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Stereo-controlled substitution on tris(2-pyridylmethyl)amine ligands and chirality tuning of luminescence in their lanthanide complexes

Takashi Yamada,[a] Satoshi Shinoda,[a] Jun-ichi Uenishi[b] and Hiroshi Tsukube[a,*]

[a]*Department of Chemistry, Graduate School of Science, Osaka City University, Sugimoto, Sumiyoshi-ku, Osaka 558-8585, Japan*
[b]*Department of Pharmaceutical Organic Chemistry, Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607-8412, Japan*

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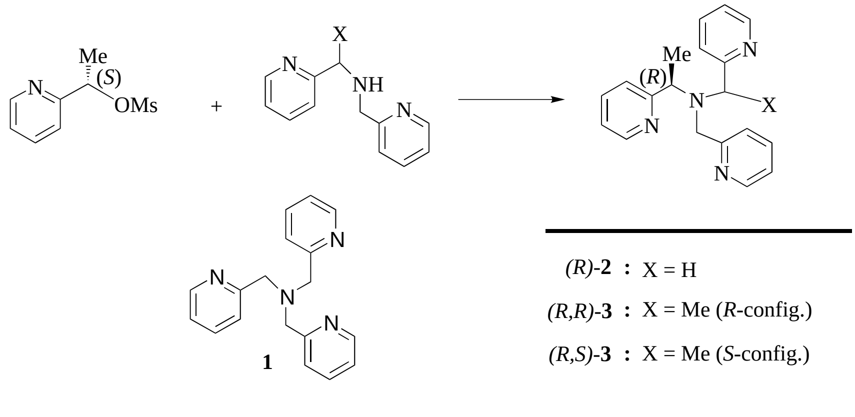
Abstract—A series of tris(2-pyridylmethyl)amine ligands including one or two asymmetric centers were synthesized in a stereo-controlled fashion, and their Tb^{3+} and Eu^{3+} complexes offered characteristic luminescence properties depending on the ligand stereochemistry.

Tris(2-pyridylmethyl)amine derivatives are representative of tripodal ligands effective for transition metal and lanthanide cations. Their complexes have been widely employed in catalysis, extraction, chemo-sensing and other chemical processes.[1,2] The asymmetric introduction of substituents into the tris(2-pyridylmethyl)amine skeleton offered interesting functions in several asymmetric synthesis.[3] Canary et al. recently presented a tris(2-pyridylmethyl)amine derivative having one asymmetric center as a chiral solvating reagent for sulfoxides and a chromophoric ligand for metal complex devices.[4] Since the examples reported earlier were limited to have only one asymmetric center, multiple substitution on the tris(2-pyridylmethyl)amine in a stereo-controlled fashion provides new potential in the development of intelligent metal complexes. Here, we report the stereo-controlled synthesis of tris(2-pyridylmethyl)amine derivatives (*R*)-**2**, (*R*,*R*)-**3** and (*R*,*S*)-**3** and chirality-enhanced luminescence of their lanthanide complexes. These tris(2-pyridylmethyl)amine derivatives, which had one and two asymmetric centers in the tris(2-pyridylmethyl)amine skeletons, were derived from chiral 1-(2-pyridyl)ethyl methanesulfonates[5] in a stereo-controlled fashion. They formed stable Tb^{3+} and Eu^{3+} complexes that exhibited characteristic luminescence properties depending on stereochemistry of the ligands.



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(*R*)-**2** : X = H
(*R,R*)-**3** : X = Me (*R*-config.)
(*R,S*)-**3** : X = Me (*S*-config.)

Scheme 1. Structures of **1**, (*R*)-**2**, (*R*,*R*)-**3** and (*R*,*S*)-**3**.

Keywords: chirality; tris(2-pyridylmethyl)amine; lanthanide complex; luminescence.

