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Synthesis of Substituted 3(2*H*)-Furanones Using Alkylative Intramolecular Cyclization of Sulfonium Salts

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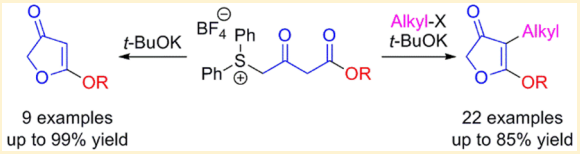
Supporting Information

ABSTRACT: The facile alkylative intramolecular cyclization of 3-alkoxycarbonyl-2-oxopropyldiphenylsulfonium salts is described. This simple method can be readily applied to the synthesis of a novel family of 4-alkylated 3(2*H*)-furanones in moderate to high yields under mild conditions via a one-pot process.

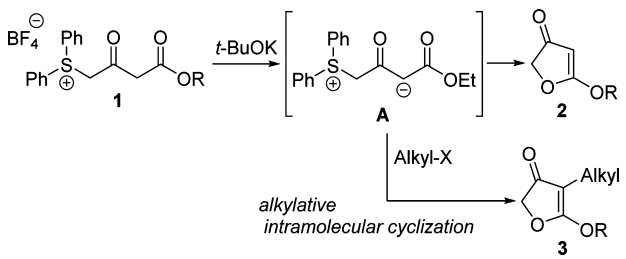


INTRODUCTION

3(2*H*)-Furanone is a core structural unit of many natural products, such as eremantholide A,[1] geiparvarin,[2] pseurotin A,[3] and jatrophone.[4] In addition, 3(2*H*)-furanone derivatives exhibit antitumor,[5] antiallergic,[6] antiulcer,[7] antiproliferactive,[8] selective COX-2 inhibitory,[9] and selective MAO-B inhibitory activities.[10] Consequently, a variety of synthetic methodologies for the functionalized 3(2*H*)-furanones have been developed, including acid-induced cyclization/dehydration of α'-hydroxy-1,3-diketones,[11] aldol reaction of 3-silyloxyfurans,[12] acid-catalyzed cyclization of α'-hydroxyenone,[13] domino reaction of α,β-acetylenic-γ-hydroxy nitriles with arenecarboxylic acids,[14] and cycloisomerization of allenic hydroxyketones in water.[15] Recently, methods based on transition-metal-catalyzed cyclizations, such as Au-catalyzed intramolecular cyclization of γ-hydroxyalkynones[16] and 2-oxo-3-butynoates,[17] Cu-catalyzed [4+1] annulation between α-hydroxyketones and nitriles,[18] and Michael addition/Pd-catalyzed ring closure of activated alkenes and 4-chloroacetoacetates,[19] have attracted considerable attention. However, the known synthetic methods have several drawbacks, such as unsatisfactory yields of the desired product, limited substrate scope, harsh conditions, and lack of a general procedure for the preparation of the starting materials. Therefore, further research is required to develop a more efficient approach to highly functionalized 3(2*H*)-furanones.

We previously reported a useful method for the synthesis of five-membered carbocycles using phosphoranes, such as allylidenetriphenylphosphorane and 2-oxopropylidenetriphenylphosphorane.[20] During the course of our study, we found that treatment of sulfonium salt **1** with *t*-BuOK produced 3(2*H*)-furanone **2** (Scheme 1). In addition, alkylative intramolecular cyclization of **1** leads to the formation of 4-alkylated 3(2*H*)-furanone **3**. To the best of our knowledge, the intramolecular cyclization of sulfonium salts to produce 3(2*H*)-furanones has not been reported to date. Herein, we report a detailed study of the intramolecular cyclization of sulfonium salts. Notably, this method involves the use of commercially available alkyl halides and *t*-BuOK, which are easy to handle, leading to a novel family of 4-alkylated 3(2*H*)-furanones via a one-pot synthesis under mild conditions.

Scheme 1. Intramolecular Cyclization of Sulfonium Salt 1



RESULTS AND DISCUSSION

Initially, 3-ethoxycarbonyl-2-oxopropyldiphenylsulfonium tetrafluoroborate (**1a**) was used as a substrate for the examination of intramolecular cyclization (Table 1). When sulfonium salt **1a** was treated with *t*-BuOK in THF at room temperature, the desired 3(2*H*)-furanone **2a** was obtained in 88% yield (entry 1). Other inorganic and organic bases were less effective (entries 2−5). Among the examined solvents, THF resulted in the best yield (entries 1 and 6−8). Having defined the optimized conditions, we next examined the scope and limitations of the ester part of sulfonium salts **1** (entries 9−16). All sulfonium salts **1b**−**1i** were prepared by the reaction of the corresponding 4-bromoacetoacetate with diphenylsulfide in the presence of silver(I) tetrafluoroborate. Sulfonium salts **1** bearing isopropyl, cyclopentyl, and cyclohexyl esters gave the corresponding 5-alkoxy-3(2*H*)-furanones **2** in high yields (entries 9−11). Similarly, 3(2*H*)-furanones with allyloxy, propargyloxy, phenyloxy, benzyloxy, or 4-bromobenzyloxy

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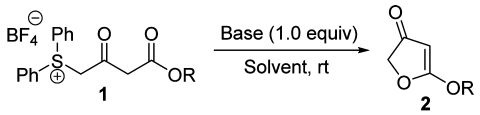
Table 1. Intramolecular Cyclization of Sulfonium Salt 1[a]



1a: R = Et **1d**: R = Cyclohexyl **1g**: R = Ph
1b: R = *i*Pr **1e**: R = Allyl **1h**: R = Bn
1c: R = Cyclopentyl **1f**: R = Propargyl **1i**: R = 4-$BrC_6H_4CH_2$

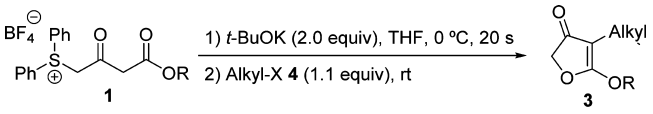
entry	1	base	solvent	time (h)	yield (%)[b]
1	**1a**	*t*-BuOK	THF	1	88
2	**1a**	K_2CO_3	THF	1	23
3	**1a**	NaH	THF	1	57
4	**1a**	Et_3N	THF	1	82
5	**1a**	LiHMDS	THF	1	2
6	**1a**	*t*-BuOK	toluene	1	71
7	**1a**	*t*-BuOK	CH_2Cl_2	1	68
8	**1a**	*t*-BuOK	Et_2O	1	30
9	**1b**	*t*-BuOK	THF	1	86
10	**1c**	*t*-BuOK	THF	1	92
11	**1d**	*t*-BuOK	THF	1	91
12	**1e**	*t*-BuOK	THF	5	90
13	**1f**	*t*-BuOK	THF	1	95
14	**1g**	*t*-BuOK	THF	1	91
15	**1h**	*t*-BuOK	THF	1	93
16	**1i**	*t*-BuOK	THF	3	99

[a]Reaction conditions: sulfonium salt **1** (0.2 mmol), base (0.2 mmol), solvent (2.0 mL). [b]Isolated yield.

groups in the 5 position were obtained in high yields from the corresponding sulfonium salts (entries 12−16). It is noteworthy that the efficient construction of 3(2*H*)-furanone with a variety of alkoxy groups was accomplished within 1−5 h, with good yields in all cases.

