

Regio- and Stereoselective Synthesis of Sulfur-Bearing Four-Membered Heterocycles: Direct Access to 2,4-Disubstituted Thietane 1-Oxides

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# 1 Regio- and Stereoselective Synthesis of Sulfur-Bearing Four- 2 Membered Heterocycles: Direct Access to 2,4-Disubstituted Thietane 3 1-Oxides

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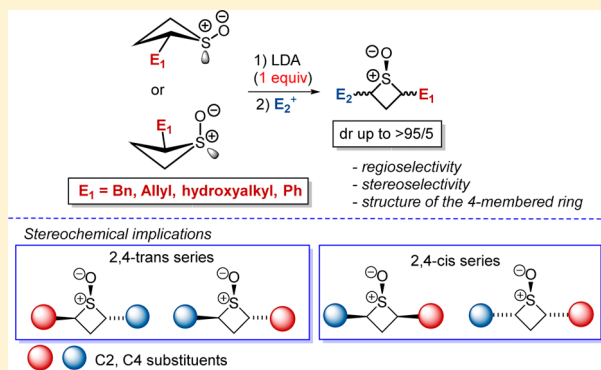
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## 11 Supporting Information

12 **ABSTRACT:** Starting from readily available C2-substituted  
13 thietane 1-oxides, a straightforward synthesis of new C2,C4-  
14 disubstituted thietane 1-oxides has been developed by using a  
15 lithiation/electrophilic trapping sequence. The chemical and  
16 configurational stability of lithiated C2-substituted thietane 1-  
17 oxides has been investigated as well as the stereochemical  
18 implications for this process. The results demonstrate that a  
19 stereoselective functionalization at the C2, C4 positions of a  
20 thietane is feasible, leaving intact the four-membered ring.



## 21 ■ INTRODUCTION

22 Sulfur-containing compounds are present in several drugs and  
23 biologically active structures and have pivotal importance in  
24 medicinal chemistry. In fact, 2 of the 21 proteinogenic amino  
25 acids contain sulfur, and some of the 2009 blockbuster drugs in  
26 the U.S. were organosulfur compounds (Figure 1).<sup>1</sup> Other  
27 interesting, and so far little explored, chemical entities bearing  
28 the sulfur atom are thietanes, sulfur-bearing four-membered  
29 heterocycles (FMHs) that are included in several bioactive  
30 molecules (Figure 1). FMHs gained recently significant  
31 prominence in medicinal chemistry and are considered as  
32 privileged scaffolds in the drug-discovery process.<sup>2</sup> In the past  
33 10 years, there has been a growing interest in structures bearing  
34 a four-membered ring due to the possibility to explore new  
35 regions of the chemical space and get new lead molecules. In a  
36 recent review, Carreira highlighted this aspect focusing on  
37 spirocyclic structures including FMHs.<sup>3</sup> Nevertheless, between  
38 the most common FMHs such as oxetanes, azetidines, and  
39 thietanes, it appears that the latter system has received much  
40 less attention.

41 Most of the reported strategies for the preparation of  
42 substituted thietanes rely on the intra- or intermolecular  
43 displacement of a suitable leaving group by a sulfur nucleophile  
44 or a [2 + 2] cycloaddition reaction as in the case of the thia  
45 Paternò–Buchi reaction.<sup>4</sup> However, these strategies could have

limits such as a competitive  $\beta$ -elimination and the use of stinking 46  
reagents or regioselectivity problems as in the case of the 47  
cycloaddition approach. 48

In a recent research program, run in our laboratory, on the 49  
chemistry of small heterocycles and functionalized FMHs as 50  
potential lead compounds,<sup>5</sup> we became interested in the 51  
preparation of C2-substituted thietane 1-oxides.<sup>6</sup> By using a 52  
direct approach, based on the functionalization of the simple 53  
and readily available parent thietane 1-oxide **1**, several C2- 54  
substituted thietane 1-oxides were obtained. In our preliminary 55  
communication, it was disclosed that thietane 1-oxide could be 56  
readily lithiated, with 1 equiv of LDA, at the C2 adjacent to the 57  
sulfinyl group and effectively trapped with electrophiles. Being 58  
**1** a prochiral substrate, the C2 functionalization led to two 59  
diastereoisomeric adducts **2** and *diast-2* with a variable degree 60  
of stereoselectivity depending on the electrophile (Scheme 1). 61 st  
However, the use of 2 equiv of LDA gave access to C2,C4 62  
doubly substituted thietane 1-oxides via a stepwise lithiation/ 63  
trapping mechanism, and a mixture of diastereomeric thietanes 64  
*cis-3* and *trans-3* was obtained. 65

This stepwise mechanism prompted us to investigate the 66  
introduction of two different electrophiles, so allowing the 67

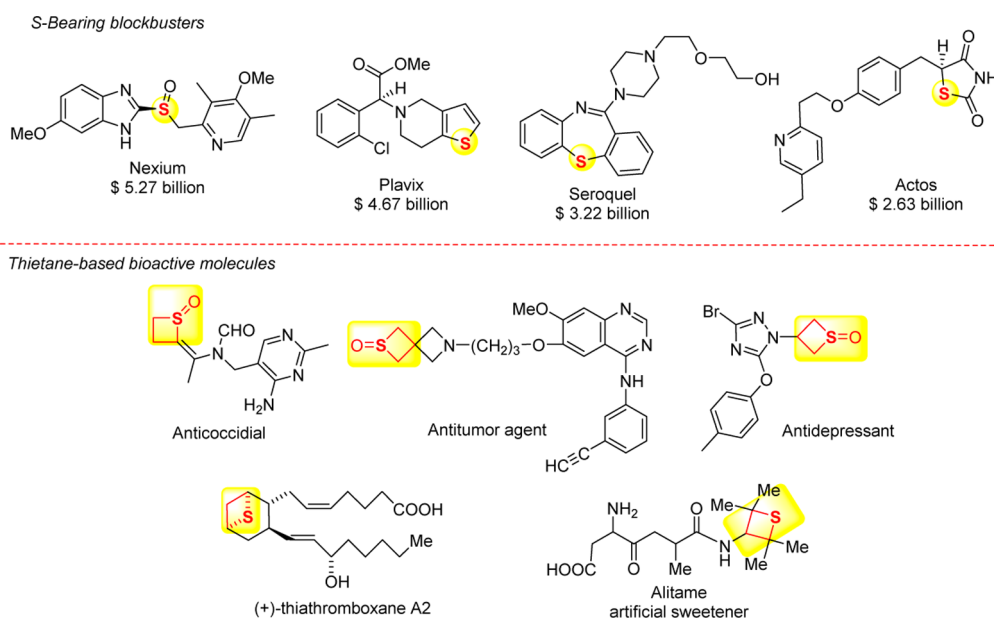
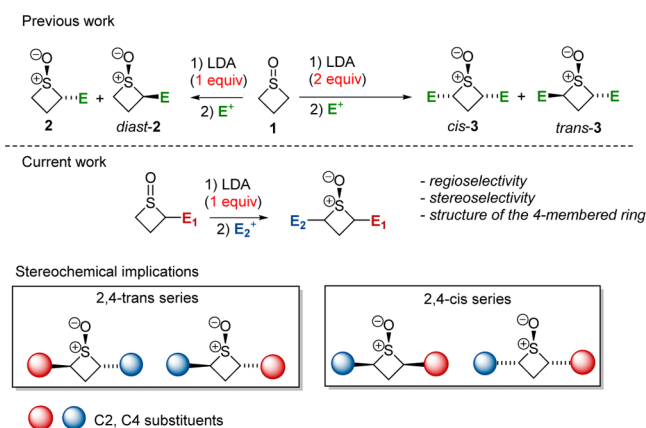


Figure 1. Sulfur- and thietane-bearing bioactive molecules.

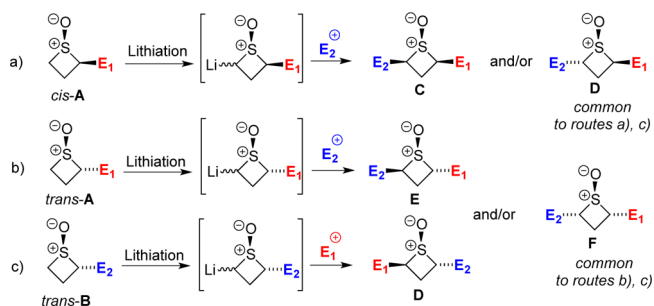
### Scheme 1. Examples of Mono and Double Functionalization of Thietane 1-Oxides



68 preparation of various 2,4-disubstituted thietane 1-oxides. We  
 69 noticed that, by a judicious choice of the starting material, the  
 70 preparation of all the stereoisomeric 2,4-disubstituted thietane  
 71 1-oxides could be achievable. In fact, stereochemical  
 72 implications related to this process suggest four different  
 73 combinations (i.e., diastereoisomers) for the same pair of C2,  
 74 C4 substituents (Schemes 1 and 2). This aspect could be  
 75 relevant for medicinal chemistry studies but also from a  
 76 structural point of view, little being known on the structural  
 77 aspects of this kind of compounds.<sup>7</sup>

78 This approach, and the corresponding stereochemical  
 79 implication, is summarized in Scheme 2 by three routes (a–  
 80 c) that can be envisaged for this lithiation/trapping sequence.  
 81 These routes could represent a selection guide when this  
 82 strategy has to be chosen for a stereoselective preparation of  
 83 C2,C4-disubstituted thietane 1-oxides. In fact, when both  
 84 diastereoisomers of C2-functionalized thietane 1-oxides are  
 85 available (i.e., *cis*-A and *trans*-A, routes a and b in Scheme 2),  
 86 further lithiation/substitution would provide all the four  
 87 stereoisomers C–F. By contrast, when only one diaster-  
 88 eoisomer of C2-functionalized thietane 1-oxides is available,

### Scheme 2



switching the sequence of introduction of the electrophile 89  
 would give access to three out of four possible stereoisomers of 90  
 C2,C4-disubstituted thietane 1-oxides (routes b and c, in 91  
 Scheme 2). 92

With the aim to address this issue, we report herein our 93  
 findings on the regio- and stereochemistry of this double 94  
 functionalization of C2-substituted thietane 1-oxides jointing to 95  
 structural features for the prepared thietanes. 96

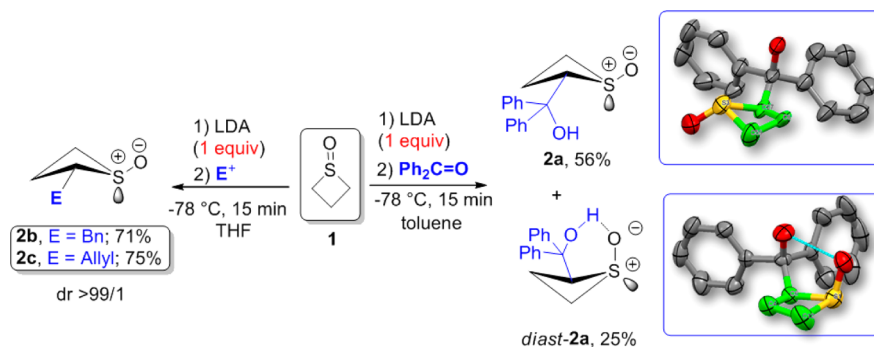
## RESULTS AND DISCUSSION

The investigation began with the preparation of representative 98  
 C2 functionalized thietane 1-oxides 2a–c and *diast*-2a by using 99  
 our reported synthetic protocol (Scheme 3).<sup>6</sup> It is worth 100 s3  
 mentioning that one main stereoisomer is observed in the 101  
 allylation and benzylation reactions of 1, leading to 2b,c, while 102  
 two diastereoisomers can be isolated in the reaction of 1 with 103  
 benzophenone (2a and *diast*-2a). 104

