Copper-Catalyzed Oxyalkynylation of C–S Bonds in Thiiranes and Thiethanes with Hypervalent Iodine Reagents

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S Supporting Information

ABSTRACT: We report the oxyalkynylation of thiiranes and thietanes using ethynylbenziodoxolone reagents (EBXs) to readily access functionalized building blocks bearing an alkyne, a benzoate, and an iodide group. The reaction proceeds with high atom efficiency most likely through an alkynyl–episulfonium intermediate. The transformation is copper-catalyzed and compatible with a large array of thiiranes and thietanes.

Strain-promoted ring opening of small saturated heterocycles (three- and four-membered rings) is an attractive way to access 1,2- or 1,3-functionalized building blocks. This approach has been thoroughly investigated for oxygen and nitrogen heterocycles including epoxides,¹ aziridines,² and oxetanes.³ In comparison, this strategy has been less explored for the sulfur analogues, thiiranes^{1,4} and thietanes,⁵ despite the importance of sulfur-containing molecules.⁶ The more reactive thiiranium ion is a well-described intermediate and has been recently involved in the development of highly enantioselective transformations.⁷ Its formation often relies on the reaction of alkenes with an electrophilic sulfur source or the nucleophilic substitution of a leaving group next to a thioether (Scheme 1a). Their generation by reaction of an electrophile with the sulfur atom is unusual.^{7a,b} A few recent reports explored this method of activation either by alkylation for a subsequent ring expansion⁸ or by arylation to induce a ring opening.⁹

In contrast, the generation of a noncyclic sulfonium ion by alkylation of thioethers is a well-known method.^{7b,10} To the best of our knowledge, only one report published by Ochiai and co-workers presented their formation by alkynylation (Scheme 1b).¹¹ Ethynyliodonium salts were used to synthesize alkynyl-(diphenyl)sulfonium salts. When thioanisole (**1**) was alkynylated with iodonium **2**, sulfonium intermediate **A** reacted with an excess of **1** to give thioalkyne **4**. Later, a mild and selective protocol for the formation of thioalkynes was proposed by our group using thiols and ethynylbenziodoxolones (EBX).¹² Iodonium salts were not suitable for this transformation, as they led to the formation of disulfides. Considering the high sulfur affinity of hypervalent iodine reagents, we anticipated that

they could be used for the generation of an alkynylated episulfonium intermediate from the corresponding thiirane (Scheme 1c).

EBX reagents were expected to be superior in this reaction, as their activation using metal catalysis is well-established¹³ and the released benzoate **5** can act directly as a nucleophile for the formed episulfonium, resulting in a highly atom-economical process.¹⁴ The obtained β -hydroxy sulfide motif is found in a large array of bioactive molecules¹⁵ and is mostly accessed by epoxide ring opening. The reverse approach exploiting thiirane chemistry has been less developed,¹⁶ except for the acetolysis of carbohydrate bearing a thiirane at the C₅–C₆ position.¹⁷

Herein, we report the successful copper-catalyzed oxyalkynylation of thiiranes using EBX reagents. The reaction probably proceeds through the formation of an episulfonium intermediate and furnishes the desired β -hydroxy sulfides in moderate to good yields using operationally simple conditions. The methodology was also applied to the ring opening of thietanes to access 1,3-difunctionalized products.

We started our investigation by optimizing the reaction conditions using TIPS-EBX (**6a**) and the commercially available cyclohexene sulfide (**7a**) as a model substrate (Table 1; see Supporting Information for a full list of tested reaction conditions, Table S1). No product was observed in the absence of catalyst or in the presence of TMSCl as Lewis acid (entries 1 and 2). However, we were pleased to see that addition of a catalytic amount of Cu(CH₃CN)₄BF₄ afforded the desired

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Scheme 1. Strategies Exploiting Thiiranium and Sulfonium Ions for C–S Bond Activation

a) Formation of a thiiranium ion: current strategies

b) Previous work by Ochiai: alkylation of thioanisole (1) using iodonium salts¹¹

c) This work: Cu-catalyzed oxy-alkynylation of thiiranes with EBX reagents

Table 1. Optimization of the Oxyalkynylation^a

entry	catalyst	solvent	T (°C)	time (h)	yield (%) ^b
1	none	THF	70	24	traces
2 ^c	TMSCl	THF	30	4	not observed
3	Cu(CH ₃ CN) ₄ BF ₄	THF	rt	24	53
4	Cu(CH ₃ CN) ₄ BF ₄	DCE	rt	24	66
5	Cu(CH ₃ CN) ₄ BF ₄	DCE	50	1.5	65
6 ^d	Cu(CH ₃ CN) ₄ BF ₄	DCE	100	0.5	67
7	Cu(OTf) ₂	DCE	50	1.5	66

^aReaction conditions: TIPS-EBX (6a) (0.1 mmol), cyclohexene sulfide (7a) (0.15 mmol), catalyst (10 mol %), solvent (0.07 M), reactions were carried out under N₂ atmosphere. ^bIsolated yield. ^c1 equiv of TMSCl was used. ^dReaction was performed under microwave irradiation.

product 8a in 53% yield as a single diastereoisomer (entry 3). The relative *trans* configuration was confirmed by X-ray crystallography. Different solvents were screened: replacing THF with DCE increased the yield to 66% (entry 4). Working at higher temperatures resulted in a significant lower reaction time with no influence on the yield (entries 4–6). Next, we examined a range of copper catalysts (see Supporting Information). A similar yield was obtained only when Cu(OTf)₂ was used (entry 7). Oligomers containing multiple cyclohexyl sulfide motifs were identified as byproducts of the reaction. To reduce this side reactivity different concentrations, stoichiometries of 6a/7a and copper loadings were examined (see Table S2 for details), but the reaction yield was constantly between 45 and 65%.¹⁸

With the optimized conditions in hand (entry 5), we first investigated a range of structurally diverse thiiranes (Scheme 2). Using cyclopentene sulfide allowed the synthesis of 8b in a slightly improved yield. Incorporation of an oxygen or a protected nitrogen atom in the ring afforded 8c and 8d in good and moderate yield, respectively. Simple ethylene sulfide 6e provided a lower yield of 8e (46%). However, this result has to be put in perspective with the known tendency of 7e to polymerize, as well as its low boiling point (55 °C).¹⁹ When the reaction was performed with unsymmetrical propylene sulfide, 8f was obtained as a mixture of regioisomers (2.1:1 rr), the major one resulting from the attack of the carboxylate at the most substituted position. A similar outcome was observed with a longer alkyl chain (product 8g). Using the disubstituted analogue 7h led to a significant improvement of the regioselectivity (15.5:1 rr), although with a diminished yield of 8h. When the reaction was run with the enantioenriched substrate 7i, it afforded 8i with full conservation of the ee for both regioisomers. In this case, we were surprised to observe an inversion of regioselectivity. We hypothesize that it could be due to the inductive effect of the nearby oxygen. The synthesis of 8j incorporating two protected alcohols was achieved in a lower yield.

Next, we examined different hypervalent iodine reagents. Substitution of the TIPS group by aryl substituents was well-tolerated and showed little impact on the reaction (8k–m). Alkyl-EBX gave also good results (8n–o). A lower yield was observed for 8p, and decreasing the temperature furnished a slightly better result. Modification of the iodobenzoic acid core with a methoxy, a nitro, or a fused benzene ring allowed the synthesis of products 8q–s in good yields. Importantly, vinylbenziodoxolone reagents (VBX) could be used successfully in the transformation, providing the oxyvinylated products 8t–u in promising yields without further optimization.

We next examined the transformation of the less strained thietane heterocycles (Scheme 3). We were pleased to see that simple thiacyclobutane (9a) reacted under similar reaction conditions to deliver 1,3-functionalized thioalcohol 10a in moderate yield. Introduction of a phenyl group at the 3-position of the thiacyclobutane did not affect the transformation (product 10b). Spirocyclic substrates 9c and 9d gave improved yields of products 10c and 10d and demonstrated the selectivity of the reaction for sulfur heterocycles. Considering the good results obtained with four-membered rings, the reaction of tetrahydrothiophene (9e) was examined next. At higher temperature (100 °C), we could obtain the 1,4-functionalized thioalcohol 10e in moderate yield.

To highlight the synthetic utility of our method, further functionalizations of 8a were performed (Scheme 4a). We first focused on the reactivity of the iodobenzoate ester: Sonogashira cross-coupling with the iodine afforded 11 in good yield, and the saponification of the iodobenzoic ester allowed the synthesis of the free alcohol 12. Next, we turned our attention toward the thioalkyne function. A sequence of TIPS deprotection followed by copper-catalyzed alkyne–azide cycloaddition afforded triazole 14 in excellent yield. A scale-up reaction (2 mmol) was then carried out using Ph-EBX (6k) and cyclohexene sulfide (7a) (Scheme 4b). The reaction gave a similar yield at this scale. The synthesized phenyl thioalkyne 8k was hydrated to afford thioester 15 in good yield.

A series of experiments were carried out to gain more insight into the reaction mechanism (Scheme 5). We first attempted the ring opening of cyclohexene sulfide (7a) in the presence of a

Scheme 2. Scope of the Oxyakynylation with Thiiranes and HIRs*

*The major regioisomer is drawn; rr = regioselectivity ratio. Reaction was carried out on 0.2 mmol scale. ^aReaction was heated to 70 °C. ^bReaction was stirred at rt.

Scheme 3. Scope Extension to Thietanes and Tetrahydrothiophene*

*Reactions were carried out on 0.2 mmol scale. ^aThe reaction mixture was heated to 100 °C under microwave irradiation.

copper catalyst and sodium benzoate or benzoic acid (Scheme 5, eq 1). No product formation was observed after 3 days, highlighting the importance of the hypervalent iodine reagents for thiirane activation. We applied our standard conditions to cyclohexene oxide (17) (eq 2). Even if epoxides are more prone to a ring-opening reaction due to their higher ring strain,^{4b} no trace of product 18 was observed. This result confirmed the selectivity of the transformation for sulfur heterocycles. The reaction was attempted using iodonium salt 6v instead of EBX (eq 3). When cesium benzoate or benzoic acid was added to

Scheme 4. Product Modifications

^aConditions: (a) 8a (1.0 equiv), 2-ethynylnaphthalene (2.0 equiv), Pd(PPh₃)₂Cl₂ (10 mol %), CuI (20 mol %), Et₃N (30 mM), 40 °C, 2.5 h; (b) 8a (1.0 equiv), K₂CO₃ (2.5 equiv), EtOH (0.1 M), 45 °C, 30 h; (c) 8a (1.0 equiv), TBAF (1.2 equiv), THF (80 mM), 0 °C, 1 h; (d) 13 (1.0 equiv), BnN₃ (1.2 equiv), Cu(H₂O)₅SO₄ (10 mol %), sodium ascorbate (20 mol %), CHCl₃/H₂O 15:1 (60 mM), rt, 24 h; (e) 8k (1.0 equiv), PTSA (1.0 equiv), SiO₂ (15.0 equiv), CH₂Cl₂ (0.2 M), 40 °C, 24 h.

replace the missing nucleophile, the desired product was formed only in trace amounts. The addition of a radical scavenger led to the formation of the desired product 8a with a decreased yield (eq 4). No TEMPO adducts were detected. Nevertheless, a radical pathway cannot be excluded at this stage, as such intermediates may be too unstable to be isolated.

Scheme 5. Additional Experiments for Mechanism Elucidation

Considering the successful ring opening of nonstrained tetrahydrothiophene (Scheme 3, 10e), we wondered if non-cyclic thioethers could be cleaved using our method. We were pleased to see that dibenzyl sulfide **20** reacted to afford the corresponding thioalkyne **21a** and benzyl ester **21b** in moderate yields at 100 °C (eq 5). A competitive experiment was carried out with **6k** and **6q** possessing different alkynes and iodobenzoic cores (eq 6). In total, four different products were isolated: the expected products **8k** and **8q** and the crossover products **8a** and **8v** bearing one functional group from each reagent. This showed that external addition can occur but is less favored (~1:2 ratio). Indeed, when the reaction was performed in the presence of an excess of methanol, ether product **8w** could be obtained in 16% yield together with 46% of **8a** (eq 7).²⁰

Based on these results, we propose a possible reaction mechanism in Scheme 6. First, the copper(I) catalyst activates EBX reagent **6**. Two different modes of activation could be envisaged: formation of the iodonium salt **II** or oxidative transfer to generate the copper(III) complex **III**.²¹ In the former case, activated iodonium salt **II** would react directly with cyclohexene sulfide (**7a**) to give sulfonium **IV**. Both a concerted α -addition–elimination or a β -addition/ α -elimination/1,2-shift pathway could be considered.²² In the latter case, coordination of the copper(III) center followed by reductive elimination would lead to sulfonium **IV**.²³ At this stage, exchange of carboxylates could happen. Sulfonium **IV** then undergoes a ring opening by

Scheme 6. Proposed Speculative Mechanism

nucleophilic attack of the copper carboxylate, affording the desired product **8** and regenerating the initial copper catalyst **I**. The product formed has a relative *trans* configuration resulting from a $\text{S}_\text{N}2$ attack of the carboxylate.

In summary, we have described an atom-efficient copper-catalyzed ring opening of thiiranes and thietanes through the use of hypervalent iodine reagents. The transformation works with different cheap copper sources at a broad range of concentrations and temperatures. In the case of unsymmetrical episulfides, the product resulting from the addition on the carbon-bearing substituents stabilizing better a partial positive charge was observed. Based on the relevant literature and our control experiments, we propose a speculative reaction mechanism involving formation of an episulfonium intermediate for C–S bond activation.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.orglett.9b04157>.

Experimental procedures and analytical data for all new compounds (PDF)

Accession Codes

CCDC 1962904 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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Supporting Information for

Copper-Catalyzed Oxy-Alkynylation of C-S Bonds in Thiiranes and Thiethanes with Hypervalent Iodine Reagents

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1. General Methods

All reactions were carried out under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et₂O, CH₃CN, toluene, hexane and CH₂Cl₂ were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 10 ppm, Karl-Fischer titration). All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Fluorochem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Silicycle silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Pre-coated TLC sheets ALUGRAM[®] Xtra SIL G/UV₂₅₄ and visualized with UV light and potassium permanganate or *p*-anisaldehyde stain. ¹H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d. All signals are reported in ppm with the internal chloroform signal at 7.26 ppm. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, bs = broad signal, coupling constant(s) in Hz, integration, assignment). ¹³C-NMR spectra were recorded with {1H} decoupling on a Bruker DPX-400 101 MHz spectrometer in chloroform-d unless otherwise stated. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm as standard unless otherwise stated. Infrared spectra were recorded on a JASCO FT-IR B4100 or a Bruker Alpha-P spectrophotometer with an ATR device and a ZnSe prisma and are reported as cm⁻¹ (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) QTOF. HPLC measurements were done on a Agilent 1260 Infinity autosampler using a CHIRALPAK IBN or IC column from DAICEL Chemical. Samples were prepared in a 90/10 hexane/isopropanol mixture, before being submitted in chiral HPLC. Microwave reactions were run in a Biotage Initiator 2.0. Cyclohexene sulfide (85%, technical grade) was purchased from Sigma-Aldrich and purified by distillation prior to use.

2. Additional tables

Table S1. Initial optimization.^a

entry	catalyst	solvent	T (°C)	time (h)	isolated yield
1	None	THF	70	24	traces ^b
2 ^c	TMSCl	THF	30	4	not observed
3	Cu(CH ₃ CN) ₄ BF ₄	THF	rt	24	53
4	Cu(CH ₃ CN) ₄ BF ₄	NO ₂ Me	rt	24	56
5	Cu(CH ₃ CN) ₄ BF ₄	AcOEt	rt	24	49
6	Cu(CH ₃ CN) ₄ BF ₄	acetone	rt	24	56
7	Cu(CH ₃ CN) ₄ BF ₄	dioxane	rt	24	64
8	Cu(CH ₃ CN) ₄ BF ₄	toluene	rt	24	62
9	Cu(CH ₃ CN) ₄ BF ₄	DCE	rt	24	66
10	Cu(CH₃CN)₄BF₄	DCE	50	1.5	65
11	Cu(CH ₃ CN) ₄ BF ₄	DCE	70	1.5	61
12 ^d	Cu(CH ₃ CN) ₄ BF ₄	DCE	100	0.5	67
13	Cu(CH ₃ CN) ₄ PF ₆	DCE	50	1.5	66
14	Cu(OTf) ₂	DCE	50	1.5	66
15	CuI	DCE	50	1.5	19
16	Cu(tfacac) ₂	DCE	50	1.5	11
17	AuCl	DCE	rt	24	not observed
18	TiCl ₄	DCE	50	24	not observed
19	Sc(OTf) ₃	DCE	50	24	not observed
20	Zn(OTf) ₂	DCE	50	24	not observed
21	AgOTf	DCE	50	24	traces ^b

^aReaction conditions: TIPS-EBX (**6a**) (0.1 mmol), cyclohexene sulfide (**7a**) (0.15 mmol), catalyst (10 mol%), solvent (0.07 M), reactions were carried out under N₂ atmosphere. ^bObserved by NMR. ^c1 equivalent of TMSCl was used. ^dReaction was performed under microwave irradiation. tfacac = trifluoroacetylacetonate.

Table S2. Attempts to reduce oligomerization^a

entry	variation from standard conditions	T (°C)	time (h)	isolated yield
1	None	50	1.5	65
2	C = 0.02 M	50	1.5	65
3	C = 0.15 M	50	1.5	65
4	$\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ loading = 5 mol%	50	3.5	65
5	$\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ loading = 20 mol%	50	1.5	53
6	+ L1 (15 mol%)	rt	24	17
7	+ L1 (15 mol%)	50	5	20
8	+ L2 (15 mol%)	50	1.5	not observed
9	Ratio 6a/7a = 1 : 2	rt	24	62
10	Ratio 6a/7a = 1 : 2.5	rt	24	61
11	Ratio 6a/7a = 1 : 1	rt	24	55
12	Ratio 6a/7a = 1.5 : 1	rt	24	56
13	Ratio 6a/7a = 2 : 1	rt	24	45
14	Ratio 6a/7a = 2.5 : 1	rt	24	46
15	+ 2-iodobenzoic acid (1 equiv.), dropwise addition of 7a	50	1.5	66

^aReaction conditions: TIPS-EBX (**6a**) (0.1 mmol), cyclohexene sulfide (**7a**) (0.15 mmol), catalyst (10 mol%), solvent (0.07 M), reactions were carried out under N_2 atmosphere.

3. Preparation of Hypervalent Iodine Reagents

The synthesis of reagents had already been described before by our group. The procedures are taken from the indicated publications to facilitate reproduction of the results by having all data in the same file.

1-Hydroxy-1,2-benziodoxol-3-(1H)-one (**23**)

Following a reported procedure,¹ NaIO₄ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**22**) (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **23** (8.3 g, 31 mmol, 98%) as a white solid. ¹H NMR (400 MHz, (CD₃)₂SO): δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1H, *ArH*), 7.97 (m, 1H, *ArH*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1H, *ArH*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1H, *ArH*); ¹³C NMR (100 MHz, (CD₃)₂SO): δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m). The values of the NMR spectra are in accordance with reported literature data.¹

Triisopropylsilyl trimethylsilylacetylene (**25**)

¹ L. Kraszkiewicz, L. Skulski, *Arkivoc* **2003**, 2003, 120.

Following a reported procedure,² ⁿBuLi (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**24**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotriisopropylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over MgSO₄, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (56-57 °C/0.25 mm of Hg) to yield **25** (7.16 g, 28.0 mmol, 92% yield) as a colorless liquid. ¹H NMR (400 MHz, CDCl₃): δ 1.08 (m, 21H, TIPS), 0.18 (s, 9H, TMS); IR ν 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). The values of the NMR spectra are in accordance with reported literature data.²

1-[(Triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**6a**)

Following a reported procedure,³ 2-iodosylbenzoic acid (**23**) (21.7 g, 82.0 mmol, 1.00 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3 vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added *via* canula and cooled to 0 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.10 equiv) was added dropwise *via* a dropping funnel over 30 min (no temperature increase was observed). After 15 min, (trimethylsilyl)(triisopropylsilyl)acetylene (**25**) (23.0 g, 90.0 mmol, 1.10 equiv) was added *via* canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added *via* syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in CH₂Cl₂ (200 mL) and

² C. J. Helal, P. A. Magriotis, E. J. Corey, *J. Am. Chem. Soc.* **1996**, *118*, 10938–10939.

³ J. P. Brand, J. Waser, *Angew. Chem. Int. Ed.* **2010**, *49*, 7304–7307.

