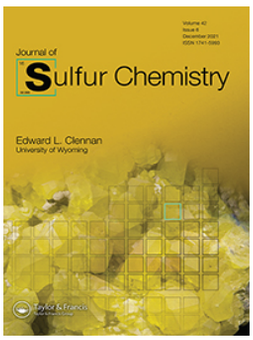

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Reactions between lithiated 1,3-dithiane oxides and trialkylboranes

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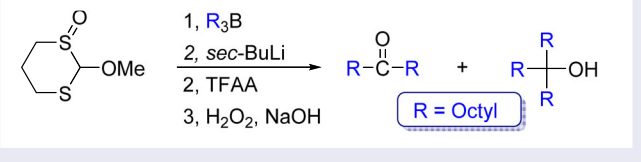
ABSTRACT

Various 2-substituted-1,3-dithiane oxides (1-oxide and 1,3-dioxide) have been metalated and reacted for the first time with a trialkylborane (trioctylborane). The 2-chloro-1,3-dioxide results in migration of an octyl group from boron to carbon with the displacement of chloride and gives nonanoic acid after oxidation, but there is no evidence for a second migration involving displacement of a sulfenate group. The reaction involving lithiation of the 2-methoxy-1-oxide results in two migrations, with the displacement of both the methoxy group and the thiolate unit of the dithiane ring, giving dioctyl ketone after oxidation, but the yield is low, primarily because thiophilic addition of the lithiating agent predominates over lithiation. Again, there is no evidence for the displacement of the sulfenate unit. However, the intermediate prior to oxidation can be treated with trifluoroacetic anhydride to induce a Pummerer rearrangement, and the presumed trifluoroacetoxyalkylthiolate group then acts as a novel leaving group and is displaced, resulting in trioctylmethanol on oxidation, but the yield is again very low.



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1. Introduction

Organoboranes are common reagents that enable many useful synthetic transformations [1–4]. Many of those reactions involve the 1,2-migration of an alkyl group from boron to an electrophilic center bearing a leaving group at the α-position. Although alkylboron compounds are quite stable as a result of the low polarity of the C–B bond, they can be oxidized easily [5,6]. Oxidation following a 1,2-migration reaction leads to the

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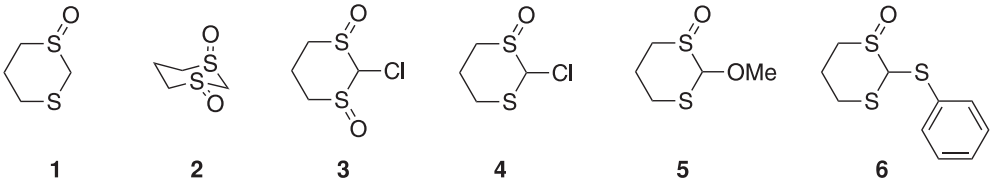


Figure 1. 1,3-Dithiane oxide derivatives **1–6**.

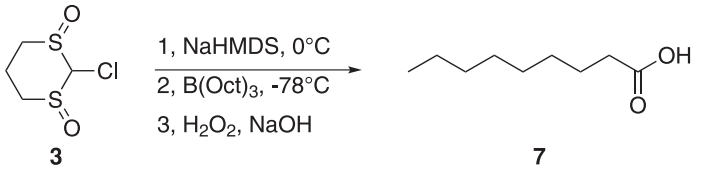
production of various products, including carbonyl compounds and alcohols [7]. Various factors affect the migration of groups in such reactions, including the steric bulk of the groups around the boron atom, which can play an important role in controlling migration [8].

Reactions of trialkylboranes with various trisubstituted methanes such as chloroform ($CHCl_3$), dichlorofluoromethane ($CHCl_2F$), chlorodifluoromethane ($CHClF_2$) and 1,1-dichloromethyl methyl ether (DCME) in the presence of a strong base result in the transfer of all three alkyl groups from boron-to-carbon in a single process [9,10]. Even trialkylboranes having a tertiary alkyl group, such as a *tert*-butyl or thexyl moiety, on reaction with DCME and lithium triethylcarboxide at 25°C, transfer all three groups successfully [9,10]. A reagent with three different leaving groups attached to a central carbon atom could, in principle, be used as an alternative to DCME, opening up possibilities for asymmetric induction to generate enantiomerically enriched chiral tertiary alcohols. Compounds having two sulfur-containing leaving groups have been used successfully to perform up to two 1,2-boron to carbon migrations [11–15], and in principle, a third leaving group could be incorporated to allow a third migration. A potential advantage of using sulfur-based leaving groups might be that stereoselectivity could be controlled, as it can, for example, in reactions of various electrophiles with metalated 1,3-dithiane oxides [16–21]. Such reagents might be able to offer possibilities for the generation of appropriately substituted chiral reagents for reactions with trialkylboranes. However, some basic studies are needed in order to underpin such possibilities.

