2-Pyridone–Fluorobenzene Complexes

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Nucleobase–Fluorobenzene Interactions: Hydrogen Bonding Wins over π Stacking**

Roman Leist, Jann A. Frey, Philipp Ottiger, Hans-Martin Frey, Samuel Leutwyler, Rafał A. Bachorz, and Wim Klopper**

Hexafluorobenzene forms an alternating π-stacking arrangement in its 1:1 cocrystal with benzene and other aromatics, while pure benzene and hexafluorobenzene crystallize in a T-shaped "herringbone" arrangement.[1] Hexafluorobenzene and polyfluorophenyl groups have hence found application in supramolecular design and crystal engineering as π-acceptor synthons that typically produce alternating stacked structures in 1:1 combination with arenes.[2–5] The face-to-face π stacking of nucleobases makes an important contribution to the stability and structures of oligonucleotides and nucleic acids. The relative importance of H-bonding and π stacking for DNA stability has been qualitatively probed in studies with nucleobase analogues whose N–H or C=O H-bonding groups of the Watson–Crick pairing edges have been partly or wholly fluorinated.[6–9] DNAs containing polyfluorinated nucleobase analogues have shown base pairing and even selective replication by DNA polymerases, and this has been interpreted in terms of base-stacking, hydrophobic, and shape-complementarity effects.[6–9]

Despite this wide interest in π stacking, there are few measurements of the properties of isolated π-stacked molecular dimers. An electric-deflection molecular-beam study on the paradigmatic benzene–hexafluorobenzene complex indicated parallel molecular planes and collinear sixfold symmetry axes,[10] but no other data are available. For the benzene dimer, microwave, Raman, and UV spectroscopic measurements have only provided data on the T-shaped dimer,[11–13] but the parallel-displaced π-stacked dimer predicted by high-level ab initio calculations[14–17] has not been observed so far. The Raman and UV vibronic spectra of the gas-phase benzene trimer and tetramer have also been interpreted in terms of locally T-shaped subunits.[13,18,19]

We have investigated H-bonding versus π stacking in isolated cold complexes formed between the nucleobase analogue 2-pyridone (2PY) and 1,2,4,5-tetrafluorobenzene (4FB), pentafluorobenzene (5FB), and hexafluorobenzene (6FB), using mass-specific ultraviolet and infrared laser spectroscopic techniques (see the Supporting Information). In the molecular-beam environment, solvation and ionic effects as well as constraints of the DNA backbone are removed. Supersonic jet cooling reduces the temperature to below 5 K and thus eliminates entropic effects. The $S_0 \rightarrow S_1$ two-color resonant two-photon ionization (2C-R2PI) spectra of both 2PY·4FB and 2PY·5FB (Figure 1 A and B) display sharp and intense origins and narrow-band vibrational excitations, which imply that these complexes are doubly H-bonded. The 2PY·*n*FB complexes with $n = 1$–4 have previously been shown to form unconventional C–H···O=C and

