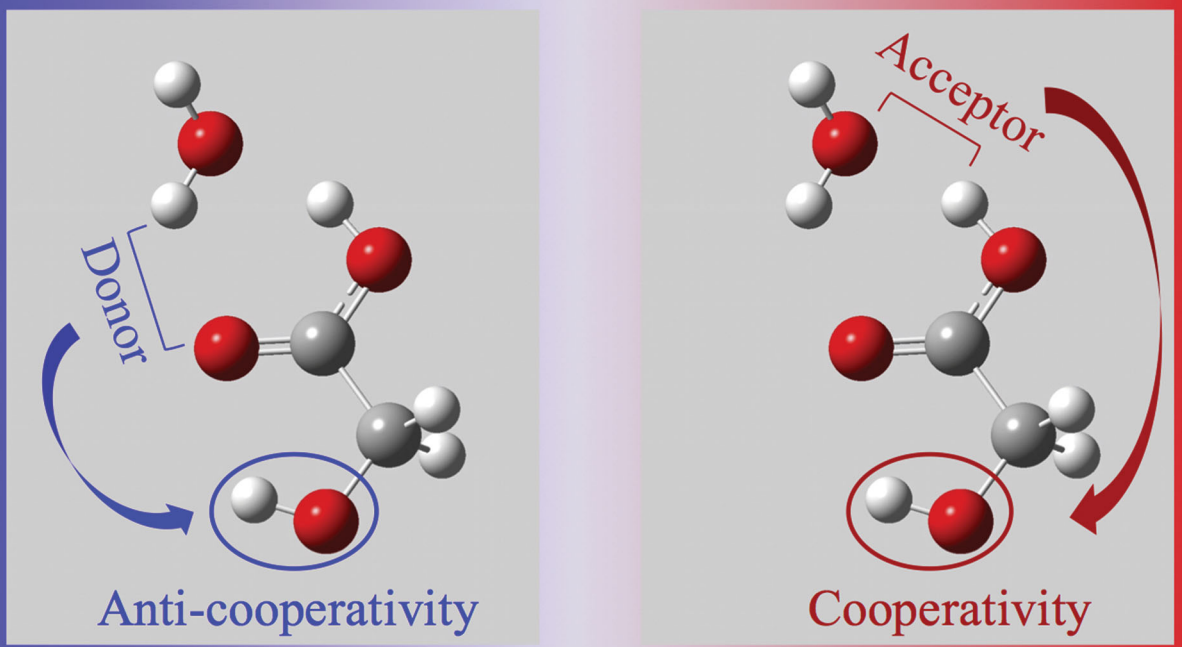

Showcasing research from the groups of Dr Peifeng Su, Dr Wei Wu, Dr Yong Xia and Dr Zhijun Yang in China, and Dr Carl Trindle and Dr Quanli Gu in the USA.

Dissection of H-bonding interactions in a glycolic acid–water dimer

This paper is a first, definitive and quantitative report of the binding strength, and competing anti-cooperative and cooperative behaviors in the glycolic acid–water dimer, with reference to the aromatic analog – 9-hydroxy-9-fluorene carboxylic acid. This work may inspire significant interest in multiple H-bond interactions for carboxylic acids and water clusters.

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Dissection of H-bonding interactions in a glycolic acid–water dimer

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The binding strength and collective effects of multiple H-bonds in the glycolic acid–water dimer were studied in comparison to the aromatic analog, 9-hydroxy-9-fluorene carboxylic acid (9HFCA). Quantitative analysis by the generalized Kohn–Sham energy decomposition analysis shows that the energy difference in each specific physical interaction, from a glycolic acid–water dimer to a 9HFCA–water dimer, is small and amounts to less than 5% of the binding energy of the 9HFCA–water dimer. Extensive comparison of further, similar H-bonded complexes with widely varying binding strengths reinforces their excellent analogy in that the fluorene group acts as a non-interfering spectator for intermolecular H-bonding interactions. With reference to the spectroscopic measurement on the 9HFCA–water dimer (8.51 ± 0.09 kcal mol^{-1}), the binding energy of the glycolic acid–water dimer is estimated to be 8.51 ± 0.31 kcal mol^{-1}, a much better accuracy than previous reports. Furthermore, correlating the infrared spectra of 9HFCA H-bonded complexes provides a circumstantial probing of the existence and consequences of cooperative and anti-cooperative behaviors in the glycolic acid–water dimer. Our studies point to the interesting H-bonding phenomena in the glycolic acid–water dimer, which may inspire challenging experiments in future.

Introduction

Hydrogen (H) bonding[1] is of broad interest in all scientific areas, and has been especially characterized for water clusters,[2] and also for clusters of carboxylic acids.[3] One exemplary case in carboxylic acids is glycolic acid, HO–CH_2–COOH, as shown in Fig. 1. As the smallest alpha hydroxy carboxylic acid, glycolic acid has two possible sites for intermolecular H-bonding, the two hydroxyl (OH) groups – one as the carboxylic OH and another as the alcoholic OH. The conformational flexibility of glycolic acid has been extensively analyzed in the past, and the global minimum isomer,[4] where an intramolecular H-bond is formed between the COOH's C=O and the alcoholic OH, is much lower than other isomers energetically. Experimentally, the infrared (IR) spectra of glycolic acid have been studied in the vapor phase[5] and in matrix isolation.[6] However, it is very difficult to unequivocally identify the vibrational frequencies of the two OH groups due to either the broadening of the IR spectra or the matrix environment complication, not to mention their IR spectra in complexes.

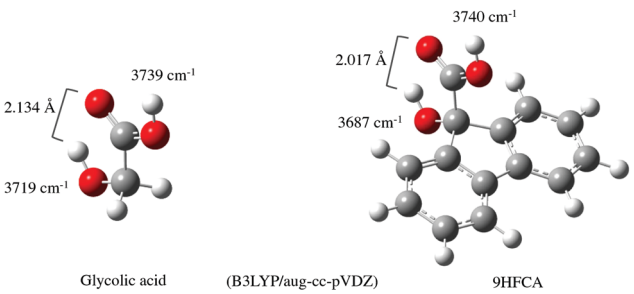

Fig. 1 Geometries, intramolecular distances and harmonic frequencies of the alcoholic and carboxylic OH stretching frequencies for glycolic acid and 9HFCA. The calculations were done by B3LYP/aug-cc-pVDZ.

