JOC The Journal of Organic Chemistry

Article

Recyclable Dirhodium(II) Catalyst Rh2(esp)2 for the Allylic Oxidation of #5-Steroids

Yi Wang, Yi Kuang, Hongyang Zhang, Ruocheng Ma, and Yuanhua Wang

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b00414 • Publication Date (Web): 12 Apr 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Recyclable Dirhodium(II) Catalyst $Rh_2(esp)_2$ for the Allylic Oxidation of Δ^5-Steroids

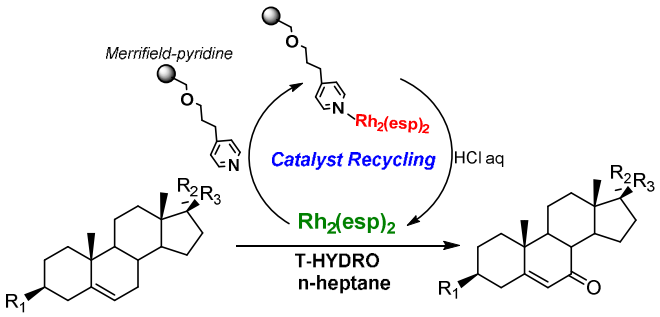
Yi Wang,[†] Yi Kuang,[†] Hongyang Zhang,[†] Ruocheng Ma,[‡] and Yuanhua Wang*[,†]

[†]College of Chemistry, Sichuan University, Chengdu, 610064, P. R. China

[‡]Jiaxiang Foreign Languages School Attached To Chengdu No.7 Middle School, Chengdu, 610023, P.R.China

E-mail: yhwang@scu.edu.cn

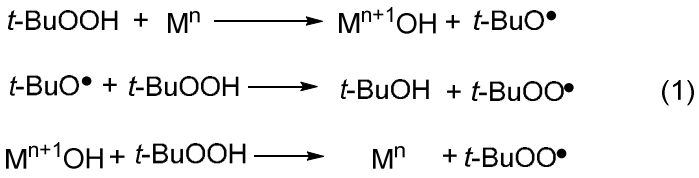
The chelating dirhodium(II) catalyst $Rh_2(esp)_2$ was shown to efficiently catalyze the allylic oxidation of Δ^5-steroids using T-HYDRO (70% tert-butyl hydroperoxide in water) as oxidant. Reaction yields were affected by the coordination ability of the solvent. The non-coordinating solvent n-heptane was determined to be an optimal solvent. At gram scale, the product, Δ^5-en-7-one steroid, precipitated from the reaction mixture. The $Rh_2(esp)_2$ complex did not undergo catalytic degradation and was recycled using Merrifield-pyridine resin for further allylic oxidation cycles. The results of ultraviolet /visible spectral analysis suggested that the Rh_2(II,II) species, rather than the Rh_2(II,III) species, was catalyst resting state during the reaction, which helps to explain the high durability of the catalyst.



Introduction

Allylic oxidation is a fundamental organic reaction that involves direct transformation of an allylic CH_2 group to a carbonyl group.[1,2] This transformation is of great importance given the versatility of the resulting unsaturated enones or 1, 4-enediones, which can act as synthetic starting materials or drug precursors.[3] In particular, the allylic oxidation of Δ^5-steroids to Δ^5-en-7-one steroids has shown promising results for the prevention and treatment of cancer and has also been shown to inhibit the biosynthesis of sterol.[4a] Further functionalization of the double bond or the carbonyl group attracted the synthetic interest.[4b-d] Although classical oxidation reactions using stoichiometric chromium(VI) have been extensively studied, the harsh reaction conditions and toxic chromium regents make these methods unfavorable.[5] Recently, highly efficient metal-catalyzed allylic oxidation methods mediated by *tert*-butyl hydroperoxide (TBHP, *t*-BuOOH) have been reported (Eq 1).[6] These procedures provided a feasible approach for the oxidation of Δ^5-steroids with moderate to good reactivity. *tert*-Butyl hydroperoxide acts as a source of the *tert*-butylperoxy radical (*t*-BuOO•), a selective one-electron oxidant. The generation of *t*-BuOO• relies on metal complexes, such as sodium chlorite,[7] copper iodide,[8] bismuth salts,[9] cobalt acetate,[10] dirhodium caprolactamate ($Rh_2(cap)_4$),[11] ruthenium trichloride,[12] and manganese(III) acetate.[6a] As one-electron reductants, the metal complexes (M^n) are thought to homolytically cleave the oxygen–oxygen bond of TBHP (Eq 1), generating *t*-BuOO• by hydrogen atom abstraction from TBHP by *tert*-butoxy radical (*t*-BuO•) and

one electron oxidative metal species ($M^{n+1}OH$).



(1)

However, due to the radical mechanism of these oxidation reactions in the presence of stoichiometric TBHP, irreversible decomposition of the high oxidative state catalytically active species can occur over the course of the reaction and lead to a loss in catalytic activity or selectivity.[11b,13] Portion-wise addition of catalysts and/or oxidants to the reaction system was done to minimize catalyst deactivation, however this can complicate the method.[8,11b,13] In addition, for practical applications, costly metals necessitate a stable and recyclable catalyst. Therefore, the use of environmentally friendly, stable, efficient, and recoverable metal catalysts would be highly beneficial for the oxidation of Δ^5-steroids.

Recently, we reported Du Bois' dirhodium (II) complex $Rh_2(esp)_2$[14] (Figure 1) as a robust, efficient, and recyclable catalyst for solvent-free allylic and benzylic oxidation.[15] This method requires a low catalyst loading and uses environmentally safe aqueous TBHP (70% *tert*-butyl hydroperoxide in water, T-HYDRO) as an oxidant. This method is also operationally simple, scalable, can occur at ambient temperatures, and does not require additives. Since Rh_2(II,II) species exists in the catalyst resting state in these reactions, the catalyst $Rh_2(esp)_2$ did not degrade under the oxidation reaction conditions

and was recyclable (Figure 1). Based on previous studies, the oxidation of Δ^5-steroids using the $Rh_2(esp)_2$/T-HYDRO protocol was investigated in the current study.

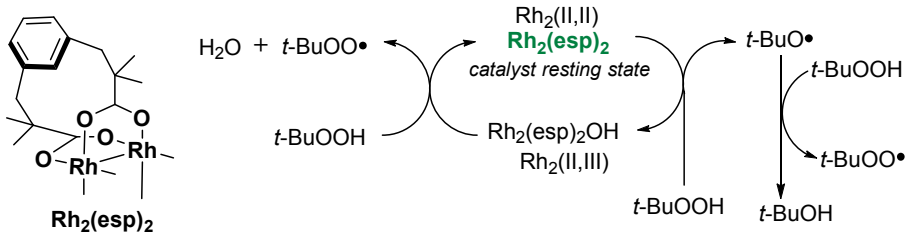


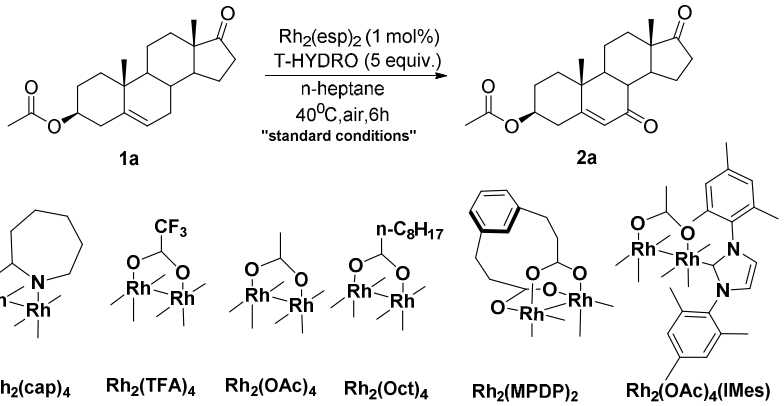
Figure 1. One-electron oxidative reaction between dirhodium(II) catalyst $Rh_2(esp)_2$.