We next carried out the alkylation of in situ-generated enolate and subsequent ring closure to afford 4-alkylated 3(2*H*)-furanones (Table 2). When sulfonium salt **1a** was treated with 2.0 equiv of *t*-BuOK and 1.1 equiv of benzyl bromide (BnBr, **4a**) in THF, the desired 4-benzyl-5-ethoxy-3(2*H*)-furanone **3aa** was obtained in 83% yield (entry 1). This simple one-pot process allowed us to use various benzyl bromides having an electron-donating as well as an electron-withdrawing group, and the corresponding alkylated products **3ab**−**3ag** were obtained in good yields (entries 2−7). Similar to benzyl bromide, use of methyl iodide (**4h**) and ethyl iodide (**4i**) gave the products **3ah** and **3ai** in 79% and 53% yields, respectively (entries 8 and 9). However, the reaction with isopropyl iodide resulted in a poor reaction yield, presumably because of the competing elimination reaction. More reactive halides, including allyl bromide (**4j**), cinnamyl bromide (**4k**), and propargyl bromide (**4l**), underwent alkylative intramolecular cyclization well (entries 10−12). Furthermore, ethyl bromoacetate (**4m**) and 2-thienylmethyl bromide (**4n**) were also tolerated in the reaction, affording **3am** and **3an**, respectively (entries 13 and 14). Finally, the reactions were attempted using sulfonium salts **1** bearing various ester moieties and benzyl bromide, and the desired products were obtained in moderate to good yields (entries 15−22). It should be emphasized that a variety of 4-alkylated 3(2*H*)-furanones were readily obtained in moderate to good yields by a simple one-pot process.

Table 2. Synthesis of 4-Alkylated 3(2*H*)-Furanones 3[a]

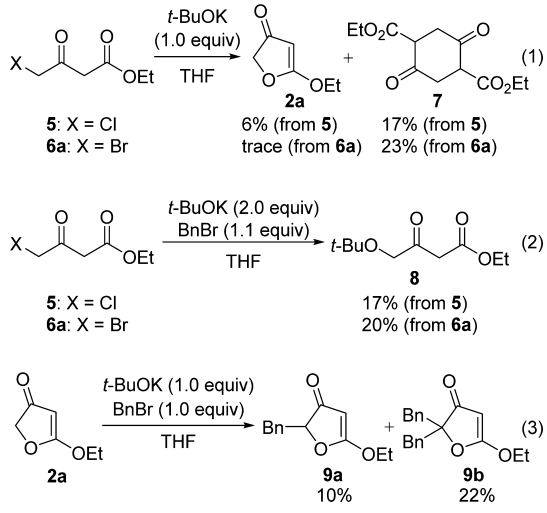


entry	1	4	time (h)	3	yield (%)[b]
1	**1a**	BnBr (**4a**)	3	**3aa**	83
2	**1a**	4-$MeOC_6H_4CH_2Br$ (**4b**)	1	**3ab**	64
3	**1a**	4-$MeC_6H_4CH_2Br$ (**4c**)	1	**3ac**	81
4	**1a**	4-$ClC_6H_4CH_2Br$ (**4d**)	2	**3ad**	76
5	**1a**	4-$BrC_6H_4CH_2Br$ (**4e**)	4	**3ae**	72
6	**1a**	2-$BrC_6H_4CH_2Br$ (**4f**)	3	**3af**	85
7	**1a**	2-$FC_6H_4CH_2Br$ (**4g**)	3	**3ag**	77
8	**1a**	methyl iodide (**4h**)	1	**3ah**	79
9	**1a**	ethyl iodide (**4i**)	1	**3ai**	53
10	**1a**	allyl bromide (**4j**)	3	**3aj**	71
11	**1a**	cinnamyl bromide (**4k**)	3	**3ak**	76
12	**1a**	propargyl bromide (**4l**)	3	**3al**	76
13	**1a**	$BrCH_2CO_2Et$ (**4m**)	3	**3am**	73
14	**1a**	2-thienylmethyl bromide (**4n**)	1	**3an**	73
15	**1b**	**4a**	2	**3ba**	70
16	**1c**	**4a**	1	**3ca**	73
17	**1d**	**4a**	1	**3da**	77
18	**1e**	**4a**	2	**3ea**	76
19	**1f**	**4a**	2	**3fa**	70
20	**1g**	**4a**	1	**3ga**	38
21	**1h**	**4a**	2	**3ha**	69
22	**1i**	**4a**	2	**3ia**	68

[a]Reaction conditions: sulfonium salt **1** (0.20 mmol), *t*-BuOK (0.40 mmol), alkyl-X **4** (0.22 mmol), THF (2.5 mL). [b]Isolated yield.

To obtain insight into the mechanism of the intramolecular cyclization of **1**, mechanistic studies were carried out. When ethyl 4-chloroacetoacetate (**5**) or ethyl 4-bromoacetoacetate (**6a**) was subjected to the optimal conditions, the formation of a trace amount of desired **2a** and dimerization product **7** was observed (Scheme 2, eq 1). Moreover, the treatment of **5** or **6a** with 2.0 equiv of *t*-BuOK in the presence of 1.1 equiv of BnBr did not afford desired **3aa**; instead, nucleophilic substitution product **8** was detected (Scheme 2, eq 2). These results clearly indicate that a bulky leaving group is important to form the

Scheme 2. Mechanistic Studies



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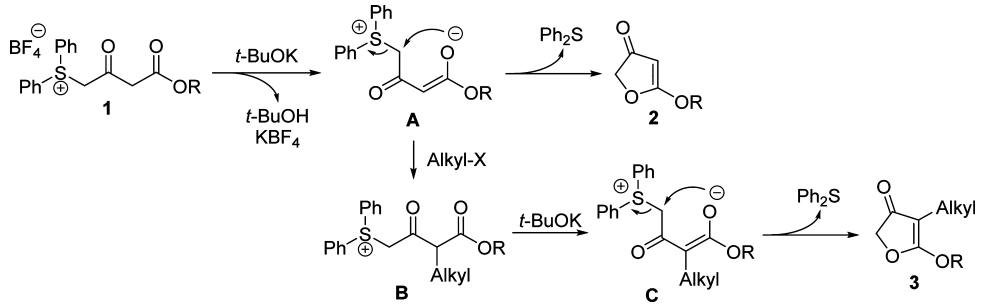
Scheme 3. Plausible Mechanism

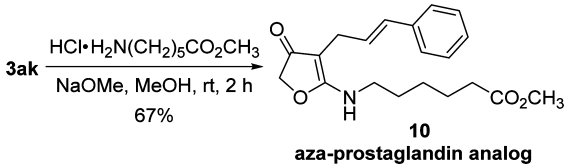


desired 3(2*H*)-furanones, because the substrates having smaller leaving groups (Cl, **5**; Br, **6a**) undergo the intermolecular S_N2 reaction. Furthermore, treatment of 3(2*H*)-furanone **2a** with 1.0 equiv of BnBr and 1.0 equiv of *t*-BuOK afforded 2-monobenzylated **9a** and 2,2-dibenzylated **9b** (Scheme 2, eq 3), revealing that alkylation of the furanone skeleton does not occur in the reaction. All of the results mentioned above disclose that a bulky diphenylsulfonio group would prevent undesired intermolecular side reaction and decomposition of substrate **1** by *t*-BuOK.

