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Enantioselective epoxidation of unfunctionalized simple olefins by non-racemic molybdenum(VI)(oxo-diperoxo) complexes

V. Schurig *, K. Hintzer, U. Leyrer, C. Mark,

Institut für Organische Chemie der Universität, Auf der Morgenstelle 18, D-7400 Tübingen (F.R.G.)

P. Pitchen and H.B. Kagan

Laboratoire de Synthèse Asymétrique, Université Paris-Sud, F-91405 Orsay (France)

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Abstract

Molybdenum(VI)(oxo-diperoxo) complexes bearing bidentate ligands with hydroxy and carbonyl functions show asymmetric induction in the stoichiometric epoxidation of simple prochiral olefins. The influence of the ligand and alkene structure on the enantiomeric excess of the oxiranes has been investigated. The addition of chiral diols to the molybdenum(VI)(oxo-diperoxo) reagents gives high enantiomeric excesses probably because of an efficient kinetic resolution of the oxiranes formed.

Introduction

The importance of chiral epoxides in biochemistry and synthetic chemistry has warranted the search for simple enantioselective routes to these compounds. While nearly enantiomerically pure α-hydroxyalkyloxiranes can be obtained by asymmetric Sharpless epoxidation of allylic alcohols with t.-butylhydroperoxide/diethyl tartrate [1] no such versatile a procedure is yet available via the peroxo-metal-mediated epoxidation of *unfunctionalized* alkenes to simple oxiranes.

Molybdenum(VI)(oxo-diperoxo) complexes **1** ($n = 1$–2; L = H_2O, DMF, HMPA, pyr) are stoichiometric reagents for the oxidation of various organic substrates such as sulfides, aliphatic amines, ketones, and olefins [2]. It has previously been shown that stoichiometric amounts of **1** containing a chiral bidentate ligand L, i.e., (*S*)-*N*,*N*-dimethyl-lactamide, epoxidize simple prochiral alkenes such as propene, 1-butene or *trans*-2-butene to give optically active oxiranes (ee = 30–35% at 20 °C and 1 bar in nitromethane) [3]. A crystal structure determination of **1** (L = (*S*)-*N*,*N*-

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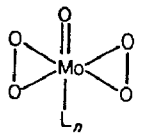


1

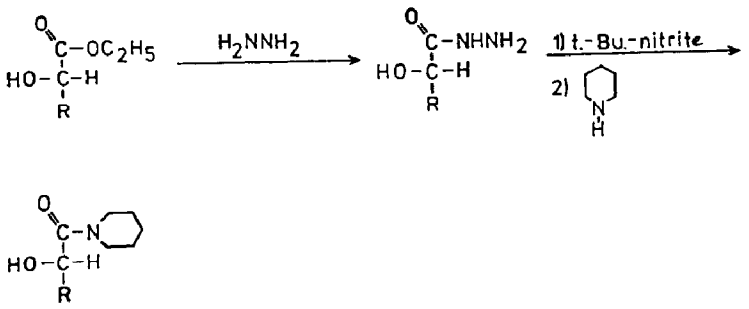
dimethyl-lactamide) has revealed a slightly distorted pentagonal-bipyramidal coordination sphere about molybdenum with two peroxo groups and the carbonyl oxygen of L in equatorial positions and an oxo group and the hydroxy function of L in axial positions [4].

1(L = (*S*)-piperidine-lactamide) [5] has successfully been employed for the enantioselective epoxidation of a prochiral tetracyclic anthracyclinone precursor containing a methylsubstituted endocyclic double bond at 0 °C with ee = 53% [6]. High dilution of the reagent (in dichloromethane) gave the enantiomeric yields of ee = 75% [7]. **1** (L = dimethyl-2-piperidinosuccinate and dimethyl-(−)-2-morpholinosuccinate) has been used in a study of the enantioselective epoxidation of *cis*-2-methyl-n-octadec-7-ene to the insect pheromone (−)-disparlure [8]. Some molybdenum(VI) (oxo-diperoxo) reagents bearing chiral monodentate ligands, such as, **1** (L = (−)-menthyl-phosphoric acid triamide, *N*,*N*-dimethyl-(−)-menthylamine *N*-oxide, (+)-α-phenyl ethyl-phosphoric acid triamide and *N*,*N*-dimethyl-(+)-α-phenyl ethylamine *N*-oxide) have shown only low asymmetric induction in the epoxidation of *trans*-2-octene (chemical yields of epoxide: 8–70%, ee = 0.7–8.5%) at 25 °C in 1,2-dichloroethane [9].

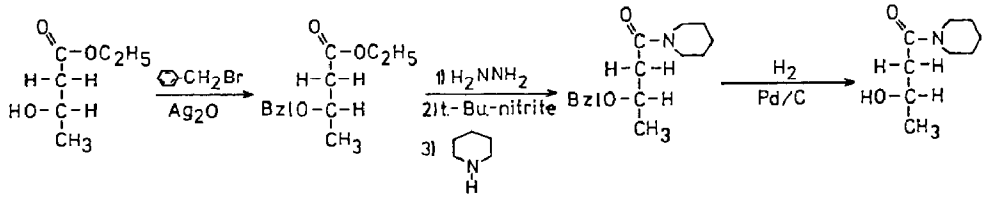
Here we describe a detailed study on the use of **1** containing various chiral ligands, as well as auxiliary additives, for the enantioselective epoxidation of simple prochiral alkenes.

Results and Discussion

(*S*)-*N*,*N*-Dimethyl-lactamide (DMLA) [3,10] and (*S*)-*N*,*N*-dimethyl-3-phenyl-lactamide (DMPLA) [10] have been used previously as chiral, non-racemic, bidentate ligands in molybdenum(VI) (oxo-diperoxo) reagents **1** for the enantioselective epoxidation of unfunctionalized simple olefins. A number of additional compounds, listed in Scheme 1, have been prepared and tested as chiral ligands in molybdenum(VI) (oxo-diperoxo) reagents **1** for asymmetric epoxidations. The new structures should throw light on the influence of (i) the size of the amide component, (ii) branching of alkyl substituents (PLA vs. HMBPA), (iii) an additional chiral center (HMPPA), and (iv) the position of the hydroxy group (PLA vs. HBPA) on enantioselective oxirane formation. In addition, ligands in which the chiral center and the hydroxy group is located in the amide function have been investigated (AcPro, BzPro). The dimethylamide ligands (DMLA, DMPLA) were prepared as described previously, by reaction of the ethyl esters with dimethylamine in good chemical yields [10]. The piperidine amide of lactic acid (PLA) was obtained from ethyl lactate and piperidine in low yields. Higher yields were obtained by reaction of the ester with hydrazine hydrate to give the hydrazide followed by azide coupling with piperidine [11].

