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INTRAMOLECULAR Sm^{2+} AND Sm^{3+} PROMOTED REACTION OF γ-OXY-δ-KETOALDEHYDE; STEREOCONTROLLED FORMATION OF PINACOL AND LACTONE

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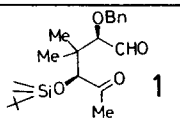
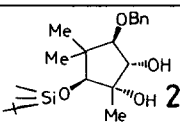
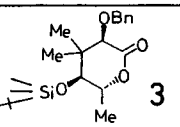
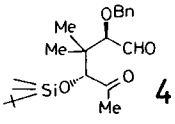
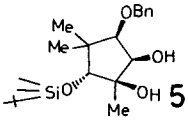
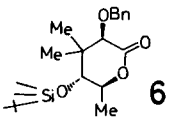
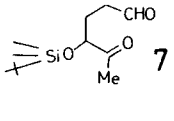
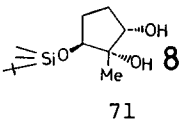
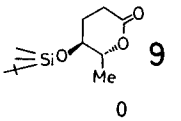
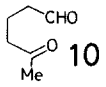
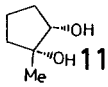
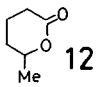
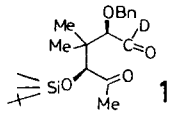
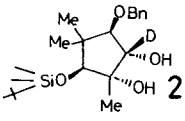
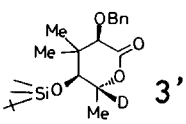
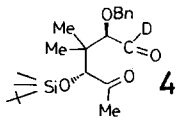
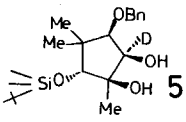
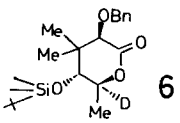
Summary: Samarium promoted intramolecular pinacol coupling and Tishchenko oxidoreduction of γ-oxy-δ-ketoaldehyde proceeded stereospecifically. Newly forming hydroxy group is oriented *anti* to γ-silyoxy group in both reactions.

Synthesis of cyclic polyoxo natural product is currently important task in organic chemistry.[1] During the course of synthetic studies for highly oxidized terpenoids, we needed to prepare polyols consecutively existing on five or six membered ring. To date there have been some strategies to build up such functional systems, e.g. osmylation of hydroxy olefin[1a] or 1,4-addition of singlet oxygene.[1b] On the other hand, intramolecular pinacol coupling is attractive for such purpose, because it provides a new ring and vicinal diols at the same time. Although a number of intramolecular pinacol coupling mediated with low valent metals, particularly SmI_2, have been reported,[2] stereochemistry of face selection to neighbouring substituents has not been elucidated well.[3]

Herein we wish to report stereochemistry of intramolecular pinacol coupling and Tishchenko oxidoreduction promoted by Sm^{2+} and Sm^{3+} species in the case of γ-oxy-δ-ketoaldehyde. Treatment of α-benzyloxy-β-dimethyl-γ-(tert-butyldimethylsilyloxy)-δ-ketoaldehyde (**1**) with SmI_2 in THF[4] at room temperature gave pinacol **2** in 80 % yield as a sole product. Ketoaldehyde **4** and **7** also afforded the corresponding diols **5** and **8** in 76 % and 71 % yields respectively. Structures of the diols including relative stereochemistry to α-benzyloxy group and/or to γ-silyloxy group were confirmed by deriving them to the corresponding 5-membered acetonides.[5] The results, shown in **Table 1**, clearly indicated that *cis* vicinal diols were produced in *trans* form to the adjacent γ-silyloxy group.

