PERSPECTIVE

NJC
www.rsc.org/njc

The development of asymmetric diamination of alkenes with imido-osmium reagents

Kilian Muñiz*

Kekulé-Institut für Organische Chemie und Biochemie, Gerhard-Domagk-Str. 1, D-53121 Bonn, Germany. E-mail: kilian.muniz@uni-bonn.de; Fax: +49 228 735813; Tel: +49 228 736553

Received (in Montpellier, France) 27th April 2005, Accepted 28th July 2005
First published as an Advance Article on the web 23rd August 2005

Defined oxidative transformations of alkenes offer a versatile route to higher-functionalised organic entities. While processes such as dihydroxylation and aminohydroxylation have reached a remarkable level of efficiency with regard to substrate scope and enantioselection, the related process of diamination has received only scant attention. This *perspective* summarises recent results in the development of asymmetric diamination of alkenes employing bis- and tris(imido)osmium oxidants. Two different asymmetric courses were developed which consist of diastereoselective diamination employing chiral auxiliaries and enantioselective diamination in the presence of a chiral metal catalyst. The diamination products are obtained as monomeric diamine-ligated osmium complexes of unprecedented stability, and all results from these studies represent a completely new chapter in osmium-mediated alkene oxidation.

Introduction

The development of hitherto unknown reactivity constitutes the central challenge in synthetic organic chemistry. It is the most fascinating part of the whole undertaking in that it allows the discovery of selective functional group introduction or transformation and thereby generates novel complex structural entities in a unique manner.

In the area of enantioselective alkene functionalisation a direct diamination of alkenes represents a highly desirable oxidation process. Enantiomerically pure vicinal diamines[1–3] represent an important class of organic compounds that are of utmost importance in various areas of today's chemistry including medicinal and biological chemistry,[1] asymmetric synthesis[2–5] and chiral oligomers.[2,3,6] In homogeneous catalysis, an unsurpassed enantioselective catalyst was developed by Noyori who described ternary ruthenium complexes for asymmetric ketone hydrogenation. These outstanding examples of highly enantioselective molecular catalysts rely crucially on diamines as one of their ligand components. In view of catalyst efficiency, these compounds are unparalleled. Peak turnover rates reach 62 per second, while enantioselectivities of up to 99% ee can commonly be obtained.[7]

The exact working mode of this unique catalyst was uncovered in 2003 when Noyori succeeded in the elucidation of the mechanism of enantioselective ketone hydrogenation with ternary BINAP/1,2-diamine Ru dihydride catalysts (Fig. 1b).[8] A structurally defined hydride/borohydride ruthenium complex,[9] whose X-ray structure is depicted in Fig. 1a, served as precursor for the unambiguous determination of underlying kinetics, influence of solvent, base and hydrogen pressure on the overall reaction profile. Finally, a pivotal role of the diamine ligand on the overall working mode of the catalysis was proven. The reaction proceeds in the outer coordination sphere of a chirally modified RuH_2 catalyst without metal–substrate interaction. Instead, the enantiofacial differentiation of the substrate is kinetically accomplished on the molecular surface of the catalyst. The final hydrogen transfer proceeds through a six-membered transition state and involves simultaneous transfer of a proton from an amino moiety of the chiral diamine ligand to the carbonyl oxygen and hydride transfer from ruthenium to the carbonyl. A molecular model of the active *trans*-RuH_2 species displaying the hydride and amine proton (H–Ru–N–H_{ax}) as involved in the transition state is depicted in Fig. 1a (right). The contribution to the chiral environment of the catalyst as well as the active performance in hydrogen transfer constitute the dual role of the prerequisite diamine ligand.[9,10]

In several cases, these catalysts contain 1,2-diphenylethylenediamine (DPEN, in Fig. 1) as the chiral ligand. It is important to note that only a very limited number of chiral, non-racemic diamines are commercially available. While for the mentioned case of enantioselective ketone hydrogenation the actual catalysts[7] can be regarded as almost perfect for a wide range of substrates, related enantioselective processes would certainly benefit from the availability of a larger number of enantiopure diamines.

The appealing possibility of generating these compounds through direct oxidative diamination of alkenes led to the decision to embark on a study of this type of reaction.

Kilian Muñiz was born in Hildesheim, Germany in 1970. From 1990 to 1996 he studied chemistry at Hannover University, Germany, at Imperial College London, UK and at the University of Oviedo, Spain. In 1996 he joined the group of Professor Carsten Bolm at the RWTH Aachen, Germany to obtain his doctorate in 1998. In 1999/2000 he worked as a postdoctoral associate with Professor Ryoji Noyori at Nagoya University, Japan. From December 2000 to January 2005 he carried out his Habilitation at the Kekulé-Department in Bonn, Germany. He was the recipient of the ADUC Prize for Habilitands in 2004.

DOI: 10.1039/b506221g

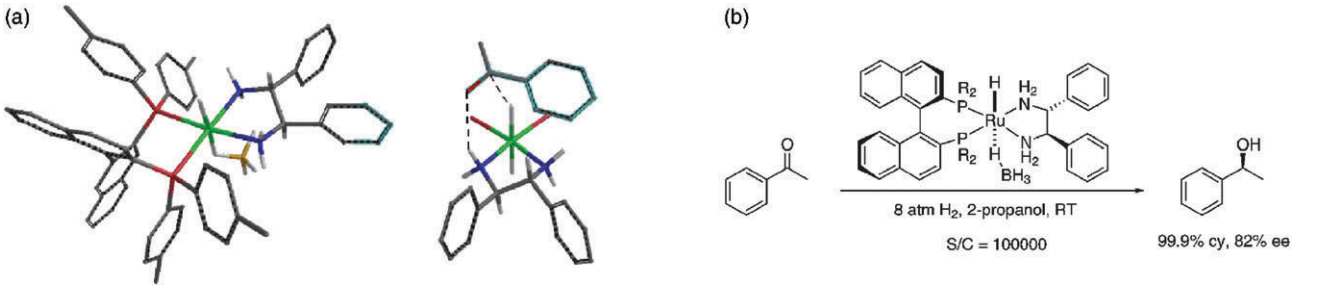


Fig. 1 (a) Left: X-Ray structure of (*R*)-TolBINAP/(*R*,*R*)-DPEN-RuH(η^1-BH_4). Right: Involvement of the H–Ru–N–H_{ax}-surface during hydrogen transfer of the active catalyst onto the *Re*-side of acetophenone. (b) Highly productive catalytic enantioselective reduction of acetophenone.

At the outset of the present work, some precedence regarding this type of reaction had already become available. In 1974, Barluenga and Aznar pioneered the direct diamination of alkenes by introducing a thallium(III)-promoted method employing anilines as nitrogen sources.[11] Later, this type of reaction was further elaborated by a related example employing mercury(II) salts.[12] Seminal work by Bäckvall introduced a two-step sequence of amino-palladation followed by oxidative lead(IV)-induced amination to give vicinal diamines in a stereocontrolled manner *via* a *trans*-selective process.[13] Apart from two disparate reports on osmium-mediated reactions,[14,15] the only other known protocol consists of a catalytic process employing *N*,*N*-dichloro tosylamide and rhodium(I) or iron(II) catalyst systems. These reactions are believed to be initiated by formation of aziridinium intermediates which undergo subsequent Ritter-type imidazolidine formation.[16] Despite all this progress, there had been no asymmetric reaction sequences to yield chiral, non-racemic diamines from alkenes and no detailed mechanistic information on the course of the respective reactions.

In view of the tremendous success of osmium-catalysed alkene oxidation, priority was given to this type of transformation. Oxidative conversion of alkenes with osmium tetroxide dates back to seminal work by Criegee[17] who in 1936 showed that dihydroxylation of alkenes is a feasible, high-yielding process which proceeds in a variety of solvents such as benzene or diethyl ether. He isolated the first osmium glycolate esters as primary addition products and described subsequent reactions of these compounds. More importantly, Criegee made the paramount observation on acceleration of the dihydroxylation reactions in the presence of tertiary amines such as pyridine. These reactions not only proceed at significantly higher rates, they also produce osmium glycolate complexes which contain coordinated pyridine moieties to stabilise the Os center and prevent decomposition of the compounds.

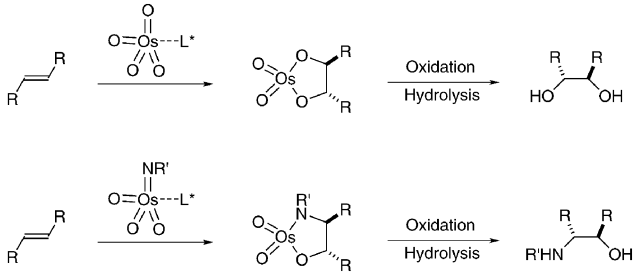
The inherent high volatility and toxicity as well as the reasonably high price represent the major drawbacks for application of this reagent in stoichiometric amounts. As a consequence, catalytic protocols were developed.[18–20] Use of *N*-methyl morpholine-*N*-oxide (NMO) or trimethylamine-*N*-oxide established the industrial Upjohn process.[21] The asymmetric osmium-catalysed conversion of unfunctionalised alkenes into diols is nowadays recognised as one of the most versatile and efficient asymmetric catalytic reactions.[22] It is regarded as an almost universally applicable reaction and its general importance in all areas of asymmetric synthesis earned its principal inventor K. B. Sharpless the 2001 Nobel Prize in Chemistry.[23]

The present system consists of a combination of an osmium(VI) salt, which replaces the rather inconvenient osmium tetroxide, potassium hexacyanoferrate as reoxidant and a chiral ligand. The development of chiral cinchona alkaloid ligands bearing a phthalazine core (PHAL ligands) has led to high asymmetric induction for nearly all types of alkenes. The popularity of the cinchona alkaloids is not only owed to their ability for efficient asymmetric induction. Upon their complexation to osmium tetroxide, the resulting 18e complex experiences a significantly enhanced reaction rate over the free 16e OsO_4. This phenomenon, which has been termed *ligand accelerated catalysis*,[24] provides a large kinetic preference for the chirally catalysed reaction pathway over the achiral one.

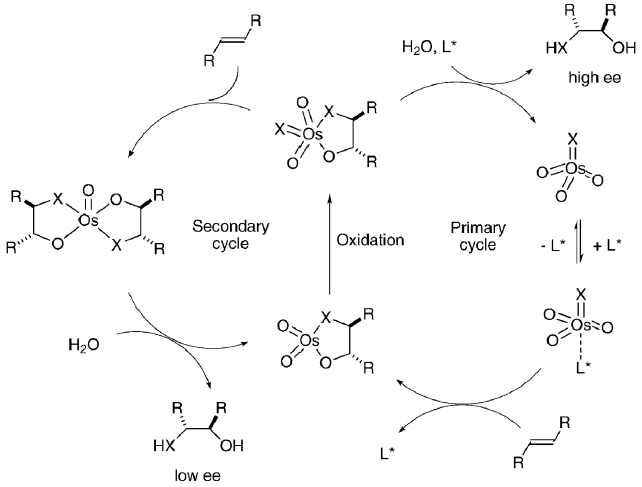
Under related conditions, suitable nitrenoids as reoxidants induce formation of imido-osmium compounds which catalyse the formation of amino alcohols *via* the corresponding azaglycolates.[25–27] As a consequence, alkenes can be transformed into vicinal diols and amino alcohols, respectively, with complete stereospecificity, high yields and usually high enantiomeric excesses (Scheme 1).

In principle, there exist two different catalytic cycles for catalytic enantioselective dihydroxylation and aminohydroxylation processes, which had already been detected during the initial stages of development. In 1980, Sharpless and co-workers gave a detailed description of their first catalytic asymmetric dihydroxylation (AD) system on the basis of chiral cinchona alkaloid ligands.[22,28] From kinetic studies, it was determined that only the first catalytic cycle proceeds with high enantioselectivities since it involves initial coordination of the chiral ligand to the osmium tetroxide reagent. The chirally modified oxidant then adds to the alkene with high face selectivity giving rise to an osmium(VI) glycolate which releases the ligand to undergo reoxidation to Os(VIII). This osmium(VIII) glycolate is the crucial overall intermediate. Its direct hydrolysis releases the diol product and regenerates OsO_4 which reenters the primary catalytic cycle. However, in case of a slow hydrolysis rate, this intermediate can also reoxidise a second alkene yielding an osmium(VI) bis(glycolate) intermediate which upon hydrolysis releases a diol product. Upon reoxidation to the osmium(VIII) glycolate the secondary cycle is closed. It is only of very low asymmetric induction since it proceeds in the absence of the chiral cinchona alkaloid ligand and with nothing other than the remote chiral information of the initial glycolate entity.

Importantly, this secondary cycle could be largely excluded by the optimised Sharpless protocol, employing hexacyanoferrate as reoxidant and working in a biphasic system of *tert*-butanol and water. Here, reoxidation occurs exclusively in the aqueous medium and, therefore, hydrolysis of the initial osmium(VI) glycolate from the organic phase is crucial in order



Scheme 1 Osmium-catalysed alkene oxidations. L* = cinchona alkaloid based ligand.



