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ALKYLATION OF 2-BUTYL-4,4-DIMETHYL-4*H*-BENZO[*d*][1,3]-OXATHIINE-1,1-DIOXIDE, A NEW CLASS OF ACYL ANION EQUIVALENTS AS AN ALTERNATIVE TO DITHIANES

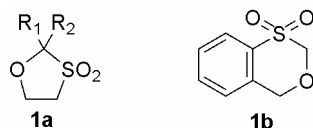
Robert K. Boeckman, Jr.,* Susan M. Hanson, and Jeremy A. Cody

University of Rochester, Department of Chemistry, P.O. Box 271216 Rochester, NY 14623, U. S. A. email: rkb@rkbmac.chem.rochester.edu.

Abstract – (2-Butyl-4,4-dimethyl-4*H*-benzo[*d*][1,3]oxathiine-1,1-dioxide has been found to react with several electrophiles, such as various halides and aldehydes, upon regioselective deprotonation. This method utilizes the sulfone group to form new carbon-carbon bonds while serving as a masked carbonyl. Subsequent hydrolysis of the sulfone provides a facile approach toward many useful synthetic intermediates. This methodology could provide a useful alternative to the use of dithiane groups.

INTRODUCTION

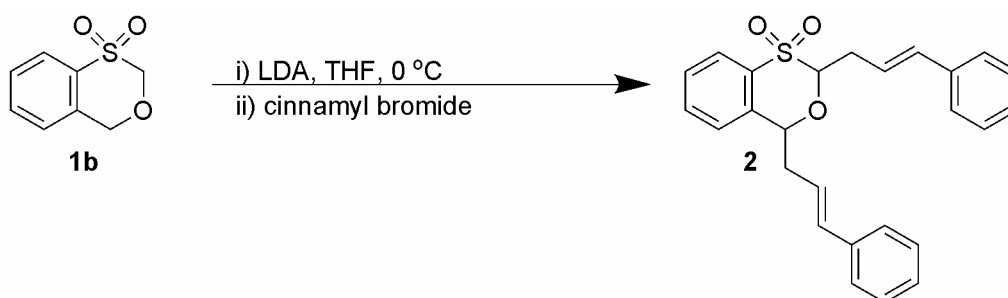
Although the use of sulfones to facilitate C-C bond formation has been in common use as a synthetic tool for several decades,¹ there are still opportunities to further exploit the utility of this functionality for organic synthesis. The sulfone is robust towards a variety of reaction conditions, and the derived α -sulfonylcarbanions have broad utility through their facile reaction with a wide variety of carbon and heteroatom electrophiles. The chemistry of α -sulfonylcarbanions has been extensively reviewed, and the potential of these substrates to be utilized as acyl anion equivalents has also been widely recognized.² Numerous examples of the lithiation and alkylation of structurally diverse sulfones have been reported in the literature.³ Pioneering work in this area was accomplished by Schlessinger, who clearly illustrated the utility and formation of acyl anion equivalents from ketene thioacetal monoxides, and Magnus, whose extensive report on developments in sulfone chemistry paved the way for organic chemists to adopt this chemistry as a useful synthetic methodology.^{1a,4} In his review on sulfone chemistry, Magnus reported the results of a preliminary investigation into the possibility that 1,3-oxathiolane-*S*-dioxides (**1a** and **1b**) might serve as useful adjuncts to hemithioacetals as protecting groups and be exploitable as a new sulfone based acyl anion equivalent^{1a} (Figure 1).

Figure 1. 1,3-Oxathiolane-*S*-dioxides and 4*H*-benzo[*d*]1,3]oxathiine-1,1-dioxides (**1a** and **1b**)

RESULTS AND DISCUSSION

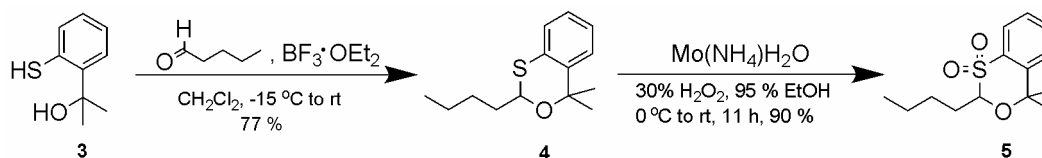
In connection with ongoing synthetic work in our laboratories that required an alternative to a dithiane as an acyl anion equivalent suitable for coupling two fragile complex synthons, we reinvestigated the preliminary unpublished observations of Magnus employing dioxide substrate (**1b**). We found that our initial attempts to deprotonate and regioselectively alkylate sulfone (**1b**) using lithium diisopropylamine as the base and cinnamyl bromide as the electrophile resulted in undesired deprotonation at the benzylic position affording the bis-alkylated sulfone (**2**) in 17% yield. Furthermore, it was noted that the anion(s) derived from (**1b**) appeared rather instable. We speculated that the source of the observed instability might result from α -elimination of the α -mono sulfone anion.

