TUTORIAL REVIEW

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Imido-osmium(VIII) compounds in organic synthesis: aminohydroxylation and diamination reactions

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Imido complexes of osmium tetroxide are versatile compounds for olefin functionalisation. This *tutorial review* offers a brief historical overview on these compounds and discusses the electronic properties and reactivities of isolated imido osmium compounds in what had been the original stoichiometric aminohydroxylation reaction. The recently emerging catalytic Sharpless aminohydroxylation is discussed with special emphasis on mechanistic details. The final section deals with diamination of olefins, which relies on the chemistry of bisimido and trisimido osmium complexes.

1 Introduction

Osmium tetroxide **1** is a versatile and highly acclaimed reagent for organic synthetic transformations. Its high preference for olefinic substrates and the availability of catalytic processes have rendered it the ideal oxidant for diol synthesis. Among various catalytic reaction conditions, the Sharpless asymmetric dihydroxylation represents a powerful version with a uniquely broad substrate scope.[1] While dihydroxylation reactions have encountered broad interest, osmium reagents bearing imido instead of oxo ligands are still far from achieving their full synthetic potential. This coincides with a gap in the development of olefin functionalisation processes since both catalytic and stoichiometric aminohydroxylation and diamination reactions require defined imido osmium reagents.

2 Complexes

The first isolated imidoosmium(VIII) complexes were synthesized in the late 1950s.[2,3] Incidentally, this represented the first syntheses of discrete transition metal complexes bearing an imido ligand.[4] To date, only a limited number of imidoosmium(VIII) complexes have actually been isolated. Fig. 1 shows the series of

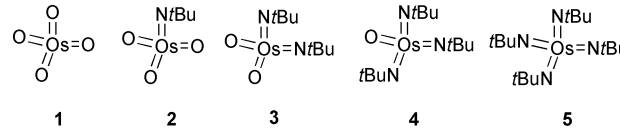
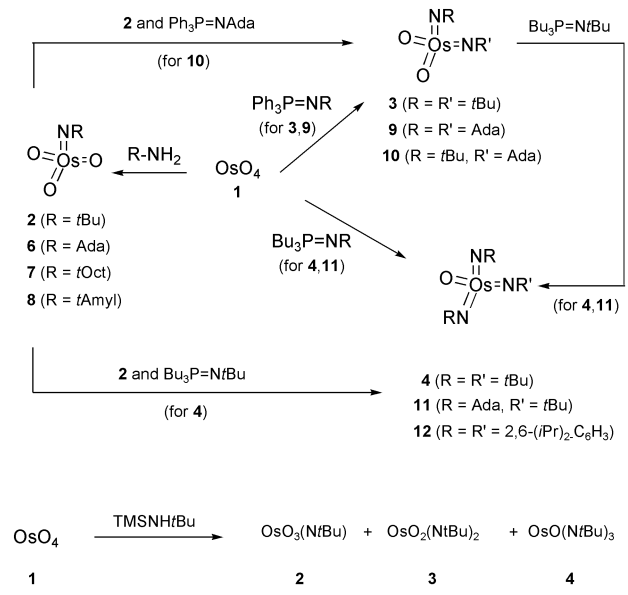


Fig. 1 *tert*-Butyl imido compounds as derivatives of OsO_4.

tert-butyl substituted imido derivatives of OsO_4 (**1**) ranging from the monoimido compound **2** to the tetrakisimido compound **5**.

Historically, monoimido osmium(VIII) compounds are accessible directly from OsO_4 by treatment with the respective amine in hydrocarbon solvent or even with an aqueous amine solution.[2,3,5] Bis and trisimido derivatives are readily available from reaction of phosporane iminates with **1** or preformed monoimido complexes, respectively.[6] The latter procedure can give rise to mixed imido complexes such as **10** and **11**. A variety of different imido compounds has been prepared by either of these synthetic approaches (Scheme 1).[2,3,5,6]



Scheme 1 Synthesis of various imidoosmium(VIII) compounds.

At present, the synthetically most convenient procedure consists of direct treatment of a solution of osmium tetroxide **1** in *n*-hexane with an excess of TMS-*N*-*tert*-butylamine, which forms a mixture of the three imido compounds **2–4** that can be separated by column chromatography. This reaction is the most economical approach since it results in a combined yield of around 90% (Scheme 1, below).[7,8] Direct treatment of **1** with neat TMS-*N*-*tert*-butylamine

Kilian Muñiz was born in Hildesheim, Germany in 1970. From 1990 to 1996 he studied Chemistry at Hannover University, Germany, at the Imperial College London, UK and at University of Oviedo, Spain working in the groups of Professors H. M. R. Hoffmann, Susan E. Gibson and José Barluenga. In 1996 he joined the group of Professor Carsten Bolm at the RWTH Aachen, Germany to obtain his doctorate in 1998. From 1999 to 2000 he carried out postdoctoral work with Professor Ryoji Noyori at Nagoya University, Japan working on ruthenium hydride catalyst precursors and on the mechanism of the BINAP/1,2-diamine-ruthenium(II)-catalysed ketone hydrogenation. Since December 2000 he has been a Habilitand associated with Professor Karl Heinz Dötz at the Kekulé Department in Bonn, Germany. His research centres on enantioselective oxidative nitrogen transfer reactions and mechanistic elucidation of asymmetric transition metal oxidations.

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was reported by Wilkinson to furnish the tetrakisimido complex **5** (Fig. 1) as a red oil.[9] Unlike the related complexes **2**-**4** it is no longer air- and moisture-stable and the synthetic approach is quite difficult. A related mono-tosylated derivative by Sharpless represents another stable tetrakisimido complex, but has only been mentioned in literature footnotes.[4,9]

The trisimido complex **12** was prepared by Schrock and coworkers *via* a two-step synthesis: reaction of **1** with (2,6-di-*iso*-propyl)phenylisocyanide yields an intermediary homoleptic trisimido osmium(VI) complex which can be reoxidised to the osmium(VIII) compound **12** with trimethylamine-*N*-oxide.[10]

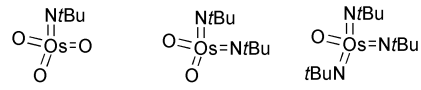
It was soon discovered[6,11] that apart from the *tert*-butyl substituent, only a limited number of other nitrogen substituents such as the mentioned *tert*-alkyl groups in compounds **6–8** would result in stable compounds. Apparently, non-tertiary substituents at nitrogen undergo hydrogen shift rearrangements that lead to Os reduction and complex degradation. According to a report by Wilkinson this also holds true for the case of aniline-based imido ligands which require a 2,6-substitution pattern for stability.[9] It should be noted within the context of stable isolable imido osmium(VIII) complexes that all derivatives **2–4** and **6–11** represent solid, non-volatile compounds that do not display the high toxicity of the parent compound **1**.

