Reductive Chloro- and Thioallylations: Stereoselective Two-Step Transformations of Esters and Lactones into Functionalized *cis*- and *trans*-Vinyloxiranes

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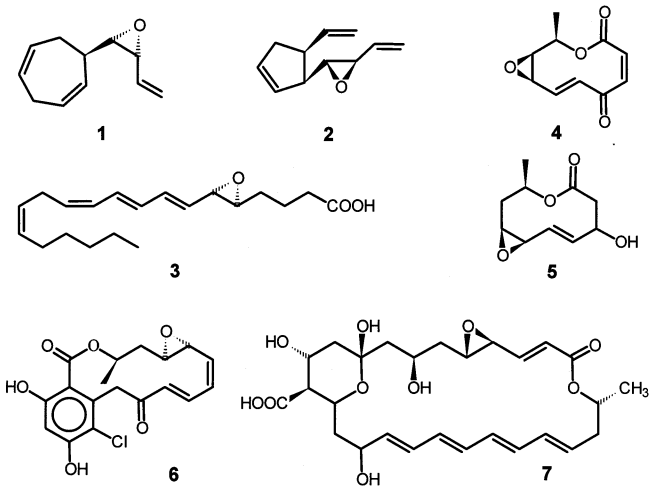
A practical and straightforward procedure is described for the diastereoselective synthesis of functionalized *cis*- and *trans*-vinyloxiranes. Readily available esters and lactones were sequentially treated in a one-pot procedure with DIBAL-H and (*Z*)-γ-chloroallyl-BBN or (*E*)-phenylthioallyltitanium reagents to give *syn*-β-chlorohydrins or *anti*-β-hydroxy thioethers in good yields with high regio- and diastereoselectivities. The β-hydroxy intermediates were stereoselectively converted into the corresponding *cis*- or *trans*-vinyloxiranes upon treatment with DBU (for halohydrins) or by alkylation/elimination (for β-hydroxy thioethers). The protocol tolerates several functional groups and promises to be of general applicability.

The vinyloxirane moiety is a structural element of many natural products, which often possess remarkably high biological activity. The eicosanoid-derived algal pheromones lamoxirene (**1**)[1] and caudoxirene (**2**)[2], for example, trigger mass release of spermatozoids from their gametangia down to a threshold concentration of 30−50 pM in seawater[3]. Other eicosanoid-derived alkenyl oxiranes were identified as important intermediates in the biosynthesis of leukotrienes **3**[4] and other oxylipins[5]. The macrocyclic lactones **4**−**7**[6] have attracted considerable attention since they appear to be promising chemotherapeutic agents for the treatment of various diseases. Common to all is an alkenyloxirane subunit carrying an additional α- or β-alkoxy or -hydroxy substituent.

Besides of being interesting synthetic targets per se, vinyloxiranes with defined configurations also represent exceedingly valuable key intermediates for the preparation of more complex, iso- and enantiomerically pure bioactive compounds. Many recent syntheses take advantage of the high reactivity and versatility of the alkenyloxirane unit that easily undergoes stereospecific ring-opening reactions with concomitant alkylation to form multifunctional compounds such as allyl and amino alcohols. For this purpose, modern Pd^0[7], lanthanoid[8] and cuprate[9] chemistry is mostly employed. As an example, the α-hydroxy-substituted vinyloxirane **10e** (Table 2) served as key substrate for Pd^0-catalyzed hydroxyamination in the synthesis of the amino sugar (−)-acosamine[10]. ω-Amino- and ω-hydroxyvinyloxiranes, such as **10g**, were used extensively for Pd^0-mediated macrocyclization in the preparation of macrolides[7][11].

Scheme 1



Thus, due to their biological and synthetic importance, vinyloxiranes have been the topic of numerous intensive research activities, although their stereoselective synthesis is unsatisfactory. Current synthetic approaches either require tedious multistep procedures by the Sharpless epoxidation method[10][12], or demand configurationally unstable aldehydes as starting material for alkylation with heterosubstituted allyl anion equivalents[13]. To bypass the isolation of, for example, sensitive α-hydroxy or α-amino aldehydes, we have developed a generally applicable reductive one-pot allylation of configurationally stable functionalized esters or lactones.

