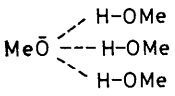
Application of Tritium Nuclear Magnetic Resonance Spectroscopy to the Determination of Isotopic Fractionation Factors in Methanol–Methoxide Solutions

By **Jasim M. A. Al-Rawi**, Chemistry Department, University of Mosul, Iraq
James P. Bloxsidge, John A. Elvidge, and **John R. Jones**,* Chemistry Department, University of Surrey, Guildford GU2 5XH
Rory A. More O'Ferrall,* Chemistry Department, University College, Belfield, Dublin 4

Tritium n.m.r. measurements of hydroxy chemical shifts in methanolic solutions of sodium methoxide have been used to determine an isotopic fractionation factor for the inner solvation shell of the methoxide ion and contributions from inner and outer solvation shells to the methoxide ion chemical shift. The identity of protium and tritium chemical shifts and the relationship between tritium and deuterium fractionation factors $\phi^T = \phi^{1.442}$ mean that measurements in MeOH and MeOD double the information available from ^1H n.m.r. measurements alone. The necessary assumption previously made to derive ϕ from ^1H measurements, that secondary solvation does not contribute to the methoxide ion chemical shift, is shown to be incorrect, but the revised value of ϕ (0.7) differs only slightly from earlier values, although treatment of the secondary solvation shift as a variable leads to some loss of precision in the definition of ϕ. At high methoxide concentrations plots of chemical shift against concentration are distinctly curved. Contributions to the curvature from breakdown of the assumption that isotopic atom fractions in the solution as a whole and in the bulk solvent are identical are evaluated.

MEASUREMENTS of the fractionation of hydrogen and deuterium isotopes within the solvation shell of the methoxide ion in isotopically mixed MeOH–MeOD solvents are important both for the interpretation of solvent isotope effects upon reaction rates and equilibria in methanolic media, [1-3] and in providing information on the structure of the solvated ion.[1,2] The magnitudes of solvent isotope effects in reactions catalysed by methoxide, $k_{MeOD}/k_{MeOH} \cong 3$ or more,[3] must indicate a substantial isotope effect on the binding of molecules in the solvation shell, because the ion itself bears no covalently bound exchangeable hydrogen. This isotope effect is conveniently expressed as a fractionation factor ϕ measuring the ratio of concentration of MeOD to MeOH molecules at a solvation site relative to the bulk solvent. Assuming that the fractionation is dominated by three equivalent hydrogen-bonded molecules in the primary solvation shell (1), the contribution to kinetic and equilibrium isotope effects k_D/k_H in pure isotopic solvents is ϕ^3, and to isotope effects k_x/k_H in mixed isotopic solvents of deuterium atom fraction x is $(1 - x + x\phi)^3$.



(1)

Both direct measurements[1,2] and the general magnitude of kinetic and equilibrium isotope effects [3] suggest $\phi \cong 0.7$. This value is comparable with that found for the ethoxide ion in ethanol [4] and is of interest in relation to similar measurements for the hydroxide ion. Solvent isotope effects upon reactions involving aqueous hydroxide ion are susceptible to alternative interpretations giving a dominant role respectively to the covalently bound O–H hydrogen or to water molecules of the ionic solvation shell.[5-7] The measurements for alkoxide ions favour the latter possibility

The most direct measurement of ϕ has been by n.m.r. spectroscopy. For dilute solutions of sodium methoxide in MeOH the concentration dependence of the hydroxy group chemical shift may be written as equation (1). The concentration is expressed as $a = N/(1 - N)$ where

$$\delta/a = \delta(MeO^-) + \delta(Na^+) \quad (1)$$

N is the mole fraction of sodium methoxide and a is used to represent correctly the atom fractions of hydroxy-hydrogen atoms in the solvent and in the solvation shells of the solute.[6,8] The chemical shifts are in p.p.m./mole fraction and $\delta(MeO^-)$ and $\delta(Na^+)$ are the single-ion chemical shifts for methoxide and sodium ions respectively.

For sodium methoxide in isotopically mixed solutions of MeOH and MeOD the concentration dependence of the chemical shift has been written as equation (2), where Q is the atom fraction of protium in the solvation shell

$$\delta/a = Q\delta(MeO^-) + \delta(Na^+) \quad (2)$$

of the methoxide ion relative to that in the bulk solvent (for MeOH, $Q = 1$). It is assumed that exchangeable hydrogens in the primary solvation shell of the methoxide ion are isotopically equivalent and that these alone contribute to the isotopic fractionation and to the methoxide chemical shift. For a solution with deuterium atom fraction x, Q is given by equation (3), where [H] and [D] denote protio- and deuterio-hydroxy concentions in the methoxide solvation shell. Since by

$$Q = \frac{1}{(1-x)}\left\{\frac{[H]}{[H]+[D]}\right\}_{Methoxide} \quad (3)$$

definition the methoxide fractionation factor, $\phi = \{[D]/[H]\}/\{x/(1 - x)\}$, is simply related to Q by equation (4),

$$Q = (1 - x + x\phi)^{-1} \quad (4)$$

it follows that ϕ may be determined from the limiting slopes at low methoxide concentrations of plots of δ

versus a in isotopically pure MeOH and in MeOD containing a small amount of MeOH, making use of the independently determined mole fraction chemical shift for the sodium ion.[1,9] In this way Gold and Grist [1] obtained $\phi = 0.74$, in good agreement with $\phi = 0.76$ reported in a preliminary communication of some of the present results.[2]