ArH), 7.80 (m, 2H, ArH), 7.63 (m, 2H, ArH), 7.48 (m, 3H, ArH); ^{13}C NMR (100 MHz, CDCl_3): δ 163.9, 134.9, 132.9, 132.5, 131.6, 131.3, 130.8, 128.8, 126.2, 120.5, 116.2, 106.6, 50.2. The characterization data corresponded to the reported values.⁴

1-(*p*-Tolylethynyl)-1,2-benziodoxol-3(1H)-one (**6l**)

Following a reported procedure,⁵ trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.32 g, 5.00 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at room temperature. The resulting suspension was stirred for 3 h, followed by the drop wise addition of trimethyl(*p*-tolylethynyl)silane (**27**) (1.04 g, 5.50 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of NaHCO_3 (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with saturated solution of NaHCO_3 (20 mL), dried over MgSO_4 , filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (*ca* 20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **6l** (0.540 g, 1.49 mmol, 30%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.43 (dd, $J = 6.1, 2.9$ Hz, 1H, ArH), 8.30–8.14 (m, 1H, ArH), 7.77 (dd, $J = 6.9, 3.1$ Hz, 2H, ArH), 7.50 (d, $J = 7.8$ Hz, 2H, ArH), 7.25 (d, $J = 7.6$ Hz, 2H, ArH), 2.43 (s, 3H, ArCH_3); ^{13}C NMR (100 MHz, CDCl_3): δ 166.6, 141.5, 134.9, 132.8, 132.5, 131.6, 131.3, 129.5, 126.2, 117.4, 116.2, 107.25, 49.1, 21.7. The characterization data corresponded to the reported values.⁵

1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (**6m**)

⁵ H. Huang, G. Zhang, L. Gong, S. Zhang, Y. Chen, *J. Am. Chem. Soc.* **2014**, *136*, 2280–2283.

Following a reported procedure,⁶ trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.32 g, 5.00 mmol, 1.00 equiv) in CH₂Cl₂ (15 mL) at room temperature. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**28**) (1.17 g, 5.50 mmol, 1.10 equiv). The resulting suspension was stirred for 6 h at room temperature. A saturated solution of NaHCO₃ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with saturated solution of NaHCO₃ (20 mL), dried over MgSO₄, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH₃CN (ca 20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **6m** (1.50 g, 3.51 mmol, 70%) as a white solid. Mp (Dec.): 174-177 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.44 (td, *J* = 7.3, 2.1 Hz, 2H, ArH), 7.84–7.74 (m, 2H, ArH), 7.68 (d, *J* = 1.1 Hz, 1H, ArH), 7.61 (dd, *J* = 7.6, 1.7 Hz, 1H, ArH), 7.36 (dtd, *J* = 22.4, 7.5, 1.5 Hz, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃): δ 166.6, 135.2, 134.7, 133.0, 132.7, 131.8, 131.3, 127.6, 126.8, 126.4, 123.2, 116.5, 104.3, 55.4; IR ν 2358 (w), 2155 (w), 1638 (s), 1616 (m), 1585 (w), 1466 (w), 1316 (m), 1147 (w). The characterization data corresponded to the reported values.⁶

1-[3,3-Dimethylbutynyl]-1,2-benziodoxol-3(1*H*)-one (**6n**)

Following a reported procedure,⁷ trimethylsilyltriflate (1.52 mL, 8.42 mmol, 1.0 equiv) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**23**) (2.69 g, 10.1 mmol, 1.2 equiv) in acetonitrile (30 mL). 3,3-dimethylbut-1-yn-1-yltrimethylsilane (**29**) (1.30 g, 8.42 mmol, 1.0 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (680 μL, 8.42 mmol, 1.0 equiv). The mixture was stirred 10 min. The solvent was then removed under reduced pressure. CH₂Cl₂ and 1 M NaOH were added. The resulting suspension was filtered. The layers were separated and the aqueous layer was extracted with CH₂Cl₂. The

⁶ F. Le Vaillant, T. Courant, J. Waser, *Angew. Chem. Int. Ed.* **2015**, *54*, 11200–11204.

⁷ C. C. Chen, J. Waser, *Org. Lett.* **2015**, *17*, 736–739.

organic layers were combined, dried over MgSO_4 , filtered and the solvent was evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (ca 20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **6n** (1.43g, 4.36 mmol, 57%) as a colorless solid." Mp (Dec.) 189 – 192°C. ^1H -NMR (400 MHz, CDCl_3) δ 8.39 (m, 1H, Ar-*H*), 8.12 (m, 1H, Ar-*H*), 7.75 (m, 2H, Ar-*H*), 1.37 (s, 9H, ^tBu). The characterization data corresponded to the reported values.⁷

2-Cyclopropylethynyl-1,2-benziodoxol-3(1*H*)-one (**6o**)

Following a reported procedure,⁸ 2-iodobenzoic acid (**22**) (6.41 g, 25.8 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate ($\text{TsOH}\cdot\text{H}_2\text{O}$, 4.91 g, 25.8 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 7.00 g, 28.4 mmol, 1.10 equiv) were dissolved in dichloromethane (48 mL) and 2,2,2-trifluoroethanol (48 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which (cyclopropylethynyl)trimethylsilane (**30**) (5.00 g, 36.2 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 12 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH_2Cl_2 (400 mL) and under vigorous stirring, a saturated solution of NaHCO_3 (400 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried over MgSO_4 , filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **6o** (2.11 g, 6.76 mmol, 26 %) as a white solid. Mp (Dec.): 174.2–177.6 °C; TLC ($\text{EtOAc}:\text{MeOH}$, 9:1 v/v): R_f = 0.46, KMnO_4 ; ^1H NMR (CDCl_3 , 400 MHz): δ 8.34 (dd, J = 7.0, 2.1 Hz, 1H, Ar*H*), 8.18–8.09 (m, 1H, Ar*H*), 7.81–7.63 (m, 2H, Ar*H*), 1.59 (tt, J = 8.2, 5.0 Hz, 1H, CH), 1.07–0.85 (m, 4H, CH_2CH_2); ^{13}C NMR (CDCl_3 , 100 MHz): δ 166.7, 134.7, 132.3, 131.7, 131.4, 126.2, 115.9, 113.3, 35.0, 9.8, 1.1; IR ν 3464 (w), 3077 (w), 3012 (w), 2238 (w), 2159 (m), 1607 (s), 1559 (m), 1438 (m), 1338 (m), 1298

⁸ D. P. Hari, J. Waser, *J. Am. Chem. Soc.* **2016**, *138*, 2190–2193.

(m), 833 (m), 744 (s), 691 (m). HRMS (ESI) calcd. for $C_{12}H_{10}IO_2^+$ $[M+H]^+$ 312.9720; found 312.9719. The characterization data corresponded to the reported values.⁸

(5-Chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (**6p**)

Following a reported procedure,⁹ 2-iodobenzoic acid (**22**) (3.76 g, 15.2 mmol, 1.00 equiv), *para*-toluenesulfonic acid monohydrate (TsOH·H₂O, 2.88 g, 15.2 mmol, 1.00 equiv) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 4.11 g, 16.7 mmol, 1.10 equiv) were dissolved in CH₂Cl₂ (30 mL) and 2,2,2-trifluoroethanol (30 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which 5-chloro-1-pentynyl-1-boronic acid pinacol ester (**31**) (4.85 g, 21.2 mmol, 1.40 equiv) was added in one portion. The reaction mixture was stirred for 90 minutes at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in CH₂Cl₂ (15 mL) and under vigorous stirring, saturated solution of NaHCO₃ (15 mL) was added. The mixture was stirred for 10 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of CH₂Cl₂ (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography using ethyl acetate to afford **6p** (3.76 g, 10.8 mmol, 71%) as a white solid. TLC (EtOAc): *R*_f = 0.15, KMnO₄; Mp: 138.5-141.7 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.41-8.34 (m, 1H, ArH), 8.22-8.13 (m, 1H, ArH), 7.82-7.68 (m, 2H, ArH), 3.71 (t, *J* = 6.1 Hz, 2H, ClCH₂CH₂), 2.82 (t, *J* = 6.9 Hz, 2H, CCCH₂CH₂), 2.18-2.05 (m, 2H, ClCH₂CH₂); ¹³C NMR (CDCl₃, 100 MHz): δ 166.8, 134.9, 132.5, 131.6, 131.6, 126.4, 115.8, 107.1, 43.4, 41.2, 30.7, 18.0; IR ν 2942 (w), 2866 (w), 2171 (w), 2091 (w), 1727 (w), 1617 (s), 1556 (w), 1441 (w), 1339 (m), 1213 (w), 1023 (w), 846 (w), 742 (s). The characterization data corresponded to the reported values.⁹

4,5-Dimethoxy-2-iodosylbenzoic acid (**33**)

⁹ R. Frei, M. D. Wodrich, D. P. Hari, P. A. Borin, C. Chauvier, J. Waser, *J. Am. Chem. Soc.* **2014**, *136*, 16563–16573.

Following a reported procedure,⁴ NaIO₄ (1.25 g, 5.84 mmol, 1.05 equiv) and 2-iodo-4,5-dimethoxybenzoic acid (**32**) (1.71 g, 5.56 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (15 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (40 mL) and allowed to cool to RT, protecting it from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 4 mL) and acetone (3 x 4 mL), and air-dried in the dark to give the pure product **33** (1.64 g, 5.06 mmol, 91%) as a colorless solid. ¹H NMR (400 MHz, DMSO); δ 7.45 (s, 1H, ArH), 7.23 (s, 1H, ArH), 3.88 (d, 6H, *J* = 0.9 Hz, Me). The characterization data corresponded to the reported values.⁴

4,5-Dimethoxy-1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**6q**)

Following a reported procedure,⁴ trimethylsilyltriflate (400 μL, 2.20 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of **33** (648 mg, 2.00 mmol, 1.0 equiv) in acetonitrile (10 mL). After 2 min, (trimethylsilyl)(triisopropylsilyl)acetylene (**25**) (560 mg, 2.20 mmol, 1.1 equiv) was added dropwise, followed, after 20 min, by the addition of pyridine (180 μL, 2.20 mmol, 1.1 equiv). The mixture was stirred 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (20 mL). The organic layer was washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH₂Cl₂ (20 mL). The organic layers were combined, washed with a saturated solution of NaHCO₃ (40 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 8 mL) and wash with hexanes afforded **6q** (575 mg, 1.18 mmol, 59%) as colorless crystals. Mp (Dec.) 180.0–183.0 °C; ¹H NMR (400 MHz, CDCl₃); δ 7.83 (s, 1H, ArH), 7.61 (s, 1H, ArH), 3.99 (s, 3H, OMe), 3.97 (s, 3H, OMe), 1.14

(m, 2H, TIPS); ^{13}C NMR (100 MHz, CDCl_3): δ 166.7, 154.9, 152.2, 124.5, 113.8, 113.2, 107.8, 104.7, 66.0, 56.7, 56.5, 18.5, 11.2; IR 2945 (w), 1616 (m), 1569 (w), 1497 (m), 1464 (w), 1396 (m), 1317 (w), 1269 (m), 1215 (m), 1181 (w), 1129 (w), 1026 (w), 921 (w), 884 (w), 778 (w), 734 (m), 708 (m), 639 (s). The characterization data corresponded to the reported values.⁴

2-Iodosyl-5-nitrobenzoic acid (**34**) and 2-iodosyl-3-nitrobenzoic acid (**35**)

Following a reported procedure,⁴ fuming nitric acid (3.3 mL) was added to 2-iodobenzoic acid (**22**) (5.0 g, 20 mmol, 1.0 equiv) in concentrated H_2SO_4 (6.7 mL). The reaction was equipped with a cooler and a nitrous vapor trap and was heated at $100\text{ }^\circ\text{C}$ for 1 h. The reaction mixture was then poured in ice-water and filtered. The resulting solid was refluxed in water (50 mL) and filtered. A second crop of precipitate was filtered from the mother liquors. Both solids were combined, washed with acetone (10 mL) and dried under vacuum to afford **34** (2.19 g, 7.10 mmol, 36 %). The mother liquors were reduced to one third and then kept at $4\text{ }^\circ\text{C}$, the resulting precipitate was filtered, washed with acetone (10 mL) and dried under vacuum to afford **35** (630 mg, 2.04 mmol, 10 %). **34**: ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$): δ 8.73 (dd, $J = 8.8, 2.6\text{ Hz}$, 1H, ArH), 8.58 (d, $J = 2.4\text{ Hz}$, 1H, ArH), 8.54 (br s, 1H, OH), 8.11 (d, $J = 8.8\text{ Hz}$, 1H, ArH). **35**: ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{SO}$): δ 7.92 (dd, $J = 7.9, 1.5\text{ Hz}$, 1H, ArH), 7.79 (m, 1H, ArH), 7.67 (m, 1H, ArH). The characterization data corresponded to the reported values.⁴

5-Nitro-1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (**6r**)

Following a reported procedure,⁴ trimethylsilyltriflate (646 μL , 3.56 mmol, 1.10 equiv, freshly distilled over CaH_2) was added dropwise to a stirred solution of 2-iodosyl-5-nitrobenzoic acid

34 (1.00 g, 3.23 mmol, 1.00 equiv) in acetonitrile (15 mL) at 0 °C. After 15 min at room temperature, (trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**25**) (906 mg, 3.56 mmol, 1.10 equiv) was added dropwise, followed, after 30 min, by the addition of pyridine (290 μ L, 3.56 mmol, 1.10 equiv). The mixture was stirred for 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH₂Cl₂ (25 mL). The organic layer was washed with 1 M HCl (25 mL) and the aqueous layer was extracted with CH₂Cl₂ (25 mL). The organic layers were combined, washed with a saturated solution of NaHCO₃ (20 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 20 mL) afforded **6r** (960 mg, 2.02 mmol, 63%) as a white solid. Mp (Dec.); 198.0-206.0 °C; ¹H NMR (400 MHz, CDCl₃): δ 9.20 (d, *J* = 2.6 Hz, 1H, Ar*H*), 8.60 (ddd, *J* = 9.0, 2.5, 0.4 Hz, 1H, Ar*H*), 8.53 (d, *J* = 8.9 Hz, 1H, Ar*H*), 1.30-1.14 (m, 21H, TIPS); ¹³C NMR (100 MHz, CDCl₃): δ 166.4, 150.7, 134.4, 129.0, 128.2, 126.5, 122.7, 115.2, 63.1, 18.5, 11.3. The characterization data corresponded to the reported values.⁴

1-Hydroxy-1,2-naphthiodoxol-3-(1*H*) (**37**)

Following a reported procedure,¹⁰ NaIO₄ (1.9 g, 8.8 mmol, 1.05 equiv) and 3-iodo-2-naphthoic acid (**36**) (2.5 g, 8.4 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (27 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 8 mL) and acetone (3 x 8 mL), and air-dried in the dark to give the pure product **37** (2.2 g, 6.9 mmol, 82%) as a colorless solid. ¹H NMR (400 MHz, DMSO): δ 8.67 (s, 1H, OH), 8.38 (s, 1H, Ar*H*), 8.28 (d, *J* = 8.0 Hz, 1H, Ar*H*), 8.18-8.20 (m, 2H, Ar*H*), 7.71-7.78 (m, 2H, Ar*H*). ¹³C NMR (100 MHz, CDCl₃): δ 168.5, 136.6, 133.5, 132.5, 130.0, 129.6, 128.8, 128.7, 128.6, 127.1, 116.6. The characterization data corresponded to the reported values.¹⁰

¹⁰ N. Declas, F. Le Vaillant, J. Waser, *Org. Lett.* **2019**, *21*, 524–528.

1-((Triisopropylsilyl)ethynyl)-1,2-naphthiodoxol-3-(1H) (6s)

Trimethylsilyltriflate (254 μ L, 1.40 mmol, 1.10 equiv) was added dropwise to a stirred solution of 1-hydroxy-1,2-naphthiodoxol-3-(1H) **37** (400 mg, 1.28 mmol, 1.00 equiv) in acetonitrile (6.4 mL) at 0 °C. After 15 min at room temperature, (trimethylsilyl)(triisopropyl)acetylene (**25**) (357 mg, 1.40 mmol, 1.10 equiv) was added dropwise, followed, after 30 min, by the addition of pyridine (113 μ L, 1.40 mmol, 1.10 equiv). The mixture was stirred for 20 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in CH₂Cl₂ (25 mL). The organic layer was washed with 1 M HCl (25 mL) and the aqueous layer was extracted with 3 x 20 mL of CH₂Cl₂. The organic layers were combined, washed successively with a saturated solution of NaHCO₃ (20 mL) and brine (20 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The resulting solid was boiled in CH₃CN (5 mL). The mixture was filtered, the solid was washed with pentane and collected with CH₂Cl₂. The resulting solution was concentrated *in vacuo* to afford **6s** (466 mg, 0.974 mmol, 76%) as a white solid. R_f 0.25 (Dichloromethane:Methanol 95:5); Mp (Dec.): >180 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ 8.95 (s, 1H, ArH), 8.79 (s, 1H, ArH), 8.16 – 8.09 (m, 1H, ArH), 7.92 – 7.84 (m, 1H, ArH), 7.75 – 7.68 (m, 2H, ArH), 1.29 – 1.18 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 166.9, 137.1, 134.4, 133.3, 129.8, 129.3, 128.8, 127.7, 126.7, 126.7, 114.5, 112.1, 65.4, 18.8, 11.4; HRMS (ESI/QTOF) *m/z*: [M + H]⁺ Calcd for C₂₂H₂₈IO₂Si⁺ 479.0898; Found 479.0900; IR (ν_{max} , cm⁻¹) 2943 (m), 2865 (m), 1649 (m), 1620 (s), 1610 (s), 1561 (m), 1462 (m), 1440 (m), 1337 (m), 1296 (m), 882 (m), 835 (m), 731 (s), 703 (s), 691 (s), 676 (s).