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Results and Discussion

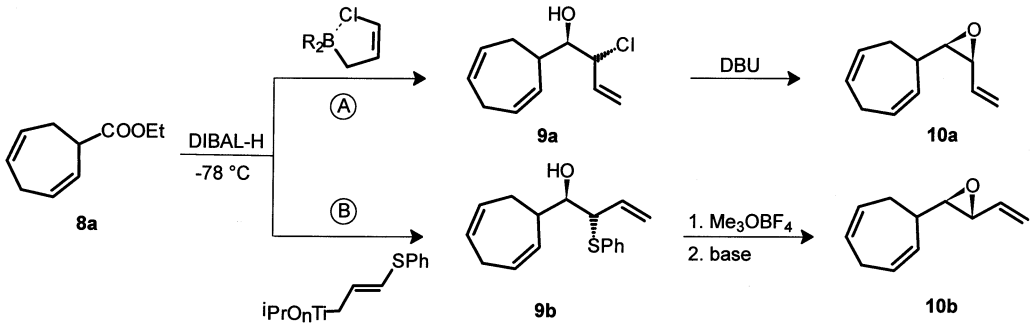
In our synthetic approach to the gamete-releasing and -attracting algal pheromone *cis*-lamoxirene (**10a**)[14], we have recently shown that an aldehyde, generated in situ from the carboxylic ester **8a** by reduction with DIBAL-H at low temperatures (−78°C)[15], is efficiently alkylated with (*Z*)-γ-chloroallyl-BBN[16] to form the *syn*-halohydrin **9a**, in preparatively useful yield and with high diastereoselectivity (Scheme 2, path A). Subsequent treatment of **9a** with a sterically hindered base, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[17], afforded the rather labile pheromone with high yield and without competing side reactions.

aldehydes generated in situ not only provides a convenient approach to compounds that are otherwise difficult to prepare, but also complement each other in their diastereoselectivity.

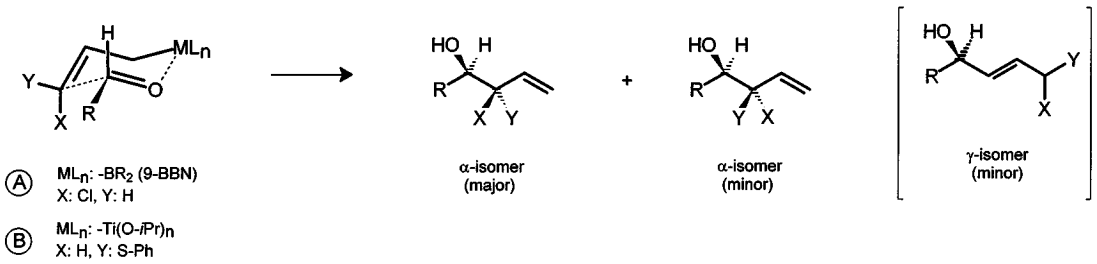
To determine the ease and limitations of this approach, a number of aliphatic and aromatic esters with (protected) functional groups were reduced in situ, and the resulting aldehydes were immediately alkylated by addition of the preformed allylation reagent (Table 1), without preceding isolation of intermediates.

The regio- and the diastereoselectivity of reductive allylations with (*Z*)-γ-chloroallyl-BBN or the [(phenylthio)allyl]titanium reagent were generally in accord with the original reports on isolated aldehydes[16][18]. In agreement with Scheme 3, allylation with the (*Z*)-γ-chloroallyl-BBN resulted almost exclusively in *syn*-chlorohydrins, while allylations with [(phenylthio)allyl]titanium predominantly led to *anti* products (*anti*/*syn* = > 90:< 10). Only reductive thioallylations of the aromatic esters **8b** and **8c** exhibited a lower degree of diastereoselection (*anti*/*syn* ≈ 85:15). With chiral esters **8d** and **8e**, a degree of simple diastereoselectivity was observed, resulting from the asymmetry of the starting material (63% *d.e.* for **9e**, 11% *d.e.* for **9f**). According to the model of Felkin−Anh[19] for allylation of α- and

Scheme 2



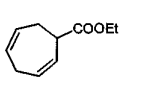
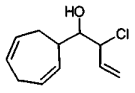
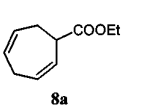
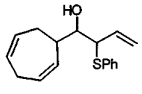
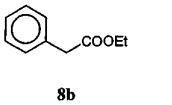
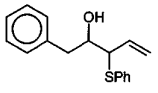
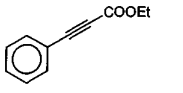
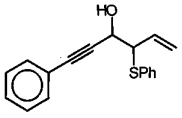
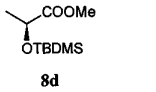
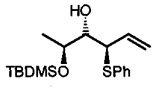
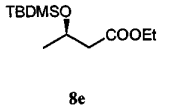
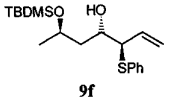
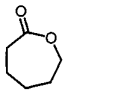
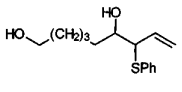
Scheme 3



Owing to the different configuration of the two allylation reagents, the phenylthio-substituent occupies the favoured equatorial position [Scheme 3, (B)], while the chlorine atom of the organoboron compound adopts an axial position in the ensuing complex [Scheme 3, (A)], accounting for the formation of the *syn*-α-chlorohydrin as the major product. In consequence, the reductive chloro- and thioallylation of β-substituted chiral aldehydes, stereoisomers **9e** and **9f** were predicted to be the major products. In all cases, however, the regioselectivity of the allylation reactions was excellent and occurred almost exclusively at the α-carbon atom (α/γ = > 97:< 3), independent of the allylation reagent used.