Scheme 2 Osmium-catalysed alkene oxidation: catalytic cycles for dihydroxylation (X = O) and aminohydroxylation (X = NR′).

to generate an osmate which can enter the aqueous phase and undergo reoxidation. Recent investigation provided an alternative electrophilic cleavage of the initial osma(VIII) glycolate from the first cycle. Upon addition of aryl boronic acids to the otherwise unchanged AD conditions, the electrophilic boron center initiates transesterification from osmium to boron. Thereby, the products are obtained as highly enantiomerically enriched boronic esters and the osmium is maintained almost exclusively in the first catalytic cycle.[29]

While believed to proceed through similar cycles, the asymmetric aminohydroxylation (AA) process still requires additional improvement. Of special importance remains the question of regioselectivity which is lacking a general solution.[30] In addition, the substrate range remains more limited when electron-rich and (*Z*)-configured alkenes are employed and mechanistic understanding of the reasons for the successful imido group transfer onto the alkene remains scarce.

One of the key interests in the optimisation of transition metal-based catalysis relies on the isolation of the major intermediates along the catalytic cycle. Usually, only the catalyst or the immediate catalyst precursor and the final organic product become directly available for studies while all intermediate steps remain elusive. However, full characterisation of major intermediates is a prerequisite for rational optimisation of reaction conditions.

Right from the beginning of osmium tetroxide-mediated alkene dihydroxylation, Criegee isolated osmaglycolates and studied their behaviour in subsequent conversions.[17] Major intermediates along the catalytic pathways of Scheme 2 are identical with those first structural determinations.

Within the area of alkene oxidation, the successful application of the original diol protocol to amino alcohol synthesis raises the question as to whether diamines can also be obtained from alkenes in a single oxidation step.

Osmium complexes for stoichiometric alkene diamination

In order to accomplish nitrogen transfer to alkenes with osmium(VIII) complexes, modification of the parent osmium tetroxide is necessary. This is best achieved by exchange of oxo groups for imido ligands. For example, osmium tetroxide reacts readily in aqueous solutions of *tert*-butylamine to furnish *tert*-butylimido trioxoosmium(VIII). This reaction, which was discovered in 1948, represents the first synthesis of a defined transition metal imido complex.[25] Subsequent reactions by Sharpless,[31] Nugent,[32] Wilkinson,[33] and Schrock[15]

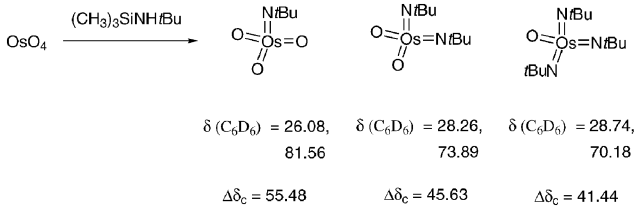


Fig. 2 *tert*-Butylimido-osmium(VIII) compounds.

have allowed for the isolation of several preformed imido-osmium(VIII) compounds bearing tertiary alkyl or sterically congested arene groups.

Within the present project, we have discovered efficient routes to the first three imido complexes in question, namely mono-, bis- and tris(imido)osmium compounds bearing *tert*-butyl substituents, by simply reacting osmium tetroxide with *N*-TMS-*tert*-butylamine in *n*-hexane–THF solutions. Separation by conventional column chromatography gives each of the three complexes in analytically pure form.

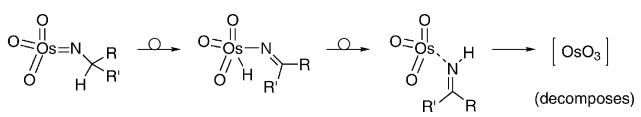
When inspecting the ^{1}H and ^{13}C nmr data for imido compounds $OsO_2(N^tBu)_2$ and $OsO(N^tBu)_3$, all imido ligands are isochronic displaying only a single set of signals. The respective ^{13}C nmr data are given in Fig. 2. In the case of these compounds, the respective shifts for the signals of the methyl and the quaternary carbon atoms are indicative of the number of imido moieties present in the complex. Regarding the ^{1}H nmr signals, a pronounced downfield shift is observed on going from $OsO_3(N^tBu)$ to $OsO(N^tBu)_3$. The relative difference in shift $\Delta\delta_C$, as observed from the respective carbon nmr spectra, can be correlated to the relative electron density at Os(VIII)[34] and thus to the respective average bond order for the imido ligands which apparently decreases from a formal 3 to a formal 2.33.

The isolation of preformed complexes crucially depends on the substitution pattern on the imido ligand. For example, alkyl substituents other than tertiary ones do not lead to stable osmium compounds. Presumably, this is due to the initiation of α-hydride elimination and thus imido tautomerisation into the organic skeleton (Scheme 3). Subsequent reductive removal of an organic imido compound gives an osmium(VI) species which only furnishes black osmium decomposition products as observed during various reactions.

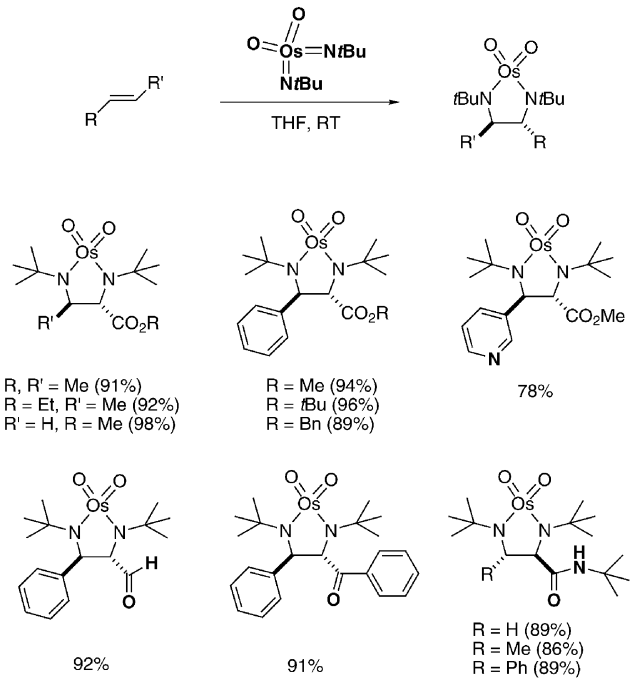
Osmium-mediated diamination

General aspects

In the presence of bis(imido)osmium reagents, virtually all alkenes are oxidised cleanly and chemoselectively. The reaction is fast and irreversible and leads to thermodynamically stable heterocycles which we have denominated osmaimidazolidines. Scheme 4 depicts selected examples of alkene diamination.[35] Among the highest yields are osmaimidazolidine formations with acrylates, crotonates and cinnamates as substrates. For the latter case, the methyl, *tert*-butyl and benzyl esters were submitted to diamination yielding the corresponding products with the orthogonally protected esters. The example of the 3-(3′-pyridinyl) acrylate is particularly noteworthy for the observed chemoselectivity with regard to exclusive oxidation of the olefinic double bond. Related dihydroxylation or aminohydroxylation conditions lead to fast and irreversible oxidation



Scheme 3 Presumed decomposition pathway for non-tertiary imido ligands.



Scheme 4 General diamination reaction and selected examples of functional group tolerance.

of the pyridine unit to give pyridine-*N*-oxide derivatives, which were not observed under the present diamination conditions. Likewise, the clean diamination reactions of cinnamic aldehyde and chalcone reflect the beneficial reactivity of imido-osmium oxidants. While free aldehyde functionalities are usually incompatible with AD or AA reactions, they are completely tolerated in the present cases. AD-based oxidation of chalcones usually encounters similar problems and calls for protection of the ketone prior to alkene dihydroxylation. Again, the related diamination did not require such precautions.

In general, the chromophoric products can be purified conveniently by column chromatography or through crystallisation. This stability of the osmaimidazolidines is noteworthy, particularly their lack of reactivity toward conventional oxidants such as chloramine-T, NMO and *tert*-butyl hydroperoxide, preventing reoxidation to Os(VIII). Concerning the alkene geometry, complete stereospecificity was observed for (*E*)-substituted alkenes which gave *trans*-configured osmaimidazolidines exclusively. Alkenes displaying a (*Z*)-substitution pattern usually do not react. As a single exception, dimethyl maleate underwent diamination, however, this oxidation was accompanied by significant isomerisation and the major product was again a *trans*-configured osmaimidazolidine, which was identical to an authentic compound from direct diamination of dimethyl fumarate.

Regarding kinetic control, several competition experiments were undertaken. A first competition experiment for oxidation of dimethyl fumarate with $OsO_2(N^tBu)_2$ or $OsO(N^tBu)_3$ revealed a higher reaction rate for these reagents than for the related compounds OsO_4 and $OsO_3(N^tBu)$.[36] In fact, the relative reactivity in the oxidation of dimethyl fumarate was found to increase in the following order: $k\{OsO(N^tBu)_3\} > k\{OsO_2(N^tBu)_2\} \gg k\{OsO_3(N^tBu)\} \geq k(OsO_4)$.

It is particularly significant that the sterically very congested tris(imido) species $OsO(N^tBu)_3$ reacts faster than the bis(imido) reagent $OsO_2(N^tBu)_2$. This indicates that electronic, not steric properties are important in the oxidation of electron-deficient alkenes with imido complexes. As a second important observation, compound $OsO_3(N^tBu)$ leads to diol and amino alcohol formation, while $OsO_2(N^tBu)_2$ and $OsO(N^tBu)_3$ display complete chemoselectivity and undergo diamination reactions exclusively. However, the mentioned reactivity order turned out to be reversed when oxidation of styrene was investigated. In this case, osmium tetroxide gave a high yield of 89% after 12 h at rt, while the imido compounds reacted more slowly. An investigation on the relative reactivity of $OsO_2(N^tBu)_2$ toward electron deficient alkenes resulted in nearly equal reactivities for diamination of methyl cinnamate and dimethyl fumarate (Fig. 3, left).[36] Apparently, the second electron-withdrawing group has only a negligible electronic influence.

Importantly, this similarity in reactivity is no longer observed for competition experiments involving monosubstituted alkenes such as styrene and methyl acrylate. Here, the electron-deficient alkene undergoes a faster reaction (Fig. 3, right).

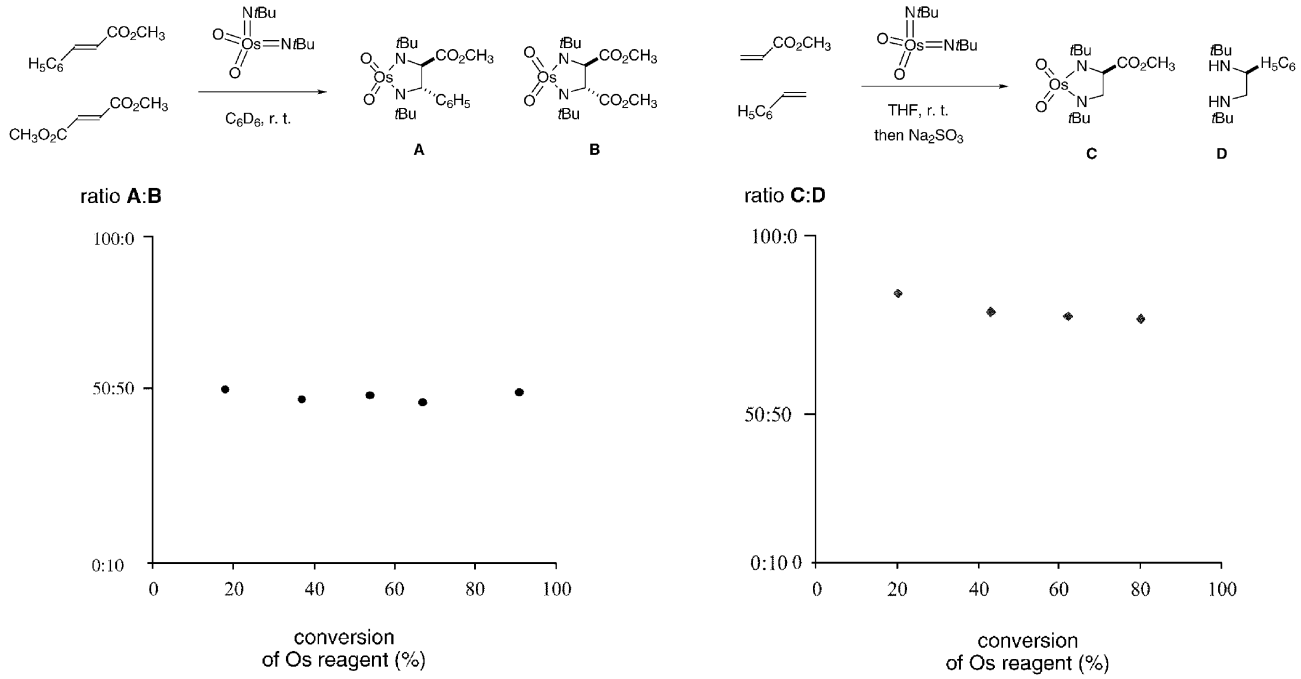
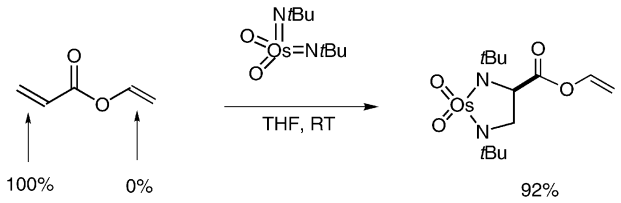


Fig. 3 Kinetic profiles for competitive diamination with $OsO_2(N^tBu)_2$: methyl cinnamate *vs.* dimethyl fumarate (left) and styrene *vs.* methyl acrylate (right).



