# INTERACTION OF LANTHANIDE SHIFT REAGENTS WITH ALKYLTOSYLATES OF HETEROCYCLIC BASES AND TOSYLATES OF CYANINE DYES

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The interaction of alkyltosylates of derivatives of pyridine, quinoline, benzothiazole, benzimidazole, and cyanine dyes with the lanthanide shift reagent Eu(fod)$_3$ is studied. The structure of the salt cations is related to their ability to interact with the LSR. Results of a calculation of the structure of the adducts of heterocyclic alkyltosylates with the LSR are presented.

It is known that lanthanide shift reagents (LSR) are able to form adducts with the anions of organic salts resulting in a pseudocontact lanthanide induced shift (LIS) of the NMR signals for the protons in the cation [1]. However, use of this property of the LSR until now has been limited since the quaternary salts (usually for the study a salt with an inorganic anion is chosen) are poorly soluble in chloroform, methylene chloride, and other solvents used in experiments with LSR. Recently we found [2] that the above difficulties can be circumvented if salts with an organic anion-p-toluenesulfonate (tosylate), are chosen for the study with LSR. Such salts are easily obtained, sufficiently soluble in chloroform and methylene chloride, and effectively interact with LSR. It is also important that the tosylate anion contains nuclei suitable for NMR spectra ($^1$H and $^{13}$C) whose LIS values can more reliably establish the structure of the adducts with the LSR, in contrast to the inorganic anions.

In this work, alkyltosylates of a series of heterocyclic bases and tosylates of cyanine dyes are used as substrates and europium 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionate, Eu(fod)$_3$, as the LSR. Table 1 gives the LIS values found for a [reagent]/[substrate] ratio of 1:1. It follows from Table 1 that the protons with the most strongly shifted signals in the presence of the LSR are those near the onium nitrogen atom, in many cases the LIS values of these protons even exceed the LIS of those in the tosylate anion, through which the LSR coordination occurs directly.

The effect of steric hindrance in the cation on the LIS can be judged from salts I-V, the cations of which contain a pyridine ring. If one of the α-positions of the pyridine ring is free, then the α-proton signal is shifted most strongly of all upon addition of LSR. If both positions next to the onium nitrogen atom have substituents, their signals are shifted much more weakly than in the case above. Even more, the LIS values of the quaternary salt can even exceed those for the heterocyclic base. The interaction of Eu(fod)$_3$ with N-methylcollidine tosylate and collidine itself (V and VI) can serve as an illustration of this. The LIS of a 4-CH$_3$ group in a salt exceeds the shift of the corresponding group in the base by 2.5 times.

On going from alkyltosylates containing a pyridine ring to quaternary salts of azoles, significant changes in their ability to coordinate to the LSR do not occur. Thus, the LIS values are near the shifts found for the pyridine salts for the alkyltosylates of substituted benzothiazoles XI and XII and for the benzimidazole salt XIII. From Table 1 it follows that the substituents on the heterocyclic nucleus located not only next to, but also away from the onium nitrogen atom have a marked effect on the LIS. For example, the methyltosylate of 4-picoline (IV) has a LIS value almost twice as small as the analogous 2-picoline salt (II). Similar effects in a series of heterocyclic bases have already been studied [3].

Cyanine dyes are important organic salts. We measured the PMR spectra of symmetric and asymmetric monomethin-, carbo-, and dicarbocyanine XIV-XX tosylates in the presence of LSR. The signals of the protons of the cations of these dyes were found to be shifted significantly

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TABLE 1. Lanthanide Induced Shifts (ppm) of Protons in Methyl-(ethyl-)tosylates of Nitrogen-containing Heterocyclic Bases*

