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A new application of solvatochromic pyridinium-*N*-phenolate betaine dyes: examining the electrophilicity of lanthanide shift reagents

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ABSTRACT

The well-known solvent polarity indicators, pyridinium-*N*-phenolate betaine dyes, appeared to be promising reactants for comparing the electrophilicity of NMR chemical shift reagents such as lanthanide(III) complexes with dipivaloylmethane [tris(2,2,6,6-tetramethylheptan-3,5-dione)]. These dyes are suitable for the UV–vis spectroscopic study of weak specific Lewis acid/base interactions in solution.

In this Letter, we report on a novel application of the well-known and widely used solvent polarity indicators pyridinium-*N*-phenolate betaine dyes, which seem to be a promising tool for comparing the electrophilicity of various neutral Lewis-acidic species, in particular of NMR chemical shift reagents such as lanthanide(III) complexes with dipivaloylmethane [dpm = tris(2,2,6,6-tetramethyl heptan-3,5-dione)], Ln(dpm)$_3$. The betaine dyes used are shown in Scheme 1.

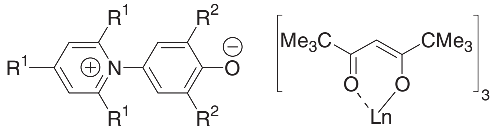
Pyridinium-*N*-phenolates are known as the most powerful solvatochromic dyes.[1] Their ground-state dipole moment amounts to ca. 15 D, which allows these betaine dyes to be considered as genuine zwitterions. They exhibit one of the largest solvent-induced hypsochromic shifts of the long-wavelength intramolecular charge transfer (CT) absorption band with increasing solvent polarity (negative solvatochromism). In the case of standard dye **2**, used to establish the empirical solvent polarity scale $E_T(30)$, this band shift is $\Delta\lambda = -357$ nm going from diphenyl ether ($\lambda_{max} = 810$ nm) to water ($\lambda_{max} = 453$ nm) as solvent.[1]

The extraordinary susceptibility of the intramolecular CT absorption of dye **2** and some of its derivatives to the nature of its microenvironment has led, in addition to their use as polarity indicators for molecular solvents,[1] to a manifold of further applications: determination of the polarity of ionic liquids,[2] study of their thermo-, halo-, piezo-, and chiro-solvatochromism,[1a–c] determination of the water content of organic solvents,[3] as tools for examining interfacial properties,[4] as molecular probes for the study of organized media such as micellar solutions of colloidal surfactants,[1c,4c,5] microemulsions,[4c,5a,6] suspensions of phospholipid liposomes,[4c,5b,7] solutions of dendrimers,[8] other supramolecular systems,[1b,9] and surfactant-doped gels.[10] Moreover, the phenolate oxygen of **2** is highly basic and can be readily protonated, resulting in the (reversible) disappearance of the solvatochromic CT band and decolorization of the dye solution. Therefore, these betaine dyes can also be used as acid/base indicators.[4c,5b,6] The acid/base interaction of protonated **2** with anions of varying basicity has been recently reported.[11] In addition, these betaine dyes are often used in sensor devices.[12]

The basic phenolate center of **2** is known to interact in organic solvents and micellar media with typical Lewis acids such as metal cations, leading to hypsochromic shifts and intensity decreases of the CT band.[13] Similar effects were registered for the interaction of the dyes with neutral molecules such as methyl-β-cyclodextrin,[9b] nonionic peptide lipids,[14a] and other biopolymers.[14b] However, such studies are only few in numbers.

Therefore, it is worthwhile to investigate the interaction of such universal probe dyes with a variety of further neutral species with electrophilic character. Within the course of such studies, we found that not only lanthanide(III) cations but also their neutral complexes with dipivaloylmethane (dpm), widely used in NMR spectroscopy as lanthanide shift reagents,[15] display the essential modifications of the long-wavelength CT band of pyridinium-*N*-phenolate betaine dyes **1–5**.

