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Substituent Effects on the Solvatochromism of 2-Phenylimidazopyrazinones: Effective Control of the Color Variation Range and Sensitivity toward an Indication of the Proton-donor Ability of Solvents by an Electron-withdrawing Group Substitution

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A *para*-substitution on the phenyl group of 2-phenylimidazopyrazinone successively resulted in a change of the solvatochromic property, especially of the color-variation range and sensitivity to solvents, demonstrating that derivatives possessing an electron-withdrawing group are preferable as potential indicators of the proton-donor ability of solvents.

The imidazo[1,2-*a*]pyrazin-3(7*H*)-one (imidazopyrazinone) ring (Chart 1) is an essential core structure of bioluminescence[1] and chemiluminescence.[2] In addition to the luminescent properties, a series of imidazopyrazinone derivatives exhibit a unique solvatochromism originating from the hydrogen-bonding interaction between a carbonyl group of imidazopyrazinone (hydrogen-bond acceptor) and protic solvent molecules (hydrogen-bond donor).[3] Because the colors of imidazopyrazinone solutions depend on the strength of the hydrogen-bonding interaction, imidazopyrazinones are applicable as colorimetric sensors of the proton-donor abilities of solvents. In fact, it was recently found that the 2-phenylimidazopyrazinone derivative (**1c**) acts as a potential indicator in various solvents, while the corresponding 2-methyl derivative does not.[3] To gain further insights into control of the color variation range and sensitivity toward the proton-donor ability of solvents, we studied the substituent effects on the solvatochromic property of **1c** using *para*-substituted derivatives (Chart 1, **1a**, R = $N(CH_3)_2$; **1b**, R = OCH_3; **1d**, R = Cl; **1e**, R = CN).[4] In this paper, we report that the spectroscopic characteristic of 2-phenylimidazopyrazinones **1** is readily modulated by the substitution of R, and that derivatives **1** with an electron-withdrawing group R are preferable as potential indicators of the proton-donor ability of solvents.

The UV–vis absorption spectra of **1a**–**1e** in water, alcoholic solvents, acetic acid, chloroform, acetonitrile, and DMSO were measured; those of **1a**, **1c**, and **1e** are shown in Figure 1. The colors of **1c** and **1e** in solutions varied from red to yellow and from pink to orange, depending on the solvent, respectively, while those of **1a** showed a small change from dark to pale orange.[6]

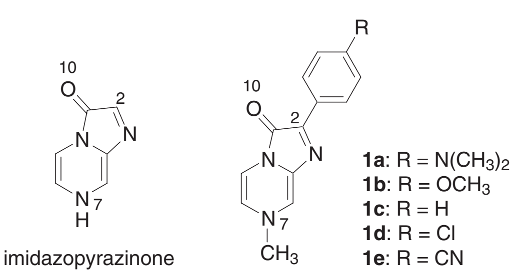


Chart 1.

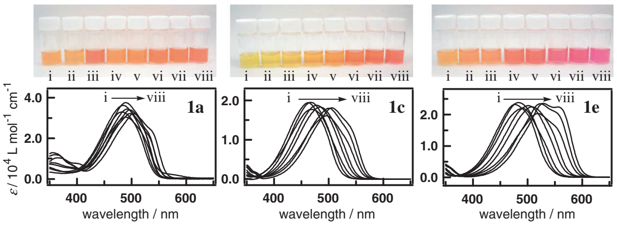


Figure 1. Graduated changes of colors and UV–vis absorption spectra of **1a**, **1c**, and **1e** in various solvents: (i) 2,2,2-trifluoroethanol ($\alpha = 1.51$), (ii) water ($\alpha = 1.17$), (iii) acetic acid ($\alpha = 1.12$), (iv) methanol ($\alpha = 0.93$), (v) 2-propanol ($\alpha = 0.76$), (vi) chloroform ($\alpha = 0.44$), (vii) acetonitrile ($\alpha = 0.19$), and (viii) DMSO ($\alpha = 0.00$).

