# 8-Endo Cyclization of (Alkoxycarbonyl)methyl Radicals: Radical Ways for Preparation of Eight-Membered-Ring Lactones

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**Abstract:** Cyclization of (alkoxycarbonyl)methyl radicals generated from bromoacetates proceeds in the 8-endo mode to generate heptanolactones. Three distinct types of 8-endo/5-exo tandem radical cyclizations produce different bicyclic heptanolactones. In certain cases, intramolecular free-radical attack on the heptanolactone carbonyl group initiates further skeletal rearrangement. Ab initio calculations indicate that the preference of the 8-endo cyclization over the 5-exo mode originates from the conformational bias of (alkoxycarbonyl)-methyl radicals favoring the *Z*- over the *E*-conformation.

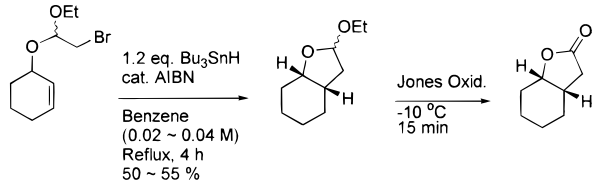
## Introduction

Radical cyclization reactions developed in the past decade are now firmly established as indispensable tools in synthetic chemistry. In forming carbo- and heterocyclic compounds, these reactions exhibit useful regio- and stereoselectivity employing a variety of functional groups as radical acceptors, and efficient synthetic schemes for a plethora of complex natural products have been formulated based on key radical cyclization reactions.[1]

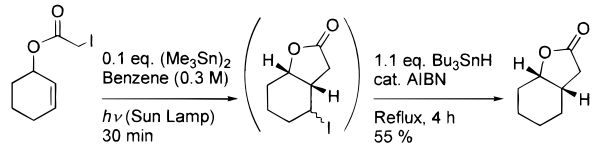
Lactones were among the primary targets in the early stage of development. Initial attempts to cyclize (alkoxycarbonyl)-alkyl radical species from α-haloalkanoate esters under standard radical-generating conditions with tributylstannane and AIBN led only to simple reduction products, and the results were attributed to the unfavorable conformational bias of these carbonyl conjugated radicals. Stork[2] and Ueno[3] solved this problem by developing tin hydride-mediated cyclization of α-haloacetals as an indirect route to γ- and δ-lactones (Scheme 1). Another practical solution to this problem was devised by Curran[4] based on the halogen atom-transfer reactions (Scheme 2). More recently, however, direct syntheses of γ- and δ-lactones via 5-exo or 6-exo radical cyclizations using α-haloalkanoates as substrates were reported[5] (Scheme 3).

In our continuing efforts to synthesize hydroazulenic sesquiterpenes, we had occasion to examine the tributylstannane-mediated radical cyclization reaction of the bromoacetate **1**. In light of the findings cited above, we hoped to obtain a tricyclic γ-lactone via 5-exo/7-endo tandem radical cyclizations, which would be used as a pivotal intermediate en route to guaianolide natural products.[6] The reaction proceeded smoothly under the standard high-dilution radical-generating conditions, and a product was obtained in 80% isolated yield. Upon careful

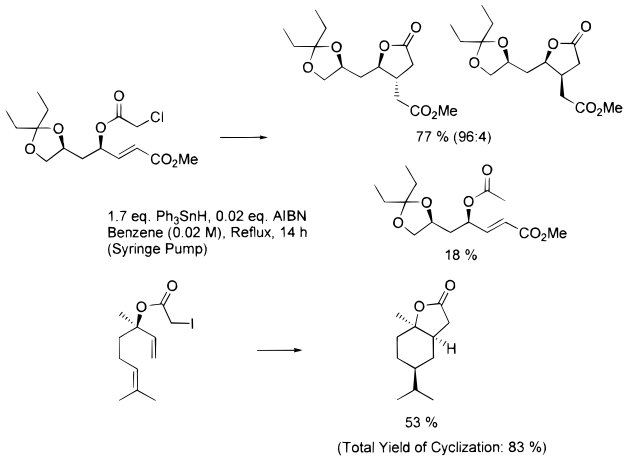
**Scheme 1**




**Scheme 2**




**Scheme 3**




(1) For recent reviews, see: (a) Giese, B.; Kopping, B.; Göbel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. *Org. React.* **1996**, *48*, 301. (b) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (c) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, pp 715, 779.

(2) (a) Stork, G.; Mook, R., Jr.; Biller, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741. (b) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765. (c) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303. (d) Stork, G.; Sher, P. M.; Chen, H. L. *J. Am. Chem. Soc.* **1986**, *108*, 6384. (e) Stork, G. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 149.

(3) (a) Ueno, Y.; Chino, K.; Watanabe, M.; Moriya, O.; Okawara, M. *J. Am. Chem. Soc.* **1982**, *104*, 5564. (b) Ueno, Y.; Moriya, O.; Chino, K.; Watanabe, M.; Okawara, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1351.

(4) (a) Curran, D. P.; Chang, C. T. *Tetrahedron Lett.* **1987**, *28*, 2477. (b) Curran, D. P.; Chang, C. T. *J. Org. Chem.* **1989**, *54*, 3140. (c) Curran, D. P.; Chang, C. T. *Tetrahedron Lett.* **1990**, *31*, 933.

(5) (a) Belletire, J. L.; Mahmoodi, N. O. *Tetrahedron Lett.* **1989**, *30*, 4363. (b) Clough, J. M.; Pattenden, G.; Wight, P. G. *Tetrahedron Lett.* **1989**, *30*, 7469. (c) Hannesian, S.; Di Fabio, R.; Marcoux, J. F.; Prud'homme, M. *J. Org. Chem.* **1990**, *55*, 3436.

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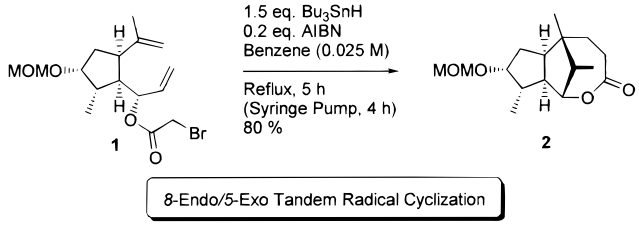
**Scheme 4**




spectroscopic analysis, we were quite surprised to find that what we had was the tricyclic heptanolactone **2**, a product of 8-endo/5-exo tandem radical cyclizations (Scheme 4). For the (alkoxycarbonyl)methyl radical generated from the bromoactate **1**, 8-endo cyclization was preferred over the usual 5-exo cyclization. In other words, eight-membered heptanolactone ring formation was kinetically much faster than five-membered $\gamma$-lactone formation!

It is well-known that the eight-membered-ring lactones are the least accessible ones via traditional lactone-forming reactions starting from $\omega$-halo- and $\omega$-hydroxycarboxylic acids and $\omega$-alkenoic acids.[7−9] Aside from a few scattered examples,[10,11] syntheses of heptanolactones frequently employ indirect schemes which may involve Baeyer−Villiger oxidation of cycloheptanones or sigmatropic rearrangements among others.[12] In this context, the preferential formation of a eight-membered heptanolactone via 8-endo cyclization reaction of an (alkoxycarbonyl)methyl radical was truly remarkable, especially when an alternative 5-exo mode of cyclization was also possible. In this paper, we report results of further experimental examples of 8-endo cyclization of (alkoxycarbonyl)methyl radicals.[13] We also provide a theoretical basis for the preferential 8-endo cyclization by presenting results of ab initio calculations.

(6) For the guaianolide synthesis via 5-exo/7endo tandem radical cyclization reactions, see: Lee, E.; Lim, J. W.; Yoon, C. H.; Sung, Y.-s.; Kim, Y. K.; Yun, M.; Kim, S. *J. Am. Chem. Soc.* **1997**, *119*, 8391.

(7) For reviews, see: (a) Back, T. G. *Tetrahedron* **1977**, *33*, 3041. (b) Rousseau, G. *Tetrahedron* **1995**, *51*, 2777.

(8) The difficulty in the formation of heptanolactones is discussed in the following examples: (a) Mukaiyama, T.; Usui, M.; Saigo, K. *Chem. Lett.* **1976**, 49. (b) Galli, C.; Illuminati, G.; Mandolini, L. *J. Am. Chem. Soc.* **1973**, *95*, 8374. (c) Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591. (d) Galli, C.; Mandolini, L. *J. Chem. Soc., Chem. Commun.* **1982**, 251. (e) Simonot, B.; Rousseau, G. *J. Org. Chem.* **1994**, *59*, 5912.

(9) In many other examples, heptanolactones are omitted as targets but it is obvious that they are the most difficult ones: (a) Corey, E. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614. (b) Kurihara, T.; Nakajima, Y.; Mitsunobu, O. *Tetrahedron Lett.* **1976**, 2455. (c) Vorbrüggen, H.; Krolikiewicz, K. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 876. (d) Kruizinga, W. H.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1979**, 286. (e) Steliou, K.; Szczygielska-Nowosielska, A.; Favre, A.; Poupart, M. A.; Hanessian, S. *J. Am. Chem. Soc.* **1980**, *102*, 7578. (f) Kruizinga, W. H.; Kellogg, R. M. *J. Am. Chem. Soc.* **1981**, *103*, 5183. (g) Regen, S. L.; Kimura, Y. *J. Am. Chem. Soc.* **1982**, *104*, 2064. (h) Steliou, K.; Poupart, M. A. *J. Am. Chem. Soc.* **1983**, *105*, 7130. (i) Kimura, Y.; Regen, S. L. *J. Org. Chem.* **1983**, *48*, 1533.

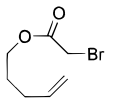
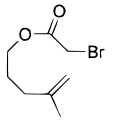
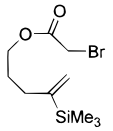
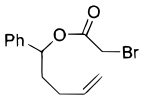
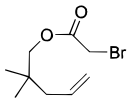
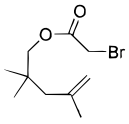
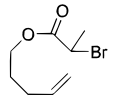
(10) There are a few recent examples of successful formation of heptanolactones from substituted 7-hydroxyheptanoic acids. In these cases, the conformational constraint imposed by the substituents is considered important: (a) Funk, R. L.; Abelman, M. M. *J. Org. Chem.* **1986**, *51*, 3247. (b) Buszek, K. R.; Sato, N.; Jeong, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5511. (c) Andrus, M. B.; Argade, A. B. *Tetrahedron Lett.* **1996**, *37*, 5049.