(E)-1-(2-Cyclohexylvinyl)-1,2-benziodoxol-3(1H)-one (6t)

Following a reported procedure,¹¹ trifluoromethanesulfonic acid (TfOH, 0.533 mL, 6.00 mmol, 1.00 equiv.) was added dropwise to a stirred solution of 2-iodobenzoic acid (**22**) (1.49 g, 6.00 mmol, 1.00 equiv.) and *meta*-chloroperoxybenzoic acid (*m*CPBA-77%, 1.48 g, 6.60 mmol, 1.10 equiv.) in dichloromethane (37.5 mL) at 0 °C. After 15 minutes stirring at room temperature, (E)-(2-cyclohexylvinyl)boronic acid (**38**) (1.85 g, 12.0 mmol, 2.00 equiv.) was added in one portion at 0 °C. The reaction mixture was stirred for an additional 1 hour at room temperature, then the resulting mixture was concentrated *in vacuo*. Diethyl ether (300 mL) was added and the resulting mixture was vigorously stirred over 30 minutes. The solid was filtered off and washed with portions of diethyl ether (5 x 50 mL). The resulting solid was dissolved in dichloromethane (50 mL) and treated with a solution of saturated aqueous sodium bicarbonate (50 mL). The mixture was vigorously stirred for 1 hour, then the organic layer was diluted with dichloromethane (100 mL) and the two layers were separated. The aqueous layer was extracted with additional portions of dichloromethane (3 x 50 mL) and the combined organic layers were washed with water (50 mL) and brine (50 mL), then dried over magnesium sulfate and filtered. The volatiles were removed to afford pure **6t** (0.654 g, 1.84 mmol, 31% yield) as a beige solid. *R*_f 0.46 (Dichloromethane:Methanol 95:5); ¹H NMR (400 MHz, CDCl₃) δ 8.44 – 8.33 (m, 1H, ArH), 7.55 (tt, *J* = 7.2, 5.3 Hz, 2H, ArH), 7.50 – 7.39 (m, 1H, ArH), 6.98 (dd, *J* = 15.4, 6.8 Hz, 1H, ICHCH), 6.55 (dd, *J* = 15.3, 1.2 Hz, 1H, ICHCHCH), 2.45 – 2.30 (m, 1H, CHCH(CH₂)₂), 1.96 – 1.75 (m, 4H, CH₂), 1.75 – 1.65 (m, 1H, CH₂), 1.45 – 1.09 (m, 5H, CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 166.7, 164.0, 133.7, 133.4, 132.9, 130.7, 125.8, 114.6, 98.9, 44.6, 31.8, 25.8, 25.6. Spectroscopic data was consistent with the values reported in literature.¹¹

(E)-1-Styryl-1,2-benziodoxol-3(1H)-one (6u)

Following a reported procedure,¹¹ trifluoromethanesulfonic acid (TfOH, 0.666 mL, 7.50 mmol, 1.50 equiv.) was added dropwise to a stirred solution of 2-iodobenzoic acid (**22**) (1.24 g, 5.00

¹¹ E. Stridfeldt, A. Seemann, M. J. Bouma, C. Dey, A. Ertan, B. Olofsson, *Chem. – Eur. J.* **2016**, *22*, 16066–16070.

mmol, 1.00 equiv.) and *meta*-chloroperoxybenzoic acid (*m*CPBA-77%, 1.23 g, 5.50 mmol, 1.10 equiv.) in dichloromethane (31.3 mL) at 0 °C. After 15 minutes stirring at room temperature, (E)-styrylboronic acid (**39**) (1.04 g, 7.00 mmol, 1.40 equiv.) was added in one portion at 0 °C. The reaction mixture was stirred for an additional 1 hour at room temperature, then the resulting mixture was treated with a solution of saturated aqueous sodium bicarbonate (50 mL). The mixture was vigorously stirred for 1 hour, then the organic layer was diluted with dichloromethane (100 mL) and the two layers were separated. The aqueous layer was extracted with additional portions of dichloromethane (3 x 50 mL) and the combined organic layers were washed with water (50 mL) and brine (50 mL), then dried over magnesium sulfate, filtered and concentrated *in vacuo*. Diethyl ether (300 mL) was added and the resulting mixture was vigorously stirred over 30 minutes. The solid was filtered off and washed with portions of diethyl ether (5 x 50 mL) to afford **6u** (0.602 g, 1.72 mmol, 34% yield) as a pale brown solid. *R*_f 0.30 (Dichloromethane:Methanol 95:5); ¹H NMR (400 MHz, CDCl₃) δ 8.36 (dt, *J* = 7.1, 1.2 Hz, 1H, *ArH*), 7.80 (d, *J* = 15.7 Hz, 1H, *ArH*), 7.61 – 7.40 (m, 8H, *ArH*), 7.33 (d, *J* = 15.7 Hz, 1H, *ArH*); ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 154.3, 135.1, 133.7, 133.4, 132.9, 131.3, 130.8, 129.3, 127.9, 126.5, 115.6, 99.8. Spectroscopic data was consistent with the values reported in literature.¹¹

Phenyl((triisopropylsilyl)ethynyl)iodonium trifluoromethanesulfonate (**6v**)

Following a reported procedure,¹² phenyliodonium diacetate (**40**) (2.53 g, 7.85 mmol, 1.00 eq.) was diluted with CH₂Cl₂ (7 mL) and the mixture was stirred for 5 minutes. Next, triflic anhydride (0.600 mL, 3.90 mmol, 0.50 eq.) was added dropwise at 0 °C and the resulting yellow mixture was stirred for 30 min. To the mixture was added (trimethylsilyl)(triisopropylsilyl)acetylene (**25**) (2.00 g, 7.86 mmol, 1.00 eq.) and stirring continued for 2 hours at 0 °C. Water was then added (30 mL) and the mixture was extracted

¹² R. Frei, J. Waser, *J. Am. Chem. Soc.* **2013**, *135*, 9620–9623.

with CH₂Cl₂ (2 x 30 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The resulting solid was triturated in hexane (10 mL). Filtration and removal of solvent *in vacuo* afforded **6v** (2.90 g, 11.2 mmol, 70%) as a colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 8.09 (m, 2 H, ArH), 7.65 (m, 1 H, ArH), 7.52 (m, 2 H, ArH), 1.15-1.01 (m, 21 H, TIPS). ¹³C NMR (100 MHz, CDCl₃) δ 133.7, 132.5, 132.4, 123.0 (J_{C-H} = 319 Hz), 117.6, 117.6, 44.9, 18.3, 11.1. IR ν 3288 (w), 3088 (m), 2949 (m), 2894 (m), 2869 (w), 1563 (m), 1467 (w), 1451 (w), 1388 (w), 1281 (s), 1236 (s), 1221 (s), 1174 (s), 1068 (w), 1028 (s), 988 (m), 916 (m), 884 (m), 736 (s), 679 (m), 639 (s). The characterization data is in accordance with reported literature values.¹²

4. Preparation of Thiiranes reagents

Thiiranes **7a**, **7e**, **7f** and **7h** were commercially available and bought from Sigma-Aldrich.

Cyclopentene sulfide (**7b**)

Following a reported procedure,¹³ to a solution of 6-oxabicyclo[3.1.0]hexane (**41**) (0.50 g, 5.9 mmol, 1.0 equiv.) in water (8.9 mL) was added KSCN (2.3 g, 24 mmol, 4.0 equiv.). The resulting mixture was stirred at 45 °C for 24 h. The reaction was cooled to rt and 2 mL of pentane and brine were added. The crude mixture was extracted with 3 x 2 mL of pentane. Combined organic layers were dried over MgSO₄ and loaded over a plug of silica, the product was eluted with pentane and concentrated in vacuo to afford **7b** (0.16 g, 1.4 mmol, 23%, 85% purity) as a colourless oil. ¹H NMR (400 MHz, Chloroform-*d*) δ 3.30 (d, *J* = 2.4 Hz, 2H, *CHS*), 2.06 (dd, *J* = 13.9, 7.0 Hz, 2H, *CH*₂ cyclopentyl), 1.90 – 1.76 (m, 2H, *CH*₂ cyclopentyl), 1.70 – 1.45 (m, 2H, *CH*₂ cyclopentyl); ¹³C NMR (100 MHz, Chloroform-*d*) δ 41.8, 29.1, 18.2. Spectroscopic data was consistent with the values reported in literature.¹³

4-Thiocyanatotetrahydrofuran-3-ol (**43**)

Compound **43** was synthesized following an adapted version of a reported procedure.¹⁴ A solution of 3,6-dioxabicyclo[3.1.0]hexane (**42**) (2.00 g, 23.2 mmol, 1.0 equiv.), NH₄SCN (1.77 g, 23.2 mmol, 1.0 equiv.) and Selectfluor™ (0.866 g, 2.32 mmol, 0.1 equiv.) in acetonitrile (35 mL) was stirred at 50 °C for 48 h. The mixture was concentrated *in vacuo*, the crude oil was

¹³ X. Chen, J. Xu, *Tetrahedron Lett.* **2017**, *58*, 1651–1654.

¹⁴ J. S. Yadav, B. V. S. Reddy, Ch. S. Reddy, *Tetrahedron Lett.* **2004**, *45*, 1291–1293.

purified by column chromatography (MeOH/CH₂Cl₂; 5:95) to afford **43** (2.29 g, 15.8 mmol, 68%) as a slightly yellow oil. *R*_f 0.25 (MeOH/CH₂Cl₂; 5:95); ¹H NMR (400 MHz, Chloroform-*d*) δ 4.59 – 4.50 (m, 1H, *CHOH*), 4.30 (dd, *J* = 10.6, 5.7 Hz, 1H, *CH*₂O), 4.16 (dd, *J* = 10.2, 4.9 Hz, 1H, *CH*₂O), 3.83 – 3.75 (m, 2H, *CH*₂O), 3.74 – 3.69 (m, 1H, *CHSCN*), 3.22 (s, 1H, *OH*); ¹³C NMR (100 MHz, Chloroform-*d*) δ 111.2, 77.2, 74.1, 70.8, 52.7 IR (*v*_{max}, cm⁻¹) 3418 (s), 2986 (w), 2883 (w), 2159 (m), 1672 (s), 1416 (s), 1177 (s), 1067 (s), 964 (s), 907 (s), 771 (s), 714 (s). No exact mass could be obtained.

3-Oxa-6-thiabicyclo[3.1.0]hexane (**7c**)

Compound **7c** was synthesized following an adapted version of a reported procedure.¹⁵ To a solution of 4-thiocyanatotetrahydrofuran-3-ol (**43**) (2.03 g, 20.0 mmol, 1.0 equiv.) in pyridine (8.8 mL) was added MsCl (1.62 mL, 21.0 mmol, 1.5 equiv.) under N₂ atmosphere at 0 °C. The mixture was allowed to warm to rt and stirred for 18 h. The reaction mixture was diluted with 50 mL of water and extracted with 3 x 30 mL of CH₂Cl₂. The combined organic layers were washed successively with 50 mL of a 1 M aq. sol. of HCl and water. The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to afford crude 4-thiocyanatotetrahydrofuran-3-yl methanesulfonate (**44**). The crude mixture was used directly without further purification. To the resulting crude oil were added water (52 mL) and NaOH (1.12 g, 28.0 mmol, 2.0 equiv.) and the mixture was stirred at rt for 38 h. The pH of the reaction mixture was adjusted to pH = 7 with addition of 1 M aq. sol. of HCl, the aqueous layer was extracted with 3 x 30 mL of CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude orange oil was purified by column chromatography (CH₂Cl₂/Pentane; 7:3) to afford **7c** (0.417 g, 4.09 mmol, 29%) as a yellow oil. *R*_f 0.3 (AcOEt/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 4.05 (d, *J* = 10.0 Hz, 2H, *CH*₂O), 3.83 (dd, *J* = 10.1, 1.4 Hz, 2H, *CH*₂O), 3.44 (d, *J* = 1.4 Hz, 2H, *CHS*); ¹³C NMR (100 MHz, Chloroform-*d*) δ 69.3, 38.0; IR (*v*_{max}, cm⁻¹) 2899 (m), 2823 (s), 2156 (s), 1669 (s), 1403

¹⁵ L. Goodman, B. R. Baker, *J. Am. Chem. Soc.* **1959**, *81*, 4924–4926.

(s), 1270 (m), 1216 (s), 1186 (s), 1074 (s), 1035 (m), 905 (s), 718 (s), 708 (s); HRMS (APPI/LTQ-Orbitrap) m/z : $[M + H]^+$ Calcd for $C_4H_7OS^+$ 103.0212; Found 103.0207.

***Tert*-butyl 3-hydroxy-4-thiocyanatopyrrolidine-1-carboxylate (**46**)**

Compound **46** was synthesized following an adapted version of a reported procedure.¹⁴ A solution of *tert*-butyl 6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (**45**) (3.00 g, 16.2 mmol, 1.0 equiv.), NH_4SCN (1.23 g, 16.2 mmol, 1.0 equiv.) and SelectfluorTM (0.60 g, 1.6 mmol, 0.1 equiv.) in acetonitrile (24 mL) was stirred at 50 °C for 48 h. The mixture was concentrated *in vacuo*, the crude oil was purified by column chromatography ($\text{MeOH}/\text{CH}_2\text{Cl}_2$; 2.5:97.5) to afford **46** (2.21 g, 9.06 mmol, 56%) an orange solid. R_f 0.28 ($\text{MeOH}/\text{CH}_2\text{Cl}_2$; 5:95); Mp: 69-70 °C; ^1H NMR (400 MHz, $\text{CHloroform-}d$) δ 4.47 (d, $J = 19.7$ Hz, 1H, CHOH), 3.94 (dd, $J = 12.6$, 6.5 Hz, 1H, CH_2N), 3.87 – 3.77 (m, 1H, CH_2N), 3.65 (dt, $J = 6.5$, 4.1 Hz, 1H, CHSCN), 3.55 – 3.31 (m, 2H, CH_2N), 3.11 – 2.93 (m, 1H, OH), 1.46 (s, 9H, $\text{C}(\text{CH}_3)_3$). ^{13}C NMR (100 MHz, $\text{CHloroform-}d$) mixture of rotamers: δ 154.3 (2 peaks), 110.2 (2 peaks), 80.8 (2 peaks), 74.6 (2 peaks), 51.6 (2 peaks), 50.6 (2 peaks), 48.8 (2 peaks), 28.5; IR (ν_{max} , cm^{-1}) 3400 (w), 2984 (w), 2885 (w), 2159 (w), 1675 (s), 1415 (s), 1167 (s), 965 (m), 774 (m); HRMS (ESI/QTOF) m/z : $[M + \text{Na}]^+$ Calcd for $\text{C}_{10}\text{H}_{16}\text{N}_2\text{NaO}_3\text{S}^+$ 267.0774; Found 267.0768.

***Tert*-butyl 6-thia-3-azabicyclo[3.1.0]hexane-3-carboxylate (**7d**)**

Compound **7d** was synthesized following an adapted version of a reported procedure.¹⁵ To a solution of *tert*-butyl 3-hydroxy-4-thiocyanatopyrrolidine-1-carboxylate (**46**) (2.0 g, 8.1 mmol, 1.0 equiv.) in pyridine (5.0 mL) was added MsCl (0.94 mL, 12 mmol, 1.5 equiv.) under N_2 atmosphere at 0 °C. The mixture was allowed to warm to rt and stirred for 22 h. The reaction mixture was diluted with 50 mL of water and extracted with 3 x 30 mL of CH_2Cl_2 . The combined organic layers were washed successively with 50 mL of a 1 M aq. sol. of HCl and

water. The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo* to afford crude *tert*-butyl 3-((methylsulfonyl)oxy)-4-thiocyanatopyrrolidine-1-carboxylate (**47**). The crude mixture was used directly without further purification. To the resulting crude oil were added water (30 mL) and NaOH (0.65 g, 16 mmol, 2.0 equiv.) and the mixture was stirred at rt for 38 h. The pH of the reaction mixture was adjusted to pH = 7 with addition of 1 M aq. sol. of HCl, the aqueous layer was extracted with 3 x 30 mL of CH_2Cl_2 . The combined organic layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude orange oil was purified by column chromatography (CH_2Cl_2 /Pentane; 7:3) to afford **7d** (1.3 g, 6.4 mmol, 79%) as a pink solid. R_f 0.2 (AcOEt/Pentane; 1:9); Mp: 47 °C ^1H NMR (400 MHz, Chloroform-*d*) δ 3.97 (d, J = 12.6 Hz, 1H, NCH_2), 3.86 (d, J = 12.5 Hz, 1H, NCH_2), 3.48 (dt, J = 12.6, 2.4 Hz, 2H, NCH_2), 3.38 – 3.29 (m, 2H, SCH), 1.43 (s, 9H, $\text{C}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, Chloroform-*d*) mixture of rotamers: δ 155.7, 80.0, 48.9 (two peaks), 37.5 (two peaks), 28.5; IR (ν_{max} , cm^{-1}) 2981 (w), 1698 (s), 1408 (s), 1172 (s), 1065 (m), 963 (w); HRMS (APCI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_9\text{H}_{15}\text{NNaO}_2\text{S}^+$ 224.0716; Found 224.0720.

2-Hexylthiirane (**7g**)

Compound **7g** was synthesized following an adapted version of a reported procedure.¹⁶ To a solution of 2-hexyloxirane (**48**) (1.5 mL, 10 mmol, 1.0 equiv.) and PPh_3S (4.4 g, 15 mmol, 1.5 equiv.) in toluene (35 mL) was added dropwise a solution of TFA (0.77 mL, 10 mmol, 1.0 equiv.) in toluene (5 mL). The reaction was stirred at rt for 16 h then quenched by the addition of 50 mL of a sat. sol. of NaHCO_3 and stirred for 15 min. Et_2O (50 mL) was added and the two layers were separated. The aqueous layer was washed with 2 x 30 mL of Et_2O . The combined organic layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. The resulting white solid was suspended in pentane, filtered and washed with pentane. The pentane solution was concentrated *in vacuo* and the resulting crude oil was purified by column chromatography (pentane) to afford **7g** (0.93 g, 6.5 mmol, 65%) as a colorless oil. R_f 0.37 (Pentane) ^1H NMR

¹⁶ T. H. Chan, J. R. Finkenbine, *J. Am. Chem. Soc.* **1972**, *94*, 2880–2882.

(400 MHz, Chloroform-*d*) δ 2.93 – 2.83 (m, 1H, *CHS*), 2.50 (dd, J = 6.3, 1.0 Hz, 1H, *CH*₂S), 2.15 (dd, J = 5.7, 1.0 Hz, 1H, *CH*₂S), 1.89 – 1.75 (m, 1H, *CH*₂ hexyl), 1.58 – 1.41 (m, 3H, *CH*₂ hexyl), 1.39 – 1.22 (m, 6H, *CH*₂ hexyl), 0.94 – 0.84 (m, 3H, *CH*₂*CH*₃); ¹³C NMR (100 MHz, Chloroform-*d*) δ 36.7, 36.2, 31.9, 29.5, 29.1, 26.1, 22.7, 14.2. Spectroscopic data was consistent with the values reported in literature.¹³

(*S*)-Triisopropyl(oxiran-2-ylmethoxy)silane (**50**)

Following a reported procedure,¹⁷ to a cold (0 °C) solution of (*R*)-oxiran-2-ylmethanol (**49**) (2.5 g, 34 mmol, 1.0 equiv.) in CH₂Cl₂ (56 mL) were added imidazole (2.8 g, 41 mmol, 1.2 equiv.) and TIPSCl (8.7 mL, 41 mmol, 1.2 equiv.). The mixture was warmed to rt and stirred for 1.5 h. The reaction mixture was filtered on celite, 80 mL of water and 50 mL of pentane were added to the filtrate and the two layers were separated. The aqueous layer was extracted with 3 x 50 mL of pentane. Combined organic layers were washed successively with 80 mL of water and 2 x 80 mL of brine, dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (Et₂O/Pentane; 5:95 to 1:9) to afford **50** (7.6 g, 33 mmol, 97%) as a colorless oil. ¹H NMR (400 MHz, Chloroform-*d*) δ 3.91 (dd, J = 11.6, 3.3 Hz, 1H, TIPSO-*CH*₂), 3.75 (dd, J = 11.7, 4.7 Hz, 1H, TIPSO-*CH*₂), 3.16 – 3.05 (m, 1H, *OCH*), 2.77 (dd, J = 5.3, 4.0 Hz, 1H, *OCH*₂), 2.66 (dd, J = 5.2, 2.6 Hz, 1H, *OCH*₂), 1.18 – 0.97 (m, 21H, TIPS); ¹³C NMR (101 MHz, Chloroform-*d*) δ 64.1, 52.7, 44.6, 18.1, 12.1. Spectroscopic data was consistent with the values reported in literature.¹⁷

(*R*)-Triisopropyl(thiiran-2-ylmethoxy)silane (**7i**)

¹⁷ S. Hoppen, S. Bäurle, U. Koert, *Chem. – Eur. J.* **2000**, *6*, 2382–2396.

Synthesized following an adapted version of a reported procedure.¹⁸ A solution of (*S*)-triisopropyl(oxiran-2-ylmethoxy)silane (**50**) (2.0 g, 8.7 mmol, 1.0 equiv.) and thiourea (0.73 g, 9.6 mmol, 1.1 equiv.) in a mixture of ethanol (4.25 mL) and water (0.85 mL) was stirred at rt for 24 h. The reaction was concentrated *in vacuo* then water (20 mL) and CH₂Cl₂ (20 mL) were added. The two layers were separated and the aqueous layer was extracted with 3 x 20 mL of CH₂Cl₂. Combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude mixture was purified by column chromatography (Toluene/Pentane; 15:85) to afford **7i** (1.6 g, 6.6 mmol, 76%) as a colorless oil. R_f 0.73 (Toluene/Pentane; 1:3); ¹H NMR (400 MHz, Chloroform-*d*) δ 3.97 (dd, *J* = 10.6, 4.9 Hz, 1H, OTIPS-CH₂), 3.61 (dd, *J* = 10.8, 6.8 Hz, 1H, OTIPS-CH₂), 3.14 – 3.02 (m, 1H, SCH), 2.54 – 2.46 (m, 1H, SCH₂), 2.24 (dd, *J* = 5.4, 1.2 Hz, 1H, SCH₂), 1.19 – 0.94 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 68.3, 35.1, 24.1, 18.1, 12.2; IR (ν_{max}, cm⁻¹) 2946 (s), 2865 (s), 1464 (m), 1388 (w), 1095 (s), 884 (m), 794 (s), 685 (s); HRMS (APPI/QTOF) *m/z*: [M + H]⁺ Calcd for C₁₂H₂₇OSSi⁺ 247.1546; Found 247.1538.

(*Z*)-1,4-Bis(benzyloxy)but-2-ene (**52**)

Following a reported procedure,¹⁹ to a cooled (0 °C) suspension of NaH (60% dispersion in mineral oil, 0.80 g, 20 mmol, 4.0 equiv.) in THF (8.1 mL) was added dropwise (*Z*)-but-2-ene-1,4-diol (**51**) (0.41 mL, 5.0 mmol, 1.0 equiv.). The mixture was stirred under reflux for 2 h then cooled to rt. A solution of BnBr (2.4 mL, 20 mmol, 4.0 equiv.) in THF (8.1 mL) was added dropwise, the mixture was stirred under reflux for 1 h, cooled to rt and stirred for 24 h. The mixture was cooled to 0 °C, quenched with a slow addition of 15 mL of water and concentrated *in vacuo*. The resulting mixture was extracted with 3 x 20 mL of DCM. Combined organic layers were washed successively with 20 mL of a sat. sol. of NH₄Cl, 20 mL of water and 20 mL of brine, dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was

¹⁸ H. Bouda, M. E. Borredon, M. Delmas, A. Gaset, *Synth. Commun.* **1989**, *19*, 491–500.

