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The Correlation of Basicity and Equilibrium Constants Evaluated from Lanthanoid-induced Shifts in the Eu(fod)$_3$-*p*-Substituted Aniline Systems

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An approximate linear correlation has been found between the basicity of substrate (pK_a) and the logarithm of the equilibrium constant K_1 for 1 : 1 adducts evaluated from the least squares analysis of lanthanoid-induced shifts (LIS) for the systems containing Eu(fod)$_3$ and a series of *p*-substituted anilines in CDCl$_3$. In contrast, both the observed *S*-values and intrinsic shifts have shown no simple correlation to pK_a's of substrates.

The equilibrium constants (K) and chemical stoichiometry for several systems containing shifts reagents (LSR) and substrates (S) in solution have quantitatively been investigated by several workers in terms of the least-squares analysis of lanthanoid-induced shifts (LIS).[1-9] The orders of magnitude of K have, though roughly, been estimated for several functional groups as a coordination site. The validity of these estimates of K values has been checked solely by the degree of fits of the LIS data to the equilibrium system and by the magnitude of the free energy change, ΔG. Indeed, it has generally been confirmed that such a fit to each envelope of proton data in a substrate molecule is satisfactory (measured in terms of the standard deviation, σ). However the variation in K-values with the position in a molecule is relatively large. It has not been investigated which of some possible origins of errors is directly related to this variation in K.

From the characteristics of LSR as a Lewis acid it is reasonable to expect that the K-values should be correlated to the basicity of the substrate, the degree of steric hindrance on complexation, and the nature of the solvent, *e.g.*, the dielectric constant. It has recently been found in our laboratory that there is a qualitative correspondence between K and the degree of steric hindrance on complexing to LSR for the Eu(fod)$_3$–alkylaniline system in CCl$_4$.[6]

This paper will report on the relation of K to the basicity of the substrate for a selected series of *p*-substituted anilines with similar steric effects and various pK_a's with Eu(fod)$_3$ in CDCl$_3$.

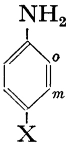
Experimental

Eu(fod)$_3$ dried over P_2O_5 in a vaccum desiccator was used immediately after sublimation. CDCl$_3$ as the solvent and liquid amine samples were dried over molecular sieves in the dark, the solid samples being recrystallized. The sample solutions were prepared by the so-called "S_0-incremental dilution method,"[1] with a constant concentration of substrate (S_0), 0.2 M. The maximum ratio, $[L_0]/[S_0]$ (ρ), was 2.4 to 3.4, where $[L_0]$ is the total concentration of Eu(fod)$_3$, the number of data points, 23 to 28. NMR spectra were recorded on a Hitachi R-20A at 60 MHz at 34 °C in the frequency-swept mode, using TMS as an internal standard. The program used for the fitting analysis was LISA[5] developed by Shapiro *et al.* and partially modified in this laboratory. All computations were made on HITAC 8800/8700 computers at The University of Tokyo.

Results and Discussion

The systems consisting of aniline and Ln(fod)$_3$ in CDCl$_3$ at room temperature fullfil "the condition of fast substrate exchange" for the measurement of NMR shifts,[6,11,12] as well as those studied in most literatures. It has been found for most substrates with Ln(fod)$_3$ that the highest complex present in solution is LS_2 for very small values of ρ.[1,3-9] Consequently, the equilibria to be considered are 1) $L+S \rightleftharpoons LS \cdots K_1$, 2) $LS+S \rightleftharpoons LS_2 \cdots K_2$, and 3) $L+2S \rightleftharpoons LS_2 \cdots K_3$. Eq. 3 may be neglected because its formation constant is expected to be much smaller than for the others. The formation of L_2 dimer ($L+L \rightleftharpoons L_2 \cdots K_L$ (4)) has been considered in the literature through vapor phase osmometric measurements.[13] The introduction of this effect to the fitting analysis of LIS gave poorer fits for several substrates in solution.[4,5] This suggests that K_L has a very small value, even if the dimerization reaction were considered. Thus, in the present analysis for each substrate, the attempts were made for fitting the LIS data to the four equilibrium systems; (a) only (1), (b) (1)+(4), (c) (1)+(2), and (d) (1)+(2)+(4). For the two step equilibrium (c), the appropriate ranges of K_1 and K_2 were first estimated on the basis of the K-values[6] already obtained for analogous substrates. The respective Q-values ($Q=\sum_i^N(\delta_{\mathrm{exp},i}-\delta_{\mathrm{calcd},i})^2$, where the δ-values represent the LIS's and N the number of data points) for *o*- and *m*-proton data, Q_o and Q_m, were calculated by the introduction of a set of K_1 and K_2 values common to the two data series. The Q_{av}-value was evaluated as the

