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Ruthenium(IV) porphyrin catalyzed highly selective oxidation of internal alkenes into ketones with Cl_2pyNO as terminal oxidant

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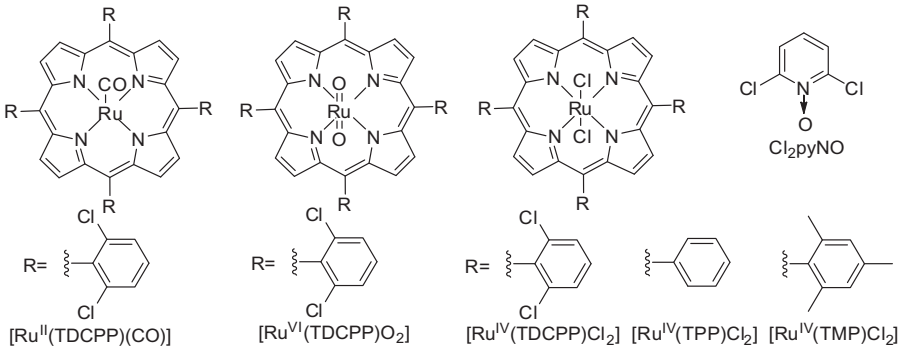
ABSTRACT

A new method for the conversion of internal alkenes into ketones without cleavage of C=C bond by using dichlororuthenium(IV) *meso*-tetrakis(2,6-dichlorophenyl)porphyrin [Ru^{IV}(TDCPP)Cl_2] as catalyst and 2,6-dichloropyridine N-oxide(Cl_2pyNO) as oxidant is developed.

Carbonyl groups have extensive applications in organic synthesis.[1] In the literature, a number of effective means have been developed for the synthesis of ketones. Terminal alkenes except ethylene can be converted to methyl ketones as the main products by aerobic $PdCl_2$-catalyzed Cu-mediated oxidation in aqueous solutions, usually referred to the Wacker oxidation.[2] However, the most important industrial application of Wacker oxidation is the conversion of ethylene to acetaldehyde,[3] and it is difficult to obtain ketones having long aliphatic alkyl chains through Wacker oxidation of alkenes.[4] The rearrangement of epoxides induced by a Lewis acid is a useful tool for constructing carbonyl compounds but has a shortcoming of low selectivity as the products are a mixture of aldehydes and ketones.[5] The oxidative cleavage of alkenes is another method used for the preparation of ketones but this is also a method used to truncate carbon chains.[6] Undoubtedly, oxidation of alkenes is one of the most straightforward routes for the synthesis of ketones. Therefore, highly selective oxidation of internal alkenes to ketones without cleavage of C=C bond remains



Scheme 1. Ruthenium porphyrin catalysts and oxidant Cl_2pyNO.

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a challenge. Our previous studies revealed the epoxidation–isomerization reaction (E–I) of alkenes catalyzed by [Ru^{IV}(TDCPP)Cl_2] (TDCPP = *meso*-tetrakis(2,6-dichlorophenyl)porphyrin) with 2,6-dichloropyridine N-oxide (Scheme 1).

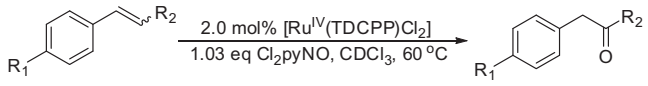
(Cl_2pyNO) or air as a terminal oxidant gave aldehydes as the major product.[7] The main objective of this work was to prepare ketones using the ruthenium porphyrin catalyzed E–I reaction of alkenes under optimized conditions, which we conceive to be a supplement of Wacker oxidation.

At the outset, compared to the previous work[7] on the ruthenium porphyrin catalyzed E–I reaction, a solution of alkene 1-phenyl-1,3-heptdiene which was a mixture of *cis* and *trans*-isomers (about 1:1 ratio), Cl_2pyNO (1.03 equiv) and catalyst [Ru^{IV}(TDCPP)Cl_2] (2.0 mol %) in $CDCl_3$ was stirred for 5 h at 60 °C. The β,γ-unsaturated ketone 1-phenyl-1-heptene-4-one was formed in 87% yield. A trace amount of aldehyde product was detected in the reaction mixture.

