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Pot-Economy Autooxidative Condensation of 2-Aryl-2-lithio-1,3-dithianes

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ABSTRACT: The autooxidative condensation of 2-aryl-2-lithio-1,3-dithianes is here reported. Treatment of 2-aryl-1,3-dithianes with *n*-BuLi in the absence of any electrophile leads to condensation of three molecules of 1,3-dithianes and formation of highly functionalized α-thioether ketones orthothioesters in 51-89% yields upon air exposure. The method was further expanded to benzaldehyde dithioacetals, affording corresponding orthothioesters and α-thioether ketones in 48-97% yields. The experimental results combined with density functional theory studies support a mechanism triggered by the autooxidation of 2-aryl-2-lithio-1,3-dithianes to yield a highly reactive thioester that undergoes condensation with two other molecules of 2-aryl-2-lithio-1,3-dithiane.

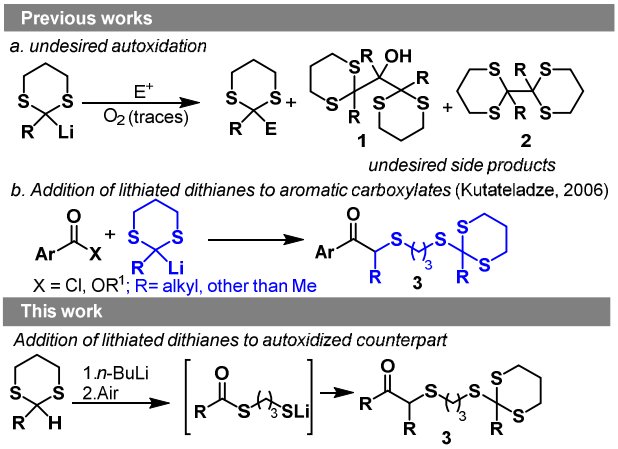
INTRODUCTION

Organolithium compounds can undergo autoxidation towards formation of highly unstable organolithium peroxides, which upon fast interaction with another organolithium leads to the ultimate formation of lithium alkoxides.[1] Oxidation of RLi with ROOLi was proven by Müller and Töpel[2] in 1939 and used in several oxidative processes,[3] and the autoxidation of organolithiums further explored in preparation of alcohols.[4]

The first reports of Corey and Seebach[5] on the use of lithiated 1,3-dithianes as synthetic equivalents to acyl anions have rapidly gathered the attention of the synthetic community. The umpolung strategy rendered by transformation of aldehydes to 2-substituted 1,3-dithianes and subsequent formation of the lithiated acyl anion equivalent have been explored for preparation of a wide array of products,[6,7] namely in natural product synthesis.[8] Other thioacetals can lead to the formation of similar acyclic lithiated anions,[9] but it was soon realized that cyclic 2-lithio-1,3-dithianes were advantageous due to their ease of preparation and general suitability.[6b] Despite the undisputable importance of 2-lithio-1,3-dithianes in synthetic chemistry, inconsistent yields and formation of side products have been reported.[10] Problems derived from its high reactivity and strong basicity have been overcome either by transmetalation,[11,12,13] or using less reactive silyl,[14,15,16] or tin[10a,17] analogues. The autoxidation of 2-lithio-1,3-dithiane (Scheme 1) upon air exposure has been reported by Wade and co-workers,[18] after observing formation of **1** and **2** in absence of an electrophile. The formation of **1** was also later reported by Argade and co-workers when preparing 2-lithio-1,3-dithiane.[19] The presence of an oxidizing impurity in older bottles of *n*-BuLi was advanced as the cause for the formation of the oxidized products. The same compound was reported to be formed in 25% yield when preparing 2-lithio-1,3-dithiane in THF, proposed by the authors to arise from the unlikely reaction of the desired intermediate with solvent.[20] Presence of dimers derived from single electron transfer processes have been observed in several other works,[12a,14c,21] especially in presence of nitro substituted compounds.[22] The nucleophilic addition of 2-lithio-1,3-dithianes to acyl chlorides and esters reported by Kutateladze and co-workers[23] is one example from the vast array of dithiane umpolung reactivity of carbonyl compounds (Scheme 1). Interestingly, when an aldehyde other than acetaldehyde is used, the reaction proceeds through addition of a second dithiane molecule through ring-opening of the firstly installed dithiane unit.[24]

Considering the previous reports on the autoxidation of 2-lithio-1,3-dithianes, we envisioned that 2-aryl-2-lithio-1,3-dithianes could be oxidized *in situ* to yield a thioester capable of undergoing a similar attack by the excess organolithium eventually forming compounds similar to those described by Kutateladze in a pot economy.[25] Previously reported transformations of the envisioned products include desulfurizing difluorination of the α-thioether ketone and dithioketal moieties[26] or trifluoromethylation of benzylic orthothioesters.[26b, 27] Orthothioesters can be converted to esters, thioesters or orthoesters[28] and α-thioether ketones have also been used in the oxidative coupling of benzyl ketones.[29]

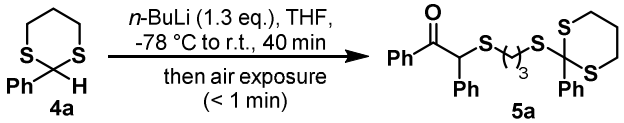
Scheme 1.



RESULTS AND DISCUSSION

Gratifyingly, when reacting 2-phenyl-2-lithium-1,3-dithiane with *S*-benzyl benzothioate, product **5a** was obtained in 89% yield (Table 1, entry 1). The ability of the thioester group to undergo the same transformation as benzoylchloride (entry 2) prompted us to assess the possibility for *in situ* formation of the thioester by oxidation of the lithium dithiane. Hence, the argon atmosphere of a solution of 2-phenyl-2-lithium-1,3-dithiane from **4a** was replaced by oxygen and kept for 5 minutes to afford the thioorthoester in 69% yield (entry 3). The simple exposure of the reaction mixture to air for 30 min allowed formation of thioorthoester **5a** in 41% yield (entry 4), which was increased to 68% by decreasing exposure to air to less than a minute (entry 5), and to 71% by forming the lithiated dithiane at 0 °C (entry 6). Modification of the stoichiometric amounts of *n*-BuLi or other solvents (entries 7-10) did not improve the reaction success. Although a fast process at 0 °C, air exposure of the organolithium at -78 °C led to only traces of product and unreacted dithiane (entry 11).

Table 1. Optimization of reaction conditions

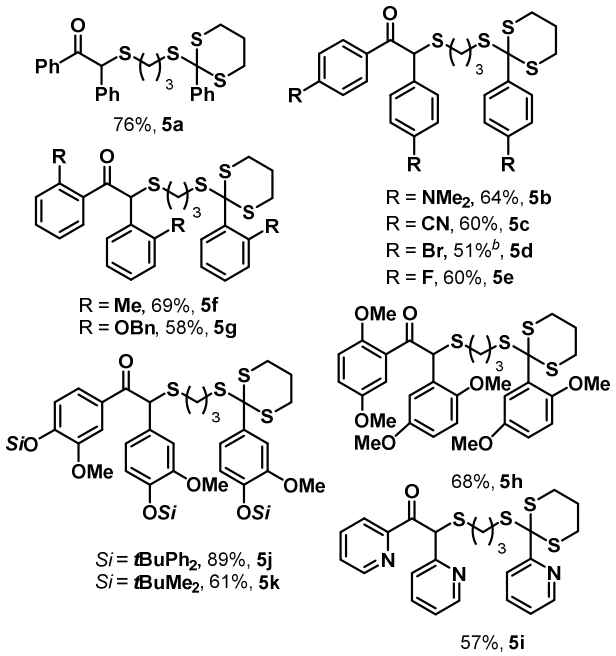


Entry	Deviation from reaction conditions[a]	Yield (%)[b]
1	PhC(O)SBn (0.65 eq.), no air	89
2	PhC(O)Cl (0.65 eq.), no air	71
3	O_2 balloon for 5 min	69
4	30 min air exposure	41
5	r.t., 20 min	68
6	0°C to r.t., 20 min	71
7	1.0 eq. *n*-BuLi, 0°C to r.t., 20 min	66
8	1.6 eq. *n*-BuLi, 0°C to r.t., 20 min	60
9	Et_2O, 0°C to r.t., 20 min	46
10	Toluene	39
11	air exposure at -78 °C	traces

[a] *n*-BuLi (2.5 M in hexanes, 1.3 mmol) was added dropwise to a solution of dithiane **4a** (1 mmol) in THF (5 ml) under argon atmosphere at -78 °C. The mixture was left to reach rt after 20 min, and opened to air 1 minute before addition of NH_4Cl saturated aqueous solution. [b] Isolated Yield

Finally, the optimized protocol retrieved formation of orthothioester **5a** in 76% and the scope of the method was evaluated (Scheme 2). Formation of ortholithiation derived products was not observed even in presence of directing metalating groups. The correspondent orthothioesters derived from electron rich or electron poor aryl dithianes could be obtained in reasonable yields. Phenyl-1,3-dithianes decorated with halogens at the *para*-position were successfully transformed into the corresponding orthothioesters **5d** and **5e**, although LDA had to be used for the bromide derivative to avoid transmetalation with *n*-BuLi. TBDMS and TBDPS silyl protective groups were stable to the reaction conditions, and silyl ethers **5j** and **5k** could be obtained in up to 89% yield. A dithiane derived from 2-formylpyridine resulted in formation of **5i** in 57% yield. Despite several attempts on the autooxidative addition of nitrophenyl-1,3-dithianes, only alkylated derivatives or starting materials were obtained. Other electron deficient dithianes such as pentafluorophenyl or para-trifluoromethylphenyl derivatives were unstable towards the lithiation conditions tested.