Equation 1. Alkylation of (**1b**) with Cinnamyl Bromide



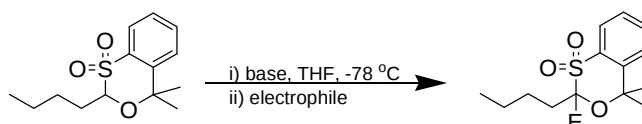
This unforeseen lack of regioselective anion formation was easily circumvented by replacing the benzylic protons in parent sulfone (**1b**) with methyl groups. We also reasoned that geminal substitution might retard the undesired α -elimination process leading to a more stable anion. Consequently, subsequent experimentation was performed on 4,4-dimethyl-4*H*-benzo[*d*][1,3]oxathiine-1,1-dioxides, specifically *n*-butyl derivative (**5**), which was readily obtained as a white crystalline solid in 69% overall yield from known benzyl alcohol (**3**) and pentanal by $\text{BF}_3\cdot\text{Et}_2\text{O}$ catalyzed hemithioacetalization followed by ammonium molybdate catalyzed oxidation with H_2O_2 (Scheme 1).⁵

Scheme 1. Preparation of 2-Butyl-4,4-dimethyl-4*H*-benzo[*d*][1,3]oxathiine 1,1-dioxide (**5**)



With this substrate in hand, optimal conditions for facile α -sulfone anion formation were explored. (Table 1) Treatment of sulfone (**5**) with LDA or LTMP, in this case, failed to facilitate efficient conversion to alkylated products, even when HMPA was employed to facilitate deprotonation and/or alkylation. Optimal results were obtained when alkyllithium reagents were employed for deprotonation. We found that *n*-BuLi worked well, with PhLi also providing satisfactory results. Non-alkyllithium bases such as sodium amide and KHMDS failed to facilitate deprotonation as well. Further exploration of less nucleophilic alkyllithium bases such as trityl or fluorenyl lithium may prove fruitful as the use of nucleophilic alkyllithium bases could serve to limit functional group compatibility when more sensitive and complex aldehydes are employed as substrates.

Table 1. Alkylation of Sulfone (**5**) Employing Various Lithium Bases

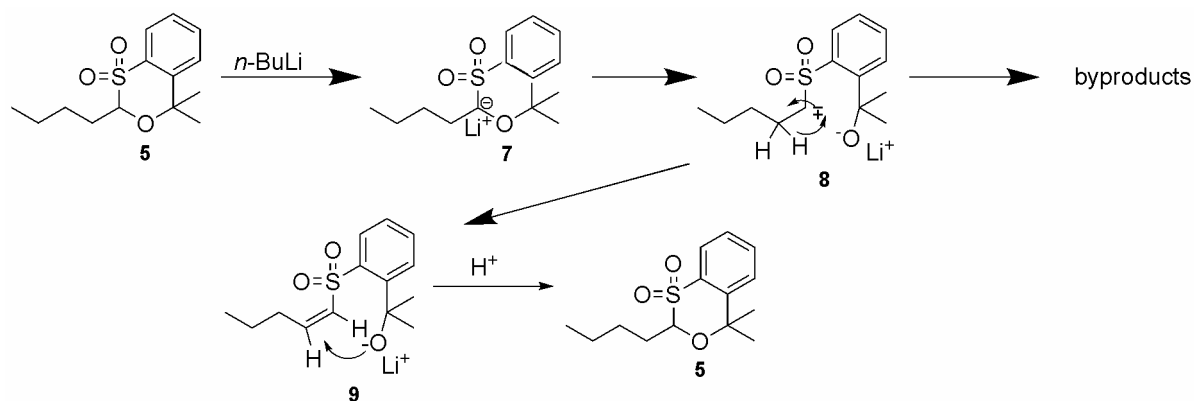


entry	Base	HMPA Equivalents	Electrophile	Product	Yield (%)
1	LTMP	0		SM recovered	NR
2	LTMP	1.4		R= SM recovered	30 (1:1 SM:Pdt)
3	LDA	0		SM recovered	NR
4	LDA	1.4		SM recovered Polar byproducts	NR
5	<i>n</i> -BuLi	0		R=	56
6	PhLi	0		R= SM recovered	49 (1:3 SM:Pdt)

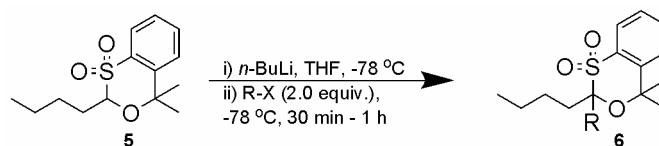
Initially, we had assumed that anion formation would proceed relatively slowly, but we expected that once formed the anion would be reasonably stable. Thus, sulfone (**5**) was stirred in the presence of *n*-BuLi for 15-30 min prior to addition of the electrophile. However, only fair and irreproducible yields were

obtained, and some starting material was recovered under those reaction conditions. Based on these observations, we surmised that the α -sulfonylcarbanion was either very short-lived or involved in other chemistry leading to byproducts that were not isolated on workup. Therefore, we speculated that a non-nucleophilic base such as lithium tetramethylpiperidine might allow for the generation of the anion in the presence of the electrophile. An experiment was run in which sulfone (**5**), cinnamyl bromide and LTMP were all combined at $-78\text{ }^{\circ}\text{C}$ and warmed to room temperature over the course of an hour. However, only starting material was recovered. When HMPA was added to the reaction, a 1:1 ratio of starting material : product was recovered in 30% yield. Based on this preliminary experimentation, we concluded that the anion derived from (**5**) was apparently unstable, and that yields might be improved by immediate trapping of the anion with the electrophile. When (**5**) was treated with *n*-BuLi and prenyl bromide was added after 10 min, we reproducibly obtained 56% yield of the alkylated sulfone (**6a**), an improvement but still less than satisfactory. We further optimized this procedure by examining the order of addition of the reagents and varying the temperature. From these experiments, we concluded that addition of the electrophile after a short time to the α -sulfone anion at $-78\text{ }^{\circ}\text{C}$ was optimal.

