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Non-Dehydrative Pinacol Rearrangement Using a Lewis Acid-Trialkyl Orthoester Combined System

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Abstract: An efficient pinacol rearrangement mediated by trialkyl orthoformate has been developed. The reactions of various types of diols with a catalytic amount of a Lewis acid in the presence of an ortho ester afforded the rearranged product in good yields *via* a cyclic ortho ester intermediate. This combined system is applicable not only to cyclic and acyclic tri- and tetra-substituted diols but also to the diols having acid-sensitive acetals.

Introduction

Carbon skeletal rearrangement reactions are very powerful synthetic tools to construct new carbon frames, and many reactions have been developed so far. Among them, pinacol rearrangement is one of the oldest known transformations of the carbon skeleton. The reaction is typically catalyzed by a Brønsted acid or Lewis acid and the diols (pinacols) are converted to the corresponding pinacolone. During the reaction, dehydration occurs intrinsically (eq. 1). As a result, several disadvantages are encountered in this reaction. For instance, 1) excess Lewis acid is usually required for the completion of the reaction, and 2) acid labile functional groups are sensitive to the reaction conditions and hence cannot coexist.[1] In order to overcome these difficulties, non-dehydrative rearrangements such as semi-pinacol rearrangement[2] and the rearrangement of epoxides[3] have been widely used instead of pinacol rearrangement. However, recent remarkable progress in the stereoselective synthesis of pinacols by pinacol coupling using low valent metals,[4] samarium diiodide[5] or by dihydroxylation of olefins using OsO_4 in the presence of a chiral ligand[6] would make pinacol rearrangement itself quite attractive, if its drawbacks are overcome. Recently, Mukaiyama developed an efficient pinacol rearrangement reaction using a catalytic amount (0.2 eq.) of $SbCl_5$-$AgSbF_6$, where the bis-silylether of the diol was used and siloxane was produced instead of H_2O.[7] Sands developed another catalytic method (0.5 eq. of BF_3•Et_2O) using $MgSO_4$ as a dehydrating agent.[8] However, in this case the formation of H_2O could not be suppressed.

Quite recently, we have reported an attractive alternative method[9] to overcome the disadvantage of the pinacol rearrangement, using a Lewis acid-trimethyl orthoformate [$HC(OMe)_3$] combined system, wherein the

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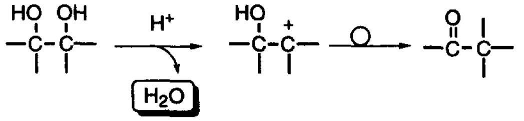
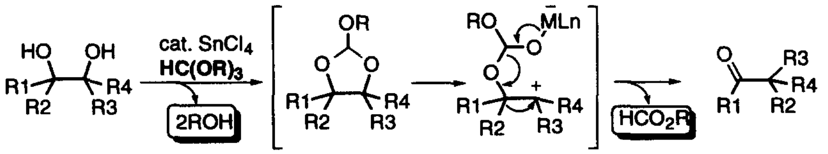
reaction proceeds under non-dehydrative circumstances (eq. 2). This Lewis acid-$HC(OMe)_3$ was found to be effective even with a catalytic amount of Lewis acid. On further investigation, however, it has been found that this system has some limitations. Subsequent detailed study of this new pinacol rearrangement revealed that several trialkyl orthoformates [$HC(OR)_3$] are effective in this reaction and among them, ethyldiphenyl orthoformate [$(PhO)_2CHOEt$], in particular, proved to be an efficient choice and can be applied to such diols where $HC(OMe)_3$ failed to give fruitful results. More importantly, it has also been observed that this orthoformate method is effective for the rearrangement reaction of dihydroxy acetals which are prone to undergo hydrolysis in the conventional Lewis acid catalyzed pinacol rearrangement. Full details of these studies are presented here.



(eq. 1)



(eq. 2)

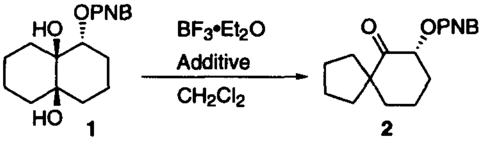
Results and Discussion

Perspective of the Reaction System

First, we investigated the pinacol rearrangement of **1** using $BF_3 \cdot Et_2O$ as a Lewis acid (Table 1). The spiro compound **2**[10] was obtained in 60% yield *via* the carbocation intermediate at the β-position of the acyloxy group.[11] However, 8 equivalents of $BF_3 \cdot Et_2O$ was required to accomplish the transformation and only under a reflux condition (entry 1). We then examined the reported improved methods. Sands's method[8] was found to be ineffective in the present case (entry 2). Mukaiyama's method using $SbCl_5$-$AgSbF_6$ with bis-silylether[7] was also not successful, because silylation of the 1,2-diol hardly occurred due to the bulkiness of the substrate. Use of molecular sieves also did not have any significant effect (entry 3). The failure of these methods to bring about an effective pinacol transformation of **1**, coupled with our earlier successful mild synthesis of oxocyclic compounds from triols using a Brønsted acid-orthoester system,[12] encouraged us to examine this reaction using our methodology. The sole purpose of using the orthoester is to activate the diol, thus trapping the water.[13] Although $PhC(OMe)_3$ and $MeC(OMe)_3$ were found to be inert so that no reaction occurred (entries 4 and 5), $HC(OMe)_3$ was effective in producing the reaction very well and afforded the rearranged product **2** in 83 % yield at 0°C-r.t. with only 1 equiv. of $BF_3 \cdot Et_2O$ (entry 6).

We then focused our attention on the effect of Lewis acids in the presence of $HC(OMe)_3$ as an additive (Table 2). All the Lewis acids tried efficiently performed this transformation and afforded **2** in good yields. However, $SnCl_4$ was found to be superior to others (entry 2). It is quite interesting to note that none of these Lewis acids afforded **2** in the absence of $HC(OMe)_3$.

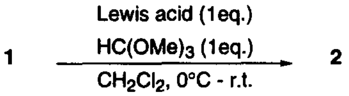
Table 1. Effect of Additives on the Pinacol Rearrangement



Entry	Additive	BF_3•Et_2O (eq.)	Conditions	Yield (%)
1	none	8	0°C - reflux, 3 h	60
2	$MgSO_4$	10	0°C - r.t., 48 h	15 (68)[a]
3	MS 4 Å	1	"	NR
4	$PhC(OMe)_3$	1	"	NR
5	$MeC(OMe)_3$	1	"	NR
6	$HC(OMe)_3$	1	"	83

[a] Yield in the parenthesis is recovered starting material.

