Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gsrp20

The base-mediated cyclization of selected benzyl alkynyl sulfones with aromatic aldehydes: novel synthetic access to aryl-substituted 5,6-dihydro-1,4-oxathiin S,S-dioxides

Lilly U. Ho [a], Mohanad Gh. Shkoor [a], M. Selim Hossain [a], Matthew C. Deen [a], Dmitriy V. Soldatov [a] & Adrian L. Schwan [a]
[a] Department of Chemistry, University of Guelph, Guelph, ON, Canada, N1G 2W1

Version of record first published: 18 Sep 2012.

To cite this article: Lilly U. Ho , Mohanad Gh. Shkoor , M. Selim Hossain , Matthew C. Deen , Dmitriy V. Soldatov & Adrian L. Schwan (2013): The base-mediated cyclization of selected benzyl alkynyl sulfones with aromatic aldehydes: novel synthetic access to aryl-substituted 5,6-dihydro-1,4-oxathiin S,S-dioxides, Journal of Sulfur Chemistry, 34:1-2, 79-87

To link to this article: http://dx.doi.org/10.1080/17415993.2012.719509

Journal of Sulfur Chemistry, 2013
Vol. 34, Nos. 1–2, 79–87, http://dx.doi.org/10.1080/17415993.2012.719509

SHORT COMMUNICATION

The base-mediated cyclization of selected benzyl alkynyl sulfones with aromatic aldehydes: novel synthetic access to aryl-substituted 5,6-dihydro-1,4-oxathiin *S*,*S*-dioxides

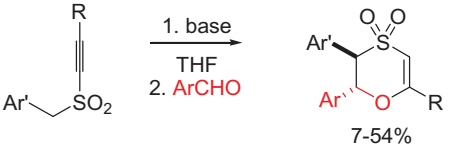
Lilly U. Ho, Mohanad Gh. Shkoor, M. Selim Hossain, Matthew C. Deen, Dmitriy V. Soldatov[†] and Adrian L. Schwan*

Department of Chemistry, University of Guelph, Guelph, ON, Canada N1G 2W1

(*Received 10 July 2012; final version received 6 August 2012*)

On the occasion of his 70th birthday, this paper is dedicated to Professor Eric Block, a valued mentor and a recognized leader in the international sulfur community.

Based on an unexpected product isolated during the LDA-mediated intramolecular cyclization of a benzyl alkynyl sulfones, a conceptually new cyclization method for the formation of 5,6-dihydro-1,4-oxathiin *S*,S-dioxides is demonstrated. The reaction affords products with (het)aryl groups at the 5- and 6-positions in 7–54% yield.



Keywords: sulfone; cyclization; 1,4-oxathiin *S*,*S*-dioxides; base-mediated; alkyne

1. Introduction

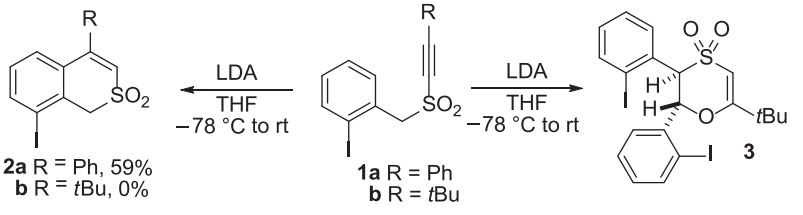
In a previous publication, the Schwan group introduced the LDA-mediated intramolecular cyclization of selected benzyl alkyl sulfones (*1*). In that communication, we indicated that either direct or indirect formation of a carbanion at the benzylic position brought about a new mode for the formation of 1*H*-2-benzothiopyran *S*,*S*-dioxides (isothiochroman 2,2-dioxides) (*2*). The cyclization has similarities and differences compared to established anionic cyclizations involving the dearomatization of aryl sulfones (*3–7*).

Herein, we introduce a recently discovered product from an intramolecular cyclization attempt and demonstrate, on a proof-of-principle basis, that one of the possible reactions involved in its formation can serve as an inspiration for the preparation of 5,6-dihydro-1,4-oxathiin *S*, *S*-dioxides.

*Corresponding author. Email: schwan@uoguelph.ca
[†]Author to whom correspondence regarding the X-ray analysis should be directed: Email: dsoldato@uoguelph.ca.

