FULL PAPER

Mn(III)-Based Oxidative Cyclization of Alkenes Using Tricarbonyl System

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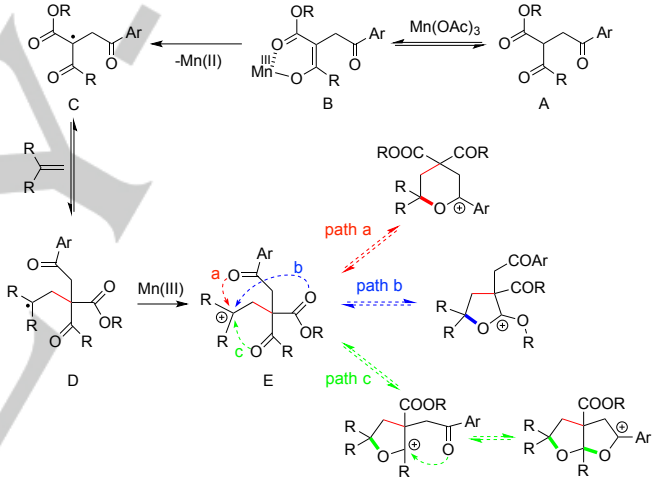
Abstract: The Mn(III)-based oxidation of 1,1-disubstituted ethenes with 2-(2-aryl-2-oxoethyl)malonates, 2-acetyl-4-aryl-4-oxobutanoates, and 3-acetyl-1-arylpentane-1,4-diones was evaluated. The reaction using the malonates mainly gave the 2,3-dihydro-4*H*-pyran-4,4-dicarboxylates along with γ-lactones. A similar reaction using the acetyloxobutanoates and acetylpentanediones produced the 2,3,3a,6a-tetrahydrofuro[2,3-*b*]furans and the corresponding dihydropyrans. The cyclization was strongly affected by the nucleophilicity of the carbonyl oxygen in the carbocation intermediate, and the kinetic and thermodynamic controls of the following reaction. The structure determination and the mechanisms are discussed.

Introduction

Cyclization using the carbonyl double bond is one of the most important techniques to prepare oxygen heterocycles.[1] The oxidation of 1,3-dicarbonyl compounds with transition metal oxidants, such as Mn, Ce, Co, Tl, Hg, Cu, Ru, Pb, Ni, Ag, VO, etc., is able to generate carbon radicals at the α position to the carbonyl group,[2] and if an electron-rich alkene is present in the reaction system, the carbon radicals immediately attack the C–C double bond, followed by *O*-cyclization to produce the oxygen heterocycles, such as furans and lactones.[3] Manganese(III) acetate, $Mn(OAc)_3$, is the best oxidant to produce 1,3-dicarbonyl radicals via the Mn(III)-enolate complex, which are allowed to react with alkenes and aromatics, producing many types of heterocyclic compounds.[4,5] 1,3-Dicarbonyl compounds bearing another carbonyl functionality between the 1,3-dicarbonyl group, such as A in Scheme 1, are similarly oxidized with $Mn(OAc)_3$ and the corresponding radicals C are produced via the Mn(III)-enolate complex B. Radical C, for example, adds to 1,1-disubstututed alkenes to give tertiary carbon radicals D. Radicals D are easily oxidized under the stated conditions to produce cations E, which next compete for cyclization at the three carbonyl oxygens (paths a, b, and c in Scheme 1).[6,7] At this time, the cyclization is controlled by the kinetics and thermodynamics, and also the nucleophilicity of the carbonyl oxygen. We previously reported the reactions using tricarbonyl substrates, giving dihydro-2*H*-pyrans, dihydrofuro[2,3-*b*]furans,[7] azadioxa[4.3.3]-, azadioxa[5.3.3]-, azadioxa[6.3.3]-,[8] and azatrioxa[4.4.3]-propellanes.[9] In this paper, we concentrated on the reaction using the 3-acetyl-1-arylalkane-1,4-dione derivatives and examined the difference in the reactivity for the nucleophilicity of the carbonyl oxygen. As a result, the keto carbonyl oxygen was the best for the cyclization and 2,3,3a,6a-tetrahydrofuro[2,3-*b*]furans were mainly produced via a tandem cyclization, while the reaction using 2-(2-aryl-2-oxoethyl)malonates gave the dihydro-2*H*-pyrans. We describe the reactions in detail.



Scheme 1. Cyclization mode in the Mn(III)-based reaction of 2-alkanoyl-4-aryl-4-oxobutanoates.

