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# γ-Lactones as templates in ring-closing metathesis: Enantioselective synthesis of medium sized carbocycles fused to butyrolactones

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**Abstract**

A methodology for accessing enantiomerically enriched carbocyclic systems fused to γ-lactones is described. Key steps are the stereoselective synthesis of highly substituted γ-lactones and ring-closing metathesis of the suitable ramifications. The process permits the choice of stereochemistry, regioselectivity and ring size of the fused compounds.


*Keywords:* γ-Lactone; RCM; Carbocycles; Stereoselective synthesis

## 1. Introduction

γ-Lactones are widely distributed in nature in many biologically important natural products [1]. This structural unit also plays a very important role in the synthesis of biologically active natural products [2]. In addition, the γ-lactone unit is often found fused to medium-sized rings [3]. Included among these structures are the ambrosin (**1**) [4], vernolepin (**2**) [5], elephantopin (**3**) [6] and Corey lactone (**4**) [2a]. Approaches to the stereocontrolled synthesis of such complex system are highly desirable [7] (Fig. 1).

The base-induced cyclization of enantiomerically enriched α-[(phenylthio)acyloxy]-α,β-unsaturated esters **7** produces highly substituted butyrolactones **8** with a high degree of stereocontrol (Scheme 1) [8]. After oxidation, the alkylation of the anion generated α to the lactone carbonyl of these α-benzenesulfonyl γ-lactones proceeded with excellent diastereoselection [9]. On the other hand, ring-closing metathesis (RCM) [10] reaction of densely functionalized dienes has been extensively utilized in the synthesis of various organic frameworks [11].

Guided by this set of construction reactions, we pondered a general methodology to the stereoselective access to carbocyclic systems fused to a γ-lactone ring (**9**, and **11**) based on the retrosynthetic simplification outlined in Scheme 2. In both α,β- or β,γ-fused systems the cyclic double bond could arise via RCM of the suitable diene system (**10** and **12**). Both molecules should be available either by diastereoselective alkylation or proper homologation of the stereochemically defined butyrolactone **8**. This methodology could ensure stereochemistry, ring size of the fused system and divergence from a common intermediate [12] (see Scheme 2).

## 2. Results and discussion

Based on the retrosynthetic analysis presented above, the first critical issue on the way to testing the RCM strategy for the synthesis of carbocyclic fused system was the enantioselective construction of the polysubstituted butyrolactone **14**. In general, the basic sequence outlined in Scheme 1 was followed to access the necessary γ-lactone.

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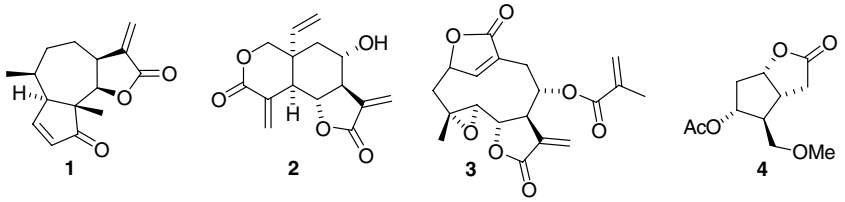
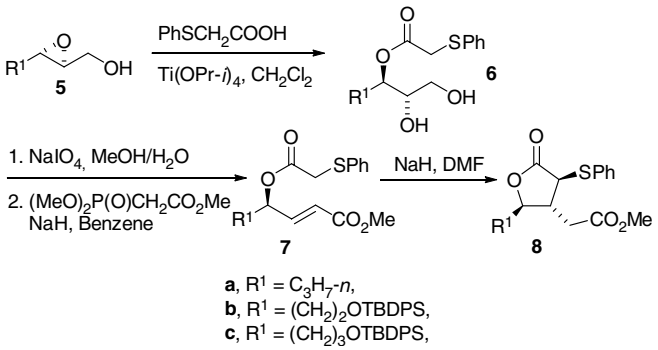
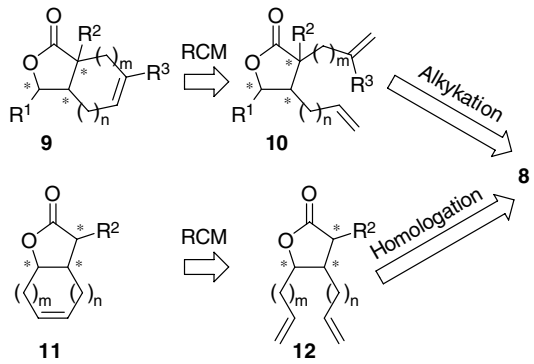


Fig. 1. Representative structures featuring a fused carbocycle to a butyrolactone.



Scheme 1.



Scheme 2.

It should be pointed out that in order to homologate the $R^1$ substituent it must contain a suitable functional group at this end. In our case a *tert*-butyl diphenyl silyl ether was adequate for this propose. Known epoxides **5** [13], were submitted to our previously reported sequence [8] yielding satisfactorily the common intermediate **8**. At this point of the synthesis, two alternative ways were followed depending if α,β- or β,γ-fused systems are the desired target.

The synthesis of the diene **10** needs stereoselective alkylation at the α-carbon of the lactone system and proper functional group manipulation on the ester functionality. In order to accomplish both tasks, **8a** was saponified to the corresponding carboxylic acid that was reduced to the primary alcohol and the sulfide group was oxidated to the sulfone **13**. The base-induced alkylation with a series of unsaturated alkylating agents proceeded chemo- and stereoselectively yielding the contrasteric product **14** [14]. The

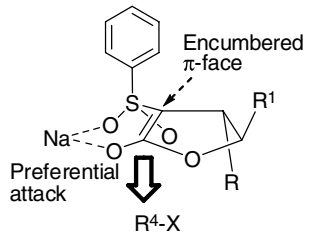
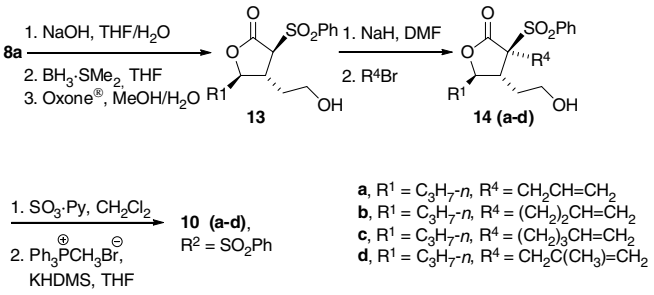


Fig. 2. Stereochemical model for the alkylation of α-benzenesulfonyl-γ-lactones.



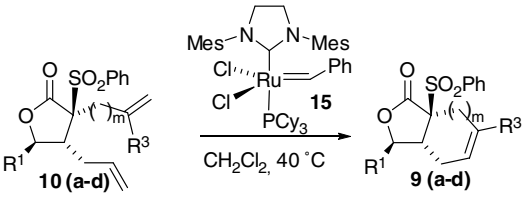
Scheme 3.

coordination of the sodium cation with one oxygen of the sulfone group and the oxygen of the enolate causes the *anti*-π-face of the enolate relative to the β-substituent to be encumbered by the phenyl group of the phenylsulfone, directing the alkylating agents to the *syn* face (Fig. 2) [9]. Oxidation of the primary alcohol **14** and Wittig reaction provided the necessary diene system **10** for the ring-closing metathesis step (Scheme 3).

Having reached these advanced intermediates, we tested the ring-closing olefin metathesis reaction. Exposure of the dienes **10** to second generation Grubbs' catalyst **15** provided the corresponding α,β-fused unsaturated cycles **9** in good to high yield depending of the ring size (Table 1) [15]. The coupling between geminal disubstituted olefins with terminal alkenes provided the corresponding trisubtituted cyclic alkene also in good yield (entry 4).

As mentioned earlier, the synthesis of the alternative diene **12** from the common γ-lactone **8** needed the necessary manipulation of the functional group at the $R^1$ and the ester substituents. Thus, proceeding with the synthesis, the above mentioned sequence of saponification of the ester functionality, reduction to primary alcohol, oxidation and

Table 1
Stereoselective synthesis of α,β-fused unsaturated cycles to γ-lactones




| Entry | 10 | Yield (9) |
|---|---|---|
| 1 | **10a**, $R^3$ = H, $m = 1$ | 85 |
| 2 | **10b**, $R^3$ = H, $m = 2$ | 85 |
| 3 | **10c**, $R^3$ = H, $m = 3$ | 45 |
| 4 | **10d**, $R^3$ = Me, $m = 1$ | 85 |

Wittig homologation provided the suitable terminal alkene **16**. To fulfill the diene system the silyl protecting group was readily removed and an almost identical sequence of oxidation and Wittig reaction was performed yielding **12** ($n = 1$, $R^2$ = SPh), regardless of the carbon chain length. Again, these intermediates were submitted to carbene **15** affording the corresponding β,γ-unsaturated fused γ-lactones **11b** and **11c** in excellent yields as the only detected products (Scheme 4).