| Compound | Base | Position of Positions of protons or substituents | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | in the cation | | | | | | | | in the anion | | |
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 4 | 3 | 2 |
| I | Pyridine | (CH$_3$) 6,9 | (H) 8,2 | (H) 3,4 | (H) 2,5 | (H) 3,4 | (H) 8,2 | — | — | 0,3 | 1,1 | 4,7 |
| II | α-Picoline | (CH$_3$) 8,1 | (CH$_3$) 2,8 | — | (H) 2,1 | (H) 4,7 | (H) 12,6 | — | — | 0,2 | 0,6 | 4,6 |
| III | β-Picoline | (CH$_3$) 6,4 | (H) 5,6 | (CH$_3$) 1,3 | (H) 1,8 | (H) 3,6 | (H) 9,7 | — | — | 0,1 | 0,4 | 4,4 |
| IV | γ-Picoline | (CH$_3$) 4,6 | (H) 5,8 | (H) 2,4 | (CH$_3$) 0,6 | (H) 2,4 | (H) 5,8 | — | — | 0,2 | 0,3 | 3,5 |
| V | Collidine | (CH$_3$) 7,6 | (CH$_3$) 4,8 | (H) 3,8 | (CH$_3$) 2,4 | (H) 3,8 | (CH$_3$) 4,8 | — | — | 0,4 | 1,4 | 7,8 |
| VI | Collidine, base | — | (CH$_3$) 4,5 | (H) 2,0 | (CH$_3$) 1,1 | (H) 2,0 | (CH$_3$) 4,5 | — | — | — | — | — |
| VII | Quinoline | (CH$_3$) 8,6 | (H) 14,9 | (H) 7,6 | (H) 2,9 | (H) 2,2 | (H) 0,6 | (H) 1,0 | (H) 2,5 | 0,2 | 0,8 | 5,0 |
| VIII | Quinaldine | (CH$_3$) 4,1 | (CH$_3$) 3,1 | (H) 2,5 | (H) 2,3 | (H) 1,9 | (H) 0,9 | (H) 1,3 | (H) 2,1 | 0,3 | 0,6 | 4,9 |
| IX | Lepidine | (CH$_3$) 6,9 | (H) 13,5 | (H) 4,3 | (CH$_3$) 1,1 | — | — | — | (H) 2,3 | 0,2 | 0,4 | 4,7 |
| X | Isoquinoline | (H) 11,1 | (CH$_3$) 7,1 | (H) 7,0 | (H) 2,4 | (H) 1,0 | (H) 0,3 | (H) 0,6 | (H) 2,8 | 0,6 | 0,8 | 5,4 |
| XI | 2-Methylbenzothiazole | — | (CH$_3$) 3,8 | (CH$_2$) 4,5<br>(CH$_3$) 1,3 | (H) 1,4 | (H) 0,9 | (H) 0,9 | (H) 2,4 | — | 0,3 | 0,8 | 5,1 |
| XII | 2-Methyl-5-methoxy-6-methylmercaptobenzothiazole | — | (CH$_3$) 4,6 | (CH$_2$) 6,6<br>(CH$_3$) 2,2 | (H) 1,8 | (CH$_3$) 0,6 | (CH$_3$) 0,9 | (H) 2,6 | — | 0,5 | 0,7 | 6,0 |
| XIII | 2-Methyl-3-phenyl-6-cyanobenzimidazole | — | (CH$_3$) 5,0 | (CH$_2$) 8,3<br>(CH$_3$) 1,2 | (H) 1,1 | (H) 0,9 | — | (H) 2,1 | — | 0,6 | 1,1 | 5,8 |

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*The proton form is given in parentheses.

TABLE 2. Lanthanide Induced Shifts (ppm) of Protons in the Tosylates of Symmetric Cyanine Dyes, $X^+ = CH(CH{=}CH)_nXTos^-$*

| Compound | Heterocyclic nucleus X | n | Solvent | Cation† | | | | | | Anion | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | N—R | 1-H | 2-H | 3-H | 4-H | 5-H | CH$_3$ | 3-H | 2-H |
| XIV | N-Ethylbenzothiazolyl-2 | 0 | CD$_2$Cl$_2$ | (CH$_2$) 1,6<br>(CH$_3$) 1,1 | 1,6 | — | — | — | — | 0,0 | 0,2 | 2,9 |
| XV | N-Ethylbenzothiazolyl-2 | 1 | CD$_2$Cl$_2$ | (CH$_2$) 0,7<br>(CH$_3$) 0,5 | 0,5 | 0,5 | 0,5 | — | — | 0,1 | 0,3 | 2,5 |
| XVI | N-Ethylbenzothiazolyl-2 | 2 | CD$_2$Cl$_2$ | (CH$_2$) 0,8<br>(CH$_3$) 0,6 | 0,3 | 0,4 | — | 0,4 | 0,3 | 0,1 | 0,2 | 3,5 |
| XVII | N-Methyl-3,3-dimethylindolenyl-2 | 1 | CDCl$_3$ | (CH$_3$) 3,1 | 2,3 | 0,9 | 2,3 | — | — | −0,1 | 0,0 | 2,1 |

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*The proton form is given in parentheses.

