$PhI(OAc)_2$-Promoted Rearrangement of the Hydroxyl Group: Ring Expansion of 4-Hydroxy-2-cyclobutenone to 2(5*H*)-Furanone in Comparison with Ring Cleavage of the α-Hydroxycycloalkanone to the ω-Formyl Ester

Masatomi Ohno*

Department of Materials Science and Engineering, Toyota Technological Institute, 2−12−1 Hisakata, Tempaku, Nagoya 468-8511, Japan

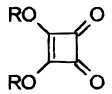
Isamu Oguri and Shoji Eguchi

Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa, Nagoya 464-8603, Japan

Received April 27, 1999

Reaction of 4-hydroxy-2-cyclobutenones with $PhI(OAc)_2$ in 1,2-dichloroethane at reflux temperature gave rise to 5-acetoxy-2(5*H*)-furanones as a rearranged product, formation of which is explained by ring cleavage of the once formed hypervalent iodine intermediate and following recyclization of the resulting acyl cation with a carbonyl oxygen. Likewise, 5-methoxy-2(5*H*)-furanones were obtained in better yields by using methanol as both a solvent and a nucleophile. Extension of this reaction to simple 2-hydroxycycloalkanones resulted in ring cleavage to methyl ω-formylalkanoates under milder conditions. In this case, the mechanism is explained by known glycol cleavage with $PhI(OAc)_2$.

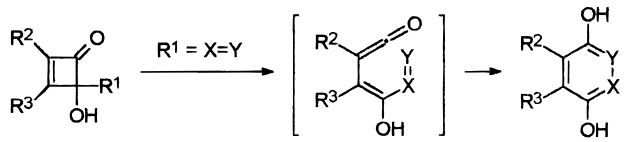
Squaric acid (**1**) has been exploited as a useful C-4 synthon in organic syntheses,[1] which are realized mainly with 4-hydroxy-2-cyclobutenone derivatives **3** obtained



1 R = H
2 R = Et

from **1**.[2] While tandem electrocyclic ring-opening and -closure reactions have been demonstrated to be effective for the ring transformation of **3** to poly-substituted six-membered carbo- and heterocycles **4** (Scheme 1),[1,3] another reaction induced by a reactive intermediate is also considered to be alternative and useful for ring expansion to five-membered ring systems.[4] Ring strain of **3** can be relieved by the trigger of a reactive intermediate, and the opened structure of this intermediate is ready for recyclization with an unsaturated end. This sequence was first realized in the radical-mediated reaction to give 2(5*H*)-furanones **5** via an oxy-centered radical and 4-cyclopentene-1,3-dione **6** via an carbon-centered radical (Scheme 2).[5] In the former case, unusual nonradical

Scheme 1



3 **4**

recombination between carbonyl and ketene ends was estimated by the calculations,[6] and such a unique process is in fact utilized for a new annulation method by Pattenden.[7] Similar ring transformation was achieved by the trigger of carbocation and carbene (carbenoid) intermediates generated from diazo-functionalized 4-hydroxy-2-cyclobutenones; the cationic route produced both 2-ylidenefuranone **7** and 4-cyclopentene-1,3-diones **8** but the carbenoid route directed predominant formation of **8** via a metallacyclic intermediate.[8]

We have now envisaged an additional reaction involving an electron-deficient oxygen center for the above type of ring transformation. To this end, an effective leaving group is necessary on an oxygen atom and desirable to be introduced on a hydroxyl group with ease. A hypervalent iodine reagent seems to satisfy these requirements. Facile displacement on hypervalent iodine with nucleophiles and super-leaving ability of newly formed hypervalent iodine intermediate have been highlighted recently.[9] On an amino group, Hofmann rearrangement is known to be effected by such propensity (Scheme 3).[10]

On the other hand, none of rearrangements on a hydroxyl group have yet been reported; because of

(1) (a) Schmidt, A. H. *Synthesis* **1980**, 961. (b) Liebeskind, L. S. *Tetrahedron* **1989**, *45*, 3053. (c) Moore, H. W.; Yerxa, B. R. *Chemtracts. Org. Chem.* **1992**, *5*, 273.

(2) (a) Kraus, J. L. *Tetrahedron Lett.* **1985**, *26*, 1867. (b) Reed, M. W.; Polart, D. J.; Perri, S. T.; Foland, L. D.; Moore, H. W. *J. Org. Chem.* **1988**, *53*, 2477. (c) Liebeskind, L. S.; Fengl, R. W.; Wirtz, K. R.; Shawe, T. T. *J. Org. Chem.* **1988**, *53*, 2482.

(3) For recent examples, see: (a) Sun, L.; Liebeskind, L. S. *Tetrahedron Lett.* **1997**, *38*, 3663. (b) Onofrey, T. J.; Gomez, D.; Winters, M.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 5658. (c) Liu, F.; Liebeskind, L. S. *J. Org. Chem.* **1998**, *63*, 2835. (d) Heileman, M. J.; Moore, H. W. *Tetrahedron Lett.* **1998**, *39*, 3643.

(4) Ohno, M.; Yamamoto, Y.; Eguchi, S. *Synlett* **1998**, 1167.

(5) Yamamoto, Y.; Ohno, M.; Eguchi, S. *J. Am. Chem. Soc.* **1995**, *117*, 9653.

