On the kinetics of epoxidation of olefins by *cis* and *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] complexes

André L. Bogado [a,*], Roberto F. de Souza [b], Ulf Schuchardt [c], Alzir A. Batista [a,1]

[a] *Departamento de Química, Universidade Federal de São Carlos, Rod. Washington Luís km 235, São Carlos 13565-905, SP, Brazil*
[b] *Instituto de Química, Universidade Federal do Rio Grande do Sul, Av. Bento Gonçalves 9500,
P.O. Box 15003, Porto Alegre 91501-970, RS, Brazil*
[c] *Instituto de Química, Universidade Estadual de Campinas, P.O. Box 6154, Campinas 13083-970, SP, Brazil*

Abstract

The kinetics of the epoxidation of *cis*-cyclooctene, 2-norbornene and limonene catalyzed by *cis*-[RuCl$_2$(dppb)(2,2′-bipy)] (**1**) or *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] (**2**) (where, dppb: 1,4-bis(diphenylphosphino)butane; 2,2′-bipy: 2,2′-bipyridine) in the presence of iodosylbenzene (PhIO) follow a Michaelis–Menten type mechanism. The performance of **1** and **2** in the epoxidation of *cis*-cyclooctene, 2-norbornene and limonene are respectively (**1**) $V_{max} = 8.62$, 11.6 and 4.98 mol l^{-1} min^{-1} and (**2**) $V_{max} = 4.28$, 7.55 and 5.66 mol l^{-1} min^{-1}. The activation energies of the epoxidations catalyzed by **1** are 1.5–3.3 kcal mol^{-1} lower than those measured for **2**.
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1. Introduction

The epoxidation of alkenes with transition metal complexes is a valuable tool for the synthesis of chemical and pharmaceutical products [1]. Ruthenium and osmium are prominent catalysts for these reactions due to their ability to form high-valent oxo-metal species that have been recognized as active intermediates in the oxygen transfer reactions [2–7]. These complexes can assume a large range of coordination numbers and oxidation states [8].

Selective epoxidations have been achieved by the controlled modification of the ligand and/or symmetry of these complexes [9,10]. The epoxidation of alkenes catalyzed by pentacoordinated ruthenium(II) like [RuCl(P–P)$_2$]$^+$ (where P–P can be an achiral diphosphine as 1,3-bis(diphenylphosphino)propane [3] or a chiral one like chiraphos 4S,5S-(+)-o-isopropylidene-2,3-dihidroxi-1,4-bis-(diphenylphosphino)butane [9]) involve ruthenium(IV)-oxo as active species. The latter is formed by the reaction of iodosylbenzene (PhIO) with ruthenium(II) catalyst precursors. Using bipyridines, the tailoring of the catalytic selectivity of ruthenium(IV)-oxo complexes has been described [11]. This suggests that the use of selected N donor ligands can favor the epoxidation reaction at the expense of the oxidative cleavage of double bonds [12].

A Michaelis–Menten mechanism can be a valuable tool in order to understand the contribution of the different steps of the overall epoxidation reaction.

* Corresponding author. Tel.: +55-16-260-8285;
fax: +55-16-260-8209.
E-mail address: alzir@dq.ufscar.br (A.A. Batista).
[1] Cocorresponding author.

$$S + C \xrightleftharpoons[k_{-1}]{k_1} CS \xrightarrow{k_2} P + C$$
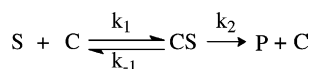
Scheme 1. Michaelis–Menten type mechanism. (S: substrate; C: catalyst; CS: reactive intermediate catalyst–substrate complex; P: product; k_1, k_{-1} and k_2 are the receptivity rate constants).

Scheme 1 shows the rationale of the epoxidation process under such a viewpoint.

The Michaelis–Menten parameters can be obtained through a Lineweaver–Burk graphical treatment of the reactivity data [13], providing easy calculation of the characteristic reaction constants necessary for a close evaluation of the catalytic reaction.