## 3. Conclusions

We have shown that the conjunction of our protocol for accessing to highly substituted γ-lactones and ring-closing metathesis provides a suitable methodology to enantiomeric unsaturated carbocyclic systems fused to γ-lactones. In addition to the high stereochemical control in all substituent in the butyrolactone system and control in the ring size, we synthesize systems with enough functional groups to elaborate more complicated molecules, such us the generation of α-methylene γ-lactones [8], butenolides [8] and series of structures resulting of manipulation of the generated cyclic alkene [12]. Applications of the reported strategy to the synthesis of bioactive natural compounds are subject of study in our laboratory and well be reported in due course.

## 4. Experimental

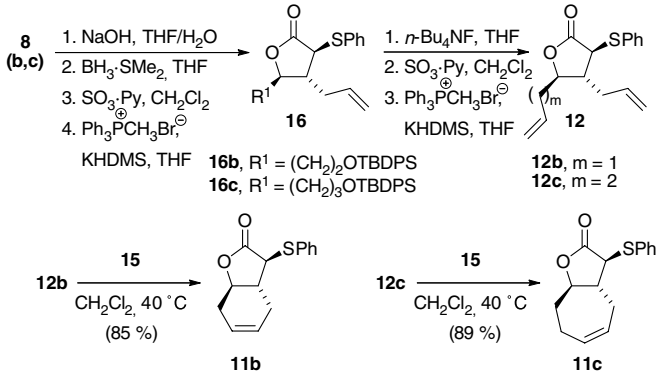
### 4.1. General remarks

$^1$H and $^{13}$C NMR spectra were recorded at 25 °C on a Bruker Avance-400 and/or 300 spectrometer in $CDCl_3$ as solvent, and chemical shifts are reported relative to $Me_4Si$. Low- and high-resolution mass spectra were taken using a Micromass Autospec spectrometer. Elemental analyses were performed on a Fisons Instruments EA 1108 CHNS-O. Optical rotations were determined for solutions in chloroform or *n*-hexane with a Perkin–Elmer Model 241 polarimeter. Column chromatography was performed on Merck silica gel, 60 Å and 0.2–0.5 mm. Visualization of spots was performed with UV light and/or phosphomolybdic acid in ethanol stain. All solvents were purified by standard techniques [16]. Reactions requiring anhydrous conditions were performed under argon. Anhydrous magnesium sulfate was used for drying solutions.

### 4.2. General procedure to obtain 3-(phenylthio)acyloxy 1,2-diols from enantiomerically enriched 2,3-epoxy alcohols

#### 4.2.1. Preparation of (2S,3R)-1,2-dihydroxyhexan-3-yl 2-(phenylthio)acetate (*6a*)

To a stirred solution of (2*S*, 3*S*)-epoxy-1-hexanol [13] (5 g, 0.043 mol) in dry $CH_2Cl_2$ (430 mL) was added (phenylthio)acetic acid (10.9 g, 0.065 mol) at 0 °C under argon. The mixture was stirred for 15 min, and Ti(OPr-*i*)$_4$ (15.4 mL, 0.052 mol) was added. After the addition, the mixture was allowed to warm to room temperature and the solution was stirred for 2 h. A solution of aqueous tartaric acid (15% w/v, 400 mL) was added, and this final mixture was stirred until clear phases were reached (30 min). The phases were separated and the aqueous phase was extracted with $CH_2Cl_2$. The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ and brine, dried, concentrated, and purified by column chromatography, to yield **6a** (11.51 g, 94% yield) as an oil: $[\alpha]_D^{25} = +11.1$ (*c* 1.32, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0,85 (t, $J = 7.21$ Hz, 3H), 1.28 (m, 2H), 1.57 (m, 2H), 3.12 (br s, 1H), 3.45 (br s, 1H), 3.56 (m, 3H), 3.66 (s, 2H), 4.88 (m, 1H), 7.25 (m,




Scheme 4.

2H), 7.39 (m, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.8 (q), 18.4 (t), 32.3 (t), 36.7 (t), 62.6 (t), 72.8 (d), 75.7 (d), 127.1 (d), 129.1 (d), 129.9 (d), 134.8 (s), 170.1 (s); MS *m/z* (relative intensity) 284 $(M)^+$ (25), 253 (2), 168 (61), 123 (100); HRMS Calc. for $C_{14}H_{20}O_4S$ $(M)^+$ 284.1082, found 284.1078.

#### 4.2.2. Preparation of (2S,3R)-1,2-dihydroxy-5-tert-butyldiphenylsilyloxy-pentan-3-yl-2-(phenylthio)-acetate (**6b**)

Prepared from (2*S*,3*S*)-epoxy-5-*tert*-butyldiphenylsilyloxy-1-pentanol [13] (4.16 g, 11.7 mmol) to give **6b** (4.9 g, 80% yield) as an oil: $[\alpha]_D^{25} = -2.85$ (*c* 1.44, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,05 (s, 9H), 1.89 (m, 2H), 2.09 (br s, 1H), 3.21 (br s, 1H), 3.45 (dd, $J = 11.8$, 5.4 Hz, 1H), 3.56 (s, 2H), 3.62 (m, 1H), 3.69 (m, 3H), 5.05 (m, 1H), 7.38 (m, 9H), 7.63 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.0 (s), 26.7 (q), 33.2 (t), 36.6 (t), 59.9 (t), 62.6 (t), 72.5 (d), 73.1 (d), 127.1 (d), 127.7 (d), 129.1 (d), 129.8 (d), 133.1 (s), 135.5 (d), 169.7 (s); MS *m/z* (relative intensity) 449 $(M - 75)^+$ (3), 269 (16), 199 (100), 123 (64); HRMS Calc. for $C_{25}H_{25}O_4SiS$ $(M - 75)^+$ 449.1243, found 449.1251.

#### 4.2.3. Preparation of (2S,3R)-1,2-dihydroxy-6-tert-butyldiphenylsilyloxy-hexan-3-yl-2-(phenylthio)acetate (**6c**)

Prepared from 6-*tert*-butyldiphenylsilyloxy-hexen-2(*E*)-ol [13] (3.65 g, 9.86 mmol) to give **6c** (4.3 g, 81% yield) as an oil: $[\alpha]_D^{25} = +0.91$ (*c* 4.39, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,08 (s, 9H), 1.58 (m, 4H), 2.9 (br s, 1H), 3.48 (dd, $J = 11.9$, 5.9 Hz, 1H), 3.62 (m, 2H), 3.65 (s, 2H), 3.69 (m, 2H), 4.92 (m, 1H), 7.42 (m, 9H), 7.69 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.9 (s), 26.3 (t), 26.6 (q), 27.8 (t), 36.2 (t), 62.1 (t), 63.0 (t), 72.3 (d), 75.3 (d), 126.8 (d), 127.4 (d), 128.8 (d), 129.3 (d), 129.6 (d), 133.5 (s), 134.3 (s), 135.2 (d), 169.8 (s); MS *m/z* (relative intensity) 463 $(M - 75)^+$ (15), 349 (37), 235 (43), 199 (100); HRMS Calc. for $C_{26}H_{27}O_4SiS$ $(M - 75)^+$ 463.3029, found 463.3035.

### 4.3. General procedure to transform 3-(phenylthio)acyloxy-1,2-diols into γ-(phenylthio)acyloxy-α,β-unsaturated esters

#### 4.3.1. Preparation of methyl (4R)-4-[(phenylthio)-acetoxy]hepte-2(E)-enoate (**7a**)

To a stirred solution of **6a** (10 g, 0.035 mol) in MeOH/$H_2O$ (20:1, 70 mL) were added $NaIO_4$ (18.83 g, 0.088 mol) and a catalytic amount of tetrabutylammonium periodate at room temperature. After 1 h, the mixture was filtered through a pad of celite and washed with ether. The resulting solution was concentrated, yielding an oil of the crude aldehyde, which was used without purification.

To a suspension of sodium hydride (1.9 g, 0.063 mol, 80% in mineral oil) in benzene (500 mL), at 0 °C was added slowly (trimethylphosphono)acetate (11.34 mL, 0.070 mol) in benzene (50 mL). After complete addition the mixture was stirred for 5 min and the crude aldehyde dissolved in benzene (150 mL) was added dropwise. The reaction mixture was stirred for 30 min, after which time TLC showed complete conversion to the unsaturated ester. The reaction was quenched with acetic acid (4 mL), extracted with ether (500 mL), and washed with a saturated aqueous solution of $NaHCO_3$ (200 mL) and brine (200 mL), dried over $MgSO_4$, filtered and concentrated, and purified by column chromatography, to give **7a** (7.92 g, 73% yield) as an oil: $[\alpha]_D^{25} = +19,9$ (*c* 1.24, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.84 (t, $J = 7.19$ Hz, 3H), 1.24 (m, 2H), 1.57 (m, 2H), 3.64 (s, 2H), 3.69 (s, 3H), 5.37 (m, 1H), 5.90 (dd, $J = 15.7$, 1.5 Hz, 1H), 6.77 (dd, $J = 15.7$, 5.3 Hz, 1H), 7.24 (m, 2H), 7.38 (m, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.3 (q), 17.70 (t), 35.4 (t), 36.3 (t), 51.2 (q), 73.0 (d), 121.1 (d), 126.7 (d), 128.7 (d), 129.8 (d), 134.4 (s), 144.71 (d), 165.9 (s), 166.4 (s); MS *m/z* (relative intensity) 308 $(M)^+$ (18), 168 (6), 141 (54), 123 (100); HRMS Calc. for $C_{16}H_{20}O_4S$ $(M)^+$ 308.1082, found 308.1093.