Scheme 2.[a]



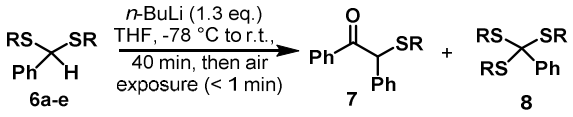
[a] for reaction conditions see footnote *a*, table 1 [b]LDA as base

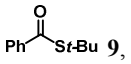
Acyclic benzaldehyde dithioacetals derived from primary and secondary thiols undergo the same process to yield α-thioether ketones **7** and orthothioesters **8** (Table 2). Dithioacetal **6e** derived from *tert*-butyl mercaptan failed to provide the corresponding ketone or orthothioesters likely due to steric hindrance as only thioester **9** could be obtained. The use of O_2 instead of air was observed to be detrimental for the reaction yield, as complex mixtures of products were obtained in such cases.

In order to evaluate the scope of the transformation concerning the nature of the 2-substituent of 1,3-dithianes, several 2-alkyl-1,3-dithianes were submitted to our autooxidative conditions (Scheme 3). The autooxidation of 2-lithio-1,3-dithiane under our reaction conditions resulted in the

unsurprised formation of alcohol **1a** as previously reported by Wade and co-workers (Scheme 3, eq 1).[18] 2-Alkyl substituted 1,3-dithianes undergo autooxidation to some extent, however the reaction is halted before orthothioester formation and **10** are obtained in up to 27% yields (Scheme 3, eq 2) probably due to the competitive formation of the lithium enolate of product. Similar yields of the products were observed when increasing the amount of *n*-BuLi. The presence of a bulky *t*-butyl substituent alters the outcome of the reaction. Dithioester **11**, resulting from condensation of two oxidized species was the only product identified (Scheme 3, eq 3). The autooxidative addition of 1,3-dithiane derived from silyl protected glycoaldehyde yields **10p** together with hexyl substituted 1,3-dithiane. The formation of the later is likely to occur by trapping of the ketene dithiane with *n*-butyl lithium.[30] Several attempts to apply this procedure to 2-silyl substituted 1,3-dithianes, such as 2-TMS-1,3-dithiane 2-TBDPS-1,3-dithiane, resulted in the formation of complex mixtures of unidentified products.

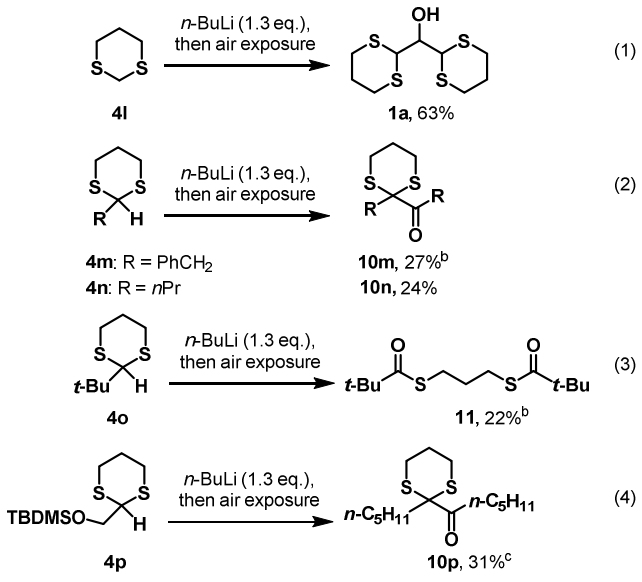
Table 2. Autooxidative condensation of benzaldehyde-derived dithioacetals



Entry[a]	R	**7** Yield (%)[b]	**8** Yield (%)[b]
1	Ph	**7a**, 48	**8a**, -[c]
2	*n*-Bu	**7b**, 97	**8b**, 72
3	$(CH_2)_{11}Me$	**7c**, 73	**8c**, 56
4	*sec*-Bu	**7d**, 67	**8d**, -[c]
5	*t*-Bu	 **9**, 62	

[a] For reaction conditions see footnote *a*, table 1. [b] Isolated Yield. [c] Observed in ^{1}H NMR of the crude mixture but not isolated.

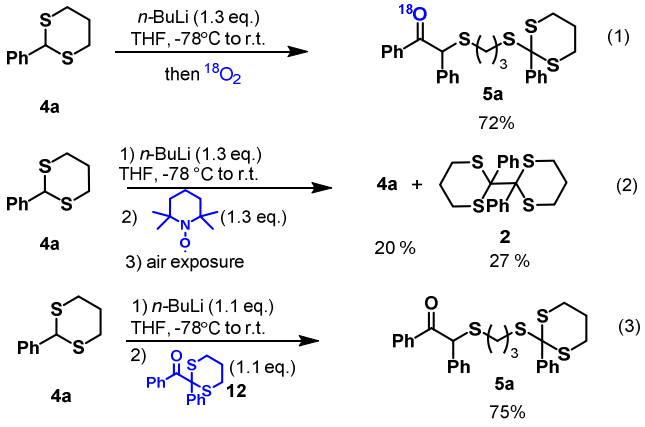
Scheme 3.[a]



[a] For reaction conditions see footnote *a*, table 1. Isolated Yields [b] unreacted dithiane **4** was isolated as the major species. [c] 2-(*n*-hexyl)-1,3-dithiane was also isolated in 23%.

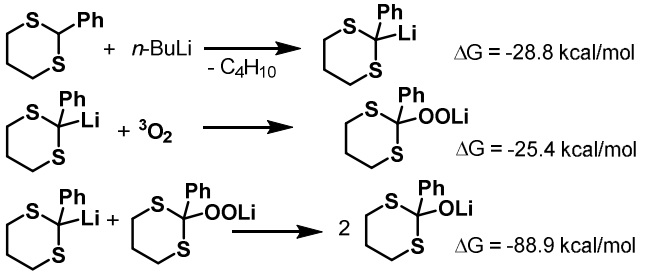
The role of atmospheric oxygen as the oxidant species in the process was confirmed by running the autooxidative condensation reaction under $^{18}O_2$, affording the ^{18}O isotopically labeled **5a** in 72% yield (Scheme 4, eq 1). Impelled by the previous suggestions that a SET mechanism could be involved, the exposure to air in presence of TEMPO was performed (Scheme 4, eq 2). Trapped intermediates were not identified and only compound **2** was isolated**,** already known to derive from SET.[12a, 14c, 21] Notably, formation of compound **5a** was not observed, which might indicate the SET process to be a pitfall prior to the organolithium autooxidation. The presence of **12** as intermediate in the reaction was supported by its reaction with lithium dithiane derived from **4a** (Scheme 4, eq 3).

Scheme 4.



In order to get some insight on the reaction mechanism, the several putative processes involved in the transformation were studied by DFT calculations.[31] The spontaneous autooxidation of the organolithium compound was verified through optimization of relevant intervenient species (Scheme 5). The process seems highly favorable, as the lithium alkoxide formation is balanced by the release of 25.4 kcal/mol upon reaction of lithium dithiane with triplet oxygen[3a] followed by release of 88.9 kcal/mol upon reaction of the lithium peroxide with lithium dithiane to form the corresponding lithium alkoxide.

Scheme 5.



According to our calculations, formation of thioester **B** from lithium alkoxide **A** requires only 2.7 kcal/mol (**Figure 1**). The thiolate charge in thioester **B** is highly stabilized by lithium and becomes more stabilized upon interaction with a lithium dithiane molecule (**C**). The presence of lithium increases the C=O polarization of the thioester assisting the nucleophilic

attack of a lithium dithiane molecule, and requires 11.2 kcal/mol. The transition state $\mathbf{TS_{CD}}$ resembles an early one, as suggested by the rather long forming C-C bond and small