(11) There are more successful examples for synthesis of unsaturated heptanolactones: Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.

(12) (a) McWilliams, J. C.; Clardy, J. *J. Am. Chem. Soc.* **1994**, *116*, 8378. (b) Robinson, R. A.; Clark, J. S.; Holmes, A. B. *J. Am. Chem. Soc.* **1993**, *115*, 10400. (c) Curtis, N. R.; Holmes, A. B.; Looney, M. G. *Tetrahedron* **1991**, *47*, 7171.

(13) Part of this work has appeared in communication form: Lee, E.; Yoon, C. H.; Lee, T. H. *J. Am. Chem. Soc.* **1992**, *114*, 10981.

**Table 1**

| Substrates | Products | |
|---|---|---|
|  **3a** | **3b** (31 %) | **3c** (38 %) |
|  **4a** | **4b** (18 %) | **4c** (38 %) |
|  **5a** | **5b** (32 %) | **5c** (54 %) |
|  **6a** | **6b** (24 %) | **6c** (52 %) |
|  **7a** | **7b** (16 %) | **7c** (53 %) |
|  **8a** | **8b** (50 %) | **8c** (25 %) |
|  **9a** | **9b** (32 %) | **9c** (13 %) |

## Results

The bromoacetates **3a**−**20a** were obtained via reaction of the corresponding alkenols and alkadienols with bromoacetic acid in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP). Most alkenols and alkadienols used are known, and they were either purchased or synthesized by employing procedures in the literature. Other alkenols and alkadienols were obtained by following procedures described in the Experimental Section.

Slow addition (via a syringe pump) of a solution of tributylstannane (1.4 equiv) in benzene containing azobisisobutyronitrile (AIBN) (0.1 equiv) over 5 h into a benzene solution (0.015 M) of 4-pentenyl bromoacetate (**3a**) under reflux gave 4-pentenyl acetate (**3b**, 31%) and heptanolactone (**3c**, 38%).[14] The presence of the 4-methyl substituent did not increase the yield of the lactone **4c** (38%), but substitution with the 4-trimethylsilyl group facilitated the cyclization considerably in forming lactone **5c** (54%). Further examples of the simple 8-endo cyclization are presented in Table 1. 1-Phenyl and 2,2-dimethyl substitutents increased the yield of the lactones **6c** (52%) and **7c** (53%) as expected. The lower yield for **8c** (25%)

(14) (a) Matsubara, S.; Takai, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2029. (b) Wiberg, K. B.; Waldron, R. F. *J. Am. Chem. Soc.* **1991**, *113*, 7697.

**Table 2**

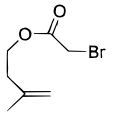
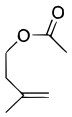
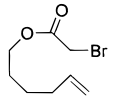
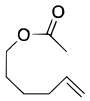
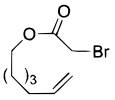
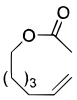
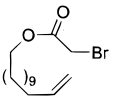
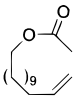
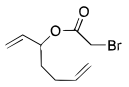
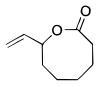
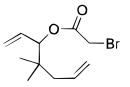
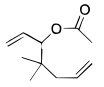
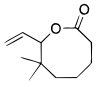
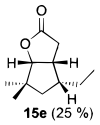
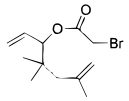
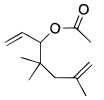
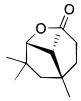
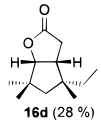
| Substrates | Products |
|---|---|
|  **10a** |  **10b** (42 %) |
|  **11a** |  **11b** (79 %) |
|  **12a** |  **12b** (57 %) |
|  **13a** |  **13b** (90 %) |

**Table 3**

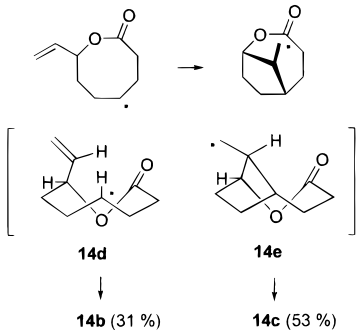
| Substrates | Products (Isolated Yield) | | | |
|---|---|---|---|---|
|  **14a** |  **14b** (31 %) |  **14c** (53 %) | | |
|  **15a** |  **15b** (25 %) |  **15c** (25 %) |  **15d** (23 %) |  **15e** (25 %) |
|  **16a** |  **16b** (44 %) | |  **16c** (14 %) |  **16d** (28 %) |

may be attributed to the steric crowding in the transition-state conformations. (Alkoxycarbonyl)ethyl radicals are presumably much less active in this type of cyclization as shown by the low yield of the lactone **9c** (13%) from the α-bromopropionate **9a**. From the results shown in Table 1, it was concluded that 8-endo cyclization of (alkoxycarbonyl)methyl radicals was indeed generally applicable.

On the contrary, reactions of the lower and higher homologues **10a** and **11a** did not yield cyclization products (6-exo or 7-endo mode for **10a** and 8-exo or 9-endo mode for **11a**) (Table 2). The reaction of **10a** produced a complex product mixture from which **10b** was isolated in 42% yield. The conversion of **11a** into the acetate **11b** (79%) was accompanied by one major byproduct, which appeared to be a dimeric species formed by the intermolecular attack of the (alkoxycarbonyl)methyl radical and subsequent reduction. Formation of larger lactone rings was also unfavorable, as the acetates **12b** (57%) and **13b** (90%) were the only products isolated after reaction of the substrates **12a** and **13a**. These results indicate that 8-endo mode of cyclization is the intrinsically favored pathway for (alkoxycarbonyl)methyl radicals.

Next, substrates **14a**−**16a** were reacted under the same conditions for 5-exo/8-endo competition experiments (Table 3). Radical cyclization of the bromoacetate **14a** proceeded smoothly to yield the heptanolactone **14b** (31%) and the bicyclic heptanolactone **14c** (53%). The result of the reaction of **15a** was more interesting. Thin-layer chromatographic analysis (silica gel, 7:1 hexane/ethyl acetate) of the crude reaction mixture revealed four clean spots for the simple acetate **15b** (25%), the heptanolactone **15c** (25%), the bicyclic butyrolactone **15e** (25%), and the bridged bicyclic lactone **15d** (23%). The reaction of **16a** yielded mainly three products: the acetate **16b** (44%), the butyrolactone **16d** (28%), and the bicyclic lactone **16c** (14%). The heptanolactones **14b** and **15c** were clearly obtained via 8-endo cyclization, and the bicyclic heptanolactones **14c**, **15d**, and **16c** are products of 8-endo/5-exo tandem radical cyclizations. No simple 5-exo mode cyclization products were obtained. It is now quite clear that 8-endo mode cyclization is much faster than 5-exo cyclization for (alkoxycarbonyl)methyl radicals. It is to be noted that the combined yield (84%) of **14b** and **14c** from **14a** for 8-endo cyclization is substantially higher than the yield (38%) of **3c** from **3a**. This could be the effect of an extra substituent on the reactive conformation.

**Scheme 5**




Comments on the structural elucidation of the bicyclic heptanolactones are warranted. The secondary methyl group in **14c** was determined to be exo oriented whereas the secondary methyl groups in **15d** and **16c** were assigned to be endo oriented. The NOE difference spectrum of **16c** showed that the intensity of the signals ($\delta$ 1.57 and 1.69, ABq, $J$ = 14.4 Hz) from the protons of the isolated methylene group of the carbocyclic ring did not change upon irradiation of the secondary methyl group signals ($\delta$ 0.94, d, $J$ = 7.2 Hz) but the signals ($\delta$ 1.67, dd, $J$ = 4.5, 13.5 Hz) from one of the methylene protons $\beta$ to the carbonyl group were enhanced.

In the formation of the bicyclic heptanolactone **14c**, the conformation **14d** may be important, in which the pendant vinyl group is directed away from the heptanolactone center (Scheme 5). Apparently, the transition-state conformation for the 5-exo cyclization of the heptanolactone radical formed by 8-endo cyclization of the initial (alkoxycarbonyl)methyl radical from **15a** (and **16a**) is much influenced by the presence of the gem dimethyl groups so that the conformation **15f** may become more important (Scheme 6). In the ensuing methyl radical **15g**, the radical center is directed toward the center of the lactone ring, enticing further rearrangement. It may be assumed that the reaction proceeds from the methyl radical **15g** via transannular attack to the lactone carbonyl group and fragmentation of the oxy radical **15h** to the ethyl radical **15i**. The mechanism delineated in Scheme 6 calls for the cis relationship of the lactone ring and the ethyl group in **16d**. This was convincingly shown in the NOE difference spectrum: irradiation of the lactone methylene proton signals ($\delta$ 2.49, d, $J$ = 7.6 Hz) resulted in the enhancement of the signals ($\delta$ 1.29, q, $J$ = 7.4 Hz) from the methylene protons of the ethyl group. We believe this is

