CHEMISTRY LETTERS, pp. 1491-1494, 1993.

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[1)]

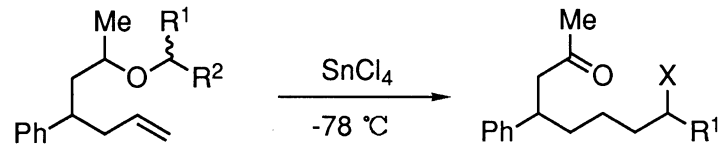
Mitsuhiro YOSHIMATSU, Noriyuki HATAE, Hiroshi SHIMIZU,
and Tadashi KATAOKA*
Gifu Pharmaceutical University, 6-1 Mitahora-higashi 5-chome, Gifu 502

Oxacyclooctyl (oxocanyl) carbenium ions generated by treatment of *O*-(5-hexenyl)-*Se*,*O*-heteroacetals or *O*,*O*-acetals with $SnCl_4$ underwent intramolecular 1,5-hydride transfer, and the α-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.[2)] Overman *et al.* have intensively studied not only the cyclization of iminium ions but also the cyclization of α-alkoxycarbenium ions.[3)] Very recently we reported the intramolecular cyclization of α-seleno carbenium ions generated by the selective C-O bond cleavage of the *Se*,*O*-heteroacetals.[4)] As part of our developing studies on this cyclization reaction, we have been studying the cyclization of the α-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 $SnCl_4$. 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.[5)] This paper describes that reactions of hexenyl *Se*,*O*-heteroacetals or *O*,*O*-acetals bearing no 5-trimethylsilyl group with $SnCl_4$ cause the 1,7-acetal carbon transfer to give 7-oxohexanols or 7-oxohexyl chlorides.

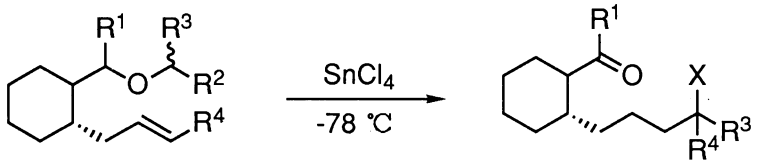
Treatment of ene-*Se*,*O*-heteroacetal **1a** with $SnCl_4$ (4 equiv.) in CH_2Cl_2 (0.15 M solution) at -78 °C under an Ar atmosphere afforded a keto alcohol **2a** in 62% yield.[6)] The structure of **2a** was determined by ^1H- and ^{13}C-NMR, IR and mass spectrometry. Other ene-*Se*,*O*-heteroacetals **4a-c**, **7a** and **10** similarly reacted with $SnCl_4$ 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 α-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**[7)] were prepared in order to cleave one of the C-O bonds site-selectively and allowed to react with $SnCl_4$. However, rearranged products, keto alcohols **2b-c** and keto chlorides **3b-c**[8)] were obtained in low yields. Some methoxy acetals **4d**, **e**, **7b**[7)] more smoothly



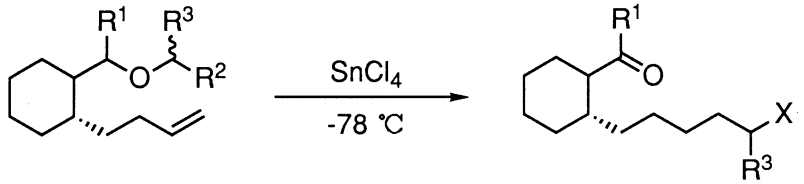
1a (R^1=H; R^2=SePh)
1b (R^1=CH_2CH_2Ph; R^2=OCH_2CH_2OMe)
1c (R^1=$(CH_2)_5CH_3$; R^2=OCH_2CH_2OMe)

2a (R^1=H; X=OH)(62%)
2b (R^1=CH_2CH_2Ph; X=OH)(25%)/
3b (R^1=CH_2CH_2Ph; X=Cl)(13%)
2c (R^1=$(CH_2)_5CH_3$; X=OH)(10%)/
3c (R^1=$(CH_2)_5CH_3$; X=Cl)(30%)



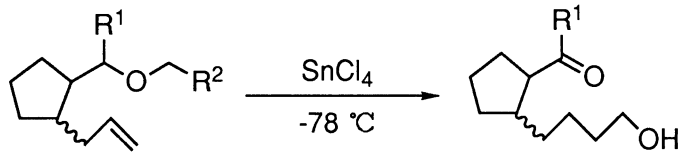
4a (R^1=R^3=R^4=H; R^2=SePh)
4b (R^1=Me; R^2=SePh; R^3=R^4=H)
4c (R^1=Me; R^2=SePh; R^3=H; R^4=*n*-Pr)
4d (R^1=R^4=H; R^2=OMe; R^3=Me)
4e (R^1=Me; R^2=OMe; R^3=CH_2CH_2Ph; R^4=H)

