Dichlororuthenium(IV) Complex of *meso*-Tetrakis(2,6-dichlorophenyl)porphyrin: Active and Robust Catalyst for Highly Selective Oxidation of Arenes, Unsaturated Steroids, and Electron-Deficient Alkenes by Using 2,6-Dichloropyridine *N*-Oxide

Jun-Long Zhang and Chi-Ming Che*[a]

Abstract: $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$, prepared in 90% yield from the reaction of $[Ru^{VI}(2,6\text{-}Cl_2tpp)O_2]$ with Me_3SiCl and structurally characterized by X-ray crystallography, is markedly superior to $[Ru^{IV}(tmp)Cl_2]$, $[Ru^{IV}(ttp)Cl_2]$, and $[Ru^{II}(por)(CO)]$ (por = 2,6-Cl_2tpp, F_{20}-tpp, F_{28}-tpp) as a catalyst for alkene epoxidation with 2,6-Cl_2pyNO (2,6-Cl_2tpp = *meso*-tetrakis(2,6-dichlorophenyl)porphyrinato dianion; tmp = *meso*-tetramesitylporphyrinato dianion; ttp = *meso*-tetrakis(*p*-tolyl)porphyrinato dianion; F_{20}-tpp = *meso*-tetrakis(pentafluorophenyl)porphyrinato dianion; F_{28}-tpp = 2,3,7,8,12,13,17,18-octafluoro-5,10,15,20-tetrakis(pentafluorophenyl)-porphyrinato dianion). The "$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ + 2,6-Cl_2pyNO" protocol oxidized, under acid-free conditions, a wide variety of hydrocarbons including 1) cycloalkenes, conjugated enynes, electron-deficient alkenes (to afford epoxides), 2) arenes (to afford quinones), and 3) Δ^5-unsaturated steroids, Δ^4-3-ketosteroids, and estratetraene derivatives (to afford epoxide/ketone derivatives of steroids) in up to 99% product yield within several hours with up to 100% substrate conversion and excellent regio- or diastereoselectivity. Catalyst $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ is remarkably active and robust toward the above oxidation reactions, and turnover numbers of up to 6.4×10^3, 2.0×10^4, and 1.6×10^4 were obtained for the oxidation of α,β-unsaturated ketones, arenes, and Δ^5-unsaturated steroids, respectively.

Keywords: homogeneous catalysis · oxidation · porphyrinoids · ruthenium · structure elucidation

Introduction

Metalloporphyrin oxidation catalysts not only constitute unique biomimetic models for cytochrome P-450 enzymes (which play an important role in biosynthesis, metabolism, and oxidative transformations) but also have practical applications in organic oxidation reactions. A significant number of metalloporphyrin oxidation catalysts have been developed since the leading works by Groves and co-workers,[1a] and some of these can catalyze the hydroxylation of alkanes and epoxidation of unfunctionalized alkenes with high regio-, shape- and stereoselectivity under mild conditions.[1] Ruthenium–porphyrin complexes are among the most extensively studied metalloporphyrin catalysts for hydrocarbon oxidation.

In 1985, Groves and Quinn discovered that a sterically bulky dioxoruthenium(VI) porphyrin, $[Ru^{VI}(tmp)O_2]$ (tmp = *meso*-tetramesitylporphyrinato dianion), can catalyze the aerobic epoxidation of alkenes.[2] Afterwards, Marchon and co-workers observed the $[Ru^{VI}(tmp)O_2]$-catalyzed aerobic oxidation of unsaturated steroids.[3] Hirobe and co-workers discovered the epoxidation of alkenes, hydroxylation of alkanes, and oxidation of arenes and steroids with heteroaromatic *N*-oxides such as 2,6-dichloropyridine *N*-oxide (2,6-Cl_2pyNO) in the presence of catalyst $[Ru^{VI}(por)O_2]$ or $[Ru^{II}(por)(CO)]$ (por = porphyrin in general).[4] Groves and co-workers reported the hydroxylation/epoxidation of hydrocarbons with 2,6-Cl_2pyNO catalyzed by the highly fluorinated ruthenium porphyrin $[Ru^{II}(F_{20}\text{-tpp})(CO)]$ (F_{20}-tpp = *meso*-tetrakis(pentafluorophenyl)porphyrinato dianion).[5] By employing chiral $[Ru^{VI}(por^*)O_2]$ or $[Ru^{II}(por^*)(CO)]$ as catalysts (por* = chiral porphyrin in general), we and Gross, Berkessel, and Simonneaux realized the enantioselective ox-

[a] J.-L. Zhang, Prof. C.-M. Che
Department of Chemistry and
Open Laboratory of Chemical Biology of the
Institute of Molecular Technology for Drug Discovery and Synthesis
The University of Hong Kong, Pokfulam Road (Hong Kong)
Fax: (+852) 2857-1586
E-mail: cmche@hku.hk

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

 DOI: 10.1002/chem.200401008

idation of hydrocarbons with 2,6-Cl_2pyNO, PhIO, or dioxygen.[6–9] We also reported the epoxidation of alkenes with 2,6-Cl_2pyNO catalyzed by the [Ru^{II}(por)(CO)] grafted onto mesoporous molecular sieve MCM-41[10a] and MCM-48,[10c] Merrifield's peptide resin,[10b] dendrimers,[10d] and soluble polymers.[10e] A catalyst of [Ru^{II}(por)(CO)] immobilized in a highly cross-linked polymer for the alkene epoxidation with 2,6-Cl_2pyNO was subsequently reported by Severin and Nestler.[11] The alkene epoxidation catalyzed by [Ru^{VI}(tmp)O_2] can also be performed with N_2O as oxidant, as found by Yamada and co-workers.[12] Recently, we reported the epoxidation of cycloalkenes with 2,6-Cl_2pyNO catalyzed by [Ru^{II}(2,6-Cl_2tpp)(CO)] (2,6-Cl_2tpp = *meso*-tetrakis(2,6-dichlorophenyl)porphyrinato dianion).[13]

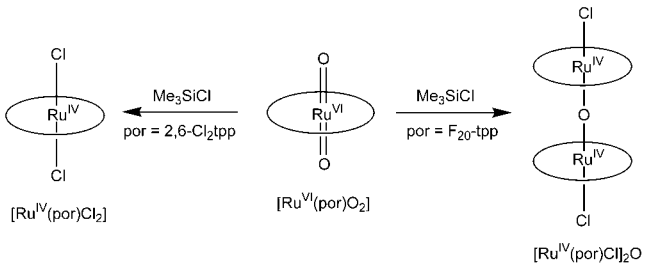
The [Ru^{VI}(por)O_2]- or [Ru^{II}(por)(CO)]-catalyzed oxidations show attractive features such as 1) almost complete β-selectivity in the epoxidation of cholesteryl esters;[3a–c,10c–10e] 2) extremely high turnover number of up to 1.2×10^5 in the hydroxylation of adamantane;[4e,5] 3) high selectivity, versatility, and reusability in the epoxidation of alkenes catalyzed by the polymer-supported [Ru^{II}(por)(CO)];[10b] and 4) high enantioselectivity for the asymmetric epoxidation of styrene.[6c,7] However, [Ru^{VI}(por)O_2] catalysts are unstable and must be freshly prepared or generated in situ, whereas the oxidation by stable catalysts [Ru^{II}(por)(CO)] (except for por = F_{20}-tpp) usually requires a long reaction time (24–48 h) to complete. It would be of particular interest to develop a stable ruthenium porphyrin oxidation catalyst that not only shows extraordinary selectivity and versatility, but also exhibits a high reactivity.

In a previous work, we found that the stable chiral dichlororuthenium(IV) porphyrin [Ru^{IV}(D_4-por*)Cl_2] (D_4-por* = D_4-symmetric 5,10,15,20-tetrakis((1*S*,4*R*,5*R*,8*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracen-9-yl)-porphyrinato dianion), characterized by spectroscopic means, exhibited substantially higher catalytic activity toward asymmetric alkene epoxidation with 2,6-Cl_2pyNO than the carbonyl analogue [Ru^{II}(D_4-por*)(CO)].[14a] This finding prompted us to further develop the chemistry of dichlororuthenium(IV)–porphyrin complexes including the methods of preparation and structural and reactivity studies. Herein are described the epoxidation of a wide variety of alkenes and oxidation of arenes and steroids with 2,6-Cl_2pyNO catalyzed by the dichlororuthenium(IV)–porphyrin complexes [Ru^{IV}(por)Cl_2] (por = 2,6-Cl_2tpp, tmp, ttp) (ttp = *meso*-tetrakis(*p*-tolyl)porphyrinato dianion), along with the crystal structures of [Ru^{IV}(por)Cl_2] (por = 2,6-Cl_2tpp, tmp) and [{Ru^{IV}(F_{20}-tpp)Cl}$_2$O]. The selective oxidation of alkenes to aldehydes catalyzed by [Ru^{IV}(2,6-Cl_2tpp)Cl_2] has recently been reported.[14b] The present work also reports comparative oxidation studies using [Ru^{II}(2,6-Cl_2tpp)(CO)], [Ru^{II}(F_{20}-tpp)(CO)], [Ru^{II}(F_{28}-tpp)(CO)] (F_{28}-tpp = 2,3,7,8,12,13,17,18-octafluoro-5,10,15,20-tetrakis(pentafluorophenyl)porphyrinato dianion), [{Ru^{IV}(F_{20}-tpp)Cl}$_2$O], and other related ruthenium catalysts. Strikingly, [Ru^{IV}(2,6-Cl_2tpp)Cl_2] is a highly efficient catalyst for 2,6-Cl_2pyNO oxidation of electron-deficient α,β-unsaturated ketones (which are usually poor substrates for metalloporphyrin-mediated oxidation) with excellent substrate conversions (up to 95%) and product yields (up to 99%) within several hours. Oxidation of α,β:γ,δ-unsaturated alkenes and 2-substituted naphthalenes by the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol shows that the electronic properties of the substrates can affect the product regioselectivity. Prior to this work, reports in the literature on ruthenium–porphyrin-catalyzed oxidations of arenes and steroids were sparse,[3,4d,10c–10e] and in very few cases metalloporphyrin complexes have been employed as catalysts for the oxidation of electron-deficient alkenes.[10b,e,14a,15] Therefore, [Ru^{IV}(2,6-Cl_2tpp)Cl_2] is an exceptionally active, versatile, and robust metal catalyst toward 2,6-Cl_2pyNO oxidation of alkenes compared with other metalloporphyrin catalysts.

Results and Discussion

Syntheses and X-ray crystal structures of [Ru^{IV}(2,6-Cl_2tpp)Cl_2], [Ru^{IV}(tmp)Cl_2], and [{Ru^{IV}(F_{20}-tpp)Cl}$_2$O]: Several methods are known for preparation of [Ru^{IV}(por)Cl_2] complexes.[16] Gross and co-workers reported that [Ru^{IV}(por)Cl_2] could be obtained by heating a solution of [Ru^{II}(por)(CO)] in CCl_4.[16b,d] The chiral complex [Ru^{IV}(D_4-por*)Cl_2] was prepared by this method in 95% yield.[14a] We attempted to prepare [Ru^{IV}(2,6-Cl_2tpp)Cl_2] using this procedure, but found that the conversion of [Ru^{IV}(2,6-Cl_2tpp)(CO)] to [Ru^{IV}(2,6-Cl_2tpp)Cl_2] was only 50% even after refluxing a solution of [Ru^{IV}(2,6-Cl_2tpp)(CO)] in CCl_4 for 48 h.

Interestingly, the reaction of freshly prepared [Ru^{VI}(2,6-Cl_2tpp)O_2] with excess Me_3SiCl in CH_2Cl_2 at room temperature gave [Ru^{IV}(2,6-Cl_2tpp)Cl_2] in 90% yield (Scheme 1),



Scheme 1. Preparation of [Ru^{IV}(2,6-Cl_2tpp)Cl_2] and [{Ru^{IV}(F_{20}-tpp)Cl}$_2$O].

similar to the reaction of [Ru^{VI}(ttp)O_2] with Me_3SiCl to give [Ru^{IV}(ttp)Cl_2].[16c] A similar treatment of [Ru^{VI}(tmp)O_2] with Me_3SiCl afforded [Ru^{IV}(tmp)Cl_2] in 80% yield. However, when the reaction was extended to [Ru^{VI}(F_{20}-tpp)O_2], a dinuclear complex, [{Ru^{IV}(F_{20}-tpp)Cl}$_2$O], was obtained in 62% yield (Scheme 1); no [Ru^{IV}(F_{20}-tpp)Cl_2] was isolated.

The ^{1}H NMR spectrum of [Ru^{IV}(2,6-Cl_2tpp)Cl_2] shows the signal of the pyrrolic protons (H_β) at $\delta = -53.4$ ppm, similar to the corresponding signals reported for the paramagnetic

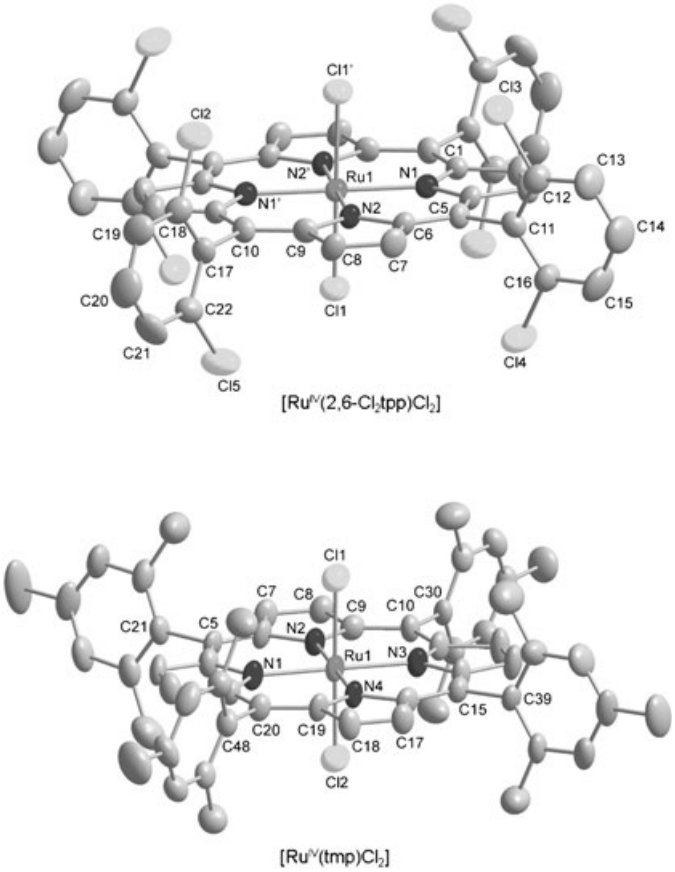


Figure 1. Structures of $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and $[Ru^{IV}(tmp)Cl_2]$ with omission of hydrogen atoms. Thermal ellipsoids were drawn at a 30% probability level. Note that the unit cell of $[Ru^{IV}(tmp)Cl_2]$ contains two independent types of molecules, only one of which is shown here.