**Scheme 6**

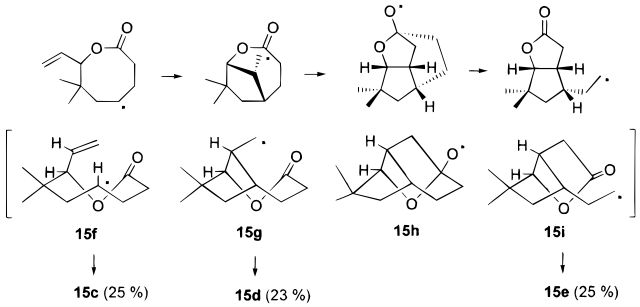
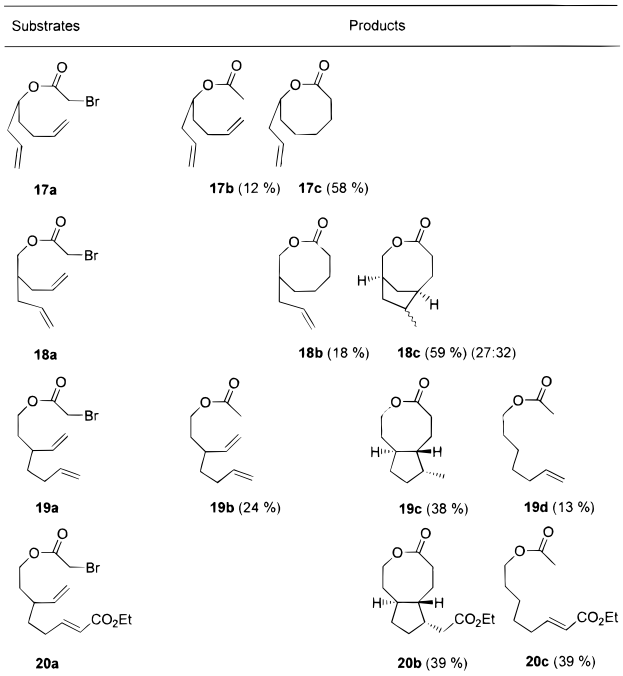



**Table 4**

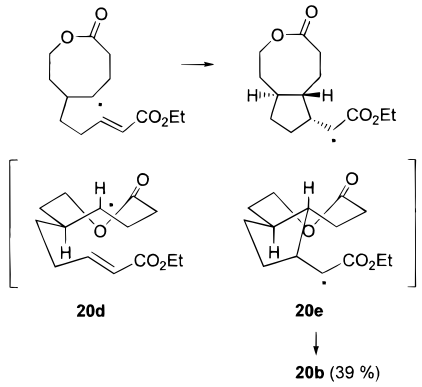



the first clear-cut example of the radical rearrangements involving ester or lactone carbonyl functionalities.[15,16]

Further examples of 8-endo radical cyclization were collected (Table 4). The reaction of the bromoacetate **17a** yielded the acetate **17b** (12%) and the heptanolactone **17c** (58%). Obviously, transannular 6-exo cyclization was not feasible after initial 8-endo cyclization. However, the substrate **18a** was transformed into a mixture (27:32) of the bicyclic lactones **18c** (59%) and the heptanolactone **18b** (18%). The formation of **18c** may be explained by a second type of 8-endo/5-exo tandem radical cyclization. A third type of 8-endo/5-exo tandem radical cyclization is also possible: the reaction of the bromoacetate **19a** afforded the acetate **19b** (24%), 6-heptenyl acetate (**19d**, 13%), and the bicyclic heptanolactone **19c** (38%). The straight-chain acetate **20c** (39%) and the bicyclic heptanolactone **20b** (39%) were also isolated from the reaction of the bromoacetate **20a**.

The stereoselectivity in the formation of **20b** (and **19c**) may be explained as shown in Scheme 7. From two different

**Scheme 7**




bromoacetates **19a** and **20a**, almost identical yields of **19c** and **20b** were obtained, and it may be argued that the initial 8-endo radical cyclization proceeded under irreversible conditions. The efficiency of 8-endo radical cyclizations in general may thus have to be explained by assuming that the reactions proceeded irreversibly.

In the reaction of **19a** and **20a**, products **19d** and **20c** were isolated, and their structures were confirmed by independent syntheses. One obvious (but unlikely) explanation was the vinyl hydrogen abstraction by the initial (alkoxycarbonyl)methyl radicals followed by the loss of acetylene. When **20a** was reacted in the presence of deuteriotributylstannane instead of tributylstannane, deuterium-labeled **20b** (45%) and **20c** (36%) were isolated. Spectroscopic analysis of **20c** easily located the deuterium atom at the acetate methyl carbon. Obviously, the rationalization given above is not operational and an alternative explanation is needed.

## Discussion

There are several known examples of 8-endo radical cyclization. Some of them involve relatively rigid templates, and it is difficult to correlate these results with the present one.[17] For flexible carbocycle synthesis, it is predicted that 8-endo mode of cyclization of a 7-octenyl radical is preferred over the alternative 7-exo mode of cyclization,[18] and examples of cyclooctane synthesis were indeed reported.[19] But the preferential formation of heptanolactones cannot be explained on the same grounds as the formation of cyclooctanes. Contemporary to our initial reports,[13] Speckamp and co-workers reported medium-sized lactone synthesis via copper(I)-catalyzed atom-transfer cyclizations of dichloroacetates and trichloroacetates,[20] which is probably more closely related to the present study. More recently, 8-endo cyclization of unsaturated acrylates upon reaction with t-BuHgI/KI has been reported by Russell and Li.[21]

The preferred 8-endo mode of cyclization of (alkoxycarbonyl)methyl radicals reflects the conformational bias of these

(15) For a review for radical-mediated rearrangements, see: Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091.

(16) For some examples of intramolecular addition of alkyl radicals to aldehyde and ketone carbonyl groups, see: (a) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 2116. (b) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 8102. (c) Tsang, R.; Dickson, J. K. Jr.; Park, H.; Walton, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1987**, *109*, 3484. (d) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 3493. (e) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 6548.

(17) (a) Sato, T.; Ishida, S.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 353. (b) Crich, D.; Chen, C.; Hwang, J. T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937.

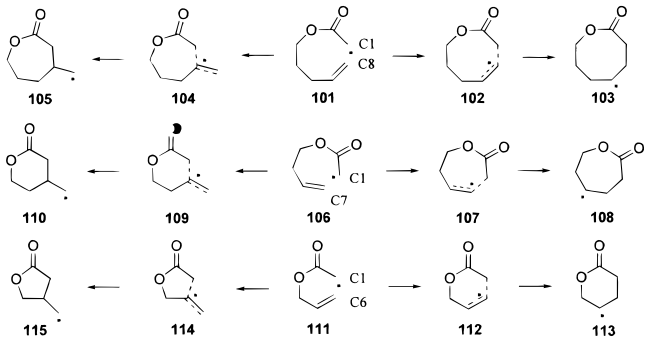
(18) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925.

(19) (a) Merritt, J. E.; Sasson, M.; Kates, S. A.; Snider, B. B. *Tetrahedron Lett.* **1988**, *29*, 5209. (b) Snider, B. B.; Merritt, J. E. *Tetrahedron* **1991**, *47*, 8663. (c) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1994**, *59*, 3186.

(20) (a) Pirrung, F. O. H.; Steeman, W. J. M.; Hiemstra, H.; Speckamp, W. N.; Kaptein, B.; Boesten, W. H. J.; Schoemaker, H. E.; Kamphuis, J. *Tetraheron Lett.* **1992**, *33*, 5141. (b) Pirrung, F. O. H.; Hiemstra, H.; Kaptein, B.; Sobrino, M. E. M.; Petra, D. G. I.; Schoemaker, H. E.; Speckamp, W. N. *Synlett* **1993**, 739. (c) Pirrung, F. O. H.; Hiemstra, H.; Speckamp, W. N.; Kaptein, B.; Schoemaker, H. E. *Tetrahedron* **1994**, *50*, 12415. (d) Pirrung, F. O. H.; Hiemstra, H.; Speckamp, W. N.; Kaptein, B.; Shoemaker, H. E. *Synthesis* **1995**, 458.

(21) Russell, G. A.; Li, C. *Tetrahedron Lett.* **1996**, *37*, 2557.

**Scheme 8**




radicals favoring *Z*-conformation (*s*-trans) over *E*-conformation (*s*-cis). In line with many theoretical and experimental studies corroborating the relative stability of *Z*-ester conformations, the *Z*-conformation of the (alkoxycarbonyl)alkyl radicals was also judged to be more stable than the *E*-conformation.[22] Atom-transfer cyclization of allyl iodoacetates is much more efficient at 80 °C than at 25 °C. This beneficial effect of temperature arises because, at higher temperature, there is relatively larger population of the less stable *E*-conformer (which can cyclize in the 5-exo mode) of (allyloxycarbonyl)methyl radicals than at lower temperature.[23] The selective formation of eight-membered-ring heptanolactones in these cyclization reactions is probably also connected with the finding that heptanolactone is the smallest lactone for which *Z*-conformers are found as low-energy conformers.[14b]

For a better understanding of the selectivity shown in the above experimental results, ab initio calculations were performed on a number of cyclizations of (alkoxycarbonyl)methyl radicals. All calculations were carried out with the GAMESS[24] series of programs using the ROHF[25] method. All structures reported were fully optimized with the 3-21G basis sets[26] and were characterized by harmonic frequency analysis. Energies are obtained with second-order Møller−Plesset perturbation theory (MP2).[27] The intrinsic reaction coordinate calculations (IRC)[28] were performed to confirm the connectivity between the respective reactant and product via a proposed transition structure.

Results from ab initio calculations on the cyclizations of homologues of (alkoxycarbonyl)methyl radicals (Scheme 8) are given in Figure 1 and Table 5. The *Z*-conformations of (alkoxycarbonyl)methyl radicals are calculated to be more stable than the *E*-conformations along the reaction pathway up to the transition state.