Results and Discussion

Dehydroepiandrosterone acetate **1a** was chosen as a substrate for initial studies. Based on a previously reported solvent-free reaction protocol,[15] the oxidation of **1a** to **2a** was carried out with 1 mol% $Rh_2(esp)_2$ catalyst and 5 equiv T-HYDRO at 40°C. In the absence of solvent, **1a** did not fully dissolve in the aqueous TBHP and conversion to **2a** was very low. Solvent screenings were performed to determine the ideal solvent to solubilize the steroidal substrate. However, due to the unique structure of the dirhodium(II) complexes, some solvent molecules likely acted as labile ligands and bind to the dirhodium(II) core axially.[16a] The interaction between the axial solvent molecule ligands and the dirhodium(II) core affects the electronic properties of the dirhodium(II) complex. The energy of the Rh_2 π^* to Rh_2 σ^* HOMO to LUMO transition band in the dirhodium(II) complex has been shown to be strongly affected by axial ligand coordination.[16] Recently, Berry *et al.* and our group have reported that axial ligand coordination to $Rh_2(esp)_2$ can change the redox potential of the complex.[17] Therefore,

selecting the appropriate solvent for this oxidation is important.

Table 1. Optimization of Reaction Conditions[a]



entry	deviation from the standard conditions	**2a** yield (%)[b]
1	none	85
2	n-hexane instead of n-heptane	83
3	n-pentane instead of n-heptane	75
4	EtOAc instead of n-heptane	70
5	acetone instead of n-heptane	72
6	DCE instead of n-heptane	52
7	CH_3CN instead of n-heptane	42
8	DME instead of n-heptane	18
9	TBHP[c] instead of T-HYDRO	71
10	80% CHP instead of T-HYDRO	66
11	30% H_2O_2 instead of T-HYDRO	trace
12	60^0C instead of 40^0C	72
13	$Rh_2(cap)_4$ instead of $Rh_2(esp)_2$	87[11]
14	$Rh_2(OAc)_4$ instead of $Rh_2(esp)_2$	39
15	$Rh_2(TFA)_4$ instead of $Rh_2(esp)_2$	25
16	$Rh_2(Oct)_4$ instead of $Rh_2(esp)_2$	30
17	$Rh_2(OAc)_4$(IMes) instead of $Rh_2(esp)_2$	63
18	$Rh_2(MPDP)_2$ instead of $Rh_2(esp)_2$	49
19	0.1 mol % $Rh_2(esp)_2$ instead	50

[a]Unless otherwise noted, all reactions were performed with **1a** (0.4 mmol), T-HYDRO (2.0 mmol), n-heptane (0.5 mL), dirhodium catalyst (1.0 mol%). [b]Yield after column chromatography. [c]TBHP (5-6 M solution in decane).

Several commonly used solvents such as ethyl acetate (EtOAc), acetone,

1,2-dichloroethane (DCE), acetonitrile (CH_3CN), dimethyl ether (DME), and alkanes (n-petane, n-hexane, n-heptane) were evaulated. The reaction yields were found to be sensitive to the type of solvent used in the reaction. High yields of **2a** were obtained rapidly with non-coordinating alkanes (Table 1, entries 1-3). These results were similar to those given by Doyle's dirhodium(II) caprolactamate ($Rh_2(cap)_4$), which has been reported to catalyze the reaction with 87% yield in DCE.[11] n-Heptane was used in further screening, because it is suitable for practical applications compared to n-pentane (flammable) and n-hexane (neurological toxicity).[18] Conversely, reactions performed in coordinating solvents, such as acetone, EtOAc, DCE, CH_3CN, and DME, resulted in lower yields (Table 1, entries 4-8). It is possible that coordinating solvents bind to $Rh_2(esp)_2$, influence the reaction rates, and even deactivate the catalyst. To understand the effect of the solvent on $Rh_2(esp)_2$ in this oxidation reaction, UV/vis spectroscopy was used to monitor the behavior of $Rh_2(esp)_2$ in different solvents (Figure 2).

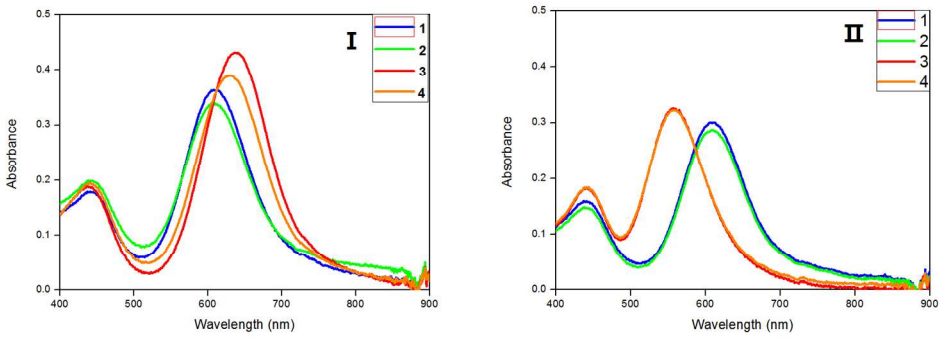


Figure 2. UV/vis spectroscopy of $Rh_2(esp)_2$ in different solvents. I (1) $Rh_2(esp)_2$ in acetone (λ_{max} = 613 nm). (2) $Rh_2(esp)_2$ and T-HYDRO in acetone (λ_{max} = 608 nm). (3) $Rh_2(esp)_2$ in EtOAc (λ_{max} = 636 nm). (4) $Rh_2(esp)_2$ and T-HYDRO in EtOAc (λ_{max} = 631 nm). II (1) $Rh_2(esp)_2$ in DME (λ_{max} = 608 nm). (2) $Rh_2(esp)_2$ and T-HYDRO in DME (λ_{max} = 610 nm). (3) $Rh_2(esp)_2$ in CH_3CN (λ_{max} = 557 nm). (4) $Rh_2(esp)_2$ and T-HYDRO in CH_3CN (λ_{max} = 559 nm).

