

Radical Cyclizations of Alkenyl Acylphosphonate Derivatives under Thermal and Photochemical Conditions

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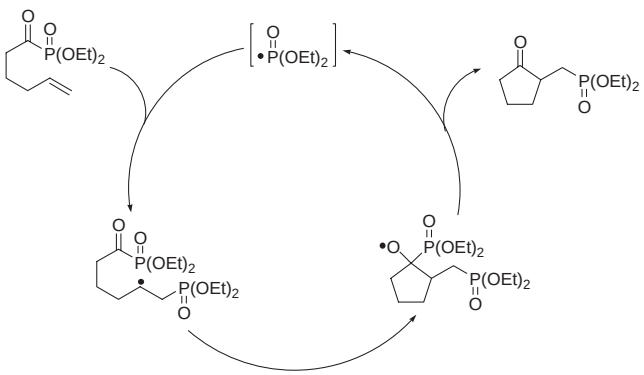
Received March 16, 2005; E-mail: skim@kaist.ac.kr

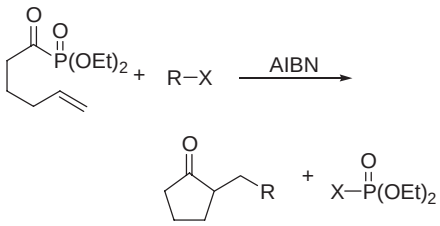
The use of alkenyl acylphosphonate and acylphosphine oxide derivatives as acceptors in radical cyclizations was studied under thermal and photochemical conditions, respectively. The cyclizations of alkenyl acylphosphonates under thermal conditions occurred smoothly in refluxing dioxane using benzoyl peroxide as an initiator; the addition of diethyl phosphite increased the chemical yield. Photochemically induced cyclizations of alkenyl acyldiphenylphosphine oxides at 300 nm gave similar results, although a notable difference was observed in one case. The intramolecular cyclization of *S*-but-3-enyl phosphinothiolformates occurred under thermal and photochemical conditions, providing thiolactones, whereas *S*-pent-4-enyl phosphinothiolformate afforded the tetrahydrothiophene derivative under similar conditions.

Radical cyclizations proved to be synthetically useful for the construction of 5- and 6-membered rings, and mostly utilized carbon–carbon multiple bonds as radical acceptors.[1] Recently, carbon–nitrogen double bonds, such as imines, oximes, and hydrazones, have been known to be very effective radical acceptors.[2] However, the carbonyl group, one of the most important functional groups, has not been widely used as an acceptor because the addition of an alkyl radical to the carbonyl group is energetically unfavorable and reversible due to the strong π-bond strength of the carbonyl group.[3] Although an aldehyde and a ketone are not suitable as acceptors, due to unfavorable equilibrium at the cyclization, acyl sulfides, acyl selenides,[4] and acylgermanes[5] have been effectively used as carbonyl group equivalent radical acceptors.

The acylphosphonates were known as acylating agents, and react with various nucleophiles, such as alcohols, amines, and carbanions.[6] In radical reactions, acyl and bis(acyl)phosphine oxides have been widely employed as photochemical sources of acyl radicals for use as initiators in the polymerization reactions.[7] Very recently, Kim et al. have shown intramolecular acylation reactions using an acylphosphonate group as a carbonyl group equivalent radical acceptor.[8] The intramolecular acylation involves the addition of an electrophilic alkyl radical onto an alkenyl bond, followed by cyclization to the acylphosphonate group along with the β-elimination of a diethyl phosphonyl group from an alkoxyl radical (Eq. 1). In the reaction, the finally eliminated phosphonyl radical reacts with an alkyl halide to generate an alkyl radical along with diethyl phosphoryl halide. Since the phosphonyl radical is known to add efficiently to alkenes,[9] we investigated the cyclization of alkenyl acylphosphonates based on a plausible mechanism, depicted in Scheme 1. If the eliminated phosphonyl radical generated by the radical cyclization could add to the starting alkenyl moiety of the acylphosphonate, the phosphonyl radical would mediate the acylphosphorylation of alkenyl acylphosphonates to provide cyclic ketones bearing the diethyl phosphonyl group.



Scheme 1. Phosphonyl radical-mediated acylphosphorylation of an alkene.



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Results and Discussion

To initiate the radical reaction, two reaction conditions involving thermal and photochemical conditions were employed. We first examined the combination of benzoyl peroxide/diethyl phosphite in benzene.[9a] When butenyl benzoylphosphonate

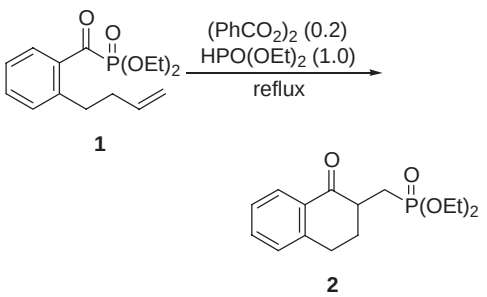
Published on the web August 30, 2005; DOI 10.1246/bcsj.78.1665

Table 1. Solvent Effect in the Radical Reaction of Acylphosphonate **1**[a)]

Solvent	Time	Yield of **2**
2,2,5,5-Tetramethyltetrahydrofuran	6 h	trace
Benzene	6 h	trace
Toluene	6 h	27%
Propionitrile	1 h	75%
1,4-Dioxane	1 h	82%

a) Ratio of the reagents was **1**:$(PhCO_2)_2$:$HPO(OEt)_2$ = 1.0:0.2:1.0.

