JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2003; **16:** 682–690
DOI: 10.1002/poc.623

Syntheses and UV–visible spectroscopic properties of two new hydrophilic 2,6-di(carbamoyl)-substituted solvatochromic pyridinium *N*-phenolate betaine dyes[†,‡]

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Received 6 December 2002; revised 4 February 2003; accepted 4 February 2003

ABSTRACT: Syntheses and negative solvatochromism of two 2,6-di(carbamoyl)-substituted pyridinium *N*-phenolate betaines dyes, **3** and **4**, are described for the purpose of obtaining more hydrophilic zwitterionic dyes which are better soluble in water and other aqueous media (such as binary water–solvent mixtures or aqueous ionophore solutions) than the rather hydrophobic standard betaine dyes **1** and **2**, which have been used to establish an empirical scale of solvent polarity, called the $E_T(\mathbf{30})$ or E_T^N scale. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: betaine dyes; $E_T(\mathbf{30})$ values; solvatochromism; solvent effects; UV–visible spectroscopy

INTRODUCTION

Solutions of the pyridinium *N*-phenolate betaine dye **1** (Scheme 1) are solvatochromic, thermochromic, piezochromic and halochromic.[3–5] This means that the longest-wavelength intramolecular charge-transfer (CT) absorption band in the visible spectrum of dye **1** depends on solvent polarity,[3–5] solution temperature,[6] external pressure[7] and the nature and concentration of added ionophores.[8] *Ionophores* are ionic compounds (such as $Na^+ Cl^-$) which, in contrast to ionogens, consist of ions in the crystal, in the melt, and in solution. *Ionogens* (such as H—Cl) are compounds with molecular crystal lattices which produce ions only when dissolved in appropriate solvents, inducing the ionization of the covalent compound.[9] By definition, negative (positive) solvatochromism means that solvent-influenced UV–Vis absorption bands of the solute chromophore are shifted hypsochromically (bathochromically) with increasing solvent polarity.[5] The exceptionally large negative solvatochromism of the standard betaine dye **1** has been used to establish a UV–Vis spectroscopically derived scale of solvent polarity, called the $E_T(\mathbf{30})$ or E_T^N scale.[3,4,10] The $E_T(\mathbf{30})$ values are simply defined as the molar transition energy (in kcal mol^{-1}; 1 kcal = 4.184 kJ) of the standard betaine dye **1**, measured in solvents of different polarity at room temperature (25 °C) and normal pressure (1 bar), according to the equation

$$\begin{aligned} E_T(\mathbf{30})(\text{kcal mol}^{-1}) &= h \cdot c \cdot \tilde{\nu}_{\max} \cdot N_A \\ &= (2.8951 \times 10^{-3}) \cdot \tilde{\nu}_{\max}(\text{cm}^{-1}) \\ &= 28591/\lambda_{\max}(\text{nm}) \end{aligned} \quad (1)$$

where $\tilde{\nu}_{\max}$ is the wavenumber and $\lambda_{\max}$ the wavelength of the maximum of the long-wavelength solvatochromic absorption band of betaine dye **1** in the visible spectral region.

High $E_T(\mathbf{30})$ values correspond to high solvent polarity, here defined as the overall solvation capability of a solvent.[4,5,11] The $E_T(\mathbf{30})$ solvent polarity scale ranges from 63.1 kcal mol^{-1} for water to 30.7 kcal mol^{-1} for tetramethylsilane (TMS) as the most and least polar solvents, respectively. In order to avoid use of the non-SI unit kcal mol^{-1}, the dimensionless, normalized E_T^N scale was later introduced, using water ($E_T^N = 1.000$) and TMS ($E_T^N = 0.000$) as extreme reference solvents to fix the scale.[12]

The primary indicator dye **1** is sufficiently soluble in most organic solvents, although insoluble or only sparingly soluble in non-polar solvents such as aliphatic hydrocarbons, perfluoroalkanes and TMS, and also in water. For the indirect determination of $E_T(\mathbf{30})$ values of such non-polar solvents, the lipophilic penta-*tert*-butyl-substituted betaine dye **2** was introduced as a secondary indicator dye, the $E_T(\mathbf{2})$ values of which correlate linearly with that of the primary indicator dye **1** for those solvents in which both betaine dyes are soluble.[12] Thus, based on the excellent linear correlation between the E_T values of **1**

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[†] Part XXVII in the series Pyridinium *N*-Phenoxide Betaine Dyes and Their Application to the Determination of Solvent Polarities. For Part XXVI, see Ref. 1.

[‡] Dedicated to Professor Dr T. M. Krygowski, Warsaw, in recognition of his remarkable contributions in the areas of physical organic chemistry, on the occasion of his 65th birthday.

[§] Based on the Diploma and PhD Thesis of A. Röchling.[2]

Contract/grant sponsor: Deutsche Forschungsgemeinschaft.
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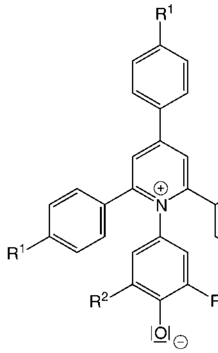


	R^2	R^2
1	H	H_5C_6–
2	Me_3C–	4-Me_3C–H_4C_6–
3	H	Me–NH–CO–
4	H	Me_2N–CO–

Scheme 1. Molecular structure of the betaine dyes **1**–**4**

and **2**, $E_T(\mathbf{30})$ values can be calculated for such non-polar solvents in which the primary probe dye is not soluble enough for UV–Vis spectroscopic measurements.[4,12,13]

