The Correlation of Steric Effects and Equilibrium Constants Evaluated from Lanthanoid-induced ^{1}H Shifts in Aniline Derivative-Eu(fod)$_3$ Systems

Masatoshi Hirayama and Norio Ishida
Department of Chemistry, Ibaraki University, Bunkyo, Mito 310

(Received June 7, 1976)

The equilibrium constants, K_1 and K_2, between a series of *o*- and *N*-substituted anilines and Eu(fod)$_3$ in CCl$_4$ were evaluated using a four-parameter analysis of lanthanoid-induced shifts. It was found that the order of magnitudes of the values of K corrected for the effect of the pK_a-value well corresponds to the accessibility of the nitrogen lone-pair to the Eu ion on the complexation.

Ernst *et al.*[1] have found that in a series of *p*-substituted anilines, the Eu(dpm)$_3$-induced ^{1}H-NMR shifts (the so-called *S*-values) can be linearly correlated to its basicity, and furthermore, that no such relation exists in comparisons of amines with a different steric accessibility of the N-lone pair. However, one may consider that the use of pure intrinsic shifts[2–5] should lead to a more precise discussion of the correlation between shift and basicity. The intrinsic shifts should be related to the tightness of the interaction between the N-lone pair and the Eu ion, while the equilibrium between an Eu-chelate and amine depends on the frequency of occurrence of the interaction between these in solution. Therefore, it may be reasonable to consider that the magnitudes of the equilibrium constants should be dependent on both the basicity of amine and the steric accessibility of the N-lone pair to the Eu ion, as would be expected from the amounts of the lanthanoid-induced intrinsic shifts.

The present paper describes the correspondence between the equilibrium constants obtained from a least-squares analysis of the experimental Eu(fod)$_3$-induced shifts for a series of *o*- and *N*-substituted anilines and the predicted steric hindrance on complexing to Eu(fod)$_3$.

Experimental

All the liquid aniline derivatives used were distilled *in vacuo* and dried over molecular sieves, and 2-aminobiphenyl, recrystallized from ethanol. CCl$_4$ (spectro grade) dried over molecular sieves was used as the solvent without further purification. Eu(fod)$_3$ obtained commercially was used after drying over P$_2$O$_5$ in a vacuum desiccator.[6] In order to prepare the observed lanthanoid-induced shifts (LIS) *vs.* [Eu(fod)$_3$]/[Aniline] (ρ) plots, an original complex solution with the largest value of ρ was first prepared in a ^{1}H-NMR tube. This solution was then diluted step by step with an amine solution of concentration [S_0], while the NMR spectrum was measured. The total amine concentration [S_0] was 0.19 to 0.25 M, the largest ρ value 2.1 to 3.4, and the number of data points 19 to 22.

The NMR spectra were recorded on a Hitachi R-20A spectrometer at a probe temperature of 34 °C at 60 MHz in the frequency-swept mode using TMS as an internal standard.

All computations for the fitting analysis were carried out on HITAC-8800/8700 computers at the Computer Center of the University of Tokyo, except for some of which were performed on the HITAC-8250 computer at the Computer Center of Ibaraki University. The program used was LISA2 which was prepared by Shapiro *et al.* and partially modified in this laboratory.

Results and Discussion

Several *o*- and *N*-substituted anilines were chosen, because various degrees of steric hindrance may be expected with these amines upon complexing to Eu(fod)$_3$ in solution, and moreover, because the basicities (given in terms of pK_a-values) of these amines do not vary widely in magnitude.

The fitting analysis of the LIS *vs.* ρ plot was made by postulating an equilibrium system in which a self-association effect of Eu(fod)$_3$ was added to the two-step mechanism for the complexation of amine to Eu(fod)$_3$, that is, $L+S \rightleftarrows LS$ (K_1), $LS+S \rightleftarrows LS_2$ (K_2) and $L+L \rightleftarrows L_2$ (K_L).[2,7] These examinations using K_L-values up to 100 led to a monotonic increase or decrease in the standard deviation (σ) with increasing K_L-value for most proton resonances, although in a few cases a minimum value of σ was reached within this range of K_L. Therefore, the inclusion of this effect may be unfavorable. All the systems studied were therefore analyzed assuming K_L to be zero. Table 1 shows the intrinsic shifts (δ_1 and δ_2) and the σ-values obtained by the least-squares analysis. It can be said that these σ-values are adequately small. Representative examples are shown in Figs. 1 and 2. Table 2 shows the pK_a-values[8] and the averages of the K-values, for which the K-values were weighted according to the δ_1-value of each resonance in the molecule. The variation of K-values obtained from the various resonance lines in the molecule was fairly large (with a standard deviation of 18 to 50%). However, the averaged K-value changed considerably with the kind, position and number of substituents on aniline, as seen from Table 2. Therefore, these values may be useful for a qualitative discussion of the steric effect.

