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EFFICIENT SYNTHESIS OF 2-ALKYLIDENE-4*H*-3,1-BENZOXATHIIN-4-ONES AND DETERMINATION OF THEIR DOUBLE BOND CONFIGURATION

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Abstract – 2-Alkylidene-4*H*-3,1-benzoxathiin-4-ones were efficiently synthesized by reaction of 2-(acylthio)benzoic acids with condensation reagents in the presence of base. The *E* and *Z* isomers of the products were distinguished by comparison of the chemical shifts of the vinylic protons in the ^{1}H NMR spectra of the 4*H*-3,1-benzoxathiin-4-ones and their corresponding 1-oxides.

INTRODUCTION

4*H*-3,1-Benzoxathiin-4-ones have been reported to have insecticidal and fungicidal activities,[1,2] and various 4*H*-3,1-benzoxathiin-4-ones have been patented for use as crop protection agents.[3] However, the reactivity of 4*H*-3,1-benzoxathiin-4-ones has not been extensively investigated: ring-opening reactions with nucleophiles,[4-7] oxidation reactions,[6,8] sulfurization reactions,[4,5] photoreactions,[8] and thermolysis[9] are the only reactions to have been reported. In a previous paper, we reported the synthesis of 1,2-benzisothiazolin-3(2*H*)-ones by ring transformation of 4*H*-3,1-benzoxathiin-4-one 1-oxides with amines,[10] and 4*H*-3,1-benzoxathiin-4-ones are increasingly being used as starting materials.

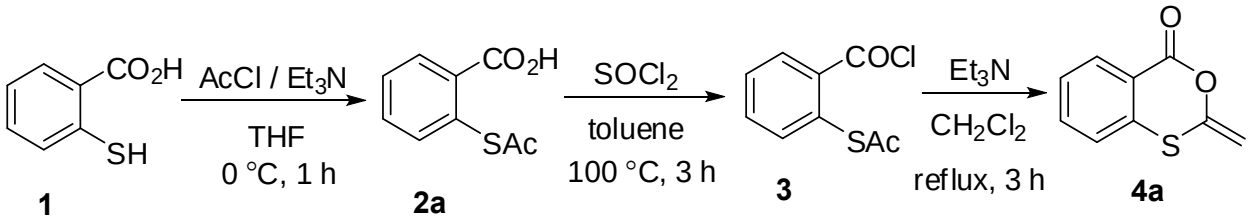
4*H*-3,1-Benzoxathiin-4-ones are usually synthesized by the reaction of thiosalicylic acids with carbonyl compounds or their acetals.[2,6,11] The use of acetylene compounds instead of carbonyl compounds has recently been reported,[12] and various 2-monosubstituted and 2,2-disubstituted 4*H*-3,1-benzoxathiin-4-one derivatives were synthesized in this way. However, the synthesis of 2-functionalized group substituted 4*H*-3,1-benzoxathiin-4-ones, such as 2-alkoxy-[13] and 2-alkylamino-derivatives,[14] has rarely been reported.

In contrast, the chemistry of 4*H*-1,3-benzodioxin-4-ones, which are oxo analogs of 4*H*-3,1-benzoxathiin-4-ones, has been thoroughly investigated, and 2-alkoxy-4*H*-1,3-benzodioxin-4-ones are of interest as prodrugs of acylsalicylic acids.[15] The synthesis of 2-methylene-4*H*-1,3-benzodioxin-4-one as a key intermediate for 2-alkoxy-4*H*-1,3-benzodioxin-4-one derivatives has been reported,[16] but this 2-methylene-substituted compound was obtained unexpectedly from the reaction of 2-acetoxybenzoyl chloride and triethylamine; the authors had intended to synthesize isoflavone derivatives. 2-Methylene-4*H*-3,1-benzoxathiin-4-one was also reported to be formed, in low yield, as an unexpected product of the reaction of 2-(acetylthio)benzoic acid with amines in the presence of a condensation reagent; the intended products were 2-(acetylthio)benzamides.[17] However, no characterization data for this unexpected byproduct were presented in the report.

As a part of our research on 4*H*-3,1-benzoxathiin-4-ones, we are interested in 2-alkylidene-4*H*-3,1-benzoxathiin-4-one chemistry. In this paper, we present a simple method for the synthesis of 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones, and we also describe the determination of their double bond configuration.

RESULTS AND DISCUSSION

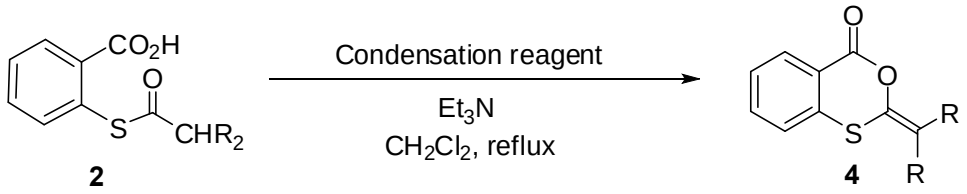
On the basis of the previously reported method for the synthesis of 2-alkylidene-4*H*-3,1-benzodioxin-4-ones,[16] we attempted to cyclize 2-(acylthio)benzoyl chlorides in the presence of base. Thiosalicylic acid (**1**) was converted to its *S*-acetyl derivative (**2a**) by reaction with acetyl chloride in THF, and **2a** was allowed to react with thionyl chloride in refluxing toluene to afford 2-(acetylthio)benzoyl chloride (**3**). Although 2-methylene-4*H*-3,1-benzodioxin-4-one was previously synthesized under severe reaction conditions (e.g., reaction for 15 h at 110 °C in toluene), we were able to synthesize 2-methylene-4*H*-3,1-benzoxathiin-4-one (**4a**) under mild conditions, refluxing dichloromethane for 3 h, in 72% yield (Scheme 1). The structure of the product was confirmed by observation of the two vinylic proton peaks in the NMR spectrum.



