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# Articles

## Three- to Six-Carbon Ring-Enlargement Reaction of Cyclic Ortho Esters Bearing a Diazocarbonyl Side Chain. Use of the Intramolecular Formation of Tricyclooxonium Ylides

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Two types of bicyclic ortho esters **14** and **18**, which are tethered to a diazocarbonyl group by polymethylene linkages -$(CH_2)_n$- of different lengths ($n$ = 1−3 for **14** and 1−4 for **18**), were prepared and catalytically decomposed by treatment with $Rh_2(OAc)_4$ either in the presence or absence of a protic nucleophile (MeOH, PhOH, AcOH) to give ring-enlargement product lactones **25** and **30** of different sizes. With **14**, the enlargement took place when $n$ = 1 or 2, but not when $n$ = 3. With **18**, in which the diazo carbon is substituted with a methoxycarbonyl group, the length of the chain can be extended further to $n$ = 4 to obtain ring-enlargement products or their derivatives. All of these reactions could be explained in terms of the intermediacy of tricyclooxonium ylides **22** and **28**. The ylides form an equilibrium with the corresponding ring-opened zwitterions **22′** and **28′**, respectively, which, after protonation by a protic nucleophile, undergo mainly ring-enlargement to form medium-sized or large oxalactones rather than 1,2-rearrangement.

### Introduction

Ethereal oxonium ylides are highly reactive and short-lived intermediates compared to other onium ylides. While they continue to elude spectroscopic identification,[1] their intervention has been proposed frequently and verified indirectly[2] in carbene reactions when singlet carbenes were generated in ethereal solvents or in the presence of ethereal substrates.[3,4] However, in comparison with carbonyl ylides[5] and hydroxonium ylides[6] which have been studied extensively, ethereal ylides have been used very little for synthetic purposes. This limitation may be due to the lability of the ylides which exist as extremely short-lived components in equilibrium with carbenes or carbenoids.[7] In an effort to develop the synthetic utility of ethereal oxonium ylides, we recently designed[8] an intramolecular reaction of carbenes with cyclic ethereal substituents to form ethereal bicyclooxonium ylides, i.e, as kinetically formed intermediates, which was followed by release of the strain of the constrained bicyclic intermediates to give open-ring

(1) (a) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263. (b) Tomioka, H,; Kobayashi, N,; Murata, S.; Ohtawa, T. *J. Am. Chem. Soc.* **1991**, *113*, 8771.

(2) (a) Naito, I.; Oku, A.; Otani, N.; Fujiwara, Y.; Tanimoto, Y. *J. Chem. Soc., Perkin Trans. 2* **1996**, 725. (b) Naito, I.; Oku, A.; Fujiwara, Y.; Tanimoto, Y. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1051.

(3) For examples of intermolecular oxonium ylide formation, see: (a) Nozaki, H.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, *7*, 2563. (b) Friedrich, K.; Jansen, U.; Kirmse, W. *Tetrahedron Lett.* **1985**, *26*, 193. (c) Kirmse, W.; Chiem. P. V. *Tetrahedron Lett.* **1985**, *26*, 197. (d) Pirrung, M. C.; Brown. W. L.; Rege, S.; Laughton, P. *J. Am. Chem. Soc.* **1991**, *113*, 8561. (e) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; van Leusen, D. *J. Org. Chem.* **1984**, *49*, 1917. (f) Iwamura, H.; Imahasi, Y. *Tetrahedron Lett.* **1975**, 1401. (g) Olah, G. A.; Doggweiler, H.; Felberg, J. D. *J. Org. Chem.* **1984**, *49*, 2116. (h) Baird, M. S.; Baxter, A. G. W.; Hoorter, A.; Jefferion, I. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2575. (j) Oku, A.; Ohwaki, S.; Kimura, K. *Acta Chem. Scand.* **1993**, *47*, 391.

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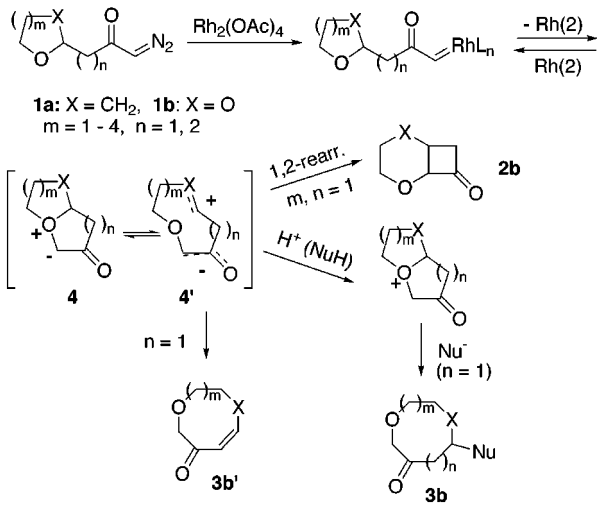
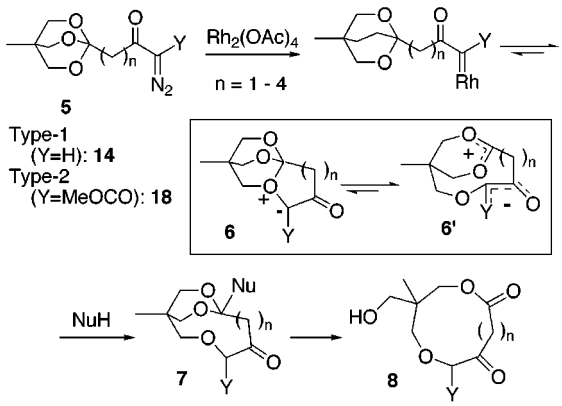
**Scheme 1**



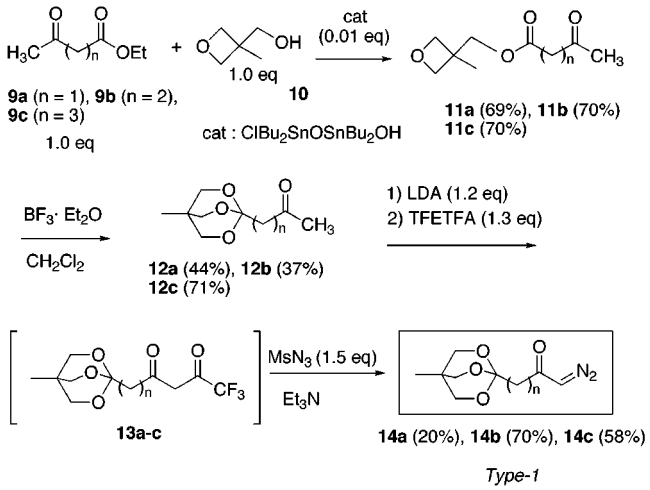

products, i.e., the thermodynamically favorable products. The consequence of this reaction was a three-carbon ring-enlargement reaction, which is of synthetic interest (Scheme 1). We adopted three conditions for this reaction: (1) use of medium-sized cyclic ethers as intramolecular nucleophiles toward carbenes; (2) diazoketone side chains whose transition-metal carbenoids can form entropically favorable, though short-lived, five-membered oxonium ylide intermediates,[9] and ylide formation must be followed by fast irreversible reactions such as protonation or an intramolecular proton shift; and (3) presence of ylide-stabilizing groups such as carbonyl groups.[10]

A limitation we encountered with diazocarbonyl-substituted cyclic ethers was the length of the diazocarbonyl side-chain: as the chain was elongated to more than $n = 1$ (Scheme 1), the expected enlargement did not take place and a ring-switching reaction took place instead.[8,11] We presumed that if a cation-stabilizing group was positioned adjacent to the bridgehead carbon of both bicyclic ylides and oxonium ions, cleavage of the central bond would be facilitated. In fact, cyclic acetals with a longer diazocarbonyl side chain ($n = 2$, X = O in Scheme 1) facilitated the expected ring-enlargement reaction.[12] However, those with a long side chain ($n > 2$) were not effective for extending the scope of this enlargement reaction. Therefore, we extended the search for an ylide-stabilizing system to bicyclic ortho esters **5** in hope of demonstrating the stabilizing effects of oxygen atoms on oxonium ylides **6** and zwitterions **6′** (Scheme 2). Indeed, we have found with these ortho ester systems that the stabilization of both charges of the ylides is more important than the release of strain and, consequently, the ring-enlargement is facilitated more than with cyclic acetal systems.[13] This report deals with three- to six-carbon ring-enlargement reactions of cyclic ortho esters to give 9- to 12-membered trioxa-5-oxobicyclo[4+*n*.2.2]-cyclanones **7** and their derivative oxalactones **8**.

