Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 1471–1476

TETRAHEDRON:
*ASYMMETRY*

# Diastereoselective ring opening of limonene oxide with water catalysed by β-ketophosphonate complexes of molybdenum(VI)

Laurent Salles, Andrew F. Nixon, Nicholas C. Russell, Russell Clarke, Peter Pogorzelec and
David J. Cole-Hamilton *

*School of Chemistry, University of St. Andrews, St. Andrews, Fife, KY16 9ST, Scotland, UK*

Received 25 February 1999; accepted 8 April 1999

**Abstract**

In the presence of catalytic quantities of [$MoO_2Cl_2L$] (L=β-ketophosphonate derived from camphor), water initiates the selective ring opening of *cis* (+) or (−)-limonene oxide to give the *trans*-diaxial diol. The *trans* isomer of the limonene oxide remains almost completely unreacted, thus providing a method for the kinetic separation of the *trans* diastereomer. $^1H$ and $^{13}C$ NMR studies of the interaction of the epoxide with the molybdenum complex show that the metal coordinates to the epoxide oxygen atom and that the diastereo-discriminating step is attack of Mo=O onto the *tertiary* carbocation formed by cleavage of a C–O bond in the epoxide. © 1999 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

The ring opening of epoxides by water can be either base or acid catalysed and is used extensively for the production of diols.[1] In the case of limonene, it has been shown that the acid catalysed ring opening of either the *cis* or the *trans* isomer leads to the same (*trans*-diaxial) diol.[2–4] The same product is expected from both isomers because the isopropenyl group anchors the ring conformation and diaxial opening predominates.[4] Since formation of this product from the *cis* isomer requires nucleophilic attack on the tertiary centre rather than on the secondary centre, which occurs for the *trans* isomer, it is expected that the *cis* isomer might open more slowly than the *trans*. Generally, there is, however, no data on the relative reactivities of the *cis* and *trans* isomers.[4,5] In the reaction with $LiAlH_4$, the *trans* isomer was definitely more reactive.[4] Enantioselective ring opening of limonene oxides by water was observed in the presence of the yeast *Rhodotorula glutinis*[6] or in the presence of rabbit mEH.[7]

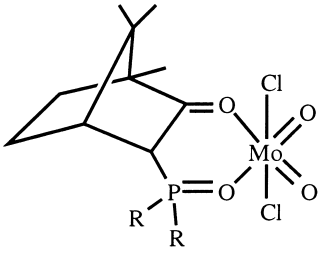
During the course of studies[8] on the epoxidation of a variety of alkenes in the presence of β-ketophosphonate complexes of molybdenum(VI), we noted that the *cis*:*trans* ratio of the product epoxide obtained from limonene (originally 1:1) changed upon standing in air. We reasoned that this

---

* Corresponding author. Tel: 44-(0)1334-463805; fax: 44-(0)1334-463808; e-mail: djc@st-and.ac.uk

*PII:* S0957-4166(99)00136-6

might arise because of a reaction of the epoxide with moisture from the air since it did **not** occur for the products of epoxidation reactions carried out in the presence of molecular sieves.[8,9] We have, therefore, studied the ring opening of limonene oxide by water in the presence of the same β-ketophosphonate complexes of molybdenum and now report the results of this study which show that the *cis* isomer opens selectively, thus providing a method for separating the *trans*-diastereomer of the epoxide.



**1**

| | R | Camphor |
|---|---|---|
| **a** | EtO | (+) |
| **b** | EtO | (-) |
| **c** | (+)-2-BuO | (+) |
| **d** | Ph | (+) |