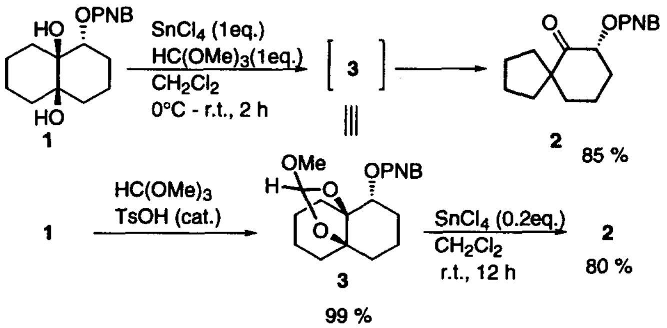
Table 2. Effect of Lewis Acids in the Presence of $HC(OMe)_3$



Entry	Lewis acid	Time	Yield of **2** (%)	
1	BF_3•Et_2O	48 h	83	(NR)[a]
2	$SnCl_4$	2 h	85	(trace)
3	TMSOTf	2 h	74	(NR)
4	$EtAlCl_2$ (2eq.)	8 h	70	(NR)

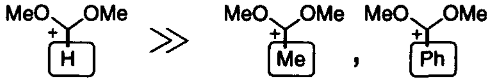
[a] Result in parentheses is observed in the absence of $HC(OMe)_3$.

From the above observation, it is clearly evident that $HC(OMe)_3$ plays an important role and accelerates the pinacol rearrangement to a great extent. The reaction proceeds *via* a cyclic ortho ester intermediate **3**, which could be easily observed on TLC, and its structure was confirmed by comparison with the authentic one prepared by the reaction of **1** and $HC(OMe)_3$ in the presence of a catalytic amount of *p*-TsOH. It was also ascertained that treatment of cyclic orthoester **3** with a catalytic amount of $SnCl_4$ afforded the rearranged product **2** in good yield thereby proving unambiguously that the reaction proceeds through the cyclic intermediate **3** (Scheme 1). On the other hand, no cyclic orthoester intermediate was observed when $PhC(OMe)_3$ and $MeC(OMe)_3$ were used. This could be due to the difference in the reactivities of the dioxycarbenium ions towards tertiary alcohols because of their bulkiness (Figure 1).

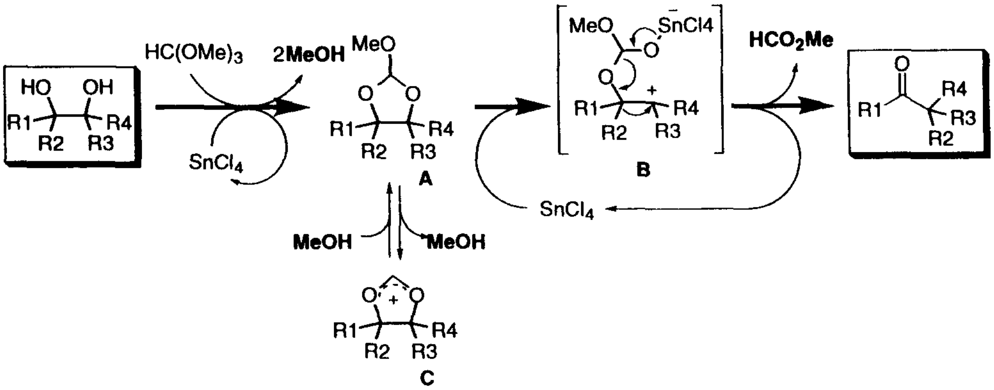


Scheme 1

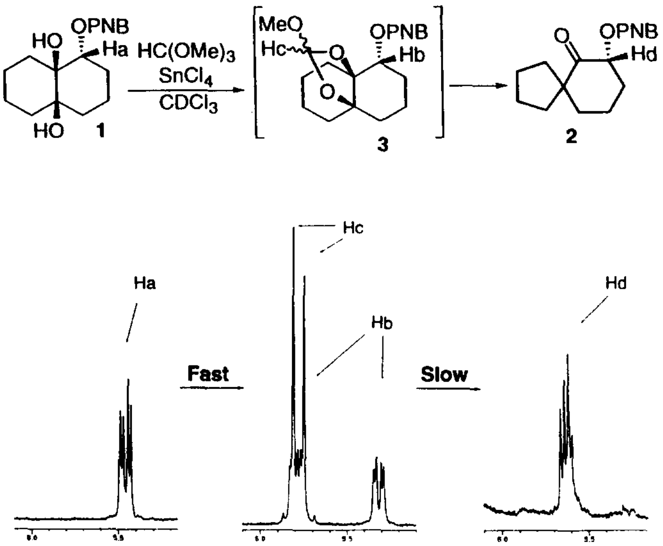
Figure 1. Reactivity of the Dioxenium Ions towards *tert*-Alcohols



Based on these results, the most probable mechanism that could be envisaged for the rearrangement reaction has been depicted in Scheme 2. Formation of the cyclic intermediate **A** by the reaction of the diol with $HC(OMe)_3$ in presence of Lewis acid and subsequent conversion to the cationic intermediate **B** would give rise to the rearranged product. Although the formation of another cationic intermediate C[14] cannot be ruled out, because of the equilibrium between the intermediates C and A in the presence of MeOH, eventually one might expect that the equilibrium would be shifted towards A during the course of the reaction, which in turn would give rise to intermediate B. The irreversible nature of the intermediate B to A as well as its instability coupled with its tendency to undergo a very fast rearrangement could be considered as the driving force for this reaction. It is worth noting that only 2 eq. of MeOH and 1 eq. of HCO_2Me were formed but no H_2O was released during this reaction. This was further confirmed by ^1H NMR experiments. Scheme 3 shows the ^1H NMR spectra of the reaction measured at different time intervals. Approximately 1:1 signal of "Hc" proton derived from diastereomixture of intermediate 3 was observed.



Scheme 2

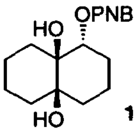
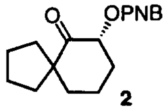
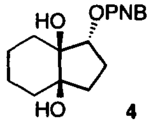
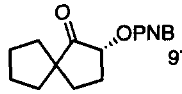
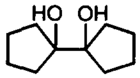
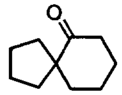
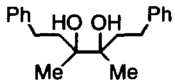
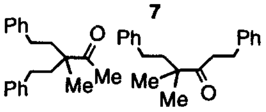
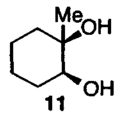
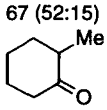


Scheme 3

Reaction of Various Diols in the Presence of HC(OMe)3

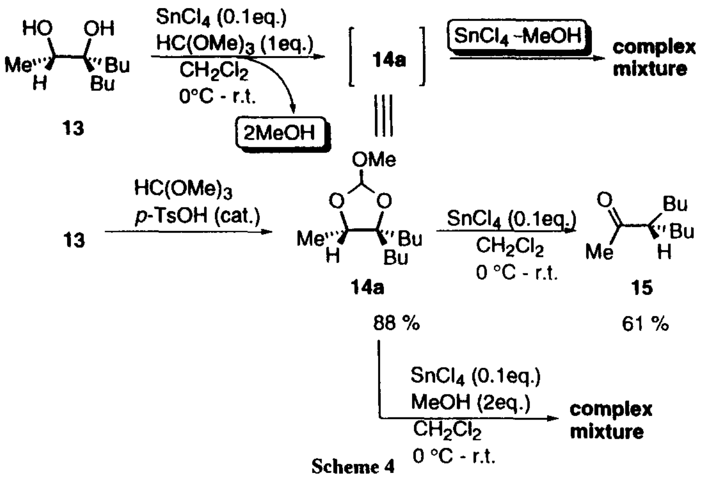
From the mechanistic consideration depicted in Scheme 2 and the result of the reaction of **3** with a catalytic amount of $SnCl_4$ as in Scheme 1, it appeared to us that this rearrangement reaction might even proceed with a catalytic amount of Lewis acid. We then examined the generality of the reaction using several types of diols. The results are shown in Table 3. Compound **1**, to our surprise, afforded a better yield under catalytic condition, although the reaction time was quite long (entry 1). Bicyclo[4.3.0]nonane system **4** gave the rearrangement product **5** in extremely high yield. This ortho ester method is applicable not only to typical tetrasubstituted diols (**6**[15] and **8**) for pinacol rearrangement (entries 3 and 4) but also to cyclic trisubstituted diol **11**[16] (entry 5).