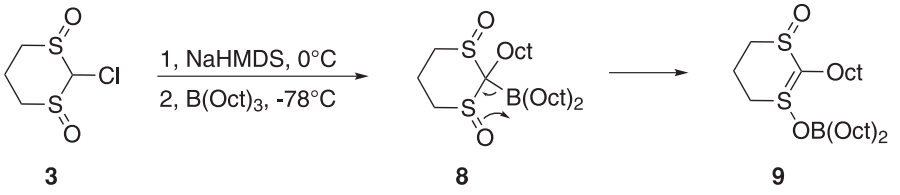
We have been extensively involved in the development of useful synthetic methods that utilize boron and lithium intermediates [22–31]. We therefore turned our attention towards reactions between trialkylboranes and appropriate lithiated 1,3-dithiane oxides derived from **1**, including *trans*-1,3-dithiane-1,3-dioxide **2**, a mixture of *cis*- and *trans*-2-chloro-1,3-dithiane-1,3-dioxides **3**, and 2-substituted 1,3-dithiane-1-oxides **4–6** (Figure 1). Our intention was to investigate what kinds of reactions, if any, would take place. We now report the results.

2. Results and discussion

Reaction of *trans*-1,3-dithiane-1,3-dioxide **2** (Figure 1) and *n*-butyllithium (*n*-BuLi) in a mixture of pyridine and tetrahydrofuran (THF), followed by the addition of an aldehyde as an electrophile, gives the corresponding alcohol as a mixture of two diastereoisomers in a ratio of around 1:2 [32]. The reaction of **2** and *n*-BuLi (two mole equivalents), followed by the addition of tri-*n*-octylborane at –78°C and then $HgCl_2$ was attempted. After work-up, 1-octanol was the only product, indicating that no migration had taken place



Scheme 1. Reaction of **3** and trioctylborane to produce nonanoic acid **7**.



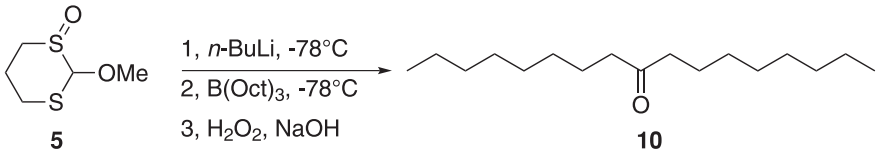
Scheme 2. Possible rearrangement of the intermediate after the first migration step.

under the conditions tried. Possibly, no boron–carbon adduct was produced as a result of the steric hindrance caused by the two sulfoxide groups. Alternatively, the sulfoxide group might not be a good leaving group. In order to try to distinguish these possibilities, the reaction of trioctylborane and metalated **3**, which contains a good leaving group (Cl), was attempted.

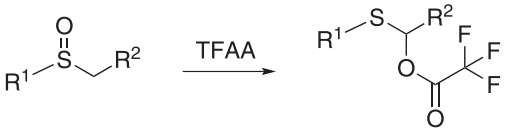
Metalation of **3** (Figure 1) was attempted using sodium *bis*(trimethylsilyl)amide (NaHMDS) at 0°C. The metalated intermediate was allowed to react with trioctylborane at −78°C followed by oxidation using a basic solution of hydrogen peroxide (H_2O_2; Scheme 1). Following work-up, nonanoic acid (**7**) was obtained in 50% yield along with 1-octanol. The GC–MS spectrum showed the presence of traces of dioctyl ketone as a result of two migrations, but the amount was not significant. Attempts to encourage the second migration by the use of a higher temperature were not successful.

Clearly, an octyl group had replaced the chlorine, although apparently in only moderate yield. It is possible that steric hindrance caused by the two sulfoxide groups inhibited the complete formation of the B–C adduct. The failure to give more than one boron to carbon migration could suggest that the sulfoxide group might not act as a good leaving group so that the reaction stops after the first migration. However, it could also be that the intermediate **8** formed after the first migration rearranges to a more stable boron enolate-like compound **9** (Scheme 2), in a manner similar to that which occurs in reactions of trialkylboranes with anions of α-bromocarbonyl compounds [33,34], as we have experienced previously in a phenylsulfoxide system [24]. The product of the rearrangement **9** would no longer be of the type that is susceptible to B–C migrations.

Some insight into such possibilities might be provided by reactions of 2-substituted-1,3-dithiane-1-oxides **4–6** (Figure 1) because after the first migration, there would still be another potential leaving group (a thiolate anion), even if the sulfoxide moiety is not a good enough leaving group. First, we decided to attempt metalation of **4** followed by reaction with several electrophiles (*e.g.* iodoethane, 3,4-dimethoxybenzaldehyde and benzaldehyde) to ensure that appropriate conditions for metalation had been found. Several bases (*e.g.* *n*-BuLi, NaHMDS and LDA) at different temperatures (0°C, −78°C and



Scheme 3. Reaction of **5** and trioctylborane to produce 9-heptadecanone (dioctyl ketone), **10**.