Based on these experimental results, a plausible mechanism for intramolecular cyclization of **1** is described in Scheme 3. Initially, enolate **A** is generated by the treatment of **1** with *t*-BuOK. Subsequently, intramolecular nucleophilic attack of the oxygen of **A** gives 3(2*H*)-furanone **2** and diphenylsulfide (Ph_2S). With regard to the alkylative intramolecular cyclization, enolate **A** reacts with alkyl halides to form alkylated intermediate **B**. Subsequent deprotonation of **B** by another equivalent of *t*-BuOK and intramolecular cyclization of alkylated enolate **C** gives 4-alkylated 3(2*H*)-furanone **3** and Ph_2S.

The 4-alkylated 3(2*H*)-furanones can undergo further transformations to afford useful substances. For example, treatment of **3ak** with methyl 6-aminohexanoate and sodium methoxide in methanol for 2 h at room temperature afforded aza-prostaglandin analogue **10** in 67% yield (Scheme 4),[21] indicating that a 4-alkyl-5-alkoxy-3(2*H*)-furanone **3** serves as an important synthetic intermediate for the synthesis of a variety of biologically important compounds.

Scheme 4. Conversion of 3ak into Aza-prostaglandin Analogue 10



CONCLUSION

In summary, we have developed a one-pot synthesis of substituted 3(2*H*)-furanones from sulfonium salts **1** via alkylation followed by intramolecular cyclization under mild conditions. The proposed procedure shows wide substrate scope and functional group tolerance. This reaction can be extended to a few-step synthesis of an aza-prostaglandin analogue. The aza-prostaglandin analogue was prepared in 51% overall yield over two steps from the sulfonium salt **1a**. This method would provide novel synthetic routes for biologically important compounds containing a furanone skeleton.

EXPERIMENTAL SECTION

All reactions were performed under an argon atmosphere. The reagents and solvents were used as received from commercial suppliers without any further purification, unless otherwise indicated. Alkyl halides **4b** and **4n** were prepared according to the literature procedure.[22] Silica gel (40−50 mesh) was used for flash column chromatography. Components separated by thin-layer chromatography (TLC) were detected under UV light at 254 nm or by staining by using ethanoic *p*-anisaldehyde. IR spectra were recorded on an FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra recorded in $CDCl_3$ were referenced to TMS (0.00 ppm) and the solvent peak (77.0 ppm), respectively. ^{1}H NMR and ^{13}C NMR spectra recorded in CD_2Cl_2 were referenced to the residual solvent peaks (5.32 and 53.8 ppm, respectively). High-resolution mass spectra (HRMS) were measured by using FAB, ESI-TOF, and APCI-Orbitrap mass spectrometers.

General Procedure for Synthesis of 4-Bromoacetoacetates 6. Dry CH_2Cl_2 (20 mL) and diketene (1.94 mL, 25.4 mmol) were added to a four-necked round-bottom flask equipped with two dropping funnels and a thermometer, after the solution was cooled to −20 °C. Bromine (1.3 mL, 25.4 mmol) in dry CH_2Cl_2 (5 mL) was slowly added to the mixture at such a rate that the temperature did not rise above −10 °C, and the mixture was stirred until the color of bromine disappeared. Pyridine (2.06 mL, 25.5 mmol) and alcohol (1.0 equiv) in dry CH_2Cl_2 (5 mL) were added slowly to the mixture at such a rate that the temperature did not rise above −10 °C. The mixture was allowed to warm to room temperature and was stirred for 1 h. The mixture was treated with water and extracted with EtOAc. The extract was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc = 12:1) gave the 4-bromoacetoacetate **6** (keto−enol mixture).

*Ethyl 4-Bromoacetoacetate (**6a**).*[23] Pale yellow oil (4.40 g, 84%). R_f = 0.40 (*n*-hexane/EtOAc = 4:1). IR (neat): 1746, 1728 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.22 (q, J = 7.2 Hz, 2 H), 4.06 (s, 2 H), 3.71 (s, 2 H), 1.30 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.6, 166.6, 61.8, 46.0, 33.8, 14.0. HRMS (FAB): m/z [M+H]$^+$ calcd for $C_6H_{10}{}^{81}BrO_3$, 210.9793; found, 210.9802; calcd for $C_6H_{10}{}^{79}BrO_3$, 208.9813; found, 208.9816.

*Isopropyl 4-Bromoacetoacetate (**6b**).* Pale yellow oil (4.56 g, 81%). R_f = 0.48 (*n*-hexane/EtOAc = 4:1). IR (neat): 1741, 1724 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.07 (sept, J = 6.3 Hz, 1 H), 4.05 (s, 2 H), 3.67 (s, 2 H), 1.27 (d, J = 6.3 Hz, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.8, 166.1, 69.6, 46.4, 33.9, 21.7. HRMS (FAB): m/z [M+H]$^+$ calcd for $C_7H_{12}{}^{81}BrO_3$, 224.9949; found, 224.9935; calcd for $C_7H_{12}{}^{79}BrO_3$, 222.9970; found, 222.9960.

*Cyclopentyl 4-Bromoacetoacetate (**6c**).* Pale yellow oil (5.20 g, 82%). R_f = 0.50 (*n*-hexane/EtOAc = 4:1). IR (neat): 2966, 1723 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.25−5.22 (m, 1 H), 4.04 (s, 2 H), 3.67 (s, 2 H), 1.91−1.86 (m, 2 H), 1.76−1.70 (m, 4 H), 1.64−1.58 (m, 2 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 194.8, 166.3, 78.8, 46.3, 33.9, 32.5, 23.6. HRMS (FAB): m/z [M+H]$^+$ calcd for $C_9H_{14}{}^{81}BrO_3$,

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251.0106; found, 251.0111; calcd for $C_9H_{14}{}^{79}BrO_3$, 249.0126; found, 249.0111.

*Cyclohexyl 4-Bromoacetoacetate (**6d**).* Pale yellow liquid (4.09 g, 62%). R_f = 0.52 (*n*-hexane/EtOAc = 4:1). IR (neat): 2938, 2860, 1722 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 4.87−4.81 (m, 1 H), 4.05 (s, 2 H), 3.69 (s, 2 H), 1.89−1.85 (m, 2 H), 1.76−1.71 (m, 2 H), 1.57−1.53 (m, 1 H), 1.49−1.33 (m, 4 H), 1.31−1.24 (m, 1 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 194.8, 166.0, 74.4, 46.4, 33.9, 31.3, 25.2, 23.6. HRMS (FAB): *m*/*z* $[M+H]^+$ calcd for $C_{10}H_{16}{}^{81}BrO_3$, 265.0262; found, 265.0273; calcd for $C_{10}H_{16}{}^{79}BrO_3$, 263.0283; found, 263.0255.

*Allyl 4-Bromoacetoacetate (**6e**).* Pale yellow liquid (4.70 g, 85%). R_f = 0.44 (*n*-hexane/EtOAc = 4:1). IR (neat): 1747, 1730 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 5.92 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1 H), 5.36 (dq, *J* = 17.2, 1.3 Hz, 1 H), 5.29 (dq, *J* = 10.4, 1.3 Hz, 1 H), 4.66 (dt, *J* = 5.8, 1.3 Hz, 2 H), 4.05 (s, 2 H), 3.75 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.4, 166.3, 131.2, 119.2, 66.3, 45.9, 33.8. HRMS (FAB): *m*/*z* $[M+H]^+$ calcd for $C_7H_{10}{}^{81}BrO_3$, 222.9793; found, 222.9802; calcd for $C_7H_{10}{}^{79}BrO_3$, 220.9813; found, 220.9803.