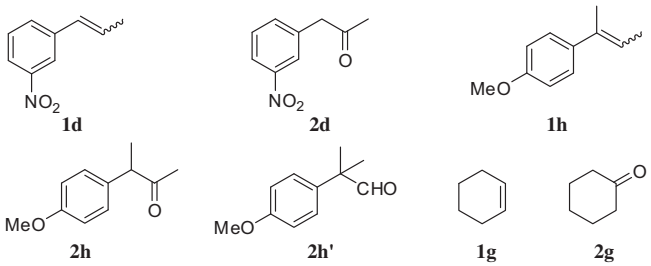
Subsequently, the effects of solvent, catalyst, temperature, and equivalent of oxidant were examined and the results are depicted in Table 1. Similar results were obtained with $CHCl_3$, CH_2Cl_2, or $ClCH_2CH_2Cl$ as the solvent. Other solvents, such as toluene, acetonitrile, and ethyl acetate, were inferior (entries 1–7). Probably, the ruthenium porphyrin catalyst is more soluble in $CHCl_3$, CH_2Cl_2, or $ClCH_2CH_2Cl$, thereby such a halide solvent is advantageous for the catalysis. $CDCl_3$ was chosen as the solvent and the catalysis was monitored/followed by ^{1}H NMR. The reaction of 1-phenyl-1,3-heptdiene with Cl_2pyNO was more efficiently catalyzed by [Ru^{IV}(TDCPP)Cl_2] than that by other porphyrin catalysts, one of which, the [Ru^{II}(TDCPP)(CO)] complex, was a relatively inactive catalyst in the reaction (entries 8–12). This finding is in a good agreement with our previous work reported in the literature.[7] The use of 1.03 equiv of Cl_2pyNO gave the best results in terms of the yield of ketone product (87%). The conversion of 1-phenyl-1,3-heptdiene became incomplete if insufficient Cl_2pyNO was used. If excess oxidant was used, no ketone product could be observed at all (entries 12–14). Changing the temperature to 25 °C resulted in a lower yield of the ketone (entry 1).

With the optimized conditions in hand, we examined the scope of substrates for the [Ru^{IV}(TDCPP)Cl_2] catalyzed oxidation of styrene compounds to ketones. As depicted in Table 2, various aryl alkenes underwent the catalytic reaction to give the corresponding ketones with most of them obtained in good or moderate yields. The substituent on the phenyl ring was found to affect the reaction time and product yield dramatically. For example, with substrate **1a** having a strong electron rich substituent, the reaction time was shortened to 2 h and the ketone was obtained in 85% yield, while for **1b**, **1c** having weak electron rich substituents, a longer reaction time was required and the product was obtained in lower yield (entries 1–3). When a strong electron-withdrawing group nitro was used, epoxide was obtained without the ketone product observed even an increase in catalyst loading and a longer reaction time (entry 4) were used. The substrate with a longer carbon chain gave a lower product yield (entries 5 and 6) whereas alkyl alkene, which is not a conjugated olefin, could not be converted into ketone (entry 7).

Table 2
Oxidation of internal styrene compounds with Cl_2pyNO catalyzed by [Ru^{IV}(TDCPP)Cl_2]



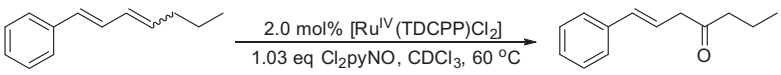
R_1= OMe, R_2= Me: **1a**, **2a**; R_1= Me, R_2= Me: **1b**, **2b**; R_1= H, R_2= Me: **1c**, **2c**; R_1=OMe, R_2= n-propyl: **1e**, **2e**; R_1= OMe, R_2= n-pentyl: **1f**, **2f**



Entry	Substrate[a]	Time (h)	Product	Yield[b] (%)
1	**1a**	2	**2a**	85
2	**1b**	24	**2b**	52
3	**1c**	24	**2c**	15
4	**1d**	24	**2d**	0[c]
5	**1e**	2	**2e**	76
6	**1f**	5	**2f**	67
7	**1g**	6	**2g**	0[c]
8	*cis*-**1f**	2	**2f**	71
9	*trans*-**1f**	2	**2f**	33
10	**1h**	2	**2h**	23
			2h′	9

[a] 0.1 mmol alkene.
[b] Yield determined by ^{1}H NMR with PhTMS as the internal standard.
[c] Only epoxide has been obtained.