Scheme 5 Chemoselectivity in diamination of alkenes: an intramolecular competition reaction.

This result again underlines the importance of electron-deficient substituents in order to ensure high reactivity in alkene diamination. These general trends in reactivity of $OsO_2(N^tBu)_2$ and $OsO(N^tBu)_3$ toward electronically different C–C double bonds are best illustrated by the reaction of $OsO_2(N^tBu)_2$ with vinyl acrylate which represents a substrate with two electronically different C–C double bonds (Scheme 5). In this competition experiment, complete chemoselectivity regarding the reagent (exclusive diamination, no dihydroxylation or aminohydroxylation) and the substrate (exclusive oxidation of the acrylate C–C double bond over the vinylic one) takes place and the observed osmaimidazolidine product is formed selectively as the only product out of 8 possibilities!

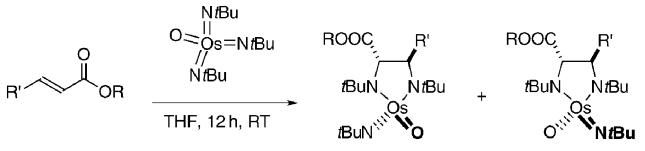
Stereogenic osmium centers from diamination of alkenes

Investigations of diaminations employing tris(imido) osmium(VIII) reagents had only been undertaken for ethylene and symmetrical (*E*)-substituted alkenes such as fumarates (*vide supra*). When subjecting methyl cinnamate to diamination with the tris(imido)osmium reagent, formation of two independent new products was observed. Due to the non-equivalence of the two nitrogen atoms in the osmaimidazolidine ring and the two different remaining oxo and imido groups at the tetrahedral environment of the osmium atom, the latter atom turns into a stereogenic center itself.[37] These chiral-at-osmium compounds contain a tetrahedral coordination sphere. Most chiral organometallic and inorganic compounds with stereogenic metal centers[38] belong to the half sandwich type and therefore display an octahedral coordination sphere of four different ligands and thus have the isomerisation possibilities of a tetrahedron only. Real tetrahedral coordination is rarely found for chiral-at-metal complexes.[39]

Investigation of several unsymmetrical esters revealed that the substituent at the 3-position has a deleterious influence on the overall diastereoselectivity of the diamination. Alkenes such as cinnamates and crotonates consistently yield products with a diastereomeric ratio (dr) of about 60 : 40 (Scheme 6, Table 1).

The relative configuration of the major diastereoisomers was determined by X-ray analysis of the one obtained from diamination of methyl cinnamate. A [(2*R*,4*R*,5*S*)/(2*S*,4*S*,5*R*)]-configuration is observed for those compounds which consequently demands a [(2*S*,4*R*,5*S*)/(2*R*,4*S*,5*R*)]-configuration for the related minor diastereoisomers. Regarding these relative configurations, it is interesting to note that in the preferred stereoisomer the remaining bulky imido moiety and the ester group are *syn*-positioned across the osmaimidazolidine ring.

For acrylates and methacrylates, respectively, a remarkable increase in diastereomeric ratio is observed. In these cases,



Scheme 6 Stereogenic osmium centers from diamination of 3-substituted acrylates.

Table 1 Stereogenic osmium centers from diamination of 3-substituted acrylates

R′	R	Diastereomeric ratio	Combined yield (%)
C_6H_5	CH_3	62 : 38	90
C_6H_5	C_2H_5	60 : 40	91
C_6H_5	$C(CH_3)_3$	64 : 36	90
CH_3	CH_3	62 : 38	89

values ranging from 90 : 10 dr up to more than 98 : 02 dr were observed (Scheme 7, Table 2).

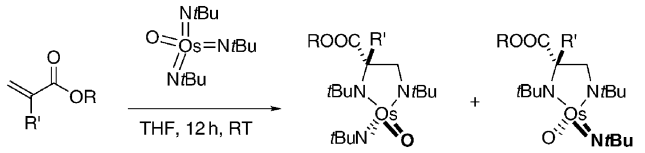
Clearly, there is a pronounced influence on the overall diastereoselectivity in this reaction, which strongly depends on the alkene substitution pattern and on the alcohol moiety in the ester substituent. As observed, 3-substituents appear to have a deleterious influence, while bulky substituents in the ester group benefit high diastereomeric ratios. This influence on the overall diastereoselectivity is intriguing.

All diastereomers could be readily separated from their crude reaction mixtures *via* conventional column chromatography. For all reactions of cinnamic esters, diastereomeric ratios were unchanged between 10 and 95% conversion within nmr accuracy and did not show temperature-dependence within a range of 0–30 °C. Moreover, nmr experiments with isolated diastereomers in toluene-d_8 proved that there is no change in dr over a temperature range of −80–90 °C and the same experiment led to no detectable epimerisation. These results prove the configurational stability of chiral-at-metal osmaimidazolidines.

Electronic characterisation of imido-osmium(VIII) reagents

Regardless of the exact course of diamination with bis- and tris(imido)osmium reagents, the question of electronic preferences remained open. Electronic evaluation of imido-osmium (VIII) reagents is a necessary tool in order to establish the substrate–reagent reactivity correlation for these compounds. Already in one of the first reports, Sharpless qualified isolated mono(imido) compounds such as $OsO_3(N^tBu)$ to be milder oxidants than the parent osmium tetroxide OsO_4.[40] A more detailed investigation employing Hammett correlations led to a conclusive picture for oxidation of cinnamic esters with the osmium oxidants in question.[36] While OsO_4 as a 16e oxidant must display a pronounced electrophilic character ($\rho = -0.55$), reactions of $OsO_2(N^tBu)_2$ reveal a negligible electronic influence for cinnamate oxidation ($\rho = 0.05$). Moreover, no rate difference in diamination of methyl cinnamate and dimethyl fumarate with $OsO_2(N^tBu)_2$ was observed, indicating that one electron-withdrawing group is sufficient in order to achieve the maximum rate. In contrast, tris(imido) compound $OsO(N^tBu)_3$ displays an electronic influence for cinnamate diamination and the observed ρ-value of 0.25 suggests a rather nucleophilic nature for this oxidant (Scheme 8, Fig. 4).

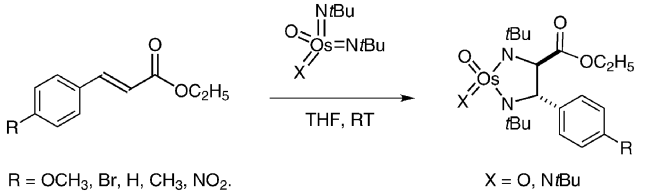
Within this context, one should notice the relative change of preferred substrate geometry in going from OsO_4 to $OsO(N^tBu)_3$. While performance of osmium tetroxide is most efficient in the oxidation of (*Z*)-configured neutral or electron-rich alkenes, imido compounds such as $OsO_3(N^tBu)$, with their reduced electrophilicity, give best results with terminal or (*E*)-substituted neutral alkenes. In contrast, the electronically saturated bis(imido) complex $OsO_2(N^tBu)_2$ has a strong pre-



Scheme 7 Stereogenic osmium centers from diamination of acrylates.

Table 2 Stereogenic osmium centers from diamination of acrylates

R′	R	Diastereomeric ratio	Combined yield (%)
H	CH_3	90 : 10	97
H	$C(CH_3)_3$	93 : 7	95
CH_3	CH_3	96 : 4	97
CH_3	$C(CH_3)_3$	>98 : <2	99



Scheme 8 Diamination of 4′-substituted cinnamates with $OsO_2(N^tBu)_2$ and $OsO(N^tBu)_3$.

ference for (*E*)-configured electron-deficient alkenes. The corresponding tris(imido) complex $OsO(N^tBu)_3$ is a neatly nucleophilic oxidant with strong steric hindrance. As a consequence it reacts only with terminal or (*E*)-substituted alkenes.

Chemoselectivity

A variety of reactions of neutral alkenes with bis- and tris(imido)osmium reagents showed very high chemoselectivity in favour of diamination, and electron-deficient alkenes usually display complete chemoselectivity yielding osmaimidazolidines as the sole products.[35,36] With these experimental results in hand, a computational investigation of the reaction course was undertaken[41] that, for reaction of $O_2Os(NH)_2$ with ethylene, suggested a [3 + 2] mechanism to be operating. Furthermore, two major conclusions were drawn regarding the exclusive nitrogen transfer. Fig. 5 shows the respective transition states and calculated product structures for the corresponding reaction pathways of ethylene diamination with $O_2Os(NH)_2$. First, elongation of the Os=NH moieties toward the transition state geometry is energetically preferred over the competing Os=O bond elongation. Secondly, the energy contribution of π-back donation from the imido ligands to the π*-orbital of the alkene is greatly enhanced in the case of diamination. This suggests that the diamination pathway represents both the kinetically and thermodynamically preferred reaction course.

The viability of this theoretical investigation is strengthened by the excellent agreement between the calculated values for the final osmaimidazolidine bond lengths and the ones obtained from solid state measurements (*vide infra*).

Diamine liberation

The inherent stability of the osmaimidazolidine core prevents hydrolytic or related release of the diamine product and reductive liberation of the respective diamines was found to be impossible even with sulfite or thiosulfate.[35] Strong metal hydrides are necessary to release the osmium from the diamine chelate. This overall sequence thus generates diamines directly from alkenes employing a stoichiometric amount of osmium reagent. While lithium aluminium hydride leads to clean removal of the osmium metal, the efficiency of this reaction is hampered by the concomitant reduction of the carbonyl substituent as well. However, a convenient synthesis of 2,3-diamino alcohols is feasible through this sequence. Use of borohydrides leaves the carbonyl moieties intact and leads to exclusive reduction of the metallaheterocycle. Thus, 2,3-diamino carboxylic acids and derivatives are obtained by this procedure. In several cases, 2,3-diamino carboxylic esters underwent conversion to β-lactams under the reaction conditions and it was found convenient to convert ester functionalities into their corresponding amides prior to Os removal (Scheme 9).[35]

In addition, acidic work-up represents another alternative for those cases without acid-labile functional groups. If desired, recycling of the osmium after the final reduction step is possible. Dissolution in dichloromethane of the remaining black cap from column chromatographical purification and addition of a suitable oxidant such as hydrogen peroxide allows for the preparation of an aqueous solution of osmium tetroxide which is directly treated with *tert*-butylamine to form the mono(imido)osmium(VIII) complex. This compound is non-volatile and can be converted to the required bis- and tris(imido)osmium reagents upon treatment with TMS-*tert*-butylamine. The overall procedure thus avoids isolation of the poisonous osmium tetroxide.

Osmaimidazolidine structures

The stability of monomeric osmaimidazolidines is surprising, especially when compared to the chemistry of related osmaheterocycles from related dihydroxylation and aminohydroxylation reactions. It is a well-established fact that both osmium mono(glycolate) and azaglycolate complexes require additional donor molecules in order to gain the necessary stability. Several examples have become known, including pyridine and quinuclidine moieties.[42] In the absence of such donor molecules, glycolate exchange between two molecules leads to the formation of a stable bis(glycolate) osmium compound[43] and osmium trioxide, as had been already observed by Criegee[17] in his seminal initial studies on the course of

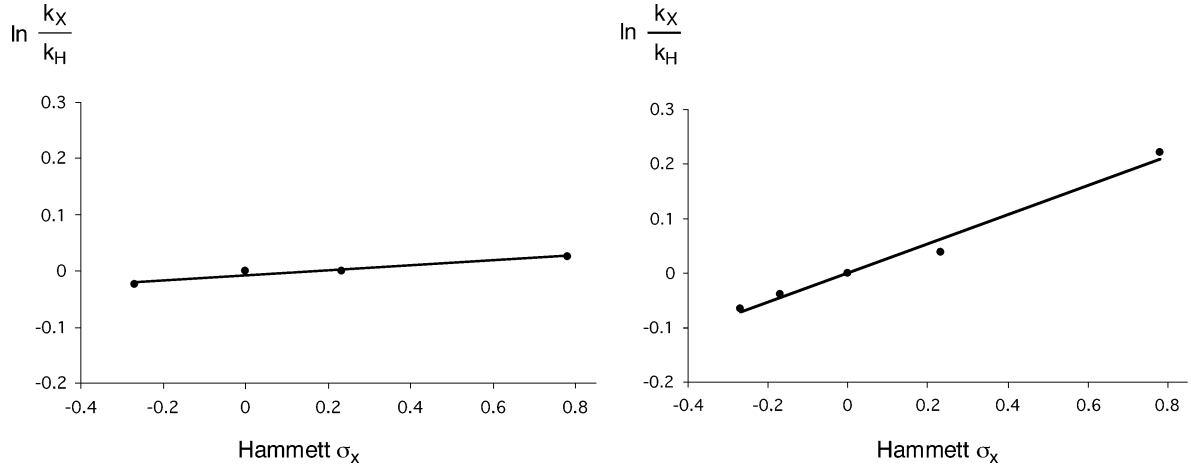


Fig. 4 Hammett correlation diagrams for diamination of 4′-substituted cinnamates with $OsO_2(N^tBu)_2$ (left) and $OsO(N^tBu)_3$ (right).