The transition band of Rh_2 π^*-Rh_2 σ^* was observed to shift to higher energy in coordinating solvents (acetone, EtOAc, CH_3CN, and DME). For example, the Rh_2 π^*-Rh_2 σ^* band shifts to 557 nm when $Rh_2(esp)_2$ is dissolved in CH_3CN, which indicates that CH_3CN binds strongly to rhodium. Previous reports have shown that the characteristic band of $Rh_2(esp)_2$ dissolved in DCM appears at 661 nm.[17b] After adding T-HYDRO in one portion to the different $Rh_2(esp)_2$ solutions, all UV/vis spectra remained relatively unchanged. These results indicate that the solvated $Rh_2(esp)_2$ remained stable under oxidative conditions and that oxidative cleavage of the Rh-Rh bond did not occur. Furthermore, the characteristic band at *ca.* 800 nm of a one-electron oxidized Rh_2(II,III) species was not detected, which suggests that Rh_2(II,II) exists in the catalyst resting state.[14d-f,15] Lower yields of **2a** were obtained when coordinating solvents were used (Table 1). The solvents coordinated to $Rh_2(esp)_2$ did not destroy the catalyst, but inhibited catalysis and decreased the reaction rate. When more strongly coordinating solvents were used, even lower yields were observed: 42% for CH_3CN (Table 1, entry 7) vs. 70% in EtOAc (Table 1, entry 4). These results are consistent with the high yield of **2a** that was obtained when the oxidation was carried out in non-coordinating n-heptane. $Rh_2(esp)_2$ was also shown to be very stable in n-heptane during oxidation (Figure 3).

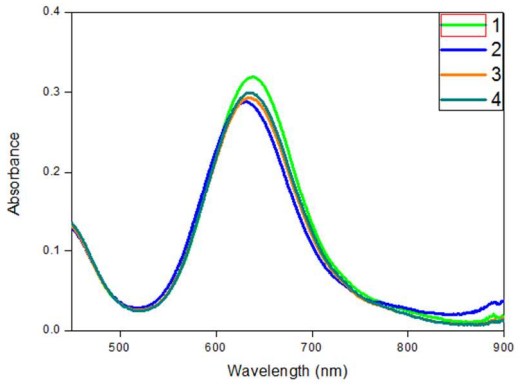


Figure 3. UV/vis spectroscopy of $Rh_2(esp)_2$ catalyst in n-heptane during the oxidation reaction. (1) $Rh_2(esp)_2$ and 1**a** in heptane (λ_{max} = 642 nm). (2) $Rh_2(esp)_2$, **1a** and T-HYDRO in heptane (1 h, λ_{max} = 637nm). (3) $Rh_2(esp)_2$, **1a** and T-HYDRO in heptane (3 h, λ_{max} = 638 nm). (4) $Rh_2(esp)_2$, **1a** and T-HYDRO in heptane (6 h, λ_{max} = 638 nm).

However, DCE was found to be an oxidizing solvent (likely through C-H abstraction) and not a suitable solvent in the current system. The UV/vis spectra for oxidation in DCE exhibited a typical band at 847 nm for the one-electron oxidized Rh_2(II,III) species (Figure 4),[14d-f,15] indicating that the Rh_2(II,III) species existed in the catalyst resting state during oxidation. This active Rh_2(II,III) intermediate was unstable and readily to decrease in the concentration under oxidative reaction conditions. The gradually degraded Rh_2(II,III) species in the reaction resulted in a low yield of **2a** (Table 1, entry 6). Rh(II,III) has been previously shown to exist in a resting state in DCE, with the one electron oxidized $Rh_2(esp)_2^+$ species reacting with DCE to give $Rh_2(esp)_2Cl$. The Cl^- is then axially coordinated to the oxidized species, which results in catalyst arrest.[14d-f,16b]

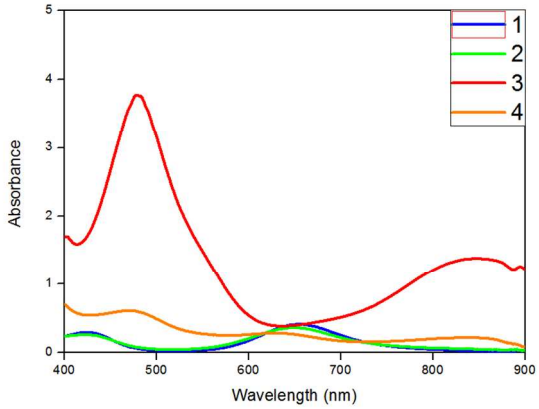


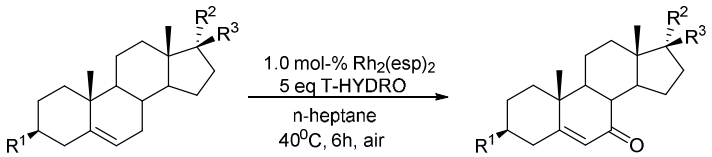
Figure 4. UV/vis Spectroscopy of $Rh_2(esp)_2$ catalyst in DCE during the oxidation. (1) $Rh_2(esp)_2$ in DCE (λ_{max} = 654 nm). (2) $Rh_2(esp)_2$ and **1a** in DCE (λ_{max} = 648 nm). (3) $Rh_2(esp)_2$, **1a** and T-HYDRO in DCE (5 min, λ_{max} = 483 nm). (4) $Rh_2(esp)_2$, **1a** and T-HYDRO in DCE (6 h, λ_{max} = 475 nm).

After screening for the optimal solvent, other commercially available oxidants were tested (Table 1, entries 9-11). The yield dropped when TBHP (5-6 M solution in decane) was used (Table 1, entry 9). An aqueous solution of 80% cumene hydroperoxide (80% CHP) resulted in a low yield, while 30% hydrogen peroxide resulted in only a trace amount of product **2a**. The effect of reaction temperature was also investigated. The yield was observed to decrease to 72% when the temperature was increased from 40°C to 60°C (Table 1, entry 12). Different dirhodium(II) catalysts were also screened, with only $Rh_2(OAc)_4$, $Rh_2(TFA)_4$ and $Rh_2(Oct)_4$ producing the desired product **2a** at yields ranging from 25 to 39% (Table 1, entries 14-16). Additionally, $Rh_2(OAc)_4(IMes)$[20] and the structurally-similar chelating dirhodium(II) catalyst $Rh_2(MPDP)_2$[21] were found to be less efficient compared with $Rh_2(esp)_2$ (Table 1, entries 17-18). Further evaluation revealed that reducing the catalyst loading to 0.1 mol% $Rh_2(esp)_2$ catalysed the reaction,

but only resulted in a 50% yield after 6 h (Table 1, entry 19). The oxidation catalysed by $Rh_2(esp)_2$ was an overall clean reaction. NMR analysis of the crude products (Table 1, entry 1) showed that the only detectable impurities were small amounts of over-oxidized products. In addition, peroxides or epoxides were not detected.

Once the optimal reaction conditions were determined, a variety of Δ^5-steroidal substrates **1a-g** were oxidized using 1 mol% of catalyst with 5 equiv of oxidant T-HYDRO and heating at 40°C for 6 h. The different functional groups of 3-acetate-Δ^5-steroids substrates **1a-d** were each oxidized into the desired ketone products **2a-d** with good yields (Table 2, entries 1-4). Oxidation of 3-hydroxy-Δ^5-steroids **1e-f** was also successful but these substrates gave relatively lower isolated yields of 7-ketocholesterol **2e-f** (Table 2, entries 5-6). If the alcohol group was protected, as with *tert*-butyl dimethylsilyl ethers (**1g**), the yield of the desired product was observed to increase (Table 2, entry 7).

