REGIOCONTROLLED RING OPENING REACTIONS OF A CYCLIC ACETAL

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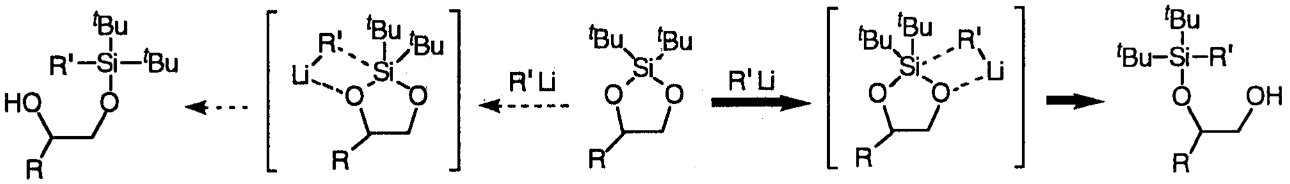
Abstract —— Regiocontrol in ring opening reactions of 2-alkyl-4,4-dimethyl-1,3-dioxolane with allyltrimethylsilane was investigated. In the reactions promoted by $TiCl_4$, the ratio of the isomers can be changed from 91:9 to 1:99 simply by adopting different experimental procedures based on the sequence of adding the substrates.

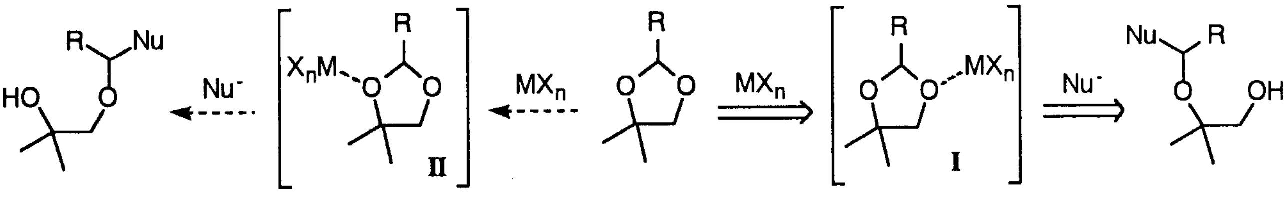
Recently, we have reported a new method for inside selective silylation of 1,2-diols on the basis of kinetically controlled cleavage of a five-membered cyclic silyl ether.[1] In this reaction, the preferential formation of a 2-siloxy-1-alkanol is attributable to complexation of lithium at the sterically less hindered oxygen (Scheme 1).

Scheme 1



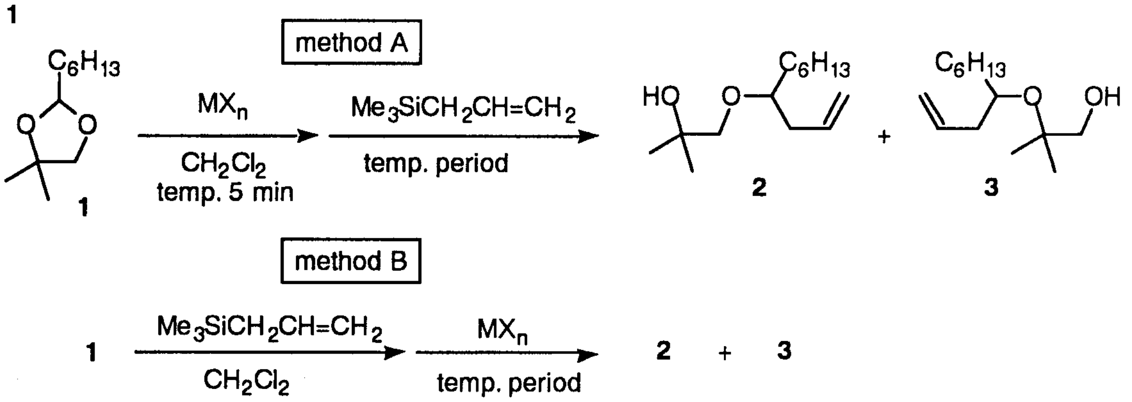
On the other hand, ring cleavage reactions of cyclic acetals promoted by a Lewis acid has found widespread use in organic synthesis.[2,3] In relation to the chemistry shown above, we became intrigued by control of regiochemistry in the ring opening reaction of a 2-alkyl-4,4-dimethyl-1,3-dioxolane.[4] Thus, a Lewis acid would prefer complexation at the sterically less hindered oxygen to form **I**, which would be cleaved by a nucleophile to give a primary alcohol selectively (Scheme 2).

