

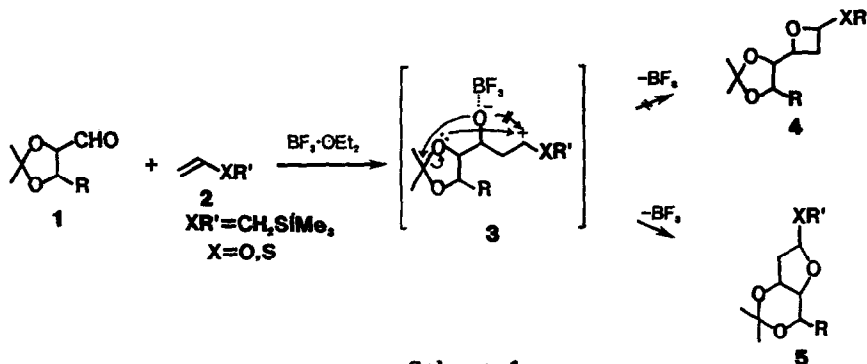
STRUCTURAL ELUCIDATION OF THE CYCLIC PRODUCTS FORMED BY THE REACTION OF 2,3-O-ISOPROPYLIDENE DERIVATIVES OF aldehydo-ALDOSE WITH ALLYLSILANES, VINYL ETHERS, OR VINYL SULFIDES IN THE PRESENCE OF BORON TRIFLUORIDE ETHERATE

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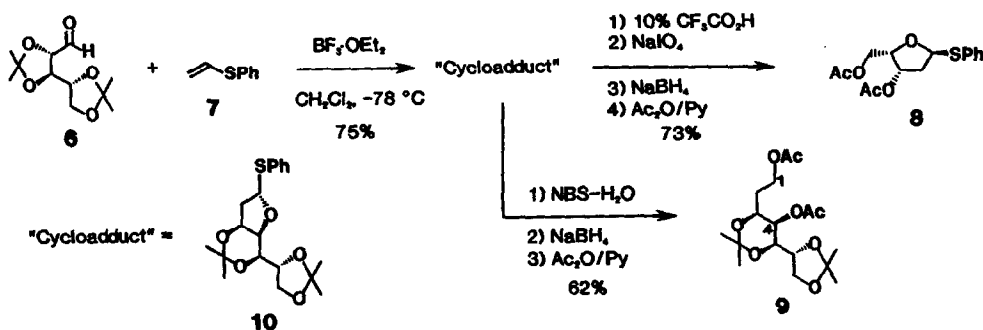
Summary: The structural elucidation of the cyclic products derived from 2,3-O-isopropylidene derivatives of aldehydo-aldose and allylsilanes, vinyl ethers, or vinyl sulfides indicated that tetrahydrofuran derivatives were formed by cyclization accompanied with migration of the isopropylidene group.

Reactions of carbonyl compounds with allylsilanes in the presence of a Lewis acid have been shown to be useful for the synthesis of homoallyl alcohols.¹ When this allylation was applied to 2,3-O-isopropylidene derivatives of aldehydo-aldose **1** using boron trifluoride etherate as a Lewis acid, 1:1 cycloadducts were predominantly formed instead of the expected homoallyl alcohols.² Furthermore, the reaction using vinyl ethers or vinyl sulfides in place of the allylsilanes provided similar cycloadducts.³ It seemed reasonable to speculate that the structures of the cycloadducts might be oxetanes **4** formed by intramolecular cyclization of cationic intermediates **3**⁴ as reported in the previous papers. In the course of our laboratory's continuing study of the cycloadducts, we noticed that the structures should correctly be tetrahydrofuran derivatives **5** rather than oxetanes **4**.⁵ The reaction would proceed accompanied with migration of the isopropylidene group and the simultaneous formation of a tetrahydrofuran ring from the cationic intermediate **3** (Scheme 1). In the present letter, structural elucidation of the tetrahydrofuran **5** by means of chemical transformations and by an X-ray crystallographic structure analysis is described.