1 was heated with diethyl phosphite (1 equiv) in the presence of benzoyl peroxide (20 mol %) in benzene for 6 h, the reaction did not proceed, yielding a trace amount of the desired product **2** (Eq. 2). As shown in Table 1, a similar result was obtained using 2,2,5,5-tetramethyltetrahydrofuran as a solvent. However, when toluene and propionitrile were used as solvents, the desired product **2** was obtained in 27% and 75% yields, respectively. An even better result was obtained when the reaction was carried out in refluxing 1,4-dioxane, indicating that solvents with active hydrogen are essential for the success of the reaction.



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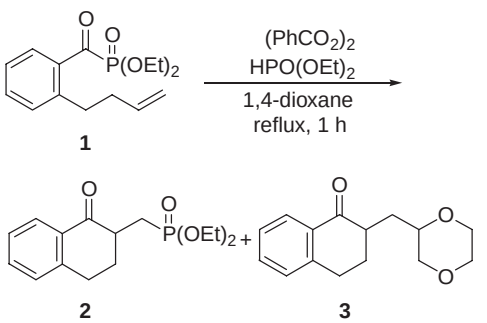


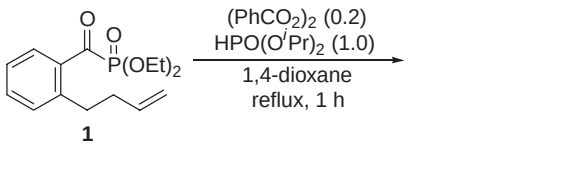
(3)

When **1** was treated with diethyl phosphite (1 equiv) and benzoyl peroxide (20 mol %) in 1,4-dioxane, it was consumed smoothly and, after 1 h refluxing, acylphosphorylation product **2** was obtained in 82% yield along with the formation of 1,4-dioxanyl compound **3** (5%) (Eq. 3). Although it is not yet clear, the key mediator, the phosphonyl radical, may be generated via i) hydrogen abstraction from diethyl phosphite by a solvent-derived radical and/or ii) an initial addition of the solvent-derived radical to the alkenyl part of **1**, followed by radical cyclization and the elimination of the phosphonyl radical. Furthermore, if the cyclization proceeded by the radical chain mechanism depicted in Scheme 1, the acylphosphorylation product **2** should have been obtained with a catalytic amount or even in the absence of diethyl phosphite. Thus, we investigated the effect of the amount of diethyl phosphite in the reaction (Table 2). As anticipated, the use of 40 mol % of diethyl phosphite gave 72% yield of **2**, which revealed that the phosphonyl part of product **2** came not only from the added phosphite, but also from the starting acylphosphonate **1**. Moreover, even in the absence of diethyl phosphite, **2** was obtained in 64% yield along with **3** (7%). The formation of 1,4-dioxanyl byproduct **3** in all cases indicates that the reaction seems to have been initiated by the addition of 1,4-dioxan-2-yl radical, which was generated by hydrogen abstraction from 1,4-dioxane by benzoyloxyl radical. Since the use of a large excess of diethyl phosphite (5 equiv) gave a similar result, as compared to 1 equiv of diethyl phosphite, the remaining reactions were carried out with benzoyl peroxide (20 mol %) as an initiator and diethyl phosphite (1 equiv) in refluxing 1,4-dioxane.

Table 2. Effect of the Amount of Diethyl Phosphite in the Radical Cyclization of Acylphosphonate **1**[a)]

$HPO(OEt)_2$ (x)[b)] /mol amt.	Yield	
	2	**3**
5.0	88%	3%
1.0	82%	5%
0.4	72%	7%
0	64%	7%

a) The reaction was performed by using reagents in the ratio of **1**:$(PhCO_2)_2$:$HPO(OEt)_2$ = 1.0:0.2:x in 1,4-dioxane for 1 h. b) Molar amounts of diethyl phosphite to **1**.



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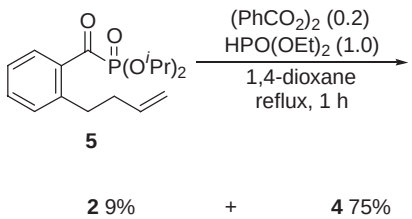
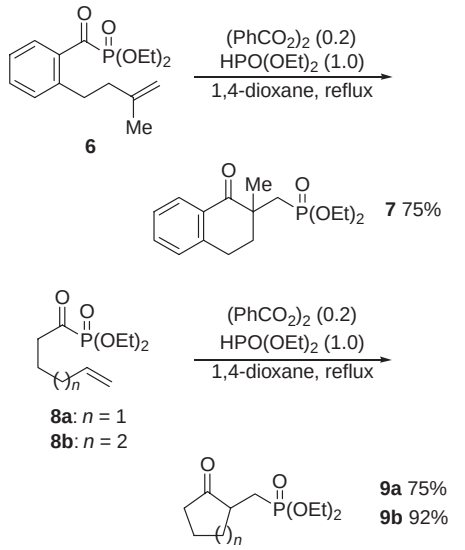
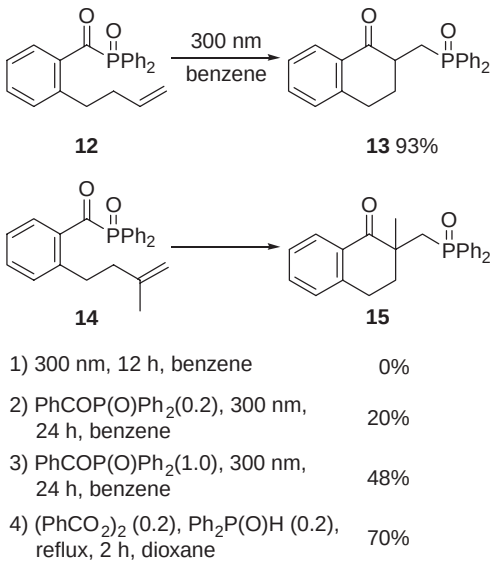