2. Results and discussion

While pursuing the scope of the aforementioned intramolecular cyclization chemistry of benzyl alkyl sulfones, it was discovered that cyclization was severely hindered by placement of a *t*-butyl group on the alkyne opposite the sulfone (*1*). Whereas **2a** could be formed in 59% yield by cyclization, compound **2b** was not observed at all. The reaction mixture did, however, yield a different and unexpected compound as a major product (Scheme 1).



Scheme 1. Divergent directions of benzyl alkynyl sulfone cyclizations.

That main product, eventually identified as **3**, was isolated and purified and a single-crystal X-ray diffraction study was conducted to confirm the molecular structure and elucidate the molecular geometry. The study revealed two crystallographically different, but chemically identical molecules of **3** in the crystal structure (referred to as molecules **3A** and **3B** further in the text). Molecule **3A** is shown in Figure 1. The distances S1A–C1A (1.806(8) Å), C1A–C2A (1.55(1) Å), C2A–O3A (1.457(9) Å), O3A–C3A (1.342(9) Å), C3A–C4A (1.36(1) Å) and C4A–S1A (1.713(9) Å) are within the expected range and confirm the double character of the C3A–C4A bond. The corresponding distances in the molecule **3B** are 1.801(8), 1.54(1), 1.445(9), 1.351(9), 1.34(1) and 1.719(9) Å. Two crystal structures showing the same six-membered ring fragment with the sulfone group and the adjacent double bond have been reported previously (*8, 9*). The overall geometry of the ring is similar in these structures. In the 3,3,5,6-tetraphenyl-2-one derivative (*8*), the S–C(sp^3), C(sp^3)–C(sp^3), C(sp^3)–O, O–C(sp^2), C(sp^2)–C(sp^2) and C(sp^2)–S distances are

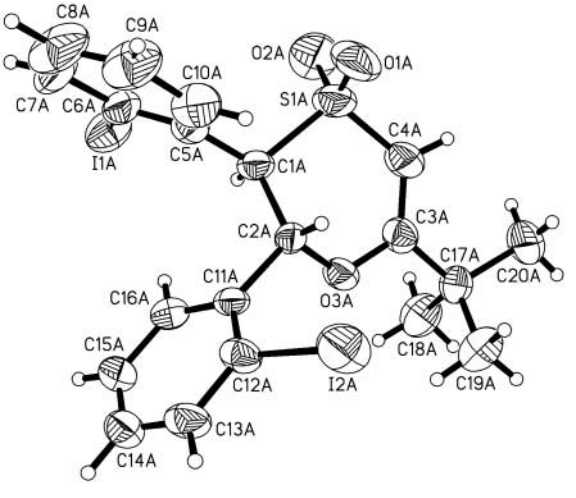
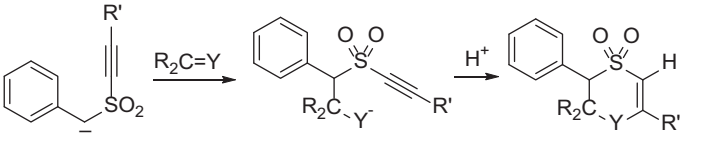


Figure 1. ORTEP view of molecule **3A** as found in the crystal structure of **3**. The thermal ellipsoids are at the 50% probability level.

1.838(6), 1.541(8), 1.364(7), 1.383(7), 1.341(8) and 1.761(6) Å, respectively. The corresponding distances for another structure, systemic fungicide oxycarboxin (*9*), are 1.761(4), 1.509(5), 1.432(5), 1.346(5), 1.357(5) and 1.754(4) Å. As expected, the sulfone S atom and the O atom of the ring are coplanar with the C=C double bond in **3** (within 0.005 Å), while the two C(sp^3) atoms deviate from the plane by 0.3–0.5 Å. The conformational geometry of the molecule is quite rigid: the dihedral angles between the least-squares plane of the S-containing ring and the phenyl rings C5A–C10A and C11A–C16A are 89.6(2)°and 69.1(3)°, respectively, while the corresponding angles in molecule B are 88.1(3)°and 67.9(3)°. The arrangement of the molecules in the crystal is consistent with van der Waals type of packing and the only found short intermolecular contact is between I2A and I2B of 3.8 Å.

