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Lanthanide Induced Shifts of the PMR Spectra of Polyaza-aromatic Compounds

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The LIS's were determined with the equimolar mixtures of two monoaza-aromatic compounds, and the relative coordinating ability of each ligand was estimated from these LIS's. The coordinating ability index is defined as the ratio of the complexed species of the monoaza-aromatics to that of pyridine, and is proved to be transferable to the nitrogen atom of similar steric circumstances. Thus, Eu(fod)$_3$ induced shifts of the protons in several unsymmetrical naphthyridines and related heterocycles were estimated by the sum of the induced shifts of the corresponding monofunctional equivalents weighted by the relative abundances of the complexed species which were obtained from the coordinating ability measurements. The method is applicable to other bifunctional compounds of rigid conformation.

Since the first success reported by Hinckley,1) lanthanide shift reagents have been applied to many stereochemical problems, and their uses are known as a routine technique of resolving the overlapping NMR signals. However, their application is limited within the monofunctional compounds in most cases, and relatively few examples have previously been reported concerning the lanthanide-induced shifts (LIS) of bi- and poly-functional compounds.2) In the field of the chemistry of nitrogen heterocycles, their uses were focused on relatively simple compounds, such as pyridine, quinoline, and related compounds. An extensive work on six-membered nitrogen heterocycles including diazanaphthalenes has also been reported by Armarego and coworkers.3) However, the discussion on the preferred site of complexation is qualitative and rather inconclusive.

In order to use shift reagents on polyfunctional compounds, it is necessary to decide the preferred site of complexation. Further, it is desirable to know quantitatively the relative abundances of the complexed molecules on two or more competing sites. In general, the coordinating ability of the ligand is affected by the electronic and steric factors.4) In the case of shift reagent-substrate complexes, it is demonstrated that the coordinating ability is mainly governed by the steric factors which control the approach of the bulky Eu(III) complexes.

In this investigation, the LIS's were determined on the equimolar mixture of the two monofunctional compounds carrying similar functional groups in different steric circumstances. This offers an approach to determine the coordinating abilities of various substrates to the shift reagent by intermolecular competition.5) Then, the LIS's of bifunctional compounds were estimated by the weighted summation of the induced shift of every equivalent monofunctional compound [$S_i^{(m)}$]. To accomplish this, the induced shifts of each monofunctional compound carrying a functional group of almost same circumstances as in the bifunctional one were measured first. Then, their induced shifts were again determined with an equimolar mixture of the two equivalent monofunctional compounds. The ratios of the induced shifts in the mixed solution to the one component LIS's give the relative abundances of the complexed monofunctional equivalents. The ratios thus obtained are nearly indifferent irrespective of the nature of protons in the molecule, and may be usable as a measure for the relative coordinating ability of the two substrates. The sequence of the relative coordinating ability indices will be a more reliable criterion for the steric effect than the LIS itself, since the steric factor of the McConnel-Robertson equation,6) $(3\cos^2\theta-1)/r^3$, will also affect the LIS values

The coordinating ratios can be assumed to reproduce the complexation in two sites of the bifunctional compound. Then, the induced shifts (S_i) of each proton (i) in a bifunctional compound is calculated by summing up the each induced shift of the monofunctional model compound ($S_i^{(m)}$) weighted by the normalized relative abundance ($P^{(m)}$) obtained by the competitive complexation among the monofunctional model compounds.

$$S_i = \sum_{(m)} S_i^{(m)} \cdot P^{(m)} \tag{1}$$

The above equation is derived by assuming that the electronic and other through bond effects between the two functional groups are negligible, and applies to the bifunctional compounds in which the two functional groups are located moderately apart from each other. Diaza-aromatic compounds carrying nitrogen atoms in different rings are suitable examples, and the LIS's of these heterocycles can be estimated properly from those of monoaza-aromatic compounds of similar structural feature.

Experimental

Materials used in this investigation were synthesized according to the methods previously reported,7) or obtained by purification of commercially available materials. Proton NMR spectra were measured with chloroform-*d* solutions employing a JNM C-60H spectrometer operating at 60 MHz. The concentrations of the solutions were adjusted approximately at 0.3 mol·l^{-1} with respect to substrates, and Eu(fod)$_3$ was employed as the shift reagent throughout this work except the cases otherwise remarked. The induced shift was measured by adding the shift reagent in small portions to the solution containing an excess of the substrate. To eliminate the

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effect of imperfect complexation (equilibrium constants), the concentration of substrates were carefully adjusted to be constant throughout this investigation.