Table 3. Pinacol Reaction of Various Diols with $HC(OMe)_3$ and a Catalytic Amount of $SnCl_4$ in CH_2Cl_2 at 0°C~r.t.

Entry	Substrate	Equiv. of $SnCl_4$	Reaction time	Product	Yield (%)
1	 **1**	0.4	52 h	 **2**	82
2	 **4**	0.2	7 h	 **5**	97
3	 **6**	0.2	5 min	 **7**	90
4	 **8**	0.4	4 d	 **9** 67 (52:15) **10**	
5	 **11**	0.4	9 h	 **12**	66

Study on Orthoformate Reagent

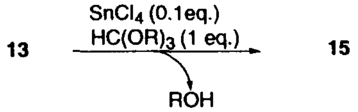
Pinacol rearrangement of many diols, mostly tetrasubstituted ones using HC(OMe)3, was indeed effective with a catalytic amount of Lewis acid (Table 3). On the other hand, under the same reaction conditions, the reaction of acyclic trisubstituted diol **13**[17] gave a complex mixture (see Scheme 4). In this reaction, the initial formation of cyclic orthoester **14a** was ascertained by TLC, but the subsequent rearrangement was found to be slow and afforded only a complex mixture. We then examined the reactivity of this cyclic orthoester intermediate **14a**, which was synthesized independently using *p*-TsOH as a catalyst. Treatment of **14a** with 0.1 eq. of $SnCl_4$ afforded the rearranged product **15** in 61% yield. However, use of $SnCl_4$ (0.1 eq.)-MeOH (2 eq.), the reagent combination which was supposed to be formed *in situ* during the reaction of the diol with $SnCl_4$ (0.1 eq.)-HC(OMe)3 (1 eq.) system, resulted in a complex mixture. This result clearly suggested that presence of MeOH inhibits the Lewis acidity of $SnCl_4$, and hence the $SnCl_4$-HC(OMe)3 combined system is not suitable for the rearrangement of diols such as **13**.



Scheme 4

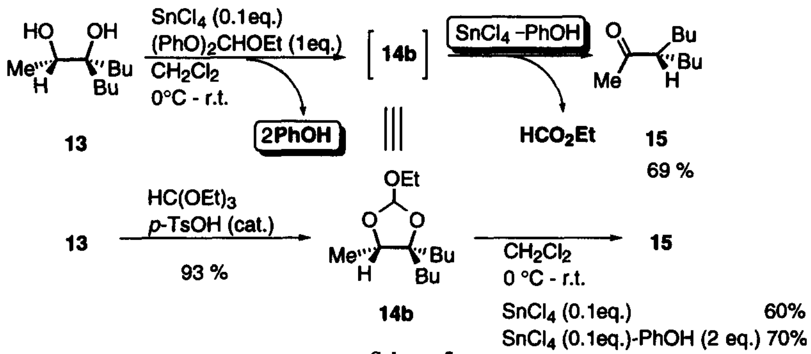
Because of the above limitations in the use of $HC(OMe)_3$, we then focused our attention on the reaction of **13** with other such orthoformate reagents, wherein alcohols other than MeOH could be released during the reaction. Results of these reactions are shown in Table 4. Reaction of **13** in the absence of any orthoester was fruitless and afforded **15** only in a trace amount (entry 1). As mentioned earlier, use of $HC(OMe)_3$ resulted in a complex mixture, and use of other orthoformate derivatives such as $HC(OEt)_3$, $HC(O\text{-}iPr)_3$, $PhOCH(OEt)_2$ and $(PhO)_2CHOEt$ improved the yield of the reaction (entries 3, 4, 5, and 6). Among them, a more attractive result was achieved with the use of $(PhO)_2CHOEt$;[18] the rearranged product **15** was obtained in 69% yield (entry 6). Because of the great difficulty involved in the preparation of $HC(OPh)_3$, use of this reagent in the above reaction was not attempted.

Table 4. Study of Ortho Esters



Entry	$HC(OR)_3$	Yield	Time	ROH
1	none	trace	10h	H_2O
2	$HC(OMe)_3$	complex	18h	MeOH
3	$HC(OEt)_3$	31%	4h	EtOH
4	$HC(O\text{-}iPr)_3$	51%	15h	i-PrOH
5	$PhOCH(OEt)_2$	57%	4h	EtOH,PhOH
6	$(PhO)_2CHOEt$	69%	4h	PhOH

The reason for the superiority of $(PhO)_2CHOEt$ in bringing about an efficient rearrangement of the diol **13** could be rationalized as follows (Scheme 5). As observed earlier, in the present case also, the initial formation of the cyclic orthoester intermediate and its subsequent rearrangement could be followed by TLC. The structure of the intermediate was ascertained by comparison with the authentic ethyl cyclic orthoester **14b** obtained by reaction of **13** with $HC(OEt)_3$. Unlike in the case of $HC(OMe)_3$ which produces MeOH during the reaction, in the present system, PhOH is released. PhOH, which is acidic, is not expected to react with or inhibit the Lewis acid, and thus its presence does not seem to affect the course of the reaction. In fact, $SnCl_4$ (0.1 eq.)-PhOH (2 eq.) mediated the rearrangement of **14b** in a way similar to that of $SnCl_4$ (0.1 eq.) itself.



Scheme 5

Reaction of Various Diols in the Presence of $(PhO)_2CHOEt$

We then examined several types of diols which were not suitable for the foregoing pinacol rearrangement reaction in the presence of $HC(OMe)_3$. The results are shown in Table 5. For the purpose of comparison, the results using $HC(OMe)_3$ are also listed. First, the effect of $(PhO)_2CHOEt$ was observed in the reaction of **16**, and the yield of **17** was dramatically increased compared to that with $HC(OMe)_3$ (entry 1). In the case of $HC(OMe)_3$, a moderate yield of bicyclohexyl-1,1'-diene was obtained. Even in the case of compounds **8** and **11**, a slight increment in the yields was observed with the use of $(PhO)_2CHOEt$ (entries 2 and 3). This $SnCl_4$-$(PhO)_2CHOEt$ combined system was also found to be effective in the case of **13**, and the desired product **15** was obtained in 69% yield as mentioned earlier (entry 4).