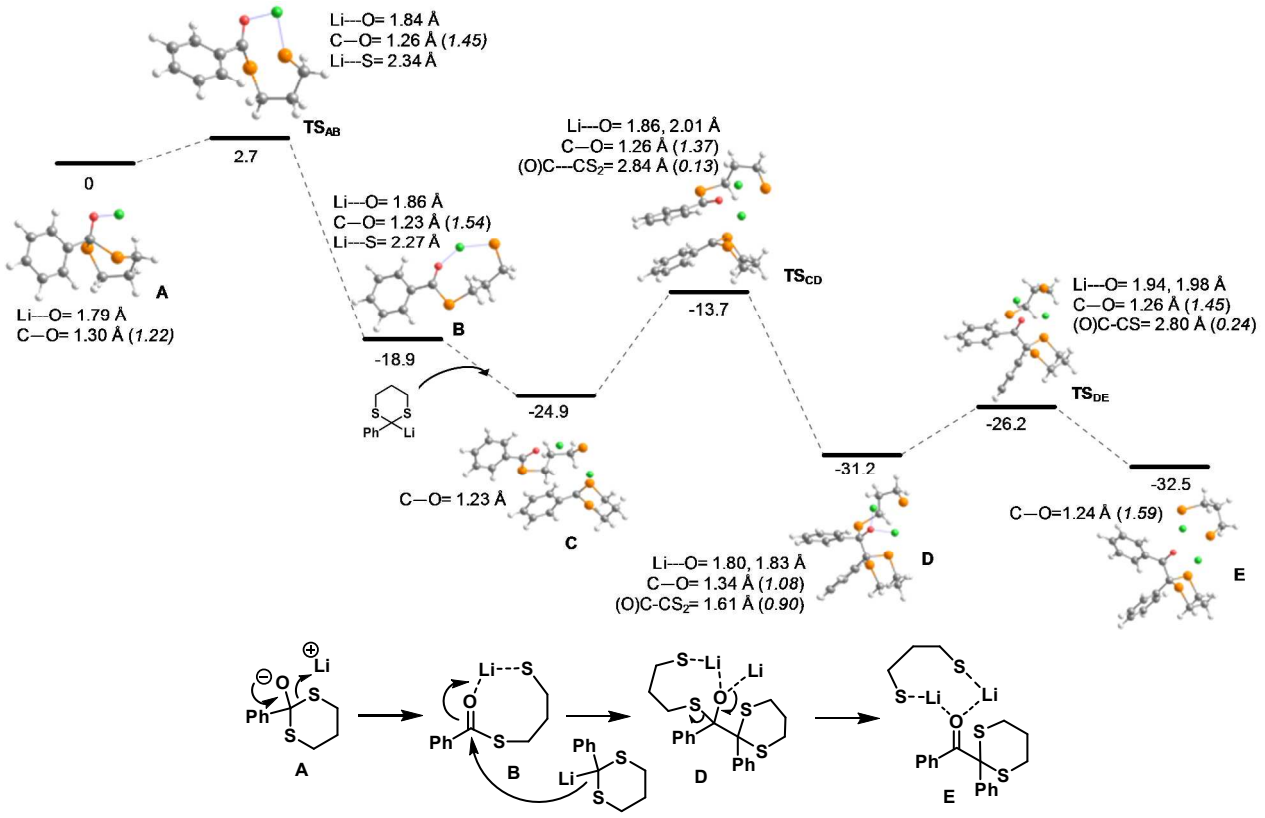


Figure 1. Free energy profile (PBE0) for deterioration of lithium alkoxide and reaction with 2-phenyl-2-lithio-1,3-dithiane, and mechanistic representation. Optimized structures of minima and transition states are presented with bond distances and Wiberg indexes (in italics) for the more relevant bonds. Free energies values are presented in kcal/mol, referring to the initial intermediate **A**.

Wiberg index[32] (d = 2.84 Å and WI = 0.13), which becomes considerably shorter in the tetrahedral intermediate **D** (d = 1.61 Å and WI = 0.90). The collapse of intermediate **D** to the more stable pair of ketone and lithium thiolate (**E**) requires only 5.0 kcal/mol to overcome the transition state $\mathbf{TS_{DE}}$ energy barrier. Interaction of the lithium cations with sulfur atoms is visible in calculated $\mathbf{TS_{DE}}$, although such stabilization is likely to take place by the solvent molecules. The pair of products represented in **E** is highly stabilized by interaction of lithium cations with both sulfur atoms of the thiolate and the carbonyl oxygen.

Condensation of the ketone **12** in **E** with another lithium dithiane molecule was considered, as observed experimentally (Scheme 4, eq 3), by taking the nucleophilic attack of the organolithium to a sulfur atom of the α-disubstituted ketone (Figure 2).[24] The calculated transition state for this reaction $\mathbf{TS_{FG}}$ is characterized by distension of the C-S bond of the ketone (2.11 Å in $\mathbf{TS_{FG}}$ and 1.85 Å in **F**) and formation of a new C-S bond (2.49 Å and WI = 0.29) with the lithium dithiane molecule, demanding for 11.2 kcal/mol. Weakening of the carbon-oxygen bond from **F** to **G** is visible by its length (1.23 Å in **F** and 1.29 Å in **G**) and weaker Wiberg index in the lithium enolate product **G** (WI = 1.65 in **F** and 1.31 in **G**), accompanied by strengthening of the C-C bond (1.55 Å; WI = 0.95 in **F** and 1.40 Å; WI = 1.47 in **G**). Although we cannot rule out a radical mechanism based on our calculations (as suggested by Kutateladze[23] and considered in supporting information), the low energy barrier determined for the ionic nucleophilic attack might indicate this as the main route for formation of the orthothioester product.

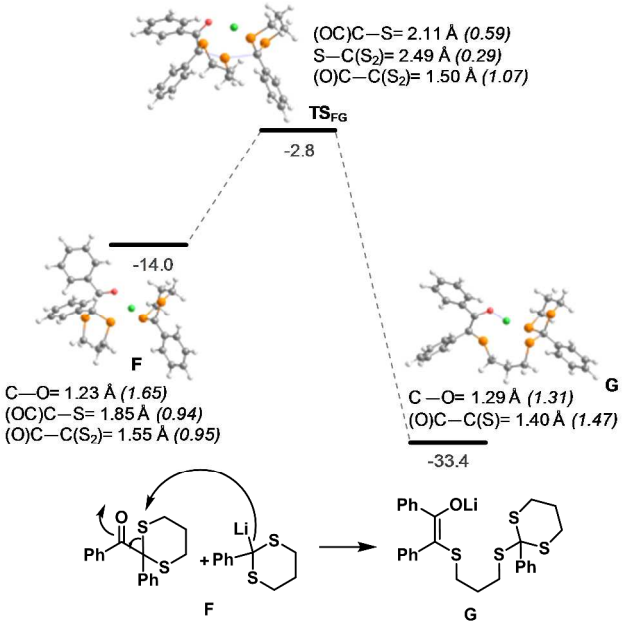


Figure 2. Free energy profile (PBE0) for nucleophilic condensation of α-disubstituted ketone with 2-phenyl-2-lithio-1,3-dithiane and mechanistic representation. Optimized structures of minima and transition states are presented with bond distances

and Wiberg indexes (in italics) for the more relevant bonds. Free energies values are presented in kcal/mol, referring to the initial intermediate **A** from Figure 1.

CONCLUSION

In summary, we have shown that 2-aryl-2-lithium-1,3-dithianes undergo autooxidative condensation forming α-thioether ketones orthothioesters in reasonable to good yields upon aerobic oxidation. The procedure can be expanded to other benzaldehyde derived dithioacetals, affording orthothioesters and α-thioether ketones in good to excellent yields. 2-Alkyl substituted 1,3-dithianes also undergo a similar autooxidative process upon treatment with *n*-BuLi and air exposure, however condensation of a third dithiane unit is hampered by presence of enolizable positions on the condensation intermediate. DFT calculations support a reaction mechanism that starts with the highly thermodynamic favorable autoxidation of the organolithium dithiane, leading to formation of the thioester that is further trapped by another 2-lithium-1,3-dithiane. The herein described process might be on the basis of the known limitations on the use of 2-lithio-1,3-dithianes in synthetic chemistry, and it is also a way to achieve highly functionalized and stable orthothioesters.

EXPERIMENTAL SECTION

General remarks: Reactions were monitored through thin-layer chromatography (TLC) with commercial silica gel plates (Merck silica gel, 60 F254). Visualization of the developed plates was performed under UV lights at 254 nm and by staining with cerium ammonium molybdate, 2,4-dinitrophenylhydrazine and vanillin stains. Flash column chromatography was performed on silica gel 60 (40-63 μm) as stationary phase. Preparative TLCs were conducted on PLC silica gel 60 F254, 1 mm.^{1}H NMR spectra were recorded at 300 MHz, ^{13}C NMR spectra were recorded at 75 MHz and ^{19}F spectrum was recorded at 282 MHz in a 300 MHz Varian Mercury spectrometer, using $CDCl_3$ as solvent. Chemical shifts (δ) are reported in ppm referenced to the $CDCl_3$ residual peak (δ 7.26) or TMS peak (δ 0.00) for ^{1}H NMR and to $CDCl_3$ (δ 77.16) for ^{13}C NMR. The following abbreviations were used to describe peak splitting patterns: s = singlet, d = doublet, t = triplet, m = multiplet. Coupling constants, *J*, were reported in Hertz (Hz). High-resolution mass spectra were recorded on a Waters ESI-TOF MS spectrometer. Tetrahydrofuran (THF) was dried by distillation under argon with sodium metal and benzophenone as indicator. Dichloromethane (DCM) was dried by distillation under argon with calcium hydride. Isotope labelled oxygen-18 (99% isotopic purity) was purchased from Sigma-Aldrich (CAS Number 32767-18-3). A small balloon was filled with oxygen-18 and used directly in the oxidation reaction.

General procedure for preparation of 2-substituted 1,3-dithianes (Method A), based on modified previously reported method.[33] Aldehyde (15 mmol, 1 equiv.) and 1,3-propanedithiol (3mL, 16.5 mmol, 1.1 equiv.) were dissolved in dichloromethane (50 mL) in a round-bottom flask. Iodine (381 mg, 1.5 mmol, 0.1 equiv.) was slowly added do the stirring solution as to prevent vigorous boiling of the solvent. The reaction was quenched with a 2% $Na_2S_2O_3$ aqueous solution (10 mL) 30 minutes after complete iodine addition. Upon separation, the organic layer was washed successively with a 10% aqueous NaOH solution (10 mL), water (10 mL) and brine (10 mL). The organic solvent was dried over $MgSO_4$ and filtered. After evaporating the solvent, the product was recrystallized in isopropanol. Note: Reactions were conducted in different scales depending on availability of aldehyde starting material.

4a: Prepared according to method A. 77% yield (3.425 g, 17.45 mmol), white crystals. Obtained with same spectral characterization as previously described.[34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.49-7.45 (m, 2H), 7.37-7.29 (m, 3H), 5.17 (s, 1H), 3.12-3.02 (m, 2H), 2.95-2.88 (m, 2H), 2.22-2.14 (m, 1H), 2.01-1.86 (m, 1H).

4b: Prepared according to a modified previously reported method.[35] 4-(Dimethylamino)benzaldehyde (1 g, 6.7 mmol, 1 equiv.) and 1,3-propanedithiol (0.74 mL, 7.4 mmol, 1.1 equiv.) were dissolved in 10 mL of dry DCM in an argon purged round-bottom flask. The solution was cooled to 0°C and BF_3•OEt_2 (1.16 mL, 9.4 mmol, 1.4 equiv.) was added dropwise. The solution was then left warming to room temperature for 1 hour. The reaction was quenched with a 10% aqueous NaOH solution (10 mL). The layers were separated and the organic phase collected and washed with water (10 mL) and Brine (10 mL). The organic solvent was dried over $MgSO_4$ and filtered. After evaporation of the solvent, the product was recrystallized from isopropanol to give **4b** as yellow crystals in 93% yield (1.498 g, 6.26 mmol). Obtained with same spectral characterization as previously described.[36] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.33 (d, *J*=8.8 Hz, 2H), 6.67 (d, *J*=8.8 Hz, 2H), 5.12 (s, 1H), 3.17-2.86 (m, 4H), 2.94 (s, 6H), 2.20-2.10 (m, 1H), 1.97-1.82 (m, 1H).

