Hydrogen-bond basicity pK_{HB} scale of aldehydes and ketones

François Besseau, Maryvonne Luçon, Christian Laurence and Michel Berthelot

Laboratoire de Spectrochimie, Faculté des Sciences et des Techniques, Université de Nantes, 2 rue de la Houssinière, BP 92208, 44322 Nantes Cedex 3, France

The thermodynamic hydrogen-bond basicity scale pK_{HB} (logarithm of the formation constant of 4-fluorophenol–aldehyde or ketone complexes in CCl_4 at 298 K) has been determined for aldehydes, aliphatic ketones, cycloalkanones, diketones and quinones, halogenated ketones, pyrones and related compounds, acetophenones, benzophenones and various other conjugated ketones. The relationship between pK_{HB} and a spectroscopic scale of basicity is obscured by the presence of two stereoisomeric complexes. In the R^1COMe series the electronic and steric effects of the alkyl R^1 almost cancel out, whereas steric effects prevail in R^1COR^2. Among alkyl substituents the 1-adamantyl is the most electron-donating. In cycloalkanones the basicity sequence with ring size is 4 < 11 ~ 12 ~ 15 < 5 < 6 < 7 < 8. Quantitative structure–basicity relationships have been established in the aromatic 3- and 4-XC_6H_4COMe and the aliphatic XCOMe series. Intramolecular hydrogen bonding causes a basicity decrease in acetylacetone. Hydrogen bonding sites are discussed.

The first thermodynamic scale of hydrogen-bond basicity was set up in 1969–1972 by Taft and co-workers,[1–3] who defined pK_{HB} as log K_f for the 1:1 complexation of bases with 4-fluorophenol in carbon tetrachloride at 298 K [eqns. (1)–(3)].

$$B + 4\text{-}FC_6H_4OH \rightleftharpoons 4\text{-}FC_6H_4OH \cdots B \quad (1)$$

$$K_f = [\text{Hydrogen-bond complex}]/[B][4\text{-}FC_6H_4OH] \quad (2)$$

$$pK_{HB} = -\log_{10}(\text{dissociation constant of the complex}) = \log_{10} K_f \quad (3)$$

Little further work on the pK_{HB} scale was reported between 1972 and 1988, when we began to extend systematically the pK_{HB} scale to the various families of organic bases. Nitrogen,[4,5] oxygen,[6,7] sulfur[8] and π bases[9] have already been studied. In the carbonyl base family, the pK_{HB} scale has been published for esters,[10] amides[11] and amidates[12] but not for aldehydes and ketones.

Previous measurements of equilibrium constants for the hydrogen bonding of phenols to aldehydes and ketones have been reported by Gramstad,[13] Kelm and Brauer,[14] Bellon and co-workers[15] and others.[16–19] However, they refer to a too limited a number of compounds to give a wide view of the influence of structure on ketone hydrogen-bond basicity. Moreover they were carried out with different phenols (*e.g.* phenol[13] and 2-naphthol[15]), different solvents (*e.g.* CCl_4[14] and cyclohexane[15]) and different temperatures (293,[13] 298[16] or 303 K[18]). Statistical procedures could be used to set up a homogeneous basicity scale from these data but this would inevitably result in a loss of fine structural information. We prefer to build a scale defined from a reference process [eqn. (1)] rather than a statistical scale, and we present here the pK_{HB} scale of aldehydes and (mainly) ketones. We have assembled 79 primary and 25 secondary pK_{HB} values (*vide infra*). Our sample of compounds is numerous and diverse enough to study the influence on hydrogen-bond basicity of: (*i*) electronic and steric effects of alkyl R^1 and R^2 groups in the R^1COR^2 series; (*ii*) ring size in cycloalkanones; (*iii*) field, resonance and polarisability effects in the aliphatic series XCOMe; (*iv*) field and resonance effects in ring-substituted acetophenones, benzophenones and benzaldehydes.

Experimental

Chemicals

Ketones and aldehydes were mostly commercially available and after purification were generally 99.5% pure according to GLC or TLC. Compounds **27** and **28** were generously given by Dr Abboud (Madrid), **37** by Dr Morris (Glasgow), **62** by Dr Reichardt (Marburg) and **94** and **100** by Drs Geribaldi and Gal (Nice).

4-Fluorophenol was sublimed and dried over P_2O_5. The spectroscopic grade CCl_4 was dried before use on activated molecular sieves. All the procedures for the preparation of solutions and filling the IR cell were conducted in a dry glove-box.

Spectra

IR spectra were recorded with a Fourier transform spectrometer, either a Bruker IFS 48 or a Nicolet 510 M, at a resolution of 1 cm^{-1} with 256 scans. An infrasil quartz cell of 1 cm was used. The temperature was maintained at 25 ± 0.2 °C.