The mode of formation of heterocycle **3** presumably follows the principles of Scheme 2, where $R_2C{=}Y$ is *o*-iodobenzaldehyde. Whereas the mechanism for the apparent *in situ* formation of the aldehyde from **1b** in the reaction mixture is still under investigation, the proposed mode of formation of **3** provided the impetus to evaluate the chemistry of Scheme 2 directly. The chemistry would provide a facile synthetic access to the 5,6-dihydro-1,4-oxathiin *S*,*S*-dioxide (Y=O). The oxathiin *S*,S-dioxide heterocyclic core is central to a well-recognized family of fungicides (*10–12*). Whereas a variety of synthetic approaches to the ring system are documented (*10, 13–16*), generally applicable methodologies are rare, as are accesses to substrates with multiple aryl substituents (*14*).

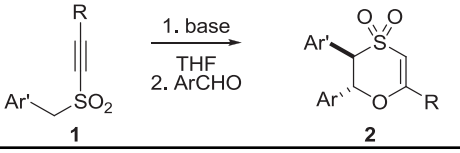


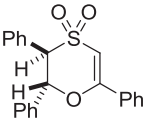
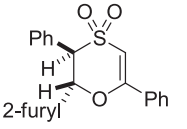
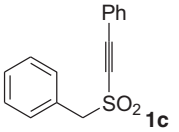
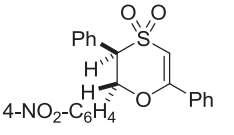
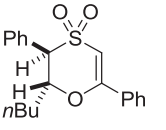
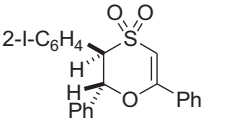
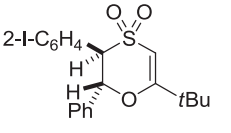
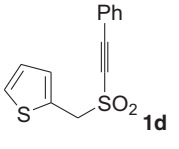
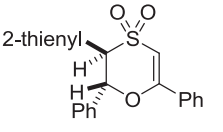
Scheme 2. Proposed formation of sulfone-containing heterocycles.

The premise of Scheme 2 forms the model for a conceptually new preparation of 5,6-dihydro-1,4-oxathiin *S*,*S*-dioxides and this chemistry was pursued by our group. Specifically, compounds of type **1b** were deprotonated and an aldehyde was then introduced to effect electrophilic capture and subsequent intramolecular conjugate addition to the triple bond. The key to establishing the chemistry is to intercept the benzyl anion prior to its intramolecular cyclization or competitive polymerization (*1*). Several experiments were carried out at temperatures below −10°C in order to probe incorporation of aldehyde. For several reaction temperatures, a cyclization product was observed, but the mixture still contained significant starting material. Eventually, the selected conditions involved the exposure of sulfones **1** in THF to base (LDA or *n*BuLi, *vide infra*) at −35°C for 2 h. Introduction of the aldehyde in THF was followed by stirring overnight at −35°C, followed by aq. acid quench at the same temperature. Under these conditions, the amount of starting sulfone **1** that typically remained was 0–40%.

Products **4** were isolated after multiple flash chromatographies and were typically characterized by diagnostic peaks in the proton NMR. Specifically, the lone vinylic proton was evident as a sharp singlet in the 5.85–6.46 ppm range. The two lone methine protons appeared each as doublets in the 5.81–6.38 and 4.81–5.57 ppm regions of the ^{1}H NMR spectrum. Their ^{1}H–^{1}H coupling constant was typically in the 11.4–11.7 Hz range, in keeping with that observed for **3** (11.4 Hz). Indeed the H−C−C−H dihedral angle of the trans-disposed protons of the oxathiin ring skeleton established by the X-ray crystal structure analysis [168.2(7)°(**3A**) and 170.2(7)°(**3B**)] are consistent with the large ^{1}H–^{1}H coupling constant according to the Karplus curve. Thus, the 5,6-(het)aryl groups of all cyclization products **4a–c**, **e–g** possessed the *trans*-stereochemistry.

Table 1. Formation of 5,6-dihydro-1,4-oxathiin *S*,*S*-dioxides (**2**) by reaction of alkynyl sulfones **1** with aldehydes.



