

STEREODIVERGENT SYNTHESIS OF 1,3-POLYOLS

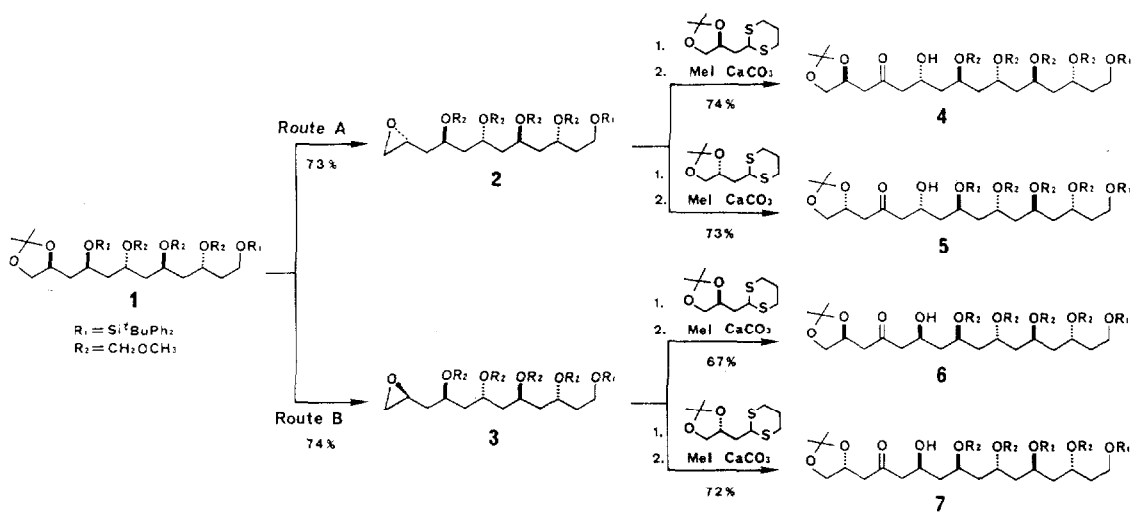
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Summary: A method for the stereoselective synthesis of 1,3-polyols containing both *anti*- and *syn*-1,3-diol units based on a 1,3-*syn*-stereoselective reduction is reported.

Recent stereochemical studies on polyene macrolide antibiotics demonstrated the presence of both *anti*- and *syn*-1,3-diol units in a polyhydroxylated chain.<sup>1)</sup> Therefore, development of an efficient synthesis for stereochemically defined 1,3-polyols is a prerequisite for structural and synthetic studies. We have developed highly stereocontrolled methods for preparing *syn*-1,3- and *anti*-1,3-polyols based on *syn*-1,3-asymmetric reduction of  $\beta$ -alkoxy  $\beta'$ -hydroxy ketones.<sup>2, 3)</sup> In this letter we would like to report an efficient stereodivergent synthesis of 1,3-polyols which contain both *anti*- and *syn*-1,3-diol units in a polyol chain.

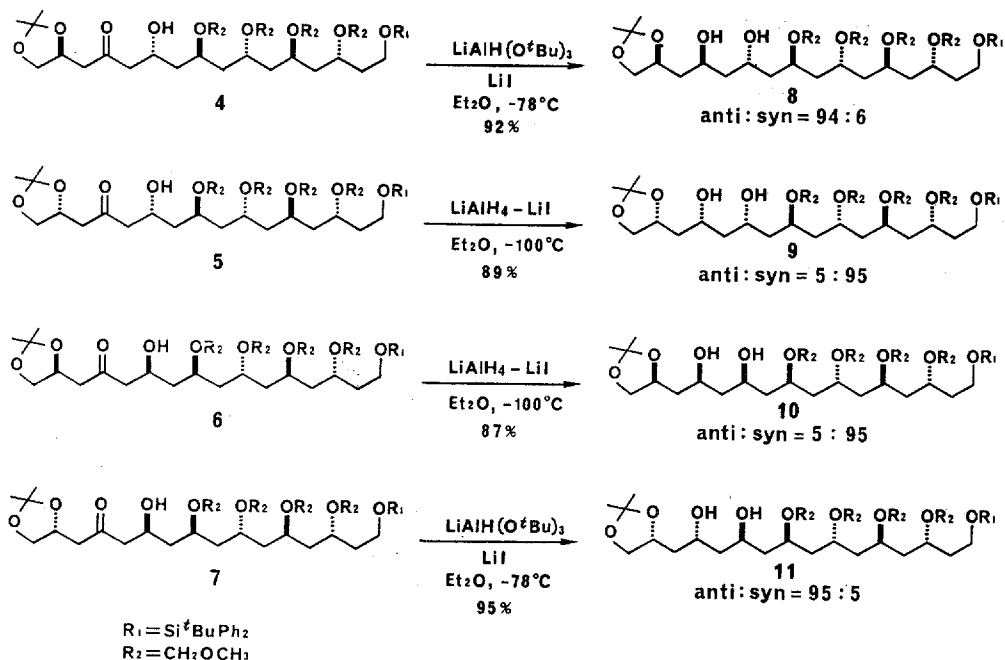
Our approach utilizes an *anti*-polyol derivative (1),  $[\alpha]_D^{24} +0.63^\circ$  (CHCl<sub>3</sub>), which was prepared by the method developed in our laboratory.<sup>3)</sup> The terminal dioxolane group of (1) was converted to the epoxides (2),  $[\alpha]_D^{25} -1.24^\circ$  (CHCl<sub>3</sub>), and (3),  $[\alpha]_D^{25} -7.22^\circ$  (CHCl<sub>3</sub>), by the routes A and B, respectively. The epoxides (2) and (3) are good precursors for higher homologs and introduction of enantiomeric C<sub>4</sub> units could lead to stereochemically divergent 1,3-polyols.



