JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2001; **14:** 247–255

Linear solvation energy (LSE) correlations of the solvatochromic response and x-ray structure analysis of hydrophilically *N*-substituted Michler's ketone derivatives

Mohamed El-Sayed,[1] Hardy Müller,[1] Gerd Rheinwald,[2] Heinrich Lang[2] and Stefan Spange[1]*

[1]Department of Polymer Chemistry, Institute of Chemistry, Chemnitz University of Technology, Strasse der Nationen 62, D-09111 Chemnitz, Germany
[2]Department of Inorganic Chemistry, Institute of Chemistry, Chemnitz University of Technology, Strasse der Nationen 62, D-09111 Chemnitz, Germany

Received 1 September 2000; revised 18 December 2000; accepted 18 December 2000

ABSTRACT: Bathochromic UV–Vis spectral shifts of two hydrophilically *N*-substituted Michler's ketone derivatives, 4,4′-bis[di(2-hydroxyethyl)amino]benzophenone [MK$(OH)_4$] (**1**) and 4-(dimethylamino)-4′-[di(2-hydroxyethyl)-amino]benzophenone [MK$(OH)_2$] (**3**), were measured in 28 solvents of different polarity. For MK$(OH)_4$ and MK$(OH)_2$ in non-polar, dipolar aprotic and hydrogen-bonding solvents, the solvatochromic responses of the two solutes conform exactly to the requirements of the Kamlet-Taft linear solvation free energy model of solvent–solute interactions. The contribution of the hydrogen-bond accepting property of the solvent on the bathochromic band shift of MK$(OH)_4$ and MK$(OH)_2$ increases with increasing number of their OH groups at the N-substituent. The x-ray crystallographic analysis for MK$(OH)_2$ reveals the presence of strong intermolecular hydrogen bonds between the carbonyl oxygen atom and the 2-hydroxyethyl group, which plays a significant role in the colour of the crystals. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: LSE correlations; Michler's ketone; solvatochromism; substituent effects; 4-(dimethylamino)-4′-[di(2-hydroxyethyl)amino]benzophenone; x-ray crystal structure analysis

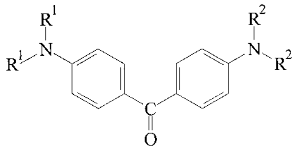
INTRODUCTION

Quantification of the general properties of solvents and micelle environments has been studied by physical organic chemists for many years.[1] The responses of solvatochromic indicators on changing solvent environments have been used as the phenomenological basis for several empirical 'solvent polarity' scales.[1b] Among such quantitative scales, the Kamlet–Taft system[2] is the most comprehensive with respect to all solvent types and it is well supported by theoretical reaction field models for the solvent influences upon the solvatochromic probes.[3,4] The simplified linear solvation energy (LSE) relationship in the Kamlet–Taft system is given by the equation[2]

$$XYZ = (XYZ)_0 + s(\pi^* + d\delta) + a\alpha + b\beta \qquad (1)$$

In this equation three major intrinsic solvent properties are included: the solvent's dipolarity-polarizability (π^* and its $d\delta$ correction term for the polarizability), hydrogen-bonding acidity (α) and hydrogen/bonding basicity (β). The coefficients s, d, a and b are solvent-independent coefficients reflecting the susceptibility of the solute property XYZ to the parameters π^*, δ, α and β. A wide variety of spectral probes have been used to determine the π^*, α and β values for solvents in addition to the usual solvatochromic UV–Vis indicators. For instance, solvent-dependent shifts from ^{19}F and ^{15}N NMR chemical shifts of suitable probes have been utilized in interpreting solvent effects.[5] Solvatochromic methods have also been used in order to characterize polar surfaces, such as alumina and silica.[6–8] The nature of the silica surface, for example, was found to be best described by both π^* and α.[7,8] The bare silica surface exhibits both HBD (hydrogen-bond donating) and dipolarity/polarizability properties which are differently reflected by the respective polar dye adsorbed on the surface. The early work with UV–Vis solvatochromic indicators employed relatively simple species, e.g. substituted nitroanilines; however, these studies were extended to merocyanines and betaines as the solvatochromic probes.[9] Recently, benzophenone and stilbene derivatives have been applied to dipolarity measurements of alkylbenzenes.[10]

**Correspondence to:* S. Spange, Department of Polymer Chemistry, Institute of Chemistry, Chemnitz University of Technology, Strasse der Nationen 62, D-09111 Chemnitz, Germany.
E-mail: stefan.spange@chemie.tu-chemintz.de
Contract/grant sponsor: Fonds der Chemischen Industrie.
Contract/grant sponsor: Deutsche Forschungsgemeinschaft.



Compound	Name	Substituent
1	4,4′-Bis[di(2-hydroxyethyl) amino]benzophenone	$R^1 = R^2$ $= CH_2CH_2OH$
2	4-(dimethylamino)-4′-[di(2-acetoxyethyl)amino]benzophenone	$R^1 = CH_3$ $R^2 = CH_2CH_2OCOCH_3$
3	4-(dimethylamino)-4′-[di(2-hydroxyethyl) -amino]benzophenone	$R^1 = CH_3$ $R^2 = CH_2CH_2OH$
4	4,4′-bis(dimethylamino) benzophenone	$R^1 = R^2$ $= CH_3$

Scheme 1. Different Michler's ketone derivatives: 4,4′-bis[di(2-hydroxyethyl)amino]benzophenone (**1**), 4-(dimethylamino)-4′-[di(2-acetoxyethyl)amino]benzophenone (**2**), 4-(dimethylamino)-4′-[di(2-hydroxyethyl)amino]benzophenone (**3**) and 4,4′-bis(dimethylamino)benzophenone (**4**)

