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A study of the formation and application of new chiral water soluble lanthanoid benzoates using real-time infrared spectroscopy

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ABSTRACT

A range of water soluble lanthanoid benzoate complexes of composition $[Ln(Bz)_3(H_2O)_n]$ (Ln = La, Gd, Ho and Yb; Bz = 3,5-bis((*R*)-2,3-dihydroxypropoxy)benzoate and 3,4,5-tris((*R*)-2,3-dihydroxypropoxy)benzoate) have been prepared by reaction of lanthanoid bicarbonates with three equivalents of the corresponding optically active benzoic acid in water. Application of $[Ln(Bz)_3(H_2O)_n]$ as asymmetric catalysts for epoxide ring opening reactions has been investigated using styrene oxide, showing complete conversion after 20 h, albeit with no significant enantiomeric excess observed. The formation of the lanthanoid complexes and subsequent catalytic conversion of styrene oxide to phenylethane-1,2-diol were monitored using real-time infrared (RTIR) spectroscopy, yielding information about reaction pathways and intermediates.

1. Introduction

In recent years the metal organic complexes of the lanthanoid metals have come to be identified and studied as useful and highly adaptable catalysts in a variety of important organic transformations including, for instance, hydroelemention, Michael addition, asymmetric aldol and hetero Diels–Alder reactions [1]. This has been largely predicated on properties intrinsic to the metal cations; high Lewis acidity, variations in charge, size and coordination numbers, as well as the low toxicity and relatively high stability of the complexes. While many chiral complexes have been prepared [2], the lability of the ligands and strong oxophilicity of metal cations has limited their application to use in anhydrous solvents since water has a tendency to close down the catalysts, either through restricting coordination of organic substrates at the metal center or through hydrolysis. The development of complexes which can be used as water soluble catalysts [1b] has centered almost exclusively on the triflates, which are achiral and require the addition of chiral auxiliaries to support enantioselective reactions. In terms of epoxide opening reactions lanthanoid complexes are typically used to facilitate regioselectivity as opposed to enantioselectivity [3]. The few attempts made have focused on lipophilic ligands (e.g. PyBOX = 2,6-Bis[4-phenyl-2-oxazolinyl]pyridine) which limit application to non-polar solvents [4]. In searching for alternative complexes which meet the 'sustainability' objectives of being non-corrosive, of low toxicity and able to be utilized in an aqueous environment [5], we recently described the first efficient and highly effective use of substituted lanthanoid benzoate complexes in the kinetic separation of the pure diastereomer of *trans*-limonene oxide through selective ring opening of the *cis*-isomer of a racemic mixture in water [6]. Since lanthanoid benzoates are generally highly insoluble in water the benzoic acids need to be modified with polar groups to support aqueous solubility while bulky groups can prevent polymeric aggregation. Our previous ligands, amide functionalized benzoates, while imparting water solubility were achiral in nature. In advancing this chemistry, we now describe the synthesis of two new optically active benzoate ligands incorporating chiral diol side arms, and their use in the formation of a series of *tris*-substituted benzoate complexes of La, Gd, Ho and Yb. Both complex formation and their application as ring opening catalysts have been studied using real-time infrared (RTIR) spectroscopy; an in situ analytical technique which in recent years has been successfully applied in the study of reaction kinetics [7] and in elucidating reaction mechanisms [8].

2. Experimental

2.1. General procedures

Chemicals were obtained from Sigma–Aldrich and were used as received. Methyl 3,4,5-trihydroxybenzoate was synthesized

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according to a known literature procedure [9]. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 300 spectrometer and Varian Unity Nova 500 spectrometer. Chemical shifts were recorded on the δ scale and referenced to the solvent. Solid-state IR spectra were recorded on a Bruker Equinox 55 Infrared Spectrometer fitted with a Specac Diamond ATR source. Solution RTIR scanning measurements were recorded using a Mettler Toledo ReactIR 10 spectrometer fitted with a DiComp probe connected to an MCT detector with a K6 Conduit and scanning in the region of 4000–650 wavenumbers at 8 wavenumber resolution. Water content was determined by TGA using Setaram TG92 with a heating rate of 10 K/min under argon in a range from 50 to 200 °C. Melting points were measured on a Stuart Scientific Melting Point Apparatus SMP3 in an open capillary and are uncorrected. Optical rotation was measured using a PolAAr 2001 automatic polarimeter at the sodium D line (587 nm) at 25 °C. Elemental analyses were performed by Campbell Microanalytical Laboratory, Department of Chemistry, University of Otago, Dunedin, New Zealand. Lanthanoid metal analyses were determined by first digesting the accurately weighed samples with conc. H_2SO_4 and HNO_3. Then the residual solids were dissolved in minimal water and made into a standardized 100 mL solution followed by complexometric titrations with standardized 0.0100 M Na_2H_2EDTA solution with Xylenol Orange indicator and hexamethylenetetramine buffer. Solubility measurements were obtained by incremental addition of analyte to a known volume of deionised water each hour until no further dissolution was observed. Results shown represent an average of three repetitions.

*2.2. Synthesis of (R)-(2,2-dimethyl-1,3-dioxolan-4-yl)methyl 4-methylbenzenesulfonate (**1**)*

Synthesized according to a literature procedure [9]. Yield: 5.6 g (94%). $[\alpha]_D^{25} = -5.1°$ (lit. −4.8°) [9]. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.27 (s, 6H, CH$_3$), 2.47 (s, 3H, Ar-CH$_3$), 3.66 (dd, J_1 = 8.5 Hz J_2 = 5.5 Hz, 1H, 1$_A$-H), 3.99 (m, 2H, 3$_B$-H, 1$_B$-H), 4.13 (dd, J_1 = 7.0 Hz J_2 = 3.5 Hz, 1H, 3$_B$-H), 4.26 (m, 1H, 2H), 7.54 (d, J = 8.0 Hz, 2H, ArH), 7.82 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR (50 MHz, CDCl$_3$): δ = 21.8, 25.3, 26.8, 66.3, 69.6, 73.0, 110.2, 128.2, 130.0, 132.8, 145.2. IR (Diamond ATR): ν 3056, 2997, 2895, 1595, 1486, 1373, 1356, 1341, 1266, 1213, 1191, 1168, 1098, 1084, 967, 934, 981, 820, 735, 664 cm^{-1}. MS (ESI): m/z = 309.0 [MNa]$^+$.