For (4-pentenyloxycarbonyl)methyl radical **101**, the *Z*-conformation (**101Z**) is more stable than the *E*-conformation (**101E**) by 8.7 kcal/mol. The activation energies for the 8-endo and 7-exo cyclizations of **101E** are 4.5 and 7.6 kcal/mol, respectively (Figure 1b and d). The activation energy (4.0 kcal/mol) of the 8-endo cyclization of **101Z** is much smaller than that (13.5 kcal/mol) of the 7-exo cyclization (Figure 1a and c). Therefore, ROHF/MP2/3-21G//ROHF/3-21G ab initio calculations predict that 8-endo cyclization of the *Z*-conformation is the most preferred mode of reaction for **101**. Figure 2 shows the calculated structure of the transition-state **102Z** for 8-endo cyclization. In the transition-state **102Z**, the C1−C8 bond length is 2.12 Å, and the radical approach angle C1−C8−C7 is 106.6°. The pyramidalization at C8 is 158.3°. These values

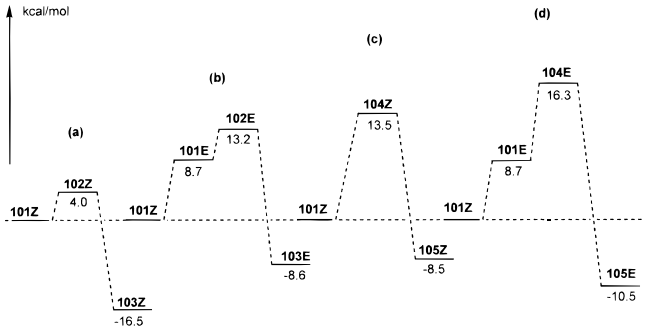



**Figure 1.** Schematic representation of possible reaction modes of **101**: (a) 8-endo cyclization of the *Z*-conformation; (b) 8-endo cyclization of the *E*-conformation; (c) 7-exo cyclization of the *Z*-conformation; (d) 7-exo cyclization of the *E*-conformation.

**Table 5.** Energies and Geometry Data for Cyclization of (Alkoxycarbonyl)methyl Radicals (ROHF/MP2/3-21G//ROHF/3-21G)

| structure[a] | energy (hartree) | distance (Å) |
|---|---|---|
| **101** Z | −419.653 628 | $d$(C1−C8) = 4.19 |
| E | −419.639 786 | $d$(C1−C8) = 4.94 |
| **102** Z | −419.647 271 | $d$(C1−C8) = 2.12 |
| E | −419.632 564 | $d$(C1−C8) = 2.12 |
| **103** Z | −419.679 941 | $d$(C1−C8) = 1.57 |
| E | −419.669 688 | $d$(C1−C8) = 1.56 |
| **104** Z | −419.632 049 | $d$(C1−C7) = 2.14 |
| E | −419.627 706 | $d$(C1−C7) = 2.13 |
| **105** Z | −419.667 150 | $d$(C1−C7) = 1.55 |
| E | −419.670 360 | $d$(C1−C7) = 1.55 |
| **106** Z | −380.743 785 | $d$(C1−C7) = 4.59 |
| E | −380.727 826 | $d$(C1−C7) = 3.95 |
| **107** Z | −380.725 982 | $d$(C1−C7) = 2.12 |
| E | −380.719 304 | $d$(C1−C7) = 2.13 |
| **108** Z | −380.753 889 | $d$(C1−C7) = 1.55 |
| E | −380.760 319 | $d$(C1−C7) = 1.56 |
| **109** (E) | −380.719 333 | $d$(C1−C6) = 2.12 |
| **110** (E) | −380.760 378 | $d$(C1−C6) = 1.55 |
| **111** (E) | −341.817 171 | $d$(C1−C6) = 3.29 |
| **112** (E) | −341.798 573 | $d$(C1−C6) = 2.13 |
| **113** (E) | −341.851 156 | $d$(C1−C6) = 1.54 |
| **114** (E) | −341.807 211 | $d$(C1−C5) = 2.09 |
| **115** (E) | −341.853 688 | $d$(C1−C5) = 1.54 |

[a] Z or E means *Z*- and *E*-conformation.

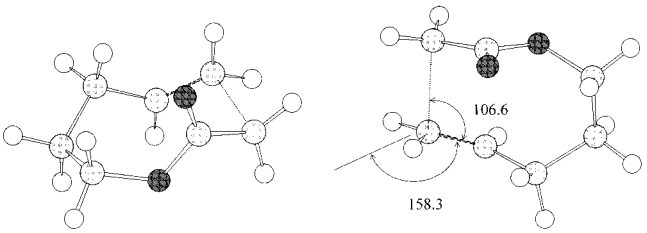



**Figure 2.** Calculated structure of the transition state for 8-endo cyclization (**102Z**).

(22) (a) Fisher, H.; Wu, L. M. *Helv. Chim. Acta* **1983**, *66*, 138. (b) Beckwith, A. L. J.; Glover, S. A. *Aust. J. Chem.* **1987**, *40*, 157.

(23) Curran, D. P.; Tamine, J. *J. Org. Chem.* **1991**, *56*, 2746.

(24) GAMESS version 11/96: Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347.

(25) (a) McWeeny, R.; Diercksen, G. *J. Chem. Phys.* **1968**, *49*, 4852. (b) Faegri, K.; Manne, R. *Mol. Phys*. **1976**, *31*, 1037. (c) Hsu, H.; Davidson, E. R.; Pitzer, R. M. *J. Chem. Phys.* **1976**, *65*, 609.

(26) Bikley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc*. **1980**, *102*, 939.

(27) (a) Knowles, P. J.; Andrews, J. S.; Amos, R. D.; Handy, N. C.; Pople, J. A. *Chem. Phys. Lett.* **1991**, *186*, 130. (b) Lauderdale, W. J.; Stanton, J. F.; Gauss, J.; Watts, J. D.; Bartlett, R. J. *Chem. Phys. Lett.* **1991**, *187*, 21.

(28) (a) Schmidt, M. W.; Gordon, M. S.; Dupuis, M. *J. Am. Chem. Soc*. **1985**, *107*, 2585. (b) Gonzales, C.; Schlegel, H. B. *J. Phys. Chem*. **1990**, *94*, 5523.

**Scheme 9**

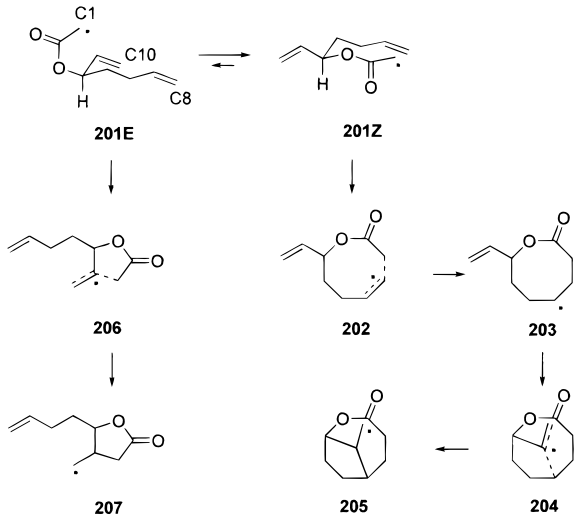



**Table 6.** Energies and Geometry Data for the 8-Endo/5-Exo Tandem Cyclization of (Alkoxycarbonyl)methyl Radicals (ROHF/MP2/3-21G//ROHF/3-21G)

| structure[a] | energy (hartree) | distance (Å) |
|---|---|---|
| **201** Z | −496.280 597 | $d$(C1−C8) = 3.72 |
| E | −496.262 789 | $d$(C1−C8) = 3.95 |
| **202** | −496.272 977 | $d$(C1−C8) = 2.12 |
| **203** | −496.309 176 | $d$(C1−C8) = 1.56 |
| **204** | −496.281 915 | $d$(C7−C9) = 2.10, $d$(C9−C10) = 1.35 |
| **205** | −496.324 056 | $d$(C7−C9) = 1.55, $d$(C9−C10) = 1.51 |
| **206** | −496.256 771 | $d$(C1−C9) = 2.09, $d$(C9−C10) = 1.35 |
| **207** | −496.304 592 | $d$(C1−C9) = 1.55, $d$(C9−C10) = 1.51 |

[a] Z or E means *Z*- and *E*-conformation.

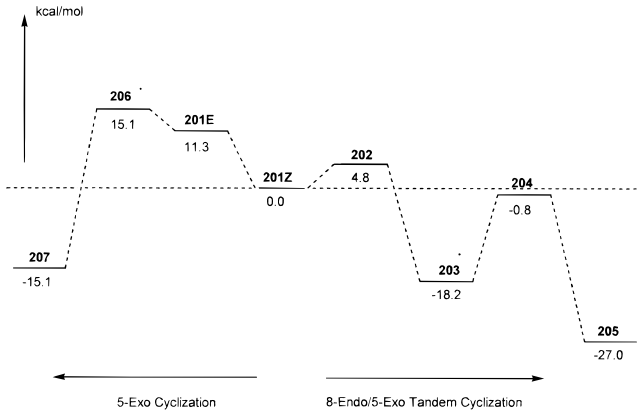



**Figure 3.** Schematic representation of 8-endo/5-exo tandem radical cyclizations of **201**.

are comparable to those calculated for intermolecular addition of various radicals to different alkenes.[29]

Results from ab initio calculations on the 8-endo/5-exo tandem radical cyclizations of the radical **201** (Scheme 9) are summarized in Figure 3 and Table 6. The *Z*-conformation (**201Z**) of the radical **201** is more stable than the *E*-conformation (**201E**) by 11.3 kcal/mol. The activation barrier (3.8 kcal/mol) for the 5-exo cyclization of **201E** is comparable to that (4.8 kcal/mol) of the 8-endo cyclization of **201Z**. These calculations therefore indicate that the preference of the 8-endo cyclization

(29) (a) Zipse, H.; He, J.; Houk, K. N.; Giese, B. *J. Am. Chem. Soc.* **1991**, *113*, 4324. (b) Wong, M. W.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, *116*, 6284. (c) Wong, M. W.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, *116*, 11938.

