A SIMPLE SYNTHESIS OF (R)-GLYCEROL ACETONIDE FROM ASCORBIC ACID

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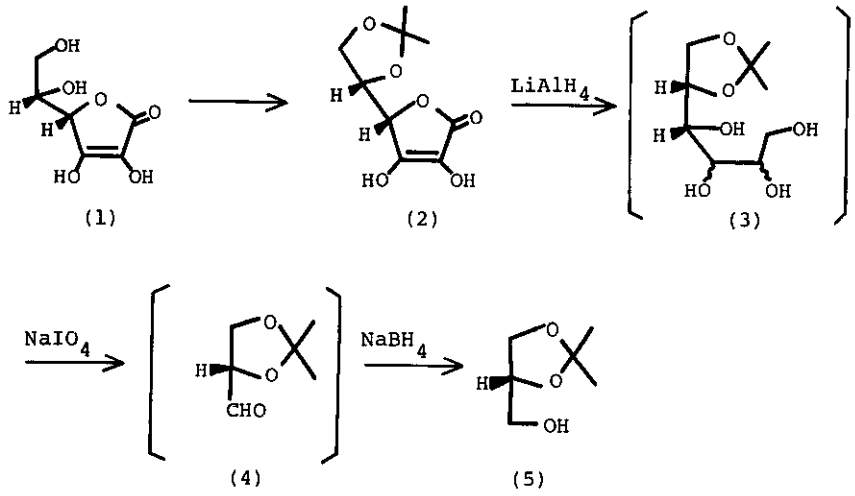
Abstract-----A simple synthesis of (R)-glycerol acetonide(5) has been developed using (L)-ascorbic acid(1) as a chiral precursor.

Recent developments in the total synthesis of optically active natural products call for efficient preparation of both (S)- and (R)-enantiomers of glycerol acetonide as versatile chiral precursors[1]. Of the enantiomers, the (S)-isomer is readily available, but acquisition of the (R)-counterpart(5) is very difficult because of unavailability of a suitable chiral progenitor[2]. Recently, Jung and Shaw[1c] have developed an ingenious method for the preparation of the (R)-isomer(5) using (L)-ascorbic acid acetonide(2) obtained easily from a readily available chiral precursor, (L)-ascorbic acid(1). However the method involved so tedious manipulations that it can hardly be applicable to a large scale preparation. We report here an improved one-pot procedure for the preparation of (R)-glycerol acetonide(5) from (L)-ascorbic acid acetonide(2) which allows a larger scale production employing much simpler experimental conditions. The present procedure consists of the following sequences in the same flask: (i) reduction of the all carbonyl groups contained in the acetonide(2), (ii) oxidative cleavage of all the vicinal glycols of the reduction product(3), (iii) reduction of (S)-glyceraldehyde acetonide(4) formed.

To a stirred suspension of $LiAlH_4$[3](2.85 g, 75 mmol) in THF(100 ml) was added freshly prepared (L)-ascorbic acid acetonide(2)[1c](13.5 g, 62.5 mmol) in portions under the current of argon at 0°C and the mixture was then refluxed for 2 h until hydrogen evolution ceased. The cooled reaction mixture was treated with minimum amount of saturated aqueous NaCl to decompose remaining $LiAlH_4$. To the brown suspension was added saturated aqueous $NaIO_4$ solution(43.0 g, 200 mmol) dropwise with vigorous stirring at 0°C. After 1 h, a suitable amount of methanol was added to the mixture in order to facilitate stirring and the resulting colorless slurry was treated with $NaBH_4$(9.5 g, 250 mmol) at 0°C. After being stirred for 1 h at the

same temperature, the mixture was filtered by suction through a bed of Celite. The filtrate was evaporated in vacuo and the residue was extracted with ethyl acetate, dried over sodium sulfate, and evaporated in vacuo. The residual oil was distilled using a Kugelrohl to give pure (R)-glycerol acetonide(5)[4](2.41 g, 29.2 %), bp 110°C(20 mmHg)(lit.[5] 86-87°C(16 mmHg) for opposite enantiomer), $[\alpha]_D$ -11.17°(c= 5.148, MeOH)(lit.[1c] $[\alpha]_D$ -10.76°).



(1) (2) (3) (4) (5)

REFERENCES AND NOTES

1. Recent examples: (a) (+)-Brefeldin A: T. Kitahara, K. Mori, and M. Matsui, Tetrahedron Lett., 3021(1979), (b) (-)-ipsdienol: K. Mori, T. Takigawa, T. Matsuo, Tetrahedron, 35, 933(1979), (c) (-)-GABOB(γ-Amino-β-hydroxybutyric acid): M.E. Jung and T.J. Shaw, J. Am. Chem. Soc., 102, 6304(1980), (d) (-)-mesembrine: S. Takano, Y. Imamura, and K. Ogasawara, Tetrahedron Lett., 22, 4479(1981).
2. See, ref. 1c.
3. Increasing amount of $LiAlH_4$ did not effect the overall yield of (5): 2.0 equimol-26.0 %($[\alpha]_D$ -11.10°(c=4.236, MeOH)); 3.0 equimol-29.6 %($[\alpha]_D$ -11.17° (c=5.215, MeOH)).
4. The compound was identical(IR, ^{1}H-NMR, MS) with an authentic specimen of the opposite configuration prepared from (D)-mannitol[5].
5. S. Takano, E. Goto, M. Hirama, and K. Ogasawara, Heterocycles, 16, 381(1981).

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