Results and Discussion

Reaction using 2-(2-aryl-2-oxoethyl)malonates 2a-g.[7] 1,1-Disubstituted ethenes **1a-g** were prepared by the Grignard reaction of the corresponding acetopheneones with arylmagnesium bromide or methylmagnesium iodide followed by dehydration. The malonates **2a-g** containing one keto-carbonyl and two ester carbonyl groups were prepared by the reaction of malonates with α-bromoacetophenone derivatives in the presence of a base in alcohol.[10] With the reactants in hand, the oxidation of a mixture of **1a** (R^1 = R^2 = Ph) and **2a** (R^3 = R^4 = OMe, Ar = Ph) with $Mn(OAc)_3$ was carried out at an almost stoichiometric amount (Table 1, Entry 1). To our delight, two cyclization compounds were produced in low yields, one was the dihydropyran **3aa** and the other was the lactone **4aa** (eq. 1 in Scheme 2). Products **3aa** and **4aa** were easily characterized by NMR spectroscopy (See Experimental Section and Supporting Information). For example, two singlets assigned to the H-5 sp^2

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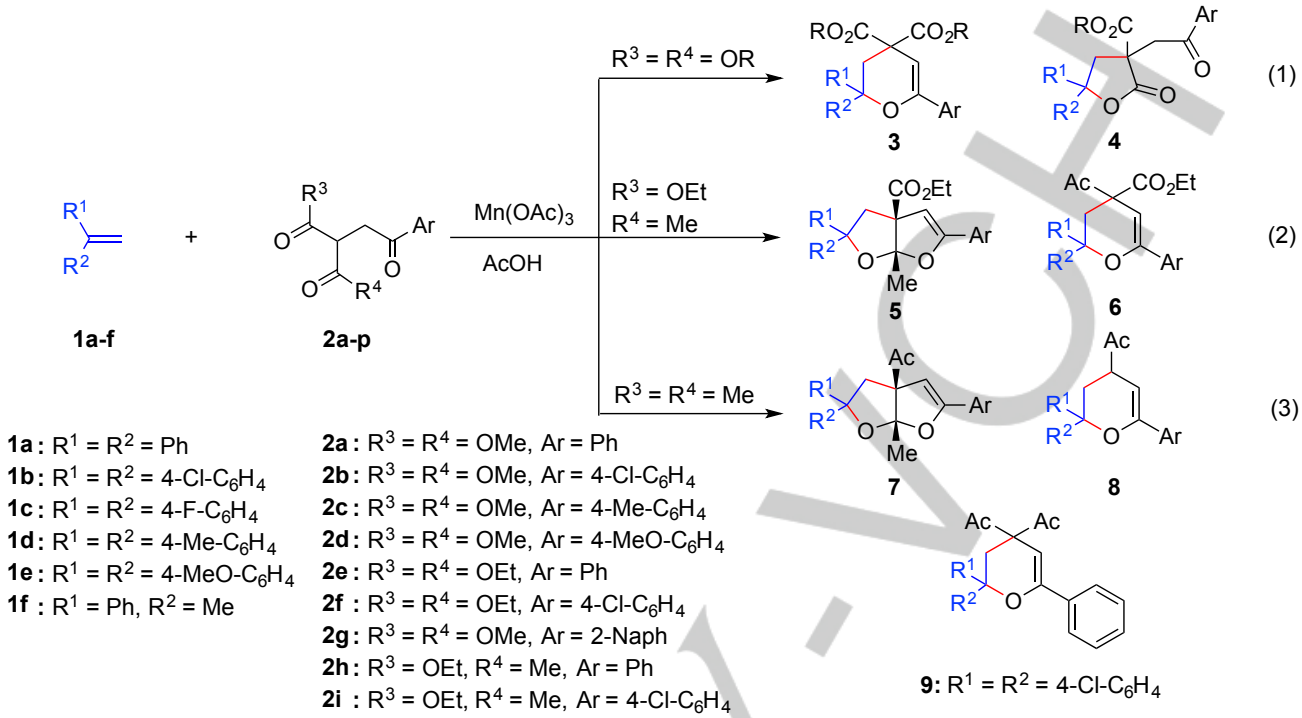


1a : $R^1 = R^2$ = Ph
1b : $R^1 = R^2$ = 4-Cl-C_6H_4
1c : $R^1 = R^2$ = 4-F-C_6H_4
1d : $R^1 = R^2$ = 4-Me-C_6H_4
1e : $R^1 = R^2$ = 4-MeO-C_6H_4
1f : R^1 = Ph, R^2 = Me

2a : $R^3 = R^4$ = OMe, Ar = Ph
2b : $R^3 = R^4$ = OMe, Ar = 4-Cl-C_6H_4
2c : $R^3 = R^4$ = OMe, Ar = 4-Me-C_6H_4
2d : $R^3 = R^4$ = OMe, Ar = 4-MeO-C_6H_4
2e : $R^3 = R^4$ = OEt, Ar = Ph
2f : $R^3 = R^4$ = OEt, Ar = 4-Cl-C_6H_4
2g : $R^3 = R^4$ = OMe, Ar = 2-Naph
2h : R^3 = OEt, R^4 = Me, Ar = Ph
2i : R^3 = OEt, R^4 = Me, Ar = 4-Cl-C_6H_4
2j : R^3 = OEt, R^4 = Me, Ar = 4-F-C_6H_4
2k : R^3 = OEt, R^4 = Me, Ar = 4-Me-C_6H_4
2l : R^3 = OEt, R^4 = Me, Ar = 2-Naph
2m : $R^3 = R^4$ = Me, Ar = Ph
2n : $R^3 = R^4$ = Me, Ar = 4-Cl-C_6H_4
2o : $R^3 = R^4$ = Me, Ar = 4-F-C_6H_4
2p : $R^3 = R^4$ = Me, Ar = 4-Me-C_6H_4
2q : $R^3 = R^4$ = Me, Ar = 4-MeO-C_6H_4
2r : $R^3 = R^4$ = Me, Ar = 2-Naph

