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Amino-acid-functionalized solvatochromic probes

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***N*-(4-nitrophenyl)-L-proline (2) has been obtained by a nucleophilic aromatic substitution reaction of 4-fluoronitrobenzene with L-proline. The corresponding amide derivatives 3–5 have been synthesized by peptide coupling of 2 with different amino acid derivatives and chiral amines. Solvatochromism of the long-wavelength UV/Vis band in the electronic absorption spectra of the compounds 2–5 has been studied and analyzed using the empirical Kamlet–Taft solvent polarity parameters π^* (dipolarity/polarizability), α (hydrogen bond donating ability), and β (hydrogen bond accepting ability). Reasonable Kamlet–Taft solvatochromic correlations ($r > 0.95$) were established for the three amide derivatives 3–5 in a range of common solvents and three room temperature ionic liquids (RTILs). The UV/Vis absorption of the 4-nitroaniline derivative 2 showed a hypsochromic shift with increasing concentration due to intermolecular hydrogen bonded aggregate formation in protic solvents, which is not observed for compounds 3–5.**

Keywords: amino acid; chirality; nucleophilic substitution; chromophores; solvatochromism

INTRODUCTION

The development of specific molecular probes for the recognition of specific binding sites in peptides and proteins is a challenge due to the manifold interaction which can possibly occur in those complex systems.[1–6]

The detection of separate di- or tripeptide sequences in rapid protein scans requires the application of suitable sets of sequence specific UV/Vis sensors. However, the pioneering works of Still[7–17] and other scientists[18–30] have shown that specific peptide sequences can be recognized by artificial receptors, which are based on cage-compounds and related molecular structures. The usage of such a complementary di- or tripeptide sequence, which is suitable to interact specifically with a target peptide sequence, seems a promising concept, because the same principle occurs in nature. However, even the distinct differentiation of the 20 common genetically encoded amino acids by a suitable UV/Vis probe is still not established, because of the chemical similarity of the amino acids due to their ionic nature.[31,32]

The objective of this study is the synthesis of novel UV/Vis probes bearing amino acid sequences linked to the chromophoric π-electron system. The direct linking of amino acid moieties to UV/Vis and fluorescence probes for environment responsive probing is a new field where scientific activities have been started since the last 5 years.[33–38] For preliminary and basic studies we chose 4-nitroaniline derivatives as these have been widely used in materials science (nonlinear optics)[39–43] and analysis (solvatochromism).[44–55] There are a large number of substituted *p*-nitroaniline derivatives, which are used as solvent-sensitive indicators for setting up polarity scales,[44–52] as lipophilic indicators in micelles, bi-layers, and biological membranes.[53–55] In this context, amino acid (L-proline) substituted nitroaniline derivatives are chiral organic compounds suitable as materials for optical second harmonic generation.[56] 4-*N*-proline substituted nitroaniline derivatives have been also used as the guest component in a α- and β-cyclodextrine complex, respectively.[57,58]

The aim of the present work was the synthesis and structural characterization of several amino acid and dipeptide functionalized 4-nitroaniline derivatives **2**–**5** and the investigation of their solvatochromic properties in detail (Scheme 1).

Compound **2** was first synthesized by Yoshino *et al.*,[56] however, no details of the preparation procedure and chemical analysis were reported. The synthesis of **2** was also reported by Lo Meo *et al.*[58] using another synthetic procedure. Major attention was devoted to the study of the complex formation with α- and β-cyclodextrine.[58] At the same time, nitroanilines such as **2** are an interesting object studying the specific solvatochromic effects, in view of the fact that these compounds can form several types of hydrogen bonded complexes. However, interpretation of preliminary solvatochromic investigations of **2** by El-Sayed[59] showed inadequate conclusions.

In this work we wanted to show particularly whether and how the peptide moiety of **3**, **4**, and **5** has an effect on the chromophoric π-electron system as a result of interactions with the surroundings of the molecules. It is to clarify, what proportion of these environment effects are dipole–dipole and/or hydrogen bond or acid–base interactions. To separate the individual solvation effects we used the simplified Kamlet–Taft equation[49,50] [Eqn (1)] from which the coefficients of the individual interaction

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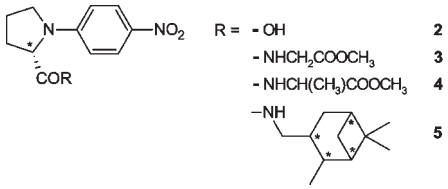
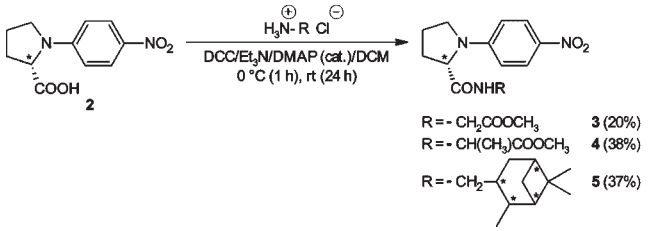


Scheme 1. Compounds **2**–**5** studied in this work



Scheme 3. Reaction scheme for peptide coupling reactions

contributions can be determined using multiple correlation analysis.[44,45]

$$\tilde{\nu}_{max} = \tilde{\nu}_{max,0} + a\alpha + b\beta + s\pi^* \quad (1)$$

where $\tilde{\nu}_{max}$ is the longest wavelength UV/Vis absorption maximum of the compound measured in a particular solvent, $\tilde{\nu}_{max,0}$ is that of a nonpolar reference solvent, α [46] reflects solvent hydrogen bond donor (HBD) ability, β [47] reflects solvent hydrogen bond acceptor (HBA) ability, and π^*[48,49] describes the dipolarity/polarizability of the solvent. *a*, *b*, and *s* are the solvent-independent correlation coefficients, which allow the effects of a particular parameter on the solvatochromic properties of the compound to be determined.

RESULTS AND DISCUSSION

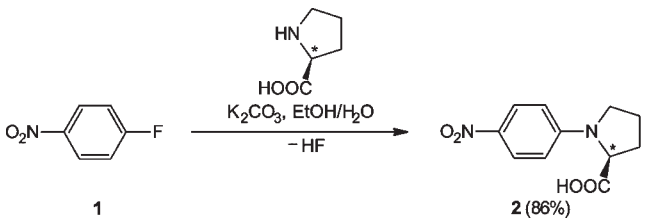
Synthesis

As extension of our studies on solvatochromic compounds[60–71] and to establish the influence of intermolecular hydrogen bonds between crystals in combination with a chiral center on the photophysical properties of these compounds, we prepared *N*-(4-nitrophenyl)-L-proline (**2**) by nucleophilic aromatic substitution in a mixture of EtOH/H_2O (3:1) (Scheme 2). Due to the high reactivity of 1-fluoro-4-nitrobenzene[72] and the cyclic amine[73] L-proline a high yield was obtained with aqueous ethanol[74] as solvent.

Compound **2** can be coupled with other amino acids, dipeptides or oligopeptides via the remaining C-terminus, which allows the extension of the recognition sequence.

Principally, two synthetic strategies can be applied to the synthesis of oligopeptide functionalized UV/Vis probes.

I. The amino-acid-functionalized chromophoric system is synthesized in a first step and then the peptide moiety is coupled using established synthetic procedures to extend peptide sequences (Scheme 3).
II. The whole peptide moiety is linked directly by a chemical reaction to the chemically activated chromophore in one step.



Scheme 2. Reaction scheme for the nucleophilic aromatic substitution of fluoro compound **1** with L-proline

The method of choice was the synthetic strategy I in presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC)/Et_3N/*N*,*N*-dimethylamino pyridine (DMAP)[75,76] to afford the corresponding amides **3**–**5** (Scheme 3).

