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Di- and tetracarboxylate ligands for highly luminescent terbium(III) complexes on the basis of sulfonylcalix[4]arene scaffold

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Abstract—New di- (**2**) and tetracarboxylate ligands (**4**) were prepared on a sulfonylcalix[4]arene platform by O-alkylation of thiacalix[4]arene with ethyl bromoacetate, followed by hydrolysis of the ester function and oxidation of the sulfide bridges. The sulfonyl-based ligands **2** and **4** formed luminescent 1:1 complexes with terbium(III) ion having higher luminescent quantum yield ($\Phi = 0.29_1$ and 0.28_7, respectively) than 1:1 complexes of the corresponding thiacalix[4]arene-based di- (**1**) and tetracarboxylate ligands (**3**) ($\Phi = 0.03_8$ and 0.00_3, respectively), implying higher efficiency of sulfonyl ligands (**2** and **4**) than those of thia ligands (**1** and **3**) in the energy transfer process.

Energy-transfer luminescence is the emission from the metal center of a lanthanide(III) complex, the excitation energy for which is transferred from the coordinated ligand in T_1 state. Owing to the mechanism, the energy-transfer luminescence has characteristic features such as long lifetime (μs–ms order), large Stokes shift (200–300 nm), and sharp emission band, which are attractive from the viewpoint of applications to luminescent labeling and sensing.[1] For such purposes, design of the ligand plays the key role, where the prerequisites are (1) thermodynamic and kinetic stability of the formed complex; (2) ability to shield Ln^{III} ion from solvent molecule; and (3) availability of light absorbing antenna having suitable T_1 level responsible for the energy transfer. So far, calixarenes have served as a hopeful molecular scaffold to construct ligands for such use owing to the feasibility of chemical modifications at the phenol moiety with functional groups to fulfill the above-mentioned requirements.[2] On the contrary, Shinkai and co-workers reported energy transfer luminescence of a Tb^{III} complex with calix[4]arene-*p*-tetrasulfonate (CAS), which, notably, does not have any auxiliary ligating and antenna groups.[3] Recently, we found that sulfur-bridged calix[4]arenes, that is, thia- and sulfonylcalix[4]arene-*p*-tetrasulfonates (TCAS and SO_2CAS, respectively) can also be used as the ligand to give Tb^{III} complexes, giving higher luminescent intensity and longer lifetime (τ) than CAS did.[4] The high efficiency of the sulfur-containing ligands is ascribed to the high efficiency in light absorption, namely large molar absorptivity (ε) as well as the coordination ability of the bridging sulfur-group to reduce the number of the coordinated water molecules. In quest of superior ligands for the luminescence, we designed ligands **2** and **4** based on sulfonylcalix[4]arene (SO_2CA) as a scaffold because of the larger ε than that of thiacalix[4]arene (TCA), where two and four carboxymethyl groups are introduced to afford more stable complexes with better shielding ability of the metal center from water. Here, we report the synthesis of the ligands, their complexation behavior toward Tb^{III} ion, and the luminescence properties.

Although ligands **2** and **4** were designed on a SO_2CA scaffold, we were reluctant to take the direct etherification route by reacting with ethyl bromoacetate considering the low nucleophilicity of the phenoxide O^- flanked by two *o,o′*-sulfonyl groups via delocalization of the charge through resonance.[5,6] Instead, we took the route of the initial O-functionalization of TCA followed by oxidation of the bridging sulfur to sulfone: Heating a

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Keywords: Calixarenes; Ligand; Luminescence; Terbium.

