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# Towards the Asymmetric Synthesis of Ascochlorin

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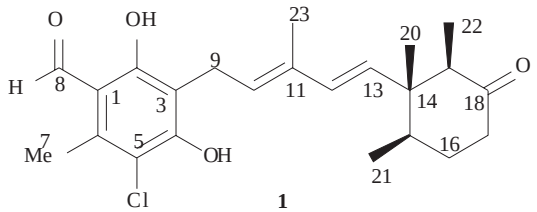
A synthetic approach is described to the asymmetric synthesis of ascochlorin (**1**), an antiviral antibiotic, based on the construction of a sesquiterpene unit via asymmetric Diels-Alder reaction of tigloyl sultam **4** & butadiene, and the introduction of the aromatic side chain (C9-C12 unit) by employing cuprate chemistry.

## Introduction

Ascochlorin (**1**) is an antiviral antibiotic obtained from the filter cake of the fermented broth of *Ascochyta viciae* Libert[1]. It has a strong inhibitory effect on viral growth in cultured cells[2]. The compound features three stereogenic centers, a sesquiterpene unit, a 1,3-diene system, and an aromatic unit having an aldehyde, a methyl, a chloride, and two hydroxy substituents. The absolute stereochemistry of this antibiotic was determined by X-ray analysis[3]. Due to high biological activity, the ascochlorin family has attracted the attention of synthetic chemists. So far only the total synthesis of (±) ascochlorin with a totally different strategy has been reported in the literature[4]. In this paper we describe our studies aimed at applying asymmetric Diels-Alder, cuprate, and Julie olefination reactions as the key strategies in the total synthesis of this biologically active natural compound (**1**).

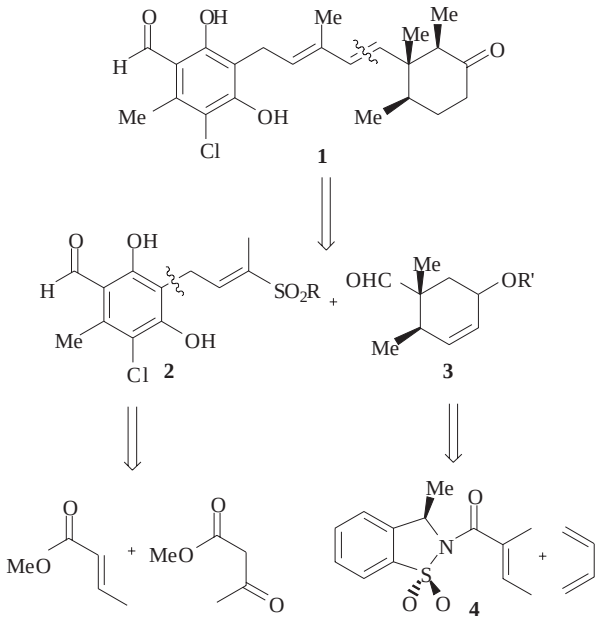



**1**

*Deceased $15^{th}$ March 1996.

## Results and Discussion

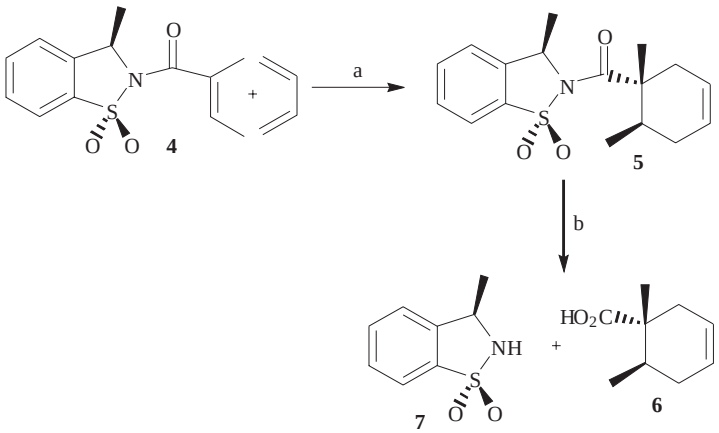
Our strategy for achieving the asymmetric synthesis of ascochlorin was to synthesize the sesquiterpene unit **3** by asymmetric Diels-Alder reaction of tigloyl sultam **4** and butadiene. This reaction was developed by Oppolzer's group[5] and used in the synthesis of substituted cyclohexane derivatives which were obtained in high diastereoselectivities. Construction of aromatic unit **2** is achieved easily, as reported in the literature[6]. Our approach to the unification of aromatic and sesquiterpene units by forming a $C_{12}$-$C_{13}$ double bond was based on the Julia olefination reaction (Scheme 1).



