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Selective Oxidation of Benzylic Hydrocarbons to Carbonyl Compounds Catalyzed by Mn(III) Salen Complexes

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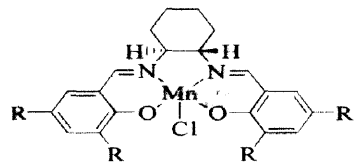
Abstract: Selective oxidation of benzylic hydrocarbons to the carbonyl compounds was achieved using a racemic Mn(III) salen complex **1** as the catalyst. The reaction proceeds in good yields under mild reaction conditions using iodosobenzene or aq. sodium hypochlorite as a stoichiometric oxidant. © 1998 Elsevier Science Ltd. All rights reserved.

The oxidation of benzylic C-H bonds constitutes one of the most fundamental transformations in organic synthesis.[1] Metal-oxo species have long been investigated for the activation of hydrocarbons to the corresponding carbonyl compounds.[2] Recently, (salen)Mn(III) complexes have been utilized for the enantioselective epoxidation of olefins,[3] where manganese-oxo species have been considered as the active intermediate. In addition, studies of C-H hydroxylation have been reported using chiral (salen)Mn complexes as reaction mediators.[4] Salen-manganese complexes whose preparation and handle are relatively easy, however, have not been utilized for the synthesis of carbonyl compounds from hydrocarbons. As a part of our research on the application of Mn(III) salen complexes in organic synthesis, we decided to investigate these catalysts for the benzylic C-H activation.



R = H **1**
= ^{t}Bu **2**

Using ethylbenzene as the typical benzylic substrate, the salen-Mn complex **1**[5] and the commercial Jacobsen's catalyst (S,S)-**2** were examined under various reaction conditions. The results are summarized in Table 1. The reaction produced acetophenone (**4**) as the major product, along with α-methylbenzyl alcohol (**3**) as the only side product as determined by GC analysis. In terms of reactivity and selectivity to the carbonyls, the complex **1** was found to be better catalyst for the benzylic oxidation. This type of reactivity difference is documented in the literature,[6] where the catalytic activity of the salen-Mn(III) complex is dependent on the steric and electronic environment of the salen ligand. Thus, the racemic complex **1**, which can be more easily prepared than the complex **2**, can be used as the choice of catalyst for this reaction. For the oxidant, iodosobenzene was found to be better than aq. sodium hypochlorite[7] or hydrogene peroxide.[8] The reaction also proved to be dependant on the choice of solvent (entries 3, 5). Although the reaction improved

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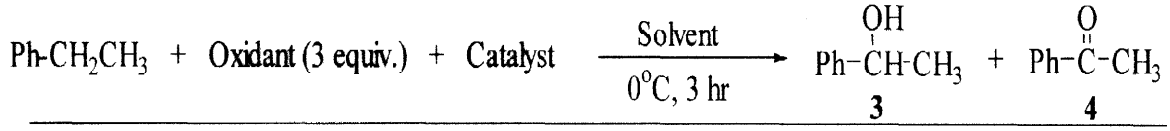
with more catalyst, the yield increase was small with employing more than 15% of the catalyst (entries 1, 3). Trial of the reaction using manganese salt such as $Mn(OAc)_2$ or $Mn(OAc)_3$ as the catalyst provided no product at all (entries 10, 11). External addition of salen ligand to the condition of entry 11 or 12 afforded some conversion, which indicates that salen chelated manganese is essential to the reaction.

Table 1. Examination of Reaction Conditions for the Oxidation of Ethylbenzene.



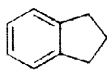
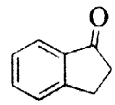
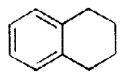
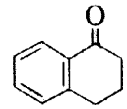
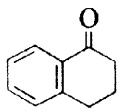
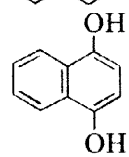
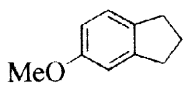
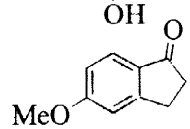
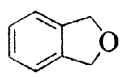
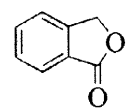
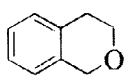
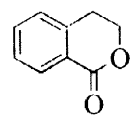
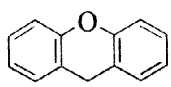
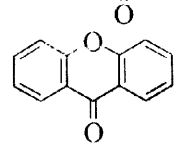
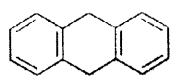
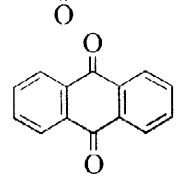
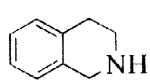
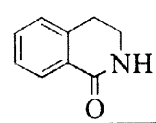
Entry	Oxidant	Catalyst (Equiv.)	Solvent	Conversion(%)[a]	Ratio (**3**:**4**)[a]
1	PhI=O	**1**(0.08)	CH_3CN	61	7 : 93
2		**2**(0.08)		7	13 : 87
3		**1**(0.15)		77	6 : 94
4		**2**(0.15)		11	14 : 86
5		**1**(0.15)	CH_2Cl_2	42	7 : 93
6		**2**(0.15)		5	30 : 70
7	aq. NaOCl	**1**(0.15)		15	11 : 89
8		**2**(0.15)		13	13 : 87
9	35% H_2O_2	**1**(0.15)	CH_3CN	12	38 : 62
10		**2**(0.15)		3	33 : 67
11	PhI=O	$Mn(OAc)_2 \cdot 4H_2O$(0.15)		0	
12		$Mn(OAc)_3 \cdot 2H_2O$(0.15)		0	

[a] Based on GC analysis with a commercial HP-5 capillary column, 25m × 0.20mm × 1.5 μ m.

