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A theoretical study on the basicity of carbonyl compounds in CCl_4

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Abstract—The basicity of 21 carbonyl compounds, measured in CCl_4 in the presence of 4-fluorophenol as reference, was interpreted in terms of two theoretical descriptors, the global energy of protonation ΔE and the charge variation on the oxygen atom Δq_O, calculated with a hybrid DFT method (B3LYP/6-31G(d)). © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The study of acid–base equilibria of organic compounds and the effect of solvent contributions to acidity shifts is a permanent area of interest, with a variety of approaches by different authors. The behaviour of a variety of CH acids in gas phase and DMSO has been recently compared and shifts in acidity interpreted in terms of solvent-attenuating factors.[1] In a related paper, the effect of different solvents on the relative acidities of organic acids has been investigated.[2] The acidity of organic molecules in the gas phase and in aqueous solvent has been probed with ab initio, DFT and continuum solvation methods.[3]

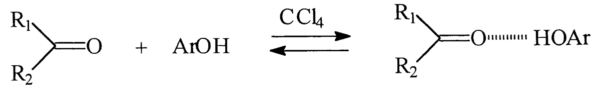
The search for correlations between acid–base properties and theoretical descriptors of organic compounds[4,5] has led our attention to the basicity of carbonyl compounds. Various authors have measured the basicity of these compounds in water and in other solvents,[6] so that there should in principle exist a wealth of data available in the literature for comparisons with theoretically derived parameters. Unfortunately, the wide range of reported values of basicity for the same compounds by different authors often preclude their use in trustworthy studies. Thus, various authors have arrived at pK_a values in water of protonated acetone that span a range of nearly 7 units. A similar observation applies to other carbonyl bases like acetophenone, benzaldehyde and benzophenone.[6]

In a survey of the pK_a values in water of 32 carbon acids, we have recently shown that their acid behaviour correlated with two descriptors, their deprotonation energy (ΔE) and the total charge variation on all hard centres conjugated with the anionic carbon atom of their conjugate bases ($\sum\Delta q_X$).[5] The former descriptor was associated with the intrinsic, or gas-phase acidity, whereas the charge descriptor was used to rationalize solvation effects on the acidity of these compounds. The results also showed no improvement on the correlations when the relatively modest HF/3-21G method was replaced by the more sophisticated hybrid DFT B3LYP method with the larger 6-31G(d) basis set. This relative insensitivity of the obtained correlation on the method of calculation had been observed before by us[4,5] and others[7–9] in the study of the acidic properties of different families of compounds, in the gas-phase and in solution.

In the present communication, we decided to investigate the correlations of the same descriptors with the basic behaviour of various carbonyl compounds in tetrachloromethane. The basicity of a variety of compounds in this solvent had been evaluated in the presence of 4-fluorophenol, by measuring the IR absorbance of the free OH band of that reference compound (Scheme 1).[10]

The resulting pK_{HB} values, calculated from the dissociation constant K_{HB} of the hydrogen-bond complex, spanned a range of ca. 3 units.

The analysis of these data seemed interesting to us for several reasons. In the first place, the data covered a wide range of carbonyl functionalities, such as aromatic and aliphatic aldehydes and ketones, vinylogous esters and amides. They were obtained under the same conditions, so that any deviations observed in our correlations could not be ascribed to experimental errors originating from different laboratories. The pK_{HB} scale correlated well with other hydrogen-bond basicity data corresponding to other aldehydes and/or ketones. In addition, the set constituted a comparatively simple acid–base system, since solvation effects could be regarded as negligible in such a non-polar



Scheme 1.

Keywords: carbonyl compounds; basicity; DFT calculations.

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medium. The question on the meaning and validity of the previously defined energy and charge descriptors for this new system was worth investigating. DFT-based local and global descriptors had been employed with success in a study of the reactivity of some aldehydes towards acid-catalysed ^{18}O exchange reactions with H_2O^{18}.[11] In the present work, the hybrid DFT method B3LYP/6-31G(d) was employed for the calculation of theoretical parameters for the description of the basic behaviour of a series of carbonyl compounds in CCl_4.

2. Method of calculation

Calculations were performed with the Gaussian 94w package.[12] The structures of all carbonyl compounds and their protonated derivatives had geometries fully optimised by the B3LYP method, using the 6-31G(d) basis set. Frequency calculations were performed with a few carbonyl compounds and their protonated forms, to ensure that the obtained structures corresponded in all cases to ground states.