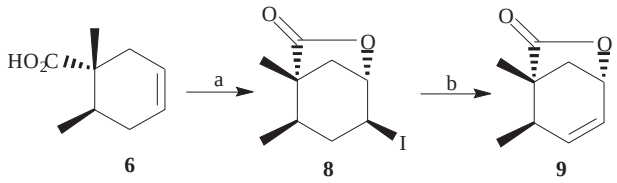

**Scheme 1.** Synthetic Strategy

For the synthesis of a sesquiterpene unit, we started with tigloylsultam **4** and *trans*-piperylene, which gave the desired Diels-Alder adduct in high yield but with the wrong stereochemistry at C-19. Therefore we decided to introduce the C-19 methyl group at a later stage and perform the same reaction with 1,3-butadiene instead of *trans*-piperylene. This reaction gave the desired Diels-Alder adduct **5** in 85% yield and in 96% de (determined by HPLC). The chiral auxiliary was easily removed by treatment of cycloadduct **5** with LiOH in the presence of $H_2O_2$, which gave cyclohexenecarboxylic acid **6** in 94% yield and the recovered sultam auxiliary **7** in 80% yield (Scheme 2).

In order to introduce oxygen on C-18 (ascochlorin numbering), standard iodolactonization methodology was applied to the crude carboxylic acid **6**. The reaction yielded the desired iodolactone **8** in 98% yield. Treatment of this lactone with DBU gave compound **9** in 96% yield (Scheme 3).

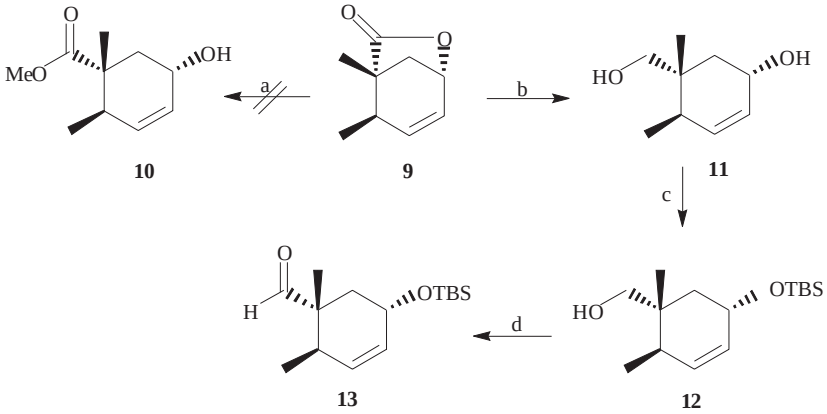



**Scheme 2.** (a) $MeAlCl_2$, toluene, 144 h, -30°C, 85% yield; (b) $LiOH{\cdot}H_2O$, $H_2O_2$ (30% ), $THF/H_2O$, **6**: 94% yield, **7**: 80% yield.