Results and Discussion

The LIS's of Monoaza-Aromatic Compounds and Evaluation of the $P^{(m)}$ *Values.* The lanthanide-induced shift was estimated, as usual, from the slope of the $\Delta\delta$ *vs.* [Eu(fod)$_3$]/[Substrate] plot, where $\Delta\delta$ refers to the chemical shift change induced by the shift reagent. The slope from the least squares fit of the plot was used as the LIS value (denoted by S in Tables and equations). The LIS's of various six-membered monoaza-aromatic compounds are given in Table 1. As expected, both the LIS's and the coordinating abilities (in Tables 2 and 5) decrease with increasing streic hindrance around the nitrogen atoms. This tendency is illustrated by the fact that the LIS decreases in the order of pyridine>2-methylpyridine>2,6-dimethylpyridine in the series of pyridine homologs. A remarkable difference is observed between the LIS's of 3- and 5-protons of 2-methylpyridine (**2**). Though the influence of the contact shift is not negligible for this compound, its contribution is concluded to be not predominant in the case of proton spectra.[8] Thus, the magnitudes of the LIS's can be interpreted that the bulkier methyl group expels the coordinated Eu(fod)$_3$ molecule to the opposite side of the C$_4$–N axis and changes the contribution of the steric factor on the 3- and 5-protons. This effect will be discussed quantitatively in the succeeding part of this paper. Similar deviations in coordination sites are also observed with 6-chloro-2-methylquinoline (**5**) and 6-chloro-8-methylquinoline (**6**). In the case of the 6-chloro-2-methyl derivative (**5**), the LIS of 7-proton is considerably larger than that in the 6-chloro-8-methyl derivative (**6**). This must also be the consequence of the different location of Eu(III) ion relative to the nitrogen ligand.

In order to determine the coordinating ability by intermolecular competition method, the LIS's of each substrate in the solution of the equimolar mixture of the two substrates were measured in a similar manner. Then the coordination ratio for every proton was calculated by comparison of the apparent LIS value ($S_i^{\mathrm{ap(m)}}$) with that of each component ($S_i^{\mathrm{o(m)}}$). By averaging the coordination ratios $P_i^{(m)}$ of all protons in the molecule m, the coordination ratio of the molecule ($P^{(m)}$) is calculated.[9] The coordination ratios of several aza-aromatic compounds to Eu(fod)$_3$ are given in Table 2. In the cases of shift reagents, the coordinating ability is mainly governed by the steric factor. Thus, the ability estimated from the coordination ratios of quinoline is nearly identical with those of 2-methylpyridine (**2**) and 6-chloroquinoline (**4**) with which the steric circumstances of the donor nitrogen atoms are similar to quinoline. Analogously, the coordinating abilities of 2,6-dimethylpyridine (**3**) and 6-chloro-8-methylquinoline (**6**) are almost identical with those of 6-chloro-2-methylquinoline (**5**) and 1-azaphenanthrene (**7**), respectively. 2-Methylpyridine might possess a little larger coordinating ability than 6-chloroquinoline, because the free rotation of the methyl group in the former can operate to lessen the steric hindrance in contrast to the rigid 8-H in quinoline. The same discussion is also applicable to the series of 2,6-dimethylpyridine (**3**), 6-chloro-2-methylquinoline (**5**), and acridine (**8**). The order of coordinating ability is: 2,6-dimethylpyridine > 6-chloro-2-methylquinoline > acridine. However, the differences in coordinating abilities among these compounds are smaller than those among the compounds of dissimilar steric circumstances. In short, the competitive complexation experiments given in Table 2 reveal the fact that the steric circumstances are the dominating factor to the coordinating abilities of these heterocycles.

