CHEMISTRY
A EUROPEAN JOURNAL

A New Pyridine-2,6-bis(oxazoline) for Efficient and Flexible Lanthanide-Based Catalysts of Enantioselective Reactions with 3-Alkenoyl-2-oxazolidinones

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Abstract: A new pyridine-2,6-bis(oxazoline) (**4**) has been easily synthesised from the reaction of (1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol (**1**) and dimethyl pyridine-2,6-dicarboximidate (**2**), followed by TIPS (TIPS = triisopropylsilyl) protection of the 4′-CH_2OH group. The catalysts derived from **4** and eight lanthanide(III) triflates have been tested over three reactions involving 3-acryloyl- and 3-crotonoyloxazolidinones (**5a**,**b**): the Diels–Alder (DA) reaction with cyclopentadiene, the 1,3-dipolar cycloaddition with diphenyl nitrone and the Mukaiyama–Michael reaction with 2-trimethylsilyloxyfuran. Several reactions exhibit very good enantioselectivity (*ee* > 90%), and the opposite enantiomers can be easily obtained simply by changing the cation. This specific feature of the ligand can be appreciated in the DA reaction of **5a**, since the catalyst [Sc^{III}(**4**)] gives the adduct (2′S)-**9a** with 99% *ee*, whereas the catalyst [Y^{III}(**4**)] gives the opposite enantiomer with 95% *ee*. A rationale of the enantioselectivity is proposed on the basis of the NMR spectra of La-based complexes involving **4** and **5** as ligands.

Keywords: asymmetric synthesis · cations · enantioselectivity · lanthanides · N ligands

Introduction

The formation of carbon–carbon bonds through asymmetric catalytic processes has attracted a great deal of interest and the art of organic synthesis has progressed impressively. In general, the catalysts consist of a cation coordinating an optically active organic ligand and the complex must have at least one free binding site to coordinate one reagent, promoting the formation of the reactive complex involved in the catalytic cycle.

The ideal ligand should offer some advantages: it should be easily prepared, cheap, resistant under the reaction conditions and very selective for a large number of processes, hence very flexible. The ideal ligand has not yet been discovered (and probably never will), but pyridine-2,6-bis(oxazolines) (pybox) provide efficient catalysts for such a variety of processes that a search in this field is certainly attractive.[1]

The reaction between (1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol (**1**) and dimethyl pyridine-2,6-dicarboximidate (**2**) has several of the advantages described above, and if the hydroxy group involved in the oxazoline formation is in the 1-position, the resulting pybox will have a phenyl group in position 5′, which has been found to be very useful in the development of efficient catalysts of the Mukaiyama–Michael (MM)[2] and Diels–Alder (DA)[3,4] reactions of alkenoyl-1,3-oxazolidinones. The residual CH_2OH groups in the 4′-position could interfere in the formation of the reactive complex that involves the nitrogen atoms of the pybox, the cation and the reagent, but a suitable protection of the hydroxy groups should both avoid this and increase the shielding effect exerted by the substituent at the 4′-position.

Following the protocol reported by Aggarwal[5] for the preparation of the analogous box from dimethylmalonyldinitrile and **1**, Müller and Boléa[6] and Reiser and co-workers[7] synthesised the desired 5-aryl-4-hydroxymethylpybox in a regioselective manner and in good yields starting from the corresponding *p*-nitrophenyl and *p*-methylthiophenyl (thiomicamine) analogues of **1** (Scheme 1). These ligands were

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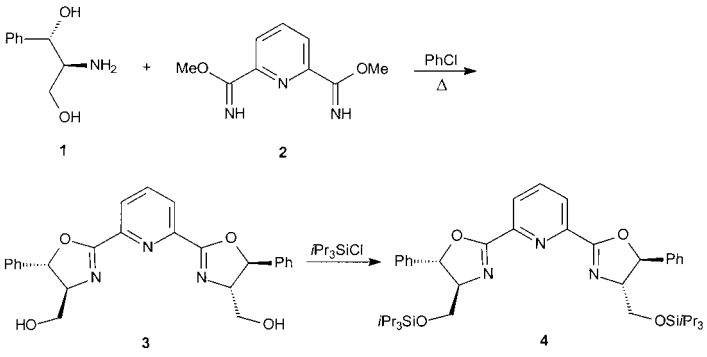
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

DOI: 10.1002/chem.200401213



Scheme 1.

Table 1. Diels–Alder reactions between **5a** and **6** at −50 °C in CH_2Cl_2 in the presence of 10 % mol of catalyst and 4 Å molecular sieves.

Entry	r[a] [Å]	Triflate	t [h]	[**9a**]/[**10a**][b]	**9a** *ee* %[c]	**10a** *ee* %[c]
1	0.870	Sc	16	96:4	99 (2′*S*) *Re*	>95 (2′*S*) *Re*
2	0.977	Lu	48	90:10	24 (2′*R*) *Si*	racemic
3	0.985	Yb	24	91:9	83 (2′*R*) *Si*	55 (2′*R*) *Si*
4	1.015	Ho	48	95:5	91 (2′*R*) *Si*	60 (2′*R*) *Si*
5	1.019	Y	48	90:10	95 (2′*R*) *Si*	67 (2′*R*) *Si*
6	1.066	Eu	48	91:9	90 (2′*R*) *Si*	50 (2′*R*) *Si*
7	1.126	Pr	24	93:7	86 (2′*R*) *Si*	24 (2′*R*) *Si*
8	1.160	La	16	94:6	80 (2′*R*) *Si*	racemic

[a] r = ionic radius. [b] Yields were all quantitative. [c] The configuration is given in parentheses, followed by the face approach.

tested in the addition of diethylzinc to benzaldehyde and cyclohexenone[7] and, after silylation with several trialkylsilyl chlorides, in the intramolecular Cu^{II}-catalysed cyclopropanation reaction, but the enantioselectivity was always disappointing.

Despite these unpleasant precedents, a test of the catalysts based on silylated pybox derived from **1** was planned.

Results

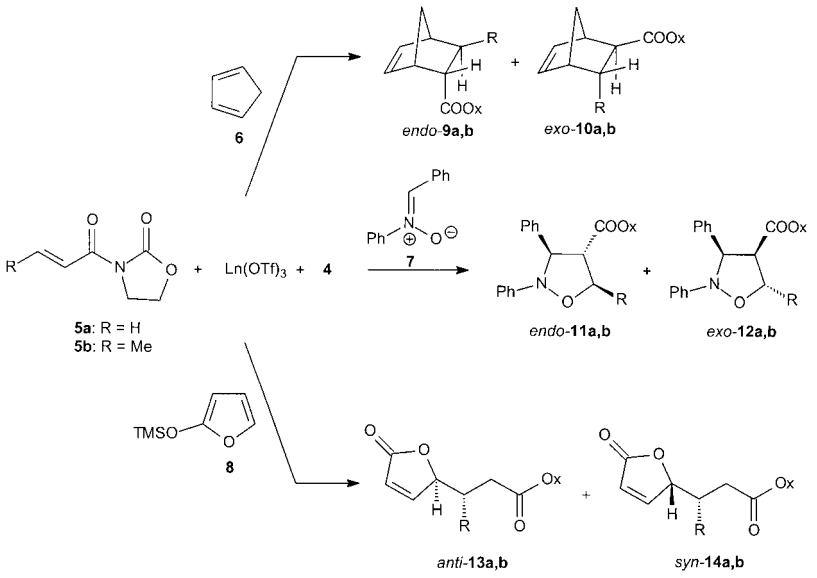
Pybox **4** was synthesised by refluxing **1** and **2** in chlorobenzene to give **3**, which was isolated and silylated with iPr$_3$SiCl and imidazole (Scheme 1) to give **4** in good yield on a multigram scale. Compound **4** was the ligand used for the formation of the complexes with eight lanthanide triflates, taking into account the specific affinity of pybox for these trivalent cations[1] and the interesting effects on the enantioselectivity exerted by such cations.