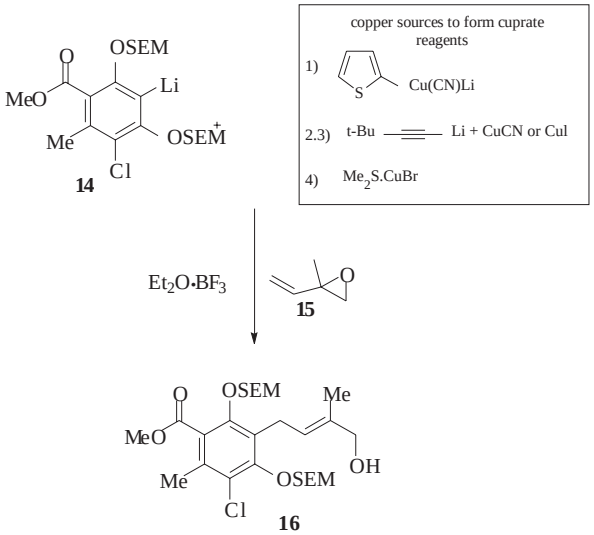

**Scheme 3.** (a) $NaHCO_3$, KI, $I_2$, $THF/H_2O$, rt, 98% yield; (b) DBU, THF, reflux, 96% yield.

Cleavage of the lactone unit on compound **9** by treatment with TRITON-B then MeI, which was recently employed[7] to cleave a similar lactone, did not give the expected hydroxy ester **10** (Scheme 4), and most of the starting material was recovered with minor decomposition. Therefore, we decided to cleave the lactone unit with $LiAlH_4$, which worked cleanly and gave the desired diol **11** in 98% yield. Oxidation of the allylic alcohol on compound **11** with $MnO_2$ afforded the desired $\alpha,\beta$-unsaturated ketone in low yield, so we decided to protect the primary alcohol selectively and carry out the oxidation reaction on the resulting compound. For this purpose, alcohol **11** was treated with TBDMSCl, which surprisingly attached to the secondary alcohol and gave mono protected alcohol **12** in 48% yield. The remaining product of the reaction was the diprotected form of alcohol **11**. Similar results were obtained when TBDPSCl was used as the protecting group. Apparently, the C-14 methyl group hinders the primary alcohol. Oxidation of this alcohol by Swern oxidation reaction conditions or by TPAP[8] cleanly gave aldehyde **13** (Scheme 4), which could be used without purification in the Julie olefination reaction (Scheme 6).



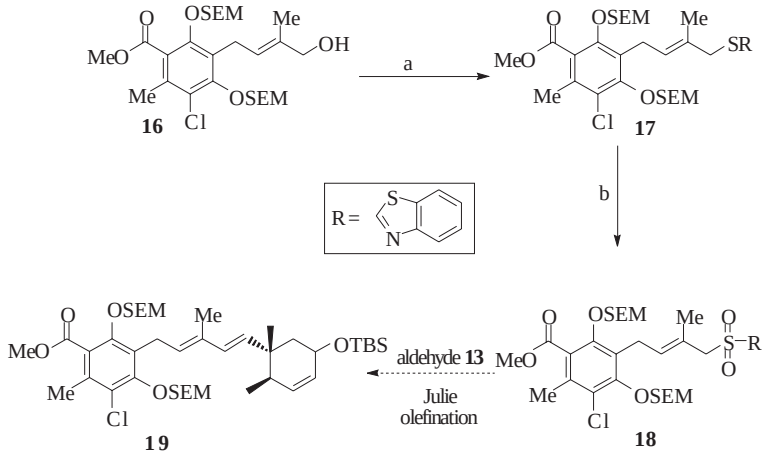

**Scheme 4.** (a) TRITON-B, then MeI; (b) $LiAlH_4$, $Et_2O$, rt, 98% yield; (c) TBDMSCl, imidazole, $CH_2Cl_2$, 0°C 48% yield; (d) $(COCl)_2$, DMSO, $Et_3N$, $CH_2Cl_2$, -78°C or TPAP, NMO, $CH_2Cl_2$, rt, 90% yield.

For the synthesis of the aromatic unit of ascochlorin, compound **14** was synthesized as in the literature[7] and the alkene side chain was introduced to this compound by cuprate chemistry[9]. Although the yield (50%) of 1,4-addition reaction of either lower or higher order cuprates to epoxide **15** was not very satisfactory, we were able to carry out the reaction on a gram scale using easily available starting materials. In order to increase the yield of this reaction, we tried different ligands and copper sources to form the cuprate reagent: 2-thienyl(cyano)copper lithium, *ter*-butylethenyl lithium with CuI/CuCN, or $Me_2S{\cdot}CuBr$. Of these reagents, CuCN with *tert*-butylethenyl lithium gave the desired product in a resonable yield (50%) as a mixture of **E** and **Z** isomers in a ratio of 20/1 (Scheme 5).




