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Determination of a Solvent Hydrogen-Bond Acidity Scale by Means of the Solvatochromism of Pyridinium-N-phenolate Betaine Dye 30 and PCM-TD-DFT Calculations

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Ⓢ Supporting Information

ABSTRACT: Empirical parameters of solvents describing their hydrogen-bond (HB) acidity (e.g., the Kamlet−Taft α parameter) are often difficult to determine for new solvents because they are not directly related to a single definition process. Here, we propose a simple method based on one probe, the betaine dye **30**, and one reference process, the solvatochromism of this dye, measured by its first electronic transition energy, $E_T(30)$. These $E_T(30)$ values are calculated within the time-dependent density functional theory framework, using a polarizable continuum solvent model (PCM). The part of $E_T(30)$ values that is not included in the PCM calculation is taken as the HB component of the measured $E_T(30)$ values, allowing us to deduce a solvent HB acidity parameter α_1. The validity of this simple model is assessed by good linear correlations between α_1 and a variety of solute properties mainly depending on the solvent's HB acidity. The quality of fit observed with α_1 is at least comparable with that obtained by previous solvent HB acidity scales. The simplicity of our method is illustrated by the determination of α_1 and of its companion, the electrostatic solvent parameter ES, for some new green solvents derived from glycerol.
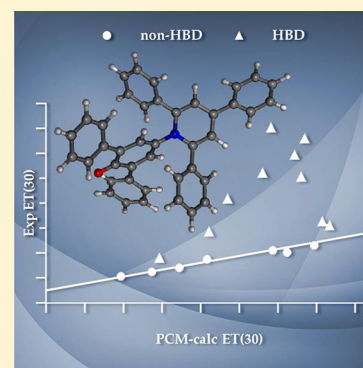
INTRODUCTION

Hydrogen-bond (HB) acidity is a category of Lewis acidity in which Lewis acids are O−H, N−H, or C−H hydrogen-bond donors (HBDs[1]) such as, for example, water, formamide, or trichloromethane. Indeed, when they form hydrogen-bonded complexes with hydrogen-bond acceptors (HBAs[1]), these compounds can accept electron density in their antibonding $\sigma*$(O−H, N−H, or C−H) orbitals from HBAs acting as Lewis bases.[2] Many properties of HBDs (as solutes or solvents) are related to their acid strength.[3] Accordingly, many hydrogen-bond acidity scales have been introduced for use in various fields such as drug design,[4] absorption spectra, adsorption, distribution, metabolism, and elimination properties,[5,6] correlation analysis of solvent effects,[7,8] prediction of hydrogen-bonding constants,[9] and partition[10] and separation techniques.[11]

At present, the measurement of the HB acidity of molecules dissolved in inert solvents (the so-called *solute* HB acidity scale) can be considered as achieved thanks to the α_2^H,[12] A,[13] and log K_α scales[4] as well as to a spectroscopic NMR scale,[14] all introduced by Abraham et al. However, the measurement of the HB acidity of molecules in bulk, acting as solvents (the so-

called *solvent* HB acidity scale) represents a much greater challenge, because two terms are involved in this solvent property: (i) the nonspecific solvent/solute interactions and (ii) the specific hydrogen-bond solvent/solute interactions. The first contribution must be subtracted from the measured property to isolate the hydrogen-bonding contribution. To perform this task, either one can use the solvatochromic comparison method[15,16] or one can calculate the contribution of the nonspecific interactions by means of linear solvation energy relationships (LSERs).[7,8,17] Both methods have been used for defining the two "pure" solvent HB acidity scales in current use: the α scale proposed by Kamlet and Taft,[7,8,15] and revisited by Marcus,[18,19] and the SA scale proposed by Catalán et al.[16,17]

In spite of these achievements, a further somewhat improved solvent HB acidity scale seems to be necessary for two reasons: (i) it is rather difficult to extend the existing α and SA scales to new solvents because the α scale emerges from a complex
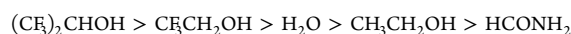
averaging process[7,8,15] and the construction of the *SA* scale requires no less than five solvatochromic probes;[16,17,20] (ii) both existing scales do not agree very well with each other ($r^2 = 0.812$ for 51 solvents common to both scales) and disagree particularly for important HBD solvents such as water and formamide, as shown by the following deviating HB acidity sequences:

SA scale:

$$H_2O > (CF_3)_2CHOH(HFIP) > CF_3CH_2OH > HCONH_2 > CH_3CH_2OH$$

α scale:

$$(CF_3)_2CHOH > CF_3CH_2OH > H_2O > CH_3CH_2OH > HCONH_2$$

To circumvent these major drawbacks, we propose here a new methodology, based on the extraordinary solvent-induced shifts of the intramolecular charge-transfer absorption band of the pyridinium *N*-phenolate betaine dye **30** as reference process (Scheme 1),[21−25] and the polarizable continuum model (PCM)

Scheme 1. Molecular Structure and $S_0 \rightarrow S_1$ Transition of Betaine Dye 30
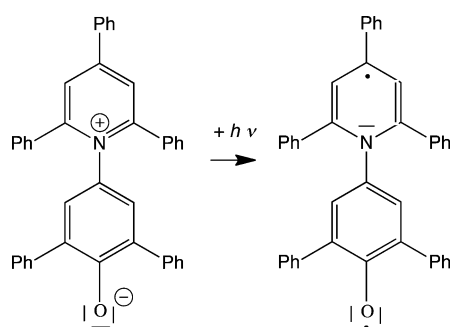
method[26] for the calculation of the contribution of nonspecific solvent/solute interactions. This proceeding is simple (only one reference process and one straightforward theoretical calculation) and offers the following advantages: (i) betaine dye **30** is well suited for the construction of a solvent HB acidity scale because, in HBD solvents, the solvatochromism of this zwitterionic dye is mainly determined by hydrogen-bonding to its phenolate oxygen atom;[21−25,27] (ii) the solvatochromic band shift corresponding to the $S_0 \rightarrow S_1$ transition of **30**, translated into its molar transition energy $E_T(30)$, is known for more than 100 HBD solvents, and can easily be measured by vis/NIR spectrometry for new solvents because **30** is commercially available;[23,24] (iii) the nonspecific solvent/dye interactions contributing to the $E_T(30)$ values are mainly caused by electrostatic interaction forces between the permanent multipoles of **30** and the surrounding solvent molecules, because the red-shifting dispersion forces are nearly canceled out by the blue-shifting induction forces,[27−30] and the PCM method is well suited for the calculation of such electrostatic solvent/solute interactions;[26] (iv) the PCM method is implemented in several user-friendly software packages and more than 50 HBD solvents have been already parametrized in one of the most popular ab initio program, Gaussian 09.[31]