A difficulty with this method of measuring ϕ is that equations (1) and (2) represent rather drastic simplifications of the full expression for the chemical shift which is given by equation (5). In this equation the summation $\Sigma Q_i\delta_i$ implies consideration of all molecules in the sodium and methoxide solvation shells differing in chemical shift and fractionation factor from those of the bulk solvent. Perhaps the least satisfactory assumption

$$\delta = a\Sigma Q_i\delta_i \qquad (5)$$

is that the only molecules contributing to the methoxide chemical shift are the strongly fractionating molecules of its innermost solvation shell. This assumption is simply removed by replacing $\delta(Na^+)$ in equations (1) and (2) by δ_0, where δ_0 is the sum of contributions from non-fractionating and weakly fractionating hydrogens in the solvation shells of both Na^+ and MeO^-. Unfortunately the number of unknowns in the two equations is increased from two to three, and ϕ is no longer determinable. It is thus clear that the assumption $\delta_0 = \delta(Na^+)$ is enforced by the necessity of obtaining ϕ from a too limited number of measurements.

A simple way of resolving this difficulty and providing a more satisfactory evaluation of ϕ is to combine the proton n.m.r. measurements with corresponding tritium n.m.r. measurements. Tritium n.m.r. spectroscopy has some important advantages in this application. Tritium chemical shifts are virtually identical to proton chemical shifts,[10,11] and, since there should be little vibrational coupling of the hydroxy-hydrogen with other hydrogens in the methanol molecules, fractionation factors for tritium can be expected [12] to be accurately related to those for deuterium by the Swain–Schaad relationship,[13] $\phi^T = \phi^{1.442}$.

The general relationship (5) is applicable to tritium as well as protium n.m.r. with the Q_i values now representing atom fractions of tritium at a fractionating position relative to solvent (Q_i^T). In the presence of H, D, and T isotopes Q_i^T is given by equation (6). If we recognise

$$Q_i^T = \left\{\frac{[T]}{[H]+[D]+[T]}\right\}_i \Big/ \left\{\frac{[T]}{[H]+[D]+[T]}\right\}_{solvent} \qquad (6)$$

that $[T] \ll [H] + [D]$ and use the Swain relationship between tritium and deuterium fractionation factors, the relationship between Q_i^T and the corresponding fractionation factor ϕ, for a solution of deuterium atom fraction x, is straightforwardly obtained * as equation (7).

If we rewrite equations (1) and (2) for the protium chemical shifts in their less approximate form, with δ_0 replacing $\delta(Na^+)$, and, since it now represents only a fraction of the methoxide ion chemical shift, δ_M replacing

$$Q_i^T = \frac{\phi_i^{1.442}}{(1 - x + x\phi_i)} \qquad (7)$$

$\delta(MeO^-)$, we can now add two equations for the corresponding tritium measurements in pure MeOH and in an MeOH–MeOD mixture [equations (8)]. The tritium results therefore double the number of measurements

$$\begin{aligned}
\delta/a &= \delta_0 + \delta_M && \delta_H\ (MeOH)\\
\delta/a &= \delta_0 + \frac{\delta_M}{(1 - x + x\phi)} && \delta_H\ (MeOD)\\
\delta/a &= \delta_0 + \delta_M\phi^{1.442} && \delta_T\ (MeOH)\\
\delta/a &= \delta_0 + \frac{\delta_M\phi^{1.442}}{(1 - x + x\phi)} && \delta_T\ (MeOD)
\end{aligned} \qquad (8)$$

from which chemical shifts and fractionation factors may be determined without correspondingly increasing the number of parameters. They thus make possible a realistic test of the approximations required of determinations based on ^1H n.m.r. spectroscopy alone.

EXPERIMENTAL

[*O*-^{2}H]methanol was analysed by the method described by Streitwieser.[14] [*O*-^{3}H]methanol was prepared simply by exchanging methanol (3 ml) with tritiated water (10 μl; 50 Ci ml^{-1}) for a few minutes. After being dried the product was fractionally distilled. Before use each sample of methanol was dried by distillation from activated magnesium. Sodium methoxide solutions were made up by volume and molar concentrations determined by titration. Mole fractions were calculated using available density results for sodium methoxide solutions.[15] As the relationshp between molarity and mole fraction is practically unaffected by isotopic substitution the same values were used for all three methanols.