Table 2. Oxidation of Steroids Using Optimized Condition[a]



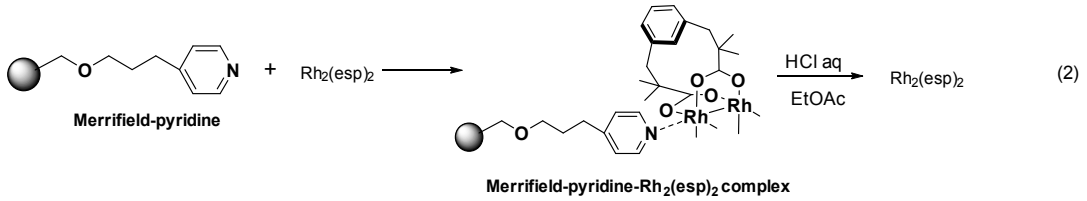
1a-g **2a-g**

entry	substrate	**2** yield (%)[b]
1	R^1 = OAc, R^2 = O, R^3 = O (**1a**)	85 (**2a**)
2	R^1 = OAc, R^2 = C_8H_{17}, R^3 = H (**1b**)	72 (**2b**)
3	R^1 = OAc, R^2 = Ac, R^3 = H (**1c**)	87 (**2c**)
4	R^1 = Cl, R^2 = C_8H_{17}, R^3 = H (**1d**)	77 (**2d**)
5	R^1 = OH, R^2 = C_8H_{17}, R^3 = H (**1e**)	38 (**2e**)
6	R^1 = OH, R^2 = Ac, R^3 = H (**1f**)	43 (**2f**)
7	R^1 = OTBS, R^2 = C_8H_{17}, R^3 = H (**1g**)	70 (**2g**)

[a]All reactions were performed using **1a-g** (0.4 mmol), T-HYDRO (2 mmol), n-heptane (0.5 mL), $Rh_2(esp)_2$ (1.0 mol%). [b]Yield after column chromatography.

Since many transition metal catalysts easily degrade under oxidative conditions in Δ^5-steroids oxidations, the stable Rh_2(II,II) species in a catalyst resting state may aid in catalyst stability, recovery, and recyclability. To test the recyclability of the catalyst, the oxidation reactions were scaled up to gram levels and tested in catalyst recycling experiments. At this scale, highly pure product **2a** was observed to precipitate from the reaction mixture when **1a** (1.1 g, 3.3 mmol) was treated with 25 mg $Rh_2(esp)_2$ in 2 mL heptane under standard conditions. Pure product **2a** was readily obtained by gravity filtration at a yield of 76%. This precipitation reaction demonstrated that this oxidation method was operationally simple. Initial attempts to recover the $Rh_2(esp)_2$ catalyst used column chromatography. Though the $Rh_2(esp)_2$ was successfully recovered, the recovery rate was low (< 50%) and the method was inefficient. Using a previously described method for immobilization of dirhodium catalysts,[22] a convenient and efficient way was developed to recovery the $Rh_2(esp)_2$ catalyst. A Merrifield resin was synthesized as a polymer backbone and functionalized with a pyridine group. The resin was then applied to coordinate to rhodium atoms and scavenge the $Rh_2(esp)_2$ catalyst from the homogenous solution (Eq 2). After filtration of product **2a,** 80 mg of Merrifield-pyridine resin was added to the above residue solution. After stirring for 10 min, the red Merrifield-pyridine-$Rh_2(esp)_2$ complex was recovered by filtration. The obtained Merrifield-pyridine-$Rh_2(esp)_2$ complex was then directly added to a 2 mL

EtOAc with 3M HCl (aq) mixed solution to release the $Rh_2(esp)_2$. A green organic solvent containing $Rh_2(esp)_2$ released from the polymer was separated. Finally, 24 mg of $Rh_2(esp)_2$ (96% recovery rate) was obtained after the EtOAc was removed (Figure 5).

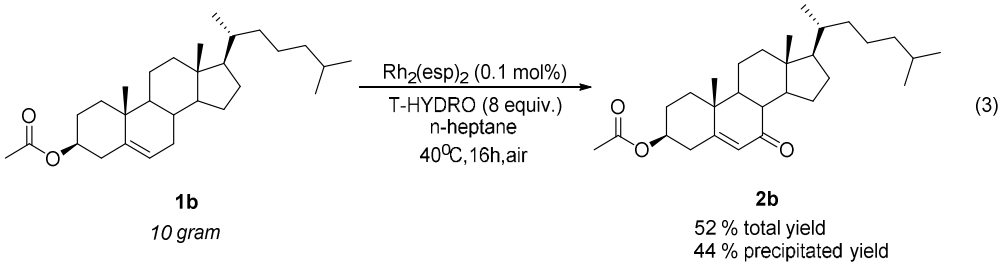


(a) (b) (c) (d) (e)

Figure 5. Recovery of $Rh_2(esp)_2$. (a) Merrifield-pyridine resin. (b) Residue solution after the filtration of product. (c) Merrifield-pyridine resin was added to $Rh_2(esp)_2$ complex in heptane. (d) Merrifield-pyridine-$Rh_2(esp)_2$ complex. (e) The release of $Rh_2(esp)_2$ in HCl $_{(aq)}$/EtOAc.

As it serves as an important intermediate product in vitamin D_3 manufacturing, 7-keto-cholesteryl acetate **2b** was selected for further scaled-up reactions.[11-12] After preliminary optimization of the reaction conditions, a lower $Rh_2(esp)_2$ loading (0.1 mol%) was observed to efficiently catalyse the allylic oxidation of 10 g of **1b** using 8 equiv T-HYDRO, resulting in a total yield of 52% after 16 h and 44% yield of product **2b** precipitate (Eq. 3). These results indicate that the $Rh_2(esp)_2$ catalyst tolerates scale-up for a long time under mild reaction conditions. This robust and environmentally-friendly oxidation procedure may be applied in the synthesis of fine

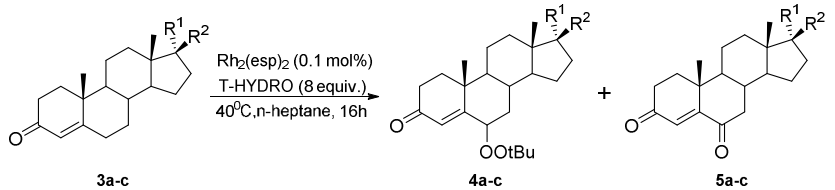
chemicals and pharmaceuticals.



(3)

The less reactive 17-acetyltestosterone **3a** (due to a conjugated system of double bonds and the presence of a carbonyl group) was successfully oxidized using modified conditions (8 equiv T-HYDRO and 16 h reaction time instead of the standard 5 equiv T-HYDRO and 6h). Although extension of the reaction time (16h), a catalyst loading of 0.1 mol% still resulted in the desired diketone product **5a** at a 53% yield and a 10% yield of the peroxide product **4a** (Table 3, entry 1). These results may be attributed to the high stability of the $Rh_2(esp)_2$ catalyst during the reaction. The formation of *tert*-butyl peroxide product **4a** indicates that the reaction mechanism involved a free radical. Similar results were obtained with the oxidation of 4-cholesten-3-one **3b** and 4-androstene-3, 17-dione **3c** (Table 3, entries 2-3).