Scheme 4. Pummerer rearrangement induced by TFAA.

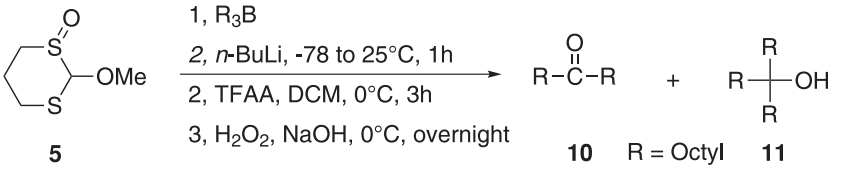
−100°C) were used. However, no new products were identified under the conditions used. One explanation for such observations is that the metalated intermediate of **4** is not stable under the conditions attempted. Therefore, in order to stabilize the anion produced *in-situ*, the chlorine in **4** was replaced by a methoxy group (*i.e.* **5**). Compound **5** (Figure 1) was a mixture of two diastereomers in a ratio of 81:19.

The reaction of **5** with *n*-BuLi followed by trioctylborane (Scheme 3) was investigated to test for possible boron-to-carbon 1,2-migrations. Indeed, the use of **5** led to the formation of dioctyl ketone (**10**; Scheme 3), which was isolated in 13% yield along with 1-octanol (72% of all octyl groups of tri–*n*–octylborane). However, no product of a triple migration was seen.

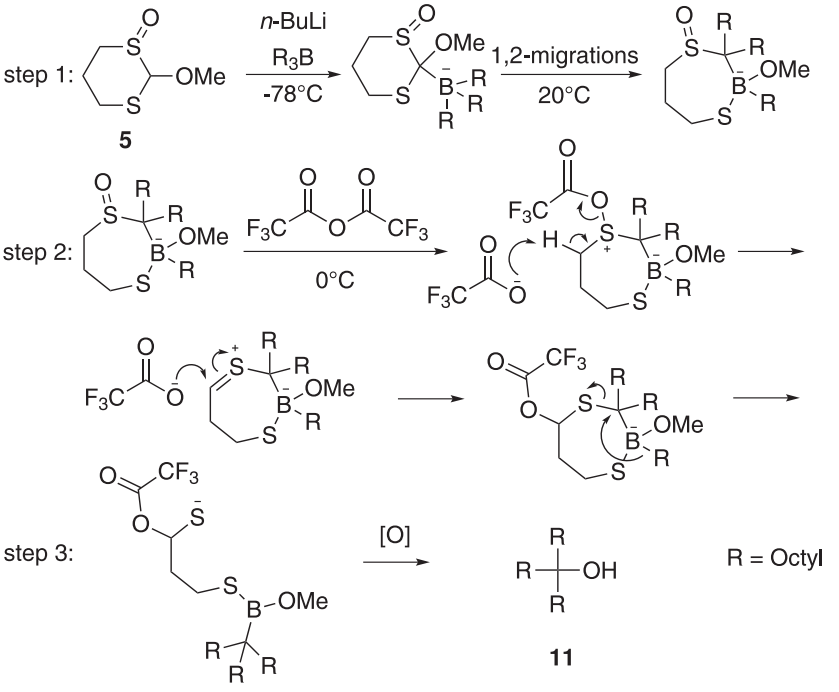
Although it was not clear why the yield of **10** was so low, it was encouraging that some dioctyl ketone had been formed, indicating that not only the methoxy group but also a second group, presumably the thiolate group, could be displaced by an octyl group during the process. However, it was disappointing that a third migration, presumably involving displacement of a sulfoxide moiety, did not take place. Whether this was due to the inability of the sulfoxide to act as a leaving group or whether the intermediate formed after two migrations could undergo a rearrangement akin to that shown in Scheme 2 to prevent a further migration was unclear. Therefore, before attempting to improve the yield of **10**, it was important to understand whether the intermediate after two migrations was still capable of being induced to undergo a further migration.

The Pummerer rearrangement is a common way to convert an alkyl sulfoxide into an α-acyloxyalkyl sulfide by the use of acetic anhydride or trifluoroacetic anhydride (TFAA; Scheme 4) [35].