*2.3. Synthesis of methyl 3,5-bis(((S)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)benzoate (**2a**)*

A solution of tosylate **1** (10.0 g, 35 mmol), methyl 3,5-dihydroxybenzoate (1.46 g, 8.70 mmol) and potassium carbonate (4.83 g, 35 mmol) in DMF (50 mL) was stirred for five days at 100 °C. The mixture was then allowed to cool, and diluted with diethyl ether (1.5 L). The solution was washed with water (10 × 350 mL) and the organic phase dried (MgSO$_4$) and concentrated to dryness under reduced pressure. The crude product was subjected to column chromatography (3:1 hexane:EtOAc) to yield the title compound. Yield: 2.1 g (96%). M.p. 78–79 °C. $[\alpha]_D^{25}$ +2.1°. *Anal.* Calc. for $C_{20}H_{28}O_8$: C, 60.6; H, 7.1. Found: C, 60.7; H, 7.1%. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.40 (s, 6H, CH$_3$), 1.46 (s, 6H, CH$_3$), 3.87–3.90 (m, 5H, 3$_A$-H, CH$_3$), 3.94–3.97 (ddd, 2H, J_1 = 9.5 Hz J_2 = 5.5 Hz J_3 = 2.0 Hz, 3$_B$-H), 4.04–4.07 (ddd, 2H, J_1 = 9.5 Hz J_2 = 5.5 Hz J_3 = 2.0 Hz, 1$_A$-H), 4.14–4.17 (dd, 2H, J_1 = 8.5 Hz J_2 = 6.0 Hz, 1$_B$-H), 4.47 (p, 2H, J = 6.0 Hz, 2-H), 6.69 (s, 1H, ArH), 7.19 (s, 2H, ArH) ppm. ^{13}C NMR (50 MHz, CDCl$_3$): δ = 25.6, 27.0, 52.5, 66.9, 69.4, 74.1, 107.1, 108.4, 110.1, 132.3, 159.8, 166.8 ppm. IR (Diamond ATR): ν 2985, 2937, 2881, 1714, 1599, 1442, 1411, 1369, 1354, 1304, 1236, 1211, 1177, 1157, 1105, 1053, 1030, 1009, 974, 936, 894, 833, 795, 765, 670, 641 cm^{-1}. MS (ESI): m/z = 419.2 [MNa]$^+$.

*2.4. Synthesis of methyl 3,4,5-tris(((S)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)benzoate (**2b**)*

The methyl benzoate **2b** was obtained using a similar procedure as in 4.1.2 from **1** and methyl 3,4,5-trihydroxybenzoate (1.61 g, 8.70 mmol). Yield: 1.1 g (23%). M.p. 77.5–78.5 °C. $[\alpha]_D^{25}$ = +8.7°. *Anal.* Calc. for $C_{26}H_{38}O_{11}$: C, 59.3; H, 7.3. Found: C, 59.4; H, 7.4%. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.37 (s, 3H, CH$_3$), 1.39 (s, 6H, CH$_3$), 1.41 (s, 3H, CH$_3$), 1.46 (s, 6H, CH$_3$), 3.89 (s, 3H, OCH$_3$), 3.91–4.03 (m, 6H, 1$_B$-H, 3$_A$-H, 4$_B$-H), 4.10–4.19 (m, 6H, 1$_A$-H, 3$_B$-H, 6$_A$-H), 4.42 (p, 1H, J = 6.0 Hz, 5-H), 4.48 (pd, 2H, J_1 = 1.0 Hz J_2 = 5.5 Hz, 2-H), 7.31 (s, 2H, ArH). ^{13}C NMR (50 MHz, DMSO): δ 26.2 (2C), 27.4 (2C), 53.1, 66.4, 67.1, 70.6, 74.2, 74.6, 74.9, 109.0, 109.4, 109.7, 125.65, 142.2, 152.7, 166.6. IR (Diamond ATR): ν 2987, 2937, 1717, 1591, 1503, 1429, 1371, 1330, 1248, 1204, 1121, 1079, 1046, 1023, 1002, 978, 938, 895, 838, 763 cm^{-1}. MS (ESI): m/z = 549.2 [MNa]$^+$.

*2.5. Synthesis of 3,5-bis(((S)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)benzoic acid (**3a**)*

A solution of methyl benzoate **2a** (1.67 g, 4.2 mmol) in 1:2 mixture of THF and H_2O was adjusted to pH 12 using aqueous sodium hydroxide (0.5 M). This solution was refluxed for 12 h, after which time the THF was removed and the aqueous remainder adjusted to pH 2 and extracted with diethyl ether (10 × 350 mL). The combined organics were combined, dried (MgSO$_4$) and evaporated to dryness yielding a white powder. Yield: 1.46 g (91%). M.p. 99–101 °C. $[\alpha]_D^{25}$ = +2.7°. *Anal.* Calc. for $C_{19}H_{26}O_8$: C, 59.7; H, 6.8. Found C 59.7, H 6.8%. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.34 (s, 6H, CH$_3$), 1.40 (s, 6H, CH$_3$), 3.82–3.84 (dd, 2H, J_1 = 8.5 Hz J_2 = 6.0 Hz, 3$_A$-H), 3.89–.93 (ddd, 2H, J_1 = 11.5 Hz J_2 = 7.5 Hz J_3 = 2.0 Hz, 1$_B$-H), 3.99–4.12 (ddd, 2H, J_1 = 9.0 Hz J_2 = 5.5 Hz J_3 = 2.0 Hz, 3$_B$-H), 4.09–4.12 (dd, 2H, J_1 = 8.5 Hz J_2 = 7.0 Hz, 1$_A$-H), 4.42 (p, 2H, J = 6.0 Hz, 2-H), 6.68 (s, 1H, ArH), 7.20 (s, 2H, ArH). ^{13}C NMR (50 MHz, CDCl$_3$): δ = 26.3, 27.4, 66.5, 67.0, 74.5, 106.6, 108.7, 109.8, 133.8, 160.4, 167.7. IR (Diamond ATR): ν 2990, 2937, 2878, 1685, 1601, 1446, 1422, 1371, 1309, 1256, 1235, 1210, 1157, 1053, 1028, 943, 834, 766, 732, 671, 642 cm^{-1}. MS (ESI): m/z = 405.2 [MNa]$^+$.