4c: Prepared according to method A. 89% yield (2.997 g, 13.54 mmol), white crystals. Obtained with same spectral characterization as previously described. [34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.65-7.57 (m, 4H), 5.17 (s, 1H), 3.11-3.01 (m, 2H), 2.96-2.90 (m, 2H), 2.23-2.15 (m, 1H), 2.01-1.86 (m, 1H).

4d: Prepared according to method A. 81% yield (3.628 g, 13.18 mmol), white crystals. Obtained with same spectral characterization as previously described. [34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.49-7.44 (m, 2H), 7.37-7.32 (m, 2H), 5.11 (s, 1H), 3.10-3.00 (m, 2H), 2.94-2.86 (m, 2H), 2.22-2.12 (m, 1H), 1.99-1.84 ppm (m, 1H).

4e: Prepared according to method A. 76% yield (1.515 g, 7.07 mmol), white crystals. Obtained with same spectral characterization as previously described.[37] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.47-7.42 (m, 2H), 7.05-6.99 (m, 2H), 5.14 (s, 1H), 3.10-3.01 (m, 2H), 2.94-2.87 (m, 2H), 2.22-2.13 (m, 1H), 1.99-1.84 (m, 1H).

4f: Prepared according to method A. 69% yield (1.253 g, 5.96 mmol), white crystals. Obtained with same spectral characterization as previously described. [34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.61-7.57 (m, 1H), 7.24-7.13 (m, 3H), 5.33 (s, 1H), 3.14-3.04 (m, 2H), 2.95-2.88 (m, 2H), 2.45 (s, 3H), 2.23-2.14 (m, 1H), 2.02-1.87 (m, 1H).

4g: Prepared according to method A. 88% yield (1.681 g, 5.56 mmol), pale yellow solid. Product was isolated by flash chromatography (Hex:AcOEt, 95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.60 (dd, *J*=7.6, 1.8 Hz, 1H), 7.47-7.30 (m, 5H), 7.21 (td, *J*=7.8, 1.5 Hz, 1H), 7.00 -6.95 (m, 1H), 6.89 (d, *J*=8.2 Hz, 1H), 5.76 (s, 1H), 5.13 (s, 2H), 3.13-2.85 (m, 2H), 2.92-2.85 (m, 2H), 2.20-2.11 (m, 1H), 2.00-1.85 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 154.8, 137.2, 129.4, 129.3, 128.7, 128.1, 128.0, 127.3, 121.5, 112.7, 70.6, 44.2, 44.1,

32.5, 25.5. HR-MS (ESI) m/z calculated for $C_{17}H_{19}OS_2^+$ $[M+H]^+$ 303.0872, found 303.0884.

4h: Prepared according to method A. 76% yield (1.172 g, 4.57 mmol), white crystals. Obtained with same spectral characterization as previously described. [34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.15 (dd, *J*=2.3, 1.2 Hz, 1H), 6.83-6.76 (m, 2H), 5.67 (s, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.16-3.06 (m, 2H), 2.93-2.86 (m, 2H), 2.20-2.12 (m, 1H), 2.01-1.86 (m, 1H).

4i: Prepared according to a modified previously reported method.[38] Freshly distilled picolinaldehyde (1 mL, 10.51 mmol, 1 equiv.) and 1,3-propanedithiol (1.16 mL, 11.56 mmol, 1.1 equiv.) were dissolved in DCE (20 mL). *p*-Toluenosulfonic acid (200 mg, 1.05 mmol, 0.1 equiv.) was added to the mixture and the solution refluxed for 24 hours. The reaction was cooled to room temperature and quenched with a 10% aqueous NaOH solution (10 mL). The layers were separated and the organic phase collected and washed with water (10 mL) and brine (10 mL). The organic solvent was dried over $MgSO_4$ and filtered. The solvent was evaporated and the product isolated by flash chromatography (Hex:AcOEt, 70:30) to give **4i** as a yellow solid in 54% yield (1.111 g, 5.63 mmol), with same spectral characterization as previously described.[38] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.57 (dd, *J*=4.4, 1.5 Hz, 1H), 7.67 (td, *J*=7.6, 1.8 Hz, 1H), 7.46 (d, *J*=7.6 Hz, 1H), 7.22-7.18 (m, 1H), 5.35 (s, 1H), 3.11-2.92 (m, 4H), 2.23-2.13 (m, 1H), 2.05-1.90 (m, 1H).

4-(1,3-Dithian-2-yl)-2-methoxyphenol: Prepared according to method A and used in preparation of **4j** and **4k**. 84% yield (6.723 g, 27.73 mmol), white crystals. Obtained with same spectral characterization as previously described.[39] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.00-6.84 (m, 2H), 6.87-6.84 (m, 1H), 5.64 (s, 1H), 5.11 (s, 1H), 3.90 (s, 3H), 3.10-2.87 (m, 2H), 2.93-2.86 (m, 2H), 2.21-2.12 (m, 1H), 1.99-1.84 (m, 1H).

4j: 4-(1,3-Dithian-2-yl)-2-methoxyphenol (0.5 g, 2.06 mmol, 1 equiv.), imidazole (155 mg, 2.27 mmol, 1.1 equiv.) and 4-dimethylaminopyridine (25 mg, 0.2 mmol, 0.1 equiv.) were dissolved in dry DCM (10 mL), in an argon purged round-bottom flask. Then, *tert*-butyl(chloro)diphenylsilane was added dropwise to the stirring solution. The mixture was left stirring at room temperature for 24 h. The reaction was quenched with H_2O (10 mL) and the layers were separated. The organic layer was collected and washed with water (10 mL) and Brine (10 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by flash chromatography (Hex:DCM, 1:1) to yield **4j** in 93% yield (918 mg, 1.91 mmol) as a colorless thick oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.69 (dd, *J*=7.6, 1.8 Hz, 4H), 7.42-7.31 (m, 6H), 6.89 (d, *J*=1.8 Hz, 1H), 6.76-6.73 (m, 1H), 6.55-6.63 (m, 1H), 5.05 (s, 1H), 3.57 (s, 3H), 3.07-2.98 (m, 2H), 2.91-2.83 (m, 2H), 2.18-2.09(m, 1H), 1.96-1.81 (m, 1H), 1.10 ppm (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 150.6, 145.2, 135.5, 133.6, 132.3, 129.7, 127.6, 120.2, 120.0, 111.8, 55.5, 51.5, 32.3, 26.8, 25.2, 19.9. HR-MS (ESI) m/z calculated for $C_{27}H_{33}O_2S_2Si^+$ $[M+H]^+$ 481.1686, found 481.1687.

4k: 4-(1,3-Dithian-2-yl)-2-methoxyphenol (0.8 g, 3.30 mmol, 1 equiv.), imidazole (270 mg, 3.96 mmol, 1.2 equiv.) and 4-dimethylaminopyridine (42 mg, 0.34 mmol, 0.1 equiv.) were dissolved in dry DCM (10 mL), in an argon purged round-bottom flask. Then, *tert*-butyldimethylsilyl chloride (597 mg, 3.96 mmol, 1.2 equiv.) was added dropwise to the stirring solution. The mixture was left stirring at room temperature for 24 h. The reaction was quenched with H_2O (10 mL) and the layers were separated. The organic layer was collected and washed with water (10 mL) and Brine (10 mL), dried over $MgSO_4$, filtered and evaporated. The product was purified by flash chromatography (Hex:EtOAc, 95:5) to yield **4k** in 90% yield (1.056 mg, 2.86 mmol) as a colorless thick oil with same spectral characterization as previously described.[40] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 6.97 (d, *J*=1.8 Hz, 1H), 6.92-6.89 (m, 1H), 6.79-6.76 (m, 1H), 5.11 (s, 1H), 3.81 (s, 3H), 3.10-3.01 (m, 2H), 2.93-2.86 (m, 2H), 2.21-2.11 (m, 1H), 1.99-1.84 (m, 1H), 0.98 (s, 9H), 0.14 (s, 6H).

4l: Prepared according to a modified previously reported method.[41] In an argon purged round-bottom flask were added 10 mL of dry DCM, 5 mL of glacial acetic acid, and BF_3•OEt_2 (2.47 mL, 20 mmol, 1 equiv.). Then, a solution of 1,3-propanedithiol (2 mL, 20 mmol, 1 equiv.) and chloromethyl methyl ether (1.67 mL, 22 mmol, 1.1 equiv.) in 30 mL of dry DCM was added dropwise for 10 min at room temperature. The solution was left stirring for 3 hours at room temperature, and then quenched with 40 mL of water. The layers were separated and the organic phase collected and washed with water (40 mL), a 10% aqueous NaOH solution (2 × 40 mL) and brine (40 mL). The organic solvent was dried over $MgSO_4$, filtered and evaporated. Sublimation under reduced pressure gave pure **4l** as a white solid in 32% yield (778 mg, 6.47 mmol), with same spectral characterization as previously described.[42] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.78 (s, 2H), 2.84-2.80 (m, 4H), 2.11-2.03 (m, 2H).

4m: Prepared according to method A. 53% yield (560 mg, 2.66 mmol), pale green solid. 1.2 equiv. of 1,3-propanedithiol were used. Obtained with same spectral characterization as previously described,[43] after purification by flash chromatography (Hex:EtOAc, 85:15). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.34-7.22 (m, 5H), 4.24 (t, J = 7.3 Hz, 1H), 3.02 (d, J = 7.3 Hz, 2H), 2.85-2.80 (m, 4H), 2.15-2.05 (m, 1H), 1.92-1.79 (m, 1H).