For the peptide coupling reaction, the hydrochlorides of glycine methyl ester and L-alanine methyl ester have been selected. For this study we also considered a sterically demanding bicyclic amine linked via a peptide bond to the proline carboxylic group to show the influence of twisting of the L-proline ring upon solvation. In regard to the configuration of the amide derivatives it proved to be more difficult than expected. The absolute configurations of the chiral crystals of **2**, **3**, and **4** were determined by X-ray crystal structure analysis using the Flack[77–79] parameter method. X-ray crystal structure analyses reveal that partial racemization was only obtained for compound **4**. In a subsequent paper we will report on the solid state structures.[80]

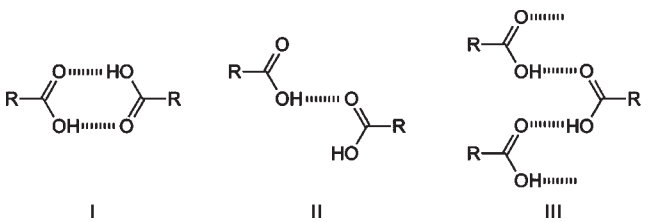
An associated problem derives from the unknown influence of the push–pull π-electron system on the electronic properties of the amino acid or dipeptide linkage. This point plays a role in the interpretation of the results.

Solvent effects on the UV/Vis absorption spectra

For the solvatochromic investigations we used the four nitroaniline derivatives **2**–**5** (Scheme 1). All four chromophores investigated have a push–pull-substituted aromatic π-electron system, which is responsible for the solvatochromic properties.

Due to the high polarity and HBD/HBA capability of the amino-acid-functionalized chromophores, it is likely that association will occur in different solvents and this can have an influence on the UV/Vis absorption maximum. UV/Vis measurements of compound **2** show a significant indication of probe aggregation.[81] It is well-known that carboxylic acids form intermolecular hydrogen bonded aggregates such as I–III (Scheme 4).[82–86] The existence of monomeric, dimeric (I, II) and polymer (III) species depends on acid concentration, temperature and solvent polarity.

At the high concentration range from $c = 0.5 \times 10^{-4}$ to 4.0×10^{-4} M, the long-wavelength UV/Vis absorption maximum



Scheme 4. Intermolecular hydrogen bonded aggregates of carboxylic acids: I cyclic dimer, II linear dimer, III polymer

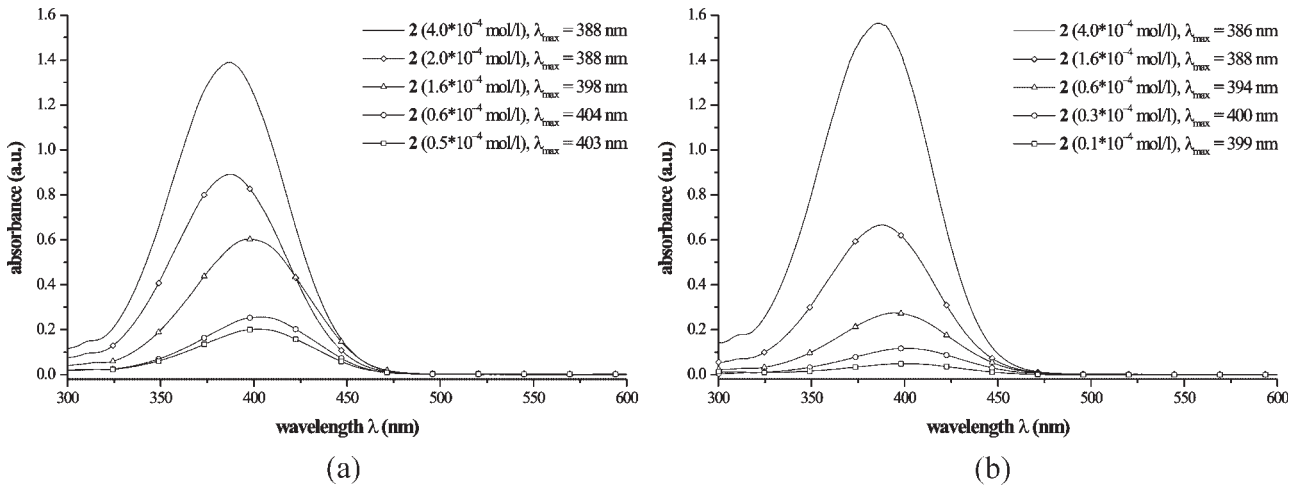


Figure 1. UV/Vis absorption spectra of **2** in ethanol (a) and methanol (b)

of **2** was hypsochromically shifted from $\lambda_{max} = 403$ to 388 nm in ethanol and from $\lambda_{max} = 400$ to 386 nm in methanol, respectively (Fig. 1). Thus, dye aggregation in solution is observed in the concentration interval studied for the solvatochromic measurements.

Furthermore, UV/Vis absorption spectra of compound **2** in ethanol were recorded in a temperature range from 223 to 323 K in 10 K intervals. The UV/Vis absorption maximum is shifted to longer wavelength from 393 to 399 nm with increasing temperature. An isosbestic point was observed at around 419 nm by the temperature changes. Thus, the resulting changes of the UV/Vis spectra observed by the temperature-sensitive measurements in protic solvents are enthalpically controlled.

UV/Vis spectroscopic measurements reveal a concentration dependence of **2** only for protic solvents. It is possible that different types of aggregation of **2** occur in protic and also aprotic solvents. But in the concentration interval studied for UV/Vis measurements a displacement of the UV/Vis absorption band of compound **2** is observed only in protic solvents. However, at this time we are not able to determine which species of **2** is present in aprotic solvents as well as in the investigated concentration range of protic solvents.

Probe **2** was also measured in solvents, in which no change of the UV/Vis absorption was observed with changing the concentration of the probe. UV/Vis absorption spectra of **2** in these selected solvents and additionally in ethanol and methanol (Table 1) have been considered for the solvatochromic linear solvation energy (LSE) correlation analysis. Furthermore, UV/Vis measurements of compounds **3**–**5** show no significant contribution of probe aggregation in protic and nonprotic solvents. Thus, the solvatochromism of **3**–**5** could be investigated in protic solvents, too. Hence, UV/Vis measurements were carried out on compound **2** in 25 and compounds **3**–**5** in 38 and 39, respectively, common solvents of different polarity and hydrogen bond ability at 293 K as shown in Table 1 to determine the coefficients *a*, *b*, and *s* from Eqn (1).

UV/Vis spectra of compound **5** in eight solvents of different polarity are shown in Fig. 2.

Overall, as the solvent polarity increases from cyclohexane to water (compounds **3**, **4**) and formamide (compound **5**), respectively, the UV/Vis absorption spectra of the compounds **3**–**5** show a significant bathochromic shift of the solvatochromic long-wavelength symmetric UV/Vis absorption band. Compound **2**, which has been quantified only in 25 solvents due to the observed probe aggregation in protic solvents, shows also a bathochromic shift with increasing the solvent polarity. These bathochromic shifts are in agreement with an increased delocalization of electron density due to the conjugation of the lone-pair of electrons on the nitrogen atom of substituted proline derivative donors with the aromatic π-electron system and the nitro-group acceptor.

