Solvent Effects on the Conformational Equilibrium of 1,1,2-Trichloroethane

Michael H. Abraham,[a] **Raymond J. Abraham,**[b] **Paul Leonard,**[b] **Nancy S. True**[c] **and Cristina Suarez**[c]
[a] *Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK*
[b] *School of Chemistry, The University of Liverpool, Liverpool L69 3BX, UK*
[c] *Chemistry Department, The University of California, Davis, California 95616, USA*

Proton coupling constants, *J*, and proton chemical shifts, $\delta(CH)$ and $\delta(CH_2)$, are reported for 1,1,2-trichloroethane in 32 protic and aprotic solvents, and in the gas phase. These have been analysed in terms of a conformational equilibrium between conformers **I** and **II** using multiple linear regression analysis through the Abraham–Kamlet–Taft equation. The main solvent influence on all three NMR parameters arises through reaction field effects as modelled by the Kamlet–Taft solvent dipolarity parameter π_1^*. There is a small effect of solvent hydrogen-bond basicity on $\delta(CH)$ but not on $\delta(CH_2)$ indicating that the $CHCl_2$ proton is slightly acidic. A similar effect of solvent basicity on the coupling constant *J* shows that not only is conformer **II** more dipolar than conformer **I** but that the $CHCl_2$ proton in **II** is more acidic than the $CHCl_2$ proton in **I**. The gas phase values of *J*, $\delta(CH)$ and $\delta(CH_2)$ are more comparable with a suggested value of −0.4 for π_1^* than with the directly measured value of −1.1 units.

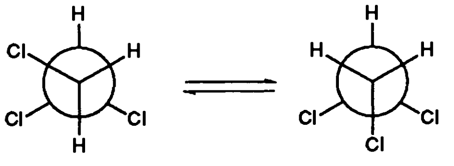
The effect of solvents on conformational equilibria, especially in terms of the variation of ΔG^0 with solvent, has been quite well studied.[1,2] Such equilibria are almost unique in that several properties of the reactant and the product are identical,* or nearly identical, and hence lead to cancellation of a number of solute–solvent and solvent–solvent interaction terms. Thus, because the reactant and product have almost the same volume or surface area, cavity effects that arise through the disruption of solvent–solvent interactions will cancel as between reactant and product, and general dispersion interactions of the solute–solvent type will also tend to cancel in the same way. If, however, the two conformers have different dipole moments and/or different quadrupole moments, their effects on a dielectric reaction field will be different. Hence conformational equilibria are extremely useful as tests of reaction field theories that can correlate or predict how ΔG^0 varies with solvent relative permittivity.[3,4] Now reaction field theories are restricted to solvents that are non-associated, and hence should properly exclude common solvents such as water and the alcohols. Hence although there are many examples of the effect of non-associated (generally aprotic) solvents on ΔG^0 for conformational equilibria, there are few such studies in which a wide range of solvents, including both aprotic and hydroxylic solvents have been studied.

This is unfortunate from the point of view of application of multiple linear regression analysis (MLRA) to solvent effects on conformational equilibria, because MLRA requires that the solvent properties used as explanatory variables be reasonably orthogonal, and span as wide a range as possible.[5] Without the inclusion of hydroxylic solvents, it is difficult to meet these criteria, and if solvents are restricted to apolar only, then very little information can be obtained by application of MLRA.

The two most useful general equations used to apply MLRA to solvent effects are those devised by Koppel, Palm, Makitra and Pirig (the KPMP equation) and by Abraham, Kamlet and Taft and their co-workers (the AKT equation). Both of these have been reviewed recently,[5] and have been applied to numerous sets of kinetic and equilibrium processes. The general AKT equation is given in eqn. (1), where the solvent parameters

$$Y = c + d\delta + s\pi_1^* + a\alpha_1 + b\beta_1 + h(\delta_H^2)_1 \qquad (1)$$

