Electrostatic Interactions Are Key to C=O n-π* Shifts: An Experimental Proof

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S *Supporting Information*

ABSTRACT: Carbonyl n-π* transitions are known to undergo blue shift in polar and hydrogen-bonding solvents. Using semiempirical expressions, previous studies hypothesized several factors like change in dipole moment and hydrogen-bond strength upon excitation to cause the blue shift. Theoretically, ground-state electrostatics has been predicted to be the key to the observed shifts, however, an experimental proof has been lacking. Our experimental results demonstrate a consistent linear correlation between IR (ground-state phenomenon) and n-π* frequency shifts (involves both ground and excited electronic-states) of carbonyls in hydrogen-bonded and non-hydrogen-bonded environments. The carbonyl hydrogen-bonding status is experimentally verified from deviation in n-π*/fluorescence correlation. The IR/n-π* correlation validates the key role of electrostatic stabilization of the ground state toward n-π* shifts and demonstrates the electrostatic nature of carbonyl hydrogen bonds. n-π* shifts show linear sensitivity to calculated electrostatic fields on carbonyls. Our results portray the potential for n-π* absorption to estimate local polarity in biomolecules and to probe chemical reactions involving carbonyl activation/stabilization.
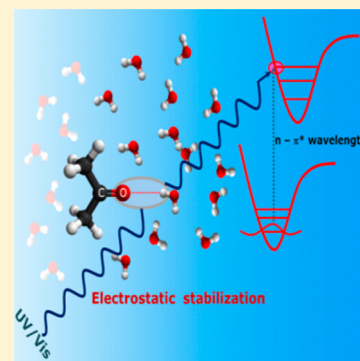
Solute–solvent interactions are widely known to have significant effects on the behavior of molecular systems. In the near-ultraviolet (UV) region, anomalous solvatochromic shifts of carbonyl (C=O) electronic absorption bands to shorter wavelengths with increasing solvent polarity were first reported in the 1920s.[1] Later it was recognized that such absorption bands arise from n-π* transitions, where the nonbonding electron localized on the oxygen atom of the carbonyl (C=O) is excited to the antibonding π* orbital.[2,3] The largest sensitivity to solvents arises when the lone pair on C=O is available for hydrogen bonding (H-bonding) in protic solvents. The blue shift in n-π* electronic transition of C=O has been of great interest for a long time, from both theoretical and experimental points of view. Several factors like change in the dipole moment and H-bonding in the excited state,[4] size of the solvent molecules,[4] H-bonding of the solvent with the solute,[5] Franck–Condon principle, and the changes in H-bond strength upon excitation[6] have been proposed to cause the solvatochromic blue shifts in C=O n-π* transition. Several semiempirical expressions have been derived to dissect the role of H-bonding and electrostatics toward the n-π* blue shifts in carbonyls.[7,8] Recently, Catalan and coworkers have proposed a new photophysical model that includes solvent acidity, dipolarity, and polarizability to explain the spectroscopic data.[9] Various other theoretical studies have also contributed to the understanding of the solvatochromic blue shifts of n-π* transitions of carbonyls.[10–12] It has been theoretically postulated that the solute–solvent interactions in the excited state do not appreciably contribute to the blue shift of the n-π* transitions;[13] however, to the best of our knowledge, a direct experimental demonstration of the origin of the blue shift in n-π* transitions has never been reported. Because C=O

chromophore is present in a wide range of chemical/biological molecules, experimental determination of the interactions leading to the blue shift will have an immense effect on the molecular level mechanistic understanding of chemical/biological reactions involving C=O stabilization/activation by the catalyst/solvent.[14–16]

The C=O chromophore is potentially a versatile spectroscopic probe to intermolecular interactions by means of UV, IR, ^{13}C NMR, and Raman spectroscopy. The high sensitivity of the spectroscopic observables involved in spectroscopic transitions localized on C=O toward solvent polarity, H-bonding, and formation of donor–acceptor complex have been reported.[17,18] These shifts have been explained either through theoretical calculations or through indirect semiempirical models derived from experimental data. In this study, we report direct experimental results using IR/n-π* correlations on various C=O molecules to explain the C=O n-π* solvatochromic shifts. Previous studies have dissected electrostatic and H-bonding contribution to n-π* transitions. Our experimental results show a unique correlation for both protic and aprotic solvents to underpin the electrostatic nature of carbonyl H-bonds in a consistent manner. Moreover, we demonstrate that the H-bonding status of C=O can be experimentally probed using deviations in n-π*/fluorescence correlations.