Scheme 1. Synthesis of 2-methylene-4*H*-3,1-benzoxathiin-4-one **4a** from acid chloride **3**

Next, we investigated the one-step synthesis of 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones **4** from 2-(acylthio)benzoic acids **2** by using condensation reagents. In the literature,[17] the use of *O*-benzotriazole-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate as a condensation reagent for the synthesis **4a** has been reported. We investigated three commercially available condensation reagents:

Table 1. Cyclization of 2-(acylthio)benzoic acid (**2**) with condensation reagents[a)]

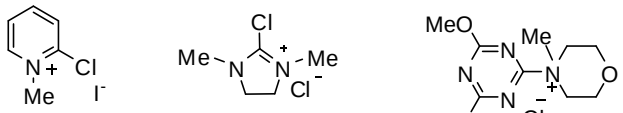


2 **4**

Entry	**2**	R	Condensation reagent[b)]	Time / h	Product	Yield[c)] /%
1	**2a**	H	MR	5	**4a**	41
2	**2b**	Ph	MR	1	**4b**	86
3	**2a**	H	DMC	7	**4a**	80
4	**2b**	Ph	DMC	3	**4b**	94
5	**2a**	H	DMT-MM	8	**4a**	13
6	**2b**	Ph	DMT-MM	3	**4b**	90

a) **2**, 1.5 mmol; condensation reagent, 2.0 mmol; Et_3N, 7.5 mmol; CH_2Cl_2, 20 mL.

b)



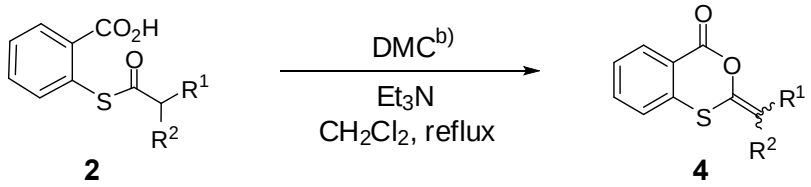
MR DMC DMT-MM

c) Isolated product.

2-chloro-1-methylpyridinium iodide (Mukaiyama reagent),[18] 2-chloro-1,3-dimethylimidazolinium chloride (DMC),[19] and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride[20] (Table 1). Cyclization of 2-(acylthio)benzoic acids **2** proceeded with these condensation reagents in the presence of base, and 2-methylene-4*H*-3,1-benzoxathiin-4-ones **4** were obtained. Although the three condensation reagents gave similar yields in the cyclization of 2-(diphenylacetylthio)benzoic acid (**2b**), DMC gave a substantially higher yield than the other condensation reagents in the cyclization of 2-(acetylthio)benzoic acid (**2a**). Therefore, we used DMC as a condensation reagent to investigate the cyclization of various substituted 2-(acylthio)benzoic acids **2** (Table 2). Monophenyl derivatives **2d**–**f** gave 2-benzylidene-4*H*-3,1-benzoxathiin-4-ones **4d**–**f** in good yields as single isomers (>99:1, entries 4–6).

Reactions of 2-(acylthio)benzoic acids with ether substituents resulted in mixtures of *E* and *Z* isomers, which were separated by silica gel column chromatography (entries 7–9). 2-(Propionylthio)benzoic acid (**2j**) gave a 1:1 mixture of the product isomers (entry 10). Under these reaction conditions, the treatment of 2-(isobutyrylthio)benzoic acid (**2c**) with DMC afforded **4c** in 56% yield, but further investigation revealed that **4c** could be synthesized in 88% yield if pyridine was used as a base in 1,2-dichloroethane at 80 °C (entry 3).

Table 2. Synthesis of 2-alkylidene-4*H*-3,1-benzoxathiin-4-one **4**[a)]



2 **4**

Entry	**2**	R^1	R^2	Time / h	Product	Yield[c)] /%	Ratio of isomers[d)] (*E* : *Z*)
1	**2a**	H	H	7	**4a**	80	-
2	**2b**	Ph	Ph	3	**4b**	94	-
3[e)]	**2c**	Me	Me	5	**4c**	88	-
4	**2d**	Ph	H	5	**4d**	88	>99 : 1
5	**2e**	4-ClC_6H_4	H	3	**4e**	91	>99 : 1
6	**2f**	4-$MeOC_6H_4$	H	5	**4f**	85	>99 : 1
7	**2g**	PhO	H	5	**4g**	89	77 : 23
8	**2h**	MeO	H	7	**4h**	82	72 : 28
9	**2i**	AcO	H	5	**4i**	81	77 : 23
10	**2j**	Me	H	5	**4j**	77	50 : 50

a) **2**, 1.5 mmol; DMC, 2.0 mmol; Et_3N, 7.5 mmol; CH_2Cl_2, 20 mL.
b) DMC: 2-chloro-1,3-dimethylimidazolinium chloride.
c) Isolated product.
d) Determined with ^{1}H-NMR. See Table 3.
e) 1,2-Dichloroethane (20 mL); 80 °C; pyridine (7.5 mmol).