The UV/Vis shifts range from $\lambda = 361$ nm in tetrachloromethane to $\lambda = 403$ nm in hexamethylphosphoramide (**2**), from $\lambda = 354$ nm in tetrachloromethane to $\lambda = 402$ nm in water (**3**), from $\lambda = 355$ nm in tetrachloromethane to $\lambda = 406$ nm in water (**4**), and from $\lambda = 349$ nm in cyclohexane to $\lambda = 405$ nm in formamide (**5**). The extent of the solvatochromic shift of *N*-(4-nitrophenyl)-L-proline (**2**) ($\Delta\tilde{\nu} = 2890\ cm^{-1}$) as function of the solvent polarity is lower than that of the amide derivative **3** ($\Delta\tilde{\nu} = 3370\ cm^{-1}$), **4** ($\Delta\tilde{\nu} = 3540\ cm^{-1}$), and **5** ($\Delta\tilde{\nu} = 3960\ cm^{-1}$).

Furthermore, solvatochromic investigations were performed in room temperature ionic liquids (RTILs). RTILs are salts whose melting point (mp) is $<100\ ^{\circ}C$ and therefore represent a class of solvents with ionic character. These solvents show strong solvating power which is utilized to investigate specific HBA effects caused by the anion of RTILs. Of topical interest is also the investigation of the true polarity of ionic liquids, because this point is controversially discussed in literature.[89,90] Measurements were taken on compounds **2**–**5** in 1-hexyl-3-methylimidazolium [C_6-mim] salts at 293 K as shown in Table 2.

There is a significant influence of the anion of RTIL observed on the shift of the solvatochromic UV/Vis absorption band. As expected, the UV/Vis absorption spectra of these compounds show a bathochromic shift from [C_6-mim][PF_6] to [C_6-mim][Cl] of the solvatochromic long-wavelength symmetric UV/Vis band with increasing ability of the anion of ionic liquids to interact as H-bond acceptor or electron-pair donor (EPD), respectively (Table 2).

LSE correlation analyses

In order to determine the respective contributions of solvent properties on $\tilde{\nu}_{max}$, the simplified form of the Kamlet–Taft linear solvation energy relationship (LSER) was used [Eqn (1)] The

Table 1. UV/Vis absorption maxima of **2** measured in 25 and of **3–5** in 38 and 39, respectively, solvents[a] of different polarity and hydrogen bond ability.

	$\tilde{\nu}_{max} \times 10^{-3}\,cm^{-1}$				Kamlet–Taft parameters		
Solvent	(**2**)	(**3**)	(**4**)	(**5**)	α	β	π^*
Cyclohexane	[b]	[b]	[b]	28.65	0.00	0.00	0.00
n-Hexane	[b]	[b]	[b]	28.33	0.00	0.00	−0.04
Triethylamine	26.60	27.55	27.47	27.78	0.00	0.71	0.14
Tetrachloromethane	27.70	28.25	28.17	28.17	0.00	0.10	0.28
p-Xylene	27.03	27.40	27.32	27.40	0.00	0.12	0.43
o-Xylene[a]	27.03	27.17	27.25	27.17	0.00	0.12	0.51
Toluene	26.81	27.25	27.17	27.25	0.00	0.11	0.54
Benzene	26.81	27.17	27.17	27.17	0.00	0.10	0.59
Diethyl ether	27.10	27.47	27.32	27.40	0.00	0.47	0.27
1,4-Dioxane	26.53	26.81	26.81	26.74	0.00	0.37	0.55
Anisole	25.97	26.60	26.53	26.53	0.00	0.32	0.73
Tetrahydrofurane	26.04	26.46	26.32	26.32	0.00	0.55	0.58
Ethyl acetate	26.32	26.67	26.46	26.60	0.00	0.45	0.55
1,2-Dimethoxyethane	26.11	26.39	26.25	26.18	0.00	0.41	0.53
Chloroform	26.18	26.95	26.95	26.88	0.20	0.10	0.58
1,1,2,2-Tetrachloroethane	25.71	26.32	26.18	26.11	0.00	0.00	0.95
Pyridine	25.13	25.51	25.45	25.45	0.00	0.64	0.87
Dichloromethane	26.11	26.63	26.60	26.53	0.13	0.10	0.82
Hexamethylphosphoramide	24.81	25.19	25.06	25.06	0.00	1.05	0.87
Tetramethylurea	25.45	25.25	25.19	25.25	0.00	0.80	0.83
1,2-Dichloroethane	25.97	26.63	26.46	26.32	0.00	0.10	0.81
Benzonitrile	25.45	25.71	25.64	25.58	0.00	0.37	0.90
Acetone	25.77	25.84	25.84	25.77	0.08	0.43	0.71
N,*N*-dimethylacetamide	[c]	25.32	25.25	25.25	0.00	0.76	0.88
N,*N*-dimethylformamide	[c]	25.25	25.25	25.13	0.00	0.69	0.88
4-Butyrolactone	[c]	25.38	25.32	25.25	0.00	0.49	0.87
Dimethyl sulfoxide	[c]	24.94	24.81	24.75	0.00	0.76	1.00
Acetonitrile	25.77	25.91	25.84	25.71	0.19	0.40	0.75
Nitromethane	25.71	25.77	25.71	25.64	0.22	0.06	0.85
1-Decanol	[c]	26.81	26.67	26.60	0.70	0.82	0.45
1-Butanol	[c]	26.39	26.18	26.11	0.84	0.84	0.47
2-Propanol	[c]	26.25	26.11	26.11	0.76	0.84	0.48
1-Propanol	[c]	26.25	26.18	25.91	0.84	0.90	0.52
Ethanol	24.81	26.39	26.11	26.18	0.86	0.75	0.54
Methanol	25.00	26.18	26.04	26.11	0.98	0.66	0.60
Ethane-1,2-diol	[c]	25.38	25.32	25.32	0.90	0.52	0.92
Formamide	[c]	25.00	24.88	24.69	0.71	0.48	0.97
2,2,2-Trifluoroethanol	[c]	25.84	25.84	25.84	1.51	0.00	0.73
Water	[c]	24.88	24.63	[b]	1.17	0.47	1.09
1,1,1,3,3,3-Hexafluoro-2-propanol	[c]	25.64	25.58	25.71	1.96	0.00	0.65
$\Delta\tilde{\nu}_{max}(cm^{-1})$	2890	3370	3540	3960			

[a] α, β, and π^* values for all solvents were taken from Refs [87,88].
[b] Probe is insoluble in this solvent.
[c] Probe shows significant contribution of probe aggregation in this solvent.

solvatochromic parameters α, β, and π^* for the multiple–linear regression analysis were taken from Refs [87,88]. The results of the multiple–linear regression analyses are summarized in Table 3.

The correlations statistically provide a solid base to understand the manifold solvent effects on the solvatochromic long-wavelength UV/Vis absorption band of these molecules. The correlation coefficient *r* is greater than 0.95 for LSERs, which indicates a high validity of the multiparameter equations and allows significant conclusions to be drawn.

The best regression fit for **2** is obtained from a two-parameter equation with β and π^*. However, including the results in methanol and ethanol at low concentration of **2** ($c \leq 4.0 \times 10^{-4}$ mol/L) also a significant regression fit with a three-parameter equation is obtained.

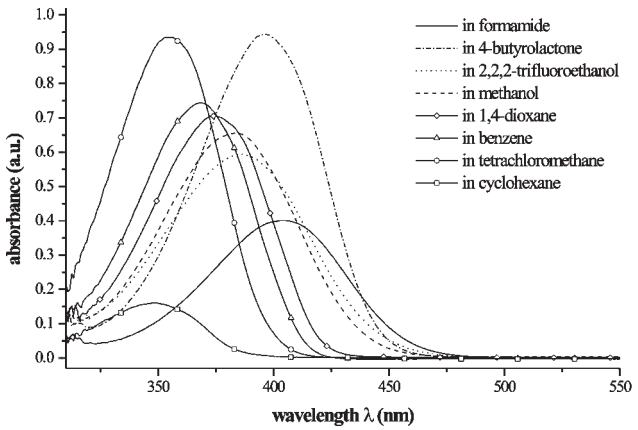


Figure 2. UV/Vis absorption spectra of **5** in different solvents

All investigated compounds **2**–**5** show a positive solvatochromism with increasing acidity, basicity, and dipolarity/polarizability of the solvents.