Table 2 shows that the large variation of K-values does not correspond to the small change in pK_a-values. This clearly indicates that the pK_a-value does not play a major role in the equilibria and suggests that steric hindrance may predominantly affect the complexation. *o*-Toluidine, *o*-ethylaniline and 2,3- and 2,4-, and 2,5-xylidines have much smaller equilibrium constants (both K_1 and K_2) than does aniline, in spite of the fact that their pK_a-values are similar in magnitude to that of aniline. Of these five compounds, *o*-ethylaniline has extraordinarily small values of K_1 and K_2. Consequently, the four remaining derivatives may be regarded as a

TABLE 1. THE INTRINSIC SHIFTS, δ_1 AND δ_2,$^{a)}$ AND THE STANDARD DEVIATIONS, $\sigma^{h)}$

Compound		2H	3H	4H	5H	6H	Ethyl	
							CH$_2$	CH$_3$
o-Toluidine	δ_1	−7.16$^{b)}$	−2.14	−3.07	−3.22	−10.52		
	δ_2	−5.12$^{b)}$	−1.27	−2.03	−2.27	−6.66		
	σ	0.032	0.019	0.020	0.021	0.100		
o-Ethylaniline	δ_1		−3.51	−3.29	−2.41	−11.74	−8.82	−3.73
	δ_2		−2.08	−1.87	−2.41	−6.51	−5.47	−2.54
	σ		0.013	0.012	0.010	0.032	0.040	0.012
2,3-Xylidine	δ_1	−9.24$^{b)}$	−2.85$^{b)}$	−3.99	−2.74	−13.45		
	δ_2	−6.66$^{b)}$	−2.08$^{b)}$	−2.86	−1.42	−7.63		
	σ	0.047	0.014	0.015	0.013	0.040		
2,4-Xylidine	δ_1	−8.38$^{b)}$	−3.72	−0.73$^{b)}$	−2.59	−12.93		
	δ_2	−5.81$^{b)}$	−2.41	−0.29$^{b)}$	−1.38	−7.24		
	σ	0.044	0.018	0.005	0.011	0.048		
2,5-Xylidine	δ_1	−8.06$^{b)}$	−3.71	−3.61	−1.53$^{b)}$	−12.05		
	δ_2	−5.23$^{b)}$	−2.35	−2.21	−0.90$^{b)}$	−6.67		
	σ	0.032	0.015	0.028	0.007	0.066		
2,6-Xylidine	δ_1	−7.04$^{b)}$	−3.47	−4.10	−3.47	−7.04$^{b)}$		
	δ_2	−4.49$^{b)}$	−1.97	−2.56	−1.97	−4.49$^{b)}$		
	σ	0.030	0.019	0.019	0.019	0.030		
N-Methyl-*m*-toluidine	δ_1	−12.52	−1.37$^{b)}$	−2.99	−2.97	−13.33		−14.94$^{c)}$
	δ_2	−8.45	−1.94$^{b)}$	−3.37	−2.50	−14.26		−15.86$^{c)}$
	σ	0.072	0.008	0.022	0.018	0.076		0.083
N-Ethyl-*m*-toluidine	δ_1	−13.40	−1.85$^{b)}$	−3.00	−3.55	−13.84	−17.77$^{d)}$	−7.83$^{d)}$
	δ_2	−4.45	−0.57$^{b)}$	−1.21	−1.11	−4.45	−6.85$^{d)}$	−2.97$^{d)}$
	σ	0.041	0.010	0.014	0.011	0.048	0.056	0.022
2-Aminobiphenyl$^{e)}$	δ_1	−6.68$^{f)}$	−4.26	−4.23$^{g)}$		−12.76		
	δ_2	−7.49$^{f)}$	−1.81	−3.02$^{g)}$		−11.90		
	σ	0.044	0.021	0.016		0.028		

