

# Enantioselective catalytic diamination of alkenes with a bisimidoosmium oxidant†

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A first example of an enantioselective catalytic diamination of olefins has been developed which employs enantiopure titanium complexes as catalysts and bis(*t*butylimido)dioxoosmium(VIII) as nitrogen source.

Current protocols for direct diamination of olefins rely on transition metals, a process which was pioneered by Barluenga and Aznar who reported on the use of thallium and mercury promoters,<sup>1,2</sup> followed by later investigation on palladium,<sup>3</sup> osmium,<sup>4</sup> and, more recently, catalytic amounts of iron and ruthenium.<sup>5</sup> Still, enantioselective variants of all these diamination reactions have remained unexplored.

We have recently been interested in the development of asymmetric diamination of olefins employing preformed imido osmium(VIII) compounds such as **1**. These reactions are characterised by complete chemoselectivity and excellent stereoselectivity, but are incompatible with Cinchona alkaloids as ligands. Hence, currently available methods for asymmetric diamination require the use of stoichiometric amounts of chiral auxiliary.<sup>6,7</sup>

During studies on the scope of reactivity in the diaminations with osmium oxidants, we encountered a surprisingly low reaction rate for oxidation of crotoyl oxazolidinone **2** with dioxo bisimidoosmium compound **1** (Scheme 1). For example, <sup>1</sup>H NMR experiments revealed that diamination of **2** is about 18 times slower than for the related methyl crotonate.

This observation established the basis for an enantioselective transition metal catalysed diamination process which is reported herein. The oxazolidinone moiety as in **2** represents one of the most successful groups in stereoselective synthesis, either as enantiomerically pure Evans auxiliary<sup>8</sup> or as achiral directing group in enantioselective catalysis.<sup>9</sup>

We briefly explored the former reaction. Upon use of enantiopure oxazolidinones, diastereoselective diamination reactions

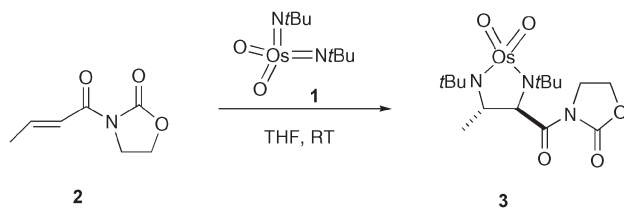
should become available. As an illustrative example, reaction of **1** with *N*-crotoyl (*S*)-4-benzyl oxazolidinone led to 92 : 08 d.r. This value compares well with related stereoinductions in diaminations of chiral acrylates.<sup>6</sup>

Extensive work on the electronic properties of imidoosmium compounds had previously revealed an electronically neutral to nucleophilic reaction pattern for these reagents.<sup>10</sup> Thus, activation of the carbonyl moiety in **2** by transition metal complexes should enhance the electron deficiency of the olefinic bond and thereby accelerate the overall reaction rate as well as introduce enantioselectivity into this process for those cases where the metal complex bears defined stereochemical information.

To this end, a variety of Lewis acids were screened. Obviously, the present oxidation reaction conditions employing **1** as oxidant preclude a number of metal ion candidates because of oxidation state incompatibility. For example, tin(II) and copper(I) complexes were found to readily react with the osmium(VIII) reagent leading to low conversions regarding diamination, if any. This limits potential candidates to high-oxidation-state Lewis acids.<sup>11</sup> Among these, titanium(IV) reagents were considered promising, especially in view of their rich application in combination with the oxazolidinone group.<sup>12</sup>

Since in the present case the achiral background reaction is comparably slow, the overall reaction should proceed *via* the catalytic pathway. The validity of this assumption was demonstrated, when 5 mol% of dichloro-bis(isopropoxy)titanium(IV) were added to diamination of **2** in toluene. In this case, a significant rate increase was observed leading to a 37% isolated yield after a reaction time of 6 h. The uncatalysed reaction gives less than 7% yield of **3** after this period (Fig. 1).

In order to render the overall diamination process enantioselective, chiral ligands were screened employing the reaction from



Scheme 1 Diamination of oxazolidinone **2**.

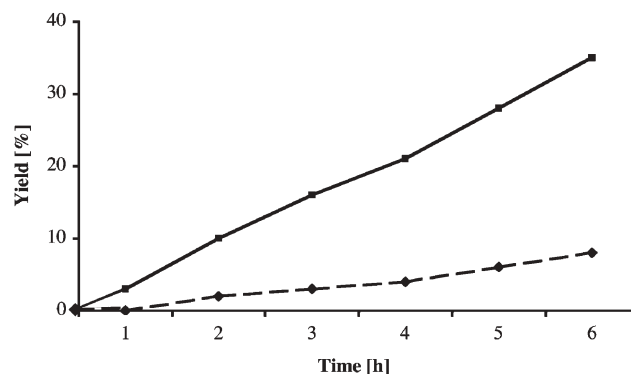


Fig. 1 Initial reactivity in diamination of **2** in the absence of any catalyst (dashed line) and with a catalytic 5 mol% of  $\text{TiCl}_2(\text{O}i\text{Pr})_2$  (straight line).