A shift to higher field is observed with the 2-H of 1,8-naphthyridine (**10**) by addition of Eu(fod)$_3$. 1,8-

TABLE 1. THE LIS'S OF SEVERAL MONOAZA-AROMATIC COMPOUNDS

Compound	2-CH$_3$	8-CH$_3$	2-H	3-H	4-H	5-H	6-H	7-H	8-H	9-H	10-H
Pyridine (**1**)	—	—	35.37	11.11	11.00	11.11	35.37	—	—	—	—
	—	—	(1.00)	(0.31)	(0.31)	(0.31)	(1.00)	—	—	—	—
2-Methylpyridine (**2**)	23.37	—	—	8.56	5.34	4.60	13.89	—	—	—	—
	(1.00)	—	—	(0.37)	(0.23)	(0.20)	(0.59)	—	—	—	—
2,6-Dimethylpyridine (**3**)	7.29	—	—	2.48	2.09	2.48	—	—	—	—	—
	(1.00)	—	—	(0.34)	(0.29)	(0.34)	—	—	—	—	—
6-Chloroquinoline (**4**)	—	—	26.64	8.80	10.33	7.34	—	5.57	33.63	—	—
	—	—	(0.79)	(0.26)	(0.31)	(0.22)	—	(0.17)	(1.00)		
6-Chloro-2-methylquinoline (**5**)	5.06	—	—	1.75	1.29	0.84	—	0.57	5.92	—	—
	(0.85)	—	—	(0.30)	(0.22)	(0.14)	—	(0.10)	(1.00)	—	—
6-Chloro-8-methylquinoline (**6**)	—	4.13	4.04	0.44	0.59	0.18	—	1.29	—	—	—
	—	(1.00)	(0.98)	(0.11)	(0.14)	(0.04)	—	(0.31)	—	—	—
1-Azaphenanthrene (**7**)	—	—	2.72	0.43	0.55	<0.5	<0.5	<0.5	<0.5	<0.5	3.92
	—	—	(0.69)	(0.11)	(0.14)	(<0.13)	(<0.13)	(<0.13)	(<0.13)	(<0.13)	(1.00)
Acridine (**8**)	—	—	1.0	1.0	8.05	8.05	<1.0	<1.0	<1.0	1.71	—
	—	—	(0.12)	(0.12)	(1.00)	(1.00)	(<0.12)	(<0.12)	(<0.12)	(0.21)	—
2,8-Dimethylquinoline (**9**)	1.79	1.98	—	0.81	0.75	<0.5	<0.5	<0.5	—	—	—
	(0.90)	(1.00)	—	(0.41)	(0.38)	(<0.25)	(<0.25)	(<0.25)	—	—	—
1,8-Naphthyridine	—	—	−1.04	3.63	5.17	5.17	3.63	−1.04	—	—	—
	—	—	(−0.20)	(0.70)	(1.00)	(1.00)	(0.70)	(−0.20)	—	—	—

The LIS's defined by $S^\circ = \Delta\delta / ([\mathrm{Eu(fod)_3}]/[\mathrm{Substrate}])$ are given in this table. Relative LIS values with respect to the largest are given in parentheses.

TABLE 2. RESULTS ON THE COMPETITIVE COORDINATION EXPERIMENTS BETWEEN TWO SUBSTRATES

Run No.	Predominantly Complexed Substrate		Less Predominantly Complexed Substrate	
	Compound 1	P_1 (%)	Compound 2	P_2 (%)
1	1,8-Naphthyridine	92	Pyridine	8
2	Isoquinoline	56	Pyridine	44
3	Pyridine	87	2-Me-Pyridine	13
4	Pyridine	88	2,6-Me_2-Pyridine	12
5	Pyridine	87	6-Cl-Quinoline	13
6	Pyridine	91	6-Cl-2-Me-Quinoline	9
7	Pyridine	93	6-Cl-8-Me-Quinoline	7
8	Pyridine	88	Acridine	12
9	Pyridine	93	1-Azaphenanthrene	7
10	Pyridine	97	2,8-Me_2-Quinoline	3
11	2-Me-Pyridine	58	6-Cl-Quinoline	42
12	2-Me-Pyridine	78	2,6-Me_2-Pyridine	22
13	Quinoline	52	6-Cl-Quinoline	48
14	6-Cl-Quinoline	77	2,6-Me_2-Pyridine	23
15	6-Cl-Quinoline	72	6-Cl-2-Me-Quinoline	28
16	6-Cl-Quinoline	74	6-Cl-8-Me-Quinoline	26
17	6-Cl-Quinoline	71	Acridine	29
18	2,6-Me_2-Pyridine	68	6-Cl-2-Me-Quinoline	32
19	2,6-Me_2-Pyridine	73	6-Cl-8-Me-Quinoline	27
20	2,6-Me_2-Pyridine	65	Acridine	35
21	6-Cl-2-Me-Quinoline	63	6-Cl-8-Me-Quinoline	37
22	6-Cl-2-Me-Quinoline	51	Acridine	49
23	6-Cl-2-Me-Quinoline	62	1-Azaphenanthrene	38
24	Acridine	64	6-Cl-8-Me-Quinoline	36
25	Acridine	61	1-Azaphenanthrene	39
26	1-Azaphenanthrene	54	6-Cl-8-Me-Quinoline	46
27	6-Cl-8-Me-Quinoline	53	2,8-Me_2-Quinoline	47