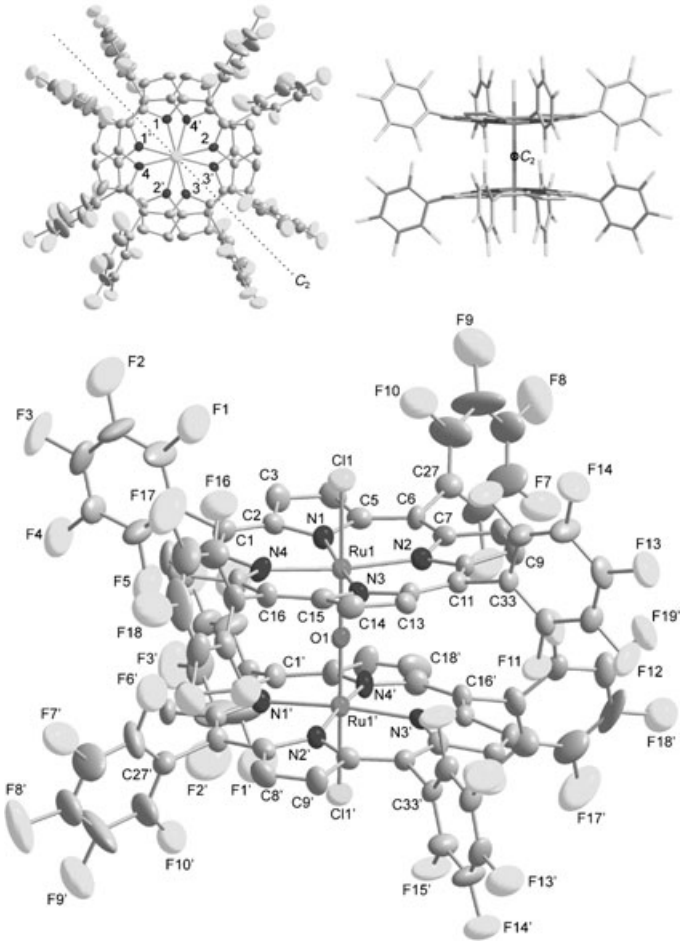


Figure 2. Structure of $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ with omission of hydrogen atoms. Thermal ellipsoids were drawn at a 30% probability level. The upper part of this figure shows top and side views of the molecule along the Cl1-Ru1-O1-Ru1′-Cl′ axis and the C_2 axis, respectively.

$[Ru^{IV}(tmp)Cl_2]$[16d] and $[Ru^{IV}(ttp)Cl_2]$.[16c] The electrospray mass spectrum of $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ shows the parent ion peak at $m/z = 1059.7$. Complex $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ is diamagnetic and features the H_β signal at $\delta = 8.98$ ppm in the ^1H NMR spectrum; its FAB mass spectrum shows peaks at $m/z = 1109$ and 1090 assignable to the fragments $[Ru(F_{20}\text{-}tpp)Cl]^+$ and $[Ru(F_{20}\text{-}tpp)O]^+$, respectively.

Figures 1 and 2 depict the structures of $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$, $[Ru^{IV}(tmp)Cl_2]$, and $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$. The crystallographic data and selected bond lengths and angles are given in Tables 1 and 2. Note that there are two independent molecules in the asymmetric unit of $[Ru^{IV}(tmp)Cl_2]$. The $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ molecule (Figure 1, upper) has a crystallographic center of symmetry at the Ru atom. For $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ (Figure 2, Ru–O: 1.8088(6) Å), there is a crystallographic C_2 axis that passes through the bridging O atom and is perpendicular to the Cl-Ru-O-Ru-Cl axis. The porphyrin rings are almost planar in the two mononuclear complexes, with mean displacement of 0.0125 Å for $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and 0.0208, 0.0560 Å for $[Ru^{IV}(tmp)Cl_2]$ from the least-squares planes. Appreciable dome distortions (mean displacement: 0.0935 Å) are observed for the porphyrin rings in $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$, with the Ru atoms being 0.30 Å out of the corresponding mean planes toward the O atoms. The Ru–Cl distances of 2.288(2) Å in $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and 2.292(4) Å (average) in $[Ru^{IV}(tmp)Cl_2]$ are slightly shorter than that in $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ (2.322(2) Å) and in the previously reported $[\{Ru^{IV}(oep)Cl\}_2O]$ (2.320(6) Å, oep = 2,3,7,8,12,13,17,18-octaethylporphyrinato dianion).[17] $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and $[Ru^{IV}(tmp)Cl_2]$ are the first structurally characterized mononuclear dichlororuthenium(IV)–porphyrin complexes.

We measured the cyclic voltammogram of $[Ru^{IV}(tmp)Cl_2]$ (Figure 3), which shows a quasi-reversible oxidation couple at $E_{1/2} = 0.80$ V and a reversible reduction couple at $E_{1/2} = -0.02$ V (vs $Cp_2Fe^{+/0}$). With reference to previous studies on the electrochemistry of related ruthenium–porphyrin complexes,[16c,18] the quasi-reversible oxidation couple can be assigned to the porphyrin-centered process, $[Ru^{IV}(tmp)Cl_2] - e^- \rightarrow [Ru^{IV}(tmp^{\bullet+})Cl_2]$, whereas the reduction couple can be assigned to the reduction of Ru^{IV} to Ru^{III}. The $E_{1/2}$ of the $Ru^{IV/III}$ couple for the related $[Ru^{IV}(dpp)(pz)_2]$ (dpp = 2,3,5,7,8,10,12,13,15,17,18,20- dodecaphenylporphyrinato dianion, pz = pyrazolate) was reported to

Table 1. Crystallographic data for $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$, $[Ru^{IV}(tmp)Cl_2]$, and $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$.

	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]\cdot 2CHCl_3\cdot C_6H_{14}$	$[Ru^{IV}(tmp)Cl_2]\cdot 0.5CHCl_3$	$[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]\cdot 2H_2O\cdot CHCl_3$
formula	$C_{44}H_{20}Cl_{10}N_4Ru\cdot 2CHCl_3\cdot C_6H_{14}$	$C_{56}H_{52}Cl_2N_4Ru\cdot 0.5CHCl_3$	$C_{88}H_{16}Cl_2F_{40}N_8ORu_2\cdot 2H_2O\cdot CHCl_3$
M_r	1385.12	1012.67	2389.53
crystal system	monoclinic	monoclinic	tetragonal
space group	$P2_1/c$	$P2_1/c$	$I4_1/a$
λ [Å]	0.71073	0.71069	0.71073
T [K]	301	293	294
a [Å]	12.322(3)	19.141(4)	27.128(3)
b [Å]	18.903(4)	25.293(5)	27.128(3)
c [Å]	12.828(3)	24.875(5)	31.137(5)
α [°]	90	90	90
β [°]	95.65(3)	94.95(3)	90
γ [°]	90	90	90
V [Å^3]	2973(1)	11998(4)	22914(5)
Z	2	8	8
ρ_{calcd} [g cm^{-3}]	1.547	1.121	1.385
$\mu(Mo_{K\alpha})$ [mm^{-1}]	1.022	0.452	0.490
$F(000)$	1384	4184	9344
crystal size [mm]	$0.25\times0.1\times0.05$	$0.4\times0.4\times0.1$	$0.38\times0.10\times0.10$
R_1	0.059	0.081	0.079
wR_2	0.15	0.25	0.21
goodness-of-fit	0.93	0.97	1.16
largest diff. peak/hole [e Å^{-3}]	0.618/−0.426	1.171/−0.503	0.998/−0.991

Table 2. Selected bond lengths [Å] and angles [°] for $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$, $[Ru^{IV}(tmp)Cl_2]$, and $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$.

$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$			
Ru1−N1	2.035(7)	Ru1−C1	2.288(2)
Ru1−N2	2.045(6)		
N1-Ru1-N2	89.5(3)	N1-Ru1-N2′	90.5(3)
N1-Ru1-Cl1′	89.0(2)	N1′-Ru1-Cl1′	91.0(2)
N2-Ru1-Cl1′	90.9(2)	N2′-Ru1-Cl1′	89.1(2)
$[Ru^{IV}(tmp)Cl_2]$[a]			
Ru1−N1	2.023(9)	Ru1−N2	2.011(9)
Ru1−N3	2.033(8)	Ru1−N4	2.029(9)
Ru2−N5	2.04(1)	Ru2−N6	2.041(9)
Ru2−N7	2.014(9)	Ru2−N8	2.04(1)
Ru1−Cl1	2.302(4)	Ru1−Cl2	2.282(4)
Ru2−Cl3	2.290(3)	Ru2−Cl4	2.292(3)
N1-Ru1-N2	89.5(4)	N2-Ru1-N4	178.8(4)
N1-Ru1-N4	89.6(4)	N2-Ru1-N3	90.6(4)
N1-Ru1-N3	179.5(4)	N4-Ru1-N3	90.4(4)
Cl1-Ru1-Cl2	179.3(1)	Cl3-Ru2-Cl4	179.3(1)
$[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$			
Ru1−O1	1.8088(6)	Ru1−N2	2.019(5)
Ru1−N4	2.047(5)	Ru1−N3	2.051(5)
Ru1−N1	2.056(5)	Ru1−Cl1	2.322(2)
Ru1′−O1	1.8088(6)		
O1-Ru1-N2	93.6(2)	O1-Ru1-N4	93.4(2)
O1-Ru1-N1	93.0(2)	O1-Ru1-N3	93.0(2)
N2-Ru1-N4	173.0(2)	N2-Ru1-N3	89.9(2)
N3-Ru1-N4	89.5(2)	N2-Ru1-N1	90.4(2)
N3-Ru1-N1	174.0(2)	N1-Ru1-N4	89.5(2)
O1-Ru1-Cl1	179.6(2)	N2-Ru1-Cl1	86.8(2)
N4-Ru1-Cl1	86.2(2)	N3-Ru1-Cl1	87.2(2)
N1-Ru1-Cl1	86.9(2)	Ru1-O1-Ru1′	180.0(3)

[a] There are two types of independent molecules in the unit cell.

be −0.41 V versus $Cp_2Fe^{+/0}$,[18b] revealing that pz^- is more effective than Cl^- in stabilizing the Ru^{IV} oxidation state.

Epoxidation of styrene catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and other ruthenium–porphyrin complexes

Effect of oxidants: Table 3 gives the results for the reactions of styrene with oxidants PhIO, TBHP (*tert*-butyl hydroperoxide), UHP (urea hydrogen peroxide adduct), and 2,6-X_2pyNO (X = Cl, Br, Me, H) in the presence of catalytic amounts of $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ or $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$. Complex $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ displayed a markedly higher reactivity than $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ for all these oxidants except PhIO (see the conversion values in Table 3). The main product in the oxidation with UHP and 2,6-X_2pyNO (entries 5–11, 13) is styrene oxide (up to 90% yield). However, the oxidation with PhIO or TBHP afforded benzaldehyde as the main product (up to 70% yield, entries 1–4).

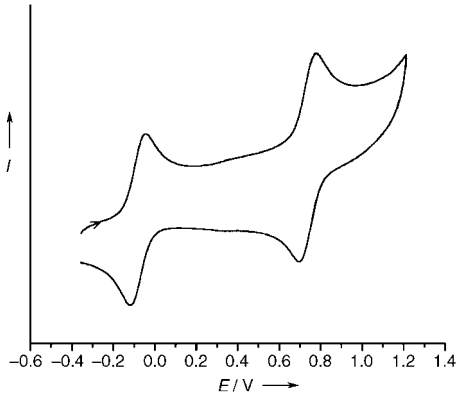
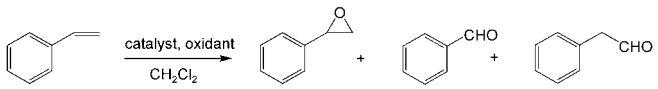


Figure 3. Cyclic voltammogram of $[Ru^{IV}(tmp)Cl_2]$ measured at a scan rate of 50 mV s^{-1} in CH_2Cl_2 containing 0.1 mol dm^{-3} tertrabutylammonium hexafluorophosphate at room temperature.

Of the four pyridine *N*-oxides shown in Table 3, 2,6-Cl_2pyNO was the most effective oxidant for the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed styrene epoxidation, featuring a substrate conversion of 99% and an epoxide yield of 89% (entry 7). The highest yield of styrene oxide in Table 3 corresponds to UHP, but this oxidant resulted in a low conversion of $\leq$38% (entries 5 and 6). Therefore, UHP was not used as oxidant in subsequent oxidation reactions.

Table 3. Epoxidation of styrene catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ with different oxidants.[a]



I II III

Entry	Catalyst	Oxidant	Conv [%][b]	Yield [%][c] I	II	III
1	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	PhIO	5	32	63	5
2	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	PhIO	41	30	61	9
3	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	TBHP	64	12	70	18
4	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	TBHP	42	20	66	14
5	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	UHP	38	90	2	8
6	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	UHP	20	86	8	6
7	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	2,6-Cl_2pyNO	99	89	8	3
8	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	2,6-Cl_2pyNO	32	80	15	5
9	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	2,6-Br_2pyNO	76	85	10	5
10	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	2,6-Br_2pyNO	20	86	8	6
11	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	2,6-Me_2pyNO	28	66	20	12
12	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	2,6-Me_2pyNO	[d]	[d]	[d]	[d]
13	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	pyNO	10	60	35	5
14	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	pyNO	[d]	[d]	[d]	[d]

[a] Reaction conditions: CH_2Cl_2, 40 °C, catalyst/oxidant/styrene molar ratio = 1:550:500 (entries 1–6, 13 and 14, for 24 h), 1:1100:1000 (entries 7–12 for 5 h). [b] Conversions were determined by GC using 1,4-dichlorobenzene as standard. [c] Based on the amount of consumed substrates. [d] No reaction.

Surprisingly, complex $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ could also catalyze the oxidation of styrene with 2,6-Cl_2pyNO, PhIO, and TBHP (see Table S1 in the Supporting Information), although this complex exhibited a lower catalytic efficiency for styrene epoxidation than $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$. The 2,6-$Cl_2$pyNO oxidation of styrene in CH_2Cl_2 at 40 °C in the presence of 0.1 mol % of $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ afforded styrene oxide, benzaldehyde, and phenylacetaldehyde in 67 %, 8 %, and 25 % yield, respectively, with 25 % conversion within 24 h. With TBHP as oxidant, the oxidation of styrene catalyzed by $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$ gave benzaldehyde in 90 % yield. This contrasts with the low catalytic activity observed for $[\{Ru^{IV}(ttp)X\}_2O]$ (X = Cl, OMe, OEt).[19]

Time course: The 2,6-Cl_2pyNO epoxidation of styrene catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ in benzene or dichloromethane at room temperature with a catalyst/substrate/oxidant molar ratio of 1:1000:1100 exhibited no apparent induction period and proceeded much more rapidly than by $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ (which showed an induction period of around 2 h) and $[\{Ru^{IV}(F_{20}\text{-}tpp)Cl\}_2O]$, as is evident from the time course plots depicted in Figure 4 (cf. curves B, F, and G). Dichloromethane is a better solvent than benzene for the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed reaction (cf. curves B and E); in the former solvent, the oxidation catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ was even faster than by $[Ru^{VI}(2,6\text{-}Cl_2tpp)O_2]$ (cf. curves B and C) and was only slightly affected by the presence of dioxygen (cf. curves B and D). No appreciable oxidation of styrene occurred with $[\{Ru^{IV}(ttp)(OEt)\}_2O]$ as catalyst (curve H).

