Pergamon

Tetrahedron 58 (2002) 7049–7064

TETRAHEDRON

Isomerization of cyclic ethers having a carbonyl functional group: new entries into different heterocyclic compounds

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Received 19 March 2002; accepted 23 May 2002

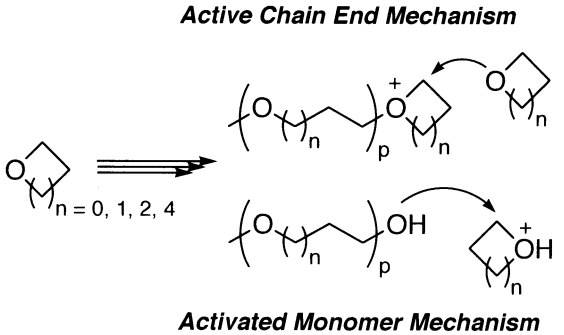
Abstract—Oxiranes (epoxides) and oxetanes having a carbonyl functional group are chemoselectively isomerized to different heterocyclic compounds via Lewis acid-promoted 1,6- and 1,7-intramolecular nucleophilic attacks of the carbonyl oxygen on the electron-deficient carbon neighboring the oxonium oxygen: for example, cyclic imides to bicyclic acetals, esters to bicyclic orthoesters, *sec*-amides to 4,5-dihydrooxazole or 5,6-dihydro-4*H*-1,3-oxazines, and *tert*-amides to bicyclic acetals or azetidines. The intramolecular attack of a 1,5-positioned carbonyl oxygen predominantly results in a propagating-end isomerization polymerization. On the other hand, cyclic ethers having a 1,8- or farther positioned carbonyl group undergo conventional ring-opening polymerization. A tetrahydrofuran (oxolane) ring does not open, even with a 1,6-positioned carbonyl group.

1. Introduction

Strained cyclic ethers are especially useful intermediates in synthetic organic chemistry, because of their high reactivity and the variety of their reactions.[1] Moreover, epoxide/oxirane, oxetane, and tetrahydrofuran/oxolane are of major interest in the field of polymer chemistry.[2] The cationic ring-opening polymerization of these cyclic ethers has been examined at a level of detail comparable to the polymerization of familiar vinyl monomers such as styrene and (meth)acrylates. As shown in Scheme 1, it is generally known that the cationic ring-opening polymerization proceeds in two modes: the active chain end mechanism in usual cases, or the activated monomer mechanism in elaborated cases.[3]

Among cationically polymerizable cyclic ethers, oxetanes have an advantage in that various chemical modifications are permitted under neutral or basic conditions and the introduction of bulky substituents causes little or no decrease of polymerizability. We have previously reported the preparation and application of various functionalized poly(oxetane)s.[4] Because of the high nucleophilicity of oxetanyl oxygen,[2] the ring-opening polymerization of substituted oxetanes by the active chain end mechanism proceeds readily in the presence of common functional groups including vinyl, halo, ether, acetal, ketone, ester, amide, imide, azo, nitro, nitrile, sulfonate, etc. Notably, we found that the polymerization of oxetanes having a carbonyl functional group at the 3-position gives unusual polymers with cyclic structures in the main chain.[5–7] This new type of polymerization involves the isomerization of the starting oxetanes to bicyclic compounds as the real monomers. We have intended to develop this isomerization process to a new synthetic method for preparing various heterocyclic compounds from oxetanes by suppressing the polymerization.

This paper describes the Lewis acid-promoted isomerization of oxiranes and oxetanes having a carbonyl functional group to different heterocyclic compounds, as outlined in Scheme 2. The chemoselective isomerization affords bicyclic acetals, bicyclic orthoesters, 4,5-dihydrooxazole, 5,6-dihydro-4*H*-1,3-oxazines, and azetidines, depending on the nature of the starting carbonyl functional groups. The formation of azetidines appears as if the endocyclic oxygen is exchanged with the exocyclic nitrogen, but the rearrangement proceeds by an interesting double isomerization involving ring expansion to bicyclic acetals and subsequent ring contraction to different four-membered azetidines. In addition, these results present a new elementary reaction process in the cationic ring-opening polymerization of cyclic ethers.



Scheme 1. Cationic ring-opening polymerization of cyclic ethers.

Keywords: oxetanes; epoxides; carbonyl compounds; isomerization.

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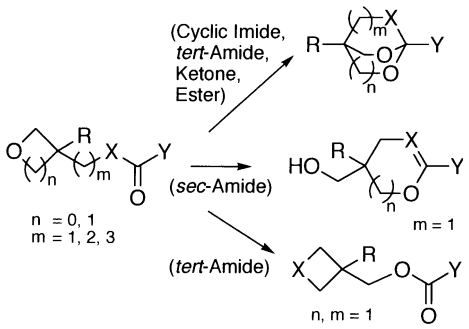


Synthetic utility:

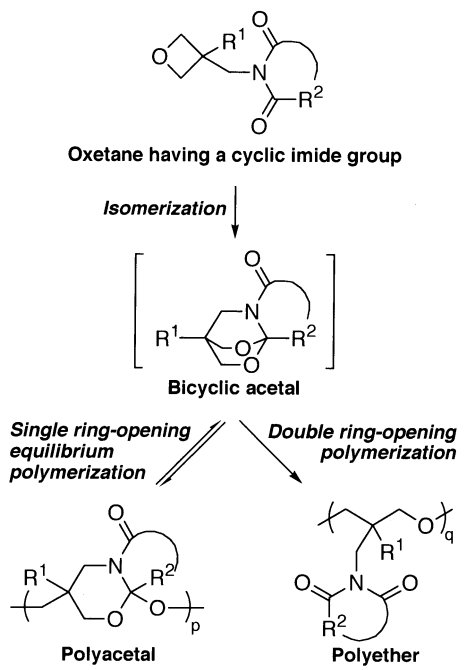
1° entries into different heterocyclic compounds and cyclic monomers
2° carbonyl protection with oxetane as a propanediol equivalent
3° rearrangement of exocyclic element to endocyclic element
4° new elementary reaction in cationic ring-opening polymerization

Scheme 2. Lewis acid-promoted isomerization of small cyclic ethers having a carbonyl functional group.

2. Results and discussion

2.1. Isomerization of oxetanes having a carbonyl functional group

2.1.1. Oxetane imides. Recently we have reported the cationic polymerization of oxetanes having a cyclic imide group at the 3-position (Scheme 3).[5,6] The polymerization gave two kinds of polymers with different structures depending on the temperature: one is a polyacetal containing tetrahydro-1,3-oxazine rings in the main chain, and the other is a polyether carrying pendant imide groups. The latter appears as if it is formed via a straightforward ring opening. However, both polymerizations can be distinguished from conventional cationic ring-opening polymerization. The oxetane imides undergo isomerization prior to polymerization, and the resulting bicyclic acetals polymerize cationically in situ by single ring opening at low temperature (usually at room temperature and below) or by double ring opening at high temperature (usually above 80°C). This new mode of polymerization involving such an isomerization has been termed 'monomer-isomerization polymerization'.[5]



Scheme 3. Monomer-isomerization polymerization of oxetane imides (**1**).

The above isomerization of oxetanes can provide a new entry into bicyclic acetals and a useful method for breaking the symmetry of cyclic imides. However, the yields of isomerization products were more or less compensated by the subsequent polymerization of these as the real monomers. Fortunately, it was found that the single ring-opening polymerization is an equilibrium process, although double ring-opening polymerizations are virtually irreversible. The equilibrium constant (K) of the single ring-opening polymerization of a bicyclic acetal can be defined as follows:

$$K = \frac{[\text{polyacetal}]_e}{[\text{bicyclic acetal}]_e[\text{polyacetal}]_e} = [\text{bicyclic acetal}]_e^{-1} \quad (1)$$

If no side reaction occurs, the following mass balance can be established:

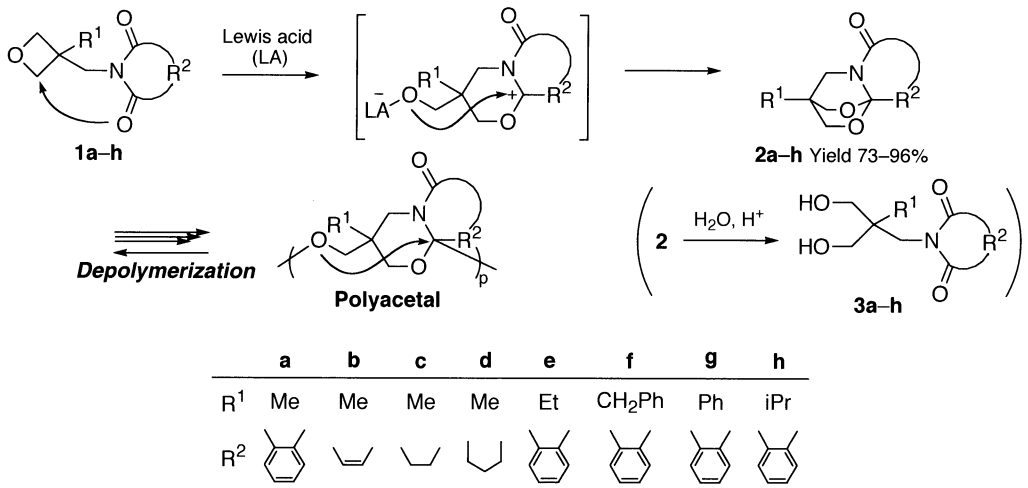
$$[\text{bicyclic acetal}]_e = [\text{oxetane}]_0 - [\text{polyacetal}]_e \quad (2)$$

K is dependent on temperature, and hence $\ln K$ can be expressed as Dainton's equation:[8]

$$\ln K = -\ln[\text{bicyclic acetal}]_e = \Delta S^\circ/R - \Delta H^\circ/RT \quad (3)$$

where T, ΔH°, and ΔS° are the polymerization temperature in degrees Kelvin, and the standard enthalpy and entropy changes of polymerization, respectively. As already reported,[5,6] the plots of ln[bicyclic acetal] vs T^{-1} showed good linear correlations in low-temperature polymerizations. This clearly indicated that equilibrium exists between bicyclic acetals and polyacetals via ring-opening polymerization and ring-closure depolymerization. The maximum yield of an isomerization product will be achieved when the equilibrium is completely shifted to the monomer state. Eqs. (1) and (2) imply that K is equal to $[\text{oxetane}]_0^{-1}$ in such an equilibrium, and thus Eq. (3) gives a certain equilibrium temperature, which is called the ceiling temperature (T_c) in the field of polymer chemistry.

We examined the Lewis acid-promoted isomerization of some oxetane imides (**1a**–**h**) (Scheme 4) and the results are shown in Table 1. Lewis acids and Brønsted acids, such as CF_3SO_3H and *d*-camphorsulphonic acid, were effective catalysts. The isomerization took place above −10°C and, of course, proceeded more rapidly at higher temperature. However, isomerization at room temperature and below was sometimes accompanied by the single ring-opening polymerization, and above 80°C the double-ring opening polymerization of **2** took place. To obtain **2** in high yields, it was necessary to use weak Lewis acids, such as trimethylaluminium (Me_3Al) and methylaluminium bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD), which initiated neither polymerization.[9] The nature of the cyclic imide (R^2) and the steric demand of the 3-R^1 substituent exerted little or no effect on the isomerization yield. The choice of catalyst was



Scheme 4. Isomerization of oxetane imides (**1**).

Table 1. Isomerization of oxetane imides (**1**) to bicyclic acetals (**2**) under the optimized conditions

Entry	Substrate			Lewis acid[a]	Conditions[b] (solvent, °C, h)	Yield[c] (%)
		R^1	R^2			
1	**1a**	Me	Phthalimide	Me_3Al	PhCl, 120, 12	96
2	**1a**	Me	Phthalimide	MAD[d]	PhCl, 120, 12	91
3	**1b**	Me	Maleimide	BnTA[e]	PhCl, 120, 24	73
4	**1c**	Me	Succinimide	TMSOTf[f]	PhCl, 120, 3	74
5	**1d**	Me	Glutarimide	TMSOTf[f]	PhCl, 120, 12	84
6	**1e**	Et	Phthalimide	Me_3Al	PhCl, 120, 3	77
7	**1f**	CH_2Ph	Phthalimide	$BF_3{\cdot}Et_2O$	CH_2Cl_2,[g] 35, 72	74
8	**1g**	Ph	Phthalimide	CF_3SO_3H	PhCl,[h] 80, 10 min	82
9	**1h**	*i*Pr	Phthalimide	Me_3Al	PhCl, 120, 12	82

[a] 5 mol%.
[b] **1** (0.5 g) in 2.0 mL of the solvent.
[c] Isolated yield of **2**.
[d] Methylaluminium bis(2,6-di-*tert*-butyl-4-methylphenoxide).
[e] 1-Benzyltetrahydrothiophenium hexafluoroantimonate.
[f] Trimethylsilyl trifluoromethanesulfonate.
[g] 7.5 mL.
[h] 3.5 mL.

not so crucial since the single ring-opening polymerization is an equilibrium phenomenon. If the polyacetals are formed, dilution of the reaction mixture allows regeneration of **2** through depolymerization.[5,6] Selecting the appropriate concentration of **1** was rather critical for avoiding polymerization, namely, the isomerization temperature ought to be higher than the T_c under the experimental conditions. The concentration can be predicted from the T_c, which has been estimated to be -14 to 95°C under the standard conditions (1.0 mol L^{-1} in CH_2Cl_2).[5,6] For example, the reaction of **1f** with $BF_3{\cdot}Et_2O$ at 35°C (entry 7) proceeded without polymerization in a relatively dilute solution of CH_2Cl_2 (0.2 mol L^{-1}). For the most part **2a**–**h** showed sufficient stability for chromatographic manipulation and recrystallization, except that **2d** was relatively sensitive toward moisture. On the other hand, **2a**–**h** were readily hydrolyzed in aqueous THF containing a small amount of ca. 1 M HCl at room temperature, to give 2-(imidomethyl-substituted)propane-1,3-diols **3a**–**h** almost quantitatively.

The isomerization likely involves coordination of Lewis acid (LA) to the oxetanyl oxygen rather than the imide-carbonyl.[6] The intramolecular nucleophilic attack of the carbonyl oxygen on the α-carbon of the oxetane oxonium cation is entropically preferred over the intermolecular attack of the other oxetane molecule. Ring closure of the resulting 1,3-oxazin-2-ylium cation then affords **2** (oxonium form). Oxetanes having a phthalimide group separated by longer spacers such as $CH_2O(CH_2)_n$ (n=4 and 6) did not isomerize under the influence of $BF_3{\cdot}Et_2O$, but polymerized in the conventional ring-opening manner[10] to give the corresponding polyether. Detailed X-ray crystallographic and ^1H NMR spectroscopic analyses of **2a**–**d** revealed an interesting difference between the bicyclic structures, as

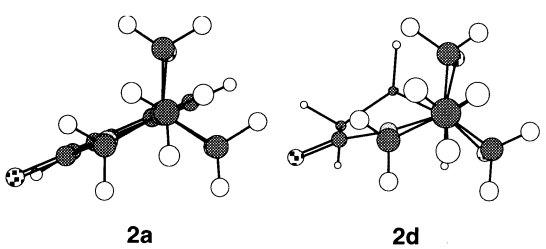
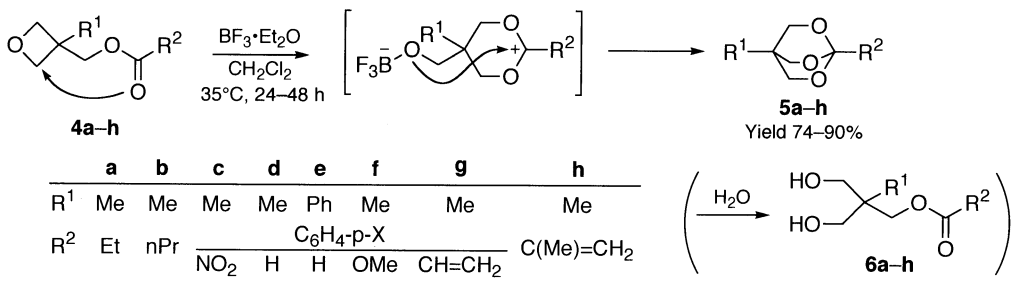
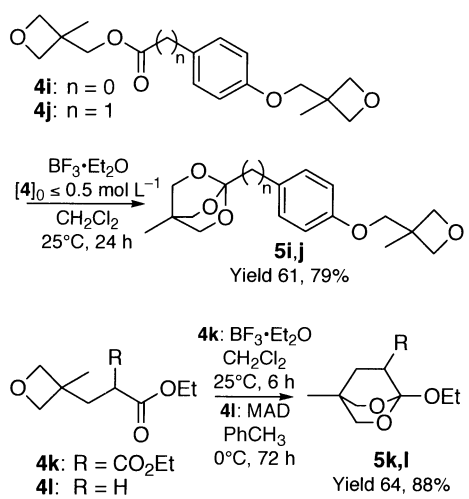


Figure 1. Molecular modes of **2a** and **2d** based on X-ray crystallographic data.



Scheme 5. Isomerization of oxetane esters (**4**).



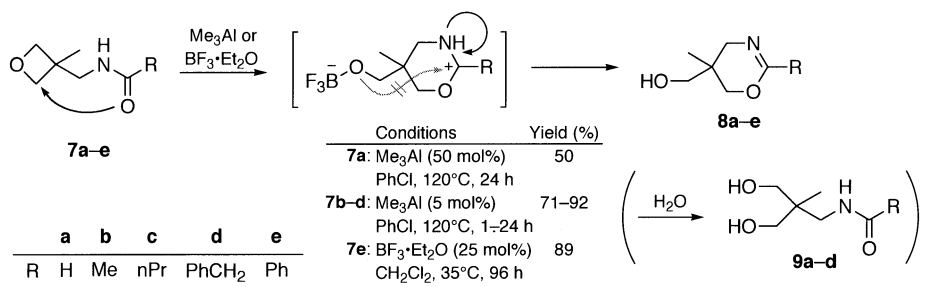
Scheme 6. Isomerization of other oxetane esters (**4**).

shown in Fig. 1.[5,6] In the cases of **2a**–**c**, the bicycles attached to a five-membered ring are highly symmetrical. In contrast, the bicycle of **2d** is considerably twisted both in the solid state and in $CDCl_3$ solution, probably due to an additional six-membered lactam ring.[6]

2.1.2. Oxetane esters. Similarly, oxetanes having an ester substituent (**4**) also brought about a monomer-isomerization polymerization to give poly(orthoester)s and polyethers (Scheme 5).[7] In contrast to the cases of **1a**–**h**, the isomerization of **4** was not accompanied by polymerization even in ca. 1.0 M CH_2Cl_2 solution at room temperature, due to the relatively low T_c of bicyclic orthoesters (**5**). For example, the T_c temperatures of **5b** and **5d** under the standard conditions in CH_2Cl_2 are −7.5 and −22.5°C, respectively.[7] Thus, the isomerization of **4a**–**h** with BF_3·Et_2O in CH_2Cl_2 at 35°C gave **5a**–**h** in good yields, as shown in Scheme 5. These results mirror Corey's orthoester synthesis,[11] which is regarded as a special phenomenon that can occur in a limited temperature range between T_c of the equilibrium single-ring opening polymerization and the lowest temperature needed for the double-ring opening polymerization. Pseudo first-order rate constants (k_i) of the isomerizations of **1** and **4** were determined by NMR analysis using 5 mol% of BF_3·Et_2O in $CDCl_3$ at 25°C.[6,7] The k_i values showed that **4** isomerized more slowly than **1** did. However, **4** was sufficiently reactive to permit the slow isomerization even at −78°C, while **1** did not isomerize below −10°C. It is most likely that the isomerization of **4** also proceeds by 1,6-intramolecular nucleophilic attack of the ester-carbonyl oxygen. The similarity between the yields of **5c** and **5f** (91% for X in R^2=NO_2, and 78% for X in R^2=OCH_3) suggests that the stability of a 1,3-dioxolan-2-ylium cation intermediate can overcome the strong electron-withdrawing nature of the 4-nitrophenyl group. Moisture-sensitive **5a**–**h** were hydrolyzed under neutral conditions in aqueous THF at 35°C, to give 2-(ester-substituted)propane-1,3-diols (**6a**–**h**) almost quantitatively. In addition, lower aliphatic acid orthoesters, such as **5a** and **5b**, underwent rapid hydrolysis even in air at room temperature.[7]

Orthoesters (OBO esters)[11,12] are useful groups for protecting carboxylic esters from nucleophilic attack. The oxetane esters of 4-vinylbenzoic acid and methacrylic acid (**4g** and **4h**) were readily converted into the bicyclic orthoesters (**5g** and **5h**) without affecting the vinyl groups.[13] Compounds **4i** and **4j** (Scheme 6) possess two oxetane rings bound through ether and ester linkages. When the isomerizations were conducted in dilute CH_2Cl_2 solutions (ca. 0.5 mol L^{-1}), only oxetanes proximal to the esters were converted into bicyclic orthoesters. Notably, BF_3·Et_2O had no influence on the other ether-linked oxetanes. This isomerization was also applicable to oxetanes linked with an ester moiety in the reverse direction. Thus, **4k** and **4l** were rearranged to the orthoesters (**5k** and **5l**) of an exocyclic type.

2.1.3. Oxetane *sec*-amides. Oxetanes having an amide group are also candidates for the present isomerization. In a



Scheme 7. Isomerization of oxetane *sec*-amides (**7**).

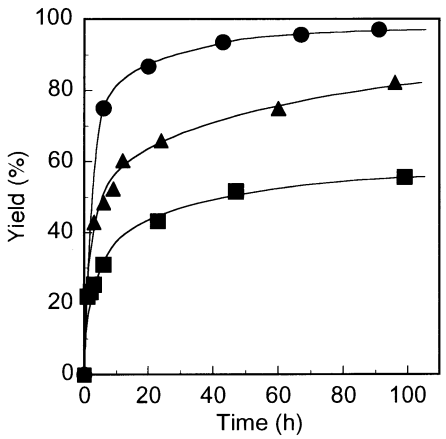


Figure 2. Time-conversion curves in the isomerization of **7e** (0.5 g) with $BF_3{\cdot}Et_2O$ in CH_2Cl_2(2.4 mL). Conditions ($BF_3{\cdot}Et_2O$ in mol%, temperature in °C); ■ (10, 25), ▲ (25, 25), • (25, 35).

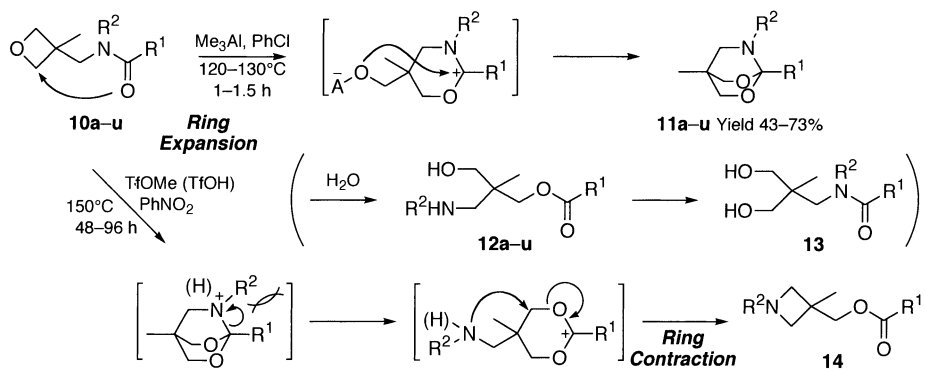
preliminary experiment, the isomerization of oxetane benzamide (**7e**) was examined using 10 mol% of $BF_3{\cdot}Et_2O$ in CH_2Cl_2 at 25°C (Scheme 7). The result sharply differed from the isomerization of **1** and **4**. First, the product was the monocyclic 1,3-oxazine (**8e**), instead of a bicyclic compound. Also, as can be seen from the time-conversion curve shown in Fig. 2, the rapid reaction in the initial stage slowed down remarkably halfway, with unreacted **7e** remaining. In contrast, both **1** and **4** isomerized according to good pseudo first-order kinetics up to high conversions. This self-quenching phenomenon suggested that the catalytic cycle of $BF_3{\cdot}Et_2O$ was disturbed owing to the basicity of the product **8e**. As shown in Fig. 2, the isomerization was virtually complete after four days by increasing both the amount of $BF_3{\cdot}Et_2O$ and the reaction temperature (25 mol%, 35°C).

Additional examples are also given in Scheme 7. The isomerization of these oxetane *sec*-amides (**7a–d**) required higher temperatures and, therefore, the competing polymerization by $BF_3{\cdot}Et_2O$ occurred to a greater extent. The use of Me_3Al suppressed oligomer formation, and the corresponding 1,3-oxazine derivatives (**8a–d**) were obtained in satisfactory yields even at 120°C.[14] This method allows the preparation of 5,6-dihydro-4*H*-1,3-oxazines with various 2-R substituents including hydrogen.[15] The products were sufficiently stable to distillation and recrystallization. However, **8a–d** hydrolyzed to (2-amide-substituted)propane-1,3-diols (**9a–d**) during chromatography on alumina with AcOEt. When **8e** was exposed to in THF containing a small amount of 0.5 M H_2SO_4 at room temperature, the benzoate of **8e** was obtained in 24% yield.[14]

Like the formation of **2**, the mechanism for the reaction giving **8** can also be explained by a 1,6-intramolecular nucleophilic attack of the amide-carbonyl oxygen. In this case, cation intermediates have a nitrogen atom with amine character, unlike the amide nitrogen in the cations formed from **1**. Therefore, the oxazinium cations are interconvertible to the stable iminium cations without cyclization. This isomerization mode supports the intervention of the cation intermediates presumed in the isomerizations of **1** and **4**, i.e. a 1,3-oxazin-2-ylium cation for **1** and a 1,3-dioxolan-2-ylium cation for **4**.

2.1.4. Oxetane *tert*-amides. In contrast to the *sec*-amides (**7**), isomerization of oxetane *tert*-amides (**10a–u**) gave bicyclic acetals (**11a–u**).[14,16] This reaction mode (Scheme 8) apparently resembles that of the cyclic imides **1**. However, the reactions are self-quenching, because **11** can function as an amine base to trap the acid catalyst. Therefore, the isomerization of **10** with $BF_3{\cdot}Et_2O$ required a high temperature (120–130°C) for completion. To suppress polymerization, the reactions were quenched by the addition of Et_3N immediately after disappearance of the starting materials (1–1.5 h). Although oligomeric products had formed, highly moisture-sensitive **11a–u** were obtained in moderate yields by direct distillation of the reaction mixture from CaH_2 under nitrogen. Analogous bicyclo-[n.3.0] amino-acetals (n=3 and 4) have previously been obtained by intermolecular cycloaddition or transacetalization, and the high susceptibility of these compounds to nucleophiles has been reported.[17] Similarly, **11a–u** were immediately hydrolyzed in air to give **12a–u** as a result of C–N bond fission. The hydrolysis products having less bulky R^1 or R^2 group, such as **12a–c**, **e**, **f**, **n**, and **r**, on standing, were spontaneously converted into **13** via acyl exchange.[18]

When the above isomerization was continued for a further 24 h, the initially formed **11** disappeared and oligomeric products with a polyether backbone were formed, along with a small amount of the azetidine having an ester group at the 3-position (**14**). The more forcing conditions of methyl trifluoromethanesulfonate (TfOMe, 2 mol%) in nitrobenzene at 150°C improved the yield of **14** in some



Scheme 8. Isomerization of oxetane *tert*-amides (**10**) with ring expansion and contraction: substituents R^1 and R^2 refer to Table 2.

Table 2. Double isomerization of oxetane *tert*-amides (**10**) to azetidine ester (**14**)

R^1 / R^2	Me	Et	nPr	Bn	-C_6H_4-*p*-X				iPr	tBu
					NO_2	Cl	H	OMe		
Me		**a** 0		**b** 0			**c** 6			**d** 54
Et	**e** 0	**f** 2	**g** 10		**h** 58	**i** 56	**j** 73	**k** 64	**l** 47	**m** 42
nPr	**n** 0	**o** 6	**p** 12				**q** 70			
Bn	**r** 0	**s** 47	**t** 62				**u** 75		compd. no. yield (%)	

NMR conversion of **14**. The reaction of **10** (0.9 mmol) in anhydrous nitrobenzene (1.0 mL) was carried out using TfOMe (2 mol%) at 150°C for 48–96 h.

cases.[16] The results are summarized in Table 2, where the R^1 and R^2 groups are arranged according to the bulkiness. Apparently, the product yields are governed by the bulkiness of both substituents. The scope of the reaction for constructing azetidine rings may be limited by the vigorous reaction conditions and the steric requirements for a bulky R^1 or R^2 group. However, this method offers an alternative to the general syntheses, including the cyclization of α,γ-difunctionalized alkanes or the reduction of β-lactams and malonimides.[19]

The unusual, counter-intuitive isomerization of **10** to **14** was of primary interest from a mechanistic point of view. The fate of **10j** was examined by NMR analysis of the isomerization accelerated with 2.5 times the usual amount of TfOMe in nitrobenzene-d_5 (Fig. 3). The product distribution suggests that **14j** could be formed via **11j**. This possibility was substantiated from the fact that the isomerization starting from **11j** in place of **10j** also yielded **14j**. We refer to this reaction sequence as 'double isomerization' distinguishing it from the 'single' isomerizations of carbonyl-functionalized oxetanes. The potential intervention of **11** as the intermediate is shown in the

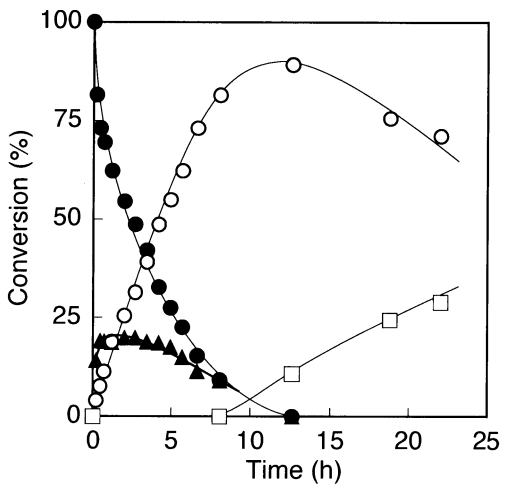
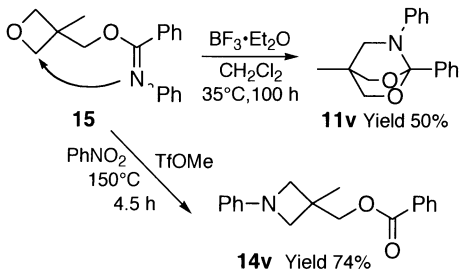


Figure 3. Time-conversion curves in the double isomerization of **10j** with TfOMe (5 mol%) in nitrobenzene-d_5 at 150°C: (•) **10j**, (▲) **11j**, (○) **14j**, (□) oligomeric products.

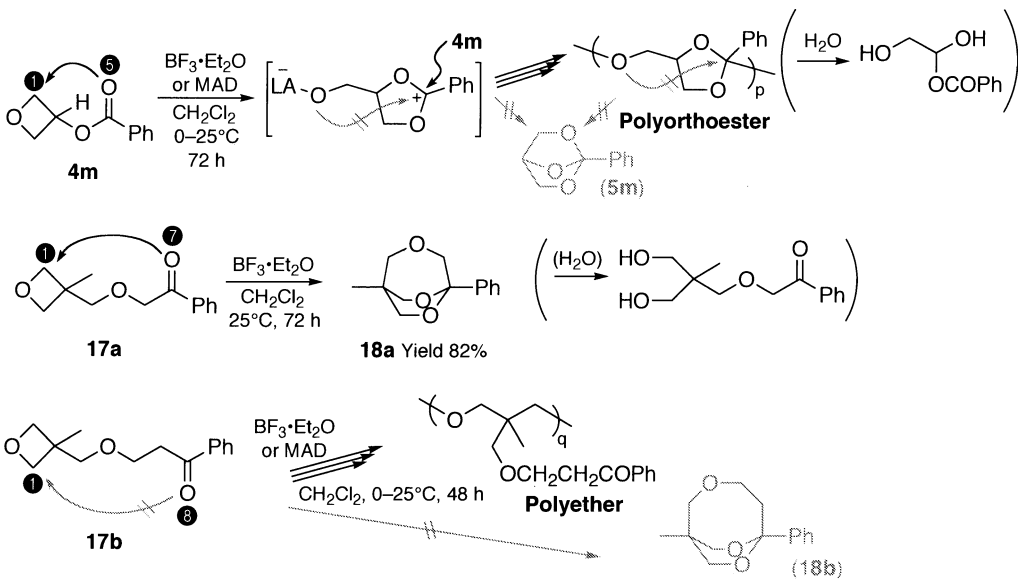


Scheme 9. Double isomerization of oxetane benzimidate (**15**).

mechanism proposed in Scheme 8. The double isomerization involves two key steps: a four-membered oxetane ring in **10** is first expanded to a [2.2.2]-bicycle in **11**, which is in turn contracted to a different four-membered azetidine ring in **14**. The ammonium ion of **11** suffers steric repulsion between the adjacent R^1 and R^2 groups, making the C–N^+ bond scission feasible. The resulting 1,3-dioxan-2-ylium cation closes to form an azetidine ring. Stabilization of the 1.3-dioxan-2-ylium cation does not seem to be important, because the double isomerization of *N*-ethylbenzamides (**10h–k**) results in similar yields of **14h–k** regardless of the nature of the *p*-X-substituent. It is likely that **14** are ring-opening monomers, and hence **14** would be consumed by oligomerization in the latter half of reaction, as shown in Fig. 3. In our examination, TfOMe is the preferred catalyst. The very reactive methylating reagent is likely to be extremely short-lived, and may simply serve to generate in situ the true catalytic species, presumably TfOH, following methylation or hydrolysis with water impurity. However, TfOH itself was less suitable as the catalyst in that the oligomerization of **14** was accelerated to a greater extent (48% yield of **14j** in 68 h).

Oxetane benzimidate (**15**) is a functional-group isomer of **10**, and the unsaturated nitrogen can also act as an intramolecular nucleophile (Scheme 9). Thus, a bicyclic acetal (**11v**) and an azetidine benzoate (**14v**) were alternatively obtained by choosing different reaction conditions. The mode of isomerization is fundamentally similar to that of the double isomerization of **10**. On the other hand, oxetane tosylate (**16**: 3-methyloxetan-3-ylmethyl toluene-4-sulfonate) underwent an ordinary ring-opening polymerization.[20] This indicates that the unsaturated oxygen attached to a sulfur lacks nucleophilicity.

2.1.5. Effect of the carbonyl position in the 3-substituent of oxetane. As mentioned above, we have demonstrated the isomerization of oxetanes having varied carbonyl functionality, such as cyclic imides, esters, and amides. It has been shown that the isomerization modes of these oxetanes are extremely chemoselective toward the nature of carbonyl functional group and all of the isomerizations are preferred over the conventional cationic ring-opening polymerization of the oxetane moiety. Irrespective of the variety of the isomerization modes, there is a common step passing through an intramolecular nucleophilic attack of the 1,6-positioned carbonyl oxygen on the α-carbon of the oxetane oxonium cation. Our next focus was on the importance of the positional relationship between the nucleophilic oxygen and the electrophilic carbon. The first example is the reaction of 1,5-positioned oxetane benzoate **4m**, as shown in



Scheme 10. Effect of the carbonyl position in the 3-substituent of oxetane.

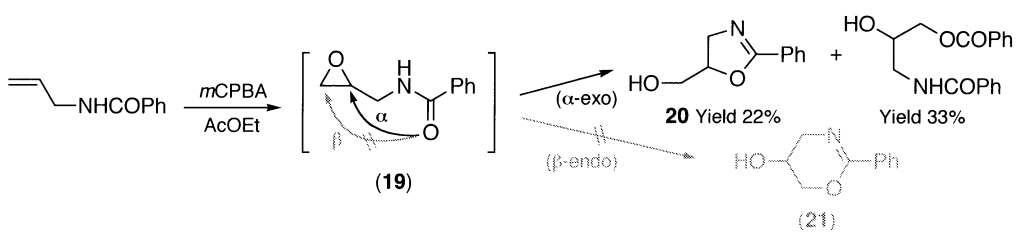
Scheme 10.[21] If the isomerization takes place in the same mode as that of 1,6-positioned oxetane benzoate **4e**, bicyclo[2.2.1]-orthoester **5m** could be formed. Contrary to this expectation, the acid-promoted reaction of **4m** predominately resulted in polymerization to give a poly(orthoester) composed of five-membered dioxolane rings. When the poly(orthoester) was subjected to degradation under depolymerization conditions, no formation of **5m** was detected. The cyclic orthoester structure provided a piece of evidence for the occurrence of a 1,5-intramolecular attack of the carbonyl oxygen. Presumably, the subsequent ring closure would suffer from a higher ring strain to form **5m**, and hence the cation intermediate would preferentially undergo the intermolecular attack of **4m** (propagating-end isomerization polymerization).

A keto-carbonyl oxygen is also expected to possess good nucleophilicity. Oxetane ketone (**17a**) has the carbonyl oxygen at the 1,7-position. The BF_3·Et_2O-promoted isomerization to a bicyclo[3.2.2]-acetal (**18a**) indicated that the 1,7-intramolecular attack took place as readily as the 1,6-intramolecular attack did. On the other hand, farther 1,8-positioned oxetane ketone (**17b**) predominately brought about the ordinary ring-opening polymerization to give a polyether alone. The observation deserves the following comments: the intramolecular attack of the 1,8-positioned carbonyl oxygen becomes less favorable than the intermolecular attack of **17b** (polymerization), as rationally predicted from common organic chemistry. In addition, the potential ring strain of a hypothetical product bicyclo[4.2.2]-acetal **18b** would be ruled out as the reason why it was not formed, because an isomerization to a possibly more strained bicyclo[4.2.1]-acetal (**23b**) was realized, as mentioned later.

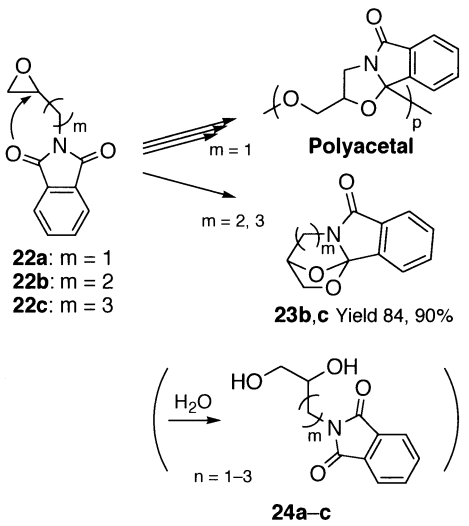
2.2. Isomerization of other cyclic ethers having a carbonyl functional group

2.2.1. Oxirane *sec*-amide. A series of isomerizations of oxetanes strongly suggests that similar isomerizations should be possible for smaller three-membered cyclic ethers, as long as the carbonyl group is properly positioned. Thus, we examined the acid-promoted isomerization of oxirane benzamide **19**. The amide-carbonyl oxygen can attack on either the electrophilic α- or β-carbon in the oxirane ring or both. *m*CPBA oxidation of *N*-allylbenzamide for preparing **19** directly gave five-membered 2-phenyl-5-hydroxymethyl-4,5-dihydrooxazole (**20**) in a quantitative NMR conversion, instead of six-membered 2-phenyl-5,6-dihydro-4*H*-1,3-oxazin-5-ol (**21**), as outlined in Scheme 11. The rather low isolated yield of **20** arises from hydrolytic ring opening and benzoyl transfer during chromatographic work-up (see Section 2.1.3). Apparently, the epoxidation was followed by the isomerization of intermediate **19**, probably catalyzed by *m*-chlorobenzoic acid that was produced in situ from *m*CPBA. Consequently, the formation of a five-membered ring reveals that the attack of the 1,5-positioned carbonyl oxygen leads to α-exo cyclization, in accord with Baldwin's rules.[22]

2.2.2. Oxirane imides. The isomerization of homologous oxirane phthalimides (**22a–c**) was investigated to elucidate



Scheme 11. Isomerization of oxirane benzamide (**19**).



Scheme 12. Isomerization of oxirane phthalimides (**22**).

the effect of the relative position of the carbonyl oxygen (Scheme 12). In the reaction of 1,5-positioned **22a**, an isomerization polymerization occurred predominately to give only polyacetal with five-membered 4,5-dihydrooxazole rings in the main chain.[23] This result was similar to the isomerization polymerization of 1,5-positioned oxetane benzoate **4m**. In contrast, the isomerization of 1,6-positioned **22b** and 1,7-positioned **22c** gave the expected bicyclic acetals (**23b**, **c**). All of the cyclic structures of these products including the polyacetal are apparently formed as a result of the α-*exo* attack. The hydrolysis of **23b** and **23c** as well as the polyacetal of **22a** gave phthalimido-substituted ethylene glycols **24a**–**c** under the same conditions as those for **2**.

Similar neighboring assistance was previously observed by Chamberlin et al.[24] in the preparation of stereochemically controlled tetrahydrofurans, tetrahydropyrans, and oxepans from ester- and ketone-substituted oxiranes in cooperation with nucleophiles and Lewis acids. They postulated or isolated the five-membered monocyclic cations and the six- and seven-membered bicyclic acetals as key intermediates. This agrees with our observations, which complements Chamberlin's method mechanistically.

2.2.3. Other cyclic ethers having a carbonyl functional group. As an example of a five-membered cyclic ether, oxolane phthalimide (**25**: 2-(tetrahydrofuran-3-ylmethyl)-isoindole-1,3-dione) was prepared. Although the imide-carbonyl oxygen is placed at the 1,6-position, neither isomerization nor polymerization took place, unlike 1,6-positioned analogues of oxetane and oxirane (**1a** and **22b**). It is not surprising because the less strained five-membered cyclic oxonium cation is expected to be an insufficient electron acceptor. For the same reason, substituted tetrahydrofuran, except when the substituents form additional rings, cannot polymerize cationically.[2b]

Since our finding of the monomer-isomerization polymerization, similar ring-opening polymerizations involving neighboring carbonyl-group assistance have been reported by other polymer chemists.[25,26] Miyamoto et al. have reported the cationic polymerization of oxirane esters and oxirane carbonates having the 1,5-positioned carbonyl groups.[25] Also therein, poly(orthoester)s and poly(carbonate)s of cyclic structures were obtained instead of polyethers. Based on the present outcomes, we consider it reasonable that the polymerization of these oxiranes can be categorized as a propagating-end isomerization polymerization involving the same 1,5-intramolecular nucleophilic attack as those of **4m** and **22a**.

3. Conclusion

In this study we investigated the Lewis acid-promoted isomerization of small cyclic ethers having a carbonyl functional group. The oxiranes (epoxides) and oxetanes were chemoselectively isomerized to different heterocyclic compounds via 1,6- and 1,7-intramolecular nucleophilic attacks of the carbonyl oxygen (neighboring carbonyl-group assistance in an expanded meaning): for example, cyclic imides to bicyclic acetals, esters to bicyclic orthoesters, *sec*-amides to 4,5-dihydrooxazole or 5,6-dihydro-4*H*-1,3-oxazines, and *tert*-amides to bicyclic acetals or azetidines. Interestingly, the rearrangement to azetidines proceeded through a double isomerization mechanism involving ring expansion of four-membered oxetanes to bicyclo[2.2.2]-acetals and subsequent ring contraction to different four-membered azetidines. The intramolecular attack of a 1,5-positioned carbonyl oxygen predominantly resulted in a propagating-end isomerization polymerization. On the other hand, cyclic ethers having a 1,8- and farther positioned carbonyl group underwent the conventional ring-opening polymerization. A tetrahydrofuran (oxolane) ring did not open, even with a 1,6-positioned carbonyl group. The above isomerizations of small-membered oxiranes and oxetanes can be extended to other carbonyl precursors, except for the carbonates, which failed in the tandem cyclization under the conditions examined. In addition, some of the above bicyclic acetals and orthoesters further underwent complicated cyclodimerization to afford unexpected products having a dioxane or dioxolane ring, which will be reported in the following paper in this journal issue.

4. Experimental

4.1. General

All of melting points are uncorrected, and all boiling ranges denote bath temperatures. NMR spectra were measured on JEOL JNM GSX-500, LA-400, EX-270, and FX-100S NMR spectrometers using $CDCl_3$ as the solvent. The chemical shifts were determined with respect to TMS (δ 0.00 ppm) for ^1H nuclei and $CDCl_3$ (δ 77.00 ppm) for ^{13}C nuclei as internal standards. Spectral data were reported at 270 MHz for ^1H nuclei unless otherwise noted. In NMR measurement of moisture-sensitive compounds, they were taken into NMR tubes filled with dry nitrogen by evacuation, and dissolved in anhydrous $CDCl_3$ that was freshly distilled from powdered CaH_2. IR spectra were recorded on JASCO FT/IR-3 and JASCO A-202 infrared spectrometers. High resolution mass spectroscopic analyses (HRMS) and microanalyses were accomplished at the Center for Instrumental Analysis, Kanazawa University,

using a JEOL JMS-SX102 A mass spectrometer (ionization potential, 70 eV for EIMS) and a YANAKO CHN Corder MT-5, respectively. GPC was performed on a Shimadzu LC-10A high-speed liquid chromatography system equipped with a differential refractometer, using THF as the eluent with a flow rate of 1.0 mL min^{-1} at room temperature. Number-average molecular weights ($M_{n\ GPC}$) were determined on the basis of the molecular weight calibration curve obtained using polystyrene standards. All heterocyclic compounds obtained by the isomerization in this study were hydrolyzed to ring-opened diols, amino-alcohols, or the related compounds, which were characterized by IR, NMR, and MS analyses. These spectroscopic data are omitted for simplicity.

In experiments requiring anhydrous solvents, dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), and chlorobenzene (PhCl) were freshly distilled from powdered CaH_2 under nitrogen, and toluene and nitrobenzene were freshly distilled from butyllithium and phosphorus pentoxide, respectively. Triethylamine (Et_3N) used as a quencher was freshly distilled from powdered CaH_2. 1-Benzyltetrahydrothiophenium hexafluoroantimonate (BnTA)[27] as a thermally latent Lewis acid was prepared by Endo's method: 60% yield, mp 112–113°C (lit.[27] mp 121.5–122°C). Methylaluminium bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) was prepared by Aida's method[28] and recrystallized from toluene–hexane under a nitrogen atmosphere: 60% yield. 3-Methyloxetanylmethanol (**26**)[11] and its tosylate (**16**),[29] which were used as the principal precursors of oxetane derivatives reported here, were prepared from 2-hydroxymethyl-2-methylpropane-1,3-diol according to literature methods. For purification of products by preparative column chromatography, alumina (Merck Art. 101097, aluminium oxide 90, 70–230 mesh ASTM) was used throughout this work.

4.2. Preparation of cyclic ethers having a cyclic imide substituent

Oxetane imides **1a**–**h**[5,6,9] and oxirane phthalimide **22a**[23,30] were prepared as described in our previous reports, and the spectroscopic properties and analytical data were reported therein.

4.2.1. 2-(2-Oxiranylethyl)isoindole-1,3-dione (22b). *p*-Toluenesulfonyl chloride (14.5 g, 76.3 mmol) was added by portions to a solution of but-3-enol (5.00 g, 69.3 mmol) in pyridine (50 mL) at 0°C. After stirring at room temperature for 1 h, the mixture was acidified with 1 M HCl, and extracted with Et_2O. The organic layer was successively washed with 5% aq NaOH and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was distilled in vacuo to give but-3-enyl *p*-toluenesulfonate (12.2 g, 78%) as a colorless oil: bp 90–100°C (1 mmHg). The above tosylate (11.6 g, 51.4 mmol) and potassium phthalimide (10.9 g, 59.1 mmol) were dissolved in DMF (30 mL), and the solution was stirred at 80°C for 2 h. After addition of a large amount of H_2O (300 mL), the mixture was extracted with Et_2O. The organic layer was successively washed with 5% aq NaOH and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was recrystallized from Et_2O–hexane to give 2-(but-3-enyl)-isoindole-1,3-dione (8.44 g, 82%) as colorless crystals: mp 48–49°C. *m*CPBA (9.19 g, 37.3 mmol) was added by portions to a solution of the above imide (7.50 g, 37.3 mmol) in AcOEt (30 mL). After stirring at 80°C for 1 h, the mixture was successively washed with sat. aq $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, and evaporated in vacuo. The crude product was recrystallized from AcOEt–hexane to give **22b** (6.46 g, 80%). Colorless crystals; mp 83–85°C; IR (KBr) 1770, 1710, 1400, 915, 803 cm^{-1}; ^1H NMR δ 1.84 (dq, J=14.1, 7.1 Hz, 1H, NCH_2CH_2), 2.10 (ddt, J=14.2, 6.6, 4.6 Hz, 1H, NCH_2CH_2), 2.45 (dd, J=5.0, 2.6 Hz, 1H, OCH_2 *cis* to 2-ethyl), 2.72 (dd, J=4.8, 4.1 Hz, 1H, OCH_2 *trans* to 2-ethyl), 2.97–3.03 (m, 1H, OC*H*), 3.86, 3.93 (both dt, J=13.7, 6.8 Hz, 1H, NCH_2CH_2), 7.72, 7.85 (both dd, J=5.5, 3.1 Hz, 2H, *m*- and *o*-Ar*H*); ^{13}C NMR δ 31.6, 35.1, 46.4, 50.2, 123.3, 132.1, 134.0, 168.3; EI HRMS Calcd for $C_{12}H_{11}NO_3$: 217.0739. Found: 217.0742.

4.2.2. 2-(3-Oxiranylpropyl)isoindole-1,3-dione (22c). Pent-4-enol (18.8 g, 219 mmol), which was prepared from tetrahydrofuran-2-ylmethanol according to the Organic Syntheses method,[31] was added to a solution of NaOH (35.0 g, 874 mmol) in H_2O (150 mL). To the aqueous solution cooled to 0°C, a solution of *p*-toluenesulfonyl chloride (47.9 g, 251 mmol) in THF (150 mL) was added dropwise for 1.5 h, and then the mixture was stirred at room temperature for 24 h. The THF was removed in vacuo and the remaining mixture was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo to give pent-4-enyl *p*-toluenesulfonate (40.3 g, 77%) as an oil. The crude product was used in the next step without further purification. In the same procedure for **22b**, 2-(pent-4-enyl)isoindole-1,3-dione (1.35 g, 86%) was obtained from the above tosylate (1.72 g, 7.26 mmol), potassium phthalimide (2.02 g, 10.9 mmol), and DMF (5 mL). The crude product was purified by vacuum distillation: colorless oil; bp 80–90°C (1 mmHg). Then, 2-(3-oxyranylpropyl)isoindole-1,3-dione was obtained from the above olefin (1.35 g, 6.27 mmol), *m*CPBA (1.55 g, 6.27 mmol), and AcOEt (10 mL). The crude product was purified by alumina column chromatography using toluene as the eluent, followed by vacuum distillation to give pure **22c** (0.79 g, 55%). Colorless oil; bp 130–140°C (1 mmHg); IR (liquid film) 1770, 1710, 1395, 915, 795 cm^{-1}; ^1H NMR δ 1.56 (ddt, J=14.0, 8.4, 6.8 Hz, 1H, $NCH_2CH_2CH_2$), 1.67 (ddt, J=14.0, 6.1, 4.5 Hz, 1H, $CH_2CH_2CH_2N$), 1.75–1.95 (m, 2H, $NCH_2CH_2CH_2$), 2.50 (dd, J=4.9, 2.6 Hz, 1H, OCH_2 *cis* to propyl), 2.75 (t, J=4.5 Hz, 1H, OCH_2 *trans* to propyl), 2.93–3.00 (m, 1H, OC*H*), 3.72 (dt, J=13.5, 6.9 Hz, 1H, $NCH_2CH_2CH_2$), 3.78 (dt, J=13.5, 7.3 Hz, 1H, NCH_2CH_2-CH_2), 7.72, 7.85 (both dd, J=5.6, 3.0 Hz, 2H, *m*- and *o*-Ar*H*); ^{13}C NMR δ 25.1, 29.8, 37.6, 46.9, 56.6, 123.2, 132.1, 134.0, 168.4; EI HRMS Calcd for $C_{13}H_{13}NO_3$: 231.0896. Found: 231.0896.

4.2.3. 2-(Tetrahydrofuran-3-ylmethyl)isoindole-1,3-dione (25). *p*-Toluenesulfonyl chloride (10.3 g, 53.5 mmol) was added by portions to a solution of tetrahydrofuran-3-ylmethanol (5.00 g, 49.0 mmol) in pyridine (16 mL) at 0°C, and stirring was continued at room temperature for 3 h. The solution was acidified with 1 M HCl and extracted with Et_2O. The organic layer was

successively washed with 5% aq NaOH and brine, dried over Na_2SO_4, and evaporated in vacuo. The resulting crude tosylate (11.1 g, 88%) was used in the next step without further purification. Potassium phthalimide (9.22 g, 49.8 mmol) was suspended in a solution of the above tosylate (11.1 g, 43.3 mmol) in DMF (45 mL), and the mixture was stirred at 80°C for 4 h. A large amount of water (450 mL) was added to deposit white precipitates, which were collected by filtration and dissolved in $CHCl_3$. The organic layer was washed with water, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by recrystallization from CH_2Cl_2–hexane to give **25** (7.18 g, 72%). Colorless crystals; mp 121–122°C; IR (KBr) 1770, 1706, 1399, 912, 720 cm^{-1}; ^1H NMR (400 MHz) δ 1.71, 2.00 (both dq, J=13.2, 6.7 Hz, 1H, C4H_2), 2.72 (septet, J=6.8 Hz, 1H, C3H), 3.59 (dd, J=8.8, 5.9 Hz, 1H, OC2H_2), 3.68 (dd, J=13.7, 7.8 Hz, 1H, NCH_2), 3.73 (dd, J=13.7, 7.3 Hz, 1H, NCH_2), 3.75 (q, J=7.6 Hz, 1H, OC5H_2), 3.81 (dd, J=8.8, 6.8 Hz, 1H, OC2H_2), 3.92 (q, J=7.3 Hz, 1H, OC5H_2), 7.72, 7.84 (both dd, J=5.4, 2.9 Hz, 2H, *m*- and *o*-ArH); ^{13}C NMR (100 MHz) δ 30.0, 38.9, 40.4, 67.6, 71.1, 123.3, 131.9, 134.0, 168.4; EI HRMS Calcd for $C_{13}H_{13}NO_3$: 231.0896. Found: 231.0886. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.60; H, 5.68; N, 5.96.

4.3. Preparation of oxetanes having an ester group

Oxetane esters **4b**, **d**, and **e** were prepared as described in our previous report,[7] and the spectroscopic properties and analytical data were reported therein.

4.3.1. 3-Methyloxetan-3-ylmethyl propionate (4a). Propionyl chloride (2.20 g, 23.8 mmol) was added dropwise to a solution of **26** (2.00 g, 19.6 mmol) and Et_3N (13.9 mL, 100 mmol) in CH_2Cl_2 (10 mL) at 0–6°C. After stirring at 5°C for 5 h, the mixture was successively washed with 1 M HCl, 10% aq NaOH, and brine, dried over Na_2SO_4, and distilled in vacuo to give **4a** (1.14 g, 37%). Colorless oil; bp 94–98°C (10 mmHg); IR (liquid film) 1740, 1180, 1080, 980, 830 cm^{-1}; ^1H NMR δ 1.17 (t, J=7.6 Hz, 3H, CH_2CH_3), 1.34 (s, 3H, 3-CH_3), 2.39 (q, J=7.6 Hz, 2H, CH_2CH_3), 4.17 (s, 2H, 3-CH_2O), 4.38, 4.52 (both d, J=5.9 Hz, 2H, OCH_2 *trans* and *cis* to 3-CH_2O); ^{13}C NMR δ 9.13, 21.2, 27.5, 39.1, 68.4, 79.5, 174.2; FAB HRMS Calcd for $C_8H_{15}O_3$ (M^++H): 159.1022. Found: 159.1015.

4.3.2. 3-Methyloxetan-3-ylmethyl 4-nitrobenzoate (4c). Diethyl azodicarboxylate (40% toluene solution, 1.90 mL, 4.36 mmol) was added dropwise to a toluene (10 mL) solution of **26** (0.217 g, 2.13 mmol), 4-nitrobenzoic acid (0.735 g, 4.40 mmol), and Ph_3P (1.12 g, 4.26 mmol) at 0°C under nitrogen. The mixture was stirred overnight, treated with aq $NaHCO_3$, and then extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by alumina column chromatography using AcOEt–hexane=1:1 as the eluent, followed by vacuum distillation, to give pure **4c** (0.400 g, 75%) as a yellow liquid, which solidified at room temperature. Bp 125–130°C (1 mmHg); mp 62–64°C; IR (liquid film) 1730, 1530, 1350, 1280, 1100, 980, 845 cm^{-1}; ^1H NMR δ 1.45 (s, 3H, 3-CH_3), 4.47 (s, 2H, 3-CH_2O), 4.50, 4.65 (both d, J=6.1 Hz, 2H, OCH_2 *trans* and *cis* to 3-CH_2O), 8.24, 8.31 (both d, J=8.8 Hz, 2H, *m*- and *o*-ArH to 4-NO_2); ^{13}C NMR δ 21.2, 39.3, 69.8, 79.4, 123.5, 130.6, 135.1, 150.5, 164.5; FAB HRMS Calcd for $C_{12}H_{14}NO_5$ (M^++H): 252.0872. Found: 252.0867.

4.3.3. 3-Methyloxetan-3-ylmethyl 4-methoxybenzoate (4f). In the same procedure for **4c**, **4f** was obtained from **26** (0.267 g, 2.62 mmol), 4-methoxybenzoic acid (0.648 g, 4.26 mmol), diethyl azodicarboxylate (40% toluene solution, 1.90 mL, 4.36 mmol), and Ph_3P (1.12 g, 4.26 mmol) in toluene (10 mL). The crude product was purified by alumina column chromatography using AcOEt–hexane=1:9 as the eluent, followed by vacuum distillation, to give pure **4f** (0.553 g, 89%). Colorless liquid; bp 122–125°C (1 mmHg); IR (liquid film) 1710, 1255, 1100, 980, 845 cm^{-1}; ^1H NMR δ 1.42 (s, 3H, 3-CH_3), 3.87 (s, 3H, ArOCH_3), 4.37 (s, 2H, 3-CH_2O), 4.46, 4.65 (both d, J=5.9 Hz, 2H, OCH_2 *trans* and *cis* to 3-CH_2O), 6.94, 8.02 (both d, J=7.8 Hz, 2H, *m*- and *o*-ArH to 4-OCH_3); ^{13}C NMR δ 21.4, 39.4, 55.4, 68.7, 79.6, 113.6, 122.2, 131.5, 163.3, 166.1; EI HRMS Calcd for $C_{13}H_{16}O_4$: 236.1049. Found: 236.1050.

4.3.4. 3-Methyloxetan-3-ylmethyl 4-vinylbenzoate (4g). *N*,*N*′-Dicyclohexylcarbodiimide (1.39 g, 6.76 mmol) was added by portions to a THF (30 mL) solution of **26** (0.690 g, 6.76 mmol), 4-vinylbenzoic acid (1.00 g, 6.76 mmol), and 4-dimethylaminopyridine (cat. amount) at 0°C. After the mixture was stirred at 0°C for 2 h and then at room temperature for 3 h, the urea precipitated was filtered off. The filtrate was evaporated in vacuo, and the residue was dissolved in Et_2O. The organic layer was successively washed 5% aq NaOH and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was distilled from CuCl in vacuo to give **4g** (0.911 g, 53%). Yellowish oil; bp 100–105°C (1 mmHg); IR (liquid film) 1720, 1630, 1280, 1100, 980, 830 cm^{-1}; ^1H NMR δ 1.43 (s, 3H, 3-CH_3), 4.39 (s, 2H, 3-CH_2O), 4.46, 4.65 (both d, J=5.9 Hz, 2H, OCH_2 *trans* and *cis* to 3-CH_2O), 5.40 (d, J=10.9 Hz, 1H, *trans*-CH_2=CH), 5.87 (d, J=17.6 Hz, 1H, *cis*-CH_2=CH), 6.76 (dd, J=17.6, 10.8 Hz, 1H, CH_2=CH), 7.47, 8.01 (both d, J=8.4 Hz, 2H, *o*- and *m*-ArH to 4-vinyl); ^{13}C NMR δ 21.4, 39.4, 69.0, 79.6, 116.6, 126.1, 128.9, 129.8, 135.8, 142.1, 166.1; FAB HRMS Calcd for $C_{14}H_{17}O_3$ (M^++H): 233.1178. Found: 233.1176.

4.3.5. 3-Methyloxetan-3-ylmethyl methacrylate (4h). In the same procedure for **4c**, **4h** was obtained from **26** (1.52 g, 14.9 mmol), methacrylic acid (2.57 g, 29.4 mmol), diethyl azodicarboxylate (40% toluene solution, 8.65 mL, 29.8 mmol), and Ph_3P (7.81 g, 29.8 mmol) in toluene (10 mL). Extractive work-up with AcOEt gave the crude product, which was purified by vacuum distillation to give pure **4h** (1.79 g, 72%).[32] Colorless liquid; bp 40–43°C (1 mmHg); IR (liquid film) 1720, 1640, 1160, 980, 835 cm^{-1}; ^1H NMR δ 1.37 (s, 3H, 3-CH_3), 1.97 (pseudo d, J=1.0 Hz, 3H, CH_2=C–CH_3), 4.23 (s, 2H, 3-CH_2O), 4.40, 4.56 (both d, J=5.9 Hz, 2H, OCH_2 *trans* and *cis* to 3-CH_2O), 5.60 (pseudo qui, J=1.6 Hz, 1H, *cis*-CH_2=CMe), 6.14 (pseudo s, 1H, *trans*-CH_2=CMe); ^{13}C NMR δ 18.4, 21.3, 39.3, 68.8, 79.6, 125.8, 135.9, 167.2; FAB HRMS Calcd for $C_9H_{15}O_3$ (M^++H): 171.1022. Found: 171.1034.

4.3.6. 3-Methyloxetan-3-ylmethyl 4-(3-methyloxetan-3-ylmethoxy)benzoate (4i). A solution of **16** (10.0 g,

39.06 mmol) and sodium bromide (8.04 g, 78.13 mmol) in DMF (25 mL) was stirred at 40°C for 3 h. The solvent was removed in vacuo and the residue was dissolved in Et_2O and water. The organic layer was washed with brine, dried over Na_2SO_4, and distilled in vacuo to give 3-bromomethyl-3-methyloxetane (4.79 g, 74%) as a colorless oil; bp 35–40°C (1 mmHg).

A solution of 4-hydroxybenzoic acid (0.310 g, 2.24 mmol) and KOH (0.264 g, 4.71 mmol) in EtOH (10 mL) was stirred at room temperature for 1 h, and evaporated in vacuo. The above bromide (0.741 g, 4.49 mmol) and DMF (10 mL) were added to the residue. The solution was stirred at 100°C for 3 h, and then the solvent was evaporated in vacuo. After dilution with water, the mixture was extracted with Et_2O. The organic layer was successively washed with 1 M HCl, 5% aq NaOH, and brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was distilled in vacuo and recrystallized from CH_2Cl_2–hexane to give **4i** (0.489 g, 65%). The residue was 'ester' and 'ether' in ^{1}H NMR assignment denote the ester- and ether-linked oxetanyl groups, respectively. Colorless plates; bp 150–160°C (1 mmHg); mp 68–70°C; IR (KBr) 1710, 1250, 1100, 1050, 975, 850 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.43, 1.45 (both s, 3H, ester- and ether-CH_3), 4.09 (s, 2H, CH_2OAr), 4.37 (s, 2H, CH_2OCOAr), 4.46, 4.48 (both d, J=5.9 Hz, 2H, ester- and ether-OCH_2 *trans* to 3-CH_2O), 4.63, 4.65 (both d, J=5.9 Hz, 2H, ester- and ether-OCH_2 *cis* to 3-CH_2O), 6.97, 8.03 (both d, J=8.3 Hz, 2H, *o*- and *m*-ArH to ether); ^{13}C NMR (100 MHz) δ 21.2, 21.3, 39.3, 39.6, 68.7, 72.9, 79.6, 114.2, 122.6, 131.7, 162.9, 166.2; EI HRMS Calcd for $C_{17}H_{22}O_5$: 306.1468. Found: 306.1465. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.36; H, 7.20.

4.3.7. 3-Methyloxetan-3-ylmethyl [4-(3-methyloxetan-3-ylmethoxy)phenyl]acetate (4j). In the same procedure for **4i**, **j** was obtained from the above bromide (0.432 g, 2.62 mmol), 4-hydroxylphenylacetic acid (0.203 g, 1.31 mmol), KOH (0.226 g, 4.03 mmol), and DMF (10 mL) at 100°C for 4 h. The crude product was distilled in vacuo from CaH_2 to give pure **4j** (0.323 g, 70%). Ester and ether in ^{1}H NMR assignment denote the ester- and ether-linked oxetanyl groups, respectively. Colorless oil; bp 160–170°C (1 mmHg); IR (KBr) 1730, 1240, 1140, 975, 830 cm^{-1}; ^{1}H NMR δ 1.29, 1.43 (both s, 3H ester- and ether-CH_3), 3.61 (s, 2H, ArCH_2CO$_2$), 4.00 (s, 2H, CH_2OAr), 4.16 (s, 2H, CH_2OCO), 4.35, 4.45 (both d, J=5.9 Hz, 2H, ester- and ether-OCH_2 *trans* to 3-CH_2O), 4.48, 4.62 (both d, J=5.9 Hz, 2H, ester- and ether-OCH_2 *cis* to 3-CH_2O), 6.89, 7.21 (both d, J=8.5 Hz, 2H, *o*- and *m*-ArH to ether); ^{13}C NMR δ 21.2, 21.3, 39.1, 39.7, 40.4, 68.9, 72.8, 79.4, 79.7, 114.6, 126.2, 130.2, 158.1, 171.7; EI HRMS Calcd for $C_{18}H_{24}O_5$: 320.1624. Found: 320.1623.

4.3.8. Diethyl 2-(3-methyloxetan-3-ylmethyl)malonate (4k). A solution of **16** (15.0 g, 55.2 mmol) and sodium iodide (18.0 g, 120 mmol) in acetone (40 mL) was refluxed for 3 h. The solvent was removed in vacuo, and the residue was dissolved in Et_2O and water. The organic layer was washed with brine, dried over Na_2SO_4, and distilled in vacuo to give 3-iodomethyl-3-methyloxetane (8.88 g, 76%) as a yellowish oil; bp 90–95°C (20 mmHg). Small pieces of Na metal (0.223 g, 9.70 mmol) were slowly added to EtOH (16 mL) below 5°C, and then diethyl malonate (0.905 g, 5.65 mmol) and the above iodide (1.00 g, 4.72 mmol) were added successively. The resulting solution was refluxed for 1.5 h, cooled, and quenched by adding MeOH (1 mL) and then water (6 mL). Keeping the mixture at pH=6 with acetic acid, it was concentrated halfway in vacuo and extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was separated into unreacted diethyl malonate and **4k** (0.53 g, 50%) by fractional distillation in vacuo. Colorless oil; bp 80–85°C (1 mmHg); IR (liquid film) 1725, 1150, 1090, 1025, 1090, 980, 825 cm^{-1}; ^{1}H NMR δ 1.27 (t, J=7.2 Hz, 6H, OCH$_2$CH_3), 1.34 (s, 3H, 3-CH_3), 2.30 (d, J=7.1 Hz, 2H, 3-CH_2CH), 3.35 (t, J=7.1 Hz, 1H, 3-CH$_2$CH), 4.19 (q, J=7.1 Hz, 4H, OCH_2CH$_3$), 4.29, 4.45 (both d, J=5.9 Hz, 2H, oxetane OCH_2 *trans* and *cis* to 3-CH_2CH); ^{13}C NMR δ 14.1, 22.9, 37.2, 38.5, 48.5, 61.7, 82.4, 169.2; EI HRMS Calcd for $C_{12}H_{20}O_5$: 244.1311. Found: 244.1319.

4.3.9. Ethyl 3-(3-methyloxetan-3-yl)propionate (4l). According to Krapcho's method,[33] the decaroboethoxylation of **4k** (5.04 g, 20.6 mmol) was carried out in DMSO (30 mL) containing H_2O (0.74 mL, 41 mmol) and NaCl (1.21 g, 20.6 mmol) with stirring at 110°C for 5 h. The reaction mixture was diluted with H_2O (30 mL), and extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and distilled in vacuo to give pure **4l** (2.53 g, 71%). Colorless oil; bp 40–45°C (1 mmHg); IR (liquid film) 1740, 1175, 980, 830 cm^{-1}; ^{1}H NMR δ 1.27 (t, J=7.1 Hz, 3H, OCH$_2$CH_3), 1.30 (s, 3H, 3-CH_3), 1.99 (pseudo t, J=8.0 Hz, 2H, 3-CH$_2$CH_2), 2.29 (pseudo t, J=8.0 Hz, 2H, 3-CH_2CH$_2$), 4.14 (q, J=7.1 Hz, 2H, OCH_2CH$_3$), 4.34, 4.42 (both d, J=5.7 Hz, 2H, oxetane OCH_2 *trans* and *cis* to 3-CH$_2$CH$_2$); ^{13}C NMR δ 14.2, 23.0, 29.8, 33.8, 38.8, 60.5, 82.2, 173.1; EI HRMS Calcd for $C_9H_{16}O_3$: 172.1100. Found: 172.1105.

4.3.10. Oxetan-3-yl benzoate (4m). Oxetan-3-ol was prepared from epichlorohydrin according to Baum's method,[34] except using 3,4-dihydro-2*H*-pyran in place of ethyl vinyl ether as an OH-protecting reagent. 1,3-Dicyclohexylcarbodiimide (1.72 g, 8.31 mmol) was added to a solution of the alcohol (0.615 g, 8.31 mmol), benzoic acid (1.02 g, 8.31 mmol), and 4-(dimethylamino)pyridine (0.10 g, 0.83 mmol) in THF (50 mL) at 0°C. The mixture was stirred at 0°C for 1 h and then at room temperature for 3 h, and the resulting precipitates were filtered off. The solvent was removed in vacuo from the filtrate, and the residue was extracted with Et_2O. The organic layer was successively washed with 1 M HCl, 10% aq NaOH, and brine, dried over Na_2SO_4, and distilled in vacuo to give **4m** (0.355 g, 24%). Colorless oil; bp 55–60°C (1 mmHg); IR (liquid film) 1720, 1275, 1115, 975, 840 cm^{-1}; ^{1}H NMR δ 4.79 (dd, J=7.8, 5.4 Hz, 2H, OCH_2 *cis* to 3-benzoate), 5.00 (t, J=7.1 Hz, 2H, OCH_2 *trans* to 3-benzoate), 5.67 (qui, J=5.9 Hz, 1H, C3H), 7.46 (t, J=7.8 Hz, 2H, *m*-ArH), 7.60 (t, J=7.4 Hz, 1H, *p*-ArH), 8.09 (d, J=8.3 Hz, 2H, *o*-ArH); ^{13}C NMR δ 68.4, 77.6, 128.5, 129.3, 129.7, 133.5, 165.8; EI HRMS Calcd for $C_{10}H_{10}O_3$: 178.0632. Found: 178.0630.

4.4. Preparation of cyclic ethers having an amide group

Oxetane *sec*-amides (**7a–e**)[14] and oxirane benzamide (**19**)[23]

were prepared as described in our previous reports. Oxetane *tert*-amides (**10a**–**u**) were prepared by *N*-alkylation[35] of **7** as described in our previous reports,[14,16] and obtained as a mixture of *s-cis* and *s-trans* isomers at room temperature, except for stereochemically pure pivalamides (*Z*)-**10d** and (*Z*)-**10m**. The spectroscopic properties and analytical data of these oxetane amides were reported therein.

4.4.1. Preparation of 3-methyloxetan-3-ylmethyl *N*-phenylbenzimidate (15). Small pieces of Na metal (0.105 g, 4.58 mmol) and **26** (0.539 g, 5.28 mmol) were refluxed in benzene (10 mL) for 6 h, and then *N*-phenylbenzimidoyl chloride[36] (0.759 g, 3.52 mmol) was added to the mixture, which was refluxed for a further 2 h. The benzene layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was repeatedly washed with hexane, and purified by alumina column chromatography using AcOEt–hexane=1:3 as the eluent, to give pure **15** (0.375 g, 35%). Colorless solid; mp 75–76°C; IR (KBr) 1650, 1150, 730, 980, 845 cm^{-1}; ^1H NMR (400 MHz) δ 1.44 (s, 3H, 3-CH_3), 4.42 (s, 2H, 3-CH_2O), 4.44, 4.69 (both d, J=5.9 Hz, 2H, OCH_2 *trans* and *cis* to 3-CH_2O), 6.73 (d, J=8.1 Hz, 2H, *o*-ArH to N=C), 6.64 (t, J=7.3 Hz, 1H, *p*-ArH to N=C), 7.16, 7.19 (both t, J=7.6 Hz, 2H, *m*-ArH to N=C and 3-ArH-*m*), 7.27 (t, J=7.3 Hz, 1H, 3-ArH-*p*), 7.32 (d, J=8.0 Hz, 2H, 3-ArH-*o*); ^{13}C NMR (100 MHz) δ 21.4, 39.3, 70.6, 79.8, 121.3, 122.6, 127.8 (overlapped), 128.8, 129.2, 129.9, 130.8, 148.0, 158.3; EI HRMS Calcd for $C_{18}H_{19}NO_2$: 281.1417. Found: 281.1415.

4.5. Preparation of oxetanes having a ketone substituent

4.5.1. 2-(3-Methyloxetan-3-ylmethoxy)-1-phenylethanone (17a). A solution of 3-iodomethyl-3-methyloxetane (1.26 g, 5.90 mmol, see Section 4.3.8) and (2-phenyl-1,3-dioxolan-2-yl)methanol[37] (1.00 g, 5.54 mmol) in benzene–hexane=1:1 (15 mL) was refluxed over solid NaOH (3.01 g, 75.3 mmol) with stirring for 12 h, while tetrabutylammonium bromide (0.895 g, 2.78 mmol) was added by 90 mg portions every 1 h. After water (25 mL) was added to the mixture, the organic layer was separated, washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by alumina column chromatography using AcOEt–hexane=1:3 as the eluent, to give 2-(3-methyloxetan-3-ylmethoxymethyl)-2-phenyl-1,3-dioxolane (0.220 g, 58%) as a colorless oil. The ketal (0.475 g, 1.80 mmol) was stirred in 0.5 M aq H_2SO_4 (23 mL) at room temperature for 10 h. The reaction mixture was neutralized with sat. aq $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by alumina column chromatography using AcOEt–hexane=2:3 as the eluent, followed by vacuum distillation, to give **17a** (0.249 g, 63%). Colorless oil; bp 100–105°C (1 mmHg); IR (liquid film) 1700, 1135, 975, 830 cm^{-1}; ^1H NMR δ 1.35 (s, 3H, CH_3), 3.64 (s, 2H, 3-CH_2O), 4.38, 4.58 (both d, J=5.7 Hz, 2H, CH_2O *trans* and *cis* to 3-CH_2O), 4.79 (s, 2H, OCH_2CO), 7.47 (pseudo t, J=7.4 Hz, 2H, *m*-ArH), 7.59 (pseudo t, J=7.3 Hz, 1H, *p*-ArH), 7.94 (pseudo d, J=7.0 Hz, 2H, *o*-ArH); ^{13}C NMR δ 21.3, 40.0, 65.3, 74.2, 79.9, 126.0, 127.9, 133.5, 134.8, 196.5; EI HRMS Calcd for $C_{13}H_{16}O_3$: 220.1100. Found: 220.1104.

4.5.2. 3-(3-Methyloxetan-3-ylmethoxy)-1-phenylpropan-1-one (17b). According to the procedure for **17a**, the phase-transfer-catalysis reaction of 3-iodomethyl-3-methyloxetane (0.335 g, 1.58 mmol, see Section 4.3.8), 2-(1,3-dioxolan-2-yl)-2-phenylethanol[38] (0.307 g, 1.58 mmol), solid NaOH (0.60 g, 15 mmol), and tetrabutylammonium hydrogensulfate (cat. amount) in benzene (15 mL), followed by chromatographic purification of the crude product using AcOEt–hexane=1:9 as the eluent, gave 2-[2-(3-methyloxetan-3-ylmethoxy)ethyl]-2-phenyl-1,3-dioxolane (0.221 g, 50%) as a colorless oil. The above oxolane (0.300 g, 1.08 mmol) was dissolved in a mixture of acetone (15 mL)–H_2O (7.5 mL) containing *p*-toluenesulfonic acid (cat. amount), and the solution was refluxed for 10 h. The acetone was removed in vacuo, and then the remaining mixture was extracted with Et_2O. The organic layer was dried over Na_2SO_4, and distilled in vacuo to give **17b** (0.202 g, 80%). Pale yellowish oil; bp 115–120°C (1 mmHg); IR (liquid film) 1680, 1120, 980, 835 cm^{-1}; ^1H NMR δ 1.27 (s, 3H, CH_3), 3.27 (t, J=6.4 Hz, 2H, OCH_2CH_2), 3.53 (s, 2H, 3-CH_2O), 3.92 (t, J=6.4 Hz, 2H, OCH_2CH_2), 4.43, 4.48 (both d, J=5.7 Hz, 2H, CH_2O *trans* and *cis* to 3-CH_2O), 7.45 (pseudo t, J=7.4 Hz, 2H, *m*-ArH), 7.56 (pseudo t, J=7.3 Hz, 1H, *p*-ArH), 7.97 (pseudo d, J=7.1 Hz, 2H, *o*-ArH); ^{13}C NMR δ 21.4, 38.8, 39.9, 66.8, 76.4, 80.0, 128.0, 128.5, 133.0, 136.9, 198.3; EI HRMS Calcd for $C_{14}H_{18}O_3$: 234.1256. Found: 234.1255.

4.5.3. Isomerization of imide-substituted cyclic ethers. Typically, a hexane solution of Me_3Al (1.70 mL, 1.0 mol L^{-1}, 1.70 mmol) was added to a solution of **1a** (8.02 g, 34.7 mmol) in anhydrous PhCl (32 mL) under dry nitrogen. The resulting solution was allowed to stand at 120°C for 12 h, and the reaction was quenched by adding anhydrous Et_3N (1.6 mL). The mixture was diluted with CH_2Cl_2 (50 mL) to deposit insoluble materials, which were removed by filtration. After decolorization of the filtrate with charcoal followed by evaporation, the residue was recrystallized from CH_2Cl_2–hexane to give 2,3-benzo-7-methyl-9,10-dioxa-5-azatricyclo[5.2.2.$0^{1,5}$]undeca-2-en-4-one (**2a**; 7.28 g, 91%). Colorless needles; mp 172–174°C; IR (KBr) 1721, 1711, 1132, 1055–968 cm^{-1}; ^1H NMR (400 MHz) δ 0.95 (s, 3H, 7-CH_3), 3.63 (s, 2H, NCH_2), 3.94, 4.07 (both d, J=8.3 Hz, 2H, equatorial and axial OCH_2 with respect to a boat-type 1,3-dioxane ring), 7.44–7.53 (m, 3H, carbonyl *m*- and *p*-ArH), 7.72 (d, J=7.3 Hz, 1H, carbonyl *o*-ArH); ^{13}C NMR (100 MHz) δ 15.6, 31.2, 49.3, 74.0, 101.2, 121.8, 123.2, 130.5, 132.0, 132.9, 139.6, 163.9; EI HRMS Calcd for $C_{13}H_{13}NO_3$: 231.0896. Found: 231.0885. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.29; H, 5.73; N, 5.98.

The preparation, spectroscopic properties, and analytical data of bicyclic acetals **2b**–**h** were described in our previous reports.[5,6,9]

4.5.4. 2,3-Benzo-10,11-dioxa-5-azatricyclo[6.2.1.$0^{1,5}$]undec-2-en-4-one (23b). Reaction conditions: **22b** (0.205 g, 0.943 mmol), MAD (5 mol%), toluene (2.1 mL), 25°C, 72 h. **23b** (0.172 g, 84%); colorless crystals; mp 105–107°C (Et_2O–hexane); IR (KBr) 1700, 1145, 1040–935 cm^{-1}; ^1H NMR δ 1.71 (ddd, J=13.9, 5.4, 1.8 Hz, 1H, C7H_2), 2.21 (dddd, J=13.9, 11.9, 7.3, 3.3 Hz, 1H, C7H_2), 3.45 (ddd,

J=13.5, 11.9, 5.6 Hz, 1H, NC6H_2), 4.18 (dd, J=13.5, 7.3 Hz, 1H, NC6H_2), 4.23 (d, J=2.6 Hz, 2H, OC9H_2), 4.96 (m, 1H, OC8H), 7.52–7.61 (m, 3H, ArH other than carbonyl o-ArH), 7.77–7.81 (m, 1H, carbonyl o-ArH); ^{13}C NMR δ 26.1, 32.8, 68.0, 74.2, 111.3, 122.5, 123.3, 131.2, 132.1, 133.6, 137.6, 163.2; EI HRMS Calcd for $C_{12}H_{11}NO_3$: 217.0739. Found: 217.0738.

4.5.5. 2,3-Benzo-11,12-dioxa-5-azatricyclo[7.2.1.0^{1,5}]dodec-2-en-4-one (23c). Reaction conditions: **22c** (0.500 g, 2.16 mmol), BF_3·Et_2O (250 mol%), CH_2Cl_2 (14.5 mL), 25°C, 72 h. **23c** (0.452 g, 90%); the large amount of BF_3·Et_2O was required to suppress polymerization. Colorless oil; bp 140–150°C (1 mmHg); IR (KBr) 1700, 1140, 1060–940 cm^{-1}; ^{1}H NMR δ 1.87–2.16 (m, 4H, C7H_2C8H_2), 3.26 (ddd, J=13.7, 11.5, 2.1 Hz, 1H, NC6H_2), 3.94 (ddd, J=13.9, 5.4, 2.5 Hz, 1H, NC6H_2), 4.19 (dd, J=7.4, 0.8 Hz, 1H, OC10H_2), 4.21 (t, J=6.6 Hz, 1H, OC10H_2), 4.86 (m, 1H, OC9H), 7.44–7.58 (m, 3H, ArH other than carbonyl o-ArH), 7.73 (d, J=7.1 Hz, 1H, carbonyl o-ArH); ^{13}C NMR δ 20.6, 34.8, 41.1, 69.4, 76.1, 116.7, 121.7, 122.8, 130.6, 132.0, 132.4, 141.9, 166.5; EI HRMS Calcd for $C_{13}H_{13}NO_3$: 231.0896. Found: 231.0896.

4.5.6. Isomerization of ester-substituted cyclic ethers. Typically, BF_3·Et_2O (1.80 mL, 0.432 mol L^{-1} in CH_2Cl_2, 0.778 mmol) was added to an CH_2Cl_2 (12 mL) of **4d** (3.00 g, 15.6 mmol) under dry nitrogen. The resulting solution was allowed to stand at 25°C for 24 h, and quenched by adding anhydrous Et_3N (1.6 mL). The volatile materials were evaporated to dryness, and then the crude product was purified by alumina column chromatography using toluene as the eluent, followed by recrystallization from CH_2Cl_2–hexane, to give 4-methyl-1-phenyl-2,6,7-trioxabicyclo[2.2.2]octane (**5d**; 2.37 g, 74%). Colorless needles; mp 128–129°C; IR (KBr) 1105–990 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.87 (s, 3H, 4-CH_3), 4.08 (s, 6H, OCH_2), 7.33–7.36 (m, 3H, m- and p-ArH), 7.62 (dd, J=6.6, 3.2 Hz, 2H, o-ArH); ^{13}C NMR (126 MHz) δ 14.5, 30.5, 73.3, 107.4, 125.6, 128.0, 129.1, 135.7; EI HRMS Calcd for $C_{12}H_{14}O_3$: 206.0943. Found: 206.0949.

Moisture-sensitive **5** was isolated by direct distillation of the reaction mixture from CaH_2, and stored under nitrogen. The preparation, spectroscopic properties, and analytical data of bicyclic orthoesters **5b** and **5e** were described in our previous report.[7]

4.5.7. 1-Ethyl-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (5a). Reaction conditions: **4a** (0.315 g, 1.99 mmol), BF_3·Et_2O (5 mol%), CH_2Cl_2 (6.2 mL), 35°C, 24 h. **5a** (0.283 g, 90%); colorless oil, which was rapidly hydrolyzed with moisture in air; bp 30–35°C (1 mmHg); IR (liquid film) 1065, 1050, 990 cm^{-1}; ^{1}H NMR (anhydrous $CDCl_3$) δ 0.73 (s, 3H, 4-CH_3), 0.87 (t, J=7.5 Hz, 3H, 1-CH_2CH_3), 1.62 (q, J=7.5 Hz, 2H, 1-CH_2CH_3), 3.82 (s, 6H, CH_2O); ^{13}C NMR (anhydrous $CDCl_3$) δ 7.57, 14.6, 29.9, 30.3, 72.6, 109.2; FAB HRMS Calcd for $C_8H_{15}O_3$ (M^++H): 159.1022. Found: 159.1025.

4.5.8. 4-Methyl-1-(4-nitrophenyl)-2,6,7-trioxabicyclo[2.2.2]octane (5c). Reaction conditions: **4c** (101 mg, 0.398 mmol), BF_3·Et_2O (5 mol%), CH_2Cl_2 (1.2 mL), 35°C, 48 h. **5c** (90.5 mg, 91%); pale yellowish crystals; mp 160–162°C; IR (KBr) 1520, 1340, 1100, 1010, 980, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 3H, 4-CH_3), 4.10 (s, 6H, OCH_2), 7.78, 8.19 (both d, J=8.8 Hz, 2H, m- and o-ArH to 4-NO_2); ^{13}C NMR ($CDCl_3$) δ 14.5, 30.7, 73.3, 106.6, 123.1, 127.1, 143.6, 148.2; EI HRMS Calcd for $C_{12}H_{13}NO_5$: 251.0794. Found: 251.0800.

4.5.9. 1-(4-Methoxyphenyl)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (5f). Reaction conditions: **4f** (0.306 g, 1.30 mmol), BF_3·Et_2O (5 mol%), CH_2Cl_2 (1.4 mL), 35°C, 48 h. **5f** (0.240 g, 78%); colorless crystals; mp 82–84°C; IR (KBr) 1250, 1095, 1050–985 cm^{-1}; ^{1}H NMR δ 0.87 (s, 3H, 4-CH_3), 3.79 (s, 3H, OCH_3), 4.07 (s, 6H, OCH_2), 6.85 (d, J=8.7 Hz, 2H, o-ArH to 4-OCH_3), 7.54 (d, J=8.6 Hz, 2H, m-ArH to 4-OCH_3); ^{13}C NMR δ 14.6, 30.5, 55.3, 73.2, 107.4, 113.2, 126.9, 129.9, 160.0; EI HRMS Calcd for $C_{13}H_{16}O_4$: 236.1049. Found: 236.1041.

4.5.10. 4-Methyl-1-(4-vinylphenyl)-2,6,7-trioxabicyclo[2.2.2]octane (5g). Reaction conditions: **4g** (100 mg, 0.431 mmol), BF_3·Et_2O (10 mol%), CH_2Cl_2 (0.4 mL), 25°C, 24 h. **5g** (79 mg, 79%); colorless plates; mp 107–109°C (CH_2Cl_2–hexane); IR (KBr) 1630, 1100–950 cm^{-1}; ^{1}H NMR δ 0.87 (s, 3H, orthoester 4-CH_3), 4.08 (s, 6H, OCH_2), 5.24 (dd, J=10.9, 0.8 Hz, 1H, *trans*-CH_2=CH), 5.74 (dd, J=17.6, 0.8 Hz, 1H, *cis*-CH_2=CH), 6.70 (dd, J=17.6, 10.9 Hz, 1H, CH_2=CH), 7.38, 7.57 (both d, J=8.2 Hz, 2H, o- and m-ArH to 4-vinyl); ^{13}C NMR δ 14.5, 30.5, 73.2, 107.3, 114.3, 125.5, 125.7, 136.4, 136.7, 138.1; EI HRMS Calcd for Calcd for $C_{14}H_{16}O_3$: 232.1100. Found: 232.1103.