Equilibrium constants

The equilibrium constant is defined by $K_f = C_c/C_aC_b = (C_a^\circ - C_a)/[C_a(C_b^\circ - C_a^\circ + C_a)]$ where C_c, C_b and C_a are the equilibrium concentrations of complex, base (ketone or aldehyde) and acid (4-fluorophenol), respectively, and C_a° and C_b° are the initial concentrations determined by weight. C_a is obtained from the IR absorbance of the free OH band of 4-fluorophenol at 3614 cm^{-1} ($\varepsilon = 235$ dm^3 mol^{-1} cm^{-1}). The equilibrium constants are taken as the mean of four values corresponding to four base concentrations. These concentrations are chosen such that the complex percentage is kept in the range 20–80% of the initial acid concentration. Typical concentration ranges are 0.3–0.6 M for $MeCOCF_3$ and 0.02–0.04 M for the most basic ketone **100**. All measurements are carried out in a cell of 1 cm path length and the 4-fluorophenol concentration is *ca.* 4×10^{-3} M in order to minimize self-association. K_f is estimated to be accurate to within 5–10% and consequently pK_{HB} values are given to within ±0.02–0.05 pK units.

Results

Primary pK_{HB} values are assembled in Table 1. They all refer to

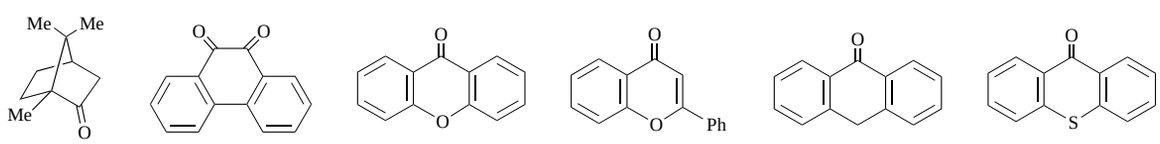
Table 1 Hydrogen-bond basicity of aldehydes and ketones: frequency shifts $\Delta\nu$(OH)/cm^{-1}, primary and secondary pK_{HB} values and β_2^H values

No.	Compound	Formula	$\Delta\nu$(OH)[a]	pK_{HB}[b]	β_2^H
	Aldehydes				
1	Acetaldehyde	MeCOH		0.65	0.38
2	Benzaldehyde	PhCOH	65	0.78	0.41
3	4-Chlorobenzaldehyde	4-ClC_6H_4COH		0.63	0.37
4	4-Methoxybenzaldehyde	4-$MeOC_6H_4COH$	93	1.10	0.47
5	4-(Dimethylamino)benzaldehyde	4-$Me_2NC_6H_4COH$	123	1.53	0.57
6	*trans*-Cinnamaldehyde	PhCH=CHCOH		1.13	0.48
7	2-Methoxybenzaldehyde	2-$MeOC_6H_4COH$		1.11	0.48
	Aliphatic ketones				
8	Propan-2-one	MeCOMe	115	1.18	0.49
9	Butan-2-one	MeCOEt	91	1.22	0.50
10	3-Methylbutan-2-one	$MeCOPr^i$		(1.20)	0.50
11	3,3-Dimethylbutan-2-one	$MeCOBu^t$		(1.17)	0.49
12	Pentan-2-one	$MeCOPr^n$		(1.17)	0.49
13	Pentan-3-one	EtCOEt		(1.14)	0.48
14	3-Methylpentan-2-one	$MeCOBu^s$		(1.22)	0.50
15	4-Methylpentan-2-one	$MeCOBu^i$		(1.17)	0.49
16	2,4-Dimethylpentan-3-one	Pr^iCOPr^i		(1.08)	0.47
17	2,2,4,4-Tetramethylpentan-3-one	Bu^tCOBu^t	77	0.96	0.44
18	Hexan-2-one	$MeCOBu^n$		(1.18)	0.49
19	Hexan-3-one	$EtCOPr^n$		(1.13)	0.48
20	Heptan-4-one	Pr^nCOPr^n		(1.14)	0.48
21	2,6-Dimethylheptan-4-one	Bu^iCOBu^i		(1.07)	0.47
22	3,5-Dimethylheptan-4-one	Bu^sCOBu^s		(1.07)	0.47
23	1-Adamantyl methyl ketone	MeCOAd	87	1.30	0.52
24	Cyclohexyl methyl ketone	$MeCOcC_6H_{11}$		(1.24)	0.50
25	Methyl cyclopropyl ketone	MeCOcPr		(1.32)	0.52
26	Dicyclopropyl ketone	cPrCOcPr	110	1.36	0.53
27	1-Adamantyl *tert*-butyl ketone	$AdCOBu^t$	79	1.08	0.47
28	Di-(1-adamantyl) ketone	AdCOAd	89	1.17	0.49
	Cycloalkanones				
29	Cyclobutanone	$CH_2(CH_2)_2CO$		1.00	0.45
30	Cyclopentanone	$CH_2(CH_2)_3CO$	121	1.27	0.51
31	Cyclohexanone	$CH_2(CH_2)_4CO$	126	1.39	0.54
32	2-Methylcyclohexanone	$CH_2(CH_2)_3CH(CH_3)CO$		(1.27)	0.51
33	Cycloheptanone	$CH_2(CH_2)_5CO$	127	1.41	0.54
34	Cyclooctanone	$CH_2(CH_2)_6CO$		1.45	0.55
35	Cycloundecanone	$CH_2(CH_2)_9CO$	89	1.20	0.50
36	Cyclododecanone	$CH_2(CH_2)_{10}CO$	85	1.23	0.50
37	Cyclopentadecanone	$CH_2(CH_2)_{13}CO$	83	1.22	0.50
38	Camphor	*c*	103	1.31	0.52
	Diketones, quinones				
39	Biacetyl	MeCOCOMe	36	0.53	0.35
40	Benzil	PhCOCOPh	46	0.74	0.40
41	1,4-Benzoquinone	CH=CHCOCH=CHCO		0.81	0.41
42	9,10-Phenanthrenequinone	*c*		(1.00)	0.45
43	Acetyl acetone	$MeCOCH_2COMe$		0.90	0.43
	Halogenated quinones				
44	1,1,1-Trifluoropropan-2-one	$MeCOCF_3$	39	−0.06	0.22
45	1,1,1-Trichloropropan-2-one	$MeCOCCl_3$		0.00	0.24
46	1,1-Dichloropropan-2-one	$MeCOCHCl_2$		0.25	0.29
47	1,3-Dichloropropan-2-one	$ClCH_2COCH_2Cl$		0.32	0.31
48	Chloropropan-2-one	$MeCOCH_2Cl$	55	0.66	0.38
	Pyrones and related compounds				
49	γ-Pyrone	CH=CHOCH=CHCO	185	2.03	0.68
50	2,6-Dimethyl-γ-pyrone	CH=C(Me)OC(Me)=CHCO	220	2.50	0.78
51	Xanthone	*c*	119	1.36	0.53
52	Flavone	*c*	167	1.99	0.67
53	Anthrone	*c*		1.16	0.49
54	Thioxanthen-9-one	*c*		(1.18)	0.49
55	10-Methyl-9(10*H*)-acridone	*c*		(1.92)	0.65
	Conjugated ketones: acetophenones				
56	4-(Diethylamino)acetophenone	4-$Et_2NC_6H_4COMe$		1.82	0.63
57	4-(Dimethylamino)acetophenone	4-$Me_2NC_6H_4COMe$	134	1.76	0.62
58	4-Piperidinoacetophenone	$CH_2(CH_2)_4NC_6H_4COMe$		1.71	0.61