Scheme 2. Mn(III)-based reaction of alkenes **1a-f** with 2-carbonylalkane-1,4-diones **2a-r**.

Table 1. Reaction of alkenes **1a-f** with malonates **2a-g** in the presence of manganese(III) acetate[a]

Entry	Alkene **1**	Malonate **2**	**1**:**2**:$Mn(OAc)_3$[b]	Time/min	Product (yield/%)[c]	
1	**1a**: $R^1 = R^2$ = Ph	**2a**: $R^3 = R^4$ = OMe, Ar = Ph	1:1.2:2.2	7	**3aa** (37)	**4aa** (5)
2	**1a**	**2a**	1:2:3	15	**3aa** (79)	**4aa** (10)
3	**1b**: $R^1 = R^2$ = 4-Cl-C_6H_4	**2a**	1:2:3	14	**3ba** (73)	**4ba** (15)
4	**1c**: $R^1 = R^2$ = 4-F-C_6H_4	**2a**	1:2:3	14	**3ca** (74)	
5	**1d**: $R^1 = R^2$ = 4-Me-C_6H_4	**2a**	1:2:3	11	**3da** (64)	**4da** (9)
6	**1e**: $R^1 = R^2$ = 4-MeO-C_6H_4	**2a**	1:2:3	11	Complex mixture	
7	**1f**: R^1 = Ph, R^2 = Me	**2a**	1:2:3	11	**3fa** (37)	**4fa** (38)
8	**1a**	**2b**: $R^3 = R^4$ = OMe, Ar = 4-Cl-C_6H_4	1:2:3	8	**3ab** (71)	
9	**1a**	**2c**: $R^3 = R^4$ = OMe, Ar = 4-Me-C_6H_4	1:2:3	7	**3ac** (74)	**4ac** (13)
10	**1a**	**2d**: $R^3 = R^4$ = OMe, Ar = 4-MeO-C_6H_4	1:2:3	7	**3ad** (23)	
11	**1a**	**2e**: $R^3 = R^4$ = OEt, Ar = Ph	1:2:3	6	**3ae** (61)	
12	**1a**	**2f**: $R^3 = R^4$ = OEt, Ar = 4-Cl-C_6H_4	1:2:3	6	**3af** (57)	
13	**1a**	**2g**: $R^3 = R^4$ = OMe, Ar = 2-Naph	1:2:3	5	**3ag** (51)	**4ag** (9)

[a] The reaction of alkene **1** (1 mmol) was carried out in AcOH (15 mL) at reflux temperature. [b] Molar ratio. [c] Isolated yield based on the amount of the alkene **1** used.

and H-3 methylene protons appeared at δ 5.64 (1H) and 3.44 (2H), respectively, in the ^{1}H NMR spectrum of **3aa**, and the ^{13}C NMR spectrum showed two characteristic peaks due to the sp^2 enolate carbons at C-5 (δ 95.1) and C-6 (δ 151.5) and a quaternary carbon (δ 81.4) assigned to the C-2 sp^3 carbon attached to the oxygen. While the minor product **4aa** was certainly the γ-lactone based on the IR spectrum ($\nu_{C=O}$ 1778 cm^{-1}) and the ^{1}H NMR spectrum showed two sets of AB gemimal couplings, at δ 3.87 (H_a-CH) and 3.26 (HC-H_b) (J_{ab} = 18.0 Hz), and at δ 3.85 (H_c-CH) and 3.31 (HC-H_d) (J_{cd} = 15.0 Hz). These NMR data supported the fact that the oxidative cyclization undoubtedly occurred and the major dihydropyran and minor γ-lactone skeleton must have been constructed. The reaction was then optimized and the best yield of **3aa** was achieved in 79% along with **4aa** (10%) (Entry 2). The use of 4-chlorophenyl- **1b** and 4-fluorophenyl-substituted ethenes **1c** gave a similar result (Entries 3 and 4), but the bis(4-methylphenyl)ethene (**1d**) and 2-phenylpropene (**1f**) led to an inferior yield (Entries 5 and 7). The reaction of the alkene **1e** (R^1 = R^2 = 4-MeOC_6H_4) substituted by a strong electron-donating group became complicated and no products were isolated (Entry 6). On the other hand, although the electronic effect of the 2-arylethyl group in **2b** (Ar = 4-Cl-C_6H_4) and **2c** (Ar = 4-Me-C_6H_4) was not observed during the cyclization (Entries 8 and 9), the use of **2d** bearing the 4-MeOC_6H_4 group that produced the low yield of **3ad** and steric effect of **2g** having the (2-naphthyl)ethyl group was remarkable (Entries 10 and 13). In addition, the reaction using the diethyl malonates **2e** and **2f** gave a slightly inferior result (Entries 11 and 12).

