DOI: 10.1002/ejoc.200600955

Pybox/Lanthanide-Catalysed Diels–Alder Reactions with an Unsaturated α-Oxo Ester or 3-Alkenoyl-2-oxazolidinone as Dienophile: The Sense of Stereoinduction in Five- or Six-Membered Bidentate Reagent Coordination

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Keywords: Asymmetric synthesis / Enantioselectivity / Lanthanides / Pybox

The enantioselective Diels–Alder (DA) reactions of cyclopentadiene with 3-cinnamoyl-1,3-oxazolidinone (**3**) and methyl (*E*)-2-oxo-4-phenyl-3-butenoate (**4**) carried out in the presence of lanthanide triflate complexes of (4′*S*,5′*S*)-2,6-bis[4′-(triisopropylsilyloxymethyl)-5′-phenyl-1′,3′-oxazolin-2′-yl]pyridine (**1**) have been compared. The aim of this work was to compare the effect of the α- and β-dicarbonyl derivatives, coordinated to the cationic site of the catalysts through a five- or six-membered ring chelation, respectively, on the face-selectivity of the reaction. Only the Sc^{III} triflate complex of **1** was found to be a very selective catalyst in the reaction with cinnamoyloxazolidinone **3**, which allowed almost complete stereocontrol. The reaction between cyclopentadiene and methyl keto ester **4** was more complicated because, in addition to the expected normal DA adducts **7** and **8**, the less expected *endo*-**9** product of the [4+2] hetero-DA (HDA) reaction, which resulted from the α-keto ester behaving as a heterodiene, was obtained. [3,3] Claisen rearrangement of HDA adduct **9** stereospecifically gave the *endo* DA product, which allowed a correlation to be made between the absolute configuration of these products. The scandium complex was found to be the best catalyst in both reactions: the DA reaction gave an *endo*-**7**:*exo*-**8** ratio of 95:5 and the *ee* of (2*R*,3*R*)-**7** was 99.5 %, whereas the HDA reaction was strongly selective and gave a single stereoisomer: (4*R*,4a*S*,7a*R*)-**9** with an *ee* > 99.5 %. The lanthanum complex furnished the opposite enantiomer in both reactions, albeit with low *ee*; the lanthanides with intermediate ionic radius gave results that were in between those of scandium and lanthanum. A rationale of the stereochemical outcome is proposed.

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 made impressive progress as a result of this research. In general, the catalyst consists of a cation coordinating an optically active organic ligand to give a complex with at least one free binding site to coordinate one reagent, which promotes the formation of the reacting complex involved in the catalytic cycle. Among the great variety of ligands having gone on stage in the last 15 years, C_2-symmetric bis(oxazolines) having either a single carbon atom or a pyridine ring as the spacer between the two heterocyclic rings (box[1] and pybox,[2] respectively) have been widely used in the formation of chiral catalysts.

To induce a good level of stereoselectivity, it is not enough to have at least one vacant Lewis acid site in the chiral complex suitable for coordination and activation of the reagent, but the resulting supramolecular complex [ligand/cation/reagent] must be rigidly oriented to favour the selective attack of the second reagent at one specific face of the coordinated substrate. This is the reason for the great success of dicoordinating reagents and, among them, of α- and β-dicarbonyl derivatives. These coordinating substrates, which differ in their dichelation with the cationic centre of the catalyst giving either a five- or six-membered structure, rigidly bind the reagent to the catalyst and hence induce face selectivity in the catalysed reaction. A great variety of enantioselective reactions of α- and β-dicarbonyl derivatives, catalysed by box and pybox complexes, have been reported: the dicarbonyl pendant may be the site of the reaction (aldol, Henry, Friedel–Crafts and carbonyl hetero-Diels–Alder reactions) or an attached group may be involved (Mannich, Michael, Diels–Alder and 1,3-dipolar cycloaddition reactions),[1,2] but a direct comparison of the effect of the different dicarbonyl pendants on face selectivity has not been extensively explored.

