

A METHOD FOR EASY PREPARATION OF OPTICALLY PURE (S)-5-HYDROXY-2-PENTEN-4-OLIDE AND (S)-5-HYDROXPENTAN-4-OLIDE

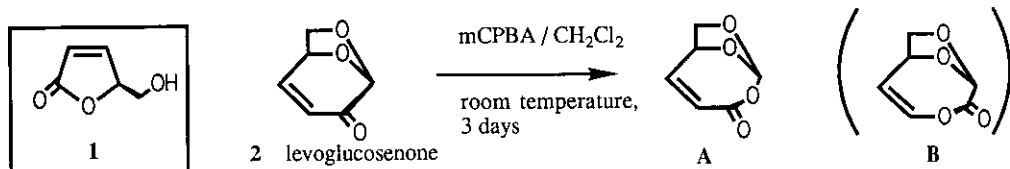
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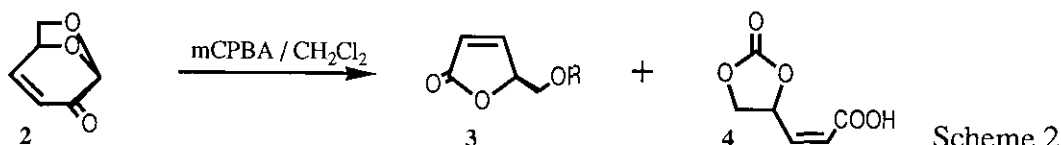
Abstract — A new method for preparation of (S)-5-hydroxy-2-penten-4-olide **1** and (S)-5-hydroxypentan-4-olide **8** starting from levoglucosenone **2** is described.

(S)-5-Hydroxy-2-penten-4-olide **1** is a very useful chiral source for synthesizing natural products because of its highly functionalized structure containing one chiral center.¹ Despite several syntheses of **1**² being known, an efficient method to produce a large quantity has been unknown. In this paper, we report a new method for convenient preparation of **1** from levoglucosenone **2**.³ As can be seen from Scheme 1, levoglucosenone **2** has an adequate functionalized framework for this purpose with the exception of one carbon atom.

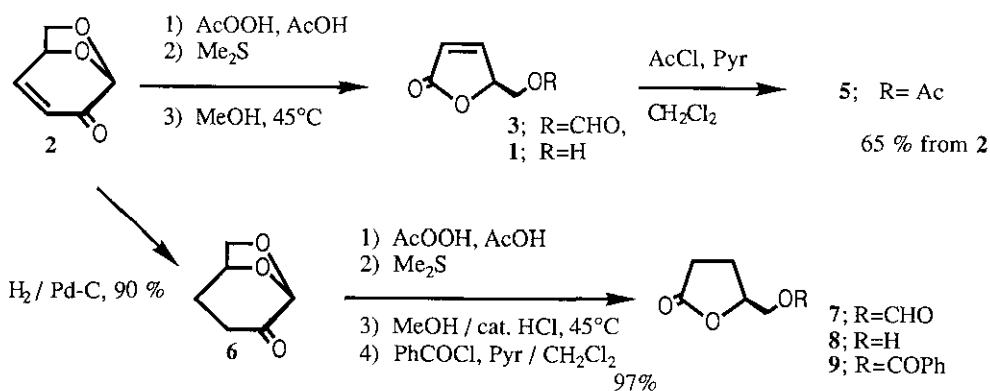


Scheme 1

Shafizadeh et al.⁴ has previously reported the Baeyer Villiger oxidation of **2** with mCPBA. They suggested that the oxidation product was not **B** but **A** based on uv and ir spectral data. We noted that this lactone **A** was a good precursor of **1**. We proceeded by investigating the Baeyer Villiger oxidation of **2** carefully and in detail.



The result showed that the formic ester **3**⁵ was the main product (59 %) when Shafizadeh's procedure was used. In addition, carbonate **4**⁶ was obtained as a minor product (16 %) (Scheme 2). To avoid a complicated oxidation process, other peracids were examined. The best result was obtained by using peracetic acid, and a new preparation method of the butenolide **1** was established (Scheme 3).



A typical procedure is as follows: To a solution of levoglucosenone **2** (15 g, 119 mmol) in acetic acid (60 ml), 1.2 molar equivalent peracetic acid (ca. 40 % in acetic acid) was added over 30 min. The mixture was stirred for 2 days at room temperature. Dimethyl sulfide (1.4 ml, 19 mmol) was added to the mixture. After 1 h, the reaction mixture was concentrated in vacuo. The residue contained butenolide **1** and a small quantity of formate **3** (about 10%). To the residue methanol (50 ml) was added and the mixture was stirred overnight at 45°C in order to convert the formate **3** into the free (*S*)-5-hydroxy-2-penten-4-olide **1** completely. If necessary, a small amount of HCl could be added to the mixture.

The methanol solution was concentrated in vacuo and butenolide **1** was obtained as brown oil.⁷ The nmr analysis of this crude **1** showed only a single product. The optical rotation value of the corresponding acetate **5**⁸ indicates its high optical purity. The total yield from **2** was 65 %.