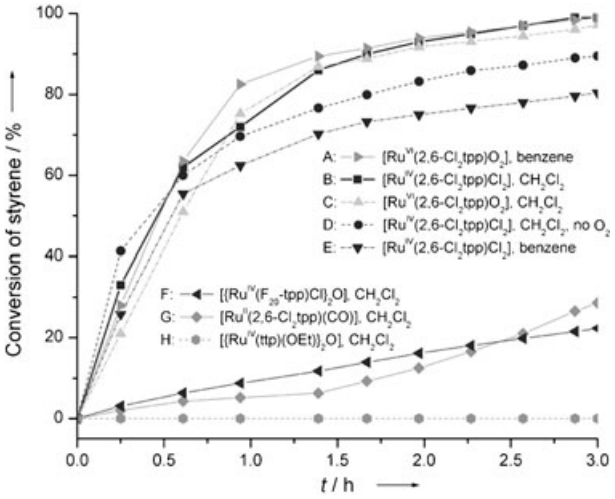


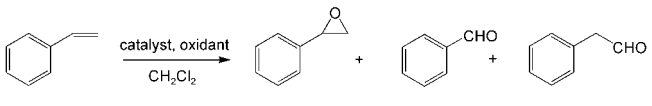
Figure 4. Time course plots for epoxidation of styrene with 2,6-Cl_2pyNO catalyzed by various ruthenium–porphyrin complexes at room temperature (catalyst/substrate/oxidant molar ratio = 1:1000:1100).

Comparison with ruthenium complexes of perfluorinated porphyrin and Schiff bases: In view of the rapid oxidation of hydrocarbons with 2,6-Cl_2pyNO catalyzed by $[Ru^{II}(F_{20}\text{-}tpp)(CO)]$,[5] we examined the catalytic activity of the perfluorinated porphyrin complex $[Ru^{II}(F_{28}\text{-}tpp)(CO)]$ toward epoxidation of styrene by 2,6-Cl_2pyNO, PhIO, or TBHP. To our surprise, $[Ru^{II}(F_{28}\text{-}tpp)(CO)]$ is a less efficient catalyst than $[Ru^{II}(F_{20}\text{-}tpp)(CO)]$, and even exhibited a lower catalytic efficiency than $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ (see Table 4). For example, when 2,6-Cl_2pyNO was used as oxidant, < 5 % conversion was observed after 24 h, with styrene oxide formed in 32 % yield (entry 1 of Table 4). Addition of HBr or HCl did not improve the conversion and product yield, in contrast to the marked acceleration of the $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$- or $[Ru^{II}(tmp)(CO)]$-catalyzed hydrocarbon oxidation upon addition of HX (X = Cl and Br).[4c]

Ruthenium Schiff base complexes depicted in Figure 5 are poor or ineffective catalysts for the 2,6-Cl_2pyNO epoxidation of styrene (see Table S2 in the Supporting Information). After a 24 h reaction, the conversions were < 15 %, and the main product was benzaldehyde, with an enantioselectivity (if any) of < 10 % *ee* for the epoxide product.

Reaction mechanism: The progress of the catalytic reaction was followed through monitoring the changes of the Soret (408 nm) and β band (515 nm) of $[Ru^{IV}(tmp)Cl_2]$ (4×

Table 4. Epoxidation of styrene with different oxidants catalyzed by $[Ru^{II}(F_{28}\text{-tpp})(CO)]$, $[Ru^{II}(F_{20}\text{-tpp})(CO)]$, and $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$.[a]



I II III

Entry	Catalyst	Oxidant	Conv. [%][b]	Yield [%][c] I	II	III
1	$[Ru^{II}(F_{28}\text{-tpp})(CO)]$	2,6-Cl_2pyNO	<5	32	64	4
2	$[Ru^{II}(F_{20}\text{-tpp})(CO)]$	2,6-Cl_2pyNO	54	67	20	13
3	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	2,6-Cl_2pyNO	62	92	7	1
4	$[Ru^{II}(F_{28}\text{-tpp})(CO)]$	PhIO	15	32	56	14
5	$[Ru^{II}(F_{20}\text{-tpp})(CO)]$	PhIO	44	21	68	11
6	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	PhIO	41	30	61	9
7	$[Ru^{II}(F_{28}\text{-tpp})(CO)]$	TBHP	35	0	92	0
8	$[Ru^{II}(F_{20}\text{-tpp})(CO)]$	TBHP	74	0	99	0
9	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	TBHP	42	20	66	14

[a] Reaction conditions: CH_2Cl_2, 40°C, 24 h, catalyst/oxidant/styrene molar ratio = 1:1100:1000. [b] Conversions were determined by GC using 1,4-dichlorobenzene as standard. [c] Based on the amount of consumed substrates.

10^{-4} M). For a solution of styrene and $[Ru^{IV}(tmp)Cl_2]$ in a molar ratio of 10000:1 in CH_2Cl_2, the absorbance at 408 nm decreased slightly (<5%) and the 515 nm band shifted to 526 nm after 2 h. One equivalent of 2,6-Cl_2pyNO (relative to styrene) was then added to this solution, but the conversion of styrene was low (15%) after a reaction time of 1 h. This is in contrast to the styrene conversion of 68% found when a similar CH_2Cl_2 solution of $[Ru^{IV}(tmp)Cl_2]$ and 2,6-Cl_2pyNO (also in the molar ratio of 10000:1) was allowed to react with styrene for 1 h. Thus, addition of 2,6-Cl_2pyNO at the beginning of the reaction was important for the catalysis. In the absence of styrene, a solution of 2,6-Cl_2pyNO and $[Ru^{IV}(tmp)Cl_2]$ (10000:1) in dichloromethane was monitored by UV-visible spectrophotometry. For the initial 2 h, the absorbance at 408 and 515 nm did not change and no shift of the β band was observed. Upon subsequent addition of one equivalent of styrene (relative to 2,6-Cl_2pyNO) and stirring the mixture for 1 h, the conversion of styrene and the yield of styrene oxide based on consumed styrene were found to be 69% and 90%, respectively; there was no shift in λ_{max} of the Soret band (408 nm) and β band (515 nm), but only a slight decrease (10%) in the absorbance at 408 nm.

^{1}H NMR spectroscopy (in $CDCl_3$) was employed to monitor the progress of styrene oxidation with 2,6-Cl_2pyNO catalyzed by $[Ru^{IV}(tmp)Cl_2]$ with 1,3,5-tribromobenzene as internal standard. Figure 6 shows the time course of the reaction. The amount of $[Ru^{IV}(tmp)Cl_2]$ slightly decreased (<5%, based on the intensity of the phenyl proton signal at 12.5 ppm) in the absence of styrene (catalyst/2,6-Cl_2pyNO molar ratio = 1:100) for the first 20 min. After styrene was added, the conversion of styrene was only 14% and the amount of the catalyst $[Ru^{IV}(tmp)Cl_2]$ was reduced to 83% of its initial amount after 2 min. After that, the conversion of styrene and the yield of styrene oxide based on consumed styrene dramatically increased (from 14% to 96% and 10% to 90%, respectively), but the amount of the $[Ru^{IV}(tmp)Cl_2]$ catalyst only decreased from 83% to 77% after 20 min. This is not consistent with $[Ru^{IV}(tmp)Cl_2]$ being the active species in these catalytic reactions.

We scaled up the epoxidation reaction [catalyst (0.02 mmol), styrene (20 mmol), and 2,6-Cl_2pyNO (22 mmol)], which was completed within 2 h. The ^{1}H NMR

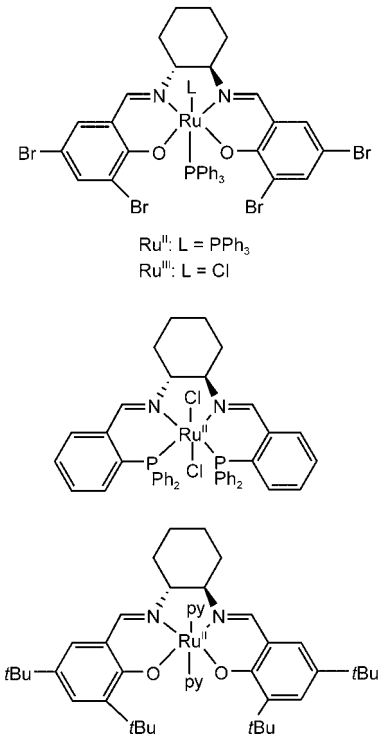


Figure 5. Schematic structures of ruthenium Schiff base complexes.

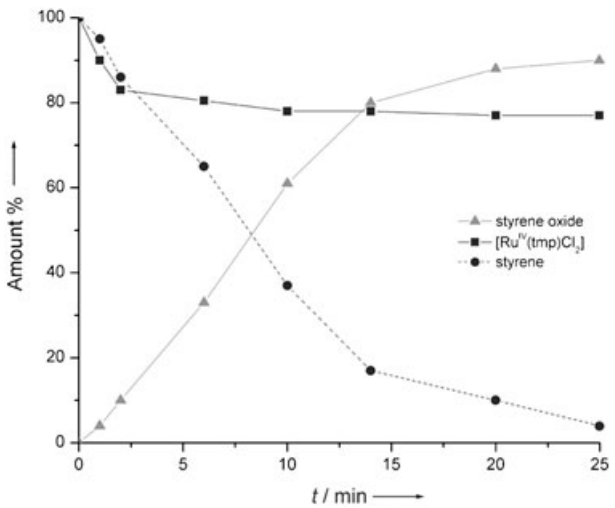


Figure 6. Time course plots for epoxidation of styrene with 2,6-Cl_2pyNO catalyzed by $[Ru^{IV}(tmp)Cl_2]$ (catalyst/styrene/2,6-Cl_2pyNO = 1:100:100). The reactions were monitored by ^{1}H NMR spectroscopy (300 MHz, $CDCl_3$) with 1,3,5-tribromobenzene as internal standard.

spectrum of the reaction mixture showed that the pyrrolic proton signal of $[Ru^{IV}(tmp)Cl_2]$ at −54 ppm decreased in intensity (30%) and some unassigned broad peaks at −10, −12, and −23 ppm developed.[20] Interestingly, when the reaction mixture was stirred for 72 h at room temperature, styrene oxide was found to be partly converted into phenyl acetylaldehyde in 14% yield (based on styrene epoxide). We note that neither $[Ru^{II}(tmp)(CO)]$ nor $[Ru^{IV}(tmp)Cl_2]$ catalyzed ring opening of styrene epoxide. Based on this finding, we propose that the $[Ru^{IV}(tmp)Cl_2]$ catalyst converts to some other species, presumably a Ru^{III} species according to the work by Groves and co-workers,[5] which functions as Lewis acid for epoxide-ring-opening reactions similar to that of iron(III)–porphyrin catalysts.[21]

Ru^{V}–oxo species or Ru^{IV}–oxo–porphyrin radical cation have generally been proposed as the reactive intermediate in ruthenium–porphyrin-catalyzed oxidation of hydrocarbons by 2,6-Cl_2pyNO.[5,22] In this work, $[Ru^{II}(F_{28}\text{-tpp})(CO)]$ provided an opportunity to examine the electronic effect of the porphyrinato ligand on catalytic oxidation. It is known that β-halogenation induces a large anodic shift in the oxidation potential of porphyrinato ring, thus disfavoring the formation of porphyrin π radical cation in the $[Ru(F_{28}\text{-tpp})]$ case, and Ru^{V}–oxo species of F_{28}-tpp would be expected to be oxidizing. Indeed, we found that the reaction of $[Ru^{VI}(F_{28}\text{-tpp})O_2]$ with styrene is ten times faster than that of $[Ru^{VI}(F_{20}\text{-tpp})O_2]$ in CH_2Cl_2 at room temperature.[23] However, as shown by entries 1–3 of Table 4, with 2,6-Cl_2pyNO as oxidant and at 40°C for 24 h, $[Ru^{II}(F_{28}\text{-tpp})(CO)]$ exhibited lower reactivity (conversion: <5%) toward epoxidation of styrene than $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ and $[Ru^{II}(F_{20}\text{-tpp})(CO)]$ (conversion: 62% and 54%, respectively). Similar findings were found with PhIO or TBHP used as a terminal oxidant. Thus $[Ru^{II}(F_{28}\text{-tpp})(CO)]$ is not an effective catalyst for catalytic oxidation, in contrast to the increased reactivity of $[Ru^{VI}(F_{28}\text{-tpp})O_2]$ relative to that of $[Ru^{VI}(F_{20}\text{-tpp})O_2]$ and $[Ru^{VI}(2,6\text{-}Cl_2tpp)O_2]$.[23]

Nam, Que, and co-workers reported the formation and characterization of an adduct complex formed between an iron–porphyrin and iodosylbenzene;[24a] Collman and co-workers showed small but appreciable dependence of selectivity on the nature of oxygen atom donor used in the iron–porphyrin- and manganese–corrole-catalyzed epoxidation of styrene and *cis*-cyclooctene.[25] Figure 7 depicts the plots of $\log k_{rel}$ (see Experimental Section) versus Hammett σ^+ substituent constant for the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed epoxidation of styrenes with 2,6-Cl_2pyNO, 2,6-Br_2pyNO, and 2,6-Me_2pyNO as oxidants, which show linear correlation with slopes (ρ^+) of −1.35, −1.07, and −0.61, respectively (R = 0.998, 0.995, and 0.996, respectively). With 2,6-Cl_2pyNO, the ρ^+ value is −0.72 when a heterogenized $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ catalyst was used,[10a] which is about twofold smaller than that using $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ as catalyst. The ligation of pyridine *N*-oxide, solvent, or other nucleophile generated during the catalysis to the putative "Ru^{V}=O" intermediate[5] could account for the different ρ^+ values.

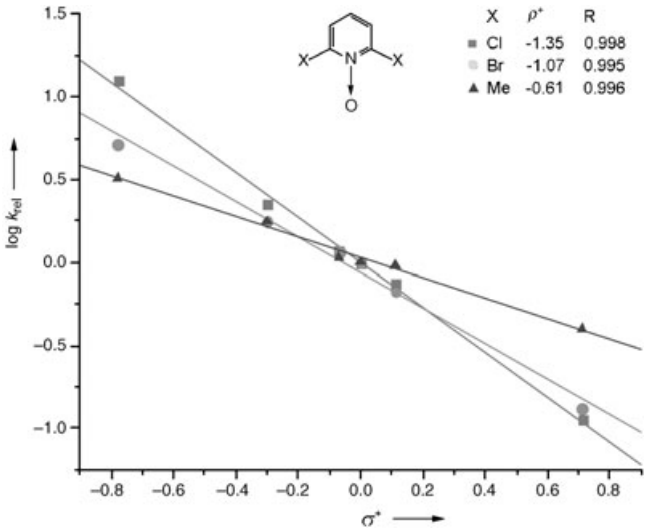
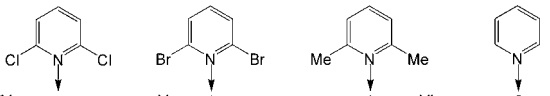


Figure 7. Hammett correlation studies ($\log k_{rel}$ vs σ^+) for $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed epoxidation of styrenes *p*-$YC_6H_4CH{=}CH_2$ (Y = MeO, Me, F, H, Cl) and 3-$NO_2C_6H_4CH{=}CH_2$ with 2,6-Cl_2pyNO, 2,6-Br_2pyNO, and 2,6-Me_2pyNO.

