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Studies on the Synthesis of Olivin: Diastereoselective Synthesis of a Functionalized D-Fucose Derivative

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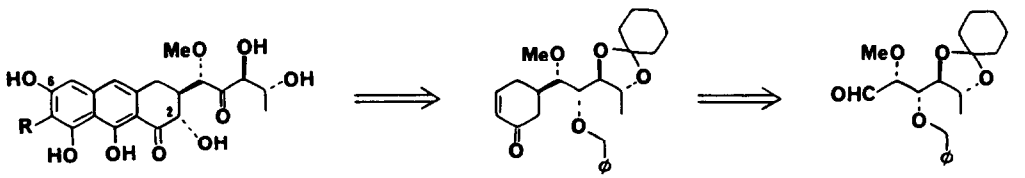
Abstract. A short, highly diastereoselective synthesis of D-fucose derivative 4 by a route involving the addition of allylboronate reagent 7 to aldehyde 6 is described.

The aureolic acid group of antitumor antibiotics is a class of complex polysaccharides based on two aglycones, olivin (1) and chromomycinone (2).[2] Each of the naturally occurring antibiotics possess a disaccharide at the C.6 phenolic hydroxyl group and a trisaccharide attached to C.2-OH. Certain members of this group, including aureolic acid itself, have found application in the clinical treatment of human cancers.[2,3]

We are currently exploring an approach to 1 based on the sequence 4 → 3 → 1.[4] Towards this end we describe herein a short, highly diastereoselective synthesis of D-fucose deri-



1 R = H
2 R = CH_3

3

4

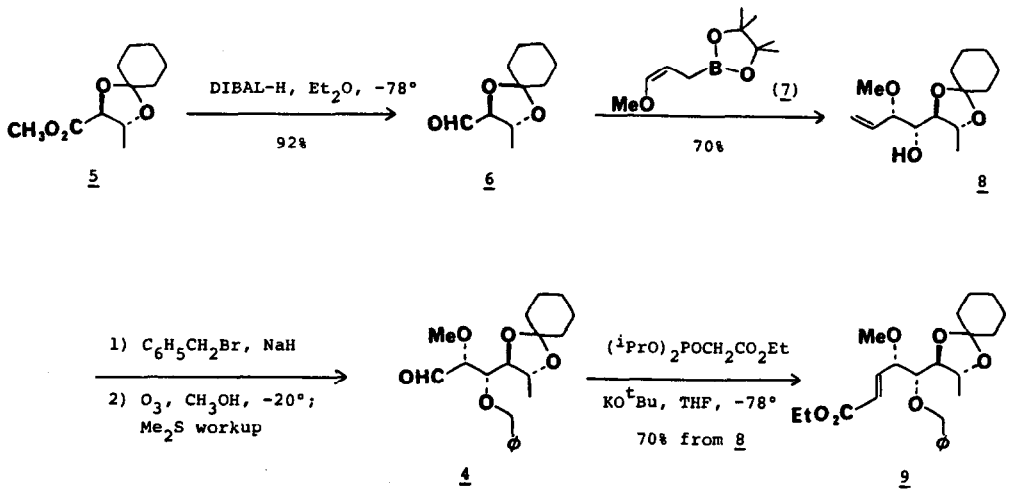
vative 4. This accomplishment has bearing not only on our approach to olivin, but also on the general problem of carbohydrate synthesis.

A renaissance of interest in the chemical synthesis of carbohydrates and functionalized monosaccharides has occurred in recent years.[5] A conceptually simple approach to carbohydrate derivatives involves the addition of a synthetic equivalent of an allyl-ether anion to an aldehyde.[6] Although recent publications from a number of laboratories have reported such transformations with achiral aldehydes,[7] with one exception[5e] the issue of aldehyde diastereofacial selectivity (i.e., the Cram-anti-Cram addition problem)[8] has not been addressed.