**Scheme 5.** Cuprate Reactions for the Introduction of Alkene Side Chain

In order to carry out the Julie olefination reaction[10], alcohol **16** was transferred to its thioether derivative **17** under standard reaction conditions in 87% yield. Oxidation of this thioether gave the corresponding sulfone **18** in 63% yield. Now, the project is at the stage of Julie olefination, which is expected to give compound **19**. With the synthesis of compound **19**, only a couple of steps will be left for the completion of asymmetric synthesis of ascochlorin.




**Scheme 6.** (a) 2-mercaptobenzothiazole, $Ph_3P$, DEAD, 86% yield; (b) $Mo_7O_{24}(NH_4)_{64}H_2O$, $H_2O_2$, 63% yield

# Experimental

*General.* All reactions were carried out under argon atmosphere. Solvents were dried by distillation with drying agents as follows: $Et_2O$, THF (Na/benzophenone), toluene (Na metal), $CH_2Cl_2$, triethylamine ($CaH_2$). Column flash chromatography (FC): $SiO_2$ (Merck 60 0.040-0.060 nm). TLC (Merck 60F254 0.025nm). HPLC: Waters *Waters 501*, $^1$H- and $^{13}$C-NMR spectra were recorded on a *Bruker AMX-400* spectrometer at operating frequencies of 400.1 and 100.6 MHz respectively in $CDCl_3$. New compounds were named by the Chem Draw Ultra program.

**(1,6-Dimethyl-cyclohex-3-enyl)-(3-methyl-1,1-dioxo-1,3-dihydro-1$\lambda^6$-benzo [d]isothiazol-2-yl)-methanone (5).** $MeAlCl_2$ in hexanes (26 mL, 25.70 mmol) was added slowly to a solution of the tigloylsultam **4** (1.70 g, 6.42 mmol) in toluene (35 mL) at -30°C. After 30 min, butadiene (5.6 mL, 64.2 mmol, condensed in a graduated cylinder at -78°C) was added via a cannula to the reaction mixture. After 96 h TLC showed the major cycloadduct with some starting material and a great amount of polymer formation. Therefore another 5 eq of butadiene was added to the reaction mixture. After another 48 h, the reaction mixture was quenched at -30°C by the addition of HCl (10% , 20 mL), warmed up to rt, diluted with ether (20 mL) and stirred at rt for 6 h to remove excess butadiene. The aqueous layer was extracted with ether, and the combined organic layer was dried over $Na_2SO_4$, filtered and concentrated to give a light yellow solid, which was subjected to FC ($SiO_2$, hexanes/Ether 8/2 to 6/4), which gave 1.8 g of pure cycloadduct **5** in 85% yield. *Rf* 0.48 (2/3 hexanes/$Et_2O$); $^1$H-NMR $\delta$ 0.97(d, J = 7.5Hz, 3H), 1.34(s, 3H), 1.61(d, J=7.5Hz, 3H), 1.80(m, 1H), 1.93(d, J=18.1Hz, 1H), 2.24(m, 1H), 2.81(m, 1H), 3.12(d, J=16.3Hz, 1H), 5.65(s, 2H), 5.71(q, J=13.0& 6.4Hz, 1H), 7.40(d, J=7.5Hz, 1H), 7.55(t, J=7.5Hz, 1H), 7.67(t, J=7.5Hz, 1H), 7.75(d, J=8.0Hz, 1H); $^{13}$C-NMR $\delta$ 16.53(q), 18.00(q), 21.24(q), 31.12(t), 31.33(d), 33.81(t), 48.97(s), 57.49(d), 121.45(d), 123.89(d), 124.56(d), 125.19(d), 129.32(d), 133.67(d), 134.69(s), 137.81(s), 177.43(s).