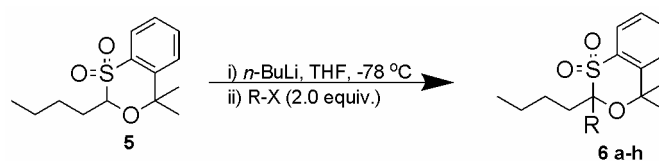
Figure 2. Plausible Mechanism for Decomposition of (**7**)



The apparent instability of the α -oxygenated sulfone anion (**7**) derived from (**5**) is most likely arising from the formation of the highly reactive carbene intermediate (**8**) by α -elimination (Scheme 2).⁶ Upon addition of *n*-BuLi, the α -sulfonylcarbanion is rapidly generated. A competition then ensues between reaction with the electrophile to form alkylation products and α -elimination to (**8**) which can further react by multiple pathways; including possible rearrangement to vinyl sulfone (**9**) with eventual recyclization to starting sulfone (**5**). We did not further investigate the mechanism of decomposition of (**7**) or the fate of (**7**) upon decomposition. Fortunately, rapid anion formation followed by addition of the electrophile permitted us to minimize the recovery of (**5**).

Figure 3. Reaction Conditions for the Alkylation of Sulfone (**5**) with Various Halides

Based on the results above, the following general reaction conditions were established (Scheme 3). The α -sulfonylcarbanion of (**5**) was generated by the addition of *n*-BuLi at $-78\text{ }^{\circ}\text{C}$. Upon addition of the base, the solution turned bright yellow-orange, which is indicative of anion formation. The addition of base was followed by addition (5-10 min later) of the electrophile. A number of different halides were examined to probe the reactivity and generality of this reaction with respect to electrophile (Table 3). As expected, the highest yields were observed when iodides are used as electrophiles, although allylic bromides afforded moderate yields. Less reactive secondary iodides failed to react. Although we did not examine any such

Table 2. Alkylation of Sulfone (**5**) with Various Halides

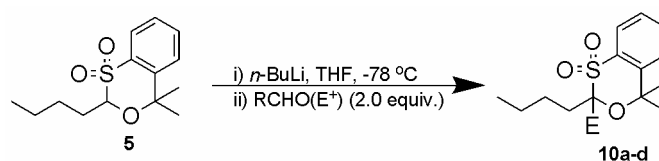
entry	Halide	Product	Yield (%)
1		6a, R =	56
2		6b, R =	65
3		6c, R =	74
4	CH ₃ I	6d, R = CH ₃	55
6		6e, R =	50 ^a
7		6f, R =	57 ^a
8		NR	NR
9		6h, R =	49 ^a

^aYield based on recovered starting material.

electrophiles, it is possible that triflates would provide an additional boost in reactivity. To permit utilization of more readily available bromides, we incubated the bromides with tetrabutylammonium iodide (1 equiv) in THF prior to addition to the reaction mixture. Under these conditions, a 10-15% improvement in the yields of alkylation products was obtained.

To further demonstrate the utility of this process, reactions with various aldehydes were attempted as shown in Table 2. Tolerance of such moieties as silyl protecting groups and nitro groups to the reaction conditions was also briefly explored. Our method proved to be quite versatile with the aforementioned functionalities proving tolerant of the reaction conditions. For example, the use of TMS-protected propargyl bromide provided the desired alkylation product in modest yield. Aldehydes with α -chiral centers also proved to be suitable electrophiles for this substrate as well, with no epimerization of the adjacent chiral center observed, although mixtures of diastereomers were observed. No attempt was made to optimize the diastereoselectivity of these reactions.

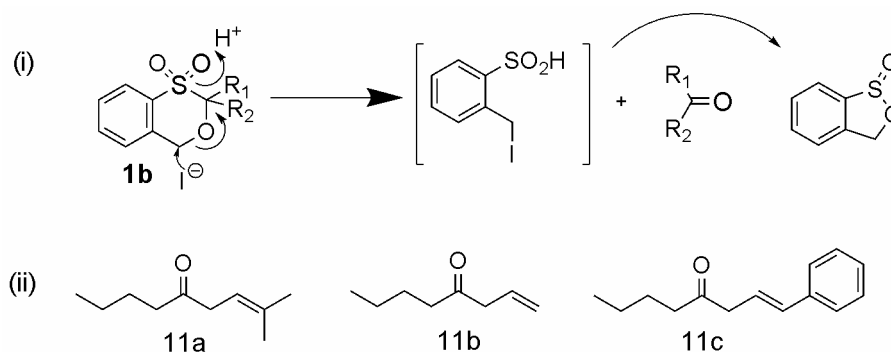
Table 3. Reaction of Sulfone (**5**) with Various Carbonyl Substrates



entry	Carbonyl	Product ^a	Yield (%)
1		10a, E=	70
2		10b, E=	52
3		10c, E=	63
4		10d, E=	59

^a A mixture of diastereomers was obtained.