4n: Prepared according to a modified previously reported method.[35] Butyraldehyde (0.45 mL, 5 mmol, 1 equiv.) and 1,3-propanedithiol (0.6 mL, 6 mmol, 1.2 equiv.) were dissolved in 20 mL of dry DCM under argon. The solution was stirred at room temperature and BF_3•OEt_2 (0.43 mL, 0.7 mmol, 0.7 equiv.) was added dropwise. After 90 minutes, the reaction was quenched by washing the reaction mixture twice with 20 mL of 10% aqueous NaOH. The combined aqueous layers were then extracted twice with 20 mL of DCM. The organic layers were combined, washed with 25 mL of brine and dried over $MgSO_4$. The organic solvent was evaporated under reduced pressure and the resulting oil was purified by flash chromatography (hexane/EtOAc 97:3), which afforded **4n** as a colorless oil in 99% yield (808 mg, 4.98 mmol). Obtained with same spectral characterization as previously described.[34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 4.05 (t, J=6.7 Hz, 1H), 2.92-2.76 (m, 4H), 2.14-2.06 (m, 1H), 1.90-1.77 (m, 1H), 1.75-1.67 (m, 2H), 1.59-1.45 (m, 2H), 0.85-0.97 (m, 3H).

4o: Prepared according to a modified previously reported method.[44] Pivalaldehyde (5 mmol, 1 equiv.) and N-bromosuccinimide (178 mg, 1 mmol, 0.2 equiv.) were dissolved in CH_2Cl_2 (25 ml). The solution was then stirred under argon at r.t. and 1,3-propanedithiol (1.2 equiv.) was added dropwise. The reaction was monitored by TLC and quenched with 10% aqueous NaOH (25 ml) when the aldehyde was consumed (30-80 min). Aqueous and organic

layers were separated and the aqueous layer was washed with CH_2Cl_2 (2 x 25 ml). The combined organic layers were washed with 25 ml brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. 62% yield (544 mg, 3.08 mmol), white solid was obtained with same spectral characterization as previously described.[34] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.99 (s, 1H), 2.90-2.86 (m, 4H), 2.11-2.02 (m, 1H), 1.86-1.74 (m, 1H), 1.10 (s, 9H).

4p: Prepared according to method A. Flash chromatography gradient eluent: Hex:AcOEt (85:15 to 60:40). 33% yield (433 mg, 1.64 mmol), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 4.17-4.17 (m, 1H), 3.85 (d, J=6.4 Hz, 2H), 2.90-2.75 (m, 4H), 2.15-2.06 (m, 1H), 1.96-1.85 (m, 1H), 0.90 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 66.1, 48.6, 29.1, 26.2, 26.0, 18.6, -5.2. HR-MS (ESI) m/z calculated for $C_{11}H_{24}OS_2SiNa^+$ $[M+Na]^+$ 287.0930, found 287.0953.

General procedure for preparation of dithioacetals 6 (Method B), based on modified previously reported method.[44] Aldehyde (5 mmol, 1 equiv.) and *N*-bromosuccinimide (178 mg, 1 mmol, 0.2 equiv.) were dissolved in CH_2Cl_2 (25 ml). The solution was then stirred under argon at r.t. and thiol (2.5 equiv.) was added dropwise. The reaction was monitored by TLC and quenched with 10% aqueous NaOH (25 ml) when the aldehyde was consumed (30-80 min). Aqueous and organic layers were separated and the aqueous layer was washed with CH_2Cl_2 (2 x 25 ml). The combined organic layers were washed with 25 ml brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was then purified by recrystallization or by flash chromatography.

6a: Prepared according to a modified previously reported method.[33] Benzaldehyde (0.51 ml, 5 mmol, 1 equiv.) and benzenethiol (1.08 ml, 10.5 mmol, 2.1 equiv.) were dissolved in $CHCl_3$ (25 ml). The solution was then stirred at r.t. and I_2 (0.13 g, 0.5 mmol, 0.1 equiv.) was added. The reaction was monitored by TLC. When the aldehyde was consumed (30 min) the reaction was quenched with aqueous $Na_2S_2O_3$ (0.1 M, 25 ml) and then washed twice with 10% aqueous NaOH (25 ml). Aqueous and organic layers were separated and the aqueous layer was washed with $CHCl_3$ (25 ml). The combined organic layers were washed with 20 ml of H_2O, dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield the crude product. The crude product was then purified by recrystallization from hexane to afford **6a** as white crystals in 66% yield (1.01 g, 3.28 mmol) with the same spectral characterization as previously described.[45] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.39-7.20 (m, 15H), 5.42 (s, 1H).

6b: Prepared according to method B. Flash chromatography eluent: Hex:AcOEt (97.5:2.5). 91% yield (1.218 g, 4.54 mmol), colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.45-7.42 (m, 2H), 7.34-7.22 (m, 3H), 4.87 (s, 1H), 2.63-2.46 (m, 4H), 1.58-1.48 (m, 4H), 1.42-1.30 (m, 4H), 0.87 (t, J = 7.3 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 140.7, 128.5, 127.8, 127.8, 53.3, 32.0, 31.3, 22.1, 13.7. HR-MS (ESI) m/z calculated for $C_{15}H_{23}S_2^+$ $[M-H]^+$ 267.1236, found 267.1246.

6c: Prepared according to a modified previously reported method.[33] Benzaldehyde (2 mL, 19.7 mmol, 1 equiv.) and dodecanethiol (10.4mL, 43.3 mmol, 2.2 equiv.) were dissolved in dichloromethane (30 mL) in a round-bottom flask. Then, iodine (508, 2 mmol, 0.1 equiv.) was slowly added do the stirring solution as to prevent vigorous boiling of the solvent. After 2 hours of complete addition, the reaction was quenched with a 2% $Na_2S_2O_3$ aqueous solution (10 mL). The layers were separated and the organic layer collected and washed successively with a 10% aqueous NaOH solution (10 mL), water (10 mL) and brine (10 mL). The organic solvent was dried over $MgSO_4$ and filtered. After evaporating the solvent, the product was purified by flash chromatography (hexane) to give **6c** as a white amorphous solid in 57% yield (5.563 g, 11.29 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.45-7.42 (m, 2H), 7.35-7.22 (m, 3H), 4.86 (s, 1H), 2.62-2.45 (m, 4H), 1.59-1.49 (m, 4H), 1.35-1.24 (m, 36H), 0.90-0.86 (m, 6H). ^{13}C NMR ($CDCl_3$, 75MHz) δ ppm 140.8, 128.6, 127.9, 127.8, 53.3, 32.4, 32.1, 29.8, 29.7, 29.6, 29.5, 29.3, 29.3, 29.0, 22.8, 14.3. HR-MS (ESI) m/z calculated for $C_{31}H_{55}S_2^+$ $[M-H]^+$ 491.3740, found 491.3757.

6d: Prepared according to method B. 86% yield (1.150 g, 4.29 mmol), colorless oil. Flash chromatography eluent: Hex:AcOEt (97.5:2.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.47 (d, J = 7.6 Hz, 2H), 7.34-7.22 (m, 3H), 4.94 (s, 1H), 2.88-2.63 (m, 2H), 1.66-1.42 (m, 4H), 1.24-1.20 (m, 6H), 0.97-0.88 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 141.1, 128.5, 127.8, 127.7, 50.8, 50.6, 42.5, 42.4, 29.5, 29.5, 20.7, 20.6, 20.6, 11.2, 11.1. HR-MS (ESI) m/z calculated for $C_{15}H_{23}S_2^+$ $[M-H]^+$ 267.1236, found 267.1243.

6e: Prepared according to method B. 87% yield (1.171 g, 4.37 mmol), white solid. Flash chromatography eluent: Hex:AcOEt (97.5:2.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.48-7.44 (m, 2H), 7.32-7.26 (m, 2H), 7.23-7.18 (m, J = 1.3 Hz, 1H), 5.02 (s, 1H), 1.29 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 144.1, 128.7, 127.7, 127.4, 48.8, 45.8, 31.3. HR-MS (ESI) m/z calculated for $C_{15}H_{23}S_2^+$ $[M-H]^+$ 267.1236, found 267.1243.

12: Prepared according to a modified previously reported method.[46] Benzil (1g, 4.76 mmol, 1.2 equiv.) was dissolved in dry DCM (5 mL) in an argon purged round-bottom flask. The solution was cooled to 0°C in an ice bath bath. A solution of 1,3-propanedithiol (398 µL, 3.96 mmol, 1 equiv.) and BF_3•Et_2O (489 µL, 3.96 mmol, 1 equiv.) in dry DCM (1.5 mL) was added dropwise at 0 °C. The solution was warmed to room temperature for 3 hours and quenched with 10 mL of a saturated aqueous $NaHCO_3$ solution. The layers were separated and the organic phase collected. The aqueous phase was extracted with DCM (3 × 10 mL) and the organic phases combined, dried over $MgSO_4$, filtered and the solvent evaporated. The dry crude was dissolved in hot isopropanol and left cooling at room temperature. After 3 hours, the product precipitated as a white solid and was filtered and washed with cold isopropanol to yield **12** as a white solid in 54% yield (641 mg, 2.13 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.69-7.66 (m, 2H), 7.57 (dd, *J*=7.9, 1.5 Hz, 2H), 7.38-7.28 (m, 4H), 7.22-7.17 (m, 2H), 3.26 (ddd, *J*=14.4, 12.0, 2.9 Hz, 2H), 2.80-2.73 (m, 2H), 2.17-2.08 (m, 1H), 2.01-1.86 (m, 1H). ^{13}C NMR (300 MHz, $CDCl_3$): δ ppm 192.8, 139.0, 134.5, 132.2, 130.8, 129.2, 128.8, 127.7, 127.5, 63.5, 29.3, 24.1. HR-MS (ESI) m/z calculated for $C_{17}H_{17}OS_2^+$ $[M+H]^+$ 301.0715, found 301.0734.

