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Manganese(III)-Based Oxidative Dual Cyclization of 4,4-Diaryl-3-butenyl-3-oxobutanoates

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Abstract—The oxidative intramolecular tandem cyclization of 4,4-diaryl-3-butenyl 3-oxobutanoates **3a-e** and 4,4-diaryl-3-butenyl 2-(2-aryl-2-oxoethyl)-3-oxobutanoates **5aa-ee** using manganese(III) acetate was investigated. The reaction of oxobutanoates **3a-e** gave the desired dual cyclization products, 7,7-diaryl-9-methyl-3,8-dioxabicyclo[4.3.0]non-9-en-2-ones **4a-e**, in excellent yields. A similar cyclization of oxobutanoates **5aa-ee** did not give the tricyclic compounds **7** but 1-acetyl-7,7,9-triaryl-3,8-dioxabicyclo[4.4.0]dec-9-en-2-one **6aa-ee** in good yields.

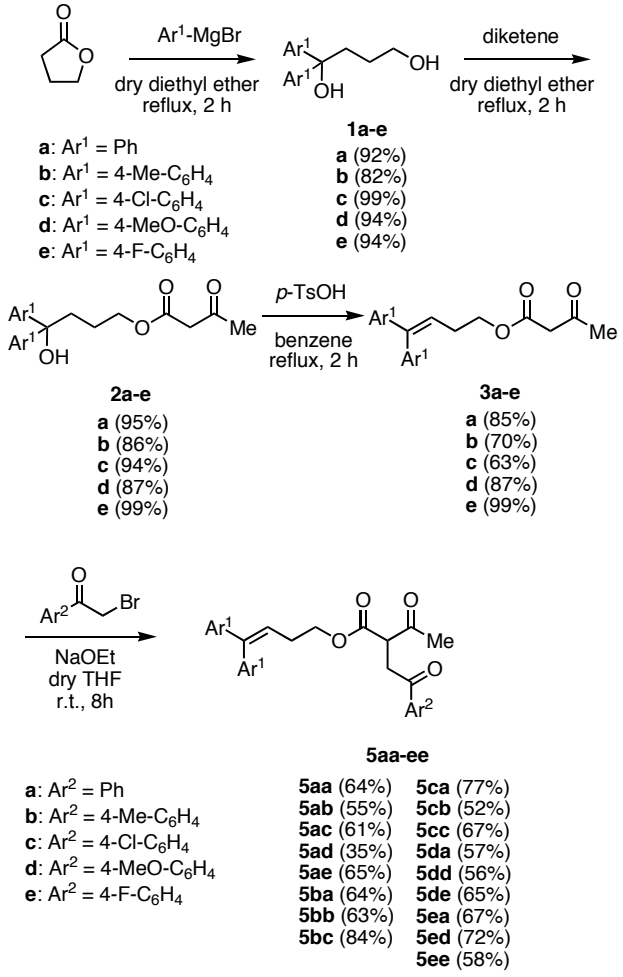
1. Introduction

One of the synthetic targets in the organic synthesis is heterocyclic compounds which have chemically interesting structure and useful actions in human life.[1] There are many naturally occurring oxygen-containing heterocyclic compounds, some of which have very strong biological activities.[2] For example, the trioxabicyclo[4.3.0]non-3-ene framework is also found in artemisinin, yingzhausu A and C, and etc.[3] Artemisinin and yingzhaosu A and C have an antimaralial activity. Moreover, these heterocyclic compounds are important as a building block that is essential for the total synthesis of many natural products.[1] For these reasons, to construct the dioxabicyclo[4.3.0]non-9-en-2-one and dioxabicyclo[4.4.0]dec-9-en-2-one skeleton is very significant in organic chemistry.[4-6]

Recently, we reported the synthesis of dioxabicyclo[3.3.0]oct-3-enes and dihydropyranes using manganese(III)-based tandem cyclization of malonates or pentanediones with alkenes.[7] In the course of our study, we planed to investigate a similar dual and/or three-dimensional cyclization using 4,4-diaryl-3-butenyl 3-oxobutanoates.[8,9,10]

2. Results and Discussion

4,4-Diaryl-3-butenyl 3-oxobutanoates **3a-e** were prepared by the reaction of γ-butylolactone with arylmagnesium bromides and then, the monoesterification of the obtained diols **1a-e** with diketene followed by dehydration. 4,4-Diaryl-3-butenyl 2-(2-aryl-2-oxoethyl)-3-oxobutanoates **5aa-ee** were synthesized by the reaction of 4,4-diaryl-3-butenyl 3-oxobutanoates **3a-e** with α-bromoacetophenones which were prepared by the reaction of the corresponding acetophenones with bromine in methanol (Scheme 1).