* P_1 and P_2 are the coordinating ratios in percent, which are estimated by employing the following equation: $P_i = S_i^{ap}/S_i^{o}$

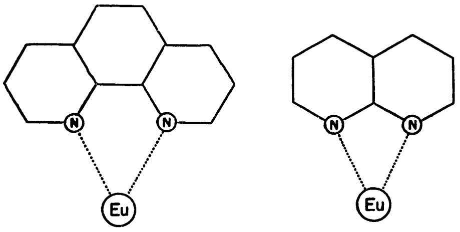


Fig. 1. Eu^{3+}–1,10-phenanthroline and 1,8-naphthyridine complexes. These bases behave as bidentate ligands in the complex formation.

naphthyridine (**10**) is a bidentate ligand, forming a chelate compound with $Eu(fod)_3$ (as shown in Fig. 1), and this may be the reason for its anomalous LIS. Thus, the system gains additional stabilization energy, and its coordinating power is strengthened remarkably. The above discussion applies to the peculiar stability of the 1,10-phenanthroline- and 2,2'-bipyridine-$Eu(fod)_3$ complexes.

The $P^{(m)}$ values are convenient to compare the coordinating abilities of the two nitrogen donors, but inconvenient for the comparison among several nitrogen donors of different steric circumstances. Thus, the coordinating ability index (C) is defined as the ratio of $P^{(m)}$ to the $P^{(m)}$ of pyridine. The most probable values of coordinating ability indices were calculated from the $P^{(m)}$'s listed in Table 2 by least squares optimization technique, and are given in Table 5.

The intermolecular competition offers a more reliable method to determine the abundances of the complexed species, since the LIS's depend not only on the population of the complexed species but also on the steric factor (in Eq. 3). The LIS's of some protons are shown in Table 3. These protons occupy nearly equivalent positions relative to the nitrogen atoms. By comparing these LIS's with the coordinating ability

TABLE 3. THE LIS'S OF SOME PROTONS OCCUPYING NEARLY EQUIVALENT POSITIONS RELATIVE TO THE NITROGEN ATOMS

Compound	1	2	3	4	5	6	7	8	9	10
LIS	35.37	13.89	7.29	26.64	5.06	4.04	8.05	2.72	1.79	−1.04[a]
Position	2-H	6-H	2-CH_3	2-H	2-CH_3	2-H	4-H	2-H	2-CH_3	2-H

a) Shift to the higher field.

indices in Table 5, it is shown that the LIS's are not always proportional to the coordinating abilities. The coordinating ability indices are rather insensitive to the electronic effect. Thus, the coordinating ability indices for quinoline and its 6-chloro-derivative are 0.153 and 0.145, respectively. However, a small but definite effect is observed when a substituent is attached directly to the hetero-aromatic ring. The coordinating ability indices for pyridine, 4-chloropyridine, and 4-methylpyridine are 1.00, 0.79, and 1.22, respectively, and, as expected, the electron donating ability of the substituent favors the complex formation. In conclusion the relative values of the coordinating ability indices are transferable to the nitrogen ligand of similar local steric circumstances.