We describe herein the use of *cis* and *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] complexes in the epoxidation of alkenes with iodosylbenzene as oxidant.

2. Experimental

2.1. General considerations

Reagent grade solvents were distilled from CaH$_2$ (CH$_2$Cl$_2$), Na (Et$_2$O and hexanes) or 4 Å molecular sieves (MeCN) prior to use. RuCl$_3$·xH$_2$O, hexadecane, *cis*-cyclooctene, limonene, 2-norbornene, tetrabutyl-ammonium hexafluorophosphate (HTBA), 2,2′-bipy-ridine (2,2′-bipy), 1,4-bis(diphenylphosphino)butane (dppb) and triphenylphosphine (PPh$_3$) were used as supplied by Aldrich.

All operations were performed under argon. The ruthenium(II) complexes were synthesized from [Ru-Cl$_2$(dppb)]$_2$(μ-dppb) or [RuCl$_2$(dppb)(PPh$_3$)] as reported in [14]. Iodosylbenzene was synthesized by Sharefikin's method [15] and purified by Lucas's method [16]. The reaction products were analyzed by gas chromatography using a Shimadzu GC-17A chromatograph equipped with an FID detector. An LM-120 column (poly(ethyleneglycol), 25 m long, 0.25 mm i.d., 0.25 μm film thickness), was used for the characterization of *cis*-cyclooctene and limonene epoxidation products and a DB-1 column (dimethyl-polysiloxane, 30 m long, 0.25 mm i.d., 0.25 μm film thickness), used for the characterization of 2-norbornene epoxidation products and N$_2$ was the gas carrier (1.0 ml min^{-1}). The temperature program

was from 50 to 120 °C (2 min) at a heating rate of 10 °C min^{-1}, and from 120 to 150 °C (2 min) at heating rate of 5 °C min^{-1} (*cis*-cyclooctene and cy-clooctene oxide). When the epoxidation of limonene was investigated, the temperature program was from 50 to 200 °C (2 min) at a heating rate of 10 °C min^{-1}. When the epoxidation of 2-norbornene was investi-gated, the temperature program was from 40 to 65 °C (1 min) at a heating rate of 7 °C min^{-1}, then to 78 °C at a heating rate of 5 °C min^{-1} and finally to 200 °C (2 min) at a heating rate of 7 °C min^{-1}.

Mass spectra were obtained using a GC/MS Shi-madzu QP-5000 spectrometer (EI, 70 eV). Ruthenium complexes were analyzed by ^{31}P (^{1}H) NMR on an ARX 200 MHz and a DRX 400 MHz Bruker instru-ment. Samples were prepared under an inert atmo-sphere of argon and analyzed at room temperature using a D$_2$O capillary and dichloromethane (CH$_2$Cl$_2$) as solvent. Chemical shifts were calculated with re-spect to the phosphorus signal of phosphoric acid 85% (H$_3$PO$_4$).

The experiments involving the oxidation and la-bility of the biphosphine were carried out by ^{31}P (^{1}H) NMR on a DRX 400 MHz Bruker instrument. Ruthenium complexes *cis*-[RuCl$_2$(dppb)(2,2′-bipy)] (**1**) or *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] (**2**) (5.0 mg; 6.6 μmol) were dissolved in CH$_2$Cl$_2$ without oxygen. PhIO (58.0 mg; 26.0 μmol) was added after first spec-tra had been acquired. All spectra were obtained with 20 min of acquisition and 10 min of delay between each spectrum during several hours.

Cyclic voltammetry measurements were carried out on BAS workstation model 100 B, using acetonitrile with HTBA (0.1 mol l^{-1}) as supporting electrolyte. Glassy carbon was used as both the working and aux-iliary electrode and Ag/AgCl was used as reference electrode. A scan rate of 200 mV s^{-1} and a sensi-tivity of 100 μA were used. Under these conditions ferrocene gave $E_{1/2} = 0.348$ mV.