**1,6-Dimethyl-cyclohex-3-enecarboxylic acid (6).** To a stirring solution of Diels-Alder adduct **5** (785 mg, 2.46 mmol) in THF/ $H_2O$ (2/1, 15 mL) was added $H_2O_2$ (1.5 mL from a 30% soln. in water) at rt. The resulting reaction was stirred for 2 h at this temperature and TLC showed complete consumption of the starting material, so the reaction was worked up. First, a saturated solution of $Na_2S_2O_3$ (15 mL)

was added to destroy excess peroxide, and then the mixture was acidified to pH=1 by adding 10% HCl solution. The aqueous layer was extracted with ether (3x25 mL). The combined ether layer was dried over $MgSO_4$, filtered and concentrated to give the cleaved auxiliary **7** in 80% yield and the desired acid **6** in 94% yield, both as white solids after flash column chromatography ($SiO_2$, 2/1, $Et_2O$/hexanes). For acid **6**, *Rf* 0.30 (1/1 hexanes/$Et_2O$); $^1$H-NMR $\delta$ 0.91(d, J=6.4Hz, 3H), 1.09(s, 3H), 1.73(m, 1H), 1.94(d, J=17.8Hz, 1H), 2.15(m, 2H), 2.58(d, J= 17.8 Hz 1H), 5.63(s, 2H); $^{13}$C-NMR $\delta$ 15.47(q), 16.39(q), 30.69(t), 32.88(d), 35.50(t), 44.77(s), 124,13(d), 125.56(d), 184.29(s).

**4-Iodo-1,2-dimethyl-6-oxa-bicyclo[3.2.1]octan-7-one (8).** To a stirring solution of acid **6** (110 mg, 0.71 mmol) in THF/$H_2O$ (1/1, 4 mL) was added solid $NaHCO_3$ (299 mg, 3.60 mmol). After stirring the reaction mixture for 10 min, KI (141 mg, 0.85 mmol) and $I_2$ (541 mg, 2.13 mmol) were added. The resulting dark yellow colored reaction mixture was stirred overnight and worked up in the morning. First, 10% solution of $Na_2S_2O_3$ was added until the disappearance of iodine color, and then the aqueous layer was extracted with ether (3x8mL), and the combined organic layer was dried over $MgSO_4$, filtered and concentrated to give the desired crude lactone **8** (196 mg, 0.70 mmol) in 98% yield as white solids, which was recrystallized from ether/hexanes (1/1) as colorless needles. *Rf* 0.50 (1/1 hexanes/ $Et_2O$); $^1$H-NMR $\delta$ 1.19(d, J=7.5Hz, 3H), 1.35(s, 3H), 1.99-2.06(3H), 2.70(dt, J=17.2& 7.1Hz, 1H), 2.93(d, J=12.8Hz, 1H), 4.37(m, 1H), 4.79(m, 1H); $^{13}$C-NMR $\delta$ 15.36(q), 19.09(q), 34.13(t), 34.22(d), 35.09(t), 45.32(s), 72.28(d), 79.47(d), 180.69(s).

**1,2-Dimethyl-6-oxa-bicyclo[3.2.1]oct-3-en-7-one (9).** To a stirring solution of iodolactone **8** (570 mg, 2.03 mmol) in THF (10 mL) was added DBU (619 mg, 4.07 mmol). The resulting reaction mixture was refluxed under $N_2$ atmosphere for 2 h, at which time TLC showed no starting material. The reaction mixture was diluted with ether (5 mL) and hydrolized with 10% HCl (5 mL), and the two layers were separated. The aqueous layer was extracted with ether (3x15 mL). The combined organic layer was washed with saturated soln. of $NaHCO_3$ (20 mL) and brine (20 mL) and then dried over $MgSO_4$. Lastly, it was filtered and concentrated to give the desired compound **9** (283 mg, 1.86 mmol) as a solid in 96% yield after flash column chromatography ($SiO_2$, 1/1, $Et_2O$/hexanes). *Rf* 0.40 (1/1 hexanes/$Et_2O$); $^1$H-NMR $\delta$ 1.05(d, J=7.5Hz, 3H), 1.25(s, 3H), 2.10-240(m, 3H), 4.69(t, J=5.1Hz, 1H), 5.90-6.20(m, 2H); $^{13}$C-NMR $\delta$ 14.42(q), 19.9(q), 34.70(t), 37.63(d), 44.41(s), 72.12(d), 128.10(d), 137.76(d), 180.15(s).