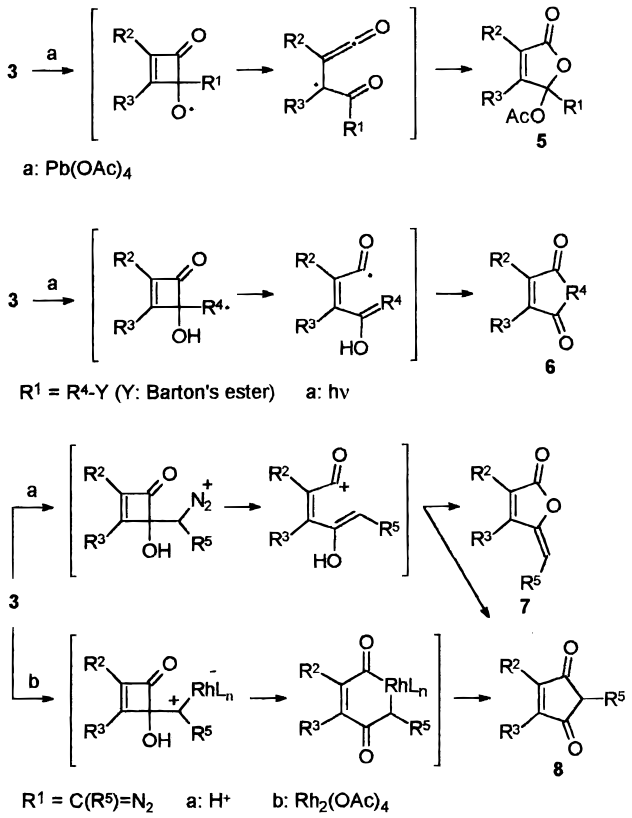
(6) Yamamoto, Y.; Ohno, M.; Eguchi, S. *J. Org. Chem.* **1996**, *61*, 9264

(7) Boeck, B. D.; Herbert, N.; Pattenden, G. *Tetrahedron Lett.* **1998**, *39*, 6971.

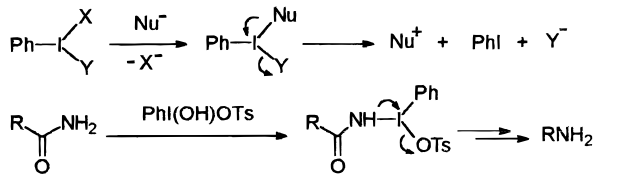
(8) Ohno, M.; Noda, M.; Yamamoto, Y.; Eguchi, S. *J. Org. Chem.* **1999**, *64*, 707. For synthesis of dimethylgloiosiphone by a cationic rearrangement, see: Paquette, L. A.; Sturino, C. F.; Dousso, P. *J. Am. Chem. Soc.* **1996**, *118*, 9456.

10.1021/jo990704v CCC: $18.00
Published on Web 11/19/1999

Scheme 2



Scheme 3

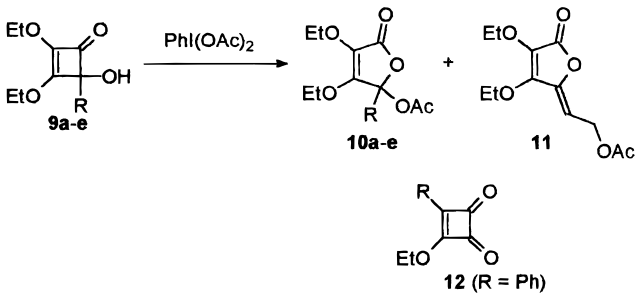


similarity to $Pb(OAc)_4$, the major applications of this reagent fall into alcohol (phenol) oxidation and glycol cleavage.[9a] Nevertheless, the exceeding ability as a leaving group is expected to assist a rearrangement on the hydroxyl group if it were cooperative with some structural factor such as ring strain. This is the case for 4-hydroxy-2-cyclobutenones. We report here the first example of $PhI(OAc)_2$-promoted rearrangement of these compounds and comparison with simple 2-hydroxycycloalkanones.

Results and Discussion

The starting 4-hydroxy-2-cyclobutenones **9** were prepared from diethyl squarate (**2**) according to the established procedure.[5] $PhI(OAc)_2$ is the reagent of choice for the purpose because it is one of the most popular and accessible hypervalent iodine compounds. Typically, the reaction between them was examined by using 4-methyl-substituted cyclobutenone **9a**. Thus, **9a** was treated with a slight excess of $PhI(OAc)_2$ in dichloromethane at room temperature under exclusion of moisture. The reaction took place quite slowly as judged by TLC analysis, and the product was obtained in 30% yield by chromatographic separation after stirring for 3 days. The structure was determined to be 5-acetoxy-3,4-diethoxy-5-methyl-2-(5*H*)-furanone (**10a**) by direct comparison with an authentic sample obtained by our previous method.[5] As the expected rearrangement was effected by the action of $PhI(OAc)_2$ on the hydroxyl group of cyclobutenone, we next tried to improve the yield; reflux in dichloromethane for 2 days slightly raised the yield to 34% and better yield of 64% was obtained by reflux in 1,2-dichloroethane within 6 h. Oppositely, the yield decreased to 24% at higher temperature such as refluxing in toluene. We then carried out the reaction of other cyclobutenones **9b**−**e** under refluxing conditions in 1,2-dichloroethane, and comparative results were obtained (Table 1). In the phenyl-substituted case (entry 6), 18% yield of a byproduct, 4-ethoxy-3-phenyl-3-cycobutene-1,2-dione (**12**, R= Ph), was isolated as a result of acid-catalyzed rearrangement.[2b,c] This was suppressed by addition of molecular sieves to trap the formed acetic acid, and the yield was increased to 84% (entry 7). The vinyl-substituted **9d** gave 5-vinylfuranone **4d** and (*Z*)-5-ethylidenefuranone **11** with a ratio of 1:2 (^{1}H NMR measurement).