*Propargyl 4-Bromoacetoacetate (**6f**).* Pale yellow liquid (4.31 g, 78%). R_f = 0.32 (*n*-hexane/EtOAc = 4:1). IR (neat): 3289, 1751, 1734 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 4.76 (d, *J* = 2.4 Hz, 2 H), 4.04 (s, 2 H), 3.78 (s, 2 H), 2.53 (t, *J* = 2.4 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.0, 165.8, 76.7, 75.7, 53.0, 45.6, 33.7. HRMS (FAB): *m*/*z* $[M+H]^+$ calcd for $C_7H_8{}^{81}BrO_3$, 220.9636; found, 220.9632; calcd for $C_7H_8{}^{79}BrO_3$, 218.9657; found, 218.9660.

*Phenyl 4-Bromoacetoacetate (**6g**).* Pale yellow liquid (4.61 g, 72%). R_f = 0.38 (*n*-hexane/EtOAc = 4:1). IR (neat): 1765, 1728, 733, 690 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.42−7.38 (m, 2 H), 7.28−7.25 (m, 1 H), 7.14−7.12 (m, 2 H), 4.09 (s, 2 H), 3.96 (s, 2 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 194.3, 165.3, 150.1, 129.5, 126.4, 121.3, 46.0, 26.9. HRMS (FAB): *m*/*z* $[M+H]^+$ calcd for $C_{10}H_{10}{}^{81}BrO_3$, 258.9793; found, 258.9794; calcd for $C_{10}H_{10}{}^{79}BrO_3$, 256.9813; found, 256.9828.

*Benzyl 4-Bromoacetoacetate (**6h**).*[24] Pale yellow liquid (5.39 g, 79%). R_f = 0.40 (*n*-hexane/EtOAc = 4:1). IR (neat): 1745, 1730, 749, 699 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.40−7.34 (m, 5 H), 5.19 (s, 2 H), 4.02 (s, 2 H), 3.76 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.4, 166.4, 134.9, 128.7, 128.6, 128.4, 67.5, 46.0, 33.8. HRMS (FAB): *m*/*z* $[M+H]^+$ calcd for $C_{11}H_{12}{}^{81}BrO_3$, 272.9949; found, 272.9954; calcd for $C_{11}H_{12}{}^{79}BrO_3$, 270.9970; found, 270.9965.

*4-Bromobenzyl 4-Bromoacetoacetate (**6i**).* White solid (7.00 g, 80%). Mp 72.0−72.8 °C. R_f = 0.34 (*n*-hexane/EtOAc = 4:1). IR (KBr): 1741, 1720, 708 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.4 Hz, 2 H), 7.24 (d, *J* = 7.4 Hz, 2 H), 5.14 (s, 2 H), 4.01 (s, 2 H), 3.76 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.3, 166.3, 134.0, 131.9, 130.1, 122.7, 66.6, 45.9, 33.7. HRMS (APCI-Orbitrap): *m*/*z* $[M-H]^-$ calcd for $C_{11}H_9{}^{81}Br_2O_3$, 350.8882; found, 350.8883; calcd for $C_{11}H_9{}^{81}Br^{79}BrO_3$, 348.8904; found, 348.8904; calcd for $C_{11}H_9{}^{79}Br_2O_3$, 346.8927; found, 346.8924.

General Procedure for Synthesis of Sulfonium Salts 1. Diphenylsulfide (5.4 mL, 33 mmol) was added to a suspension of silver(I) tetrafluoroborate (1.25 g 6.42 mmol) in dry CH_2Cl_2 (5.4 mL) at 0 °C, and the mixture was stirred for 5 min. A solution of 4-bromoacetoacetate **6** (1.0 equiv) in dry CH_2Cl_2 (1.0 mL) was added to the mixture via cannula, and the mixture was allowed to warm room temperature and then stirred for 48 h in the dark. The mixture was filtered through a Celite pad and concentrated under reduced pressure. The residue was applied on silica gel and eluted with CH_2Cl_2 (to remove excess Ph_2S) followed by CH_2Cl_2/MeOH = 15:1. The latter solution was concentrated under reduced pressure, and *tert*-butyl methyl ether was added to the residue. The mixture was stirred until a precipitate was observed, and then the *tert*-butyl methyl ether phase was decanted. After washing of the solid with *tert*-butyl methyl ether was repeated several times, the solid was collected and dried under vacuum to give sulfonium salt **1**.

*3-Ethoxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1a**).* White solid (1.58 g, 61%). Mp 117.4−117.5 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 1748, 1719, 1058, 741, 689 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.96−7.94 (m, 4 H), 7.74−7.71 (m, 2 H), 7.69−7.65 (m, 4 H), 5.77 (s, 2 H), 4.17 (q, *J* = 7.2 Hz, 2 H), 3.84 (s, 2 H), 1.25 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.4, 166.9, 134.7, 131.6, 130.4, 123.8, 62.1, 56.2, 47.0, 13.9. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{18}H_{19}O_3S$, 315.1055; found, 315.1047.

*3-Isopropyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1b**).* White solid (1.66 g, 62%). Mp 104.1−104.7 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 1745, 1720, 1105, 1082, 741, 690 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.96−7.74 (m, 4 H), 7.74−7.72 (m, 2 H), 7.70−7.67 (m, 4 H), 5.80 (s, 2 H), 5.02 (sept, *J* = 6.3 Hz, 1 H), 3.84 (s, 2 H), 1.24 (d, *J* = 6.3 Hz, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.6, 166.6, 134.7, 131.6, 130.4, 123.8, 70.2, 56.3, 47.3, 21.6. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{19}H_{21}O_3S$, 329.1211; found, 329.1215.

*3-Cyclopentyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1c**).* White solid (1.62 g, 57%). Mp 123.2−123.6 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 2966, 1741, 1723, 1067, 740, 690 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.96−7.93 (m, 4 H), 7.75−7.71 (m, 2 H), 7.70−7.66 (m, 4 H), 5.78 (s, 2 H), 5.19−5.15 (m, 1 H), 3.83 (s, 2 H), 1.84−1.80 (m, 2 H), 1.71−1.68 (m, 4 H), 1.59−1.56 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.6, 166.9, 134.7, 131.6, 130.4, 123.8, 79.3, 56.3, 47.3, 32.5, 23.6. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{21}H_{23}O_3S$, 355.1368; found, 355.1370.

*3-Cyclohexyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1d**).* White solid (1.78 g, 61%). Mp 137.7−137.9 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 2941, 2858, 1748, 1717, 1085, 1037, 750, 689 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.96−7.93 (m, 4 H), 7.74−7.71 (m, 2 H), 7.66−7.69 (m, 4 H), 5.78 (s, 2 H), 4.79−4.74 (m, 1 H), 3.84 (s, 2 H), 1.83−1.81 (m, 2 H), 1.71−1.69 (m, 2 H), 1.53−1.50 (m, 1 H), 1.45−1.38 (m, 2 H), 1.36−1.19 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.6, 166.5, 134.7, 131.6, 130.4, 123.8, 75.0, 56.3, 47.3, 31.3, 25.1, 23.6. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{22}H_{25}O_3S$, 369.1524; found, 369.1508.

