Radical-Mediated Ring Enlargement of Cyclobutenones: New Synthetic Potential of Squaric Acid

Yoshihiko Yamamoto, Masatomi Ohno, and Shoji Eguchi*

Contribution from the Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Chikusa, Nagoya 464-01, Japan

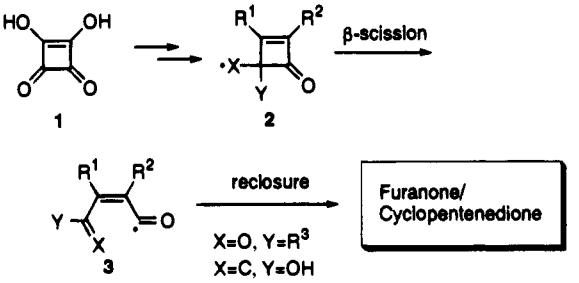
Received May 2, 1995[⊗]

Abstract: 4-Hydroxy-2-cyclobutenones, which are readily obtainable from diethyl squarate, reacted with lead tetraacetate to give 5-acetoxy-2(5*H*)-furanones and 5-alkylidene-2(5*H*)-furanones *via* oxy-radical-triggered ring opening (β-scission) and subsequent 5-*endo* reclosure. This method was extended to saturated four-membered α-ketol and applied to the synthesis of a natural product (*Z*-isomer of multicolanate). A carbon-centered radical-triggered reaction was also performed in which photolysis of a mixed anhydride of thiohydroxamic acid and (4-oxo-2-cyclobutenyl)-acetic acid afforded a 4-cyclopentene-1,3-dione rather than the furanone as a rearranged product. The similarity of these rearrangements is discussed using a PM3 calculation in terms of pentadienoyl radical to cyclopentenone radical cyclization and its oxa version.

Introduction

Cyclobutenes have received considerable attention as versatile synthetic intermediates because of their stereospecific ring-opening reactivity and its applicability to organic syntheses.[1] While these ring systems are obtainable primarily through cycloaddition, squaric acid (**1**) is a commercially available four-membered ring oxocarbon compound which has recently emerged as a C_4-synthon in the synthesis of highly substituted biologically active compounds based on the regioselective conversion to cyclobutenones and subsequent ring expansions.[2] Although various ring-transforming methods for the synthesis of naturally occurring products have been developed, previous studies principally focused on the electrocyclic ring opening of cyclobutenones and successive ring closure of the resulting vinyl ketene intermediates.[3] Nevertheless, some examples do not fall into this category; for example, the $Pd(OCOCF_3)_2$-catalyzed ring enlargement of 4-alkynylcyclobutenone to alkylidenecyclopentenone[4] and the rhodium(I)-catalyzed ring expansion of 4-cyclopropylcyclobutenones to cycloheptadienones[5] have been reported by Liebeskind and co-workers. With this perspective, we previously reported a novel ring transformation of 4-hydroxycyclobutenones *via* radical intermediates.[6] In this method, ring opening was effected by β-scission of a radical generated at the position adjacent to the cyclobutene ring, and the subsequent 5-*endo* reclosure of the resulting acyl radical intermediate gave rise to a cyclized product, 2(5*H*)-furanone, selectively.

Scheme 1



This new ring transformation can be further extended to the case of a carbon-centered radical. Thus, as illustrated in Scheme 1, acyl radical intermediates **3**, which are generated by β-scission from the initial radicals **2** (X = O, C), contribute to subsequent intramolecular reclosure, in the 5-*endo* mode, to form five-membered ring systems. In this paper, we provide a detailed examination of both ring transformations from squaric acid including mechanistic considerations. Associated methodologies have recently been reviewed by Dowd and Zhang.[7]

Results

Oxidative Rearrangement of 4-Hydroxycyclobutenones to 2(5*H*)-Furanones. The cycloalkoxy radical is a fascinating intermediate because it can be readily generated from a parent alcohol by various methods (*e.g.*, nitrite ester photolysis, hypohalite thermolysis, one-electron oxidation, *etc.*).[8] Once formed, the oxy radical is so reactive that C−C bonds adjacent to the radical center are efficiently cleaved to produce a carbonyl and a new carbon radical (β-scission). These features have been exploited in organic synthesis. For example, the β-scission of a fused bond in bridgehead-hydroxylated bicyclic compounds results in the synthesis of medium and large rings.[9] Recyclization *via* the addition of a transient radical produced by β-scission

[⊗] Abstract published in *Advance ACS Abstracts*, September 1, 1995.

(1) Durst, T.; Breau, L. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 5, Chapter 6.1.

(2) For a review, see: Moore, H. W.; Yerxa, B. R. *Chemtracts: Org. Chem.* **1992**, *5*, 273.

(3) For recent examples, see: (a) Liebeskind, L. S.; Wang, J. *J. Org. Chem.* **1993**, *58*, 3550. (b) Edwards, J. P.; Krysan, D. J.; Liebeskind, L. S. *Ibid.* **1993**, *58*, 3942. (c) Liebeskind, L. S.; Wang, J. *Tetrahedron* **1993**, *49*, 5461. (d) Gruski, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 6101. (e) Birchler, A. G.; Liu, F.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 7737. (f) Liu, H.; Gayo, L. M.; Sullivan, R. W.; Choi, A. Y. H.; Moore, H. W. *Ibid.* **1994**, *59*, 3284. (g) Winters, M. P.; Stranberg, M.; Moore, H. W. *Ibid.* **1994**, *59*, 7572. (h) Yamamoto, Y.; Ohno, M.; Eguchi, S. *Tetrahedron* **1994**, *50*, 7783.

(4) (a) Liebeskind, L. S.; Mitchell, D.; Foster, B. S. *J. Am. Chem. Soc.* **1987**, *109*, 7908. (b) Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 291. (c) Liebeskind, L. S.; Bombrum, A. *J. Org. Chem.* **1994**, *59*, 1149.

(5) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 4895.

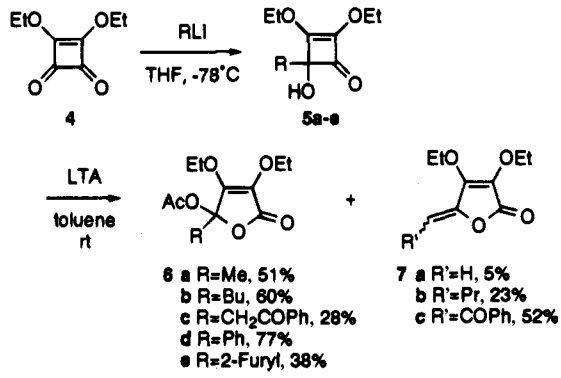
(6) Yamamoto, Y.; Ohno, M.; Eguchi, S. *J. Org. Chem.* **1994**, *59*, 4707.

(7) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091.

(8) Burn, P.; Waegelll, B. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1983; Vol. 3, Chapter 6.

0002-7863/95/1517-9653$09.00/0

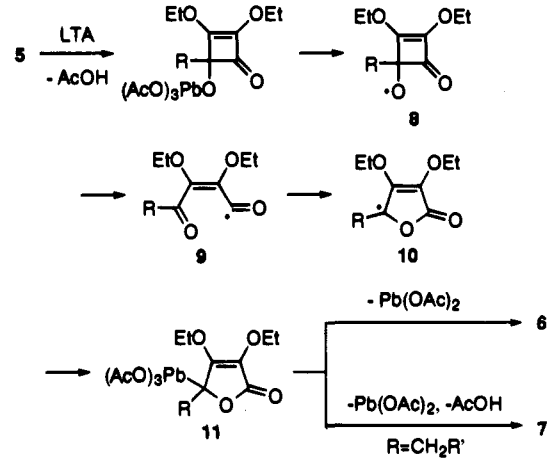
Scheme 2



to a radicophilic bond within the same molecule is also an important synthetic tactic.[10] Strained cyclobutoxy radicals inevitably undergo these types of reactions.[11] Accordingly, 4-hydroxycyclobutenones, which are derived from **1**, are believed to be susceptible to ring expansion *via* the oxy radical.

The action of lead tetraacetate (LTA)[12] on alcohols is the preferred method for generating the oxy radical in this system. The required alcohols **5a**−**e** were obtained from diethyl ester **4** and appropriate organolithium reagents.[13] Typically, the 4-methyl-substituted alcohol **5a** was treated with LTA (2 equiv) in dry toluene at ambient temperature. The reaction was monitored by TLC and was completed within 1 h. Standard workup and separation by preparative TLC gave the rearranged products 5-acetoxy-2(5*H*)-furanone **6a** and 5-methylene-2(5*H*)-furanone **7a** in a ratio of 10/1 (total yield 56%) (Scheme 2). The structure of major product **6a** was determined from spectral data. The IR spectrum indicated, instead of the hydroxy group of **5a**, two new carbonyl absorptions at 1782 and 1769 cm^{-1} corresponding to the acetoxy and furanone moieties. The ^{13}C NMR spectrum indicated the furanone structure due to the presence of one quaternary carbon (δ 99.1) and two pairs of olefinic and carbonyl carbons (δ 121.4, 156.4, 166.8, and 168.4). In the mass spectrum, the required M^+ (*m/z* 244, 85%) was observed together with the parent peak (*m/z* 202, $M^+-H_2C{=}C{=}O$). Minor product **7a** was characterized by carbonyl absorption at 1779 cm^{-1}, methylene signals in both the ^1H NMR (δ 4.95; s, 2 H) and ^{13}C NMR spectra (δ 92.1), and M^+ (*m/z* 184, 55%). In the same manner, rearranged products **6b** and **7b** were obtained in a ratio of 2.6/1 (total yield 83%) and **6c** and **7c**

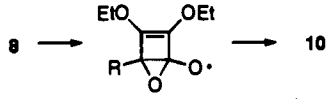
Scheme 3



were obtained in a ratio of 1/2.4 (total yield 80%) from **5b** and **5c**, respectively. In these cases, (*Z*)-isomers were formed selectively, as deduced from ^1H NMR.[14] However, only 5-acetoxy-2(5*H*)-furanones **6d** and **6e** were produced from **5d** and **5e**, respectively, which have no α-hydrogens to eliminate (Scheme 2). With **5d**, in which a phenyl group is located at a position at which it might interact with the acyl radical,[15a] the reaction with a carbonyl group was unaffected (*vide infra*).

Scheme 3 illustrates a possible mechanism for the formation of furanones **6** and **7** from **5**. The initial alkoxy radical **8** generated from alcohol **5** and LTA undergoes β-scission to produce acyl radical intermediate **9**. Recyclization (**9** → **10**) proceeds through addition of the radical to the carbonyl oxygen. The resulting lead(IV) intermediate **11** finally collapses *via* the reductive elimination of lead(II) acetate to give acetoxyfuranone **6** or alternatively *via* the concomitant elimination of acetic acid to give 5-ylidenefuranone **7**. A related *endo*-cyclization of the 4-oxo-2-butenyl radical has been reported in the photorearrangement of benzocyclobutenol to phthalide[11d] and is supported by recent calculations.[16] Oxy radical **8** might be added to a carbonyl group intramolecularly to give a 5-oxabicyclo-[2.1.0]pent-2-enyloxy radical intermediate which leads to the product by means of the process in Dowd's ring-expansion reaction.[17] However, this route seems to be energetically less favored (*vide infra*).