General procedure for autooxidative addition of dithianes 4a-c and 4e-k: Dithiane (1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in an argon purged round-bottom flask. The solution was cooled to -78 °C in an acetone/liquid nitrogen bath. *n*-BuLi (1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78 °C for 20 minutes and then left to warm up to room temperature for 40 minutes. The argon balloon was

replaced with an atmospheric air balloon and an additional needle was inserted in the septum as to allow air flow through the surface of the solution. As oxidation took place the solution warmed up and color change was usually observed. After 1 minute the solution was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered and evaporated. The product was purified by flash chromatography.

5a: 76% yield (128 mg, 0.26 mmol), pale yellow oil. Flash chromatography eluent: Hex:AcOEt (90:10). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.96 - 7.90 (m, 4 H) 7.54 - 7.23 (m, 11 H) 5.51 (s, 1 H) 3.30 (ddt, *J*=13.8, 10.8, 2.9, 2.9 Hz, 2 H) 2.75 - 2.68 (m, 2 H) 2.57 - 2.44 (m, 4 H) 2.15 - 2.04 (m, 1 H) 1.96 - 1.83 (m, 1 H) 1.76-1.66 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 195.1, 141.6, 136.7, 135.8, 133.4, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.1, 128.0, 64.3, 55.6, 32.7, 30.6, 29.2, 28.4, 24.4. HR-MS (ESI) m/z calculated for $C_{27}H_{28}OS_4Na^+$ $[M+Na]^+$ 519.0915, found 519.0894.

5b: 64% yield (135 mg, 0.22 mmol), amorphous yellow solid. Flash chromatography eluent: Hex:AcOEt (60:40). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.90-7.87 (m, 2H), 7.79-7.76 (m, 2H), 7.30-7.26 (m, 2H), 6.67-6.56 (m, 6H), 5.47 (s, 1H), 3.36-3.26 (m, 2H), 3.01 (s, 6H), 2.95 (s, 6H), 2.90 (s, 6H), 2.72-2.67 (m, 2H), 2.59-2.45 (m, 4H), 2.12-2.03 (m, 1H), 1.94-1.84 (m, 1H), 1.81-1.71 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 193.5, 153.4, 150.2, 150.0, 131.3, 129.5, 129.0, 128.4, 124.9, 123.6, 112.7, 111.9, 110.7, 64.4, 54.9, 40.6, 40.5, 40.1, 32.9, 30.6, 29.4, 28.7, 24.5. HR-MS (ESI) m/z calculated for $C_{33}H_{43}N_3OS_4Na^+$ $[M+Na]^+$ 648.2181, found 648.2187.

5c: 60% yield (232 mg, 0.41 mmol), amorphous white solid. Flash chromatography eluent: Hex:AcOEt (70:30). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.05 – 8.02 (m, 4H), 7.75 (d, *J*=8.8 Hz, 2H), 7.67 - 7.56 (m, 6H), 5.43 (s, 1H), 3.20 (tdd, *J*=2.3, 9.9, 14.1 Hz, 2H), 2.73 (ddd, *J*=2.9, 6.9, 14.2 Hz, 2H), 2.60-2.44 (m, 4H), 2.12 - 2.02 (m, 1H), 1.97 - 1.84 (m, 1H), 1.73-1.64 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 192.3, 146.8, 141.1, 138.4, 132.7, 132.4, 129.8, 129.4, 129.0, 118.5, 118.3, 117.7, 117.1, 112.4, 112.3, 63.5, 54.2, 32.4, 30.8, 29.3, 28.1, 23.9. HR-MS (ESI) m/z calculated for $C_{30}H_{25}N_3OS_4Na^+$ $[M+Na]^+$ 594.0773, found 594.0773.

5e: 60% yield (112 mg, 20 mmol), colorless oil. Flash chromatography eluent: Hex:AcOEt (94:6). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.00-7.88 (m, 4H), 7.42-7.38 (m, 2H), 7.12-7.00 (m, 6H), 5.44 (s, 1H), 3.26 (ddt, *J*=13.8, 10.9, 2.6 Hz, 2H), 2.76-2.68 (m, 2H), 2.57-2.46 (m, 4H), 2.13-2.04 (m, 1H), 1.96-1.82 (m, 1H), 1.76-1.66 (m, 2H). ^{19}F NMR (282MHz, $CDCl_3$): δ ppm -104.01--104.09 (m, 1F), -113.35--113.45 (m, 1F), -113.56--113.66 ppm (m, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 193.3, 167.6, 164.2, 164.2, 160.9, 137.4, 137.4, 132.3, 132.2, 131.9, 131.9, 131.8, 131.7, 130.6, 130.5, 130.1, 130.0, 116.2, 115.9, 115.5, 115.2, 63.6, 54.4, 32.7, 30.7, 29.3, 28.3, 24.2. HR-MS (ESI) m/z calculated for $C_{27}H_{25}F_3OS_4Na^+$ $[M+Na]^+$ 573.0633, found 573.0640.

5f: 66% yield (120 mg, 0.22 mmol), colorless oil. Flash chromatography eluent: Hex:AcOEt (95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.97-7.94 (m, 1H), 7.42 (d, *J*=5.9 Hz, 2H), 7.32-7.27 (m, 1H), 7.19-7.12 (m, 8H), 5.52 (s, 1H), 3.40-3.30 (m, 2H), 2.83 (s, 3H), 2.75-2.68 (m, 2H), 2.55-2.48 (m, 4H), 2.37 (s, 3H), 2.33 (s, 3H), 2.15-2.04 (m, 1H), 1.98-1.84 (m, 1H), 1.74-1.64 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 199.0, 138.7, 138.4, 138.0, 137.7, 136.1, 134.2, 133.8, 131.9, 131.2, 130.9, 129.2, 129.0, 128.4, 128.1, 127.6, 126.7, 125.6, 125.5, 64.9, 54.7, 32.8, 31.1, 29.2, 28.6, 24.3, 23.6, 20.8, 19.8. HR-MS (ESI) m/z calculated for $C_{30}H_{34}OS_4Na^+$ $[M+Na]^+$ 561.1385, found 561.1389.

5g: 58% yield (324 mg, 0.40 mmol), pale yellow oil. Flash chromatography eluent: Hex:AcOEt (80:20). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.87-7.85 (m, 1H), 7.59 (d, *J*=7.6 Hz, 2H), 7.43 (dt, *J*=7.6, 2.1 Hz, 2H), 7.36-7.13 (m, 16H), 6.94-6.76 (m, 6H), 6.12 (s, 1H), 5.17 (s, 2H), 4.95-4.79 (m, 4H), 3.32-3.24 (m, 2H), 2.71-2.64 (m, 2H), 2.40-2.30 (m, 4H), 2.07-1.96 (m, 1H), 1.94-1.80 (m, 1H), 1.56-1.46 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 198.0, 157.1, 156.8, 156.0, 137.5, 136.9, 136.4, 132.8, 130.8, 130.3, 129.8, 129.6, 129.4, 128.8, 128.7, 128.6, 128.6, 128.4, 128.1, 127.9, 127.5, 127.5, 127.3, 127.2, 125.7, 121.0, 120.8, 120.5, 114.8, 112.7, 111.8, 71.0, 70.4, 70.2, 63.1, 52.5, 32.9, 31.0, 28.9, 28.5, 24.3. HR-MS (ESI) m/z calculated for $C_{48}H_{46}O_4S_4Na^+$ $[M+Na]^+$ 837.2171, found 837.2196.

5h: 68% yield (157 mg, 0.23 mmol), colorless oil. Flash chromatography eluent: Hex:AcOEt (80:20). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.45 (d, *J*=2.9 Hz, 1H), 7.13 (d, *J*=3.5 Hz, 1H), 6.99 (t, *J*=1.5 Hz, 1H), 6.95-6.78 (m, 4H), 6.71 (d, *J*=1.8 Hz, 2H), 6.03 (s, 1H), 3.82 (s, 3H), 3.76 (s, 6H), 3.73 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H), 3.36-3.26 (m, 2H), 2.74-2.68 (m, 2H), 2.54-2.49 (m, 4H), 2.10-2.01 (m, 1H), 1.96-1.83 (m, 1H), 1.75-1.65 ppm (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 197.4, 153.7, 153.4, 153.2, 152.6, 152.4, 151.1, 130.7, 128.2, 126.7, 119.5, 116.0, 115.6, 115.6, 114.8, 114.2, 113.8, 113.0, 111.8, 62.5, 57.6, 56.2, 55.9, 55.8, 55.8, 52.1, 32.9, 30.9, 29.0, 28.6, 24.4. HR-MS (ESI) m/z calculated for $C_{33}H_{40}O_7S_4Na^+$ $[M+Na]^+$ 699.1549, found 699.1572.

5i: 62% yield (63 mg, 0.13 mmol), yellow oil. Flash chromatography was run with eluent Hex:AcOEt:Et_3N (50:50:2) because the compound was unstable on silica without treatment with triethylamine. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.65-8.61 (m, 1H), 8.52-8.45 (m, 2H), 8.10-8.07 (m, 1H), 7.85-7.78 (m, 2H), 7.70-7.66 (m, 3H), 7.49-7.41 (m, 1H), 7.19-7.11 (m, 2H), 6.39 (s, 1H), 3.46-3.34 (m, 2H), 2.75-2.68 (m, 2H), 2.64-2.49 (m, 2H), 2.42 (t, *J*=7.3 Hz, 2H), 2.18-2.10 (m, 1H), 1.95-1.81 (m, 1H), 1.61-1.51 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 195.4, 161.0, 157.8, 152.3, 149.2, 149.1, 148.0, 137.1, 137.1, 136.8, 127.4, 124.0, 123.2, 123.2, 122.3, 122.2, 65.9, 53.2, 32.7, 31.2, 28.3, 28.2, 24.9. HR-MS (ESI) m/z calculated for $C_{24}H_{25}N_3OS_4Na^+$ $[M+Na]^+$ 522.0773, found 522.0806.

