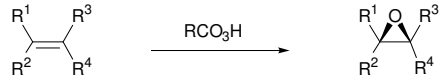
# *Part 2: Investigation into a Novel Molybdenum Oxo Imido Epoxidation Catalyst*

# *Chapter 1: Introduction*

## 1.1 Epoxides

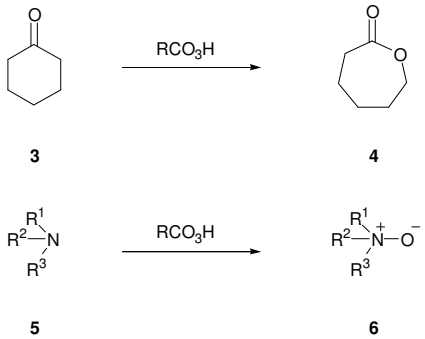
Epoxides are found in natural products and can be used as synthetically useful compounds to introduce stereochemistry. It is a three membered cyclic ether which is highly strained and is susceptible to nucleophilic attack. A variety of methods have been developed to produce epoxides. A traditional method is to react an alkene **1** with a peroxy acid such as *meta*-chloroperoxybenzoic acid (mCPBA) (Scheme 1).[1]




**1** **2**

**Scheme 1**. General preparation of an epoxide.

The reaction can be performed in the presence of alkyl, aryl, hydroxyl, esters and other functional groups. However the peroxy acid can also react with some functional groups, ketones **3** or aldehydes, to form an ester **4** by insertion of an oxygen atom next to the carbonyl. This type of reaction is known as a Baeyer-Villiger reaction.[1] Generally the R group which migrates is the more substituted group i.e. the most stable to positive charge. In addition tertiary amines **5** can react with peroxy acids to form N-oxides **6**.



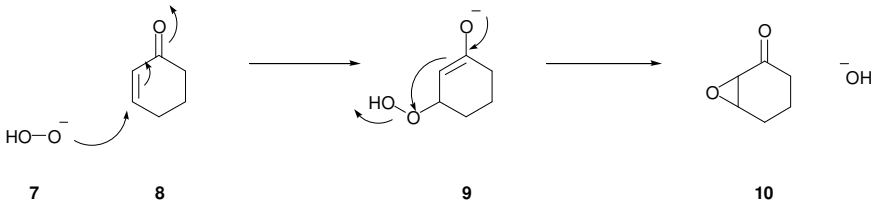

**3** **4**

**5** **6**

**Scheme 2**. Baeyer-Villiger reaction and N-oxide formation.

The reaction of an alkene with a peroxy acid is concerted and therefore the stereochemistry of the alkene is retained i.e. stereospecific. Peroxy acids do not react with alkenes when an electron withdrawing group is present indicating it is an electrophilic reagent.

Michael acceptors such as enone **8** can be epoxidised by a hydroperoxide anion **7** to form epoxy ketones **10** (Scheme 3).[2] The reaction is not concerted and involves the conjugate addition of a hydroperoxide anion **7**. The intermediate enolate **9** attacks the peroxide losing the hydroxide anion to form the epoxide **10**.

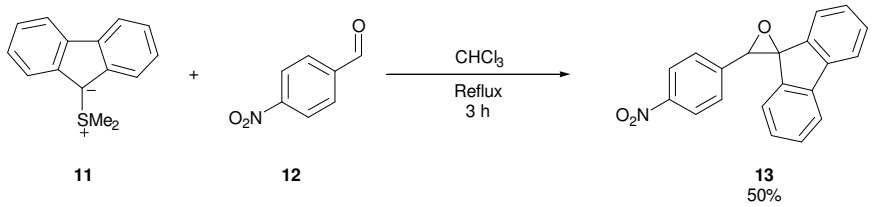



**Scheme 3**. Nucleophilic epoxidation

A variety of other methods to synthesise epoxides have been developed and several of these methods and their asymmetric developments will be discussed below.

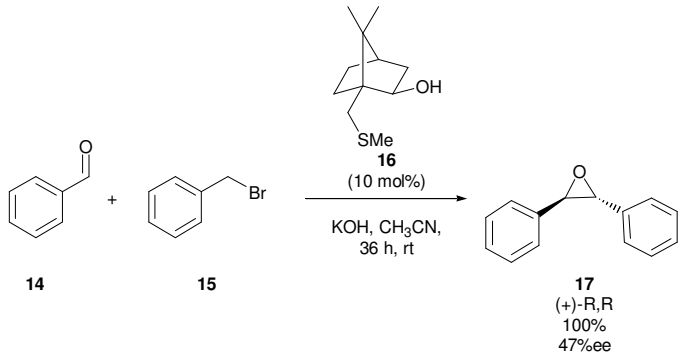
## 1.2 Sulfur ylide epoxidation

In 1958 Johnson reported the first epoxidation of an aldehyde using a sulfur ylide (Scheme 4).[3] This involved the reaction of 9-dimethylsulfonium fluorenylide **11** with *p*-nitrobenzaldehydes **12** and produced the benzafluorene oxide **13** in 50% yield. In the early 1960s Corey also investigated the reaction of sulfur ylides and further developed this area of chemistry.[4]



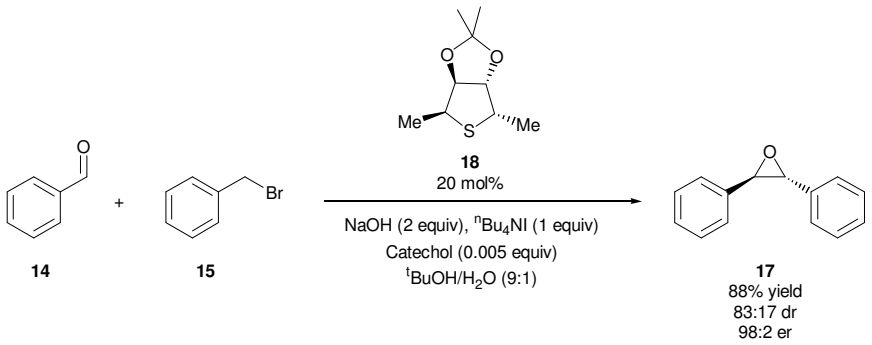

**Scheme 4**. First reported epoxidation using sulfur ylides

In 1987, Furukawa reported the first catalytic sulfur ylide epoxidation and two years later reported the first example of an enantioselective reaction using sulfur ylides (Scheme 5).[5] The reaction involved alkylation of catalytic chiral sulfide **16** with a benzyl bromide **15** to form the sulfonium salt. The ylide was formed by *in-situ* deprotonation of the sulfonium salt. Reaction of the ylide with benzaldehyde **14** gave the epoxide **17** and regenerated the sulfide.



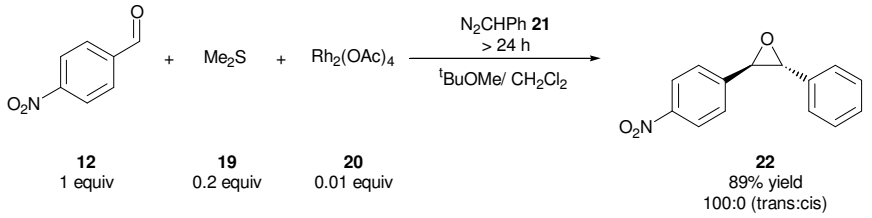

**Scheme 5**. Enantioselective catalytic sulfur ylide mediated epoxidation.

A number of research groups have developed this field of chemistry and have investigated a variety of conditions. One of the most promising systems was developed by Metzner (Scheme 6).[6] This involved a catalytic loading of 20 mol% of sulfide **18** and gave an 88% yield of **17**. The dr of the reaction was 83:17 and produced an ee of 96%.



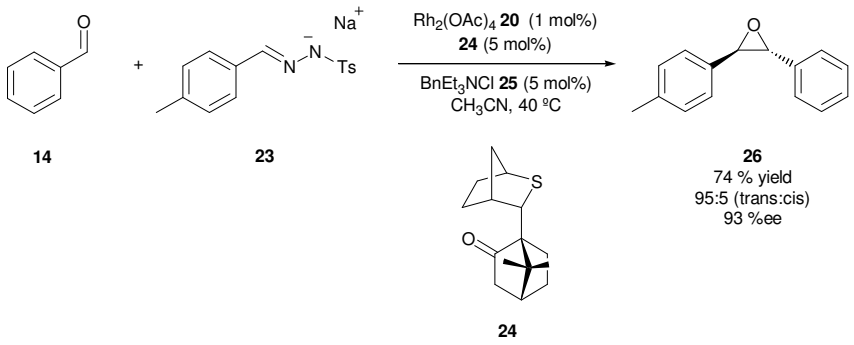

**Scheme 6**. Metzner conditions for enantioselective catalytic sulfur ylide epoxidation

In addition sulfur ylides have also been generated by reaction of dimethyl sulfide **19** with a carbene. This method was first reported by Aggarwal in 1994 and involved the generation of a carbene from decomposition of a diazo compound **21** using a metal such as $Rh_2(OAc)_4$ **20** (Scheme 7).[7] The reaction no longer required base and therefore base sensitive aldehydes could be used. In addition less reactive sulfides and aldehydes could also be used. Further developments have led to *in situ* generation of diazo compounds to avoid the hazards associated with working with diazo compounds.[8]




**Scheme 7**. First catalytic cycle using a diazo compound to form sulfur ylide

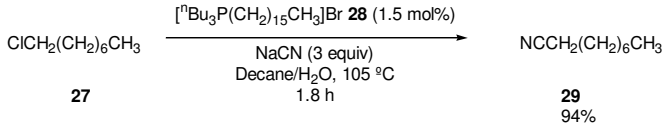
The N-tosylhydrazone salt **23** method for the *in situ* generation of the diazo compound has been investigated as an enantioselective reaction.[9] The reaction used catalytic amounts of chiral sulfide **24**, $Rh_2(OAc)_4$ **20** and the phase transfer catalyst $BnEt_3NCl$ **25** (Scheme 8). This produced a 75% yield of *p*-methylstilbene oxide **26** with a dr of 95:5 (*trans*:*cis*) and an enantiomeric excess of 95%.




**Scheme 8**. Enantioselective epoxidation reaction using catalytic chiral sulfide and *in situ* formation of diazo compound

## 1.3 Phase transfer catalysed epoxidation

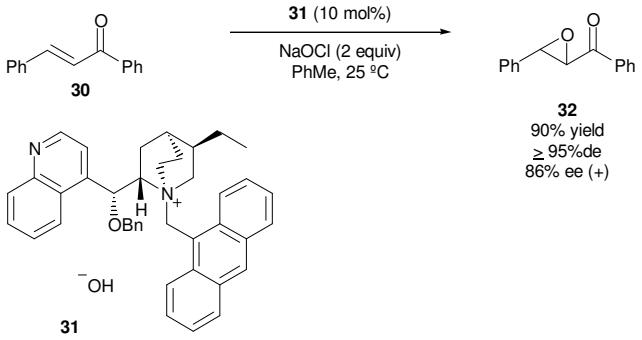
The term phase transfer catalysis was introduced in 1971 by Starks to explain the role of tetra-alkylammonium or phosphonium salts in the reaction of 1-chlorooctane **27** with sodium cyanide to give 1-cyanooctane **29** (Scheme 9).[10] When the ammonium salt or phosphonium salt was not present no reaction was observed. Phase transfer catalysis has been investigated extensively and a variety of reactions can be performed and these include alkylation, aldol, Horner-Wadsworth-Emmons, cyclopropanation and epoxidation to name a few.




