The hydrogen bond acidity and other descriptors for oximes

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The solvation descriptors for cyclohexanone oxime and acetone oxime have been obtained from measurements on water–solvent partitions, and gas–liquid chromatographic retention data. These yield values of 0.33 and 0.37 for the Abraham hydrogen bond acidity, A, in reasonable agreement with a value of 0.37 for cyclohexanone oxime obtained by our recent NMR method. The other descriptors E, S, B, L and V have also been obtained for cyclohexanone oxime and acetone oxime, and have been estimated for a number of other oximes as well. The value for A, the overall or effective hydrogen bond acidity of the oximes is reasonably close to the 1 : 1 hydrogen bond acidity, $\alpha_2^H = 0.39$ to 0.46, that can be deduced from previous literature measurements on oximes, and to the 1 : 1 hydrogen bond acidity, $\alpha_2^H = 0.43$ for another NOH compound, *N*,*N*-dibenzylhydroxylamine, that again can be deduced from literature measurements.

Introduction

The oximes were important derivatives of aldehydes and ketones, often used for identification in the 19th and early 20th century. Their use as derivatives has declined, but a number of oximes are important. Nifuroxime is a drug, and diacetylmonooxime is a cholinesterase reactivator. In order to predict physicochemical and biochemical properties of the oximes, a knowledge of their Abraham descriptors[1,2] (or solvation parameters) is needed. One of the key descriptors is the overall, or effective, hydrogen bond acidity, A, in which we were particularly interested, especially as we have recently developed a new method for the experimental determination of this parameter.[3] In this work, we showed that the difference ($\Delta\delta$) in the ^{1}H NMR chemical shift of a protic hydrogen in DMSO *vs.* $CDCl_3$ solvent is directly related to the hydrogen bond acidity. This correlation was valid over 54 compounds and 72 protic hydrogens varying from cyclohexane to the OH proton of phenol. An important advantage of the NMR method is that it allows the determination of A values for individual protic hydrogens in multifunctional solutes.

As we have pointed out,[1] the overall or effective hydrogen bond acidity, A, is the important type of acidity when considering processes in which a solute is in dilute solution and surrounded by solvent molecules, or is present in the gas phase as an isolated molecule. A related acidity is the 1 : 1 hydrogen bond acidity, α_2^H, in which a solute complexes with a hydrogen bond base in an inert solvent such as tetrachloromethane.[1,4] The defining equations for α_2^H are eqn (1),[4] where K is the 1 : 1 complexation constant for an acid against a reference base B, eqn (2) in which log K is put on a general scale of hydrogen bond acidity K_A^H, and finally eqn (3) in which K_A^H is transformed into the α_2^H scale. In eqn (2), L_B and D_B are the fitting coefficients.

$$\text{A–H} + :\text{B} \rightarrow \text{A–H}\cdots\text{B};\ K \qquad (1)$$

$$\log K \text{ (for an acid against a reference base B)} = L_B \log K_A^H + D_B \qquad (2)$$

$$\alpha_2^H = (1.1 + K_A^H)/4.636 \qquad (3)$$

The term $(1.1 + K_A^H)$ serves to define the origin of the scale where $\alpha_2^H = 0$ for zero acidity, and the factor 4.636 is used only to provide a suitable range of the scale. A number of equations on the lines of eqn (2) were constructed for various reference bases.

The only acid–base measurements that seem to have been made on oximes are those of Ossart *et al.*,[5] who measured 1 : 1 complexation constants for a number of oximes against the base tetrahydrofuran in tetrachloromethane. The 1 : 1 complexation constants, K, in units of mol^{-1} dm^3, are in Table 1, together with the corresponding values of α_2^H that we have deduced from the L_B and D_B values for the base tetrahydrofuran[4] in Table 2, through eqn (2) and (3). Feuer *et al.*[6] have measured 1 : 1-complexation constants for the NOH compound *N*,*N*-dibenzylhydroxylamine against a number of hydrogen bond bases in tetrachloromethane, as shown in Table 2, where we give the deduced values of α_2^H.

