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Nucleophilic Epoxidation of α′-Hydroxy Dienyl Sulfoxides

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A novel route to enantiopure densely functionalized epoxy sulfinyl tetrahydrofurans, based on the unexpected and highly stereoselective remote nucleophilic epoxidation of hydroxy 1-sulfinyl butadienes with *t*-BuOOK, followed by ring closure and subsequent epoxidation of the resulting sulfinyl dihydrofurans, is described. Alternatively, the treatment of these dienes with *m*-CPBA followed by acid-catalyzed cyclization gives rise to related sulfonyl dihydrofurans in high yields but with low selectivity. The stereochemical outcome of the nucleophilic epoxidation of these substrates has also been studied.

Introduction

The nucleophilic epoxidation of simple vinyl sulfoxides is a general and efficient route to enantiopure sulfinyl and sulfonyl oxiranes,[1] versatile synthetic intermediates.[2] For a number of years we have been engaged in an in-depth study of the scope of this unique process. Our initial survey of the epoxidation of vinyl sulfoxides bearing additional oxygenated substituents at allylic positions indicated that the selectivity of the process was primarily controlled by the chiral sulfur center.[3] Subsequent detailed studies have revealed that this control by sulfur was not always operative,[4] but at the time, and seeking to apply our methodology to the preparation of carbohydrate fragments, we considered that the nucleophilic epoxidation of hydroxy dienyl sulfoxides, **A** (Scheme 1), should produce oxiranes **B**, adequate precursors of carbohydrates by simple manipulations.[5] At this stage we realized that the 1,4 conjugate addition pathway could be operative to some extent,[6] but we considered that it would just result in diminished yields. On the other hand, if this 1,4-pathway were selective, which was perceived as unlikely, oxiranes **C** could be produced and this could outline a simple entry to the tetrahydrofuran core, an ubiquitous building block for bioactive products.[7] In this report we describe in full our studies on the development of a novel strategy for the expedient preparation of highly substituted tetrahydrofurans **D** from hydroxy sulfinyl dienes **A**. This unexpected process takes place primarily by an unusually selective remote nucleophilic epoxidation of dienes **A** followed by ring closure of vinyl sulfinyl

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(2) For a review on the preparation and applications of α-oxy sulfones, including sulfonyl oxiranes, see: (a) Chemla, F. *J. Chem. Soc., Perkin Trans. 1* **2002**, 275−299. For other reviews on aspects of the synthesis and reactivity of sulfinyl and sulfonyl oxiranes, see: (b) Satoh, T.; Yamakawa, K. *Synlett* **1992**, 455−468. (c) Satoh, T. *Chem. Rev.* **1996**, *96*, 3303−3325. For recent references on applications of sulfinyl and sulfonyl oxiranes, see: (d) Mori, Y.; Hayashi, H. *J. Org. Chem.* **2001**, *66*, 8666−8668. (e) Satoh, T.; Taguchi, D.; Kurabayashi, A.; Kanoto, M. *Tetrahedron* **2002**, *58*, 4217−4224. (f) Mori, Y.; Hayashi, H. *Tetrahedron* **2002**, *58*, 1789−1797. (g) Mori, Y.; Yaegashi, K.; Furukawa, H. *J. Am. Chem. Soc.* **1996**, *118*, 8158−8159. (h) Mori, Y.; Yaegashi, K.; Furukawa, H. *J. Am. Chem. Soc.* **1997**, *119*, 4557−4558. (i) For a recent application of these building blocks within synthetic studies toward Yessotoxin and Adriatoxin, see: Mori, Y.; Takase, T.; Noyori, R. *Tetrahedron Lett.* **2003**, *44*, 2319−2322.

(3) Fernández de la Pradilla, R.; Manzano, P.; Priego, J.; Viso, A.; Martínez-Ripoll, M.; Rodríguez, A. *Tetrahedron Lett.* **1996**, *37*, 6793−6796.

(4) Fernández de la Pradilla, R.; Fernández, J.; Manzano, P.; Méndez, P.; Priego, J.; Tortosa, M.; Viso, A.; Martínez-Ripoll, M.; Rodríguez, A. *J. Org. Chem.* **2002**, *67*, 8166−8177.

(5) For reviews on the synthesis of carbohydrate derivatives from acyclic precursors, see: (a) Ager, D. J.; East, M. B. *Tetrahedron* **1993**, *49*, 5683−5765. (b) Ager, D. J.; East, M. B. *Tetrahedron* **1992**, *48*, 2803−2894. We subsequently developed an alternative route to vinyl oxiranes related to **B**; see: Fernández de la Pradilla, R.; Méndez, P.; Priego, J.; Viso, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1247−1249.

(6) For 1,4-additions of lithiated protected cyanohydrins to a dienyl sulfoxide, see: (a) Guittet, E.; Julia, S. *Tetrahedron Lett.* **1978**, *37*, 1155−1158. (b) Guittet, E.; Julia, S. *Synth. Commun.* **1981**, *11*, 697−708. (c) Guittet, E.; Julia, S. *Synth. Commun.* **1981**, *11*, 709−722.