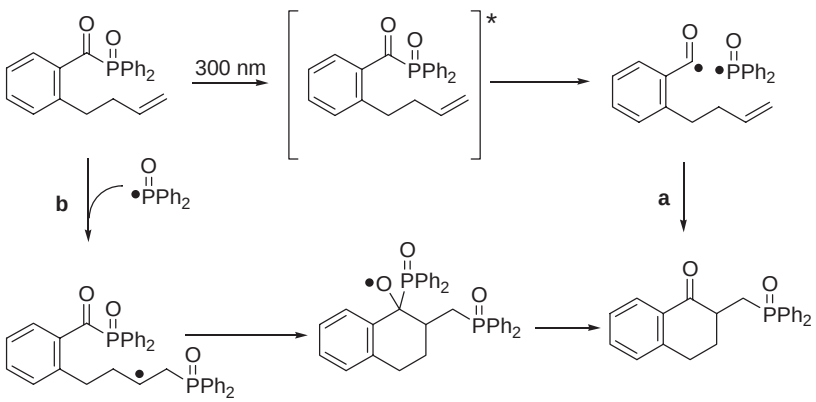
To clearly confirm whether the phosphonyl group of the product **2** originated from diethyl phosphite or **1**, phosphonyl group scrambling experiments were performed. As shown in Eq. 4, when **1** was reacted with diisopropyl phosphite under the same condition, **2** bearing the diethyl phosphonyl group originated from the starting acylphosphonate **1** was isolated as a major product (71%) along with **4** (10%). A similar result was also obtained with **5**. The results obtained here clearly indicate that the eliminated phosphonyl radical not only works as a radical carrier, but also efficiently adds to the alkenyl moiety of the acylphosphonate. This acylphosphorylation reaction exhib-



Scheme 2. Cyclizations of alkenyl acylphosphonates under thermal conditions.



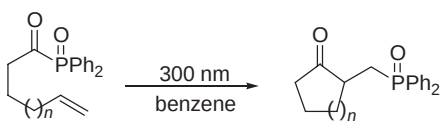
Scheme 3. Cyclizations of **12** and **14** under photochemical and thermal conditions.



Scheme 4. Plausible mechanism of a photochemically induced acylphosphorylation.

ited a wide generality. As shown in Scheme 2, the presence of a methyl group in **6** did not cause any problems, yielding **7** in 75% yield. Furthermore, the reaction of aliphatic acylphosphonates **8a** and **8b** under the same conditions provided α-phosphonomethyl cyclopentanone **9a** and cyclohexanone **9b** in 75% and 92% yield, respectively.

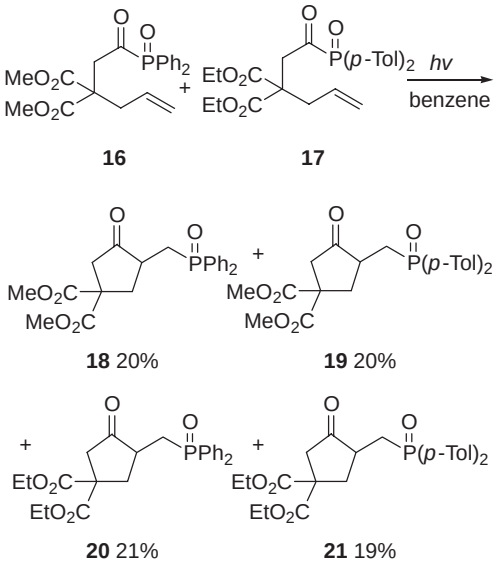
We next studied a photochemically induced acylphosphorylation. As we anticipated, the irradiation of a benzene solution of **8a** at 300 nm for 6 h did not afford **9a**, and the starting material was recovered. Evidently, an acyl radical was not generated under the condition due to weak UV absorption. However, when acyldiphenylphosphine oxide **10a** was used to generate the acyl radical under the photochemically initiated condition, the reaction proceeded smoothly, yielding cyclopentanone **11a** in 73% yield under the same condition. A similar result was obtained with **10b**, yielding diphenylphosphinoyl cyclohexanone **11b** in 95% yield (Eq. 5). Furthermore, the irradiation of a benzene solution of **12** at 300 nm for 2 h afforded the desired product **13** in 93% yield. However, contrary to the result obtained with **6** in Scheme 2, the irradiation of **14** in benzene at 300 nm did not give **15**. When a benzene solution of **14** was irradiated at 300 nm for 12 h, the reaction did not occur, and the starting material (91%) was recovered unchanged (Scheme 3).