Indeed, the intermolecular H-bonding interactions between glycolic acid and water raise some fundamentally interesting questions. First, what is the accurate dissociation energy (D_0) between glycolic acid and water? This number is still not measured so far. Obviously, knowing how tightly water binds to glycolic acid is imperative to fundamentally understand the micro-solvation of glycolic acid as a good humectant and moisturizer in pharmaceutical science. It may also be useful for

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kinetic modeling in atmospheric chemistry[7] where a range of carboxylic acids and water vapor are present since the glycolic acid–water binding geometry represents a standard structure for the general carboxylic acid–water interactions.[8] Another question is related to the collective interactions involving multiple intra- and intermolecular H-bonds in glycolic acid complexes such as with water or formic acid. Will the intramolecular H-bond be influenced by the intermolecular H-bond(s)? If so, what is the mechanism behind this? Not too surprisingly, these seemingly simple questions in fact present tremendous challenges and have not been reported so far by experimentalists. The difficulties are because glycolic acid has no strong electronic absorption bands, and the ionization potential lies in the vacuum ultraviolet (UV) region, ~120 nm; glycolic acid homo-dimers are also abundant.

Recently, gas phase spectroscopy and dynamics of 9-hydroxy-9-fluorene carboxylic acid (9HFCA) and its H-bonded complexes have been intensively studied using IR and UV laser spectroscopy under molecular beam conditions.[9–11] Only the global minimum isomer in 9HFCA (in Fig. 1) was observed in the gas phase molecular beam experiment.[12] Using IR-UV double resonance spectroscopy, the binding energy of the 9HFCA–water dimer was accurately determined as 2975 ± 30 cm^{-1} (8.51 ± 0.09 kcal mol^{-1}).[9] Also, the alcoholic OH and the carboxylic OH stretching frequencies in 9HFCA were clearly measured to be two separable peaks at 3538 and 3579 cm^{-1}, respectively. More interestingly, the intramolecular H-bond in 9HFCA has been found to be either red or blue shifted upon complexation with water or formic acid.[10] These types of experimental work are relatively easier to perform because the fluorene component has strong UV absorption, ~300 nm, and was well studied by electronic and ionization spectroscopy.[13]

Here, we show that using qualitative and quantitative approaches, from several aspects, one can closely correlate 9HFCA with glycolic acid upon intermolecular H-bonding interactions, so the spectroscopic information obtained from the 9HFCA–water dimer can be extended to confidently infer the binding energy for the glycolic acid–water dimer. Furthermore, correlating quantitative IR spectra of 9HFCA H-bonded complexes allows revealing of, for the first time, the cooperative and anti-cooperative H-bonding effects in the glycolic acid–water dimer.

Computational and experimental details

The recently developed generalized Kohn–Sham energy decomposition analysis[14] (GKS-EDA) has been established to quantify the specific intermolecular interactions in a physically meaningful way.[15,16] Comparing the energy difference in each intermolecular physical interaction between the glycolic acid–water dimer and the 9HFC–water dimer allows complete characterization of the detailed influence of the fluorene fragment (in 9HFCA) on the intermolecular interactions. So the analogy between 9HFCA and glycolic acid in terms of intermolecular H-bonding can be better evaluated along with the total intermolecular interaction energy.

GKS-EDA, which was developed based on localized molecular orbital EDA[17] and EDA polarizable continuum model,[18] was performed in GAMESS.[19] Basis set superposition error (BSSE) corrections were performed with geometry optimized on a counterpoise-corrected surface.[20] GKS-EDA divides the total interaction ΔE^{int} into electrostatic ΔE^{ele}, Pauli repulsion ΔE^{Pauli}, polarization ΔE^{pol}, correlation ΔE^{corr} and/or dispersion ΔE^{disp}. The BSSE corrected interaction energy ΔE^{int} can be decomposed as:

$$\Delta E^{int} = \Delta E^{ele} + \Delta E^{Pauli} + \Delta E^{pol} + \Delta E^{disp} + \Delta E^{corr}$$

The dissociation (binding) energy, D_0, is then calculated using the equation below.

$$D_0 = |\Delta E^{int} + \Delta E(geo) + \Delta E(ZPE)|$$

wherein ΔE(geo) is the geometrical relaxation energy, which is the sum of each fragment's energy difference between the fragment in the complex and the free fragment and ΔE(ZPE) is the change in the zero point energy (ZPE) corrections between the monomers and the complex. The negative (or attractive) energy terms are ΔE^{ele}, ΔE^{pol}, ΔE^{corr} and ΔE^{disp}, contributing to a higher D_0; the positive energy terms are ΔE^{Pauli}, ΔE(ZPE) and ΔE(geo), resulting in a smaller D_0.

The benchmark calculations, based on the coupled cluster double (triple) excitation approach using complete basis set limit extrapolations, namely the CCSD(T)/CBS method, were performed for the binding energy of the glycolic acid–water dimer. To do so, first, the glycolic acid–water dimer geometry was optimized at the counterpoise-corrected surface using the second-order Møller–Plesset (MP2)[21] method with a basis set, aug-cc-pVTZ,[22] followed by the MP2 single point energy evaluation on a larger basis set, aug-cc-pVQZ.[22] Second, the CCSD(T) single point energy was estimated from the two-point (aug-cc-pVTZ and aug-cc-pVQZ) CBS extrapolation with separate extrapolations on the Hartree–Fock and correlation energies.[23] Note that the zero point energy was calculated by MP2/aug-cc-pVTZ. For the 9HFCA–water dimer, the same type of CCSD(T)/CBS calculation is prohibitive to us.

The CCSD(T)/CBS benchmark calculations do not necessarily warrant an accurate value, but provide a good reference point to the estimated binding energy of the glycolic acid–water dimer. Table 1 shows the calculated binding energy based on the MP2 and CCSD(T) methods using aug-cc-pVTZ and aug-cc-pVQZ basis sets as well as the CCSD(T)/CBS method. It suggests the accuracy

Table 1 MP2 and CCSD(T) D_0 (in kcal mol^{-1}) calculations on glycolic acid–water dimer using the basis sets of aug-cc-pVTZ and aug-cc-pVQZ, as well as the two-points CBS extrapolation. The ZPE correction was obtained by MP2/aug-cc-pVTZ

	MP2[a]	MP2[b]	CCSD(T)[a]	CCSD(T)[b]	CCSD(T)/CBS
D_0	7.77	8.09	7.85	8.20	8.38

[a] aug-cc-pVTZ. [b] aug-cc-pVQZ.

and necessity of the CCSD(T)/CBS calculations. As the basis set increases from aug-cc-pVTZ to aug-cc-pVQZ, the calculated D_0 value also increases, from 7.77 kcal mol^{-1} to 8.09 kcal mol^{-1} by MP2, and from 7.85 kcal mol^{-1} to 8.20 kcal mol^{-1} by CCSD(T), respectively. Then, the CCSD(T)/CBS calculations show that the calculated binding energy is even higher, 8.38 kcal mol^{-1}.