Ground state electrostatic interactions have been hypothesized to cause the solvatochromic blue shift in C=O n-π* transitions from direct reaction field (DRF) calculations.[13]
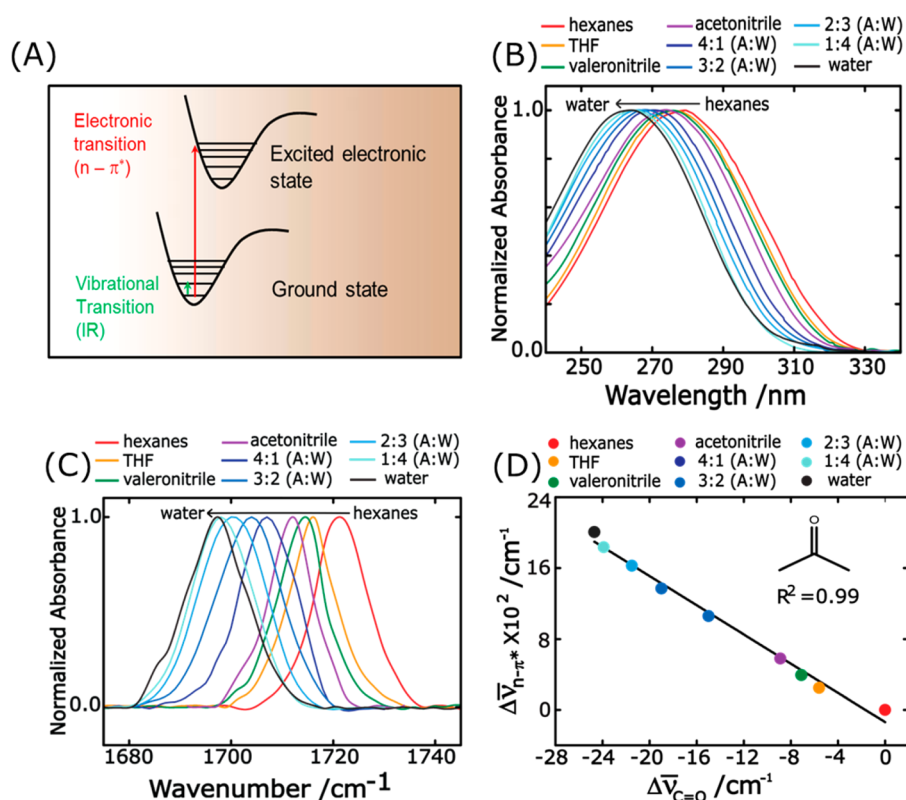
Figure 1. (A) Energy diagram representation of the IR transition (a ground-state phenomenon) and the n-π^* transition (involves ground and excited electronic states). Solvatochromic (B) n-π^* electronic absorption spectra and (C) IR absorption spectra of the C=O stretch of acetone in aprotic and protic solvation environments. (D) Shifts of n-π^* absorption ($\Delta\bar{\nu}_{n\text{-}\pi^*}$) plotted against shifts of C=O IR stretching frequencies ($\Delta\bar{\nu}_{C=O}$) of acetone in different solvation environments. The black line indicates best fit line. The regression value (R^2) of the fitted line is shown in the figure.