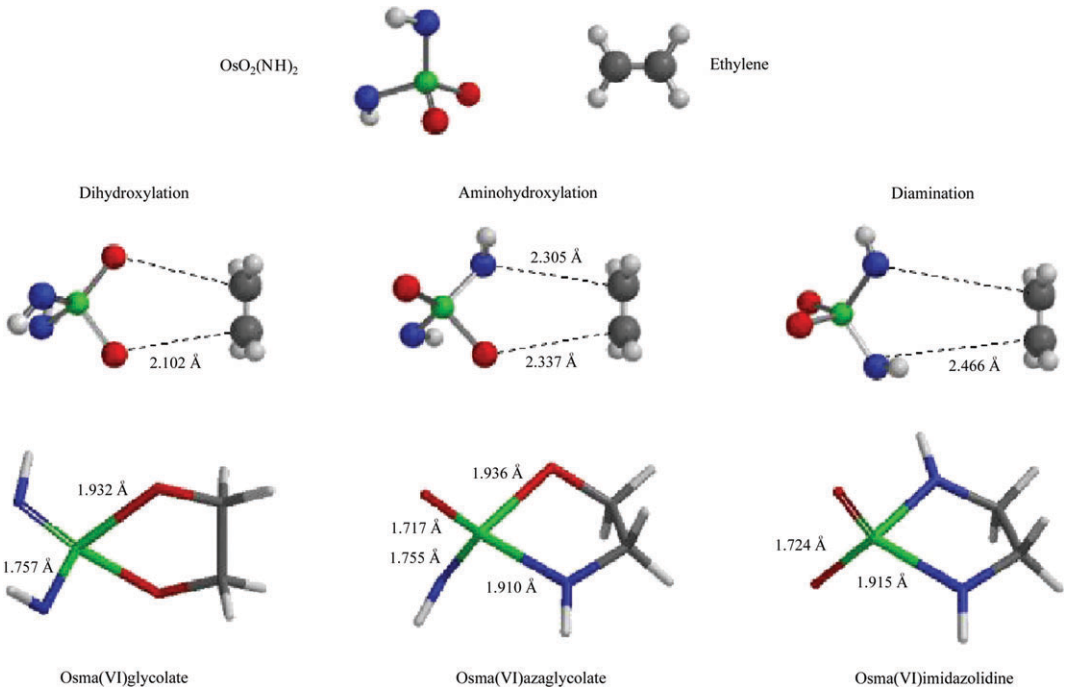


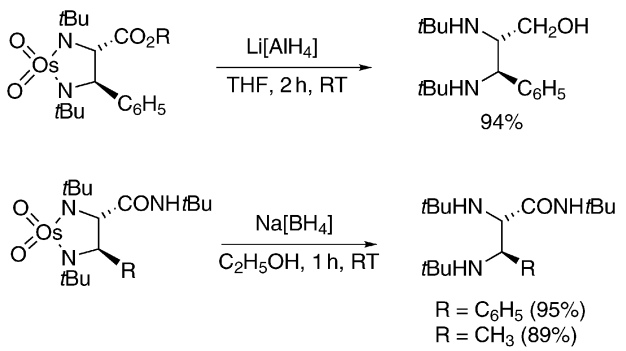
Fig. 5 DFT-derived structures for reactants (top), transition states (middle) and products (bottom) for concerted additions of $O_2Os(NH)_2$ to ethylene.

dihydroxylation. Alternatively, dimerisation might occur.[44] The same behaviour is usually observed for related azaglycolates from aminohydroxylation reactions.[45]

In contrast, osmaimidazolidines from diamination with bis- and tris(imido)osmium compounds are of impressive stability, despite the fact that these represent 16 electron compounds as well. Several attempts to achieve coordination of pyridine or DMAP as potential ligands did not meet with success. Apparently, the presence of the two basic lone pairs at the nitrogen ring atoms saturate the overall electron demand of the Os center, rendering it electronically saturated.

NMR data

The respective nmr data for all osmaimidazolidines are in full agreement with the proposed heterocyclic ring structure. Fig. 6 contains two representative ^{1}H nmr spectra depicting the data for the osmaimidazolidines from diamination of *tert*-butyl cinnamate and diethyl fumarate, respectively. For the former, the most interesting observation is on the singlets from the two hydrogens on the osmaimidazolidine backbone. Given that the overall process of diamination of (*E*)-substituted alkenes occurs with complete stereospecificity, these two hydrogens must be *trans*-positioned with respect to each other. The apparent absence of any measurable ^3J coupling constant suggests a



Scheme 9 Reductive cleavage of Os-diamine chelates to liberate vicinal diamines.

90–120° angle between the two hydrogen atoms within the inflexible heterocycle backbone. In accordance, the respective carbon atoms display slight derivation from tetrahedral arrangement. This observation turned out to be general for all products from the diamination of unsymmetrical alkenes.

The product from diamination of diethyl fumarate with the tris(imido)osmium oxidant gives an osmaimidazolidine which contains a remaining imido ligand at osmium. The signals for the *tert*-butyl groups of these imido substituents generally experience a more pronounced downfield shift than the ones on the two ring amines. For the depicted example, the signal occurs at 1.31 ppm downfield from TMS, a value that indicates significant bent-character for this imido moiety, suggesting that the electronic stabilisation of the osmaheterocycle derives almost entirely from the lone pairs of the ring nitrogens. Additional careful examination of the nmr spectra revealed a pronounced non-symmetry for the signals both of the hydrogen atoms and the carbon atoms of the heterocyclic part of the osmaimidazolidine. This is not surprising since the arrangement at Os locates the oxo and the imido ligands on different sides of the osmaimidazolidine and thus enforces non-equivalency of the incorporated atoms and functional groups.

Solid state structures

In view of the significant stability and thus the unprecedented monomeric structure of osmaimidazolidines, a variety of different derivatives were recrystallised and submitted to X-ray analysis (Fig. 7).[35] Their overall stereochemical features coincide perfectly with the suggested structures. As can be seen from the structure of the osmaimidazolidine from diamination of methyl cinnamate, the two ring hydrogens are indeed positioned at around 120° to each other which matches the conclusions derived from the nmr data as discussed above. This three-dimensional arrangement may also explain the observed pronounced instability of osmaimidazolidines derived from (*Z*)-disubstituted alkenes since it would require an almost parallel positioning of two large substituents along the heterocyclic backbone.

The other most important characteristics are the pseudo-tetrahedral coordination at the central Os atom and the

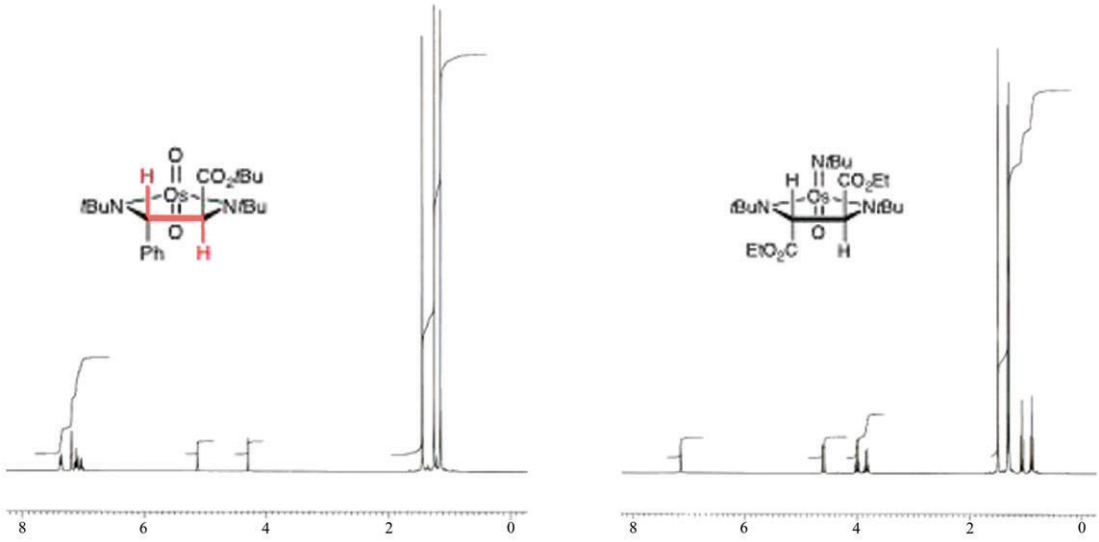


Fig. 6 ^{1}H nmr spectra of the osmaimidazolidines from diamination of *tert*-butyl cinnamate (left) and diethyl fumarate (right) with bis- and tris(imido)osmium oxidant, respectively.

relatively small difference in Os–O double bond and Os–N bond lengths. For the former, values in the usual range of 1.72–1.73 Å were determined while the latter showed bond lengths of about 1.88–1.89 Å. These values are in excellent agreement with the ones obtained from DFT calculations for the respective hydrogen substituted osmaimidazolidines as diamination products (Fig. 5).[41] They indicate significant π-character for the Os–N bonds and point to an increased stability of the osmium diamine chelate structure. From a chemical point of view and apart from their monomeric character, the stabilities of the two products derived from diamination of chalcone and *N*-*tert*-butyl cinnamic amide, respectively, are unprecedented. To the best of our knowledge, dihydroxylation and aminohydroxylation reactions of chalcones or related α,β-unsaturated ketones have remained particularly difficult to accomplish. This is mainly due to the product diol's strong electron-withdrawing neighbouring group which induces a rapid and irreversible retro-aldol process to take place. Apparently, the osmaimidazolidine product obtained from diamination prevents the corresponding retro-Mannich process due to the incorporation of the nitrogens' lone pairs into the heterocyclic ring. Even more surprising, cinnamic amides and related acrylamides give clean and stable products as well. In view of the prominent role of amides in turnover in secondary Sharpless aminohydroxylation reactions,[46] the complete absence of any interaction between the amide group and the osmium center in the crystal structure is noteworthy and once more reflects the unprecedented general stability of these compounds.

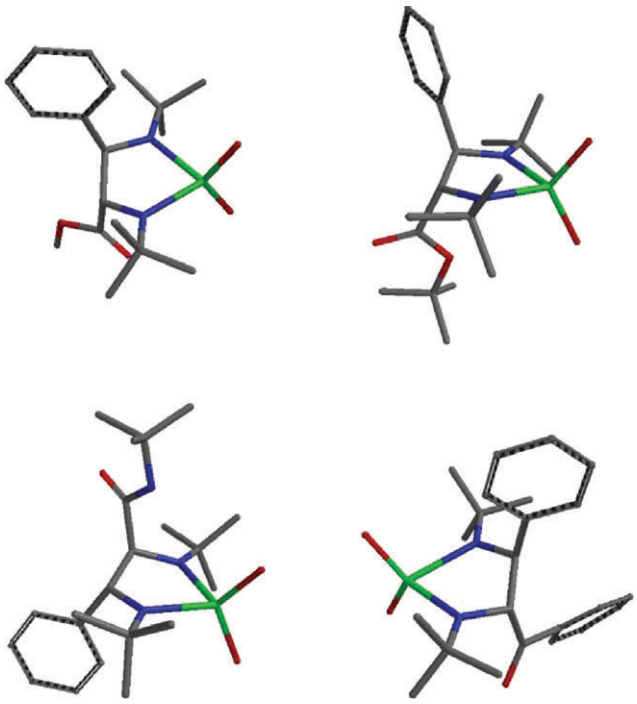


Fig. 7 Solid state structures of osmaimidazolidines from diamination of methyl cinnamate (top left), *tert*-butyl cinnamate (top right), chalcone (below left) and *N*-*tert*-butyl cinnamic amide (below right).