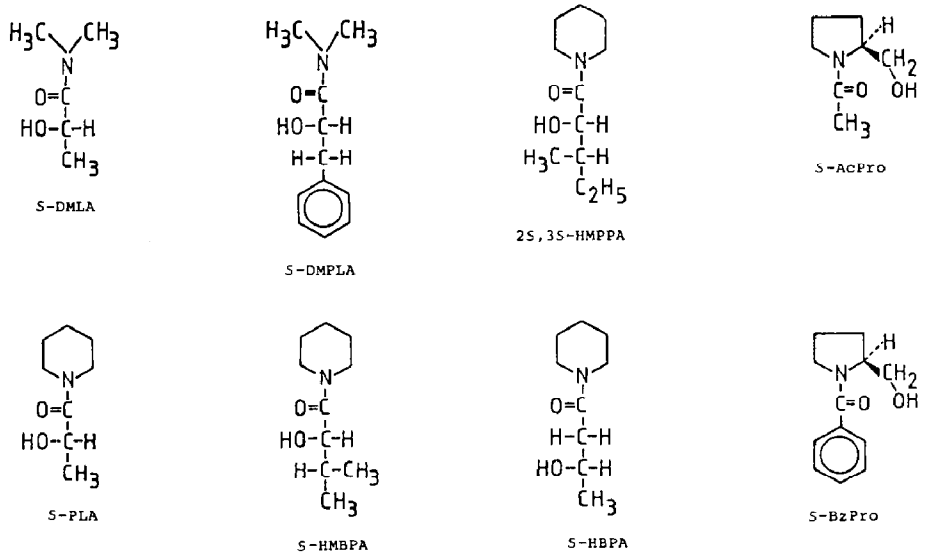


For the synthesis of HBPA the β-hydroxy group was protected as the benzyl ether [12] to avoid side-reactions in the azide coupling.



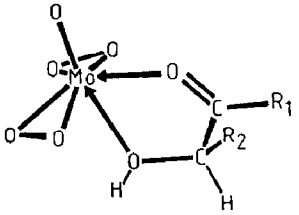
Hydroxy acid amides with bulky amine components such as tetramethylpiperidine or diisopropylamide could not been prepared in sufficient yields. The acylation of prolinol was straightforward.

The molybdenum(VI) (oxo-diperoxo) complexes **1** were obtained by stoichiometric reaction of the ligands with MoO_3 and H_2O_2 by the procedure as described by Mimoun et al. [2]. The complexes **1** were obtained after concentration of the reaction mixture as yellow powders which exhibit the characteristic Mo=O vibration at $\nu = 950–970\ cm^{-1}$ and the O–O vibration (doublet) at $\nu = 850–880\ cm^{-1}$ in the infrared spectra. In the reaction of HBPA with MoO_3 and H_2O_2 a water-containing product, which could not be dehydrated by P_4O_{10}, was formed.



Scheme 1

In analogy to the structure of $MoO(O_2)_2 \cdot H_2O \cdot HMPT$ [13] and of $MoO(O_2)_2 \cdot DMLA$ [4] a pentagonal bipyramidal geometry is assumed for the new molybdenum(VI)(oxo-diperoxo) complexes **1** in which the carbonyl group occupies an equatorial position while the hydroxy group is coordinated from an axial position:



In the reaction of PLA with MoO_3 and H_2O_2 not only the expected yellow complex $MoO(O_2)_2 \cdot PLA$ was formed but another yellow-orange compound, which exerted better solution properties in organic solvents, could be isolated. A Mo/O ratio of 1:7 was inferred from elemental analysis; hereafter this complex is abbreviated as 'Mo · PLA'.

The enantiomeric excess (ee) of the oxiranes was determined by complexation gas chromatography on chiral stationary phases such as nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] [14]. This method readily permits the chemical yield, enantiomeric yield and absolute configurations of the volatile oxiranes to be determined by simple headspace analysis after short intervals [3], without the usual requirements of isolation, chemical manipulation, and interruption of the reaction. In a typical experiment, the reaction was performed in 'head-space'-vials, which were charged with approx. 20 mg molybdenum(VI)(oxo-diperoxo) complex, dissolved in 2–3 ml nitromethane, and 1–2 ml gaseous olefin. Figures 1 and 2 show typical complexation chromatograms characterizing the enantioselective epoxidation of *trans*-2-butene with $MoO(O_2)_2 \cdot DMPLA$ and 'Mo · PLA', respectively. The results of a the epoxidation of *trans*-2-butene with various molybdenum(IV) (oxo-diperoxo) complexes **1** are listed in Table 1. The results merit some comment. The molybdenum(VI) (oxo-diperoxo) complexes **1** epoxidize *trans*-2-butene enantioselectively to (2*R*,2*R*)-*trans*-2,3-dimethyloxirane with distinct enantiomeric excesses (ee). Unless stated otherwise in Table 1, the ee values remain constant during the entire reaction period (10 min–10 h). Rather unexpectedly, the enantiomeric bias is reduced when the temperature is lowered. As the temperature is increased above 23° C the ee remains essentially constant up to 53° C while the chemical yield of the oxirane decreases. The enantioselectivity is randomly influenced by the nature of the chiral ligands of molybdenum. Thus, while the substitution of acyclic dimethylamine for cyclic piperidine in the amide function does not alter the enantiomeric composition of the oxirane formed, an increase in the steric bulk of the ligand (HMBPA, HMPPA, DMPLA vs. DMLA) results in a decrease in enantioselectivity. A remarkable timedependence of the enantiomeric composition of the oxirane has been observed for the other complexes whereas for molybdenum(VI) (oxo-diperoxo)DMLA and PLA reagents the ee remained constant during the epoxidation reaction. Thus, in the case of $MoO(O_2)_2 \cdot DMPLA$, the ee dropped from 40.2% (20 min) to 17.6% (20 h) (cf. Fig. 1). The position of the hydroxy group in respect of the carbonyl group in the ligand has a striking influence on the enantioselective

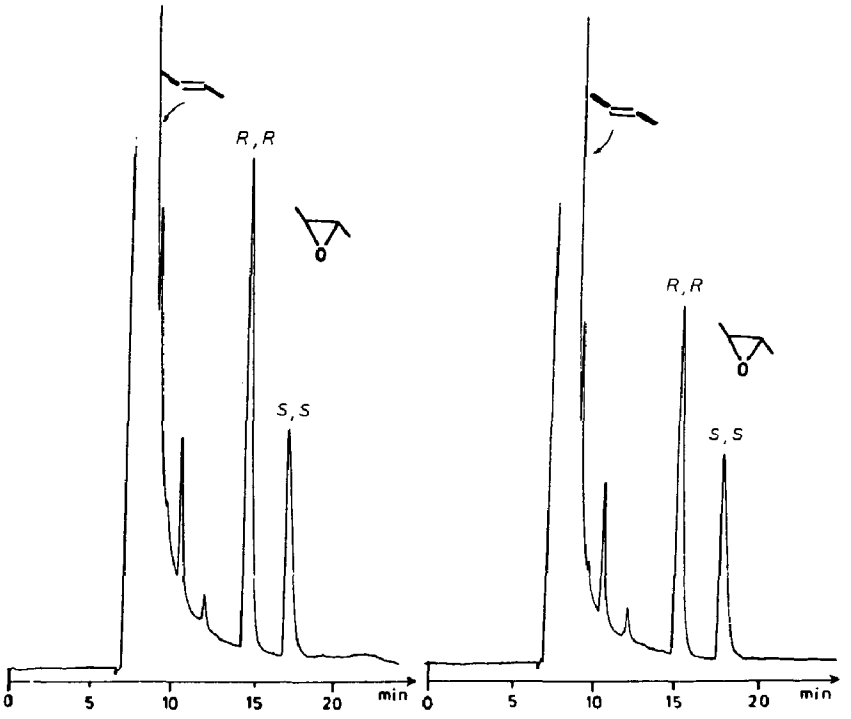
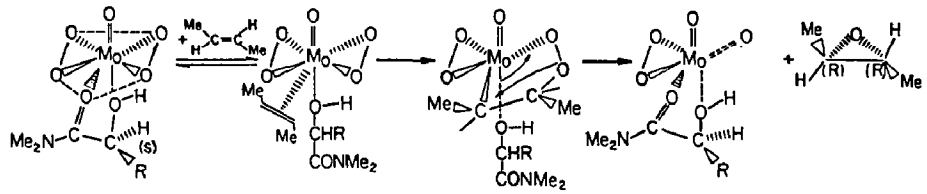