In the choice of the reactions to be tested, the well-known bicoordination ability of 3-alkenoyl-1,3-oxazolidin-2-ones **5** with pybox and lanthanide cations was considered;[1] therefore the DA reaction of cyclopentadiene (**6**), the 1,3-dipolar cycloaddition (1,3-DC) with diphenylnitrone (**7**) and the MM reaction with 2-trimethylsilyloxyfuran (**8**), with either 3-acryloyl- or 3-crotonoyloxazolidinones (**5a**,**b**), were tested (Scheme 2).

The Diels–Alder (DA) reaction: The DA reaction of **5a** and **6** is strongly *endo* selective and the *endo*-**9a**/*exo*-**10a** ratio was always more than 90:10 (Table 1). The enantioselectivity is strongly influenced by the nature of the cation: Ho, Y and Eu give very good enantioselectivities (entries 4–6: *ee* in the range 90–95 %) and Sc (entry 1) gives an excellent enantioselectivity (*ee* 99 %); in fact this catalyst gives one of the best results reported in the literature.

This ligand produces another remarkable result, since the enantioselectivity can be simply driven by changing the cation: the Sc-based catalyst gives (2′*S*)-**9a** in 99 % *ee*, while the Y-based catalyst furnishes the opposite enantiomer with up to 95 % *ee*. This specific property makes pybox **4** a unique ligand, better by far than *cis*-4′,5′-diphenyl-pybox, which gave a similar effect, but with a less pronounced shift in the enantioselectivity.[4]

The analogous DA reaction run on the crotonoyl derivative **5b** requires a higher temperature to be complete within 1–2 days and is less *endo* selective than the cycloaddition involving **5a**: if Sc is excluded, products **9b** and **10b** are obtained in a ratio varying from 2:1 to about 1:1. The enantioselectivity obtained with the Sc catalyst (Table 2, entry 1) is excellent, since the *ee*'s of (2′*S*)-**9b** and **10b** are 93 and 99 %, respectively. The catalysts with any other lanthanide revert the sense of the induction, but good results in terms of enantioselectivity are observed only for the *endo* isomer and for Ho, Y and Eu (Table 2, entries 4–6).



Scheme 2.

Table 2. Diels–Alder reactions between **5b** and **6** at 17 °C in CH_2Cl_2 in the presence of 10 % mol of catalyst and 4 Å molecular sieves.

Entry	Triflate	*t* [h]	[**9b**]/[**10b**][a]	**9b** *ee* %[b]	**10b** *ee* %[b]
1	Sc	24	92:8	93 (2′*S*,3′*R*) *Re*	>99 (2′*S*,3′*R*) *Re*
2	Lu	48	70:30	30 (2′*R*,3′*S*) *Si*	racemic
3	Yb	48	63:37	64 (2′*R*,3′*S*) *Si*	35 (2′*R*,3′*S*) *Si*
4	Ho	48	45:55	90 (2′*R*,3′*S*) *Si*	56 (2′*R*,3′*S*) *Si*
5	Y	48	55:45	90 (2′*R*,3′*S*) *Si*	54 (2′*R*,3′*S*) *Si*
6	Eu	48	68:32	90 (2′*R*,3′*S*) *Si*	49 (2′*R*,3′*S*) *Si*
7	Pr	48	71:29	87 (2′*R*,3′*S*) *Si*	30 (2′*R*,3′*S*) *Si*
8	La	16	74:26	81 (2′*R*,3′*S*) *Si*	18 (2′*R*,3′*S*) *Si*

[a] Yields were all quantitative. [b] The configuration is given in parentheses, followed by the face approach.

The behaviour of both dienophiles in terms of enantioselectivity response to the change of the cation is similar. Sc gives (*S*)-**9** as the preferred enantiomer, then, with the increasing of the ionic radius, the enantioselectivity is reverted with a maximum occurring with the medium-sized cations (Ho, Y, Eu). If log[(*S*)-**9**/(*R*)-**9**] or log[(*S*)-**10**/(*R*)-**10**] are plotted versus the lanthanide ionic radius (*r*), a two lines are obtained that intercept each other at Y, as clearly evidenced by the graph of Figure 1 in the case of **9a**. This is the same behaviour already observed in the asymmetric catalysis with other 4′-alkyl-substituted pybox ligands.[4,8]

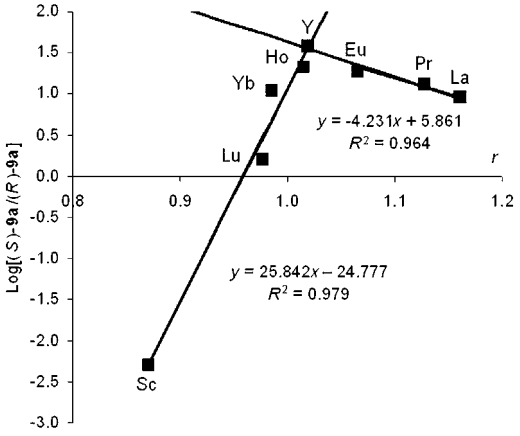


Figure 1. Plot of log[(*S*)-**9a**/(*R*)-**9a**] versus the lanthanide ionic radius (*r*).

1,3-Dipolar cycloaddition (1,3-DC): The 1,3-DC between **5a** and diphenylnitrone **7** was run at −20 °C, the yields are nearly quantitative, all catalysts are *exo*-selective and **12a** is the major product, an unusual behaviour in the pybox-catalysed 1,3-DC between **7** and **5a**.[1] For box-based catalysts *exo*-selectivity is much more usual; for example, compound **12a** was obtained with optical purity suitable to determine its absolute configuration through the X-ray structure of a derivative only by using *trans*-4,5-diphenyl bis(oxazoline) as the chiral ligand.[9]

If the *exo* selectivity is remarkable, the *ee* of **12a** obtained with the lanthanide/**4** complexes (Table 3) is unsatisfactory and cannot compete with the *ee* obtained with the above-mentioned box-based catalysts.

Table 3. 1,3-Dipolar cycloaddition of **5a** and **7** at −20 °C in CH_2Cl_2 in the presence of 10 % mol of catalyst and 4 Å molecular sieves.

Entry	Triflate	*t* [h]	[**11a**]/[**12a**][a]	**11a** *ee* %[b]	**12a** *ee* %[b]
1	Sc	48	22:78	50 (3′*S*,4′*R*) *Re*	20 (3′*R*,4′*R*) *Re*
2	Lu	48	10:90	24 (3′*S*,4′*R*) *Re*	67 (3′*R*,4′*R*) *Re*
3	Yb	48	9:91	5 (3′*R*,4′*S*) -	62 (3′*R*,4′*R*) *Re*
4	Ho	48	8:92	53 (3′*R*,4′*S*) *Si*	racemic
5	Y	48	10:90	53 (3′*R*,4′*S*) *Si*	7 (3′*S*,4′*S*) -
6	Eu	48	6:94	68 (3′*R*,4′*S*) *Si*	51 (3′*S*,4′*S*) *Si*
7	Pr	48	6:94	56 (3′*R*,4′*S*) *Si*	66 (3′*S*,4′*S*) *Si*
8	La	16	10:90	26 (3′*R*,4′*S*) *Si*	65 (3′*S*,4′*S*) *Si*

[a] Yields were all quantitative. [b] The configuration is given in parentheses, followed by the face approach.