A single crystal of the major isomer of 2-(phenoxymethylene)-4*H*-3,1-benzoxathiin-4-one (**4g**) was obtained, and the *E* configuration was confirmed by X-ray crystallography (Figure 1). However, the double bond configurations of the other products still had to be determined. The ^{1}H NMR chemical shifts of the *E* and *Z* isomers of methyl styryl sulfide and methyl styryl sulfoxide have been measured,[21] and the oxidation reaction was found to shift the protons β to the sulfur atoms to lower field; the change in chemical shift for the *E* isomer ($\Delta\delta$ = 0.59 ppm) is larger than that for the *Z* isomer ($\Delta\delta$ = 0.26 ppm). We used these results to determine the double bond structures of 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones **4**.

2-(Phenoxymethylene)-4*H*-3,1-benzoxathiin-4-one (**4g**), the structure of which had been determined by X-ray crystallography, was oxidized with *m*-chloroperoxybenzoic acid (*m*CPBA) in dichloromethane to afford the corresponding 1-oxide (**5g**) in 79% yield. The oxidation shifted the vinylic proton signal

downfield by 0.56 ppm. In contrast, oxidation of **4′g**, a minor product of the cyclization, with *m*CPBA gave sulfoxide **5′g** in 76% yield, and the signal for the vinylic proton in the oxidized compound was

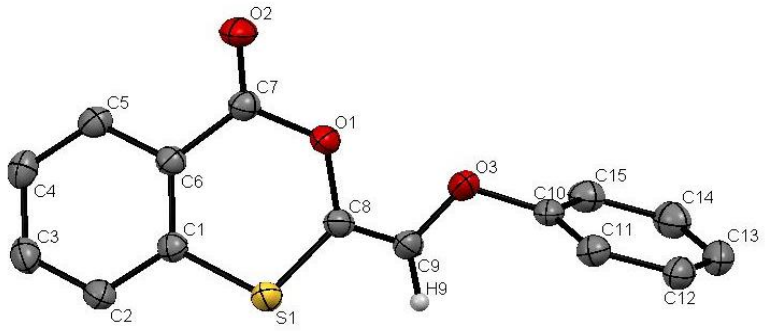
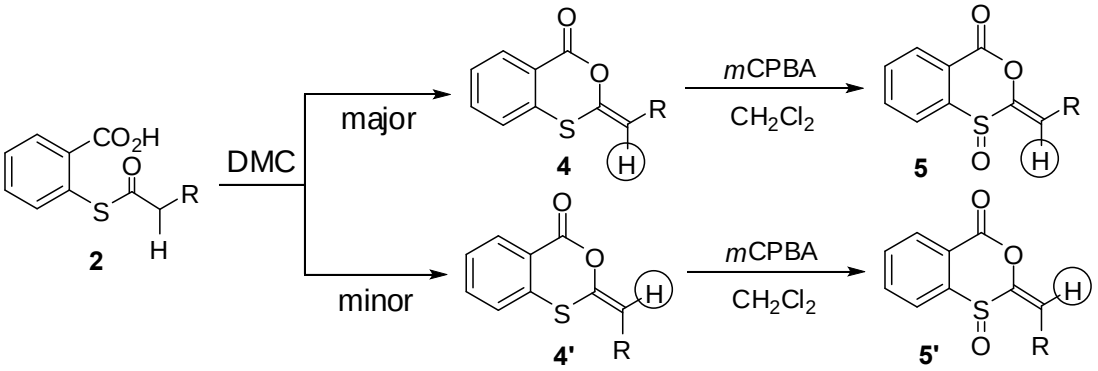


Figure 1. ORTEP drawing of **4g** (showing thermal ellipsoids at the 50% probability level).

Table 3. Oxidation of 4*H*-3,1-benzoxathiin-4-ones[a] and chemical shifts of vinylic protons



Entry	4	R	Product	Yield[b] (%)	^{1}H-NMR chemical shift			Conformation
					4 or 4'	5 or 5'	Δδ	
1	**4d**	Ph	**5d**	85 [c]	6.09	6.67	0.58	*E*
2	**4e**	4-ClC$_6$H$_4$	**5e**	70 [c]	6.04	6.62	0.58	*E*
3	**4f**	4-MeOC$_6$H$_4$	**5f**	88 [c]	6.05	6.61	0.56	*E*
4	**4g**	PhO	**5g**	79	6.51	7.07	0.56	*E* [d]
5	**4'g**	PhO	**5'g**	76	7.12	7.37	0.25	*Z*
6	**4h**	MeO	**5h**	67	6.02	6.60	0.58	*E*
7	**4'h**	MeO	**5'h**	61	6.72	6.97	0.25	*Z*
8	**4i**	AcO	**5i**	62	7.17	7.72	0.55	*E*
9	**4'i**	AcO	**5'i**	64	7.70	7.93	0.23	*Z*