Fig. 1. Complexation-gas-chromatographic determination of the enantiomeric yield of *trans*-2,3-dimethyloxirane (formed by asymmetric epoxidation of *trans*-2-butene with $MoO(O_2)_2 \cdot$DMPLA) on nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] (0.12 *M* in squalane) at 60 °C [14]. Left: ee = 40.2% (after 20 min), right: ee = 17.6% (after 20 h). Column: 70 m × 0.5 mm nickel capillary, carrier: 3.0 ml/min N_2.

oxirane formation. Thus, the asymmetric induction decreases in the order: α (DMLA, PLA) > β (HBPA) ≫ γ (AcPro, BzPro). The highest enantiomeric bias is observed with the reagent 'Mo · PLA'. The interpretation of the findings is difficult because the mechanism of the stoichiometric epoxidation of alkenes by molybdenum(VI) (oxo-diperoxo) complexes **1** is still unclear. An equatorial ligand can be replaced by olefin by the Mimoun mechanism [15]. The alkene–metal bonding can only be σ, since Mo^{VI} has no π-electrons for back-donation. An increase in the rate of epoxidation with alkyl substitution at the olefin-double bond, thus increasing the Lewis donor property of the alkene, has been observed previously [3,16]. Upon coordination the alkene loses its nucleophilic character and becomes electrophilic, thus becoming susceptible to nucleophilic attack by the peroxo group via an intramolecular 1,3-dipolar cycloaddition to give a five-membered dioxametallacycle which eventually collapses into a molybdenum(VI) (dioxo-peroxo) species and an alkene oxide. In keeping with this mechanism, the carbonyl



function of the bidentate ligand must dissociate from the equatorial position. This is

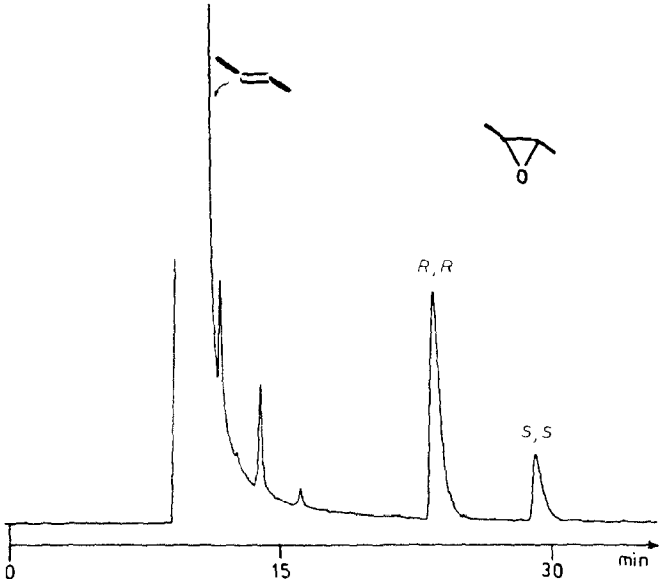
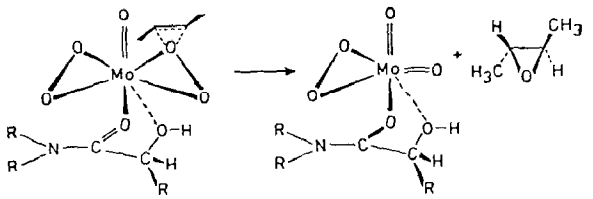


Fig. 2. Complexation-gas-chromatographic determination of the enantiomeric yield of *trans*-2,3-dimethyloxirane (formed by asymmetric epoxidation of *trans*-2-butene with 'Mo·PLA'] on nickel(II) bis[3-heptafluorobutanoyl)-(1*R*)-camphorate) (0.12 *M* in squalane) at 60 °C [14]. ee = 55.0% (at −20 °C). Column: 70 m × 0.5 mm nickel capillary, carrier: 3.0 ml/min N_2.

a contradiction in terms of the structural data, which reveal a very strong equatorial (2.07 Å), but a weak axial (2.36 Å) bond of the DMLA ligand in the molybdenum(VI) (oxo-diperoxo) complex [4]. In regard to enantioselectivity, it should be mentioned that also monodentate chiral ligands have recently been shown to exert relatively low prochiral recognition of alkenes. The mechanism of the oxygen transfer from the molybdenum(VI) (oxo-diperoxo) complex to the olefin remains in doubt [9]. On the basis of the Modena mechanism [17] the olefin is not coordinated to the molybdenum(VI) (oxodiperoxo) reagent at all, but is directly oxidized by electrophilic attack of the peroxo group, in analogy to the epoxidation of alkenes with peroxo acids [18].



A third mechanism, advanced by Sheldon, involves molybdenum-diol complexes, in which the diol originates from the epoxide formed [19].

Unfortunately, the results of the asymmetric epoxidation obtained here are currently inadequate to differentiate between either of these mechanistic proposals. For those cases in which the ee remained constant during the course of the epoxidation reaction, it was concluded that the formation of the oxirane is induced asymmetrically (absence of kinetic resolution of the oxirane), and that only one peroxo group is involved in the oxidation. Attempts to recycle the molybdenum(VI)

Table 1

Enantiomeric excess (ee) [a] of (2*R*,3*R*)-*trans*-2,3-dimethyloxirane formed in the stoichiometric asymmetric epoxidation of *trans*-2-butene with molybdenum(VI) (oxo-diperoxo) reagents **1** at different temperatures in nitromethane.

