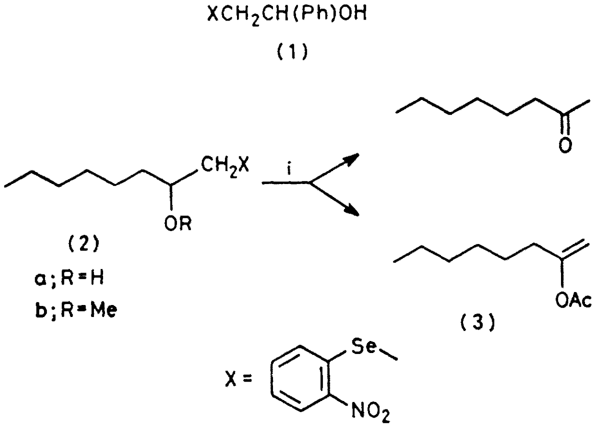
New Ketone Synthesis *via* β-Hydroxy *o*-Nitrophenyl Selenoxides; a One-step Synthesis of Deoxy-keto Sugars

By Kimiaki Furuichi, Sadamu Yogai, and Toshio Miwa*
(*Faculty of Science, Osaka City University, Osaka* 558, *Japan*)

Summary β-Hydroxy *o*-nitrophenyl selenides and their *O*-alkyl or *O*-acyl derivatives were prepared and converted into ketones or the corresponding enol derivatives in satisfactory yields; these reactions were applied to the synthesis of sugar derivatives.

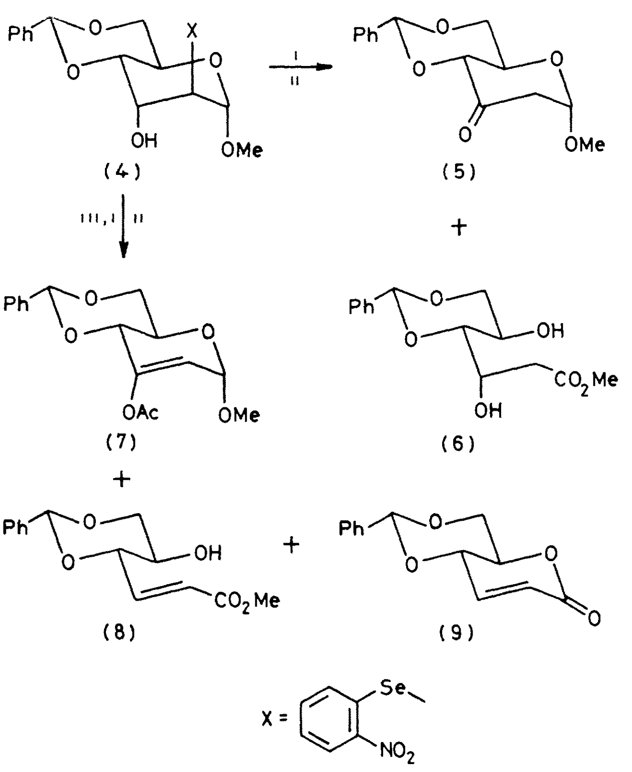
RECENTLY, many organoselenium compounds have been synthesised which effectively introduce many kinds of groups into organic molecules.[1] For example, β-hydroxy phenyl selenides were converted into olefins or allylic alcohols *via* selenoxides under mild conditions. When this method is applied to β-hydroxy phenyl selenides having an available hydrogen on the carbon atom bearing the hydroxy group, *cis*-elimination affords the enol form of ketones.[2] Here, we describe the results of studies on such eliminations using *o*-nitrophenyl selenoxides as intermediates.



Reagents: i, H_2O_2, $CHCl_3$.