The utility of this method lies in the ability to expose the masked carbonyl functionality to give various aldehydes and ketones. In his review,^{1a} Magnus reports that treatment of sulfone (**1b**) with catalytic hydrogen iodide in dichloromethane at room temperature facilitates this transformation. (Figure 4) Since the determination of effective hydrolysis conditions can be very substrate specific, we sought to demonstrate the feasibility of this conversion.

Figure 4. Formation of Ketones or Aldehydes Via Sulfone Hydrolysis

Therefore, we briefly investigated the acid-assisted hydrolysis of the alkylated 1,3-oxathiolane-S-dioxide substrates. We found that the aforementioned hydrolysis could be achieved via three different sets of acidic reaction conditions: (i) concentrated HCl-methanol (1:10) with heating to 50 °C (ii) conc. H₂SO₄-methanol (1:20) at rt (iii) Amberlite strongly acidic resin (pH~1)-methanol/H₂O with heating to 60 °C. When substrates (**6a**, **6b**, and **6e**) were subjected to these conditions, the corresponding unsymmetrical ketones (**11 a-c**) were obtained in 50-60% yield. Also, several examples of photochemical-induced heterolytic cleavage of the C-S bond in the presence of base have been reported in the literature.^{7a} Catalytic hydrolysis with 70% perchloric acid or HCl in the presence of a mercuric salt have been demonstrated as well.^{7b} These alternatives may provide viable options for more sensitive aldehydes or ketones.

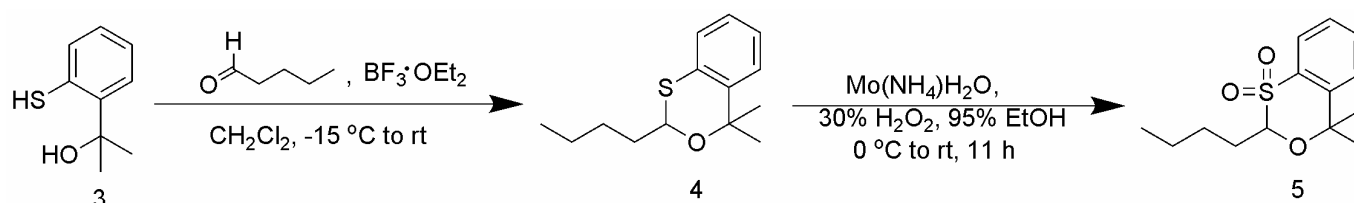
The alkylation of 2-butyl-4,4-dimethyl-4*H*-benzo[*d*][1,3]oxathiine-1,1-dioxide with various aldehyde and halide electrophiles has been disclosed. Although the generality of this method is somewhat limited by the inherent instability of the intermediate α -oxygen substituted sulfonyl anions, this method has reasonable generality and good versatility, and thus may provide a potentially useful alternative to the use of dithianes in some cases owing to the greater ease with which the resulting ketones can be unmasked.

EXPERIMENTAL

General Procedures: All non-aqueous reactions were carried out using flame-dried glassware under an atmosphere of argon. Unless stated otherwise, reactions were stirred magnetically. Moisture-sensitive reagents and solutions were introduced via syringe, cannula, or addition funnel. Reactions were cooled using ice water (0 °C), dry ice-acetone (-78 °C), dry ice-benzyl alcohol (-15 °C) or an external cryocool immersion bath. Volatile solvents were removed using a Büchi rotary evaporator attached to a variable pressure vacuum pump. Samples were rigorously dried under high vacuum. Liquid chromatography was performed on EM Reagents silica gel 60 (230-400 mesh) using the specified solvent system as eluent. Unless noted otherwise, all work-up procedures and extractions involved the use of reagent grade solvents.

Tetrahydrofuran and diethyl ether were distilled from sodium-benzophenone ketyl, and dichloromethane was distilled from calcium hydride.

Proton and carbon nuclear magnetic resonance (NMR) spectra were obtained on a Bruker Avance 400 (400 MHz). Infrared spectra (IR) were acquired on a Shimadzu FT-IR. High resolution mass spectra were provided by the Department of Chemistry at the State University of New York (SUNY) at Buffalo. Ionization techniques consisted of chemical ionization (CI), electron impact (EI), and electrospray (ES).



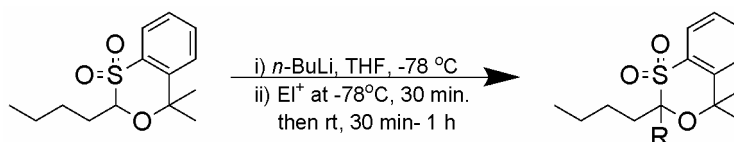
2-Butyl-4,4-dimethyl-4H-benzo[d][1,3]oxathiane-1,1-dioxide (5):