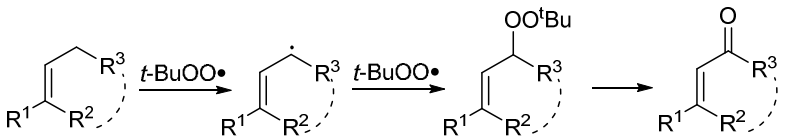
Table 3. Oxidation of Steroids Using Lower Catalyst Loading[a]



entry	substrate	yield(%)[b] 4	5
1	R^1 = OAc, R^2 = H (**3a**)	10(**4a**)	53(**5a**)
2	R^1 = C_8H_{17}, R^2 = H (**3b**)	13(**4b**)	38(**5b**)
3	R^1 = Ac, R^2 = H (**3c**)	6(**4c**)	48(**5c**)

[a]Reaction conditions: **3a-c** (4.0 mmol), T-HYDRO (20.0 mmol), n-heptane (2.0 mL), $Rh_2(esp)_2$ (0.1 mol%). [b]Yields after column chromatography.

Doyle et al. previously described the mechanism of allylic oxidation.[6c,11] In the case of $Rh_2(cap)_4$, the metal catalyst generates *t*-BuOO•, which then facilitates hydrogen abstraction from the allylic C-H bond (Scheme 1). The exceptional catalytic activity of $Rh_2(cap)_4$ is provided its low oxidation potential and rapid reduction of oxidized Rh_2(II,III) species to the catalytically active Rh_2(II,II) species to complete the catalytic cycle. Interestingly, the UV/visible spectroscopy results indicate a different catalyst resting state for $Rh_2(esp)_2$-catalyzed *t*-BuOO• generation than the previously reported $Rh_2(cap)_4$-catalyzed reaction (Scheme 1). In the $Rh_2(cap)_4$ ($E_{1/2}$ = 11 mV *vs* SCE)[6c] catalysed oxidation reactions, the mixed-valent Rh_2(II,III) species exists in a resting state. This active Rh_2(II,III) intermediate is unstable and is rapidly consumed under oxidative conditions.[11b] In contrast, $Rh_2(esp)_2$ has a high oxidation potential ($E_{1/2}$ = 1130 mV *vs* SCE)[14d] and can facilitate oxidation reactions and be easily recovered at the end of the reaction. One-electron oxidation to $Rh_2(esp)_2^+$ can be considered the rate limiting step. Therefore, the catalyst resting state is the stable Rh_2(II,II) state. Since the reaction (Table 1, entry 14) catalysed by $Rh_2(OAc)_4$, which has a similarly high oxidation potential ($E_{1/2}$ = 1170 mV *vs* SCE)[23] as $Rh_2(esp)_2^+$ produces low yields of the target product, the chelating ligand of $Rh_2(esp)_2$ likely aids in stabilizing the Rh_2(II,II) oxidation state.



Scheme 1. Proposed Reaction Mechanism.

Conclusion

The optimized $Rh_2(esp)_2$/T-HYDRO system exhibited efficient catalytic performance under allylic oxidations for conversion of a variety of Δ^5-steroids to corresponding keto-products. Reaction yields were affected by the type of coordinated solvents. Reactions with this catalyst generally exhibited high stability in heptane, due to the Rh_2(II,II) catalyst resting state which is less prone to decomposition and allows for recycling of the catalyst. A Merrifield resin functionalized with a pyridine group was used to recover the $Rh_2(esp)_2$ catalyst from a homogenous solution. Future experiments will focus on elucidating the stabilization mechanism of the chelating ligand of $Rh_2(esp)_2$ and broadening the scope of this oxidation protocol.

Experimental Section

General. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz. Chemical shifts (δ) were referenced to either TMS or the residual solvent peak. The ^{1}H NMR spectra data are

presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). High-resolution mass spectra were obtained by ESI-TOF and LCMS-IT-TOF. Elemental analyses were performed with a Vario MICRO select instrument.

Typical Allylic Oxidation of Δ^5-Steroids Procedure. A steroid substrate (0.4 mmol) and $Rh_2(esp)_2$ (3 mg, 0.004 mmol) were added to a 10 mL tube equipped with a stir bar. The tube was sealed with a rubber septa and a purge needle. T-HYDRO (0.28 mL, 2 mmol) was added dropwise via syringe. After stirring for 6 h, a saturated sodium thiosulfate solution was added to the mixture to quench the reaction. The mixture was extracted with ethyl acetate (3 × 5 mL) and washed with water (2 × 10 mL). The organic layers were combined and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography (ethyl acetate/hexane) to obtain the desired products.

Procedure for Preparation of Merrifield-pyridine Resin.[22] In a 100 mL flask, Merrifield resin (2 g, 2 mmol, 1 mmol/g) was added to a solution of *t*-butyl ammonium iodide (0.37 g, 1 mmol) in N,N-Dimethylformamide (DMF, 25 mL). In a separate 50 mL round bottom flask, 4-pyridinepropanol (1.1 g, 8 mmol) was added to a mixture of sodium hydride (0.12 g, 5 mmol) in THF (5 mL). An additional 10 mL of DMF was added to the round bottom flask and the mixture was allowed to sit for 1 h. The mixture was then added to the Merrifield resin and stirred overnight. The resin was then drained

and sequentially washed with THF, THF/DMF (v/v = 1/1), DMF, DMF/H_2O (v/v = 1/11/1), DMF, THF/DMF (v/v = 1/1), THF, THF/DCM (v/v = 1/1), DCM. The resin was dried under vacuum to give the Merrifield-pyridine resin. Loading of pyridine was determined by elemental analysis for nitrogen 1.24 % N, 0.88 mmol/g.

Typical Procedure for Precipitating the product 2a and Catalyst Recycling Experiment. A steroid substrate **1a** (1.1 g, 3.3 mmol) and $Rh_2(esp)_2$ (25 mg, 0.033 mmol) were added to a 10 mL round bottom flask equipped with a stir bar. After 2 mL of n-heptane was added, the flask was sealed with a rubber septa and a purge needle. T-HYDRO (2.37 mL, 16.5 mmol) was added dropwise via syringe. After completion of the reaction, product **2a** was directly precipitated from the mixture and separated by filtration. The obtained products were washed with cold n-heptane, then dried under vacuum to give a yield of 76%. After filtration and washing of the product **2a**, 80 mg Merrifield-pyridine resin was added to the combined residue solution. After stirring for 10 min, the red Merrifield-pyridine-$Rh_2(esp)_2$ complex was recovered by filtration. The obtained Merrifield-pyridine-$Rh_2(esp)_2$ complex was directly added to a 2 mL EtOAc with 3M HCl (aq) mixed solution to release the $Rh_2(esp)_2$. After stiring for some hours, the green organic solvent containing $Rh_2(esp)_2$ released from the polymer was separated. After the EtOAc was removed 24 mg of $Rh_2(esp)_2$ (96% recovery rate) was obtained. Catalyst recovered from the first reaction was directly added to a 2 mL of **1a** (1.1 g, 3.3 mmol) in 2 mL heptane and 5 equiv T-HYDRO in order to initiate the second oxidation.