TABLE 1. SUBSTRATES AND pK_a[a)]-VALUES

		Compound	pK_a[a)]
	1	X=CH_3	4.90
	2	F	4.48
	**3**	C_6H_5	4.22
	4	Cl	3.83
	5	Br	3.73
	6	I	3.65
	7	CN	1.75
	8	NO_2	0.93
	9	OCH_3	5.16
	10	$COOCH(CH_3)_2$	2.49
	11	$COCH_3$	2.20

a) Taken from Ref. 10.

TABLE 2. FQUILIBRIUM CONSTANTS AND INTRINSIC SHIFTS[a)]

Coupound		δ_1[b)]	δ_2[b)]	K_1	K_2	$Q_{av,min}(\sigma)$[c)]
1	*o*-H	-10.00 ± 0.21	-7.07 ± 0.05	212 ± 30.5	13 ± 12.7	1.03×10^{-2} (0.021)
	m-H	-2.38 ± 0.16	-1.54 ± 0.08			
2	*o*-H	-13.89 ± 0.21	-8.91 ± 0.11	228 ± 100.0	55 ± 14.5	8.00×10^{-3} (0.018)
	m-H	-2.89 ± 0.03	-1.91 ± 0.03			
3	*o*-H	-10.73 ± 0.19	-7.03 ± 0.09	153 ± 29.9	26 ± 14.1	9.20×10^{-3} (0.019)
	m-H	-2.56 ± 0.08	-1.22 ± 0.06			
4	*o*-H	-10.60 ± 1.27	-6.59 ± 0.36	69 ± 7.4	20 ± 27.6	4.50×10^{-2} (0.046)
	m-H	-2.17 ± 0.23	-1.52 ± 0.10			
5	*o*-H	-9.91 ± 0.13	-5.67 ± 0.82	91 ± 33.9	15 ± 6.4	3.27×10^{-1} (0.128)
	m-H	-2.07 ± 0.03	-1.27 ± 0.21			
6	*o*-H	-13.60 ± 0.35	-5.51 ± 0.04	84 ± 4.0	193 ± 61.6	7.50×10^{-2} (0.061)
	m-H	-2.84 ± 0.66	$-1.25\pm0.00_7$			
7[e)]	*o*-H	-11.30 ± 0.14	-3.93 ± 0.14	14.8 ± 1.14	2.6 ± 0.14	2.42×10^{-2} (0.032)
	m-H	-6.93 ± 0.88	-2.65 ± 0.10			
	o-H	-11.90 ± 0.16		11.2 ± 0.76	0.7 ± 0.07[d)]	2.83×10^{-2} (0.035)
	m-H	-7.37 ± 0.12				
8	*o*-H	-11.47 ± 2.39		3.0 ± 0.57	23.0 ± 5.7[d)]	2.60×10^{-3} (0.011)
	m-H	-8.98 ± 1.85				

a) The values of K_1, K_2, δ_1 and δ_2 are those corresponding to $Q_{av,min}$. The standard deviations given in parentheses were evaluated on the basis of each pair of parameters corresponding to $Q_{o,min}$ and $Q_{m,min}$. b) Measured in ppm. Negative signs designate shifts to lower field. c) See text for $Q_{av,min}$. σ is the standard deviation for the fitting analysis, $\sqrt{Q_{av,min}/N}$, where N is the number of date points. d) K_L-values. e) Two sets of parameters obtained by the fitting analyses to both the equilibrium systems are listed. See text.

average which was weighted for the respective δ_1-values corresponding to Q_o and Q_m, where δ_1 is the intrinsic shift for the 1 : 1 complex (LS). The minimum value of Q_{av}, $Q_{av,min}$, was found from the Q_{av}-map in the range of K_1 and K_2 selected above. In the equilibrium system (d), after the introduction of the appropriate value ($0.01\leq K_L\leq50$) into K_L, the above procedure was conducted. For the one step mechanisms, (a) and (b), the Q_{av}-map for K_1 and K_L was prepared, where K_L was assumed to be zero for (a).