used as explanatory variables are: δ, a polarisability correction term; π_1^*, the solvent dipolarity: α_1, the solvent hydrogen-bond acidity; β_1, the solvent hydrogen-bond basicity; and δ_H^2, the Hildebrand cohesive energy density. The π_1^*, α_1 and β_1 parameters are the well-known Kamlet–Taft 'solvatochromic parameters'.[6] We did not explore the KPMP equation, because lack of a number of key solvent parameters prevented an exact comparison with AKT. R. J. Abraham[7] has measured the NMR coupling constant, *J*, between the C-1 and C-2 protons in 1,1,2-trichloroethane in 22 aprotic solvents, to use as a test of reaction field theories; these *J*-values and also Abraham and Bretschneider's calculated[2] ΔG^0 values for the equilibrium (2) were subsequently used[5] as the independent variable, *Y*, in eqn. (1).



(2)

μ = 1.2 D μ = 2.6 D

I II

For 19 of the aprotic solvents, M. H. Abraham and co-workers derived[5] eqns. (3) and (4), where *n* is the number of

$$J/\mathrm{Hz} = (6.27 \pm 0.05) + (0.25 \pm 0.01)\delta - (0.70 \pm 0.09)\pi_1^* - (0.45 \pm 0.12)\beta_1 \qquad (3)$$
$$n = 19, \mathrm{sd} = 0.01, \rho = 0.967$$

$$\Delta G^0/\mathrm{kcal\ mol^{-1}} = (1.22 \pm 0.05) + (0.29 \pm 0.11)\delta - (1.13 \pm 0.10)\pi_1^* - (0.30 \pm 0.13)\beta_1 \qquad (4)$$
$$n = 19, \mathrm{sd} = 0.10, \rho = 0.978$$

data points (solvents), sd is the overall standard deviation, and ρ is the overall correlation coefficient. As expected, the term in $(\delta_H^2)_1$ is not significant, because the cavity effect of **I** and **II** exactly cancels out, and the π_1^* term is significant and negative

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* Reactant and product here refer to two conformers in equilibrium. In the present case, conformers I and II are reactant and product, respectively.

because increase in solvent dipolarity favours the more dipolar conformer **II** over **I**. What is not expected is that solvent hydrogen-bond basicity also slightly favours **II** over **I**, which implies that 1-H *trans* to the 2-Cl chlorine atom in **II** is more acidic than 1-H *trans* to 2-H in **I**.

As mentioned above, a soundly-based application of MLRA requires a selection of solvents that cover as wide a range of parameters as possible, and the main aim of the present work is to determine values of J for equilibrium (2) in a wider selection of solvents, and then to reinvestigate the possible effect of solvent hydrogen-bond basicity on J-values for the equilibrium, eqn. (2).

Although the vicinal proton–proton couplings are almost intrinsically solvent independent, which allows the rotamer energy values to be obtained from their values, this is not the case with the proton chemical shifts. These are known to vary considerably with solvent even when no rotational equilibrium is present, and a number of possible interactions have been put forward as explanations.[8] These include van der Waals interactions with the solvent, solvent magnetic anisotropy effects, the solvent reaction field and hydrogen-bond interactions. The use of an internal reference to measure proton chemical shifts will tend to compensate for van der Waals interactions and solvents with large magnetic anisotropies are well known (*e.g.* aromatic solvents, carbon disulphide, acetonitrile, *etc*). Here, the use of an internal shift difference, *i.e.* $\delta(CHCl_2) - \delta(CH_2Cl)$ may tend to diminish these effects.

The reaction field effect is a direct function of solvent relative permittivity, which in our treatment is related to the solvent dipolarity π_1^*, and hence in principle can be deduced through an equation such as eqn. (1). Hydrogen bonding is a more selective and chemically sensitive interaction: although hydrogen-bonding shifts on the proton of chloroform have been documented, evidence for hydrogen-bonding shifts in the $CHCl_2$ and CH_2Cl protons is not unequivocal.[8,9]

Thus a secondary aim of this work is to determine whether proton chemical shifts in 1,1,2-trichloroethane can be analysed by MLRA in order to provide further information on solute–solvent interactions.

Experimental

The various solvents and 1,1,2-trichloroethane were all obtained commercially and used without further purification. The proton spectra indicated that no significant amounts of impurities were present.