¹⁹ F.-L. Wu, B. P. Ross, R. P. McGeary, *Eur. J. Org. Chem.* **2010**, *2010*, 1989–1998.

purified by column chromatography (AcOEt/Pentane; 5:95) to afford **52** (1.1 g, 4.0 mmol, 80%) as a colorless oil. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.27 (m, 10H, PhH), 5.80 (t, J = 3.8 Hz, 2H, CH=CH), 4.50 (s, 4H, PhCH₂O), 4.07 (d, J = 4.9 Hz, 4H, OCH₂CH=CH); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 138.3, 129.7, 128.6, 127.9, 127.8, 72.4, 65.9. Spectroscopic data was consistent with the values reported in literature.¹⁹

2,3-Bis((benzyloxy)methyl)oxirane (**53**)

Following a reported procedure,²⁰ to a cooled (0 °C) solution of (*Z*)-1,4-bis(benzyloxy)but-2-ene (**52**) (1.08 g, 4.00 mmol, 1.0 equiv.) in CH₂Cl₂ (4.0 mL) was added dropwise a solution of *m*CPBA (1.35 g, 6.01 mmol, 1.5 equiv.) in CH₂Cl₂ (6.5 mL) over 15 minutes. The mixture was warm to rt and stirred for 24 h. The mixture was cooled to 0 °C, filtered through a plug of silica and eluted with cold CH₂Cl₂ (40 mL). The resulting solution was washed sequentially with 20 mL of a sat. sol. of NaHCO₃, 20 mL of a sat. sol. of Na₂S₂O₃ and 20 mL of brine. The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (AcOEt/Pentane; 5:95) to afford **53** (0.536 g, 1.88 mmol, 47%) as a colorless oil. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 10H, PhH), 4.62 (d, J = 11.9 Hz, 2H, PhCH₂O), 4.52 (d, J = 11.9 Hz, 2H, PhCH₂O), 3.69 (dd, J = 11.2, 3.8 Hz, 2H, OCH₂CH), 3.58 – 3.49 (m, 2H, OCH₂CH), 3.30 – 3.23 (m, 2H, CHO); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 137.9, 128.6, 128.0, 127.9, 73.4, 68.2, 54.6. Spectroscopic data was consistent with the values reported in literature.²⁰

2,3-Bis((benzyloxy)methyl)thiirane (**7j**)

²⁰ Y. Schmidt, B. Breit, *Chem. - Eur. J.* **2011**, *17*, 11780–11788.

Compound **7j** was synthesized following an adapted version of a reported procedure.¹⁸ A solution of 2,3-bis((benzyloxy)methyl)oxirane (**53**) (305 mg, 1.07 mmol, 1.0 equiv.) and thiourea (90 mg, 1.2 mmol, 1.1 equiv.) in a mixture of water (105 μ L) and ethanol (530 μ L) was stirred at rt for 65 h. The reaction was concentrated *in vacuo*. The crude mixture was purified by column chromatography (AcOEt/Pentane; 5:95 then 10:90) to afford **7j** (136 mg, 0.452 mmol, 42%) as a colorless oil and unreacted **53** (143 mg, 0.504 mmol, 47%). Rf 0.47 (AcOEt/Pentane; 1:9) ¹H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 10H, PhH), 4.60 (d, *J* = 12.0 Hz, 2H, PhCH₂O), 4.54 (d, *J* = 11.9 Hz, 2H, PhCH₂O), 3.72 – 3.65 (m, 4H, OCH₂CH), 3.26 – 3.18 (m, 2H, CHS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 138.0, 128.6, 127.9, 127.9, 73.3, 70.2, 36.7. Spectroscopic data was consistent with the values reported in literature.¹⁹

5. Preparation of Thietanes reagents

Thiethane **9a** was commercially available and purchased from Sigma-Aldrich.

(1,3-Dibromopropan-2-yl)benzene (**55**)

Following a reported procedure,²¹ to a cold (0 °C) solution of 2-phenylpropane-1,3-diol (**54**) (1.00 g, 6.57 mmol, 1.0 equiv.) and PPh₃ (3.79 g, 14.5 mmol, 2.2 equiv.) in CH₂Cl₂ (33 mL) was added NBS (2.57 g, 14.5 mmol, 2.2 equiv.). The mixture was warmed to rt and stirred for 4.5 h. The mixture was concentrated in vacuo, the resulting crude product was purified by column chromatography (Et₂O/Pentane; 0:100 to 1:99) to afford **55** (1.48 g, 5.32 mmol, 81%) as a colorless oil. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.30 (m, 3H, ArH), 7.25 – 7.20 (m, 2H, ArH), 3.80 (dd, *J* = 10.3, 6.8 Hz, 2H, CH₂Br), 3.73 (dd, *J* = 10.3, 6.3 Hz, 2H, CH₂Br), 3.39 (p, *J* = 6.6 Hz, 1H, PhCH); ¹³C NMR (101 MHz, Chloroform-*d*) δ 139.7, 128.9, 128.1, 127.7, 49.1, 35.7. Spectroscopic data was consistent with the values reported in literature.²¹

3-Phenylthietane (**9b**)

Following a reported procedure,²¹ to a solution of (1,3-dibromopropan-2-yl)benzene (**55**) (0.80 g, 2.9 mmol, 1.0 equiv.) in dry DMF (19.2 mL) was added portion wise Na₂S·9H₂O (0.83 g, 3.5 mmol, 1.2 equiv.). The mixture was stirred at 100 °C for 8 h. The reaction was quenched with 50 mL of water and extracted with 3 x 40 mL of AcOEt. Combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was purified by

²¹ T. Zheng, J. Tan, R. Fan, S. Su, B. Liu, C. Tan, K. Xu, *Chem. Commun.* **2018**, 54, 1303–1306.

column chromatography (Et₂O/Pentane; 0:100 to 4:96) to afford **9b** (76 mg, 0.50 mmol, 17%) as a colorless oil. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.16 (m, 5H, PhH), 4.53 (p, *J* = 9.0 Hz, 1H, CH), 3.57 (t, *J* = 9.1 Hz, 2H, SCH₂), 3.32 (t, *J* = 8.9 Hz, 2H, SCH₂); ¹³C NMR (100 MHz, Chloroform-*d*) δ 144.2, 128.8, 127.1, 126.0, 45.3, 33.2. Spectroscopic data was consistent with the values reported in literature.²¹

7,7-Dimethyl-6,8-dioxa-2-thiaspiro[3.5]nonane (**9c**)

Following a reported procedure,²¹ to a solution of 5,5-bis(bromomethyl)-2,2-dimethyl-1,3-dioxane (**56**) (0.97 g, 3.2 mmol, 1.0 equiv.) in dry DMF (12.8 mL) was added portion wise Na₂S·9H₂O (0.84 mg, 3.5 mmol, 1.1 equiv.). The mixture was stirred at 100 °C for 6 h. The reaction was quenched with 50 mL of water and extracted with 3 x 50 mL of Et₂O. Combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (AcOEt/Pentane; 5:95) to afford **9c** (0.49 g, 2.8 mmol, 88%) as a white solid. ¹H NMR (400 MHz, Chloroform-*d*) δ 3.88 (s, 4H, OCH₂), 2.97 (s, 4H, SCH₂), 1.38 (s, 6H, C(CH₃)₂); ¹³C NMR (100 MHz, Chloroform-*d*) δ 98.1, 68.5, 41.2, 30.9, 23.7. Spectroscopic data was consistent with the values reported in literature.²¹

2-Oxa-6-thiaspiro[3.3]heptane (**9d**)

Compound **9d** was synthesized following an adapted version of a reported procedure.²¹ To an oven dried 2-neck round bottom flask were added 3,3-bis(bromomethyl)oxetane (**57**) (1.5 g, 6.2 mmol, 1.0 equiv.) and dry DMF (25 mL) then Na₂S·9H₂O (1.6 g, 6.8 mmol, 1.1 equiv.) was added portionwise. The mixture was stirred at 50 °C for 6.5 h. The reaction was cooled to rt and quenched by the addition of 50 mL of water. The resulting mixture was extracted with 3 x

50 mL of AcOEt. Combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (AcOEt/PE; 1:9) to afford **9d** (0.32 g, 2.7 mmol, 44%) as an orange oil. R_f 0.29 (AcOEt/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 4.67 (s, 4H, OCH₂), 3.39 (s, 4H, SCH₂); ¹³C NMR (100 MHz, Chloroform-*d*) δ 84.6, 48.0, 36.1; IR (ν_{max}, cm⁻¹) 2932 (m), 2858 (m), 1179 (w), 976 (s), 836 (m); HRMS (APCI/QTOF) m/z: [M + H]⁺ Calcd for C₅H₉OS⁺ 117.0369; Found 117.0367.

6. Oxy-alkynylation

General procedure A: Oxy-alkynylation of thiiranes

To a microwave vial containing hypervalent iodine reagent (**6**) (0.20 mmol, 1 equiv.) was added Cu(CH₃CN)₄BF₄ (6.3 mg, 20 μmol, 0.1 equiv.) under N₂ atmosphere. The vial was sealed, DCE (2.5 mL) and a solution of thiirane (**7**) (0.30 mmol, 1.5 equiv.) in DCE (0.5 mL) were added under N₂ atmosphere. The resulting mixture was stirred at 50 °C for 24 h (unless otherwise indicated). The reaction was cooled to rt and concentrated *in vacuo*. The crude product was purified as described.

2-(((Triisopropylsilyl)ethynyl)thio)cyclohexyl 2-iodobenzoate (**8a**)

To a microwave vial containing TIPS-EBX (**6a**) (43 mg, 0.10 mmol, 1.0 equiv.) was added Cu(CH₃CN)₄BF₄ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N₂ atmosphere. The vial was sealed then DCE (1.5 mL) and cyclohexene sulfide (**7a**) (16 μL, 0.15 mmol, 1.5 equiv.) were added under N₂ atmosphere. The resulting mixture was stirred at 50 °C for 1.5 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude oil was purified by preparative TLC (Toluene/Pentane; 1:3) to afford **8a** (35 mg, 0.065 mmol, 65%) as a colorless oil. The compound crystallized as a white solid after long-time storage in a freezer at -5 °C. Mp: 50 °C. R_f 0.4 (Toluene/Pentane; 1:3); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.97 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.84 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.05 (td, *J* = 10.0, 4.4 Hz, 1H, OCH), 2.95 (ddd, *J* = 11.3, 9.8, 4.2 Hz, 1H,

SCH), 2.43 – 2.24 (m, 2H, CH₂ cyclohexyl), 1.93 – 1.75 (m, 3H, CH₂ cyclohexyl), 1.62 – 1.34 (m, 3H, CH₂ cyclohexyl), 1.08 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.7, 141.2, 135.7, 132.6, 131.0, 128.0, 100.1, 94.1, 92.5, 75.0, 50.5, 32.0, 31.9, 25.5, 24.0, 18.8, 11.5; IR (ν_{max}, cm⁻¹) 2942 (s), 2865 (s), 2089 (m), 1731 (s), 1460 (m), 1283 (s), 1253 (s), 1103 (m), 1014 (m), 867 (m), 741 (s), 674 (s); HRMS (ESI) m/z: [M+Na]⁺ calcd for C₂₄H₃₅INaO₂SSi⁺ 565.1064; found 565.1070.

2-(((Triisopropylsilyl)ethynyl)thio)cyclopentyl 2-iodobenzoate (**8b**)

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and cyclopentene sulfide (**7b**) (35 mg, 0.30 mmol). The crude oil was purified by column chromatography (AcOEt/Pentane; 1:99) to afford **8b** (75 mg, 0.14 mmol, 71%) as a light yellow oil. R_f 0.43 (Toluene/Pentane; 1:3); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.75 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.49 – 5.41 (m, 1H, OCH), 3.56 – 3.48 (m, 1H, SCH), 2.38 – 2.23 (m, 2H, CH₂ cyclopentyl), 1.98 – 1.83 (m, 4H, CH₂ cyclopentyl), 1.07 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.9, 141.4, 135.6, 132.7, 131.1, 128.0, 99.2, 94.0, 93.6, 82.2, 51.6, 31.7, 30.7, 23.1, 18.8, 11.5; IR (ν_{max}, cm⁻¹) 2948 (m), 2866 (m), 2088 (m), 1723 (s), 1461 (m), 1436 (w), 1285 (s), 1247 (s), 1127 (m), 853 (m), 741 (s); HRMS (ESI/QTOF) m/z: [M + Na]⁺ Calcd for C₂₃H₃₃INaO₂SSi⁺ 551.0907; Found 551.0922.

4-(((Triisopropylsilyl)ethynyl)thio)tetrahydrofuran-3-yl 2-iodobenzoate (**8c**)

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and 3-oxa-6-thiabicyclo[3.1.0]hexane (**7c**) (31 mg, 0.30 mmol). The reaction was stirred at 70

°C for 48 h. The crude oil was purified by column chromatography (CH₂Cl₂/Pentane; 4:6) to afford **8c** (64 mg, 0.12 mmol, 61%) as a colorless oil. *R*_f 0.55 (AcOEt/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 7.9, 1.2 Hz, 1H, *ArH*), 7.79 (dd, *J* = 7.8, 1.7 Hz, 1H, *ArH*), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H, *ArH*), 7.17 (td, *J* = 7.7, 1.7 Hz, 1H, *ArH*), 5.59 (dt, *J* = 4.4, 1.9 Hz, 1H, *OCH*), 4.37 (dd, *J* = 9.9, 6.6 Hz, 1H, *OCH*₂CHS), 4.25 (dd, *J* = 10.9, 4.7 Hz, 1H, *OCH*₂CHO), 4.07 (dd, *J* = 10.9, 1.8 Hz, 1H, *OCH*₂CHO), 3.91 (dd, *J* = 9.9, 5.0 Hz, 1H, *OCH*₂CHS), 3.74 (ddd, *J* = 7.0, 5.0, 2.1 Hz, 1H, *SCH*), 1.07 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.6, 134.5, 133.1, 131.3, 128.1, 100.5, 94.2, 92.0, 80.7, 73.0, 71.5, 50.3, 18.7, 11.4; IR (ν_{max}, cm⁻¹) 2864 (m), 2090 (m), 1738 (w), 1462 (m), 1284 (m), 1238 (m), 1088 (s), 881 (m), 852 (s), 740 (s); HRMS (ESI/QTOF) *m/z*: [M + Na]⁺ Calcd for C₂₂H₃₁INaO₃SSi⁺ 553.0700; Found 553.0713.

***Tert*-butyl 3-((2-iodobenzoyl)oxy)-4-(((triisopropylsilyl)ethynyl)thio)pyrrolidine-1-carboxylate (**8d**)**

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and *tert*-butyl 6-thia-3-azabicyclo[3.1.0]hexane-3-carboxylate (**7d**) (60 mg, 0.30 mmol). The reaction was stirred at 70 °C for 48 h. The crude oil was purified by column chromatography (AcOEt/Pentane; 5:95) to afford **8d** (47 mg, 0.075 mmol, 38%) as an orange oil. *R*_f 0.48 (AcOEt/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.74 (d, *J* = 7.8 Hz, 1H, *ArH*), 7.41 (t, *J* = 7.6 Hz, 1H, *ArH*), 7.17 (t, *J* = 7.7 Hz, 1H, *ArH*), 5.57 (d, *J* = 15.0 Hz, 1H, *OCH*), 4.00 (dd, *J* = 12.8, 4.9 Hz, 1H, *NCH*₂), 3.97 – 3.86 (m, 1H, *NCH*₂), 3.83 – 3.76 (m, 1H, *SCH*), 3.75 – 3.62 (m, 1H, *NCH*₂), 3.58 (dd, *J* = 12.3, 2.9 Hz, 1H, *NCH*₂), 1.46 (s, 9H, C(CH₃)₃), 1.08 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) mixture of rotamers: δ 165.6 (two peaks), 154.2, 141.5 (two peaks), 134.8 (two peaks), 133.1 (two peaks), 131.3, 128.1, 101.0, 94.0, 91.7 (two peaks), 80.3, 78.1, 50.1 (two peaks), 49.3 (two peaks), 48.8 (two peaks), 28.6, 18.8, 11.4; IR (ν_{max}, cm⁻¹) 2971 (w), 2873 (w), 2093 (w), 1696 (s), 1399 (s),

1238 (m), 1165 (s), 1116 (s), 877 (m), 858 (m), 738 (s); HRMS (ESI/QTOF) m/z : $[M + Na]^+$ Calcd for $C_{27}H_{40}INNaO_4SSi^+$ 652.1384; Found 652.1395.

2-(((Triisopropylsilyl)ethynyl)thio)ethyl 2-iodobenzoate (**8e**)

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and ethylene sulfide (**7e**) (18 μ L, 0.30 mmol). The crude oil was purified by column chromatography (Et₂O/Pentane; 2:98) to afford **8e** (45 mg, 93 μ mol, 46%) as a light yellow oil. R_f 0.38 (Toluene/Pentane; 1:3); 1H NMR (400 MHz, Chloroform-*d*) δ 8.00 (dd, J = 8.0, 1.2 Hz, 1H, *ArH*), 7.85 (dd, J = 7.8, 1.7 Hz, 1H, *ArH*), 7.41 (td, J = 7.6, 1.2 Hz, 1H, *ArH*), 7.16 (td, J = 7.7, 1.7 Hz, 1H, *ArH*), 4.64 (t, J = 6.5 Hz, 2H, *OCH*₂), 3.10 (t, J = 6.5 Hz, 2H, *SCH*₂), 1.07 (s, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.2, 141.5, 134.8, 133.0, 131.3, 128.1, 98.5, 94.3, 94.1, 63.1, 34.2, 18.8, 11.4; IR (ν_{max} , cm⁻¹) 2946 (m), 2866 (m), 2090 (m), 1729 (s), 1460 (m), 1433 (m), 1286 (s), 1245 (s), 1129 (m), 1008 (m), 854 (s), 741 (s); HRMS (ESI/QTOF) m/z : $[M + H]^+$ Calcd for $C_{20}H_{30}IO_2SSi^+$ 489.0775; Found 489.0790.

1-(((Triisopropylsilyl)ethynyl)thio)propan-2-yl 2-iodobenzoate (**8f**) and 2-(((Triisopropylsilyl)ethynyl)thio)propyl 2-iodobenzoate (**8f'**)

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and propylene sulfide (**7f**) (24 μ L, 0.30 mmol). The crude oil was purified by column chromatography (Toluene/Pentane; 1:3) to afford an inseparable 2.1:1 mixture of **8f/8f'** (64 mg, 0.13 mmol, 64%) as a colorless oil (ratio was determined using the integrals of NMR signal for H_a and H_b). R_f 0.43 (Toluene/Pentane; 1:3) **8f**: 1H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.95 (m, 1H, *ArH*), 7.80 (d, J = 7.8 Hz, 1H, *ArH*), 7.44 – 7.36 (m, 1H, *ArH*), 7.20 – 7.11 (m, 1H, *ArH*), 5.42 (h, J = 6.2 Hz, 1H, *OCH*), 3.12 (dd, J = 13.4, 6.0 Hz, 1H, *SCH*₂), 3.00 (dd, J =

13.4, 6.1 Hz, 1H, SCH₂), 1.55 (d, *J* = 6.5 Hz, 3H, CH₃CH), 1.11 – 1.03 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.4, 135.4, 132.7, 131.1, 128.1, 97.7, 95.1, 94.1, 71.1, 41.2, 19.2, 18.8, 11.4; **8f'**: ¹H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.95 (m, 1H, ArH), 7.85 (d, *J* = 7.8 Hz, 1H, ArH), 7.45 – 7.36 (m, 1H, ArH), 7.20 – 7.11 (m, 1H, ArH), 4.52 (dd, *J* = 11.3, 6.7 Hz, 1H, OCH₂), 4.43 (dd, *J* = 11.3, 6.6 Hz, 1H, OCH₂), 3.32 (h, *J* = 6.8 Hz, 1H, SCH), 1.51 (d, *J* = 6.9 Hz, 3H, CH₃CH), 1.14 – 1.01 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 166.2, 141.5, 134.9, 133.0, 131.3, 128.1, 100.4, 94.3, 92.3, 67.7, 41.9, 18.8, 17.7, 11.5; IR (ν_{max}, cm⁻¹) 2952 (s), 2867 (s), 2090 (s), 1736 (s), 1463 (m), 1281 (s), 1242 (s), 1123 (s), 1021 (m), 878 (s), 856 (s), 741 (s), 675 (s); HRMS (ESI/QTOF) *m/z*: [M + H]⁺ Calcd for C₂₁H₃₂IO₂SSi⁺ 503.0932; Found 503.0938.

