JOC*Note*

Second-Generation Synthesis of *syn*- and *anti*-Cycloheptadienylsulfone Polyketide Stereodiads

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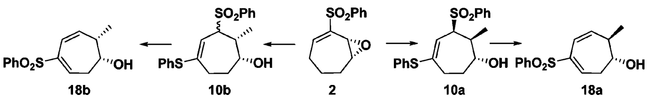
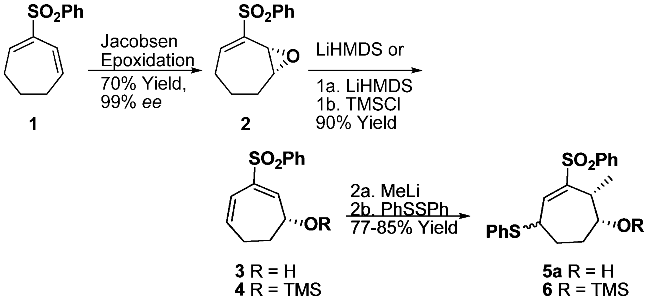


Stereodiad sulfones **18a** and **18b** are key intermediates for polyketide synthesis. This note describes the synthesis of **18a** and **18b** from enantiopure epoxide **2**. The two sequences have been optimized for large-scale synthesis to give 80−85% overall yields in one operation (one operation implies that no crystallization or distillation is required throughout the synthesis) while avoiding chromatography.

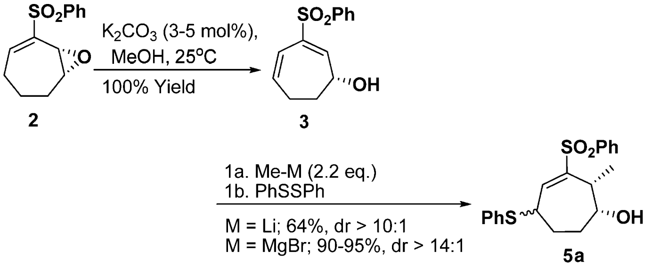
1. Diastereoselective Methylation/Epoxide Opening−Sulfenylation: 1.1. *syn*-Methylation−Sulfenylation. The *anti*- and *syn*-stereodiads **18a** and **18b** are pivotal intermediates of polypropionate segments for many synthetic targets in our laboratory. The first-generation synthesis of **18b** subjected achiral dienylsulfone **1**[1] to Jacobsen asymmetric epoxidation (now 1% catalyst loading)[2] to give epoxide **2** in good yield and very high enantiomeric excess (99%), both antipodes of **2** being equally accessible. Base-promoted isomerization of epoxide **2** afforded dienyl alcohol **3** or its TMS ether **4**, both in 90% yield. MeLi addition to vinylsulfones **3** or **4** resulted in anticipated OH-directed *syn*-selective methylation with the former and unusual TMSO-directed *syn*-selective methylation[3] with the latter. The resulting allyl sulfonyl anion was quenched with PhSSPh to give vinylsulfones **5a** and **6** in 77−85% yield (Scheme 1).

In the second-generation strategy, base-promoted isomerization of epoxide **2** to dienyl alcohol **3** was found to be quantitative employing 3−5 mol % of K_2CO_3/MeOH. As shown above, the lithiated oxido anion of **3** was known to direct methyllithium with superior stereocontrol than did substrate **4**, simultaneously avoiding deprotection of the TMS ether,[4] but only afforded **5a** in 64% yield and dr > 10:1 (Scheme 2).[2] Fortunately, favorable results with MeMgBr on other substrates[5] prompted its application to **3** resulting in a 90−95% yield of **5a** and dr > 14:1. It is worth mentioning that **5a** is initially received as an inseparable 3:1 diastereomeric mixture along with allylsulfone **10b** and epimers of **5a** and **10b** at the methyl position as judged by ^{1}H NMR. Thus, the 14:1 ratio was determined after transforming **5a** to dienylsulfone **18b**.