Again, the enantioselectivity largely depends upon the cation: Lu and Yb (entries 2,3) give **12a** with the (3′*R*,4′*R*) configuration (67 and 62 % *ee* respectively), whereas Pr and La (entries 7,8) give the opposite enantiomer with comparable *ee*.

The reaction between the crotonoyloxazolidinone (**5b**) and **7** was run at room temperature; the yields are about quantitative and nearly equal amounts of *endo*-**11b** and *exo*-**12b** are obtained (Table 4). The *ee* of *endo*-**11b** is very disappointing with small cations, and only Pr and La (the larger cations; entries 7,8) give the (3′*R*,4′*S*,5′*R*) enantiomer with up to 64 % *ee*. In the case of *exo*-**12b**, a preferential approach of nitrone to the *Re*-face of the coordinated dipolarophile is observed with the smaller cations, and (3′*R*,4′*R*,5′*S*)-**12b** is the favoured stereoisomer (Sc, Lu and Yb; Table 4, entries 1–3), while the favoured approach with the larger cations is on the opposite *Si*-face (Table 4, entries 4–8), and a very good selectivity (90 % *ee*) of (3′*S*,4′*S*,5′*R*)-**12b** is obtained by using Pr (Table 4, entry 7).

The relationships between enantioselectivity and ionic radius are somewhat different from those observed in the case of the DA reaction, with trends that depend upon the dipolarophile.

Table 4. 1,3-Dipolar cycloaddition of **5b** and **7** at 25 °C in CH_2Cl_2 in the presence of 10 % mol of catalyst and 4 Å molecular sieves.

Entry	Triflate	*t* [h]	[**11b**]/[**12b**][a]	**11b** *ee* %[b]	**12b** *ee* %[b]
1	Sc	72	37:63	racemic	54 (3′*R*,4′*R*,5′*S*) *Re*
2	Lu	72	45:55	8 (3′*R*,4′*S*,5′*R*) -	50 (3′*R*,4′*R*,5′*S*) *Re*
3	Yb	72	49:51	11 (3′*R*,4′*S*,5′*R*) *Si*	34 (3′*R*,4′*R*,5′*S*) *Re*
4	Ho	72	59:41[c]	30 (3′*R*,4′*S*,5′*R*) *Si*	48 (3′*S*,4′*S*,5′*R*) *Si*
5	Y	72	56:44[d]	30 (3′*R*,4′*S*,5′*R*) *Si*	47 (3′*S*,4′*S*,5′*R*) *Si*
6	Eu	72	50:50[e]	45 (3′*R*,4′*S*,5′*R*) *Si*	81 (3′*S*,4′*S*,5′*R*) *Si*
7	Pr	72	50:50	64 (3′*R*,4′*S*,5′*R*) *Si*	90 (3′*S*,4′*S*,5′*R*) *Si*
8	La	72	56:44	64 (3′*R*,4′*S*,5′*R*) *Si*	85 (3′*S*,4′*S*,5′*R*) *Si*

[a] Yields were quantitative unless stated otherwise. [b] The configuration is given in parentheses, followed by the face approach. [c] Yield: 94 %. [d] Yield: 98 %. [e] Yield: 93 %.

The Mukaiyama–Michael (MM) reaction: The MM reaction of **5a** and **8** to give the enantiomers **13a** and **14a** is not easy, and only a few asymmetric catalysts have been applied to such a reaction. Two catalysts were first tested: the (*R*)-3,3′-bis(*N*,*N*-diethylaminomethyl)BINOL/Sc(OTf)$_3$, and [(*S*,*S*)-*tert*-butyl-box/Cu(OTf)$_2$ systems, both giving only moderate enantioselectivity.[10] Recently, after a careful optimisation of the reaction conditions and by using 4 Å molecular sieves (MS) and pentafluorophenol as additives, the (*R*)-*N*,*N*′-bis(2-quinolylmethylene)BINIM/Ni(ClO$_4$)$_2$ system has been reported to give the *S* enantiomer in excellent yield (93%) and enantioselectivity (with up to 91% *ee*).[11]

Of the eight lanthanide complexes of **4** tested, seven destroyed the reagents, and only the Sc-based complex was an efficient catalyst when one equivalent of alcohol with poor coordinating ability (trifluoroethanol (TFE), hexafluoroisopropanol (HFIP) or *tert*-butyl alcohol) and MS were used as additives (Table 5). In the presence of TFE, HFIP or *t*BuOH (Table 5, entries 5–7) the yields are quantitative and the enantioselectivity of **13a** is comparable with the best results reported in the literature.

Table 5. Mukaiyama–Michael reaction of **5a** and **7** at −50 °C in CH_2Cl_2 in the presence of 10% mol of catalyst, 4 Å molecular sieves (MS), and several additives.[a]

Entry	Triflate	Additives	*ee*%[b]
1	Sc	–	
2	Sc	MS	78 (*S*)
3	Sc	CF_3CH_2OH[c]	89 (*S*)
4	Sc	MS/EtOH[c]	89 (*S*)
5	Sc	MS/CF_3CH_2OH[c]	92 (*S*)
6	Sc	MS/$(CF_3)_2CHOH$[c]	92 (*S*)
7	Sc	MS/*t*BuOH[c]	93 (*S*)

[a] Yields were quantitative except for entry 1 for which no reaction occurred. [b] The configuration is given in parentheses. [c] One equivalent.

The conditions required to catalyse the reaction of **5b** and **8** were less selective and, in the presence of MS and one equivalent of TFE, the results reported in Table 6 (entries 2,5–11) were obtained.

Table 6. Mukaiyama–Michael reaction of **5b** and **7** at −20 °C in CH_2Cl_2 in the presence of 10% mol of catalyst, 4 Å molecular sieves, and several additives.

Entry	Triflate	Additives	[**13b**]/[**14b**][a]	**13b** *ee*%[b]	**14b** *ee*%[b]
1	Sc	–	96:4	82 (*S*,*S*) *Re*	44 (*R*,*S*) *Re*
2	Sc	[c]	98:2	94 (*S*,*S*) *Re*	>90 (*R*,*S*) *Re*
3	Sc	[d]	98:2	94 (*S*,*S*) *Re*	>90 (*R*,*S*) *Re*
4	Sc	[e]	96:4	94 (*S*,*S*) *Re*	>95 (*R*,*S*) *Re*
5	Lu	[c]	96:4	54 (*S*,*S*) *Re*	19 (*S*,*R*) *Si*
6	Yb	[c]	95:5	46 (*S*,*S*) *Re*	8 (*S*,*R*) –
7	Ho	[c]	90:10	42 (*R*,*R*) *Si*	3 (*R*,*S*) –
8	Y	[c]	93:7	26 (*R*,*R*) *Si*	18 (*R*,*S*) *Re*
9	Eu	[c]	87:13	70 (*R*,*R*) *Si*	33 (*R*,*S*) *Re*
10	Pr	[c]	75:25	53 (*R*,*R*) *Si*	4 (*R*,*S*) –
11	La	[c]	61:39	33 (*R*,*R*) *Si*	20 (*S*,*R*) *Si*

[a] Yields were all quantitative. [b] The configuration is given in parentheses, followed by the face approach. [c] With one equivalent of CF_3CH_2OH. [d] With one equivalent of *t*BuOH. [e] With one equivalent of $(CF_3)_2CHOH$.