*2.6. Synthesis of 3,4,5-tris(((S)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)benzoic acid (**3b**)*

The benzoic acid **3b** was synthesized by a method identical to that of **3a**: Yield: 1.6 g (76%). M.p. 117.0–119.5 °C. $[\alpha]_D^{25}$ = +6.8°. *Anal.* Calc. for $C_{25}H_{36}O_{11}$: C, 59.3; H, 7.3. Found: C, 59.2; H, 7.4%. ^{1}H NMR (500 MHz, CDCl$_3$): δ = 1.37 (s, 3H, CH$_3$), 1.39 (s, 6H, CH$_3$), 1.41 (s, 3H, CH$_3$), 1.46 (s, 6H, CH$_3$), 3.91–4.03 (m, 6H, 1$_B$-H, 3$_A$-H, 4$_B$-H), 4.10–4.19 (m, 6H, 1$_A$-H, 3$_B$-H, 6$_A$-H), 4.42 (p, 1H, J = 6.0 Hz, 5-H), 4.48 (qd, 2H, J_1 = 1.0 Hz J_2 = 5.5 Hz, 2-H), 7.31 (s, 2H, ArH). ^{13}C NMR (50 MHz, DMSO): δ = 26.2 (2C), 27.4 (2C), 53.1, 66.4, 67.1, 70.6, 74.2, 74.6, 74.9, 109.0, 109.4, 109.7, 125.65, 142.2, 152.7, 166.6. IR (Diamond ATR): ν 2987, 2937, 1717, 1591, 1503, 1429, 1371, 1330, 1248, 1204, 1121, 1079, 1046, 1023, 1002, 978, 938, 895, 838, 763 cm^{-1}. MS (ESI): m/z = 549.2 [MNa]$^+$.

*2.7. Synthesis of 3,5-bis((R)- 2,3-dihydroxypropoxy)benzoic acid (**4aH**)*

Benzoic acid **3a** (0.50 g, 1.31 mmol) was dissolved in a solution of H_2O and trifluoroacetic acid (1:3, 4 mL) and stirred for 2 h. After this time solvent was removed under high vacuum and the crude product dissolved in methanol. The methanol was removed under high vacuum and the process repeated a second time to ensure complete removal of trifluoroacetic acid, yielding the title compound as a viscous colorless oil. Yield: 0.40 g (~99%). $[\alpha]_D^{25}$ = +8.2°. *Anal.* Calc. for $C_{13}H_{18}O_8$: C, 51.7; H, 6.0. Found: C, 51.4; H, 6.2%. ^{1}H NMR (500 MHz, D_2O): δ = 3.69 (dq, 4H, J_1 = 12.0 Hz J_2 = 6.5 Hz, 3-H), 4.05 (m, 6H, 1-H, 2-H), 6.79 (s, 1H, ArH), 7.15 (s, 2H, ArH). ^{13}C NMR (50 MHz, DMSO): δ = 63.6, 70.8, 71.0, 106.8, 108.5, 133.7, 160.8, 167.9. IR (Diamond ATR): ν 3302, 2941, 1697, 1597, 1447, 1301, 1239, 1174, 1118, 1060, 864, 769, 633 cm^{-1}. MS (ESI): *m/z* = 325.2 [MNa]$^+$.

*2.8. Synthesis of 3,4,5-tris((R)- 2,3-dihydroxypropoxy)benzoic acid (**4bH**)*

The trisubstituted **4bH** was synthesized as colorless viscous oil by a method identical to that of **4aH**. Yield: 0.38 g (~99%). $[\alpha]_D^{25}$ = −1.0°. *Anal.* Calc. for $C_{16}H_{24}O_{11}$: C, 49.0; H, 6.2. Found: C, 48.8; H, 6.5%. ^{1}H NMR (500 MHz, D_2O): δ = 3.70 (dq, 6H, J_1 = 18.5 Hz J_2 = 4.5 Hz, 1-H, 4-H), 4.05 (m, 9H, 2-H, 3-H, 5-H, 6-H), 7.22 (s, 2H, ArH). ^{13}C NMR (50 MHz, DMSO): δ = 63.6, 63.7, 70.9, 71.5, 71.7, 75.6, 101.8, 126.5, 142.4, 153.1, 167.8. IR (Diamond ATR): ν 3192, 2956, 2928, 2871, 1674, 1589, 1505, 1428, 1328, 1209, 1142, 1104, 1047, 1011, 957, 922, 890, 863, 771, 715 cm^{-1}. MS (ESI): *m/z* = 415.2 [MNa]$^+$.

*2.9. General synthesis of complexes **5a–5h***

Benzoic acid **4aH** or **4bH** (3 equiv) was dissolved in water and rapidly stirred as $LnHCO_3$ (0.9 equiv) was added in one portion. A further 0.2 equivalents of $LnHCO_3$ were added by small increments. Generation of carbon dioxide bubbles and dissolution of the formed emulsion were indicative of reaction occurring. The solution was stirred for 12 h after which time the solution was filtered and the solvent removed under high vacuum yielding Ln complexes **5a–h** with yields of 88–95% (Table 1).

*2.10. Synthesis of [La(**4a**)$_3$(H_2O)$_2$]·2H_2O (**5a**)*

Yield: 93%. M.p. 83.0–87.2 °C. $[\alpha]_D^{25}$ = −5.2°. *Anal.* Calc. for $C_{39}H_{55}LaO_{26}\cdot 4H_2O$: C, 42.0; H, 5.3; La, 10.0. Found: C, 41.5; H, 5.0; La, 9.6%. ^{1}H NMR (500 MHz, D_2O): δ = 3.42–3.52 (m, 4H, 3-H), 3.91 (m, 6H, 1-H, 2-H), 6.60 (s, 1H, ArH), 6.96 (s, 2H, ArH). ^{13}C NMR (50 MHz, DMSO): δ = 62.5, 69.3, 70.1, 105.9, 108.3, 144.2, 159.4, 182.9. IR (Diamond ATR): ν 3231, 2942, 1531, 1391, 1214, 1096, 1033, 927, 869, 768, 682 cm^{-1}. MS (ESI): *m/z* = 740.7 [LaL$_2$]$^+$, 814.8 [LaL$_2$KOH.H$_2$O]$^+$, 1042.6 [LaL$_3$H]$^+$, 1117.0 [LaL$_3$K.H$_2$O]$^+$.