Route A 1. PPTS, MeOH 2. <sup>t</sup>BuCOCl, Py 3. MsCl, Et<sub>3</sub>N 4. MeOK

Route B 1. PPTS, MeOH 2. TsCl, Py 3. MeOK

$R_1 = \text{Si}^t\text{BuPh}_2$   
 $R_2 = \text{CH}_2\text{OCH}_3$



In fact, couplings of the epoxides (2) and (3) with the anions of the enantiomeric dithianes prepared by the treatment of  $^n\text{BuLi}$  (THF,  $-30^\circ\text{C}$ , 2h and then  $-20^\circ\text{C}$ , 24h) gave dithioacetals, which were deprotected with  $\text{MeI}-\text{CaCO}_3$  in 80% aqueous  $\text{MeCN}$ , yielding the four  $\beta$ -alkoxy  $\beta'$ -hydroxy ketones (4), (5), (6), and (7),<sup>4)</sup> respectively. We already realized a  $\beta$ -alkoxy-induced syn-1,3-asymmetric reduction of  $\beta$ -alkoxy  $\beta'$ -hydroxy ketones<sup>2, 3)</sup>;  $\text{LiAlH}(\text{O}^t\text{Bu})_3$ -LiI reduction is suited for the ketones (4) and (7) with anti-relationship of alkoxy and hydroxy groups, whereas  $\text{LiAlH}_4$ -LiI reduction for the ketones (5) and (6) with syn-relationship. Reduction of the ketones (4), (5), (6), and (7) with these reducing agents gave the 1,3-polyols (8), (9), (10), and (11),<sup>5)</sup> respectively, in good yield with excellent anti:syn ratios.

Since the present technology could provide facile access to 1,3-polyols by the combinations of chiral epoxides, enantiomeric dithianes, and reducing agents of  $\text{LiAlH}_4$ -LiI and  $\text{LiAlH}(\text{O}^t\text{Bu})_3$ -LiI, the flexibility of the above sequence in preparing any desired stereochemical combination is considerably enhanced.

#### References and notes

- (a) S. L. Schreiber and M. T. Goulet, *J. Am. Chem. Soc.*, **109**, 8120 (1987). (b) J. Pawlak, K. Nakanishi, T. Iwashita, and E. Borowski, *J. Org. Chem.*, **52**, 2896 (1987).
- (a) Y. Mori, M. Kuhara, A. Takeuchi, and M. Suzuki, *Tetrahedron Lett.*, **29**, 5419 (1988). (b) Y. Mori, A. Takeuchi, H. Kageyama, and M. Suzuki, *Tetrahedron Lett.*, **29**, 5423 (1988).
- Y. Mori and M. Suzuki, preceding communication of this issue.
- 4:  $[\alpha]_D^{25} +3.15^\circ$  (c 1.0,  $\text{CHCl}_3$ ); 5:  $[\alpha]_D^{25} -3.42^\circ$  (c 1.0,  $\text{CHCl}_3$ ); 6:  $[\alpha]_D^{25} +7.95^\circ$  (c 1.0,  $\text{CHCl}_3$ ); 7:  $[\alpha]_D^{25} +1.08^\circ$  (c 1.0,  $\text{CHCl}_3$ ).
- 8:  $[\alpha]_D^{25} +7.88^\circ$  (c 0.68,  $\text{CHCl}_3$ ); 9:  $[\alpha]_D^{25} +5.08^\circ$  (c 0.92,  $\text{CHCl}_3$ ); 10:  $[\alpha]_D^{25} +1.89^\circ$  (c 0.8,  $\text{CHCl}_3$ ); 11:  $[\alpha]_D^{25} +1.82^\circ$  (c 0.5,  $\text{CHCl}_3$ ).

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