Scheme 2



Allyltrimethylsilane[5] was chosen as a nucleophile, and its addition with 2-hexyl-4,4-dimethyl-1,3-dioxolane (**1**) were performed under the influence of several Lewis acids. We employed two different experimental procedures based on the sequence of adding the Lewis acid: either allylsilane was added to a solution of acetal (**1**) pre-treated with a Lewis acid (method A) or a Lewis acid was added to a mixture of acetal (**1**) and allylsilane (method B). The combined yields of adducts (**2**) and (**3**) were estimated by ^1H NMR using bromoform as an internal standard, and the product ratios were determined by capillary GC analysis. Structural assignment of the product was achieved by treating **3** with PDC, which gave the corresponding aldehyde. The results are summarized in Table 1.

Table 1

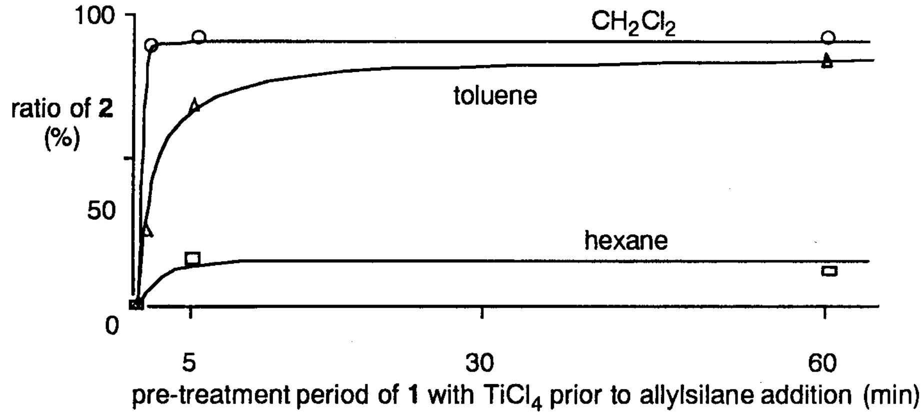


entry	MX_n	method	temp. (°C)	period (h)	yield (%)	2 : 3
1	$TiCl_4$	A	-78	1	99	91 : 9
2		B			91	1 : 99
3	$TiCl_3(O^iPr)$	A	-78	2	61	91 : 9
4		B			87	91 : 9
5	$AlCl_3$	A	-78	5	87	<1 :>99
6		B			88	<1 :>99
7	$SnCl_4$	A	-23	4	58	1 : 99
8		B			68	1 : 99

The ratios of regioisomers (**2**) and (**3**) were significantly dependent on the choice of Lewis acids and were virtually independent of the methods A or B. In the reactions with $TiCl_4$, however, the regioselectivity was dramatically changed from 91:9 to 1:99 simply by adopting procedure method B in lieu of method A.