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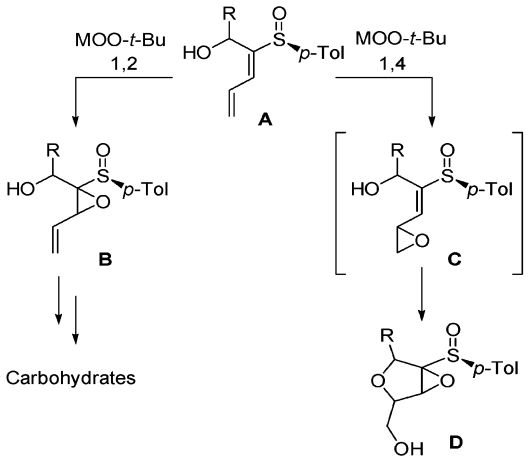
SCHEME 1



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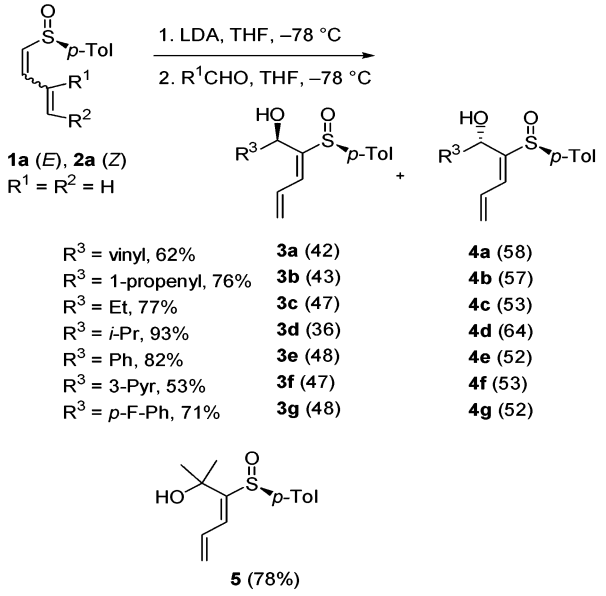


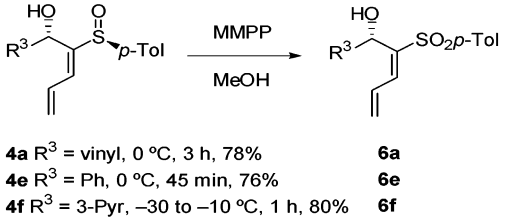
oxiranes **C**, and a second nucleophilic epoxidation of the resulting sulfinyl dihydrofurans in a single synthetic operation.

Preparation of Starting Materials

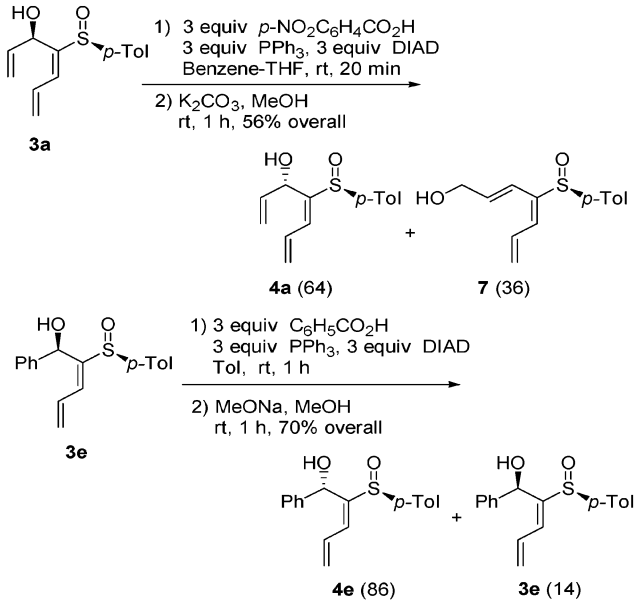
Scheme 2 shows the preparation of a number of dienols **3a**−**g** and **4a**−**g**, obtained by lithiation of the mixture of dienes **1a**−**2a**, available in one step by the method of Craig,[8] and reaction with a variety of aldehydes followed by chromatographic separation.[9,10] To explore the behavior of some dienyl sulfones in this process, dienes **4a** and **4e** were oxidized smoothly under standard conditions (MMPP, Scheme 3). Pyridine-containing substrate **4g** required carefully controlled reaction conditions to prevent substantial overoxidation to the corresponding *N*-oxide from taking place (see Supporting Information for details).

To enhance the efficiency of this methodology, the transformation of the "unreactive" diastereomers **3** (see

SCHEME 3



SCHEME 4



below) into the "reactive" diastereomers **4** was explored. Initially we intended to carry out a nucleophilic substitution with KO_2 on the mesylate of **3a** (Scheme 4);[11] however, the use of MsCl/Et_3N resulted in S_N2' displacement by chloride to produce a conjugated trienyl chloride related to **7**. The use of Ms_2O with a number of different bases (Et_3N, pyr, DBU) gave exclusively the mesylate of trienol **7**, presumably due to conjugate addition of methanesulfonate anion to the mesylate of **3a**. We then turned our attention to the Mitsunobu protocol using *p*-$NO_2C_6H_4CO_2H$,[12] followed by deprotection of the *p*-nitrobenzoate. Under these conditions, (Scheme 4) still a substantial

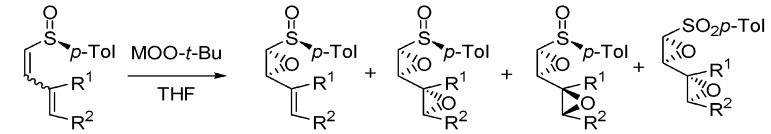
(8) Craig, D.; Daniels, K.; McKenzie, A. R. *Tetrahedron* **1993**, *49*, 11263−11304.