It should be mentioned that the presence of the aluminum alkoxides, resulting from the reduction of the esters or

Table 1. Reductive chloro- and thioallylations of esters and lactones

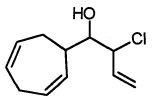
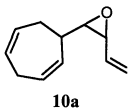
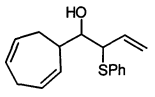
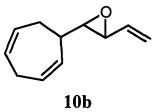
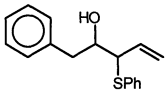
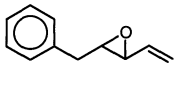
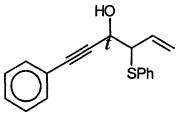
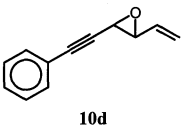
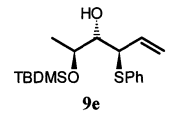
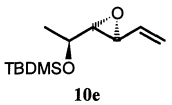
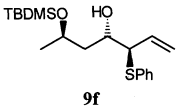
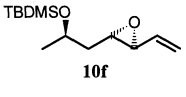
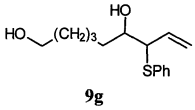
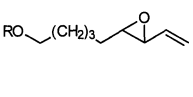
Substrate	Method[a]	Product	*anti/syn*[b]	α/γ	Yield[c]
 **8a**	A	 **9a**	3/97	>99/1	57 %
 **8a**	B	 **9b**	95/5	98/2	69 %
 **8b**	B	 **9c**	86/14	99/1	85 %
 **8c**	B	 **9d**	83/17	97/3	80 %
 **8d**	B	 **9e**	90/10 63% *d.e.*	98/2	62 %
 **8e**	B	 **9f**	89/11 11% *d.e.*	98/2	73%
 **8f**	B	 **9g**	94/6	97/3	77 %

[a] All reactions were performed on a 5.0-mmol scale according to the general procedure given in the Experimental Section; (for **9a** see ref.[14]). Method A: 1.0 equiv. of DIBAL−H, −78°C; 1.5 equiv. of (*Z*)-γ-chloroallyl-BBN (in situ), −78°C to room temp.; method B: 1.0 equiv. of DIBAL−H, −78°C; 1.5 equiv. of (*E*)-γ-[(phenylthio)allyl]titanium (in situ), −78°C to room temp. − [b] The diastereomeric ratio of products was determined by NMR analysis of the crude reaction mixture. − [c] Isolated yield.

lactones, did not interfere with the allylation reactions (e.g. by transmetallation). In no case was the high *syn*/*anti* selectivity of the organoboron- or the organotitanium reagent altered. The method is of particular value for the transformation of lactones, since no protection/deprotection of functionalities is required.

For the conversion of β-hydroxy thioethers into the vinyloxiranes the desulfurization procedure, by Meerwein methylation and subsequent base-assisted cyclization of the ensuing sulfonium salts, is well known and established[18][20]. Usually, this transformation is achieved by consecutive treatment of the thioethers with $(CH_3)_3OBF_4$ in CH_2Cl_2, followed by stirring with an aqueous sodium hydroxide solution. However, for most of the rather unstable and base-sensitive vinyloxiranes in Table 2, the relatively harsh conditions (using aqueous NaOH, pH = 12) had to be avoided. Superior results were obtained with the non-nucleophilic nitrogen base 1,8-diazabicylo[5.4.0]undec-7-ene (DBU). In particular, yields of the very sensitive vinyloxiranes **10b** and **10d** were substantially increased by using this mild anhydrous variant.

Table 2. Cyclizations of β-hydroxy sulfides and chlorohydrins

Substrate	Method[a]	Product	*trans/cis*	Yield[b]
 **9b**	*i)*	 **10a**	3/97	81 %
 **9a**	*iii)*	 **10b**	95/5	89 %
 **9c**	*ii)*	 **10c**	86/14	84 %
 **9d**	*iii)*	 **10d**	83/17	76 %
 **9e**	*iii)*	 **10e**	90/10 63% *d.e.*	69 %
 **9f**	*iii)*	 **10f**	89/11 11% *d.e.*	72%
 **9g**	*ii)*	 **10g** R=H, CH_3	94/6	80 %[c]

[a] All reactions were performed on a 1−2-mmol scale, as described in the Experimental Section; (for **10a** see ref.[14]). Method *i):* 3 equiv. of DBU/DCM, 0°C. Method *ii):* 1. 1.2 equiv. of Me_3OBF_4/DCM, 0°C, 2. 0.25 M $NaOH_{aq.}$ (see ref.[18b]). Method *iii):* 1. 1.1 equiv. of Me_3OBF_4/DCM, 2. 3 eq. of DBU, 0°C. − [b] Isolated yield. − [c] Formation of up to 40% of the *O*-methylated product has been observed when excess Me_3OBF_4 was used.