Tritium and protium spectra were recorded with a Perkin-Elmer R10 instrument operating at 64 and 60 MHz respectively, and on a Bruker WH90 pulse (Fourier-transform) spectrometer at 96 and 90 MHz. For the latter instrument the deuteriated methanol provided the field-locking signal. ^1H Spectra were also recorded on a Varian A60 spectrometer. In all three instruments the probe temperature was kept at 25 °C.

Dioxan (<1%) was used as an internal reference for protium chemical shifts and a ghost referencing procedure [11] was used to obtain the tritium chemical shifts, *i.e.* the shift $\Delta^T - \Delta^T_{dioxan}$ was calculated from relation (9).

$$\Delta^T - \Delta^T_{dioxan} = 1.0664\,(\Delta^H - \Delta^H_{dioxan}) \qquad (9)$$

RESULTS

Tritium and protium hydroxy chemical shifts relative to solvent methanol for sodium methoxide solutions in MeOH and MeOH–MeOD mixtures of deuterium atom fraction 0.90 are listed in Table 1. Tritium chemical shifts were measured for solutions containing a small amount of tritiated methanol and protium shifts were recorded for the same solutions. The results also include some protium measurements, reported previously in graphical form for solutions not containing tritium.[2]

* Numerator and denominator in the top and bottom of (6) are divided by [H].[T]/[H] is put equal to 0 in both denominators. The substitution $\phi^T = \{[T]/[H]\}_i/\{[T]/[H]\}_{solvent}$ is made.

TABLE 1

Tritium and protium hydroxy chemical shifts in p.p.m. relative to pure solvent (δ) for sodium methoxide solutions in MeOH and 90 : 10 v/v MeOD–MeOH

a	δ/p.p.m.	a	δ/p.p.m.	a	δ/p.p.m.
δ_H (MeOH) [a]		δ_H (MeOD) [b]		δ_T (MeOH) [c]	
0.0101	0.273	0.0101	0.310	0.0166	0.345
0.0166	0.680	0.0135	0.488	0.0336	0.528
0.0277	0.610	0.0204	0.640	0.0509	0.760
0.0336	0.789	0.0273	0.943	0.0687	1.010
0.0352	0.819	0.0309	0.953	0.0868	1.210
0.0417	0.889	0.0409	1.265	0.1056	1.386
0.0482	1.189	0.0427	1.279	0.1241	1.490
0.0508	1.127	0.0537	1.494	0.1442	1.640
0.0582	1.269	0.0554	1.509	0.1641	1.680
0.0661	1.446	0.0661	1.789	δ_T (MeOD) [d]	
0.0687	1.508	0.0698	1.766	0.0135	0.288
0.0868	1.644	0.0741	1.969	0.0273	0.628
0.0893	1.789	0.0775	2.068	0.0409	0.803
0.1056	2.126	0.0994	2.439	0.0554	0.998
0.1240	2.184	0.1146	2.767	0.0698	1.080
0.1442	2.317	0.1298	2.927	0.0840	1.385
0.1641	2.688	0.0080 [f]	0.267	0.0994	1.554
0.0087 [e]	0.202	0.0153	0.512	0.1146	1.850
0.0163	0.380	0.0238	0.770	0.1298	2.026
0.0252	0.572	0.0307	0.975		
0.0327	0.747	0.0384	1.200		
0.0403	0.910	0.0470	1.387		
0.0485	1.068	0.0544	1.595		
0.0548	1.235	0.0606	1.783		
0.0637	1.363	0.0831	2.100		
0.0775	1.647				

[a] For solvent MeOH $\delta_H = 1.100$ p.p.m. [b] For solvent MeOH–MeOD $\delta_H = 1.200$ p.p.m. [c] For solvent MeOH $\delta_T = 1.105$ p.p.m. [d] For solvent MeOH–MeOD $\delta_T = 1.176$ p.p.m. [e] Following results from ref. 2, $\delta_H = 1.23$ p.p.m. for MeOH. [f] Following results from ref. 2, $\delta_H = 1.20$ p.p.m. for MeOH–MeOD.

TABLE 2

Slopes $S = \Sigma Q_i \delta_i$ of plots of protium and tritium hydroxy chemical shifts in p.p.m. *vs.* concentration (a) [a] of sodium methoxide in MeOH or MeOH—MeOD [c] mixtures

Measurement	$S = (\delta/a)_{a \to 0}$		σ_S [b]
	Obs.	Calc. for $\phi = 0.7$	
δ_H (MeOH)	−25.0 [d]	−25.9	0.4
δ_T (MeOH)	−17.3	−17.1	0.2
δ_H (MeOD)	−34.5 [e]	−34.1	0.5
δ_T (MeOD)	−22.2	−21.9	1.0

[a] $a = N/(1 - N)$ where N is the mole fraction of sodium methoxide. [b] Standard deviation of the mean in S. [c] Atom fraction of deuterium = 0.90. [d] For the data from ref. 2 alone: −23.7. [e] For the data from ref. 2 alone: −34.9.