After this second reaction, the solution was cooled to 0°C, **2a** precipitated (78% yield) and 22 mg of $Rh_2(esp)_2$ complex (93% recovery rate) was recovered. This catalyst was cycled twice more according to the procedure of cycle 2. The stable $Rh_2(esp)_2$ catalytst system was found to maintain high activity and produce high yields after 5 cycles (see Supporting Information (SI)).

$Rh_2(esp)_2$:[14a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (t, *J* = 7.5 Hz, 2H), 6.92 (s, 2H), 6.87 (dd, *J* = 7.5, 1.5 Hz, 4H), 2.66 (s, 8H), 1.03 (s, 24H). HRMS (ESI^+) *m/z* calculated for $C_{32}H_{40}O_8Rh_2$ 759.0906 ($[M+H]^+$), found 759.0913.

$Rh_2(MPDP)_2$: [21a] ^{1}H NMR (400 MHz, 1% v/v d_4-MeOH in $CDCl_3$): δ 7.09 (t, *J* = 7.5 Hz, 2H), 6.86 (dd, *J* = 7.6, 1.5 Hz, 4H), 6.80 (s, 2H), 2.77-2.67 (m, 8H), 2.36-2.28 (m, 8H). HRMS (ESI^+) *m/z* calculated for $C_{24}H_{24}O_8Rh_2$ 646.9653 ($[M+H]^+$), found 646.9633.

$Rh_2(OAc)_4(IMes)$:[20c] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (s, 2H), 6.80 (s, 4H), 2.23 (s, 12H), 2.22 (s, 6H), 1.55 (s, 12H). HRMS (ESI^+) *m/z* calculated for $C_{29}H_{36}N_2O_8Rh_2$ 746.0582 ($[M]^+$), found 746.0584.

3β-Acetoxyandrost-5-en-7.17-dione (2a):[8] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 2/1) afforded 116 mg (85%); white solid, mp 185-187 ℃, R_f = 0.21 (*n*-hexane/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.76 (d, *J* = 1.8 Hz, 1H), 4.68-4.76 (m, 1H), 2.85-1.26 (comp, 20H), 2.05 (s, 3H), 1.24 (s, 3H), 0.89 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.8, 170.3, 164.8, 126.5, 72.0, 50.0, 47.9, 45.7, 44.4, 38.5, 37.8, 36.0, 35.7, 30.7, 27.3, 24.2, 21.3, 20.6, 17.4, 13.8.

HRMS (ESI^+) *m/z* calculated for $C_{21}H_{28}O_4$ 285.1849 ($[M+H-CH_3COOH]^+$), found 285.1862.

3β-Acetoxycholest-5-ene-7-one (2b):[24] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 5/1) afforded 126 mg (72%); repeated column chromatography gave analytically pure product (105 mg, 60%), white solid, mp 157-159 ℃, R_f = 0.49 (*n*-hexane/EtOAc = 5/1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.70 (d, *J* = 1.6 Hz, 1H), 4.67-4.75 (m, 1H), 2.57-0.99 (comp, 32H), 2.05 (s, 3H), 1.21 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.9 Hz, 3H), 0.85 (d, *J* = 1.9 Hz, 3H,), 0.68 (s, 3H). $^{13}C\{^1H\}$ NMR (100MHz, $CDCl_3$): δ 201.9, 170.3, 163.9, 126.7, 72.2, 54.8, 49.9, 45.4, 43.1, 39.5, 38.7, 38.3, 37.7, 36.1, 35.7, 28.6, 28.0, 27.4, 26.3, 23.8, 22.8, 22.6, 21.2, 18.87, 17.3, 12.0. HRMS (ESI^+) *m/z* calculated for $C_{29}H_{46}O_3$ 383.3309 ($[M+H-CH_3COOH]^+$), found 383.3295.

3β-Acetoxypregn-5-ene-7, 20-dione (2c):[24] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 2/1) afforded 128 mg (87%); white solid, mp 140-142 ℃, R_f = 0.24 (*n*-hexane/EtOAc = 3/1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (d, *J* = 1.6 Hz, 1H), 4.67-4.75 (m, 1H), 2.58-1.24 (comp, 24H), 2.13 (s, 3H), 2.05 (s, 3H), 1.21 (s, 3H), 0.65 (s, 3H). $^{13}C\{^1H\}$ NMR (100MHz, $CDCl_3$) δ 209.8, 201.2, 170.4, 164.2, 126.5, 72.1, 62.3, 50.0, 49.6, 45.2, 44.4, 38.4, 37.7, 36.0, 31.7, 27.3, 26.5, 23.6, 21.3, 21.1, 17.3, 13.3. HRMS (ESI^+) *m/z* calculated for $C_{23}H_{32}O_4$ 313.2162 ($[M+H-CH_3COOH]^+$), found 313.2146.

3β-Chlorocholest-5-ene-7-one (2d):[11] Typical procedure was followed and flash

chromatography (*n*-hexane/EtOAc = 10/1) afforded 127 mg (77%); white solid, mp 143-144 ℃, R_f = 0.79 (*n*-hexane/EtOAc = 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.68 (s, 1H), 3.80-3.88 (m, 1H), 2.70 (d, *J* = 8.3 Hz, 2H), 2.35-2.43 (m, 1H), 2.14-2.26 (m, 2H), 1.88-2.05 (m, 4H), 2.71-0.99 (comp, 20H), 1.22 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.9 Hz, 3H), 0.86 (d, *J* = 1.9 Hz, 3H), 0.68 (s, 3H). ^{13}C{^{1}H} NMR (100MHz, $CDCl_3$) δ 202.0, 163.9, 126.2, 57.8, 54.8, 49.9, 45.5, 43.1, 42.7, 39.5, 38.6, 38.1, 36.2, 35.7, 32.8, 28.5, 28.0, 26.3, 23.8, 22.8, 22.6, 21.1, 18.9, 17.2, 12.0. HRMS (ESI$^+$) *m/z* calculated for $C_{27}H_{43}ClO$ 419.3075 ([M+H]$^+$), found 419.3062.

3β-Hydroxycholest-5-ene-7-one (2e):[11] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 2/1) afforded 60 mg (38%); white solid, mp 168-170 ℃, R_f = 0.16 (*n*-hexane/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 (d, *J* = 1.7 Hz, 1H), 3.64-3.71 (m, 1H), 2.52-0.99 (comp, 30H), 1.19 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.9 Hz, 3H), 0.85 (d, *J* = 1.9 Hz, 3H), 0.68 (s, 3H). ^{13}C{^{1}H} NMR (100MHz, $CDCl_3$) δ 202.5, 165.4, 126.0, 70.5, 54.8, 50.0, 49.9, 45.4, 43.1, 41.8, 39.5, 38.7, 38.3, 36.3, 35.7, 31.1, 28.6, 28.0, 26.3, 23.8, 22.8, 22.6, 21.2, 18.9, 17.3, 12.0. HRMS (ESI$^+$) *m/z* calculated for $C_{27}H_{44}O_2$ 401.3414 ([M+H]$^+$), found 401.3404.