Reagent	ee (%) [b] at 23 °C	ee (%) [b] at 0 °C	ee (%) [b] at −20 °C
$MoO(O_2)_2$·DMLA	28.0	20.6	18.6
$MoO(O_2)_2$·PLA	25.6	22.4	15.4
'Mo·PLA'	48.6	53.0	55.0
$MoO(O_2)_2$·HBPA	11.2	6.9	–
$MoO(O_2)_2$·AcPro	3.0	2.5	–
$MoO(O_2)_2$·BzPro	3.4	1.2	–
$MoO(O_2)_2$·DMPLA	40.2	22.2	–
	after 20 min	after 2 h	
	17.2	16.8	
	after 20 h	after 26 h	
$MoO(O_2)_2$·HMPPA	22.2	14.7	–
	after 30 min		
	12.7		
	after 6 h		
$MoO(O_2)_2$·HMBPA	20.6	12.6	–
	after 30 min		
	16.8		
	after 6 h		

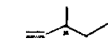
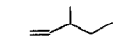
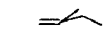
[a] Unless stated otherwise, the ee values remained constant during the entire reaction period (10 min–10 h). Error in ee: ±2% (by complexation gas chromatography).
[b] After 20 min.
$MoO(O_2)_2$·DMLA 53 °C: ee 27.9%
$MoO(O_2)_2$·DMLA 38 °C: ee 31.2%
$MoO(O_2)_2$·DMLA 70 °C: no oxirane detectable
$MoO(O_2)_2$·PLA 38 °C: ee 26.3%
$MoO(O_2)_2$·PLA 53 °C: ee 27.0%

(oxo-diperoxo) reagents, without isolation, for use in consecutive asymmetric epoxidations, by re-oxidation with H_2O_2 failed.

In Table 2 are compared the asymmetric epoxidations of various prochiral (and chiral) alkenes with $MoO(O_2)_2$ · DMLA and 'Mo · PLA' at 23 °C. The enantiomeric yield of the oxiranes is dependent on the degree of alkyl substitution at the double bond of the prochiral olefins. The asymmetric induction decreases in the order propene > 1-butene > 3-methyl-1-butene [3] with the preferential formation of (*R*)-alkyloxiranes. But ee increases with inversion of prochiral recognition for dimethyl-1-butene, resulting in the preferential formation of (*S*)-t-butyloxirane. *Trans*-2-butene undergoes higher asymmetric induction than does *trans*-2-pentene, whereby (2*S*,3*S*)-*trans*-2-methyl/ethyl-3-methyloxiranes are preferentially formed. The asymmetric epoxidation of *cis*-2-pentene, containing a *re*- and *si*-prochiral center, respectively, leads to the preferential formation of (2*S*,3*R*)-2-ethyl-3-methyloxirane. Geminal ethyl/methyl-disubstitution at the double bond in 2-methyl-1-butene shows no enantiofacial discrimination and, consequently, only racemic 2-ethyl-2-methyloxirane is formed. Trisubstitution at the double bond in 2-methyl-2-butene leads only to modest enantioselectivity.

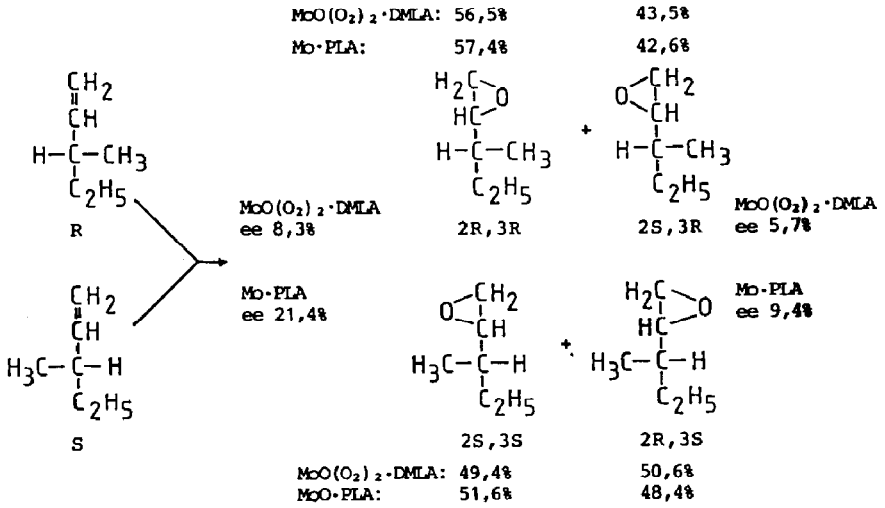
Table 2

Enantiomeric [c] composition and absolute configuration of oxiranes formed in excess in the stoichiometric asymmetric epoxidation of aliphatic alkenes with $MoO(O_2)_2$·DMLA and 'Mo·PLA' in nitromethane at 23° C.

Alkene	$MoO(O_2)_2$·DMLA ee%	'Mo·PLA' ee%
	32.1 (*R*)	42.1 (*R*)
	27.4 (*R*)	31.4 (*R*)
	– [a]	– [a]
	34.5 (*S*)	31.5 (*S*)
	6.3 (*R*) [b]	9.6 (*R*) [b]
	11.8 (2*S*,3*R*)	23.2 (2*S*,3*R*)
	24.3 (*R*,*R*)	40.0 (*R*,*R*)
 rac	8.3 (2*R*,3*R*) 5.7 (2*R*,3*S*)	21.4 (2*R*,3*R*) 9.4 (2*S*,3*R*)
 s	50.6% (2*S*,3*S*) [d] 49.4% (2*R*,3*S*)	51.1% (2*S*,3*S*) [d] 48.9% (2*R*,3*S*)
	28.0 (*R*,*R*)	48.6 (*R*,*R*)
	0 [e]	– [e]

[a] No oxirane detectable. [b] $MoO(O_2)_2$·DMLA at 0° C: ee 7%; 'Mo·PLA' at −5° C: ee 8.8%. [c] Reaction at 0° C, at 23° C no oxirane detectable after 30 min. [d] Diastereomeric ratio in %. [e] Error in ee: ±2% (by complexation gas chromatography).

The diastereoselectivity of $MoO(O_2)_2$ · DMPLA and 'Mo · PLA' towards chiral alkenes was tested with the substrate 3-methyl-1-pentene. Epoxidation of the racemic alkene leads to two pairs of enantiomeric diastereoisomers. The diastereoselectivity is very low for the (*S*)-olefin. The (*R*)-olefin, however, gave predominantly the (2*R*,3*R*)-configuration oxirane. The ratio of the pairs of diastereomers is almost the same as in the case of $MoO(O_2)_2$ · DMLA, while for 'Mo · PLA' the diastereomers originating from the (*R*)-olefin are formed in preponderance as the result of kinetic resolution of the alkene. When enantiomerically pure (*S*)-3-methyl-1-pentene [20] was used (cf., Table 1) the diastereomeric ratio of the oxiranes was again found to be nearly 1 : 1.