Following the work of Nam[24b] and Collman,[25] we examined competitive epoxidation of styrene and *cis*-cyclooctene using different pyridine *N*-oxides as oxidants and $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ as catalyst. As shown in Table 5, the use of different pyridine *N*-oxides did not affect the selectivity of the reactions. This is consistent with the proposal that a reactive "Ru^{V}=O" species was responsible for the oxidation.[5] Based on these observations, and the suggestion by Groves and co-workers,[5] a small amount of Ru^{III} species, generated from the Ru^{IV} in situ, was transformed to a "Ru^{V}=O" species upon addition of 2,6-Cl_2pyNO. However, the possibility of the formation of pyridine *N*-oxide-coordinated Ru^{IV}=O species similar to that proposed by Gross and Ini[6d] cannot be excluded.

Table 5. Competitive epoxidation of styrene and *cis*-cyclooctene with different pyridine *N*-oxides catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$.[a]

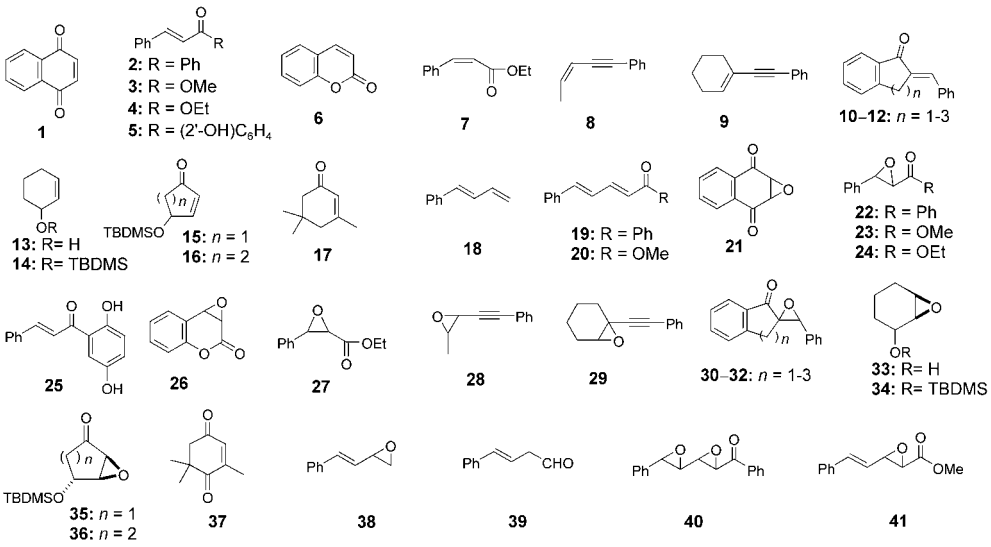


Entry	Catalyst	$Conv_{cis\text{-cyclooctene}}/Conv_{styrene}$[b]				
		T [°C]	IV	V	VI	VII
1	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	25	1.70	1.77	1.84	1.88
2	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	0	2.40	2.45	2.65	2.46
3	$[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$	25	1.67	1.70	[c]	[c]

[a] Reaction conditions: CH_2Cl_2, 40°C, catalyst/oxidant/styrene/*cis*-cyclooctene molar ratio = 1:1100:1000:1000. [b] Determined by GC using 1,4-dichlorobenzene as standard. [c] No reaction.

Epoxidation of conjugated enynes and electron-deficient alkenes: Epoxidation of conjugated enynes and electron-deficient alkenes (such as α,β-unsaturated ketones) provides useful intermediates for organic synthesis.[26] Although several efficient methods for these reactions with metal catalysts,[27] including the Weitz–Scheffer reaction, can give the corresponding epoxides in high yields and enantioselectivity, electrophilic oxidants are less studied for these transformations.[10b,14a,15,28] The previously reported "[Ru^{II}(Pybox)(Pydic)]+PhI($OAc)_2$" protocol (Pybox = bis(oxazolinyl)pyridine; Pydic = pyridine-2,6-dicarboxylate)[28] and ferric porphyrin–peroxo complexes[15] could only give the epoxides in moderate yields (60–70%). Jacobsen and co-workers have reported the asymmetric epoxidation of cinnimate esters catalyzed by chiral Mn–salen complexes.[29] Recently, we reported that [Ru^{IV}(D_4-por*)Cl_2][14a] and other ruthenium–porphyrin complexes[10b,e] catalyzed the epoxidation of electron-deficient alkenes with less than 70% conversion. In this work, we found that the [Ru^{IV}(2,6-Cl_2tpp)Cl_2]-catalyzed 2,6-Cl_2pyNO oxidation of 1) electron-deficient alkenes (**1**–**7**, **10**–**12**, **19**, **20**); 2) allylic substituted cyclohexenes (**13**, **14**); 3) cyclopentenone (**15**) and cyclohexenones (**16**, **17**); 4) conjugated alkene (**18**); and 5) conjugated enynes (**8**, **9**) (see Table 6) afforded the corresponding epoxides **21**–**24**, **26**–**36**, **38**, **40**, and **41** or other oxidation products (**25**, **37**, **39**) in up to 99% yield with up to 99% substrate conversion and with high regio- and diastereoselectivity and catalytic product turnover after a reaction time of 6–8 h. These results are unprecedented for metalloporphyrin catalysts.

Table 6. Oxidation of α,β-unsaturated ketones and conjugated enynes with 2,6-Cl_2pyNO catalyzed by ruthenium–porphyrin complexes.[a]



Entry	Catalyst	Substrate	Product	t [h]	Conv [%]	Yield [%][b]	TON[c]
1	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**1**	**21**	6	95	99	940
2	[Ru^{IV}(tmp)Cl_2]	**1**	**21**	8	90	99	890
3	[Ru^{IV}(ttp)Cl_2]	**1**	**21**	10	80	95	760
4	[Ru^{II}(2,6-Cl_2tpp)(CO)]	**1**	**21**	48	80	99	790
5	[Ru^{II}(F_{20}-tpp)(CO)]	**1**	**21**	12	90	99	890
6	[{Ru^{IV}(F_{20}-tpp)Cl}$_2$O]	**1**	**21**	24	7	99	69
7[d]	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**1**	**21**	48	65	99	6.4×10^3
8	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**2**	**22**[e]	6	96	99	950
9	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**3**	**23**[e]	6	80	99	790
10	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**4**	**24**[e]	6	78	99	770
11	[Ru^{IV}(tmp)Cl_2]	**4**	**24**[e]	6	65	99	640
12[f]	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**5**	**25**	12	42	85	350
13	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**6**	**26**	6	85	99	840
14	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**7**	**27**[g]	6	98	90	880
15	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**8**	**28**[h]	6	95	88	840
16	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**9**	**29**	6	99	99	980
17	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**10**	**30**	8	38	90	340
18	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**11**	**31**	8	46	92	420
19	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**12**	**32**	8	72	90	650
20	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**13**	**33**	2	99	99	980
21	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**14**	**34**	2	99	99	980
22	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**15**	**35**	6	95	99	940
23	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**16**	**36**	6	95	90	860
24	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**17**	**37**	8	75	99	740
25	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**18**	**38**+**39**	6	99	50 (**38**), 50 (**39**)	490
26[f]	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**19**	**40**	8	99	80	790
27	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**20**	**41**	8	95	85	810

[a] Reaction conditions: CH_2Cl_2, 40°C, catalyst/oxidant/substrate molar ratio = 1:1100:1000, unless otherwise noted. [b] Isolated yield based on the amount of consumed substrate. [c] Turnover number. [d] Catalyst/oxidant/substrate molar ratio = 1:10000:11000. [e] Configuration: *trans*. [f] Catalyst/oxidant/substrate molar ratio = 1:2200:1000. [g] *cis*:*trans* = 9:1. [h] *cis*:*trans* = 10:1.

Treatment of 1,4-naphthoquinone (**1**, 1 mmol) with 2,6-Cl_2pyNO (1.1 mmol) and catalyst [Ru^{IV}(2,6-Cl_2tpp)Cl_2] (1 μmol) in CH_2Cl_2 at 40°C for 6 h afforded **21** in 99% yield with substrate conversion of 95% (entry 1 in Table 6). When [Ru^{IV}(tmp)Cl_2], [Ru^{IV}(ttp)Cl_2], [Ru^{II}(2,6-Cl_2tpp)(CO)], or [Ru^{II}(F_{20}-tpp)(CO)] was used as catalyst, a considerably longer reaction time was required to attain similar substrate conversion (>80%, entries 2–5 in Table 6). The μ-oxo dimer [{Ru^{IV}(F_{20}-tpp)Cl}$_2$O] was not effective for this transformation, as only 7% substrate conversion was attained after a reaction time of 24 h (entry 6 in Table 6). To further investigate the stability of the catalyst toward the ox-

idation process, we examined the epoxidation of **1** in the presence of 0.01 mmol% of $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$, and a turnover number of up to 6.4×10^3 was achieved (entry 7 in Table 6).

Complex $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ can efficiently catalyze the epoxidation of chalcone and *trans*-cinnimate esters **2**–**4**, producing the corresponding epoxides **22**–**24** in 99% yield with substrate conversions of 78–96% within 6 h (entries 8–10 in Table 6). In contrast, the $[Ru^{IV}(D_4\text{-por*})Cl_2]$-catalyzed 2,6-$Cl_2$pyNO epoxidation of **2** and **4** gave **22** and **24** with substrate conversion of 18 and 48%, respectively, after 16 h.[14a] For the oxidation of **4**, $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ also exhibited a higher catalytic efficiency than $[Ru^{IV}(tmp)Cl_2]$ (entries 10 and 11 in Table 6). The oxidation of 2′-hydroxychalcone (**5**) was also examined. The aromatic ring hydroxylation product **25** was obtained with the C=C bond remaining intact (yield: 85%, conversion: 42%, entry 12 in Table 6). It should be noted that when coumarin (**6**) was employed as a substrate, the epoxide **26** was obtained in nearly quantitative yield (entry 13 in Table 6) within 6 h, whereas a similar epoxidation by dimethyldioxirane would require 14 days.[30]

Epoxidation of **7** and **8** catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ (entries 14 and 15 in Table 6) gave **27** and **28**, respectively, with high conversions. *trans*-Epoxides were found as side products (for **27**, *cis*/*trans* = 9:1; for **28**, *cis*/*trans* = 10:1). This is comparable to the epoxidation catalyzed by chiral Mn–salen complexes (which gave a mixture of *cis*- and *trans*-**27** in a ratio of 73:10),[29] $[Ru^{IV}(D_4\text{-por*})Cl_2]$ (*cis*-/*trans*-**28** = 86:12),[14a] and polymer-supported ruthenium porphyrin (*cis*-/*trans*-**28** = 13:1).[10b] In addition, conjugated enyne **9** with a double bond in the cyclohexene ring could be epoxidized to afford **29**, which is an important intermediate in the synthesis of α-allenic alcohols,[31] in high yield (entry 16 in Table 6).

Due to electronic and steric effects, cyclic enones **10**–**12** derived from indanone, tetralone, and benzosuberone are known to be sluggish substrates toward oxidation.[32] Interestingly, these substrates were epoxidized to **30**–**32**, respectively, in 90–92% yields with up to 72% conversion within 8 h by using catalyst $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ (entries 17–19 in Table 6).

trans-Epoxides of allylic cycloalkenes are versatile building blocks for organic synthesis and construction of biologically active natural products,[33,34] and recently manganese– and ruthenium–porphyrin complexes were proved to be efficient catalysts for the synthesis of this class of epoxides.[13] As shown in entry 20 of Table 6, by using $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2)]$ as catalyst, **13** was converted into **33** in 99% yield and 99% conversion within 2 h at 40 °C, with a moderate selectivity of *trans*/*cis* = 1:5, which is different from that obtained using manganese–porphyrin catalysts (*cis*/*trans* = 1:4).[13] Strikingly, for **14** with a protected 3-hydroxyl group, the *trans*-epoxide **34** was obtained in 99% yield with turnover number (TON) of 980 within 2 h (entry 21 in Table 6).

To examine the diastereoselectivity in epoxidation of electron-deficient cycloalkenes catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$, we performed the epoxidation of allylic substituted cyclopentenone **15** and cyclohexenone **16**. As shown in entries 22 and 23 of Table 6, **15** and **16** were converted into *trans*-epoxides **35** and **36**, respectively, in up to 99% yield with 95% conversion and with a TON of up to 940 after 6 h at 40 °C. A TON of 3000 was achieved when the epoxidation of **15** was performed for 48 h with lower catalyst loading. Evidently, $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ exhibited a markedly higher reactivity and product turnover than $[Ru^{II}(2,6\text{-}Cl_2tpp)(CO)]$ (48 h, TON = 80)[13] in catalyzing these epoxidation reactions.

It is interesting to note that the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed oxidation of isophorone **17** afforded α,β-unsaturated diketone **37** in 99% yield (entry 24 in Table 6). This is different from the results using metal peroxide as oxidant, which gave the epoxide as major product.[35] A manganese porphyrin has also been reported to catalyze the oxidation of **17** to the diketone product **37** (with oxygen as oxidant in the presence of triethyl amine).[36] This may be due to the presence of γ-CH_2 and α-CH_3 groups in **17**; the γ-CH_2 group would be more readily oxidized than the alkene double bond, the latter is obstructed by the α-CH_3 group.

