Solvation of Fluoride Ions

Carmen Carmona, Graham Eaton, and Martyn C. R. Symons*

Department of Chemistry, The University, Leicester LE1 7RH, U.K.

I.r. and n.m.r. studies of solutions of fluorides in various solvents including amides are compared with those for chlorides and xenon; it is concluded that there is no strong case for postulating any special interaction between N–H groups and F^- ions in solution, and that ^{19}F shifts are not a good measure of the strengths of hydrogen bonds to fluoride.

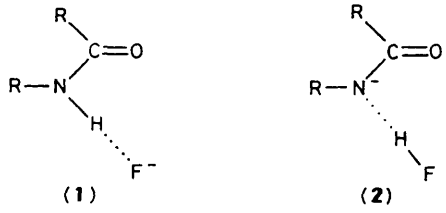
Fluoride ions, despite their similarity to the biologically ubiquitous chloride ions, and the necessary role that they play in various biological systems, are the butt of much controversy, and are blamed, by some, for several biologically harmful processes, including cancer.[1] It is, therefore, important to learn about the solvation of F^- and especially its mode of interaction with biological compounds.

It has recently been suggested that F^- forms remarkably strong hydrogen bonds to the N–H protons of amides and hence that it may actively compete for structurally important N–H groups in proteins and in DNA.[2–4] In summary, these ideas stem from the following. (a) Theoretical calculations for unit (**1**, R = H, Me) which suggest that the hydrogen bond is the second strongest known.[2] [This statement is somewhat of an understatement, since the actual hydrogen bond is between N and H, the proton having been transferred to fluoride (**2**) according to these calculations.] This implies that the interaction is enormously greater than that between F^- and water or methanol. (b) In support of these calculations, it is claimed that, for CsF in *N*-methylformamide (NMF), a band at *ca.* 1600 cm^{-1} is due to the N–H (or H–F) stretch.[2] This very large shift from 3465 cm^{-1} (for monomeric NMF) would certainly indicate extremely strong bonding, whichever be the species involved, (**1**) or (**2**). (c) Work on the ^{19}F resonance shifts and N–H proton shifts are also cited in favour of this concept. [Unfortunately, our results for the ^{19}F resonance of F^- in NMF are quite different from those reported in ref. 2 (Figure 1)].

The contribution made by the NH proton resonance studies for the N–H proton is said to be unimportant mainly because of the extreme line broadening obtained.[3] [The suggestion that an n.m.r. peak at *ca.* 5.8 p.p.m. obtained on adding CsF is due to the ionized amide $(HCONCH_3)^-$ can in our view be dismissed. This band is almost certainly due to traces of water.]

Thus the major experimental evidence is the new i.r. band at 1600 cm^{-1}. As stressed in ref. 2, this is very close to the C–N–H bending mode for NMF, and our own studies suggest that the new band is indeed simply this mode shifted to high frequencies as a result of hydrogen bonding to F^-. Such a high-frequency shift is expected on increasing the hydrogen bond strength, and curve analysis shows that this is a narrow band rather than one with the extreme width expected for a band due to very strong hydrogen bonding.

Our results indicate that a broad band at *ca.* 2950 cm^{-1}, that is, shifted from $(N–H)_{free}$ by 515 cm^{-1}, is the true N–H band, modified by bonding to F^-. Very similar broad bands, shifted to about this extent, were also obtained from solutions of F^- in methanol and in water (*HOD* in D_2O). These low frequency shifts are expected by analogy with the effect of F^- on the ^1H