The Sc complex (entry 2) gives excellent results both in terms of diastereo- (*anti*:*syn* = 98:2) and enantioselectivity (the *ee* of (*S*,*S*)-**13b** is 94%) and it can compete with the best asymmetric catalysts, specific for the MM reaction of **5a** and **8**, the bis[(4′*R*,5′*R*)-diphenyl]pybox complexes of La, Eu and Ce triflate.[2]

The enantioselectivity changes with the cation: the *ee* of (*S*,*S*)-**13b** decreases from Sc to Yb (entries 2,5,6); with Ho and the following lanthanides (entries 7–11), adduct (*R*,*R*)-**13b** is obtained as the preferential enantiomer, with a maximum corresponding to the medium-sized lanthanide (Eu, entry 9). Therefore, the relationship between enantioselectivity and ionic radius becomes again a net broken line as previously observed in the DA reaction.

Discussion

Some points deriving from the above-presented results require discussion and rationalisation:

1) The enantioselectivity reversion with the change of the cation taking the chiral ligand as constant.
2) The different selectivity induced by the catalysts with the change of the second reaction partner taking the coordinating reagent as constant.

The formation of opposite enantiomers by simply changing the lanthanide cation in the pybox-based catalyst has already been observed[4,8,12–14] and in the DA reaction the relationships between enantioselectivity and lanthanide ionic radius evidenced two different typologies. When the pybox had a phenyl group at the 4′-position on the oxazoline ring, a linear relationship was obtained, but when the 4′-substituent was an alkyl group, two lines were obtained that intercepted each other at one of the medium-sized cations, with the extremes being Sc and La.[4,8] This effect was interpreted as the result of a change in the coordination of chiral ligand and reagents (**4** and **5** in this research) around the different cations.

The relationship between enantioselectivity and lanthanide ionic radius described above (see Figure 1) suggests that, in spite of its complex structure, ligand **4** largely behaves as a 4′-alkyl-substituted pybox, and that (keeping the cation constant) **5a**,**b** could generate the same reacting intermediate in each catalytic process (DA, 1,3-DC and MM reaction) with the attack of the different reagents (**6**–**8**) on the same unshielded enantioface of the coordinated reagent.

This hypothesis was tested first with the predominant *endo* products of the DA reaction by plotting log[(*S*)-**9b**/(*R*)-**9b**] versus log[(*S*)-**9a**/(*R*)-**9a**] (Figure 2). When the cation is kept constant, the linear relationship strongly supports a similar behaviour of the reacting intermediates involving **5a** and **5b** versus **6**, independent of the coordination number (CN) of the complex.

To compare the reacting intermediates involved in the 1,3-DC and MM reactions with those of the DA cycloaddi-

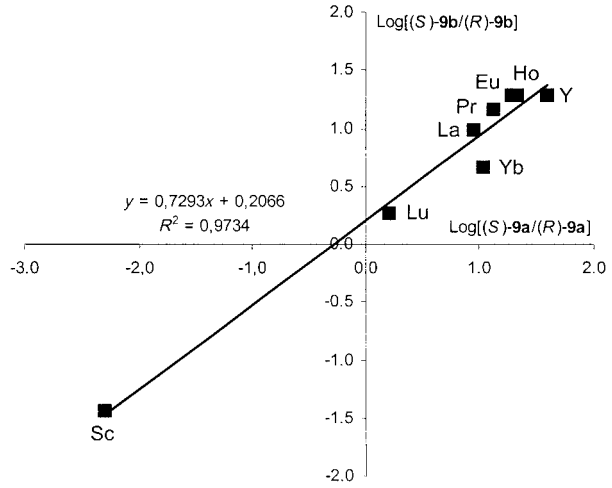


Figure 2. Plot of log[(*S*)-**9b**/(*R*)-**9b**] versus log[(*S*)-**9a**/(*R*)-**9a**].

tion, the enantioselectivity of the major products obtained from the reactions of **5b** (**12b** for the 1,3-DC and **13b** for the MM addition) were plotted versus the enantioselectivity of the *endo* product **9b**. Only the correlation between DA and MM data is linear (Figure 3), and this is a good experimental proof that similar reacting intermediates are involved in both the reactions. After the coordination of **4** and **5b** around the cation, the attack of either **6** (DA reaction) or **8** (MM addition) is on the same enantioface of the coordinated **5b**, to produce the same stereochemical outcome.

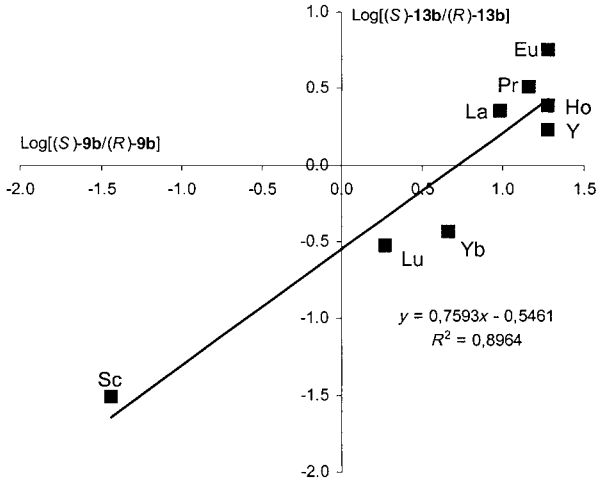


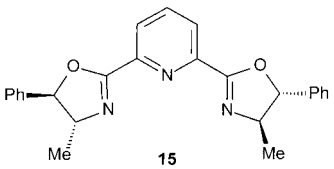
Figure 3. Plot of log[(*S*)-**13b**/(*R*)-**13b**] of the *anti*-adduct of the Mukaiyama–Michael versus log[(*S*)-**9b**/(*R*)-**9b**] of the *endo*-adduct of the Diels–Alder.

A linear relationship between enantioselectivity and ionic radius can be interpreted as the result of two competing pathways, each involving a reactive complex, the specific configuration of which induces the preferred attack to the *Re* or the *Si* face of the complexed reagent.[4,8] A broken linear relationship requires a more complicated model. To gain information about the reactive intermediates involved in the catalytic cycles of the above DA, 1,3-DC and MM reactions, possible tools are ^{1}H and ^{13}C NMR spectroscopic investigations and X-ray structure analysis of lanthanide pybox complexes.

Starting from the X-ray structure of a pybox-based complex, the substitution of some ligands (generally one or more triflate ions, one or more water molecules) with the coordinating reagent allows us to propose a model of a reactive intermediate that is able to rationalise the stereochemical outcome of the reaction. There have been reports in the literature of two crystal structures of Sc–pybox complexes; [Sc(Ph-pybox)$(OTf)_3(H_2O)$] and [Sc(Inda-pybox)$(OTf)_3$-(H_2O)].[15,16] In both cases, Sc has a CN of seven: the three nitrogen atoms of the pybox, one triflate ion, and one water molecule define the equatorial plane of the complex, while the two remaining triflate anions occupy the two residual apical positions. In the case of La, the reported crystal structure of [La(*trans*-4′,5′-diPh-pybox)$(OTf)_3(H_2O)_4$] shows that La has a CN of nine, because besides the three nitrogen atoms of the chiral ligand, two axial triflates and four water molecules are bound to La.[2]

To rationalise the relationship between cation and enantioselectivity, a homogenous set of crystal structures involving pybox and different lanthanides is required. Unfortunately, such a homogenous set of data is not available in the literature, but recently the molecular structures of six lanthanide(III) complexes have been determined. The ligands around the cation were the bidentate and negatively charged $PhC(NAr)_2$, the CH_2SiMe_3 group, and a variable number of THF molecules;[17] the crucial point is that the CN clearly increases with the increasing of ionic radius: the CN is five for the Sc-based complex, six for Lu, Y and Gd, and seven for Nb and La.