For compounds **1** to **6**, the best results were obtained from the analysis using (c), satisfactorily small values being observed for $Q_{av,min}$. Thus, the set of K_1 and K_2 values which gives the $Q_{av,min}$ value, is a reasonable one, and the values are shown in Table 2 together with the $Q_{av,min}$ values. Simultaneously, the $Q_{o,min}$ and $Q_{m,min}$ for the *o*- and *m*-proton data were independently determined from the Q_o and Q_m maps, respectively. The values of Q_{min} were satisfactorily small except for the *o*-proton data of **5**. The standard deviations for each of the values of K_1 and K_2 decided above were evaluated from the respective K_1 and K_2 values corresponding to $Q_{o,min}$ and $Q_{m,min}$ (Table 2). Representative examples of the analysis and Q-map's are shown in Figs. 1 and 2 for the two step equilibrium, respectively. The values of K vary widely from the *o*- to the *m*-system, especially for the K_2-values as presumed. It is, however, difficult to determine the error responsible for this variation and some explanations will be given later.

The optimum values for the intrinsic shifts, δ_1 and δ_2, were obtained from the set of K_1 and K_2 values which gave $Q_{av,min}$, and each standard deviation was calculated on the basis of the δ_1 and δ_2 values corresponding to $Q_{o,min}$ and $Q_{m,min}$, as the case of K. As may be seen from Table 2, the values of the intrinsic shift do not vary so widely as the K-values, since they are not so

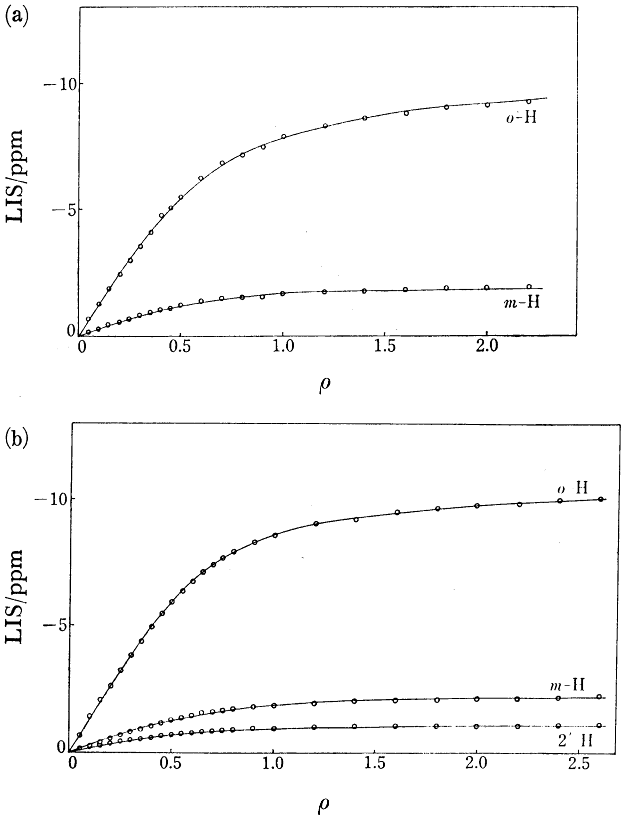


Fig. 1. Results of theoretical fits of the observed $Eu(fod)_3$-induced shifts to the two step mechanism for (a) *p*-chloroaniline and (b) 4-aminobiphenyl.
○: The observed data.