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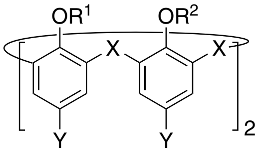

	X	Y	R^1	R^2
CAS	CH_2	SO_3^-	H	H
TCA	S	Bu^t	H	H
TCAS	S	SO_3^-	H	H
SO_2CA	SO_2	Bu^t	H	H
SO_2CAS	SO_2	SO_3^-	H	H
1	S	Bu^t	CH_2CO_2H	H
2	SO_2	Bu^t	CH_2CO_2H	H
3	S	Bu^t	CH_2CO_2H	R^1
4	SO_2	Bu^t	CH_2CO_2H	R^1
5	S	Bu^t	CH_2CO_2Et	H
6	S	Bu^t	CH_2CO_2Et	R^1
7	SO_2	Bu^t	CH_2CO_2Et	R^1

mixture of TCA, 8-fold excess of ethyl bromoacetate, and Na_2CO_3 as a base catalyst in acetone gave cone-shaped tetra-O-alkylated **6**.[7] According to the method reported by Lhotak[8] oxidation of compound **6** by use of large excess of 3-chloroperoxybenzoic acid (MCPBA) afforded sulfonyl **7** in a good yield (74%). However, attempted hydrolysis of the ester function of **7** by heating with K_2CO_3 as the base in DMSO–water gave a mixture of bare SO_2CA and mono-, di-, and tricarboxylates of one. This suggests that the *o*,*o*′-disulfonyl-substituted phenoxy moiety of **7** is highly susceptible to nucleophilic attack by OH^- to release the (carbonyl)methoxy moiety to give the phenols rather than the desired ester-hydrolysis products. In other words, SO_2CA behaved as a 'good' leaving group as indicated above.

Hence, as an alternative route to **4**, cone-shaped **6** was first subjected to hydrolysis to give tetracarboxylic acid **3** as reported elsewhere,[9] which was in turn oxidized with MCPBA to afford **4** in a good yield (85%).[10] X-ray analysis of **4** (Fig. 1)[11] showed high disorder mainly in *tert*-butyl groups to result in a large *R* value, but the resolution is sufficient to establish that the cone-shaped structure was maintained during the initial hydrolysis and subsequent oxidation processes as well as to show that one 1,4-dioxane molecule (disordered) was included in the cavity. ^{1}H NMR of **4** in methanol-d_4 exhibited three singlet but broad peaks for Bu^t, $–CH_2O–$ (Fig. 2), and ArH protons, suggesting certain molecular motion reducing molecular symmetry from ideal C_4 symmetry of cone conformation. This can be rationalized by assuming C_{2v}–C_{2v} conformational interconversion observed in tetra-O-alkylated calix-,[12] thiacalix-,[13,14] and sulfonylcalix[4]arenes in solutions.[8]

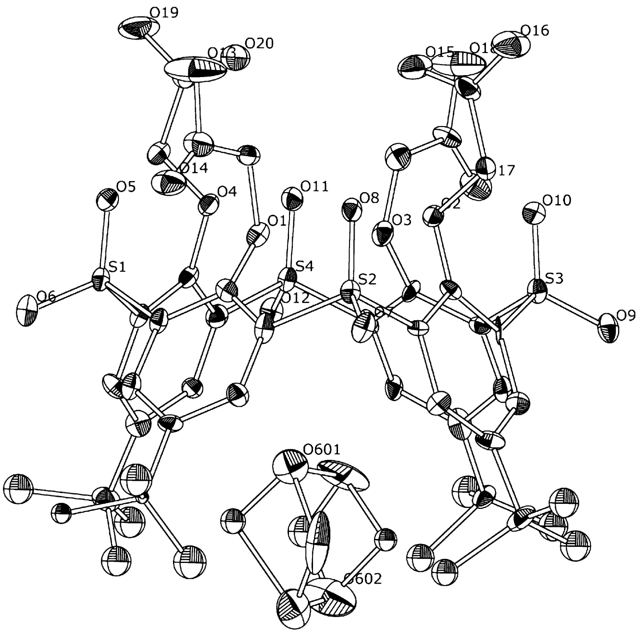

Figure 1. ORTEP drawing of ligand **4** with thermal ellipsoids drawn at 30% probability. For clarity, parts of methyl groups found in disordered Bu^t moiety are shown.

