Diastereoselective β-Hydroxy Vinylsulfone Isomerizations

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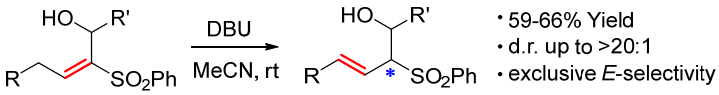
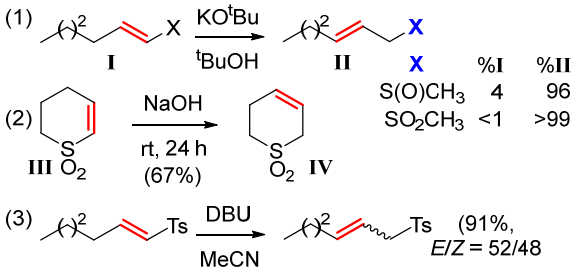


Abstract. Vinylic phenylsulfones containing a β-hydroxyl stereocenter undergo a diastereoselective isomerization to the corresponding allylic isomer upon treatment with 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU). Diastereoselectivity of this reaction increases with increasing size of the group attached to the carbinol carbon (up to >20:1 d.r. with a *tert*-butyl). Isolated yields of the isomerized allylic 1,2-hydroxy phenylsulfone products were comparable among the different vinylsulfones tested (59-66%). The major competing pathway was a C-C bond cleavage process, proposed to occur after the initial isomerization event. The sense of diastereoselection was consistent among all substrates investigated, in favor of the *erythro*-isomer based on NMR analysis.

The positional isomerization of carbon-carbon double bonds continues to attract considerable attention as a synthetic tool,[1] owing to the wide availability of olefins as feedstock chemicals and the presence of C-C double bonds in final target structures. Additionally, this transformation benefits from perfect atom economy,[2] in line with green chemistry principles.[3] Often, but not always,[4-6] these processes are driven by thermodynamic considerations, where a less-stable C-C double bond is selectively isomerized to a more stable position. Examples include the isomerization of γ,β-unsaturated esters[7] and allylbenzenes[8] to their conjugated isomers. Isomerization can also occur sequentially over longer distances in the presence of metal catalysts such as palladium[9,10] and ruthenium,[11,12] favoring formation of the most stable double bond positional isomer. Preventing this thermodynamically controlled chain walking isomerization, for example to select for a monoisomerization product, presents a challenge for these types of processes.[13]

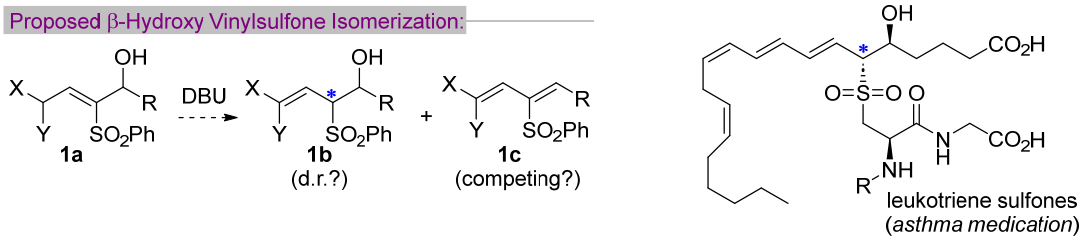
In 1964, O'Connor and Lyness reported a deconjugative monoisomerization of vinyl sulfoxides and sulfones to their allylic isomers upon treatment with potassium *tert*-butoxide (Scheme 1, eq. 1).[14] This was consistent with Fehnel's previous observation that cyclic vinylsulfone **III** readily tautomerizes to **IV** in the presence of sodium hydroxide (eq. 2).[15] Later, Inomata and coworkers showed that a weaker base DBU is similarly capable of vinylic- to allylic sulfone isomerizations, and also studied stereochemical aspects (e.g. *E*:*Z* ratios of the products) of this transformation (eq. 3).[16-19] Inomata's protocol was subsequently adopted for the total synthesis of the natural products ingenol[20] and avermectin B1a,[21] and has also featured in the synthesis of vinyl azides.[22] Theory supports a thermodynamic preference for the allylic isomer in these systems, explained by the electron-withdrawing nature of sulfoxide and sulfone groups being inductively unfavorable for attachment to an sp^2 hybridized carbon.[23]

Scheme 1. Previously reported isomerization of vinylsulfones to their allylic isomer.



Recently our group has been investigating reactions of allylic β-hydroxy phenyl sulfones of type **1b** (Scheme 2).[24] Among the different preparative approaches considered for these compounds, one option that surfaced was an isomerization from a vinyl precursor **1a**. This proposal, however, raised several important questions and concerns. Foremost, it was expected that dehydration and formation of the corresponding conjugated diene **1c** would compete. If successful, however, the reaction would produce a new sulfone-containing carbon stereocenter (*). Sulfone stereocenters can be found in a number of medicinally relevant molecules,[25] with pertinent examples being the leukotriene sulfones.[26] New approaches to their synthesis could therefore be of value to drug discovery programs. Moreover, the presence of an existing hydroxyl stereocenter in **1a** might render the reaction diastereoselective, providing a handle to control the absolute geometry of the final product.

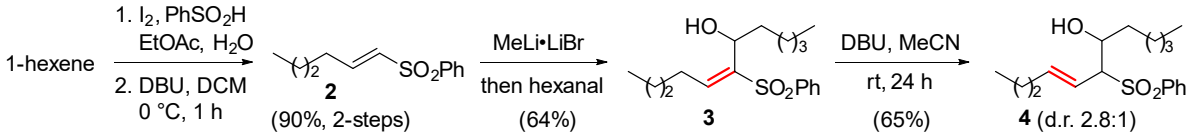
Scheme 2. Proposed isomerization of **1a** for the preparation of allylic β-hydroxy phenylsulfones **1b**.



