

1,7-Acetal Carbon Rearrangement *via* 1,5-Hydride Transfer in an Oxocanyl Carbenium  
Ion. Conversion of *O*-(5-Hexenyl)-*Se,O*-heteroacetals or *O,O*-Acetals  
into 7-Oxohexanols or 7-Oxohexyl Chlorides<sup>1)</sup>

Mitsuhiro YOSHIMATSU, Noriyuki HATAE, Hiroshi SHIMIZU,  
and Tadashi KATAOKA\*

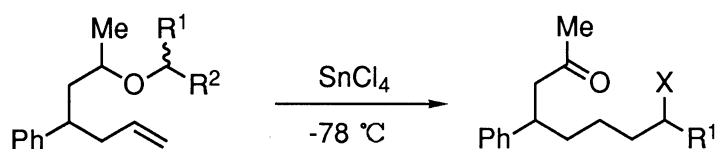
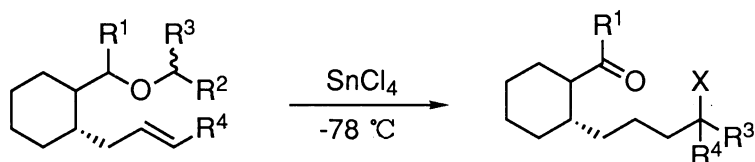
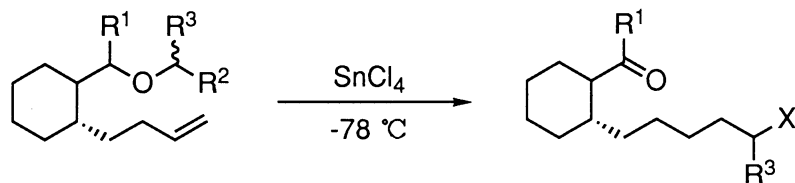
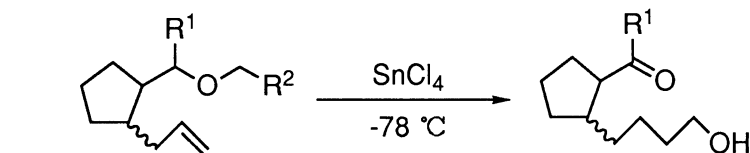
Gifu Pharmaceutical University, 6-1 Mitahora-higashi 5-chome, Gifu 502

Oxacyclooctyl (oxocanyl) carbenium ions generated by treatment of *O*-(5-hexenyl)-*Se,O*-heteroacetals or *O,O*-acetals with SnCl<sub>4</sub> underwent intramolecular 1,5-hydride transfer, and the  $\alpha$ -oxy carbenium ions newly formed were hydrolyzed to give the 7-oxohexanols or 7-oxohexyl chlorides in good yields. Various *O*-(5-hexenyl)-*Se,O*-heteroacetals or *O,O*-acetals were converted into 7-oxohexanols or 7-oxohexyl chlorides.

Much attention has been focused on cationic cyclizations as one of the more interesting subjects in organic syntheses.<sup>2)</sup> Overman *et al.* have intensively studied not only the cyclization of iminium ions but also the cyclization of  $\alpha$ -alkoxycarbenium ions.<sup>3)</sup> Very recently we reported the intramolecular cyclization of  $\alpha$ -seleno carbenium ions generated by the selective C-O bond cleavage of the *Se,O*-heteroacetals.<sup>4)</sup> As part of our developing studies on this cyclization reaction, we have been studying the cyclization of the  $\alpha$ -oxy carbenium ions generated by the selective C-Se bond cleavage of the *Se,O*-heteroacetals and found that *Se,O*-heteroacetals or *O,O*-acetals underwent the 1,7-migration of the acetal moiety during treatment with SnCl<sub>4</sub>. This migration involves a 1,5-hydride transfer of the oxacyclooctyl (oxocanyl) carbenium ions. Although Overman *et al.* reported that the Lewis acid promoted cyclization of 5-(trimethylsilyl)-5-hexenyl acetals afforded 7-keto alcohols together with 4-(trimethylsilyl)-4-oxocenes, their objective was the synthesis of 4-oxocenes and they did not pay their attention to the formation of 7-keto alcohols.<sup>5)</sup> This paper describes that reactions of hexenyl *Se,O*-heteroacetals or *O,O*-acetals bearing no 5-trimethylsilyl group with SnCl<sub>4</sub> cause the 1,7-acetal carbon transfer to give 7-oxohexanols or 7-oxohexyl chlorides.