5a (R^1=R^3=R^4=H; X=OH)(63%)
5b (R^1=Me; R^3=R^4=H; X=OH)(93%)
5c (R^1=Me; R^3=H; R^4=*n*-Pr; X=OH)(94%)
5d (R^1=R^4=H; R^3=Me; X=OH)(67%)
6e (R^1=Me; R^3=CH_2CH_2Ph; R^4=H; X=Cl)
(60%)



7a (R^1=Me; R^2=H; R^3=SePh)
7b (R^1=Me; R^2=OMe; R^3=CH_2CH_2Ph)

8a (R^1=Me; R^3=H; X=OH) (quant.)
9b (R^1=Me; R^3=CH_2CH_2Ph; X=Cl)(65%)



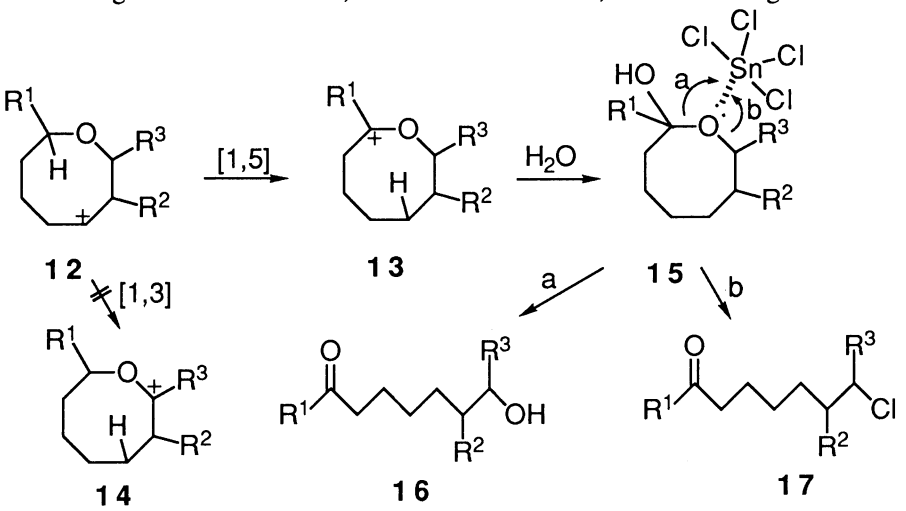
trans-**10** (R^1=Me; R^2=SePh)
cis-**10**

trans-**11**(R^1=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 $SnCl_4$ 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 transfered 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 α-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 β-hydrogen but the δ-hydrogen adjacent to the oxygen atom (1,5-hydride transfer) and changes into the α-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-$SnCl_4$ 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.[9] 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 α-position to the oxygen (R^1=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 $SnCl_4$. 4-Phenylhept-1-en-6-one was synthesized from benzalacetone, allyl trimethylsilane and $TiCl_4$ [G. Majetich, A. Casares, D. Chapman, and M. Behnke, *J. Org. Chem.*, **51**, 1745 (1986)]. Reduction of 4-phenylhept-1-en-6-one with $NaBH_4$ in EtOH gave 4-phenylhept-1-en-6-ol in quantitave yield. The alcohol (2.0 g, 11 mmol) was treated with NaH (0.5 g, 21 mmol) and Bu_3SnCH_2I (4.5 g, 13 mmol) in THF to give tributylstannane (4.2 g, 78%). Transmetallation of the tributylstannane with *n*-BuLi (12.5 mmol) followed by treatment with $(PhSe)_2$ (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_2Cl_2 (6 ml) was added dropwise to a solution of $SnCl_4$ (1.0 g, 4.0 mmol) in CH_2Cl_2(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 $NaHCO_3$ 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 $MgSO_4$. 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 ν: 3600-3200 (OH), 1720 (CO). ^{1}H NMR (400 MHz; $CDCl_3$) δ: 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_2OH), 7.15-7.20 (3H, m, ArH), 7.21-7.31 (2H, m, ArH). ^{13}C NMR (100 MHz; $CDCl_3$) δ: 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 ν: 1720 (CO). ^{1}H NMR (400 MHz; $CDCl_3$) δ: 1.16-1.96 (8H, m, alkyl H), 2.01 (3H, s, COMe), 2.64-2.76 (3H, m, benzyl H and CH_2CO), 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). ^{13}C NMR (100 MHz; $CDCl_3$) δ: 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), 128.49 128.55 (d), 141.13 (s), 144.09 (s), 207.77 (s). Anal. Found: C, 77.21; H,8.14%. Calcd for $C_{22}H_{27}ClO$: C, 77.06; H, 7.94%. The structures of the other products were similarly determined by ^{1}H and ^{13}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)