In addition, bond distance and harmonic frequency calculations involving the intramolecular H-bond in monomers and complexes were performed on optimized geometries using B3LYP,[24] ωB97X-D,[25] M06-2X[26] and MP2 with a basis set of 6-311++G(d,p)[27] or aug-cc-pVDZ.[22] Charge analysis was performed by the natural bond orbital (NBO).[28]

The UV hole burning experiments on the 9HFCA–water dimer were performed in the molecular beam apparatus. A supersonic helium beam carrying 9HFCA and its water complexes was produced by a pulsed nozzle (series 9, 20 Hz). A thin film of high vacuum silicone grease was coated on the inside of the nozzle with the solid sample placed in the cap of its valve to avoid the 9HFCA decomposition upon heating at 120 °C. After a skimmer, laser spectroscopy was performed downstream in a second chamber at a distance of 10 cm from the nozzle. The binding partner, water, was seeded in helium *via* a variable flow controller and adjusted so that significant amounts of hetero dimers were formed while limiting the production of larger clusters.

Two independently tunable UV laser pulses were generated. Each is a pulsed nanosecond Nd-YAG (Continuum NY-61 or Quanta-Ray GCR-3) pumping a tunable dye laser (Lumonics HD500) with a visible bandwidth of 0.05 cm^{-1}. Both of the dye lasers are equipped with frequency doubling capabilities (Spectra-Physics WEX). One UV laser (scanning) has a power of ~0.1 mJ per pulse and another (burning) ~0.5 mJ per pulse. Each laser beam was focused using an appropriate lens, and spatially and temporally overlapped with another in a counter propagating geometry.

The 9HFCA–water complex ions of interest were collected using a standard Wiley–Mclaren time of flight mass spectrometer.[29] The burning laser frequency was fixed at the electronic origin band, and another UV laser was fired ~0.1 μs later and scanned and alternated on *vs.* off while monitoring the complex ion signal to obtain the electronic spectrum.

Results and discussion

A. Geometries of glycolic acid and 9HFCA

Comparing 9HFCA with glycolic acid, the only difference is the fluorene moiety as seen in Fig. 1. In order to make 9HFCA a useful substitute for the glycolic acid reference, the fluorene group must not participate in the complex's H-bonding geometry, but 9HFCA must still be able to reflect all effects in the complex's H-bonding network. So it is important to compare the H-bonding sites and geometries of the 9HFCA monomer to those of a glycolic acid monomer in order to establish the quality of their analogy upon water complexation. For glycolic acid and 9HFCA complexes with water, the source for the intermolecular strength presumably comes from the binding motif – the two intermolecular H-bonds formed between the carboxylic acid group and water. So it is useful to analyze and compare the two OH groups in the monomers.

Table 2 B3LYP, M06-2X and MP2 calculated two OH stretching frequencies (in cm^{-1}) in glycolic acid and 9HFCA. The calculated D_0 values for their water complexes (global minima in kcal mol^{-1}) are also included. The basis set is aug-cc-pVDZ

	B3LYP[a]	B3LYP[b]	M06-2X[a]	M06-2X[b]	MP2[a]	MP2[b]
Alcoholic OH	3719	3687	3800	3775	3731	3677
Carboxylic OH	3739	3740	3808	3813	3739	3723
D_0	6.97	7.03	8.88	8.77	7.03	—

[a] Glycolic acid. [b] 9HFCA.

In Table 2, geometry optimization and harmonic frequency calculations[30] by B3LYP, M06-2X and MP2 with the aug-cc-pVDZ basis set show a consensus. From glycolic acid to 9HFCA, the carboxylic OH stretching frequency is nearly identical, and the alcoholic OH stretching frequency is slightly different. Based on the B3LYP/aug-cc-pVDZ calculations quoted below, glycolic acid's carboxylic OH stretching harmonic frequency (no scaling) is 3739 cm^{-1}, almost identical to that of 9HFCA, 3740 cm^{-1}, suggesting a negligible influence of the fluorene moiety. On the other hand, glycolic acid's alcoholic OH stretching harmonic frequency is calculated to be 3719 cm^{-1}, 32 cm^{-1} higher than that of the 9HFCA counterpart, 3687 cm^{-1}. In glycolic acid or 9HFCA, the alcoholic OH stretching frequency is smaller than that of the carboxylic OH, due to the formation of the intramolecular H-bond between the alcoholic OH and the carbonyl group. Based on the calculated frequency shifts, the intramolecular H-bond strength in glycolic acid is weaker than in 9HFCA. This is consistent with a calculated longer intramolecular H-bond distance, 2.134 Å in glycolic acid *vs.* 2.017 Å in 9HFCA. Overall, glycolic acid and 9HFCA are nearly identical in the carboxylic OH stretching mode, and slightly different in the alcoholic OH group. This is verified by M06-2X and MP2 calculations. So, it suggests that the influence of the fluorene moiety on glycolic acid upon the intermolecular H-bonding interactions is not significant and may not impact too much.

B. Geometries of water complexes with glycolic acid and 9HFCA

Several isomers for the 9HFCA–water dimer are possible since water can bind to either the COOH group, or the alcoholic OH group, or even the fluorene moiety. The most stable configuration is for water binding to the COOH group through two typical intermolecular H-bonds. Experimentally, only a single isomer of 9HFCA–water was identified using the UV hole burning spectra. From the spectra obtained by the UV-UV burning experiments, in Fig. 2, the burning UV laser fixed at the electronic origin band (32 767 cm^{-1}) and alternated on and off while another UV laser was scanned across the spectra range of 32 720 to 33 220 cm^{-1}. The resulting difference spectrum (the bottom spectrum in blue color) shows that all the vibronic bands are associated with a single isomer, assigned as the global isomer. Previous IR spectra of the 9HFCA–water$_{(1,2)}$ complexes

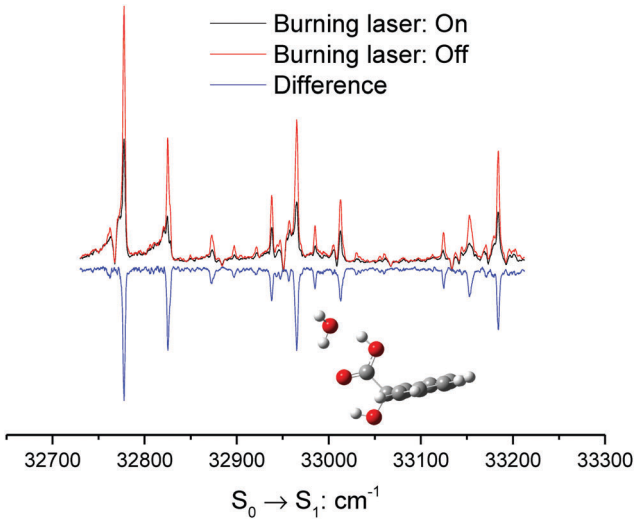

Fig. 2 UV–UV hole burning spectra on 9HFCA–water complex. It shows that only a single isomer was present in the gas phase molecular beam experiment; it is assigned as the global minimum (the inserted structure).

also confirmed that the observed 9HFCA–water complex is the global minimum.

