Polyaniline Doping by α,α-Difluoro-β-amino Acids

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Supporting Information

ABSTRACT: Currently, polyaniline (PANI) is considered as a promising polymer that can be used in biosensors, drug delivery systems, bioelectronics, etc. Its biocompatibility can be strongly improved by using dopants with biofunctionality. This study reveals the protonation/doping of PANI by fluorinated analogs of natural amino acids, namely, α,α-difluoro-β-amino acids (DFAAs) with alkyl and aromatic tails in N-methylpyrrolidone solutions. We find that these acids can dope PANI due to both the weakened basicity of their amino groups because of two fluorine atoms in α,α-positions and specific intermolecular interactions (π−π stacking, alkyl−π, F−π) of their tails with units of PANI chains. These interactions did not give the doped PANI salts with high conductivity but led to formation of stable PANI-DFAA complexes, which were confirmed both by clear changes in the UV–Vis and Fourier transform infrared spectra of the protonated/doped PANI and by their conductivity of ~10^-6 S/cm. Our results suggest an applicability of such PANI complexes as carriers of DFAA for their biomedical applications.

1. INTRODUCTION

Although biomedical applications of polyaniline (PANI) are still in the shadow of other well-known high-tech ones (e.g., ref 3), currently, we can see a significant growth of publications on this important issue of PANI-based materials (e.g., ref 4). This increase in interest appeared not only due to an encouraging set of PANI properties, namely, conductivity, electrochemical activity, sensing and biosensing abilities, near-IR absorption, ion-exchange capacity, high environmental stability and low cost, etc., but also due to recently confirmed biocompatibility. The last PANI feature was first suggested to have a good bio/histocompatibility with the rat tissue in vivo. But recently, it has been shown that extracts of PANI base and its conducting (doped) salt PANI-HCl have excellent biocompatibility. Nevertheless, even the simple PANI purification via deprotonation/reprotonation cycle allowed significant reduction in cytotoxicity. This fact, in turn, evidenced a responsibility of low-molecular-weight impurities/by-products rather than PANI for the observed cytotoxicity. The finding agrees well with the fact that the toxicity effect of lowered concentration of nanodiamond-PANI nanocomposite was shown to be negligible. Therefore, one can consider the redoping approach as a suitable method for preparation of biocompatible conducting PANI. It is obvious that this approach can be enhanced when using biologically active substances with acidic functionalities as dopants. However, typically, these substances are weak acids and, at quite high concentrations of >0.5 M (e.g., tartaric acids) or even ≥5 M (e.g., pyroglaualic acid), are unable to completely dope the dedoped PANI dissolved in N-methylpyrrolidone (NMP), DMF, or DMSO. Moreover, the optically active aminosulfonic acid containing simultaneously acidic and amino functional groups appeared to be unable to dope emeraldine base (EB) dissolved in NMP or DMF that was presumably explained by formation of the zwitterion. Remarkably, however, while the impossibility of doping of weakly basic EB by the zwitterionic form of phenylalanine was emphasized, it was found that the film of chiral dedoped (after either (S)-(−)-camphorsulfonic acid or (R)-(−)-camphorsulfonic acid) PANI upon exposure to l-phenylalanine (or d-phenylalanine) solution for 3 weeks showed in circular dichroism (CD) spectra a new peak revealing an interaction of both participants unlike the case of the enantiomer with the opposite chirality (d-phenylalanine or l-phenylalanine, respectively). On the other hand, the absence of the interaction in the opposite case suggests that peaks induced by the respective enantiomer in the CD spectra appeared probably not due to a specific protonation/doping in the system but mainly to conformationally facilitated geometrical docking of the l-phenylalanine (or d-phenylalanine) to the chiral dedoped PANI.

At the same time, the existence of amino acids in zwitterionic form cannot be the main reason of their inability to dope EB as the protonated amino group contains quite...
labile H⁺ ion and loses it (becomes deprotonated) at pH higher than the isoelectric point of the amino acid. This lability of the zwitterionic H⁺ means that it can be taken by substances, which are stronger bases than amino group in the amino acid. However, the NH₂ group in amino acids (typical pKₐ values are roughly in the range of 9–11) is much more basic than imine and amine groups of EB (pKₐ values are 5.5 and 2.5, respectively), and therefore, these groups are unable to withdraw zwitterionic H⁺ only due to stronger donor–acceptor bonding. Taking into account this aspect, we suggest considering EB doping by amino acids, which contain amino groups with basicity weakened due to introduction of electron-withdrawing substituents in the molecule. To our best knowledge, our work is the first attempt to realize this possibility by using fluorinated β-amino acids, namely, α,α-difluoro-β-amino acids (DFAAs) as dopants. Although these amino acids are unnatural, they are not only biocompatible but can be applied and even already applied in biological research and in some synthetic pharmaceuticals due to enhanced biological interactions, increased proteolytic and thermal stability, and biophysical attributes. Hopefully, these applications can improve not only therapeutic properties through introduction of electron-withdrawing fluorine containing substituents in the molecule but biocompatibility of polyaniline also.