The stoichiometric epoxidation of simple prochiral olefins with chiral molybdenum(VI) (oxodiperoxo) reagents can also be performed preparatively. Thus, reaction of equimolar amounts of *trans*-stilbene and molybdenum(VI) (oxo-diperoxo)-(*S*)-lactic acid piperidineamide, $MoO(O_2)_2 \cdot$ PLA, in dichloromethane for 15 h

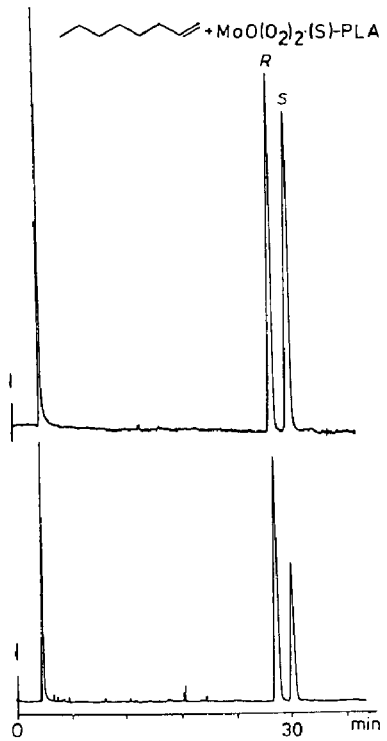


Fig. 3. Complexation-gas-chromatographic determination of the enantiomeric yield of (*R*)-1,2-epoxyoctane (formed by preparative asymmetric epoxidation of 1-octene with $MoO(O_2)_2$·(S)-PLA) on manganese(II) bis[3-(heptafluorobutanoyl)-(1R)-camphorate] (0.125 *M* in OV 101) at 70 °C. ee = 27% (at 22 °C). Column: 40 m×0.25 mm glass capillary, carrier: 1 bar N_2. (Top: racemic sample; bottom: asymmetrically formed product).

Table 3

Enantiomeric composition and absolute configuration of oxiranes formed in excess in the stoichiometric asymmetric epoxidation of aliphatic alkenes with molybdenum(VI) (oxo-diperoxo) reagents **1** in the presence of equivalent additives in nitromethane at 23° C.

Reagent	Equivalents of additive	Alkene	ee (%)
$MoO(O_2)_2$·PLA	1 DMF	*trans*-2-Butene	25.3 (*R*)
$MoO(O_2)_2$·PLA	2 DMF	*trans*-2-Butene	17.8 (*R*)
$MoO(O_2)_2$·PLA	1 *S*-PLA	*trans*-2-Butene	25.8 (*R*)
$MoO(O_2)_2$·PLA	1 *S*-1,2-Propanediol	*trans*-2-Butene	52.2 (*R*)
$MoO(O_2)_2$·PLA	1 2*S*,3*S*-Butanediol	*trans*-2-Butene	93.2 (*R*)
$MoO(O_2)_2$·PLA	2 2*S*,3*S*-Butanediol	*trans*-2-Butene	76.8 (*R*)
$MoO(O_2)_2$·PLA	1 2*R*,3*R*-Butanediol	*trans*-2-Butene	89.8 (*S*)
$MoO(O_2)_2$·PLA	1 *S*-3-Methyl-pentane-1-ol	*trans*-2-Butene	30.0 (*R*)
$MoO(O_2)_2$·PLA	1 2*S*,3*S*-3-Methyl-1,2-pentanediol	*trans*-2-Butene	23.4 (*R*)
$MoO(O_2)_2$·PLA	1 *S*-3-Methyl-1,2-butanediol	*trans*-2-Butene	28.0 (*R*)
$MoO(O_2)_2$·PLA	1 *R*-3,3-Dimethyl-1,2-butanediol	*trans*-2-Butene	0
$MoO(O_2)_2$·PLA	1 *S*-1,3-Butanediol	*trans*-2-Butene	19.4 (*R*)
$MoO(O_2)_2$·PLA	1 2*S*,3*S*-Butanediol + 1 DMF	*trans*-2-Butene	59.2 (*R*)
$MoO(O_2)_2$·BzPro	1 2*S*,3*S*-Butanediol	*trans*-2-Butene	83.6 (*R*)
$MoO(O_2)_2$·DMLA	1 2*S*,3*S*-Butanediol	*trans*-2-Butene	75.6 (*R*)
$MoO(O_2)_2$·DMLA	1 2*S*,3*S*-Butanediol + 1 DMF	*trans*-2-Butene	56.4 (*R*) (after 14 h) 75.2 (*R*) (after 48 h)
$MoO(O_2)_2$·DMLA	1 2*R*,3*R*-Diethyl-tartrate	*trans*-2-Butene	22.6 (*R*)
$MoO(O_2)_2$·HMPT	1 2*S*,3*S*-Butanediol	*trans*-2-Butene	59.6 (*R*)
$MoO(O_2)_2$·PLA	1 2*S*,3*S*-Butanediol	*trans*-2-Pentene	95.4 (*R*)
$MoO(O_2)_2$·PLA	1 2*S*,3*S*-Butanediol	1-Butene	> 70 (*R*)

at 22° C led to a 55% yield (isolated) of trans-(2*R*,3*R*)-diphenyloxirane showing $[\alpha]_D^{20}$ +115.7° (*c*, 1.1 benzene) (lit. [21] $[\alpha]_D^{20}$ +357° (c, 0.59 benzene, ee = 95%)), corresponding to an optical purity, *p*, of 31%. Extension of the reaction time did not change the optical yield, but drastically reduced the chemical yield (after 24 h: 49%; after 40 h: no oxirane detected). The preparative asymmetric epoxidation of 1-octene with molybdenum(VI) (oxo-diperoxo)-(*S*)-lactic acid piperidineamide, $MoO(O_2)_2$ · PLA, in dichloromethane for 13 h at 22° C gave (*R*)-1,2-epoxyoctane in 53% yield (isolated), with an ee of 27% (cf. Fig. 3).

Rearrangements of oxiranes which can take place in the presence of Lewis acids to give ketones or aldehydes diminish the chemical yield in the epoxidation reaction, and can be minimized by the addition of amides to molybdenum(VI) (oxo-diperoxo) reagents **1** [22]. We have found that the addition of one equivalent DMF or PLA to the reaction mixture did not affect the enantiomeric yield in the asymmetric epoxidation of *trans*-2-butene, whereas an excess of DMF significantly lowers the asymmetric induction (cf. Table 3). These Lewis bases probably compete with the olefin for coordination sites on molybdenum or replace the chiral ligand.

Very high enantiomeric excesses (ee) for the oxiranes were found when enantiomerically pure 1,2-alkanediols were added to the epoxidation reagent molybdenum(VI) (oxo-diperoxo)-(*S*)-lactic acid piperidineamide, $MoO(O_2)_2$ · PLA (cf. Table 3, Fig. 4).