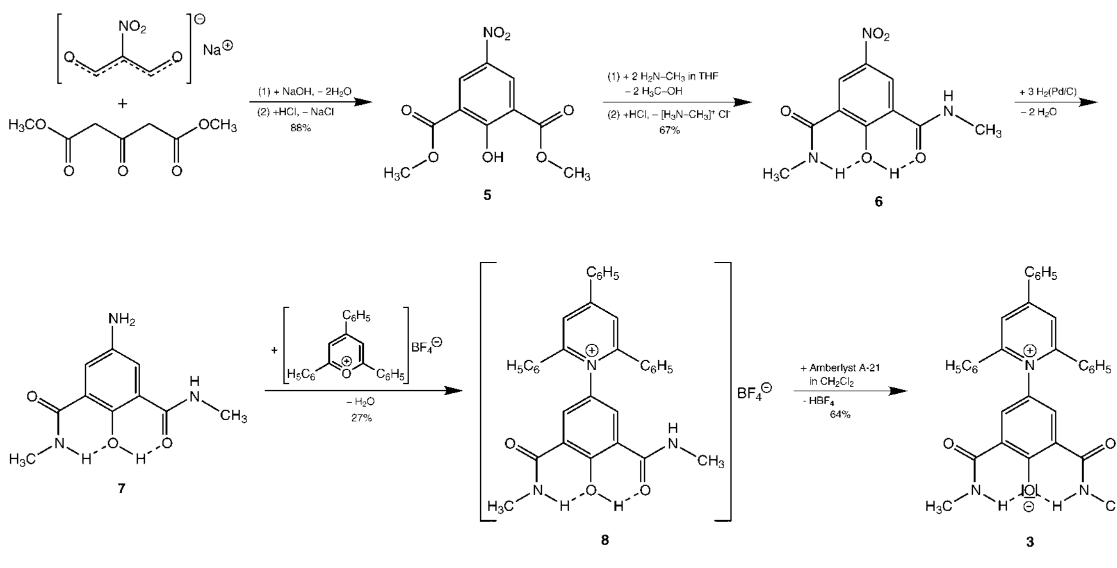
Unfortunately, the primary indicator dye **1** is only sparingly soluble in water (its solubility in water is only about $2 \times 10^{-6}\,\mathrm{mol\,l^{-1}}$),[14] just enough to determine its $E_T(\mathbf{30})$ values directly with a saturated solution in a 10 cm quartz cell. This low solubility of **1** in water is obviously caused by the core of five hydrophobic phenyl groups around its zwitterionic pyridinium *N*-phenolate chromophore. In order to obtain better water-soluble betaine dyes, the peripheral phenyl rings of **1** should be modified either by introduction of hydrophilic substituents into these phenyl groups or through replacement by other more hydrophilic groups, but without changing the essential solvatochromic chromophore. For this reason, we synthesized pyridinium *N*-phenolates with hydrophilic carboxylate (—$CO_2^-Na^+$)[15] and methanesulfonate (—SO_2CH_3) substituents[16] in the 2,4,6-phenyl rings of the pyridinium moiety, but with limited success.[15,16] However, replacement of at least two of the five peripheral phenyl groups by 2-, 3- or 4-pyridyl rings leads to comparatively good water-soluble pyridinium *N*-phenolate betaine dyes, as has been shown recently.[17] This increased solubility in water is obviously due to the possibility of forming intermolecular hydrogen bonds between water and the pyridyl-nitrogen atoms, thus pulling the whole dye into the aqueous solution. Other hydrophilic groups which should lead to better water solubility of **1** are carbamoyl groups of the type —CO—NH—CH_3 and —CO—$N(CH_3)_2$. Here, we report on the synthesis and solvatochromism of the new pyridinium *N*-phenolate betaine dyes **3** and **4** with two methyl-substituted carbamoyl groups in 2,6-positions of the phenolate moiety as hydrogen-bond acceptors (Scheme 1).

RESULTS AND DISCUSSION

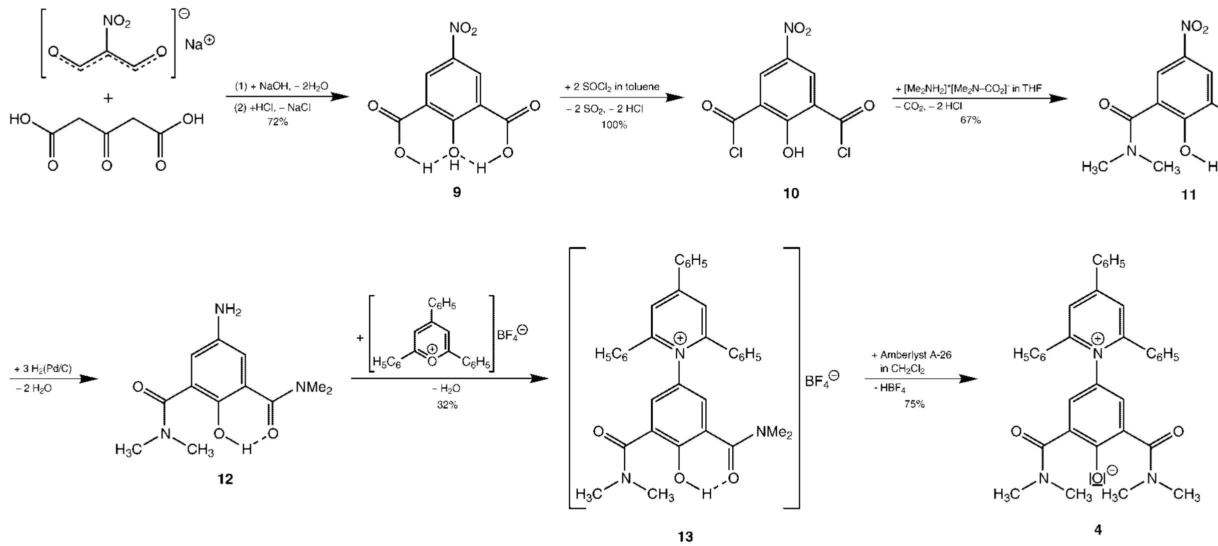
Syntheses of betaine dyes 3 and 4

The key step in the synthesis of such betaine dyes is the condensation reaction between 2,4,6-triaryl-substituted pyrylium salts and 2,6-disubstituted 4-aminophenols, producing *N*-(4-hydroxyphenyl)pyridinium salts, which are eventually deprotonated to give the corresponding betaine dyes (Schemes 2 and 3). For the synthesis of **3** and **4**, the known 2,4,6-triphenylpyrylium tetrafluoroborate[18] has to be reacted with the unknown 2,6-disubstituted 4-aminophenols **7** (Scheme 2) and **12** (Scheme 3), which were prepared as follows.