4,4′-Bis(dimethylamino)benzophenone (Michler's ketone; MK) is one of the widely studied[11–15] positively solvatochromic compounds, which has a solvatochromic absorption range of $\Delta\lambda = 68$ nm ($\Delta\nu = 5080\ \mathrm{cm}^{-1}$) on going from *n*-hexane to 3-methoxyphenol as solvent.[14]

The application of MK (**4**) is limited because it is insoluble in water. As extension of our studies on MK (**4**),[14] we intended to prepare 4,4′-bis[di(2-hydroxyethyl)-amino] benzophenone, [MK(OH)$_4$] (**1**), [MK(OH)$_4$ (**1**) was mentioned in the summary of Ref. 16. However, neither the detailed synthesis nor its chemical structure data have been reported], and 4-(dimethylamino)-4′-[di(2-hydroxyethyl)amino] benzophenone, [MK(OH)$_2$] (**3**) (Scheme 1) in order to establish the strong positive solvatochromic effect for this type of hydrophilic compound. In addition, functional substituents (e.g. hydroxy groups) are useful for chemical incorporation of dye molecules in polymers or bonding to chiral groups. MK(OH)$_4$[16] and MK(OH)$_2$ are new compounds, the applications of which are based on their large variations in the visible spectrum as a function of the environmental polarity and the good solubility in all kinds of solvents, especially in water.

Table 1. UV–Vis absorption maxima for 4,4′-bis[di(2-hydroxyethyl)amino]benzophenone (**1**), 4-(dimethylamino)-4′-[di(2-hydroxyethyl)amino]benzophenone (**3**) and 4,4′-bis(dimethylamino)benzophenone (**4**)

Solvent	α[a]	β[a]	π^*[a]	ν_{max} (**1**) (10^{-3}cm^{-1})	ν_{max} (**3**) (10^{-3}cm^{-1})	ν_{max}[b] (**4**) (10^{-3}cm^{-1})
Triethylamine	0.00	0.71	0.14	28.82	29.33	29.68
Tetrachloromethane	0.00	0.00	0.28	Insoluble	29.24	29.24
Diethyl ether	0.00	0.47	0.27	29.07	29.15	No data
p-Xylene	0.00	0.12[c]	0.43	29.07	28.99	29.00
Toluene	0.00	0.11	0.54	28.74	28.9	28.92
Ethyl acetate	0.00	0.45	0.55	28.65	28.82	29.04
1,4-Dioxane	0.00	0.37	0.55	28.49	28.74	28.92
Tetrahydrofuran	0.00	0.55	0.58	28.49	28.74	28.84
Benzene	0.00	0.10	0.59	28.65	28.74	28.76
1,2-Dimethoxyethane	0.00	0.41	0.53	28.57	28.65	No data
Acetone	0.08	0.48	0.71	28.17	28.41	28.64
1,2-Dichloroethane	0.00	0.00	0.81	28.33	28.33	28.20
Acetonitrile	0.19	0.31	0.75	28.01	28.17	28.32
Chloroform	0.44[d]	0.00	0.58	28.41	28.09	28.04
Benzonitrile	0.00	0.41	0.90	27.78	27.78	27.88
N,*N*-Dimethylformamide	0.00	0.69	0.88	27.7	27.78	28.04
1,1,2,2-Tetrachloroethane	0.00[c]	0.00	0.95	27.86	27.78	27.88
Pyridine	0.00	0.64	0.87	27.62	27.7	27.88
Dimethyl sulfoxide	0.00	0.76	1.00	27.25	27.47	27.64
1-Butanol	0.79	0.88[d]	0.47	27.17	27.32	27.36
Ethanol	0.83	0.77[d]	0.54	27.17	27.25	27.32
Methanol	0.93	0.62[d]	0.60	27.03	27.03	27.08
Acetic acid	1.12	0.45[c]	0.64	26.67	26.67	26.68
Formamide	0.71	0.48[c]	0.97	26.53	26.6	26.64
1,2-Ethanediol	0.90	0.52[d]	0.92	26.46	26.46	26.40
Water	1.17	0.18[d]	1.09	25.97	26.11	Insoluble
2,2,2-Trifluoroethanol	1.51	0.00	0.73	26.32	25.91	25.76
1,1,1,3,3,3-Hexafluoro-2-propanol	1.96	0.00	0.65	25.51	25.00	24.96

[a] Solvatochromic parameters α, β and π^* from Ref. 2.
[b] Results from Ref. 14.
[c] Data from Ref. 19.
[d] Data are relatively less certain (see Ref. 2).