The Sc^{III}-mediated processes are discussed first, since the model is simple and because Sc gives the best enantioselective catalysts. The Sc complex of (4′*R*,5′*R*)-2,6-bis(4′-methyl-5′-phenyl-1′,3′-oxazolin-2′-yl)pyridine (**15**) was found to be a highly efficient catalyst of the DA reaction between **5a** and **6**, since (2′*S*)-**9a** was obtained with up to 97% *ee*;[4] the Sc complex of **4**, even if its configuration is opposite to that of **15**, gives the same (2′*S*)-**9a** with 99% *ee* (Table 1, entry 1).



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The models of the reacting complexes can be derived from the Sc^{III}–pybox molecular structures, if two vicinal triflates and the bound water are removed and substituted with **5**, through a complexation with the oxazolidinone CO group occupying the apical position of the complex.[4,8,18]

When a methyl group is at the 4′-position (pybox **15**), the *Si* face of the coordinated dienophile in the reacting intermediate **18** is shielded by the *trans*-phenyl group in the 5′-position; the increased steric demand of the substituent in the 4′-position of pybox **4** becomes the crucial factor in determining the face selectivity. The favoured attack of either cyclopentadiene **6** or trimethylsilyloxyfuran (**8**) on the reacting intermediate **19** will involve the *Re* face to give (2′*S*)-**9a**,**b** and (2′*S*)-**10a**,**b** from the attack of **6** to the coordinated dienophile (DA reaction), and (*S*,*S*)-**13b** from the attack of **8** in the MM reaction, Figure 4.

The reacting complexes of the diamagnetic trivalent cations Sc, Y, Lu and La, were tentatively characterised by NMR spectroscopy in $CDCl_3$, the common ligand being the pybox **4**, and **5a**, **5b** or 3-acetyl-1,3-oxazolidin-2-one (**5c**) (the last taken as an unreactive model of the dipolarophile used to test diphenylnitrone as potential auxiliary ligand) being alternatively involved in the formation of the complex.

The ^{1}H NMR spectra with Sc^{III} show the selective formation of complexes involving pybox and the cation, a behaviour with some precedents in pybox–Sc-catalysed reactions,[8,19] with **5a–c** not appreciably involved in the complexation. When nitrone is added to the sample containing **5c**, **4** and Sc, it is clearly coordinated to the cation.

The ^{1}H NMR spectra of [Y(**4**)] complexes are poorly resolved, but show the unequivocal coordination of **4**, **5c**, and (when added) **7** to the cation. The ^{1}H and ^{13}C NMR spectra of the [1:1:1] complex [Lu(**4**)-(**5c**)] are sufficiently resolved to demonstrate the formation of a complex involving both ligands and at least one triflate around the cation (q at 119.4 ppm, ^2J-(C,F) = 316 Hz). When one equivalent of **7** is added, the broadening and shifting of the methyne proton from 7.95 to 8.02 ppm, and the absence of the carbon absorptions formerly at 148.7 and 135.8 ppm, support the formation of a new complex that indeed retains the triflate and in addition contains nitrone.

When one equivalent of La-(OTf)$_3$ is added to an equimolar mixture of **4** and either **5a**, **5b** or **5c** in CH_2Cl_2, by diluting the solutions with pentane, three solid complexes (**20a**, **20b** and **20c** respectively) can be isolated and their ^{1}H and ^{13}C NMR spectra are reported in Table 7 with those of the uncomplexed reagents.

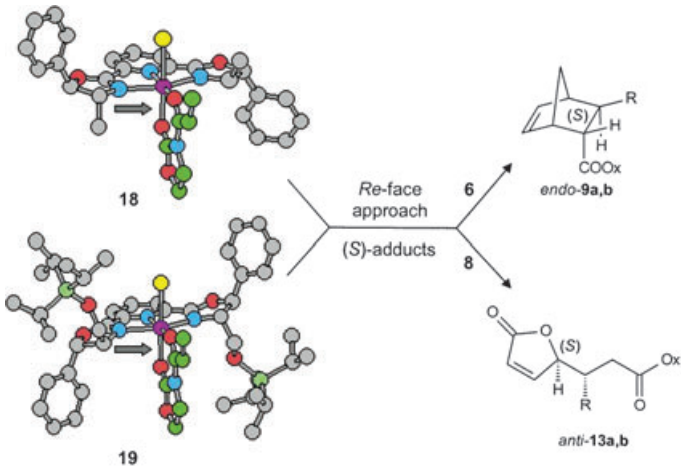
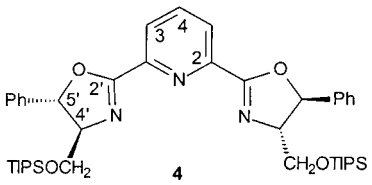
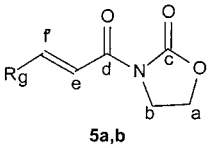


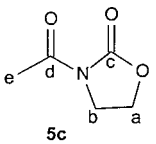
Figure 4. Assumed reactive intermediates for the reactions of **5** with both **6** (Diels–Alder) and **8** (Mukaiyama–Michael), catalysed by the Sc(OTf)$_3$ complexes of pybox **15** (reactive intermediate **18**) and **4** (reactive intermediate **19**).

The complexes of **5a**, **5b** and **5c** have very similar NMR spectra, with the oxazolidinone behaving as a bidentate ligand through its carbonyl groups, **4** is always a tridentate ligand, and each complex shows absorption of the triflate carbon as a quartet at 119.4 ppm. When one equivalent of **7** is added to complex **20c**, the nitrone is not involved in any

Table 7. ^{1}H- and ^{13}C NMR spectra of the La^{III} triflate complexes between **4** and **5a**, **5b**, or **5c** in $CHCl_3$.







