Reductive Ring Opening of 6-Deoxy-6-iodopyranosides and 5-Deoxy-5-iodofuranosides by Manganese. A Convenient Procedure for the Preparation of Chiral 5-Hexenals and 4-Pentenals

Kazuho Tanaka, Shinjiro Yamano, Oyo Mitsunobu*

Department of Chemistry, College of Science and Engineering, Aoyama Gakuin University, Chitosedai, Setagayaku, Tokyo 157-8572, Japan
E-mail: mitsu@chem.aoyama.ac.jp

Received 15 July 2001

Abstract: Reaction of fully protected 6-iodopyranosides and 5-iodofuranosides with Mn in the presence of trimethylsilyl chloride and $PbCl_2$ (Takai-conditions) afforded the corresponding 5-hexenals and 4-pentenals in good to moderate yields.

Key words: reductive sugar-ring opening, manganese, chiral 5-hexenals, chiral 4-pentenals

Grob-type fragmentation of 6-deoxy-6-halopyranosides and 5-deoxy-5-halofuranosides leading to the corresponding 5-hexenals and 4-pentenals has been performed by a variety of metallic reagents, which involves activated Zn,[1a-c] Zn/Ag-graphite,[1d,e] BuLi,[1a,b] SmI_2,[1f] In,[1g] and acetyliron anion.[1h] Since the resulting enals could be utilized for the construction of natural products with multiple center of chirality, there is an ever increasing demand for more simple and mild procedures for the reductive sugar-ring opening. In the course of preparation of the carbon framework of mycinamicin IV, we attempted Rieke-Zn[2] mediated reductive ring opening of a 6-iodopyranoside.[3] Although the fragmentation reaction gave the expected 5-hexenal in moderate yield, the use of potassium in the preparation of Rieke-Zn prompted a search for more simple procedure.

Takai and his coworkers reported that the reaction of alkyl halides with carbonyl compounds could be promoted by Mn in the presence of $PbCl_2$ and trimethylsilyl chloride (TMSCl), where strong reduction potential of Mn would play an important role in the success of the reaction.[4] The reaction system would therefore be expected to be utilized in the halosugar-ring opening.

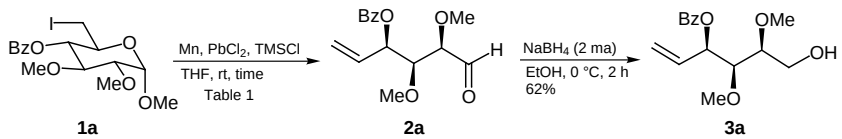
At the outset, methyl 4-*O*-benzoyl-6-deoxy-6-iodo-2,3-di-*O*-methyl-α-D-glucofuranoside (**1a**) reacted with Mn (4 molar amount: ma), $PbCl_2$ (0.01 ma), and TMSCl (0.4 ma) in THF at room temperature.[5] Under these conditions, however, the expected 5-hexenal **2a** was obtained in 13% yield with 82% recovery of **1a** (Scheme 1, Table 1, entry 1). Since **2a** was unstable and began to decompose even in refrigerator, the aldehyde was converted into stable alcohol **3a** by reduction with $NaBH_4$ for characterization (Scheme 1).

In order to find the optimum conditions, the amounts of $PbCl_2$ and TMSCl were increased to 0.3 ma and 4.5 ma, respectively, where **2a** was obtained in 62% yield (entry 2). The yield of **2a** was increased to 81% by the use of 5 ma of Mn (entry 3). In this reaction, however, a small amount of unidentified sugar derivative containing trimethylsilyl group was formed. Thus, the amount of TMSCl was decreased to 4.0 ma, where **2a** was isolated in 96% yield without any detectable formation of the silylated side product (entry 4).[6,7] In the following experiments, the conditions shown in entry 4 in Table 1 were used as the standard conditions.

The β-anomer of **1a** (**1b**) also reacted with Mn under the standard conditions to give the expected 5-hexenal **2a** in 79% yield with 16% recovery of **1b** (Scheme 2).

Methyl 6-iodo-2, 3, 4-tri-*O*-benzoyl-α-D-glucopyranoside (**1c**) and methyl 4-*O*-benzoyl-6-iodo-2,3-di-*O*-methyl-α-D-mannopyranoside (**1d**) reacted smoothly with Mn under the standard conditions to afford the expected 5-hexenals **2c** and **2d** in 96% and 97% yields, respectively (Scheme 2).

