## New Method for the Preparation of an Active Manganese Species and its Use for Radical Cyclization Reactions

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**Abstract:** Reduction of  $\text{Li}_2\text{MnCl}_4$  with magnesium in THF afforded a fairly active manganese species which readily initiated radical cyclization of 2-iodoethanal allylic acetals at room temperature. The corresponding 2-bromoethanal acetals also provided the same cyclized products upon treatment with the activated manganese reagent at reflux in THF.

Recently, we have reported that treatment of 2-iodoethanal acetals with trialkylmanganate such as n-Bu<sub>3</sub>MnMgBr afforded tetrahydrofuran derivatives in good yields. The catalytic reaction proceeded smoothly, as well as the stoichiometric reaction, and the same cyclized products were obtained upon treatment of the acetals with butylmagnesium bromide in the presence of a catalytic amount of manganese(II) chloride.<sup>1</sup> Low-valent manganese such as Mn(0) could be an active catalyst and play a critical role in the manganese-catalyzed cyclization reaction. Here we will to describe the preparation of low-valent manganese and its use for radical cyclization of 2-haloethanal acetals.

The manganese reagent was obtained upon reduction of the well soluble ate-complex Li2MnCl4 with magnesium turnings activated by 1,2dibromoethane. 1,2-Dibromoethane (5.0 mmol) was added to a suspension of magnesium<sup>2</sup> (40 mmol) in THF (4 mL). Exothermic reaction took place. After being stirred for another 5 min, THF and the produced MgBr<sub>2</sub> were removed by a syringe and the resulting magnesium turnings were washed with THF (3 x 4 mL).<sup>3</sup> Then, a pale yellow-green solution of Li2MnCl44 (15 mmol), derived from MnCl2 (15 mmol) and LiCl (30 mmol), in THF (40 mL) was added to the above magnesium turnings. The mixture was stirred for 24 h at room temperature. The original pale yellow-green color turned dark. This resulting finely divided black powder<sup>5,6</sup> was partially soluble in THF. A clear dark supernatant solution of manganese in THF (5.0 mL, ~1.8 mmol) was added by a syringe to a solution of 2-iodoethanal acetal 1a (1.0 mmol) in THF (2.0 mL) at 25 °C under argon atmosphere. The mixture was stirred for 6 h at 25 °C. The resulting mixture was quenched with sat. NH<sub>4</sub>Cl, extracted with ethyl acetate (3 x 10 mL), and the combined organic layers were washed with NaCl solution, dried over anhydrous  $Na_2SO_4$ , and concentrated. Silica gel column chromatography provided a cyclized product 2a in 70% yield (Scheme 1).



The representative results of the reaction of various acetals with lowvalent manganese are shown in Table 1. This new method has some characteristics compared to the reaction with *n*-Bu<sub>3</sub>MnMgBr and several comments are worth noting. (1) In the case of the substrates (1a, 1b, 1e, and 1f) which have terminal alkene or disubstituted olefins, products having a methyl group or an alkyl group on the tetrahydrofuran ring were obtained exclusively. In contrast, the substrates which are

Table 1.	Cyclization of 2-Haloethanal Allylic Acetals, 2-	-
Iodoethvl	Allyl Ether (Amine) with Active Manganese <sup>a)</sup>	



a) The reaction was performed at 25 °C (X=I) or 70 °C (X=Br). b) Diastereomeric ratio = 1/1 c) E/Z = 45/55 d) Diastereomeric ratio = 66/34 e) Diastereomeric ratio could not be determined. f) Diastereomeric ratio = 52/48

derived from  $\gamma,\gamma$ -disubstituted allylic alcohol (**1d** and **1g**) gave the cyclized products having an alkenyl moiety in addition to the products bearing an alkyl group. Thus, 4-alkyl-substituted tetrahydrofuran derivatives were obtained principally in this new procedure. These results show sharp contrast to those of the reaction with *n*-Bu<sub>3</sub>MnMgBr which provides alkenyl-substituted tetrahydrofuran products

