Synthesis of Chiral 4,5-Dihydroxy-2-Pentenal Derivatives from D-Ribose

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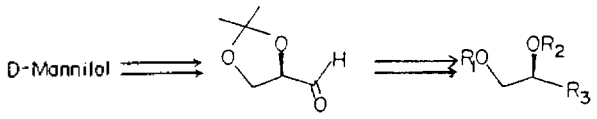
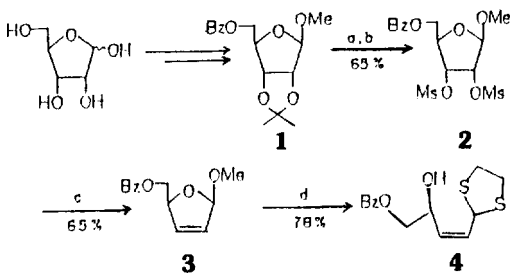
Received June 29, 1987

D-Ribose is the source of chiral intermediates which can be utilized for the synthesis of chiral natural products such as streptolidine[1], leukotriene C-1[2], pseudomonic acid[3], etc.

As part of our efforts toward the synthesis of leukotriene intermediate from D-ribose, a new method for the preparation of (S)-4,5-dihydroxy-2-pentenal derivatives was found. Conventionally these were synthesized from D-glyceraldehyde acetonide[4]. Therefore in this case it is necessary to remove acetonide group to free dihydroxyl group and manipulate one of dihydroxyl group in order to utilize it for further transformation.



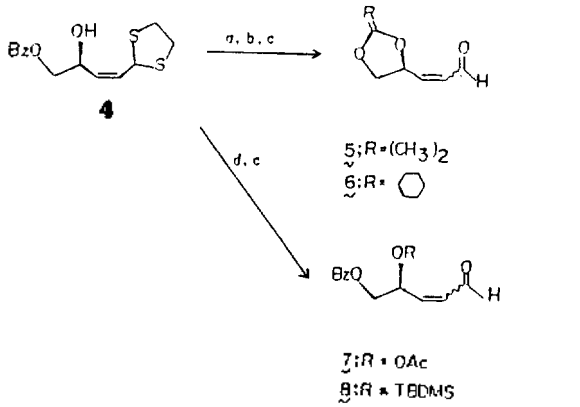
In contrast, our approach was the initial protection of primary hydroxyl group and exposure of secondary hydroxyl group after series of chemical transformation of a D-ribose ring. Our synthetic pathway was based on the conversion of dihydroxyl groups to cis-double bond and the conversion of cyclic acetal to acyclic dithioacetal derivative as depicted in Scheme 1.



Reagents: (a) 50% CH_3COOH, 70°C, 6hrs; (b) MsCl, Pyridine, rt, 16 hrs; (c) NaI, Zn, DMF, reflux, 2hrs; (d) $HS(CH_2)_2SH$, $BF_3.Et_2O$, 0-5°C, 5min.

Scheme 1

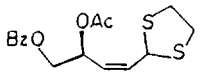
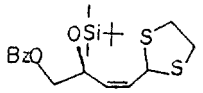
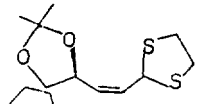
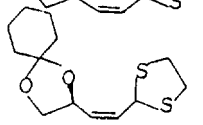
D-Ribose was easily derivatized to the acetonide, which was subsequently converted to benzoate **1**. The removal of acetonide group was performed in 50% aqueous acetic acid at 70°C for 6 hrs to afford 82% yield of cis-diol. This vicinal cis-diol was transformed to dimesylate **2** by treatment with mesyl chloride in pyridine at room temperature in 91% yield. Although in general reaction of cis-dimesylate with NaI has been known to give relatively low yield compared with that of trans compound and from cis-diol the alkene was better prepared via ortho ester[5] or thionocarbonate[6], we could manage to obtain 65% of isolated yield of alkene from cis-dimesylate by employing NaI and Zn in DMF[7]. The use of DMF dried over 3 Å molecular sieves was found to be critical in this reaction. Wet DMF always gave poor yields. The resulting dihydrofuran **3** was so labile that it was easily converted to furan ring with elimination of methanol in the presence of trace amount of acid. Thus this cyclic acetal was converted directly to acyclic 1,3-dithiol without conversion to hemiacetal. Employing the ratio of 1 equivalent of $BF_3 \cdot Et_2O$ to ethanedithiol in anhydrous dichloromethane we could get 78% yield of the desired dithioacetal **4**.



