



An investigation into oxo analogues of molybdenum olefin metathesis complexes as epoxidation catalysts for alkenes

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ABSTRACT

The oxo-imido molybdenum complex **2a** is an effective catalyst at low catalyst loadings (0.5 mol % or below) for the epoxidation of a range of alkenes with ^tBuOOH in PhMe at 90 °C. Reactions are complete in less than 4 h and the products are isolated in high yields. The catalytic system is chemoselective for the epoxidation of electron-rich alkenes and allylic alcohols.

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Metal-catalysed olefin epoxidation has received interest from both academic and industrial research laboratories because epoxides are important building blocks in organic synthesis and polymer science.¹ Although numerous procedures have been developed,² there is still a need for the development of new catalysts that may uncover a more detailed understanding of oxidation pathways and inform the design of more efficient catalytic systems. Since the first example of a molybdenum oxo complex catalysing the epoxidation of alkenes with peroxides such as organic hydroperoxides and hydrogen peroxide,³ a variety of different complexes have been developed.^{4–6} It has been reported that the mixed oxo-imido complex **1** epoxidised *cis*-cyclooctene,⁷ but was not investigated further due to the instability of the catalyst to the reaction conditions (PhMe, 55 °C). Due to the similarity between this complex and our own oxo analogues of molybdenum olefin metathesis catalysts **2**,⁸ we chose to investigate the thermally more stable complex **2a** as a catalyst for the epoxidation of a broad range of substrate alkenes (Fig. 1).

Initial investigation involved the optimisation of the epoxidation of *trans*-stilbene with complex **2a** using the conditions originally described for the epoxidation of *cis*-cyclooctene with **1**.⁷ These were essentially those of Sharpless,⁹ namely ^tBuOOH (2 equiv), **1** (0.4 mol %) and Na₂HPO₄ (1 mol %) in PhMe at 55 °C. Consistent and high yielding results for the epoxidation were obtained with catalyst **2a** with ^tBuOOH (3 equiv) and **2a** (0.5 mol %) in PhMe at 90 °C. Significant differences from the original literature example with **1** were that catalyst **2a** was active at a higher temperature which ensured efficient conversion and the redundant use of Na₂HPO₄ which seemed to retard the reaction.¹⁰

The scope of the reaction was examined using the optimised conditions (Table 1).¹¹ The epoxidation of *trans*-stilbene, *cis*-stilbene, styrene, *cis*-cyclooctene and decene showed complete conversion by TLC or HPLC (entries 1–5). The isolated yields were high, except for the reactive styrene oxide. It is noteworthy that the epoxidation of *cis*-stilbene generated only *cis*-epoxide: no *trans* product was detected. Functionalised alkenes were investigated to probe the limitations of the catalyst system. Cyclohexenol (entry 6) underwent directed epoxidation to give the *cis*-epoxide as the sole product isolated in 87% yield, indicating hydrogen bonding or coordination of the hydroxy group to the catalyst. This is an unusual feature of molybdenum oxo catalysts which has not been commonly investigated.^{4–6} This directing effect was supported by the regiospecific epoxidation of geraniol (entry 9) in 96% isolated yield. Epoxidation of geraniol acetate (entry 10) indicates, that in the absence of a coordinating group, the electronic character of the competing alkenes dictates the regiochemistry to give a 72% isolated yield of the dimethyl epoxide. A 23% yield of the bis-epoxide was also isolated with no mono-epoxidation of the allylic acetate detected. However, the limitations of the present catalyst **2a** and reaction conditions are clear with limonene (entry 7) where a moderate 58% yield of the most substituted mono epoxide was isolated.

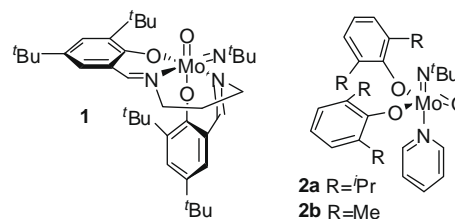

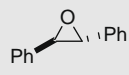

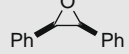





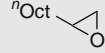
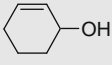
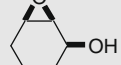
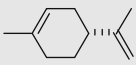
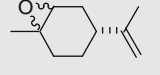

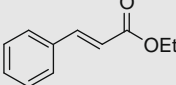
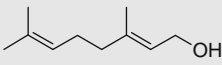
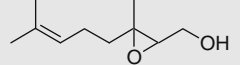
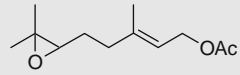
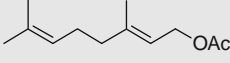
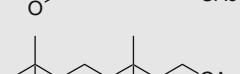
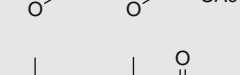
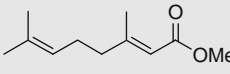
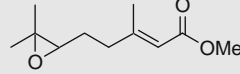


Figure 1.

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Table 1
MoO(N^tBu)(2,6-ⁱPr₂C₆H₃O)₂py (**2a**)-catalysed epoxidation of alkenes^a

Entry	Alkene	Product	Yield ^b (%)
1			85 (99) ^c
2			99 (99) ^c
3			50
4			98 ^d
5			80
6			87
7 ^e			58
			26
8		—	—
9 ^f			96
			72
10 ^g			23
			23
11			99

^a Alkene (4.0 mmol), **2a** (0.02 mmol) and ^tBuOOH (12.1 mmol) in PhMe (7.4 mL), 90 °C, 1–4 h.

^b Isolated yield.