Contrary to the interaction with 'bare' cations, neutral lanthanide complexes **6a–c** do not decolorize the betaine dye solutions,



1: R^1 = Ph, R^2 = H; **2**: R^1 = R^2 = Ph; **3**: R^1 = Ph, R^2 = CMe$_3$; **4**: R^1 = Ph, R^2 = Cl; **5**: R^1 = R^2 = 4-Me$_3$C-C$_6$H$_4$; Ln = La (**6a**), Eu (**6b**), Yb (**6c**).

Scheme 1. Molecular structure of betaine dyes **1–5** and the NMR shift reagents Ln(dpm)$_3$ **6a–c**.

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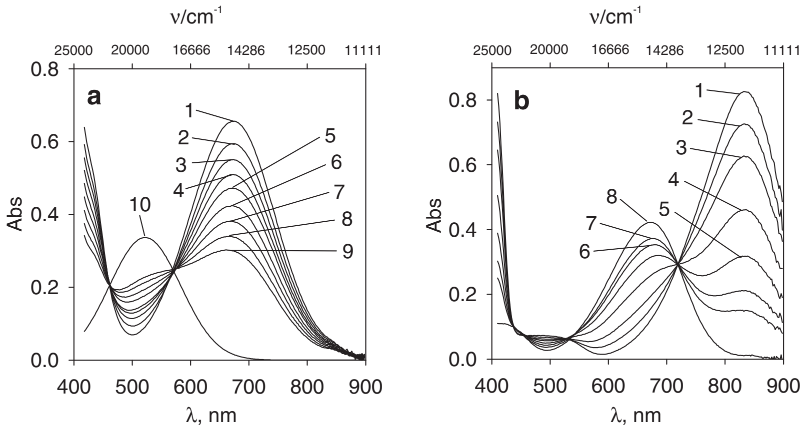

Figure 1. (a) Visible absorption spectra of pyridinium-*N*-phenolate **2** ($c = 1.0 \times 10^{-4}$ M, 1.00 cm cell), measured in acetone at 25 °C with increasing amounts of added Yb(dpm)$_3$: c(Yb(dpm)$_3$) = 0 (1); 2.0×10^{-4} (2); 5.0×10^{-4} (3); 8.0×10^{-4} (4); 12.0×10^{-4} (5); 18.0×10^{-4} (6); 26.0×10^{-4} (7); 36.0×10^{-4} (8); and 48.0×10^{-4} M (9); the calculated visible spectrum of the 2/Yb(dpm)$_3$ associate (10). (b) Visible absorption spectra of pyridinium-*N*-phenolate **5** ($c = 1.00 \times 10^{-3}$ M, 0.10 cm cell), measured in benzene at 25 °C with increasing amounts of added Eu(dpm)$_3$: c(Eu(dpm)$_3$) = 0 (1); 0.30×10^{-3} (2); 0.40×10^{-3} (3); 0.60×10^{-3} (4); 0.80×10^{-3} (5); 1.00×10^{-3} (6); 1.20×10^{-3} (7); 10.0×10^{-3} M (8).

but produce hypsochromic band shifts of up to $\Delta\nu = (2.6–4.8) \times 10^3$ cm^{-1}. In this case, the spectra of dyes **1–5** change, with increasing concentration of Ln(dpm)$_3$, in a similar manner, as shown in Figure 1, with a distinct isosbestic point. The corresponding Ln(dpm)$_3$-induced hypsochromic band shifts of dyes **1–5** are collected in Table 1.

