REGIOCONTROLLED RING OPENING REACTIONS OF A CYCLIC ACETAL

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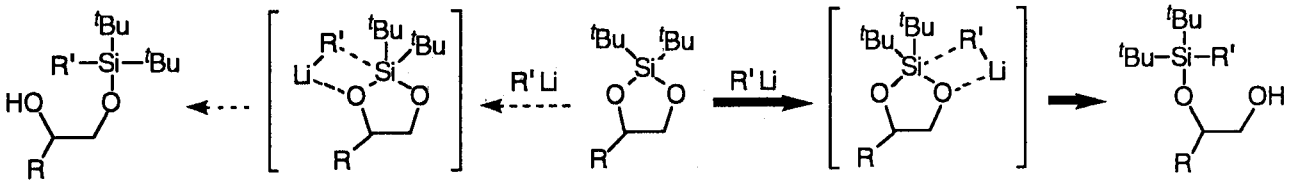
Abstract —— Regiocontrol in ring opening reactions of 2-alkyl-4,4-dimethyl-1,3-dioxolane with allyltrimethylsilane was investigated. In the reactions promoted by $TiCl_4$, the ratio of the isomers can be changed from 91:9 to 1:99 simply by adopting different experimental procedures based on the sequence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

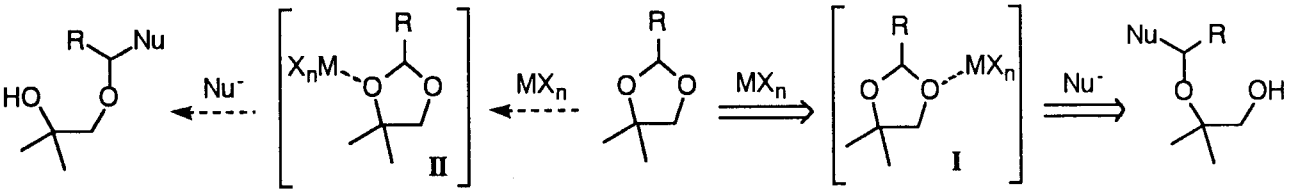
Recently, we have reported a new method for inside selective silylation of 1,2-diols on the basis of kinetically controlled cleavage of a five-membered cyclic silyl ether.[1] In this reaction, the preferential formation of a 2-siloxy-1-alkanol is attributable to complexation of lithium at the sterically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

Scheme 1



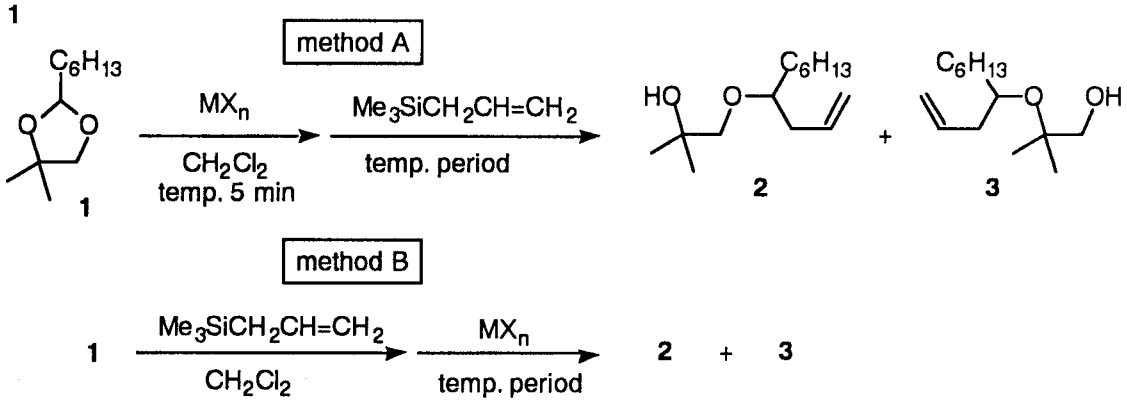
On the other hand, ring cleavage reactions of cyclic acetals promoted by a Lewis acid has found widespread use in organic synthesis.[2,3] In relation to the chemistry shown above, we became intrigued by control of regiochemistry in the ring opening reaction of a 2-alkyl-4,4-dimethyl-1,3-dioxolane.[4] 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