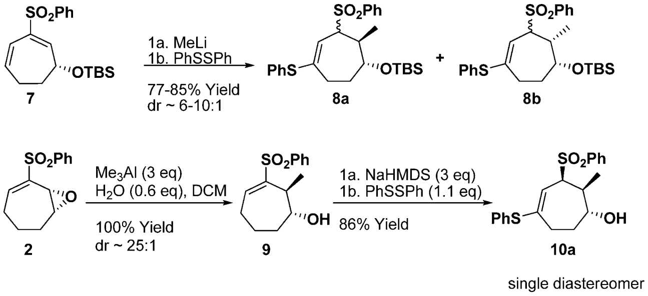
SCHEME 1. First-Generation *syn*-Selective Methylation-Sulfenylation



SCHEME 2. MeMgBr versus MeLi Addition to 3



SCHEME 3. First- versus Second-Generation Syntheses of *anti*-Diad 10a



1.2. *anti*-Methylation−Sulfenylation. The first-generation reaction of **7** with MeLi followed by PhSSPh resulted in a mixture of **8a** and diastereomer **8b** in ratios ranging from 6 to 10:1 (Scheme 3). Since $AlMe_3$ typically methylates cross-conjugated vinyl epoxides in an *anti* fashion,[6] reaction of epoxide **2** with $AlMe_3$ was investigated in the second-generation strategy, giving the *anti*-1,2-addition product **9** with 25:1 selectivity with respect to alternative *syn*-1,2- and 1,4-addition products (Scheme 3). Conversion of **9** to allylsulfone **10a** required O,C-dimetalation followed by PhSSPh quenching (sulfenylation). It was expected that the initial mixture of vinylsulfones obtained would need to be subsequently equilibrated to allylsulfone **10a** employing DBU. However, this reaction interestingly produced the "already equilibrated" allylsulfone **10a**. Crude **10a** contains residual PhSH/PhSSPh impurities that complicate large-scale reactions. A continuous

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(1) (a) Meyers, D. J.; Fuchs, P. L. *J. Org. Chem.* **2002**, *67*, 200. (b) Park, T.; Torres, E.; Fuchs, P. L. *Synthesis* **2004**, *11*, 1895.

(2) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063.

(3) Torres, E. Ph.D. Thesis, Purdue University, May 2004.

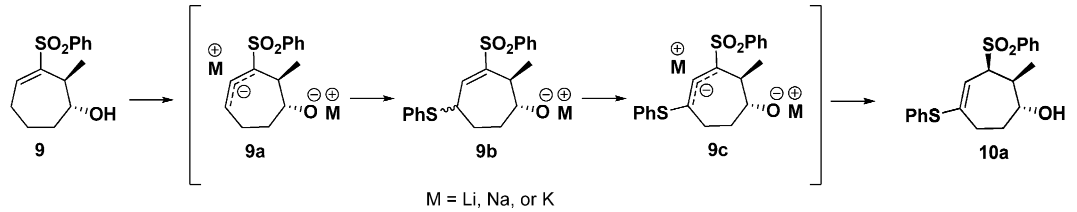
(4) See discussion in the Supporting Information.

(5) El-Awa, A. Ph.D. Thesis, Purdue University, 2007.

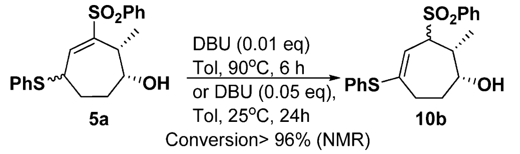
(6) Abe, N.; Hanawa, H.; Maruoka, K.; Sasaki, M.; Miyashita, M. *Tetrahedron Lett.* **1999**, *40*, 5369.