Table 1. Absolute Values and Shifts in n-π^* and C=O Stretching Frequencies of Acetone in Non-Hydrogen-Bonding and Hydrogen-Bonding Solvation Environments

solvent	carbonyl stretch ($\bar{\nu}_{C=O}$)/cm^{-1}	($\bar{\nu}_{C=O}$)/cm$^{-1 b}$	n-π^* wavelength ($\lambda_{n\text{-}\pi^*}$)/nm	n-π^* wavenumber ($\bar{\nu}_{n\text{-}\pi^*}$)/cm^{-1}	($\Delta\bar{\nu}_{n\text{-}\pi^*}$)/cm^{-1}
hexanes	1721.6	0.0	278.0	35971	0.0
tetrahydrofuran	1716.0	−5.6	276.1	36219	248
valeronitrile	1714.5	−7.1	275.0	36364	393
acetonitrile	1712.7	−8.9	273.6	36550	579
4:1 A:W^a	1706.6	−15.0	270.0	37030	1059
3:2 A:W^a	1702.6	−19.0	267.8	37341	1370
2:3 A:W^a	1700.1	−21.5	266.0	37598	1627
1:4 A:W^a	1697.7	−23.9	264.5	37807	1836
water	1696.9	−24.7	263.3	37979	2008

^{a}A:W represents acetonitrile−water solution (v/v). ^{b}Negative sign represents red shift with respect to hexane.

From an experimental viewpoint, parameters derived from solvent dielectric constant have shown reasonable linear correlation with the shift in n-π^* transition frequencies in a selected set of aprotic solvents;[7,8] however, using the semiempirical parameter, similar correlation could not be seen for protic solvents that can form an H-bond with the carbonyl. C=O stretching frequencies have also been reported to show linear sensitivity with similar semiempirical expressions for aprotic solvents.[19] Other semiempirical polarity parameters/scales like Kosower's Z scale and Onsager reaction field have been extensively used to correlate the solvent effects on n-π^* and C=O stretching frequencies;[20,21] however, H-bonding pose a challenging task to describe solute−solvent interactions. The continuum semiempirical models do not account for the microscopic nature of the solvent and thereby cannot describe specific chemical interactions like H-bonding. Electrostatic field

can serve as a quantitative and microscopic descriptor of solute−solvent interactions.[22] Stark effect provides a calibration of the transition frequency to the electrostatic field in terms of the difference dipole associated with the transition. Recent studies from vibrational Stark effect (VSE), arising from IR transitions) have demonstrated that the field arising from electrostatic interactions varies linearly with C=O IR frequency in both H-bonding and non-H-bonding environments;[23] however, deviations from linear field-frequency correlation have been observed for nitriles in protic solvents.[24−26] Because both the solvatochromic shifts in C=O IR frequencies and n-π^* frequencies have shown linear sensitivity to multiple semiempirical expressions for aprotic solvents, we wanted to check whether a linear correlation exists between n-π^* and IR shifts in carbonyls. On the basis of the results of VSE on C=O, we hypothesized that a correlation

between IR shift (ground electronic state phenomenon) and n-π^* shift (involves both ground and excited states) would provide model-free direct experimental evidence of the role of ground-state electrostatic interactions toward the solvatochromic blue shifts observed for carbonyls (Figure 1A). Incorporating both protic and aprotic solvents in our study will enable us to confirm if electrostatic interactions are key toward the spectral shifts in both H-bonding and non-H-bonding solvation environments.