Table 5. Pinacol Reaction of Various Diols with $(PhO)_2CHOEt$ and a Catalytic Amount of $SnCl_4$ in CH_2Cl_2 at 0°C~r.t.

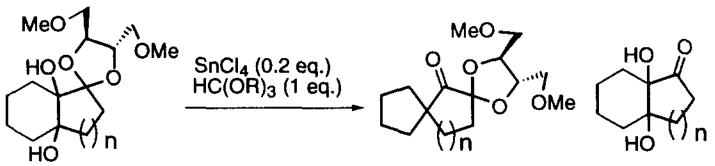
Entry	Substrate	Equiv. of $SnCl_4$	Product	Yield (%) $(PhO)_2CHOEt$	Yield (%) $HC(OMe)_3$
1	16	0.4	17	75	36[a]
2	8	0.4	9, 10	87 (64:23)	67 (52:15)
3	11	0.4	12	77	66
4	13	0.1	15	69	complex

[a] Bicyclohexyl-1,1'-diene was obtained in 55% yield.

Reaction of Dihydroxy Acetals

A characteristic feature of our rearrangement reaction is exemplified by the reaction of the substrates having an acetal functionality in the molecule (Table 6).[19] Treatment of the dihydroxy acetals **18a** with $SnCl_4$ gave the rearranged product **19a**[20] in low yield with a reasonable amount of dihydroxy ketone **20a** obtained by acid hydrolysis of **18a** (entry 1). Very surprisingly, use of $SnCl_4$-$HC(OMe)_3$ and $SnCl_4$-$(PhO)_2CHOEt$ systems afforded **19a** in good yields without the formation of **20a** respectively (entries 2 and 3). It is a remarkable finding that the acid labile acetal groups remained intact under these reaction conditions. On the other hand, in the reaction of the bicyclo[4.4.0]decane system **18b**, $SnCl_4$-$(PhO)_2CHOEt$ systems gave a poor result (entry 6). This is because of the bulkiness of the acetal moiety so that $(PhO)_2CHOEt$ could hardly react with the diols.

Table 6. Pinacol Reaction of Dihydroxy Acetals with a Catalytic Amount of $SnCl_4$ in CH_2Cl_2 at 0°C~r.t.



18a, b **19a,b** **20a,b**

Entry	Substrate	HC(OR)3	Reaction time	Yield (%) 19	Yield (%) 20
1	**18a** n= 1	none	20 h	34	39
2		$HC(OMe)_3$	3 h	88	-
3		$(PhO)_2CHOEt$	3 h	77	-
4	**18b** n= 2	none	24 h	trace	33
5		$HC(OMe)_3$	2.5 h	76	-
6		$(PhO)_2CHOEt$	12 h	19	30

Conclusion

We have developed an efficient and mild reaction system for the pinacol rearrangement reaction. The reaction proceeds without formation of H_2O using a catalytic amount of Lewis acid. The present method described here offers a new solution to the disadvantages of the usual pinacol rearrangement and would be a promising one for the successful transformation of various other types of 1,2-diols.

Experimental Section

All melting points are uncorrected. NMR spectra were measured on 270 MHz, 300 MHz and 500 MHz spectrometers with $CDCl_3$ as a solvent and with $SiMe_4$ as an internal standard. Infrared (IR) absorption spectra were recorded as a KBr pellet. All solvents were distilled and dried according to standard procedure.

Preparation of Diol Derivatives

Dihydroxy acylates **1** and **4** were prepared from the corresponding α,β-unsaturated ketones (3,4,5,6,7,8-Hexahydro-1(2*H*)-naphthalenone and 2,3,4,5,6,7-Hexahydro-1*H*-inden-1-one, respectively) in a three-step sequence: (i) formation of allylic alcohol by reduction of the α,β-unsaturated ketones with DIBAH in CH_2Cl_2 at 0 °C, (ii) triol formation by OsO_4 oxidation of allylic alcohol in acetone-H_2O (1:1, 10 mL), and (iii) acylation of the triol with *p*-nitrobenzoyl chloride in pyridine. Dihydroxy acetals **18a, b** were also prepared by a two-step sequence: (i) formation of the diol-ketone by the Swern oxidation of the triol which was synthesized by the above method, (ii) acetalization of the diol-ketone with (2*R*, 3*R*)-1,4-dimethoxybutanediol in the presence of TMSOTf in CH_2Cl_2 at 0 °C. Tetrasubstituted diols **6, 8, 16** were prepared by pinacol coupling of the corresponding ketones using Mg-Hg/$TiCl_4$.[15] Trisubstituted diol **11** was synthesized by OsO_4 oxidation of 1-methylcyclohexene, and **13** was synthesized by the nucleophilic addition of butylmagnesium chloride to ethyl lactate.[17]

r-1,c-6-Dihydroxybicyclo[4.4.0]dec-t-2-yl 4-nitrobenzoate (1): colorless crystals; mp 167-169 °C (AcOEt-*n*-hexane); IR 3500, 2940, 2869, 1723, 1528, 1279 cm^{-1}; ^1H NMR δ 1.43-2.01 (m, 14H), 2.16 (s, 1H), 2.71 (s, 1H), 5.46 (dd, 1H, *J* = 5.5, 12.0 Hz), 8.20 (d, 2H, *J* = 8.0 Hz), 8.28 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (C_6D_6) δ 19.1, 20.6, 23.2, 27.4, 28.7, 32.6, 36.3, 74.5, 75.4, 78.8, 123.4, 130.7, 136.1, 150.6, 165.1. Anal. Calcd. for $C_{17}H_{21}NO_6$: C, 60.89; H, 6.31; N, 4.18. Found: C, 60.84; H, 6.18; N, 4.21.

r-1,c-6-Dihydroxybicyclo[4.3.0]non-t-7-yl 4-nitrobenzoate (4): colorless crystals; mp 64–66 °C (CH_2Cl_2–MeOH); IR 3480, 2942, 2863, 1725, 1530 cm^{-1}; ^1H NMR δ 1.20-1.94 (m, 12H), 2.06-2.24 (m, 1H), 2.44-2.64 (m, 1H), 5.52 (dd, 1H, *J* = 6.0, 10.0 Hz), 8.23 (d, 2H, *J* = 8.0 Hz), 8.30 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR δ 19.9, 23.2, 24.9, 29.5, 29.7, 33.5, 79.5, 79.7, 86.3, 123.5, 130.8, 134.9, 150.7, 166.3. Anal. Calcd. for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.65; H, 5.91; N, 4.40.

1-(Hydroxycyclopentyl)cyclopentane-1-ol (6): colorless crystals; mp 111–112.5 °C (AcOEt–*n*-hexane) (lit[15] mp. 111–112 °C) IR 3328 cm^{-1}; ^1H NMR δ 1.55-1.90 (m, 16H), 1.92 (brs, 2H).