10.1021/jo702353e CCC: $40.75

SCHEME 4. In situ Equilibration in the *anti* Series



SCHEME 5. Optimized Vinylsulfone to Vinyl Sulfide Rearrangement



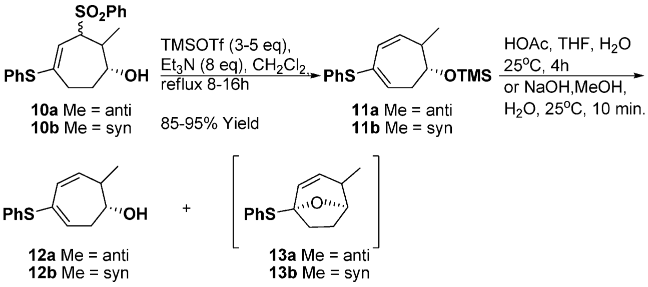
extraction employing CH_3CN/hexane was effective in completely removing these impurities on 30 g scale (Table 1 in Supporting Information).[7]

2. Vinyl Sulfone to Vinyl Sulfide Rearrangement. It is well-documented that vinylsulfones rearrange to allylsulfones under basic conditions.[8] While this equilibration occurs in the same step of sulfinylation for the *anti* series, it requires an additional step in the case of the *syn* series. In the *anti* series, treating epoxide **9** with base quantitatively forms dianion **9a**. Subsequent sulfenylation of **9a** affords vinylsulfone monoanion **9b** presumably as a diastereomeric mixture. Under the strongly basic conditions, **9b** is deprotonated to yield dianion **9c** which undergoes regio- and stereoselective quenching to **10a** upon workup (Scheme 4).

In contrast, in the *syn* series, the weakly basic[9] benzenethiolate anion requires ~3 days for complete equilibration. Hence, **5a** was isolated and subsequently treated with catalytic DBU[10] (0.05 equiv at ambient temperature for 1 day, or 0.01 equiv at 90 °C for 6 h), which effected almost quantitative conversion of **5a** to **10b** (Scheme 5). Crude **5a** contains a significant amount of PhSH. Attempting DBU equilibration of the crude mixture is difficult because the catalytic DBU is deactivated by the PhSH impurity. However, utilizing CH_3CN/hexane extraction on crude **5a** rendered it sufficiently pure to undergo the DBU equilibration without chromatographic purification.

3. Benzenesulfinic Acid Elimination. The secondary phenyl sulfone moiety is a poor nucleofuge.[11] Upon treatment with a strong base, the proton α to the sulfone is abstracted,[12] effectively preventing 1,2-elimination of the benzenesulfinate group.[13] However, in certain cases, base-promoted elimination of sulfones is possible.[14] Under E_1 elimination conditions, tertiary, allylic, and α-heteroatom-substituted sulfones can act as nucleofuges followed by proton abstraction or nucleophilic trapping.[15] Finally, allylsulfones are viable substrates for oxidative addition by metals to form π-allyl complexes,[16] which can be either attacked by a nucleophile or transformed to a diene in the presence of a base.[17]

SCHEME 6. First-Generation Elimination of Benzenesulfinic Acid



Compounds **10a** and **10b** are allylic sulfones bearing a vinylogous γ-heteroatom and the first-generation reaction with excess TMSOTf and Et_3N produces dienyl sulfides **12a** and **12b** in high yield after desilylation.[4] However, the expense of TMSOTf prompted a search for more economical elimination conditions. Moreover, the original conditions afforded silyloxy dienyl sulfides **11a** and **11b** requiring an additional deprotection step. Desilylation could be performed employing $HOAc/THF/H_2O$ or $NaOH/MeOH/H_2O$. While $NaOH/MeOH/H_2O$ requires 10 min for completion and does not produce any side products, $HOAc/THF/H_2O$ requires 4 h and gives a significant amount of cyclized products **13a** and **13b** (Scheme 6). In the second-generation strategy, aluminum-based Lewis acids were used. Initially, treating **10a** or **10b** with $AlCl_3/Et_3N$ in CH_2Cl_2 for 12−18 h afforded **12a** or **12b** in 70−78% yield.[18] Technical difficulties associated with $AlCl_3$

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(7) Table 1 in the Supporting Information describes detailed optimization for dianion formation−sulfenylation reaction of **9** to **10a**.