**Scheme 2**




**Scheme 3**




## Results and Discussion

To investigate the scope of the present ring-enlargement of bicyclic ortho esters, two types of diazocarbonyl-substituted bicyclic ortho esters were prepared. Ortho esters **14** (Type 1) possess no ethoxycarbonyl group at the diazo-substituted carbon, whereas ortho esters **18** (Type 2) have such a group to stabilize the negative charge of ylides in its enolate form.

**Preparation of Diazocarbonyl-Substituted Bicyclic Ortho Esters of Type 1 (14)** (Scheme 3). The ester exchange reaction of ketoesters **9** ($n = 1-3$) with oxethanemethanol by the catalysis of distannoxane[14] gave

(4) For intramolecular oxonium ylide formation, see: (a) Pirrung, M. C.; Werner, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 6060. (b) Clark, J. S.; Dossetter, A. G.; Whittingham, W. G. *Tetrahedron Lett.* **1996**, *37*, 5603. (c) Clark, J. S.; Whitlock, G. A. *Tetrahedron Lett.* **1994**, *35*, 6381. (d) ref 23. (e) Brogan, J. B.; Bauer, C. B.; Rogers, R. D.; Zercher, C. K. *Tetrahedron Lett.* **1996**, *37*, 5053.

(5) Reviews: (a) Reference 1a. (b) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385.

(6) (a) Moody, C. J.; Taylor, R. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 721. (b) Davies, M. J.; Heslin, C. J.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2473. (c) Davies, M. J.; Moody, C. J.; Taylor, R. J. *Synlett* **1990**, 93.

(7) (a) See ref 1a. (b) T. Sueda, T. Nagaoka, S. Goto, M. Ocjiai *J. Am. Chem. Soc.* **1996**, *118*, 10141.

(8) Oku, A.; Ohki, S.; Yoshida, T.; Kimura, K. *J. Chem. Soc. Chem. Commun.* **1996**, 1077.

(9) For cyclic five-membered carbonyl ylides, see (a) Hamaguchi, M.; Ibata, T. *Tetrahedron Lett.* **1974**, 4475. (b) Ibata, T.; Toyoda, J. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1787.

(10) This is not always the requisite because free carbenes such as alkylidenecarbenes bearing a cyclic acetal ring also undergo a similar enlargement. See ref 13.

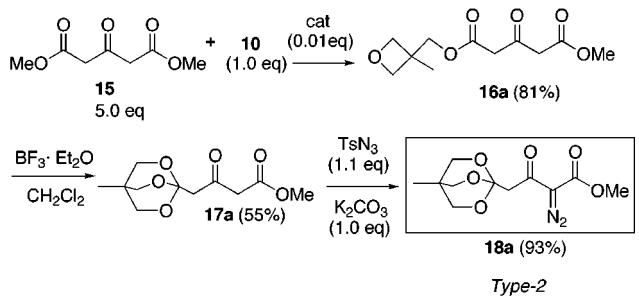
(11) Kamada, T.; Ge-Quing; Abe, M.; Oku, A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 413.

(12) Oku, A.; Murai, N.; Baird, J. *J. Org. Chem.* **1997**, *62*, 2123.

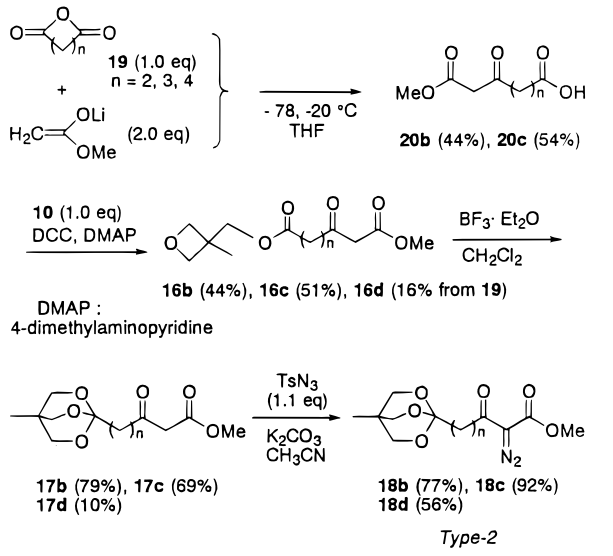
(13) (a) Mori, T.; Taniguchi, M.; Suzuki, F.; Doi, H.; Oku, A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3623. (b) Mori, T.; Oku, A. *J. Chem. Soc. Chem. Commun.* **1999**, 1339.

(14) (a) Otera, J.; Yano, T.; Okawara, R. *Organometallics* **1986**, *5*, 1167. (b) Yano, T.; Nakashima, K.; Otera, J. *Organometallics* **1985**, *4*, 1501.

**Scheme 4**




**Scheme 5**




esters **11** in 70% yield.[15] Treatment of **11** with $BF_3$-etherate produced ketones **12** bearing a bicyclic ortho ester (**a**, $n$ = 1, 44%; **b**, $n$ = 2, 37%; **c**, $n$ = 3, 71%).[16] Ketones **12** were transformed to the expected diazoketones **14** (**a**, 20%; **b**, 70%; **c**, 58%) by treatment of their lithium enolate with trifluoroethyl trifluoroacetate **13** and then with mesyl azide.[17]

**Preparation of Ortho Esters of Type 2**. **18a** ($n$ = 1, Scheme 4): The ester exchange reaction of diester **15** (5 equiv) with oxethanemethanol **10** (1 equiv) gave singly exchanged ester **16a** ($n$ = 1, 81%).[15] Treatment of **16a** with $BF_3$·$Et_2O$ gave ortho ester **17a** (55%), which was treated with tosyl azide[18] in the presence of $K_2CO_3$ to give diazoester **18a** ($n$ = 1, 93%).

**18b**−**d** ($n$ = 2−4) (Scheme 5): The methoxycarbonylmethylation of cyclic acid anhydrides **19** ($n$ = 2−4) with the Li-enolate of methyl acetate gave carboxylic acid **20**.[19] Esterification of **20** with **10** in the presence of DCC gave **16**,[20] which was converted to **17** by procedures analogous to those used for **17a**.[16] The diazotization of **17** finally gave **18**.[18] Overall yields from **20** were **18b** (12%), **18c** (18%), and **18d** (28%).

**Rh(II)-Catalyzed Reaction of Type 1 Bicyclic Diazo Ortho esters 14 in the Presence of MeOH. Choice of Protic Nucleophiles**. In general, the reaction of cyclic and acyclic ethereal oxonium ylides typically proceeds via a few different mechanisms, e.g., 1,2-rearrangement (Stevens rearrangement),[21] sigmatropic rearrangement,[4] or intra- and intermolecular proton shift.[22] Roskamp and Johnson[23] reported that the transition metal-catalyzed reaction of diazoacetonyldioxolane **1b** ($n$ = 1) yielded mainly the 1,2-rearrangement product **2b** with a minor amount of ring-enlargement product **3b** (Scheme 1). We thought that **3b** would be a major product if the 1,2-rearrangement could be suppressed by protonating the bicyclooxonium ylide **4** with a protic nucleophile (NuH). Indeed, we found that the reaction in the presence of acetic acid dramatically facilitated the ring-enlargement to produce **3b** and **3b′** in high yields (combined yield 87%).[12] The reasons for this facilitation are (1) faster protonation of ylide **4** than its 1,2-rearrangement, and (2) stabilization of ylide **4**, its protonated oxonium ion, and the corresponding monocyclic zwitterion **4′** by charge delocalization in the two-oxygen system. On the basis of these hypotheses, we expected that the ring-opening of tricyclic oxonium ylides, which can be generated from bicyclic ortho esters, should be facilitated (Scheme 2: Y = H, COOEt) more than the dioxolane system **4** derived from **1b**.

Suppressing the 1,2-rearrangement and facilitating the enlargement by adoption of a protic nucleophile which is less acidic than AcOH seems to be applicable to ortho ester systems because of the longevity of the ylides. Therefore, methanol was used in place of acetic acid. Indeed, the ring-enlargement of **14a** took place quantitatively in the presence of MeOH and afforded **24**. This indicates that ylide **22** and its zwitterion **22′**, which are formed from tricyclic ortho ester **14** (Scheme 6), are longer-lived and presumably more basic than the dioxolanyl ylide **4** (Scheme 1).[24]

**Reactions of 14a and 14b.** The Rh-catalyzed reaction of **14a** ($n$ = 1) in the presence of MeOH proceeded smoothly to give ring-enlargement product **24a** (93%, determined by $^1$H NMR). However, **24a** is very labile under chromatographic conditions and, upon isolation, it was transformed to nine-membered lactone **25a** (73% from **14a**) (Scheme 6, Table 1).

