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Dimerization Constants for Phosphoric Acid Diesters

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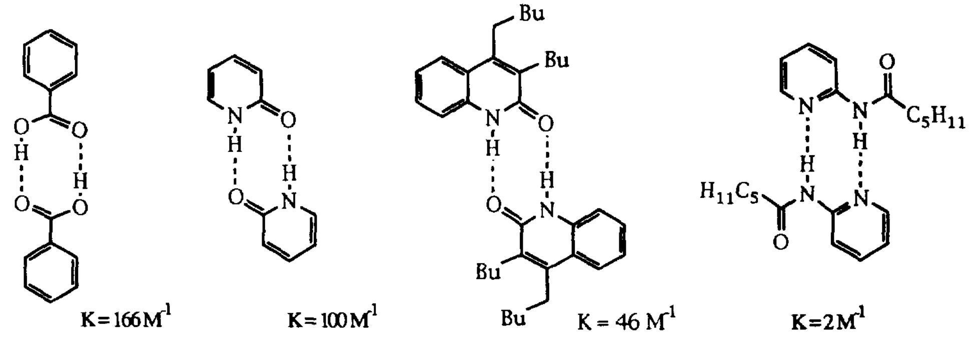
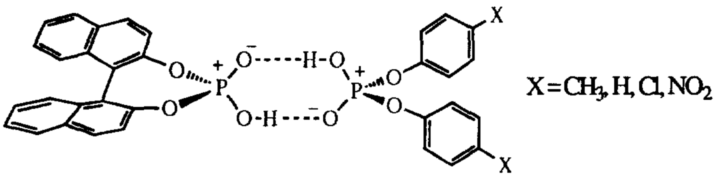
Abstract: Phosphoric acid diesters are found to dimerize in dry chloroform with dimerization constants of 10^4 to 10^5 M^{-1}. A correlation between dimerization constants and Hammett sigma values exists.

Molecular recognition via hydrogen bonding has recently been used to self-assemble monomers into controllable aggregates in solution[1] and to control crystal packing in the solid state.[2] For example, the well known dimerization of carboxylic acid,[3] 2-aminopyridine,[4] and 2-pyridone[5] derivatives has been used to such ends. However, as shown below, dimerization constants for such compounds are small to moderate in chloroform.[6] Therefore, it is likely that multiple interactions of such magnitude will be required as a means to guide a self-assembly process into discrete and robust aggregates in solution. The requirement of multiple interactions could be alleviated with larger self-association constants.



During the study of polyaza-receptors for phosphoric acid diesters in chloroform, we found extensive dimerization of the phosphoric acid diesters, and were lead to measure a dimerization constant.[7] Using a fluorescence technique, we found that the dimerization constant of dinaphthylphosphoric acid with dibenzylphosphoric acid in dry chloroform was 6.5 x 10^4 M^{-1}. Dimerization constants of alkylphosphoric acid diesters in water saturated chloroform have been found to be near 3 x 10^4 M^{-1}.[8] Herein, we report that arylphosphoric acid diesters have even larger dimerization constants that increase with increasing phosphoric acid acidity.

The assay for determination of dimerization constants involved a fluorescense quenching technique that has been described in detail previously.[7] However, instead of using dinaphthylphosphoric acid as previously reported, R-(-)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate was used as the fluorescence probe due to its higher emission intensity. The fluorescence probe and the required phosphoric acid diesters were either purchased from Aldrich or prepared by literature methods.[9] A chloroform solution of the probe was made (1.24 x 10^{-4} M) and diluted to approximately 5.0 x 10^{-8} M. The solution was excited at 260 nm, and emission was recorded between 300 and 500 nm. In separate cuvettes, the fluorescence of the same concentration of probe with varying concentrations of the desired arylphosphoric acid diesters (typically between 5 x 10^{-8} to 2.5 x 10^{-5} M) was measured. The concentration of the diesters were determined by Beer's law analysis. Using the Benesi-Hildebrand method,[10] plots of 1/Δf vs 1/[arylphosphoric acid diester] gave the dimerization constants. Emission was integrated over 345-365 nm, 345-360 nm, 335-400 nm, and 325-390 nm for bis-(4-methylphenyl) phosphoric acid, diphenylphosphoric acid, bis-(4-chlorophenyl)phosphoric acid, and bis-(4-nitrophenyl)phosphoric acid respectively. A typical plot is shown in Figure 1. All the plots were linear, with the exception of the plot for bis-(4-nitrophenyl) phosphoric acid, which was slightly concave. Dimerization constants of the fluorescent probe with bis-(4-methylphenyl) phosphoric acid, diphenylphosphoric acid, bis-(4-chlorophenyl)phosphoric acid, and bis-(4-nitrophenyl)phosphoric acid were determined to be 5.7 x 10^4, 1.3 x 10^5, 2.6 x 10^5, and 8.4 x 10^5 M^{-1} respectively.