2. EXPERIMENTAL SECTION

2.1. Materials. NMP (Aldrich) was of UV−Vis spectroscopy grade and used as received. In the doping experiments, we used PANI in the EB state (PANI-POL).

DFAAs (Table 2) were synthesized in accordance with the protocol described elsewhere. The short description of this protocol is given in the Supporting Information also.

2.2. PANI Doping with the Fluorinated Amino Acids. This process was realized in 0.0125% (w/v) (~0.0014 M) solutions of EB in NMP upon slow addition of different quantities of DFAA powder under constant stirring at ambient conditions to get 0.005, 0.01, and 0.02 M concentrations of the acids. In particular, we used both the stoichiometric molar ratio of the EB/DFAA = 1:0.5 and higher ones: 1:3.6, 1:7.2, and 1:14.4. The concentrations were doubled on the basis of the UV−Vis monitoring as follows. Once the interaction at the first molar ratio (e.g., 1:3.6 molar ratio, 0.005 M concentration of DFAA) slowed down, the next double portion of the DFAA was added to this solution to get a 1:7.2 molar ratio (0.01 M concentration of DFAA). The same procedure was repeated for the next doubled molar ratio 1:14.4 (0.02 M concentration of DFAA). This means that the last UV−Vis spectrum of the joint solution with the previous molar ratio of the EB/DFAA was followed by the first UV−Vis spectrum of the joint solution with the next molar ratio and doubled DFAA concentration.

To check the possibility of PANI doping by DFAA in a water medium, EB films were prepared by casting of 2% (w/v) EB solution in NMP on quartz plates (0.8 cm × 3 cm) followed by their drying in ambient conditions for 7 days to a solid state and then for 1 day in dynamic vacuum at 60 °C to a constant weight. The dried film on the plate was then placed in a 1 cm quartz cuvette filled with 0.01 M solution of the DFAA (on the example of DFAA2) for subsequent monitoring of the EB state by UV−Vis spectroscopy.

2.3. Characterization. pKₐ values of the synthesized DFAAs and their unsubstituted counterparts were calculated with the help of the Calculator Plugin within the Marvin software package (Table 1). Interactions of these acids with EB in joint solutions in NMP, placed in a 1 cm quartz cuvette, were monitored by UV−Vis spectrophotometer Specord M40 for up to 17 days. Similarly, we studied a possibility of interaction of EB films on quartz plate with water solutions of the acids in a 1 cm quartz cuvette.

The samples of PANIs doped with a stoichiometric molar ratio of the EB unit/acid = 1:0.5 by the aromatic DFAAs, which demonstrated the strongest interaction with EB (DFAA2, DFAA3, and DFAA4), were separated from their solutions as follows. At first stage, the solutions were concentrated while blowing an argon stream. These concentrated solutions were cast on glass plates and dried at ambient conditions and then at 60 °C until constant weight was achieved. The formed doped PANIs films were scraped off the glass plates and ground in an agate mortar to a fine powdery state. These powders were used for conductivity and Fourier transform infrared (FTIR) spectroscopy measurements. In particular, there were prepared small pellets of the pure doped PANIs to measure their DC conductivity by standard two-probe technique. This simple technique was used as the conductivities of these doped PANIs were quite low (see Section 3.3). The powders were also used to prepare their pellets with KBr for FTIR measurements (Bruker Vertex 70 spectrometer).