A new pybox class of catalyst has been obtained from (4′*S*,5′*S*)-2,6-bis[4′-(triisopropylsilyloxymethyl)-5′-phenyl-1′,3′-oxazolin-2′-yl]pyridine (**1**) and lanthanide(III) triflates, which works nicely in the Diels–Alder (DA) reaction between 3-acryloyl- and 3-crotonoyloxazolidinones and cy-

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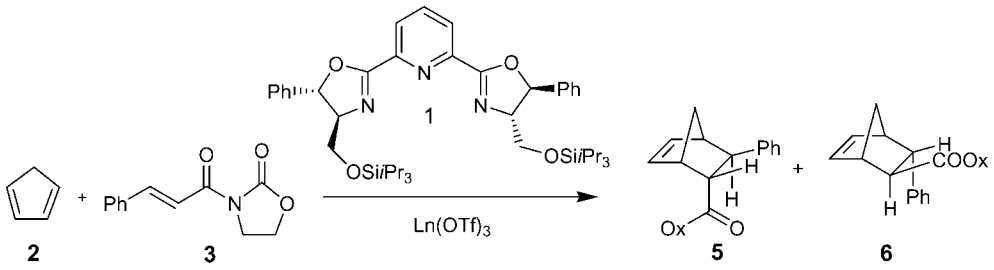
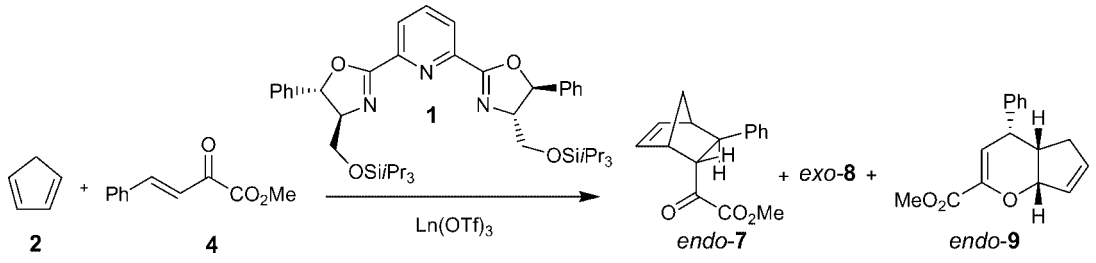


Scheme 1.



Scheme 2.

clopentadiene[3a] and in the Mukaiyama aldol reaction of pyruvates and 1-phenyl-1-trimethylsilyloxyethene.[3b] Therefore, the enantioselective DA reactions of cyclopentadiene (**2**) with 3-cinnamoyl-2-oxazolidinone (**3**) (Scheme 1) and methyl (*E*)-2-oxo-4-phenyl-3-butenoate (**4**) (Scheme 2) with the same catalyst and under comparable conditions may test the effect of five- and six-membered ring chelation on face selectivity.

The DA reaction between **2** and cinnamoyloxazolidinone **3** has been used by several groups as a benchmark to test the efficiency of a catalyst. Since the very first experiments with Ti/TADDOLates,[4] several other catalysts have been tested [lanthanides/BINAPH complexes,[5] Ni^{II}/ or Cu^{II}/bis(imines)[6] and catalysts involving a variety of chiral ligands[7]], but only Zn^{II} complexed to a ligand derived from pseudoephedrine[7e] gave an enantioselectivity comparable to that obtained by Evans and coworkers with the *t*Bu-box/Cu^{II} catalyst: yield 96%, *endo*/*exo* ratio 81:19, (*R*)-**5** *ee* 96%.[8]

The DA reaction between **2** and keto ester **4** has been explored less and only two results have been reported in the literature. The [Cu(SbF$_6$)$_2$] complex of (*R*,*R*)-dibenzofuran-2,2′-diylbis(4-phenyloxazoline) catalyses the DA reaction between **2** and **4** to yield **7** with an acceptable yield (50%), excellent stereoselectivity (*endo*/*exo* ratio 94:6) and promising enantioselectivity [68% *ee* for (2*R*,3*R*)-**7**].[9] Interestingly, the Ni^{II} complex of the same ligand catalyses the reaction of **2** with **3** to give (*R*)-**5** in 74% *ee*.[9] The second catalyst, the (*S*)-1,2,2-tris(4-*sec*-butyl-1,3-oxazolin-2-yl)propane/Cu(ClO$_4$)$_2$ complex, gives somewhat similar results [yield 64%, *endo*/*exo* ratio 97:3, (2*R*,3*R*)-**7** *ee* 71%].[10]

With these results as benchmarks, the specific affinity of pybox for lanthanide trivalent cations and the interesting effects on the enantioselectivity exerted by such cations[1] suggested that the complexes of pybox (**1**) with seven lanthanide triflates in the above DA reactions of cyclopentadiene with **3** and **4** should be tested.