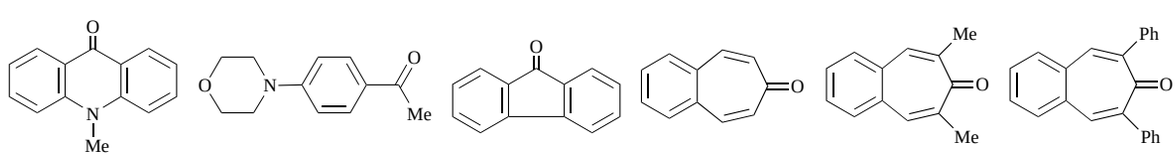
Table 1 (*Contd*)

No.	Compound	Formula	$\Delta\nu$(OH)[a]	pK_{HB}[b]	β_2^H
59	4-Morpholinoacetophenone	*c*	117	1.61	0.58
60	4-Aminoacetophenone	4-$H_2NC_6H_4COMe$		(1.50)	0.56
61	4-Methoxyacetophenone	4-$MeOC_6H_4COMe$	111	1.33	0.52
62	4-(1-Adamantyl)acetophenone	4-AdC_6H_4COMe	106	1.30	0.52
63	4-*tert*-Butylacetophenone	4-$Bu^tC_6H_4COMe$	92	1.25	0.51
64	4-Isopropylacetophenone	4-$Pr^iC_6H_4COMe$	98	1.21	0.50
65	4-Ethylacetophenone	4-EtC_6H_4COMe	86	1.25	0.51
66	4-Methylacetophenone	4-MeC_6H_4COMe	102	1.24	0.50
67	4-Methylthioacetophenone	4-$MeSC_6H_4COMe$	87	1.21	0.50
68	Acetophenone	C_6H_5COMe	92	1.11	0.48
69	4-Fluoroacetophenone	4-FC_6H_4COMe	80	1.00	0.45
70	4-Chloroacetophenone	4-ClC_6H_4COMe	84	0.93	0.44
71	1,4-Diacetylbenzene	4-$MeCOC_6H_4COMe$	71	1.22	0.50
72	4-Cyanoacetophenone	4-$N{\equiv}CC_6H_4COMe$	65	0.97	0.45
73	4-(Trifluoromethyl)acetophenone	4-$F_3CC_6H_4COMe$	67	0.78	0.41
74	4-Nitroacetophenone	4-$O_2NC_6H_4COMe$		0.69	0.39
75	3-Methoxyacetophenone	3-$MeOC_6H_4COMe$	88	1.16	0.49
76	3-Methylacetophenone	3-MeC_6H_4COMe	88	1.10	0.47
77	3-Fluoroacetophenone	3-FC_6H_4COMe		0.83	0.42
78	3-Chloroacetophenone	3-ClC_6H_4COMe	77	0.82	0.41
79	3-(Trifluoromethyl)acetophenone	3-$F_3CC_6H_4COMe$	68	0.72	0.39
80	1,3-Diacetylbenzene	3-$MeCOC_6H_4COMe$		1.16	0.49
81	3-Nitroacetophenone	3-$O_2NC_6H_4COMe$		0.69	0.39
82	2-Chloroacetophenone	2-ClC_6H_4COMe	64	0.90	0.43
83	2-Methoxyacetophenone	2-$MeOC_6H_4COMe$		1.34	0.53
	Conjugated ketones: benzophenones				
84	Benzophenone	PhCOPh	52	1.07	0.47
85	4-Methoxybenzophenone	4-$MeOC_6H_4COPh$	97	1.27	0.51
86	4,4′-Bis(methoxy)benzophenone	$(4\text{-}MeOC_6H_4)_2CO$	95	1.49	0.56
87	4-(Dimethylamino)benzophenone	4-$Me_2NC_6H_4COPh$	123	1.67	0.60
88	4,4′-Bis(dimethylamino)benzophenone	$(4\text{-}Me_2NC_6H_4)_2CO$		(1.93)	0.65
89	4,4′-Bis(diethylamino)benzophenone	$(4\text{-}Et_2NC_6H_4)_2CO$	160	2.33	0.74
90	Dimesityl ketone	$(2,4,6\text{-}Me_3C_6H_2)_2CO$		(1.01)	0.46
	Conjugated ketones: miscellaneous				
91	But-3-yn-2-one	HC≡CCOMe	58	0.68	0.38
92	9-Fluorenone	*c*	105	1.09	0.47
93	2-Acetylnaphthalene	$C_{10}H_7COMe$	89	1.13	0.48
94	3-Chloro-5,5-dimethylcyclohexenone	$CH{=}C(Cl)CH_2C(Me)_2CH_2CO$	119	1.21	0.50
95	*trans*-4-Phenylbut-3-en-2-one	PhCH=CHCOMe	124	1.38	0.53
96	Acetylferrocene	$C_5H_5FeC_5H_4COMe$		1.65	0.59
97	3-Methyl-5,5-dimethylcyclohexenone	$CH{=}C(Me)CH_2C(Me)_2CH_2CO$	154	1.74	0.61
98	Tropone	$CH{=}CH(CH{=}CH)_2CO$		1.97	0.66
99	Diphenylcyclopropenone	$PhC{=}C(Ph)CO$	214	2.30	0.73
100	3-Dimethylamino-5,5-dimethylcyclohexenone	$CH{=}C(NMe_2)CH_2C(Me)_2CH_2CO$	248	2.92	0.87