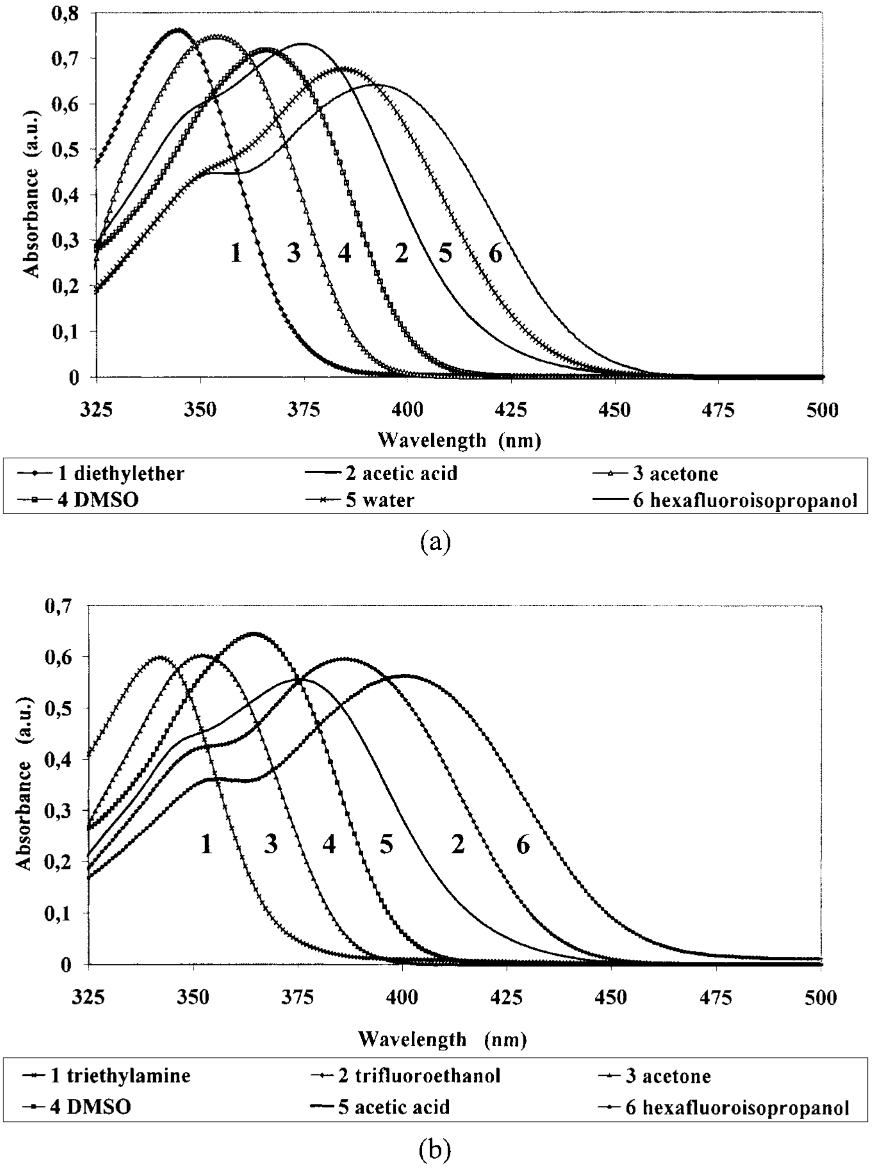


Figure 1. UV–Vis absorption spectra of (a) $MK(OH)_4$ and (b) $MK(OH)_2$, dissolved in different solvents with different polarity, i.e. water, triethylamine, diethyl ether, acetone, dimethyl sulfoxide (DMSO), acetic acid and hexafluoro-2-propanol

RESULTS AND DISCUSSION

Solvatochromic measurements

The long-wavelength UV–Vis absorption bands of $MK(OH)_4$ (**1**) and $MK(OH)_2$ (**3**) undergo a significant red shift with increasing polarity of the solvent (Table 1). This band shift can be analyzed by means of various solvatochromic scales.

For the evaluation of the solvatochromic properties of the probes $MK(OH)_4$ and $MK(OH)_2$, we chose the solvatochromic comparison method first introduced by Kamlet and Taft.[17,18] The absorption maxima of the solvatochromic UV–Vis bands of $MK(OH)_4$ and $MK(OH)_2$ were determined in 28 liquid solvents at 293 K (see Table 1). The solvents were selected in order to obtain large variations in the solvent parameters π^*, α and β.

Figure 1 shows the UV–Vis absorption spectra of $MK(OH)_4$ and $MK(OH)_2$ in six solvents of different polarity.

In the case of HBA and weak polar solvents such as diethyl ether, $MK(OH)_4$ and $MK(OH)_2$ show a symmetrical UV–Vis band because the n–π^* and π–π^* transitions interfere,[12] whereas in strong HBD solvents such as 2,2,2-trifluoroethanol (TFE), acetic acid, and water, an additional shoulder at about $\lambda = 300$ nm is observed which is probably caused by a separate n–π^*

Table 2. Values of the solvent-independent correlation coefficients (*a*, *b* and *s* of the Kamlet-Taft parameters α, β and π^*), solute property of a reference system $(XYZ)_0$, standard deviation (SD) and number of solvents (*n*) for the solvatochromism of $MK(OH)_4$, $MK(OH)_2$ and MK

Compound	$(XYZ)_0$	*a*	*b*	*s*	*r*	SD	Probe>*F*	*n*
$MK(OH)_4$	29.948	−1.472	−0.768	−1.995	0.992	0.134	<0.0001	27
	29.566	−1.423	–	−1.899	0.970	0.252	<0.0001	27
	29.575	–	−0.374	−2.527	0.568	0.857	0.00924	27
	28.602	−1.589	−0.664	–	0.890	0.474	<0.0001	27
	28.331	−1.546	–	–	0.873	0.498	<0.0001	27
	29.392	–	–	−2.471	0.559	0.846	0.00242	27
	27.767	–	−0.114	–	0.031	1.020	0.87725	27
$MK(OH)_2$	29.912	−1.661	−0.343	−2.005	0.990	0.168	<0.0001	28
	29.774	−1.643	–	−2.001	0.986	0.192	<0.0001	28
	29.656	–	−0.008	−2.761	0.575	0.956	0.00656	28
	28.642	−1.823	−0.328	–	0.901	0.507	<0.0001	28
	28.513	−1.806	–	–	0.898	0.505	<0.0001	28
	27.804	–	−0.061	–	0.015	1.146	0.93891	28
	29.653	–	–	−2.761	0.575	0.937	0.00136	28
MK	30.082	−1.809	−0.065	−2.236	0.992	0.152	<0.0001	25
	30.059	−1.807	–	−2.241	0.992	0.150	<0.0001	25
	28.644	−1.856	−0.151	–	0.899	0.527	<0.0001	25
	29.481	–	0.159	−2.490	0.468	1.065	0.06598	25
	28.585	−1.851	–	–	0.899	0.5172	<0.0001	25
	27.858	–	−0.070	–	0.018	1.178	0.93266	25
	29.534	–	–	−2.479	0.466	1.0426	0.0188	25

transition. For the regression analysis, only the intense absorption (π–π^* transition) at the longer wavelength was used.