2.2. Catalytic experiments

Alkene epoxidations were performed using a 3.0 ml reactor. The temperature was controlled within ±0.5 °C using a NESLAB cryostat. The ruthenium(II) complexes, *trans* and *cis*-[RuCl$_2$(dppb)(2,2′-bipy)] (1.0 mg; 1.32 μmol) and iodosylbenzene (PhIO) (8.7–44.0 mg; 40–200 μmol) were added under argon.

Table 1
Epoxidation of cyclooctene, norbornene and limonene

Entry	Pre-catalyst	Substrate	Conversion (%)	Epoxide selectivity (%)	Yield (%)	Reference
1	**1**	*cis*-Cyclooctene	58	34	20	This work[a]
2	**2**	*cis*-Cyclooctene	44	45	20	This work[a]
3	**1**	2-Norbornene	65	27	18	This work[a]
4	**2**	2-Norbornene	58	43	25	This work[a]
5	**1**	Limonene	36	47	17	This work[a]
6	**2**	Limonene	23	48	11	This work[a]
7	**3**	2-Norbornene	7	60	4.2	[3][b]
8	**4**	2-Norbornene	13	45	5.8	[3][b]
9	**3**	*cis*-Cyclooctene	4	65	2.6	[3][b]
10	**4**	*cis*-Cyclooctene	7	55	3.8	[3][b]

[a] Catalyst/substrate molar ratio = 1/40; substrate/PhIO molar ratio = 1/1.5; *cis*-[RuCl$_2$(dppb)(2,2′-bipy)] (**1**); *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] (**2**); temperature = 25 °C; time = 154 min.

[b] Catalyst/substrate molar ratio = 1/50; substrate/PhIO molar ratio = 1/2; [RuCl(dppp)$_2$]$^+$ (**3**) and [RuCl(ppy)$_2$]$^+$ (**4**); temperature = 22 °C; time = 10 h.

Dichloromethane (1 ml), hexadecane as internal standard (3.0 μl; 10 μmol) and *cis*-cyclooctene or limonene (3.0–14.0 μl; 18–86 μmol) were transferred using a micro syringe. The 2-norbornene epoxidation followed the same procedure, but only the 2-norbornene (2.4–12.4 mg; 26–132 μmol) was dissolved in dichloromethane (1 ml). The mixture was magnetically stirred for 154 min. With the progress of the epoxidation reaction, samples were withdrawn at regular time intervals and analyzed by gas chromatography.

3. Results and discussion

The epoxidation reactions of *cis*-cyclooctene, 2-norbornene and limonene catalyzed by **1** and **2** have been studied in detail. Typical results are shown in Table 1.

These results show that complexes **1** and **2** are active in olefins epoxidation. In all reactions, complex **1** is more active than **2**, however, **2** is generally more selective than **1** for the epoxidation products, with exception of limonene for which both catalysts show similar selectivities.

It is interesting to compare the performance of complexes **1** and **2** with the related complexes [RuCl(dppp)$_2$]$^+$ (**3**) and [RuCl(ppy)$_2$]$^+$ (**4**) (where dppp: 1,3-bis(diphenylphosphino)propane and ppy: 1-(diphenylphosphino)-2-(2-pyridyl)ethane)) previ-

ously described by Bressan and Morvillo [3], and with RuCl$_3$/bipyridine (**5**) or phenanthroline (**6**), described by Meunier and coworkers [11]. The epoxidation data using the complexes **3** and **4** under similar conditions to those used in this work are shown in Table 1. These data should be compared with the values obtained in the *cis*-cyclooctene epoxidation with **1** and **2** (Table 1). There is a significant enhancement in the reaction rate using **1** and **2** when compared with **3** and **5**, but with similar selectivities.[2]

