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Studies on the Proton Magnetic Resonance Spectra of Aromatic Systems. XXI.[1] Discussions on Stoichiometry, Equilibrium and Infinite Concentration Shift of Pyridine Base-Tris(dipivalomethanato)europium Eu(DPM)$_3$ Complex in Solution

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The 1: 1 complex formations between pyridine bases and Eu(DPM)$_3$ are approved at equimolar, excess base and excess Eu(DPM)$_3$ conditions. The equilibrium constants and complex shifts are estimated by the graphic and simulation methods of the observed results of the above three conditions.

The complex shifts thus obtained showed good correspondence with infinite concentration shifts and the so-called *S* values. The equilibrium constants are solvent dependent, whereas the complex shifts are not.

Keywords——shift reagent; complex formation; equilibrium constant; complex shift; infinite concentration shift; *S* value; nuclear magnetic resonance; lanthanaide induced shift; pyridine base

In the previous report,[1] complex formation of the pyridine bases with the shift reagent and chemical meaning of the induced paramagnetic shift parameter-S value-have been studied under the large excess of pyridine bases.

In this work, the stoichiometry of above complex formation was investigated by the measurement of nuclear magnetic resonance (NMR) and fluorescence spectra of equimolar, excess base and excess reagent mixtures, and the complex shifts as well as equilibrium constants were estimated by graphic and simulation methods. The 1: 1 complex formation was approved for the three cases. In addition, so-called infinite concentration shifts were estimated from the linear relations between successive dilution shifts and $C^{-2/3}$ of equimolar solutions—C represents the molarity of the solute—and approved to be the complex shifts.

Experimental

Pyridine bases used in this work were of the J.I.S. grade. They were dried over Linde molecular sieves 4A for some days before use. The shift reagent Eu(DPM)$_3$ purchased from Dojin Chemical Laboratories was sublimed under reduced pressure and stored over silica gel in a desiccator. Sample preparation was carried out in an air-conditioned room. All NMR spectra were taken on a Hitachi R-22 type high resolution NMR spectrometer with an external lock mode at 90 MHz. NMR measurements under elevated temperatures were achieved using a variable temperature equipment. Line positions were measured relative to an internal Me_4Si reference using a frequency counter with an error of ± 1.0 Hz.

Results and Discussion

The results are illustrated in Fig. 1—8.

1) Part XX: Y. Sasaki, H. Kawaki, and Y. Okazaki, *Chem. Pharm. Bull.* (Tokyo), **23**, 1905 (1975).
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Continuous Variations and Molar Ratio Methods

Both continuous variation and molar ratio methods of the NMR and fluorescence spectra clearly showed the formation of 1:1 complex between the pyridine base and shift reagent.

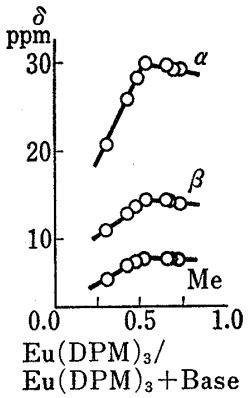

Fig. 1. Continuous Variation Method of 4-Picoline and $Eu(DPM)_3$ at 70° in CCl_4

Total concentration, 0.3 M.

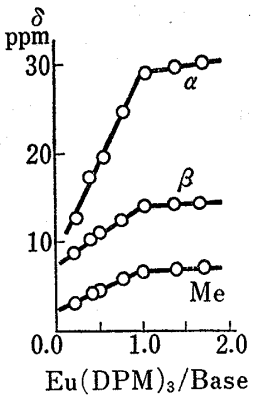

Fig. 2. Molar Ratio Method of 3-Picoline and $Eu(DPM)_3$ at 70° in CCl_4

Base concentration, 0.15 M.