We are interested in the regioselective epoxidation of electron-deficient α,β:γ,δ conjugated alkenes. Previous work has shown that the α,β-double bond is more reactive towards a nucleophilic oxidant than the γ,δ-bond, but this regioselectivity has rarely been encountered with electrophilic oxidants.[37] For example, dimethyldioxirane was reported to oxidize (*E*,*E*)-cinnamylideneacetophenones to give the corresponding diepoxides with minor α,β-monoepoxide.[37c] In this work, different conjugated alkenes **18**–**20** were employed to investigate the electronic effect of these alkenes on the regioselectivity of the oxidations under our reaction conditions (entries 25–27, Table 6). First, epoxidation of **18** gave γ,δ-monoepoxide **38** in 50% yield and aldehyde **39** in 50% yield after 6 h, revealing that the "$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$+2,6-$Cl_2$pyNO" protocol favored oxidation of terminal double bonds. The (*E*,*E*)-cinnamylideneacetophenone substrate **19** was chosen as it contains an electron-withdrawing carbonyl group. Oxidation of **19** afforded the α,β:γ,δ-diepoxide **40** as the main product (80% yield); only minor γ,δ-monoepoxide (5% yield) was detected. A 60% yield of α,β:γ,δ-diepoxide was obtained by using dimethyldioxirane as oxidant.[37c,38] For substrate **20**, which contains an electron-withdrawing COOMe group, the major product was *trans*-α,β-monoepoxide **41** (yield: 85%), with *trans*-γ,δ-monoepoxide obtained in 10% yield; this shows that the less electron-rich C=C bond of **20** was favorably epoxidized. To our knowledge, this is the first catalytic epoxidation of electron-deficient α,β:γ,δ-conjugated alkene to afford *trans*-α,β-monoepoxides with an adjacent COOMe group, which is a useful building block for natural product synthesis.[39] The present finding is comparable to the results obtained for the Darzens reaction involving stoichiometric reactions between aldehyde and α-halo carbonyl compounds.[39]

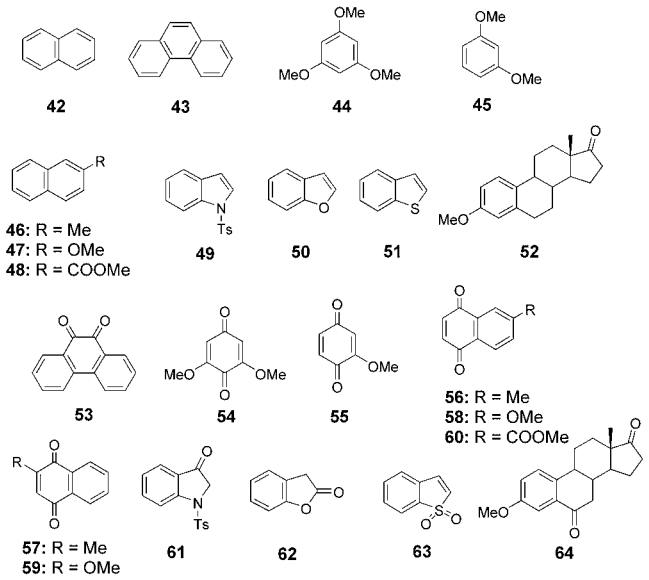
Oxidation of arenes: Oxidative transformation of arenes to quinones is of importance due to the biological activities

and synthetic applications of quinones. In particular, *p*-benzoquinones are useful building blocks for the synthesis of antitumor compounds such as chaloxone and Strepomycetes metabolite LL-C10037α.[40] From a biological perspective, arenes can be metabolized in vivo by cytochrome P-450 to form quinones.[40b] From a chemical point of view, preparation of quinones by direct oxidation of arenes would be an advanced synthetic method.[41] The most commonly employed procedures for oxidation of arenes require an excess of metal-based oxidants such as CrO_3, which pose severe problems to the environment.[42] Metal catalysts such as methyltrioxorhenium(VIII) (MTO) as well as iron– and manganese–porphyrin complexes have been reported for these oxidations.[43] However, product turnover numbers (TONs) of less than 100 were observed. Hirobe and co-workers first reported that the "ruthenium–porphyrin + 2,6-Cl_2pyNO" protocol could be employed to selectively convert aromatic compounds to quinones in the presence of HBr or HCl with turnover numbers of up to 500.[4d,f] Groves and co-workers reported that oxidation of benzene with 2,6-Cl_2pyNO catalyzed by [Ru^{II}(F_{20}-tpp)(CO)] gave 1,4-benzoquinone in the absence of acid.[5] Encouraged by these findings, we examined the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol for oxidation of arenes in the absence of an acid additive.

The oxidation reactions were carried out in CH_2Cl_2 in sealed flasks at 40 °C and were followed by TLC (Table 7). Alkoxybenzene derivatives such as *m*-trimethoxybenzene (**44**) and *m*-dimethoxybenzene (**45**) were oxidized to *p*-benzoquinones **54** and **55** in 99 % yield with 99 % and 94 % conversions, respectively (entries 3 and 5 in Table 7). For the oxidation of **44**, the turnover number can be as high as 2.0×10^4 (entry 4 in Table 7). For less reactive substrates such as naphthalene (**42**) and phenanthrene (**43**), the oxidations gave 1,4-naphthoquinone (**1**) and 9,10-phenanthroquinone (**53**) in 99 % yield with 40 and 58 % conversions, respectively (entries 1 and 2 in Table 7). Using Herrmann's "MTO + H_2O_2 + Ac_2O + HOAc" protocol, a highly concentrated (up to 83 %) H_2O_2 solution would be required to achieve good substrate conversion.[43e]

2-Methylnaphthalene (**46**) was oxidized by the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol to give 6- and 2-methyl-1,4-naphthoquinones (**56** and **57**) in a ratio of 6.6:1 with high conversion (80 %, entry 6 in Table 7); this ratio is higher than that obtained by using the "[Ru^{II}(2,6-Cl_2tpp)(CO)] + 2,6-Cl_2pyNO" protocol (the ratio of **56**/**57** is 3.3:1, conversion = 46 %). Previous work by Meunier and Bernadou showed that the Fe– and Mn–porphyrin-catalyzed oxidation of **46** resulted in lower regioselectivities (the **56**/**57** ratio varied from 0.5 to 2.5:1).[43g] Our results (**56**/**57** = 6.6:1) are also different from those observed by using the "MTO + hydrogen peroxide" protocol, in which case, compound **57** was obtained as the main product (**56**/**57** is up to 1:7.5).[44] 6-Substituted-1,4-naphthoquinones could be used as key building blocks in the synthesis of natural products such as (+)-cordiaquinone B and some terphenylquinones, which could be prepared through Diels–Alder condensation between conjugated dienes and *p*-benzoquinones.[45] In this work, we

Table 7. Oxidation of arenes with 2,6-Cl_2pyNO catalyzed by [Ru^{IV}(2,6-Cl_2tpp)Cl_2].[a]



Entry	Substrate	Product	*t* [h]	Conv [%]	Yield [%][b]	TON[c]
1	**42**	**1**	12	40	99	400
2	**43**	**53**	12	58	99	570
3	**44**	**54**	6	99	99	980
4	**44**	**54**	48	68	99	2.0×10^4
5	**45**	**55**	6	94	99	930
6	**46**	**56** + **57**	12	80	87 (**56**), 13 (**57**)	800
7	**47**	**58** + **59**	12	95	45 (**58**), 55 (**59**)	950
8	**48**	**60**	6	68	99	670
9	**49**	**61**	6	99	95	940
10	**50**	**62**	6	99	95	940
11	**51**	**63**	6	99	95	940
12	**52**	**64**	8	99	88	870

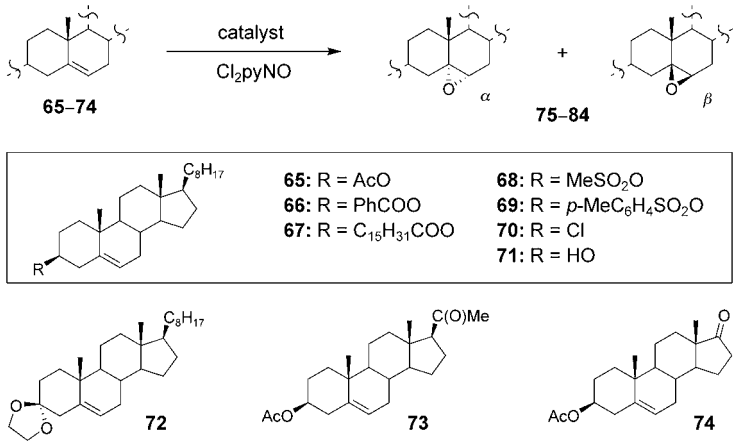
[a] Reaction conditions: CH_2Cl_2, 40 °C, catalyst/oxidant/substrate molar ratio = 1:4400:1000 (entries 1 and 2), 1:2200:1000 (entries 3, 5–12), 1:60000:30000 (entry 4). [b] Isolated yield based on the amount of consumed substrate. [c] Turnover number.

obtained this kind of product in 70 % yield through a one-step oxidation of commercially available 2-methylnaphthalene. To investigate the generality of the oxidation of 2-substituted naphthalenes, methoxyl 2-naphthalene (**47**) and methyl 2-naphthoate (**48**) were used as substrates. As shown in Table 7 (entry 7), oxidation of **47** gave two products **58** and **59** in a ratio of 45:55 and the conversion was up to 95 %. When **48** was used as substrate, only 6-substituted 1,4-naphthoquinone **60** was obtained (99 % yield, entry 8 in Table 7). These results indicate that, for 2-substituted naphthalenes, an electron-withdrawing group at the 2-position offered better regioselectivity (COOMe > Me > OMe).

For heteroatom-containing compounds such as benzoindole, benzofuran, and benzothiophene (**49**–**51**), the reactions afforded the products **61**–**63** in 95 % yield with 99 % conversion (entries 9–11 in Table 7). Previously, these oxidation products were prepared by stoichiometric oxidation with oxodiperoxomolybdenum(VI).[46]

Estrone and its methoxy derivative form an important class of arenes which are of interest in medicinal chemistry.

Table 8. Epoxidation of Δ^5-unsaturated steroids with 2,6-Cl_2pyNO catalyzed by ruthenium–porphyrin complexes.[a]



Entry	Catalyst	Substrate	Product	t [h]	Conv [%]	Yield [%][b] (α+β)	β:α ratio[c]	TON[d]
1	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**65**	**75**	0.5	100	95	>99:1	950
2	[Ru^{IV}(tmp)Cl_2]	**65**	**75**	2	100	95	84:1	950
3	[Ru^{IV}(ttp)Cl_2]	**65**	**75**	2.5	100	89	3:1	890
4	[Ru^{II}(2,6-Cl_2tpp)(CO)]	**65**	**75**	12	100	92	>99:1	920
5	[Ru^{II}(F_{20}-tpp)(CO)]	**65**	**75**	12	100	90	8:1	900
6[e]	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**65**	**75**	48	75	73	>99:1	1.6×10^4
7	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**66**	**76**	1	100	93	>99:1	930
8	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**67**	**77**	1	100	96	>99:1	960
9	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**68**	**78**	1	100	95	>99:1	950
10	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**69**	**79**	1	99	97	>99:1	960
11	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**70**	**80**	1	100	90	26:1	900
12	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**71**	**81**	1	100	85	7:1	850
13	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**72**	**82**	1	100	94	>99:1	940
14	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**73**	**83**	1	100	96	>99:1	960
15	[Ru^{IV}(2,6-Cl_2tpp)Cl_2]	**74**	**84**	1	100	92	>99:1	920

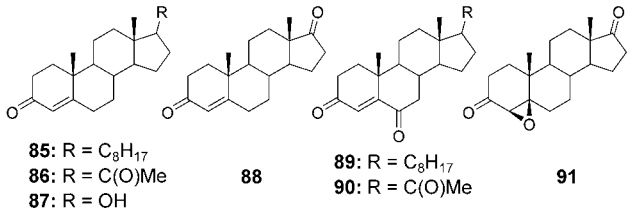
[a] Reaction conditions: CH_2Cl_2, 40 °C, catalyst/oxidant/substrate molar ratio = 1:1100:1000 (except for entry 6). [b] Isolated yield based on starting substrate. [c] Determined by ^{1}H NMR spectroscopy as described in reference [51]. [d] Turnover number. [e] Catalyst/oxidant/substrate molar ratio = 1:33000:30000.

Hirobe and co-workers first reported the oxidation of estrone with cytochrome P-450 as catalyst, resulting in selective oxidation at the C7-position of estrone to give 10β-hydroxy-1,4-estradiene-3,17-dione.[47a] The oxidation of estrone using the "[Ru^{II}(2,6-Cl_2tpp)(CO)] + 2,6-Cl_2pyNO + HX" protocol was also reported,[47a] which afforded an intractable dark liquid. In this work, a similar result was found with the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol. However, by changing the 3-hydroxy group of estrone to a methoxy group, the C6-position of **52** was oxidized with the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol to ketone **64** in 88% yield with 99% conversion (entry 12 in Table 7). The "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol therefore affords the selective oxidation of the benzylic C–H bonds at the C6-position of protected estrone.

Oxidation of Δ^5- and Δ^4-steroids and estratetraene derivatives: The biochemistry of steroids is of considerable interest in the context of drug discovery, particularly for the treatment of malignant diseases.[48] Selective oxidation of steroids could lead to new epoxide and ketone derivatives that are important intermediates for further structural elaboration of steroid skeletons. In this work, we found that the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol displayed remarkable efficiencies in 1) oxidation of Δ^5-unsaturated steroids **65**–**74** to form epoxides **75**–**84**, respectively (Table 8), 2) oxidation of Δ^4-3-ketosteroids **85**–**88** to form diketo-, or triketosteroids (Table 9), and 3) oxidation of estratetraene derivatives **92**–**94** to form epoxides **95**–**97**, respectively (Table 10).

β-*Selective epoxidation of* Δ^5-*unsaturated steroids*: 5β,6β-Epoxides can be found in some naturally occurring Δ^5-unsaturated steroids that exhibit antitumor activities.[49] Previous attempts to achieve metal-mediated stereoselective β-epoxidation of Δ^5-unsaturated steroids employed protocols such as "vanadium or molybdenum catalyst + alkyl hydroperoxide",[50a] "Fe^{III} or Ti^{III} acetylacetonates + hydrogen peroxide",[50b] "$KMnO_4$-copper or iron sulphate",[50c,f] bisoxazolineruthenium(II) complexes,[50g] and "methyltrioxorhenium(MTO) + H_2O_2".[50h] Metalloporphyrin complexes of manganese[50d] and ruthenium[3,10c–e] have previously been used as catalysts for epoxidation of Δ^5-unsaturated steroids. Nevertheless, all the reported metal-catalyzed oxidation protocols suffer from low product-turnover num-

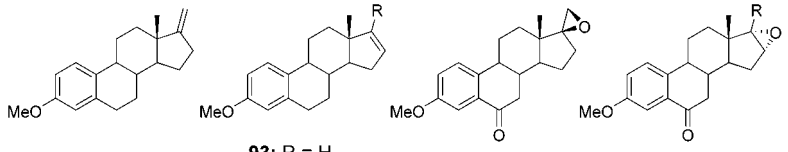
Table 9. Oxidation of Δ^4–3-ketosteroids with 2,6-Cl_2pyNO catalyzed by [Ru^{IV}(2,6-Cl_2tpp)Cl_2].[a]



Entry	Substrate	Product	t [h]	Conv [%]	Yield [%][b]	TON[c]
1	**85**	**89**	6	99	92	910
2	**86**	**90**	6	99	95	940
3	**87**	**88**	1	99	99	980
4	**88**	**91**	4	99	89	880

[a] Reaction conditions: CH_2Cl_2, 40 °C, catalyst/oxidant/substrate molar ratio = 1:2200:1000 (entries 1 and 2) or 1:1100:1000 (entries 3 and 4). [b] Isolated yield based on the amount of consumed substrate. [c] Turnover number.

Table 10. Epoxidation of estratetraene derivatives with 2,6-Cl_2pyNO catalyzed by $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$ and $[Ru^{IV}(tmp)Cl_2]$.[a]



92 **93**: R = H, **94**: R = C≡CH **95** **96**: R = H, **97**: R = C≡CH

Entry	Catalyst	Substrate	Product	Conv [%]	Yield [%][b]	TON[c]
1	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	**92**	**95**	99	90	890
2	$[Ru^{IV}(tmp)Cl_2]$	**92**	**95**	99	88	870
3	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	**93**	**96**	99	95	940
4	$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$	**94**	**97**	99	92	910

[a] Reaction conditions: CH_2Cl_2, 40 °C, 8 h, catalyst/oxidant/substrate molar ratio = 1:4000:1000. [b] Isolated yield based on the substrate consumed. [c] Turnover number.

bers (less than 100), except for the ruthenium–porphyrin complexes grafted on dendrimers or soluble polymers (which gave TONs of up to 900).[10d,e]

We first employed cholesterol acetate **65** as a substrate to examine the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed epoxidation of Δ^5-unsaturated steroids with 2,6-Cl_2pyNO. The reaction was completed within 0.5 h when conducted in CH_2Cl_2 with catalyst/2,6-Cl_2pyNO/**65** molar ratio of 1:1100:1000, and afforded a mixture of α- and β-**75** in 95% yield, with β:α ratio of >99:1 (entry 1 in Table 8).[51] Changing the catalyst to $[Ru^{IV}(tmp)Cl_2]$, $[Ru^{IV}(ttp)Cl_2]$, or $[Ru^{IV}(por)(CO)]$ (por = 2,6-Cl_2ttp, F_{20}-tpp) increased the reaction time to 2–12 h for completion of the reaction under similar conditions (entries 2–5 in Table 8). It is remarkable that, with a catalyst/2,6-Cl_2pyNO/**65** molar ratio of 1:33000:30000, the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed epoxidation of **65** gave an extremely high turnover number of 1.6×10^4, and the β:α ratio was maintained at >99:1 (entry 6 in Table 8).

