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# Mn(III)-Induced Molecular Oxygen Trapping Reaction of Alkenes with 2,3-Pyrrolidinedione Derivatives. A Novel Entry to 1-Hydroxy-8-aza-2,3-dioxabicyclo[4.3.0]nonan-9-ones

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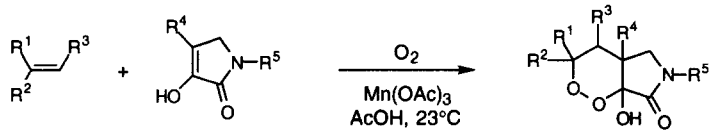
***Abstract***: Molecular oxygen trapping reaction of alkenes with 2,3-pyrrolidinedione derivatives was developed using a Mn(III)-induced oxidation system. Alkenes and 2,3-pyrrolidinediones were treated with manganese(III) acetate in acetic acid under a stream of dry air, giving 1-hydroxy-8-aza-2,3-dioxabicyclo[4.3.0]nonan-9-ones in good yields. The reaction involved molecular oxygen trapping of radicals which were formed by the addition of pyrrolidinedione radicals induced by Mn(III) to alkenes.


Although some techniques for the synthesis of cyclic peroxides based on photooxygenation[1] and electrochemical oxidation[2] are known, one area of interest in our research group is the development of synthetic methodology for the preparation of cyclic peroxides using manganese complexes.[3] A number of these cyclic peroxides have been isolated from natural sources and some of them exhibited significant biological activities.[4] Furthermore, 1,2-dioxan-3-ols could be used as starting materials for the syntheses of furans,[5] pyrazoles,[6] and 1,2-dioxolanes.[7] Manganese(III) acetate is well-known as an efficient oxidant for enolizable carbonyl compounds to produce $\alpha$-keto radicals.[8] Although Mn(III)-induced molecular oxygen trapping reactions have been extensively investigated,[3] there is, to our best knowledge, no report on the synthesis of bicyclic compounds containing both a 1,2-dioxane ring and a lactam ring. Recently, it was reported that the manganese(III) oxidation of alkenes with barbituric acid and its derivatives did not give bicyclic peroxide.[9] The reason was believed to be due to the low reactivity of the carbamoyl group towards this type of cyclization. It seemed reasonable to anticipate the formation of bicyclic compounds containing both a 1,2-dioxane ring and a lactam ring in Mn(III)-induced molecular oxygen trapping reactions of alkenes with 2,3-pyrrolidinediones having an electron-withdrawing substituent, e.g., a carbonyl or cyano group, at the 4-position. In this communication, we briefly describe the results of our study on the Mn(III)-based cyclization of alkenes, 2,3-pyrrolidinedione derivatives, and molecular oxygen.

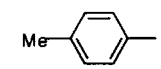
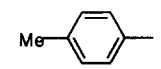
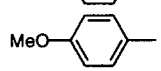
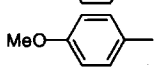
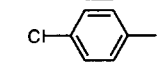
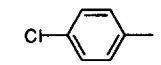
1,1-Diphenylethene (**1**, $R^1 = R^2 =$ Ph, $R^3 =$ H) (1 mmol) was treated with ethyl 1-benzyl-2,3-pyrrolidinedione-4-carboxylate (**2**, $R^4 = CO_2Et$, $R^5 =$ Bn) (2 mmol) in the presence of manganese(III) acetate (1 mmol) in acetic acid (25 mL) at 23 °C for 12 h under a dry air stream. The solvent was removed and the residue




1 2 3

was treated with water (30mL). Extraction of the aqueous solution with chloroform and then separation by a silica gel column eluting with chloroform gave 1-hydroxy-8-aza-2,3-dioxabicyclo[4.3.0]nonan-9-one **3** in 84% yield (Table 1, entry 1). The structure of the product was established by spectroscopic methods and elemental analysis.[10] The same reaction in the absence of manganese(III) acetate did not give any products. However, addition of manganese(II) acetate instead of manganese(III) acetate in the same reaction led to the production of **3** in 15% yield.[3e,f,9] Using 1,1-bis(4-methylphenyl)ethene (**1**, $R^1 = R^2 = 4\text{-}MeC_6H_4$, $R^3 = H$) which had an electron-donating group on the aromatic ring increased the yield of **3** (Entry 2). The increase in yield might be

**Table 1. Molecular Oxygen Trapping Reaction of Alkenes with 2,3-Pyrrolidinedione Derivatives in the Presence of Manganese(III) Acetate**

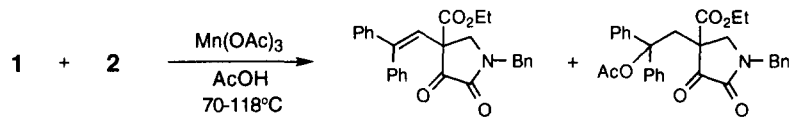
| Entry | Alkene **1** | | | 2,3-Pyrrolidinedione **2** | | **3** (yield / %)[a] |
|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | |
| 1 | Ph | Ph | H | $CO_2Et$ | Bn | 84 |
| 2 |  |  | H | $CO_2Et$ | Bn | 90 |
| 3 |  |  | H | $CO_2Et$ | Bn | 61 |
| 4 |  |  | H | $CO_2Et$ | Bn | 76 |
| 5 | Ph | Me | H | $CO_2Et$ | Bn | 79 |
| 6 | Me | Me | H | $CO_2Et$ | Bn | 73[b] |
| 7 | Et | Et | H | $CO_2Et$ | Bn | 58[c] |
| 8 | $R^1$–$R^3$ = -$(CH_2)_6$- | H | | $CO_2Et$ | Bn | 21[c] |
| 9 | Ph | Ph | H | $CO_2Me$ | Bn | 82 |
| 10 | Ph | Ph | H | $CO_2Et$ | Et | 80 |
| 11 | Ph | Ph | H | $CO_2Bu$ | Me | 83 |
| 12 | Ph | Ph | H | CN | Et | 70 |
| 13 | Ph | Ph | H | CN | Bn | 82 |

a ) Isolated yields based on the amount of the ethene used. b) The reaction was carried out under a stream of **1** and the product yield was based on **2** used. c) The molar ratio of **1**:**2**:manganese(III) acetate was 3:1:1 and the product yield was based on **2** used.