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Table 1 Values of the 1 : 1 complexation constant, K, for some oximes against tetrahydrofuran in tetrachloromethane, and the corresponding values of α_2^H

Oxime	K (ref. 5)	α_2^H
Acetaldehyde oxime	3.75	0.44
Acetone oxime	3.51	0.43
Butanone oxime	4.08	0.45
Cyclohexanone oxime	2.45	0.39
Acetophenone oxime	4.24	0.45
Benzophenone oxime	4.49	0.46
Benzaldehyde oxime (β)	4.65	0.46

Results

The complexation constants of Ossart *et al.*[5] can be transformed into K_A^H and then into α_2^H values through eqn (2) and (3). The deduced values of α_2^H range from 0.39 to 0.46 as shown in Table 1. Similarly, the complexation constants of Feuer *et al.*[6] yield the α_2^H values given in Table 2. No equation on the lines of eqn (2) has been constructed for benzene as a reference base, and so we are left with three independent values of α_2^H for *N*,*N*-dibenzylhydroxylamine. There is not very good agreement, but we can say that the 1 : 1 hydrogen bond acidity of *N*,*N*-dibenzylhydroxylamine is around 0.43 units. Once α_2^H is known, the general equation, eqn (4),[7] can be used to estimate the 1 : 1 complexation constant of the oximes or of the hydroxylamine with any base for which the 1 : 1 hydrogen bond basicity β_2^H has been determined.[8–11]

$$\log K = (7.354\alpha_2^H\beta_2^H) - 1.094 \quad (4)$$

Of more practical utility is the overall hydrogen bond acidity, A, which is one of the descriptors in our linear free energy relationships, LFERs, eqn (5) and (6).[1,2]

$$SP = c + eE + sS + aA + bB + vV \quad (5)$$

$$SP = c + eE + sS + aA + bB + lL \quad (6)$$

In eqn (5) and (6), the independent variables are solute descriptors as follows. E is the solute excess molar refractivity in units of $(cm^3\ mol^{-1})/10$, S is the solute dipolarity/polarizability, A and B are the overall or summation hydrogen bond acidity and basicity, V is the McGowan characteristic volume [12] in units of $(cm^3\ mol^{-1})/100$ and L is the logarithm of the gas to hexadecane partition coefficient at 25 °C. Eqn (5) is used for transfer of solutes from one condensed phase to another, and eqn (6) is used for processes that involve the transfer of solutes from the gas phase to a solvent phase. The dependent variable, SP, is a set of solute properties in a given system. For example, SP in eqn (5) could be the water-to-octanol partition coefficient, as $\log P_{oct}$, and SP in eqn (6) could be a gas-to-solvent partition coefficient or some measure of gas chromatographic retention. The coefficients in eqn (5) and 6 are evaluated through multiple linear regression analysis (MLRA).

Table 2 Values of L_B and D_B in eqn (2), the 1 : 1 complexation constant, K, in tetrachloromethane and derived values of α_2^H for *N*,*N*-dibenzylhydroxylamine

Base	L_B	D_B	K (ref. 6)	α_2^H
Triethylamine	1.0486	0.0517	14	0.462
Diethyl ether	0.7129	−0.3206	2.3	0.444
Dimethyl sulfoxide	1.2399	0.2656	11	0.372
Benzene	N/A	N/A	0.5	
Tetrahydrofuran	0.8248	−0.1970		

The use of eqn (5) and (6) in the determination of descriptors has been described in detail,[2] and numerous examples are available.[13–16] In brief, equations on the lines of eqn (5) and (6) are set up for a number of physicochemical processes, using solutes whose descriptors are known. The SP values for the investigated compound are then obtained by experiment for the same processes under exactly the same conditions as used in the calibration experiments. There are six descriptors that are required for any compound. However, V can be calculated from atomic and bond contributions,[1,12] and E can then be obtained by one of a variety of methods. If the refractive index of the liquid compound at 20 °C is available, E can be obtained directly. Otherwise E can be calculated by addition of fragments, either by hand or by a commercial program,[17] or can be obtained from a calculated refractive index.[18]

Cyclohexanone oxime and acetone oxime are solids, but a number of lower oximes are liquids whose refractive index has been measured,[19] and for which we have calculated E, see Table 3. Also included are values of E calculated from the ACD refractive index,[18] and values of E calculated through the PharmaAlgorithm (PHA) program.[17] The ACD values are all too low, but the PHA values show good agreement with the experimental values. We take the PHA value of 0.58 for cyclohexanone oxime and a value of 0.39 for acetone oxime (slightly larger than that for butanone oxime).