Epoxidation of Δ^5-steroids **66**–**74** by using the "$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$+2,6-$Cl_2$pyNO" protocol with catalyst/2,6-Cl_2pyNO/substrate molar ratio of 1:1100:1000 gave epoxides **76**–**84**, respectively, in 85–97% yields within 1 h (entries 7–15 in Table 8). The Δ^5-steroid with a free C3-OH group (**71**) was converted to its epoxide **81** with moderate β-selectivity (β:α = 7:1) in 85% yield (entry 12 in Table 8). No ketone product was observed. The Δ^5-steroids with other C3-substituents were oxidized to their epoxides with almost complete β-selectivity (entries 7–10 and 13–15 in Table 8). Interestingly, the methanesulfonate and tosylate derivatives **68** and **69** (key intermediates in the conversion of epoxide to diene) were converted into the epoxides without detectable decomposition of the methanesulfonyl and tosyl groups. The 17-substituted steroids **72**–**74** also gave the products **82**–**84**, respectively, in high yields and excellent selectivities (entries 13–15, Table 8), revealing that substituents at the 17-position have little effect on the reactions. It is especially striking that the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed epoxidations of the benzoic ester **66** and the long-chain aliphatic ester **67** with 2,6-Cl_2pyNO (entries 7 and 8 in Table 8) were completed within 1 h. In contrast, epoxidations of these two substrates by "$[Ru^{VI}(tmp)O_2]$+air"[3] and "dendritic ruthenium–porphyrin+2,6-Cl_2pyNO"[10d] require 24 h for completion.

Oxidation of Δ^4-3-ketosteroids: Δ^4-3-Ketosteroids exhibit useful therapeutic actions. They are involved in the biosynthetic step of the steroid nucleus in vivo and are key starting materials for the synthesis of steroid derivatives that are potential inhibitors of aromatase.[52] It should be noted that Δ^4-3-ketosteroids are α,β-unsaturated ketones. Holland and co-workers showed that oxidation of Δ^4-3-ketosteroids with excess sodium peroxide gave Δ^4-3,6-diketosteroids in moderate yields.[53a] Marchon and co-workers observed that Δ^4-3-ketosteroids such as Δ^4-cholestene-3-one **85** (Table 9) could not be oxidized using the "$[Ru^{VI}(tmp)O_2]$+air" protocol.[3b]

We performed the $[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$-catalyzed oxidation of **85** and progesterone (**86**) in CH_2Cl_2 at 40 °C for 6 h with catalyst/2,6-Cl_2pyNO/substrate molar ratio of 1:2200:1000 and obtained the Δ^4-cholestene-3,6-dione (**89**) and Δ^4-pregnene-3,6,20-trione (**90**) in 92 and 95% yields (entries 1 and 2 in Table 9), respectively. No hydroxylated products or epoxides were detected in the reaction mixtures (even with the 2,6-Cl_2pyNO/substrate molar ratio of 1.1:1). This is different from the oxidation of Δ^5-cholestene-3-one by the "$[Ru^{VI}(tmp)O_2]$+air" system,[53b] which gave a mixture of **89**, 6β-hydroxy-Δ^4-cholestene-3-one, and 6α-hydroxy-Δ^4-cholestene-3-one. The oxidation of Δ^5-cholestene-3-one to **89** can also be effected by employing the "$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$+2,6-$Cl_2$pyNO" protocol with 2,6-$Cl_2$pyNO/substrate molar ratio of 2.2:1, and again, no hydroxylated products or epoxides were detected (**89** is usually obtained from oxidation of Δ^5-3β-alcohol or Δ^5-3-one by using chromium oxidants[53c,d]).

Interestingly, changing the substituent at the C17 position in the D ring resulted in a change in the nature of the oxidation product. Oxidation of **85** and **86** using this protocol gave Δ^4-3,6-diones (**89** and **90**, entries 1 and 2 in Table 9). However, with a hydroxyl group at the C17-position (**87**), the reaction was fast, affording Δ^4-androstene-3,17-dione (**88**) in 98% overall yield within 1 h (entry 3 in Table 9). The oxidation of **88** proceeded more slowly and gave the β-epoxide **91** in 89% yield after 4 h as shown in entry 4 of Table 9 (the structure of **91** was determined by X-ray crystal analysis, see Figure S1 in the Supporting Information). Such dependence of the oxidation product on the C17-substituent has not been observed for the oxidation of Δ^4-3-ketosteroids with TBHP or sodium peroxide[53] or the oxidation of Δ^5-unsaturated steroids using the "$[Ru^{IV}(2,6\text{-}Cl_2tpp)Cl_2]$+2,6-$Cl_2$pyNO" protocol described above.

Oxidation of estratetraene derivatives with C=C bond at D ring: Steroids with an epoxide group at the C17-position of D ring are key intermediates for natural product synthesis.[54] These epoxides are usually prepared through stoichiometric reactions that either give low to moderate diastereoselectivity or require tedious experimental procedures. For example, the C17-epoxides of estrone and its derivatives (which have potential uses in oral contraceptive treatment of hyperandrogenism and in the treatment of hormone-dependent breast cancer in postmenopausal women[55]) can be obtained by oxidation using *m*-CPBA with a diastereoselectivity of $\alpha/\beta = 80{:}20$,[55a,56a,56c] by ring closure of *trans*-bromohydrin with strong inorganic base,[56c,e] and by reaction of the carbonyl group (C17) at D ring with sulfur ylide ($Me_3SOI/KO\textit{t}Bu$).[55c–e] However, there are few reports on the synthesis of the C17-epoxides of unsaturated steroids through catalytic processes.[10d,57]

We observed that treatment of the estratetraene derivatives **92**–**94** with 2,6-Cl_2pyNO in CH_2Cl_2 in the presence of catalyst [Ru^{IV}(2,6-Cl_2tpp)Cl_2] at 40 °C for 8 h (catalyst/2,6-Cl_2pyNO/substrate molar ratio = 1:4000:1000) led to epoxidation of the double bond between C17 and C19 of **92** and between C16 and C17 of **93** and **94** to give epoxides **95**–**97**, respectively, in 90–95 % yields with virtually complete β-selectivity for **95** and α-selectivity for **96** and **97** (entries 1, 3, and 4 in Table 10); the β-configuration of **95** and α-configuration of **96** were confirmed by X-ray crystal analysis, see Figure S2 in the Supporting Information). A similar reaction was observed when [Ru^{IV}(tmp)Cl_2] was used as catalyst (entry 2 in Table 10). Surprisingly, in these cases, the CH_2 group at the C6-position in B ring was concomitantly oxidized to ketone (such oxidation could not be prevented even when the 2,6-Cl_2pyNO/substrate molar ratio was reduced to 1.1:1). This is unusual in the oxidation chemistry of estratetraene derivatives and is different from the TBHP epoxidation of the analogues of **92** catalyzed by the Sharpless catalysts[57] and other oxidation methods,[56,58] and from the 2,6-Cl_2pyNO epoxidation of **92** catalyzed by a [Ru^{II}(por)(CO)]-based dendritic ruthenium–porphyrin complex,[10d] neither of which resulted in oxidation of the benzylic CH group at the C6-position.

Conclusion

The structurally characterized [Ru^{IV}(2,6-Cl_2tpp)Cl_2] shows a markedly higher efficiency in catalyzing epoxidation of electron-deficient alkenes with 2,6-Cl_2pyNO than the carbonylruthenium(II)–porphyrin complexes [Ru^{II}(por)(CO)] (por = 2,6-Cl_2ttp, F_{20}-tpp) and other dichlororuthenium(IV)–porphyrin complexes [Ru^{IV}(tmp)Cl_2] and [Ru^{IV}(ttp)Cl_2]. The epoxidation of a variety of α,β-unsaturated ketones with 2,6-Cl_2pyNO catalyzed by [Ru^{IV}(2,6-Cl_2tpp)Cl_2] can be completed in a few hours, and exhibited high regio- and diastereoselectivities with up to 99 % substrate conversion. The "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol is applicable to the oxidation of arenes and affords quinones with up to 99 % substrate conversion and almost complete product selectivity within several hours. [Ru^{IV}(2,6-Cl_2tpp)Cl_2] is also a powerful catalyst for oxidation of steroids with 2,6-Cl_2pyNO under mild conditions. By employing this catalyst, the oxidation of Δ^5-unsaturated steroids can be completed within 0.5 or 1 h and displayed up to > 99 % β-selectivity and up to 97 % epoxide yield; while the oxidation of Δ^4-3-ketosteroids to Δ^4-3,6-diketosteroids or β-epoxide (which proceeded with up to 99 % product yields within 1–6 h) is sensitive to the substituent(s) at the remote C17-position. For oxidation of estratetraene derivatives with C=C bond at D ring, both the C=C and the benzylic C–H bonds at the C6-position in B ring are oxidized, affording a new class of steroid derivatives in up to 95 % yields. Product turnover numbers in the oxidation of electron-deficient alkenes, arenes, and steroids by using the "[Ru^{IV}(2,6-Cl_2tpp)Cl_2] + 2,6-Cl_2pyNO" protocol can be as high as 6.4×10^3, 2.0×10^4, and 1.6×10^4, respectively. These results demonstrate that [Ru^{IV}(2,6-Cl_2tpp)Cl_2] is an active, robust, and versatile catalyst for highly selective oxidation of arenes, unsaturated steroids, and electron-deficient alkenes using 2,6-Cl_2pyNO as oxidant.

Experimental Section

General: *m*-CPBA, alkenes **1**–**4**, **6**, **13**, **17**, arenes **42**–**46**, **50**, **51**, and steroids **65**–**67**, **70**, **71**, **73**, **74**, **85**–**88** were purchased from Aldrich and Acros. Alkenes **5**,[59] **7**–**9**,[29,31,60] **10**–**12**,[61] **14**–**17**,[13] **18**,[62] **19**, **20**,[37] arenes **47**, **48**,[63,64] **49**,[65] estrone derivative **52**,[66] cholesteryl esters **68**, **69**,[67] **72**,[68] estratetraene derivatives **92**,[69] **93**,[70] **94**,[71] oxidant 2,6-X_2pyNO (X = Cl, Br, Me, H),[72] the porphyrin ligands,[73] and related ruthenium complexes of porphyrins[10] and Schiff bases[74] were prepared according to the published procedures. All solvents were of AR grade. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DPX 300 or 400 spectrometer by using tetramethylsilane (TMS) as an internal standard, with the chemical shifts relative to TMS. Infrared spectra were recorded by using Bio-Rad FTS-7 FT-IR spectrometer. UV-visible spectra were measured on a Milton Roy Spectronic 3000 diode-array spectrophotometer. Mass spectra were recorded on a Finnigan MAT95 (FAB), Finnigan LCQ quadrupole ion trap (electrospray), or Jasco (EI and HRMS) mass spectrometer. GC measurements were carried out on a HP 5890 Series II gas chromatograph equipped with a flame ionization detector and a 3396 Series II integrator. Electrochemical studies were performed on a Princeton Applied Research Model 273 A potentiostat/galvanostat coulometer with a three-electrode cell system (working electrode: glassy carbon, counter electrode: platinum wire, reference electrode: 0.1 M $Ag/AgNO_3$ in MeCN). Elemental analysis was performed by the Institute of Chemistry, the Chinese Academy of Sciences.

Preparation of [Ru^{IV}(2,6-Cl_2tpp)Cl_2] and [Ru^{IV}(tmp)Cl_2]:*m*-CPBA (0.17 g, 1 mmol) was added to a solution of [Ru^{II}(2,6-Cl_2tpp)(CO)] or [Ru^{II}(tmp)(CO)] (0.1 mmol) in CH_2Cl_2 (30 mL). The mixture was stirred at room temperature for 30 min and then flashed through an alumina column. Removal of solvent in vacuo gave [Ru^{VI}(por)O_2] (por = 2,6-Cl_2ttp or tmp). The freshly prepared [Ru^{VI}(por)O_2] was dissolved in CH_2Cl_2 (20 mL) and treated with Me_3SiCl (0.2 mL). The resulting mixture was stirred at room temperature under argon until the reaction reached completion (monitored by UV-visible spectroscopy). The solvent was removed by evaporation, and the residue was washed with methanol (5 × 15 mL) and recrystallized from CH_2Cl_2/MeOH, affording [Ru^{IV}(2,6-Cl_2tpp)Cl_2] or [Ru^{IV}(tmp)Cl_2] as a dark red solid.

Data for [Ru^{IV}(2,6-Cl_2tpp)Cl_2]: Yield: 90 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (d, 8H; phenyl-H), 8.81 (t, 4H; phenyl-H), −53.4 ppm (br s, 8H; pyrrole-H); IR (KBr): $\tilde{\nu}$ = 1010 cm^{-1} (oxidation state marker band); UV/

Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 410 (5.20), 520 nm (4.11); elemental analysis calcd (%) for $C_{44}H_{20}Cl_{10}N_4Ru{\cdot}CH_3OH{\cdot}0.5\,CH_2Cl_2$ (1134.76): C 48.16, H 2.22, N 4.94; found: C 48.39, H 1.91, N 4.83; electrospray MS: *m/z*: 1059.7 $[M]^+$, 1024.9 $[M-Cl]^+$, 989.9 $[M-2Cl]^+$.

Data for [Ru^{IV}(tmp)Cl$_2$]: Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.47 (s, 8H; phenyl-H), 4.08 (s, 24H; *o*-CH_3), 3.85 (s, 12H; *p*-CH_3), −54.3 ppm (br s, 8H; pyrrole-H); IR (KBr): $\tilde{\nu}$ = 1015 cm^{-1} (oxidation state marker band); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 408 (5.23), 515 nm (4.24); elemental analysis calcd (%) for $C_{56}H_{52}Cl_2N_4Ru{\cdot}2\,H_2O{\cdot}1.5\,CH_2Cl_2$ (1116.44): C 61.86, H 5.33, N 5.02; found: C 61.92, H 5.14, N 5.21; electrospray MS: *m/z*: 952.7 $[M]^+$, 917.2 $[M-Cl]^+$, 882.8 $[M-2Cl]^+$.