† Electronic supplementary information (ESI) available: characterisation of reaction products and spectral characterisation for new compounds. See <http://www.rsc.org/suppdata/cc/b5/b502150b/>  
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**Table 1** Asymmetric diamination of **2** with titanium catalysts

Entry	Diol	Product	Yield [%] <sup>a</sup>	E.r. <sup>b</sup>
1	( <i>R,R</i> )-Dimethyl tartrate <sup>c</sup>	(-)- <b>3</b>	78	56 : 44
2	(-)-BINOL <sup>c</sup>	(+)- <b>3</b>	87	59 : 41
3	(-)-BINOL	(+)- <b>3</b>	88	77 : 23
4	( <i>R,R</i> )-TADDOL <sup>c</sup>	(+)- <b>3</b>	91	61 : 39
5	( <i>R,R</i> )-TADDOL	(+)- <b>3</b>	92	94 : 06
6	( <i>S,S</i> )-TADDOL	(-)- <b>3</b>	90	93 : 07

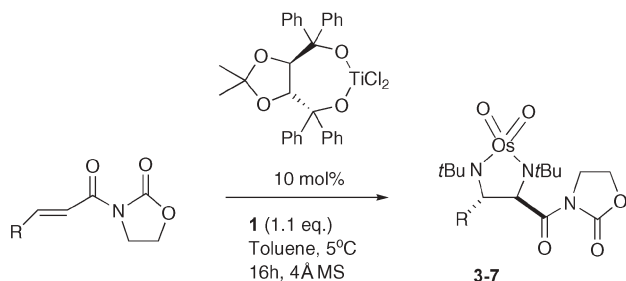
<sup>a</sup> Isolated yield after work up and column chromatography.

<sup>b</sup> Determined by Chiralpak AD (see Supporting Information for details). <sup>c</sup> With *in situ* generated catalyst.

Scheme 1 as model reaction. Toluene was employed as solvent instead of the usual thf in order to minimise potential coordination of the solvent to the titanium catalyst. Under such conditions, catalysts from BINOL (1,1'-binaphthalene-2,2'-diol), dimethyl tartrate and TADDOL (4,5-bis(diphenylhydroxymethyl)-2,2-dimethyl-1,3-dioxolane) gave the highest reactivity, with the latter one affording the best induction (Table 1). It was found decisive to perform the reactions with preformed Ti alkoxides.<sup>13</sup> Attempts to employ *in situ* conditions led to irreproducible results regarding product ee, especially in the case of BINOL-derived catalysts.

The optimised conditions thus consist of mixing a toluene solution of the preformed catalysts (10 mol%) with the substrate, cooling it to 5 °C before the bisimido osmium oxidant **1** is added. Under these optimised conditions, conversion of five different olefins in the presence of the Ti-TADDOLate catalyst led to formation of osmimidazolidines **3–7** with enantiomeric ratios in the range of 84 : 16 to 95 : 5 (Scheme 2, Table 2).

This catalytic enantioselective process benefits from the acceleration of the catalysed pathway over the potential uncatalysed background reaction.<sup>14</sup> For the reaction between **1** and **2** in the presence of a stoichiometric amount of the titanium catalyst, an enantiomeric ratio of 95 : 5 was determined. This suggests that the

**Scheme 2** Enantioselective Ti-TADDOLate catalysed diamination of olefins.**Table 2** Enantioselective Ti-TADDOLate catalysed diamination

Entry	Substrate (R)	Product	Yield [%] <sup>a</sup>	E.r. <sup>b</sup>
1	Me	(+)- <b>3</b>	92	94 : 06
2	H	(+)- <b>4</b>	97	91 : 09
3	Pr	(+)- <b>5</b>	91	93 : 07
4	Ph	(+)- <b>6</b>	95	84 : 16
5	CO <sub>2</sub> Me	(-)- <b>7</b>	83	95 : 05

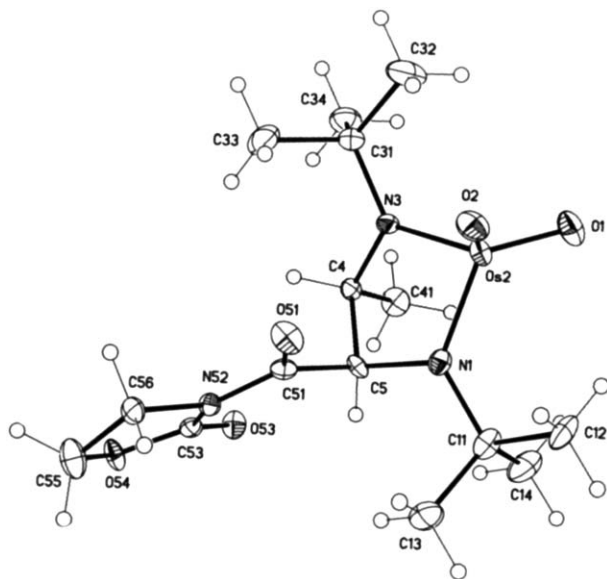
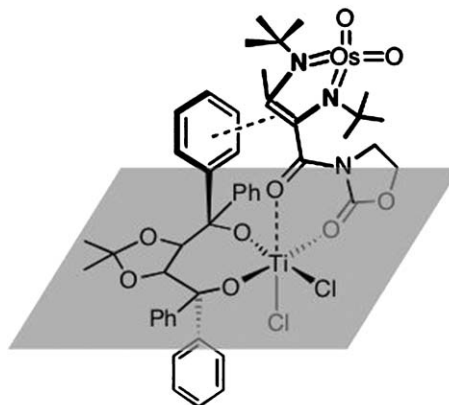
<sup>a</sup> Isolated yield after work up and column chromatography.