Fig. 3a shows the global minima in the acid–water dimers where water binds to the carboxylic acid group. Obviously, the carboxylic OH stretching frequency in the acid will dramatically change upon water complexation. From the B3LYP/aug-cc-pVDZ calculations mentioned below, the harmonic carboxylic OH frequency (no scaling) in the glycolic acid–water dimer is 3318 cm^{-1}, close to that in the 9HFCA–water dimer, 3314 cm^{-1}. The symmetric stretching frequency of water is similar in the glycolic acid–water and 9HFCA–water dimers, 3652 cm^{-1} *vs.* 3659 cm^{-1}. The alcoholic OH stretching frequency in the glycolic acid–water dimer is barely affected and slightly higher than that in the 9HFCA–water dimer, 3718 cm^{-1} *vs.* 3685 cm^{-1}. Two intermolecular H-bond distances in the glycolic acid–water dimer are 1.765 and 2.052 Å, also near the 9HFCA–water dimer, 1.765 and 2.062 Å, accordingly. This suggests that in either dimer the intermolecular H-bond with water as a proton acceptor is stronger than the other one with water as a proton donor. Then, the intramolecular H-bond is near the weaker intermolecular H-bond. Compared to that in the monomers, the intramolecular H-bond distance is reduced slightly, 2.111 Å in the glycolic acid–water dimer and 1.996 Å in the 9HFCA–water dimer. So in terms of the nature of the H-bonding networks, the glycolic acid–water dimer and 9HFCA–water dimer are similar in the intermolecular H-bonds and retain the small difference in the intramolecular H-bond (as in the monomer). Overall, the differences of H-bonding in the two dimers suggest that the fluorene group in 9HFCA may engage weaker intermolecular interactions as compared to glycolic acid with water. From their D_0 values, one may further find the following: comparing the glycolic acid–water dimer with the 9HFCA–water dimer, the calculated values are very close, 6.97 *vs.* 7.03 kcal mol^{-1} by B3LYP, 8.27 *vs.* 8.16 kcal mol^{-1} by ωB97X-D, and 8.88 *vs.* 8.77 kcal mol^{-1} by M06-2X.

Water can also bind to the alcoholic group in glycolic acid or 9HFCA, as seen in Fig. 3b, but this configuration is a high energy local minimum isomer. From the B3LYP/aug-cc-pVDZ calculations mentioned below, the harmonic carboxylic OH frequency (no scaling) in the glycolic acid–water dimer is 3734 cm^{-1}, close to that in the 9HFCA–water dimer, 3730 cm^{-1}. The symmetric stretching frequency of water is similar in glycolic acid–water and 9HFCA–water dimers, 3651 cm^{-1} *vs.* 3650 cm^{-1}. The alcoholic OH stretching frequency in the glycolic acid–water dimer is significantly red shifted, but close to that in the 9HFCA–water dimer, 3557 cm^{-1} *vs.* 3566 cm^{-1}. Two intermolecular H-bond distances in the glycolic acid–water dimer are 1.883 and 1.947 Å, moderately different from the counterparts in the 9HFCA–water dimer, 1.912 and 1.924 Å. Interestingly, in this case the fluorene group in 9HFCA may start to engage in additional direct H-bonding interaction with water. For instance, the intermolecular interactions of CH$\cdots$OH for the fluorene moiety with water occur in this 9HFCA–water configuration, but absolutely not in a similar glycolic acid–water configuration. This intermolecular distance (indicated by the dashed line) is 2.493 Å (by B3LYP/aug-cc-pVDZ), shorter than the intermolecular distance in the methane–water dimer (2.610 Å).[31] So, the analogy between glycolic acid and 9HFCA is compromised. For this configuration, the calculated D_0 values for water complexes with glycolic acid and 9HFCA are noticeably varying, 4.13 *vs.* 3.83 kcal mol^{-1} by B3LYP, 5.50 *vs.* 5.75 kcal mol^{-1} by ωB97X-D, and 5.81 *vs.* 6.43 kcal mol^{-1} by M06-2X. Also, when water binds to the π electrons of the fluorene moiety in 9HFCA, the analogy between glycolic acid and 9HFCA in their water complexes becomes much worse as the glycolic acid–water dimer completely lacks such a strong interaction (OH–π).

Discerning the intermolecular interactions for the dimers in Fig. 3a and b can be visualized in an intuitive way by the non-covalent interaction (NCI) plots,[32] so as to see the effects of the fluorene moiety. From the NCI plots in Fig. 3c where 2-dimensional plots are on both sides and 3-dimensional plots are in the middle, for the global minima isomers where water binds to the carboxylic acid group, all signatures of intermolecular H-bonding in the glycolic acid–water dimer, reflected by the blue NCI surfaces, are retained in the 9HFCA–water dimer. However, for the local isomer where water binds to the alcoholic group, a signature of CH$\cdots$OH intermolecular interactions in the 9HFCA–water dimer, reflected by the blue NCI surface to be a H-bond (a spike at −0.01 in the 2-dimensional plot), emerges between fluorene's CH group and water; such an interaction is completely non-existent in the glycolic acid–water dimer. So, a stronger influence of the fluorene moiety is evident as water binds to the alcoholic group over the carboxylic acid group, and the analogy between 9HFCA and glycolic acid is not as good with this type of configuration.

C. GKS-EDA on the glycolic acid–water dimer and the 9HFCA–water dimer

To make a detailed dissection of the binding energy of the glycolic acid–water dimer, we turn to the GKS-EDA for its comparison with the 9HFCA–water dimer. In Table 3, a specific

