DALTON COMMUNICATION

Chirality probing of amino alcohols with lanthanide complexes *via* induced circular dichroism spectroscopy

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Achiral lanthanide tris(β-diketonates) selectively formed 1 : 1 highly coordinated complexes with amino alcohols and the resulting complexes exhibited characteristic circular dichroism signals depending on the absolute configuration of the bound guests.

Induced circular dichroism (CD) spectroscopy has proved useful for the assignment of the stereochemistry of chiral guest molecules. When a probe is achiral but chromophoric and a guest is chiral but nonchromophoric, only the probe–guest complex offers induced CD which reflects the chirality of the guest. In this method, several micrograms of the guest are required without any chemical derivatization and these can be readily recovered. Although calixarenes, resorcinarenes, porphyrins and other achiral receptors have been successfully used,[1] the number of effective CD probes for sensing the chirality of specific guests remains limited.

We present achiral lanthanide tris(β-diketonates) **1**–**3** as a new type of CD probe capable of specific binding and chirality sensing of amino alcohols (Fig. 1). Although the employed complexes are electronically neutral (as they contain three diketonate ligands), they often have neutral guests in addition to the diketonate ligands and form highly coordinated complexes.[2] We demonstrate below that lanthanide complexes **1**–**3** selectively form 1 : 1 complexes with amino alcohols and the resulting highly coordinated complexes exhibit characteristic CD signals depending on the absolute configuration of the bound amino alcohols. Several lanthanide complexes are employed as shift reagents in NMR spectroscopy, catalysts in organic synthesis, probes in fluorescence/MRI analysis and hydrolytic catalysts in protein and gene technology,[3] but their receptor functions, particularly CD probe abilities, have rarely been characterized. Radzki and Giannotti reported UV spectroscopic studies demonstrating that some gadolinium porphyrins bound achiral amines, phenols and nucleic bases,[4] and we also developed extraction systems of anionic and zwitterionic amino acids *via* lanthanide coordination chemistry.[5] Here, we apply a series of lanthanide tris(β-diketonates) as specific CD probes to the chirality sensing of neutral amino alcohols of biological and chemical interest.[6]

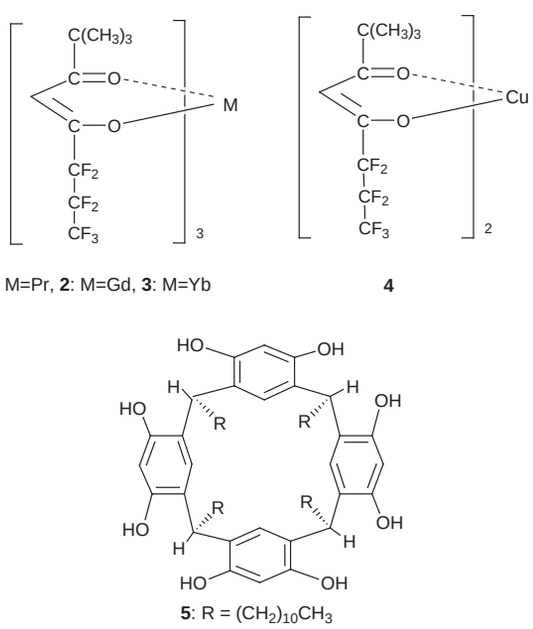


Fig. 1 Lanthanide tris(β-diketonates) **1**–**3** and reference probes **4** and **5**.

Three lanthanide tris(β-diketonates) **1**–**3** were examined which have trivalent praseodymium, gadolinium and ytterbium ions as metal centers. Their receptor and CD probing functions were compared with those of the corresponding copper bis(β-diketonate) **4**. The employed lanthanide ions have larger ionic radii (0.87–0.99 Å)[7] and higher coordination numbers (8–12) than those of transition metal cations. Chiral amine **6**, alcohol **7**, diol **8** and amino alcohols **9**–**14** were chosen as neutral guests which are nonchromophoric and CD silent under the conditions employed (>250 nm). Fig. 2 illustrates the CD spectra of the CH_2Cl_2 solutions containing several combinations of chiral guests **6**–**9** and achiral probes **3** and **4**. Ytterbium tris(β-diketonate) **3** exhibited a split Cotton effect in its CD spectrum as well as significant UV changes upon addition of the chiral amino alcohol **9**. Since chiral monoamine **6**, monoalcohol **7** and diol **8** did not induce any change in the UV or CD spectra of **3**, it is concluded that the ytterbium tris(β-diketonate) **3** chemo-selectively formed a complex with chiral amino alcohol **9**. The copper bis(β-diketonate) **4** did not give any perceptible CD or UV changes for guests **6**–**9**. When the enantiomers (*S*)- and (*R*)-**9** were compared, they afforded symmetrical CD spectra in the presence of ytterbium complex **3**, while they gave exactly the same UV changes. The achiral praseodymium and