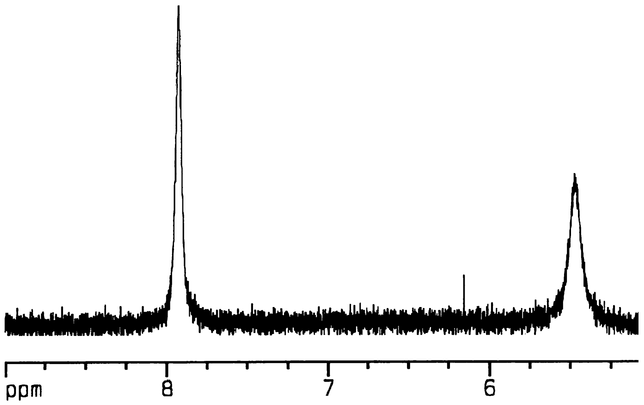

Figure 2. Aromatic and methylene part of ^{1}H NMR spectrum for ligand **4** (298 K, CD_3OD).

For preparation of SO_2CA-based dicarboxylic acid **2**, synthetic route similar to that for **4** was employed: First, a mixture of TCA, 2-fold excess of ethyl bromoacetate, and Na_2CO_3 in acetone were heated to afford *syn*-di-*O*-alkylated TCA (**5**),[9] in which a pair of distal phenol oxygen atoms have two (ethoxycarbonyl)methyl groups directing *syn* with respect to a mean plane of four sulfur atoms. Then the ester function of **5** was hydrolysed by heating with KOH in ethanol–water mixture to give TCA-dicarboxylate **1**,[9] which was further treated with MCPBA to afford **2** in a yield of 84% from **1**.[15] The *syn* conformation of **2** was evidenced by the ^{1}H NMR spectrum showing two sets of sharp singlet peaks for Bu^t and ArH, which was maintained during the transformations from *syn*-di-O-alkylated **5**.

In methanolic solution, SO_2CA-based dicarboxylic acid **2** has an absorption maximum at 290 nm, which originates from π–π* transition at the aromatic ring.[16] In the presence of an excess of triethylamine, another absorption band around 350 nm appeared, suggesting dissociation of the phenolic OH of **2**. Upon addition of terbium(III) nitrate, the absorption at 338 nm linearly increased up to $[Tb^{III}]_T/[\mathbf{2}]_T = 1$ (Fig. 3), meaning that **2** formed 1:1 complex. TCA-based **1** similarly behaved to

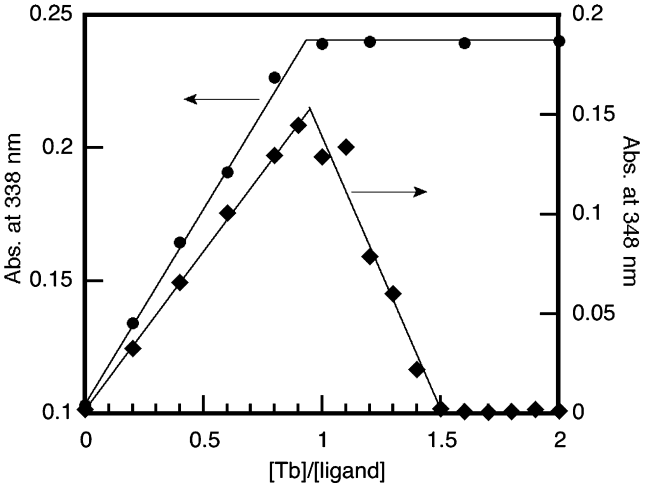

Figure 3. Molar ratio plots for Tb^{III}-sulfonyl ligand systems. Closed circle: $[\mathbf{2}]_T = 2.0 \times 10^{-5}$ M, $[NEt_3]_T = 2.0 \times 10^{-4}$ M, diamond: $[\mathbf{4}]_T = 2.0 \times 10^{-5}$ M, $[NEt_3]_T = 1.0 \times 10^{-4}$ M.

form 1:1 complex with Tb^{III}, the absorption maximum of which is at 320 nm originating from π–π* transition at the phenoxy moiety. Notably, the ε value for Tb^{III} complex with SO_2CA-based **2** at the absorption maximum is larger than that with TCA-based **1** (Table 1), meaning that higher efficiency of SO_2CA scaffold in light absorption than that of TCA one is retained after di-O-alkylation.