Herein we report results from studies on the diastereoselective isomerization of hydroxy vinylphenylsulfones to *E*-allylic sulfone products. Our results indicate that diastereoselectivity is affected by sterics associated with the group attached to the carbinol carbon ("R" in Scheme 2), and that the sense of diastereoselectivity was the same for all substrates tested in favor of the *erythro*-isomer. Rather than dehydration, the primary competing reaction was a C-C bond cleavage process. Nonetheless, good yields (59-66%) and excellent diastereoselectivity (up to >20:1) of the allylic sulfone product could be obtained.

Our studies began with the preparation of β-hydroxy vinylsulfone **3** (Scheme 3). This was accomplished through the union of 1-hexene and hexanal via intermediate vinylsulfone **2** according to the combined procedures of Inomata[16,17] (for vinylsulfone synthesis) and Eisch and Galle[27] (for aldehyde addition). Treatment of **3** with DBU in acetonitrile (MeCN) at room temperature for 24 h resulted in a mixture of products, where the major component was the double-bond isomerized allylic sulfone **4** that was isolated in 65% yield and diastereomeric ratio (d.r.) of 2.8:1.

Scheme 3. Synthesis and DBU isomerization of β-hydroxy vinyl phenylsulfone **3**.



The use of COSY NMR allowed for the assignment of signals belonging to major- and minor diastereomers of **4** as well as identification of a single component giving rise to unexpected signals in the alkene region that were coupled to a doublet at 3.72 ppm (Figure 1). Further analysis led to the assignment of these signals belonging to allylic sulfone **5**, which was confirmed by comparison to reported NMR data[28] as well as its independent synthesis by the isomerization of **2** with DBU. Interestingly, a ~1:1 *cis*:*trans* mixture of **5** was obtained from **2** (consistent with Inomata's results[16]), whereas formation of **5** from **3** was highly *trans*-selective under the same conditions.[29] Similarly, only the *trans*-isomer of **4** was observed from the isomerization of **3** by ^{1}H NMR analysis (J_{ab} = 15.5 Hz).

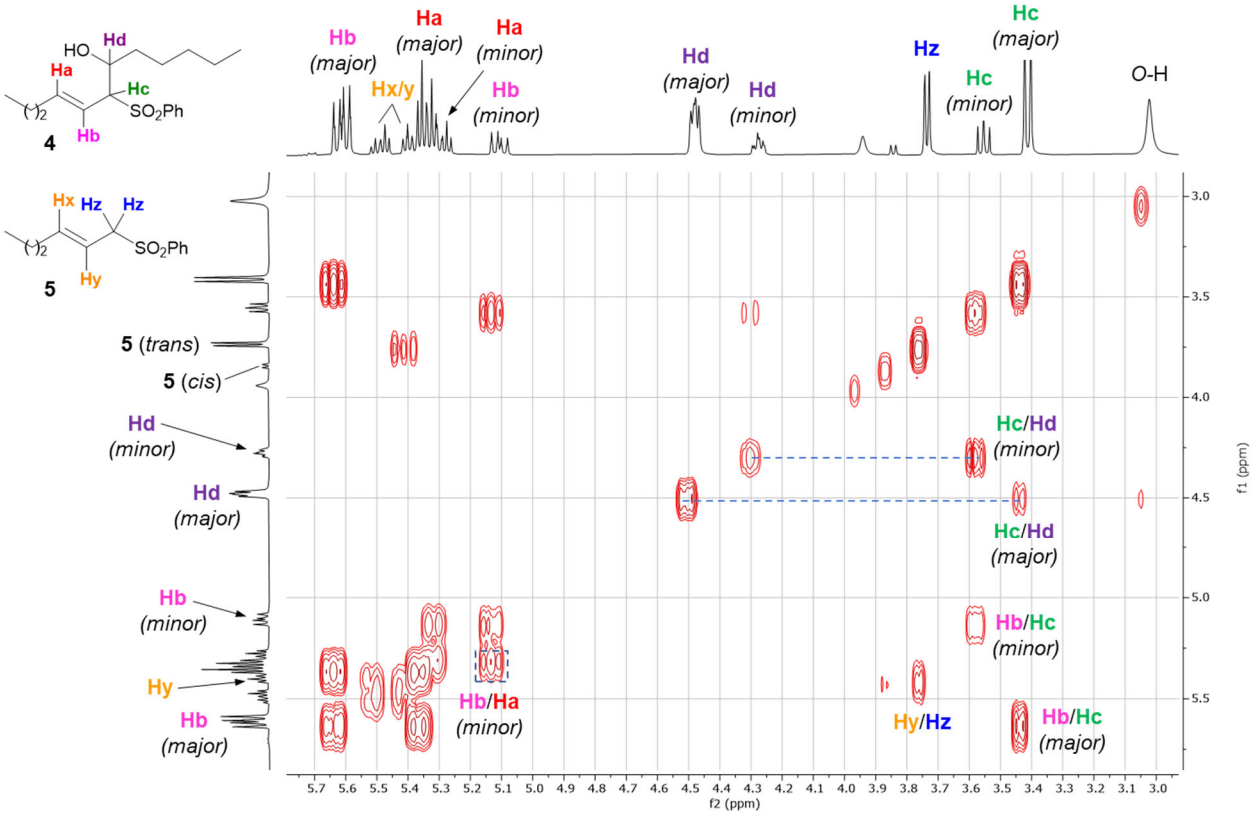
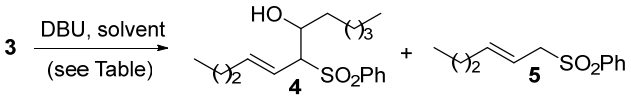


Figure 1. COSY NMR spectrum of the product mixture obtained upon treatment of vinylsulfone **3** with DBU in MeCN at room temperature for 24 h. Cross-peak analysis allowed for the assignment of signals H_a-H_d belonging to major- and minor diastereomers of **4** (d.r. 2.8:1) as well as identification of compound **5** as the major byproduct.