(9) Lithiation of *Z* vinyl sulfoxides with organolithium reagents and LDA yields *E* lithio derivatives. Substantial racemization was reported for the lithiation of *Z* vinyl sulfoxides with organolithium reagents, see: (a) Posner, G. H. In *Asymmetric Reactions and Processes in Chemistry*; Eliel, E. L., Otsuka, S., Eds.; ACS Symp. Ser. No. 185; American Chemical Society: Washington, DC, 1982; p 142. (b) Fawcett, J.; House, S.; Jenkins, P. R.; Lawrence, N. J.; Russell, D. R. *J. Chem. Soc., Perkin Trans. 1* **1993**, 67−73. We have measured the optical rotations of a variety of *E* vinyl and dienyl sulfoxides arising from the lithiation of *Z* isomers (LDA, −78 °C) and we did not find significant differences with the rotations of the pure *E* isomers derived from Horner−Emmons procedures. For a recent report on the intramolecular alkylation of α-sulfinyl vinyl carbanions, see: (c) Maezaki, N.; Izumi, M.; Yuyama, S.; Sawamoto, H.; Iwata, C.; Tanaka, T. *Tetrahedron* **2000**, *56*, 7927−7945.

(10) All new products have been fully characterized. See the Supporting Information. The stereochemical assignment for dienols **3** and **4** is based on careful comparison of their ^1H and ^{13}C NMR data, as well as chromatographic behavior with the data of a series of related compounds, one of which was characterized by X-ray crystallography, see: Marino, J. P.; Viso, A.; Lee, J.-D.; Fernández de la Pradilla, R.; Fernández, P.; Rubio, M. B. *J. Org. Chem.* **1997**, *62*, 645−653.

(11) Corey, E. J.; Nicolau, K. C.; Shibashaki, M.; Machida, Y.; Shiner, C. S. *Tetrahedron Lett.* **1975**, 3183−3186.

TABLE 1. Nucleophilic Epoxidation of Simple Sulfinyl Dienes



1a (1*E*), $R^1 = R^2 = H$ **8** **9** **10** **11**
2a (1*Z*), $R^1 = R^2 = H$
2b (1*Z*), $R^1 = H$, $R^2 = Me$
2c (1*Z*), $R^1 = Me$, $R^2 = H$

entry	substrate	conditions	**8**[a]	**9**[a]	**10**[a]	**11**[a]	yield,[b] %
1	**1a**	2 equiv of KOO-*t*-Bu, 4 °C, 22 h					decomp
2	**2a**	2 equiv of NaOO-*t*-Bu, 0 °C, 4 h					NR
3[c]	**2a**	2 equiv of KOO-*t*-Bu, 0 °C, 10 min	**8a** (64)	**9a** (28)	**10a** (8)		10
4[d]	**2a**	1 equiv of KOO-*t*-Bu, −78 to 0 °C, 35 min	**8a** (9)	**9a** (76)	**10a** (15)		36
5[e]	**2a**	2 equiv of KOO-*t*-Bu, −20 to 0 °C, 1 h	**8a** (60)	**9a** (33)	**10a** (7)	traces	50
6[f]	**2b**	2 equiv of KOO-*t*-Bu, −20 to 0 °C, 135 min		**9b** (70)		**11b** (30)	ND
7	**2c**	3 equiv of KOO-*t*-Bu, −20 to 0 °C, 90 min	**8c**				56

[a] Stereochemical assignments are tentative. [b] Yields of pure products after column chromatography. [c] Reaction proceeded to ca. 30% conversion. [d] Reaction proceeded to ca. 71% conversion. [e] Reaction proceeded to ca. 91% conversion. [f] Reaction proceeded to ca. 51% conversion.

amount of trienol **7** was obtained. After some optimization, dienol **3e** gave more satisfactory results affording an 86:14 mixture of **4e** and **3e** in good yield.

Epoxidation of Simple Sulfinyl Dienes

Having established the viability and reproducibility of the first few examples of this methodology,[13] which, for clarity, will be discussed below, we chose to explore briefly the reactivity of simple sulfinyl dienes under these conditions to establish if these simpler substrates could also undergo a stereoselective remote epoxidation and the results obtained are gathered in Table 1. The simplest 1*E* diene, **1a**, gave no reaction at short times or under more forcing conditions delivered a complex reaction mixture with substantial decomposition (Table 1, entry 1). In contrast, 1*Z* isomer **2a** rapidly gave a low yield of a mixture of 1,2 monoepoxide **8a** and bisepoxides **9a** and **10a**, along with recovered starting material (entry 3). Entries 4 and 5 indicate that the outcome of the reaction is highly dependent on the temperature with low temperatures favoring initial remote epoxidation followed by a second 1,2 epoxidation. It should be pointed out that all stereochemical assignments for these products (**8**−**11**) are tentative, particularly those of the bisepoxides. In view of our lack of success with the 1*E* isomer **1a**, the rest of this exploratory study was carried out on the *Z* isomers. Thus, quite to our surprise, diene **2b**, bearing a substituent at C-4, gave a 70:30 mixture of sulfinyl and sulfonyl bisepoxides **9b** and **11b** both as single isomers. Finally, diene **2c**, bearing a substituent at C-3, gave exclusively monoepoxide **8c** derived from 1,2-attack. The results obtained in this quick survey indicate that, in some cases, simple 1*Z* sulfinyl dienes can undergo a selective remote epoxidation, followed by a second 1,2 epoxidation under the reaction conditions.

(12) (a) Martin, S. F.; Dodge, J. A. *Tetrahedron Lett.* **1991**, *32*, 3017−3020. For reviews, see: (b) Hughes, D. L. *Org. React.* **1992**, *42*, 335−668. (c) Hughes, D. L. *Org. Prep. Proced. Int.* **1996**, *28*, 127−164.

(13) For a preliminary communication, see: Fernández de la Pradilla, R.; Montero, C.; Priego, J.; Martínez-Cruz, L. A. *J. Org. Chem.* **1998**, *63*, 9612−9613.

