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A Mild Catalytic Oxidation System: Ruthenium Porphyrin and 2,6-Dichloropyridine *N*-Oxide Applied for Alkene Dihydroxylation

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Abstract: A new method was developed to transform alkenes into three types of functional molecules, including epoxides, aldehydes and 1,2-diols by using dichlororuthenium(IV) *meso*-tetrakis(2,6-dichlorophenyl)porphyrin [Ru(IV)(TDCPP)Cl_2] as catalyst and 2,6-dichloropyridine *N*-oxide (Cl_2pyNO) as the oxidant, in which the 1,2-diols were afforded *via* "one-pot" reactions in moderate yields.

Keywords: alkenes; catalytic oxidation; 2,6-dichloropyridine *N*-oxide; dihydroxylation; ruthenium porphyrin

1,2-Diols are useful building blocks in organic synthesis. This subunit can be synthesized from alkenes through alkene dihydroxylation.[1] Several group VIII transition metal oxides, such as: Fe,[2] Ru, Os, have been employed to promote these reactions, in which, OsO_4 is the most commonly used catalyst. In 1988, Sharpless and Jacobsen[3] developed the OsO_4/NMO (*N*-methylmorpholine *N*-oxide) oxidation system for asymmetric dihydroxylation of alkenes. Several similar studies[4] have been made based on this system in recent years. The industrial use of OsO_4, however, is thwarted by its expensive price and toxic properties. In 1953, the less toxic RuO_4 was introduced into this field by Carl Djerassi.[5] Shing and co-workers improved the synthetic utility of this transformation by reducing the catalyst loading of RuO_4.[6] Then, a new catalytic system lowered further the amount of the catalyst to 0.25–0.5 mol% through the combination of $RuCl_3$, $NaIO_4$ and $CeCl_3 \cdot 7H_2O$.[7] Che and co-workers recently presented the *cis*-dihydroxylation of various unfunctionalized alkenes by using [Ru(II)-(Me_3tacn)Cl_3] as catalyst and H_2O_2 as the terminal oxidant.[8] Despite these acheviements, developing milder and more efficient methods for alkene dihydroxylation reactions is still an attractive topic.

Since cytochrome P-450,[9] one of the most attractive metalloenzymes containing the porphyrin structure in nature, was found to catalyze metabolic oxygen transfer processes, porphyrins have been demonstrating a wide range of applications in catalytic oxidation reactions, including alkene cyclopropanation,[10] C–N bond formation,[11] saturated C–H bond amination,[12] and alkene epoxidation.[13] In previous work, the combination of dichlororuthenium(IV) *meso*-tetrakis(2,6-dichlorophenyl)porphyrin [Ru(IV)-(TDCPP)Cl_2] (**1**) and 2,6-dichloropyridine *N*-oxide (Cl_2pyNO) (**2**) (Figure 1) afforded aldehydes in high yields *via* epoxide rearrangement.[14] We envisioned that this reaction could provide an efficient method to prepare different types of products. For example, aldehydes can be obtained from epoxide rearrangement, while expoxides can be obtained by the blocking of this rearrangement process. The 1,2-diols can be prepared by utilizing epoxide ring opening and hydrolysis.

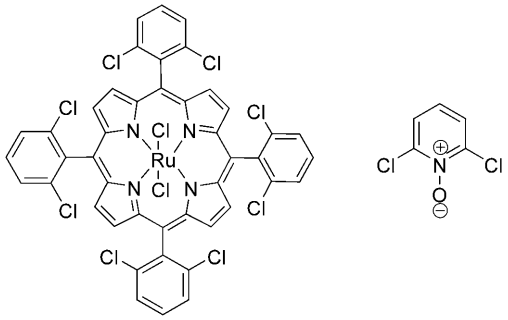
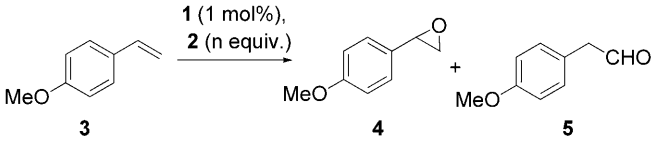


Figure 1. [Ru(IV)(TDCPP)Cl_2] and Cl_2pyNO.