The epoxidation of alkenes with PhIO is shown to be dependent on the lability of the biphosphine in the catalyst precursor **1** or **2**. Using ^{31}P (^{1}H) NMR it can be shown that the coordinated biphosphine is oxidized. The coordinated biphosphine in **1** shows two doublets at 42 and 31 ppm ($^2J_{P–P}$ = 33 Hz); in **2**, it appears as a singlet at 33 ppm. For **1**, the phosphorus oxidizing process takes place in two steps: initially the phosphorus *trans* to the heterocyclic nitrogen is oxidized, giving a singlet for dppbO (mono-oxidized—dangling with the P=O not coordinated) at 28 ppm. Then the second phosphorous is oxidized, giving a singlet for dppbO$_2$ (di-oxidized, not coordinated) at 31 ppm. For **1**, the biphosphine was completely oxidized after 17 h. For **2**, the oxidation is faster, leading directly to the fully oxidized ligand showing the typical singlet at

[2] Systems **5** and **6** has been reported to give 56% yield in norbornene epoxidation at 4 h reaction time [11], but the system is biphasic and the oxidant is different, precluding a direct comparison of this result with those herein reported.
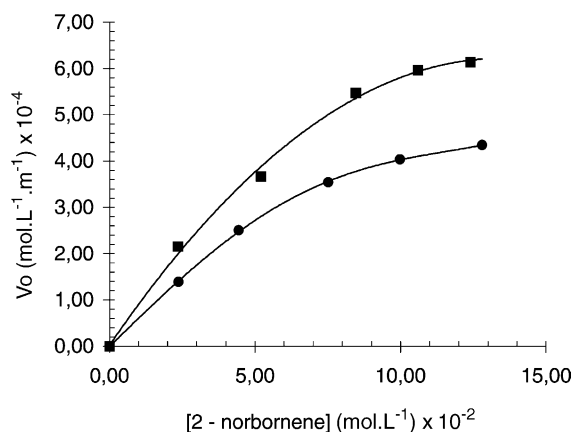
Fig. 1. Michaelis–Menten plot for the 2-norbornene epoxidation with **1** (■) and **2** (●).

Fig. 2. Lineweaver–Burk plot for the 2-norbornene epoxidation with **1** (■) and **2** (●).

31 ppm after 30 min. The structures of the ruthenium complexes after the completely oxidation and dissociation of the biphosphine ligands are the same for **1** and **2**, suggesting the presence of the Ru=O species [3]. This time difference for oxidation of the coordinated biphosphine in **1** and **2** could be determining same kinetic parameters like initial rate (V_0), V_{max} and K_M.

The enhancement of the epoxidation reaction rate is attractive but a discussion of the reasons for such an enhancement depends on the knowledge of the contribution of each individual step of the catalytic cycle. A convenient method for the kinetic study of this type of catalytic reaction is the use of Michaelis–Menten plots (Fig. 1) and their corresponding Lineweaver–Burk plots (Fig. 2), in order to obtain the corresponding V_{max} and K_M parameters.

Table 2 reports the V_{max} and K_M parameters calculated from the Lineweaver–Burk plots of reactions 1–6.

The reactions used to obtain the Michaelis–Menten parameters were performed keeping the catalyst concentration constant [catalyst loading ($1.36\,\mu$mol)] and varying the substrate concentration, in order to obtain a substrate/catalyst molar ratio from 20/1 to 100/1 while the substrate/PhIO molar ratio was kept at 1/1.5.