In Figures 1(a) and 1(b) the data are shown as plots of chemical shift *vs.* $a = N/(1 - N)$ where N is the mole fraction of sodium methoxide. The plots show quite marked curvature and limiting slopes $S = (\delta/a)_{a \to 0}$ were obtained as intercepts from a linear least-squares analysis of plots of δ/a *vs.* a. This analysis corresponds to expressing δ empirically as a quadratic function of a with linear coefficient S, as in equation (10). Values of S are listed in

$$\delta = Sa + Ra^2 \qquad (10)$$

Table 2 and were used to calculated the limiting slopes shown as dashed lines in Figure 1.

Previous treatments have taken $a = N$ instead of $N/(1 - N)$.[1,2] This is legitimate for measurements at low mole fractions of sodium methoxide and when limiting slopes of

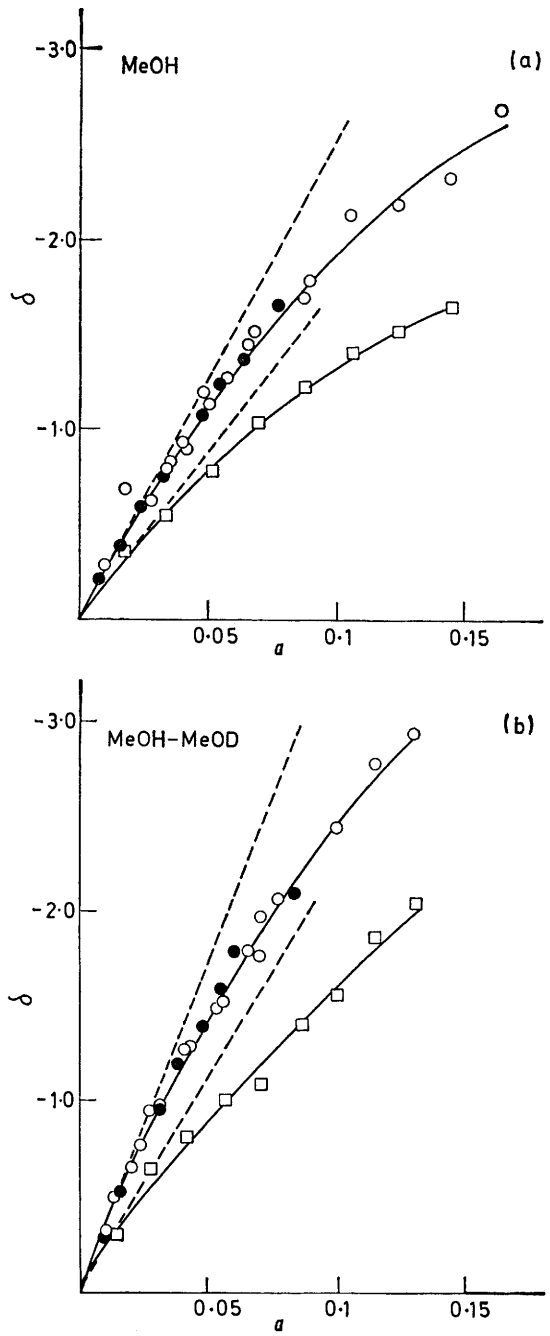


FIGURE 1 Plots of protium (δ_H) and tritium (δ_T) hydroxy chemical shifts in p.p.m. relative to solvent *versus* concentration of sodium methoxide [$a = N/(1 - N)$] for (a) MeOH (δ_H, ○ or ●) and MeOH (δ_T, □), and (b) MeOH–MeOD (δ_H, ○ or ●) and MeOH–MeOD (δ_T, □). The MeOH–MeOD mixtures contain 0.9 atom fraction of deuterio-solvent. The full lines are unweighted quadratic fits to the data, and the dotted lines limiting slopes obtained as intercepts of plots of δ *versus* a. The closed circles indicate data from ref. 2

plots of δ/a *vs.* a were considered, but for higher concentrations $N/(1 - N)$ should be used. The curvature of the plots which is clearly apparent in Figure 1 is less pronounced when $a = N$. The origin of the curvature which is a familiar feature of similar plots for aqueous solutions [5,16,17] is briefly considered later.

Analysis of the data in terms of a linear dependence of

δ/a upon a strongly weights points at low solute concentrations, and equivalent results were obtained using a direct quadratic least-squares analysis with weighting $1/a^2$ (and with δ at $a = 0$ optimised rather than taken as zero). The tritium measurement at lowest methoxide concentration in MeOH and the protium measurement for the same solution were discarded as deviating strongly from the correlations. The weighting is appropriate for determining slopes S as $a \longrightarrow 0$, but only S for the tritium measurement in MeOD was sensitive ($> \pm 5\%$) to the weighting, giving the lower value of $S = 17$ from the unweighted quadratic analysis compared with $S = 22$ from the weighted analysis.