## 2. Results and discussion

Treating a mixture of *cis*- and *trans*-(+)-limonene oxide in $CH_2Cl_2$ with water in the presence of dichloro{[(IR)-*endo*]-(+)-3-(diethoxyphosphoryl)camphor}dioxomolybdenum(VI) **1a** leads to the formation of the *trans*-diaxial diol, but only the *cis* isomer of the epoxide reacts at a significant rate, the *trans* isomer remaining largely unconverted.[†] The time course of the reaction for a 1:1:1.3 ratio of water:*cis*-limonene oxide:*trans*-limonene oxide is shown in Fig. 1. The reaction rate is very dependent upon the amount of water added; complete conversion of the *cis*-limonene oxide taking from 20 h to several days, the quickest reactions occurring when an approximately stoichiometric amount of water is used. For the longer term reactions with larger amounts of water there is evidence from NMR spectra recorded at the end of the reactions that the *trans* isomer is also partially reacted. The dependence on water is complex since excess water (2 equivalents per total limonene oxide) leads to destruction of the catalyst to give an inactive blue precipitate. Similarly, catalyst destruction occurs in THF, with which water is miscible.

Changing the chirality of the limonene oxide or of the camphor, changing the substituents on the phosphonate to (+)-2-butyl or using phenyl groups in place of alkoxides on phosphorus **1**(**b**–**d**) does not alter the selectivity of the reaction, with the *cis* isomer always reacting preferentially (Table 1) showing that there is no enantioselectivity in the reaction. Full conversion of the *cis* isomer is not always observed, however, and lower activity is observed using $[MoO_2Cl_2]$ (Table 1).

In order to determine the origins of the selectivity, we have examined the stoichiometric reaction between a mixture of *cis*- and *trans*-(+)-limonene oxide and **1a** by $^1$H NMR spectroscopy. The proton on the epoxide ring of *cis*-limonene oxide resonates as a triplet at δ 3.05, whilst that of the *trans* isomer resonates as a doublet at δ 2.95. On addition of **1a** (0.5 mol per mol of limonene oxide), the resonance from the *trans* isomer remains unchanged, but that from the *cis*-isomer shifts to 4.05. On increasing the amount of **1a**, no further changes occur in the $^1$H NMR resonances of limonene oxide up to a **1a**:limonene oxide ratio of 1:1. These results show that the catalyst binds preferentially to the *cis* isomer, and that this binding is presumably the origin of the selectivity of the ring opening reaction.

Examination of the resonances from **1a** in the presence of limonene oxide (0.5:1) shows that **1a** remains intact and, in particular, that the resonance from the H atom on $C_3$ is a doublet of multiplets at δ 3.85 ($J_{PH}$=47 Hz), indicating that the β-ketophosphonate ligand remains bidentate.[10] This proton

---

[†] If the Mo complex is replaced with the same concentration of *p*-toluenesulphonic acid, almost no conversion was observed after 1 week of stirring.

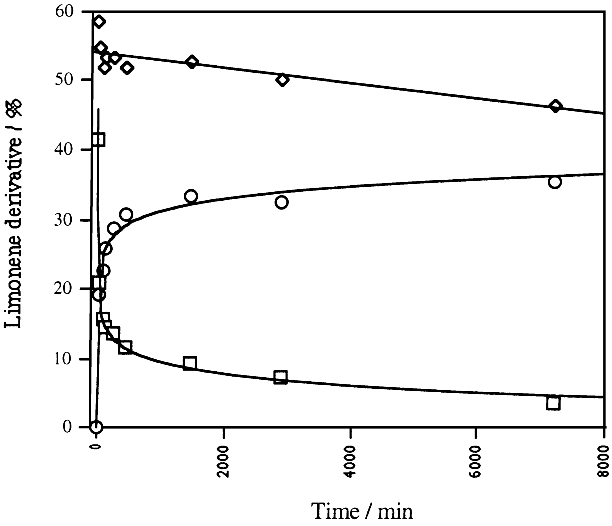


Figure 1. Time course of the reaction of *cis*- and *trans*-(+)-limonene oxide with water catalysed by **1a**. Conditions as in Experimental