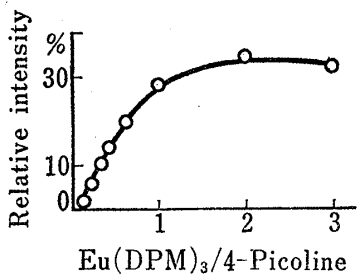

Fig. 3. Molar Ratio Method of 4-Picoline and $Eu(DPM)_3$ at Room Temperature in CCl_4 by Fluorescence Spectrometry

$Eu(DPM)_3$ concentration, 3×10^{-3} M.

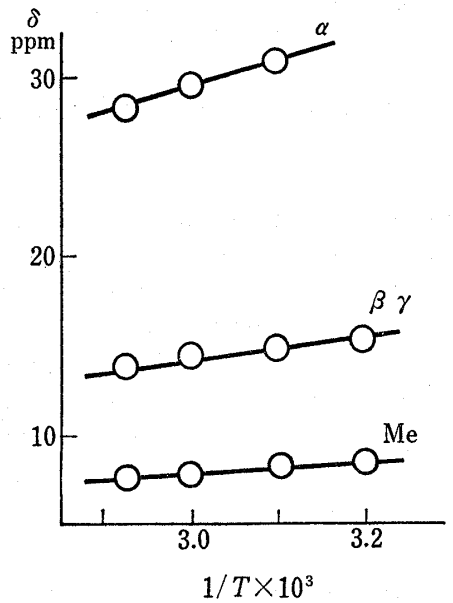

Fig. 4. Variable Temperature Experiment of 4-Picoline in CCl_4

$Eu(DPM)_3$ concentration, 0.16 M.
Base concentration, 0.15 M.

(Fig. 1—3) The formation of a 1:2 complex, which may be expected in a large excess of the base could not be realized in these experiments.

Variable Temperature Experiment

Chemical shifts of the equimolar mixtures showed linear dependence on $1/T$ (*ca.* Fig. 4), and the inflections were unobserved at equimolar points in all measurement temperatures.

Determination of the Complex Shifts and Equilibrium Constants

As a 1:1 complex formation was approved in above experiments, we next examined to interpret the concentration dependence of shifts on the basis of 1:1 complex formation under a few experimental conditions.

I. Equimolar Mixtures——For a 1:1 complex formation of Eq. 1,

$$A + D \rightleftarrows AD \qquad (1)$$

where A represents acceptor and D donor, equilibrium constant K_c is given by Eq. 2,

$$K_c = \frac{C_{AD}}{(C_A^\circ - C_{AD})(C_D^\circ - C_{AD})} \qquad (2)$$

where C_A°, C_D° and C_{AD} represent initial concentration of the acceptor and donor and equilibrium concentration of the complex, respectively. The activity coefficient of each species is assumed to be 1. Chemical shifts of the fast exchanging system can be calculated by the weighted means of the shifts of free and complexed species, and thus Eq. 3 holds for donor molecule.

$$\delta_{calc} = \frac{(C_D^\circ - C_{AD})}{C_D^\circ}\delta_D + \frac{C_{AD}}{C_D^\circ}\delta_{AD} \quad (3)$$

This equation is readily transformed to Eq. 4, where δ_{calc}-δ_D and δ_{AD}-δ_D are substituted by Δ and Δ_c, respectively.

$$\Delta/C_D^\circ = K_c\Delta_c(C_A^\circ/C_D^\circ) - K_c(1+C_A^\circ/C_D^\circ) + (\Delta^2/\Delta_c)K_c \quad (4)$$

Under the condition of $C_D^\circ = C_A^\circ$, Eq. 4 leads to Eq. 5.

$$\Delta/C_D^\circ - (\Delta^2/\Delta_c)K_c = -2K_c\Delta + K_c\Delta_c \quad (5)$$