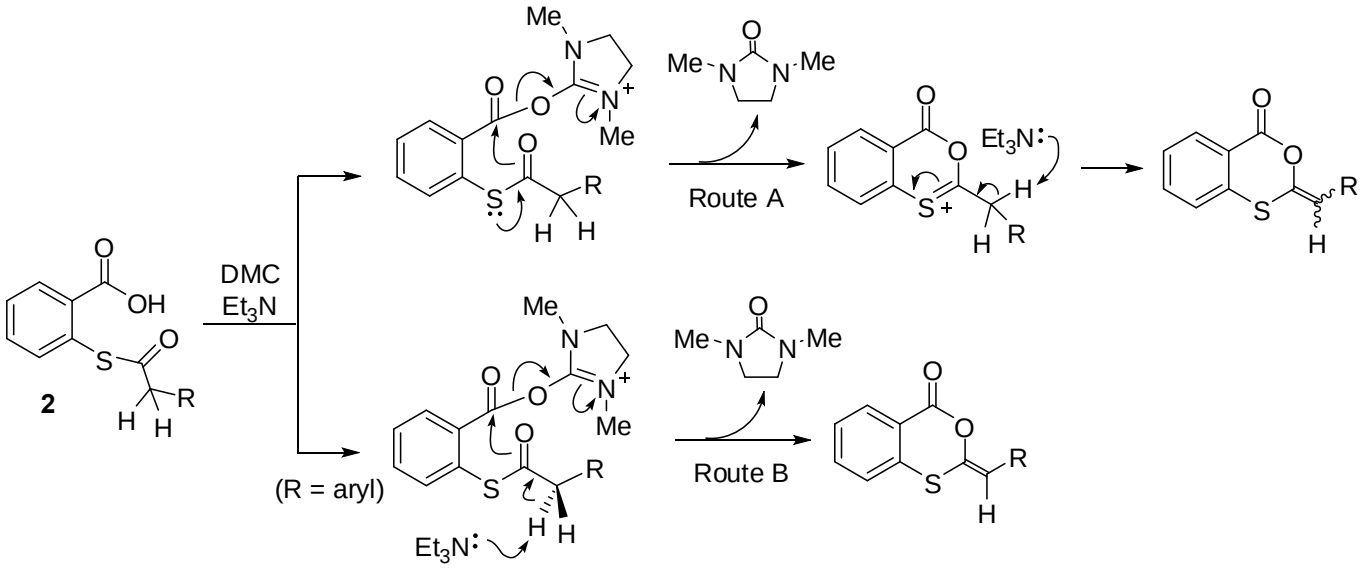
a) **4**: 1.0 mmol, *m*CPBA: 1.1 mmol, CH_2Cl_2: 10 mL, rt, 30 min.
b) Isolated product.
c) Calculated from ^{1}H-NMR spectra.
d) Determined with X-ray crystallographic analysis (see Figure 1).

shifted 0.25 ppm downfield. That is, the oxidation-induced downfield shift of the vinylic proton of the *E* isomer was larger than that of the *Z* isomer. This result was in good agreement with the results reported for methyl styryl sulfide and confirmed that the double bond configurations of the 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones could be determined by comparison of their ^{1}H NMR spectra before and after oxidation.

Isolated isomers of 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones **4** and **4′** were oxidized with *m*CPBA (Table 3). All the major isolated isomers showed behavior consistent with the *E* configuration; that is, the vinylic protons shifted downfield by approximately 0.58 ppm after oxidation. In contrast, the vinylic protons of the minor isomers shifted downfield by approximately 0.24 ppm, indicating that they were *Z* isomers. Although a single isomer was obtained from monophenyl derivatives **3d**–**f** under these reaction conditions, the oxidation results clearly indicated that the *E* isomers formed predominantly. Even when the isomers were not separable, the ^{1}H NMR peaks could be assigned by oxidation of the mixture (entry 10).

Plausible reaction mechanisms for the formation of 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones are depicted in Scheme 2. In the first step, 1 equivalent amount of triethylamine deprotonates the carboxylic acid and the resulting anion reacts with the condensation reagent. Then the functional group derived from the condensation reagent could be eliminated by attack of the oxygen atom of the acyl carbonyl group on the ester carbonyl group, facilitated by electron donation from the sulfur atom. The result would be a benzoxathiinium cation, which could undergo elimination of a proton with triethylamine (Route A). Steric repulsion between the sulfur and oxygen atoms was unlikely to be sufficient to control the double bond configuration. As a result, products were obtained as *E*/*Z* mixtures. On the centrally, in the case that the R substituents are aryl groups, it is possible that benzene and imidazolinium rings can interact each other, and that the intermediate becomes somewhat stable. Therefore, triethylamine attacks the α-proton from less hindered side and the oxygen atom of the thioester carbonyl group continuously attacks to the ester carbonyl group, which results in predominant formation of *E*-alkylidene products (Route B).

In conclusion, we synthesized 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones by means of the reactions of 2-acylthiosalicylic acids with condensation reagents. When double bond isomers were possible, the *E* isomers predominated, and the double bond configurations were determined by comparison of the vinylic proton chemical shifts with those of the corresponding 1-oxide derivatives.



Scheme 2. Plausible mechanisms for formation of 2-alkylidene-4*H*-3,1-benzoxathiin-4-ones

EXPERIMENTAL

Melting points were determined on a Mettler FP90 microscopic plate and are uncorrected. ^{1}H NMR spectra were obtained with a JEOL JNM-ECX400 spectrometer operating at 400 MHz, and chemical shifts (δ) are reported in ppm relative to internal tetramethylsilane. ^{13}C NMR spectra were obtained with a JEOL JNM-ECX400 spectrometer operating at 100 MHz, and chemical shifts (δ) are reported in ppm relative to internal tetramethylsilane. IR spectra were recorded on a JASCO FT IR-4100 spectrophotometer. Elemental analysis and high-resolution mass spectral analysis were performed by the Analytical Center at the National Institute of Advanced Industrial Science and Technology. An X-ray structure was measured with a Bruker AXS APEX2 diffractometer.

General procedure for synthesis of 2-(acylthio)benzoic acids 2. To a solution of thiosalicylic acid (**1**, 5.0 mmol, 771 mg) in THF (20 mL) cooled on an ice bath were added an acyl chloride (1.1 mmol) and triethylamine (7.5 mmol, 759 mg). The mixture was stirred for 1 h under a nitrogen atmosphere at 0 °C, and then the solvent was evaporated under reduced pressure. The reaction mixture was dissolved in water, and diluted HCl (5 mL) was added. The crude product was extracted with AcOEt, and the organic layer was dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and purification of the crude product by recrystallization from AcOEt–hexane afforded **2**.