Dicarboxylate ligands **1** and **2** formed 1:1 complex with Tb^{III} ion very rapidly, whereas tetracarboxylates **3** and **4** did very slowly. For instance, complexation of sulfonyl-based **4** with Tb^{III} ion took 10 h to reach equilibrium under $[Tb^{III}]_T/[\mathbf{4}]_T = 1$ at 45 °C. The molar ratio plot for **4** (Fig. 3) shows that 1:1 complex formed in the range $[Tb^{III}]_T/[\mathbf{4}]_T \leqslant 1$, whereas 2:3 (=ligand:metal) complex formed at $[Tb^{III}]_T/[\mathbf{4}]_T \geqslant 1.5$. Though **4** does not have protonic OH at the phenol moiety, there appeared a new absorption band at 348 nm upon formation of 1:1 complex, while intensity of the original band at 290 nm decreased but remained with significant intensity (Table 1). This strongly suggests that alkylated phenolic O groups of **4** are still able to coordinate to Tb^{III} center to significantly perturb energy levels of frontier orbitals of the phenol moiety. By contrast, the 2:3 complex does not have absorption band at 348 nm, suggesting that the phenolic O of **4** does no longer coordinate in the complex. For thia-based ligand **3**, 1:1 complex formation took 3 h under $[Tb^{III}]_T/[\mathbf{3}]_T \leqslant 1$ at 45 °C. The 1:1 complex of Tb^{III}-**3** only has absorption maximum in a short wavelength region at 285 nm rather than 348 nm as in the case of Tb^{III}-**4**, suggesting that phenolic O of ligand **3** does not coordinate to Tb^{III} center in effect. In terms of light absorbing ability, 1:1 Tb^{III}-**4** complex has smaller ε values than Tb^{III}-**3** does (Table 1), which may result from the splitting of absorption band of Tb^{III}-**4** into two at 290 and 348 nm. In summary, dicarboxylate ligands **1** and **2** rapidly formed 1:1 complex under a wide range of $[Tb^{III}]_T/[\text{ligand}]_T$ ratio, whereas tetracarboxylate ligands **3** and **4** slowly did 1:1 in the range of $[Tb^{III}]_T/[\text{ligand}]_T \leqslant 1$. The slow complex formation of, especially, SO_2CA-based tetracarboxylate **4** is indicative of high kinetic stability of the Tb^{III} complex.

Table 1. Photophysical properties of 1:1 complexes of Tb^{III} with **1**–**4**

Ligands	λ_{max} (nm)	ε (M^{-1} cm^{-1})	Φ
1	320	10,600	0.0379 ± 0.0007
2	345	13,000	0.291 ± 0.003
3	285	11,500	0.00322 ± 0.00012
4	294, 348	9300, 6500	0.287 ± 0.005

Methanolic solutions containing 1:1 complex of ligands **1**–**4** with Tb^{III} ion exhibited strong luminescence consisting of four emission bands (Fig. 4a), which correspond to the transitions from $^5D_4$ to $^7F_6$ (around 490), $^7F_5$ (545), $^7F_4$ (580), and $^7F_3$ (620 nm) at Tb^{III} center. Band shapes slightly differ among complex species, implying that the coordination environment provided by these ligands has subtle influences on the f–f electronic transition in the Tb^{III} center. Excitation spectrum of each complex shown in Fig. 4b has maxima corresponding to the absorption maxima, indicating that Tb^{III} center