The base-catalyzed, two-fold aldol condensation reaction of sodium nitromalonaldehyde monohydrate[19] with dimethyl 3-oxoglutarate yielded 4-nitrophenol **5** (Scheme 2), which was converted into the 2,6-dicarbamoyl-substituted 4-nitrophenol **6** by reaction with methylamine. Palladium-catalyzed reduction of **6** with dihydrogen



Scheme 2. Synthesis of the 2,6-di(*N*-methylaminocarbonyl)-substituted betaine dye **3**



Scheme 3. Synthesis of the 2,6-di(*N*,*N*-dimethylaminocarbonyl)-substituted betaine dye **4**

gave the oxygen-sensitive 4-aminophenol **7**, which was immediately reacted with the 2,4,6-triphenylpyrylium salt[18] to give *N*-(4-hydroxyphenyl)pyridinium salt **8**. The downfield ^{1}H NMR shift of the NH and OH signal of **8** indicates participation of these groups in intramolecular hydrogen bonds as schematically indicated by the dotted lines in formulas **6**–**8** [$\delta(\mathrm{NH}) = 7.9$ and $\delta(\mathrm{OH}) = 15.6$ ppm for **8** in $CDCl_3$]. In analogy with the intramolecular O—H···O=C hydrogen bond found experimentally in salicylic acid derivatives,[20] the most probable molecular fine structure of **6**–**8** is that given in Scheme 2, with one N—H···O—H and one O—H···O=C intramolecular hydrogen bond.

Deprotonation of **8** with a suspension of the basic anion-exchange resin Amberlyst A-21 in dichloromethane gave eventually the orange betaine dye **3** as sesquihydrate. Betaine dye **3** can now form two intramolecular N—H···$^-$O— hydrogen bonds directed to the same phenolate oxygen atom, in competition with the intermolecular hydrogen bonds formed between N—H and —O$^-$ and the water of crystallization.

An analogous two-fold aldol condensation of sodium nitromalonaldehyde monohydrate[19] with 3-oxoglutaric acid yielded the dicarboxylic acid **9** (Scheme 3), which was converted into its dichloride **10** with thionyl chloride. Reaction of **10** with dimethylammonium dimethylcarbamate (Dimcarb) as dimethylamine precursor[21] led to the 2,6-bis(dimethylaminocarbonyl)-substituted 4-nitrophenol **11**. Reduction of **11** to the 4-aminophenol **12** and its immediate reaction with 2,4,6-triphenylpyrylium tetrafluoroborate[18] gave the *N*-(4-hydroxyphenyl)pyridinium salt **13**, which was deprotonated by means of a suspension of Amberlyst A-26 (OH form) in dichloromethane to give the blue–violet betaine dye **4** as the ca dihydrate. The most probable molecular fine structure of intermediates **11**–**13** is described with one intramolecular O—H···O=C hydrogen bond, in analogy with corresponding salicylic acid derivatives.[20] The downfield ^{1}H NMR shift of the OH signal of **11** and **13** is in agreement with the participation of O—H in an intramolecular hydrogen bond ($\delta = 11.7$ and 11.3 ppm in $CDCl_3$).

The molecular structures of all new compounds were confirmed by elemental analysis and mass, UV–Vis, IR and ^{1}H and ^{13}C NMR spectra (see Experimental section).

UV–Vis spectra and solvatochromism of betaine dyes 3 and 4

In acetonitrile, a solvent of intermediate polarity, the UV–Vis spectra of betaine dyes **3** and **4** exhibit two main absorption bands of different intensity at $\lambda_{\max} =$ 451 and 544 nm ($\varepsilon \approx 2600$–2800 l mol^{-1} cm^{-1}) and $\lambda_{\max} =$ 303 nm ($\varepsilon \approx 35\,000$–38 000 l mol^{-1} cm^{-1}). The spectrum of betaine dye **3** shows an additional intermediate absorption band at $\lambda_{\max} = 369$ nm ($\varepsilon \approx$ 8800 l mol^{-1} cm^{1}). The corresponding intermediate absorption band of **4** can only be seen as shoulder because of overlap with the intensive short-wavelength band (see Table 1 and Experimental section).

Only the position of the long-wavelength band in the visible spectral region is strongly solvent (and substituent) dependent; the others are not. On going from nonpolar benzene to polar ethanol as solvent, the visible absorption bands of **3** and **4** are shifted hypsochromically by $\Delta\lambda = -128$ and -216 nm, respectively, which corresponds to a solvent-induced increase in the molar electronic transition energies of $\Delta E_{\mathrm{T}} = +15.4$ and $+19.1$ kcal mol^{-1}, respectively (see Table 1).

Various quantum-chemical calculations and different spectroscopic measurements[22–33] as well as direct evidence by terahertz (THz) spectroscopy[34] have shown that the long-wavelength Vis absorption band of betaine dyes such as **1** is related to an intramolecular charge transfer (CT) from the HOMO of the phenolate to the LUMO of the pyridinium moiety. Therefore, the position of this CT

Table 1. Long-wavelength, solvent-dependent CT absorption maxima, λ_{max} (nm) and the corresponding $E_T(\mathbf{X})$ values (kcal mol^{-1}) (in parentheses) of betaine dyes $\mathbf{X} = \mathbf{3}$ and **4**, measured in up to 19 solvents of different polarity at 25 °C and normal pressure, ordered according to decreasing $E_T(\mathbf{30})$ values [4]

No.	Solvent	$E_T(\mathbf{30})$[a]	$\lambda_{max}(\mathbf{3})$ [$E_T(\mathbf{3})$][b]	$\lambda_{max}(\mathbf{4})$ [$E_T(\mathbf{4})$][b]
1	Water	63.1	–[c]	415 (68.9)
2	Methanol	55.4	–[d]	448 (63.8)
3	*N*-Methylformamide	54.1	–	463 (61.7)
4	Ethanol	51.9	428 (66.8)	471 (60.7)
5	1-Propanol	50.7	431 (66.3)	479 (59.7)
6	1-Butanol	49.7	435 (65.7)	482 (59.3)
7	2-Propanol	48.4	434 (65.9)	506 (56.5)
8	Acetonitrile	45.6	451 (63.4)	544 (52.6)
9	Dimethyl sulfoxide	45.1	449 (63.7)	551 (51.9)
10	*N,N*-Dimethylformamide	43.2	459 (62.3)	568 (50.3)
11	Acetone	42.2	470 (60.8)	584 (48.9)
12	1,2-Dichloroethane	41.3	489 (58.5)	594 (48.1)
13	Dichloromethane	40.7	492 (58.1)	595 (48.1)
14	Pyridine	40.5	486 (58.8)	601 (47.6)
15	Trichloromethane	39.1	498 (57.4)	597 (47.9)
16	Ethyl acetate	38.1	501 (57.1)	624 (45.8)
17	Tetrahydrofuran	37.4	511 (56.0)	645 (44.3)
18	1,4-Dioxane	36.0	528 (54.1)	662 (43.2)
19	Benzene	34.3	556 (51.4)	687 (41.6)
			$\Delta\lambda = -128$ nm[e]	$\Delta\lambda = -216$ nm[e]
			$\Delta E_T = 15.4$[e]	$\Delta E_T = 19.1$ kcal mol^{-1} [e]

[a] Taken from Ref. 4.