The energy descriptor (ΔE) was calculated as the difference between the heats of formation of the fully protonated carbonyl compound and its conjugate base. The charge descriptor Δq_X was the difference between the charges on atom X, in the protonated compound and in its conjugate base.

$$\Delta E = \Delta H_f(BH^+) - \Delta H_f(B) \qquad (1)$$

$$\Delta q_X = q_X(BH^+) - q_X(B) \qquad (2)$$

3. Results and correlations

Twenty-one carbonyl compounds, comprising aliphatic and aromatic aldehydes and ketones, with pK_{HB} values spanning the full range of available basicities, were chosen from Ref. 10. The list of compounds with the corresponding pK_{HB} values is given in Table 1. Table 2 lists the descriptor values for all compounds. It also includes the variation of the C=O bond length upon protonation ($\Delta d_{C=O}$), and the calculated O–H bond length of the fully protonated carbonyl compounds (d_{O-H}), obtained from the optimised structures.

The pK_{HB} values, together with the basicity of the carbonyl compounds, increase with an increase in the absolute values of the energy descriptor. By contrast, the calculated charge variations on the carbonyl C and the O atoms do not show any monotonic trend with the increase of the basicity of the series. No correlation was observed ($r^2<0.2$) between the pK_{HB} and the charge descriptor Δq_O. An examination of the values of the charge descriptor Δq_C reveals a clear distinction between conjugated and non-conjugated carbonyl compounds. For the conjugated compounds, Δq_C values are all negative, an indication that the carbonyl carbon atom becomes slightly less positive upon protonation of the CO group. The reverse is observed for the non-conjugated compounds, where an increase in positive charge on the carbon atom is observed.

Table 1. Basicity values of carbonyl compounds **1**–**21** in tetrachloromethane

	Carbonyl compound	pK_{HB} value[a]
1	Trifluoroacetone	−0.06
2	1,3-Dichloroacetone	0.32
3	4-Chlorobenzaldehyde	0.63
4	Acetaldehyde	0.65
5	3-Nitroacetophenone	0.69
6	Benzaldehyde	0.78
7	4-Chloroacetophenone	0.93
8	Cyclobutanone	1.00
9	4-Methoxybenzaldehyde	1.10
10	Acetophenone	1.11
11	3-Methoxyacetophenone	1.16
12	2-Pentanone	1.17
13	Acetone	1.18
14	Cyclopentanone	1.27
15	Cyclohexanone	1.39
16	Cycloheptanone	1.41
17	4-Dimethylaminoacetophenone	1.76
18	Tropone	1.97
19	γ-Pyrone	2.03
20	2,6-Dimethyl-γ-pyrone	2.50
21	3-Dimethylamino-3,5-dimethylcyclohexenone	2.92

[a] From dissociation constants K_{HB} of hydrogen-bond complexes with 4-fluorophenol. Data from Ref. 10.

In Table 2 are also listed the variations of the C=O bond distance upon protonation ($\Delta d_{C=O}$). The distinction between conjugated and non-conjugated carbonyls is also apparent here. Conjugated compounds showed variations in the range 0.082–0.096 Å, whereas the values for non-conjugated carbonyls never exceeded 0.071 Å.

The values of the hydroxyl bond length of the protonated carbonyls also reveal a subtle difference between conjugated and non-conjugated compounds. The former

Table 2. Energy (ΔE), charge (Δq_X), bond-length variations ($\Delta d_{C=O}$) and hydroxyl bond length (d_{O-H}) on protonation of carbonyl bases **1**–**21**, calculated by the B3LYP/6-31G(d) method

Compound	$-\Delta E$ (a.u.)	Δq_C	Δq_O	$\Delta d_{C=O}$ (Å)[a]	d_{O-H} (Å)[b]
1	0.2933	0.036	−0.003	0.058	0.992
2	0.3052	0.019	−0.019	0.060	0.999
3	0.3345	−0.042	−0.060	0.086	0.976
4	0.3061	0.032	0.018	0.060	0.984
5	0.3279	−0.017	−0.044	0.082	0.978
6	0.3370	−0.033	−0.051	0.083	0.977
7	0.3418	−0.029	−0.049	0.087	0.976
8	0.3187	0.036	0.000	0.068	0.984
9	0.3537	−0.058	−0.065	0.093	0.975
10	0.3450	−0.021	−0.041	0.084	0.976
11	0.3487	−0.025	−0.041	0.085	0.976
12	0.3281	0.028	0.007	0.067	0.982
13	0.3235	0.027	0.012	0.065	0.983
14	0.3282	0.035	0.004	0.068	0.982
15	0.3345	0.036	0.005	0.069	0.982
16	0.3335	0.036	0.008	0.071	0.982
17	0.3726	−0.066	−0.048	0.094	0.975
18	0.3683	−0.013	−0.032	0.095	0.974
19	0.3573	−0.022	−0.021	0.086	0.976
20	0.3731	−0.027	−0.023	0.089	0.975
21	0.3927	−0.023	−0.030	0.096	0.975