Dowd's ring-expansion mechanism



In the mechanism described above, the ring-opened acyl radical intermediate recyclized with the carbonyl double bond, although it is possible in **5d** that the phenyl group participates in 6-*exo-trig* cyclization.[15a] To obtain further insight into this process, another typical cyclization, 5-*exo-trig*, was examined

(9) (a) Akhtar, M.; Marsh, S. *J. Chem. Soc. (C)* **1966**, 937. (b) Mihailovic, M. L.; Iovenic, L.; Gasic, M.; Rogic, M.; Melera, A.; Stefanovic, M. *Tetrahedron* **1966**, *22*, 2345. (c) Freire, R.; Maarrero, J. J.; Rodrígurz, M. S.; Suárez, E. *Tetrahedron Lett.* **1986**, *27*, 383. (d) O'Dell, D. E.; Loper, J. T.; Macdonald, T. L. *J. Org. Chem.* **1988**, *53*, 5225. (e) Schreiber, S. L.; Hulin, B.; Liew, W.-F. *Tetrahedron* **1986**, *42*, 2945. (f) Posner, G. H.; Webb, K. S.; Asirvathan, E.; Jew, S. S.; Degl'Innocenti, A. *J. Am. Chem. Soc.* **1988**, *110*, 4754. (g) Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073. (h) Suginome, H.; Yamada, S. *Tetrahedron Lett.* **1987**, *28*, 3963.

(10) (a) Suginome, H.; Furusaki, A.; Kato, K.; Maeda, N.; Yonebayashi, I. *J. Chem. Soc., Perkin Trans. 1* **1981**, 236. (b) Suginome, H.; Yamada, S. *J. Org. Chem.* **1984**, *49*, 3753. (c) Orito, K.; Yorita, K.; Suginome, H. *Tetrahedron Lett.* **1991**, *32*, 5999. (d) Booker-Milburn, K. I. *Synlett* **1992**, 809. (e) Iwasawa, N.; Funahashi, M.; Hayakawa, S.; Narasaka, K. *Chem. Lett.* **1993**, 545.

(11) (a) Suginome, H.; Liu, C. F.; Furusaki, A. *Chem. Lett.* **1984**, 911. (b) *Ibid.* **1985**, 27. (c) Suginome, H.; Kobayashi, K.; Itoh, M.; Furusaki, A. *Ibid.* **1985**, 727. (d) Kobayashi, K.; Itoh, M.; Suginome, H. *Tetrahedron Lett.* **1987**, *28*, 3369. (e) Snider, B. B.; Vo, N. H.; Foxman, B. M. *J. Org. Chem.* **1993**, *58*, 7228. (f) Vo, N. H.; Snider, B. B. *Ibid.* **1994**, *59*, 5419. (g) Tsunoi, S.; Ryu, I.; Tamura, Y.; Yamasaki, S.; Sonoda, N. *Synlett* **1994**, 1009. (h) Horwell, D. C.; Morrell, A. I.; Roberts, E. *Tetrahedron Lett.* **1995**, *36*, 459.

(12) House, H. O. *Modern Synthetic Reactions*, 2nd. ed.; Benjamin Inc.: Menlo Park, CA, 1972; p 359.

(13) (a) Reed, M. W.; Pollart, D. J.; Perri, S. T.; Foland, L. D.; Moore, H. W. *J. Org. Chem.* **1988**, *53*, 2477. (b) Liebeskind, L. S.; Fengel, R. W.; Wirtz, R.; Shawe, T. T. *Ibid.* **1988**, *53*, 2482.

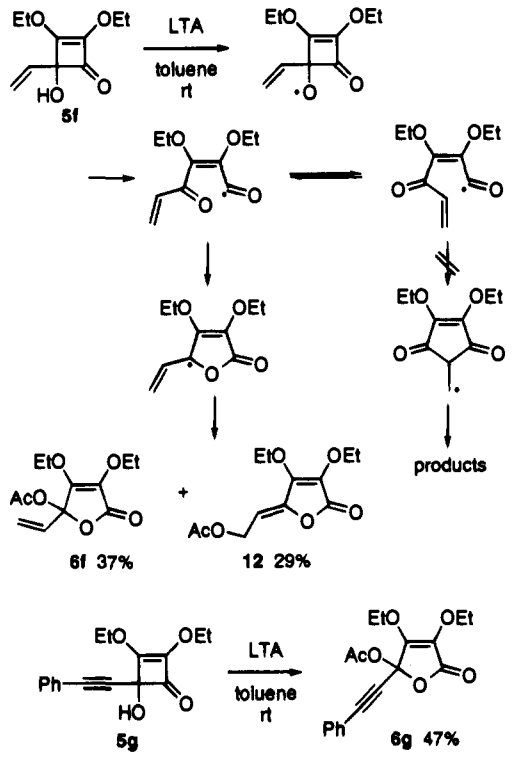
(14) Less than 3% of **7b** and none of **7c** was the (*E*)-isomer. The stereochemistry of **7b** was inferred by the relative chemical shift of the olefinic protons [(*Z*) δ 5.35, (*E*) δ 5.59; see ref 20], and that of **6c** was suggested by analogy with (*Z*)-5-phenacylidene-4-methoxy-2(5*H*)-furanone (see ref 3h). **12** is believed to have the same stereochemistry since it is the result of a similar reaction.

(15) (a) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 4, Chapter 4.2.3. (b) *Ibid.* Vol. 4, Chapter 4.2.2.

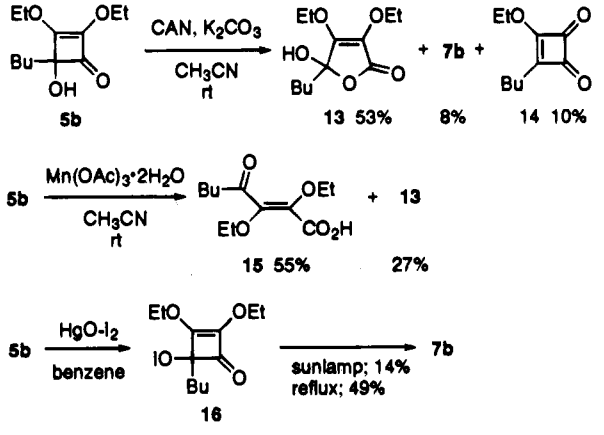
(16) The calculation for a benzo analog indicated that the 2-oxobenzocyclobutoxy radical is 27 kcal less stable than the 2-formylbenzoyl radical, which is, in turn, 26 kcal less stable than the 3-phthalidyl radical (Mendenhall, G. D.; Protasiewicz, J. D.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1994**, *116*, 1718).

(17) (a) Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 3493. (b) *Idem. Tetrahedron* **1989**, *45*, 77.

Scheme 4



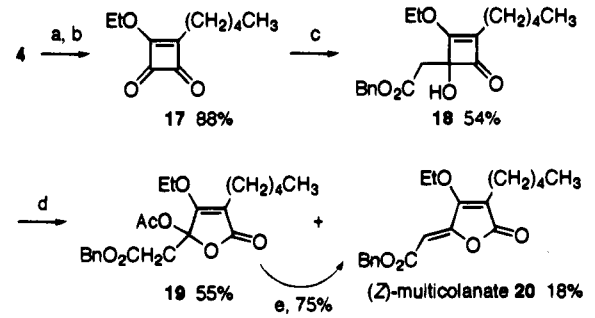
Scheme 5



using 4-vinyl-substituted **5f**.[15b] As depicted in Scheme 4, however, 2(5*H*)-furanone **6f** and alkylidene-2(5*H*)-furanone **12**[14] were obtained in a ratio of 1.3/1 (total yield 66%) rather than cyclopentenediones, which are 5-*exo-trig* cyclization products, under the same conditions. Similarly, 4-alkynyl-substituted **5g** gave 5-*endo* product **6g** at a yield of 47%. This selectivity implies that 5-*endo* cyclization involving a carbonyl terminus is a favorable process. This is supported by PM3 calculations (see Discussion). Alternatively, it can be explained by a cationic mechanism; that is, oxidation of the acyl radical intermediate **9** with Pb(IV) or Pb(III) produces an acyl cation which is responsible for the preferred interaction with a carbonyl group.[11g]

Although LTA was effective in this rearrangement, other oxidants were also tested (Scheme 5). Oxidative rearrangement of **5b** with CAN $[(NH_4)_2Ce(NO_3)_6 \cdot H_2O$ (2 equiv)/K_2CO_3/CH_3CN, room temperature, 1 h] afforded 5-hydroxyfuranone **13** together with **7b** and 3-ethoxy-4-butyl-3-cyclobutene-1,2-dione (**14**). The structure of **13** was supported by acetylation to **6b**. In addition, Mn(III) oxidation of **5b** [$Mn(OAc)_3 \cdot 2H_2O$ (2 equiv)/CH_3CN, room temperature, 1.5 h] afforded **13** together with **15**. However, anhydrous ferric chloride did not promote the rearrangement of **5b** and instead catalyzed the formation of **14** as a Lewis acid. Apart from this metallic oxidation, the

Scheme 6[a]



[a] Key: (a) $CH_3(CH_2)_4MgBr$, THF, −78 °C; (b) Cat. HCl, CH_2Cl_2, room temperature; (c) CH_2=COLi(OBn), THF, −78 °C; (d) LTA, toluene, room temperature; (e) DBU, THF, room temperature.

reaction occurred through a distinct free radical pathway by photolysis and thermolysis of hypoiodite **16** generated from **5b** and $HgO-I_2$.[9a-c] A solution of **5b** in benzene was treated with HgO (3 equiv) and I_2 (3 equiv) followed by irradiation (sunlamp) for 1 h to afford furanone **7b** at a yield of 14%, which was then refluxed in benzene for 1 h to give a higher yield (49%). Thus, free radical mechanism undoubtedly participates in the formation of furanones (Scheme 3).

A wide variety of 5-ylidenetetronic acid derivatives are found in nature[18] and some show useful biological properties (*e.g.*, agglomerin,[19a] tetronomycin,[19b] piperolide,[19c] pulvinic acid,[19d] and variabilin[19e]). The versatility of the furanone synthetic method described above was demonstrated in the stereoselective synthesis of (*Z*)-isomer of multicolanate **20**. Multicolanic acid[20] has a 4-(acylmethylene)tetronic acid skeleton, and its (*E*)-stereochemistry was previously established in the synthesis of a 1:3 mixture of methyl (*E*)- and (*Z*)-*O*-methylmulticolanate by the Wittig condensation of acid anhydride.[21] Our synthetic route is shown in Scheme 6. First, an alkyl side chain was introduced by reacting **4** with the corresponding Grignard reagent.[13b] The resulting **17** was functionalized with the lithium enolate of benzyl acetate to 4-hydroxycyclobutenone **18** having an ester group at the 4-position. The oxidative rearrangement of **18** with LTA occurred smoothly to give **19** and **20** in a ratio of 1/3 (total yield 73%); acetoxy tetronate **19** was converted to **20** in good yield with DBU in THF. The structure of **20** was confirmed by comparing the spectral data to those reported for the methyl ester.[21a]

Oxidative rearrangement with LTA was also attempted in a saturated ring system[22] (Scheme 7). Thus, α-hydroxycyclobutanones[23] **21a,b** were subjected to LTA oxidation to give the expected γ-acetoxy-γ-lactones **22a,b** in moderate yields. The success of this reaction implies that unsaturation is not required for ring closure. On the contrary, oxidation of the related α-hydroxycyclopentanone **21c** resulted in the formation of open-chain product **23** in a yield of 49% together with a trace amount

(18) (a) Pattenden, G. *Fortschr. Chem. Org. Naturst.* **1978**, *35*, 133. (b) Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625. (c) Yamamoto, M. *Yuki Gosei Kagaku Kyokaishi* **1981**, *39*, 25.