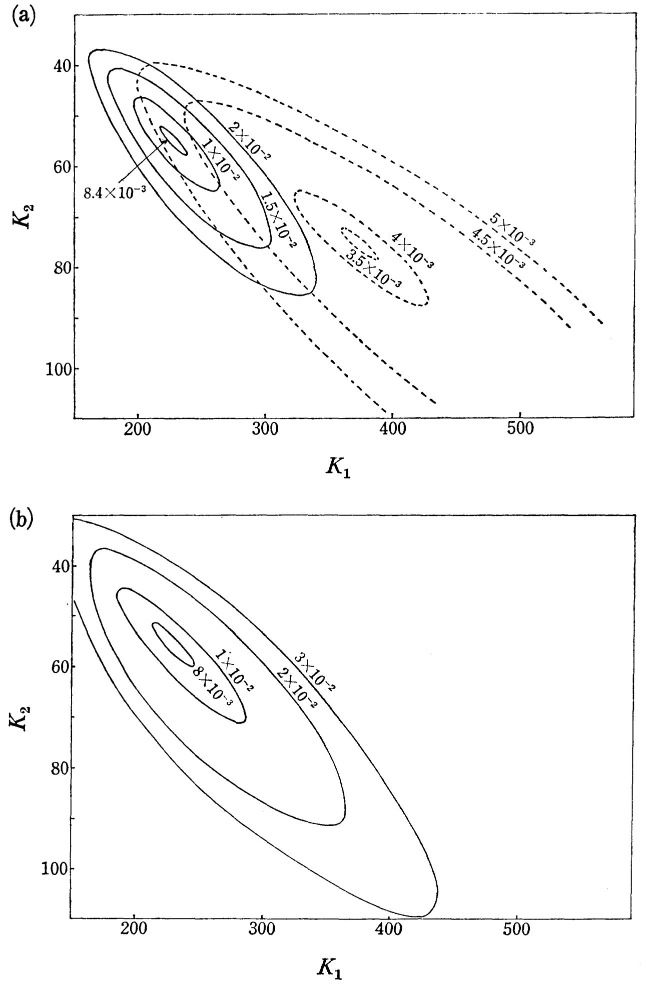


Fig. 2. Contour plots of Q calculated by fitting the LIS's to the equilibrium system, $L+S \rightleftarrows LS$ and $LS+S \rightleftarrows LS_2$, for the *p*-fluoroaniline–Eu(fod)$_3$ system in CDCl$_3$ at 34 °C. a) The results calculated independently for *o*- and *m*-proton data. Solid and broken lines denote Q_o and Q_m, respectively. b) The average of Q_o and Q_m, Q_{av}.

