

An NMR Spectroscopic Method for Mapping Reactions in Solution

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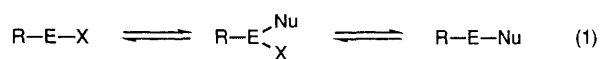
By monitoring changes in NMR chemical shifts of a chelating pyridone ring, as substituents are varied, the progress of a reaction in solution can be mapped in a somewhat analogous way to the X-ray spectroscopic techniques in the solid state.

The X-ray crystallographic studies by Bürgi, Dunitz^{1,2} and others^{3,4} have helped to elucidate the molecular pathways of reaction at, for example, carbon,¹ tin² and silicon^{3,4} nuclei. The essence of that method is that bond lengths and angles for a series of structurally related model compounds are compared and used to infer coordination and bond angle changes during the course of a reaction.

We sought to develop a method that would enable the progress of a particular reaction to be mapped in solution by preparing a series of compounds that represent species 'frozen' at various points on the reaction profile. Whereas X-ray crystallography gives very detailed structural informa-

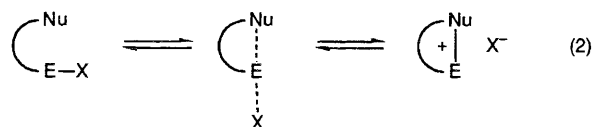
tion solution studies will necessarily be more qualitative. Nevertheless we have produced a system in which the progress of a nucleophilic substitution from reactants to products, through intermediates, can be monitored in solution in a reasonably quantitative manner.

For a system R-E-X undergoing substitution to R-E-Nu in reaction (1) the minimum requirements for studying the progress of reaction are (i) a measure of the extent of Nu-E



bond formation (and/or E-X bond breaking) and (ii) a measure of the coordination state of the nucleus E.

The coordination state of E, for NMR active nuclei, can usually be accurately determined from the chemical shift of E. The extent of Nu-E bond making is more difficult to measure. In a chelating system, equation (2), the coordination of Nu can



be estimated with some accuracy if it is accompanied by a significant change in the nature of the molecule, as for example in an aromatization. We chose for a first study, the 2-pyridone molecule which can undergo the changes shown in eqn. (3). The major assumption is that, as the reaction progresses from **1** to **3**, the NMR chemical shifts in the ring can be closely approximated by the chemical shifts of an appropriate mixture of the model compounds such as **4** and **5** when E is SiMe₂.

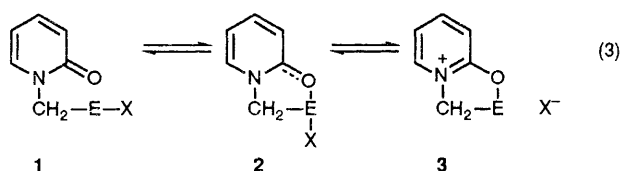


Fig. 1 shows the ¹³C NMR chemical shift changes as *N*-methylpyridone, **4** 10% w/w in CDCl₃, is titrated with successive amounts of trimethylsilyl trifluorosulphonate (TMSOTf) to give **5**. It was shown that complete silylation occurred at all mole ratios and that equilibrium between **4** and **5** is rapid on the NMR time scale, so there is only one resonance for each of the carbon atoms C-2, C-3, C-4, C-5 and C-6 in any mixture of **4** and **5**. There is a very good linear correlation between the chemical shifts of the carbon nuclei in a mixture of **4** and **5** and the mole fraction of **5**. (Similar results are obtained from the ¹H NMR spectra.) Hence, we have made the assumption that the O-E bond in the **1,2,3** manifold is *x* per cent formed ('extent of reaction' *x*%) if the pyridone

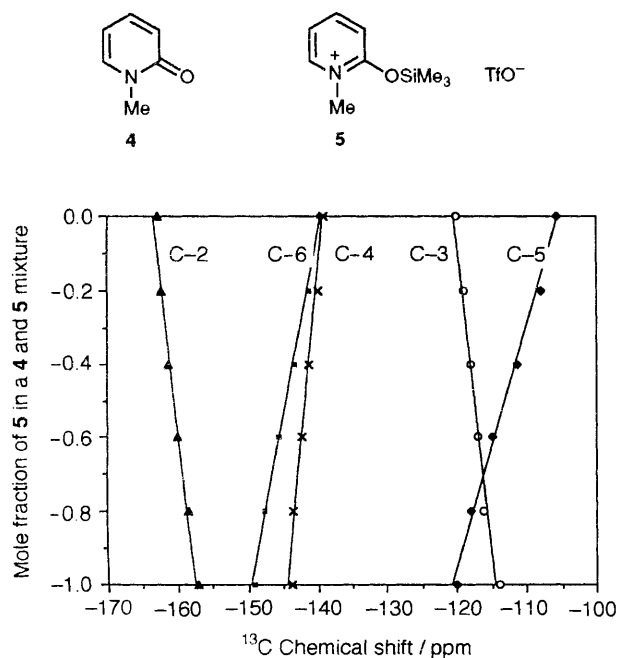


Fig. 1 NMR chemical shift changes during the pyridone to pyridinium ion transformation

¹³C resonances indicate *x*% **5** (*0.x* mole fraction of **5**). This 'extent of reaction' can then be correlated with the coordination state of E, as measured by the NMR chemical shift of E. Compounds **6**, **7** and **8** demonstrate that the assumptions are firmly based. There is ample evidence from X-ray crystallography that chelated amide complexes of dimethylchlorosilanes are five-coordinated with bond orders of about 0.5 for both Si-O and Si-Cl bonds.⁵

The chemical shifts of the ring carbon nuclei in **6** in CD₃CN (C-2, 160.1; C-3, 115.8; C-4, 139.3; C-5, 113.6; C-6, 143.3 ppm) resemble closely those of an equimolar mixture of **4** and **5** with chemical shifts differing by less than about ±1 ppm from those in the mixture. This corresponds to an 'extent of reaction' of 50% for compound **6**. Although the fit of chemical shifts is currently determined visually the accuracy is estimated to be approximately ±5%. There is generally an excellent correlation with C-5 and C-6 chemical shifts where the differences between **4** and **5** are greatest and a good correlation with C-3 and C-4. The correlation with C-2 is generally poor for chelated compounds such as **6-8**.

The ²⁹Si NMR spectrum of **6** is a sharp single resonance at about δ -40. This represents a low frequency shift of over 70 ppm relative to Me₃SiCl and is unambiguous evidence of pentacoordination at silicon.⁶ The ²⁹Si and ¹³C NMR spectra of **6** are temperature independent and a solution of **6** in MeCN does not conduct electricity. The compounds **6** being unequivocally five-coordinate at silicon confirms that the changes in the ¹³C NMR pyridone ligand with increasing O-E coordination are consistent with those observed for the **4, 5** equilibrium.

For **6** the O-Si bond is about 50% formed and the structure corresponds to **2**. Evidence is given in the accompanying paper that **6** does represent the closest approximation to a true five-coordinate intermediate in a substitution at silicon.

It is well-established that the tendency to five-coordination increases in the order R₃SiCl < R₂SiCl₂ < RSiCl₃.⁴ The expectation for the series **6, 7, 8** is that as *n* increases so the O-Si and Si-Cl apical bond lengths will decrease⁷ as the complexes increasingly resemble stable five-coordinate compounds with all bond orders approaching unity. The ¹³C NMR chemical shifts of **7** in CDCl₃ (C-2, 162.2; C-3, 114.5; C-4, 139.0; C-5, 113.9; C-6, 144.8 ppm) suggest about 65% O-Si bond formation, and those of **8** in CDCl₃ (C-2, 160.8; C-3, 114.0; C-4, 140.0; C-5, 115.4; C-6, 146.1 ppm) about 75% O-Si bond formation. Fig. 2 shows the variation in Si-O bond

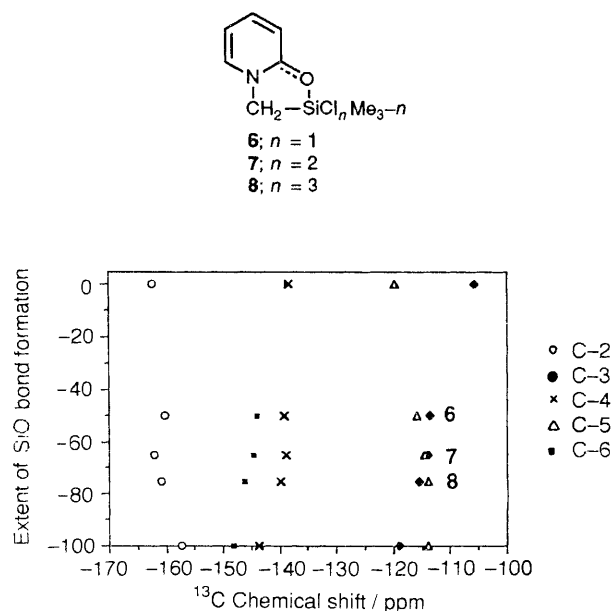


Fig. 2 Extent of Si-O bond formation for compounds **6-8**

formation for the series 6-8. The ^{29}Si NMR chemical shifts of -52.4 ppm for 7 and -77.7 ppm for 8 are entirely consistent with fully five-coordination at silicon. This combination of an increasing extent of O-Si bond formation while maintaining five-coordination at silicon is what is expected as the silicon centre becomes more susceptible to addition and less susceptible to substitution.

The solution mapping of the course of nucleophilic substitution at E can therefore be modelled by studying the NMR spectra of a series of compounds 1 in which X is varied and substituents may be placed in the ring to modify the nucleophilicity of the oxygen atoms. (For each ring substituent the chemical shift limits of the analogues of 4 and 5 must be determined individually.) For each compound the extent of O-E bond-making can be determined and the coordination state of E may be also estimated. With a sufficiently large number of compounds a picture of the bond making and coordination changes during a reaction may therefore be assembled. The accompanying paper shows how this new

method has been applied to map the structure of complexes in the series 1, 2, 3 during nucleophilic substitution at RSiMe_2X .

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