On the *trans–cis* controversy in Ti–TADDOLate-catalysed cycloadditions. Experimental indications for the structure of the reactive catalyst–substrate intermediate

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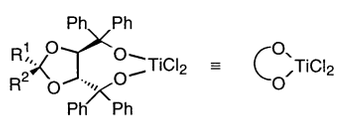
In order to investigate the structure of the reactive intermediate in the titanium-catalysed 1,3-dipolar cycloaddition, a series of reactions catalysed by $TiX(Pr^iO)_3$ and $TiX(Pr^iO)$-TADDOLate [X = Cl, Br, CF_3SO_3 (OTf)] complexes have been performed. The 1,3-dipolar cycloaddition between benzylidenephenylamine *N*-oxide and 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one is catalysed by 20 mol% $TiCl(Pr^iO)_3$ to give primarily the *exo*-isoxazolidine. If the chloride ligand of the catalyst is substituted with more bulky ligands such as bromide and trifluoromethanesulfonate, the selectivity of the reaction changes to give primarily the *endo*-isoxazolidine. The same change in diastereoselectivity from *exo* to *endo* is also observed by the application of $TiX(Pr^iO)$-TADDOLate (X = Cl, Br, OTf) complexes as catalysts for the analogous reaction. On the basis of these results, NMR spectral investigations and MM2 models, the most reactive intermediate in the $TiCl(Pr^iO)_3$ catalysed cycloaddition is proposed to be an octahedral complex in which the chloride ligand is located in the axial position relative to the plane defined by the two carbonyl oxygen atoms from 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one and two alkoxide ligands. The structure of the reactive intermediate in the Ti^{IV}-TADDOLate-catalysed 1,3-dipolar cycloaddition and Diels–Alder reactions is also briefly discussed on the basis of the results obtained.

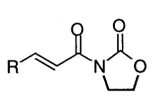
Introduction

TADDOLs (α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols) first reported by Seebach *et al*. have been widely applied as ligands in various Ti^{IV}-catalysed addition reactions.[1,2] For example the $TiCl_2$–TADDOLates **1** can catalyse important reactions such as the asymmetric Diels–Alder[3,4] and 1,3-dipolar cycloadditions[5] frequently inducing high diastereo- and enantio-meric excesses.



1

One of the challenges of catalytic asymmetric reactions such as the Diels–Alder and the 1,3-dipolar cycloadditions catalysed by the $TiCl_2$–TADDOLates **1** is to understand the catalytic properties of the catalyst and how the reaction proceeds. It is important to understand the structure of the reactive intermediate in these, as well as other reactions, in order to make improvements to the catalysts.



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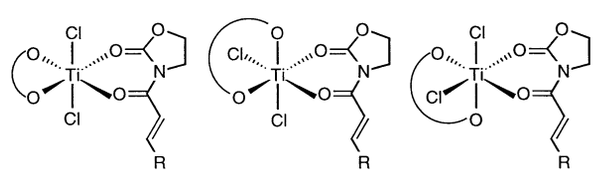
The mechanism of the asymmetric Diels–Alder reactions catalysed by $TiCl_2$–TADDOLates **1** using *N*-alkenoyloxazolidinone **2** as the dienophile have been the subject of debate.[6–10] The interest and controversy is related to the geometrical arrangement of the chiral ligand and the two chloride ligands at the titanium centre when **2** is coordinated to the metal.[6–10] Corey and Matsumura were the first to propose an intermediate to account for the stereochemical outcome of the $TiCl_2$–TADDOLate catalysed Diels–Alder reaction.[7] In this model the α,β-unsaturated carbonyl moiety of *N*-acryloyloxazolidinone was proposed to be in an s-*trans* geometry. More recently, DiMare and co-workers have studied similar complexes in solution by NMR spectroscopy.[8] In these studies three different intermediates were observed, and, in contrast to Corey's model, they all have the α,β-unsaturated carbonyl moiety in an s-*cis* conformation.[8] The three proposed intermediates **3a–c** are outlined below. The most abundant structure in solution **3a** (70%) has the four oxygen atoms in the same plane and the two chloride atoms perpendicular to this plane. In the two less abundant structures **3b** (24%) and **3c** (6%), the two chloride ligands are *cis* to each other. MM2-optimized structures of **3b** and **3c**, indicate that the α-*Si* face of the alkene is effectively shielded in **3b**, leading to an α-*Re* approach of the conjugated diene to the alkene in the Diels–Alder reaction, which is in agreement with experimental data.[4g] In **3c** the opposite α-*Si* approach would be favoured.[8]