When compared to osmium(VIII) oxide **1**, the structural chemistry of these complexes is dominated by the alkylimido ligand. To date, structural information on monomeric imido osmium(VIII) complexes is rather scarce being limited to the three solid state structure elucidations of compounds **2**, **3** and **6** (Fig. 2).[8,12]

The structure of **2** displays a nearly tetrahedral coordination sphere around Os and an almost linear imido ligand with an Os–N distance of 1.69 Å and an Os–N–C angle of 175°. This suggests an additional electron donation involving the nitrogen lone pair rendering the imido moiety a 4e ligand and thus leading to an Os centre of a formal 18e count. Related structural features are found in the X-ray structure of compound **6**. Here, the Os–N bond length of 1.7 Å and the Os–N–C angle of 171° suggest a comparable Os–N triple bond character. For the tetrahedral complex **3** the two imido ligands result non-equivalent. While one is bound in a nearly perfect linear fashion (Os–N–C angle of 179°), the other one is bent by an Os–N–C angle of 155°. As a consequence, the two imido ligands figure as a 4e- and a 2e-donor, respectively, and the overall electron count for Os is 18 again. Additional theoretical calculations by the authors indicate that the different arrangements of the two imido ligands might not only result from electronic reasons alone, but also from intramolecular packing forces.

When inspecting the ^{1}H and ^{13}C NMR data for imido compounds **3** and **4** all imido ligands are isochronic displaying only a single set of signals. The respective ^{13}C data for **2–4** are given in Fig. 3.

In case of compounds **2–4**, the respective shifts for the signals of the methyl and the quaternary carbon atoms are indicative for the number of imido moieties present in the complex. Regarding the ^{1}H NMR signals, a pronounced downfield shift is observed in going from **2** to **4**. The relative difference in shift $\Delta\delta_C$ as observed from the respective carbon NMR can be correlated to the relative electron density at Os(VIII)[4] and thus of the respective average bond order for the imido ligands which apparently decreases from a formal 3 to a formal 2.33.



	2	**3**	**4**
^{1}H nmr, δ (C_6D_6)/ppm	0.87	1.12	1.27
^{13}C nmr, δ (C_6D_6)/ppm	26.1, 81.6	28.3, 73.9	28.7, 70.2
$\Delta\delta_C$	55.5	45.6	41.5

Fig. 3 NMR data for compounds **2**–**4**.

3 Aminohydroxylation: stoichiometric reactions

In 1975, Sharpless discovered the reaction of monoimido complexes **2** and **6** with olefins.[5] Although against all statistical odds, aminoalcohols were the major products. These reactions initiated the development of osmium-mediated aminohydroxylation and a representative example is given for the oxidation of α-methyl styrene (Scheme 2).[5,12]

The following reaction features were generally observed in oxidation reactions with **2**: the aminohydroxylations are *cis*-stereoselective and occur in a stereospecific manner. The preferred olefin classes are terminal and (*E*)-substituted olefins and a high regioselectivity was generally observed for the former yielding products with the amino group placed at the more accessible terminal carbon atom. However, sterically congested olefins gave exclusive diol formation. Based on the paramount observation by Criegee that osmylation reactions are significantly accelerated by pyridine, olefin functionalisation with **2** was tested in pyridine as solvent. Significantly higher yields were generally obtained. For example, aminoalcohol formation from styrene occurs with 92% yield in pyridine while other solvents such as dichloromethane, tetrahydrofuran or *tert*-butanol give lower yields in the range of 37 to 64%. For those cases with competing diol formation, pyridine also influences the chemoselectivity, *i.e.* the aminoalcohol/diol ratio. For example, oxidation of (*E*)-5-decene in dichloromethane forms a 50:20-mixture of diol and aminoalcohol, while exclusive formation of the latter is observed in pyridine solvent (Scheme 2). This beneficial effect is induced by tertiary amine additives such as quinuclidine and [2,2,2]-diazabicyclooctane (dabco) as well.[13]

† CCDC-reference codes for structural data in this article are as follows: KEWMEE (compound **2**), ADOOSB (compound **3**), ADOOSA (compound **6**), DEVZEJ (compound **13**), QAGBEG (compound **35**, CCDC-204560) and HUTXOJ (compound **40a**, CCDC-192700).

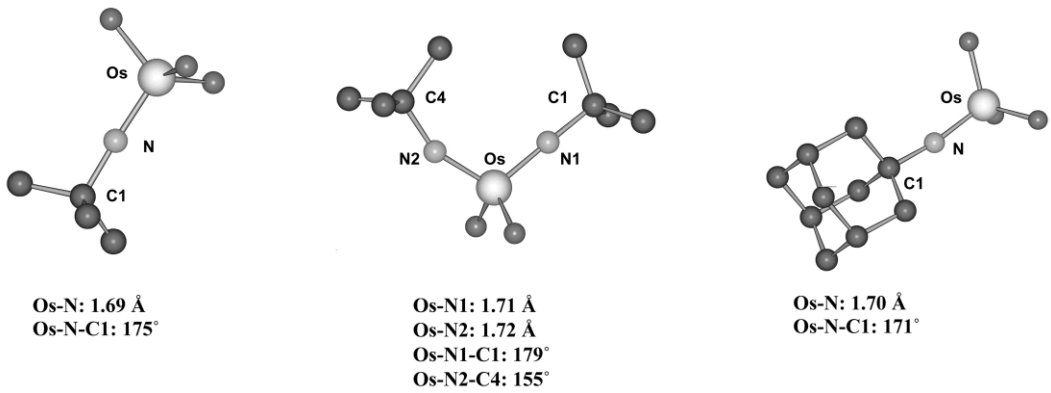
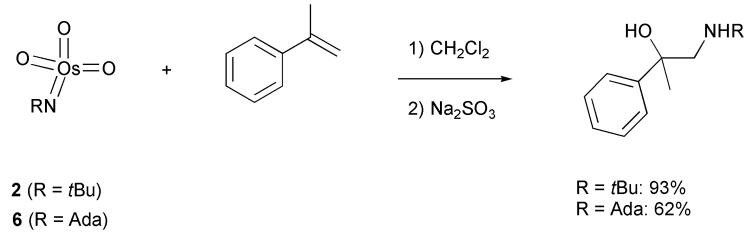
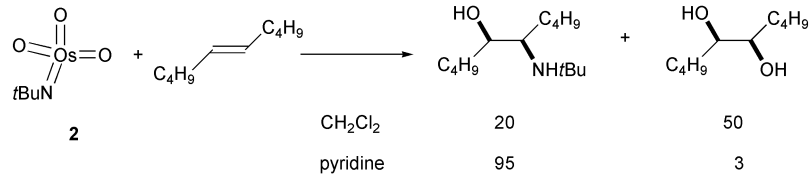


Fig. 2 X-ray structures of complexes **2** (left), **3** (middle) and **6** (right).†





Scheme 2 Aminohydroxylation of α-methyl styrene and (*E*)-5-decene.