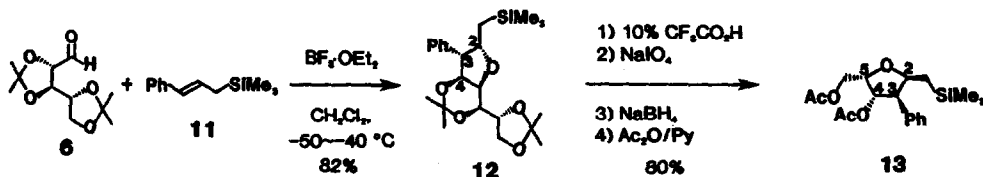
Scheme 1

The reaction of 2,3;4,5-di-O-isopropylidene-aldehydo-D-arabinose (6) with phenyl vinyl sulfide (7) in the presence of 1.1 equivalent of boron trifluoride etherate in dichloromethane at -78°C for 15 min gave a diastereomerically pure cycloadduct⁶ (75% yield), which was then transformed according to the following procedure. The isopropylidene groups were removed by acid hydrolysis. Oxidative cleavage of the resulting tetraol with sodium metaperiodate and subsequent sodium borohydride reduction and acetylation provided, unexpectedly, a tri-substituted tetrahydrofuran 8.⁷ In the sequence of these reactions, the possibility of ring expansion of an oxetane such as 4 to a tetrahydrofuran during the acid hydrolysis cannot be ruled out. Therefore, another transformation was carried out under non-acidic conditions; treatment of the cycloadduct with *N*-bromosuccinimide in the presence of water, followed by reduction and acetylation led to 1,4-di-O-acetyl-3,5;6,7-di-O-isopropylidene-2-deoxy-D-gluc_o-heptitol (9).⁸ The ^1H - ^1H decoupling experiments of 9 proved that the two acetyl groups were introduced at the C-1 and C-4 hydroxyl functions. These results suggest that the tetrahydrofuran moiety is present in the starting "cycloadduct", which is illustrated as compound 10.



Scheme 2

(*E*)-Cinnamyltrimethylsilane (11) reacted with the aldehyde 6 at -50 to -40°C for 2 h to afford tetrahydrofuran 12 (80% yield), whose structure was also confirmed after the conversion to 13 as shown in Scheme 3. The relative stereochemistry of 13 was established by the coupling constants of both 12 ($J_{2,3}=5.0$ Hz, $J_{3,4}=0$ Hz) and 13 ($J_{2,3}=8.2$ Hz, $J_{3,4}=5.4$ Hz, $J_{4,5}=5.4$ Hz).



Scheme 3

It should be pointed out that the trimethylsilylmethyl and the phenyl substituents on the tetrahydrofuran bear a cis relationship even when (E)-cinnamylsilane is used as a starting material.

Similarly, tetrahydrofuran **15** was produced as a single diastereomer by each of the reactions using three different E/Z-ratio mixtures of methyl styryl ether (**14**) in the presence of 10 mol% of boron trifluoride etherate at $-78\text{ }^{\circ}\text{C}$ (Eq. 1). This stereoselectivity may be explained in terms of the combination of Cram's cyclic model and an "acyclic extended" transition state model;⁹ the most favored transition states resulting from the (Z)- and (E)-styryl ethers can be illustrated as **16** and **17**,¹⁰ each of which affords cationic intermediates **18** and **19**, respectively. The subsequent cyclization may proceed exclusively from **18** because of the steric preference to provide **15** as the sole product. For the rigorous confirmation of the molecular structure of **15**, an X-ray crystallographic analysis was carried out to give the structure of Figure 1.¹¹

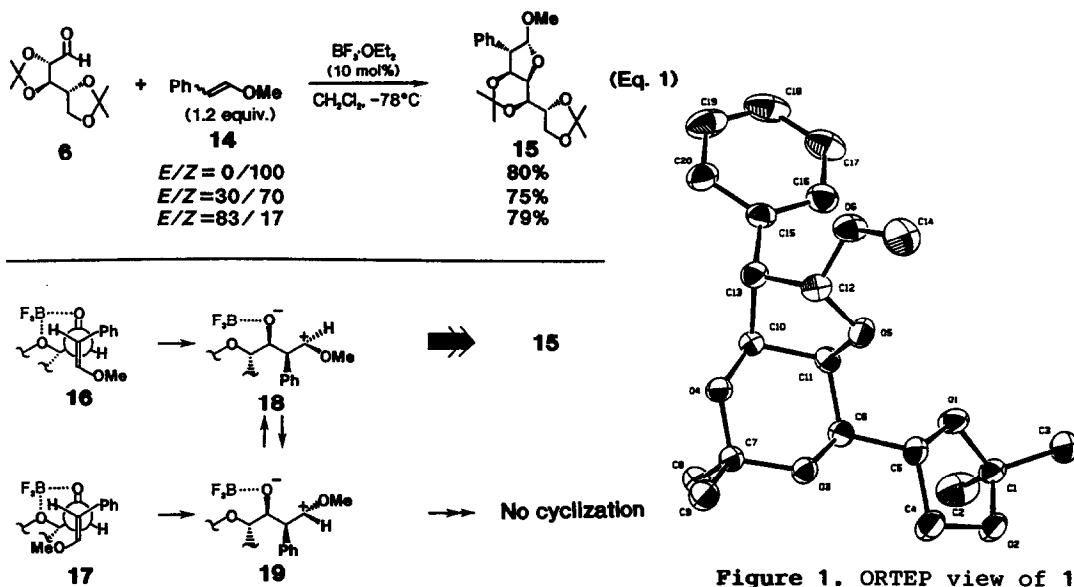


Figure 1. ORTEP view of **15**

In conclusion, it has been shown that allylsilanes, vinyl ethers, or vinyl sulfides react with 2,3-O-isopropylidene derivatives of aldehydo-aldose in the presence of boron trifluoride etherate to afford tetrahydrofuran derivatives, presumably resulting from intramolecular cyclization accompanied with migration of the isopropylidene group in the cationic intermediates (Scheme 1). This reaction is useful for the stereoselective formation of substituted tetrahydrofurans. Its application to the synthesis of biologically interesting compounds is currently in progress.