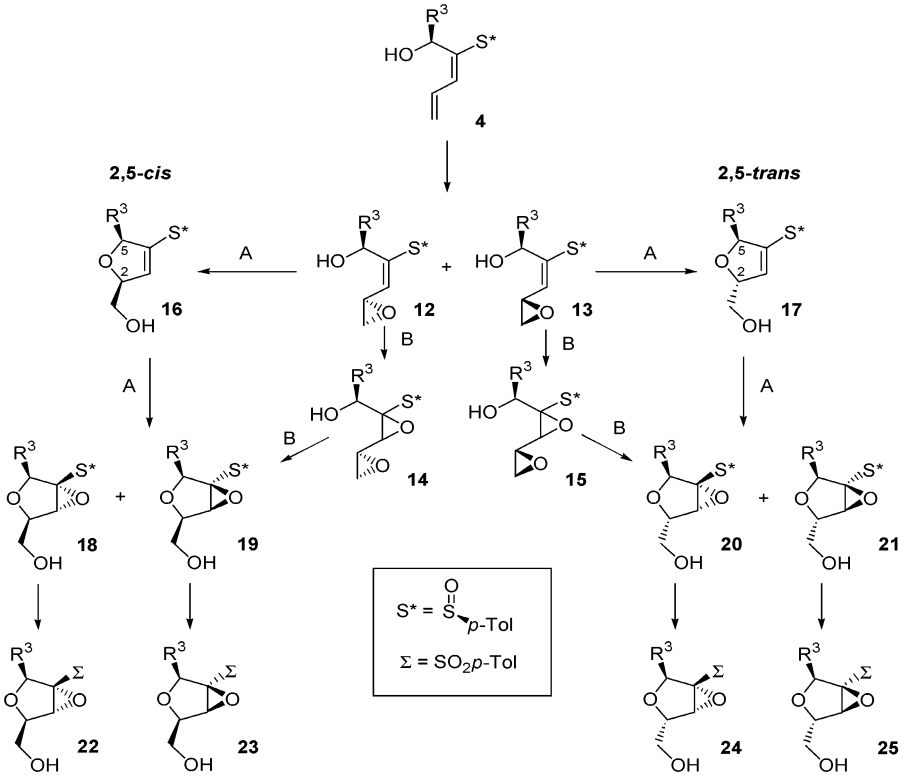
Synthesis of Tetrahydrofurans from Hydroxy Sulfinyl and Sulfonyl Dienes

The initial stage of our investigation was carried out on dienol **3a** that was found to be very unreactive to the standard conditions, and under forcing conditions led to intractable mixtures of products that were not investigated in detail. In sharp contrast, diastereomeric dienol **4a** reacted with KOO-*t*-Bu to afford a low yield of a sulfinyl tetrahydrofuran. Scheme 5 gathers the majority of intermediates and products that we considered reasonable for this complex tandem process. We believed the process to commence by a remote nucleophilic epoxidation affording monoepoxides **12** and **13**. At this point two distinct pathways were considered reasonable. Pathway A (Scheme 5) entails a 5-*exo*-trigonal cyclization leading to sulfinyl dihydrofurans **16** or **17** respectively followed by a second nucleophilic epoxidation to sulfinyl tetrahydrofurans **18**−**21** which under the reaction conditions could undergo a facile oxidation at sulfur to some extent to afford sulfonyl tetrahydrofurans **22**−**25**. On the other hand, pathway B entails a second epoxidation on monoepoxides **12** and **13** to produce bisepoxides **14** and **15** that would undergo a base-promoted 5-*exo*-trigonal cyclization to sulfinyl tetrahydrofurans **18**−**21**.[14] It should be noted that both pathways could be operative simultaneously leading to diastereomeric products due to the presumably different stereochemical outcome of the second nucleophilic epoxidation that takes place on different substrates.

With these considerations in mind, we set out on a detailed study of this complex and unexpected process with the goals of trying to isolate reaction intermediates to shed some light on the reaction pathway while, if possible, improving the yields of the process and testing the scope of the methodology. The results obtained are shown in Table 2. It should be pointed out that in many cases the substantial complexity of the process has rendered the ratios reported below just approximate; in

(14) Baldwin, J. E. *Chem. Commun.* **1976**, 734−736.

SCHEME 5



addition, this methodology is very dependent on the precise reaction conditions used, including reaction temperature, stoichiometry, and reaction time.

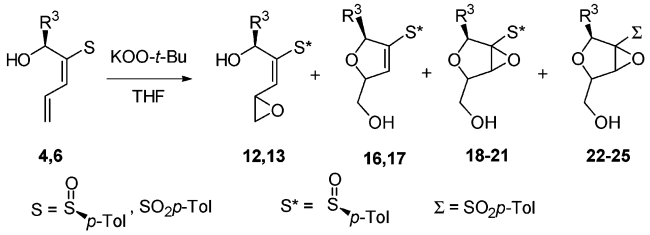
At short reaction times (10 min), a small amount of monoepoxide **12a** (7%) was isolated from the reaction between **4a** and KOO-*t*-Bu (Table 2, entry 1). Similarly, the use of 0.85 equiv of reagent gave a small amount (ca. 10%) of sulfinyl dihydrofuran **16a** (entry 2) that was epoxidized under standard conditions to produce an 85:15 mixture of **18a** and **22a** (entry 3). These findings support pathway A (Scheme 5) as a reasonable sequence of events for these processes. After considerable experimentation, it was determined that for **4a** optimal results could be obtained by slowly adding a THF solution of the substrate to a cold (−20 °C) THF solution of KOO-*t*-Bu, allowing the reaction temperature to warm to 0 °C rapidly, and then quenching after a relatively short time at 0 °C. Thus, **4a** gave an 83:17 separable mixture of sulfoxide **18a** and sulfones **22a** (90:10 mixture) in 48% yield (entry 4). The use of an excess of reagent and longer reaction time (entry 5) resulted in much more overoxidation to sulfones **22a** and in a much lower yield (18%). Finally, the possibility of using hydroxy sulfonyl dienes as substrates for this process was explored, seeking to establish the viability of the protocol and also the stereochemical implications of the allylic center as the sole element of stereocontrol, and the results obtained are shown in entries 6 and 7. Thus it appears that the process is viable even with the milder reagent NaOO-*t*-Bu, but in lower yield and with substantially diminished selectivity to produce the major isomer **22a** along with two minor isomers of unknown precise stereochemistry in 62:29:9 ratio.