Using this method, we have determined a new solvent HB acidity parameter α_1 as follows (subscript 1 indicates that this parameter is *solvent*-specific and differs from its *solute*-specific congener α_2^H). We assume that $E_T(30)$ values can be divided into three parts according to eq 1

$$E_T(30) = E_T(\text{gas}) + \Delta E_T(\text{nsp}) + \Delta E_T(\text{HBD}) \qquad (1)$$

wherein $E_T(\text{gas})$ stands for the gas phase and the last two terms for the nonspecific (nsp) and specific hydrogen-bonding components of the overall $E_T(30)$ values, respectively. For a set of non-HBD solvents it is found that the experimental and the PCM-TD-DFT calculated $E_T(30)$ values correlate linearly according to eq 2:

$$E_T(30) = aE_T(\text{PCM-TD-DFT}) + b \qquad (2)$$

In this equation the regression coefficients *a* and *b* take into account the gas-phase value and the well-known overevaluation of the electronic transition energies of cyanine dyes (betaine **30** = merocyanine dye) by conventional TD-DFT methods.[32] We then calculated $E_T(30)$ values for HBD solvents by the same method. These $E_T(30)$ values computed for HBD solvents do not obey the calibration line of eq 2 because PCM calculations do not account for the supplementary hypsochromic band shifts caused by specific solvent/solute interactions, i.e., in this case the hydrogen bonding to the phenolate oxygen atom of betaine **30**. The displacements of the HBD solvents from the calibration line, $\Delta E_T(\text{HBD})$, is hence attributed to the hydrogen-bonding contribution to $E_T(30)$ values and one can conclude that

$$\Delta E_T(\text{HBD}) = E_T(30) - [aE_T(\text{PCM-TDDFT}) + b] \qquad (3)$$

and write, by definition,

$$\alpha_1 = \Delta E_T(\text{HBD})/\text{scaling factor} \qquad (4)$$

To check the validity of this new solvent HB acidity parameter α_1, we have correlated a set of physicochemical properties highly dependent on the solvent's HB acidity by means of LSERs including the parameter α_1. A high percentage of the variance of these properties can be indeed explained by α_1. This allows the conclusion that the method reported on in this work might be useful for parametrizing the HB acidity of molecular solvents.

■ THEORETICAL MODELS

The $S_0 \rightarrow S_1$ molar electronic transition energies of betaine dye **30** have been calculated for 31 non-HBD and 55 HBD solvents, using the TD-DFT approach as implemented in the Gaussian 09 package,[31] tightening both energy (at least to 10^{-8} au) and geometry optimization thresholds (*tight* means corresponding to a residual mean force smaller than 10^{-5} au). The electronic ground-state geometries of **30** were optimized with the CAM-B3LYP exchange−correlation functional[33] and the 6-31+G-(d,p) atomic basis set, imposing the C_2 point group symmetry found in a recent TD-DFT study of betaine dye **30**.[34] The calculations have been done on the most stable conformer of **30** because the other one has a transition energy very close to that of the most stable conformer (see Table 1 of ref 34). For the sake of consistency, the first excited-state TD-DFT calculations were performed with the same functional and atomic basis set, but augmented with diffuse orbitals on the hydrogen atoms, namely 6-31++G(d,p). Betaine dye **30** has a merocyanine-like electronic structure and it is well-known that hybrid functionals (both global and range-separated hybrid) overshoot the electronic transition energies of this family of cyanine dyes. This topic is beyond the scope of this study that focuses on solvent effects only, and the reader is directed to ref 32 for a discussion of this question.

As stated before, the solvent effects have been systematically (both electronic ground-state structure and optical spectra) accounted for by using the well-known PCM model,[26] which delivers a valid approximation of solvent effects as long as no specific solvent/solute interactions play a major role. For the electronic excited states, the linear-response (LR) PCM model in its nonequilibrium limit was used, as this model is suited for UV/vis absorption spectra.[35,36] We have also performed calculations with the corrected LR model (cLR),[37] which allows a more complete account of the change of polarization of the cavity between the ground and excited states. Although the cLR model yields $E_T(30)$ values closer to the experimental ones (mean error = 9.7 kcal·mol^{-1} = 0.42 eV) than the LR model (mean error 14.0 kcal·mol^{-1} = 0.61 eV), the latter gives a slightly better relative agreement with the experiment (r^2 = 0.953) than the former (r^2 = 0.940) for the 31 non-HBD solvents of the calibration line. As, on the one hand, this calibration is at the heart of the determination of the α_1 scale (vide infra) and, on the other hand, LR calculations are both faster and available in more computational packages, we stick to the LR approximation in the following (cLR results are given in the Supporting Information part).

Solvents that are not defined by default in the Gaussian 09 package have been parametrized starting from a physically and structurally similar solvent and using its experimental relative permittivity, ε_r, and refractive index, n_D.[30] For instance, for glycerol (propane-1,2,3-triol) we started with 1-pentanol and used ε_r = 42.50 and n_D = 1.473 (which translates into an optical limit value of ε_∞ = 2.170).