(19) (a) Terui, Y.; Sakazaki, R.; Shoji, J. *J. Antibiot.* **1983**, *35*, 133. (b) Keller-Juslén, C.; King, H. D.; Kuhn, M.; Loosli, H. R.; Pache, W.; Petcher, T. J.; Weber, H. P.; Wartburg, A. *Ibid.* **1982**, *35*, 142. (c) Hänsel, R.; Pelter, A. *Phytochemistry* **1971**, *10*, 1627. (d) Pattenden, G. *Prog. Chem. Org. Nat. Prod.* **1978**, *35*, 133. (e) Faulkner, D. J. *Tetrahedron Lett.* **1973**, 3821.

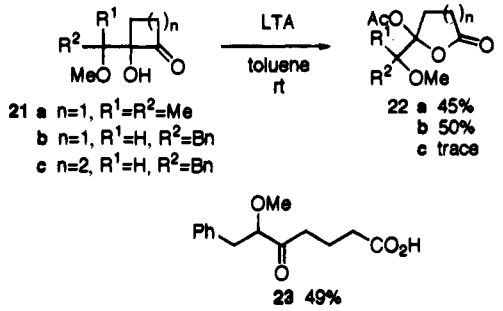
(20) Gudgeon, J. A.; Holker, J. S. E.; Simpson, T. J. *J. Chem. Soc., Chem. Commun.* **1974**, 636.

(21) (a) Begley, M. J.; Gedge, D. R.; Pattenden, G. *Ibid.* **1978**, 60. (b) Gedge, D. R.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1979**, 89.

(22) For examples of lead tetraacetate-promoted ring opening of an α-ketol, see: (a) Hurd, C. D.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1952**, *74*, 5324. (b) Anderson, R. J.; Henrick, C. A. *Ibid.* **1975**, *97*, 4327.

(23) Shimada, J.; Hashimoto, K.; Kim, B. H.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1759.

Scheme 7

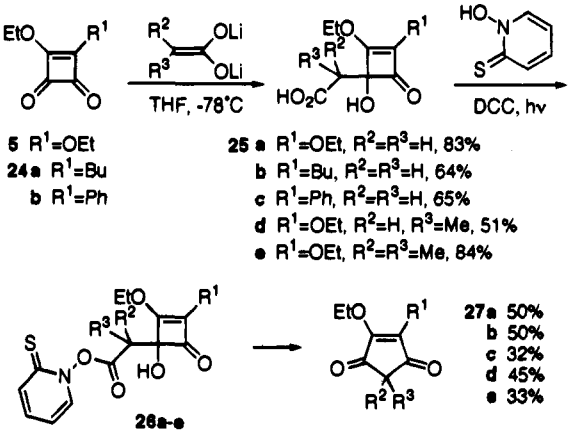


of cyclized product **22c**; 6-*endo* cyclization of the acyl radical intermediate is disfavored.[24] Thus, the present oxidative rearrangement is realized in four-membered ring α-ketols.

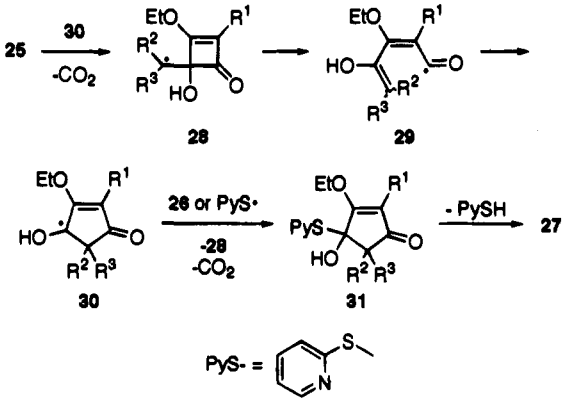
Decarboxylative Rearrangement of (1-Hydroxy-4-oxo-2-cyclobutenyl)acetic Acid to 4-Cyclopentene-1,3-dione. Naturally occurring cyclopentenediones with interesting biological activities have been isolated (*i.e.*, PGA derivatives,[25] pentenomycin,[26] terrein,[27] and similin A[28]). It may be useful to establish a general procedure for preparing highly substituted cyclopentenediones from substituted cyclobutenones.[29] In this respect, if the above oxidative rearrangement of 4-hydroxycyclobutenones can be realized faithfully with the carbon-centered radical as shown in Scheme 1, this class of compounds may be produced. Otherwise an enol-to-keto tautomerization may occur before rearrangement, leading to the furanones, exactly as with the oxy radical. It would also be interesting to determine if there were any similarity, in the respective mechanisms, or synthetic dichotomy. Therefore, we decided to investigate the reactivity of 1-hydroxy-4-oxo-2-cyclobutenylmethyl radical (**2**, X = C, Y = OH in Scheme 1).

A mixed anhydride of thiohydroxamic acid and cyclobutenyl-substituted acetic acid (Barton's ester)[30] is the reagent of choice for generating the desired starting radical.[31] Acids **25a**–**e** were prepared from the addition of ketene dilithio acetals to cyclobutenediones **5** and **24** in 51–84% yields. Barton's esters **26a**–**e** were then obtained by condensing these acids with *N*-hydroxythiopyridone in the presence of *N,N*-dicyclohexylcarbodiimide (DCC) and used without further purification. Typically, **26a** was subjected to photolysis (500 W tungsten lamp) in dichloromethane for 2 h. After removing the solvent, separation of the residue by flash chromatography gave the 5-*endo* cyclized product **27a** at a yield of 43%. When the reaction was carried out under high-dilution conditions, the yield was improved to 50% (Scheme 8). The cyclopentenedione structure of **27a** was confirmed as follows. The IR spectrum

Scheme 8



Scheme 9



showed strong absorptions at 1694 and 1622 cm^{-1} due to an enedione moiety. In the ^1H NMR spectrum, a singlet signal due to a methylene moiety (δ 2.89) was observed together with signals at δ 1.39 (6 H, t, J = 7.0 Hz) and 4.61 (4 H, q, J = 7.0 Hz) due to two ethoxy groups. The ^{13}C NMR spectrum showed one sp^3 signal (δ 41.2) and two sp^2 signals (δ 151.9 and 192.3), which were assigned to the ring carbons. The required M^+ (*m/z* 184, 65%) was demonstrated in the mass spectrum. Likewise, 3-butyl-substituted **25b** and 3-phenyl-substituted **25c** (in acetone) were transformed to the corresponding cyclopentenediones **27b** and **27c** at yields of 50 and 33%, respectively. The reaction of α-substituted acids **25d**,**e** was also examined; photolysis of monosubstituted acid **25d** gave cyclopentenedione **27d** at a yield of 45%, which is comparable to that of **27a**, while disubstituted **25e** gave **27e** at a lower yield (33%) because of a steric effect at the 5-*endo* cyclization stage (**29** → **30** in Scheme 9).

A proposed mechanism which accounts for the formation of **27** is outlined in Scheme 9. Photolysis of Barton's ester **26** produces a cyclobutenylmethyl radical **28**, which undergoes β-scission to give an unsaturated acyl radical (pentadienoyl radical) **29**. Prior to enol–keto tautomerization, recyclization (**29** → **30**) proceeds through addition of the radical to an enol end, just as with **9** → **10** in the case of the oxy-radical-initiated reaction. Finally, a product-like radical **30** is trapped with a thiyl radical to give cyclopentenedione **27** after elimination. Again, involvement of a bicyclo[2.1.0]pent-2-enyloxy radical intermediate is less likely for the same reasons as cited above.[17,32]

(24) Even acyl cation cyclization may give the same result; see ref 11g.

(25) (a) Kikuchi, H.; Tsukitani, Y.; Iguchi, K.; Yamada, Y. *Tetrahedron Lett.* **1982**, *23*, 5171. (b) Iguchi, K.; Kaneta, S.; Mori, K.; Yamada, Y.; Honda, A.; Mori, Y. *Ibid.* **1985**, *26*, 5787. (c) Baker, B. J.; Okuda, R. K.; Yu, P. T. K.; Scheuer, P. J. *J. Am. Chem. Soc.* **1985**, *107*, 2976.

(26) (a) Umino, K.; Furumai, T.; Matsuzawa, N.; Awataguchi, Y.; Ito, Y.; Okuda, T. *J. Antibiot.* **1973**, *26*, 506. (b) Shomura, T.; Hoshida, J.; Kondo, Y.; Watanabe, H.; Omoto, S.; Inoue, S.; Niida, T. *Kenkyu Nempo* **1976**, *16*, 1. (c) Noble, M.; Noble, D.; Fletton, R. A. *J. Antibiot.* **1978**, *31*, 15.

(27) Raistrick, H.; Smith, G. *Biochem. J.* **1935**, *29*, 606.

(28) Weber, H. A.; Swenson, D. C.; Gloser, J. B. *Tetrahedron Lett.* **1992**, *33*, 1157.

(29) (a) Zora, M.; Herndon, J, W. *J. Org. Chem.* **1994**, *59*, 699. (b) Sun, L.; Liebeskind, L. S. *Ibid.* **1994**, *59*, 6856; also see ref 4.

(30) (a) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1983**, 993. (b) Barton, D. H. R.; Zard, S. Z. *Pure Appl. Chem.* **1986**, *58*, 675. (c) Crich, D.; Quintero, L. *Chem. Rev.* **1989**, *89*, 1413.

(31) For examples of free-radical-mediated ring expansion using Barton's ester, see: (a) Green, S. P.; Whiting, D. A. *J. Chem. Soc., Chem. Commun.* **1992**, 1754. (b) Galatsis, P.; millan, S. D.; Faber, T. *J. Org. Chem.* **1993**, *58*, 1215.

(32) Although the energy maximum ($\Delta H^{\ddagger}$ = 8.5 kcal/mol) for expansion of the (2-oxocyclopentyl)methyl radical to the 3-oxocyclohexyl radical through Dowd's mechanism was obtained successfully by PM3 calculation; the analogous transition structure in this route was not estimated (see Discussion). Instead, a bicyclo[2.1.0]pent-2-ene-like structure was optimized by assuming a cyclopropane moiety fixed in the same geometry as in the above expansion, which gave an estimated value of $\Delta H \approx$ 35.5 kcal/mol.