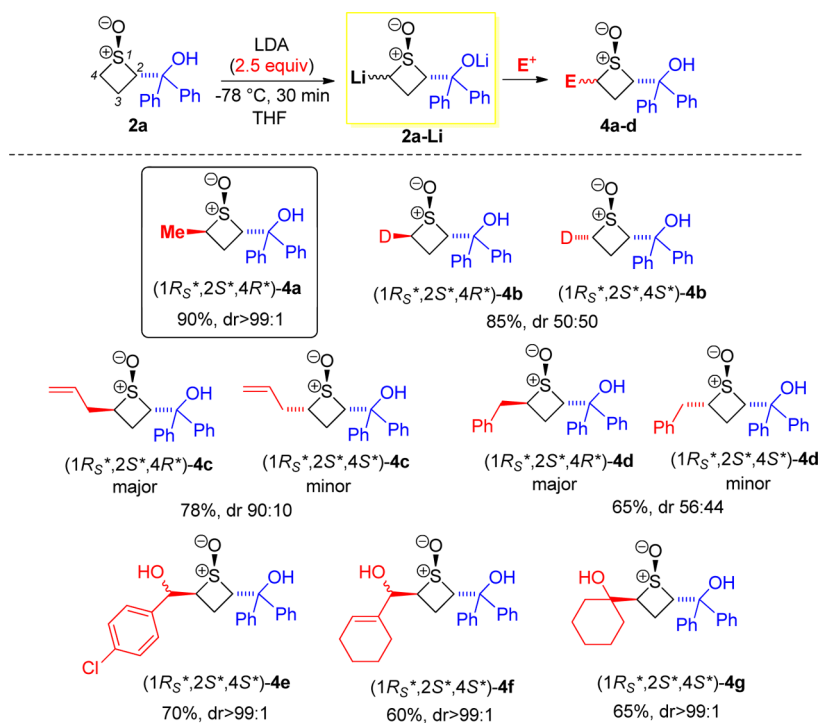
In this latter case, X-ray analysis of 2a and *diast*-2a confirmed 105  
 their structure and stereochemistry as well as differences in the 106  
 ring puckering (Scheme 3).<sup>8</sup> 107

Because of the availability of the two diastereoisomeric 108  
 thietanes 2a and *diast*-2a, disclosing different structural features 109  
 for the four-membered ring, their reactivity was investigated 110  
 first. The lithiation of 2a occurred regioselectively at the C4, in 111  
 the presence of 2.5 equiv of LDA at  $-78^{\circ}\text{C}$  in THF, and the 112  
 corresponding lithiated intermediates could be successfully 113  
 trapped with several electrophiles (including MeOD, MeI, 114

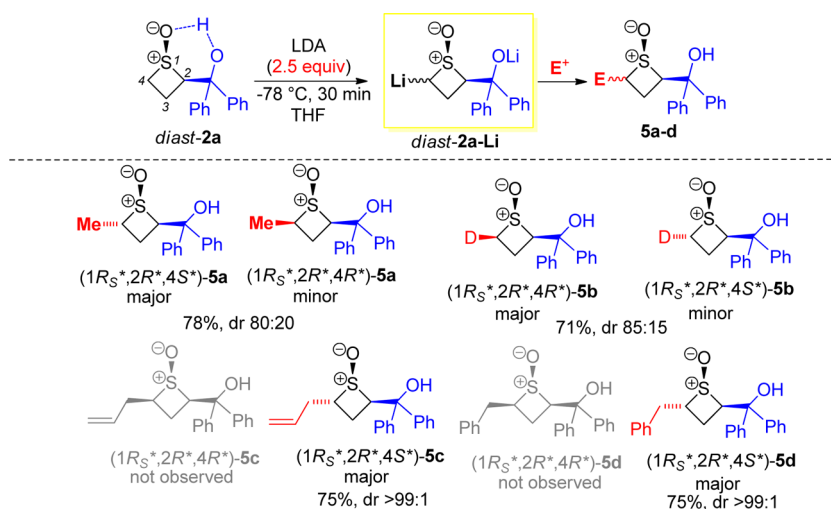
### Scheme 3. Synthesis of C2-Functionalized Thietane 1-Oxides



### Scheme 4. Lithiation/Substitution of Thietane 2a

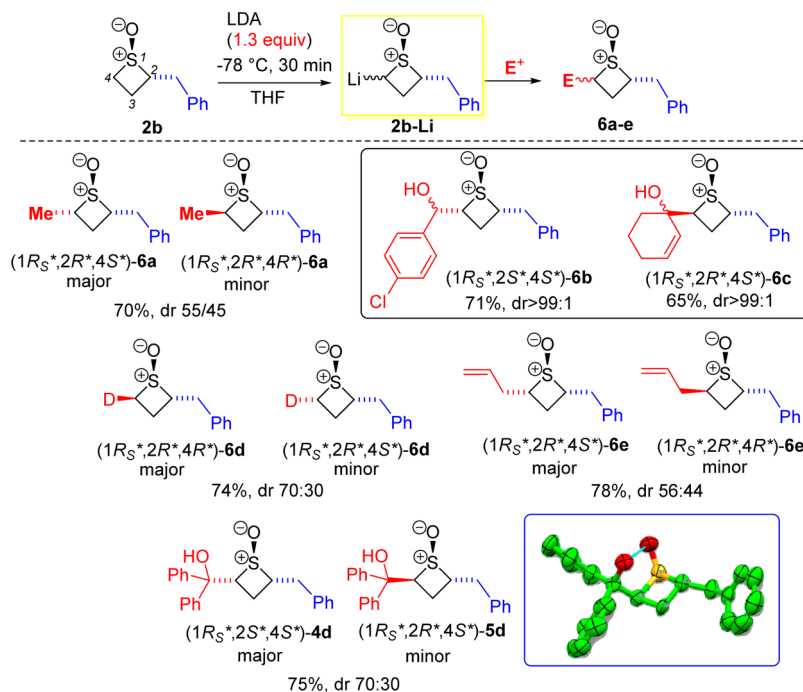


### Scheme 5. Lithiation/Substitution of Thietane diast-2a



115 BnBr, allylBr, aldehyde, and ketones), leading to disubstituted  
116 thietanes 4a–g (Scheme 4). Being the C4 prochiral, a new

stereogenic center was created upon lithiation. Nevertheless, a 117  
118 variable degree of stereoselectivity was observed in the final



119 products **4a–g**, and mixtures of two diastereoisomers were  
 120 obtained in most cases (Scheme 4). High stereoselectivity (dr >  
 121 90:10) resulted only for the reactions of lithiated **2a** with MeI  
 122 and allylBr, giving, respectively, thietanes **4a** and **4c**. By NMR  
 123 experiments (see the SI), it was demonstrated that, in these  
 124 latter cases, the introduced electrophile set preferentially *syn* to  
 125 the sulfur oxygen, leading to a relative stereochemistry  
 126 (1*R<sub>S</sub>*\*, 2*S*\*, 4*R*\*) for the main stereoisomer.<sup>9</sup> Deuteration and  
 127 benzylation occurred with very low, if any, stereoselectivity,  
 128 suggesting that the electrophile may be playing a role in  
 129 determining the stereochemical course of the reaction.<sup>10</sup> The  
 130 use of carbonyl compounds (*p*-chlorobenzaldehyde, cyclo-  
 131 hexanone, and cyclohexanone) resulted with a high level of  
 132 stereoselectivity, giving thietanes (1*R<sub>S</sub>*\*, 2*S*\*, 4*S*\*)-**4e–g**. Never-  
 133 theless, the reactions resulted poorly selective with respect to  
 134 the carbinolic carbon, and a 1:1 separable mixture of  
 135 diastereoisomers were obtained in the reactions with the  
 136 aromatic aldehyde and the prochiral ketone. The high level of  
 137 stereoselectivity observed at the C4 of the thietane ring could  
 138 be ascribed to both steric hindrance, due to the large C2  
 139 substituent, and coordination effects brought by the carbonyl  
 140 group. Attempts to use an epoxide as the electrophile failed,  
 141 and unreacted starting material was recovered.

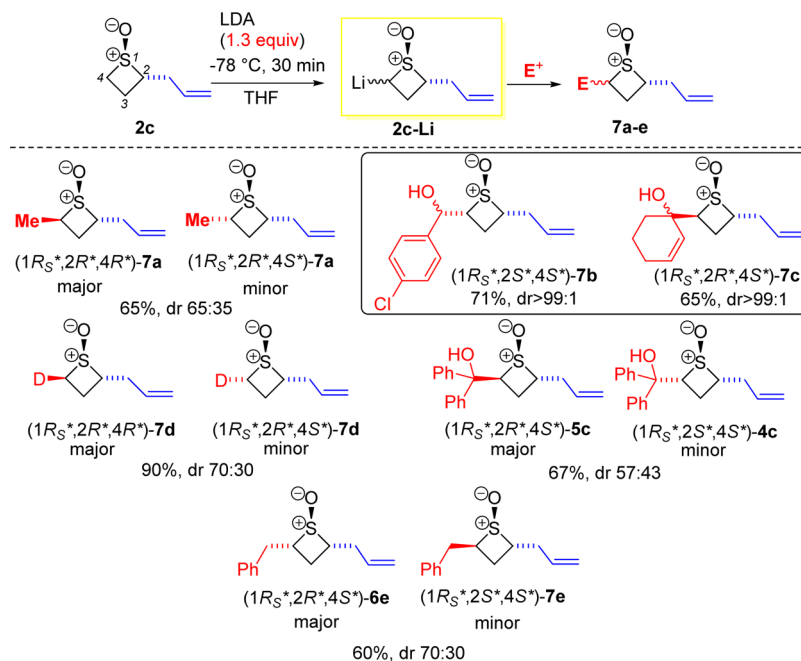
142 Next, we investigated the reactivity of *diast-2a*, whose  
 143 stereochemistry was ascertained by X-ray analysis.<sup>8</sup> From a  
 144 structural point of view, *diast-2a* discloses marked differences  
 145 with respect to **2a** such as a puckered conformation, due to an  
 146 intramolecular hydrogen bond between the hydroxyalkyl  
 147 moiety and the sulfoxide group, leading to a pseudoaxial  
 148 sulfur–oxygen bond. We were keen to verify if such different  
 149 structural features could affect the stereochemical course of the  
 150 double functionalization. When *diast-2a* was lithiated under the  
 151 same conditions used in the case of **2a** (2.5 equiv of LDA, –78  
 152 °C, 30 min), and reacted with electrophiles, still mixtures of  
 153 diastereoisomeric adducts **5a–d** were obtained (Scheme 5).  
 154 Nevertheless, while deuteration reaction led mainly to  
 155 diastereoisomer (1*R<sub>S</sub>*\*, 2*R*\*, 4*R*\*)-**5b** (dr 70:30), a switch in

stereochemical preference was observed in methylation, 156  
 allylation, and benzylation reactions perhaps due to steric 157  
 reasons. In these cases, diastereoisomers (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)-**5a**, 158  
 (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)-**5c**, and (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)-**5d** were obtained with 159  
 good stereoselectivity (Scheme 5). 160