5j: 89% yield (239 mg, 0.19 mmol), amorphous white solid. Flash chromatography eluent: Hex:AcOEt (80:20). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.69-7.61 (m, 12H), 7.41-7.15 (m, 22H), 6.79 (s, 1H), 6.66-6.59 (m, 4H), 5.28 (s, 1H), 3.53 (s, 3H), 3.52 (s, 3H), 3.47 (s, 3H), 3.24-3.15 (m, 2H), 2.63 (dt, *J*=14.1, 2.9 Hz, 2H), 2.45-2.32 (m, 4H), 2.06-1.96 (m, 1H), 1.87-1.75 (m, 1H), 1.63-1.54 (m, 2H), 1.10-1.08 ppm (m, 27H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 194.2, 151.1, 150.7, 150.4, 150.0, 145.2, 144.9, 135.5, 135.3, 134.5, 133.5, 133.5, 133.0, 130.2, 130.0, 129.7, 129.7, 129.6, 127.8, 127.6, 127.5, 123.0, 121.1, 120.2, 120.2, 119.7, 119.5, 112.4, 112.3, 112.2, 64.1, 55.5, 55.5, 55.4, 32.7, 30.5, 29.3, 28.4, 26.8, 26.7, 26.6, 24.4, 19.9, 19.9, 19.9. HR-MS (ESI) m/z calculated for $C_{78}H_{88}O_7S_4Si_3Na^+$ $[M+Na]^+$ 1371.4613, found 1371.4641.

5k: 61% yield (148 mg, 0.15 mmol), amorphous white solid. Flash chromatography eluent: Hex:DCM (1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm ^{1}H NMR ($CDCl_3$, 300MHz): d = 7.49-7.45 (m, 3H), 7.37-7.34 (m, 1H), 6.96 (d, *J*=2.3 Hz, 1H), 6.85-6.74 (m, 4H), 5.43 (s, 1H), 3.80 (s, 6H), 3.77 (s, 3H), 3.33-3.24 (m, 2H), 2.74-2.67 (m, 2H), 2.58-2.44 (m, 4H), 2.12-2.05 (m, 1H), 1.94-1.82 (m, 1H), 1.74-1.65 (m, 2H), 0.98 (s, 9H), 0.97 (s, 9H), 0.96 (s, 9H), 0.15-0.11 (m, 18H) ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 194.2, 151.4, 151.1, 150.8, 150.3, 145.2, 144.9, 134.7, 130.3, 129.8, 123.3, 121.5, 120.8, 120.5, 120.4, 120.3, 112.3, 112.2, 112.1, 64.2, 55.7, 55.6, 55.5, 55.3, 32.8, 30.7, 29.4, 28.5, 25.8, 25.7, 24.5, 18.6, 18.5, -4.4, -4.5. HR-MS (ESI) m/z calculated for $C_{48}H_{76}O_7S_4Si_3Na^+$ $[M+Na]^+$ 999.3679, found 999.3645.

5d: Dithiane **4d** (281 mg, 1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in an argon purged round-bottom flask. The solution was cooled to -78ºC in an acetone/liquid nitrogen bath. LDA (0.85mL of a 1.5 M solution, 1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 ºC. The solution was left stirring at -78 ºC for 20 minutes and then left to warm up to room temperature for 40 minutes. The argon balloon was replaced with an atmospheric air balloon and an additional needle was inserted in the septum as to allow air flow through the surface of the solution. As oxidation took place the solution warmed up and color change was observed. After 1 minute the solution was quenched with 10 mL of a saturated aqueous NH_4Cl solution. The aqueous layer was extracted three times with Et_2O (3 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was evaporated and the product purified by flash chromatography (eluent Hex:AcOEt, 90:10) to afford the desired compound **5d** in 51% yield (127 mg, 0.17 mmol) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.83-7.77 (m, 4H), 7.59-7.54 (m, 2H), 7.50-7.44 (m, 4H), 7.32-7.26 (m, 2H), 5.37 (s, 1H), 3.29-3.19 (m, 2H), 2.75-2.69 (m, 2H), 2.59-2.45 (m, 4H), 2.13-2.03 (m, 1H), 1.96-1.82 (m, 1H), 1.76-1.66 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 193.5, 140.7, 135.4, 134.2, 132.2, 132.2, 131.7, 130.6, 130.5, 129.9, 128.9, 122.7, 122.4, 63.7, 54.5, 32.6, 30.7, 29.3, 28.3, 24.2. HR-MS (ESI) m/z calculated for $C_{27}H_{24}Br_3OS_4^-$ $[M-H]^-$ 728.8266, found 728.8265.

General procedure for autooxidative addition of dithioacetals 6a-6d: Dithioacetal **6** (1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in an argon purged round-bottom flask. The solution was cooled to -78 ºC in an acetone/liquid nitrogen bath. *n*-BuLi (1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 ºC. The solution was left stirring at -78 ºC for 20 minutes and then left to warm up to room temperature for 40 minutes. The argon balloon was replaced with an atmospheric air balloon and an additional needle was inserted in the septum as to allow air flow through the surface of the solution. After 1 minute the solution was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered and evaporated. Products **7** and **8** were obtained after purification by flash chromatography.

7a: 48% yield (97 mg, 0.32 mmol), white solid. Flash chromatography eluent: Hex:AcOEt (97.5:2.5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.94-7.90 (m, 2H), 7.49-7.44 (m, 1H), 7.38-7.17 (m, 12H), 5.85 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 194.8, 136.6, 135.6, 134.1, 133.4, 133.1, 129.0, 128.9, 128.8, 128.7, 128.1, 128.0, 60.4. HR-MS (ESI) m/z calculated for $C_{20}H_{17}OS^+$ $[M+H]^+$ 305.0995, found 305.1013. The corresponding orthothioester product, **8a** could not be isolated due to low polarity and structural similarity to **6a**. However, the following characteristic peaks for the **8a** can be observed from the NMR spectrum of a mixture with the dithioacetal. **8a**: ^{1}H NMR (300 MHz, $CDCl_3$): 7.69-7.64 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 139.4, 132.9, 128.8, 128.4, 128.3, 128.0, 127.9, 77.0.

7b: 97% yield (92 mg, 0.32 mmol), white solid. Flash chromatography eluent: Hex:AcOEt (95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.99-7.96 (m, 2H), 7.53-7.23 (m, 8H), 5.55 (s, 1H), 2.56-2.42 (m, 2H), 1.58-1.48 (m, 2H), 1.41-1.29 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 195.3, 136.9, 135.9, 133.3, 129.0, 128.9, 128.9, 128.7, 128.0, 55.5, 31.3, 31.2, 22.1, 13.7. HR-MS (ESI) m/z calculated for $C_{18}H_{21}OS^+$ $[M+H]^+$ 285.1308, found 285.1328.

8b: 72% yield (86 mg, 0.24 mmol), colorless oil. Flash chromatography eluent: Hex:AcOEt (95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.87-7.84 (m, 2H), 7.35-7.21 (m, 3H), 2.58 (t, J = 7.3 Hz, 6H), 1.51-1.29 (m, 12H), 0.88-0.83 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 141.8, 131.3, 127.9, 127.6, 73.5, 31.5, 30.5, 22.3, 13.7. HR-MS (ESI) m/z calculated for $C_{15}H_{23}S_2^+$ $[M-S(CH_2)_3CH_3]^+$ 267.1236, found 267.1255.

7c: 73% yield (99 mg, 0.25 mmol), pale yellow solid. Flash chromatography gradient eluent: Hex:Toluene (80:20 to 50:50). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.99-7.96 (m, 2H), 7.54-7.23 (m, 8H), 5.55 (s, 1H), 2.55-2.41 (m, 2H), 1.59-1.49 (m, 2H), 1.30-1.22 (m, 18H), 0.90-0.86 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 195.3, 136.9, 136.0, 133.3, 129.1, 129.0, 128.9, 128.7, 128.0, 55.6, 32.1, 31.6, 29.8, 29.7, 29.6, 29.5, 29.3, 29.2, 29.0, 22.8, 14.3. HR-MS (ESI) m/z calculated for $C_{26}H_{37}OS^+$ $[M+H]^+$ 397.2560, found 397.2591.

8c: 56% yield (131 mg, 0.19 mmol), white solid. Flash chromatography eluent: Hexane (100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.87 -7.84 (m, 2H), 7.35-7.21 (m, 3H), 2.57 (t, *J*=7.3 Hz, 6H), 1.54-1.44 (m, 6H), 1.31-1.24 (m, 54H), 0.90-0.86 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 142.1, 128.1, 127.8, 73.7, 32.1, 32.0, 29.8, 29.8, 29.6, 29.5, 29.4, 29.3, 28.6, 22.9, 14.3. HR-MS (ESI) m/z calculated for $C_{31}H_{55}S_2^+$ $[M-S(CH_2)_{11}CH_3]^+$ 491.3740, found 491.3737.

7d: 67% yield (63 mg, 0.22 mmol), pale yellow solid. 1:1 mixture of diastereomers. Flash chromatography eluent: Hex:AcOEt (95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 8.01-7.97 (m, 4H), 7.54-7.23 (m, 16H), 5.61 (s, 2H), 2.75-2.61 (m, 2H), 1.72-1.42 (m, 4H), 1.30 (d, J = 6.4 Hz, 3H), 1.19 (d, J = 7.0 Hz, 3H), 0.98-0.86 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 195.5, 195.4, 137.2, 135.9, 133.3, 129.0, 128.9, 128.9, 128.7, 127.9, 54.7, 54.6, 42.1, 41.9, 29.7, 29.7, 21.0, 20.6, 11.3, 11.2. HR-MS (ESI) m/z calculated for $C_{18}H_{21}OS^+$ $[M+H]^+$ 285.1308, found 285.1303. The corresponding orthothioester product **8d** could not be isolated due to low polarity and structural similarity to **6d**. However, the following characteristic peaks for **8d** can be observed in NMR spectrum of the crude reaction mixture: **8d**:^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 69.3, 29.0 20.1, 11.5.