The initial reaction rates were determined by the *initial-rate method* [17] and these values were used to obtain the corresponding Michaelis–Menten plots which a hyperbolic limitation of the enhancement of the reaction rate with increasing substrate concentration. The abs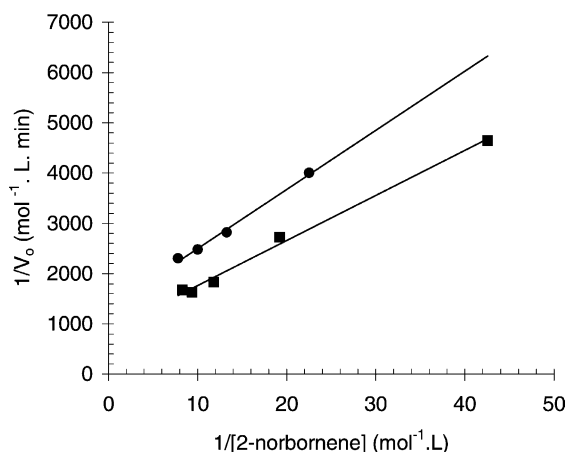ence of a linear relationship between V_0 and the concentration of the substrate [S] is characteristic of a sequential catalytic process. The value of V_0 is only proportional to [S] at low values of [S], as shown in Fig. 1.

The corresponding Lineweaver–Burk plots, with the reciprocal of the initial rate ($1/V_0$) plotted against 1/[S], give the ordinate intercept with the value $1/V_{max}$ and the slope K_M/V_{max}, thus enabling the calculation of K_M and V_{max}. The values are reported in Table 2.

The V_{max} values are the maximum rates that can be obtained and correspond to the maximum concentration of the [CS] form (reactive intermediate catalyst–substrate complex and $V_{max} = k_2 \times [C]_0$, where k_2 is the rate constant of the slow step and $[C]_0$ the initial concentration of the catalyst ($mol\,l^{-1}$)). The values of k_2 are also reported in Table 2 and reflect the difference of the activity between **1** and **2** for the epoxidation of *cis*-cyclooctene, 2-norbornene and limonene.

The activation energies (E_a) of these reactions were calculated from the reaction rates of the kinetic runs performed in the temperature range of 10–25 °C, keeping the catalyst/substrate molar ratio at 1/60 [18–20]. A typical Arrhenius plot, correlating $\ln k$ and T^{-1}, is shown in Fig. 3. The E_a values calculated from these plots are reported in column 7 of Table 2.

The higher conversions obtained for **1** compared with **2** are, in part, a consequence of lower E_a values observed for **1**. The difference between the E_a observed for **2** and **1** is $3.28\,kcal\,mol^{-1}$ in the case

Table 2
Michaelis–Menten parameters for the epoxidation of *cis*-cyclooctene, 2-norbornene and limonene

Entry	Pre-catalyst	Substrate	$V_{max} \times 10^{-4}$ (mol L^{-1} min^{-1})	K_M (mmol L^{-1})	k_2 (h^{-1})	E_a (kcal mol^{-1})	A (L mol^{-1} min^{-1})	$\Delta G^{\#a}$ (kcal mol^{-1})	$\Delta H^{\#a}$ (kcal mol^{-1})	$\Delta S^{\#a}$ (cal mol^{-1} K^{-1})	$T\Delta S^{\#a}$ (kcal mol^{-1})
1	**1**	Cyclooctene	8.62	156	39.0	11.03	7.30×10^5	3.03	10.44	24.82	7.40
2	**2**	Cyclooctene	4.28	46	19.5	14.31	7.20×10^8	2.22	13.71	38.54	11.49
3	**1**	Norbornene	11.6	104	52.7	12.68	4.86×10^7	2.18	12.09	33.20	9.90
4	**2**	Norbornene	7.55	89	34.0	14.05	1.78×10^9	1.43	13.46	40.34	12.03
5	**1**	Limonene	4.98	111	22.6	8.68	3.10×10^5	1.19	8.09	23.14	6.90
6	**2**	Limonene	5.66	122	25.5	10.37	2.40×10^5	3.03	9.78	22.64	6.75