Eq. 5 shows that the linear relation may be observable between Δ/C_D° and Δ, and K_c and Δ_c are determined from its slope and intercept, when the second term of the left-hand side is negligible. However, it was found that K_c and Δ_c thus obtained sometimes gave non-negligible values of $(\Delta^2/\Delta_c)\,K_c$. We therefore employed the iterative method, where new K_c and Δ_c values were obtained from the linear relation of Eq. 5 including the term $(\Delta^2/\Delta_c)\,K_c$ calculated from the initial values of K_c and Δ_c. Iteration was performed adopting the linear least squares method until the initial and the new values coincide so well that the agreement factor R expressed as followings becomes smaller than 0.05.

$$R = \left\{\frac{\sum_i(\Delta_{obs,i} - \Delta_{calc,i})^2}{\sum_i(\Delta_{obs,i})^2}\right\}^{1/2}$$

The two parameters thus obtained (*cf.* Table I) reproduced satisfactorily the observed shifts as shown in Fig. 5. These results approve the 1:1 complex formation of equimolar mixtures.

Table I. Complex Shifts Δ_c (ppm) and Equilibrium Constants K_c (M^{-1}) estimated from Graphic Method of Equimolar Mixtures at 38° in CCl_4

	Δ_c (ppm)[a]				K_c (M^{-1})
	α	β	γ	Me	
Pyridine	25.8	8.9	8.5		1291±164
2-Picoline	10.0	7.7	7.0	23.1	345±217
3-Picoline	28.1	9.3	9.1	6.0	3223±504
4-Picoline	27.6	9.5		7.0	2390±127
3,5-Lutidine	24.9		8.3	5.4	2737±196

a) Error being within ±5%.

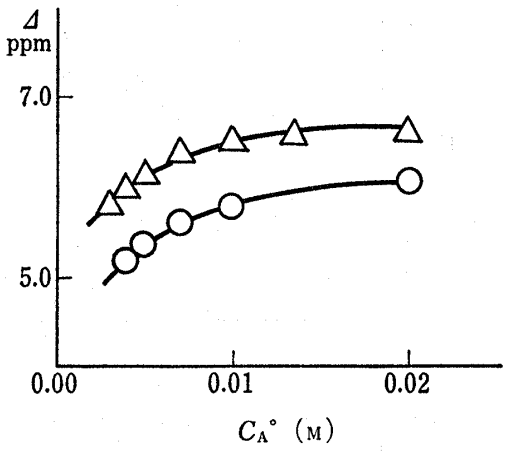

Fig. 5. Comparison between Δ_{calc} and Δ_{obs} of Me Groups of 4-Picoline at 38° in CCl_4

——: calculated curves; ○, △, experimental points of $c_A^\circ/c_D^\circ = 1$ and $c_A^\circ/c_D^\circ = 3$.

The data summarized in Table I suggest that while methyl substitution in pyridine increases K_c, methyl substituion at α-posision of nitrogen decreases K_c due to the steric hindrance of methyl group. Furthermore, as summarized in Table II, K_c's are solvent dependent, but Δ_c's are not. These results suggest that in the complex formation in this work the solvent molecule does not intervene between donor and acceptor molecule.

II. Mixtures with Excess Donor——When $C_D^\circ \gg C_A^\circ$ holds, Eq. 2 is transformed to Eq. 6, neglecting the term C_{AD}^2.

$$C_D^\circ = C_A^\circ\Delta_c(1/\Delta) - (1/K_c + C_A^\circ) \quad (6)$$

Table II. Complex Shifts Δ_c (ppm) and Equilibrium Constants K_c (M^{-1}) estimated from Dilution Method of Equimolar and Excess Acceptor Mixtures at 38°