A seminal contribution by Griffith disclosed the X-ray analysis on the complex (*tert*-OctNOsO$_3$)$_2$dabco **13** (Fig. 4).[14] The Os atoms

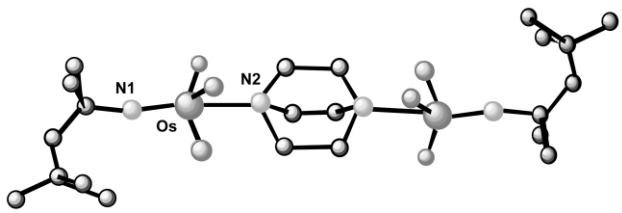


Fig. 4 X-ray structure of complex **13**.†

lie within a distorted trigonal bipyramidal coordination and the bridgehead amino moieties of the ligand are about 2.45 Å located away from the metal centres. The *trans*-position of the imido ligand with regards to the dabco nitrogen dominates the overall electronic properties. Due to this *trans*-effect, the imido ligand is no longer bound in a linear, but in a pronounced bent coordination with a rather long Os–N bond length of 1.73 Å. It functions as a 2e ligand with less to no back donation to Os. This overall arrangement indicates a higher tendency for nitrogen transfer and fits the experimentally observed increase in chemoselectivity aided by tertiary nitrogen ligands.

A footnote in the original Sharpless publication[13] stated that *Cinchona* alkaloid ligands which are chiral quinuclidine derivatives are capable of promoting an asymmetric reaction pathway. This observation was later taken up by Rubinstein and Svendsen who reported use of 4-chlorobenzoyl substituted dihydroquinine (DHQ) and dihydroquinidine (DHQD), two first generation Sharpless ligands (Fig. 5).[15] For oxidation of stilbene with reagent **2** at room temperature, the product consisted of a 40:60-aminoalcohol:diol mixture. This value could be significantly increased in the presence of the *Cinchona* alkaloids yielding 97:3 and 92:8 ratios in favor of the desired aminoalcohols. This result is indicative of a pronounced ligand acceleration effect on the oxidation since diol formation derives mainly from the uncomplexed Os compound. However, while the DHQD-based ligand gave a high 90% enantiomeric excess for the aminoalcohol, the diastereomeric DHQ led to only a low enantiomeric excess of 50%. In view of the regular pseudo-enantiomeric performance of DHQ and DHQD,[1] this reaction outcome is surprising. More importantly, estimated binding constants for **2**/quinuclidine and **2**/PCB-DHQD were found to be significantly lower than for the corresponding OsO_4 complexes. This is not surprising taking into account the presence of a donor imido ligand that diminishes the overall electrophilicity at the Os centre in **2** and compares well with the details from Griffith crystal structure of the related dabco complex (Fig. 4).

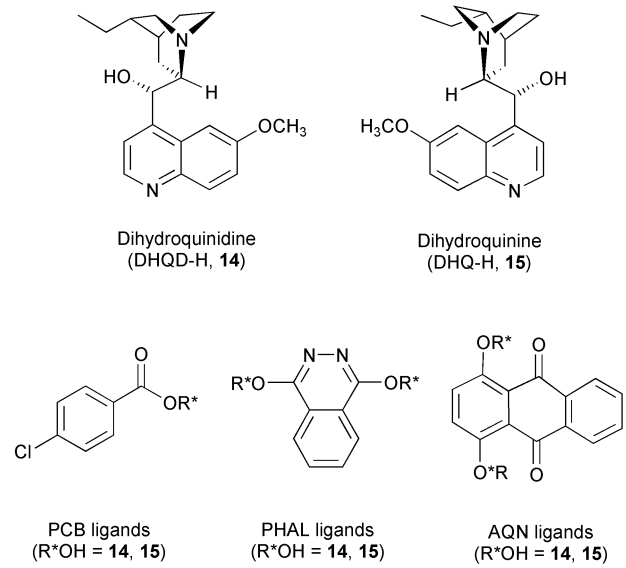


Fig. 5 Chiral *Cinchona* alkaloid ligands.

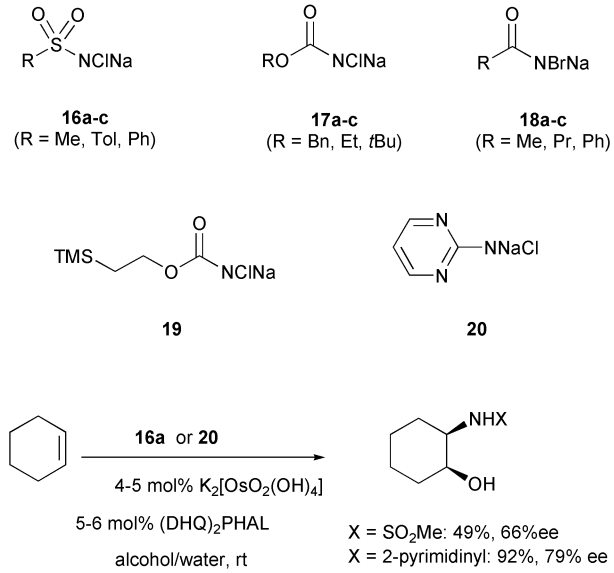
4 Aminohydroxylation: catalytic reactions

From the outset of stoichiometric aminohydroxylation reactions, three major drawbacks were identified, namely the stoichiometric use of precious osmium metal, the requirement of quaternary alkyl substituents at nitrogen and the use of strong reducing agents including hydride reagents such as $NaBH_4$ or $LiAlH_4$ to liberate the aminoalcohol. In view of the catalytic versions for homogeneous dihydroxylation employing oxo-transfer reagents such as *t*BuOOH and NMO,[1] a nitrene-based terminal oxidant was obviously desirable and chloramine-T trihydrate emerged as an ideal solution since it is commercially available, cheap and leaves no organic by-products.[16,17] Generally, the reactions were performed with 1 mol% **1** in *tert*-butanol at 60 °C. At this temperature, hydrolytic cleavage of the intermediary azaglycol osmate ester with the water from the nitrene precursor is accomplished. It was noted that in some cases the conversion could be enhanced by addition of silver salts[17] or by use of a phase transfer co-catalyst in a chloroform/water solvent mixture at room temperature.[16] *N*-Chloro salts of carbamates were introduced as an alternative nitrene precursor[18,19] leading to amino alcohol products with nitrogen substituents for more convenient deprotection. Again, application of silver or mercury salts was beneficial and increased yields to 87%.