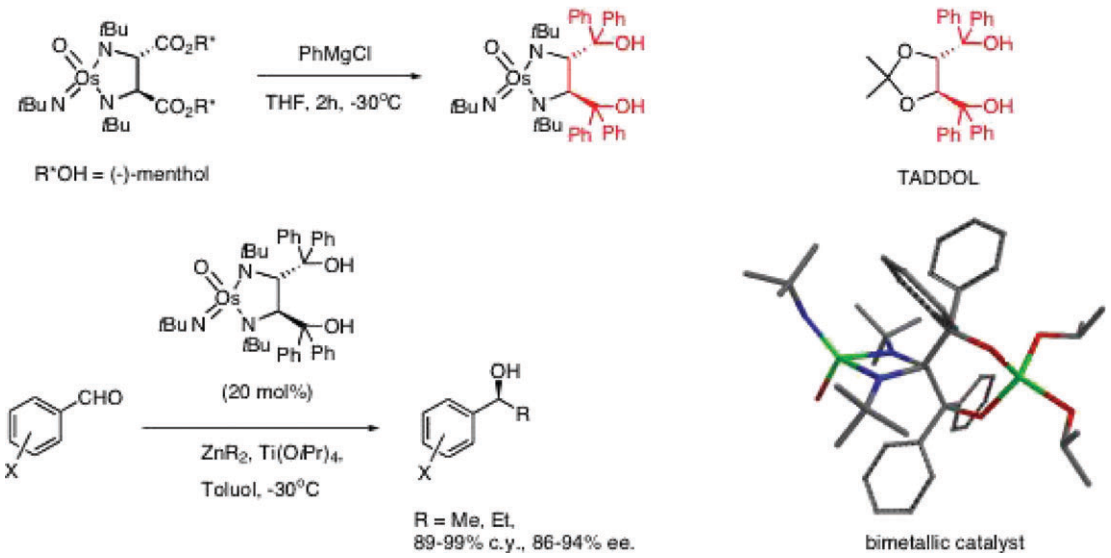
Functional group transformations on osmaimidazolidines

An interesting transformation on the functional groups in the backbones of osmaimidazolidines was achieved by conventional addition of Grignard reagents. For example, conversion of the ester groups in the diastereomerically and enantiomerically pure bis(ester) obtained from diamination of dimenthyl fumarate (*vide infra*) gave a crystalline osmaimidazolidine containing two diphenylhydroxymethyl groups in the 4- and 5-positions.[47] Regarding this backbone substitution pattern this compound is reminiscent of the related class of TADDOL ligands which were introduced by Seebach and are derivatives of tartaric acid (Scheme 10).[48]

Indeed, the newly generated osmaimidazolidine turned out to be a suitable bidentate ligand for *in situ* coordination to titanium(IV). The resulting chiral complex catalysed the enantioselective alkylation of aldehydes using diethyl- and dimethylzinc as reagents.[49] The general reaction conditions were identical to those of related TADDOL-based catalyses, as were the yields and enantiomeric excesses of the chiral secondary alcohol products.[50] Regarding the structure of the chiral catalyst, it is of bimetallic nature (Os *vs.* Ti) and the asymmetric induction could in principle be the result of either a Lewis acid osmium or titanium center. However, in view of the identical reaction outcome and of the pronounced failure of osmium centers in related osmaimidazolidines to show electrophilic behaviour, it is reasonable to assume that the active catalytic center of the bimetallic catalyst is on titanium.

The quest for a catalytic diamination of alkenes

The inherent stability of the osmaimidazolidine core has so far prevented the development of a catalytic version. In general,



Scheme 10 Stereospecific synthesis of osmaimidazolidine ligands as TADDOL analogues and application in dialkylzinc addition to aldehydes (MM3-model of the suggested bimetallic catalyst at the lower right).

one would assume such a process to require the coexistence of a nitrene precursor and an amine unit of nucleophilic character in order to promote aminolytic cleavage of the intermediary osmaimidazolidine. The simplest catalytic cycle for such a scenario is depicted in Fig. 8.

Starting from a bis(imido)osmium(VIII) catalyst, diamination of the respective olefinic substrate will furnish an intermediary osma(VI)imidazolidine. Reoxidation through a nitrene will generate an osma(VIII)imidazolidine. The required nitrene should in principle be accessible *in situ* from the corresponding *N*-halo precursor as known from the related Sharpless AA reaction.[25,27] In principle, this deprotonation should already be feasible with the free amine that is required for aminolysis of the osma(VIII)imidazolidine. This final step of aminolysis will release the diamine product, regenerate the bis(imido) osmium(VIII) catalyst and thereby close the catalytic cycle.

In order to prevent the formation of regioisomers in case of unsymmetrical alkenes, an ideal scenario would consist of the use of identical substituents R in both the nitrene precursor and the amino source for aminolysis.

All attempts toward realisation of this proposal have so far proven unsuccessful. The major drawback consists of the impossibility of generating defined bis(imido)osmium(VIII) compounds with electron-deficient nitrogen substituents as isolable starting materials. However, the presence of deactivating nitrogen substituents represents the prerequisite for aminolytic cleavage of the primary osmaimidazolidine intermediates. A further drawback was encountered within the search for nitrogen components that are able to co-exist both in their free NH_2 form (for aminolytic cleavage) and as the *N*-halo form (for nitrene generation). Two of the most promising candidates, trifluoroacetamide and trifluoromethyl sulfonamide, which display appropriate pK_a values (6 and 8, respectively) in order to substitute water in the cleavage step, did not provide stable imido ligands on osmium.

Moreover, repeated attempts to employ *in situ* generated imido-osmium(VIII) oxidants or combinations of aliphatic amines and stable nitrene precursors such as chloramine-T gave very low conversion and no diamine product could ever be detected in the crude reaction mixture. In order to overcome these problems, a theoretical investigation of an alternative pathway was undertaken. On the basis of density functional calculations, the following proposal was devised (Fig. 9).

Here, the diamination step again relies on the suprafacial addition of a bis(imido)osmium(VIII) species to an alkene. The resulting osma(VI)imidazolidine is then reoxidised by interaction with an oxo-transfer reagent to give the trioxoosma(VIII) imidazolidine which is hydrolysed by water to liberate the diamine product. These steps are comparable to those of the parent dihydroxylation process. The decisive overall step

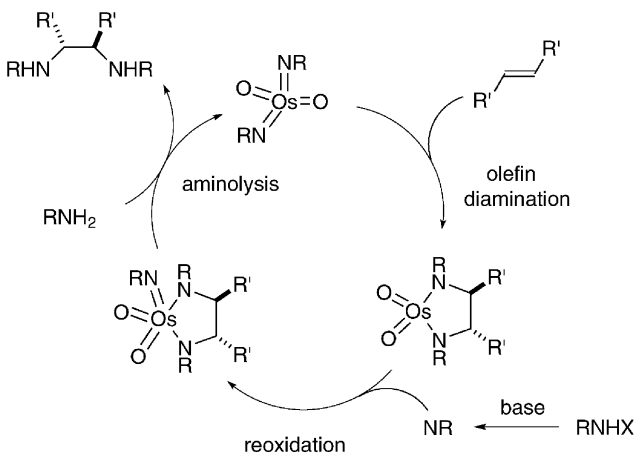


Fig. 8 Proposed catalytic cycle for diamination of alkenes.

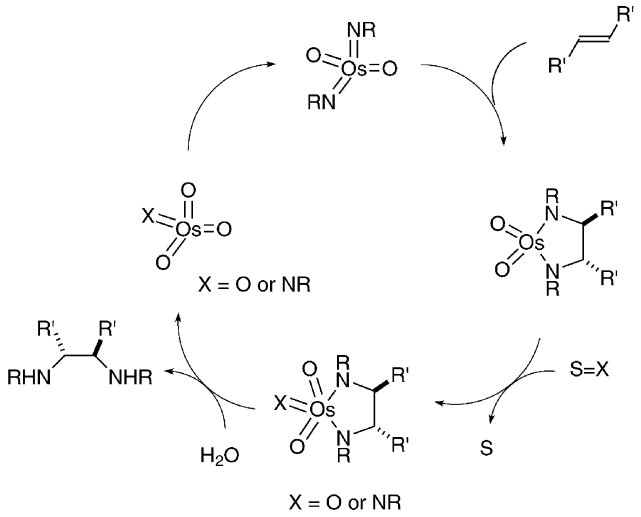


Fig. 9 Theoretical pathways for catalytic diamination of alkenes.

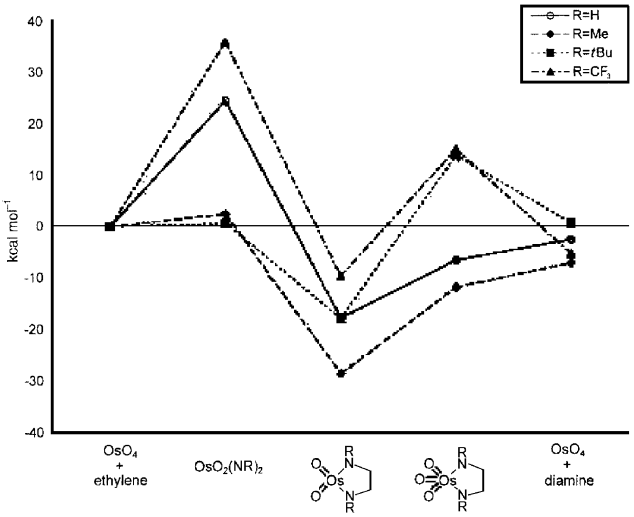


Fig. 10 Thermodynamic reaction profiles for hypothetical catalytic diamination.

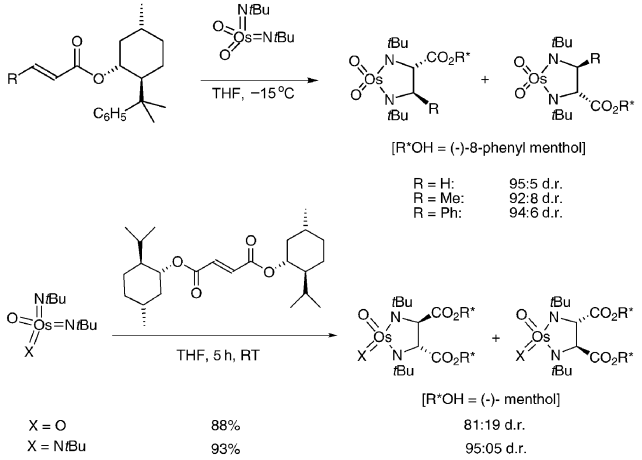
consists of the subsequent conversion of osmium tetroxide to the bis(imido)osmium(VIII) reagent. This step is calculated to be endergonic by about 24 kcal mol^{-1} (calculated *versus* NH_3/H_2O) and would require activated amine sources in order to overcome this barrier.[41]

Alternatively, the same catalytic cycle could be considered, employing a nitrene-based reoxidant to furnish an imido-dioxoosma(VIII)imidazolidine, which upon hydrolytic release of the diamine product would give a mono(imido)osmium(VIII) compound. In order to close a potential catalytic cycle, a subsequent imido for oxo exchange to the bis(imido)osmium(VIII) catalyst is required. While this proposal consists of a more balanced overall thermodynamic profile, it still bears the oxidative and non-oxidative nitrogen transfer processes as the greatest challenges. In general, calculations[41] suggest that the substituents on the imido ligands control the thermodynamic reaction profile for these diaminations to a large extent. As an example, Fig. 10 shows the influence of various imido nitrogen substituents on the overall thermodynamic reaction profile for catalytic diaminations as discussed above.

Still, several attempts toward realisation of this concept did not meet with success. Apparently, the reactivity of osmium tetroxide and mono(imido)osmium compounds within direct dihydroxylation and aminohydroxylation, respectively, is higher than for nitrogen transfer processes to form bis(imido) osmium complexes. This outcome would represent a good example for a thermodynamically feasible process of diamination which is overcome by competing alkene functionalisation reactions which involve metal species as precursors for the desired catalyst, but already show a *kinetically* preferred catalytic reaction behaviour on their own.

Asymmetric diamination of alkenes

In view of the apparent difficulty in devising catalytic diamination processes, attention was turned to the development of asymmetric reaction pathways and the use of stoichiometric amounts of a chiral auxiliary were considered. Since reaction rates and product stability favoured diamination reactions of electron-deficient alkenes it was decided to initially employ this kind of alkene. In particular, acrylates and related alkenes would offer the possibility to attach a variety of chiral, non-racemic alkenes and thus allow for a fast and efficient evaluation of the respective auxiliaries. Among Oppolzer's camphor sultam and various chiral alcohols such as 1-phenylethanol, menthol, fenchol and 8-phenylmenthol, the latter emerged as the most efficient auxiliary. For the respective esters of acrylic



Scheme 11 First asymmetric diaminations of alkenes.

acid, crotonic acid and cinnamic acid, diastereomeric ratios in the range of 72 : 28–95 : 5 were obtained (Scheme 11, top).[35,51]

Separation of all diastereomeric mixtures was accomplished cleanly either *via* conventional column chromatography or *via* semi-preparative HPLC. In order to unambiguously establish the absolute configuration of the products, the major stereoisomer from diamination of 8-phenylmenthyl cinnamate was submitted to X-ray analysis. Its structure is depicted in Fig. 11.