101	Dibenzyl ketone	$(PhCH_2)_2CO$		(1.00)	0.45
102	Benzotropone	*c*		(1.88)	0.64
103	α,α′-Dimethylbenzotropone	*c*		(1.48)	0.56
104	α,α′-Diphenylbenzotropone	*c*		(1.30)	0.52

[a] $\Delta\nu$(OH) = 3644 − ν(OH···); ν(OH···) is the apparent maximum of the bonded absorption in case of overlapping bands (see text). [b] Secondary values between brackets. [c] For structures see text.



38 **42** **51** **52** **53** **54**



55 **59** **92** **102** **103** **104**

the reference process, equilibrium (1), and come from three sources. (*i*) Six values (**4**, **5**, **50**–**52** and **96**) are from the pioneering work of Taft and co-workers[1,3] and were determined by ^{19}F NMR spectroscopy. (*ii*) Eight values (**2**, **7**, **61**, **68**, **83**–**85** and **98**) were measured by our group by Fourier transform IR spectroscopy and have been published elsewhere.[20] (*iii*) The other 65

values were determined in this work by Fourier transform IR spectroscopy.

Carbon tetrachloride is the standard solvent for establishing the pK_{HB} scale, but a few ketones (**42**, **54**, **55**, **60** and **88**) are not sufficiently soluble in this solvent. Consequently the hydrogen-bonded complexes of 4-fluorophenol with these ketones were studied in dichloromethane. Taft and co-workers[3] have shown that there is no general relationship between the logarithms of the equilibrium constants measured in these two solvents. Thus, from new measurements carried out in both solvents, we have established the conversion equation [eqn. (4)] which is restricted

$$pK_{HB} = 1.051 \log K'_{CH_2Cl_2} + 0.707 \quad (4)$$
$$n = 5\ r = 0.995\ s = 0.06\ F = 274$$

to carbonyl compounds. In this equation, r is the correlation coefficient, n the number of data points, s the standard deviation of the estimate and F the Fisher F-statistic. Secondary pK_{HB} values calculated from eqn. (4) are given in brackets in Table 1.

We have compared the pK_{HB} scale assembled in this work with other hydrogen-bond basicity data[13–15] corresponding to aldehydes and/or ketones. Results are presented in eqns. (5)–(8),

$$pK_{HB} = 1.096 \log K\,(\text{phenol, } CCl_4, 293\ K) - 0.044 \quad (5)$$
$$n = 6 \quad r = 0.995 \quad s = 0.05 \quad F = 377$$

$$pK_{HB} = 0.904 \log K\,(\text{2-naphthol, } C_6H_{12}, 293\ K) - 0.116 \quad (6)$$
$$n = 14 \quad r = 0.991 \quad s = 0.03 \quad F = 651$$

$$pK_{HB} = 0.889 \log K\,(\text{2-naphthol, } C_7H_{16}, 293\ K) - 0.092 \quad (7)$$
$$n = 14 \quad r = 0.981 \quad s = 0.04 \quad F = 306$$