Table 1



entry	compd	R	solvent[a]	time/temp.	product [yield (%)]
1	**9a**	Me	DM	3 days/rt	**10a** [30]
2	**9a**	Me	DM	2 days/reflux	**10a** [34]
3	**9a**	Me	DE	6 h/reflux	**10a** [64]
4	**9a**	Me	T	6 h/reflux	**10a** [24]
5	**9b**	Bu	DE	6 h/reflux	**10b** [65]
6	**9c**	Ph	DE	6 h/reflux	**10c** [60]/**12** [18][b]
7	**9c**	Ph/ms[c]	DE	6 h/reflux	**10c** [84]
8	**9d**	$CH=CH_2$	DE	6 h/reflux	**10d**/**11** [43][d]
9	**9e**	2-furyl	DE	6 h/reflux	**11e** [34]

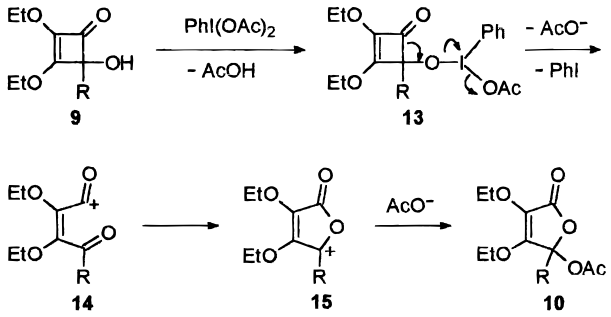
[a] DM: CH_2Cl_2. DE: $ClCH_2CH_2Cl$. T: Toluene. [b] The compound **12** was a byproduct as a result of AcOH-catalyzed rearrangement. [c] The reaction was carried out in the presence of 4A molecular sieves (ms). [d] The ratio of **10d**/**11** was determined to be 1/2 by relative ^{1}H NMR peak area.

Scheme 4 illustrates a plausible mechanism for the formation of 2(5*H*)-furanones **10** by the $PhI(OAc)_2$-promoted rearrangement of 4-hydroxy-2-cyclobutenones **9**. First, nucleophilic displacement on a hypervalent iodine with hydroxyl group of **9** generates another hypervalent iodine intermediate **13**, which involves an electron-deficient oxygen center susceptible to eliminative ring opening to an acyl cation intermediate **14**.[11] Such a ring-opening aptitude has been observed in radical-, cation-, and carbene-triggered ring expansion of 4-hydroxy-2-cyclobutenones.[4] Second, recyclization of this acyl cation **14** with an carbonyl oxygen is a facile process to

(9) (a) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, 1997. (b) Kitamura, T.; Fujiwara, Y. *Org. Prep. Proc. Int.* **1997**, *29*, 459. (c) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431. (d) Moriarty, R. M.; Vaid, R. K.; Koser, G. F. *Synlett* **1990**, 365. (e) Ochiai, M.; Nagao, Y. *J. Synth. Org. Chem. Jpn.* **1986**, 44, 660.

(10) Moriarty, R. M.; Khosrowshahi, J. S.; Awasthi, A. K.; Penmasta, R. *Synth. Commun.* **1988**, *18*, 1179. For other rearrangements, see (a) Ramsden, C. A.; Rose, H. L. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2319. (b) Wipf, P.; Venkatraman, S. *J. Org. Chem.* **1996**, *61*, 8004. (c) De Mico, A.; Roberto, M.; Piancatelli, G. *Gazz. Chim. Ital.* **1995**, *125*, 325.

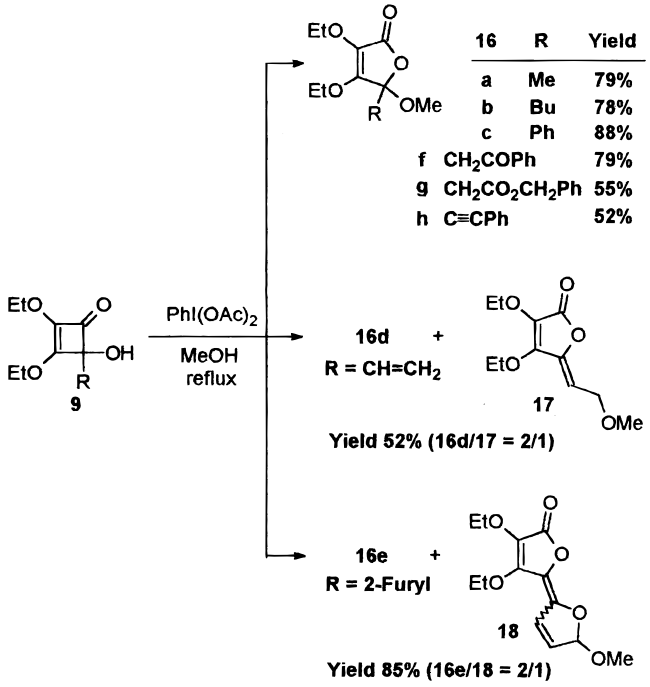
Scheme 4



give a furanone cation **15**, which is trapped with an acetate anion to give the final product **10** (and **11**).[12]

Then, the above reaction was carried out in methanol at reflux temperature. This solvent was used to avoid an acid-catalyzed side reaction to give cyclobutenedione (acetic acid should preferentially interact with a hydroxyl group of largely existing solvent rather than of a reactant) and to work as a nucleophile. A typical reaction is again with **9a**. Thus, the treatment under the same conditions as above except using methanol as a solvent for 2 h gave the expected rearrangement product, 3,4-diethoxy-5-methoxy-5-methyl-2(5*H*)-furanone (**16a**), in 79% yield. According to this procedure, other cyclobutenones **9b**−**h** were transformed to 5-methoxy-2(5*H*)-furanones **16b**−**h** (Scheme 5). Compared with the reaction conducted in 1,2-dichloroethane, yields are better in general and no byproduct **12** was obtained in the case of phenyl-substituted **9c**. Further, the vinyl-substituted **9d** gave a mixture of 5-vinylfuranone **16d** and (*Z*)-5-ethylidenefuranone **17**[13] with a ratio of 2:1 (reversal of entry 8 in Table 1), and the furyl-substituted **9e** produced

