(Schiff-Base)Mn(III)-Catalyzed Hydroxylation of α,β-Unsaturated Esters Using Molecular Oxygen in the Presence of Metal Hydrides

Jong Seok Baik, Sung-bin Han, and Nam Ho Lee*

Department of Chemistry and Research Institute for Basic Sciences, Cheju National University, Jeju 690-756, Korea
**E-mail: namho@cheju.ac.kr*
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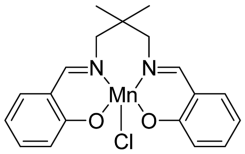
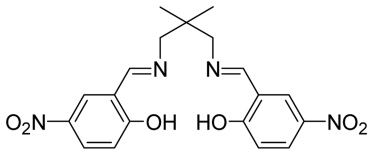
Molecular oxygen would be the most desirable oxidant in organic synthesis owing to its economically and environmentally favorable properties. Therefore, various methods have long been developed to utilize the molecular oxygen as the oxidizing reagent under mild reaction conditions. We also have reported a new oxygenation method on the olefin oxidation to corresponding alcohols, where atmospheric pressure of oxygen was involved as the oxidant along with (schiff-base)Mn(III) catalyst and sodium borohydride as the co-reagent.[1]

As a continuing effort in this field, we decided to examine the electron deficient olefins such as α,β-unsaturated esters as the reaction substrate. Direct hydroxylation of α,β-unsaturated esters would provide the α-hydroxy esters, which comprise important functional groups frequently encountered in organic synthesis. Even though various preparative method on α-hydroxy esters has been reported, relatively few reports have been made utilizing molecular oxygen as the oxidant for the synthesis of α-hydroxy esters.[2]

In order to obtain the optimized reaction conditions in this study, we have examined some experimental parameters such as (schiff-base)Mn(III) complex, reaction solvent and reaction temperature. The optimized reaction condition was described in Table 1, where Mn(III) complex **1** (10 mol%) was employed as the catalyst under atmospheric pressure of oxygen along with two equivalents of sodium borohydride. The reaction was carried out using chloroform as a solvent at 0 °C.



1

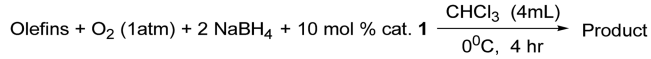


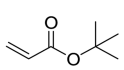
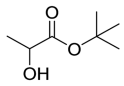
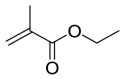
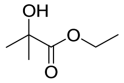
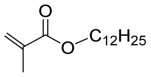
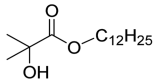
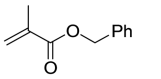
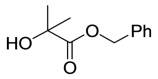
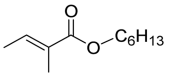
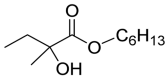
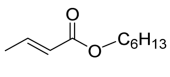
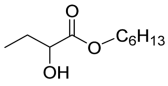
2

Some α,β-unsaturated esters were subjected to the above reaction conditions, and the results are summarized in Table 1. As seen in the Table, the examined unsaturated esters proved to be good substrates for the given oxygenation condition. *t*-Butyl acrylate (**3**) was converted to the corresponding alcohol **9** in 73% isolated yield along with small amount of reduced product, *t*-butyl propionate. Methacrylate compounds **4-6** were also converted to the corresponding tertiary alcohols **10-12** in good yields. Hexyl tigrate (**7**), where double bond is located internally, also proved to be good substrate to give the α-hydroxy ester **13** in 74% yield. When the β-methyl acrylate (**8**) was examined under the reaction condition, the expected product was obtained in only 36% yield. In order to improve the product yield, examination of other different reaction conditions was made. As a result, yield improvement up to 75% was observed when the catalyst **1** was replaced by direct addition of manganese(III) acetate coupled with electron deficient schiff-base **2** as the external ligand (entry 6).[3]

During the study of this oxidation process, we observed that ester group is reduced by sodium borohydride under some solvent condition. For example, lauryl methacrylate (**5**) was reduced to the alcohol in 11% yield when

Table 1. The oxygenation of some α,β-unsaturated esters



Entry	STM		Product		Isolated Yield (%)
1		**3**		**9**	73
2		**4**		**10**	74[a]
3		**5**		**11**	83
4		**6**		**12**	80
5		**7**		**13**	71
6		**8**		**14**	36(75[b])

[a]GC yield using dodecane as an internal standard. [b]Using 15 mol% schiff-base ligand **2** along with 15 mol% Mn(III) acetate as the catalyst instead of complex **1**

Table 2. Oxygenation of α,β-unsaturated esters under different metal hydrides

Olefins + Hydrides + 10 mol% complex **1** $\xrightarrow[\text{Solvent}]{O_2,\ 4\ hr}$ Products

Entry	Olefins	Hydrides	Temp.	Solvent	Products	Yield (%)[a]
1	**5**	2 $NaBH_4$	0 °C	$CHCl_3$ (4 mL)	**11**	83
2	**5**	2 *n*-Bu_4NBH_4	0 °C	$CHCl_3$/EtOH (4 mL/1 mL)	**11**	79
3	**5**	1.2 $PhSiH_3$	rt	*i*-PrOH/EtOH (2 mL/2 mL)	**11**	76
4	**7**	2 $NaBH_4$	0 °C	$CHCl_3$ (4 mL)	**13**	74
5	**7**	2 *n*-Bu_4NBH_4	0 °C	$CHCl_3$/EtOH (4 mL/1 mL)	**13**	73
6	**7**	1.2 $PhSiH_3$	rt	*i*-PrOH/EtOH (2 mL/2 mL)	**13**	32(50[b])