Other solvents besides MeCN were examined in the DBU isomerization of **3** (Table 1). In general, greater solvent polarity resulted in higher conversions but also increased amounts of byproduct **5**. For instance, the reaction in DMSO proceeded with complete conversion but gave a 1.6:1 ratio of **4**:**5** (Entry 5) Conversely, the use of less polar chloroform ($CHCl_3$) as solvent under otherwise identical conditions

resulted in only 41% conversion, but far greater selectivity for the isomerized product **4** (19.4:1 **4**:**5**; Entry 4). An outlier was toluene (PhMe), where lower conversion (31%) was accompanied by significant amounts of **5** (3.6:1 **4**:**5**; Entry 6), greater than what was obtained with MeCN and methanol (MeOH; 6.7-6.8:1 **4**:**5**; Entries 1 and 3). Heating the reaction increased conversion as well as compound **5** formation (Entries 7 and 8). Balancing conversion with the yield and d.r. of **4**, MeCN was selected as the optimum solvent for this transformation.

Table 1. Results from solvent studies on the DBU isomerization of **3**.

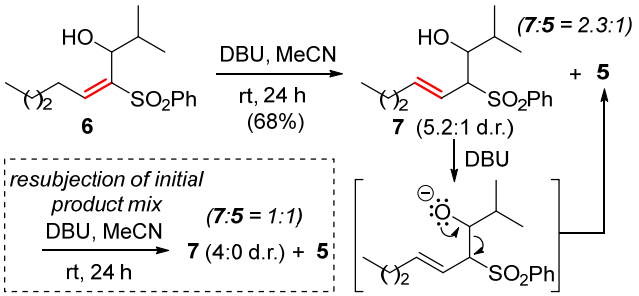


Entry	Solvent[A]	% Conv.[B]	4 d.r.[C]	4 : 5[C]
1	MeCN	88	2.8 : 1	6.8 : 1
2	THF	57	1.6 : 1	20.0 : 1
3	MeOH	68	2.5 : 1	6.7 : 1
4	$CHCl_3$	41	2.1 : 1	19.4 : 1
5	DMSO	100	3.3 : 1	1.6 : 1
6	PhMe	31	2.0 : 1	3.6 : 1
7	THF[D]	91	2.1 : 1	1 : 2.0
8	$CHCl_3$[D]	52	2.1 : 1	7.2 : 1

Notes for Table: [A]Reactions were performed by adding DBU (4.0 equiv.) to a 0.4 M solution of the vinylsulfone in MeCN and stirring at room temperature for 20 h. [B]Calculated by dividing the product ^{1}H NMR integration values (major + minor diastereomer) by the sum of product + starting material integrations. [C]From ^{1}H NMR integrations. [D]Performed at 50 °C.

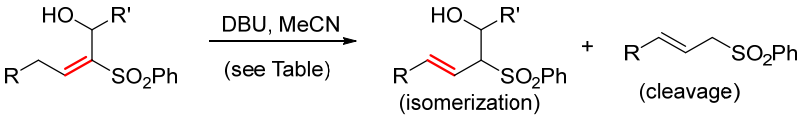
Byproduct **5** was also observed in the mixture obtained from isobutyraldehyde-derived hydroxy vinylsulfone **6** upon treatment with DBU in MeCN at rt for 24 h (Scheme 4). The isomerized product **7** was nonetheless the major component, obtained in 68% isolated yield as a 5.2:1 mixture of diastereomers. Formation of **5** from the reaction of **6** (and **3**) is proposed to proceed via a mechanism involving deprotonation of the hydroxyl group followed by a retro-sulfonyl anion aldehyde addition. In support of this mechanism, resubjection of the initially formed 2.3:1 mixture of **7** and **5** with DBU resulted in increased amounts of **5** relative to **7** (now ~1:1), supporting the intermediacy of **7** in the formation of **5**. There was also a slight erosion in the d.r. of **7** (from 5.2:1 to 4.0:1) upon resubjection, perhaps indicating differences in rate for this C-C bond cleavage process between the two diastereomers of **7**.

Scheme 4. Isomerization of **6** and resubjection of the initially formed product mixture. The increased amounts of **5** relative to **7** upon resubjection is consistent with a mechanism involving formation of **7** from **6** followed by the conversion of **7** to **5**.



A series of additional β-hydroxy vinylsulfones were synthesized and examined in their isomerization with DBU to the corresponding allylic isomer (Table 2). A clear trend was observed with larger groups attached to the carbinol carbon resulting in isomerized products with higher d.r. For instance, a methyl group at this position as in compound **8** gave the isomerized hydroxy allylic sulfone with a d.r. of 1.8:1 (Entry 1), whereas an isopropyl resulted in a d.r. of 5.2:1 (Entry 4, *i*-Pr, **6**), and *tert*-butyl produced a single diastereomer by ^{1}H NMR (Entries 7 and 10, *t*-Bu, **10**). Reducing the reaction time for **6** to 15 h (Entry 5) and 10 h (Entry 6) gave lower conversions (86% and 79% respectively) but higher ratios in favor of the isomerized product over C-C bond cleavage, again consistent with a mechanism involving first isomerization followed by retro-sulfonyl anion aldehyde addition (where the rate of isomerization is greater than cleavage). Introduction of a phenyl adjacent to the hydroxyl resulted in essentially complete C-C bond cleavage and formation of **5** (Entry 8),[29] perhaps as a result of conjugation afforded to the aldehyde coproduct by this group (i.e. benzaldehyde; *ref.* Scheme 4).

Table 2. Results from different β-hydroxy vinyl phenylsulfone reactions with DBU.