In conclusion, we have shown that *anti*-β-hydroxy thioethers and *syn*-α-chlorohydrins are most conveniently prepared by simple and sequential treatment of esters and lactones with DIBAL-H, followed by in situ allylation of the ensuing organoaluminum intermediates, with either [(phenylthio)allyl]titanium or (*Z*)-γ-chloroallyl-BBN. The predominantly formed stereoisomers can be purified by chromatography and give access to stereohomogeneous *trans*- and *cis*-vinyloxiranes by intramolecular S_N2 displacements. Since the success of the reductive allylation is not dependent on the position of the oxygen substituent (cf. Table 1, **8d**−**8f**), this new approach provides a general and reliable access to α-, β- and ω-functionalized vinyloxiranes. Moreover, the method can be extended to the synthesis of trisubstituted vinyloxiranes by employing the correspondingly substituted allylation reagents. In fact, analogous trans-

formations of amino acid esters were successful and have been developed into direct, high-yielding routes to sphingoid bases[21] and amino sugars.

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Experimental Section

Reactions were performed under argon; solvents were dried according to standard methods; allyl phenyl sulfide was prepared as described in ref.[18b] and distilled prior to use. Carbonyl compounds were distilled prior to use. Ethyl phenyl acetate, ethyl phenyl propiolate and ε-caprolactone were purchased from Aldrich Co. Ethyl cyclohepta-2,5-dienecarboxylate[14][22], silylated ethyl β-hydroxybutyrate and methyl lactate were synthesized according to literature procedures[23]. − IR: Perkin-Elmer Series 1600 FTIR Spectrophotometer. − ^{1}H and ^{13}C NMR: Bruker AC 400 spectrometer; $CDCl_3$ as solvent. Chemical shifts are given in ppm (δ values) downfield relative to TMS. − GC MS (70 eV): Finnigan ITD 800 coupled with a Carlo Erba GC 6000 gas chromatograph, Model Vega, equipped with a WCOT fuse silica column, 15 m × 0.32 mm, CP-SIL 5, Chrompack, Middelburg, The Netherlands. − HR MS: Kratos MS 50. − Chromatography: Silica gel, Si 60 (70−230 mesh, E. Merck, Darmstadt, Germany) and Florisil® (100−200 mesh, Aldrich Co.).

Reductive Thioallylation of Esters and Lactones. − General Procedure; **9c**: *Reduction of the Ester:* A solution of freshly distilled ethyl phenyl acetate (**8b**) (0.82 g, 5.0 mmol) in 15 ml of toluene/pentane (2:1, v/v) was cooled to −78°C. DIBAL-H (5.0 ml, 1.0 M in hexanes, 5.0 mmol) was added slowly through a precooled cannula with a syringe pump at a rate of 0.2 ml/min to the well-stirred solution. Stirring was continued (30 min) until GLC indicated > 95% reduction of the starting material. − *Preparation of the [3-(Phenylthio)allyl]titanium Reagent:* A stirred and cooled (−78°C) solution of allyl phenyl sulfide (1.13 g, 7.5 mmol) in THF (25.0 ml) was gradually treated with *n*BuLi (4.7 ml, 1.6 M in hexane, 7.5 mmol) with formation of a yellow solution. The mixture was stirred at −78°C for 10 min, warmed to 0°C and stirred at 0°C for 30 min. After re-cooling to −78°C, titanium tetraisopropoxide (2.13 g, 7.5 mmol) was added dropwise. − *In Situ Alkylation:* The organotitanium reagent was stirred for a further 15 min at −78°C and then, the above solution of the reduced ester was carefully added by cannulation. The resulting mixture was stirred at −78°C for 30 min and then slowly warmed to 0°C. Stirring was continued for 2 h at 0°C and then the mixture was poured into dilute hydrochloric acid (20 ml). The organic layer was separated and the aqueous layer extracted with ether (3 × 50 ml). After drying (Na_2SO_4) of the organic layer, the solvent was evaporated in vacuo at room temp., and the resulting crude oil was purified by flash chromatography (FC) on silica gel with pentane/ether (2:1) as eluant. Yield: 1.21 g (85%); colourless oil. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.38 (br. s, 1 H, O*H*), 2.88 (dd, *J* = 6, 2.5 Hz, 2 H, PhCH_2), 3.71 (dd, *J* = 10, 4 Hz, 1 H, SC*H*), 4.02 (m, 1 H, OC*H*), 5.12 (dd, *J* = 17, 1 Hz, 1 H, C=CH_2), 5.12 (dd, *J* = 10, 1 Hz, 1 H, C=CH_2), 5.96 (ddd, *J* = 17, 10, 10 Hz, 1 H, *H*C=CH_2), 7.24−7.41 (m, 10 H, Ph). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 40.8 (Ph*C*H_2), 57.9 (C-3), 73.1 (C-2), 119.5 (HC=*C*H_2), 126.7, 127.6, 129.1, 129.6, 132.8, 133.5, 133.8, 138.1 (H*C*=CH_2, Ph). − IR (KBr, film): ν = 3441 (br., OH), 3060, 3027, 2920, 1949, 1712, 1602, 1583, 1479, 1453, 1438, 1083, 1026, 995, 921, 845, 742, 700 cm^{-1}. − MS (70 eV): *m/z* (%) = 270 [$M^{+\cdot}$] (3), 253 (5), 179 (2), 150 (100), 149 (38), 135 (38), 122 (9), 121 (11), 120 (8), 110 (9), 109 (16), 105 (5), 91 (61), 77 (6), 65 (29), 51 (11), 41 (8), 39 (24). − HR MS: *m/z* calcd. for $C_{17}H_{18}OS$ ($M^{+\cdot}$) 270.1078, found 270.1072.