(8) (a) O'Connor, D. E.; Lyness, W. I. *J. Am. Chem. Soc.* **1964**, *86*, 3840. (b) Inomata, K.; Hirata, T.; Suhara, H.; Kinoshita, H.; Kotake, H.; Senda, H. *Chem. Lett.* **1988**, 2009. (c) Ozawa, M.; Iwata, N.; Kinoshita, H.; Inomata, K. *Chem. Lett.* **1990**, 1689. (d) Short, K. M.; Ziegler, C. B., Jr. *Tetrahedron Lett.* **1995**, *36*, 355. (e) Nakamura, T.; Guha, S. K.; Ohta, Y.; Abe, D.; Ukaji, Y.; Inomata, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 2031.

(9) The pK_a of benzene thiol is ca. 10 in DMSO and 6.5 in H_2O; see: Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224.

(10) The pK_a of DBU is ca. 12 in DMSO; see: Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183; Evans, D. A. Evans pK_a table http://daecr1.harvard.edu/ (April 2007); DBU or the 13000 times stronger P_2-Et phosphazene base are highly effective at promoting prototropic equilibration of simple 5−7 ring vinylsulfones (Jin, Z.; Kim, S. H.; Fuchs, P. L. *Tetrahedron Lett.* **1996**, *37*, 5247).

(11) Coulter, A. K.; Miller, R. E. *J. Org. Chem.* **1971**, *36*, 1898.

(12) The pK_a of the proton on the α carbon to a sulfone is ca. 29 in DMSO; see: Evans, D. A. Evans pK_a table http://daecr1.harvard.edu/ (April 2007).

(13) An exception is the case of *tert*-sulfones, especially in presence of a γ,δ-unsaturation. See: (a) Hamann, P. R.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 914. (b) Fuchs, P. L.; Braish, T. F. *Chem. Rev.* **1986**, *86*, 903.

(14) Trost, B. M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107.

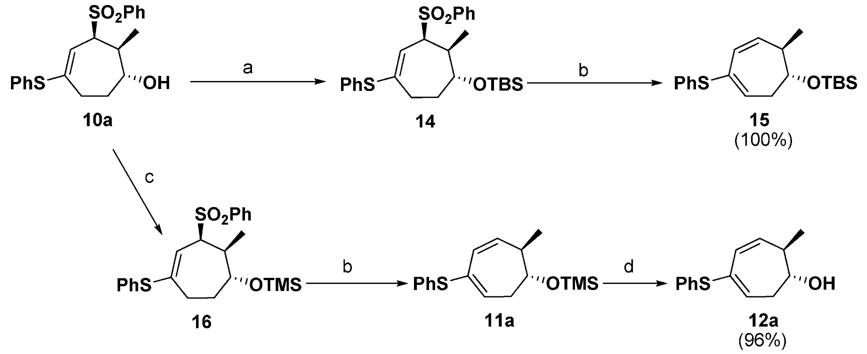
(15) (a) Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 7260. (b) Brown, D. S.; Bruno, M.; Davenport, R. J.; Ley, S. V. *Tetrahedron* **1989**, *45*, 4293. (c) Brown, S. D.; Hansson, T.; Ley, S. V. *Synlett* **1990**, 48. (d) Brown, S. D.; Carreau, P.; Ley, S. V. *Synlett* **1990**, 749. (e) Trost, B. M.; Ghadiri, M. R. *Bull. Soc. Chim. Fr.* **1993**, *130*, 433. (f) Ghosh, A. K.; Liu, C. *J. Am. Chem. Soc.* **2003**, *125*, 2374 and ref 15.

(16) (a) Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5979. (b) Trost, B. A.; Merlic, C. A. *J. Org. Chem.* **1990**, *55*, 1127 and ref 15.