Preparation of [{Ru^{IV}(F$_{20}$-tpp)Cl}$_2$O]: This complex was prepared according to the same procedure as that for the preparation of [Ru^{IV}(2,6-Cl_2tpp)Cl_2] except that [Ru^{II}(F$_{20}$-tpp)(CO)] was used instead of [Ru^{II}(2,6-Cl_2tpp)(CO)]. Yield: 62%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.98 ppm (s, 16H; pyrrole-H); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 394 (5.42), 512 (4.11), 640 nm (4.32); elemental analysis calcd (%) for $C_{88}H_{16}Cl_2F_{40}N_8ORu_2{\cdot}2\,CHCl_3{\cdot}C_6H_{14}$ (2559.03, a sample recrystallized from $CHCl_3$/hexane): C 45.06, H 1.26, N 4.38; found: C 45.10, H 1.06, N 4.26; FAB MS: *m/z*: 1109 [Ru(F$_{20}$-tpp)Cl]$^+$, 1090 [Ru(F$_{20}$-tpp)O]$^+$, 1071 [Ru(F$_{20}$-tpp)]$^+$.

General procedure for 2,6-Cl$_2$pyNO oxidation of arenes, steroids, and electron-deficient alkenes catalyzed by ruthenium–porphyrin complexes: A mixture of substrate (1 mmol), 2,6-Cl_2pyNO, and ruthenium porphyrin in CH_2Cl_2 (5 mL) was stirred under argon at 40 °C (for the molar ratio of catalyst/2,6-Cl_2pyNO/substrate, see Tables 3–10). The completion of the reaction was determined by ^{1}H NMR spectroscopy by monitoring the appropriate signal of the protons on the alkene double bond or on the aromatic ring. Pure oxidation product was obtained after flash chromatography on silica gel column with ethyl acetate-hexane (1:4 v/v) as eluent. The oxidation products **21**–**41**,[26a,30,37,75] **53**–**55**,[4d] **56**–**60**,[43] **61**–**63**,[46] **64**,[47] **75**–**84**,[3,76,77] and **89**–**91**[53] were characterized as reported in the literature. For characterization of **95**–**97**, see the spectral data included in Supporting Information.

Competitive epoxidation of substituted styrenes versus styrene with 2,6-X$_2$pyNO (X = Cl, Br, Me) catalyzed by [Ru^{IV}(2,6-Cl$_2$tpp)Cl$_2$]: Complex [Ru^{IV}(2,6-Cl_2tpp)Cl_2] (0.5 μmol) was added to a solution of styrene (0.5 mmol), substituted styrene (0.5 mmol), and 2,6-X_2pyNO (0.55 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred for 2 h at room temperature. The amounts of styrenes before and after the reaction were determined by GC. The relative rates k_{rel} were determined by the Equation (1) in which Y_f and Y_i are the final and initial quantities of substituted styrene; H_f and H_i are the final and initial quantities of styrene.

$$k_{rel} = k_Y/k_H = \log(Y_f/Y_i)/\log(H_f/H_i) \quad (1)$$

X-ray crystal structure determinations of [Ru^{IV}(2,6-Cl$_2$tpp)Cl$_2$], [Ru^{IV}(tmp)Cl$_2$], [{Ru^{IV}(F$_{20}$-tpp)Cl}$_2$O], 91, **95**, and **96**: Diffraction-quality crystals of [Ru^{IV}(2,6-Cl_2tpp)Cl_2]·2 $CHCl_3{\cdot}C_6H_{14}$, [Ru^{IV}(tmp)Cl_2]·0.5 $CHCl_3$, and [{Ru^{IV}(F$_{20}$-tpp)Cl}$_2$O]·2 $H_2O{\cdot}CHCl_3$ were obtained by slow diffusion of hexane into solutions of the complexes in $CHCl_3$, whereas those of **91**, **95**, and **96** were obtained by slow evaporation of their solutions in ethyl acetate/hexane. The data were collected on a MAR diffractometer with a 300 mm image plate detector for [Ru^{IV}(2,6-Cl_2tpp)Cl_2]·2 $CHCl_3{\cdot}C_6H_{14}$ and [Ru^{IV}(tmp)Cl_2]·0.5 $CHCl_3$, and on a Bruker SMART diffractometer for [{Ru^{IV}(F$_{20}$-tpp)Cl}$_2$O]·2 $H_2O{\cdot}CHCl_3$, **91**, **95**, and **96** using graphite-monochromatized $Mo_{K\alpha}$ radiation. The structures were refined by full-matrix least-squares against F^2 by using SHELXL-97[78] program on PC.

CCDC-251906 ([Ru^{IV}(2,6-Cl_2tpp)Cl_2]), −251907 ([Ru^{IV}(tmp)Cl_2]), −251902 ([{Ru^{IV}(F$_{20}$-tpp)Cl}$_2$O]), −251903 (**91**), −251904 (**95**), −251905 (**96**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

This work was supported by The University of Hong Kong, the Hong Kong Research Grants Council (No.7099/00P), and the University Grants Committee of the Hong Kong SAR of China (Area of Excellence Scheme, AoE/P-10/01). We thank Prof. Zhong-Yuan Zhou and Dr. Nianyong Zhu for assistance in solving the crystal structures reported in this paper.

[1] a) J. T. Groves, T. E. Nemo, *J. Am. Chem. Soc.* **1983**, *105*, 5786; b) B. R. Cook, T. J. Reinert, K. S. Suslick, *J. Am. Chem. Soc.* **1986**, *108*, 7281; c) B. Meunier, *Chem. Rev.* **1992**, *92*, 1411; d) J. P. Collman, X. Zhang, V. J. Lee, E. S. Uffelman, J. I. Brauman, *Science* **1993**, *261*, 1404; e) *Metalloporphyrins in Catalytic Oxidation*, (Ed.: R. A. Sheldon), Marcel Dekker, New York, **1994**; f) P. Bhyrappa, J. K. Young, J. S. Moore, K. S. Suslick, *J. Am. Chem. Soc.* **1996**, *118*, 5708; g) D. Dolphin, T. G. Traylor, L. Y. Xie, *Acc. Chem. Res.* **1997**, *30*, 251.

[2] J. T. Groves, R. Quinn, *J. Am. Chem. Soc.* **1985**, *107*, 5790.

[3] a) J.-C. Marchon, R. Ramasseul, *J. Chem. Soc. Chem. Commun.* **1988**, 298; b) J.-C. Marchon, R. Ramasseul, *Synthesis* **1989**, 389; c) M. Tavarès, R. Ramasseul, J.-C. Marchon, B. Bachet, C. Brassy, J.-P. Mornon, *J. Chem. Soc. Perkin Trans. 2* **1992**, 1321; d) M. Tavarès, R. Ramasseul, J.-C. Marchon, D. Valleegoyet, J. C. Gramain, *J. Chem. Res. Synop.* **1994**, 74.

[4] a) T. Higuchi, H. Ohtake, M. Hirobe, *Tetrahedron Lett.* **1989**, *30*, 6545; b) T. Higuchi, H. Ohtake, M. Hirobe, *Tetrahedron Lett.* **1991**, *32*, 7435; c) H. Ohtake, T. Higuchi, M. Hirobe, *J. Am. Chem. Soc.* **1992**, *114*, 10660; d) T. Higuchi, C. Satake, M. Hirobe, *J. Am. Chem. Soc.* **1995**, *117*, 8879; e) H. Ohtake, T. Higuchi, M. Hirobe, *Heterocycles* **1995**, *40*, 867; f) T. Higuchi, M. Hirobe, *J. Mol. Catal. A* **1996**, *113*, 403; g) T. Shingaki, K. Miura, T. Higuchi, M. Hirobe, T. Nagano, *Chem. Commun.* **1997**, 861.

[5] J. T. Groves, M. Bonchio, T. Carofiglio, K. Shalyaev, *J. Am. Chem. Soc.* **1996**, *118*, 8961.

[6] a) Z. Gross, S. Ini, M. Kapon, S. Cohen, *Tetrahedron Lett.* **1996**, *37*, 7325; b) Z. Gross, S. Ini, *J. Org. Chem.* **1997**, *62*, 5514; c) Z. Gross, S. Ini, *Org. Lett.* **1999**, *1*, 2077; d) Z. Gross, S. Ini, *Inorg. Chem.* **1999**, *38*, 1446.

[7] a) A. Berkessel, M. Frauenkron, *J. Chem. Soc. Perkin Trans. 1* **1997**, 2265; b) A. Berkessel, P. Kaiser, J. Lex, *Chem. Eur. J.* **2003**, *9*, 4746.

[8] a) T.-S. Lai, R. Zhang, K.-K. Cheung, H.-L. Kwong, C.-M. Che, *Chem. Commun.* **1998**, 1583; b) T.-S. Lai, H.-L. Kwong, R. Zhang, C.-M. Che, *J. Chem. Soc. Dalton Trans.* **1998**, 3559; c) R. Zhang, W.-Y. Yu, T.-S. Lai, C.-M. Che, *Chem. Commun.* **1999**, 409; d) R. Zhang, W.-Y. Yu, T.-S. Lai, C.-M. Che, *Chem. Commun.* **1999**, 1791; e) R. Zhang, W.-Y. Yu, H.-Z. Sun, W.-S. Liu, C.-M. Che, *Chem. Eur. J.* **2002**, *8*, 2495.

[9] P. Le Maux, M. Lukas, G. Simonneaux, *J. Mol. Catal. A* **2003**, *206*, 95.

[10] a) C.-J. Liu, W.-Y. Yu, S.-G. Li, C.-M. Che, *J. Org. Chem.* **1998**, *63*, 7364; b) X.-Q. Yu, J.-S. Huang, W.-Y. Yu, C.-M. Che, *J. Am. Chem. Soc.* **2000**, *122*, 5337; c) J.-L. Zhang, Y.-L. Liu, C.-M. Che, *Chem. Commun.* **2002**, 2906; d) J.-L. Zhang, H.-B. Zhou, J.-S. Huang, C.-M. Che, *Chem. Eur. J.* **2002**, *8*, 1554; e) J.-L. Zhang, C.-M. Che, *Org. Lett.* **2002**, *4*, 1911.

[11] O. Nestler, K. Severin, *Org. Lett.* **2001**, *3*, 3907.

[12] T. Yamada, K. Hashimoto, Y. Kitaichi, K. Suzuki, T. Ikeno, *Chem. Lett.* **2001**, 268.

[13] W.-K. Chan, P. Liu, W.-Y. Yu, M.-K. Wong, C.-M. Che, *Org. Lett.* **2004**, *6*, 1597.

[14] a) R. Zhang, W.-Y. Yu, K.-Y. Wong, C.-M. Che, *J. Org. Chem.* **2001**, *66*, 8145; b) J. Chen, C.-M. Che, *Angew. Chem.* **2004**, *116*, 5058; *Angew. Chem. Int. Ed.* **2004**, *43*, 4950.

[15] Valentine and co-workers reported that ferric porphyrin peroxo complexes could stoichiometricly oxidize electron-deficient alkenes to form epoxides in moderate yields. See for example: M. Selke, M. F. Sisemore, J. S. Valentine, *J. Am. Chem. Soc.* **1996**, *118*, 2008.

[16] a) M. Ke, C. Sishta, B. R. James, D. Dolphin, J. W. Sparapany, J. A. Ibers, *Inorg. Chem.* **1991**, *30*, 4766; b) Z. Gross, C. M. Barzilay, *J. Chem. Soc. Chem. Commun.* **1995**, 1287; c) W.-H. Leung, T. S. M. Hun, H.-W. Hou, K.-Y. Wong, *J. Chem. Soc. Dalton Trans.* **1997**, 237; d) Z. Gross, A. Mahammed, C. M. Barzilay, *Chem. Commun.* **1998**, 1105.

[17] H. Masuda, T. Taga, K. Osaki, H. Sugimoto, M. Mori, H. Ogoshi, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3887.

[18] a) J. T. Groves, R. Quinn, *Inorg. Chem.* **1984**, *23*, 3844; b) C.-J. Liu, W.-Y. Yu, S.-M. Peng, T. C. W. Mak, C.-M. Che, *J. Chem. Soc. Dalton Trans.* **1998**, 1805.

[19] We examined the oxidation of styrene with 2,6-Cl_2pyNO, PhIO, or TBHP catalyzed by [{Ru^{IV}(ttp)X}$_2$O] (X = Cl, OMe, OEt, prepared according to the method described in: J. P. Collman, C. E. Barnes, P. J. Brothers, T. J. Collins, T. Ozawa, J. C. Gallucci, J. A. Ibers, *J. Am. Chem. Soc.* **1984**, *106*, 5151). These catalytic reactions resulted in $\leq$10% styrene conversion after 12 h.

[20] The signal at -10 ppm might arise from [Ru^{IV}(tmp)O] (see: J. T. Groves, K.-H. Ahn, *Inorg. Chem.* **1987**, *26*, 3831 and ref. [6d]). A red solid was isolated by chromatography of the mixture on a silica gel column; its UV-visible and IR spectra were identical to that of [Ru^{II}(tmp)(CO)].

[21] Some iron(III)–porphyrin complexes were previously reported to catalyze epoxide isomerization to aldehyde, see for example: a) T. Takanami, M. Ueno, F. Hino, K. Suda, *Chem. Lett.* **1996**, 1031; b) K. Suda, K. Baba, S. Nakajima, T. Takanami, *Tetrahedron Lett.* **1999**, *40*, 7243; c) K. Suda, K. Baba, S. Nakajima, T. Takanami, *Chem. Commun.* **2002**, 2570.

[22] F. Ogliaro, S. P. de Visser, J. T. Groves, S. Shaik, *Angew. Chem.* **2001**, *113*, 3612; *Angew. Chem. Int. Ed.* **2001**, *40*, 2874.

[23] C.-M. Che, unpublished results.

[24] a) W. Nam, S. K. Choi, M. H. Lim, J.-U. Rohde, I. Kim, J. Kim, C. Kim, L. Que Jr., *Angew. Chem.* **2003**, *115*, 113; *Angew. Chem. Int. Ed.* **2003**, *42*, 109; b) W. Nam, M. H. Lim, H. J. Lee, C. Kim, *J. Am. Chem. Soc.* **2000**, *122*, 6641.

[25] J. P. Collman, L. Zeng, R. A. Decréau, *Chem. Commun.* **2003**, 2974.

[26] a) A. G. Myers, P. J. Proteau, *J. Am. Chem. Soc.* **1989**, *111*, 1146; b) R. C. Larock, *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*, VCH, New York, **1989**, pp. 505–520; c) R. A. Johnson, K. B. Sharpless, in *Comprehensive Organic Synthesis*, *Vol. 7* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, Chapter 3; d) M. J. Porter, J. Skidmore, *Chem. Commun.* **2000**, 1215.

[27] Selected examples for asymmetric oxidations by metal peroxides: a) C. Baccin, A. Gusso, F. Pinna, G. Strukul, *Organometallics* **1995**, *14*, 1161; b) M. Bougauchi, S. Watanable, T. Arai, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc.* **1997**, *119*, 2329; c) E. J. Corey, F.-Y. Zhang, *Org. Lett.* **1999**, *1*, 1287; d) T. Nemoto, T. Ohshima, M. Shibasaki, *J. Am. Chem. Soc.* **2001**, *123*, 9474; e) K. Funabashi, M. Jachmann, M. Kanai, M. Shibasaki, *Angew. Chem.* **2003**, *115*, 5647; *Angew. Chem. Int. Ed.* **2003**, *42*, 5489; f) B. S. Lane, K. Burgess, *Chem. Rev.* **2003**, *103*, 2457.