**5-Hydroxymethyl-4,5-dimethyl-cyclohex-2-enol (11).** To a stirring suspension of $LiAlH_4$ (50.0 mg, 1.31 mmol) in ether (5 mL) was added lactone **9** (210 mg, 1.38 mmol) in ether (5 mL) at rt. The reaction was completed in less than 1 h. It was hydrolyzed by adding $Na_2SO_410H_2O$ (1 g), and solids were filtered off and washed with ether. After concentrating the washings, the desired compound **11** was obtained as a colorless solid (210 mg, 1.35 mmol) in 98% crude yield. It was pure enough to use for the next step. *Rf* 0.19 (2/3 hexanes/EtOAc); $^1$H-NMR $\delta$ 0.81(s, 3H), 0.89(d, J=7.5Hz, 3H), 1.60(dd, J=6.2& 5.7Hz, 1H), 1.73(dd, J=6.2& 5.7Hz, 1H), 2.20(m, 1H), 3.26(d, J=11.1Hz, 1H), 3.58(d, J=11.1Hz, 1H), 4.25(bs, 1H), 5.60-5.72(m, 2H); $^{13}$C-NMR $\delta$ 14.62(q), 17.90(q), 33.21(t), 34.16(d), 42.27(s), 65.41(t), 71.76(d), 127.14(d), 134.15(d).

**[5-(*tert*-Butyl-dimethyl-silanyloxy)-1,2-dimethyl-cyclohex-3-enyl]-methanol (12).** To a stirring solution of alcohol **11** (200.0 mg, 1.28 mmol) in $CH_2Cl_2$ (5 mL) was added TBDMSCl (231.0g, 1.54 mmol) and imidazole (105.0 g, 1.54 mmol). The resulting mixture was stirred at 0°C under argon atmosphere for 1h, diluted with $CH_2Cl_2$ (10 mL), and washed with $H_2O$ (10 mL) and saturated brine (10 mL).

The organic layer was dried ($Na_2SO_4$), filtered, and concentrated. Purification by column chromatography ($SiO_2$, 3/1 hexanes/EtOAc, *Rf* 0.30) yielded 130 mg (48% ) of mono protected alcohol **12**; $^1$H-NMR $\delta$ -0.30(s, 3H), –0.13(s, 3H), 0.82 (s, 3H), 0.90(d, J=7.3Hz, 3H), 0.93 (s, 9H), 1.63(dd, J=6.4 & 5.8Hz, 1H), 1.71(dd, J=6.4 & 5.8 Hz, 1H), 2.25(m, 1H), 3.24(d, J=11.2 Hz, 1H), 3.55(d, J=11.2Hz, 1H), 4.30(m, 1H), 5.70-5.80(m, 2H); $^{13}$C-NMR $\delta$ –4.60(q), 14.42(q), 18.21(q), 18.53(s), 25.10(q), 32.94(t), 34.45(d), 42.92(s), 65.57(t), 72.34(d), 128.10(d), 133.44(d).

**5-(*tert*-Butyl-dimethyl-silanyloxy)-1,2-dimethyl-cyclohex-3-enecarbaldehyde (13).** To a stirring solution of oxalyl chloride (90 $\mu$L, 0.74 mmol) in anhydrous $CH_2Cl_2$ (2.0 mL) at –78°C was slowly added DMSO (115$\mu$L, 1.6 mmol). As soon as gas evolution subsided, a solution of alcohol **12** in 0.5 mL $CH_2Cl_2$ was added dropwise over a 20 min period. With further stirring at –78°C, triethylamine (410 uL, 3 mmol) was added and the mixture was allowed to warm to ambient temperature over 20 min before quenching with saturated $NH_4Cl$ (2 mL). The aqueous phase was extracted twice with $CH_2Cl_2$ and combined organic phase was washed with saturated $NaHCO_3$, dried ($Na_2SO_4$), filtered, and concentrated. Purification by column chromatography ($SiO_2$, 5/1 hexanes/EtOAc, *Rf* 0.3) yielded 180 mg (90% ) of aldehyde **13**; $^1$H-NMR $\delta$ -0.32(s, 3H), –0.14(s, 3H), 1.01(s, 9H), 1.10(d, J=7.3Hz, 3H), 1.27(s, 3H), 1.85-2.30(m, 3H), 4.33(m, 1H), 5.70-5.80(m, 2H), 9.60(s, 1H); $^{13}$C-NMR $\delta$ –4.41(q), 15.63(q), 18.37(s), 19.22(q), 24.60(q), 36.23(d), 37.41(t), 46.14(s), 73.24(d), 129.02(d), 134.51(d), 205.02(s).