The results of the regression analyses show that the extent of the solvatochromic shift of the amide bond containing chromophores **3**–**5** show a significantly stronger dependence on the π^* term of the solvent compared to compound **2** as indicated by the *s* coefficient < -3. The negative sign of the *s* correlation coefficient indicates that the electronically excited state of these molecules becomes stronger solvated and consequently stabilized with increasing the solvents dipolarity/polarizability. On the strength of the higher dipole moment the energy of the electronically excited state decreases more than the ground state. This is well in agreement with bathochromic shifted UV/Vis absorption maxima with increasing polarity of the solvents.

The influence of the β-term of the solvent on the shift of λ_{max} for compound **2** in comparison to compounds **3**–**5** is similar (refer to Table 3). The results of the regression analyses indicate that the influence of the HBA property arises from the formation of hydrogen bonds donated from the carboxyl group and amide group (Scheme 5), respectively, of the probe to the lone-pair of the solvent molecule. This effect is new and noteworthy. We found a related effect of the β-parameter on the solvatochromism of *N*-(2-hydroxyethyl)-substituted Michler's ketone and *N*-methyl-*N*-[1-(2,3-dihydroxypropyl)]-4-nitroaniline derivatives.[68–71] The sign of the correlation coefficient *b* is negative, indicating that hydrogen bonding with a protophilic solvent leads to displacement of λ_{max} to lower frequencies.

The comparison of the value of coefficients *a* shows that specific interactions between HBD solvents and the solute are larger for compound **2** than for the compounds **3**–**5**. Then, the stronger bathochromic shift of the nitroaniline derivative **2** observed in protic solvents is caused by the HBD strength of the solvent. This effect is of importance for the construction of peptide bond containing UV/Vis probes. Obviously the carboxyl group disturbs the HBA solvation of the proline-N-atom at the push–pull aromatic π-electron system. Thus, the HBD solvation of the nitro group has a stronger effect on the bathochromic shift of the UV/Vis absorption band of **2**.

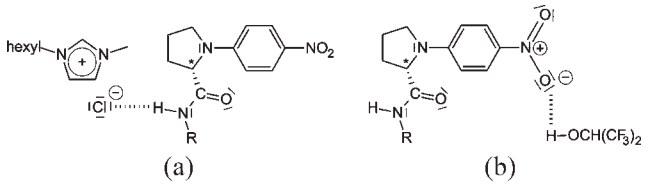
Table 2. UV/Vis absorption maxima of **2**–**5** measured in 3 RTIL[89,90]

	$\tilde{\nu}_{max} \times 10^{-3}\,cm^{-1}$				Kamlet–Taft parameters		
Ionic liquid	(**2**)	(**3**)	(**4**)	(**5**)	α	β	π^*
[C_6-mim][PF_6]	25.13	25.38	25.32	25.25	0.57[89]	0.50[90]	0.91[90]
[C_6-mim][BF_4]	25.19	25.25	25.19	25.13	0.68[89]	0.61[90]	0.90[90]
[C_6-mim][Cl]	24.94	24.75	24.63	24.51	0.23[89]	0.97[90]	0.91[90]

Table 3. Solvent-independent correlation coefficients *a*, *b*, and *s* of the Kamlet–Taft parameters α, β, and π^*, respectively, solute property of the reference system $\tilde{\nu}_{max,0}$, correlation coefficient (*r*), significance (*f*), standard deviation (sd), and number of solvents (*n*) calculated for the solvatochromism of compounds **2**–**5**

Compound	$\tilde{\nu}_{max,0}$	*a*	*b*	*s*	*n*	*r*	*f*	sd
(**2**)[a]	28.234 ± 0.150	—	-1.213 ± 0.167	-2.578 ± 0.209	23	0.956	<0.0001	0.215
(**2**)[b]	28.240 ± 0.135	-1.101 ± 0.160	-1.302 ± 0.145	-2.476 ± 0.187	25	0.971	<0.0001	0.193
(**3**)[c]	28.912 ± 0.145	-0.379 ± 0.082	-1.005 ± 0.135	-3.138 ± 0.184	38	0.958	<0.0001	0.248
(**4**)[c]	28.872 ± 0.142	-0.416 ± 0.080	-1.115 ± 0.133	-3.116 ± 0.180	38	0.961	<0.0001	0.243
(**5**)[d]	28.765 ± 0.119	-0.402 ± 0.088	-1.031 ± 0.137	-3.081 ± 0.167	39	0.967	<0.0001	0.261

[a] Only in solvents in which no probe aggregation of **2** is observed.
[b] In methanol and ethanol (low concentration of **2**) and in solvents in which no probe aggregation of **2** is observed.
[c] Insoluble in *n*-hexane and cyclohexane.
[d] Insoluble in water.



Scheme 5. (a) HBA/EPD solvents such as the chloride ion of [C_6-mim][Cl] lower the (−I)-effect of the CONH-substituent, which causes a bathochromic band shift compared to nitroaniline derivative. (b) HBD/EPA solvents such as 1,1,1,3,3,3-hexafluoro-2-propanol enhance the (−M)- and (−I)-effect of the NO_2-substituent, which causes a bathochromic band shift compared to nitroaniline derivative

The negative sign of correlation coefficient *a* indicates formation of hydrogen bonds between protic solvents which have HBD and electron-pair acceptor (EPA) ability, and the oxygen atoms of the nitro-group (Scheme 5).

Altogether, the absolute *s* value is significantly larger than the *a* and *b* coefficient for the calculated LSERs for the compounds **2**–**5**. This result demonstrates that the ability of the used solvents to donate or accept hydrogen bonds is much weaker than solute–solvent dipole–dipole interactions.

$$\tilde{\nu}_{max} * 10^{-3}\,[\mathbf{2}] = 28.061 - 0.879\alpha - 1.198\beta - 2.232\pi^{*}$$
$$r = 0.959,\ f < 0.0001,\ sd = 0.235,\ n = 28$$

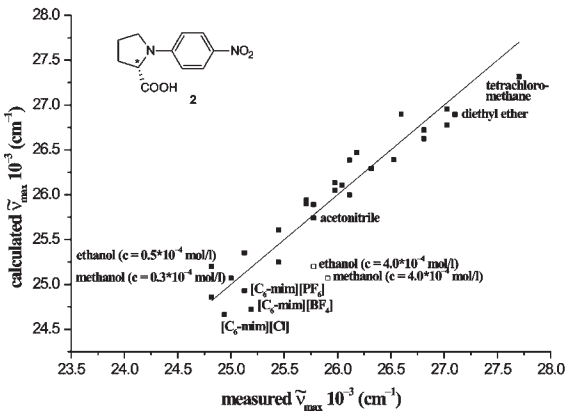


Figure 3. Relationship between calculated and measured $\tilde{\nu}_{max}$ values for **2** (28 solvents)

Steric effects of the substituent at the amide bond seem to be of minor importance due to the observation that the solvatochromic properties of **3**–**5** do not differ significantly from each other.