*3-Allyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1e**).* White solid (1.69 g, 64%). Mp 114.0−114.7 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 1750, 1720, 1060, 1032, 753, 684 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.96−7.93 (m, 4 H), 7.73−7.70 (m, 2 H), 7.68−7.65 (m, 4 H), 5.83 (ddt, *J* = 17.2, 10.5, 5.9 Hz, 1 H), 5.77 (s, 2 H), 5.30 (dq, *J* = 17.2, 1.3 Hz, 1 H), 5.25 (dq, *J* = 10.5, 1.3 Hz, 1 H), 4.61 (dt, *J* = 5.9, 1.3 Hz, 2 H), 3.87 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.3, 166.5, 134.7, 131.6, 131.1, 130.4, 123.8, 119.2, 66.5, 56.1, 46.9. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{19}H_{19}O_3S$, 327.1055; found, 327.1046.

*3-Propargyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1f**).* White solid (1.37 g, 52%). Mp 87.6−87.9 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 3291. 1754, 1727, 1059, 741, 689 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.95−7.93 (m, 4 H), 7.73−7.70 (m, 2 H), 7.68−7.64 (m, 4 H), 5.75 (s, 2 H), 4.70 (d, *J* = 2.5 Hz, 2 H), 3.87 (s, 2 H), 2.49 (t, *J* = 2.5 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 165.9, 134.7, 131.6, 130.4, 123.8, 76.8, 75.7, 56.0, 53.2, 46.7. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{19}H_{17}O_3S$, 325.0898; found, 325.0895.

*3-Phenyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1g**).* White solid (1.07 g, 37%). Mp 115.5−115.9 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 1764, 1719, 1057, 747, 686 cm^{-1}. ^1H NMR (500 MHz, CD_2Cl_2): δ 7.93−7.91 (m, 4 H), 7.76−7.73 (m, 2 H), 7.69−7.65 (m, 4 H), 7.40−7.36 (m, 2 H), 7.28−7.25 (m, 1 H), 7.12−7.09 (m, 2 H), 5.75 (s, 2 H), 4.10 (s, 2 H). ^{13}C NMR (126 MHz, CD_2Cl_2): δ 193.4, 166.1, 150.5, 135.2, 132.0, 130.8, 129.9, 126.8, 124.0, 121.9, 56.6, 47.4. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{22}H_{19}O_3S$, 363.1055; found, 363.1053.

*3-Benzyloxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1h**).* White solid (1.74 g, 58%). Mp 66.8−67.5 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 1749, 1720, 1056, 742, 691 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.90−7.89 (m, 4 H), 7.68−7.60 (m, 6 H), 7.35−7.29 (m, 5 H), 5.73 (s, 2 H), 5.13 (s, 2 H), 3.85 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.2, 166.5, 134.9, 134.6, 131.5, 130.4, 128.6, 128.5, 128.4, 123.8, 67.7, 56.1, 47.0. HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{23}H_{21}O_3S$, 377.1211; found, 377.1195.

*3-(4-Bromobenzyl)oxycarbonyl-2-oxopropyldiphenylsulfonium Tetrafluoroborate (**1i**).* White solid (1.87 g, 54%). Mp 110.6−111.0 °C. R_f = 0.40 (DCM/MeOH = 9:1). IR (KBr): 1748, 1723, 1070, 805, 741, 690 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.91−7.89 (m, 4 H),

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7.69−7.66 (m, 2 H), 7.63−7.60 (m, 4 H), 7.45 (d, J = 8.4 Hz, 2 H), 7.19 (d, J = 8.4 Hz, 2 H), 5.74 (s, 2 H), 5.07 (s, 2 H), 3.86 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.2, 166.4, 134.6, 133.9, 131.7, 131.5, 130.4, 130.1, 123.8, 122.5, 66.8, 56.1, 46.9. HRMS (FAB): m/z $[M]^+$ calcd for $C_{23}H_{20}{}^{81}BrO_3S$, 457.0296; found, 457.0295; calcd for $C_{23}H_{20}{}^{79}BrO_3S$, 455.0317; found, 455.0315.

General Procedure for Synthesis of 5-Alkoxy-3(2*H*)-furanones 2. *t*-BuOK (1.0 equiv) was added to a suspension of sulfonium salt **1** (0.2 mmol) in dry THF (2.0 mL) at room temperature. The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the reaction, the mixture was treated with brine and extracted with EtOAc. The organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc = 1:4) gave the desired 5-alkoxy-3(2*H*)-furanone **2**.

*5-Ethoxy-3(2H)-furanone (**2a**).*[25] White solid (22.0 mg, 88%). Mp 58.3−58.5 °C. R_f = 0.30 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1687, 1571 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.81 (s, 1 H), 4.57 (s, 2 H), 4.28 (q, J = 7.1 Hz, 2 H), 1.46 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.2, 185.7, 80.5, 75.1, 67.9, 14.2. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_6H_9O_3$, 129.0552; found, 129.0551.

*5-Isopropyloxy-3(2H)-furanone (**2b**).* Colorless oil (24.6 mg, 86%). R_f = 0.36 (*n*-hexane/EtOAc = 1:4). IR (neat): 1698, 1574 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.80 (s, 1 H), 4.70 (sept, J = 6.2 Hz, 1 H), 4.57 (s, 2 H), 1.43 (d, J = 6.2 Hz, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.3, 185.0, 80.8, 76.7, 74.8, 21.7. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_7H_{11}O_3$, 143.0708; found, 143.0704.

*5-Cyclopentyloxy-3(2H)-furanone (**2c**).* White solid (30.8 mg, 92%). Mp 65.6−65.8 °C. R_f = 0.32 (*n*-hexane/EtOAc = 1:4). IR (KBr): 2970, 1693, 1571 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.92−4.89 (m, 1 H), 4.79 (s, 1 H), 4.56 (s, 2 H), 1.96−1.91 (m, 4 H), 1.90−1.78 (m, 2 H), 1.71−1.65 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.3, 185.3, 85.7, 81.2, 74.9, 32.7, 23.6. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_9H_{13}O_3$, 169.0865; found, 169.0867.

*5-Cyclohexyloxy-3(2H)-furanone (**2d**).* White solid (33.1 mg, 91%). Mp 89.2−89.7 °C. R_f = 0.48 (*n*-hexane/EtOAc = 1:4). IR (KBr): 2937, 2865, 1710, 1596 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$):δ 4.79 (s, 1 H), 4.56 (s, 2 H), 4.47−4.40 (m, 1 H), 1.99−1.96 (m, 2 H), 1.84−1.79 (m, 2 H), 1.68−1.61 (m, 2 H), 1.58−1.55 (m, 1 H), 1.43−1.32 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.3, 185.0, 81.4, 80.8, 74.8, 31.3, 24.9, 23.2. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{10}H_{15}O_3$, 183.1021; found, 183.1024.

*5-Allyloxy-3(2H)-furanone (**2e**).* White solid (25.1 mg, 90%). Mp 40.3−40.5 °C. R_f = 0.38 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1697, 1581 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.03−5.97 (m, 1 H), 5.48−5.40 (m, 2 H), 4.84 (s, 1 H), 4.71 (dt, J = 5.8, 1.3 Hz, 2 H), 4.59 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.3, 185.5, 129.8, 120.6, 81.1, 75.2, 72.1. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_7H_9O_3$, 141.0552; found, 141.0544.