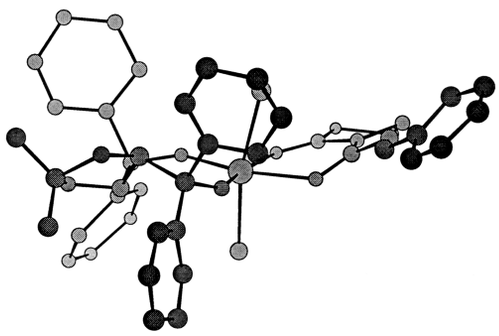


3a **3b** **3c**

DiMare and co-workers and Seebach *et al*. assumed that in **3a**, neither of the alkene faces are shielded sufficiently to account for the high enantioselectivities frequently obtained in the $TiCl_2$–TADDOLate-catalysed Diels–Alder reaction.[8,9] Furthermore, they propose **3b** to be more reactive than **3a**. In **3a** the carbonyl oxygen atoms of the *N*-alkenoyloxazolidinone **2** are located *trans* to the π-donating TADDOLate oxygen atoms, whereas in **3b** and **3c** one of the carbonyl oxygen atoms of **2** is located *trans* to one chloride ligand. This is proposed to lead to a higher degree of Lewis acid activation of the dienophile in **3b** and **3c** compared to **3a**.[8,9]

Recently, we obtained the crystal structure of a complex resulting from the mixing of $TiCl_2(Pr^iO)_2$, (2*R*,3*R*)-2,3-*O*-(2-

propylidene)-1,1,4,4-tetraphenylbutane-1,2,3,4-tetraol and 3-*N*-[(*E*)-cinnamoyl]-1,3-oxazolidin-2-one.[10a] This complex is similar to **3a**, the intermediate proposed to be most abundant in these asymmetric titanium-catalysed Diels–Alder reactions.[8] The X-ray structure of this complex, **4**, which we have proposed to be an intermediate in the Ti^{IV}–TADDOLate catalysed asymmetric Diels–Alder and the 1,3-dipolar cycloadditions, shows the TADDOLate and the *N*-cinnamoyl oxazolidinone ligands in the equatorial plane and the two chloride ligands in axial positions—*trans* to each other.[10a]



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It was found that complex **4**, both as a catalyst in the presence of different *N*-alkenoyloxazolidinones, and in a stoichiometric reaction, reacts with cyclopentadiene giving the same Diels–Alder product as obtained in the $TiCl_2$–TADDOLate-catalysed Diels–Alder reaction.[10b] Furthermore, it was shown that the diastereoselectivity was dependent on the axial ligands in **4**. Exchange of the chloride ligands in the complex with the more bulky tosylato ligands, leads to an increase in the *exo*-Diels–Alder product and a decreased amount of the *endo*-Diels–Alder product. We have also applied the knowledge of the structure of **4** to the development of a highly diastereo- and enantio-selective TiX_2–TADDOLate catalysed 1,3-dipolar cycloaddition of alkenes with nitrones, where *endo*:*exo* selectivities >95 : < 5 and enantiomeric excesses > 90% for some of the *endo*-isoxazolidines formed were obtained.[5c] The development of this highly selective reaction was also based on an exchange of the chloride ligands at the titanium atom with more bulky ligands leading to a change in the approach of the nitrone from an *exo* to an *endo* mode.[5c] The *endo*- and enantioselectivity of $Ti(OTos)_2$–TADDOLate-catalysed reaction was explained by an intermediate directly derived from **4**.

Thus, the question is: which of the intermediates **3a** or **3b**, in which the chloride ligands are located *trans* and *cis*, respectively, is the most probable intermediate in the TiX_2–TADDOLate catalysed reactions?[6–10] We have therefore investigated whether a chloride ligand in the position *trans* to the *N*-alkenoyloxazolidinone carbonyl groups, as in **3b** and **3c**, leads to a more reactive intermediate, and affects the stereochemical outcome of the reaction, than locating the chloride ligand in the axial position as in **3a**.