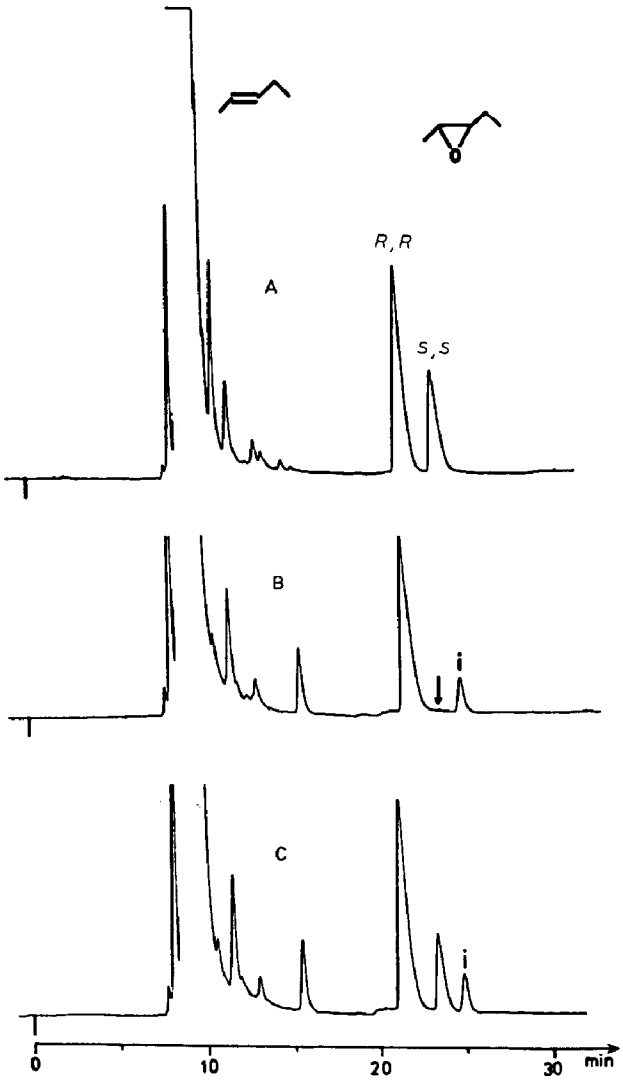


Fig. 4. Complexation-gas-chromatographic determination of the enantiomeric yield of (2*R*,3*R*)-*trans*-2-ethyl-3-methyloxirane (formed by the reaction of *trans*-2-pentene with $MoO(O_2)_2 \cdot (S)$-PLA/(2*S*,3*S*)-butanediol (1 : 1)) on nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] (0.125 *M* in OV 101) at 70 °C. Column: 40 m × 0.25 mm glass capillary, carrier: 1 bar N_2. (Top: after 30 min; center: after 14 h, ee = 95.4% (integrated); bottom: after 15 h, with added racemic oxirane for peak-identification; i = unidentified impurity formed during the reaction).

The enantiomeric composition of the oxiranes increased with time and reached a maximum after 12–16 h. The chirality of the added diol exclusively determines the chirality of the oxirane enantiomers formed in excess. Previous investigations have shown [5,23] that equimolar mixtures of molybdenum(VI) (oxo-diperoxo) reagents **1** and chiral 1,2-alkane diols represent a very efficient catalytic system for the kinetic resolution of simple oxiranes such as methyloxirane, *trans*-2,3-dimethyloxirane, epichlorohydrin or phenyloxirane. The present results indicate that the molybdenum(VI) (oxo-diperoxo) reagents **1** epoxidize alkenes into oxiranes which

subsequently undergo kinetic resolution by an efficient molybdenum-diol catalyst of unknown structure.

Experimental

(S)-N,N-Dimethyl lactamide (DMLA)

This amide was prepared from (*S*)-ethyl lactate by a previously published procedure [24].

(S)-Piperidine lactamide (PLA)

A solution containing 118.1 g (1 mol) (*S*)-ethyl lactate (Fluka AG, Buchs, Switzerland) (ee = 94.6%, by GC) in 200 ml methanol was treated with 135 g (1.6 mol) piperidine. The mixture was stirred for 7 days at 20 °C, concentrated and distilled. Yield: 43.7 g (28%); b.p. 86 °C/0.2 torr. α_D^{20} −8.3° (neat), $[\alpha]_D^{20}$ −3.5° (*c*, 2 $CHCl_3$). MS: *m/e* 157 (M^+; 69 (100%)). ^{13}C NMR ($CDCl_3$): 172.8, 63.6, 45.4, 43.1, 25.7, 25.1, 24.0, 21.1 ppm.

(S)-N,N-Dimethyl-3-phenyl lactamide (DMPLA)

a. Ethyl ester: A mixture of 8.3 g (50 mmol) (*S*)-3-phenyl-lactic acid, 20 ml ethanol, 150 ml chloroform and 0.5 g ion exchanger (Dowex 50WX8) was refluxed in a water separator for two days. The ion exchanger was filtered off and the residue was distilled in vacuo. Yield: 8.5 g (88%), b.p. 92 °C/0.04 torr. The distillate crystallized in the refrigerator (m.p. 48 °C). ^{13}C NMR ($CDCl_3$): 173.9. 136.3, 129.3, 128.1, 126.6, 71.1, 61.4, 40.5, 14.0 ppm.

b. Amide: A solution of 6.0 g (30.9 mmol) of the ester in 10 ml methanol, was treated with 7 ml dimethylamine. The mixture was stirred for three days at 20 °C, concentrated, and chromatographed on silica (ethyl acetate). Yield: 5.2 g (87%), m.p. 66 °C. $[\alpha]_D^{20}$ 37.3° (*c*, 2 EtOH). ^{13}C NMR ($CDCl_3$): 173.4, 136.8, 129.1, 128.2, 126.5, 68.8, 41.8, 36.1, 35.6 ppm.

(S)-2-Hydroxy-3-methylbutanoic acid piperidineamide (HMBPA)

A solution containing 5.0 g (34.2 mmol) (*S*)-ethyl 2-hydroxy-3-methylbutanoate in 40 ml ethanol was treated with 17.1 g (0.34 mol) hydrazine hydrate at 0 °C. The mixture was stirred for 12 h at 5 °C, then concentrated, and treated with diethyl ether. The hydrazide formed was recrystallized from ethanol/ether. Yield: 3.8 g (84%). m.p. 141 °C. $[\alpha]_D^{20}$ −68.0° (*c*, 1.5 EtOH).

A suspension containing 1.57 g (11.9 mol) of the hydrazide in 10 ml of a 2.9 *N* hydrochloric acid/tetrahydrofuran solution, was treated with 1.5 g (14.5 mmol) of t-butylnitrite at −25 °C. The mixture was stirred for 20 min until the solution became clear, then 100 ml cold ethyl acetate was added, the mixture was washed separately with $NaHCO_3$ and NaCl solutions at low temperature, and dried over sodium sulfate. The azide solution was then treated at −20 °C with 2.0 g (23.5 mmol) of piperidine. After stirring for 20 h at 0 °C the mixture was treated with ethyl acetate and washed separately with citric acid, $NaHCO_3$ and NaCl solutions at low temperature, and dried over sodium sulfate. The concentrated residue was purified by chromatography on silica (ethyl acetate-petroleum ether 60/90, 2 : 3).

Yield: 1.7 g (77%), colorless oil. MS: *m/e* 185(M^+; 113 (100%)). ^{13}C NMR ($CDCl_3$): 172.0, 71.8, 61.4, 44.7, 31.3, 29.6, 28.9, 24.1, 19.4, 14.6 ppm.

(2S,3S)-2-Hydroxy-3-methylpentanoic acid piperidineamide (HMPPA)

A solution containing 5.0 g (31.2 mmol) (2*S*,3*S*)-ethyl 2-hydroxy-3-methylpentanoate in 40 ml ethanol was treated with 15.6 g (0.31 mol) hydrazine hydrate at 0 °C. Yield (after work-up (vide supra)): 1.6 g (78%). MS: *m/e* 199(M^+; 55 (100%)). ^{13}C NMR ($CDCl_3$): 172.2, 61.6, 44.7, 38.5, 29.7, 28.9, 24.2, 22.0, 16.2, 11.7 ppm.