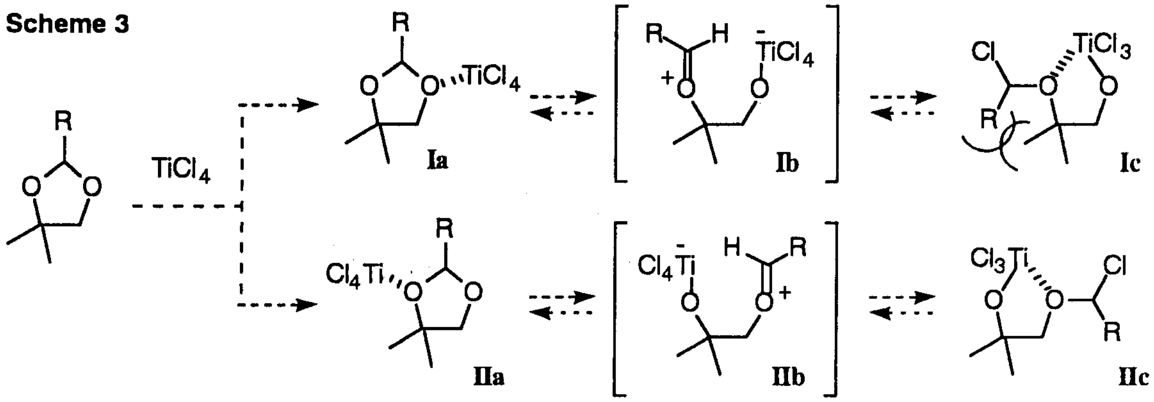
The origin of the unique property of $TiCl_4$ was further investigated. Our attention to monitoring the reaction course in detail was given to the initial 5 minutes of method A. The relationship between pre-treatment period and the ratio of **2** and **3** was examined in dichloromethane, toluene, and hexane. The results were plotted as a function of pre-treatment period in Figure 1. These results clearly indicate that product (**2**) arises from some stable intermediate which is slowly generated during treatment of acetal (**1**) with $TiCl_4$. Judging from the observation that the polar solvent preferentially affords **2**, the intermediate is presumed to have ionic character.

Figure 1

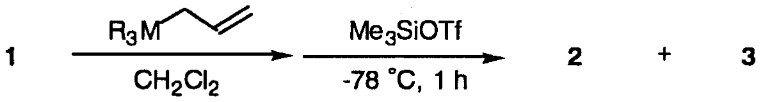


Although formation of oxonium ion intermediates (**Ib**) or (**IIb**) *via* ring cleavage may be postulated (Scheme 3), these ionic intermediate seems not to exist for such a long time. Therefore, we suggest that chloride (**Ic**) or (**IIc**) which could be in rapid equilibrium with oxonium ion (**Ib**) or (**IIb**), respectively, may be the actual intermediate of the "pseudo SN1-type reaction".[6] The preferential formation of **IIc** over **Ic** can be rationalized by the steric interaction between the R group and the methyl groups in **Ic**. Similarly, the reactions with $TiCl_3(O^iPr)$, which lead to selective formation of **2**, may also proceed via the "pseudo SN1-type reaction".[7]

Scheme 3



In contrast with this, the highly selective formation of **3** observed with $AlCl_3$ and $SnCl_4$ would come from an SN2-type reaction of complex (**I**) in Scheme 2. The rate of an SN2-type reaction should be enhanced by the nucleophilicity of the allylmetal.[8] Indeed, under the influence of TMSOTf, **1** underwent ring cleavage by allyltributyltin to afford **3** in almost quantitative yield, while allyltrimethylsilane failed to react with **1** under the same conditions. These results indicate that an SN2-type reaction tends to give **3** selectively.



$R_3M = Me_3Si$: no reaction

Bu_3Sn: 97% (**2**:**3** =<1:>99)

Consequently, we have demonstrated that the regiochemistry in nucleophilic ring-opening of **1** can be controlled by the choice of a Lewis acid as well as the experimental procedure. Further studies on the reactions of **1** with other nucleophiles are currently under investigation.

ACKNOWLEDGEMENT
This work was partially supported by Grants from the Ministry of Education, Science, Sports, and Culture of the Japanese Government. M.T. thanks JSPS for a predoctral fellowship.

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Received, 20th May, 1999