3 4 5

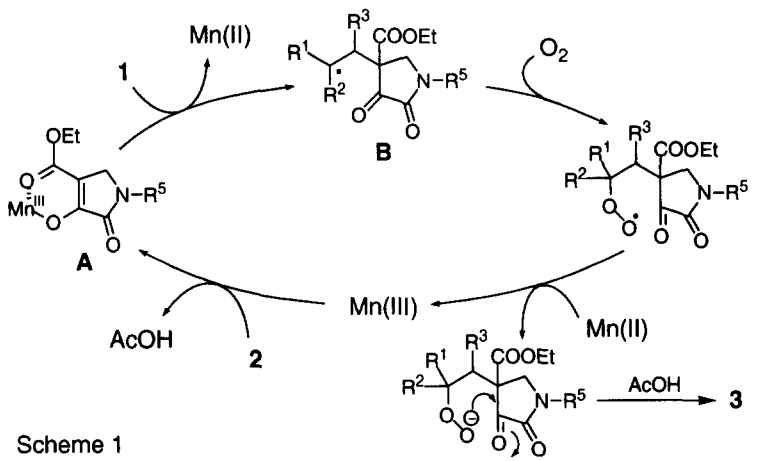
ascribed to the stability of radical **B** formed from the reaction of manganese(III) enolate complex **A** with alkene **1** (Scheme 1).[11] However, a similar reaction of 1,1-bis(4-methoxyphenyl)ethene (**1**, $R^1 = R^2 = 4\text{-}MeOC_6H_4$, $R^3 = H$) afforded the corresponding **3** in only 61% yield (Entry 3) together with pyrrolidinedione **4** (18%) and phenol **5** (10%). The formation of the two by-products **4** and **5** could be explained by acid-catalyzed decomposition of **3** under the reaction conditions.[2,5] In fact, stirring **3** in acetic acid at 23 °C for 16 h gave **3** (83% recovered), **4** (16%), and **5** (15%). The reaction was also applicable to other substituted ethenes (Entries 4-8). Similar reactions of **1** with other 2,3-pyrrolidinedione derivatives also gave the corresponding **3** in comparable yields (Entries 9-13).

On the other hand, the reaction of **1** ($R^1 = R^2 = Ph$, $R^3 = H$) with **2** ($R^4 = CO_2Et$, $R^5 = Bn$) at 70 °C for 6 min gave two compounds **6** (18%) and **7** (46%) in which no molecular oxygen incorporation took place.[12] It




6 7

would be rationalized that the oxidation of tertiary alkyl radical **B** to the corresponding cation becomes more facile at the high temperature than the molecular oxygen trapping process.[3c,f] When the reaction was repeated under an argon atmosphere for 30 min, the yields of **6** and **7** were somewhat improved to 21% and 52%, respectively. The reaction at reflux temperature for 2 min afforded the same products, **6** (50%) and **7** (24%).




Scheme 1

In summary, we have demonstrated the utility of 4-substituted 2,3-pyrrolidinedione **2** in the reaction with alkenes **1** and molecular oxygen. This methodology provides a convenient synthesis of the 8-aza-2,3-dioxabicyclo[4.3.0]nonane skeleton. The compounds obtained in this work have a pyrrolidinone ring bearing

an ester or a cyano group at the 4-position. It is noteworthy that analogs of these compounds were designed to be endothelin receptor antagonists.[13] Efforts are currently underway in our laboratories to investigate similar reactions of 2,3-pyrrolidinediones **2** having an acyl group and a carbamoyl group at the 4-position.

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10. 8-Benzyl-6-ethoxycarbonyl-1-hydroxy-4,4-diphenyl-8-aza-2,3-dioxabicyclo[4.3.0]nonan-9-one: Colorless prisms (from ethanol), mp 171-172 °C; IR (KBr) $\nu$ 3500-2900, 1730, 1707; $^1$H NMR (DMSO-$d_6$) $\delta$ 8.28 (1H, s), 7.6-6.8 (15H, m), 4.54 (1H, d, $J$ = 15.62 Hz), 4.09 (1H, d, $J$ = 15.62 Hz), 4.00 (2H, q, $J$ = 7.33 Hz), 3.22 (1H, d, $J$ = 15.14 Hz), 3.18 (1H, d, $J$ = 10.75 Hz), 3.05 (1H, d, $J$ = 15.14 Hz), 2.92 (1H, d, $J$ = 10.75 Hz), 1.15 (3H, t, $J$ = 7.33 Hz); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 170.6, 166.4, 145.2, 142.4, 135.3, 128.3, 127.4, 126.9, 126.7, 125.7, 125.0, 100.0, 83.6, 60.9, 48.9, 47.1, 46.0, 32.1, 13.7. Anal. Calcd for $C_{28}H_{27}NO_6$: C, 71.02; H, 5.75; N, 2.96. Found: C, 70.82; H, 5.87; N, 2.91.
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