This then leaves four descriptors, S, A, B and L to be obtained by experiment. In principle, if four values of SP are obtained in four calibrated systems, we have four unknowns (S, A, B and L) that can be deduced from four equations. In practice, it is much better to have a larger number of equations and then to find the best solution of the equations by trial-and-error, the best solution being the values of the descriptors that provide the best fit of calculated and experimental SP values. We used the procedure in Microsoft 'Solver' to obtain the best fit descriptors. We can extend the number of equations through eqn (7), where P_s is a water-to-solvent partition coefficient, K_s is the corresponding gas-to-solvent partition coefficient, and K_w is the corresponding gas-to-water partition coefficient. In the case of a solvent such as octanol, that takes

Table 3 Some experimental and calculated values of E for oximes

Oxime	$\eta(20)$	V	E(exptl.)[a]	ACD (calc.)	PHA (calc.)
Formaldehyde oxime		0.3650			0.37
Acetaldehyde oxime	1.4264	0.5059	0.390	0.300	0.40
Propanal oxime	1.4303	0.6468	0.366	0.293	0.40
Butanal oxime	1.4367	0.7877	0.357	0.288	0.40
Isobutanal oxime		0.7877	(0.37)		0.41
Acetone oxime		0.6468	(0.39)	0.296	0.38
Butanone oxime	1.4431	0.7877	0.383	0.292	0.38
Pentan-2-one oxime	1.4455	0.9286	0.369	0.290	0.37
Pentan-3-one oxime	1.4465	0.9286	0.375	0.290	0.37
Hexan-2-one oxime	1.4470	1.0695	0.354	0.288	0.37
Heptan-4-one oxime	1.4475	1.2104	0.335	0.288	0.37
Cyclopentanone oxime		0.8200	(0.58)		0.59
Cyclohexanone oxime		0.9609	(0.58)	0.728	0.58

[a] Values in parenthesis are estimated.

up a considerable amount of water when in equilibrium with water, both $\log P_s$ and $\log K_s$ refer to the water-saturated octanol. Then eqn (7) can be applied provided that $\log K_w$ as obtained for pure water is the same for water saturated with octanol. There is a considerable amount of experimental evidence that $\log K_w$ is indeed the same, within any realistic experimental error, for water and octanol saturated water,[20] and so eqn (7) can be applied to wet octanol as well as to solvents that take up only very small quantities of water.

$$\log P_s = \log K_s - \log K_w \quad (7)$$

If we allow the value of $\log K_w$ to float, we have increased the number of 'descriptors' to be determined from four to five. However, the $\log P_s$ values for the four solvents listed in

Table 4 Coefficients in the equations used to calculate descriptors for cyclohexanone oxime, and the corresponding observed and calculated values (P_s is the water-to-solvent partition coefficient, K_s is the corresponding gas-to-solvent partition coefficient, K_w is the corresponding gas-to-water partition coefficient, k is the gas to stationary phase partition coefficient, t_r' is the retention time relative to the standard)