(5)

There are two possible reaction pathways in the photochemically induced acylphosphorylation of **12**. Pathway **a** involves the intramolecular addition of a photochemically generated radical pair of the acyl radical and the phosphinoyl radical to the pendant alkenyl moiety, as shown in Scheme 4,[10] whereas pathway **b** involves the addition of the photochemically generated diphenyl phosphinoyl radical onto the alkenyl group, followed by cyclization onto the acylphosphonate group. Thus, pathway **b** would follow a similar mechanism to that shown in the thermally induced cyclization of alkenyl acylphospho-

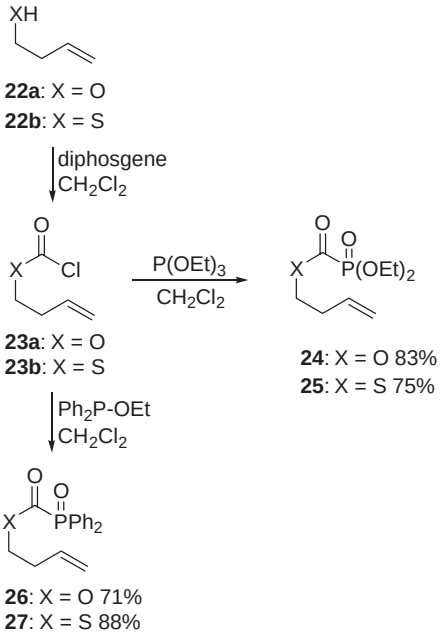
nates (Scheme 1). To gain mechanistic insights of the photochemically induced cyclization, we performed a cross-over experiment using an equimolar mixture of two different acylphosphine oxides, **16** and **17**. When an equimolar mixture of **16** and **17** in benzene was irradiated at 300 nm for 2 h, the product consisted of a mixture of four products, from which a mixture of **18** and **19** was separated from a mixture of **20** and **21** by column chromatography. The ratio of each product was determined by ^{1}H NMR analysis (Eq. 6). The result obtained in this study indicates that the photochemically induced reaction does not proceed via the addition of the radical pair, and supports pathway **b**.



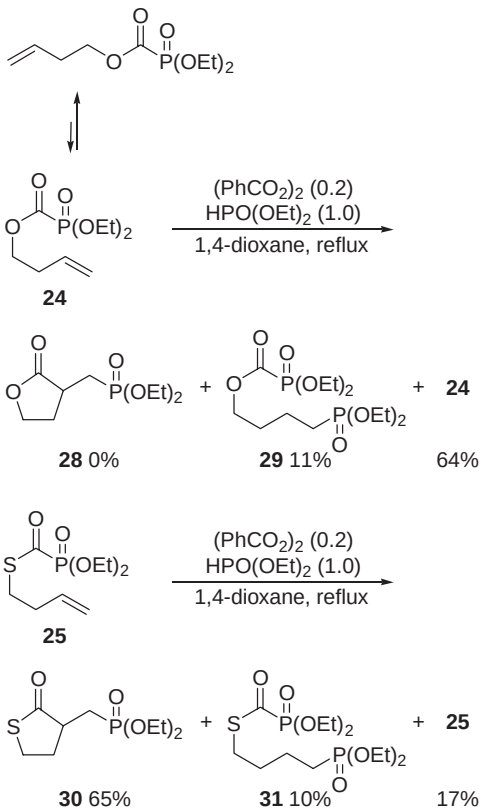
(6)

In order to explain why **14** acts differently under photochemical conditions, several experiments were performed, as shown in Scheme 3. To initiate the reaction, when the reaction was carried out in the presence of 0.2 equiv of benzoyl diphenylphosphine oxide, **15** was obtained in 20% yield, whereas the use of 1 equiv of benzoyl diphenylphosphine oxide gave **15** in 48% yield. Furthermore, a thermal reaction of **14** with benzoyl peroxide (20 mol %) and diphenylphosphine oxide (0.2 equiv) in refluxing dioxane gave **15** in 70% yield. The results suggest that cleavage of the carbon–phosphorous bond in **14** did not occur under photochemical conditions, thereby failing to generate the diphenylphosphinoyl radical. However, we do not know why **14** does not undergo photolysis to initiate the reaction.

We next briefly studied a feasibility of using a phosphonoformate and a phosphonothiolformate as a radical acceptor to explore whether the present acylation would be further extended to the synthesis of lactone **28**[11] and thiolactone **30**,[12] respectively (Scheme 6). Diethylphosphonoformate **24** was prepared by the treatment of chloroformate **23a** with triethyl phosphite in dichloromethane at room temperature for 2 h (Scheme 5).[13] Similarly, *S*-but-3-enyl diethylphosphonothiolformate (**25**) was prepared from **22b** by a two-step procedure.[14] The treatment of **22b** with diphosgene in dichloromethane afforded **23b**, which was further treated with triethyl phosphite to give phosphonothiolformate **25** in 75% yield. Furthermore, the treatment of **23a** with ethyl diphenylphosphinite in dichloromethane at room temperature gave *S*-but-3-enyl diphenylphosphinoformate (**26**) in 71% yield. Similarly, diphenylphosphinothiolformate **27** was prepared in 88% yield by the treatment of **23b** with ethyl diphenylphosphinite under the same condition.



Scheme 5. Preparation of phosphonoformate **24**, phosphonothiolformate **25**, phosphinoformate **26**, and phosphinothiolformate **27**.



Scheme 6. Cyclizations of **24** and **25** under thermal conditions.