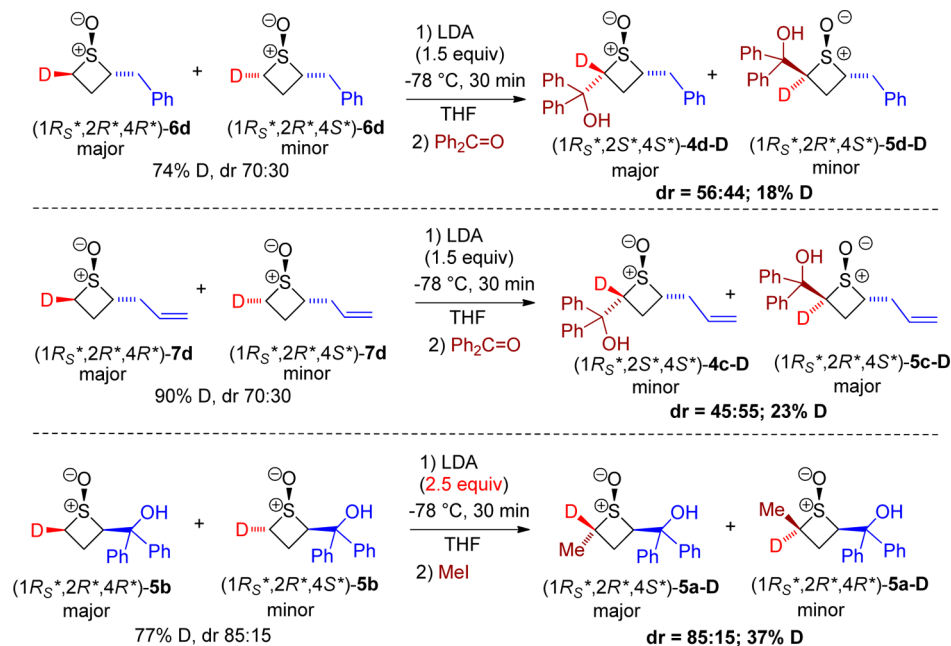
It is worth pointing out that, regardless of the degree of 161  
 stereoselectivity observed in the lithiation/trapping of **2a** and 162  
*diast-2a*, the availability of both diastereoisomers gives the 163  
 possibility to potentially access three of the four possible 164  
 stereoisomers of C2,C4-disubstituted thietane 1-oxides. In fact, 165  
 the benzylation or allylation reactions of lithiated **2a** furnished 166  
 stereoisomers (1*R<sub>S</sub>*\*, 2*S*\*, 4*R*\*)-**4c,d** and (1*R<sub>S</sub>*\*, 2*S*\*, 4*S*\*)-**4c,d**, 167  
 while the same protocol applied on lithiated *diast-2a* gives 168  
 derivatives (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)-**5c,d** derivatives. Such stereochem- 169  
 ical implications could be of great importance in drug discovery 170  
 programs or when different stereoisomers need to be tested. 171

Alternatively, when only one stereoisomer of the C2- 172  
 substituted thietane 1-oxide is available, as in the case of **2b** 173  
 and **2c**, control on the stereochemistry could be achieved by 174  
 switching the sequence of introduction of the electrophiles. To 175  
 this end, the reactivity of thietanes **2b,c** was investigated. First, 176  
**2b** was lithiated by using 1.3 equiv of LDA at –78 °C in THF 177  
 as the solvent (Scheme 6). Trapping of **2b-Li** with electrophiles 178  
 gave C2,C4-disubstituted thietanes **6a–e**. Modest to low levels 179  
 of stereoselectivity were observed in the trapping reactions with 180  
 MeI, MeOD, and allylBr, leading, respectively, to mixtures of 181  
 (1*R<sub>S</sub>*\*, 2*R*\*, 4*R*\*)-**6a,d,e** and (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)-**6a,d,e** (Scheme 182  
**6**).<sup>11</sup> In the reactions with benzophenone, a 70:30 mixture of 183  
 thietanes (1*R<sub>S</sub>*\*, 2*S*\*, 4*S*\*)-**4d** and (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)-**5d** was 184  
 obtained (Scheme 6). It is important to recall that this 185  
 sequence gives the same stereoisomers observed in separate 186  
 benzylation reactions carried out on lithiated **2a** and *diast-2a* 187  
 (see Schemes 3 and 4) but with a different ratio. Even in this 188  
 case, structure and relative stereochemistry of (1*R<sub>S</sub>*\*, 2*R*\*, 4*S*\*)- 189  
**5d** was unambiguously assigned by X-ray analysis.<sup>11</sup> In the 190  
 reactions of **2b-Li** with *p*-chlorobenzaldehyde and cyclo- 191  
 hexanone, leading, respectively, to (1*R<sub>S</sub>*\*, 2*S*\*, 4*S*\*)-**6b** and 192

### Scheme 7. Lithiation/Substitution of Thietane 2c



### Scheme 8. Attempts to Establish Configurational Stability of Lithiated Thietane 1-Oxides



193  $(1R_S^*, 2R^*, 4S^*)$ -**6c**, an opposite and high stereochemical  
194 preference was observed (Scheme 6) with reference to the  
195 C4 of the heterocyclic ring.<sup>13</sup>

196 The reactivity of **2c** was also investigated using the same  
197 conditions and electrophiles as in the case of **2b**. The results are  
198 reported in Scheme 7. The lithiation/trapping of **2c** occurred  
199 with modest stereoselectivity, just as observed in the case of **2b**  
200 in the reactions with MeI, MeOD, and BnBr, leading,  
201 respectively, to diastereomeric mixtures of thietanes  
202  $(1R_S^*, 2R^*, 4R^*)$ -**7a, d, e**,  $(1R_S^*, 2R^*, 4S^*)$ -**7a, d**, and  
203  $(1R_S^*, 2R^*, 4S^*)$ -**6e**. Again, an opposite and high stereochemical  
204 preference was observed in the reactions of **2c-Li** with *p*-  
205 chlorobenzaldehyde and cyclohexanone, leading, respectively,

206 to  $(1R_S^*, 2S^*, 4S^*)$ -**7b** and  $(1R_S^*, 2R^*, 4S^*)$ -**7c** (Scheme 7).<sup>13</sup> It  
207 is worth noting that, in the reaction of **2c-Li** with  
208 benzophenone stereoisomers,  $(1R_S^*, 2S^*, 4S^*)$ -**4c** and  
209  $(1R_S^*, 2R^*, 4S^*)$ -**5c** were obtained as seen in the lithiation/  
210 allylation of **2a** and *diast*-**2a**. Similarly, benzylation of **2c-Li** led  
211 to thietanes  $(1R_S^*, 2S^*, 4S^*)$ -**7e** and  $(1R_S^*, 2R^*, 4S^*)$ -**6e**, the  
212 latter still as the major stereoisomer, just as observed in  
213 lithiation/allylation of **2b** (Scheme 6).

214 The above study allows us to assess that the lithiation/  
215 electrophile trapping sequence on C2-substituted thietane 1-  
216 oxides occurs with a variable degree of stereoselectivity  
217 depending on the electrophile and on the structure of the  
218 starting C2-substituted thietane. However, with the exception 218

219 of deuterated derivatives, diastereomeric C2,C4-disubstituted  
220 thietane 1-oxides were easily separable by flash chromatog-  
221 raphy, and their structure and relative stereochemistry were  
222 established by NMR experiments and chemical shift  
223 correlations (see the SI).

224 With the aim to shed light on the stereochemical course of  
225 this lithiation/trapping sequence, the configurational stability of  
226 lithiated thietane 1-oxides was investigated using deuterated  
227 thietanes **5b**, **6d**, and **7d** as starting materials (Scheme 8). In  
228 fact, as already reported by us in the case of aziridines, further  
229 lithiation on deuterated systems could furnish evidence on the  
230 configurational stability of the corresponding lithiated inter-  
231 mediates, provided the existence of an intramolecular kinetic  
232 isotope effect (KIE).<sup>14</sup>

233 Assuming an appreciable KIE, a preferential removal of the  
234 proton over deuterium, in thietanes **5b**, **6d**, and **7d**, would lead  
235 to lithiated intermediates possessing opposite stereochemistry  
236 with respect to those generated from parent thietanes **2b,c** or  
237 *diast-2a*. If the so-generated lithiated intermediates are  
238 configurationally unstable, the diastereoselectivity observed,  
239 upon reaction with an electrophile, should match that found in  
240 the lithiation/trapping on protonated parent thietanes.  
241 Conversely, with configurationally stable lithiated intermedi-  
242 ates, trapping with the electrophile would lead to a different  
243 diastereomeric ratio. As a consequence of the KIE, in both  
244 cases, the final products should keep a high level of deuterium  
245 content. Thus, simply comparing the diastereomeric ratios  
246 resulting from the lithiation/trapping of deuterated thietanes  
247 with that observed with the corresponding parent fully  
248 protonated thietanes, evidence on the configurational stability  
249 or instability of the lithiated intermediates could be obtained.  
250 However, prior to running the lithiation reactions, the relative  
251 stereochemistry of deuterated thietanes **5b**, **6d**, and **7d** needed  
252 to be assessed. In the case of **5b**, NOESY experiments allowed  
253 us to assign the relative configuration for (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**5b**  
254 and (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**5b** (see the SI). In the case of thietanes **6d**  
255 and **7d**, because of overlapping signals in their <sup>1</sup>H NMR  
256 spectra, the relative stereochemistry was assigned by compar-  
257 ison between real and simulated proton NMR spectra.<sup>15</sup> We  
258 have found this approach very useful and reliable for other  
259 small-sized heterocycles,<sup>6,5c,d,16</sup> and it allowed us to assign, even  
260 in this case, the stereochemistry of deuterated thietanes  
261 (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**6d**, (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**6d**, (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**7d**,  
262 and (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**7d** (see the SI for details).

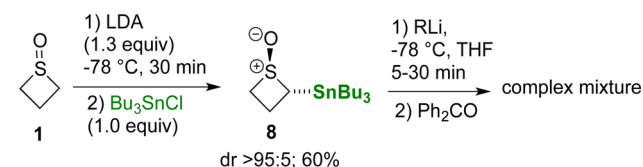
263 When a diastereomeric mixture of deuterated thietanes **6d**  
264 and **7d** was subjected to lithiation, followed by trapping with  
265 benzophenone, a mixture of the corresponding hydroxyalky-  
266 lated adducts was obtained (Scheme 8). In both experiments,  
267 ESI-MS analysis showed a sensible reduction of deuterium  
268 content as a consequence of a weak KIE. As reported in  
269 Scheme 8, thietanes **6d** or **7d** behave similarly. In the reaction  
270 of (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**6d** and (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**6d**, the correspond-  
271 ing adducts (1*R*<sub>S</sub><sup>\*</sup>,2*S*<sup>\*</sup>,4*S*<sup>\*</sup>)-**4d-D** and (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**5d-D**  
272 formed with 72% yield and a diastereomeric ratio of 56:44,  
273 respectively. The deuterium content was reduced to 18% in  
274 each diastereomer, which is about 75% less with respect to the  
275 starting material. Similarly, lithiation/trapping of  
276 (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**7d** and (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**7d** furnished thietanes  
277 (1*R*<sub>S</sub><sup>\*</sup>,2*S*<sup>\*</sup>,4*S*<sup>\*</sup>)-**4c-D** and (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**5c-D** in 65% yield  
278 and 45:55 ratio, respectively. The deuterium content of the  
279 products was reduced even in this case to 23% (about 70% less  
280 than the starting material).

The lithiation/methylation of (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**5b** and  
(1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**5b** led to (1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*S*<sup>\*</sup>)-**5a-D** and  
(1*R*<sub>S</sub><sup>\*</sup>,2*R*<sup>\*</sup>,4*R*<sup>\*</sup>)-**5a-D** in 80% yield and 85:15 diastereomeric  
ratio, respectively (Scheme 8). The deuterium erosion was of  
about 48%, leaving a content of 37% in the final products.