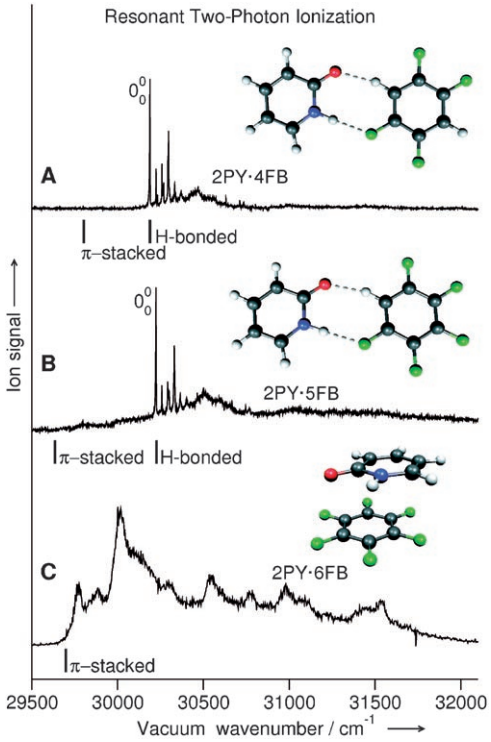

Figure 1. Two-color resonant two-photon ionization spectra of A) 2-pyridone·1,2,4,5-tetrafluorobenzene (2PY·4FB), B) 2-pyridone·pentafluorobenzene (2PY·5FB), and C) 2-pyridone·hexafluorobenzene (2PY·6FB). Vertical bars indicate the RI-CC2 calculated $S_0 \rightarrow S_1$ origins, scaled by a factor of 0.86.

[*] Dr. R. Leist, Dr. J. A. Frey, P. Ottiger, Dr. H.-M. Frey, Prof. Dr. S. Leutwyler
Department of Chemistry and Biochemistry
Universität Bern, Freiestrasse 3, 3012 Bern (Switzerland)
Fax: (+41) 31-631-3994
E-mail: leutwyler@iac.unibe.ch

R. A. Bachorz, Prof. Dr. W. Klopper
Center for Functional Nanostructures (CFN) and
Institut für Physikalische Chemie
Universität Karlsruhe (TH), 76128 Karlsruhe (Germany)

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N–H···F–C hydrogen bonds, and their UV spectra are similar to those in Figure 1 A and B.[20,21]

In contrast, 2PY·6FB (Figure 1 C) exhibits about 60-cm^{-1} broad bands that are 40 times wider than those of 2PY·4FB and 2PY·5FB. This dramatic changeover to a broad-band spectrum reflects a structural change from an H-bonded to a π-stacked complex that exhibits ultralow-frequency vibrations (see below). Using the UV–UV hole-burning technique[21] and tuning the hole-burning laser to any location within the strong band II centered at 30050 cm^{-1} removes the entire spectrum of 2PY·6FB (Figure 2 A and C). Thus, the

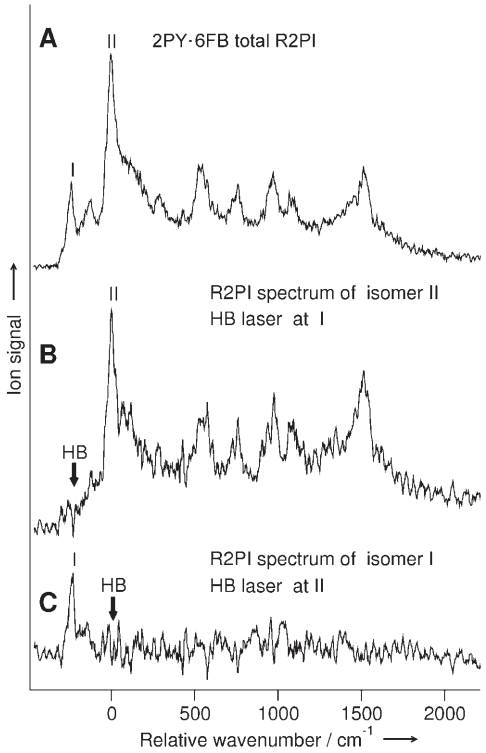

Figure 2. A) Two-color resonant two-photon ionization spectrum of 2PY·6FB. B, C) Separation of spectrum A into subspectra of two isomers denoted I and II by UV–UV laser hole burning (HB) at the laser frequencies indicated by arrows. In C), the entire spectrum of isomer II is removed, although the HB laser is only 0.4 cm^{-1} wide.

absorption spectrum of 2PY·6FB is mainly homogeneously broadened. Analogous UV–UV hole-burning experiments at the lowest lying band at 29770 cm^{-1}, marked as I in Figure 2 A, removes the two lowest bands, as shown in Figure 2 B. The subspectrum in Figure 2 C probably corresponds to a π-stacked isomer of 2PY·6FB (isomer I) that also exhibits considerable homogeneous broadening. Despite the broadening, the characteristic signature of the optically active in-plane vibronic modes of the 2-pyridone chromophore[22] can be clearly identified in the spectrum of the more intense component of 2PY·6FB.