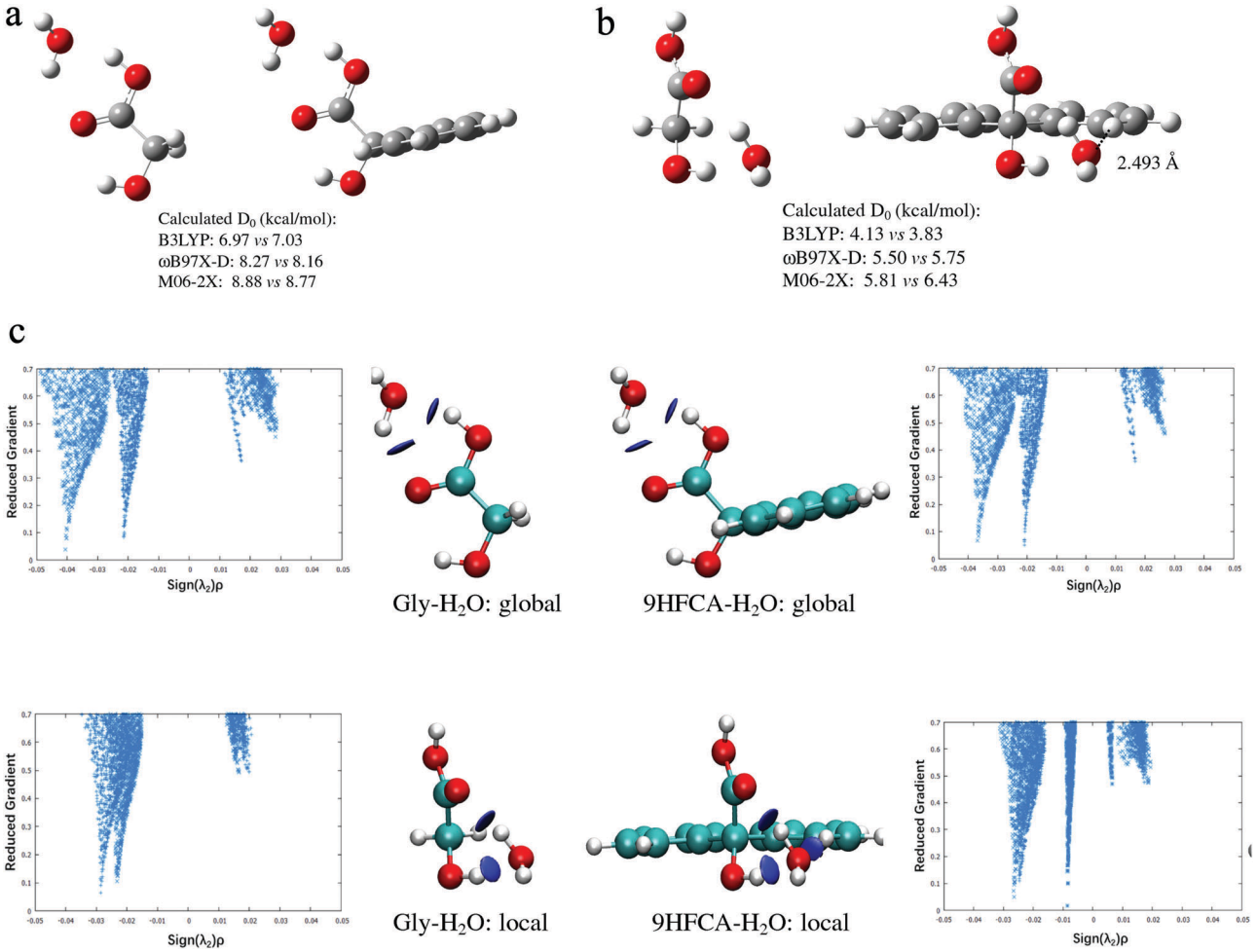

Fig. 3 (a) Calculated geometries and D_0 values for water complexes with glycolic acid and 9HFCA (the global minima) where water is bound to the carboxylic acid group. Calculations were done with the basis set of aug-cc-pVDZ, and ZPE and counterpoise correction were included. (b) Calculated geometries and D_0 values for water complexes with glycolic acid and 9HFCA (the local minima) where water is bound to the alcoholic group. Calculations were done with the basis set of aug-cc-pVDZ, and ZPE and counterpoise correction were included. (c) NCI analysis of water complexes with glycolic acid and 9HFCA where water binds to the carboxylic group to form the global minimum isomer and to the alcoholic group to form the local minimum isomer. The blue NCI surfaces, 2-dimension plots on both sides and 3-dimension plots in the middle, reflect the intermolecular H-bonding interactions in the dimers. Geometries were optimized by M06-2X/aug-cc-pVDZ, and the NCI iso-surfaces were set as 0.5 a.u.

component in the GKS-EDA is evaluated for its contribution to the total intermolecular interactions. The calculations were based on the aug-cc-pVDZ basis set with three popular density functionals, B3LYP, ωB97X-D and M06-2X. The calculated D_0 values for the 9HFCA–water dimer or the glycolic acid–water dimer are, as expected, method dependent. For the global minimum isomer (corresponding to Fig. 3a), each term's energy difference (glycolic acid–water dimer minus 9HFCA–water dimer) is very small, less than 0.40 kcal mol^{-1} among the three methods. So it eliminates a concern of large cancellation effects that could come across all the energy terms. More importantly, each term's energy difference represents only less than 5% of the binding energy of the glycolic acid–water dimer, supporting that each specific physical interaction, arising from the intermolecular interactions between 9HFCA and water, is minimally impacted with the addition of the fluorene group. So, the nature of the intermolecular H-bonding in these two acid–water dimers is basically identical in each specific physical interaction, and no cancellation effect occurs across the EDA terms. In short, the GKS-EDA comparison of the two dimers suggests that the intermolecular interaction between water and the fluorene moiety in 9HFCA is non-significant in terms of any attraction of electrostatic, polarization, correlation and dispersion, or any Pauli repulsion. Overall, the GKS-EDA results show that the amount of a long-range interaction between water and the fluorene moiety in the 9HFCA–water dimer is minimal.

However, for the local minimum isomer (corresponding to Fig. 3b), particularly referring to ωB97X-D and M06-2X calculations, the energy differences in some of the GKS-EDA terms such as ΔE^{Pauli}, ΔE^{ele} and ΔE^{disp} along with D_0 values start to be more dramatic than the counterparts in the global minima isomers. The biggest difference amid the attractive forces is ΔE^{ele} but its value is modest, consistent with the

Table 3 GKS-EDA results on the global and local minima isomers of 9HFCA–H_2O dimer and glycolic acid–H_2O (Gly–H_2O) dimer. The basis set used is aug-cc-pVDZ

		ΔE^{Pauli}	ΔE^{ele}	ΔE^{pol}	ΔE^{disp}	ΔE^{corr}	ΔE(geo)	ΔE(ZPE)	D_0
B3LYP[a]	9HFCA–H_2O	23.14	−20.37	−9.48	—	−2.96	0.46	2.18	7.03
	Gly–H_2O	23.38	−20.72	−9.73	—	−2.85	0.65	2.29	6.97
	Difference	0.24	−0.35	−0.25	—	0.11	0.19	0.11	0.06
ωB97X-D[a]	9HFCA–H_2O	22.47	−20.16	−8.88	−1.02	−3.48	0.59	2.32	8.16
	Gly–H_2O	22.57	−20.44	−9.05	−0.90	−3.39	0.62	2.31	8.27
	Difference	0.10	−0.28	−0.17	0.12	0.09	0.03	−0.01	0.11
M06-2X[a]	9HFCA–H_2O	21.94	−19.90	−9.12	—	−4.26	0.41	2.16	8.77
	Gly–H_2O	22.16	−20.27	−9.35	—	−4.18	0.58	2.17	8.88
	Difference	0.22	−0.37	−0.23	—	0.08	0.17	0.01	0.11
B3LYP[b]	9HFCA–H_2O	19.94	−17.98	−7.58	—	−2.57	2.21	2.14	3.83
	Gly–H_2O	19.64	−17.88	−7.41	—	−2.75	1.81	2.46	4.13
	Difference	−0.30	0.10	0.17	—	−0.18	−0.40	0.32	0.30
ωB97X-D[b]	9HFCA–H_2O	21.45	−19.02	−7.80	−1.70	−3.50	2.57	2.24	5.75
	Gly–H_2O	20.06	−18.23	−7.36	−1.15	−3.30	1.97	2.51	5.50
	Difference	−1.39	0.79	0.44	−0.55	0.20	−0.60	0.27	−0.25
M06-2X[b]	9HFCA–H_2O	19.88	−18.21	−7.43	—	−5.05	2.16	2.22	6.43
	Gly–H_2O	19.61	−17.41	−7.18	—	−4.15	1.98	2.35	5.81
	Difference	−1.27	0.80	0.25	—	0.90	−0.18	0.13	−0.62