Table 1 shows the UV–Vis absorption maxima of $MK(OH)_4$ (**1**) and $MK(OH)_2$ (**3**) compared with MK (**4**). This positive solvatochromism can be explained by the

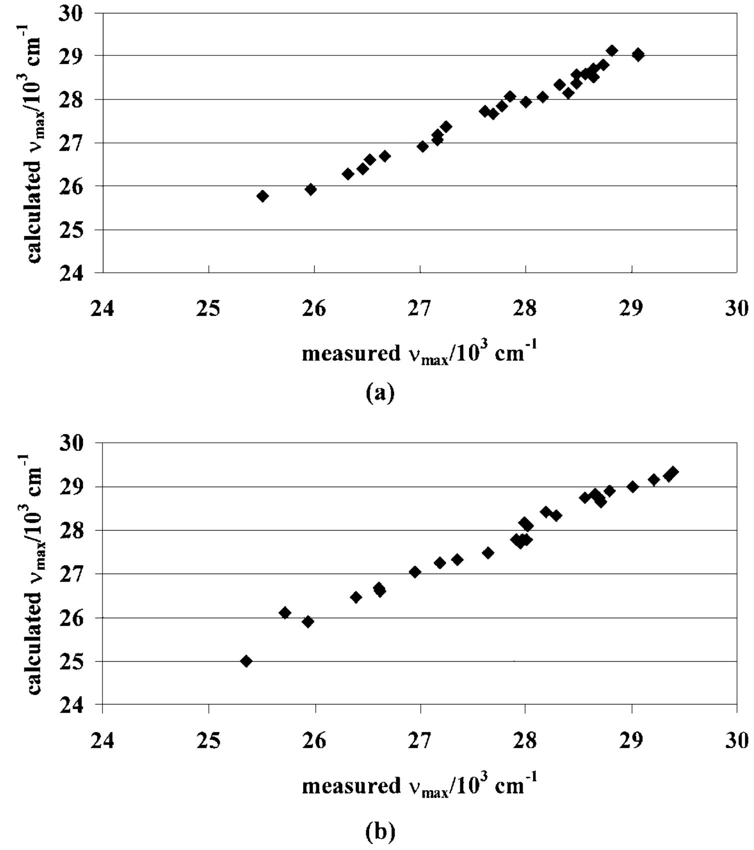


Figure 2. Relationships between calculated and measured ν_{max} values for (a) $MK(OH)_4$ and (b) $MK(OH)_2$ in 28 different solvents

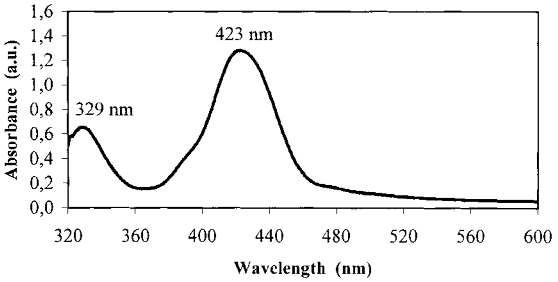


Figure 3. UV–Vis reflectance spectrum of $MK(OH)_2$ (**3**) as crystal powder in the solid state

assumption that the electronic ground state of $MK(OH)_4$, $MK(OH)_2$ and MK is less stabilized than the first excited state with increasing solvent polarity.[11–14]

The long-wavelength UV–Vis absorption maximum of $MK(OH)_4$ ranges from $\lambda = 344$ nm in diethyl ether to 392 nm in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), corresponding to $\Delta\lambda = 48$ nm ($\Delta\nu = 3560\ \text{cm}^{-1}$) stabilization energy over a wide range of solvent polarity. The solvatochromic band shift is even more pronounced for $MK(OH)_2$, ranging from $\lambda = 341$ nm in triethylamine (TEA) to 400 nm in HFIP, corresponding to $\Delta\lambda = 59$ nm ($\Delta\nu = 4330\ \text{cm}^{-1}$), whereas in the case of MK the shift ranges from $\lambda = 337$ nm in TEA to 401 nm in HFIP, corresponding to $\Delta\lambda = 64$ nm ($\Delta\nu = 4720\ \text{cm}^{-1}$).

The results of multiple linear regression analyses of the UV–Vis data from Table 1 according to Eqn (1) are summarized in Table 2.

The best regression fits obtained for $MK(OH)_4$ and $MK(OH)_2$ are given by Eqns (2) and (3), respectively and are shown in Fig. 2.

$$\nu_{\max} \times 10^{-3}[\text{MK(OH)}_4] = 29.948 - 1.995\pi^* - 1.472\alpha - 0.768\beta \quad (2)$$

$$n = 27;\ r = 0.992;\ \text{SD} = 0.134$$

$$\nu_{\max} \times 10^{-3}[\text{MK(OH)}_2] = 29.912 - 2.005\pi^* - 1.661\alpha - 0.343\beta \quad (3)$$

$$n = 28;\ r = 0.990;\ \text{SD} = 0.168$$

Note that Eqn (2) shows a significant dependence of the UV-Vis absorption maximum of $MK(OH)_4$ on both the π^* and α terms, as expected from the presence of both dipolar character and basic sites in the molecule. The strongest dependence of the UV–Vis absorption maximum of $MK(OH)_4$, however, is clearly on π^*. The coefficient b of the β-term in Eqn. (2) is twice as large as that in Eqn (3), whereas the solvatochromic band shift of pure Michler's ketone (MK) shows no dependence on the β term of the solvent.[14] Accordingly, the UV–Vis absorption bands of $MK(OH)_4$ compared with MK show the largest bathochromic shift in strong HBA solvents with $\alpha = 0$ such as TEA, ethyl acetate, 1,4-dioxane, tetrahydrofuran, dimethylformamide and dimethyl sulfoxide, as shown by the UV–Vis data in Table 2.