The possible intermolecular solute–solvent interactions with 1,3-dialkylimidazolium-based ionic liquids as solvent are manifold, because the imidazolium cation interacts as a weak HBD/EPA and the effect of the anion is that of a HBA/EPD (Scheme 5). The behavior of the probes **3**–**5**, which are sensitive mainly to π^* and in the second instance to β, also can confirm former studies that have characterized the polarity of ionic liquids, in this case of ionic liquids with 1-hexyl-3-imidazolium cations with various anions [X^-]. A previous analysis determined π^*-parameter to be 1.08[90] for [C_6-mim][PF_6], 1.07[90] for [C_6-mim][BF_4], and 1.27[90] for [C_6-mim][Cl] corresponding to the values in the order of magnitude of dimethyl sulfoxide or water.

The improved UV/Vis spectroscopic method for determining β and π^* for RTILs (Table 2)[90] provides much better agreement with the observed UV/Vis absorption maxima than the data from the Ref. [89]. Hence, the use of the novel nitroaniline solvatochromic probes confirms these new aspects of the HBA strength and dipolarity/polarizability on the overall polarity of ionic liquids.

The position of the UV/Vis absorption band of compound **2** in the investigated ionic liquids is independent from the concentration. The quantitatively best regression fit obtained for the key compound **2** is shown in Fig. 3.

The results of the multiple–linear regression analyses are summarized in Table 4.

Solvatochromic measurements in RTILs which interact as hydrogen bond acceptor confirm the β sensitivity of the probes.

CONCLUSION

Amino acid functionalities as substituents of push–pull π-electron systems such as *N*-(4-nitrophenyl)-L-proline derivatives can be used to achieve information on aggregation *versus* solvatochromic properties of polar compounds. However, compound **2** shows a hypsochromic shift of the UV/Vis absorption maxima with increasing concentration in protic solvents. A comprehensive study of the solvent effects on the position of the long-wavelength UV/Vis absorption band of the compounds **2**–**5** is presented. The UV/Vis absorption maxima have been measured in a variety of protic and aprotic solvents, and especially in RTILs. Overall, the four amino acid derivatives **2**–**5**

Table 4. Solvent-independent correlation coefficients *a*, *b*, and *s* of the Kamlet–Taft parameters α[89], β,[90] and π^*[90], respectively, solute property of the reference system $\tilde{\nu}_{max,0}$, correlation coefficient (*r*), significance (*f*), sd, and number of solvents (*n*) calculated for the solvatochromism of compounds **2**–**5**

Compound	$\tilde{\nu}_{max,0}$	*a*	*b*	*s*	*n*	*r*	*f*	sd
(**2**)[a]	28.061 ± 0.152	−0.879 ± 0.173	−1.198 ± 0.164	−2.232 ± 0.212	28	0.959	<0.0001	0.235
(**3**)[b]	28.932 ± 0.136	−0.373 ± 0.078	−1.036 ± 0.126	−3.155 ± 0.172	41	0.962	<0.0001	0.241
(**4**)[b]	28.886 ± 0.133	−0.408 ± 0.077	−1.143 ± 0.124	−3.123 ± 0.169	41	0.965	<0.0001	0.237
(**5**)[c]	28.785 ± 0.114	−0.394 ± 0.086	−1.073 ± 0.131	−3.097 ± 0.159	42	0.969	<0.0001	0.256

[a] Only in solvents in which no probe aggregation of **2** is observed.
[b] Insoluble in *n*-hexane and cyclohexane.
[c] Insoluble in water.

show a positive solvatochromism. The data have been analyzed and interpreted in terms of empirically derived LSERs using the Kamlet–Taft solvents parameter set. The results of correlation analyses suggest that the influence of solvent dipolarity/polarizability on the long-wavelength absorption maximum for all compounds is more predominant. Also, the effect of β-term on the bathochromic band shift is more pronounced than that of the α term, particularly with regards to the dipeptide functionalized 4-nitroaniline derivatives **3** and **4**, and the pinane derivative **5**. Furthermore, the solvatochromism of the compounds **3**–**5** was used to investigate the reliability of the Kamlet–Taft solvent parameter β and π^* of RTILs from Ref. [90].

EXPERIMENTAL SECTION

General remarks

Solvents from Merck, Fluka, Lancaster, and Aldrich were redistilled over appropriate drying agents prior to use. Dichloromethane was dried over calcium hydride and distilled under argon. All the following ionic liquids were purchased in the highest available grade from commercial sources and used without further purification: Merck: 1-hexyl-3-methylimidazolium chloride, 1-hexyl-3-methylimidazolium tetrafluoroborate, 1-hexyl-3-methylimidazolium hexafluorophosphate. All commercial reagents were used without further purification, they were purchased from the following suppliers: Acros: L(−)-proline, Lancaster: glycine methyl ester hydrochloride, L(−)-alanine methyl ester hydrochloride, ABCR: 1-fluoro-4-nitrobenzene, DCC.

All mps were measured on a Boetius mp apparatus and were uncorrected. The UV/Vis absorption spectra were obtained by MCS 400 diode array UV/Vis spectrometer from Carl Zeiss, Jena, connected via glass-fiber optics. ^{1}H NMR and ^{13}C NMR spectra were measured at 20 °C on a Bruker Avance 250 NMR spectrometer at 250 and 69.9 MHz and on a Varian Gemini 300 FT NMR spectrometer at 300 and 75.5 MHz, respectively. The residue signals of the solvents (DMSO-d_6, CD_2Cl_2, $CDCl_3$) were used as internal standards. The FT-IR spectra were measured by means of diffuse reflection diluted with KBr at room temperature in the wave number range from 400 to 4000 cm^{-1} on a Perkin-Elmer Fourier transform 1000 spectrometer. Elemental analysis was determined with a Vario-EL analysis.

Correlation analysis

Multiple regression analysis was performed with Origin 5.0 statistical program.

*N-(4-nitrophenyl)-L-proline (**2**)*

As mentioned above, the synthesis of **2** was previously described.[54,56,59,91]

An equimolar amount of L-proline (8.17 g, 0.071 mol) was added at 25 °C to a mixture of 1-fluoro-4-nitrobenzene (10.00 g, 0.071 mol) and threefold molar amount of K_2CO_3 (29.02 g, 0.210 mol) in EtOH/H_2O (100 ml, v/v = 3/1). The mixture was refluxed at 90 °C for 38 h and then cooled to room temperature (rt). The mixture was poured into ice water and neutralized with 2 M HCl. The precipitate was filtered off, washed with H_2O, and recrystallized (EtOAc) to give **2** (14.43 g, 0.061 mol) as a yellow solid. 86% yield. M.p. > 220 °C (dec). ^{1}H NMR (250 MHz, DMSO-d_6, 25 °C): δ = 1.91–2.37 (m, 4 H, proH-3/4), 3.39–3.58 (m, 2 H, proH-5), 4.42 (dd, $^3J_{H,H}$ = 8.7 Hz, $^3J_{H,H}$ = 2.3 Hz, 1 H, proH-2), 6.58 (d, $^3J_{H,H}$ = 9.2 Hz, 2 H, ArH), 8.07 (d, $^3J_{H,H}$ = 9.2 Hz, 2 H, ArH). ^{13}C NMR (69.9 MHz, DMSO-d_6, 25 °C): δ = 23.2, 30.2, 48.3, 60.3, 111.3, 125.9, 136.1, 151.4, 173.5. IR (KBr): $\tilde{\nu}$ = 3569 m (carboxylic OH), 2974 m, 2871 m, 1718 s (C═O), 1601 s, 1515 s (NO_2), 1313 *vs* (NO_2), 1199 m, 1115 s, 827 m cm^{-1}. Anal. Calcd for $C_{11}H_{12}N_2O_4$: C, 55.93; H, 5.12; N, 11.86. Found: C, 55.82; H, 4.95; N, 11.86.