1-Propenyl-substituted substrate **4b** gave a comparable outcome to **4a** with slightly diminished selectivity (Table 2, entry 8). The behavior of substrates bearing aliphatic substituents of different size (**4c**, R^3 = Et and **4d**, R^3 = *i*-Pr) was then examined and the results obtained are gathered in entries 9−13. In most cases the overall yields obtained were higher (44−59%), important amounts of sulfinyl dihydrofurans were isolated, and the overall selectivity of the process was substantially diminished for the second epoxidation of the dihydrofurans, in the case of **4c** (**18c**:**19c**, ca. 70:30) and also for the remote epoxidation in the case of **4d** (**16d**:**17d**, 77:23).

In contrast with the results above, the reaction of Ph-substituted **4e** gave diminished yields and a substantial amount of a bisepoxide (ca. 25%), presumably **14e**, when the process was started at −20 °C (Table 2, entry 14). Furthermore, a substantial reduction of both cis:trans and α:*β* selectivities was also found. Carrying out the process at 0 °C gave an improvement in yield but with comparable selectivities (entry 15). Dienyl sulfone **6e** was also tested and a rather complex mixture of products was obtained with an estimated 87:13, 2,5-cis:2,5-trans selectivity (entry 16). This result is comparable to that shown in entry 17 that gathers the results obtained by sequential epoxidation of sulfinyl dienol **4e** followed by oxidation of the crude with *m*-CPBA. It should be mentioned that the selectivity found for the major 2,5-cis products from the sulfoxide (entry 17; **22e**:**23e**, 91:9) is slightly better than that obtained from the dienyl sulfone (entry 16; **22e:23e**, 79:21).

This chemistry was also extended to heteroaromatic substrate **4f**, bearing a 3-pyridyl moiety, and to evaluate the stereodirecting capabilities of the allylic center, to dienyl sulfone **6f**, and the results obtained are shown in Table 2, entries 18 and 19. The results obtained parallel those found for **4e** and **6e** (R^3 = Ph), except for the fact that bisepoxides were not isolated in this case.

TABLE 2. Synthesis of Tetrahydrofurans from Hydroxy Sulfinyl Dienes (4) and Hydroxy Sulfonyl Dienes (6)