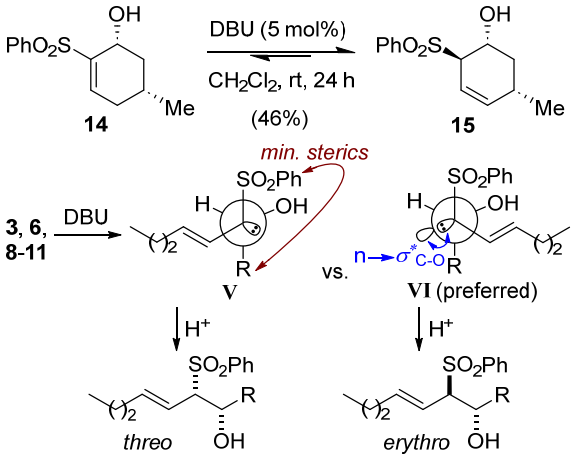
Entry	R	R' (compound #)	% Conversion[A] (% Yield[B])	d.r.[C]	Isom : Cleav[C]
1	$(CH_2)_2CH_3$	Me (**8**)	92 (59)	1.8 : 1	2.6 : 1
2	$(CH_2)_2CH_3$	*n*-pent (**3**)	89 (65)	2.8 : 1	6.0 : 1
3	$(CH_2)_2CH_3$	*i*-Bu (**9**)	89 (61)	2.6 : 1	3.3 : 1
4	$(CH_2)_2CH_3$	*i*-Pr (**6**)	95 (60)	5.2 : 1	2.3 : 1
5	$(CH_2)_2CH_3$	*i*-Pr (**6**)	86[C]	5.8 : 1	5.3 : 1
6	$(CH_2)_2CH_3$	*i*-Pr (**6**)	79[D]	4.9 : 1	6.9 : 1
7	$(CH_2)_2CH_3$	*t*-Bu (**10**)	100 (64)	>20 : 1	3.2 : 1
8	$(CH_2)_2CH_3$	Ph (**11**)	100	--	1:>10
9	$(CH_2)_3OTIPS$	*i*-Pr (**12**)	94 (61)	6.1 : 1	3.1 : 1
10	$(CH_2)_3OTIPS$	*t*-Bu (**13**)	100 (66)	>20 : 1	3.2 : 1

Notes: [A]Reactions were performed by adding DBU (4.0 equiv.) to a 0.4 M solution of the vinylsulfone in MeCN and stirring at room temperature for 24 h. Percent conversions were calculated by dividing the product integration values (major + minor diastereomer) by the product + starting material integrations.

[B]Isolated yield after chromatography on silica. [C]Determined by ^{1}H NMR. [C]The reaction was run for 15 h. [D]The reaction was run for 10 h.

Marcantoni and Cingolani noted an upfield shift in the ^{13}C NMR spectrum for the carbinol carbons of β-hydroxy phenylsulfones in the *erythro*-isomer compared with those in the *threo*-isomer.[30] For all products listed in Table 2, the major diastereomer consistently displayed an upfield carbinol signal (as well as an upfield sulfonyl carbon signal) in their ^{13}C NMR spectrum. Assuming the same trend observed by Marcantoni and Cingolani applies to the β-hydroxy phenylsulfones obtained here, the major diastereomer of the allylic sulfone product for all substrates is the *erythro*-isomer. To our knowledge, only one diastereoselective vinylic to allylic sulfone isomerization has been reported, in this case from cyclic vinylsulfone **14** as part of a synthesis of the C21-C26 segment of apoptolidin natural products[31] (Scheme 5). Treatment of **14** with DBU resulted in a 1:2.5 equilibrium mixture in favor of the allylic isomer from which **15** could be isolated in 46% yield. Compound **15** was described as a single diastereomer, yet in this case the stereochemical outcome is presumably controlled by the cyclohexene ring conformation energetics (i.e. all groups in **15** are equatorial). Other studies indicate that α-phenylsulfonyl carbanions exist largely with the lone-pair of electrons in an sp^3-hybridized orbital.[32,33] The structure of the intermediate anion formed upon deprotonation of the β-hydroxy vinylsulfone with DBU might therefore be best represented by the two Newman projections **V** and **VI**. Sterics are minimized between the phenylsulfonyl- and R groups, which becomes increasingly influential as R becomes larger. Dipole-minimization and hyperconjugation[34] (n→$\sigma^*_{C\text{-}O}$) would then favor **VI** from which the *erythro*-isomer would be formed.

Scheme 5. Previously reported diastereoselective β-hydroxy vinylsulfone isomerization of **14** to **15** and proposed model for selective formation of the *erythro*-isomer from acyclic substrates **3**, **6**, and **8**-**11**.



In summary, β-hydroxy vinyl phenylsulfones undergo diastereoselective isomerization to the corresponding allylic isomer upon treatment with DBU at room temperature. Diastereoselectivity increases with increasing sterics associated with the group attached to the carbinol carbon (e.g. 1.8:1 for Me vs 5.2:1 for *i*-Pr and >20:1 for *tert*-butyl). A competing C-C bond cleavage also occurs during the reaction, which appears to be promoted by higher polarity solvents like DMSO and higher temperature.

When performed at room temperature in acetonitrile for 24 h, isolated yields of the isomerized allylic β-hydroxy sulfone products were consistently around 60%. Current efforts are directed at further optimizations and scope studies, as well as investigating strategic applications of the isomerization reaction (and C-C bond cleavage) to the preparation of valuable synthetic targets.

Experimental Section

General Information. All reactions were carried out in vessels under a nitrogen atmosphere unless otherwise specified. Dry solvents were prepared by passing the solvent through a column of activated alumina under nitrogen immediately prior to use. All reagents were purchased and used as received unless mentioned otherwise. TLC analysis used 0.25 mm silica layer fluorescence UV_{254} plates. Column chromatography: silica gel (230-400 mesh). IR: FT-IR with single-bounce diamond ATR. NMR: Spectra were recorded on a 500 MHz spectrometer in $CDCl_3$; chemical shifts (d) are given in ppm, coupling constants (*J*) in Hz. Solvent signals were used as references ($CDCl_3$: δ 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δ 7.26 ppm). HRMS: quadrupole time-of-flight LC-MS with electrospray ionization (ESI positive and negative).