Benzyl alcohol (10.00 g, 59.5 mmol) was added to anhydrous methylene chloride (375 mL) at rt. Pentanal (5.12 g, 59.5 mmol, 1 equiv.) was added in one portion, and the solution was cooled to $-15\text{ }^{\circ}\text{C}$. BF_3 -etherate (8.44 g, 7.50 mL, 59.5 mmol, 1 equiv.) was added slowly via syringe pump over 10 min. The mixture was stirred and slowly warmed to RT over the course of 1 h yielding an orange solution. The reaction was quenched with 1N NaOH (250 mL) and stirred for 10 min. The aqueous layer was separated and extracted with methylene chloride (3 x 100 mL). The combined organics were dried over magnesium sulfate and filtered. Concentration in vacuo afforded clear, yellow oil. Purification by column chromatography (500 mL silica gel, gradient 90% hexanes/EtOAc) yields (4) as a clear, pale yellow oil (10.84 g, 77%). However, crude product (4) is pure enough for further conversion. ^1H NMR (400 MHz, CDCl_3) δ 7.25-7.04 (m, 4H), 5.14-5.12 (m, 1H), 1.94-1.79 (m, 8H), 1.56-1.38 (m, 4H), 0.96 (t, 3H). IR (film) 2947, 2857, 1595, 1444, 1062, 939, 742 cm^{-1} . LRMS m/z : 237.3 ($\text{M}+\text{H}$) $^+$ Calculated for (M^+): 236.12

Thiooxoacetal (10.84 g, 45.9 mmol) was added to 95% EtOH (450 mL), and the solution was cooled to $0\text{ }^{\circ}\text{C}$. A solution of ammonium molybdate (6.25 g, 5.04 mmol, 0.11 eq.) in 30% H_2O_2 (78.0 mL, 0.689 mol, 15 eq.) was added dropwise to the reaction mixture over 50 min via an additional funnel. Once the addition was complete, the ice bath was removed. The mixture was warmed to rt and stirred for 12 h. The reaction was diluted with brine (200 mL) and extracted with Et_2O (3 x 150 mL). The combined organics were washed with brine (2 x 100 mL), dried over magnesium sulfate and filtered. Concentration in vacuo yielded an off-white oil. Purification by column chromatography (500 mL silica gel, gradient 90-50% hexanes/EtOAc) provided 11.07 g of (5) as a white solid (90%) having mp $114\text{--}116\text{ }^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3) δ 7.95 (dd, $J = 7.8, 1.2\text{ Hz}$, 1H), 7.53 (ddd, $J = 7.8, 7.7, 1.3\text{ Hz}$, 1H), 7.45 (ddd, $J = 7.8, 7.7, 1.0\text{ Hz}$, 1H), 7.18 (dd, $J = 7.7, 1.3\text{ Hz}$, 1H), 4.86 (dd, $J = 9.6, 3.2\text{ Hz}$, 1H), 2.19-2.09 (m,

1H), 2.28-2.24 (m, 1H), 1.99-1.85 (m, 1H), 1.72-1.58 (m, 7H), 1.53-1.38 (m, 3H), 0.97 (t, $J = 7.3\text{Hz}$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.1, 136.2, 132.4, 128.0, 126.0, 123.8, 84.7, 78.4, 31.3, 26.6, 26.5, 24.6, 22.3, 13.8; IR (film) 2927, 2867, 1434, 1376, 1297, 1264, 1141, 1083, 1016, 947, 803, 755 cm^{-1} . HRMS (ESI) m/z 291.1026 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 291.1031; MP $114\text{ }^\circ\text{C}$ - $116\text{ }^\circ\text{C}$.



General Procedure for Alkylation: Sulfone (100 mg, 1.87 mmol) was added to anhydrous THF and cooled to $-78\text{ }^\circ\text{C}$. To the cooled solution, a solution of $n\text{-BuLi}$ (0.9 mL, 2.05 mmol, 1.1 equiv.) was added dropwise via syringe. The solution changed from clear to bright yellowish orange after the addition of $n\text{-BuLi}$. The reaction was stirred for 5-10 min at $-78\text{ }^\circ\text{C}$, and then the electrophile was added via syringe. The reaction was stirred at $-78\text{ }^\circ\text{C}$ for 30 min. The solution was then warmed to rt and stirred for 30 min-1 h. The reaction was quenched with saturated aqueous NaHCO_3 (2 mL). The aqueous layer was separated, extracted with Et_2O (3 x 10 mL), dried over sodium sulfate and filtered. Concentration in vacuo yielded products as pale yellow oils. Purification by column chromatography (50 mL silica gel, gradient 98-70% hexanes/ethyl acetate) provided products (**6a-h**) and (**7a-d**) as thick, clear oils.

2-butyl-4,4-dimethyl-2-(3-methyl-but-2-enyl)-4H-benzo[d][1,3]oxathiane 1,1-dioxide (6a):

^1H NMR (400 MHz, CDCl_3) δ 8.00 (dd, $J = 7.7\text{ Hz}$, 1.4 Hz, 1H), 7.57 (ddd, $J = 7.6$, 7.6, 1.4 Hz, 1H), 7.47 (ddd, $J = 7.7$, 7.6, 0.90 Hz, 1H), 7.23 (dd, $J = 7.6$, 0.9 Hz, 1H), 5.28 (m, 1H), 2.86 (dd, $J = 15.8$, 7.5 Hz, 1H), 2.48 (dd, $J = 15.8$, 5.4 Hz, 1H), 2.10 (m, 1H), 1.83-1.20 (m, 17 H), 0.89 (t, $J = 7.3\text{Hz}$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.5, 135.3, 132.7, 127.7, 125.6, 124.3, 115.9, 109.4, 92.2, 76.6, 33.0, 32.4, 31.3, 30.4, 25.9, 24.7, 22.9, 18.1, 13.8. IR (film) 2960, 2931, 2872, 1718, 1700, 1684, 1654, 1636, 1534, 1507, 1458, 1438, 1385, 1363, 1300, 1152, 1069, 965, 876, 763, 591, 559 cm^{-1} . HRMS (ESI) m/z 359.1648 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 359.1657.