#### 4.3.2. Preparation of methyl (4R)-4-[(phenylthio)-acetoxy]-6-tert-butyldiphenylsilyloxy-hexen-2(E)-oate (**7b**)

Prepared from **6b** (4.5 g, 8.58 mmol) to give **7b** (3.57 g, 76% yield) as an oil: $[\alpha]_D^{25} = +10,97$ (*c* 1.44, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.86 (m, 2H), 3.58 (s, 2H), 3.66 (m, 2H), 3.72 (s, 3H), 5.64 (m, 1H), 5.92 (dd, $J = 15.7$, 1.4 Hz, 1H), 6.81 (dd, $J = 15.7$, 5.4 Hz, 1H), 7.39 (m, 9H), 7.62 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.9 (s), 26.5 (q), 36.3 (t), 36.4 (t), 51.4 (q), 59.0 (t), 70.7 (d), 121.2 (d), 127.5 (d), 129.5 (d), 133.2 (s), 135.3 (d), 144.8 (d), 166.2 (s), 168.4 (s); MS *m/z* (relative intensity) 491 $(M - 57)^+$ (27), 413 (2), 349 (68), 199 (93); HRMS Calc. for $C_{27}H_{27}O_5SiS$ $(M - 57)^+$ 491.1348, found 491.1354.

#### 4.3.3. Preparation of methyl (4R)-4-[(phenylthio)-acetoxy]-7-tert-butyldiphenylsilyloxy-hepten-2(E)-oate (**7c**)

Prepared from **6c** (4 g, 7.43 mmol) to give **7c** (3.09 g, 74% yield) as an oil: $[\alpha]_D^{25} = +4.87$ (*c* 2.3, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.50 (m, 2H), 1.72 (m, 2H), 3.60 (m, 2H), 3.67 (s, 2H), 3.75 (s, 3H), 5.40 (m, 1H), 5.90 (dd, $J = 15.7$, 0.9 Hz, 1H), 6.78 (dd, $J = 15.7$, 5.2 Hz, 1H), 7.40 (m, 9H), 7.63 (m, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.2 (s), 26.8 (q), 27.7 (t), 30.1 (t), 36.7 (t), 51.7 (q), 63.1 (t), 73.4 (d), 121.6 (d), 127.6 (d), 129.1 (d), 133.7 (s), 135.5 (d), 144.9 (d), 166.3 (s), 168.8 (s); MS *m/z* (relative intensity) 505 $(M - 57)^+$ (29), 349 (100), 213 (31), 199 (63); HRMS Calc. for $C_{28}H_{29}O_5SiS$ $(M - 57)^+$ 505.1505, found 505.1505.

### 4.4. General cyclization procedure of γ-(phenylthio)acyloxy α,β-unsaturated esters

#### 4.4.1. Preparation of methyl 2-((2R,3R,4S)-5-oxo-4-(phenylthio)-2-propyl-tetrahydrofuran-3-yl)acetate (**8a**)

To a suspension of sodium hydride (1.43 g, 0.036 mmol, 80% in mineral oil) in dry DMF (162 mL) under argon at −50 °C was added dropwise the unsaturated ester **7a** (10 g, 0.032 mmol) in dry DMF (162 mL). The reaction mixture was stirred for 4 h, after which time TLC showed complete conversion into the lactone. The reaction was quenched with acetic acid (4 mL) and extracted with ether. The combined organic phases were washed with a saturated

aqueous solution of $NaHCO_3$ and brine, dried and concentrated. Purification by silica gel column chromatography gave **8a** (9.5 g, 95% yield) as an oil: $[\alpha]_D^{25} = +7.1$ (*c* 11.4, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.86 (t, $J = 7.05$ Hz, 3H), 1.35 (m, 4H), 2.40 (m, 1H), 2.56 (d, $J = 5.8$, Hz, 2H), 3.68 (s, 3H), 3.75 (d, $J = 10.3$, Hz, 1H), 4.22 (m, 1H), 7.32 (m, 3H), 7,55 (m, 2H); $^{13}C$ NMR (300 MHz, $CDCl_3$) $\delta$ 13.6 (q), 18.4 (t), 34.7 (t), 36.0 (t), 43.1 (d), 51.3 (d), 51.8 (q), 82.2 (d), 128.7 (d), 129.2 (d), 131.5 (s), 134.1 (d), 171.0 (s), 173.5 (s); MS *m*/*z* (relative intensity) 308 $(M)^+$ (86), 277 (3), 249 (7), 168 (32), 109 (96); HRMS Calc. for $C_{16}H_{20}O_4S$ $(M)^+$ 308.1082, found 308.1083.

#### 4.4.2. Preparation of methyl 2-(2R,3R,4S)-5-oxo-4-(phenylthio)-2-(2-tert-butyldiphenylsilyloxy)ethyl-tetrahydrofuran-3-yl-acetate (8b)

Prepared from **7b** (3.4 g, 6.2 mmol) to give **8b** (3.23 g, 95% yield) as an oil: $[\alpha]_D^{25} = +12,75$ (*c* 2.51, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1,03 (s, 9H), 1.83 (m, 2H), 2.43 (m,1H), 2.63 (d, $J = 5.9$ Hz, 2H), 3.69 (s, 3H), 3.81 (d, $J = 7.6$ Hz, 1H), 4.47 (m, 1H), 7.31 (m, 3H), 7.41 (m, 6H), 7.56 (m, 2H), 7.62 (m, 4H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 18.9 (s), 26.6 (q), 34.1 (t), 36.9 (t), 43.0 (q), 50.9 (d), 51.7 (d), 59.4 (t), 78.9 (d), 127.5 (d), 128.6 (d), 129.0 (d), 129.5 (d), 131.1 (s), 133.1 (s), 133.9 (d), 135.2(d), 170.8 (s), 173.4 (s); MS *m*/*z* (relative intensity) 491 $(M - 57)^+$ (10), 255 (100), 199 (81); HRMS Calc. for $C_{27}H_{27}O_5SiS$ $(M - 57)^+$ 491.1348, found 491.1344.

#### 4.4.3. Preparation of methyl 2-(2R,3R,4S)-5-oxo-4-(phenylthio)-2-(3-tert-butyldiphenylsilyloxy)propyl-tetrahydrofuran-3-yl-acetate (8c)

Prepared from **7c** (2.8 g, 4.98 mmol) to give **8c** (2.66 g, 95% yield) as an oil: $[\alpha]_D^{25} = +5.07$ (*c* 2.6, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.55 (m, 2H), 1.68 (m,2H), 2.39 (m, 1H), 2.60 (d, $J = 6.1$ Hz, 2H), 3.63 (m, 2H), 3.69 (s, 3H), 3.76 (d, $J = 10.2$ Hz, 1H), 4.20 (ddd, $J = 8.2$, 8.2, 3.3 Hz, 1H), 7.32 (m, 3H), 7.41 (m, 6H), 7.58 (m, 2H), 7.64 (m, 4H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.1 (s), 26.8 (q), 28.0 (t), 30.4 (t), 34.5 (t), 42.9 (d), 50.4 (q), 51.3 (d), 63.0 (t), 82.2 (d), 127.6 (d), 128.9 (d), 129.3 (d), 129.6 (d), 131.2 (s), 133.6 (s), 134.2 (d), 135.5(d), 171.0 (s), 173.6 (s); MS *m*/*z* (relative intensity) 505 $(M - 57)^+$ (40), 427 (20), 269 (100), 199 (66); HRMS Calc. for $C_{28}H_{29}O_5SiS$ $(M - 57)^+$ 505.1505, found 505.1496.

