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Aerobic Oxygenation of Olefinic Compounds into the Corresponding α-Hydroxy Ketones Using the Catalyst System of OsO_4 and Ni(II) Complex

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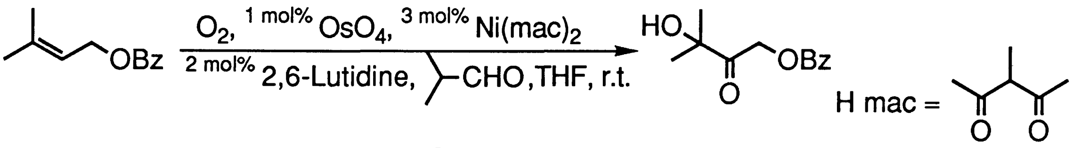
In the presence of the catalyst system of OsO_4 and bis(3-methyl-2,4-pentanedionato)nickel(II), various olefinic compounds are directly converted into the corresponding α-hydroxy ketones in good yields with molecular oxygen and an aldehyde.

α-Hydroxy ketones are useful intermediates for the synthesis of various natural products including biologically active compounds, sugars, and β-hydroxy-α-amino acids. Concerning the preparative method of α-hydroxy ketones, oxidation of oxygen-containing substrates, such as ketones,1) silyl enol ethers2) or lithium enolates,3) have been widely investigated. The oxidation of C-C double bonds of olefinic compounds to compose two oxygen-containing functions is also considered as an alternative method for the preparation of α-hydroxy ketones, and OsO_4 catalyzed oxidation of $\Delta^{17,20}$ position of steroids with Milas's reagent (hydrogenperoxide in anhydrous *t*-butyl alcohol),4) $RuCl_3$ catalyzed oxidation of olefins with acetic peracid5) or stoichiometric $KMnO_4$ oxidation of olefins6) have been reported.

It was already shown from our laboratory that a catalytic amount of bis(1,3-diketonato)nickel(II) efficiently promotes monooxygenation reaction of olefins into the corresponding epoxides with an atmospheric pressure of oxygen and an aldehyde.7a) Furthermore, the above aerobic epoxidation has been extended to the oxygenation of cyclic or acyclic ketones into the corresponding lactones or esters,7b) aldehydes into the corresponding carboxylic acids,7c) or enolates into the corresponding α-hydroxy carbonyl compounds.2) In order to develop more useful aerobic oxygenation to introduce two oxygen atoms into C-C double bond, it was expected that aerobic bifuctionalization reaction of olefinic compounds could be achieved by choosing a suitable combination of two metallic species such as OsO_4 and second transition metal catalyst.

In this communication, we would like to describe a novel and convenient preparative method of α-hydroxy ketones from olefinic compounds with molecular oxygen (safe and the most available oxidant) and an aldehyde



Scheme 1.

Bz = PhCO-

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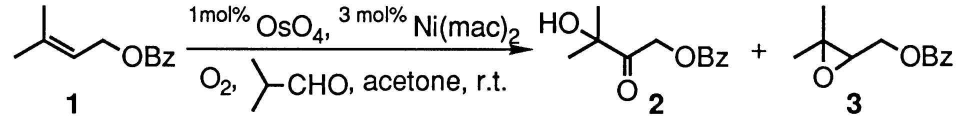
using the catalyst system of OsO_4 and bis(3-methyl-2,4-pentanedionato)nickel(II) (=$Ni(mac)_2$).2)

First, OsO_4 catalyzed aerobic oxygenation of prenyl benzoate (**1**) was taken as a model reaction, and various second transition metals were examined in order to achieve the bifuctionalization of olefin **1**. After screening several metals, it was found that, in the coexistence of 1 mol% of OsO_4 and 3 mol% of $Ni(mac)_2$, two oxygen-containing functions, hydroxyl group and carbonyl group, were composed on C-C double bond of prenyl benzoate (**1**) to afford the corresponding α-hydroxy ketone **2** in 62% yield along with epoxide **3** (Entry 1 in Table 1). In the present oxygenation reaction, it was confirmed that the combined use of OsO_4 and $Ni(mac)_2$ is essential to form α-hydroxy ketone by treating olefin **1** with an atmospheric pressure of oxygen and an aldehyde (Entries 2-5).

