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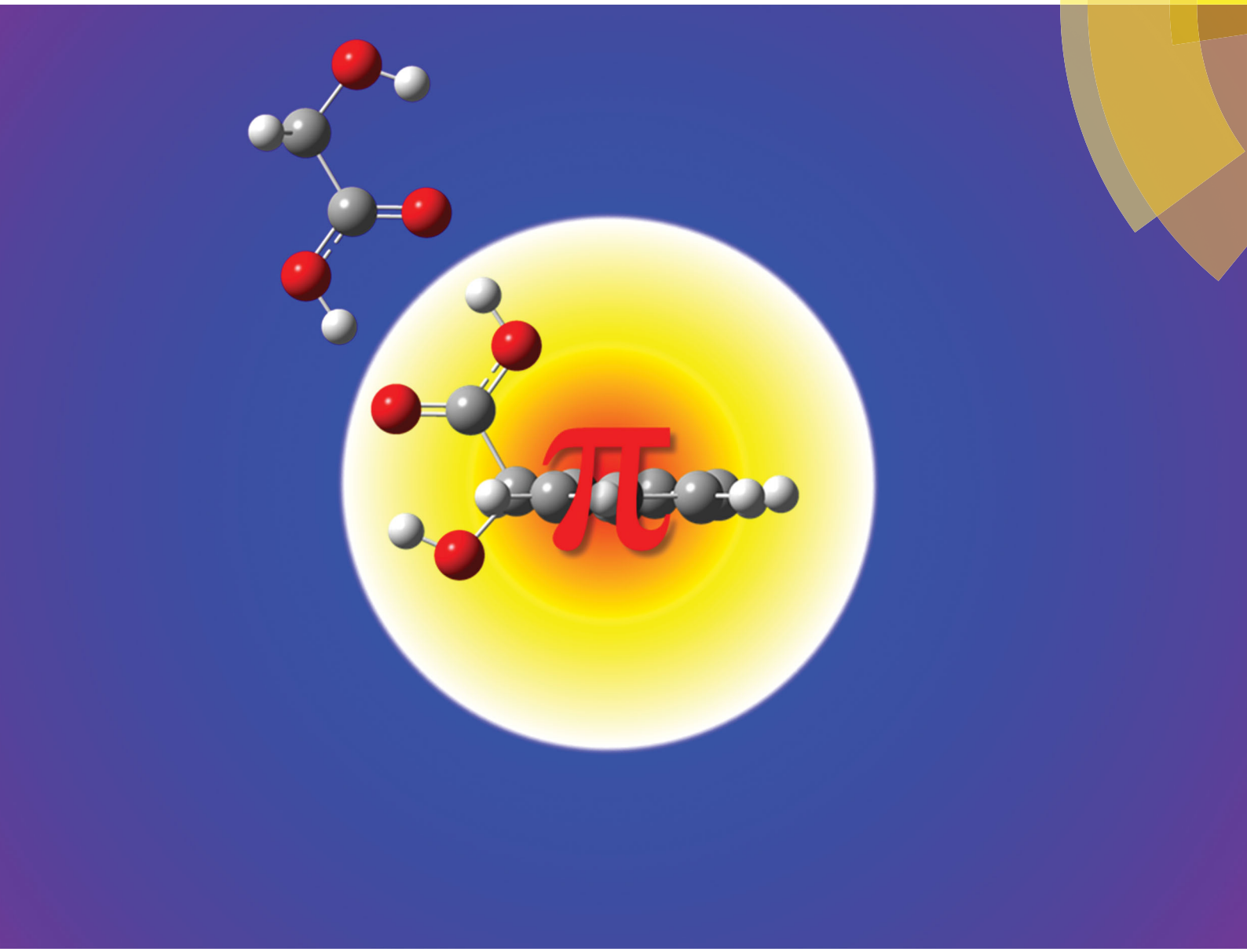

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Infrared spectroscopy of gas phase alpha hydroxy carboxylic acid homo and hetero dimers

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New gas phase infrared spectroscopy is reported for an aromatic alpha hydroxy carboxylic acid homo dimer of 9-hydroxy-9-fluorene carboxylic acid $(9HFCA)_2$, and the hetero dimer of 9HFCA with glycolic acid. In terms of the 9-hydroxy stretching frequency, the 16 cm^{-1} blue-shift in the homo dimer and the 17 cm^{-1} blue-shift in the hetero dimer, relative to that in 9HFCA monomer, are attributed to collective effects with anti-cooperativity stronger than cooperativity. Furthermore, for the hetero dimer, the two alpha hydroxy groups' stretching frequencies are clearly resolved, and differ by 30 cm^{-1}. This difference represents a modest, quantitative enhancement of the intramolecular H-bond by the fluorene moiety in 9HFCA monomer, as opposed to that in glycolic acid. Accurate vibrational frequencies of the alpha OH, 3568 cm^{-1} in the bare glycolic acid, and 3584 cm^{-1} in the glycolic acid homo dimer are determined for the first time by comparison to 9HFCA monomer, homo and hetero dimers. The quantitative studies by infrared spectroscopy reveal subtle interactions among intra- and intermolecular H-bonds in the alpha hydroxyl acid dimers, which are also uniquely extended to probe each monomer's subtle intramolecular interactions.

Introduction

Hydrogen (H) bonding[1] has been extensively characterized for water clusters,[2] but also clusters of carboxylic acids.[3,4] Alpha hydroxy carboxylic acids, *e.g.* glycolic acid (HO–CH_2–COOH) in Fig. 1, are particularly interesting with important applications, such as in organic synthesis, food processing and skin care.[5] They also serve to probe subtle intra- and intermolecular H-bonding interactions. In the lowest energy isomer, an intramolecular H-bond forms between COOH's C=O and the alpha OH; other isomers lacking this interaction are much higher in energy.[6] Past work on glycolic acid shows that it is difficult to study the intramolecular H-bond for the monomer and multiple H-bonds for its complexes such as with water or formic acid.[7] Glycolic acid readily forms clusters, making it difficult to synthesize, separate and characterize the size-specific homo and/or hetero complexes. For example, it was not possible to unequivocally identify the vibrational stretching frequencies of the two OH groups in glycolic acid, due to the broadening of the infrared (IR) spectra, or the matrix environment complication,[8] not to mention the superimposed IR spectra of the complexes which have not been reported to date.