Acetone is chosen as the model carbonyl because the C=O stretching frequencies and n-π^* frequencies of acetone have been extensively characterized in various solvents of varying polarity.[9,27−29] As previously reported, we observe a gradual increase in n-π^* frequencies and a decrease in C=O stretching frequencies with increasing polarity of the aprotic solvents (Figure 1B,C). The n-π^* frequencies are obtained using the methodology provided by Renge.[29] The overall frequency dispersion observed from the aprotic nonpolar solvent hexane to the aprotic polar solvent acetonitrile in the IR experiment is ca. 9 cm^{-1} (Table 1). For n-π^* transitions, the dispersion is ca. 579 cm^{-1} (Table 1). When acetone is dissolved in water, where the C=O can form a H-bond with water, a further red shift and blue shift are observed in IR and n-π^* frequencies, respectively. To further understand the interactions in H-bonding environment, we have scanned the polarity range between acetonitrile and water using acetonitrile/water solutions, where the percentage of water is gradually increased by 20% (v/v) increments. The C=O IR and n-π^* frequencies of acetone in various solvents/solvent mixtures are listed in Table 1. The reported frequencies shifts (as shown in Table 1) are calculated with respect to hexane, as it is the most nonpolar solvent in the solvatochromic series. Moreover, theoretical calculations have predicted approximately zero electrostatic field along the C=O in hexane.[23] The solvatochromic red shifts in IR frequencies show a linear correlation with the corresponding n-π^* blue shifts (Figure 1D). The linear sensitivity, as seen in aprotic solvents, where the interactions are predominantly electrostatic, continues in protic solvation environments, and the regression value of the best-fit line is 0.99. The solvatochromic C=O IR shifts has been previously shown to arise from VSE, where the local electrostatic field from the solvation environment affects the vibrational frequencies.[23] Thus, the observed linear correlation between a ground state phenomenon and n-π^* shifts in Figure 1D demonstrates that the electrostatic interactions are key toward the acetone n-π^* blue shift in both H-bonding and non-H-bonding environments.

To check the generality of the role of electrostatics toward the n-π^* blue shifts in carbonyls, we have carried out similar solvatochromic UV and IR absorption experiments on other molecules containing the C=O moiety. C=O connected to an aromatic ring (acetophenone), α,β-unsaturated ketone (mesityl oxide), and ester (ethyl acetate) are the different carbonyls chosen to check the validity of the IR/n-π^* correlation in a similar sets of solvents/solvent mixtures. Because the n-π^* absorption frequency of ethyl acetate is within the solvent cutoff limit in most solvents, the solvatochromic response of ethyl acetate has been studied in hexane, acetonitrile, water, and acetonitrile/water solutions (Figure 2A). Excellent IR/n-π^* correlation in ethyl acetate, as shown in Figure 2B, demonstrates that electrostatic stabilization of the ground state also determines the n-π^* blue shifts of ester C=O. Acetophenone and mesityl oxide also show excellent linear
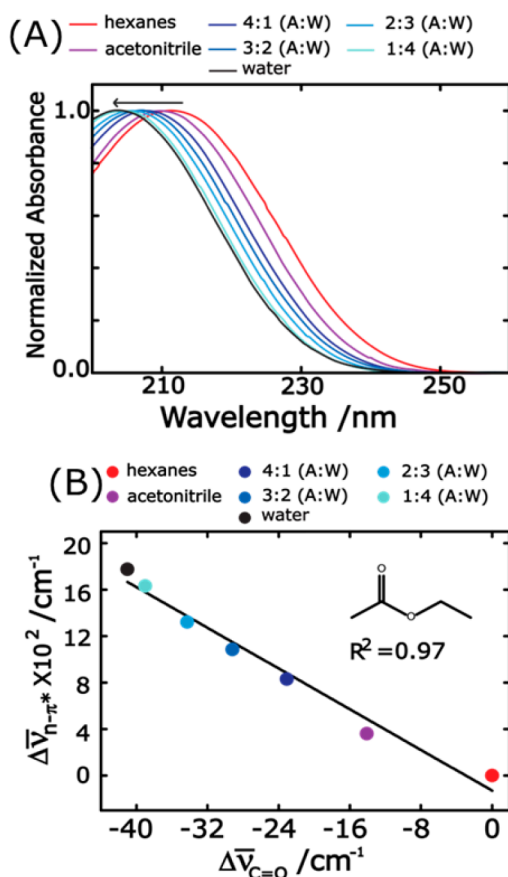

Figure 2. (A) n-π^* electronic absorption spectra of ethyl acetate in non-hydrogen-bonding and hydrogen-bonding solvation environments. The polarity increases in the direction of the arrow. (B) Shifts of n-π^* absorption ($\Delta\bar{\nu}_{n-\pi^*}$) plotted against shifts of C=O IR stretching frequencies ($\Delta\bar{\nu}_{C=O}$) of ethyl acetate in different solvation environments. The black line indicates best fit line. The regression value (R^2) of the fitted line is shown in the figure.