1-(((Triisopropylsilyl)ethynyl)thio)octan-2-yl 2-iodobenzoate (8g) and 2-(((Triisopropylsilyl)ethynyl)thio)octyl 2-iodobenzoate (8g')

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and 2-hexylthiirane (**7g**) (43 mg, 0.30 mmol). The crude oil was purified by column chromatography (Toluene/Pentane; 15:85) to afford an inseparable 1.9:1 mixture of **8g/8g'** (68 mg, 0.12 mmol, 60%) as a colorless oil (ratio was determined using the integrals of NMR signal for H_a and H_b). R_f 0.55 (Toluene/Pentane; 1:3); **8g**: ¹H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.95 (m, 1H, ArH), 7.80 (dd, *J* = 7.8, 1.8 Hz, 1H, ArH), 7.45 – 7.37 (m, 1H, ArH), 7.20 – 7.11 (m, 1H, ArH), 5.42 – 5.33 (m, 1H, OCH), 3.08 (d, *J* = 5.9 Hz, 2H, SCH₂), 1.96 – 1.73 (m, 2H, CH₂ hexyl), 1.53 – 1.22 (m, 8H, CH₂ hexyl), 1.10 – 1.03 (m, 21H, TIPS), 0.88 (t, *J* = 6.5 Hz, 3H, CH₂CH₃); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.9, 141.3, 135.5, 132.7, 131.0, 128.0, 97.5, 95.3, 94.1, 74.2, 39.9, 33.1, 31.8, 29.2, 25.5, 22.7, 18.8, 14.2, 11.4; **8g'**: ¹H NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.96 (m, 1H, ArH), 7.85 (dd, *J* = 7.8, 1.7 Hz, 1H, ArH), 7.45 – 7.37 (m, 1H, ArH), 7.20 – 7.10 (m, 1H, ArH), 4.51 (qd, *J* = 11.4, 6.6 Hz, 2H, OCH₂), 3.16 – 3.10 (m, 1H, SCH), 1.95 – 1.73 (m, 2H, CH₂ hexyl), 1.51 – 1.22 (m, 8H, CH₂ hexyl), 1.12 – 1.03 (m, 21H, TIPS), 0.92 – 0.85 (m, 3H, CH₂CH₃); ¹³C NMR (100 MHz, Chloroform-*d*) δ 166.2, 141.5, 134.9, 132.9, 131.3, 128.1, 99.7, 94.3, 92.3, 66.8, 47.6, 31.8, 30.8, 29.1, 26.8,

22.7, 18.8, 14.2, 11.5; IR ($\nu_{\max}$, cm^{-1}) 2933 (m), 2862 (m), 2089 (m), 1730 (s), 1461 (m), 1281 (s), 1245 (s), 1126 (m), 1101 (m), 1009 (m), 856 (m), 739 (s); HRMS (ESI/QTOF) m/z : $[M + H]^+$ Calcd for $\text{C}_{26}\text{H}_{42}\text{IO}_2\text{SSi}^+$ 573.1714; Found 573.1724.

2-Methyl-1-(((triisopropylsilyl)ethynyl)thio)propan-2-yl 2-iodobenzoate (8h) and 2-Methyl-2-(((triisopropylsilyl)ethynyl)thio)propyl 2-iodobenzoate (8h')

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and isobutylene sulfide (**7h**) (27 mg, 0.30 mmol). The reaction was stirred at 50 °C for 48 h. The crude oil was purified by column chromatography (Toluene/Pentane; 1:3) to afford an inseparable 15.5:1 mixture of **8h/8h'** (41 mg, 0.080 mmol, 40%) as a colorless oil (ratio was determined using the integrals of NMR signal for H_a and H_b). R_f 0.43 (Toluene/Pentane; 1:3); **8h**: ^1H NMR (400 MHz, Chloroform- d) δ 7.95 (dd, $J = 8.0, 1.2$ Hz, 1H, ArH), 7.75 (dd, $J = 7.7, 1.8$ Hz, 1H, ArH), 7.39 (td, $J = 7.6, 1.2$ Hz, 1H, ArH), 7.12 (td, $J = 7.6, 1.7$ Hz, 1H, ArH), 3.39 (s, 2H, SCH_2), 1.75 (s, 6H, CCH_3), 1.15 – 0.98 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform- d) δ 165.8, 141.1, 136.4, 132.3, 130.9, 127.9, 96.6, 96.5, 93.6, 83.8, 46.5, 25.6, 18.6, 11.3; **8h'**: ^1H NMR (400 MHz, Chloroform- d) δ 8.00 (dd, $J = 7.9, 1.2$ Hz, 1H, ArH), 7.85 (dd, $J = 7.8, 1.7$ Hz, 1H, ArH), 7.45 – 7.41 (m, 1H, ArH), 7.20 – 7.16 (m, 1H, ArH), 4.40 (s, 2H, OCH_2), 1.50 (s, 6H, CCH_3), 1.11 – 1.00 (m, 21H, TIPS); ^{13}C NMR spectrum was not resolved due the too small signals intensities; IR ($\nu_{\max}$, cm^{-1}) 2945 (s), 2866 (s), 2089 (m), 1722 (s), 1462 (m), 1377 (m), 1297 (s), 1252 (s), 1208 (m), 1105 (s), 1009 (m), 874 (s), 859 (s), 742 (s); HRMS (ESI/QTOF) m/z : $[M + \text{Na}]^+$ Calcd for $\text{C}_{22}\text{H}_{33}\text{INaO}_2\text{SSi}^+$ 539.0907; Found 539.0907.

(S)-1-(((Triisopropylsilyl)ethynyl)thio)-3-(((triisopropylsilyl)oxy)propyl 2-iodobenzoate (8i) and (S)-2-(((triisopropylsilyl)ethynyl)thio)-3-(((triisopropylsilyl)oxy)propyl 2-iodobenzoate (8i')

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and (*R*)-triisopropyl(thiiran-2-ylmethoxy)silane (**7i**) (74 mg, 0.30 mmol). The reaction was stirred at 50 °C for 48 h. The crude oil was purified by column chromatography (CH₂Cl₂/Pentane; 1:9) to afford **8i** (21 mg, 0.032 mmol, 16%) and **8i'** (48 mg, 0.071 mmol, 36%). **8i**: *R_f* 0.21 (CH₂Cl₂/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, *ArH*), 7.84 (dd, *J* = 7.8, 1.7 Hz, 1H, *ArH*), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H, *ArH*), 7.14 (td, *J* = 7.7, 1.8 Hz, 1H, *ArH*), 5.43 – 5.34 (m, 1H, *OCH*), 4.06 (dd, *J* = 4.4, 2.1 Hz, 2H, TIPS-*CH*₂), 3.25 (dd, *J* = 13.4, 5.8 Hz, 1H, *SCH*), 3.16 (dd, *J* = 13.4, 6.8 Hz, 1H, *SCH*), 1.16 – 0.98 (m, 42H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.7, 141.4, 135.1, 132.8, 131.3, 128.0, 97.7, 95.0, 94.3, 74.2, 63.1, 36.6, 18.8, 18.1, 12.0, 11.4; IR (*v*_{max}, cm⁻¹) 2950 (m), 2867 (m), 2095 (m), 1737 (m), 1463 (m), 1244 (m), 1122 (s), 1006 (s), 881 (s), 788 (m), 737 (s), 675 (s); HRMS (ESI/QTOF) *m/z*: [*M* + Na]⁺ Calcd for C₃₀H₅₁INaO₃SSi₂⁺ 697.2034; Found 697.2048. Chiral HPLC conditions: *ee* > 95% ; Chiralpak IC 99.95:0.05 Hexane/*i*PrOH, 1.0 mL/min, 60 min. *tr* = 9.2 min, λ = 230.4 cm⁻¹. The stereochemistry drawn is based on the assumption that the reaction proceed under inversion of configuration. **8i'**: *R_f* 0.18 (CH₂Cl₂/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H, *ArH*), 7.84 (dd, *J* = 7.8, 1.7 Hz, 1H, *ArH*), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H, *ArH*), 7.16 (td, *J* = 7.6, 1.7 Hz, 1H, *ArH*), 4.71 (dd, *J* = 11.5, 5.7 Hz, 1H, *OCH*₂), 4.60 (dd, *J* = 11.5, 6.8 Hz, 1H, *OCH*₂), 4.12 (dd, *J* = 10.3, 5.0 Hz, 1H, TIPS-*CH*₂), 4.01 (dd, *J* = 10.3, 7.2 Hz, 1H, TIPS-*CH*₂), 3.45 – 3.32 (m, 1H, *SCH*), 1.17 – 0.98 (m, 42H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 166.1, 141.5, 134.9, 132.9, 131.3, 128.1, 99.3, 94.3, 92.9, 64.0, 63.1, 49.6, 18.8, 18.1, 12.0, 11.5; IR (*v*_{max}, cm⁻¹) 2933 (s), 2864 (s), 2091 (m), 1738 (s), 1463 (m), 1286 (s), 1243 (s), 1189 (m), 1127 (s), 1099 (s), 885 (m), 741 (s), 682 (s); HRMS (ESI/QTOF) *m/z*: [*M* + Na]⁺ Calcd for C₃₀H₅₁INaO₃SSi₂⁺ 697.2034; Found 697.2048. Chiral HPLC conditions: *ee* > 95% ; Chiralpak IBN 100:0 Hexane/*i*PrOH, 1.0 mL/min, 60 min. *tr* = 15.9 min, λ = 230.4 cm⁻¹.

1,4-Bis(benzyloxy)-3-(((triisopropylsilyl)ethynyl)thio)butan-2-yl 2-iodobenzoate (**8j**)

Synthesized following **general procedure A** starting from TIPS-EBX (**6a**) (86 mg, 0.20 mmol) and 2,3-bis((benzyloxy)methyl)thiirane (**7j**) (90 mg, 0.30 mmol). The reaction was stirred at 70 °C for 48 h. The crude oil was purified by column chromatography (CH₂Cl₂/Pentane; 1:1) to afford **8j** (56 mg, 0.077 mmol, 38%) as a colorless oil. *R_f* 0.55 (AcOEt/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 7.9, 1.2 Hz, 1H, *ArH*), 7.79 (dd, *J* = 7.8, 1.7 Hz, 1H, *ArH*), 7.39 – 7.21 (m, 11H, *ArH*), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H, *ArH*), 5.76 (q, *J* = 5.1 Hz, 1H, *OCH*), 4.64 – 4.49 (m, 4H, PhCH₂O), 3.93 – 3.76 (m, 4H, OCH₂CH), 3.69 – 3.60 (m, 1H, *SCH*), 1.04 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.4, 141.4, 137.9, 137.8, 134.7, 132.9, 131.5, 128.5, 128.5, 128.0, 128.0, 127.9, 127.8, 127.8, 98.8, 94.5, 93.8, 73.7, 73.4, 72.1, 69.2, 69.0, 50.5, 18.8, 11.5; IR (ν_{max}, cm⁻¹) 2864 (m), 2359 (m), 2089 (m), 1740 (m), 1456 (m), 1238 (m), 1089 (s), 882 (m), 854 (m), 736 (s), 697 (s), 678 (s); HRMS (ESI/QTOF) *m/z*: [M + H]⁺ Calcd for C₃₆H₄₆IO₄SSi⁺ 729.1925; Found 729.1930.

2-((Phenylethynyl)thio)cyclohexyl 2-iodobenzoate (**8k**)

Synthesized following **general procedure A** starting from 1-[Phenylethynyl]-1,2-benziodoxol-3(1*H*)-one (**6k**) (70 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μL, 0.30 mmol). The reaction was stirred for 1.5 h. The crude oil was purified by column chromatography (Toluene/Pentane; 1:1) to afford **8k** (46 mg, 0.10 mmol, 50%) as an orange oil; *R_f* 0.47 (Toluene/Pentane; 1:1) ¹H NMR (400 MHz, Chloroform-*d*) δ 7.97 (dd, *J* = 8.0, 1.2 Hz, 1H, *ArH*), 7.90 (dd, *J* = 7.8, 1.7 Hz, 1H, *ArH*), 7.44 – 7.38 (m, 2H, *ArH*), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H, *ArH*), 7.30 – 7.25 (m, 3H, *ArH*), 7.12 (td, *J* = 7.7, 1.7 Hz, 1H, *ArH*), 5.14 (td, *J* = 10.0, 4.4 Hz, 1H, *OCH*), 3.08 (ddd, *J* = 11.3, 9.8, 4.2 Hz, 1H, *CHS*), 2.42 – 2.28 (m, 2H, CH₂ cyclohexyl),

1.90 – 1.76 (m, 2H, CH_2 cyclohexyl), 1.64 – 1.33 (m, 4H, CH_2 cyclohexyl); ^{13}C NMR (100 MHz, Chloroform- d) δ 165.8, 141.3, 135.5, 132.6, 131.8, 131.1, 128.4, 128.2, 128.0, 123.5, 95.3, 94.2, 76.8, 75.5, 51.1, 32.2, 32.0, 25.6, 24.0; IR (ν_{max} , cm^{-1}) 3060 (w), 2931 (m), 2855 (w), 2164 (w), 1725 (s), 1587 (w), 1440 (m), 1281 (s), 1250 (s), 1131 (m), 1100 (m), 1015 (s), 746 (s), 693 (m); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{19}\text{INaO}_2\text{S}^+$ 485.0043; Found 485.0057.

2-((*p*-Tolylethynyl)thio)cyclohexyl 2-iodobenzoate (**8l**)

Synthesized following **general procedure A** starting from 1-(*p*-Tolylethynyl)-1,2-benziodoxol-3(1H)-one (**6l**) (72 mg, 0.20 mmol, 1.0 equiv.) and cyclohexene sulfide (**7a**) (33 μL , 0.30 mmol). The reaction was stirred at 50 $^{\circ}\text{C}$ for 2 h. The crude oil was purified by column chromatography (Toluene/Pentane; 35:65) to afford **8l** (48 mg, 0.10 mmol, 50%) as a yellow oil. R_f 0.5 (Toluene/Pentane; 1:1); ^1H NMR (400 MHz, Chloroform- d) δ 7.97 (dd, $J = 8.0, 1.2$ Hz, 1H, *ArH*), 7.90 (dd, $J = 7.8, 1.7$ Hz, 1H, *ArH*), 7.40 – 7.28 (m, 3H, *ArH*), 7.16 – 7.05 (m, 3H, *ArH*), 5.13 (td, $J = 10.0, 4.4$ Hz, 1H, *OCH*), 3.12 – 3.02 (m, 1H, *SCH*), 2.42 – 2.28 (m, 5H, CH_2 cyclohexyl + PhCH_3), 1.88 – 1.78 (m, 3H, CH_2 cyclohexyl), 1.64 – 1.32 (m, 3H, CH_2 cyclohexyl); ^{13}C NMR (100 MHz, Chloroform- d) δ 165.8, 141.3, 138.5, 135.5, 132.6, 131.8, 131.1, 129.1, 128.0, 120.4, 95.4, 94.2, 75.8, 75.5, 51.1, 32.2, 32.0, 25.6, 24.0, 21.6; IR (ν_{max} , cm^{-1}) 3031 (w), 2931 (w), 2165 (w), 1723 (s), 1575 (w), 1509 (w), 1440 (m), 1281 (s), 1249 (s), 1131 (m), 1100 (s), 1014 (s), 945 (m), 818 (s), 741 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{22}\text{H}_{21}\text{INaO}_2\text{S}^+$ 499.0199; Found 499.0201.

2-(((2-Bromophenyl)ethynyl)thio)cyclohexyl 2-iodobenzoate (**8m**)

Synthesized following **general procedure A** starting from 1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1*H*)-one (**6m**) (85 mg, 0.20 mmol, 1.0 equiv.) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The reaction was stirred at 50 °C for 2 h. The crude oil was purified by column chromatography (Toluene/Pentane; 1:1) to afford **8m** (59 mg, 0.11 mmol, 54%) as a yellow oil. R_f 0.47 (Toluene/Pentane; 1:1); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.96 (dd, J = 7.9, 1.2 Hz, 1H, Ar*H*), 7.89 (dd, J = 7.8, 1.7 Hz, 1H, Ar*H*), 7.54 (dd, J = 8.0, 1.2 Hz, 1H, Ar*H*), 7.40 (dd, J = 7.7, 1.7 Hz, 1H, Ar*H*), 7.35 (td, J = 7.6, 1.2 Hz, 1H, Ar*H*), 7.22 (td, J = 7.6, 1.2 Hz, 1H, Ar*H*), 7.12 (tt, J = 7.6, 1.7 Hz, 2H, Ar*H*), 5.19 (td, J = 10.0, 4.5 Hz, 1H, OCH), 3.12 (ddd, J = 11.6, 9.9, 4.2 Hz, 1H, SCH), 2.39 (m, 2H, CH_2 cyclohexyl), 2.03 – 1.89 (m, 1H, CH_2 cyclohexyl), 1.89 – 1.79 (m, 2H, CH_2 cyclohexyl), 1.64 – 1.32 (m, 3H, CH_2 cyclohexyl); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.3, 135.5, 133.1, 132.6, 132.4, 131.2, 129.0, 128.0, 127.1, 125.7, 125.1, 94.2, 94.0, 82.4, 75.5, 51.3, 32.3, 32.0, 25.7, 24.0; IR (ν_{max} , cm^{-1}) 3060 (w), 2925 (w), 2167 (m), 1724 (s), 1577 (w), 1460 (m), 1428 (m), 1251 (s), 1129 (m), 1099 (m), 1017 (s), 943 (m), 743 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{18}\text{BrINaO}_2\text{S}^+$ 562.9148; Found 562.9151.

2-((3,3-Dimethylbut-1-yn-1-yl)thio)cyclohexyl 2-iodobenzoate (**8n**)

Synthesized following **general procedure A** starting from 1-[3,3-Dimethylbutynyl]-1,2-benziodoxol-3(1*H*)-one (**6n**) (66 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The reaction was stirred at 50 °C for 4.5 h. The crude oil was purified by column chromatography (CH_2Cl_2 /Pentane; 3:7) to afford **8n** (47 mg, 0.11 mmol, 53%) as a colorless oil. R_f 0.38 (Toluene/Pentane; 1:3); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.97 (dd, J = 8.0, 1.2

Hz, 1H, *ArH*), 7.87 (dd, $J = 7.8, 1.7$ Hz, 1H, *ArH*), 7.40 (td, $J = 7.6, 1.2$ Hz, 1H, *ArH*), 7.14 (td, $J = 7.6, 1.7$ Hz, 1H, *ArH*), 5.03 (td, $J = 9.9, 4.4$ Hz, 1H, *OCH*), 2.90 (ddd, $J = 11.2, 9.8, 4.2$ Hz, 1H, *SCH*), 2.41 – 2.30 (m, 1H, CH_2 cyclohexyl), 2.29 – 2.19 (m, 1H, CH_2 cyclohexyl), 1.88 – 1.69 (m, 3H, CH_2 cyclohexyl), 1.61 – 1.31 (m, 3H, CH_2 cyclohexyl), 1.23 (s, 9H, $\text{C}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.2, 135.8, 132.6, 131.1, 128.0, 105.0, 94.1, 75.1, 64.0, 50.1, 32.0, 31.8, 31.1, 29.0, 25.5, 24.0; IR (ν_{max} , cm^{-1}) 2975 (w), 1723 (m), 1442 (w), 1251 (s), 1097 (m), 1014 (m), 944 (m), 737 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{23}\text{INaO}_2\text{S}^+$ 465.0356; Found 465.0345.