[28] H. Nishiyama, T. Shimada, H. Itoh, H. Sugiyama, Y. Motoyama, *Chem. Commun.* **1997**, 1863.

[29] For examples of epoxidation of electron-deficient alkenes catalyzed by Mn^{III}–Schiff base complex, see: L. Deng, E. N. Jacobsen, *J. Org. Chem.* **1992**, *57*, 4320.

[30] S. L. Born, P. A. Rodriguez, C. L. Eddy, L. D. Lehman-McKeeman, *Drug Metab. Dispos.* **1997**, *25*, 1318.

[31] A. Alexakis, I. Marek, P. Mangeney, J. F. Normant, *Tetrahedron* **1991**, *47*, 1677.

[32] D. Enders, J. Zhu, L. Kramps, *Liebigs Ann./Recl.* **1997**, 1101.

[33] A. H. Hoveyda, D. A. Evans, G. C. Fu, *Chem. Rev.* **1993**, *93*, 1307.

[34] W. Adam, T. Wirth, *Acc. Chem. Res.* **1999**, *32*, 703.

[35] T. Honma, M. Nakajo, T. Mizugaki, K. Ebitani, K. Kaneda, *Tetrahedron Lett.* **2002**, *43*, 6229.

[36] N. Ito, T. Etoh, H. Hagiwara, M. Kato, *Synthesis* **1997**, 153.

[37] For epoxidation of α,β:γ,δ-unsaturated alkenes by nucleophilic oxidant, see: a) M. E. Lasterra-Sánchez, U. Felfer, P. Mayon, S. M. Roberts, S. R. Thorton, C. J. Todd, *J. Chem. Soc. Perkin Trans. 1* **1996**, 343; b) J. V. Allen, M. J. Bergeron, S. Griffiths, S. M. Mukherjee, S. M. Roberts, N. M. Williamson, L. E. Wu, *J. Chem. Soc. Perkin Trans. 1* **1998**, 3171; c) A. Lévai, A. M. S. Silva, J. A. S. Cavaleiro, T. Patonay, V. L. M. Silva, *Eur. J. Org. Chem.* **2001**, 3213.

[38] In this work, we obtained a mixture of α,β:γ,δ-diepoxides at a 2:1 ratio, and the selectivity was different from that obtained by dimethyldioxirane.[37c] ^{1}H NMR: δ = 3.18 (dd, J = 1.8, 4.5 Hz, 0.34H), 3.28 (dd, J = 2.1, 3.0 Hz, 0.66H), 3.35 (dd, J = 1.9, 4.5 Hz, 0.34H), 3.46 (dd, J = 2.1, 3.0 Hz, 0.66H), 3.93 (d, J = 1.8 Hz, 0.33H), 3.96 (d, J = 1.8 Hz, 0.66H), 4.33 (d, J = 1.8 Hz, 0.33H), 4.36 (d, J = 1.8 Hz, 0.64H), 7.23–7.36 (m, 5H), 7.48–7.52 (m, 2H), 7.57 (t, J = 7.5 Hz, 1H), 8.05 (dd, J = 7.6 Hz, 1H).

[39] a) W. Eberbach, B. Burchardt, *Chem. Ber.* **1978**, *111*, 3665; b) T. Hirashita, K. Kinoshita, H. Yamamura, M. Kawai, S. Araki, *J. Chem. Soc. Perkin Trans. 1* **2000**, 825.

[40] a) T. Fex, B. Wickberg, *Acta Chem. Scand. Ser. B* **1981**, *35*, 97; b) O. Block, G. Klein, H.-J. Altenbach, D. J. Brauer, *J. Org. Chem.* **2000**, *65*, 716.

[41] a) J. B. Pridham, *Enzyme Chemistry of Phenolic Compounds*, Pergamon, New York, **1963**; b) P. J. Dudfield, in *Comprehensive Organic Synthesis*, *Vol. 7* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, Chapters 2.10 and 2.11.

[42] S. Yamazaki, *Tetrahedron Lett.* **2001**, *42*, 3355.

[43] Selected examples: a) G. Labat, B. Meunier, *J. Org. Chem.* **1989**, *54*, 5008; b) G. Labat, J.-L. Séris, B. Meunier, *Angew. Chem.* **1990**, *102*, 1488; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1471; c) B. Meunier, *New J. Chem.* **1992**, *16*, 203; d) I. Artaud, K. Ben-Aziza, D. Mansuy, *J. Org. Chem.* **1993**, *58*, 3373; e) W. Adam, W. A. Herrmann, J. Lin, C. R. Saha-Möller, R. W. Fisher, J. D. G. Correia, *Angew. Chem.* **1994**, *106*, 2545; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2475; f) W. Adam, W. A. Herrmann, J. Lin, C. R. Saha-Möller, *J. Org. Chem.* **1994**, *59*, 8281; g) R. Song, A. Sorokin, J. Bernadou, B. Meunier, *J. Org. Chem.* **1997**, *62*, 673.

[44] a) W. Adam, P. A. Ganeshpure, *Synthesis* **1993**, 280, and references therein; b) W. A. Herrmann, J. J. Haider, R. W. Fisher, *J. Mol. Catal. A* **1999**, *138*, 115.

[45] Selected examples: a) J. M. M. del Corral, M. Gordaliza, M. A. Castro, M. M. Mahiques, A. San Feliciano, M. D. García-Grávalos, *Bioorg. Med. Chem.* **1998**, *6*, 31; b) T. Kuramochi, M. Asaoka, T. Ohkubo, H. Takei, *Tetrahedron Lett.* **1996**, *37*, 7075; c) J.-L. Ioset, A. Marston, M. P. Gupta, K. Hostettmann, *Phytochemistry* **2000**, *53*, 613.

[46] a) C. S. Chien, T. Suzuki, T. Kawasaki, M. Sakamoto, *Chem. Pharm. Bull.* **1984**, *32*, 3945; b) C. S. Chien, T. Kawasaki, M. Sakamoto, *Chem. Pharm. Bull.* **1985**, *33*, 5071.

[47] a) T. Ohe, M. Hirobe, T. Mashino, *Drug Metab. Dispos.* **2000**, *28*, 110; b) J. Yang, R. Weinberg, R. Breslow, *Chem. Commun.* **2000**, 531.

[48] a) R. F. Witzmann, *Steroids-Key to Life*, Van Nostrum Reinhold, New York, **1981**; b) W. Klyne, *The Chemistry of Steroids*, Methuen, London, **1957**; c) F. L. Zeelen, *Medicinal Chemistry of Steroids*, Elsevier, Amsterdam, **1990**; d) P. B. Reese, *Steroids* **2001**, *66*, 481; e) D. C. Johannessen, P. E. Lønning, *Drugs Aging* **1992**, *2*, 530.

[49] a) S. M. Kupchan, W. K. Anderson, P. Bollinger, R. W. Doskotch, R. M. Smith, J. A. Saenz-Renauld, H. K. Schnoes, A. L. Burlingame, D. H. Smith, *J. Org. Chem.* **1969**, *34*, 3858; b) K. Gamoh, M. Hirayama, N. Ikekawa, *J. Chem. Soc. Perkin Trans. 1* **1984**, 449.

[50] a) K. B. Sharpless, R. C. Michaelson, *J. Am. Chem. Soc.* **1973**, *95*, 6136; b) M. Tohma, T. Tomita, M. Kimura, *Tetrahedron Lett.* **1973**, *14*, 4359; c) T. Muto, J. Umehara, H. Masumori, T. Miura, M. Kimura, *Chem. Pharm. Bull.* **1985**, *33*, 4749; d) R. Ramasseul, C. Scheer, M. Tavarès, J. C. Marchon, *J. Mol. Catal.* **1990**, *63*, 167; e) E. J. Parish, S. Li, *J. Org. Chem.* **1996**, *61*, 5665; f) J. A. R. Salvador, M. L. Sáe Melo, A. S. Campos Neves, *Tetrahedron Lett.* **1996**, *37*, 687; g) V. Kesavan, S. Chandrasekaran, *J. Org. Chem.* **1998**, *63*, 6999; h) D. Musumeci, D. Sica, *Steroids* **2002**, *67*, 661.

[51] The β:α ratios were determined by integration of the C6 proton signals in the ^{1}H NMR spectra of the reaction mixtures. The proton

NMR signal of 6α-H of 5β,6β-epoxides appears at $\delta = 3.00$–3.15 ppm, while that of 6β-H of 5α,6α-epoxides appears at $\delta = 2.75$–2.95 (see A. D. Cross, *J. Am. Chem. Soc.* **1962**, *84*, 3206).

[52] D. F. V. Lewis, *Cytochrome P 450-Structure, Function and Mechanism*, Taylor & Francis, London, **1996**.

[53] a) H. L. Holland, E. Riemland, U. Daum, *Can. J. Chem.* **1982**, *60*, 1919; b) M. Tavarès, R. Ramasseul, J. C. Marchon, M. Maumy, *Catal. Lett.* **1991**, *8*, 245; c) A. Nangia, A. Anthony, *Synth. Commun.* **1996**, *26*, 225; d) M. Hector, R. W. Hartmann, V. C. O. Njar, *Synth. Commun.* **1996**, *26*, 1075.

[54] Selected examples: a) S. A. Sadek, S. M. Shaw, W. V. Kessler, G. C. Wolf, *J. Org. Chem.* **1981**, *46*, 3259; b) J. Wang, P. J. De Clercq, *Tetrahedron Lett.* **1996**, *37*. 3395; c) M. Jarman, S. E. Barrie, J. M. Llera, *J. Med. Chem.* **1998**, *41*, 5375; d) B. Schönecker, C. Lange, M. Kötteritzsch, W. Günther, J. Weston, E. Anders, H. Görls, *J. Org. Chem.* **2000**, *65*, 5487; e) A. Anderson, A. C. Boyd, J. K. Clark, L. Fielding, D. K. Gemmell, N. M. Hamilton, M. S. Maidment, V. May, R. McGuire, P. McPhail, F. H. Sansbury, H. Sundaram, R. Taylor, *J. Med. Chem.* **2000**, *43*, 4118; f) W. Yu, Z. Jin, *J. Am. Chem. Soc.* **2002**, *124*, 6576.

[55] a) M. Baum, *J. Steroid Biochem.* **1990**, *36*, 187; b) S. Top, H. El Hafa, A. Vessières, J. Quivy, J. Vaissermann, D. W. Hughes, M. J. McGlinchey, J.-P. Mornon, E. Thoreau, G. Jaouen, *J. Am. Chem. Soc.* **1995**, *117*, 8372; c) E. von Angerer, *The Estrogen Receptor as a Target for Rational Drug Design*, Landes, Austin, Texas, USA, **1995**; d) G. S. Chetrite, J. R. Pasqualini, *J. Steroid Biochem. Mol. Biol.* **2001**, *76*, 95.

[56] a) G. P. Muller, W. F. Johns, *J. Org. Chem.* **1961**, *26*, 2403; b) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965**, *87*, 1353; c) A. R. Daniewski, W. Wojciechowka, *Synthesis* **1984**, 132; d) A. Kohl, W. Kreser, *Helv. Chim. Acta* **1998**, *81*, 2264; e) L. R. Falvello, F. Foubelo, T. Soler, M. Yus, *Tetrahedron: Asymmetry* **2000**, *11*, 2063.

[57] C. L. J. Ewers, M. Harre, J. Mohr, K. Nickisch, U. Tilstam, *Tetrahedron* **1998**, *54*, 4277.

[58] a) L. A. Van Dijick, B. J. Lankwerden, J. G. C. M. Vermeer, A. J. M. Weber, *Recueil. Trav. Chim. Pays-Bas* **1983**, *24*, 2939; b) A. Alexakis, I. Marek, P. Mangeney, J. F. Normant, *Tetrahedron* **1991**, *47*, 1677.

[59] E. V. Stoyanov, Y. Champavier, A. Simon, J.-P. Basly, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2685.

[60] R. L. Halcomb, S. J. Danishefsky, *J. Am. Chem. Soc.* **1989**, *111*, 6661.

[61] G. A. Wächter, R. W. Hartmann, T. Sergejew, G. L. Grün, D. Ledergerber, *J. Med. Chem.* **1996**, *39*, 834.

[62] Y. Wang, F. G. West, *Synthesis* **2002**, 99.

[63] S. Ouk, S. Thiebaud, E. Borredon, P. Le Gars, *Appl. Catal. A* **2003**, *241*, 227.

[64] E. Mohacsi, *Synth. Commun.* **1982**, *12*, 453.

[65] Y. Kikugawa, *Synthesis* **1981**, 460.

[66] K. Hanada, N. Miyazawa, K. Ogasawara, *Chem. Pharm. Bull.* **2003**, *51*, 104.

[67] a) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax, J. H. Williams, *J. Org. Chem.* **1952**, *17*, 1341; b) H. J. Buchanan, P. J. Cox, S. M. S. V. Doidge-Harrison, R. A. Howie, M. Jaspars, J. L. Wardell, *J. Chem. Soc. Perkin Trans. 1* **1997**, 3657.

[68] A. E. Dann, J. B. Davis, M. J. Nagler, *J. Chem. Soc. Perkin Trans. 1* **1979**, 158.

[69] A. Kuhl, W. Kreiser, *Helv. Chim. Acta* **1998**, *81*, 2264.

[70] S. A. Sadek, S. M. Shaw, W. V. Kessler, G. C. Wolf, *J. Org. Chem.* **1981**, *46*, 3259.

[71] C. J. Elsevier, H. J. T. Bos, P. Vermeer, A. L. Spek, J. Kroon, *J. Org. Chem.* **1984**, *49*, 379.

[72] R. J. Rousseau, R. K. Robins, *J. Heterocycl. Chem.* **1965**, *2*, 196.

[73] J. S. Lindsey, R. W. Wagner, *J. Org. Chem.* **1989**, *54*, 828.

[74] a) W.-H. Leung, C.-M. Che, *Inorg. Chem.* **1989**, *28*, 4619; b) P. Barthazy, A. Togni, A. Mezzetti, *Organometallics* **2001**, *20*, 3472; c) J. A. Miller, W. C. Jin, S. T. Nguyen, *Angew. Chem.* **2002**, *114*, 3077; *Angew. Chem. Int. Ed.* **2002**, *41*, 2953.

[75] a) S. Colonna, A. Manfredi, R. Annunziata, M. Spadoni, *Tetrahedron* **1987**, *43*, 2157; b) N. H. Lee, E. N. Jacobsen, *Tetrahedron Lett.* **1991**, *32*, 6533; c) A. Kumar, V. Bhakuni, *Tetrahedron Lett.* **1996**, *37*, 4751; d) D. Enders, J. Zhu, G. Raabe, *Angew. Chem.* **1996**, *108*, 1827; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1725; e) G. A. Kraus, M. Kirihara, *J. Org. Chem.* **1992**, *57*, 3256.

[76] R. C. Young, T. K. Nagle, T. J. Meyer, D. G. Whitten, *J. Am. Chem. Soc.* **1978**, *100*, 4773.

[77] A. S. Demir, *Tetrahedron* **2001**, *57*, 227.

[78] G. M. Sheldrick, SHELXL-97, Program for the Refinement of Crystal Structures, University of Göttingen, Germany, **1997**.

Received: October 5, 2004
Published online: April 5, 2005