Results

The DA reaction between **2** and 3-cinnamoyl-1,3-oxazolidin-2-one (**3**) (Scheme 1) was carried out at –20 °C and the majority of lanthanide cations gave either poor yields or unsatisfactory *ee*'s (Table 1). Only the Sc^{III} triflate complex of **1** proved to be very efficient and selective as the catalyst: the *endo*-**5**/*exo*-**6** ratio is 99:1, and the enantioselectivity is excellent with an *ee* of 98% for (2′*R*,3′*R*)-**5** (Table 1, Entry 1).

Table 1. DA reaction between **2** and **3**.[a]

Entry	Triflate	Time [d]	Yield[b] [%]	[**5**]/[**6**]	*ee* **5** (Config.) [%]	*ee* **6**[c] [%]
1	Sc	2	89	99:1	98 (2′*R*,3′*R*)	n.d.
2	Lu	10	traces	67:33	36 (2′*R*,3′*R*)	52 (2°)
3	Yb	8	57	76:24	4 (2′*R*,3′*R*)	11 (2°)
4	Y	8	71	76:24	5 (2′*S*,3′*S*)	5 (1°)

[a] Carried out at –20 °C in CH_2Cl_2 in the presence of 10 mol-% of the complex formed between **1** and Ln^{III} triflate and 4 Å molecular sieves (MS). [b] Isolated yields. [c] 1° and 2° refer to the HPLC order of elution.

The reaction between **2** and methyl (*E*)-2-oxo-4-phenyl-3-butenoate (**4**) (Scheme 2), carried out at –50 °C in CH_2Cl_2 in the presence of 10 mol-% of the **1**/lanthanide triflate complex, was more complicated because, in addition to the expected normal DA *endo* and *exo* adducts (**7** and **8**, respectively), the less usual product (*endo*-**9**) of the [4+2] hetero-DA (HDA) reaction, which results from the α-keto ester behaving as a heterodiene, was obtained. The enantioselective HDA reaction with cyclopentadiene behaving as a dienophile has rarely been observed and, to the best of our

knowledge, a single example has been reported in the literature: the reaction between crotonoylphosphonate and **2**.[11]

The two sets of isomers derived from the two competitive pericyclic processes can be easily separated by column chromatography.

The DA reaction is always strongly *endo* selective with the *endo*-**7**/*exo*-**8** ratio around 90:10 (or better), whereas the HDA adduct *endo*-**9** was obtained as a single regio- and diastereoisomer (^{1}H NMR NOESY experiments).

The enantioselectivity of the normal DA *endo* product **7** was strongly influenced by the nature of the cation: whereas the lanthanum-, europium-, holmium- and yttrium-based catalysts gave unsatisfactory *ee*'s, the ytterbium and lutetium catalysts gave results (84–88% *ee*) that were better than those reported in the literature. The best catalyst was again the scandium complex, which induced a high diastereoselectivity and almost complete enantioselectivity to nearly give a single *endo* enantiomer (Table 2, Entry 1). These pybox complexes produced another remarkable result as the enantioselectivity can simply be driven towards the selective formation of the opposite enantiomers by changing the cation. The scandium-based catalyst (Table 2, Entry 1) gave (–)-**7** in 99.5% *ee*, whereas the lanthanum-based one (Table 2, Entry 7) furnished the opposite (+) enantiomer in 31% *ee*. Results in between the two extremes were obtained with other cations and are a function of the lanthanide ionic radius. This specific aspect, already observed in the DA reactions of **2** with 3-acryloyl- and 3-crotonoyloxazolidinones catalysed by the lanthanide complexes of either **1** or *cis*-4′,5′-diphenyl-pybox,[3,12] seems to be a specific property of this type of ligand. These results allowed us to consider the Sc^{III} triflate complex of **1** as the best diastereo- and enantioselective catalyst for the DA reactions of both **3** and **4** with cyclopentadiene to be reported in the literature. The enantioselectivity of the HDA *endo* adduct **9** is again strongly influenced by the cation (Table 2). As chiral HPLC does not allow an optimum separation of the enantiomers, the *ee* of **9** was determined by a combination of HPLC and optical rotation (see the Experimental Section) as the scandium-catalysed reaction (Table 2, Entry 1) gave **9** as a single enantiomer whose optical rotation was never higher than –226.4.