General procedure for preparation of *3*–*5*

Compound **2** (0.500 g, 2.12 mmol) was dissolved in anhydrous dichloromethane (100 ml), and the solution was cooled to 0 °C. An equimolar amount of amine hydrochloride (2.12 mmol), DCC (0.437 g, 2.12 mmol), triethylamine (0.215 g, 0.3 ml, 2.12 mmol), and a 10th part of an equimolar amount of 4-*N*,*N*-dimethylaminopyridine (0.026 g, 0.21 mmol) were added. The mixture was then allowed to warm up to room temperature and stirred for 24 h. The precipitate was filtered off and washed with dichloromethane. The filtrate was washed with 10% HCl, 5% aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was purified by flash column chromatography (silica gel, dichloromethane/ethyl acetate), affording **3**–**5** as yellow crystals.

N-(4-nitrophenyl)-L-prolylglycine methyl ester **3**

(Dichloromethane/ethyl acetate, 1:1), 20% yield. M.p. 177–178 °C. ^{1}H NMR (300 MHz, CD_2Cl_2, 25 °C): δ = 2.04–2.14 (m, 2 H, proH-3 or proH-4), 2.25–2.33 (m, 2 H, proH-3 or proH-4), 3.34–3.43 (m, 1 H, proH-5), 3.67 (s, 3 H, OCH_3), 3.69–3.76 (m, 1 H, proH-5), 3.87–4.07 (m, 2 H, CH_2CO), 4.20 (dd, $^3J_{H,H}$ = 7.8 Hz, $^3J_{H,H}$ = 3.4 Hz, 1 H, proH-2), 6.60 (d, $^3J_{H,H}$ = 9.3 Hz, 2 H, ArH), 6.60 (1 H, NH), 8.08 (d, $^3J_{H,H}$ = 9.3 Hz, 2 H, ArH). ^{13}C NMR (75.5 MHz, CD_2Cl_2, 25 °C): δ = 24.1, 31.8, 41.2, 49.8, 52.6, 64.1, 112.3, 126.2, 138.7, 152.1, 170.3, 172.7. IR (KBr): $\tilde{\nu}$ = 3303 s (NH), 2965 m, 1747 s (C═O), 1736 s (C═O), 1655 *vs* (C═O), 1556 m, 1518 m (NO_2), 1334 *vs* (NO_2), 1217 s (COC), 1117 m, 823 m cm^{-1}. $C_{14}H_{17}N_3O_5$ (307.292): calcd C 54.72, H 5.58, N 13.67; found C 54.73, H 5.56, N 13.55.

N-(4-nitrophenyl)-L-prolylalanine methyl ester **4**

(Dichloromethane/ethyl acetate, 1:1), 38% yield. M.p. 174–176 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.38 (d, $^3J_{H,H}$ = 7.1 Hz, 3 H, CH_3), 1.98–2.16 (m, 2 H, proH-3 or proH-4), 2.29–2.37 (m, 2 H, proH-3 or proH-4), 3.35–3.44 (m, 1 H, proH-5), 3.67 (s, 3 H, OCH_3), 3.70–3.77 (m, 1 H, proH-5), 4.18 (dd, $^3J_{H,H}$ = 7.4 Hz, $^3J_{H,H}$ = 4.0 Hz, 1 H, proH-2), 4.50–4.63 (m, 1 H, CH), 6.59 (d, $^3J_{H,H}$ = 9.3 Hz, 2 H, ArH), 6.59 (1 H, NH), 8.11 (d, $^3J_{H,H}$ = 9.3 Hz, 2 H, ArH). ^{13}C NMR (75.5 MHz, CD_2Cl_2, 25 °C): δ = 18.1, 23.9, 31.4, 47.9, 49.5, 52.5, 63.8, 112.0, 126.0, 138.7, 151.6, 171.8, 172.7. IR (KBr): $\tilde{\nu}$ = 3303 s (NH), 2954 m, 1750 s (C═O), 1666 s (C═O), 1601 s, 1535 m, 1515 m (NO_2), 1312 *vs* (NO_2), 1241 m (COC), 1111 s, 828 m cm^{-1}. $C_{15}H_{19}N_3O_5$ (321.318): calcd C 56.07, H 5.96, N 13.08; found C 55.93, H 5.92, N 12.95.

1-(4-Nitrophenyl)-N-[(2,6,6-trimethylbicyclo[3.1.1]hept-3-yl)methyl]-pyrrolidin-2-carboxamide **5**

(Dichloromethane/ethyl acetate, 20:1), 37% yield. M.p. 156–158 °C. ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 0.62 (m, 1 H, CH_2), 0.92 (s, 3 H, CH_3), 0.97 (d, $^3J_{H,H}$ = 7.1 Hz, 3 H, CH_3), 1.15 (s, 3 H, CH_3), 1.33–1.40 (m, 1 H, CH_2), 1.56–1.65 (m, 1 H, CH),

1.69–1.74 (m, 1 H, CH), 1.77–1.87 (m, 1 H, CH), 1.78–1.85 (m, 1 H, CH), 1.88–2.06 (m, 1 H, CH_2), 2.09–2.17 (m, 2 H, proH-3 or proH-4), 2.21–2.30 (m, 1 H, CH_2), 2.32–2.37 (m, 2 H, proH-3 or proH-4), 3.09–3.18 (m, 1 H, CH_2N), 3.27–3.34 (m, 1 H, CH_2N), 3.35–3.44 (m, 1 H, proH-5), 3.69–3.76 (m, 1 H, proH-5), 4.19 (dd, $^3J_{H,H} = 7.7$ Hz, $^3J_{H,H} = 3.9$ Hz, 1 H, proH-2), 6.14 (t, $^3J_{H,H} = 6.1$ Hz, 1 H, NH), 6.59 (d, $^3J_{H,H} = 9.3$ Hz, 2 H, ArH), 8.13 (d, $^3J_{H,H} = 9.3$ Hz, 2 H, ArH). ^{13}C NMR (69.9 MHz, $CDCl_3$, 25 °C): $\delta = 21.9$, 23.0, 24.1, 28.0, 31.6, 32.2, 33.7, 36.2, 38.8, 40.8, 41.4, 47.5, 47.8, 49.7, 64.3, 112.1, 126.2, 138.9, 151.8, 172.1. IR (KBr): $\tilde{\nu} = 3269$ bs (NH), 2900 s, 1655 s (C═O), 1598 s, 1567 m, 1515 m (NO_2), 1312 s (NO_2), 1108 m, 821 m cm^{-1}. $C_{22}H_{31}N_3O_3$ (385.500): calcd C 68.54, H 8.11, N 10.90; found C 68.45, H 8.03, N 10.79.