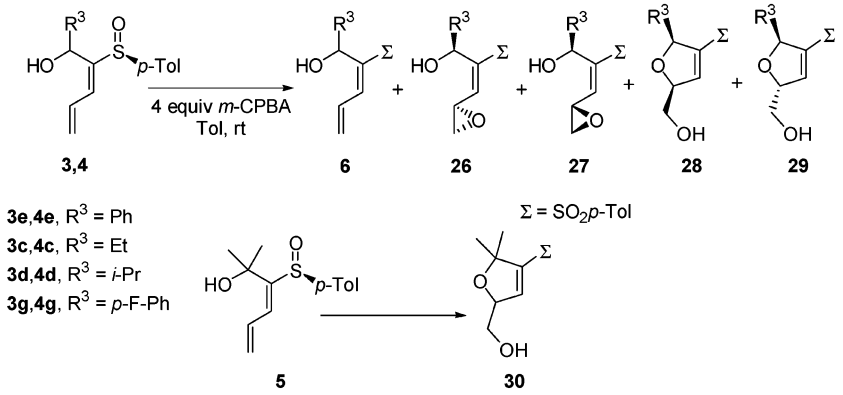


entry	substrate	conditions	**12**, **13**	**16**, **17**[a]	**18**−**21**[a]	**22**−**25**[a]	yield,[b] %
1	**4a**	2 equiv of KOO-*t*-Bu, −20 to 0 °C, 10 min	**12a**	ND	ND	ND	7
2	**4a**	0.85 equiv of KOO-*t*-Bu, −78 to 4 °C, 18 h		**16a** (38)	**18a** (54)	**22a** (8)	10[c]
3	**16a**	4.0 equiv of KOO-*t*-Bu, −20 to 0 °C, 1 h			**18a** (85)	**22a** (15)	47
4	**4a**	2.0 equiv of KOO-*t*-Bu, −20 to 0 °C, 40 min		traces	**18a** (83)	**22a** (17) [90:10]	48[d]
5	**4a**	3.0 equiv of KOO-*t*-Bu, −20 to 0 °C, 4 h			**18a** (18)	**22a** (82) [90:10]	18[d]
6	**6a**	2.0 equiv of KOO-*t*-Bu, −20 to 0 °C, 10 min				**22a**−**25a** [62:29:9]	29[d]
7	**6a**	4.0 equiv of NaOO-*t*-Bu, 0 °C to rt, 8 h				**22a**−**25a** [62:29:9]	ND[d]
8	**4b**	2.0 equiv of KOO-*t*-Bu, 0 °C, 30 min			**18b** (90) [90:10]	**22b** (10)	36[d]
9	**4c**	1.5 equiv of KOO-*t*-Bu, −25 to 0 °C, 105 min		**16c** (27)	**18c:19c** (47) [73:27]	**22c:23c** (26) [70:30]	50
10	**4c**	1.5 equiv of KOO-*t*-Bu, −25 to 0 °C, 1 h		**16c** (37)	**18c:19c** (19) [70:30]	**22c:23c** (25) [70:30]	44[e]
11	**4c**	3.0 equiv of KOO-*t*-Bu, −25 to 0 °C, 1 h			**18c:19c** (17)	**22c:23c** (83) [77:23]	50
12	**4d**	1.6 equiv of KOO-*t*-Bu, −30 to −5 °C, 25 min		**16d:17d** (35) [77:23]	**18d**−**20d** (40) [73:12:15]	**22d**−**25d** (25) [53:13:13:11]	59
13	**4d**	1.5 equiv of KOO-*t*-Bu, −30 to −5 °C, 75 min		**16d:17d** (38)	**18d**−**20d** (29)	**22d**−**25d** (33)	59[f]
14	**4e**	1.8 equiv of KOO-*t*-Bu, −20 to 0 °C, 50 min		**16e:17e** (12) [80:20]	**18e**−**20e** (77) [77:18:5]	**22e**−**24e** (11) [65:35]	33[g]
15	**4e**	1.8 equiv of KOO-*t*-Bu, 0 °C, 50 min			**18e**−**20e** (87) [74:14:12]	**22e**−**24e** (13) [62:38]	42
16	**6e**	2.0 equiv of KOO-*t*-Bu, −10 to 0 °C, 30 min				**22e:23e/24e:25e** (87/13) [79:21/85:15]	ND
17	**4e**	(1) 1.8 equiv of KOO-*t*-Bu, 0 °C, 70 min; (2) *m*CPBA, CH_2Cl_2				**22e:23e/24e:25e** (86/14) [91:9/76:24]	30
18	**4f**	2.0 equiv of KOO-*t*-Bu, −20 to 0 °C, 75 min		**16f:17f** (20) [90:10]	**18f**−**20f** (76) [95:5:5]	**22f**−**25f** (4) [68:32]	39
19	**6f**	2.0 equiv of KOO-*t*-Bu, −30 to −5 °C, 1.5 h				**22f:23f/24f:25f** (85/15) [87:13/73:27]	28
20	**4g**	2.0 equiv of KOO-*t*-Bu, −40 to 0 °C, 40 min			**18g**−**21g** (47)	**22g**−**25g** (20)	36[g]
21	**4g**	2.0 equiv of KOO-*t*-Bu, 0 °C, 70 min		**16g:17g** (9) [89:11]	**18g**−**20g** (78) [62:21:17]	**22g**−**25g** (13) [61:21:11:7]	41
22	**4g**	3.0 equiv of KOO-*t*-Bu, CH_2Cl_2, 0 °C, 70 min		**16g**−**17g** (40) [90:10]	**18g**−**20g** (50) [75:15:10]	**22g**−**25g** (10) [52:32:10:6]	36
23	**4g**	2.0 equiv of KOO-*t*-Bu, CH_2Cl_2, 0 °C, 40 min		**16g:17g** (47)	**18g**−**20g** (45)	**22g**−**25g** (8)	67[h]
24	**4 g**	3.0 equiv of KOO-*t*-Bu, Tol, 0 °C, 24 h		**16g:17g** (67)	**18g**−**20g** (20)	**22g**−**25g** (13)	ND[i]
25	**5**	1.8 equiv of KOO-*t*-Bu, 4 °C, 3.5 days		**16h:17h** (20) [75:25]	**18h**−**21h** (50) [48:0:31:21]	**22h:23h** (30) [77:23]	61[j]

[a] Relative amounts of products are shown in parentheses and the diastereomeric ratios for each type of product are shown in brackets; in some cases these ratios were not measured. [b] Combined yields of pure products after column chromatography. [c] This yield refers only to sulfinyl dihydrofuran **16a**. [d] The stereochemistry of the minor products was not established. [e] Reaction carried out on a 4 mmol scale with reagent "aged" for 90 min; a sulfenate byproduct was obtained (see Supporting Information). [f] Reaction carried out on a 4 mmol scale. [g] Acyclic bis-epoxides **14** were also isolated (see Supporting Information). [h] Yield includes 20% recovered starting material. [i] About 40% ratio of starting material was present in the crude mixture (^{1}H NMR); the yield was not determined. [j] Yield includes 40% recovered starting material.

Entries 20−24 gather our efforts on substrate **4g** (R^3 = *p*-F-Ph) that gave comparable results to those found for **4e** (R^3 = Ph), including the production in ca. 23% yield of bisepoxide **14g** when the reaction was started at