3β-Hydroxypregn-5-ene-7, 20-dione (2f):[11] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 1/1) afforded 56 mg (43%); white solid, mp 208-210 ℃, R_f = 0.30 (*n*-hexane/EtOAc = 1/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (d, *J* = 1.6 Hz, 1H), 3.64-3.72 (m, 1H), 2.55-1.22 (comp, 22H), 2.13 (s, 3H), 1.20 (s, 3H), 0.66 (s, 3H). ^{13}C{^{1}H} NMR (100MHz, $CDCl_3$) δ 209.9, 201.6, 165.7, 125.9, 70.4, 62.3,

50.0, 49.8, 45.2, 44.4, 41.8, 38.4, 37.7, 36.4, 31.6, 31.1, 26.5, 23.6, 21.1, 17.3, 13.3. HRMS (ESI^+) *m/z* calculated for $C_{21}H_{30}O_3$ 331.2268 ($[M+H]^+$), found 331.2287.

3β-[(1,1-dimethylethyl)dimethylsilyl]oxycholest-5-ene-7-one (2g):[11] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 20/1) afforded 136 mg (70%); white solid, mp 215-216 ℃, R_f = 0.37 (*n*-hexane/EtOAc = 20/1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.66 (d, *J* = 1.2 Hz, 1H), 3.56-3.64 (m, 1H), 2.42-1.07 (comp, 29H), 1.18 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J* = 1.8 Hz, 3H), 0.85 (d, *J* = 1.8 Hz, 3H), 0.67 (s, 3H), 0.06 (s, 6H). $^{13}C\{^1H\}$ NMR (100MHz, $CDCl_3$) δ 202.5, 165.9, 125.8, 71.3, 54.8, 50.0, 45.4, 43.1, 42.6, 39.5, 38.7, 38.4, 36.4, 36.2, 35.7, 31.8, 28.6, 28.0, 26.3, 25.9, 23.8, 22.8, 22.6, 21.2, 18.9, 18.2, 17.3, 12.0, -4.7.

17β-Acetoxyandrost-4-en-3,6-dione (4a): Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 3/1) afforded 165 mg (10%); repeated column chromatography gave analytically pure product (121 mg, 7%), colourless oil, R_f = 0.55 (*n*-hexane/EtOAc = 3/1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.86 (s, 1H), 4.60 (dd, *J* = 8.9, 8.0 Hz, 1H), 4.39 (t, *J* = 2.8 Hz, 1H), 2.58-0.90 (comp, 32H), 2.05 (s, 3H), 1.20 (s, 9H), 1.18 (s, 3H), 0.85 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 200.3, 171.2, 163.9, 128.5, 83.8, 82.5, 80.1, 53.5, 50.4, 42.5, 38.0, 36.9, 36.6, 34.6, 34.2, 30.2, 28.2, 27.4, 26.5, 26.4, 23.4, 21.2, 20.4, 18.1, 12.1. HRMS (ESI^+) *m/z* calculated for $C_{25}H_{38}O_5$ 837.5511 ($[2M+H]^+$), found 837.5487.

Cholest-4-ene-3,6-dione (4b): Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 10/1) afforded 243 mg (13%); colourless oil, R_f =

0.65 (*n*-hexane/EtOAc = 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (s, 1H), 4.37 (t, *J* = 2.7 Hz, 1H), 2.58-0.96 (comp, 38H), 1.26 (s, 3H), 1.20 (s, 9H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 1.8 Hz, 3H), 0.85 (d, *J* = 1.7 Hz, 3H), 0.71 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.5, 164.5, 128.3, 84.0, 80.0, 56.1, 53.7, 42.5, 39.6, 37.9, 36.9, 36.1, 35.8, 35.1, 34.3, 30.4, 28.1, 26.6, 24.1, 23.8, 22.8, 22.6, 20.9, 18.7, 18.0, 12.0. This compound is unstable to obtain a good HRMS or elemental analysis.

Pregn-4-ene-3,6,20-trione (4c): Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 5/1) afforded 95 mg (6%); colourless oil, R_f = 0.65 (*n*-hexane/EtOAc = 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (s, 1H), 4.38 (t, *J* = 2.6 Hz, 1H), 2.55-1.10 (comp, 33H), 2.13 (s, 3H), 1.27 (s, 3H), 1.20 (s, 9H), 0.68 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 209.4, 200.3, 163.9, 128.5, 83.8, 80.1, 63.5, 56.2, 53.5, 44.0, 38.7, 37.9, 37.0, 35.0, 34.3, 31.5, 30.4, 28.2, 26.5, 24.3, 22.8, 20.9, 18.1, 13.4. HRMS (ESI$^+$) *m/z* calculated for $C_{25}H_{38}O_4$ 403.2843 ([M+H]$^+$), found 403.2829.

17β-Acetoxy-6-*tert*-butylperoxy-androst-4-en-3-one (5a):[25] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 2/1) afforded 722 mg (53%); white solid, mp 193-195 ℃, R_f = 0.21 (*n*-hexane/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (d, *J* = 0.7 Hz, 1H), 4.64 (dd, *J* = 9.0, 8.0 Hz, 1H), 2.71-1.21 (comp, 20H), 2.05 (s, 3H), 1.17 (s, 3H), 0.84 (s, 3H). ^{13}C{^{1}H} NMR (100MHz, $CDCl_3$) δ 201.7, 199.3, 171.1, 160.6, 125.7, 82.0, 50.9, 46.2, 42.6, 39.8, 36.2, 35.5, 34.0, 27.3, 23.3, 21.1, 20.4, 17.6, 12.0. HRMS (ESI$^+$) calculated for $C_{21}H_{28}O_4$ 345.2060 ([M+H]$^+$), found 345.2059.

Cholest-6-*tert*-butylperoxy-4-ene-3-one (5b):[26] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 5/1) afforded 598 mg (38%); white solid, mp 123-125 ℃, R_f = 0.45 (*n*-hexane/EtOAc = 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (d, *J* = 0.8 Hz, 1H), 2.70-0.99 (comp, 29H), 1.16 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 1.8 Hz, 3H), 0.86 (d, *J* = 1.8 Hz, 3H), 0.72 (s, 3H). ^{13}C{^{1}H} NMR (100MHz, $CDCl_3$) δ 202.4, 199.6, 161.1, 125.4, 56.5, 55.9, 51.0, 46.8, 42.5, 39.8, 39.5, 39.1, 36.1, 35.6, 34.2, 34.0, 28.0, 23.9, 22.8, 22.6, 20.9, 18.6, 17.5, 11.9. HRMS (ESI$^+$) *m/z* calculated for $C_{27}H_{42}O_2$ 399.3258 ([M+H]$^+$), found 399.3240.

Pregn-6-*tert*-butylperoxy-4-ene-3,20-dione (5c):[26] Typical procedure was followed and flash chromatography (*n*-hexane/EtOAc = 3/1) afforded 623 mg (48%); white solid, mp 197-199 ℃, R_f = 0.63 (*n*-hexane/EtOAc = 3/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (s, 1H), 2.72-1.22 (comp, 21H), 2.14 (s, 3H), 1.17 (s, 3H), 0.68 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 208.9, 201.7, 199.4, 160.5, 125.7, 63.1, 56.5, 50.7, 46.5, 43.9, 39.7, 38.1, 35.5, 34.0, 33.9, 31.5, 24.1, 22.8, 20.8, 17.5, 13.3. HRMS (ESI$^+$) *m/z* calculated for $C_{21}H_{28}O_3$ 329.2111 ([M+H]$^+$), found 329.2105.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Pictures of the oxidation reaction, complete catalysts recycling experiments, and copies of ^{1}H and ^{13}C NMR spectra for all compounds.