Table 1. Oxidation of 4-methoxystyrene catalyzed by [Ru(IV)(TDCPP)Cl_2] with varying loadings of Cl_2pyNO.[a]



Entry	Cl_2pyNO [equiv.]	Conversion [%]	Yield [%][b]	
			4	**5**
1	2.0	100	76	24
2	1.03	100	0	99
3	0.9	90	0	>99

[a] *Reaction conditions:* **3**: 0.1 mmol, **1**: 0.5 mol%, $CDCl_3$: 0.5 mL; 25 °C, open to the air.

[b] Determined by ^{1}H NMR spectroscopy (based on consumed substrate).

The reaction of 4-methoxystyrene was chosen as the model system for our initial investigation. A series of experiments were performed and representative results are listed in Table 1. As shown in Table 1, the amount of oxidant loading affected the reaction pathway. The optimal conditions for the formation of the aldehyde were to use 1.03 equivalents of oxidant.[14] However, when 2.0 equivalents of oxidant was used, the epoxide **4** was obtained as the major product in 76% yield, along with the formation of aldehyde **5** in 24% yield.

We reasoned that the *in-situ* ring opening (epoxide hydrolysis) would prevent the synthesis of aldehyde and epoxide. In order to get the optimal reaction conditions for the formation of the diols, a carboxylic acid was introduced to promote the reaction. Indeed, when AcOH and 1.5 equivalents of Cl_2pyNO were added, the ring-opened diol products were obtained as a mixture of regioisomers in excellent yield (95%). Formic acid was later found to be a better promoter for the ring opening process.

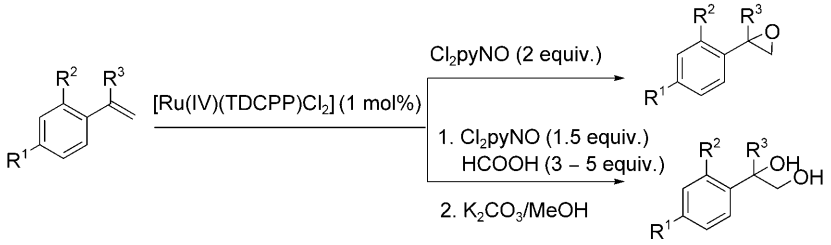
Under the same optimized conditions, a series of styrenes were tested to prepare epoxides and diols. As depicted in Table 2, all the epoxide derivatives were obtained in high yields. Most of the epoxidation reactions were complete in less than 1 hour, giving the desired products in moderate to good yields. The substituent(s) on the phenyl ring was found to affect the reaction time dramatically. For example, the reaction of compounds **c, f** and **i** took only ten minutes, while the reactions of compounds **b** and **d** took 17 h to give the corresponding products in 96% and 97% yields respectively.

Almost all the diol products were synthesised in 2 h in good yields (Table 2). The reaction of compound **k** took 3 h to give the diol, possibly because of the presence of the methyl group attached at the double bond. It was interesting to mention that compound **h** took 22 h. The total yields were higher than 80% except for compounds **f** and **i**.

A plausible mechanism has been proposed. In the process, [Ru(IV)(TDCPP)Cl_2] is supposed to be a precatalyst, not the effective or active one, which, as illustrated in Figure 2, is transformed into the real catalyst, [Ru(TDCPP)LL′]. L and L′ are other ligands from the reaction system, probably containing the elements Cl or O. [Ru(TDCPP)LL′] promotes the transformation of the alkenes into aldehydes, epoxides and diols. When the loading of oxidant was increased from 1.03 equivalents to 2.0 equivalents, the aldehyde formation was prohibited. We speculated that Cl_2pyNO acts as ligand coordinated to the ruthenium atom of the catalyst. Therefore, there is a competition between oxidant and epoxide for this coordination reaction. In the case of 1.03 equivalents of oxidant, the epoxide interacts with Ru complex again, which initiates the epoxide rearrangement. On the other hand, excess oxidant interacts with the Ru complex, which pushes away the resulting epoxide and shifts the equilibrium to epoxide formation. The ring-opening reagent, such as protic acid, was added to give diols through epoxide hydrolysis.

In summary, a mild oxidation system has been developed to convert alkenes into various types of functional molecules, including aldehydes, epoxides, and diols in moderate to excellent yields by controlling the loadings of oxidant and reaction procedures. This is the first time, to the best of our knowledge, that an efficient method has been developed to prepare three different types of compounds from alkenes by using a single catalytic system *via* "one-pot" cascade reactions.