We expected that elongation of the diazocarbonyl sidechain by one more methylene unit will still enable a similar but four-carbon enlargement reaction because tricyclic ylide **22b** is still sufficiently strained to isomerize into zwitterion **22′b** with relief of strain. Indeed, the analogous reaction of **14b** ($n$ = 2) in the presence of MeOH produced ring-enlargement product **24b** (81%) and O−H insertion product **23b** (9%), and the former was

(15) (a) Otera, J.; Dan-Oh, N.; Nozaki, H. *Tetrahedron* **1993**, *49*, 3065. (b) Otera, J.; Dan-Oh, N.; N. Nozaki, H. *J. Org. Chem*. **1991**, *56*, 5037.

(16) Corey, E. J.; Raju, N. *Tetrahedron Lett*. **1983**, *24*, 5571.

(17) Rick, L. D.; Raymond, F. M.; Ronald, G. B.; Saung, Z. P. *J. Org. Chem*. **1990**, *55*, 1959.

(18) For diazotization with tosyl azide, see: (a) Regitz, M. *Organic Syntheses*; Wiley: New York, 1988; Coll. Vol. VI, p 389. (b) Koshinen, A. M. P.; Munoz, L. *J. Chem. Soc. Chem. Commun*. **1990**, 652. (c) Taber, D. F.; Ruckle, R. E. *J. Org. Chem*. **1986**, *51*, 4077. (d) Taber, D. F.; Gleave, D. M.; Herr, R. J.; Moody, K.; Hennesy, M. *J. Org. Chem*. **1995**, *60*, 2283.

(19) Montforts, F. P.; Ofner, S. *Angew. Chem., Int. Ed. Engl*. **1979**, *18*, 632.

(20) Parish, R. C.; Stock, L. M. *J. Org. Chem*. **1965**, *30*, 927.

(21) (a) Tester, R. W.; West, F. G. *Tetrahedron Lett*. **1998**, *39*, 4631. (b) West, F. G.; Naidu, B. N.; Tester, R. W. *J. Org. Chem*. **1994**, *59*, 6892. (c) West, F. G.; Eberlein, T. H.; Tester, R. W. *J. Org. Chem*. **1992**, *57*, 3479.

(22) (a) Reference 13. (b) Unpublished results: The deuterium scrambling reaction of dithiolane-substituted diazocarbonyl compounds indicated that both intra- and intermolecular proton-transfer reactions can take place with bicyclic sulfonium ylides.

(23) Roskamp, E. J.; Johnson, C. R. *J. Am. Chem. Soc*. **1986**, *108*, 6062.

(24) When AcOH was used in place of MeOH, the reaction resulted in the formation of a complex mixture.

**Scheme 6**

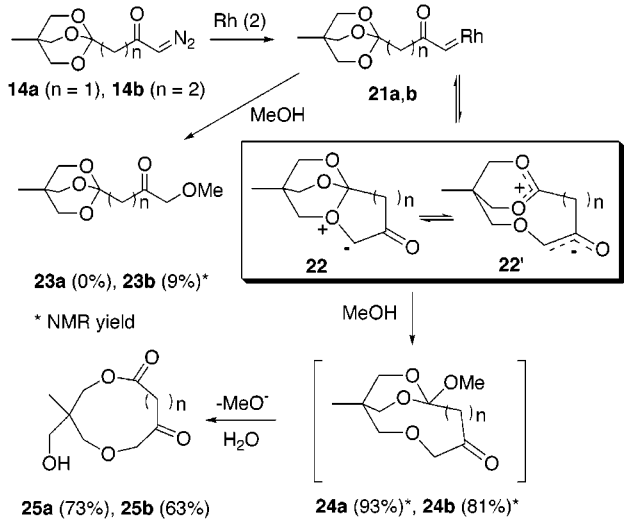
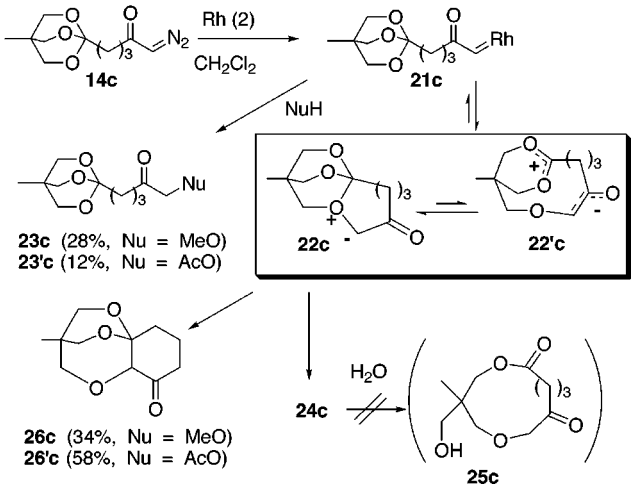



**Table 1. Ring-Enlargement Reaction of Diazoketone (Type 1)**

| diazo-ketone | *n* | NuH (equiv) | product yield, % | | | |
|---|---|---|---|---|---|---|
| **14a** | 1 | MeOH (1) | **24a** (93%)[a] | **25a** (73%) | _ | _ |
| **14b** | 2 | MeOH (1) | **24b** (61%)[a] | **25b** (63%) | **23b** (9)[a] | _ |
| **14c** | 3 | MeOH (1) | _ | _ | **23c** (28) | **26c** (34) |
| **14c** | 3 | AcOH (1) | _ | _ | **23c** (12) | **26c** (58) |
| **14c** | 3 | AcOH (1.5) | _ | _ | **23c** (24) | **26c** (51) |

[a] NMR yield.

**Scheme 7**

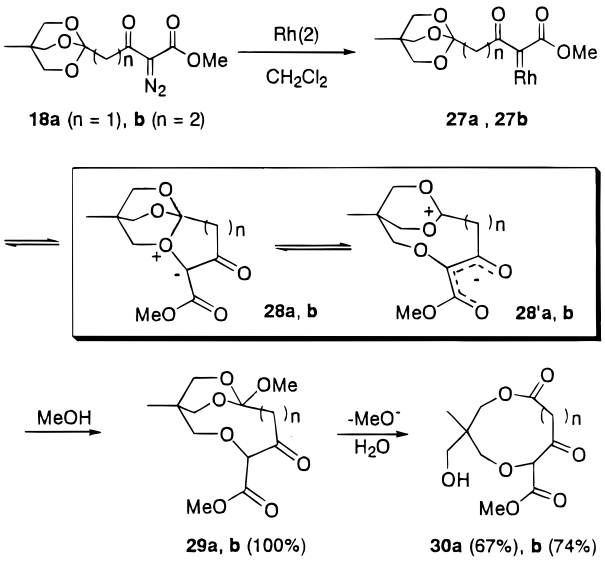



transformed to **25b** (63% from **14b**) after treatment with a silica gel column (Scheme 6).

From the difference in the ring-enlargement reactivity between **14a** and **14b**, it seems that the enlargement of **22b** is slower than that of more strained ylide **22a** and charge-stabilization by the oxygen atoms in zwitterion **22′** is not the sole factor to facilitate the ring-transformation.

**Reaction of 14c.** The reaction of **14c** ($n = 3$) was also examined in the presence of MeOH (Scheme 7). Isolated products were insertion product **23c** (28%) and 1,2-rearrangement product **26c** (34%), but the expected enlargement product **24c** or **25c** was not found. The use of AcOH in place of MeOH to suppress the 1,2-rearrangement was unsuccessful, and again **23′c** (24%) and **26′c** (51%) were formed.

**Scheme 8**




This result indicates that the favorable reaction of tricyclooxonium ylide **22c** (Type 1) may be ring-reassembly from a weakly strained and polarized tricyclic ylide **22c** to a less-strained and nonpolar 1,2-rearrangement product **26c**, rather than ring-opening to zwitterion **22′c** (Scheme 7). In addition, albeit ring-opening from slightly strained **22c** to less-strained **22′c** seems favorable, the change in the distance of the charge separation between the ylide and zwitterion structure may disfavor the formation of a zwitterion more in structure **22′c** than **22′b**. Thus, while maintaining equilibrium with carbenoid **21c**,[2a] ylide **22c** is converted to either **26c** or **23c**.

