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Manganese(III) acetate based tandem oxidation of various cyclic β-alkoxy α,β-unsaturated ketones

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Abstract

We describe the unusual preliminary results of manganese(III) acetate based tandem oxidation of various β-alkoxy 2-cyclopentenone and 2-cyclohexenone derivatives to afford corresponding α′-acetoxy-α′-phenyl substituted oxidation products in good yields. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

1,3-Diketones possess a central position in synthetic organic chemistry as starting materials in natural product synthesis. In particular, enol ethers of these cyclic diketones, namely β-alkoxy α,β-unsaturated ketones, are very valuable synthetic intermediates in the construction of various biologically active materials, such as antibiotics[1] and several alkaloid families.[2,3] Furthermore, most of these synthetic strategies rely on regioselective oxidation at the α′ position of β-alkoxy α,β-unsaturated ketones.[4,5] In connection with our synthetic studies with manganese(III) acetate,[6–8] we attempted to prepare α′-acetoxy β-alkoxy α,β-unsaturated ketones via a $Mn(OAc)_3$ acetoxylation method.[6,7,9] Here we report our results obtained from the $Mn(OAc)_3$ oxidation of various β-alkoxy α,β-unsaturated ketones and an optimization of the reaction conditions.

2. Results and discussion

β-Alkoxy α,β-unsaturated ketones **1** were prepared from the corresponding 1,3-diketones using slightly modified literature procedures[1] and allowed to react with $Mn(OAc)_3$. β-Alkoxy α,β-unsaturated ketones **1** (with benzene as the solvent) underwent a tandem oxidation with

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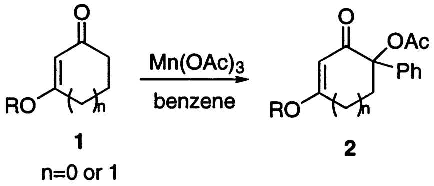
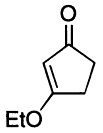
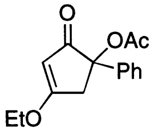
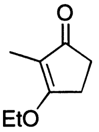
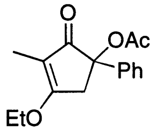
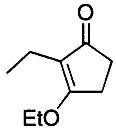
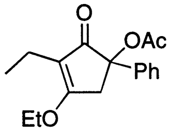
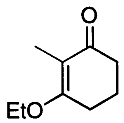
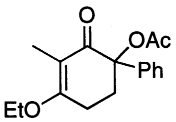
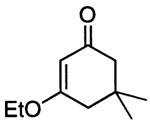
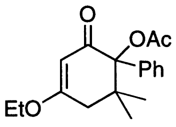
Mn(OAc)$_3$ to afford products **2**. Characterization of the products revealed the introduction of a phenyl group together with an acetoxy moiety on the α′ position (Scheme 1).



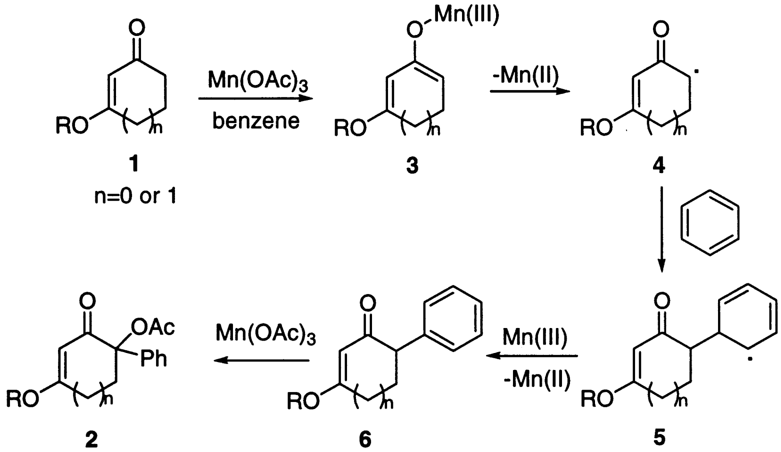
Scheme 1.

The results are summarized in Table 1.

Table 1
Tandem oxidation of β-alkoxy α,β-unsaturated ketones with Mn(OAc)$_3$ in benzene

Reactant	Product[10]	Yield (%)	Time (h)
		61	8
		73	10
		68	11
		75	8
		73	10

The reaction presumably proceeds via the formation of the Mn(III) enolate **3**, which loses Mn(II) upon one-electron oxidation to give α′-keto radical **4**[11] (Scheme 2). Addition of this radical to benzene yields another radical, **5**. One-electron oxidation of the resultant radical **5** gives α′-phenyl β-alkoxy α,β-unsaturated ketones **6**. The introduction of aryl groups adjacent to ketones was reported to be confined to acetone, by Vinogradov et al.[12] since α′-keto radicals generated by higher ketones would result in secondary radicals which would dimerize, or tertiary radicals that are prone to further oxidation. In contrast to this conclusion, in this study no dimerization was observed. Oxidation of intermediate **6** by another equivalent of $Mn(OAc)_3$ provides α′-acetoxy α′-phenyl β-alkoxy α,β-unsaturated ketones **2**. The oxidation of **6** to **2** must be more rapid than the formation of **6**, since no intermediate product **6** could be obtained in any case.