General Experimental Procedures.

General Procedure A: Vinyl Phenylsulfone Synthesis.[18] To a solution of sodium benzenesulfinate (1.08 g, 6 mmol) in ethyl acetate (EtOAc, 25 mL) and water (25 mL) open to air was added the 1-alkene (4 mmol) and iodine (1.02 g, 4 mmol) and the mixture was stirred vigorously at room temperature for 2 h. The reaction was quenched with aq. $Na_2S_2O_3$ (25 mL) and extracted with EtOAc (2 x 25 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The crude product was redissolved in DCM (25 mL) in a flask open to air and cooled to 0 °C. DBU (0.9 mL, 6 mmol) was then added, and the mixture was stirred for 1 h. The reaction was quenched with aq. HCl (1M, 25 mL), and extracted with DCM (2 x 25 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. Purification of the crude product by chromatography on silica (10:1 to 4:1 hexanes:EtOAc) gave the *E*-vinylsulfone as a colorless oil.

General Procedure B: Vinylsulfone Aldehyde Additions.[27] To a solution of (*E*)-(hex-1-en-1-ylsulfonyl)benzene (**2**) or (*E*)-triisopropyl((6-(phenylsulfonyl)hex-5-en-1-yl)oxy)silane in THF (to make a 0.5 M solution) at -95 °C was added a solution of MeLi•LiBr (1.5 M, 1.2 equiv.) and the resulting mixture was warmed to -78 °C and stirred for 30 min. The aldehyde (1.5 equiv.) was then added and the reaction was stirred for 2 h before quenching with aq. NH_4Cl and extracting with EtOAc. The organic phase was dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. Purification of the crude product by chromatography on silica (4:1 to 1:1 hexanes:EtOAc) gave the β-hydroxy vinylsulfone as a colorless oil.

General Procedure C: β-Hydroxy Vinylsulfone Isomerizations. To a solution of the β-hydroxy vinylsulfone in MeCN (to make a 0.4 M solution) at room temperature was added DBU (4 equiv.) and the mixture was stirred for 24 h. The reaction was quenched with 1M HCl and extracted with DCM (2x). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. Purification of the crude product by chromatography on silica (4:1 to 1:1 hexanes:EtOAc) gave the β-hydroxy allylic phenylsulfone as a colorless oil.

(*E*)-(hex-1-en-1-ylsulfonyl)benzene (2). Prepared according to procedure A. Compound **2** was obtained as a colorless oil (0.67 g, 75%). *Spectral data matched that previously reported*:[35] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.78 (m, 2H), 7.64 – 7.52 (m, 1H), 7.53 – 7.43 (m, 2H), 6.95 (dt, *J* = 15.1, 6.9 Hz, 1H), 6.28 (dt, *J* = 15.1, 1.6 Hz, 1H), 2.19 (dtd, *J* = 8.3, 6.9, 1.6 Hz, 2H), 1.49 – 1.34 (m, 2H), 1.34 – 1.23 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H).

(*E*)-triisopropyl((6-(phenylsulfonyl)hex-5-en-1-yl)oxy)silane. Prepared according to procedure A. (*E*)-Triisopropyl((6-(phenylsulfonyl)hex-5-en-1-yl)oxy)silane was obtained as a colorless oil (1.2 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.66 – 7.56 (m, 1H), 7.55 – 7.49 (m, 2H), 6.99 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.31 (dt, *J* = 15.1, 1.6 Hz, 1H), 3.65 (t, *J* = 5.9 Hz, 2H), 2.26 (td, *J* = 6.9, 5.3 Hz, 2H), 1.60 – 1.47 (m, 4H), 1.12 – 0.94 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 140.7, 133.1, 130.4, 129.1, 127.5, 62.7, 32.1, 31.2, 24.0, 17.9, 11.9.

(*E*)-7-(phenylsulfonyl)dodec-7-en-6-ol (3). Prepared according to procedure B using vinyl sulfone **2** (0.20 g, 0.89 mmol) and hexanal. Compound **3** was obtained as a colorless oil (0.184 g, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.81 (m, 2H), 7.62 – 7.56 (m, 1H), 7.56 – 7.42 (m, 2H), 6.94 (t, *J* = 7.7 Hz, 1H), 4.53 (dd, *J* = 8.8, 5.5 Hz, 1H), 2.56 (s, 1H), 2.41 – 2.29 (m, 2H), 1.73 (dddd, *J* = 13.4, 9.6, 8.7, 4.8 Hz, 1H), 1.52 – 1.40 (m, 3H), 1.40 – 1.32 (m, 2H), 1.32 – 1.23 (m, 1H), 1.23 – 1.00 (m, 4H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.81 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 143.0, 141.2, 133.1, 129.1, 127.7, 69.0, 36.7, 31.3, 30.7, 28.2, 25.6, 22.40, 22.38, 13.9, 13.8.

(*E*)-7-(phenylsulfonyl)dodec-8-en-6-ol (4). Prepared according to procedure C using β-hydroxy vinyl sulfone **3** (0.13 g, 0.40 mmol). Compound **4** was obtained as a colorless oil (0.085 g, 65%) and 2.8:1 mixture of diastereomers. *Spectral data for the mixture of diastereomers:* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 4H), 7.65 – 7.60 (m, 2H), 7.55 – 7.50 (m, 4H), 5.61 (ddt, *J* = 15.5, 9.9, 1.5 Hz, 1H), 5.34 (dt, *J* = 15.5, 6.8 Hz, 1H), 5.30 – 5.25 (m, 1H), 5.11 (ddt, *J* = 15.3, 10.1, 1.4 Hz, 1H), 4.48 (ddd, *J* = 8.4, 5.2, 1.4 Hz, 1H), 4.28 (td, *J* = 8.3, 2.9 Hz, 1H), 3.94 (s, *O*H), 3.55 (dd, *J* = 10.1, 8.7 Hz, 1H), 3.41 (dd, *J* = 9.9, 1.4 Hz, 1H), 3.02 (s, *O*H), 1.93 (dddd, *J* = 15.7, 13.9, 6.5, 1.3 Hz, 4H), 1.62 – 1.50 (m, 2H), 1.49 – 1.34 (m, 2H), 1.33 – 1.15 (m, 12H), 0.85 (td, *J* = 7.0, 3.4 Hz, 3H), 0.76 (dt, *J* = 9.2, 6.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 141.6, 141.0, 137.5, 133.7, 129.1, 128.90, 128.87, 128.83, 128.77, 128.5, 119.3, 117.0, 116.0, 74.9, 73.0, 68.6, 68.1, 34.7, 34.5, 31.4, 25.0, 22.4, 21.8, 13.9, 13.5.