The results show a not significant KIE effect for the lithiation  
reactions, removal of deuterium being a competitive event.<sup>17</sup>  
However, some conclusion can be drawn considering the  
observed stereochemical preferences. In fact, in all cases, the  
diastereomeric ratios are slightly different from those observed  
with the corresponding parent undeuterated thietanes (see  
Schemes 5–7) but, most importantly, the major diaster-  
eoisomers are the same. A reasonable hypothesis, according to  
the above results, is that the lithiated intermediates are  
configurationally unstable and likely equilibrate under the  
reaction conditions. Thus, the observed diastereoselectivities  
perhaps could depend only on the activation barrier of the  
reaction with the electrophiles.<sup>18</sup>

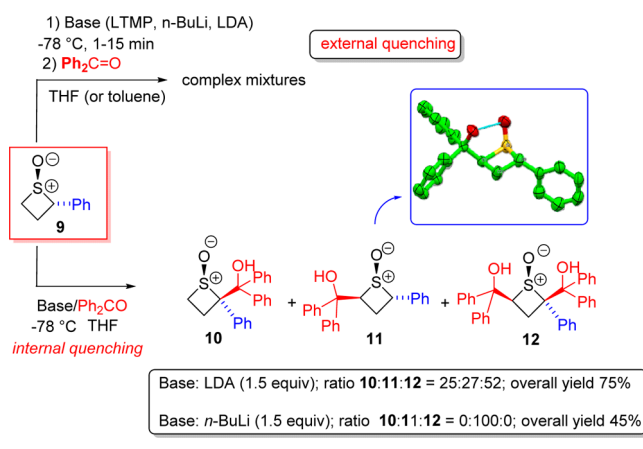
We also explored an alternative pathway, involving thietane  
**8**, to get more insights about the configurational (in)stability of  
lithiated thietanes. Thietane **8** was prepared by a lithiation/  
trapping sequence of **1**, using Bu<sub>3</sub>SnCl as the electrophile.  
Nevertheless, attempts to generate the corresponding lithiated  
thietane stereospecifically,<sup>19</sup> by a tin–lithium exchange reaction  
on stannylated thietane **8**, failed (Scheme 9).

#### Scheme 9



For the sake of comparison, we also investigated the  
lithiation of 2-phenyl substituted thietane 1-oxide **9** (Scheme  
10). In this case, a switch in regioselectivity was expected for

#### Scheme 10. Lithiation/Substitution of 2-Phenylthietane **9**



the presence of a benzylic position. However, when a solution  
of **9** was added to a cooled (-78 °C) THF (or toluene)  
solution of a base (LTMP, LDA or *n*-BuLi), further trapping  
with benzophenone returned only complex reaction mixtures  
likely because of an intrinsic chemical instability of the  
corresponding lithiated 2-aryl thietane 1-oxide. With the aim  
to get some insights on the regioselectivity, the internal quenching

316 of the lithiated 2-aryl thietane **9** was pursued. By addition of a  
317 solution of LDA (1.5 equiv) to a precooled THF solution ( $-78$   
318  $^{\circ}\text{C}$ ) of **9** and benzophenone (1 equiv), a mixture of  
319 functionalized 2-arylthietane 1-oxides **10**, **11**, and **12** was  
320 obtained in 75% overall yield (Scheme 10). The presence of  
321 derivatives **11** and **12** shows that the kinetic acidity of the  
322 methylene protons competes very well with the thermodynamic  
323 acidity of the benzylic proton.

324 In striking contrast, the use of the stronger organolithium *n*-  
325 BuLi, under internal quenching conditions, led to higher  
326 regioselectivity with the exclusive formation of adduct **11**,  
327 whose structure has been confirmed by X-ray analysis,<sup>20</sup> in a  
328 modest 45% yield due to the competitive addition of *n*-BuLi to  
329 the electrophile (Scheme 10). It is worth noting the preferential  
330 functionalization at the methylene position (kinetic preference)  
331 by using *n*-BuLi, and the possibility to introduce a third  
332 electrophile as in **12** when LDA is used as the base. The  
333 stereochemistry of **10** and **12** likely suggests a configurational  
334 stability of the corresponding lithiated thietane. However, this  
335 kind of lithiated 2-arylthietane 1-oxides would deserve further  
336 studies of their chemical and configurational stability that is out  
337 of the scope of the present work.

## 338 ■ CONCLUSIONS

339 In conclusion, this investigation tries to fill a gap on the  
340 reactivity and stereoselectivity of lithiated C2-functionalized  
341 thietane 1-oxides. The results showed that the C4 position is  
342 involved in the proton/lithium permutation and that likely the  
343 corresponding lithiated thietane 1-oxides are configurationally  
344 unstable. Concerning the stereoselectivity, it is dependent on  
345 either the stereochemistry of the starting thietane 1-oxides or  
346 the nature of the electrophile. A higher level of stereoselectivity  
347 could be obtained with thietane *diast-2a* having a *syn*  
348 relationship between the sulfinyl oxygen and the C2-  
349 substituent. In the case of thietane 1-oxides **2a–c**, having a  
350 *trans* relationship between the sulfinyl oxygen and the C2-  
351 substituent, variable degrees of stereoselectivity have been  
352 observed. Nevertheless, this approach allows us to prepare  
353 three of the four possible stereoisomers of C2,C4-disubstituted  
354 thietane 1-oxides by simply choosing one of the sequences  
355 reported in Scheme 2. It is worth pointing out that, to the best  
356 of our knowledge, this stereochemical aspect has never been  
357 explored previously. Importantly, by this sequential lithiation/  
358 trapping strategy, new products can be obtained starting from  
359 the readily available thietane 1-oxide **1**, and leaving intact the  
360 four-membered ring.<sup>21</sup> Further developments on the asym-  
361 metric version of this strategy are underway in our laboratory  
362 and will be reported in due course.

## 363 ■ EXPERIMENTAL SECTION

364 **General Methods.** THF was freshly distilled under a nitrogen  
365 atmosphere over Na/benzophenone. Toluene was freshly distilled  
366 under a nitrogen atmosphere over CaH<sub>2</sub>. Diisopropylamine (DIPA)  
367 was distilled over finely powdered CaH<sub>2</sub>, *n*-butyllithium was purchased  
368 as hexane solution, and the title was established by a titration  
369 method.<sup>22</sup> All the other chemicals were commercially available and  
370 used without further purification. Magnetic resonance spectra were  
371 recorded using 400, 500, and 600 MHz spectrometers. For the <sup>1</sup>H, <sup>13</sup>C  
372 NMR spectra (<sup>1</sup>H NMR 400, 500, 600 MHz, <sup>13</sup>C NMR 100, 125, 150  
373 MHz), CDCl<sub>3</sub>, methanol-*d*<sub>4</sub>, and toluene-*d*<sub>8</sub> were used as the solvents.  
374 MS-ESI analyses were performed on an LC/MSD trap system VL.  
375 Melting points were uncorrected. GC-MS spectrometry analyses were  
376 carried out on a gas chromatograph (dimethylsilicon capillary column,  
377 30 m, 0.25 mm i.d.) equipped with a mass selective detector operating

at 70 eV (EI). The high-resolution mass spectrometry (HRMS) 378  
analyses were performed using a mass spectrometer equipped with an 379  
electrospray ion source (ESI) operated in positive ion mode and a 380  
time-of-flight analyzer. The sample solutions (CH<sub>3</sub>OH) were 381  
introduced by continuous infusion with a syringe pump at a flow 382  
rate of 180  $\mu\text{L min}^{-1}$ . The instrument was operated with end-plate 383  
offset and capillary voltages set to  $-500$  and  $-4500$  V, respectively. 384  
The nebulizer pressure was 0.4 bar (N<sub>2</sub>), and the drying gas (N<sub>2</sub>) flow 385  
rate was 4.0 L  $\text{min}^{-1}$ . The capillary exit and skimmer voltages were 90 386  
and 30 V, respectively. The drying gas temperature was set at 180  $^{\circ}\text{C}$ . 387  
The calibration was carried out with a sodium formate solution (10 388  
mM NaOH in isopropanol/water 1:1 (+0.2% HCOOH). For flash 389  
chromatography, silica gel 60, 0.04–0.063 mm particle size was used. 390  
All reactions involving air-sensitive reagents were performed under 391  
argon in oven-dried glassware using a syringe septum cap technique. 392

### General Procedure for Lithiation/Electrophile Trapping 393 Sequence on C2-Substituted Thietane 1-Oxide. Starting 394

materials were prepared following a reported procedure.<sup>6</sup> To a 395  
stirred solution of DIPA (2.5 equiv for **2a** and *diast-2a* and 1.3 equiv 396  
for **2b,c**) in 8.0 mL of dry THF at 0  $^{\circ}\text{C}$ , a solution of *n*-BuLi (2.5 M in 397  
hexane, 2.5 equiv for **2a** and *diast-2a* and 1.3 equiv for **2b,c**) was added 398  
dropwise. After 20 min at 0  $^{\circ}\text{C}$ , the solution of LDA was cooled down 399  
to  $-78$   $^{\circ}\text{C}$  and thietanes 1-oxide (1.0 mmol, 1.0 equiv) in 2.0 mL of 400  
dry THF was added dropwise. After stirring for 30 min at  $-78$   $^{\circ}\text{C}$ , the 401  
electrophile (1.3 equiv) was added neat if liquid and in 1.0 mL of 402  
solvent if solid. After the reaction was complete, as ascertained by GC 403  
or TLC, the reaction mixture was quenched with 2 mL of saturated 404  
NH<sub>4</sub>Cl, poured in water (10 mL), and extracted with AcOEt (3  $\times$  10 405  
mL). The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and 406  
concentrated in vacuo. Flash chromatography on silica gel (Hexane/  
AcOEt) afforded 2,4-disubstituted thietanes 1-oxides. 407

(1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)-2-(Hydroxydiphenylmethyl)-4-methylthietane 1- 409  
Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)-4*a*. Column chromatography on silica gel 410  
(Hexane/AcOEt 70:30), pale yellow solid, mp 173–176  $^{\circ}\text{C}$ , 90% (255 411  
mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  1.51 (d, *J* = 7 Hz, 3 H), 1.82 (t, *J* 412  
= 11 Hz, 1 H), 2.45–2.55 (m, 1 H), 2.8 (br s, OH), 3.44 (quintet, *J* = 413  
7 Hz, 1 H), 4.38 (t, *J* = 9 Hz, 1 H), 7.20–7.25 (m, 1 H), 7.25–7.30 414  
(m, 5 H), 7.30–7.40 (m, 2 H), 7.50–7.55 (m, 2 H). <sup>13</sup>C NMR (125 415  
MHz, CDCl<sub>3</sub>)  $\delta$  0.2, 22.1, 47.4, 71.8, 78.6, 125.9, 127.3, 127.5, 128.2, 416  
128.4, 128.9, 143.7, 144.4. FT-IR (KBr,  $\text{cm}^{-1}$ )  $\nu$  699, 747, 1002, 1035, 417  
1170, 1447, 2953, 3317. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for 418  
C<sub>17</sub>H<sub>18</sub>SO<sub>2</sub>Na 309.0920; found 309.0927.

(1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)/(1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*b*. Mixture of diastereoisomers *dr* 420  
50:50. Column chromatography on silica gel (Hexane/AcOEt 70:30), 421  
waxy solid, 85% D (235 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  1.96– 422  
2.02 (m, 1 H), 2.07–2.15 (m, overlapping s at 2.10 Acetone, 1 H), 423  
2.75 (bs, 1 H), 2.87–2.93 (m, 0.6 H), 3.30–3.34 (m, 0.57 H), 4.30 424  
(dd, *J* = 9.9, 11.4 Hz, 1 H), 7.16–7.19 (m, 1 H), 7.22–7.26 (m, 5 H), 425  
7.29–7.32 (m, 2 H), 7.45–7.46 (m, 2 H). <sup>13</sup>C NMR (125 MHz, 426  
CDCl<sub>3</sub>)  $\delta$  13.1, 46.4 (t, *J* = 22.2 Hz), 46.5 (t, *J* = 24.4 Hz), 46.7, 75.4, 427  
75.5, 78.3, 126.0, 127.4, 127.5, 127.6, 128.3, 128.5, 128.9, 143.8, 144.3. 428  
ESI-MS: *m/z* (rel. int.): 295 [M<sub>H</sub> + Na]<sup>+</sup>(32); 296 [M<sub>D</sub> + Na]<sup>+</sup>(100). 429