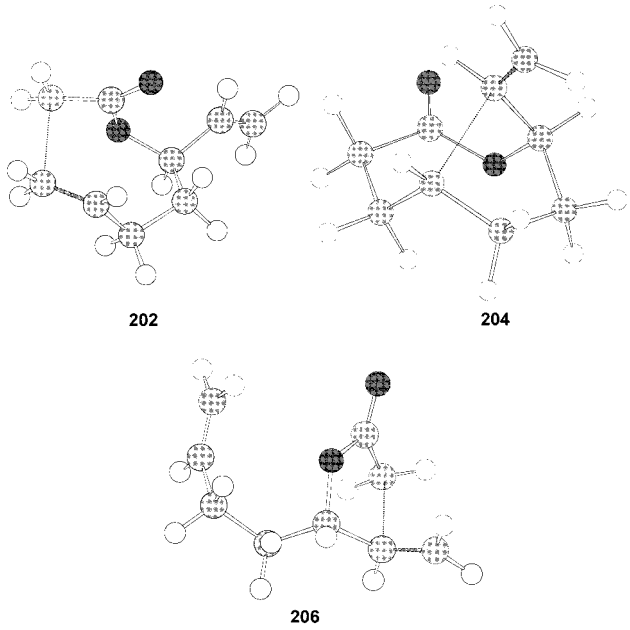



**Figure 4.** Calculated structures of the transition states **202**, **204**, and **206**.

of **201** over the 5-exo mode originates from the conformational bias of this radical favoring the *Z*- over the *E*-conformation. The 7-exo mode of cyclization is also possible for **201Z**, but the activation energy for this mode of reaction should be much higher than that of the 8-endo cyclization (cf. Figure 1a and c). Figure 4 shows the calculated transition-state structures **202**, **204**, and **206**.

In conclusion, 8-endo cyclization is the fundamentally preferred mode of reaction for (alkoxycarbonyl)methyl radicals and eight-membered heptanolactones are obtained in reasonably good yields from bromoacetates. Further mechanistic details and synthetic utility of these unique reactions[30] will be reported in due course.

## Experimental Section

NMR spectra were obtained on Varian EM-360A (60 MHz), Bruker AC-80 (80 MHz), Bruker AW-80 (80 MHz), Varian VXR-200 (200 MHz), Varian Gemini-300BB (300 MHz), and Bruker AMX 500 (500 MHz) instruments. Chemical shifts are reported as $\delta$ values relative to internal tetramethylsilane. Mass spectra were recorded on a VG-Trio 2 spectrometer using electron impact (EI) or chemical ionization (CI) method, and high-resolution mass spectra (HRMS) were recorded on a JEOL JMS GSX-300 spectrometer. Infrared spectra were taken on a Perkin-Elmer model 782 spectrometer or a Bruker IFS48 FT-IR spectrophotometer as neat oil. Optical rotations were measured on a Jasco DIP-360 digital polarimeter. GC chromatograms were recorded on a Hewlett-Packard model HP 5880A gas chromatograph using nitrogen as carrier gas.

TLC was performed on Merck precoated silica gel plates (no. 5554), and the TLC spots were visualized under 254-nm UV light and/or by charring after dropping the plate into vanillin solution in 5% sulfuric acid/methanol. Purification of products was accomplished via Merck silica gel (no. 7734 and no. 9385) flash chromatography. Hexane and ethyl acetate were simple distilled and used in column chromatography.

Unless otherwise specified, all reactions were conducted under a slight positive pressure of dry nitrogen and the usual workup

(30) For an example in the synthesis of (−)-clavukerin A, see: Lee, E.; Yoon, C. H. *Tetrahedron Lett.* **1996**, *37*, 5929.

refers to washing of the quenched reaction mixture with saturated sodium chloride solution, drying over anhydrous $MgSO_4$, and evaporating under reduced pressure using a rotary evaporator.

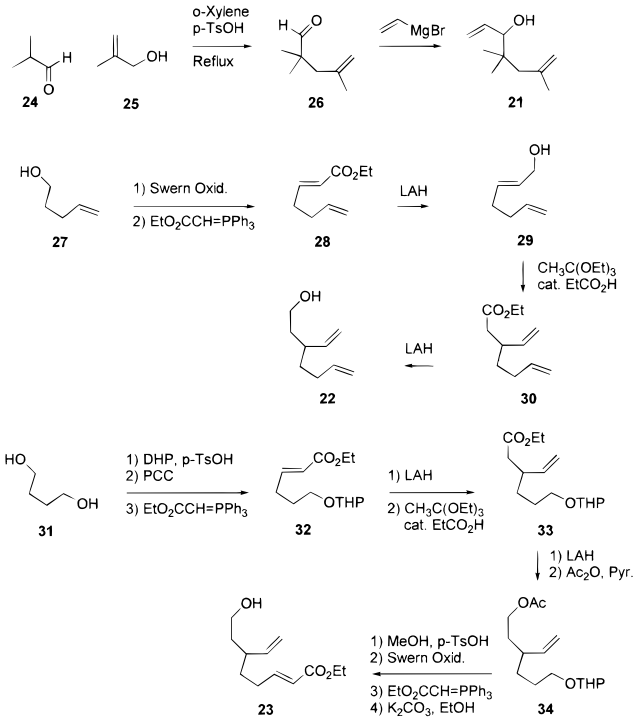
All solvents used in reactions were dried under nitrogen or argon atmosphere. THF was distilled from Na-benzophenone. Dichloromethane and benzene were washed with concentrated $H_2SO_4$ and distilled from $P_2O_5$ and stored over 4-Å molecular sieves. Ethyl ether was distilled from lithium aluminum hydride (LAH). Pyridine was dried over KOH and stored over 4-Å molecular sieves.

**Bromoacetate 1.** To a stirred solution of DCC (280 mg, 1.31 mmol) in 10 mL of dry dichloromethane was added bromoacetic acid (210 mg, 1.48 mmol) at 0 °C, and the reaction mixture was stirred for 30 min at that temperature. To this mixture was added the solution of the allylic alcohol (210 mg, 0.87 mmol) in 5 mL of dichloromethane followed by a catalytic amount (40 mg) of DMAP, and the reaction mixture was stirred for 30 min at room temperature. After filtration on a silica gel pad, the filtrate was concentrated under reduced pressure. Flash chromatography (silica gel, 1.5 × 15 cm, 12:1 hexane/ethyl acetate) afforded the bromoacetate **1** (300 mg, 95%): $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 1.07 (d, 3 H, $J$ = 7.1 Hz), 1.79 (br s, 3 H), 2.34−2.44 (m, 1 H), 2.91−2.97 (m, 1 H), 3.35 (s, 3 H), 3.98 (s, 2 H), 4.08 (t, 1 H, $J$ = 4.6 Hz), 4.58 and 4.65 (ABq, 2 H, $J$ = 6.8 Hz), 4.82 (br, 1 H), 5.07−5.29 (m, 4 H), 5.77 (ddd, 1 H, $J$ = 5.4, 11.0, 17.0 Hz).

**Heptanolactone 2.** To a stirred solution of the bromoacetate **1** (310 mg, 0.86 mmol) in dry benzene (34 mL, 0.025 M) under reflux was added a mixture of tributylstannane (0.28 mL, 1.2 equiv) and a catalytic amount of AIBN in 5 mL of benzene via a syringe pump for 4 h. After complete addition, the reaction mixture was heated under reflux for 1 h. After evaporation of solvent, flash chromatography (silica gel, 1.5 × 15 cm, 10:1 hexane/ethyl acetate) afforded the heptanolactone **2** (194 mg, 80%): $[\alpha]_D^{30}$ −86.3° (*c* 2.35, $CCl_4$); $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.929 (d, 3 H, $J$ = 7.1 Hz), 0.936 (s, 3 H), 1.162 (d, 3 H, $J$ = 6.8 Hz), 1.20−2.00 (m, 6 H), 2.28−2.64 (m, 4 H), 3.38 (s, 3 H), 3.99 (br t, 1 H, $J$ = 3.2 Hz), 4.14 (d, 1 H, $J$ = 5.6 Hz), 4.58 and 4.69 (ABq, 2 H, $J$ = 6.7 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 174.8, 95.02, 88.89, 81.32, 55.41, 55.31, 50.78, 46.69, 44.66, 43.07, 34.08, 32.96, 30.57, 22.70, 13.83, 7.68; IR (neat, cm$^{-1}$) 2932, 1777, 1725, 1446, 1403, 1281, 1245, 1194, 1149, 1091, 1038; MS (EI) *m*/*z* (relative intensity) 282 ($M^+$, 7), 264 (6), 250 (25), 237 (59), 219 (64), 209 (21), 193 (32), 178 (29), 165 (100), 147 (66), 133 (33), 121 (47), 111 (42), 107 (37), 81 (78), 69 (30), 55 (31); HRMS *m*/*z* calcd for $C_{16}H_{26}O_4$ 282.1832, found 282.1839.

**Preparation of Alkenols and Alkadienols.** 4-Penten-1-ol, 3-methyl-3-buten-1-ol, and 5-hexen-1-ol were purchased from Aldrich. 4-Methyl-4-penten-1-ol,[31] 4-(trimethylsilyl)-4-penten-1-ol,[32] 1-phenyl-4-penten-1-ol,[33] 2,2-dimethyl-4-penten-1-ol,[20c] 2,2,4-trimethyl-4-penten-1-ol,[34] 6-hepten-1-ol,[35] 12-tridecen-1-ol,[36] 1,6-heptadien-3-ol,[37] 4,4-dimethyl-1,6-heptadien-3-ol,[38] 1,7-octadien-4-ol,[39] and 2-(2′-propenyl)-4-penten-1-ol[40] were synthesized according to the literature procedures. 4,4,6-Trimethyl-1,6-heptadien-3-ol (**21**), 3-ethenyl-6-hepten-1-ol (**22**), and ethyl 6-(2′-hydroxyethyl)-2,7-octadienoate (**23**) were prepared as described below (Scheme 10).

**Scheme 10**




**4,4,6-Trimethyl-1,6-heptadien-3-ol (21).** Isobutyraldehyde (**24**; 10 g, 138 mmol) and methallyl alcohol (**25**; 15 g, 208 mmol) were dissolved in *o*-xylene (50 mL) containing *p*-TsOH (0.1 g). The solution was heated 48 h under reflux with continuous removal of water on a Dean−Stark trap. The product aldehyde **26** (7.8 g, 45%) was obtained via fractional distillation through a short packed column. A sample of the aldehyde **26** (5.0 g, 41 mmol) in dry THF (50 mL) was added dropwise at 0 °C to the THF solution (50 mL) of vinylmagnesium bromide obtained from magnesium (1.25 g, 51 mmol) and vinyl bromide (6.6 g, 62 mmol). The reaction mixture was stirred 30 min at room temperature and poured into ice/2 N HCl. The resulting mixture was extracted three times with ether. The combined ether extracts were washed with water, saturated $NaHCO_3$ solution, and brine and dried over anhydrous $MgSO_4$. Concentration and flash chromatography afforded 4,4,6-trimethyl-1,6-heptadien-3-ol (**21**, 4.8 g, 78%): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 0.92 (s, 6 H), 1.59 (s, 1 H), 1.80−1.82 (m, 3 H), 1.99 and 2.16 (ABq, 2 H, $J$ = 12.9 Hz), 3.84 (br d, 1 H, $J$ = 7.5 Hz), 4.70−4.74 (m, 1 H), 4.84−4.93 (m, 1 H), 5.10−5.36 (m, 2 H), 5.77−6.19 (m, 1 H).