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REFERENCES

[1] F. Eblinger, M. Sirish, H. J. Schneider, *Adv. Supramol. Chem.* **2000**, *6*, 185–216.
[2] J. H. Hartley, T. D. James, C. J. Ward, *J. Chem. Soc., Perkin Trans 1* **2000**, 3155–3184. DOI:10.1039/a909641h
[3] J. L. Lavigne, E. V. Anslyn, *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 3118–3130. DOI: 10.1002/1521-3773(20010903)40:17<3118
[4] J. Zhang, R. E. Campbell, A. Y. Ting, R. Y. Tsien, *Nature Rev. Mol. Cell Biol.* **2002**, *3*, 906–918. DOI: 10.1038/nrm976
[5] A. Verma, V. M. Rotello, *Chem. Commun.* **2005**, 303–312. DOI: 10.1039/b410889b
[6] R. Paulini, K. Müller, F. Diederich, *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 1788–1805. DOI: 10.1002/anie.200462213
[7] S. S. Yoon, T. M. Georgiadis, W. C. Still, *Tetrahedron Lett.* **1993**, *34*, 6697–6700. DOI: 10.1016/S0040-4039(00)61678-7
[8] S. S. Yoon, W. C. Still, *Tetrahedron Lett.* **1994**, *35*, 2117–2120. DOI: 10.1016/S0040-4039(00)76774-8
[9] S. S. Yoon, W. C. Still, *Angew. Chem. Int. Ed. Engl.* **1995**, *33*, 2458–2460. DOI: 10.1002/anie.199424581
[10] S. S. Yoon, W. C. Still, *Tetrahedron Lett.* **1994**, *35*, 8557–8560. DOI: 10.1016/S0040-4039(00)78435-8
[11] H. Wennemers, W. C. Still, *Tetrahedron Lett.* **1994**, *35*, 6413–6416. DOI: 10.1016/S0040-4039(00)78233-5
[12] S. S. Yoon, W. C. Still, *Tetrahedron* **1995**, *51*, 567–578. DOI: 10.1016/0040-4020(94)00916-I
[13] H. Wennemers, S. S. Yoon, W. C. Still, *J. Org. Chem.* **1995**, *60*, 1108–1109.
[14] C. Gennari, H. P. Nestler, B. Salom, W. C. Still, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1765–1768. DOI: 10.1002/anie.199517651
[15] M. Maletic, H. Wennemers, D. Q. McDonald, R. Breslow, W. C. Still, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1490–1492. DOI: 10.1002/anie.199614901
[16] C. T. Chen, H. Wagner, W. C. Still, *Science* **1998**, *279*, 851–853. DOI: 10.1126/science.279.5352.851
[17] K. Ryan, W. C. Still, *Bioorg. Med. Chem. Lett.* **1999**, *20*, 2673–2678. DOI: 10.1016/S0960-894X(99)00463-1
[18] MdA. Hossain, H. J. Schneider, *J. Am. Chem. Soc.* **1998**, *120*, 11208–11209. DOI: 10.1021/ja982435g
[19] F. Eblinger, H. J. Schneider, *Chem. Commun.* **1998**, 2297–2298. DOI: 10.1039/a805720f
[20] M. Sirish, H. J. Schneider, *Chem. Commun.* **1999**, 907–908. DOI: 10.1039/a901325c
[21] T. W. Bell, A. B. Khasanov, M. G. B. Drew, A. Filikov, T. L. James, *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 2543–2547. DOI: 10.1002/(SICI)1521-3773(19990903)38:17<2543
[22] T. W. Bell, Z. Hou, S. C. Zimmermann, P. A. Thiessen, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2163–2165. DOI: 10.1002/anie.199521631
[23] T. W. Bell, J. Liu, *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 923–925. DOI: 10.1002/anie.199009231
[24] H. Hachisako, Y. Murata, H. Ihara, *J. Chem. Soc., Perkin Trans. 2* **1999**, 2569–2577. DOI: 10.1039/a903956b
[25] T. Fessmann, J. D. Kilburn, *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1993–1996. DOI: 10.1002/(SICI)1521-3773(19990712)38:13/14<1993
[26] H. Wennemers, *Chimia* **1999**, *53*, 229–230.
[27] M. Conza, M. Nold, H. Wennemers, ECSOC-4 **2000**, 1334–1337.
[28] H. Wennemers, M. Conza, M. Nold, P. Krattiger, *Chem. Eur. J.* **2001**, *7*, 3342–3347. DOI: 10.1002/1521-3765(20010803)7:15<3342
[29] M. Conza, H. Wennemers, *J. Org. Chem.* **2002**, *67*, 2696–2698. DOI: 10.1021/jo016152+
[30] N. Douteau-Guével, F. Perret, A. W. Coleman, J. P. Morel, N. Morel-Desrosiers, *J. Chem. Soc., Perkin Trans. 2* **2002**, 524–532. DOI: 10.1039/b109553f
[31] S. H. Li, C. W. Yu, J. G. Xu, *Chem. Commun.* **2005**, 450–452. DOI: 10.1039/b414131h
[32] A. Buryak, K. Severin, *J. Am. Chem. Soc.* **2005**, *127*, 3700–3701. DOI: 10.1021/ja042363v
[33] B. E. Cohen, T. B. McAnaney, E. S. Park, Y. N. Jan, S. G. Boxer, L. Y. Jan, *Science* **2002**, *296*, 1700–1703. DOI: 10.1126/science.1069346
[34] S. M. B. Fraga, M. S. T. Gonçalves, J. C. V. P. Moura, K. Rani, *Eur. J. Org. Chem.* **2004**, 1750–1760. DOI: 10.1002/ejoc.200300692
[35] M. P. Brun, L. Bischoff, C. Garbay, *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 3432–3436. DOI: 10.1002/anie.200454116
[36] M. Nitz, A. R. Mezo, M. H. Ali, B. Imperiali, *Chem. Commun.* **2002**, 1912–1913. DOI: 10.1039/b205224e
[37] M. E. Vázquez, D. M. Rothman, B. Imperiali, *Org. Biomol. Chem.* **2004**, *2*, 1965–1966. DOI: 10.1039/b408001g
[38] C. G. Knight, *Biochem. J.* **1991**, *274*, 45–48.
[39] M. Kato, M. Kiguchi, N. Sugita, Y. Taniguchi, *J. Phys. Chem. B* **1997**, *101*, 8856–8859. DOI: 10.1021/jp970488z
[40] I. Ledoux, J. Zyss, in *Novel Optical Materials and Applications*, Chapter 1, (Eds: I. C. Khoo, F. Simoni, C. Umeton) John Wiley & Sons, New York, **1997**. 1–48.
[41] P. Gangopadhyay, S. Venugopal Rao, D. Narayana Rao, T. P. Radhakrishnan, *J. Mater. Chem.* **1999**, *9*, 1699–1705. DOI: 10.1039/a901591d
[42] F. L. Huyskens, P. L. Huyskens, A. P. Persoons, *J. Chem. Phys.* **1998**, *108*, 8161–8171. DOI: 10.1063/1.476171
[43] P. Norman, Y. Luo, D. Jonsson, H. Agren, K. O. Sylvester-Hvid, K. V. Mikkelsen, *J. Chem. Phys.* **1997**, *107*, 9063–9066. DOI: 10.1063/1.475196
[44] C. Reichardt, in *Solvents and Solvent Effects in Organic Chemistry* (3rd edn, updated and enlarged ed.), Wiley-VCH, Weinheim, **2003**.
[45] C. Reichardt, *Chem. Rev.* **1994**, *94*, 2319–2358. DOI: 10.1021/cr00032a005
[46] R. W. Taft, M. J. Kamlet, *J. Am. Chem. Soc.* **1976**, *98*, 2886–2894. DOI: 10.1021/ja00426a036
[47] M. J. Kamlet, R. W. Taft, *J. Am. Chem. Soc.* **1976**, *98*, 377–383. DOI: 10.1021/ja00418a009
[48] M. J. Kamlet, T. N. Hall, J. Boykin, R. W. Taft, *J. Org. Chem.* **1979**, *44*, 2599–2604. DOI: 10.1021/jo01329a001
[49] M. J. Kamlet, J. L. M. Abboud, R. W. Taft, *J. Am. Chem. Soc.* **1977**, *99*, 6027–6038. DOI: 10.1021/ja00460a031
[50] M. J. Kamlet, J. L. M. Abboud, M. H. Abraham, R. W. Taft, *J. Org. Chem.* **1983**, *48*, 2877–2887. DOI: 10.1021/jo00165a018
[51] C. Laurence, P. Nicolet, M. Tawfik Dalati, J. L. M. Abboud, R. Notario, *J. Phys. Chem.* **1994**, *98*, 5807–5816. DOI: 10.1021/j100074a003
[52] R. R. Minesinger, E. G. Kayser, M. J. Kamlet, *J. Org. Chem.* **1971**, *36*, 1342–1345. DOI: 10.1021/jo00809a005
[53] G. Mansour, W. Creedon, P. C. Dorrestein, J. Maxka, J. C. MacDonald, R. Helburn, *J. Org. Chem.* **2001**, *66*, 4050–4054. DOI: 10.1021/jo0014764
[54] R. Helburn, Y. Dijiba, G. Mansour, J. Maxka, *Langmuir* **1998**, *14*, 7147–7154. DOI: 10.1021/1a980787v
[55] R. Helburn, N. Ullah, G. Mansour, J. Maxka, *J. Phys. Org. Chem.* **1997**, *10*, 42–48. DOI: 10.1002/(SICI)1099-1395(199701)10:1<42
[56] K. Yoshino, M. Ozaki, A. Nakano, M. Honma, *Technol. Reports Osaka Univ.* **1990**, *40*, 81–85.
[57] P. Lo Meo, F. D'Anna, S. Riela, M. Gruttadauria, R. Noto, *Tetrahedron* **2004**, *60*, 9099–9111. DOI: 10.1016/j.tet.2004.07.079