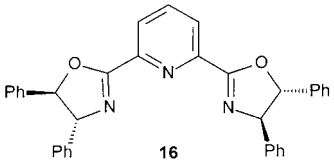
	4 δH, δC	**5a** δH, δC	**5b** δH, δC	**5c** δH, δC	**20c** δH, δC	**20a** δH, δC	**20b** δH, δC
H3	8.24	–	–	–	8.23	8.25	8.24
H4	7.93	–	–	–	8.17	8.19	8.18
H4′	4.40	–	–	–	4.77	4.74	4.74
H5′	5.76	–	–	–	6.00	5.96	5.96
Ha	–	4.44	4.28	4.36	4.50	4.55	4.55
Hb	–	4.10	4.04	4.04	4.18	4.21	4.21
He	–	7.50	7.25	2.56	2.12	6.95[a]	6.62[a]
Hf	–	6.55	7.10	–	–	6.42[a]	7.06
Hg	–	5.91	1.95	–	–	5.85[a]	1.83[a]
C2	147.0	–	–	–	144.3	144.3	144.3
C2′	162.8	–	–	–	166.6	166.5	166.6
C4′	76.9	–	–	–	74.0	74.1	74.1
C5′	84.9	–	–	–	88.4	88.1	88.2
Ca	–	62.0	61.9	61.6	62.5	63.0	63.0
Cb	–	42.5	42.5	41.9	42.9	43.4	43.6
Cc	–	153.2	153.4	153.4	–	–	–
Cd	–	164.9	165.0	169.9	–	–	–
Ce	–	126.9	121.3	22.8	23.5	–	–
Cf	–	131.6	146.6	–	–	–	–
SO_3CF_3	–	–	–	–	119.4	119.4	119.4

[a] Data at 50 °C.

kind of coordination (methyne H is a narrow singlet at 7.95 ppm, sharp carbon absorptions are observed at 148.7, 135.8 and 121.7 ppm). Further information on the structures of **20a–c** was derived from their HPLC-MS, which evidenced the presence of two triflate ions in each complex. In conclusion, the spectroscopic investigations demonstrate that La^{III} coordinates three nitrogen and two oxygen atoms, belonging to **4** and **5** respectively, and two triflate ions around the cation, while the addition of nitrone had no apparent effects.

To test the relevance of the isolated La-based complexes in the catalytic cycle, cyclopentadiene was added to samples of **20a** (cooled to −50 °C) and **20b** (at 17 °C), with molecular sieves, in CH_2Cl_2. After 16 h quantitative yields of adducts were obtained and the stereochemical results (see Experimental Section) were nearly superimposable to those reported in Tables 1 and 2 (entries 8). Thus it seems reasonable to assume that **20a**,**b** do not differ from the reacting intermediate involved in the La-catalysed DA and MM reactions.

The La complexes give two further pieces of information. There is a strong analogy between the NMR spectrum of **20b** and that of a complex with the same composition, but with *trans*-4′,5′-diPh-pybox (**16**) as chiral ligand,[2] even if the latter has been registered in CD_3CN. The absorptions belonging to coordinated **5b** are very similar; the crotonoyl



protons in the ^1H NMR spectra are well resolved at 50–70 °C and the δ values of the complex including **16** are nearly identical to those reported in Table 7. The signals Ca and Cb carbon atoms have nearly identical δ values in their ^{13}C NMR spectra; other signals of **5b** disappear upon complexation. The δ values of the triflate C atom signals are identical.

Even if the configuration of pybox **16** is opposite to that of **4**, the sense of induction of the DA and the MM reactions for both catalysts derive from the attack to the same *Si* face of **5b**.[2,3] Therefore, in order to rationalise the stereochemical outcome, it is necessary to assume that, in going from pybox **16** to **4**, the increased steric hindrance of the substituent in the 4′-position determines a deformation of the catalyst geometry without any change in the cation coordination sphere (see structures **21** and **22**, Figure 5). In the reactive intermediate **21**, derived from pybox **16**, the *Re* face of the coordinated alkenoyloxazolidinone is shielded by the phenyl group at the 5′-position of the ligand, while in the deformed complex **22** the shielding effect is exerted by the bulky substituent in the 4′-position of pybox **4**. In both cases, despite the opposite configuration of the chiral ligands, the reactive complex will favour an approach to the same *Si* face of the

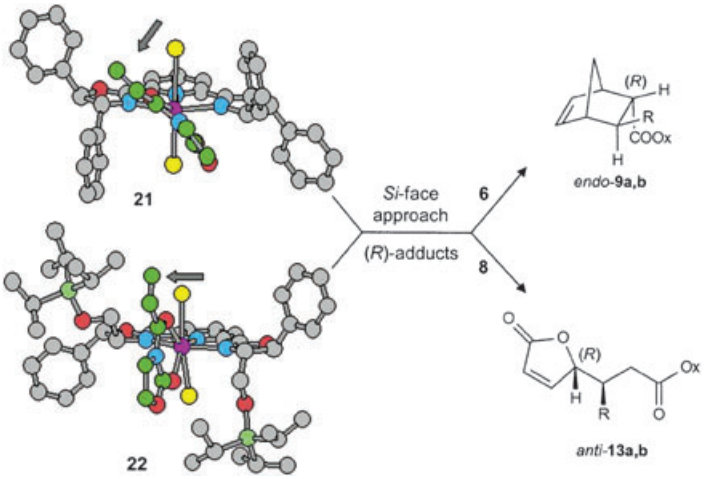


Figure 5. Assumed reactive intermediates for the reactions of **5** with both **6** (Diels–Alder) and **8** (Mukaiyama–Michael), catalysed by the $La(OTf)_3$ complexes of pybox **16** (reactive intermediate **21**) and **4** (reactive intermediate **22**).

coordinated reagent and only a reduction in the enantioselectivity will be observed.

The nonhomogenous behaviour of the set of catalysts with respect to 1,3-DC may also be rationalised from the above NMR spectra. The enantioselectivity induced into the DA and MM reactions by changing the lanthanides is similar because the second reagent is not involved in any reactive complexes, while the coordination ability of nitrone **7** has been found to depend upon the cation. Hence the relationship between enantioselectivity and lanthanide catalyst of the 1,3-DC reactions will not be comparable with that observed in the DA and MM reactions.

Conclusion

The new pybox ligand **4** described in this paper can be easily synthesised on a multigram scale, and, with lanthanide triflates, gives efficient enantioselective catalysis of the DA and the MM reactions of **5a**,**b**. The catalyst is less enantioselective in the 1,3-DC between diphenylnitrone **7** and **5**, even if some isoxazolidines are obtained with up to 90 % *ee*.

These results make pybox **4** competitive with 2,6-bis-[(4′*R*,5′*R*)-diphenyl-1,3-oxazolin-2′-yl]pyridine (**16**), one of the more flexible pybox ligands suitable for the preparation of catalysts with lanthanide cations. The new ligand has an important advantage over **16**, since the enantioselectivity is a function of the lanthanide with formation of opposite enantiomers simply by changing the cation. This specific character can be appreciated in the DA reaction of **5a**, since the complex [Sc^{III}(**4**)] gives the adduct (2′*S*)-**9a** with 99 % *ee*, whereas the complex [Y^{III}(**4**)] gives the opposite enantiomer with 95 % *ee*.

Experimental Section

General methods and materials: Melting points were determined by the capillary method and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. HPLC-MS spectra were carried out by using an LCQ DECA ion trap mass spectrometer equipped with electrospray ionisation (ESI) ion source and controlled by Xcalibur software 1.1 (Thermo-Finnigan, San Jose, CA, USA). For sample injection the instrument syringe pump was used at a flow rate of 5 μL min^{-1}. Samples were dissolved in CH_3CN. Experiments were carried out in positive ion mode under constant instrumental conditions: source voltage 2.0 keV, capillary voltage 37 V, sheet gas flow 29 (arbitrary units), capillary temperature 200 °C, tube lens voltage 0 V. Dichloromethane was the hydrocarbon-stabilised Aldrich ACS grade, distilled from calcium hydride and used immediately; lanthanide triflates were Aldrich ACS reagents; powdered molecular sieves 4 Å were obtained from Aldrich and heated under vacuum at 300 °C for 5 h and kept in sealed vials in a dryer. (1*S*,2*S*)-2-Amino-1-phenylpropane-1,3-diol (**1**) and 3-acetyl-1,3-oxazolidin-2-one (**5c**) were Aldrich commercial products. Dimethyl pyridine-2,6-dicarboximidate (**2**) was prepared from 2,6-dicyanopyridine following the literature method.[6] 3-Acryloyl- and 3-crotonoyl-1,3-oxazolidin-2-ones (**5a**,**b**) were prepared following the literature method.[20,21]