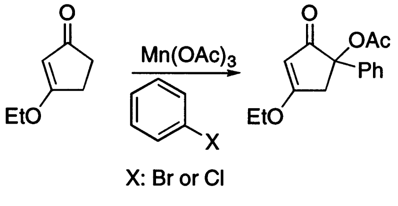


Scheme 2.

In the next step of this study, 3-ethoxy-2-cyclopentenone was chosen as a model compound. The $Mn(OAc)_3$ oxidation was performed in various solvents. Firstly, nitrobenzene was used to examine the effect of a radical scavenger on the reaction propagation. As expected from the proposed reaction mechanism, no product formation was observed.

When anisole and aniline were introduced as solvents, only uncharacterized oxidation products were obtained.

In another attempt, bromobenzene and chlorobenzene were used. In both of these solvents, the reaction propagated in a similar manner to the one in benzene, with the elimination of bromine or chlorine, to yield 5-acetoxy-3-ethoxy-5-phenyl-2-cyclopentenone (Scheme 3) in 38 and 12% yields, respectively.



Scheme 3.

From the heteroaromatic solvents, furan was reacted with $Mn(OAc)_3$ to give polymeric materials and in pyridine no product formation was observed.

In conclusion, an exciting and synthetically valuable $Mn(OAc)_3$ based tandem oxidation is demonstrated. The applicability of a one-pot double oxidation method is attractive for further use in synthesis.

3. Experimental

^{1}H NMR spectra were recorded in $CDCl_3$ on Bruker Spectrospin Avance DPX 400 spectrometers. Chemical shifts are given in ppm from tetramethylsilane. IR spectra were obtained from a Perkin–Elmer Model 1600 series FT-IR spectrometer and are reported in cm^{-1}. Mass spectra were recorded with Varian MAT 212.

3.1. General procedure for the Mn(OAc)$_3$ oxidation of β-alkoxy α,β-unsaturated ketones **2**

A mixture of $Mn(OAc)_3$ (4.64 g, 20.0 mmol) in benzene (or corresponding solvent) (200 ml) was refluxed for 45 min under a Dean–Stark trap. Then the mixture was cooled down to room temperature and the β-alkoxy α,β-unsaturated ketone (7.0 mmol) was gradually added. The mixture was allowed to reflux until the dark brown colour disappeared (TLC monitoring). The reaction mixture was diluted with an equal amount of ethyl acetate and the organic phase was washed with 1N HCl followed by saturated $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$ and evaporated in vacuo. The crude product was separated by flash column chromatography using ethyl acetate/hexane as eluent to afford the product.

3.1.1. Mn(OAc)$_3$ oxidation of 3-ethoxy-2-cyclopentenone in benzene

$C_{15}H_{16}O_4$ (0.84 g, 61% yield) mp: 94–96°C. ^{1}H NMR : δ 1.36 (t, 3H, $J=7$ Hz), 2.10 (s, 3H), 3.13 (d, 1H, $J=18$ Hz), 3.30 (d, 1H, $J=18$ Hz), 4.05 (m, 2H), 5.25 (s, 1H), 7.18–7.34 (m, 5H). ^{13}C NMR : δ 14.5, 21.7, 43.0, 68.2, 84.1, 102.5, 125.1, 128.5, 129.0, 138.6, 170.1, 185.8, 199.4. IR (neat): 1740, 1715 cm^{-1}. MS *m/e* 260 (9), 218 (32), 217 (28), 200 (25), 105 (100), 77 (22). HRMS (observed): 260.1049, (calculated): 260.1048.

References

1. Quesada, M. L.; Schlessinger, R. H.; Parsons, W. H. *J. Org. Chem.* **1978**, *43*, 3968–3970.
2. Chen, Y. L.; Mariano, P. S.; Little, G. M.; O'Brien, D.; Huesmann, P. L. *J. Org. Chem.* **1981**, *46*, 4643–4654.
3. Hackett, S.; Livinghouse, T. *J. Org. Chem.* **1986**, *51*, 879–884.
4. Boschelli, D.; Smith, A. B.; Stringer, O. D.; Jenkins, R. H.; Davis, F. A. *Tetrahedron Lett.* **1981**, *22*, 4385–4388.
5. Koreeda, M.; Chen, Y. P. L. *Tetrahedron Lett.* **1981**, *22*, 15–18.
6. Tanyeli, C.; Demir, A. S.; Dikici, E. *Tetrahedron: Asymmetry* **1996**, *7*, 2399–2402.
7. Demir, A. S.; Hamamci, H.; Tanyeli, C.; Akhmedov, I. M.; Doganel, F. *Tetrahedron: Asymmetry* **1998**, *9*, 1673–1677.
8. Demir, A. S.; Tanyeli, C.; Altinel, E. *Tetrahedron Lett.* **1997**, *38*, 7267–7270.
9. Demir, A. S.; Sayrac, T.; Watt, D. S. *Synthesis* **1990**, 1119–1121.
10. All the products were characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS.
11. Snider, B. B.; Kiselgof, E. Y. *Tetrahedron* **1996**, *52*, 6073–6084.
12. Vinogradov, M. G.; Verenchikov, S. P.; Fedorova, T. M.; Nikishin, G. I. *Zh. Org. Khim.* **1975**, *11*, 947–952.