Table 1. Aerobic Oxygenation of Prenyl Benzoate (**1**) into α-Hydroxy Ketone **2**a)

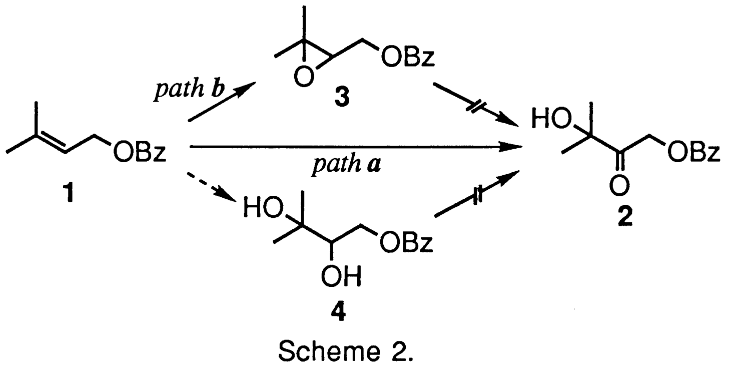


Entry	Catalyst	Aldehyde	Atmosphere	Yield /%b) **2**	**3**
1	OsO_4, $Ni(mac)_2$	isobutyraldehyde	O_2	62	23
2	$Ni(mac)_2$	isobutyraldehyde	O_2	0	75
3	OsO_4	isobutyraldehyde	O_2	trace	0
4	OsO_4, $Ni(mac)_2$	none	O_2	0	0
5	OsO_4, $Ni(mac)_2$	isobutyraldehyde	Ar	0	0

a) Reaction conditions; prenyl benzoate (**1**) 3.0 mmol, isobutyraldehyde 9.0 mmol, OsO_4 0.03 mmol (1.0 mol%), $Ni(mac)_2$ 0.09 mmol (3.0 mol%), in acetone 5.0 ml, 1 atm O_2, r.t., 14 h. b) Isolated yield.

In the above oxygenation, it was found that α-hydroxy ketone **2** was not obtained at all and unchanged epoxide **3** or 1,2-diol **4** was recovered, when epoxide **3** or 1,2-diol **4**8) was employed as a starting material. On the other hand, no 1,2-diol **4** was detected in the oxygenation described in Entry 1 in Table 1. Thus, it is reasonable to consider that α-hydroxy ketone **2** is formed directly from olefinic compound **1** *via path **a*** and not from epoxide **3** or 1,2-diol **4** (Scheme 2). Concerning the active oxidant for the conversion of olefin **1** into α-hydroxy ketone **2**, it is postulated that olefin **1** is attacked with OsO_4 first, then resulting *osmate ester* is oxidatively converted with epoxidation species generated from nickel(II) complex, O_2, and an aldehyde into α-hydroxy ketone **2** along with regeneration of OsO_4.

The assumed reaction pathway suggested that the yield of α-hydroxy ketone **2** could be improved by an