Reduction of ester 5 (available by three steps from L-threonine)[9] with 2.5 equiv of DIBAL-H in Et_2O (-78°C; H_2O quench) afforded a hydrate[4e] which was dehydrated (CH_2Cl_2, reflux, sohxlet extractor containing 4Å molecular sieves) to give 6 in 92% yield. A solution

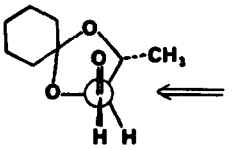
of 6 and (Z)-boronate 7[7a] in dry hexane were mixed at -78°C and allowed to warm to room temperature. The mixture was then stirred for 24-48 h before being quenched with triethanol amine. In this manner alcohol 8[10a,b] (mp 61-62°C; $[\alpha]_D^{19}$ + 32.0° (c=0.3, CH_2Cl_2)) was obtained in 70% yield with greater than 95% diastereoselectivity. Benzylation of 8 ($C_6H_5CH_2Br$, NaH, DME, reflux, 80% yield[10a,b]) followed by ozonolysis (O_3, CH_3OH, -20°C; Me_2S workup) afforded crude aldehyde 4[10a] which, without purification, was transformed to ester

Scheme I



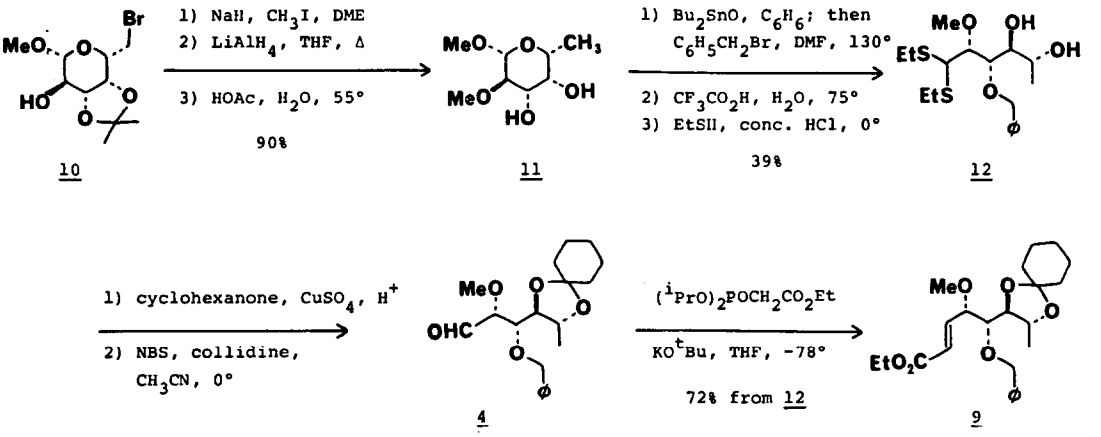
9[10a,b] ($[\alpha]_D^{19}$ + 24.8° (c=0.68, CH_2Cl_2)) in 70% overall yield from 8 by a modified Wadsworth-Emmons reaction.[11] We are currently exploring routes to cyclohexenone 3 from 9.[12]

The stereochemistry of 4 and 9, and hence 8, was confirmed by the independent synthesis of 4 and 9 from D-galactose derivative 10[13] as outlined in Scheme II.[14] These data are consistent with the interpretation that 8 is produced by a Felkin-type addition[5g,15] of boronate 7 to 6 with carbon-carbon bond formation occurring anti to the polar C-O bond, as illustrated by the following diagram. Efforts to develop a general synthesis of carbo-



hydrates based on the addition of allyl ether anion equivalents to aldehydes are in progress and will be reported in due course.

Scheme II



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References

1. Roger and Georges Firmenich Assistant Professor of Natural Products Chemistry.

2. Remers, W.A. "The Chemistry of Antitumor Antibiotics," Wiley-Interscience: New York, 1979; Chapter 3, and references cited therein.