Results and discussion

In a recent paper we described a TiX_2–TADDOLate catalysed 1,3-dipolar cycloaddition between alkenes and nitrones such as 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one and benzylidenephenylamine *N*-oxide.[5c] In the cases where X = Cl in the catalyst, the reaction proceeded with *exo*-selectivity, but when the chloride ligands were substituted with a more bulky ligand such as bromide or tosylato the reaction proceeded with *endo*-selectivity.[5c]

This change from *exo*- to *endo*-selectivity was explained by steric repulsion between the *C*-phenyl substituent of the benzylidenephenylamine *N*-oxide and the axial ligand at the

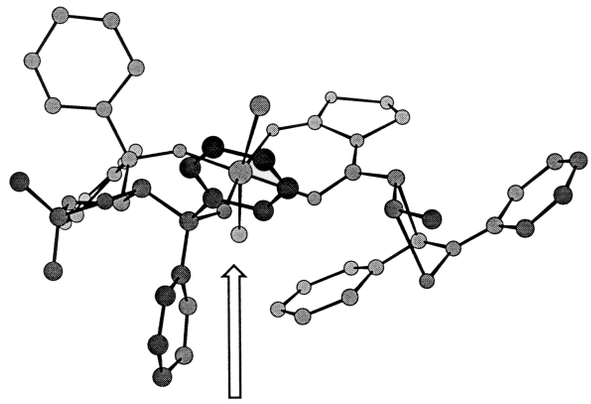
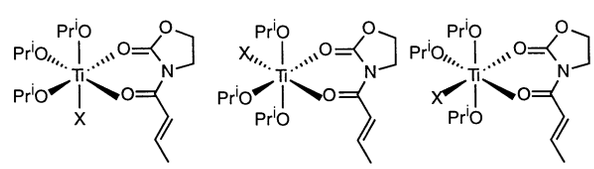


Fig. 1

titanium atom when the steric bulk of the ligand is increased (Fig. 1). However, since both our proposed intermediate **4**/**3a** and DiMare's and Seebach's suggested intermediate **3b** contain at least one chloride ligand axial to the plane defined by the titanium atom and the two carbonyl groups of *N*-alkenoyloxazolidinone **2**, the change in *endo*/*exo* selectivity when exchanging the chloride ligands with bulkier ligands can to a certain extent be accounted for by both intermediates. Thus, we have turned our attention to monochlorotitanium trialkoxides,[11] since in these complexes the chloride ligand can either be located in the axial position or in the equatorial plane, *trans* to the carbonyl group of **2**. In order to investigate the effect of the position of the chloride ligand on the reactivity of the intermediates a number of reactions, presented in the following, have been performed.

The $Ti(Pr^iO)_3X$ (X = Cl, Br, OTf; Tf = CF_3SO_2)-3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one case

There are three possible intermediates **5a–c** when 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one (**2a**) is coordinated to $TiX(Pr^iO)_3$ (X = Cl, Br, OTf) **6a–c**. For **5a** which is a chiral structure the mirror image also exists but it will not alter the reaction course. The structures **5b** and **5c** are achiral. Intermediate **5a** has ligand **2a** and two alkoxide ligands in the equatorial plane, while the remaining alkoxide ligand and the X ligand occupy axial positions. The two intermediates **5b** and **5c** have two alkoxide ligands in axial positions while one alkoxide ligand and the X ligand are at the two alternative sites in the equatorial plane.



5a-X X = Cl, Br, OTf

5b-X X = Cl, Br, OTf

5c-X X = Cl, Br, OTf

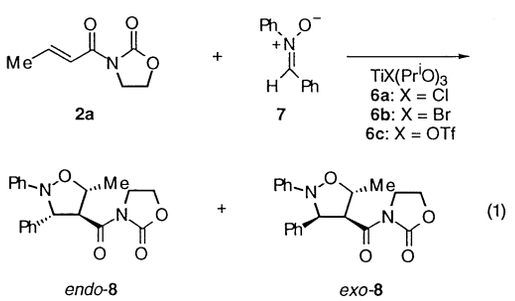
The reaction of 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one **2a** with benzylidenephenylamine *N*-oxide **7** in the presence of $TiX(Pr^iO)_3$ (X = Cl, Br, OTf) as the catalyst leads to the isoxazolidines *endo*-**8** and *exo*-**8** [eqn. (2)].