(1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-(3-propenyl)- 430  
thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*c*. Column chromatography on 431  
silica gel (Hexane/AcOEt 50:50), white solid mp 144–146  $^{\circ}\text{C}$ , 8% (24 432  
mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  1.81 (q, *J* = 12.1 Hz, 1 H), 2.05– 433  
2.14 (m, 1 H), 2.32–2.39 (m, 1 H), 2.46–2.54 (m, 1 H), 3.10–3.19 434  
(m, 1 H), 4.07 (dd, *J* = 11.6, 9.7 Hz, 1 H), 5.00–5.08 (m, 2 H), 5.67 435  
(ddt, *J* = 17.0, 10.2, 6.7 Hz, 1 H), 7.14–7.31 (m, 8 H), 7.44–7.46 (m, 436  
2 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  19.1, 35.9, 61.0, 71.1, 78.2, 437  
118.3, 125.9, 127.4, 127.5, 128.3, 128.4, 128.9, 133.1, 143.9, 144.4. FT- 438  
IR (KBr,  $\text{cm}^{-1}$ )  $\nu$  700, 749, 764, 1043, 1266, 1447, 2981, 3056, 3272. 439  
HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>19</sub>H<sub>20</sub>SO<sub>2</sub>Na 335.1076; 440  
found 335.1069. 441

(1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)-2-(Hydroxydiphenylmethyl)-4-(3-propenyl)- 442  
thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)-4*c*. Column chromatography on 443  
silica gel (Hexane/AcOEt 70:30), pale yellow solid, mp 173–176  $^{\circ}\text{C}$ , 444  
70%, (219 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  1.85–1.92 (m, 1 H), 445  
2.36 (dt, *J* = 9.5, 13.5 Hz, 2 H), 2.62–2.71 (m, 1H), 3.23–4.14 (m, 1 446  
H), 4.25 (t, *J* = 10.4 Hz, 1 H), 4.98–5.05 (m, 2 H), 5.63–5.73 (m, 1 447

448 H), 7.13–7.16 (m, 1 H), 7.18–7.22 (m, 5 H), 7.25–7.27 (m, 2 H),  
449 7.41–7.42 (m, 2 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 20.4, 30.7, 50.7,  
450 71.5, 78.3, 117.8, 125.8, 127.2, 128.3, 128.7, 133.6, 143.7, 144.3. FT-IR  
451 (KBr, cm<sup>-1</sup>) ν 698, 754, 913, 1052, 1447, 1493, 2948, 3059, 3256.  
452 HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>19</sub>H<sub>20</sub>SO<sub>2</sub>Na 335.1076;  
453 found 335.1069.

454 (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4-Benzyl-2-(hydroxydiphenylmethyl)thietane 1-  
455 Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*d*. Column chromatography on silica gel  
456 (Hexane/AcOEt 70:30), white solid, mp 128–131 °C. 29% (105 mg).  
457 <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.80 (q, *J* = 12 Hz, 1 H), 1.94–2.00  
458 (m, 1 H), 2.76 (dd, *J* = 10, 14 Hz, 1 H), 3.14 (dd, *J* = 6, 14 Hz, 1 H),  
459 3.01 (bs, 1 H, OH), 3.24–3.30 (m, 1 H), 4.03 (t, *J* = 11 Hz, 1 H), 7.05  
460 (d, *J* = 8 Hz, 2 H), 7.11–7.13 (m, 2H), 7.17–7.21 (m, 7H), 7.25 (t, *J* =  
461 8 Hz, 2H), 7.43 (d, *J* = 8 Hz, 2H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ  
462 19.4, 37.9, 62.3, 71.3, 78.0, 125.9, 126.9, 127.3<sub>9</sub>, 127.4<sub>3</sub>, 128.1, 128.4,  
463 128.7, 128.7<sub>9</sub>, 128.8<sub>4</sub>, 137.4, 144.0, 144.5. FT-IR (film, cm<sup>-1</sup>) ν 705,  
464 759, 1027, 1059, 1166, 1343, 1447, 1496, 1603, 2918, 3026, 3062,  
465 3314. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>23</sub>H<sub>22</sub>SO<sub>2</sub>Na  
466 385.1233; found 385.1216.

467 (1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)-4-Benzyl-2-(hydroxydiphenylmethyl)thietane 1-  
468 Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*R*\*)-4*d*. Column chromatography on silica gel  
469 (Hexane/AcOEt 70:30), pale yellow solid, mp 139–141 °C. 36% (134  
470 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 2.03–2.11 (m, 1 H), 2.46 (ddd, *J*  
471 = 9, 10, 13 Hz, 1 H), 2.97 (dd, *J* = 10, 14 Hz, 1 H), 3.41 (dd, *J* = 6, 14  
472 Hz, 1 H), 3.51–3.59 (m, 1H), 4.38–4.41 (m, 1 H), 7.20–7.25 (m, 4  
473 H), 7.28–7.32 (m, 7 H), 7.36–7.38 (m, 2 H), 7.52–7.54 (m, 2 H).  
474 <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 21.1, 32.3, 52.7, 71.4, 78.5, 125.9,  
475 127.2, 128.5, 128.8, 128.9, 129.3, 137.8, 143.7, 144.3. FT-IR (KBr,  
476 cm<sup>-1</sup>) ν 700, 754, 1032, 1384, 1448, 1494, 1601, 1628, 2924, 3027,  
477 3059, 3418. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for  
478 C<sub>23</sub>H<sub>22</sub>SO<sub>2</sub>Na 385.1233; found 385.1247.

479 (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-(4-chlorophenyl-  
480 hydroxymethyl)thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*e*. First eluted  
481 diastereoisomer. Column chromatography on silica gel (Hexane/  
482 AcOEt 50:50), white solid mp. 186–188 °C. 35% (144 mg). <sup>1</sup>H NMR  
483 (600 MHz, CD<sub>3</sub>OD) δ 2.47 (m, 1 H), 2.78–2.83 (m, 1 H), 3.59–3.62  
484 (m, 1 H), 4.73 (t, *J* = 10.1 Hz, 1 H), 5.33 (d, *J* = 4.6 Hz, 1H), 7.23–  
485 7.27 (m, 2 H), 7.31–7.33 (m, 6H), 7.37–7.41 (m, 4H), 7.50 (d, *J* = 9.1  
486 Hz, 2H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 19.3, 57.0, 69.3, 74.5, 78.9,  
487 127.4, 127.9, 128.4, 128.5, 128.9, 129.3<sub>0</sub>, 129.3<sub>1</sub>, 129.5, 134.3, 142.2,  
488 145.7, 145.9. FT-IR (KBr, cm<sup>-1</sup>) ν 699, 1004, 1013, 1399, 1447, 1491,  
489 1598, 3058, 3390. HRMS (ESI-TOF) *m/z* [M + Na] calcd for  
490 C<sub>23</sub>H<sub>21</sub>ClSO<sub>3</sub>Na 435.0792; found 435.0787.

491 (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-(hydroxydiphenylmethyl)-4-(4-chlorophenyl-  
492 hydroxymethyl)thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*e*. Second eluted  
493 diastereoisomer. Column chromatography on silica gel (Hexane/  
494 AcOEt 50:50), white solid, mp 164–166 °C. 35% (147 mg). <sup>1</sup>H NMR  
495 (600 MHz, CDCl<sub>3</sub>) δ 1.94–1.99 (m, 1 H), 2.36–2.41 (m, 1 H), 3.49–  
496 3.52 (m, 1 H), 4.15 (bs, 1 H), 4.45 (t, *J* = 10.5 Hz, 1 H), 5.39 (d, *J* =  
497 9.5 Hz, 1 H), 7.17–7.28 (m, 10 H), 7.34 (t, *J* = 7.7 Hz, 2 H), 7.44 (d, *J*  
498 = 7.7 Hz, 2H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 18.6, 56.0, 71.4, 73.5,  
499 78.5, 125.9, 127.0, 127.9, 128.57, 128.65, 128.70, 129.08, 129.14,  
500 134.5, 138.2, 143.2, 143.8. FT-IR (KBr, cm<sup>-1</sup>) ν 701, 1013, 1032,  
501 1447, 1491, 1638, 1733, 2924, 3413. HRMS (ESI-TOF) *m/z* [M +  
502 Na]<sup>+</sup> calcd for C<sub>23</sub>H<sub>21</sub>ClSO<sub>3</sub>Na 435.0792; found 435.0790.

503 (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-(1-hydroxy-  
504 cyclohex-2-en-1-yl)thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*f*. First eluted  
505 diastereoisomer. Column chromatography on silica gel (Hexane/  
506 AcOEt 70:30), waxy solid. 31% (109 mg). <sup>1</sup>H NMR (500 MHz,  
507 CDCl<sub>3</sub>) δ 1.39–1.47 (m, 1H), 1.48–1.57 (m, 1H), 1.71–1.85 (m, 2H)  
508 1.94–2.02 (m, 1H) 2.03–2.13 (m, 1H) 2.53–2.62 (m, 1H), 2.83–  
509 2.92 (m, 1H), 3.34 (dd, *J* = 9.9, 5.7 Hz, 1H), 4.56 (dd, *J* = 10.6, 9.4 Hz,  
510 1H) 5.86 (dt, *J* = 10.1, 3.7 Hz, 1H), 6.08 (d, *J* = 10.2 Hz, 1H), 7.28–  
511 7.35 (m, 6H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H). <sup>13</sup>C  
512 NMR (125 MHz, CDCl<sub>3</sub>) δ 18.4, 19.3, 25.1, 32.5, 56.0, 72.0, 72.8,  
513 78.6, 125.8, 126.6, 127.6, 128.2, 128.5, 128.9, 129.9, 130.9, 143.2,  
514 143.7. FT-IR (KBr, cm<sup>-1</sup>) ν 700, 732, 910, 1031, 1165, 1447, 1493,  
515 1646, 2929, 3400. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for  
516 C<sub>22</sub>H<sub>24</sub>SO<sub>3</sub>Na 391.1338; found 391.1345.

(1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-(1-hydroxy- 517  
518 cyclohex-2-en-1-yl)thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*f*. Second  
519 eluted diastereoisomer. Column chromatography on silica gel  
520 (Hexane/AcOEt 70:30), sticky oil. 30% (110 mg). <sup>1</sup>H NMR (500  
521 MHz, CDCl<sub>3</sub>) δ 1.57–1.68 (m, 1H), 1.80–1.88 (m, 1H), 1.89–2.03  
522 (m, 2H), 2.01–2.16 (m, 2H), 2.58–2.66 (m, 1H), 2.93–3.01 (m, 1H),  
523 3.32 (dd, *J* = 9.8, 6.0 Hz, 1H), 4.56 (t, *J* = Hz, 1H), 5.58 (d, *J* = 10.1  
524 Hz, 1H), 5.90–5.83 (m, 1H) 7.25–7.35 (m, 6H), 7.36–7.41 (m, 2H),  
525 7.47–7.50 (m, 2H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 18.7, 19.7, 24.9,  
526 29.7, 35.5, 55.3, 71.6, 72.8, 78.6, 1258.8, 126.6, 126.9, 127.6, 128.2,  
527 128.5, 128.9, 131.4, 143.2, 143.7. FT-IR (KBr, cm<sup>-1</sup>) ν 700, 735, 910,  
528 1031, 1160, 1448, 1493, 1713, 2929, 3369. HRMS (ESI-TOF) *m/z* [M  
529 + Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>24</sub>SO<sub>3</sub>Na 391.1338; found 391.1343.

(1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-(1-hydroxy- 530  
531 cyclohexyl)thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-4*g*. Column chromatog-  
532 raphy on silica gel (Hexane/AcOEt 30:70), sticky oil. 65% (240 mg).  
533 <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 1.08–1.22 (m, 1H), 1.24–1.34 (m,  
534 2H), 1.35–1.52 (m, 3H), 1.54–1.78 (m, 4H) 2.5–2.57 (m, 1 H),  
535 2.87–2.96 (m, 1 H), 3.24 (dd, *J* = 9.8, 5.9 Hz, 1H), 4.53 (dd, *J* = 11.0,  
536 8.7 Hz, 1H), 7.34–7.24 (m, 6H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.48 (d, *J* =  
537 7.8 Hz, 2H). FT-IR (film, cm<sup>-1</sup>) ν 701, 753, 999, 1264, 1447, 1493,  
538 1599, 1694, 2858, 2932, 3058, 3391. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ  
539 19.3, 21.2, 21.4, 25.9, 33.3, 34.0, 55.6, 71.7, 74.5, 48.5, 125.9, 126.6,  
540 127.6, 128.1, 128.5, 128.8, 143.2, 143.8. HRMS (ESI-TOF) *m/z* [M +  
541 Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>26</sub>SO<sub>3</sub>Na 393.1495; found 393.1504.