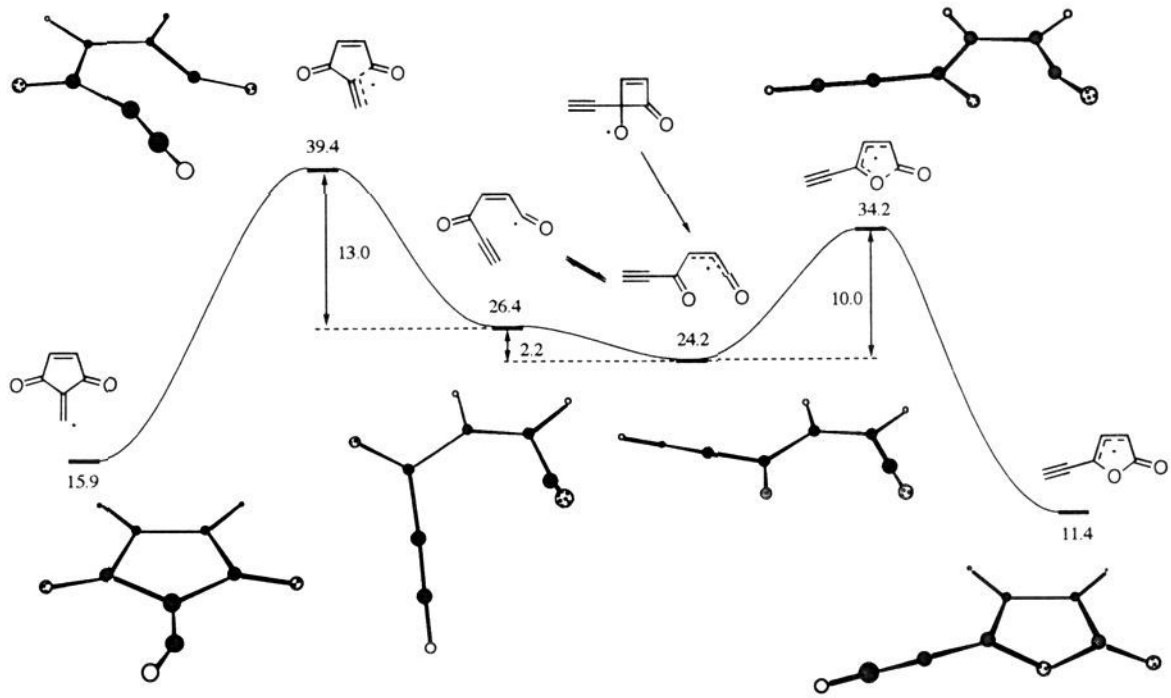


Figure 1. Schematic energy diagram for 5-*endo* vs 5-*exo* cyclizations from (1-ethynyl-4-oxo-2-cyclobutenyl)oxy radical. Indicated values show the heat of formation, ΔH, in kcal/mol with optimized geometries (UHF/PM3).

Discussion

Both oxygen- and carbon-centered radicals generated at the position adjacent to a cyclobutenone ring induced the present rearrangement. Ring strain relief prompted ring opening, and the resulting terminal acyl radical underwent intramolecular 5-*endo* ring closure as a carbonyl bond and an enol bond were formed. The resulting products were furanones from **5** and cyclopentenediones from **25**. If tautomerism were to predominate in **29**, the same furanone structure should result from the common intermediate. Furthermore, cyclization in **5f,g** occurred in the 5-*endo* mode rather than in the 5-*exo* mode. These facts indicate that the cyclizations of pentadienoyl radical to cyclopentenone radical (**29** → **30**) and its oxa version (**9** → **10**) occur with a relatively low energy barrier. To understand synthetically different but mechanistically similar results, we used UHF/PM3 calculations,[33] to study the energy of each of the possible radical intermediates and the transition states. The default routines in MOPAC version 5.0 were used for full optimization of geometry and to compute the heats of formation using the keyword PRECISE. Geometry optimizations of transition structures were performed using the nonlinear least-squares (NLLSQ) minimization routine. The resulting transition structures were subjected to a FORCE analysis, and in each case, only one negative value was found.

The calculation was first carried out for the 5-*endo vs* 5-*exo* cyclization reactions; for simplicity, 2,3-diethoxy and phenyl substituents were omitted from **5g**. A schematic representation of the minimum-energy path for each cyclization is given in Figure 1. The resulting oxy radical opens a cyclobutene ring with no saddle point to give an acyl radical with a carbonyl group inside, and with all of the atoms in the same plane. The formation of an ethynyl group inside results in a slightly higher energy. The 5-*endo* cyclized product (right hand) and 5-*exo* cyclized product (left hand) are then formed with an energy difference of 5.2 kcal. The former product is relatively more stable than the latter one. Thus, the 5-*endo* cyclization is an energetically favored process.

(33) Stewart, J. P. *Comput. Chem.* **1989**, *10*, 221.

We next performed calculations for the rearrangement of the carbon-centered radical; again, the molecule was simplified by not considering substituents (Figure 2). In this case, the carbon radical generated opens a cyclobutenone ring with a very low-energy transition state (6.2 kcal). At this stage, the transition structure for forming a bicyclo[2.1.0]pentenoxy radical (*i.e.*, Dowd's mechanism)[17] is estimated to have a much higher energy.[32] The acyl radicals formed have two extreme geometries with a hydroxyl group and a vinyl group inside. From these intermediates, the slightly stable radical which faces a vinyl group cyclizes, in the 5-endo mode, to a cyclopentenone radical with an energy barrier of only 14.4 kcal.

These calculations indicate that the resulting acyl radical is, in fact, a conjugated pentadienoyl radical with a flat U-shaped geometry, which can readily undergo rearrangement to a cyclopentenone radical. This is also true for the oxa version (*i.e.*, 5-oxapentadienoyl radical → furanone radical). Houk *et al.* discussed the analogous pattern of cationic and anionic pentadienyl → cyclopentenyl rearrangement using *ab initio* quantum mechanics.[34] Facile pentadienyl radical to cyclopentenone radical cyclization seems to be associated with the Nazarov reaction, which includes pentadienone to cyclopentenone cyclization.

Conclusion

4-Hydroxycyclobutenones **5** prepared from diethyl squarate and organolithium reagents were transformed to 5-acetoxy-2(5*H*)-furanones and 5-ylidene-2(5*H*)-furanones by treatment with LTA. This novel oxidative rearrangement can be explained in terms of an oxy-radical triggered ring opening (β-scission) and subsequent ring closure with the addition of the resulting acyl radical to a carbonyl oxygen. Similarly, the oxidation of cyclobutenones with an alkenyl (alkynyl) substituent at the 4-position also gave 2(5*H*)-furanones. The versatility of this oxidative rearrangement was demonstrated in the stereoselective

(34) Houk, K. N.; Li, Y.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682.

(35) Yamamoto, Y.; Nunokawa, K.; Okamoto, K.; Ohno, M.; Eguchi, S. *Synthesis* **1995**, 571.

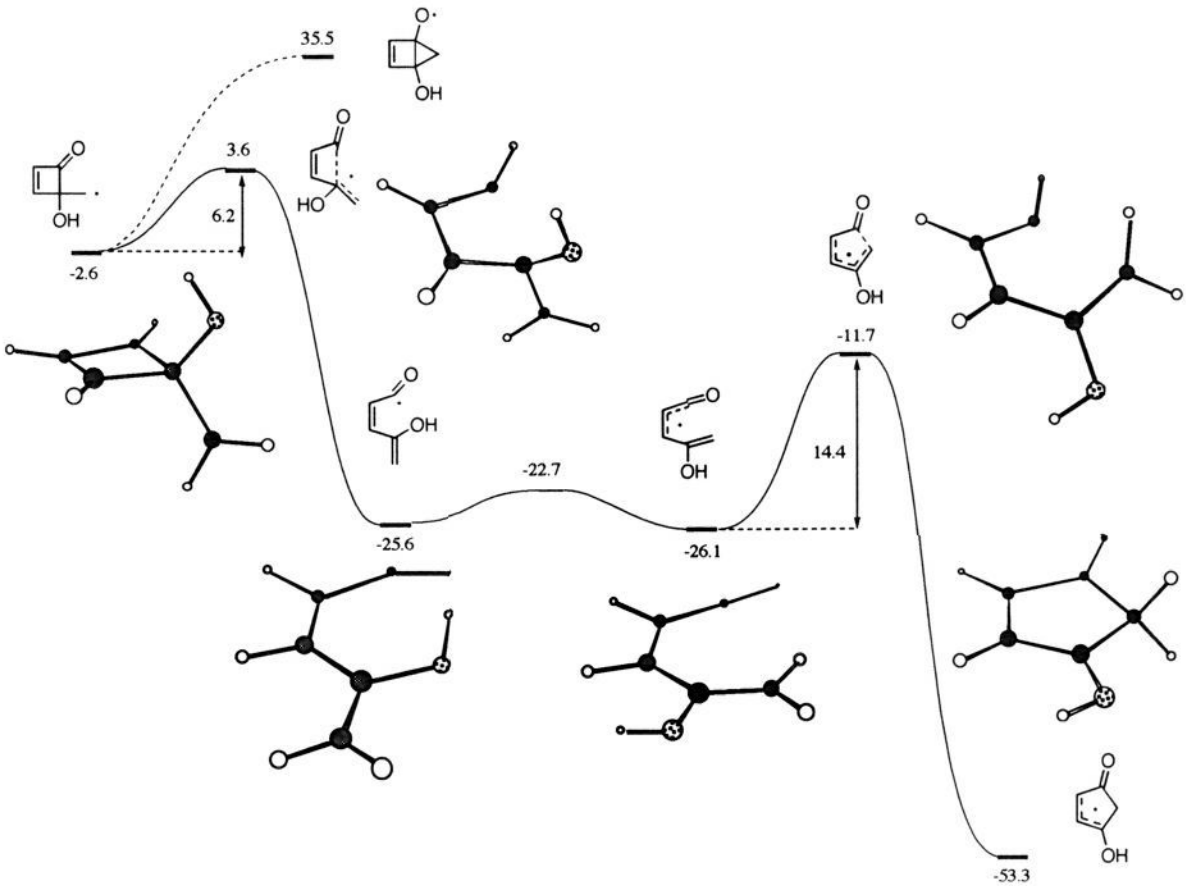


Figure 2. Schematic energy diagram for 5-*endo* cyclization from (1-hydroxy-4-oxo-2-cyclobutenyl)methyl radical. Indicated values show the heat of formation, ΔH, in kcal/mol with optimized geometries (UHF/PM3).

synthesis of the (*Z*)-isomer of a multicolanate. This rearrangement was further extended to saturated four-membered α-ketols to give γ-lactones; however, in the case of a five-membered ring, 6-*endo* cyclization was disfavored. While cationic 5-*endo* cyclization could not be ruled out in the above metallic oxidation reactions (*e.g.*, with LTA), the distinctive reaction with HgO/I_2 *via* a hypoiodite revealed that the radical intermediate was definitely involved in the ring-closure step.