		CCl_4		Cyclohexane		$CH_2Cl_2(CD_2Cl_2)$		$CDCl_3$	
		Δ_c(ppm)[a]	$K_c(M^{-1})$[b]	Δ_c(ppm)[a]	$K_c(M^{-1})$[b]	Δ_c(ppm)[a]	$K_c(M^{-1})$[b]	Δ_c(ppm)[a]	$K_c(M^{-1})$[b]
2-Picoline	I	23.1	345	21.6	558	28.9	76	30.7	31
	II			21.3	663			32.6	34
3-Picoline	I	6.0	3223	5.0	2523			6.2	194
	II	5.7	3063	5.5	2828	5.4	1359		
4-Picoline	I	7.0	2390	7.1	2865			7.9	196
	II	6.8	2521	6.6	3916	6.9	1015	7.7	252
3,5-Lutidine	I	5.4	2737	5.7	3536			5.7	209
	II	5.5	3656			5.4	1877	6.2	396

I) Graphic method of equimolar mixtures; $C_D^\circ = C_A^\circ = 0.002$—$0.02$ M.
II) Simulation method of excess acceptor mixtures; $C_D^\circ = 0.001$—0.007 M, $C_A^\circ = 0.002$—0.02 M.
a) Complex shifts of Me groups. Error being within ±5%.
b) Equilibrium constants estimated from Me groups. Error being within ±10%.

Armitage, *et al.*[3] employed Eq. 6 to determine K_c and Δ_c, however, this equation was proved ineffective, since contribution of the term $1/K_c$ becomes negligible when K_c is much larger than $1/C_D^\circ$. In fact, although plots of C_D° *vs.* $1/\Delta$ resulted in a linear relation as expected from Eq. 6, the intercept was too close to zero to obtain the reliable value of $(1/K_c + C_A^\circ)$. K_c's and Δ_c's in this experimental conditions are considered comparable to those in I, because the observed shifts are well reproduced by Eq. 3 using K_c and Δ_c derived from equimolar mixtures (*cf.* Table I). The S values derived from linear relations in Fig. 2 are correlated with Δ_c as follows, and thus S values may be accepted as the 1:1 complex shifts Δ_c in CCl_4.

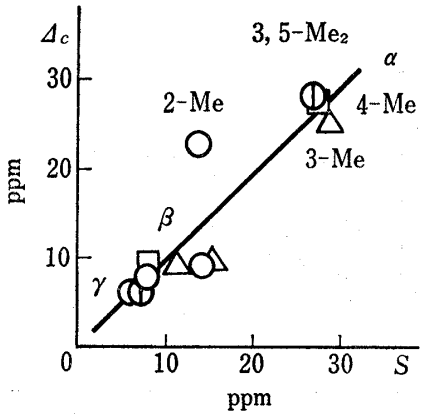

Fig. 6. Correlations between Complex Shifts Δ_c and Paramagnetic Shift Parameters S

S: shift parameter obtained at Eu(DPM)$_3$/Substrate$\lesssim$0.02.
Substrate concentration, 0.2 M.

$$\Delta_c = 0.96S + 0.45 \qquad (7)$$

III. Mixtures with Excess Acceptor——Dilution experiments with mixtures of excess acceptor resulted in a similar concentration dependence to those with equimolar mixtures (*cf.* Fig. 5). For the present case Eq. 5 or 6 is not applicable any more, but δ_{calc} is expressed as a function of K_c and Δ_c (*cf.* Eq. 8). We employed a simulation method to obtain K_c and Δ_c; these were determined so as to give the best fit between δ_{calc}'s and δ_{obs}'s.[4]

$$\delta_{calc} = \delta_D + \frac{\{K_c(C_A^\circ + C_D^\circ) + 1\} \pm \sqrt{\{K_c(C_A^\circ + C_D^\circ) + 1\}^2 - 4K_c^2 C_A^\circ C_D^\circ}}{2K_c C_D^\circ} (\delta_{AD} - \delta_D) \qquad (8)$$

The values thus derived are comparable to those of equimolar mixtures (*cf.* Table II) and the 1:1 complex formation is confirmed.

3) I. Armitage, G. Dunsmore, L.D. Hall, and A.G. Marshall, *Can. J. Chem.*, **50**, 2119 (1972).
4) Root mean square deviations were minimized with NEAC 2200 Model 500 computer at Osaka University Computer Center utilizing a library program DAVID. For equimolar mixtures, both simulation and graphic methods gave consistent results.