Reaction using 2-acetyl-4-aryl-4-oxobutanoates 2h-l. In order to explore the reaction using a compound including two keto-carbonyl and one ester carbonyl groups instead of the oxoethylmalonates **2a-e**, 2-acetyl-4-aryl-4-oxobutanoates **2h-l** were prepared by the reaction of the 3-oxobutanoates with the corresponding α-bromoacetophenones in the presence of NaOEt in dry CH_2Cl_2. With the oxobutanoates **2h** (84%), **2i** (78%), **2j** (71%), **2k** (82%), and **2l** (54%), respectively, in hand, the reaction of alkene **1a** with **2h** (R^3 = OEt, R^4 = Me, Ar = Ph) was first evaluated (eq. 2 in Scheme 2 and Table 2, Entries 1-4). As a result, bicyclic compound **5ah** and dihydropyran **6ah** were produced in moderate yields. The best yield was achieved under reflux temperature using a stoichiometric amount of Mn(OAc)$_3$ (Entry 3). The IR spectrum of **5ah** showed strong absorption bands at 1722 cm^{-1} and 1250 cm^{-1} assigned to the ester group, and a singlet of an sp^2 proton assigned to H-4 (δ 4.90) and an AB quartet due to H-3 methylene proton (δ 3.32 and 3.23, J = 13.1 Hz) appeared in the ^{1}H NMR spectrum (See Experimental Section and Supporting Information). In addition, a diastereotopic methylene signal (δ 4.21) of the ethoxy group was also observed. In the ^{13}C NMR spectrum of **5ah**, three characteristic sp^3 quaternary carbons appeared, three of which were assigned to the C-6a ring junction (δ 118.5) attached to two oxygens, C-2 (δ 89.6) connected to an oxygen and two phenyl groups, and a C-3a ring junction (δ 67.3) joined to an ester carbonyl and an alkenic sp^2 carbon. Therefore, the product **5ah** consisted of a bicyclic structure and was determined to be ethyl 6a-methyl-2,2,5-triphenyl-2,3-dihydrofuro[2,3-*b*]furan-3a(6a*H*)-carboxylate. The stereochemistry should be a cis-fused bicyclic compound (vide infra for an X-ray single crystal structure of **7bm**). Although the ^{1}H NMR spectrum of **6ah** was similar to that of the dihydropyran **3aa**, the methylene protons of H-3 and ethoxy group appeared as an AB quartet and a diastereotopic multiplet, respectively, due to the existence of an asymmetric carbon at C-4 in **6ah**.

With the exact structure of the product in hand, we next examined the reaction using various combinations of alkenes **1b-e** and 2-acetyl-4-aryl-4-oxobutanoates **2h-l**. However, the product distribution was similar to that using **1a** and **2h** (Table 2, Entries 5-16). In any event, a tandem cyclization predominantly occurred using two keto-carbonyl groups of the 2-acetyl-4-aryl-4-oxobutanoates **2h-l**, but no γ-lactonization at the ester carbonyl group occurred.

Table 2. Reaction of alkenes **1a-e** with 4-oxobutboates **2h-l** in the presence of manganese(III) acetate[a]