TABLE 3. Oxidation−Epoxidation of Hydroxy Sulfinyl Dienes



entry	substrate	conditions	**6**:**26**,**27**:**28**,**29**	monoepoxides **26**:**27**	dihydrofurans **28**:**29**	yield,[a] %
1	**3e**	CH_2Cl_2, 4 days	0:81:19	**26e** (57):**27e** (43)	**28e** (57):**29e** (43)	73
2	**3e**	Et_2O, 5 days	0:50:20	**26e** (50):**27e** (50)	**28e** (50):**29e** (50)	76
3	**3e**	Tol, 3.5 days	0:80:20	**26e** (61):**27e** (39)	**28e** (61):**29e** (39)	76
4	**3c**,**4c**	Tol, 20 h	9:91:0	**26c** (62):**27c** (38)	0:0	85
5	**3d**,**4d**	Tol, 38 h	0:70:30	**26d** (58):**27d** (42)	**28d** (75):**29d** (25)	84
6	**3g**,**4g**	Tol, 3 days	0:83:17	**26g** (59):**27g** (41)	**28g** (75):**29g** (25)	94
7	**3g**,**4g**	5 equiv of *m*CPBA, Tol, 3 days; then 0.2 equiv of CSA	0:0:0	0:0	**28g** (60):**29g** (40)	84
8	**6g**	oxone, MeOH, H_2O, rt, 22 h	80:0:20	0:0	**28g** (60):**29g** (40)	18
9	**6g**	acetone, oxone, $NaHCO_3$, H_2O, rt, 46 h	80:10:10	**26g** (45):**27g** (55)	**28g** (45):**29g** (55)	ND
10	**6g**	DMDO, CH_2Cl_2, 0 °C, 4 h	9:77:14	**26g** (50):**27g** (50)	**28g** (50):**29g** (50)	74
11	**3g**	CH_3CN, H_2O_2, $NaHCO_3$, MeOH, rt, 6 days	30:0:70	0:0	**28g** (70):**29g** (30)	61
12	**3g**	PhCN, H_2O_2, $NaHCO_3$, MeOH, rt, 4 days	20:0:80	0:0	**28g** (70):**29g** (30)	ND
13	**5**	*m*CPBA, Tol, rt, 2 days	0:0:0	0:0	30	85

[a] Combined yields of pure products after column chromatography, including starting material.

−40 °C (entry 20) and the production of a 9:78:13 mixture of dihydrofurans, sulfinyl, and sulfonyl tetrahydrofurans (entry 21). In an effort to understand better this process, particularly the cause of the lower yields obtained for substrates bearing R^3 = Aryl, alkenyl, relative to those bearing alkyl groups, and guided by finding variable amounts of *p*-fluorobenzaldehyde in the crude reaction mixtures, we examined the stability of dienol **4g** to KO-*t*-Bu (THF, 0 °C, 2 h); this experiment resulted in substantial fragmentation with recovery of just 62% of **4g** and the corresponding amounts of aldehyde and sulfinyl diene **1a**. Thus it appears that another competing reaction pathway, this undesired fragmentation provoked by the KO-*t*-Bu released as the epoxidation takes place, or even perhaps by KOO-*t*-Bu, is also operative in these processes.

In view of these findings we surveyed the use of other solvents to try to improve the overall efficiency of the process. Toluene gave rise to a very slow reaction (entry 24) and CH_2Cl_2 gave slightly better results by enhancing the rate of cyclization of monoepoxide **12**, which, in contrast with the standard conditions, could not be detected by TLC, but diminishing the rate of the second epoxidation, affording important amounts of dihydrofurans (entry 22). Entry 23 shows that a slightly better overall yield can be obtained by performing the reaction in CH_2Cl_2 at short reaction times to produce a mixture of products in 66% yield, including 20% recovered starting material. Finally, the behavior of substrate **5**, bearing *gem*-dimethyl substituents, was examined and a rather complex mixture of products was obtained in low yield and with low conversion (entry 25).

Preparation and Nucleophilic Epoxidation of Sulfonyl Dihydrofurans

At this stage we decided to explore an alternative route to 2,5-cis and 2,5-trans sulfonyl dihydrofurans related to **16** and **17** (Scheme 5). We were attracted by the synthetic potential of these intermediates that have scarcely been documented in the literature.[15] More relevant to this project, we believed that a careful study of the nucleophilic epoxidation of these substrates could allow for firm structural assignments for our sulfinyl and sulfonyl tetrahydrofurans. On the basis of literature precedents,[16] we envisioned the simplest route to achieve this goal to be the simultaneous oxidation and epoxidation with *m*-CPBA, followed by acid- or base-catalyzed cyclization of the resulting vinyl oxiranes.

Table 3 gathers our results on this oxidation−epoxidation protocol. Treatment of hydroxy sulfinyl diene **3e** with *m*-CPBA in CH_2Cl_2 resulted in a fast oxidation to the dienyl sulfone followed by a slow epoxidation at the distal double bond to produce a separable mixture of monoepoxides **26e** and **27e**, along with significant amounts of dihydrofurans **28e** and **29e** in good overall yield (Table 3, entry 1). The influence of the solvent on the rate and

(15) Craig, D.; Ikin, N. J.; Mathews, N.; Smith, A. M. *Tetrahedron* **1999**, *55*, 13471−13494.

(16) (a) For the use of *m*-CPBA with high selectivity within this context, see: Iqbal, J.; Pandey, A.; Chauban, B. P. S. *Tetrahedron* **1991**, *47*, 4143−4154. (b) For a related report with MMPP followed by CSA, see: Kang, S. H. *Tetrahedron Lett.* **1989**, *30*, 5915−5918. See also: (c) Urones, J. G.; Marcos, I. S.; Garrido, N. M.; Basabe, P.; San Feliciano, S. G.; Coca, R.; Díez, D. *Synlett* **1998** 1364−1365. (d) Díez, D.; Beneitez, M. T.; Marcos, I. S.; Garrido, N. M.; Basabe, P.; Urones, J. G. *Tetrahedron*: *Asymmetry* **2002**, *13*, 639−646

selectivity of the process was then briefly examined (entries 2 and 3), with toluene providing a slightly better selectivity and faster rate of reaction. In view of the poor selectivity found we chose to carry out this part of the study using racemic materials, therefore it was appropriate in some cases to use diastereomeric mixtures of hydroxy dienes **3** and **4** that would produce racemic sulfones **6**, eventually leading to racemic dihydrofurans. Thus, entries 4−6 show the results obtained for the other substrates of this study that paralleled those above except that for R^3 = Et, *i*-Pr the epoxidations were a little faster. It was also possible to carry out a one-pot protocol by adding catalytic CSA to the crude epoxidation mixture affording sulfonyl dihydrofurans **28g** and **29g** that, unlike for most of the previous examples, were separated readily.