**Scheme 9**. Starks phase transfer catalysis reaction

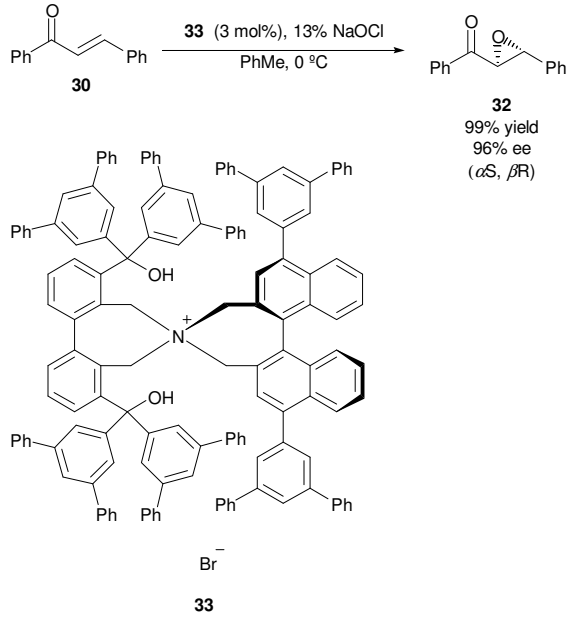
Efficient methods to asymmetrically epoxidise electron-deficient alkenes such as α,β-unsaturated ketones have been developed using asymmetric phase transfer catalysts.[11] In 1998 Lygo reported that epoxidation of α,β-unsaturated ketones **30** could be achieved in high yields with relatively high ee's (69-87%

ee) using an N-anthracenylmethylcinchodinium salt **31** (Scheme 10).[12] This was a large increase in enantiomeric excess as previously only a 55% ee had been achieved using phase transfer catalysts.




**Scheme 10**. Lygo N-anthracenylmethylcinchodinium salt for epoxidation

A new type of phase transfer catalyst for epoxidation of α,β-unsaturated ketones has been developed by Marouka since the cinchona derived phase transfer catalysts (Scheme 11). These new catalysts **33** produced a higher yield of 99% and an enantiomeric excess of 96%.

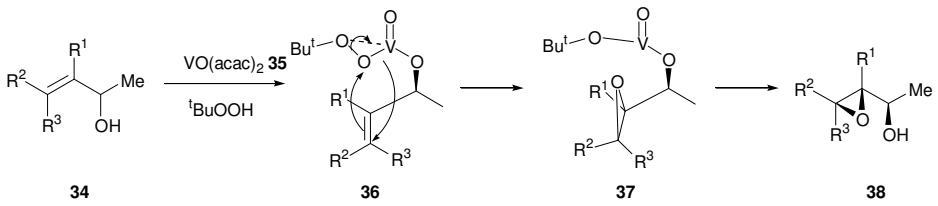



**Scheme 11**. Marouka phase transfer catalyst system for epoxidation

## 1.4 Metal catalysed epoxidation

In 1965 Brill and Indictor investigated the potential of *tert*-butylhydroperoxide (TBHP) as an epoxidising reagent.[13] It was found that small quantities of metal acetonates such as Cr (III), $MoO_2$ (II), VO(I) and V(III) produced a significant increase in epoxide yield. In addition the reaction was observed to be stereospecific as pure *trans*-alkenes gave pure *trans*-epoxides.

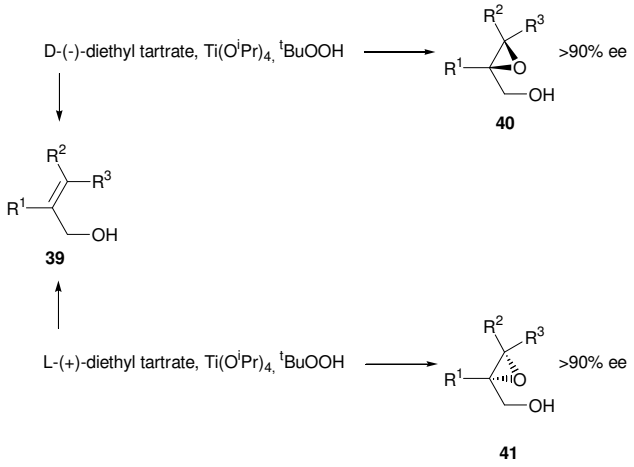
In the particular case of $VO(acac)_2$ **35**, it was found to be a very efficient catalyst for the epoxidation of allylic alcohols **34** when TBHP was used as the oxidant. The mechanism is generally reported as occurring *via* a cyclic transition state **36** (Scheme 12). The epoxide occurs on the same side as the alcohol to give *cis*-product **38** which occurs due to site directed epoxidation by coordination of the alcohol to the metal centre.




**Scheme 12**. Mechanism of $VO(acac)_2$ catalysed allylic alcohol epoxidation.

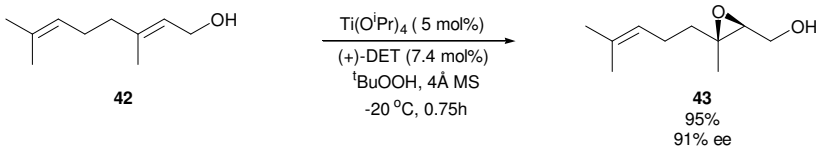
Sharpless reported the first practical method for asymmetric epoxidation of allylic alcohols in 1980.[14] The reaction involved the reaction of titanium tetra-isopropoxide in stoichiometric to catalytic quantities, with tert-butylhydroperoxide and (+)- or (-)- diethyl tartrate. Within several years, developments in this chemistry had led to the reaction requiring only catalytic quantities of titanium and tartrate for the epoxidation of a broad range of allylic alcohols.[15] The Sharpless asymmetric epoxidation has been extensively used in

academia and industry due to its predictable results. The reaction of primary allylic alcohols **39** gives complete conversion to the asymmetric epoxide **40** or **41**. The epoxide formed is dependent on which enantiomer of the tartrate is used and is predicted using the mnemonic below (Scheme 13).




**Scheme 13**. Facial selectivity of Sharpless asymmetric epoxidation using Diethyl tartrate.[14]

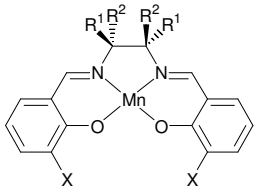
In addition, the Sharpless asymmetric epoxidation is highly selective for allylic alcohols, in that other double bonds in the substrate are not epoxidised (Scheme 14). It can also be used to kinetically resolve racemic secondary allylic alcohols.




**Scheme 14**. A standard Sharpless epoxidation[15]

The success of the Sharpless asymmetric epoxidation of allylic alcohols led to investigations into the asymmetric epoxidation of non-functionalised alkenes. Jacobsen and Katsuki developed the asymmetric epoxidation of non-functionalised alkenes simultaneously in 1990.[16] These manganese-salen complexes were based on biological oxidation systems and produced outstanding stereoselectivity.[17] The original catalysts by Jacobsen **44** and

Katsuki **45** were very similar in design; differing only at the ortho position of the phenoxide (Figure 1).




**44** $R^1$=H, $R^2$=Ph, X=$^t$Bu (Jacobsen)
**45a** $R^1$=H, $R^2$=Ph, X=CHPhEt (Katsuki)
**45b** $R^1$=Ph, $R^2$=H, X=CHPhEt (Katsuki)

**Figure 1**. Original Jacobsen and Katsuki catalysts for epoxidation of non-functionalised alkenes

The catalyst system **46** was designed to work by side on approach to Mn-oxo ligand along the N-Mn bond (Figure 2). The bulky group at X on the phenoxide would create an unfavourable steric interaction with the most hindered side of the alkene. Thus the smallest group on the alkene would be closest to the bulky substituent at X. In addition the phenyl groups on the salen backbone would only allow one approach easily.

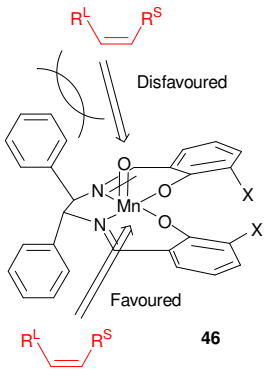
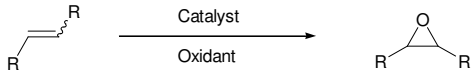
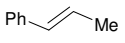
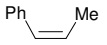
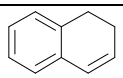



**Figure 2.** Model to explain enantioselectivity

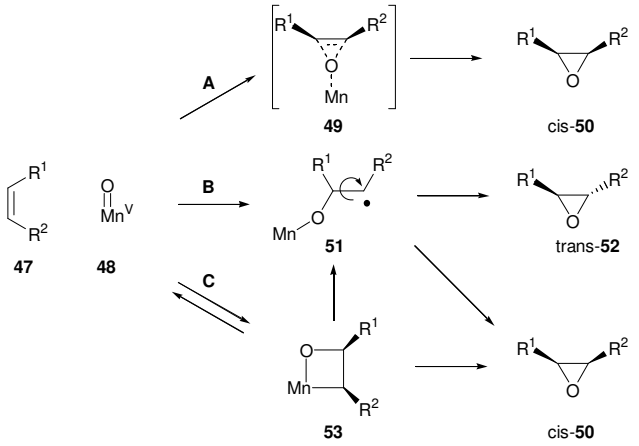
Initially the Jacobsen catalyst **44** was superior for *cis*-alkenes producing better selectivities than the Katsuki catalyst **45** (Table 1, Entry 4 & 7). Interestingly under Katsuki epoxidation conditions using catalyst **45a**, gave *cis*- and *trans*-epoxide of *cis*-$\beta$-methylstyrene (Entry 5 & 6). This result occurs probably due to the mechanism of oxygen transfer.

