UNUSUAL [2+2]CYCLOADDITION REACTION OF ALLYLSILANES WITH 2,3-O-ISOPROPYLIDENE DERIVATIVES OF ALDEHYDE-ALDOSE CATALYZED BY BORON TRIFLUORIDE ETHERATE

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Summary: In the reaction of allylsilanes with $2,3-\underline{0}$ -isopropylidene derivatives of <u>aldehyde</u>-aldose, [2+2]cycloaddition occurred predominantly rather than allylation in the presence of boron trifluoride etherate to give oxetane derivatives as major products together with small amounts of homoallyl alcohols.

The Lewis acid mediated reaction of allylsilanes with carbonyl compounds is well known as a useful method for the preparation of homoallyl alcohols.¹⁾ However, when the reaction of allyltrimethylsilane($\underline{2}$) with 2,3:4,5-di- $\underline{0}$ isopropylidene-<u>aldehyde</u>- \underline{D} -arabinose($\underline{1}$) was attempted in the presence of boron trifluoride etherate, we found that the desired homoallyl alcohol $\underline{4}$ was obtained in only 16% yield and an unexpected oxetane $\underline{3}$ was produced in 72% yield as a single isomer with a <u>trans</u> configuration revealed by ¹H-NMR analysis²) (Eq. 1). We were interested in the unusual behavior of this reaction and undertook a detailed investigation. In this communication, we wish to present the first example of [2+2]cycloaddition reaction between allylsilanes and aldehydes catalyzed by a Lewis acid.



The following description of the experimental procedure for the above reaction is typical. To a solution of aldehyde 1^{3} (2.732 g, 11.9 mmol) and allylsilane 2 (1.62 g, 14.2 mmol) in dry CH_2Cl_2 (100 ml) was slowly added boron trifluoride etherate (1.85 g, 13.0 mmol) in CH_2Cl_2 (10 ml) at -78 °C under an argon atmosphere. After 10 min, Et_3N (3 ml) was added at the same temperature. The reaction mixture was warmed to room temperature and a saturated aqueous solution of NaHCO₃ was added. The organic layer was separated and washed with water. After drying and evaporation of the solvent, flush column chromatography gave the oxetane 3^{4} (2.946 g, 72%) and the homoallyl alcohol 4 (0.522 g, 16%).

First, we attempted the reaction of $\underline{1}$ and $\underline{2}$ in the presence of other Lewis acids such as TiCl₄, SnCl₄, AlCl₃, MgBr₂, and ZnCl₂. TiCl₄ and SnCl₄ complicated the reaction, and MgBr₂ and ZnCl₂ gave only the homoallyl alcohol $\underline{4}$. Though AlCl₃ essentially catalyzed the [2+2]cycloaddition reaction, another allylation of the isopropylidene ketal moiety of 3 took place.⁵⁾

Run	Aldehyde	Reaction time	Oxetane ^{b)}	Yield/% ^{c)}	Alcohol ^{b)}	Yield/% ^C
1	χ ⁰) ^{CHO}	15 min	X0 6 SiMe3	30 (3:2:1) ^{d)}	χ_0^{OH}	3 (-) ^{e)}
2	X0 XCH0 <u>8</u> 0Bn	1 h		3 77 (5:4) ^{d)}	λ_0^{OH}	9 (5:4) ^{d)}
3	X0***CH0 X0****CH0 *******************************	2 h	O SiMe OBn <u>12</u>	59 (-) ^{f)}	OH OBn <u>13</u>	15 (-) ^{f)}
4	$\begin{array}{c} \chi_0^0 \chi^{CHO} \\ H_3 C \chi_0^0 \chi \\ \underline{14} \end{array}$	1 h	×0 H ₃ C ↓0 ↓0 ↓0 ↓0 ↓0 ↓0 ↓0 ↓0 ↓0 ↓0	72 (4:1) ^{g)}	λ_{0} $H_{3}C$ μ_{0} μ_{1} μ_{0} μ_{1} $\mu_{$	15 (4:1) ^{g)}
5	X0.+CH0 Bn0 - 0 <u>17</u>	1 h Br	0 0 SiMe3 0 0 0 0 0 0 0 0 0 0 0 0 0	67 (2:1) ^{g)}	DH X0,	10 (2:1) ^{g)}

Table 1. Reaction of allylsilane with 2,3-<u>O</u>-isopropylidene-<u>aldehyde</u>-aldoses^{a)}

- a) All the reactions were carried out at -78 °C in CH_2Cl_2 using 1.2-1.5 equiv. of the silane and 1.1-1.2 equiv. of $BF_3 \cdot OEt_2$ to aldehyde.
- b) All new compounds were characterized by ^{1}H -NMR and ^{13}C -NMR spectra.
- c) Isolated yield. Ratio in parentheses is that of stereoisomers. The oxetane <u>6</u> was produced as stereoisomeric mixtures of two <u>trans</u>-isomers and a <u>cis</u>-one (<u>trans:cis</u>=5:1). The oxetanes <u>9</u>, <u>15</u>, and <u>18</u> were obtained as mixtures of two <u>trans</u>-isomers.
- d) Determined by the isolation of each isomer.
- e) Not determined.
- f) Obtained as a single isomer with a trans configuration.
- g) Determined by $^{13}C-NMR$.

Since it can be presumed that the presence of a cyclic ketal adjacent to carbonyl group is required for the formation of an oxetane ring,⁶⁾ we next carried out the reaction of the allylsilane $\underline{2}$ and other $2,3-\underline{0}$ -isopropylidene derivatives of <u>aldehyde</u>-aldose as shown in Table 1. All the aldehydes employed in this examination, expectedly, underwent the [2+2]cycloaddition reaction in a regiospecific manner to yield the oxetanes as major products. Low yields of the products in the reaction of the aldehyde $\underline{5}$ probably resulted from its lability under the boron trifluoride condition. The \underline{D} -arabinose derivative $\underline{11}$

gave the oxetane 12 as a single isomer again, but from the other aldehydes the corresponding oxetanes were produced as mixtures of two or three stereoisomers.