3,4-Dimethyl-1,6-diphenyl-3,4-hexanediol (8): white powder (1:1 diastereomixture); mp 74–75 °C (AcOEt–*n*-hexane); IR 3532, 3027, 2959, 1497, 1455 cm^{-1}; ^1H NMR δ 1.26 (s, 6/2H), 1.28 (s, 6/2H), 1.66-1.74 (m, 4/2H), 1.87-2.01 (m, 4/2H), 1.95 (s, 2H), 2.69 (dt, 4/2H, *J* = 5.0, 13.0 Hz), 2.77-2.85 (m, 4/2H), 7.15-7.24 (m, 10H); ^{13}C NMR (C_6D_6) δ 20.7, 21.1, 30.7, 38.4, 39.0, 76.8, 76.9, 126.0, 128.7, 128.8, 143.2, 143.3. Anal. Calcd. for $C_{20}H_{26}O_2$: C, 80.50; H, 8.78. Found: C, 80.45; H, 8.62.

1-Methylcyclohexane-*cis*-1,2-diol (11): white powder; mp 67–68 °C (AcOEt–*n*-hexane); (lit[16] 68 °C); IR 3438 cm^{-1}; ^1H NMR δ 1.26 (s, 3H), 1.27-1.95 (m, 10H), 3.41 (m, 1H).

3-Butyl-2,3-heptanediol (13): colorless oil; bp 148–150 °C/9 mmHg (lit[17] 168–173 °C / 20 mmHg); IR 3400, 2940, 2872 cm^{-1}; ^1H NMR δ 0.92 (t, 6H, *J* = 7.0 Hz), 1.16 (d, 3H, *J* = 6.5 Hz), 1.20-1.70 (m, 12H), 1.79 (brs, 1H), 2.05 (brs, 1H), 3.72 (m, 1H). ^{13}C NMR (C_6D_6) δ 14.5, 14.6, 17.7, 24.0, 24.1, 26.0, 26.1, 34.5, 36.2, 71.7, 76.0.

1-(Hydroxycyclohexyl)cyclohexan-1-ol (16): colorless crystals; mp 125–126 °C (Diethyl ether) (lit[15] mp. 124–125 °C) IR 3457 cm^{-1}; ^1H NMR δ 1.05-1.16 (m, 2H), 1.32-1.40 (m, 4H), 1.55-1.73 (m, 14H), 1.77 (s, 2H).

cis-1,6-Dihydroxybicyclo[4.3.0]nonane-2-spiro-1'-(3'S,4'S)-3',4'-bis(methoxymethyl)-2',5'-dioxolane (18a): [1:1 diastereomixture] colorless oil; IR 3528, 2934, 2864 , 1456 cm^{-1}; ^1H NMR δ 1.24-1.40 (m, 2H), 1.45-1.70 (m, 6H), 1.84-2.12 (m, 4H), 2.73 (brs, 1/2H), 2.94 (brs, 1/2H), 3.10 (brs, 1/2H), 3.39 (s, 3H), 3.41 (s, 3H), 3.46-3.73 (m, 4H), 3.79 (brs, 1/2H), 3.96-4.04 (m, 1H), 4.14-4.21 (m, 1H). Anal. Calcd. for $C_{15}H_{26}O_6$: C, 59.58; H, 8.67. Found: C, 59.75; H, 8.52.

cis-1,6-Dihydroxybicyclo[4.4.0]decane-2-spiro-1'-(3'S,4'S)-3',4'-bis(methoxymethyl)-2',5'-dioxolane (18b): [A single isomer (more polar isomer on TLC : AcOEt-*n*-hexane)] colorless oil; IR 3544, 2930, 2867, 1453 cm^{-1}; ^1H NMR δ 1.26-1.96 (m, 14H), 3.05 (brs, 1H), 3.39 (s, 3H), 3.41 (s, 3H), 3.52 (d, 2H, J = 4.5 Hz), 3.60 (dd, 2H, J = 3.0, 4.5 Hz), 3.82 (brs, 1H), 4.03 (dt, 1H, J = 4.5, 8.0 Hz), 4.20 (dt, 1H, J = 4.5, 8.0 Hz); ^{13}C NMR δ 17.8, 20.5, 23.0, 30.3, 32.8, 33.8, 34.6, 59.4, 59.5, 72.6, 73.2, 75.2, 75.4, 77.3, 79.0, 113.7. Anal. Calcd. for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.70; H, 8.99.

Treatment of Diols with Lewis Acid-Ortho Ester: General Procedure for Table 1-6

To a solution of the diol (0.1 mmol) in dry CH_2Cl_2 (1 mL) was added the ortho ester (0.1 mmol), and BF_3•Et_2O or other Lewis acid (0.01–0.1 mmol) at 0 °C under N_2, and the reaction mixture was stirred for the time shown in the Table. After dilution with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over $MgSO_4$ or Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel (AcOEt–*n*-hexane) to give the pure product.

Reactions for Table 1

(entry 1)

6-Oxospiro[4.5]dec-7-yl 4-nitrobenzoate (2): 1 (39.0 mg, 0.116 mmol) and BF_3•Et_2O (0.117ml, 0.928 mmol) gave **2** as colorless crystals (22.0 mg, 60%): mp 103–104 °C (MeOH); IR 2869, 1736, 1721 cm^{-1}; ^1H NMR δ 1.14-2.00 (m, 12H), 2.38-2.55 (m, 2H), 5.63 (dd, 1H, J = 5.5, 6.5 Hz), 8.25 (d, 2H, J = 6.5 Hz), 8.29 (d, 2H, J = 6.5 Hz); ^{13}C NMR δ 20.7, 24.5, 25.4, 32.6, 33.6, 35.6, 39.3, 57.0, 76.1, 123.3, 130.8, 135.2, 150.4, 163.7, 206.1. Anal. Calcd. for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.03; N, 4.41. Found: C, 64.29; H, 6.06; N, 4.41.

(entry 2, Sands' method)

To a solution of **1** (41.2 mg, 0.123 mmol) in dry CH_2Cl_2 (1.23 mL) was added $MgSO_4$ (14.0 mg) at r.t. under N_2, and the reaction mixture was stirred for 1 h. BF_3•Et_2O (0.156 mL, 1.23 mmol) was then added to the reaction mixture at 0 °C, and the reaction mixture was stirred at 0 °C ~ r.t. for the time shown in the Table. After dilution with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The same procedure as stated above then gave **2** (5.9 mg, 15%).

(entry 6)

1 (101 mg, 0.301 mmol), $HC(OMe)_3$ (0.033 mL, 0.301 mmol), and BF_3•Et_2O (0.0382 mL, 0.301 mmol) gave **2** (79.0 mg, 83%).