Correlation of powder reflectance UV–Vis spectroscopy and x-ray crystal structure analysis of $MK(OH)_2$ (3)

Crystals of $MK(OH)_2$ show two strong UV–Vis absorption bands, a less intense band at $\lambda = 329$ nm ($\nu = 30395\ \text{cm}^{-1}$) and a strong band at $\lambda = 423$ nm ($\nu = 23641\ \text{cm}^{-1}$) (Fig. 3). This proves strong specific and dipolar interactions between the single molecules in the crystal. The x-ray structure analysis confirms the predicted interactions.

$MK(OH)_2$ crystallizes in the monoclinic space group $P2(1)/n$ with $a = 475.17(2)$ pm, $b = 1481.78(5)$ pm, $c = 2378.810(10)$ pm and $\beta = 93.588(2)°$. The results of the x-ray structure determination for $MK(OH)_2$ are shown in Fig. 4. The positions of the hydrogen atoms in the hydrogen bonds were experimentally determined. In the crystal lattice, the molecules are bridged by two kinds of hydrogen bonds, first between the hydroxyl group O2—H2O and the keto group C1=O1 and second between the two hydroxyl groups of neighboring molecules (the oxygen O2 and the hydrogen H3O). The two hydrogen-bonding motif build up a two-dimensional structure.

The strong hydrogen bridge to the carbonyl oxygen is responsible for the intense colour of the crystals, because the hydroxyethyl substituents force the chromophore into acentric environments through hydrogen-bonding network, and this enhances the extent of the overlap between the nitrogen lone-pair orbital and the aromatic π-electron cloud, resulting in an increased bathochromic shift of the π–π^* transition.

X-ray structure analysis of acid–base adducts of $MK(OH)_2$ with pentachlorophenol and trifluoromethansulfonic acid was carried out by Gramstad *et al.*,[20] who reported that depending on the coordination of either the carbonyl group or the nitrogen atom, different colours of the adducts were observed. The result of the structure analysis of $MK(OH)_2$ is in agreement with the results of the solvatochromic measurements.

DISCUSSION

Overall, the three types of MK derivatives show a positive solvatochromism significantly dependent on both the dipolarity/dipolarizability and the HBD capacity of the solvent. According to the literature,[14] this result was expected. The coefficient a [from Eqn (1)] decreases in the order MK > $MK(OH)_2$ > $MK(OH)_4$, indicating a smaller influence of the α term on the bathochromic band shift of $MK(OH)_4$ than for MK. For all three compounds,

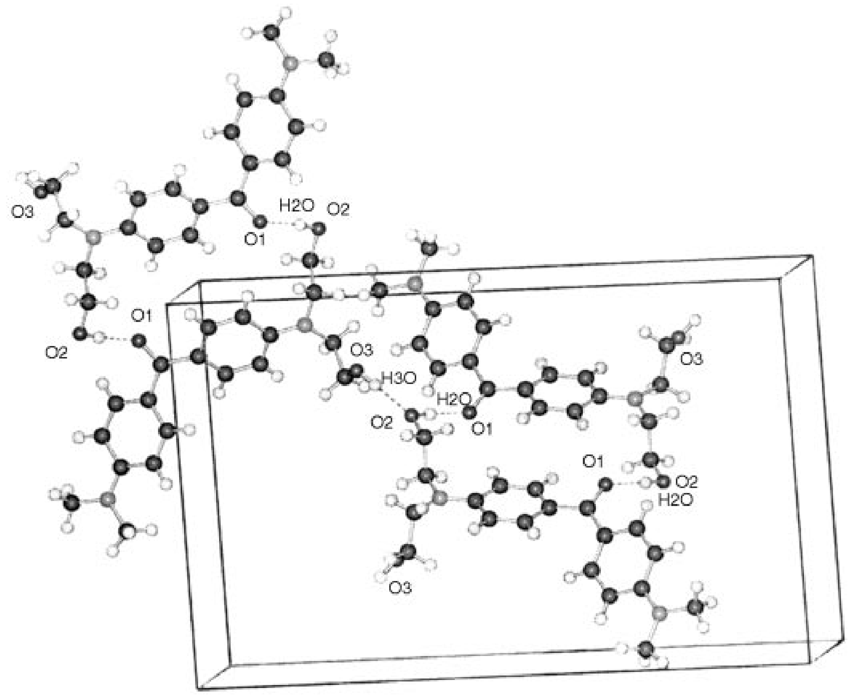
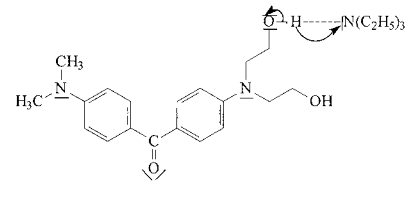


Figure 4. Molecular packing of MK(OH)$_2$ (**3**) with intermolecular hydrogen bonds (dashed lines)

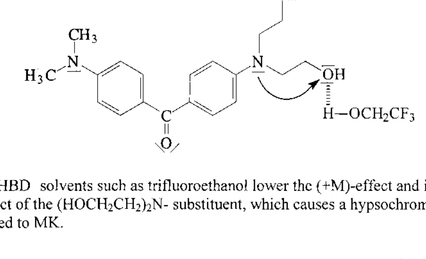
the difference in the influence of the π^* term on the bathochromic band shift is not significant. The influence of the β term on the bathochromic band shift is negligible for MK, but the coefficient b [from Eqn (1)] increases with increasing number of 2-hydroxyethyl substituents on the amino groups. Despite the fact that the improvement of the correlation coefficient r (Table 2) does not seem to change significantly on going from a two-parameter equation with α and π^* only to a three-parameter equation with π^*, α and β.