**3-Ethenyl-6-hepten-1-ol (22).** DMSO (3.56 mL, 41.8 mmol) was added to a dichloromethane solution (60 mL) of oxalyl chloride (1.84 mL, 18.9 mmol) under a nitrogen atmosphere at −78 °C. After 5 min, 4-penten-1-ol (**27**; 1.5 g, 17.4 mmol) was added dropwise to this solution, followed by triethylamine (31 mL, 120 mmol) after another 15 min at the same temperature. This reaction mixture was stirred for 30 min at −78 °C and allowed to warm to room temperature. To this solution,

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(carbethoxymethylene)triphenylphosphorane (6.7 g, 41.8 mmol) in dry dichloromethane (10 mL) was added. After being stirred for 2 h at room temperature, the reaction was quenched by adding water and the aqueous layer was extracted with dichloromethane three times. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated to afford 2.0 g of the ester **28**. The product was dissolved in anhydrous ether (10 mL), and this solution was added dropwise to a suspension of LAH (661 mg, 17.3 mmol) in anhydrous ether at 0 °C. After stirring 30 min at room temperature, water (0.8 mL), 15% NaOH solution (0.8 mL), and water (2.1 mL) were added successively. This mixture was filtered on a silica gel pad, and the filtrate was concentrated. Flash chromatography on silica gel gave 2,6-hepatadien-1-ol (**29**; 750 mg, 60% yield from 4-penten-1-ol): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.95−2.20 (m, 4 H), 3.57−3.80 (m, 2 H), 4.87−6.05 (m, 5 H). A sample (1.56 g, 13.9 mmol) of **29** was heated with triethyl orthoacetate (15.8 g, 97.4 mmol) in the presence of propionic acid (0.15 g) at 130−140 °C for 20 h with continuous removal of ethanol. The reaction was quenched with 2 N HCl, and the reaction mixture was extracted with ether three times. The combined ether extracts were washed with saturated $NaHCO_3$ solution and brine, dried over anhydrous $MgSO_4$, and concentrated. Flash chromatography afforded the product ester **30** (1.55 g, 60%). A sample (822 mg, 4.4 mmol) of the ester **30** was dissolved in anhydrous ether (10 mL), and this solution was added dropwise into a suspension of LAH (168 mg, 4.4 mmol) in ether (10 mL) at 0 °C. After being stirred for 30 min at room temperature, this reaction mixture was worked up as described above. Flash chromatography afforded 3-ethenyl-6-hepten-1-ol (**22**; 430 mg, 70%): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.24−1.73 (m, 5 H), 1.91−2.30 (m, 3 H), 3.64 (t, 2 H, $J$ = 6.5 Hz)), 4.86−6.06 (m, 6 H).

**Ethyl 6-(2′-Hydroxyethyl)-2,7-octadienoate (23).** To a solution of 1,4-butanediol (**31**; 10.2 g, 113 mmol) and a catalytic amount (0.2 g) of *p*-TsOH in dichloromethane (150 mL) was added DHP (10.3 mL, 113 mmol) in dichloromethane (40 mL) via a syringe pump for 5 h. After complete addition, the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched with water, and the reaction mixture was extracted three times with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated. Flash chromatography yielded the THP-protected diol (10.4 g, 60%). This sample of the alcohol was reacted with PCC (25.4 g, 118 mmol) in dichloromethane (100 mL) in the presence of NaOAc and 4-Å molecular sieves. The reaction mixture was filtered through a silica gel pad, and the filtrate was concentrated to yield the aldehyde (7.11 g, 70%). The aldehyde sample was dissolved in dry THF (20 mL), and this solution was added to (carbethoxymethylene)triphenylphosphorane (2.58 g, 15 mmol) in dry THF (80 mL) at 0 °C. The reaction mixture was stirred for 2 h at room temperature. Concentration and flash chromatography afforded the ester **32** (8.51 g, 85%): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.28 (t, 3 H, $J$ = 7.1 Hz), 1.43−1.91 (m, 8 H), 2.18−2.37 (m, 2 H), 3.26−3.91 (m, 4 H), 4.18 (q, 2 H, $J$ = 7.1 Hz), 4.56 (br s, 1 H), 5.83 (dt, 1 H, $J_t$ = 1.5 Hz, $J_d$ = 15.6 Hz), 7.00 (dt, 1 H, $J_t$ = 6.8 Hz, $J_d$ = 15.6 Hz). The ester **32** (8.0 g, 33 mmol) was dissolved in anhydrous ether (75 mL), and this solution was added dropwise into a solution of LAH (1.26 g, 33 mmol) in anhydrous ether (75 mL) at 0 °C. After being stirred 1 h at room temperature, this reaction mixture was worked up as described above. Flash chromatography afforded the allylic alcohol (5.95 g, 30 mmol). This sample of the allylic alcohol was heated with triethyl orthoacetate (34.1 g, 210 mmol) and a catalytic amount (0.2 g) of propionic acid at 160−170 °C for 12 h with continuous removal of ethanol. The reaction mixture was worked up as described above. Flash chromatography afforded the ester **33** (4.06 g, 50%): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.24 (t, 3 H, $J$ = 7.1 Hz), 1.20−1.80 (m, 10 H), 2.30−2.70 (m, 3 H), 3.24−3.87 (m, 4 H), 4.12 (q, 2 H, $J$ = 7.1 Hz), 4.55 (br s, 1 H), 4.90−5.88 (m, 3 H). This sample of the ester **33** was dissolved in anhydrous ether (30 mL), and the solution was added to a suspension of LAH (573 mg, 15 mmol) in anhydrous ether (40 mL) under reflux. After being stirred for 30 min at room temperature, the reaction mixture was worked up as described above. The alcohol (3.40 g, 100%) was obtained via flash chromatography. This sample of the alcohol was treated with pyridine (1.25 mL) and acetic anhydride (1.53 g, 15 mmol) at 0 °C. After stirring 1 h at 0 °C, the reaction mixture was warmed to room temperature and stirred for 12 h. The reaction mixture was washed with 2 N HCl and brine, dried over anhydrous $MgSO_4$, and concentrated. Flash chromatography afforded the protected diol **34** (4.0 g, 98%): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.30−1.80 (m, 13 H). 2.04 (s, 3 H), 3.23−3.87 (m, 4 H), 3.96−4.15 (m, 2 H), 4.55 (br s, 1 H), 4.85−5.78 (m, 3 H). This sample of the protected diol **34** was dissolved in methanol (40 mL) containing a catalytic amount (0.2 g) of *p*-TsOH, and the solution was stirred for 90 min at room temperature. The reaction mixture was concentrated, and the residue was dissolved in ether. The ether solution was washed with brine, dried over anhydrous $MgSO_4$, and concentrated to give the alcohol (2.64 g, 95%). Oxalyl chloride (1.40 mL, 14.5 mmol) in dry dichloromethane (50 mL) was treated with DMSO (2.67 mL, 31.3 mmol) at −78 °C under a nitrogen atmosphere. After 5 min, the sample of the alcohol (2.64 g, 14.1 mmol) in dry dichloromethane (15 mL) was added dropwise to this solution, and the reaction mixture was further stirred for 15 min at −78 °C. Triethylamine (23 mL, 89.9 mmol) was added to the reaction mixture, which was stirred for 30 min at −78 °C before warming to 0 °C. The reaction mixture was quenched with water, and the aqueous layer was extracted three times with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated to give the aldehyde (2.34 g, 90%). This sample of the aldehyde was dissolved in dry THF (10 mL) and the solution was treated with (carbethoxymethylene)triphenylphosphorane (2.20 g, 12.8 mmol) dissolved in dry THF (20 mL) at 0 °C. The reaction mixture was stirred for 2 h at room temperature. Concentration and flash chromatography afforded the acetoxy ester (3.07 g, 95%). This sample of the acetoxy ester was dissolved in ethanol (50 mL) with $K_2CO_3$ (0.3 g). The solution was stirred for 1 day at room temperature. Concentration and flash chromatography afforded ethyl 6-(2′-hydroxyethyl)-2,7-octadienoate (**23**, 2.17 g, 85%): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.28 (t, 3 H, $J$ = 7.1 Hz), 1.35−1.79 (m, 5 H), 1.97−2.34 (m, 3 H), 3.65 (t, 2 H, $J$ = 6.5 Hz), 4.18 (q, 2 H, $J$ = 7.1 Hz), 4.89−7.14 (m, 5 H).

**General Procedure for Preparation of Bromoacetates.** To a stirred solution of DCC (1.2 equiv) in dry dichloromethane was added bromoacetic acid (1.4 equiv) at room temperature, and the reaction mixture was stirred for 30 min. To this mixture was added an alcohol solution in dichloromethane followed by a catalytic amount (0.1 equiv) of DMAP, and the reaction mixture was stirred for 30 min at room temperature. After filtration on a silica gel pad, the filtrate was concentrated under reduced pressure. Flash chromatography afforded the corresponding bromoacetate in good yield.

**General Procedure for Radical Cyclizations.** To a stirred solution of a bromoacetate in benzene (0.015 M) under reflux was added a mixture of tributylstannane (1.4 equiv) and AIBN (0.1 equiv) in benzene via a syringe pump for 5 h (typical scale: 1.0 mmol of bromoacetate in 67 mL of benzene). The reaction mixture was further heated under reflux for 1 h and concentrated under reduced pressure. The products were separated by flash chromatography.