From a mechanistic point of view, the electron-withdrawing properties of the tosylamide and the carbamate moiety enhance hydrolytic cleavage and thus enable the prerequisite catalyst turn-over to occur, but the overall catalytic performance was not

satisfying. It is noteworthy that the use of chiral terpene-based carbamates did not yield significant diastereomeric excess[18] and an asymmetric version of the catalytic protocol clearly remained in demand.

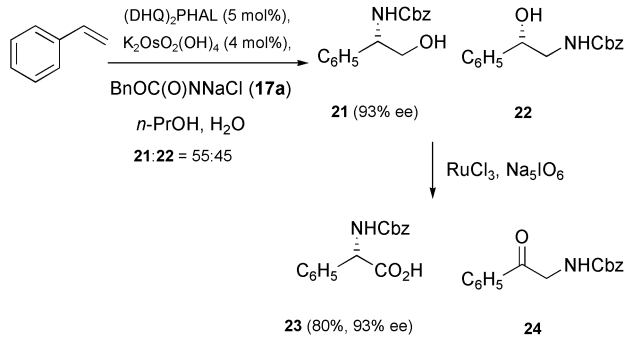
In what turned out to be the birth of the long-sought catalytic asymmetric aminohydroxylation, Sharpless and co-workers reported in 1996 that a combination of an osmium(VI) salt, chloramine-T and a chiral *Cinchona* alkaloid (Fig. 5) catalysed the oxidation of various olefins in alcohol/water or acetonitrile/water solvent mixtures.[20] At present, several different nitrene precursors compatible with the general conditions of catalytic AA have been introduced (Scheme 3).[21–23]



Scheme 3 Nitrene precursor and AA reaction of cyclohexene.

Derivatives **16–20** were employed in asymmetric reactions together with the standard *Cinchona* alkaloid ligands. Except for some special cases involving chloramine-T (**16b**) all these aminohydroxylations benefit from ligand acceleration by the *Cinchona* alkaloids. In reactions with carbamates **17a–c**, the nitrene precursors are usually generated *in situ* prior to the AA reaction. In contrast, sulfonamide and amide precursors have to be prepared in advance. The original procedures called for three equivalents of nitrene precursor, however, the development of amide-based nitrenes **18a–c** afforded protocols which work with only a slight excess of oxidant. Although the AA may be accompanied by diol formation in some cases, the aminohydroxylation pathway is generally dominating the catalysis. The reaction works best for electron-deficient olefins such as cinnamates, although it also proceeds smoothly for neutral olefins such as styrene or cyclohexene and electron-rich ones such as enol ethers. In particular, AA reaction of cyclohexene, a symmetrical (*Z*)-olefin illustrates an advantage over the AD procedure. While the latter one gives rise to an achiral *meso*-compound oxidation of this olefin leads to chiral aminoalcohol formation with acceptable enantiomeric excesses (Scheme 3). Due to the high crystallinity of the products, their enantiomeric excesses can be increased to 99% by recrystallisation.

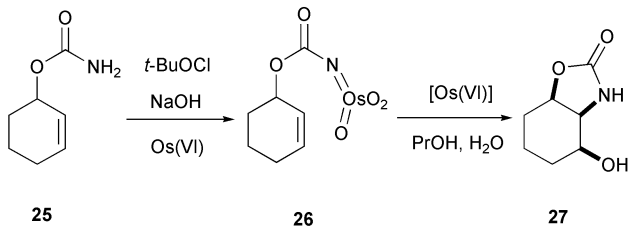
Despite all improvements, the regioselectivity problem has remained the Achilles' heel of the catalytic AA. While some solutions were introduced for special substrate or ligand classes these suffer from limited applicability.[24,25] For α,β-unsaturated carbonyl compounds, the preferred product contains a β-positioned nitrogen atom. However, only a 2:1 mixture was obtained from the original catalytic aminohydroxylation employing a silver salt additive.[16] This preference is significantly enhanced for catalytic AA in the presence of the standard PHAL ligands, especially for the amide-based nitrene precursors **18a–c**.[26] A reversal in regioselectivity was reported for the respective AQN ligands which in carbamate-based AA reaction tend to favor formation of the α-amino derivative.[27] In contrast to styrene aminohydroxylation with **2**, the regioselectivity outcome of the catalytic AA is also dominated by the ligand of choice. This feature was elegantly employed by Reddy and Sharpless who developed a two-step procedure to convert styrenes into enantiomerically enriched or pure α-aryl glycines (Scheme 4).[28] After AA reaction of the



Scheme 4 Two-step synthesis of α-aryl glycines from styrenes.

respective styrenes, the mixture of the resulting two regiosiomers **21**/**22** is submitted to further oxidation. While thereby the secondary alcohol in **22** is transferred into the ketone **24**, the terminal alcohol **21** furnishes the desired α-phenyl glycine **23**, which can be easily separated from **24** *via* acid/base extraction.