In order to extend the reductive fragmentation of 6-iodopyranosides by Mn to furanosides, 5-iodofuranosides **4a** was subjected to ring opening under the standard conditions for 1 h to give a complex mixture of products, and the expected aldehyde **5a** could hardly be obtained presumably because of its instability. Thus, after **4a** had been consumed, the resulting mixture was successively treated



1a **2a** **3a**

Scheme 1

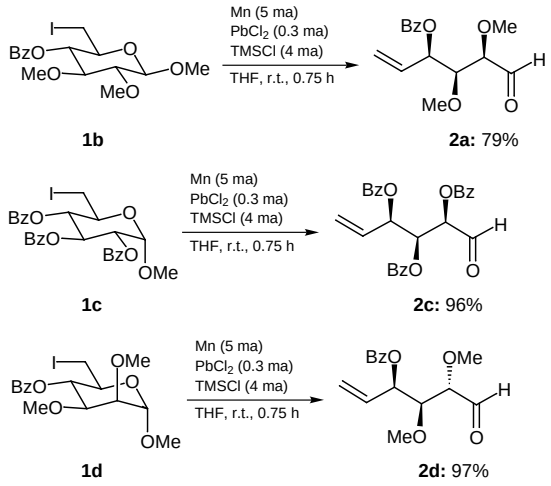
Synlett 2001, No. 10, 28 09 2001. Article Identifier:
1437-2096,E;2001,0,10,1620,1622,ftx,en;Y13601st.pdf.

ISSN 0936-5214

Table 1 Ring Opening of **1a** with Mn in THF at Room Temperature[6,]

Entry	Reagents used (molar amounts)			Time h	Product %	Recovery %
	Mn	$PbCl_2$	TMSCl		**2a**	**1a**
1	4	0.01	0.4	1.5	13[a]	82
2	4	0.3	4.5	1.5	62[a]	22
3	5	0.3	4.5	0.75	81[b]	nd
4	5	0.3	4.0	0.75	96[b]	nd

[a] Yields were determined by ^1H NMR.
[b] Isolated yield.



Scheme 2

with $NaBH_4$ (2 ma) to afford the corresponding alcohol **6a** in 13% isolated yield. When **4a** reacted with 14 ma of Mn in the presence of $PbCl_2$ (0.3 ma) and TMSCl (4.5 ma), followed by treatment with $NaBH_4$ as above, alcohol **6a** was isolated in 48% yield. By the similar procedure, furanoside **4b** and **4c** afforded alcohol **6b** and **6c** in 55% and 48% yields, respectively (Scheme 3).

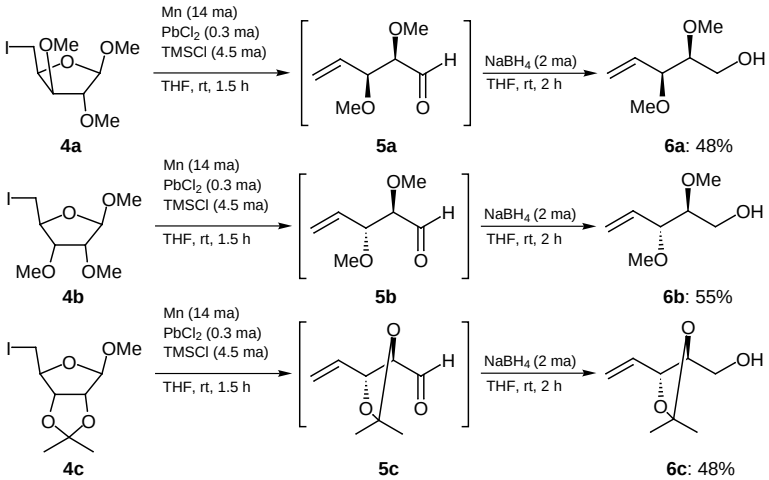
In summary, we have shown that manganese activated by Takai procedure could be successfully utilized in reductive sugar ring opening of 6-iodopyranosides and 5-iodofuranosides leading to 5-hexenals and 4-pentenals, which are versatile intermediates in organic synthesis. The procedure can be carried out by standard bench-top technique at room temperature, and would therefore be more convenient than reported methods.

Acknowledgement

This work was partially supported by a Grant-in-Aid for Scientific Research from Ministry of Education, Science, Sports and Culture of Japan, the Science Fund of Japan Private School Promotion Foundation, and Research Institute of Aoyama Gakuin University.

References and Notes

(1) (a) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1984**, *67*, 1328. (b) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990. (c) Vitamin B_{12} catalyst of zinc mediated ring opening has recently been reported: Kleban, M.; Kautz, U.; Greul, J.; Hilgers, P.; Kugler, R.; Dong, H.-Q.; Jäger, V. *Synthesis* **2000**, 1027. (d) Fürstner, A.; Jumbam, D.; Feslic, J.; Weidmann, H. *J. Org. Chem.* **1991**, *56*, 2213. (e) See also: Fürstner, A.; Weidmann, H. *J. Org. Chem.* **1989**, *54*, 2307. (f) Chiara, J. L.; Martínez, S.; Bernabé, M. *J. Org. Chem.* **1996**, *61*, 6488; and references therein. (g) Hyldtoft, L.; Madsen, R. *J. Am. Chem. Soc.* **2000**, *122*, 8444; and references therein. (h) Bartnicka, E.; Zamojski, A. *Polish J. Chem.* **1998**, *72*, 688.
(2) Rieke, R. D.; Hudnall, P. M. *J. Chem. Soc., Chem. Commun.* **1973**, 269.