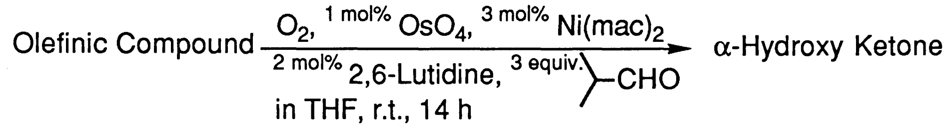


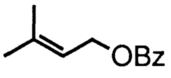
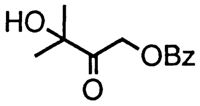
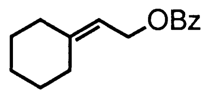
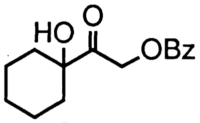
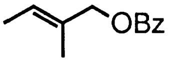
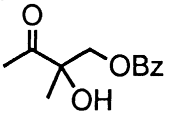
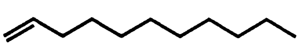
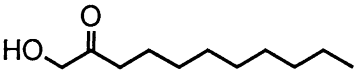
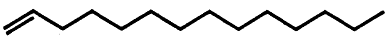
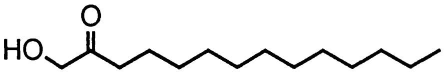
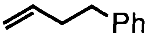
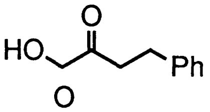
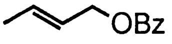
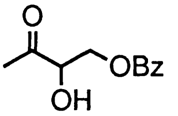
Scheme 2.

acceleration of the oxidation of olefin **1** with OsO_4 *via path a* or a suppression of the competitive epoxidation of olefin **1** *via path b*. Based on the reported evidence that several amines were effectively employed as additives to increase the reaction rate of OsO_4 catalyzed oxidation of olefins into the corresponding *cis*-1,2-diols.[9)] Then, the present oxygenation reaction was tried by adding 2 mol% of 2,6-lutidine (2 equiv. against OsO_4), and the yield of α-hydroxy ketone **2** increased up to 72%, as expected.[10)] It was also found that reaction solvent influenced notably to suppress the competitive formation of epoxide **3** *via path b*, and it was shown that THF was an appreciable solvent to afford α-hydroxy ketone **2** in 82% yield, and that undesirable formation of epoxide **3** was decreased down to 7%, probably because THF is unfavorable reaction solvent for the aerobic epoxidation of olefins catalyzed by nickel(II) complexes in terms of its slow reaction rate.[7d)]

The above procedure was successfully applied to various olefinic compounds as shown in Table 2. Benzoates of trisubstituted allylic alcohols were oxygenated into the corresponding α-hydroxy ketones in good yields (Entries 1-3). Terminal olefins also afforded α-hydroxy ketones in all the cases without accompanying α-hydroxy aldehydes (Entries 4-6). In the case of 1,2-disubstituted olefin, only one regio isomer of α-hydroxy

Table 2. Aerobic Oxygenation of Various Olefinic Compounds into the Corresponding α-Hydroxy Ketones[a)]



Entry	Olefinic compound	α-Hydroxy ketone[b)]	Yield /%[c)]
1			82
2			80
3[d)]			65
4			67
5			62
6			49[e)]
7			31[f)]

a) Reaction conditions; olefinic compound 3.0 mmol, isobutyraldehyde 9.0 mmol, OsO_4 0.03 mmol (1.0 mol%), $Ni(mac)_2$ 0.09 mmol (3.0 mol%), 2,6-lutidine 0.06 mmol (2.0 mol%) in THF 5.0 ml, 1 atm O_2, r.t., 14 h. b) satisfactory ^1H NMR and IR spectra were obtained. c) Isolated yield. d) Acetone was used as a solvent. *See* Ref. 11. e) Conversion of 4-phenyl-1-butene was 63% and yield of 1,2-epoxy-4-phenylbutane was 7%. f) Conversion of *trans*-2-butenyl benzoate was 69%.

ketone was isolated in 31% yield at 69% conversion (Entry 7).

A typical procedure for the oxygenation of prenyl benzoate (**1**) is described as follows; prenyl benzoate (**1**) (570 mg, 3.0 mmol), $Ni(mac)_2$ (30 mg, 0.09 mmol, 3.0 mol%), OsO_4 (7 mg, 0.03 mmol, 1.0 mol%), 2,6-lutidine (17 μl, 0.06 mmol, 2.0 mol%), and isobutyraldehyde (9.0 mmol) in dry THF were stirred under an atmospheric pressure of oxygen at room temperature for 14 h. Then solvent was removed *in vacuo*, and residue was purified by silicagel column chromatography (hexane / ethyl acetate) to afford the corresponding α-hydroxy ketone **2**12) (544 mg, 82% yield).