(1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-methylthietane 1- 542  
543 Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-5*a*. Column chromatography on silica gel  
544 (Hexane/AcOEt 70:30), pale yellow solid, mp 134–137 °C. 62% (178  
545 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.43 (d, *J* = 7 Hz, 3 H), 1.92–  
546 2.08 (m, 1H), 3.03–3.20 (m, 1 H), 3.58–3.70 (m, 1 H), 4.25–4.42  
547 (m, 1 H), 7.11–7.13 (m, 1 H), 7.17–7.23 (m, 3 H), 7.25–7.33 (m, 4  
548 H), 7.46 (d, *J* = 8 Hz, 2 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 17.6,  
549 26.1, 55.2, 59.4, 80.2, 125.8, 126.0, 127.0, 127.6, 128.4, 128.7, 143.6,  
550 145.9. FT-IR (KBr, cm<sup>-1</sup>) ν 701, 740, 758, 984, 998, 1068, 1172, 1258,  
551 1407, 1450, 1493, 2962, 3026, 3362. HRMS (ESI-TOF) *m/z* [M +  
552 Na]<sup>+</sup> calcd for C<sub>17</sub>H<sub>18</sub>SO<sub>2</sub>Na 309.0920; found 309.0928.

(1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-2-(Hydroxydiphenylmethyl)-4-methylthietane 1- 553  
554 Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-5*a*. Column chromatography on silica gel  
555 (Hexane/AcOEt 70:30), pale yellow oil. 16% (45 mg). <sup>1</sup>H NMR (600  
556 MHz, CDCl<sub>3</sub>) δ 1.31 (d, *J* = 6.7 Hz, 3 H), 2.70 (dt, *J* = 7.2, 11.2 Hz,  
557 1H), 3.39–3.50 (m, 2 H), 4.02 (dd, *J* = 8.0, 10.5 Hz, 1 H), 7.11–7.13  
558 (m, 1 H), 7.18–7.22 (m, 2 H), 7.25–7.33 (m, 5 H), 7.51–7.53 (m, 4  
559 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 12.0, 31.6, 47.8, 54.3, 79.6, 125.6,  
560 126.1, 127.2, 127.7, 128.4, 128.8, 143.7, 145.2. FT-IR (film, cm<sup>-1</sup>) ν  
561 701, 740, 758, 984, 998, 1068, 1172, 1258, 1407, 1450, 1493, 2962,  
562 3026, 3362. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for  
563 C<sub>17</sub>H<sub>18</sub>SO<sub>2</sub>Na 309.0920; found 309.0918.

(1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)/(1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-5*b*. Mixture of diastereoisomers *dr* 564  
565 70:30. Column chromatography on silica gel (Hexane/AcOEt 70:30),  
566 white solid, 71% D (194 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 2.39–  
567 2.46 (m, 1 H), 3.08–3.14 (m, 0.38 H), 3.28–3.35 (m, 1 H), 3.41–3.47  
568 (m, 0.82 H), 4.35 (t, *J* = 8.3 Hz, 0.90 H), 5.77 (bs, 1 H), 7.09–7.29  
569 (m, 8 H), 7.43–7.46 (m, 2 H). 295 [M<sub>H</sub> + Na]<sup>+</sup>(37); 296 [M<sub>D</sub> +  
570 Na]<sup>+</sup>(100).

(1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-(3-propenyl)- 571  
572 thietane 1-Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-5*c*. Column chromatography on  
573 silica gel (Hexane/AcOEt 50:50), white solid, mp 132–135 °C. 75%  
574 (234 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 2.01–2.07 (m, 1 H), 2.41–  
575 2.46 (m, 1 H), 2.50–2.55 (m, 1 H), 3.03 (ddd, *J* = 13.4, 11.4, 6.2 Hz, 1  
576 H), 3.59–3.65 (m, 1 H), 4.33 (dd, *J* = 9.5, 6.2 Hz, 1 H), 5.07–5.10  
577 (m, 2 H), 5.49 (bs, 1 H), 5.67–5.75 (m 1 H), 7.10 (t, *J* = 7.7 Hz, 1 H),  
578 7.16–7.22 (m, 3 H), 7.26–7.29 (m, 4 H), 7.45 (d, *J* = 8.7 Hz, 2 H).  
579 <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 23.8, 36.1, 55.4, 63.0, 80.2, 118.7,  
580 125.8, 125.9, 127.1, 127.6, 128.4, 128.7, 132.8, 143.6, 145.9. FT-IR  
581 (KBr, cm<sup>-1</sup>) ν 703, 739, 1013, 1266, 1450, 2984, 3054, 3342. HRMS  
582 (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>19</sub>H<sub>20</sub>SO<sub>2</sub>Na 335.1076; found  
583 335.1066.

(1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-(Hydroxydiphenylmethyl)-4-benzylthietane 1- 584  
585 Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-5*d*. Column chromatography on silica gel  
586 (Hexane/AcOEt 70:30), white solid, mp 143–146 °C. 75% (271 mg). 586

587 <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 2.07 (ddd, *J* = 8, 10, 13 Hz, 1 H),  
588 2.94–3.00 (m, 2 H), 3.15 (dd, *J* = 7, 14 Hz, 1 H), 3.80–3.86 (m, 1 H),  
589 4.29 (ddd, *J* = 1, 6, 10 Hz, 1 H), 5.44 (bs, 1 H, OH), 7.08–7.11 (m, 3  
590 H), 7.15–7.27 (m, 10H), 7.42–7.44 (m, 2 H). <sup>13</sup>C NMR (125 MHz,  
591 CDCl<sub>3</sub>) δ 23.9, 38.1, 55.4, 65.5, 80.2, 125.7, 125.9, 127.0, 127.2, 127.6,  
592 128.4, 128.7, 128.8<sub>9</sub>, 128.9<sub>4</sub>, 136.9, 143.6, 145.9. FT-IR (KBr, cm<sup>-1</sup>) *ν*  
593 675, 700, 759, 769, 1016, 1033, 1060, 1178, 1193, 1407, 1450, 1493,  
594 1601, 2919, 2935, 3025, 3308. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup>  
595 calcd for C<sub>23</sub>H<sub>22</sub>SO<sub>2</sub>Na 385.1233; found 385.1216.  
596 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-Benzyl-4-methylthietane 1-Oxide  
597 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-6a. Column chromatography on silica gel (AcOEt),  
598 pale yellow oil. 39% (75 mg). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 1.36 (q,  
599 *J* = 12.2 Hz, 1H), 1.45 (d, *J* = 6.8 Hz, 3H), 2.49 (dt, *J* = 12.6, 9.5 Hz,  
600 1H), 2.97 (dd, *J* = 14.2, 8.5 Hz, 1H), 3.18–3.23 (M, 1H), 3.25 (dd, *J* =  
601 14.0, 6.4 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H),  
602 7.31 (t, *J* = 7.4 Hz, 2H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 16.8, 24.2,  
603 37.9, 59.3, 64.2, 126.9, 128.64, 128.8, 137.2. FT-IR (film, cm<sup>-1</sup>) *ν* 702,  
604 1065, 1376, 1453, 1496, 2925, 3467. HRMS (ESI-TOF) *m/z* [M +  
605 Na]<sup>+</sup> calcd for C<sub>11</sub>H<sub>14</sub>SONa 217.0658; found 217.0664.  
606 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-2-Benzyl-4-methylthietane 1-Oxide  
607 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-6a. Column chromatography on silica gel (AcOEt),  
608 pale yellow oil, 31% (61 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.49 (d,  
609 *J* = 7 Hz, 3 H), 1.99–2.16 (m, 2 H), 2.98 (dd, *J* = 8, 14 Hz, 1 H), 3.24  
610 (dd, *J* = 7, 14 Hz, 1 H), 3.52 (quintet, *J* = 7 Hz, 1 H), 3.69 (quintet, *J* =  
611 8 Hz, 1 H), 7.10–7.37 (m, 5 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 11.6,  
612 25.3, 38.0, 49.5, 65.3, 127.0, 128.8, 128.9, 137.4. FT-IR (film, cm<sup>-1</sup>) *ν*  
613 702, 1065, 1376, 1453, 1496, 2925, 3467. HRMS (ESI-TOF) *m/z* [M  
614 + Na]<sup>+</sup> calcd for C<sub>11</sub>H<sub>14</sub>SONa 217.0658; found 217.0661.  
615 (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-[(4-Chlorophenyl)hydroxymethyl]-4-benzyl-  
616 thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-6b. Mixture of diastereomers at the  
617 chiral carbon, *dr* 50:50. Column chromatography on silica gel  
618 (AcOEt), colorless oil. 71% (224 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ  
619 1.44 (q, *J* = 12.2 Hz, 1 H), 1.72 (q, *J* = 12.2 Hz, 1 H), 2.07–2.13 (m,  
620 overlapping s Acetone at 2.09, 2 H), 2.83–2.90 (m, 2 H), 3.14–3.20  
621 (m, 2 H), 3.26–3.37 (m, 4 H), 4.69 (d, *J* = 8.7 Hz, 1 H), 5.09 (d, *J* =  
622 3.7 Hz, 1 H), 7.08–7.09 (m, 3 H), 7.15–7.25 (m, 15 H). <sup>13</sup>C NMR  
623 (125 MHz, CDCl<sub>3</sub>) δ 17.4, 20.4, 37.8, 63.3, 69.1, 70.1, 73.5, 127.1–  
624 126.5, 128.6–129.1, 133.9, 133.3, 136.9, 137.0, 139.1, 139.2. FT-IR  
625 (film, cm<sup>-1</sup>) *ν* 703, 735, 841, 1047, 1245, 1454, 1493, 1602, 1732,  
626 2925, 3334. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for  
627 C<sub>17</sub>H<sub>17</sub>ClSO<sub>2</sub>Na 343.0530; found 343.0516.  
628 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-4-Benzyl-2-(1-hydroxycyclohex-2-en-1-yl)thietane  
629 1-Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-6c. Major diastereomer. Column chromatog-  
630 raphy on silica gel (Hexane/AcOEt 50:50), pale yellow oil. 42% (110  
631 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.50–1.57 (m, 1 H), 1.75–1.82  
632 (m, 1 H), 1.84–1.94 (m, 2 H), 1.98–2.44 (m, overlapping s, AcOEt, 2  
633 H), 2.92–3.04 (m, 2 H), 3.14 (dd, *J* = 7, 14 Hz, 1 H), 3.30 (ddd, *J* = 6,  
634 7, 15 Hz, 1 H), 3.87–3.97 (m, 1 H), 4.21 (bs, 1 H, OH), 5.54 (d, *J* =  
635 10 Hz, 1 H), 5.80 (dt, *J* = 4, 1 Hz, 1 H), 7.13–7.14 (m, 2 H), 7.17–  
636 7.20 (m, 1 H), 7.24–7.26 (m, 2 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ  
637 18.8, 22.7, 25.0, 35.8, 38.3, 57.2, 65.2, 72.9, 127.0<sub>9</sub>, 127.1<sub>4</sub>, 128.8,  
638 128.9, 131.6, 137.0. FT-IR (film, cm<sup>-1</sup>) *ν* 700, 735, 1010, 1186, 1262,  
639 1429, 1454, 1496, 1672, 1707, 2866, 2935, 3027, 3392. HRMS (ESI-  
640 TOF) *m/z* [M + Na]<sup>+</sup> calcd for C<sub>16</sub>H<sub>20</sub>SO<sub>2</sub>Na 299.1076; found  
641 299.1078.  
642 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-4-Benzyl-2-(1-hydroxycyclohex-2-en-1-yl)thietane  
643 1-Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-6c. Minor Diastereomer. Column chromatog-  
644 raphy on silica gel (Hexane/AcOEt 50:50), pale yellow oil. 23% (70  
645 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.32–1.36 (m, 1 H), 1.43–1.49  
646 (m, 1 H), 1.68–1.76 (m, 1 H), 1.86–1.93 (m, 1 H), 1.97–2.09 (m, 2  
647 H), 2.90–2.97 (m, 2 H), 3.15 (dd, *J* = 7, 14 Hz, 1 H), 3.31 (dd, *J* =  
648 9.5, 5.1 Hz, 1 H), 3.86–3.97 (m, 1 H), 4.19 (bs, 1 H, OH), 5.77 (dt, *J* =  
649 = 10, 4 Hz, 1 H), 5.99 (d, *J* = 10.2 Hz, 1 H), 7.13–7.14 (m, 2 H),  
650 7.17–7.19 (m, 1 H), 7.23–7.26 (m, 2 H). <sup>13</sup>C NMR (125 MHz,  
651 CDCl<sub>3</sub>) δ 20.5, 24.5, 27.3, 34.6, 40.6, 60.5, 67.5<sub>9</sub>, 129.2, 130.8, 130.9,  
652 132.0, 133.39. FT-IR (film, cm<sup>-1</sup>) *ν* 700, 734, 1029, 1188, 1454, 1496,  
653 1712, 2851, 2930, 3027, 3400. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup>  
654 calcd for C<sub>16</sub>H<sub>20</sub>SO<sub>2</sub>Na 299.1076; found 299.1067.  
655 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)/(1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-6d. Mixture of diastereoisomers *dr*  
656 70:30. Column chromatography on silica gel (AcOEt), yellow oil,