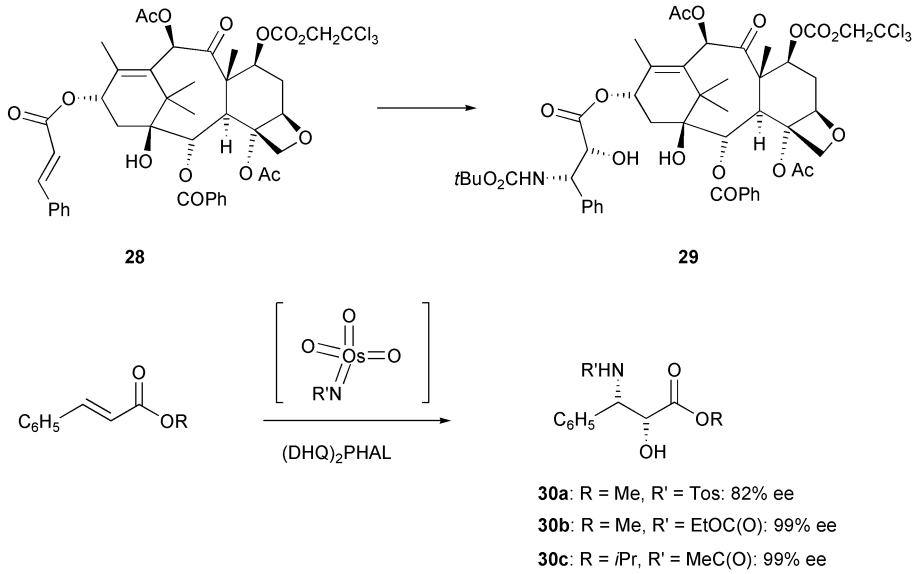
Recently, the inherent problem of regioselectivity in aminohydroxylation reactions has been tackled by an alternative approach. Donohoe has described intramolecular aminohydroxylations which rely on carbamate tethers as in **25**.[29] It is assumed to proceed *via* intermediary Os imido compounds such as **26** which provides **27** and related products under standard conditions with the expected complete chemo and stereoselectivity and in moderate to high yields (Scheme 5). Interestingly, the reaction shows only a slight



Scheme 5 Intramolecular aminohydroxylation.

increase in rate in the presence of tertiary amines. However, *Cinchona* alkaloids do not induce enantioselectivity and all attempts toward kinetic resolution on substrates such as **25** were unsuccessful. Obviously, either the olefin face distinction does not apply in this intramolecular version or, more probably, the carbamoylimido osmium intermediate releases the ligand in a step prior to olefin functionalisation.

The advancement of aminohydroxylation by the development of a catalytic protocol is probably illustrated best with the examples of TAXOL® side chain synthesis which represents a phenyl isoserine derivative. With the catalytic AA still undiscovered, Guéritte and co-workers investigated the aminohydroxylation of 13-cinnamoylbaccatin III **28**.[30] In view of the milder deprotection conditions, the carbamate route was chosen. From various screening experiments with *N*-chloro-*N*-argento *tert*-butyl carbamate yields of up to 80% were obtained for stoichiometric reactions and 50% conversion was reached in catalytic processes. Both methods provide all four possible stereo and regioisomers in nearly equimolar amounts. Apparently, the bulky chiral taxane skeleton offers no efficient asymmetric induction. Yields of the catalytic reactions could be improved by dihydroquinine esters and furnished a notable diastereomeric excess of 46% in favour of the desired (2′*R*,3′*S*)-configurated stereoisomer **29** (Scheme 6). Final protecting group



Scheme 6 AA approaches to TAXOL® side chain synthesis.

manipulation gave the natural product TAXOL®. Although hampered by the low catalytic efficiency, this work represents the first detailed report on catalytic AA reaction under the influence of *Cinchona* alkaloids.

Given the general availability of Baccatin III, synthesis of the isoserine side chain as a separated molecule and final attachment to the Baccatin III core is a much more advantageous procedure. Several reports on aminohydroxylation of cinnamates have appeared that all follow the general principle outlined in Scheme 6. It should be noted that the amide variant displays a significant advantage over the sulfonamide and carbamate variants in that it employs only 1.1 equivalents of the nitrene precursor. Thereby, highly enantioselective multigram synthesis of the TAXOL® side chain **30c** on a 1.25 mol scale could be accomplished.[21,26]

In view of the importance of the resulting aminoalcohol functionality for synthesis of organic ligands and auxiliaries, introduction in total synthesis or related biological and medicinal application, an impressive body of work has already been produced. As a consequence, the Sharpless AA reaction has been extensively reviewed over recent years[21–23] and general experimental recommendations can be found in ref. 21. In the following section, special focus is made on the role of the imido complex in this reaction.

Mechanistic implications of catalytic Sharpless AA reactions

While the chemistry of isolated osmium(VIII) complexes bearing alkylimido ligands has been well investigated, surprisingly few data have become available on the nature and reactivity of the respective compounds with tosylimido or carbamoylimido ligands. These compounds remain elusive both in isolated form or as stabilised adducts with nitrogen ligands. As a consequence, a full investigation on the mechanistic pathways of the AA reaction has not yet been undertaken. For the reaction of the active trioxo imidoosmium species two mechanistic proposals on the basis of the related dihydroxylation reaction[1] have been discussed: a direct and concerted [3+2]-mechanism and a stepwise [2+2]-addition involving an intermediary four-membered osmacycle (Fig. 6).[21–23] A concerted 3+2 cycloaddition reaction would require a simultaneous transfer of both the nitrogen and the osmium group from the osmium complex onto the olefin. This irreversible oxidation step directly determines the final absolute configuration of the product. The active osmium complex responsible for the stereoselective reaction course is believed to be a *Cinchona* alkaloid ligated complex **B** which is able to distinguish the prochiral C–C double bond faces of the substrate (Scenario **C**). Although **B** exists in an

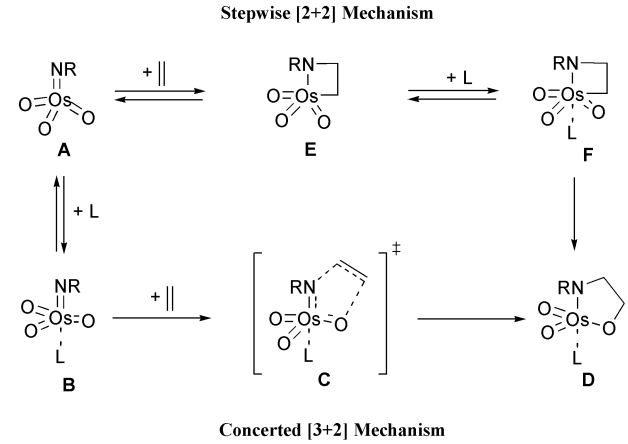
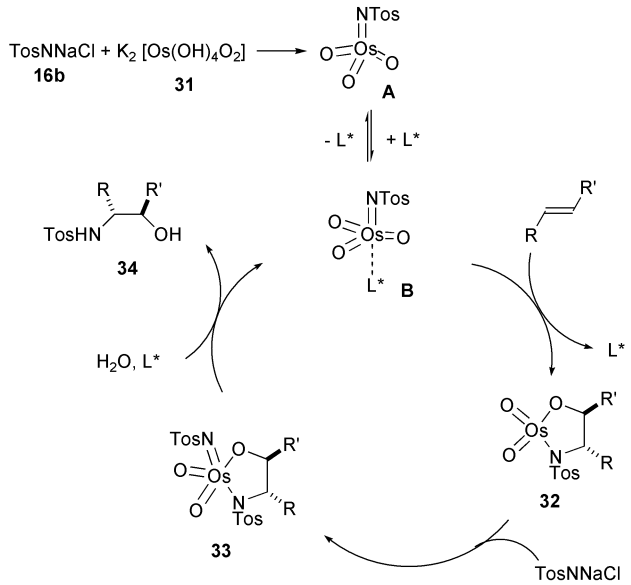