Table 1
Oxidation of 1-phenyl-1,3-heptdiene under various conditions[a]



Entry	Solvent	Catalyst	Cl_2pyNO (eq)	Temperature (°C)	Conversion ratio (%)	Yield[b] (%)
1	$CDCl_3$	[Ru^{IV}(TDCPP)Cl_2]	1.03	25	100	73
2	CH_3CN	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	37	31
3	$PhCH_3$	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	93	66
4	$CH_3COOCH_2CH_3$	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	85	71
5	$ClCH_2CH_2Cl$	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	91	83
6	CH_2Cl_2	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	92	85
7	$CHCl_3$	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	93	85
8	$CDCl_3$	[Ru^{IV}(TPP)Cl_2]	1.03	60	57	19
9	$CDCl_3$	[Ru^{IV}(TMP)Cl_2]	1.03	60	100	71
10	$CDCl_3$	[Ru^{II}(TDCPP)(CO)]	1.03	60	46	0[c]
11	$CDCl_3$	[Ru^{VI}(TDCPP)O_2]	1.03	60	100	68
12	$CDCl_3$	[Ru^{IV}(TDCPP)Cl_2]	1.03	60	100	87
13	$CDCl_3$	[Ru^{IV}(TDCPP)Cl_2]	0.5	60	61	81
14	$CDCl_3$	[Ru^{IV}(TDCPP)Cl_2]	2.0	60	100	0[c]

[a] 0.1 mmol substrate and catalyst(2 mol %).
[b] Yield determined by ^{1}H NMR with PhTMS as the internal standard.
[c] Only epoxide has been obtained.

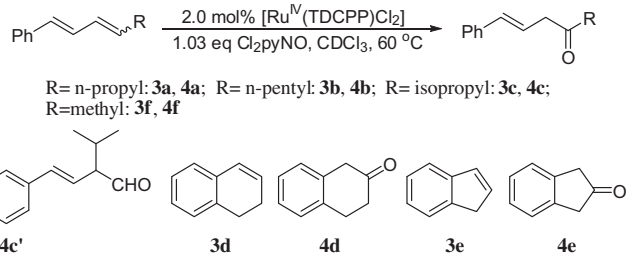
The alkene substrates mentioned above were a mixture of *cis*- and *trans*-isomers with an approximate 1:1 ratio. One of them was separated by column chromatography. It turned out that under the [Ru^{IV}(TDCPP)Cl_2] catalyzed conditions, the *cis*-isomer was oxidized by Cl_2pyNO to give ketone 2 times higher in yield than that from the *trans*-isomer under the same conditions (entries 8 and 9).

When a trisubstituted alkene was used, a complicated mixture was obtained containing the desired ketone and the byproduct 2-(4-methoxyphenyl)-2-methylpropanal. The byproduct aldehyde was produced via methyl migration probably owing to the multi-substitutes on the double bond (entry 10).

Then other internal dienes and cyclic alkenes were examined (Table 3). Lengthening the carbon chain was found to have little impact on the reaction with corresponding ketones obtained in 87% yield (entries 1 and 2). When an isopropyl diene was used, the product ketone was obtained in 62% yield (entry 3) and 2-isopropyl-4-phenyl-3-enal was observed. The byproduct aldehyde was presumably obtained via isopropyl migration in the isomerization step.

Cyclic alkenes like benzocyclopentene and benzocyclohexene can also be converted into their respective ketones in high yields with longer reaction time (entries 4 and 5).