[b] The $E_T(\mathbf{X})$ values given in parentheses are calculated from the long-wavelength absorption maxima of $\mathbf{X} = \mathbf{3}$ and **4** according to Eqn (1).

[c] Not soluble in this solvent.

[d] Not measurable because of overlap with the intense UV absorption band.

[e] $\Delta\lambda = \lambda_{max}(\text{EtOH}) - \lambda_{max}(C_6H_6)$; $\Delta E_T = E_T(\text{EtOH}) - E_T(C_6H_6)$.

band should depend on the ionization energy of the electron donor (i.e. the phenolate part) and on the electron affinity of the electron acceptor (i.e. the pyridinium part). On protonation of the phenolate part of betaine dyes **1**–**4**, the solvent-dependent CT band disappears and the corresponding *N*-(4-hydroxyphenyl)pyridinium salts formed (e.g. **8** and **13**) absorb only at $\lambda_{max} \approx 300$–$310$ nm, corresponding to the $\pi \rightarrow \pi^*$ absorption of the 2,4,6-triphenylpyridinium chromophore.

Replacement of the two 2,6-phenyl groups in the phenolate part of the standard betaine dye **1** ($\lambda_{max} = 627$ nm in acetonitrile) by the two *N*-methyl-substituted aminocarbonyl groups results in both cases in a hypsochromic shift of the long-wavelength CT band, amounting to $\Delta\lambda = 451 - 627 = -176$ nm ($\Delta E_T = +17.8$ kcal mol^{-1}) for **3** (with two —CO—NH—CH$_3$ groups) and to $\Delta\lambda = 544 - 627 = -83$ nm ($\Delta E_T = +7.0$ kcal mol^{-1}) for **4** [with two —CO—N(CH$_3$)$_2$ groups] in acetonitrile as solvent. The replacement of the two 2,6-phenyl groups [Hammett substituent constant $\sigma_p = 0.02$ for —C$_6$H$_5$ (For comprehensive collections of Hammett constants, see Ref. 35)] by the two electron-withdrawing aminocarbonyl groups ($\sigma_p = 0.31$ for —CO—NH$_2$[35,36]) increases the ionization energy of the phenolate moiety, with the experimentally observed hypsochromic CT band shift as a consequence. The σ_p value of —CO—NH—CH$_3$ is 0.36,[35,37] similar to that of the —CO—NH$_2$ group;[36] the corresponding σ_p value for —CO—N(CH$_3$)$_2$ seems not to be known.[35] According to the $\Delta\lambda$ or ΔE_T values observed experimentally, the electron-withdrawing effect increases in the order —CO—N(CH$_3$)$_2$ < —CO—NH—CH$_3$, which seems reasonable. The greater hypsochromic band shift observed for betaine dye **3** reflects an increased ionization energy of the phenolate moiety of **3**. This increase is presumably caused by the formation of intramolecular hydrogen bonds of the two —CO—NH—CH$_3$ groups with the phenolate oxygen atom, as shown in Scheme 2.

In Table 1, the molar transition energies $E_T(\mathbf{3})$ and $E_T(\mathbf{4})$ of the new betaine dyes **3** and **4**, measured for up to 19 HBD and non-HBD solvents, are also given (in parentheses), together with the corresponding $E_T(\mathbf{30})$ values of the primary indicator dye **1**. In both cases, there exists a good linear correlation between the E_T values of the new dyes **3** and **4** and the $E_T(\mathbf{30})$ values of dye **1** with correlation coefficients $r \approx 0.98$–0.99 for all HBD and non-HBD solvents, as shown by the following regression equations and Fig. 1:

$$E_T(\mathbf{3})/(\text{kcal mol}^{-1}) = 0.854 \cdot E_T(\mathbf{30})/(\text{kcal mol}^{-1}) + 23.89 \quad (2)$$

($n = 16$; $r = 0.979$; $\sigma = 0.982$ kcal mol^{-1})

$$E_T(\mathbf{4})\ (\text{kcal mol}^{-1}) = 1.016 \cdot E_T(\mathbf{30})/(\text{kcal mol}^{-1}) + 6.86 \quad (3)$$

($n = 19$; $r = 0.992$; $\sigma = 0.983$ kcal mol^{-1}); see also Fig. 1)