3. RESULTS

The calculated pKₐ values of carboxylic and amine groups of all the synthesized DFAAs reveal their stronger acidic and weaker basic properties compared to their unsubstituted counterparts (Table 1). This effect is predictable and appears due to the high electronegativity of fluorine. Nevertheless, the pKₐ values are still too high compared to those of imino and

| No. | α,ω-Difluoro-β-amino acids | α,ω-difluorinated amino acids | Non-α,ω-difluorinated analogs |
|-----|-----------------------------|-------------------------------|-------------------------------|
| 1   | α,ω-Difluoro-2,2-difluorocarboxylic acid (DFAA1) | -CO₂H, pKₐ = 2.87 | -NH₂, pKₐ = 7.99 | -CO₂H, pKₐ = 4.49 | -NH₂, pKₐ = 10.55 |
| 2   | α,ω-Difluoro-2,2-difluoro-3-phenoxy/propanoic acid (DFAA2) | 2.56 | 7.3 | 4.03 | 9.65 |
| 3   | α,ω-Difluoro-2,2-difluoro-3,4-fluoro phenyl/propanoic acid (DFAA3) | 2.06 | 7.25 | 3.43 | 9.58 |
| 4   | α,ω-Difluoro-2,2-difluoro-3-(4-trifluoro methyl) phenyl/propanoic acid (DFAA4) | 1.88 | 7.26 | 3.43 | 9.6 |
amino groups of PANI (5.5 and 2.5, respectively\textsuperscript{18}). Obviously, this means that the amino groups of DFAAs are very strong bases and dedoped PANI (EB) is unable to take off protons from their zwitterions. Therefore, at first view, PANI cannot be doped in their solutions. Indeed, we could not register the PANI doping in the amino acid solutions in NMP at the stoichiometric molar ratio of EB/DFAA = 1:0.5 or even at 2–3-fold surplus of the amino acids for a long time (up to 1 month). Nevertheless, at lower ratios (3.6–14.4-fold surplus of the amino acids), the PANI doping became possible even in the case of DFAA1 having the most weak base and acid functionalities with highest pK\textsubscript{a} among the synthesized DFAAs (Table 1).

3.1. PANI Doping with the Aliphatic Fluorinated Amino Acid. As one can see in Figure 1a, there are an almost negligible decrease in the exciton band of EB at 641 nm and an increase of absorption in the near-infrared region (above \textasciitilde 750 nm) of the UV–Vis spectra scanned for 23 h in the joint solution of EB and DFAA1 at the 1:3.6 molar ratio. Nevertheless, even these very weak changes reveal some interaction of EB with DFAA1.

A double increase of the amino acid concentration (EB/DFAA1 = 1:7.2 molar ratio) causes a small enhancement of changes in both the exciton band height and near-infrared absorption as well as a small red shift (\textasciitilde 2 nm) of the band maximum for 24 h (Figure 1b and Table 2). Moreover, at around 710 nm, a quite clear isosbestic point appears, which indicates the EB direct protonation by DFAA1.\textsuperscript{25} As expected, these changes were enhanced at another doubled DFAA1 concentration (molar ratio of EB/DFAA1 = 1:14.4) that led to the stronger red shift (\textasciitilde 5 nm) for 6 h (Figure 1c). Moreover, prolongation of the interaction time up to 1–2 weeks caused strong changes in the joint EB and DFAA1 solution. In particular, the exciton band significantly dropped and shifted to \textasciitilde 700 nm at the 15th day with simultaneous appearance of shoulder at \textasciitilde 780 nm (Figure 1c). These changes are accompanied with some dropping of the band intensity probably due to formation of a small quantity of an insoluble phase that, in total, confirms PANI doping with DFAA1.

3.2. PANI Doping with the Aromatic Fluorinated Amino Acids. Replacement of the alkyl (octyl) tail in DFAA1 by the unsubstituted phenyl one in DFAA2 led to a quite dramatic decrease in pK\textsubscript{a1} and pK\textsubscript{a2} of these amino acids (Table 1). This change indicates a significant enhancement of the acidity and weakening of the basicity of the carboxyl and amino groups, respectively, under the effect of the aromatic substituent. Moreover, introducing additional electronegative substituents (with different inductive and mesomeric effects) in the para position of the benzene ring of the amino acids caused the further acidity enhancement from pK\textsubscript{a1} = 2.56 (DFAA2) to pK\textsubscript{a1} = 1.88 (DFAA4), while the basicities of the amino groups were almost the same. Nevertheless, despite these strong changes in acid–base properties of the acids and increase in their acidity in the series of DFAA2 < DFAA3 < DFAA4 at their lowest concentration of 0.005 M (i.e., at EB/DFAA = 1:3.6 molar ratio), a red shift of the maximum of the EB exciton band is not observed (Table 2). At the same time, as in the above case of the aliphatic DFAA1, one can see a very small decrease of this band and a weak increase of absorption in the near-infrared region of the in situ UV–Vis spectra of the solutions of EB and the aromatic DFAAs monitored during the first day (Table 2 and Figures 2a–5a).

