

0040-4039(95)01873-5

## Competition between Catalytic Epoxidation and Oxidative Cleavage of *trans*-Stilbene by Ruthenium Complexes Associated with Bidentate Ligands.

C. Augier, L. Malara, V. Lazzeri and B. Waegell\*.

Laboratoire de stéréochimie, associé au CNRS, Faculté des Sciences St-Jérôme, Case 532, av. Escadrille Normandie-Niemen, F-13397 Marseille Cedex 20, France.

**Abstract :** Bidentate ligands featuring two different nitrogen heterocycles (pyridine, oxazoline, oxazolidine and thiophene) directly linked together or separated by a spacer, have been prepared and used as ruthenium ligands to epoxidize *trans*-stilbene and to study the competition between this reaction and oxidative cleavage of the double bond.

There has been considerable interest devoted to the reactivity of oxometal species in biological processes<sup>1</sup>, especially as for as hydroxylation of carbon-hydrogen bonds and epoxidations of double bonds are concerned. Catalytic and enantioselective epoxidation of double bonds undoubtedly present a stimulating challenge for organic synthesis and homogeneous catalysis<sup>2</sup>.

Following our work reported earlier on mechanistic aspects of the oxidation of alkanes with RuO<sub>4</sub> generated *in* situ<sup>3</sup>, we present here preliminary results on the catalytic epoxidation of double bonds with ruthenium complexes associated with non porphyrinic chiral ligands. Balavoine and all.<sup>4</sup> had shown that bipyridine or substituted phenantroline ruthenium complexes catalyse the epoxidation of stilbenes. Furthermore the [RuO<sub>2</sub>(bipy){IO<sub>3</sub>(OH)<sub>3</sub>}] complex<sup>5</sup> could be isolated and its crystal structure was determined. This complex where the ruthenium is associated with a bipyridine ligand is an excellent epoxidation catalyst.



Scheme 1.

As a consequence, it was reasonable to synthesise various chiral bidentate ligands mainly derived from pyridine coupled with oxazolines and oxazolidines with the hope that they would bind to the ruthenium so that to form complexes able to epoxidise double bonds possibly with chirality transfer.

Prior to achieve enantioselectivity with such ruthenium complexes, it is essential to control the epoxidation process relatively to the oxidative cleavage of the double bond which must be avoided or at least minimised. According to the molecular investigations of Drago<sup>6</sup> trans dioxo ruthenium species are able to epoxidize double bonds, whereas oxidative cleavage of the latter will be achieved by the corresponding *cis* isomer (Scheme 1). Although these considerations do not take into account the oxidising or reoxidising reagent (O<sub>2</sub>, H<sub>2</sub>O<sub>2</sub>, NaClO, NaIO<sub>4</sub>), they are supported by experimental results<sup>5</sup> especially those which involve porphyrins as ruthenium ligand<sup>7</sup>.

We have undertaken this work in order to check whether the pairing of bidentate ligands so that to form a square planar structure around the ruthenium core (A in Scheme 1), analogous to what is found in porphyrins<sup>8</sup>, would favour epoxidation reactions via *trans* dioxo ruthenium species. Conversely with bidentate ligands where the two heterocyclic rings are linked by a more important spacer, rather than a single carbon-carbon bond, it should be more difficult to associate such ligands in a *trans* stereo chemistry around the central ruthenium atom<sup>9</sup>. Consequently the formation of the *cis* dioxo ruthenium species (B in Scheme 1) should be favoured and oxidative cleavage of the double bond ought to be the major process.

We have selected *trans*-stilbene as a model of alkene, because it generally gives good yields of epoxide<sup>4,5</sup>, and is not epoxidised in presence of air in absence of any catalysts, as norbornene does<sup>9</sup>.

Ligands have been synthesised according to known procedures<sup>11</sup>. A preliminary systematic study<sup>12</sup> with oxazolines had shown that with 2,2'-pyridyloxazoline, it was necessary to use at least a tenfold excess of ligand relatively to ruthenium, and a reaction time of around 16 hours, in order to obtain good conversions of the alkene, and high selectivity in epoxide which is exclusively *trans* <sup>13</sup>. Control experiments have shown that once formed the epoxide is stable under the reaction conditions used.



These parameters had to be slightly modified with oxazolidines derivatives<sup>14</sup>. The ratio of epoxide 2 formed relatively to the aldehyde 3 are reported in Table 1 and 2. It can be seen from Table 1, that it is difficult to avoid oxidative cleavage as the ratio of epoxide relatively to the initial stilbene does not exceed the value of four.

Ligand	4	5	6	7	8	9
n eq. / Ru	13	12	5	12	5	5
Reaction time (h)	17	16	20	18	20	20
Conversion (%)	98	98	100	99	88	70
Yield 2 (%)	80	73	74	59	39	10
Selectivity 2 (%)	81	75	74	60	44	15
Ratio 2/3	4	3	3	1,5	0,8	0,2
		Tabl	e 1.			

On the other hand, according to the analysis of the results obtained with ligands reported in Table 2, the oxidative cleavage now becomes a major process.