(17) Such elimination reactions are precedented. See for example: Suzuki, S.; Fujita, Y.; Nishida, T. *Tetrahedron Lett.* **1983**, *24*, 5737 and ref 17.

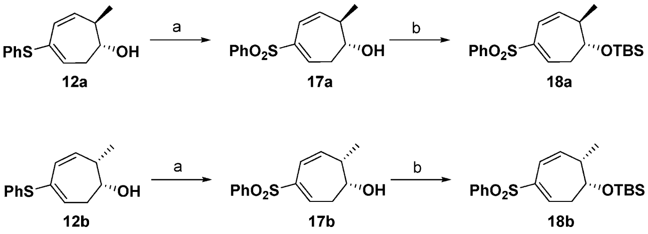
(18) See Supporting Information (Table 2, optimization of $AlCl_3/Et_3N$ elimination of benzenesulfinic acid).

SCHEME 7. Second-Generation Desulfonylation of Silyl Ethers 14 and 16[a]



[a] Conditions: (a) TBSOTf (1.1 equiv), 2,6-lutidine (1.5 equiv), CH_2Cl_2; (b) i-Pr_2NEt (3 equiv), $AlMe_3$ (2.2 equiv), −78 to 25 °C, 45 min; (c) HMDS (0.5 equiv), I_2 (0.01 equiv), CH_2Cl_2, 25 °C, 10 min; (d) 10% NaOH/MeOH.

SCHEME 8. Oxidation/TBS Protection of 12a and 12b[a]



[a] Conditions: (a) 30% H_2O_2 (2 equiv), Na_2WO_4 (0.02 equiv), $PhP(O)(OH)_2$ (0.02 equiv), $Oct_3MeNHSO_4$ (0.02 equiv), toluene, 0 to 25 °C, 3 h; (b) TBSOTf (1.1 equiv), Et_3N (2 equiv), CH_2Cl_2, 0 to 25 °C, 2 h (yields are quantitative for Noyori's oxidation and −OTBS protection).

(especially on large scale)[19] led to further optimization employing $AlMe_3$/i-Pr_2NEt in CH_2Cl_2 for 45 min, giving **12a** or **12b** in >90% yield. TMS or TBS protection of **10a** afforded the desired dienyl sulfides **12a** and **15** in 96 and 100% overall yields (from **10a**), respectively (Scheme 7).[20]

4. Dienyl Sulfide to Dienyl Sulfone Oxidation/TBS Protection. The final hurdle in the second-generation syntheses of **18a** and **18b** is the oxidation of dienyl sulfides to **17a** and **17b**. The difficulty arises because many oxidants cannot selectively oxidize a sulfoxide to a sulfone in the presence of an olefin bearing a free alcohol.[21] The first-generation reaction relied on stoichiometric MCPBA as an oxidant, which indeed provided unwanted epoxidation. On the basis of successful results from the optimized synthesis of **1**, Noyori's catalyst system was initially investigated in the second-generation strategy.[22] This protocol was well-suited to this transformation and afforded **17a** and **17b** in 90−100% yield from **12a** and **12b**, respectively. Subsequent TBS protection of **17a** and **17b** quantitatively delivered **18a** and **18b** (Scheme 8).[10]

Experimental Section[23]

Preparation of *syn*-Cycloheptadienylsulfone 18b. Chromatographically purified dienyl alcohol **3** (1.04 g, 4.2 mmol) was azeotropically dried with toluene (2 × 30 mL) followed by addition of THF under Ar, and the resultant light yellow solution was cooled to −70 °C. MeMgBr (6.4 mL, 8.9 mmol, 1.4 M in tol/THF = 3:1) was added at once, and the dry ice bath was immediately removed. As the reaction warmed to 25 °C, its color changed to deep orange.[24] After vigorous stirring for 1 h at 25 °C, PhSSPh (1.3 g, 5.9 mmol) was added via a solids addition arm,[25] and the reaction was stirred for an additional hour[26] and then quenched by addition of 5% HCl (10 mL). The crude reaction mixture was transferred to a separatory funnel; 40 mL of water was added, and the mixture was extracted with ether (2 × 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and purified by flash column chromatography (hex/EtOAc = 2:1 to hex/EtOAc = 1:1) to give 1.49 g (95%) of **5a** (as an inseparable 3:1 mixture of epimers)[27] as a light yellow oil. This procedure was repeated successfully on 10 g of **3**, quantitatively affording **5a**. Continuous extraction employing CH_3CN/hexane (see preparation of **10a**) is necessary before the next transformation.