Treatment of styrene oxide (7·93 mmol) with *o*-nitrophenyl selenocyanate (7·93 mmol) and sodium borohydride (8·83 mmol) in absolute ethanol (35 ml) at room temperature for 2 days under nitrogen[3] gave 2-(*o*-nitrophenylselenyl)-1-phenylethanol (**1**)† (m.p. 73—74 °C, 39%‡). Oxidation of (**1**) (1·0 g) with 30% hydrogen peroxide (5 equiv.) in dichloromethane (20 ml) under reflux for 1 h gave, with simultaneous elimination of *o*-nitrophenylselenous acid, acetophenone in 42% yield. Likewise, 1-(*o*-nitrophenylselenyl)octan-2-ol (**2a**) (m.p. 42—43 °C, obtained from oct-1-ene oxide in 87% yield) or its methyl ether (**2b**) [obtained from (**2a**) in 24% yield§ (NaOH, Me_2SO_4, H_2O, Me_2SO)] gave octan-2-one (30% H_2O_2–$CHCl_3$, reflux, 24 h, 45%). When the selenoxide of (**2a**) was isolated and heated at 100 °C (0·1 Torr), the yield of octan-2-one increased to 73%. With the acetate of (**2a**), oxidation (30% H_2O_2–$CHCl_3$, reflux, 6 h) and simultaneous elimination again took place to give 2-acetoxyoct-1-ene (**3**) (83%). However, similar selenides having unsubstituted phenyl groups were oxidized with hydrogen peroxide in boiling chloroform to give the corresponding oxides.

Application of this reaction to the synthesis of carbohydrate derivatives gave satisfactory results. Thus, treatment of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside[4] (2·72 mmol) with *o*-nitrophenyl selenocyanate (2·56 mmol) and sodium borohydride (2·56 mmol) in a mixture of dichloromethane (9 ml) and ethanol (3 ml) at room temperature for 6 h gave methyl 4,6-*O*-benzylidene-2-deoxy-2-*o*-nitrophenylselenyl-α-D-altropyranoside (**4**) ($[\alpha]_D^{18}$ = − 9·8°) in 30% yield§ after chromatography on silica. In contrast, methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside[4] was found to be unreactive towards the selenyl anion under the same conditions. Oxidation of (**4**) (30% H_2O_2–CH_2Cl_2, reflux, 30 min) gave, without elimination of selenous acid, the selenoxide in quantitative yield. Thermolysis of this selenoxide in toluene under reflux for 1·5 h, followed by chromatography on silica, gave two products, methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (**5**)[5] (m.p. 177—178 °C, $[\alpha]_D^{17}$ = + 133·8, 50%) and methyl 4,6-*O*-benzylidene-2-deoxy-D-*ribo*-hexonate (**6**) (m.p. 121—122 °C, $[\alpha]_D^{26}$ = − 52·1°, 16%). In the same way, the acetate of (**4**) was allowed to react under the above conditions to give three products, methyl-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hex-2-enopyranoside (**7**) (m.p. 123—124 °C, $[\alpha]_D^{17}$ = + 87·8°, 45%), methyl 4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hex-2-enonate (**8**) ($[\alpha]_D^{27}$ = − 44·0°, 17%), and 4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hex-2-eno-1,5-lactone (**9**) (m.p. 136—137 °C, $[\alpha]_D^{27}$ = + 33·0°, 22%). The structure of (**7**) was established by hydrolysis (K_2CO_3, MeOH) to



Reagents: i, H_2O_2, CH_2Cl_2; ii, toluene, reflux; iii, Ac_2O, pyridine.

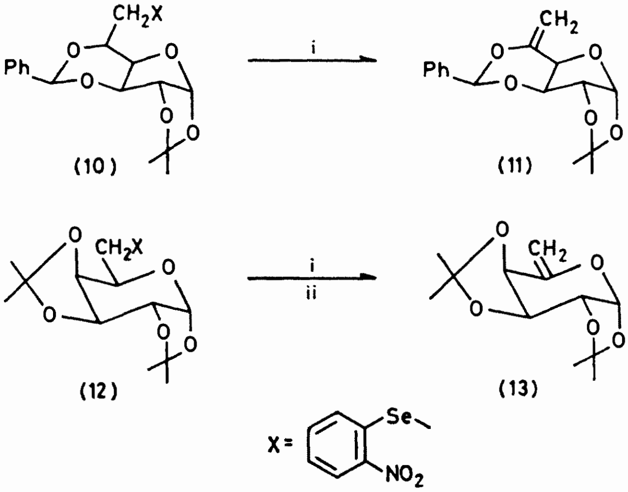
---

† All m.p.s are uncorrected. Optical rotations were measured in chloroform solution (*c* = 1). The i.r., ^1H, and ^{13}C n.m.r. spectra of new compounds were compatible with the assigned structures, and crystalline compounds gave satisfactory analytical data.