(*E*)-(hex-2-en-1-ylsulfonyl)benzene (5). Prepared according to procedure C using vinylsulfone **2** (0.05 g, 0.22 mmol). Compound **5** was obtained as a colorless oil (0.048 g, 96%) and ~1:1 *cis*:*trans* mixture. *Spectral data for the mixture matched that previously reported:*[28] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.87 – 7.84 (m, 2H), 7.70 – 7.61 (m, 2H), 7.54 (dd, *J* = 8.4, 7.1 Hz, 4H), 5.72 (dtt, *J* = 10.0, 7.4, 1.3 Hz, 1H), 5.59 – 5.46 (m, 1H), 5.45 – 5.36 (m, 2H), 3.85 (dd, *J* = 7.9, 1.2 Hz, 2H), 3.74 (dd, *J* = 7.3, 1.0 Hz, 2H), 2.07 – 1.92 (m, 2H), 1.71 (qd, *J* = 7.4, 1.7 Hz, 2H), 1.29 (h, *J* = 7.4 Hz, 2H), 1.15 (h, *J* = 7.4 Hz, 2H), 0.81 (t, *J* = 7.4 Hz, 2H), 0.75 (t, *J* = 7.4 Hz, 3H).

(*E*)-2-methyl-4-(phenylsulfonyl)non-4-en-3-ol (6). Prepared according to procedure B using vinyl sulfone **2** (0.20 g, 0.89 mmol) and isobutyraldehyde. Compound **6** was obtained as a colorless oil (0.16 g, 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.62 – 7.55 (m, 1H), 7.54 – 7.45 (m, 2H), 6.93 (t, *J* = 7.6 Hz, 1H), 4.11 (dd, *J* = 10.1, 4.0 Hz, 1H), 2.75 (s, *J* = 6.7 Hz, *O*H), 2.32 (q, *J* = 7.7 Hz, 2H), 2.01 (dt, *J* = 9.6, 6.6 Hz, 1H), 1.49 – 1.40 (m, 2H), 1.33 (dq, *J* = 8.9, 7.2 Hz, 2H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.54 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.5, 142.4, 141.3, 133.1, 129.0, 127.7, 74.9, 33.2, 30.5, 28.4, 22.3, 19.4, 18.9, 13.7.

(*E*)-2-methyl-4-(phenylsulfonyl)non-5-en-3-ol (7). Prepared according to procedure C using β-hydroxy vinyl sulfone **6** (0.13 g, 0.44 mmol). Compound **7** was obtained as a colorless oil (0.88 g, 68%) and 5.2:1 mixture of diastereomers. *Spectral data for the major diastereomer:* 1H NMR (500 MHz, CDCl3) δ 7.91 – 7.79 (m, 2H), 7.67 – 7.59 (m, 1H), 7.58 – 7.49 (m, 2H), 5.64 (ddt, J = 15.6, 9.9, 1.5 Hz, 1H), 5.45 – 5.30 (m, 1H), 4.08 (dd, J = 9.0, 1.4 Hz, 1H), 3.60 (dd, J = 9.8, 1.2 Hz, 1H), 2.01 – 1.88 (m, 2H), 1.67 (dp, J = 9.0, 6.7 Hz, 1H), 1.35 – 1.12 (m, 4H), 1.02 (d, J = 6.6 Hz, 3H), 0.80 – 0.74 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 137.4, 133.7, 129.0, 128.8, 117.1, 73.3, 71.3, 34.7, 31.7, 21.8, 19.1, 18.3, 13.5.

(*E*)-3-(phenylsulfonyl)oct-3-en-2-ol (8v). Prepared according to procedure B using vinyl sulfone **2** (0.20 g, 0.89 mmol) and acetaldehyde. Compound **8v** was obtained as a colorless oil (0.13 g, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.66 – 7.59 (m, 1H), 7.55 (ddt, *J* = 8.2, 6.7, 1.2 Hz, 2H), 6.95 (t, *J* = 7.7 Hz, 1H), 4.79 (p, J = 6.7 Hz, 1H), 2.46 (d, *J* = 6.5 Hz, 1H), 2.41 (qd, *J* = 7.4, 2.3 Hz, 2H), 1.55 – 1.46 (m, 2H), 1.43 – 1.36 (m, 2H), 1.34 (d, *J* = 6.7 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.9, 143.6, 141.1, 133.2, 129.2, 127.7, 65.0, 30.7, 28.2, 23.2, 22.4, 13.8.