DBU (24 μL, 0.16 mmol)[28] was added to a solution of **5a** (1.18 g, 3.2 mmol) in toluene (13 mL) and stirred at 110 °C.[29] The reaction color changed from light yellow to dark brown a few minutes after addition of the DBU. After 4 h, the reaction mixture was cooled to 25 °C and concentrated by rotary evaporation followed by vacuum drying to give 1.18 g (100%) of **10b** as a dark brown oil. ^1H NMR analysis of the crude mixture showed two components in ca. 2:1 ratio.[30] For analytical purposes, an enriched sample of each component was obtained by flash column chromatography (hex/EtOAc = 2:1 → hex/EtOAc = 3:2) and are named here as **10b-A** and **10b-B**.[31] This procedure was repeated successfully on 10 g of **5a**, quantitatively affording **10b**.

Vinyl sulfide **10b** (10 g, 26.7 mmol) was dissolved in CH_2Cl_2 (90 mL) and treated with HMDS (3.34 mL, 16.0 mmol) and I_2 (68 mg, 0.27 mmol). The reaction was stirred at 25 °C for 10 minutes then i-Pr_2NEt (13.9 mL, 80.1 mmol) was added. The mixture was

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[19] See detailed discussion in Supporting Information.

[20] See Supporting Information (Table 3, optimization of $AlMe_3$/$i$$Pr_2$-NEt elimination of benzenesulfinic acid).

[21] See for example: (a) Schultz, S. H.; Freyermuth, H. B.; Buc, S. R. *J. Org. Chem.* **1963**, *28,* 1140. (b) Charette, A. B.; Berthelette, C.; St-Martin, D. *Tetrahedron Lett.* **2001**, *42*, 5149. (c) Sivaramakrishnan, A.; Nadolski, G. T.; McAlexander, I. A.; Davidson, B. S. *Tetrahedron Lett.* **2002**, *43*, 213.

[22] (a) Sato, K.; Hyodo, M.; Aoki, M.; Zheng, X.; Ryoji, N. *Tetrahedron* **2001**, *57*, 2469. (b) Noyori, R.; Aoki, M.; Sato, K. *Chem. Commun.* **2003**, 1977.

[23] See Supporting Information for detailed experimental and characterization data.

[24] If crude **3** is used for the reaction, its THF solution is colored orange and no color change is observed upon MeMgBr addition.

[25] PhSSPh can also be added via cannula as a THF solution with similar reaction outcome.

[26] Stirring for longer than 1 h after PhSSPh should be avoided as the desired product starts to decompose.

[27] Other minor isomers co-elute with **5a**, which include **10b** and epimers of **5a** and **10b** at the Me position. Because of that, the reported 14:1 diastereoselectivity of the reaction is determined after conversion to dienylsulfone **18b**.

[28] Runs of this reaction with as low as 1 mol% of DBU were equally successful.

[29] Running the reaction for 24 h at 100 °C resulted in intramolecular addition of the alcohol group to the vinylsulfone.

[30] That both components were converted to **10b** indicates that they are epimeric at the vinylsulfone position.