### 4.5. General procedure to obtain α-benzenesulfonyl-β-hydroxyethyl-γ-lactones

#### 4.5.1. Preparation of (3S,4R,5R)-3-benzenesulfonyl-4-(2-hydroxyethyl)-5-propyldihydrofuran-2-one (13)

To a stirred solution of the lactone **8a** (9 g, 0.029 mol) in THF/$H_2O$, 4:1 (146 mL, 0.2 M) was added NaOH (11.7 g, 0.29 mol). The reaction was stirred for 1 h, until starting material was not detected by TLC. Then concentrated HCl was added at 0 °C until pH 1 was reached and the reaction was extracted in AcOEt. The combined organic phases were washed with a saturated aqueous solution of brine, dried and concentrated. Purification by column chromatography yielded (2*R*,3*R*,4*S*)-[5-oxo-4-(phenylthio)-2-propyltetrahydrofuran-3- yl]acetic acid (7.9 g, 92% yield) as an oil: $[\alpha]_D^{25} = +2.3$ (*c* 2.7, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.87 (t, $J = 7.1$ Hz, 3H), 1.41 (m, 2H), 1.56 (m, 2H), 2.39 (m, 1H), 2.66 (d, $J = 5.9$ Hz, 2H), 3.75 (d, $J = 10.2$ Hz, 1H), 4,20 (m, 1H), 7.32 (m, 3H), 7.55 (m, 2H), 10.98 (br s, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.5 (t), 34.3 (t), 35.4 (t), 42.7 (d), 51.2 (d), 82.2 (d), 129.0 (d), 129.3 (d), 131.1 (s), 134.4 (d), 173.7 (s), 175.9 (s); MS *m*/*z* (relative intensity) 294 $(M)^+$ (100), 168 (29), 149 (21), 110 (68); HRMS Calc. for $C_{15}H_{18}O_4S$ $(M)^+$ 294.0926, found 294.0938. Anal. Calc. for $C_{15}H_{18}O_4S$: C, 61.22, H, 6.45, S, 10.56. Found: C, 61.20, H, 6.16, S, 10.89.

To a stirred solution of (2*R*,3*R*,4*S*)-[5-oxo-4-(phenylthio)-2-propyltetrahydrofuran-3-yl]acetic acid (7.5 g, 0.025 mol) in dry THF (127 mL, 0.2 M) under argon was added dropwise the complex $BH_3 \cdot SMe_2$ (2 M) in THF (15.3 mL, 0.031 mol) at −10 °C. The mixture was allowed to warm slowly to room temperature and stirred additionally for 6–8 h until TLC showed the end of the reaction. Then the mixture was cooled to 0 °C and quenched by careful addition of MeOH (10.3 mL, 0.25 mol). The resulting solution was evaporated in vacuo and the obtained crude was purified by column chromatography to give (3*S*,4*R*,5*R*)-4-(2-hydroxyethyl)-3-phenylthio-5-propyldihydrofuran-2-one (6.28 g, 88% yield) as an oil: $[\alpha]_D^{25} = +28.4$ (*c* 0.38, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.89 (t, $J = 7.0$ Hz, 3H), 1.43 (m, 2H), 1.59 (m, 2H), 1.84 (m, 2H), 2.18 (m, 1H), 2.55 (br s, 1H), 3.59 (d, $J = 10.1$ Hz, 1H), 3.85 (m, 2H), 4.09 (m, 1H), 7.34 (m, 3H), 7.59 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.7 (t), 36.4 (t), 43.6 (d), 52.3 (d), 60.0 (t), 83.3 (d), 128.8 (d), 129.3 (d), 131.7 (s), 133.9 (d), 174.6 (s); MS *m*/*z* (relative intensity) 280 $(M)^+$ (100), 262 (47), 149 (12), 110 (82); HRMS Calc. for $C_{15}H_{20}O_3S$ $(M)^+$ 280.1133, found 280.1131. Anal. Calc. for $C_{15}H_{20}O_3S$: C, 64.26, H, 7.19, S, 11.44. Found: C, 64.27, H, 7.47, S, 11.29.

To a stirred solution of (3*S*,4*R*,5*R*)-4-(2-hydroxyethyl)-3-phenylthio-5- propyldihydrofuran-2-one (6 g, 0.021 mol) in MeOH (71.4 mL, 0.3 M) was added $KHSO_5$ (19.76 g, 0.032 mol) in $H_2O$ (42.8 mL, 0.5 M) at 0 °C. The mixture was vigorously stirred for 5 h, until TLC showed completion. Then it was diluted with EtOAc and the organic phase was washed with $H_2O$ and brine, dried, concentrated and purified by silica gel column chromatography, yielding **13** (6.2 g, 93% yield) as an oil: $[\alpha]_D^{25} = +28.79$ (*c* 3.64, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.88 (t, $J = 7.3$ Hz, 3H), 1.37 (m, 2H), 1.61 (m, 2H), 1.85 (m, 2H), 2.78 (br s, 1H), 2.91 (m, 1H), 3.75 (m, 2H), 4.16 (m, 1H), 4.23 (d, $J = 7.1$ Hz, 1H), 7.55 (m, 2H), 7.66 (m, 1H), 7.90 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.6 (q), 18.6 (t), 36.0 (t), 37.1 (t), 38.8 (d), 59.7 (t), 69.3 (d), 84.3 (d), 129.2 (d), 129.9 (d), 134.7 (d), 136.6 (s), 167.4 (s); MS *m*/*z*

(relative intensity) 313 $(M+1)^+$ (31), 295 (7), 203 (45), 141 (44), 77 (100); HRMS Calc. for $C_{15}H_{21}O_5S$ $(M+1)^+$ 313.1110, found 313.1111. Anal. Calc. for $C_{15}H_{20}O_5S$: C, 57.67, H, 6.45, S, 10.26. Found: C, 57.68, H, 6.65, S, 10.03.

### 4.6. General procedure for the alkylation of α-(benzenesulfonyl)γ-lactones

#### 4.6.1. Preparation of (3S,4R,5R)-3-allyl-3-benzenesulfonyl-4-(2-hydroxyethyl)-5-propyldihydrofuran-2-one (**14a**)

To a suspension of NaH (51,7 mg, 1,92 mmol, 80% in mineral oil) in dry DMF (4 mL) under argon was added dropwise the sulfone **13** (500 mg, 1.6 mmol) in dry DMF (4 mL) at 0 °C. The reaction mixture was stirred for 15 min, after which time allyl bromide (166.4μL, 1.92 mmol) was added. The reaction was allowed to warm to room temperature and stirred for 4 h. After this period TLC showed complete conversion. Then to the reaction mixture were added AcOH (50 μL) and $H_2O$ (10 mL), and it was extracted with ether. The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ and brine, dried over $MgSO_4$, concentrated and purified by column chromatography, giving **14a** (423 mg, 75% yield) as an oil: $[\alpha]_D^{25} = +39.9$ (*c* 1.73, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.86 (t, $J = 7.2$ Hz, 3H), 1.45 (m, 2H), 1.75 (m, 2H), 2.13 (m, 2H), 2.49 (br s, 1H), 2.80 (m, 2H), 3.16 (m, 1H), 3.71 (m, 1H), 3.84 (m, 1H), 3.98 (m, 1H), 5.19 (m, 2H), 5.56 (m, 1H), 7.59 (m, 2H), 7.68 (m, 1H), 7.92 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.6 (t), 30.6 (t), 34.0 (t), 36.5 (t), 40.9 (d), 60.4 (t), 75.1 (s), 83.5 (d), 122.3 (t), 129.93 (d), 129.8 (d), 131.5 (d), 134.3 (s), 134.7 (d), 170.7 (s); MS *m*/*z* (relative intensity) 353 $(M+1)^+$ (13), 211 (100), 193 (64), 71 (95); HRMS Calc. for $C_{18}H_{25}O_5S$ $(M+1)^+$ 353.1423, found 353.1423. Anal. Calc. for $C_{18}H_{24}O_5S$: C, 61.34, H, 6.86, S, 9.10. Found: C, 61.64, H, 6.95, S, 8.87.

#### 4.6.2. Preparation of (3S,4R,5R)-3-benzenesulfonyl-3-butenyl-4-(2-hydroxyethyl)-5- propyldihydrofuran-2-one (**14b**)

Prepared from **13** (500 mg, 1.6 mmol) using 4-bromo-1-butene as alkylating agent to give **14b** (352 mg, 60% yield) as an oil: $[\alpha]_D^{25} = +37.8$ (*c* 0.27, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.86 (t, $J = 7.1$ Hz, 3H), 1.40 (m, 2H), 1.71 (m, 2H), 2.0 (m, 4H), 2.6 (br s, 1H), 3.16 (m, 1H), 3.74 (m, 1H), 3.82 (m, 1H), 4.04 (m, 1H), 4.97 (m, 2H), 5.63 (m, 1H), 7.57 (m, 2H), 7.67 (m, 1H), 7.91 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.7 (q), 17.5 (t), 28.6 (t), 29.2 (t), 30.8 (t), 36.8 (t), 40.8 (d), 60.3 (t), 75.1 (s), 83.8 (d), 116.5 (t), 127.9 (d), 131.5 (d), 134.4 (s), 135.3 (d), 136.8 (d), 170.7 (s); MS *m*/*z* (relative intensity) 367 $(M+1)^+$ (39), 297 (10), 154 (100), 125 (24), 77 (54); HRMS Calc. for $C_{19}H_{27}O_5S$ $(M+1)^+$ 367.1579, found 367.1571. Anal. Calc. for $C_{18}H_{24}O_5S$: C, 62.27, H, 7.15, S, 8.75. Found: C, 62.47, H, 7.25, S, 8.87.