a) Measured in ppm. b) Values for methyl protons. c) Values for *N*-methyl protons. d) Values for *N*-ethyl protons. e) Only four curves were thoroughly analyzed. f) This resonance line was assigned to the 2′ proton in the neighboring ring. This assignment is probably correct from the amount of shift and the coupling pattern of this line. g) It cannot be determined whether this signal should be assigned to 4H or 5H. h) $\left[\sum_{i=1}^{N}(\delta_{\mathrm{obsd},i}-\delta_{\mathrm{calcd},i})^2/(N-1)\right]^{1/2}$ measured in ppm, where δ_{obsd} and δ_{calcd} are the observed and calculated LIS, respectively and N is the number of data points.

group having K-values larger than those of *o*-ethylaniline, in view of the accuracy of the present estimates for the K. *N*-Methyl, *N*-ethyl, and *N,N*-dimethyl derivatives have particularly small values of K_1 and K_2, in contrast to their relatively large pK_a-values, especially those which are much smaller for the latter derivative. However, it cannot be clearly decided which K-values, those for the *N*-methyl or *N*-ethyl derivatives, are the larger. Thus, the order of magnitudes of K_1 and K_2, after correction for the effect of basicity, is as follows:

aniline > *o*-methyl > *o*-ethyl > *N*-methyl, *N*-ethyl >
N,N-dimethyl.

2,6-Xylidine and 2-aminobiphenyl have comparatively small pK_a-values. It may be said that the K_1 for 2,6-xylidine is located between those for *o*-ethylaniline and the *N*-monoalkyl-derivatives, but that the K_2 is similar in magnitude to that for the *N*-monoalkyl-derivatives, and that the K_1 and K_2 for 2-aminobiphenyl are similar in magnitude to those for the *N*-monoalkyl-derivatives having larger pK_a-values. Thus, the order, corrected for the effect of the pK_a-values, is

o,o-dimethyl > *o*-phenyl > *N*-methyl, *N*-ethyl,

which holds for both K_1 and K_2. From the trend in the variation of K_1 relative to that of pK_a for the four *o*-methyl derivatives, it is difficult to consider that the equilibrium constant for *o*-ethylaniline, which is about six times that for 2,6-xylidine (for both K_1 and K_2), can be ascribed to the difference in the pK_a-values, which is about 0.5 (see Table 2). Consequently, the overall order of the K-values corrected for the effect of the pK_a-values, is[9]

aniline > *o*-methyl > *o*-ethyl > *o,o*-dimethyl >
o-phenyl > *N*-methyl, *N*-ethyl > *N,N*-dimethyl.

On the other hand, one may assume that the aniline adduct of Eu(fod)$_3$ has a geometry similar to those of Eu(dpm)$_3$Py$_2$[10] and Ho(dpm)$_3$(4-picoline)$_2$,[11] although correct information about the present adduct is not known. Then, on the basis of this assumption, the degrees of steric hindrance for these aniline derivatives

Table 2. The equilibrium constants, K_1 and K_2,[a] and pK_a[b]

Compound	K_1	K_2	pK_a
o-Toluidine	1188	109	4.39
o-Ethylaniline	282	65	4.37
2,3-Xylidine	1081	95	4.72
2,4-Xylidine	1101	128	4.89
2,5-Xylidine	740	105	4.53
2,6-Xylidine	48.8	9.3	3.95
N-Methyl-*m*-toluidine	11.3	1.6	5.00
N-Ethyl-*m*-toluidine	9.2	9.0	5.12[c]
2-Aminobiphenyl[d]	9.5	5.5	3.83
N,*N*-dimethylaniline[e]	<0.1	—	5.07
N,*N*-Diethylaniline[f]	—	—	5.11
Aniline[g]	5230	582	4.62

