PYRROLE STUDIES—XX[1]

THE INFLUENCE OF STERIC HINDRANCE UPON THE H-BONDED ASSOCIATION OF PYRROLES WITH PYRIDINES

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Abstract—The association constants for α,α'-dialkylpyrrole:pyridine systems determined from infrared intensity measurements of the NH absorption band of the non-bonded pyrroles indicate that, although the α-substituents sterically hinder the formation of the NH–N bonded complexes, there is little evidence for any significant NH–π bonding.

Pyrrole behaves as a proton donor in the presence of molecules which have centres of high electron density. In general, strong colinear NH–X complexes are formed with electronegative atoms, but autoassociation of pyrrole and the association of pyrrole with other aromatic systems appears to occur through orthogonal NH–π bonds.[2] In contrast with these generalisations, the dipole moment of pyrrole, when measured in the presence of alkyl nitriles, is consistent with NH–π association between the pyrrole and the nitrile group.[3] Similarly, although there is overwhelming evidence that the H-bonded association between pyrrole and pyridine involves a colinear NH–H bond,[4] the dipole moment data for pyrrole, when measured in the presence of 2,4,6-trimethylpyridine, has been interpreted in terms of NH–π bonding.[5,6] Although complexes of this type involving hydrogen bonding with a π-deficient ring would appear to be unfavourable, the postulate has been extended to suggest that pyrrole simultaneously forms both NH–N and NH–π bonded complexes with pyridine and its methyl derivatives.[7] It was of interest, therefore, to examine the infrared spectra of pyrrole and 2,5-dialkyl-pyrroles in the presence of a series of methylpyridines to establish whether steric hindrance promotes the formation of NH–π bonded complexes.

Measurement of the intensity of the non-bonded νNH absorption band for *ca.* 5×10^{-3} M solutions of pyrrole in the presence of 0.1–1.0 M concentrations of pyridine and its 4-methyl-, 2,6-dimethyl- and 2,4,6-trimethyl derivatives provided values for the H-bonded association constants (Table 1), which are in close agreement with those calculated from earlier IR and NMR spectroscopic measurements. However, both the present and the previously recorded association constants obtained from spectroscopic data are consistently lower than those calculated from dipole moment[5–7] and calorimetric measurements.[8] These anomalies probably arise from differences in the concentrations of the pyrrole used in the various analytical techniques. Previous work has shown that the most consistent set of equilibrium constants are obtained when the concentration of the pyrrole is less than 1×10^{-2} M.[9] At higher concentrations autoassociation of the pyrrole is significant and generally introduces errors in the measurement of the equilibrium constants for the formation of complexes between the

pyrrole and proton acceptors. It has also been noted[9] that the measurement of equilibrium constants from IR data becomes inaccurate at concentrations below 1×10^{-3} M, when the bonded and non-bonded νNH absorption bands frequently are not well resolved.

The strength of the NH–N bond of the pyrrole: substituted pyridine complexes, as given by the difference between the frequencies of the bonded and non-bonded νNH absorption bands, is related to the basicity of the pyridines, but the association constants, which correspond to the ease of formation and stability of the complexes, reflect the steric effects of the α-methyl groups on the pyridine rings. This is clearly seen in the correlation of log $K_{assoc.}$ with the pK_a values for the pyridines (Fig. 1). It is apparent that the electron donating character of the 4-methyl substituent, which
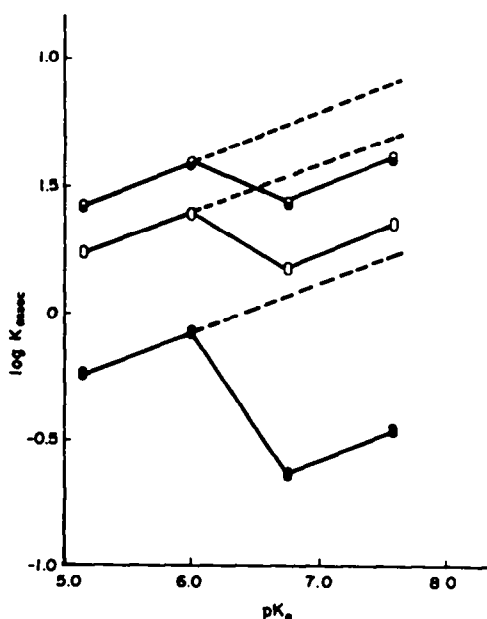