Scheme 3

(3) Yamano, S.; Teranishi, M.; Mitsunobu, O. The 74th Meeting of Chemical Society of Japan, Kyoto, March 30, 1998, 4E5 11
(4) (a) Takai, K.; Ueda, T.; Hayashi, T.; Moriwake, T. *Tetrahedron Lett.* **1996**, *37*, 7049. (b) Takai, K.; Ueda, T.; Ikeda, N.; Moriwake, T. *J. Org. Chem.* **1996**, *61*, 7990.
(5) An optimum conditions for manganese promoted allylation of cyclododecanone (see ref 4a).
(6) The synthesis of 4-benzoyloxy-2,3-dimethoxyhex-5-enal (**2a**) is representative (Table 1, entry 4). Mn powder (138 mg, 2.5 mmol; purchased from Kanto Chemical Co. Inc. Cat. No. 25061-32) and $PbCl_2$ (42 mg, 0.15 mmol) placed in a flask were dried by heating with heat-gun in vacuo for 30 min and then THF (1 mL) and TMSCl (0.25 mL, 2.25 mmol) were successively added. The resulting mixture was stirred for 30 min, followed by the addition of **1a** (218 mg, 0.5 mmol) in THF (1.5 mL). After 45 min, the mixture was filtered through Hyfro Super Cel®. The flask was rinsed with ethyl acetate and the mixture was filtered through the Hyfro Super Cel®. The filtrate was washed with H_2O. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was separated by silica gel column chromatography (hexane:AcOEt = 3:2) to afford **2a** (134 mg, 96%). ^{1}H NMR (270 MHz; in $CDCl_3$): δ 9.84 (1H, d, J = 1.37 Hz, H-1), 8.09-8.04 (2H, m, Ph), 7.60-7.45 (3H, m, Ph), 5.96 (1H, ddd, J = 17.41, 10.54, 6.41 Hz, H-5), 5.85-5.81 (1H, m, H-4), 5.48 (1H, ddd, J = 17.41, 1.37, 0.92 Hz, H-6a), 5.36 (1H, ddd, J = 10.54, 1.37, 0.92 Hz, H-6b), 3.62 (1H, dd, J = 6.41, 3.21 Hz, H-3), 3.39 (1H, dd, J = 3.21, 1.37 Hz, H-2), 3.52 (3H, s, CH_3O), 3.49 (3H, s, CH_3O).
(7) Reduction of **2a** by $NaBH_4$: To a solution of **2a** (100 mg, 0.36 mmol) in ethanol (1 mL) was added $NaBH_4$ (27 mg, 0.72 mmol) at 0 °C. After the solution was stirred at 0 °C for 2 h, the reaction was quenched by the addition of 5% HCl. The mixture was extracted with ethyl acetate. The organic layer was separated, dried ($MgSO_4$), and concentrated. The residue was separated by silica gel column chromatography (ethyl acetate:hexane = 1:1) to give alcohol **3a** (62 mg, 61%). ^{1}H NMR (500 MHz) In $CDCl_3$: δ 8.09-8.07 (2H, m, Ph), 7.60-7.44 (3H, m Ph), 6.01 (1H, ddd, J = 16.95, 11.00, 6.42 Hz, H-5), 5.78-5.75 (1H, m, H-4), 5.44 (1H, dt, J = 16.45, 1.37 Hz, H-6a), 5.32 (1H, dt, J = 11.00, 1.37 Hz, H-6b), 3.87 (1H, dd, J = 11.46, 4.58 Hz, H-1a), 3.70 (1H, dd, J = 11.46, 4.58 Hz, H-1b), 3.60-3.58 (1H, m, H-3), 3.45 (1H, q, 4.58, H-2), 3.59 (3H, s, CH_3O), 3.50 (3H, s, CH_3O). In C_6D_6: δ 8.22-8.20 (2H, m, Ph), 7.10-7.01 (3H, m, Ph), 6.05 (1H, ddt, J = 5.96, 4.58, 1.37 Hz, H-4), 5.93 (1H, ddd, J = 17.41, 10.54, 5.96 Hz, H-5), 5.36 (1H, dt, J = 17.4, 1.37 Hz, H-6a), 5.05 (1H, dt, J = 10.54, 1.37 Hz, H-6b), 3.71-3.69 (1H, m, H-1a), 3.57-3.54 (1H, m, H-1b), 3.47 (1H, dd, J = 5.96, 4.59 Hz, H-3), 3.26 (1H, dt, J = 5.96, 4.58 Hz, H-2), 3.31 (3H, s, CH_3O), 3.14 (3H, s, CH_3O).