Reagents: (a) K_2CO_3, MeOH, rt, 30min; (b) **5**; $(CH_3)_2C(OMe)_2$, **6**; , p-TsOH, CH_2Cl_2, rt, 2hrs; (c) $HgCl_2$, HgO, 80% CH_3CN, reflux, 50min.

Scheme 2

Table 1.

Entry	1,3-Dithiole	Ratio of products[a] E/Z	Isolated yield
1		5:1	62%
2		1:1.5	84%
3		1:1.5	46%
4		1:1.5	73%

[a] Ratios determined by 80 MHz ^1H NMR.

The next steps in the sequence were the protection of free secondary hydroxyl group and oxidative cleavage of dithiol to aldehyde. However in order to confirm the streochemistry of secondary alcohol, the benzoate group was removed and the resulting diol was converted to acetonide. Consequently dithioacetal was converted to aldehyde **5** by treatment with 1.1 equivalent of HgO and 2.2 equivalent of $HgCl_2$. Although the chirality at the secondary hydroxyl group was conserved, the isomerization of double bond gave a mixture of Z/E iso-

mers. (Scheme 2). The predominant isomer was separated by chromatography on SiO_2 and its ^1H NMR showed the presence of trans-double bond (J = 15 Hz). This aldehyde was further reduced to the previously known trans-allylic alcohol with $[\alpha]_D^{17} = 33.8°$ ($CHCl_3$, c = 2.28)[8].

This isomerization prompted us to prepare several derivatives and examine the ratio of E/Z isomers of the corresponding aldehydes **6-8**. The results are exhibited in Table 1. When we used CH_3I instead of $HgO/HgCl_2$ in order to circumvent the metallic effect, we could obtain exclusively thermodynamically stable trans-aldehyde. Currently we are looking for the reactions which can furnish the exclusive generation of E isomers.

References and Notes

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2. E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Samuelsson, and S. Hammarstrom, *J. Am. Chem. Soc.*, **102**, 1436 (1980).
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5. S. Hanessian, A. Bargiotti, and M. Larue, *Tetrahedron Lett.*, 737 (1978) and mp of the elimination product was identical with this reference value. mp 62-63°C.
6. E. J. Corey and J. I. Shulman, *Tetrahedron Lett.*, 3655 (1968).
7. (a) R. S. Tipson and A. Cohen, *Carbohydr. Res.*, **1**, 338 (1965). (b) H. R. Schuler and K. N. Slessor, *Can. J.* Chem., **55**, 3280 (1977). (c) S.-Y. Chen and M. M. Joullie, *J. Org. Chem.*, **49**, 1769 (1984).
8. The trans allyl alcohol was prepared according to the method reported by N. Minami, S. S. Ko and Y. Kishi (*J. Am. Chem. Soc.* **104**, 1109 (1982)) and also it was further converted to aldehyde by Swern oxidation in order to confirm Z-**5**.