Scheme 5

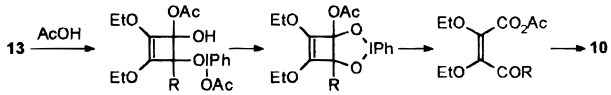


5-[2(5*H*)-furylidene]furanone **18**[13] in 28% yield with a 1:1 *E*/*Z* ratio as an inseparable mixture together with 5-(2-furyl)furanone **16e** in 57% yield. Carbonyl- and alkynyl-substituted furanones **16f**−**h** were also obtained by this method. The structures of these products were confirmed by analogy with 5-acetoxyfuranones **10**. For example, **16a** was characterized on the basis of spectral patterns similar to **10a** as follows; IR showed absorptions at 1771 and 1681 cm^{-1} (enone), and ^{1}H NMR and ^{13}C NMR indicated reasonable signals at δ 1.61 (methyl) and 3.23 (methoxy) and at δ 23.1 (*C*H$_3$), 50.8 (O*C*H$_3$), 102.2 (*C*-5), and 167.5 (*C*-2), respectively, and MS involved the required M$^+$ peaks at *m*/*z* 216. The ylidenefuranone structure of **18** could be deduced even as a mixture; chemical shifts observed in both ^{1}H and ^{13}C NMR spectra were compatible with fully conjugated and thermodynamically more stable 5-methoxy-2(5*H*)-furylidene rather than deconjugated 3-methoxy-2(3*H*)-furylidene as a C-5 substituent (see Experimental Section).[14]

While methanol was employed as an external nucleophile in the above reaction, intramolecular version may be attained by locating a hydroxyl group within the same molecule. Thus, **9i** was prepared from **2** and benzyl alcohol/BuLi−TMEDA[15] and allowed to react with PhI(OAc)$_2$. In this case, however, the reaction proceeded at room temperature, and the expected spiro compound **21** to be formed according to Scheme 4 was not obtained. The spectral data of the product were consistent with the eight-membered lactone **20** rather than the furanone **21**, since a chiral carbon (such as C-5 of **21**) was absent and another carbonyl bond appeared instead of an ether bond; methylene protons of ethoxy groups were no longer diastereotopic as judged by simple quartet in ^{1}H NMR, and two carbonyl groups were indicated by absorptions at 1738 and 1685 cm^{-1} in IR and signals at δ 166.3 and

(11) While the similar reaction was effected by both PhI(OAc)$_2$ and Pb(OAc)$_4$, the mechanistic difference between them lies in the fate of the initially formed intermediate ROIPh (OAc) and ROPb(OAc)$_3$ (R = 2-oxo-3,4-diethoxy-3-cyclobutenyl). The latter case was proposed to generate an oxy radical species from the above intermediate because of the intrinsic nature of alkoxylead(IV) and the resemblance of reactivity to the related hypoiodite (ref 5). The former case of hypervalent iodine is likely to involve an oxy cation-like species (or else an electron-deficient oxygen center), based on super-leaving ability of this group. As an extreme, phenyliodinium(III) reagents have recently been proposed to effect phenolic oxidation with the intervention of phenoxenium ions as intermediates (Kürti, L.; Herczegh, P.; Visy, J.; Simonyi, M.; Antus, S.; Pelter, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 379). The independent reaction course of ROIPh(OAc) from that of ROPb(OAc)$_3$ may be reflected in somewhat different product distributions (e.g., entries 3, 5, and 8 in Table 1). At the ring expansion step, stepwise (via acyl cation **14**) and concerted (via 1,2-acyl shift) processes are conceivable. Nevertheless, the former type of process was favored in the related α-carbocation-induced ring expansion reaction of cyclobutenones and cyclobutanones (ref 8 and its footnotes 5f and 12) and is believed to participate also in the present reaction. The similar ring expansion route might be realized by using Me$_2$SO/(COCl)$_2$ (in this case Me$_2$S is a leaving group); however, the reaction of **9a** resulted in the formation of 4-ethoxy-3-methyl-2-cyclobutene-1,2-dione (**12**, R = Me), indicating PhI(OAc)$_2$ to be a useful reagent with a high leaving ability for the aimed rearrangement.

(12) Liberated acetic acid seemed to play no significant role in the rearrangement, since intentional removal of the acid caused the better yield of the rearranged product (entry 7 in Table 1); thus, a glycol cleavage pathway as depicted below is not likely.

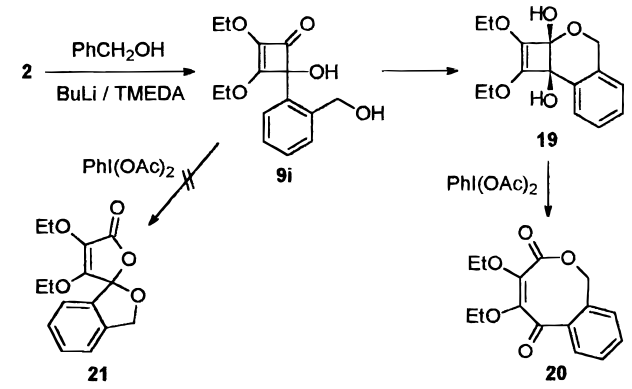


(13) Predominant formation of the (*Z*)-isomer **17** from **9e** was suggested by analogy with the reaction of **9e** to **11**. In the case of **18**, no selectivity was observed because of no stereochemical difference between (*Z*)- and (*E*)-isomers. PM3 calculations indicated that **17** was more stable than the corresponding *E*-isomer by 4.1 kcal/mol but energy difference was only 0.5 kcal/mol between (*Z*)- and (*E*)-**18**.

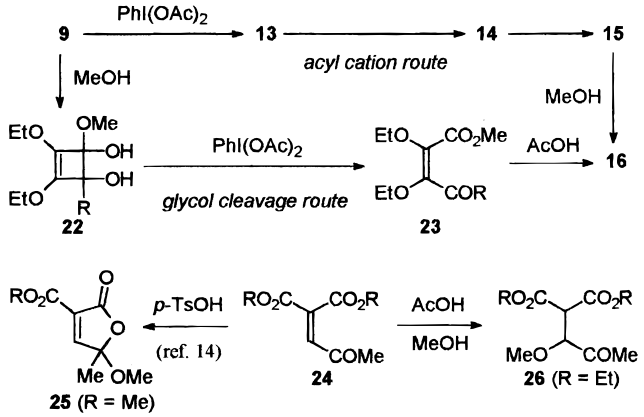
(14) Coupling constants of 2(5*H*)-furylidene ($J_{3,4}$ = 5.8−6.0 Hz and $J_{4,5}$ = 1.0−1.2 Hz) were nicely correlated with those of 2,5-dihydrofuran: Lozach, R.; Braillon, B. *J. Magn. Reson.* **1973**, *12*, 244.