*2.11. Synthesis of [Gd(**4a**)$_3$(H_2O)$_4$]·H_2O (**5b**)*

Yield: 88%. M.p. 92.8–95.7 °C. $[\alpha]_D^{25}$ = −5.2°. *Anal.* Calc. for $C_{39}H_{55}GdO_{26}\cdot 5H_2O$: C, 40.7; H, 5.3; Gd, 11.1. Found: C, 41.3; H, 5.5; Gd, 11.9%. IR (Diamond ATR): ν 3251, 2941, 1569, 1502, 1408, 1334, 1209, 1099, 1035, 865, 761 cm^{-1}. MS (ESI): *m/z* = 759.8 [GdL$_2$]$^+$, 1061.9 [GdL$_3$H]$^+$.

Table 1
Summary of yields and solubilities for lanthanoid complexes **5a–h**.

Complex	Formula	Yield (%)	Water solubility (mol L^{-1})
5a	[La(**4a**)$_3$(H$_2$O)$_2$]	93	0.16
5b	[Gd(**4a**)$_3$(H$_2$O)$_4$]	88	0.05
5c	[Ho(**4a**)$_3$(H$_2$O)$_2$]	95	0.09
5d	[Yb(**4a**)$_3$(H$_2$O)$_3$]	93	0.04
5e	[La(**4b**)$_3$(H$_2$O)]	90	0.05
5f	[Gd(**4b**)$_3$(H$_2$O)$_2$]	92	0.05
5g	[Ho(**4b**)$_3$(H$_2$O)$_3$]	90	0.08
5h	[Yb(**4b**)$_3$(H$_2$O)$_3$]	94	0.09

*2.12. Synthesis of [Ho(**4a**)$_3$(H_2O)$_2$]·2H_2O (**5c**)*

Yield: 95%. M.p. 89.4–93.6 °C. $[\alpha]_D^{25}$ = −4.9°. *Anal.* Calc. for $C_{39}H_{55}HoO_{26}\cdot 4H_2O$: C, 41.1; H, 5.2; Ho, 11.5. Found: C, 40.7; H, 4.9; Ho, 10.8%. IR (Diamond ATR): ν 3256, 2942, 1569, 1504, 1411, 1335, 1211, 1104, 1035, 929, 868, 761 cm^{-1}. MS (ESI): *m/z* = 766.9 [HoL$_2$]$^+$, 1069.0 [HoL$_3$H]$^+$, 1143.2 [HoL$_3$K.(H$_2$O)$_2$]$^+$, 1067.0 [HoL$_3$-H]$^-$, 1369.2 [HoL$_4$]$^-$.

*2.13. Synthesis of [Yb(**4a**)$_3$(H_2O)$_3$]·2H_2O (**5d**)*

Yield: 93%. M.p. 90.0–96.0 °C. $[\alpha]_D^{25}$ = −5.0°. *Anal.* Calc. for $C_{39}H_{55}O_{26}Yb\cdot 5H_2O$: C, 40.4; H, 5.3; Yb, 12.8. Found: C, 40.1; H, 4.8; Yb, 12.8%. ^{1}H NMR (500 MHz, D_2O): δ = 3.40–3.87 (m, 10H, 1-H, 2-H, 3-H), 4.69 (s, 2H, ArH), 6.06 (s, 1H, ArH). IR (Diamond ATR): ν 3256, 2942, 1705, 1567, 1503, 1425, 1334, 1209, 1100, 1035, 929, 876, 761 cm^{-1}. MS (ESI): *m/z* = 775.7 [YbL$_2$]$^+$, 1077.9 [YbL$_3$H]$^+$.

*2.14. Synthesis of [La(**4b**)$_3$(H_2O)] (**5e**)*

Yield: 90%. M.p. 59.8–62.9 °C. $[\alpha]_D^{25}$ = −9.5°. *Anal.* Calc. for $C_{48}H_{69}LaO_{33}\cdot H_2O$: C, 43.3; H, 5.4; La, 13.1. Found. C, 43.0; H, 5.4; La, 12.2%. ^{1}H NMR (500 MHz, D_2O): δ = 3.50–3.64 (m, 6H, 1-H, 4-H), 3.78–3.96 (m, 9H, 2-H, 3-H, 5-H, 6-H), 7.26 (s, 2H, ArH). ^{13}C NMR (50 MHz, DMSO): δ = 63.3 (2C), 70.6, 71.3 (2C), 75.1, 104.3, 107.8, 125.6, 152.2, 166.9. IR (Diamond ATR): ν 3221, 2951, 1534, 1442, 1391, 1334, 1164, 1105, 1046, 930, 862, 782, 676 cm^{-1}. MS (ESI): *m/z* = 920.8 [LaL$_2$]$^+$, 1312.8 [LaL$_3$H]$^+$.

*2.15. Synthesis of [Gd(**4b**)$_3$(H_2O)$_2$]·2.5H_2O (**5f**)*

Yield: 92%. M.p. 51.4–57.2 °C. $[\alpha]_D^{25}$ = −8.4°. *Anal.* Calc. for $C_{48}H_{69}GdO_{33}\cdot 4.5H_2O$: C, 40.8; H, 5.6; Gd, 13.7. Found: C, 40.6; H, 5.6; Gd, 13.1%. IR (Diamond ATR): ν 3256, 2942, 1553, 1466, 1403, 1164, 1112, 1050, 930, 861, 783, 677 cm^{-1}. MS (ESI): *m/z* = 939.6 [GdL$_2$]$^+$, 1330.6 [GdL$_3$H]$^+$.

*2.16. Synthesis of [Ho(**4b**)$_3$(H_2O)$_3$] (**5g**)*

Yield: 90%. M.p. 58.8–64.0 °C. $[\alpha]_D^{25}$ = −9.0°. *Anal.* Calc. for $C_{48}H_{69}HoO_{33}\cdot 3H_2O$: C, 41.4; H, 5.4; Ho, 15.4. Found: C, 41.1; H, 5.6; Ho, 15.0%. IR (Diamond ATR): ν 3265, 2938, 1570, 1443, 1408, 1329, 1301, 1164, 1107, 1044, 930, 859, 784, 763, 675 cm^{-1}. MS (ESI): *m/z* = 1337.2 [HoL$_3$-H]$^-$, 1410.9 [HoL$_3$Cl.(H$_2$O)$_2$]$^-$.