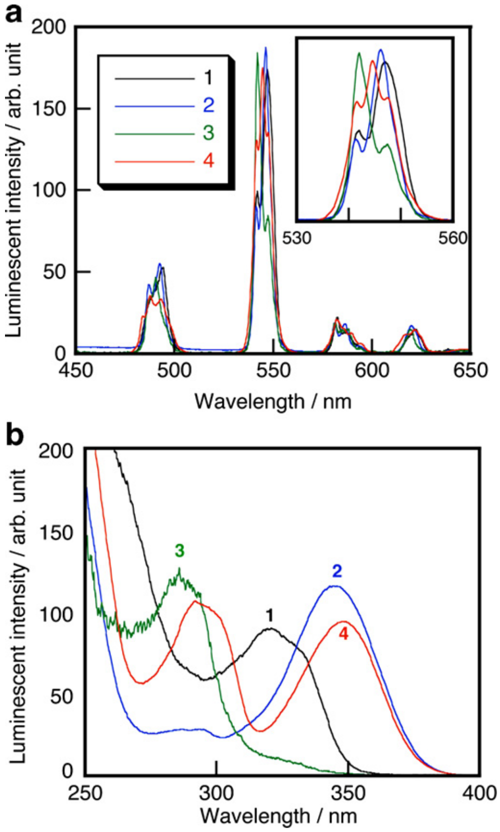

Figure 4. Emission (a) and excitation (b) spectra for Tb^{III} complexes with ligands **1**–**4**. (a) (1) $[\mathbf{1}] = 2 \times 10^{-5}$, $[Tb] = 5 \times 10^{-6}$, $[NEt_3] = 5 \times 10^{-4}$ M, $\lambda_{ex} = 320$ nm; (2) $[\mathbf{2}] = 6 \times 10^{-6}$, $[Tb] = 1 \times 10^{-6}$, $[NEt_3] = 1 \times 10^{-4}$ M, $\lambda_{ex} = 345$ nm; (3) $[\mathbf{3}] = 6 \times 10^{-5}$, $[Tb] = 2 \times 10^{-5}$, $[NEt_3] = 6 \times 10^{-4}$ M, $\lambda_{ex} = 290$ nm and (4) $[\mathbf{4}] = 6 \times 10^{-6}$, $[Tb] = 1 \times 10^{-6}$, $[NEt_3] = 1 \times 10^{-4}$ M, $\lambda_{ex} = 348$ nm and (b) (1) $[\mathbf{1}] = 2 \times 10^{-6}$, $[Tb] = 1 \times 10^{-6}$, $[NEt_3] = 5 \times 10^{-5}$ M, $\lambda_{em} = 546$ nm; (2) $[\mathbf{2}] = 2 \times 10^{-6}$, $[Tb] = 1 \times 10^{-6}$, $[NEt_3] = 5 \times 10^{-5}$ M, $\lambda_{em} = 545$ nm; (3) $[\mathbf{3}] = 3 \times 10^{-6}$, $[Tb] = 1 \times 10^{-6}$, $[NEt_3] = 4 \times 10^{-5}$ M, $\lambda_{em} = 544$ s nm and (4) $[\mathbf{4}] = 2 \times 10^{-5}$, $[Tb] = 2 \times 10^{-6}$, $[NEt_3] = 2 \times 10^{-4}$ M, $\lambda_{em} = 544$ nm.

Table 2. Emission lifetimes of 1:1 complexes of Tb^{III} with **1**–**4** in CH_3OH (τ_H) and CD_3OD (τ_D) and the number of coordinating methanol (q) ($N = 5$)

Ligands	τ_H (ms)	τ_D (ms)	q
1	0.183 ± 0.001	0.190 ± 0.001	1.8
2	1.40 ± 0.01	2.34 ± 0.01	2.4
3	1.57 ± 0.03	2.71 ± 0.01	2.2
4	$1.47 \pm 0.00_4$	2.42 ± 0.01	2.2

is excited by energy absorbed by and transferred from the phenol moiety. Luminescence quantum yields (Φ) for 1:1 complexes of Tb^{III} with ligands **1**–**4** were determined (Table 1). Surprisingly, TCA-based di- (**1**) and tetracarboxylate ligands (**3**) gave complexes with substantially smaller Φ values than un-*O*-functionalized TCAS did ($\Phi = 0.15$),[4] implying that energy-transfer efficiency decreased by introducing substituents at the phenolic O to affect the T_1 level responsible for excitation of Tb^{III} center. On the other hand, SO_2CA-based ligands **2** and **4** have much higher quantum yield as compared to TCA-based **1** and **3**. Detailed analysis of the energy levels of the complexes should wait further study, but at least one can say that SO_2CA-based **2** and **4** are essentially more efficient ligands to transfer the absorbed energy from its T_1 state to $^5D_4$ level of Tb^{III} center than thia-based **1** and **3**. In order to evaluate the ability of carboxylate ligands **1**–**4** to shield Tb^{III} center from solvent molecules, we estimated the number of coordinating methanol (q) for the complex by use of Horrocks equation, $q = 8.4(\tau_H^{-1} - \tau_D^{-1})$,[17] where τ_H and τ_D are luminescent lifetimes of the complex in CH_3OH and CD_3OD, respectively (Table 2). As can be seen, the values of τ_H as well as τ_D are in the scale of ms order except for Tb^{III}-**1**. Irrespective of ligand species, the number q is ca. 2, which is smaller than the number of coordinating water to Tb^{III}-TCAS ($q = 4.5$) and SO_2-CAS ($q = 4.2$) complexes.[4] This implies that introducing carboxylate groups to TCA and SO_2CA scaffolds successfully enhances the ability to shield the Tb^{III} center.

