COMMUNICATION

Stereospecific and regioselective catalytic epoxidation of alkenes by a novel ruthenium(II) complex under aerobic conditions

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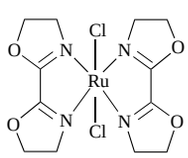
Epoxidation of alkenes by molecular oxygen is effected in high yields by catalysis of $RuCl_2(biox)_2$ using isobutyraldehyde as the co-reductant: the reaction is stereospecific and regioselective.

There has been considerable interest in recent years in both the homogeneous transition metal-catalysed epoxidation of alkenes[1] and in the use of oxoruthenium complexes as catalysts for organic oxidations.[2] With regard to aerobic oxidation catalysed by transition metal complexes several reactions involving the combined use of molecular oxygen with reducing agents have been reviewed.[3] The combination of three components, that is, a transition metal, organic ligands and a reductant is considered to create an effective oxygenation system for such aerobic reactions.

In 1985, Groves and Quinn reported a successful aerobic epoxidation of olefins with a ruthenium–porphyrin catalyst.[4] All the other epoxidations catalysed by ruthenium complexes involved the use of $NaIO_4$ or PhIO as the terminal oxidants under biphasic conditions.[5] Nishiyama *et al.*[6] used dichlorobis(oxazolinyl)bipyridylruthenium(II) complex for the oxidation of alkenes in the presence of PhIO and found oxidative cleavage as the major pathway, while Barf *et al.* reported the epoxidation of alkenes with a combination of (bipyridyl)$RuCl_2$-$(DMSO)_4$ and *tert*-butylhydroperoxide.[7]

C_2-symmetric 4,4′,5,5′-tetrahydro-2,2′-bisoxazoles have been used as ligands in catalytic asymmetric transfer hydrogenation of ketones.[8] Prior to achieving enantioselectivity in epoxidation with ruthenium complexes it is essential to find conditions in favour of epoxidation rather than oxidative cleavage. Drago has demonstrated that in general *trans*-dioxoruthenium complexes catalysed oxidation of alkenes to yield epoxides while the *cis*-isomers mediate oxidative cleavage.[9] The aim of the present work is to use bisoxazoles as bidentate ligands so that they form a square planar structure around the ruthenium core, analogous to ruthenium–porphyrin systems.[4] Accordingly, ruthenium–bisoxazole complex **1** was synthesized[10] and our successful results of an oxo-transfer reaction with **1** are presented in this communication.



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In the preliminary investigations of oxidation of alkenes with **1**, PhIO, $NaIO_4$, urea–H_2O_2, NaOCl and TBHP were used as terminal oxidants. In all cases the reaction was incomplete (30–50% conversion) and the product was always a mixture of epoxides and cleavage products. However, when the oxidation of alkenes was carried out with **1** (2.5 mol%) in CH_2Cl_2 (25 °C, 6–12 h) in the presence of molecular oxygen as the oxidant and isobutyraldehyde as the co-reductant excellent yields of epoxides **2**–**21** were obtained. The results are summarized in Table 1.

As can be gauged from Table 1 this catalytic epoxidation with **1** is highly stereospecific. Thus, *trans*-stilbene **2** and *cis*-stilbene **4** under the reaction conditions afford the *trans*-stilbene oxide **3** and *cis*-stilbene oxide **5** respectively in high yields. Styrene epoxide **11** which is highly unstable under conditions of peracid epoxidation is quite stable under the present reaction conditions. Another salient feature of the present methodology is the high regioselectivity. Thus in the oxidation of 4-vinylcyclohexene **16** and limonene **18** catalysed by **1**, the monoepoxides **17** and **19** respectively were the exclusive products isolated in very good yields. A more dramatic example of stereoselectivity is illustrated in the epoxidation of cholest-5-ene **20**. Under conditions of catalytic epoxidation the 5β,6β-epoxide **21A** is obtained in excess of 94% selectivity and in excellent yields.

Thus we have developed a non-porphyrin ruthenium(II) system which catalyses the epoxidation of alkenes under aerobic conditions with great efficiency. The reaction is stereospecific and regioselective and this kind of high stereospecificity and regioselectivity has not been reported with other catalytic epoxidation methodologies.[5–7] Since C_2-symmetric bisoxazoles can be easily derived from optically active amino alcohols, chiral ruthenium complexes are readily accessible and studies of catalytic asymmetric epoxidation of unfunctionalized alkenes with these systems are under progress.

Experimental

Synthesis of complex 1

trans-Tetrakis(acetonitrile)dichlororuthenium(II)[11] (0.336 g, 1 mmol) was refluxed with 4,4′,5,5′-tetrahydro-2,2′-bisoxazole (0.308 g, 2.2 mmol) for 6 h in ethanol (10 ml). The solvent was removed under reduced pressure to give a red coloured solid. The solid was recrystallized from EtOH–Et_2O (1 : 3) and stored in a desiccator; mp 280 °C (uncorrected); ν_{max}(thin film)/cm^{-1} 2950, 1610; δ_H(90 MHz, D_2O) 3.4 (m, 8H), 3.8 (m, 8H); δ_C(22.5 MHz, D_2O) 53.61, 68.87, 155.26 (Calc. for $C_{12}H_{16}Cl_2N_4O_4Ru$: C, 31.86; H, 3.56; N, 12.38. Found: C, 31.81; H, 3.48; N, 12.40%).

Typical experimental procedure for epoxidation

Ruthenium complex **1** (2.5 mol%) was added to the alkene (1 mmol) dissolved in dichloromethane (4 ml). To this homogeneous solution $NaHCO_3$ (1.5 equiv.) and isobutyraldehyde (1.5 equiv.) were added. The mixture was stirred under an atmosphere of oxygen at 25 °C and the reaction was monitored by TLC. Once the reaction was over, the reaction mixture was diluted with CH_2Cl_2 and filtered through a pad of Celite and silica gel. Removal of solvent yielded the crude product which was purified by flash chromatography over neutral alumina or distillation under reduced pressure.

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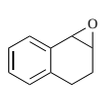
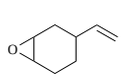
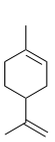
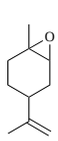
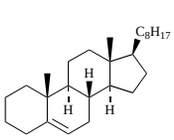
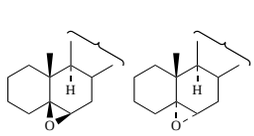
Table 1 Epoxidation of alkenes catalysed by $RuCl_2(biox)_2$

Entry	Substrate	Reaction time/h	Product	Yield[a] (%)
1	 **2**	8	 **3**	95
2	 **4**	10	 **5**	88
3	 **6**	9	 **7**	85
4	Undec-1-ene **8**	12	Undec-1-ene oxide **9**	100[b]
5	 **10**	8	 **11**	85
6	 **12**	10	 **13**	72
7	 **14**	6	 **15**	100
8	 **16**	10	 **17**	90
9	 **18**	8	 **19**	92
10	 **20**	6	 **21A**[c] **21B**[c]	95

[a] Isolated yields. [b] Yield based on 75% conversion. [c] The ratios were determined by ^1H NMR spectroscopy.

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