Acknowledgments: The author wishes to thank Professor Nobuo Tanaka, Tokyo Institute of Technology, for the X-ray crystallographic determination of the structure of 15 and also to thank Professors Teruaki Mukaiyama, Science University of Tokyo, and Hisashi Takei, Tokyo Institute of Technology, for many helpful discussions.

References and Notes

- 1) E. W. Colvin, "Silicon in Organic Synthesis", Butterworths, London (1980) p. 97; A. Hosomi and H. Sakurai, Tetrahedron Lett., **1976**, 1295; I. Ojima and M. Kumagai, Chem. Lett., **1978**, 575.
- 2) H. Sugimura and M. Uematsu, Tetrahedron Lett., **1988**, 29, 4953.
- 3) H. Sugimura and K. Osumi, Tetrahedron Lett., **1989**, 30, 1571.
- 4) For examples of Lewis acid promoted [2+2] cycloaddition through similar cationic intermediates (a) using allylsilanes, see: R. Pardo, J.-P. Zahra, and M. Santelli, Tetrahedron Lett., **1979**, 4557; A. Hosomi, H. Kobayashi, and H. Sakurai, Tetrahedron Lett., **1980**, 21, 955; H. O. House, P. C. Gaa, and D. VanDerveer, J. Org. Chem., **1983**, 48, 1661; G. Majetich, J. Defauw, and C. Ringold, J. Org. Chem., **1988**, 53, 50; (b) using unsaturated ethers, see: H. Vieregge, H. M. Schmidt, J. Renema, H. J. T. Bos, and J. F. Arens, Rec. Trav. Chim., **1966**, 85, 929; J. Pornet, A. Rayadh, and L. Miginiac, Tetrahedron Lett., **1988**, 29, 4717; J. Mattay and K. Buchkremer, Helv. Chim. Acta, **1988**, 71, 981.
- 5) The author would like to correct the previously assigned structure 4 to 5 with his sincere apology.
- 6) The selected physical properties are as follows: mp 69-70 °C (hexane); $[\alpha]_D^{27}$ -227° (c 1.00, CHCl₃); 400 MHz ¹H NMR(CDCl₃) δ=1.36(s, 3H), 1.39 (s, 3H), 1.43(s, 3H), 1.44(s, 3H), 2.07(ddd, J=4.88, 7.32, 14.16 Hz, 1H), 2.47(dd, J=7.08, 14.16 Hz, 1H), 3.92-3.97(m, 2H), 3.99(t, J=2.20, 1H), 4.06(dd, J=6.35, 8.54 Hz, 1H), 4.33(q, J=6.35 Hz, 1H), 4.41(dd, J=2.20, 4.64 Hz, 1H), 5.70(t, J=7.08 Hz, 1H), 7.24-7.30(m, 3H), 7.56-7.58(m, 2H); Anal. Calcd for C₁₀H₂₆O₅S: C, 62.28; H, 7.15; S, 8.73%. Found: C, 62.51; H, 7.18; S, 9.05%.
- 7) **8**: 90 MHz ¹H NMR(CDCl₃) δ=2.07(s, 3H), 2.08(s, 3H), 2.37(dd, J=5.5, 7.0 Hz, 1H), 2.45(dd, J=2.8, 7.0 Hz, 1H), 4.20-4.55(m, 3H), 5.40(ddd, J=2.7, 2.8, 5.5 Hz, 1H), 5.75(t, J=7.0 Hz, 1H), 7.22-7.60(m, 5H).
- 8) The details of confirmation of the 2-deoxy-D-gluco-heptitol structure have been described in reference 3.
- 9) S. Murata, M. Suzuki, and R. Noyori, J. Am. Chem. Soc., **1980**, 102, 3248.
- 10) A similar transition state has been proposed previously; M. T. Reetz, Angew. Chem. Int. Ed. Engl., **1984**, 23, 556.
- 11) The crystal data are as follows: C₂₀H₂₈O₆, Mr=364.44, orthorhombic, P2₁2₁2₁, a=12.464(3), b=19.374(2), c=8.129(2) Å, Z=4, D_x=1.233g/cm³, F(000)=784, R=0.035 for 1823 unique observed [$|F_0| > 3\sigma(F_0)$] reflections. Atomic coordinates have been deposited with the Cambridge Crystallographic Data Center.