A clear difference in the doping ability of all the synthesized DFAAs appeared at their higher concentrations or long-term interactions (a few days) (Table 2 and Figures 1–5).

Thus, even the weakest aromatic amino acid DFAA2 with an unsubstituted benzene ring at 0.01 M concentration (EB/DFAA2 = 1:7.2 molar ratio) shows much faster interaction with EB compared to the aliphatic one DFAA1 (compare Figures 1b and 2b; see Table 2). Furthermore, the isosbestic point in the DFAA2 case red-shifted to \textasciitilde 730 nm, which indicated probably an involvement of additional interactions of...
PANI with this acid. Moreover, the interaction is so fast that, for 1440 min, one can see a quite strong shift to 668 nm and decrease in the exciton band maximum compared with the first (3 min) UV–Vis spectrum registered just after the addition of the next DFAA2 portion to the solution (Figure 2b and Table 2). The rate and degree of the PANI doping (position of the exciton band maximum) increased at the next doubled DFAA2 concentration of 0.02 M (EB/DFAA2 = 1:14.4 molar ratio) that was accompanied also by a quite strong red shift of the exciton band maximum up to 714 nm at 1440 min of the interaction (Figures 2c and 3 and Table 2).

Interestingly, unlike the aliphatic amino acid DFAA1, the interaction of the unsubstituted aromatic amino acid DFAA2 with EB was practically completed at the first day (1440 min) and resulted in the exciton band position at 714 nm, which did not change even for 10 days (14,400 min) (Figure 3). As in the former case, these spectral features were accompanied with some dropping of the band intensity probably due to formation of a small quantity of an insoluble phase of PANI doped by DFAA2.

The substitution in the para position of the benzene ring of DFAA by electron-withdrawing substituents such as fluorine atom (DFAA3) and especially as the trifluoromethyl group (DFAA4) dramatically enhances interaction of these amino acids with EB (Figures 3–5).

In particular, at the highest DFAA3 and DFAA4 concentration (0.02 M), the interaction with EB becomes saturated at the fifth day with the final positions of the exciton band at 731 and 754 nm, respectively (Table 2 and Figure 3). This result indicates that, in both cases, the interaction runs slower but deeper with the higher EB exciton band red shifts than in the case of DFAA2. Moreover, a degree of this interaction increases with increasing electronegativity of the p-substituent (i.e., from F to CF3) in the benzene ring. However, at lower concentrations of 0.005 and 0.01 M, the rate of the acid dopant interaction with EB is lower in the case DFAA4 compared with DFAA2 and DFAA3. Thus, at these concentrations, one can observe mainly a quite strong decrease in the exciton band maximum practically without its red shift during the first day of the interaction of DFAA4 with EB (Table 2 and Figure 5a,b).

In general, the UV–Vis spectral measurements testify to some dissimilarity in the doping behavior of the aliphatic and aromatic fluorinated amino acids as well as to a delayed interaction of the former with the dissolved EB compared with the latter (see slopes of kinetic profiles of the interactions at the highest DFAA concentration in Figure 3). Considering the same functionalities of these DFAA and differences in their hydrocarbon tails, one may assume that both similarity and dissimilarity in their behavior can be associated with specific interactions of these tails with EB macromolecules and NMP molecules. It should be emphasized here that this assumption ignores a gradual increase in their acidity and a decrease in basicity from aliphatic amino acid DFAA1 to aromatic amino acids DFAAs (Table 1). But we take into account, in this case, the critically important fact that the amino group of these acids is still much a stronger base than imino and amino groups of EB (Table 1 and above discussion) and, therefore, inevitably binds the carboxylic group hydrogen with formation of the zwitterion.

### 3.3. Properties of the PANI Doped with the Aromatic Fluorinated Amino Acids

The above UV–Vis spectroscopy evidences of the binding affinity of PANI for DFAA are strongly supported with studies of FTIR spectra and conductivity of the formed PANI salts/complexes. In particular, we confirmed the PANI doping phenomenon on the example of the PANIs doped by the aromatic amino acids DFAA2–DFAA4 with the stoichiometric molar ratio of the EB unit to the DFAA (1:0.5)5. These amino acids manifested the most significant changes in their above-discussed UV–Vis spectra (see Figures 2, 4, and 5). As one can see in Figure 6 and Table 3, albeit most bands of the EB and the amino acids overlap due to differences in the acids’ FTIR spectra and their inputs in the spectra of the doped PANIs, a few changes in positions and shapes of some characteristic PANI bands can be revealed.