9b: This compound was prepared from ethyl cyclohepta-2,5-dienecarboxylate (**8a**) (0.83 g, 5.0 mmol) in an analogous manner to **9c**. The crude product was purified by FC on silica gel with a pentane/ether (10:1 → 1:1) gradient as eluent. Yield: 0.95 g (69%); colourless oil. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.13−2.65 (m, 3 H, CH_2, C*H*), 2.68 (m, 2 H, CH_2), 3.61 (d″t″, *J* = 5, 2.4 Hz, 1 H, SC*H*), 3.74 (dd, *J* = 9, 4.6 Hz, 1 H, OC*H*), 5.03 (ddd, *J* = 17, 1.4, 0.5 Hz, 1 H, HC=CH_2), 5.11 (dd, *J* = 10.2, 1.4 Hz, 1 H, HC=CH_2), 5.45−5.88 (m, 5 H, *H*C=C*H*, *H*C=CH_2), 7.06−7.39 (m, 5 H, Ph). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 29.4 (C-4′), 30.4 (C-7′), 41.0 (C-1′), 57.3 (SCH), 75.5 (OCH), 119.7 (HC=*C*H_2), 127.3, 129.3, 129.6, 130.3, 132.2, 133.3, 133.8, 134.2, 134.4 (H*C*=CH_2, H*C*=*C*H, Ph). − IR (KBr, film): ν = 3448 (br., OH), 3075, 3015, 2914, 1635, 1583, 1480, 1438, 1230, 1088, 1025, 989, 920, 739, 691 cm^{-1}. − MS (70 eV): *m/z* (%) = 272 [$M^{+\cdot}$] (12), 179 (8), 163 (6), 161 (14), 150 (67), 149 (62), 147 (20), 145 (88), 135 (63), 117 (29), 116 (29), 115 (32), 110 (30), 109 (58), 195 (31), 91 (100), 79 (43), 77 (62), 69 (33), 67 (29), 65 (59), 51 (30), 41 (49), 39 (74). − HR MS: *m/z* calcd. for $C_{17}H_{20}OS$ ($M^{+\cdot}$) 272.1235, found 272.1238.

9d: This compound was prepared from ethyl phenylpropiolate (**8c**) (0.87 g, 5.0 mmol) in an analogous manner to **9c**. The crude product was purified by FC on silica gel with a pentane/ether (5:1 → 1:1) gradient as eluent. Yield: 1.12 g (80%); yellow oil. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.78 (d, *J* = 6 Hz, 1 H, O*H*), 3.84 (dd, *J* = 9 Hz, 1 H, SC*H*), 4.75 (m, 1 H, OC*H*), 5.19 (m, 2 H, HC=CH_2), 5.95 (ddd, *J* = 15, 11, 10 Hz, 1 H, *H*C=CH_2), 7.21−7.44 (m, 10 H, Ph). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 58.6 (SCH), 64.5 (OCH), 86.8, 87.0 (Ph*C*≡*C*), 118.9 (HC=*C*H_2), 122.2, 127.8, 127.9, 128.3, 128.7, 129.0, 129.1, 131.9, 132.9, 133.2, 133.3, 133.8, 134.2 (H*C*=CH_2, Ph). − IR (KBr, film): ν = 3418 (br., OH), 3058, 2925, 2230, 2196, 1953, 1882, 1634, 1583, 1489, 1439, 1383, 1316, 1176, 1025, 988, 921, 795, 690 cm^{-1}. − MS (70 eV): *m/z* (%) = 281 [$MH^{+\cdot}$] (4), 263 (10), 210 (2), 171 (48), 150 (100), 149 (71), 147 (23), 135 (12), 131 (24), 116 (25), 115 (38), 109 (19), 103 (26), 77 (18), 65 (12), 51 (13), 50 (8), 39 (17). − HR MS: *m/z* calcd. for $C_{18}H_{15}OS$ ($M^{+\cdot}$ − H) 279.0843, found 279.0833.