Reactions for Table 2 (Reaction conditions and times : see table 2 in the text)

entry	amount of **1**	$HC(OMe)_3$	Lewis acid	yield of **2** (%)
2	36.1 mg (0.108 mmol)	0.012 ml (0.108 mmol)	$SnCl_4$ 0.0126 ml (0.108 mmol)	85 (29.1 mg)
3	30.6 mg (0.0912 mmol)	0.010 ml (0.0912 mmol)	TMSOTf 0.018 ml (0.0912 mmol)	74 (21.5 mg)
4	34.4 mg (0.103 mmol)	0.011 ml (0.103 mmol)	$EtAlCl_2$ (2eq.) 0.22 ml [0.98 M *n*-hexane solution] (0.206 mmol)	70 (22.8 mg)

Reactions for Table 3 (Reaction conditions and times : see table 3 in the text)

entry	substrate	$HC(OMe)_3$	$SnCl_4$	product yield (%)
1	**1** 32.6 mg (0.108 mmol)	0.012 ml (0.108 mmol)	4.5 µl (0.039 mmol)	**2** 82 (25.4 mg)
2	**4** 32.0 mg (0.10 mmol)	0.011 ml (0.10 mmol)	0.023 ml 10% CH_2Cl_2 solution (0.02 mmol)	**5** 97 (29.4 mg)
3	**6** 101.1 mg (0.594 mmol)	0.071 ml (0.653 mmol)	0.014 ml (0.12 mmol)	**7** 90 (81.4 mg)
4	**8** 100 mg (0.335 mmol)	0.037 ml (0.335 mmol)	0.016 ml (0.134 mmol)	**9** 52 (49.1 mg) **10** 15 (14.1 mg)
5	**11** 202.1 mg (1.55 mmol)	0.17 ml (1.55 mmol)	0.073 ml (0.624 mmol)	**12** 66 (114.0 mg)

1-Oxospiro[4.4]non-2-yl 4-nitrobenzoate (5): colorless crystals; mp 108-109 °C (CH_2Cl_2-*n*-hexane); IR 2955, 2869, 1750, 1730 cm^{-1}; ^1H NMR δ 1.20-2.20 (m, 11H), 2.40-2.60 (m, 1H), 5.43 (dd, 1H, *J* = 8.5, 10.0 Hz), 8.24 (d, 2H, *J* = 8.5 Hz), 8.30 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR δ 25.8, 26.0, 26.7, 33.2, 37.9, 39.0, 54.5, 77.0, 123.8, 131.3, 135.2, 150.9, 164.2, 216.6. Anal. Calcd. for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.31; H, 5.63, N, 4.62.

Spiro[4.5]decan-6-one (7)[15]: colorless oil; IR 2944, 2865, 1707, 1451 cm^{-1}; ^1H NMR δ 1.32-1.46 (m, 2H), 1.55-1.60 (m, 4H), 1.62-1.89 (m, 6H), 2.00-2.13 (m, 2H), 2.40 (t, 2H, *J* = 6.5 Hz).

3-Methyl-3-phenethyl-5-phenyl-2-pentanone (9): colorless oil; IR 3020, 3950, 1701 cm^{-1}; ^1H NMR δ 1.28 (s, 3H), 1.81 (dt, 2H, *J* = 5.5, 12.5 Hz), 1.96 (dt, 2H, *J* = 5.0, 12.5 Hz), 2.18 (s, 3H), 2.43 (dt, 2H, *J* = 5.0, 12.5 Hz), 2.53 (dt, 2H, *J* = 5.5, 12.5 Hz), 7.15-7.32 (m, 10H); ^{13}C NMR δ 20.7, 25.3, 30.8, 40.4, 51.4, 125.9, 128.2, 128.4, 142.0, 212.8. Anal. Calcd. for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.84; H, 8.74.

4,4-Dimethyl-1,6-diphenyl-3-hexanone (10): colorless oil; IR 3027, 2967, 1703, 1455 cm^{-1}; ^1H NMR δ 1.15 (s, 6H), 1.77-1.80 (m, 2H), 2.38-2.42 (m, 2H), 2.79 (t, 2H, *J* = 7.5 Hz), 2.88 (t, 2H, *J* = 7.5 Hz), 7.08-7.29 (m, 10H); ^{13}C NMR δ 24.3, 29.9, 31.1, 38.9, 42.1, 47.5, 125.8, 126.0, 128.2, 128.3, 128.4, 128.5, 141.5, 142.1, 214.2. Anal. Calcd. for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.78; H, 8.75.

Reactions for Table 4 (Reaction conditions and times : see table 4 in the text)

entry	amount of **13**	$HC(OR)_3$		$SnCl_4$	yield of **15** (%)
3	107.9 mg (0.573 mmol)	$HC(OEt)_3$	0.09 ml (0.572 mmol)	6.7 μl (0.057 mmol)	31 (30.0 mg)
4	195 mg (1.04 mmol)	$HC(O\text{-}iPr)_3$	197 mg (1.04 mmol)	0.012 ml (0.104 mmol)	51 (90.0 mg)
5	100 mg (0.53 mmol)	$PhOCH(OEt)_2$	0.102 ml (0.53 mmol)	6.2 μl (0.053 mmol)	57 (51.4 mg)
6	100 mg (0.53 mmol)	$(PhO)_2CHOEt$	130 mg (0.53 mmol)	6.2 μl (0.053 mmol)	69 (62.4 mg)

3-Butyl-2-heptanone (15): colorless oil: IR 2959, 2930, 2866, 1713 cm^{-1}; ^1H NMR δ 0.88 (t, 6H, J= 7.0Hz), 1.16-1.35 (m, 8H), 1.37-1.46 (m, 2H), 1.52-1.64 (m, 2H), 2.11 (s, 3H), 2.42 (m, 1H); ^{13}C NMR δ 13.9, 22.8, 28.7, 29.6, 31.4, 53.3, 213.4. HRMS m/z Calcd. for $C_{11}H_{23}O$ (M^++1): 171.1749. Found: 171.1745.

Reactions for Table 5 (Reaction conditions : see table 5 in the text)

entry	substrate	$HC(OR)_3$		$SnCl_4$	product	yield (%)
1	**16** 100.8 mg (0.504 mmol)	$HC(OMe)_3$	0.055 ml (0.504 mmol)	0.024 ml (0.020 mmol)	**17**	36 (32.7 mg)
1	**16** 99.0 mg (0.499 mmol)	$(PhO)_2CHOEt$	129 mg (0.499 mmol)	0.023 ml (0.20 mmol)	**17**	75 (67.5 mg)
2	**8** 253.0 mg (0.847 mmol)	$(PhO)_2CHOEt$	206 mg (0.847 mmol)	0.04 ml (0.34 mmol)	**9** **10**	64 (150.8 mg) 23 (55.3 mg)
3	**11** 205.5 mg (1.57 mmol)	$(PhO)_2CHOEt$	385 mg (1.58 mmol)	0.075 ml (0.64 mmol)	**12**	77 (135.7 mg)

Spiro[5.6]dodecan-7-one (17): colorless oil; IR 2926, 2855, 1700, 1453 cm^{-1}; ^1H NMR δ 1.37-1.82 (m, 18H), 2.50 (t, 2H, J = 6.0 Hz).