On the other hand, an aromatic analog to glycolic acid, 9-hydroxy-9-fluorene carboxylic acid (9HFCA), has proven to be an excellent vehicle for spectroscopic investigation of H-bonding.[9] As shown in Fig. 1, 9HFCA has C_s symmetry with the chromophore fluorene perpendicular to the glycolic acid moiety. Owing to this orthogonality, the fluorene component does not participate in intermolecular H-bonding interactions of the hydroxy acid component upon complexation. Thus, 9HFCA acts as glycolic acid in the formation of H-bonded complexes because the fluorene moiety has negligible influence on the binding partners.[9] The advantage of 9HFCA and its H-bonded complexes is the strong ultraviolet (UV) absorption of the fluorene chromophore in the easily accessible ~300 nm region, which makes it well suited for H-bonding study by resonance enhanced multiphoton (REMPI) spectroscopy[10] including mass resolved IR-UV double resonance.[11]

One question to address is within the 9HFCA monomer itself – shown by the blue arrow in Fig. 1 – between the fluorene moiety and the glycolic acid moiety. What influence, if any, does the chromophore moiety have on the intramolecular H-bond? Does this aromatic group enhance or weaken the

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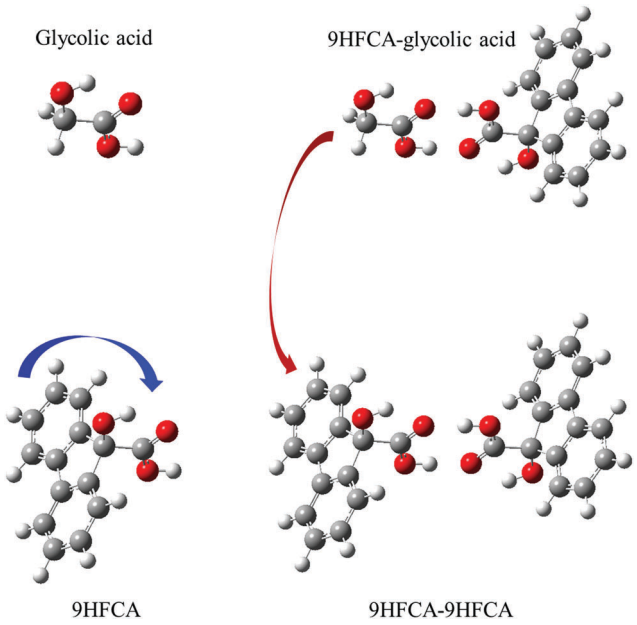

Fig. 1 Glycolic acid, 9HFCA, 9HFCA–glycolic acid and 9HFCA–9HFCA dimers. The blue arrow indicates the possible influence of the fluorene moiety on the glycolic acid moiety in 9HFCA. The red arrow indicates the difference from 9HFCA–glycolic acid hetero dimer to 9HFCA homo dimer.

intramolecular H-bonding strength? How can one measure this presumably small effect in a definitive way? These tricky questions on 9HFCA monomer turn out to be nicely answered by studying and comparing the homo and hetero dimers, $(9HFCA)_2$ and 9HFCA–glycolic acid, as shown in Fig. 1. 9HFCA can form a complex *via* its carboxylic acid group binding to glycolic acid or another 9HFCA. In the two dimers' structures, the fluorene moiety is far away from the binding partner, and it has been shown to have minimal impact on the H-bonding motif.[12] From homo dimer to hetero dimer, the only difference – indicated by the red arrow – is the fluorene moiety, which hardly impacts the intermolecular interactions at all. So, from the structural perspective, one anticipates that any spectroscopic difference between the two dimers essentially corresponds to 9HFCA monomer's intramolecular interactions between fluorene and glycolic acid moieties.

Here, we report that the combination of IR spectra of the homo and hetero dimers permits a clear and definitive judgement for the monomer's subtle intramolecular interactions – that is, the enhancement of the intramolecular H-bonding strength in the 9HFCA monomer, as opposed to that in the glycolic acid monomer. We overcame experimental difficulties to successfully produce, isolate and cool the homo dimer, $(9HFCA)_2$, and the hetero dimer, 9HFCA–glycolic acid *via* the gas phase molecular beam. We subsequently recorded their mass resolved IR spectra using IR-UV double resonance spectroscopy. For the first time, we attribute the measured blue frequency shift of the 9-hydroxy (9-OH) group in the dimers to the collective effects among intra- and intermolecular H-bonds; this is due to the competition of anti-cooperativity and cooperativity – even in a small H-bonding network. Furthermore, we are able to experimentally infer accurate values for the vibrational frequencies of the alpha OH in the bare glycolic acid and its homo dimer.

Experiments and calculations

The molecular beam apparatus has been documented in previous publications.[13,14] In brief, it consists of two vacuum chambers where in the first chamber the pulsed supersonic molecular beam containing the clusters of interest is produced by a standard general valve (series 9). The beam is skimmed by a conical skimmer with a millimeter diameter and enters into the second differentially pumped chamber where the IR-UV double resonance spectroscopy experiment was performed. The formation of 9HFCA–9HFCA homo dimer and 9HFCA–glycolic acid hetero dimer in the molecular beam has been particularly challenging. This is because 9HFCA has low vapor pressure and is easily decomposed upon heating, even to temperatures below its melting point (160 °C).

Recently, we inhibited sample decomposition by coating the entire nozzle with a thin teflon film (Donwell Company) to substantially reduce the thermal decomposition of solid 9HFCA samples before supersonic expansion. Then, we were able to see a modest 9HFCA–9HFCA dimer ion signal at 120 °C, significantly below its melting point (160 °C); the signal would decrease at higher temperatures. For the formation of 9HFCA–glycolic acid hetero dimer, the temperature range was even more constrained due to glycolic acid decomposition. Therefore, the 9HFCA/glycolic acid samples were heated more gently to approximately 60 °C. Although the ion signal of 9HFCA–glycolic acid hetero dimer was modest, we were able to acquire quality spectra.