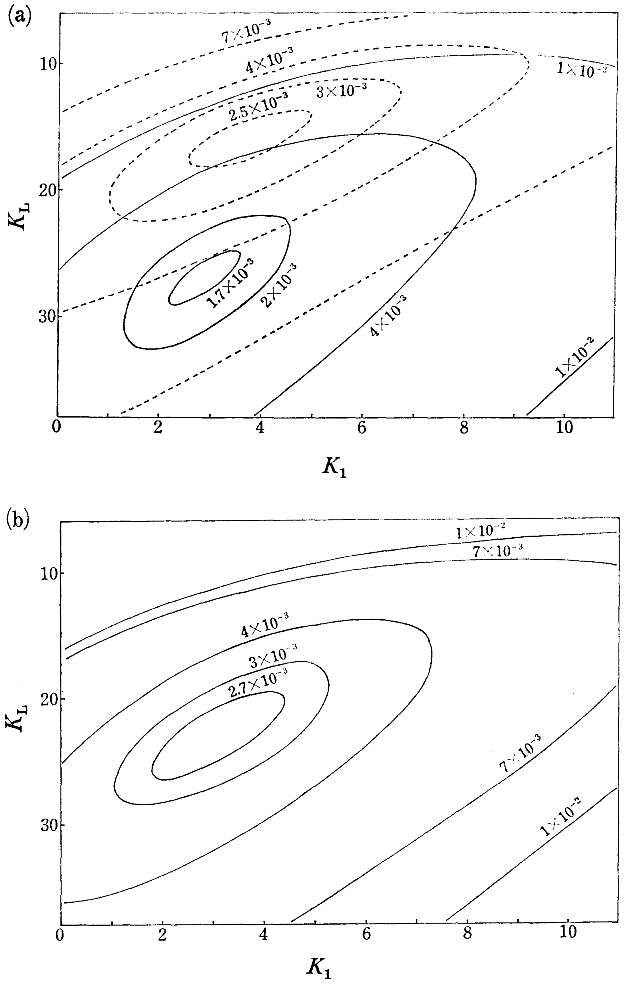


Fig. 3. Contour plots of Q calculated by fitting the LIS's to the equilibrium system, $L+S \rightleftarrows LS$ and $L+L \rightleftarrows L_2$, for the *p*-nitroaniline–Eu(fod)$_3$ system in CDCl$_3$ at 34 °C. a) Solid and broken lines denote Q_o and Q_m, respectively. b) Q_{av}.

sensitive to small variations in Q near Q_{min} as the *K*-value.

For **8**, while the data did not fit well (c), the considerably small value of $Q_{av,min}$ was observed solely by the application of (b) to the analysis of data; the Q-map's are shown in Fig. 3. Attempts to fit the data for **7** to both (b) and (c) resulted in similar small magnitudes of $Q_{av,min}$, and further small variation in values of K, δ_1 and δ_2. It is difficult to select the equilibrium system for the determination of K_1, and however, (b) appears preferable to (c), from the view point of the linearity of log K_1 *vs.* pK_a (Fig. 4). The considerably small or zero values of K_2 obtained for compounds **7** and **8**, appear consistent with the fact that these pK_a values are smaller than for **1** to **6**. Furthermore, it is very plausible from the view point of the competing effect of coordination that only the data for the compound **8** having the smallest pK_a value can be well explained in terms of the addition of the effect of self-association of Eu(fod)$_3$ in solution. In Fig. 4, log K_1 is plotted *vs.* pK_a, where the approximately linear relationship is valid from the nature of the Lewis acid of Eu(fod)$_3$. This is supported by the larger shifts observed for methoxy protons than those expected from the adduct formed by coordination through the N-lone pair. For **10** and **11**, the fits of data to (a) were relatively good for the envelope of *m*-proton shifts ($Q \approx 0.01$), but very poor for the *o*-proton shifts. These two substrates did not lead to a clear minimum of Q from the fitting analysis to any other equilibrium systems. This may be due also to the expected effect of coordination of the X-group to the Eu(fod)$_3$. For this type of bifunctional substrate, an additional coordination state, Eu···X-ϕ-NH$_2$ needs to be taken into account in the equilibrium system.[14] However, the number of parameters determined by least squares analysis becomes considerably greater. Even if more parameters could be evaluated, the results would have no physical significance.

The possible sources of scatter in data in Fig. 4 may be attributed to the following facts; (1) the steric accessibility of the substrate to Eu(fod)$_3$ may be affected by X, (2) the substrate molecule in the present system may be under somewhat different condition from that under which the pK_a-value was measured in Ref. 10, (3) the effect of the coordination effect of X to Eu(fod)$_3$

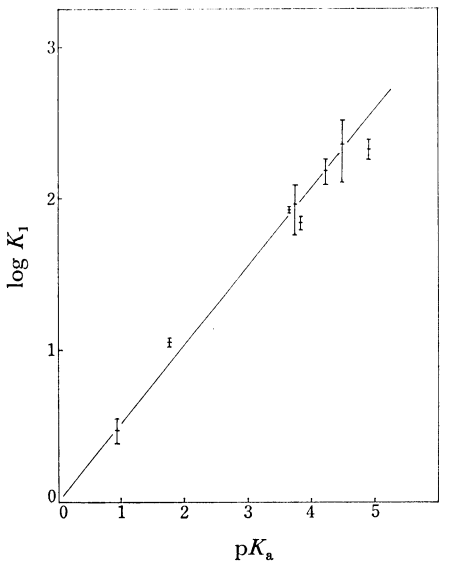


Fig. 4. The logarithms of the equilibrium constants for 1: 1 adducts (K_1) formed between $Eu(fod)_3$ and *p*-substituted anilines in $CDCl_3$ at 34 °C, *vs.* pK_a-values. The range of each data point corresponds to its standard deviation.

on the observed shifts is not taken into account for all the groups, and (4) a small error may be inherent in the measurement of the concentration of substrate or shift reagent.