In conclusion, here we prepared new di- and tetracarboxylate ligands (**2** and **4**, respectively) on a SO_2CA scaffold to form 1:1 complex having high luminescence quantum yields resulting from high efficiency in the energy transfer process. Considering additional advantages of Tb^{III} complexes derived from SO_2CA-based ligands such as longer wavelength of absorption maxima of Tb^{III}-**2** and -**4** complexes suitable for N_2 laser excitation, larger molar absorptivity of Tb^{III}-**2** complex, and high kinetic stability of Tb^{III}-**4** complex, **2** and **4** are promising ligands for analytical applications.

References and notes

1. *Lanthanide Probes in Life, Chemical and Earth Sciences: Theory and Practice*; Bünzli, J. C. G., Choppin, G. R., Eds.; Elsevier, 1989.
2. Sabbatini, N.; Guardigli, M.; Manet, I.; Ziessel, R. *Calixarenes 2001* **2001**, 583–597.
3. Sato, N.; Yoshida, I.; Shinkai, S. *Chem. Lett.* **1993**, 1261–1264.
4. Iki, N.; Horiuchi, T.; Oka, H.; Koyama, K.; Morohashi, N.; Kabuto, C.; Miyano, S. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2219–2225.
5. Oae, S.; Yoshihara, M.; Tagaki, W. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 951–958.
6. Matsumiya, H.; Takahashi, Y.; Iki, N.; Miyano, S. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1166–1172.
7. Iki, N.; Narumi, F.; Fujimoto, T.; Morohashi, N.; Miyano, S. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2745–2750.
8. Lhotak, P. *Tetrahedron* **2001**, *57*, 4775–4779.
9. Iki, N.; Morohashi, N.; Narumi, F.; Fujimoto, T.; Suzuki, T.; Miyano, S. *Tetrahedron Lett.* **1999**, *40*, 7337–7341.
10. Compound **4**: A mixture of cone **3**[9] (95.3 mg, 0.100 mmol) in acetonitrile (9 ml) and MCPBA (0.863 g, 5.00 mmol) in chloroform (8 ml) was heated at reflux for 12 h. After evaporation to dryness, the solid residue was washed with chloroform (10 ml) to remove *m*-chlorobenzoic acid. Recrystallization from methanol–water mixture afforded essentially pure sample of **4** (92.3 mg, Yield. 85.4%). Mp 345 °C (decomp.). IR (KBr, cm^{-1}): 3435 (OH), 2966 (CH), 1742 (C=O), 1331 (SO_2). ^1H NMR (400 MHz, acetone-d_6, 300 K) δ 1.22 (36H, br s, $C(CH_3)_3$), 5.54 (8H, br s, OCH_2), 7.96 (8H, br s, Ar*H*). FAB MS (NBA): *m*/*z* 1081.4 $[M+H]^+$.
11. *Crystallographic analysis*: A 20-ml glass vial containing 10 ml of a solution of **4** (30 mg) in 1,4-dioxane was left open in a dark place to allow slow evaporation of the solvent. After 5 days, colorless crystal suitable for X-ray analysis was obtained. X-ray data: $C_{64}H_{104}O_{32}S_4$, FW = 1513.75, monoclinic, C2 (#5), crystal dimensions $0.20 \times 0.20 \times 0.02$ mm, $T = 223$ K, Mo-Kα radiation, $a = 34.886(5)$, $b = 16.021(2)$, $c = 15.972(2)$ Å, $\beta = 103.7313(7)°$, $V = 8671.7(1)$ Å^3, $Z = 4$, $D_{Calcd} = 1.159$ g/cm^3, Full-matrix least-squares, $R = 0.103$ and $R_w = 0.317$ for observed 10,814 reflections, GOF = 1.24. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 612397. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
12. Arduini, A.; Fabbi, M.; Mantovani, M.; Mirone, L.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Org. Chem.* **1995**, *60*, 1454–1457.
13. Lang, J.; Dvorakova, H.; Bartosova, I.; Lhotak, P.; Stibor, I.; Hrabal, R. *Tetrahedron Lett.* **1999**, *40*, 373–376.
14. Lhotak, P.; Stastny, V.; Zlatuskova, P.; Stibor, I.; Michlova, V.; Tkadlecova, M.; Havlicek, J.; Sykora, J. *Collect. Czech. Chem. Commun.* **2000**, *65*, 757–771.
15. Compound **2**: A mixture of *syn*-**1**[9] (100 mg, 0.119 mmol) and MCPBA (616 mg, 3.57 mmol) in chloroform (10 ml) was heated at reflux for 6 h. After evaporating the mixture to dryness, solid residue was triturated twice with warm hexane (10 ml) followed by filtration to remove *m*-chlorobenzoic acid. The residue was washed with warm 1,2-dichloroethane (10 ml) and recrystallized from acetone–hexane mixture to afford essentially pure sample of **2** (96.5 mg, yield 84.0%). Mp 323 °C (decomp.). IR (KBr, cm^{-1}): 3378 (OH), 2967 (CH), 1735 (C=O), 1318 (SO_2). ^1H NMR (400 MHz, acetone-d_6, 300 K) δ 1.33 (18 H, s, $C(CH_3)_3$), 1.40 (18H, s, $C(CH_3)_3$), 4.90 (4H, s, OCH_2), 8.18 (4H, s, Ar*H*), 8.43 (4H, s, Ar*H*). FAB MS (NBA): *m*/*z* 965.3 $[M+H]^+$.
16. *Spectroscopic measurement*: Stock solutions were prepared by dissolving ligands (**1**–**4**), $Tb(NO_3)_3{\cdot}6H_2O$, and NEt_3 in methanol. For preparation of Tb^{III} complex, appropriate