[31] **10b-A** is the component with higher R_f, and **10b-B** is the one with lower R_f.

then cooled to −78 °C for 10 minutes and 25% AlMe$_3$ in hexanes (23.5 mL, 58.7 mmol) was added dropwise at −78 °C then the dry ice bath was immediately removed. The reaction was stirred at 25 °C for 45 minutes and the reaction was checked for completion by TLC (50% ethyl acetate/hexanes). The reaction was then carefully poured into a beaker containing 10% NaOH (50 mL/ice). The reaction flask was washed with CH$_2$Cl$_2$ (2 × 10 mL) and the washings were added to the beaker then the mixture was stirred at 25 °C for 30 minutes. MeOH (50 mL) was added to give a homogenous phase, and the reaction was stirred for 30 min. Brine (100 mL) was added, the aqueous phase was discarded, and the organic phase was washed with brine (100 mL) containing 5% HCl (60 mL, 82.2 mmol) to remove *i*-Pr$_2$NEt. The mixture was then carefully neutralized with 5% HCl using phenolphthalein as indicator. The organic phase was separated, dried over Na$_2$SO$_4$, and then concentrated via rotary evaporation to give a crude yellow oil.[32] After celite-pad filtration, the crude oil was submitted to Noyori oxidation as described below to give sulfone **17b** as a yellow oil (6.8 g, 96%). The ^{1}H NMR of the crude material was clean enough for the next transformation.

EtOAc (270 mL) was added to crude[33] **12b** (18.8 g, 0.081 mol) and stirred under air to give a brown solution. Na$_2$WO$_4$ (2 mL, 4 mmol, 1 M in H$_2$O), PhP(O)(OH)$_2$ (2 mL, 4 mmol, 1 M in H$_2$O), MeOct$_3$NHSO$_4$ (4 mL, 4 mmol, 0.5 M in tol), and H$_2$O$_2$ (28 mL, 0.24 mol, 30% in H$_2$O) were added to the above solution and vigorously stirred at 25 °C. After 4 h, the reaction was judged complete by TLC,[34,35] and the mixture was transferred to a separatory funnel, and brine (200 mL) was added. The aqueous layer was extracted with ether (2 × 100 mL), and the combined organic layers were washed with saturated Na$_2$SO$_3$ solution, dried over Na$_2$SO$_4$, and concentrated via rotary evaporation to give **17b** as an orange oil. The crude oil was purified by flash column chromatography (hex/EtOAc = 1:1 → hex/EtOAc= 2:3) to give 14 g (65% overall yield) of **17b** as a light yellow viscous oil.[36] TLC (50% ethyl acetate/hexanes) R_f 0.39. Silylation of **17b** as previously described provides a quantitative yield of *syn*-stereodiad **18b**.

Preparation of *anti*-Cycloheptadienylsulfone 18a. A solution of 25% AlMe$_3$ in hexanes (30 mL, 60 mmol) in dry CH$_2$Cl$_2$ (50 mL) was cooled to −20 °C for 30 min, then DI−H$_2$O (216 μL, 12 mmol) was added dropwise and very carefully over 30 min. The dry ice bath was removed, and the reaction was stirred for 1 h. Solid epoxide **2** (5 g, 20 mmol) was added in portions, and the reaction was stirred at 25 °C for 40 min. Reaction was checked for completion using TLC (50% ethyl acetate/hexanes), then the reaction mixture was cooled again to −40 °C for 30 min. Careful dropwise addition of aq 10% NaOH (until CH$_4$ gas evolution stopped) was followed by adding aq 10% NaOH (50 mL), then the mixture was allowed to stir at 25 °C for 30 min (alternatively, pouring the cold reaction on 10% NaOH/ice is more convenient and safer). The organic phase was separated, washed with brine (50 mL), dried over Na$_2$SO$_4$, then concentrated via rotary evaporation to afford a crude yellowish oil (dr 25:1). Purification by flash column chromatography (20% ethyl acetate/hexanes) afforded **9** as a colorless oil (4.9 g, 93%). Crystallization from ether gave **9** as white prisms (3.2 g, 60%). Mp 74.8−75.4 °C. TLC (50% ethyl acetate/hexanes) R_f 0.26.