The UV–Vis data from Table 2 show that an enhanced bathochromic band shift is caused by pure HBA solvents (with $\alpha = 0$) from MK to MK(OH)$_4$. The bathochromic band shift can be interpreted in terms of the lone pair of the HBA solvents coordinated to the O-bonded hydrogen atom of the 2-hydroxyethyl group. Owing to this specific solvation, the positive mesomeric effect of the 4-(HOCH$_2$CH$_2$)$_2$N substituent on the benzene ring is slightly enhanced. Accordingly, a small bathochromic shift is expected. A lowering of the negative inductive effect would also cause a bathochromic effect. A specific solvation of the carbonyl carbon atom by the HBA solvent would result in a hypsochromic band shift. However, the solvation of the (HOCH$_2$CH$_2$)$_2$N substituent by HBA solvents can also cause a polarized solvent shell of MK(OH)$_4$ or MK(OH)$_2$ which has a larger (induced) dipole moment than the remaining bulk solvent phase. This explanation corresponds to an increase in the value of the π^* term of the solvating molecules near the (HOCH$_2$CH$_2$)$_2$N substituent.

A hypsochromic band shift from MK to MK(OH)$_4$ is observed when strong HBD solvents (trifluoroethanol, water or hexafluoro-2-propanol) are considered. This result indicates a specific solvation of the oxygen atoms of the (HOCH$_2$CH$_2$)$_2$N substituent by the active hydrogen atoms of the HBD solvents. Consequently, the positive mesomeric effect of the (HOCH$_2$CH$_2$)$_2$N substituent is lowered. A solvation of the lone pair of the nitrogen atom is unlikely, since in that case a significant



(a) HBA solvents such as triethylamine enhance the (+M)-effect or/and lower the (–I) effect of the (HOCH$_2$CH$_2$)$_2$N- substituent, which causes a bathochromic band shift compared to MK.



(b) Strong HBD solvents such as trifluoroethanol lower the (+M)-effect and increase the (-I) effect of the (HOCH$_2$CH$_2$)$_2$N- substituent, which causes a hypsochromic band shift compared to MK.

Scheme 2. Suggested solvation mechanism of MK(OH)$_2$ in (a) HBA solvents and (b) HBD solvents deviation (hypsochromic shift) from the straight line given in Eqn (2) should be observed for these solvents. We assume that the specific interaction between the HBA solvent and the $(HOCH_2CH_2)_2N$ substituent plays the major role (see Scheme 2), because the bathochromic band shift obtained in going from MK to $MK(OH)_4$ is negligible for common alcohols (methanol, ethanol, *n*-butanol). These solvents show both HBD and HBA properties of similar strength. In aromatic and halogenated solvents also no significant difference of λ_{max} between $MK(OH)_4$, $MK(OH)_2$ and MK is observed.

Consequently, the positive solvatochromism of $MK(OH)_4$ and $MK(OH)_2$ can be expressed as the difference of the LSE equations of $MK(OH)_2$ or $MK(OH)_4$, respectively, with MK:

$$\nu_{max} \times 10^{-3}[MK(OH)_4] = 2.362 + 1.863 \times 10^{-3}\nu_{max}[MK(OH)_2] - 0.947 \times 10^{-3}\nu_{max}[MK] \quad (4)$$

$$n = 24;\ r = 0.991;\ SD = 0.133$$

The measured ν_{max} data for all three Michler's ketone derivatives, **1**, **2** and **3**, were fitted by multiple regression in order to obtain a relationship between these ketones as shown in Eqn (4).

The crystals of $MK(OH)_2$ show a strengthening of all three effects in the same molecule—HBA property of the carbonyl oxygen, HBD capacity of the 4-$(HOCH_2CH_2)_2N$ substituent and high dipolarity/polarizability of the substituted aromatic ring—which consequently results in a significant bathochromically shifted long-wavelength UV–Vis absorption band. Therefore, we think that the novel functionalized MK derivatives $MK(OH)_4$ (**1**) and $MK(OH)_2$ (**2**) are suitable polarity indicators for the surface of a variety of solid materials. Furthermore, the 2-hydroxyethyl group can also be used for chemical derivatization reactions with carboxylic acids, isocyanates or epoxides in order to be linked at polymers or surface groups.

EXPERIMENTAL

Materials. Solvents obtained from Merck, Fluka, Lancaster and Aldrich were redistilled over appropriate drying agents prior to use.

Spectral measurements. The UV–Vis absorption spectra of freshly prepared solutions were obtained by means of an MCS 400 diode-array spectrometer (Carl Zeiss Jena), connected with an immersion cell (TSM 5) via glass-fibre optics. NMR measurements were made at 20 °C on a Varian Gemini 300 FT NMR spectrometer, operating at 300 MHz for ^1H and 75 MHz for ^{13}C. The signals of the solvents ($CDCl_3$ or CD_3OD) were used as internal standards. IR spectra were recorded with a Bio-Rad FTS 165 spectrometer.

Correlation analysis. Multiple regression analysis was performed with the Origin 5.0 statistical program.