†Numbering of the chain: $X{-}C^1H{=}C^2H{-}C^3H{=}\ldots{=}X^+$.

TABLE 3. Lanthanide Induced Shifts of Protons of the $N-CH_3(N-C_2H_5)$ Group in Tosylates of Asymmetric Cyanine Dyes $X_1^+{=}CH-CH{=}CH-X_2Tos^-$*

| Compound | Nucleus $X_1$ | Nucleus $X_2$ | Shifts (ppm) of protons of $N-CH_3$ ($N-C_2H_5$) group | |
|---|---|---|---|---|
| | | | in $X_1$ | in $X_2$ |
| XVIII | 1-Methyl-3,3-dimethylindolenyl-2 | 3-Methylbenzothiazolyl-2 | ($CH_3$) 2,2 | ($CH_3$) 8,7 |
| XIX | 1-Methyl-3,3-dimethylindolenyl-2 | 1-Methylquinolyl-2 | ($CH_3$) 0,9 | ($CH_3$) 4,2 |
| XX | 3-Ethylbenzoxazolyl-2 | 1-Ethylquinolyl-2 | ($CH_2$) 1,0<br>($CH_3$) 0,8 | ($CH_2$) 1,7<br>($CH_3$) 1,1 |

*The proton form is given in parentheses.

more weakly than the proton signals of the corresponding quaternary salts. This can be explained by the positive charge of the cation in the cyanine dyes of symmetric structure being delocalized over the extended conjugation chain as a result of which the anion is paired with the cation less stably and the residence time near the heterocyclic moieties in the complex is decreased. The coordination of the LSR to the tosylate anion remains almost the same (Table 2). Especially interesting are the results of coordination of $Eu(fod)_3$ to the tosylates of asymmetric dyes XVIII-XX (Table 3). The LIS observed for the protons of the cation are found to be strongly dependent on the electronic asymmetry of the dye cation, which is explained by the difference in the electron-donating ability (D) of the heterocyclic nucleus of the dye. If the electron-donating ability is high, as for example in dyes XVIII and XIX, then the proton signals of the more electron-donating heterocyclic nucleus are shifted more strongly under the effect of the LSR than the proton signals of the less electron-donating heterocycle. If the dye contains residues of similar electron-donating ability (XX), then the signals of both auxochromes are shifted practically identically under the effect of the LSR, and the absolute value of the signals falls.

The difference in the LIS for the $NCH_3$ ($NC_2H_5$) group can be used for comparison of the relative electron-donating ability of heterocyclic residues in the asymmetric dyes. In Table 4, the values of D for some heterocycles in the asymmetric dye tosylates are given. The values of D from deviations of the corresponding terminal groups [4, 5] are given for comparison. A satisfactory correlation between the values of D found by us and those taken from the literature is seen. The lowered value of D from the PMR data for the 3,3-dimethylindolene nucleus by comparison with those from the deviations can be related to the presence of steric hindrances which the geminal methyl groups create with the tosylate anion near the heterocyclic nucleus.

The method of determination of the relative electron-donating ability of heterocyclic residues from LIS values (accounting for steric factors) can be recommended in those cases when the symmetric dyes are difficultly obtained or the determination of deviations from electronic spectra cause difficulties.

The mode of coordination and geometric structure which is formed by the adducts are important to know when studying organic molecules by the LSR method. It is known in the literature [1] that the coordination of the LSR in complexes with organic salts occurs through the anion, with the cation and anion forming a tight ion pair. An exemplary diagram of such a complex ($Eu(fod)_3$ with N-methylquinoline tosylate) is shown in Fig. 1, a.

Using the graphics program LINIYa [6], we attempted to determine the structure of LSR adducts with the salts II-IV, VII, X, XI, and XIII. Since the exact location of the localized coordination center (anion) in this case is unknown, its coordinates together with those sought for the lanthanide ion in the adduct were optimized by a gradient method. The minimum of the function S was determined:

$$S=f(x_{Eu}, y_{Eu}, z_{Eu}; x_A, y_A, z_A), \tag{1}$$

where S is the sum of the root mean square deviations for the calculated and experimental LIS; $x_{Eu}$, $y_{Eu}$, and $z_{Eu}$ are the europium ion coordinates in the adduct, and $x_A$, $y_A$, and $z_A$ are the coordinates of the anion.