(15) Meyer, N.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1978**, *7*, 521.

Scheme 6



Scheme 7

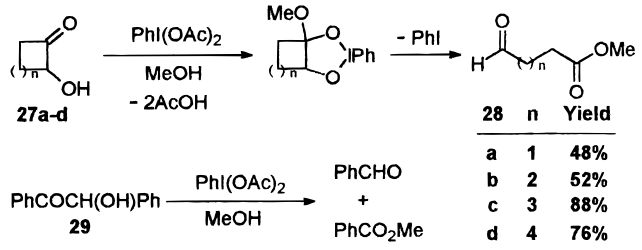


195.5 in ^{13}C NMR. Mechanistically, the lactone formation was elucidated by intramolecular hemiacetalization and ring cleavage of the formed glycol **19** with $PhI(OAc)_2$ leading to a different product (Scheme 6).

As the glycol cleavage route was revealed to participate with the above intramolecular reaction, this might be also the case for the intermolecular reaction with methanol as shown in Scheme 7 (i.e., **9** → **22** → **23** → **16**). Nevertheless, the reactivity, which was reflected in the foregoing reaction temperature (reflux conditions), seemed to be fit for the acyl cation route via **14** rather than the glycol cleavage route via **22** (cf., the reaction of **9a** in 1,2-dichloroethane vs those of **27a** and **9i** as described above and below). Furthermore, the formation of an intermediate compound [for example, methyl (*Z*)-4-oxo-2,3-diethoxy-2-pentenoate (**23**, R = Me) from **9a**] was not found throughout the reaction. Although **23** might cyclize to **16** with the aid of acetic acid, the following reaction is not an exact but rather a suggestive reference. An olefinic compound **24** with the cis relationship of acetyl and alkoxycarbonyl groups, which was reported to lactonize to **25** under *p*-TsOH-catalyzed conditions,[16] underwent only Michael addition to give **26** under refluxing conditions in methanol with acetic acid. These facts inclined us to suppose that the intermolecular reaction is different from the intramolecular one and still obeys the same mechanism as shown in Scheme 4. [17]

Then, the above reaction was extended to simple 2-hydroxycycloalkanones, because it is interesting to examine and compare with the hypervalent iodine chemistry of α-ketols. Until now, this class of compound is only

Scheme 8



known to react with $PhI(OAc)_2$ as its enolate form to give a β-lactone.[18] In the same manner employed for cyclobutenones **9**, four- to seven-membered cycloalkanones **27a**−**d** were treated with $PhI(OAc)_2$ in methanol, and the reaction was found to occur smoothly at room temperature. After chromatographic separation, the products were obtained in moderate to good yields and identified as methyl ω-formylalkanoate **28a**−**d** by spectral comparison with authentic samples.[19] In addition, the reaction with benzoin (**29**) gave fragmented methyl benzoate and benzaldehyde in nearly quantitative yield and 27% yield (GLC), respectively. On the other hand, the reaction of **27c** in 1,2-dichloroethane was found to be suppressed, and the related α-hydroxy ester (e.g., methyl lactate) difficult to acetalize did not show any reactivity under the same conditions as employed for α-hydroxy ketones. These results imply the significancy of hemiacetal formation and agree with the glycol cleavage mechanism as shown in Scheme 8.[20] From a synthetic viewpoint, $PhI(OAc)_2$ is known to be used in a way similar to $Pb(OAc)_4$, and this is also the case for bond-scission of α-ketols.[21]

In summary, the ring expansion reaction of 4-hydroxy-2-cyclobutenones **9** was promoted by $PhI(OAc)_2$ to give 2(5*H*)-furanones **10** and **16** (and, in some cases, 2-ylidenefuranones **11**, **17**, and **18**), providing the first example for the rearrangement initiated by action of a hypervalent iodine reagent on a hydroxyl group. The formation of furanone products can be explained by tandem eliminative ring opening to an acyl cation and its recyclization with an carbonyl oxygen, and the first key-step resulted from the high leaving ability of a hypervalent iodine intermediate consonant with ring strain relief of a cyclobutenone. Such a mechanism was operative in 1,2-dichloroethane (as a solvent) and presumably also in methanol (as both a solvent and a nucleophile). On the other hand, an intramolecular version of the latter reaction favored a glycol cleavage route, and this route also participated with simple 2-hydroxycycloalkanones **27**. Apart from the mechanism, $PhI(OAc)_2$ is useful for

(16) Levison, B. S.; Miller, D. B.; Salomon, R. G. *Tetrahedron Lett.* **1984**, *25*, 4633.

(17) In this case the opened acyl cation **14** might be trapped with a solvent to give **23**, but this possibility could be subdued by preferential cyclization of this cation with a proximate carbonyl end in the cis-olefinic configuration

(18) Turuta, A. M.; Kamernitsky, A. V.; Fadeeva, T. M.; Zhulin, A. V. *Synthesis* **1985**, 1129.

(19) (a) Taylor, W. G. *J. Org. Chem.* **1981**, *46*, 4290. (b) Doleschall, G.; Toth, G. *Tetrahedron* **1979**, *36*, 1649. (c) Claus, R. E.; Schreiber, S. L. *Org. Synth.* **1986**, *64*, 150. (d) Finke, R. G.; Sorrell, T. N. *Org. Synth.* **1980**, *59*, 102.

(20) If the ring expansion mechanism was operative also for **27a**, a butyrolactone might be produced. However, this is not the case, and the difference in reactivity between cyclobutenone such as **9a** and cyclobutanone such as **27a** seems to be attributed to ring strain relief of the four-membered rings and stabilization of the opened acyl cations by conjugation, both of which are influenced by double vs single bond nature adjacent to the carbonyl group. These are apparently advantageous for **9a** to undergo ring-opening.