In particular, there is the band overlapping of asymmetrical (asym) NH3+ deformation vibration and asym COO− stretching vibration of the amino acids with quinonoid ring stretching vibration of the pristine EB (in the range of about 1550–1600 cm−1). Nevertheless, their changes are clearly identified in the doped PANIs despite the presence of the wide band of C=O stretching vibration in NMP at 1665(6) cm−1 (Figure 6 and Figure S1). Thus, one can see in all cases a blue shift of the asym NH3+ vibration (Table 3) that suggests at least a partial transfer of protons from the protonated amino groups of the amino acids to PANI imine sites. This suggestion is supported with the red shift of the quinonoid ring stretching vibrations typical of PANI doping29–31 (from 1583 to 1573/1572/1562 cm−1 in cases of DFAA2/DFAA3/DFAA4, respectively; Table 3). These new positions of quinonoid ring stretching vibrations are quite close to asym COO− stretching vibrations of the amino acids (1569/1570/1578 cm−1; Table 3). At first view, we cannot resolve these vibrations especially for asym COO− stretching vibrations of DFAA2 and DFAA3 (Figure 6a,b), which are located at a little lower wavenumbers (1569/1570 cm−1) than those of the PANI-DFAA2 and PANI-DFAA3 salts (1573/1572 cm−1). At the same time, the symmetrical (sym) COO− stretching vibrations of the amino acids shifted after their interaction with

### Table 2. Exciton Band Positions of EB in Solutions of DFAA

| acid, tail           | exciton band position at 360 min, nm | exciton band position at 1440 min (24 h), nm | exciton band position for long-term interactions, nm |
|----------------------|-------------------------------------|-----------------------------------------------|------------------------------------------------------|
| DFAA1 octyl          | 641/641/641                         | 641/643/646                                   | n/a/662/668 (7 days), 683/714 (10 days), 698/714 (15 days) |
| DFAA2 phenyl         | 661/683                             | 641/686/714                                   | n/a/648/714 (3 days), n/a/714 (10 days)               |
| DFAA3 p-F-phenyl     | 641/691                             | 643/676/691                                   | n/a/691 (8–11 days), n/a/723 (5–13 days)              |
| DFAA4 p-CF3-phenyl   | 644/690                             | 643/684/698                                   | n/a/758 (3–5 days)                                    |

*The band initial position is ca. 640 nm. n/a, not applicable.
PANI to lower wavenumbers (from 1416/1415/1416 to 1414/1410/1406 cm$^{-1}$) (Table 3). Comparison of this red shift of the sym COO$^-$ stretching vibrations with positions of the asym COO$^-$ stretching vibrations allows us to assume that bands at 1573/1572/1562 cm$^{-1}$ may be assigned to the new positions of quinonoid ring stretching vibrations in the doped PANIs. This assignment agrees well with a red shift of the C$-$N stretching vibrations from 1304 to 1299/1301/1303 cm$^{-1}$ in aromatic amine structures (Table 3) typical of PANI protonation (doping).29

Unexpectedly, unlike the quinonoid ring stretching vibrations, the benzenoid ring stretching vibrations of the parent EB blue-shifted from 1495 to 1502/1509/1504 cm$^{-1}$ (Table 3, Figure 6, and Figure S1) after its interaction with these DFAAs. This phenomenon both differs from the typical doping behavior of PANI$^{7,29}$ and confirms the above-described specificity of interaction of the fluorinated amino acids with EB.

The specificity of this interaction is also confirmed by the quite low conductivity of the PANI doped with these acids (Table 4), which is, however, much higher than that of the parent EB ($\sim$10$^{-10}$ S/cm).

Interestingly, in the case of DFAA2 with an unsubstituted benzene ring, the conductivity value is around by 2.5–3.6 times higher than in the DFAA3 and DFAA4 cases. This fact agrees with the highest red shift (to 1299 cm$^{-1}$, Table 3) of C$-$N stretching vibration in protonated secondary aromatic amine structures of PANI-DFAA2. The differences in the red shifts of C$-$N stretching vibrations and in the conductivity values of the doped PANIs (Table 4), although small, are opposite and, therefore, contradict to the more significant doping degree in the DFAA3 and DFAA4 cases (Figures 2−5).