By keeping the cation fixed, a close parallel between the *ee*'s of *endo*-**7** and *endo*-**9** in the DA and HDA reactions can be seen. The scandium-catalysed reactions (Table 2, Entry 1) were almost completely enantioselective and both products were obtained in 99.5% *ee*. The similar behaviour of the DA and HDA reaction, which includes the inversion of the enantioselectivity observed with the europium- and lanthanum-based catalysts, is illustrated by plotting the log of the enantiomeric ratio (*er*) of *endo*-**7** and *endo*-**9** versus the ionic radius of the lanthanide cation. The resulting graph (Figure 1) consists of two nearly superimposable linear relationships, analogous to that obtained with the lanthanide complex of 4′-phenyl- and *cis*-4′,5′-diphenylpybox.[12,13] These overlapping relationships can be interpreted as the result of two competing pathways, the DA and HDA processes, which occur with the same reacting complex for each single cation, whose specific configuration induces the same preferred attack on the *Re* or *Si* face of the complexed reagent with the same degree of enantioselectivity.

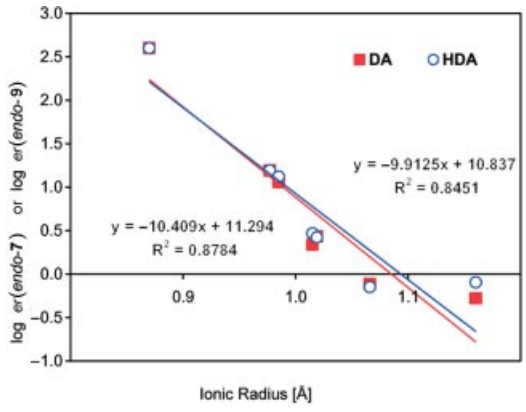


Figure 1. Plot of log*er* for the DA (*endo*-**7**) and HDA (*endo*-**9**) processes versus the lanthanide ionic radius.

Discussion

The Sc^{III}-mediated DA reaction between **2** and **3** will be discussed first because only scandium, of the different lanthanides tested, acts as an enantioselective catalyst. The reacting complex may have a [Sc^{III}/pybox] molecular structure in which dicoordinated **3** is bound to scandium with the oxazolidinone CO in the apical position of complex **10** and a triflate anion *anti* to it (Figure 2).[3,12] The steric demands of the substituent in the 4′ position of pybox (**1**)

Table 2. Diels–Alder and hetero-Diels–Alder reactions between **2** and **4**.[a]

Entry	Ionic radius [Å]	Triflate	Time [h]	Yield [b] [%]	[7+8]/[9]	[7]/[8]	*ee* **7** (Config.) [%]	*ee* **8** [c] [%]	*ee* **9** (Config.)[d] [%]
1	0.870	Sc	12	90	66:34	95:5	99.5 (2*R*,3*R*)	35 (2°)	99.5 (4*R*,4a*S*,7a*R*)
2	0.977	Lu	12	96	70:30	93:7	88 (2*R*,3*R*)	48 (2°)	88 (4*R*,4a*S*,7a*R*)
3	0.985	Yb	12	94	85:15	92:8	84 (2*R*,3*R*)	48 (2°)	86 (4*R*,4a*S*,7a*R*)
4	1.015	Ho	12	86	79:21	94:6	37 (2*R*,3*R*)	30 (2°)	49 (4*R*,4a*S*,7a*R*)
5	1.019	Y	12	82	85:15	93:7	46 (2*R*,3*R*)	40 (2°)	45 (4*R*,4a*S*,7a*R*)
6	1.066	Eu	12	77	78:22	92:8	13 (2*S*,3*S*)	7 (1°)	17 (4*S*,4a*R*,7a*S*)
7	1.160	La	24	98	81:19	91:9	31 (2*S*,3*S*)	36 (1°)	11 (4*S*,4a*R*,7a*S*)

[a] Carried out at –50 °C in CH_2Cl_2 in the presence of 10 mol-% of the complex formed between **1** and Ln^{III} triflate and 4 Å molecular sieves (MS). [b] Isolated yields. [c] 1° and 2° refer to the HPLC order of elution. [d] Determined by chiral HPLC and optical rotation.

becomes the crucial factor in determining face selectivity. If the favoured attack of cyclopentadiene **2** is at the less shielded *Re* face of bound dienophile **3**, then the formation of (2*R*,3*R*)-**7** can be rationalised.