On processing the experimental visible spectral data by standard methods, it was found that interaction of the basic betaine oxygen center with the electrophilically neutral Ln(dpm)$_3$ complexes can be satisfactorily described in terms of the formation of 1:1 associate. The association constants, K_{ass}, for the formation of the $^{+}$D^{-}/Ln(dpm)$_3$ associates, were determined in acetone for dyes **1–5** and are collected in Table 2. Similar Ln(dpm)$_3$-induced band shifts could be registered for the more lipophilic dye **5** in CCl$_4$ and benzene as solvents because of its better solubility in these nonpolar solvents (Fig. 1b), as well as in acetonitrile and DMSO, in which, however, the lanthanide complexes **6a–c** are less soluble, and eventually in CHCl$_3$, in which the $^{+}$D^{-}/Ln(dpm)$_3$ formation is somewhat weaker. As a result of the sufficient solubility of both components in acetone, this solvent seems to be the best for this type of investigation.

The dyes **1–5** were synthesized as reported earlier,[1,5d] and the Ln(dpm)$_3$ reagents were prepared as described.[16] The dyes, except **3**, are actually crystal hydrates.[5d] Therefore, they were dried in vacuo at 120 °C for 6 h before the measurements. All lanthanide chelates are very hygroscopic and should be handled with care. On absorption of water, their shifting power is reduced drastically. Therefore, in insufficiently dried solvents, the calculated K_{ass} values would be underestimated. It should be mentioned that storing the betaine dyes in CHCl$_3$ and CCl$_4$ solutions for long times can lead to irreversible decoloration.

Table 1
Hypsochromic shifts of the visible absorption maxima of betaine dyes **1**–**5**, caused by addition of Ln(dpm)$_3$ **6a**–**c**, measured in acetone, benzene, and tetrachloromethane CCl$_4$ at room temperature

Betaine dye (solvent)	$\Delta\nu_{max} \times 10^{-3}$/cm^{-1} ($\Delta\lambda$/nm)		
	6a	**6b**	**6c**
1 (Acetone)	–	2.62 (73)	–
2 (Acetone)	4.00 (142)	3.76 (135)	4.25 (149)
3 (Acetone)	4.82 (201)	4.47 (184)	4.34 (183)
4 (Acetone)	4.13 (108)	3.40 (88)	3.22 (85)
5 (Acetone)	3.73 (143)	3.51 (137)	2.98 (114)
5 (Benzene)	3.06 (170)	2.90 (163)	2.76 (157)
5 (CCl$_4$)	2.72 (170)	2.58 (163)	2.43 (155)

Table 2
Calculated K_{ass} values for the formation of the $^{+}$D^{-}/Ln(dpm)$_3$ associates

Betaine dye (solvent)	$K_{ass} \times 10^{-3}$/M^{-1}		
	6a	**6b**	**6c**
1 (Acetone)	–	21.0 ± 1.6	–
2 (Acetone)	4.3 ± 0.1	1.57 ± 0.05	0.361 ± 0.008
3 (Acetone)	61.0 ± 1.5	4.5 ± 0.2	0.381 ± 0.006
4 (Acetone)	5.06 ± 0.03	1.47 ± 0.04	0.634 ± 0.003
5 (Acetone)	3.79 ± 0.01	1.81 ± 0.01	0.202 ± 0.004
5 (Benzene)	39 ± 3	16.6 ± 0.7	1.44 ± 0.04

The largest Ln(dpm)$_3$-induced band shift was exhibited by dye **3** (Table 1); the K_{ass} values for this dye are also rather high (Table 2). It should be noted that the interaction of **3** with H^{+} is the strongest of the compared betaine dyes.[17] On going from acetone to benzene as solvent, an increase in K_{ass} by one order of magnitude was registered for dye **5** (Table 2), which reflects the strengthening of the $^{+}$D^{-}/Ln(dpm)$_3$ interaction in nonpolar solvents. It should be noted that both the λ_{max} of the free dye **5** and of its associates are substantially higher in nonpolar solvents as compared with that in acetone.