The wavenumbers (ν in cm^{-1}) of the lowest energy bands of **1a**–**1e** are linearly correlated to Kamlet–Taft's α value (Figure 2),[7,8] indicating that the hydrogen-bonding interaction between **1a**–**1e** (hydrogen-bond acceptor) and the solvent molecules (hydrogen-bond donor) regulates the solvatochromism.[3] The linear lines were obtained as follows: **1a**: $\nu = 550\alpha + 19920$ ($r = 0.94$), **1b**: $\nu = 1110\alpha + 19970$ ($r = 0.99$), **1c**: $\nu = 1360\alpha + 19690$ ($r = 0.99$), **1d**: $\nu = 1340\alpha + 19540$ ($r = 0.99$), and **1e**: $\nu = 1420\alpha + 18770$ ($r = 0.98$). The slope gradually increases with increasing the electron-withdrawing property of R: **1a** $\ll$ **1b** $<$ **1c** $\approx$ **1d** $<$ **1e**. In particular, the value of **1a** (R = $N(CH_3)_2$) is remarkably small. On the other hand, the intercept gradually decreases with increasing the electron-withdrawing property of R: **1a** $\approx$ **1b** $>$ **1c** $>$ **1d** $\gg$ **1e**. Especially, a significantly small value was found for **1e** (R = CN).

The smallest slope value of **1a** among **1a**–**1e** was readily explained by AM1 COSMO calculations ($\varepsilon = 46.5$ for DMSO).[9,10]

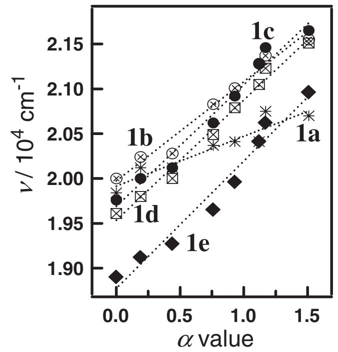
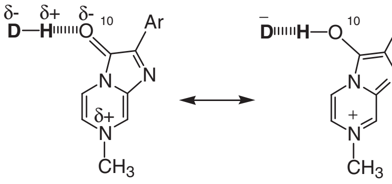


Figure 2. Plots of wavenumbers ν (cm^{-1}) of the lowest energy bands for **1a**–**1e** against Kamlet–Taft's α values: **1a** (✳), **1b** (⊗), **1c** (●), **1d** (☒), and **1e** (◆).



I **II**

Scheme 1.

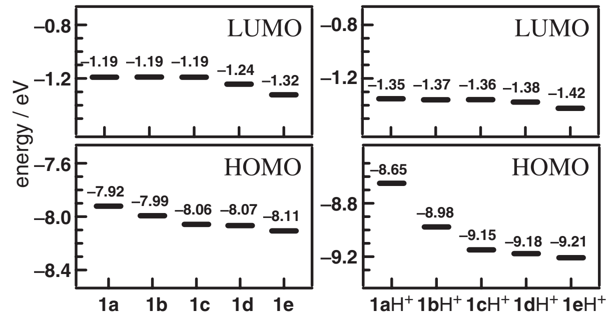


Figure 3. Energy levels of HOMO and LUMO for **1a**–**1e** and protonated molecules **1a**H^+–**1e**H^+ calculated with the AM1-COSMO method ($\varepsilon = 46.5$ for DMSO).

The HOMO and LUMO energy levels of **1a**–**1e** and the corresponding protonated molecules **1a**H^+–**1e**H^+ were calculated,[11] because the hydrogen-bonded structure of **1a**–**1e** with a solvent molecule (D–H) is depicted by resonance structures **I** and **II**, possessing neutral and protonated imidazopyrazinone parts, respectively (Scheme 1).[3] As summarized in Figure 3, the HOMO–LUMO energy gap of **1a**H^+ (R = $N(CH_3)_2$) is the smallest among **1a**H^+–**1e**H^+ because of a steep rise of the HOMO level, while the HOMO–LUMO energy gaps of **1a**–**1e** do not change very much. The resulting difference (0.57 eV) in the HOMO–LUMO energy gaps between **1a** and **1a**H^+ is much smaller than those (0.8–1.0 eV) of other derivatives. Thus, this reasonably explains the observation that **1a** had the smallest slope of the α–ν correlation.