* Corresponding author. Tel./fax: +81-6-6605-2560; e-mail: tsukube@sci.osaka-cu.ac.jp

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Since the luminescence intensity of the lanthanide complex was remarkably enhanced by tuning of the ligand chirality, the stereo-controlled substitution on the ligand proved to be an effective means of manipulating the functions of lanthanide complexes in the non-asymmetric luminescence process.[6,7]

A series of tris(2-pyridylmethyl)amine derivatives (*R*)-**2**, (*R*,*R*)-**3** and (*R*,*S*)-**3** were synthesized by reaction of corresponding chiral pyridylethanol methanesulfonates with di(pyridylmethyl)amines (Scheme 1). Mono-substituted derivative (*R*)-**2** was typically prepared from (*S*)-1-(2-pyridyl)ethyl methanesulfonate and di(2-pyridylmethyl)amine in 30% yield. Its molar circular dichroic absorption $\Delta\varepsilon$ was recorded as +3.60 cm^2 $mmol^{-1}$ (1.00×10^{-4} mol/L in CH_3OH). Since this value was comparable with that reported ($\Delta\varepsilon=+3.55$ cm^2 $mmol^{-1}$, 1.00×10^{-4} mol/L in CH_3OH),[4] the substitution proceeded via S_N2 mechanism with complete inversion of the asymmetric center. Disubstituted ligands (*R*,*R*)-**3** and (*R*,*S*)-**3** were newly synthesized as follows: 6 equiv. of (*S*)-1-(2-pyridyl)ethyl methanesulfonate was treated with 2-aminomethylpyridine in the presence of *N*-ethyldiisopropylamine (CH_3CN, 60°C, 2 days) to give (*R*,*R*)-**3** in 30% yield;[8] 1.5 equiv. of 2-aminomethylpyridine was treated with (*S*)-1-(2-pyridyl)ethyl methanesulfonate, followed by addition of 3 equiv. of (*R*)-1-(2-pyridyl)ethyl methanesulfonate (*N*-ethyldiisopropylamine, CH_3CN, 60°C, 3 days) to give (*R*,*S*)-**3** in 9% yield.[8] Their stereochemical purities were confirmed >95% *de* for (*R*,*S*)- and (*R*,*R*)-**3** by GPC (JAIGEL-1H and 2H, Japan Analytical Ind. Ltd, $CHCl_3$) and ^{1}H NMR determinations. These ligands had sufficient optical purities to evaluate the stereochemical effects on metal complex functions.

As reported with tris(2-pyridylmethyl)amine **1**,[2] (*R*)-**2**, (*R*,*R*)-**3** and (*R*,*S*)-**3** readily formed Tb^{3+} and Eu^{3+} complexes that exhibited characteristic emission spectra in acetonitrile.[9] Fig. 1 illustrates notable differences in emission intensity among the lanthanide complexes of tris(2-pyridylmethyl)amine derivatives, though they showed similar absorption spectra. When four kinds of Tb^{3+} complexes were excited at 260 nm, characteristic luminescence bands were recorded at 487, 543, 585 and 620 nm via ligand-to-metal energy transfer. The largest enhancement of luminescence intensity was observed with disubstituted ligand (*R*,*S*)-**3**. The relative emission intensity at 543 nm was estimated to be 4.3 for (*R*,*S*)-**3**/**1**, 1.6 for (*R*)-**2**/**1** and 1.5 for (*R*,*R*)-**3**/**1**. (*R*,*S*)-**3** was confirmed to offer 2.9 times more intense emission than (*R*,*R*)-**3**. The lifetime of the luminescence increased in a similar order: 1.41 ms for (*R*,*R*)-**3** <1.47 ms for **1**=1.48 ms for (*R*)-**2** <1.80 ms for (*R*,*S*)-**3**. The significant effects of ligand chirality were also confirmed in the Eu^{3+} luminescence processes and the enhanced luminescence bands were observed at 590, 614 and 698 nm. (*R*,*S*)-**3** gave 2.2 fold more intense luminescence, while (*R*)-**2** and (*R*,*R*)-**3** showed almost the same intensity as unsubstituted **1**. The relative intensity of the emission band at 614 nm to that at 590 nm was compared, because this is a sensitive indication of the symmetry of Eu^{3+} complex.[10] The complex with (*R*,*S*)-**3** exhibited much smaller value (2.6) than those (ca. 4.3) with **1**, (*R*)-**2** and (*R*,*R*)-**3**, indicating that (*R*,*S*)-**3** formed the Eu^{3+} complex with higher symmetry than **1**, (*R*)-**2** or (*R*,*R*)-**3**. To avoid ligand-to-metal energy transfer, direct excitation of the Eu^{3+} ion at 395 nm was performed with these four complexes.[11] Interestingly, (*R*,*S*)-**3** gave 1.7 times more intense emission than the other three ligands, demonstrating that the stereochemistry of the tris(2-pyridylmethyl)amine derivatives had great influences on the metal luminescence and the ligand-to-metal energy transfer processes. (*R*,*S*)-**3** probably provides highly symmetric coordination with lanthanide centers and effectively isolates them from the solvent molecules. The stereoisomers can, in principle, be considered different ligands, but the effects of ligand chirality on the lanthanide luminescence phenomena have rarely been reported.[12] The present results revealed that the tuning of the ligand chirality effectively enhanced the functions of lanthanide complexes in the apparently non-asymmetric luminescence process.