Treatment of ene-*Se,O*-heteroacetal **1a** with SnCl<sub>4</sub> (4 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (0.15 M solution) at -78 °C under an Ar atmosphere afforded a keto alcohol **2a** in 62% yield.<sup>6)</sup> The structure of **2a** was determined by <sup>1</sup>H- and <sup>13</sup>C-NMR, IR and mass spectrometry. Other ene-*Se,O*-heteroacetals **4a-c**, **7a** and **10** similarly reacted with SnCl<sub>4</sub> to give keto alcohols **5a-c**, **8a** and **11** in moderate-to-high yields, respectively. From these results, the acetal carbon migrated to the olefinic terminal carbon to form a hydroxymethyl group.

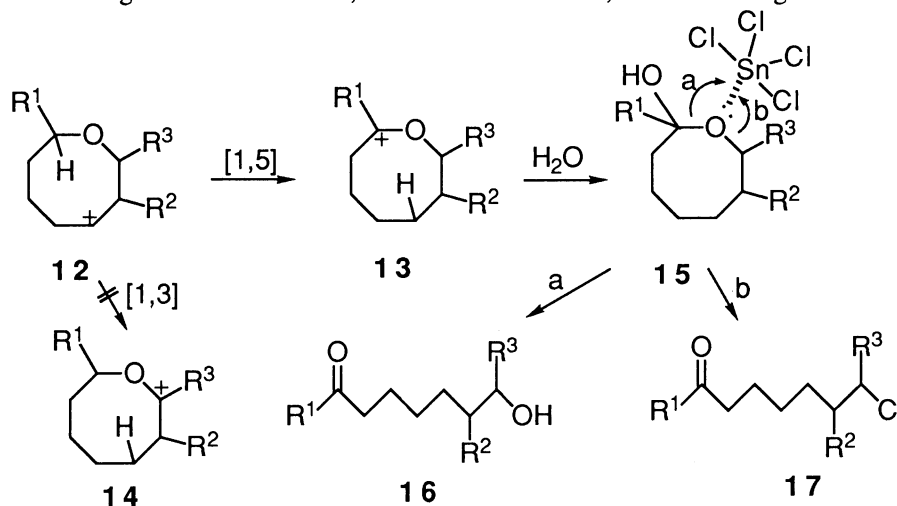
If the  $\alpha$ -oxy carbenium ions can be generated from *O,O*-acetals, this 1,7-migration of the acetal carbon is more conveniently applicable to the synthesis of the 7-keto alcohols, because the *O,O*-acetals are known much more than the *Se,O*-heteroacetals. The methoxyethoxyacetals **1b-c**<sup>7)</sup> were prepared in order to cleave one of the C-O bonds site-selectively and allowed to react with SnCl<sub>4</sub>. However, rearranged products, keto alcohols **2b-c** and keto chlorides **3b-c**<sup>8)</sup> were obtained in low yields. Some methoxy acetals **4d, e**, **7b**<sup>7)</sup> more smoothly

**1a** ( $\text{R}^1=\text{H}$ ;  $\text{R}^2=\text{SePh}$ )**1b** ( $\text{R}^1=\text{CH}_2\text{CH}_2\text{Ph}$ ;  $\text{R}^2=\text{OCH}_2\text{CH}_2\text{OMe}$ )**1c** ( $\text{R}^1=(\text{CH}_2)_5\text{CH}_3$ ;  $\text{R}^2=\text{OCH}_2\text{CH}_2\text{OMe}$ )**2a** ( $\text{R}^1=\text{H}$ ;  $\text{X}=\text{OH}$ )(62%)**2b** ( $\text{R}^1=\text{CH}_2\text{CH}_2\text{Ph}$ ;  $\text{X}=\text{OH}$ )(25%)/**3b** ( $\text{R}^1=\text{CH}_2\text{CH}_2\text{Ph}$ ;  $\text{X}=\text{Cl}$ )(13%)**2c** ( $\text{R}^1=(\text{CH}_2)_5\text{CH}_3$ ;  $\text{X}=\text{OH}$ )(10%)/**3c** ( $\text{R}^1=(\text{CH}_2)_5\text{CH}_3$ ;  $\text{X}=\text{Cl}$ )(30%)**4a** ( $\text{R}^1=\text{R}^3=\text{R}^4=\text{H}$ ;  $\text{R}^2=\text{SePh}$ )**4b** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^2=\text{SePh}$ ;  $\text{R}^3=\text{R}^4=\text{H}$ )**4c** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^2=\text{SePh}$ ;  $\text{R}^3=\text{H}$ ;  $\text{R}^4=n\text{-Pr}$ )**4d** ( $\text{R}^1=\text{R}^4=\text{H}$ ;  $\text{R}^2=\text{OMe}$ ;  $\text{R}^3=\text{Me}$ )**4e** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^2=\text{OMe}$ ;  $\text{R}^3=\text{CH}_2\text{CH}_2\text{Ph}$ ;  $\text{R}^4=\text{H}$ )**5a** ( $\text{R}^1=\text{R}^3=\text{R}^4=\text{H}$ ;  $\text{X}=\text{OH}$ )(63%)**5b** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^3=\text{R}^4=\text{H}$ ;  $\text{X}=\text{OH}$ )(93%)**5c** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^3=\text{H}$ ;  $\text{R}^4=n\text{-Pr}$ ;  $\text{X}=\text{OH}$ )(94%)**5d** ( $\text{R}^1=\text{R}^4=\text{H}$ ;  $\text{R}^3=\text{Me}$ ;  $\text{X}=\text{OH}$ )(67%)**6e** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^3=\text{CH}_2\text{CH}_2\text{Ph}$ ;  $\text{R}^4=\text{H}$ ;  $\text{X}=\text{Cl}$ )  
(60%)**7a** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^2=\text{H}$ ;  $\text{R}^3=\text{SePh}$ )**7b** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^2=\text{OMe}$ ;  $\text{R}^3=\text{CH}_2\text{CH}_2\text{Ph}$ )**8a** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^3=\text{H}$ ;  $\text{X}=\text{OH}$ ) (quant.)**9b** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^3=\text{CH}_2\text{CH}_2\text{Ph}$ ;  $\text{X}=\text{Cl}$ )(65%)*trans*-**10** ( $\text{R}^1=\text{Me}$ ;  $\text{R}^2=\text{SePh}$ )*cis*-**10***trans*-**11**( $\text{R}^1=\text{Me}$ )(45%)*cis*-**11**(79%)