[a] Variation of the carbonyl bond distance upon protonation.

[b] Calculated hydroxyl bond-length of the protonated carbonyls.

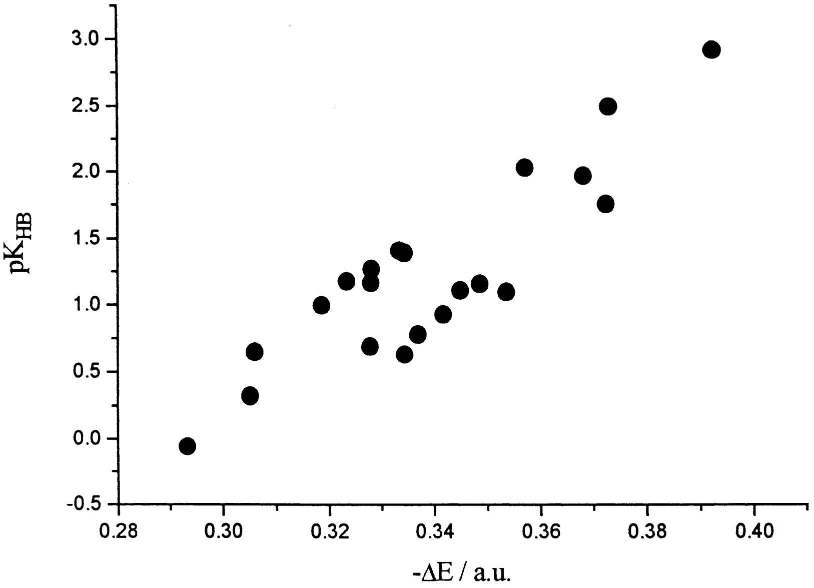


Figure 1. Correlation between the experimental pK_{HB} values of compounds **1–21** and the energy descriptor ΔE.

compounds exhibited slightly smaller d_{O-H} values (<0.978 Å) than the latter (>0.982 Å).

Fig. 1 is a plot of the experimental pK_{HB} values vs the energy descriptor ΔE. As can be seen, the obtained correlation was only fair (r^2=0.785). An inspection of the plot reveals two sets of points, corresponding to conjugated and non-conjugated carbonyls, by which two roughly parallel straight lines might be drawn. The observed dispersion led to the incorporation of a second descriptor into a two-parameter regression equation. For both methods of calculation, the best choice was the charge descriptor Δq_O. This parameter was fairly independent of the energy descriptor (r^2=0.238). The dispersion of the data points of Fig. 1 was thus reduced, and the correlation improved by the regression Eq. (3)

$$\mathrm{p}K_{HB}^{calc} = -32.28\Delta E + 13.51\Delta q_O - 9.41$$
$$[n = 21,\ r^2 = 0.978,\ F = 392,\ \mathrm{S.D.} = 0.11] \tag{3}$$

The obtained standard deviation of 0.11 pK_{HB} units was about twice the maximum experimental error estimated for the reported pK_{HB} values (0.05).[10] The resulting plot of experimental vs calculated pK_{HB} values is shown in Fig. 2.

4. Discussion

For all compounds **1–21**, the site of protonation was the carbonyl oxygen. This was based on previous evidence of