The observed configuration for this major isomer is in agreement with a stereochemical transition state in which the diastereotopic *Si*-face of the reactive C–C double bond is selectively shielded by the adjacent phenyl moiety of the chiral terpene auxiliary (Fig. 11). Thus, diamination occurs preferentially at the more accessible *Re*-face of the alkene, furnishing the observed (4*R*,5*S*)-configuration for the major diastereomer, a reaction outcome that is reminiscent of an AD reaction on methyl acrylates.[52] Such a stereochemical model of a π-stacking interaction had previously been suggested by several groups for diastereoselective reactions of 8-phenylmenthyl acrylates.[53]

In view of the excellent reactivities of the imido complexes $OsO_2(N^tBu)_2$ and $OsO(N^tBu)_3$ toward alkyl fumarates, their reaction with a chiral non-racemic analogue, the commercially available bis[(−)-menthyl] fumarate, was investigated as well. Thus, its reaction with $OsO_2(N^tBu)_2$ led to two diastereomers in a ratio of 81 : 19. This ratio could be significantly increased when complex $OsO_2(N^tBu)_2$ was changed for the tris(imido) derivative $OsO(N^tBu)_3$ and the two corresponding products were isolated in >95 : <5 dr (Scheme 11, below). Finally, a single crystal X-ray analysis of the major product from diamination of bis(menthyl) fumarate with the tris(imido) osmium(VIII) reagent unambiguously confirmed the absolute stereochemistry from this process (Fig. 12) which resulted to be of (*R*,*R*)-configuration. Understanding that there should be no

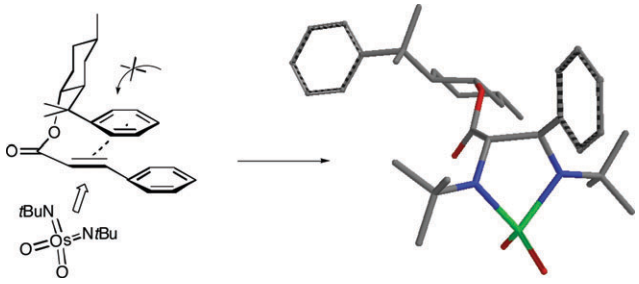


Fig. 11 Selectivity model for explanation of stereodiscrimination in asymmetric diamination of acrylates and solid state structure of the major diastereoisomer from diamination of 8-phenylmenthyl cinnamate with $O_2Os(N^tBu)_2$.

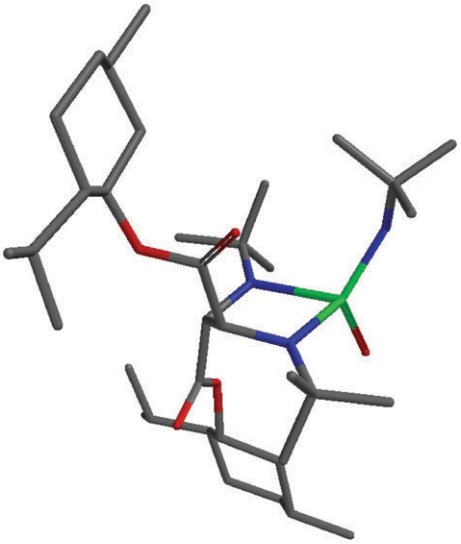
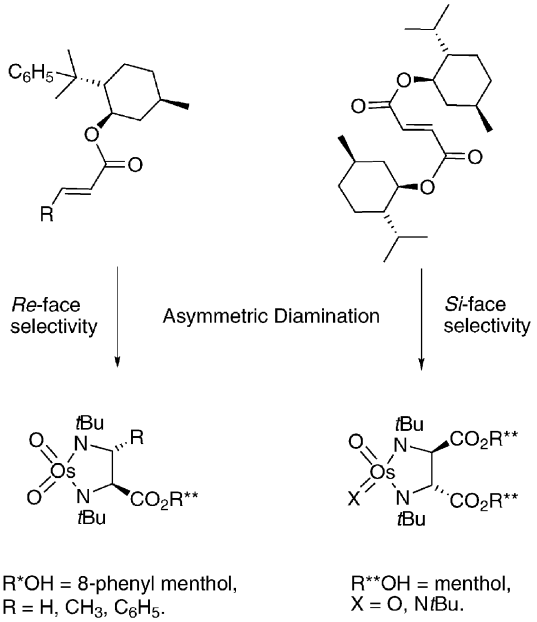


Fig. 12 Solid state structure of the major diastereomer from diamination of bis(menthyl) fumarate.



Scheme 12 Comparison of face selectivity in auxiliary-controlled asymmetric diamination of alkenes.

severe difference in the course of diamination reactions with $OsO_2(N^tBu)_2$ and $OsO(N^tBu)_3$, respectively, an identical absolute configuration is assumed for the corresponding dioxo derivative. It is important to note that the (*R*,*R*)-configuration results from *Si*-face addition, an approach that is opposite to the one in the related case employing the 8-phenylmenthyl auxiliary. This latter auxiliary dominates the stereoselective diamination *via* an active π-stacking conformation that apparently overrides the given preference in stereodiscrimination with the (−)-menthyl moiety. Thus the two chiral terpene auxiliaries exercise opposite face selectivity in the asymmetric diamination of alkenes (Scheme 12). The oxidative conversion of chiral dimenthyl fumarate has been previously described to occur with oxidants such as osmium tetroxide[54] and potassium permanganate,[55] yielding mixtures of diastereomers with an analogous preference for the (*R*,*R*)-diastereomer, albeit with lower dr.

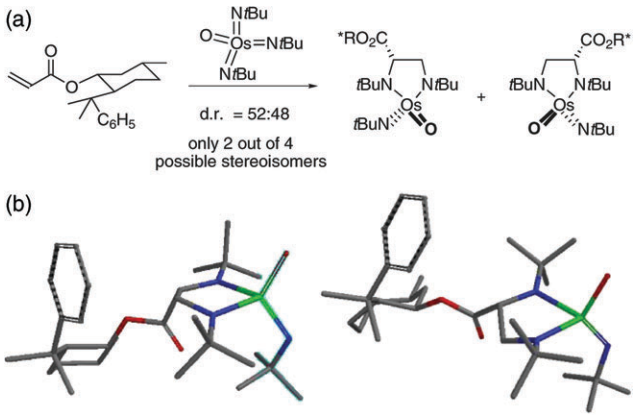
Regarding the structure of the major diastereoisomer itself, it is important to note that the remaining imido ligand coordinates in a bent fashion with a 157° angle. This indicates that the ring nitrogen atoms contribute most of the electronic stabilisation to the Os center and that the imido ligand is involved only to a much lower extent. In contrast, Schrock's arylimido osmaimidazolidine structure[15] displays a nearly linear imido ligand with an N–Os–C angle of 178°, indicative of a reversed electron donation *via* the imido lone pair.

The synthesis of chiral-at-metal osmaimidazolidines from diamination of unsymmetrical alkenes with a tris(imido) osmium reagent had been discussed above. In addition, it appears noteworthy that this example is the first one of generating such metal atoms in the course of oxidative alkene functionalisation. Since the formation of the stereogenic metal centers concomitantly occurs within the alkene diamination process, any reasonable mechanistic assumption on the precise course of the diamination reaction must correctly explain the correlation of all newly established stereocenters. This was taken into account in a preliminary investigation employing 8-phenylmenthyl acrylate as alkene (Scheme 13). Here, only two out of four possible stereoisomers were observed and separated by semi-preparative HPLC. Their solid state structures were determined and unambiguously prove that the absolute configurations do not match the inherent stereodiscrimination of a concerted [3 + 2]-cycloaddition pathway as discussed for related diaminations with the bis(imido) reagent. Hence, alternative stepwise processes must be taken into account.[37]

An extensive discussion on the mechanistic course of the related dihydroxylation of alkenes had focused on whether this reaction followed a concerted [3 + 2]-cycloaddition[56,57] or a stepwise [2 + 2]-reaction pathway.[58] Obviously, the present diamination and the electronic properties of its tris(imido) osmium reagent cannot be compared with dihydroxylations in the presence of osmium tetroxide. Still, the proposed nucleophilic reaction between the tris(imido) reagent and the acrylate substrate shows that there might be reactivity within osmium(VIII)-promoted alkene oxidation that does not follow concerted cycloaddition.

In order to accomplish an enantioselective diamination of alkenes, it was intended to employ cinchona alkaloid based ligands as introduced by Sharpless in his respective AD and AA reactions.[22,28] Despite several attempts and variation of all reaction parameters, it was not possible to achieve any measurable asymmetric induction in diaminations of various alkenes with the bis- and tris(imido)osmium(VIII) reagents. This is a noteworthy difference to the respective stoichiometric and catalytic oxidations with osmium tetroxide[59] and mono(imido) derivatives thereof.[60]

Careful ^{1}H nmr titration studies for different ratios of $O_2Os(N^tBu)_2$ and the standard first-generation 4-chloroben-



Scheme 13 X-Ray structures (b) of the two diastereoisomers from diamination of (−)-8-phenylmenthyl acrylate with the tris(imido) osmium reagent (a).

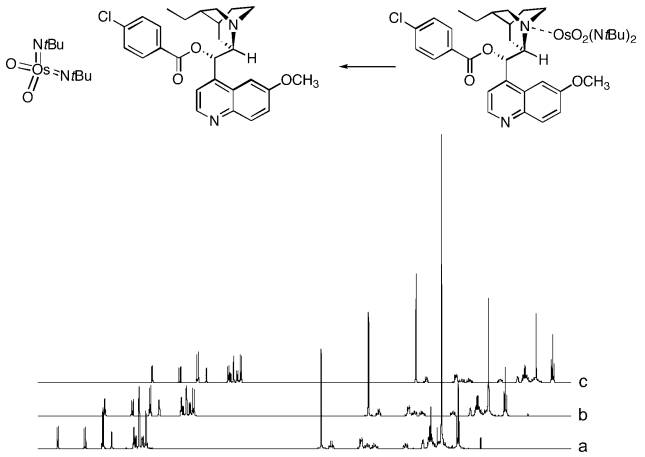
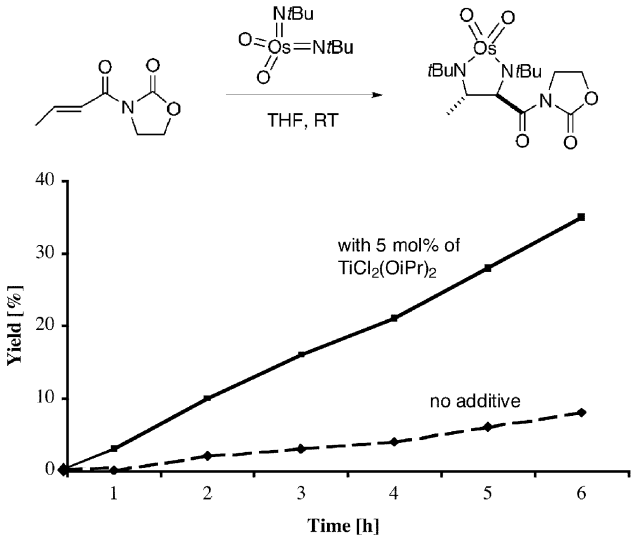


Fig. 13 ^{1}H nmr spectra for titration of $O_2Os(N^tBu)_2$ with cinchona alkaloid DHQ-PCB [for ratios of 1 : 1 (a), 5 : 1 (b) and 20 : 1 (c), respectively].



Scheme 14 Diamination of crotonyl oxazolidinone and reaction acceleration in the presence of a Lewis acid.

zoyl ligand of dihydroquinine (DHQ-PCB) did not suggest any complexation at all. Apparently, even in the presence of a 20-fold excess of DHQ-PCB there was no change in the nmr shifts of the respective sets of signals for the two compounds (Fig. 13).[36] This is a pronounced difference from the related situation for both osmium tetroxide and the mono(imido) complex $O_3Os(N^tBu)$ which form cinchona alkaloid complexes that can be detected spectroscopically. For these two Os compounds, an equilibrium between the free complex and the ligated derivative has been established.[22,59,60] Such behaviour which is indispensable for *ligand accelerated catalysis*[24] can prove rather problematic in asymmetric stoichiometric transformations. In such cases, tight binding between the ligand and metal center is preferable. The inability of bis- and tris(imido) complexes, $O_2Os(N^tBu)_2$ and $OOs(N^tBu)_3$, respectively, to undergo complexation with standard cinchona alkaloids originates from the *tert*-butylimido ligands at osmium. Since these entities contain a basic lone pair at each nitrogen of the imido ligand, donation of electron density to the formally 16e osmium center is enhanced and results in a significantly diminished Lewis acidity at the metal center, if any. As a consequence, no σ-coordination of external ligands is feasible. This result also explains the apparent ease of diamination of the 3-pyridyl acrylate (*vide supra*) since a potentially competing coordination of the pyridino group to the Os(VIII) reagent cannot take place.

These results preclude a general enantioselective diamination on the basis of cinchona alkaloid induction. However, certain solutions for enantioselective diamination may be available for special substrate classes.

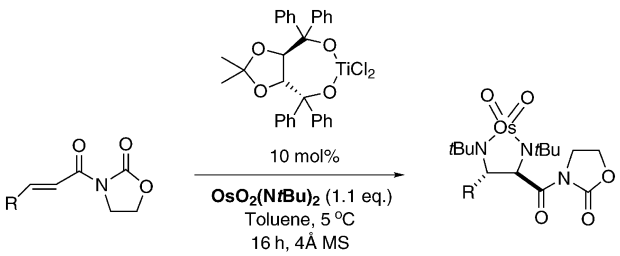
For example, during studies on the scope of reactivity in the diaminations with osmium oxidants, a surprisingly low reaction rate for oxidation of crotonyl oxazolidinone with a dioxo bis(imido)osmium compound (Scheme 14) was encountered. ^{1}H nmr experiments revealed that diamination of related methyl crotonate is about 18 times faster than for the present oxazolidinone derivative.