Table 2. Alkenes that were oxidized with [Ru(IV)(TDCPP)Cl_2] and Cl_2pyNO.[a]



Compound	R^1	R^2	R^3	Time[b]	Yield[d] of epoxide	Time[c]	Yield[d] of diol
a	MeO	H	H	15 min	76%	2 h	95%
b	H	H	H	17 h	96%	2 h	85%
c	Me	H	H	10 min	97%	2 h	92%
d	F	H	H	17 h	97%	2 h	81%
e	*i*-Bu	H	H	11 min	82%	2 h	90%
f	*t*-Bu	H	H	10 min	90%	2 h	63%
g	*i*-PrO	H	H	48 min	46%	2 h	98%
h	PhO	H	H	52 min	75%	22 h	88%
i	BnO	H	H	10 min	90%	2 h	63%
j	Me	Me	H	15 min	–[e]	2 h	86%
k	H	H	Me	19 min	–[e]	3 h	83%

[a] Yields of the aldehydes were reported in the previous works.[14]
[b] The reaction times of epoxidation.
[c] The reaction times for the nucleophilic ring opening of epoxides.
[d] The yields were determined by ^{1}H NMR with internal standard of trimethylphenylsilane.
[e] Epoxides from **j** and **k** were crudely obtained and directly used for their conversions to diols.

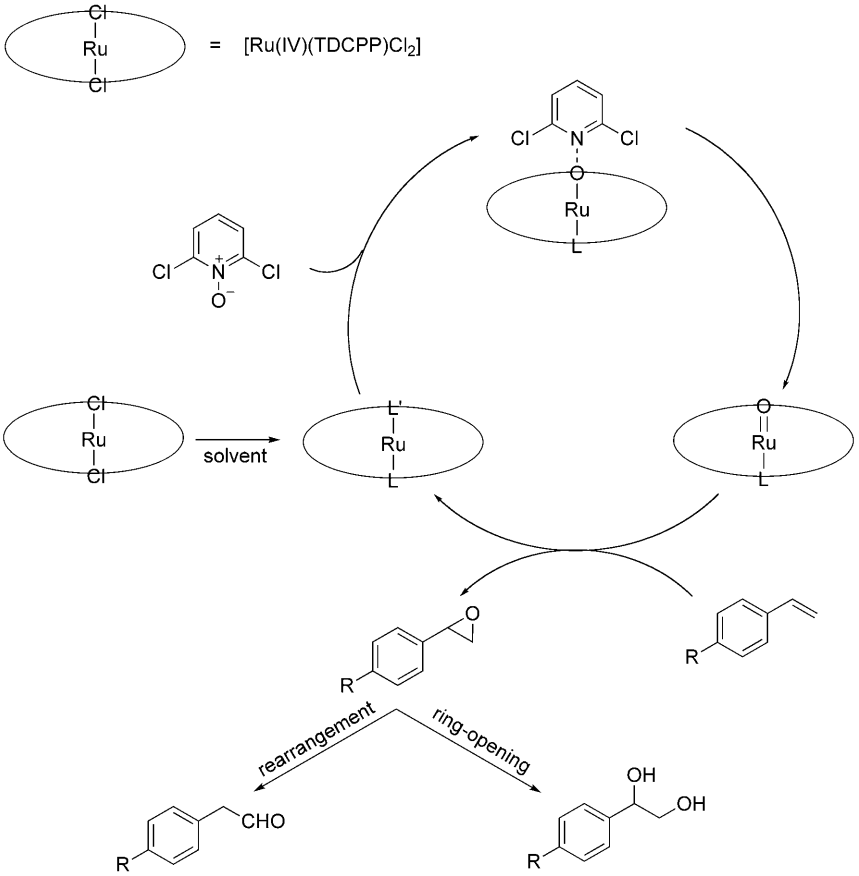


Figure 2. Probable mechanism leading to aldehydes, epoxides and diols.

Experimental Section

[Ru(II)(TDCPP)(CO)]

A mixture of $Ru_3(CO)_{12}$ (178 mg, 0.28 mmol) and porphyrin H_2TDCPP (165 mg, 0.19 mmol) was heated to reflux in 1,2,4-trichorobenzene under an argon atmosphere for 4–6 h. After the mixture was cooled to room temperature, the residue was loaded onto an alumina column and the column was first eluted with hexane to remove the trichlorobenzene, followed by eluting with dichloromethane. A dark red band containing the desired ruthenium complex was collected; yield: 187 mg (99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.48 (s, 8H), 7.73–7.80 (m, 8H), 7.65 (dd, 4H, J = 7.8 Hz); IR (KBr): ν = 2921, 2851, 1951, 1429, 1009, 799 cm^{-1}; UV-vis (CH_2Cl_2): λ_{max} (log ε) = 410, 531, 609 nm; MS (FAB) m/z = 1018 (M + 1), 990 (M + 1 − CO).