Synthesis of 2-methylene-4*H*-3,1-benzoxathiin-4-one (4a) from acid chloride 3. 2-(Acetylthio)benzoic acid (**2a**, 5.0 mmol, 980 mg) was dissolved in toluene (50 mL), and thionyl chloride (1 mL) was added to the solution. The reaction mixture was heated to 100 °C for 3 h. After the reaction, the solvent was evaporated to give 2-(acetylthio)benzoyl chloride (**3**). To a solution of **3** (2 mmol, 429 mg) in

CH_2Cl_2 (30 mL) was added triethylamine (6.0 mmol, 607 mg), and the mixture was stirred at reflux for 3 h. The solvent was evaporated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent 4 : 1 CH_2Cl_2 : hexane) to afford **4a** in 72% yield.

2-Methylene-4*H*-3,1-benzoxathiin-4-one (4a): mp 51.3-53.0 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 4 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.92 (1H, d, *J* = 2.4 Hz), 5.19 (1H, d, *J* = 2.4 Hz), 7.21 (1H, d, *J* = 7.6 Hz), 7.29 (1H, td, *J* = 7.6, 1.2 Hz), 7.51 (1H, td, *J* = 7.6, 1.2 Hz), 8.15 (1H, dd, *J* = 7.6, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 102.2, 121.9, 125.5, 126.6, 132.5, 134.5, 136.2, 145.0, 160.5; IR (KBr) ν_{max} 3029, 1747, 1616, 1440, 1283, 1099, 853 cm^{-1}. Anal. Calcd for $C_9H_6O_2S$: C 60.66; H 3.39. Found: C 60.69; H 3.31.

General procedure for the synthesis of 4 with condensation reagents. To a solution of **2** (1.5 mmol) in CH_2Cl_2 (20 mL) were added a condensation reagent (2.0 mmol) and triethylamine (7.5 mmol, 759 mg), and the mixture was stirred at reflux for 3–8 h. After water was added to the reaction mixture, the products were extracted with CH_2Cl_2. The organic layer was washed with water and dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and the crude product was purified by silica gel column chromatography with an appropriate solvent.

2-Diphenylmethylene-4*H*-3,1-benzoxathiin-4-one (4b): mp 165-166 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 2 : 1) 0.5; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.13 (1H, d, *J* = 7.6 Hz), 7.22-7.48 (12H, m), 8.18-8.21 (1H, m); ^{13}C-NMR (100 MHz, $CDCl_3$): 121.7, 125.5, 126.4, 127.8, 128.1, 128.3, 128.5, 129.9, 130.1, 130.3, 132.4, 134.4, 135.7, 136.8, 137.5, 138.0, 160.8; IR (KBr) ν_{max} 3062, 3020, 1734, 1587, 1439, 1275, 1093, 735 cm^{-1}. Anal. Calcd for $C_{21}H_{14}O_2S$: C 76.34; H 4.27. Found: C 76.40; H 4.13.

2-Isopropylidene-4*H*-3,1-benzoxathiin-4-one (4c): mp 77.1-77.6 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 3 : 1) 0.55. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.86 (3H, s), 1.91 (3H, s), 7.25-7.27 (2H, m), 7.47 (1H, td, *J* = 7.8, 1.5 Hz), 8.14 (1H, d, *J* = 7.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.6, 19.8, 123.2, 124.0, 125.7, 126.2, 131.0, 132.4, 133.9, 138.0, 162.1; (KBr) ν_{max} 2918, 1741, 1655, 1442, 1286, 1227, 1139, 1122, 1099, 739 cm^{-1}. Anal. Calcd for $C_{11}H_{10}O_2S$: C 64.05; H 4.89. Found: C 64.20; H 4.79.

(*E*)-2-Benzylidene-4*H*-3,1-benzoxathiin-4-one (4d): mp 84.9-85.5 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 2 : 1) 0.5; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.09 (1H, s), 7.25-7.38 (5H, m), 7.51 (1H, td, *J* = 7.8, 1.6 Hz), 7.68 (2H, d, *J* = 7.8 Hz), 8.17 (1H, dd, *J* = 8.0, 1.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 116.9, 122.0, 125.5, 126.6, 128.0, 128.6, 129.1, 132.5, 133.0, 134.5, 137.2, 137.6, 160.4; IR (KBr) ν_{max} 3055, 3025, 1737, 1622, 1586, 1265, 1101, 733 cm^{-1}. Anal. Calcd for $C_{15}H_{10}O_2S$: C 70.84; H 3.96. Found: C 70.91; H 3.88.

(*E*)-2-(4-Chlorobenzylidene)-4*H*-3,1-benzoxathiin-4-one (4e): mp 131-132 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 2 : 1) 0.5; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.03 (1H, s), 7.25 (1H, dd, *J* = 7.6, 1.2 Hz), 7.29-7.33 (3H, m), 7.52 (1H, td, *J* = 7.6, 1.2 Hz), 7.61 (2H, dt, *J* = 8.4, 2.4 Hz), 8.16 (1H, dd, *J* = 7.6, 1.2

Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 115.4, 121.8, 125.5, 126.7, 128.8, 130.3, 131.5, 132.6, 133.6, 134.6, 136.9, 138.3, 160.0; IR (KBr) ν_{max} 3048, 1743, 1584, 1442, 1265, 1102, 854, 736 cm^{-1}. Anal. Calcd for $C_{15}H_9ClO_2S$: C 62.39; H 3.14. Found: C 62.18; H 3.11.