The measurement of the ground state IR spectrum is *via* an IR-UV double resonance technique with mass resolution. Tunable IR and UV laser pulses were generated using solid state Nd:YAG lasers pumping tunable dye lasers, followed by nonlinear frequency conversions. The UV laser was used to perform the REMPI spectroscopy on monomer or dimer where the ions were collected with a standard Wiley–Mclaren time of flight mass spectrometer.[15] To scan the IR spectrum, the UV laser was fixed to the electronic origin transition of interest (monomer or dimer), and the IR laser was then introduced 30 ns earlier in time, softly focused and spatially aligned with the UV laser spot in a counter propagating geometry.

With basis sets of Pople[16] (6-311++G(d,p)), and Dunning[17] (aug-cc-pVTZ) types, B3LYP,[18] M06-2X,[19] B3LYP-D3[20] and second-order Møller–Plesset[21] (MP2) methods were applied to calculate the isomer with lowest energy, and its associated dimer conformations and energies. Molecular structures, harmonic vibrational frequencies and bond lengths were computed in Gaussian 16.[22]

The non-covalent interaction (NCI) analysis scheme, implemented by Yang *et al.*,[23] was used to identify noncovalent interactions. A NCI index is derived from a two-dimension plot

of the reduced density gradient (RDG), s, and the electron density, ρ. The RDG, s, is expressed as:

$$s = \frac{1}{2(3\pi^2)^{1/3}} \cdot \frac{|\nabla\rho|}{\rho^{4/3}}$$

when s is plotted against the product of electron density (ρ) and the sign of the second Hessian eigenvalue, *i.e.*, sign(λ_2)ρ various types of weak non-covalent interactions can be revealed. The signatures of the non-covalent interactions appear in the regions where the electron density and reduced density gradient are small. The value of ρ at the spike is an indicator for the binding strength of the interaction. With a negative λ_2 value, a ρ value in the range of 0.01–0.05 (a.u.) represents a normal (attractive) H-bond.

Results and discussion

A. NCI analysis of glycolic acid, 9HFCA, 9HFCA–9HFCA and 9HFCA–glycolic acid dimers

NCI analysis offers a direct, qualitative way to visualize the intra- and intermolecular interactions. The structures were stringently optimized using M06-2X/aug-cc-pVTZ methods. Fig. 2a and b shows the NCI plots for the intra- and intermolecular H-bonds in glycolic acid and 9HFCA monomers, 9HFCA–9HFCA and 9HFCA–glycolic acid dimers. For monomers in Fig. 2a, the intramolecular H-bond of glycolic acid has an electron density trough value (isovalue) of −0.022 a.u., close in magnitude but different from that of 9HFCA, −0.026 a.u. The small difference in trough value indicates the fluorene moiety has modest influence on the glycolic acid

