carbonyl oxygen) ---					
		σ Bond	O-H ($water^{closer}$)	π antibond	C=O (carboxyl)	σ to π*	0.10
		--- From H_2O (near carbonyl group) to H_2O (near carboxyl group) ---					
		Lone Pair (1)	O (water)	σ antibond	O-H ($water^{away}$)	p to σ*	0.11
		Lone Pair (2)	O (water)	σ antibond	O-H ($water^{away}$)	p to σ*	10.80

Table S17B Orbital interactions of DHPA calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. SMD was used for the aqueous phase calculations.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, Kcal/mol
		Variant	Atom/s	Variant	Atom/s		
DHPA	Gas	Lone Pair	O (carboxyl)	σ antibond	O-H (alcohol^{bottom})	p to σ*	2.28
		Lone Pair	O (alcohol^{top})	σ antibond	O-H (carboxyl)	p to σ*	1.88
		sp3 Bond	C-OH (alcohol^{top})	σ antibond	O-H (alcohol^{bottom})	sp3 to σ*	0.58
		π Bond	C=O (carboxyl)	σ antibond	O-H (carboxyl)	π to σ*	0.85
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	7.02
		σ Bond	O-H (carboxyl)	π antibond (2)	C=O (carboxyl)	σ to π*	2.20
		σ Bond	O-H (alcohol^{top})	sp3 antibond	C-OH (alcohol^{bottom})	σ to sp3*	2.09
		σ Bond	O-H (alcohol^{bottom})	sp3 antibond	C-OH (alcohol^{top})	σ to sp3*	3.36
		σ Bond	O-H (alcohol^{bottom})	sp2 antibond	C-OH (carboxyl)	σ to sp2*	0.61
	Aqueous	Lone Pair	O (carboxyl)	σ antibond	O-H (alcohol^{bottom})	p to σ*	1.80
		Lone Pair	O (alcohol^{top})	σ antibond	O-H (carboxyl)	p to σ*	0.95
		π Bond	C=O (carboxyl)	σ antibond	O-H (carboxyl)	π to σ*	0.88
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	6.84
		σ Bond	O-H (carboxyl)	π antibond (2)	C=O (carboxyl)	σ to π*	2.33
		σ Bond	O-H (alcohol^{top})	sp3 antibond	C-OH (alcohol^{bottom})	σ to sp3*	1.09
		σ Bond	O-H (alcohol^{bottom})	sp3 antibond	C-OH (alcohol^{top})	σ to sp3*	2.45
		σ Bond	O-H (alcohol^{bottom})	sp2 antibond	C-OH (carboxyl)	σ to sp2*	0.61

Table S18B Orbital interactions of DHPA–H_2O in gas phase, calculated by NBO at B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
DHPA–H_2O	Gas	--- From within DHPA ---					
		Lone Pair	O (carboxyl)	σ antibond	O-H (alcohol^{bottom})	p to σ*	0.93
		π Bond	C=O (carboxyl)	σ antibond	O-H (carboxyl)	π to σ*	1.26
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	6.81
		σ Bond	O-H (carboxyl)	π antibond (2)	C=O (carboxyl)	σ to π*	1.42
		σ Bond	O-H (alcohol^{top})	sp3 antibond	C-OH (alcohol^{bottom})	σ to sp3*	2.32
		σ Bond	O-H (11-12)	sp3 antibond	C-OH (alcohol^{top})	σ to sp3*	2.18
		σ Bond	O-H (11-12)	sp2 antibond	C-OH (carboxyl)	σ to sp2*	0.69
		--- From DHPA to H_2O ---					
		Lone Pair (1)	O (alcohol^{top})	σ antibond	O-H (water^{away})	p to σ*	0.07
		Lone Pair (1)	O (alcohol^{top})	σ antibond	O-H (water^{closer})	p to σ*	3.96
		Lone Pair (2)	O (alcohol^{top})	σ antibond	O-H (water^{closer})	p to σ*	2.10
		σ Bond	O-H (carboxyl)	σ antibond	O-H (water^{away})	σ to σ*	0.07
		--- From H_2O to DHPA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.27
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	22.86
		σ Bond	O-H (water^{closer})	sp3 antibond	C-OH (alcohol^{top})	σ to sp3*	0.10
		σ Bond	O-H (water^{closer})	σ antibond	O-H (carboxyl)	σ to σ*	0.92
		σ Bond	O-H (water^{closer})	σ antibond	O-H (alcohol^{top})	σ to σ*	0.14