2-((Cyclopropylethynyl)thio)cyclohexyl 2-iodobenzoate (**8o**)

Synthesized following **general procedure A** starting from 2-Cyclopropylethynyl-1,2-benziodoxol-3(1*H*)-one (**6o**) (62 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μL , 0.30 mmol). The reaction was stirred at 50 °C for 4 h. The crude oil was purified by column chromatography (Toluene/Pentane; 3:7 to 5:5) to afford **8o** (40 mg, 0.09 mmol, 47%) as a colorless oil. R_f 0.25 (Toluene/Pentane; 1:3); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.97 (dd, $J = 8.0, 1.2$ Hz, 1H, *ArH*), 7.87 (dd, $J = 7.8, 1.7$ Hz, 1H, *ArH*), 7.40 (td, $J = 7.6, 1.2$ Hz, 1H, *ArH*), 7.14 (td, $J = 7.7, 1.7$ Hz, 1H, *ArH*), 5.02 (td, $J = 9.9, 4.4$ Hz, 1H, *OCH*), 2.88 (ddd, $J = 11.3, 9.8, 4.2$ Hz, 1H, *SCH*), 2.38 – 2.29 (m, 1H, CH_2 cyclohexyl), 2.28 – 2.16 (m, 1H, CH_2 cyclohexyl), 1.86 – 1.64 (m, 3H, CH_2 cyclohexyl), 1.60 – 1.22 (m, 4H, CH_2 cyclohexyl + CH cyclopropyl), 0.82 – 0.63 (m, 4H, CH_2 cyclopropyl); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.2, 135.6, 132.6, 131.1, 128.0, 100.9, 94.2, 75.3, 61.2, 50.3, 32.0, 31.9, 25.5, 23.9, 9.2, 1.0; IR (ν_{max} , cm^{-1}) 3087 (w), 3010 (m), 2936 (m), 2171 (w), 1723 (s), 1401 (m), 1281 (m), 1250 (s), 1128 (m), 1097 (s), 1016 (s), 803 (s), 739 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{19}\text{INaO}_2\text{S}^+$ 449.0043; Found 449.0051.

2-((5-Chloropent-1-yn-1-yl)thio)cyclohexyl 2-iodobenzoate (**8p**)

Synthesized following **general procedure A** starting from (5-Chloropent-1-ynyl)-1,2-benziodoxol-3(1*H*)-one (**6p**) (70 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The reaction was stirred at rt for 24 h. The crude oil was purified by column chromatography (Toluene/Pentane; 3:7 to 5:5) to afford **8p** (28 mg, 0.061 mmol, 31%) as a colorless oil. R_f 0.15 (Toluene/Pentane; 1:3); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, J = 8.0, 1.2 Hz, 1H, Ar*H*), 7.87 (dd, J = 7.8, 1.7 Hz, 1H, Ar*H*), 7.41 (td, J = 7.6, 1.2 Hz, 1H, Ar*H*), 7.15 (td, J = 7.7, 1.7 Hz, 1H, Ar*H*), 5.05 (td, J = 9.9, 4.4 Hz, 1H, OCH), 3.64 (td, J = 6.5, 1.1 Hz, 2H, ClCH₂), 2.98 – 2.83 (m, 1H, SCH), 2.49 (t, J = 6.8 Hz, 2H, C $\equiv$ CCH₂), 2.37 – 2.29 (m, 1H, CH₂ cyclohexyl), 2.28 – 2.19 (m, 1H, CH₂ cyclohexyl), 1.94 (p, J = 6.6 Hz, 2H, CH₂CH₂CH₂Cl), 1.86 – 1.69 (m, 3H, CH₂ cyclohexyl), 1.57 – 1.31 (m, 3H, CH₂ cyclohexyl); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.3, 135.5, 132.7, 131.1, 128.0, 94.8, 94.2, 75.2, 66.9, 50.2, 43.9, 32.1, 31.8, 31.5, 25.5, 23.9, 17.8; IR (ν_{max} , cm⁻¹) 2948 (s), 2864 (m), 2090 (m), 1732 (s), 1577 (w), 1461 (m), 1281 (s), 1245 (s), 1127 (s), 1102 (m), 1016 (m), 856 (m), 676 (m); HRMS (ESI/QTOF) m/z : [M + Na]⁺ Calcd for C₁₈H₂₀ClINaO₂S⁺ 484.9809; Found 484.9801.

2-(((Triisopropylsilyl)ethynyl)thio)cyclohexyl 2-iodo-4,5-dimethoxybenzoate (**8q**)

Synthesized following **general procedure A** starting from 4,5-Dimethoxy-1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**6q**) (98 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The reaction was stirred at 50 °C for 5 h. The crude oil was purified by column chromatography (AcOEt/Pentane; 5:95) to afford **8q** (73 mg, 0.12 mmol, 61%) as a yellow oil. R_f 0.4 (AcOEt/Pentane; 1:9); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.50 (s, 1H, Ar*H*), 7.36 (s, 1H, Ar*H*), 4.98 (td, J = 10.1, 4.5 Hz, 1H, OCH),

3.90 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 3.05 – 2.92 (m, 1H, SCH), 2.44 – 2.34 (m, 1H, CH₂ cyclohexyl), 2.34 – 2.25 (m, 1H, CH₂ cyclohexyl), 1.96 – 1.74 (m, 3H, CH₂ cyclohexyl), 1.61 – 1.30 (m, 3H, CH₂ cyclohexyl), 1.06 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 164.7, 151.9, 148.8, 126.8, 123.7, 114.2, 100.1, 92.4, 84.6, 75.0, 56.4, 56.1, 50.5, 32.1, 32.0, 25.6, 24.0, 18.8, 11.5; IR (ν_{max}, cm⁻¹) 2943 (m), 2865 (w), 2085 (w), 1506 (m), 1453 (w), 1371 (m), 1334 (m), 1257 (s), 1206 (s), 1173 (s), 1110 (m), 1020 (m), 874 (m), 856 (m), 731 (m); HRMS (ESI/QTOF) *m/z*: [M + Na]⁺ Calcd for C₂₆H₃₉INaO₄SSi⁺ 625.1275; Found 625.1279.

2-(((Triisopropylsilyl)ethynyl)thio)cyclohexyl 2-iodo-5-nitrobenzoate (**8r**)

Synthesized following **general procedure A** starting from 5-Nitro-1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**6r**) (95 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μL, 0.30 mmol). The reaction was stirred at 50 °C for 3 h. The crude oil was purified by column chromatography (Toluene/Pentane; 4:6) to afford **8r** (70 mg, 0.12 mmol, 60%) as a light yellow solid. *R*_f 0.2 (Toluene/Pentane; 3:7); Mp: 92-94 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ 8.62 (d, *J* = 2.7 Hz, 1H, Ar*H*), 8.20 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.97 (dd, *J* = 8.6, 2.7 Hz, 1H, Ar*H*), 5.14 (td, *J* = 10.2, 4.5 Hz, 1H, OCH), 2.92 (ddd, *J* = 11.5, 9.9, 4.2 Hz, 1H, SCH), 2.43 – 2.24 (m, 2H, CH₂ cyclohexyl), 1.97 – 1.77 (m, 3H, CH₂ cyclohexyl), 1.65 – 1.55 (m, 1H, CH₂ cyclohexyl), 1.51 – 1.32 (m, 2H, CH₂ cyclohexyl), 1.08 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 163.8, 147.9, 142.8, 137.0, 126.3, 125.6, 102.5, 100.5, 91.9, 75.8, 50.2, 32.0, 31.9, 25.6, 24.0, 18.8, 11.5; IR (ν_{max}, cm⁻¹) 2940 (s), 2862 (s), 2089 (s), 1737 (s), 1527 (s), 1459 (m), 1348 (s), 1263 (s), 1243 (s), 1142 (s), 1116 (m), 1019 (s), 856 (s), 737 (s), 677 (s), 659 (s); HRMS (ESI/QTOF) *m/z*: [M + Na]⁺ Calcd for C₂₄H₃₄INNaO₄SSi⁺ 610.0915; Found 610.0911.

2-(((Triisopropylsilyl)ethynyl)thio)cyclohexyl 3-iodo-2-naphthoate (**8s**)

Synthesized following **general procedure A** starting from 1-((triisopropylsilyl)ethynyl)-1,2-naphthiodoxol-3-(1*H*) (**6s**) (96 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The reaction was stirred at 50 °C for 4 h. The crude oil was purified by column chromatography (Toluene/Pentane; 3:7) to afford **8s** (82 mg, 0.14 mmol, 69%) as a yellow oil. R_f 0.5 (Toluene/Pentane; 3:7); ^1H NMR (400 MHz, Chloroform-*d*) δ 8.49 (s, 1H, Ar*H*), 8.36 (s, 1H, Ar*H*), 7.92 – 7.86 (m, 1H, Ar*H*), 7.77 – 7.71 (m, 1H, Ar*H*), 7.56 (pd, J = 6.9, 1.5 Hz, 2H, Ar*H*), 5.11 (td, J = 10.1, 4.4 Hz, 1H, OCH), 3.02 (ddd, J = 11.4, 9.8, 4.2 Hz, 1H, SCH), 2.49 – 2.38 (m, 1H, CH_2 cyclohexyl), 2.38 – 2.28 (m, 1H, CH_2 cyclohexyl), 1.96 – 1.78 (m, 3H, CH_2 cyclohexyl), 1.67 – 1.55 (m, 1H, CH_2 cyclohexyl), 1.52 – 1.35 (m, 2H, CH_2 cyclohexyl), 1.15 – 0.99 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.8, 140.7, 135.8, 131.9, 131.8, 131.6, 129.0, 128.8, 127.4, 126.7, 100.1, 92.5, 88.8, 75.1, 50.5, 32.0, 32.0, 25.6, 24.0, 18.8, 11.5; IR (ν_{max} , cm^{-1}) 2940 (s), 2863 (s), 2089 (m), 1731 (s), 1622 (s), 1611 (s), 1462 (m), 1449 (m), 1276 (s), 1264 (s), 1197 (s), 1103 (s), 1015 (m), 882 (s), 744 (s), 707 (s), 677 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{28}\text{H}_{37}\text{INaO}_2\text{SSi}^+$ 615.1220; Found 615.1227.

2-(((*E*)-2-Cyclohexylvinyl)thio)cyclohexyl 2-iodobenzoate (**8t**)

Synthesized following **general procedure A** starting from (*E*)-1-(2-cyclohexylvinyl)-1,2-benziodoxol-3(1*H*)-one (**6t**) (71 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The crude oil was purified by column chromatography (Toluene/Pentane; 1:1) to afford **8t** (29 mg, 0.062 mmol, 31%) as a colorless oil. R_f 0.53 (Toluene/Pentane; 1:1); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, J = 8.0, 1.2 Hz, 1H, Ar*H*), 7.84 (dd, J = 7.8, 1.8 Hz, 1H, Ar*H*), 7.39 (td, J = 7.6, 1.2 Hz, 1H, Ar*H*), 7.14 (td, J = 7.6, 1.8 Hz, 1H, Ar*H*), 5.95 (dd, J = 15.1, 1.2 Hz, 1H, CH=CHS), 5.73 (dd, J = 15.2, 6.8 Hz, 1H, CH=CHS), 5.01 (td, J = 9.3, 4.2 Hz, 1H,

OCH), 2.95 (ddd, $J = 10.6, 9.1, 4.1$ Hz, 1H, CHS), 2.31 – 2.21 (m, 1H, CH₂ cyclohexyl), 2.20 – 2.11 (m, 1H, CH₂ cyclohexyl), 1.97 – 1.85 (m, 1H, CH cyclohexyl), 1.84 – 1.71 (m, 2H, CH₂ cyclohexyl), 1.71 – 1.50 (m, 7H, CH₂ cyclohexyl), 1.50 – 1.31 (m, 2H, CH₂ cyclohexyl), 1.30 – 1.06 (m, 3H, CH₂ cyclohexyl), 1.06 – 0.92 (m, 2H, CH₂ cyclohexyl); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.9, 141.3, 140.7, 135.8, 132.5, 131.1, 128.0, 118.7, 94.2, 76.5, 48.7, 41.5, 32.8, 31.6, 31.2, 26.2, 26.1, 25.1, 23.7; IR ($\nu_{\max}$, cm⁻¹) 2924 (s), 2853 (m), 1727 (s), 1574 (w), 1453 (m), 1440 (m), 1285 (s), 1246 (s), 1132 (s), 1099 (m), 1011 (m), 946 (m), 741 (s); HRMS (ESI/QTOF) m/z : [M + Na]⁺ Calcd for C₂₁H₂₇INaO₂S⁺ 493.0669; Found 493.0680.

(*E*)-2-(Styrylthio)cyclohexyl 2-iodobenzoate (8u**)**

Synthesized following **general procedure A** starting from (*E*)-1-styryl-1,2-benziodoxol-3(1*H*)-one (**6u**) (70 mg, 0.20 mmol) and cyclohexene sulfide (**7a**) (33 μ L, 0.30 mmol). The reaction was stirred at 70 °C for 16 h. The crude oil was purified by column chromatography (AcOEt/Pentane; 5:95) to afford **8u** (33 mg, 0.071 mmol, 36%) as a colorless oil. R_f 0.34 (Toluene/Pentane; 1:1); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.90 (dd, $J = 7.9, 1.2$ Hz, 1H, ArH), 7.75 (dd, $J = 7.8, 1.7$ Hz, 1H, ArH), 7.26 – 7.14 (m, 6H, ArH), 7.04 (td, $J = 7.6, 1.7$ Hz, 1H, ArH), 6.79 (d, $J = 15.6$ Hz, 1H, CH=CHPh), 6.59 (d, $J = 15.6$ Hz, 1H, CH=CHPh), 5.10 (td, $J = 9.4, 4.2$ Hz, 1H, OCH), 3.16 (ddd, $J = 10.9, 9.1, 4.1$ Hz, 1H, SCH), 2.35 – 2.20 (m, 2H, CH₂ cyclohexyl), 1.89 – 1.74 (m, 2H, CH₂ cyclohexyl), 1.68 – 1.52 (m, 2H, CH₂ cyclohexyl), 1.51 – 1.36 (m, 2H, CH₂ cyclohexyl); ¹³C NMR (100 MHz, Chloroform-*d*) δ 166.0, 141.2, 136.9, 135.5, 132.5, 131.0, 129.6, 128.6, 127.9, 127.1, 125.8, 124.1, 94.1, 77.2, 49.3, 31.8, 31.4, 25.2, 23.8; IR ($\nu_{\max}$, cm⁻¹) 2932 (m), 2861 (m), 2089 (m), 1726 (s), 1592 (m), 1457 (m), 1281 (s), 1248 (s), 1104 (m), 1010 (m), 943 (m), 858 (m), 741 (s); HRMS (ESI/QTOF) m/z : [M + Na]⁺ Calcd for C₂₁H₂₁INaO₂S⁺ 487.0199; Found 487.0205.

General procedure B: Oxy-alkynylation of thiethanes

To a microwave vial containing 1-[(*triisopropylsilyl*)ethynyl]-1,2-benziodoxol-3(1H)-one (**6a**) (0.20 mmol, 1 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (6.3 mg, 20 μmol , 0.1 equiv.) under N_2 atmosphere. The tube was sealed, DCE (2.5 mL) and a solution of thietane (**9**) (0.30 mmol, 1.5 equiv.) in DCE (0.5 mL) were added under N_2 atmosphere. The resulting mixture was stirred at 70 °C for 48 h (unless otherwise indicated). The reaction was cooled to rt and concentrated *in vacuo*. The crude product was purified as described.

3-(((Triisopropylsilyl)ethynyl)thio)propyl 2-iodobenzoate (**10a**)

Synthesized following **general procedure B** starting from trimethylene sulfide (**9a**) (23 μL , 0.30 mmol). The crude oil was purified by column chromatography (Toluene/Pentane; 3:7) to afford **10a** (44 mg, 0.088 mmol, 44%) as a colorless oil. R_f 0.3 (Toluene/Pentane; 1:3); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, $J = 7.9, 1.2$ Hz, 1H, Ar*H*), 7.77 (dd, $J = 7.8, 1.7$ Hz, 1H, Ar*H*), 7.40 (td, $J = 7.6, 1.2$ Hz, 1H, Ar*H*), 7.16 (td, $J = 7.7, 1.7$ Hz, 1H, Ar*H*), 4.49 (t, $J = 6.0$ Hz, 2H, OCH_2), 2.90 (t, $J = 7.0$ Hz, 2H, CH_2S), 2.27 (q, $J = 6.1$ Hz, 2H, CH_2 aliphatic), 1.06 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.6, 141.4, 135.4, 132.8, 131.1, 128.1, 98.0, 95.0, 94.1, 63.7, 32.4, 28.2, 18.8, 11.5; IR (ν_{max} , cm^{-1}) 2953 (m), 2861 (m), 2091 (m), 1728 (s), 1464 (m), 1430 (m), 1285 (s), 1248 (s), 1129 (s), 1009 (m), 882 (m), 857 (m), 741 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{31}\text{INaO}_2\text{SSi}^+$ 525.0751; Found 525.0758.

2-Phenyl-3-(((triisopropylsilyl)ethynyl)thio)propyl 2-iodobenzoate (**10b**)

Synthesized following **general procedure B** starting from 3-phenylthietane (**9b**) (45 mg, 0.30 mmol). The crude oil was purified by column chromatography (Toluene/Pentane; 1:1) to afford **10b** (52 mg, 0.090 mmol, 45%) as an orange oil. R_f 0.53 (Toluene/Pentane; 1:1); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, $J = 7.9, 1.2$ Hz, 1H, ArH), 7.65 (dd, $J = 7.8, 1.7$ Hz, 1H, ArH), 7.41 – 7.31 (m, 3H, ArH), 7.33 – 7.25 (m, 3H, ArH), 7.14 (td, $J = 7.7, 1.7$ Hz, 1H, ArH), 4.73 – 4.58 (m, 2H, OCH₂), 3.60 (p, $J = 6.9$ Hz, 1H, PhCH), 3.27 (dd, $J = 13.0, 7.2$ Hz, 1H, SCH₂), 3.06 (dd, $J = 13.0, 7.8$ Hz, 1H, SCH₂), 1.14 – 1.00 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.3, 141.5, 139.7, 135.0, 132.8, 131.1, 128.9, 128.1, 128.0, 127.7, 98.2, 95.0, 94.2, 67.6, 44.1, 38.6, 18.8, 11.5; IR (ν_{max} , cm⁻¹) 2947 (m), 2865 (m), 2088 (s), 1728 (s), 1589 (w), 1460 (m), 1283 (s), 1248 (s), 1102 (s), 1017 (m), 857 (m), 743 (s); HRMS (ESI/QTOF) m/z : [M + Na]⁺ Calcd for C₂₇H₃₅INaO₂SSi⁺ 601.1064; Found 601.1071.

(2,2-Dimethyl-5-((((triisopropylsilyl)ethynyl)thio)methyl)-1,3-dioxan-5-yl)methyl 2-iodobenzoate (10c)

Synthesized following **general procedure B** starting from 7,7-dimethyl-6,8-dioxaspiro[3.5]nonane (**9c**) (52 mg, 0.30 mmol). The reaction was stirred at 70 °C for 60 h. The crude oil was purified by column chromatography (AcOEt/Pentane; 5:95) to afford **10c** (80 mg, 0.13 mmol, 66%) as an orange oil. R_f 0.5 (AcOEt/Pentane; 1:9); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, $J = 7.9, 1.2$ Hz, 1H, ArH), 7.76 (dd, $J = 7.8, 1.7$ Hz, 1H, ArH), 7.40 (td, $J = 7.6, 1.2$ Hz, 1H, ArH), 7.16 (td, $J = 7.7, 1.7$ Hz, 1H, ArH), 4.54 (s, 2H, COOCH₂), 3.97 (d, $J = 12.1$ Hz, 2H, OCH₂), 3.87 (d, $J = 12.0$ Hz, 2H, OCH₂), 3.04 (s, 2H, SCH₂), 1.44 (s, 3H, CCH₃), 1.43 (s, 3H, CCH₃), 1.04 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.4, 141.5, 135.3, 132.9, 131.2, 128.1, 98.7, 96.9, 96.3, 94.0, 65.7, 64.1, 39.3, 38.9, 25.3, 22.2, 18.7, 11.4; IR (ν_{max} , cm⁻¹) 2995 (m), 2948 (m), 2871 (m), 2089 (m), 1732 (m), 1462 (w), 1380 (m), 1246 (m), 1080 (m), 854 (m), 737 (s); HRMS (ESI/QTOF) m/z : [M + Na]⁺ Calcd for C₂₆H₃₉INaO₄SSi⁺ 625.1275; Found 625.1286.