*5-Propargyloxy-3(2H)-furanone (**2f**).* White solid (26.2 mg, 95%). Mp 96.3−96.4 °C. R_f = 0.46 (*n*-hexane/EtOAc = 1:4). IR (KBr): 3226, 1690, 1566 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.96 (s, 1 H), 4.84 (d, J = 2.5 Hz, 2 H), 4.62 (s, 2 H), 2.69 (t, J = 2.5 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.1, 185.0, 81.7, 78.2, 75.6, 75.0, 58.6. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_7H_7O_3$, 139.0395; found, 139.0385.

*5-Phenyloxy-3(2H)-furanone (**2g**).* White solid (32.1 mg, 91%). Mp 82.0−82.4 °C. R_f = 0.60 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1694, 1550 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47−7.43 (m, 2 H), 7.36−7.33 (m, 1 H), 7.22−7.19 (m, 2 H), 4.69 (s, 2 H), 4.63 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.9, 185.9, 152.3, 130.2, 127.3, 120.3, 82.5, 75.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{10}H_9O_3$, 177.0552; found, 177.0554.

*5-Benzyloxy-3(2H)-furanone (**2h**).* White solid (35.6 mg, 93%). Mp 75.1−75.5 °C. R_f = 0.48 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1702, 1566 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42−7.39 (m, 5 H), 5.23 (s, 2 H), 4.89 (s, 1 H), 4.59 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.2, 185.5, 133.3, 129.3, 128.9, 128.1, 81.4, 75.3, 73.2. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{11}H_{11}O_3$, 191.0708; found, 191.0716.

*5-(4-Bromobenzyloxy)-3(2H)-furanone (**2i**).* White solid (53.5 mg, 99%). Mp 126.5−126.6 °C. R_f = 0.48 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1682, 1563 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, J = 8.4 Hz, 2 H), 7.42 (d, J = 8.4 Hz, 2 H), 5.18 (s, 2 H), 4.88 (s, 1 H), 4.60 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.1, 185.2, 132.3, 132.1, 129.6, 123.5, 81.4, 75.4, 72.2. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{11}H_{10}{}^{81}BrO_3$, 270.9793; found, 270.9784; calcd for $C_{11}H_{10}{}^{79}BrO_3$, 268.9813; found, 268.9803.

General Procedure for Synthesis of 4-Alkylated 3(2*H*)-Furanones 3. *t*-BuOK (2.0 equiv) was added to a suspension of sulfonium salt **1** (0.2 mmol) in THF (2.5 mL) at 0 °C. After 20 s, the reaction mixture appeared yellow. The alkyl halide **4** (1.1 equiv) was then added, and the reaction mixture was allowed to warm to room temperature, monitored by TLC. After the reaction was complete, the mixture was treated with brine and extracted with EtOAc. The extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (*n*-hexane/EtOAc = 1:2) gave the desired 4-alkylated 3(2*H*)-furanone **3**.

*4-Benzyl-5-ethoxy-3(2H)-furanone (**3aa**).* Pale yellow oil (36.3 mg, 83%). R_f = 0.34 (*n*-hexane/EtOAc = 1:4). IR (neat): 1697, 1604, 728, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27−7.13 (m, 4 H), 7.18−7.15 (m, 1 H), 4.57 (s, 2 H), 4.41 (q, J = 7.1 Hz, 2 H), 3.42 (s, 2 H), 1.39 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.5, 181.6, 140.2, 128.3, 128.2, 125.9, 93.7, 74.9, 65.8, 25.5, 14.7. HRMS (APCI-Orbitrap): m/z $[M+H]^+$ calcd for $C_{13}H_{15}O_3$, 219.1021; found, 219.1016.

*5-Ethoxy-4-(4-methoxybenzyl)-3(2H)-furanone (**3ab**).*[26] Pale yellow oil (31.6 mg, 64%). R_f = 0.42 (*n*-hexane/EtOAc = 1:4). IR (neat): 1696, 1604 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (d, J = 8.7 Hz, 2 H), 6.79 (d, J = 8.7 Hz, 2 H), 4.55 (s, 2 H), 4.42 (q, J = 7.1 Hz, 2 H), 3.77 (s, 3 H), 3.35 (s, 2 H), 1.40 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.6, 181.6, 157.9, 132.5, 129.3, 113.7, 94.2, 74.9, 65.8, 55.2, 24.7, 14.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{14}H_{17}O_4$, 249.1127; found, 249.1115.

*5-Ethoxy-4-(4-methylbenzyl)-3(2H)-furanone (**3ac**).* Pale yellow solid (37.5 mg, 81%). Mp 60.8−60.9 °C. R_f = 0.46 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1693, 1612, 823 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.16 (d, J = 7.8 Hz, 2 H), 7.06 (d, J = 7.8 Hz, 2 H), 4.55 (s, 2 H), 4.41 (q, J = 7.1 Hz, 2 H), 3.37 (s, 2 H), 2.29 (s, 3 H), 1.40 (t. J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.5, 181.5, 137.3, 135.3, 128.9, 128.2, 94.0, 74.9, 65.8, 25.1, 20.9, 14.7. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{14}H_{17}O_3$, 233.1178; found, 233.1169.

*4-(4-Chlorobenzyl)-5-ethoxy-3(2H)-furanone (**3ad**).* Pale yellow solid (38.4 mg, 76%). Mp 55.4−55.9 °C. R_f = 0.30 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1686, 1593, 803 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22−7.17 (m, 4 H), 4.57 (s, 2 H), 4.43 (q, J = 7.1 Hz, 2 H), 3.38 (s, 2 H), 1.40 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.4, 181.5, 138.7, 131.6, 129.7, 128.3, 93.3, 74.9, 66.0, 24.9, 14.7. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{13}H_{14}ClO_3$, 253.0631; found, 253.0612.

*4-(4-Bromobenzyl)-5-ethoxy-3(2H)-furanone (**3ae**).* White solid (42.6 mg, 72%). Mp 53.5−53.6 °C. R_f = 0.58 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1687, 1592, 798 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 8.3 Hz, 2 H), 7.13 (d, J = 8.3 Hz, 2 H), 4.57 (s, 2 H), 4.42 (q, J = 7.1 Hz, 2 H), 3.56 (s, 2 H), 1.40 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.4, 181.5, 139.2, 131.3, 130.1, 119.7, 93.3, 75.0, 66.0, 25.1, 14.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{13}H_{14}{}^{81}BrO_3$, 299.0106; found, 299.0114; calcd for $C_{13}H_{14}{}^{79}BrO_3$, 297.0126; found, 297.0128.

*4-(2-Bromobenzyl)-5-ethoxy-3(2H)-furanone (**3af**).* Pale yellow oil (50.5 mg, 85%). R_f = 0.58 (*n*-hexane/EtOAc = 1:4). IR (neat): 1697, 1604, 749 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (dd, J = 7.9, 1.3 Hz, 1 H), 7.27−7.25 (m, 1 H), 7.22−7.19 (m, 1 H), 7.08−7.02 (m, 1 H), 4.61 (s, 2 H), 4.40 (q, J = 7.1 Hz, 2 H), 3.55 (s, 2 H), 1.40 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.5, 181.6, 138.5, 132.4, 130.1, 127.6, 127.1, 124.2, 91.7, 74.9, 65.9, 26.1, 14.6. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{13}H_{14}{}^{81}BrO_3$, 299.0106; found, 299.0084; calcd for $C_{13}H_{14}{}^{79}BrO_3$, 297.0126; found, 297.0108.