**Table 1**. Comparison of early Jacobsen and Katsuki catalysts of non-functionalised alkenes



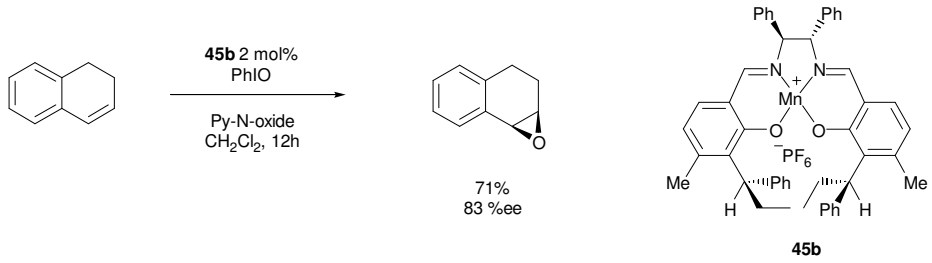

| Entry | Substrate | Catalyst | Oxidant | Yield | %ee | Config |
|---|---|---|---|---|---|---|
| 1 |  | **44** | Iodosyl mesitylene | 63 | 20 | 1S,2S |
| 2 | | **45a** | PhIO | 28 | 21 | 1S,2S |
| 3 | | **45b** | PhIO | 12 | 50 | 1R,2R |
| 4 |  | **44** | Iodosyl mesitylene | 73 | 84 | 1R,2S |
| 5 | | **45a** | PhIO | 26 | 44 | 1R, 2S |
| 6 | | | | 17 | 47 | 1S,2S |
| 7 |  | **44** | Iodosyl mesitylene | 72 | 78 | 1R,2S |
| 8 | | **45a** | PhIO | 93 | 49 | 1R,2S |

The mechanism for the Jacobsen-Katsuki epoxidation has been debated in the literature with the potential for three possible mechanisms (Scheme 15).[18] Alkyl substituted alkenes appear to preferentially undergo mechanism **A**, were formation of the epoxide is concerted as charge cannot be easily stabilised i.e. *cis*-alkene **47** produces *cis*-epoxide **50**. However for conjugated alkenes mechanism **B** can occur, where rotation about the C-C single bond **51** leads to both the *cis*-**50** and *trans*-**52** epoxides. This explains why the *trans*- and *cis*-epoxide are obtained for *cis*-$\beta$-methylstyrene (Table 1, Entry 5 & 6) as the benzene radical formed would be stable long enough for rotation to occur. Several authors have suggested mechanism **C** for the epoxidation of alkenes conjugated to aryl, alkenyl or alkynyl groups. The general consensus appears to be the side on approach of the alkene to the metal-oxo complex from the Jacobsen-Katsuki reaction, and this is followed by a stepwise C-O bond formation. The level of asymmetric induction in the [Mn(salen)]-catalysed epoxidation is dependent on the degree of C-O bond formation during the transition state.



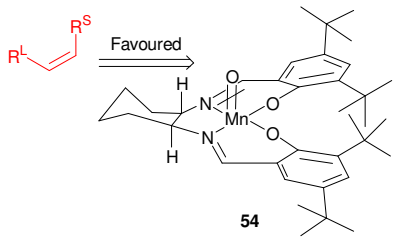

**Scheme 15**. Three possible mechanisms for oxygen transfer in Jacobsen-Katsuki reaction.

Introduction of donor ligands, such as pyridine-N-oxide, to the Katsuki catalyst increased the yield and selectivities to the same level as the Jacobsen catalyst (Scheme 16).[19]




**Scheme 16.** An early example of a Katsuki epoxidation

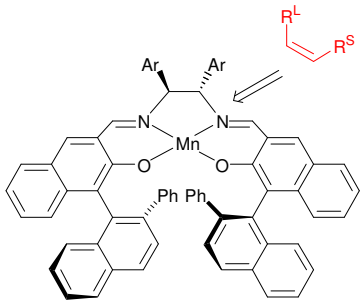
Jacobsen further modified his catalyst to increase the selectivity. This altered the approach of the alkene from the side on approach where the phenyl groups directed the alkene, to the top on approach for **54** (Figure 3). The alkene now approached the oxo group over the cyclohexyl salen backbone. The steric *tert*-butyl groups at *ortho* and *para* position on the phenoxide prevented approach from the other 3 sides. The unfavourable interaction with the axial proton on the salen backbone means that the most hindered substituent is forced to approach from the opposite side. The epoxidation of *cis*-$\beta$-methylstyrene using this new catalyst gave an 84% yield and a 92% ee.[20]




**54**

**Figure 3**. Modified Jacobsen catalyst model for enantioselectivity.

Katsuki also modified his catalyst but retained the original method for enantioselectivity of using side-on approach of the alkene along the N-Mn bond (Figure 4).[21] The new catalyst **55** used electronic repulsion between the salen benzene ring and the unsaturated alkene substituent to orientate the unsaturated alkene substituent away from the salen benzene ring.



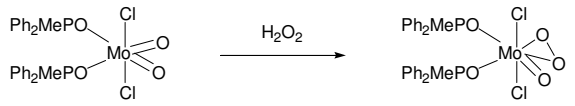

**55**
Ar=3,5-$Me_2C_6H_3$

**Figure 4**. Modified Katsuki catalyst

Jacobsen-Katsuki catalysts have been found to asymmetrically epoxidise *cis*-, tri- and tetra-substituted alkenes.[22] Although the Jacobsen-Katsuki reaction was first published in 1990, there is limited use in synthesis at the moment. Sharpless epoxidation is still favoured for asymmetric epoxidations due to the simple and often predictable results.

## 1.5 Molybdenum epoxidation catalysts

Molybdenum oxo complexes have been investigated as epoxidation catalysts of alkenes in the presence of an oxidant since 1965.[13] A variety of achiral and chiral molybdenum complexes have been investigated. The choice of oxidant is dependent on the stability of the molybdenum complex as hydrogen peroxide degrades to water which may degrade the complex. Although hydrogen peroxide is more environmentally friendly, *tert*-butyl hydroperoxide is generally preferred in industry as an oxidant due to its relative stability and solubility in organic solvents.

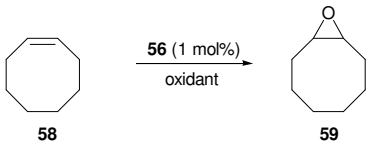



**56** **57**

**Scheme 17**. Preparation of a peroxo molybdenum complex

One of the most common features of molybdenum complexes which catalyse epoxidations is the dioxo ligand which can react with an oxidant to produce a peroxo ligand (Scheme 17).[23] Two oxidants, $^{t}$BuOOH and $H_2O_2$, were reacted with the molybdenum complex **56** to epoxidise *cis*-cyclooctene **58** and the results are shown below (Table 2). The molybdenum catalyst was more active using $^{t}$BuOOH as an oxidant, compared to $H_2O_2$, as the reaction was complete within 6 h (Entry 1). The reaction with $H_2O_2$ only yielded 35% after 24 h at 55 °C (Entry 2) and increasing the temperature actually reduced the yield (Entry 3). In addition, the reactions were clean and only the epoxide product was observed. The observed difference in yield for the two oxidants may be due to decomposition of the molybdenum complex in the presence of $H_2O_2$.

**Table 2**. Epoxidation of *cis*-cyclooctene using $MoO_2Cl_2(OPMePh_2)_2$ **56** as catalyst




| Entry | Time (h) | Oxidant | Temp (°C) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | 6 | $^t$BuOOH | 55 | 100 |
| 2 | 24 | $H_2O_2$ | 55 | 35 |
| 3 | 24 | $H_2O_2$ | 90 | 20 |

[a] GCMS quantitative

A variety of different achiral complexes of molybdenum have been used to epoxidise cyclooctene; a few are shown below (Figure 5). These ligands vary from cyclopentadienyl **60**,[24] bipyridine **61**,[25,26] bisimine **62**[27] and salen type ligands **64**.[28]

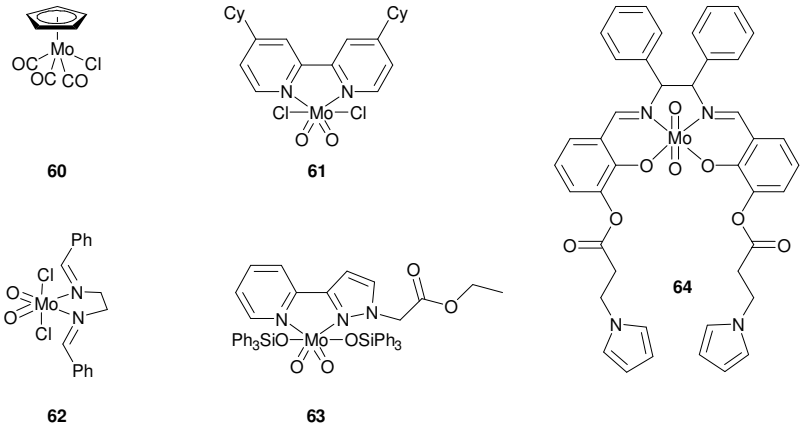
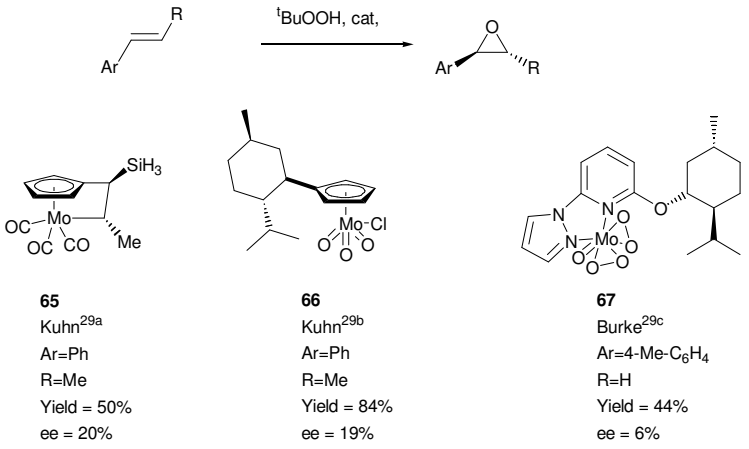



**Figure 5**. Achiral molybdenum complexes tested as epoxidation catalysts

In addition a number of chiral molybdenum complexes have been prepared in an attempt to produce an effective asymmetric epoxidation catalyst for non-functionalised alkenes. A chiral ansa-bridged cyclopentadienyl molybdenum complex **65** was reacted with *trans*-$\beta$-methylstyrene using $^t$BuOOH as the oxidant (Scheme 18).[29]After 4 h there was a 50% conversion to the epoxide,

however the enantiomeric excess was only 20%. This was the best observed enantiomeric excess with these types of ligand.



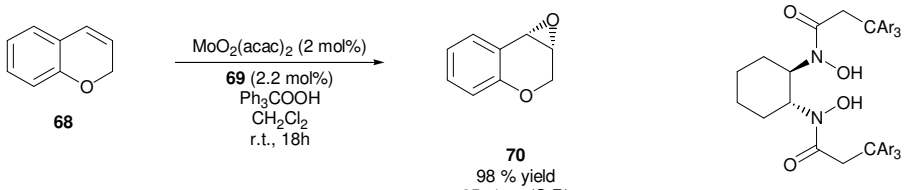

**65**
Kuhn[29a]
Ar=Ph
R=Me
Yield = 50%
ee = 20%

**66**
Kuhn[29b]
Ar=Ph
R=Me
Yield = 84%
ee = 19%

**67**
Burke[29c]
Ar=4-Me-$C_6H_4$
R=H
Yield = 44%
ee = 6%

**Scheme 18**. Attempted chiral epoxidation.

In 2006 Yamamoto used a chiral bishydroxyamic acid **69** as a ligand and $MoO_2(acac)_2$ to produce an asymmetric epoxidation reaction using an achiral oxidant.[30] The Yamamoto molybdenum epoxidation protocol produced a higher yield of 98% with a relatively similar selectivity (Scheme 19), compared to the Katsuki catalyst **55** which gave only 80% yield with 97% ee for **70**.[21b] In addition the catalyst system was stable in air and the reactions occurred at ambient temperature where as the Katsuki catalyst had to be cooled to 0 °C to obtain the higher yield. This suggested that the Yamamoto asymmetric epoxidation protocol was as selective as the Jacobsen-Katsuki catalysts and higher yielding.