(21) (a) Hazen, J. R. *J. Org. Chem.* **1970**, *35*, 973. (b) Crimmins, M. T.; Jung, D. K.; Gray, J. L. *J. Am. Chem. Soc.* **1993**, *115*, 3146.

bond-scission of α-ketol as is $Pb(OAc)_4$ and preferable to that of the latter toxic reagent.

Experimental Section

General Remarks. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ or DMSO-d_6 solution with $SiMe_4$ as an internal standard. 1,2-Dichloroethane was dried over $CaCl_2$, distilled, and kept over 4 Å molecular sieves, while THF was dried over Na/Ph_2CO and distilled before use. Methanol was dried over 3 Å molecular sieves. Flash chromatography was carried out using a Fuji-Davison BW-300 with hexane (H) and ethyl acetate (A) as an eluent. Squaric acid was provided by Kyowa Hakko Kogyo Co., Ltd. Preparation of the squaric acid derivatives **9a**−**h** has been reported previously.[5]

Representative Procedure for the Synthesis of 10a−**e.** To a solution of **9a** (49 mg, 0.26 mmol) in 1,2-dichloroethane (3 mL) was added $PhI(OAc)_2$ (90 mg, 0.28 mmol) under exclusion of moisture, and the solution was stirred at reflux temperature for 6 h. After cooling, the solvent was removed under vacuum, and the residue was chromatographed on a silica gel column (H/A 10/1) to give 5-acetoxy-2(5*H*)-cyclobutenone **10a** (40 mg, 64%). The other cyclobutenones **10b**−**e** were obtained in the same manner except elution with H/A 15/1 for **9b** and 20/1 for **9c** in yields shown in Table 1. For phenyl-substituted **9c**, the reaction was also carried out in the presence of powdered 4 Å molecular sieves (300 mg) with the yield increased to 84%. All of the products were identical with those obtained by our previous method.[5]

Representative Procedure for the Synthesis of 16a−**h.** To a solution of **6a** (123 mg, 0.66 mmol) in methanol (3 mL) was added $PhI(OAc)_2$ (218 mg, 0.68 mmol) at room temperature under exclusion of moisture, and the solution was stirred at reflux temperature for 2 h. The same workup and purification as above gave 5-methoxy-2(5*H*)-cyclobutenone **16a** (79 mg, 79%). The yields for **16b**−**h** are summarized in Scheme 5.

3,4-Diethoxy-5-methoxy-5-methyl-2(5*H*)-furanone (16a): Elution with (H/A 10/1); oil; IR (neat) 1771, 1687 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.32 (3 H, t, J = 7.0 Hz), 1.41 (3 H, t, J = 7.0 Hz), 1.61 (3 H, s), 3.23 (3 H, s), 4.15 and 4.22 (each 1 H, dq, J = 7.0, 9.6 Hz), 4.52 (2 H, q, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 15.30, 15.33, 23.1, 50.8, 68.1, 68.5, 102.2, 122.0, 155.2, 167.5; MS (EI) *m*/*z* (relative intensity) 216 (M$^+$, 86), 185 (31), 157 (47), 143 (100). Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.59; H, 7.45.

5-Butyl-3,4-diethoxy-5-methoxy-2(5*H*)-furanone (16b): Elution with (H/A 12/1); oil; IR (neat) 1771, 1688 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (3 H, t, J = 6.9 Hz), 1.32 (3 H, t, J = 7.0 Hz), 1.41 (3 H, t, J = 7.0 Hz), 1.23−1.39 (4 H, m), 1.76−1.97 (2 H, m), 3.23 (3 H, s), 4.16 and 4.22 (each 1 H, dq, J = 7.0, 9.6 Hz), 4.51 (2 H, q, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 15.3, 15.4, 22.5, 24.8, 35.6, 50.59, 68.0, 68.6, 104.2, 122.7, 154.4, 167.8; MS (EI) *m*/*z* (relative intensity) 258 (M$^+$, 32), 227 (11), 201 (100). Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.44; H, 8.59. Found: C, 60.51; H, 8.55.

3,4-Diethoxy-5-methoxy-5-phenyl-2(5*H*)-furanone (16c): Elution with (H/A 10/1); oil; IR (neat) 1773, 1684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 (3 H, t, J = 7.0 Hz), 1.32 (3 H, t, J = 7.0 Hz), 3.39 (3 H, s), 4.17 and 4.25 (each 1 H, dq, J = 7.0, 9.6 Hz), 4.40 and 4.50 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.35−7.42 (3 H, m), 7.51−7.59 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 15.1, 15.4, 51.6, 68.3, 68.6, 102.5, 122.0, 126.5 (2C), 128.7 (2C), 129.8, 136.1, 155.8, 167.9; MS (EI) *m*/*z* (relative intensity) 278 (M$^+$, 97), 247 (26), 205 (21), 105 (100). Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.72; H, 6.55.

5-Ethenyl-3,4-diethoxy-5-methoxy-2(5*H*)-furanone (16d). This was eluted as the first fraction (H/A 10/1). The analytical sample was obtained by further purification on preparative TLC ($CHCl_3$) as an oil; IR (neat) 1772, 1685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.32 (3 H, t, J = 7.0 Hz), 1.39 (3 H, t, J = 7.0 Hz), 3.33 (3 H, s), 4.16 and 4.22 (each 1 H, dq, J = 7.0, 9.6 Hz), 4.45 and 4.48 (each 1 H, dq, J = 7.0, 9.8 Hz), 5.42 (1 H, dd, J = 1.2, 10.4 Hz), 5.66 (1 H, dd, J = 1.2, 17.2 Hz), 5.89 (1 H, dd, J = 10.4, 17.2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.3, 51.3, 68.3, 68.5, 101.2, 120.1, 122.0, 132.7, 155.0, 167.6; MS (EI) *m*/*z* (relative intensity) 228 (M$^+$, 76), 197 (38), 169 (32), 156 (49), 127 (100). Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 57.92; H, 7.05.