In addition, an analogous ring enlargement triggered by a carbon-centered radical was realized by photolysis of Barton's esters **26** obtained from (1-hydroxy-4-oxo-2-cyclobutenyl)acetic acids **25** and *N*-hydroxythiopyridone. In this case, β-scission of the (4-oxo-2-cyclobutenyl)methyl radical produced a pentadienoyl radical, which underwent the same 5-*endo* cyclization as above to give a cyclopentene-1,3-dione. As a result, a common rearrangement was observed in the reactions of both **5** and **26**; pentadienoyl radical to cyclopentenone radical cyclization (or its oxa version) was a significant key process. In fact, this cyclization prevailed over keto−enol tautomerism as seen in **29** → **30** and 5-*exo-trig* ring closure as seen in **5f** → **6f**. PM3 calculations supported the energetic preference for this process.

In conclusion, this new method involving cyclobutenone ring opening suggests a new synthetic application for squaric acid. In addition, we believe that radical-mediated ring opening of cyclobutene and subsequent 5-*endo* ring closure may constitute a general ring-expansion methodology.

Experimental Section

General Procedure. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as an internal standard. Mass spectra were recorded on a JEOL JMS-AX 505 HA mass spectrometer. Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. THF was freshly distilled from Na and benzophenone. Toluene was dried over Na. Acetonitrile and diisopropylamine were dried over CaH_2, distilled, and stored over CaH_2. Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

Synthesis of 4-Hydroxycyclobutenones 5. Alcohols **5a**,**d**,**e**−**g** were prepared from diester **4** and the corresponding organolithium reagents (vinyl magnesium bromide for **5f**) using procedures in previous reports[13] which have described **5b**.[13a]

2,3-Diethoxy-4-hydroxy-4-methyl-2-cyclobutenone (5a): 84%; oil (elution H−A (3:1)); IR (neat) 3389, 1769, 1628 cm^{-1}; ^1H NMR δ 1.29 (3 H, t, J = 7.0 Hz), 1.43 (3 H, t, J = 7.0 Hz), 1.52 (3 H, s), 3.72 (1 H, br s), 4.28 (2 H, q, J =7.0 Hz), 4.44 and 4.51 (each 1 H, dq, J = 7.0, 10.4 Hz); ^{13}C NMR δ 15.2, 15.5, 19.3, 66.8, 69.2, 83.4, 132.0, 169.3, 188.5; MS (EI) *m/z* (relative intensity) 186 (M^+, 35), 169 (4), 129 (100), 113 (12). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.87; H, 7.76.

2,3-Diethoxy-4-hydroxy-4-phenyl-2-cyclobutenone (5d): 54%; oil (elution H−A (4:1)); IR (neat) 3383, 1771, 1620 cm^{-1}; ^1H NMR δ 1.33 (3 H, t, J = 7.0 Hz), 1.35 (3 H, t, J = 7.0 Hz), 3.71 (1 H, br s), 4.34 (2 H, q, J =7.0 Hz), 4.31 and 4.44 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.30−7.55 (5 H, m); ^{13}C NMR δ 15.1, 15.6, 67.2, 69.6, 87.7, 126.2, 128.6, 128.9, 134.6, 137.8, 166.5, 184.7; MS (EI) *m/z* (relative intensity) 248 (M^+, 100), 219 (41), 191 (82), 163 (24), 145 (48), 105 (88). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.74; H, 6.49.

2,3-Diethoxy-4-(2-furyl)-4-hydroxy-2-cyclobutenone (5e): 79%; oil (elution H−A (3:1)); IR (neat) 3383, 1775, 1624 cm^{-1}; ^1H NMR δ 1.34 (3 H, t, J = 7.0 Hz), 1.36 (3 H, t, J = 7.0 Hz), 3.96 (1 H, br s), 4.35 (2 H, q, J =7.0 Hz), 4.35 and 4.47 (each 1 H, dq, J = 7.0, 10.2 Hz), 6.38 (1 H, dd, J = 1.8, 3.4 Hz), 6.46 (1 H, dd, J = 1.0, 3.4 Hz),

7.40 (1 H, dd, J = 1.0, 1.8 Hz); ^{13}C NMR δ 15.1, 15.5, 67.3, 69.6, 84.5, 108.6, 111.3, 135.2, 143.1, 150.6, 165.4, 182.9; MS (EI) *m/z* (relative intensity) 238 (M^+, 100), 210 (14), 192 (15), 181 (22), 153 (38), 125 (16). Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.31; H, 6.11.

4-Ethenyl-2,3-diethoxy-4-hydroxy-2-cyclobutenone (5f): 46%; oil (elution H−A (5:1)); IR (neat) 3391, 1771, 1620 cm^{-1}; ^{1}H NMR δ 1.31 (3 H, t, J = 7.0 Hz), 1.41 (3 H, t, J = 7.0 Hz), 3.76 (1 H, br s), 4.30 (2 H, q, J =7.0 Hz), 4.39 and 4.47 (each 1 H, dq, J = 7.0, 10.2 Hz), 5.36 (1 H, dd, J = 1.0, 10.6 Hz), 5.54 (1 H, dd, J = 17.4, 1.0 Hz), 5.98 (1 H, dd, J = 17.4, 10.6 Hz); ^{13}C NMR δ 15.1, 15.5, 67.1, 69.5, 87.0, 109.9, 118.5, 135.0, 167.0, 185.4; MS (EI) *m/z* (relative intensity) 198 (M^+, 55), 170 (31), 142 (71), 113 (100). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.55; H, 7.16.

2,3-Diethoxy-4-hydroxy-4-(phenylethynyl)-2-cyclobutenone (5g): 100%; oil (elution H−A (5:1)); IR (neat) 3374, 2226, 1777, 1622 cm^{-1}; ^{1}H NMR δ 1.31 (3 H, t, J = 7.0 Hz), 1.47 (3 H, t, J = 7.0 Hz), 4.03 (1 H, br s), 4.32 (2 H, q, J =7.0 Hz), 4.59 (2 H, q, J = 7.0 Hz), 7.25−7.50 (5 H, m); ^{13}C NMR δ 15.2, 15.5, 67.4, 69.8, 79.1, 83.6, 88.9, 122.1, 128.6, 129.2, 132.2, 135.0, 165.1, 181.5; MS (EI) *m/z* (relative intensity) 272 (M^+, 15), 244 (28), 229 (53), 216 (46), 188 (32), 129 (100). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.58; H, 5.91.

Preparation of 2,3-Diethoxy-4-hydroxy-4-phenacyl-2-cyclobutenone (5c). To a solution of LDA prepared from *n*-BuLi (0.51 mL of 1.6 M hexane solution, 0.82 mmol) and diisopropylamine (83 mg, 0.82 mmol) in dry THF (1 mL) at −78 °C was added acetophenone (99 mg, 0.82 mmol) under a nitrogen atmosphere. The solution was stirred for 30 min and then transferred by syringe to a solution of diethyl squarate (**4**) (70 mg, 0.41 mmol) in dry THF (1 mL) at −78 °C. The solution was stirred for 30 min and then quenched with 5% aqueous NH_4Cl (5 mL) at −78 °C. The product was extracted with dichloromethane (5 mL × 4), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by flash chromatography (H−A (2:1)) to afford alcohol **5c** (86 mg, 72%): oil; IR (neat) 3397, 2226, 1773, 1678, 1632 cm^{-1}; ^{1}H NMR δ 1.29 (3 H, t, J = 7.0 Hz), 1.37 (3 H, t, J = 7.0 Hz), 3.45 and 3.55 (each 1 H, d, J = 17.2 Hz), 4.30 (2 H, q, J = 7.0 Hz), 4.44 (2 H, q, J = 7.0 Hz), 5.01 (1 H, br s), 7.43−8.00 (5 H, m); ^{13}C NMR δ 15.1, 15.5, 40.2, 67.0, 69.5, 84.2, 128.7, 129.0, 133.1, 134.2, 136.7, 166.9, 184.7, 200.0; MS (EI) *m/z* (relative intensity) 290 (M^+, 2), 170 (31), 120 (32), 113 (17), 105 (100). Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.10; H, 6.34.

Typical Procedure for Oxidation of Alcohol 5 with Lead Tetraacetate. To a solution of $Pb(OAc)_4$ (444 mg, 0.70 mmol) in dry toluene (2 mL) at ambient temperature was added a solution of alcohol **5a** (65 mg, 0.35 mmol) in dry toluene (1 mL), and the solution was stirred for 1 h under a nitrogen atmosphere. The reaction mixture was poured into water (10 mL), and insoluble materials were filtered off. The products in the filtrate were then extracted with dichloromethane (5 mL × 4), and the extract was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by preparative TLC (H−A (3:1)) to afford methylenefuranone **7a** (3 mg, 5%) and acetoxyfuranone **6a** (44 mg, 51%). The other alcohols **5b−e,g** were treated in the same manner to give products **6b−e,g** and **7b,c**. Furanones **6f** and **12** obtained from alcohol **5f** were separated by chromatography (H−A (15:1)).

5-Acetoxy-3,4-diethoxy-5-methyl-2(5*H*)-furanone (6a): oil; IR (neat) 1782, 1769, 1694 cm^{-1}; ^{1}H NMR δ 1.32 (3 H, t, J = 7.0 Hz), 1.38 (3 H, t, J = 7.0 Hz), 1.68 (3 H, s), 2.06, (3 H, s), 4.17 (2 H, q, J =7.0 Hz), 4.48 and 4.55 (each 1 H, dq, J = 7.0, 10.2 Hz); ^{13}C NMR δ 15.0, 15.2, 21.4, 23.5, 68.2, 68.3, 99.1, 121.4, 156.4, 166.8, 168.4; MS (EI) *m/z* (relative intensity) 244 (M^+, 85), 202 (100), 185 (33), 174 (39), 159 (21), 157 (52), 128 (68). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.02; H, 6.67.

3,4-Diethoxy-5-methylene-2(5*H*)-furanone (7a): oil; IR (neat) 1779, 1669, 1651 cm^{-1}; ^{1}H NMR δ 1.33 (3 H, t, J = 7.0 Hz), 1.40 (3 H, t, J = 7.0 Hz), 4.24 (2 H, q, J =7.0 Hz), 4.50 (2 H, q, J = 7.0 Hz), 4.95 (2 H, s); ^{13}C NMR δ 15.3, 15.4, 67.9, 68.5, 92.1, 124.0, 148.2, 148.6, 165.4; MS (EI) *m/z* (relative intensity) 184 (M^+, 55), 156 (27), 128 (100). Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.66; H, 6.60.

5-Acetoxy-5-butyl-3,4-diethoxy-2(5*H*)-furanone (6b): 60%; oil; IR (neat) 1782, 1692 cm^{-1}; ^{1}H NMR δ 0.90 (3 H, t, J = 6.8 Hz), 1.32 (3 H, t, J = 7.0 Hz), 1.37 (3 H, t, J = 7.0 Hz), 1.35−1.43 (6 H, m), 2.06, (3 H, s), 4.18 (2 H, q, J =7.0 Hz), 4.48 and 4.53 (each 1 H, dq, J = 7.0, 13.2 Hz); ^{13}C NMR δ 13.8, 15.2, 15.3, 21.6, 22.3, 24.0, 35.6, 68.2, 68.4, 101.0, 122.2, 155.4, 167.1, 168.5; MS (EI) *m/z* (relative intensity) 286 (M^+, 83), 244 (100), 227 (27), 216 (50), 199 (20), 170 (39), 159 (40). Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.73; H, 7.78.