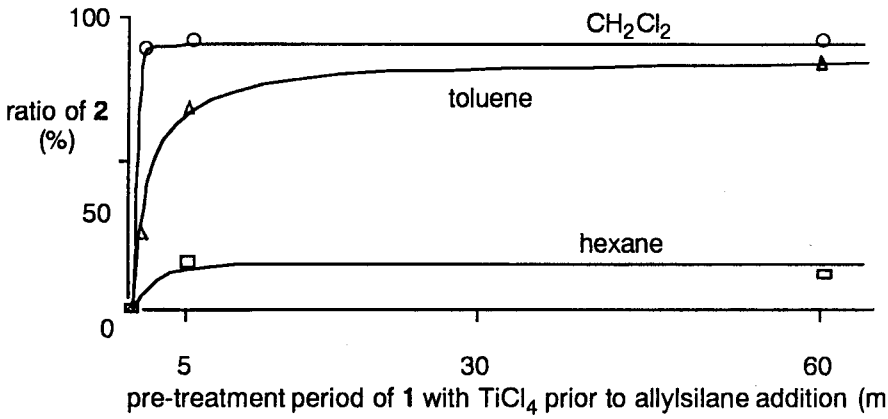


entry	MX_n	method	temp. (°C)	period (h)	yield (%)	**2** : **3**
1	$TiCl_4$	A	-78	1	99	91 : 9
2		B			91	1 : 99
3	$TiCl_3(O^iPr)$	A	-78	2	61	91 : 9
4		B			87	91 : 9
5	$AlCl_3$	A	-78	5	87	<1 :>99
6		B			88	<1 :>99
7	$SnCl_4$	A	-23	4	58	1 : 99
8		B			68	1 : 99

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.

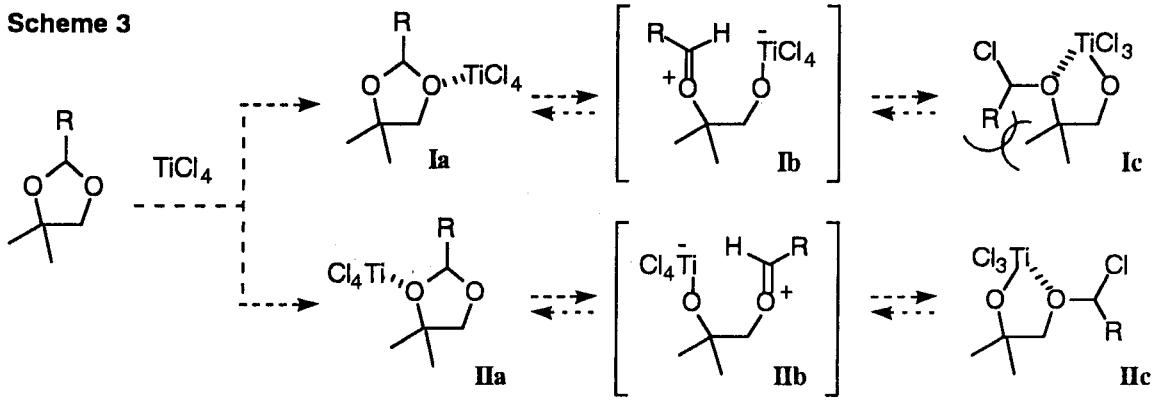
The origin of the unique property of $TiCl_4$ was further investigated. Our attention to monitoring the reaction course in detail was given to the initial 5 minutes of method A. The relationship between pre-treatment period and the ratio of **2** and **3** was examined in dichloromethane, toluene, and 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

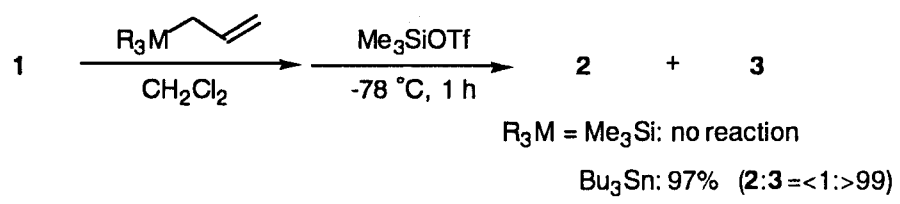


Although formation of oxonium ion intermediates (**Ib**) or (**IIb**) *via* ring cleavage may be postulated (Scheme 3), these ionic intermediate seems not to exist for such a long time. Therefore, we suggest that chloride (**Ic**) or (**IIc**) which could be in rapid equilibrium with oxonium ion (**Ib**) or (**IIb**), respectively, may be the actual intermediate of the "pseudo S_N1-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 S_N1-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 S_N2-type reaction of complex (**I**) in Scheme 2. The rate of an S_N2-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 S_N2-type reaction tends to give **3** selectively.



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

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