3,4-Diethoxy-5-(2-methoxyethylidene)-2(5*H*)-furanone (17). This was eluted as the second fraction and further purified as above: oil; IR (neat) 1777, 1687, 1655 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3 H, t, J = 7.0 Hz), 1.39 (3 H, t, J = 7.0 Hz), 3.35 (3 H, s), 4.19 (2 H, d, J = 7.0 Hz), 4.23 (2 H, q, J = 7.0 Hz), 4.94 (2 H, q, J = 7.0 Hz), 5.45 (1 H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 15.3, 15.4, 58.5, 65.7, 68.0, 68.6, 105.1, 123.8, 143.8, 148.4, 165; MS (EI) *m*/*z* (relative intensity) 228 (M$^+$, 100), 197 (17), 169 (21), 156 (49). Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 57.94; H, 7.04.

3,4-Diethoxy-5-(2-furyl)-5-methoxy-2(5*H*)-furanone (16e). This was eluted as the first fraction (H/A 10/1): oil; IR (neat) 1778, 1688 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (3 H, t, J = 7.0 Hz), 1.36 (3 H, t, J = 7.0 Hz), 3.40 (3 H, s), 4.21 and 4.27 (each 1 H, dq, J = 7.0, 9.8 Hz), 4.47 and 4.54 (each 1 H, dq, J = 7.0, 10.4 Hz), 6.40 (1 H, dd, J = 1.8, 3.4 Hz), 6.59 (1 H, dd, J = 1.0, 3.4 Hz), 7.44 (1 H, dd, J = 1.0, 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.3, 51.6, 68.4, 68.5, 99.0, 110.2, 110.8, 122.6, 143.9, 148.3, 153.6, 167.2; MS (EI) *m*/*z* (relative intensity) 268 (M$^+$, 49), 237 (16), 195 (21), 167 (15), 111 (20), 95 (100). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.19; H, 6.04.

3,4-Diethoxy-5-[5-methoxy-2(5*H*)-furylidene]-2(5*H*)-furanone (18). This was eluted as the second fraction and obtained as an inseparable 1:1 *E*/*Z*-mixture (oil). Attempted further separation of these stereoisomers on thin-layer chromatography caused gradual decomposition. Therefore the following spectral data were analyzed as a mixture form; IR (neat) 1750, 1680, 1632 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 and 1.34 (each 1/2 × 3 H, t, J = 7.0 Hz), 1.42 and 1.44 (each 1/2 × 3 H, t, J = 7.0 Hz), 3.50 and 3.52 (each 1/2 × 3 H, s), 4.21 and 4.23 (each 1/2 × 2 H, q, J = 7.0 Hz), 4.54 and 4.55 (each 1/2 × 2 H, q, J = 7.0 Hz), 6.15 and 6.25 (each 1/2 × 1 H, dd, J = 1.2, 1.5 Hz and 1.0, 1.5 Hz, respectively), 6.27 and 6.29 (each 1/2 × 1 H, dd, J = 1.5, 5.8 Hz and 1.5, 6.0 Hz, respectively), 6.89 and 6.94 (each 1/2 × 1 H, dd, J = 1.0, 5.8 Hz and 1.2, 6.0 Hz, respectively); ^{13}C NMR ($CDCl_3$) δ 15.4 (overlapped 2C), 55.4 and 55.8, 68.2 and 68.4, 68.6 and 68.7, 110.7 and 112.1, 122.2 and 122.8, 123.9 and 124.1, 126.3 and 126.7, 132.3 and 133.4, 143.3 and 147.2, 150.4 and 150.7, 164.6 and 165.0; MS (EI) *m*/*z* (relative intensity) 268 (M$^+$, 100), 237 (50), 180 (46). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.27; H, 6.06.

3,4-Diethoxy-5-methoxy-5-phenacyl-2(5*H*)-furanone (16f): Elution with (H/A 10/1); oil; IR (neat) 1779, 1693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (3 H, t, J = 7.0 Hz), 1.36 (3 H, t, J = 7.0 Hz), 3.26 (3 H, s), 3.42 and 3.74 (each 1 H, d, J = 15.6 Hz), 4.14 and 4.50 (each 1 H, dq, J = 7.0, 9.8 Hz), 4.39 and 4.55 (each 1 H, dq, J = 7.0, 10.2 Hz), 7.42−7.62 (3 H, m), 7.91−7.97 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 15.3 (2C), 43.2, 50.2, 68.2, 68.5, 101.6, 123.7, 128.8 (2C), 129.0 (2C), 133.8, 137.4, 153.0, 167.2, 194.7; MS (EI) *m*/*z* (relative intensity) 320 (M$^+$, 28), 201 (15), 105 (100). Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.82; H, 6.30.

5-(Benzyloxycarbonylmethyl)-3,4-Diethoxy-5-methoxy-2(5*H*)-furanone (16 g): Elution with (H/A 10/1); oil; IR (neat) 1779, 1743, 1692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (3 H, t, J = 7.0 Hz), 1.35 (3 H, t, J = 7.0 Hz), 2.97 and 3.07 (each 1 H, d, J = 15.2), 3.23 (3 H, s), 4.04 and 4.19 (each 1 H, dq, J = 7.0, 9.8 Hz), 4.41 and 4.54 (each 1 H, dq, J = 7.0, 10.3 Hz), 5.11 (2 H, s), 7.35 (5 H, s); ^{13}C NMR ($CDCl_3$) δ 15.3, 15.4, 40.7, 50.4, 67.0, 68.2, 68.5, 101.0, 123.5, 128.8 (3C), 129.0 (2C), 135.8, 152.7, 167.1, 167.7; MS (EI) *m*/*z* (relative intensity) 350 (M$^+$, 20), 319 (1), 201 (7), 91 (100). Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.70; H, 6.33. Found: C, 61.70; H, 6.36.