Notes

The authors declare no competing financial interest.

Acknowledgements.

We are grateful for financial support from National Science Foundation of China (grant no. 21272162).

References

(1) (a) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds*; Academic Press: New York, 1981. (b) Newhouse, T.; Baran, P. S. *Angew. Chem., Int. Ed*. **2011**, *50*, 3362-3374.

(2) (a) Muzart, J. *Bull. Soc. Chim. Fr*. **1986**, 65-77. (b) Page, P. C. B.; McCarthy, T. J. *Comprehensive Organic Synthesis*; Vol. 7; Trost, B. M., Flemming, I. Eds.; Pergamon: Oxford, 1991.

(3) (a) *Modern Oxidation Methods*, 2nd ed., Backvall, J.-E. Eds.; Wiley-VCH: Weinheim, 2010. (b) Weidmann, V.; Maison, W. *Synthesis* **2013**, *45*, 2201-2221.

(4) (a) Numazawa, M.; Tachibana, M. *Steroids* **1997**, *62*, 516-522 and references cited therein. (b) Arsenou, E. S.; Fousteris, M. A.; Koutsourea, A. I.; Nikolaropoulos, S. S.; *Mini Reviews in Medicinal Chemistry* **2003**, *3*, 557-567. (c) Parish, E. J.; Kizito, S. A.; Qiu, Z.H. *Lipids* **2004**, *39*, 801-804. (d) Wendell, S. G.; Edward, J. P. *J Steroids Horm*

Sci. **2016**, *7*, 171-175.

(5) Manahan, S. E. *Environmental Chemistry*; 7th ed., Lewis Pub: Boca Raton, FL, 2000.

(6) (a) Shing, T. K. M.; Yeung, Y. -Y.; Su, P. L. *Org. Lett*. **2006**, *8*, 3149-3151. (b) Yu, J. Q.; Corey, E. J. *J. Am. Chem. Soc*. **2003**, *125*, 3232-3233. (c) Ratnikov, M. O.; Doyle, M. P. *Mendeleev Communications* **2014**, *24*, 187-196 and references cited therein. (d) Wusiman, A.; Lu, C. D. *Appl. Organomet. Chem*. **2015**, *29*, 254-258 and references cited therein. (e) Nakanishi, M.; Bolm, C. *Adv. Synth. Catal*. **2007**, *349*, 861-864.

(7) Silvestre, S. M.; Salvador, J. A. R. *Tetrahedron* **2007**, *63*, 2439-2445.

(8) Arsenou, E. S.; Koutsourea, A. I.; Fousteris, M. A.; Nikolaropoulos, S. S. *Steroids* **2003**, *68*, 407-414.

(9) Salvador, J. A. R.; Silvestre, S. M. *Tetrahedron Lett*. **2005**, *46*, 2581-2584.

(10) Salvador, J. A. R.; Clark, J. H. *Chem. Commun*. **2001**, 33-34.

(11) (a) Choi, H.; Doyle, M. P. *Org. Lett*. **2007**, *9*, 5349-5352. (b) McLaughlin, E. C.; Choi, H.; Wang, K.; Chiou, G.; Doyle, M. P. *J. Org. Chem*. **2009**, *74*, 730-738.

(12) (a) Miller, R. A.; Li, W. J.; Humphrey, G. R. *Tetrahedron Lett*. **1996**, *37*, 3429-3432. (b) Shingate, B. B.; Hazra, B. G.; Salunke, D. B.; Pore, V. S. *Tetrahedron Lett*. **2011**, *52*, 6007-6010.

(13) Li, Y. C.; Wu, X. H.; Lee, T. B.; Isbell, E. K.; Parish, E. J.; Gorden, A. E. V. *J. Org.Chem*. **2010**, *75*, 1807-1810.

(14) (a) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*,

15378-15379. (b) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417-422. (c) Zalatan, D. N.; Du Bois, J. *Top. Curr. Chem.* **2009**, *292*, 347-378. (d) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2009**, *131*, 7558-7559. (e) Kornecki, K. P.; Berry, J. F. *Chem. - Eur. J.* **2011**, *17*, 5827-5832. (f) Kornecki, K. P.; Berry, J. F. *Chem. Commun.* **2012**, *48*, 12097-12099.

(15) Wang, Y.; Kuang, Y.; Wang, Y. H. *Chem. Commun*. **2015**, *51*, 5852-5855.

(16) (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley and Sons: New York, 1998. (b) Kornecki, K. P.; Berry, J. F.; Powers, D. C.; Ritter, T. *Prog. Inorg. Chem.* **2014**, *58*, 225-302.

(17) (a) Warzecha, E.; Berto, T. C.; Berry, J. F. *Inorg. Chem*. **2015**, *54*, 8817-8824. (b) Zhao, L. L.; Zhang, H. Y.; Wang, Y. H. *J. Org. Chem*. **2016**, *81*, 129−136.

(18) Anderson, N. G. in *Practical Process Research and Development;* 2nd ed., Academic Press: Oxford, 2012, pp. 121-168.

(19) Beckwith, A. L. J.; Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 4983-4992.

(20) (a) Na, S. J.; Lee, B. Y.; Bui, N. N.; Mho, S. I.; Jang, H. Y. *J. Organomet. Chem.* **2007**, *692*, 5523-5540. (b) Bui, N. N.; Hong, J. T.; Ho, X. H.; Mho, S. I.; Jang, H. Y. *Bull. Korean Chem. Soc.* **2008**, *29*, 1624-1626. (c) Gois, P. M. P.; Trindade, A. F.; Veiros, L. F.; Andre, V.; Duarte, M. T.; Afonso, C. A. M.; Caddick, S.; Cloke, F. G. N. *Angew. Chem.*, *Int. Ed.* **2007**, *46*, 5750–5753. (d) Coelho, J. A. S.; Trindade, A. F.; Wanke, R.; Rocha, B. G. M.; Veiros, L. F.; Gois, P. M. P.; Pombeiro, A. J. L.; Afonso, C.

A. M. *Eur. J. Org. Chem.* **2013**, 1471-1478.

(21) (a) Bickley, J.; Bonar-Law, R.; McGrath, T.; Singh, N.; Steiner, A. *New J. Chem.* **2004**, *28*, 425-433. (b) Taber, D. F.; Meagley, R. P.; Louey, J. P.; Rheingold, A. L. *Inorg. Chim. Acta* **1995**, *239*, 25-28.

(22) Davies, H. M. L.; Walji, A. M. *Org. Lett.* **2005**, *7*, 2941–2944.

(23) Zhu, T. P.; Ahsan, M. Q.; Malinski, T.; Kadish, K. M.; Bear, J. L. *Inorg. Chem.* **1984**, *23*, 2-3.

(24) Pearson, A. J.; Chen, Y. S.; Han, G. R.; Hsu, S. Y.; Ray, T. *J. Chem. Soc.*, *Perkin Trans.*, *I* **1985**, 267-273.

(25) Marwah, P.; Marwah, A.; Lardy, H. A. *Green Chem.* **2004**, *6*, 570-577.

(26) Hunter, C. A.; Priest, S. M. *Steroids* **2006**, *71*, 30-33.