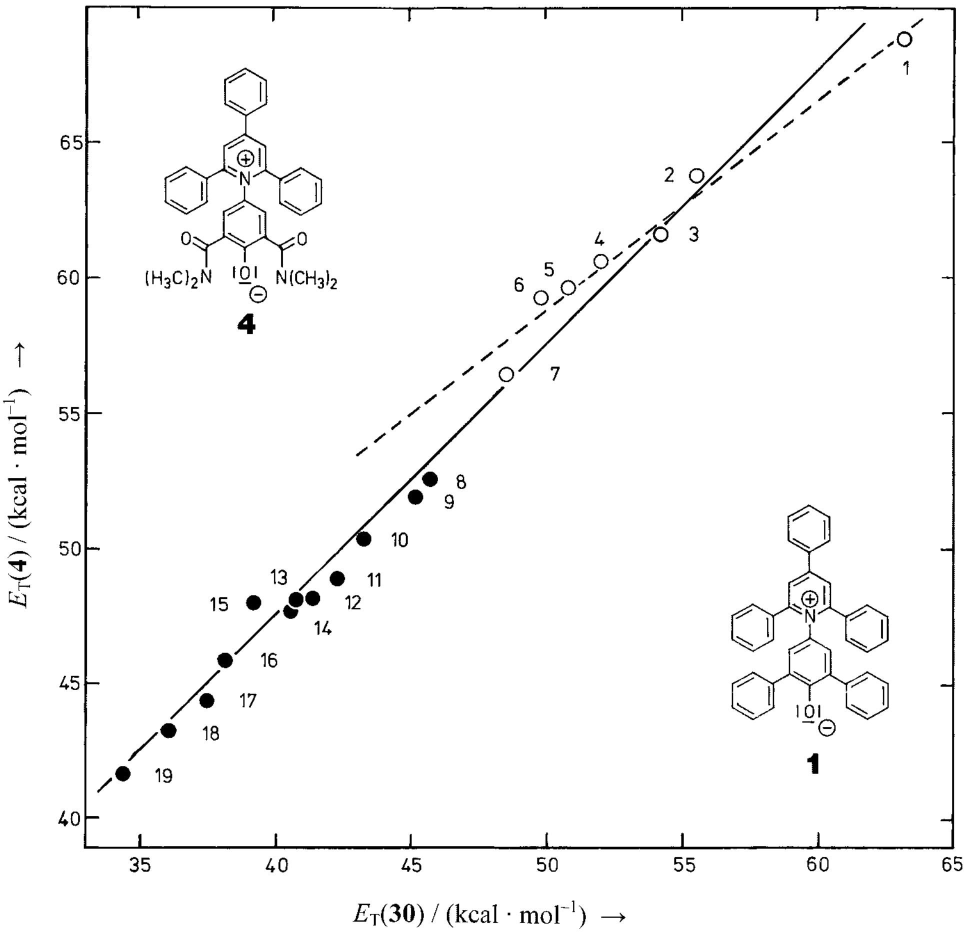


Figure 1. Linear correlation between the $E_T(\mathbf{30})$ values of standard betaine dye **1** and the $E_T(\mathbf{4})$ values of betaine dye **4**, measured in seven HBD solvents (open circles) and 12 non-HBD solvents (full circles), according to Eqn (3). The separate dashed line represents the linear correlation for the seven HBD solvents only, according to Eqn (4). Solvent numbering as in Table 1

The slope of correlation Eqn (2) is distinctly smaller than unity, indicating that betaine dye **3** is less sensitive to a change in solvent polarity than standard dye **1**, whereas Eqn (3) exhibits a slope of almost unity, demonstrating the high susceptibility of betaine dye **4** against changes in solvent polarity, comparable to that of dye **1**. The good quality of both correlations allows the calculation of $E_T(\mathbf{30})$ values for such media for which a direct experimental determination is not possible for reasons of limited solubility or strong solvent acidity, thus using betaines **3** and **4** as additional standard dyes.

A closer look at the correlation line given by Eqn (3) and illustrated in Fig. 1 reveals some family-dependent behaviour for betaine dye **4**. The group of seven HBD solvents (i.e. water, *N*-methylformamide and the alcohols; the very weak C—H hydrogen-bond donors $CHCl_3$, CH_2Cl_2 and CH_3CN are considered as non-HBD solvents) follow a regression line with a slope smaller than the regression line given by Eqn (3), which can be described by the equation

$$E_T(\mathbf{4})/(\text{kcal mol}^{-1}) = 0.789 \cdot E_T(\mathbf{30})/(\text{kcal mol}^{-1}) + 19.47 \qquad (4)$$

($n = 7$ HBD solvents; $r = 0.986$; $\sigma = 0.716\,\text{kcal mol}^{-1}$; see also Fig. 1)

Analogous HBD/non-HBD solvent dispersions of linear E_T/E_T correlations have also been found for some other pyridinium *N*-phenolate betaine dyes.[17] Surprisingly, the specific solvation of betaine dye **4** in HBD solvents leads to an altogether smaller susceptibility (slope only 0.789) of **4** against a solvent change. Nevertheless, Eqn (3) can be used for the calculation of $E_T(\mathbf{30})$ values for aqueous media, with the aid of $E_T(\mathbf{4})$ values of the more hydrophilic betaine dye **4**, with sufficient precision.

The new betaine dyes **3** and **4** are sufficiently soluble in most organic solvents, including benzene as non-polar hydrocarbon, but both dyes are insoluble in *text*-butyl methyl ether, tetrachloromethane and cyclohexane. Betaine dye **4** is suitably soluble in water, whereas dye **3** is surprisingly and disappointingly not water-soluble. Dissolution of a solid in a solvent means that the solvent gradually destroys the crystal lattice by non-specific and specific solvation of the molecules located on the crystal surface. In the crystal lattice of **3**, intra- and intermolecular hydrogen bonds between the zwitterionic dye molecules are presumably formed, which obviously prevent the interaction of the dye molecules with water, a solvent which can usually act as a hydrogen-bond donor (HBD) and hydrogen-bond acceptor (HBA) solvent simultaneously. In solutions of **3** in non-HBD and non-HBA solvents, intramolecular N—H···O hydrogen bonds are probably formed to such an extent, that the formation of intermolecular hydrogen bonds with added HBD solvents seems to be reduced. In the case of betaine dye **4** as solid, intra- and intermolecular hydrogen bonding between the dye molecules is not possible, and the dimethylaminocarbonyl and phenolate oxygen atoms are now prone to specific intermolecular interaction with HBD solvents such as water, leading to the desired water solubility. Unfortunately, the results of an x-ray structure determination of **3** and **4** are not yet available because of the difficulty in obtaining suitable single crystals.

CONCLUSION

The new carbamoyl-substituted pyridinium *N*-phenolate betaine dyes **3** and **4**, synthesized according to the reaction pathways given in Schemes 1 and 2, enlarge the supply of highly solvatochromic indicator dyes for the empirical determination of solvent polarities, in addition to the already known standard betaine dyes **1** and **2**. In particular, betaine dye **4** should be useful for the indirect determination of E_T(**30**) values for all kinds of aqueous media because of its water solubility, in addition to the hydrophilic, also water-soluble pyridyl-substituted betaine dyes described recently.[17] The advantage of betaine dye **4** over these pyridyl-substituted betaine dyes[17] is their simpler and less expensive synthesis. Disappointingly, in spite of the introduction of two hydrophilic *N*-methylaminocarbonyl groups, betaine dye **3** is not sufficiently soluble in water, presumably because of the preferred formation of intramolecular hydrogen bonds with the phenolate oxygen atom of **3** instead of intermolecular hydrogen bonds with the solvent.

EXPERIMENTAL

General methods. Melting-points (not corrected): Kofler–Mikroheiztisch (Reichert) and Mel-Temp apparatus. Elemental analyses: performed with a CHN-Automat Vario EL (Heraeus) at the Analytik-Servicelabor of the Department of Chemistry, Marburg. UV–Vis spectra: double-beam UV–Vis–NIR U-3410 spectrophotometer (Hitachi) with 1.00 cm quartz cells Suprasil (Hellma). IR spectra: IFS 88 spectrophotometer (Bruker) with KBr discs. ^{1}H and ^{13}C NMR: ARX 200 and AC-300 spectrometers (Bruker) in $CDCl_3$ and CD_3SOCD_3 with tetramethylsilane as internal standard. Mass spectra: MAT CH-7A spectrometer (Varian) with electron ionization (EI, 70 eV) and MAT 711 (Varian) with field desorption (FD). Analytical TLC: 60F-245 plates with silica gel and fluorescence indicator on aluminium foil (Merck). Flash chromatography: silica gel 60 (Merck), particle size 0.040–0.063 mm. Solvents: solvents for the solvatochromic measurements were used as commercially available in the highest available quality (analytical or spectroscopic grade) and were additionally dried and purified by means of molecular sieves and, if necessary, by filtration through a column of basic alumina, activity grade I, in order to remove traces of acids. For these measurements the solvents must be absolutely acid free, otherwise the betaine dyes are protonated and the long-wavelength solvatochromic CT absorption band disappears. Solvents for synthetic work were purified according to the usual standard methods (see Chapter A-2 and Table A-3 in Ref. 5).