An α-trifluoroacetoxyalkylthiolate group should be a better leaving group than a simple alkylthiolate group. Therefore, if the second octyl migration had involved the displacement of the thiolate group and the intermediate thus produced had not undergone a rearrangement akin to that shown in Scheme 2, a Pummerer rearrangement conducted on the intermediate might induce the third migration. In order to test this possibility, the reaction of **5** with *n*-BuLi and trioctylborane was conducted as before, but then excess TFAA (1.3 mole equivalents) was added at 0°C and the mixture was stirred for 3 h. Following oxidation of the mixture and work-up, a mixture of **10** (4%), trioctylmethanol (**11**) (6%),



Scheme 5. Induction of the third migration *via* a Pummerer rearrangement.

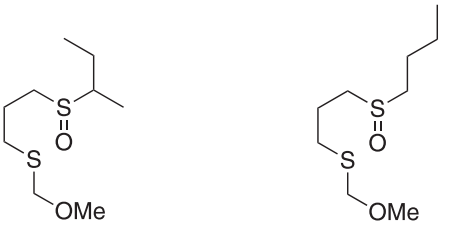


Scheme 6. A possible mechanism for the formation of **11**.

and 1-octanol (69% of all octyl groups of tri-*n*-octylborane) was produced (Scheme 5). A possible mechanism for the formation of **11** is shown in Scheme 6.

The combined yields of **10** and **11** were not very different from the yield of **10** achieved when no Pummerer rearrangement was incorporated. Not, all of the double migrated product was converted into a triple migrated product, which could indicate that the Pummerer rearrangement had not gone to completion under the conditions attempted or that some of the double migration intermediates had undergone a rearrangement akin to that in Scheme 2. However, the most significant result was that triple migration could be induced, and before investigating whether the conversion of double migrated product into the triple migrated product could be improved, it was important to try to improve the yield of the double migration product itself.

It was thought that the low yield of **10** using *n*-BuLi as the lithiating agent might be due to the poor formation of 2-lithio-2-methoxy-1,3-dithiane-1-oxide with this reagent.



12 **13**

Figure 2. Structures of **12** and **13**.

Table 1. The GC yield of **10** according to Scheme 3 but using different lithium reagents.

Entry	Lithium reagent	Mole equivalents	GC Yield of **10** (%)
1	*n*-BuLi	1.1	16[a]
2	*tert*-BuLi	1.1	12
3	*sec*-BuLi	1.0	20
4	*sec*-BuLi	1.1	28
5	*sec*-BuLi	1.2	31
6	*sec*-BuLi	1.4	5
7	*sec*-BuLi	1.8	–
8	LDA	1.1	20
9	LDA	1.1	30[b]
10	LDA	5.0	3
11	LiTMP	1.1	12
12	LiHDMS	1.1	18

[a]The yield estimated by GC of the crude product mixture is a little higher than that which could be isolated (13%).
[b]Reaction conducted at 0°C.

Therefore, other lithium reagents were used in attempts to improve the yield of **10**. The GC yields of **10** obtained under the conditions used are reported in Table 1.

The use of 1.1 mole equivalents of *sec*-BuLi led to the production of **10** in 28% yield (Table 1; Entry 4) compared to 16% when *n*-BuLi (1.1 mole equivalents) was used (Table 1; Entry 1). To our surprise, *tert*-BuLi, which is a stronger base compared with both *n*-BuLi and *sec*-BuLi, led to the formation of **10** in only 12% yield (Table 1; Entry 2). *sec*-BuLi is less sterically hindered than *tert*-BuLi and is a stronger base than *n*-BuLi. Since *sec*-BuLi provided the highest yield, it was of interest to test the effect of the quantity of *sec*-BuLi on the yield of **10**. Therefore, several experiments were carried out using different mole equivalents (1.0–1.8) and the GC yields of **10** are recorded in Table 1 (Entries 3–7), which showed that the yield of **10** peaked at 31% when *sec*-BuLi (1.2 mole equivalents) was used (Table 1; Entry 5). Several other attempts were made to improve the yield of **10** with *sec*-BuLi. For example, cooling the reaction mixture to −100°C led to a similar yield to that obtained at −78°C (31%).

It was suspected that the lithium intermediate of **5** was not produced cleanly under the conditions attempted. To test this theory, lithiation of **5** was attempted using *sec*-BuLi (1.2 mole equivalents) at −78°C followed by protonation using aqueous ammonium chloride (NH_4Cl), which would regenerate **5** in quantitative yield if there were to be clean formation of the lithiated derivative. The crude product was purified, and a new product was identified as **12** (Figure 2; See Experimental Section for characterization). Compound

12 would have resulted from the initial thiophilic addition of *sec*-BuLi to the sulfoxide group followed by ring-opening, and it was isolated in 49% yield as a 1:1 mixture of two diastereoisomers. Such a result explains why the yield of **10** dropped to 0% when a large excess of *sec*-BuLi (1.8 mole equivalents) was used.