#### 4.6.3. Preparation of (3S,4R,5R)-3-benzenesulfonyl-3-pentenyl-4-(2-hydroxyethyl)-5-propyldihydrofuran-2-one (**14c**)

Prepared from **13** (500 mg, 1.6 mmol) using 5-bromo-1-pentene as alkylating agent to give **14c** (353 mg, 58% yield) as an oil: $[\alpha]_D^{25} = +22.6$ (*c* 0.31, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.96 (t, $J = 7.1$ Hz, 3H), 1.33 (m, 2H), 1.44 (m, 2H), 1.53 (m, 2H), 1.96 (m, 2H), 2.16 (m, 2H), 3.17 (m, 1H), 3.75 (m, 1H), 3.82 (m, 1H), 4.05 (m, 1H), 4.99 (m, 2H), 5.65 (m, 1H), 7.67 (m, 2H), 7.71 (m, 1H), 7.94 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.6 (t), 28.6 (t), 29.2 (t), 30.1 (t), 30.8 (t), 36.8 (t), 40.8 (d), 61.3 (t), 75.1 (s), 83.6 (d), 116.0 (t), 124.0 (d), 129.2 (d), 129.6 (s), 130.9 (d), 136.8 (d), 174.5 (s); MS *m*/*z* (relative intensity) 381 $(M+1)^+$ (10), 269 (43), 125 (10), 69 (100); HRMS Calc. for $C_{20}H_{29}O_5S$ $(M+1)^+$ 381.1735, found 381.1739. Anal. Calc. for $C_{20}H_{28}O_5S$: C, 63.13, H, 7.42, S, 8.43. Found: C, 63.30, H, 7.55, S, 8.62.

#### 4.6.4. Preparation of (3S,4R,5R)-3-(2-methyl)allyl-3-benzenesulfonyl-4-(2-hydroxyethyl)-5-propyl-dihydrofuran-2-one (**14d**)

Prepared from **13** (500 mg, 1.6 mmol) using 3-chloro-2-methyl-1-propene as alkylating agent to give **14d** (352 mg, 60% yield) as an oil: $[\alpha]_D^{25} = +38.2$ (*c* 1.07, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.87 (t, $J = 7.3$ Hz, 3H), 1.41 (m, 2H), 1.52 (m, 2H), 1.67 (s, 3H), 1.76 (m, 2H), 2.17 (m, 2H), 3.22 (m, 1H), 3.72 (m, 1H), 3.82 (m, 1H), 4.07 (m, 1H), 4.85 (s, 1H), 4.93 (s, 1H), 7.59 (m, 2H), 7.68 (m, 1H), 7.94 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.7 (t), 23.4 (q), 30.8 (t), 36.8 (t), 37.1 (t), 60.8 (t), 69.4 (d), 74.7 (s), 83.7 (d), 116.9 (t), 128.8 (d), 131.7 (d), 134.1 (s), 134.7 (d), 138.9 (s), 171.6 (s); MS *m*/*z* (relative intensity) 367 $(M+1)^+$ (39), 297 (10), 154 (100), 125 (24), 77 (54); HRMS Calc. for $C_{19}H_{27}O_5S$ $(M+1)^+$ 367.1579, found 367.1571. Anal. Calc. for $C_{18}H_{24}O_5S$: C, 62.27, H, 7.15, S, 8.75. Found: C, 62.47, H, 7.25, S, 8.87.

### 4.7. General procedure for the preparation of terminal alkenes from primary alcohols

#### 4.7.1. Preparation of (3S,4R,5R)-3,4-diallyl-3-benzenesulfonyl-5-propyldihydrofuran-2-one (**10a**)

To a stirred solution of the alcohol **14a** ($R^1 = $ Pr-*n*, $R^4 = CH_2CH{=}CH_2$) (400 mg, 1.14 mmol) in dry $CH_2Cl_2$ (3.8 mL) were added methyl sulfoxide (750 μL, 0.66 mL/mmol) and triethylamine (1.11 mL, 7.9 mmol) at 0 °C. The mixture was stirred for 15 min and then the complex $SO_3 \cdot Py$ (723 mg, 4.5 mmol) was added. The reaction was allowed to warm to room temperature and stirred for 4 h. After this period TLC showed complete conversion. The reaction was extracted with ether. The combined organic phases were washed with $H_2O$ and brine, dried and concentrated, yielding an oil of the crude aldehyde, which was used without purification.

A solution of potassium hexamethyldisilazane (5.45 mL, 2.73 mmol) 0.5 M in toluene was added dropwise to a stirred mixture of methyltriphenylphosphonium bromide (974 mg,

2.73 mmol) in THF (6 mL) at −40 °C. The mixture was stirred for 1 h at −40 °C to give a deep yellow coloration. A solution of the crude aldehyde in THF (3 mL) was added dropwise to the ylide solution and stirring was maintained for 1 h at −40 °C. The reaction mixture was quenched by dropwise addition of an ammonium chloride solution, followed by warming to room temperature, at which point ether was added. The organic layer was washed with water, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography to obtain the diene **10a** (316 mg, 80% yield) as an oil: $[\alpha]_D^{25} = +32.5$ (*c* 1.53, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.86 (t, $J = 7.2$ Hz, 3H), 1.27 (m, 2H), 1.45 (m, 2H), 1.75 (m, 1H), 2.33 (m, 1H), 2.76 (m, 2H), 3.06 (m, 1H), 4.03 (m, 1H), 5.10 (m, 2H), 5.22 (m, 2H), 5.58 (m, 1H), 5.78 (m, 1H), 7.60 (m, 2H), 7.72 (m, 1H), 7.94 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.4 (t), 32.8 (t), 33.9 (t), 37.2 (t), 43.6 (d), 74.2 (s), 83.8 (d), 117.6 (t), 122.0 (t), 129.2 (d), 130.1 (d), 131.4 (d), 133.4 (s), 134.6 (d), 135.4 (d), 170.6 (s); MS *m*/*z* (relative intensity) 349 $(M+1)^+$ (27), 207 (52), 91 (43), 71 (100); HRMS Calc. for $C_{19}H_{25}O_4S$ $(M+1)^+$ 349.1473, found 349.1475. Anal. Calc. for $C_{19}H_{24}O_4S$: C, 65.49, H, 6.94, S, 9.20. Found: C, 65.83, H, 7.14, S, 8.86.

#### 4.7.2. Preparation of (3S,4R,5R)-4-allyl-3-benzenesulfonyl-3-butenyl-5-propyldihydrofuran-2-one (*10b*)

Prepared from **14b** (300 mg, 0.82 mmol) to give **10b** (237 mg, 80% yield) as an oil: $[\alpha]_D^{25} = +57.4$ (*c* 1.08, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.89 (t, $J = 7.2$ Hz, 3H), 1.33 (m, 2H), 1.48 (m, 2H), 1.78 (m, 1H), 2.02 (m, 3H), 2.23 (m, 1H), 2.70 (m, 1H), 3.10 (m, 1H), 4.07 (m, 1H), 5.01 (m, 2H), 5.13 (m, 2H), 5.63 (m, 1H), 5.78 (m, 1H), 7.56 (m, 2H), 7.68 (m, 1H), 7.92 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.5 (t), 28.5 (t), 29.4 (t), 30.0 (t), 37.5 (t), 43.4 (d), 74.1 (s), 83.9 (d), 116.4 (t), 117.8 (t), 128.8 (d), 131.4 (d), 134.6 (d), 134.7 (s), 135.1 (d), 135.4 (d), 170.6 (s); MS *m*/*z* (relative intensity) 363 $(M+1)^+$ (100), 255 (5), 154 (45), 109 (31), 77 (18); HRMS Calc. for $C_{20}H_{27}O_4S$ $(M+1)^+$ 363.1630, found 363.1621. Anal. Calc. for $C_{20}H_{26}O_4S$: C, 66.27, H, 7.23, S, 8.85. Found: C, 66.58, H, 7.35, S, 8.45.

#### 4.7.3. Preparation of (3S,4R,5R)-4-allyl-3-benzenesulfonyl-3-pentenyl-5-propyldihydrofuran-2-one (*10c*)

Prepared from **14c** (300 mg, 0.79 mmol) to give **10c** (237 mg, 80% yield) as an oil: $[\alpha]_D^{25} = +56.9$ (*c* 2.15, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.87 (t, $J = 7.1$ Hz, 3H), 1.42 (m, 5H), 1.57 (m, 1H), 1.76 (m, 1H), 2.03 (m, 3H), 2.17 (m, 1H), 2.66 (m, 1H), 3.05 (m, 1H), 4.05 (m, 1H), 4.97 (m, 2H), 5.12 (m, 2H), 5.65 (m, 1H), 5.76 (m, 1H), 7.58 (m, 2H), 7.67 (m, 1H), 7.92 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.5 (t), 24.7 (t), 28.7 (t), 33.0 (t), 33.6 (t), 37.5 (t), 43.4 (d), 74.4 (s), 84.0 (d), 116.1 (t), 117.7 (t), 128.8 (d), 131.3 (d), 134.5 (d), 134.7 (s), 135.2 (d), 136.7 (d), 170.7 (s); MS *m*/*z* (relative intensity) 377 $(M+1)^+$ (84), 307 (12), 267 (94), 235 (100), 141 (40); HRMS Calc. for $C_{21}H_{29}O_4S$ $(M+1)^+$ 377.1786, found 377.1775. Anal. Calc. for $C_{21}H_{28}O_4S$: C, 66.99, H, 7.50, S, 8.52. Found: C, 67.27, H, 7.78, S, 8.04.