Reactions for Table 6 (Reaction conditions and times : see table 6 in the text)

entry	substrate	$HC(OR)_3$	$SnCl_4$	product	yield (%)
1	**18a**[a] 30.5 mg (0.101 mmol)	none	0.011 ml (0.101 mmol)	**19a** **20a**	34 (9.7 mg) 39 (6.7 mg)
2	**18a** 41.1 mg (0.136 mmol)	$HC(OMe)_3$ 0.015 ml (0.136 mmol)	0.032 ml 10% CH_2Cl_2 solution (0.027 mmol)	**19a**	88 (33.9 mg)
3	**18a** 50.0 mg (0.165 mmol)	$(PhO)_2CHOEt$ 40.4 mg (0.165 mmol)	0.039 ml 10% CH_2Cl_2 solution (0.033 mmol)	**19a**	77 (36.0 mg)
4	**18b**[b] 39.7 mg (0.125 mmol)	none	0.015 ml (0.125 mmol)	**20b**	33 (7.7 mg)
5	**18b** 29.5 mg (0.093 mmol)	$HC(OMe)_3$ 0.010 ml (0.093 mmol)	0.022 ml 10% CH_2Cl_2 solution (0.0186 mmol)	**19b**	76 (21.2 mg)
6	**18b** 45.2 mg (0.143 mmol)	$(PhO)_2CHOEt$ 34.9 mg (0.143 mmol)	0.034 ml 10% CH_2Cl_2 solution (0.029 mmol)	**19b** **20b**	19 (8.8 mg) 30 (7.8 mg)

[a] 1:1 diastereomixture was used. [b] A single isomer (more polar isomer on TLC: AcOEt-*n*-hexane) was used.

(2*S*,3*S*)-2,3-Bis(methoxymethyl)-1,4-dioxadispiro[4.1.4.2]tridecan-6-one (19a): colorless oil; IR 2872, 2816, 1746, 1450 cm^{-1}; ^{1}H NMR δ 1.47-1.54 (m, 2H), 1.61-1.91 (m, 8H), 2.09 (t, 2H, *J* = 7.5 Hz), 3.39 (s, 3H), 3.40 (s, 3H), 3.49-3.56 (m, 3H), 3.73 (dt, 1H, *J* = 7.5, 10.0 Hz), 4.03 (dt, 1H, *J* = 4.5, 7.5 Hz), 4.28-4.34 (m, 1H); ^{13}C NMR δ 25.7, 25.7, 31.6, 32.5, 37.5, 38.1, 54.0, 59.3, 59.4, 72.5, 74.0, 78.1, 78.6, 108.8, 218.7. Anal. Calcd. for $C_{15}H_{24}O_5$: C, 63.36; H, 8.51. Found: C, 63.61; H, 8.63.

(2*S*,3*S*)-2,3-Bis(methoxymethyl)-1,4-dioxadispiro[4.1.4.3]tetradecan-6-one (19b): colorless oil; IR 2940, 2872, 1719, 1530, 1449 cm^{-1}; ^{1}H NMR δ 1.42-1.71 (m, 8H), 1.81-1.87 (m, 2H), 1.97-2.02 (m, 2H), 2.12-2.26 (m, 2H), 3.37 (s, 3H), 3.40 (s, 3H), 3.40-3.44 (m, 1H), 3.44-3.63 (m, 3H), 3.99-4.03 (m, 2H); ^{13}C NMR δ 19.6, 25.0, 25.1, 35.9, 36.1, 37.6, 38.2, 56.9, 59.2, 59.4, 72.4, 73.3, 78.0, 78.7, 107.6, 209.1. Anal. Calcd. for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.56; H, 8.75.

cis-3a,7a-Dihydroxyoctahydro-1*H*-inden-1-one (20a): colorless oil; IR 3461, 2940, 2865, 1750 cm^{-1}; ^{1}H NMR δ 1.23-1.97 (m, 8H), 2.13-2.26 (m, 2H), 2.42-2.54 (m, 2H), 2.67 (brs, 1H), 3.09 (brs, 1H). ^{13}C NMR δ 19.6, 23.2, 26.8, 31.0, 31.5, 33.2, 76.4, 80.3, 219.3. MS (EI) m/z (rel intensity) 170 (M^+, 37), 152 (100), 124 (73), 114 (100), 96 (86), 86 (99), 79 (23), 67 (98), 55 (100).

cis-4a,8a-Dihydroxyoctahydro-1(2*H*)-naphthalenone (20b): colorless crystals; mp 64-65 °C (Diethyl ether-*n*-hexane); IR 3480, 2944, 2867, 1709 cm^{-1}; ^{1}H NMR δ 1.49-1.56 (m, 2H), 1.58-1.74 (m, 6H), 1.88-1.96 (m, 2H), 2.14 (tq, 1H, *J* = 4.5, 13.5 Hz), 2.27 (ddt, 1H, *J* = 2.5, 4.5, 13.5 Hz), 2.42-2.47 (m, 1H), 2.60 (s, 1H), 2.61 (dt, 1H, *J* = 7.0, 14.0 Hz), 4.11 (s, 1H); ^{13}C NMR δ 20.3, 21.0, 23.1, 30.9, 34.3, 36.3, 36.6, 76.3, 80.2, 214.1. Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.28; H, 8.62.

Synthesis of cyclic ester intermediate (3) (Scheme 1)

11,13-Dioxa-12-methoxytricyclo[4.4.0.3^{1,6}]tridec-2-yl *p*-nitrobenzoate (3): To a suspension of **1** (100 mg, 0.298 mmol) in $HC(OMe)_3$ (2.98 mL) was added a catalytic amount of *p*-TsOH at r.t. under N_2, and the reaction mixture was stirred for 1.5 h. K_2CO_3 was then added to the reaction mixture, and the mixture was stirred for 10 min. After filtration, the organic layer was concentrated to give **3** as a colorless oil (1:1 diastereomixture, 111.4 mg, 99%); compound **3** is very labile and its structure was determined by IR and ^{1}H NMR: IR 2944, 2869, 1727, 1530, 1277 cm^{-1}; ^{1}H NMR δ 1.18-1.29 (m, 2H), 1.35-2.04 (m, 10H), 2.19-2.36 (m, 2H), 3.40 (s, 3/2H), 3.42 (s, 3/2H), 5.33 (dd, 1/2H, *J* = 4.0, 12.0 Hz), 5.75 (s, 1/2H), 5.82 (s, 1/2H), 5.82 (dd, 1/2H, *J* = 4.0, 12.0 Hz), 8.19-8.33 (m, 4H) .

Reaction of 3 with $SnCl_4$

To a solution of **3** (50.2 mg, 0.133 mmol) in dry CH_2Cl_2 (1.33 mL) was added $SnCl_4$ (10% CH_2Cl_2 solution, 0.032 mL, 0.027 mmol) at 0 °C under N_2, and the reaction mixture was stirred at 0 °C for 30 min and at r.t. for 15 min. After dilution with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over or N a_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel (AcOEt–*n*-hexane) to give **2** (33.7 mg, 80%).

NMR Experiment (Scheme 3)

To a solution of **1** (10.4 mg, 0.031 mmol) in $CDCl_3$ (1.0 mL) was added $HC(OMe)_3$ (8 μL, 0.062 mmol), and $SnCl_4$ (one drop by micro syringe). The reaction was monitored by ^1H NMR every 1 h.