3,4-Diethoxy-5-methoxy-5-(phenylethynyl)-2(5*H*)-furanone (16h): Elution with (H/A 15/1); oil; IR (neat) 2234, 1780, 1691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.34 (3 H, t, J = 7.0 Hz), 1.44 (3 H, t, J = 7.0 Hz), 3.63 (3 H, s), 4.22 (2 H, q, J = 7.0 Hz), 4.55 (2 H, q, J = 7.0 Hz), 7.30−7.55 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.4, 53.5, 68.5, 68.6, 80.4, 88.0, 95.7, 121.1, 122.0, 128.8 (2C), 130.0, 132.5 (2C), 154.1, 166.8; MS (EI) *m*/*z* (relative

intensity) 302 (M^+, 17), 229 (30), 129 (100). Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.59; H, 5.98.

Preparation of 3,4-Diethoxy-4-hydroxy-4-[(2-hydroxymethyl)phenyl)]-2-cyclobutenone (9i). To a solution of benzyl alcohol (324 mg, 3 mmol) and tetramethylethylenediamine (697 mg, 6 mmol) in pentane (12 mL) was added *n*-BuLi (1.6 M hexane solution, 7.14 mL, 12 mmol) gradually at room temperature under a nitrogen atmosphere, and the mixture was refluxed for 11 h and diluted with THF (12 mL). To this solution was added a solution of **2** (510 mg, 3 mmol) in THF (6 mL) at −78 °C, and the mixture was stirred for 1 h. Then 1 N HCl (6 mL) was added at this temperature, and subsequently the solution was basified with sat. $NaHCO_3$. The product was extracted repeatedly with ether, while a separating funnel was cooled by adding ice. The extracts were combined, washed with brine, and dried over Na_2SO_4. After evaporation of the solvent, the residue was chromatographed on a silica gel column (H/A 2/1) to give **9i** (94 mg, 10%) as an oil: IR (neat) 3335, 1769, 1622 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.23 (3 H, t, J = 7.0 Hz), 1.37 (3 H, J = 7.0 Hz), 4.17 and 4.23 (each 1 H, dq, J = 7.0, 10.4 Hz), 4.42 and 4.51 (each 1 H, dq, J = 7.0, 10.2 Hz), 4.88 (2 H, br s), 5.11 (1 H, br s), 6.61 (1 H, s), 7.15−7.58 (5 H, m); ^{13}C NMR (DMSO-d_6) δ 15.0, 15.4, 61.3, 66.4, 69.5, 88.7, 126.0, 126.7, 127.8, 128.2, 132.4, 135.8, 142.4, 167.9, 186.0; MS (EI) *m*/*z* (relative intensity) 260 (M^+ − 18, 16), 203 (65), 169 (21), 133 (40), 118 (100). Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.81; H, 6.49.

Reaction of 9i with $PhI(OAc)_2$. To a solution of **9i** (73 mg, 0.26 mmol) in methanol (3 mL) was added $PhI(OAc)_2$ (85 mg, 0.26 mmol) under exclusion of moisture, and the solution was stirred at room temperature for 1.5 h. After evaporation of the solvent, the residue was chromatographed on a silica gel column (H/A 10/1) to give 5,6-benzo-2,3-diethoxy-4-oxo-2-hepten-7-olide (**20**) as an oil (50 mg, 70%); IR (neat) 1738, 1685, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (3 H, t, J = 7.0 Hz), 1.41 (3 H, J = 7.0 Hz), 4.02 (2 H, q, J = 7.0 Hz), 4.25 (2 H, q, J = 7.0 Hz), 5.42 (2 H, s), 7.12−7.45 (4 H, m); ^{13}C NMR ($CDCl_3$) δ 15.4, 15.6, 66.9, 68.4, 68.9, 125.8, 126.9, 128.8, 130.4, 135.4, 136.6, 139.3, 154.8, 166.3, 195.5; MS (EI) *m*/*z* (relative intensity) 276 (M^+, 17), 203 (12), 174 (28), 135 (21), 118 (100). Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.20; H, 5.85.

Attempted AcOH-Catalyzed Reaction of Ethyl 2-Acetonylidenemalonate (24). A solution of **24**[22] (64 mg, 0.3 mmol) in methanol (2 mL) including acetic acid (36 mg, 0.6 mmol) was refluxed for 2 h. The solvent and acetic acid were removed under vacuum to give almost pure ethyl 2-(1-methoxyacetonyl)malonate (**26**) as an oil (76 mg, 98%); IR (neat) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (3 H, t, J = 7.2 Hz), 1.29 (3 H, t, J = 7.2 Hz), 2.31 (3 H, s), 3.51 (3 H, s), 3.93 (1 H, d, J = 6.8 Hz), 4.18 (1 H, dq, J = 11.0, 7.2 Hz), 4.24 (1 H, dq, J = 11.0, 7.2 Hz), 4.25 (2 H, q, J = 7.2 Hz) ^{13}C NMR ($CDCl_3$) δ 14.0 (2C), 26.9, 54.4, 59.8, 62.0 (2C), 84.4, 167.2, 167.4, 208.5; MS (CI) *m*/*z* (relative intensity) 247 (M^+ + 1, 89), 215 (100), 169 (69). Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.70; H, 7.35.

Representative Procedure for the Synthesis of methyl *ω*-formylalkanoate 28: To a solution of cyclohexanone **27c** (55 mg, 0.5 mmol) in methanol (2.5 mL) was added $PhI(OAc)_2$ (161 mg, 0.5 mmol) under exclusion of moisture, and the mixture was stirred at room temperature for 3 h. After evaporation of the solvent, the residue was chromatographed (H/A 3/1) to give methyl 6-oxohexanoate (**28c**) (64 mg, 88%). The other reactions were carried out for periods of 1.5 h (**27a**), 2 h (**27b**), and 12 h (**27d**). The isolated yields were summarized in Scheme 8. The reaction of benzoin (**29**) was carried out with 1.5 equiv of $PhI(OAc)_2$ for 24 h, and the yield was estimated with GLC (see text).

JO990704V

(22) Ouall, M. S.; Vaulter, M.; Carrie, R. *Synthesis* **1977**, 626.