Fig. 6 Mechanistic pathways for aminohydroxylation.

equilibrium with the free ligand and uncomplexed monoimido compound **A**, it is understood to react at a higher rate than the latter. This process which is denominated *Ligand Accelerated Catalysis*[31] ensures product formation is dominated *via* the chiral pathway involving **B** and not *via* the achiral one. As an alternative pathway, the electrophilic Os center in **A** upon coordination to an olefin might undergo a 2+2 addition to form an metallacycle. This process can involve formation of an osmaazetane intermediate **E** as depicted in Fig. 6 or, alternatively, an osmaoxetane arising from involvement of an Os–O bond. In such a scenario, the reaction sequence is reversible until coordination of the chiral ligand which triggers an irreversible stereospecific rearrangement *via* **F** to yield the azaglycolate osmium ester **D**.

The experimentally observed regioselectivity has been quoted as an indication for a stepwise 2+2 pathway since it would match the electronic polarisation within the Os–N bond and the standard acrylate substrates. However, such argumentation does not provide a rationale for the change in regioselectivity with AQN ligands[27] and in addition, experimental or theoretical proof for the observed chemoselectivity in these reactions is still missing. Whatever the exact course of the heteroatom transfer from the imidoosmium compound to the olefin, the generally accepted catalytic cycle for *Cinchona* alkaloid aided AA reaction is believed to proceed *via* three key species (Scheme 7). Starting from an imido osmium catalyst **A** that is formed *in situ* from the nitrene precursor (for convenience, chloramine-T **16b**) and **31**, an Os(VI) compound, and that in the presence of the chiral *Cinchona* alkaloid adds stereoselectively to the olefin to furnish the azaglycol osmate ester

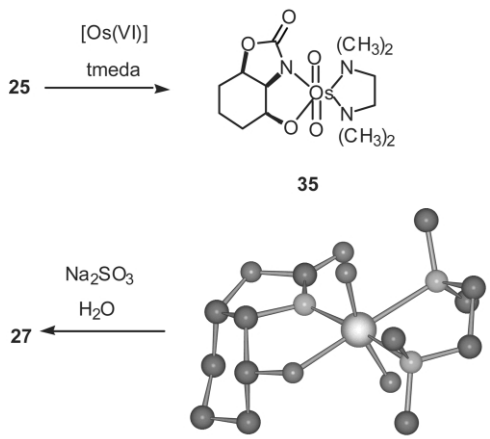


Scheme 7 General catalytic cycle for Sharpless asymmetric aminohydroxylation.

32. Reoxidation of the central osmium atom to Os(VIII) by chloramine-T gives the osmate intermediate **33** which upon ligand-aided hydrolysis releases the enantiomerically enriched aminoalcohol **34** and regenerates the catalytically active species **B**.

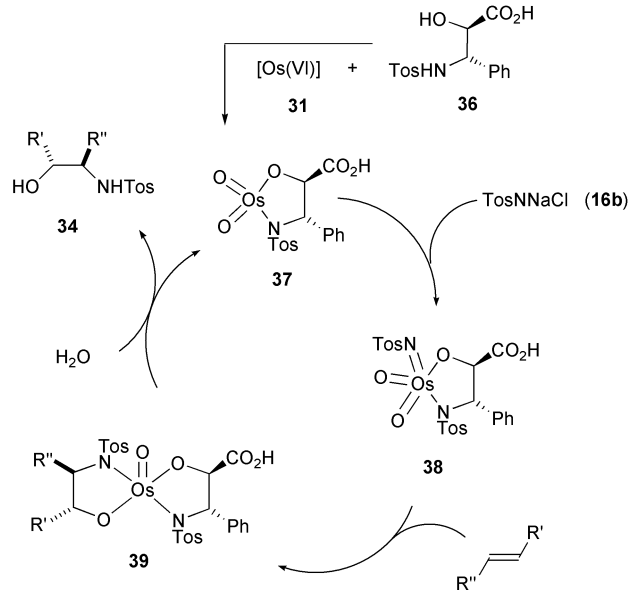
This overall process is based on several well equilibrated factors that include the beneficial acceleration by the tertiary amine ligand. Thus, unselective aminoalcohol formation is largely prevented since the complexed species shows a significantly higher reaction rate over the uncomplexed compound. Moreover, the ligand acceleration also holds true for the hydrolysis step thereby preventing a subsequent second olefin oxidation with **33**. Such a step would lead to entering the so-called secondary cycle which is ligand-independent and results in a significantly diminished enantiomeric excess. Apart from the asymmetric induction, the *Cinchona* alkaloid ligand is exercising a pronounced influence on regio and chemoselectivity in the initial step of olefin oxidation.

Few experimental data on the intermediates in this catalytic cycle have become available. For one of the intramolecular reactions described above, the azaglycolate ester intermediate originating from **25** could be trapped by addition of tmeda.[29] Reduction with sulfite releases **27** and confirms the nature of **35** as an isolated intermediate of the original catalytic circle. Adduct **35** was characterised by X-ray analysis and represents a rare example of isolated intermediates in catalytic aminohydroxylation reactions (Scheme 8).



Scheme 8 Intermediate **35** from intramolecular aminohydroxylation.†

In the original development of the catalytic AA reaction, involvement of the secondary cycle was suppressed because of its independence from the stereoinducing ligand. However, Sharpless discovered that some special substrates such as acrylates or acrylamides undergo highly selective aminohydroxylation that are unaffected by tertiary amine ligands.[32] In addition, a certain class of ligands, namely 2,3-dihydroxy carboxylic acids or 3-tosylamino, 2-hydroxy carboxylic acids such as **36** form osmium azaglycolates which are capable of catalysing AA reactions in the secondary



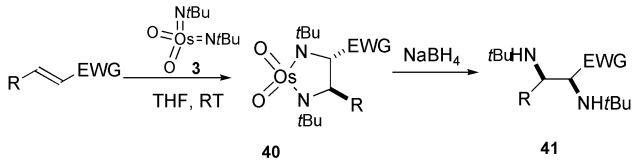
Scheme 9 Sharpless AA reaction in the secondary cycle.

cycle (Scheme 9).[33] For example, when a combination of the aminoalcohol **36** and the usual Os(VI) salt **31** was employed as chiral catalyst precursor, aminohydroxylation of styrene and methyl cinnamate was accomplished in high yield together with a moderate regioselectivity of 2:1. Enantioselectivites in the range of 24 to 59% enantiomeric excess were obtained proving the validity of this second cycle AA process. It is believed to be initiated by formation of an azaglycolate osmium(VI) compound **37** from **31** and **36**. Reoxidation to Os(VIII) by chloramine-T **16b** furnishes the active catalyst **38**. When adding to a prochiral olefin, asymmetric induction relies exclusively on the stereogenic centres of the azaglycolate backbone. The resulting bis(azaglycolate) **39** is cleaved under the influence of the free carboxylate moiety to selectively release the aminoalcohol product **34**. By this mode, the catalyst precursor **37** is regenerated for subsequent olefin oxidation.