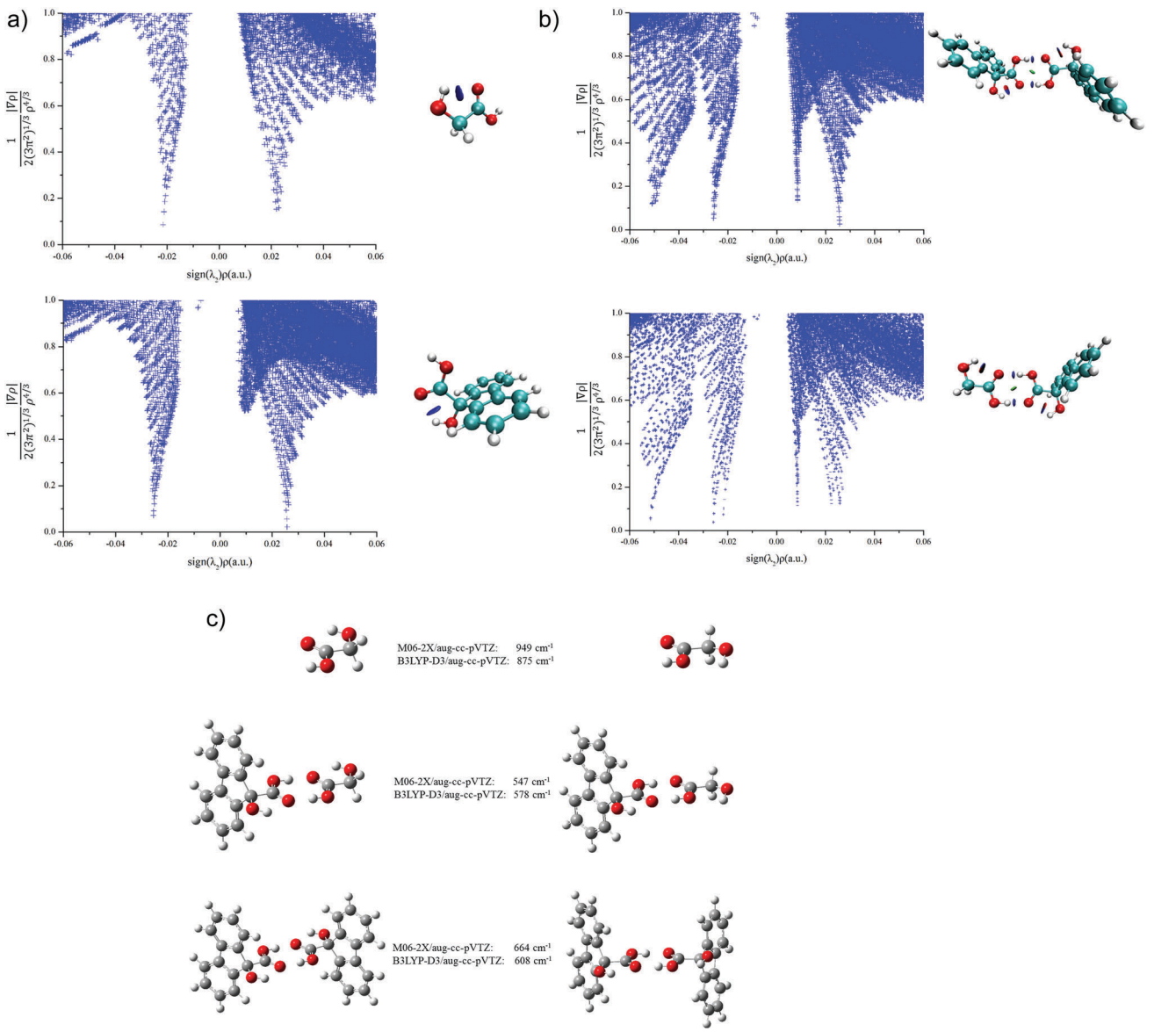

Fig. 2 (a) NCI plots for glycolic acid and 9HFCA. (b) NCI plots for 9HFCA homo dimer and 9HFCA–glycolic acid hetero dimer. (c) Calculated conformational energetics for glycolic acid, 9HFCA–glycolic acid hetero dimer and 9HFCA homo dimer. The left side represents the global energy minima while the right side represents the second lowest energy minima.

entity, as manifested from the intramolecular H-bonding strength.

The variation in intramolecular H-bonding strength persists in the dimers 9HFCA–9HFCA and 9HFCA–glycolic acid, as shown in Fig. 2b. For the 9HFCA–9HFCA dimer, there are two identical intramolecular H-bonds (association with 9-OH). The corresponding trough value is −0.026 a.u., which is barely changed upon dimerization. For the 9HFCA–glycolic acid dimer, the 9-OH associated intramolecular H-bond has the same trough value −0.026 a.u., also barely affected upon glycolic acid complexation. The intramolecular H-bond of glycolic acid in the hetero dimer has a trough value −0.022 a.u., identical with that in bare glycolic acid, but different from the one in bare 9HFCA. So, the difference of the intramolecular H-bond between bare glycolic acid and 9HFCA is retained in the dimers 9HFCA–9HFCA and 9HFCA–glycolic acid. In addition, NCI analysis of the repulsive intermolecular interactions between O···O and H···H in the two dimers are the same, expressed by a isovalue of 0.009 a.u.

For the (attractive) intermolecular H-bonding interactions, the two H-bonds (OH···O=C) in each dimer are linear, parallel to each other, and have the same trough value, −0.051 a.u. On the other hand, the intermolecular H-bonds distances, 1.653 Å *vs.* 1.653 Å in the 9HFCA–9HFCA dimer, are barely changed, 1.646 Å *vs.* 1.645 Å in the 9HFCA–glycolic acid dimer. These identical trough values for all the intermolecular H-bonds and the tiny change of bond distances suggest that the aromatic moiety has minimal impact on the intermolecular binding strength. They also suggest that with either glycolic acid or 9HFCA as complexation partner to 9HFCA, the intermolecular H-bonds have alike impact on the 9-OH of that remote 9HFCA molecule. Moreover, the calculated binding energies and H-bonds distances for the homo and hetero dimers in Table 1 are consistent within a particular method. The similarity in binding energies further shows that the fluorene chromophore's impact on the intermolecular H-bonding strength is minimal as it is far away from the binding partner, does not participate in the intermolecular interactions and thus acts as a non-interfering spectator in the dimers.

Several other isomers in the homo or hetero acid–acid dimers are certainly possible, and the global energy minimum turns out to be quite symmetric in geometry. The calculated conformational energetics for the two lowest energy isomers – from monomer to dimer – is shown in Fig. 2c. For the optimal intermolecular H-bonding motif in an acid–acid dimer, the two equal and parallel intermolecular H-bonds, C=O···HO and HO···C=O, are strongly coupled to maximize the intermolecular interactions. Then, a secondary contribution to the conformational energetics comes from the intramolecular H-bonding motif. Past work has well characterized the intramolecular H-bonding energetics for glycolic acid[6] and 9HFCA,[14] which unequivocally shows that the binding geometry of C=O···HO (between carbonyl group and alpha OH group in monomer) is much stronger than that of HO···HO (between two OH groups in monomer). A third consideration here is the long range fluorene–fluorene interaction in the 9HFCA homo dimer. However, the two chromophores are far away from each other, as separated by the intermolecular H-bonding motif, so their interaction turns out to be too weak to make a difference. The calculations still show that the more symmetric homo (or hetero) dimer is significantly more stable. Note that the long range fluorene–fluorene interaction in the 9HFCA homo dimer becomes different from the fluorene–fluorene dimer itself[24,25] where the π–π electrons interaction primarily contributes to the intermolecular binding strength.

In short, the NCI analysis on the optimized, global minimum structures of glycolic acid, 9HFCA, 9HFCA–9HFCA and 9HFCA–glycolic acid dimers show consistent similarity in intermolecular H-bonds and difference in intramolecular H-bonds. So, the information gathered on intramolecular interactions between fluorene and glycolic acid moieties can be inferred from the difference in the dimers of 9HFCA–9HFCA and 9HFCA–glycolic acid – due to their similar intermolecular H-bonds and strengths. Also, complication from local isomers is not a concern.