(*E*)-3-(phenylsulfonyl)oct-4-en-2-ol (8a). Prepared according to procedure C using β-hydroxy vinyl sulfone **8v** (0.14 g, 0.51 mmol). Compound **8a** was obtained as a colorless oil (0.08 g, 59%) and 1.8:1 mixture of diastereomers. *Spectral data for the mixture of diastereomers:* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (ddd, *J* = 8.6, 3.9, 1.3 Hz, 4H), 7.69 – 7.63 (m, 2H), 7.57 (dd, *J* = 8.5, 7.1 Hz, 4H), 5.65 (ddt, *J* = 15.5, 10.0, 1.5 Hz, 1H), 5.43-5.32 (m, 2H), 5.13 (ddt, *J* = 15.4, 10.1, 1.4 Hz, 1H), 4.72 (qd, *J* = 6.5, 1.5 Hz, 1H), 4.47 (dq, *J* = 8.6, 6.3 Hz, 1H), 4.03 (bs, *O*H), 3.53 (dd, *J* = 10.1, 8.5 Hz, 1H), 3.40 (dd, *J* = 9.9, 1.5 Hz, 1H), 3.10 (bs, *O*H), 2.03 – 1.90 (m, 4H), 1.32 – 1.23 (m, 4H), 1.22 (d, *J* = 6.4 Hz, 6H), 0.88 – 0.76 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.1, 141.2, 137.5, 137.2, 133.9, 133.8, 129.1, 128.90, 128.88, 128.8, 119.3, 116.8, 75.9, 74.0, 34.7, 34.5, 21.84, 21.76, 21.1, 20.6, 13.54, 13.49.

(*E*)-2-methyl-5-(phenylsulfonyl)dec-5-en-4-ol (9v). Prepared according to procedure B using vinyl sulfone **2** (0.50 g, 2.2 mmol) and isovaleraldehyde. Compound **9v** was obtained as a colorless oil (0.35 g, 51%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.61 – 7.56 (m, 1H), 7.54 – 7.49 (m, 2H), 6.91 (t, *J* = 7.7 Hz, 1H), 4.61 (dd, *J* = 10.2, 4.2 Hz, 1H), 2.54 (s, 1H), 2.35 (td, *J* = 7.4, 3.1 Hz, 2H), 1.72 (ddd, *J* = 13.9, 9.8, 5.2 Hz, 1H), 1.60 (dpd, *J* = 8.7, 6.7, 5.2 Hz, 1H), 1.51 – 1.43 (m, 2H), 1.39 – 1.30 (m, 2H), 1.14 (ddd, *J* =

14.0, 8.6, 4.3 Hz, 1H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.73 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 143.4, 141.2, 133.1, 129.1, 127.8, 67.1, 45.8, 30.7, 28.2, 24.6, 23.2, 22.4, 21.4, 13.8.

(*E*)-2-methyl-5-(phenylsulfonyl)dec-6-en-4-ol (9a). Prepared according to procedure C using β-hydroxy vinyl sulfone **9v** (0.10 g, 0.32 mmol). Compound **9a** was obtained as a colorless oil (0.061 g, 61%) and 2.6:1 mixture of diastereomers. *Spectral data for the major diastereomer*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.79 (m, 2H), 7.67 – 7.60 (m, 1H), 7.58 – 7.50 (m, 2H), 5.63 (ddt, *J* = 15.4, 10.0, 1.5 Hz, 1H), 5.33 (dt, *J* = 15.4, 6.8 Hz, 1H), 4.61 (ddd, *J* = 9.0, 4.8, 1.3 Hz, 1H), 3.38 (dd, *J* = 10.5, 1.2 Hz, 1H), 2.97 (s, 1H), 2.01 – 1.87 (m, 2H), 1.73 (dh, *J* = 8.4, 6.6 Hz, 1H), 1.51 (ddd, *J* = 13.7, 9.0, 5.9 Hz, 1H), 1.28 – 1.16 (m, 2H), 1.09 (ddd, *J* = 13.8, 8.3, 4.8 Hz, 1H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.76 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.7, 137.5, 133.8, 128.93, 128.90, 117.1, 73.3, 66.2, 43.5, 34.7, 24.2, 23.0, 22.0, 21.9, 13.5.

(*E*)-2,2-dimethyl-4-(phenylsulfonyl)non-4-en-3-ol (10v). Prepared according to procedure B using vinyl sulfone **2** (0.20 g, 0.89 mmol) and pivaldehyde. Compound **10v** was obtained as a colorless oil (0.16 g, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.88 (m, 2H), 7.60 – 7.56 (m, 1H), 7.54 – 7.49 (m, 2H), 6.70 (s, 1H), 4.40 (d, *J* = 9.1 Hz, 1H), 2.26 (dq, *J* = 15.4, 8.0 Hz, 2H), 1.40 – 1.29 (m, 2H), 1.21 (h, *J* = 7.1 Hz, 2H), 1.02 (s, 9H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.8, 143.1, 142.6, 132.9, 129.0, 127.5, 77.6, 37.7, 30.6, 29.7, 26.9, 22.3, 13.7.

(*E*)-2,2-dimethyl-4-(phenylsulfonyl)non-5-en-3-ol (10a). Prepared according to procedure C using β-hydroxy vinyl sulfone **10a** (0.07 g, 0.24 mmol). Compound **10v** was obtained as a colorless oil (0.048 g, 64%) and >20:1 mixture of diastereomers. *Spectral data for the major diastereomer*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.77 (m, 2H), 7.68 – 7.59 (m, 1H), 7.56 – 7.49 (m, 2H), 5.69 (ddt, *J* = 15.7, 9.8, 1.5 Hz, 1H), 5.26 (dt, *J* = 15.7, 6.9 Hz, 1H), 4.26 (dd, *J* = 3.4, 0.9 Hz, 1H), 3.71 (dt, *J* = 9.8, 0.8 Hz, 1H), 2.78 (d, *J* = 3.3 Hz, 1H), 1.89 (dtdd, *J* = 8.0, 6.7, 5.6, 1.5 Hz, 2H), 1.25 – 1.15 (m, 2H), 0.91 (s, 9H), 0.77 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.7, 137.0, 133.6, 129.2, 128.8, 118.7, 74.0, 70.6, 35.9, 34.9, 26.6, 21.7, 13.7.