6 Diamination: stoichiometric reactions

Already back in 1977, Sharpless reported the reaction of bis and trisimido complexes **3** and **4** with olefins. For neutral olefins diamine formation was accompanied by small amounts of aminoalcohol, but reaction with fumarates resulted in complete chemoselectivity.[6] As an additional important result, the primary reaction products were stable enough for isolation and were identified as monomeric osmaimidazolidines. In order to understand this high chemoselectivity in olefin functionalisation with **3**, a computational investigation of the reaction course was undertaken 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. First, elongation of the Os=NH moieties toward the transition state geometry is energetically preferred over the competing Os=O bond elongation. Secondly, energy contribution of π-backdonation from the imido ligands to the π*-orbital of the olefin is greatly enhanced in the case of diamination.[34]

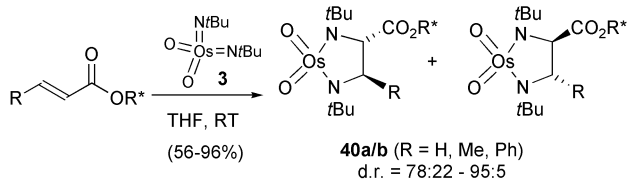
A complete survey of the chemistry behind the reaction of **3** with various olefins was undertaken recently.[7] Apparently, imido species **3** and **4** display a pronounced preference for olefin oxidation tolerating all kinds of functional groups such as aldehydes and ketones and even organometallic moieties such as ferrocene. The reaction proceeds with complete stereospecificity and in excellent yields. The chromophoric products **40** can be purified by convenient column chromatography or through crystallization. The stability of the osmaimidazolidines is noteworthy, particularly their unreactivity toward conventional oxidants such as chloramine-T, NMO and *tert*-butylhydroperoxide. Moreover, reductive liberation of the respective diamines is not feasible with sulfite or thiosulfate and strong metal hydrides are necessary to release the osmium from the diamine chelate. This overall sequence generates diamines **41** directly from olefins employing a stoichiometric amount of osmium reagent (Scheme 10). If desired, recycling of the osmium after the final reduction step is possible.



Scheme 10 Stereospecific diamination of olefins. EWG = electron-withdrawing group.

An asymmetric version of this diamination reaction appeared problematic since it was found that the standard *Cinchona* alkaloid derivatives for catalytic AD and AA reaction (Fig. 5) would not coordinate bisimido complex **3** or trisimido complex **4**.[7] This observation can be rationalised taking into account the specific electronic properties of these compounds and an electronic saturation of the Os centre through the basic lone pair at the imido nitrogen atoms. This overall scenario in **3** and **4** with formal 18e-Os centres removes all tendency for tertiary amine coordination.

Instead, an asymmetric diamination was accomplished by use of chiral enantiopure auxiliaries (Scheme 11).[35] Among various chiral



Scheme 11 Diastereoselective diamination of olefins with bisimido osmium(VIII) reagent **3**. R*OH = (−)-8-phenyl menthol.

alcohols, (−)-8-phenyl menthol performed best and led to diastereomeric ratios of up to 95:5. This sequence represents the first direct asymmetric diamination of olefins. Its success relies on the well-established ability of the terpene auxiliary to promote efficient π-stacking between the *Si*-face of the prochiral olefin thereby enhancing nitrogen transfer from the osmium reagent to the unshielded *Re*-face. A crystal structure analysis on the major product from diamination of (−)-8-phenyl menthyl cinnamate revealed the (*S*,*R*)-configuration for the newly generated stereocentres and thereby confirmed that the oxidation had taken place from the *Re*-face (Fig. 7).

While theoretical investigation suggests a concerted mechanism to be operating, the observed outcome could also arise from a stepwise reaction sequence involving an intermediary osmaazetane. The latter one could either arise from a direct [2+2]-reaction as discussed above for related aminohydroxylations (Fig. 6) or from a stepwise sequence involving an interaction between the electrophilic C3-terminus of the olefin and an imido ligand.

Electronic evaluation of imido osmium(VIII) reagents is a necessary tool in order to establish substrate–reagent reactivity correlation for these compounds. Already in one of the first reports,