Synthesis of betaine dye 3 (Scheme 2). *2,6-Bis(methoxycarbonyl)-4-nitrophenol (**5**).* The preparation analogous to Ref. 38. To a stirred solution of NaOH (2.47 g, 61.8 mmol) in water (180 ml) and methanol (190 ml) were added dimethyl 3-oxoglutarate (34.6 ml, 41.5 g, 238 mmol) and subsequently sodium nitromalonaldehyde monohydrate (37.4 g, 238 mmol).[19] The mixture was stirred at room temperature for ca 24 h. The yellow precipitate formed was filtered off, washed with ice-cold water and then suspended in cold water. The suspension was acidified with ice-cold aqueous 2 M HCl (pH ≈ 1) and stirred until the yellow solid was dissolved and a new colourless precipitate was formed. This precipitate was filtered off, washed with cold water, recrystallized twice from ethanol–water (1:1) and dried *in vacuo*, to afford **5** (53.2 g, 88%) as colourless crystals with m.p. 141 °C. IR (KBr): ν (cm^{-1}) = 3456 (OH), 1736 (C═O), 1528 and 1340 (NO_2). ^{1}H NMR ($CDCl_3$): δ (ppm) = 3.95 (s, 6 H, CH_3), 8.85 (s, 2 H, aromatic H), 12.39 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ (ppm) = 53.1 (CH_3), 117.1 and 131.2 (phenol-C-2 and C-3), 138.9 (C—NO_2), 165.6 (C—OH), 166.3 (C═O). MS (EI): m/z (%) = 255 (100) [M^+], 223 (34), 192 (68), 165 (66). $C_{10}H_9NO_7$ (255.2): calcd C 47.07, H 3.55, N 5.49; found C 46.92, H 3.70, N 5.62%.

*2,6-Bis(N-methylaminocarbonyl)-4-nitrophenol (**6**).* Gaseous methylamine (b.p. −6.5 °C), prepared by heating an aqueous methylamine solution ($c = 40\,\mathrm{cg\,g^{-1}}$) in a hot-water bath, was passed through two wash-bottles (the first empty and cooled, the second filled with KOH pellets) into a solution of **5** (5.00 g, 19.6 mmol) in tetrahydrofuran (350 ml) for ca 5 h. The excess of methylamine leaving the reaction vessel was condensed in a cooling trap, cooled with liquid nitrogen. After 5 h, the system reaction vessel–cooling trap (with condensed methylamine) was closed, provided with a bubble counter and the cooling agent (liquid N_2) was removed. Then, the reaction mixture was stirred at room temperature for 4 days in the closed system, filled with methylamine. Eventually, the solvent was distilled off in a rotary evaporator to give the yellow methylammonium salt of the product. This salt was dissolved in a mixture of water, methanol, and ethanol and cold 2 M HCl was added with stirring. The colourless flocculent precipitate formed was filtered off, washed with cold water, recrystallized twice from ethanol and dried *in vacuo* to yield colourless flakes of **6** (3.31 g, 67%), which sublime at ca 268 °C. IR (KBr): $\nu(\text{cm}^{-1}) = 3379$ (OH), 3321 (NH), 1670 (C═O), 1344 (NO_2). ^{1}H NMR (CD_3SOCD_3): δ (ppm) = 2.76 (d, 6 H, CH_3), 8.75 (s, 2 H, aromatic H), 9.12 (broad m, 2 H, NH); the OH signal is not discernible. ^{13}C NMR (CD_3SOCD_3): δ (ppm) = 26.2 (CH_3), 119.1 (*C*—CO—NH—), 127.6 (phenol-C-3), 137.3 (C—NO_2), 160.5 (C—OH), 165.9 (C═O). MS (EI): *m/z* (%) = 253 (100) [M^+], 223 (30), 192 (76), 146 (23). $C_{10}H_{11}N_3O_5$ (253.2): calcd C 47.44, H 4.38, N 16.60; found C 47.60, H 4.23, N 16.90%.

*4-Amino-2,6-bis(N-methylaminocarbonyl)phenol (**7**).* A suspension of a palladium catalyst (10% Pd on charcoal; ca 100 mg) in a solution of **6** (2.03 g, 8.00 mmol) in water–methanol (200 ml) was reduced with dihydrogen at room temperature and normal pressure until the necessary amount was absorbed (ca 530 ml H_2; time ca 18 h). The catalyst was filtered off under nitrogen, the solvent was distilled off *in vacuo* and the residue was dried *in vacuo*, to give **7** as yellow solid, which turned dark on contact with air. Because of its sensitivity to oxygen, **7** was immediately converted into the pyridinium salt **8** without further characterization.

*1-[4-Hydroxy-3,5-bis(N-methylaminocarbonyl)phenyl]-2,4,6-triphenylpyridinium tetrafluoroborate (**8**).* A solution of freshly prepared **7** (see above) and 2,4,6-triphenylpyrylium tetrafluoroborate (2.70 g, 6.80 mmol)[18] in dry dichloromethane (75 ml) and dry methanol (75 ml) was stirred at room temperature for 2 h. Then, three drops of acetic acid were added and stirring was continued for 2 days. The dark reddish-brown solution was filtered and the solvents were nearly completely distilled off in a rotary evaporator. The liquid residue was dissolved in acetone (20 ml) and this solution was slowly dropped with stirring into diethyl ether (800 ml). The precipitate formed was filtered off, washed with diethyl ether, recrystallized twice from methanol, and dried *in vacuo* (40 °C, 10^{-3} mbar, P_4O_{10}), to afford **8** (1.30 g, 27%) as an orange solid with m.p. 211–214 °C. IR (KBr): ν (cm^{-1}) = 3404 (OH), 1084 (BF_4). UV–Vis (CH_3CN): $\lambda_{\max}$ (log ε) = 309 nm (4.57). ^{1}H NMR ($CDCl_3$): δ (ppm) = 2.85 (d, 6 H, CH_3), 7.27–7.30 (m, 6 H, aromatic H), 7.37–7.40 (m, 4 H, aromatic H), 7.51–7.58 (m, 4 H, aromatic H), 7.81–7.84 (m, 3 H, aromatic H), 7.93 (s, 2 H, NH), 8.05 (s, 2 H, pyridinium-3-H), 15.62 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ (ppm) = 26.6 (CH_3), 125.8, 128.3, 128.8, 129.3, 129.6, 129.9, 130.6, 132.4, 132.7, 133.9, 157.4, and 157.6 (aromatic C), 161.2 (C═O); not all expected 17 signals are discernible. MS (FD): *m/z* (%) = 513 (100) [$M+\ -HBF_4 - H$]. $C_{33}H_{28}BF_4N_3O_3$ (601.4): calcd C 65.91, H 4.69, N 6.99; found C 65.72, H 4.61, N 6.97%.