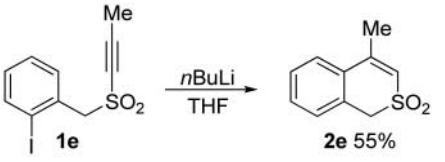
	Starting sulfone	Aldehyde/base	5,6-dihydro-1,4-oxathiin *S*,*S*-dioxide	% Yield[a]
1		Benzaldehyde/*n*BuLi	**4a**: 	54 (57)
2		Furfural/*n*BuLi	**4b**: 	19 (22)
3	 **1c**	4-Nitro-benzaldehyde/*n*BuLi	**4c**: 	7[b]
4		*n*−Butyraldehyde/*n*BuLi	**4d**: 	0[c]
5	**1a**	Benzaldehyde/LDA	**4e**: 	11
7	**1b**	Benzaldehyde/LDA	**4f**: 	25 (37)
8	 **1d**	Benzaldehyde/*n*BuLi	**4g**: 	25[d]

Notes: [a]Isolated yield is indicated. Yield in parenthesis indicates yield based on the consumed starting material.
[b]Low intensity peaks were observed in the ^{1}H NMR that could be attributable to a minor stereoisomer of **4c**.
[c]No cyclization product was obtained.
[d]Product could not be obtained in pure form. Yield is estimated from the ^{1}H NMR spectrum of the crude reaction mixture. See Section 5 for partial characterization of **4g**.

^{13}C NMR and IR spectroscopies and mass spectrometry data are also fully consistent with the assigned structures.

Judging by the outcome of the reactions, the identity of the base exhibited little influence on the chemical yield. *n*BuLi was the most convenient, but a control experiment indicated that

*n*BuLi prefers to react with an *o*-iodobenzyl substrate by way of lithium–halogen exchange, as evidenced by the intramolecular cyclization of **1e** to **2e** (Scheme 3). Hence, *o*-iodobenzyl containing substrates **1a** and **1b** were treated with LDA.



Scheme 3. Intramolecular cyclization from chemoselective reaction of *n*BuLi with *o*-iodobenzyl sulfone **1e**.

Assuming equally effective benzyl anion formation with either LDA or *n*BuLi, the cyclization proceeded in poor to fair yields with a number of substrates (Table 1). NMR evidence suggests polymerization was competitive in a number of instances. Moreover, difficult separations also led to reduced yields. Since the optimized conditions for **4a** and benzaldehyde provided the best yield, it is possible that each of the other reactions requires a separate optimization assessment. Thienyl containing substrate **4d** reacted with benzaldehyde only in low yield; the product (**4g**) could not be obtained pure, but diagnostic NMR and MS data indicated some cyclization occurred. The reaction proved unsuitable for aliphatic aldehydes (Table 1, Entry 4). The reaction is also not amenable to replacement of the aromatic aldehydes with carbon disulfide (Scheme 2, $R_2C{=}Y = S{=}C{=}S$), an *N*-phenyl aldimine (Scheme 2, $R_2C{=}Y = PhCH{=}NPh$) or phenyl isothiocyanate (Scheme 2, $R_2C{=}Y = PhNCS$): no 1,4-dithiin or 1,4-thiazine based heterocycles were obtained in those trials. In the latter instance, with sulfone **1c** as the starting substrate, only after warming the product of fully intramolecular cyclization was observed.

3. Conclusion

The chemistry of this communication successfully demonstrates the principle that the benzyl anion derived from selected benzyl alkynyl sulfones can be captured with aromatic aldehydes for the eventual formation of 5,6-di(het)aryl-5,6-dihydro-1,4-oxathiin *S*,*S*-dioxides, albeit in poor to fair yields. Clearly, additional optimization is required to increase the yields, and there is potential for cyclization with catalytic base. The chemistry suggests that the inclusion of an aldehyde unit may be a component of the mechanism leading to the unexpected formation of a 5,6-di-(2-iodophenyl)-5,6-dihydro-1,4-oxathiin *S*,*S*-dioxide (**3**) when *o*-iodobenzyl 3,3-dimethylbutynyl sulfone (**1b**) was treated with base.

4. Experimental

Flash column chromatography was performed with silica gel particle size 30–63 (mesh 230–400) supplied by Silicycle®. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 300 (300 MHz ^{1}H), a Bruker Avance 400 (400 MHz ^{1}H, 100.6 MHz ^{13}C) or a Bruker Avance 600 (600 MHz ^{1}H, 150.9 MHz ^{13}C). High-resolution mass spectrometry was carried out using a Q-TOF micro (Waters, Cambridge, MA, USA). Samples were infused at a concentration of approximately 10 μM in 9:1 acetonitrile:water with 0.1 mM ammonium acetate at a flow rate of 5 μL/min through an ESI source in positive ionization mode with a spray voltage of 3700 V.

Gentle source conditions including a cone voltage of 20 V and a collision cell voltage of 8 V were used with N_2 nebulizer (300 l/h) and cone (30 l/h) gas. External mass calibration was carried out using [Glu^1]-Fibrinopeptide.