The *endo*/*exo*-selectivity[5a,c] is dependent on the approach of benzylidenephenylamine *N*-oxide **7** to the alkene part of 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one **2a** when coordinated to the catalyst $TiX(Pr^iO)_3$. The three intermediates **5a–c** should thus be expected to show different *endo*/*exo*-selectivity in their reaction with **7**. For intermediate **5a** a dependence on X should be expected since this ligand is close to the reaction path for the approach of **7** to the alkene part of **2a**, whereas for the intermediates **5b**,**c**, in which X is more distant from the reaction centre a less significant dependence on X should be expected.

Table 1 Effects of various $TiX(Pr^iO)_3$ (X = Cl, Br, OTf) complexes on the *exo*/*endo* selectivity of the 1,3-dipolar cycloaddition of 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one **2a** and benzylidenephenylamine *N*-oxide, **7**. The catalysts **6a–c** are achiral, while the catalysts **10a–c**, in the presence of α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol ligand, are chiral.

Entry[a]	Catalyst (20 mol%)	*endo*:*exo*[b] (%)	ee (*endo*)[c] (%)	ee (*exo*)[d] (%)
1	**6a**	32:68	—	—
2	**6b**	70:30	—	—
3	**6c**	93:7	—	—
4	**10a**	16:84	47	51
5	**10b**	83:17	84	42
6	**10c**	89:11	30	42[e]

[a] After reaction time of 48 h, conversions >80% were obtained in all entries. [b] *endo*:*exo* ratios were determined by ^{1}H NMR spectroscopy of the crude product. [c] The ee of *endo*-**8** was determined by HPLC (Daicel Chiralcel OD using hexane: Pr^iOH 90:10). [d] The ee of *exo*-**8** was determined by ^{1}H NMR spectroscopy using $Eu(hfc)_3$ as chiral shift reagent. [e] Opposite enantiomer compared with **10a,b** as the catalyst.

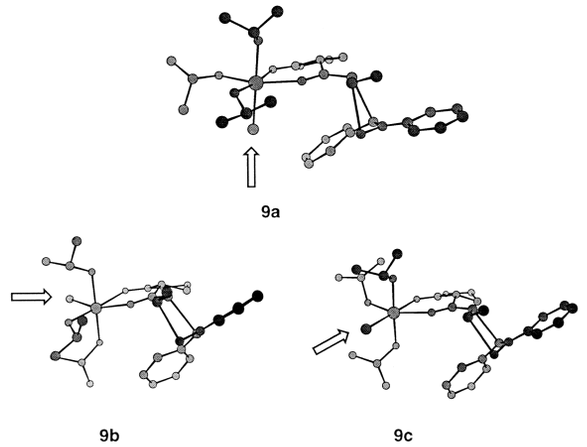


The results for the reaction of **2a** with **7** in the presence of the catalysts **6a–c** are presented in Table 1 (for details see Experimental section).

The diastereoselectivities obtained in the three first entries in Table 1 clearly show a significant dependence on X in the $TiX(Pr^iO)_3$ (X = Cl, Br, OTf) **6a–c** catalysts. Increasing the steric volume of X from chloride to bromide to triflato in the catalyst leads to a significant change in the diastereoselectivity of the reaction between **7** and **2a**. For the reaction catalysed by $TiCl(Pr^iO)_3$ an *endo*-**8**:*exo*-**8** ratio of 32:68 is obtained, while $TiBr(Pr^iO)_3$ gives a ratio of 70:30 and finally by the application of $TiOTf(Pr^iO)_3$ as the catalyst a total change in the *endo*-**8**:*exo*-**8** ratio to 93:7 in favour of *endo*-**8** is obtained.[12]

Inspection of the results for the influence of the X ligand in the $TiX(Pr^iO)_3$ (X = Cl, Br, OTf) **6a–c** catalysts on the diastereoselectivity of the reaction of **2a** with **7** adds some interesting restrictions to the catalytic intermediates **5a–c** in this reaction. The approach of **7** to the alkene part in **5a–c** assuming a distance of 2.5 Å between the reacting atoms is presented in **9a–c**. These three approaches have been obtained using MM2 calculations[13] assuming an octahedral intermediate and X = Cl (the chloride atom is indicated with an arrow).