(4′*S*,5′*S*)-2,6-Bis(4′-hydroxymethyl-5′-phenyl-1′,3′-oxazolin-2′-yl)pyridine (3): A mixture of **1** (3.34 g, 20 mmol) and **2** (1.93 g, 10 mmol) in 1,2-dichloroethane (20 mL) was heated under reflux for 24 h. After cooling for a few hours at 5 °C, **3** precipitated as a white solid which was filtered, dried (2.67 g, 67 % yield), and directly used in the following reaction. A sample was crystallised from ethyl acetate as soft white crystals. M.p. 210–211 °C; $[\alpha]_D^{25} = +20.5$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 3.84$ (brs, 2H; -C*H*OH), 4.31 (m, 4H; 4′-H, -C*H*OH), 5.23 (brs, 2H; -OH), 5.79 (d, ^3J(H,H) = 8.3 Hz, 2H; 5′-H), 7.3–7.5 (m, 10H; aromatic protons), 7.69 (t, ^3J(H,H) = 7.8 Hz, 1H; 4-H), 7.92 ppm (d, ^3J(H,H) = 7.8 Hz, 2H; 3-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 62.7$ (-CH_2OH), 76.7 (4′-C), 83.3 (5′-C), 125.4 (3-C), 125.9, 128.4, 128.8, 137.0 (4-C), 146.3, 163.0 ppm; IR (Nujol): $\tilde{\nu} = 3308$ (OH), 1653 cm^{-1}; elemental analysis calcd (%) for $C_{25}H_{23}N_3O_4$ (429.5): C 69.91, H 5.40, N 9.79; found: C 70.05, H 5.33, N 10.00.

(4′*S*,5′*S*)-2,6-Bis[4′-(triisopropylsilyl)oxymethyl-5′-phenyl-1′,3′-oxazolin-2′-yl]pyridine (4): A suspension of **3** (2.14 g, 0.5 mmol), triisopropylsilyl chloride (2.12 g, 1.1 mmol) and imidazole (2.04 g, 3 mmol) in CH_2Cl_2 was stirred overnight at RT. The solvent was evaporated and the residue was subjected to chromatography over a short column of neutral Al_2O_3 with cyclohexane/AcOEt 85:15 as eluant. Pure **4** (3.15 g, 85 % yield) soon separated as a white solid. M.p. 111–112 °C; $[\alpha]_D^{25} = +62.2$ ($c = 1.0$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.07$ (m, 42H; TIPS), 3.84 (dd, ^3J(H,H) = 9.0, 9.8 Hz, 2H; -C*H*HO), 4.21 (dd, ^3J(H,H) = 4.1, 9.8 Hz, 2H; -C*H*HO), 4.40 (m, 2H; 4′-H), 5.76 (d, ^3J(H,H) = 6.4 Hz, 2H; 5-H), 7.3–7.4 (m, 10H; aromatic protons), 7.93 (t, ^3J(H,H) = 7.8 Hz, 1H; 4-H), 8.24 ppm (d, ^3J(H,H) = 7.8 Hz, 2H; 3-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 11.8$ (CH TIPS), 17.9 (CH_3 TIPS), 65.5 (CH_2O), 76.9 (4′-C), 84.9 (5′-C), 125.8, 127.9 (3-C), 128.4, 137.1, 140.8 (4-C), 147.0, 172.6 ppm; IR (Nujol): $\tilde{\nu} = 1642$ cm^{-1}; elemental analysis calcd (%) for $C_{43}H_{63}N_3O_4Si_2$ (742.2): C 69.59, H 8.56, N 5.66; found: C 69.75, H 8.48, N 5.78.

General procedure for the enantioselective Diels–Alder reaction between 5a and 6: Compound **5a** (0.042 g, 0.30 mmol), pybox **4** (0.03 mmol), the lanthanide triflate (0.03 mmol) and molecular sieves (about 0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient temperature in a rubber-septum-sealed vial; the mixture was stirred 1 h and then cooled at −50 °C. Compound **6** (100 μL, ca. 1.5 mmol) was added with a microsyringe and stirring was continued at −50 °C until TLC showed that all of the dienophile had reacted. The reaction was quenched in water, extracted with CH_2Cl_2, dried, the mixture of adducts **9a** and **10a** was separated from pybox **4** by column chromatography (silica gel, 30 cm L, 1,5 cm diameter, cyclohexane/ethyl acetate 75:25 was the eluant), and subjected to HPLC analysis using a Chiralcel OD column with hexane/2-propanol (9:1) as eluant (1.0 mL min^{-1}). The average retention times were 20 and 21 min for (1′*S*,2′*R*,4′*S*)- and (1′*R*,2′*S*,4′*R*)-3-(bicyclo[2.2.1]hept-5′-ene-2′-carbonyl)-2-oxazolidinone (**10a**) respectively, 22.5 and 25 min for (1′*S*,2′*S*,4′*S*)- and (1′*R*,2′*R*,4′*R*)-**9a** respectively, largely dependant on small variations of the solvents, and were checked with reference mixtures.

General procedure for the enantioselective Diels–Alder reaction between 5b and 6: Compound **5b** (0.046 g, 0.30 mmol), the chiral ligand pybox **4** (0.03 mmol), the lanthanide triflate (0.03 mmol) and molecular sieves (0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient temperature in a rubber-septum-sealed vial; the mixture was stirred 1 h and then kept at a constant temperature of 17 °C. Compound **6** (100 μL, ca. 1.5 mmol) was added and the reaction was worked up as previously described for the reaction between **5a** and **6**, except the HPLC analysis was performed on a Chiralpak AD column with hexane/2-propanol (98:2) as eluant (0.5 mL min^{-1}). The average retention times were 32 and 36 min for (1′*S*,2′*R*,3′*S*,4′*R*)- and (1′*R*,2′*S*,3′*R*,4′*S*)-3-(3-methylbicyclo[2.2.1]hept-5′-ene-2′-carbonyl)-2-oxazolidinone (**10b**) respectively, 34.5 and 40.5 min for (1′*S*,2′*S*,3′*R*,4′*R*)- and (1′*R*,2′*R*,3′*S*,4′*S*)-(**9b**) respectively.

General procedure for the enantioselective 1,3-dipolar cycloaddition between 5a and 7: Compound **5a** (0.042 g, 0.30 mmol), pybox **4** (0.03 mmol), the lanthanide triflate (0.03 mmol) and molecular sieves (about 0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient temperature in a rubber-septum-sealed vial, and the mixture was stirred for about 1 h. The mixture was then cooled at −20 °C and after about 10 min **7** (0.060 g, 0.30 mmol) was added and stirring was continued at −20 °C until TLC showed that all dipolarophile had reacted. The reaction was quenched in water, extracted with CH_2Cl_2, dried, the mixture of adducts **11a** and **12a** was separated from pybox ligand by column chromatography (silica gel, cyclohexane/ethyl acetate 80:20 was the eluant), and subjected to HPLC analysis using a Chiralpack AD column with hexane/2-propanol (8:2) as eluant (1.0 mL min^{-1}). The quality of 2-propanol was crucial for the separation and C. Erba solvent was the best. The average retention times were 17 and 19 min for (3′*S*,4′*S*)- and (3′*R*,4′*R*)-3-[(2′,3′-diphenylisoxazolidin-4′yl)carbonyl]-1,3-oxazolidin-2-one (**12a**) respectively; 20.5 and 24.4 min for (3′*R*,4′*S*)- and (3′*S*,4′*R*)-**11a** respectively.