‡ 1-(*o*-Nitrophenylselenyl)-1-phenylethanol (m.p. 88—89 °C, 59%) was obtained along with (**1**).

§ In addition to the starting materials, selenides were obtained as products in each of the reactions.

the known ketone (**5**). The compounds (**6**), (**8**), and (**9**) are assumed to be formed *via* unstable intermediates produced by *cis*-elimination of the C-1 proton together with the selenoxy group.



Reagents: i, H_2O_2, CH_2Cl_2; ii, heat.

Another example of applying this reaction to carbohydrate chemistry is shown in the synthesis of 5,6-unsaturated sugar derivatives. Treatment of 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose with *o*-nitrophenyl selenocyanate and tri-n-butylphosphine in tetrahydrofuran[6] gave 3,5-*O*-benzylidene-6-deoxy-1,2-*O*-isopropylidene-6-*o*-nitrophenylselenyl-α-D-glucofuranose (**10**) (m.p. 147—148 °C, $[\alpha]_D^{15} = +28\cdot8°$, 85%), which was transformed directly to 3,5-*O*-benzylidene-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose[7] (**11**) (m.p. 126—128 °C, $[\alpha]_D^{15} = +68\cdot4°$ 72%) under mild conditions (30% H_2O_2–CH_2Cl_2, reflux, 30 min). Although selenation of 1,2:3,4-*O*-di-isopropylidene-α-D-galactopyranose with the same reagents[6] (45 °C, 12 h) gave the corresponding selenide (**12**) ($[\alpha]_D^{16} = -89\cdot3°$) in poor yield (24%§), 6-deoxy-1,2:3,4-*O*-di-isopropylidene-β-L-*arabino*-hex-5-enopyranose (**13**)[8] (m.p. 85—86 °C, $[\alpha]_D^{29} = -135\cdot8$, 85%) was obtained as sole product by oxidation of (**12**) (30% H_2O_2–CH_2Cl_2, reflux, 1 h), followed by sublimation of the resulting selenoxide at 90 °C (0·05 Torr).

(*Received*, 21*st September* 1979; *Com.* 1018.)

[1] D. L. J. Clive, *Tetrahedron*, 1978, **34**, 1049; H. J. Reich, *Accounts Chem. Res.*, 1979, **12**, 22.
[2] N. Zylber and J. Zylber, *J.C.S. Chem. Comm.*, 1978, 1084.
[3] K. B. Sharpless and M. W. Young, *J. Org. Chem.*, 1975, **40**, 947.
[4] R. L. Whistler and M. L. Wolform, 'Method in Carbohydrate Chemistry,' Academic Press, New York, 1963, vol. 2, p. 189.
[5] A. Klemer and G. Rodermeyer, *Chem. Ber.*, 1974, **107**, 2612; A. Rosental and P. Catsoulacos, *Canad. J. Chem.*, 1968, **46**, 2868; B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), 1966, 398.
[6] P. A. Greico, S. Gilman, and M. Nishizawa, *J. Org. Chem.*, 1976, **41**, 1485.
[7] A. S. Meyer and T. Reichstein, *Helv. Chim. Acta*, 1946, **29**, 139; N. Nakajima and S. Takahashi, *Agric. and Biol. Chem.* (*Japan*), 1967, **31**, 1709.
[8] B. Helferich and E. Himmem, *Ber.*, 1929, **62**, 2136; G. Descotes, A. Faure, and J. C. Martin, *J. Carbohydrates, Nucleosides, Nucleotides*, 1974, **1**, 133.