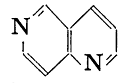
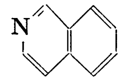
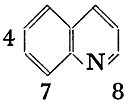
Estimation of the LIS's of Polyaza-aromatic Compounds. As the coordinating abilities of the nitrogen atoms in the heterocycles are dependent mainly upon their steric circumstances, the LIS's of polyaza-aromatic compounds can be estimated from the coordinating abilities of monoaza-aromatic compounds of which nitrogen atoms occupy similar steric circumstances. The method is quite successful in estimating the LIS's of polyaza-aromatic compounds without polyaza-rings. Thus, the induced shifts of the ring protons of 1,6- and 1,7-naphthyridines were estimated from those of quinoline and isoquinoline. Eu(fod)$_3$ was employed as the shift reagent throughout this work, and the induced shift was measured by adding the shift reagent in small portions. To avoid the effect of the di-coordinated species $C_8H_6N_2 \cdot 2Eu(fod)_3$, the induced shift was estimated from the chemical shift displacement ($\Delta\delta$) in the range of lower [Eu(fod)$_3$]/[substrate] ratios. From the experiment of the competitive complexation with the equimolar quinoline–isoquinoline mixture in chloroform-*d*, the mean coordinating abilities for quinoline ($P^{(1)}$) and isoquinoline ($P^{(2)}$) have already been estimated to be 0.14 and 0.86, respectively. Then, the induced shifts for the protons in the naphthyridines were estimated by Equation 1 as shown in Table 4.

The estimated relative induced shifts agree almost quantitatively with the observed values except the case of 8-H in 1,7-naphthyridine. The lower estimated value of S_8 in 1,7-naphthyridine can be improved considerably by assuming the equal $S_i^{(2)}$ values for 6-H and 8-H of 1,7-naphthyridine (which correspond to those of 3-H and 1-H in isoquinoline, respectively). This assumption is exactly true if pyridine is employed as a model monofunctional compound.

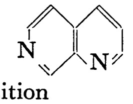
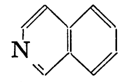
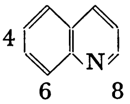
Similar estimations again result proper relative values for the LIS's of 2-methyl- and 4-methyl-1,5-naphthyridines (as shown in Table 4). The magnitudes of the induced shifts can also be estimated in fair agreement by this method. However, the relative values fit more closely with the observed ones.

Table 4. The observed and the estimated LIS's of some naphthyridines

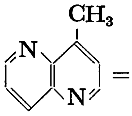
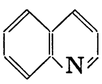
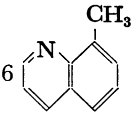
Naphthyridine — Reference monoaza-aromatics and the ratios

(1)  = 0.86  + 0.14 

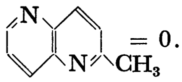
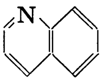
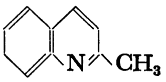
Position		2	3	4	5	7	8
S_i	obsd	8.46	5.63	8.23	29.20	37.74	16.28
	calcd	6.45	4.58	7.76	25.55	31.06	13.30
$S_i/(S_i)_{max}$	obsd	0.22	0.15	0.22	0.77	1.00	0.43
	calcd	0.21	0.15	0.25	0.82	1.00	0.42

(2)  = 0.86  + 0.14 

Position		2	3	4	5	6	8
S_i	obsd	6.25	4.31	7.39	9.29	29.27	32.62
	calcd	6.49	4.58	7.76	9.96	31.06	28.89
$S_i/(S_i)_{max}$	obsd	0.19	0.13	0.23	0.28	0.90	1.00
	calcd	0.22	0.16	0.27	0.34	1.08	1.00

(3)  = 0.74  + 0.26 

Position		2	3	6	7	8	CH_3
S_i	obsd	42.02	15.06	11.95	10.28	58.71	15.68
	calcd	19.84	6.85	5.49	4.23	25.04	—
$S_i/(S_i)_{max}$	obsd	0.72	0.26	0.20	0.18	1.00	0.27
	calcd	0.79	0.27	0.22	0.17	1.00	—

(4)  = 0.72  + 0.28 

position		3	4	6	7	8	CH_3
S_i	obsd	6.41	33.66	25.43	9.44	12.18	5.41
	calcd	4.50	24.57	19.37	6.50	9.10	—
$S_i/(S_i)_{max}$	obsd	0.19	1.00	0.76	0.28	0.36	0.16
	calcd	0.18	1.00	0.79	0.26	0.37	—

Estimation of the Locations of Eu(III) in the Shift Reagent-Substrate Complexes and Calculation of the $S_i^{(m)}$*'s for the Protons Void in the Model Monofunctional Compounds.* In order to correlate the coordinating ability with the location of Eu(III) ion and to use in estimating some LIS's of polyfunctional compounds, the most probable location of the complexed Eu(III) ion was determined by evaluating the agreement factors[10] defined by the folowing equation.