4.1. *Formation of 1,4-oxathiin S,S-dioxide 3*

Freshly prepared LDA (1.00 equiv.) in THF was slowly added to a solution of 2-iodobenzyl-3,3-dimethyl-1-butynyl sulfone (**1b** [R = *t*Bu], 0.500 g, 1.38 mmol) (0.05 M concentration of substrate, 27.60 ml of THF) at −78°C. The cold bath was removed and the reaction mixture was permitted to warm to rt for overnight. The mixture was quenched with saturated aqueous NH_4Cl. The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 10 ml). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. After flash chromatography (hexanes and EtOAc) and recrystallization (hexanes and EtOAc), 0.201 g of **3** was isolated (68% based on the recovery of 0.139 g of the starting material). Mp: 184–185°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ: 7.77 (m, 2H), 7.46 (dd, J = 1.5 and 7.9 Hz, 1H), 7.37 (dd, J = 1.6 and 7.9 Hz, 1H), 7.31–7.22 (m, 2H), 6.97–6.89 (m, 2H), 6.38 (d, J = 11.4 Hz, 1H), 5.93 (s, 1H), 5.51 (d, J = 11.4 Hz, 1H), 1.18 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ: 171.14, 140.15, 139.87, 137.15, 131.44, 131.11, 130.68, 129.30, 128.82, 128.75, 128.21, 103.87, 101.38, 100.36, 85.96, 69.47, 37.21, 27.41. IR (neat, ν_{max}): 2969, 1608, 1471, 1305, 1136, 1101, 1013, 911 cm^{-1}. ESI HRMS, calculated for $[C_{20}H_{20}SO_3I_2+H]^+$: 594.9296; found: 594.9374.

4.2. *X-ray analysis of 3*

A crystal of **3** (thin colorless sheet, 0.4 × 0.2 × 0.01 mm) was selected from a bulk product obtained by crystallization from ethyl acetate–hexane. The crystal was mounted on the tip of a glass fiber and studied at room temperature on a SuperNova Agilent single-crystal X-ray diffractometer equipped with a microfocus CuK_α (λ = 1.54184 Å) radiation source and Atlas CCD detector. Diffraction intensity data were collected using ω-scan to the maximum 2θ angle of 130° (resolution of 0.85 Å), with the redundancy factor of 4. The unit cell parameters were refined using the entire data set.

The data were processed using CrysAlisPro software (*17*). Absorption corrections were applied using the multiscan method. Since the crystal was very thin (<0.01 mm) and displayed lower quality data, the SADABS software (*18*) was used to introduce the absorption correction through a special treatment procedure for plate-like crystals (face {010}, min glancing angle 5°). The structure was solved (direct methods) and refined (full-matrix least-squares on F^2) using SIR-92 (*19*) and SHELXL-97 (*20*). Non-hydrogen atoms were refined anisotropically, while hydrogen atoms were introduced at calculated positions as riding on their corresponding carbon atoms and refined isotropically. All significant residual extrema on the final electron density map were located near the iodine atoms. Geometric calculations were carried out using the WinGX (*21*) and Olex (*22*) software packages and molecular graphics was prepared using ORTEP-3 for Windows (*23*).

Crystal data: $C_{20}H_{20}I_2O_3S$, formula weight 594.22; temperature of study 293(2) K; triclinic, $P-1$; a = 10.347(1), b = 12.185(1), c = 17.087(2) Å; α = 95.87(2)°, β = 90.05(2)°, γ = 101.89(2)°; V = 2096.5(4) Å^3; Z = 4; D_{calc} = 1.883 g/cm^3; μ (CuK_α) = 24.63 mm^{-1}; $F(000)$ = 1144 e; reflections collected/unique 23565/6932 (R_{int} = 0.058); refinement of 476 parameters with full-matrix least-squares on F^2; final R indices [5393 data with $I > 2\sigma_I$] R_1 = 0.074, wR_2 = 0.197; goodness-of-fit 1.097. Full crystallographic data including a CIF file have been deposited with the Cambridge Crystallographic Data Centre with the deposition number CCDC 886549 and can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif or by e-mail deposit@ccdc.cam.ac.uk.

4.3. *Preparation of sulfones 1*

Sulfones **1** were prepared from the corresponding sulfides (*1,24*) by oxidation. Compounds **1a–d** have been previously reported (*1*).