<sup>b</sup> Determined by Chiralpak AD (see Supporting Information for details).

above diamination reactions proceed almost entirely *via* the catalysed pathway. Due to their high crystallinity, all products **3–7** from Table 2 could be crystallised to enantiopurity (> 99.5 : < 0.5 e.r., according to analytical HPLC).

The absolute configuration of the major enantiomers was determined through single crystal X-ray analysis of product **3** (Fig. 2).<sup>‡</sup> An absolute (*R,S*)-configuration was established [Flack's parameter<sup>15</sup>  $X = -0.003(5)$ ] which matches a diamination from the *Re,Si*-face of the olefin as depicted in Fig. 3. Such a stereodiscriminating transition state is in complete agreement with those postulated by Seebach for related Ti-TADDOLate catalysed reactions.<sup>12</sup>

Under the assumption of a concerted [3 + 2]-addition<sup>17</sup> of the bisimido osmium reagent **1** to the Ti-TADDOLate coordinated

**Fig. 2** Solid state structure of diamination product (+)-**3**.<sup>‡</sup> Only one of two independent molecules from the asymmetric unit is shown. Selected bond lengths (Å) and angles (°): N(1)–Os(2) 1.886(4), Os(2)–O(2) 1.723(3), Os(2)–O(1) 1.728(3), Os(2)–N(3) 1.885(3), N(3)–Os(2)–N(1) 81.93(14), O(2)–Os(2)–O(1) 120.14(13) [N(1')–Os(2') 1.892(3), Os(2')–O(2') 1.730(3), Os(2')–O(1') 1.715(2), Os(2')–N(3') 1.897(4), N(3')–Os(2')–N(1) 81.55(14), O(2')–Os(2')–O(1') 119.58(13)].**Fig. 3** Transition state for diamination.

olefin, the role of **1** can be compared to that of organic 4π-compounds in related cycloaddition reactions, for which there exist significant literature precedents.<sup>8,12,16</sup>

Regarding general concepts in catalytic enantioselective oxidation reactions, the use of a chiral transition metal catalyst in combination with a high-oxidation state reagent represents a rarely observed concept. Usual combinations consist of a pre-oxidation of the metal centre for chiral catalyst generation preceding oxidative conversion of the organic substrate or activation of the organic substrate by a chiral metal complex prior to oxidation with an organic reagent.

The present example represents an extension which is based on a fortunate coexistence between the actual titanium catalyst and the imido osmium oxidant. This effect was found to be unique since attempts towards realisation of related oxidation reactions with osmium tetroxide did not induce an enantioselective dihydroxylation of **2**. Apparently, the electrophilic oxidant OsO<sub>4</sub> does not meet the specific electronic requirements for oxidation of olefins such as **2** within a transition metal catalyst accelerated pathway.

In summary, we have reported on a transition metal catalysed process for enantioselective diamination of alkenes with a preformed imido osmium reagent. This first enantioselective catalytic diamination reaction is characterised by a marked rate enhancement for the catalysed process, efficient stereoselectivity and high overall yields.

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## Notes and references

‡ Data for crystal structure analysis were measured on a Nonius KappaCCD diffractometer. (+)-**3**: C<sub>15</sub>H<sub>27</sub>N<sub>3</sub>O<sub>5</sub>Os, monoclinic, *P*2(1) (No. 4), *a* = 10.8391(2), *b* = 14.8658(2), *c* = 11.5981(2) Å, β = 99.432(1)°, *V* = 1843.56(5) Å<sup>3</sup>, *Z* = 4, *T* = 123 K, μ(MoKα) =

6.945 mm<sup>-1</sup>, 19723 reflections, 8200 unique reflections (2θ<sub>max</sub> = 50°), *R*1 = 0.0206 [*I* > 2σ(*I*)], *wR*2 = 0.0421 (all data), 433 parameters and 1 restraint. Empirical absorption correction was applied. Full details for the crystal structure analysis were deposited with the Cambridge Crystallographic Data Centre (CCDC). CCDC 260572. See <http://www.rsc.org/suppdata/cc/b5/b502150b/> for crystallographic data in CIF or other electronic format.

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