For calculation of quadratic coefficients R in the equation (10) an unweighted quadratic analysis was considered more appropriate. The parameter of interest here is R/S rather than R but as R is much more sensitive to the weighting than S the values listed in Table 3 are based on the unweighted analysis. Again only the δ_T (MeOD) value depends importantly ($> \pm 20\%$) upon the weighting: weighted, $R/S = -2.7$; unweighted, $R/S = -1.1$. The treatment of comparable data has been discussed by Taylor and Tomlinson.[5] The calculated dependences of δ upon a shown as full lines in Figure 1 are based on the values of R and S in Table 3.

For MeOH the limiting slope of -25.0 ± 0.4 for the plot of δ/a *vs.* a from Table 2 and Figure 1(a) is in good agreement with the value of -25.4 ± 0.2 found by Gold and Grist.[1] Gold and Grist noted a discrepancy between their value and that of the measurements reported previously.[2] These measurements are included as closed circles in Figure 1(a) and, when considered alone, in the present analysis still yield the lower value of $S = -23.7$. From Figure 1(a), however, it is apparent that the difference between the two sets of measurements is small, and the discrepancy in S no doubt in part reflects the sensitivity of the quadratic analysis to minor fluctuations in the data, especially where the concentration range is insufficient for the quadratic coefficient to be realiably determined, as is certainly true of the earlier measurements. The same comparison for the MeOD measurements showed a discrepancy in limiting slopes of only 1%, although in both comparisons, as expected of the different concentration ranges involved, the discrepancies in quadratic parameters are relatively large (*e.g.* for MeOH, $R = 35$ compared with $R = 57$ for the combined data).

TABLE 3

Quadratic coefficients R for the dependence of protium and tritium hydroxy chemical shifts (p.p.m.) upon concentration (a) of NaOMe in MeOH and MeOH–MeOD mixtures [a]

Measurement	R	R/S	$\Sigma(1 - Q_i)$ calculated
δ_H (MeOH)	57	−2.3 [b]	0
δ_T (MeOH)	46	−2.6	1.2
δ_H (MeOD)	73	−2.3 [b]	−1.1
δ_T (MeOD)	19	−1.1	0.5

[a] Mole fraction of MeOD is 0.9. [b] From data of ref. 2, $R/S = -1.5$ for δ_H(MeOH) and −3.6 for δ_H(MeOD); see comment in Results section.

DISCUSSION

The limiting slopes S of plots of δ *versus* a [$= N/(1 - N)$] as a falls to zero for the protium and tritium hydroxy chemical shifts of solutions of sodium methoxide in MeOH and MeOH–MeOD mixtures of deuterium atom fractions $x = 0.90$ are listed in Table 2 and shown as the dashed lines in Figures 1(a) and 1(b). The necessity of considering limiting slopes is indicated by the marked curvature of the plots in the figures, and this curvature is discussed below. The measured slopes themselves allow us to determine whether the data are consistent with the simple model implied by the equations (8) which relate the slopes to a single methoxide fractionation factor ϕ and to two sets of chemical shifts: that for the strongly fractionating hydrogens of the primary methoxide solvation shell, δ_M, and that for the molecules in methoxide and sodium solvation shells not subject to appreciable fractionation, δ_0.

First we may test the assumption of previous determinations based on protium n.m.r. alone, that contributions to δ_0 arise solely from the solvation shell of the sodium ion. In this case $\delta_0 = \delta(Na^+)$ and ϕ is obtained from equation (11), where S_0 and S_x are the limiting

$$\frac{S_0 - \delta(Na^+)}{S_x - \delta(Na^+)} = (1 - x + x\phi) \qquad (11)$$

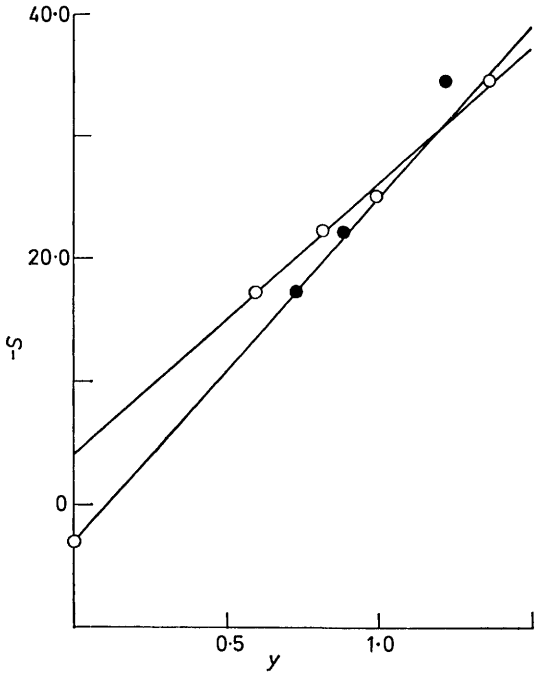


FIGURE 2 Slopes of plots of tritium and protium hydroxy chemical shifts *versus* concentration of sodium methoxide in MeOH and MeOH–MeOD mixtures [$-S = -(\delta/a)_{a \to 0}$] plotted against $y = \phi^{1.442}$, $(1 - x + x\phi)^{-1}\phi^{1.442}$, 1.0, and $(1 - x + x\phi)^{-1}$ for $\phi = 0.7$ (○) and $\phi = 0.8$ (●). The point at $y = 0$ is for $S = \delta(Na^+)$