(S)-3-Hydroxybutanoic acid piperidineamide (HBPA)

a. (*S*)-ethyl benzyloxybutanoate. A mixture of 24.0 g (0.18 mol) (*S*)-ethyl 3-hydroxybutanoate and 47.0 g (0.27 mol) benzylbromide in 200 ml diethyl ether was treated with 42.0 g silver oxide [12]. The mixture was distilled and chromatographed on silica (dichloromethane, petroleum ether 60/90, 2 : 3) and redistilled. Yield: 12.5 g (31%). b.p. 98 °C, 0.04 torr. ^{13}C NMR ($CDCl_3$): 171.5, 138.5, 128.3, 127.6, 72.0, 70.8, 60.4, 42.1, 19.8, 14.1 ppm.

b. (*S*)-3-Benzyloxybutanoic acid piperidineamide. A solution containing 8.0 g (36 mmol) of the ester in 60 ml ethanol was treated with 18 g (0.36 mol) hydrazine hydrate for 12 h at 0 °C. The mixture was concentrated and chromatographed on silica (benzene-chloroform-methanol-water, 40 : 40 : 40 : 5). Yield: 4.9 g (65%). A suspension of the hydrazide (2.5 g, 12 mmol) in 10 ml of a 2.9 *N* hydrochloric/tetrahydrofuran solution was treated with 1.6 g (15.5 mmol) of t-butylnitrite at −30 °C. The mixture was stirred for 20 min, then 100 ml cold ethyl acetate was added, and the mixture was washed separately with $NaHCO_3$ and NaCl solutions at low temperature, and dried over sodium sulfate. To the filtered solution was added 2.0 g (23.5 mmol) piperidine at −20 °C. The mixture was stirred for 20 h at 0 °C. Yield (after work-up (vide supra)): 2.2 g (70%), colorless oil. ^{13}C NMR ($CDCl_3$): 169.3, 138.6, 128.1, 127.6, 127.3, 72.8, 70.9, 61.5, 44.7, 40.4, 29.7, 28.9, 24.3, 20.0 ppm.

c. (*S*)-3-Hydroxybutanoic acid piperidineamide. A solution containing 3 g (11.5 mmol) of the protected amide in 50 ml methanol and 0.5 ml ethyl acetate was hydrogenated over 0.5 g palladium/charcoal. After 6 h the mixture was filtered, concentrated, and distilled. Yield: 1.5 g (76%). b.p. 88 °C/0.05 torr. $[\alpha]_D^{20}$ 17.3° (*c*, 0.7 $CHCl_3$). MS: *m/e* 171 (M^+; 55 (100%)). ^{13}C NMR ($CDCl_3$): 170.6, 64.1, 44.7, 40.4, 29.7, 28.9, 24.1, 22.0 ppm.

(S)-N-Acetylprolinol (AcPro) and (S)-N-benzoylprolinol (BzPro)

a. Prolinol. To an ice-cold suspension of 50 g (1.32 mol) $LiAlH_4$ in 1000 ml dry tetrahydrofuran was added 57.6 g (0.5 mol) (*S*)-proline in portions. The mixture was refluxed for 72 h. The precipitate, obtained after hydrolysis (170 ml water), was extracted with tetrahydrofuran for 48 h in a Soxhlet apparatus. The prolinol was distilled. Yield: 30 g (59%) b.p. 107 °C/0.06 torr. $[\alpha]_D^{20}$ 3.3° (*c*, 4 methanol). ^{13}C NMR ($CDCl_3$): 63.0, 59.0, 45.0, 26.4, 24.3.

b. (*S*)-*N*-Acetylprolinol [25]. To 5.0 g (49.4 mmol) of (*S*)-prolinol was added 5.0 g (49 mmol) acetanhydride at such a rate as to keep the temperature at 50 °C. Afterwards the mixture was heated to 65 °C and stirred for 1 h and then distilled. Yield: 5.1 g (72%) b.p. 107 °C/0.06 torr. $[\alpha]_D^{20}$ −68.5° (*c*, 3 methanol). ^{13}C NMR

($CDCl_3$): 174.5, 174.2, 66.4, 65.7, 63.6, 62.7, 52.2, 51.7, 31.3, 30.6, 27.2, 25.2, 24.6 ppm.

c. (*S*)-*N*-Benzoylprolinol. To a mixture of 5.0 g (49.4 mmol) of (*S*)-prolinol and 5.0 g (49.4 mmol) triethylamine in 100 ml chloroform was added dropwise 7.0 g (49.8 mmol) benzoyl chloride at −10 °C. The mixture was stirred for 12 h at 0 °C, then diluted with chloroform, and washed separately with citric acid, $NaHCO_3$ and NaCl solutions, and dried over sodium sulfate. Yield (after work-up): 8.9 g (88%), colorless oil. ^{13}C NMR ($CDCl_3$): 171.3, 136.5, 129.7, 127.9, 126.7, 65.5, 60.4, 50.7, 27.8, 24.5 ppm.

General procedure for the preparation of molybdenum(VI) (oxo-diperoxo) complexes:

N.B. *The necessary care should be taken when preparing and handling peroxometal compounds, although we are not aware of any reports on violent decompositions of molybdenum(VI) (oxo-diperoxo) compounds at normal conditions.*

To a 5-ml aqueous hydroperoxide solution (30%) was added, in portions, 1.0 g molybdenum(VI) oxide at 20 °C. The mixture was stirred at 20 °C for 20 min and at 40 °C for 4 h. After most of the molybdenum oxide had dissolved the mixture was filtered. The yellow solution was treated at 10 °C with one equivalent of ligand dissolved in approx. 4 ml methanol. The mixture was stirred for 30 min at 20 °C, concentrated, and kept 12 h at 0 °C. When the complex did not crystallize after addition of dichloromethane or benzene, the mixture was diluted with ethanol and carefully (!) (shield protection) concentrated on a rotary evaporator. This procedure was repeated five times. The mixture was then further concentrated. The complex is usually obtained as a yellow, microcrystalline powder. But if it is obtained as an oil, the addition of diethyl ether with stirring at 5 °C yields a yellow powder. The complexes were washed with diethyl ether and dried in vacuo.

Warning: Fast and complete concentration of the reaction mixture may lead to deflagration of the complexes. All complexes prepared decompose at temperatures above 100 °C, some violently, changing color from yellow to blue and black. The complexes were stored at 5 °C in < 0.5 g portions.

Molybdenum(VI) (oxo-diperoxo)-(S)-N,N-dimethyl lactamide, $MoO(O_2)_2 \cdot DMLA$. 2.5 g (17.4 mmol) MoO_3, 12.5 ml H_2O_2, 2.04 g (17.4 mmol) DMLA. Yield: 3.6 g (71%) lemon-yellow powder. $[\alpha]_D^{20}$ −27.5° (*c*, 1.8 H_2O). Anal. Found: C, 20.21; H, 4.20; N, 5.00. $C_5H_{11}MoNO_7$ (293.08) calc: C, 20.94; H, 3.78; N, 4.77%.