In some cases of the above reactions, formations of δ-lactone were observed, but always the yields were found largely dependent on the

Table 1 Samarium Promoted Reactions of δ-Ketoaldehyde

Entry	Substrate	Reagent	Product (yield %) Pinacol	δ-Lactone
	 1		 2	 3
1		SmI_2 a)	80	0
2		SmI_2 b)	18	65
3		SmI_2OBu^t c)	0	89
	 4		 5	 6
4		SmI_2 a)	76	0
5		SmI_2 b)	21	62
6		SmI_2OBu^t c)	0	75
	 7		 8	 9
7		SmI_2 a)	71	0
8		SmI_2 b)	35	41
9		SmI_2OBu^t c)	0	75
	 10		 11	 12
10		SmI_2 a)	68	0
11		SmI_2OBu^t c)	0	~10 d)
	 1'		 2'	 3'
12		SmI_2 e)	67	20
	 4'		 5'	 6'
13		SmI_2 e)	62	16

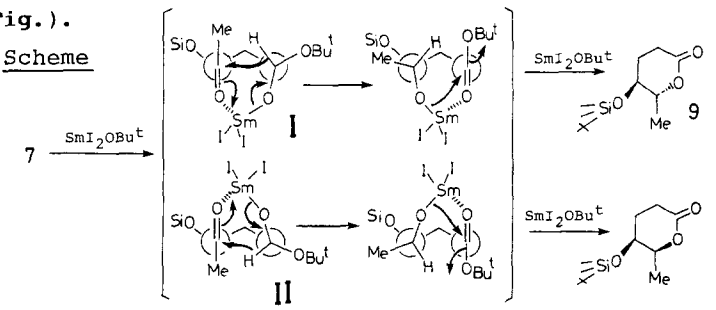
(a) THF, r.t. One eq. of SmI_2 prepared freshly in THF (0.1 M) was used (b) THF:hexane (1:1), r.t. THF solution of SmI_2 (0.1 M) was premixed with methanol in a ratio of 99:1 before the addition. (c) THF, r.t. (d) This reaction was messy and aldol products were isolated. (e) Older SmI_2 was used.

quality of the reagent.[6] The lactones were resulted by intramolecular Tishchenko oxidoreduction[7] between aldehydes and methyl ketones. These results imply that Sm^{3+} species, presumably present in SmI_2 reagent, might mediate the reaction. In fact when SmI_2OBu^t[8] was employed instead of SmI_2, lactones ware produced exclusively and none of the pinacol was obtained (entries 3, 6 and 9). Addition of small amount of methanol also promoted lactone formation (entries 2, 5 and 8) in which SmI_2OMe might be formed *in situ* from methanol and Sm^{3+} species. In this reaction, somehow γ-silyloxy group is required essentially. Although the reason is not clear at present, a simple δ-ketoaldehyde **10** provided lactone **12** very poorly even by the use of SmI_2OBu^t (entry 11). However it gave pinacol **11** by the reaction with SmI_2 in good yield (entry 10).

The obtained lactones **3** and **6** were consisted of a single stereoisomer and the structures were shown in **Table 1**. The stereochemistry of the newly produced secondary hydroxy center was found to be *anti* in relation to the ajacent silyloxy group along the zig-zag carbon chain in all cases. The stereochemistry was determined by transformation of the lactones **3** and **6** to *trans* epoxides (both, J=2.2 Hz) respectively by 3 steps conversion (*cis* epoxides both, J=4.4 Hz).[9] A source of proton used in reduction was found to come from aldehyde by an experiment using deuterated aldehyde in which the produced lactone possessed quantitative incorporation of deuterium in the NMR spectrum (entries 12 and 13).

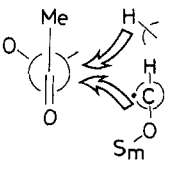
The reaction mechanism could be explained as follow (shown in the next **scheme**). Addition of Sm^{3+} (e.g. SmI_2OBu^t) to aldehyde followed by cordination with methyl ketone formed cyclic intermediate. Then hydrogen shifted to the ketone, and successively lactone was formed after elimination of SmI_2OBu^t. Intermediary samarium complex may take two possible configurations, such as the **form I** and the **form II**. The reaction may undergo through the **form I** and non-chelation type of face selection to γ-silyloxy methyl ketone (in **Fig.**) was postulated by considering the stereochemical analysis of the product. Same stereochemical face selection was observed in the former pinacol coupling process (in the **Fig.**).