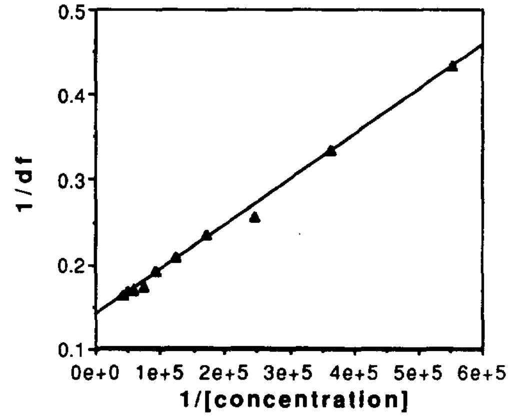


Figure 1: A typical Benesi-Hildebrand Plot. This plot is for bis-(4-chlorophenyl) phosphoric acid with the probe.

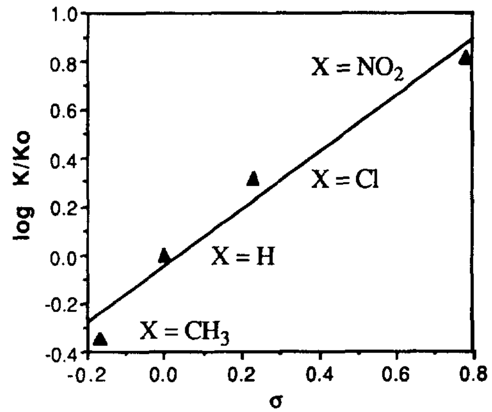


Figure 2: Hammett plot.

Figure 2 shows a Hammett plot of the dimerization constants. The rho value was found to be 1.2, which is larger than that found (0.6) for the dimerization of substituted benzoic acids.[8] The curve, however, is not perfectly linear. We postulate that this is primarily due to an under estimation of the dimerization constant between the fluorescent probe and bis-(4-nitrophenyl) phosphoric acid, which results from a breakdown of the assay. If the dimerization constant between bis-(4-nitrophenyl) phosphoric acid and another of itself is near 10^6 M^{-1}, as with its binding to the probe, then the dimerization constant will be underestimated by our method, and the Benesi-Hildebrand plot will be curved downward as observed.

Since the dimerization constants of phosphoric acid diesters were determined to be exceptionally large, we were prompted to test if the fluorescence assay was just measuring the equilibrium with the corresponding pyrophosphate. Mixing diphenylphosphoric acid with the probe at mM concentrations (conditions for which essentially all the esters would be dimerized or giving pyrophosphate) resulted in no mass spectral evidence of pyrophosphates, but instead resulted in a spectra indicative of the individual phosphodiesters. However, subjecting a known sample of the pyrophosphate (synthesized from chlorodiphenylphosphate and the probe) to the same mass spectral analysis resulted in a strong parent ion peak. Therefore, it was concluded that no pyrophosphate is formed under the conditions of the binding studies.

The dimerization constants reported herein for phosphoric acid diesters are orders of magnitude higher than those for carboxylic acids and pyridine based dimers used in hydrogen bond driven self-assembly. The strong dimerization is likely due in part to the large dipolar nature of the P-O bond of the phosphoric acid, and as we have now shown, is partially a result of the highly acidic nature of this class of compounds. We predict that the strong driving force for recognition between phosphoric acids will be useful in controlling the strenght and nature of self-assembled systems. In addition, the ability to tune dimerization constants via manipulation of substituents should allow subtle control of aggregation state.

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