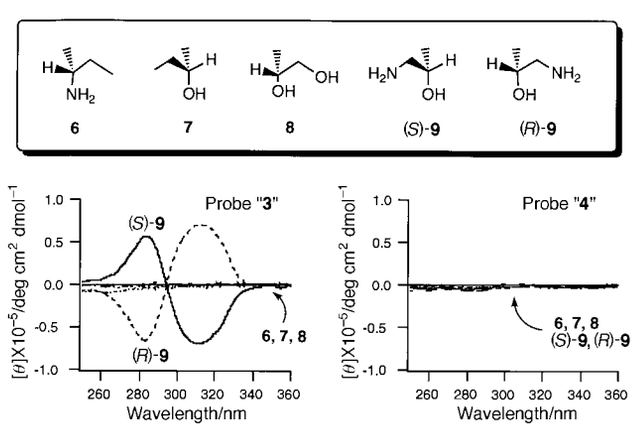
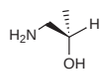
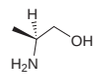
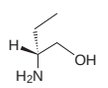
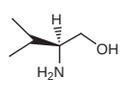
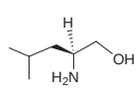
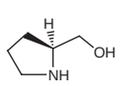


Fig. 2 CD Spectra of **3** and **4** in the presence of chiral guests (**6**, **7**, **8** and **9**). [**3** or **4**] = 3.5×10^{-5} mol l^{-1}; [guest] = 3.5×10^{-4} mol l^{-1} in CH_2Cl_2.

Table 1 CD Data of amino alcohols with **3** in CH_2Cl_2 [a]

Amino alcohol		Configuration	1st λ/nm (θ) [b] 2nd λ/nm (θ) [b]	Amp [c]
	**9** [d]	*S*	284 (+0.57) 312 (−0.68)	+1.25
	**10** [d]	*S*	285 (+0.67) 313 (−0.87)	+1.54
	**11**	*R*	283 (−0.60) 312 (+0.71)	−1.31
	**12** [d]	*S*	284 (+1.12) 311 (−1.22)	+2.34
	**13**	*S*	284 (+0.83) 312 (−0.97)	+1.80
	**14**	*S*	298 (+0.25) 325 (−0.24)	+0.49

[a] Conditions: [**3**] = 3.5×10^{-5} mol l^{-1}; [amino alcohol] = 3.5×10^{-4} mol l^{-1}. [b] They are indicated as [θ] $\times 10^{-5}$/deg cm^2 dmol^{-1}. [c] Amp = [θ at 1st λ] − [θ at 2nd λ]. [d] Their enantiomers showed mirror image CD spectra.

gadolinium complexes **1** and **2** similarly acted as CD probes specific for chiral amino alcohol **9**. The three lanthanide complexes employed produced induced CD signals with the same sign for amino alcohol **9** of the same configuration, and their amplitudes (Amp = [θ at 1st λ] − [θ at 2nd λ] $\times 10^{-5}$ deg cm^2 dmol^{-1}) were shown to be dependent on the size of the central metal cations: Pr^{3+} (+0.24) < Gd^{3+} (+0.83) < Yb^{3+} (+1.25) for (*S*)-**9**. This order indicates that the largest CD signal was observed in the complex with the smallest ion system. The UV and CD titration experiments confirmed 1:1 complexation between amino alcohol and lanthanide tris(β-diketonates), and the stability constant (log *K*) was typically determined as 5.6 for the highly coordinated complex between **2** and **9** in CH_2Cl_2. Resorcinarene **5** was reported to form hydrogen-bonded complexes with chiral polyols and to offer induced CD signals specific for their stereochemistry.[1a] This macrocycle operated for chiral amino alcohols, but the amplitude of the CD signals for (*S*)-**9** (Amp < 0.1) was much smaller than that with lanthanide tris(β-diketonate) **1**, **2** or **3** under the employed conditions. Thus, the present type of lanthanide complexes can be considered as being sensitive and selective CD probes for chiral amino alcohols.

This CD probing method does not require any chemical modification of the guest and can be extended to various amino alcohols **10**–**14**. Table 1 indicates that the absolute configurations of the six amino alcohols were well determined with ytterbium tris(β-diketonate) **3**. The amino alcohols of the same configuration exhibited the same Cotton effect sign, and the magnitude of the CD greatly depended on the nature of the attached substituent to the asymmetric carbon of the guest: **12** (Me_2CH) > **13** (Me_2CHCH_2) > **10** (CH_3) > **11** ($MeCH_2$). Although the type of amino function (primary amine **9**–**13** *vs.* secondary amine **14**) influenced the locations of the CD signals, their signs can be used as effective probes for chirality and stereochemical assignments of the amino alcohols. As reported earlier,[3b] the lanthanide tris(β-diketonates) **1**–**3** caused serious broadening of the ^{1}H NMR signals of all the guests examined. Thus, these achiral lanthanide complexes are not chemoselective probes and offer no enantiomer-selective change in the NMR spectroscopy. When we applied them as CD probes, the situation dramatically changed. They preferred amino alcohols to amine, alcohol and diol guests and sensitively responded to their chirality.† Thus, further combinations of central lanthanide ions and achiral ligands can provide wide variations in the design of a new chirality sensory system for other important guests.

Acknowledgements

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Notes and references

† Chiral diamine, (*S*)-2-pyrrolidinemethylamine, also gave induced CD signals in the presence of lanthanide complexes, but their amplitudes were smaller than those with the corresponding amino alcohol **14**.

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