(*E*)-1-phenyl-2-(phenylsulfonyl)hept-2-en-1-ol (11v). Prepared according to procedure B using vinyl sulfone **2** (0.20 g, 0.89 mmol) and benzaldehyde. Compound **11v** was obtained as a colorless oil (0.21 g, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 2H), 7.50 – 7.44 (m, 1H), 7.40 – 7.31 (m, 3H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.12 (s, 5H), 5.80 (d, *J* = 5.7 Hz, 1H), 3.47 (d, *J* = 8.0 Hz, 1H), 2.27 (q, *J* = 7.6 Hz, 2H), 1.42 (m,, 2H), 1.33 – 1.23 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.2, 142.7, 140.7, 139.8, 132.8, 128.9, 128.2, 127.6, 127.3, 125.5, 69.1, 30.4, 28.3, 22.4, 13.7.

(*E*)-2-methyl-4-(phenylsulfonyl)-9-((triisopropylsilyl)oxy)non-4-en-3-ol (12v). Prepared according to procedure B using triisopropyl((6-(phenylsulfonyl)hex-5-en-1-yl)oxy)silane (0.20 g, 0.50 mmol) and

isobutyraldehyde. Compound **12v** was obtained as a colorless oil (0.16 g, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.84 (m, 2H), 7.61 – 7.55 (m, 1H), 7.55 – 7.47 (m, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 4.12 (d, *J* = 9.7 Hz, 1H), 3.71 – 3.65 (m, 2H), 2.73 (s, 1H), 2.36 (tdd, *J* = 7.3, 5.1, 2.2 Hz, 2H), 2.02 (dh, *J* = 9.7, 6.6 Hz, 1H), 1.62 – 1.49 (m, 4H), 1.11 – 1.02 (m, 21H), 1.01 (d, J = 6.5 Hz, 3H), 0.55 (d, J = 6.8 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 146.4, 142.7, 141.4, 133.2, 129.1, 127.8, 75.0, 62.8, 33.4, 32.6, 28.6, 25.1, 19.4, 19.0, 18.0, 12.0.

(*E*)-2-methyl-4-(phenylsulfonyl)-9-((triisopropylsilyl)oxy)non-5-en-3-ol (12a). Prepared according to procedure C using β-hydroxy vinyl sulfone **12v** (0.08 g, 0.18 mmol). Compound **12a** was obtained as a colorless oil (0.048 g, 61%) and 6.1:1 mixture of diastereomers. *Spectral data for the major diastereomer*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.77 (m, 2H), 7.66 – 7.59 (m, 1H), 7.53 (ddt, *J* = 8.4, 6.5, 1.4 Hz, 2H), 5.65 (ddt, *J* = 15.5, 9.9, 1.5 Hz, 1H), 5.37 (dt, *J* = 15.6, 6.8 Hz, 1H), 4.07 (dt, *J* = 9.0, 1.6 Hz, 1H), 3.73 (dd, *J* = 7.3, 1.0 Hz, 1H), 3.63 – 3.48 (m, 2H), 3.05 (d, *J* = 2.5 Hz, 1H), 2.12 – 1.95 (m, 2H), 1.66 (dh, *J* = 9.0, 6.6 Hz, 1H), 1.41 (dtd, *J* = 13.6, 6.5, 1.9 Hz, 2H), 1.05 – 1.02 (m, 21H), 1.01 (d, *J* = 3.6 Hz, 3H), 0.77 (d, *J* = 6.7 Hz, 3H). *Spectral data for the mixture of diastereomers:* ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 141.5, 138.4, 137.4, 133.7, 133.6, 129.04, 128.95, 128.9, 128.6, 117.1, 116.1, 73.3, 71.3, 62.6, 62.5, 60.2, 32.0, 31.8, 29.2, 29.0, 19.1, 18.4, 18.0, 12.0.

(*E*)-2,2-dimethyl-4-(phenylsulfonyl)-9-((triisopropylsilyl)oxy)non-4-en-3-ol (13v). Prepared according to procedure B using triisopropyl((6-(phenylsulfonyl)hex-5-en-1-yl)oxy)silane (0.20 g, 0.50 mmol) and pivaldehyde. Compound **13v** was obtained as a colorless oil (0.17 g, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.86 (m, 2H), 7.59 – 7.54 (m, 1H), 7.53 – 7.47 (m, 2H), 6.71 (s, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 3.61 (t, *J* = 5.8 Hz, 2H), 2.29 (ddd, *J* = 14.2, 7.9, 6.0 Hz, 1H), 1.52 – 1.37 (m, 4H), 1.11 – 0.97 (m, 30H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 143.2, 142.6, 132.9, 129.0, 127.4, 77.5, 62.8, 37.7, 32.4, 29.8, 27.0, 25.1, 18.0, 12.0.

(*E*)-2,2-dimethyl-4-(phenylsulfonyl)-9-((triisopropylsilyl)oxy)non-5-en-3-ol (13a). Prepared according to procedure C using β-hydroxy vinyl sulfone **13v** (0.08 g, 0.17 mmol). Compound **13a** was obtained as a colorless oil (0.053 g, 66%) and >20:1 mixture of diastereomers. *Spectral data for the major diastereomer:* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.76 (m, 2H), 7.65 – 7.58 (m, 1H), 7.53 (dt, *J* = 8.6, 6.9 Hz, 2H), 5.70 (ddt, *J* = 15.6, 9.7, 1.5 Hz, 1H), 5.27 (dt, *J* = 15.7, 6.8 Hz, 1H), 4.26 (s, 1H), 3.70 (d, J = 9.7 Hz, 1H), 3.56 (td, *J* = 6.4, 3.5 Hz, 2H), 2.85 – 2.73 (m, 1H), 1.99 (dddd, *J* = 14.7, 13.0, 10.6, 6.8 Hz, 2H), 1.44 – 1.34 (m, 2H), 1.12 – 0.97 (m, 21H), 0.91 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.4, 136.9, 133.6, 129.2, 128.7, 118.7, 74.0, 70.6, 62.6, 35.9, 31.8, 29.2, 26.5, 18.0, 11.9.

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