Table 1 (a) Calculated binding energies (cm^{-1}) for the dimers. The basis set aug-cc-pVTZ was used and zero point energies were included. GA is the acronym of glycolic acid. (b) Calculated intermolecular H-bonds distances (Å) for the dimers. The basis set aug-cc-pVTZ was used. GA is the acronym of glycolic acid

Methods	9HFCA–9HFCA	9HFCA–GA	GA–GA
(a)			
B3LYP	4732	4809	4893
B3LYP-D3	5866	5814	5809
ωB97X-D	5602	5527	5538
M06-2X	5395	5473	5625
(b)			
B3LYP	1.672/1.672	1.667/1.669	1.663/1.663
B3LYP-D3	1.657/1.657	1.653/1.655	1.651/1.651
ωB97X-D	1.664/1.664	1.664/1.664	1.663/1.663
M06-2X	1.653/1.653	1.645/1.646	1.639/1.639

B. UV and IR spectra of 9HFCA, 9HFCA–9HFCA and 9HFCA–glycolic acid

The experimental results from IR spectroscopy support the NCI analysis that the alpha OH stretching frequency is different from glycolic acid monomer to 9HFCA monomer, but show that the 9-OH stretching frequency is actually changed, blue-shifted upon dimerization. First, we obtained one color two photon S_1 origin band spectra for 9HFCA monomer, 9HFCA–9HFCA and 9HFCA–glycolic acid dimers, as shown in Fig. 3a. Their S_1 origin bands are located at 32 768 cm^{-1}, 32 733 cm^{-1} and 32 728 cm^{-1}, respectively. From monomer to homo and hetero dimers, the frequency shifts of the S_1 origin bands are small, −35 and −40 cm^{-1}. This agrees with the dimer geometry in that when a binding partner, such as 9HFCA or glycolic acid, binds to the side chain of 9HFCA, the electronic excitation of chromophore sees slight interference from the binding partner. Note that in fluorene homo dimer where two chromophores are strongly interacted, there is a much larger red-shift of S_1 origin band (more than 200 cm^{-1}).[24,25] On the other hand, in 9HFCA monomer, a hot band which is red-shifted by 9 cm^{-1} from the S_1 origin band, has been assigned as the side chain rocking

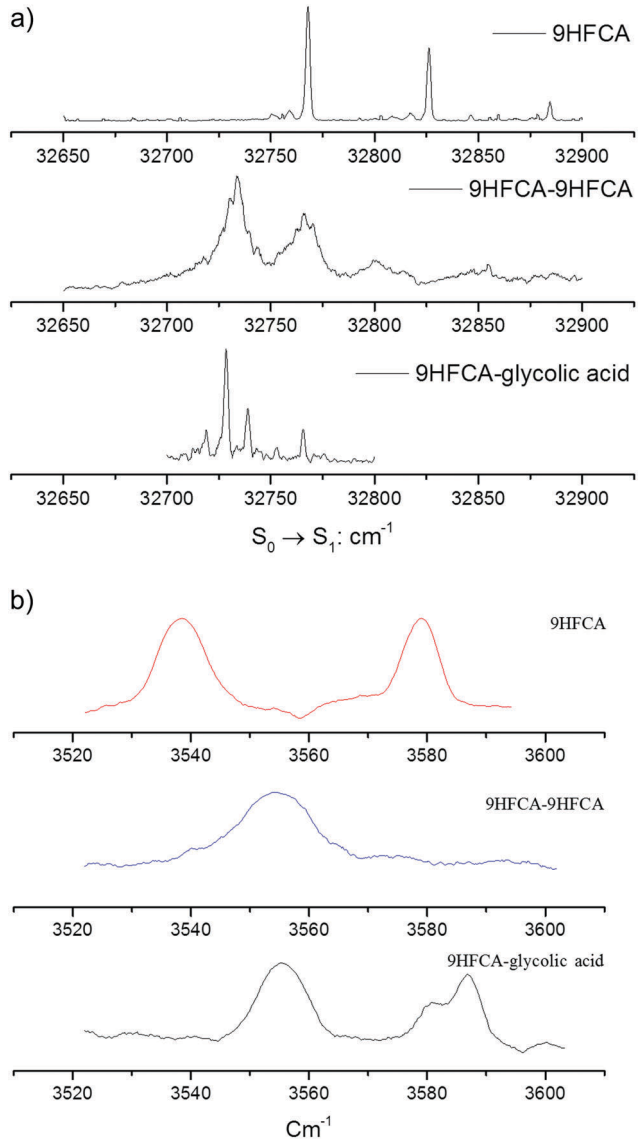

Fig. 3 (a) Mass resolved one color two photon REMPI spectra near S_1 origin bands for 9HFCA, 9HFCA homo dimer and 9HFCA–glycolic acid hetero dimer. (b) IR spectra of 9HFCA, 9HFCA homo dimer and 9HFCA–glycolic acid hetero dimer in the gas phase. The UV laser wavelength was fixed at each S_1 origin band.

mode.[14] (UV-UV hole burning experiments confirmed one single conformation in monomer or dimer.)

In the S_1 spectra of dimers, the hot bands are expected to appear as well. For the homo dimer, it is no surprise that the vibronic bands, besides the hot bands, are much broader as there are a lot of low frequencies modes to overlap so to make assignments difficult. For the hetero dimer, the vibronic band at 32 919 cm^{-1} is also red-shifted by 9 cm^{-1} from the S_1 origin band, which is the same with that in monomer. So, it is assigned as the hot band with glycolic acid H-bonding to the (side chain) carboxylic group of 9HFCA. The band at 32 739 cm^{-1} with a vibrational frequency of 11 cm^{-1} is assigned as the side chain torsional mode. The band at 32 765 cm^{-1} with a vibrational frequency of 37 cm^{-1} is assigned as the side chain rocking mode,[14] which appears strongly in the monomer as 58 cm^{-1}. We did not see any fragmentation signal upon ionizing the two dimers by the UV laser. This is because the energy of the S_1 excited state to cation is close to the neutral to S_1 transition energy, and the cation geometry remains largely the same as in neutral preferring an adiabatic transition. In addition, trimer or larger clusters were barely seen as the samples were only heated modestly to minimize 9HFCA and/or glycolic acid decomposition.

Fig. 3b shows their IR spectra from 3500 to 3600 cm^{-1} pumping each S_1 origin band. In the IR spectra, 9HFCA displays two distinct peaks at 3538 and 3579 cm^{-1}. Previously, we definitively assigned the first peak as the 9-OH stretch, and the second as the carboxylic acid OH stretch.[26] However, the intermolecular carboxylic OH stretching frequencies in the carboxylic acid dimers did not display well defined peaks as their IR spectra were so messy, structure-less, and very broad,[27–29] spanning a range of 2600 to 3200 cm^{-1}.