Single crystal structure analysis. Rod-shaped, yellowish crystals were embedded in a perfluoroalkyl ether (ABCR) (viscosity 1600 cSt) for protection against oxygen or moisture. The unit cell was determined with the program SMART (Bruker AXS, Madison, WI, USA). For data integration and refinement of the unit cell the program SAINT (Bruker AXS) was used. The space group was determined using the programs XPREP (Bruker AXS) and the empirical absorption correction was done with SADABS (Bruker AXS). In the structure solution by direct methods the program SHELX97[21] was employed; the structure refinement was based on least-squares methods based on F^2 with SHELX97[21]. The plots of the molecular structures were visualized using the programs ZORTEP (L. Zsolnai and G. Huttner, University of Heidelberg, 1994) and Schakal 97 (E. Keller, University of Frieburg, Germany, 1997).

All non-hydrogen atoms were fully refined in the calculated positions, when possible; the hydrogen atoms were taken from the electron density difference map and in both their position and their thermal parameters refined freely. The structural data (without structural factors) were deposited at the Cambridge Crystallographic Data Centre and can be obtained by citing the depositing number CCDC-147477.

*4,4′-Bis[di(2-hydroxyethyl)amino]benzophenone $MK(OH)_4$ (**1**).* A mixture of 7.64 g (35 mmol) of 4,4′-difluorobenzophenone and 70.00 g (666 mmol) of diethanolamine was stirred at 150–160 °C for 48 h. The resulting reaction mixture was distilled under reduced pressure to remove the excess of diethanolamine. The residue was purified by column chromatography on silica gel using ethanol–ethyl acetate (1:1) as eluent, affording **1** (8.15 g, 21 mmol, 60%) as a pure yellow, viscous oil. All attempts to obtain **1** as a crystalline solid failed.

IR (film) v (cm^{-1}), 3308 (OH), 1721 (C═O); ^1H NMR (CD_3OD), δ 7.63 (d, $J = 8.79$ Hz, 4H, ArH-2,6,2′,6′), 6.78 (d, $J = 8.79$ Hz, 4H, ArH-3,5,3′,5′), 3.75 (t, $J = 5.50$ Hz, 8H, CH_2O), 3.62 (t, $J = 5.50$ Hz, 8H, CH_2N); ^{13}C NMR (CD_3OD), δ 196.5 (C═O), 152.8 (ArC-4,4′), 133.6 (ArC-1,1′), 126.7 (ArC-2,6,2′,6′), 111.8 (ArC-3,5,3′,5′), 60.2 (CH_2O), 54.8 (CH_2N); MS (DEI-desorption electron ionisation), *m/z* (relative abundance,%) 388 (M^+, 2), 357 (3.5), 208 (2.5), 180 (3), 132 (10.5), 61 (14.5), 45 (84), 43 (100), 31 (30); MS (ESI-electron spray ionisation), *m/z* 389.2 (M^++1).

*4-(Dimethylamino)-4′-[di(2-acetoxyethyl)amino]benzophenone $MK(OAc)_2$ (**2**).* The synthesis of [di(2-acetoxyethyl)amino]benzene was described previously.[22] A

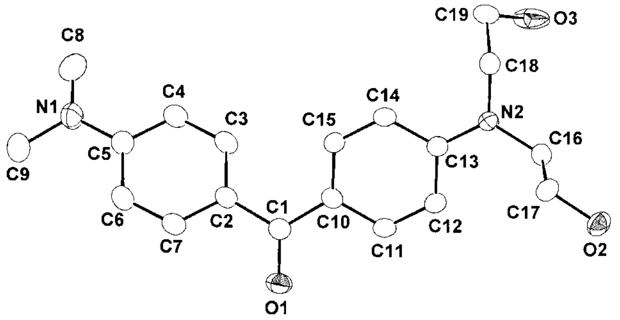


Figure 5. Molecular structure of MK(OH)$_2$ (**3**) (without hydrogen atoms)

solution of 4-(dimethylamino)benzoyl chloride (9.64 g, 52.5 mmol) in 30 ml of 1,2-dichloroethane was gradually added to a suspension of anhydrous AlCl$_3$ (8.00 g, 60 mmol) in 20 ml of 1,2-dichloroethane at 23 °C. The reaction mixture was further stirred for 1 h and then treated with a solution of [di(2-acetoxyethyl)amino]benzene (9.64 g, 50 mmol) in 20 ml of 1,2-dichloroethane for 1 h at 23 °C. After being stirred for 4 h at the same temperature, the reaction mixture was poured into water, acidified with 1 M HCl, extracted with ethyl acetate, and the ethyl acetate extract was washed with water, dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel 60 with ethyl acetate–*n*-hexane (2:1) as eluent, affording **2** (10.91 g, 26.48 mmol, 53%) as a pale yellow, viscous oil.

IR (pure) ν (cm^{-1}), 1739 (C=O); ^{1}H NMR (CDCl$_3$), δ 7.66 (dd, J = 9.06, 3.02 Hz, 4H, ArH-2,6,2′,6′), 6.68 (d, J = 9.06 Hz, 2H, ArH-3,5), 6.56 (d, J = 9.06 Hz, 2H, ArH-3′,5′), 4.16 (t, J = 5.91 Hz, 4H, CH$_2$O), 3.59 (t, J = 5.91 Hz, 4H, CH$_2$N), 2.91 (s, 6H, NCH$_3$), 1.94 (s, 6H, CCH$_3$); ^{13}C NMR (CDCl$_3$), δ 192.9 (C=O), 170.2 (C=O ester), 152.2 (ArC-4), 149.5 (ArC-4′), 131.7 (ArC-2,6), 131.6 (ArC-2′,6′), 126.2 (ArC-1), 125.2 (ArC-1′), 110.1 (ArC-3,5), 109.9 (ArC-3′,5′), 60.7 (CH$_2$O), 49.1 (CH$_2$N), 39.6 (NCH$_3$), 20.4 (CCH$_3$); MS (DEI), *m/z* (relative abundance, %) 413 (M$^+$+1, 1.5), 412 (M$^+$, 4), 339 (15), 148 (30), 106 (26), 87 (100), 45 (15), 43 (81); MS (ESI), *m/z* 413.2 (M$^+$+1).