correlations between shifts in IR and n-π^* frequencies (Figure 3A,B) in aprotic as well as protic solvation environments. n-π^* electronic absorption spectra of mesityl oxide and acetophenone in non-H-bonding and H-bonding solvation environments are shown in the Supporting Information (Figures S1 and S2); however, because of the intrinsic overlap of the n-π^* and $\pi-\pi^*$ bands of acetophenone and mesityl oxide in polar protic solvation environments, the conjugated ketones have been studied up to 1:1 acetonitrile/water (50% v/v). For acetophenone and mesityl oxide, the water concentration in binary solvent mixtures has been increased by 10% (v/v) to maintain the same number of data points in the linear fit. The IR and n-π^* frequencies for acetophenone, ethyl acetate, and mesityl oxide, along with their shifts with respect to hexane, are listed in the Supporting Information (Tables S1−S3).

The explanation of the above-mentioned experimental correlation is as follows. During the ultrafast n-π^* excitation process, the solvent shells cannot reorient and adapt to the excited state dipole, and thus the carbonyl moiety in the excited state is surrounded by the solvent molecules adapted to the ground state electrostatic interactions. A better stabilization of the ground state C=O dipole in polar solvation environment as compared with a nonpolar solvent leads to the n-π^* blue shift with increasing solvent polarity. This stability can be associated with a greater electrostatic field exerted by the
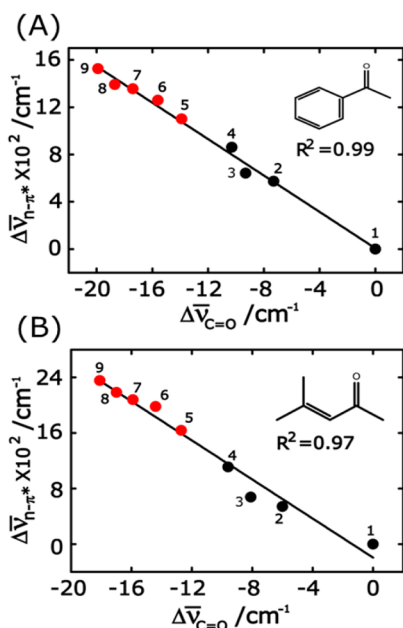
Figure 3. Plots of n-π^* frequency shifts ($\Delta\bar{\nu}_{n-\pi^*}$) versus IR frequency shifts ($\Delta\bar{\nu}_{C=O}$) of (A) acetophenone and (B) mesityl oxide in different solvents and binary solvent mixtures. The black lines indicate the best-fit lines. The black solid circles represent aprotic solvents [(1) hexanes, (2) tetrahydrofuran, (3) valeronitrile, (4) acetonitrile] and red solid circles represent aqueous acetonitrile solutions (v/v) [(5) 90% acetonitrile, (6) 80% acetonitrile (7) 70% acetonitrile, (8) 60% acetonitrile, (9) 50% acetonitrile]. The regression values (R^2) of the fitted lines are shown in the figures.