Table 5. The Eu–N distances (d_{Eu-N}), distortion angles (φ), and coordinating ability indices (C) of some aza-aromatic compounds

Compound	1	2	3	4	5	6	7	8	9	10
d_{Eu-N}, Å	3.3	—	4.0	—	4.2	5.1	4.2	5.3	—	—
	(3.9)	4.7		(4.8)	(5.7)	(4.6)				
φ°	0	—	0	—	4	10	18	0	—	—
	(0)	(5)		(16)	(9)	(23)				
C	[1.00]	0.177	0.097	0.158	0.084	0.058	0.070	0.096	0.040	11.5

a) The distances and angles in paretheses refer to those of Pr(fod)$_3$–substrate complexes.

$$R = \left(\frac{[(S_{\text{obsd}})_i-(S_{\text{calcd}})_i]^2}{(S_{\text{obsd}})_i{}^2}\right)^{1/2} \tag{2}$$

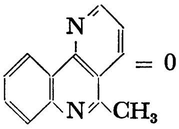
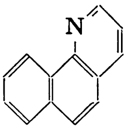
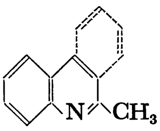
The calculations were carried out with a HITAC 8250 digital computer by assuming the following: a) The lanthanide-substrate interaction is entirely, or at least predominantly, of pseudocontact nature usually evaluated by the McConnell-Robertson equation,

$$S = K(3\cos^2\theta-1)/r^3 \tag{3}$$

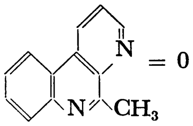
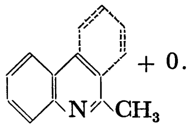
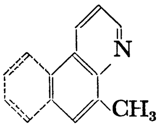
where θ is the N–Ln–H internuclear angle and r is the Ln–H distance. b) The coordination site is located on the plane of the heteroaromatic ring. The Eu–N distances thus obtained are given, together with the relative coordinating ability indices, in Table 5. Some of the results are illustrated also in Fig. 2. The calculated locations of Eu(III) ions are in accordance with the degree of the steric hinrdance qualitatively estimated from the coordinating abilities. The results illustrate that there exists an approximately linear relation between the coordinating ability indices and the Eu–N distances. If the substrate molecule carries some groups, such as methyl, which cause the steric hindrance to the coordination, the coordination site of Eu(fod)$_3$ may shift, and both the Eu–N distance and the orientation of the Eu–N axis deviate from those of pyridine. The methyl and the benzo groups of 8-methylquinoline and 1-azaphenanthrene, respectively, hinder the access of the shift reagent more remarkably than those of 2-methylquinoline and acridine. Angular distortion of the Eu–N axes in the Eu complexes of the former may play an important role to increase the steric hindrance. The steric circumstances of the electron

Table 6. The observed and the estimated LIS's of some diazaphenanthrenes

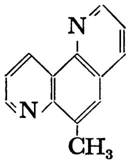
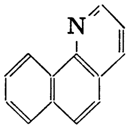
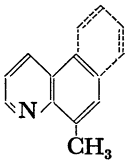
Diazaphenanthrene — Reference monoaza-aromatics and the ratio[a)]

(5)  = 0.38  + 0.62 

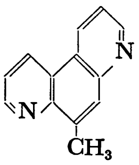
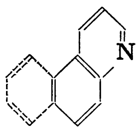
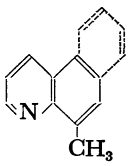
Position		2	3	4	7	8	9	10	CH_3
S_i	obsd	1.52	0.59	1.06	4.71	<0.5	<0.5	2.37	3.46
	calcd	1.52	0.65	1.15	3.75	0.54	0.61	2.01	—
$S_i/(S_i)_{\max}$	obsd	0.32	0.13	0.23	1.00	<0.1	<0.1	0.50	0.73
	calcd	0.40	0.17	0.30	1.00	0.14	0.16	0.53	—

(6)  = 0.63  + 0.37 

Position		1	2	3	7	8	9	10	CH_3
S_i	obsd	0.80	0.54	1.55	4.62	<0.5	<0.5	0.74	4.17
	calcd	0.84	0.58	1.94	3.90	0.49	0.59	0.82	—
$S_i/(S_i)_{\max}$	obsd	0.17	0.12	0.34	1.00	<0.1	<0.1	0.16	0.90
	calcd	0.22	0.15	0.50	1.00	0.13	0.15	0.21	—