The ^1H NMR spectrum of 1,1,2-trichloroethane was obtained as 5% (v/v) solutions on a Bruker WM. 250 FT NMR spectrometer, with a probe temperature of *ca.* 20 °C. A [$^2H_6$]propanone capillary was used as the deuterium lock signal and all measurements were referred to tetramethylsilane as an internal reference. Typical instrumental conditions were SW 2000 Hz in 16K data points giving an AT of 4.4 s; PW 3.0 μs (40 °C), 16 scans. The FIDs were transformed into 64K data points to give a digital resolution of 0.06 Hz point^{-1}. Both the CH_2 and CH splittings were measured to obtain the required $^3J_{HH}$ coupling, and the measurements usually agreed to <0.02 Hz. In some cases the CH_2 peak was partially obscured by the solvent peak, and in these cases only the triplet $CHCl_2$ signal was used for measurements of J. The δ values are quoted to 0.001 ppm. Some experiments with more dilute solutions were performed but no significant change in either the couplings or the chemical shifts was observed. The spectra are all strictly first order at the field strength used. The gas phase spectrum of 1,1,2-trichloroethane was obtained on a Nicolet NT300 FT spectrometer using a 12 mm ^1H probe, as previously described.[10] The sample temperature was 60 °C and the sample tube contained 1,1,2-trichloroethane (3 Torr) tetramethylsilane (1 Torr), and sulphur hexafluoride (300 Torr), the latter to improve sensitivity and resolution by increasing the relaxation times. The HH coupling is estimated to be accurate to ±0.04 Hz and the chemical shift is given to 0.001 ppm from tetramethylsilane, although this may not be directly comparable with the solution spectra for reasons given earlier.

Results of the NMR experiments are given in Table 1, together with the solvent parameters used in the MLRA.

Discussion

For the 32 solvents in Table 1, we have all the necessary parameters to apply the AKT eqn. (1) to values of J. We find that the explanatory variables α_1 and $(\delta_H^2)_1$ are not significant, exactly as we found before.[5] Eqn. (5) therefore

$$J/\text{Hz} = (6.35 \pm 0.04) + (0.28 \pm 0.06)\delta - (0.87 \pm 0.07)\pi_1^* - (0.33 \pm 0.07)\beta_1 \quad (5)$$
$$n = 32,\ \text{sd} = 0.10,\ \rho = 0.948$$

results. Thus results for the wider set of 32 solvents used to obtain eqn. (5) are, within experimental error, exactly the same as those for the limited set of 19 aprotic solvents used before [see eqn. (3)]. We can therefore confirm that the two major solvent influences on the J-values are solvent dipolarity and solvent hydrogen-bond basicity. These arise because conformer **II** is more dipolar than conformer **I**, and because 1-H in **II** is slightly more acidic than 1-H in **I**.

As mentioned before,[5] two values for the gas phase π_1^* parameter have been suggested, a directly measured value[11] from UV shifts of indicators of −1.1, and an indirect value[12] of 0.4 from gas-phase effects on the 1,2-dibromo-4-*tert*-butylcyclohexane equilibrium. Our measured gas phase J-value for the equilibrium (2) of 6.20 at 60 °C is in better accord with the −0.4 value, rather than with the measured value of −1.1 units.* Although the absence of general van der Waals interactions in the gas phase suggests that UV gas phase shifts may not be comparable to those in solution,[13] this is probably not the case with J-values because of a cancellation of effects between conformers **I** and **II**.

It is of some interest to see if solvent effects on the $CHCl_2$ and CH_2Cl proton chemical shifts can also be interpreted through MLRA, using the AKT equation (1). In the case of δ(CH) we find that neither α_1 nor $(\delta_H^2)_1$ are significant, but that δ, π_1^* and (just) β_1 all contribute [eqns. (6) and (7)]. In equation (6) the exploratory variable β_1 is significant

$$\delta(\text{CH}) = (5.31 \pm 0.08) - (0.80 \pm 0.11)\delta + (1.16 \pm 0.13)\pi_1^* + (0.23 \pm 0.13)\beta_1 \quad (6)$$
$$n = 32,\ \text{sd} = 0.19,\ \rho = 0.915$$