Entry	Alkene **1**	Oxobutanoate **2**	**1**:**2**:Mn(OAc)$_3$[b]	Time/min	Product (yield/%)[c]	
1	**1a**: R^1 = R^2 = Ph	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:2	7[d]	**5ah** (42)	**6ah** (23)
2	**1a**: R^1 = R^2 = Ph	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:2	1[e]	**5ah** (47)	**6ah** (28)
3	**1a**: R^1 = R^2 = Ph	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:2	1	**5ah** (49)	**6ah** (29)
4	**1a**: R^1 = R^2 = Ph	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:4	7	**5ah** (30)	**6ah** (20)
5	**1b**: R^1 = R^2 = 4-Cl-C_6H_4	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:2.1	1	**5bh** (55)	**6bh** (33)
6	**1c**: R^1 = R^2 = 4-F-C_6H_4	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:2.2	1	**5ch** (54)	**6ch** (24)
7	**1d**: R^1 = R^2 = 4-Me-C_6H_4	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2:2.1	1	**5dh** (68)	**6dh** (27)
8	**1e**: R^1 = R^2 = 4-MeO-C_6H_4	**2h**: R^3 = OEt, R^4 = Me, Ar = Ph	1:1.2.2	1	**5eh** (58)	**6eh** (15)
9	**1a**: R^1 = R^2 = Ph	**2i**: R^3 = OEt, R^4 = Me, Ar = 4-Cl-C_6H_4	1:1.2:2.1	1	**5ai** (54)	**6ai** (25)
10	**1a**: R^1 = R^2 = Ph	**2j**: R^3 = OEt, R^4 = Me, Ar = 4-F-C_6H_4	1:1.2.2	1	**5aj** (51)	**6aj** (28)
11	**1a**: R^1 = R^2 = Ph	**2k**: R^3 = OEt, R^4 = Me, Ar = 4-Me-C_6H_4	1:1.2.2	1	**5ak** (41)	**6ak** (34)
12	**1a**: R^1 = R^2 = Ph	**2l**: R^3 = OEt, R^4 = Me, Ar = 2-Naph	1:1.2:2.1	1	**5al** (31)	**6al** (25)
13	**1b**: R^1 = R^2 = 4-Cl-C_6H_4	**2i**: R^3 = OEt, R^4 = Me, Ar = 4-Cl-C_6H_4	1:1.2:2.1	1	**5bi** (51)	**6bi** (31)
14	**1b**: R^1 = R^2 = 4-Cl-C_6H_4	**2k**: R^3 = OEt, R^4 = Me, Ar = 4-Me-C_6H_4	1:1.2:2.1	1	**5bk** (43)	**6bk** (32)
15	**1d**: R^1 = R^2 = 4-Me-C_6H_4	**2i**: R^3 = OEt, R^4 = Me, Ar = 4-Cl-C_6H_4	1:1.2:2.1	1	**5di** (60)	**6di** (26)
16	**1d**: R^1 = R^2 = 4-Me-C_6H_4	**2k**: R^3 = OEt, R^4 = Me, Ar = 4-Me-C_6H_4	1:1.2:2.1	1	**5dk** (57)	**6dk** (22)

[a] The reaction of alkene **1** (0.5 mmol) was carried out in AcOH (20 mL) at reflux temperature. [b] Molar ratio. [c] Isolated yield based on the amount of the alkene **1** used. [d] The reaction was carried out at 80 °C. [e] The reaction was carried out at 100 °C.

Table 3. Reaction of alkenes **1a-f** with pentane-1,4-diones **2m-r** in the presence of manganese(III) acetate[a]

Entry	Alkene **1**	Pentanedione **2**	**1**:**2**:Mn(OAc)$_3$[b]	Time/min	Product (yield/%)[c]		
1	**1a**: $R^1 = R^2$ = Ph	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	5[d]	**7am** (62)	**8am** (19)	
2	**1a**: $R^1 = R^2$ = Ph	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	3[e]	**7am** (64)	**8am** (20)	
3	**1a**: $R^1 = R^2$ = Ph	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	1	**7am** (67)	**8am** (22)	
4	**1b**: $R^1 = R^2$ = 4-Cl-C_6H_4	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	1	**7bm** (82)	**8bm** (9)	**9** (7)
5[f]	**1b**: $R^1 = R^2$ = 4-Cl-C_6H_4	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	7	**7bm** (77)		**9** (15)
6	**1c**: $R^1 = R^2$ = 4-F-C_6H_4	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	1	**7cm** (52)	**8cm** (14)	
7	**1d**: $R^1 = R^2$ = 4-Me-C_6H_4	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1:2:3	1	**7dm** (76)		
8	**1e** $R^1 = R^2$ = 4-MeO-C_6H_4	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1: 2: 3	1	**7em** (78)		
9	**1f**: R^1 = Ph, R^2 = Me	**2m**: $R^3 = R^4$ = Me, Ar = Ph	1: 2: 3	1	**7fm** (53)		
10	**1a**: $R^1 = R^2$ = Ph	**2n**: $R^3 = R^4$ = Me, Ar = 4-Cl-C_6H_4	1: 2: 3	1	**7an** (66)	**8an** (19)	
11	**1a**: $R^1 = R^2$ = Ph	**2o**: $R^3 = R^4$ = Me, Ar = 4-F-C_6H_4	1: 2: 3	1	**7ao** (61)	**8ao** (14)	
12	**1a**: $R^1 = R^2$ = Ph	**2p**: $R^3 = R^4$ = Me, Ar = 4-Me-C_6H_4	1: 2: 3	1	**7ap** (61)	**8ap** (24)	
13	**1a**: $R^1 = R^2$ = Ph	**2q**: $R^3 = R^4$ = Me, Ar = 4-MeO-C_6H_4	1: 2: 3	1	**7aq** (39)	**8aq** (36)	
14	**1a**: $R^1 = R^2$ = Ph	**2r**: $R^3 = R^4$ = Me, Ar = 2-Naph	1: 2: 3	1	**7ar** (54)	**8ar** (18)	