a) These are average values in which the values of K are weighted according to the value of δ_1 for each resonance. When convergence of a K-value was unobtainable in the fitting analysis or one K-value was extremely different in magnitude from the other K-values for the resonances of the molecule, this value was excluded from the estimate of the averages. b) These values were taken from Ref. 8. c) Since the pK_a-value of *N*-ethyl-*m*-toluidine could not be found in the literature, that of *N*-ethylaniline is listed. This value is situated between 4.96 (*N*-ethyl-*o*-toluidine) and 5.72 (*N*-ethyl-*p*-toluidine) and appears to be plausible in analogy with the pK_a-values of aniline and toluidines: 4.62 (aniline), 4.39 (*o*-toluidine), 4.69 (*m*-toluidine), and 5.12 (*p*-toluidine). d) The averages of the K-values for only three resonances. e) All the values of K_2, δ_1 and δ_2 are very unreliable because the observed shifts are too small. However, the K_1-value is consistently less than 0.1 for all the protons. f) Analysis is almost impossible due to further small shift values. g) Listed for comparison with the present compounds, as a representative which may be considered to have no particular effect due to the steric hindrance.

have been discussed using the Eu-N distance, 2.65 Å,[10,12] and the angle (θ) between the Eu-N and N-C bonds, 120—140°.[12] Such a comparison of steric hindrance was made qualitatively based mainly on the access of substituent groups to several oxygen atoms of the β-diketonato ligands in both the 1 : 1 and 1 : 2 adducts. One may recognize that the order is unaffected by a slight variation of the geometry, and thus

aniline < *o*-methyl < *o*-ethyl < *o*-phenyl

holds for steric hindrance. For *o*-derivatives, in order to decrease the steric effect, the N-C bond can be slightly twisted so as to increase the distances between the *o*-substituent group and several oxygen atoms, at a small expense of the π-overlap in the N-C bond. However, no such possibility can be expected for the complexation of 2,6-xylidine.[13] Thus, it seems reasonable to consider that the steric effect for 2,6-xylidine is more rigorous than that for *o*-ethylaniline, because the methyl group in the ethyl group can be oriented in the direction away from the oxygen atoms. In *o*-aminobiphenyl, the two rings are considerably twisted with respect to each other and the neighboring ring may be fairly close to the *t*-butyl or heptafluoropropyl group. These must cause a fairly large hindrance, although whether 2,6-xylidine

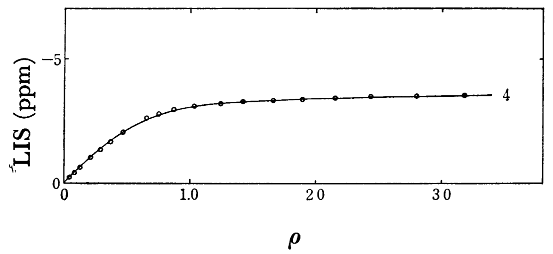

Fig. 1 (a)

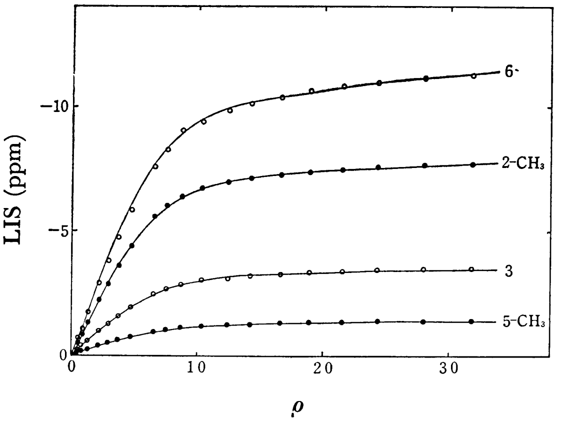

Fig. 1 (a)

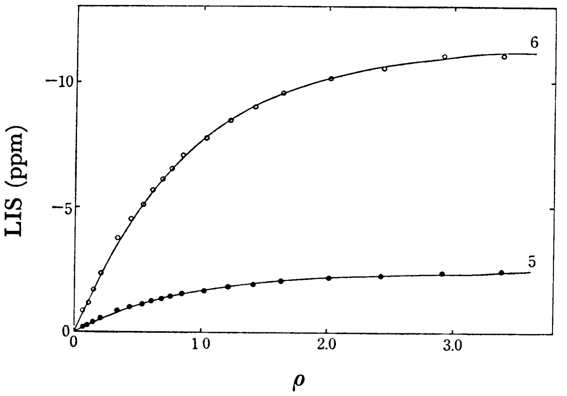

Fig. 1 (b)