A solution of alcohol **9** (30 g, 120 mmol) in THF (300 mL) was cooled to −78 °C for 30 min, then 2 M NaHMDS in THF (180 mL, 360 mmol) was added dropwise over 10 min to give a clear yellow solution that eventually turned into a deep red clear solution. The dry ice bath was removed, and the mixture was stirred at 25 °C for 4 h to give a bright orange suspension. Reaction is checked for complete dianion formation using TLC (50% ethyl acetate/hexane). Dianion **9a** quantitatively quenches on TLC to produce allyl sulfone **20** and does not return any vinyl sulfone **9** (see Supporting Information). A solution of PhSSPh (26.4 g, 120 mmol) in THF (120 mL) was added via cannula at 25 °C to the reaction mixture where the orange suspension dissolves and re-forms immediately. After stirring for 1 h, reaction was quenched with 5% HCl (300 mL) and diluted with ether (300 mL). Five percent HCl (300 mL) was added, and the mixture was stirred for 1 h. After discarding the aqueous phase, a solution of K$_2$CO$_3$ (168 g, 1.2 mol) in DI−H$_2$O (600 mL) was added and the mixture was stirred at 25 °C for another 1 h. Organic phase was separated, washed with brine, and dried over Na$_2$SO$_4$ for 2 h. Concentration of the organic phase via rotary evaporation afforded **10a** as a brown oil.

Continuous Extraction Purification of 10a. The brown oil from above was dissolved in CH$_3$CN (300 mL) and was transferred to a 6840 continuous extraction apparatus (ACE Glass Catalog 2005 p. 150) that was fitted with an overhead condenser and a side arm 500 mL round-bottom flask. Hexane (400 mL) was added to give a biphasic system where the lower layer was the CH$_3$CN layer (clear, brown) and the upper was the hexane layer (clear, colorless). The inner glass tube was filled completely with hexanes and inserted into the extractor. The side arm flask containing hexanes was placed in an oil bath and was heated at 80 °C. The extraction was continued for 10 h during which time the hexane layer turns yellow and the color is gradually transferred to the side arm flask. After cooling the system to 25 °C, the CH$_3$CN phase was separated and concentrated via rotary evaporation to give highly pure (as checked by ^{1}H NMR) vinyl sulfide **10a** as a brown oil. Crystallization from boiling ether afforded **10a** as tan crystals (72%). Repeating the above procedure employing alcohol **9** (1.0 g, 4 mmol) followed by purification via flash column chromatography (20% ethyl acetate/hexanes) afforded **10a** as a yellowish crystalline solid (1.28 g, 86%). Mp range 114.4−117.8 °C; TLC (50% ethyl acetate/hexanes) R_f 0.5. Elimination of **10a** to **12a**, oxidation to **17a**, and silylation to **18a** was carried out as with **18b** (see Supporting Information for the detailed experimental procedure).

Acknowledgment. We are grateful to Dr. Douglas Lantrip for his intellectual and technical support. We acknowledge Arlene Rothwell and Karl Wood for providing the MS data. M.N. deeply thanks Nelson Vinueza for technical support. We thank Dr. Phillip Fanwick for providing the crystal structure data.

Supporting Information Available: Detailed discussion, detailed experimental procedures, schemes, optimization tables, ^{1}H NMR, ^{13}C NMR, X-ray, and MS data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(32) The celite-pad filtration step is performed to eliminate Cl$^-$ ions from the product as they inhibit the catalyst used in the subsequent oxidation step.

(33) **12b** must be purified from any traces of halide ions as they inhibit the Na$_2$WO$_4$ catalyst used in this reaction.

(34) The reaction time may vary due to the possible presence of trace halide ions.

(35) The reaction starts as a dark brown solution and slowly changes to a yellowish orange solution, which usually signifies complete conversion.

(36) Because of the high viscosity of **17b**, it is more accurate to determine the yield after conversion to TBS derivative **18b**.