72.4% D (134 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.56–1.65 (m, 1  
657 H), 2.24–2.33 (m, 1 H), 2.86–2.96 (m, 1.47 H), 3.17 (dd, *J* = 6.3,  
658 14.3 Hz, 1 H), 3.32–3.37 (m, 0.83 H), 3.52–3.61 (m, 1 H), 7.12–7.14  
659 (m, 2 H), 7.15–7.20 (m, 1 H), 7.23–7.26 (m, 2 H). <sup>13</sup>C NMR (125  
660 MHz, CDCl<sub>3</sub>) δ 16.3, 16.4, 38.1, 48.1 (t, *J* = 22.4 Hz), 48.2 (t, *J* = 23.3  
661 Hz), 48.5, 68.9, 127.0, 128.8, 128.9, 137.1. 153 ESI-MS: *m/z* (rel. int.):  
662 203[M<sub>H</sub> + Na]<sup>+</sup>(34); 204 [M<sub>D</sub> + Na]<sup>+</sup>(100).  
663 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-2-Benzyl-4-(3-propenyl)thietane 1-Oxide  
664 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-6e. Column chromatography on silica gel (Hexane/  
665 AcOEt 50:50), colorless oil. 35% (76 mg). <sup>1</sup>H NMR (600 MHz,  
666 CDCl<sub>3</sub>) δ 1.92 (ddd, *J* = 8, 11, 13 Hz, 1 H), 2.21 (ddd, *J* = 3, 10, 13  
667 Hz, 1 H), 2.35–2.44 (m, 1 H), 2.69–2.77 (m, 1), 2.92 (dd, *J* = 9, 14  
668 Hz, 1 H), 3.17 (dd, *J* = 6, 14 Hz, 1 H), 3.35–3.39 (m, 1 H), 3.58–3.64  
669 (m, 1 H), 5.03–5.08 (m, 2 H), 5.68–5.77 (m, 1 H), 7.11–7.13 (m, 2  
670 H), 7.16–7.19 (m, 1 H), 7.23–7.26 (m, 2 H). <sup>13</sup>C NMR (125 MHz,  
671 CDCl<sub>3</sub>) δ 23.4, 30.3, 38.1, 53.0, 65.2, 118.0, 127.0, 128.8, 128.9, 133.8,  
672 137.3. FT-IR (film, cm<sup>-1</sup>) *ν* 701, 749, 917, 1005, 1062, 1437, 1454,  
673 1496, 1602, 1639, 2929, 3028, 3062, 3445. HRMS (ESI-TOF) *m/z* [M  
674 + Na]<sup>+</sup> calcd for C<sub>13</sub>H<sub>16</sub>SONa 243.0814; found 243.0818.  
675 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-Benzyl-4-(3-propenyl)thietane 1-Oxide  
676 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-6e. Column chromatography on silica gel (Hexane/  
677 AcOEt 50:50), pale yellow oil. 43% (96 mg). <sup>1</sup>H NMR (600 MHz,  
678 CDCl<sub>3</sub>) δ 1.34 (like q, 1 H), 2.37–2.45 (m, 2 H), 2.49–2.53 (m, 1 H),  
679 2.90 (dd, *J* = 9, 14 Hz, 1 H), 3.15–3.24 (m, 2 H), 3.31–3.40 (m, 1 H),  
680 5.04–5.12 (m, 2 H), 5.71 (ddt, *J* = 7, 10, 17 Hz, 1 H), 7.10–7.13 (m, 2  
681 H), 7.16–7.19 (m, 1 H), 7.22–7.28 (m, 2 H). <sup>13</sup>C NMR (125 MHz,  
682 CDCl<sub>3</sub>) δ 22.6, 35.9, 38.0, 63.1, 64.4, 118.3, 127.0, 128.8, 128.9, 133.1,  
683 137.3. FT-IR (film, cm<sup>-1</sup>) *ν* 702, 749, 921, 1061, 1299, 1454, 1496,  
684 1640, 2919, 3028, 3063, 3437. ESI-MS: *m/z* (rel. int.): 221 [M +  
685 H]<sup>+</sup>(100).  
686 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-2-(3-Propenyl)-4-methylthietane 1-Oxide  
687 (1*R*<sub>5</sub>\*,2*R*\*,4*R*\*)-7a. Column chromatography on silica gel (AcOEt),  
688 pale yellow oil, 42% (61 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.47 (d,  
689 *J* = 7.4 Hz, 3 H), 1.98 (ddd, *J* = 8.3, 11.9, 13.0 Hz, 1 H), 2.12–2.19  
690 (m, 1 H), 2.43–2.48 (m, 1 H), 2.52–2.57 (m, 1 H), 3.46–3.53 (m,  
691 2H), 5.09–5.15 (m, 2 H), 5.76 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1 H). <sup>13</sup>C  
692 NMR (125 MHz, CDCl<sub>3</sub>) δ 11.7, 25.2, 36.0, 49.4, 63.6, 118.2, 133.1.  
693 FT-IR (film, cm<sup>-1</sup>) *ν* 920, 997, 1060, 1123, 1439, 1641, 2867, 2929,  
694 2976, 3079, 3467. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for  
695 C<sub>7</sub>H<sub>12</sub>SONa 167.0501; found 167.0500.  
696 (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-2-[(4-Chlorophenyl)hydroxymethyl]-4-(3-  
697 propenyl)thietane 1-Oxide (1*R*<sub>5</sub>\*,2*S*\*,4*S*\*)-7b. Mixture of diaster-  
698 eomers *dr* 70:30. Column chromatography on silica gel (AcOEt),  
699 yellow oil. 71% (192 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.40 (q, *J* =  
700 12.1 Hz, 1 H), 1.66 (q, *J* = 12.2 Hz, 1 H), 2.11–2.17 (m, 2 H), 2.34–  
701 2.49 (m, 4 H), 3.08–3.17 (m, 2 H), 3.31–3.38 (m, 2 H), 4.66 (d, *J* =  
702 8.5 Hz, 1 H), 5.02–5.09 (m, 5 H), 5.63–5.70 (m, 2 H), 7.17–7.24 (m,  
703 8 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 17.3, 20.2, 35.7, 35.8, 61.9, 69.1,  
704 69.2, 69.9, 73.5, 118.4, 118.5, 127.3, 127.5, 128.8, 129.0, 132.7, 132.8,  
705 133.7, 139.3, 139.4. IR (film, cm<sup>-1</sup>) *ν* 757, 841, 923, 1043, 1089, 1490,  
706 1641, 2923, 2979, 3081, 3339. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup>  
707 calcd for C<sub>13</sub>H<sub>15</sub>ClSO<sub>2</sub>Na 293.0373; found 293.0374.  
708 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-(1-Hydroxycyclohex-2-en-1-yl)-4-(3-propenyl)-  
709 thietane 1-Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-7c. Minor diastereomer. Column  
710 chromatography on silica gel (Hexane/AcOEt 50:50), yellow oil. 20%  
711 (47 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.41–1.61 (m, overlapping s  
712 H<sub>2</sub>O at 1.60, 2 H), 1.93–2.15 (m, overlapping s AcOEt at 2.04, 3 H),  
713 2.46–2.62 (m, 2 H), 3.07 (ddd, *J* = 13.2, 11.4, 5.3 Hz, 1 H), 3.37–3.42  
714 (m, 1 H), 3.73–3.84 (m, 1 H), 4.32 (bs, 1 H), 5.15–5.20 (m, 2 H),  
715 5.75–5.88 (m, 2 H), 6.06–6.09 (m, 1 H). <sup>13</sup>C NMR (125 MHz,  
716 CDCl<sub>3</sub>) δ 18.6, 22.4, 25.2, 32.7, 36.4, 58.4, 64.1, 72.8, 118.6, 130.0,  
717 131.1, 132.9. FT-IR (film, cm<sup>-1</sup>) *ν* 710, 1025, 1266, 1435, 1707, 2943,  
718 3054, 3400. HRMS (ESI-TOF) *m/z* [M + Na]<sup>+</sup> calcd for  
719 C<sub>12</sub>H<sub>18</sub>SO<sub>2</sub>Na 249.0925; found 249.0920.  
720 (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-2-(1-Hydroxycyclohex-2-en-1-yl)-4-(3-propenyl)-  
721 thietane 1-Oxide (1*R*<sub>5</sub>\*,2*R*\*,4*S*\*)-7c. Major diastereomer. Column  
722 chromatography on silica gel (Hexane/AcOEt 50:50), yellow oil. 45%  
723 (109 mg). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 1.55–1.66 (m, 1 H), 1.82–  
724 2.17 (m, 6 H), 2.49–2.60 (m, 2 H), 3.11 (ddd, *J* = 13.2, 11.4, 5.4 Hz, 1  
725 H), 3.38 (ddd, *J* = 9.5, 5.4, 1.3 Hz, 1 H), 3.75–3.81 (m, 1 H), 4.31 (bs,  
726

727 1 H), 5.15–5.20 (m, 2 H), 5.63–5.65 (m, 1 H), 5.80 (ddt,  $J = 17.0$ ,  
728 10.3, 6.7 Hz, 1 H), 5.89 (dt,  $J = 10.1$ , 3.7 Hz, 1 H).  $^{13}\text{C}$  NMR (125  
729 MHz,  $\text{CDCl}_3$ )  $\delta$  18.8, 22.7, 35.8, 36.4, 57.3, 63.8, 72.9, 118.6, 127.1,  
730 131.6, 132.9. FT-IR (film,  $\text{cm}^{-1}$ )  $\nu$  710, 1025, 1266, 1435, 1707, 2943,  
731 3054, 3400. HRMS (ESI-TOF)  $m/z$  [ $M + \text{Na}$ ] $^+$  calcd for  
732  $\text{C}_{12}\text{H}_{18}\text{SO}_2\text{Na}$  249.0925; found 249.0921.

733  $(1R_5^*,2R^*,4R^*)/(1R_5^*,2R^*,4S^*)$ -7d. Mixture of diastereoisomers  $dr$   
734 = 71:29. Column chromatography on silica gel (AcOEt), pale yellow  
735 oil, 89% D (118 mg).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  1.62–1.70 (m, 1  
736 H), 2.39–2.63 (m, 3 H), 2.94–3.02 (m, 0.3 H), 3.40–3.52 (m, 1.72  
737 H), 5.13–5.20 (m, 2 H), 5.74–5.85 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  
738  $\text{CDCl}_3$ )  $\delta$  16.2, 36.1, 48.0<sub>6</sub> (t,  $J = 22.8$  Hz), 48.1<sub>5</sub> (t,  $J = 23.2$  Hz), 48.4,  
739 67.6, 118.4, 132.9. ESI-MS:  $m/z$  (rel. int.): 153 [ $M_{\text{H}} + \text{Na}$ ] $^+$ (13); 154  
740 [ $M_{\text{D}} + \text{Na}$ ] $^+$ (100).