(7)  = 0.54  + 0.46 

Position		2	3	4	5	8	9	10	CH_3
S_i	obsd	2.09	0.61	0.77	1.26	4.07	0.55	3.39	4.35
	calcd	1.64	0.42	0.52	0.86	2.13	0.47	2.39	—
$S_i/(S_i)_{\max}$	obsd	0.62	0.18	0.23	0.37	1.20	0.16	1.00	1.28
	calcd	0.69	0.18	0.22	0.36	0.89	0.20	1.00	—

(8)  = 0.74  + 0.26 

Position		1	2	3	5	8	9	10	CH_3
S_i	obsd	9.78	8.60	24.94	28.71	3.86	3.30	6.97	3.08
	calcd	7.82	6.61	19.80	25.22	2.35	1.78	3.28	—
$S_i/(S_i)_{\max}$	obsd	0.34	0.30	0.87	1.00	0.13	0.11	0.24	0.11
	calcd	0.31	0.26	0.79	1.00	0.09	0.07	0.13	—

a) The reference monoaza-aromatic compound is lacking in the aromatic ring illustrated by the broken line, and the $S_i^{(m)}$ values were estimated by the method described in the text.

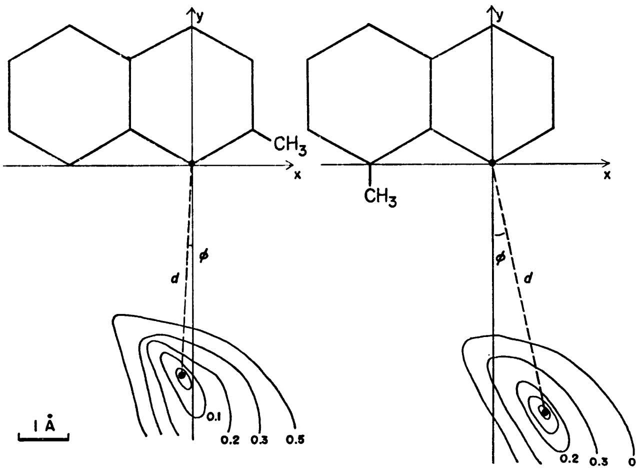


Fig. 2. The most probable location of europium (III) ion in the shift reagent–substrate complex estimated by the evaluation of the R values.

donating nitrogen atom affect remarkably the coordination with the shift reagent.

On estimating the induced shifts (S_i's) of the protons in bifunctional compounds by Eq. 1, the induced shifts of the monofunctional reference compounds ($S_i^{(m)}$'s) are required. When the reference monofunctional compounds have the same skeletal structure with that of the bifunctional compound, the $S_i^{(m)}$ values can be obtained experimentally, as exemplified by the cases (1) to (4) in Table 4. However, such reference monofunctional compounds are not always available easily when the bifunctional compound has a more complex structure. Even in such cases, the induced shifts $S_i^{(m)}$ of the protons on the rings distant from the functional group can be estimated from the $d_{\mathrm{Eu-N}}$ and ϕ values by employing the McConnell-Robertson equation. For example, the induced shifts of the protons in 5-methyl-1,6-diazaphenanthrene is estimated from the $S_i^{(m)}$'s of 2-methylquinoline and 1-azaphenanthrene (as shown in Table 6). Since 2-methylquinoline is void of the aromatic ring illustrated by the broken lines in Table 6, the $S_i^{(m)}$'s for the protons at 2, 3, and 4 positions due to the complexation on the 6-nitrogen atom are estimated by calculating relative LIS's of these protons by Eq. 3. As the induced shifts $S_i^{(m)}$'s of the distant protons are small, the approximation is permissible in spite of the considerable inaccuracy accompanying to this method of evaluation. The results are shown in Table 6, together with those of 5-methyl-4,6-diaza-, 6-methyl-1,7-diaza-, and 6-methyl-4,7-diaza-phenanthrenes. Here again the estimated LIS's are rather smaller than the observed ones, however, the agreement between the relative values is excellent in most cases. And the method is proved to be applicable to the prediction of the LIS's of the heteroaromatic compounds of this class.

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9) The procedure is formulated as follows;

$$P_i^{(m)} = \frac{(S_i^{ap})_i^{(m)}}{(S^0)_i^{(m)}} \qquad P^{(m)} = \sum_{i=1}^{n} P_i^{(m)}/n,$$

where n is the number of protons over which $P_i^{(m)}$'s are averaged.

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