This method was also applied to the preparation of (S)-5-hydroxypentan-4-olide **8**. The oxidation of the dihydrolevoglucosenone **6**⁹ proceeded very fast. The excellent efficiency of this procedure was demonstrated in the high total yield (87 %) of **9** from **2**.¹⁰

ACKNOWLEDGEMENT

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3. IUPAC name is 1,6-anhydro-3,4-dideoxy- β -D-glycero-hex-3-enopyranos-2-ulose. Y. Halpern, R. Riffer, and A. Broid, J. Org. Chem., 1973, **38**, 204 ; levoglucosenone **2** is available from Yuki Gosei Kogyo Co., Ltd.
4. F. Shafizadeh, R. H. Hurneaux, and T. T. Stevenson, Carbohydr. Res., 1979, **71**, 169 .
5. bp 85~90°C/0.5 torr.; $n_D=1.4743$ (23°C); $[\alpha]_D -125^\circ$ (c 1.18, 23°C, CHCl₃); ir (film) ν cm⁻¹ 3495, 3105, 2960, 1760, 1725, 1605, 1165, 1110(s); uv λ max(95% EtOH) 208 nm, ϵ 6300 and 258 nm, ϵ 210; hrms calcd for C₆H₆O₄, 142.0266, found 142.0270; ¹H-nmr (CDCl₃, 300 MHz): δ 4.49(2H, m), 5.27(1H, m), 6.35(1H, dd, J=2.2, 5.7 Hz), 7.45(1H, dd, J=1.6, 5.7 Hz), 8.15(1H, br s); ¹³C-nmr (CDCl₃, 75 MHz): δ 61.8, 80.2, 123.6, 131.8, 151.9, 160.1. Formate **3** was synthesized by P. Camps, J. Cardellach, J. Font, R. M. Ortuno, and O. Ponsati, Tetrahedron, 1982, **38**, 2395.
6. Ir (film) ν cm⁻¹ 3400, 1720, 1650(s); ¹H-nmr (CDCl₃, 300 MHz): δ 4.18(1H, dd, J=7.3, 8.8 Hz), 4.92(1H, dd, J=8.5, 8.8 Hz), 6.03(1H, dddd, J=2.0, 5.8, 7.3, 8.5 Hz), 6.08(1H, dd, J=2.0, 11.4 Hz), 6.63(1H, dd, J=5.8, 11.4 Hz). Me ester of **4**; $[\alpha]_D -178^\circ$ (c 2.26, 23°C, CHCl₃); ¹³C-nmr (CDCl₃, 75 MHz): δ

57.1, 75.3, 79.9, 127.9, 151.1, 160.3, 171.2.

7. Ir (film) ν cm^{-1} 3450, 1750, 1600; ^1H -nmr (CDCl_3 , 300 MHz): δ 3.80(1H, dd, $J=5.0$, 12.2 Hz), 4.00(1H, dd, $J=3.8$, 12.2 Hz), 5.17(1H, m), 6.22(1H, dd, $J=2.1$, 5.7 Hz), 7.50(1H, dd, $J=1.5$, 5.7 Hz).
8. bp $96^\circ\text{C}/0.3$ torr; $[\alpha]_D -126^\circ$ (c 3.56, 23°C , CHCl_3) ($[\alpha]_D -123.6^\circ$ (c 3.68, 20°C , CHCl_3) was reported in ref.[5]); ir (film) ν cm^{-1} 1740(s), 1600(w), 1230(s); ^1H -nmr (CDCl_3 , 300 MHz): δ 2.08(3H, s), 4.35(2H, m), 5.25(1H, m), 6.23(1H, dd, $J=2.1$, 5.8 Hz), 7.45(1H, dd, $J=1.6$, 5.8 Hz).
9. IUPAC name, 1,6-anhydro-3,4-dideoxy- β -D-glycero-hexopyranos-2-ulose. F. Shafizadeh and P. S. Chin, Carbohydr. Res., 1977, **58**, 79.
10. Dihydrolevoglucosenone **6** (7.32 g, 57.2 mmol) in acetic acid (25 ml) was treated with 40% peracetic acid (8 ml) below 30°C for 1 h. After the mixture was stirred for 1 h at room temperature, dimethyl sulfide (0.23 ml) was added and the mixture was stirred for an additional 20 min. The solvent was evaporated in vacuo. The crude butyrolactone was treated with MeOH (50 ml) and conc. HCl (2 ml) overnight at 45°C . The solvent was evaporated in vacuo to provide **8** (6.7 g); ir ν cm^{-1} 3400, 2950, 1770, 1180, 1060; ^1H -nmr (CDCl_3 , 300 MHz): δ 2.1~2.35(2H, m), 2.5~2.7(2H, m), 3.65(1H, dd, $J=4.0$, 12.0 Hz), 3.92(1H, dd, $J=3.2$, 12.0 Hz). The 5-benzoate **9** (12.2 g, 97.3 % yield) was obtained from **8** (6.7 g), benzoyl chloride (8.85 g) and pyridine (70 ml); mp $60\sim60.5^\circ\text{C}$; $[\alpha]_D +49.7^\circ$ (c 1.03, 25°C , EtOH); ir (film) ν cm^{-1} 1780, 1730(sh); ^1H -nmr (CDCl_3 , 300 MHz): δ 2.15 (1H, m), 2.45(1H, m), 2.63(2H, m), 4.44(1H, dd, $J=5.3$, 12.3 Hz), 4.55(1H, dd, $J=3.2$, 12.3 Hz), 4.90(1H, m), 7.45(2H, t, $J=7.5$ Hz), 7.59(1H, t, $J=7.5$ Hz), 8.03(2H, d, $J=7.5$ Hz). M. Taniguchi et al. (ref.[1]) synthesized **9** and reported $[\alpha]_D +48.2^\circ$; mp $59\sim60.5^\circ\text{C}$.

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