**68**

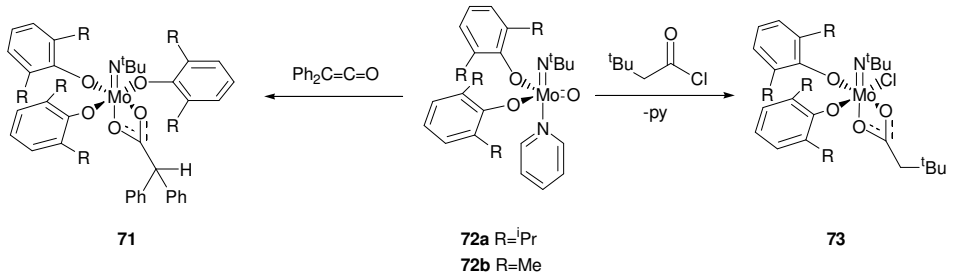
**70**
98 % yield
95 % ee (S,R)

**69**
Ar =4-isopropylphenyl

**Scheme 19**. Yammoto asymmetric epoxidation protocol

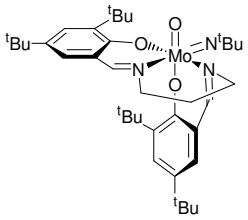
## 1.6 Proposed Research

The novel molybdenum oxo imido complex **72** was previously synthesised in the Anderson group.[31] It had been shown to react with diphenylketene to give **71** and acid chlorides to give **73** (Scheme 20).[32] Therefore due to their similarity to the molybdenum complexes above (Chapter 1.5), they were screened as epoxidation catalysts.



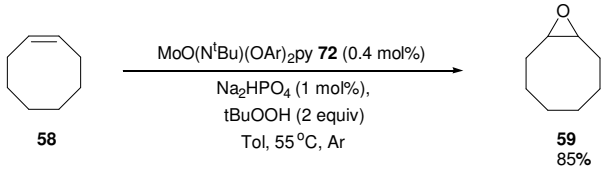

**Scheme 20**. Molybdenum oxo-imido complexes

In 2004 Sullivan reported the molybdenum oxo-imido Schiff base complex **74** would epoxidise alkenes (Figure 6).[33] Thus we wished to examine whether our novel complex **72** would epoxidise alkenes. Using the conditions reported by Sullivan, an initial investigation of *cis*-cyclooctene with $^{t}$BuOOH using **72** by Cross showed an 85% conversion to *cis*-cyclooctene oxide (Scheme 21).[32] We decided to investigate the potential of the novel molybdenum oxo imido complex **72** as an epoxidation catalyst. This would involve exploring the optimisation of the reaction conditions; the substrate scope and the potential as an enantioselective epoxidation catalyst.



**74**

**Figure 6**. Sullivan molybdenum oxo imido Schiff base complex

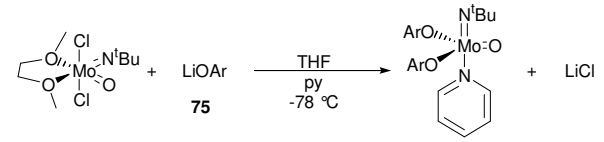



**Scheme 21**. Epoxidation of *cis*-cyclooctene using $MoO(N^tBu)(OAr)_2py$

# *Chapter 2: Results & Discussion*

## 2.1 Initial investigations

The complex **72** could be prepared using the method previously developed in our group using $MoO(N^tBu)Cl_2dme$ **74** and the lithium salt of the phenol **75**. This produced the complex **72a** in 31% (lit.[31] 48%) and **72b** in 39% (lit.[31] 45%). The complex **72** agreed with the literature data and was judged pure by $^1H$ NMR.



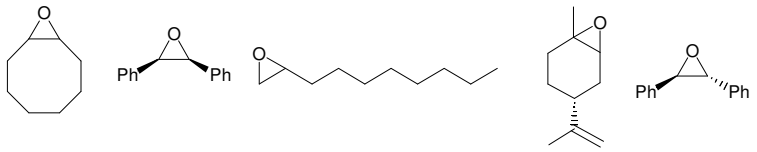

**74** **72**

LiOAr= Li(2,6-$^i$Pr$_2$C$_6$H$_3$O) **75a**
LiOAr= Li(2,6-Me$_2$C$_6$H$_3$O) **75b**

OAr= (2,6-$^i$Pr$_2$C$_6$H$_3$O) **72a**
OAr= (2,6-Me$_2$C$_6$H$_3$O) **72b**

**Scheme 22**

We decided to quickly investigate the scope of the epoxidation reaction using **72** as epoxidation catalysts. A variety of alkenes, which are regularly used in epoxidation methodology, were tested (Figure 7). The reactions were performed using the same conditions as stated in Scheme 21. These produced varying results from 33% to 86%. Thus having proved **72** would epoxidise a variety of alkenes we decided to optimise the conditions.




**58** 44% **76** 86% **77** 58% **78** 33% **79** 59%

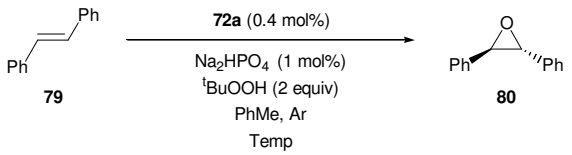
**Figure 7**

## 2.2 Optimisation

During our initial investigation into the scope of the reaction the complex **72b** was found to be less stable under the epoxidation conditions than **72a**. Therefore our optimisation reactions were investigated using the catalyst **72a** and involved reaction temperature, catalyst loading, oxidant equivalents, time and additive $Na_2HPO_4$.

The original test reaction by Cross used *cis*-cyclooctene in toluene at 55 °C with a catalyst loading of 0.4 mol%, 2 equivalents of $^tBuOOH$ and 1 mol% of $Na_2HPO_4$ (Scheme 21, pg 95).[32] We decided to investigate the optimisation using *trans*-stilbene **79** as the substrate due to the ease of isolation of *trans*-stilbene oxide **80**.

**Table 3** – Optimisation of temperature



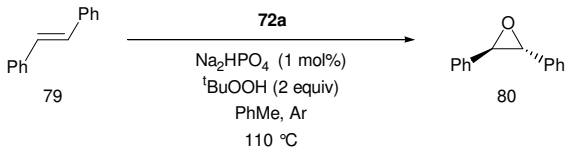

| Entry | Temp (°C) | Yield (%)[a] |
|---|---|---|
| 1 | 55 | 59 |
| 2 | 110 | 75 |
| 3 | 80 | 61 |
| 4 | 90 | 76 |

[a] Isolated yield

The first area of the reaction we decided to optimise was temperature (Table 3). At 55 °C, an isolated yield of 59% was obtained (Entry 1) and when the temperature was increased to reflux (110 °C) a yield of 75% was obtained

(Entry 2). The reaction was repeated at 90 °C and an isolated yield of 76% was obtained (Entry 4). However reducing the temperature further to 80 °C gave only a 61% yield (Entry 3). This suggested that the optimal temperature was 90 °C.

**Table 4** - Optimisation of catalyst loading




| Entry | **72a** (mol%) | Yield (%)[a] |
|---|---|---|
| 1 | 0.4 | 75 |
| 2 | 0 | 2[b] |
| 3 | 1 | 76 |
| 4 | 5 | 59 |
| 5 | 0.2 | 75 |

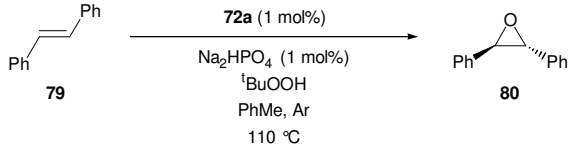
[a] Isolated yield

[b] % conversion determined by $^1$H NMR

Subsequently the catalyst loading was investigated (Table 4); the original catalyst loading used only 0.4 mol% and gave an isolated yield of 75% (Entry 1). An initial control reaction where **72a** was not present, produced only a 2% conversion determined by $^1$H NMR (Entry 2). Increasing the catalyst loading to 1 mol% produced an isolated yield of 76% of *trans*-stilbene oxide **80** (Entry 3). Further increasing the catalyst loading to 5 mol% had a detrimental effect as only a 59% yield was obtained (Entry 4). Finally reducing the catalyst loading of **72a** to 0.2 mol% (Entry 5) produced the same yield as 0.4 mol% catalyst loading. This suggested the catalyst could work at even lower catalyst loading and still generate the same yield.

The number of equivalent of oxidant $^{t}$BuOOH was investigated (Table 5). The optimisation reactions for the number of equivalents of oxidant used were performed on a smaller scale with a 1 mol% catalyst loading. The original conditions had used two equivalents of oxidant and produced a yield of 53% (Entry 1). Reducing the number of equivalents of $^{t}$BuOOH to one reduced the yield to 34% (Entry 2). Increasing the number of equivalents to three increased the yield to 65% (Entry 3). Further increases in oxidant to four equivalents or eight equivalents did not produce any further increase in yield (Entry 4 & 5). Thus three equivalents of $^{t}$BuOOH appeared to be the optimum number of equivalents.

**Table 5 –** Optimisation of number of equivalents of $^{t}$BuOOH.



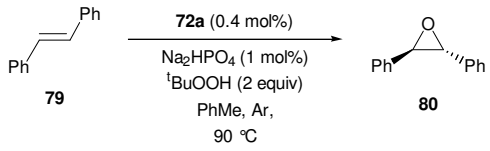

| Entry | $^{t}$BuOOH (equiv) | Yield (%)[a] |
|---|---|---|
| 1 | 2 | 53 |
| 2 | 1 | 34 |
| 3 | 3 | 65 |
| 4 | 4 | 65 |
| 5 | 8 | 64 |

[a] Isolated yield

The reaction had, until this point, been performed overnight. However we wished to investigate the rate of conversion to *trans*-stilbene oxide **80** (Table 6). When the epoxidation reaction was run at 90 °C for 20 h an isolated yield of 76% was obtained (Entry 1). Reducing the time to only 15 min showed a 38% conversion to *trans*-stilbene oxide **80** by $^{1}$H NMR (Entry 2). After one hour, a 70% conversion was obtained (Entry 3) and after two hours only an increase of

5% to 75% conversion was observed (Entry 4). This suggested that the majority of the epoxidation of *trans*-stilbene **79** occurred within the first 1-2 hours and therefore the reaction time could be significantly reduced.

