

FORMATION OF 1,2-DIOXACYCLOHEXANES BY THE REACTION OF ALKENES WITH TRIS(2,4-PENTANEDIONATO)MANGANESE(III) OR WITH β -KETOCARBONYL COMPOUNDS IN THE PRESENCE OF MANGANESE(III) ACETATE

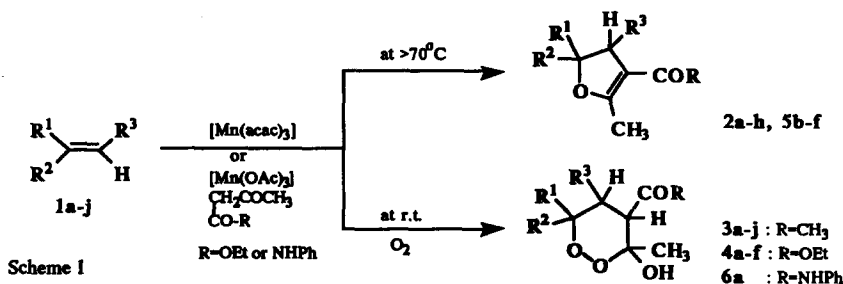
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Summary: The reactions of 1,1-disubstituted ethenes, styrene, 1-octene, 1-nonene, cyclohexene and cyclooctene with tris(2,4-pentanedionato)manganese(III) in acetic acid at room temperature give 4-acetyl-3-hydroxy-3-methyl-1,2-dioxacyclohexanes in 8-92 % yields. The reactions of 1,1-disubstituted ethenes with ethyl 3-oxobutanoate or acetoacetanilide in the presence of manganese(III) acetate also give corresponding 1,2-dioxacyclohexanes in good to moderate yields.

Recently one of the unique synthetic methodology utilizing manganese(III)-mediated radical inter- or intramolecular cyclization reactions have been reported.¹⁾ Particularly, manganese(III) acetate (abbreviated [Mn(OAc)₃]) or tris(2,4-pentanedionato)manganese(III) (abbreviated [Mn(acac)₃]) in acetic acid performs very interesting role in these reactions. [Mn(acac)₃] produces ligand radicals in acetic acid very easily over 70 °C. When alkenes (1) are present in this reaction system, 3-acetyl-2-methyl-4,5-dihydrofurans (2) are obtained in good yields.^{1c)} However, we found that the reaction mode was dramatically changed at room temperature and molecular oxygen inserted 4-acetyl-3-hydroxy-3-methyl-1,2-dioxacyclohexanes (3) were formed (Scheme 1).



Although a lot of cyclic peroxides were synthesized by the use of photosensitized oxygenation²⁾ and electrochemical cycloaddition,³⁾ the present reaction is the first example that molecular oxygen is trapped to the manganese(III)-induced radical intermolecular cyclization.

Table 1. Reaction of Alkenes with [Mn(acac)₃] or β -Ketocarbonyl Compounds in the Presence of [Mn(OAc)₃] in AcOH at 23 °C

Alkene	Molar ratio ^{a)}	Time h	Product (yield/%) ^{b)}	
1a : R ¹ =R ² =Ph, R ³ =H	1 : 1	11	3a (92)	
1b : R ¹ =R ² =4-ClC ₆ H ₄ , R ³ =H	1 : 2	12	3b (90)	
1c : R ¹ =R ² =4-CH ₃ OC ₆ H ₄ , R ³ =H	1 : 2	12	3c (87)	
1d : R ¹ =R ² =4-CH ₃ C ₆ H ₄ , R ³ =H	1 : 1	13	3d (77)	
1e : R ¹ =R ² =4-FC ₆ H ₄ , R ³ =H	1 : 1	12	3e (72)	
1f : R ¹ =Ph, R ² =R ³ =H	1 : 1	12	3f (34)	
1g : R ¹ =C ₆ H ₁₃ , R ² =R ³ =H	5 : 1	15	3g (8) ^{c)}	
1h : R ¹ =C ₇ H ₁₅ , R ² =R ³ =H	5 : 1	14	3h (35) ^{c)}	
1i : R ¹ ,R ³ =(CH ₂) ₄ , R ² =H	4 : 1	12	3i (11) ^{c)}	
1j : R ¹ ,R ³ =(CH ₂) ₆ , R ² =H	5 : 1	14	3j (43) ^{c)}	
1a	1 : 3 : 1 ^{d)}	10	4a (82)	
1b	1 : 3 : 1 ^{d)}	12	4b (27)	5b (34)
1c	1 : 3 : 1 ^{d)}	12	4c (54)	5c (46)
1d	1 : 3 : 1 ^{d)}	12	4d (55)	5d (46)
1e	1 : 3 : 1 ^{d)}	12	4e (50)	5e (17)
1f	1 : 3 : 1 ^{d)}	12	4f (50)	5f (13)
1a	1 : 3 : 1 ^{e)}	12	6a (91)	

a) Alkene : [Mn(acac)₃]. b) Isolated yield based on the amount of the alkene used. c) Isolated yield based on the amount of the [Mn(acac)₃] used. d) Alkene : ethyl 3-oxobutanoate : [Mn(OAc)₃]. e) Alkene : acetoacetanilide : [Mn(OAc)₃].