Table 1
Ring opening of limonene oxide by water catalysed by molybdenum(VI) complexes[a]

| Limonene oxide | Catalyst | Camphor | Time to 50% conversion of *cis* isomer/min | Time reaction terminated/h | Ratio of *cis:trans* limonene at termination |
|---|---|---|---|---|---|
| (+) | **1(a)** | (+) | 20 | 98 | 1:99[b] |
| (–) | **1(a)** | (+) | 75 | 503 | 10:100 |
| (+) | **1(b)** | (–) | 10 | 71 | 15:85 |
| (–) | **1(b)** | (–) | 60 | 27 | 13:87 |
| (+) | **1(c)** | (+) | 35 | 264 | 3:97 |
| (–) | **1(c)** | (+) | 60 | 648 | 0:100 |
| (+) | **1(d)** (+) | (+) | 30 | 768 | 20:80 |
| (–) | **1(d)** (+) | (+) | 60 | 672 | 24:76 |
| (+) | $MoO_2Cl_2$ | – | – | 96.5 | 36:64 |
| (–) | $MoO_2Cl_2$ | – | 1470 | 96 | 32:68 |

[a] Conditions as in experimental ($H_2O$ = 0.04 g).

[b] $^1$H NMR studies show that, after 2 weeks standing in air 94% of the *cis* isomer and 40% of the *trans* isomer have reacted to form diol.

resonates as a doublet of multiplets at δ 3.85 ($J_{PH}$=33.6 Hz) for **1a** but is at δ 2.95 ($J_{PH}$=27 Hz) for the free ligand or δ 3.4 (br $J_{PH}$~30 Hz) if the ligand is bound in a unidentate fashion through the phosphoryl O atom.[10] Comparison of the $^1$H (Table 2) and $^{13}$C NMR spectra of solutions containing *cis*- and *trans*-limonene oxide, the mixture of *trans*-limonene oxide and the *trans*-diaxial diol, and solutions obtained from mixing *cis*- and *trans*-limonene oxide with **1a** (0.5:0.5:1) show that the spectrum from the last of

Table 2
Selected $^1$H NMR parameters for limonene derived moieties[a]

| Compound | δ Vinyl H | δ ($J_{HH}$/Hz) Epoxide H | δ Methyl groups |
|---|---|---|---|
| *cis* limonene oxide | 4.65, 4.72 | 3.05 t (3.5) | 1.34, 1.68 |
| *trans* limonene oxide | 4.65 | 3.0 d (7) | 1.32, 1.65 |
| *trans*-diaxial diol | 4.72 | 3.62 t (4) | 1.28. 1.72 |
| Mo complex | 4.75 | 4.02 bs | 1.30. 1.72 |

[a] In all cases, the ring protons resonate as a complex series of multiplets δ 1.2-2.1.

these solutions bears a much closer resemblance to that of the *trans*-limonene oxide–diol mixture than to that of the limonene oxides themselves. In particular, the resonances from the epoxide C atoms of the *cis*-limonene oxide, which originally resonate at δ 59.1, 57.3 are shifted to 66.3 and 74.6 in the presence of **1a**, whilst those from the *trans*-limonene oxide remain unshifted at δ 60.4 and 57.2. This suggests firstly that the diastereo-discriminating step is the coordination and attack of the molybdenum complex rather than the attack of water and secondly that the product of the interaction of **1a** with *cis*-limonene oxide has a diol like structure. Fig. 2 shows the proposed mechanism by which this diolato complex forms and leads to the *trans*-diaxial diol. The molybdenum complex could bind to either lone pair on the epoxide O atom, but we suggest that it does not bind over the ring because there are two alkyl substituents on this side of the epoxide as opposed to only one on the other side. There should be little preference for binding to the *cis* or *trans* isomers. The binding of the Lewis acid then promotes cleavage of the C–O bond in the epoxide which leads to the more stable carbocation (tertiary). The oxo group on the molybdenum then attacks the carbocation to give the five membered diolato ring, but this can only occur for the intermediate derived from the *cis*-limonene oxide, because for the *trans*, the C–O(–Mo) bond is equatorial and hence almost coplanar with the C–methyl bond. $S_N1$ like mechanisms have been proposed before to explain minor products in the ring opening of limonene oxide by an acetate ion.[4] $S_N2$ attack of water on the same C atom then leads to the observed *trans*-diaxial diol. Although attack of water on the *tertiary* C atom might be expected to be disfavoured, it occurs preferentially in cases such as this because of the preference for the diaxial product.[4]