TABLE 4. Comparison of the Relative Electron-Donating Ability, D, of Heterocyclic Nuclei in Carbocyanine Dyes*

| Heterocyclic Nucleus | D, % | | |
|---|---|---|---|
| | from deviations of indocarbocyanines | from deviations of indocarbocyanines | from PMR spectral data |
| N-Methyl-3,3-indolenyl-2 | 49,5 | — | 21,4 |
| N-Ethylbenzoxazolyl-2 | 65,7 | 44,8 | 58.8 |
| N-Methylbenzothiazolyl-2 | 71,5 | 69,0 | 84.6 |
| N-Methylquinolyl-2 | 100,0 | 100,0 | 100.0 |

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*Electron-donating ability of the quinoline nucleus was taken as 100%.

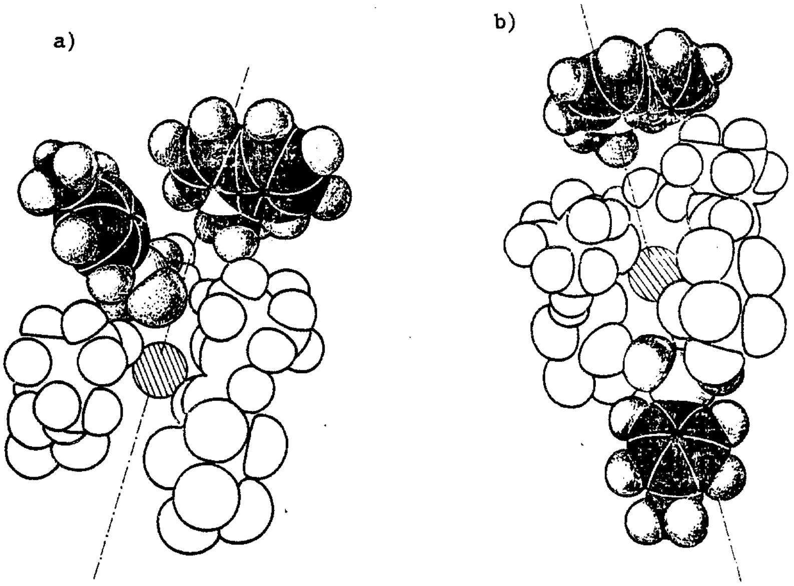

Fig. 1. Diagram of a possible structure of LSR adducts with organic salts for the Eu(fod)$_3$ complex with N-methylquinolinium tosylate (the cation and anion are shaded; the LSR is not shaded but the central Eu$^{3+}$ ion is striped; the main magnetic axis is shown by a dashed—dotted line): a) the cation and anion form a tight ion pair; and b) the cation and anion are located on opposite sides of the LSR.

Several variations of the calculations were carried out for each of the salts II-IV. (1) Calculations were based only on the LIS of protons in the anion; a global minimum of the function was obtained which corresponded to the position of the lanthanide ion in the adduct at a distance of 2.3-2.5 Å from the sulfo group of the anion. (2) A variation in the position of the anion relative to the cation was done, where (a) it was assumed that the cation and anion form a tight ion pair; (b) a structure with an ion pair separated by the chelate was assumed, in which the anion and cation are located on opposite sides of the LSR (Fig. 1, b). As it happened, for both variations a point with good correlation of the calculated LIS with the experimental values could be found. The distance from the europium ion to the coordination center in both cases for the salts II-IV were 2.4-2.5 Å, i.e., practically coincident with that calculated using the LIS of the protons in the anion.

Thus, the structure proposed earlier for the LSR adducts with the heterocyclic ammonium salts [1] is not the only one possible. Calculations based on the pseudocontact nature of the LIS allow two structural variants which are practically equivalent from a mathematical point of view to be found for the LSR—substrate adduct for compounds I-XIII. This result is related to the multivalued character of the function (1). For choosing between the structural variants found for the adducts, additional studies by other methods should obviously be pursued.

## EXPERIMENTAL

PMR spectra were done on a Bruker WP-100 SY spectrometer with a working frequency of 100.13 MHz. TMS was used as an internal standard, deuterated chloroform and methylene chloride were used as solvents, $Eu(fod)_3$ served as the shift reagent. Spectra were measured at 25°C. Calculations were carried out on an IBM CM-1.

Alkyltosylates of heterocyclic bases were obtained by melting equimolar quantities of bases with methyl- or ethyltosylate. The solid products obtained were crystallized from acetone or a mixture of ethanol—ethylacetate, 1:6.

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