

(Salen)Mn-Catalyzed Oxygenation of Vinyl Arenes to the Corresponding Alcohols in the Presence of Sodium Borohydride

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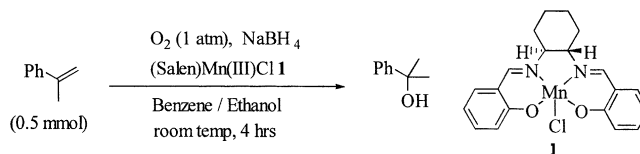
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Oxygen molecule plays a pivot role in the biological systems. In addition, it is probably the most desirable oxidant in organic synthesis in terms of economical and environmental viewpoints. Therefore, lots of efforts have long been focused to utilize molecular oxygen for the oxidation of organic compounds especially using transition metals as an activator.¹ Recent studies have been directed to the development of more mild and efficient oxygenation procedures,² and indeed some excellent examples have been published very recently in the case of alcohol oxidation.³ Undoubtedly, development of novel and mild oxygenation methods is still in demand.

As a series of our attempts to use salen-manganese complexes in organic synthesis,⁴ we tried to develop a biomimetic mono-oxygenation procedure using catalytic (salen) Mn(III) complex **1**, which is easily accessible from readily available precursors. In nature, oxygen gas is employed as an effective oxidant in biomolecules. In this biological process, an enzyme such as cytochrome P-450 is catalytically involved to activate O₂ molecule, where one-oxygen reductant such as NAD(P)H is necessarily consumed. As a synthetic model of an enzyme P-450, metal porphyrine complexes in conjunction with appropriate reductants have been studied for the aerobic oxidation of olefins to afford hydrated products.⁵ While most of these studies were focused on the reaction mechanism to access the better understanding of the biological oxidation process, few synthetically useful procedures were developed partly due to low reactivities or product selectivities providing olefin dimers as a side product. In this letter, we want to disclose that (Salen)Mn(III) complex **1** and sodium borohydride under the atmospheric pressure of oxygen can comprise a useful synthetic method for the oxidation of vinyl arenes to the corresponding alcohols.

Our investigation began with an effort to optimize reaction conditions for the oxidation of vinyl arenes using catalytic salen-manganese complex **1** and stoichiometric NaBH₄ under O₂ atmosphere. α -Methylstyrene was chosen as a model substrate to give the oxidized product, 2-phenyl-2-propanol. The first variable examined was the amount of NaBH₄ as a hydride source (entries 1-3). It proved that 1.5 equivalent of sodium borohydride is necessary to complete the reaction. Among the examined alcohols including methanol and isopropyl alcohol, ethanol was found to be the most efficient in this reaction, which is presumably due to the increased solubility of the catalyst at least in part (entries 6-8). Oxygen gas, which was supplied *via* a balloon, was of

Table 1. Examination of Reaction Conditions for the Oxygenation of α -methylstyrene







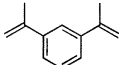
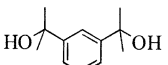


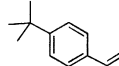
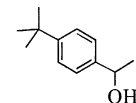
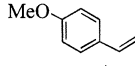
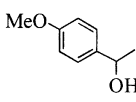
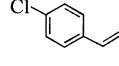
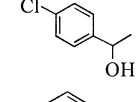

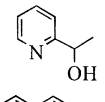
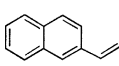
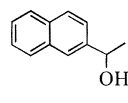




Entry	NaBH ₄ (equiv)	Complex 1 (mol %)	Benzene (mL)	Ethanol (mL)	Product (Yield %) ^a
1	0.5	10	10	2.0	38
2	1.0	10	10	2.0	53
3	1.5	10	10	2.0	92
4	1.5	5	10	2.0	84
5	1.5	5	1.0	2.0	94
6	1.5	10	10	0	39
7	1.5	10	10	0.5	67
8	1.5	10	10	1.0	92
9	1.5	10	10	2.0	7 ^b
10	1.5	10	10	2.0	34 ^c

^aGC yields using dodecane as an internal standard. ^bReaction under N₂ gas in place of O₂. ^cReaction under air in place of oxygen gas.

course indispensable for this procedure. For example, when the reaction was performed under nitrogen gas atmosphere, very low conversion was obtained (entry 9). Use of air in place of oxygen under otherwise identical conditions gave worse result (entry 10). We also found that the amount of benzene is another important factor, *i.e.* improved result was obtained with lesser amount of solvent (entries 4, 5). In fact, using the condition in entry 5 as the optimized one, we were able to let the reaction go completion with 5 mol% of the catalyst **1**.