**Representative Procedure for the Cuprate Reaction:** To a stirring suspension of CuCN (17.0 mg, 0.19 mmol, dried by isotropic removal of water with toluene, 3x2 mL, under vacuum line) in THF (5 mL) at -78°C was added red colored aryllithium derivative which was formed by mixing compound **14** (100 mg, 0.18 mmol) with *n*-BuLi (0.11 mL 0.19 mmol from 1.50 M solution in hexanes) at -78°C via a cannula. As soon as the addition was over, the cooling bath was replaced with an ice-bath. The reaction mixture turned brownish-yellow. After stirring, the reaction mixture was kept total of 30 min at 0°C and 25 min at rt, it was cooled back to -78°C and was added epoxide **15** (19.0 $\mu$L, 0.189 mmol) and $Et_2O$ $BF_3$ (0.023 mL, 0.19 mmol) were added respectively. After 2 h stirring at this temperature, the reaction mixture was quenched with $NH_4Cl/NH_4OH$ solution (2.0 mL, 9/1 mixture) while it was still cold. After 30 min stirring, the aqueous layer became dark blue and was extracted with ether (3x4 mL). The combined organic layer was dried over $MgSO_4$, filtered and concentrated to give a light yellow oil. This crude oil was purified by flash column on silica gel (10/1 hexanes/EtOAc) to give **16E** in 47% yield with a trace amount of **16Z**.

**3-Chloro-5-(4-hydroxy-3-methyl-but-2-enyl)-2-methyl-4,6-bis-(2-trimethyl silanyl-ethoxymethoxy)-benzoic acid methyl ester (16E).** *Rf* 0.26 (4/1 hexanes/EtOAc); $^1$H-NMR $\delta$ 0.00(s, 18H), 0.95(dd, J=8.3& 8.7Hz, 4H), 1.78(s, 3H), 2.26(s, 3H), 3.50(d, J=6.4 Hz, 2H), 3.75-3.85(m, 4H), 3.88(s, 3H), 3.98(s, 2H), 5.06(d, J=20.0Hz, 4H), 5.45(m, 1H); $^{13}$C-NMR $\delta$ -1.40(q), 13.98(q), 17.62(q), 18.12(t), 18.21(t), 24.19(t), 52.41(q), 67.76(t), 67.92(t), 68.80(t), 97.86(t), 99.20(t), 125.22(d), 124.98(s), 126.92(s), 128.70(s), 132.95(s), 135.40(s), 151.65(s), 153.63(s), 167.94(s). **16Z:** *Rf* 0.28 (4/1 hexanes/EtOAc); $^1$H-NMR $\delta$ 0.00(s, 18H), 0.99(m, 4H), 1.76(s, 3H), 2.26(s, 3H), 3.54(d, J=6.4Hz, 2H), 3.74-3.93 (m, 4H), 3.90(s, 3H), 4.20(s, 2H), 5.05(d, J=23.4Hz, 4H), 5.30(m, 1H); $^{13}$C-NMR $\delta$ -1.24(q), 17.60(q), 18.10(t), 18.20(t), 21.40(q), 24.08(t), 52.43(q), 67.96(t), 68.15(t), 97.43(t), 99.07(t), 125.04(s), 125.12(d), 127.06(s), 128.82(s), 135.05(s), 135.81(s), 151.27(s), 153.22(s), 167.91(s).