The formation of the $^{+}$D^{-}/Ln(dpm)$_3$ associate can be described in terms of a weak Lewis acid/base interaction. The formation of the associate between Ln(dpm)$_3$ and pyridinium-*N*-phenolates depends on electronic and steric factors. According to the McConnell–Robertson relationship, the ^{1}H NMR pseudocontact shift is inversely proportional to a geometric factor in the following manner:[15a] $\Delta\nu_i/\nu_i = [K\cdot(3\cdot\cos 2\Theta_i - 1)]/r_i^3$. Here r_i is the distance between the lanthanide-ion and the i-th H-atom, Θ_i is the angle between this distance vector and the principal magnetic dipolar axis of the complex, K is a constant characteristic of the magnetic susceptibility of the metal-ion. Therefore, the principal factor influencing the shift of a particular ^{1}H NMR signal is the distance between the metal-ion and the signal-producing H-atom.

The rather small lanthanide-induced ^{1}H NMR chemical shifts ($\Delta\delta$ <1 ppm), observed for the signals produced by the H-atoms of the phenolate moiety in the presence of Eu(dpm)$_3$ in CDCl$_3$ or CD$_3$COCD$_3$, are probably the result of steric hindrance in the associate formed between the phenolate oxygen and the lanthanide-ion, as well as by the efficient delocalization of the negative charge of the phenolate oxygen into the phenolate ring. Even for compound **1**, without bulky substituents (R^2 = H), the tight interaction appeared to be less probable. Thus, this associate should also be considered as a solvent-shared one. Moreover, $CDCl_3$ is capable of forming weak hydrogen bonds with the phenolate oxygen and the π-system of both partners, thus inhibiting further the approach of both associate-forming components. The decrease in stability of the $^+D^-/Ln(dpm)_3$ associates in the sequence **6a**→**6b**→**6c** is in line with the 'lanthanide contraction'.

Our results clearly demonstrate that pyridinium-*N*-phenolate betaine dyes are not only suitable for the solvent polarity determinations, but can also be used for the UV–vis spectroscopic study of weak specific Lewis acid/base interactions, as shown by their association with lanthanide complexes in solution. We anticipate that the results obtained will be useful in studying the electrophilicity of further neutral species by means of such weak Lewis-basic solvatochromic betaine dyes.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.06.057.

