# Theoretical Study of the Solvatochromic Properties of Rhodamines using the AM1 and PM3/COSMO Solvation Model†

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AM1 and PM3 SCF-MO/COSMO solvation modelling of the solvatochromic properties of the rhodamine-based colour forming dyes reproduces the known relative stabilities of these molecules and demonstrates how theoretically constructed linear-free-energy relationships could be used in the rational design of new systems.

There is considerable current interest in the solvatochromic properties of betaine dyes such as the Reichardt systems[1] or the industrially important colour formers based on the rhodamine ring system.[2] In this latter system, an equilibrium between a neutral colourless form (*e.g.* **1**) and an intensely coloured quinoid form (*e.g.* **2**) is dependent almost entirely on the polarity of the surrounding medium. Rational design of such systems involves, *inter alia*, a delicate positioning of this equilibrium such that the colour forms only when needed. In systems such as rhodamine B (**1**, $X = O$, $R^1 = R^2 = NH_2$),[2] this can be achieved by fine tuning the substituents R^1 and R^2, as well as by adjusting the nature of X. We report in this paper an SCF-MO investigation of the rhodamine equilibria using the AM1 and PM3 COSMO solvation model.

1a, X = O
1b, X = NH

2a, X = O
2b, X = NH

3a, X = O
3b, X = NH

4a, X = O
4b, X = NH
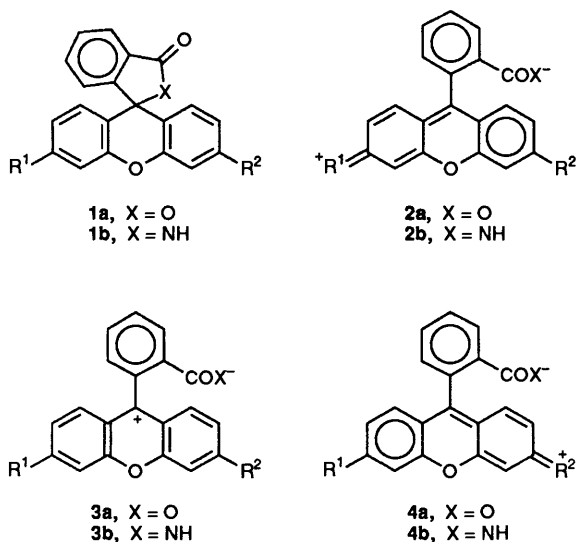
Theoretical studies of systems such as **1** have been limited to spectral studies,[3] rather than to the position of the solvent-sensitive equilibrium. In part, this has been due to the relatively poor solvation models that can be applied to large organic molecules, particularly when geometry optimisation is essential. Recent progress in developing continuum solvation models such as the COSMO method[4] now enables calculation of enthalpies and free energies of such equilibria.[5] We show here that application of the COSMO/semiempirical AM1 or PM3 model enables theoretically estimated linear free energy relationships (LFER) for systems such as **1** to be evaluated, and geometrical responses to solvation to be estimated.

The calculated gas phase enthalpy (ΔH_g) for the open

zwitterionic forms **2a** ($R^2 = NH_2, OMe, H, Cl, CO_2, CN, NO_2$) is 50–56 or 38–45 kcal mol^{-1} higher than **1a** at the PM3 or AM1 levels,§ values similar to the glycine equilibrium.[7] For $R^1 = R^2 = NH_2$ at the COSMO/AM1 level, the quinonoid form is predicted to be more stable in water [$\Delta\Delta H_{aq}$ (**2a**) − $\Delta\Delta H_{aq}$(**1a**) = −2.7 kcal mol^{-1}], as found experimentally.[8] This value is little changed when corrected to $\Delta\Delta G_{aq}$ (−2.8 kcal mol^{-1}) using the vibrationally estimated entropies. To see how such theoretically derived energetics might be used in linear free-energy relationships, we initially plotted both $\Delta\Delta H_g$(**2a**) − $\Delta\Delta H_g$(**1a**) and $\Delta\Delta H_{aq}$(**2a**) − $\Delta\Delta H_{aq}$(**1a**), $R^1 = NH_2$ against the Hammett σ_p value of R^2. The plots are reasonably linear ($r^2 = 0.94$–0.96) for both the AM1 and PM3 methods (Fig. 1), suggesting a high degree of self-consistency in the theoretical procedure. Indeed, we expect that such correlations may prove a good test of new parameters derived for other elements.

Several interesting trends are discernible from the slopes of these plots. Firstly, for $R^1 = NH_2$, the gas phase slopes (5.2/AM1, 4.9/PM3) are significantly larger than the COSMO solution values (2.9/AM1, 0.85/PM3). If $R^1 = H$, this reduction is attenuated from 7.3 (AM1) and 7.1 (PM3) to 5.9 (AM1) and 5.0 (PM3). Secondly, the R^1 substituent attenuates the electronic effect of the R^2 group (Fig. 2). In this, the PM3 effect (*e.g.* slopes of 5.0 and 0.85 for $R^1 = H$ and NH_2, respectively) is more pronounced than the AM1 effect (5.9 and 2.9).