Such a contradiction probably can be explained by the fact that conductivity of the doped PANI in the solid state depends not only on the doping degree but also on packing of the charged PANI macromolecules, which is affected, in turn, by space orientation and plasticization ability of the dopant anions.

Judging by small changes of optical band gaps of the PANI-DFAA complexes (Table 4), which decrease in the series

\[ \text{EB} > \text{PANI} − \text{DFAA1} > \text{PANI} − \text{DFAA2} > \text{PANI} − \text{DFAA3} > \text{PANI} − \text{DFAA4} \] (1)

the packing factor is not important in their diluted solutions. This series, unlike the conductivity changes in these complexes, matches with changes in the exciton band position of the PANI (EB) under the interaction with DFAAs (Figure 3) and, therefore, confirms enhancement of this interaction the from DFAA1 case to DFAA4 one.

Figure 2. In situ UV−Vis spectra of the joint solutions of 0.0125 wt % (≈0.0014 M) EB and different concentrations of DFAA2 monitored during up to 10 days: (a) 0.005 M DFAA2 (EB/DFAA1 = 1:3.6 molar ratio); (b) 0.01 M DFAA2 (EB/DFAA2 = 1:7.2 molar ratio); (c) 0.02 M DFAA2 (EB/DFAA2 = 1:14.4 molar ratio).

Figure 3. Kinetic profiles of changes of the PANI exciton band position upon interaction with DFAA (at their highest concentration of 0.02 M; EB/DFAA = 1:14.4 molar ratio).
4. DISCUSSION

The above results clearly reveal the interaction/protonation/doping of EB with the synthesized DFAAs in the joint solutions in NMP. Nevertheless, taking into account much lower basicity of imino and amino groups of EB (pKₐ = 5.5 and 2.5, respectively) compared with that of amino groups of DFAAs (pK₂ approximately in the range of 7.25−7.99, Table 1), it is difficult to understand the existence of this interaction unless additional facilitating factors are considered. In particular, the most important factor here is probably a competition of imine nitrogen atoms of EB, amino groups of the acid(s), and carbonyl groups of NMP molecules for carboxylic hydrogens of these amino acids. Naturally, there are also other important additional physicochemical factors

Figure 4. In situ UV−Vis spectra of the joint solutions of 0.0125 wt % (~0.0014 M) EB and different concentrations of DFAA3: (a) 0.005 M DFAA3 (EB/DFAA3 = 1:3.6 molar ratio); (b) 0.01 M DFAA3 (EB/DFAA3 = 1:7.2 molar ratio); (c) 0.02 M DFAA3 (EB/DFAA3 = 1:14.4 molar ratio).

Figure 5. In situ UV−Vis spectra of the solutions of 0.0125 wt % (~0.0014 M) EB with different concentrations of DFAA4 monitored during 24 h: (a) 0.005 M DFAA4 (EB/DFAA4 = 1:3.6 molar ratio); (b) 0.01 M DFAA4 (EB/DFAA4 = 1:7.2); (c) 0.02 M DFAA4 (EB/DFAA4 = 1:14.4).
affecting the participants. Specifically, this competition begins only after addition of the acid in the EB solution, where EB macromolecules have already been involved in hydrogen bonding with carbonyl groups of NMP molecules through mutual hydrogen bonds and obviously are both in coiled and agglomerated conformations. The addition of the fluorinated amino acid inevitably changes the physicochemical situation in this solution due to the following factors: (1) an involvement of NMP molecules both from the solution bulk and from the solvation shells of the EB macromolecules into formation of the solvation shells of the amino acid molecules (or their zwitterions) (Figure 7). This change, in turn, is accompanied with a partial weakening of the proton interaction with the amino group of the zwitterion due to its involvement in hydrogen bonding with the carbonyl group of the NMP molecule.

This important input of NMP in the PANI doping by DFAAs in the NMP solutions is strongly supported by the fact that we have found no changes in the UV−Vis spectrum of EB film placed in 0.01 M water solution of DFAA2 for a long time (up to 17 days, Figure S2). (2) The factor (1) facilitates protonation of imine nitrogen atoms in the PANI macromolecules by the amino acid (or more probably by its zwitterion) that is accompanied with both an appearance of positive charges on their chains and a transition from their quite compact coil conformation to a more expanded one.