Different types of vinyl substrates were subjected to the reaction conditions examined above. As seen in Table 2, the complex **1** coupled with NaBH₄ proved to be an efficient catalyst to effect the oxygenation of styrene derivatives to give the alcoholic compounds. The necessary amount of NaBH₄ was dependent on the substrate structures, *i.e.* there needed 1.5 equiv. borohydride for α -substituted styrenes whereas 2.0 equivalence was necessary for vinyl derivatives. With 4.0 equiv. of reductant, double oxygenation was also efficiently achieved (entry 3). This reaction was generally applicable to other aromatic compounds such as pyridinyl and naphthyl derivatives (entries 8, 9). Functionality change in the benzene ring did not affect the reactivity showing low electronic effect in this reaction (entries 4-7). However, the

Table 2. The oxygenation of styrene derivatives catalyzed by (Salen)Mn(III) complex **1** in the presence of NaBH₄

Entry	Substrate	A	Product	Isolated Yield (%)
1		1.5		85
2		1.5		90
3		4.0		77
4		2.0		81
5		2.0		80
6		2.0		87
7		2.0		87
8		2.0		73
9		2.0		79
10		2.0		35 (65) ^a
11		2.0		7

^aReaction was performed with molecular sieve (4 Å) as an additive.

styrene reactivity was decreased sharply by introduction of a substitution at terminal carbon of the C–C bond (entry 10). Interestingly, by addition of 4 Å molecular sieves in this condition, yield improvement was observed. For the non-conjugated vinyl compound, this procedure displays very low conversion leaving most of the starting material intact (entry 11). This oxygenation procedure turned out to be a very clean reaction, e.g. following the reaction by GC and GC-MS, the only distinguished side products were dimers usually observed in less than 5% yields. The typical experimental procedure is as follows: In a 50 mL two-neck round bottomed flask were placed α -methylstyrene (1.0 mmol, 118 mg), racemic (Salen)Mn(III)Cl complex **1** (0.05 mmol, 20 mg) and benzene (2 mL) as a solvent. After oxygen balloon was adapted to the reaction flask, flushing the vessel with O₂ was undertaken by evacuation/charging procedure three times. To this was added *via* syringe NaBH₄ (1.5 mmol, 56 mg) dissolved in 4 mL ethanol over 20 min with stirring. After the mixture was stirred for 4 h at rt, it was poured into

sat. NH₄Cl solution and extracted with diethyl ether. The organic layer was dried, concentrated in *vacuo* and purified by flash chromatography to give 2-phenyl-2-propanol (116 mg, 85 % yield) as the product.

In summary, we have shown that vinyl arene compounds could be efficiently oxidized into the corresponding alcohols using (salen)Mn(III) complex **1** as the catalyst in the presence of NaBH₄, where O₂ gas was used as the ultimate oxidant. This procedure could comprise a mild and selective oxygenation method for the conjugated olefins. Even though the reaction mechanism is not elucidated yet, by judging from the product distribution, in this oxidation is not involved in the high valent Mn–O species⁶ which is commonly encountered in (salen)Mn-mediated oxidation process and well documented to lead to olefin epoxidation.⁷ Further studies to understand the reaction mechanism⁸ and to expand the scope of this process are in progress.

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7. Subjection of styrene oxide to the identical reaction conditions described in the text provided no reaction, which eliminates the possible reaction pathway involving the epoxide formation followed by selective opening mediated by NaBH₄.
8. For example, trial of asymmetric induction with styrene using Jacobsen catalyst such as (*R,R*)-*N,N'*-bis(3,5-di-*t*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride provided no selectivities giving the phenethyl alcohol as a racemic mixture.