9e: This compound was prepared from **8d** (1.16 g, 5.0 mmol) in an analogous manner to **9c**. The crude product was purified by FC on silica gel with pentane/ether (3:1) as eluent. Yield: 1.05 g (62%); colourless oil. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.00 (s, 3 H, H_3CSi), 0.01 (s, 3 H, H_3CSi), 0.83 [s, 9 H, (CH_3)$_3$CSi], 1.13 (d, *J* = 6 Hz, 3 H, CH_3), 2.45 (br. s, 1 H, OH), 3.49−3.56 (m, 1 H, SC*H*), 3.88 (dd, *J* = 9, 6 Hz, 1 H, OC*H*), 3.91 (″t″, *J* = 6 Hz, 1 H, OC*H*), 5.02 (ddd, *J* = 17, 2, 1 Hz, 1 H, HC=CH_2), 5.07 (dd, *J* = 10, 2 Hz, 1 H, HC=CH_2), 5.82 (ddd, *J* = 17, 10, 9 Hz, 1 H, *H*C=CH_2), 7.11−7.37 (m, 5 H, Ph). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = −4.8 (H_3C*S*i), −3.9 (H_3C*S*i), 16.9 (CH_3), 18.0 [(H_3C)$_3$*C*], 25.8 [3 C, (H_3C)$_3$C], 54.1 (SCH), 69.3 (OCH), 75.8 (HOCH), 118.5 (HC=*C*H_2), 126.3, 127.3, 128.6, 128.9, 132.5, 133.4, 134.0 (H*C*=CH_2, Ph). − IR (KBr, film): ν = 3462 (br., OH), 3076, 2929, 2856, 1584, 1472, 1439, 1388, 1256, 1086, 1004, 967, 915, 835, 776, 738, 690 cm^{-1}. − MS (70 eV): *m/z* (%) = 321 [$M^{+\cdot}$ − OH] (4), 281 (3), 263 (3), 233 (6), 207 (18), 189 (65), 173 (22), 171 (29), 159 (60), 149 (100), 137 (25), 127 (54), 119 (41), 109 (19), 103 (16), 75 (34), 73 (33), 65 (11), 45 (12), 41 (23), 39 (21). − HR MS: *m/z* calcd. for $C_{18}H_{30}O_2SSi$ ($M^{+\cdot}$) 338.1736, found 338.1729.

9f: This compound was prepared from **8e** (1.11 g, 5.0 mmol) in an analogous manner to **9c**. The crude product was purified by FC on silica gel with pentane/ether (3:1) as eluent. Yield: 1.28 g (73%); colourless, viscous oil. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.00 (s, 3 H, H_3CSi), 0.01 (s, 3 H, H_3CSi), 0.80 [s, 9 H, $(H_3C)_3C$], 1.09 (d, J = 6 Hz, 3 H, CH_3), 1.53−1.68 (m, 2 H, CH_2), 3.10 (br. s, 1 H, OH), 3.53 (dd, J = 9, 4 Hz, 1 H, SCH), 3.89−4.05 (m, 2 H, OCH), 4.87 (ddd, J = 17, 1, 0.7 Hz, 1 H, HC=CH_2), 4.98 (dd, J = 10, 1 Hz, 1 H, HC=CH_2), 5.79 (ddd, J = 17, 10, 9 Hz, 1 H, HC=CH_2), 7.11−7.25 (m, 5 H, Ph). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = −4.8 (H_3CSi), −4.0 (H_3CSi), 17.9 [$(H_3C)_3C$], 24.4 (CH_3), 25.9 [3 C, $(H_3C)_3$C], 43.4 (CH_2), 59.2 (SCH), 69.4, 72.1 (OCH), 117.9 (HC=CH_2), 127.3, 128.8, 128.9, 132.9, 133.0, 134.3, 134.6 (C=CH_2, Ph). − IR (KBr, film): ν = 3382 (br., OH), 2930, 2885, 1727, 1584, 1472, 1440, 1362, 1255, 1089, 835, 775, 738, 690 cm^{-1}. − MS (70 eV): *m/z* (%) = 335 [$M^{+\cdot}$ − OH] (10), 293 (21), 249 (38), 219 (10), 203 (78), 159 (100), 141 (12), 135 (14), 119 (57), 103 (34), 75 (92), 73 (44), 57 (14), 41 (36), 39 (27). − HR MS: *m/z* calcd. for $C_{19}H_{30}OSSi$ ($M^{+\cdot}$ − H_2O) 334.1787, found 334.1799.