5-Butylidene-3,4-diethoxy-2(5*H*)-furanone (7b): 23%; oil; IR (neat) 1773, 1688, 1653 cm^{-1}; ^{1}H NMR δ 0.94 (3 H, t, J = 7.2 Hz), 1.33 (3 H, t, J = 7.0 Hz), 1.39 (3 H, t, J = 7.0 Hz), 1.22−1.56 (2 H, m), 2.27 (2 H, q, J = 7.2 Hz), 4.20 (2 H, q, J =7.0 Hz), 4.49 (2 H, q, J = 7.0 Hz), 5.35 (1 H, t, J = 8.0 Hz); ^{13}C NMR δ 13.8, 15.2, 15.3, 22.4, 27.2, 67.8, 68.6, 110.2, 123.0, 142.1, 149.0, 165.9; MS (EI) *m/z* (relative intensity) 226 (M^+, 100), 198 (32), 169 (75), 156 (91), 141 (57), 128 (75), 113 (26). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.66; H, 8.06.

5-Acetoxy-3,4-diethoxy-5-phenacyl-2(5*H*)-furanone (6c): 28%; oil; IR (neat) 1786, 1771, 1694 cm^{-1}; ^{1}H NMR δ 1.31 (3 H, t, J = 7.0 Hz), 1.32 (3 H, t, J = 7.0 Hz), 2.08 (3 H, s), 3.46 and 4.02 (each 1 H, d, J = 15.2 Hz), 4.13 and 4.20 (each 1 H, dq, J = 7.0, 10.0 Hz), 4.44 and 4.51 (each 1 H, dq, J = 7.0, 10.0 Hz), 7.43−8.00 (5 H, m); ^{13}C NMR δ 15.1, 15.3, 21.7, 42.4, 68.3, 68.4, 99.0, 123.0, 128.8, 129.0, 134.0, 137.3, 154.4, 166.4, 168.3, 193.8; MS (EI) *m/z* (relative intensity) 348 (M^+, 38), 261 (19), 233 (16), 105 (100). Anal. Calcd for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found: C, 62.12; H, 5.71.

3,4-Diethoxy-5-phenacylidene-2(5*H*)-furanone (7c): 52%; crystals (mp 89−91 °C); IR (KBr) 1786, 1657, 1618 cm^{-1}; ^{1}H NMR δ 1.35 (3 H, t, J = 7.0 Hz), 1.44 (3 H, t, J = 7.0 Hz), 4.34 (2 H, q, J =7.0 Hz), 4.56 (2 H, q, J = 7.0 Hz), 6.48 (1 H, s), 7.42−7.99 (5 H, m); ^{13}C NMR δ 15.3, 15.4, 68.4, 68.6, 99.8, 125.3, 128.8, 128.9, 133.5, 138.4, 147.5, 150.8, 164.1, 188.4; MS (EI) *m/z* (relative intensity) 288 (M^+, 26), 183 (24), 147 (18), 105 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.61; H, 5.64.

5-Acetoxy-3,4-diethoxy-5-phenyl-2(5*H*)-furanone (6d): 77%; oil; IR (neat) 1783, 1690 cm^{-1}; ^{1}H NMR δ 1.28 (3 H, t, J = 7.0 Hz), 1.32 (3 H, t, J = 7.0 Hz), 2.15 (3 H, s), 4.18 and 4.24 (each 1 H, dq, J = 7.0, 9.8 Hz), 4.42 and 4.49 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.36−7.58 (5 H, m); ^{13}C NMR δ 15.0, 15.3, 21.6, 68.5 (2 C), 99.0, 121.6, 125.7, 128.8, 130.0, 135.6, 156.5, 167.1, 168.3; MS (EI) *m/z* (relative intensity) 306 (M^+, 60), 264 (84), 247 (31), 191 (35), 105 (100). Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.78; H, 5.88.

5-Acetoxy-3,4-diethoxy-5-(2-furyl)-2(5*H*)-furanone (6e): 38%; oil; IR (neat) 1782, 1691 cm^{-1}; ^{1}H NMR δ 1.33 (3 H, t, J = 7.0 Hz), 1.34 (3 H, t, J = 7.0 Hz), 2.16 (3 H, s), 4.21 and 4.26 (each 1 H, dq, J = 7.0, 9.8 Hz), 4.52 (2 H, q, J = 7.0 Hz), 6.41 (1 H, dd, J = 1.8, 3.4 Hz), 6.59 (1 H, dd, J = 1.0, 3.4 Hz), 7.45 (1 H, dd, J = 1.0, 1.8 Hz); ^{13}C NMR δ 15.1, 15.3, 21.5, 68.5, 68.6, 95.5, 109.9, 110.9, 122.4, 144.1, 147.3, 154.3, 166.5, 168.0; MS (EI) *m/z* (relative intensity) 296 (M^+, 81), 254 (100), 237 (60), 209 (28), 181 (44). Anal. Calcd for $C_{14}H_{16}O_7$: C, 56.76; H, 5.44. Found: C, 56.75; H, 5.45.

5-Acetoxy-5-ethenyl-3,4-diethoxy-2(5*H*)-furanone (6f): 37%; oil; IR (neat) 1784, 1690 cm^{-1}; ^{1}H NMR δ 1.32 (3 H, t, J = 7.0 Hz), 1.37 (3 H, t, J = 7.0 Hz), 2.10 (3 H, s), 4.19 (2 H, q, J = 7.0 Hz), 4.48 and 4.53 (each 1 H, dq, J = 7.0, 10.2 Hz), 5.42 (1 H, dd, J = 1.0, 10.6 Hz), 5.67 (1 H, dd, J = 1.0, 17.4 Hz), 5.92 (1 H, dd, J = 10.6, 17.4 Hz); ^{13}C NMR δ 15.1, 15.3, 21.6, 68.4 (2 C), 97.9, 120.0, 121.7, 132.1, 155.7, 166.8, 168.3; MS (EI) *m/z* (relative intensity) 256 (M^+, 65), 214 (100), 197 (35), 186 (50), 169 (27), 159 (14), 140 (47). Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.35; H, 6.17.

5-(Acetoxyethylidene)-3,4-diethoxy-2(5*H*)-furanone (12): 29%; oil; IR (neat) 1782, 1746, 1690, 1655 cm^{-1}; ^{1}H NMR δ 1.33 (3 H, t, J = 7.0 Hz), 1.39 (3 H, t, J = 7.0 Hz), 2.08 (3 H, s), 4.24 (2 H, q, J = 7.0 Hz), 4.50 (2 H, q, J = 7.0 Hz), 4.81 (2 H, d, J = 7.2 Hz), 5.45 (1 H, t, J = 7.2 Hz); ^{13}C NMR δ 15.2, 15.3, 20.8, 57.8, 68.0, 68.6, 102.0, 123.9, 144.7, 148.1, 164.6, 171.1; MS (EI) *m/z* (relative intensity) 256 (M^+, 48), 214 (100), 185 (73), 157 (54), 141 (24). Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.34; H, 6.19.

5-Acetoxy-3,4-diethoxy-5-(phenylethynyl)-2(5*H*)-furanone (6g): 51%; oil; IR (neat) 2240, 1792, 1692 cm^{-1}; ^{1}H NMR δ 1.35 (3 H, t, J = 7.0 Hz), 1.44 (3 H, t, J = 7.0 Hz), 2.15 (3 H, s), 4.21 and 4.27 (each 1 H, dq, J = 7.0, 9.6 Hz), 4.56 and 4.62 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.29−7.52 (5 H, m); ^{13}C NMR δ 15.1, 15.3, 21.4, 68.5, 68.8,

80.2, 87.7, 91.4, 120.8, 121.9, 128.7, 130.0, 132.5, 153.8, 165.8, 167.6; MS (EI) *m/z* (relative intensity) 330 (M^+, 77), 287 (24), 273 (63), 215 (22), 175 (18), 129 (100). Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.54; H, 5.40.

Oxidation of Alcohol 5b with Ceric Ammonium Nitrate. To a mixture of alcohol **5b** (88 mg, 0.39 mmol) and powdered potassium carbonate (216 mg, 1.56 mmol) in dry acetonitrile (1 mL) at ambient temperature was added a solution of $(NH_4)_2Ce(NO_3)_6 \cdot H_2O$ (428 mg, 0.78 mmol) in dry acetonitrile (2 mL) dropwise over 40 min. The reaction mixture was stirred for 1 h under a nitrogen atmosphere, poured into water (10 mL), and extracted with dichloromethane (5 mL × 4). The extract was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by preparative TLC (H—A (3:1)) to afford methylenefuranone **7b** (7 mg, 8%), hydroxyfuranone **13** (50 mg, 53%), and cyclobutenedione **14** (7 mg, 10%).

5-Butyl-3,4-diethoxy-5-hydroxy-2(5*H*)-furanone (13): oil; IR (neat) 3378, 1767, 1752, 1682 cm^{-1}; ^1H NMR δ 0.87 (3 H, t, J = 6.8 Hz), 1.15—1.45 (4 H, m), 1.31 (3 H, t, J = 7.2 Hz), 1.40 (3 H, t, J = 7.2 Hz), 1.91 (2 H, m), 4.13 (2 H, q, J =7.2 Hz), 4.15 (1 H, br s), 4.50 (2 H, q, J = 7.2 Hz); ^{13}C NMR δ 13.9, 15.2, 15.3, 22.4, 24.9, 35.7, 68.2, 68.8, 101.1, 121.1, 157.2, 168.6; MS *m/z* (relative intensity) 244 (M^+, 84), 187 (76), 171 (31), 159 (56), 131 (100). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00 ; H, 8.25 . Found: C, 58.74 ; H, 8.51.

Oxidation of Alcohol 5b with Manganese(III) Acetate. To a suspension of $Mn(OAc)_3 \cdot 2H_2O$ (113 mg, 0.42 mmol) in dry acetonitrile (2 mL) was added a solution of alcohol **5b** (49 mg, 0.21 mmol) in dry acetonitrile (1 mL) at ambient temperature. The reaction mixture was stirred for 1.5 h under a nitrogen atmosphere and poured into water (10 mL), and insoluble materials were filtered off. The products were then extracted with dichloromethane (5 mL × 4), and the extract was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by preparative TLC (H—A (3:1)) to afford carboxylic acid **15** (28 mg, 55%) and hydroxyfuranone **13** (14 mg, 27%).