This observation set the basis for an enantioselective transition metal catalysed diamination process. Thus, activation of the carbonyl moiety by transition metal complexes which incorporate defined stereochemical information, should enhance the electron deficiency of the olefinic bond and thereby accelerate the overall reaction rate as well as introduce enantioselectivity into the overall process.[61,62]

To this end, a variety of Lewis acids were screened. Obviously, the present oxidation reaction conditions employing the bis(imido)osmium oxidant preclude a number of metal ion candidates because of oxidation state incompatibility. Within this context, tin(II) and copper(I) complexes were found to react readily with the osmium(VIII) reagent and thus led to low diamine formation, if any. It is interesting to note that there exists surprisingly little precedence for investigation on oxygen transfer between osmium reagents such as OsO_4 and other metals. As a noteworthy exception, an interesting (reversible) transfer between osmium and selenium has become available.[63] These observations limit potential candidates to high-oxidation-state Lewis acids. Among these, titanium(IV) reagents were considered promising, especially in view of their rich application in combination with the oxazolidinone group. 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 for a diamination of crotonyl oxazolidinone in toluene and in the presence of 5 mol% of dichloro-bis(isopropoxy)titanium (IV). A significant rate increase was observed which led to a 37% isolated yield after a reaction time of 6 h. The uncatalysed reaction gave less than 7% yield after this period (Scheme 14).

In order to render the overall diamination process enantioselective, chiral ligands were screened, employing the reaction from Scheme 14 as model reaction. Toluene was employed as solvent instead of the usual THF in order to prevent a decrease in Lewis acidity of the titanium catalyst upon THF coordination. A preformed catalyst from TADDOL and a titanium salt gave the highest reactivity and afforded the best induction. Under such optimised conditions, conversion of five different alkenes in the presence of the Ti-TADDOLate catalyst[48] led to the formation of different osmaimidazolidines with enantiomeric ratios in the range of 84 : 16–95 : 5 (Scheme 15).

This catalytic enantioselective process benefits from the acceleration of the catalysed pathway over the potential



Scheme 15 First enantioselective diamination of alkenes.

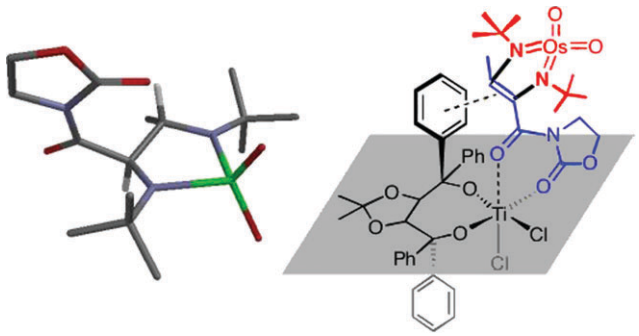


Fig. 14 X-Ray structure of the major enantiomer from the catalytic enantioselective diamination of crotonyl oxazolidinone and the stereodiscriminating transition state.

uncatalysed background reaction.[24] For the corresponding stoichiometric reaction, an enantiomeric ratio of 95 : 5 was obtained. This suggests that the above diamination reactions proceed almost entirely *via* the catalysed pathway. The absolute configuration of the major enantiomers was determined through single crystal X-ray analysis of the product from diamination of crotonyl oxazolidinone. An absolute (*R*,*S*)-configuration was established, which matches a diamination from the *Re*,*Si*-face of the alkene as depicted in Fig. 14. Such a stereodiscriminating transition state is in complete agreement with those postulated for related Ti-TADDOLate catalysed reactions. Under the assumption of a concerted [3 + 2]-addition[48] of the bis(imido)osmium reagent to the Ti-TADDOLate coordinated alkene, its role can be compared to that of organic 4π-compounds in related cycloaddition reactions, for which there exists significant literature precedence.[48]

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 rather unique since attempts towards realisation of related oxidation reactions with osmium tetroxide did not induce any enantioselectivity. Apparently, the electrophilic oxidant OsO_4 does not meet the specific electronic requirements for oxidation of alkenes such as crotonyl oxazolidinone within a transition metal catalyst accelerated pathway.

Summary and perspectives for future development

Imido-osmium compounds represent versatile reagents for direct, stereospecific diamination of alkenes. Osmaimidazolidines are formed as stable, monomeric products of these reactions. For diamination of unsymmetrical alkenes with tris(*tert*-butylimido)oxoosmium(VIII), osmaimidazolidines with a stereogenic metal center are obtained. Asymmetric versions of all these diamination reactions have been developed on the basis of both chiral auxiliaries and chiral catalysts. Thus, diastereomerically and enantiomerically enriched osmaimidazolidines have become available in what represents the *status quo* of this type of oxidative alkene transformation.

Future development in this area will have to devise two novelties regarding imido-osmium compounds. Firstly, the development of suitable monomeric complexes with electron-deficient imido ligands are required in order to allow for coordination of external chiral ligands and thus enable for a more general way of enantioselective induction. In addition, these electron-withdrawing substituents could allow for suitable destabilisation of the osmaimidazolidine products which may ultimately allow for the release of the osmium metal after the alkene functionalisation step and thus devise a reaction truly catalytic in osmium. Secondly, the question on differentiation of the nitrogen atoms in the diamine product leads to the challenge of developing complexes with defined different substitution patterns at the imido groups.

At the present stage, it appears of prime interest to investigate the fundamental oxidation properties of defined imido-osmium complexes. One must devise compounds that are of different nature than those from aminohydroxylation since this reaction proceeds in water and, as a consequence, continuously generates a third oxo ligand at osmium. In addition to these remarks, the exciting chemistry of related stoichiometric diamination processes which rely on thallium, mercury or palladium may well lead to the development of catalytic activity with complimentary applicability. At present, one conclusion is obvious: the enantioselective catalytic diamination of alkenes represents an extremely exciting task and an important synthetic process to be developed.

Acknowledgements

My research over the recent years has been generously supported by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft, the German-Israeli Foundation, the Deutscher Akademischer Austauschdienst and the Alexander-von-Humboldt Foundation/Japanese Society for the Promotion of Science. I am particularly grateful to my former academic teachers Prof. H. M. R. Hoffmann, Prof. S. E. Gibson, Prof. J. Barluenga, Prof. C. Bolm and Prof. R. Noyori for their support and continuous advice. Dr D. Deubel significantly contributed to the development of alkene diamination by providing the theoretical background, and Dr M. Nieger has provided all solid state structures over the past years. I am also grateful to Dr A. Iesato, C. H. Hövelmann, J. Streuff, I. Almodovar, A. Villar and R. Vicente for their contributions to imido-osmium chemistry and to Dr A. Minatti and Dr J. Hildebrand for numerous discussions and suggestions. The expert composition of the cover artwork was provided by Martin Muñiz.

References

1 F. Fache, E. Schulz, M. L. Tommasio and M. Lemaire, *Chem. Rev.*, 2000, **100**, 2159.
2 D. Lucet, T. Le Gall and C. Mioskowski, *Angew. Chem. Int. Ed.*, 1998, **37**, 2580.
3 Y. L. Bennani and S. Hanessian, *Chem. Rev.*, 1997, **97**, 3161.
4 (*a*) E. J. Corey, S. Sarshar, M. D. Azimioara, R. C. Newbold and M. C. Noe, *J. Am. Chem. Soc.*, 1996, **118**, 7851; (*b*) M. Asami, T. Suga, K. Honda and S. Inoue, *Tetrahedron Lett.*, 1997, **38**, 6425; (*c*) S. Hanessian, P. Meffre, M. Girard, S. Beaudoin, J.-Y. Sancéau and Y. Bennani, *J. Org. Chem.*, 1993, **58**, 1991; (*d*) K. Murata, H. Konishi, M. Ito and T. Ikariya, *Organometallics*, 2002, **21**, 253; (*e*) M. Nakajima, I. Miyoshi, K. Kanayama, S.-I. Hashimoto, M. Noji and K. Koga, *J. Org. Chem.*, 1999, **64**, 2264; (*f*) L. Cavallo, M. E. Cucciolito, A. De Martino, F. Giordano, I. Orabona and A. Vitagliano, *Chem. Eur. J.*, 2000, **6**, 1127.
5 (*a*) R. Noyori, M. Yamakawa and S. Hashiguchi, *J. Org. Chem.*, 2001, **66**, 7931; (*b*) T. Katsuki, *Adv. Synth. Catal.*, 2002, **344**, 131; (*c*) A. Magnus, S. K. Bertilsson and P. G. Andersson, *Chem. Soc. Rev.*, 2002, **31**, 223; (*d*) K. Kubota and J. L. Leighton, *Angew. Chem. Int. Ed.*, 2003, **42**, 946; (*e*) M. J. Palmer and M. Wills, *Tetrahedron: Asymmetry*, 1999, **10**, 2045; (*f*) J. Balsells and P. J. Walsh, *J. Am. Chem. Soc.*, 2000, **122**, 1802.
6 (*a*) J. Gawronski, K. Gawronska, J. Grajewski, K. Kacprzak and U. Rychleska, *Chem. Commun.*, 2002, 582; (*b*) P. Wittung, P. Nielsen and B. Norden, *J. Am. Chem. Soc.*, 1997, **119**, 3189; (*c*) F. Lagriffoule, P. Wittung, M. Eriksson, K. K. Jensen, B. Norden, O. Buchardt and P. E. Nielsen, *Chem. Eur. J.*, 1997, **3**, 912; (*d*) K. Hanabusa, M. Yamada, M. Kimura and H. Shirai, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1949.
7 (*a*) R. Noyori and T. Ohkuma, *Angew. Chem. Int. Ed.*, 2001, **40**, 40; (*b*) R. Noyori, *Angew. Chem. Int. Ed.*, 2002, **41**, 2008; (*c*) R. Noyori, *Adv. Synth. Catal.*, 2003, **345**, 15; (*d*) R. Noyori and T. Ohkuma, *Pure Appl. Chem.*, 1999, **71**, 1493.
8 C. Sandoval, T. Ohkuma, K. Muñiz and R. Noyori, *J. Am. Chem. Soc.*, 2003, **125**, 13490.
9 T. Ohkuma, M. Koizumi, K. Muñiz, G. Hilt, C. Kabuto and R. Noyori, *J. Am. Chem. Soc.*, 2002, **124**, 6508.
10 S. E. Clapham, A. Hadzovic and R. H. Morris, *Coord. Chem. Rev.*, 2004, **248**, 2201.