Reaction of **5** with *n*-BuLi followed by protonation led in the same way to the production of **13** (Figure 2) in 40% yield. On the other hand, the reaction of **5** with *tert*-BuLi under similar reaction conditions did not lead to any new products and the starting material was recovered. In the latter case, both thiophilic addition and deprotonation might be restricted due to the hindrance of the *tert*-butyl group.

Next, our attention turned to the use of less nucleophilic lithium reagents such as lithium diisopropylamide (LDA), lithium tetramethylpiperidide (LiTMP) and lithium *bis*(trimethylsilyl)amide (LiHDMS). First, we attempted reaction of **5** and LDA followed by protonation. Only starting material was recovered, indicating that **5** did not undergo thiophilic addition such as was seen with *sec*- and *n*-BuLi. However, when the lithiated intermediates were treated with trioctylborane the yields of **10** were still disappointingly low (Table 1; Entries 8–12). The best yield of **10** with the lithium amide reagents was 30% when the reaction was carried out with LDA (1.1 equivalents) at 0°C (Table 1; Entry 9). The use of a superbase (Schlosser's reagent, LICKOR [36]) provided no improvement.

Finally, we investigated the use of reagent **6**, in the hope that the sulfur atom of the SPh group would provide better stabilization of the lithiated species than the OMe group and might lead to a greater preference for lithiation over thiophilic addition, leading to an improvement in the yield of **10**. However, on reaction of **6** with trioctylborane, **10** was obtained in only 4% yield along with 1-octanol as the main product. Therefore, no further studies were conducted.

3. Conclusion

Reactions of lithiated dithiane oxides, generated using different bases, with trialkylboranes, followed by oxidation, have been investigated. The use of 2-chloro-1,3-dithiane-1,3-dioxide led to only one migration, producing nonanoic acid in moderate yield (50%). 2-Methoxy-1,3-dithiane-1-oxide led to two migrations, giving dioctyl ketone in up to 31% yield and a third migration could be induced, leading eventually to trioctylmethanol, by addition of trifluoroacetic anhydride to bring about a Pummerer rearrangement prior to oxidation. Various attempts have been made to try to find conditions under which the yields could be improved, but no conditions were found that would render the reactions useful for synthetic methodology. The major problem appears to be in bringing about quantitative formation of an appropriate lithiated sulfoxide species, but if this issue can be resolved, the reactions would potentially offer an approach for the synthesis of chiral tertiary alcohols.

4. Experimental section

4.1. General

Chemicals, reagents and solvents were purchased from Aldrich Chemical Company. The solvents were purified using standard procedures [37]. The concentration of BuLi was

determined prior to use [38]. LDA-LICKOR superbase was prepared based on a literature procedure [36]. Bruker AV400 or AV500 spectrometers were used to record the ^{1}H (400 or 500 MHz) and ^{13}C NMR (100 or 125 MHz) spectra. Low- and high-resolution mass spectra were recorded on a Waters GCT Premier spectrometer and a Waters LCT Premier XE instrument, respectively. GC measurements were carried out using a Shimadzu GC-2014 gas chromatograph fitted with a ZB-5 column (30, 0.32 mm inner diameter, 1.0 μm film thickness). The carrier gas was He at 69.3 kPa, and a split injection mode was used. The oven temperature was increased from 70°C to 260°C at 6°C min^{-1} and then held for 4 min. Tetradecane was used as an external standard to allow quantification of products.

4.2. Preparation of 1,3-dithiane-1-oxide (1) [39]

Sodium periodate (1.07 g, 5 mmol) in H_2O (35 mL) was added slowly over 30 min to a stirred solution of 1,3-dithiane (0.60 g, 5.0 mmol) in MeOH (40 mL) in a round-bottom flask (250 mL) at a temperature less than 20°C. The mixture was stirred for 30 min, and the solid formed was collected by filtration, washed with dichloromethane (DCM; 3 × 20 mL) and the filtrate and washings were combined and concentrated under reduced pressure. The residue obtained was extracted with DCM (3 × 20 mL), the extract was dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure to give **1** (0.58 g, 85%) as a colorless solid, m.p. 85–86°C (lit [39]. 86–87°C). ^{1}H NMR (400 MHz; $CDCl_3$) δ 3.99 (d, J = 12.7 Hz, 1H), 3.63 (d, J = 12.7 Hz, 1H), 3.39–3.24 (m, 1H), 2.71–2.43 (m, 4H), 2.32–2.10 (m, 1H). ^{13}C NMR (125 MHz; $CDCl_3$) δ 52.9, 50.5, 28.3, 27.1.