$$pK_{HB} = 1.241 \log K\,(\text{phenol, } CCl_4, 293\ K) - 0.131 \quad (8)$$
$$n = 15 \quad r = 0.943 \quad s = 0.12 \quad F = 104$$

where K is the formation constant expressed in $dm^3\ mol^{-1}$. Our data agree well with those of Kelm and Brauer[14] [eqn. (5)] and of Bellon and co-workers[15] [eqns. (6) and (7)]. Since the standard deviations of the estimate in eqns. (5)–(7) are within experimental errors, secondary pK_{HB} values can safely be calculated from the results of these authors. They are also given in brackets in Table 1. On the contrary, the Gramstad data[13] [eqn. (8)] do not seem satisfactory ($s = 0.12$). For example, Gramstad finds that 4-chlorobenzaldehyde is more basic than benzaldehyde, in contradiction of our results and with the electron-withdrawing effect of the 4-chloro substituent.

We give also in Table 1 the β_2^H and $\Delta\nu$(OH) values. β_2^H, calculated from eqn. (9), has proved useful in linear solvation energy

$$\beta_2^H = (pK_{HB} + 1.1)/4.636 \quad (9)$$

relationships[21,22] and for prediction of the stability of many hydrogen-bonded complexes.[23] $\Delta\nu$(OH) is the lowering of the methanol ν(OH) frequency on going from the free to the hydrogen-bonded absorption.

Discussion

Two 1:1 complexes of 4-fluorophenol with ketones

The ν(OH) band of the complex of 4-fluorophenol (and other OH hydrogen-bond donors) with aldehydes or ketones is generally abnormally broad and unsymmetrical, and can be resolved into Gauss–Lorentzian component bands (Fig. 1).[24–28] A general agreement[24,27,28] exists for attributing the low-frequency component band to the bent n complex **A**, whereas the high-frequency component band was tentatively attributed to the linear n complex **B**[27] or the out-of-plane π complex **C**.[28]

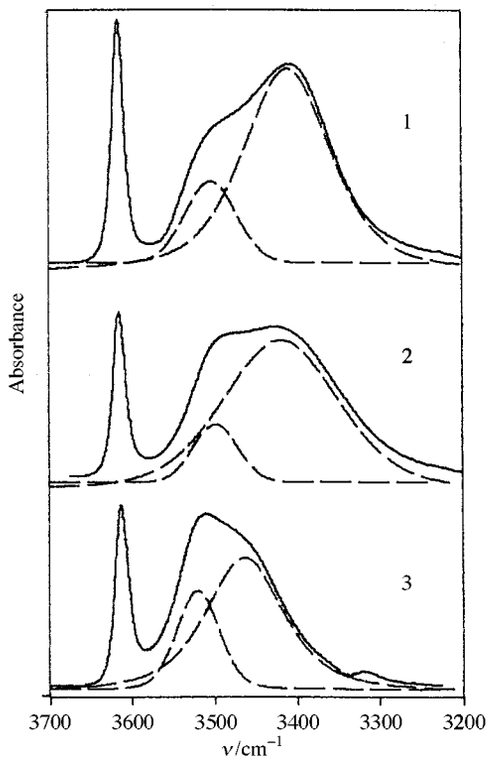
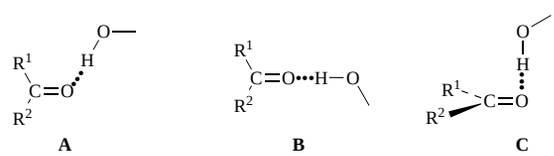


Fig. 1 Variation of the OH bandshape of 4-fluorophenol hydrogen bonded in CCl_4 with (1) cyclobutanone; (2) 2-chloroacetophenone; (3) benzil. The dotted lines show the two component bands attributed to the stereoisomeric complexes **A** or **B**(**C**).



Accordingly, K_f is a global formation constant which is the sum of the formation constants for each stereoisomeric complex. Methods have been presented[25,26,28] for evaluating the individual constants, but we prefer keeping the global constant K_f for measuring the basicity of the whole carbonyl oxygen, *i.e.* reasoning in terms of atoms rather than in terms of electrons in order to avoid evident experimental and theoretical difficulties.

It is, however, useful to recall[27] that complex **B** is strongly favoured by bulky R^1 and R^2 substituents (*e.g.* *tert*-butyl or 1-adamantyl) and electron-withdrawing substituents (*e.g.* CF_3). On the contrary, acetone, with small and electron-donating methyl groups, and pyrones, cyclohexenones and cycloalkanones, where cyclisation minimizes steric effects, form mainly complex **A**.

For a series of 12 ketones forming mainly **A** complexes we have found a good relationship (Fig. 2) between the thermodynamic pK_{HB} scale and the spectroscopic scale of hydrogen-bond basicity $\Delta\nu$(OH). For other ketones, and aldehydes, we have presented elsewhere[29] the difficulties encountered in establishing meaningful relationships between spectroscopic and thermodynamic scales of basicity.