General procedure for the enantioselective 1,3-dipolar cycloaddition between 5b and 7: Compound **5b** (0.046 g, 0.30 mmol), the chiral ligand pybox **4** (0.03 mmol), the lanthanide triflate (0.03 mmol) and molecular sieves (about 0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient temperature in a rubber-septum-sealed vial; the mixture was stirred for 1 h and then kept at a constant temperature of 25 °C. After about 10 min **7** (0.060 g, 0.30 mmol) was added and stirring was continued until TLC showed that all of the dipolarophile had reacted. The reaction was worked up as previously described for the reaction between **5a** and **7** and HPLC analysis was performed on a Chiralpak AD column with hexane/2-propanol (90:10) as eluant (1.0 mL min^{-1}). The average retention times were 17 and 18 min for (3′*R*,4′*R*,5′*S*)- and (3′*S*,4′*S*,5′*R*)-3-[(4′-methyl-2′,3′-diphenylisoxazolidin-4′-yl)carbonyl]-1,3-oxazolidin-2-one (**12b**) respectively; 31 and 43 min for (3′*R*,4′*S*,5′*R*)- and (3′*S*,4′*R*,5′*S*)-**11b** respectively.

General procedure for the enantioselective Mukaiyama–Michael reaction between 5a and 8: Compound **5a** (0.042 g, 0.30 mmol), pybox **4** (0.03 mmol), $Sc(OTf)_3$ (0.015 g, 0.03 mmol) and molecular sieves (about 0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient temperature in a rubber-septum-sealed vial; the mixture was stirred for about 1 h. The mixture was then cooled to −20 °C, the required amount (0.30 mmol) of the additive reported in Table 5 was added, and after about 10 min, **8** (0.047 g = 50 μL, 0.30 mmol) was added with a microsyringe. Stirring was continued at −20 °C until TLC showed that all **5a** reacted, the reaction was quenched in water, extracted with CH_2Cl_2 and dried; the mixture of enantiomers **13a** and **14a** was separated from the pybox ligand by column chromatography (silica gel, cyclohexane/ethyl acetate 50:50 was the eluant), and submitted to HPLC analysis using a Chiralpack AD column with hexane/2-propanol (1:1) as eluant (1.0 mL min^{-1}). The average retention times were 16 and 23 min for (*S*)-3-(2′,5′-dihydro-5′-oxo-2′-furyl)propanoyl-1,3-oxazolidin-2-one (**13a**) and (*R*)-**14a** respectively.

General procedure for the enantioselective Mukaiyama-Michael reaction between 5b and 8: Compound **5b** (0.046 g, 0.30 mmol), the pybox **4** (0.03 mmol), the lanthanide triflate (0.03 mmol) and molecular sieves (about 0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient

temperature in a rubber-septum-sealed vial; the mixture was stirred for 1 h and then cooled to −20 °C. The required amount (0.30 mmol) of the additive reported in Table 6 was added, and after about 10 min, **8** (0.047 g = 50 μL, 0.30 mmol) was added with a microsyringe. The reaction was worked up as previously described for **5a** and **8** and the HPLC analysis was performed on a Chiralpak AD column with hexane/2-propanol (2:1) as eluant (1.0 mL min^{-1}). The average retention times were 19 and 27 min for (*R*,*S*)- and (*S*,*R*)-3-(2′,5′-dihydro-5′-oxo-2′-furyl)butanoyl-1,3-oxazolidin-2-one (**14b**) respectively, 22 and 25 min for (*R*,*R*)- and (*S*,*S*)-**13b** respectively.

Complexes of 4, 5a–c and lanthanum triflate (20a–c)—general procedure: The pybox **4** (0.111 g, 0.15 mmol), La(OTf)$_3$ (0.088 g, 0.15 mmol) and **5a–c** (0.15 mmol) were dissolved in CH_2Cl_2 (2.0 mL). After one night the small amount of undissolved solid was filtered through a pipette, and pentane (about 15 mL) was added. After a few hours a white solid separated (about 75 % yield) that could be crystallised from benzene/hexane. The ^{1}H and ^{13}C NMR spectra are reported in Table 7, additional analytical and spectroscopic data are listed below.

Complex 20a: M.p. 140–142 °C; $[\alpha]_D^{25} = -22.4$ ($c = 0.5$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1761$ (C=O), 1653 cm^{-1}; MS (2.0 keV, ESI): *m/z* (%): 1319 (5) [**4**+**5a**+La(OTf)$_2$]$^+$, 1178 (100) [**4**+La(OTf)$_2$]$^+$; elemental analysis calcd (%) for $C_{52}H_{70}F_9LaN_4O_{16}S_3Si_2$ (1469.4): C 42.51, H 4.80, N 3.81; found: C 42.31, H 5.02, N 3.77.

Complex 20b: M.p. 148–150 °C; $[\alpha]_D^{25} = -27.6$ ($c = 0.5$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1757$ (C=O), 1653 cm^{-1}; MS (2.0 keV, ESI): *m/z* (%): 1333 (25) [**4**+**5b**+La(OTf)$_2$]$^+$, 1178 (100) [**4**+La(OTf)$_2$]$^+$; elemental analysis calcd (%) for $C_{53}H_{72}F_9LaN_4O_{16}S_3Si_2$ (1482.3): C 42.91, H 4.89, N 3.78; found: C 42.77, H 5.03, N 3.91.

Complex 20c: M.p. 160–162 °C; $[\alpha]_D^{25} = -24.2$ ($c = 0.5$ in $CHCl_3$); IR (Nujol): $\tilde{\nu} = 1758$ (C=O), 1653 cm^{-1}; MS (2.0 keV, ESI): *m/z* (%): 1307 (3) [**4**+**5c**+La(OTf)$_2$]$^+$, 1178 (100) [**4**+La(OTf)$_2$]$^+$; elemental analysis calcd (%) for $C_{51}H_{70}F_9LaN_4O_{16}S_3Si_2$ (1456.2): C 42.03, H 4.84, N 3.84; found: C 42.31, H 5.02, N 3.89.

Diels–Alder reaction between 20a and 6: Complex **20a** (0.050 g, 0.035 mmol) and molecular sieves (about 0.020 g) were added to anhydrous CH_2Cl_2 (0.2 mL) at ambient temperature under the conditions of the DA reaction of **5a** described above. Cyclopentadiene (**6**, 0.015 mL) was added at −50 °C and worked up as above (the chromatographic column was a pipette). The HPLC analysis gave a ratio **9a**/**10a** = 90:10; (2′*R*)-**9a** 75 % *ee*; **10a** was nearly racemic.

Diels–Alder reaction between 20b and 6: Complex **20b** (and molecular sieves) in anhydrous CH_2Cl_2 was reacted with **6** at 17 °C and worked up as above. The HPLC analysis gave a ratio **9b**/**10b** = 70:30; (2′*R*,3′*S*)-**9a** 80 % *ee*; (2′*R*,3′*S*)-**10b** *ee* was about 10 %.

Acknowledgements

This work was supported by MIUR and the University of Pavia. Thanks are due to CINMPIS for a fellowship to A.L.

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Received: November 26, 2004
Published online: April 13, 2005