Temperature = 298.15 K; *cis*-[RuCl$_2$(dppb)(2,2′-bipy)] (**1**); *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] (**2**).
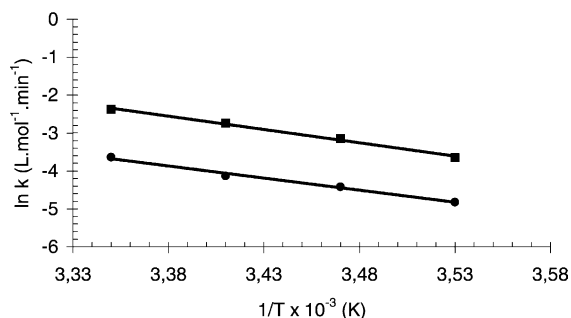
Fig. 3. Arrhenius plot for the 2-norbornene epoxidation with **1** (■) and **2** (●).

of *cis*-cyclooctene, $1.37 \, \text{kcal mol}^{-1}$ in the case of 2-norbornene and $1.69 \, \text{kcal mol}^{-1}$ for limonene. Certainly the fact that complex **2** forms the catalyst species Ru=O more rapidly, this can contribute to its faster decomposition allowing the observed higher conversion and lower selectivity for the complex **1** when compared with the complex **2**.

The activation parameters, A and E_a, and the corresponding activated state thermodynamic parameters ($\Delta G^{\#}$, $\Delta H^{\#}$ and $\Delta S^{\#}$) have been calculated in order to explain the origin of the activity control for **1** and **2**.

The relationship between the observed activities and the entropic contribution, seen through the values of A or, more directly, from $T \Delta S^{\#}$, is straightforward. For the epoxidation of *cis*-cyclooctene and 2-norbornene the entropic contributions for **1** and **2** show differences of 4.1 and $2.1 \, \text{kcal mol}^{-1}$, respectively, which are the origin of the control of activity. For limonene, the A values as well as the $T \Delta S^{\#}$ are similar, with a difference of $-0.15 \, \text{kcal mol}^{-1}$, thus explaining the similar activities that have been observed.

Epoxidation reactions in the temperature range of 10–25 °C gave a linear relationship of $\Delta G^{\#}$ values with temperature, indicating that the same mechanism is preserved in this range.

The discussion on the origin of the observed E_a values should take into account the oxidation potential of the epoxidized olefins. The anodic peak potential (E_{pa}) in the cyclic voltammetry for *cis*-cyclooctene, 2-norbornene and limonene in acetonitrile were found to be 2.21, 2.25 and 1.89 V, respectively. The E_a values of Table 2 have a straight relationship with these E_{pa} values, i.e. the oxidation of the olefin is easier when lower E_a values are observed.

4. Conclusions

Our study shows that the complexes *cis*-[RuCl$_2$(dppb)(2,2′-bipy)] (**1**) and *trans*-[RuCl$_2$(dppb)(2,2′-bipy)] (**2**) are active in the epoxidation of olefins like *cis*-cyclooctene, limonene, 2-norbornene. In all reactions, complex **1** is more active than **2**, however, **2** is generally more selective than **1** for the epoxidation products. The epoxidation of the alkenes is shown to be dependent on (a) the lability of the biphosphine in the catalyst precursors and (b) the chelating capacity of the ligands that remain coordinated to the metal after the dissociation of the biphosphine.

For the epoxidation reactions performed in the temperature range of 10–25 °C, the $\Delta G^{\#}$ values have a linear relationship with the temperature, indicating that the same mechanism is preserved in this temperature range.

The E_a values for the epoxidation of the olefins show a linear relationship with their electrochemical anodic peak potential (E_{pa}), i.e. the oxidation of the olefin is easier when lower E_a values are observed.

The use of Michaelis–Menten plots and their corresponding Lineweaver–Burk plots, has shown to be a convenient method for the kinetic study of this catalytic reaction. From these plots, the corresponding V_{max} and K_M parameters are obtained and then used in the analysis of the behavior of this system.

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