$$\delta(\text{CH}) = (5.36 \pm 0.08) - (0.92 \pm 0.10)\delta + (1.26 + 0.13)\pi_1^* \quad (7)$$
$$n = 32,\ \text{sd} = 0.20,\ \rho = 0.905$$

at the 92% confidence level, using students t-test. Hence the main factor that affects δ(CH) is solvent dipolarity, with a minor factor being solvent hydrogen-bond basicity. Now this is exactly what one would expect if reaction field effects are important, see Introduction, and if the $CHCl_2$ proton is very slightly acidic.

On the other hand, a similar analysis of $\delta(CH_2)$ shows that the CH_2Cl proton is not acidic at all, there being no significant dependence of $\delta(CH_2)$ on the explanatory variable β_1: in eqn. (8) the confidence level of β_1 is only 66%. Hence the main

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* Our gas phase value of J corresponds, *via* eqn. (5), to a gas phase value for π_1^* of +0.2 units.

Table 1 Solvent parameters[a] used in the calculations, and experimental values of J/Hz, δ(CH) and $\delta(CH_2)$ for 1,1,1-trichloroethane

Solvent	δ	π_1^x	α_1	β_1	$(\delta_H^2)_1$[a]	J	δ(CH)	$\delta(CH_2)$
Methanol	0.00	0.60	0.93	0.62	2.052	5.664	6.113	4.045
Ethanol	0.00	0.54	0.83	0.77	1.621	5.673	5.653	3.555
Propan-2-ol	0.00	0.48	0.76	0.95	1.331	5.677	6.060	3.978
tert-Butyl alcohol	0.00	0.41	0.68	1.01	1.119	5.733	6.004	3.954
2,2,2-Trifluoroethanol	0.50	0.73	1.51	0.00	1.371	5.819	5.811	3.939
1,1,1,3,3,3-Hexafluoropropan-2-ol	0.50	0.65	1.96	0.00	0.893	5.829	5.760	3.926
N-Methylpyrrolidin-2-one	0.00	0.92	0.00	0.77	1.276	5.221	6.602	4.249
Nitrobenzene	1.00	1.01	0.00	0.30	1.222	5.600	5.982	4.030
Benzonitrile	1.00	0.90	0.00	0.37	1.229	5.618	6.002	3.999
Bromobenzene	1.00	0.79	0.00	0.06	0.974	5.980	5.344	3.517
Chlorobenzene	1.00	0.71	0.00	0.07	0.936	5.995	5.302	3.485
Methyl phenyl ether	1.00	0.73	0.00	0.22	0.929	5.926	5.266	3.436
n-Pentane	0.00	−0.08	0.00	0.00	0.499	6.265	5.223	3.448
n-Hexane	0.00	−0.08	0.00	0.00	0.528	6.254	5.161	3.386
Decalin	0.00	0.09	0.00	0.00	0.754	6.222	5.566	3.796
Tetrachloromethane	0.50	0.28	0.00	0.00	0.738	6.225	4.908	3.134
Benzene	1.00	0.59	0.00	0.10	0.838	5.954	4.882	3.095
1,1,2-Trichloroethene	0.50	0.53	0.00	0.00	0.848	6.156	5.705	3.905
Diisopropyl ether	0.00	0.27	0.00	0.47	0.557	6.046	5.997	3.958
Diethyl ether	0.00	0.27	0.00	0.47	0.562	6.039	6.034	3.994
Trichloromethane	0.50	0.58	0.44	0.00	0.887	6.070	5.758	3.950
1-Bromoheptane	0.00	0.48	0.00	0.00	0.732	6.049	5.785	3.933
Dichloromethane	0.50	0.82	0.30	0.00	0.977	5.926	5.829	3.990
1,2-Dichloroethane	0.50	0.81	0.00	0.00	0.983	5.855	5.868	4.000
Butanone	0.00	0.67	0.06	0.48	0.860	5.478	6.273	4.143
Propanone	0.00	0.71	0.08	0.48	0.906	5.515	6.274	4.155
Acetonitrile	0.00	0.75	0.19	0.37	1.378	5.509	6.066	4.066
Nitromethane	0.00	0.85	0.22	0.25	1.585	5.495	6.223	4.270
N,*N*-Dimethylformamide	0.00	0.88	0.00	0.69	1.389	5.286	6.545	4.267
Dimethyl sulphoxide	0.00	1.00	0.00	0.76	1.688	5.126	6.600	4.281
Triethylamine	0.00	0.14	0.00	0.71	0.555	6.136	5.633	3.462
1,1,2-Trichlorethane	0.50	0.85	0.00	0.00	0.968	5.959	5.816	3.979
Gas phase	–	—	—	—	—	6.200	5.537	3.770