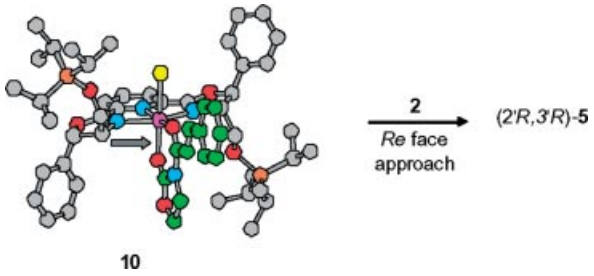


Figure 2. Assumed reacting intermediate **10** in the DA reaction between **2** and **3**, catalysed by the $Sc(OTf)_3$ complex of pybox (**1**); the yellow sphere represents a triflate ligand.

The rationale of the reaction between **2** and keto ester **4** suffers from the uncertainty of the absolute configuration of products **7** (the DA adduct) and **9** (the HDA one). The former has been reported twice in the literature[9,10] and the major *endo* enantiomer with a negative optical rotation was proposed to be (2*R*,3*R*)-**7** on the basis of considerations about the reactive intermediates and by analogy with the configuration of other products obtained from the same catalyst.[9]

Because the best reaction stereoselectivity was obtained with the Sc^{III} complex (Table 2, Entry 1), an attempt to rationalise the observed results will begin with this cation. A [Sc^{III}/pybox] molecular structure with dicoordinated ethyl glyoxylate bound to scandium with the ketonic CO in the equatorial position and the ester moiety (equivalent to the oxazolidinone CO in **3**) in the apical position has been reported in the literature.[14] If methyl (*E*)-2-oxo-4-phenyl-3-butenoate (**4**) is docked on **1** instead of glyoxylate and a triflate residue is placed in the apical position, then structure **11** is the model of the reacting complex (Figure 3).

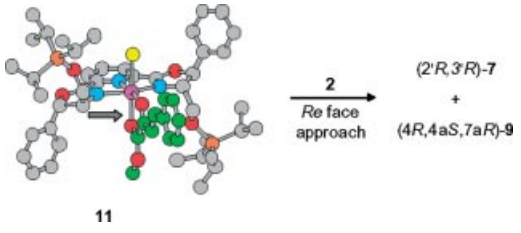
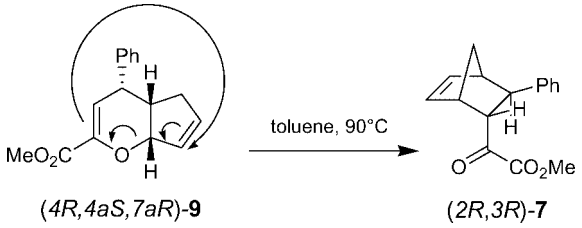


Figure 3. Assumed reacting intermediate **11** in the DA and HDA reactions between **2** and **4**, catalysed by the $Sc(OTf)_3$ complex of pybox (**1**); the yellow sphere represents a triflate anion.

The substituent in the 4′-position of pybox (**1**) becomes again the crucial factor in determining face selectivity. The formation of (2*R*,3*R*)-**7**, the same absolute configuration already proposed for the *endo* product with a negative optical rotation,[9] can be rationalised if the favoured attack of cyclopentadiene occurs at the less shielded *Re* face of bound dienophile **4**. This is the DA product arising from cyclopentadiene behaving as a diene. If attack occurs at the same *Re* face of **4** with cyclopentadiene behaving as a dienophile, (4*R*,4a*S*,7a*R*)-**9** must be the *endo* product of the HDA reaction.

Under these assumptions, there is a clear relationship between the absolute configurations of **7** and **9**. To test this, two pure samples of the DA and HDA products (which are fully stable under the reaction conditions), derived from the same reaction, were heated at 90 °C in toluene. Whereas the retro-DA reaction with formation of **4** is the only reaction of **7** after several days of heating, HDA adduct **9** was partly converted into **7** [ratio **9**/**7** = 40:60] after 12 hours. Chromatographic separation allowed us to isolate both **9** (with again the same composition of the starting product) and a pure sample of *endo*-**7** uncontaminated by *exo*-**8** (Scheme 3). The enantiomeric composition of **7** was determined by chiral HPLC; the major enantiomer was (2*R*,3*R*)-**7**, with nearly the same *ee* assigned earlier to **9**. This is a result of an asymmetric Claisen-type [3,3] sigmatropic rearrangement[15] from **9** to **7**, a reaction that has seldom been reported for DA/HDA reactions,[16,17] and never enantioselectively. Heating of the reaction cannot be continued until complete conversion of the starting material has occurred because **9**, after a longer time, begins to undergo the retro-DA reaction and ^1H NMR spectroscopic analysis shows the formation of **4**. This rearrangement is a clear demonstration that if (2*R*,3*R*) is the configuration of **7**, then **9** must be the (4*R*,4a*S*,7a*R*) enantiomer.