Scheme



Figure

Tishchenko Reaction



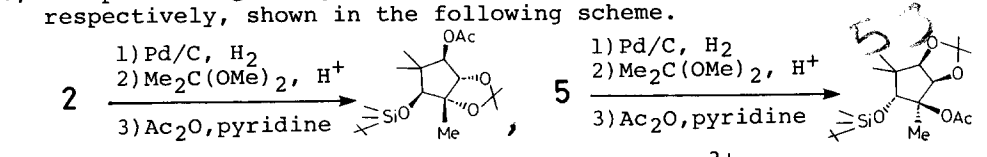
Pinacol Coupling

In conclusion in both the pinacol coupling and the lactone formation recation, a hydroxy group forming at the new stereogenic center orients *anti* to the silyloxy group in both cases. The novel lactone formation reported here is the first intramolecular Tishchenko oxidoreduction and is perfectly stereocontrolled. These results will be useful for polyoxo natural product synthesis.

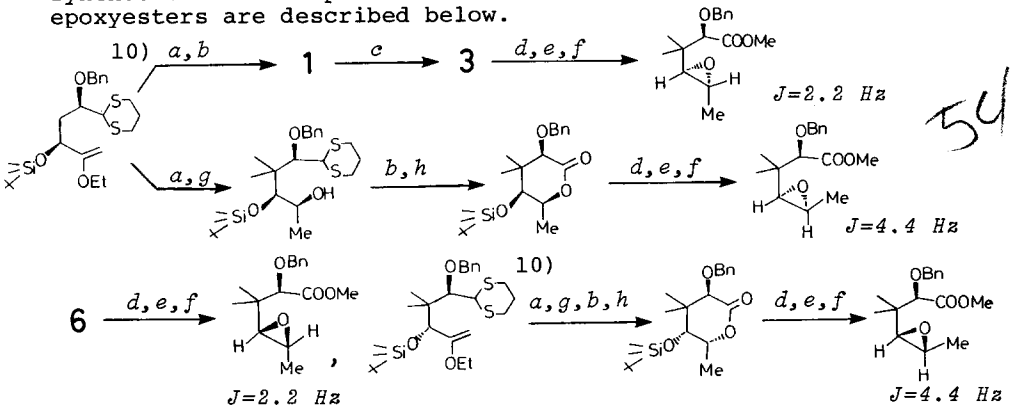
Aknowledgement: Authors are appreciate to Prof. J. Inanaga for valuable discussions and technical advice.

References and Notes

1, For example; Forskolin syntheses, a)S.Hashimoto, S.Sakata, M.Sonegawa and S.Ikegami, J.Am.Chem.Soc., 110, 3670 (1988). b)E.J.Corey, P.D.S.Jardine and J.C.Rohloff, ibid., 110, 3672 (1988).
2, G.A.Molander and C.Kenny, J.Am.Chem.Soc., 111, 8236 (1989) and references cited therein.
3, J.L.Chiana, W.Cabri and S.Hanessian, Tetrahedron Lett., 32, 1125 (1991).
4, T.Inamoto and M.Ono, Chem.Lett., 501 (1986).
5, The pinacols 2 and 5 were transformed to acetonide monoacetate respectively, shown in the following scheme.



6, When older SmI_2, presumably containing some Sm^{3+} species by the result of air oxidation, was used, a ratio of lactone/diol was increased.
7, Recent intermolecular Tishchenko oxidoreduction, see D.A.Evans and A.H.Haveyda, J.Am.Chem.Soc., 112, 6447 (1990).
8, J.Collin, J.-N.Namy and H.Kagan, Nouv.J.Chem., 10, 229 (1986).
9, Transformations of the δ-lactones 3 and 6 to *trans* epoxyesters and synthesis of other possible stereoisomeric δ-lactones and *cis* epoxyesters are described below.



a)CF_3COOH, *b*)NCS,$AgNO_3$, *c*)SmI_2OBu^t, *d*)$Bu^n{}_4NF$, *e*)MsCl,pyridine, *f*)K_2CO_3,MeOH, *g*)DIBAL, *h*)Jones Oxidation

10, J.Uenishi, Y.Kawachi and S.Wakabayashi, J.Chem.Soc., Chem.Commun., 1033 (1990).

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