4.3. Preparation of trans-1,3-dithiane-1,3-dioxide (2) [40]

Sodium periodate (5.35 g, 25 mmol) was added to a suspension of 1,3-dithiane (1.20 g, 10 mmol) in a mixture of MeOH (35 mL) and H_2O (3.5 mL). The mixture was stirred for 96 h then Me_2S (0.75 mL, 10 mmol) was added, and the mixture stirred for 30 min. The solvent was removed under reduced pressure, and the white solid obtained was extracted with a mixture of acetone and EtOH (5:1 by volume). The extract was passed through a short pad of silica with a mixture of acetone and EtOH (5:1 by volume) as the eluent. The solvent was removed under reduced pressure, and the *cis* and *trans* mixture was purified by flash column chromatography (silica; acetone) to give **2** (0.94 g, 62%) as a colorless solid, m.p. 171–172°C (lit [40]. 170–171°C). ^{1}H NMR (500 MHz; DMSO-d_6) δ 4.34 (s, 2H), 3.27–3.15 (m, 2H), 3.02–2.91 (m, 2H), 2.66–2.15 (m, 2H). ^{13}C NMR (125 MHz; DMSO-d_6) δ 61.8, 47.6, 14.9.

4.4. Preparation of 2-chloro-1,3-dithiane-1,3-dioxide (3) [21]

N-Chlorosuccinimide (147 mg, 1.1 mmol) was added to a stirred solution of **2** (152 mg, 1.0 mmol) in dry DCM (10 mL). The mixture was stirred at 20°C for 23 h and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica; EtOH:EtOAc = 1:9 by volume) to afford **3** (158 mg, 85%) as a colorless solid, m.p. 139–141°C (lit [21]. 141–142°C). ^{1}H NMR (500 MHz; $CDCl_3$) δ 5.93 (s, 1H), 3.46–3.08 (m, 3H), 2.97 (m, 1H), 2.85–2.60 (m, 1H), 2.48–2.16 (m, 1H). ^{13}C NMR (125 MHz; $CDCl_3$) δ 75.3, 45.4, 41.5, 14.5.

4.5. Synthesis of 2-chloro-1,3-dithiane-1-oxide (4)

N-Chlorosuccinimide (147 mg, 1.1 mmol) was added to a stirred solution of **1** (136 mg, 1.0 mmol), prepared as described in Section 4.2, in dry DCM (10 mL). The mixture was stirred at 20°C for 23 h and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica; EtOAc:Et_2O = 1:10 by volume) to give **4** (0.103 g, 60%) as a mixture of two diastereomers (58:42 ratio) as a light yellow solid, m.p. 48–70°C. ν_{max} (NaCl film) 2995, 2940, 2844, 1423 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$) the signals for the two isomers overlapped except for the C*H*Cl proton; δ 5.90 (s, 1H of major isomer), 5.49 (s, 1H of minor isomer), 3.33–3.04 (m, 3H), 3.04–2.89 (m, 2H), 2.87–2.74 (m, 1H), 2.68–2.55 (m, 1H), 2.46–2.17 (m, 4H), 1.83–1.64 (m, 1H). ^{13}C NMR (100 MHz; $CDCl_3$) major isomer: δ 74.0, 45.9, 28.9, 23.2; minor isomer: 70.2, 41.0, 29.7, 23.4. MS (EI) *m/z* (%) 172 ($^{37}ClM^+$, 12%), 170 ($^{35}ClM^+$, 36), 135 (16), 106 (100), 90 (95), 64 (30). HRMS: Found for $^{35}ClM^+$ ($C_4H_7ClOS_2$): 169.9630, calculated: 169.9627.

4.6. Synthesis of 2-methoxy-1,3-dithiane-1-oxide (5)

MeOH (10 mL) was added to sodium metal (14 mg, 0.6 mmol) under nitrogen in an ice bath and stirred for 10 min. The solution obtained was transferred in a dropwise manner through a syringe to a stirred cooled (0°C) solution of **4** (103 mg, 0.6 mmol) in dry THF (4 mL). The mixture was allowed to warm to room temperature and stirred for 1 h. The solvents were removed under reduced pressure, and the solid obtained was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were washed with brine, separated and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the crude product was purified by flash column chromatography (silica; EtOAc:Et_2O = 1:10 by volume) to yield **5** (70 mg, 70%), as a mixture of two diastereomers in a ratio of 81:19, as light yellow oil. ν_{max} (neat) 2935, 2907, 2831, 1424, 1084 and 1029 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$) δ 5.32 (s, 1H of major isomer), 5.01 (s, 1H of minor isomer) 3.75 (s, 3H of major isomer), 3.64 (s, 3H of minor isomer), 3.36 (td, J = 12.8, 2.8 Hz, 1H of major isomer), 3.12 (t, J = 6.6 Hz, 1H of minor isomer), 3.01–2.95 (m, 1H of each isomer), 2.87–2.80 (m, 1H of each isomer) 2.69–2.54 (m, 1H of minor isomer), 2.42–2.20 (m, 3H of major isomer and 2H of minor isomer). ^{13}C NMR (100 MHz; $CDCl_3$) major isomer: δ 90.2, 59.5, 45.2, 29.3, 22.2; minor isomer: δ 93.2, 58.7, 42.2, 31.1, 23.2. MS (EI) *m/z* (%) 166 (M^+, 68%), 135 (5), 106 (100), 90 (98) and 64 (95). HRMS: Found for M^+ ($C_5H_{10}O_2S_2$): 166.0125, calculated: 166. 0122.