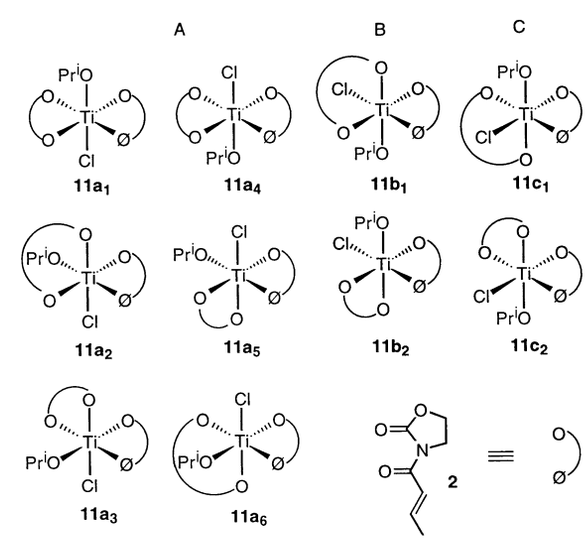
The approach of **7** in an *exo*-fashion to the alkene moiety of **2a** coordinated to $TiCl(Pr^iO)_3$ outlined in **9a–c** shows that for the approach of **7** to **5a** (**9a**) steric repulsion between the α-C-phenyl substituent of **7** will dominate when the axial chloride ligand is substituted with the more steric demanding bromide and triflato ligands. This increased steric repulsion between the α-C-phenyl substituent of **7** and the axial ligand in the catalyst might force a change of the reaction path for the nitrone from an *exo*-approach to an *endo*-approach giving *endo*-**8** as the major diastereomer as the bulkiness of the axial ligand increases. It should be noted that for the titanium-catalysed reaction of **7** with **2a** in the absence of steric repulsion between the ligands at the titanium centre, the *exo*-transition state is lower in energy than the *endo*-transition state.[5b] Thus *exo*-**8** is primarily formed if the spatial arrangement of the ligands at



the titanium catalyst allows for it.[5b] The approach of **7** to the alkene in intermediate **5b**, outlined in **9b**, probably occurs *via* the *endo*-transition state due to the steric bulk of the axial isopropoxy ligands. A substitution of the chloride ligand in **9b** with bromide or triflato will not be expected to have any significant influence on the diastereoselectivity of the reaction since the equatorial ligand is not in close contact with the incoming nitrone in the *exo*-transition state. The behaviour of intermediate **9c** is expected to parallel that of **9b**. Thus, when X = Cl most of the reaction probably takes place through intermediate **5a** and for X = Br and OTf intermediate **5a** might also account for the reaction path, but for the two latter catalysts, we cannot exclude that an important part of the reaction occurs through intermediate **5b** and/or **5c**.

The $TiX(Pr^iO)$–TADDOLate (X = Cl, Br, OTf)-3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one case

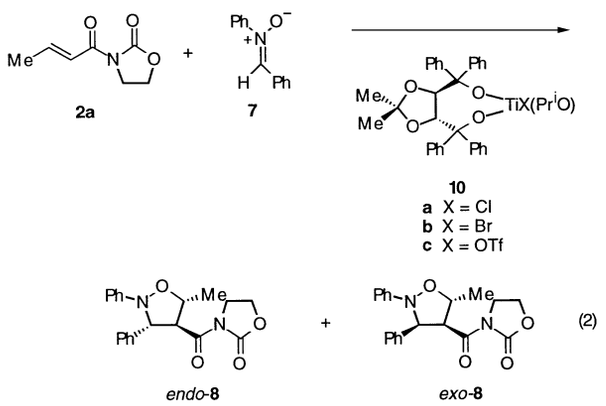
Compared with the $TiX(Pr^iO)_3$ (X = Cl, Br, OTf)-3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one case presented above, the exchange of two of the alkoxide ligands with a TADDOL ligand leads to an increase in the number of possible intermediates when 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one **2a** coordinates to the $TiX(Pr^iO)_3$–TADDOLate (X = Cl, Br, OTf) **10a–c** catalyst. The possible intermediates can be separated into three groups. (A) The chloride ligand can be located in the axial position as in **5a**. Examining **5a**, a substitution of two isopropoxy ligands with the TADDOL ligand can be performed to give three different structures $\mathbf{11a_{1-3}}$, three aditional structures $\mathbf{11a_{4-6}}$ can be obtained in a similar manner from the mirror image of **5a**. (B) The chloride ligand can be located in the *trans*-position to the α,β-unsaturated carbonyl group as in **5b**. Substitution of two isopropoxy ligands in **5b** with the TADDOL ligand can be per-