741  $(1R_5^*,2S^*,4S^*)$ -2-Benzyl-4-(3-propenyl)thietane 1-Oxide  
742  $(1R_5^*,2S^*,4S^*)$ -7e. Column chromatography on silica gel, (Hexane/  
743 AcOEt 50:50), yellow oil. 18% (40 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  
744  $\delta$  1.95 (ddd,  $J = 13.3$ , 10.8, 8.3 Hz, 1H), 2.40 (ddd,  $J = 13.3$ , 10.3, 3.1  
745 Hz, 1H), 2.51 (dt,  $J = 15.20$ , 6.8 Hz, 1H), 2.62 (dt,  $J = 14.5$ , 7.2 Hz,  
746 1H), 3.00 (dd,  $J = 14.5$ , 10.2 Hz, 1H), 3.42 (dd,  $J = 14.5$ , 5.5 Hz, 1H),  
747 3.69–3.54 (m, 2H), 5.23–5.12 (m, 2H), 5–78–587(m, 1H), 7.38–  
748 7.18 (m, 5H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  23.5, 31.7, 35.9, 54.8,  
749 63.4, 118.3, 126.7, 128.7, 129.2, 132.9, 137.7. FT-IR (film,  $\text{cm}^{-1}$ )  $\nu$   
750 703, 720, 1061, 1266, 1454, 1496, 1641, 2983, 3053, 3437. HRMS  
751 (ESI-TOF)  $m/z$  [ $M + \text{Na}$ ] $^+$  calcd for  $\text{C}_{13}\text{H}_{16}\text{SONa}$  243.0814; found  
752 243.0818.

753  $(1R_5^*,2R^*)$ -2-(Tributylstannyl)thietane 1-Oxide 8. Column chro-  
754 matography on silica gel (Hexane/AcOEt 50:50), colorless oil (60%).  
755  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (t,  $J = 7$  Hz, 9 H), 0.96–0.99 (m,  
756 6 H), 1.25–1.34 (m, 6 H), 1.45–1.54 (m, 6 H), 2.05–2.14 (m, 1H),  
757 2.47–2.55 (m, 1 H), 3.27–3.37 (m, 2 H), 3.68–3.72(m, 1 H).  $^{13}\text{C}$   
758 NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  9.2, 13.7, 16.4, 27.4, 29.1, 53.1, 58.0, 74.2.  
759 FT-IR ( $\text{cm}^{-1}$ )  $\nu$  657, 691, 1050, 1101, 1464, 1643, 2871, 2853, 2927,  
760 2956. HRMS (ESI-TOF)  $m/z$  [ $M + \text{H}$ ] $^+$  calcd for  $\text{C}_{15}\text{H}_{33}\text{OSSn}$   
761 381.1274; found 381.1271.

762 **General Procedure for Synthesis of 2-Phenyl Thietane-1-**  
763 **Oxide 9.** 2-Phenyl thietane was prepared following a reported  
764 procedure.<sup>23</sup> To a stirred solution of 1,3-dichloro-1-phenylpropane  
765 (10.0 mmol, 1.880 g, 1.0 equiv) in EtOH/ $\text{H}_2\text{O} = 80:20$  (100 mL) at  
766 room temperature was added  $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ , and then the solution was  
767 heated at 70 °C overnight. After the reaction was complete, as  
768 determined by GC or TLC, EtOH was removed in vacuo and the  
769 aqueous layer was extracted with  $\text{Et}_2\text{O}$  (3  $\times$  10 mL). The combined  
770 organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and concentrated in  
771 vacuo. Chromatography on silica gel (Hexane/AcOEt) afforded the 2-  
772 phenyl thietane as a pale orange oil (65% yield). To a solution of 2-  
773 phenyl thietane (9.05 mmol, 1.358 g, 1 equiv) in glacial acetic acid (2.7  
774 mL, 5.4 equiv) at 0 °C was added  $\text{H}_2\text{O}_2$  (30 w/w %) (11.76 mmol, 1.4  
775 mL, 1.3 equiv) dropwise. After 5 h at 0–10 °C, a water solution of  
776 NaOH (1 M) was slowly added to neutralize the excess of  
777  $\text{CH}_3\text{COOH}$ . The reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$   
778 10 mL). The combined organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), filtered,  
779 and concentrated in vacuo. Chromatography on silica gel (AcOEt)  
780 gave the 2-phenyl thietane 1-oxide 9 as a pale yellow solid (40% yield).

781 **2-Phenylthietane 1-Oxide 9.** The spectral data fit those already  
782 reported.<sup>22</sup> Column chromatography on silica gel (AcOEt), pale  
783 yellow solid, 40%.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  2.16 (dq,  $J = 9.5$ ,  
784 13.7 Hz, 1 H), 2.65–2.70 (m, 1 H), 3.02–3.08 (m, 1 H), 3.43–3.45  
785 (m, 1 H), 4.40–4.44 (m, 1 H), 7.32–7.37 (m, 5 H).  $^{13}\text{C}$  NMR (125  
786 MHz,  $\text{CDCl}_3$ )  $\delta$  16.7, 47.3, 72.3, 127.3, 128.5, 128.9, 136.3.

787 **General Procedure for Lithiation–Electrophile Trapping in**  
788 **Situ Sequence of trans 2-Phenyl Thietane 1-Oxide 9.** To a  
789 stirred solution of DIPA (1.5 mmol, 0.212 mL, 1.5 equiv) in 8.0 mL of  
790 THF at 0 °C was added a solution of *n*-butyllithium (2.5 M in hexane,  
791 1.5 mmol, 0.6 mL, 1.5 equiv) dropwise. After 20 min at 0 °C, the  
792 solution of LDA was cooled to –78 °C and a mixture of 2-phenyl  
793 thietanes-1-oxide (1.0 mmol, 166.0 mg, 1.0 equiv) and benzophenone  
794 (1.0 mmol, 182 mg, 1.0 equiv) in 2.0 mL of solvent was added  
795 dropwise. After 1 h, as determined by GC or TLC, the reaction  
796 mixture was poured in water (10 mL) and extracted with AcOEt (3  $\times$

10 mL). The combined organic layers were dried ( $\text{Na}_2\text{SO}_4$ ), filtered,  
797 and concentrated in vacuo. Chromatography on silica gel (Hexane/  
798 AcOEt) afforded the 2,4-disubstituted thietanes 1-oxide and 2,2,4-  
799 trisubstituted thietanes 1-oxide.  
800

801  $(1R_5^*,2S^*)$ -2-(Hydroxydiphenylmethyl)-2-phenylthietane 1-Oxide  
802 **10.** Column chromatography on silica gel (Hexane/AcOEt 80:20),  
803 white solid, 185–188 °C.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  2.83–2.91  
804 (m, 2 H), 3.24–3.30 (m, 1 H), 4.52–4.58 (m, 1 H), 6.88 (d,  $J = 7.4$   
805 Hz, 2 H), 7.11–7.26 (m, 11 H), 7.40 (d,  $J = 7.2$  Hz, 2 H).  $^{13}\text{C}$  NMR  
806 (125 MHz,  $\text{CDCl}_3$ )  $\delta$  31.0, 43.0, 74.1, 84.8, 127.5, 127.6, 127.8, 127.9,  
807 128.0, 128.1, 128.2, 128.5, 128.6, 128.9, 130.9, 131.5, 137.2<sub>0</sub>, 137.2<sub>3</sub>,  
808 143.5. FT-IR (KBr,  $\text{cm}^{-1}$ )  $\nu$  702, 737, 1032, 1266, 1447, 1493, 1599,  
809 2927, 3058, 3351. HRMS (ESI-TOF)  $m/z$  [ $M + \text{Na}$ ] $^+$  calcd for  
810  $\text{C}_{22}\text{H}_{20}\text{SO}_2\text{Na}$  371.1082; found 371.1076.

811  $(1R_5^*,2R^*,4R^*)$ -2-(Hydroxydiphenylmethyl)-4-phenylthietane 1-  
812 **Oxide 11.** Column chromatography on silica gel (Hexane/AcOEt  
813 80:20), white solid, mp 194 °C – dec.  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$   
814 2.53 (dt,  $J = 9.5$ , 13.7 Hz, 1 H), 3.22 (ddd,  $J = 5.6$ , 11.8, 13.7 Hz, 1 H),  
815 4.40–4.50 (m, 1 H), 4.76–4.87 (m, 1 H), 5.37 (bs, 1 H), 7.12–7.15  
816 (m, 1 H), 7.18–7.35 (m, 12 H), 7.48–7.50 (m, 2 H).  $^{13}\text{C}$  NMR (125  
817 MHz,  $\text{CDCl}_3$ )  $\delta$  24.4, 55.4, 69.0, 80.4, 125.9, 126.0, 127.2, 127.5,  
818 127.7, 128.5, 128.8, 129.2, 136.8, 143.7, 146.0. FT-IR (KBr,  $\text{cm}^{-1}$ )  $\nu$   
819 700, 755, 1037, 1062, 1161, 1447, 1494, 2854, 2924, 3058, 3454.  
820 HRMS (ESI-TOF)  $m/z$  [ $M + \text{Na}$ ] $^+$  calcd for  $\text{C}_{22}\text{H}_{20}\text{SO}_2\text{Na}$  371.1082;  
821 found 371.1076.

822  $(1R_5^*,2S^*,4S^*)$ -2,4-Bis(hydroxydiphenylmethyl)-2-phenylthietane  
823 **1-Oxide 12.** Column chromatography on silica gel (Hexane/AcOEt  
824 80:20), white solid mp 139–142 °C, 70%.  $^1\text{H}$  NMR (600 MHz,  
825  $\text{CDCl}_3$ )  $\delta$  2.81 (dd,  $J = 12.8$ , 7.2 Hz, 1 H), 3.83 (dd,  $J = 11.8$ , 7.2 Hz, 1  
826 H), 5.43 (t,  $J = 12.5$  Hz, 1 H), 5.68 (bs, 1 H), 6.79 (d,  $J = 8.0$  Hz, 2  
827 H), 6.84 (bs, 1 H), 7.10–7.39 (m, 23 H).  $^{13}\text{C}$  NMR (125 MHz,  
828  $\text{CDCl}_3$ )  $\delta$  32.9, 52.4, 69.4, 79.5, 84.9, 125.6, 125.9, 127.4<sub>7</sub>, 127.5<sub>2</sub>,  
829 127.7, 127.8, 127.9, 128.2, 128.3, 128.5<sub>0</sub>, 128.5<sub>3</sub>, 128.5<sub>9</sub>, 128.6<sub>3</sub>, 128.8,  
830 131.0, 135.3, 140.7, 143.0, 143.5, 144.5. FT-IR (film,  $\text{cm}^{-1}$ )  $\nu$  700, 735,  
831 1010, 1186, 1262, 1429, 1454, 1496, 1672, 1707, 2866, 2935, 3027,  
832 3392. HRMS (ESI-TOF)  $m/z$  [ $M + \text{Na}$ ] $^+$  calcd for  $\text{C}_{35}\text{H}_{30}\text{SO}_3\text{Na}$   
833 553.1813; found 553.1808.

## ■ ASSOCIATED CONTENT

### ● Supporting Information

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra for new compounds (PDF),  
and X-ray and calculation data (PDF)  
X-ray crystallographic data for (CIF)  
X-ray crystallographic data for (CIF)  
X-ray crystallographic data for (CIF)  
X-ray crystallographic data for (CIF)

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### Notes

The authors declare no competing financial interest.

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