(*E*)-2,3-Diethoxy-4-oxo-2-octenoic Acid (15): oil; IR (neat) 3341, 1763, 1686 cm^{-1}; ^1H NMR δ 0.89 (3 H, t, J = 7.4 Hz), 1.15—1.45 (4 H, m), 1.32 (3 H, t, J = 7 Hz), 1.42 (3 H, t, J = 7 Hz), 1.85 (2 H, m), 4.16 (2 H, q, J = 7 Hz), 4.54 (2 H, q, J = 7 Hz), 9.82 (1 H, br s); ^{13}C NMR δ 13.8, 15.2, 22.5, 24.6, 31.8, 68.3, 68.7, 107.6, 122.6, 154.5, 168.9; MS *m/z* (relative intensity) 244 (M^+, 5), 227 (100), 199 (35). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00 ; H, 8.25 . Found: C, 58.79 ; H, 8.46 .

Oxidation of Alcohol 5b with Mercury(II) Oxide and Iodine. A solution of alcohol **5b** (76 mg, 0.33 mmol), HgO (214 mg, 0.99 mmol), and I_2 (251 mg, 0.99 mmol) in dry benzene (10 mL) was irradiated with a 500 W tungsten lamp at ambient temperature for 1 h. The reaction mixture was washed with 10% $Na_2S_2O_3$ (5 mL), and the organic layer was dried (Na_2SO_4) and evaporated. The product was purified by preparative TLC (H—A (3:1)) to afford methylenefuranone **7b** (15 mg, 14%).

When a solution of **5b** (110 mg, 0.48 mmol), HgO (312 mg, 1.44 mmol), and I_2 (365 mg, 1.44 mmol) in dry benzene (10 mL) was refluxed for 1 h, the product was obtained at a yield of 49% after the same workup and separation.

Synthesis of Benzyl *O*-Ethyl-(*Z*)-multicolanate 20. Preparation of 3-Ethoxy-4-pentyl-3-cyclobutene-1,2-dione (17). To a solution of diethyl squarate (**4**) (340 mg, 2.0 mmol) in dry THF (2 mL) at −78 °C was added a solution of pentylmagnesium bromide prepared from Mg (97 mg, 4.0 mmol) and 1-bromopentane (604 mg, 4.0 mmol) under a nitrogen atmosphere. The reaction mixture was stirred for 30 min, quenched with 5% aqueous NH_4Cl (10 mL), and extracted with dichloromethane (5 mL × 4). The extracts were dried (Na_2SO_4) and evaporated. The residue was treated with 2 drops of concentrated HCl in dichloromethane (5 mL) for 1 h. The solution was then diluted with another 5 mL of dichloromethane and dried over K_2CO_3. After the solvent was evaporated, the residue was purified by chromatography (H—A (10:1)) to afford cyclobutenedione **17** (308 mg, 80%): oil; IR (neat) 1794, 1753, 1597 cm^{-1}; ^1H NMR δ 0.91 (3 H, m), 1.25—1.40 (4 H, m), 1.49 (3 H, t, J = 7.2 Hz), 1.59—1.78 (2 H, m), 2.61 (2 H, t, J = 7.2 Hz), 4.79 (2 H, q, J = 7.2 Hz); ^{13}C NMR δ 13.9, 15.6, 22.2, 25.0, 25.5, 31.8, 70.7, 185.2, 194.8, 196.0, 199.0; MS *m/z* (relative intensity) 196 (M^+, 9), 168 (20), 139 (100). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.28; H, 8.25.

Preparation of Benzyl (2-Ethoxy-1-hydroxy-4-oxo-3-pentyl-2-cyclobutenyl)acetate (18). To a solution of LDA prepared from *n*-BuLi (1.18 mL of 1.6 M hexane solution, 1.9 mmol) and diisopropylamine (192 mg, 1.9 mmol) in THF (2 mL) at −78 °C was added benzyl acetate (285 mg, 1.9 mmol) by syringe. The solution was stirred for 30 min and then transferred by syringe to a solution of **17** (308 mg, 1.6 mmol) in dry THF (1 mL) at −78 °C. The solution was stirred for 30 min and then quenched with 5% aqueous NH_4Cl (10 mL) at −78 °C. The product was extracted with dichloromethane (5 mL × 4), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by flash chromatography (H—A (4:1)) to afford ester **18** (301 mg, 54%): oil; IR (neat) 3366, 1750, 1615 cm^{-1}; ^1H NMR δ 0.88 (3 H, t, J = 6.8 Hz), 1.23—1.55 (6 H, m), 1.40 (3 H, t, J = 7.2 Hz), 2.08 (2 H, t, J = 7.4 Hz), 2.84 and 2.94 (each 1 H, d, J = 20 Hz), 4.33 and 4.41 (each 1 H, dq, J = 7.0, 9.6 Hz), 4.45 (1 H, br s), 5.14 and 5.21 (each 1 H, d, J = 12.2 Hz), 7.37 (5 H, s); ^{13}C NMR δ 14.0, 15.0, 22.4, 22.7, 27.5, 31.8, 37.6, 67.3, 68.9, 88.1, 127.5, 128.8, 128.9, 129.0, 135.6, 171.4, 181.0, 190.7; MS (EI) *m/z* (relative intensity) 300 (2), 253 (100), 213 (33), 209 (61): (CI), 347 (MH^+, 100). Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.56. Found: C, 69.08; H, 7.82.

Oxidation of Alcohol 18 with Lead Tetraacetate. As described for **5**, oxidation of **18** (301 mg, 0.87 mmol) with $Pb(OAc)_4$ (771 mg, 1.7 mmol) and chromatographic separation (H—A (8:1)) afforded acetoxyfuranone **19** (195 mg, 55%) and (*Z*)-multicolanate **20** (56 mg, 18%).

Spectral Data for 19: oil; IR (neat) 1773, 1744, 1676 cm^{-1}; ^1H NMR δ 0.89 (3 H, t, J = 6.2 Hz), 1.23—1.56 (6 H, m), 1.33 (3 H, t, J = 7.0 Hz), 2.01 (3 H, s), 2.28 (2 H, q, J = 7.4 Hz), 3.04 and 3.22 (each 1 H, d, J = 15.0 Hz), 4.27 and 4.35 (each 1 H, dq, J = 7.0, 9.2 Hz), 5.06 and 5.14 (each 1 H, d, J = 12.2 Hz), 7.35 (5 H, m); ^{13}C NMR δ 14.0, 15.1, 21.5, 22.4, 23.2, 29.4, 31.6, 40.4, 67.0, 67.9, 99.6, 104.6, 128.7 (2 C), 128.9, 135.6, 166.9, 167.0, 168.1, 171.2; MS (EI) *m/z* (relative intensity) 404 (M^+, 15), 344 (7), 210 (16), 185 (55), 91 (100). Anal. Calcd for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found: C, 65.27; H, 7.04.

Spectral Data for 20: oil; IR (neat) 1790, 1725, 1638 cm^{-1}; ^1H NMR δ 0.89 (3 H, t, J = 6.4 Hz), 1.2—1.6 (6 H, m), 1.42 (3 H, t, J = 7 Hz), 2.45 (2 H, t, J = 8 Hz), 4.40 (2 H, q, J =7 Hz), 5.24 (2 H, s), 7.3—7.5 (5 H, m); ^{13}C NMR δ 13.9, 15.2, 22.4, 23.6, 29.8, 31.6, 66.6, 68.0, 95.1, 107.4, 128.6 (2 C), 128.9, 136.1, 153.5, 161.2, 163.8, 169.6; MS *m/z* (relative intensity) 344 (M^+, 2), 238 (100), 210 (26), 181 (32). Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.62; H, 7.12.

Transformation of Acetoxytetronate 19 to 20. To a solution of **19** (96 mg, 0.24 mmol) in THF (1 mL) was added diazabicyclo[5.4.0]-undec-7-ene (40 mg, 0.26 mmol), and the solution was stirred for 10 min at ambient temperature. The reaction mixture was diluted with dichloromethane (10 mL), washed with water, and dried over Na_2SO_4. After evaporating the solvent, the residue was subjected to chromatography (H—A (8:1)) to afford **20** (63 mg, 75%).

General Procedure for Oxidation of Alcohols 21 with Lead Tetraacetate. Alcohols **21a—c** were oxidized by the procedure described for **5**, and the products were separated by chromatography (eluent H—A (2:1)).

4-Acetoxy-4-(1-methyl-1-methoxyethyl)-4-butanolide (22a): 45%; oil; IR (neat) 1792, 1748 cm^{-1}; ^1H NMR δ 1.25 and 1.30 (each 3 H, s), 2.09 (3 H, s), 2.19—3.02 (4 H, m), 3.26 (3 H, s); ^{13}C NMR δ 18.0, 19.3, 21.8, 26.3, 29.4, 50.2, 77.8, 111.2, 169.7, 176.6; MS (EI) *m/z* (relative intensity) 157 (7), 125 (20), 73 (100); (CI) 217 (MH^+, 13), 157 (100). Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.51; H, 7.48.

4-Acetoxy-4-(2-phenyl-1-methoxyethyl)-4-butanolide (22b): 50% (diastereomeric mixture *ca.* 3:1); oil; IR (neat) 1821, 1751 cm^{-1}; ^1H NMR δ 1.99 and 2.22 (1 H and 2 H, respectively, s), 1.5—3.1 (6 H, m), 3.23 and 3.34 (1 H and 2 H, respectively, s), 3.69 and 3.89 ($^1/_3$ H and $^2/_3$ H, respectively, dd, J = 5.0, 7.4 Hz), 7.12—7.34 (5 H, m); ^{13}C NMR δ 28.5 and 28.6, 32.8 and 32.7, 38.3 and 38.1, 58.7 and 60.6, 87.9 and 84.9, 109.7, 127.0 and 126.8, 128.7, 129.7 and 129.8, 137.2 and 138.5, 169.1 and 168.9, 175.9; MS (EI) *m/z* (relative intensity) 218 (23), 187 (17), 135 (100); (CI) 276 (MH^+, 4), 220 (100). Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.55; H, 6.71.

6-Methoxy-5-oxo-7-phenylheptanoic acid (23): 49%; oil; IR (neat) 3500−2500 (broad), 1713 cm^{-1}; ^1H NMR δ 1.84 (2 H, tt, J = 7.0, 7.2 Hz), 2.33 (2 H, t, J = 7.2 Hz), 2.43 and 2.56 (each 1 H, dt, J = 7.0, 18.6 Hz), 2.88 (1 H, dd, J = 7.4, 14.2 Hz), 2.98 (1 H, dd, J = 5.2, 14.2 Hz), 3.32 (3 H, s), 3.84 (1 H, dd, J = 5.2, 7.4 Hz), 7.17−7.34 (5 H, m), 10.03 (1 H, br s); ^{13}C NMR δ 17.9, 33.0, 37.4, 38.2, 58.6, 88.0, 127.0, 128.8, 129.7, 137.2, 179.7, 212.4; MS (EI) *m/z* (relative intensity) (no molecular ion) 218 (11), 163 (1), 135 (100), 103 (27); (CI) 251 (MH^+, 100), 219 (29). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.00; H, 7.43.