The reactions of other allylsilanes with 1 were also examined as described in Eqs. 2 and 3. Although (\underline{E}) -cinnamyltrimethylsilane $(\underline{20})$ exclusively



16%

24

underwent the [2+2]cycloaddition reaction, 3-methyl-2-butenyltrimethylsilane $(\underline{22})$ was allowed to produce the two regionsomers of oxetanes, $\underline{23}$ and $\underline{24}$. The production of <u>24</u> is thought to be caused by an electrophilic attack predominantly occurring at the β -carbon of the silane on account of the steric hindrance of the γ -carbon as well as the stability of the carbonium cation in its intermediate.

A possible reaction mechanism of the present [2+2]cycloaddition is illustrated in Fig. 1. The process of allylation through an intermediate \underline{I}



Fig. 1. Mechanism of the [2+2]cycloaddition reaction

(path b) has been discussed in detail by other investigators.⁷⁾ On the other hand, when the ring closure proceeds in the intermediate \underline{I} (path a), an oxetane ring will be formed. A similar ring closure mechanism has been proposed by Vieregge and his colleagues⁸⁾ in the [2+2]cycloaddition reaction between 1alkynyl ethers and carbonyl compounds in the presence of Lewis acids. To confirm the reaction mechanism (path a), we re-examined the reaction of $\underline{1}$ and $\underline{2}$ under a catalytic condition; $\underline{1}$ was treated with $\underline{2}$ (1.2 equiv.) in the presence of $BF_3 \cdot OEt_2$ (0.2 equiv.) at -78 °C for 3 h to yield the oxetane <u>3</u> and the alcohol 4 in 62% and 10%, respectively. This result seems to well agree with the above mechanism. The role of 1,3-dioxolane ring adjacent to carbonyl group in the formation of an oxetane is not apparent at the present stage. Further investigation of the mechanistic features as well as the application in organic synthesis is currently under way.

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References and Notes

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- 2) A <u>trans</u> relationship between the two substituents on the oxetane ring was confirmed by the values of the coupling constants.⁴) The absolute configuration, however, could not be assigned.
- 3) H. Zinner, E. Wittenburg, and G. Rembarz, Chem. Ber., <u>92</u>, 1614 (1959).
- 4) Compound <u>3</u>: mp 42-44 °C (methanol-water); $[\alpha]_D^{28}$ -19.5 °(<u>c</u> 1.0, CHCl₃); IR (KBr) 2980, 2945, 2875, 1380, 1370, 1245, 1200, 1155, 1085, 1070, 957, 855, 840 cm⁻¹; ¹H-NMR (CDCl₃, 400MHz) $\delta = 0.00$ (s, 9H, (CH₃)₃Si-), 1.01 (dd, $J_{1,1}$ '=14.0, $J_{1,2}=8.7$ Hz, 1H, 1-H), 1.23 (dd, $J_{1,1}$ '=14.0, $J_{1',2}=6.0$ Hz, 1H, 1'-H), 1.33, 1.34, 1.39, 1.40 (4s, 12H, C(CH₃)₂), 1.61 (dd, $J_{2,3}=4.4$, $J_{3,3}$ '= 13.3Hz, 1H, 3-H), 2.23 (ddd, $J_{2,3}$ '=8.7, $J_{3,3}$ '=13.3, $J_{3',4}=5.3$ Hz, 1H, 3'-H), 3.52 (t, $J_{4,5}=2.7$, $J_{5,6}=2.7$ Hz, 1H, 5-H), 3.78 (dd, $J_{5,6}=2.7$, $J_{6,7}=8.3$ Hz, 1H, 6-H), 3.93 (dd, $J_{7,8}=4.4$, $J_{8,8}$ '=8.7Hz, 1H, 8-H), 4.03 (dd, $J_{7,8}$ '=6.0, $J_{8,8}$ ' =8.7Hz, 1H, 8'-H), 4.18 (dddd, $J_{1,2}=8.7$, $J_{1',2}=6.0$, $J_{2,3}=4.4$, $J_{2,3}$ '=8.7Hz, 1H, 2-H), 4.31 (ddd, $J_{6,7}=8.3$, $J_{7,8}=4.4$, $J_{7,8}$ '=6.0Hz, 1H, 7-H), 4.32 (dd, $J_{3',4}=5.3$, $J_{4,5}=2.7$ Hz, 1H, 4-H); ¹³C-NMR(CDCl₃) $\delta = -0.9$ ((CH₃)₃Si-), 20.2 (q), 26.0 (q), 26.7 (t), 27.7 (q), 30.4 (q), 41.9 (t), 67.8 (t), 71.0 (d), 72.5 (d), 73.6 (d), 75.5 (d), 77.1 (d), 98.5 (s), 109.8 (s); Anal. Calcd for $C_{17}H_{32}O_5Si:$ C, 59.27; H, 9.36%. Found: C, 59.55; H, 9.45%.
- The reaction was carried out as described in Eq. 4. Recently, a similar ring opening of an isopropylidene ketal with allylation has been reported;
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- 6) In practice, according to our previous experiment, the reaction of the allylsilane with $2-\underline{0}$ -benzyl-3,4- $\underline{0}$ -isopropylidene-<u>aldehyde</u>- \underline{D} -erythrose in the presence of BF₃.OEt₂ gave the corresponding homoallyl alcohol in 58% yield, but no oxetane product.
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