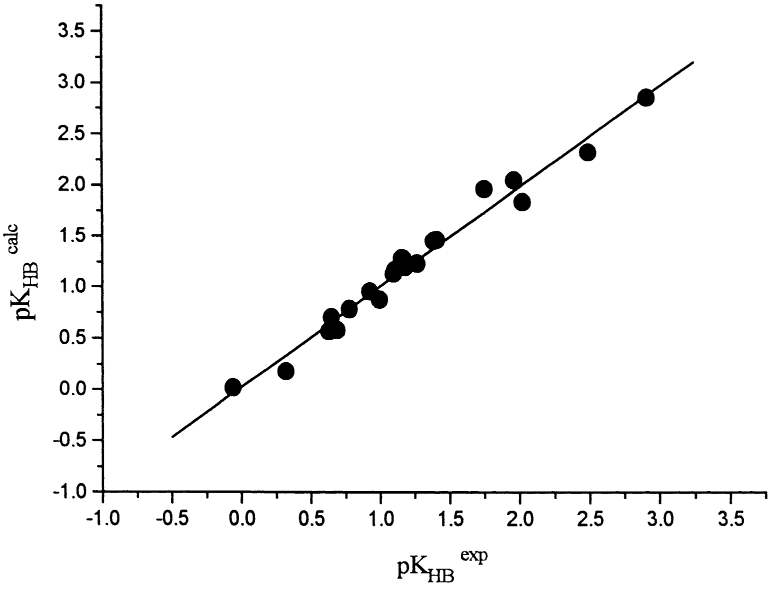
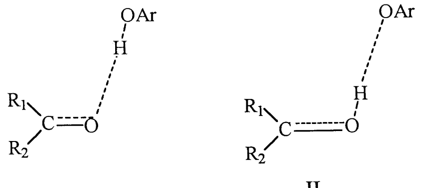


Figure 2. Experimental vs. calculated pK_{HB} values of compounds **1–21**, from regression equation (3) and the B3LYP/6-31G(d) descriptor values of Table 2.



I II

Scheme 2.

the site of protonation of aromatic aldehydes, from the O (1s) core electron binding energies,[13] and on the spectroscopic evidence that, in the case of pyrones and vinylogous amides, the carbonyl group, and not the conjugated heteroatom, was hydrogen-bonded to the phenol donor.[10]

The absolute value of the protonation energy (ΔE) increases with the basicity of the carbonyl compound. This is the result, to a first approximation, of the exergonic formation of an O–H bond in the protonated base. The strength of this bond increases with the basicity of the C=O group.

For both sets of conjugated and non-conjugated carbonyl compounds, the variation of the calculated C=O bond distance on protonation ($\Delta d_{\mathrm{C=O}}$) increases with the basicity of the compound. This may be taken as an indication of the degree of proton transfer from the phenol to the carbonyl compound in the complex. Thus, for the series of conjugated compounds, the weakest base, 4-chlorobenzaldehyde (**3**), has a $\Delta d_{\mathrm{C=O}}$ value of 0.086 Å, corresponding to a hydrogen-bond complex approaching the extreme situation (I) below. The strongest base of the series, compound **21**, has a $\Delta d_{\mathrm{C=O}}$ value of 0.096 Å. Structure II depicts this extreme situation for a complex where the maximum elongation of the C=O bond is accompanied by maximum shortening of the O–H bond with the phenolic proton (Scheme 2).

The basic behaviour of compounds **1–21** in CCl_4 should approach a gas-phase situation, since solvation effects by the non-polar medium are negligible. Therefore, a reasonable correlation is observed between the pK_{HB} and the ΔE descriptor, which is a measure of the intrinsic basicity of all compounds (Fig. 1). The observed dispersion reflects the fact that the series comprises two different sets of carbonyl compounds, with conjugated and non-conjugated C=O groups. The behaviour of compounds **1–21** may be regarded as a composite of two factors, the global molecular stabilization of the protonated base and the specific interaction of the C=O group with the proton donor. The contribution of these factors to the basicity of the studied compounds differs for conjugated and non-conjugated carbonyls. For the latter, protonation of the C=O group leads to localized enthalpic and bond changes, concentrated mainly on the carbonyl group of the molecule. In a conjugated compound, however, the enthalpic changes are shared with other portions of the molecule and the C=O bond deformation is only a part of the overall bond-length modifications of the whole molecule. This interpretation is supported by the different values of the Δq_{C} descriptor for conjugated and non-conjugated compounds (Table 2). In the non-conjugated compounds, C=O protonation transfers positive charge to the carbon atom. In the conjugated compounds, this positive charge-transfer is shared with the rest of the molecule to such an extent that electron donation by the rest of the molecule results in an increase of negative charge on the C=O carbon atom of practically all members of the set.