[a] Global minimum isomer. [b] Local minimum isomer.

difference in H-bonding networks between the 9HFCA–water dimer and the glycolic acid–water dimer, which is a weaker CH···OH H-bond.

Fortunately, for the 9HFCA–water dimer, the spectroscopic measurement of the D_0 value, 8.51 ± 0.09 kcal mol^{-1}, is associated with the global minimum (in Fig. 3a) which is also the only isomer observed. So, based on the above analysis, the D_0 value of the glycolic acid–water dimer (the global minimum isomer) is expected to be very close to 8.51 kcal mol^{-1}. This is an important conclusion especially concerning the difficulty of the spectroscopic measurement for the glycolic acid–water dimer, as well as the variation in *ab initio* calculations due to the available choices and limitations in the method and basis set.

D. Binding energies of 9HFCA and glycolic acid complexes with an array of partners

Besides the water binding, changing the intermolecular H-bonding partners for complexes with 9HFCA and glycolic acid allows a comprehensive diagnosis of the intermolecular H-bonding networks, and further confirms that the presence of the fluorene moiety does not introduce any complication with the intermolecular H-bonding interactions. From the M06-2X/aug-cc-pVDZ calculations, which have been well established to accurately describe the intermolecular H-bonding interactions,[33] Fig. 4a shows the optimized geometries and D_0 for glycolic acid complexes with a variety of H-bonding partners, NH_3, CH_3CHO, H_2NCHO, HCOSH, $(H_2O)_2$, HCOOH, HCl and HF. For these H-bonded complexes, the intermolecular H-bonds' distances, angles and D_0 values vary substantially and highly depend on the binding partner.

Each of the H-bonding partners serves as a good probe of the influence of the fluorene moiety on the intermolecular interactions. Fig. 4b shows the M06-2X/aug-cc-pVDZ calculated D_0 values for glycolic acid complexes in the *y*-axis and for 9HFCA complexes in the *x*-axis, while all the binding partners in Fig. 4a are included. Taking two extreme cases, the D_0 value of the HCl complex with glycolic acid is small, 5.19 kcal mol^{-1}, and for 9HFCA it gets slightly higher, 5.43 kcal mol^{-1}. The D_0 value of the HCOOH complex with glycolic acid is very high, 15.04 kcal mol^{-1}, and for 9HFCA it gets slightly smaller, 14.77 kcal mol^{-1}. Fitting the array of the data extracts the variation and displays a perfectly linear regression: R^2 is 0.998 and the slope is 1.036. This fitting unambiguously shows that the fluorene moiety does not seriously affect 9HFCA's intermolecular H-bonding interactions. Additional calculations using the B3LYP, ωB97X-D and MP2 methods deliver the same linearity. In short, the fluorene moiety purely acts as a non-interfering spectator over a wide range of D_0 values for these prototypical H-bonded complexes as the binding partner is bound to the carboxylic acid group in 9HFCA.

E. Binding energy determination of the glycolic acid–water dimer

Since the fluorene moiety in 9HFCA is non-significantly impactful when water binds to the carboxylic acid group in the glycolic acid moiety, based on the fitted slope in Fig. 4b and the experimental number of the 9HFCA–water dimer (8.51 ± 0.09 kcal mol^{-1}), the D_0 value of the glycolic acid–water dimer is determined to be 8.51 ± 0.31 kcal mol^{-1} (8.51 × 0.036). This is in line with the CCSD(T)/CBS results, −8.38 kcal mol^{-1}. This number is considerably higher than the estimation at the earlier stage,[34] 6.96 kcal mol^{-1}, calculated by B3LYP/6-311++G(3df,3pd), which is understandable due to the lack of dispersion treatment by B3LYP. More importantly, it highlights the necessity and importance of the recent experimental work

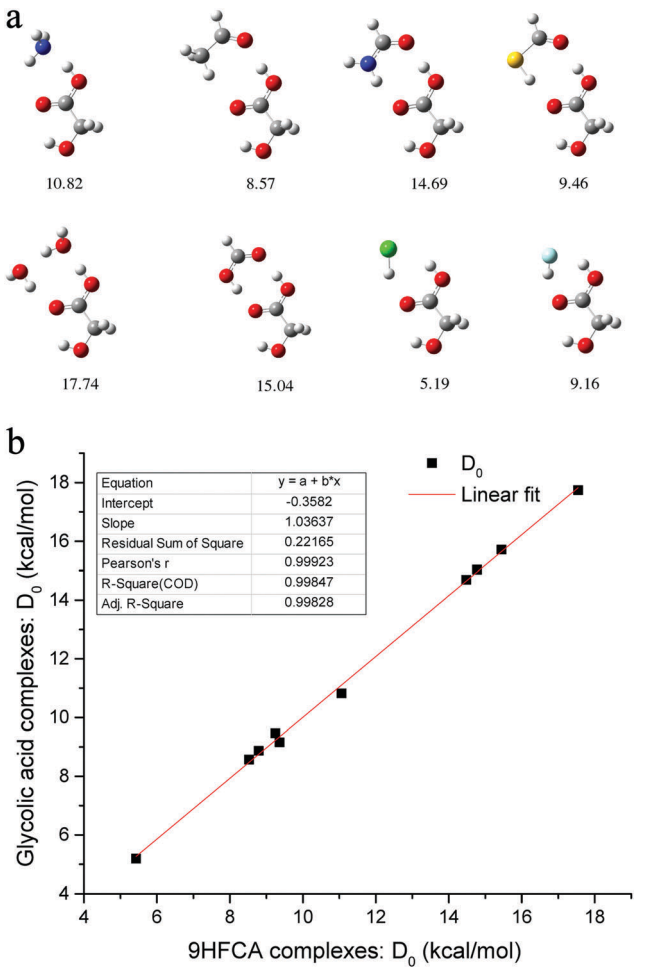

Fig. 4 (a) M06-2X/aug-cc-pVDZ calculated geometries and D_0 (kcal mol^{-1}) for a variety of H-bonding complexes with glycolic acid. (b) Linear fitting on the calculated D_0 values for a variety of H-bonding complexes with glycolic acid and 9HFCA. D_0 calculations were done by M06-2X/aug-cc-pVDZ.

of the 9HFCA–water dimer,[9] which establishes a spectroscopic accuracy.