Scheme 3.

The low *ee* of the opposite enantiomer (Table 2, Entry 7) obtained from **4**, when bound to La^{III}, can be explained by assuming the same reactive intermediate as already involved in the Diels–Alder and Mukaiyama–Michael reactions of 3-acryloyl-oxazolidinones catalysed by **1**/$La(OTf)_3$.[3] This reacting complex is derived from the X-ray crystal structure of [La^{III}(*trans*-4′,5′-diPh-pybox)$(H_2O)_4(OTf)_2$],[18] but the increased steric hindrance of the substituent in the 4′-position of pybox (**1**) determines a deformation of the catalyst geometry. The presence of two apical triflates shifts **4** into the equatorial region of the complex and the bulky substituent in the 4′-position favours attack of cyclopentadiene at the less shielded *Si* face of bound keto ester **4**.

Conclusions

The lanthanide complexes of pybox (**1**), which have already been used as efficient catalysts in enantioselective DA and Mukaiyama–Michael reactions with acryloyl- and crotonoyloxazolidinones, are very efficient stereoselective cata-

lysts of the DA reaction of cyclopentadiene with 3-cinnamoyl-2-oxazolidinone (**3**) and methyl (*E*)-2-oxo-4-phenyl-3-butenoate (**4**), which gives both diastereo- and enantioselective results not easily obtained with other optically active catalysts.

These reagents, α- and β-dicarbonyl derivatives, are involved through bidentate coordination in the formation of reactive complexes characterised by either five- or six-membered structures. These rigid structures, when Sc^{III} is the Lewis acid core of the catalyst, give excellent facial discriminations with respect to the attack of cyclopentadiene. Both give DA adducts with high diastereo- and enantiomeric excesses. The latter, in addition to the DA reaction, undergoes the HDA reaction with the formation of a single stereoisomer. These results suggest **1** is one of the more versatile pybox ligands and is suitable for the preparation of excellent catalysts with lanthanide cations.

Experimental Section

General Methods and Materials: Melting points were determined by the capillary method with a Büchi 510 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 300 (300 MHz) spectrometer. Lanthanide triflates were purchased from Aldrich (ACS reagents); dichloromethane (Aldrich) was hydrocarbon-stabilised (ACS grade), distilled from calcium hydride and used immediately; powdered molecular sieves (4 Å; Aldrich) were heated under vacuum at 300 °C for 5 h and then kept in sealed vials in a dryer. 3-Cinnamoyl-1,3-oxazolidin-2-one (**3**) and methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**4**) were prepared following literature methods.[19,20] (4′*S*,5′*S*)-2,6-Bis[4′-(triisopropylsilyloxymethyl)-5′-phenyl-1′,3′-oxazolin-2′-yl]pyridine (**1**) was prepared as described previously.[3]

General Procedure for the Enantioselective Diels–Alder Reaction between Cyclopentadiene and 3-Cinnamoyl-1,3-oxazolidin-2-one (3): 3-Cinnamoyl-1,3-oxazolidin-2-one (**3**) (0.064 g, 0.30 mmol), pybox (**1**; 0.022 g, 0.03 mmol), the lanthanide triflate (0.03 mmol) and MS (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 15 min and then cooled to –50 °C. Cyclopentadiene (**2**, 100 μL, about 1.5 mmol) was added through a microsyringe and stirring was continued at –50 °C for the time reported in Table 1. The reaction was quenched with water, extracted with CH_2Cl_2 and dried. The mixture of adducts **5** and **6** was separated from **1** by column chromatography (silica gel, 30 cm, 1.5 cm, cyclohexane/ethyl acetate 75:25) and analysed by HPLC with the use of a Chiralcel AD column (hexane/2-propanol 95:5, 1.0 mL/min). t_R = 25 and 52 min for 3-(1′*S*,2′*S*,3′*S*,4′*S*)- and 3-[(1′*S*,2′*R*,3′*R*,4′*R*)-3′-phenylbicyclo[2.2.1]hept-5′-en-2′-ylcarbonyl]-1,3-oxazolidin-2-one (**5**), respectively, and t_R = 22 and 34 min for the enantiomers of *exo*-**6**, respectively, and may depend on small variations of the solvents and were checked with reference mixtures.