*4-(Dimethylamino)-4′-[di(2-hydroxyethyl)amino]benzophenone MK(OH)$_2$ (**3**).* 4-(Dimethylamino)-4′-[di(acetoxyethyl)amino]benzophenone (0.412 g, 1 mmol) was added to a solution of potassium carbonate (0.276 g, 2 mmol) dissolved in 20 ml of methanol–water (1:1). The

Table 3. Crystal data for MK(OH)$_2$ (**3**)

Crystal size	0.35 × 0.2 × 0.2 mm	
Empirical formula	C$_{19}$H$_{24}$N$_2$O$_3$	
Chemical formula	C$_{19}$H$_{24}$N$_2$O$_3$	
Formula weight	328.40	
Crystal system	Monoclinic	
Space group	*P*2$_1$/*n*	
Unit cell dimensions	a = 475.17(2) pm	α = 90°
	b = 1481.78(5) pm	β = 93.588(2)°
	c = 2378.810(10) pm	γ = 90°
Volume	1671.63 × 10^6(9) pm^3	
Z	4	
Density (calculated)	1.305 g cm^{-3}	
Radiation used	Mo Kα	
Wavelength	71.073 pm	
Linear absorption coefficient	0.089 mm^{-1}	
Temperature	173(2) K	
Diffractometer	Bruker SMART CCD	
Scan method	ω scans	
Absorption correction	Empirical	
Max. and min. transmission	0.962453 and 0.762955	
Number of measured reflections	7023	
Number of independent reflections	3687	
Number of observed reflections	2359	
Criterion of recognition (σ-limit)	>2 $\sigma(I)$	
R(int)	0.0435	
θ range for data collection	1.62–30.37°.	
Completeness to θ = 30.37°	73.1%	
Index ranges	$-6 \leq h \leq 5$, $-21 \leq k \leq 3$, $-30 \leq l \leq 28$	
Final R indices [$I > 2\Sigma(I)$]	$R1$ = 0.0526, $wR2$ = 0.1026	
R indices (all data)	$R1$ = 0.0979, $wR2$ = 0.1221	
Maximum δ/σ	0.004	
Maximum e-density	0.191 e A^{-3}	
Minimum e-density	−0.210 e A^{-3}	

Table 4. Selected bond lengths, atomic distances and angles for $[MK(OH)_2]$ (**3**)

	Bond length (pm)		Atomic distance (pm)
O2–H(2O)	94.0(3)	O3–O2	269.9(2)
O3–H(3O)	90.0(3)	O2–O1	267.1(2)
O1–H2O	174.0(3)		Angle (°)
O2–H3O	180.0(3)	O1–H1–O2	168(3)
		O2–H2–O3	176(3)

mixture was refluxed for 2 h at 80 °C in a water-bath. After cooling to room temperature, the mixture was poured into ice–water and neutralized with concentrated HCl. The precipitate was filtered off, washed with water and recrystallized from ethanol to give **3** (0.289 g, 0.88 mmol, 88%), m.p. 161–162 °C as yellow needles.

Found: C, 69.40; H, 7.42; N, 8.41; $C_{19}H_{24}N_2O_3$ requires C, 69.49; H, 7.37; N, 8.53%; IR (Nujol), v (cm^{-1}) 3350 (OH), 1729 (C═O); ^1H NMR (CD_3OD), δ 7.66 (dd, $J = 9.06$, 4.39 Hz, 4H, ArH-2,6,2′,6′), 6.81 (d, $J = 9.06$ Hz, 2H, ArH-3,5), 6.76 (d, $J = 9.06$ Hz, 2H, ArH-3′,5′), 3.77 (t, $J = 5.91$ Hz, 4H, CH_2O), 3.65 (t, $J = 5.91$ Hz, 4H, CH_2N), 3.06 (s, 6H, NCH_3); ^{13}C NMR (CD_3OD), δ 197.1 (C═O), 155.1 (ArC-4), 153.2 (ArC-4′), 134.0 (ArC-2,6), 133.8 (ArC-2′,6′), 127.2 (ArC-1), 122.3 (ArC-1′), 112.22 (ArC-3,5), 112.16 (ArC-3′,5′), 60.6 (CH_2O), 55.2 (CH_2N), 40.6 (NCH_3); MS (DEI), *m/z* (relative abundance, %) 329 ($M^+ + 1$, 3), 328 (M^+, 12.5), 298 (19), 297 (100), 148 (64), 132 (23), 45 (15), 43 (100), 31 (21); MS (ESI), *m/z* 329.2 ($M^+ + 1$).

The UV–Vis reflectance spectrum of **3** is shown in Fig. 5 and crystal and structural data are given in Tables 3 and 4.

CONCLUSION

Hydrophilically substituted derivatives of Michler's ketone, $MK(OH)_4$ and $MK(OH)_2$, were obtained through successive replacement of the dimethylamino groups by $(HOCH_2CH_2)_2N$ groups. The new compounds $[MK(OH)_4]$ (**1**) and $[MK(OH)_2]$ (**3**) are water soluble. The solvatochromism of these new MK derivatives is slightly modified compared with MK (**4**). Hydrogen bonds of strong HBA and of strong HBD solvents with the $(HOCH_2CH_2)_2N$ group can be interpreted with the help of regression analysis using the Kamlet–Taft solvent parameter set. A crystallographic structure analysis of $MK(OH)_2$ (**3**) and the UV–Vis spectrum of the crystal are in accord with the proposed solvation mechanism.

Acknowledgements

Financial support by the Fonds der Chemischen Industrie, Frankfurt am Main, and in particular by the Deutsche Forschungsgemeinschaft, Bonn, is gratefully acknowledged.

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