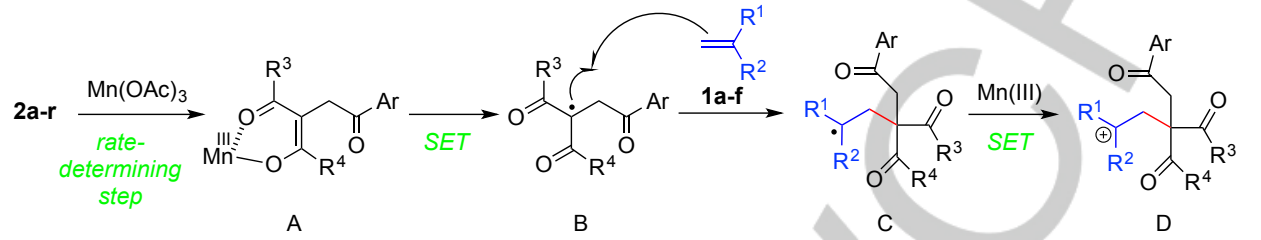
[a] The reaction of alkene **1** (1 mmol) was carried out in AcOH (15 mL) at reflux temperature. [b] Molar ratio. [c] Isolated yield based on the amount of the alkene **1** used. [d] The reaction was carried out at 70 °C. [e] The reaction was performed at 100 °C. [f] The reaction was conducted at room temperature in an AcOH (6 mL) and HCO_2H (2 mL) mixed solvent.