**Table 6** - Optimisation of reaction time.



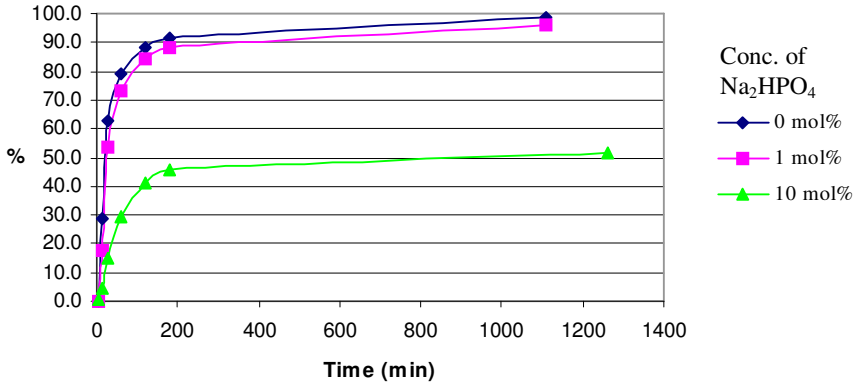

| Entry | Time (h) | Yield (%)[a] |
|---|---|---|
| 1 | 20 | 76[b] |
| 2 | 0.25 | 38 |
| 3 | 1 | 70 |
| 4 | 2 | 75 |

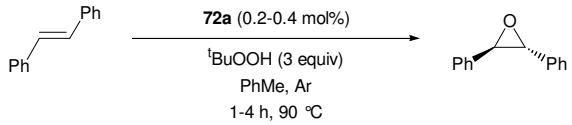
[a]% conversion determined by $^1$H NMR

[b]Isolated yield

Thus our reaction conditions had been altered to a catalyst loading of 0.2-0.4 mol%, using three equivalents of $^t$BuOOH at 90 °C for several hours. Using these conditions we decided to investigate the additive $Na_2HPO_4$. The reactions were monitored by hplc and an interesting result was observed. The removal of $Na_2HPO_4$ actually produced a faster rate of reaction compared to when 1 mol% of $Na_2HPO_4$ was present (Graph 1). The $Na_2HPO_4$ was found to have a detrimental effect on the rate of the reaction and indeed when 10 mol% of $Na_2HPO_4$ was used the reaction was hindered as only a 50% conversion was observed. A literature investigation into the use of the $Na_2HPO_4$ additive in epoxidation reactions appears to stem from a review by Sharpless, in which he comments the additive reduces the number of side products obtained.[34] As the rate had been consistently faster without $Na_2HPO_4$, the new optimized conditions no longer contained the additive (Scheme 23).

**Graph 1.** Time course of **72a** catalysed epoxidation of *trans*-stilbene with varying concentration of $Na_2HPO_4$ present.




**Scheme 23**

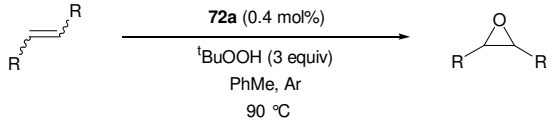
## 2.3 Epoxidation of various alkenes

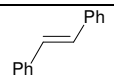
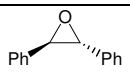
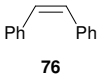
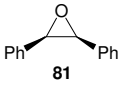
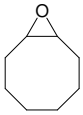
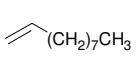
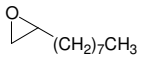
Once the optimised epoxidation reaction conditions had been obtained we examined the scope of the reaction in greater detail. Wherever possible the reactions were monitored by hplc for completion, otherwise they were followed by tlc.

The epoxidation of *trans*-stilbene **79** and *cis*-stilbene **76** produced isolated yields of 85% and 99% respectively (Table 7, Entry 1 & 2). The epoxidation of styrene **82** was followed by tlc and showed **82** had been consumed. However after silica column chromatography only a 50% isolated yield of **83** was obtained (Entry 3). This may be due to decomposition on the column. In

addition *cis*-cyclooctene **58** was epoxidised in 98% yield (Entry 4) and decene oxide **84** was obtained in 80% yield (Entry 5).

**Table 7**. Epoxidation of non-functionalised alkenes




| Entry | Alkene | Product | Yield (%)[a] |
|---|---|---|---|
| 1 |  **79** |  **80** | 85 (99[b]) |
| 2 |  **76** |  **81** | 99 (99[b]) |
| 3 |  **82** |  **83** | 50 |
| 4 |  **58** |  **59** | 98[c] |
| 5 |  **77** |  **84** | 80 |

[a] Isolated yield [b] Yield determined by hplc

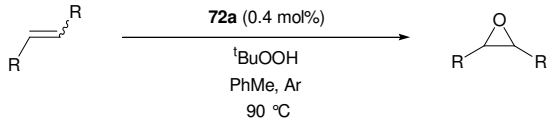
[c] Yield determined by $^1$H NMR

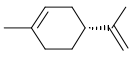
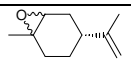
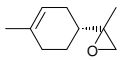
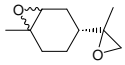
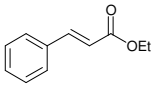
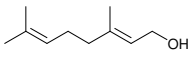
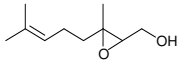
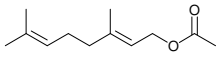
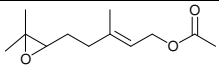
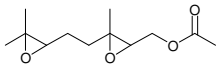
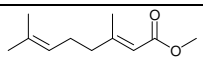
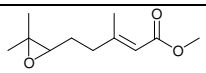
In addition we decided to investigate more functionalized alkenes in an attempt to discover more about the actual catalytic species. The epoxidation of cyclohexenol **85** gave the *cis*-epoxide of cyclohexenol **86** relative to the alcohol (Table 8, Entry 1). This suggested that the alcohol was coordinating to the metal centre and therefore encouraging epoxidation to occur on the same face. This suggests a similar mechanism to $VO(acac)_2$ **35** for allylic alcohols (Scheme 12, pg 86) The epoxidation of limonene **78** (Entry 2) with 1.2 equiv of $^t$BuOOH showed some selectivity as the major product was that from epoxidation of the most electron rich alkene to give **87** as a 1:1 mixture of

diastereomers. In addition the bis-epoxidised limonene **89** was obtained in 26% yield. None of the mono-epoxidised limonene **88** was observed. We decided to investigate an electron deficient alkene and chose ethyl-*trans*-cinnamate **90** (Entry 3). This particular alkene did not react with our epoxidation catalyst **72a**. The ethyl-*trans*-cinnamate **90** was also tested with our other complex **72b** and still no epoxidation was observed. Thus far we had discovered that **72a** would direct epoxidation of allylic alcohols *via* the pendant hydroxyl group and preferred electron rich alkenes.

An investigation into substrates containing more than one alkene group was also performed. The terpene geraniol **91** was investigated and the reaction was monitored until **91** had been consumed by tlc (Entry 4). In this particular case the allylic alcohol was epoxidised preferentially over the non-functionalised alkene to give **92** with an isolated yield of 96%. This indicated that the alcohol coordination to the metal centre influenced which alkene would be epoxidised first. The reaction was repeated with 3 equivalents of $^{t}$BuOOH and monitored by tlc until geraniol had been consumed. Epoxidation of both alkenes did occur to obtain 75% of the bis-epoxidised geraniol and only 25% of **92** determined by $^{1}$H NMR. We decided to protect the alcohol of geraniol **91** with an acetate group to give **93**, which would prevent the coordination to the metal centre. Thus when it was epoxidised, it was found that the non-functionalised alkene was preferentially epoxidised to give **94** in 72% (Entry 5), however the bis-epoxidised geraniol acetate **95** was also observed in 23%. Finally we decided to investigate methyl geranate **96** and this gave only **97,** where the most electron rich alkene was epoxidised (Entry 6).

**Table 8**. Epoxidation of functionalised alkenes

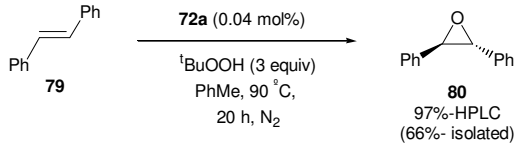



| Entry | Alkene | Product | $^{t}$BuOOH (equiv) | Yield (%)[a] |
|---|---|---|---|---|
| 1 |  **85** |  **86** | 3 | 87 |
| 2 |  **78** |  **87**<br>  **88**<br>  **89** | 1.2 | 58<br>0<br>26 |
| 3 |  **90** | - | 3 | 0 |
| 4 |  **91** |  **92** | 2 | 96 |
| 5 |  **93** |  **94**<br>  **95** | 1.2 | 72<br>23 |
| 6 |  **96** |  **97** | 2 | 99 |

[a] Isolated yield

We decided to also investigate a large scale epoxidation of *trans*-stilbene **79** and reduce the catalyst loading to only 0.04 mol% (Scheme 24). A substrate to catalyst loading of 2500 to 1. Again the reaction was monitored by hplc and showed a 97% conversion to **80**. The crude reaction was purified by crystallisation in petrol and produced a 66% yield of *trans*-stilbene oxide **80**.

The hplc conversion suggested that the catalyst loading may be reduced even further without loss of reactivity.

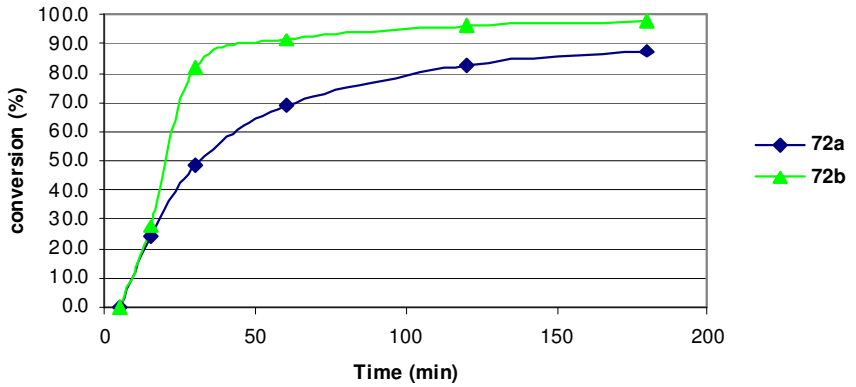



**Scheme 24**

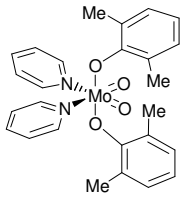
## 2.4 Rate comparison

The rate of epoxidation of *cis*-stilbene using catalysts MoO(N$^t$Bu)(2,6-$^i$Pr$_2$C$_6$H$_3$O)$_2$py **72a** and MoO(N$^t$Bu)(2,6-Me$_2$C$_6$H$_3$O)$_2$py **72b** were examined to investigate whether they had the same rate of reaction (Graph 2). When the two rates were compared the methyl derivative **72b** was faster as an 82% conversion was obtained after 30 minutes compared to 49% conversion for **72a**. On leaving the reactions to run longer both reactions gave isolated yields of 99%. This suggested the methyl derivative **72b** was initially a more active catalyst than the *iso*-propyl derivative **72a** but both catalysts would produce the same yield of epoxide.