The adduct *endo*-**5** can be separated from its diastereoisomer *exo*-**6** by column chromatography (silica gel, 30 cm, 1.5 cm, cyclohexane/ethyl acetate 85:15). White crystals, m.p. 130–131 °C (hexane), Ref.[4h] 118 °C. IR (Nujol): $\tilde{\nu}$ = 1769 ($\nu_{C=O}$), 1693 ($\nu_{C=O}$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.10 (m, 5 H, aromatic protons), 6.55 (dd, *J* = 5.6 Hz, 3.2 Hz, 1 H), 5.95 (dd, *J* = 5.6 Hz, 2.7 Hz, 1 H), 4.50–4.30 (m, 2 H), 4.23 (dd, *J* = 5.2 Hz, 3.4 Hz, 1 H), 4.10–3.90 (m, 2 H), 3.49 (m, 1 H), 3.38 (dd, *J* = 5.1 Hz, 1.5 Hz, 1 H), 3.0 (m, 1 H), 1.97 (d, *J* = 8.7 Hz, 1 H), 1.59 (dd, *J* = 8.8 Hz, 1.7 Hz, 1 H) ppm. ^{1}H NMR data are identical to that in Ref.[21] ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.8, 173.8, 143.6, 140.1, 132.1, 128.4, 127.5, 126.0, 61.8, 50.2, 49.6, 48.0, 47.4, 46.8, 42.9 ppm. From the experiment reported in Table 1, Entry 1: (1′*S*,2′*R*,3′*R*,4′*R*)-**5** was obtained in 98% *ee*, $[\alpha]_D$ = –169.5 (*c* = 0.9, $CHCl_3$), Ref.[6e] 90% *ee* of (1′*R*,2′*S*,3′*S*,4′*S*)-**5**: $[\alpha]_D$ = +130.83 (*c* = 1.0, $CHCl_3$).

Adduct **6** was obtained by column chromatography as a thick oil. IR (Nujol): $\tilde{\nu}$ = 1778 ($\nu_{C=O}$), 1694 ($\nu_{C=O}$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.15 (m, 5 H, aromatic protons), 6.50 (dd, *J* = 5.6 Hz, 3.1 Hz, 1 H), 6.07 (dd, *J* = 5.6 Hz, 2.8 Hz, 1 H), 4.50–4.35 (m, 2 H), 4.13–4.00 (m, 3 H), 3.75 (dd, *J* = 5.4 Hz, 1.1 Hz, 1 H), 3.14 (d, *J* = 8.8 Hz, 1 H), 1.87 (d, *J* = 8.6 Hz, 1 H), 1.51 (dd, *J* = 8.6 Hz, 1.5 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.5, 153.3, 142.9, 137.0, 135.7, 127.9, 126.1, 61.8, 50.1, 49.9, 49.0, 47.0, 46.7, 42.9 ppm. $C_{17}H_{17}NO_3$ (283.32): C 72.07, H 6.05, N 4.94; found C 72.02, H 6.17, N 5.02.

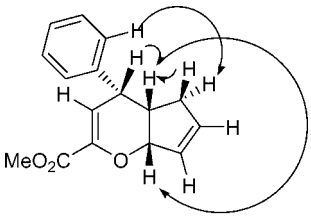
General Procedure for the Enantioselective Reaction between Cyclopentadiene and Methyl (*E*)-2-Oxo-4-phenylbut-3-enoate (4): Methyl (*E*)-2-oxo-4-phenylbut-3-enoate (**4**) (0.057 g, 0.30 mmol), pybox (**1**, 0.03 mmol), the lanthanide triflate (0.03 mmol) and MS (about 0.040 g) were added to anhydrous CH_2Cl_2 (0.3 mL) at ambient temperature in a rubber-septum-sealed vial, and the mixture was stirred for 15 min and then cooled to –50 °C. Cyclopentadiene (**2**; 100 μL, about 1.5 mmol) was added through a microsyringe and stirring was continued at –50 °C for the time reported in Table 2. The reaction was quenched with water, extracted with CH_2Cl_2, dried and the mixture of adducts was separated by column chromatography (silica gel, 30 cm, 1.5 cm, cyclohexane/ethyl acetate 92:8). The inseparable mixture of the Diels–Alder products **7** and **8** eluted first, then the hetero-Diels–Alder product **9**.

The mixture of **7** and **8** was submitted to HPLC analysis performed on a Chiralpak AD column (hexane/2-propanol 96:4, 1.0 mL/min). t_R = 13 and 15.5 min for methyl (1*R*,2*S*,3*S*,4*S*)- and (1*S*,2*R*,3*R*,4*R*)-3-phenylbicyclo[2.2.1]hept-5-en-2-ylglyoxylate (**7**), respectively, and t_R = 12 and 14 min for the two *exo* enantiomers (**8**) {Ref.[10] t_R = 9.55, 11.86, 8.66 and 10.76 min}.