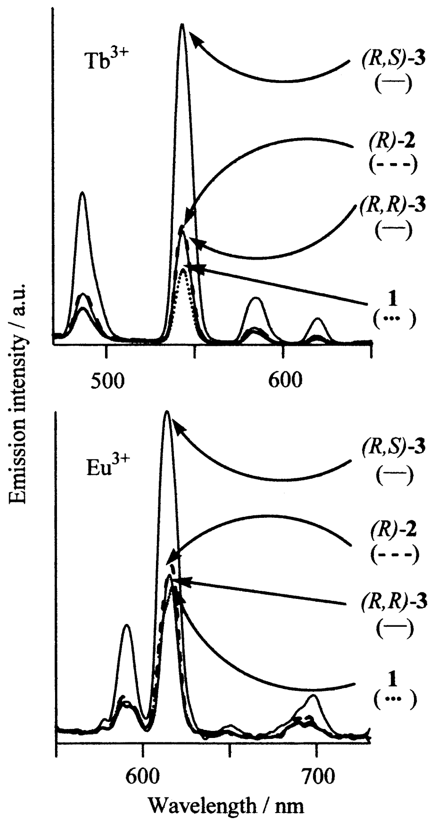

Figure 1. Emission spectra of Tb^{3+} (upper) and Eu^{3+} (lower) complexes with **1**, (*R*)-**2**, (*R*,*R*)-**3** and (*R*,*S*)-**3**. $Ln(CF_3SO_3)_3$: 0.1 mM; ligand; 0.3 mM in CH_3CN at room temperature. Excitation at 260 nm.

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8. (*R*,*R*)-**3**: Yellow oil, >95% *de*; $[\alpha]_D^{20}$ +108 (c=1.05, $CHCl_3$); R_f=0.53 (5% EtOAc in CH_2Cl_2), ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (2H, dq, J=4.9, 1.0 Hz), 8.42 (1H, dq, J=4.9, 1.0 Hz), 7.67–7.52 (4H, m), 7.30 (2H, d, J=8.0 Hz), 7.15–7.00 (3H, m), 4.36 (1H, d, J_{gem}=16.6 Hz), 4.13 (2H, q, J=6.8 Hz), 3.83 (1H, d, J_{gem}=16.4 Hz), 1.43 (6H, d, J=6.8Hz); ^{13}C NMR (400 MHz, $CDCl_3$): δ 163.4, 163.3, 148.7, 148.5, 136.1, 122.8, 122.3, 121.7, 121.2, 60.4, 52.8 and 17.8; HRMS calcd for $C_{20}H_{23}N_4$: $M+H^+$, 319.1922. Found: m/z 319.1920. (*R*,*S*)-**3**: Yellow crystals, mp 91–92°C; >95% *de*; $[\alpha]_D^{20}$ −4 (c=0.52, $CHCl_3$); R_f=0.54 (5% EtOAc in CH_2Cl_2), ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (2H, dq, J=4.9, 1.0 Hz), 8.43 (1H, dq, J=4.9, 1.0 Hz), 7.65 (2H, td, J=7.8, 2.0 Hz), 7.58–7.53 (3H, m), 7.42 (1H, d, J=7.8 Hz), 7.15–7.04 (3H, m), 4.20 (2H, q, J=6.8 Hz), 4.02 (2H, s), 1.27 (6H, d, J=6.8 Hz); Anal. calcd for $C_{20}H_{22}N_4$: C, 75.44; H, 6.96; N, 17.60. Found: C, 75.56; H, 6.98; N, 17.60.
9. We carried out luminescence experiments with 3:1 complexes (ligand: Tb^{3+} or Eu^{3+}). Based on UV titrations, tris(2-pyridylmethyl)amines **1**–**3** had similar log K values for 3:1 complexation: 18.6–19.1 for Tb^{3+} and 17.8–18.4 for Eu^{3+}.
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