11 (*a*) V. Gómez Aranda, J. Barluenga and F. Aznar, *Synthesis*, 1974, 504; (*b*) F. Aznar, PhD thesis, University of Zaragoza, 1975.
12 (*a*) J. Barluenga, L. Alonso-Cires and G. Asensio, *Synthesis*, 1979, 962; (*b*) J. Barluenga, F. Aznar, M. C. S. de Mattos, W. B. Kover, S. García-Granda and E. Pérez-Carreño, *J. Org. Chem.*, 1991, **56**, 2930.
13 J.-E. Bäckvall, *Tetrahedron Lett.*, 1975, **16**, 2225.
14 A. O. Chong, K. Oshima and K. B. Sharpless, *J. Am. Chem. Soc.*, 1977, **99**, 3420.
15 (*a*) J. T. Anhaus, T. P. Kee, M. H. Schofield and R. R. Schrock, *J. Am. Chem. Soc.*, 1990, **112**, 1642; (*b*) M. H. Schofield, T. P. Kee, J. T. Anhaus, R. R. Schrock, K. H. Johnson and W. M. Davis, *Inorg. Chem.*, 1991, **30**, 3595; note, however, that all products from these reactions are achiral.
16 (*a*) G. Li, H.-X. Wei, S. H. Kim and M. Carducci, *Angew. Chem. Int. Ed.*, 2001, **40**, 4277; (*b*) H.-X. Wei, S. H. Kim and G. Li, *J. Org. Chem.*, 2002, **67**, 4777; (*c*) W. Pei, C. Timmons, N.-W. Wie and G. Li, *Org. Biomol. Chem.*, 2003, **1**, 2919; (*d*) C. Timmons, D. Chen, X. Xu and G. Li, *Eur. J. Org. Chem.*, 2003, 3850; (*e*) H.-X. Wie, S. Siruta and G. Li, *Tetrahedron Lett.*, 2002, **43**, 3809; (*f*) G. Li, S. H. Kim and H.-X. Wie, *Tetrahedron Lett.*, 2000, **41**, 8699.
17 (*a*) R. Criegee, *Justus Liebigs Ann. Chem.*, 1936, **522**, 75; (*b*) R. Criegee, *Angew. Chem.*, 1937, **50**, 153; (*c*) R. Criegee, *Angew. Chem.*, 1938, **51**, 519; (*d*) R. Criegee, B. Marchand and H. Wannowius, *Justus Liebigs Ann. Chem.*, 1942, **550**, 99.
18 (*a*) K. A. Hofmann, *Chem. Ber.*, 1912, **45**, 3329; (*b*) K. A. Hofmann, O. Ehrhardt and O. Schneider, *Chem. Ber.*, 1913, **46**, 1657.
19 (*a*) N. A. Milas and S. Sussmann, *J. Am. Chem. Soc.*, 1936, **58**, 1302; (*b*) N. A. Milas and S. Sussmann, *J. Am. Chem. Soc.*, 1937, **59**, 2345; (*c*) N. A. Milas, S. Sussmann and H. S. Mason, *J. Am. Chem. Soc.*, 1939, **61**, 1844; (*d*) N. A. Milas, J. H. Treptagnier, J. T. Nolan and M. I. Iliopulos, *J. Am. Chem. Soc.*, 1959, **81**, 4730.
20 (*a*) K. B. Sharpless and K. Akashi, *J. Am. Chem. Soc.*, 1976, **98**, 1986; (*b*) K. Akashi, R. E. Palermo and K. B. Sharpless, *J. Org. Chem.*, 1978, **43**, 2063.
21 (*a*) W. P. Schneider and A. V. McIntosh, US-2.769.824, 1956 (*Chem. Abs.*, 1957, **51**, 8822e); (*b*) V. VanRheenen, R. C. Kelly and D. Y. Cha, *Tetrahedron Lett.*, 1976, **17**, 1973.
22 (*a*) H. C. Kolb, M. S. VanNieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483; (*b*) C. Bolm, J. P. Hildebrand and K. Muñiz, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, Wiley-VCH, Weinheim, 2000, p. 299; (*c*) I. E. Marko and J. S. Svendsen, in *Comprehensive Asymmetric Catalysis II*, ed. E. N. Jacobsen, A. Pfaltz, H. Yamamoto, Springer, Berlin, 1999, p. 713; (*d*) H. Becker and K. B. Sharpless, in *Asymmetric Oxidation Reactions: A Practical Approach*, ed. T. Katsuki, Oxford University Press, London, 2001, p. 81; (*e*) M. Beller and K. B. Sharpless, in *Applied Homogeneous Catalysis*, ed. B. Cornils, W. A. Herrmann, VCH, Weinheim, 1996, p. 1009.
23 http://www.nobel.se/chemistry/laureates/2001/index.html; K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2002, **41**, 2024.
24 D. J. Berrisford, C. Bolm and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1059.
25 K. Muñiz, *Chem. Soc. Rev.*, 2004, **33**, 160.
26 First report: G. Li, H.-T. Chang and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 451.
27 (*a*) Reviews: C. Bolm, J. P. Hildebrand and K. Muñiz, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, Wiley-VCH, Weinheim, 2000, p. 299; (*b*) J. A. Bodkin and M. D. McLeod, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2733; (*c*) G. Schlingloff and K. B. Sharpless, in *Asymmetric Oxidation Reactions: A Practical Approach*, ed. T. Katsuki, Oxford University Press, London, 2001, p. 104; (*d*) D. Nilov and O. Reiser, *Adv. Synth. Catal.*, 2002, **344**, 1169; (*e*) P. O'Brien, *Angew. Chem. Int. Ed.*, 1999, **38**, 326; (*f*) G. Casiraghi, G. Rassu and F. Zanardi, *Chemtracts: Org. Chem.*, 1997, **10**, 318; (*g*) O. Reiser, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1308.
28 E. N. Jacobsen, I. Marko, M. B. France, J. S. Svendson and K. B. Sharpless, *J. Am. Chem. Soc.*, 1989, **111**, 737.
29 C. H. Hövelmann and K. Muñiz, *Chem. Eur. J.*, 2005, **11**, 3951.
30 (*a*) Special solutions: H. Han, C.-W. Cho and K. Janda, *Chem. Eur. J.*, 1999, **5**, 1565; (*b*) C.-Y. Chuang, V. C. Vassar, Z. Ma, R. Geney and I. Ojima, *Chirality*, 2002, **14**, 151.
31 (*a*) K. B. Sharpless, D. W. Patrick, L. K. Truesdale and S. A. Biller, *J. Am. Chem. Soc.*, 1975, **97**, 2305; (*b*) D. W. Patrick, L. K. Truesdale, S. A. Biller and K. B. Sharpless, *J. Am. Chem. Soc.*, 1978, **100**, 2628.
32 W. A. Nugent, R. L. Harlow and R. J. McKinney, *J. Am. Chem. Soc.*, 1979, **101**, 7265.
33 A. A. Danopoulos, G. Wilkinson, B. Hussain-Bates and M. B. Hursthouse, *J. Chem. Soc., Dalton Trans.*, 1991, 269.
34 W. A. Nugent and B. L. Haymore, *Coord. Chem. Rev.*, 1980, **31**, 123.
35 K. Muñiz, A. Iesato and M. Nieger, *Chem. Eur. J.*, 2003, **9**, 5581.
36 K. Muñiz, *Eur. J. Org. Chem.*, 2004, 2243.
37 K. Muñiz, M. Nieger and H. Mansikkamäki, *Angew. Chem. Int. Ed.*, 2003, **42**, 5958.
38 (*a*) H. Brunner, *Angew. Chem. Int. Ed.*, 1999, **38**, 1194; (*b*) C. Ganter, *Chem. Soc. Rev.*, 2003, **32**, 130; (*c*) H. Brunner, *Eur. J. Inorg. Chem.*, 2001, 905.
39 (*a*) H. Brunner and W. Miehling, *Angew. Chem. Suppl.*, 1983, 84; (*b*) H. Brunner, P. Faustmann, A. Dietl and B. Nuber, *J. Organomet. Chem.*, 1997, **542**, 255; (*c*) H. Brunner, P. Faustmann and B. Nuber, *J. Organomet. Chem.*, 1998, **556**, 129; (*d*) H. Brunner, P. Faustmann and B. Nuber, *J. Organomet. Chem.*, 1999, **579**, 1. The author is very grateful to Prof. H. Brunner for pointing out this context.
40 (*a*) K. B. Sharpless, D. W. Patrick, L. K. Truesdale and S. A. Biller, *J. Am. Chem. Soc.*, 1975, **97**, 2305; (*b*) D. W. Patrick, L. K. Truesdale, S. A. Biller and K. B. Sharpless, *J. Am. Chem. Soc.*, 1978, **100**, 2628.
41 D. V. Deubel and K. Muñiz, *Chem. Eur. J.*, 2004, **10**, 2475.
42 (*a*) R. M. Pearlstein, B. K. Blackburn, M. W. Davis and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 639; (*b*) Selected recent structural determinations of pyridine adducts: J. M. Wallis and J. K. Kochi, *J. Am. Chem. Soc.*, 1988, **110**, 8207; (*c*) W. A. Herrmann, S. J. Eder and W. Scherer, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 1345; (*d*) W. A. Herrmann, S. J. Eder and W. Scherer, *Chem. Ber.*, 1993, **126**, 39. Further structures deposited at CCDC bear the following identification codes: OLATOS, QERCUL, MBAOOS, MTOLOS, OSOTYM, MAYDIZ, ADPYOS10, HOMMAX, HOMMEB and VIGPIK.
43 (*a*) Recent structural determinations: A. Lehtonen, J. Jokela, P. G. Edwards and R. Sillanpää, *J. Chem. Soc., Dalton Trans.*, 1999, 2785; (*b*) M. R. Sivik, J. C. Gallucci and L. A. Paquette, *J. Org. Chem.*, 1990, **55**, 391; (*c*) F. L. Philipps and A. C. Skapski, *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.*, 1975, **31**, 1814; (*d*) L. O. Atovmyan and Y. A. Sokolova, *Zh. Strukt. Khim.*, 1979, **20**, 754.
44 (*a*) F. L. Philipps and A. C. Skapski, *J. Chem. Soc., Dalton Trans*, 1975, 2586; (*b*) B. A. Cartwright, W. P. Griffith, M. Schröder and A. C. Skapski, *J. Chem. Soc., Chem. Commun.*, 1978, 853.
45 (*a*) Structural determinations: T. J. Donohoe, P. D. Johnson, A. Cowley and M. Keenan, *J. Am. Chem. Soc.*, 2002, **124**, 12934; (*b*) W. P. Griffith, N. T. McManus, A. C. Skapski and A. J. Nielson, *Inorg. Chim. Acta*, 1985, **103**, L5.
46 (*a*) A. E. Rubin and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2637; (*b*) H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem. Int. Ed.*, 2001, **40**, 2004.
47 K. Muñiz, *Tetrahedron Lett.*, 2003, **44**, 3547.
48 D. Seebach, A. K. Beck and A. Heckel, *Angew. Chem. Int. Ed.*, 2001, **40**, 92.
49 (*a*) R. Noyori and M. Kitamura, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 49; (*b*) K. Soai and S. Niwa, *Chem. Rev.*, 1992, **92**, 833; (*c*) P. Knochel and R. D. Singer, *Chem. Rev.*, 1993, **93**, 2117; (*d*) L. Pu and H.-B. Yu, *Chem. Rev.*, 2001, **101**, 757.
50 D. Seebach, A. K. Beck, B. Schmidt and Y. M. Wang, *Tetrahedron*, 1994, **50**, 4363.
51 K. Muñiz and M. Nieger, *Synlett*, 2003, 211.
52 S. Hatakeyama, Y. Matsui, M. Suzuki, K. Sakurai and S. Takano, *Tetrahedron Lett.*, 1985, **26**, 6485.
53 (*a*) J. Barluenga, J. M. Montserrat, J. Flórez, S. García-Granda and E. Martín, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1392; (*b*) J. Barluenga, J. M. Montserrat, J. Flórez, S. García-Granda and E. Martín, *Chem. Eur. J.*, 1991, **1**, 236; (*c*) I. Fleming and N. D. Kindon, *J. Chem. Soc., Perkin Trans. 1*, 1995, 303; (*d*) J. d'Angelo and J. Maddaluno, *J. Am. Chem. Soc.*, 1986, **108**, 8112.
54 (*a*) A. McKenzie and H. Wren, *J. Chem. Soc.*, 1907, **91**, 1215; (*b*) J. Micklefield, K. J. Harris, S. Gröger, U. Mocek, H. Hilbi, P. Dimroth and H. G. Floss, *J. Am. Chem. Soc.*, 1995, **117**, 1153.
55 F. Fernández, G. García and J. E. Rodríguez, *Synth. Commun.*, 1990, **20**, 2837.
56 (*a*) E. J. Corey and M. C. Noe, *J. Am. Chem. Soc.*, 1996, **118**, 319; (*b*) J. Böeseken and J. van Giffen, *Recl. Trav. Chim. Pays-Bas*, 1920, **39**, 183; (*c*) J. Böeseken, *Recl. Trav. Chim. Pays-Bas*, 1922, **41**, 199; (*d*) M. Torrent, M. Sola and G. Frenking, *Chem. Rev.*, 2000, **100**, 439.

57 A. J. DelMonte, J. Haller, K. N. Houk, K. B. Sharpless, D. A. Singleton, T. Strassner and A. A. Thomas, *J. Am. Chem. Soc.*, 1997, **119**, 9907.

58 (*a*) K. B. Sharpless, A. Y. Teranishi and J.-E. Bäckvall, *J. Am. Chem. Soc.*, 1977, **99**, 3120; (*b*) Z. Göbel and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1329.

59 (*a*) J. S. Svendsen, I. Markó, E. N. Jacobsen, C. P. Rao, S. Bott and K. B. Sharpless, *J. Org. Chem.*, 1989, **54**, 2263; (*b*) D. V. Deubel and G. Frenking, *Acc. Chem. Res.*, 2003, **36**, 645.

60 H. Rubenstein and J. S. Svendsen, *Acta Chem. Scand.*, 1994, **48**, 439.

61 For a review see: J. S. Johnson and D. A. Evans, *Acc. Chem. Res.*, 2000, **33**, 325.

62 (*a*) Selected recent work in this area: M. P. Sibi and J. B. Sausker, *J. Am. Chem. Soc.*, 2002, **124**, 984; (*b*) K. Li and K. K. Hii, *Chem. Commun.*, 2003, 1132; (*c*) K. Li, P. N. Horton, M. B. Hursthouse and K. K. Hii, *J. Organomet. Chem.*, 2003, **665**, 250; (*d*) W. Zhuang, R. G. Hazell and K. A. Jorgensen, *Chem. Commun.*, 2001, 1240; (*e*) J. Huang and R. P. Hsung, *J. Am. Chem. Soc.*, 2005, **127**, 50.

63 (*a*) A. Krief and C. Colaux-Castillo, *Pure Appl. Chem.*, 2002, **74**, 107; (*b*) A. Krief, A. Destree, V. Durisotti, N. Moreau, C. Smal and C. Colaux-Castillo, *Chem. Commun.*, 2001, 558; (*c*) A. Krief and C. Colaux-Castillo, *Tetrahedron Lett.*, 1999, **40**, 4189; (*d*) A. Krief and C. Castillo-Colaux, *Synlett*, 2001, 501.