Steric and electronic effects of alkyl substituents

From steric substituent scales,[30] it is well known that branching and/or lengthening alkyl groups increase their steric effects. Obviously steric effects always decrease hydrogen-bond basicity,[4,31] *i.e.* pK_{HB}. There is some dispute as to whether alkyl groups present significant and not constant electronic effects, and what kind of electronic effects (electronegativity, field, polarisability and/or hyperconjugation)[32] should operate. We

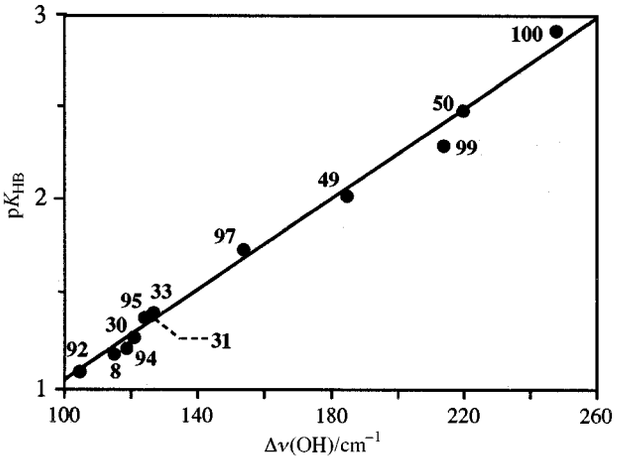


Fig. 2 Comparison of the thermodynamic and spectroscopic hydrogen-bond basicity scales for carbonyl bases showing mainly the stereoisomeric complex **A**. Numbers refer to Table 1. The regression line obeys the equation $pK_{HB} = 1.217$, $\Delta\nu(OH) - 0.183$, $n = 12$, $r = 0.995$, $s = 0.06$, $F = 1047$.

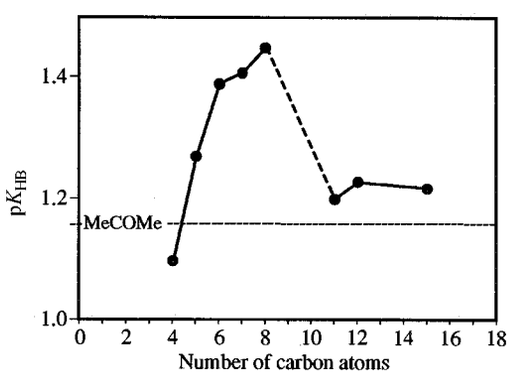


Fig. 3 Variation of pK_{HB} with the ring size of cycloalkanones

have recently obtained repeated evidence[5,7,9] that the hydrogen-bond basicity of functions not too sensitive to steric effects increases not only when hydrogen is substituted by a methyl group, but also when the methyl is lengthened and/or branched. For example, MeOH has a higher pK_{HB} value than H_2O,[7] and Bu^{t}CN is more basic than MeCN.[5]

For the carbonyl function we have found that the steric effect of R^1 predominates in the R^1CONMe_2 series,[11] whereas the opposite electronic and steric effects of R^1 almost cancel out in the R^1COOEt series.[10] The R^1COMe series resembles the R^1COOEt series since the pK_{HB} values do not change more than ±0.03 units around a mean value of 1.20. However, electronic effects clearly prevail over steric effects for the cyclohexyl and 1-adamantyl substituents since $cC_6H_{11}COMe$ and AdCOMe are respectively more basic than MeCOMe by 0.07 and 0.12 pK units.

In the R^1COR^2 series, steric effects prevail over electronic effects. For example di-*tert*-butyl ketone is less basic than acetone by 0.22 units. We again point out the significant electron-donating effect of the 1-adamantyl substituent since AdCOBu^t approaches and AdCOAd equals the MeCOMe basicity.

The well-known unsaturated character of the cyclopropyl substituent ($\sigma_R^+ = -0.15$) accounts for cyclopropyl methyl ketone and dicyclopropyl ketone being the most basic ketones in the R^1COMe and R^1COR^2 series.

Cyclisation

Within the cycloalkanones series, we observe (Fig. 3) that hydrogen-bond basicity increases with ring size, from the four-membered cyclobutanone to eight-membered cyclooctanone. We have not studied cyclononanone and cyclodecanone and cannot affirm that cyclooctanone is the most basic cycloalkanone. However, as ring size increases further basicity decreases asymptotically to $pK_{HB} = 1.21 \pm 0.02$. As expected the bicyclic camphor stands between cyclopentanone and cyclohexanone.