Fig. 1. Correlation of the basicities of pyridine and its 4-, 2,6- and 2,4,6-methylated derivatives with log $K_{assoc.}$ for the formation of complexes with pyrrole (⊖), 2,5-dimethylpyrrole (○) and 2,5-di-*tert*-butylpyrrole (●).

Table 1. Enthalpies and association constants for the formation of H-bonded complexes between pyrrole, 2,5-dimethylpyrrole and 2,5-di-*tert*-butylpyrrole and substituted pyridines

	$K_{assoc.}^{a}$ (1 mol^{-1})	$\Delta\nu NH^{b}$ (cm^{-1})	ΔH^{a} (kJ)
Pyrrole:Pyridine Complexes			
Pyridine	2.65 ± 0.16	290 ± 5	22.5
4-Methylpyridine	3.97 ± 0.23	295 ± 10	22.7
2,6-Dimethylpyridine	2.77 ± 0.13	295 ± 10	22.7
2,4,6-Trimethylpyridine	4.10 ± 0.10	305 ± 10	23.2
2,5-Dimethylpyrrole:Pyridine Complexes			
Pyridine	1.74 ± 0.06	220 ± 10	18.9
4-Methylpyridine	2.49 ± 0.12	235 ± 10	19.6
2,6-Dimethylpyridine	1.52 ± 0.30	240 ± 10	19.9
2,4,6-Trimethylpyridine	2.30 ± 0.30	240 ± 10	19.9
2,5-Di-*tert*-butylpyrrole:Pyridine Complexes			
Pyridine	0.58 ± 0.04	200 ± 5	17.8
4-Methylpyridine	0.84 ± 0.06	205 ± 10	18.1
2,6-Dimethylpyridine	0.23 ± 0.02	210 ± 10	18.3
2,4,6-Trimethylpyridine	0.34 ± 0.02	210 ± 10	18.3

a Measured at 25°C

b $\Delta\nu NH = \nu NH$ (non-bonded) $- \nu NH$ (H-bonded)

c Calculated from $-\Delta H(kJ) = 0.0515 \times \Delta\nu NH + 7.53$ See ref. 8.

increases the basicity of the pyridine without introducing any steric hindrance to the formation of the H-bonded complexes, has an effect of increasing log K_{assoc} by *ca.* 0.16, irrespective of the pyrrole involved in the association complex. In contrast, extrapolation of the data for the pyrrole:pyridine system shows that, although α-methyl substituents on the pyridine ring increases the basicity of the pyridine nitrogen atom, steric hindrance to the formation of the complex decreases log K_{assoc} by *ca.* 0.29 from the expected value. Similarly, comparison of the data for the pyrrole:pyridine and 2,5-dimethylpyrrole:pyridine systems shows that the 2,5-dimethyl groups lower the value of log K_{assoc} by only *ca.* 0.19. This difference in the steric effects of the α-methyl substituents on the pyridine and pyrrole rings is readily rationalised in terms of the geometry of the two rings. The steric effects appear to be additive, within experimental error. Thus, the calculated effect of the steric hindrance to the complex formation of 2,5-dimethylpyrrole with 2,6-dimethylpyridines would be a decrease in log K_{assoc} of *ca.* 0.48 from the value derived from the extrapolation of the correlation of the basicity of the pyridines with the values of log K_{assoc} for systems in which no steric hindrance is present. The observed effect was a decrease of 0.55 ± 0.07 in the value of log K_{assoc}.

Predictably, the steric effect of the α-*tert*-butyl groups on the pyrrole ring upon the formation of the association complexes with the pyridines was considerably greater than that of the α-methyl groups. Comparison of the data for the pyrrole:pyridine and 2,5-di-*tert*-butylpyrrole:pyridine systems indicate that the steric effect of the *tert*-butyl groups reduces the log K_{assoc} by *ca.* 0.66.