2-Allyl-2-butyl-4,4-dimethyl-4H-benzo[d][1,3]oxathiane 1,1-dioxide (6b,6c):

^1H NMR (400 MHz, CDCl_3) δ 7.97 (dd, $J = 7.8\text{ Hz}$, 1.4 Hz, 1H), 7.60 (ddd, $J = 7.6$, 7.6, 1.2 Hz, 1H), 7.49 (ddd, $J = 7.7$, 7.6, 0.90 Hz, 1H), 7.26 (dd, $J = 8.0$, 1.0 Hz, 1H), 5.96 (m, 1H), 5.28 (m, 2H), 2.89 (dd, $J = 15.2$, 7.2 Hz, 1H), 2.63 (dd, $J = 15.2$, 6.8 Hz, 1H), 2.10 (dt, $J = 7.6$, 4.4 Hz, 1H), 1.83-1.20 (m, 17 H), 0.89 (t, $J = 7.2\text{ Hz}$, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 136.7, 134.1, 132.7, 130.2, 127.8, 125.7, 124.3, 119.8, 91.2, 65.8, 36.2, 32.8, 32.6, 32.5, 31.1, 28.6, 28.5, 24.2, 22.9, 13.8. IR (film) 3078, 2933, 2873, 1718, 1638, 1540, 1508, 1458, 1385, 1365, 1120, 996, 975, 917, 873, 678, 502 cm^{-1} . HRMS (ESI) m/z 331.1338 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 331.1344.

2-Butyl-2,4,4-trimethyl-4H-benzo[d][1,3]oxathiine 1,1-dioxide (6d): ^1H NMR (400 MHz, CDCl_3) δ 7.97 (dd, $J = 7.8, 1.0$ Hz, 1H), 7.55 (ddd, $J = 7.8, 7.6, 1.2$ Hz, 1H), 7.48 (ddd, $J = 7.8, 7.7, 1.3$ Hz, 1H), 7.23 (dd, $J = 7.8, 0.9$ Hz, 1H), 2.05-1.97 (m, 2 H), 1.70 (s, 3 H), 1.65-1.57 (m, 6 H), 1.47-1.35 (m, 4 H), 0.96 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.6, 132.6, 127.7, 125.9, 125.7, 124.4, 89.8, 76.4, 33.6, 32.5, 31.4, 24.6, 22.2, 19.4, 13.9. IR (film) 2932, 2873, 1597, 1479, 1375, 1365, 1262, 1116, 1076, 987, 620 cm^{-1} . HRMS (ESI) m/z 305.1180 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 305.1187.

2-Butyl-4,4-dimethyl-2-(3-phenyl-allyl)-4H-benzo[d][1,3]oxathiine 1,1-dioxide (6e): ^1H NMR (400 MHz, CDCl_3) δ 8.07 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.59 (ddd, $J = 7.8, 7.6, 1.2$ Hz, 1H), 7.54 (ddd, $J = 7.8, 7.7, 1.2$ Hz, 1H), 7.43-7.26 (m, 6H), 6.56 (dd, $J = 15, 1.0$ Hz, 1H), 6.40-6.32 (m, 1H), 3.09 (dd, $J = 15.6, 7.6$ Hz, 1H), 2.82 (dd, $J = 15.6, 7.6$ Hz, 1H), 2.17-2.11 (m, 1H), 1.88 (dt, $J = 9.6, 3.2$ Hz, 1H), 1.78 (s, 3H), 1.74-1.60 (m, 5H), 1.35-1.29 (m, 2H), 0.90 (t, 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.4, 137.0, 134.2, 132.8, 132.7, 128.5, 127.8, 127.4, 126.2, 125.6, 124.4, 122.4, 91.8, 76.2, 35.6, 32.8, 32.6, 24.4, 22.9, 13.8. IR (film) 3061, 2958, 1478, 1364, 1260, 1152, 1085, 969, 803 cm^{-1} . HRMS (ESI) m/z 407.1655 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 407.1657.

2-Butyl-4,4-dimethyl-2-(3-methyl-butyl)-4H-benzo[d][1,3]oxathiine 1,1-dioxide (6f): ^1H NMR (400 MHz, CDCl_3) δ 8.01 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.59 (ddd, $J = 7.7, 7.6, 1.3$ Hz, 1H), 7.49 (ddd, $J = 7.7, 7.6, 1.3$ Hz, 1H), 7.23 (dd, $J = 8.0, 1.0$ Hz, 1H), 2.19-2.07 (m, 2H), 1.81-1.79 (m, 2H), 1.20-1.37 (m, 16H), 0.97-0.90 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.5, 132.9, 132.7, 127.7, 125.5, 125.4, 124.4, 123.8, 93.4, 32.8, 32.5, 31.5, 31.0, 30.9, 29.3, 28.5, 22.9, 22.5, 22.2, 13.8. IR (film) 3065, 2255, 1722, 1596, 1439, 1384, 1366, 1156, 1087, 1062, 881, 764, 645 cm^{-1} . HRMS (ESI) m/z 361.1806 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 361.1813.