Ligand	10	11	12			
n eq. / Ru	10	12	10			
Reaction time (h)	18	16	18			
Conversion (%)	53	67	80			
Yield 2 (%)	6	7	2			
Selectivity 2 (%)	11	10	2			
Ratio 2 / 3	0,1	0,1	0,02			

7	l'a	Ы	e	2.
			-	

The later results can be interpreted by the formation of a complex with only one ligand<sup>15</sup> (B without b in Scheme 1), in such a way that a *cis* dioxo ruthenium can be easily formed and then cleaves the double bond. Ligand 10 probably only complexes the metal with the nitrogen of the oxazoline as the sulfur atom electrons are too much involved in the aromatic thiophene ring<sup>16</sup>. With the ligands reported in Table 1, it is most likely that two ligands associate with ruthenium so as to favour the formation of a *trans* dioxo species (such as A in Scheme 1) which epoxidises *trans*-stilbene. We are presently making efforts to obtain related complexes in a preparative fashion in order to check this hypothesis.

Although the various ligands used in this work have been synthesised with a high optical purity or enantiomeric excess (ee>95%), the ee of the epoxide obtained is below 5% except for 7 where it reaches 18%; because of these low scores, the corresponding data are not reported in details in this paper. In any event, the present work provides useful informations on the structure of chiral ligands which have to be prepared to

achieve epoxidation of double bonds with ruthenium complexes.

## References and notes :

- a) Mansuy, D. Coord. Chem. Rev., 1993, 125, 129-142; b) Murahashi, S.I. Pure Appl. Chem., 1992, 64, 403-412; c) "Bioinorganic Chemistry of Copper" Karlin, D.; Tyeklar, Z. Chapman and Hall, New-York London, 1993.
- 2. "Catalytic Asymmetric Synthesis" Ojima I., Ed. VCH : New-York, 1993.
- 3. a) Tenaglia, A.; Terranova, E.; Waegell B. J. Org. Chem., 1992, 57, 5523-5528; b) Coudret, J.L.; Waegell, B. Inorg. Chem. Act., 1994, 222, 115-122 and references cited therein.
- a) Eskenazi, C.; Balavoine, G.; Meunier, F.; Riviere, H. Tetrahedron Lett., 1984, 25, 3187-3190; b) Eskenazi, C.; Balavoine, G.; Meunier, F.; Riviere, H. J. Chem. Soc., Chem. Commun., 1985, 1111-1113.
- 5. Bailey, A.T.; Griffith, W.P.; White, A.J.P.; Williams, D.J. J. Chem. Soc., Chem. Commun., 1994, 1833-1834.
- a) Cundari, T.R.; Drago, R.S. Inorg. Chem., 1990, 29, 487-493; b) Cundari, T.R.; Drago, R.S. Inorg. Chem., 1990, 29, 2303-2308.
- 7. Groves, J.T.; Quinn, R. J. Am. Chem. Soc., 1985, 107, 5790-5792.
- a) Groves, J.T.; Nemo, T.E. J. Am. Chem. Soc., 1983, 105, 5786-5791; b) Groves, J.T.; Myers, R.S. J. Am. Chem. Soc., 1983, 105, 5791-5796.
- 9. Goldstein, A.S.; Beer, R.H.; Drago, R.S. J. Am. Chem. Soc., 1994, 116, 2424-2429.
- 10. Tenaglia, A.; Terranova, E.; Waegell, B. unpublished observations.
- Compound 4-6 : a) Peters, G.A. ; Schaeffer, F.C. J. Org. Chem., 1961, 26, 412-418 ; b) Obermann, U. ; Brunner, H. Chem. Ber., 1989, 122, 499-507 ; Compound 7-9 : c) Takahashi, H. ; Suzuki, Y. ; Kametani, T., Heterocycles, 1983, 20, 607-615 ; Compound 10,11 : d) Bolm, C. ; Weickhardt, K. ; Zehnder, M. ; Rauff, T. Chem. Ber., 1991, 124, 1173-1180 ; Compound 12 : e) Nishiyama, H. ; Sakaguchi, H. ; Nakamura, T. ; Horihata, M. Kondo, M. ; Itoh, K. Organometallics, 1989, 8, 846-848.
- 12. Linde, C.; Malara, L. results to be published.
- 13. Experiments done with *cis*-stilbene give exclusively *cis*-stilbene epoxide with lower yields (See also ref.4).
- 14. Reaction conditions : RuCl<sub>3</sub>, 3H<sub>2</sub>O (0,06 mmoles), n eq. ligand and 10 ml of water are stirred at 2°C during 30 mn ; *trans*-stilbene (3 mmoles) in 15 ml of CH<sub>2</sub>Cl<sub>2</sub> and NaIO<sub>4</sub> (6 mmoles) are then added during 16 to 20 h ; the reaction is quenched by addition of 1 ml of propan-2-ol and extracted with CH<sub>2</sub>Cl<sub>2</sub> in the usual way. Data reported in Table 1 and 2 are related to isolated products which have been identified by <sup>1</sup>H NMR with an authentic sample of *trans*-stilbene epoxide prepared by using mCPBA, "*Reagent for Organic Synthesis*" Fieser, L. ; Fieser, M. Wiley, New-York London Sydney, 1967, 1, p136-137.
- 15. Computer modelling (© Discover Force Field ESFF, Biosym Technologies, Inc.) has shown that it is difficult to introduce in a *cis* fashion two ligands such as 11 or 12 in B type complexes (Scheme 1).
- 16. Barton, D.; Ollis, W.D. "Comprehensive Organic Chemistry"; Pergamon Press, 1979, 4, 789-838.