References and notes

1. (a) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, 2003. Chapter 7, pp 389–469; (b) Reichardt, C. *Pure Appl. Chem.* **2004**, *76*, 1903–1919; (c) Reichardt, C. *Pure Appl. Chem.* **2008**, *80*, 1415–1432.
2. Reichardt, C. *Green Chem.* **2005**, *7*, 339–351.
3. (a) Langhals, H. *Angew. Chem.* **1982**, *94*, 739–749; *Angew. Chem., Int. Ed. Engl.*. **1982**, *21,* 724–733.; (b) Vitha, M. F. *J. Chem. Educ.* **2001**, *78*, 370–372; (c) Machado, C.; Machado, V. G. *J. Chem. Educ.* **2001**, *78*, 649–651.
4. (a) Spange, S.; Vilsmeier, E.; Zimmermann, Y. *J. Phys. Chem. B* **2000**, *104*, 6417–6428; (b) Khristenko, I. V.; Kholin, Yu. V.; Mchedlov-Petrossyan, N. O.; Reichardt, C.; Zaitsev, V. N. *Kolloidny Zh.* **2006**, *68*, 558–565; *Colloid J. (Russian Acad. Sci.)* **2006**, *68*, 511–517.; (c) Mchedlov-Petrossyan, N. O. *Pure Appl. Chem.* **2008**, *80*, 1459–1510.
5. (a) Zachariasse, K.; Van Phuc, N.; Kozankiewicz, B. *J. Phys. Chem.* **1981**, *85*, 2676–2683; (b) Drummond, C. J.; Grieser, F.; Healy, T. W. *Faraday Discuss. Chem. Soc.* **1986**, *81*, 95–106; (c) Kessler, M. A.; Wolfbeis, O. S. *Chem. Phys. Lipids* **1989**, *50*, 51–56; (d) Mchedlov-Petrossyan, N. O.; Vodolazkaya, N. A.; Kornienko, A. A.; Karyakina, E. L.; Reichardt, C. *Langmuir* **2005**, *21*, 7090–7096.
6. Mchedlov-Petrossyan, N. O.; Isaenko, Yu. V.; Goga, S. T. *Russ. J. Gen. Chem.* **2004**, *74*, 1741–1747.
7. Gorbenko, G. P.; Mchedlov-Petrossyan, N. O.; Chernaya, T. A. *J. Chem. Soc., Faraday Trans.* **1998**, *94*, 2117–2125.
8. (a) Pan, Y.; Ford, W. T. *Macromolecules* **2000**, *33*, 3731–3738; (b) Morgan, M. T.; Carnahan, M. A.; Finkelstein, S.; Prata, C. A. H.; Degoricija, L.; Lee, S. J.; Grinstaff, M. W. *Chem. Commun.* **2005**, 4309–4311.
9. (a) Sutherland, I. O.; Dolman, M. *J. Chem. Soc., Chem. Commun.* **1993**, 1793–1795; (b) Venturini, G. C.; Andreaus, J.; Machado, V. G.; Machado, C. *Org. Biomol. Chem.* **2005**, *3*, 1751–1756.
10. Rottman, C.; Avnir, D. *J. Am. Chem. Soc.* **2001**, *123*, 5730–5734.
11. (a) Zimmermann-Dimer, L. M.; Reis, D. C.; Machado, C.; Machado, V. G. *Tetrahedron* **2009**, *65*, 4239–4248; (b) Zimmermann-Dimer, L. M.; Machado, V. G. *Dyes Pigm.* **2009**, *82*, 187–195.
12. For typical example, see: (a) Seeboth, A.; Kriwanek, J.; Vetter, R. *J. Mater. Chem.* **1999**, *9*, 2277–2278; (b) Zhang, C.; Suslick, K. S. . *J. Am. Chem. Soc.* **2005**, *127*, 11548–11549; (c) Fiorilli, S.; Onida, B.; Barolo, C.; Viscardi, G.; Brunel, D.; Garrone, E. *Langmuir* **2007**, *23*, 2261–2268.
13. (a) Hollmann, G.; Vögtle, F. *Chem. Ber.* **1984**, *117*, 1355–1363; (b) Pocker, Y.; Ciula, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4728–4735; (c) Gageiro, V.; Aillon, M.; Rezende, M. C. *J. Chem. Soc., Faraday Trans.* **1992**, *88*, 201–204; (d) Binder, D. A.; Kreevoy, M. M. *J. Phys. Chem.* **1994**, *98*, 10008–10016.
14. (a) Hachisako, H.; Ryu, N.; Hashimoto, H.; Murakami, R. *Org. Biomol. Chem.* **2009**, *7*, 2338–2346; (b) Sinkeldam, R. W.; Greco, N. J.; Tor, Y. *ChemBioChem* **2008**, *9*, 706–709.
15. (a) Cockerill, A. F.; Davis, G. L. O.; Harden, R. C.; Rackham, D. M. *Chem. Rev.* **1973**, *73*, 553–588; (b)*Nuclear Magnetic Resonance Shift Reagents*; Sievers, R. E., Ed.; Academic Press: New York, 1973.
16. (a) Kopecky, K. R.; Nonhebel, D.; Morris, G.; Hammond, G. S. *J. Org. Chem.* **1962**, *27*, 1036–1037; (b) Eisentraut, K. J.; Sievers, R. E. *J. Am. Chem. Soc.* **1965**, *87*, 5254–5256.
17. Mchedlov-Petrossyan, N. O.; Isaenko, Yu. V.; Goga, S. T.; Vilkova, L. N.; Borodenko, V. I.; Shekhovtsov, S. V.; Reichardt, C. *Ukr. Khim. Zh. (Russ. Ed.)* **2007**, *73*, 118–123.