Concentration Dependence of the Shifts in Successive Dilution Experiments

Plots of the dilution shifts *vs.* $(C_D^\circ)^{-2/3}$ result in good linear lines, (*cf.* Fig. 7), and Eq. 9 is deduced;

$$\ln\Delta = -B(C_D^\circ)^{-2/3} + \ln\Delta_{ic} \quad (9)$$

where B and ln Δ_{ic} are the slope and intercept. Δ_{ic}'s can be regarded as the shifts of infinitely concentrated mixtures, and they are correlated with Δ_c by Eq. 10 in CCl_4, cyclohexane, $CDCl_3$ and $CH_2Cl_2(CD_2Cl_2)$. (Fig. 8)

$$\Delta_c = 1.16\Delta_{ic} + 0.44 \quad (10)$$

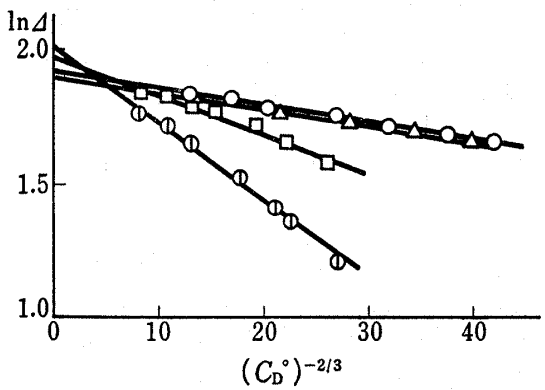

Fig. 7. Correlations between Dilution Shifts of Me Groups of 4-Picoline and $(C_D^\circ)^{-2/3}$

$C_A^\circ = C_D^\circ = 0.002$—$0.02$ M.
Solvent: ○; cyclohexane, △; CCl_4, □; CD_2Cl_2, ⊕; $CDCl_3$.

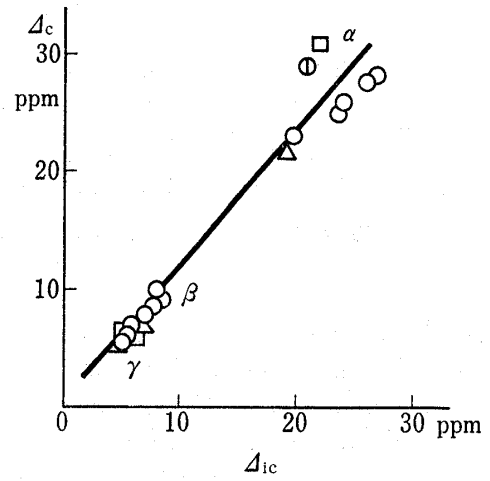

Fig. 8. Correlations between Complex Shifts Δ_c and Δ_{ic}

Solvent: ○; CCl_4, △; cyclohexane, □; $CDCl_3$, ⊕; $CH_2Cl_2(CD_2Cl_2)$.

The term $(C_D^\circ)^{-2/3}$ means the $V^{2/3}$, where V represents the volume of collision complex in solution, and $V^{2/3}$ means the surface area of spherical complex.[5] Eq. 10 therefore implies that this type of interaction is interpreted by the spherical model, which also supports the reciprocal relation between induced shift and r^{-2},[6] where r represents the distance between Eu^{3+} and H of the ligand.

5) *a*) L.D. Landau and E.M. Lifshitz, *Statistical Physics*, Chapter 1, Pergamon, New York (1958); *b*) F.W. Sears and G.L. Salinger, *Thermodynamic, Kinetic Theory*, and *Statistical Thermodynamics*, Chapter 10, Addison-Wesley, Mass. (1975).
6) A.F. Cockerill and D.M. Rackham, *Tetrahedron Lett.*, **1970**, 5149.