[3-(2-Butyl)-4,4-dimethyl-1,1-dioxo-1,4-dihydro-2H-1 λ ⁶-benzo[d][1,3]oxathiin-2-yl)-prop-1-ynyl]-trimethylsilane (6h): ^1H NMR (400 MHz, CDCl_3) δ 7.97 (dd, $J = 7.8, 1.0$ Hz, 1H), 7.60 (ddd, $J = 7.8, 7.7, 1.2$ Hz, 1H), 7.47 (ddd, $J = 7.8, 7.7, 1.2$ Hz, 1H), 7.24 (dd, $J = 7.8, 1.0$ Hz, 1H), 3.10 (dd, $J = 16, 0.9$ Hz, 1H), 2.72 (dd, $J = 16, 1.0$ Hz, 1H), 2.39-2.24 (m, 1H), 2.12-2.01 (m, 1H), 0.96 (t, $J = 7.3$ Hz, 3H), 0.19 (s, 9 H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 132.9, 132.6, 127.9, 125.7, 124.4, 99.1, 90.5, 89.4, 33.7, 32.2, 31.4, 25.0, 24.5, 23.0, 13.6, -0.2. IR (film) 3805, 3448, 2734, 2655, 2339, 1947, 1829, 1716, 1636, 1562, 1540, 1516, 1480, 1388, 1366, 1226, 1062, 911, 719.3, 464.7 cm^{-1} . HRMS (ESI) m/z 401.1580 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 401.1583.

1-(2-Butyl-4,4-dimethyl-1,1-dioxo-1,4-dihydro-2H-1 λ ⁶-benzo[d][1,3]oxathiin-2-yl)-3-methyl-butan-1-ol (10a): ^1H NMR (400 MHz, CDCl_3) δ 7.97-7.93 (m, 1H), 7.61-7.39 (m, 2H), 7.25-7.23 (m, 1H), 4.42 (m, 1H), 4.16 (m, 1H), 3.07 (br s, 1H), 2.51 (br s, 1H), 2.27-2.07 (m, 2H),

1.97-1.40 (m, 11H), 1.31-1.13 (m, 2H), 0.97-0.93 (m, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.4, 143.2, 136.2, 133.2, 132.9, 127.9, 127.8, 125.5, 125.4, 124.1, 123.8, 93.1, 92.3, 84.7, 70.3, 39.8, 39.6, 33.9, 33.3, 31.4, 31.3, 30.9, 30.3, 28.4, 26.5, 26.4, 25.4, 25.2, 24.7, 24.6, 23.9, 23.8, 23.2, 23.3, 23.2, 21.6, 21.3, 13.7. IR (film) 3751, 3690, 3648, 3523, 2932, 2254, 1716, 1636, 1572, 1540, 1437, 1366, 1226, 1102, 1073, 1040, 956, 864, 679 cm^{-1} . HRMS (ESI) m/z 377.1763 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 377.1762.

(2-Butyl-4,4-dimethyl-1,1-dioxo-1,4-dihydro-2H-1 λ^6 -benzo[d][1,3]oxathiin-2-yl)-4-nitro-phenyl)-methanol (10b): ^1H NMR (400 MHz, CDCl_3) δ 8.12 (dd, $J = 7.7, 1.0$ Hz, 2H), 7.85 (dd, $J = 7.7, 1.3$ Hz, 1H), 7.50-7.37 (m, 5H), 5.56 (s, 1H), 5.42 (s, 1H), 4.72 (s, 1H), 3.53 (s, 1H), 2.13 (m, 2H), 1.69-1.40 (m, 10H), 0.93 (t, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 147.3, 143.2, 143.0, 136.5, 133.4, 132.7, 127.8, 127.6, 125.4, 124.3, 93.0, 92.7, 70.6, 30.7, 26.5, 26.4, 25.3, 25.1, 24.8, 24.6, 23.1, 22.5, 22.3, 14.1. IR (film) 2927, 2867, 1434, 1376, 1297, 1264, 1141, 1083, 1016, 947, 803, 755 cm^{-1} . HRMS (ESI) m/z 442.1300 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 442.1300.

1-(2-Butyl-4,4-dimethyl-1,1-dioxo-1,4-dihydro-2H-1 λ^6 -benzo[d][1,3]oxathiin-2-yl)-3-(tert-butyl-diphenyl-silanoxy)-2-methyl-propan-1-ol (10c): ^1H NMR (400 MHz, CDCl_3) δ 8.01 (m, 1H), 7.53-7.57 (m, 5H), 7.23-7.17 (m, 3H), 4.87 (m, 1H), 4.52 (m, 1H), 4.41-4.17 (m, 1H), 3.62-3.52 (m, 1H), 2.59-2.47 (m, 1H), 2.39-1.85 (m, 2H), 1.45-1.03 (m, 9H), 0.99-0.83 (m, 24H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.7, 143.3, 143.0, 136.2, 135.6, 133.8, 133.6, 133.1, 132.9, 129.8, 127.8, 125.9, 123.8, 95.5, 94.6, 84.7, 67.8, 66.5, 37.1, 36.5, 34.6, 33.5, 33.1, 32.3, 31.5, 31.0, 26.8, 26.9, 26.5, 25.7, 25.2, 23.3, 22.2, 14.0, 11.25, 10.5. IR (film) 3822, 3134, 3070, 2738, 2254, 1962, 1826, 1733, 1572, 1365, 1109, 948, 704 cm^{-1} . HRMS (ESI) m/z 617.2748 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 617.2733.