**Oxocan-2-one (3c).** From 207 mg of **3a**, 48 mg (38%) of **3c** was obtained after chromatographic separation (10:1−3:1 hexane/ether): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.56−2.05 (m, 8 H), 2.52 (t, 2 H, $J$ = 5.6 Hz), 4.32 (t, 2 H, $J$ = 5.6 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 176.7, 67.83, 31.24, 30.90, 28.31, 25.79, 23.91; IR (neat, cm$^{-1}$) 2920, 2860, 1725, 1450, 1232, 1130, 1097; MS (EI) *m*/*z* (relative intensity) 128 ($M^+$, 0.1), 110 (6), 100 (19), 98 (16), 70 (27), 69 (48), 55 (100), 42 (70); HRMS *m*/*z* calcd for $C_7H_{12}O_2$ 128.0837, found 128.0844.

**5-Methyloxocan-2-one (4c).** From 221 mg of **4a**, 54 mg (38%) of **4c** was obtained after chromatographic separation (4:1 hexane/ethyl acetate): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 0.98 (d, 3 H, $J$ = 5.8 Hz), 1.25−2.00 (m, 7 H), 2.48−2.79 (m, 2 H), 4.32 (t, 2 H, $J$ = 5.6 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 176.4, 68.19, 36.12, 32.34, 32.29, 30.36, 30.09, 24.68; MS (EI) *m*/*z* (relative intensity) 142 ($M^+$, 0.2), 124 (4), 113 (19), 112 (11), 101 (10), 94 (21), 83 (39), 70 (38), 69 (51), 55 (100); HRMS *m*/*z* calcd for $C_8H_{14}O_2$ 142.0995, found 142.0988.

**5-Trimethylsilyloxocan-2-one (5c).** From 150 mg of **5a**, 54 mg (54%) of **5c** was obtained after chromatographic separation (5:1 hexane/ethyl acetate): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ −0.04 (s, 9 H), 0.45−0.55 (m, 1 H), 1.06−1.20 (m, 1 H), 1.46−1.61 (m, 2 H), 1.77−1.85 (m, 1 H), 1.96−2.09 (m, 2 H), 2.49 (ddd, 1 H, $J$ = 4.3, 9.0, 12.3 Hz), 2.70 (ddd, 1 H, $J$ = 4.1, 8.0, 12.3 Hz), 4.29−4.46 (m, 2 H); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 176.6, 67.73, 32.58, 31.79, 29.08, 25.15, 24.41, −3.777; IR (neat, cm$^{-1}$) 2955, 2858, 2254, 1722, 1448, 1249, 1124, 837; MS (CI) *m*/*z* (relative intensity) 241 (M + 41, 1), 201 (M + 1, 40), 185 (38), 172 (7), 157 (3), 143 (10), 129 (3), 111 (53), 103 (3), 83 (100), 73 (55), 69 (21); HRMS *m*/*z* calcd for $C_{10}H_{20}O_2Si$ 200.1233, found 200.1206.

**8-Phenyloxocan-2-one (6c).** From 283 mg of **6a**, 107 mg (52%) of **6c** was obtained after chromatographic separation (8:1−4:1 hexane/ether): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.60−2.20 (m, 8 H), 2.58 (t, 2 H), 5.69 (t, 1 H, $J$ = 6.9 Hz), 7.29−7.44 (m, 5 H); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 176.2, 140.2, 128.3, 127.7, 125.8, 79.63, 39.71, 32.93, 29.27, 26.53, 24.31; MS (EI) *m*/*z* (relative intensity) 204 ($M^+$, 0.5), 144 (17), 117 (25), 105 (26), 99 (59), 77 (36), 69 (36), 55 (100); HRMS *m*/*z* calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1180.

**7,7-Dimethyloxocan-2-one (7c).** From 235 mg of **7a**, 83 mg (53%) of **7c** was obtained after chromatographic separation (7:1 hexane/ethyl acetate): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 0.96 (s, 6 H), 1.20−2.00 (m, 6 H), 2.45−2.62 (m, 2 H), 3.94 (s, 2 H); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 176.1, 75.36, 37.27, 36.51, 31.32, 28.74, 25.12, 22.01; MS (EI) *m*/*z* (relative intensity) 156 ($M^+$, 0.5), 126 (5), 124 (11), 111 (3), 95 (3), 83 (15), 82 (100), 69 (19), 55 (37); HRMS *m*/*z* calcd for $C_9H_{16}O_2$ 156.1150, found 156.1178.

**5,7,7-Trimethyloxocan-2-one (8c).** From 210 mg of **8a**, 35 mg (25%) of **8c** was obtained after chromatographic separation (8:1−4:1 hexane/ether): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.927 (s, 3 H), 0.969 (d, 3 H, $J$ = 6.8 Hz), 0.994 (s, 3 H), 1.14−1.95 (m, 5 H), 2.55−2.60 (m, 2 H), 3.80 and 4.08 (ABq, 2 H, $J$ = 12.1 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 175.9, 75.53, 46.02, 36.79, 36.18, 30.86, 28.68, 27.36, 25.59, 22.70; IR (neat, cm$^{-1}$) 2960, 2925, 1725, 1455, 1375, 1340, 1165, 1120, 1075; MS (EI) *m*/*z* (relative intensity) 170 ($M^+$, 1), 155 (1), 96 (100), 83 (45), 69 (28), 55 (45); HRMS *m*/*z* calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1313.

**8-Ethenyloxocan-2-one (14b).** From 233 mg of **14a**, 48 mg (31%) of **14b** and 82 mg (53%) of **14c** were obtained after chromatographic separation (8:1 hexane/ether): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 1.36−2.03 (m, 8 H), 2.43−2.59 (m, 2 H), 5.08−5.43 (m, 3 H), 5.93 (ddd, 1 H, $J$ = 5.5, 10.0, 17.0 Hz); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 176.4, 136.7, 115.8, 78.55, 37.33, 32.99, 29.14, 26.59, 24.02; IR (neat, cm$^{-1}$) 2920, 2850, 1725, 1445, 1360, 1240; MS (EI) *m*/*z* (relative intensity) 154 ($M^+$, 0.2), 126 (3), 111 (8), 98 (52), 80 (14), 69 (32), 55 (100); HRMS *m*/*z* calcd for $C_9H_{14}O_2$ 154.0995, found 154.0975.

**9-Methyl-2-oxabicyclo[4.2.1]nonan-3-one (14c).** $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 1.06 (d, 3 H, $J$ = 7.1 Hz), 1.20−2.75 (m, 10 H), 4.61 (dd, 1 H, $J$ = 5.4, 7.7 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 175.3, 83.55, 42.77, 40.20, 33.45, 32.25, 28.97, 22.36, 10.21; IR (neat, cm$^{-1}$) 2940, 2860, 1730, 1720, 1430, 1350, 1250, 1190, 1170, 1105, 1040; MS (EI) *m*/*z* (relative intensity) 154 ($M^+$, 3), 125 (2), 110 (89), 97 (72), 82 (27), 67 (64), 55 (100); HRMS *m*/*z* calcd for $C_9H_{14}O_2$ 154.0995, found 154.0999.

**7,7-Dimethyl-8-ethenyloxocan-2-one (15c).** From 340 mg of **15a**, 60 mg (25%) of **15c**, 59 mg (25%) of **15e**, and 55 mg (23%) of **15d** were obtained after chromatographic separation (30:1−5:1 hexane/ether): $^1$H NMR (80 MHz, $CDCl_3$) $\delta$ 0.89 (s, 3 H), 0.93 (s, 3 H), 1.10−2.00 (m, 6 H), 2.35−2.59 (m, 2 H), 4.76 (d, 1 H, $J$ = 6.0 Hz), 5.16−5.43 (m, 2 H), 5.89 (ddd, 1 H, $J$ = 5.9, 9.7, 17.3 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 175.4, 133.0, 117.8, 84.18, 39.56, 32.93, 29.12, 24.75, 21.97, 21.63; IR (neat, cm$^{-1}$) 2960, 2920, 2855, 2830, 1720, 1460, 1350, 1325, 1270, 1205, 1140, 1105; MS (EI) *m*/*z* (relative intensity) 182 ($M^+$, 0.1), 126 (24), 111 (4), 82 (100), 69 (22), 55 (44); HRMS *m*/*z* calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1279.

**8,8,9-Trimethyl-2-oxabicyclo[4.2.1]nonan-3-one (15d).** $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.025 (d, 3 H, $J$ = 7.1 Hz), 1.138 (s, 3 H), 1.178 (s, 3 H), 1.29−1.39 (m, 1 H), 1.49 (d, 1 H, $J$ = 14.3 Hz), 1.75−1.85 (m, 1 H), 1.89 (dd, 1 H, $J$ = 8.3, 14.3 Hz). 2.40−2.78 (m, 4 H), 3.97 (d, 1 H, $J$ = 4.7 Hz); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 175.4, 93.18, 43.54, 42.13, 40.87, 40.33, 34.04, 33.70, 23.42, 22.29, 10.83; IR (neat, cm$^{-1}$) 3010, 2920, 1705, 1460, 1215, 1160, 1140; MS (EI) *m*/*z* (relative intensity) 182 ($M^+$, 1), 167 (1), 154 (3), 138 (19), 125 (42), 110 (16), 97 (32), 83 (16), 81 (37), 69 (40), 55 (100); HRMS *m*/*z* calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1316.

**6-Ethyl-8,8-dimethyl-2-oxabicyclo[3.3.0]octan-3-one (15e).** $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.902 (t, 3 H, $J$ = 7.3 Hz), 0.985 (s, 3 H), 1.106 (s, 3 H), 1.21 (t, 1 H, $J$ = 12.7 Hz), 1.27−1.41 (m, 2 H), 1.58 (dd, 1 H, $J$ = 5.3, 12.7 Hz), 2.05−2.20 (m, 1 H), 2.50 (d, 1 H, $J$ = 1.6 Hz), 2.52 (d, 1 H, $J$ = 5.0 Hz), 2.98−3.07 (m, 1 H), 4.39 (d, 1 H, $J$ = 6.3 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 177.7, 93.20, 43.49, 41.79, 40.49, 39.98, 29.36, 25.61, 24.25, 23.39, 12.92; MS (EI) *m*/*z* (relative intensity) 182 ($M^+$, 2), 153 (12), 140 (2), 125 (17), 111 (7), 97 (100), 85 (13), 69 (45), 55 (59); HRMS *m*/*z* calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1271.