formed to give two different structures **11b**$_{1–2}$. (C) The chloride ligand can be located in the *trans*-position to the oxazolidinone-carbonyl group as in **5c**. Substitution of two isopropoxy ligands in **5c** with the TADDOL ligand can be performed to give two different structures **11c**$_{1–2}$. The ten possible intermediates **11** are shown (for the definition of the TADDOL ligand, see above).

The reaction of 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one **2a** with benzylidenephenylamine *N*-oxide **7** in the presence of **10a–c** as the catalyst [eqn. (2)] have been performed and the results are presented as entries 4–6 in Table 1.

The results in Table 1 for the reaction of **2a** with **7** in the presence of **10a–c** as the catalyst show the same trends as the reactions performed with TiX(Pr^{i}O)$_3$ (X = Cl, Br, OTf) **6a–c** as the catalyst. The catalyst **10a** (entry 4) gives an *endo*-**8**:*exo*-**8** ratio of 16:84, whereas the catalysts **10b,c** give *endo*-**8**:*exo*-**8** ratios of 83:17 (entry 5) and 89:11 (entry 6), respectively. The trends of the *endo*-**8**:*exo*-**8** ratio for the catalysts **10a–c** are thus the same as for the catalysts **6a–c** showing an increase in the bulkiness of the X ligand changes the approach of **7** to the alkene part in **2a** when coordinated to the catalyst from an *exo*-



to an *endo*-approach. The ee values induced by the chloride containing catalyst **10a** are 47 and 51% of *endo*-**8** and *exo*-**8**, respectively, which is *ca*. 10% lower than those obtained by the analogous TiCl$_2$–TADDOLate catalyst **1**.[5a] Surprisingly, the ee of 84% of *endo*-**8** obtained by catalyst **10b**, is higher than the one obtained by the analogous TiBr$_2$–TADDOLate catalyst, whereas the ee of the *exo*-isomer is *ca*. 20% lower.[5c] The triflato containing catalyst **10c** induces lower ee values than the halide analogues. However, as demonstrated in earlier work,[5c] the analogous Ti(OTf)$_2$–TADDOLate catalyst leads to a racemic reaction with respect to the formation of *endo*-**8**. The *exo*-isomer of **8** is obtained with 42% ee by the application of **10c** as the catalyst. To our surprise the opposite enantiomer of *exo*-**8** is obtained in an excess by the use of catalyst **10c** compared with the reactions applying **10a** and **10b** as the catalysts.

Based on the same arguments as for the TiX(Pr^{i}O)$_3$ case, we propose that the reason for change in the *exo*/*endo*-selectivity in the 1,3-dipolar cycloaddition of **2a** with **7**, when the chloride ligand in the TiX(Pr^{i}O)–TADDOLate catalyst is exchanged with more bulky ligands is that the reaction proceeds *via* a transition state in which the chloride ligand is located in the axial position.

Now, there are at least two possible explanations for the change in *exo*/*endo* selectivity of the 1,3-dipolar cycloaddition reaction between **2a** and **7**, in the presence of TiCl(Pr^{i}O)$_3$ **6a** or TiCl(Pr^{i}O)–TADDOLate **10a** as the catalysts. (*i*) The only present intermediates have the chloride ligand or the more bulky ligands in the axial position or (*ii*) the intermediate with the chloride ligand in the axial position (**5a**-Cl or **11a**$_{1–6}$-Cl) are more reactive than the other possible intermediates.