We interpreted these results using highly accurate ab initio calculations of the ground S_0 and excited S_1 states of the H-bonded and π-stacked forms of the 2PY·*n*FB ($n = 4$–6) complexes. The electron correlation energy was evaluated by means of the resolution-of-identity second-order Møller–Plesset R12 method (RI-MP2-R12).[23,24] For the Hartree–Fock (HF) and RI-MP2-R12 contributions we used the Dunning augmented correlation-consistent polarized valence quadruple-zeta (aVQZ) basis set.[25,26] We evaluated the additional correlation energy contributions using coupled-cluster theory with singles and doubles excitations (CCSD, with the analogous double-zeta (aVDZ) basis set) and with perturbative triples [CCSD(T), with a modified aVDZ basis set (aVDZ′)]; see also the Supporting Information. The binding energies were calculated by adding the contributions from the four levels of theory, using the largest basis set possible at each level [Eq. (1)].

$$\Delta E = \Delta E_{\mathrm{HF}}^{\mathrm{aVQZ}} + \Delta E_{\mathrm{RI\text{-}MP2\text{-}R12}}^{\mathrm{aVQZ}} + \Delta E_{\mathrm{CCSD}}^{\mathrm{aVDZ}} + \Delta E_{\mathrm{CCSD(T)}}^{\mathrm{aVDZ'}} \quad (1)$$

The optimized S_0 ground-state structures are planar (see insets in Figure 1 A and B). The two moieties are held together by unconventional C–H···O=C and N–H···F–C hydrogen bonds. With increasing number of F atoms in the fluorobenzene the C–H···O bond become stronger (up to 17.2 kJ mol^{-1} for 2PY·4FB), while the N–H···F interaction decreases (to about 7.5 kJ mol^{-1} for 2PY·4FB).[21] The H-bonded form of 2PY·6FB is mainly stabilized by such a weak N–H···F H-bond, plus a very weak C–H···F–C interaction.

In both the π-stacked 2PY·4FB and 2PY·5FB complexes, the C=O and N–H groups of the 2PY rings are vertically aligned with a C–H and a C–F group of the lower fluorobenzene ring, and this indicates weak stabilizing interactions. In the π-stacked equilibrium structure of 2PY·6FB (Figure 1 C) the 2-pyridone edge with the C=O and N–H functional groups lies closer to the hexafluorobenzene plane, and 2PY is laterally displaced. These structures are similar to those recently calculated for the slipped-parallel benzene dimer[14] and for the stacked benzene–hexafluorobenzene complex.[27] The calculated binding energies D_e of the H-bonded 2PY·4FB and 2PY·5FB complexes are −27.9 and −28.2 kJ mol^{-1}, respectively, while those of the π-stacked forms are smaller by 5.0 and 2.5 kJ mol^{-1} (Figure 3). Increasing the degree of fluorination of the fluorobenzene moiety does not monotonically increase the binding energy of the π-stacked form: the 2PY·6FB dimer is slightly less strongly bound than 2PY·5FB (Figure 3). This difference can be traced to the attractive dipole–dipole interaction between 2PY and 5FB, which does not exist between 2PY and the nonpolar 6FB.

How much would the binding energies change by optimizing the geometries at the CCSD(T) level in place of the MP2 level (see the Supporting Information)? Of course, all binding energies would increase by the geometry relaxation, but the π-stacked structures would probably gain more energy than the H-bonded complexes. We tried to estimate the effect by optimizing the interplanar distance in the 2PY·6FB complex with the spin-component-scaled MP2 method (SCS-MP2),[28] which is known to give results close to CCSD(T) for the benzene dimer.[17] Relative to MP2, the SCS-MP2 method elongates the interplanar distance by about 0.2 Å and the CCSD(T) binding energy D_e at the SCS-MP2 minimum is −27.6 kJ mol^{-1}.