Synthesis of Cationic Rhodium(I) Complex of But-2-en-1-ol

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Reactions of $Rh(ClO_4)(CO)(PPh_3)_2$ (**1**) with unsaturated nitriles,[1] aldehydes[2] and esters[3] (L) produce four coordinated cationic rhodium(I) complexes, $[Rh(L)(CO)(PPh_3)_2]ClO_4$ which are catalytically active for isomerization, oligomerization and hydrogenation of L. Complex **1**[4] and $[Rh(CO)(PPh_3)_3]ClO_4$[5] catalyze various reactions of unsaturated alcohols. Accordingly, we launched an investigation into the rhodium complexes presented in the reaction mixtures of **1** and unsaturated alcohols, and we now wish to report a new cationic rhodium(I) complex, $[Rh(CH_3CH=CHCH_2OH)(CO)(PPh_3)_2]ClO_4$ (**2**) where $CH_3CH=CHCH_2OH$ (**3**) is coordinated through the oxygen atom but not through the olefinic group. To our knowledge, no metal complexes of unsaturated alcohols coordinated through the oxygen atom have been reported before while some metal complexes of unsaturated alcohols coordinated through the olefinic group have been reported.[6,7]

Addition of **3** (mixture of *cis* and *trans* isomers) into the benzene solution of **1** immediately results in precipitation of yellow micro-crystals of **2** (eq. 1). Attempts to prepare the similar complexes of the other unsaturated alcohols (prop-2-en-1-cl, 2-methylprop-2-en-1-ol, but-3-en-1-ol, but-2-en-2-ol, 3-methylbut-2-en-1-ol) have not been successful thus far

$$\underset{\mathbf{1}}{Rh(ClO_4)(CO)(PPh_3)_2} + \underset{\mathbf{3}}{CH_3CH=CHCH_2OH} \longrightarrow \underset{\mathbf{2}}{[Rh(CH_3CH=CHCH_2OH)(CO)(PPh_3)_2]ClO_4} \quad (1)$$

whereas the reaction of 3-phenylprop-2-en-1-ol with **1** produces a rhodium (I) complex of an unsaturated aldehyde, $[Rh(C_6H_5CH=CHCHO)(CO)(PPh_3)_2]ClO_4$ apparently *via* dehydrogenation of 3-phenylprop-2-en-1-ol.[4]

Table 1. Spectral and Conductivity Data for $[Rh(CH_3CH=CHCH_2OH)(CO)(PPh_3)_2]ClO_4$ (2)

compound	electronic absorption, nm (ε)[a]		
2[b]	350 (3820)		
	infrared absorption, cm^{-1}[c]		
compound	ν(O-H)	ν(C=C)	ν(C≡O)
$CH_3CH=CHCH_2OH$[b]	3325	1675	
2[b]	3205	1667	1994
compound	proton NMR, ppm[d]		
$CH_3CH=CHCH_2OH$[b]	1.70(m, CH_3), 2.31 (s, OH),[e] 4.09 (m, CH_2), 5.70 (m, CH=CH)		
2[b]	1.60 (m, CH_3), 3.51 (s, OH),[f] 3.29 (m, CH_2), 5.20 (m, CH=CH), 7.50 (m, $P(C_6H_5)$)		
compound	molar conductivity, $ohm^{-1}\ cm^2\ mol^{-1}$[g]		
$(n\text{-}Bu)_4NClO_4$	34		
2[b]	33		

[a] In CH_2Cl_2. [b] *cis* and *trans* isomers. [c] In Nujol. [d] In $CDCl_3$ under nitrogen at 25°C at 60 MHz. Chemical shifts are relative to Me_4Si. [e] One drop of $CH_3CH=CHCH_2OH$ in 0.4 ml of $CDCl_3$. chemical shift varies depending on the concentration of $CH_3CH=CH_2OH$ [f] 7.5×10^{-5} mole of **2** in 0.4 ml of $CDCl_3$. Chemical shift varies depending on the concentration of **2**. [g] $[(n\text{-}Bu)_4NClO_4] = [Rh] = 4.4 \times 10^{-4}$ M in CH_2Cl_2 at 25°C.

Spectral and conductivity data (Table 1) unambiguously indicate that complex **2** is a four coordinated cationic rho-