Typical Procedure for Synthesis of Carboxylic Acids 25. To a solution of LDA prepared from *n*-BuLi (3.71 mL of 1.6 M hexane solution, 6.0 mmol) and diisopropylamine (607 mg, 6.0 mmol) in THF (4 mL) at −78 °C was added acetic acid (180 mg, 3.0 mmol) by syringe. The solution was stirred for 30 min and then transferred by syringe to a solution of diester **4** (170 mg, 1.0 mmol) in dry THF (2 mL) at −78 °C. The solution was stirred for 2 h and then quenched with 1 N HCl (10 mL) at −78 °C. The product was extracted with dichloromethane (5 mL × 4), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by flash chromatography (H−A (1:1)) to afford carboxylic acid **25a** (190 mg, 83%). The other acids **25b−e** were obtained in the same manner from the corresponding esters and alkanoic acids.

(2,3-Diethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)acetic Acid (25a): oil; IR (neat) 3300, 1771, 1717, 1618 cm^{-1}; ^1H NMR δ 1.30 (3 H, t, J = 7.0 Hz), 1.43 (3 H, t, J = 7.0 Hz), 2.82 and 2.95 (each 1 H, d, J = 16.0 Hz), 4.31 (2 H, q, J = 7.0 Hz), 4.47 and 4.52 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.82 (2 H, br s); ^{13}C NMR δ 15.1, 15.5, 37.6, 67.2, 70.0, 83.0, 133.0, 167.0, 175.1, 185.7; MS (EI) *m/z* (relative intensity) 230 (M^+, 75), 212 (12), 202 (67), 184 (64), 173 (25), 168 (42), 156 (89), 145 (68), 128 (62), 112 (100). Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.40; H, 5.90.

(3-Butyl-2-ethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)acetic Acid (25b). This was obtained from **24a**[13a] and acetic acid in 64% yield: oil (eluent H−A (1:1)); IR (neat) 3300, 1748, 1717, 1605 cm^{-1}; ^1H NMR δ 0.90 (3 H, t, J = 7.2 Hz), 1.46 (3 H, t, J = 7.0 Hz), 1.22−1.58 (4 H, m), 2.12 (2 H, t, J = 8.4 Hz), 2.81 and 2.96 (each 1 H, d, J = 15.6 Hz), 4.42 and 4.52 (each 1 H, dq, J = 7.0, 9.6 Hz), 7.55 (2 H, br s); ^{13}C NMR δ 13.7, 15.0, 22.2, 22.6, 29.7, 38.2, 69.3, 87.6, 127.2, 174.3, 182.2, 193.2; MS (EI) *m/z* (relative intensity) 242 (M^+, 19), 196 (48), 167 (22), 154 (48), 125 (100). Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.15; H, 7.78.

(2-Ethoxy-1-hydroxy-4-oxo-3-phenyl-2-cyclobutenyl)acetic Acid (25c). This was obtained from **24b**[35] and acetic acid in 65% yield: crystals (mp 159−162 °C) (eluent H−A (1:1)); IR (KBr) 2970, 1740, 1709, 1620, 1593 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.45 (3 H, t, J = 7.0 Hz), 2.84 (2 H, s), 4.56 and 4.64 (each 1 H, dq, J = 7.0, 10.0 Hz), 6.85 (1 H, br s), 7.24−7.65 (5 H, m), 12.45 (1 H, br s); ^{13}C NMR (DMSO-d_6) δ 15.0, 39.4, 69.4, 90.3, 122.6, 126.5, 128.1, 129.1, 129.3, 170.9, 182.3, 188.8; MS (EI) *m/z* (relative intensity) 262 (M^+, 16), 216 (100), 188 (9), 145 (21). Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.15; H, 5.34.

2-(2,3-Diethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)propanoic Acid (25d). This was obtained from **4** and propanoic acid in 51% yield (*ca.* 1:1 diastereomeric mixture); oil (eluent H−A (2:1)); IR (neat) 3400, 1771, 1717, 1620 cm^{-1}; ^1H NMR δ 1.24 and 1.30 (each $^3/_2$ H, d, J = 7.2 Hz), 1.31 (3 H, t, J = 7.0 Hz), 1.42 and 1.44 (each $^3/_2$ H, t, J = 7.0 Hz), 2.96 and 3.01 (each $^1/_2$ H, q, J = 7.2 Hz), 4.31 (2 H, q, J = 7.0 Hz), 4.41−4.58 (2 H, m), 7.27 (2 H, br s); ^{13}C NMR δ 12.8 and 13.1, 15.5 (2 C) and 15.2 (2 C), 42.4 and 42.3, 67.2 (2 C), 70.1 and 70.0, 86.2 and 86.9, 133.6 and 133.9, 166.6 and 166.3, 178.2 and 177.6, 185.3 and 185.5; MS (EI) *m/z* (relative intensity) 244 (M^+, 39), 198 (44), 170 (53), 142 (32), 113 (36), 85 (100). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.35; H, 6.30.

2-(2,3-Diethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)-2-methylpropanoic Acid (25e). This was obtained from **4** and 2-methylpropanoic acid in 84% yield: oil (eluent H−A (2:1)); IR (neat) 3300, 1769, 1705, 1616 cm^{-1}; ^1H NMR δ 1.31 (3 H, d, J = 7.0 Hz), 1.31 and 1.39 (each 3 H, s), 1.43 (3 H, t, J = 7.0 Hz), 4.29 and 4.35 (each 1 H, dq, J = 7.0, 10.2 Hz), 4.47 and 4.53 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.27 (2 H, br s); ^{13}C NMR δ 15.2, 15.6, 21.8, 22.1, 45.3, 67.2, 70.1, 89.1, 134.0, 166.3, 180.1, 185.8; MS (EI) *m/z* (relative intensity) 258 (M^+, 34), 212 (61), 184 (63), 156 (51), 127, (42), 115 (100). Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 56.02; H, 6.81.

Typical Procedure for Photorearrangement of Barton's Ester of Carboxylic Acid 25. A solution of carboxylic acid **25a** (111 mg, 0.48 mmol) in dry dichloromethane (20 mL) was added dropwise to a solution of *N*-hydroxy-2-thiopyridone (74 mg, 0.58 mmol) and *N,N*-dicyclohexylcarbodiimide (119 mg, 0.58 mmol) in dry dichloromethane (5 mL), while being irradiated with a 500 W tungsten lamp for 40 min (a Dimroth condenser was attached because the solution was heated to reflux). The solution was irradiated for an additional 3 h. Insoluble materials were filtered off and the filtrate was evaporated to dryness. Flash chromatography (H−A (10:1)) of the residue afforded cyclopentenedione **27a** (44 mg, 50%). The other carboxylic acids **25b−e** were treated similarly to give cyclopentenediones **27b−e**.

4,5-Diethoxy-4-cyclopentene-1,3-dione (27a): oil; IR (neat) 1748 (sh), 1694, 1622 cm^{-1}; ^1H NMR δ 1.39 (6 H, t, J = 7.0 Hz), 2.89 (2 H, s), 4.61 (4 H, q, J = 7.0 Hz); ^{13}C NMR δ 15.7, 41.2, 68.2, 151.9, 192.3; MS (EI) *m/z* (relative intensity) 184 (M^+, 65), 156 (21), 128 (34), 100 (100). Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.49; H, 6.77.

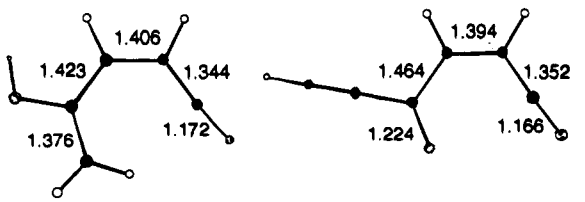
5-Butyl-4-ethoxy-4-cyclopentene-1,3-dione (27b): 50%; oil (eluent H−A (10:1)); IR (neat) 1742 (sh), 1696, 1616 cm^{-1}; ^1H NMR δ 0.92 (3 H, t, J = 7.2 Hz), 1.38 (3 H, t, J = 7.0 Hz), 1.24−1.56 (4 H, m), 2.39 (2 H, t, J = 7.8 Hz), 2.89 (2 H, s), 4.69 (2 H, q, J = 7.0 Hz); ^{13}C NMR δ 13.8, 15.9, 21.7, 22.7, 29.7, 42.3, 68.0, 142.2, 166.5, 196.3, 196.9; MS (EI) *m/z* (relative intensity) 196 (M^+, 5), 168 (100), 154 (66), 139 (43), 125 (73). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.27; H, 8.27.

4-Ethoxy-5-phenyl-4-cyclopentene-1,3-dione (27c): 32%; crystals (mp 41−43 °C) (eluent H−A (10:1)); IR (KBr) 1736 (sh), 1688, 1586 cm^{-1}; ^1H NMR δ 1.41 (3 H, t, J = 7.0 Hz), 3.06 (2 H, s), 4.76 (2 H, q, J = 7.0 Hz), 7.38−7.91 (5 H, m); ^{13}C NMR δ 15.9, 42.7, 69.1, 128.4, 128.6, 129.9 (2 C + 1 C), 135.4, 164.8, 195.7, 196.1; MS (EI) *m/z* (relative intensity) 216 (M^+, 71), 188 (54), 160 (100), 145 (59), 132 (77), 118 (79). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.17; H, 5.63.

4,5-Diethoxy-2-methyl-4-cyclopentene-1,3-dione (27d): 45%; crystals (mp 57−58 °C) (eluent H−A (10:1)); IR (KBr) 1682, 1620 cm^{-1}; ^1H NMR δ 1.24 (3 H, d, J = 7.4 Hz), 1.39 (6 H, t, J = 7.0 Hz), 2.75 (1 H, q, J = 7.4 Hz), 4.58 and 4.64 (each 2 H, dq, J = 7.0, 10.2 Hz); ^{13}C NMR δ 11.0, 15.7, 44.8, 68.1, 150.5, 196.3; MS (EI) *m/z* (relative intensity) 198 (M^+, 100), 170 (21), 142 (37), 114 (94). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.61; H, 7.10.

4,5-Diethoxy-2,2-dimethyl-4-cyclopentene-1,3-dione (27e): 33%; crystals (mp 54−55 °C) (eluent H−A (10:1)); IR (KBr) 1680, 1624 cm^{-1}; ^1H NMR δ 1.18 (6 H, s), 1.39 (6 H, t, J = 7.0 Hz), 4.61 (4 H, q, J = 7.0 Hz); ^{13}C NMR δ 15.7, 20.2, 46.6, 68.0, 148.8, 199.6; MS (EI) *m/z* (relative intensity) 212 (M^+, 100), 184 (27), 156 (81), 128 (31), 100 (18). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.20; H, 7.65.

Calculations. A semiempirical calculation (UHF/PM3) was carried out using MOPAC program Ver. 5.00 (QCPE No. 445): Stewart, J. P. *QCPE Bull.* **1989**, *9*, 10. Hirano, T. *JCPE Newsl.* **1989**, *1* (2), 36. Revised as Ver. 5.01 by J. Toyoda for Apple Macintosh. The representative bond length (Å) of a pentadienoyl radical (left) and an oxa analog (right) can be obtained as follows:



In the transition state to a cyclopentenone radical (or its oxa analog), the partial C···C=O single bond is 2.232 Å long (the O···C=O single bond is 1.931 Å long).

Acknowledgment. Y.Y. is grateful to JSPS for Research Fellowships for Young Scientists.

JA951416T