To investigate which of the two possibilities accounts for the diastereoselectivity of the reaction, a simple ^{1}H NMR spectroscopy investigation was performed on the intermediates **5a–c**, X = Cl, to determine if there are intermediates other than **5a**-Cl. A mixture of TiCl(Pr^{i}O)$_3$ and an excess of **2a** in CD_2Cl_2 was studied at −40 °C. One doublet appears at 1.91 ppm corresponding to the methyl substituent of non-coordinated **2a**. Two doublet of doublets signals appear at 1.83 and 2.07 ppm, respectively, with relative integrals of 1.25 to 1.00. These signals are proposed to correspond to the methyl substituent of the *N*-alkenoyloxazolidinone in two of the three possible intermediates **5a–c** with X = Cl. Contrary to **5b**-Cl and **5c**-Cl, **5a**-Cl does not have isopropoxy ligands facing *trans* to each other and **5a**-Cl is proposed to be more stable than **5b**-Cl or **5c**-Cl. Thus, the more abundant intermediate appearing at 1.83 ppm in the ^{1}H NMR spectrum is assumed to be **5a**-Cl. The less abundant intermediate appearing at 2.07 ppm in the ^{1}H NMR spectrum can be either **5b**-Cl or **5c**-Cl.

In conclusion both the intermediate with an axial chloride ligand **5a** and one of the two intermediates without an axial chloride ligand **5b** or **5c** are present in solution in 56 and 44%, respectively. Since the *exo*-isoxazolidine is primarily obtained in the reaction between **2a** with **7**, catalysed by **6a**, the reaction probably primarily occurs *via* a transition state having an axial chloride (*vide supra*) **5a**. Thus, the present results indicate that the intermediate **5a**, having an axial chloride ligand is more reactive in the 1,3-dipolar cycloaddition reaction, than the intermediates **5b** and **5c** in which the chloride ligand is located *trans* to one of the carbonyl groups of **2a**. This conclusion also seems to account for the results obtained in the reactions between **2a** and **7** in the presence of catalyst **10**, although we have not been able to measure the relative abundance of the intermediates **11** by ^{1}H NMR spectroscopy due to the relative high number of possible intermediates. It appears to us that the degree of Lewis acid activation of **2a** by lowering the LUMO energy by coordination to the titanium catalyst **6a** is primarily controlled by the axial ligand rather than the ligands in the *trans* position to the carbonyl groups of **2a**. If we accept this hypothesis, the application of the above reasoning on the reactions catalysed by the TiCl$_2$–TADDOLate complexes **1** indicates that the most reactive intermediate is the one having two chloride ligands in the axial positions (**3a**). This is based on the experimental results obtained from the 1,3-dipolar cycloaddition; however, the principle of Lewis acid activation is similar in the Diels–Alder reactions between **2a** and the conjugated dienes. In contrast to the arguments used by Seebach *et al*.[8] and DiMare *et al*.,[7] the experiments in this work indicate that the axial ligands in **3a–c** control the reactivity of the complex. In agreement with previous reports from our laboratories,[5c,10b] we propose that intermediate **3a**, which is in principle similar to the crystallographically characterized **4**[10a] is probably the most reactive intermediate in 1,3-dipolar cycloaddition and Diels–Alder reactions.

Experimental

General methods

^{1}H NMR spectra were recorded at 300 or 200 MHz, respectively, and are reported in ppm downfield from SiMe$_4$. *J* values are given in Hz. HPLC analysis was performed using a 4.6 mm × 25 cm Daicel Chiralcel OD column. Preparative thin layer chromatography (TLC) was performed on 200 × 200 × 1.8 mm silica gel ($PF_{254+366}$ Art. 7748, Merck) on glass plates. Solvents were dried using standard procedures. 4 Å powdered molecular sieves were activated by heating to 250 °C for 3 h under high vacuum. All glass equipment and syringes were dried in an oven at 130 °C prior to use.

Materials

The starting materials 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one **2a**,[14] benzylidenephenylamine *N*-oxide **7**[15] and (2*R*,3*R*)-2,3-*O*-(2-propylidene)-1,1,4,4-tetraphenylbutane-1,2,3,4-tetraol[1b,4g] were synthesized according to the literature. Silver trifluoro-

methanesulfonate was used as obtained from EGA Chemie. 4 Å powdered molecular sieves were received from Aldrich. Millex filter units 45 μm pore size were received from Millipore.