It is interesting to notice that a previous study on linear relationships between the ionisation potentials of carbonyl oxygens and their enthalpies of complexation with BF_3 led to the conclusion that the effect of substituents on the basicity of the carbonyl group differed for various classes of compounds. This was ascribed to the variable, strong conjugative interactions observed in the protonated state, but not in the free carbonyl compound.[14] Our theoretical results thus confirm these observations, by drawing a clear distinction between conjugated and non-conjugated carbonyl compounds.

5. Cross-validation: examples of a hybrid behaviour

The predictive power of the correlation equation (3) may be estimated from its good cross-validated correlation coefficient ($r_{\mathrm{cv}}^2=0.882$), obtained from a leave-one-out procedure. In order to test the model with other compounds not included in the regression, we decided to compare the estimated pK_{HB} value of two new carbonyl compounds, with their reported values. We chose cyclopropylmethylketone (**22**) and dicyclopropylketone (**23**) as interesting examples of a hybrid behaviour. Both compounds belong to the series of non-conjugated carbonyl compounds. However, the cyclopropyl ring is known to stabilize an adjacent carbocation, because of interactions of the C–C σ bonding orbitals with an empty p orbital.[15] Conjugation of the ring σ bonds with the π system of an adjacent carbonyl group should also occur for compounds **22** and **23**, and should be reflected in the values of the local descriptors calculated for these compounds. Table 3 lists the descriptor values for these compounds, together with the estimated pK_{HB} values, obtained with the regression equation (3). The hybrid nature of these ketones is seen in the values of the local descriptors. The values for the C=O bond elongation, $\Delta d_{\mathrm{C=O}}=0.081$ and 0.086 Å for compounds **22** and **23**, respectively, fall in the range observed for conjugated carbonyls. Cyclopentanone **14** and cyclohexanone **15**, with similar pK_{HB}

Table 3. Descriptor values and estimated pK_{HB}s for cyclopropylmethylketone (**22**) and dicyclopropylketone (**23**)

Compound	$-\Delta E$ (a.u.)	$\Delta d_{\mathrm{C=O}}$ (Å)	Δq_{O}	Δq_{C}	Calcd pK_{HB}[a]	Lit. pK_{HB}[b]
22	0.3397	0.081	−0.024	0.009	1.23	(1.32)[c]
23	0.3469	0.086	−0.027	0.024	1.42	1.36

[a] With Eq. (3).
[b] From Ref. 10.
[c] Secondary value.

values (1.27 and 1.39, respectively) have shorter $\Delta d_{C=O}$ values (0.068 and 0.069 Å), characteristic of non-conjugated carbonyls. The hydroxyl bond length (d_{O-H}) of the protonated forms of both ketones, 0.977 Å for compound **22**, and 0.975 Å for ketone **23**, also fall in the range observed for all conjugated carbonyls ($d_{O-H}<0.978$ Å). The charge variations on the oxygen atom ($\Delta q_O=-0.024$ and -0.027 for compounds **22** and **23**), are, in absolute value, larger than the variation calculated for any non-conjugated carbonyl. Similar values were obtained for the conjugated γ-pyrone **20** ($\Delta q_O=-0.023$) and the cyclohexenone **21** ($\Delta q_O=-0.030$).

The behaviour of ketones **22** and **23** departs from that of the other conjugated ketones if their charge variations on the carbonyl carbon are compared. Unlike what is observed for the conjugated π systems, the Δq_C parameter is not negative. Upon protonation, positive charge is built up on the carbonyl C atom of **22** and **23**, as is the case for all non-conjugated ketones.

Thus, the hybrid nature of compounds **22** and **23** is evident from the calculated values of their local descriptors. While the $\Delta d_{C=O}$ and the Δq_O parameters are characteristic of conjugated ketones, their positive Δq_C descriptor values position them among the non-conjugated carbonyl derivatives.

6. Conclusions

A parallel may now be drawn between the present study and the behaviour of carbon acids in water.[5] We have shown that the acid–base equilibria of two different series of compounds in distinct media could be described with the aid of two theoretical parameters, a global and a local descriptor, without explicit consideration of the solvent. The first one, the global molecular descriptor ΔE, has proved successful in correlations with various acid–base pairs in the gas-phase and in distinct solvents.[4,5,16] The second one, the local charge descriptor Δq_X, has been used to interpret solvation contributions to the acid–base equilibrium in water.[5] In the present study, in spite of the lack of significant solvation effects by the non-polar medium, this parameter may likewise be regarded as a measure of specific interactions between the carbonyl base and a proton donor, which also acts as an equimolar 'solvent'.

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