*2,6-Bis(N-methylaminocarbonyl)-4-(2,4,6-triphenylpyridinium-1-yl)phenolate (**3**).* To a stirred suspension of tetrafluoroborate **8** (0.51 g, 0.85 mmol) in dry dichloromethane (30 ml) was added the macroreticular basic anion-exchange resin Amberlyst A-21 (2.27 g; Rohm and Haas). The suspension was stirred for 6 h at room temperature, the resin was filtered off and the solvent was distilled off in a rotary evaporator. The solid residue was washed several times with n-hexane and diethyl ether, and dried *in vacuo* (10^{-3} mbar) at 50 °C with P_4O_{10}, to give **3** (0.28 g, 64%) as orange crystals with m.p. 360–361 °C. IR (KBr): ν (cm^{-1}) = 3427 (OH), 1650 (C═O). UV–Vis (CH_3CN): $\lambda_{\max}$ (log ε) = 451 (3.44), 369 (3.94), 303 nm (4.58). ^{1}H NMR ($CDCl_3$): δ (ppm) = 2.83 (d, 6 H, CH_3), 7.24–7.30 (aromatic H), 7.55–7.62 (m, 3 H, aromatic H), 7.66 (s, 2 H, phenolate-3-H), 7.80–7.83 (m, 2 H, aromatic H), 8.03 (s, 2 H, pyridinium-3-H), 11.00 (m, 2 H, NH). ^{13}C NMR ($CDCl_3$): δ (ppm) = 25.5 (CH_3), 120.6, 122.3, 125.3, 127.9, 129.0, 130.1, 130.6, 131.7, 132.5, 132.7, 133.7, 156.0, 158.5, 167.7, and 172.1 (aromatic C and C═O). MS (FD): *m/z* (%) = 513 (100) [M^+]. $C_{33}H_{27}N_3O_3$. 1.5 H_2O (513.6 + 27.0 = 540.6): calcd C 73.32, H 5.03, N 7.77; found C 73.50, H 5.32, N 7.82%.

Synthesis of betaine dye 4 (Scheme 3). *2-Hydroxy-5-nitrobenzene-1,3-dicarboxylic acid (**9**).* The preparation is analogous to Ref. 38. To a solution of NaOH (16.1 g, 403 mmol) in water (200 ml) were added 3-oxoglutaric acid (26.2 g, 179 mmol) and subsequently sodium nitromalonaldehyde monohydrate (28.2 g, 179 mmol).[19] The mixture was stirred at room temperature for ca 12 h. The dark-red solution was acidified with 2 M HCl (pH ≈ 1). The colourless precipitate formed was filtered off, recrystallized from water and dried *in vacuo* (with P_4O_{10}), to give **9** (29.3 g, 72%) as colourless crystals with m.p. 213–214 °C (lit.[39] 213–214 °C). IR (KBr): ν (cm^{-1}) = 3532 (carboxylic OH), 3485 (phenolic OH), 1714 (C═O), 1531 and 1344 (NO_2). ^{1}H NMR (CD_3SOCD_3): δ (ppm) = 8.68 (s, 2 H, aromatic H), 9.69 (broad s, 3 H, OH). ^{13}C NMR (CD_3SOCD_3): δ (ppm) = 118.1 (*C*—CO_2H), 130.8 (phenol-C-3), 136.4 (C—NO_2), 167.2 (C—OH), 170.5 (C═O). $C_8H_5NO_7$ (227.1): calcd C 42.31 H 2.22, N 6.17; found C 41.90, H 2.45, N 6.23%.

*2-Hydroxy-5-nitrobenzene-1,3-dicarbonyl dichloride (**10**).* To a stirred suspension of **9** (4.00 g, 17.6 mmol) in dry toluene (100 ml) was added thionyl chloride (25.0 ml, 41.0 g, 340 mmol) and stirring was continued at 80 °C for ca 8 h, until the generation of gas stopped and a light-yellow solution was formed. Toluene and the excess thionyl chloride were distilled off *in vacuo* (at 10 mbar) and the residue was dried *in vacuo* (10^{-3} mbar, with KOH) to yield **10** (4.65 g, ca 100%) as colourless solid with m.p. 186–191 °C, which should be stored under dry N_2 or Ar. IR (KBr): ν (cm^{-1}) = 3520 (OH), 1776 (C=O), 1535 and 1350 (NO_2). ^1H NMR (CD_3SOCD_3): δ (ppm) = 8.64 (s, 2 H, aromatic H), 14.27 (s, 1 H, OH). ^{13}C NMR (CD_3SOCD_3): δ (ppm) = 117.6 (*C*—COCl), 130.3 (phenol-C-3), 136.4 (C—NO_2), 163.2 (COCl), 166.7 (C—OH). MS (FD): *m/z* (%) = 264 (100) [M^+]. $C_8H_3Cl_2NO_5$ (264.0): calcd C 36.40, H 1.15, N 5.31; found C 36.24, H 1.34, N 5.29%.