solvents along the C=O bond dipole through VSE. The larger stability in protic solvation environments of C=O can be rationalized by considering that a H-bond positions a large dipole near the IR probe due to the small van der Waals radius of hydrogen, which, in turn, exerts a greater stabilizing electrostatic field on the C=O. The linear sensitivity of IR frequency shifts with that of n-π^* frequency in a range of different C=O compounds demonstrates that electrostatic interactions in the ground electronic state play a key role toward the n-π^* blue shifts in carbonyls. Being a function of the coordinates of the individual atoms of the solvent molecules as well as their partial charges, the electrostatic field provides a microscopic description of the solute−solvent interaction and accounts for specific chemical interactions like H-bonding. Thus, the IR/n-π^* linearity obtained in the aprotic solvents can be extended to the protic solvation environments. Very recently, Boxer and coworkers have demonstrated a linear correlation between electrostatic field and C=O IR stretching frequencies using VSE, consistently for both H-bonding and non-H-bonding solvents.[23] Theoretical calculations have predicted a redistribution of electron density along the C=O bond in the excited state, leading to a reduced dipole moment that in turn reduces the electrostatic interactions.[30] A smaller dipole moment would result in a blue shift with increasing solvent polarity through electronic Stark effect. In Stark effect interpretation the slope of the IR/n-π^* plot would be related to the difference dipoles of the two transitions. Considering the slopes of the IR/n-π^* plots along with the reported values of the difference dipoles for IR transitions (from VSE), the difference dipoles for the C=O n-π^* transitions are on the order of ~3−5 D (see Table S5 in the Supporting Information), which is consistent with the reported values for

other electronic transitions.[31] The similarity in difference dipoles supports the argument that the observed linear correlations arise from the underlying solvent electrostatic field. To further establish this point, we have calculated the electrostatic fields being exerted along the C=O using molecular dynamics (MD) simulations, and a linear correlation is obtained between n-π^* shifts and shifts in electrostatic fields for different C=O-containing molecules (Figure 4) in both
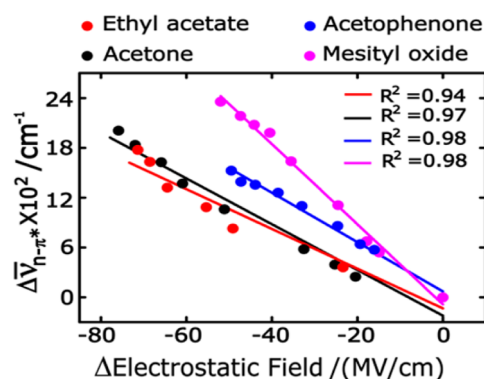

Figure 4. Shifts in n-π^* absorption wavenumber ($\Delta\bar{\nu}_{n-\pi^*}$) versus shifts in C=O electrostatic fields ($\Delta\vec{F}_{C=O}$) for ethyl acetate, acetone, acetophenone, and mesityl oxide. The solid circles represent the [$\Delta\bar{\nu}_{n-\pi^*}, \Delta\vec{F}_{C=O}$] paired points and the solid lines denote best linear fits. The regression values (R^2) of the fitted lines are shown in the Figure.

protic and aprotic solvation environments; however, previous studies involving semiempirical scales could not accommodate specific interactions like H-bonding, and thus the linearity between absorption frequencies and the polarity parameter was confined within a selected set of non-H-bonding solvents. The slopes of the best-fit lines in Figure 4 also provide us an estimate of the difference dipole for the C=O n-π^* transitions. The values of the slopes obtained using the calculated electrostatic fields (listed in Table S4 of the Supporting Information) are smaller by a factor of ~2.5 (see Table S6 of the Supporting Information). This factor is consistent with the correction factor arising from local field effect.[16,23,26]

Our experimental results show that the linearity is extendable from non-H-bonding to H-bonding environments of C=O, and thus it is unnecessary to consider separately the contribution from electrostatic interactions and H-bonding interactions for C=O spectroscopic probes. These results support the electrostatic nature of C=O H-bonding interactions.[17] Because both the axes in IR/n-π^* correlation are experimental observables, there are no assumptions involved in elucidating the highly debated origin of the n-π^* blue shifts. The only assumption is whether the C=O is H-bonded in acetonitrile/water solutions. To experimentally prove this assumption, we have used UV/fluorescence covariance of acetone in protic and aprotic solvents. An acetone molecule that is H-bonded in the ground state probably cannot sustain the H-bond in the excited state as one of the electrons in the n-orbital is removed during the n-π^* transition. Two lone pairs on C=O oxygen can presumably form two H-bonds; however, a previous study reported negligible contribution of solvent acidity to fluorescence solvatochromism of acetone. For aprotic solvents, both the ground and excited states are not H-bonded and are stabilized by the electrostatic interactions by the surrounding solvent molecules, leading to a linear correlation between n-π^* shifts