9g: This compound was prepared from ε-caprolactone (**8f**) (0.57 g, 5.0 mmol) in an analogous manner to **9c**. The crude product was purified by FC on silica gel with pentane/ether (1:2, v/v) as eluent. Yield: 1.02 g (77%); colourless, very viscous oil. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.22−1.36 (m, 8 H, CH_2), 1.78 (br. s, 1 H, OH), 2.46 (br. s, 1 H, OH), 3.54 (t, J = 6 Hz, 2 H, HOCH_2), 3.59−3.67 (m, 2 H, SCH, OCH), 5.03 (dd, J = 17, 1 Hz, 1 H, HC=CH_2), 5.08 (dd, J = 10, 2 Hz, 1 H, HC=CH_2), 5.77 (ddd, J = 17, 10, 9 Hz, 1 H, HC=CH_2), 7.05−7.39 (m, 5 H, Ph). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.6, 25.7, 32.6, 34.1 (CH_2), 59.3 (SCH), 62.7 (OCH), 71.9 (OCH), 119.0 (HC=CH_2), 127.5, 127.7, 128.9, 129.0, 132.8, 133.4, 133.9 (HC=CH_2, Ph). − IR (KBr, film): ν = 3376 (br., OH), 3075, 2935, 2859, 1634, 1583, 1479, 1438, 1051, 919, 741, 692 cm^{-1}. − MS (70 eV): *m/z* (%) = 249 [$M^{+\cdot}$ − OH] (18), 150 (100), 149 (36), 135 (44), 117 (13), 116 (13), 110 (10), 109 (18), 81 (11), 69 (12), 55 (14), 43 (11), 41 (22), 39 (22). − HR MS: *m/z* calcd. for $C_{15}H_{20}OS$ ($M^{+\cdot}$ − H_2O) 248.1235, found 248.1237.

Cyclization of β-Hydroxy Sulfides. − General Procedure; Method ii), Biphasic, Analogous to ref.[18b]: To a cooled (0°C) and well-stirred suspension of trimethyloxonium tetrafluoroborate (1.2 mmol) in dry dichloromethane (5 ml), a solution of β-hydroxy sulfide (1.0 mmol) in dichloromethane (5 ml) was added dropwise. The resulting mixture was stirred at 0°C for 2 h, warmed to 20°C and stirred until TLC analysis indicated quantitative formation of the sulfonium salt by the expense of the starting material (ca. 1−2 h). After re-cooling to 0°C, the solution was diluted with dichloromethane (5 ml) and treated with 0.25 M aqueous NaOH (10 ml). Stirring was continued for 2−4 h (TLC control) and then the pH was adjusted to 8.0 by titration with 10% aq. NH_4SO_4. The organic layer was separated and the aqueous phase extracted with ether (3 × 30 ml). After washing with brine (15 ml) and drying with Na_2SO_4, the organic phase was concentrated under reduced pressure. The residue is submitted to FC on Florisil® (100−200 mesh) using a pentane/ether gradient. − *Method iii), Anhydrous:* Methylation was conducted as described under *ii)*, but in lieu of NaOH a solution of DBU (3.0 mmol) in DCM (5 ml) was added to the sulfonium salt under argon. After stirring at 0°C for 4 h, water (15 ml) was added and the mixture was quickly partitioned between water/ether (3 × 30 ml). For work-up and purification, vide supra.

10b: This compound was prepared from **9b** (0.41 g, 1.5 mmol) according to method *iii)*. The crude product was purified by FC on Florisil® (100−200 mesh) with a pentane/ether (10:1 → 4:1) gradient as eluent. Yield: 216 mg (89%); intensively fruity smelling, colourless liquid. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.17 (m, 3 H, HC-1′, H_2C-7′), 2.70−2.91 (m, 2 H, H_2C-4′), 2.78 (dd, J = 7, 2 Hz, 1 H, HC-2), 3.13 (dd, J = 7, 2 Hz, 1 H, HC-3), 5.19 (ddd, J = 10, 2, 1 Hz, 1 H, HC=CH_2), 5.39 (dd, J = 17, 2 Hz, 1 H, HC=CH_2), 5.50−5.78 (m, 5 H, HC=CH_2, HC=CH)[14]. − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.5 (C-4′), 29.4 (C-7′), 39.8 (C-1′), 57.6 (C-3) 63.6 (C-2), 119.1 (HC=CH_2), 128.5 (C=C), 129.1 (C=C), 129.3 (C=C), 130.8 (C=C), 135.6 (C=C). − IR (KBr, film): ν = 3015, 2957, 2934, 2848, 1643, 1453, 1406, 1260, 986, 925, 887, 800, 679 cm^{-1}. − MS (70 eV): *m/z* (%) = 147 [$M^{+\cdot}$−15] (2), 129 (6), 117 (5), 105 (16), 93 (12), 92 (29), 91 (100), 79 (33), 78 (44), 77 (51), 65 (20), 51 (16), 43 (15), 39 (68). − HR MS: *m/z* calcd. for $C_{11}H_{14}O$ ($M^{+\cdot}$) 162.1045, found 162.1051.

10c: This compound was prepared from **9c** (203 mg, 0.75 mmol) according to method *ii)*. The crude product was purified by FC on Florisil® (100−200 mesh) with pentane/ether (4:1) as eluent. Yield: 101 mg (84%); colourless, odoriferous liquid. For spectroscopic data see ref.[24].

10d: This compound was prepared from **9d** (375 mg, 1.5 mmol) according to method *iii)*. The crude product was purified by FC on Florisil® (100−200 mesh) with pentane/ether (3:1) as eluent. Yield: 194 mg (76%); colourless, odoriferous liquid. For spectroscopic data see ref.[25].