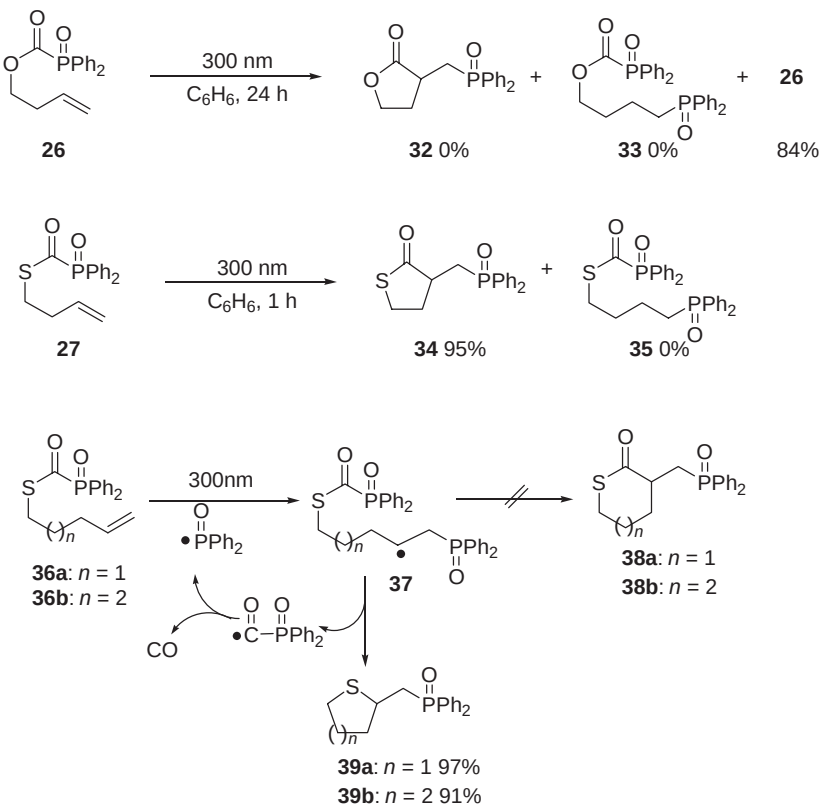
The reaction of **24** with diethyl phosphite (1 equiv) and benzoyl peroxide (20 mol %) in refluxing 1,4-dioxane for 6 h did not afford lactone **28**, yielding **29** in 11% yield along with recovery of the starting material (64%). The failure of the cyclization may be explained as an unfavorable *E*-conformation in carboxylic esters, although the low reactivity of the alkoxycarbonyl group as a radical acceptor can not be excluded.[15] However, it is known that the differences in energy are generally smaller for the *E*- and *Z*-conformations in thiol esters than for the corresponding carboxylic esters.[16] When the radical cyclization of **25** was carried out under similar conditions, the desired thiolactone **30** was obtained in 65% yield along with **31** (10%) and the starting material (17%).

The photochemically induced radical cyclization of phosphonothiolformates occurred smoothly and was cleaner than the thermally induced reaction, as shown in Scheme 7. As we observed previously, the irradiation of **26** in benzene at 300 nm for 24 h did not afford lactone **32**. However, the photochemically induced reaction of **27** in benzene at 300 nm for 1 h afforded thiolactone **34** in 95% yield without the formation of addition product **35**. However, this approach turned out to be effective only for the synthesis of 5-membered thiolactones. The irradiation of a benzene solution of *S*-pent-4-enyl diphenylphosphinothiolformate (**36a**) at 300 nm for 1 h did not give thiolactone **38a**, yielding tetrahydrothiophene **39a** in 97% yield. A similar result was also obtained with **36b**. Since 6-*exo* and 7-*exo* ring closures in **37** are slower than 5-*exo* ring closure in the cyclization of **27**, intramolecular homolytic substitution at sulfur occurred, yielding **39** along with the liberation of a phosphonocarbonyl radical. The loss of carbon monoxide from the phosphonocarbonyl radical would generate the diphenyl phosphinoyl radical for radical chain propagation. The generation of acyl radicals from thiol esters under tin-free conditions was noted previously.[17]

Conclusion

The results obtained in this study suggest that alkyl radicals add to acylphosphonates, and β-fragmentation of the resulting alkoxyl radicals affords 5- and 6-membered cyclic ketones along with the liberation of phosphonyl radicals under thermal and photochemical conditions. The eliminated phosphonyl radicals mainly mediate the acylphosphorylation of alkenyl acylphosphonates by their facile additions to alkenyl bonds. A small portion of phosphonyl radicals is generated from the added dialkyl phosphite, and the use of solvents with active hydrogen, like 1,4-dioxane, is essential for the success of the thermal acylphosphorylation. The photochemically induced cyclizations of alkenyl acyldiphenylphosphine oxides are initiated by the generation of acyl radicals and diphenylphosphinoyl radicals; the reactions then proceed by similar pathway as that involved under thermal conditions.

The cyclizations of alkenyl phosphonoformates do not occur under thermal and photochemical conditions, apparently due to an unfavorable *E*-conformation in carboxylic esters. However, the cyclization of *S*-but-3-enyl phosphinothiolformates gives thiolactones under thermal and photochemical conditions, whereas *S*-pent-4-enyl phosphinothiolformate affords the tetrahydrothiophene derivative under similar conditions, apparently due to an intramolecular homolytic substitution at sulfur.



Scheme 7. Cyclizations of phosphonoformates and phosphonothiolformates under photochemical conditions.

Experimental

General. ^{1}H, ^{13}C, and ^{31}P NMR spectra were determined for solutions in $CDCl_3$ or benzene-d_6 on Bruker DRX500, Bruker Avance-400, or JEOL AL-400 NMR spectrometers, and recorded with tetramethylsilane (TMS) ($\delta = 0$), $CDCl_3$ ($\delta = 77.0$), and 85% H_3PO_4 aq ($\delta = 0$) as internal or external references, unless otherwise noted. Infrared spectra (IR) were recorded on HORIBA FT-300S or VECTOR-33 spectrometers. High-resolution mass spectra (HRMS) were obtained on JEOL JMS-SX 102A using FAB ionization with *m*-nitrobenzylalcohol (NBA) as a matrix or a VG AUTOSPEC Ultma GC/MS system using a direct insertion probe (DIP) and an electron impact (EI) (70 eV) method. Elemental analyses were carried out at the Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, The University of Tokyo.

1,4-Dioxane was distilled over $LiAlH_4$ under argon before use. Dichloromethane (CH_2Cl_2) was distilled twice from P_4O_{10}, then from CaH_2, and stored over molecular sieves 4A. Triethyl phosphite and diethyl phosphite were purchased from Tokyo Kasei Kogyo Co., Ltd. and distilled before use. Benzoyl peroxide (Kishida Kagaku) was used as purchased. Wako Gel B-5F (Wako Pure Chemical Industries, Ltd.) was used for preparative TLC. Column chromatography was performed with PSQ100B (spherical, neutral, Fuji Silicia Kagaku).

Typical Procedure for the Preparation of Acylphosphonates. All acylphosphonates (**1**, **5**, **6**, **8a**, and **8b**) and acylphosphine oxides (**10a**, **10b**, **12**, **14**, and **16**) were synthesized by the Arbuzov reaction from the corresponding acid chloride and triethyl phosphite or ethyl diphenylphosphinite, respectively. The acid chloride was in situ prepared from the corresponding carboxylic acid according to literature.[13]

To a solution of 2-but-3-enylbenzoic acid (0.524 g, 2.97 mmol) in CH_2Cl_2 (3 mL) was slowly added oxalyl chloride (2 M in CH_2Cl_2, 3.0 mL, 6.00 mmol, Aldrich Chemical Co., Inc.) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and allowed to warm up to room temperature. The solvent and volatiles were removed in vacuo after gas generation ended. To the crude acid chloride was added 3 mL of CH_2Cl_2 and cooled to 0 °C; then, triethyl phosphite (0.51 mL, 0.494 g, 2.97 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and overnight at room temperature. The solvent was removed under reduced pressure to afford almost pure acylphosphonate **1**. The crude product was quickly subjected to short silica-gel column chromatography (hexane/ethyl acetate 1:1 v/v) to give pure acylphosphonate **1** (0.744 g, 2.51 mmol, 85%).

Diethyl 2-But-3-enylbenzoylphosphonate (1): Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (distorted t, $J = 7.0$ Hz, 6H), 2.31–2.35 (m, 2H), 2.95 (t, $J = 7.8$ Hz, 2H), 4.23–4.29 (m, 4H), 4.95–5.03 (m, 2H overlapped), 5.82–5.90 (m, 1H), 7.29 (distorted d, $J = 7.5$ Hz, 1H), 7.36 (distorted dd, $J = 7.6$, 7.8 Hz, 1H), 7.49 (distorted dd, $J = 7.5$, 7.6 Hz, 1H), 8.43 (distorted d, $J = 7.8$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3 (d, $J_{CP} = 5.6$ Hz), 33.5, 35.4, 63.9 (d, $J_{CP} = 7.4$ Hz), 115.0, 126.1, 131.5 (d, $J_{CP} = 3.9$ Hz), 132.5, 133.2, 134.6 (d, $J_{CP} = 63.0$ Hz), 137.9, 143.6 (d, $J_{CP} = 9.3$ Hz), 201.6 (d, $J_{CP} = 170.5$ Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ −1; IR (ZnSe) 568, 744, 773, 922, 974, 1016, 1250, 1652, 2981 cm^{-1}; Found: C, 60.81; H, 7.12%. Calcd for $C_{15}H_{21}O_4P$: C, 60.80; H, 7.14%.

Typical Procedure for the Intramolecular Acylphosphorylation (Thermal Conditions). To benzoyl peroxide (15.4 mg, 0.06 mmol) were added a solution of acylphosphonate **1** (88.9 mg, 0.30 mmol) in 1,4-dioxane (2 mL), diethyl phosphite (38.6 μL, 41.3 mg, 0.30 mmol), and 1,4-dioxane (1 mL), successively. The mixture was refluxed for 1 h and evaporated to dryness. The residue was subjected to silica-gel column chromatography or preparative TLC (hexane/acetone 3:2 v/v) to afford γ-ketophosphonate **2** (72.9 mg, 0.25 mmol, 82%).

Diethyl 1-Oxo-1,2,3,4-tetrahydronaphthalen-2-ylmethylphosphonate (2): Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (distorted t, $J = 7.1$ Hz, 6H), 1.68–1.76 (m, 1H), 1.90–1.99 (m, 1H), 2.61–2.66 (m, 1H), 2.80–2.91 (m, 2H overlapped), 2.96–3.01 (m, 1H), 3.09–3.15 (m, 1H), 4.08–4.20 (m, 4H), 7.25 (distorted d, $J = 7.5$ Hz, 1H), 7.31 (distorted dd, $J = 7.6$, 7.8 Hz, 1H), 7.48 (distorted ddd, $J = 1.1$, 7.5, 7.6 Hz, 1H), 8.03 (distorted d, $J = 7.8$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3 (d, $J_{CP} = 6.0$ Hz), 25.0 (d, $J_{CP} = 143.3$ Hz), 29.0, 30.0, 43.0, 61.5 (d, $J_{CP} = 6.4$ Hz), 61.7 (d, $J_{CP} = 6.5$ Hz), 126.5, 127.5, 128.7, 131.8, 133.4, 143.9, 197.7 (d, $J_{CP} = 15.6$ Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 32; IR (ZnSe) 517, 744, 960, 1020, 1053, 1234, 1456, 1599, 1682, 2981 cm^{-1}; Found: C, 60.64; H, 7.26%. Calcd for $C_{15}H_{21}O_4P$: C, 60.80; H, 7.14%.