[a] All values from ref. 5. The units of $(\delta_H^2)_1$ are 10^{-2} cal cm^{-3}.

$$\delta(CH_2) = (3.53 \pm 0.08) - (0.65 \pm 0.11)\delta + (0.95 \pm 0.13)\pi_1^x - (0.12 \pm 0.12)\beta_1 \quad (8)$$
$$n = 32,\ \mathrm{sd} = 0.18,\ \rho = 0.853$$

$$\delta(CH_2) = (3.51 \pm 0.07) - (0.59 \pm 0.09)\delta + (0.90 \pm 0.12)\pi_1^x \quad (9)$$
$$n = 32,\ \mathrm{sd} = 0.18,\ \rho = 0.848$$

solvent effect on $\delta(CH_2)$ is that of the reaction field, with solvent basicity playing no part.

The deduction of a slight acidity of the $CHCl_2$ proton, eqns. (6) and (7), and of lack of any acidity of the CH_2Cl proton, eqns. (8) and (9), is in line with our analysis of the solvent effect on J-values, namely that the $CHCl_2$ proton in **II** is more acidic than the $CHCl_2$ proton in **I**. Our conclusion is, therefore, that MLRA through an equation such as (1) can successfully be applied to proton chemical shifts as well as to coupling constants.

For reasons explained above, we feel that the gas phase proton chemical shifts may not be directly comparable to the solution values. But our gas phase values, Table 1, still seem to be more consistent with $\pi_1^x = -0.4$ rather than $\pi_1^x = -1.1$ for the gas phase.

Finally, we note the three constraints on MLRA suggested[5] by M. H. Abraham and co-workers: (i) there must be enough data points taken, (ii) the explanatory variables must cover as wide a range as possible, and (iii) the explanatory variables must not be colinear. In our case, we have 32 data points, ample for the 2- or 3-parameter regressions we have laid out above, and enough to test the full five-parameter eqn. (1). The solvent parameters in Table 1 used as explanatory variables do indeed cover a very wide range—almost as wide as is practicable. We have tested possible colinearity between the explanatory variables and find that only between π_1^x and $(\delta_H^2)_1$ is there any significant effect, $\rho = 0.621$ and $\rho^2 = 0.368$, as shown below for the individual correlation coefficients.

	δ	π_1^x	α	β
π_1^x	0.399			
α	−0.065	0.058		
β_1	−0.488	0.112	0.071	
$(\delta_H^2)_1$	−0.089	0.621	0.360	0.458

Thus for the two-parameter equations in δ and π_1^x the inter-parameter ρ value is only 0.399, and for the three-parameter equation in δ, π_1^x and β the maximum cross-correlation is only −0.488 between δ and β_1. We therefore feel that our regression equations are reasonably soundly based.

In conclusion, we have been able to apply MLRA through the AKT equation (1) to solvent effects on proton coupling constants and on proton chemical shifts, and have thus been able to uncover quite subtle solute properties and consequent solute–solvent interactions. The reaction field effects are as expected, but we have also shown that the $CHCl_2$ proton in 1,1,2-trichloroethane is slightly acidic, whereas the CH_2Cl proton has negligible acidity, and furthermore that the acidity of the $CHCl_2$ proton is higher in conformer **II** than in conformer **I**, thus leading to a small but significant dependence of the J-value on the solvent hydrogen-bond basicity.

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