Interestingly, the alpha OH vibrations remained sharp and resolved, and were thus informative.[30] Here, our study focuses on the further frequency shifts of the two alpha OH groups in the dimers. The vibrational bands of the two 9-OH groups in the homo dimer have the same frequencies (one is IR active and another is Raman active). The 9-OH stretching frequency is then blue-shifted by 16 cm^{-1} in the homo dimer and by 17 cm^{-1} in the hetero dimer. Observation of nearly equal frequency shifts of the 9-OH group in the two dimers reinforces the analogy between 9HFCA and glycolic acid (as 9HFCA's binding partners). The only difference of the two dimers, the fluorene moiety, is confirmed to have minimal influence on the remote 9-OH group. In the hetero dimer, there are only two alpha OH groups – one from 9HFCA and another from glycolic acid – lie in this IR region; it is unlikely the left shoulder of the peak centered at 3584 cm^{-1} is from the intermolecular H-bonds, or from another isomer. Plus, the complex ion signal was very small and could fluctuate quite bit while IR laser was scanning with UV laser fixed. So, we consider it as a whole single peak, which is assigned as the alpha OH group of glycolic acid in the hetero dimer.

The assignments and measurements of the frequency shifts of the alpha OH groups in the homo and hetero dimers of 9HFCA are completely supported by extensive calculations, as summarized in Table 2. A large basis set aug-cc-pVTZ calculation was used to perform the stringent structural optimization. The consensus of the array of calculations agrees well with the experiments in that (1) the stretching frequency of the 9-OH group from 9HFCA monomer to its dimers (with itself and glycolic acid) is blue-shifted, and the amount of the shift is almost the same between the homo and hetero dimers. This is also the case for alpha OH group from glycolic acid monomer to its dimers. (2) The stretching frequency of the alpha OH group (from glycolic acid side) in the hetero dimer is appreciably larger than that of 9-OH in the homo or hetero dimers. This is also the case for alpha OH group as comparing glycolic acid monomer with 9HFCA monomer.

C. Anti-cooperativity *vs.* cooperativity along H-bonding networks

Collective physical effects, such as anti-cooperativity and cooperativity, are widespread in large H-bonded water clusters

Table 2 Calculated harmonic frequencies of alpha OH (cm^{-1}) groups from monomer to dimers. The basis set aug-cc-pVTZ was used. GA is the acronym of glycolic acid

	Alpha OH (cm^{-1}) from monomer to complexes					
Methods	9-OH in 9HFCA	9-OH in 9HFCA–9HFCA	9-OH in 9HFCA–GA	Another alpha OH in 9HFCA–GA	Alpha OH in GA	Alpha OH in GA–GA
B3LYP	3691	3707	3708	3735	3723	3736
Difference	0	16	17	44	32	45
B3LYP-D3	3701	3716	3716	3741	3731	3743
Difference	0	15	15	40	30	42
ωB97X-D	3776	3790	3791	3818	3800	3816
Difference	0	24	25	42	24	40
M06-2X	3775	3794	3792	3812	3801	3815
Difference	0	19	17	37	26	40
Difference (exp.)	0	16	17	46	—	—

and solution.[31,32] They are also present in a simple beta hydroxy dimer,[33] as revealed by the 16 (or 17) cm^{-1} blue-shift of 9-OH group in the dimers here. To model the physical effects, we performed harmonic frequency calculations based on B3LYP and MP2 methods with a basis set of 6-311++G(d,p), which have proved to reproduce a wide array of experimental results with remarkable accuracy.[34] We optimized structures and simulated harmonic vibrational spectra for 9HFCA, glycolic acid and their complexes with carboxylic acids, formamide, acetaldehyde and ammonia. Note that frequency scaling factor is not important for alpha OH vibrational frequency shifts.

These computed structures, shown in Fig. 4a, nicely reproduce the experimental trend of frequencies and identify the source of frequency shifts for the alpha OH group in the 9HFCA complexes. In each H-bonded complex, the fluorene chromophore is far away from the binding partner, does not participate in the intermolecular H-bonding interactions, and acts as a non-interfering spectator. As estimated by B3LYP/6-311++G(d,p) calculations described below, the intramolecular H-bond distance is almost unchanged for the entire series of complexes, ranging from 1.98 Å to 2.00 Å. The intermolecular H-bond distance for the proton donation from 9HFCA to the binding partner varies over a narrow interval, 1.65 Å to 1.77 Å, and correlates with blue-shift of the 9-OH stretching frequency. This is associated with anti-cooperativity. In contrast, the intermolecular H-bond distance for proton acceptance from 9HFCA to the partner varies over a much wider range, 1.69 Å to 2.67 Å. 9HFCA's C═O···HX (X = O, N or C from the binding partners) intermolecular H-bond distances relate to familiar ideas of H-bonding strengths, and attend in red-shift of the 9-OH stretching frequency. This is associated with cooperativity. The ultimate sign and specific 9-OH frequency shift is thus the net outcome of the competition between anti-cooperativity and cooperativity. The frequency calculations agree with the measurements and reveal the reasons for the observed blue-shift of 9-OH stretching frequency in the 9HFCA–9HFCA and 9HFCA–glycolic acid dimer. In short, effective H-bonding donation from the partner to 9HFCA leads to a blue-shift of the 9-OH stretching frequency, a consequence of stronger anti-cooperativity than cooperativity. Ineffective donation leads to a red-shift of the 9-OH stretching frequency, a manifestation of weaker anti-cooperativity than cooperativity.