From racemic or nearly racemic mixtures, **7** can be crystallised as colourless crystals, m.p. 45 °C (hexane); the same cannot be obtained from enantiomerically pure products. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 5 H, aromatic protons), 6.47 (dd, *J* = 5.6 Hz, 3.2 Hz, 1 H), 5.97 (dd, *J* = 5.6 Hz, 2.8 Hz, 1 H), 3.87 (s, 3 H), 3.77 (dd, *J* = 5.1 Hz, 3.4 Hz, 1 H), 3.51 (m, 1 H), 3.27 (dd, *J* = 5.0 Hz, 1.5 Hz, 1 H), 3.08 (m, 1 H), 1.96 (d, *J* = 8.7 Hz, 1 H), 1.63 (dd, *J* = 8.7 Hz, 1.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.0, 162.1, 143.3, 139.8, 132.6, 128.5, 127.3, 126.1, 56.5, 52.8, 49.0, 47.6, 47.1, 45.4 ppm. From the experiment reported in Table 2, Entry 1, a mixture of (1*S*,2*R*,3*S*,4*R*)-**7** and **8**, with the diastereomeric and enantiomeric composition therein reported, was obtained as a colourless oil. $[\alpha]_D$ = –152.8 (*c* = 1.3, $CHCl_3$).

The HDA product was isolated from each reaction reported in Table 2 (Entries 1–7) as a single diastereoisomer (*endo*-**9**, ^{1}H NMR: the results of NOESY experiments are schematically illustrated in Scheme 4). From the reaction reported in Entry 1 (4*R*,4a*S*,7a*R*)-2-methoxycarbonyl-4-phenyl-4,4a,5,7a-tetrahydrocyclopenta[*b*]pyran (**9**) was obtained as a colourless oil. $[\alpha]_D$ = –226.4 (*c* = 1.2, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1734 ($\nu_{C=O}$), 1649 ($\nu_{C=C\ dihydropyran}$) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.25 (m, 5 H, aromatic protons), 6.35 (dd, *J* = 3.0 Hz, 1.3 Hz, 1 H), 6.07 (s, 2 H), 5.14 (dd, *J* = 5.9 Hz, 2.1 Hz, 1 H), 4.10 (dd, *J* = 6.8 Hz, 2.9 Hz, 1 H), 3.84 (s, 3 H), 2.91 (m, 1 H), 2.13 (dd, *J* = 16.2 Hz, 8.4 Hz, 1 H), 1.74 (ddd, *J* =

17.0 Hz, 7.5 Hz, 1.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.3, 146.1, 141.7, 138.3, 130.6, 128.4, 127.6, 126.6, 112.1, 82.2, 52.1, 43.6, 38.1, 33.6 ppm. $C_{16}H_{16}O_3$ (256.30): C 74.98, H 6.29; found C 75.08, H 6.15.



(*4R,4aS,7aR*)-**9**

Scheme 4.

[3,3] Sigmatropic Rearrangement of (4*R*,4a*S*,7a*R*)-9 to (2*R*,3*R*)-7: Tetrahydrocyclopenta[*b*]pyran (4*R*,4a*S*,7a*R*)-**9** with an optical rotation of –210 (0.012 g), dissolved in anhydrous toluene (5 mL), was heated at 90 °C for 12 h. The solvent was evaporated, and the residue was purified by chromatography over silica gel (cyclohexane/ethyl acetate 92:8). The first fraction was (2*R*,3*R*)-**7** (0.004 g) and HPLC analysis performed on a Chiralpak AD column (hexane/2-propanol 96:4,1.0 mL/min) gave a mixture of (2*S*,3*S*)-**7** and (2*R*,3*R*)-**7** (t_R = 13.2 and 16.4 min, respectively) in a ratio of 3:97. Hence, the *ee* of starting product **9** was assumed to be 94%. The second fraction was (4*R*,4a*S*,7a*R*)-**9** (0.005 g), identical in every respect to the starting product.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of products **5**–**7** and **9** and some significant HPLC chromatograms of both DA and HDA products obtained from Sc^{III}- and La^{III}-catalysed reactions and of the Claisen rearrangement.

Acknowledgments

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

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Received: November 2, 2006
Published Online: February 2, 2007