Our result for the binding energy of the glycolic acid–water dimer, 8.51 ± 0.31 kcal mol^{-1}, lies between that for the water dimer,[35] 3.16 ± 0.03 kcal mol^{-1}, and for the formic acid dimer,[36] 14.22 ± 0.12 kcal mol^{-1}. This suggests a general binding strength of about 8.5 kcal mol^{-1} between water and a carboxylic acid, which may be interesting to the wider scientific communities in studying water and acid clusters and their applications in atmospheric chemistry[37] and biological medicine.[38] So far, reports on definitive evaluation of interaction energy between water and any kind of carboxylic acids are still scarce in the literature.

F. Cooperative and anti-cooperative effects in the glycolic acid–water dimer

The intramolecular H-bond in glycolic acid may be affected upon H-bonding with water. Since the fluorene moiety in 9HFCA does not present any significant impact on the intermolecular H-bonding network in the complexes, we further extend the previous studies on 9HFCA complexes to surmise the cooperative and anti-cooperative effects[39] associated with the multiple H-bonds in the glycolic acid complexes such as with water,[40] formamide or formic acid.

In the glycolic acid–water dimer as already described, water binds to glycolic acid's COOH group through two distinct intermolecular H-bonds involving water's HO acceptor and OH donor groups. The intramolecular H-bond from the alcoholic OH group may then be affected. Illustrated in Fig. 5, intuition suggests that relative to its frequency in the glycolic acid monomer, the alcoholic OH frequency in the water complex would be blue shifted due to the familiar anti-cooperative effect[41] between the intramolecular H-bond and the nearby intermolecular H-bond (OH···O=C). We may ask, will the presence of another intermolecular H-bond (HO···OH–C=O) make a difference? If so, will the emerging cooperative effect between the intramolecular H-bond and the more remote intermolecular H-bond shift the alcoholic OH frequency to the red? Which effect, anti-cooperative or cooperative, is dominant among the three H-bonds? Anticipating the ultimate sign of the alcoholic OH frequency shift starts to be tricky; in fact, some interesting patterns of behavior can be actually discerned.

IR spectra involving the intramolecular H-bond in 9HFCA complexes such as with water, formamide and formic acid have been clearly measured. Red and blue frequency shifts of the alcoholic OH (9-hydroxy group) in the complexes have been rationalized as the competition between the two intermolecular H-bonds.[10] Using the B3LYP method, we optimized the structures and simulated vibrational spectra of glycolic acid, 9HFCA and their complexes with carboxylic acids, formamide, acetaldehyde, water, thioformic acid, ammonia, hydrochloric acid and hydrofluoric acid. The results of the computations and experiments are included in Table 4. The consensus of this array of calculations agrees with the experiments and show that the alcoholic OH stretch at issue is blue shifted in complexes of 9HFCA (or glycolic acid) with carboxylic acids, hydrochloric acid and hydrofluoric acid, but red shifted in complexes with water, thioformic acid, formamide, ammonia and acetaldehyde.

In Fig. 6, these structures provide a simple guide to the source of a certain frequency shift. The intermolecular bond lengths and harmonic frequency shift values mentioned are

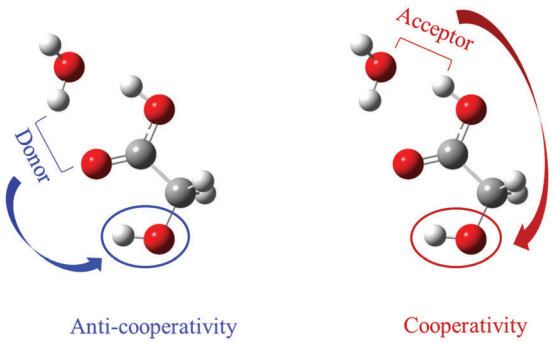

Fig. 5 Anti-cooperative and cooperative effects in the glycolic acid–water dimer.

Table 4 Computed intramolecular OH shifts in complexes of 9HFCA and glycolic acid compared to their monomers. The calculations were done by B3LYP/6-311++G(d,p). Experimental (Exp.) measurements for 9-hydroxyl frequency shifts in the 9HFCA complexes are included as well

	Shift (cm^{-1}) of intramolecular OH in the clusters										
Methods	NH_3	CH_3CHO	$HCONH_2$	HCOSH	H_2O	$(H_2O)_2$	CH_3COOH	CH_3CH_2COOH	HCOOH	HCl	HF
Glycolic acid	−23	−15	−8	−2	−5	−5	1	1	5	11	18
9HFCA	−30	−21	−9	−4	−4	−3	4	4	9	15	25
Exp. (9HFCA)	—	—	−11	—	−7	−7	7	7	13	—	—

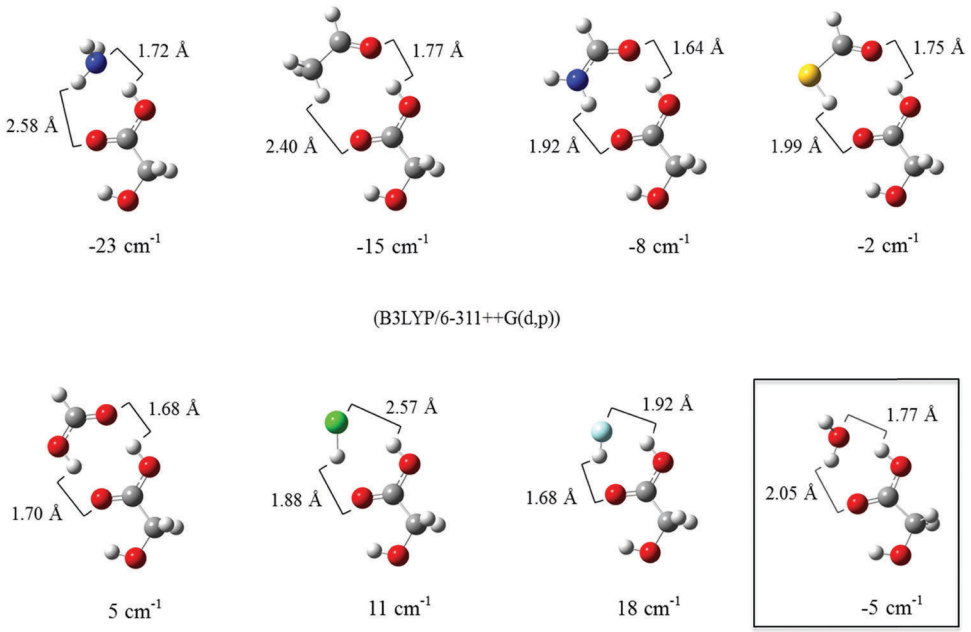

Fig. 6 B3LYP/6-311++G(d,p) computed intermolecular H-bonds distances and alcoholic OH frequency shifts for glycolic acid complexes with several H-bonding partners.