The weighting average of K_1, 667, obtained for aniline (pK_a=4.46) with $Eu(fod)_3$ in $CDCl_3$ is very large in the tendency of variation of K_1 in Fig. 4. It may be thought that aniline is not subject to the steric hindrance anticipated for *p*-substituted anilines.[16] However, such a large magnitude of K_1 may not be ascribed solely to this effect. From Table 2, no correlation may be seen between the K_2 and pK_a values for **1** to **6**. This seems acceptable from the possible expectation that the relative acidity and geometry of 1: 1 adducts (LS) and the steric effect of LS on the accessibility of the second amine molecule may vary with X. On the other hand, the *S*-values and intrinsic shifts estimated in the present investigation also showed no correlation to the pK_a values, in contrast to the linear correlation of *S*-values to pK_a's for the same substrate with $Eu(dpm)_3$ obtained by Ernst *et al.*[11] There may be several explanations to account for such different results with the Eu-chelete, containing the observation of the larger *S*-values with $Eu(dpm)_3$ than with $Eu(fod)_3$.[17] It appears that the difference in contact shift contribution to LIS may dominate among the various explanations.

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References

1) B. L. Shapiro and M. D. Johnston, Jr., *J. Am. Chem. Soc.*, **94**, 8185 (1972).

2) J. K. M. Sanders, S. W. Hanson, and D. H. Williams, *J. Am. Chem. Soc.*, **94**, 5325 (1972).

3) J. W. ApSimon, H. Beierbeck, and A. Fruchier, *J. Am. Chem. Soc.*, **95**, 939 (1973).

4) J. Reuben, *J. Am. Chem. Soc.*, **95**, 3534 (1973).

5) M. D. Johnston, Jr., B. L. Shapiro, M. J. Shapiro, T. W. Proulx, A. D. Godwin, and H. S. Pearce, *J. Am. Chem. Soc.*, **97**, 542 (1975).

6) M. Hirayama and N. Ishida, *Bull. Chem. Soc. Jpn.*, **50**, 779 (1977).

7) F. Inagaki, S. Takahashi, M. Tasumi, and T. Miyazawa, *Bull. Chem. Soc. Jpn.*, **48**, 853 (1975).

8) F. Inagaki, M. Tasumi, and T. Miyazawa, *Bull. Chem. Soc. Jpn.*, **48**, 1427 (1975).

9) H. N. Cheng and H. S. Gutowsky, *J. Phys. Chem.*, **82**, 914 (1978).

10) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solutions," Butterworth, London, 1965.

11) L. Ernst and A. Mannschreck, *Tetrahedron Lett.*, **1971**, 3023.

12) M. Hirayama, M. Sato, M. Saito, and M. Takeuchi, *Bull. Chem. Soc. Jpn.*, **48**, 2690 (1975).

13) C. S. Springer, Jr., *et al.*, "NMR Shift Reagents," ed by R. E. Sievers, Academic Press, New York, N. Y. (1973); R. Porter, T. J. Marks, and D. F. Schriver, *J. Am. Chem. Soc.*, **98**, 3548 (1973); J. F. Desreaux, L. E. Fox, and C. N. Reilley, *Anal. Chem.*, **44**, 2217 (1972).

14) Such discussion has been carried out for 1: 1 adducts[2] and the shifts explained in terms of the superposition of the corresponding monofunctional substrate.[15] This treatment, however, may not be explicitly applied to the present system.

15) H. Hart and G. M. Love, *Tetrahedron Lett.*, **1971**, 625.

16) It has been reported that such aniline derivatives coordinate to $Eu(fod)_3$ with the angle between the N–C and N–Eu bonds ranging from 120° to 140°.[12] It may be presumed on the basis of this assertion that the *p*-substituent causes the aniline molecule to be less accessible to $Eu(fod)_3$.

17) B. L. Shapiro, M. D. Johnston, Jr., A. D. Godwin, T. W. Proulx, and M. J. Shapiro, *Tetrahedron Lett.*, **1972**, 3233.