								SP	
System	*SP*	*c*	*e*	*s*	*a*	*b*	*v*/*l*	Obs	Calc
Water–octanol	$\log P_s$	0.088	0.562	−1.054	0.034	−3.460	3.814[a]	0.988	1.031
Water–chloroform	$\log P_s$	0.327	0.157	−0.391	−3.191	−3.437	4.191[a]	0.821	0.944
Water–hexane	$\log P_s$	0.361	0.579	−1.723	−3.599	−4.764	4.344[a]	−0.599	−0.773
Water–toluene	$\log P_s$	0.143	0.527	−0.720	−3.010	−4.824	4.545[a]	0.260	0.232
Gas–water[b]	$\log K_w$	−0.994	0.577	2.549	3.813	4.841	−0.869[a]	5.115	5.011
Gas–octanol	$\log K_s$	−0.198	0.002	0.709	3.519	1.429	0.858	6.103	6.181
Gas–chloroform	$\log K_s$	0.116	−0.467	1.203	0.138	1.432	0.994	5.936	6.141
Gas–hexane	$\log K_s$	0.292	−0.169	0.000	0.000	0.000	0.979	4.516	4.423
Gas–toluene	$\log K_s$	0.121	−0.222	0.938	0.467	0.099	1.012	5.375	5.423
Gas–water[c]	$\log K_w$	−1.271	0.822	2.743	3.904	4.814	−0.213	5.115	4.979
CW-20M	$\log t_r'$	−3.270	0.144	1.420	1.950	0.000	0.467	0.824	0.752
OV-275	$\log t_r'$	−2.822	0.355	1.650	1.797	0.325	0.341	1.106	1.133
Hp-Innowax	$\log t_r'$	−2.675	0.033	1.290	1.703	−0.051	0.386	0.765	0.704
DEGS	$\log t_r'$	−3.296	0.327	1.568	1.882	0.297	0.424	0.964	0.939
HP-5 80	$\log k$	−1.927	−0.051	0.360	0.303	0.000	0.636	1.258	1.215
100	$\log k$	−1.970	−0.022	0.329	0.243	0.000	0.573	0.916	0.869
120	$\log k$	−2.008	0.000	0.305	0.200	0.000	0.518	0.613	0.570
160	$\log k$	−2.552	0.050	0.229	0.145	0.000	0.389	−0.557	−0.589
SPB-Octyl 80	$\log k$	−2.645	0.165	0.062	0.000	0.000	0.703	0.600	0.543
100	$\log k$	−2.719	0.181	0.057	0.000	0.000	0.644	0.267	0.219
120	$\log k$	−2.738	0.189	0.076	0.000	0.000	0.578	−0.016	−0.063
160	$\log k$	−1.980	0.174	0.059	0.000	0.000	0.431	0.084	0.036
180	$\log k$	−1.996	0.182	0.060	0.000	0.000	0.391	−0.104	−0.147
200	$\log k$	−1.965	0.186	0.048	0.000	0.000	0.350	−0.250	−0.302
240	$\log k$	−1.979	0.192	0.052	0.000	0.000	0.287	−0.530	−0.581
Rtx-440 80	$\log k$	−2.452	−0.038	0.505	0.389	0.000	0.667	1.001	0.990
100	$\log k$	−2.537	0.000	0.461	0.316	0.000	0.613	0.647	0.630
120	$\log k$	−2.584	0.021	0.427	0.271	0.000	0.559	0.337	0.317
160	$\log k$	−2.419	0.046	0.336	0.211	0.000	0.427	−0.168	−0.176
180	$\log k$	−2.398	0.048	0.312	0.192	0.000	0.382	−0.368	−0.376
200	$\log k$	−2.403	0.067	0.288	0.181	0.000	0.346	−0.549	−0.550
220	$\log k$	−2.479	0.077	0.270	0.174	0.000	0.323	−0.730	−0.739
240	$\log k$	−2.393	0.098	0.226	0.156	0.000	0.284	−0.842	−0.854
DB-1701 160	$\log k$	−2.119	−0.007	0.553	0.575	0.000	0.409	0.238	0.331
180	$\log k$	−2.078	−0.001	0.511	0.488	0.000	0.362	0.024	0.106
200	$\log k$	−2.083	0.020	0.471	0.419	0.000	0.328	−0.164	−0.092
220	$\log k$	−2.070	0.039	0.428	0.356	0.000	0.295	−0.333	−0.270
Rxi-50 160	$\log k$	−2.104	0.124	0.592	0.283	0.000	0.390	0.264	0.279
180	$\log k$	−2.110	0.145	0.536	0.258	0.000	0.352	0.059	0.062
200	$\log k$	−2.118	0.160	0.486	0.250	0.000	0.319	−0.114	−0.127
220	$\log k$	−2.111	0.169	0.446	0.216	0.000	0.288	−0.297	−0.296
240	$\log k$	−2.093	0.181	0.402	0.192	0.000	0.259	−0.446	−0.444
80	$\log k$	−2.192	0.090	0.807	0.398	0.000	0.623	1.448	1.409
120	$\log k$	−2.236	0.117	0.713	0.302	0.000	0.505	0.778	0.755
140	$\log k$	−2.242	0.143	0.648	0.269	0.000	0.455	0.504	0.479
HP-Innowax 160	$\log k$	−2.568	0.215	1.157	1.544	0.000	0.356	0.634	0.645
180	$\log k$	−2.383	0.202	0.998	1.363	0.000	0.299	0.367	0.374
200	$\log k$	−2.350	0.204	0.926	1.198	0.000	0.265	0.133	0.142
220	$\log k$	−2.334	0.209	0.854	1.071	0.000	0.237	−0.077	−0.067
DB-225 160	$\log k$	−2.784	0.055	0.980	0.853	0.000	0.340	−0.210	−0.120
180	$\log k$	−2.833	0.074	0.909	0.776	0.000	0.311	−0.354	−0.372
200	$\log k$	−2.826	0.091	0.842	0.691	0.000	0.278	−0.600	−0.586
220	$\log k$	−2.775	0.096	0.754	0.612	0.000	0.251	−0.731	−0.754