(3-(((Triisopropylsilyl)ethynyl)thio)methyl)oxetan-3-yl)methyl 2-iodobenzoate (10d)

Synthesized following **general procedure B** starting from 2-oxa-6-thiaspiro[3.3]heptane (**9d**) (35 mg, 0.30 mmol). The crude oil was purified by column chromatography (AcOEt/PE; 1:9) to afford **10d** (60 mg, 0.11 mmol, 55%) as a colorless oil. R_f 0.33 (AcOEt/Pentane; 1:9); ^1H NMR (400 MHz, Chloroform- d) δ 7.99 (dd, $J = 8.0, 1.1$ Hz, 1H, ArH), 7.77 (dd, $J = 7.8, 1.7$ Hz, 1H, ArH), 7.41 (td, $J = 7.6, 1.2$ Hz, 1H, ArH), 7.17 (td, $J = 7.7, 1.7$ Hz, 1H, ArH), 4.77 (s, 2H, COOCH₂), 4.72 (d, $J = 6.6$ Hz, 2H, OCH₂), 4.61 (d, $J = 6.6$ Hz, 2H, OCH₂), 3.30 (s, 2H, SCH₂), 1.09 – 1.00 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform- d) δ 166.5, 141.5, 135.2, 133.0, 131.3, 128.1, 98.1, 94.8, 94.0, 77.8, 67.0, 44.2, 40.1, 18.7, 11.4; IR (ν_{max} , cm⁻¹) 2952 (m), 2871 (m), 2089 (w), 1733 (m), 1464 (m), 1422 (m), 1286 (s), 1243 (s), 1129 (m), 984 (m), 855 (m), 738 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for C₂₃H₃₄IO₃SSi⁺ 545.1037; Found 545.1044.

4-(((Triisopropylsilyl)ethynyl)thio)butyl 2-iodobenzoate (10e)

To a microwave vial containing TIPS-EBX (**6a**) (86.0 mg, 0.20 mmol, 1.0 equiv.) was added Cu(CH₃CN)₄BF₄ (6.3 mg, 0.020 mmol, 0.1 equiv.) under N₂ atmosphere. The vial was sealed then DCE (3 mL) and tetrahydrothiophene (**9e**) (27 μL , 0.30 mmol, 1.5 equiv.) were added under N₂ atmosphere. The resulting mixture was stirred at 100 °C under microwave irradiation for 24 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude oil was purified by column chromatography (CH₂Cl₂/Pentane; 2:8) to afford **10e** (40 mg, 0.077 mmol, 39%) as a colorless oil. R_f 0.28 (Toluene/Pentane; 1:3); ^1H NMR (400 MHz, Chloroform- d) δ 7.99 (dd, $J = 7.9, 1.2$ Hz, 1H, ArH), 7.78 (dd, $J = 7.8, 1.7$ Hz, 1H, ArH), 7.40 (td, $J = 7.6, 1.2$ Hz, 1H, ArH), 7.15 (td, $J = 7.7, 1.7$ Hz, 1H, ArH), 4.44 – 4.31 (m, 2H, OCH₂), 2.87 – 2.74 (m, 2H,

SCH₂), 2.04 – 1.89 (m, 4H, CH₂ aliphatic), 1.05 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 166.7, 141.4, 135.4, 132.7, 131.0, 128.0, 97.6, 95.5, 94.2, 65.2, 35.4, 27.3, 25.9, 18.7, 11.4; IR (ν_{max}, cm⁻¹) 2954 (m), 2869 (m), 2088 (s), 1722 (m), 1464 (m), 1288 (m), 1248 (m), 1128 (m), 996 (m), 856 (s), 741 (s); HRMS (ESI/QTOF) m/z: [M + Ag]⁺ Calcd for C₂₂H₃₃AgIO₂SSi⁺ 623.0061; Found 623.0073.

7. Product modifications

Sonogashira cross-coupling

Compound **11** was synthesized following an adapted version of a reported procedure.²² To a microwave vial containing 2-(((triisopropylsilyl)ethynyl)thio)cyclohexyl 2-iodobenzoate (**8a**) (50 mg, 92 μ mol, 1.0 equiv.) and 2-ethynylnaphthalene (**58**) (28 mg, 0.18 mmol, 2.0 equiv.) were added CuI (3.5 mg, 18 μ mol, 0.2 equiv.) and Pd(PPh₃)₂Cl₂ (6.5 mg, 9.2 μ mol, 0.1 equiv.) under N₂ atmosphere. The vial was sealed and degassed trimethylamine (3.1 mL) was added under N₂ atmosphere. The reaction was heated at 40 °C for 2.5 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude solid was dissolved in CH₃Cl and filtered over MgSO₄. The filtrate was successively extracted with 15 mL of a 1 M aq. sol. of HCl and 15 mL of brine. Combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (CH₂Cl₂/Pentane; 1:9 to 2:8) to afford 2-(((triisopropylsilyl)ethynyl)thio)cyclohexyl 2-(naphthalen-2-ylethynyl)benzoate (**11**) (36 mg, 63 μ mol, 68%) as a yellow oil. R_f 0.45 (Toluene/Pentane; 1:3); ¹H NMR (400 MHz, Chloroform-*d*) δ 8.09 (s, 1H, ArH), 8.04 (dd, *J* = 7.9, 1.4 Hz, 1H, ArH), 7.86 – 7.80 (m, 3H, ArH), 7.69 (dd, *J* = 7.7, 1.3 Hz, 1H, ArH), 7.62 (dd, *J* = 8.5, 1.6 Hz, 1H, ArH), 7.55 – 7.47 (m, 3H, ArH), 7.40 (td, *J* = 7.7, 1.4 Hz, 1H, ArH), 5.12 (td, *J* = 9.8, 4.4 Hz, 1H, OCH), 3.00 (ddd, *J* = 11.0, 9.6, 4.2 Hz, 1H, SCH), 2.44 – 2.34 (m, 1H, CH₂ cyclohexyl), 2.34 – 2.24 (m, 1H, CH₂ cyclohexyl), 1.91 – 1.75 (m, 3H, CH₂ cyclohexyl), 1.60 – 1.30 (m, 3H, CH₂ cyclohexyl), 1.07 (s, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.1, 134.3, 133.2, 133.1, 132.2, 131.7, 131.7, 130.7, 128.6, 128.1, 128.1, 128.0, 127.9, 126.9, 126.7, 123.9, 120.9, 99.8, 94.8, 92.9,

²² N. Zhou, L. Wang, D. W. Thompson, Y. Zhao, *Org. Lett.* **2008**, *10*, 3001–3004.

88.9, 74.4, 50.5, 31.9, 31.7, 25.4, 23.9, 18.8, 11.5; IR ($\nu_{\max}$, cm^{-1}) 3058 (m), 2936 (s), 2859 (m), 2211 (w), 2085 (m), 1718 (s), 1598 (w), 1495 (m), 1451 (m), 1246 (s), 1139 (m), 1067 (s), 857 (m), 814 (m), 750 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{36}\text{H}_{43}\text{O}_2\text{SSi}^+$ 567.2748; Found 567.2754.

Saponification

Alcohol **12** was synthesized following an adapted version of a reported procedure.⁸ To a microwave vial containing 2-(((triisopropylsilyl)ethynyl)thio)cyclohexyl 2-iodobenzoate (**8a**) (50.0 mg, 92 μmol , 1.0 equiv.) and K_2CO_3 (31.8 mg, 0.230 mmol, 2.5 equiv.) was added EtOH (0.92 mL). The vial was sealed and the reaction was stirred at 45 °C for 30 h. The mixture was cooled to rt and concentrated *in vacuo*. The crude product was purified by column chromatography (Toluene/Pentane; 1:1 then AcOEt/Pentane; 5:95) to afford 2-(((triisopropylsilyl)ethynyl)thio)cyclohexan-1-ol (**12**) (24.9 mg, 80 μmol , 86%) as a colourless oil. R_f 0.53 (AcOEt/Pentane; 1:9); ^1H NMR (400 MHz, Chloroform- d) δ 3.63 (td, $J = 10.0, 4.4$ Hz, 1H, OCH), 2.70 (s, 1H, OH), 2.49 (ddd, $J = 11.9, 9.5, 4.1$ Hz, 1H, SCH), 2.20 – 2.05 (m, 2H, CH_2 cyclohexyl), 1.83 – 1.72 (m, 3H, CH_2 cyclohexyl), 1.43 – 1.20 (m, 3H, CH_2 cyclohexyl), 1.07 (m, 21H, TIPS); ^{13}C NMR (100 MHz, Chloroform- d) δ 99.5, 91.8, 71.6, 55.3, 33.9, 31.7, 26.3, 24.5, 18.8, 11.5; IR ($\nu_{\max}$, cm^{-1}) 3411 (w), 2935 (s), 2864 (m), 2087 (m), 1461 (m), 1224 (m), 1195 (m), 1068 (s), 857 (s); HRMS (ESI/QTOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{33}\text{OSSi}^+$ 313.2016; Found 313.2013.

TIPS deprotection

Terminal alkyne **13** was synthesized following an adapted version of a reported procedure.⁸ A microwave vial containing a solution of 2-(((triisopropylsilyl)ethynyl)thio)cyclohexyl 2-iodobenzoate (**8a**) (0.4 g, 0.74 mmol, 1.0 equiv.) in THF (9.2 mL) was cooled to 0 °C. Then, a 1 M solution of TBAF in THF was added (0.89 mL, 0.89 mmol, 1.2 equiv.) and the mixture was stirred at 0 °C for 1 h. The reaction was allowed to warm to rt and quenched by the addition of 20 mL of a sat. sol. of NH₄Cl. The mixture was extracted with 3 x 20 mL of Et₂O, combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude compound was purified by column chromatography (AcOEt/Pentane; 3:97) to afford 2-(ethynylthio)cyclohexyl 2-iodobenzoate (**13**) (0.27 g, 0.71 mmol, 97%) as a brown oil.. R_f 0.15 (Toluene/Pentane; 1:3); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.86 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 7.40 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.07 (td, *J* = 10.0, 4.4 Hz, 1H, OCH), 2.99 (ddd, *J* = 11.1, 9.8, 4.2 Hz, 1H, SCH), 2.85 (s, 1H, C≡CH), 2.41 – 2.23 (m, 2H, CH₂ cyclohexyl), 1.89 – 1.77 (m, 3H, CH₂ cyclohexyl), 1.62 – 1.33 (m, 3H, CH₂ cyclohexyl); ¹³C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.3, 135.4, 132.7, 131.1, 128.0, 94.2, 84.5, 75.0, 71.7, 50.2, 31.9, 31.9, 25.5, 23.9; IR (ν_{max}, cm⁻¹) 3285 (m), 2938 (m), 2861 (w), 1726 (s), 1284 (s), 1252 (s), 1132 (m), 1103 (s), 1039 (m), 1015 (m), 743 (s); HRMS (ESI/QTOF) *m/z*: [M + Na]⁺ Calcd for C₁₅H₁₅INaO₂S⁺ 408.9730; Found 408.9731.

CuAAC

Triazole **14** was synthesized following an adapted version of a reported procedure.¹² A microwave vial containing 2-(ethynylthio)cyclohexyl 2-iodobenzoate (**13**) (77 mg, 0.20 mmol, 1.0 equiv.) in a mixture of CHCl₃ (3.1 mL) and water (0.2 mL) were added Cu(H₂O)₅SO₄ (5.0 mg, 0.020 mmol, 0.1 equiv.), sodium ascorbate (7.9 mg, 0.040 mmol, 0.2 equiv.) and BnN₃ (32 μL, 0.24 mmol, 1.2 equiv.). The vial was sealed and the reaction was stirred at rt for 24 h. The mixture was diluted with 2 mL of water then extracted with 3 x 2 mL of CH₂Cl₂. Combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product

was purified by column chromatography (AcOEt/Pentane; 0:1 to 3:7) to afford 2-((1-benzyl-1*H*-1,2,3-triazol-4-yl)thio)cyclohexyl 2-iodobenzoate (**14**) (84 mg, 0.16 mmol, 80%) as a colorless oil. R_f 0.22 (AcOEt/Pentane; 1:9); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, J = 8.0, 1.2 Hz, 1H, Ar*H*), 7.78 (dd, J = 7.8, 1.7 Hz, 1H, Ar*H*), 7.56 (s, 1H, C=CH), 7.42 – 7.30 (m, 4H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 7.14 (td, J = 7.7, 1.7 Hz, 1H, Ar*H*), 5.44 (d, J = 14.8 Hz, 1H, PhCH₂), 5.39 (d, J = 14.8 Hz, 1H, PhCH₂), 4.89 (td, J = 9.9, 4.4 Hz, 1H, OCH), 3.18 (ddd, J = 11.2, 9.6, 4.1 Hz, 1H, SCH), 2.31 – 2.12 (m, 2H, CH₂ cyclohexyl), 1.84 – 1.69 (m, 2H, CH₂ cyclohexyl), 1.63 – 1.41 (m, 2H, CH₂ cyclohexyl), 1.40 – 1.27 (m, 2H, CH₂ cyclohexyl); ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.8, 141.4, 137.4, 135.2, 134.3, 132.8, 131.2, 129.3, 128.9, 128.2, 128.1, 128.0, 94.3, 75.7, 54.4, 50.5, 32.3, 31.7, 25.4, 23.9; IR (ν_{max} , cm⁻¹) 2934 (w), 2359 (w), 2093 (m), 1720 (m), 1448 (m), 1429 (m), 1290 (s), 1252 (s), 1193 (m), 1139 (s), 1099 (s), 1042 (s), 1014 (s), 742 (s), 722 (s); HRMS (ESI/QTOF) m/z : [M + H]⁺ Calcd for C₂₂H₂₃IN₃O₂S⁺ 520.0550; Found 520.0558.

Large scale experiment

To a round bottom flask containing 1-[phenylethynyl]-1,2-benziodoxol-3(1*H*)-one (**6k**) (696 mg, 2.00 mmol, 1.0 equiv.) was added Cu(CH₃CN)₄BF₄ (62.9 mg, 0.200 mmol, 0.1 equiv.) under N₂ atmosphere. Then, DCE (30 mL) and cyclohexene sulfide (**7a**) (0.33 mL, 3.0 mmol, 1.5 equiv.) were added under N₂ atmosphere. The resulting mixture was stirred at 50 °C for 3 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude oil was purified by column chromatography (Toluene/Pentane; 1:1) to afford **8k** (503 mg, 1.09 mmol, 54%) as an orange oil.

Thioalkyne hydration

Thioester **15** was synthesized following an adapted version of a reported procedure.²³ To a microwave vial containing a solution of 2-((phenylethynyl)thio)cyclohexyl 2-iodobenzoate (**8k**) (0.14 g, 0.30 mmol, 1.0 equiv.) in CH₂Cl₂ (1.5 mL) were added PTSA (57 mg, 0.30 mmol, 1.0 equiv.) and SiO₂ (0.27 g, 4.5 mmol, 15.0 equiv.). The vial was sealed and the reaction was stirred at 40 °C for 24 h. The reaction was cooled to rt and the silica was filtrated and rinsed with AcOEt. The resulting solution was concentrated *in vacuo*. The crude product was purified by column chromatography (AcOEt/Pentane; 5:95) to afford 2-((2-phenylacetyl)thio)cyclohexyl 2-iodobenzoate (**15**) (0.12 g, 0.25 mmol, 83%) as an orange oil. *R*_f 0.45 (AcOEt/Pentane; 1:9); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 7.9 Hz, 1H, *ArH*), 7.63 (dd, *J* = 7.8, 1.7 Hz, 1H, *ArH*), 7.31 – 7.15 (m, 6H, *ArH*), 7.12 (t, *J* = 7.7, 1.7 Hz, 1H, *ArH*), 4.96 (td, *J* = 9.9, 4.2 Hz, 1H, *OCH*), 3.82 – 3.69 (m, 3H, *SCH* + *PhCH*₂), 2.23 – 2.07 (m, 2H, *CH*₂ cyclohexyl), 1.87 – 1.77 (m, 1H, *CH*₂ cyclohexyl), 1.76 – 1.67 (m, 1H, *CH*₂ cyclohexyl), 1.66 – 1.50 (m, 2H, *CH*₂ cyclohexyl), 1.49 – 1.36 (m, 2H, *CH*₂ cyclohexyl); ¹³C NMR (100 MHz, Chloroform-*d*) δ 196.4, 165.5, 141.5, 134.5, 133.5, 132.8, 131.2, 129.6, 128.7, 128.0, 127.5, 94.5, 74.9, 50.8, 46.1, 32.3, 31.9, 25.4, 23.8; IR (*v*_{max}, cm⁻¹) 3060 (w), 2933 (m), 1721 (s), 1688 (s), 1439 (m), 1282 (s), 1250 (s), 1137 (m), 1101 (m), 1011 (s), 712 (s); HRMS (ESI/QTOF) *m/z*: [*M* + Na]⁺ Calcd for C₂₁H₂₁INaO₃S⁺ 503.0148; Found 503.0161.

²³ A. L. Braga, T. L. C. Martins, C. C. Silveira, O. E. D. Rodrigues, *Tetrahedron* **2001**, 57, 3297–3300.

8. Control experiments

Ring opening of thiirane without copper in the presence of a carboxylic acid

To a microwave vial containing sodium benzoate (14.0 mg, 0.100 mmol, 1.0 equiv.) or benzoic acid (12.2 mg, 0.100 mmol, 1.0 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N_2 atmosphere. The vial was sealed then CD_2Cl_2 (1.5 mL) and cyclohexene sulfide (**7a**) (16 μL , 0.15 mmol, 1.5 equiv.) were added under N_2 atmosphere. The resulting mixture was stirred at rt for 72 h. No trace of the expected product was observed, only unreacted starting material.

Oxy-alkynylation of cyclohexene oxide (**17**)

To a microwave vial containing TIPS-EBX (**6a**) (43.0 mg, 0.100 mmol, 1.0 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N_2 atmosphere. The vial was sealed then DCE (1.5 mL) and cyclohexene oxide (**17**) (15 μL , 0.15 mmol, 1.5 equiv.) were added under N_2 atmosphere. The reaction was stirred at 50 °C for 48 h. No trace of the expected product was observed, only unreacted starting material.

Oxy-alkynylation with iodonium salt

To a microwave vial containing phenyl((triisopropylsilyl)ethynyl)iodonium trifluoromethanesulfonate (**6v**) (53.0 mg, 0.100 mmol, 1.0 equiv.) and cesium benzoate (25.0 mg, 0.100 mmol, 1.0 equiv.) or benzoic acid (12.0 mg, 0.100 mmol, 1.0 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N_2 atmosphere. The vial was sealed then DCE (1.5 mL) and cyclohexene sulfide (**7a**) (16 μL , 0.15 mmol, 1.5 equiv.) were added under N_2 atmosphere. The reaction was stirred at 50 °C for 6 h. Only traces of the desired product **19** could be detected by NMR.

Oxy-Alkynylation in the presence of TEMPO

To a microwave vial containing TIPS-EBX (**6a**) (43.0 mg, 0.100 mmol, 1.0 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N_2 atmosphere. The vial was sealed then DCE (1.0 mL), cyclohexene sulfide (**7a**) (16 μL , 0.15 mmol, 1.5 equiv.) and a solution of TEMPO (15.9 mg, 0.100 mmol, 1.0 equiv.) in DCE (0.5 mL) were added under N_2 atmosphere. The reaction was stirred at 50 °C for 4 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude oil was purified by preparative TLC (Toluene/Pentane; 1:3) to afford **8a** as a colorless oil (15 mg, 0.027 mmol, 27%).

Oxy-alkynylation of benzyl sulfide (20)

To a microwave vial containing TIPS-EBX (**6a**) (86.0 mg, 0.200 mmol, 1.0 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (6.3 mg, 0.020 mmol, 0.1 equiv.) under N_2 atmosphere. The vial was sealed then DCE (2.5 mL) and a solution of benzyl sulfide (**20**) (64.3 mg, 0.300 mmol, 1.5 equiv.) in DCE (0.5 mL) were added under N_2 atmosphere. The reaction was stirred at 100 °C under microwave irradiation for 24 h. The reaction was cooled to rt and concentrated *in vacuo*. The

crude oil was purified by column chromatography (Toluene/Pentane; 0:1 to 1:1) to afford ((benzylthio)ethynyl)triisopropylsilane (**21a**) (21 mg, 0.068 mmol, 34%) and benzyl 2-iodobenzoate (**21b**) (26 mg, 0.078 mmol, 39%) as colourless oils. **21a**: ^1H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 5H, ArH), 3.94 (s, 2H, PhCH₂), 1.07 – 0.99 (m, 21H, TIPS). Spectroscopic data was consistent with the values reported in literature.¹² **21b**: ^1H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H, ArH), 7.82 (dd, *J* = 7.8, 1.7 Hz, 1H, ArH), 7.51 – 7.44 (m, 2H, ArH), 7.44 – 7.32 (m, 4H, ArH), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H, ArH), 5.38 (s, 2H, PhCH₂). Spectroscopic data was consistent with the values reported in literature.²⁴

Competitive experiment

To a microwave vial containing 1-[phenylethynyl]-1,2-benziodoxol-3(1*H*)-one (**6k**) (34.8 mg, 0.100 mmol, 0.5 equiv.) and 4,5-dimethoxy-1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**6q**) (48.8 mg, 0.100 mmol, 0.5 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (6.3 mg, 0.020 mmol, 0.1 equiv.) under N₂ atmosphere. The vial was sealed then DCE (3 mL) and cyclohexene sulfide (**7a**) (33 μL , 0.30 mmol, 1.5 equiv.) were added under N₂ atmosphere. The reaction was stirred at 50 °C for 4.5 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude oil was purified by column chromatography (Toluene/Pentane; 0:1 to 1:1 then AcOEt/Pentane; 5:95 to 10:90) to afford **8a** (14 mg, 0.025 mmol, 13%), **8k** (18 mg, 0.039 mmol, 19%), **8q** (28 mg, 0.046 mmol, 23%) and **8v** (13 mg, 0.024 mmol, 12%). **8v**: *R*_f 0.2 (AcOEt/Pentane; 1:9); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.52 (s, 1H, ArH), 7.40 – 7.36 (m, 2H, ArH), 7.35 (s, 1H,

²⁴ W. G. Whitehurst, J. H. Blackwell, G. N. Hermann, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2019**, *58*, 9054–9059.