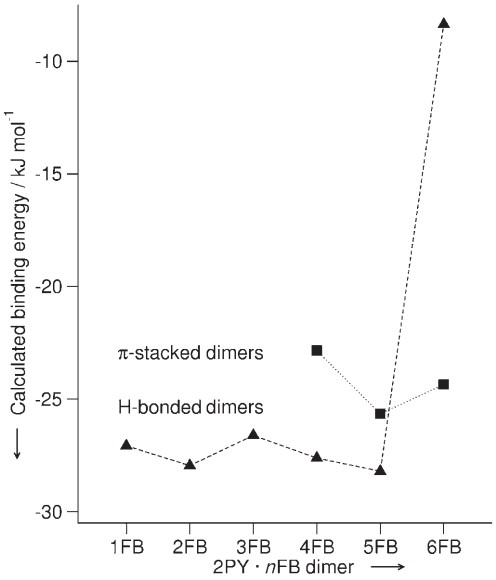

Figure 3. Ab initio CCSD(T) calculated binding energies of the H-bonded and π-stacked isomers of the 2PY·*n*FB complexes ($n=1$–6; 1FB = fluorobenzene, 2FB = 1,4-difluorobenzene, 3FB = 1,3,5-trifluorobenzene). Note the crossing of the calculated binding energies of the hydrogen-bonded and π-stacked isomers between $n=5$ and 6.

What is the reason for the unexpectedly broad $S_0 \rightarrow S_1$ absorption spectrum of 2PY·6FB? At the low temperature achieved in the supersonic jet for 2PY·4FB and 2PY·5FB (see Figure 1 A and B), the broadening of the 2PY·6FB spectrum can only be due to vibrational states of extremely low energy.

For a π-stacked dimer, the lowest-frequency intermolecular mode is the "coplanar twisting" vibration τ (Figure 4 C).

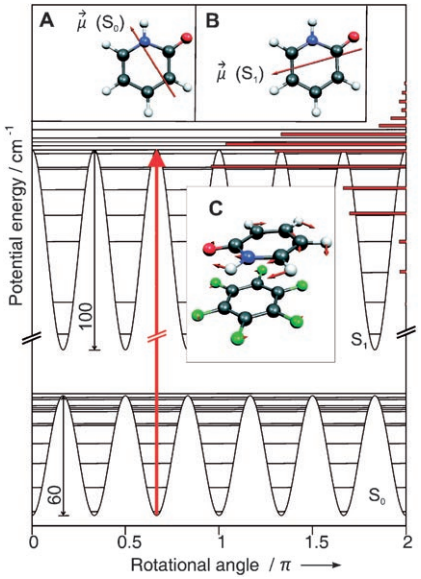

Figure 4. S_0- and S_1-state hindered-rotation potentials and vibrational levels for the "coplanar twisting" mode of 2PY·6FB. The normal mode is shown in (C). Electronic excitation (red arrow) is most probable to levels near the top of the hindered-rotation potential of the S_1 state. The calculated vibronic intensities are shown as horizontal red bars on the right.

The calculated S_0- and S_1-state τ potentials exhibit six equivalent minima and maxima, spaced by 60°, that derive from the sixfold rotational symmetry of the hexafluorobenzene moiety (Figure 4). The S_0- and S_1-state barriers, calculated at the RI-MP2 and RI-CC2/aVTZ level, are about 60 and about 100 cm^{-1}, respectively.