[a] These coefficients are for *v*, the remainder are for *l*. [b] Eqn (5). [c] Eqn (6).

Table 5 Solvation descriptors for cyclohexanone and acetone oxime

Oxime	*E*	*S*	*A*	*B*	*V*	*L*	log K_w
Cyclohexanone oxime	0.58	0.90	0.33	0.61	0.9609	4.320	5.11
Acetone oxime	0.39	0.66	0.37	0.56	0.6488	2.557	4.46

Table 4 then yield four extra log K_s values, and in addition we have two equations, one from eqn (5) and one from eqn (6) for log K_w, making an extra six equations. In Table 4 are given the systems that we have used for cyclohexanone oxime, the coefficients in eqn (5) and (6), and the observed and calculated *SP* values. The extra equations lead to a total of 53 equations for which the *SP* values can be fitted with a standard deviation, *SD*, of only 0.063 log units with the descriptors shown in Table 5.

For acetone oxime, we have the GLC data obtained at UCL. We also have an equation derived from the retention indices, *I*, obtained by Zenkevich[21] on Porapak Q for a large number of volatile compounds. Application of eqn (6) yielded eqn (8).

$$I = 154.68 - 69.354E + 38.611B + 175.622L \quad (8)$$

$$N = 214,\ R^2 = 0.9873,\ SD = 28.7,\ F = 2702.6$$

In eqn (8), *N* is the number of compounds, *R* is the correlation coefficient, *SD* is the standard deviation and *F* is the F-statistic. There is also a set of GLC data on a Perkin–Elmer column that includes acetone oxime.[22] The relevant equation is eqn (9), making a total of 16 equations for acetone oxime. Details of the calculations for acetone oxime are in Table 6; the standard deviation between observed and calculated values is only 0.040 log units.