3-Benzyloxy-1-(2-Butyl-4,4-dimethyl-1,1-dioxo-1,4-dihydro-2H-1 λ^6 -benzo[d][1,3]oxathiin-2-yl)-2-methyl-propan-1-ol (10d): ^1H NMR (400 MHz, CDCl_3) δ 8.04 (dd, $J = 7.8, 0.9$ Hz, 1H), 7.61-7.48 (m, 4H), 7.45-7.31 (m, 4H), 5.12 (s, 1H), 5.08 (s, 1H), 4.57 (s, 2H), 3.63-3.37 (m, 2H), 3.29-3.15 (m, 1H), 2.13-1.85 (m, 3H), 1.79-1.43 (m, 10H), 0.99-0.85 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.3, 132.4, 128.5, 128.4, 128.2, 127.9, 127.6, 125.9, 123.8, 84.7, 78.3, 65.3, 63.1, 31.3, 26.5, 26.4, 24.6, 25.2, 23.1, 22.2, 13.8, 11.9. IR (film) 3822, 3134, 3070, 2738, 2254, 1962, 1826, 1733, 1572, 1365, 1109, 948, 704 cm^{-1} . IR (film) 3855, 3063, 1948, 1817, 1639, 1597, 1572, 1024, 906, 804, 680 cm^{-1} . HRMS (ESI) m/z 469.2030 ($\text{M}+\text{Na}$) $^+$ Calculated for ($\text{M}+\text{Na}$) $^+$: 469.2025.

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REFERENCES (AND NOTES)

1. a) P. D. Magnus, *Tetrahedron*, 1977, **33**, 2019. b) L. Field, *Synthesis*, 1978, 713.
2. a) B. T. Grobel and D. Seebach, *Synthesis*, 1977, 357. b) D. Seebach, *Angew. Chem.*, 1969, **81**, 690. c) D. Seebach, *Angew. Chem., Int. Ed., Engl.*, 1979, **18**, 239. d) E. Block, "Reactions of Organosulfur Compounds," Academic Press, New York (1978).
3. a) K. Kondo and D. Tunemoto, *Tetrahedron Let.*, 1975, **12**, 1007. b) K. Kondo, E. Saito, and D. Tunemoto, *Tetrahedron Let.*, 1975, **27**, 2275. c) K. Tanaka, S. Matsui, and A. Kaji, *Bull. Chem. Soc. Jpn.* 1980, **53**, 3619. d) S. V. Ley, B. Lygo, F. Sternfield, and A. Wonnacott, *Tetrahedron*, 1986, **42**, 4333. e) M. Ashwell and R. F. W. Jackson, *J. Chem. Soc., Perkin Trans. 1*, 1989, **4**, 835. f) M. B. Anderson, M. Lamothe, and P. L. Fuchs, *Tetrahedron Let.*, 1991, **35**, 4457. g) K. Fuji, Y. Usami, Y. Kiryu, and M. Node, *Synthesis*, 1992, 852.
4. a) J. L. Herrmann, J. E. Richman, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **35**, 3271. b) J. E. Richman, J. L. Herrmann, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **35**, 3267. c) J. L. Herrmann, J. E. Richman, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **35**, 3275. d) J. L. Herrmann, J. E. Richman, P. J. Wepplo, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **47**, 4707. e) J. L. Herrmann, G. R. Kieczkowski, R. F. Romanet, P. J. Wepplo, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **47**, 4711. f) J. L. Herrmann, G. R. Kieczkowski, R. F. Romanet, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **47**, 4715. g) R. F. Romanet and R. H. Schlessinger, *J. Am. Chem. Soc.*, 1974, **96**, 3701. h) G. R. Kieczkowski, C. S. Pogonowski, J. E. Richman, and R. H. Schlessinger, *J. Org. Chem.*, 1977, **42**, 175. i) G. R. Kieczkowski, M. L. Quesada, and R. H. Schlessinger, *J. Am. Chem. Soc.*, 1980, **102**, 782.
5. a) T. Durst, J. C. Huang, N. K. Sharma, and D. J. H. Smith, *Can. J. Chem.*, 1978, **56**, 512. b) G. D. Figuly, C. K. Loop, and J. C. Martin, *J. Am. Chem. Soc.*, 1989, **111**, 654.
6. a) K. Schank, W. Abdel, A. Aboel-Magd, S. Buegler, P. Eigen, J. Jager, and K. Jost, *Tetrahedron*, 1994, **50**, 3721; and references therein. b) N. Kamigata and M. Kobayashi, *Sulfur Reports*, 1982, **2**, 87. c) R. J. Mulder, J. Strating, and J. Strating, *Tetrahedron Lett.*, 1967, **32**, 3057. d) R. H. Rynbrandt and F. E. Dutton, *J. Org. Chem.*, 1975, **40**, 2282.
7. a) J. E. Richman, J. L. Herrmann, and R. H. Schlessinger, *Tetrahedron Let.*, 1973, **35**, 3267; and references therein. b) K. Ogura, K. Ohtsuki, M. Nakamura, N. Yahata, K. Takahashi, and H. Iida, *Tetrahedron Lett.*, 1985, **26**, 2455; and references therein.