Interestingly, however, the significantly small intercept of **1e** (R = CN) could not be explained only by changes of the HOMO–LUMO energy gaps. This may be attributed to a specific solvation, which is not considered in the AM1-COSMO calculation, because **1e** has a large calculated dipole moment (24 D) compared to the others (18–22 D), which may work for an electrostatic interaction with solvent molecules.

In conclusion, we found that the *para*-substituent R on the phenyl group efficiently modulates the solvatochromic property of 2-phenylimidazopyrazinones **1**. In particular, the α–ν correlations revealed that the small intercept and the steep slope of **1e** (R = CN) lead to a wide color variation range and a high sensitivity toward the proton-donor ability of solvents. Therefore, 2-phenylimidazopyrazinone derivatives **1** possessing an electron-withdrawing group on *para*-position are preferable as potential indicators of the proton-donor ability of solvents.

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4 Imidazopyrazinones **1a**–**1e** were prepared by *N*-methylation of the corresponding 7-NH derivatives.[3,5] Satisfactory elemental microanalyses were obtained for all new compounds in this report. Selected data were as follows. **1a**: red powder, mp 220 °C (dec.); ^{1}H NMR (CD_3OD) δ 8.32 (2H, m), 7.69 (1H, d, $J = 1.3$ Hz), 7.48 (1H, d, $J = 5.9$ Hz), 6.88 (1H, dd, $J = 5.9$, 1.3 Hz), 6.82 (2H, m), 3.71 (3H, s), 3.04 (6H, s); IR (KBr) 1675, 1604, 1533 cm^{-1}; EIMS m/z 268 (M^+, 100), 94 (98). **1b**: red powder, mp 205 °C (dec.); ^{1}H NMR (CD_3OD) δ 8.39 (2H, m), 7.85 (1H, d, $J = 1.3$ Hz), 7.54 (1H, d, $J = 5.6$ Hz), 7.01 (2H, m), 6.93 (1H, dd, $J = 5.6$, 1.3 Hz), 3.86 (s, 3H), 3.74 (s, 3H); IR (KBr) 1670, 1587, 1515 cm^{-1}; EIMS m/z 255 (M^+, 100), 94 (70). **1d**: red powder, mp >250 °C; ^{1}H NMR (CD_3OD) δ 8.43 (2H, m), 8.05 (1H, d, $J = 1.3$ Hz), 7.64 (1H, d, $J = 5.9$ Hz), 7.45 (2H, m), 6.99 (1H, dd, $J = 5.9$, 1.3 Hz), 3.80 (3H, s); IR (KBr) 1668, 1592, 1494 cm^{-1}; EIMS m/z 259 (M^+, 62), 94 (100). **1e**: gold powder, mp >250 °C; ^{1}H NMR (CD_3OD) δ 8.61 (2H, m), 8.20 (1H, d, $J = 1.3$ Hz), 7.79 (2H, m), 7.72 (1H, d, $J = 5.9$ Hz), 7.03 (1H, dd, $J = 5.9$, 1.3 Hz), 3.84 (3H, s); IR (KBr) 2223, 1666, 1594, 1506 cm^{-1}; EIMS m/z 250 (M^+, 81), 94 (100).

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11 Each of **1a**H^+–**1e**H^+ has a proton at the O10. AM1-COSMO calculations showed that the O10 atoms of **1a**–**1e** are the most negatively charged (net atomic charge = ca. −0.6) among all the atoms, supporting that the O10 atoms are the key participants for the hydrogen-bonding interactions with solvent molecules.

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