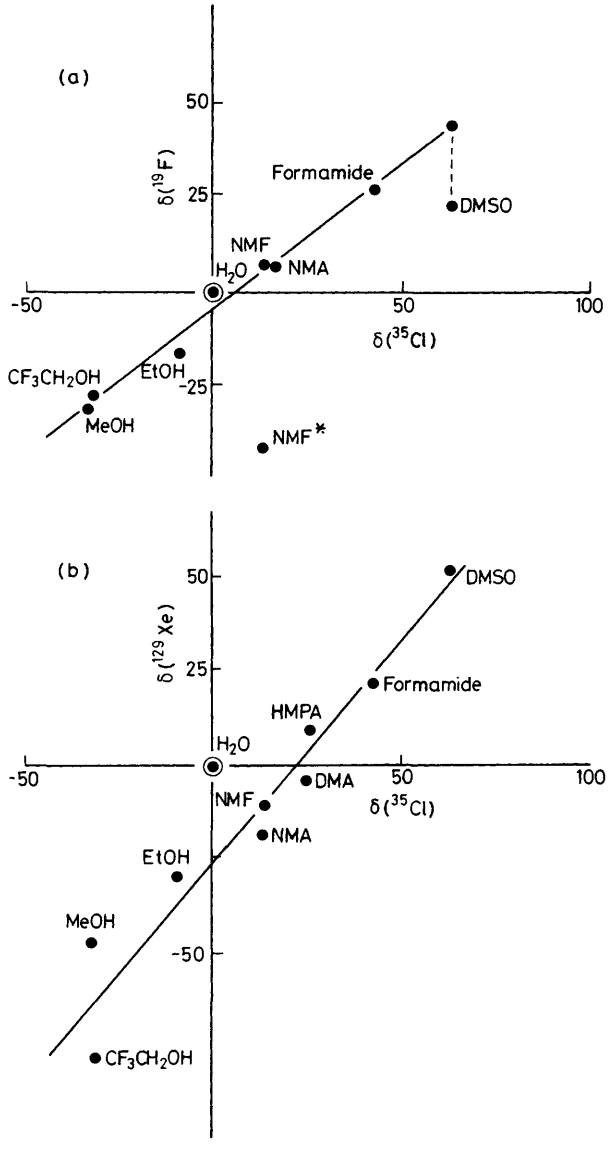


Figure 1. Trends in chemical shifts for F^- (a) and Xe (b) in a range of solvents relative to those for Cl^- ions in the same solvents. Cations were Na^+, Li^+, or Bu_4N^+, and shifts were largely independent of the concentrations used. All shifts (p.p.m.) are given relative to aqueous solutions. The value for F^- in DMSO is uncertain, because of the difficulty of removal of traces of water. (Positive shifts are downfield: NMF = *N*-methylformamide, NMA = *N*-methylacetamide, DMSO = dimethyl sulphoxide, HMPA = hexamethylphosphoramide.) *NMF (F^-) data from ref. 2.

resonance of methanol[5] and water,[6] but they do not indicate proton transfer or even unusually strong hydrogen bonding.

If the calculations are accepted, and we point out that another recent calculation for the F^-–formamide unit gives a significantly different value,[7] the model is quite inappropriate for F^- in pure amide solutions or, indeed, for aqueous amides. This is because the number of solvent molecules hydrogen bonded to F^- is probably between 4 and 6, and the greater this solvation number, the weaker the individual hydrogen bonds.[8,9]

We have studied trends in the ^{19}F resonance for F^- in mixed water–amide and methanol–amide systems. These deviate from linearity in favour of the hydroxylic solvents but not to a great extent. Trends for $^{35}Cl^-$ are similar and we see no reason for supposing that there is any marked tendency for F^- to single out strongly bound NH groups in biological aqueous systems.

Our proton resonance studies for solutions of fluorides in water, methanol, and amides support these statements. Using the arguments outlined for a range of salts in methanol,[10] it has been possible to obtain approximate solvation numbers from combined i.r. and ^1H resonance studies. The resulting values of *ca.* 4—6 are in accord with expectation and compare well with results for Cl^-.[11]

We conclude that there is no case for the suggestion that NH ···· F^- bonds are unusually strong for *solvated* fluoride ions.

Our other aim is to establish that, although $^{19}F^-$ shifts for mixed binary solvent systems may give information regarding preferential solvation, the absolute values of these shifts in pure solvents appear to bear little relationship to the strength of the hydrogen bonds formed to F^-. This is important since many workers argue that the shifts are dominated by changes in hydrogen bonding.[2—4,12] We find that overall trends for F^-, Cl^-, and Xe are broadly similar in a range of solvents (Figure 1) suggesting that the dominant factors controlling the shifts are also similar. This rules out hydrogen bonding as a controlling factor, since xenon atoms are not expected to form hydrogen bonds in any of these solvents.

C. C. is a Visiting Research Fellow from the University of Seville, Spain.

Received, 18th December 1986; Com. 1795

References

1 G. L. Waldbott, A. W. Burgstahler, and H. L. McKinney, 'Fluoridation: The Great Dilemma,' Caronado Press, Kansas, 1978.
2 J. Emsley, D. J. Jones, J. M. Miller, R. E. Overill, and R. A. Waddilove, *J. Am. Chem. Soc.*, 1981, **103**, 24.
3 J. H. Clark and E. M. Goodman, *Spectrochim. Acta, Sect. A*, 1986, **42**, 457.
4 J. H. Clark, J. Sherwood Taylor, and A. J. Goodwin, *Spectrochim. Acta, Sect. A*, 1982, 1101.
5 R. N. Butler and M. C. R. Symons, *Trans. Faraday Soc.*, 1969, **65**, 2559.
6 J. Davies, S. Ormondroyd, and M. C. R. Symons, *Trans. Faraday Soc.*, 1971, **67**, 3465.
7 K. Miaskiewicz and J. Sadlej, *J. Mol. Struct. (Theochem.)*, 1985, **124**, 223.
8 P. Kebarle, W. R. Davidson, M. French, J. B. Cumming, and T. B. McMahon, *Faraday Discuss. Chem. Soc.*, 1978, **64**, 220.
9 I. M. Strauss and M. C. R. Symons, *J. Chem. Soc., Faraday Trans. 1*, 1978, **74**, 2146.
10 M. C. R. Symons, *J. Chem. Soc., Faraday Trans. 1*, 1983, **79**, 1273.
11 G. W. Neilson and J. E. Enderby, *Ann. Rep. Chem. Soc. C*, 1979, **76**, 185.
12 J. P. K. Tong, C. H. Langford, and T. R. Stengle, *Can. J. Chem.*, 1974, **52**, 1721.