4.4. *General procedure for preparation of 1,4-oxathiin S,S-dioxides 4*

To a solution of starting sulfone in THF (1.0 equiv., 0.05 M) at −78°C, *n*BuLi (1.2 equiv., 1.6 M in hexanes) or LDA (1.2 equiv. in THF) was added dropwise. The mixture was allowed to warm up to −35°C and stirred for 2 h. A solution of the aldehyde in THF (2.0 equiv., 0.4 M) was added to the reaction mixture which was then left to stir at −35°C overnight. The reaction was quenched with sat. aq. NH_4Cl at −35°C, and the aq. layer was extracted with EtOAc (3 × 10 ml). The combined organic layers were washed with H_2O, brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Two to three flash chromatography separations on silica gel (EtOAc or ethyl ether/hexane: 5–15%:95–85%) gave pure product, unless otherwise noted.

4.4.1. *3,5,6-Triphenyl-5,6-dihydro-1,4-oxathiin S,S-dioxide **4a***

From sulfone **1c** and benzaldehyde, 1,4-oxathiin *S*,*S*-dioxide **4a** was obtained as a white solid, 54% yield; mp = 187–189°C (dec.). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.47–7.25 (m, 15H), 6.46 (s, 1H), 6.18 (d, J = 11.7 Hz, 1H), 4.81 (d, J = 11.7 Hz, 1H); ^{13}C NMR (150.9 MHz, $CDCl_3$), δ: 159.49, 134.92, 132.03, 131.52, 131.13, 129.47, 129.29, 128.79, 128.71, 128.64, 128.12, 126.38, 125.42, 101.37, 83.08, 67.96; IR (neat, ν_{max}): 3067, 1609, 1575, 1364, 1283, 1127, 1078, 910, 695 cm^{-1}; ESI HRMS, calculated for $[C_{22}H_{18}SO_3+H]^+$: 363.1050; found: 363.1066.

4.4.2. *3,6-Diphenyl-5-(2-furyl)-5,6-dihydro-1,4-oxathiin S,S-dioxide **4b***

From sulfone **1c** and furfural, 1,4-oxathiin *S*,*S*-dioxide **4b** was obtained as a white solid, 19% yield; mp = 144–146°C (dec.). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.63 (d, J = 7.8 Hz, 2H), 7.48–7.26 (m, 9H), 6.42 (s, 1H), 6.39 (s, 1H), 6.24, (d, J = 11.7 Hz, 1H), 6.23 (s, 1H), 4.96 (d, J = 11.7 Hz, 1H); ^{13}C NMR (150.9 MHz, $CDCl_3$), δ: 159.25, 147.37, 143.91, 131.94, 131.56, 130.72, 129.44, 128.44, 128.79, 128.63, 126.43, 125.20, 112.18, 110.49, 101.52, 65.61; IR (neat, ν_{max}): 3070, 1609, 1575, 1496, 1283, 1127, 1078 cm^{-1}; ESI HRMS, calculated for $[C_{20}H_{16}SO_4+H]^+$: 353.0843; found: 353.0878.

4.4.3. *3,6-Diphenyl-5-(4-nitrophenyl)-5,6-dihydro-1,4-oxathiin S,S-dioxide **4c***

From sulfone **1c** and 4-nitrobenzaldehyde, 1,4-oxathiin *S*,*S*-dioxide **4c** was obtained as a pale pink solid, 7% yield; mp = 213–215°C (dec.). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 8.14 (d, J = 8.8 Hz, 2H) 7.63 (d, J = 7.2 Hz, 2H), 7.55–7.28 (m, 10H), 6.52 (s, 1H), 6.31 (d, J = 11.6 Hz, 1H), 4.79 (d, J = 11.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 159.13, 148.30, 141.65, 131.80, 131.55, 130.92, 129.83, 129.02, 128.96, 128.92, 126.28, 124.73, 123.90, 102.02, 81.90, 67.82; IR (neat, ν_{max}): 3072, 1609, 1523, 1349, 1281, 1127, 1086 cm^{-1}; ESI HRMS, calculated for $[C_{22}H_{17}SO_5N+H]^+$: 408.0901; found: 408.0923. Low-intensity peaks were observed in the ^{1}H NMR that could be attributable to a minor stereoisomer of **4c**.