(*E*)-2-(4-Methoxybenzylidene)-4*H*-3,1-benzoxathiin-4-one (4f): mp 95.8-96.6 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 4 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.82 (3H, s), 6.05 (1H, s), 6.89 (2H, d, *J* = 8.7 Hz), 7.26-7.30 (2H, m), 7.51 (1H, td, *J* = 8.0, 1.2 Hz), 7.64 (2H, d, *J* = 8.7 Hz), 8.17 (1H, dd, *J* = 8.0, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 55.3, 114.0, 117.0, 122.3, 125.5, 125.9, 126.5, 130.6, 132.6, 134.4, 135.4, 137.7, 159.3, 160.7; IR (KBr) ν_{max} 2991, 1733, 1604, 1506, 1440, 1260, 1233, 1176, 1103, 1032, 849, 739 cm^{-1}. Anal. Calcd for $C_{16}H_{12}O_3S$: C 67.59; H 4.25. Found: C 67.65; H 4.17.

(*E*)-2-Phenoxymethylene-4*H*-3,1-benzoxathiin-4-one (4g: major product): mp 110-111 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 4 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.51 (1H, s), 7.03 (2H, m), 7.10 (1H, t, *J* = 7.5 Hz), 7.27-7.35 (4H, m), 7.51 (1H, td, *J* = 7.5, 1.2 Hz), 8.17 (1H, dd, *J* = 7.5, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 116.5, 123.8, 123.9, 125.9, 126.1, 126.9, 129.7, 130.9, 132.9, 134.2, 137.7, 156.6, 160.7; IR (KBr) ν_{max} 3073, 1745, 1673, 1590, 1487, 1438, 1220, 1092, 767, 739, 692 cm^{-1}. Anal. Calcd for $C_{15}H_{10}O_3S$: C 66.65; H 3.73. Found: C 66.78; H 3.63.

(*Z*)-2-Phenoxymethylene-4*H*-3,1-benzoxathiin-4-one (4'g: minor product): oil; R_f (CH_2Cl_2 : hexane = 4 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.99-7.12 (4H, m), 7.25-7.34 (4H, m), 7.50 (1H, td, *J* = 7.5, 1.2 Hz), 8.17 (1H, dd, *J* = 7.5, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 116.1, 122.3, 123.6, 125.9, 126.5, 130.0, 131.0, 132.7, 134.3, 134.4, 136.7, 156.4, 161.3; IR (KBr) ν_{max} 3061, 1743, 1591, 1490, 1440, 1226, 1140, 740, 688 cm^{-1}; HRMS (EI): Calcd for $C_{15}H_{10}O_3S$: 270.0351. Found: 270.0362.

(*E*)-2-Methoxymethylene-4*H*-3,1-benzoxathiin-4-one (4h: major product): mp 81.7-82.8 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 5 : 1) 0.4; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.74 (3H, s), 6.02 (1H, s), 7.23 (1H, dd, *J* = 8.0, 0.8 Hz), 7.29 (1H, td, *J* = 7.8, 1.2 Hz), 7.46 (1H, td, *J* = 7.8, 1.2 Hz), 8.14 (1H, dd, *J* = 7.8, 1.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 61.0, 121.4, 124.1, 125.7, 126.6, 132.8, 133.9, 137.1, 138.8, 161.3; IR (KBr) ν_{max} 2937, 1737, 1666, 1440, 1276, 1221, 1143, 1100, 974, 741 cm^{-1}. Anal. Calcd for $C_{10}H_8O_3S$: C 57.68; H 3.87. Found: C 57.79; H 3.80.

(*Z*)-2-Methoxymethylene-4*H*-3,1-benzoxathiin-4-one (4'h: minor product): mp 72.4-73.9 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 5 : 1) 0.5; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.71 (3H, s), 6.72 (1H, s), 7.25-7.27 (2H, m), 7.47 (1H, td, *J* = 7.8, 1.4 Hz), 8.14 (1H, dd, *J* = 7.8, 1.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$): 60.9, 122.9, 125.2, 125.9, 126.3, 132.7, 134.1, 137.6, 140.8, 162.1; IR (KBr) ν_{max} 2941, 1738, 1666, 1440, 1278, 1221, 1149, 1099, 983, 741 cm^{-1}. Anal. Calcd for $C_{10}H_8O_3S$: C 57.68; H 3.87. Found: C 57.66; H 3.77.

(*E*)-2-Acetoxymethylene-4*H*-3,1-benzoxathiin-4-one (4i: major product): mp 138-139 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 5 : 1) 0.4; ^{1}H-NMR (400 MHz, $CDCl_3$) δ2.23 (3H, s), 7.16 (1H, s), 7.27 (1H,

d, *J* = 7.8 Hz), 7.33 (1H, td, *J* = 7.8, 1.4 Hz), 7.52 (1H, td, *J* = 7.8, 1.4 Hz), 8.15 (1H, dd, *J* = 7.8, 1.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.5, 123.1, 123.4, 126.1, 127.0, 128.1, 132.8, 134.4, 136.7, 160.2, 166.6; IR (KBr) ν_{max} 3095, 1751, 1587, 1439, 1377, 1215, 1098, 1051, 945, 822, 737 cm^{-1}. Anal. Calcd for $C_{11}H_8O_4S$: C 55.92; H 3.41. Found: C 56.04; H 3.31.