Scheme 1.

underwent the migration reaction to afford the keto alcohol **5d** and keto chlorides **6e**, **9b** in good yields. Reactions of *Se,O*-heteroacetals afforded the single products, keto alcohols, while reactions of *O,O*-acetals afforded keto alcohols and keto chlorides. The reasons for the different behavior between the *Se,O*-heteroacetals and the *O,O*-acetals are not clear at the moment. The keto alcohol **2b** was treated with  $\text{SnCl}_4$  under the same conditions as *O,O*-acetal **1b**, but the keto chloride **3b** was not obtained. It is interesting from the view point of the formation mechanism of the keto chlorides that a chlorine atom is bound with the transferred carbon. Cis-trans isomerization of cyclohexane acetals, **4** and **7**, and cyclopentane derivatives **10** was not observed under these reaction conditions.

The plausible mechanism for the 1,7-migration of the acetal moiety is proposed as shown in Scheme 2. The  $\alpha$ -oxy carbenium ion generated from an *Se,O*-heteroacetal or an *O,O*-acetal undergoes intramolecular cyclization



Scheme 2.

to form the oxocanyl carbenium ion **12**. The carbenium ion **12** abstracts not the  $\beta$ -hydrogen but the  $\delta$ -hydrogen adjacent to the oxygen atom (1,5-hydride transfer) and changes into the  $\alpha$ -oxy carbenium ion **13** stabilized by the oxygen atom. The hydrolysis of the cation **13** via a hemiacetal **15** produces a keto alcohol **16**. A keto chloride **17** would be formed via the reductive elimination or ligand-coupling of the hemiacetal- $\text{SnCl}_4$  complex **15**. The 1,3-hydride shift of the cation **12** would not be observed because of the unfavorable steric requirement. According to the conformational analysis of oxocane, interconversion of its conformations can take place very easily.<sup>9)</sup> Therefore, the conformations of the oxocanyl carbenium ion **12** would be changed by the positions and the kinds of substituents. The 1,5-hydride shift, the key step in this rearrangement, would be strongly affected by the substituents from a conformational and electronic point of view. When the methyl group was introduced at the  $\alpha$ -position to the oxygen ( $\text{R}^1=\text{Me}$  in **12**), i.e., **4b** and **4c**, the yields of the products **5b** and **5c** were surprisingly increased. The introduction of a phenethyl group or a *n*-hexyl group to the acetal carbon lowered the yields of the rearranged products. The acetal **4c** substituted with a *n*-propyl group at the olefinic terminus also gave a keto alcohol **5c** in good yield.

In summary, we found the intramolecular 1,5-hydride transfer in an oxocanyl carbenium ion and the 1,7-migration of the acetal carbon. This reaction is applicable to the syntheses of 7-oxohexanols or 7-oxohexyl chlorides with long alkyl substituents.