1,1-Diphenylethene (1a, 1 mmol) was dissolved in acetic acid (25 cm³) in a 100 cm³ round-bottomed flask equipped with a calcium chloride drying tube and [Mn(acac)₃] (1 mmol) was added to the mixture. The mixture was stirred at 23 °C under air until the brown color of Mn(III) species turned transparent pale yellow (for 11 h). The solvent was removed in vacuo, and the residue was triturated with 2M HCl (30 cm³), followed by extraction with chloroform. The products were separated on TLC (Wakogel B-10) with chloroform as the developing agent to yield 3a which was recrystallized from ethanol, mp 161-162 °C. Although all of the spectral data and elemental analysis of 3a supported a structure of 4-acetyl-3-hydroxy-3-methyl-6,6-diphenyl-1,2-dioxacyclohexane, we finally determined the structure of 3a by the use of X-ray crystallography as shown in Fig. 1.⁴⁾ The similar reactions of 1,1-disubstituted ethenes (1b-e), styrene (1f), 1-octene (1g), 1-nonene (1h), cyclohexene (1i), and cyclooctene (1j) were carried out at room temperature to give corresponding 1,2-dioxacyclohexanes (3b-j) (Table 1). On the other hand, reaction of alkenes (1a-e) with ethyl 3-oxobutanoate in the presence of [Mn(OAc)₃] gave similar 1,2-dioxacyclohexanes (4a-e) along with dihydrofurans (5b-e).^{1c, 5)} Similarly, 1a reacted with acetoacetanilide in the presence of [Mn(OAc)₃] to yield cyclic peroxide (6a) in good yield (Table 1).⁶⁾

It is worth noting that the cyclic peroxide (3a) was obtained as the 3,4-*threo*-1,2-dioxacyclohexane based on the X-ray analysis. It means that cyclization of peroxy radical is reversible (step 1 in Scheme 2) and leads to a

thermodynamically stable configuration, that is to say, 3,4-*threo* form.⁷⁾

When the reaction of 1b with $[\text{Mn}(\text{acac})_3]$

was carried out at 23 °C for 12 h under nitrogen, 1b was recovered and 3b was not detected.⁸⁾

On the other hand, the yield of 3a decreased and 3-acetyl-4-hydroxy-3-hexene-2,5-dione (7) was formed as a major product, when the reaction was carried out under oxygen.⁹⁾ The hexenedione (7) is normally produced as a by-product in the $[\text{Mn}(\text{acac})_3]$ -AcOH reaction system.¹⁰⁾ Therefore, we postulate, based on prior literature and our results, a likely sequence of steps to account for the formation of 1,2-dioxacyclohexanes that we obtained as shown in Scheme 2.

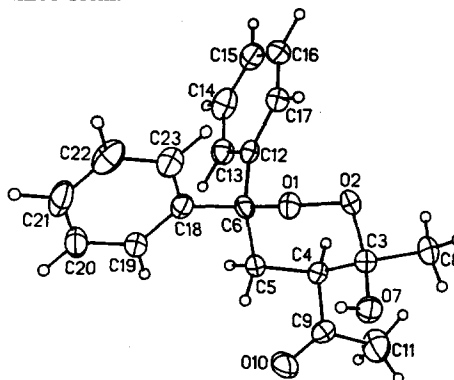
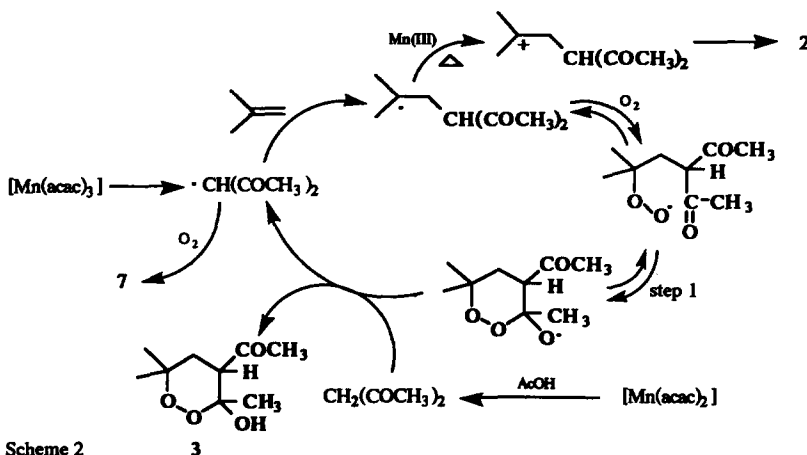


Fig. 1. ORTEP view of 3a

It was expected that the cyclic peroxides (3,4,6) might have some biological activities since 3, 4, and 6 are consisted of a basic structure of natural occurring cyclic peroxides, some of which have biological activities.¹¹⁾ However, any activities were not observed for the products (3a,b,d,e, and 4a).¹²⁾

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Scheme 2

References and Notes

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 - 4) Crystal data for **3a**: $C_{19}H_{20}O_4$, orthorhombic space group $P2_12_12_1$ with $a = 7.856$ (3), $b = 12.823$ (6), $c = 15.820$ (8) Å, $V = 1594$ Å³, and $\rho = 1.30$ g cm⁻³ for $Z = 4$. The structure was solved by use of the SHELXTL direct methods program TREF, which revealed the positions of all of the nonhydrogen atoms. Atomic parameters, bond lengths and angles for **3a** have been deposited at the Cambridge Crystallographic Data Center.
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 - 6) Nishino, H. *Bull. Chem. Soc. Jpn.* 1985, *58*, 217.
 - 7) See the reference 3) (a).
 - 8) Nitrogen gas which was passed through an aqueous KOH-pyrogallol solution and then a silica gel column was used.
 - 9) The reaction gave **1a** (57 % recovered), **3a** (21 %), and **7** (26 % based on the amount of $[Mn(acac)_3]$ used).
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 - 12) Biological activity tests were performed by Sumitomo Chemical Co., Inc., Takarazuka, Hyogo, Japan.

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