slopes for protium chemical shifts at deuterium atom fractions 0 and x respectively. Taking Gold and Grist's value of $\delta(Na^+) = 3.0$ p.p.m./mole fraction we obtain $\phi = 0.72$ which is a little smaller than, but in substantial agreement with, the value of 0.74 found by Grist and Gold.[1] However, on replacing S_0 and S_x by the corresponding tritium results we obtain the significantly higher value of $\phi = 0.78$, and if we combine H and T measurements we find for MeOH $\phi = 0.80$, and for MeOH–MeOD mixtures $\phi = 0.76$.

Although the lower limiting slopes and small numbers of points make ϕ values based on the tritium measurements less precise than those from protium, Figure 2 shows that the differences are unlikely to represent random errors. According to the equations (8) the four limiting slopes S of Table 2 may be expressed in the form $S = \delta_0 + \delta_M y$ where $y = 1.0$, $(1 - x + x\phi)^{-1}$, $\phi^{1.442}$, and $\phi^{1.442}(1 - x + x\phi)^{-1}$. Values of y may be calculated for any value of ϕ, but if the model is adequate the correct value of ϕ should yield a linear dependence of S upon y with intercept δ_0. Figure 2 shows plots of $-S$ *versus* y for two values of ϕ. The open circles are for $\phi = 0.7$, and the value $\delta(Na^+) = 3.0$ is included at $y = 0$. In this case a straight line through the points for the protium measurements, which appear to the right of the tritium points, intersects the S axis at $\delta_0 = \delta(Na^+)$, but the tritium measurements deviate from the line. The tritium measurements can be brought on to the line by taking $\phi = 0.8$, as shown by the closed circles (the point $y = 1$ is common to both values of ϕ) but now the protium measurement in MeOD deviates. The smooth variation of S with y suggests that the discrepancies are systematic in origin.

The protium and tritium results may be reconciled by no longer requiring that $\delta_0 = \delta(Na^+)$. Thus Figure 2 shows that for $\phi = 0.7$ a satisfactory straight line can be drawn through the open circles if it intersects the S axis at $\delta_0 = -4$. The value of ϕ is only slightly smaller than values determined previously [1,2] and on the basis of a simple interpretation of the model in structure (1) is perhaps more in line with the rather large kinetic solvent isotope effects common for methoxide reactions.[3] The value of $\delta_0 - \delta(Na^+) = -7$ and $\delta_M = -22$ p.p.m./mole fraction seem reasonable relative magnitudes for contributions to the net methoxide chemical shift from its primary and secondary solvation shells.

A possible interpretation of the sign of the chemical shift, and also of the lack of isotope fractionation in the secondary solvation shell, is suggested by the rather large positive increase in hydroxy chemical shift accompanying increases in temperature in methanol and other alcohols, which is usually considered a consequence of breaking hydrogen bonds.[18] A negative shift characterising the secondary methoxide solvation need not, however, imply binding of further molecules to the primary shell but simply increased hydrogen-bonding in the surrounding solvent. Such a structure-making effect [16,19] would be consistent with the presumed hydrophobic character of the primary solvated ion. It would not be expected to be associated with an isotope effect because the presence of MeOD has practically no effect on the OH chemical shift of methanol itself.[1]

Some systematic curvature can perhaps still be detected for the open circles of Figure 2, and the best fit to a straight line is achieved with $\phi = 0.6$. However, the correlation is not very sensitive to the magnitude of ϕ when δ_0 is allowed to vary and ϕ is near its optimum value, and the calculated slopes for $\phi = 0.7$ in Table 2 show an average difference of only 2% from the observed values. The value of $\phi = 0.7$ is preferred to 0.6 both because 0.6 seems too small to be consistent with observed kinetic and equilibrium isotope effects and because the associated values of $\delta_0 - \delta(Na^+) = -13$ and $\delta_M = -16$ appear unreasonable in ascribing similar chemical shifts to the primary and secondary methoxide solvation shells. Thus while the measurements offer improved values of ϕ and chemical shifts over those for which it was assumed that $\delta_0 = \delta(Na^+)$, the lack of an independent measurement of δ_0 is reflected in a loss of precision in determining ϕ.