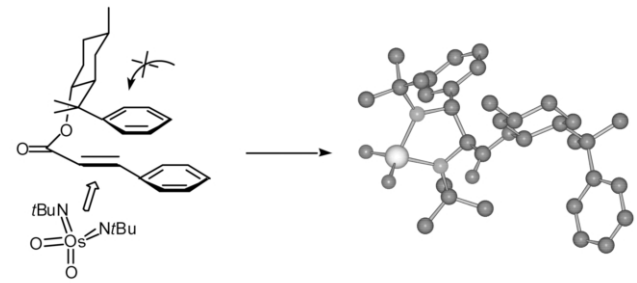


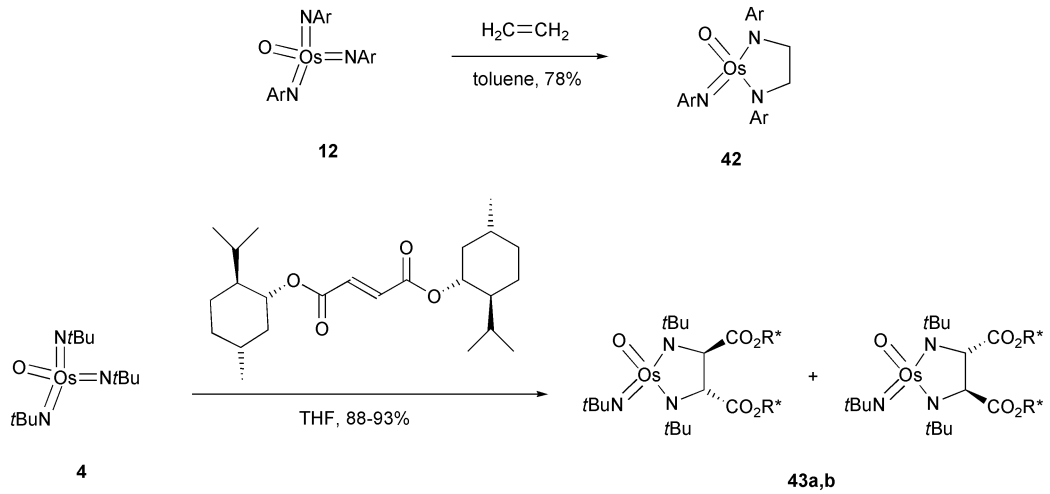
Fig. 7 Transition state for stereoselection in asymmetric diamination of (−)-8-phenyl menthyl cinnamate and solid state structure of the major diastereoisomer **40a** (R = Ph).†

Sharpless qualified isolated monoimido compounds such as **2** and **6** to be milder oxidants than the parent osmium tetroxide **1**.[11] A more detailed investigation employing Hammett correlations has led to a conclusive picture for oxidation of cinnamic esters with compounds **1–4**. While **1** as a 16e oxidant must display a pronounced electrophilic character, reactions of compound **3** reveal a negligible electronic influence for cinnamate oxidation (ρ = 0.05).[36] Moreover, no rate difference in diamination of methyl cinnamate and dimethyl fumarate with **3** was observed indicating that one EWG is sufficient in order to achieve maximium rate.[7] In contrast, trisimido compound **4** displays an electronic influence for cinnamate diamination and the observed ρ-value of 0.28 suggests a rather nucleophilic nature for this oxidant.

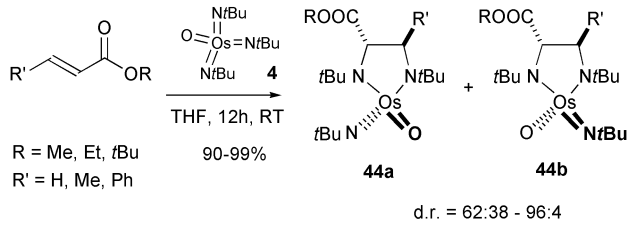
Within this context, one should notice the relative change of preferred substrate geometry in going from **1** to **4**. While performance of **1** is most efficient in the oxidation of (*Z*)-configurated neutral or electron-rich olefins, imido compounds such as **2** with their reduced electrophilicity give best results with terminal or (*E*)-substituted neutral olefins. In contrast, the electronically saturated bisimido complex **3** has a strong preference for (*E*)-configurated electron-poor olefins. The corresponding trisimido complex **4** is a neatly nucleophilic oxidant with strong sterical hindrance. As a consequence it reacts only with terminal or (*E*)-substituted olefins. This was first observed by Sharpless in the reaction of **4** with dimethylfumarate, styrene, 1- and 5-decene, respectively.[6] Later, Schrock[10] who reported complete chemoselectivity in reaction of trisimido compound **12** with ethylene, norbornene and cyclopentene to yield osmaimidazolidines such **42** (Scheme 12). Use of bis(−)-menthyl fumarate, an enantiopure olefin, gave rise to a highly diastereoselective diamination (d.r. = 95:5 for **43a**:**43b**).[7,35] Importantly, the related bisimido reagent **3** gives a significantly lower de of 62%.

When the trisimido complex **4** is submitted to reaction with unsymmetrical esters such as methyl cinnamate, clean formation of two new compounds is observed. These were identified as a pair of diastereomeric *chiral-at-metal* osmaimidazolidines (Scheme 13).[37] Diastereomeric ratios in the range of 3:2 were detected for cinnamates and crotonates, and separation of the two diastereomers could be accomplished by conventional column chromatography. The relative [(2*R*,4*R*,5*S*)/(2*S*,4*S*,5*R*)] configuration of the major diastereomer **44a** was established by X-ray crystallography.

In vast contrast, diastereomeric ratios for osmaimidazolidines from the methyl and *tert*-butyl esters of acrylic and methacrylic acid were significantly higher and in some cases only one diastereomer was observed. Apparently, steric bulk in the 3-position has a deteriorating effect on the diastereomeric ratio, while resulting advantageous when placed in the ester group. 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 to 30 °C. Moreover, NMR experiments with isolated diastereomers in toluene-d_8 proved that there is no change in diastereomeric ratio over a temperature range of −80 to 90 °C and the same experiments led to no detectable epimerisation for both isolated diastereoisomers. These results prove the configurational stability of *chiral-*



Scheme 12 Diamination of symmetrical olefins with trisimidoosmium reagents **4** and **12**. R*OH = (−)-menthol.



Scheme 13 Stereogenic Os centres from diamination of unsymmetrical, electron-deficient olefins with trisimido reagent **4**.

at-metal osmaimidazolidines. Thus, diamination of unsymmetrical olefins with osmium reagent **4** represents a conceptually novel approach in that it concomitantly creates stable and isolable products with both stereogenic carbon and osmium centres within a single reaction step of olefin functionalisation. For future investigation on mechanistic details regarding oxidative diamination, the configurational stability of the resulting central Os chirality may serve as an interesting stereochemical probe.[37]

Although a theoretical study of defined reaction courses for elaboration of imidoosmium(VIII) catalysed diaminations has been undertaken,[34] the development of such an olefin functionalisation remains elusive. To date, all available experimental data suggests that osmaimidazolidines, the primary oxidation products from such a pathway, are too stable toward hydrolysis, aminolysis and reoxidation and thus prevent elaboration of a catalytic cycle. Alternative concepts in Os chemistry have thus to be developed in order to realise new reactivity in this field.

7 Conclusion

To summarise, while the catalytic AA reaction has already reached a remarkable level of synthetic applicability over the past few years, the chemistry of related bis and trisimido complexes of osmium(VIII) is merely in its infancy. Nevertheless, further mechanistic investigation in order to clarify the exact course of heteroatom transfer from Os imido reagents to olefins is required and within this task the detection and characterisation of non-stabilised monoimido osmium(VIII) compounds is of major interest. Regarding stoichiometric reactions, bis and trisimido osmium complexes represent defined reagents that offer a suitable approach to stereochemically defined diamines. Further work to gain complete understanding of their reactivity is necessary and will be of utmost importance for the development of Os(VIII)-catalysed diamination reactions.

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