$$I = 83.84 - 19.68E + 63.46S + 118.44A + 11.85B + 196.853L \quad (9)$$

$$N = 48,\ R^2 = 0.9880,\ SD = 13.9,\ F = 713.13$$

The ^{1}H NMR spectra of oximes in $CDCl_3$ and DMSO solvents have been recorded previously. There is exchange between the NH and OH protons in hydroxylamines in DMSO solution which was noted by Feuer *et al.*[6] in their measurements of the self-association of these compounds in this solvent. However the OH chemical shift in oximes in DMSO solution is independent of concentration and this was used by Kurtz and D'Silva[23] in their estimation of the pK_a of twenty oximes in DMSO solvent. The ^{1}H NMR data of *ca.* forty oximes in $CDCl_3$ solution, including acetone and cyclohexanone oxime are given in the Aldrich Spectral catalogue.[24] The OH proton chemical shift is always very deshielded, for example acetone oxime 9.97 ppm, cyclohexanone oxime 9.78 ppm. Very similar shifts are obtained in DMSO solution: 10.12,[23] 10.14 (this work) for acetone oxime, and 10.02,[23] 10.05 (this work) for cyclohexanone oxime. The values for chloroform are for relatively concentrated solutions (8/10%, weight to volume,[24] *i.e.* for cyclohexanone oxime 0.9 mol dm^{-3}). The chemical shift of the OH proton in oximes in $CDCl_3$ solvent is known to be concentration dependent[6] due to intermolecular hydrogen bonding; thus a dilution experiment was performed in $CDCl_3$ solution on cyclohexanone oxime to obtain the ∞ dilution chemical shift required for this study. The oxime concentration was decreased until the OH chemical shift showed very little change with concentration (Table 7). The concentrations were measured by using the integral of the α-CH_2 protons of the oxime with respect to the residual $CHCl_3$ peak. The results are given in Table 7. The plot of δ(OH) *vs.* concentration is linear until a dilution of *ca.* 0.06 mol dm^{-3} is reached when the plot is essentially independent of concentration. Thus the value of 4.45 ppm may be regarded as the ∞ dilution chemical shift in this experiment. However the OH peak of the oxime at the lowest concentration measured was a broad peak of intensity 2H, with respect to the α-CH_2 protons of the oxime (see above). This value was interpreted as due to the oxime OH (intensity 1) plus an equal amount of water protons present despite careful drying of the $CDCl_3$ solvent over molecular sieves. There is rapid exchange on the NMR time scale between the oxime OH proton and the water protons to give the broad peak observed. The chemical shift of this peak is therefore the weighted average of the chemical shifts of the oxime OH and the water protons. Thus eqn (10) applies where δ_{obs}, δ and δ_2 are the observed chemical shift and the chemical shifts of the oxime OH and the water protons at these concentrations and n_1 and n_2 the mole fractions of the two species.

$$\delta_{obs} = n_1\delta_1 + n_2\delta_2 \quad (10)$$

The ∞ dilution chemical shift of water in $CDCl_3$ solvent is 1.56 ppm[25] and inserting this in eqn (10) with δ_{obs} = 4.45 ppm and $n_1 = n_2 = 1/2$ gives the ∞ dilution value for the OH shift in cyclohexanone oxime as 7.34 ppm. This value, when inserted into the *A vs.* $\Delta\delta$, eqn (3), gives an *A* value of 0.37.

Table 6 Observed and calculated values for acetone oxime (see Table 4 for definitions)

		SP	
System	*SP*	Obs.	Calc.
Water–octanol	log P_s	0.120	0.154
Water–chloroform	log P_s	−0.351	−0.264
Water–hexane	log P_s	−1.725	−1.740
Water–toluene	log P_s	−0.960	−1.002
Gas–water[a]	log K_w	4.464	4.472
Gas–octanol	log K_s	4.584	4.580
Gas–chloroform	log K_s	4.113	4.137
Gas–hexane	log K_s	2.739	2.744
Gas–toluene	log K_s	3.504	3.484
Gas–water[b]	log K_w	4.464	4.452
CW-20M	log t_r'	−0.287	−0.354
OV-275	log t_r'	0.058	0.129
HP-Innowax	log t_r'	−0.227	−0.217
DEGS	log t_r'	−0.152	−0.181
Porapak Q[21]	*I*/100	5.980	6.009
See text[22]	*I*/100	6.700	6.748

[a] Eqn (5). [b] Eqn (6).