ArH), 7.27 (d, $J = 2.7$ Hz, 3H, ArH), 5.09 (td, $J = 10.1, 4.4$ Hz, 1H, OCH), 3.90 (s, 3H, OCH₃), 3.87 (s, 3H, OCH₃), 3.13 (ddd, $J = 11.3, 9.9, 4.2$ Hz, 1H, SCH), 2.42 – 2.28 (m, 2H, CH₂ cyclohexyl), 1.91 – 1.77 (m, 3H, CH₂ cyclohexyl), 1.68 – 1.31 (m, 3H, CH₂ cyclohexyl); ¹³C NMR (100 MHz, Chloroform-*d*) δ 164.9, 152.0, 148.8, 131.7, 128.3, 128.2, 126.7, 123.7, 123.5, 114.3, 95.3, 84.7, 76.7, 75.5, 56.4, 56.1, 51.1, 32.3, 32.1, 25.7, 24.0; IR ($\nu_{\max}$, cm⁻¹) 2937 (m), 2853 (w), 2108 (m), 1714 (m), 1595 (w), 1506 (m), 1444 (w), 1370 (m), 1337 (m), 1263 (s), 1207 (s), 1177 (s), 1111 (w), 1028 (m), 917 (m), 762 (m); HRMS (ESI/QTOF) m/z : [M + Na]⁺ Calcd for C₂₃H₂₃INaO₄S⁺ 545.0254; Found 545.0270.

Addition of an external nucleophile

To a microwave vial containing TIPS-EBX (**6a**) (43.0 mg, 0.100 mmol, 1.0 equiv.) was added Cu(CH₃CN)₄BF₄ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N₂ atmosphere. The vial was sealed then DCE (1.5 mL), cyclohexene sulfide (**7a**) (16 μ L, 0.15 mmol, 1.5 equiv.) and MeOH (41 μ L, 1.0 mmol, 10.0 equiv.) were added under N₂ atmosphere. The reaction was stirred at 50 °C for 3 h. The reaction was cooled to rt and concentrated *in vacuo*. The crude oil was purified by column chromatography (Toluene/Pentane; 1:4) to afford **8a** (25 mg, 0.046 mmol, 46%) and **8w** (5.0 mg, 0.016 mmol, 16%) as a colorless oil. **8w**: R_f 0.21 (Toluene/Pentane; 3:7); ¹H NMR (400 MHz, Chloroform-*d*) δ 3.44 (s, 3H, OCH₃), 3.20 (td, $J = 9.2, 4.3$ Hz, 1H, OCH), 2.75 – 2.65 (m, 1H, SCH), 2.25 – 2.14 (m, 2H, CH₂ cyclohexyl), 1.82 – 1.65 (m, 3H, CH₂ cyclohexyl), 1.38 – 1.18 (m, 3H, CH₂ cyclohexyl), 1.11 – 1.03 (m, 21H, TIPS); ¹³C NMR (100 MHz, Chloroform-*d*) δ 99.0, 94.1, 80.3, 57.4, 51.8, 31.9, 31.0, 25.6, 24.0, 18.8, 11.5; IR ($\nu_{\max}$, cm⁻¹) 2935 (s), 2862 (s), 2088 (s), 1738 (s), 1529 (s), 1461 (m), 1451 (m), 1349 (m), 1263 (s), 1243 (s), 1118 (s), 1099 (s), 1019 (s), 858 (s), 737 (s), 676 (s), 660 (s); HRMS (ESI/QTOF) m/z : [M + Ag]⁺ Calcd for C₁₈H₃₄AgOSSi⁺ 433.1145; Found 433.1155.

To a microwave vial containing 5-Nitro-1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (**6r**) (47.0 mg, 0.100 mmol, 1.0 equiv.) was added $\text{Cu}(\text{CH}_3\text{CN})_4\text{BF}_4$ (3.2 mg, 0.010 mmol, 0.1 equiv.) under N_2 atmosphere. The vial was sealed then DCE (1.5 mL), cyclohexene sulfide (**7a**) (16 μL , 0.15 mmol, 1.5 equiv.) and MeOH (41 μL , 1.0 mmol, 10.0 equiv.) were added under N_2 atmosphere. The reaction was stirred at 50 $^\circ\text{C}$ for 3 h. The reaction was cooled to rt and concentrated *in vacuo*. Based on the crude NMR using dibromomethane as internal standard we obtained **8r** (37%) and **8w** (17%).

9. Crystal structure of **8a**

Crystals were grown by storing a large (1g) batch of **8a** in the freezer (-5 $^\circ\text{C}$) for an extensive period of time. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (CCDC 1962904) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

10. Spectra of new compounds

^1H NMR (400 MHz, CDCl_3) of compound **6s**:

^{13}C NMR (100 MHz, CDCl_3) of compound **6s**:

^1H NMR (400 MHz, CDCl_3) of compound **7c**:

^{13}C NMR (100 MHz, CDCl_3) of compound **7c**:

^1H NMR (400 MHz, CDCl_3) of compound **7d**:

^{13}C NMR (100 MHz, CDCl_3) of compound **7d**:

^1H NMR (400 MHz, CDCl_3) of compound **7g**:

^{13}C NMR (100 MHz, CDCl_3) of compound **7g**:

^1H NMR (400 MHz, CDCl_3) of compound **7i**:

7i

^{13}C NMR (100 MHz, CDCl_3) of compound **7i**:

7i

^1H NMR (400 MHz, CDCl_3) of compound **8a**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8a**:

^1H NMR (400 MHz, CDCl_3) of compound **8b**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8b**:

¹H NMR (400 MHz, CDCl₃) of compound **8c**:

¹³C NMR (100 MHz, CDCl₃) of compound **8c**:

^1H NMR (400 MHz, CDCl_3) of compound **8d**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8d**:

^1H NMR (400 MHz, CDCl_3) of compound **8e**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8e**:

^1H NMR (400 MHz, CDCl_3) of compound **8f** and **8f'**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8f** and **8f'**:

^1H NMR (400 MHz, CDCl_3) of compound **8g** and **8g'**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8g** and **8g'**:

^1H NMR (400 MHz, CDCl_3) of compound **8h** and **8h'**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8h** and **8h'**:

¹H NMR (400 MHz, CDCl₃) of compound **8i**:

¹³C NMR (100 MHz, CDCl₃) of compound **8i**:

HPLC of compound **8i**:

Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.280	BB	0.4055	8766.47949	320.11829	100.0000

HPLC of racemic **8i**:

Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.163	BV	0.3009	1908.99768	98.16668	43.1583
2	9.685	VB	0.3817	2514.24341	96.59779	56.8417

Totals : 4423.24109 194.76447

^1H NMR (400 MHz, CDCl_3) of compound **8i'**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8i'**:

HPLC of compound **8i'**:

Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.663	MM	0.3125	64.51215	3.44074	0.6439
2	15.937	MM	0.4347	9955.09570	381.71094	99.3561

Totals : 1.00196e4 385.15168

HPLC of racemic **8i'**:

Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.508	MM	0.3254	3525.26782	180.54846	50.2045
2	15.987	MM	0.3925	3496.54175	148.46820	49.7955

Totals : 7021.80957 329.01666

¹H NMR (400 MHz, CDCl₃) of compound **8j**:

¹³C NMR (100 MHz, CDCl₃) of compound **8j**:

^1H NMR (400 MHz, CDCl_3) of compound **8k**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8k**:

¹H NMR (400 MHz, CDCl₃) of compound **8I**:

¹³C NMR (100 MHz, CDCl₃) of compound **8I**:

¹H NMR (400 MHz, CDCl₃) of compound **8m**:

¹³C NMR (100 MHz, CDCl₃) of compound **8m**:

¹H NMR (400 MHz, CDCl₃) of compound **8n**:

¹³C NMR (100 MHz, CDCl₃) of compound **8n**:

^1H NMR (400 MHz, CDCl_3) of compound **8o**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8o**:

¹H NMR (400 MHz, CDCl₃) of compound **8p**:

¹³C NMR (100 MHz, CDCl₃) of compound **8p**:

^1H NMR (400 MHz, CDCl_3) of compound **8q**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8q**:

¹H NMR (400 MHz, CDCl₃) of compound **8r**:

¹³C NMR (100 MHz, CDCl₃) of compound **8r**:

CC(C)(C)C1CCC(CC1)S(=O)(=O)C2=CC=CC=C2

¹H NMR spectrum (CDCl₃) of compound 8s. The spectrum shows peaks at 8.56, 8.55, 8.43, 8.42, 8.41, 8.40, 8.39, 8.38, 8.37, 8.36, 8.35, 8.34, 8.33, 8.32, 8.31, 8.30, 8.29, 8.28, 8.27, 8.26, 8.25, 8.24, 8.23, 8.22, 8.21, 8.20, 8.19, 8.18, 8.17, 8.16, 8.15, 8.14, 8.13, 8.12, 8.11, 8.10, 8.09, 8.08, 8.07, 8.06, 8.05, 8.04, 8.03, 8.02, 8.01, 8.00, 7.99, 7.98, 7.97, 7.96, 7.95, 7.94, 7.93, 7.92, 7.91, 7.90, 7.89, 7.88, 7.87, 7.86, 7.85, 7.84, 7.83, 7.82, 7.81, 7.80, 7.79, 7.78, 7.77, 7.76, 7.75, 7.74, 7.73, 7.72, 7.71, 7.70, 7.69, 7.68, 7.67, 7.66, 7.65, 7.64, 7.63, 7.62, 7.61, 7.60, 7.59, 7.58, 7.57, 7.56, 7.55, 7.54, 7.53, 7.52, 7.51, 7.50, 7.49, 7.48, 7.47, 7.46, 7.45, 7.44, 7.43, 7.42, 7.41, 7.40, 7.39, 7.38, 7.37, 7.36, 7.35, 7.34, 7.33, 7.32, 7.31, 7.30, 7.29, 7.28, 7.27, 7.26, 7.25, 7.24, 7.23, 7.22, 7.21, 7.20, 7.19, 7.18, 7.17, 7.16, 7.15, 7.14, 7.13, 7.12, 7.11, 7.10, 7.09, 7.08, 7.07, 7.06, 7.05, 7.04, 7.03, 7.02, 7.01, 7.00, 6.99, 6.98, 6.97, 6.96, 6.95, 6.94, 6.93, 6.92, 6.91, 6.90, 6.89, 6.88, 6.87, 6.86, 6.85, 6.84, 6.83, 6.82, 6.81, 6.80, 6.79, 6.78, 6.77, 6.76, 6.75, 6.74, 6.73, 6.72, 6.71, 6.70, 6.69, 6.68, 6.67, 6.66, 6.65, 6.64, 6.63, 6.62, 6.61, 6.60, 6.59, 6.58, 6.57, 6.56, 6.55, 6.54, 6.53, 6.52, 6.51, 6.50, 6.49, 6.48, 6.47, 6.46, 6.45, 6.44, 6.43, 6.42, 6.41, 6.40, 6.39, 6.38, 6.37, 6.36, 6.35, 6.34, 6.33, 6.32, 6.31, 6.30, 6.29, 6.28, 6.27, 6.26, 6.25, 6.24, 6.23, 6.22, 6.21, 6.20, 6.19, 6.18, 6.17, 6.16, 6.15, 6.14, 6.13, 6.12, 6.11, 6.10, 6.09, 6.08, 6.07, 6.06, 6.05, 6.04, 6.03, 6.02, 6.01, 6.00, 5.99, 5.98, 5.97, 5.96, 5.95, 5.94, 5.93, 5.92, 5.91, 5.90, 5.89, 5.88, 5.87, 5.86, 5.85, 5.84, 5.83, 5.82, 5.81, 5.80, 5.79, 5.78, 5.77, 5.76, 5.75, 5.74, 5.73, 5.72, 5.71, 5.70, 5.69, 5.68, 5.67, 5.66, 5.65, 5.64, 5.63, 5.62, 5.61, 5.60, 5.59, 5.58, 5.57, 5.56, 5.55, 5.54, 5.53, 5.52, 5.51, 5.50, 5.49, 5.48, 5.47, 5.46, 5.45, 5.44, 5.43, 5.42, 5.41, 5.40, 5.39, 5.38, 5.37, 5.36, 5.35, 5.34, 5.33, 5.32, 5.31, 5.30, 5.29, 5.28, 5.27, 5.26, 5.25, 5.24, 5.23, 5.22, 5.21, 5.20, 5.19, 5.18, 5.17, 5.16, 5.15, 5.14, 5.13, 5.12, 5.11, 5.10, 5.09, 5.08, 5.07, 5.06, 5.05, 5.04, 5.03, 5.02, 5.01, 5.00, 4.99, 4.98, 4.97, 4.96, 4.95, 4.94, 4.93, 4.92, 4.91, 4.90, 4.89, 4.88, 4.87, 4.86, 4.85, 4.84, 4.83, 4.82, 4.81, 4.80, 4.79, 4.78, 4.77, 4.76, 4.75, 4.74, 4.73, 4.72, 4.71, 4.70, 4.69, 4.68, 4.67, 4.66, 4.65, 4.64, 4.63, 4.62, 4.61, 4.60, 4.59, 4.58, 4.57, 4.56, 4.55, 4.54, 4.53, 4.52, 4.51, 4.50, 4.49, 4.48, 4.47, 4.46, 4.45, 4.44, 4.43, 4.42, 4.41, 4.40, 4.39, 4.38, 4.37, 4.36, 4.35, 4.34, 4.33, 4.32, 4.31, 4.30, 4.29, 4.28, 4.27, 4.26, 4.25, 4.24, 4.23, 4.22, 4.21, 4.20, 4.19, 4.18, 4.17, 4.16, 4.15, 4.14, 4.13, 4.12, 4.11, 4.10, 4.09, 4.08, 4.07, 4.06, 4.05, 4.04, 4.03, 4.02, 4.01, 4.00, 3.99, 3.98, 3.97, 3.96, 3.95, 3.94, 3.93, 3.92, 3.91, 3.90, 3.89, 3.88, 3.87, 3.86, 3.85, 3.84, 3.83, 3.82, 3.81, 3.80, 3.79, 3.78, 3.77, 3.76, 3.75, 3.74, 3.73, 3.72, 3.71, 3.70, 3.69, 3.68, 3.67, 3.66, 3.65, 3.64, 3.63, 3.62, 3.61, 3.60, 3.59, 3.58, 3.57, 3.56, 3.55, 3.54, 3.53, 3.52, 3.51, 3.50, 3.49, 3.48, 3.47, 3.46, 3.45, 3.44, 3.43, 3.42, 3.41, 3.40, 3.39, 3.38, 3.37, 3.36, 3.35, 3.34, 3.33, 3.32, 3.31, 3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.99, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.92, 2.91, 2.90, 2.89, 2.88, 2.87, 2.86, 2.85, 2.84, 2.83, 2.82, 2.81, 2.80, 2.79, 2.78, 2.77, 2.76, 2.75, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.68, 2.67, 2.66, 2.65, 2.64, 2.63, 2.62, 2.61, 2.60, 2.59, 2.58, 2.57, 2.56, 2.55, 2.54, 2.53, 2.52, 2.51, 2.50, 2.49, 2.48, 2.47, 2.46, 2.45, 2.44, 2.43, 2.42, 2.41, 2.40, 2.39, 2.38, 2.37, 2.36, 2.35, 2.34, 2.33, 2.32, 2.31, 2.30, 2.29, 2.28, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 2.19, 2.18, 2.17, 2.16, 2.15, 2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93, 1.92, 1.91, 1.90, 1.89, 1.88, 1.87, 1.86, 1.85, 1.84, 1.83, 1.82, 1.81, 1.80, 1.79, 1.78, 1.77, 1.76,

Chemical structure of compound **8s** is shown above the spectrum. The structure features a cyclohexane ring substituted with a TIPS group, a carbonyl group, and a 2-iodophenyl group. The spectrum displays peaks corresponding to the structure, with the following chemical shifts (ppm) labeled above the peaks:

Chemical Shift (ppm)
165.75
140.65
135.81
134.66
131.78
131.57
128.96
128.79
127.57
126.72
100.10
92.53
88.80
75.11
50.50
32.02
31.96
25.68
24.03
18.81
11.51

¹H NMR (400 MHz, CDCl₃) of compound **8t**:

¹³C NMR (100 MHz, CDCl₃) of compound **8t**:

^1H NMR (400 MHz, CDCl_3) of compound **8u**:

^{13}C NMR (100 MHz, CDCl_3) of compound **8u**:

¹H NMR (400 MHz, CDCl₃) of compound **8v**:

¹³C NMR (100 MHz, CDCl₃) of compound **8v**:

8w

CSi(C)(C)C#CC1CCCCC1OC

1H NMR spectrum (CDCl₃) of compound **8w**. The spectrum shows a singlet at 3.64 ppm (3H, OCH₃), a multiplet between 1.9 and 2.3 ppm (6H, cyclohexane protons), and a singlet at 0.1 ppm (9H, TIPS methyls). An inset shows the region from 2.7 to 3.2 ppm.

COC[C@H]1CCCC[C@@H]1SC#CC2=CC=CC=C2C(F)(F)F

8w

1H NMR spectrum (CDCl₃) of compound **8w**. The x-axis represents the chemical shift in ppm, ranging from -10 to 190. The spectrum shows several peaks corresponding to the structure of **8w**.

Chemical Shift (ppm)	Assignment
~7.2	Aromatic protons (triplet)
~5.5	CH-O (multiplet)
~4.5	CH-O (multiplet)
~3.5	CH ₂ -O (multiplet)
~2.5	CH ₂ (multiplet)
~1.8	CH ₂ (multiplet)
~1.2	CH ₂ (multiplet)
~0.1	Me (small peak)
77.0, 77.1, 77.2	Solvent (CDCl ₃)

^1H NMR (400 MHz, CDCl_3) of compound **9d**:

^{13}C NMR (100 MHz, CDCl_3) of compound **9d**:

^1H NMR (400 MHz, CDCl_3) of compound **10a**:

^{13}C NMR (100 MHz, CDCl_3) of compound **10a**:

^1H NMR (400 MHz, CDCl_3) of compound **10b**:

^{13}C NMR (100 MHz, CDCl_3) of compound **10b**:

^1H NMR (400 MHz, CDCl_3) of compound **10c**:

^{13}C NMR (100 MHz, CDCl_3) of compound **10c**:

^1H NMR (400 MHz, CDCl_3) of compound **10d**:

^{13}C NMR (100 MHz, CDCl_3) of compound **10d**:

^1H NMR (400 MHz, CDCl_3) of compound **10e**:

^{13}C NMR (100 MHz, CDCl_3) of compound **10e**:

¹H NMR (400 MHz, CDCl₃) of compound **11**:

¹³C NMR (100 MHz, CDCl₃) of compound **11**:

^1H NMR (400 MHz, CDCl_3) of compound **12**:

^{13}C NMR (100 MHz, CDCl_3) of compound **12**:

¹H NMR (400 MHz, CDCl₃) of compound **13**:

¹³C NMR (100 MHz, CDCl₃) of compound **13**:

¹H NMR (400 MHz, CDCl₃) of compound **14**:

¹³C NMR (100 MHz, CDCl₃) of compound **14**:

^1H NMR (400 MHz, CDCl_3) of compound **15**:

^{13}C NMR (100 MHz, CDCl_3) of compound **15**:

^1H NMR (400 MHz, CDCl_3) of compound **43**:

^{13}C NMR (100 MHz, CDCl_3) of compound **43**:

^1H NMR (400 MHz, CDCl_3) of compound **46**:

^{13}C NMR (100 MHz, CDCl_3) of compound **46**: