through sintered glass funnels and analyzed by gas chromatography.

The gas chromatograph used in this study was a Varian Aerograph 90-P. The column used was $1/4$ in. × 8 ft 5% Carbowax 20M with Chromosorb G was column support and the column temperatures were 60–80 °C and 180–200 °C. The internal standard selected was 1-bromonaphthalene. In each run the results were normalized to the conversion percentage. Then the average of the duplicated results were entered into the tables. The precision in the yields is ±6%.

Preparation of Iron Oxide.[12] Ferrous sulfate (115 g) was dissolved in 1 L of water by heating and adding a small amount of concentrated sulfuric acid (~10 mL). Aqueous ammonium sulfide (22.3%, J. T. Baker, Phillipsburg, N.J.) was added until the precipitation was complete and then an additional 5 mL was added. Ammonium hydroxide was added until the acidity was gone, and the mixture was filtered and washed with water until a negative sulfate ion test was achieved (BaCl$_2$). The solid was air-dried and calcined at 500 °C for 3 h to a dark red solid powder which does not produce hydrogen sulfide on exposure to dilute sulfuric acid. Because the product is magnetic, it is probably Fe$_3$O$_4$.

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Communications

Self-Association and the Protomeric Equilibria of 4-Hydroxypyridine–4-Pyridone and Related Compounds

Summary: Extensive self-association of 4-pyridone is reported and suggested to shift the apparent position of the protomeric equilibrium between 4-pyridone and 4-hydroxypyridine in favor of the former in chloroform and cyclohexane. Self-association of 4-pyridones is shown to be suppressed by 2,6-substitution of the ring.

Sir: We have estimated the protomeric equilibrium constant for 4-hydroxypyridine (1)–4-pyridone (2) to be ca. 10^{-5} (K_T

1, R = H
3, R = C(CH$_3$)$_3$

2, R = H
4, R = C(CH$_3$)$_3$
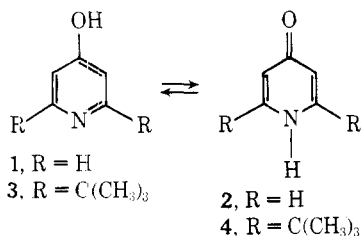
= [NH]/[OH] = 2/1) in the gas phase.[1,2] While it might be expected that 1 would also be the only detectable protomer in nonpolar weakly hydrogen bonding solvents,[3] a K_T of $10^{0.11}$ has been reported recently for this system in chloroform and a K_T of 10^{-1} may be estimated for cyclohexane.[4] Because of a continuing interest in this area we have reinvestigated that work. We wish to report that the apparent equilibrium between 1 and 2 in chloroform and cyclohexane, in fact, is dominated by the extensive oligomerization of 2 and that this self-association can be suppressed in derivatives of 4-pyridones by appropriate substitution of the 4-pyridone ring.
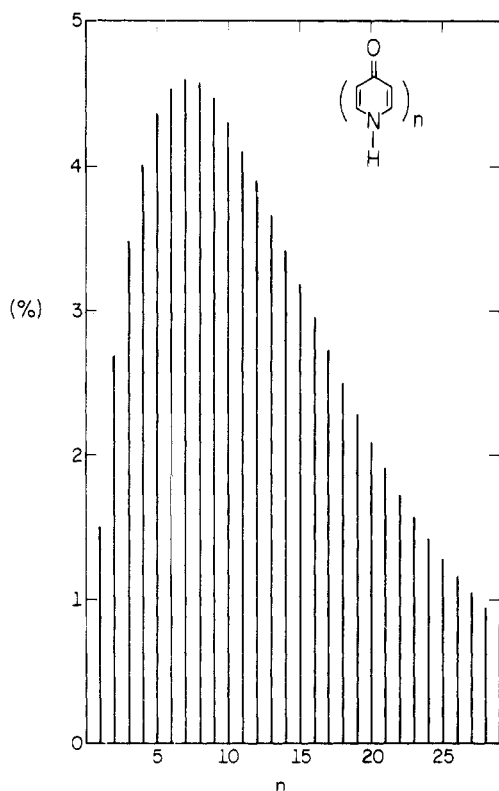
Multiwavelength analysis of the ultraviolet spectrum of 1–2 in cyclohexane and chloroform at 10^{-7} and 10^{-5} M, respectively, shows an absorption attributable to the chromophore of 2 to be the only detectable species. If that result is expressed

in terms of K_T for 1–2 a value >10 in favor of 2 is obtained. Such an equilibrium would be even further from the expected predominance of 1 than suggested by the recent work from East Anglia.[3,4]

Vapor-pressure osmometry of solutions of 4-pyridone in chloroform establishes that 2 is very strongly associated by hydrogen bonding. We find, for example, the modal association number of 4-pyridone at 0.049 M in chloroform to be 9. In fact, some years ago Coburn and Dudek suggested that 4-pyridone was a hydrogen-bonded trimer at ca. 10^{-3} M in chloroform.[5,6] If the association of 4-pyridone is analyzed as a statistical distribution of oligomers, an association free energy of −6.1 kcal/mol, an association constant of 30 000 ± 700, and the distribution of oligomers shown in Figure 1 may be derived from studies of molecular weight as a function of dilution. For this model <30% of the material would be monomeric under the conditions of the ultraviolet determination. Direct determination of the association in cyclohexane was precluded by limited solubility.

The 6.1 kcal/mol self-association energy of 2 in chloroform is clearly more than sufficient to dominate the position of protomeric equilibrium for 1–2 under the conditions reported. In fact this energy of hydrogen bonding is 1.5 kcal/mol stronger than for the dimerization of 2-pyridone in chloroform. The apparent position of protomeric equilibrium between 2-pyridone and 2-hydroxypyridine also has been shown to be determined by self-association in chloroform and cyclohexane under most conditions of measurement.[5–9] It is noteworthy that the association of 2-pyridone in cyclohexane is several kilocalories per mole stronger than in chloroform, a result which is taken to suggest that the apparent equilibrium for 1–2 is also dominated by association in cyclohexane.

These results again show the importance of correctly assessing the effect of molecular environment and association effects on molecular energies of protomeric systems.[1,2,7] Interpretation of equilibria determined on associated material

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Figure 1. Composition of oligomers to $n = 29$ for 0.025 M 4-pyridone in chloroform.

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(3) If the effect of non-hydrogen-bonding solvents on the position of equilibrium is, as a first approximation, attributed to differential stabilization of the dipoles of **1** and **2** by a dielectric effect, the equilibrium for **1–2** in solvents of low dielectric should still highly favor **1**. For example, on the basis of the Onsager equation with 4-methoxypyridine and 1-methyl-4-pyridone as models the equilibrium constant for **1–2** may be predicted to change from 10^{-5} in the vapor to $10^{-3.5}$ in cyclohexane and to $10^{-1.5}$ in chloroform. Such an application of the Onsager equation has been noted to provide a useful approximation of solvent effects on the protomeric equilibria of some 2-pyridones.[1,2] However, the limitations of this approach must be noted and our recent work suggests solvent hydrogen-bonding effects become significant in many cases: P. Beak and J. Covington, unpublished results.
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(8) The association of 4-pyridone is quite strong and persists in ethanol. Comparison of the association with that of 2-pyridone using the statistical distribution model of Figure 1 shows the free energies of hydrogen bonding in ethanol are: 4-pyridone, −2.6 kcal/mol; 2-pyridone, −1.95 kcal/mol.
(9) It is possible that the equilibrium constant for association of monomers is different from that for addition to the polymer chain. If previous work on amide association is a useful guide the dimer association constant would be less than the subsequent oligomer association constant and the amount of monomer present would be then less than the above estimate: L. L. Graham and C. Y. Chang, *J. Phys. Chem.*, **25**, 776, 784 (1977); M. Davies and D. K. Thomas, *ibid.*, **60**, 763, 767 (1956).
(10) We find that 4-pyridone is monomeric in acetonitrile, the other solvent in which the equilibrium constant for **1–2** was determined for the proposed correlation.[4]
(11) In private discussions with Professor A. R. Katritzky regarding possible problems of association of 2- and 4-pyridones which began in April, 1976, he also noted the possibility that **3–4** and **5–6** would be less associated than the parent materials. The correlations of the equilibrium constants of these substituted systems with Z values may be accorded more significance than those of the parent system.

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in terms of the relative energies of the monomers would be erroneous and the significance of the suggested correlation of the overall equilibrium constants of 2-pyridone and 4-pyridone with solvent Z values is open to question.[4,10] It is essential that the nature of the species being compared be known if fundamental understanding of medium effects on protomeric equilibria is to be achieved.

While the complication of association may be removed, in principle, by operating at very low concentrations, for some solvents the necessary dilutions may provide solutions in which the chromophore of interest is beyond the present limits of detection. Another approach is suggested by the studies of 2,6-di-*tert*-butyl-4-hydroxypyridine (**3**)–2,6-di-*tert*-butyl-4-pyridone (**4**) and 3-decyl-2,8-dimethyl-4-hydroxyquinoline (**5**)–3-decyl-2,8-dimethyl-4-quinolone (**6**), compounds which
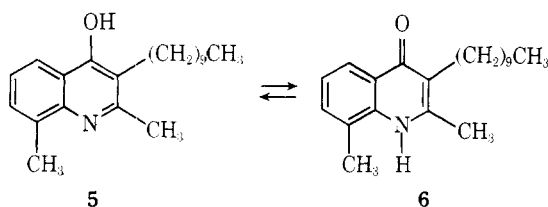
were chosen by Frank and Katritzky for their favorable solubility.[4] The structures of **3–4** and **5–6** might be expected to offer substantial hindrance to association by hydrogen bonding.[11] In fact, both **3–4** and **5–6** are shown by vapor-pressure osmometry to be essentially monomeric in chloroform at the concentrations used to measure their ultraviolet spectra. The possible association of these compounds in less polar solvents, their position of equilibrium in the vapor, and the effect of substitution on the position of equilibria need to be determined. Compounds which are designed and shown to be monomeric under the conditions of measurement should be useful in providing information about the effect of molecular environment on tautomeric equilibria.

New Synthetic Methods for the Regioselective Annelation of Aromatic Rings: 1-Hydroxy-2,3-disubstituted Naphthalenes and 1,4-Dihydroxy-2,3-disubstituted Naphthalenes

Summary: Respective condensation of the anion of ethyl 2-carboxybenzyl phenyl sulfoxide and 1*H*-2-benzofuran-1-one 3-(phenyl sulfone) with α,β-unsaturated esters and ketones results in regioselective formation of 1-hydroxy-2,3-disubstituted naphthalenes in moderate yield and 1,4-dihydroxy-2,3-disubstituted naphthalenes in good yield.

Sir: Extension of our recently reported strategy for the construction of linear polynuclear aromatic systems[1,2] has resulted in the development of two new methods for the regioselective annelation of aromatic rings. Each route can be incorporated into the original strategy with the notable advantage that abbreviated syntheses of naphthalenes with a