[58] P. Lo Meo, F. D'Anna, S. Riela, M. Gruttadauria, R. Noto, *Org. Biomol. Chem.* **2003**, *1*, 1584–1590. DOI: 10.1039/b300330b
[59] M. El-Sayed, S. Spange, *J. Phys. Chem. B* **2007**, *111*, 7224–7233. DOI: 10.1021/jp070024t
[60] S. Spange, E. Vilsmeier, K. Fischer, S. Prause, A. Reuter, *Macromol. Rapid Commun. (Feature)* **2000**, *21*, 643–659. DOI: 10.1002/1521-3927(20000601)21:10<643
[61] S. Spange, C. Schmidt, H. R. Kricheldorf, *Langmuir* **2001**, *17*, 856–865. DOI: 10.1021/1a000997j
[62] S. Spange, E. Vilsmeier, Y. Zimmermann, *J. Phys. Chem. B* **2000**, *104*, 6417–6428. DOI: 10.1021/jp000231s
[63] S. Spange, A. Reuter, *Langmuir* **1999**, *15*, 141–150. DOI: 10.1021/1a980991i
[64] S. Spange, A. Reuter, D. Lubda, *Langmuir* **1999**, *15*, 2103–2111. DOI: 10.1021/1a980328u
[65] S. Spange, A. Reuter, E. Vilsmeier, D. Keutel, T. Heinze, W. Linert, *J. Polym. Sci. A* **1998**, *36*, 1945–1955. DOI: 10.1002/(SICI)1099-0518(199808)31:11<1945
[66] S. Spange, Y. Zimmermann, A. Gräser, *Chem. Mat.* **1999**, *11*, 3245–3251. DOI: 10.1021/cm990308t
[67] S. Spange, E. Vilsmeier, A. Reuter, K. Fischer, S. Prause, Y. Zimmermann, C. Schmidt, *Macromol. Rapid Commun.* **2000**, *21*, 643–659. DOI: 10.1002/1521-3927(20000601)21:10<643
[68] M. El-Sayed, H. Müller, G. Rheinwald, H. Lang, S. Spange, *J. Phys. Org. Chem.* **2001**, *14*, 247–255. DOI: 10.1002/poc.359
[69] S. Spange, M. M. El-Sayed, H. Müller, G. Rheinwald, H. Lang, W. Poppitz, *Eur. J. Org. Chem.* **2002**, 4159–4168. DOI: 10.1002/1099-0690(20021)2002:24<4159
[70] M. M. El-Sayed, H. Müller, G. Rheinwald, H. Lang, S. Spange, *Chem. Mater.* **2003**, *15*, 746–754. DOI: 10.1021/cm020197p
[71] S. Spange, K. Hofmann, B. Walfort, T. Rüffer, H. Lang, *J. Org. Chem.* **2005**, *70*, 8564–8567. DOI: 10.1021/jo051097g
[72] H. Suhr, *Chem. Ber.* **1964**, *97*, 3268–3276. DOI: 10.1002/cber.19640971203
[73] H. Suhr, *Liebigs Ann.* **1965**, *689*, 109–117. DOI: 10.1002/jlac.19656890109
[74] H. Suhr, *Tetrahedron Lett.* **1966**, *47*, 5871–5874. DOI: 10.1016/S0040-4039(00)76099-0
[75] S. Hu, D. C. Neckers, *Tetrahedron* **1997**, *53*, 7165–7180. DOI: 10.1016/S0040-4020(97)00420-1
[76] S. Hu, D. C. Neckers, *Tetrahedron* **1997**, *53*, 2751–2766. DOI: 10.1016/S0040-4020(97)00044-6
[77] H. D. Flack, G. Bernardinelli, *Acta Cryst.* **1999**, *A55*, 908–915. DOI: 10.1107/S0108767399004262
[78] H. D. Flack, G. Bernardinelli, *J. Appl. Cryst.* **2000**, *33*, 1143–1148. DOI: 10.1107/S0021889800007184
[79] H. D. Flack, *Helv. Chim. Acta* **2003**, *86*, 905–921. DOI: 10.1002/hlca.200390109
[80] S. Spange, K. Schreiter, B. Walfort, T. Rüffer, H. Lang, Unpublished results.
[81] Ref. 59 describes that UV/Vis measurements of **2** as a function of its concentration show no significant indication of probe aggregation in the concentration interval studied for the solvatochromic measurements. This estimation is incorrect because the long wavelength absorption maximum shifts hypsochromically with increasing the concentration of **2** in protic solvents.
[82] J. T. Bulmer, H. F. Shurvell, *J. Phys. Chem.* **1973**, *77*, 256–262. DOI: 10.1021/j100621a024
[83] N. Tanaka, H. Kitano, N. Ise, *J. Phys. Chem.* **1990**, *94*, 6290–6292. DOI: 10.1021/j100379a027
[84] F. Laborie, *J. Polym. Sci.* **1977**, *15*, 1255–1274. DOI: 10.1002/pol.1977.170150521
[85] T. Kuppens, W. Herrebout, B. Veken, P. Bultnick, *J. Phys. Chem. A* **2006**, *110*, 10191–10200. DOI: 10.1021/jp0608980
[86] I. Wolfs, H. O. Desseyn, *J. Mol. Struct. (THEOCHEM)* **1996**, *360*, 81–97.
[87] Y. Marcus, *Chem. Soc. Rev.* **1993**, *22*, 409–416. DOI: 10.1039/CS9932200409
[88] Y. Marcus, *J. Phys. Chem.* **1991**, *95*, 8886–8891. DOI: 10.1021/j100175a086
[89] J. G. Huddleston, G. A. Broker, H. D. Willauer, R. D. Rogers, in *Ionic Liquids: Industrial Applications to Green Chemistry, ACS Symp. Ser.* **2002**, *818*, 270–288.
[90] A. Oehlke, K. Hofmann, S. Spange, *New J. Chem.* **2006**, *30*, 533–536. DOI: 10.1039/b516709d
[91] S. Spange, K. Schreiter, K. Hofmann, *Synthesis* **2006**, *13*, 2100–2102. DOI: 10.1055/s-2006-942408