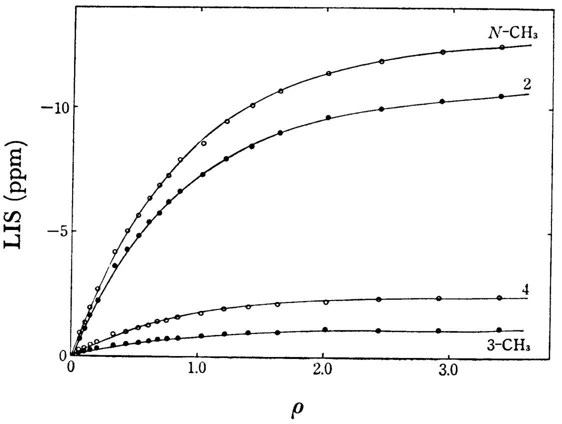

Fig. 1 (b)

Fig. 1. Results of theoretical fits of the two step mechanism, $L+S \rightleftarrows LS$, $LS+S \rightleftarrows LS_2$, to the observed Eu(fod)$_3$-induced data for (a) 2,5-xylidine at $[S_0]=0.25$ M and (b) *N*-methyl-*m*-toluidine at $[S_0]=0.19$ M. The numbers indicate the positions.
○, ●: The observed data.

or *o*-aminobiphenyl has the larger steric effect cannot be determined. In *N*-methyl, *N*-ethyl, and *N,N*-dimethyl derivatives, the *N*-methyl and *N*-methylene groups generally become much closer to some of the oxygen atoms than the ring-substituents in the other compounds, even though the degree of proximity is appreciably sensitive to a slight variation of θ. Such a situation allows us to consider that these *N*-derivatives are expected to have a steric effect that is considerably larger than those for the other amines mentioned above. *N,N*-Dimethylaniline should be less accessible to the Eu ion than the *N*-methyl or *N*-ethyl aniline, for the same reason as in the case of 2,6-xylidine.

Thus, it was found that the K_1- and K_2-values obtained from the present investigation in the aniline derivative–Eu(fod)$_3$ systems correspond well to the predicted steric accessibility of the *N*-lone pair to Eu(fod)$_3$, without any large discrepancy.

A quantitative correlation of the intrinsic shifts with the steric hindrance in the present systems is difficult to elucidate for the following reasons: (1) the steric effect possibly alters the geometry of the adduct, and consequently, the intramolecular distribution of the dipolar shifts may be changed, and (2) the variation of the extent of the steric effect may lead to a change in the cs-contribution to the LIS.

The authors would like to express their grateful appreciation to Professor B. L. Shapiro for providing them with the LISA2 program.

References

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

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

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

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

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

6) Since the use of Eu(fod)$_3$ in a few samples after purification by sublimation did not result in so much variation of the LIS as *K*-values are significantly affected, Eu(fod)$_3$ was used after only drying over P_2O_5 *in vacuo*.

7) The parameters derived from this sort of curve fitting have physical significance only when the number of data points is far larger than that of the parameters to be fit. Such a requirement is adequately satisfied for the present data.

8) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solutions," Butterworths, London (1965).

9) There are two other possible values representative of the equilibrium constants, the simple average of the *K*-values obtained from all the separate determinations performed on the molecule and the *K*-value found for the proton with the largest δ_1.[2)] However, it was confirmed that the choice of either of these two values for *K* does not influence the order of *K*-values estimated here.

10) R. E. Cramer and K. Seff, *Chem. Commun.*, **1972**, 400.

11) W. D. Horrocks, Jr., J. P. Sipe, III, and J.R. Luber, *J. Am. Chem. Soc.*, **93**, 5258 (1971).

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

13) It is anticipated, from the molecular model, that a severe restriction on rotation about the Eu–N bond arises due to the potential barrier formed between the benzene ring or the substituent groups and the *t*-butyl or heptafluoropropyl group.