It is of course not possible to rule out contributions from fractionation at more than one site for the methoxide ion. However, only fractionation factors departing appreciably from unity will affect the results. An accumulation of small fractionation effects, for example associated with solvation shells, can make an appreciable contribution to solvent isotope effects through a medium effect.[7,20] From the general form of equation (5), however, it is evident that they do not have a corresponding influence upon isotopic chemical shifts because their contributions are averaged between molecules not accumulated. The effect indeed will be particularly small when, as may often be true, small fractionation effects are associated with small chemical shifts.

With respect to additional fractionation sites it should also be recognised that the equations (8) themselves include as special cases two-site fractionations with the second $\phi = 1.0$ and 0.7; *i.e.* where the second fractionation factor is the same as the first or the same as for the solvent. Therefore an important influence on the results can be expected only when ϕ is appreciably >1.0 or <0.7. It is not easy to imagine a model for the methoxide ion for which this would be likely to be true.

It seems clear that the tritium results, while pointing to the inadequacy of the assumption required of earlier measurements, that contributions to chemical shifts other than from the primary solvation shell of the methoxide ion are confined to the solvation shell of the cation, are nonetheless consistent with the previously proposed fractionation model for the methoxide ion [1] and require only minor revision of the currently accepted value of the methoxide fractionation factor. On the other hand the measurements lack the required precision for simultaneously defining a fractionation factor and two chemical shifts and thus emphasise the need for an independent measurement of ϕ.

Curvature of Plots of δ versus a.—The curvature of the plots in Figure 1 may be expressed in terms of the quadratic coefficient R of equation (10), and values of R are given in Table 3. Although poorly defined quantitatively the curvature is sufficiently pronounced that it deserves some comment. As a number of factors may be responsible,[16,17] discussion will be confined mainly to one relating to isotopic fractionation.

An isotopically dependent cause of curvature can be recognised from the derivation of the dependence of δ upon a given in the Appendix. Previous derivations, applicable to dilute solutions, have assumed that the

atom fraction of deuterium in the solution, z, differs insignificantly from that in the bulk solvent, x. At appreciable concentrations of solute, however, this assumption breaks down and the Q_i values of equation (5) require modification so that they reflect atom fractions of protium at a site i relative to the solution as a whole rather than to the solvent alone. Applying this adjustment to equation (5) gives equation (12).

The atom fraction of hydrogen in the solution $(1 - z)$ may be expressed as a sum of protium fractions at individual sites which, as shown in the Appendix,

$$\delta = [(1 - x)/(1 - z)]a\Sigma Q_i\delta_i \qquad (12)$$

simplifies to equation (13), where it can be seen that, as expected, $(1 - z) \longrightarrow (1 - x)$ as a (and N) $\longrightarrow 0$. Since the departure of $(1 - z)$ from $(1 - x)$ represents only a small correction term it is convenient to incorporate it in the numerator rather than denominator of

$$(1 - z) = (1 - x)[1 - a\Sigma(1 - Q_i)] \qquad (13)$$

equation (12) to give as a good approximation for the dependence of δ upon a equation (14).

$$\delta = a[1 + a\Sigma(1 - Q_i)]\Sigma Q_i\delta_i \qquad (14)$$

Equation (14) has the quadratic form of the equation (10) used to analyse the experimental measurements. $\Sigma Q_i\delta_i$ is the limiting slope of plots of δ *versus* a, and if deviation of $(1 - z)$ from $(1 - x)$ is the only factor responsible for curvature of these plots, values of R/S of Table 3 correspond to $\Sigma(1 - Q_i)$. The latter identification is of interest because it potentially offers additional parameters for evaluating methoxide fractionation factors, free indeed of associated chemical shifts. The same information is obtainable from the isotope separation factor between solvent and solution $\alpha = \{z(1 - x)\}/\{x(1 - z)\}$ which is experimentally determinable as the appropriate ratio of liquid–vapour separation factors.[21] For solutions of NaOMe in MeOH and MeOH–MeOD mixtures $\Sigma(1 - Q_i)$ may be expressed in terms of the single fractionation model (1) for the methoxide ion with three equivalent solvating hydrogens as in equations (15).

$$\begin{aligned}
&\delta_H\ (\text{MeOH}) : \Sigma(1 - Q_i) = 0 \\
&\delta_H\ (\text{MeOD}) : \Sigma(1 - Q_i) = \frac{-3x(1 - \phi)}{(1 - x + x\phi)} \qquad (15) \\
&\delta_T\ (\text{MeOH}) : \Sigma(1 - Q_i) = 3(1 - \phi^{1.442}) \\
&\delta_T\ (\text{MeOD}) : \Sigma(1 - Q_i) = 3\left[1 - \frac{\phi^{1.442}}{1 - x + x\phi}\right]
\end{aligned}$$

Values of $R/S = \Sigma(1 - Q_i)$ calculated for $\phi = 0.7$ are listed in Table 3 for comparison with the experimental values. It is at once apparent that $\Sigma(1 - Q_i)$ cannot be the only factor responsible for curvature, otherwise no curvature would be observed for the protium chemical shifts in isotopically pure MeOH. Nonetheless it is noteworthy that where more than one isotope is present the predicted curvature is of a magnitude comparable with that observed and presumably must contribute to it.