Synthesis of cyclic ester intermediate (Scheme 4)

4,4-Dibutyl-2-methoxy-5-methyl-1,3-dioxolane (14a): To a suspension of **13** (199.7 mg, 1.06 mmol) in $HC(OMe)_3$ (1.0 mL) was added a catalytic amount of *p*-TsOH at r.t. under N_2, and the reaction mixture was stirred for 10 min. K_2CO_3 was then added to the reaction mixture, and the mixture was stirred for an additional 10 min. After filtration, the organic layer was concentrated to give **14a** as a colorless oil (2:1 diastereomixture, 215.7 mg, 88%); compound **14a** is very labile and its structure was determined by IR and ^1H NMR: IR 2874, 1468 cm^{-1}; ^1H NMR δ 0.90 (t, 4H, *J*= 6.5 Hz), 0.92 (t, 2H, *J*= 6.5 Hz), 1.24 (d, 3H, *J*= 6.5 Hz), 1.18-1.80 (m, 12H), 3.20 (s, 2H), 3.34 (1H, s), 3.99 (q, 2/3H, *J*= 6.5 Hz), 4.10 (q, 1/3H, *J*= 6.5 Hz), 5.62 (s, 2/3H), 5.63 (s, 1/3H).

*Reaction of **14a** with $SnCl_4$*

To a solution of **14a** (66.4 mg, 0.288 mmol) in dry CH_2Cl_2 (2.9 mL) was added $SnCl_4$ (3.5 μL, 0.030 mmol) at 0 °C under N_2, and the mixture was stirred at 0 °C for 30 min and at r.t. for 15 min. After dilution with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel (AcOEt–*n*-hexane) to give **15** (29.7 mg, 61%).

Synthesis of cyclic ester intermediate (Scheme 5)

4,4-Dibutyl-2-ethoxy-5-methyl-1,3-dioxolane (14b): To a suspension of **13** (99.0 mg, 0.526 mmol) in $HC(OEt)_3$ (0.5 mL) was added *p*-TsOH (5.4 mg, 0.0263 mmol) at r.t. under N_2, and the reaction mixture was stirred for 10 min. K_2CO_3 was then added to the reaction mixture, and the reaction mixture was stirred for an additional 10 min. After filtration, the organic layer was concentrated to give **14b** as a colorless oil (2:1 diastereomixture, 119.5 mg, 93%); compound **14b** is very labile and its structure was determined by IR and ^1H NMR: IR 2872, 1377 cm^{-1}; ^1H NMR δ 0.91 (t, 4H, *J*= 7.0 Hz), 0.92 (t, 2H, *J*= 7.0 Hz), 1.15-1.80 (m, 18H), 3.58 (q, 4/3H, *J*= 7.0 Hz), 3.61 (q, 2/3H, *J*= 7.0 Hz), 3.97 (q, 1/3H, *J*= 6.5 Hz), 4.11 (q, 2/3H, *J*= 6.5 Hz), 5.70 (s, 1H).

*Reaction of **14b** with $SnCl_4$ (Scheme 5)*

To a solution of **14b** (63.5 mg, 0.260 mmol) in dry CH_2Cl_2 (2.6 mL) was added $SnCl_4$ (3.0 μL, 0.026 mmol) at 0 °C under N_2, and the reaction mixture was stirred at 0 °C for 30 min and at r.t. for 15 min. After dilution with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel (AcOEt–*n*-hexane) to give **15** (26.7 mg, 60%).

*Reaction of **14b** with $SnCl_4$ and PhOH (Scheme 5)*

To a solution of **14b** (62.5 mg, 0.256 mmol) in dry CH_2Cl_2 (2.5 mL) was added a solution of $SnCl_4$ (3.0 μL, 0.026 mmol)-PhOH (48 mg, 0.51 mmol) in dry CH_2Cl_2 (0.1 mL) at 0 °C under N_2, and the reaction mixture was stirred at 0 °C for 15 min and at r.t. for 1 hr. After dilution with CH_2Cl_2, saturated aqueous $NaHCO_3$ was added to the mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography on silica gel (AcOEt–*n*-hexane) to give **15** (30.5 mg, 70%).

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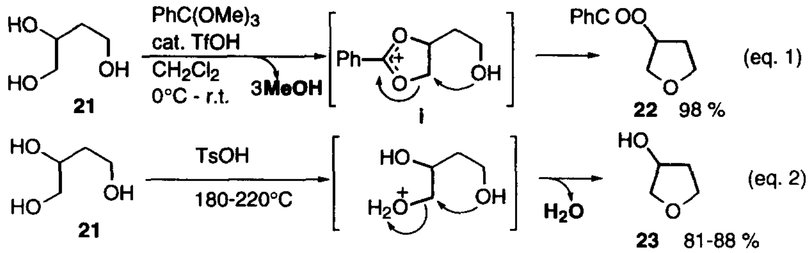
11. For a remarkable effect of the acyloxy group on the stability of the cationic intermediate, see ref. 10.
12. We have developed a mild and efficient synthesis of oxacyclic compound **22** from the triols **21**, with a suitably positioned hydroxy function, in the presence of trialkyl orthoesters (eq. 1) : (a) Fujioka, H.; Kitagawa, H.; Kondo, M.; Matsunaga, N.; Kitagaki, S.; Kita, Y. *Heterocycles.* **1993**, *35*, 665. (b) Fujioka, H.; Kitagawa, H.; Kondo, M.; Kita, Y. *ibid.* **1994**, *37*, 743. The reaction proceeds *via* cyclic orthoester intermediate **i** under mild condition. A characteristic point of the reaction is that the reaction is non-dehydrative and MeOH is formed as a by-product, whereas the usual acidic condition converts compound **21** to the cyclic ether **23** with formation of H_2O as a by-product (eq. 2) : Wynberg, H.; Bantjes, A. "Organic Synthesis Collective Volume 4"; Ragjohn, N., Ed.; John Wiley: New York, **1963**, *4*, 534.



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19. We have studied asymmetric synthesis using chiral acetals derived from C_2-symmetric 1,4-dimethoxy-2,3-butanediol. Then, pinacol rearrangement of the dihydroxy acetals derived from 1,4-dimethoxy-2,3-butanediol was examined. For our study on representative studies asymmetric synthesis using chiral acetals derived from 1,4-dimethoxy-2,3-butanediol, see: (a) Fujioka, H.; Kitagawa, H.; Yamanaka, T.; Kita, Y. *Chem. Pharm. Bull.* **1992**, *40*, 3118. (b) Fujioka, H.; Annoura, H.; Murano, K.; Kita, Y.; Tamura, Y. *Chem. Pharm. Bull.* **1989**, *37*, 2047. (c) Tamura, Y.; Annoura, H.; Yamamoto, H.; Kondo, H.; Kita, Y.; Fujioka, H. *Tetrahedron Lett.* **1987**, *28*, 5709 and references cited therein.

20. We have already found that the Lewis acid treatment of epoxy acetals **24** afforded rearrangement product **25** *via* an oxirane ring cleavage at the β-postion of an acetal due to the electron-withdrawing nature of the acetal. Unpublished results.