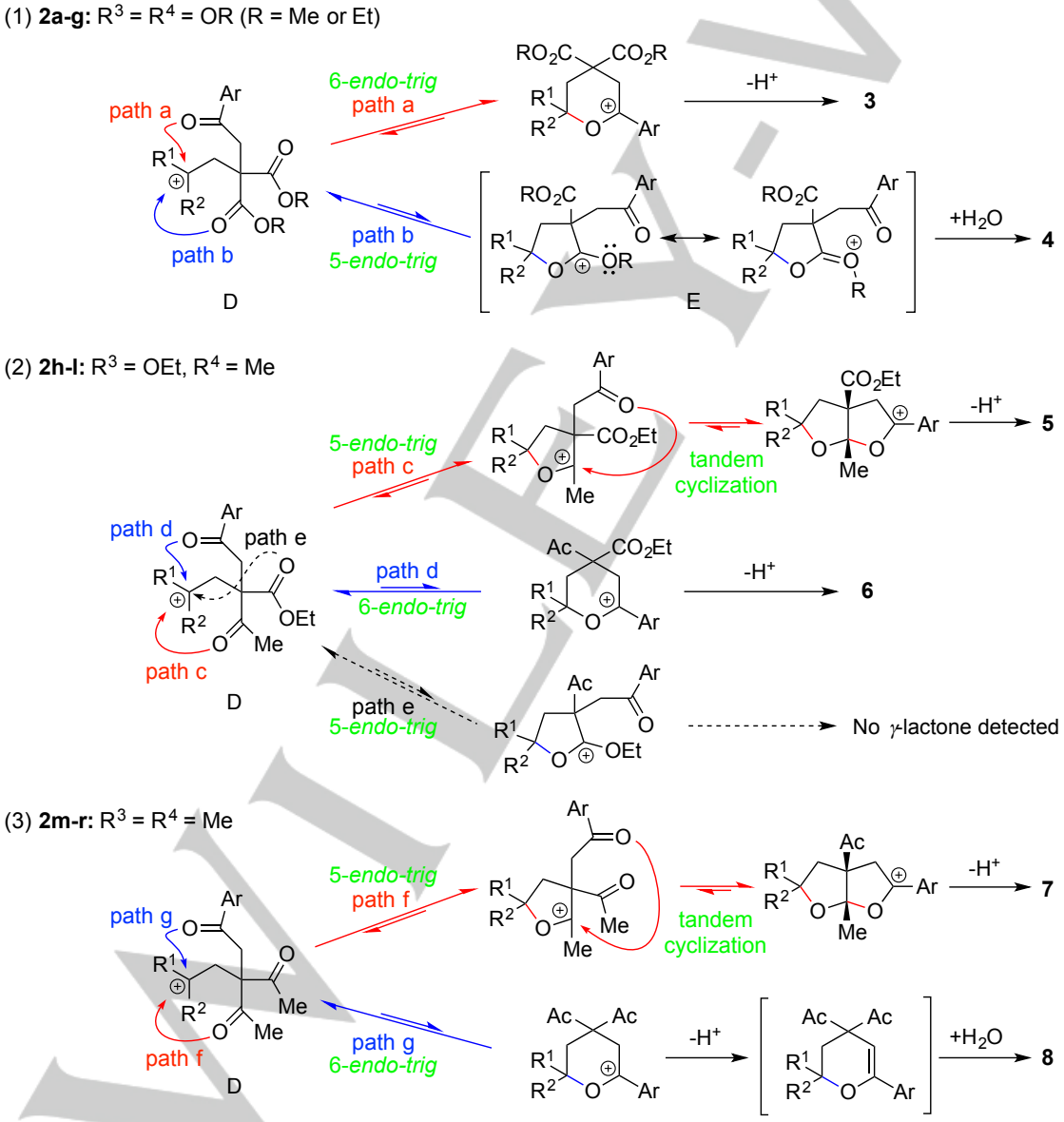
Reaction using 3-acetyl-1-arylpentane-1,4-diones 2m-r. In order to investigate the reaction with the triketones instead of the oxoethylmalonates **2a-f** and 2-acetyl-4-aryl-4-oxobutanoates **2h-l**, 3-acetyl-1-arylpentane-1,4-diones **2m-r** were prepared by the reaction of 2,4-pentanedione with α-bromoacetophenones similar to that already mentioned. With the triketones **2m-r** in hand, the reaction of **1a** with triketone **2m** ($R^3 = R^4$ = Me, Ar = Ph) was evaluated in AcOH at 70 °C (eq.3 in Scheme 2). After the work-up, two cyclization products **7am** and **8am** similar to those in the reaction of **1a** with **2h** were obtained (Table 3, Entry 1). When the reaction was carried out at reflux temperature, the reaction times shortened and the yields somewhat increased (Entry 3). The ^{1}H NMR spectrum of **7am** was similar to that of the bicyclic compound **5ah**, but the H-3 methylene protons appeared at δ 3.38 and 3.00 (J = 13.1 Hz) as an AX pattern ($\Delta\delta$ 0.38). The ^{13}C chemical shifts of **7am** (δ 118.0 and 72.4) derived from the ring junction were quite similar to those of **5ah**. Therefore, the cyclization product of **7am** was undoubtedly 3a-acetyl-6a-methyl-2,2,5-triphenyl-2,3,3a,6a-tetrahydrofuro[2,3-*b*]furan. Surprisingly, in the ^{1}H NMR spectrum of the minor product **8am**, only one acetyl group existed. In addition, a complex signal assigned to the methine proton appeared at δ 3.13 (ddd, J = 11.5, 5.8, and 2.5 Hz), and the sp^2 proton due to H-5 showed at δ 5.47 with vicinal (J = 2.5 Hz) and long-range couplings (J = 1.5 Hz). The methylene protons due to H-3 also appeared at δ 3.00 (ddd, J = 13.6, 5.8, 1.5 Hz) and δ 2.50 (dd, J = 13.6, 11.5 Hz) with germinal, vicinal, and long-range couplings. Accordingly, the minor product **8am** should be 4-acetyl-2,2,6-triphenyl-3,4-dihydro-2*H*-pyran. Probably, one acetyl group of the desired dihydropyran was lost during the reaction. With a similar result of the reaction using 2-acetyl-4-phenyl-4-oxobutanoate **2h** in hand, we next examined the reaction of 1,1-bis(4-chlorophenyl)ethene (**1b**) with **2m** (Entry 4), which gave the bicyclic product **7bm** (82% yield) along with the monoacetyl- **8bm** (9% yield) and the desired diacetyl-dihydropyran **9** (7% yield). Since we recently reported the efficient Mn(III)-based oxidative cyclization using an AcOH and HCO_2H mixed solvent,[5j] the reaction was subjected to similar conditions at room temperature. As a result, the bicyclic product **7bm** (77%) and the desired dihydropyran **9** (15% yield) were produced (Entry 5). Pleasingly, we obtained the X-ray single crystal structure of the cis-fused bicyclic product **7bm** (See Experimental Section and Supporting Information).[7]

Reaction pathway. In the above reactions, the use of malonates **2a-g** needed a longer reaction time than that of the 4-oxobutanoates **2h-l** and pentane-1,4-diones **2m-r**. This is attributed to the formation of the Mn(III)-enolate complex A which would be the rate-determining step (upper in Scheme 3).[6a] That is, the formation of A should be the fastest in the reaction with the triketones **2m-r** and slowest in that with the malonate esters **2a-g**. Once complex A was formed, the tertiary radical B was produced via a single-electron transfer (SET) oxidation and attacked the electron-rich 1,1-disubstituted ethenes **1a-f** to give the corresponding tertiary radical C which should be easily oxidized by Mn(III) species in situ to finally produce the carbocation intermediate D.