We also investigated the effect of entropy by correcting $\Delta\Delta H$ to $\Delta\Delta G$. Correlating this with the Hammett σ_p value produces a slope which is formally equivalent to the Hammett ρ values. This entropic correction has almost no effect on the slopes derived from $\Delta\Delta H_g$, but appears to induce a small increase compared with those derived from $\Delta\Delta H_{aq}$, indicating that entropic factors can indeed play a role in free energy relationships. The use of $\Delta\Delta G_{ag}$ values also produces more scatter in the Hammett plots, possibly due to errors in calculating low frequency modes in the contributions to ΔS_{aq}. In all cases, the point corresponding to $R^2 = CN$ deviates significantly, suggesting a systematic error in both the AM1 and PM3 for this particular substituent. The corresponding lactams (X = NH) show similar behaviour (Fig. 3), although the

† Non-S.I. unit employed: 1 cal = 4.18 J.
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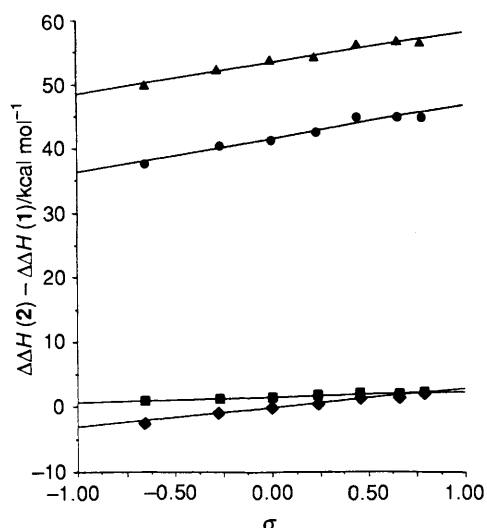
Fig. 1 Plot of the Hammett σ_p substituent constant for R^1 = NH$_2$ for (◆) $\Delta\Delta H_{aq}(2a)$ − $\Delta\Delta H_{aq}(1a)$/AM1; (■) $\Delta\Delta H_{aq}(2a)$ − $\Delta\Delta H_{aq}(1a)$/PM3; (●) $\Delta\Delta H_g(2a)$ − $\Delta\Delta H_{aq}(1a)$/AM1; (▲) $\Delta\Delta H_g(2a)$ − $\Delta\Delta H_g(1a)$/PM3

Fig. 2 Plot of the Hammett σ_p substituent constant for R^1 = H for (◆) $\Delta\Delta H_{aq}(2a)$ − $\Delta\Delta H_{aq}(1a)$/AM1; (■) $\Delta\Delta H_{aq}(2a)$ − $\Delta\Delta H_{aq}(1a)$/PM3; (●) $\Delta\Delta H_g(2a)$ − $\Delta\Delta H_g(1a)$/AM1; (▲) $\Delta\Delta H_g(2a)$ − $\Delta\Delta H_g(1a)$/PM3

equilibrium is predicted to favour the closed neutral form by a substantial margin under all circumstances. The calculated COSMO geometries reveal some interesting trends. With the PM3 method and R^1 = NH$_2$, all the calculated geometries show bond localisation as in **2**, even when R^1 = R^2 = NH$_2$, whereas with AM1, this latter combination, and also to some extent R^1 = NH$_2$, R^2 = OMe, are more delocalised, as in **3**. In one instance (R^1 = NH$_2$, R^2 = Cl, PM3), we were able to locate two valence isomers differing in energy by 17.3 kcal mol^{-1}, the lower energy one corresponding to **2** r_{NC} 1.317, r_{CIC} 1.683 Å), the other to **4** (r_{NC} 1.42, r_{CIC} 1.462 Å).

For the series R_1 = H, differing geometrical behaviour was observed. With the exception of R^2 = NH$_2$, all the geometries were analogous to **3**, whilst with R^2 = NH$_2$ only, localisation to the quinoid form **2** occurred at both the AM1 and PM3 levels. This effect is also visible in the Hammett plots, the values of $\Delta\Delta H_{aq}$ and $\Delta\Delta G_{aq}$ for this substituent deviating significantly from the regression line formed by the other substituents (Fig. 2). For this reason, these points are excluded from the regression
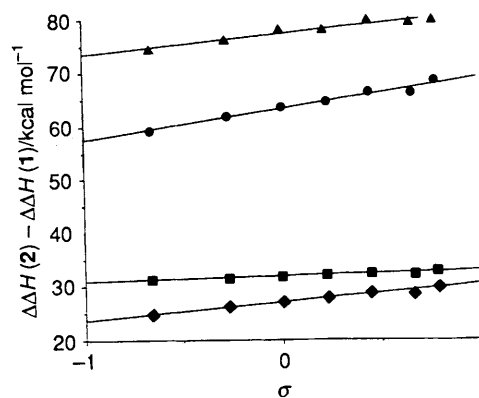

Fig. 3 Plot of the Hammett σ_p substituent constant for R^1 = NH$_2$ for (◆) $\Delta\Delta H_{aq}(2b)$ − $\Delta\Delta H_{aq}(1b)$/AM1; (■) $\Delta\Delta H_{aq}(2b)$ − $\Delta\Delta H_{aq}(1b)$/PM3; (●) $\Delta\Delta H_g(2b)$ − $\Delta\Delta H_g($ − $(1b)$/AM1; (▲) $\Delta\Delta H_g(2b)$ − $\Delta\Delta H_g(1b)$/PM3

slopes noted above. One explanation for this anomalous behaviour might lie in the neglect in the COSMO model of terms corresponding to the cavitation and dispersion free energies, which are generally taken as being proportional to the solute surface area.[9] Whilst these terms would be expected to cancel for a homologous series of compounds, this would not be true if any unusual changes in surface area between **1** and **2** or **3** due to bond localisation occurred. In practice, we found the changes in surface area between **1** and **2** are small and show no correlation with the R^1 = NH$_2$ substituent. The abnormal behaviour for this system therefore remains unclear.

We conclude that the application of the COSMO method allows the effect of substituents on solvatochromic equilibria involving major changes in substrate polarity to be studied theoretically in a systematic way.

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