4.7. Synthesis of 2-thiophenyl-1,3-dithiane-1-oxide (6)

Thiophenol (0.4 mL g, 3.9 mmol) was added to sodium metal (89 mg, 3.9 mmol) in a small amount of THF under nitrogen, and the mixture was stirred for 10 min. The sodium phenylthiolate obtained was added to a solution of **4** (0.667 g, 3.9 mmol) in THF (10 mL), and the mixture was stirred for 12 h. Aqueous saturated NaCl solution (10 mL) was added, and the organic layer was separated. The aqueous layer was extracted using $CHCl_3$ (3 × 20 mL), and the extracts and original organic layer were combined and dried ($MgSO_4$). The solvent was removed under reduced pressure to give **6** as a mixture of two diastereoisomers in a ratio of 65:35. One diastereoisomer was separated (290 mg, 30%) by flash column chromatography (silica; EtOAc:Et_2O = 1:10 by volume) as a yellow oil. ^1H

NMR (400 MHz; $CDCl_3$) δ 7.75–7.60 (m, 2H), 7.36–7.29 (m, 3H), 5.09 (s, 1H), 3.20–2.88 (m, 3H), 2.49–2.16 (m, 3H). ^{13}C NMR (125 MHz; $CDCl_3$) δ 133.9, 132.8, 129.5, 128.8, 69.2, 47.3, 28.7, 24.2.

4.8. Reaction of 2-chloro-1,3-dithiane-1,3-dioxide (3) and trioctylborane

1-Octene (0.40 mL, 2.5 mmol) was added in a dropwise manner to a stirred solution (0°C) of borane (0.08 mL, 0.8 mmol; 10.0 M in Me_2S) in THF (5 mL). The mixture was warmed up to 20°C and stirred for 1 h, and then cooled to –78°C. A solution of NaHMDS in THF (0.96 mL, 1.2 equiv.; 1.0 M) was added to a cooled (0°C) suspension of **3** (150 mg, 0.8 mmol) in THF (6 mL) and the mixture was cooled (–78°C). To that solution, tri-*n*-octylborane prepared earlier was transferred through a cannula. The mixture was stirred at –78°C for 3 h and allowed to warm up to 20°C over 1 h. A solution of aqueous NaOH (3.0 M, 10 mL) was added, followed by aqueous H_2O_2 (30%; 6 mL), and the mixture was stirred overnight. The organic layer was separated, followed by removal of solvent to give 1-octanol (230 mg, 72% of all octyl groups of tri-*n*-octylborane). The aqueous layer was acidified (HCl; 12 M) and extracted with DCM (3 × 20 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent was removed under reduced pressure to give **7** (64 mg, 50%) as a colorless oil. ^1H NMR (500 MHz; $CDCl_3$) δ 11.09 (br s, 1H), 2.34 (t, J = 7.5 Hz, 2H), 1.68–1.58 (app. quintet, J = 7.4 Hz, 2H), 1.40–1.17 (m, 10H), 0.87 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz; $CDCl_3$) δ 180.6, 34.3, 31.9, 29.3, 29.2, 29.2, 24.8, 22.8, 14.2.

4.9. Reaction of 2-methoxy-1,3-dithiane-1-oxide (5) and trioctylborane

1-Octene (0.23 mL, 1.44 mmol) was added in a dropwise manner to a stirred solution of borane (48 µL, 0.48 mmol; 10.0 M in Me_2S) in dry THF (5 mL). The mixture was warmed up to 20°C and stirred for 1 h. To the mixture, a solution of **5** (80 mg, 0.48 mmol) in THF (5 mL) was added. The mixture was cooled (–78°C) and *n*-BuLi in hexane (0.36 mL, 1.47 M, 0.53 mmol) was added dropwise. The mixture was stirred at –78°C for 1 h and allowed to warm up to 20°C and stirred for 1 h. The mixture was oxidized using an aqueous solution of NaOH (3.0 M, 10 mL), followed by aqueous H_2O_2 (30%, 6 mL). The mixture was stirred overnight and then saturated with NaCl. The crude product was extracted with $CHCl_3$ (3 × 20 mL), and the organic layers were combined and dried ($MgSO_4$). The solvents were removed under reduced pressure, and the residue obtained was purified by flash column chromatography (silica; EtOAc:Et_2O = 4:96 by volume) to give **10** (16 mg, 13%) as a colorless solid, m.p. 48–49°C (lit [41]. 48.5–49°C). ^1H NMR (400 MHz; $CDCl_3$) δ 2.38 (t, J = 7.5 Hz, 4H), 1.60–1.44 (m, 4H), 1.34–1.16 (m, 20H), 0.87 (t, J = 6.9 Hz, 6H). ^{13}C NMR (125 MHz; $CDCl_3$) δ 211.7, 43.0, 32.0, 29.5, 29.5, 29.3, 24.1, 22.8, 14.2.