(*Z*)-2-Acetoxymethylene-4*H*-3,1-benzoxathiin-4-one (4'i: minor product): mp 93.2-94.7 °C (AcOEt-hexane); R_f (CH_2Cl_2 : hexane = 5 : 1) 0.35; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.23 (3H, s), 7.27 (1H, d, *J* = 7.7 Hz), 7.31 (1H, td, *J* = 7.7, 1.2 Hz), 7.52 (1H, td, *J* = 7.7, 1.2 Hz), 7.69 (1H, s), 8.16 (1H, dd, *J* = 7.7, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.5, 122.0, 125.8, 126.8, 128.7, 132.0, 132.7, 134.6, 135.7, 160.7, 166.6; IR (KBr) ν_{max} 3093, 1750, 1592, 1442, 1370, 1196, 1139, 1030, 909, 799, 737 cm^{-1}. Anal. Calcd for $C_{11}H_8O_4S$: C 55.92; H 3.41. Found: C 55.97; H 3.30.

2-Ethylidene-4*H*-3,1-benzoxathiin-4-one (4j): a mixture of stereoisomers (*E* : *Z* = 1 : 1); Oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.77 (1.5H, d, *J* = 7.2 Hz), 1.82 (1.5H, d, *J* = 7.2 Hz), 5.34 (0.5H, q, *J* = 7.2 Hz), 5.76 (0.5H, q, *J* = 7.2 Hz), 7.21 (0.5H, d, *J* = 8.0 Hz), 7.25-7.30 (1.5H, m), 7.48 (0.5H, td, *J* = 8.0, 1.4 Hz), 7.49 (0.5H, td, *J* = 8.0, 1.4 Hz), 8.13 (0.5H, dd, *J* = 8.0, 1.4 Hz), 8.14 (0.5H, dd, *J* = 8.0, 1.4 Hz); IR (KBr) ν_{max} 2921, 1740, 1649, 1594, 1294, 1227, 1139, 1122, 1099, 740 cm^{-1}; HRMS (EI): Calcd for $C_{15}H_{10}O_3S$: 270.0351: Found: 270.0362.

General procedure for oxidation of 4 or 4'. To a solution of **4** or **4'** (1.0 mmol) in CH_2Cl_2 (10 mL) was added 70% *m*CPBA (1.0 mmol, 247 mg). The mixture was stirred for 30 min at room temperature, and then aqueous Na_2SO_3 was added. The products were extracted with CH_2Cl_2, and the organic layer was washed with water and dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent 5 : 1 CH_2Cl_2 : AcOEt). Crude **5d**, **5e**, and **5f** were recrystallized from AcOEt–hexane.

(*E*)-2-Benzylidene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5d): mp 88.0-90.6 °C (AcOEt-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.67 (1H, s), 7.37-7.43 (3H, m), 7.73-7.77 (3H, m), 7.84-7.91 (2H, m), 8.16 (1H, dd, *J* = 8.0, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 119.3, 121.4, 126.8, 128.9, 130.0, 130.4, 131.0, 132.6, 132.7, 135.4, 142.3, 147.1, 158.7; IR (KBr) ν_{max} 3055, 3025, 1747, 1639, 1586, 1446, 1266, 1238, 1082, 1055, 1036, 867, 749, 689 cm^{-1}; HRMS (EI): $C_{15}H_{10}O_3S$: 270.0351: Found: 270.0340.

(*E*)-2-(4-Chlorobenzylidene)-4*H*-3,1-benzoxathiin-4-one 1-oxide (5e): mp 65.3-66.9 °C (AcOEt-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.63 (1H, s), 7.38 (2H, dt, *J* = 8.8, 2.3 Hz), 7.70 (2H, dt, *J* = 8.8, 2.3 Hz), 7.76 (1H, td, *J* = 7.8, 1.2 Hz), 7.86-7.92 (2H, m), 8.27(1H, dd, *J* = 7.8, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 117.8, 121.2, 126.7, 129.2, 129.4, 131.5, 132.6, 132.8, 135.5, 135.9, 142.1, 147.6, 158.5; IR (KBr) ν_{max} 3043, 1753, 1587, 1488, 1406, 1265, 1233, 1089, 1031, 869, 743 cm^{-1}; HRMS (EI): $C_{15}H_9ClO_3S$: 303.9961: Found: 303.9937.

(*E*)-2-(4-Methoxybenzylidene)-4*H*-3,1-benzoxathiin-4-one 1-oxide (5f): mp 93.1-95.3 °C (AcOEt-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.84 (3H, s), 6.61 (1H, s), 6.93 (2H, d, *J* = 8.0 Hz), 7.74-7.76 (3H, m), 7.85-7.87 (2H, m), 8.29 (1H, dd, *J* = 7.6, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 55.4, 114.3, 120.4, 121.7, 123.7, 127.3, 132.4, 132.6, 132.9, 135.3, 142.0, 144.9, 159.0, 160.9; IR (KBr) ν_{max} 3005, 1752, 1604, 1511, 1255, 1179, 1086, 1055, 872, 748, 688 cm^{-1}; HRMS (EI): Calcd for $C_{16}H_{12}O_4S$: 300.0456: Found: 300.0449.

(*E*)-2-Phenoxymethylene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5g): mp 145-146 °C (AcOEt-hexane); R_f (CH_2Cl_2 : AcOEt = 5 : 1) 0.5; 1H-NMR (400 MHz, $CDCl_3$) δ 7.07 (1H, s), 7.11 (2H, dd, *J* = 8.4, 1.2 Hz), 7.21 (1H, t, *J* = 7.2 Hz), 7.38 (2H, t, *J* = 8.0 Hz), 7.79-7.89 (3H, m), 8.39 (1H, dd, *J* = 7.6, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 117.1, 122.6, 125.3, 128.5, 130.1, 132.8, 133.5, 135.1, 135.7, 137.5, 141.1, 156.2, 158.4; IR (KBr) ν_{max} 3077, 1741, 1669, 1589, 1487, 1441, 1227, 1162, 1062, 1041, 752, 695 cm^{-1}. Anal. Calcd for $C_{15}H_{10}O_4S$: C 62.93; H 3.52. Found: C 62.83; H 3.43.