4.4.4. *3,5-Diphenyl-6-(2-iodophenyl)-5,6-dihydro-1,4-oxathiin S,S-dioxide* ***4e***

From sulfone **1a** and benzaldehyde, 1,4-oxathiin *S*,*S*-dioxide **4e** was obtained as a white solid, 11% yield. ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.71 (dd, $J = 8.0$, 1.0 Hz, 1H), 7.58 (d, $J = 7.4$ Hz, 2H), 7.46–7.02 (m, 11H), 6.85 (m, 1H), 6.39 (s, 1H), 6.07 (d, $J = 11.4$ Hz, 1H), 5.57 (d, $J = 11.4$ Hz, 1H); ^{13}C NMR (150.9 MHz, $CDCl_3$), δ: 159.48, 140.29, 134.34, 131.91, 131.56, 131.27, 130.69, 129,67, 129.38, 128.78, 128.67, 128.27, 128.06, 126.44, 104.48, 101.69, 83.94, 70.12; IR (neat, ν_{max}): 3068, 2931, 1609, 1575, 1495, 1451, 1307, 1283, 1120, 1078 cm^{-1}; ESI HRMS, calculated for $[C_{22}H_{17}SO_3I+H]^+$: 489.0016; found: 488.9979.

4.4.5. *3-(t-*Butyl*)-6-(2-iodophenyl)-5-phenyl-5,6-dihydro-1,4-oxathiin S,S-dioxide* ***4f***

From sulfone **1b** and benzaldehyde, 1,4-oxathiin *S*,*S*-dioxide **4f** was obtained as a white solid, 25% yield; mp = 180–182°C (dec.). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 7.66 (dd, $J = 8.4$, 1.2 Hz, 1H), 7.42 (dd, $J = 8.1$, 1.8 Hz, 1H), 7.20–7.17 (m, 6H), 6.82 (dt, $J = 7.8$, 1.2 Hz, 1H), 5.85 (s, 1H), 5.81 (d, $J = 11.5$ Hz, 1H), 5.19 (d, $J = 11.5$ Hz, 1H), 1.12 (s, 9H); ^{13}C NMR (150.9 MHz, $CDCl_3$), δ: 171.40, 140.25, 134.62, 131.14, 130.62, 129.52, 129.48, 128.56, 128.03, 127.98, 104.45, 100.08, 83.45, 69.75, 37.27, 27.48; IR (neat, ν_{max}): 2967, 1608, 1468, 1305, 1287, 1218, 1136, 1103 cm^{-1}; ESI HRMS, calculated for $[C_{20}H_{21}SO_3I+H]^+$: 469.0329; found: 469.0310.

4.4.6. *3,5-Diphenyl-6-(2-thienyl)-5,6-dihydro-1,4-oxathiin S,S-dioxide* ***4g***

From sulfone **1d** and benzaldehyde, 1,4-oxathiin *S*,*S*-dioxide **4g** was obtained in impure form in low yield. Estimated chemical yield: 25%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: (partial spectrum) 6.45 (s, 1H), 6.02 (d, $J = 11.7$ Hz, 1H), 5.08 (d, $J = 11.7$ Hz, 1H); ESI HRMS, calculated for $[C_{20}H_{16}S_2O_3+H]^+$: 369.0614; found: 369.0628.

4.5. *Intramolecular cyclization of sulfone 1e.*

*n*BuLi (1.0 equiv., 1.83 mmol) in THF was slowly added to a solution of sulfone **1e** (0.750 g, 1.83 mmol) in THF (15 ml) at −78°C. The cold bath was removed and the reaction mixture was permitted to warm to rt over 45 min. The mixture was quenched with saturated aqueous NH_4Cl. The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 5 ml). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The product was purified by flash chromatography (hexanes/EtOAc) followed by recrystallization from hexanes/EtOAc to give cyclic sulfone **2e** (0.250 g, 1.28 mmol, 55%) as white crystals. mp: 99–100°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ: 7.54 (d, $J = 8.7$ Hz, 1H, Ar H), 7.45–7.36 (m, 2H, Ar H), 7.28 (d, $J = 6.9$ Hz, 1H, Ar H), 6.52 (s, 1H, CH), 4.35 (s, 2H, CH_2), 2.32 (s, 3H, CH_3). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ: 146.26, 130.57, 130.23, 130.03, 129.09, 128.66, 126.35, 124.58, 54.73, 21.15. IR (neat, ν_{max}): 3019, 2922, 1586, 1537, 1483, 1314, 1127, 941 cm^{-1}. ESI HRMS, calculated for $[C_{10}H_{10}SO_2+H]^+$: 195.0475; found: 195.0454.