10e: This compound was prepared from **9e** (0.68 g, 2.0 mmol) according to method *iii)*. The crude product was purified by FC on Florisil® (100−200 mesh) with a pentane/ether (10:1 → 2:1) gradient as eluent. Yield: 315 mg (69%); colourless, odoriferous liquid. For spectroscopic data see ref.[10].

10f: This compound was prepared from **9f** (0.35 g, 1.0 mmol) according to method *iii)*. The crude product was purified by FC on Florisil® (100−200 mesh) with a pentane/ether (10:1 → 2:1) gradient as eluent. Yield: 174 mg (72%); colourless, odoriferous liquid. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.04 (s, 3 H, H_3CSi), 0.06 (s, 3 H, H_3CSi), 0.84 [s, 9 H, $(H_3C)_3C$], 1.25 (d, 3 H, CH_3), 1.58 (m, 1 H, CH_2), 1.79 (m, 1 H, CH_2), 2.94 (t, J = 8 Hz, 1 H), 3.08 (d, J = 9 Hz, 1 H), 4.01 (m, 1 H, CHOSi), 5.25 (dd, J = 10, 1 Hz, HC=CH_2), 5.45 (dd, J = 17, 1 Hz, HC=CH_2), 5.54 (ddd, J = 17 Hz, 10 Hz, 7 Hz, HC=CH_2). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = −4.4 (SiCH_3), −4.1(SiCH_3), 14.5 (CH_3), 26.2 [C(CH_3)$_3$], 42.3 (CH_2), 58.1 (C-4), 58.9 (C-5), 66.9 (CHOSi), 119.4 (C=CH_2), 136.2 (C=CH_2). − IR (KBr, film): ν = 2957, 2928, 2856, 1735, 1701, 1696, 1643, 1584, 1462, 1440, 1407, 1378, 1362, 1257, 1129, 1085, 1036, 1006, 915, 870, 836, 808, 775, 738 cm^{-1}. − MS (70 eV): *m/z* (%) = 243 (2), 227 (7), 185 (100), 169 (3), 159 (36), 143 (15), 142 (18), 141 (92), 127 (5), 115 (5), 103 (20), 101 (13), 99 (31), 93 (11), 75 (60), 73 (37), 59 (15), 57 (11), 41 (45), 43 (43).

10g: This compound was prepared from **9g** (213 mg, 0.8 mmol) according to method *ii)*. The crude product was purified by FC on Florisil® (100−200 mesh) with ether as eluent. Yield: 101 mg (80%); colourless, odoriferous liquid. − R = H: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.25−1.56 (m, 8 H, CH_2), 2.73 (m, 1 H, 6-H), 2.98 (d, J = 7 Hz, 1 H, 7-H), 3.51 (t, 2 H, J = 6 Hz, H_2COH), 5.15 (d, 1 H, J = 10 Hz, H_2C=C), 5.38 (d, 1 H, J = 17 Hz, H_2C=C), 5.49 (ddd, 1 H, J = 17, 10, 7 Hz, HC=C). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.1, 26.3, 32.5, 33.2 (CH_2), 59.3 (C-6), 61.0 (C-7), 63.4 (HOCH_2), 119.5 (HC=CH_2), 136.4 (HC=CH_2). − IR (KBr, film): ν = 3407 br., 3087, 2935, 2860, 1643, 1462, 1406, 1261, 1055, 987, 923, 876, 795, 733 cm^{-1}. − MS (70 eV): *m/z* (%) = 157 [$MH^{+\cdot}$] (4), 139 (31), 121 (13), 115 (6), 109 (7), 97 (26), 95 (55), 81 (77), 79 (20), 71 (26), 69 (100), 67 (43), 57 (21), 55 (33), 43 (28), 41 (41). − R = CH_3: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.19−1.55 (m, 8 H, CH_2), 2.75 (m, 1 H, 6-H), 3.00 (d, J = 7 Hz, 1 H, 7-H), 3.26 (s, 3

H, CH_3), 3.31 (t, 2 H, J = 6 Hz, H_2COH), 5.18 (d, 1 H, J = 10 Hz, H_2C=C), 5.39 (d, 1 H, J = 17 Hz, H_2C=C), 5.50 (ddd, 1 H, J = 17, 10, 7 Hz, HC=C). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.1, 26.3, 29.9, 32.3, 33.2 (CH_2), 58.9 (C-6), 59.1 (C-7), 60.7 (H_3COCH_2), 73.1 (OCH_3), 119.2 (HC=CH_2), 136.3 (HC=CH_2). – IR (KBr, film): ν = 3087, 2934, 2860, 2827, 1642, 1462, 1406, 1388, 1203, 1119, 986, 922, 881, 798, 734 cm^{-1}. – MS (70 eV): *m/z* (%) = 171 [$MH^{+\cdot}$] (6), 140 (5), 139 (66), 121 (28), 113 (12), 111 (8), 109 (8), 97 (14), 95 (46), 81 (100), 79 (10), 71 (45), 69 (34), 67 (19), 55 (10), 45 (46), 43 (13), 41 (16), 39 (65).

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