**Graph 2**. Time course of epoxidation of *cis*-stilbene catalysed by **72a** and **72b**



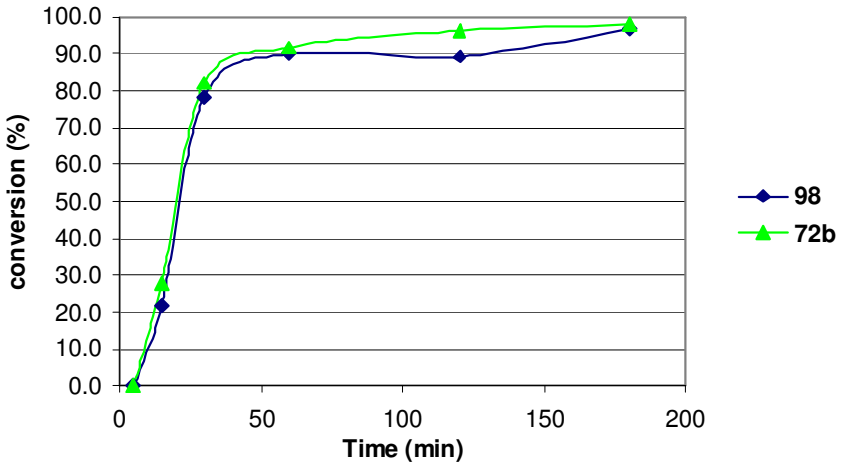
The presence of the imido group instead of an oxo group on the metal centre was investigated to discover whether any benefit was gained by the presence of an imido group. The complex $MoO_2(2,6\text{-}Me_2C_6H_3O)_2py_2$ **98** had previously been prepared by Hanna (Figure 8), but had not been tested as an epoxidation catalyst.[35] The rate of epoxidation of *cis*-stilbene using **72b** and $MoO_2(2,6\text{-}Me_2C_6H_3O)_2py_2$ **98** as catalysts was compared (Graph 3). The results obtained showed that the rate of epoxidation with either catalyst appeared to be approximately the same. This suggested the actual catalytic species was very similar as no real benefit was observed by having the imido group present. However the fact that only one oxo group was present in our complex **72** may be beneficial if a chiral complex could be developed for asymmetric epoxidation.




**98**

**Figure 8**

**Graph 3.** Time course of epoxidation of *cis*-stilbene using **72a** and **98** as catalysts



## 2.5 Investigation into a chiral molybdenum oxo imido complex

Thus far our investigation had involved the scope of the complex **72** in achiral epoxidation reactions. We decided to focus our attention into preparing a chiral molybdenum oxo imido complex in the hope of generating a chiral epoxidation reaction for non-functionalised alkenes.

The complex **72** had originally been based on the achiral Schrock olefin metathesis complexes. A literature investigation into developments of chiral Schrock olefin metathesis complexes found that in 1993 Schrock reported the preparation of BINOL, TADDOL and biphenol type molybdenum alkylidene imido complexes (Figure 12).[36] These complexes were investigated in ring opening metathesis polymerisation.

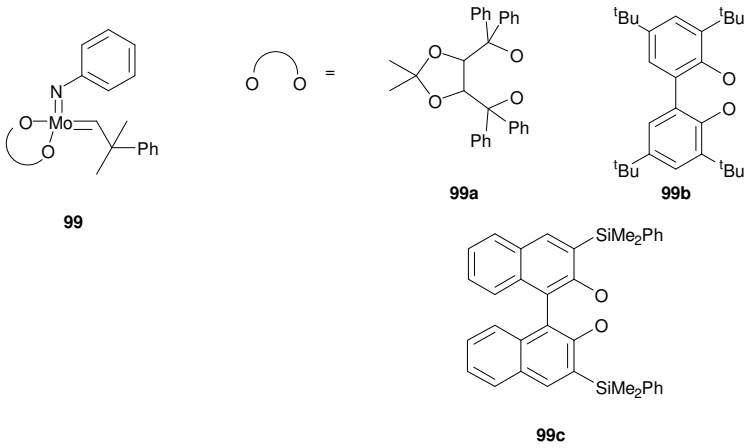
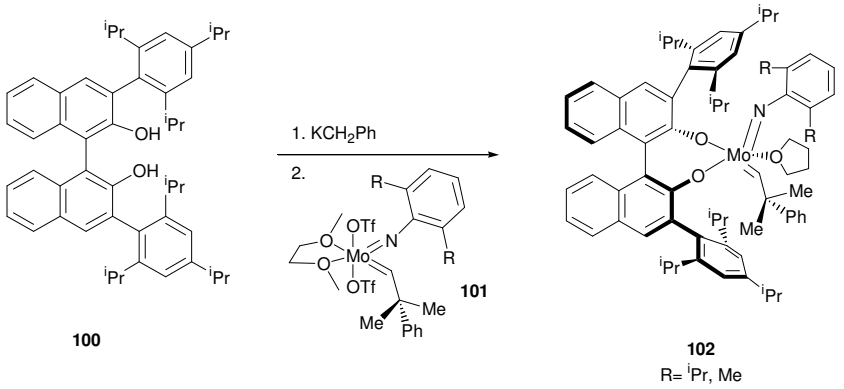



**Figure 12**

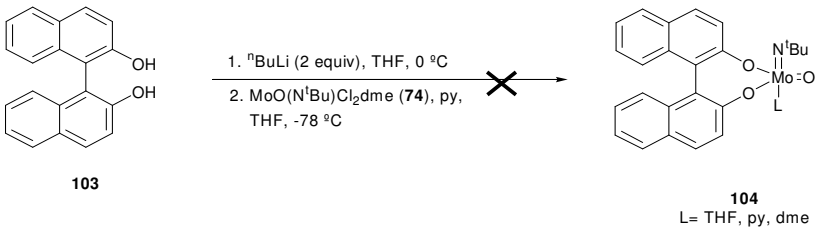
These were further investigated by Hoveyda and Schrock to produce complexes such as **102**.[37] Due to the similarities around the metal centre of our mixed oxo-imido complexes we decided to investigate the ligands BINOL **103**

and TADDOL. We hoped to isolate and characterise a chiral complex. The complex **102** was prepared by Hoveyda and Schrock by forming the potassium salt of **100** and reacting with Mo(2,6-$R_2C_6H_3N$)($CHCMe_2Ph$)$(OTf)_2$dme **101** (where R=Me or $^i$Pr). This produced **102** in 36% yield.




**Scheme 25**

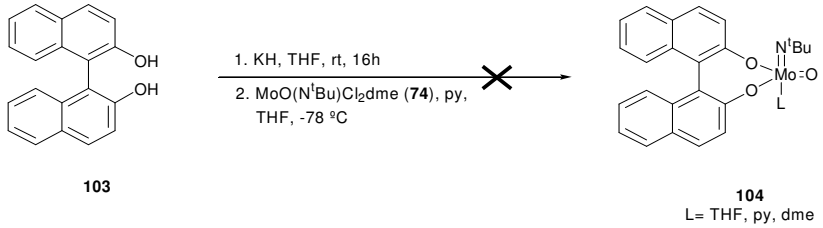
The lithium salt of **103** was prepared as the preparation of **72** had used the lithium phenoxide salt **75** (Scheme 26). Previously **72** had been isolated by crystallisation, however attempts to grow crystals from the reaction of **103** and **74** were unsuccessful. The crude reaction mixture was filtered and the precipitate and filtrate had solvent removed *in vacuo*. The analysis of the precipitate and filtrate did not show the presence of N$^t$Bu group. In addition there appeared to multiple signals for the BINOL.




**Scheme 26**

The reaction was repeated using potassium hydride as the base (Scheme 27). Again attempts to grow crystals from the reaction were unsuccessful. The

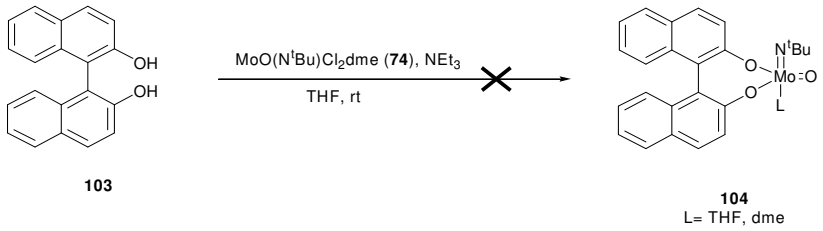
analysis of the reaction by $^1$H NMR did not show a distinct singlet for N$^t$Bu group. The BINOL residue did not contain the signal for the hydroxyl protons and therefore may still be the potassium salt of BINOL. The reaction was repeated but again complexation did not occur as **103** was observed by $^1$H NMR.




**103** **104**
L= THF, py, dme

**Scheme 27**

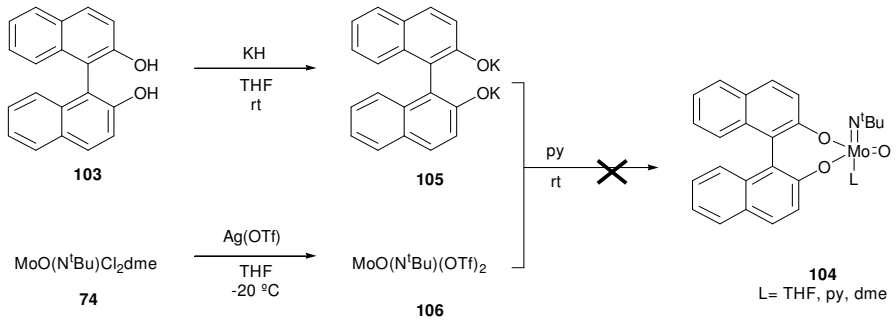
The compound **103** was reacted with MoO(N$^t$Bu)Cl$_2$dme **74** in the presence of triethylamine in the hope to form the complex **104** (Scheme 28). Unfortunately only degradation was observed.




**103** **104**
L= THF, dme

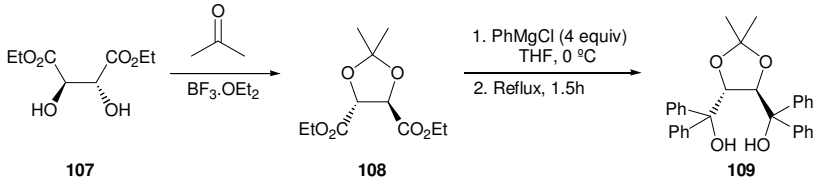
**Scheme 28**

The work by Hoveyda and Schrock had used a triflate ligand on the molybdenum complex **101** instead of chloride ligands and therefore we decided to investigate converting the chloride to triflate ligands.[37] The complex **74** was reacted with AgOTf in the hope of forming MoO(N$^t$Bu)(OTf)$_2$ **106** *in situ* (Scheme 29). The potassium salt of BINOL **105** was added to a solution of **106** and pyridine was added. Unfortunately no complexation was observed as **103** was observed by $^1$H NMR.



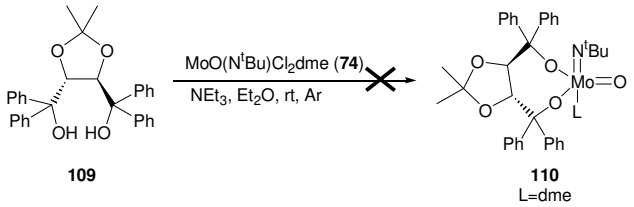

**Scheme 29**

TADDOL **109** was prepared following the method by Seebach by reacting diethyl tartrate with acetone in the presence of $BF_3.OEt_2$ followed by reaction with PhMgCl (Scheme 30).[38] This produced **109** in 39% yield over two steps and agreed with the literature data.