Acknowledgements

The authors are grateful to NSERC of Canada and the University of Guelph for funding in support of this research and for funding to M.C.D. for a USRA scholarship. D.V.S. thanks CFI (Canada) and MRI (Ontario) for providing funds for the X-ray diffraction instrumentation. M.Gh.S. thanks the Ontario MRI PDF Program for providing partial postdoctoral support.

References

(1) Hossain, M.S.; Schwan, A.L. *Org. Lett.* **2011,** *13,* 5330–5333.
(2) Shyshkina, O.O.; Tkachuk, T.M.; Volovnenko, T.A.; Volovenko, Y.M.; Zubatyuk, R.I.; Medviediev, V.V.; Shishkin, O.V. *Tetrahedron Lett.* **2012,** *53,* 4296–4299.
(3) Lopez Ortiz, F.; Iglesias, M.J.; Fernandez, I.; Andujar Sanchez, C.M.; Ruiz Gomez, G. *Chem. Rev.* **2007,** *107,* 1580–1691.
(4) Clayden, J.; Kenworthy, M.N. *Synthesis* **2004,** 1721–1736.
(5) Clayden, J.; Kenworthy, M.N.; Helliwell, M. *Org. Lett.* **2003,** *5,* 831–834.
(6) Padwa, A.; Filipkowski, M.A.; Kline, D.N.; Murphree, S.S.; Yeske, P.E. *J. Org. Chem.* **1993,** *58,* 2061–2067.
(7) Crandall, J.K.; Ayers, T.A. *J. Org. Chem.* **1992,** *57,* 2993–2995.
(8) Yasuoka, N.; Kasai, N; Tanaka, M.; Nagai, T.; Tokura, N. *Acta Crystallogr.* **1972,** *B28,* 3393–3399.
(9) Brown, J.E.; Baughman, R.G. *Acta Crystallogr.* **2010,** *E66,* o2654.
(10) Caputo, R.; Ferreri, C.; Guaragna, A.; Palumbo, G.; Pedatella, S. *J. Chem. Soc., Perkin Trans. 1* **1995,** 1971–1973.
(11) (a) Graham, B.A.; Puttock, M.A.; Felauer, E.E.; Neidermyer, R.W. DE2513202A1, 1975, Uniroyal, Inc., Can.; (b) Graham, B.A.; Puttock, M.A.; Felauer, E.E.; Neidermyer, R.W. US4043792A, 1977, Uniroyal, Inc., USA.
(12) Ulrich, J.T.: Mathre, D.E. *J. Bacteriol.* **1972,** *110,* 628–632.
(13) Nguyen, V.-H.; Nishino, H.; Kajikawa, S.; Kurosawa, K. *Tetrahedron* **1998,** *54,* 11445–11460.
(14) (a) Capozzi, G.; Fratini, P.; Menichetti, S.; Nativi, C. *Tetrahedron Lett.* **1995,** *36,* 5089–5092. (b) Capozzi, G.; Fratini, P.; Menichetti, S.; Nativi, C. *Tetrahedron* **1996,** *52,* 12233–12246.
(15) Arya, V.P.; Shenoy, M.S.J.; Gokhale, N.G. *Indian J. Chem., Sect. B* **1977,** *15,* 67–69.
(16) Bandera, Y.P.; Emets, S.V.; Timoshenko, V.M.; Shermolovich, Y.G. *Ukr. Khim. Zh. (Russ. Ed.)* **2005,** *71,* 105–113.
(17) *Agilent Technologies*, version 1.171.35.8; Xcalibur CCD system, CrysAlisPro software system; 2011.
(18) Sheldrick, G.M. SADABS; University of Göttingen, Germany, 1996.
(19) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Gualardi, A. *J. Appl. Crystallogr.* **1993,** *26,* 343–350.
(20) Sheldrick, G.M. SHELXL-97, Program for refinement of crystal structures; University of Göttingen, Germany, 1997.
(21) Farrugia, L.J. *J. Appl. Crystallogr.* **1999,** *32,* 837–838.
(22) Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. *J. Appl. Crystallogr.* **2009,** *42,* 339–341.
(23) Farrugia, L.J. *J. Appl. Crystallogr.* **1997,** *30,* 565.
(24) Motto, J.M.; Castillo, A.; Greer, A.; Montemayer, L.K.; Sheepwash, E.E.; Schwan, A.L. *Tetrahedron* **2011,** *67,* 1002–1010.