exclusively in the case of the substrates which have disubstituted or trisubstituted alkenic moieties. We are tempted to assume that a hydrogen abstraction of the intermediary carbon radical is a major step in the reaction with  $Mn(0)^*$ , whereas recombination with *n*-BuMn(I) followed by β-elimination of Mn-H producing an alkenyl substituent becomes the main route in the reaction with n-Bu<sub>3</sub>MnMgBr. (2) The bromo acetals (1b and 1d, X=Br) reacted with Mn(0)\* smoothly and as well as the iodoocetals and provided comparable yields of the desired tetrahydrofuran derivatives, although the reaction of bromo acetals required heating of the reaction mixture at reflux in THF. (3) Acetylenic triple bonds were equally effective as carbon-carbon double bonds for trapping the radical intramolecularly. Quenching the reaction mixture with D<sub>2</sub>O afforded a mixture of deuterated alkene (2c-d) and 2c (2c-d:2c = 35:65). (4) The allylic ether 1f and allylic amine 1h provided the tetrahydrofuran or pyrrolidine derivative in better yield (62% or 60%) compared to the reaction with n-Bu3MnMgBr which afforded the desired product in only 35% or 7%, respectively, and the starting allylic alcohol or allylic amine was obtained as the main product. The latter compound could be formed via E2 elimination by the attack of the ate complex (probably a butyl anion) on iodine.

We are tempted to assume the following reaction mechanism. Single electron transfer from  $Mn(0)^*$  to 2-iodoethanal acetals would give an anion radical which provides radical 3 after departure of iodide. 5-Exo mode cyclization could afford a carbon radical 4 which abstracts hydrogen from the solvent THF (Scheme 2).7



Scheme 2

The reagent  $Mn(0)^*$  also reacts with the most reactive substrates such as allylic bromides or  $\alpha$ -bromoesters at 25 °C. In contrast, simple secondary iodides such as 2-iodotridecane<sup>8</sup> was recovered unchanged upon treatment with  $Mn(0)^*$  at 25 °C for 12 h. The cyclization of N,Ndiallyl-2-iodoaniline with  $Mn(0)^*$  was not so effective as 2-iodoethanal acetals 1. For instance, treatment of 2-iodoaniline 5 (1.0 mmol) with  $Mn(0)^*$  (1.8 mmol) in THF at reflux for 6 h afforded an indoline derivative 6 in only 45% yield along with reduced N,N-diallylaniline (15%) (Scheme 3).



Scheme 3

Finally,  $Mn(0)^*$ -catalyzed reaction of acetals 1 was examined. Treatment of a solution of 1a (1.0 mmol) in THF (5 mL) with butylmagnesium bromide (1.0 M THF solution, 2 mL, 2 mmol) in the presence of  $Mn(0)^*$  (0.4 mL of a clear dark supernatant, -0.15 mmol) gave 7 which was identical with a sample prepared by the reaction of 1a with n-BuMgBr in the presence of a catalytic amount of MnCl<sub>2</sub>. The result might support our reaction mechanism which has been suggested in a previous paper<sup>1</sup> (Scheme 4).





This metallic manganese, prepared according to the methodology described above, exhibits appropriate reduction potential to investigate its use as a co-reductant with other metals. The scope and the limitation of its mediated radical cyclization will soon be reported.

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## **References and Notes**

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- 3 The blank test without manganese species was performed as follows. The supernatant liquid containing magnesium species in THF (5 mL) was added to the flask containing 1d (X=I) (1.0 mmol) in THF (2 mL). No reaction was observed after 24 h from which 90% of the starting material was recovered unchanged.
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- 5 We are tempted to assume the manganese species to be an active metallic manganese  $(Mn(0)^*)$ . Several reductive procedures have been reported for the preparation of active manganese from manganese(II) halides. LiAlH<sub>4</sub>: Hiyama, T.; Obayashi, M.; Nakamura, A. Organometallics, 1982, 1, 1249; Li-naphthalene: Kim, S.-H.; Hanson, M. V.; Rieke, R. D. Tetrahedron Lett., 1996, 37, 2197; C<sub>8</sub>K: Fürstner, A.; Brunner, H. Tetrahedron Lett., 1996, 37.7009.
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