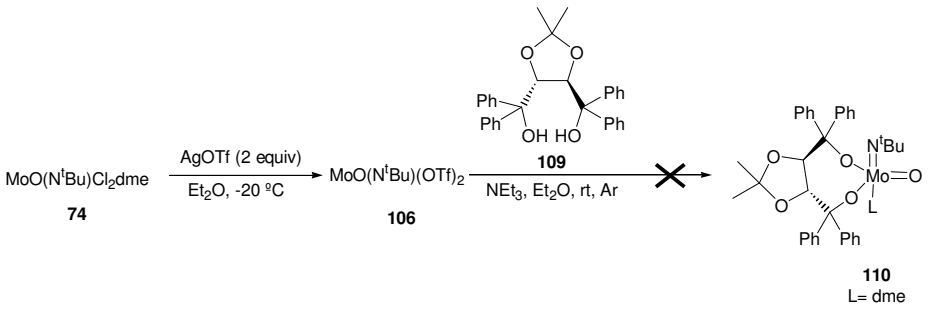

**Scheme 30**

Schrock reported TADDOL **109** had been reacted with $Mo(CHCMe_2Ph)(2,6\text{-}R_2C_6H_3N)(OTf)_2dme$ **101** in the presence of $NEt_3$ to produce $Mo(CHCMe_2Ph)(2,6\text{-}R_2C_6H_3N)$(TADDOL)L **99a** (Where R=Me, $^i$Pr and L= $NEt_3$ and dme) in 70% yield.[36] Therefore we reacted **109** with **74** under the same conditions (Scheme 31). However the crude reaction mixture showed no distinct product by $^1$H NMR. The IR of the crude reaction mixture showed hydrogen bonding as a broad signal from 3500-3200 $cm^{-1}$ was observed. This suggested the presence of the hydroxyl groups from **109** and therefore no complexation occurred.




**Scheme 31**

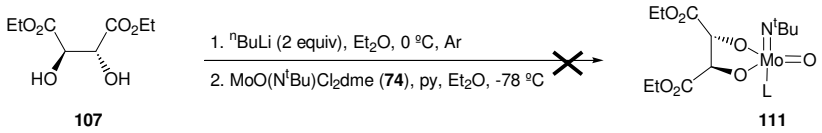
Again we attempted to convert **74** to **106** *in situ* followed by reaction with **109** in the presence of $NEt_3$ (Scheme 32). The reaction was analysed by $^1$H NMR however the N$^t$Bu group was not observed. The $^1$H NMR appeared to show signals which could correspond to **109**. Analysis by mass spectrometry was found to match data for uncomplexed **109**.




**Scheme 32**

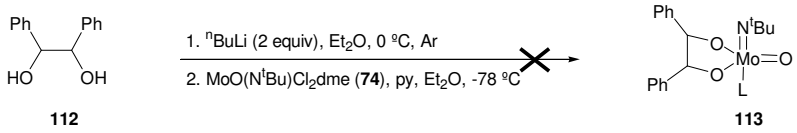
The lithium salts of diethyl tartrate **107** (Scheme 33) and hydrobenzoin **112** (Scheme 34) were also reacted with **74**, however these reactions were also unsuccessful and only degradation was observed. Unfortunately all our attempts to synthesise a chiral molybdenum oxo imido complex was unsuccessful in our hands. One possible theory is the chiral complexes were formed *in situ* but were too soluble to be isolated as crystals. This may also explain the low isolated yield of the complex **72**. Several possibilities exist to further investigate these complexes such as preparing the Schrock-Hoveyda complex **102** and followed by reaction with a carbonyl to form the chiral molybdenum oxo imido complex. In addition the crude reaction mixture of a

chiral ligand with the molybdenum oxo imido complex **74** could be tested in an asymmetric epoxidation reaction to investigate whether selectivity is observed.




**107** **111**

**Scheme 33**




**112** **113**

**Scheme 34**

# *Chapter 3: Conclusion*

## 3.1 Conclusion

The novel catalyst **72** which was developed within our group has been shown to be an effective catalyst for the epoxidation of a wide variety of alkenes. The catalyst **72** is effective for the epoxidation of electron rich alkenes. In the case of cyclohexenol (**85**), site directed epoxidation of the alkene occurred to produce only a single diastereomer. In the case of geraniol (**91**) the allylic alcohol was epoxidised preferentially over the most electron rich alkene. The epoxidation of geranyl acetate **93** gave **94** where the most electron rich alkene was epoxidised preferentially as the protection of the alcohol with an acetate group prevented coordination of the alcohol to the molybdenum centre. The catalyst **72** does not epoxidise electron deficient alkenes as demonstrated by the reaction with ethyl-*trans*-cinnamate (**90**) and methyl geranate (**96**). The $^{i}$Pr derivative of the catalyst **72a** was found to be slower than the methyl derivative **72b** but still produced the same yield. The rate comparison of mixed oxo-imido catalyst **72b** and dioxo catalyst **98** with *cis*-stilbene **76** suggested possibly the same catalytic species was formed during the reaction as the rate of reaction was the same. Unfortunately the attempts to produce a chiral molybdenum oxo imido complex were unsuccessful and therefore we were unable to investigate an asymmetric epoxidation reaction.

# *Chapter 4: Experimental*

## 4.1 General Experimental Details

All experimental procedures were performed under an atmosphere of argon. All glassware was oven dried and flame dried prior to use. Cooling to 0 °C was achieved using an ice-water bath. Cooling to temperatures below 0 °C was achieved by using dry ice/acetone mixtures.

### Purification of Solvents and Reagents:

The lithium aryloxides Li(2,6-$^{i}Pr_2C_6H_3O$) **75a** and Li(2,6-$Me_2C_6H_3O$) **75b** were prepared from $^{n}$BuLi and the appropriate phenol in hexane at -78 °C. Commercial solvents and reagents were used as supplied or purified in accordance with standard procedures, as described below.

Solvents were either dried by passing through activated alumina (THF, diethyl ether, toluene, hexane and pentane) or distilled and dried using: $Et_3N$ ($CaH_2$), THF (Na/Benzophenone), DCM ($CaH_2$), Pyridine ($CaH_2$), DMSO ($CaH_2$). When necessary DMF, $Et_3N$ and pyridine were stored under Ar and over 4Å molecular sieves (activated by heating (250 ºC) under vacuum (0.1 mbar) for 24 h).

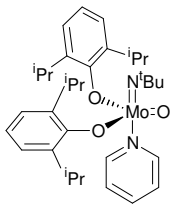
The compounds MoO($N^{t}Bu$)$Cl_2$dme **74**,[39] $MoO_2Cl_2$dme,[40] Mo($N^{t}Bu$)$_2Cl_2$dme,[40] geranyl acetate **93**[41]and TADDOL **109**[38] were prepared by literature methods.

## Characterisation:

Solid IR spectra were recorded using an Avatar 320 FTIR. All NMR spectra were recorded on Bruker AM-400 and DRX-500 NMR spectrometer. The chemical shifts were recorded relative to the solvent standard or tetramethylsilane. NMR spectra were recorded using $CDCl_3$ ($\delta_H$ = 7.27, $\delta_C$ = 77.1 ppm) or $C_6D_6$ ($\delta_H$ = 7.16, $\delta_C$ = 128.6 ppm). Multiplicities for coupled signals are denoted as: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, br = broad. All resonances that were recorded were in parts per million (ppm). All coupling constants (*J*) were recorded in Hertz (Hz). Elemental analysis was performed by the School of Chemistry, University of Nottingham on an Exeter Analytical CE-440 elemental analyser. Melting points are uncorrected and were recorded on a Gallenkamp melting point apparatus.

## 4.2 Experimental Procedures

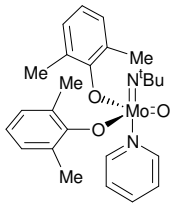
**MoO(N$^t$Bu)(2,6-$^i$Pr$_2$C$_6$H$_3$O)$_2$py (72a)**[31]




**72a**

Complex **72a** was prepared according to literature procedure (412 mg, 31% lit.[31] 48%); Data for **72a**: m.p. 125 °C (lit.[31] m.p. 117-121 °C); IR $\nu_{max}$ (solid) 2962, 1603, 1444, 1426, 1381, 1358, 1326, 1252, 1215, 1193, 1153, 1114, 934, 899 (Mo-O), 798, 767, 753 cm$^{-1}$; $^1$H NMR (400 MHz, $C_6D_6$) δ 9.26 (2H, brd, *J*=4.4, *o*-H-py), 7.13 (4H, d, *J*=7.6, *m*-H-Ar), 6.97 (2H, t, *J*=7.6, *p*-H-Ar), 6.84 (1H, t, *J*=7.6, *p*-H-py), 6.66 (2H, dd, *J*=7.2, 6.6, *m*-H-py), 3.95 (4H, sept, *J*=6.8, CH(CH$_3$)$_2$), 1.38 (12H, d, *J*=6.8, CH(CH$_3$)$_2$), 1.37 (12H, d, *J*=6.8, CH(CH$_3$)$_2$), 0.75 (9H, s, NC(CH$_3$)$_3$); $^{13}$C NMR (100.6 MHz, $C_6D_6$) δ 165.3 (C-O), 149.2, 137.6, 136.2, 124.0, 123.1, 121.6, 72.7 (NC(CH$_3$)$_3$), 28.9, 27.4, 23.3, 23.1.

**MoO(N$^t$Bu)(2,6-Me$_2$C$_6$H$_3$O)$_2$py (72b)**[31]




**72b**

Complex **72b** was prepared according to literature procedure (284 mg, 39%, lit.[31] 45%); Data for **72b**: m.p. 125 °C (lit.[31] m.p. 122-126 °C); IR $\nu_{max}$ (solid) 2974, 2925, 1602, 1466, 1423, 1358, 1265, 1237, 1200, 1160, 1092, 1072, 1038, 1011, 902 (Mo-O), 856, 775, 760, 743, 709 cm$^{-1}$; $^1$H NMR (400 MHz, $C_6D_6$) δ 9.11 (2H, brd, *J*=4.4, *o*-H-py), 6.97 (4H, d, *J*=7.6, *m*-H-Ar), 6.88 (1H, t, *J*=7.6, *p*-H-py), 6.78 (2H, t, *J*=7.4, *p*-H-Ar), 6.62 (2H, m, *m*-H-py), 2.57 (12H, s, Ar-C$H_3$), 0.70 (9H, s, NC(C$H_3$)$_3$); $^{13}$C NMR (100.6 MHz, $C_6D_6$) δ 167.9, 149.3, 138.1, 137.2, 126.1, 124.0, 121.2, 72.5 (NC(CH$_3$)$_3$), 28.51 (NC(CH$_3$)$_3$), 17.51 (Ar-CH$_3$).

**General procedure for epoxidation**

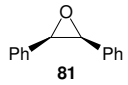
To a solution of the alkene (4.0 mmol, 1.0 equiv) and MoO(N$^t$Bu)(2,6-$^i$Pr$_2$C$_6$H$_3$O)$_2$py (0.02 mmol, 0.4 mol %) in toluene (20 mL) under an argon/nitrogen atmosphere at rt was slowly added $^t$BuOOH (12.1 mmol of 5.5 M solution in decane, 3.0 equiv). The reaction was monitored by tlc or hplc until starting material had been consumed. The reaction was cooled to rt and solvent removed under vacuum to obtain a residue. Purification by silica gel column chromatography gave the pure epoxide.