#### 4.7.4. Preparation of (3S,4R,5R)-4-allyl-3-(2-methyl)allyl-3-benzenesulfonyl-5- propyldihydrofuran-2-one (*10d*)

Prepared from **14d** (300 mg, 0.82 mmol) to give **10d** (237 mg, 80% yield) as an oil: $[\alpha]_D^{25} = +48.8$ (*c* 2.01, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.88 (t, $J = 7.1$ Hz, 3H), 1.34 (m, 2H), 1.49 (m, 2H), 1.69 (s, 3H), 1.74 (m, 1H), 2.43 (m, 1H), 2.72 (m, 2H), 3.11 (m, 1H), 4.09 (m, 1H), 4.87 (s, 1H), 4.95 (s, 1H), 5.09 (m, 2H), 5.79 (m, 1H), 7.69 (m, 2H), 7.79 (m, 1H), 7.94 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.5 (t), 23.4 (q), 32.8 (t), 37.0 (t), 37.1 (t), 44.0 (d), 73.9 (s), 84.0 (d), 116.7 (t), 117.5 (t), 128.7 (d), 131.5 (d), 134.4 (s), 134.5 (d), 137.7 (d), 139.1 (d), 171.4 (s); MS *m*/*z* (relative intensity) 363 $(M+1)^+$ (2), 257 (34), 221 (100), 179 (59), 77 (98); HRMS Calc. for $C_{20}H_{27}O_4S$ $(M+1)^+$ 363.1630, found 363.1593. Anal. Calc. for $C_{20}H_{26}O_4S$: C, 66.27, H, 7.23, S, 8.85. Found: C, 66.58, H, 7.35, S, 8.45.

### 4.8. General experimental procedure for RCM of dienes tethered to γ-lactones

#### 4.8.1. Preparation of (3R,3aR,7aS)-7a-(phenylsulfonyl)-3-propyl-3a,4,7,7a-tetrahydroisobenzofuran-1(3H)-one (*9a*)

A 250 mL flask equipped with a condenser was flame-dried in vacuo. The diene **10a** (100 mg, 0.29 mmol) in dry $CH_2Cl_2$ (71.8 mL, 4 mM) was added and the solution was degassed by bubbling argon through the mixture for 1 h. Second-generation Grubbs catalyst **15** (24.4 mg, 10 mol%) in 2 mL of dry $CH_2Cl_2$ was added through the condenser and the argon bubbling was continued for an additional 30 min. The mixture was heated and stirred at 40 °C for 3 h until TLC showed the reaction was complete. The solvent was removed in vacuo and the residue was purified by silica gel chromatography to afford the desired cyclic product **9a** (78 mg, 85% yield) as an oil: $[\alpha]_D^{25} = +1.07$ (*c* 1.7, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.94 (t, $J = 7.3$ Hz, 3H), 1.45 (m, 2H), 1.68 (m, 2H), 2.25 (m, 1H), 2.33 (m, 1H), 2.42 (m, 1H), 2.54 (m, 1H), 3.27 (m, 1H), 3.91 (m, 1H), 5.85 (m, 1H), 5.98 (m, 1H), 7.60 (m, 2H), 7.70 (m, 1H), 7.93 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.8 (t), 25.5 (t), 26.8 (t), 41.1 (d), 72.4 (s), 83.7 (d), 125.1 (d), 128.3 (d), 128.8 (d), 131.2 (d), 134.4 (s), 134.6 (d), 172.2 (s); MS *m*/*z* (relative intensity) 320 $(M)^+$ (6), 179 (100), 123 (69), 77 (61); HRMS Calc. for $C_{17}H_{20}O_4S$ $(M)^+$ 320.1082, found 320.1087. Anal. Calc. for $C_{17}H_{20}O_4S$: C, 63.73, H, 6.29, S, 10.01. Found: C, 63.91, H, 6.32, S, 9.61.

#### 4.8.2. Preparation of (3R,3aR,8aS,Z)-8a-(phenylsulfonyl)-3-propyl-3a,4,8,8a-tetrahydro-3H-cyclo-heptafuran-1(7H)-one (*9b*)

Prepared from **10b** (200 mg, 0.55 mmol) to give **9b** (157 mg, 85% yield) as an oil: $[\alpha]_D^{25} = +1.05$ (*c* 3.06, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.93 (t, $J = 7.2$ Hz, 3H),

1.49 (m, 2H), 1.67 (m, 2H), 2.03 (m, 2H), 2.30 (m, 2H), 2.57 (m, 1H), 2.84 (m, 1H), 3.28 (m, 1H), 4.38 (m, 1H), 5.50 (m, 1H), 5.57 (m, 1H), 7.57 (m, 2H), 7.69 (m, 1H), 7.93 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.8 (q), 18.8 (t), 25.8 (t), 26.6 (t), 29.0 (t), 36.9 (t), 45.0 (d), 75.2 (s), 81.0 (d), 124.8 (d), 128.7 (d), 130.0 (d), 131.3 (d), 134.4 (s), 134.5 (d), 171.4 (s); MS *m/z* (relative intensity) 334 $(M)^+$ (10), 267 (12), 193 (100), 147 (42); HRMS Calc. for $C_{18}H_{22}O_4S$ $(M)^+$ 334.1238, found 334.1225. Anal. Calc. for $C_{18}H_{22}O_4S$: C, 64.64, H, 6.63, S, 8.76. Found: C, 65.23, H, 6.82, S, 9.05.

#### 4.8.3. Preparation of (3R,3aR,9aS,Z)-9a-(phenylsulfonyl)-3-propyl-3a,4,7,8,9,9a-hexahydrocycloocta furan-1(3H)-one (**9c**)

Prepared from **10c** (200 mg, 0.55 mmol) to give **9c** (83 mg, 45% yield) as an oil: $[\alpha]_D^{25} = +0.72$ (*c* 2.5, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.88 (t, $J = 7.2$ Hz, 3H), 1.34 (m, 4H), 1.67 (m, 2H), 2.03 (m, 2H), 2.25 (m, 2H), 2.40 (m, 2H), 3.07 (m, 1H), 4.24 (m, 1H), 5.68 (m, 1H), 5.80 (m, 1H), 7.59 (m, 2H), 7.68 (m, 1H), 7.97 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.8 (q), 18.8 (t), 25.8 (t), 28.6 (t), 35.2 (t), 36.9 (t), 45.0 (d), 75.2 (s), 81.0 (d), 124.8 (d), 128.7 (d), 129.7 (d), 131.3 (d), 134.4 (s), 134.5 (d), 171.4 (s); MS *m/z* (relative intensity) 348 $(M)^+$ (2), 267 (7), 207 (68), 193 (59), 71 (100); HRMS Calc. for $C_{19}H_{24}O_4S$ $(M)^+$ 348.1395, found 348.1380. Anal. Calc. for $C_{19}H_{24}O_4S$: C, 65.49, H, 6.94, S, 9.20. Found: C, 65.93, H, 7.38, S, 7.78.

#### 4.8.4. Preparation of (3R,3aR,7aS)-6-methyl-7a-(phenylsulfonyl)-3-propyl-3a,4,7,7a-tetrahydro-iso-benzofuran-1(3H)-one (**9d**)

Prepared from **10d** (200 mg, 0.55 mmol) to give **9d** (157 mg, 85% yield) as an oil: $[\alpha]_D^{25} = +3.63$ (*c* 1.9, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.94 (t, $J = 7.2$ Hz, 3H), 1.44 (m, 2H), 1.62 (m, 2H), 1.72 (s, 3H), 2.18 (m, 1H), 2.29 (s, 2H), 2.55 (m, 1H), 3.24 (m, 1H), 3.88 (m, 1H), 5.63 (s, 1H), 7.59 (m, 2H), 7.73 (m, 1H), 7.93 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.7 (q), 18.8 (t), 23.0 (q), 29.7 (t), 31.8 (t), 36.8 (t), 41.0 (d), 73.2 (s), 84.0 (d), 121.1 (d), 128.6 (s), 128.8 (d), 131.1 (d), 134.1 (s), 134.6 (d), 172.1 (s); MS *m/z* (relative intensity) 334 $(M)^+$ (10), 267 (12), 193 (100), 147 (42); HRMS Calc. for $C_{18}H_{22}O_4S$ $(M)^+$ 334.1238, found 334.1225. Anal. Calc. for $C_{18}H_{22}O_4S$: C, 64.64, H, 6.63, S, 8.76. Found: C, 65.23, H, 6.82, S, 9.05.