*2.17. Synthesis of [Yb(**4b**)$_3$(H_2O)$_3$] (**5h**)*

Yield: 94%. M.p. 62.0–66.5 °C. $[\alpha]_D^{25}$ = −9.6°. *Anal.* Calc. for $C_{48}H_{69}YbO_{33}\cdot 3H_2O$: C, 41.1; H, 5.4; Yb, 15.3. Found: C, 40.9; H, 5.4; Yb, 14.6%. ^{1}H NMR (500 MHz, D_2O): δ = 3.50–3.64 (m, 6H, 1-H, 4-H), 3.78–3.96 (m, 9H, 2-H, 3-H, 5-H, 6-H), 4.17 (s, 2H, ArH). IR (Diamond ATR): ν 3265, 2943, 1556, 1406, 1333, 1163, 1111, 1046, 930, 861, 784, 677 cm^{-1}. MS (ESI): *m/z* = 1029.9 [YbL$_2$KOH.H$_2$O]$^+$, 1347.7 [YbL$_3$H]$^+$, 1421.7 [YbL$_3$K·(H$_2$O)$_2$]$^+$.

2.18. General procedure for catalytic testing

Catalytic epoxide ring opening reactions were undertaken using lanthanoid complexes **5a–h** by the following method. To 5 mL of deionised water were added styrene oxide (1 mL, 8.76 mmol) and catalyst (0.044 mol) at room temperature with stirring. After 4 h the reaction was found to be complete. Removal of the solvent under vacuum gave the crude phenylethane-1,2-diol which was purified by recrystallisation.

3. Results and discussion

3.1. Synthesis of poly diol substituted benzoate ligands

To obtain water soluble chiral ligands, 3,4-dihydroxybenzoic acid (α-resorcylic acid) and 3,4,5-trihydroxybenzoic acid (gallic acid) were modified to contain two and three 1,2-diol groups respectively. The introduction of these polar functionalities is convenient for two reasons; the use of d-mannitol, a naturally occurring sugar from the pool of chiral substances, is cheap and the protection and deprotection reactions through the acetonide derivatives are relatively straightforward and efficient. The overall synthetic route to the ligands is summarized in Scheme 1.

Synthesis of the tosylated precursor **1** was achieved in three steps in an overall yield of 40% following a literature procedure [10]. After nucleophilic attack from the phenolic groups of either methyl 3,4,5-trihydroxybenzoate, or methyl 3,5-dihydroxybenzoate to give the protected ligands **2a–b** in yields of 96% and 23% respectively after four days. The low isolated yield of methyl benzoate **2a** is attributed to contamination of the reaction by water, resulting in early cleavage to the benzoate **3a**, a desired product. However, strict adherence to anhydrous conditions would increase the isolated yield of **2a** if required. A subsequent slow increase of polarity from 3:1 hexane:ethyl acetate to neat ethyl acetate during chromatographic workup yielded an additional 53% of product as the substituted benzoic acid.

A dual deprotection performed in basic conditions, followed by treatment with acid, was found to improve purity of ligands **4aH, 4bH** resulting in isolated yields of 91% and 76% respectively. The ligands were found to be soluble in water with solubilities of 0.46 mol L^{-1} for **4aH** and 0.38 mol L^{-1} for **4bH**. Optical purity of both ligands was monitored throughout the synthetic procedure and no racemisation was observed.

3.2. Synthesis of lanthanoid tris-benzoate complexes

The *tris*-substituted lanthanoid benzoate complexes were obtained by reaction of three equiv of **4aH, 4bH** with the appropriate lanthanoid bicarbonate in water, as depicted in Scheme 2.

By using lanthanoid bicarbonate as lanthanoid precursor, the reactions were high yielding and clean, with only carbon dioxide and water as by-products. Due to the highly polar nature of the ligands and their tendency to retain H_2O an exact stoichiometric ratio of reactants is difficult to achieve. As such, the reaction involved using an initial 0.9 equivalents of the lanthanoid bicarbonate, followed by the addition of further 0.2 equivalents in small increments until the reaction was deemed to have gone to completion, evidenced by cessation of CO_2 emission. Excess insoluble bicarbonate was then removed by filtration prior to workup. The water solubilities and isolated yields for each of the lanthanoid complexes is summarized in Table 1.

$$\mathrm{Ln(HCO_3)_3} + 3(\mathbf{4aH, 4bH}) \longrightarrow [\mathrm{Ln}(\mathbf{4a,4b})_3(\mathrm{H_2O})_n] + 3\mathrm{CO_2} + 3\mathrm{H_2O}$$

Ln = La, $[La(\mathbf{4a})_3(H_2O)_2]$, **5a**
Gd, $[Gd(\mathbf{4a})_3(H_2O)_4]$, **5b**
Ho, $[Ho(\mathbf{4a})_3(H_2O)_2]$, **5c**
Yb, $[Yb(\mathbf{4a})_3(H_2O)_3]$, **5d**
La, $[La(\mathbf{4b})_3(H_2O)]$, **5e**
Gd, $[Gd(\mathbf{4b})_3(H_2O)_2]$, **5f**
Ho, $[Ho(\mathbf{4b})_3(H_2O)_3]$, **5g**
Yb, $[Yb(\mathbf{4b})_3(H_2O)_3]$, **5h**

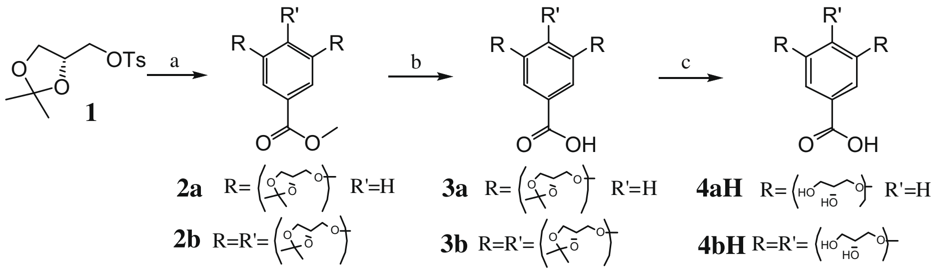
Scheme 2. Reagents and conditions: (a), H_2O, room temp. 8 h.