4.5.11. 1-Isopropenyl-4-methyl-2,6,7-trioxabicyclo-[2.2.2]octane (5h). Reaction conditions: **4h** (0.206 g, 1.21 mmol), BF_3·Et_2O (5 mol%), CH_2Cl_2 (2.0 mL), 25°C, 24 h. **5h** (0.156 g, 76%); colorless plates; mp 56–58°C; IR (KBr) 1625, 1170, 1040, 980 cm^{-1}; ^{1}H NMR δ 0.83 (s, 3H, 4-CH_3), 1.81 (pseudo t, J=1.2 Hz, 3H, CH_2=C–CH_3), 3.97 (s, 6H, CH_2O), 5.00 (pseudo qui, J=1.6 Hz, *cis*-CH_2=CMe), 5.37 (pseudo q, 1H, *trans*-CH_2=CMe); ^{13}C NMR δ 14.6, 17.8, 30.3, 72.9, 107.0, 114.0, 140.6; EI HRMS Calcd for $C_9H_{14}O_3$: 170.0943. Found: 170.0941.

4.5.12. 4-Methyl-1-[4-(3-methyloxetan-3-ylmethoxy)-phenyl]-2,6,7-trioxabicyclo[2.2.2]octane (5i). Reaction conditions: **4i** (0.200 g, 0.653 mmol), BF_3·Et_2O (5 mol%), CH_2Cl_2 (3.1 mL), 25°C, 24 h. **5i** (0.122 g, 61%); colorless plates; mp 160–162°C (CH_2Cl_2–hexane); IR (KBr) 1240, 1090, 1030, 1000, 960, 830 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.87 (s, 3H, orthoester 4-CH_3), 1.42 (s, 3H, oxetane 3-CH_3), 4.00 (s, 2H, CH_2OAr), 4.07 (s, 6H, orthoester OCH_2), 4.43, 4.61 (both d, J=6.2 Hz, 2H, oxetane OCH_2 *trans* and *cis* to 3-CH_2O), 6.89, 7.55 (both d, J=8.8 Hz, 2H, o- and m-ArH to 4-OCH_2); ^{13}C NMR (125 MHz) δ 14.5, 21.3, 30.4, 39.7, 72.8, 73.2, 79.8, 107.1, 113.9, 127.1, 130.4, 159.6; EI HRMS Calcd for $C_{17}H_{22}O_5$: 306.1468. Found: 306.1467. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.72; H, 7.35.

4.5.13. 4-Methyl-1-[4-(3-methyloxetan-3-ylmethoxy)-benzyl]-2,6,7-trioxabicyclo[2.2.2]octane (5j). Reaction

conditions: **4j** (0.103 g, 0.322 mmol), $BF_3{\cdot}Et_2O$ (5 mol%), CH_2Cl_2 (6.1 mL), 25°C, 24 h. **5j** (79 mg, 79%); colorless oil, which solidified gradually at room temperature; bp 160–170°C (1 mmHg); mp 67–68°C; IR (KBr) 1250, 1040, 1010, 990, 970, 830 cm^{-1}; ^1H NMR δ 0.70 (s, 3H, orthoester 4-CH_3), 1.34 (s, 3H, oxetane 3-CH_3), 2.86 (s, 2H, CH_2Ar), 3.80 (s, 6H, orthoester OCH_2), 3.91 (s, 2H, CH_2OAr), 4.36, 4.54 (both d, J=5.8 Hz, 2H, oxetane OCH_2 *trans* and *cis* to 3-CH_2O), 6.77, 7.14 (both d, J=8.5 Hz, 2H, *o*- and *m*-Ar*H* to 4-OCH_2); ^{13}C NMR δ 14.6, 21.4, 30.5, 39.7, 42.0, 72.6, 79.8, 108.5, 113.8, 127.4, 131.4, 157.6; FAB HRMS Calcd for $C_{18}H_{25}O_5$ (M^++H): 321.1703. Found: 321.1706.

4.5.14. Ethyl 1-ethoxy-4-methyl-2,6-dioxabicyclo-[2.2.2]octane-7-carboxylate (5k). Reaction conditions: **4k** (195 mg, 0.789 mmol), $BF_3{\cdot}Et_2O$ (5 mol%), CH_2Cl_2 (2.0 mL), 25°C, 6 h. **5k** (125 mg, 64%); colorless oil; bp 80–90°C (1 mmHg); IR (liquid film) 1720, 1150, 1050, 990 cm^{-1}; ^1H NMR δ 0.84 (s, 3H, 4-CH_3), 1.16 (t, J=7.1 Hz, 3H, 1-OCH_2CH_3), 1.27 (t, J=7.1 Hz, 3H, 7-$CO_2CH_2CH_3$), 1.90 (ddd, J=13.2, 11.0, 3.3 Hz, 1H, C8H_2 *trans* to 7-$CO_2CH_2CH_3$), 2.17 (ddd, J=13.1, 4.9, 3.1 Hz, 1H, C8H_2 *cis* to 7-$CO_2CH_2CH_3$), 3.15 (dd, J=11.0, 4.9 Hz, 1H, C7*H*), 3.74–3.97 (m, 5H of 1-OCH_2CH_3, *endo*-C3*H*, and C5H_2), 4.06–4.33 (m, 3H of *exo*-C3*H* and 7-$CO_2CH_2CH_3$): the carbons of *syn*- and *anti*-OCH_2 to 7-CO_2Et in an enantiomer of **5k** are defined as the 3- and 5-positions, respectively; ^{13}C NMR δ 14.3, 15.4, 17.8, 28.9, 34.2, 47.2, 58.2, 60.8, 75.6, 108.8, 171.8; EI HRMS Calcd for $C_{12}H_{20}O_5$: 244.1311. Found: 244.1309.

4.5.15. 1-Ethoxy-4-methyl-2,6-dioxabicyclo[2.2.2]octane (5l). Reaction conditions: **4l** (200 mg, 1.16 mmol), MAD (15 mol%), toluene (1.2 mL), 0°C, 96 h. **5l** (168 mg, 82%); colorless oil, which was rapidly hydrolyzed with moisture under air; bp 30–35°C (1 mmHg); IR (liquid film) 1000–1100 cm^{-1}; ^1H NMR (anhydrous $CDCl_3$) δ 0.81 (s, 3H, 4-CH_3), 1.20 (t, J=7.1 Hz, 3H, 1-OCH_2CH_3), 1.76–1.82 (m, 2H, C8H_2), 2.06–2.12 (m, 2H, C7H_2), 3.80 (q, J=7.2 Hz, 2H, 1-OCH_2CH_3), 3.88–3.96 (m, 4H, C3H_2 and C5H_2); ^{13}C NMR (anhydrous $CDCl_3$) δ 15.7, 18.3, 29.8, 31.0$_7$, 31.1$_3$, 58.0, 76.1, 110.3; FAB HRMS Calcd for $C_9H_{17}O_3$ (M^++H): 173.1178. Found: 173.1181.

4.5.16. Poly(orthoester) from 4m: poly{oxy(2-phenyl-1,3-dioxolane-2,5-diyl)methylene}. Reaction conditions: **4m** (0.209 g, 1.17 mmol), MAD (5 mol%), CH_2Cl_2 (1.2 mL), 0°C, 72 h. The poly(orthoester) obtained in 95% NMR conversion was purified by precipitation from a CH_2Cl_2 solution with MeOH. IR (cast film) 1720 (vw), 1310–1280, 1110–980 cm^{-1}; ^1H NMR (500 MHz) δ 3.76–3.44 (m, 2H, OCH_2), 4.05–3.76 (m, 2H, CH_2 in ring), 4.28–4.05 (m, 1H, C*H* in acetal ring), 7.40–7.10 (br s, 3H, *m*- and *p*-Ar*H*), 7.72–7.40 (br s, 2H, *o*-Ar*H*), 8.07–7.91 (br s, *o*-Ar*H* of the benzoate pendant group in the ether-type units contained in 7%); ^{13}C NMR (125 MHz) δ 63.0, 67.3, 75.2, 121.3, 125.9, 126.0, 128.1, 129.1, 137.9–137.8. $M_{n\ GPC}$=8160.

4.5.17. Isomerization of *sec*-amide-substituted cyclic ethers. Typically, a hexane solution of Me_3Al (0.054 mL, 0.98 mol L^{-1}, 0.052 mmol) was added to an anhydrous PhCl (1.0 mL) solution of **7b** (150 mg, 1.05 mmol). The resulting solution was allowed to react at 120°C for 24 h, and quenched by adding Et_3N (0.1 mL) followed by MeOH (3.0 mL). The solvents were replaced by CH_2Cl_2 (1.0 mL), and then vacuum distillation of the soluble part afforded 5-hydroxymethyl-2,5-dimethyl-5,6-dihydro-4*H*-1,3-oxazine (**8b**; 139 mg, 93%). Colorless oil; bp 110–120°C (1 mmHg); IR (liquid film) 3300, 1670 cm^{-1}; ^1H NMR δ 0.94 (s, 3H, 5-CH_3), 1.90 (s, 3H, 2-CH_3), 2.96, 3.24 (both d, J=16.1 Hz, 1H, NCH_2), 3.41 (s, 2H, CH_2OH), 3.74, 3.98 (both dd, J=10.9, 1.0 Hz, 1H, OCH_2); ^{13}C NMR δ 19.0, 20.9, 32.2, 50.4, 65.1, 70.3, 157.8. EI HRMS Calcd for $C_7H_{13}NO_2$: 143.0948. Found: 143.0948.

4.5.18. 5-Hydroxymethyl-5-methyl-5,6-dihydro-4*H*-1,3-oxazine (8a). Reaction conditions: Me_3Al (50 mol%), PhCl, 120°C, 24 h. The reaction was quenched with Et_3N followed by MeOH containing a small amount of aq NaOH. **8a** (50%); colorless oil; bp 50–70°C (1 mmHg); IR (liquid film) 3300, 1650 cm^{-1}; ^1H NMR δ 0.98 (s, 3H, 5-CH_3), 2.30 (br s, 1H, OH), 3.00, 3.27 (both d, J=14.9 Hz, 1H, NCH_2), 3.48 (s, 2H, CH_2OH), 3.64 (d, J=10.7 Hz, 1H, OCH_2,), 4.03 (dd, J=10.7, 2.0 Hz, 1H, OCH_2,), 7.01 ppm (br s, 1H, C2*H*).

4.5.19. 5-Hydroxymethyl-5-methyl-2-propyl-5,6-dihydro-4*H*-1,3-oxazine (8c). Reaction conditions: Me_3Al (5 mol%), PhCl, 120°C, 24 h. **8c** (89%); colorless oil; bp 100–120°C (1 mmHg); IR (liquid film) 3300, 1670 cm^{-1}; ^1H NMR δ 0.93 (t, J=7.2 Hz, 3H, $CH_2CH_2CH_3$), 0.95 (s, 3H, 5-CH_3), 1.59 (sex, J=7.4 Hz, 2H, $CH_2CH_2CH_3$), 2.14 (t, J=7.8 Hz, 2H, C$H_2CH_2CH_3$), 2.7 (br s, 1H, O*H*), 2.98, 3.28 (both d, J=15.4 Hz, 1H, NCH_2), 3.44 (s, 2H, CH_2OH), 3.72 (d, J=10.8 Hz, 1H, OCH_2), 3.99 (dd, J=10.7, 2.2 Hz, 1H, OCH_2).

4.5.20. 2-Benzyl-5-hydroxymethyl-5-methyl-5,6-dihydro-4*H*-1,3-oxazine (8d). Reaction conditions: Me_3Al (5 mol%), PhCl, 120°C, 24 h. **8d** (71%); colorless oil; bp 140–160°C (1 mmHg); IR (neat) 3300, 1670 cm^{-1}; ^1H NMR δ 0.91 (s, 3H, 5-CH_3), 3.07 (br s, 1H, O*H*), 3.30, 3.53 (both d, J=17.1 Hz, 1H, NCH_2), 3.38 (s, 2H, PhCH_2), 3.45 (s, 2H, CH_2OH), 3.70 (d, J=10.7 Hz, 1H, OCH_2), 3.97 (dd, J=10.6, 2.1 Hz, 1H, OCH_2), 7.23–7.35 ppm (m, 5H, Ar*H*).

4.5.21. 5-Hydroxymethyl-5-methyl-2-phenyl-5,6-dihydro-4*H*-1,3-oxazine (8e). Reaction conditions: $BF_3{\cdot}Et_2O$ (25 mol%), CH_2Cl_2, 35°C, 96 h. **8e** (89%); colorless oil; mp 135–137°C (CH_2Cl_2–hexane); IR (KBr) 3200, 1645 cm^{-1}; ^1H NMR δ 1.02 (s, 3H, 5-CH_3), 2.02 (br s, 1H, O*H*), 3.27 (d, J=16.6 Hz, 1H, NCH_2), 3.48 (dd, J=16.9, 2.2 Hz, 1H, NCH_2), 3.47, 3.57 (both d, J=10.7 Hz, 1H, CH_2OH), 3.92 (d, J=10.7 Hz, 1H, OCH_2), 4.23 (dd, J=10.7, 2.4 Hz, 1H, OCH_2), 7.33–7.44 (m, 3H, *m*- and *p*-Ar*H*), 7.89 ppm (dd, J=6.9, 1.5 Hz, 2H, *o*-Ar*H*); ^{13}C NMR δ 19.0, 32.7, 51.1, 65.8, 127.0, 128.0, 130.5, 133.3, 155.0; EI HRMS Calcd for $C_{12}H_{15}NO_2$: 205.1104. Found: 205.1115. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 69.96; H, 7.33; N, 6.76.

4.5.22. Isomerization of *tert*-amide-substituted oxetanes. Typically, $BF_3{\cdot}Et_2O$ (0.112 mL, 0.43 mol L^{-1} in PhCl,

0.048 mmol) was added to a PhCl (1.0 mL) solution of **10j** (0.224 g, 0.961 mmol). The resulting solution was allowed to stand at 130°C for 1.5 h, and quenched by adding anhydrous Et_3N (1.0 mL) and a small amount of CaH_2. Moisture-sensitive isomerization product, 7-ethyl-4-methyl-1-phenyl-2,6-dioxa-7-azabicyclo[2.2.2]octane (**11j**; 0.121 g, 54%), was isolated by direct distillation of the reaction mixture from CaH_2, and stored under nitrogen. Colorless liquid; bp 100–120°C (1 mmHg); ^{1}H NMR (100 MHz, anhydrous $CDCl_3$) δ 0.88 (s, 3H, 4-CH_3), 0.94 (t, J=7.3 Hz, 3H, CH_2CH_3), 2.36 (q, J=7.2 Hz, 2H, CH_2CH_3), 2.99 (s, 2H, NCH_2), 3.98 (s, 4H, OCH_2), 7.29–7.38 (m, 3H, *m*- and *p*-ArH), 7.60 (dd, J=6.8, 3.2 Hz, 2H, *o*-ArH); EI HRMS Calcd for $C_{14}H_{19}NO_2$: 233.1417. Found: 233.1439.