The rule for ring closure during the cyclization is generally accepted.[11] Normally, the 6-*endo-trig* cyclization is thermodynamically favored over that of the 5-*endo-trig* though the steric and electronic effects and also the existence of heteroatoms in the backbone must be considered. For the reaction with the malonates **2a-g**, the 6-*endo-trig* cyclization was favored and the dihydropyrans **3** were preferentially produced (Table 1). In some cases, the minor γ-lacones **4** were not obtained (Table 1, Entries 4, 8, 10-12). Although the 5-*endo-trig* mode might be kinetically faster that the 6-*endo* and the oxonium ion E would be somewhat stabilized by resonance (Scheme 3 (1) path b), the nucleophilicity of the keto-carbonyl oxygen is stronger than that of the ester carbonyl, so that the equilibrium shifted to path a (Scheme 3 (1) path a). The reactivity of the keto and ester carbonyls during the cyclization of D was 8:1 for the reaction of **1a** with **2a** (Table 1, Entry 2). On the other hand, the *5-endo-trig* mode at the keto-carbonyl was favorable for the reaction using 4-oxobutanoates **2h-l** because of the kinetic control[11] and the successive tandem cyclization which produced the more rigid bicyclic framework **5** (Table 2 and Scheme 3 (2) path c). In addition, it is clear that the cyclization depended on the nucleophilicity of the keto and ester carbonyl oxygens from the result that no γ-lactones were

produced during the reaction using the 4-oxobutanoates **2h-l** (Scheme 3 (2) path e). The reactivity of the 5-*endo-trig* tandem cyclization and 6-*endo-trig* mode at the keto carbonyls was 5:3 for the reaction of **1a** with **2h** (Table 2, Entry 3). Finally, the kinetically controlled 5-*endo-trig* tandem cyclization preferentially occurred for the reaction using the pentane-1,4-diones **2m-r** (Table 3 and Scheme 3 (3) path f). In some cases, only the bicyclic compounds **7** were produced (Table 3, Entries 7-9). The reactivity of the 5-*endo-trig* tandem cyclization and 6-*endo-trig* mode at the keto carbonyls was 3:1 for the reaction of **1a** with **2m** (Table 3, Entry 3).





Scheme 3. Mechanism for the formation of the products **3-8**.

Conclusions

It was concluded that the 6-*endo-trig* cyclization was favored for the carbocation intermediate D in Scheme 3, mainly giving dihydropyrans **3** when the malonates **2a-g** were used for the reaction. However, the kinetically controlled tandem cyclization preferred in D in the reaction using the pentane-1,4-diones **2m-r** produced the bicyclic compounds **7**. On the other hand, the use of the 4-oxobutanoates **2h-l** led to the result that the kinetically controlled 5-*endo* tandem cyclization somewhat preferred the thermodynamically controlled 6-*endo* mode in D, affording the bicyclic compounds **5** and the dihydropyrans **6**. It was found that the cyclization was strongly affected by the nucleophilicity of the carbonyl oxygen of the carbocation D, and the kinetic and thermodynamic controls of the following reaction. As a result, the relative feasibility of the 5-*endo-trig* tandem cyclization, 6-*endo-trig* cyclization, and 5-*endo-trig* lactonization in the carbocation intermediate D was estimated as 24-13:8:1 for the reaction of **1a** with the triketone **2m**, the diketo-monoester **2h**, and the keto-diester **2a**, when both the electronic effects of the methyl in the acetyl group and the phenyl in the benzoyl group were ignored.

Supporting Information Summary

Experimental Section (Measurements, Materials, Full reaction procedures, and spectroscopic data of all the products **3**-**9**), crystal structure of **7bm** (Fig. 1), ^{1}H and ^{13}C NMR spectral charts of all the products **3**-**9**, and X-ray Structure Report of **7bm** are available in Supporting Informatiom.

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Keywords: 2-Acetyl-4-aryl-4-oxobutanoates • 3-Acetyl-1-arylpentane-1,4-diones • 2-(2-Aryl-2-oxoethyl)malonates • Dihydro-2*H*-pyrans • 5-*endo-trig* • 6-*endo-trig* • Manganese(III) acetate • Oxidative cyclization • Tandem cyclization • 2,3,3a,6a-Tetrahydrofuro[2,3-*b*]furans

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[12] X-ray coordinates of **7bm** were deposited with the Cambridge Crystallographic Data Centre (https://www.ccdc.cam.ac.uk), deposition number: CCDC 230145.

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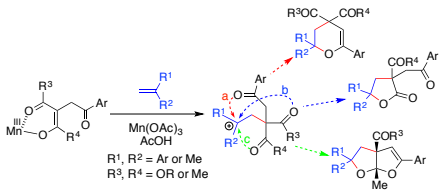

The Mn(III)-based oxidative cyclization of tricarbonyl compounds with alkenes occurred depending on the nucleophilicity of the carbonyl oxygen and the kinetic and thermodynamic controls of the following reaction, and 2,3-dihydro-4*H*-pyran-4,4-dicarboxylates, γ-lactones, and 2,3,3a,6a-tetrahydrofuro[2,3-*b*]furans were produced.

Oxidative Cyclization

*Thanh-Truc Huynh, Hiroyasu Yamakawa, Van-Ha Nguyen and Hiroshi Nishino**

Page No. – Page No.

Mn(III)-Based Oxidative Cyclization of Alkenes Using Tricarbonyl System