Considerable time and effort was spent in an attempt to grow single crystals suitable for X-ray crystallography. Unfortunately due to the high aqueous solubility of complexes **5a**–**5h**, slow evaporation of solutions in alcohols (methanol, ethanol) or water yielded glassy solids. Layering concentrated alcoholic solutions of each complex with various organic solvents (e.g. 1-propanol, *tert*-butanol, DMF, acetonitrile, diethylether etc.) resulted in eventual deposition of oily residues within each vial. This result was also observed when hot saturated methanolic solutions of **5a**–**5h** were allowed to slowly cool.

3.3. Spectroscopic analyses

Characterization of the compounds in solution was attempted by ^1H and ^{13}C NMR spectroscopy. However, in the ^1H spectra only the lanthanum and ytterbium complexes gave observable signals in the region of 2–8 ppm. Paramagnetic up field shifting of the aromatic region was observed for ligands in the ytterbium complex, with the effects less pronounced as the distance from the metal increased. The aromatic resonances were observed for complex **5d** at 6.06 and 4.69 ppm, compared with resonances at 6.60 and 6.96 ppm respectively for the corresponding lanthanum complex **5a** (Fig. 1, asterisked resonances are those for the protons *ortho* to the carboxylate group). In both cases the signals for the aliphatic diol arms were observed across the region of 3.40–4.00 ppm. The single aromatic signal for complexes **5e** and **5h** was observed at 4.17 ppm and 6.22 ppm for the ytterbium and lanthanum complexes respectively, with the aliphatic resonances magnetically equivalent in the range of 3.50–4.00 ppm. Resonances for the gadolinium and holmium complexes were not identifiable in the range −300–600 ppm, likely due to obscuration in the baseline by signal broadening. Attempts to obtain clear and informative ^{13}C NMR spectra proved unsuccessful for the Yb complexes mainly due to broadening from paramagnetic Yb^{3+}.

The water content of each complex was determined by thermogravimetric analysis. The mass losses observed indicated between



Scheme 1. Reagents and conditions: (a), **2a**:methyl 3,5-trihydroxybenzoate 2.5eq., **2b**:methyl 3,4,5-dihydroxybenzoate 3.5eq., dry DMF, K_2CO_3, 100 °C, 4d; (b), aq. NaOH, THF:H_2O (1:1), 12 h; (c), TFA, H_2O, 2 h.

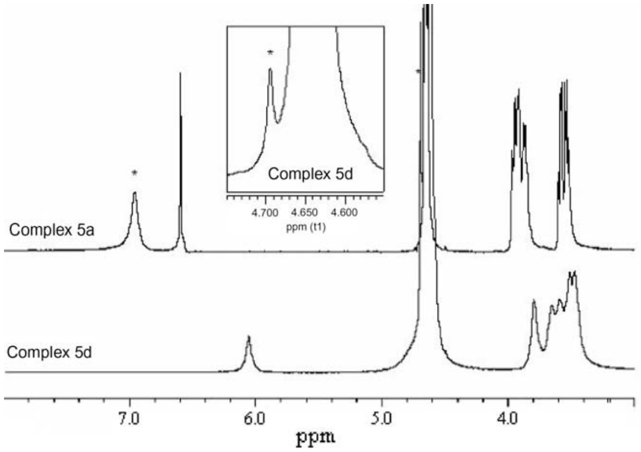


Fig. 1. Comparative NMR spectra of lanthanum complex **5a** and ytterbium complex **5d** displaying up field shifting of aromatic resonances. Asterisked resonances are those for the protons ortho to the carboxylate group in both compounds. The inset highlights the upfield shift of the ortho protons influenced by the paramagnetic Yb^{3+}.

one and four molecules of water per complex and these are shown in Table 1. However, there was a slight discrepancy in the water content of each complex when compared with the microanalytical data, which indicated additional molecules of water. This is attributed to the highly hygroscopic nature of the complexes which were not stored or handled under completely anhydrous conditions prior to elemental analysis.

Analyses of each complex by electrospray mass spectrometry identified charged species consistent with the protonated molecular ion, $[M+H]^+$, with isotopic patterns consistent with each metal investigated. Evidence of complex fragmentation yielding the dominant $[M-L]^+$ ion was evident for all complexes with the exception of the holmium complex **5g**. Higher order molecular fragments were sought to determine if polymerization by the displacement of metal bound water by diol arms of adjacent complexes was seen to occur. No evidence of polynuclear species was observed for any of the complexes.

Solid-state IR analyses of the symmetric and asymmetric carboxylate stretches for each complex allows for a prediction of the coordination mode of each benzoate relative to the metal [11]. The difference between both stretches ($\Delta\nu$) was typically less than 150 cm^{-1} strongly suggesting the ligands bind to the metal in a chelating mode, with values closer to ionic bonding (164–171 cm^{-1}) were observed for gadolinium and holmium complexes **5b** and **5c**. These results are summarized in Table 2. In all cases vibrations assigned to scissoring of water molecules were observed in the region of 800–500 cm^{-1}.

3.4. Solution real-time infrared (RTIR) analysis of complex formation

The reaction profile for the formation of the ytterbium complex **5d** as a model for the general displacement of lanthanoid bicarbonates by the substituted benzoic acids was studied using RTIR scanning spectroscopy coupled with ConcIRT™ software. This technique allows for the visualization of starting compounds, reagents, intermediates and products present in solution, without the need for invasive sampling or interruption of the reaction process. IR spectra were collected every 15 s in the wavenumber range of 4000–650 cm^{-1} at a resolution of 8 cm^{-1}. An iterative comparison of accrued spectra by ConcIRT™ allows the appearance or disappearance of the spectrum of any given component to be displayed. This allows species to be monitored using all observable vibrations across a broad spectral region, as opposed to following single isolated bands. To follow the loss of carbon dioxide the asymmetric absorption for CO_2 was monitored in the region around 2400 cm^{-1}, while the relative changes in the asymmetric and symmetric stretches, corresponding to the relative concentrations of benzoic/benzoate, were monitored in the region of 1900–900 cm^{-1}. This resulted in the identification of a reaction pathway proceeding to the *tris*-substituted complex *via* a bis-substituted intermediate.

Table 2
Infrared and structural data for complexes **5a–h**.