Different type of benzylic substrates was subjected to the reaction conditions examined above. As seen in Table 2, the complex **1**-catalyzed oxidation was efficiently effected to give the carbonyl compounds in good yields. For alkyl benzene derivatives, benzylic oxidation products were obtained with high selectivity employing iodosobenzene as an oxidant (entries 1-7). Even though the oxidation was considered to proceed *via* alcohol, only a minute amount of the corresponding alcohol was detected by GC analysis. Cyclic alkyl substrates such as indan and tetrahydronaphthalene were identified to give mono-oxidation products selectively under the reaction condition (entries 4, 5). Oxidation of 5-methoxyindan proved to be regioselective to provide the 5-methoxy-1-indanone as the major product (entry 7). GC analysis showed the product ratio of the major product and its regioisomer, 6-methoxy-1-indanone, is 8.6:1.0 for this reaction. The products were identified by comparison to the authentic samples obtained from Aldrich Co. using GC and GC-MS analysis. In this reaction, the C-H activation took place preferentially at the *para* position of the methoxy group, indicating the electrophilic nature of the manganese-oxo intermediate. During the course of this study, it was found that aq. NaOCl which is more practical oxidant than PhI=O can also effect an efficient oxidation for the reactive electron-rich compounds. Therefore, using NaOCl as an oxidant, benzyl ethers such as phthalan and isochroman were oxidized to give the corresponding phthalide and 1-isochromanone (entries 8, 9). Trial of 5 equivalent of sodium hypochlorite made a clean transformation of

Table 2. Oxidation of Benzylic Hydrocarbons Catalyzed by Racemic (Salen)Mn(III) complex **1**.

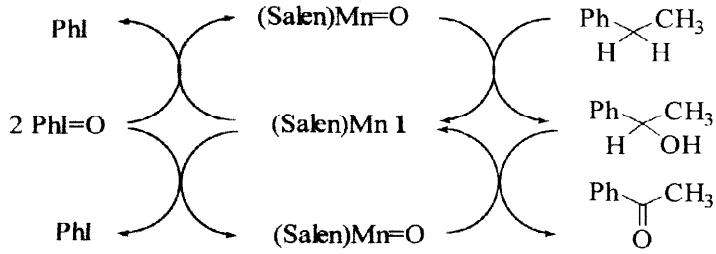
Substrate + Cat. **1** (8-15 mol%) —PhI=O (3 equiv.) or aq. NaOCl (3 equiv.)→ Product

Entry	Substrate	Method [a]	Product	Conversion (%) [b]	Isolated Yield (%)
1	Ph-CH_2CH_3	A	Ph-C(=O)-CH_3	77	60
2	Ph-CH_2-Ph	A	Ph-C(=O)-Ph	97	72
3	Ph-$CH_2CH_2CH_3$	A	Ph-C(=O)-CH_2CH_3	53	42
4		A		99	74
5		A		31	22
6		A		68	63
7		A		91	57
8		B		98	75
9		B		98	87
10		B		98	92
11[c]		B		99	66
12		B		Not Determined	27

[a] **Method A**: A mixture of substrate (0.5 mmol), iodosobenzene (1.5 mmol), and catalyst **1** (0.075 mmol) in CH_3CN (5 ml) was stirred at 0°C for 3 hr. **Method B**: To a mixture of substrate (0.5 mmol) and catalyst **1** (0.04 mmol) in CH_2Cl_2 (3 ml) was added buffered NaOCl (pH 11.3, 1.5 mmol).[6] The mixture was stirred at 0°C under N_2 atmosphere for 4 hr. [b] Based on the consumption of starting material determined by GC analysis. [c] 5 equivalents of NaOCl was used.

dihydroanthracene to anthraquinone (entry 11). Tetrahydroisoquinoline was also examined to afford the corresponding lactone , where isoquinoline was identified as a side product (entry 12).

It is reasonable to assume that the reaction proceed through Mn=O intermediate. The probable reaction pathway for the oxidation of ethylbenzene is illustrated in Scheme 1. Based on the experimental results, it is considered that the second catalytic cycle where alcohol is converted to ketone is faster than the first step.



Scheme 1

In summary, we have demonstrated the utility of Mn(III) salen complex **1** as the catalyst for the oxidation of benzylic hydrocarbons to the carbonyl compounds under mild reaction conditions. Further work is now directed to study the scope and limitation of this oxidation process.

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References and Notes

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5. This complex was prepared from the racemic *trans*-1,2-diaminocyclohexane and salicylaldehyde according to the literature procedure. See, Larrow, J. F.; Jacobsen, E. N.; Gao, Y.; Hong, Y.; Nie, X.; Zepp, C. M. *J. Org. Chem.* **1994**, 59, 1939. The complex **1** has been characterized in the literature. See, ref. 3c.
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