9: Dithioacetal **6e** (0.5 mmol, 1 equiv.) was dissolved in dry THF (2.5 mL) in an argon purged round-bottom flask. The solution was cooled to -78 ºC in an acetone/liquid nitrogen

bath. *n*-BuLi (1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78 °C for 20 minutes and then left to warm up to room temperature for 40 minutes. The argon balloon was replaced with an atmospheric air balloon and an additional needle was inserted in the septum as to allow air flow through the surface of the solution. After 1 minute the solution was quenched with 5 mL of a saturated aqueous NH_4Cl solution. 5 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 5 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was evaporated and the product was purified by preparative TLC (eluent: pentane) to yield **9** as a colorless oil (62%, 60 mg, 0.31 mmol) with the same spectral characterization as previously described.[47] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.93-7.90 (m, 2H), 7.56-7.51 (m, J = 7.3 Hz, 1H), 7.44-7.39 (m, 2H), 1.58 (s, 9H).

General Procedure for autoxidative addition of 2-alkyl-1,3-dithianes 4l-p: Dithiane (1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in an argon purged round-bottom flask. The solution was cooled to -78 °C in an acetone/liquid nitrogen bath. *n*-BuLi (1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78°C for 20 minutes and then left to warm up to room temperature for 40 minutes. The argon balloon was replaced with an atmospheric air balloon and an additional needle was inserted in the septum as to allow air flow through the surface of the solution. After 5 minutes the solution was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered and evaporated. The product was purified and separated from unreacted starting material by flash chromatography.

1a: 63% yield (47 mg, 0.18 mmol), white solid. Flash chromatography eluent: DCM (100%). Obtained with same spectral characterization as previously described.[19] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 4.28 (s, 3H), 3.15 (s, 1H), 3.07-2.95 (m, 4H), 2.78-2.62 (m, 4H), 2.07-2.00 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 74.7, 47.4, 27.9, 27.2, 25.5.

10m: 27% yield, (45 mg, 0.14 mmol), white solid. Flash chromatography eluent: Hex:AcOEt (95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.33-7.21 (m, 10H), 4.00 (s, 2H), 3.41 (s, 2 H), 2.86-2.76 (m, 2H), 2.60-2.53 (m, 2H), 1.99-1.90 (m, 1H), 1.84-1.73 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 200.6, 134.9, 134.3, 130.2, 129.9, 128.5, 128.5, 127.7, 127.0, 62.5, 44.3, 43.4, 28.0, 24.2. HR-MS (ESI) m/z calculated for $C_{19}H_{21}OS_2^+$ $[M+H]^+$ 329.1028, found 329.1052.

10n: 24% yield (29 mg, 0.12 mmol), colorless oil. Flash chromatography eluent: Hex:DCM (55:45). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.02-2.92 (m, 2H), 2.66-2.56 (m, 4H), 2.09-2.00 (m, 1H), 1.96-1.91 (m, 2H), 1.97-1.76 (m, 1H), 1.71-1.59 (m, 2H), 1.47-1.34 (m, 2H), 0.95-0.89 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 204.3, 61.4, 40.6, 37.8, 27.9, 25.0, 18.4, 18.0, 14.4, 13.9. HR-MS (ESI) m/z calculated for $C_{11}H_{21}OS_2^+$ $[M+H]^+$ 233.1028, found 233.1050.

11: 22% yield (61 mg, 0.22 mmol), colorless oil. Flash chromatography eluent: Hex:AcOEt (97:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 2.86 (t, J=7.0 Hz, 4H), 1.79 (quin, J=7.2 Hz, 2H), 1.20 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 206.6, 46.5, 29.7, 27.5, 27.5. HR-MS (ESI) m/z calculated for $C_{13}H_{25}O_2S_2^+$ $[M+H]^+$ 277.1290, found 277.1323.

10p: 31% yield (44 mg, 0.13 mmol), colorless oil. Flash chromatography gradient eluent: Hex:DCM (85:15 to 60:40). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.02-2.92 (m, 2H), 2.67-2.57 (m, 4H), 2.07-2.01 (m, 1H), 1.97-1.92 (m, 2H), 1.87-1.71 (m, 1H), 1.66-1.57 (m, 2H), 1.42-1.28 (m, 10H), 0.90-0.83 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 204.5, 61.5, 38.5, 35.8, 32.1, 31.6, 27.9, 25.0, 24.7, 24.1, 22.6, 22.3, 14.1, 14.0. 2-(*n*-hexyl)-1,3-dithiane was isolated in 23% yield (44 mg, 23 mmol), colorless oil with same spectral characterization as previously described:[48] ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 4.03 (t, J=7.0 Hz, 1H), 2.91-2.76 (m, 4H), 2.14-2.06 (m, 1H), 1.91-1.79 (m, 1H), 1.76-1.68 (m, 2H), 1.54-1.44 (m, 2H), 1.32-1.24 (m, 4H), 0.89-0.85 (m, 3H). HR-MS (ESI) m/z calculated for $C_{15}H_{29}OS_2^+$ $[M+H]^+$ 289.1654, found 289.1676.

Reaction of 4a with benzoyl chloride: Dithiane **4a** (200 mg, 1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in an argon purged round-bottom flask. The solution was cooled to -78 °C in an acetone/liquid nitrogen bath. *n*-BuLi (0.53 mL of a 2.5 M solution, 1.32 mmol, 1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78 °C for 20 minutes and then left to warm up to room temperature for 40 minutes. Benzoyl chloride (77 µL, 0.66 mmol, 0.65 equiv.) was added dropwise to the solution and after 2 minutes, while under argon, the reaction was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered and evaporated. The product was purified by flash chromatography (eluent Hex:AcOEt, 90:10) to afford **5a** in 71% yield (180 mg, 0.36 mmol) as a pale yellow oil.

Reaction of 4a with *S*-benzyl benzothioate: Dithiane **4a** (200 mg, 1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in an argon purged round-bottom flask. The solution was cooled to -78 °C in an acetone/liquid nitrogen bath. *n*-BuLi (0.53 mL of a 2.5 M solution,1.32 mmol, 1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78 °C for 20 minutes and then left to warm up to room temperature for 40 minutes. Then, *S*-benzyl benzothioate (151 mg, 0.66 mmol, 0.65 equiv.) in dry THF (1 mL) was added dropwise to the solution. After 2 minutes, while under argon, the reaction was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered and evaporated. The product was purified by flash chromatography (eluent Hex:AcOEt, 90:10) to afford **5a** in 89% yield (226 mg, 0.45 mmol) as a pale yellow oil.

Reaction of 4a in presence of $^{18}O_2$: General procedure for autooxidative addition of dithianes was used, although a small ballon filled with $^{18}O_2$ was used directly in the oxidation reaction. HR-MS (ESI) m/z calculated for $C_{27}H_{28}{}^{18}OS_4Na^+$ $[M+Na]^+$ 521.0958, found 521.0930.

Reaction of 4a in presence of TEMPO: Dithiane **4a** (200 mg, 1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL) in

an argon purged round-bottom flask. The solution was cooled to -78°C in an acetone/liquid nitrogen bath. *n*-BuLi (0.53 mL of a 2.5 M solution, 1.3 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78 °C for 20 minutes and then left to warm up to room temperature for 40 minutes. Then, TEMPO (206 mg in 1.5 mL of dry THF, 1.12 mmol, 1.3 equiv.) was added dropwise to the solution. After 2 minutes, the argon balloon was replaced with an atmospheric air balloon and an additional needle was inserted in the septum as to allow air flow through the surface of the solution. After 1 minute the solution was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered and evaporated. Flash chromatography (Hex:AcOEt, 95:5) yielded starting material **4a** (20%, 39 mg, 0.20 mmol) and dimer **2** (27%, 53 mg, 0.14 mmol) as a white solid, with same spectral characterization as previously described.[49] **2**:^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 7.54-7.15 (m, 10H), 2.70-2.49 (m, 8H), 2.01-1.75 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 135.0, 133.0, 127.6, 127.3, 70.9, 29.0, 24.7.

Reaction of 4a with 12: Dithiane **4a** (200 mg, 1.02 mmol, 1 equiv.) was dissolved in dry THF (5 mL, 0.2 M) in an argon purged round-bottom flask. The solution was cooled to -78 °C in an acetone/liquid nitrogen bath. *n*-BuLi (0.45 mL of a 2.5 M solution, 1.12 mmol, 1.1 equiv.) solution in hexanes was added dropwise to the reaction mixture at -78 °C. The solution was left stirring at -78 °C for 20 minutes and then left to warm up to room temperature for 40 minutes. Phenyl(2-phenyl-1,3-dithian-2-yl)methanone **12** (337 mg, 1.12 mmol, 1.1 equiv.) in THF (5 mL) was added dropwise to the solution. After 2 minutes, while under argon, the reaction was quenched with 10 mL of a saturated aqueous NH_4Cl solution. 10 mL of Et_2O were added and the layers were separated. The organic phase was collected and the aqueous phase was extracted two times with Et_2O (2 × 10 mL). The organic phases were combined and dried over $MgSO_4$. The solvent was filtered, evaporated and the product purified by flash chromatography (eluent Hex:AcOEt, 90:10) to afford **5a** in 75% yield (381 mg, 0.77 mmol) as a pale yellow oil.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website and includes full accounts on computational calculations and copies of spectra for all reported compounds.

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All authors have given approval to the final version of the manuscript.

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