**Rh(II)-Catalyzed Reaction of Type 2 Bicyclic Ortho Esters 18 in the Presence of MeOH**. Since the dioxacarbenium ion structure did not always have as strong a stabilizing effect on the positive charge of zwitterion **22′c** as initially expected, we investigated other factors that might enhance the preference of zwitterion **22′c** over ylide **22c**. We expected that the enolate charge of **22′c** would be stabilized by a newly introduced carbonyl group to suppress 1,2-rearrangement by the delocalization of negative charge. In this regard, the Rh-catalyzed reaction of Type 2 diazocarbonyl compounds was investigated.

**Reactions of 18a and 18b** ($n = 1$ and 2). As expected by analogy to the reactions of **14a**,**b**, the reactions of **18a** and **18b** produced ring-enlargement products **29a** and **29b** in nearly quantitative yields, as determined by $^1$H NMR analysis. Similar to the reactions of **14**, primary bicyclic products **29** were transformed to a diastereomeric mixture of the corresponding oxalactones **30a** (67%) and **30b** (74%) under hydrolysis conditions on silica gel chromatography (Scheme 8). Although the results were similar to those with **14**, the efficacy of the enlargement of **18a** and **18b** was greater than that with **14**. This enhancement can be mainly attributed to stabilization of the enolate ion by the newly introduced methoxycarbonyl group which delocalizes the negative charge and, consequently, favors the ring-opened structure **28′c** in the equilibrium with **28c**.

An intriguing observation was made in the reaction of **18a** when AcOH was used as a protic nucleophile in place of MeOH. Ring-enlargement product **30a** was obtained in only 38% yield together with the recovery of **18a** (21%).

**Scheme 9**

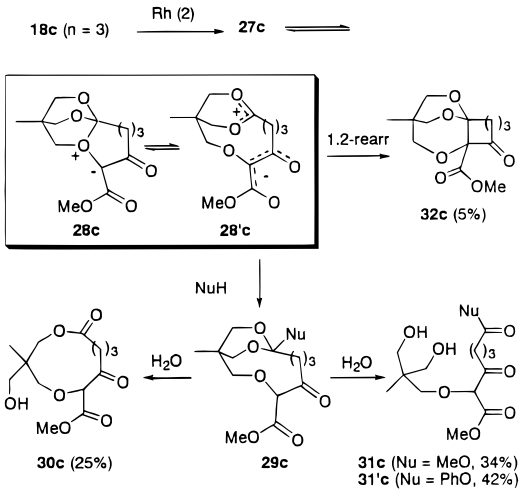



**Table 2. Ring-Enlargement Reaction of Diazoketone (Type 2)**

| diazo-ketone | *n* | NuH (equiv) | product yield, % | | | |
|---|---|---|---|---|---|---|
| **18a** | 1 | MeOH (1) | **29a** (100) | **30a** (67) | _ | _ |
| **18a** | 1 | PhOH (1.5) | _ | **30a** (54) | _ | _ |
| **18a** | 1 | AcOH (1) | _ | **30a** (38%)[a] | _ | _ |
| **18b** | 2 | MeOH (1) | **29b** (100) | **30b** (74) | _ | _ |
| **18c** | 3 | MeOH (1) | _ | **30c** (25) | **31c** (34) | **32c** (5) |
| **18c** | 3 | PhOH (1.5) | _ | _ | | **32c** (41) |
| **18d** | 4 | | _ | _ | **31d** (27) | **32d** (15) |

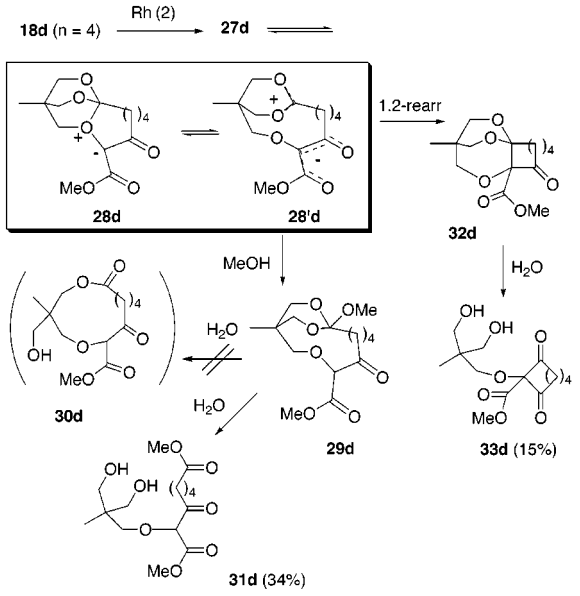
[a] **18a** was recovered in 21% yield.

In comparison with the high conversion of **14a** with MeOH, this unsatisfactory result with AcOH implies that AcOH, which is more acidic than MeOH, will protonate **18a** and retard its Rh-catalyzed decomposition. A similar phenomenon was also observed with cyclic acetal systems.[12]

**Reaction of 18c** ($n = 3$). The reaction of **18c**, which has a trimethylene tethering chain ($n = 3$) and is longer than **18b** by one methylene unit, was examined in the presence of MeOH. In contrast to the results with **14c**, the reaction realized the ring-enlargement with the formation of 11-membered oxalactone **30c** (25%) and acyclic dihydroxyketodiester **31c** (34%) in addition to a minor amount of 1,2-rearrangement product **32c** (5%) (Scheme 9). The combined yield (59%) of **30c** and **31c** indicates that the expected ring-enlargement indeed took place to give primary ring-enlargement product **29c** in more than 60% yield. This efficacy is primarily attributable to the charge separation and stabilization of the negative charge of zwitterion **28′c** by the methoxycarbonyl group. Synchronously, the positive charge, which is separated from the negative charge, is effectively delocalized in the dioxacarbenium ion moiety of **28′c** (Scheme 9). Acyclic product **31c** is presumably formed directly from the hydrolysis of primary product **29c**, since treatment of oxalactone **30c** with moistened silica gel did not give **31c**.

An analogous reaction of **18c** with PhOH as a protic nucleophile, which has a smaller p$K_a$ than MeOH, resulted in the increased formation of **32c** (41%) and decreased formation of **30c** (7%). The same trend was also observed in the reaction of **18a** with PhOH (see Table 2). There are at least two possible explanations for this trend: (1) protonation of **18c** by PhOH; and (2) the nucleophilicity of NuH is important for trapping **28′c** in equilibrium with **28c**. In structure **28′**, the negative charge is delocalized by the 1,3-diketone functionality while the separated positive charge remains unchanged at the same level of **22′**. Without nucleophiles, the reactions of both **18c** and **18d** resulted in the exclusive formation of **32c** and **32d**.

**Scheme 10**




**Reaction of 18d** ($n = 4$). The reaction of **18d**, which has a tetramethylene tethering chain ($n = 4$), was examined in the presence of MeOH (Scheme 10). Isolated products were acyclic products **31d** (27%) and **33d** (15%), but no cyclic primary or secondary enlargement products were obtained. Therefore, it seemed that further elongation of the side chain disfavors the enlargement reaction. However, the structural analysis of **31d** led us to conclude that it should be derived from the primary enlargement product **29d** via a route similar to that for the formation of **31c**.

Although enlargement products **29d** and **30d** were not isolated, **31d** was unequivocally derived from the 12-membered bicyclic intermediate **29d**, the primary enlargement product, which must be labile because of its unsymmetrical ortho ester structure. As depicted in Scheme 10, ylide **28d** prefers a tricyclic oxonium ylide structure, which is less strained and less polarized than the zwitterion structure **28′d**, and, therefore, it may undergo ring-contracting 1,2-rearrangement from **28d** to cycloheptanone **32d** faster than protonation by MeOH. Concurrently, the extensively charge-separated zwitterion **28′d**, albeit as a minor component of the equilibrium, undergoes nucleophilic attack by MeOH faster than the Type 1 series. Therefore, regarding the equilibrium between **28** and **28′**, the equilibrium is most likely shifted toward **28′** when $n = 1$ or 2 because **28′** is less strained in its bicyclic structure. On the other hand, when $n > 3$, the equilibrium is shifted toward **28**, which is less strained in its tricyclic framework.