Similar alpha OH frequency shifts and collective effects may be expected to occur in glycolic acid complexes. The results of B3LYP and MP2 calculations with the basis set 6-311++G(d,p) are summarized in Table 3 and Fig. 4b. Both types of calculations agree with each other and are in line with the experimental results on 9HFCA complexes. This again reinforces the excellent analogy between glycolic acid and 9HFCA upon H-bonding complexation. Furthermore, in light of the tremendous experimental difficulties to study the IR spectra for the glycolic acid complexes, the calculated dynamic pattern of the alpha OH frequency shifts, as revealed by modeling on glycolic acid complexes and with references to 9HFCA counterparts, indeed convincingly identify the collective effects among H-bonds. The existence and competition of anti-cooperativity and cooperativity among the intra- and intermolecular H-bonds are then established, even in such a small dimer of glycolic acid. The computational studies show that upon dimerization the stretching frequency of the alpha OH group from glycolic acid monomer to glycolic acid homo dimer will be blue-shifted, which owes to stronger anti-cooperativity than cooperativity. This type of analysis is expected to be widely applicable to many other carboxylic acids[35] including salicylic acid dimer.[33]

One thing worth noting is that the alpha OH frequency shift has no relationship with the intermolecular H-bonding energies: a more frequency shift of alpha OH group does not mean stronger intermolecular H-bonding energies and *vice versa*. The frequency shift in intramolecular H-bond reflects the cancellation and net effect of the two competing intermolecular H-bonds, while the intermolecular H-bonding energies correspond to a sum of the two individual intermolecular H-bonds' strengths.

D. Alpha OH group in glycolic acid and glycolic acid–glycolic acid dimer

The clear separation of the alpha OH group (of glycolic acid) from the 9-OH group in the hetero dimer is new, interesting, and must be attributed to the absence of the fluorene group in the bare glycolic acid. Since the two intermolecular H-bonds are almost the same in bond distance and strength between the dimers, any influence of 9HFCA on glycolic acid (in the hetero dimer) shall be the same with that on another 9HFCA (in the homo dimer), thus any sensitive spectroscopic difference between

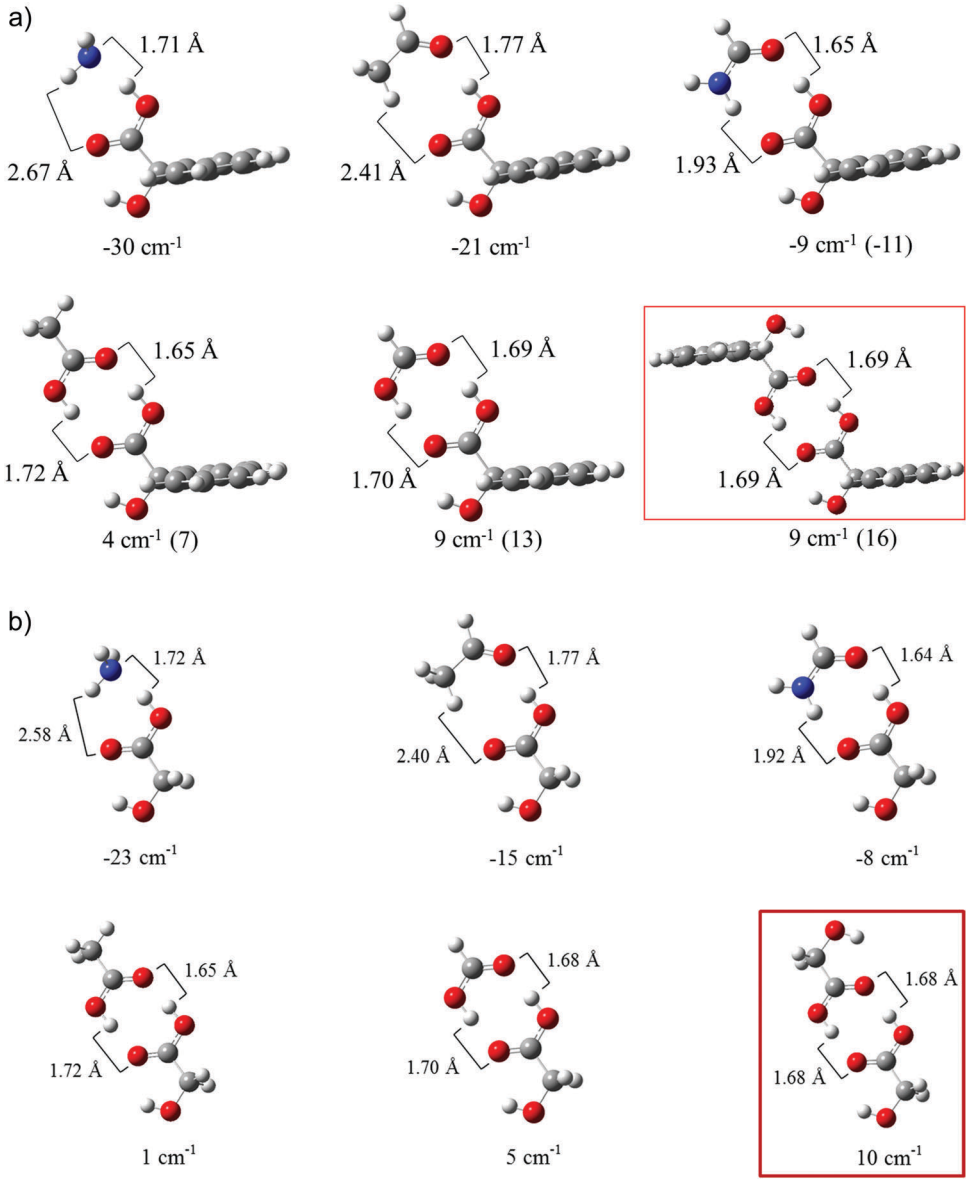

Fig. 4 (a) B3LYP/6-311++G(d,p) computed structures, intermolecular H-bonds distances and alpha OH frequency shifts in 9HFCA complexes. Experimental values appear in brackets. The trend represents an increasing anti-cooperativity. The anti-cooperativity is weaker than cooperativity in the first row, seen from a red-shift of 9-OH. It becomes stronger than cooperativity in the second row, seen from a blue-shift of 9-OH. (b) B3LYP/6-311++G(d,p) computed structures, intermolecular H-bonds distances and alpha OH frequency shifts in glycolic acid complexes. This pattern is similar to that in 9HFCA complexes.