Table 7 δ(OH) *vs.* concentration of cyclohexanone oxime in $CDCl_3$

Conc. (mol dm^{-3} × 10^{-2})	2.00	6.97	9.26	11.76	20.0
δ(OH)	4.45	4.68	5.77	6.27	8.82

Discussion

The descriptors for cyclohexanone oxime have been derived from fits to 53 equations and can be regarded as soundly based. Those for acetone oxime are based on 16 equations, and so should also be quite reliable. The value of the hydrogen bond acidity descriptor, *A*, is 0.33 or 0.37 for cyclohexanone oxime and 0.37 for acetone oxime, as compared to the 1 : 1 hydrogen bond acidity 0.39 and 0.43, respectively, see Table 1, and 0.43 for the NOH compound, *N*,*N*-dibenzylhydroxylamine, see Table 2. For alcohols, *A* and α_2^H do not differ too much : 0.37 and 0.32 for propan-1-ol, 0.33 and 0.33 for isopropanol, and 0.31 and 0.32 for *tert*-butanol. Hence, for *N*,*N*-dibenzylhydroxylamine we expect *A* to be near 0.43 units. The hydrogen-bond acidity of the two types of NOH compound, the oximes and the hydroxylamines, are thus quite close.

The value of 0.37 for the hydrogen bond acidity of cyclohexanone oxime by the NMR method is a little higher than the value of 0.33 from the GLC and partition measurements. However, the NMR method is rendered more difficult than usual because of the large concentration dependence of the chemical shift in $CDCl_3$, and the necessity of obtaining the ∞ dilution chemical shift of the oxime from the observed shift due to the oxime and water. For other acyclic oximes, we suggest that an *A*-value of 0.35 could be taken.

In the calculation of the descriptors for the oximes, we used the method of fitting by trial-and-error. If, for a given oxime, we have four unknown descriptors *S*, *A*, *B* and *L*, then four equations of the type of eqns (5) and (6) would suffice to yield values for the four descriptors. It is obviously better to have more equations, but then the solution can only be obtained by trial-and-error. We used the 'Solver' add-on programme in Microsoft Excel to obtain the best-fit descriptors. Inspection of Table 4 shows that the various equations that can be used in the calculation of descriptors have very different coefficients. The larger the coefficient the more accurately can the corresponding descriptor be obtained. Several of the GLC phases have reasonably large values of the *s*- and *a*-coefficients, because they are dipolar and are hydrogen bond bases and so they are useful in the determination of the *S* and *A* descriptors: note that the solvent hydrogen bond basicity is complementary to the solute hydrogen bond acidity. However, the values of the *a*-coefficients for the GLC phases are never more than 2.0, whereas a number of other processes, including partitions from water to non-polar solvents, have *a*-coefficients numerically almost twice as large. It is therefore an advantage to include water-to-solvent partitions in the set of equations when calculating *S* and *A*. Of course, since there are no commercially available GLC stationary phases with any significant hydrogen bond acidity (the *b*-coefficients are zero), it is then absolutely essential to include other processes such as water to solvent partitions in order to obtain the *B* descriptor.

For a few other oximes, water-to-octanol partition coefficients[26] and retention data by Zenkevich[21] are available, and we give in Table 8 approximate values for descriptors, with *A* fixed at 0.35 for the acyclic oximes, and at 0.33 for cyclopentanone oxime.

Reversed phase HPLC systems have been used instead of water-to-solvent systems in the calculation of descriptors,[27] but this is only possible if rather unusual HPLC systems are used. Du *et al.*[28] and Valko *et al.*[29] have shown that most of the common isocratic elution and gradient elution systems have similar coefficients, with rather small *a*-coefficients. Hence if HPLC systems are used, it is preferable to include some water-to-solvent partition systems as well as GLC systems.

Probably the best set of experimental data to use in order to obtain all the descriptors is a combination of retention data on GLC stationary phases and partition coefficients in a number of water-to-solvent partition systems, as we have used here.

Table 8 Approximate solvation descriptors for some oximes

Oximes	*E*	*S*	*A*	*B*	*V*	*L*	log K_w
Cyclopentanone oxime	0.580	0.94	0.33	0.61	0.8200	3.700	5.23
Acetaldehyde oxime	0.390	0.50	0.35	0.54	0.5059	1.931	3.98
Propanal oxime	0.366	0.52	0.35	0.54	0.6468	2.498	3.92
Butanal oxime	0.357	0.58	0.35	0.54	0.7877	3.149	3.96
Isobutanal oxime	0.370	0.59	0.35	0.57	0.7877	2.992	4.13
Butanone oxime	0.383	0.71	0.35	0.56	0.7877	3.173	4.40