It is noted that, by the combined use of 1 mol% of OsO_4 and 3 mol% of bis(3-methyl-2,4-pentanedionato)-nickel(II) (=$Ni(mac)_2$), various olefinic compounds are directly converted into the corresponding α-hydroxy ketones in good yields with an atmospheric pressure of oxygen and an aldehyde. Further, it was shown that the yield of α-hydroxy ketone is improved by the addition of 2 mol% of 2,6-lutidine. Thus the present aerobic oxygenation procedure provides a convenient method for the preparation of α-hydroxy ketones just starting from olefinic compounds.

References

1) E. Vedejs, D. A. Engler, and J. E. Telschow, *J. Org. Chem.*, **43**, 188 (1978).
2) T. Takai, T. Yamada, O. Rhode, and T. Mukaiyama, *Chem. Lett.*, **1991**, 281. References are cited therein.
3) K. R. Guertin and T. H. Chan, *Tetrahedron Lett.*, **32**, 715 (1991).
4) K. Miescher and J. Schmidlin, *Helv. Chim. Acta*, **33**, 1840 (1950); B. Gadsby, M. R. G. Leeming, G. Greenspan, and H. Smith, *J. Chem. Soc., C*, **1968**, 2647; E. G. Brain, F. Cassidy, A. W. Lake, P. J. Cox, and G. A. Sim, *J. Chem. Soc., Chem. Commun.*, **1972**, 497.
5) S. Murahashi, T. Saito, H. Hanaoka, T. Naota, H. Kumobayashi, and S. Akutagawa, 61th National Meeting of the Chemical Society of Japan, Yokohama, March 1991, Abstr., No. 1C918; S. Murahashi, T. Saito, Y. Murakami, T. Naota, H. Kumobayashi, and S. Akutagawa, *ibid.*, Abstr., No. 1C925.
6) S. Baskaran, J. Das, and S. Chandrasekaran, *J. Org. Chem.*, **54**, 5182 (1989).
7) a) T. Yamada, T. Takai, O. Rhode, and T. Mukaiyama, *Chem. Lett.*, **1991**, 1; *Bull. Chem. Soc. Jpn.*, in print; b) T. Yamada, K. Takahashi, K. Kato, T. Takai, S. Inoki, and T. Mukaiyama, *Chem. Lett.*, **1991**, 641; c) T. Yamada, O. Rhode, T. Takai, and T. Mukaiyama, *Chem. Lett.*, **1991**, 5; d) T. Yamada, T. Takai, O. Rhode, and T. Mukaiyama, unpublished result.
8) The 1,2-diol **4** was prepared by the oxidation of prenyl benzoate (**1**) with *N*-methylmorphorine *N*-oxide in the presence of 1 mol% of OsO_4 by usual manner.
9) E. N. Jacobsen, I. Markó, W. S. Mungall, G. Schröder, and K. B. Sharpless, *J. Am. Chem. Soc.*, **110**, 1968 (1988).
10) When tertiary amine, *N*-methylmorphorine, was added into the present oxygenation to utilize its strong coordination ability for OsO_4, both conversion of olefin **1** and yield of α-hydroxy ketone **2** were decreased compared with that in the case of 2,6-lutidine.
11) In THF solvent, 2-methyl-2-butenyl benzoate was oxygenated much more slowly than in acetone.
12) ^1H NMR ($CDCl_3$) δ=1.46 (6H, s), 3.5 (1H, s), 5.28 (2H, s), 7.45 (2H, m), 7.55 (1H, m), 8.08 (2H, m); IR (neat) 3510, 1736, 1715, 1276 cm^{-1}.

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