(*Z*)-2-Phenoxymethylene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5'g): mp 132-134 °C (AcOEt-hexane); R_f (CH_2Cl_2 : AcOEt = 5 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.07 (2H, d, *J* = 8.0 Hz), 7.20 (1H, t, *J* = 7.8 Hz), 7.37 (1H, s), 7.39 (2H, t, *J* = 8.0 Hz), 7.81-7.88 (2H, m), 7.93 (1H, dd, *J* = 7.8, 1.8 Hz), 8.39 (1H, dd, *J* = 7.8, 1.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 116.6, 122.5, 125.0, 129.5, 130.1, 132.8, 133.8, 135.1, 139.2, 140.3, 141.0, 155.9, 159.5; IR (KBr) ν_{max} 3039, 1749, 1651, 1588, 1490, 1229, 1141, 1036, 857, 749, 686 cm^{-1}. Anal. Calcd for $C_{15}H_{10}O_4S$: C 62.93; H 3.52. Found: C 62.69; H 3.39.

(*E*)-2-Methoxymethylene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5h): mp 107-108 °C (AcOEt-hexane); R_f (CH_2Cl_2 : AcOEt = 5 : 1) 0.4; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.94 (3H, s), 6.61 (1H, s), 7.76-7.84 (3H, m), 8.35 (1H, dd, *J* = 6.8, 1.2 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.5, 122.5, 128.5, 132.7, 132.8, 133.3, 135.0, 141.3, 143.2, 158.6; IR (KBr) ν_{max} 3065, 2945, 1747, 1670, 1443, 1233, 1119, 1042, 968, 740, 868, 745, 687 cm^{-1}. Anal. Calcd for $C_{10}H_8O_4S$: C 53.56; H 3.60. Found: C 53.63; H 3.51.

(*Z*)-2-Methoxymethylene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5'h): mp 126-128 °C (AcOEt-hexane); R_f (CH_2Cl_2 : AcOEt = 5 : 1) 0.5; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.87 (3H, s), 6.97 (1H, s), 7.77-7.84 (2H, m), 7.88 (1H, dd, *J* = 7.6, 1.6 Hz), 8.34 (1H, dd, *J* = 7.6, 1.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.3, 122.7, 129.4, 132.6, 133.5, 134.9, 135.3, 140.6, 147.1, 159.9; IR (KBr) ν_{max} 2941, 1738, 1440, 1278, 1221, 1149, 1099, 740 cm^{-1}. Anal. Calcd for $C_{10}H_8O_4S$: C 53.56; H 3.60. Found: C 53.60; H 3.47.

(*E*)-2-Acetoxymethylene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5i): mp 124-125 °C (AcOEt-hexane); R_f (CH_2Cl_2 : AcOEt = 5 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.30 (3H, s), 7.72 (1H, s), 7.80-7.89 (3H, m), 8.35 (1H, dd, *J* = 7.1, 1.6 Hz) ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.4, 122.3, 128.0, 128.5, 132.9, 133.7, 135.3, 137.4, 140.9, 158.0, 165.9; IR (KBr) ν_{max} 3107, 1777, 1747, 1677, 1589, 1441, 1377, 1200, 1136, 1091, 1038, 943, 814, 745, 699 cm^{-1}. Anal. Calcd for $C_{11}H_8O_5S$: C 52.38; H 3.20. Found: C 52.34; H 3.07.

(*Z*)-2-Acetoxymethylene-4*H*-3,1-benzoxathiin-4-one 1-oxide (5'i): mp 109-110 °C (AcOEt-hexane); R_f (CH_2Cl_2 : AcOEt = 5 : 1) 0.6; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.30 (3H, s), 7.82-7.92 (3H, m), 7.93 (1H, s), 8.36 (1H, dd, *J* = 7.5, 1.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.4, 122.6, 129.5, 133.0, 133.1, 134.1, 135.1, 139.9, 140.5, 159.0, 165.9; IR (KBr) ν_{max} 3043, 1766, 1659, 1370, 1202, 1140, 1057, 909, 791, 746, 672 cm^{-1}; HRMS (EI): Calcd for $C_{11}H_8O_5S$: 250.0092: Found: 250.0084.

Crystallographic data for (*E*)-2-(phenoxymethylene)-4*H*-3,1-benzoxathiin-4-one (4g). $C_{15}H_{10}O_3S$, M_w = 270.30, colorless, size: 0.35 × 0.33 × 0.29 mm, monoclinic, space group $P12_{1/c}1$, Z = 8, a = 7.2603(3) Å, b = 20.3891(9) Å, c = 16.7487(7) Å, α = 90.0000°, β = 92.2290(10)°, γ = 90.0000°, V = 2477.45(19) Å^3, D = 1.449 g/cm^3, T = 153(2) K, λ = 0.71069 Å, μ = 0.261 mm^{-1}; 13,782 reflections measured, of which 5582 were unique (R_{int} = 0.0158), R_1 = 0.0358 ($I > 2\sigma(I)$), R_w = 0.0836 (all data), goodness of fit = 1.036. The structure was solved by heavy-atom methods and refined on F^2 using all the reflections. All the non-hydrogen atoms were refined using anisotropic atomic displacement parameters, and hydrogen atoms were placed at calculated positions and included in the refinements using the riding model. Deposition number CCDC-985453. Free copies of the data can be obtained at http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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