Table 3 Calculated alpha OH frequency shifts (cm^{-1}) in glycolic acid and 9HFCA complexes. The basis set 6-311++G(d,p) was used

	Frequency shifts of alpha OH group in the complexes							
Methods	NH_3	CH_3CHO	$HCONH_2$	CH_3COOH	HCOOH	$HOCH_2COOH$	HCl	HF
Glycolic acid[a]	−35	−20	−10	2	7	8	8	16
Glycolic acid[b]	−23	−15	−8	1	5	10	11	18
9HFCA[b]	−30	−21	−9	4	9	9	15	25
Exp. (9HFCA)	—	—	−11	7	13	17	—	—

[a] MP2. [b] B3LYP.

the two dimers would uniquely measure the 9HFCA monomer's subtle intramolecular interactions – due to the presence of the fluorene group. So, the measured separation of vibrational frequency – alpha OH of glycolic acid in the 9HFCA–glycolic acid hetero dimer minus alpha OH in the 9HFCA homo dimer (3584–3554) – essentially defines the modest enhancement of the

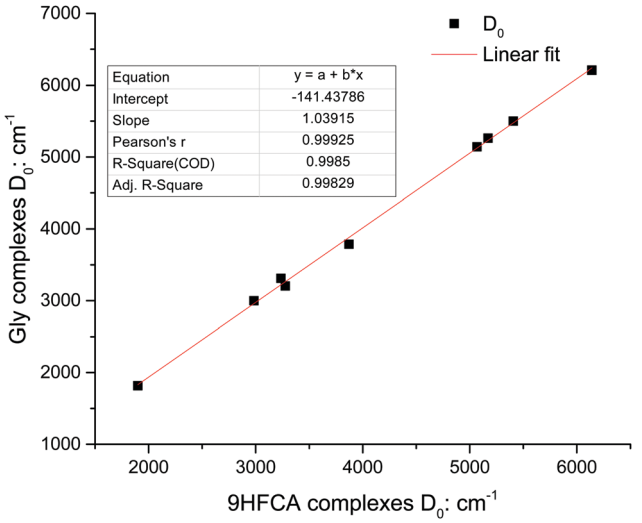

Fig. 5 Linear fitting on the binding energy (D_0) values of 9HFCA and glycolic acid complexes. The values were calculated by M06-2X/aug-cc-pVDZ.

intramolecular H-bond from the glycolic acid moiety in 9HFCA. Therefore, we can confidently conclude that by adding the 9-OH stretching frequency (3538 cm^{-1} in 9HFCA monomer) to the separation of 30 cm^{-1}; this amounts to the alpha OH stretching frequency of the bare glycolic acid, which is 3568 cm^{-1} (3538 + 30).

Moreover, as demonstrated the fluorene moiety in the 9HFCA–glycolic acid hetero dimer does not engage intermolecular H-bonding interactions, is far away from glycolic acid, so it exerts negligible influence on the stretching frequency of the alpha OH group of the glycolic acid (in the hetero dimer). This argument is corroborated by perfectly fitting the binding energy values (D_0) of 9HFCA and glycolic acid complexes (including them in Fig. 4a and b) over a wide range of 2000–6000 cm^{-1}, as shown in Fig. 5.[9] Thus, we can confidently conclude that the stretching frequency of the alpha OH group in the glycolic acid homo dimer is equal to that (of glycolic acid moiety) in the 9HFCA–glycolic acid hetero dimer, which is 3584 cm^{-1}. Interestingly, we can again confidently determine that the stretching frequency of the alpha OH group, from glycolic acid monomer to its homo dimer, is blue-shifted by 16 cm^{-1} (3584–3568).

The extrapolations of alpha OH stretching frequency for glycolic acid monomer and its homo dimer agree with the calculations summarized in Table 2. Note that from private communications with Dr Suhm, this evaluation of the alpha OH stretching band at 3568 cm^{-1} is close to that from a Fourier transform IR jet spectrum of glycolic acid, where a broad band with a range of 3566 to 3596 cm^{-1} was tentatively attributed to the two OH stretching bands of glycolic acid monomer and perhaps some small overlapping contributions from glycolic acid dimer and potential impurities.[36] This type of work on glycolic acid monomer and its homo dimer is being worked on improvement by Dr Suhm with hope to definitively quantify the vibrational frequencies for the carboxylic acid OH and alcoholic OH groups in monomer and/or dimer.

Unfortunately, we cannot evaluate the chromophore impact on the carboxylic OH since the IR spectra for the strongly coupled intermolecular H-bonds in the dimers are diffusive.

Conclusions

In conclusion, we reported the first measurement of the gas phase infrared spectra for two alpha hydroxy carboxylic acid dimers, 9HFCA–9HFCA homo dimer and 9HFCA–glycolic acid hetero dimer. First, the specific alpha OH frequency shift arises from the collective behaviors of intra- and intermolecular H-bonds in the dimers, with anti-cooperativity stronger than cooperativity. This confirms that the existence and competition of anti-cooperativity and cooperativity occur, even in a simple alpha hydroxy acid dimer such as glycolic acid dimer. Such collective behaviors among multiple H-bonds are also expected in salicylic acid dimer and can be rationalized in a similar manner. Moreover, the calculations and in particular the measurements of the two alpha OH vibrational frequencies in the homo and hetero dimers provide a unique way to quantify the intramolecular interaction – that is the aromatic acid monomer's small, but noticeable, intramolecular interactions between chromophore moiety and H-bonding moiety. At last, the alpha OH stretching frequency in the bare glycolic acid is determined as 3568 cm^{-1}, and is blue-shifted by 16 cm^{-1} in the glycolic acid homo dimer, which can be two reference points for further computational and experimental studies on glycolic acid and its complexes. In general, this new work may inspire a wide range of studies for glycolic acid and other hydroxy carboxylic acids to probe the detailed intra- and/or intermolecular interplay, a matter of continuing interest.

Conflicts of interest

There are no conflicts to declare.

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