These changes are accompanied by red shifts of the exciton band and appearance of absorption in the near-infrared range of the UV−Vis spectra of the joint EB-DFAA solutions (Figures 1−5). (3) Specific interactions of DFAAs occur both with EB and NMP molecules not only due to the protonating and hydrogen bonding abilities of carboxylic and amino groups and fluorine but also due to other noncovalent interactions involving fluorine atoms and aliphatic or aromatic tails of DFAAs with benzenoid/quinonoid units of EB. In particular, the fluorine atoms both near the amino group (all DFAAs) and in the aromatic tails (DFAA3 and DFAA4) can be involved in interactions with NH groups of the PANI chains as well as in F−π interactions with electron-deficient quinonoid rings similarly to interactions with electron-poor aromatic surfaces. The enhancement of the PANI doping by the aromatic DFAAs compared with the aliphatic DFAA1 in the course of long-term interactions can be better understood if we postulate noncovalent π−π stacking interactions of the aromatic tails of the amino acid molecules with benzenoid rings or quinonoid rings tied with protonated imine nitrogen atoms of the same EB macromolecule.

Naturally, all these changes in the solution after addition of the amino acid need some time to be completed, which obviously depends on its structure. This suggestion agrees with a more effective long-term interaction of the aromatic DFAAs with EB compared to the aliphatic DFAA1 case (Figure 3 and Table 2). In particular, for the aromatic DFAAs, we finally observed both the stronger red shift (up to 758 nm for 5 days) and the more significant decrease in the exciton band as well as the higher growth of the absorption in the near-infrared part of the spectrum (Figures 2c, 3, and 4c−5c and Table 2). For the aliphatic DFAA1, the shift was much smaller (up to 683 nm for 10 days, Figures 1c and 3 and Table 2). The same interactions with neighboring EB macromolecules should be taken into account also.

Despite a small binding energy in the PANI-DFAA complexes due to the mutual interaction sites, the residence time of the amino acids near the imine nitrogen atoms increases that facilitates the PANI protonation process. The probability of these interactions increases in the case of high amino acid concentrations, which are supported with the registered spectral changes in the joint solutions with increasing DFAA concentrations from 0.005 to 0.02 M.

If the π−π stacking interaction postulate is correct, then the PANI protonation behavior should depend also on electron density on the DFAA aromatic tail, differing only by substituents in the p-position of the benzene ring (Table 1).
is additionally decreased by two
is observed for DFAA4 having the most electron de
spectra of the PANI-DFAA complexes in Figures 1, 2, 4, and 5.

signi
in the case of the p-substituent F (DFAA3) causing the
electron-withdrawing ability. The shift is much more moderate
decreases again when transition to the unsubstituted aromatic

It should be emphasized here, however, that despite this

Table 4. Conductivity of the Pellets of the PANI Doped by
the Aromatic DFAAs

| no. | PANI   | conductivity (S/cm) | optical band gap* (eV) |
|-----|--------|---------------------|------------------------|
| 1   | EB     | ~10^-10             | 3.13                   |
|     | PANI-DFAA1 | n/a                  | 3.09                   |
| 2   | PANI-DFAA2 | 2.35 × 10^-6         | 3.08 (3.082)          |
| 3   | PANI-DFAA3 | 0.92 × 10^-6         | 3.08 (3.076)          |
| 4   | PANI-DFAA4 | 0.65 × 10^-6         | 3.06                   |

*Estimated by the π−π* absorption band edge in final UV−Vis spectra of the PANI-DFAA complexes in Figures 1, 2, 4, and 5.

It should be emphasized here, however, that despite this important p-substituent effect, the electron density on the tail is additionally decreased by two fluorine atoms in the α,α'-position to the carboxylic group of aromatic DFAA.

Let us consider, for example, the highest acid concentration of 0.02 M causing the most significant shifts in the PANI spectra during long-term interactions (Figures 2–5 and Table 2). In that case, the doping acids (including DFAA1) can be arranged in the next series, which is based on the final position of the exciton band of the doped PANI

DFAA4(758 nm) > DFAA3(723 nm) > DFAA2(714 nm)

> DFAA1(683 nm)  \hspace{1cm} (2)

As one can see, the most significant shift of the exciton band is observed for DFAA4 having the most electron deficient aromatic ring due to p-substituent CF3 with a very strong electron-withdrawing ability. The shift is much more moderate in the case of the p-substituent F (DFAA3) causing the significantly less electron deficient aromatic ring. This shift decreases again when transition to the unsubstituted aromatic tail (DFAA2) having only a weak electron deficiency induced by two α,α'-fluorine atoms separated from benzene ring by two σ-bonds (see structure of DFAA2 in Table 1). Finally, the shift is the lowest one in the case of aliphatic DFAA1.