amount of solutions of a ligand, NEt_3, and Tb^{III} ion were pipetted into a 25-ml volumetric flask, then the mixture was made up with methanol and allowed to stand for 1–4 h at room temperature or 45°C. The sample was subjected to UV-absorption measurement with a Shimadzu UV-2500-PC and/or luminescence measurement with a Hitachi F-4500 spectrometers. Luminescence quantum yields were estimated by use of the equation $\Phi = \Phi_s(A/A_s)N(\varepsilon_s/\varepsilon)\,(C_s/C)$, where A: luminescence intensity obtained by integration of luminescence spectra based on wavenumber, C: concentration of luminescent substances, subscript 's' is standard, quinine sulfate. $\Phi_s = 0.546$ ($\lambda_{ex} = 366$ nm) in 0.5 M H_2SO_4.[18] $N = (n/n_s)^2$, n, n_s: refractive indices of methanol (1.3284) and water (1.3330). λ_{ex}: Excitation wavelength for estimation of Φ, which does not necessarily correspond to absorption maximum. ε: Molar absorptivity of the complex at λ_{ex}. (λ_{ex}/ nm, $\varepsilon/\mathrm{M}^{-1}\,\mathrm{cm}^{-1}$) = (340, 5910) for **1**, (360, 9224) for **2**, (290, 13,100) for **3**, (360, 8010) for **4**.

17. Sabbatini, N.; Guardigli, M.; Lehn, J.-M. *Coord. Chem. Rev.* **1993**, *123*, 201–228.
18. Melhuish, W. H. *J. Phys. Chem.* **1961**, *65*, 229–235.