***Trans*-stilbene oxide (80)**


**80**

Data for **80** - 85 % yield (5% $Et_2O$/heptane); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.38 (10H, m, Ph-H) 3.89 (2H, s, CH-O) – Data was identical to that reported in the literature.[42]

***Cis*-stilbene oxide (81)**




**81**

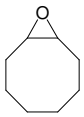
Data for **81** - 99 % yield (5% $Et_2O$/heptane); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.20-7.14 (10H, m, Ph-H) 4.38 (2H, s, CH-O) - Data was identical to that reported in the literature.[43]

**Styrene oxide (83)**


**83**

Data for **83** - 50% yield (heptane to 10% EtOAc/heptane); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.40-7.25 (5H, m, Ph-H), 3.87 (1H, m, OCHPh) 3.15 (1H, m, $OCH_2$) 2.81 (1H, m, $OCH_2$) - Data was identical to that reported in the literature.[42]

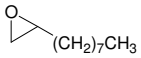
***Cis*-cyclooctene oxide (59)**



**59**

Data for **59** - 99% yield by $^1$H NMR; $^1$H NMR (400 MHz, $CDCl_3$) δ 2.95-2.90 (2H, m, OC<u>H</u>), 2.20-2.12 (2H, m, OCHC<u>H</u>$_2$) 1.6-1.4 (8H, m, -(C<u>H</u>$_2$)$_4$-) 1.24 (2H, m, C<u>H</u>$_2$) - Data was identical to that reported in the literature.[42]

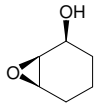
**Decene oxide (84)**



**84**

Data for **84** - 80% yield (heptane - 10% $Et_2O$/heptane); $^1$H NMR (400 MHz, $CDCl_3$) δ 2.94-2.89 (1H, m, $(CH_2)_7$C<u>H</u>-O) 2.75 (1H, dd, *J*=5.0, 3.8, OC<u>H</u>$_2$ (axial)) 2.47 (1H, dd, *J*=5.2, 2.8, OC<u>H</u>$_2$ (equatorial)) 1.58-1.39 (4H, m, C<u>H</u>$_2$) 1.39-1.23 (10H, m, C<u>H</u>$_2$) 0.89 (3H, t, *J*=6.8, $CH_2$C<u>H</u>$_3$) - Data was identical to that reported in the literature.[44]

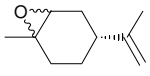
**2-Cyclohexen-1-ol oxide (86)**



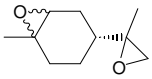
**86**

Data for **86** (single diastereomer) - 87% Yield (70% EtOAc/heptane); $^1$H NMR (400 MHz, $CDCl_3$) δ 4.00 (1H, brs, CHO<u>H</u>) 3.34 (2H, m,-C<u>H</u>-O-) 2.16 (1H, brs, C<u>H</u>OH) 1.90-1.72 (2H, m, -C<u>H</u>$_2$-) 1.62-1.40 (3H, m, -C<u>H</u>$_2$-) 1.33-1.20 (1H, m, -C<u>H</u>$_2$-) - Data was identical to that reported in the literature.[45]

**Epoxidation of (+)-Limonene**



87

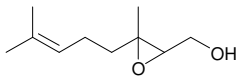


89

Only 1.2 equiv of $^{t}$BuOOH used following general reaction procedure for epoxidation. Data for **87** (mixture of 1:1 diastereomers) - 58% Yield (10% EtOAc/petrol - 30% EtOAc/petrol); $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.74 (0.5 H, brs, C=C$\underline{H}_2$), 4.68 (1.5 H, brs, C=C$\underline{H}_2$), 3.06 (0.5 H$^{cis}$, s, OC$\underline{H}$), 3.00 (0.5 H$^{trans}$, d, *J*=5.2, C=C$H_2$), 2.19-2.09 (2H, m), 1.94-1.82 (2H, m), 1.76-1.63 (4H, m), 1.59-1.50 (1H, m), 1.43-1.35 (1H, m), 1.33 (1.5H$^{cis}$, s, C$\underline{H}_3$), 1.31 (1.5H$^{trans}$, s, C$\underline{H}_3$) - Data was identical to that reported in the literature.[46]

Data for **89** - 26% Yield (10% EtOAc/petrol - 30% EtOAc/petrol); $^{1}$H NMR (400 MHz, $CDCl_3$) δ 3.07-2.95 (1H, m, OC$\underline{H}$), 2.64-2.49 (2H, m, OC$\underline{H}_2$), 2.22-1.43 (6H, m), 1.31 (3H, s, $CCH_3$), 1.26-1.20 (3H, m, $CCH_3$), 1.40-1.00 (1H, m, CH) - Data was identical to that reported in the literature.[47]

**2,3-Epoxynerol (92)**

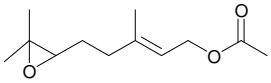



92

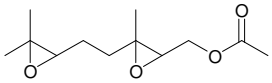
Only 2.0 equiv of $^{t}$BuOOH used following general reaction procedure for epoxidation. Data for **92** - 96 % yield (50% EtOAc/heptane); $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.09 (1H, tq, *J*=7.2, 1.4, $Me_2$C=C$\underline{H}$-$CH_2$) 3.82 (1H, m, C$\underline{H}_2$OH) 3.69 (1H, m, C$\underline{H}_2$OH) 2.98 (1H, dd, *J*=6.8, 4.4, C$\underline{H}$C$H_2$OH) 2.08 (2H, m, $CH_2$C$\underline{H}_2$C(Me)O) 1.90-1.65 (1H, m, C=CH-C$\underline{H}_2$-$CH_2$) 1.69 (3H, s, ($\underline{H}_3$C)$_2$C=CH) 1.62 (3H, s, ($\underline{H}_3$C)$_2$C=CH) 1.48 (1H, ddd, *J*=13.6, 9.2, 7.2,

C=CH-C<u>H</u>$_2$-CH$_2$) 1.23 (3H, s, C(C<u>H</u>$_3$)-O-CH$_2$) - Data was identical to that reported in the literature.[48]

**Epoxidation of Geranyl acetate**



**94**

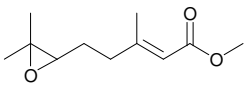


**95**

Only 1.2 equiv of $^t$BuOOH used following general reaction procedure for epoxidation. Data for **94** - 72 % yield (15% EtOAc/cyclohexane); $^1$H NMR (400 MHz, CDCl$_3$) δ 5.38 (1H, tq, *J*=7.2, 1.2, C<u>H</u>CH$_2$OAc) 4.58 (2H, d, *J*=6.8 Hz, CHC<u>H</u>$_2$OAc) 2.70 (1H, t, *J*=6.2, Me$_2$C(O)C<u>H</u>-CH$_2$) 2.19 (2H, m, Me$_2$C(O)CH-C<u>H</u>$_2$-) 2.05 (3H, s, C<u>H</u>$_3$) 1.72 (3H, s, C<u>H</u>$_3$) 1.70-1.60 (2H, m, C<u>H</u>$_2$C(Me)=CH) 1.30 (3H, s, CCH$_3$) 1.26 (3H, s, CH$_3$) - Data was identical to that reported in the literature.[49]

Data for **95** (complex mixture of diastereomers) - 23 % yield (15% EtOAc/cyclohexane); $^1$H NMR (400 MHz, CDCl$_3$) δ 4.38-4.30 (1H, m, OC<u>H</u>$_2$), 4.10-4.03 (1H, m, OC<u>H</u>$_2$), 3.05-3.00 (1H, m, OC<u>H</u>), 2.75-2.69 (1H, m, OC<u>H</u>), 2.11 (3H, s, (C=O)C<u>H</u>$_3$), 1.75-1.55 (4H, m, -(C<u>H</u>$_2$)$_2$-), 1.35-1.30 (6H, m, C<u>H</u>$_3$), 1.29-1.26 (3H, m, C<u>H</u>$_3$) - Data was identical to that reported in the literature.[49]

**Epoxidation of Methyl Geranate**



**97**

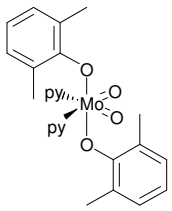
Data for **97** - 99 % yield (20% EtOAc/cyclohexane); $^1$H NMR (400 MHz, CDCl$_3$) δ 5.72 (1H, d, *J*=0.8, C=C<u>H</u>(C=O)) 3.68 (1H, s, OC<u>H</u>$_3$) 2.69 (1H, t, *J*=6.2, Me$_2$C(O)C<u>H</u>-CH$_2$) 2.40-2.20 (1H, m, Me$_2$C(O)CH-C<u>H</u>$_2$) 2.19 (3H, s, -

($\underline{H}_3C$)C=C-) 1.92 (1H, m, $Me_2C(O)CH$-$C\underline{H}_2$) 1.85-1.60 (2H, m, -$CH_2$-$C\underline{H}_2C(Me)$=CH) 1.31 (3H, s, $C(C\underline{H}_3)_2$) 1.27 (3H, s, $C(C\underline{H}_3)_2$) - Data was identical to that reported in the literature.[50]

**Large scale epoxidation of *trans*-stilbene 79**

To a solution of the *trans*-stilbene (7.30g 40.5 mmol, 1.00 equiv) and $MoO(N^tBu)(2,6\text{-}^iPr_2C_6H_3O)_2py$ (0.02 mmol, 0.04 mol%) in toluene (75 mL) under an argon atmosphere at rt was slowly added $^t$BuOOH (12.1 mmol of 5.5 M solution in decane, 3.0 equiv). The reaction was monitored by hplc and after 20 h showed 97% conversion. The reaction was cooled to rt and solvent removed under vacuum to obtain a yellow semi-solid. Purification by crystallisation using hexane produced trans-stilbene oxide **80** as clear crystals (4.78 g, 66%) – See data above.

**$MoO_2(2,6\text{-}Me_2C_6H_3O)_2py_2$ (98)**[35]




**98**

Complex **98** was prepared according to literature procedure (187 mg, 22%, lit.[35] 37%); Data for **98**: m.p. 100 °C (lit.[35] m.p. 62-63 °C); IR $\nu_{max}$ (solid) 1604, 1478, 1445, 1327, 1264, 1195, 1090, 1040, 1014, 934 (Mo-O), 901 (Mo-O), 869, 847, 760 $cm^{-1}$; $^1$H NMR (400 MHz, $C_6D_6$) δ 8.33 (4H, d, *J*=4.4, *o*-$\underline{H}$-py), 6.82 (4H, d, *J*=6.8, *m*-$\underline{H}$-Ar), 6.71 (2H, t, *J*=7.6, *p*-$\underline{H}$-Ar), 6.69 (2H, t, *J*=6.8, *p*-$\underline{H}$-py), 6.39 (4H, t, *J*=6.6, *m*-$\underline{H}$-py), 2.41 (12H, s, Ar-$C\underline{H}_3$); $^{13}$C NMR

(100.6 MHz, $C_6D_6$) δ 149.3 136.7, 129.1, 128.4, 127.8, 127.6, 126.8, 123.8, 122.2, 17.0 ($\underline{C}H_3$).

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