[Ru(VI)(TDCPP)O_2]

A dichloromethane solution of [Ru(II)(TDCPP)(CO)] (150 mg) was added to a well stirred solution of *m*-chloroperoxybenzoic acid in dichloromethane (50 mL). After 10 min, the solution was chromatographed on a short alumina column. The product was eluted by dichloromethane. The solution obtained was evaporated to dryness by rotary evaporation. A dark purple residue was obtained; yield: 123 mg (82%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.89 (s, 8H), 7.83–7.86 (m, 8H), 7.73–7.78 (m, 4H); IR (KBr): ν = 1557, 1533, 1428, 1018, 824, 801, 776 cm^{-1}; UV-vis (CH_2Cl_2): λ_{max} (log ε) = 420, 516 nm.

[Ru(IV)(TDCPP)Cl_2]

TMSCl (0.4 mL) was added into a well stirred solution of [Ru(VI)(TDCPP)O_2] (150 mg) in dichloromethane (350 mL). After 10 min, the solution was concentrated to small volume by rotary evaporation and was filtered offering a dark purple residue; yield: 139 mg (90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.56 (d, 8H, J = 8.1 Hz), 8.85 (t, 4H, J = 8.1 Hz), −53.5 (br, 8H); IR (KBr): ν = 1557, 1429, 1194, 1072, 999, 802, 776 cm^{-1}; UV-vis (CH_2Cl_2): λ_{max} (logε) = 408, 517 nm; MS (FAB): m/z = 1060 (M^+), 1025 ($M^+ - {}^{35}Cl$), 1023 ($M^+ - {}^{37}Cl$), 990 ($M^+ - 2\,{}^{35}Cl$), 988 ($M^+ - {}^{35}Cl - {}^{37}Cl$).

General Procedure for the Preparation of Diols

To a solution of styrene (0.2 mmol) in $CHCl_3$ (1–2 mL), catalyst [Ru(IV)(TDCPP)Cl_2] (2 mg, 1 mmol%), oxidant Cl_2pyNO (48 mg, 0.3 mmol), and HCOOH (22–37 μL, 0.6–1 mmol) were added at the same time. The system needs to be covered with aluminium foil paper as protection from light. With stirring, the reaction solution was kept at room temperature for 2.5–3 h. After the completion of the reaction, the mixture was diluted with 6–8 mL of petroleum ether and purified by silica gel column chromatography using petroleum ether and EtOAc (3:1–2:1) as eluent to give mixture of mono-protected diols. Then K_2CO_3 (0.3 mmol) was added to a solution of mono-protected diols (0.2 mmol) in methanol (10 mL). The mixture was stirred for 3–4 h and then concentrated with silica gel (200–300 mesh) under vacuum. The mixture was then purified by silica gel column chromatography (300–400 mesh) using petroleum ether and EtOAc (1:1–1:2) as eluent giving the pure diol.

1-(4-Methoxyphenyl) ethane-1,2-diol: yield: 32 mg (95%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.17 (brs, 1H), 2.56 (brs, 1H), 3.65 (m, 2H), 3.81 (s, 3H), 4.77 (m, 1H), 6.90 (d, J = 8.5, 2H), 7.28 (d, J = 8.5, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 55.30, 68.07, 74.28, 113.93, 127.35, 132.62, 159.42; IR: ν = 3310 cm^{-1} (br). MS: m/z = 168.0 [M^+].

1-Phenylethane-1,2-diol: yield: 23 mg (85%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.04 (brs, 1H), 2.50 (brs, 1H), 3,70 (m, 2H), 4.85 (m, 1H), 7.35 (m, 2H), 7.40 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 68.03, 74.67, 126.03, 128.60, 140.45; IR: ν = 3306 cm^{-1} (br); MS: m/z = 138.1 [M^+].

1-*p*-Tolylethane-1,2-diol: yield: 28 mg (92%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.34 (s, 3H), 2.53 (brs, 1H), 2.90 (brs, 1H), 3.70 (m, 2H), 4.76 (m, 1H), 7.16 (d, J = 7.8, 2H), 7.24 (d, J = 7.8, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.12, 68.07, 74.56, 126.01, 129.02, 137.73; IR: 3251 cm^{-1} (br); MS: m/z = 152.1 [M^+].