Diolato complexes of the kind proposed are unusual for molybdenum(VI), although a similar oxocatecholato complex, [MoO($O_2C_6H_4$)(1-piperidinolato)$_2$],[11] and the dinuclear [μ-O{MoO(2,3-dimethylbutanediolato)(2,3-dimethyl-2-hydroxy-3-butanolato)}$_2$] have been structurally characterised.[12] Simple diolato complexes are, however, well known for osmium(VI), being formed from the reaction of alkenes with [$OsO_4$] or from reactions of [$OsO_2(OMe)_2$] with 1,2-diols.[13]

## 3. Conclusion

We conclude that diastereoselective ring opening of limonene oxide with water in the presence of $Mo^{VI}$ catalysts can act selectively on the *cis* isomer to give the expected *trans*-diaxial diol, but leaves the *trans* isomer unreacted and thus provides a method for the kinetic separation of the *trans*-limonene oxide.

## 4. Experimental

NMR spectra were recorded on a Bruker Associates AM300 spectrometer operating in the Fourier transform mode. GLC analyses were performed on a Phillips gas chromatograph with a Rastex 60 M stabilwax capillary column and $N_2$ as the carrier gas. The chromatograph was programmed to run at 60°C for 4 min and then the temperature was raised to 220°C at 16°C min$^{-1}$.

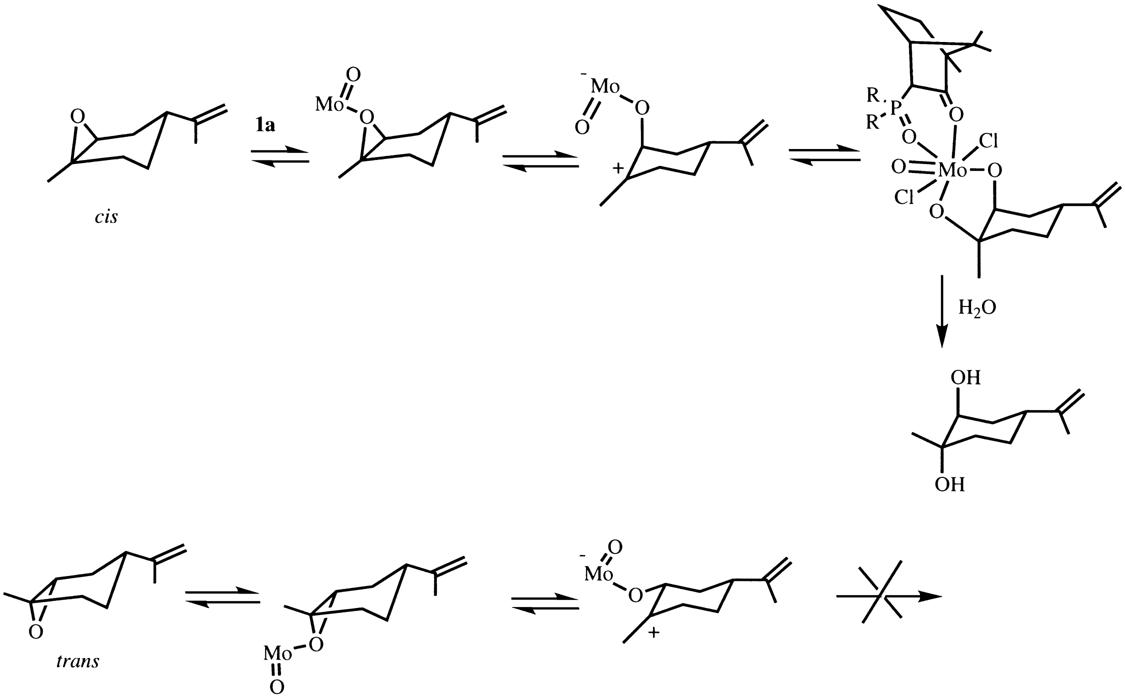


Figure 2. Proposed mechanism for the formation of the Mo diolato complex from *cis*-limonene oxide and **1a** and for the subsequent formation of the *trans* diaxial limonene diol

Limonene oxide (1:1.3 *cis*:*trans* mixture, Aldrich) was used as received and molybdenum complexes were prepared as previously described.[10]

All operations were carried out under dry deoxygenated (passage through a column containing $Cr^{2+}$ on silica) $N_2$ using standard Schlenk line and catheter tubing techniques.