The strong difference in the doping ability between the aromatic and aliphatic DFAAs is revealed also by various positions of the isosbestic point on the right side of the exciton band in the UV−Vis spectra (Figures 1, 2, 4, and 5). In particular, the amino acids with benzene rings have this isosbestic point at around 730 nm, while DFAA1 with the alkyl tail has it at around 710 nm. These differences can be probably assigned to specific doping states of PANI, which, in accordance with the above postulate, stem from various interactions of DFAA with PANI. Indeed, if π−π stacking interactions of the benzene rings of PANI are more probable with electron-deficient tails of DFAA2, DFAA3, and DFAA4 (Figure 8a), then the more electronegative p-substituent is in the benzene ring, the stronger is the red shift of the exciton band. The shift is probably further strengthened by F−π interactions (Figure 8a). This suggestion is supported with positions of these amino acids in the above series (2). Moreover, even in the case of weaker alkyl−π interactions, the aliphatic DFAA1 tail can also facilitate its immobilization near both the benzenoid rings (Figure 8b) and even electron-deficient quinonoid rings of PANI.42
spectra by two bands at around 430 nm (∼3 eV) and 800 nm (∼1.5 eV). Such behavior strongly differs from the well-known PANI doping by acids, which protonate both imine nitrogen atoms in the EB quinonoid units with formation of dications (bipolarons), followed by their intramolecular redox transformation into radical cations (polarons). At this stage, it is difficult to explain completely the found difference between the case under investigation and the typical ones without theoretical modeling of the PANI doping by DFAA, which deserves a separate study. Nevertheless, on the basis of the highly probable additional interactions of the DFAAs tails with PANI chains (see above discussion), we can consider two possibilities for the beginning. The first one is the immobilization of the charge-compensating anions of the amino acids due to such interactions near the protonated imine nitrogen atoms that hinder their redistribution and, therefore, suppress the internal redox transformation along the charged PANI chains. The next possibility can be a preferential protonation of one imine nitrogen in the quinonoid structures and formation of their cations, while the second one is not protonated probably because of an effect of Coulomb repulsion of protons by the positively charged protonated sites.

5. CONCLUSIONS

The main result of this study consists of the confirmed protonation/doping of PANI by representatives of amino acids, namely, by the α,β-difluoro-β-amino acids (DFAAs) in NMP solutions. We realized this possibility through weakening of the basicity of the DFAA amino groups due to the introduction of the electron-withdrawing substituents. On the basis of the comparison of the UV−Vis spectroscopy data and structures of the synthesized DFAAs and PANIs, we deduce that this protonation/doping process is facilitated by specific interactions (π−π stacking, alkyl−π, F−π) of DFAAs tails with the units of PANI (EB) macromolecules. This process gets saturated for the long time that depends on electron deficiency of the DFAAs tails and ends probably with the protonation of only one imine nitrogen of the quinonoid PANI unit.

Although the interactions of EB and DFAAs are not strong enough to form typical doped PANIs with high conductivity, the formation of PANI-DFAA complexes is confirmed not only by changes in the UV−Vis and FTIR spectra but also by their conductivity with convincing value of ∼10⁻⁶ S/cm. Existence of such complexes opens their applicability as carriers of DFAAs for biomedical applications.

Finally, the observed influence of the aliphatic and electron deficient aromatic tails of DFAAs on the PANI protonation/doping process suggests that similar π−π stacking, alkyl−π, and other kinds of intermolecular interactions can proceed also in the case of typical PANI doping by other organic or even inorganic acids except the simplest ones (e.g., HCl).
ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.9b00207.

Synthesis procedure of DFAA, FTIR spectra of the PANI salts with DFAs with designated peak positions, and UV–Vis spectra of the EB film in 0.01 M water solution of DFAA2 (PDF)

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ADDITIONAL NOTE

It should be emphasized here that we could apply this high ratio despite the above shown fact that, in the used diluted solutions (0.0125 wt % (~0.0014 M), EB could be doped only at much lower ratios (EB unit/amino acid ≲ 1:3.6). The formation of the respective doped PANI salts/complexes at this high ratio became possible probably due to concentration and drying of the joint PANI–amino acid solutions that resulted in the dry salts/complexes.

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