Synthesis of $TiCl(Pr^iO)_3$ (6a) and $TiBr(Pr^iO)_3$ (6b)

Toluene solutions (1 M) of **6a** and **6b** were synthesized by mixing $Ti(Pr^iO)_4$ (2.23 ml, 7.5 mmol) with $TiCl_4$ (267.5 μl, 2.5 mmol) and $TiBr_4$ (918.6 mg, 2.5 mmol), respectively, in toluene under N_2 at room temp. to give a total volume of 10 ml.

Synthesis of $TiOTf(Pr^iO)_3$ (6c)

To a suspension of silver trifluoromethane sulfonate (385.41 mg, 1.5 mmol) in toluene (4 ml) was added $Ti(Pr^iO)_3Cl$ (1 mmol in 1 ml toluene) under N_2 and stirred at room temp. for 48 h. The suspension was transferred to a syringe and filtered through a Millex filter unit into a flask containing N_2 to give a 0.2 M solution of **6c**.

Preparation of the TiX(Pr^iO)–(*R*,*R*)-[Me_2][Ph_4]TADDOLate catalysts 10a–c

To (2*R*,3*R*)-2,3-*O*-(2-propylidene)-1,1,4,4-tetraphenylbutane-1,2,3,4-tetraol (56 mg, 0.11 mmol) in a 5 ml flask under N_2 was added **6a**, **6b** or **6c** (0.1 mmol) and toluene to give a total volume of 1 ml. After stirring for 30 min the catalyst solution (0.1 M) of **10a–c** was ready for use.

General procedure for the TiX(Pr^iO)$_3$ and TiX(Pr^iO)–TADDOLate-catalysed 1,3-dipolar cycloaddition reactions (see Table 1)

To a 5 ml reaction flask containing a magnetic stirring bar, toluene (2 ml) and 4 Å powdered molecular sieves (50 mg) was added the 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one (**2a**, 15.5 mg, 0.1 mmol) and benzylidenephenylamine *N*-oxide (**7**) (25 mg, 0.13 mmol). After stirring for 15 min one of the above described catalyst solutions of **6a–c** or **10a–c** (0.02 mmol in toluene, 20 mol%) was added *via* syringe. After a total reaction time of 48 h, 2 ml of 5% MeOH in CH_2Cl_2 was added to the reaction mixture. After stirring for 10 min the mixture was filtered through a 20 mm layer of silica gel. The silica gel layer was washed with another 2 ml 5% MeOH in CH_2Cl_2 and the solvent evaporated *in vacuo*. ^{1}H NMR spectroscopy revealed that conversions of >80% were obtained in all entries in Table 1. The crude product was purified by preparative TLC (silica gel, Et_2O:light petroleum, 3:1), to give the single diastereomers *exo*-**8** and *endo*-**8**. The ee (enantiomeric excess) of *exo*-**8** was determined by ^{1}H NMR spectroscopy using $Eu(hfc)_3$ as the chiral shift reagent. The ee of *endo*-**8** was determined by HPLC (Daicel Chiralcel OD, hexane: Pr^iOH = 9:1, flow rate = 1.0 ml min^{-1}): t_R 42 min (minor), t_R = 58 min (major).

^{1}H NMR, ^{13}C NMR spectra and mass spectra of *exo*-**8** and *endo*-**8** are published elsewhere.[5]

^{1}H NMR spectroscopic investigation of the adducts between 6a and 2a

To 3-[(*E*)-but-2′-enoyl]-1,3-oxazolidin-2-one (**2a**, 25 mg, 1.6 mmol) in a 5 ml pear-shaped flask containing N_2 was added $TiCl(Pr^iO)_3$ (**6a**, 0.1 mmol, in 0.1 ml toluene). The solvent was evaporated under high vacuum at room temp. The residue was redissolved in CD_2Cl_2 (0.8 ml) and the yellow solution transferred to an NMR tube. A ^{1}H NMR spectrum was recorded of this sample at −40 °C and gave the following signals for the three different methyl groups of **2a**: $\delta(CD_2Cl_2)$: 1.83 (dd, *J* 7.3, 2.0), 1.91 (d, *J* 5.7), 2.07 (dd, *J* 7.7, 1.6).

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