### *4.1. Ring opening reactions*

[$MoO_2Cl_2L$] (L=(IR or *S*)-*endo*-(+) or (−)-3-(diethoxy) or (+)-2-butanoxy-phosphoryl) or (diphenylphosphinyl) camphor) (0.02 g, 0.04 mmol) was dissolved in (+) or (−)-limonene oxide (0.65 $cm^3$, 4 mmol) containing octan-2-ol (0.3 $cm^3$) as an internal standard. Dichloromethane (5 $cm^3$) was added followed by water (0.03 g, 1.7 mmol). The solution was stirred and the stop-watch started. Samples (0.05 $cm^3$) were taken at intervals up to 120 h, diluted with $CH_2Cl_2$ (to 5 $cm^3$) and analysed by GLC.

Similar reactions were carried out using different amounts of water or THF in place of $CH_2Cl_2$.

### *4.2. Reaction of (+)-limonene oxide with $MoO_2Cl_2$[(IR)-*endo*]-3-(diethoxy-phosphorylcamphor)*

(+)-Limonene oxide (0.31 $cm^3$, 0.194 mmol) was added to a solution of the molybdenum complex (0.047 g, 0.097 mmol) and the resulting mixture dissolved in dry degassed $CDCl_3$. The solution was examined by $^1H$ NMR spectroscopy. Selected data are collected in Table 2.

## Acknowledgements

We thank the CNRS (L. S.) and Rhône Poulenc and the EPSRC (R. C.) for funding.

## References

1. Sheldon, R. A.; Kochi, J. K. *Metal Catalysed Oxidations of Organic Compounds*; Academic Press: New York, 1981.
2. Schmidt, H. *Suomen Kemistilehti* **1958**, *B31*, 61.
3. Wylde, R.; Teulon, J. M. *Bull. Soc. Chim. Fr*. **1970**, *2*, 759.
4. Royals, E. E.; Leffingwell, J. C. *J. Am. Chem. Soc*. **1966**, *31*, 1937, and references cited therein.
5. Schmidt, H. *Chem. Ber.* **1949**, *82*, 11.
6. Weijers, C. A. G. M. *Tetrahedron: Asymmetry* **1997**, 639.
7. Bellucci, G.; Berti, G.; Ingrosso, G.; Mastrorelli, E. *J. Org. Chem.* **1980**, *45*, 299.
8. Clarke, R.; Gahagan, M.; Mackie, R. K.; Foster, D. F.; Cole-Hamilton, D. J.; Nicol, M.; Montford, A. W. *J. Chem. Soc., Dalton Trans*. **1995**, 1221.
9. Clarke, R.; Cole-Hamilton, D. J. *J. Chem. Soc., Dalton Trans*. **1993**, 1913.
10. Gahagan, M.; Mackie, R. K.; Cupertino, D. C.; Harman, M.; Hursthouse, M. B.; Cole-Hamilton, D. J. *J. Chem. Soc., Dalton Trans*. **1990**, 2195.
11. Bristow, S.; Enemark, J. H.; Garner, C. D.; Minelli, M.; Morris, G. A.; Ortega, R. B. *Inorg. Chem.* **1985**, *24*, 4070.
12. Matheson, A. J.; Penfold, B. R. *Acta. Crystallogr., Sect. B* **1979**, *35*, 2707.
13. Griffith, W. P. In *Comprehensive Coordination Chemistry*; Wilkinson, G.; Gillard, R. D.; McCleverty, J. A., Eds.; Pergamon: Oxford, 1987; Vol. 4, pp. 581–591.