4.10. Pummerer rearrangement in the reaction of 5 and trioctylborane

A solution of tri-*n*-octylborane (0.337 g, 0.96 mmol) in THF (5 mL), prepared as described above, was added to a solution of **5** (160 mg, 0.96 mmol) in THF (5 mL). The mixture was cooled to –78°C and *n*-BuLi (1.57 M in hexane; 0.72 mL, 1.13 mmol) was added in a dropwise manner. The solution was stirred at –78°C for 1 h and then allowed to warm up to 20°C. The mixture was cooled to 0°C, and a solution of TFAA (0.19 mL, 1.37 mmol) in

DCM (5 mL) was added. The mixture was stirred at 0°C for 3 h and then warmed up to 20°C. NaOH (3.0 M, 10 mL) was added to the mixture, followed by aqueous H_2O_2 (30%, 6 mL), and the mixture was stirred overnight. The mixture was saturated with NaCl and extracted with $CHCl_3$ (3 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and evaporated under reduced pressure to leave a colorless solid. The crude products were purified by flash column chromatography (silica; EtOAc:Et_2O = 4:96 by volume) to give **10** (10 mg, 4%) as a colorless oil, **11** (22 mg, 6%) as a colorless solid, and 1-octanol (258 mg, 69% of all octyl groups of tri–*n*–octylborane) as a colorless liquid.

4.11. Synthesis of (3-(sec-butylsulfinyl)propyl)(methoxymethyl)sulfane (12)

A solution of *sec*-BuLi (1.4 M in hexane, 0.37 mL, 0.52 mmol) was added in a dropwise manner to a cold (–78°C) stirred solution of **5** (79 mg, 0.48 mmol) in dry THF (10 mL). The mixture was stirred for 15 min at –78°C and saturated aqueous NH_4Cl solution (5 mL) was added. The mixture was warmed to 20°C and extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a mixture of the two diastereoisomers of **12** (55 mg, 49% yield) as a colorless oil. ν_{max} (neat) 2964, 2926, 2875, 2802, 1423, 1055, 1029, 894, 749 cm^{-1}. ^1H NMR (500 MHz; $CDCl_3$) δ 4.57 (s, 2H), 3.29 (s, 3H), 2.90–2.38 (m, 5H), 2.15–1.96 (m, 2H), 1.91–1.74 (m, 1H), 1.56–1.40 (m, 1H), 1.22, 1.14 (2d, each J = 6.9 Hz, total 3H), 1.03–0.96 (m, 3H). ^{13}C NMR (125 MHz; $CDCl_3$) δ 75.60, 75.58, 66.0, 57.3, 56.6, 56.0, 47.6, 46.9, 30.3, 23.9, 23.7, 23.3, 22.7, 15.4, 12.0, 11.5, 11.0, 10.9. EI-MS *m/z* (%) 224 (M^+, 3%), 179 (M^+ – OMe, 10), 163 (20), 148 (46), 107 (72). HRMS: Found for M^+ ($C_9H_{20}O_2S_2$): 224.0899, calculated: 224.0905.

4.12. Synthesis of (3-(butylsulfinyl)propyl)(methoxymethyl)sulfane (13)

The procedure was identical to that used in Section 4.11 except that *n*-BuLi (0.33 mL, 1.6 M in hexane, 0.53 mmol) was used instead of *sec*-BuLi. Following work-up, **13** (45 mg, 40% yield) was obtained as a colorless oil. ν_{max} (neat) 2927, 1550, 1055, 1026, 727 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$) δ 4.62 (s, 2H), 3.33 (s, 3H), 2.56–2.84 (m, 6H), 2.10 (pentet, J = 7.1 Hz, 2H), 1.73 (app. pentet, J = 7.8 Hz, 2H), 1.43–1.54 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz; $CDCl_3$) δ 75.6, 55.9, 52.4, 51.0, 30.2, 24.7, 23.1, 22.2, 13.8. EI-MS *m/z* (%) 224 (M^+, 3%), 179 (M^+ – OMe, 48), 163 (58), 148 (63), 107 (85). HRMS: Found for M^+ ($C_9H_{20}O_2S_2$): 224.0899, calculated: 224.0905.

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