■ RESULTS AND DISCUSSION

PCM-TD-DFT Calculations of $E_T(30)$ Values for Non-HBD Solvents. The empirical solvent polarity parameter $E_T(30)$ is based on the solvatochromism of 2,6-diphenyl-4-(2,4,6-triphenylpyridinium-1-yl)phenolate (Scheme 1), also called betaine dye **30** after its formula number given in the first paper.[21−24] It is defined as the molar electronic transition energy (historically in kcal·mol^{-1}; 1 cal = 4.184 J) of **30** according to eq 5

$$E_T(30)/(\text{kcal·mol}^{-1}) = hc\tilde{\nu}_{max}N_A = 28591/\lambda_{max} \quad (5)$$

where h, c, and N_A are Planck's constant, the speed of light, and Avogadro's number, respectively, and $\tilde{\nu}_{max}$ (cm^{-1}) and λ_{max} (nm) are the wavenumber and wavelength of the long-wavelength absorption band in the vis/NIR region, corresponding to an intramolecular charge-transfer transition from the phenolate to the pyridinium moiety (Scheme 1).[34]

As the PCM method principally estimates the nonspecific dye/solvent interactions and, in the case of **30**, the hydrogen-bond formation between HBD solvents and the phenolate oxygen atom is the main specific interaction, solvents have been divided into two categories: those giving and those not giving hydrogen bonds to the betaine dye, i.e., HBD and non-HBD solvents. In a recent definition of the hydrogen bond one can read "the hydrogen bond is an attractive interaction between a hydrogen atom from a .... molecular fragment X−H in which X is more electronegative than H, and an atom ... in a different molecule, *in which there is evidence of bond formation*."[38] For the 31 solvents collected in Table 1, selected to cover the widest range of $E_T(30)$ values (from alkanes to DMSO), we have not found any evidence for hydrogen-bond formation in a review on weak hydrogen bonds[39] and, therefore, consider these

Table 1. Experimental $E_T(30)$ and Calculated E_T(PCM-TD-DFT) Values as Well as Residuals ε of Eq 6 (All in kcal·mol^{-1}); Normalized Residuals $R_n = |\varepsilon|/s$

| solvent	$E_T(30)^a$	E_T(PCM-TD-DFT)	ε	R_n
n-nonane	30.8	43.2	−0.43	0.42
n-decane	30.8	43.3	−0.50	0.50
cyclohexane	30.8	43.4	−0.59	0.58
n-pentane	30.9	42.7	0.03	0.03
n-hexane	30.9	42.9	−0.10	0.10
n-heptane	30.9	43.0	−0.19	0.18
n-octane	31.0	43.1	−0.17	0.17
n-dodecane	31.0	43.4	−0.36	0.36
tetrachloroethene	31.8	44.4	−0.29	0.28
triethylamine	32.1	45.0	−0.38	0.38
1-hexene	32.4	43.7	0.80	0.79
di-*n*-butyl ether	33.0	47.3	−1.04	1.03
toluene	33.9	44.9	1.51	1.50
di-isopropyl ether	34.0	48.2	−0.69	0.68
benzene	34.3	44.4	2.20	2.18
diethyl ether	34.5	50.1	−1.52	1.50
diphenyl ether	35.3	48.9	0.14	0.14
thiophene	35.4	46.1	2.15	2.12
iodobenzene	36.2	50.5	−0.07	0.07
chlorobenzene	36.8	52.2	−0.67	0.66
fluorobenzene	37.0	51.9	−0.25	0.25
tetrahydrofuran	37.5	54.0	−1.22	1.20
methyl benzoate	38.7	53.3	0.45	0.44
cyclohexanone	40.1	57.5	−1.02	1.01
pyridine	40.5	56.7	−0.11	0.11
nitrobenzene	41.2	59.5	−1.33	1.32
benzonitrile	41.5	58.9	−0.59	0.59
N,N-dimethylacetamide	42.9	59.7	0.23	0.23
N,N-dimethylformamide	43.2	59.7	0.54	0.54
sulfolane	44.1	59.9	1.28	1.26
dimethyl sulfoxide (DMSO)	45.1	60.1	2.19	2.17

^{a}From refs 25 and 30.

solvents as non-HBD solvents (bearing in mind that this is a relative term). Satisfactorily, all these non-HBD solvents have Kamlet−Taft α values equal to 0.00 (in a scale going from α = 0.00 for alkanes to 1.96 for HFIP).[19]

As can be seen in Table 1, the PCM-TD-DFT $E_T(30)$ values are overshooting the experimental values by 10.1−18.3 kcal·mol^{-1}, as expected (see above). However, there is a good *relative* agreement between experimental and calculated values because 95.3% (100 r^2) of the variance of experimental values is explained by the calculated values. In the graph comparing experimental and calculated $E_T(30)$ values (Figure 1), the non-HBD solvents draw a calibration line according to eq 6

$$E_T(30) = 0.693(\pm 0.029) \, E_T(\text{PCM-TD-DFT})$$
$$+ 1.3(\pm 1.4) \quad (6)$$

with a number of data points n = 31, a determination coefficient r^2 = 0.953, and a standard deviation of the estimate s = 1.0 kcal·mol^{-1} (to be compared with a maximum experimental error of 0.5 kcal·mol^{-1} in the measurements of $E_T(30)$ values).[30] By comparison, an estimate of $E_T(30)$ with a solvatochromic comparison method[15] and by a LSER[18] amounts to s = 1.6 and 1.3 kcal·mol^{-1}, respectively. With our approach, the largest positive deviations (in kcal·mol^{-1}) have been found for benzene
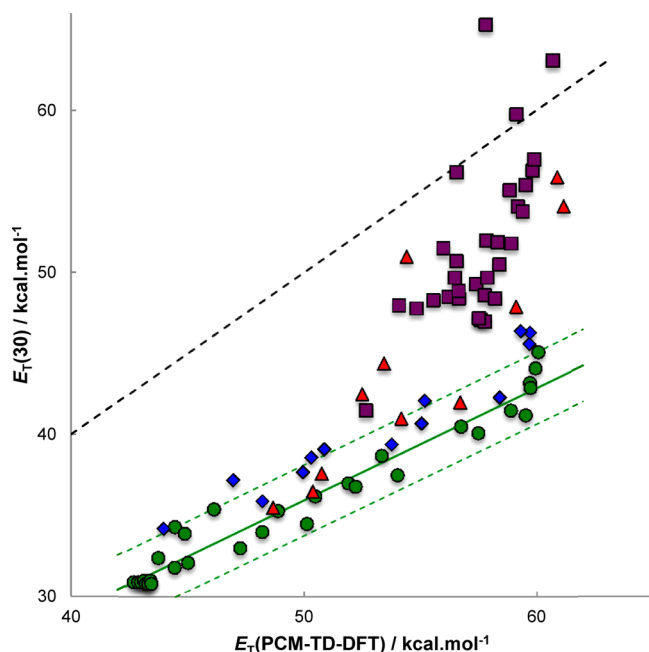
Figure 1. Plot of experimental against PCM-TD-DFT calculated $E_T(30)$ values. The green full line (with the 95% confidence interval as two dotted lines) is the calibration line drawn with non-HBD solvents only. The dotted black line is the first bisectrix corresponding to experimental value = computed value. Green circles, blue diamonds, red triangles, and purple squares correspond to non-HBD, C−H HBD, N−H HBD, and O−H HBD solvents, respectively.

(+2.20) and DMSO (+2.19), and the largest negative ones for diethyl ether (−1.52) and nitrobenzene (−1.33). However, none of these solvents can be considered as outliers because their normalized residuals R_n are smaller than the critical value of 2.92 (for $n = 31$ at the 95% confidence level[40]).

PCM-TD-DFT Calculations of $E_T(30)$ Values for HBD Solvents. With the same theoretical method, the $E_T(30)$ values of 55 HBD solvents were calculated and are collected in the third column of Table 2. All solvents containing O−H, N−H, and Csp-H groups are classified as HBD solvents. For solvents containing Csp^2−H and Csp^3−H groups, we have found in the literature spectral,[41] thermodynamic,[42−44] and crystallographic[39,45] experimental "*evidences of (H−)bond formation*"[38] with various HBAs and, therefore, we have classified the following solvents as HBD solvents: pentafluoro-benzene,[41,43] trichloroethene,[41,42] (Z)- and (E)-1,2-dichloro-ethene,[41] trichloromethane,[39,41,42,44] tribromomethane, di-chloromethane,[39,41,42,44] dibromomethane, chloroacetoni-trile,[41,42] acetonitrile,[44] nitromethane,[45] and acetone.[44]

In the plot of experimental against PCM-TD-DFT calculated $E_T(30)$ values (Figure 1) *all* data points representing HBD solvents are satisfactorily displaced *above* the calibration line of non-HBD solvents. These displacements are related to the hypsochromic band shifts induced by hydrogen bonding to the phenolate oxygen atom of **30** that are not explicitly accounted for in the PCM model. For 47 HBD solvents they are larger than 2 times the standard deviation of eq 6, i.e., $2s = 2$ kcal·mol^{-1}, ranging up to $24s$ for HFIP. Nine HBD solvents show displacements (in kcal·mol^{-1}) less than $2s$. These are the four aliphatic amines, i.e., cyclohexylamine (0.30), diethylamine (0.48), n-butylamine (1.14), and 1,2-diaminoethane (1.42), as well as five C−H donors, i.e., acetone (0.54), dibromomethane (0.86), trichloroethene (1.20), dichloromethane (1.27), and

tribromomethane (1.80). This is inherent to the weakness of their HB acidity. We have kept these nine solvents in the category of HBD solvents because there is chemical evidence for their HBD character. For example, the equilibrium constants for the formation of hydrogen-bonded complexes of acetone and dichloromethane with pyridine *N*-oxide (structurally related to betaine dye **30**) in cyclohexane are measurable and equal to 1.29 and 2.41 dm^3·mol^{-1}, respectively,[44] and those of trichloroethene, dibromomethane, and tribromomethane with hexamethylphosphoric triamide in tetrachloromethane amount to 0.27, 0.68, and 2.0 dm^3·mol^{-1}, respectively.[42] Equilibrium constants for the formation of hydrogen-bonded complexes with various HBAs have been determined also for cyclohexylamine, diethylamine, and 1,2-diaminoethane.[46]

Because the PCM approach underestimates $E_T(30)$ (no calculation of HB effects) and the TD-DFT method over-estimates the $E_T(30)$ values (merocyanine character of betaine dye **30**), a compensation of errors occurs in the PCM-TD-DFT calculations, and the calculated $E_T(30)$ values come close to their experimental ones for stronger HBD solvents. Accord-ingly, one obtains $E_T(30) \approx E_T(\text{PCM-TD-DFT})$ for 2,2,2-trifluoroethanol, water, and 3-methyphenol (standing near the first bisectrix in Figure 1), but this is the result of an error compensation. For the strongest HBD solvent, HFIP, the computed $E_T(30)$ value becomes even lower than the experimental one.

Definition of a New Solvent HB Acidity Scale. Displacements $\Delta E_T(\text{HBD})$ from the calibration line of non-HBD solvents (Figure 1), attributable to the hydrogen bonding between HBD solvents and betaine dye **30**, can be calculated from eq 7

$$\Delta E_T(\text{HBD}) = E_T(30) - [0.693 E_T(\text{PCM-TD-DFT}) + 1.31] \tag{7}$$

and they are included as a fourth column in Table 2. These $\Delta E_T(\text{HBD})$ values are assumed to measure the HB acid strength of HBD solvents. To obtain a dimensionless HB acidity scale (a common practice in the field of solvent scales[25]), we take the $\Delta E_T(\text{HBD})$ value of 12.87 kcal·mol^{-1} for methanol as the scaling factor and define an α_1 scale according to eq 8:

$$\alpha_1 = \Delta E_T(\text{HBD})/12.87 \tag{8}$$

In this way, $\alpha_1 = 0.00$ for all non-HBD solvents and $\alpha_1 = 1.00$ for methanol by definition. For the HBD solvents studied here the extreme value is that for HFIP with $\alpha_1 = 1.86$. Thus, the α_1 scale (as given in the fifth column of Table 2) has the same format as the original α scale of Kamlet and Taft (with $\alpha = 1.00$ for methanol[15]), but a wider format than the *SA* scale of Catalán (normalized to $SA = 0.4$ for ethanol[16]).

Scheme SI-1 in the Supporting Information provides a graphical comparison of the α_1 values for various C−H, O−H, and N−H HB donor solvents. The weakest HBD solvent is acetone with $\alpha_1 = 0.04$ and the strongest is HFIP with $\alpha_1 = 1.86$. The HBD solvent ordering is (with some overlaps and exceptions): C−H donors ≈ aliphatic amines < aromatic amines ≈ tertiary alcohols < primary and secondary amides ≈ primary alcohols (C$_2$ to C$_{10}$) < methanol < polyols < phenol < trifluoroethanol < water < HFIP. The observed HB acidity trend depends on three main factors: (i) the intrinsic HB acidity of the isolated molecule, as measured by the α_2^H solute

Table 2. Experimental $E_T(30)$ Values, Calculated E_T(PCM-TD-DFT) Values, Hydrogen-Bonding Component ΔE_T(HBD), and Nonspecific Component ES of $E_T(30)$ (All in kcal·mol^{-1}), as Well as the Dimensionless HB Acidity Parameter α_1

solvent	$E_T(30)^a$	E_T(PCM-TD-DFT)	ΔE_T(HBD)	$\alpha_1{}^b$	ES^c
C−H Donors					
acetone	42.3	58.4	0.54	0.04	41.76
dibromomethane	39.4	53.8	0.86	0.07	38.54
trichloroethene	35.9	48.2	1.20	0.09	34.70
dichloromethane	40.7	55.0	1.27	0.10	39.43
tribromomethane	37.7	49.9	1.80	0.14	35.90
(E)-1,2-dichloroethene	34.2	44.0	2.44	0.19	31.76
pentafluorobenzene	38.6	50.3	2.45	0.19	36.15
trichloromethane	39.1	50.9	2.56	0.20	36.54
(Z)-1,2-dichloroethene	42.1	55.2	2.57	0.20	39.53
acetonitrile	45.6	59.7	2.96	0.23	42.64
phenylacetylene	37.2	46.9	3.37	0.26	33.83
nitromethane	46.3	59.7	3.64	0.28	42.66
chloroacetonitrile	46.4	59.3	4.02	0.31	42.38
N−H Donors					
cyclohexylamine	36.5	50.4	0.30	0.02	36.20
diethylamine	35.5	48.7	0.48	0.04	35.02
n-butylamine	37.6	50.7	1.14	0.09	36.46
1,2-diaminoethane	42.0	56.7	1.42	0.11	40.58
morpholine	41.0	54.2	2.17	0.17	38.83
N-methylaniline	42.5	52.5	4.83	0.38	37.67
pyrrolidine-2-one	47.9	59.1	5.66	0.44	42.24
aniline	44.4	53.4	6.08	0.47	38.32
N-methylformamide	54.1	61.1	10.44	0.81	43.66
pyrrole	51.0	54.4	12.01	0.93	38.99
formamide	55.9	60.9	12.43	0.97	43.47
O−H Donors					
2-methyl-2-propanol	43.6	56.6	3.05	0.24	40.57
2-methyl-2-butanol	41.5	52.6	3.72	0.29	37.78
cyclopentanol	47.0	57.8	5.68	0.44	41.32
2-butanol	47.1	57.6	5.91	0.46	41.19
cyclohexanol	47.2	57.5	6.06	0.47	41.14
2-propanol	48.4	58.2	6.78	0.53	41.62
2-methyl-1-propanol	48.6	57.8	7.29	0.57	41.31
1-pentanol	49.3	57.4	8.24	0.64	41.06
1-heptanol	48.5	56.2	8.26	0.64	40.24
1-butanol	49.7	57.9	8.31	0.65	41.39
1-hexanol	48.9	56.6	8.36	0.65	40.54
1-nonanol	47.8	54.8	8.52	0.66	39.28
1-octanol	48.3	55.5	8.52	0.66	39.78
1-propanol	50.5	58.4	8.75	0.68	41.75
1-decanol	48.0	54.1	9.24	0.72	38.76
2-phenylethanol	49.7	56.5	9.28	0.72	40.42
ethanol	51.8	58.9	9.69	0.75	42.11
allyl alcohol	51.9	58.3	10.21	0.79	41.69
benzyl alcohol	50.7	56.6	10.22	0.79	40.48
2-methoxyethanol	52.0	57.8	10.63	0.83	41.37
diethylene glycol	53.8	59.4	11.36	0.88	42.44
2-phenoxyethanol	51.5	56.0	11.42	0.89	40.08
2,2,2-trichloroethanol	54.1	59.2	11.81	0.92	42.29
methanol	55.4	59.5	12.87	1.00	42.53
2-chloroethanol	55.1	58.8	13.04	1.01	42.06
ethane-1,2-diol	56.3	59.8	13.55	1.05	42.75
glycerol	57.0	59.9	14.21	1.10	42.79
3-methylphenol	56.2	56.5	15.73	1.22	40.47
2,2,2-trifluoroethanol	59.8	59.1	17.54	1.36	42.26
water	63.1	60.7	19.76	1.54	43.34
1,1,1,3,3,3-hexafluoro-2-propanol	65.3	57.8	23.95	1.86	41.35

^{a}From refs 25 and 30. ^{b}From eq 8. $^c ES = E_T(30) − \Delta E_T$(HBD).

scale of Abraham et al.;[12] (ii) the nature of the medium; and (iii) the self-association of solvent molecules into hydrogen-bonded networks. The intrinsic HB acidity α_2^H explains only 79% of the variance of α_1 for 23 HBD solvents. Therefore, a significant part of this variance cannot solely be explained on the basis of the intrinsic HB acidity, and it is crucial to make a distinction between *solute* and *solvent* HB acidity scales. A second factor arises from the fact that, for the bulk acidity, the surrounding medium changes from solvent to solvent (whereas it is constant for *solute* acidities measured in a constant inert medium), and that the formation of hydrogen-bonded complexes is favored in media of low relative permittivity.[47] A third factor might explain why pyrrolidine-2-one has a much lower α_1 value (0.44) than *N*-methylformamide (0.81): it is more difficult for the solute to break up the stable hydrogen-bonded cyclic dimer of pyrrolidine-2-one than the hydrogen-bonded linear polymer of *N*-methylformamide.

The α_1 scale is not highly correlated to either the Kamlet–Taft α scale ($r^2 = 0.876$ for $n = 41$ solvents) or the Catalán *SA* scale ($r^2 = 0.897$ for $n = 44$ solvents). Therefore, it constitutes an independent third solvent HB acidity scale, which has to be tested for its suitability in the correlation analysis of solvent effects. In the following part we show that α_1 correlates successfully with a variety of solvent HB-acidity-dependent physicochemical properties.

Correlation Analysis of Solvent Effects by Means of Solvent HB-Acidity Parameter α_1. Chemists usually tend to describe the solvation capabilities of molecular solvents in terms of empirical parameters such as the solvent's polarizability, dipolarity, HB acidity, and HB basicity. To investigate the solvent influence on a physicochemical property A in a series of solvents, the aforementioned parameters are used to construct a multiparameter relationship, called LSER, such as the popular Kamlet–Taft–Abboud–Abraham equation (9)[7,8]

$$A = A_0 + d\delta + e\pi^* + a\alpha + b\beta \qquad (9)$$

wherein A_0 is the intercept and δ, π^*, α, and β, respectively, describe the solvent's family-dependent polarizability, dipolarity/polarizability, HB acidity, and HB basicity. The regression coefficients d, e, a, and b measure the sensitivity of property A toward a change of the corresponding four parameters. An analogous LSER with differently defined solvent parameters has been recently proposed by Catalán et al.[27]

$$A = A_0 + dSP + eSdP + aSA + bSB \qquad (10)$$

in which *SP*, *SdP*, *SA*, and *SB* stand for the solvent's polarizability, dipolarity, HB acidity, and HB basicity, with the same meaning for d, e, a, and b as in eq 9.

As explained above for α, and elsewhere for π^* [48] and β,[49] the determination of these solvent parameters requires a complex averaging process, which leads, according to Marcus,[3] to a "built-in fuzziness". The solvent parameters of the Catalán equation (10) rest on clear and easily understood reference processes. Nevertheless, their determination demands no less than eight solvatochromic probes (i.e., the polyene ttbP9,[50] 2-(dimethylamino)-7-nitrofluorene,[20] 2-fluoro-7-nitrofluorene,[20] 5-nitroindole,[51] 1-methyl-5-nitroindole,[51] *o-tert*-butylstilbazo-lium betaine,[16] *o,o′*-di-*tert*-butylstilbazolium betaine,[16] and an aromatic tetrazine[17]).

For the sake of efficiency and accessibility, it is desirable to propose simpler alternatives, particularly with respect to the growing number of new solvents within the framework of green chemistry, designed to replace the older more toxic ones.

Therefore, we have been trying[30] to reparametrize the multiparameter eq 9 by (i) changing the indicator variable δ (so far equal to 0.0, 0.5, or 1.0, according to the solvent family) into the continuous Onsager function of the refractive index, $(n_D^2 - 1)/(2n_D^2 + 1)$,[52] to which the symbol *DI* is given to stress that it describes the sum of the solvent's dispersion and induction forces; (ii) changing the parameter π^* into a parameter *ES*, an acronym for electrostatic forces indicating the interaction between the permanent multipoles of solute and solvent (*ES* is equal to $E_T(30)$ for non-HBD solvents and equal to $[E_T(30) - \Delta E_T(\text{HBD})]$ for HBD solvents); and (iii) changing the parameter α into the parameter α_1 as defined by eq 8, and changing the parameter β into a parameter β_1, the definition of which will be given in a forthcoming contribution. After these changes, eq 9 will now take the form of eq 11:

$$A = A_0 + di\,DI + eES + a\alpha_1 + b\beta_1 \qquad (11)$$

To test the validity of the application of the PCM-TD-DFT method for partitioning the $E_T(30)$ solvent scale into one for HBD and one for non-HBD solvents and, consequently, to check the usefulness ("purity") of the resulting solvent parameter α_1, eq 11 should be applied to physicochemical properties A, which depend only on the solvent's HB acidity, according to $A = A_0 + a\alpha_1$.[53] However, as no such properties A can be a priori known, we have chosen to test α_1 along with the parameters *DI* and *ES* (the $b\beta_1$ contribution can be neglected when only non-HBD solutes are selected). To deal with the most appropriate properties A, we have selected those for which the regression coefficient a predominates over di and e in eq 11. We have also chosen a sample of solvents containing as many HBD solvents as possible in the widest acidity range, to get an accurate regression coefficient a. With these criteria in hand, we have tested the new solvent HB acidity parameter α_1 by means of eq 12 for the 11 properties A given in Table 3.

$$A = A_0 + di\,DI + eES + a\alpha_1 \qquad (12)$$

The results given in Table 3 correspond to numerous and varied properties A (altogether 278, including 164 for HBD solvents). Most of these properties have been already described as highly sensitive to the HB acidity of solvents, according to

Example 2: For the merocyanine dyes MePM and MePMBr2[55] the solvatochromic comparison method yields enhanced solvent-induced band shifts in HBD solvents as compared to non-HBD ones and can, consequently, be considered as "pure" descriptors of the solvent's HB acidity.

Example 3: For pyridine *N*-oxide, Schneider et al.[56] have already claimed that the difference d_{34} of the ^{13}C chemical shifts of C-3 and C-4 depends solely on the HB donation ability of the solvents.

Example 4: For *N,N*-diethylbenzamide, Schneider et al.[57] have established that the ^{13}C chemical shift of the C-2/6 ring atoms relative to that of the carbonyl carbon are primarily sensitive to the solvent's HB acidity.

Example 5: According to Taft et al.,[7] "the bimolecular substitution reactions of iodomethane with *anionic* nucleophiles depend essentially upon the solvent HBD ability."

Example 6: According to Lagalante et al.,[58] the solvatochromic band shifts of 4-nitropyridine *N*-oxide predominantly depend on the HB acidity of solvents.

Examples 7, 9, 10: These solvent-dependent spectroscopic properties have been proposed as references for the definition of solvent scales measuring the solvent's Lewis acidity (i.e., HB

Table 3. Correlations of 11 Thermodynamic, Kinetic, and Spectroscopic (UV/Vis, NMR, ESR) Properties A According to Eq 12[a]

| no.	property A	n	r^2	% a[b]	ref
	α_1 as the Only Significant Solvent Parameter[c]				
1	Gibbs energy of transfer of Cl^- from water to other solvents	10 (10)	0.973	100	54
2	$\Delta E_T(MePM-MePMBr_2)$[d]	20 (20)	0.933	100	this work, 55
3	pyridine N-oxide: NMR $d_{34} = \delta^{13}C_3 - \delta^{13}C_4$	16 (14)	0.912	100	56
4	N,N-diethylbenzamide: NMR $d_2 = \delta^{13}C_{2/6} - \delta^{13}C_{C=O}$	21 (17)	0.956	100	57
5	log k_2 of Cl^- + CH_3I	10 (7)	0.924	100	25
	α_1 and DI as Significant Solvent Parameters[c]				
6	$E_T(\pi\rightarrow\pi^*)$, 4-nitropyridine N-oxide	42 (19)	0.941	81	58
	α_1 and ES as Significant Solvent Parameters[c]				
7	$E_T(n\rightarrow\pi^*)$, 2,2,6,6-tetramethylpiperidine N-oxyl radical	47 (16)	0.954	72	59
8	methyl phenyl sulfoxide: NMR $\delta^{13}C_3$	32 (16)	0.939	82	8
	All Three Solvent Parameters α_1, ES, and DI are Significant[c]				
9	$E_T(n\rightarrow\pi^*)$, N,N-(dimethyl) thiobenzamide S-oxide	26 (16)	0.943	68	60
10	triethylphosphane oxide: NMR $\delta^{31}P$	28 (14)	0.963	76	61, 62
11	2,2,6,6-tetramethylpiperidine N-oxyl: ESR nitrogen hfs constant	26 (15)	0.935	73	63

[a]n = number of data points (number of HBD solvents in parentheses), r^2 = determination coefficient, and % a = percentage of contribution of solvent parameter α_1. [b]Explained variance in A accounted for by α_1, calculated as 100a′/(di′ + e′ + a′) where di′, e′, and a′ are the *standardized* regression coefficients. [c]Significance at the 90% confidence level from a *t* test on each regression coefficient calculated by a least-squares stepwise regression procedure [d]MePM is 4-[(E)-2-(1-methylpyridinium-4-yl)ethenyl]phenolate and MePMBr$_2$ is 2,6-dibromo-4-[(E)-2-(1-methylpyridinium-4-yl)ethenyl]phenolate. The nonspecific contribution to the transition energy E_T of dye MePM is subtracted by means of a solvatochromic comparison with the less basic, but otherwise similar, dye MePMBr$_2$, to give $\Delta E_T(MePM-MePMBr_2) = E_T(MePM) - [0.535E_T (MePMBr_2) + 20.88]$.

acidity of HBD solvents) and were called E_B,[59] E_T^{SO},[60] and AN (acceptor number).[61]

Example 8: According to Taft et al.,[8] Ph−SO−Me is a strong HBA indicator for which the solvent-dependent ^{13}C NMR shifts arise predominantly from hydrogen-bonding of HBD solvents to the sulfoxide group.

In agreement with these statements, we find indeed that 68−100% of the explained variance in A is accounted for by the α_1 solvent parameter. Therefore, the rather high determination coefficients (0.912 ≤ r^2 ≤ 0.973) found for the correlations between α_1 (alone or in minor combination with DI and ES) and these 11 solvent HB acidity-dependent properties indicate that α_1 is indeed a rather "pure" HB acidity parameter and validate its method of determination. The best and worst correlations of Table 3 are illustrated in Figures 2 and 3, respectively.

In addition, the quality of fits using α_1, α, and SA successively as solvent HB acidity parameters for correlating examples 1−5 in Table 3, which were shown to be strongly dependent on the solvent's HB acidity, are given in Table 4.
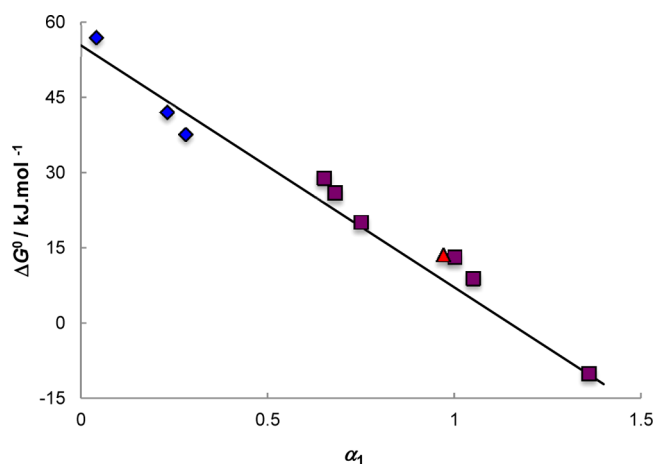
Figure 2. Plot of Gibbs energies of transfer of Cl^- from water to other solvents[54] against the solvent's hydrogen-bond acidity parameter α_1 for 10 HBD solvents. Symbols as in Figure 1.
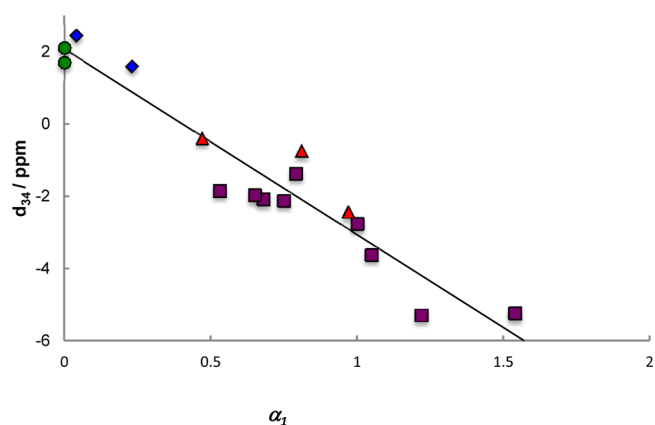
Figure 3. Plot of the differences of the ^{13}C chemical shifts between C-3 and C-4 of pyridine N-oxide[56] against the solvent's hydrogen-bond acidity parameter α_1 for 16 solvents. Symbols as in Figure 1.

Table 4. Comparison of the Goodness of Fit Given by α_1, SA, and α in Their Correlation with the Five Properties of Table 3 Depending Almost Exclusively on the Solvent HB Acidity

		r^2		
property no.	n	α_1	SA	α
1	10	0.973	0.868	0.946
2	20	0.933	0.941	0.784
3	16	0.912	0.846	0.919
4	21	0.956	0.869	0.910
5	10	0.924	0.844	0.949
1−5		0.940[a]	0.874[a]	0.902[a]

[a]Averaged r^2.

The results listed in Table 4 show that, on average, α_1 gives better fits than the other two solvent HB acidity scales. However, this comparison is not yet definitely conclusive because of the limited data sets. The parameters α and SA have already demonstrated their usefulness in the correlation analysis of solvent effects. The parameter α_1 is now proposed as a third choice for the description of the solvent's HB acidity and has still to prove its superiority. Its main advantage is the easy access for newly designed solvents. Its determination needs

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Table 5. Solvent Parameters *DI* (Dispersion+Induction), *ES* (Electrostatic Interactions between Permanent Solute and Solvent Multipoles), and α_1 (HB Acidity) of Glycerol and Three Glycerol Derivatives

solvents	DI	$E_T(30)^a$	E_T(PCM-TD-DFT)^a	ES^a	α_1
HOCH$_2$−CH(OH)−CH$_2$OH	0.219	57.0	59.9	42.79	1.10
MeOCH$_2$−CH(OH)−CH$_2$OH	0.203	53.7	58.5	41.85	0.92
MeOCH$_2$−CH(OH)−CH$_2$OMe	0.200	50.5	56.8	40.67	0.76
BuOCH$_2$−CH(OMe)−CH$_2$OBu	0.202	35.6		35.6	0

^{a}kcal·mol^{-1}.

only one probe, the betaine dye **30** (which is commercially available), and one definition process, the outstanding solvatochromism of this dye.

It should be added that the same betaine dye **30** can also be used to determine a second solvent descriptor, namely the electrostatic parameter *ES*, because $ES = E_T(30)$ for non-HBD solvents and $ES = E_T(30) - \Delta E_T(\text{HBD})$ for HBD solvents.[30] In the following we illustrate the simplicity of our method for the determination of the solvent parameters *DI*, *ES*, and α_1 for some newly developed green solvents derived from glycerol as biomass-based medium.

Determination of Solvent Parameters for Some Glycerol Derivatives. García et al.[64−66] have recently synthesized a variety of eco-friendly glycerol ethers (1-alkoxypropane-2,3-diols, 1,3-dialkoxypropan-2-ols, and 1,2,3-trialkoxypropanes) as potential substitutes for more toxic solvents and have measured many of their physicochemical properties. In particular, they determined the electro-optical properties ε_r and n_D and the empirical solvent polarity parameter $E_T(30)$. From these data and a PCM-TD-DFT calculation of $E_T(30)$, the parameter α_1 for these solvents can be obtained by means of eqs 7 and 8 as well as (13)−(15):

$$DI = (n^2_D - 1)/(2n^2_D + 1) \qquad \text{(for all solvents)} \qquad (13)$$

$$ES = E_T(30) \qquad \text{(for non-HBD solvents)} \qquad (14)$$

$$ES = 0.693E_T(\text{PCM-TD-DFT}) + 1.31$$
$$\text{(for HBD solvents)} \qquad (15)$$

The results are given in Table 5. The α_1 values decrease regularly in the order 1,2,3-triol (1.10) > 2,3-diol (0.92) > monoalkanol (0.76). The α_1 value of 1,3-dimethoxypropan-2-ol (0.76) compares well with that of propan-2-ol (0.53), taken into account the electron-withdrawing acid-strengthening influence of the two methoxy substituents (+0.11 per methoxy group, as compared to $\Delta \alpha_1 = +0.08$ in going from ethanol to 2-methoxyethanol).

CONCLUSIONS

The importance of solvent effects in science[3,25] and technology[67] has stimulated many attempts to define empirical solvent parameters for the quantification of solute/solvent interactions.[68] Although useful in many fields of science and easy to determine for a larger number of liquid media[21−24] the empirical solvent polarity parameter $E_T(30)$ cannot be expected to be generally applicable because it reflects a peculiar blend of solute/solvent interactions. In a previous paper,[30] we have described a two-parameter LSER, based on $E_T(30)$, applicable to the influence of *non-HBD solvents* on solvent-dependent processes. The data in the present contribution provide, for the first time, a simple partitioning of the $E_T(30)$ values into a hydrogen-bonding acidity parameter α_1 and an electrostatic

parameter *ES* for *HBD solvents*. Work for a safe determination of a hydrogen-bonding solvent basicity parameter β_1 will follow. Eventually, chemists will be able to use a set of four consistent parameters, known for a large number of common solvents, and to determine these parameters for newly designed solvents by rather simple methods. In the framework of green chemistry, the design of new, more eco-friendly solvents is at present a topical field of research.[69−71]

ASSOCIATED CONTENT

ⓢ Supporting Information

Scheme SI-1, graphical comparison of the solvent HB acidity of C−H, N−H, and O−H donors. Tables SI-1 and SI-2, results of cLR-PCM calculations of $E_T(30)$ for 31 non-HBD solvents and 55 HBD solvents. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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