*2,6-Bis(dimethylaminocarbonyl)-4-nitrophenol (**11**).* To a stirred solution of **10** (3.49 g, 13.2 mmol) in dry tetrahydrofuran (100 ml) was added dropwise at ca 0 °C (cooling with an ice-bath) a solution of dimethylammonium dimethylcarbamate (Dimcarb;[21] 15.0 ml, 15.8 g, 120 mmol) in dry tetrahydrofuran (50 ml). Stirring was continued for 16 h, during which the temperature gradually rose to room temperature. The solvent was distilled off in a rotary evaporator and the residue was dissolved in water (ca 100 ml). The stirred solution was acidified with HCl ($c = 10\,cg \cdot g^{-1}$; pH $\approx$ 1) and the aqueous mixture was extracted four times with dichloromethane (4×50 ml). The combined dichloromethane extracts were dried with $MgSO_4$ and the solvent was distilled off in a rotary evaporator. To the foamy yellow residue diethyl ether (ca 100 ml) was added and the suspension was heated under reflux for 2 h. After cooling to room temperature, the solid was filtered off, and dried *in vacuo* (10^{-3} mbar), to afford **11** (2.50 g, 67%) as colourless fine crystals with m.p. 142–144 °C. IR (KBr): ν (cm^{-1}) = 3430 (OH), 1643 (C=O), 1528 and 1336 (NO_2). ^1H NMR ($CDCl_3$): δ (ppm) = 3.08 (s, 12 H, CH_3), 8.25 (s, 2 H, aromatic H), 11.7 (broad s, 1 H, OH). ^{13}C NMR ($CDCl_3$): δ (ppm) = 37.6 (CH_3), 121.9 (*C*—$CONMe_2$), 125.9 (phenol-C-3), 138.8 (C—NO_2), 161.2 (C—OH). MS (FD): *m/z* (%) = 281 (100) [M^+]. $C_{12}H_{15}N_3O_5$ (281.3): calcd C 51.24, H 5.37, N 14.94; found C 51.23, H 5.44, N 14.54%.

*4-Amino-2,6-bis(dimethylaminocarbonyl)phenol (**12**).* A suspension of a palladium catalyst (10% Pd on charcoal; ca 100 mg) in a solution of **11** (2.47 g, 8.78 mmol) in dry methanol (100 ml) was reduced with dihydrogen at room temperature and normal pressure until the necessary amount was absorbed (ca 600 ml H_2; time ca 18 h). The catalyst was filtered off under nitrogen, the solvent was distilled off *in vacuo* and the residue was dried *in vacuo* (10^{-3} mbar), to yield **12** as a light-brown solid, which turned dark on contact with air. Because of its sensitivity to oxygen, **12** was immediately converted into the pyridinium salt **13** without further characterization.

*1-[4-Hydroxy-3,5-bis(dimethylaminocarbonyl)phenyl]-2,4,6-triphenylpyridinium tetrafluoroborate (**13**).* To a stirred solution of freshly prepared **12** (see above) in dry dichloromethane (50 ml) and dry methanol (50 ml) was added 2,4,6-triphenylpyrylium tetrafluoroborate (2.96 g, 7.46 mmol)[18] and stirring was continued at room temperature for 2 h. Then, five drops of acetic acid were added and stirring was continued for 5 days, until a clear red solution was formed. The red solution was filtered and the solvents were nearly completely distilled off in a rotary evaporator. The liquid residue was dissolved in acetone (20 ml) and this solution was slowly dropped with stirring into diethyl ether (1000 ml). The precipitate formed was filtered off and washed with diethyl ether. The solid residue was then dissolved in methanol, and this solution was again dropped with stirring into diethyl ether (1000 ml). The precipitate formed was filtered off, washed with diethyl ether and dried. This purification procedure was repeated until a nearly colourless, light-brown solid was observed, to yield eventually **13** as monohydrate (1.78 g, 32%) as fine crystals with m.p. 167–170 °C. IR (KBr): ν (cm^{-1}) = 3428 (OH), 1625 (C=O), 1057 (BF_4). UV–Vis (CH_3CN): λ_{max} (log ε) = 309 nm (4.54). ^1H NMR ($CDCl_3$): δ (ppm) = 2.41 (broad s, 6 H, CH_3), 2.93 (broad s, 6 H, CH_3), 7.31 (m, 8 H, aromatic H), 7.42 (m, 4 H, aromatic H), 7.48–7.56 (m, 3 H, aromatic H), 7.79–7.85 (m, 2 H, aromatic H), 8.02 (s, 2 H, pyridinium-3-H), 11.32 (s, 1 H, OH). ^{13}C NMR (CD_3SOCD_3): δ (ppm) = 34.6 (CH_3), 37.5 (CH_3), 124.9, 125.2, 128.2, 128.5, 128.8, 129.7, 130.0, 130.4, 132.6, 133.0, 133.2, 150.6, 155.6, and 156.6 (aromatic C), 166.0 (C=O); not all expected 18 signals were discernible. MS (FD): *m/z* (%) = 542 (100) [$M^+ - BF_4$]. $C_{35}H_{32}BF_4N_3O_3 \cdot H_2O$ (629.5 + 18.0 = 647.5): calcd C 64.92, H 5.29, N 6.49; found C 65.14, H 5.24, N 6.45%.

*2,6-Bis(dimethylaminocarbonyl)-4-(2,4,6-triphenylpyridinium-1-yl)phenolate (**4**).* To a stirred suspension of tetrafluoroborate **13** (0.90 g, 1.43 mmol) in dry dichloromethane (60 ml) was added the macroreticular basic anion-exchange resin Amberlyst A-26 (4.40 g; OH form; Rohm and Haas). The suspension was stirred for 18 h at room temperature, then the resin was filtered off from the dark-violet solution and washed with dichloromethane. The filtrate and the washings were combined and the solvent was distilled off in a rotary evaporator. The solid residue was washed several times with n-hexane and diethyl ether and dried *in vacuo* (10^{-3} mbar) with P_4O_{10}, to afford **4** as hydrate (0.58 g, 75%) as blue–violet crystals with m.p. 272–277 °C. IR (KBr): ν (cm^{-1}) = 3419 (OH), 1620 (C=O). UV–Vis (CH_3CN): λ_{max} (log ε) = 544 (3.42), 303 nm (4.55). ^1H NMR ($CDCl_3$): δ (ppm) = 2.60 (s, 6 H, CH_3), 2.84 (s, 6 H, CH_3), 6.59 (s, 2 H, phenolate-3-H), 7.29–7.35 (m, 8 H, aromatic H), 7.55–7.60 (m, 4 H, aromatic H), 7.79–7.83 (m, 3 H, aromatic H), 8.02 (s, 2 H, pyridinium-3-H). MS (FD): *m/z* (%) = 541 (100) [M^+]. $C_{35}H_{31}N_3O_3 \cdot 2.5\,H_2O$ (541.6 + 45.0 = 586.6): calcd C 71.66, H 6.19, N 7.16, found C 71.75, H 5.92, N 6.91%.

Acknowledgements

For financial support of this work we thank the Deutsche Forschungsgemeinschaft, Bonn, and the Fonds der Chemischen Industrie, Frankfurt/Main.

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