Typical Procedure for the Intramolecular Acylphosphorylation (Photochemical Conditions). After a dry benzene solution (2.0 mL, 0.2 M in the acylphosphine oxide) of acylphosphine oxide **10a** (119.3 mg, 0.4 mmol) in a quartz tube was degassed with nitrogen for 10 min, the solution was irradiated at 300 nm in a Rayonet photochemical reactor for 2 h. Any volatile matter was evaporated. The residue was subjected to silica-gel column chromatography (hexane/acetone 3:2 v/v) to afford γ-ketophosphine oxide **11a** (87.2 mg, 0.29 mmol, 73%).

Diphenyl 2-Oxocyclopentylmethylphosphine Oxide (11a): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27–1.50 (m, 1H), 1.52–1.70 (m, 1H), 1.82–2.05 (m, 3H), 2.10–2.32 (m, 3H), 2.95 (ddd, $J = 1.9$, 9.9, 15.3 Hz, 1H), 7.26–7.50 (m, 6H), 7.55–7.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 29.5 (d, $J_{CP} = 73.5$ Hz), 30.8, 36.4, 43.6 (d, $J_{CP} = 3.6$ Hz), 128.5 (d, $J_{CP} = 11.8$ Hz), 128.6 (d, $J_{CP} = 11.8$ Hz), 130.4 (d, $J_{CP} = 9.4$ Hz), 130.6 (d, $J_{CP} = 9.2$ Hz), 131.6 (d, $J_{CP} = 2.7$ Hz), 131.7 (d, $J_{CP} = 2.6$ Hz), 132.1 (d, $J_{CP} = 98.7$ Hz), 133.2 (d, $J_{CP} = 98.7$ Hz), 218.9 (d, $J_{CP} = 13.7$ Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 32; IR (ZnSe) 538, 698, 749, 1120, 1183 (P=O), 1438 (P–Ph), 1739 (C=O) cm^{-1}; HRMS (M^+) Found: 298.1122, Calcd for $C_{18}H_{19}O_2P$: 298.1123.

Cross-Over Experiment of a Photochemically Induced Acylphosphorylation. After a dry benzene solution (2.0 mL) of acylphosphine oxide **16** (41.4 mg, 0.1 mmol) and **17** (47.1 mg, 0.1 mmol) in a quartz tube was degassed with nitrogen for 10 min, the solution was irradiated at 300 nm in a Rayonet photochemical reactor for 2 h. Any volatile matter was evaporated. The residue was subjected to silica-gel column chromatography (hexane/acetone 3:2 v/v) to afford a mixture of γ-ketophosphine oxides, **18** and **19** (33.6 mg, ^{1}H NMR ratio 0.99:1.00, 20%, 20%), and a mixture of γ-ketophosphine oxides, **20** and **21** (37.1 mg, ^{1}H NMR ratio 1.09:1.00, 21%, 19%).

3-Oxo-4-diphenylphosphinoylmethylcyclopentane-1,1-dicarboxylic Acid Dimethyl Ester (18): Colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ 1.78–1.93 (m, 1H), 2.26 (dd, $J = 12.0$, 13.7 Hz, 1H), 2.65–2.80 (m, 2H), 2.85–2.97 (m, 2H), 3.10 (s, 3H), 3.21 (s, 3H), 3.22–3.38 (m, 1H), 6.93–7.07 (m, 6H), 7.64–7.79 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 30.6 (d, $J_{CP} = 72.4$ Hz), 37.4, 42.6 (d, $J_{CP} = 3.6$ Hz), 44.1, 52.5 (d, $J_{CP} = 2.9$ Hz), 55.2, 128.7 (d, $J_{CP} = 10.8$ Hz), 128.8 (d, $J_{CP} = 11.1$ Hz), 130.9 (d, $J_{CP} = 9.1$ Hz), 131.2 (d, $J_{CP} = 9.2$ Hz), 131.5 (d, $J_{CP} = 3.0$

Hz), 131.6 (d, $J_{CP} = 2.8$ Hz), 133.6 (d, $J_{CP} = 97.7$ Hz), 135.1 (d, $J_{CP} = 97.7$ Hz), 171.0, 171.2, 212.7 (d, $J_{CP} = 13.5$ Hz); ^{31}P NMR (121.5 MHz, C_6D_6) δ 29; IR (ZnSe) 504, 702, 744, 1121, 1439 (P–Ph), 1733 (C=O) cm^{-1}; HRMS (M^+) Found: 414.1231, Calcd for $C_{22}H_{23}O_6P$: 414.1232.

3-Oxo-4-(bis(4-methylphenyl)phosphinoyl)methylcyclopentane-1,1-dicarboxylic Acid Dimethyl Ester (19): Colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ 1.78–1.93 (m, 1H), 1.94 (d, $J = 11.9$ Hz, 6H), 2.19–2.35 (m, 1H), 2.65–2.80 (m, 2H), 2.85–2.97 (m, 2H), 3.10 (s, 3H), 3.21 (s, 3H), 3.22–3.38 (m, 1H), 6.79–6.89 (m, 4H), 7.64–7.79 (m, 4H); ^{31}P NMR (121.5 MHz, C_6D_6) δ 29.