obtained from B3LYP/6-311++G(d,p) calculations. The intramolecular H-bond distance remains almost unchanged for the entire series of complexes, ranging from 1.98 to 2.00 Å. The relative H-bonds' distances of proton acceptance *vs.* donation (from the binding partner to glycolic acid) change dramatically from NH_3 to H_2O to HF. Glycolic acid's C═O···HX (X = O, S, N or C from the binding partners) intermolecular H-bond distances correlate with familiar H-bonding strengths, so the salient differences are traced to variation in the partners' H donation effectiveness. In short, effective H-bonding donation from the partner (HCl and HF) to glycolic acid with a shorter intermolecular H-bond is associated with blue shifts, while ineffective donation from the partner (NH_3) with the longer intermolecular H-bond is related to red shifts.

As shown in Fig. 7, the alcoholic OH frequency shifts correlate well with the changes in its bond length and electron population of σ*, *i.e.*, the anti-bonding molecular orbital (MO), computed in B3LYP/6-311++G(d,p). It shows that a longer bond distance or more σ*electron population relates to red frequency shifts, and *vice versa*. The alcoholic OH's bond distance and σ* electron population in the glycolic acid monomer are 967.84 picometers and 14.83 milli-electrons, respectively. The alcoholic OH group in the NH_3 complex is most red-shifted, -23 cm^{-1}, corresponding to the largest increase in its bond distance (0.116 pm) and σ* electron population (2.68 milli-electrons). In comparison, the alcoholic OH group in the water complex is less red-shifted, -5 cm^{-1}, consistent with a smaller increase in the bond distance (0.024 pm) and σ* electron population (0.71 milli-electrons). Upon complexing with HF, the alcoholic OH group is most blue-shifted, 18 cm^{-1}, pointing to the most decrease in its bond distance (−0.088 pm) and σ* electron population (−1.82 milli-electrons). Conforming to the trend, the alcoholic OH in the formic acid complex is less blue-shifted, 5 cm^{-1}, with a smaller decrease in the bond distance (−0.031 pm) and σ* electron population (−0.21 milli-electrons).

A rationale is readily offered for the blue shifts in frequency. If the partner donates a H which engages glycolic acid's C═O, then the intramolecular H-bonding associated with the alcoholic OH is weakened. The strength of the intramolecular H-bonding is reduced, so the alcoholic OH frequency shifts to blue, as in the HCl and HF cases. It is a familiar case, anti-cooperativity, accompanied by a smaller population in the alcoholic OH σ* local MO.

How can a (further) red shift in the exo OH stretch occur? In the limiting NH_3 case, the partner literally interacts with glycolic acid's C═O, but H bonds strongly to glycolic acid's carboxylic OH. A red shift (in the alcoholic OH stretching

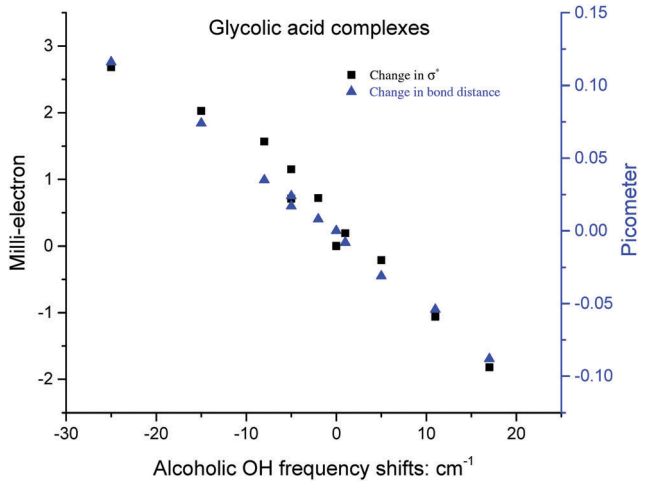

Fig. 7 Changes in σ* and bond distance of the alcoholic OH in glycolic acid complexes as function of its frequency shifts. The calculations were performed by B3LYP/6-311++G(d,p). The alcoholic OH bond distances and σ* electron populations in the complexes are given relative to the values in glycolic acid monomer, 967.84 picometers and 14.83 milli-electrons, respectively.

frequency) occurs. This shift is a consequence of cooperativity, with more electrons populating the alcoholic OH's σ* LMO. The alcoholic OH bond is thus weakened by the additional σ* population, and a red shift occurs due to the electron transfer. When the cooperativity is clear, but less effective than the anti-cooperativity, as in the formamide and water complexes, the intramolecular H-bond is still red shifted, but to a reduced amount compared with the ammonia case. With greater cooperativity, as in the formic acid complex, the intramolecular H-bond starts to blue shift which is most pronounced in the HCl and HF complexes. In short, the blue *vs.* red frequency shifts of the intramolecular H-bond are from cancellation effects, and is the consequence of the competition between anti-cooperativity and cooperativity associated with the multiple intramolecular and intermolecular H-bonds.

The quantitative correlations among bond length, bond frequency and σ* electron population show that the frequency shifts of the intramolecular H-bond can provide a sensitive probe of the existence and the influence of anti-cooperativity and cooperativity among the three H-bonds in the glycolic acid complexes with water and formic acid. Our results and analysis suggest the existence of a subtle multiple H-bonding interaction in the glycolic acid–water dimer. And they may inspire more experiments to probe quantitatively the H-bonding interactions in these prototypical acid–water and acid–acid complexes.

Conclusions

In summary, the analogy between 9HFCA and glycolic acid upon H-bonding with a range of partners including water has been investigated to demonstrate that the fluorene group in 9HFCA is not effective regarding the intermolecular H-bonding interactions associated with the global minima. With reference to the spectroscopic measurement on the 9HFCA–water dimer, the binding energy for the glycolic acid–water dimer is evaluated to have a much better accuracy, 8.51 ± 0.31 kcal mol^{-1}, in excellent accordance with the results of the CCSD(T)/CBS benchmark calculations, 8.38 kcal mol^{-1}. Moreover, from the quantitative IR spectra of 9HFCA H-bonded complexes, we deduce that the competitive anti-cooperative and cooperative behaviors in the glycolic acid–water dimer exist, which involve the multiple intramolecular and intermolecular H-bonds. To a broader impact, this work may motivate an interesting direction to conduct interesting experiments on these exemplary water–acid and acid–acid complexes.

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