Ring substitution

In ring-substituted acetophenones, the dual substituent parameter equation[33] gives excellent correlations for *meta*-substituted acetophenones [eqn. (10)] and *para*-substituted

$$pK_{HB} = 1.084 - 0.854\,\sigma_F - 0.633\,\sigma_R^+ \quad (10)$$
$$n = 7 \quad r = 0.989 \quad s = 0.03 \quad F = 88 \quad R\sigma_F/\sigma_R^+ = 0.26$$

acetophenones [eqn. (11)] provided that the pK_{HB} of diacetyl-

$$pK_{HB} = 1.67 - 0.940\,\sigma_F - 1.031\,\sigma_R^+ \quad (11)$$
$$n = 15 \quad r = 0.991 \quad s = 0.04 \quad F = 347 \quad R\sigma_F/\sigma_R^+ = 0.05$$

benzenes **71** and **80** are corrected by the statistical log 2 factor and that the nitroacetophenones **74** and **81** and the cyanoacetophenone **72** are excluded from the correlations (*vide infra*). In eqns. (10) and (11), $R\sigma_F/\sigma_R^+$ is the partial correlation coefficient between the two variables. While eqn. (10) refers to a limited number of data, the regression coefficients of eqns. (10) and (11) show that field effects measured by σ_F are about the same in the *meta*- and *para*-positions, whereas resonance effects, measured by σ_R^+, operate much more efficiently in the *para*-position. This is a generalized behaviour for proton-sharing equilibria.[5]

If we compare the effect of *para*-substituents in benzophenones, benzaldehydes and acetophenones, the regression coefficients of eqns. (12) and (13) show qualitatively that

$$pK_{HB}(XC_6H_4COH) = 1.113\,pK_{HB}(XC_6H_4COMe) - 0.411 \quad (12)$$
$$n = 5 \quad r = 0.996 \quad s = 0.04 \quad F = 347$$

$$pK_{HB}(XC_6H_4COPh) = 0.924\,pK_{HB}(XC_6H_4COMe) + 0.043 \quad (13)$$
$$n = 3 \quad r = 1.000 \quad s = 0.003 \quad F = 30\,603$$

benzaldehydes and benzophenones are respectively more and less sensitive to substituent effects than acetophenones. This behaviour is well known for other properties of $4\text{-}XC_6H_4COR$ compounds (*cf.* the carbonyl frequency[34] and the carbonyl Lewis basicity[35]) and has been explained by stereoelectronic effects of the R substituent on the conjugation between the carbonyl and the substituted phenyl groups.

Substituent effects in the XCOMe series

The dual substituent parameter equation is well suited to aromatic systems but presents some difficulties when it is applied to aliphatic systems. Provided a $\rho_\alpha\sigma_\alpha$ term (σ_α measures the electronic polarizability of the substituent) is added, Taft and Topsom[36] have however successfully extended eqn. (14) to

$$GB(pK_{HB}) = GB^\circ(pK_{HB}^\circ) + \rho_\alpha\sigma_\alpha + \rho_F\sigma_F + \rho_R\sigma_R \quad (14)$$

gas-phase proton-transfer equilibria (GB) in the aliphatic series. We have ourselves applied eqn. (14) to proton-sharing equilibria (pK_{HB}) of nitriles XC≡N,[5] esters XCOOEt,[10] amides $XCONMe_2$[11] and alcohols XOH,[37] but we encountered several problems. For example: (*i*) some substituents must be excluded, (*ii*) the statistical intercept pK_{HB}° may differ inexplicably from

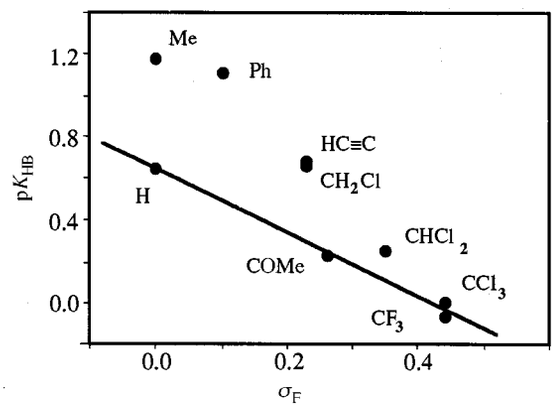


Fig. 4 Analysis of field and resonance effects of the X substituent for the XCOMe series in the pK_{HB} *vs.* σ_F plane. The line is drawn through hydrogen and substituents COMe, CF_3 and CCl_3 having insignificant resonance effects.

the experimental value of the unsubstituted compound and (*iii*) the statistical significance of the polarizability term is difficult to assess.

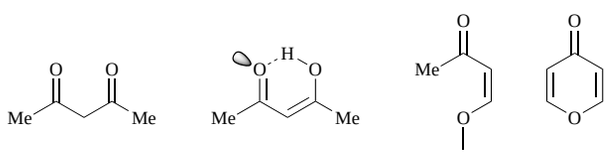
However, we have applied eqn. (14) to the XCOMe series and derived eqn. (15). We have selected only primary pK_{HB} values

$$pK_{HB} = 0.739 - 0.479\,\sigma_\alpha - 2.401\,\sigma_F - 2.455\,\sigma_R^+ \quad (15)$$
$$n = 16 \quad r = 0.976 \quad s = 0.20 \quad F = 79 \quad R\sigma_\alpha/\sigma_F = 0.005$$
$$R\sigma_\alpha/\sigma_R^+ = 0.21 \quad R\sigma_F/\sigma_R^+ = 0.23$$