Further factors suggested as responsible for curvature of δ–concentration plots at not too high solute concentrations are ion-pairing and competition for solvent molecules between ionic solvation shells.[16,17] The latter factor, except where the primary solvation shell of methoxide is affected, should be nearly isotope independent, and the absence of the fairly marked difference in curvature of tritium chemical shifts in MeOH and protium chemical shifts in MeOD implied by the calculated contributions from $\Sigma(1 - Q_i)$ perhaps again suggests that this is not the sole additional effect.

An increase in ion-pairing with increase in methoxide concentration could well be important. In so far as formation of a tight ion-pair might be supposed to release at least one solvent molecule it would presumably lead to an upfield chemical shift and a fractionation factor closer to 1.0 for the displaced molecule. However, while the change in chemical shift is consistent with the curvature observed an increase in the fractionation factor would lead to a greater value of R/S in MeOH–MeOD mixtures than in pure MeOH which, allowing for the contribution of $\Sigma(1 - Q_i)$, is the opposite of what is observed.

While no definite conclusion can be reached concerning methanolic sodium methoxide solutions it seems clear that for the interpretation of curvatures of plots of solvent chemical shifts against salt concentrations in general, isotopic measurements can offer additional information and constraints, expecially where the measurements are for lyate or lyonium ions.

APPENDIX

The general expression for the protium chemical shift Δ relative to a suitable standard for a hydroxylic solution of deuterium atom fraction z is given by equation (16). In the equation a denotes the concentration of solute in units that

$$\Delta = \frac{a(1 - x)\sum_{i=0} Q_i\Delta_i + (1 - x)(1 - \nu a)\Delta_{OH}}{(1 - z)} \qquad (16)$$

allow hydrogens introduced stoicheiometrically or associated with its solvation shells to be expressed as atom fractions of all hydrogens contributing to the shift. If the mole fraction N is used for the concentration of solute itself, $a = N/[\nu_s(1 - N) + \nu_0]$ where ν_s is the number of hydrogens per solvent molecule and ν_0 the number stoicheiometrically introduced with each molecule of solute. Δ_{OH} is the chemical shift of pure solvent and the Δ_i values are the chemical shifts of exchangeable hydrogens associated with the solute, covalently or in its solvation shells, differing from the bulk solvent; $(1 - x)$ is the isotopic atom fraction of protium in the bulk solvent and $(1 - x)Q_i$ is that at a hydrogen position i. The summation $\Sigma Q_i\delta_i$ is over all hydrogens associated with a solute molecule and implies a notional stoicheiometry for the solvation shell; ν is the stoicheiometric number of hydrogens in the solvation shell or covalently associated with the solute but derived from the solvent (*e.g.* as in H_3O^+); $(1 - \nu a)$ is the atom fraction of hydrogens in the bulk solvent.

The atom fraction of protium in the solution as a whole $(1 - z)$ may be expressed as the sum of atom fractions in the

bulk solvent and at the individual sites i [equation (17)].

$$(1 - z) = a(1 - x)\Sigma Q_i + (1 - x)(1 - \nu a) \quad (17)$$

Substituting in equation (16) and cancelling $(1 - x)$ allows the chemical shift to be written as equation (18). We wish to re-express this in terms of chemical shifts relative to the solvent OH, $\delta = \Delta - \Delta_{OH}$ and $\delta_i = \Delta_i - \Delta_{OH}$. If we recognise that $\nu - \Sigma Q_i = \Sigma (1 - Q_i)$ equation (18) can be

$$\Delta = \frac{a\Sigma Q_i\Delta_i + (1 - \nu a)\Delta_{OH}}{a\Sigma Q_i + (1 - \nu a)} \quad (18)$$

rewritten as (19), and cross multiplication yields the desired relation (20). From equation (17) we see that (20) may

$$\Delta = \frac{a\Sigma Q_i(\Delta_i - \Delta_{OH}) + [1 - a\Sigma(1 - Q_i)]\Delta_{OH}}{1 - a\Sigma(1 - Q_i)} \quad (19)$$

also be formulated as (21) and it is apparent that the usual

$$\delta[1 - a\Sigma(1 - Q_i)] = a\Sigma Q_i\delta_i \quad (20)$$

approximation $\delta = a\Sigma Q_i\delta_i$ applicable at low mole fractions

$$\delta(1 - x)/(1 - z) = a\Sigma Q_i\delta_i \quad (21)$$

of solute comes from taking $(1 - z) = (1 - x)$, as pointed out by Gold in his original derivation.[8] Equation (20) is also applicable to tritium chemical shifts when the Q_i, z, and x represent atom fractions of tritium.

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