**3-[4-(Benzothiazol-2-ylsulfanyl)-3-methyl-but-2-enyl]-5-chloro-6-methyl-2,4-bis-(2-trimethylsilanyl-ethoxymethoxy)-benzoic acid methyl ester (17).** To a stirring solution of 2-sulfanylbenzothiazole (57.0 mg, 0.34 mmol) and $Ph_3P$ (67.0 mg, 0.255 mmol) in THF(2.0 mL) at 0°C was added **16E** (96.0 mg, 0.17 mmol) in THF (2.0 mL). To this very light yellow solution was added diethyl azodicarboxylate (0.048 mL, 0.36 mmol). The resulting reaction mixture was stirred for 1 h at rt at which time TLC revealed that the starting material was consumed completely, so it was diluted with ether (4 mL) and shaken with water (3 mL). After separation of the two layers, the aqueous layer was extracted with ether (3x4 mL). The combined organic layer was dried over $MgSO_4$, filtered and concentrated to give a light yellow oil which was purified by flash column on silica gel (10/1 hexanes/EtOAc) to give 104 mg of the desired thio ether **17** in 86% yield. *Rf* 0.53 (4/1 hexanes/EtOAc); $^1$H-NMR $\delta$ 0.00(s, 18H), 0.96(dd, J=7.1& 9.7Hz, 4H), 1.92(s, 3H), 2.30(s, 3H), 3.50(m, 2H), 3.75(m, 2H), 3.85(m, 2H) 3.91(s, 3H), 3.99(s, 2H), 4.95(s, 2H), 5.05(s, 2H), 5.78(m, 1H), 7.25(m, 1H), 7.37(m, 1H), 7.72(d, J=8.8Hz, 1H), 7.84(d, J=8.5Hz, 1H); $^{13}$C-NMR $\delta$ -1.41(q), 15.60(q), 17.70(q), 18.09(t), 18.18(t), 24.68(t), 42.75(t), 52.43(q), 67.69(t), 67.82(t), 97.89(t), 99.26(t), 120.87(d), 121.50(d), 124.10(d), 124.91(s), 125.92(d), 126.85(s), 128.22(s), 128.69(d), 135.01(s), 133.02(s), 135.24(s), 151.65(s), 153.07(s), 153.62(s), 166.78(s), 167.89(s).

**3-[4-(Benzothiazole-2-sulfonyl)-3-methyl-but-2-enyl]-5-chloro-6-methyl-2,4-bis-(2-trimethylsilanyl-ethoxymethoxy)-benzoic acid methyl ester (18).** To a stirring solution of $Mo_7O_{24}(NH_4)_6.4H_2O$ (19.0 mg, 0.015 mmol) and $H_2O_2$(30%, 80.0 mL, 0.70 mmol) at 0°C was added thioether **17** (95.0 mg, 0.134 mmol) in EtOH (2 mL) which was pre-cooled to 0°C. The resulting reaction mixture was stirred for 4 h at 0°C the brought to rt slowly. After total of 5 h stirring, TLC indicated the complete disappearance of the starting material. The mixture was then diluted with ether (2 mL), and shaken with water (2 mL) and brine (2 mL). The organic layer was separated and the aqueous layer was extracted with ether (3x5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to give a light yellow oil which was purified by flash column on silica gel (10/1 hexanes/EtOAc) and 64 mg of sulfone **18** was obtained in 63% yield. *Rf* 0.42 (4/1 hexanes/EtOAc); $^1$H-NMR $\delta$ 0.00(s, 18H), 0.95(q, J=7.1& 9.7Hz, 4H), 2.01(s, 3H), 2.24(s, 3H), 3.40(d, J=6.5Hz, 2H), 3.74(ddd, J=8.4, 3.5& 8.4Hz, 2H), 3.83(m, 2H), 3.92(s, 3H), 4.14(s, 2H), 4.87(d, J=8.4Hz, 2H), 5.03(s, 2H), 5.38(m, 1H), 7.54(m, 2H), 7.88(d, J=8.9Hz, 1H), 8.12(d, J=8.4Hz, 1H); $^{13}$C-NMR $\delta$ -1.41(q), 17.10(q), 17.69(q), 18.12(t), 18.18(t), 24.85(t), 52.41(q), 64.07(t), 67.74(t), 67.82(t), 97.80(t), 99.19(t), 122.22(d), 122.67(s), 124.45(s), 125.21(d), 126.53(s), 127.05(s), 127.30(d), 127.37(d), 133.01(s), 135.27(d), 136.71(s), 151.47(s), 152.48(s), 153.43(s), 165.49(s), 167.73(s).

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