3. Calabresi, P.; Parks, R.E., Jr. in "The Pharmacological Basis of Therapeutics," 6th ed., Gilman, A.G., Goodman, L.S., Gilman, A., eds.; Macmillan: New York, 1980; p. 1296.

4. Studies on the synthesis of olivin have been reported: (a) Dodd, J.H.; Garigipati, R.S.; Weinreb, S.M. J. Org. Chem. 1982, 47, 4045; (b) Franck, R.W.; John, T.V.; Olejniczak, K.; Blount, J.F. J. Am. Chem. Soc. 1982, 104, 1106; (c) Thiem, J.; Wessel, H.-P. Annalen 1981, 2216; (d) Franck, R.W.; John, T.V. J. Org. Chem. 1980, 45, 1170; (e) Hatch, R.P.; Shringarpure, J.; Weinreb, S.M. Ibid. 1978, 43, 4172.

5. For leading references, see (a) Roush, W.R.; Brown, R.J. J. Org. Chem. 1982, 47, 1371; (b) Lee, A.W.M.; Martin, V.S.; Masamune, S.; Sharpless, K.B.; Walker, F.J. J. Am. Chem. Soc. 1982, 104, 3515; (c) Minami, N.; Ko, S.S.; Kishi, Y. Ibid. 1982, 104, 1109; (d) Danishefsky, S.; Kobayashi, S.; Kerwin, J.F., Jr. J. Org. Chem. 1982, 47, 1981; (e) Yamaguchi, M.; Mukaiyama, T. Chem. Lett. 1981, 1005; (f) Fronza, G.; Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G.; Zirotti, C. Tetrahedron Lett. 1982, 23, 4143; (g) Kozikowski, A.P.; Ghosh, A.K. J. Am. Chem. Soc. 1982, 104, 5788; (h) Mukaiyama, T.; Yamada, T.; Suzuki, K. Chem. Lett. 1983, 5.

6. For a review of the diastereoselective addition of allylmetal compounds to aldehydes, see: Hoffmann, R.W. Angew. Chem., Int. Ed. Engl. 1982, 21, 555.

7. (a) Hoffmann,R.W.; Kemper, B. Tetrahedron Lett. 1982, 23, 845; 1981, 22, 5263; (b) Wuts, P.G.M.; Bigelow, S.S. J. Org. Chem. 1982, 47, 2498; (c) Yamaguchi, M.; Mukaiyama, T. Chem. Lett. 1982, 237; (d) Yamamoto, Y.; Saito, Y.; Maruyama, K. Tetrahedron Lett. 1982, 23, 4959.

8. (a) Cram, D.J.; Abd. Elhafez, F.A. J. Am. Chem. Soc. 1952, 74, 5828; (b) Cram, D.J.; Kopecky, K.R. Ibid. 1959, 81, 2748.

9. See Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G. Tetrahedron Lett. 1981, 22, 4017; Fronza, G.; Fuganti,C.; Grasselli, P.; Marinoni, G. Ibid. 1979, 3883, and references cited therein.

10. (a) The spectroscopic properties (NMR, IR, mass spectrum) of all new compounds were fully consistent with the assigned structures. (b) A satisfactory combustion analysis (±0.3% for C,H) was obtained for this compound.

11. Nagaoka, H.; Kishi, Y. Tetrahedron 1981, 37, 3873.

12. For a study of the stereochemistry of vinyl cuprate addtions to 9 and related systems, see: Roush, W.R.; Lesur, B.M. Tetrahedron Lett., the following manuscript in this issue.

13. Bernet, B.; Vasella, A. Helv. Chim. Acta. 1979, 62, 2411.

14. The rotation of 9 prepared from 10 according to Scheme II was $[\alpha]_D^{19}$ + 21.5° (c=0.77, CH_2Cl_2).

15. Chérest, M.; Felkin, H.; Prudent, N. Tetrahedron Lett. 1968, 2199.

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