Scheme 1.

Oxidation of 4,4-diphenyl-3-butenyl 3-oxobutanoate (**3a**) with manganese(III) acetate in boiling acetic acid gave 9-methyl-7,7-diphenyl-3,8-dioxabicyclo[4.3.0]non-9-en-2-one (**4a**) in a 76% yield (Scheme 2 and Table 1, Entry 1). The reaction was scrutinized under various conditions and optimized the molar ratios, amounts of the solvent, reaction temperatures, and atmosphere. A similar reaction of other 4,4-diaryl-3-butenyl 3-oxobutanoates **3b-**

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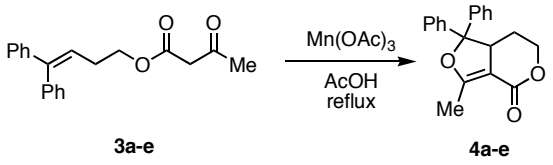
e was carried out under the optimized reaction conditions to give similar bicyclic compounds **4b-e** in moderate to good yields (Table 1, Entries 2-5). The best yield was achieved by the reaction using electoron-rich butanoate **3d**, and the corresponding bicyclic compound **4d** was obtained in a 95% yield. Probably, the dual cyclization would be accelerated during the reaction since the tertiary carbocation intermediate derived from **3d** would be stabilized by the electron-donating 4-methoxyphenyl group. As a result, the considerable substituent effect of butanoates **3a-e** was observed.



Scheme 2.

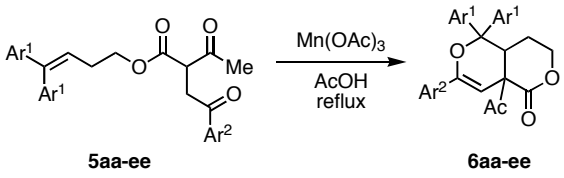
Table 1. Manganese(III)-Based Dual Cyclization of **3a-e**

Entry	**3**:Mn(III)[a]	Time/min	Yield/%[b]
1	1:4	4	**4a** (76)
2	1:4	4	**4b** (82)
3	1:4	4	**4c** (72)
4	1:4	4	**4d** (95)
5	1:4	8	**4e** (62)

[a] Molar ratio. The butanoate **3** (1.0 mmol) was used in boiling AcOH (50 mL).
[b] Isolated yield based on the butanoate **3** used.

In order to further investigate the tandem cyclization, the reaction of 4,4-diaryl-3-butenyl 2-(2-aryl-2-oxoethyl)-3-oxobutanoates **5aa-ee** was examined (Scheme 3). When the oxidation of 4,4-diphenyl-3-butenyl 2-(2-oxo-2-phenylethyl)-3-oxobutanoate (**5aa**) with manganese(III) acetate was carried out in boiling acetic acid, 1-acetyl-7,7,9-triphenyl-3,8-dioxabicyclo[4.4.0]dec-9-en-2-one (**6aa**) was obtained in a 57% yield (Table 2, Entry 1). The reaction was scrutinized under various reaction conditions and optimized the molar ratios, amounts of the solvent, reaction temperatures, and atmosphere. Unfortunately, the desired three-dimensional product **7** was not isolated. A similar oxidation of other 4,4-diaryl-3-butenyl 2-(2-aryl-2-oxoethyl)-3-oxobutanoates **5** with manganese(III) acetate was conducted under the optimized reaction conditions, giving similar bicyclic compounds **6** in moderate to good yields (Table 2, Entries 2-17). In this case, a similar substituent effect for the formation of **6** was observed as well as that for the production of dioxabicyclic compounds **4**.

The mechanism for the manganese(III)-based tandem cyclization of oxobutanoates **5** was outlined in Scheme 4.



Scheme 3.