Figure 4 also shows the vibrational levels calculated in the S_0- and S_1-state τ potentials. The horizontal lines indicating the four (five) lowest levels in the S_0 (S_1) state encompass six nearly degenerate coplanar-twisting substates with energy splittings that are too small to be shown. The homogeneous broadening of the 2PY·6FB absorption spectrum arises from the approximately 90° in-plane rotation of the dipole moment of 2PY on $S_0 \rightarrow S_1$ electronic excitation, as indicated in Figure 4 A and B. This rotation of the dipole moment displaces the minima of the S_0 and S_1 states by 30° relative to each other. The $S_0 \rightarrow S_1$ vertical excitation (red arrow in Figure 4) excites the six $v=0$ substates in the S_0-state minima to the vicinity of the S_1-state rotational barrier. Here, the very high density of τ vibrational levels gives rise to a homogeneously broadened absorption spectrum. The calculated vibronic transition intensities (horizontal red bars in Figure 4) are largest for the transitions to the τ states close to the excited-state barrier. These span a range of about 50 cm^{-1}, roughly the observed bandwidth in Figure 2.

We note that the $S_1 \leftarrow S_0$ electronic spectrum of 2PY·6FB (Figures 1 and 2) extends up to about 1635 cm^{-1} above the origin band. This places the lower limit to the S_1-state dissociation energy of 2PY·6FB at 1635 cm^{-1}, equivalent to −19.56 kJ mol^{-1}. Taking into account the shift between the electronic origins of 2PY and 2PY·6FB (+88 cm^{-1}) leads to an S_0-state dissociation energy of less than or equal to −20.61 kJ mol^{-1}. This value is in excellent agreement with the dissociation energy $D_0(S_0) = -20.56$ kJ mol^{-1} calculated for 2PY·6FB (Table 1).

Table 1: Calculated ground-state binding energies $D_e(S_0)$ and dissociation energies $D_0(S_0)$ [kJ mol^{-1}] of the hydrogen-bonded and π-stacked isomers of 2PY·*n*FB ($n=1$–6).

Complex	Isomer	D_e [Eq. (1)]	D_e [Eq. (2)][a]	D_0
2PY·1FB	H-bonded	−27.07[b]	–	−24.81
2PY·2FB	H-bonded	−27.95[b]	–	−25.65
2PY·3FB	H-bonded	−26.61[b]	–	−24.52
2PY·4FB	H-bonded	−27.85	−28.66	−24.18
2PY·5FB	H-bonded	−28.20	−29.04	−24.70
2PY·6FB	H-bonded	−9.71[b]	–	–
2PY·4FB	π-stacked	−22.86	−25.69	−20.32
2PY·5FB	π-stacked	−25.66	−28.73	−23.23
2PY·6FB	π-stacked	−24.36	−24.48	−20.56

[a] See the Supporting Information. [b] RI-MP2 complete basis-set extrapolation, according to reference [21].

In summary, we have shown experimentally that the nucleobase analogue 2-pyridone forms only H-bonded dimers with 1,2,4,5-tetrafluorobenzene and pentafluorobenzene, as have been previously observed and calculated for the 2PY·*n*FB complexes with $n=1$–3.[20,21] While both the H-bonded and π-stacked isomers of 2PY·4FB and 2PY·5FB are

calculated to be stable, the H-bonded forms are predicted to be more strongly bound by 4.99 and 2.54 kJ mol^{-1}, respectively. In contrast, 2PY·6FB is only observed in its π-stacked form. The experimental lower limit to the ground-state dissociation energy is −20.61 kJ mol^{-1}, in excellent agreement with the calculated binding energy of −20.56 kJ mol^{-1} for the π-stacked form.

Both experiment and theory show that π stacking is not the dominant binary intermolecular interaction of polyfluorinated benzenes with the model nucleobase 2-pyridone. As long as C–H···O=C hydrogen bonds can be formed, the H-bonding mode is always utilized. In 2PY·6FB, however, only very weak N–H···F and C–H···F H-bonds can be formed. Thus, hexafluorobenzene does not form a face-to-face dimer because of its especially strong π-stacking interaction, but because the alternative H-bonded form is so unfavorable. Further investigations addressing the π stacking of polyfluorobenzenes onto H-bonded nucleobase dimers are in progress.

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