Table 3
Oxidation of internal 1,3-dienes and cyclic alkenes with Cl_2pyNO catalyzed by [Ru^{IV}(TDCPP)Cl_2]



Entry	Substrate[a]	Time (h)	Product	Yield[b] (%)
1	**3a**	5	**4a**	87
2	**3b**	5	**4b**	87
3	**3c**	5	**4c**	62
			4c′	27
4	**3d**	10	**4d**	85
5	**3e**	10	**4e**	89
6[c]	**3f**	6	**4f**	99

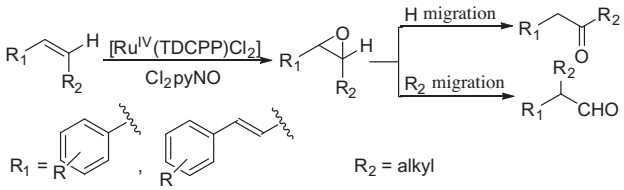
[a] 0.1 mmol alkene.
[b] Yield determined by ^{1}H NMR with PhTMS as the internal standard.
[c] Reported in the previous work.[7a]

In this work, epoxide was observed in the course of the catalysis. As depicted in Figure 1, benzocyclohexene was oxidized to epoxide and ketone by Cl_2pyNO catalyzed by [Ru^{IV}(TDCPP)Cl_2] after 2 h of reaction at 60 °C. Then the amount of epoxide decreased with concomitant increase in ketone formation upon further reaction for 4 h. In addition, the decrease of epoxide roughly matched to the increase in amount of ketone. When the reaction was conducted for 10 h, only ketone could be detected by ^{1}H NMR. If benzocyclohexene oxide was mixed with [Ru^{IV}(TDCPP)Cl_2] directly, the ketone was obtained at 60 °C. Whatever the starting material was the alkene or the epoxide, the active catalyst could be produced[7a] and it catalyzed the following reaction.

With reference to previous work,[7] a plausible mechanism is proposed as depicted in Scheme 2. Alkene is first oxidized by Cl_2pyNO to epoxide in the presence of ruthenium porphyrin catalyst. Subsequent activation of epoxide by the active ruthenium catalyst[7a] results in isomerization via H migration to give ketone as the final product (Scheme 2). However, if the C=C bond is bulky with multi-substitutes or large steric hindrance groups, such as trisubstituted alkene **1g** and bulky alkene **3c** with isopropyl, maybe the group R_2 could be forced to migrate with the inter reaction induced by the bulky porphyrin structure. So both of the H atom and group R_2 could migrate rather than H atom only.

In the rearrangement step for terminal alkene, migration of only terminal H would give β,γ-unsaturated aldehyde as the only product (Scheme 2, R_2 = H).[7] However, there could be two options in the rearrangement step for nonterminal alkene, H imigration to give β,γ-unsaturated ketones or R_2 imigration to give β,γ-unsaturated aldehydes. But these reactions with H imigrating have high selectivity to produce major product ketones.

In conclusion, a mild and convenient method has been developed to convert internal alkenes into β,γ-unsaturated ketones by Cl_2pyNO with [Ru^{IV}(TDCPP)Cl_2] catalyst without C=C cleavage. This is a useful supplement for Wacker oxidation of terminal alkenes to methyl ketones or aldehydes. The various products from this catalytic reaction are intermediate or starting materials in other reactions.[8] Further applications of this method to organic synthesis are currently under investigation.



Scheme 2. Proposed mechanism of the oxidation of alkenes with Cl_2pyNO catalyzed by [Ru^{IV}(TDCPP)Cl_2].

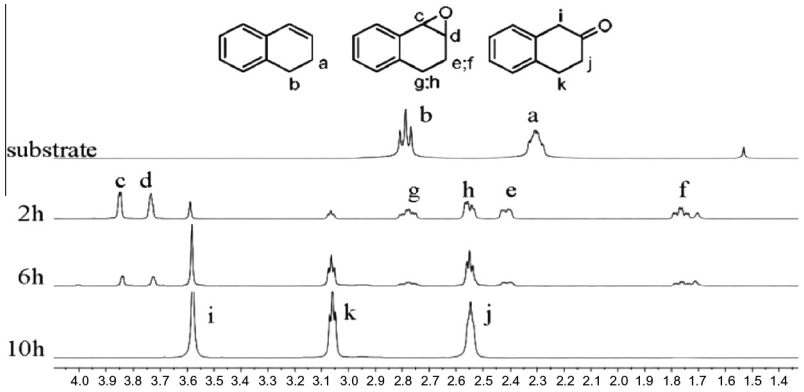


Figure 1. ^{1}H NMR of oxidation of benzocyclohexene with Cl_2pyNO catalyzed by [Ru^{IV}(TDCPP)Cl_2] changed over time.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.01.098.

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