**6,8,8,9-Tetramethyl-2-oxabicyclo[4.2.1]nonan-3-one (16c).** From 275 mg of **16a**, 54 mg (28%) of **16d** and 30 mg (14%) of **16c** were obtained after chromatographic separation (10:1−4:1 hexane/ether): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.935 (d, 3 H, $J$ = 7.2 Hz), 1.081 (s, 3 H), 1.09−1.18 (m, 1H), 1.146 (s, 3 H), 1.160 (s, 3 H), 1.568 and 1.692 (ABq, 2 H, $J$ = 14.4 Hz), 1.671 (dd, 1 H, $J$ = 4.5, 13.5 Hz), 2.18−2.24 (m, 1 H), 2.63 (ddd, 1

H, $J$ = 5.4, 13.4, 16.5 Hz), 2.75 (dt, 1 H, $J_t$ = 4.3 Hz, $J_d$ = 16.5 Hz), 4.03 (d, 1 H, $J$ = 5.0 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 175.0, 94.07, 51.75, 46.13, 44.98, 40.95, 34.61, 29.60, 28.88, 23.50, 8.659; IR (neat, cm$^{-1}$) 2960, 2920, 1720, 1715, 1460, 1390, 1340, 1285, 1240, 1190, 1120; MS (EI) *m*/*z* (relative intensity) 196 ($M^+$, 2), 153 (3), 139 (100), 121 (15), 111 (68), 109 (29), 96 (45), 83 (53), 69 (49), 55 (72); HRMS *m*/*z* calcd for $C_{12}H_{20}O_2$ 196.1465, found 196.1451.

**6-Ethyl-6,8,8-trimethyl-2-oxabicyclo[3.3.0]octan-3-one (16d).** $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.864 (t, 3 H, $J$ = 7.4 Hz), 1.067 (s, 3 H) 1.098 (s, 3 H), 1.171 (s, 3 H), 1.285 (q, 2 H, $J$ = 7.4 Hz), 1.495 and 1.674 (ABq, 2 H, $J$ = 13.7 Hz), 2.490 (d, 2 H, $J$ = 7.6 Hz), 2.60−2.75 (m, 1 H), 4.530 (d, 1 H, $J$ = 6.0 Hz); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 177.7, 94.35, 52.39, 51.02, 42.22, 41.20, 32.78, 31.11, 29.52, 27.53, 26.02, 9.203; MS (EI) *m*/*z* (relative intensity) 196 ($M^+$, 0.1), 181 (2), 167 (23), 153 (8), 139 (36), 126 (25), 111 (100), 97 (15), 83 (70), 71 (27), 69 (39), 55 (74); HRMS *m*/*z* calcd for $C_{12}H_{20}O_2$ 196.1465, found 196.1434.

**8-(2′-Propenyl)oxocan-2-one (17c).** From 247 mg of **17a**, 98 mg (58%) of **17c** was obtained after chromatographic separation (14:1−5:1 hexane/ether): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.47−1.96 (m, 8 H), 2.27−2.37 (m, 1 H), 2.41−2.59 (m, 3 H), 4.57−4.66 (m, 1 H), 5.08−5.17 (m, 2 H), 5.76−5.90 (m, 1 H); $^{13}$C NMR (50.3 MHz, $CDCl_3$) $\delta$ 176.5, 133.6, 117.7, 78.01, 39.79, 36.70, 32.28, 28.72, 26.20, 23.74; MS (EI) *m*/*z* (relative intensity) 168 ($M^+$, 0.1), 128 (7), 127 (90), 99 (14), 81 (100), 69 (15), 55 (60); HRMS *m*/*z* calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1144.

**7-(2′-Propenyl)oxocan-2-one (18b).** From 247 mg of **18a**, 45 mg (27%) of the minor isomer of **18c**, 53 mg (32%) of the major isomer of **18c**, and 30 mg (18%) of **18b** were obtained after chromatographic separation (5:1 hexane/ethyl acetate): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.19−2.20 (m, 9 H), 2.52−2.60 (m, 2 H), 4.15 (dd, 1 H, $J$ = 6.3, 12.2 Hz), 4.34 (dd, 1 H, $J$ = 3.7, 12.2 Hz), 5.03−5.10 (m, 2 H), 5.68−5.82 (m, 1 H); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 176.5, 136.0, 116.9, 70.19, 40.97, 36.37, 31.58, 29.67, 28.61, 24.21; IR (neat, cm$^{-1}$) 3020, 2930, 1732, 1248, 1217, 1047, 910; MS (CI) *m*/*z* (relative intensity) 209 (M + 41, 0.5), 169 (M + 1, 34), 151 (89), 133 (70), 123 (33), 109 (100), 81 (14), 69 (23); HRMS *m*/*z* calcd for $C_{10}H_{16}O_2$ 168.1151, found 168.1180.

**8-Methyl-3-oxabicyclo[5.2.1]decan-4-one (18c).** The minor isomer with a higher $R_f$ value on TLC: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.022 (d, 3 H, $J$ = 6.3 Hz), 1.36−1.46 (m, 1 H), 1.63−1.86 (m, 3 H), 1.89−2.14 (m, 4 H), 2.34−2.44 (m, 2 H), 2.48−2.56 (m, 1 H), 3.96 (dd, 1 H, $J$ = 3.4, 11.8 Hz), 4.59 (dd, 1 H, $J$ = 4.0, 11.8 Hz); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 180.3, 75.19, 40.10, 39.35, 38.88, 36.75, 34.19, 32.42, 24.84, 15.56; IR (neat, cm$^{-1}$) 3020, 2958, 2931, 2874, 1732, 1215; MS (EI) *m*/*z* (relative intensity) 168 ($M^+$, 0.5), 138 (36), 120 (5), 109 (8), 94 (100), 81 (63), 67 (70); HRMS *m*/*z* calcd for $C_{10}H_{16}O_2$ 168.1151, found 168.1139.

The major isomer with a lower $R_f$ value on TLC: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.030 (d, 3 H, $J$ = 6.7 Hz), 1.31−1.41 (m, 1 H), 1.50−1.55 (m, 1 H), 1.94−2.03 (m, 5 H), 2.13−2.27 (m, 1 H), 2.30−2.40 (m, 2 H), 2.50−2.60 (m, 1 H), 3.97 (dd, 1 H, $J$ = 5.4, 12.1 Hz), 4.58 (dd, 1 H, $J$ = 3.5, 12.1 Hz); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 178.4, 73.13, 43.95, 41.98, 40.88, 36.45, 34.31, 31.29, 28.82, 22.03; IR (neat, cm$^{-1}$) 3020, 2957, 2930, 2870, 1730, 1217; MS (EI) *m*/*z* (relative intensity) 168 ($M^+$, 5), 150 (17), 138 (14), 124 (49), 106 (16), 94 (98), 81 (95), 67 (74), 55 (79), 41 (100); HRMS *m*/*z* calcd for $C_{10}H_{16}O_2$ 168.1151, found 168.1173.

**9-Methyl-4-oxabicyclo[6.3.0]undecan-5-one (19c).** From 261 mg of **19a**, 70 mg (38%) of **19c** was obtained after chromatographic separation (3:1 hexane/ethyl acetate): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.875 (d, 3 H, $J$ = 7.1 Hz), 1.18−1.78 (m, 7 H), 1.89−2.19 (m, 4 H), 2.51 (ddd, 1 H, $J$ = 4.6, 8.7, 12.6 Hz), 2.68 (ddd, 1 H, $J$ = 4.4, 8.3, 12.6 Hz), 4.36 (t, 2 H, $J$ = 5.5 Hz); $^{13}$C NMR (125.7 MHz, $CDCl_3$) $\delta$ 176.8, 68.51, 45.54, 42.03, 39.04, 37.74, 33.94, 33.58, 30.79, 29.24, 15.13; IR (neat, cm$^{-1}$) 2932, 2861, 1732, 1248, 1038, 910; MS (EI) *m*/*z* (relative intensity) 182 ($M^+$, 1), 164 (1), 153 (13), 138 (24), 127 (10), 109 (28), 95 (48), 85 (49), 81 (52), 67 (51), 55 (100), 41 (69); HRMS *m*/*z* calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1311.

**9-(Ethoxycarbonyl)methyl-4-oxabicyclo[6.3.0]undecan-5-one (20b).** From 334 mg of **20a**, 100 mg (39%) of **20b** was obtained after chromatographic separation (3:1 hexane/ethyl acetate): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.25 (t, 3 H, $J$ = 7.1 Hz), 1.30−1.80 (m, 6 H), 1.82−1.96 (m, 3 H), 1.98−2.10 (m, 1 H), 2.15−2.41 (m, 2 H), 2.43−2.57 (m, 2 H), 2.63−2.71 (m, 1 H), 4.14 (q, 2 H, $J$ = 7.1 Hz), 4.30−4.41 (m, 2 H); $^{13}$C NMR (75.4 MHz, $CDCl_3$) $\delta$ 177.1, 173.9, 68.48, 60.66, 44.11, 42.56, 40.76, 37.18, 35.10, 33.60, 31.68, 30.56, 29.10, 14.34; IR (neat, cm$^{-1}$) 2939, 2864, 1726, 1278, 1194, 912; MS (EI) *m*/*z* (relative intensity) 254 ($M^+$, 2), 236 (4), 209 (19), 190 (6), 180 (59), 167 (84), 149 (18), 135 (17), 121 (39), 107 (92), 93 (78), 79 (73), 67 (61), 55 (100), 41 (81); HRMS *m*/*z* calcd for $C_{14}H_{22}O_4$ 254.1518, found 254.1527.

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