### 4.9. Preparation of (3S,4R,5R)-4-allyl-3-phenylthio-5-(2-tert-butyldiphenylsilyloxy)-ethyl-dihydrofuran-2-one (**16b**)

Prepared from **8b** by the sequence outlined in Scheme 4:

From **8b** (3 g, 5.47 mmol) was obtained (2*R*,3*R*,4*S*)-[5-oxo-4-(phenylthio)-2-(2-*tert*-butyldiphenylsilyloxy)-ethyl-tetrahydrofuran-3-yl]acetic acid (2.68 g, 92% yield) as an oil: $[\alpha]_D^{25} = +13.81$ (*c* 1.26, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.60 (m, 2H), 1.83 (m, 2H), 2.42 (m, 1H), 2.68 (d, $J = 5.7$ Hz, 2H), 3.72 (m, 2H), 3.80 (d, $J = 10.2$ Hz, 1H), 4.50 (ddd, $J = 8.8$, 8.8, 3.1 Hz, 1H), 7.31 (m, 3H), 7.39 (m, 6H), 7.55 (m, 2H), 7.62 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.9 (s), 26.6 (q), 33.7 (t), 36.9 (t), 42.6 (d), 50.9 (d), 59.3 (t), 78.8 (d), 127.5 (d), 128.8 (d), 129.1 (d), 129.5 (d), 131.2 (s), 133.2 (s), 134.0 (d), 135.2(d), 173.6 (s), 175.9 (s); MS *m/z* (relative intensity) 477 $(M - 57)^+$ (4), 349 (100), 255 (34), 199 (74); HRMS Calc. for $C_{26}H_{25}O_5SiS$ $(M - 57)^+$ 477.6321, found 477.6325.

From (2*R*,3*R*,4*S*)-[5-oxo-4-(phenylthio)-2-(2-*tert*-butyldiphenylsilyloxy)-ethyl-tetrahydrofuran-3-yl]acetic acid (2.5 g, 4.68 mmol) was obtained (3*S*,4*R*,5*R*)-4-(2-hydroxyethyl)-3-phenylthio-5-(2-*tert*-butyldiphenylsilyloxy)-ethyl-dihydrofuran-2-one (2.09 g, 86% yield) as an oil: $[\alpha]_D^{25} = +12.89$ (*c* 2.73, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.69 (m, 3H), 1.84 (m, 2H), 2.22 (m, 1H), 3.62 (d, $J = 10.1$ Hz, 1H), 3.77 (m, 4H), 4.37 (ddd, $J = 8.4$, 8.4, 2.9 Hz, 1H), 7.31 (m, 3H), 7.41 (m, 6H), 7.57 (m, 2H), 7.63 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.2 (s), 26.6 (q), 28.9 (t), 34.5 (t), 43.5 (d), 52.0 (d), 59.7 (t), 60.0 (t), 77.2 (d), 127.5 (d), 128.8 (d), 129.0 (d), 129.5 (d), 131.5 (s), 133.3 (s), 133.5 (d), 135.3 (d), 174.6 (s); MS *m/z* (relative intensity) 463 $(M - 57)^+$ (8), 385 (39), 255 (100), 199 (40); HRMS Calc. for $C_{26}H_{27}O_4SiS$ $(M - 57)^+$ 463.1399, found 463.1404.

From (3*S*,4*R*,5*R*)-4-(2-hydroxyethyl)-3-phenylthio-5-(2-*tert*-butyl-diphenyl-silyloxy)-ethyl-dihydrofuran-2-one (1.8 g, 3.46 mmol) was obtained **16b** (1.42 g, 80% yield) as an oil: $[\alpha]_D^{25} = +7.61$ (*c* 0.46, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.85 (m, 2H), 2.15 (m, 1H), 2.38 (m, 2H), 3.56 (d, $J = 9.6$ Hz, 1H), 3.75 (m, 2H), 4.41 (m, 1H), 5.14 (m, 2H), 5.72 (m, 1H), 7.30 (m, 3H), 7.40 (m, 6H), 7.54 (m, 2H), 7.60 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.0 (s), 26.6 (q), 29.5 (t), 34.9 (t), 45.8 (d), 50.9 (d), 62.9 (t), 82.5 (d), 118.7 (t), 127.5 (d), 128.5 (d), 129.0 (d), 129.5 (d), 131.8 (s), 133.3 (d), 133.6 (d), 135.2(d), 174.2 (s); MS *m/z* (relative intensity) 459 $(M - 57)^+$ (27), 279 (18), 255 (100), 199 (29); HRMS Calc. for $C_{27}H_{27}O_3SiS$ $(M - 57)^+$ 459.1450, found 459.1439.

#### 4.9.1. Preparation of (3S,4R,5R)-4-allyl-3-phenylthio-5-(3-tert-butyldiphenylsilyloxy)-propyl-dihydrofuran-2-one (**16c**)

Prepared from **8c** by the sequence outlined in Scheme 4.

From **8c** (2.5 g, 4.44 mmol) was obtained (2*R*,3*R*,4*S*)-[5-oxo-4-(phenylthio)-2-(3-*tert*-butyldiphenylsilyloxy)-propyl-tetrahydro-furan-3-yl]acetic acid (2.19 g, 90% yield) as an oil: $[\alpha]_D^{25} = +1.79$ (*c* 1.73, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1,03 (s, 9H), 1.63 (m, 2H), 1.78 (m, 2H), 2.37 (m, 1H), 2.64 (d, $J = 5.8$ Hz, 2H), 3.65 (m, 2H), 4.08 (d, $J = 7.5$ Hz, 1H), 4.22 (ddd, $J = 8.2$, 8.2, 3.8 Hz, 1H), 7.31 (m, 3H), 7.40 (m, 6H), 7.56 (m, 2H), 7.62 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.2 (s), 26.8 (q), 28.0 (t), 30.5 (t), 34.2 (t), 42.6 (d), 51.2 (d), 63.0 (t), 82.2 (d), 127.7 (d), 128.7 (d), 129.0 (d), 129.3 (d), 131.0 (s), 133.7 (s), 134.4 (d), 135.5 (d), 173.6 (s), 175.9 (s); MS *m/z* (relative intensity) 491 $(M - 57)^+$ (42), 413 (19), 269 (100), 199 (80); HRMS Calc. for $C_{27}H_{27}O_5SiS$ $(M - 57)^+$ 491.1348, found 491.1328.

From (2*R*,3*R*,4*S*)-[5-oxo-4-(phenylthio)-2-(3-*tert*-butyl-diphenylsilyloxy)-propyl-tetrahydrofuran-3-yl]acetic acid

(2 g, 3.64 mmol) was obtained (3*S*,4*R*,5*R*)-4-(2-hydroxyethyl)-3-phenylthio-5-(3-*tert*-butyldiphenylsilyloxy)-propyl-dihydrofuran-2-one (1.71 g, 88% yield) as an oil: $[\alpha]_D^{25} = +9.23$ (*c* 1.95, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1,04 (s, 9H), 1.57 (m, 2H), 1.82 (m, 5H), 2.15 (m, 1H), 3.60 (d, $J = 10.1$ Hz, 1H), 3.64 (m, 2H), 3.80 (m, 2H), 4.12 (ddd, $J = 8.1$, 8.1, 3.1 Hz, 1H), 7.32 (m, 3H), 7.41 (m, 6H), 7.58 (m, 2H), 7.63 (m, 4H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.2 (s), 26.8 (q), 28.1 (t), 30.7 (t), 34.5 (t), 43.5 (d), 52.2 (d), 60.0 (t), 63.0 (t), 83.3 (d), 126.6 (d), 128.8 (d), 129.3 (d), 129.6 (d), 131.5 (s), 133.7 (s), 133.9 (d), 135.5 (d), 174.6 (s); MS *m*/*z* (relative intensity) 477 $(M - 57)^+$ (9), 399 (61), 269 (50), 199 (100); HRMS Calc. for $C_{27}H_{29}O_4SiS$ $(M - 57)^+$ 477.1556, found 477.1558.

From (3*S*,4*R*,5*R*)-4-(2-hydroxyethyl)-3-phenylthio-5-(3-*tert*-butyldiphenylsilyloxy)-propyl-dihydrofuran-2-one (1.5 g, 2.8 mmol) was obtained **16c** (1.16 g, 78% yield) as an oil: $[\alpha]_D^{25} = -3.65$ (*c* 0.82, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1,03 (s, 9H), 1.64 (m, 2H), 1.81 (m, 2H), 2.13 (m, 1H), 2.38 (m, 2H), 3.56 (d, $J = 9.7$ Hz, 1H), 3.69 (m, 2H), 4.15 (ddd, $J = 8.0$, 8.0, 3.6 Hz, 1H), 5.12 (m, 2H), 5.76 (m, 1H), 7.34 (m, 3H), 7.43 (m, 6H), 7.59 (m, 2H), 7.66 (m, 4H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 19.0 (s), 26.7 (q), 28.0 (t), 30.8 (t), 34.9 (t), 45.7 (d), 50.9 (d), 62.9 (t), 82.5 (d), 118.7 (t), 127.5 (d), 128.5 (d), 129.0 (d), 129.5 (d), 131.8 (s), 132.9 (d), 133.3 (s), 133.8 (d), 135.3 (d), 174.2 (s); MS *m*/*z* (relative intensity) 473 $(M - 57)^+$ (58), 269 (100), 199 (39); HRMS Calc. for $C_{28}H_{29}O_3SiS$ $(M - 57)^+$ 473.1607, found 473.1604.