and the 16 substituents were: H, Me, Et, Ad, HC≡C, Ph, COMe, CF_3, CCl_3, $CHCl_2$, CH_2Cl, EtO, MeO, Me_2N, MeNH and Et_2N. The five last pK_{HB} values are taken from our previous work on esters[10] and amides.[11] The standard deviation ($s = 0.20$) of the pK_{HB} estimate is 4–10 times the experimental error, giving limited utility to this equation. We prefer analyzing substituent effects in the XCOMe series in the pK_{HB} *vs.* σ_F plane (Fig. 4). Indeed, if we neglect polarizability effects (the ρ_α regression coefficient is much smaller than ρ_F and ρ_R, the ranges of the three σ scales being about the same), we can draw the line of inductive effects through the substituents H, COMe (after correcting the biacetyl value by the statistical log 2 factor), CF_3 and CCl_3 for which the resonance effects are zero or almost zero. The deviations of the substituents $CHCl_2$, CH_2Cl, HC≡C, Me and Ph above the 'inductive line' reveal that they are resonance electron donors. The magnitude should be related to σ_R^+ and we discover, as far as the basicity of ketone is concerned, that the ethynyl group is a significant resonance donor and that the methyl and phenyl groups have very similar σ_R^+ values, at variance with published values:[38] σ_R^+ (HC≡C) ~0, σ_R^+ (Me) = −0.08 and σ_R^+ (Ph) = −0.22.

The case of acetylacetone

In CCl_4 solution, acetylacetone exists predominantly (97%)[39] as the intramolecularly hydrogen-bonded keto–enol tautomer **43b**. Consequently our pK_{HB} value of 0.90 measures mainly the basicity of the remaining available lone pair of **43b**. If we



43a **43b** **43c** **49**

roughly model the keto–enol tautomer without an intramolecular hydrogen bond, **43c**, by the molecule of γ-pyrone **49** (pK_{HB} = 2.03) we estimate that intramolecular hydrogen bonding reduces the basicity of the carbonyl group by as much as 1 pK unit. We have elsewhere[20] obtained similar results for salicylic acid derivatives. It is also interesting to note that the analysis of the partition coefficients of acetyl acetone by linear solvation energy relationships[40] gives $\beta_2^H = 0.48$, in reasonable agreement with $\beta_2^H = 0.43$ calculated from pK_{HB}.

Hydrogen-bonding sites

In addition to the carbonyl oxygen, some ketones possess other heteroatoms which are potential hydrogen-bond acceptors. The question arises as to whether pK_{HB} measures only, or mainly, the carbonyl oxygen basicity. The pK_{HB}–$\Delta\nu$(OH) relationship of Fig. 2 is site specific and indicates that the ether oxygen of pyrones **49** and **50** and the nitrogen of the vinylogous amide **100** do not contribute significantly to the pK_{HB} value. Moreover, FTIR spectrometry always shows a lower carbonyl stretching vibration in the complex than in the free ketone. No new absorption, even small, can be detected at higher frequencies. For example, the 1674 cm^{-1} carbonyl band of free 4-(dimethylamino)acetophenone is lowered to 1650 cm^{-1} in the hydrogen-bonded ketone, and even an excess of phenol (in a 22 : 1 ratio) does not allow the detection of a higher frequency carbonyl absorption which would have characterized a nitrogen fixation. This constitutes unambiguous proof that the carbonyl group is the major hydrogen-bonding acceptor site.[9,11,17]

4-Nitroacetophenone and 4-cyanoacetophenone deviate from eqn. (11) and 3-nitroacetophenone from eqn. (10). This might mean that their pK_{HB} values correspond to two simultaneous 1 : 1 complexes: OH···O_2N and OH···N≡C in addition to the expected OH···O=C complex. In the case of 4-cyanoacetophenone, this is easily verified by vibrational spectroscopy since addition of 4-fluorophenol to a solution of the cyanoacetophenone in CCl_4 not only brings about a lowering of the ν(C=O) band from 1699 to 1685 cm^{-1}, which signifies a carbonyl complex,[17] but also effects a corresponding increase of the ν(C≡N) band from 2233 to 2241 cm^{-1}, which in turn signifies a nitrile complex.[5] For the nitroacetophenones the decrease of the ν(C=O) band also shows the formation of the carbonyl complex, but the $\nu(NO_2)$ bands are not sensitive to hydrogen bonding[41] and the nitro complexes are indicated by the high global formation constants. The following analysis carried out with 3-nitroacetophenone, shows how the individual constants K_{NO_2} and K_{COMe} can be evaluated and compared to the global constant pK_{HB} = log (K_{NO_2} + K_{COMe}) = 0.69, *i.e.* K_f = 4.9 $dm^3\ mol^{-1}$. A value of K_{COMe} = 3.4 $dm^3\ mol^{-1}$ can be calculated from eqn. (10) for acetophenones and from the values $\sigma_F = 0.65$ and $\sigma_R^+ = 0$ for the 3-NO_2 substituent.[38] The difference between K_f and K_{COMe}, 1.5 $dm^3\ mol^{-1}$, is significant. It compares well with the value, 1 $dm^3\ mol^{-1}$, calculated from the correlation between pK_{HB} and substituent constants in the nitrobenzene series,[6] and is therefore attributed to K_{NO_2}.

The α-diketones **39** and **40**, the quinones **41** and **42** as well as the diacetylbenzenes **71** and **80** give also two 1 : 1 complexes but they are equivalent and the log 2 statistical correction to pK_{HB} gives the hydrogen-bond basicity of one carbonyl group.

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