Experimental

Partition coefficients

Cyclohexanone oxime and acetone oxime were used as received. Solvents were pre-equilibrated with water, and the water saturated with the solvent and the solvent saturated with water were used in the experiments. Dilute solutions of the oximes in water were gently shaken with the organic solvent and left to equilibrate at 25 °C for 30 min. Portions of the organic layer and the aqueous layer were carefully withdrawn using hypodermic syringes and directly injected into a Perkin-Elmer F-33 gas chromatograph with a stationary phase of Carbowax 20M at 101 °C. The volumes withdrawn (V_o and V_w) were arranged so that the area under the GC peaks was almost the same for the aqueous and organic layers. The ratio of the areas (A_o/A_w) could then be taken as the ratio of the quantities of oxime in the withdrawn volumes (Q_o/Q_w). Then the partition coefficient, *P*, is given by $P = (Q_o/V_o)/(Q_w/V_w) = (A_o/V_o)/(A_w/V_w)$. The partition coefficients in each water-to-solvent system are given in Table 9; this includes a value for the water-to-octanol partition coefficient from the MedChem data base.[26] From the replicate measurements we

Table 9 Partition coefficients for cyclohexanone oxime and acetone oxime between water and various solvents

Solvent	log *P*	log *P* taken
Cyclohexanone oxime		
Octanol	0.988	0.988
Toluene	0.260	0.260
Chloroform	0.805, 0.818, 0.839	0.821
Hexane	−0.570, −0.596, −0.630	−0.599
Acetone oxime		
Octanol		0.12[26]
Toluene	−0.980, −0.982	−0.981
Chloroform	−0.297	−0.297
Hexane	−1.784, −1.669, −1.751 −1.738, −1.682	−1.725

estimate that the standard deviation is about 0.03–0.04 log units. In the GC experiments, a flame ionisation detector was used; we encountered no particular problems in the analysis of the aqueous solutions.

GLC retention data

At UCL, four GLC stationary phases were each calibrated using 45–65 solutes of known descriptors: CW-20M at 101 °C, DEGS at 87 °C, HP-Innowax at 100 °C and OV-275 at 89 °C. The obtained coefficients are in Table 4, together with coefficients for all the other equations used. Cyclohexanone oxime or acetone oxime were then injected onto a given phase together with standard compounds as references, and retention data obtained under the same conditions as the calibration. The coefficients in Table 4 refer to $\log t_r'$, where t_r' is the retention time relative to the standard. The internal standards were heptanol for CW-20M, DEGS, and HP-Innowax and hexanol for OV-275. A number of secondary standards were also used. At Wayne State, retention factors at 20 °C intervals over the temperature range 60–140 or 180–240 °C were obtained with an Agilent Technologies HP-6890 gas chromatograph (Palo Alto, CA, USA) fitted with a split/splitless injector and flame ionization detector. Nitrogen was used as carrier gas at a constant linear velocity of 40 cm s^{-1} and methane was used to determine the column hold-up time. Measurements were made for seven different stationary phases on 30 m × 0.25 mm I.D. open-tubular columns with a film thickness of 0.25 μm for 60–140 °C and 1.00 μm for 180–240 °C. The system constants at each temperature were determined by calibration using 60–100 varied compounds exactly as before[30] and are summarized with the retention factors for cyclohexanone oxime in Table 4; k in $\log k$ is the gas to stationary phase partition coefficient.

NMR experiments

These were conducted exactly as described before.[3] All the compounds and solvents were obtained commercially. The $CDCl_3$ and DMSO solvents were commercial samples (Sigma-Aldrich). The $CDCl_3$ was bought in 1 ml ampoules and used directly in the experiments. Solutions of ~10 mg mL^{-1} concentration were run with TMS as internal standard in DMSO solvent. The ^1H spectra were obtained on a Bruker Avance 400 MHz NMR spectrometer operating at 400.13 MHz. Typical running conditions were 128 transients, spectral width 3300 Hz and 32 K data points, giving an acquisition time of 5 s. The FIDs were zero-filled to 64 K. The spectra were first order, and the assignments were straightforward.

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