^c Yield determined by HPLC.

^d Conversion determined by ¹H NMR.

^e 1.2 equiv ^tBuOOH.

^f 2.0 equiv ^tBuOOH.

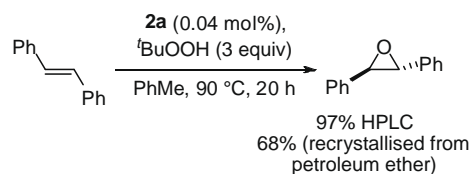
^g 1.2 equiv ^tBuOOH.

Here again, no mono terminal epoxide was isolated. The epoxidation system is electrophilic in nature as evidenced by the regioselective epoxidation of methyl geranate (entry 11) and no epoxidation was observed for the electronically deactivated ethyl *trans*-cinnamate (entry 8).

To illustrate the effectiveness of the catalytic system, a larger scale (40 mmol) epoxidation of *trans*-stilbene was investigated (Scheme 1). The catalyst loading was reduced from 0.5 mol % to 0.04 mol %, the reaction was monitored by HPLC and the product epoxide was purified by recrystallisation from petroleum ether to give an isolated yield of 68%. This represents a substrate to catalyst loading of 2500:1 and potentially this may be reduced further as the conversion by HPLC was high. This is testament to the thermal stability and extremely high reactivity of this particular molybdenum oxo catalyst compared to many others described in the literature.^{4–6}

Similar molybdenum-catalysed epoxidations are known to proceed via oxo-, peroxy- or peroxide metal intermediates and the efficiency of the oxygen transfer step is dramatically influenced by the coordination environment around the metal centre. Coordination of chiral ligands has not often led to efficient asymmetric catalysts due, in part, to the molybdenum complex being di-oxo or di-peroxy and thus being able to present two possible electrophilic oxygen atoms to the substrate alkene. The mixed oxo-imido complex **2**, which possesses just one oxygen ligand, could be a good candidate for development of an asymmetric catalyst by replacement of the phenoxide ligands with chiral alcohols or a chiral diol. In order to probe whether the mixed oxo-imido ligand set may be beneficial for asymmetric catalysis we tested the analogous di-oxo complex MoO₂(2,6-Me₂C₆H₃O)₂py₂ (**3**)¹² and **2b** for comparison purposes under our reaction conditions.¹³ The rate of epoxidation of *cis*-stilbene was compared by HPLC (Fig. 2) and was found to be identical for both complexes **2b** and **3**. This could mean that each catalyst is converted into the same active di-oxo/di-peroxy oxidant. Conversely, the comparison may not be subtle enough to differentiate between an oxo-peroxy or imido-peroxy ligand set. Attempted isolation of **2b** (or **2a** in Table 1) after the reactions was unsuccessful and led to degradation of the complex. Although this rate comparison study was inconclusive we believe that the mixed oxo-imido molybdenum complexes **2** are still attractive for investigation of an asymmetric process.

The mixed oxo-imido complex **2a** has been shown to be a highly reactive catalyst (down to 0.04% at least) and thermally stable for the epoxidation of a wide range of alkenes with ^tBuOOH. The catalytic system is susceptible to direction by a pendant hydroxy



Scheme 1. Epoxidation of *trans*-stilbene (40 mmol) with **2a** (0.04 mol %).

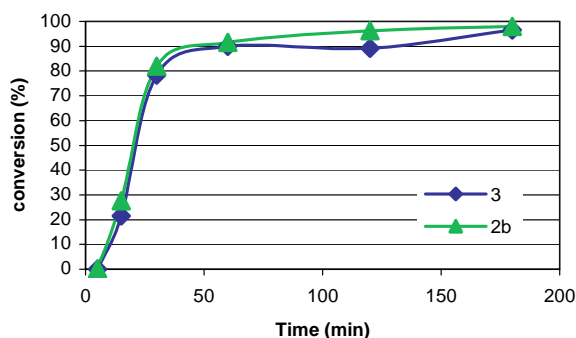


Figure 2. Time course of MoO(N^tBu)(2,6-Me₂C₆H₃O)₂py (**2b**) and MoO₂(2,6-Me₂C₆H₃O)₂py₂ (**3**) catalysed epoxidation of *cis*-stilbene. Conditions: alkene (4.0 mmol), **2a** (0.02 mmol) and ^tBuOOH (12.1 mmol) in PhMe (7.4 mL), 90 °C, 1–4 h.

group and is unreactive towards α,β -unsaturated esters, showing chemoselectivity for electron-rich alkenes. Work is ongoing to elucidate the catalytically active species and chemo- and enantioselective variants of this catalytic system are under investigation.

Acknowledgements

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- It seems that Na₂HPO₄ was originally used by Sharpless due to information suggesting that it minimised by-product formation. See Ref. 9a.
- To a solution of the alkene (4.0 mmol) and **2a** (0.02 mmol, 0.5 mol %) in PhMe (7.5 mL) under an argon atmosphere at rt was slowly added 'BuOOH (12.1 mmol of a 5.5 M solution in decane, 3.0 equiv). The reaction mixture was heated to 90 °C and monitored by TLC or HPLC until the starting material had been consumed, which was less than 4 h for all the examples studied. The reaction mixture was cooled to rt and the solvent removed under vacuum to obtain a residue. Purification by silica gel column chromatography gave pure epoxides that possessed identical physical and spectroscopic properties to those reported.
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- The corresponding Pr analogue of **3** could not be isolated. Complex **2b** gave an identical yield of *cis*-stilbene oxide as **2a**.