Table S19B. Orbital interactions of DHPA–H_2O in aqueous phase calculated by NBO at SMD-B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Phase	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
		Variant	Atom/s	Variant	Atom/s		
DHPA–H_2O	Aqueous	--- From within DHPA ---					
		Lone Pair	O (carboxyl)	σ antibond	O-H ($alcohol^{bottom}$)	p to σ*	2.95
		π Bond	C=O (carboxyl)	σ antibond	O-H (carboxyl)	π to σ*	1.28
		σ Bond	O-H (carboxyl)	π antibond (1)	C=O (carboxyl)	σ to π*	6.67
		σ Bond	O-H (carboxyl)	π antibond (2)	C=O (carboxyl)	σ to π*	1.86
		σ Bond	O-H ($alcohol^{top}$)	sp3 antibond	C-OH ($alcohol^{bottom}$)	σ to sp3*	0.88
		σ Bond	O-H ($alcohol^{bottom}$)	sp3 antibond	C-OH ($alcohol^{top}$)	σ to sp3*	1.26
		σ Bond	O-H ($alcohol^{bottom}$)	sp2 antibond	C-OH (carboxyl)	σ to sp2*	0.63
		--- From DHPA to H_2O ---					
		Lone Pair (1)	O ($alcohol^{top}$)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.55
		Lone Pair (2)	O ($alcohol^{top}$)	σ antibond	O-H ($water^{closer}$)	p to σ*	0.61
		--- From H_2O to DHPA ---					
		Lone Pair (1)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	0.49
		Lone Pair (2)	O (water)	σ antibond	O-H (carboxyl)	p to σ*	37.32
		σ Bond	O-H ($water^{away}$)	σ antibond	O-H (carboxyl)	σ to σ*	0.39
		σ Bond	O-H ($water^{closer}$)	σ antibond	O-H (carboxyl)	σ to σ*	1.20

Table S20B Orbital interactions of PAHT–H_2O complexes calculated by NBO at SMD-B2PLYP-D3BJ/aug-cc-pVTZ. Stronger (orange) and weaker (gray) intermolecular H-bonding are highlighted.

Conformer	Donor		Acceptor		Type of orbital interaction	Stabilization energy, kcal/mol
	Variant	Atom/s	Variant	Atom/s		
PAHT–H_2O_a	--- From H_2O to $PAHT_a$ ---					
	Lone Pair (1)	O	σ antibond	O-H	p to σ*	1.14
	Lone Pair (2)	O	σ antibond	O-H	p to σ*	88.03
	σ Bond	O-H ($water^{left}$)	π antibond	C=O	σ to π*	0.05
	σ Bond	O-H ($water^{left}$)	σ antibond	O-H	σ to σ*	0.99
	σ Bond	O-H ($water^{right}$)	σ antibond	O-H	σ to σ*	1.02
PAHT–H_2O_b	--- From H_2O to $PAHT_b$ ---					
	Lone Pair (1)	O	σ antibond	O-H	p to σ*	1.32
	Lone Pair (2)	O	σ antibond	O-H	p to σ*	96.86
	σ Bond	O-H ($water^{left}$)	σ antibond	O-H	σ to σ*	1.59
	σ Bond	O-H ($water^{right}$)	σ antibond	O-H	σ to σ*	1.61
PAHT–H_2O_c	--- From $PAHT_c$ to H_2O ---					
	Lone Pair (1)	O	σ antibond	O-H ($water^{closer}$)	p to σ*	0.77
	Lone Pair (2)	O	σ antibond	O-H ($water^{closer}$)	p to σ*	0.60
	π Bond	C=O	σ antibond	O-H ($water^{away}$)	π to σ*	0.11
	π Bond	C=O	σ antibond	O-H ($water^{closer}$)	π to σ*	1.51
	--- From H_2O to $PAHT_c$ ---					
	Lone Pair (1)	O	σ antibond	O-H	p to σ*	1.78
	Lone Pair (2)	O	σ antibond	O-H	p to σ*	126.39
	σ Bond	O-H ($water^{away}$)	σ antibond	O-H	σ to σ*	2.02
	σ Bond	O-H ($water^{closer}$)	π antibond	C=O	σ to π*	0.06
	σ Bond	O-H ($water^{closer}$)	σ antibond	O-H	σ to σ*	4.20