and fluorescence shifts. According to this explanation, a plot of n-π* shifts versus fluorescence shifts will maintain a linear correlation for aprotic solvents, whereas a deviation from linearity will occur for H-bonding protic solvents/solvent mixtures (Figure 5), where the ground state involves a specific
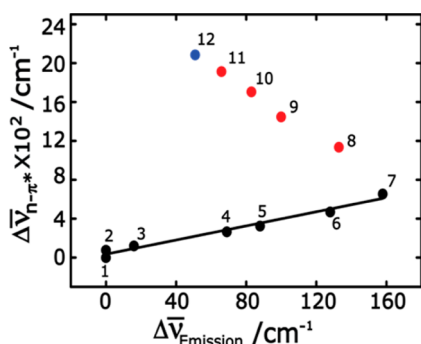

Figure 5. Shifts in n-π* absorption ($\Delta\bar{v}_{n-\pi*}$) versus shifts of emission wavenumber ($\Delta\bar{v}_{em}$) for acetone in protic and aprotic solvation environments. Black solid circles represent aprotic solvents [(1) cyclohexane, (2) hexanes, (3) n-pentane, (4) diethyl ether, (5) tetrahydrofuran, (6) valeronitrile, (7) acetonitrile], red solid circles represent aqueous acetonitrile solutions (v/v) [(8) 80% acetonitrile, (9) 60% acetonitrile, (10) 40% acetonitrile, (11) 20% acetonitrile], and blue solid circle represents water. Black line indicates best fit line in different non-hydrogen-bonding aprotic solvents. The regression value (R^2) of the best fit equals to 0.97.

chemical interaction (H-bonding) that is missing in the excited state. A plot of ($\Delta\bar{v}_{n-\pi*}$) versus fluorescence (emission) shifts ($\Delta\bar{v}_{em}$) demonstrates deviation from the linear correlation for all acetonitrile/water mixtures, thereby providing evidence that C=O is H-bonded in binary aqueous solutions of acetonitrile. The emission spectra and emission frequencies of acetone are shown in Figure S3 and Table S6 of the Supporting Information.

In summary, using IR/n-π* correlations in a range of different compounds with C=O functionalities, we have provided the first experimental evidence regarding the origin of the C=O n-π* solvatochromic shifts. Our results demonstrate that increasing solute−solvent electrostatic interactions in the ground electronic state is the key to the blue shifts in n-π* transitions. We have also experimentally demonstrated the H-bonding status of the C=O using n-π*/ fluorescence correlations. The implications of these results are manifold. These results demonstrate that n-π* frequencies can predict the electrostatic fields experienced by the carbonyl moiety. Electrostatic field has been recently proposed to be a microscopic and quantitative descriptor of noncovalent interactions and local polarity.[23] To date, IR spectroscopy has been used to predict electrostatic fields through vibrational Stark effect; however, the intrinsic overlap of the ligand C=O frequency with the amide-I band of the protein makes it extremely difficult to experimentally determine the C=O stretching frequency of the carbonyl.[16] On the contrary, long wavelength n-π* transition of ligand carbonyls (e.g., in steroids) has considerable less overlap with the protein absorption and can be a suitable alternative for determining the local polarity at the binding site of the protein. Moreover, several organic reactions are predicted to involve C=O activation through the H-bond. Metal-free organocatalysis has seen tremendous growth in recent times.[32] Recently, n-π* frequencies have been shown to correlate with organic reaction rates.[33] Our results might provide the mechanistic understanding of these organic reactions.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpclett.6b01052.

> Experimental methods and simulation protocol, table for IR frequencies and n-π* frequencies for acetophenone, ethyl acetate, and mesityl oxide, and table for MD estimated electric fields of acetone, acetophenone, mesityl oxide, and ethyl acetate in different solvation environments (PDF)

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Notes

The authors declare no competing financial interest.

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