On the other hand, TfOMe (0.05 mL, 0.43 mol L^{-1} in nitrobenzene, 0.022 mmol) was added to a nitrobenzene (1.0 mL) solution of **10j** (0.224 g, 0.961 mmol). The resulting solution was allowed to stand at 150°C for 96 h, quenched with anhydrous Et_3N (0.1 mL), and then evaporated. The residue was purified by column chromatography on alumina with AcOEt–hexane=2:3 as the eluent, followed by distillation in vacuo, to give 1-ethyl-3-methyl-azetidin-3-ylmethyl benzoate (**14j**; 0.141 g, 63%). Pale yellow liquid; bp 130–140°C (1 mmHg); IR (liquid film) 1720, 1270, 1110 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.97 (t, J=7.3 Hz, 3H, 1-CH_2CH_3), 1.38 (s, 3H, 3-CH_3), 2.51 (q, J=7.2 Hz, 2H, 1-CH_2CH_3), 3.03, 3.21 (both d, J=7.3 Hz, 2H, *cis*- and *trans*-NCH_2 to 3-CH_3), 4.33 (s, 2H, 3-CH_2O), 7.45 (t, J=7.6 Hz, 2H, *m*-ArH), 7.57 (t, J=7.3 Hz, 1H, *p*-ArH), 8.05 (d, J=7.8 Hz, 2H, *o*-ArH); ^{13}C NMR (100 MHz) δ 12.2, 22.7, 34.5, 53.4, 62.0, 70.4, 128.3, 129.5, 130.2, 132.9, 166.5; EI HRMS Calcd for $C_{14}H_{19}NO_2$: 233.1417. Found: 233.1427.

The preparation, spectroscopic properties, and analytical data of other bicyclic acetals **11**[14,16] and azetidines **14**[16] were described in our previous reports.

4.5.23. 4-Methyl-1,7-diphenyl-2,6-dioxa-7-azabicyclo-[2.2.2]octane (11v). Reaction conditions: $BF_3{\cdot}Et_2O$ (5 mol%), CH_2Cl_2, 35°C, 100 h. **11v** (50%); colorless oil; bp 120–125°C (1 mmHg); ^{1}H NMR (100 MHz, anhydrous $CDCl_3$) δ 0.91 (s, 3H, 4-CH_3), 3.69 (s, 2H, NCH_2), 3.88–4.09 (m, 4H, OCH_2), 6.80–7.15 (m, 3H, *o*- and *p*-ArH to N=C), 7.19–7.41 (m, 5H, 4-ArH-*m* and -*p*), 7.53–7.63 (m, 2H, 4-ArH-*o*).

4.5.24. 3-Methyl-1-phenylazetidin-3-ylmethyl benzoate (14v). Reaction conditions: TfOMe (35 mol%), nitrobenzene, 150°C, 4.5 h. **14v** (74%); colorless oil, which solidified at room temperature; bp 120–125°C (1 mmHg); mp 48–49°C; IR (KBr) 1720, 1120 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.44 (s, 3H, 3-CH_3), 3.64, 3.86 (both d, 2H, J=6.9 Hz, NCH_2 *trans* and *cis* to 3-CH_2O), 4.41 (s, 2H, 3-CH_2O), 6.46 (d, J=7.6 Hz, 2H, *o*-ArH to N=C), 6.75 (t, J=7.3 Hz, 1H, *p*-ArH to N=C), 7.22 (t, J=8.1 Hz, 2H, *m*-ArH to N=C), 7.40 (t, J=7.4 Hz, 2H, 1-ArH-*m*), 7.54 (t, J=7.3 Hz, 1H, 1-ArH-*p*), 7.98 (d, J=7.3 Hz, 2H, 1-ArH-*o*); ^{13}C NMR (100 MHz) δ 22.5, 35.0, 60.3, 70.2, 111.3, 117.4, 128.4, 129.0, 129.6, 130.0, 133.0, 151.2, 166.5; EI HRMS Calcd for $C_{18}H_{19}NO_2$: 281.1417. Found: 281.1412.

4.6. Isomerization of ketone-substituted oxetanes

4.6.1. 1-Methyl-5-phenyl-3,6,9-trioxabicyclo[3.2.2]nonane (18a). Reaction conditions: **17a** (200 mg, 0.909 mmol), $BF_3{\cdot}Et_2O$ (5 mol%), CH_2Cl_2 (1.1 mL), 25°C, 72 h. **18a** (164 mg, 82%); pale yellowish liquid, which solidified at room temperature; bp 100–105°C (1 mmHg); mp 98–100°C ($CHCl_3$–hexane); IR (KBr) 1120–975 cm^{-1}; ^{1}H NMR δ 0.80 (s, 3H, CH_3), 3.78 (s, 2H, C2H_2), 3.85 (s, 2H, C4H_2), 3.79, 4.19 (both d, J=9.4 Hz, 2H, equatorial and axial C7H_2 and C8H_2 with respect to a boat-type 1,3-dioxane ring), 7.21–7.28 (m, 3H, ArH-*m*- and -*p*), 7.41–7.49 (m, 2H, ArH-*o*); ^{13}C NMR δ 18.9, 37.0, 65.7, 71.9, 79.6, 105.0, 125.7, 128.0, 128.1, 138.2; FAB HRMS Calcd for $C_{13}H_{17}O_3$ (M^++H): 221.1178. Found: 221.1185.

4.6.2. Polyether from 17b: poly{oxy[2-(3-oxo-3-phenylpropoxymethyl)-2-methyltrimethylene]}. Reaction conditions: $BF_3{\cdot}Et_2O$ (5 mol%), CH_2Cl_2, 25°C, 48 h. The poly(orthoester) obtained in 100% NMR conversion was purified by precipitation from a THF solution with hexane. IR (cast film) 1680, 1100 cm^{-1}; ^{1}H NMR δ 0.84 (s, 3H, CH_3), 3.09–3.50 (m, 8H, CH_2 except for OCH_2CH$_2$CO), 3.78 (br s, 2H, OCH_2CH$_2$CO), 7.41–7.51 (m, 3H, *m*- and *p*-ArH), 7.94 (br s, 2H, *o*-ArH); ^{13}C NMR δ 17.5, 38.9, 41.1, 67.1, 73.9, 74.1, 74.4, 128.2, 128.5, 133.0, 137.2, 198.8. $M_{n\ GPC}$=4530.

Acknowledgments

The authors would like to thank Professor Amy Howell, University of Connecticut, for carefully proofreading the manuscript and also for her many valuable suggestions that were important to clarifying the presentation.

References

1. (a) Haines, A. H. Cyclic Ethers. *Comprehensive Organic Chemistry*; Stoddart, J. F., Ed.; Pergamon: Oxford, 1979; Vol. 1, pp 853–896. (b) Smith, J. G. *Synthesis* **1984**, 629–656.
2. Penczek, S.; Kubisa, P. Cationic Ring-opening Polymerization. *Comprehensive Polymer Science*; Allen, G., Bevington, J. C., Eastmond, G. C., Ledwith, A., Russo, S., Sigwalt, P., Eds.; Pergamon: Oxford, 1989; Vol. 3, pp 751–786.
3. (a) Penczek, S.; Kubisa, P.; Szymański, R. *Makromol. Chem.: Macromol. Symp.* **1986**, *3*, 203–220. (b) Wojtania, M.; Kubisa, P.; Penczek, S. *Makromol. Chem.: Macromol. Symp.* **1986**, *6*, 201–206. (c) Biedron, T.; Kubisa, P.; Penczek, S. *J. Polym. Sci., Part A: Polym. Chem.* **1991**, *29*, 619–628.
4. (a) Kanoh, S.; Motoi, M. *Bull. Chem. Soc. Jpn* **1997**, *70*, 1649–1657. (b) Hiruma, T.; Kanoh, K.; Yamamoto, T.; Kanoh, S.; Motoi, M. *Polym. J.* **1995**, *27*, 78–89. (c) Motoi, M.; Saito, E.; Kyoda, S.; Takahata, N.; Nagai, S.; Arano, A. *Polym. J.* **1991**, *23*, 1225–1241. (d) Motoi, M.; Nagahara, S.; Akiyama, H.; Horiuchi, M.; Kanoh, S. *Polym. J.* **1989**, *21*, 987–1001, and other references cited therein.
5. Kanoh, S.; Nishimura, T.; Senda, H.; Motoi, M.; Tanaka, T.; Kano, K. *Macromolecules* **1999**, *32*, 2438–2448.
6. Kanoh, S.; Nishimura, T.; Tsuchida, T.; Senda, H.; Motoi, M.;

Takani, M.; Matsuura, N. *Macromol. Chem. Phys.* **2001**, *202*, 2489–2503.
7. Kanoh, S.; Naka, M.; Yokozuka, T.; Itoh, S.; Nishimura, T.; Honda, M.; Motoi, M.; Matsuura, N. *Macromol. Chem. Phys.* **2002**, *203*, 511–521.
8. Dainton, F. S.; Ivin, K. *Q. Rev.* **1958**, *12*, 61–92.
9. Kanoh, S.; Hashiba, T.; Ando, K.; Motoi, M. *Synthesis* **1997**, 1077–1080.
10. Motoi, M.; Sekizawa, S.; Asakura, K.; Kanoh, S. *Polym. J.* **1993**, *25*, 1283–1294.
11. Corey, E. J.; Raju, N. *Tetrahedron Lett.* **1983**, *24*, 5571–5574.
12. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*. 3rd ed.; Wiley: New York, 1999; pp 437–440.
13. (a) Richardson, S. K.; Jeganathan, A.; Watt, D. S. *Tetrahedron Lett.* **1987**, *28*, 2335–2338. (b) Mori, H.; Hirao, A.; Nakahama, S. *Macromolecules* **1994**, *27*, 35–39. (c) Ishizone, T.; Okamoto, K.; Hirao, A.; Nakahama, S. *Macromolecules* **1999**, *32*, 1453–1462. (d) Ducray, P.; Lamotte, H.; Rousseau, B. *Synthesis* **1997**, 404–406.
14. Nishimura, T.; Kanoh, S.; Senda, H.; Tanaka, T.; Ando, K.; Motoi, M. *J. Chem. Soc., Chem. Commun.* **1998**, 43–44.
15. (a) Seeliger, W.; Aufderhaar, E.; Diepers, W.; Feinauer, R.; Nehring, R.; Their, W.; Hellmann, H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 875–888. (b) Ito, Y.; Inubushi, Y.; Zenbayashi, M.; Tomita, S.; Saegusa, T. *J. Am. Chem. Soc.* **1973**, *95*, 4447–4448, and references cited therein.
16. Kanoh, S.; Nishimura, T.; Kita, Y.; Motoi, M.; Takani, M.; Tanaka, T. *J. Org. Chem.* **2000**, *65*, 2253–2256.
17. (a) Feinauer, R. *Synthesis* **1971**, 16–26. (b) Lu, C.; Odian, G. *J. Polym. Sci., Part A: Polym. Chem.* **1994**, *32*, 2283–2290.
18. Porter, G. R.; Rydon, H. N.; Schofield, J. A. *J. Chem. Soc.* **1960**, 2686–2690.
19. (a) Cromwell, N. H.; Phillips, B. *Chem. Rev.* **1979**, *79*, 331–358. (b) Moore, J. A.; Ayers, R. S. In *Chemistry of Heterocyclic Compounds*. Hassner, A., Ed.; Wiley: New York, 1983; pp 1–127 Part 2. (c) Davies, D. E.; Starr, R. C. *Comprehensive Heterocyclic Chemistry*, Lwowski, W., Ed.; Pergamon: Oxford, 1984; Vol. 7, pp 237–284 Part 5.
20. Unpublished data.
21. Itoh, S.; Kanoh, S.; Motoi, M. *Polym. Preprints Jpn* **1998**, *47*, 302.
22. Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734–736.
23. Kanoh, S.; Nishimura, T.; Mitta, Y.; Ueyama, A.; Motoi, M.; Tanaka, T.; Kano, K. *Macromolecules* **2002**, *35*, 651–657.
24. Fotsch, C. H.; Chamberlin, A. R. *J. Org. Chem.* **1991**, *56*, 4141–4147.
25. (a) Miyamoto, M.; Saeki, Y.; Lee, C.-W.; Kimura, Y.; Maeda, H.; Tsutsui, K. *Macromolecules* **1997**, *30*, 6067–6073. (b) Miyamoto, M.; Saeki, Y.; Maeda, H.; Kimura, Y. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 435–444. (c) Miyamoto, M.; Tsutsui, K.; Kimura, Y. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 445–453.
26. (a) Choi, W.; Sanda, F.; Endo, T. *Macromolecules* **1998**, *31*, 9093–9095. (b) Nemoto, N.; Xu, X.; Sanda, F.; Endo, T. *Macromolecules* **2001**, *34*, 7642–7647.
27. Endo, T.; Uno, H. *J. Polym. Sci., Polym. Lett. Ed.* **1985**, *23*, 359–363.
28. Adachi, T.; Sugimoto, H.; Aida, T.; Inoue, S. *Macromolecules* **1993**, *26*, 1238–1243.
29. Kawakami, Y.; Takahashi, K.; Hibino, H. *Macromolecules* **1991**, *24*, 4531–4537.
30. Hayashi, Y.; Kayatani, T.; Sugimoto, H.; Suzuki, M.; Inomata, K.; Uehara, A.; Mizutani, Y.; Kitagawa, T.; Maeda, Y. *J. Am. Chem. Soc.* **1995**, *117*, 11220–11229.
31. Brooks, L. A.; Synder, H. R. *Organic Syntheses*; Horning, E. C., Allen, C. F. H., Shriner, R. L., Drake, N. L., Smith, L. I., Hamilton, C. S., Snyder, H. R., Eds.; Wiley: New York, 1955; Collect. Vol. 3, pp 698–700.
32. Sato, K.; Kameyama, A.; Nishikubo, T. *Macromolecules* **1992**, *25*, 1198–1199.
33. Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, *14*, 957–960.
34. Baum, K.; Berkowitz, P. T.; Grakauskas, V.; Archibald, T. G. *J. Org. Chem.* **1983**, *48*, 2953–2956.
35. Gajda, T.; Zwierzak, A. *Synthesis* **1981**, 1005–1008.
36. Schulenberg, J. W.; Archer, S. *J. Am. Chem. Soc.* **1960**, *82*, 2035–2038.
37. Mayfield, R. J.; Yates, P. *Org. Prep. Proced. Int.* **1971**, *3*, 201–204.
38. Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7777–7782.