## Conclusion

The aim of the present study, i.e., the design of a ring-enlargement reaction of tricyclic ortho esters to extend the synthetic scope of short-lived ethereal oxonium ylides, was realized by adopting two types of ortho ester-linked

diazo compounds, namely (diazomethyl)ketones (Type 1) and α-diazo-*β*-ketoesters (Type 2). The strategy for enabling the enlargement reaction is based mainly on the stabilization of intermediate oxonium ylides or their ring-opened zwitterions. With Type 1 ortho esters, the lengths of the tethering chain that enable the ring-enlargement are $n = 1, 2$, whereas with Type 2 these are $n = 1-4$. The transient formation of tricyclooxonium ylides, e.g. **22**, and their cleavage to the corresponding bicyclic zwitterions seem to be the dominant factors in facilitating the ring-enlargement reaction. The presence of three oxygen atoms of the ortho ester ring system is the primary factor in stabilizing the zwitterion to enable the enlargement of tricyclo[$(4+n)$].2.2.$0^{1,(3+n)}$]ylide intermediates to lactones. Second, delocalization of the negative charge of the zwitterion is required for the formation of larger lactones. Third, the use of sufficiently acidic protic nucleophiles NuH seems to be important. To summarize, similar enlargement reactions may be possible with other diazoalkyl-substituted cyclic ortho esters and, consequently, several medium-sized to large oxalactone derivatives **25** and **30** should be obtainable by the present method.[25]

## Experimental Section

**General Methods.** $^1$H NMR and $^{13}$C NMR spectra were recorded at 300 and 75.6 MHz, respectively, unless otherwise stated. $^1$H chemical shifts and $^{13}$C chemical shifts are expressed in $\delta$ unit (ppm). For isolation and purification of the reaction products, flash column chromatography using silica gel (Wakogel C-300) or alumina (Merck aluminum oxide 90 active basic) and solvent-recycling GPC HPLC were mainly adopted. Solvents were dried and distilled before use. Dirhodium tetraacetate was available from Aldrich Chemical Co. and dried in vacuo before use. Other transition metal catalysts such as Cu(acac) were unsuccessful in this type of reactions. 3-Chloro-1-(hydroxy)tetrabutyldistannoxane, the catalyst of the ester exchange reaction, was prepared by the method reported by Otera.[14] Oxetanylcarbinyl ketoesters **11a**−**c** were prepared from esters **9a**−**c** according to the reported method.[15] Characterization of products were carried out mostly on the bases of $^1$H NMR, $^{13}$C NMR, and sometimes IR and HRMS when necessary, and they are listed below.

**3-Methyloxetan-3-yl-carbinyl 3-oxobutanoate (11a):** $^1$H NMR 1.33 (s, 3H), 2.27 (s, 3H), 3.51 (s, 2H), 4.23 (s, 2H), 4.38 (d, $J = 6.0$ Hz, 2H), 4.50 (d, $J = 6.0$ Hz, 2H); $^{13}$C NMR 21.0, 30.1, 49.8, 69.4, 79.3, 167.0, 189.2, 209.3; IR (liquid film) 1740 (s, C=O), 1720 (m, C=O), 1150 (m, ether) cm$^{-1}$; yield 69%.

**3-Methyloxetan-3-yl-carbinyl 4-oxopentanoate (11b):** $^1$H NMR 1.32 (s, 3H), 2.19 (s, 3H), 2.63 (t, $J = 6.6$ Hz, 2H), 2.77 (t, $J = 6.6$ Hz, 2H), 4.16 (s, 2H), 4.36 (d, $J = 6.0$ Hz, 2H), 4.38 (d, $J = 6.0$ Hz, 2H); $^{13}$C NMR 21.0, 27.8, 29.7, 37.8, 39.1, 68.7, 79.5, 172.6, 206.2; yield 70%.

**3-Methyloxetan-3-yl-carbinyl 5-oxohexanoate (11c):** $^1$H NMR 1.30 (s, 3H), 1.83−1.93 (m, 2H), 2.11 (s, 3H), 2.36 (t, $J = 7.2$ Hz, 2H), 2.49 (t, $J = 7.2$ Hz, 2H), 4.13 (s, 2H), 4.35 (d, $J = 6.0$ Hz, 2H), 4.48 (d, $J = 6.0$ Hz, 2H); $^{13}$C NMR 18.8, 21.1, 29.8, 33.0, 39.0, 42.3, 68.6, 79.5, 173.1, 207.1; IR (liquid film) 1730 (s, C=O), 1710 (s, C=O) cm$^{-1}$; yield 70%.

**Preparation of Bicyclic Ortho Esters 12a**−**c.**[16] Ester **11** (21 mmol) was treated with $BF_3$·$Et_2O$ (73 $\mu$L, 15 mmol) in $CH_2Cl_2$ at −20 °C for 20 h. After quenching the reaction with $Et_3N$ (21 mmol) followed by dilution with $Et_2O$ and filtration through Celite, the filtrate was concentrated and subjected to flash chromatography (EtOAc/hexane) using silica gel which was pretreated with 1% $Et_3N$ in hexane.

**3-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)propan-2-one (12a):** $^1$H NMR 0.81 (s, 3H), 2.25 (s, 3H), 2.76 (s, 2H), 3.91 (s, 6H); $^{13}$C NMR 10.0, 14.4, 30.3, 50.9, 56.1, 72.7, 204.1; HRMS (CI) calcd for $C_9H_{15}O_4$ ($MH^+$) 187.0969, found 187.0964; IR (liquid film) 1740, 1720 (s, C=O) cm$^{-1}$; yield 44%.

**4-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)butan-2-one (12b):** $^1$H NMR 0.79 (s, 3H), 1.99 (t, $J = 7.8$ Hz, 2H), 2.13 (s, 3H), 2.57 (t, $J = 7.8$ Hz, 2H), 3.87 (s, 6H); $^{13}$C NMR 14.4, 29.7, 30.2, 30.7, 37.7, 72.5, 77.5, 207.7; HRMS (CI) calcd for $C_{10}H_{17}O_4$ ($MH^+$) 201.1125, found 201.1122; yield 37%.

**5-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)pentan-2-one (12c):** $^1$H NMR 0.78 (s, 3H), 1.61−1.77 (m, 4H), 2.10 (s, 3H), 2.44 (broad t, 2H), 3.86 (s, 6H); $^{13}$C NMR: 14.5, 17.7, 29.7, 30.2, 35.5, 35.6, 43.3, 72.5, 208.6; HRMS (CI) calcd for $C_{11}H_{19}O_4$ ($MH^+$) 215.1282, found 215.1275; IR (KBr) 1720, 1705 (s, C=O) cm$^{-1}$; Mp 67−69 °C; yield 71%.

**Preparation of Diazocarbonyl-Substituted Bicyclic Ortho Esters 14a**−**c (Type 1).**[17] To a cooled THF solution of lithium diisopropylamide (2.8 mmol) at −78 °C was added a THF solution of **12** (2.3 mmol) over 30 min under argon atmosphere. To the mixture was further added $CF_3CO_2CH_2CF_3$ (3.0 mmol) by a syringe followed by additional stirring for 10 min. After working-up the reaction mixture with AcOH (3 mmol), the concentrated oily residue, which consisted of trifluoroacetylated ortho ester **13**, was dissolved in a mixture of $CH_3CN$ (7 mL), $Et_3N$ (3 mmol), and $H_2O$ (2 mmol). To this mixture was added a $CH_3CN$ solution (7 mL) of methanesulfonyl azide (3.0 mmol), and the solution was stirred for 2.5 h. After workup followed by flash chromatographic separation over a $Et_3N$-treated silica gel, diazo esters **14** were obtained. However, **14** are too labile to be analyzed by mass spectrometry or combustion analysis.

**1-Diazo-3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-propan-2-one (14a):** $^1$H NMR 0.81 (s, 3H), 2.72 (s, 2H), 3.92 (s, 6H), 5.58 (broad, 1H); yield 20%.

**1-Diazo-4-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-butan-2-one (14b):** $^1$H NMR 0.79 (s, 3H), 1.99−2.04 (m, 2H), 2.45−2.50 (m, 2H), 3.88 (s, 6H), 5.22 (broad, 1H); $^{13}$C NMR 14.4, 16.9, 30.2, 31.5, 72.6, 108.5, 194.0, 233.2; IR (KBr) 2100 (m, =$N_2$), 1630 (s, C=O) cm$^{-1}$; yield 70%.

**1-Diazo-5-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-pentan-2-one (14c):** $^1$H NMR 0.78 (s, 3H), 1.66−1.79 (m, 4H), 2.34 (broad t, 2H), 3.86 (s, 6H), 5.23 (broad s, 1H); $^{13}$C NMR 14.3, 18.9, 19.0, 30.2, 35.6, 72.5, 108.7, 194.8, 238.7; IR (liquid film) 2100 (s, =$N_2$), 1640 (s, C=O) cm$^{-1}$; yield 58%.

**Preparation of Diazocarbonyl-Substituted Bicyclic Ortho Esters 18a (Type 2).** First, oxetanylcarbinyl ketoesters **16a** were prepared from diester **15** in 81% yield by the procedure similar to that used for **11**.[15] Preparation of bicyclic ortho ester **17a** was analogous to that described for Type 1 ortho esters **14**.[16] For the diazotization of **17a**, see the procedure described below for the preparation of **18b**−**d**.[18]

**Methyl 3-methyloxetan-3-ylcarbinyl 3-oxopentane-1,5-dioate (16a):** $^1$H NMR 1.33 (s, 3H), 3.62 (s, 2H), 3.67 (s, 2H), 3.74 (s, 3H), 4.24 (s, 2H), 4.39 (d, $J = 6.0$ Hz, 2H), 4.50 (d, $J = 6.0$ Hz, 2H); yield 81%.

**Methyl 4-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-oxobutanoate (17a):** $^1$H NMR 0.80 (s, 3H), 2.88 (s, 2H), 3.66 (s, 2H), 3.71 (s, 3H), 3.91 (s, 6H); $^{13}$C NMR 14.3, 30.3, 48.9, 50.2, 52.0, 72.7, 106.8, 167.8, 194.0; IR (KBr) 1750, 1720 (s, C=O), 1130 (ether) cm$^{-1}$; mp 69−77 °C. Anal. Calcd for $C_{11}H_{10}O_6$: C, 54.09; H, 6.60. Found: C, 54.19; H, 6.66; yield 55%.

**Methyl 2-diazo-4-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-oct-1-yl)-3-oxobutanoate (18a):** $^1$H NMR 0.78 (s, 3H), 3.34 (s, 2H), 3.82 (s, 3H), 3.90 (s, 6H); $^{13}$C NMR 14.4, 30.3, 45.0, 52.1, 72.7, 107.4, 161.4, 186.0, 230.1; IR (liquid film) 2140 (s, =$N_2$), 1720, 1650 (s, C=O) cm$^{-1}$; yield 93%.

**Preparation of Methoxycarbonyl-Substituted Keto Carboxylic Acids 20b**−**d.** Keto carboxylic acids **20b**−**d** were prepared by the reaction of lithium enolate of methyl acetate and cyclic anhydride of succinic, glutaric, and adipic acid by the analogous procedures reported.[19]

(25) Other methods for preparing medium ring lactones by C−O bond formation: (a) Clark, J. S.; Holmes, A. B. *Tetrahedron Lett.* **1988**, *34*, 4333. (b) Asaoka, M.; Naito, S.; Takei, H. *Tetrahedron Lett.* **1985**, *26*, 2103. (c) Asaki, M.; Inoue, M.; Tachibana, K. *J. Org. Chem.* **1994**, *59*, 715. (d) Boger, D. L.; Sakya, S. M.; Yohannes, D. *J. Org. Chem.* **1991**, *56*, 4204.

**5-Methoxycarbonyl-4-oxopentanoic acid (20b):** $^1$H NMR 2.38 (t, $J$ = 6.6 Hz, 2H), 2.80 (t, $J$ = 6.6 Hz, 2H), 3.64 (s, 2H), 3.70 (s, 3H); $^{13}$C NMR 27.6, 30.8, 43.1, 52.3, 169.6, 177.6; IR (liquid film) 1730 (broad, s, C=O), 1590 (s) cm$^{-1}$; yield 44%.

**6-Methoxycarbonyl-5-oxohexanoic acid (20c):** $^1$H NMR 1.92 (quint, $J$ = 6.9 Hz, 2H), 2,13 (m, 1H), 2.41 (t, $J$ = 6.9 Hz, 1H), 2.54 (t, $J$ = 6.9 Hz, 1H), 2.65 (t, $J$ = 6.9 Hz, 2H), 2.88 (d, $J$ = 16 Hz, 1H), 2.93 (d, $J$ = 16 Hz, 1H), 3.69 (s, 3H), 10 (broad, 1H); IR (liquid film) 1750, 1720 (s, C=O) cm$^{-1}$; yield 54%.

**7-Methoxycarbonyl-6-oxoheptanoic acid (20d).** Acid **20d** was not isolated but directly used for the preparation of **16d**.

**Preparation of Methyl Oxetanylcarbinyl Ketodiesters 16b−d.** To a mixture of *N*,*N*-dimethylaminopyridine (31 mmol), **20** (39 mmol), and oxetanylmethanol **10** (77 mmol) in $CH_2Cl_2$ (40 mL) was added a $CH_2Cl_2$ solution (20 mL) of DCC (43 mmol) over 15 min under argon atmosphere at 0 °C. The mixture was stirred at ambient temperature till the consumption of **20**. After workup, the product mixture was subjected to flash silica gel chromatography to isolate product **16**.

**3-Methyloxetan-3-ylcarbinyl 5-methoxycarbonyl-4-oxopentanoate (16b):** $^1$H NMR 1.33 (s, 3H), 2.66 (t, $J$ = 6.3 Hz, 2H), 2.89 (t, $J$ = 6.3 Hz, 2H), 3.51 (s, 2H), 3.74 (s, 3H), 4.16 (s, 2H), 4.38 (d, $J$ = 6.0 Hz, 2H), 4.50 (d, $J$ = 6.0 Hz, 2H); $^{13}$C NMR 16.9, 21.0, 27.8, 29.6, 37.8, 39.1, 68.7, 79.4, 161.0, 172.6, 206.2; IR (liquid film) 1740, 1720 (s, C=O), 1160 (m, ether) cm$^{-1}$; yield 44%.

**3-Methyloxetan-3-ylcarbinyl 5-methoxycarbonyl-5-oxohexanoate (16c):** $^1$H NMR 1.30 (s, 3H), 1.90 (m, 2H), 2.39 (t, $J$ = 6.9 Hz, 2H), 2.63 (t, $J$ = 6.7 Hz, 2H), 3.43 (s, 2H), 3.71 (s, 3H), 4.14 (s, 2H), 4.36 (d, $J$ = 6.0 Hz, 2H), 4.48 (d, $J$ = 6.0 Hz, 2H); $^{13}$C NMR 18.5, 21.1, 32.8, 38.8, 41.6, 48.9, 68.6, 79.5, 161.2, 172.9, 201.6; IR (liquid film) 1740, 1720 (s, m, C=O) cm$^{-1}$; yield 51%.

**3-Methyloxetan-3-ylcarbinyl 5-methoxycarbonyl-6-oxoheptanoate (16d):** $^1$H NMR 1.32 (s, 3H), 1.57−1.70 (m, 4H), 2.25−2.40 (m, 4H), 3.44 (s, 2H), 3.73 (s, 3H), 4.15 (s, 2H), 4.38 (d, $J$ = 6.0 Hz, 2H), 4.50 (d, $J$ = 6.0 Hz, 2H); yield 16% from **19**.

**Preparation of Bicyclic Ortho Esters 17b−d.** The experimental procedures for these preparations were the same to that adopted for **12**.[16]

**Methyl 5-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-oxopentanoate (17b):** $^1$H NMR 0.78 (s, 3H), 1.99 (t, $J$ = 7.5 Hz, 2H), 2.66 (t, $J$ = 7.5 Hz, 2H), 3.46 (s, 2H), 3.72 (s, 3H), 3.86 (s, 6H); $^{13}$C NMR 10.0, 14.4, 30.7, 37.2, 49.0, 52.2, 72.5, 108.4, 161.9, 214.8; yield 79%.

**Methyl 6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-oxohexanoate (17c):** $^1$H NMR 0.77 (s, 3H), 1.63−1.79 (m, 4H), 2.56 (broad t, $J$ = 6.7 Hz, 2H), 3.42 (s, 2H), 3.71 (s, 3H), 3.85 (s, 6H); $^{13}$C NMR 14.2, 17.3, 30.1, 35.3, 42.5, 48.9, 52.1, 72.4, 109.0, 167.6, 202.2; IR (KBr) 1740, 1710 (s, C=O) cm$^{-1;}$ HRMS (CI) calcd for $C_{13}H_{21}O_6$ ($MH^+$) 273.1336, found 273.1330; mp 91−97 °C; yield 69%.

**Methyl 7-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-oxoheptanoate (17d):** $^1$H NMR 0.79 (s, 3H), 1.55−1.72 (m, 6H), 2.52 (t, 2H), 3.43 (s, 2H, 3.72 (s, 3H), 3.87 (s, 6H); yield 10%.

**Preparation of Diazocarbonyl-Substituted Bicyclic Ortho Esters 18b−d (Type 2).** To a mixture of **17** (0.82 mmol) and dried $K_2CO_3$ (0.82 mmol) in $CH_3CN$ (1 mL) was added a $CH_3CN$ solution (1.3 mL) of tosyl azide (0.9 mmol) under argon atmosphere at ambient temperature. After stirring for 2 h, $Et_2O$ was added, the mixture was filtered through Celite to remove $K_2CO_3$, and again a mixture of $Et_2O$/hexane (1/2) was added to precipitate tosyl amide which was removed through Celite. The residue was purified through flash chromatography over a $Et_3N$-treated silica gel column to give **18**.

**Methyl 2-diazo-5-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-oct-1-yl)-3-oxopentanoate (18b):** $^1$H NMR 0.78 (s, 3H), 2.04 (t, $J$ = 7.5 Hz, 2H), 3.01 (t, $J$ = 7.5 Hz, 2H), 3.83 (s, 3H). 3.88 (s, 6H); $^{13}$C NMR 10.0, 14.5, 30.7, 34.7, 52.1, 56.1, 72.6, 200.2, 214.8; IR (KBr) 2125(s, =$N_2$), 1730, 1725(s, C=O) cm$^{-1}$; yield 77%.

**Methyl 2-diazo-6-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-oct-1-yl)-3-oxohexanoate (18c):** $^1$H NMR 0.78 (s, 3H), 1.67−1.83 (m, 4H), 2.84−2.89 (t, $J$ = 6.9 Hz, 2H), 3.82 (s, 3H), 3.87 (s, 6H); $^{13}$C NMR 14.4, 18.1, 30.2, 35.6, 39.6, 52.0, 72.5, 108.8, 192.3, 219.8; IR (KBr) 2120 (s, =$N_2$), 1710 (s), 1650 (s, C=O) cm$^{-1}$; yield 92%.

**Methyl 2-diazo-7-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-oct-1-yl)-3-oxoheptanoate (18d):** $^1$H NMR 0.78 (s, 3H), 1.45−1.53 (m, 2H), 1.57−1.71 (m, 4H), 2.82 (t, $J$ = 7.2 Hz, 2H), 3.81 (s, 3H), 3.87 (s, 6H); yield 56%.

**General Procedure for $Rh_2(OAc)_4$-Catalyzed Reactions of Diazoketones 14a−c (Type 1) and Diazocarbonyl Esters 18a−d (Type 2).** To a $CH_2Cl_2$ solution (12 mL) of $Rh_2(OAc)_4$ (1.0 mol % equiv) were added a protic nucleophile NuH (1.2 equiv) and diazoketone **14** or **18** (ca. 100 mg) dissolved in $CH_2Cl_2$ (5 mL) over 10−15 min under an argon atmosphere at ambient temperature. The reaction mixture was stirred for 30 min, in general, until the diazoketone was not detectable on a TLC plate. After workup with 8 mL of saturated aqueous $NaHCO_3$, the solvent was removed and the residue was chromatographed, in general, by a flash column on silica gel, or on basic alumina and gel-permeation polymer beads in the cases when products were labile on silica gel. Some products were isolated by distillation under vacuum. Determinations of unisolable bicyclic products **24a**, **29a**, and **29b** were carried out by the NMR analysis: after completion of the analogous reaction to that described above but in $CDCl_3$ or $C_6D_6$ solution, *p*-xylene was added to the solution as the internal proton standard, and an aliquot of the solution was transferred to a NMR sample tube flushed by argon.

Spectroscopic data of Rh-catalyzed reaction products are shown in the following paragraphs.

**1-Methoxy-4-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)butan-2-one (23b):** $^1$H NMR −0.23 (s, 3H), 1.95 (dt, 2H), 2.37 (broad t, $J$ = 7.2 Hz, 1H), 2.69 (broad t, $J$ = 7.2 Hz, 1H), 2.91 (s, 3H), 3.21 (broad m, 4H), 3.55 (d, 2H), 3.88 (broad s, 2H); yield 9% (NMR).

**1-Methoxy-5-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)pentan-2-one (23c):** $^1$H NMR 0.78 (s, 3H), 1.64−1.80 (m, 4H), 2.45 (t, $J$ = 7.5 Hz, 2H), 3.39 (s, 3H), 3.86 (s, 6H), 3.99 (s, 2H); HRMS (EI) calcd for $C_{12}H_{21}O_5$ ($M^+$) 245.1388, found 245.1388; yield 28%.

**1-Acetoxy-5-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)pentan-2-one (23′c):** $^1$H NMR 0.79 (s, 3H), 1.65−1.80 (m, 4H), 2.15 (s, 3H), 2.46 (t, $J$ = 7.5 Hz, 2H), 3.87 (s, 6H), 4.64 (s, 2H); HRMS (EI) calcd for $C_{13}H_{21}O_6$ ($M^+$) 273.1337, found 273.1339; yield 12%.

**1-Methoxy-7-methyl-5,9,10-trioxabicyclo[5.2.2]undecan-3-one (24a)** (not isolated)**:** $^1$H NMR −0.07 (s, 3H), 3.13 (s, 3H), 3.18−3.45 (m, 8H), 3.90 (broad s, 2H); yield 93% (NMR).

**1-Methoxy-8-methyl-6,10,11-trioxabicyclo[6.2.2]-dodecan-4-one (24b):** $^1$H NMR 0.53 (s, 3H), 2.06 (t, $J$ = 6.0 Hz, 2H), 3.27 (s, 3H), 3.65−3.93 (broad m, 8H), 4.03 (broad m, 2H); $^{13}$C NMR 9.9, 14.6, 16.8, 31.9, 34.0, 50.6, 68.1, 68.2, 80.5, 83.6, 161.9; IR (KBr) 1720 (m), 1700 (s, C=O), 1160 (m, ether) cm$^{-1}$; HRMS (EI) calcd for $C_{11}H_{19}O_5$ ($M^+$) 231.1231, found 231.1234; Mp 112−127 °C; Yield 81% (NMR).

**7-Hydroxymethyl-7-methyl-5,9-dioxa-3-oxooctanolide (25a):** $^1$H NMR 0.88 (s, 3H), 3.37 (d, $J$ = 15.6 Hz, 1H), 3.43 (d, $J$ = 9.6 Hz, 1H), 3.46 (d, $J$ = 15.9 Hz, 1H), 3.63 (broad d, $J$ = 10.5 Hz, 1H), 3.72 (broad d, $J$ = 10.5 Hz, 1H), 3.84 (dd, $J$ = 9.6, 1.5 Hz, 1H), 3.93 (d, $J$ = 16.5 Hz, 1H), 4.18 (d, $J$ = 16.5 Hz, 1H), 4.28 (dd, $J$ = 11.4, 1.5 Hz, 1H), 4.43 (d, $J$ = 11.4 Hz, 1H); $^{13}$C NMR 18.1, 41.3, 48.4, 66.2, 68.9, 78.2, 161.2, 169.1, 203.1; IR (liquid film) 3500 (m, OH), 1740 (s), 1710 (s, C=O) cm$^{-1}$; HRMS (CI) calcd for $C_9H_{14}O_5$ ($MH^+$) 203.0918, found 203.0918; Yield 73%.

**8-Hydroxymethyl-8-methyl-6,10-dioxa-4-oxononanolide (25b):** $^1$H NMR 0.84 (s, 3H), 1.60 (broad, 1H, mobile), 2.44−2.64 (m, 3H), 3.16 (2 x t, $J$ = 4.8, 10.5, 11.5 Hz, 1H), 3.38 (d, $J$ = 9.6 Hz, 1H), 3.68 (d, $J$ = 15.9 Hz, 1H), 3.72 (dd, $J$ = 9.6, 2.1 Hz, 1H), 4.02 (d, $J$ = 15.9 Hz, 1H), 4.03 (dd, $J$ = 11.4, 2.1 Hz, 1H), 4.51 (d, $J$ = 11.4 Hz, 1H); $^{13}$C NMR 17.0, 32.5, 36.5, 40.6, 65.9, 68.2, 77.0, $\delta$'s lower than 150 ppm are

not clear; IR (KBr) 3470 (m, OH), 1730, 1715 (s, C=O) $cm^{-1}$; HRMS (EI) calcd for $C_{10}H_{16}O_5$ ($M^+$) 216.0997, found 216.0999; yield 63%.

**9-Methyl-7,11,12-trioxatricyclo[7.2.2.0$^{1,6}$]tridecan-5-one (26c):** $^1$H NMR 0.80 (s, 3H), 1.75−1.99 (m, 4H), 2.22−2.46 (m, 2H), 3.57 (dd, $J$ = 9.0, 1.2 Hz, 1H), 3.67 (dd, $J$ = 9.0, 0.9 Hz, 1H), 3.84 (dd, $J$ = 11.7, 1.2 Hz, 1H), 3.96−4.00 (m, 2H), 4.04 (dd, $J$ = 11.7, 0.9 Hz, 1H), 4.37 (s, 1H); $^{13}$C NMR 17.9, 18.1, 37.1, 39.4, 71.0, 71.1, 75.4, 77.5, 88.7, 101.1, 204.7; IR (KBr) 1720 (s, C=O) $cm^{-1}$; HRMS (EI) calcd for $C_{11}H_{16}O_4$ ($M^+$) 212.1048, found 212.1041; mp 122−125 °C; yield 5%.

**1-Methoxy-4-methoxycarbonyl-7-methyl-5,9,10-trioxabicyclo[5.2.2]undecan-3-one (29a):** $^1$H NMR 0.71 (s, 3 H), 2.87 (d, $J$ = 14.1 Hz, 1 H), 3.33 (s, 1 H), 3.40 (d, $J$ = 14.1 Hz, 1 H), 3.65 (dd, $J$ = 10.8, 2.4 Hz, 1 H), 3.68 (dd, $J$ = 12.9, 1.50 Hz, 1 H), 3.77 (s, 3 H), 3.81 (dd, $J$ = 10.8, 1.5 Hz, 1 H), 3.98 (dd, $J$ = 11.1, 2.4 Hz, 1 H), 4.12 (dd, $J$ = 12.9, 2.4 Hz, 1 H), 4.22 (dd, $J$ = 11.1, 2.4 Hz, 1 H), 4.98 and 10.8 (s and s, enolic H, 1H); $^{13}$C NMR 17.9, 33.9, 49.8, 50.1, 52.3, 68.3, 70.4, 82.9, 85.0, 109.4, 169.0, 200.3; IR (liquid film) 1760, 1720 (s, C=O), 1000−1380 (broad, m, ether) $cm^{-1}$; yield 100%.

**1-Methoxy-5-methoxycarbonyl-8-methyl-6,10,11-trioxabicyclo[6.2.2]dodecan-4-one (29b)** (not isolated): $^1$H NMR 0.56 (s, 3H), 1.96 (broad s, 2H), 3.28 (s, 3H), 3.78−3.92 (m, 8H), 3.85 (s, 3H), 11.0 (s, 1H); yield 100% (NMR).

**7-Hydroxymethyl-7-methyl-4-methoxycarbonyl-5-oxa-3-oxooctanolide (30a):** $^1$H NMR (major diastereomer) 0.83 (s, 3 H), 3.33 (s, 1 H), 3.41 (d, $J$ = 9.9 Hz, 1 H), 3.42 (d, $J$ = 15.9 Hz, 1H), 3.53 (d, $J$ = 15.9 Hz, 1H), 3.81 (s, 3 H), 3.86 (s, 2 H), 4.08 (dd, $J$ = 9.9, 2.1 Hz, 1 H), 4.14 (dd, $J$ = 11.7, 2.1 Hz, 1 H), 4.47 and 10.96 (s and s, enolic H, 1H), (s, 1 H), 4.56 (d, $J$ = 11.7 Hz, 1 H); IR (liquid film) 3650−3200 (m, OH), 1740, 1720 (s, C=O) $cm^{-1}$; HRMS (EI) calcd for $C_{11}H_{10}O_7$ ($M^+$) 260.0895, found 260.0893; yield 67%.

**8-Hydroxymethyl-8-methyl-5-methoxycarbonyl-6-oxa-4-oxononanolide (30b):** (major diastereomer) $^1$H NMR 0.82 (s, 3H), 1.61 (broad, 1H), 2.49−2.66 (m, 3H), 3.17−3.26 (m, 1H), 3.40 (d, $J$ = 9.3 Hz, 1H), 3.58 (d, $J$ = 11.1 Hz, 1H), 3.72 (dd, $J$ = 11.4, 2.4 Hz, 1H), 3.79 (s, 3H), 3.84 (dd, $J$ = 9.3, 2.4 Hz, 1H), 4.00 (d, $J$ = 11.1 Hz, 1H), 4.19 (s, 1H), 4.73 (d, $J$ = 11.7 Hz, 1H); HRMS (EI) calcd for $C_{12}H_{18}O_7$ ($M^+$) 274.1051, found 274.1055; yield 74%.

**9-Hydroxymethyl-9-methyl-6-methoxycarbonyl-7-oxa-5-oxodecanolide (30c):** (major diastereomer) $^1$H NMR 0.84 and 1.20 (s and s, 3H, 2:1 ratio), 1.92−2.12 (m, two isomers, central $CH_2$, 2H), 2.32−2.77 (m, two isomers, two $COCH_2$, 4H), 3.40−3.72 and 3.88−4.60 (two groups of m, two isomers, $OCH_2$, 6H), 3.77 and 3.80 (s and s, two isomers, 1:2 ratio, $OCH_3$, 3H), 3.97 and 4.15 (pair of d, $J$ = 11.1 Hz, 1H), 4.23 and 4.29 (s and s, two isomers, 2:1 ratio, CH, 1H); HRMS (EI) calcd for $C_{13}H_{20}O_7$ ($M^+$) 288.1208, found 288.1202; yield 25%.

**Dimethyl 2-[2,2-Bis(hydroxymethyl)propyloxy]-3-oxoheptan-1,7-dioate (31c):** $^1$H NMR 0.83 (s, 3H), 1.92 (quintet, $J$ = 7.2 Hz, 2H), 2.38 (t, $J$ = 7.2 Hz, 2H), 2.74 (broad m, 2H), 2.71 (dt, $J$ = 7.2, 4.2 Hz, 2H), 3.46 (s, 3H), 3.57 (d, $J$ = 11 Hz, 2H), 3.53 (d, $J$ = 11 Hz, 2H), 3.80 (s, 3H), 4.17 (s, 2H), 4.30 (s, 1H); IR (liquid film) 3500 (broad, s, OH), 1760−1700 (broad, s, C=O) $cm^{-1}$; yield 34%.

**Dimethyl 2-[2,2-Bis(hydroxymethyl)propyloxy]-3-oxooctan-1,8-dioate (31d):** $^1$H NMR 0.82 (s, 3H), 1.59−1.68 (m, 4H), 2.36 (t, $J$ = 7.2 Hz, 2H), 2.64 (m, 2H), 2.83 (broad s, 2H), 3.46 (s, 3H), 3.51 (d, $J$ = 11.0 Hz, 2H), 3.57 (d, $J$ = 11.0 Hz, 2H), 3.80 (s, 3H), 4.17 (s, 2H), 4.29 (s, 1H); yield 35%.

**6-Methoxycarbonyl-9-methyl-7,11,12-trioxatricyclo-[7.2.2.0$^{1,6}$]tridecan-5-one (32c):** $^1$H NMR 0.80 (s, 3H), 1.73−1.83 (m, 2H), 1.89 (dm, $J$ = 14.4 Hz, 1H), 2.45 (dm, $J$ = 14.4 Hz, 1H), 2.63 (m, 1H), 2.90 (m, 1H), 3.56 (dd, $J$ = 9.3, 1.2 Hz, 1H), 3.60 (dd, $J$ = 9.3, 3.0 Hz, 1H), 3.68 (dd, $J$ = 9.0, 1.5 Hz, 1H), 3.79 (s, 3H), 3.91 (dd, $J$ = 12, 1.5 Hz, 1H), 4.27 (dd, $J$ = 9.0, 3.0 Hz, 1H), 4.37 (dd, $J$ = 12, 1.2 Hz, 1H); $^{13}$C NMR 17.4, 17.9, 35.5, 36.3, 37.7, 52.6, 70.8, 71.0, 75.6, 94.6, 101.8, 167.6, 200.7; HRMS (EI) calcd for $C_{13}H_{18}O_6$ ($M^+$) 270.1102, found 270.1097; yield 5%.

**2-[2,2-Bis(hydroxymethyl)propyloxy]-2-(methoxycarbonyl)cycloheptan-1,3-dione (33d):** $^1$H NMR 0.83 (s, 3H), 2.30−2.46 (m, 4H), 2.58 (t, $J$ = 6.2 Hz, 2H), 2.74 (broad, 2H), 2.97−3.02 (m, 2H), 3.53−3.59 (broad m, 4H), 3.76 (s, 3H), 4.13 (d, $J$ = 11.4 Hz, 1H), 4.20 (d, $J$ = 11.4 Hz, 1H); yield 15%.

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**Supporting Information Available:** Copies of $^{13}$C NMR spectra for 22 compounds: **11a**−**c**, **12a**,**b**, **14b**,**c**, **16b**,**c**, **17a**−**c**, **18a**−**c**, **24b**, **25a**,**b**, **26c**, **29a**, and **32c** described in Experimental Section. This material is available free of charge via the Internet at http://pubs.acs.org.

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