[a]Isolated yield. [b]Conversion yield detected by GC.

acetonitrile/ethanol were used as co-solvent at room temperature. This observation led us to examine other metal hydrides as a more mild hydride source. We examined tetrabutylammonium borohydride and phenyl silane as a potential metal hydride applicable in this system (Table 2). Using esters **5** and **7** as the substrates, tetrabutylammonium borohydride provided the comparable result compared to sodium borohydride (entries 2, 5), which indicates that this reagent can be the substitute for sodium borohydride depending on the experimental condition. When the substrate **5** was examined under ^{i}PrOH and ethanol as the solvent at rt, phenyl silane also proved to be the good hydride source (entry 3). For the above two cases, reduction at the carboxylate group was not observed (entries 2 and 3 in Table 2). In the case of the substrate **7**, however, phenyl silane gave the lower reactivity compared to borohydrides (entry 6). It seems that different combination of schiff-base ligand is necessary for phenyl silane as the hydride source, on which we need further study in due course.

In conclusion, we have demonstrated that α,β-unsaturated esters were oxygenated to the corresponding α-hydroxy esters in good yields. Atmospheric pressure of oxygen was used as the oxidizing agent coupled with (schiff-base) Mn(III) catalyst in the presence of metal hydrides such as borohydrides or phenyl silane. This reaction provides a mild method for the direct preparation of α-hydroxy carboxylates starting from α,β-unsaturated esters. Further studies to extend the scope of this method as well as to identify the detailed reaction mechanism are underway.

Experiment Section

Typical experimental procedure. In a 50 mL round bottom flask were placed lauryl methacrylate (**5**, 254 mg, 1.0 mmol), (schiff-base)Mn(III)Cl complex **1** (39 mg, 0.1 mmol), and $CHCl_3$ (4 mL) as a solvent. After oxygen balloon was adapted to the reaction flask, flushing the vessel with O_2 was undertaken by evacuation/charging procedure three times. To this was added *via* syringe $NaBH_4$ (74 mg, 2 mmol) dissolved in 4 mL ethanol over 20 min with stirring. After the mixture was stirred for 4 hr at rt, it was poured into sat. NH_4Cl solution and extracted with diethyl ether. The organic layer was dried with Na_2SO_4, concentrated in *vacuo* and purified by flash column chromatography to give 2-hydroxy-2-methyl-propionic acid dodecyl ester (**11**, 226 mg, 83% yield) as the product. The structure were confirmed by NMR data.

Compound 9: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.11 (1H, dd, J = 13.7, 6.8 Hz), 1.46 (9H, s), 1.34 (3H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.26, 82.32, 67.11, 28.14, 20.67.

Compound 10: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.15 (2H, t, J = 6.8 Hz), 1.37 (6H, s), 1.32 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.3, 72.1, 61.68, 27.21, 14.19.

Compound 11: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.15 (2H, t, J = 6.8 Hz), 1.65 (2H, tt, J = 7.1, 6.8 Hz), 1.44 (6H, s), 1.28 (18H, m), 0.8684 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.56, 71.88, 65.87, 31.86, 29.58, 29.57, 29.49, 29.43, 29.29, 29.11, 28.46, 27.13, 25.71, 22.64, 14.07.

Compound 12: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38 (5H, m), 5.22 (2H, s), 1.47 (6H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.56, 135.57, 128.77, 128.57, 128.13, 72.23, 67.46, 27.29.

Compound 13: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.15 (2H, t, J = 6.8 Hz), 1.76 (1H, m), 1.42 (3H, m), 1.37 (3H, s), 1.29 (6H, m), 0.86 (6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.2, 74.78, 65.77, 32.97, 31.23, 28.44, 25.6, 25.37, 22.4, 13.85, 7.86.

Compound 14: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.17 (H, dd, J = 12.7, 6.8 Hz), 4.18 (2H, m), 1.82 (1H, m), 1.66 (3H, m), 1.32 (6H, m), 0.95 (3H, t, J = 7.5 Hz), 0.87 (3H, t, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.49, 71.56, 65.87, 31.5, 28.68, 27.66, 25.62, 22.65, 14.01, 9.05.

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References and Notes

1. (a) Lee, N. H.; Baik, J. S.; Hahn, S.-B. *Bull. Korean Chem. Soc.* **1999**, *20*, 867. (b) Lee, N. H.; Byun, J. C.; Baik, J. S.; Han, C.-H.; Han, S.-B. *Bull. Korean Chem. Soc.* **2002**, *23*, 1365. (c) Lee, N. H.; Baik, J. S.; Hahn, S.-B. *Bull. Korean Chem. Soc.* **2004**, *25*, 1455.
2. (a) Inoki, S.; Kato, K.; Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1990**, 1869. (b) Magnus, P.; Payne, A. H.; Waring, M. J.; Scott, D. A.; Lynch, V. *Tetrahedron Lett.* **2000**, *41*, 9725.
3. It has been shown that employment of different external ligand provided reactivity change in this oxidation system. For the example, see ref 1c.