The general similarity of the steric effects for the three systems, as illustrated in the figure, suggests that the form of the H-bonded complexes between each of the three pyrroles with the pyridines is similar and, on the reasonable assumption that, in the absence of any steric hindrance, the pyrrole:pyridine complex essentially involves NH–N bonding, there appears to be little evidence that NH–π bonding is important in the formation of the complexes. The calculated additive effect of the steric hindrance between α-*tert*-butyl groups on the pyrrole ring and α-methyl groups on the pyridine ring, Δ log K_{assoc} = −0.95, lies outside the experimental error of the observed decrease of 1.35 ± 0.02, derived from the extrapolated graph. However, the observed steric effect of the *tert*-butyl groups is more consistent with the predominant formation of NH–N bonded complexes than with NH–π complex formation. This postulate is supported by the νNH frequency shift data. In each of the three systems, the frequency shift for the NH stretching vibration upon the formation of the association complex increases linearly with the increase in the basicity of the pyridines and, although the strength of the NH–N bond was weaker for the 2,5-di-*tert*-butylpyrrole

complexes, the frequency difference between the bonded and non-bonded νNH absorption bands was always considerably greater than that for systems which are known to involve only NH–π bonding (30–100 cm^{-1}).

EXPERIMENTAL

Commercial samples of pyrrole, pyridine, 4-methylpyridine, 2,6-dimethylpyridine and 2,4,6-trimethylpyridine were dried by standard procedures and distilled immediately before use. 2,5-Dimethylpyrrole was prepared by the method described in the lit.[10] and had b.p. 54–57°/10 mm (lit.[10] 51–53°/8 mm).

2,5-Di-tert-butylpyrrole. 1-Bromo-3,3-dimethylbutan-2-one[11] (2.2 g) and triphenylphosphine (3.6 g) in benzene (100 ml) was allowed to stand at room temperature for 3 days. The crude phosphonium salt (3.6 g, 54%) was collected, washed with benzene (2 × 10 ml), and dissolved in water (200 ml). Aqueous Na$_2$CO$_3$ (10%) was added until the pH of the solution was ca. 8.0 and the precipitated phosphorane was collected, washed with water (2 × 25 ml), and recrystallised from aqueous ethanol to give (2,2-dimethylpropionyl)methylenetriphenylphosphorane, (1.65 g, 57%) m.p. 183–185° (Found: C, 78.9; H, 6.5. C$_{24}$H$_{25}$OP requires: C, 80.0; H, 6.9%). The phosphorane (2.7 g) and 3,3-dimethylbutan-1,2-dione (0.89 g) in benzene (20 ml) were heated under reflux for 10 h. The solvent was removed under reduced pressure and the crude product extracted with diethyl ether (3 × 20 ml). Evaporation of the ether extracts gave a solid, which was recrystallised from ethanol to give 2,2,7,7-tetramethyloct-4-en-3,6-dione (1.09 g, 73.5%), m.p. 110° (lit.[12] m.p. 111°). Reduction of the octenedione with zinc dust in acetic acid[12] gave 2,2,7,7-tetramethyloctan-3,6-dione (79%) b.p. 116–117°/5 mm (lit.[12] b.p. 106–107°/10 mm), which on being heated with ammonium acetate in glacial acetic acid gave 2,5-di-tert-butylpyrrole (60%), m.p. 31.5–32.5° (lit.[13] m.p. 32–33°).

Physical measurements

The intensities of the non-bonded νNH absorption band were measured for ca. 5 × 10^{-3} M solutions of the pyrroles in CCl$_4$ in the presence of the appropriate pyridines (0.1–2.0 M) using matched 3 mm NaCl cells and a Perkin–Elmer 125 infrared spectrometer. Precalibration of the cells showed a linear correlation of the concentration of the pyrroles over a range 10^{-4} to 5 × 10^{-3} M with the apparent intensity (peak height) of the νNH absorption band.

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