3-Oxo-4-diphenylphosphinoylmethylcyclopentane-1,1-dicarboxylic Acid Diethyl Ester (20): Colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ 0.74 (t, $J = 7.2$ Hz, 3H), 0.83 (t, $J = 7.2$ Hz, 3H), 1.81–1.93 (m, 1H), 2.31 (dd, $J = 12.0$, 13.6 Hz, 1H), 2.70–2.83 (m, 2H), 2.89–3.02 (m, 2H), 3.23–3.36 (m, 1H), 3.68–3.80 (m, 2H), 3.86 (q, $J = 7.1$ Hz, 2H), 6.93–7.07 (m, 6H), 7.64–7.80 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 13.7, 13.8, 30.7 (d, $J_{CP} = 72.6$ Hz), 37.4, 42.7 (d, $J_{CP} = 3.6$ Hz), 44.1, 55.4, 61.8, 128.7 (d, $J_{CP} = 11.0$ Hz), 128.8 (d, $J_{CP} = 11.0$ Hz), 130.9 (d, $J_{CP} = 9.2$ Hz), 131.2 (d, $J_{CP} = 8.7$ Hz), 131.5 (d, $J_{CP} = 2.6$ Hz), 131.5 (d, $J_{CP} = 2.8$ Hz), 133.6 (d, $J_{CP} = 97.7$ Hz), 135.1 (d, $J_{CP} = 97.7$ Hz), 170.6, 170.9, 213.0 (d, $J_{CP} = 13.7$ Hz); ^{31}P NMR (121.5 MHz, C_6D_6) δ 29; IR (ZnSe) 505, 540, 699, 748, 1120, 1181 (P=O), 1439 (P–Ph), 1731 (C=O), 2983 cm^{-1}; HRMS (M^+) Found: 442.1546, Calcd for $C_{24}H_{27}O_6P$: 442.1545.

3-Oxo-4-(bis(4-methylphenyl)phosphinoyl)methylcyclopentane-1,1-dicarboxylic Acid Diethyl Ester (21): Colorless oil; ^{1}H NMR (400 MHz, C_6D_6) δ 0.82 (t, $J = 7.2$ Hz, 3H), 0.90 (t, $J = 7.2$ Hz, 3H), 1.85–2.12 (m, 1H), 2.00 (d, $J = 12.3$ Hz, 6H), 2.42 (dd, $J = 12.0$, 13.7 Hz, 1H), 2.77–2.92 (m, 2H), 3.01–3.11 (m, 2H), 3.47 (ddd, $J = 1.8$, 8.7, 13.6 Hz, 1H), 3.75–3.89 (m, 2H), 3.93 (q, $J = 7.0$ Hz, 2H), 6.90–6.99 (m, 4H), 7.70–7.83 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 13.7, 13.8, 21.2, 31.0 (d, $J_{CP} = 72.6$ Hz), 37.6, 42.8 (d, $J_{CP} = 3.6$ Hz), 44.2, 55.5, 61.7, 61.7, 129.4 (d, $J_{CP} = 11.8$ Hz), 129.6 (d, $J_{CP} = 11.9$ Hz), 130.7 (d, $J_{CP} = 98.9$ Hz), 131.0 (d, $J_{CP} = 9.4$ Hz), 132.3 (d, $J_{CP} = 9.2$ Hz), 132.3 (d, $J_{CP} = 100.1$ Hz), 141.7 (d, $J_{CP} = 2.6$ Hz), 170.6, 170.9, 213.0 (d, $J_{CP} = 13.5$ Hz); ^{31}P NMR (121.5 MHz, C_6D_6) δ 29; IR (ZnSe) 505, 528, 658, 741, 809, 1118, 1180 (P=O), 1446 (P–Ph), 1731 (C=O), 2982 cm^{-1}; HRMS (M^+) Found: 470.1859, Calcd for $C_{26}H_{31}O_6P$: 470.1858.

Typical Procedure for the Preparation of Phosphonoformates and Phosphonothiolformates. All phosphonoformates (**24** and **26**) and phosphonothiolformates (**25**, **27**, **36a**, and **36b**) were synthesized by the Arbuzov reaction from the corresponding chloroformate or chlorothiolformate and triethyl phosphite or ethyl diphenylphosphinite. The chloroformate and chlorothiolformate were in situ prepared from the corresponding alcohol or thiol using diphosgene and triethylamine.

To a solution of homoallyl alcohol **22a** (260 μL, 3.0 mmol) in CH_2Cl_2 (10 mL), diphosgene (540 μL, 4.5 mmol), and triethylamine (418 μL, 3.0 mmol) were added at 0 °C. After being stirred for 1 h at room temperature, the solvent and excess diphosgene were removed under reduced pressure and filtered through a celite pad using diethyl ether. After the crude chloroformate was dissolved in dichloromethane (10 mL), triethyl phosphite (510 μL, 3.0 mmol) was added at 0 °C. After being stirred for 1 h at room temperature, the solvent was evaporated under reduced pressure and the residue was separated by silica-gel column chromatography (ethyl acetate/*n*-hexane 1:1 v/v) to give phosphonoformate **24** (588.1 mg, 83%).

But-3-enyl Diethylphosphonoformate (24): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, $J = 9.5$ Hz, 6H), 2.32–2.42 (m, 2H), 4.11–4.25 (m, 6H), 4.96–5.10 (m, 2H), 5.60–5.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0 (d, $J_{CP} = 5.5$ Hz), 32.6, 64.2 (d, $J_{CP} = 11.8$ Hz), 65.6, 117.5, 133.0, 166.7 (d, $J_{CP} = 356.5$ Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ −4; IR (ZnSe) 559, 586, 1022, 1164 (P=O), 1212, 1274, 1719 (C=O), 2985 cm^{-1}; HRMS (M^+) Found: 236.0840, Calcd for $C_9H_{17}O_5P$: 236.0814.

Supporting Information

Additional spectral data of all new compounds. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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