1-(4-Fluorophenyl)ethane-1,2-diol: yield: 25 mg (81%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.11 (brs, 1H), 2.62 (brs, 1H), 3,75 (m, 2H), 4.80 (m, 1H), 7.05 (m, 2H), 7.35 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 70.70, 76.66, 118.00, 130.41, 138.85, 164.30, 165.33; IR: ν = 3313 cm^{-1} (br); MS: m/z = 156.0 [M^+].

1-(4-*tert*-Butylphenyl)ethane-1,2-diol: yield: 24 mg (63%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.31 (s, 9H), 2.35 (brs, 1H), 2.70 (brs, 1H), 3.70 (m, 2H), 4.78 (m, 1H), 7.29 (d, J = 8.2, 2H), 7.39 (d, J = 8.2, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 33.97, 37.20, 70.68, 77.16, 128.40, 140.14, 153.68; IR: ν = 3404 cm^{-1} (br); MS: m/z = 194.1 [M^+].

1-(4-Isopropoxyphenyl)ethane-1,2-diol: yield: 38 mg (98%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.32 (d, J = 6 Hz, 6H), 2.46 (brs, 1H), 2.80 (brs, 1H), 3.68 (m, 2H), 4.53 (m, 1H), 4.74 (m, 1H), 6.85 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 24.75, 70.51, 72.56, 76.86, 118.47, 130.10, 135.03, 160.35; IR: ν = 3289 cm^{-1} (br); MS: m/z = 196.1 [M^+].

1-[4-(Benzyloxy)phenyl]ethane-1,2-diol: yield: 31 mg (63%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.05 (brs, 1H), 2.43 (brs, 1H), 3.73 (m, 2H), 4.78 (m, 1H), 5.03 (s, 2H), 6.97 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 7.33 (t, J = 7.3 Hz, 1H), 7.38 (m, 2H), 7.43 (d, J = 7.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 68.05, 70.03, 74.27, 114.96, 127.40, 127.98, 128.58, 132.91, 136.90, 159.66; IR: ν = 3336 cm^{-1} (br); MS: m/z = 243.9 [M^+].

1-(2,4-Dimethylphenyl)ethane-1,2-diol: yield: 28 mg (86%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.30 (s, 6H), 2.56 (brs, 1H), 2.76 (brs, 1H), 3.65 (m, 2H), 5.01 (m, 1H), 6.96 (s, 1H), 7.04 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.55, 23.60, 69.80, 74.15, 128.40, 129.60, 133.85, 137.31, 138.12, 140.03; IR: 3242 cm^{-1} (br); MS: m/z = 166.1 [M^+].

2-Phenylpropane-1,2-diol: yield: 25 mg (83%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.52 (s, 3H), 2.01 (brs, 1H), 2.70 (brs, 1H), 3.70 (m, 2H), 7.27 (t, J = 7.3 Hz, 1H), 7.36 (m, 2H), 7.45 (d, J = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 25.98, 71.05, 74.82, 125.05, 127.16, 128.40, 144.92; IR: ν = 3391 cm^{-1} (br); MS: m/z = 152.1 [M^+].

1-(4-Isobutylphenyl)ethane-1,2-diol: yield: 35 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.6 Hz, 6H),

1.84 (m, 1H), 2.31 (brs, 1H), 2.46 (d, $J=7.1$ Hz, 2H), 2.69 (brs, 1H), 3.69 (m, 2H), 4.78 (m, 1H), 7.13 (d, $J=8$ Hz, 2H), 7.25 (d, $J=8$ Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=22.36$, 30.21, 45.09, 68.07, 74.61, 125.85, 129.29, 137.73, 141.62; IR: 3365 cm^{-1} (br); HR-MS: $m/z=194.1302$, calculated for $C_{12}H_{18}O_2$: 194.1307.

1-(4-Phenoxyphenyl)ethane-1,2-diol: yield: 40 mg (88%). ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=2.23$ (brs, 1H), 2.67 (brs, 1H), 3,70 (m, 2H), 4.81 (m, 1H), 7.00 (m, 4H), 7.11 (t, $J=$ 7.4 Hz, 1H), 7.33 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=68.05$, 74.23, 118.78, 123.42, 127.56, 129.77, 135.22, 157.10; IR: $\nu=3302$ cm^{-1} (br); HR-MS: $m/z=230.0941$, calculated for $C_{14}H_{14}O_3$: 230.0943.

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