## References

- 1) This paper is dedicated to Professor Yoshifumi Maki on this occasion of his retirement from Gifu Pharmaceutical University.
- 2) C. Thebtaranonth and Y. Thebtaranonth, *Tetrahedron*, **46**, 1385 (1990).
- 3) L. E. Overman, *Acc. Chem. Res.*, **25**, 352 (1992).
- 4) M. Yoshimatsu, M. Fujimoto, H. Shimizu, M. Hori, and T. Kataoka, *Chem. Pharm. Bull.*, **41**, 1160 (1993).
- 5) T. A. Blumenkopf, M. Bratz, A. Castaneda, G. C. Look, L. E. Overman, D. Radriguez, and A. S. Thompson, *J. Am. Chem. Soc.*, **112**, 4386 (1990).
- 6) A typical procedure for the reactions of *Se,O*- and *O,O*-acetals with SnCl<sub>4</sub>. 4-Phenylhept-1-en-6-one was synthesized from benzalacetone, allyl trimethylsilane and TiCl<sub>4</sub> [G. Majetich, A. Casares, D. Chapman, and M. Behnke, *J. Org. Chem.*, **51**, 1745 (1986)]. Reduction of 4-phenylhept-1-en-6-one with NaBH<sub>4</sub> in EtOH gave 4-phenylhept-1-en-6-ol in quantitative yield. The alcohol (2.0 g, 11 mmol) was treated with NaH (0.5 g, 21 mmol) and Bu<sub>3</sub>SnCH<sub>2</sub>I (4.5 g, 13 mmol) in THF to give tributylstannane (4.2 g, 78%). Transmetalation of the tributylstannane with *n*-BuLi (12.5 mmol) followed by treatment with (PhSe)<sub>2</sub> (3.9 g, 12.5 mmol) afforded *Se,O*-heteroacetal **1a** (1.4 g, 45%). A solution of the *Se,O*-heteroacetal **1a** (0.36 g, 1.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (6 ml) was added dropwise to a solution of SnCl<sub>4</sub> (1.0 g, 4.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (14 ml) under an Ar atmosphere at -78 °C. The reaction mixture was stirred overnight and the temperature was gradually raised to room temperature. A saturated NaHCO<sub>3</sub> solution (150 ml) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried over MgSO<sub>4</sub>. The solvent was removed under reduced pressure. The residue was purified by the preparative TLC on silica gel eluting with AcOEt-hexane(1:3) to give keto alcohol **2a** (0.14 g, 62%) as a colorless oil. IR  $\nu$ : 3600-3200 (OH), 1720 (CO). <sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>)  $\delta$ : 1.12-1.27 (2H, m, alkyl H), 1.42-1.68 (4H, m, alkyl H), 2.01 (3H, s, Me), 2.72 (2H, d, *J*=7 Hz, COMe), 3.07-3.14 (1H, m, benzyl H), 3.54 (2H, t, *J*=6 Hz, CH<sub>2</sub>OH), 7.15-7.20 (3H, m, ArH), 7.21-7.31 (2H, m, ArH). <sup>13</sup>C NMR (100 MHz; CDCl<sub>3</sub>)  $\delta$ : 23.54 (t), 30.61 (d), 32.50 (t), 36.09 (t), 41.13 (d), 50.81 (t), 62.61 (t), 126.37 (d), 127.41 (d), 128.48 (d), 144.25 (s), 208.02 (s).
- 7) The *O,O*-acetals were prepared from olefinic alcohols and enol ethers in the presence of pyridinium *p*-toluenesulfonate.
- 8) **3b**: IR  $\nu$ : 1720 (CO). <sup>1</sup>H NMR (400 MHz; CDCl<sub>3</sub>)  $\delta$ : 1.16-1.96 (8H, m, alkyl H), 2.01 (3H, s, COMe), 2.64-2.76 (3H, m, benzyl H and CH<sub>2</sub>CO), 2.79-2.86 (1H, m, benzyl H), 3.07-3.14 (1H, m, benzyl H), 3.73-3.79 (1H, m, CHCl), 7.15-7.30 (10H, m, ArH). <sup>13</sup>C NMR (100 MHz; CDCl<sub>3</sub>)  $\delta$ : 24.29 (t), 30.67 (q), 32.63 (t), 35.74 (t), 38.30 (t), 40.16 (t), 40.98 (d), 50.84 (t), 62.91 (d), 126.00 (d), 126.48 (d), 127.43 (d), 128.44 (d), 128.49 (d), 128.55 (d), 141.13 (s), 144.09 (s), 207.77 (s). Anal. Found: C, 77.21; H, 8.14%. Calcd for C<sub>22</sub>H<sub>27</sub>ClO: C, 77.06; H, 7.94%. The structures of the other products were similarly determined by <sup>1</sup>H and <sup>13</sup>C NMR, IR and mass spectrometry.
- 9) W. L. Meyer, P. W. Taylor, S. A. Reed, M. C. Leister, H.-J. Schneider, G. Schmidt, F. E. Evans, and R. A. Levine, *J. Org. Chem.*, **57**, 291 (1992).

(Received June 1, 1993)