Compound	$\nu_{asym}(CO_2)$ (cm^{-1})	$\nu_{sym}(CO_2)$ (cm^{-1})	Δ (cm^{-1})
5a	1531	1391	140
5b	1569	1408	161
5c	1569	1411	158
5d	1567	1425	142
5e	1535	1391	144
5f	1535	1403	132
5g	1541	1408	133
5h	1556	1406	150

At the start of the reaction one equivalent of ytterbium bicarbonate was added to a stirring solution of three equivalents of the ligand **5a** in deionised water. Fig. 2 shows that the emission of CO_2 quickly saturates the solution, and thereafter the rate of evolution slows exponentially until after *ca* 1 h the reaction is essentially complete.

To examine complex formation the asymmetric carbonyl stretch of the *bis*-substituted benzoic acid **4aH** was monitored during the course of the reaction. In the free acid this carbonyl stretch is observed at 1697 cm^{-1}. On deprotonation and complexation with the metal it is observed in the final *tris*-substituted complex at 1563 cm^{-1}. However, a distinct shoulder at 1557 cm^{-1} was apparent in the spectrum prior to the complete conversion of the benzoic acid to benzoate. It was anticipated that this was indicative of a relatively long-lived and stable intermediate. Trends in the variation of species present in solution were identified using the software ConcIRT™, resulting in identification of three components across the reaction lifetime, shown in Fig. 3.

Deconvolution of the combined spectrum identified two component spectra of the free ligand **4aH** and the expected *tris*-substituted complex **5d**. The data compared well with that obtained for each of the individual species. The unknown intermediate mirrored most features of the final *tris*-substituted complex, however, the asymmetric carbonyl stretch was shifted to a slightly lower wavenumber ($\Delta\nu = -16$ cm^{-1}) (Fig. 4).

To investigate this intermediate mass spectrometry was conducted on a sample of the reaction mixture shortly after the maximum in CO_2 emission was observed. This indicated the presence

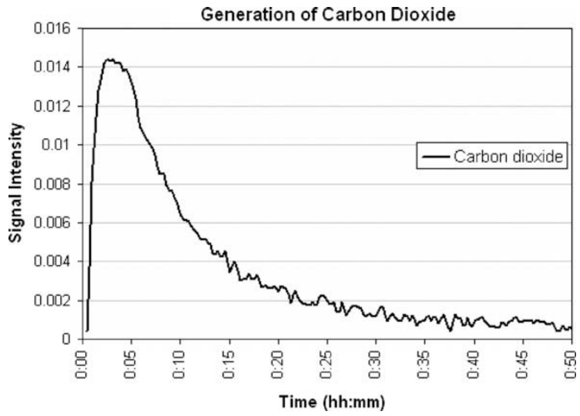


Fig. 2. Generation of carbon dioxide monitored at 2347 cm^{-1} during the formation of ytterbium complex **5d**.

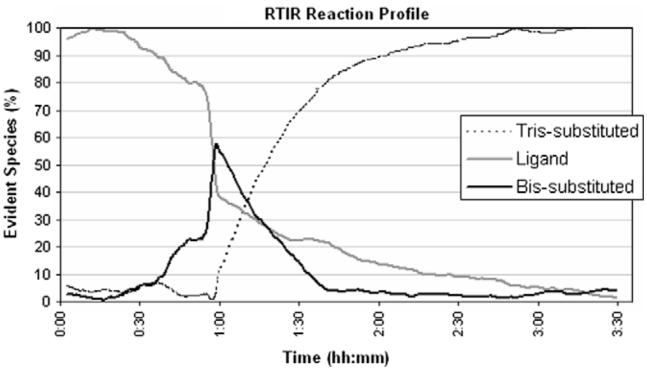


Fig. 3. RTIR reaction profile of formation of ytterbium complex **5d** as determined by monitoring the region of 1900–900 cm^{-1}.

of the heteroleptic *bis*-substituted anionic species, [Yb(**4a**)$_2$(HCO$_3$)–H]$^-$. It appears that formation of the *bis*-substituted species occurs rapidly in solution, producing the initial spike in dissolved carbon dioxide at 2347 cm^{-1}, seen in Fig. 2. The rate of ligand consumption, seen in Fig. 3 as a negative gradient, is therefore fastest during formation of the *bis*-substituted species. Formation of the *tris*-substituted complex only begins once the equilibrium concentration of the *bis*-substituted complex has reached a maximum. At this point consumption of the free acid slows coincident with the slower consumption of the *bis*-substituted complex and formation of the final *tris*-substituted complex. This rate reduction would be expected solely on grounds of steric hindrance. The slightly lower wavenumber for $\nu_{asym}(CO_2)$ in the *bis* complex can be understood by the marginally greater electrostatic interactions induced by the bicarbonate anion.

The optimum time for the reaction to go to completion under these conditions was determined to be 4 h, with the intermediate formation peaking at 1 h and 20 min.

Real-time IR analysis of complex formation using ligand **4bH** was attempted in an analogous fashion to **5d**, however meaningful trends could not be identified. This was due to broadening of the bands within the regions of interest, and an overall decrease in signal intensity for the lanthanoid species [Ln(**4b**)$_3$].

3.5. Styrene oxide ring opening reaction with lanthanoid benzoates

To assess the potential for these complexes to act as water-based asymmetric catalysts the complexes were tested for their efficacy in the stereoselective conversion of styrene oxide to 1-phenylethane-1,2-diol. The reaction, here exemplified by lanthanum complex **5e** was followed by RTIR spectroscopy, the result of which is shown in Fig. 5. A single carbon-oxygen stretch, located specifically between 861 and 883 cm^{-1} for the epoxide and 1016–1043 cm^{-1} for the diol, was selected and monitored throughout the reaction. A catalyst loading of 0.5% of **5e** was employed in the reac-

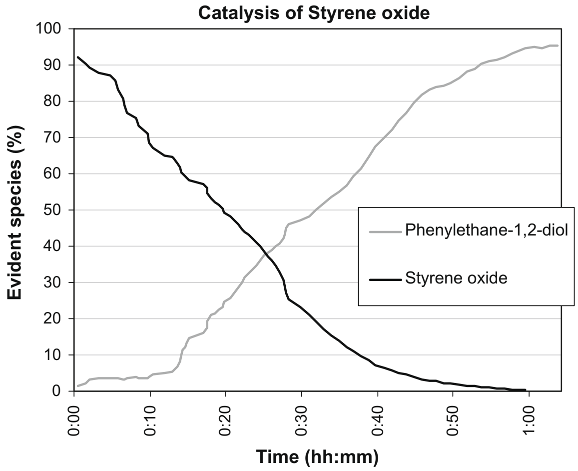


Fig. 5. RTIR monitoring of the conversion of epoxide (C–O stretches at 861 and 883 cm^{-1}) to diol (C–O stretches at 1016–1043 cm^{-1}) catalyzed by lanthanum complex **5e**.