*5-Ethoxy-4-(2-fluorobenzyl)-3(2H)-furanone (**3ag**).* Pale yellow oil (36.7 mg, 77%). R_f = 0.42 (*n*-hexane/EtOAc = 1:4). IR (neat): 1699, 1605, 759 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28−7.24 (m, 1 H), 7.17−7.12 (m, 1 H), 7.04−7.01 (m, 1 H), 7.00−6.96 (m, 1 H), 4.58

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(s, 2 H), 4.41 (q, J = 7.1 Hz, 2 H), 3.46 (s, 2 H), 1.38 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.5, 181.6, 160.8 (J = 245.6 Hz), 130.6 (J = 4.5 Hz), 127.6 (J = 8.1 Hz), 126.6 (J = 15.9 Hz), 123.8 (J = 3.6 Hz), 115.0 (J = 21.9 Hz), 92.1, 74.9, 65.9, 18.5 (J = 4.2 Hz), 14.7. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{13}H_{14}FO_3$, 237.0927; found, 237.0927.

*5-Ethoxy-4-methyl-3(2H)-furanone (**3ah**).*[27] White solid (22.6 mg, 79%). Mp 55.0−55.5 °C. R_f = 0.18 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1695, 1600 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.55 (s, 2 H), 4.44 (q, J = 7.1 Hz, 2 H), 1.61 (s, 3 H), 1.44 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.5, 181.5, 89.3, 74.7, 65.6, 14.8, 3.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_7H_{11}O_3$, 143.0708; found, 143.0695.

*5-Ethoxy-4-ethyl-3(2H)-furanone (**3ai**).* Pale yellow oil (16.5 mg, 53%). R_f = 0.24 (*n*-hexane/EtOAc = 1:4). IR (neat): 1696, 1604 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.53 (s, 2 H), 4.44 (q, J = 7.1 Hz, 2 H), 2.12 (q, J = 7.5 Hz, 2 H), 1.43 (t, J = 7.1 Hz, 3 H), 1.03 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.2, 181.4, 95.4, 74.6, 65.6, 14.8, 12.9, 12.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_8H_{13}O_3$, 157.0865; found, 157.0853.

*4-Allyl-5-ethoxy-3(2H)-furanone (**3aj**).*[28] Pale yellow oil (23.7 mg, 71%). R_f = 0.28 (*n*-hexane/EtOAc = 1:4). IR (neat): 1698, 1603 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.83 (ddt, J = 17.0, 10.0, 6.2 Hz, 1 H), 5.04 (dq, J = 17.0, 1.5 Hz, 1 H), 4.97 (dq, J = 10.0, 1.5 Hz, 1 H), 4.57 (s, 2 H), 4.44 (q, J = 7.1 Hz, 2 H), 2.85 (dt, J = 6.2, 1.5 Hz, 2 H), 1.42 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.7, 181.6, 135.0, 114.8, 91.8, 74.8, 65.8, 23.7, 14.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_9H_{13}O_3$, 169.0865; found, 169.0856.

*4-Cinnamyl-5-ethoxy-3(2H)-furanone (**3ak**).*[21] Pale yellow oil (37.1 mg, 76%). R_f = 0.28 (*n*-hexane/EtOAc = 1:4). IR (neat): 1735, 1693, 1583, 758, 700 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.32 (m, 2 H), 7.29−7.25 (m, 2 H), 7.20−7.16 (m, 1 H), 6.41 (d, J = 15.8 Hz, 1 H), 6.21 (dt, J = 15.8, 6.7 Hz, 1 H), 4.58 (s, 2 H), 4.45 (q, J = 7.1 Hz, 2 H), 3.00 (dd, J = 6.7, 1.5 Hz, 2 H), 1.43 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.6, 181.6, 137.6, 130.2, 128.4, 126.93, 126.91, 126.1, 92.1, 74.9, 65.9, 23.0, 14.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{15}H_{17}O_3$, 245.1178; found, 245.1174.

*5-Ethoxy-4-propargyl-3(2H)-furanone (**3al**).* Orange oil (22.2 mg, 76%). R_f = 0.26 (*n*-hexane/EtOAc = 1:4). IR (neat): 3245, 1701, 1605 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.59 (s, 2 H), 4.49 (q, J = 7.1 Hz, 2 H), 3.03 (d, J = 2.7 Hz, 2 H), 1.94 (t, J = 2.7 Hz, 1 H), 1.46 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.4, 181.1, 89.4, 80.9, 75.0, 67.4, 66.3, 14.8, 9.4. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_9H_{11}O_3$, 167.0708; found, 167.0708.

*5-Ethoxy-4-ethoxycarbonylmethyl-3(2H)-furanone (**3am**).* Pale yellow oil (31.3 mg, 73%). R_f = 0.18 (*n*-hexane/EtOAc = 1:4). IR (neat): 1738, 1701, 1609 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.63 (s, 2 H), 4.46 (q, J = 7.1 Hz, 2 H), 4.14 (q, J = 7.1 Hz, 2 H), 3.12 (s, 2 H), 1.43 (t, J = 7.1 Hz, 3 H), 1.26 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.0, 181.9, 170.6, 88.0, 75.2, 66.2, 60.9, 25.2, 14.7, 14.2. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{10}H_{15}O_5$, 215.0919; found, 215.0916.

*5-Ethoxy-4-(2-thienylmethyl)-3(2H)-furanone (**3an**).* Colorless oil (32.8 mg, 73%). R_f = 0.32 (*n*-hexane/EtOAc = 1:4). IR (neat): 1698, 1603, 850, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.08 (dd, J = 5.1, 1.2 Hz, 1 H), 6.88 (dd, J = 5.1, 3.4 Hz, 1 H), 6.86−6.85 (m, 1 H), 4.58 (s, 2 H), 4.46 (q, J = 7.1 Hz, 2 H), 3.62 (d, J = 0.9 Hz, 2 H), 1.43 (t, J = 7.1 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.0, 181.4, 142.9, 126.7, 124.6, 123.3, 93.4, 75.0, 66.1, 19.8, 14.8. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{11}H_{13}O_3S$, 225.0585; found, 225.0575.

*4-Benzyl-5-isopropyloxy-3(2H)-furanone (**3ba**).* Pale yellow oil (32.7 mg, 70%). R_f = 0.50 (*n*-hexane/EtOAc = 1:4). IR (neat): 1696, 1603, 731, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26−7.23 (m, 4 H), 7.18−7.14 (m, 1 H), 5.08 (sept, J = 6.2 Hz, 1 H), 4.56 (s, 2 H), 3.40 (s, 2 H), 1.37 (d, J = 6.2 Hz, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.5, 181.4, 140.4, 128.4, 128.2, 125.9, 94.1, 74.8, 74.7, 25.6, 22.4. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{14}H_{17}O_3$, 233.1178; found, 233.1181.

*4-Benzyl-5-cyclopentyloxy-3(2H)-furanone (**3ca**).* Pale yellow oil (37.6 mg, 73%). R_f = 0.56 (*n*-hexane/EtOAc = 1:4). IR (neat): 2964, 1696, 1603, 725, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26−7.23 (m, 4 H), 7.18−7.14 (m, 1 H), 5.29−5.26 (m, 1 H), 4.56 (s, 2 H), 3.39 (s, 2 H), 1.89−1.83 (m, 4 H), 1.75−1.69 (m, 2 H), 1.66−1.59 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.4, 181.4, 140.4, 128.4, 128.2, 125.9, 94.3, 83.6, 74.9, 33.2, 25.7, 23.4. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{16}H_{19}O_3$, 259.1334; found, 259.1334.

*4-Benzyl-5-cyclohexyloxy-3(2H)-furanone (**3da**).* Pale yellow oil (41.2 mg, 77%). R_f = 0.60 (*n*-hexane/EtOAc = 1:4). IR (neat): 2938, 2860, 1696, 1604, 732, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28−7.23 (m, 4 H), 7.17−7.14 (m, 1 H), 4.87−1.82 (m, 1 H), 4.55 (s, 2 H), 3.41 (s, 2 H), 1.91−1.86 (m, 2 H), 1.75−1.69 (m, 2 H), 1.69−1.57 (m, 2 H), 1.54−1.49 (m, 1 H), 1.41−1.30 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.4, 181.4, 140.4, 128.4, 128.2, 125.9, 94.1, 79.1, 74.8, 31.9, 25.7, 25.0, 23.1. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{17}H_{21}O_3$, 273.1491; found, 273.1496.

*5-Allyloxy-4-benzyl-3(2H)-furanone (**3ea**).* Pale yellow oil (35.1 mg, 76%). R_f = 0.52 (*n*-hexane/EtOAc = 1:4). IR (neat): 1696, 1604, 725, 700 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27−7.23 (m, 4 H), 7.18−7.15 (m, 1 H), 5.95 (ddt, J = 17.1, 10.5, 5.7 Hz, 1 H), 5.38−5.32 (m, 2 H), 4.84 (dt, J = 5.7, 1.4 Hz, 2 H), 4.58 (s, 2 H), 3.43 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.6, 181.3, 140.1, 130.7, 128.34, 128.30, 126.0, 119.8, 94.1, 75.0, 69.8, 25.5. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{14}H_{15}O_3$, 231.1021; found, 231.1011.

*4-Benzyl-5-propargyloxy-3(2H)-furanone (**3fa**).* White solid (32.1 mg, 70%). Mp 78.2−78.8 °C. R_f = 0.56 (*n*-hexane/EtOAc = 1:4). IR (KBr): 3210, 1693, 1601, 735, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28−7.24 (m, 4 H), 7.19−7.16 (m, 1 H), 4.95 (d, J = 2.4 Hz, 2 H), 4.61 (s, 2 H), 3.44 (s, 2 H), 2.62 (t, J = 2.4 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.8, 180.5, 139.8, 128.30, 128.28, 126.0, 94.1, 77.1, 76.0, 75.2, 56.7, 25.4. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{14}H_{13}O_3$, 229.0865; found, 229.0862.

*4-Benzyl-5-phenyloxy-3(2H)-furanone (**3ga**).* Pale yellow oil (20.5 mg, 38%). R_f = 0.74 (*n*-hexane/EtOAc = 1:4). IR (neat): 1702, 1620, 724, 690 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41−7.37 (m, 2 H), 7.31−7.25 (m, 5 H), 7.21−7.18 (m, 1 H), 7.12−7.10 (m, 2 H), 4.59 (s, 2 H), 3.53 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.4, 180.0, 151.3, 139.7, 129.7, 128.40, 128.36, 126.5, 126.1, 120.5, 95.9, 75.2, 25.7. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{17}H_{15}O_3$, 267.1021; found, 267.1003.

*4-Benzyl-5-benzyloxy-3(2H)-furanone (**3ha**).* Pale yellow oil (38.5 mg, 69%). R_f = 0.46 (*n*-hexane/EtOAc = 1:4). IR (neat): 1699, 1607, 729, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39−7.37 (m, 3 H), 7.31−7.29 (m, 2 H), 7.26−7.22 (m, 4 H), 7.19−7.15 (m, 1 H), 5.36 (s, 2 H), 4.59 (s, 2 H), 3.43 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.6, 181.3, 140.1, 134.3, 129.0, 128.8, 128.4, 128.3, 127.9, 126.0, 94.4, 75.1, 71.0, 25.6. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{18}H_{17}O_3$, 281.1178; found, 281.1191.

*4-Benzyl-5-(4-bromobenzyloxy)-3(2H)-furanone (**3ia**).* Pale yellow solid (48.7 mg, 68%). Mp 92.8−93.0 °C. R_f = 0.50 (*n*-hexane/EtOAc = 1:4). IR (KBr): 1694, 1591, 806, 720, 701 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, J = 8.5 Hz, 2 H), 7.26−7.16 (m, 5 H), 7.13 (d, J = 8.5 Hz, 2 H), 5.29 (s, 2 H), 4.58 (s, 2 H), 3.42 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.6, 181.1, 140.0, 133.2, 132.0, 129.5, 128.4, 128.3, 126.0, 123.1, 94.5, 75.1, 70.1, 25.5. HRMS (FAB): m/z $[M+H]^+$ calcd for $C_{18}H_{16}{}^{81}BrO_3$, 361.0262; found, 361.0272; calcd for $C_{18}H_{16}{}^{79}BrO_3$, 359.0283; found, 359.0296.

Synthesis of Aza-prostaglandin Analogue 10.[21] NaOMe (101.1 mg, 1.87 mmol) was added to a solution of 6-aminohexanoate hydrochloride (339.8 mg, 1.87 mmol) in dry MeOH (0.5 mL) and stirred for 30 min at room temperature. After removal of the precipitate by filtration under an argon atmosphere, to the filtrate was added **3ak** (70.3 mg, 0.288 mmol) in dry MeOH (0.5 mL) via cannula, and the mixture was stirred for 2 h at room temperature. After the solvent was concentrated under reduced pressure, the mixture was treated with 2 M HCl and extracted with diethyl ether. The extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (EtOAc/MeOH = 9:1) gave **10** as a pale yellow liquid (66.3 mg, 67%). R_f = 0.40 (EtOAc/MeOH = 9:1). IR (neat): 3217, 3024, 1737, 1677, 1651, 1573, 1496, 692 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33−

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7.27 (m, 5 H), 7.26−7.20 (m, 1 H), 6.47 (d, J = 15.9 Hz, 1 H), 6.17 (dt, J = 15.9, 6.6 Hz, 1 H), 4.55 (s, 2 H), 3.65 (s, 3 H) 3.34 (q, J = 6.6 Hz, 2 H), 3.10 (dd, J = 6.6, 1.3 Hz, 2 H), 2.20 (t, J = 7.4 Hz, 2 H), 1.59−1.51 (m, 4 H), 1.31−1.25 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.3, 178.0, 173.9, 136.8, 130.6, 128.6, 127.7, 127.3, 126.0, 88.8, 74.3, 51.5, 41.0, 33.5, 29.6, 25.9, 24.1, 23.5. HRMS (ESI-TOF): m/z [M+H]$^+$ calcd for $C_{20}H_{26}NO_4$, 344.1856; found, 344.1862.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01528.

^{1}H and ^{13}C NMR spectra data for compounds **1**, **2**, **3**, **6**, and **10** (PDF)

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Notes

The authors declare no competing financial interest.

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