### 4.10. Preparation of (3S,4R,5R)-4,5-diallyl-3-phenylthio-dihydrofuran-2-one (*12b*)

Prepared from **16b** by the sequence outlined in Scheme 4.

To a stirred solution of **16b** (1.3 g, 2.5 mmol) in dry THF (12.5 mL, 0.2 M) was added tetra-butylammonium fluoride 1 M in THF (3.02 mL, 3.02 mmol) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 1 h, until TLC showed the end. The reaction was extracted with ether and washed with brine, dried and concentrated. The residue was purified by silica gel column chromatography to obtain (3*S*,4*R*,5*R*)-4-allyl-5-(2-hydroxyethyl)-3-phenylthio-dihydrofuran-2-one (630.3 mg, 90% yield) as an oil: $[\alpha]_D^{25} = -2.25$ (*c* 0.8, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.66 (m, 2H), 1.91 (m, 1H), 2.14 (m, 1H), 2.40 (m, 2H), 3.54 (d, $J = 9.7$ Hz, 1H), 3.73 (t, $J = 5.1$ Hz, 2H), 4.32 (ddd, $J = 9.2$, 9.2, 3.0 Hz, 1H), 5.15 (m, 2H), 5.75 (m, 1H), 7.33 (m, 3H), 7.56 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 34.6 (t), 36.9 (t), 45.9 (d), 50.6 (d), 58.8 (t), 79.8 (d), 118.9 (t), 128.6 (d), 129.0 (d), 131.7 (s), 133.1 (d), 133.8(d), 174.3 (s); MS *m*/*z* (relative intensity) 278 $(M)^+$ (100), 193 (18), 149 (29), 123 (33); HRMS Calc. for $C_{15}H_{18}O_3S$ $(M)^+$ 278.0977, found 278.0982.

Prepared from (3*S*,4*R*,5*R*)-4-allyl-5-(2-hydroxyethyl)-3-phenylthio-dihydrofuran-2-one (500 mg, 1.79 mmol) using the general procedure for the preparation of alkenes from primary alcohols to obtain **12b** (3*S*,4*R*,5*R*)-4,5-diallyl-3-phenylthio-dihydrofuran-2-one (384.3 mg, 78% yield) as an oil: $[\alpha]_D^{25} = -26.0$ (*c* 2.75, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 2.18 (m, 1H), 2.29 (m, 2H), 2.42 (m, 2H), 3.54 (d, $J = 9.5$ Hz, 1H), 4.16 (ddd, $J = 7.2$, 7.2, 5.0 Hz, 1H), 5.14 (m, 4H), 5.68 (m, 2H), 7.32 (m, 3H), 7.56 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 34.8 (t), 37.9 (t), 44.5 (d), 50.7 (d), 81.4 (d), 118.7 (t), 118.8 (t), 128.5 (d), 129.0 (d), 131.6 (s), 132.8 (d),133.2 (d), 133.9(d), 174.1 (s); MS *m*/*z* (relative intensity) 274 $(M)^+$ (83), 233 (20), 168 (71), 123 (47); HRMS Calc. for $C_{16}H_{18}O_2S$ $(M)^+$ 274.1028 , found 274.1033.

#### 4.10.1. Preparation of (3S,4R,5R)-4-allyl-5-(3-butenyl)-3-phenylthio-dihydrofuran-2-one (*12c*)

Prepared from **16c** by the sequence outlined in Scheme 4.

From **16c** (1 g, 1.88 mmol) was obtained (3*S*,4*R*,5*R*)-4-allyl-5-(3-hydroxypropyl)-3-phenylthio-dihydrofuran-2-one (507 mg, 92% yield) as an oil: $[\alpha]_D^{25} = -4.92$ (*c* 0.61, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.48 (br s, 1H), 1.55 (m, 2H), 1.64 (m, 2H), 2.04 (m, 1H), 2.39 (m, 2H), 3.53 (d, $J = 9.7$ Hz, 1H), 3.63 (m, 2H), 4.15 (ddd, $J = 8.1$, 8.1, 3.2 Hz, 1H), 5.14 (m, 2H), 5.73 (m, 1H), 7.33 (m, 3H), 7.57 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 28.2 (t), 30.7 (t), 34.7 (t), 45.8 (d), 50.8 (d), 61.8 (t), 82.4 (d), 118.7 (t), 128.5 (d), 129.0 (d), 131.6 (s), 133.1 (d), 133.8 (d), 174.3 (s); MS *m*/*z* (relative intensity) 292 $(M)^+$ (100), 207 (9), 168 (12), 123 (18); HRMS Calc. for $C_{16}H_{20}O_3S$ $(M)^+$ 292.1133, found 292.1137.

From(3*S*,4*R*,5*R*)-4-allyl-5-(3-hydroxypropyl)-3-phenylthio-dihydrofuran-2-one (400 mg, 1.36 mmol) was obtained **12c** (315 mg, 80% yield) as an oil: $[\alpha]_D^{25} = -5.67$ (*c* 3.63, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.68 (m, 1H), 1.71 (m, 1H), 2.12 (m, 3H), 2.35 (m, 2H), 3.54 (d, $J = 9.6$ Hz, 1H), 4.12 (ddd, $J = 8.1$, 8.1, 3.4 Hz, 1H), 5.0 (m, 2H), 5.12 (m, 2H), 5.72 (m, 2H), 7.34 (m, 3H), 7.56 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 29.2 (t), 33.5 (t), 34.8 (t), 45.7 (d), 50.8 (d), 81.7 (d), 115.5 (t), 118.8 (t), 128.5 (d), 129.0 (d), 131.7 (s), 133.1 (d),133.8 (d), 136.7 (d), 174.2 (s); MS *m*/*z* (relative intensity) 288 $(M)^+$ (76), 247 (13), 168 (31), 149 (42), 123 (79); HRMS Calc. for $C_{17}H_{20}O_2S$ $(M)^+$ 288.1184, found 288.1182.

### 4.11. Preparation of (3S,3aR,7aR)-3-phenylthio-3a,4,7,7a-tetrahydro-isobenzofuran-2(3H)-one (*11b*)

The general experimental procedure for RCM of dienes tethered to γ-lactones was applied to **12b** on a 200 mg (0.72 mmol) scale yielding **11b** (152 mg, 85% yield) as an oil: $[\alpha]_D^{25} = -27.5$ (*c* 2.6, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 2.07 (m, 2H), 2.21 (m, 1H), 2.31 (m, 1H), 2.57 (m, 1H), 3.63 (d, $J = 12.1$ Hz, 1H), 4.10 (ddd, $J = 10.2$, 10.2, 5.5 Hz, 1H), 5.65 (m, 2H), 7.32 (m, 3H), 7.56 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 28.5 (t), 30.4 (t), 45.4 (d), 52.3 (d), 78.6 (d), 123.7 (d), 126.4 (d), 128.3 (d), 128.9 (d), 131.6 (s), 133.5 (d), 174.0 (s); MS *m*/*z* (relative intensity) 246

$(M)^+$ (97), 149 (6), 109 (15), 93 (100); HRMS Calc. for $C_{14}H_{14}O_2S$ $(M)^+$ 246.0715, found 246.0714.

*4.11.1. Preparation of (3S,3aR,8aR)-3-phenylthio-3a,4,8,8a-tetrahydro-cycloheptenfuran-2(3H)-one (**11c**)*

The general experimental procedure for RCM of dienes tethered to γ-lactones was applied to **12c** on a 200 mg (0.69 mmol) to give **11c** (160 mg, 89% yield) as an oil: $[\alpha]_D^{25} = -8.65$ (*c* 2.38, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 1.43 (m, 1H), 1.86 (m, 1H), 2.03 (m, 2H), 2.24 (m, 2H), 2.64 (m, 1H), 3.50 (d, $J = 12.4$ Hz, 1H), 4.02 (ddd, $J = 9.7$, 9.7, 2.6 Hz, 1H), 5.78 (m, 2H), 7.31 (m, 3H), 7.56 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 23.4 (t), 27.7 (t), 30.6 (t), 48.1 (d), 53.3 (d), 85.6 (d), 128.3 (d), 128.7 (d), 129.0 (d), 130.8 (d), 131.7 (s),133.5 (d), 173.9 (s); MS *m*/*z* (relative intensity) 260 $(M)^+$ (100), 162 (63), 149 (21), 107 (34); HRMS Calc. for $C_{15}H_{16}O_2S$ $(M)^+$ 260.0871, found 260.0866.

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