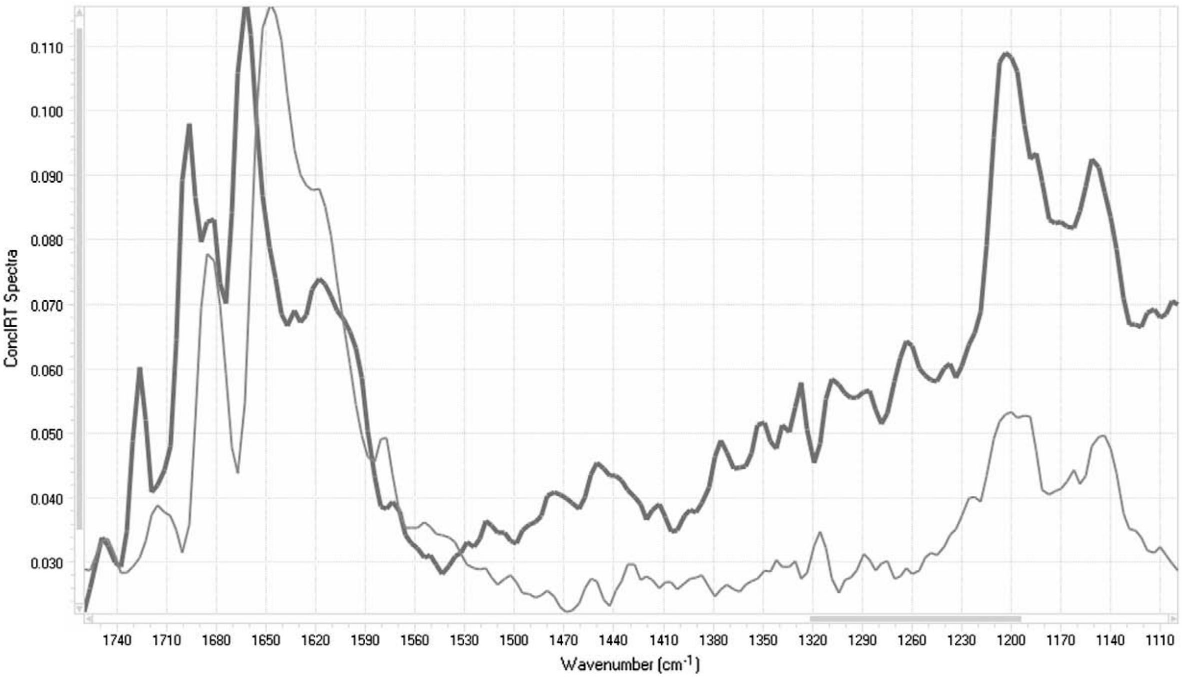
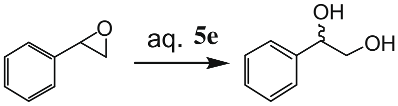


Fig. 4. Comparison of the in situ IR spectrum of known tris-substituted complex (bold) with the unknown intermediate species.



Scheme 3. Reaction of styrene oxide with **5e**.

Table 3
Observed optical rotation for 1-phenylethane-1,2-diol catalyzed by lanthanoid complexes **5a–h**.

Compound	Optical rotation of product (°)
5a	+4.8
5b	+14.2
5c	+3.1
5d	+4.5
5e	−2.8
5f	−0.7
5g	+2.1
5h	+4.7

tion conducted in deionised water at 25 °C. Total conversion of the epoxide to the diol was observed within 80 min, with a yield of 98% (Scheme 3). Repeating the reaction in absence of **5e** resulted in no observable conversion to the diol.

Disappointingly analysis of the optical activity of the products, as seen in Table 3, was indicative of the catalyst not favoring formation of either enantiomeric form (lit. $[\alpha]_D^{25}$ = +103.9° for *S* enantiomer [12], $[\alpha]_D^{25}$ = −37.8° for R enantiomer [13]). This trend was observed regardless of changes in atomic radius as a result of lanthanoid contraction. These results are likely due to the high lability of diol coordination at the metal center. Enantioselectivity is dependent on a relatively long residence time for the diol moieties at the cationic metal center, thereby inducing selectivity in the epoxide binding and the subsequent attack of the OH^- nucleophile. It is likely that H_2O coordinates more strongly than either the diol or the epoxide and so the optimum conditions for inducing selectivity are unfortunately not obtainable in a water medium. In fact, we previously observed that in an analogous complex, $[La_2(DBA)_6(H_2O)_4]_\infty$ DBA = ((*R*)-4-(2,3-dihydroxypropoxy)benzoate) [14], that polymerization through diol-metal binding occurs but not until the H_2O content is minimized and the solution heated to 60 °C to favor H_2O displacement.

4. Conclusions

Two new optically active benzoic acid ligands have been synthesized (3,5-bis((*R*)-2,3-dihydroxypropoxybenzoic acid and 3,4,5-tris((*R*)-2,3-dihydroxypropoxybenzoic acid), and their corresponding lanthanoid complexes synthesized, $[Ln(Bz)_3(H_2O)_n]$ (Ln = La, Gd, Ho, Yb), through reaction with the relevant lanthanoid bicarbonate. An RTIR study indicated that complex formation occurred in 4 h with the di-substituted benzoic acid and in 6 h with the trisubstituted benzoic acid. Evidence from analysis of the reaction with Yb suggests that the mechanism involves a metastable *bis*-carboxylate complex *en route* to the final *tris*-substituted complex. The lanthanoid complexes were all successful as Lewis acid catalysts in the ring opening of styrene oxide, with total conversion observed after one hour. Unfortunately, despite the chiral nature of the ligands no enantioselectivity was observed due, we conclude, to the high lability of the diol moieties at the metal center in an aqueous medium.

Acknowledgments

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