Table 2. Manganese(III)-Based Dual Cyclization of **5aa-ee**

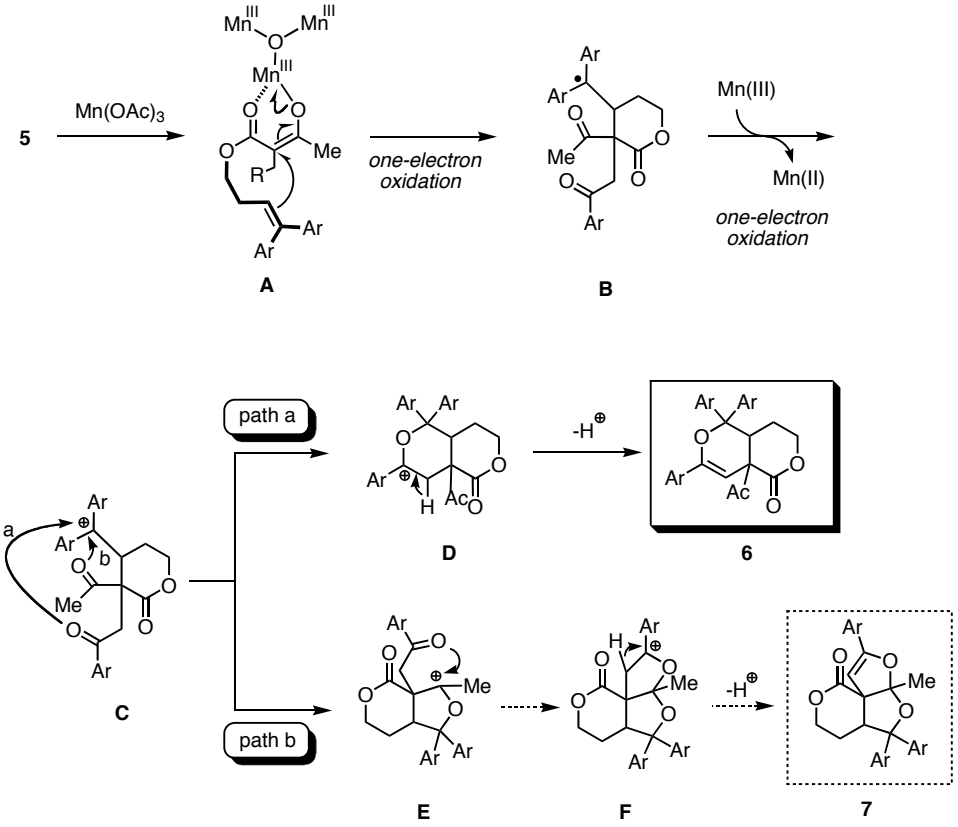
Entry	**5**:Mn(III)[a]	Time/min	Yield of **6** (%)[b]
1	1:04	5	**6aa** (57)
2	1:03	3	**6ab** (63)
3	1:03	5	**6ac** (43)
4	1:04	4	**6ad** (65)
5	1:04	10	**6ae** (35)
6	1:03	2	**6ba** (58)
7	1:04	4	**6bb** (67)
8	1:04	8	**6bc** (60)
9	1:03	4	**6ca** (43)
10	1:04	8	**6cb** (55)
11	1:03	5	**6cc** (41)
12	1:04	3	**6da** (51)
13	1:03	1	**6dd** (68)
14	1:03	2	**6de** (39)
15	1:04	7	**6ea** (42)
16	1:03	4	**6ed** (58)
17	1:04	10	**6ee** (26)

[a] Molar ratio. The butanoate **5** (0.50 mmol) was used in boiling AcOH (20 mL).
[b] Isolated yield based on the butanoate **5** used.

Although the dual cyclization of oxobutanoates **3** and **5** exactly occurred (path a), the 2-aryl-2-oxoethyl-substituted oxobutanoates **5** did not undergo the three-dimensional cyclization (path b).

3. Conclusion

The reaction of 4,4-diaryl-3-butenyl 3-oxobutanoates **3a-e** using manganese(III) acetate was investigated in detail. As a result, the reaction in acetic acid at reflux temperature gave dioxabicyclo[4.3.0]non-9-en-2-ones **4a-e**. On the other hand, a similar reaction of 4,4-diaryl-3-butenyl 2-(2-aryl-2-oxoethyl)-3-oxobutanoates **5aa-ee** was carried out using manganese(III) acetate in acetic acid at reflux temperature gave dioxabicyclo[4.4.0]dec-9-en-2-ones **6aa-ee**. The mechanism for the formation of the products **4** and **6** was explained based on the tandem cyclization pathway.



Scheme 4.

Acknowledgments

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