Molybdenum(VI) (oxo-diperoxo)-(S)-lactic acid piperidineamide, $MoO(O_2)_2 \cdot PLA$. 0.75 g (5.2 mmol) MoO_3, 3.8 ml H_2O_2, 0.82 g (5.2 mmol) PLA. Yield: 1.0 g (58%) yellow powder. $[\alpha]_D^{20}$ −4.8° (*c*, 0.7 methanol). Anal. Found: C, 29.03; H, 4.81; N, 4.52. $C_8H_{15}MoNO_7$ (333.15) calc: C, 28.84; H, 4.54; N, 4.20%. From the mother liquor was isolated 0.3 g 'Mo · PLA' at −3 °C after some time. Anal. Found: C, 25.87; H, 4.20; N, 3.74%.

Molybdenum(VI) (oxo-diperoxo)-(S)-N,N-dimethyl-3-phenyl-lactamide, $MoO(O_2)_2 \cdot DMPLA$. 0.75 g (5.2 mmol) MoO_3, 3.8 ml H_2O_2, 1.0 g (5.2 mmol) DMPLA. Yield: 1.2 g (63%) pale-yellow powder. $[\alpha]_D^{20}$ +6.9° (*c*, 1 H_2O). Anal. Found: C, 35.69; H, 4.77; N, 3.83. $C_5H_{11}MoNO_7$ (369.18) calc: C, 35.79; H, 4.10; N, 3.79%.

Molybdenum(VI) (oxo-diperoxo)-aquo-(S)-3-hydroxybutanoic acid piperidineamide, $MoO(O_2)_2 \cdot H_2O \cdot HBPA$. 0.38 g (2.6 mmol) MoO_3, 2.0 ml H_2O_2, 0.45 g (2.6 mmol) HBPA. Yield: 0.4 g (42%) pale-yellow powder. $[\alpha]_D^{20}$ +12.7° (*c* 0.6 methanol). Anal.

Found: C, 29.43; H, 4.81; N, 3.85. $C_9H_{19}MoNO_8$ (365.19) calc: C, 29.60; H, 5.24; N, 3.84%.

Molybdenum(VI) (oxo-diperoxo)-(2S,3S)-2-hydroxy-3-methyl-pentanoic acid piperidineamide, $MoO(O_2)_2$HMPPA. 0.38 g (2.6 mmol) MoO_3, 2.0 ml H_2O_2, 0.52 g (2.6 mmol) HMPPA. Yield: 0.5 g (51%) yellow powder. $[\alpha]_D^{20}$ $-3.8 \pm 0.5°$ (*c*, 0.6 methanol). Anal. Found: C, 35.12; H, 5.66; N, 3.57. $C_{11}H_{21}MoNO_7$ (375.23) calc: C, 35.21; H, 5.64; N, 3.73%.

Molybdenum(VI) (oxo-diperoxo)-(S)-2-hydroxy-3-methyl butanoic acid piperidineamide, $MoO(O_2)_2 \cdot$ HMBPA. 0.38 g (2.6 mmol) MoO_3, 2.0 ml H_2O_2, 4.9 g (2.6 mmol) HMBPA. Yield: 0.4 g (42%) yellow powder. $[\alpha]_D^{20}$ $-11.1°$ (*c*, 0.7 methanol). Anal. Found: C, 32.77; H, 5.27; N, 3.56. $C_{10}H_{19}MoNO_7$ (361.20) calc: C, 33.25; H, 5.30; N, 3.88%.

Molybdenum(VI) (oxo-diperoxo)-(S)-N-acetylprolinol, $MoO(O_2)_2 \cdot$ AcPro. 0.42 g (5.2 mmol) MoO_3, 2.0 ml H_2O_2, 0.42 g (2.9 mmol) AcPro. Yield: 0.6 g (64%) pale-yellow powder. $[\alpha]_D^{20}$ $-32.3°$ (*c* 0.5 methanol). Anal. Found: C, 26.43; H, 4.21; N, 4.40. $C_7H_{13}MoNO_7$ (319.12) calc: C, 26.34; H, 4.11; N, 4.39%.

Molybdenum(VI) (oxo-diperoxo)-(S)-N-benzoylprolinol, $MoO(O_2)_2 \cdot$ BzPro. 0.78 g (5.4 mmol) MoO_3, 3.9 ml H_2O_2, 1.1 g (5.4 mmol) BzPro. Yield: 1.6 g (78%) lemon-yellow powder. $[\alpha]_D^{20}$ $-70.7°$ (*c*, 0.5 methanol). Anal. Found: C, 37.35; H, 4.15; N, 3.98. $C_{12}H_{15}MoNO_7$ (381.19) calc: C, 37.81; H, 3.97; N, 3.67%.

Asymmetric epoxidation

The appropriate care should be taken when handling oxiranes.

Absolute configurations of oxiranes were assigned chromatographically by coinjection of optically active standards of established stereochemistry, that had been prepared separately [5]. The ee of the oxiranes were not corrected for any insufficient enantiomeric purity of the molybdenum(VI) ligands. Thus, the optimal ee might be higher in some instances.

a. Analytical procedure: Approximately 0.1 mmol molybdenum(VI) (oxo-diperoxo) complex was suspended in 3 ml nitromethane at 23°C and 1 bar in a 'head-space' vial, sealed with silicone rubber. After injection of 1 mmol alkene, the suspension became homogeneous. The enantiomeric composition of the oxirane formed was determined by complexation gas chromatography on nickel(II) bis[3-(heptafluorobutanoyl)-(1*R*)-camphorate] [14].

b. Preparative procedure: To a solution containing 1–2 g of the molybdenum(VI) (oxo-diperoxo) reagent in 400 ml dichloromethane was added an equimolar amount of the olefin, and the mixture was stirred for 12 h at 22°C. The reaction was quenched by flash chromatography over silica. The silica was washed thoroughly with dichloromethane, and the oxirane was isolated by distillation.

A mixture of 1 g (5.6 mmol) *trans*-stilbene, 1.87 g (5.6 mmol) molybdenum(VI) (oxo-diperoxo)-(*S*)-lactic acid piperidineamide, $MoO(O_2)_2 \cdot$ PLA in 400 ml dichloromethane with 15-h stirring yielded 0.6 g (55%) *trans*-(2*R*,3*R*)-diphenyloxirane $[\alpha]_D^{20}$ $+115.7°$ (*c*, 1.1 benzene) (lit [21] $[\alpha]_D^{20}$ $+357°$ (*c*, 0.59 benzene, ee = 95%)) corresponding to an optical purity, *p*, of 31%.

A mixture of 1 g (8.77 mmol) 1-octene, 2.92 g (8.77 mol) molybdenum(VI) (oxo-diperoxo)-(*S*)-lactic acid piperidineamide, $MoO(O_2)_2 \cdot$ PLA in 400 ml dichloromethane with 13-h stirring yielded 0.6 g (53%) (*R*)-1,2-epoxyoctane $[\alpha]_D^{20}$ $+3.85°$ (*c*, 1.04 benzene); ee = 27% (by complexation gas chromatography).

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