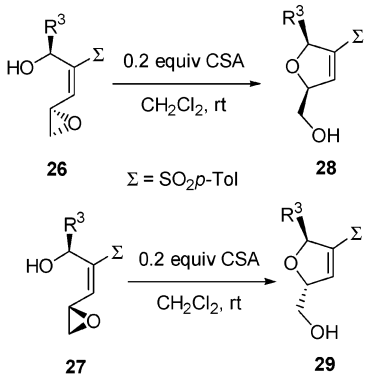
A few simple alternative epoxidizing conditions (entries 8−12) were also surveyed in an attempt to improve the selectivity of the process. Oxone in MeOH gave a similar selectivity but in a slow reaction (entry 8). Oxone in acetone also gave a poorly selective process with low conversion (entry 9). The use of freshly prepared dimethyl dioxirane in CH_2Cl_2 gave a rapid reaction, unfortunately devoid of selectivity (entry 10). Entries 11 and 12 gather the results obtained with peroxyminic acids,[17] generated in situ from H_2O_2 and nitriles, that gave a slow reaction, with slightly better selectivity (70:30) and a small (entry 11, ca. 10%) or significant (entry 12, ca. 50%) amount of epoxy sulfonyl tetrahydrofurans. Finally, the treatment of substrate **5**, bearing a *gem*-dimethyl moiety, with *m*-CPBA smoothly gave sulfonyl dihydrofuran **30** in excellent yield (entry 13).

The cyclization of diastereomeric vinyl oxiranes **26** and **27** was then examined, initially, under basic conditions. Thus *t*-BuOK (THF, rt, 8 h) led to recovered starting material and NaH (0 °C to room temperature, 5 h) afforded small amounts of dihydrofurans and a complex mixture of products. Alternatively, the use of catalytic CSA (0.2 equiv, CH_2Cl_2, rt) gave excellent yields of sulfonyl dihydrofurans **28** and **29** that are gathered in Table 4.[18]

Table 5 shows our efforts on the epoxidation of 2,5-cis sulfonyl dihydrofurans **28**. Entries 1−3 show the results obtained for model substrate **28e** with different metalated peroxides in THF for which the best selectivity was obtained with LiOO-*t*-Bu (91:9, entry 1). Under identical conditions, ethyl-substituted substrate **28c** gave a substantially diminished selectivity (71:29, entry 4), apparently independent in this case of the counterion (entry 5, 72:28). Finally, more sterically demanding substrates **28d** and **28g** gave adequate results with LiOO-*t*-Bu (entries 6 and 7). In some cases (entries 1 and 6), small amounts of sulfonyl furans **31** were also isolated; the reaction pathway that leads to these furans has not been investigated.

In contrast with the results above, the epoxidations of 2,5-trans sulfonyl dihydrofurans **29e** were significantly more selective when KOO-*t*-Bu was used (Table 6, entry 3) and in this case comparable selectivities in favor of

TABLE 4. Acid-Catalyzed Preparation of Sulfonyl Dihydrofurans from Sulfonyl Diene Monoepoxides



entry	substrate	R^3	product	yield[a]
1	**26e**	Ph	**28e**	99%
2	**26c**	Et	**28c**	98%
3	**26d**	*i*-Pr	**28d**	97%
4	**26g**	*p*-F-Ph	**28g**	99%
5	**27e**	Ph	**29e**	96%
6	**27c**	Et	**29c**	96%
7	**27d**	*i*-Pr	**29d**	99%
8	**27g**	*p*-F-Ph	**29g**	99%

[a] Yields of pure products after column chromatography.

epoxidation anti to the hydroxymethyl moiety were obtained for the other substrates tested (entries 4−6). Again, small amounts of sulfonyl furans **31** were also isolated. Finally Scheme 6 shows that dimethyl-substituted dihydrofuran **30** also gave rise to the corresponding tetrahydrofurans **22h** and **23h** with moderate selectivity under standard conditions.

Chemical Correlations

The structures of these sulfinyl and sulfonyl oxiranes were assigned by spectroscopic methods (^{1}H and ^{13}C NMR and NOE experiments in some cases). However, a definitive structural assignment was obtained by an X-ray diffraction analysis of *p*-nitrobenzoate **32**, prepared from sulfinyl tetrahydrofuran **18a** under standard conditions (Scheme 7).[19] In addition, a number of sulfinyl tetrahydrofurans and dihydrofurans were oxidized smoothly under standard conditions (MMPP or *m*-CPBA) to produce the corresponding sulfones and the results obtained are gathered in Schemes 7 and 8.

Results and Discussion

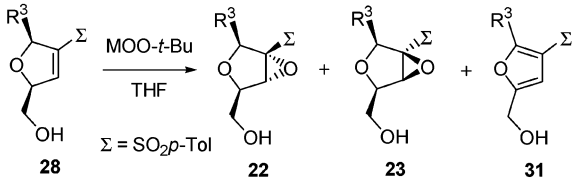
There are several stereochemical issues to address when trying to rationalize this complex process and our thoughts, assuming an early transition state for each transformation involved, are given below. The first aspect is the lack of reactivity of diastereomers **3**, relative to diastereomers **4**. This may be understood by admitting that the intramolecular hydrogen bond plays an important role for the less polar diastereomer **3** than for the more polar diastereomer **4**. In this manner, chelated

(17) (a) Payne, G. B. *Tetrahedron* **1962**, *18*, 763−765. (b) Bachmann, C.; Gesson, J.-P.; Renoux, B.; Tranoy, I. *Tetrahedron Lett.* **1998**, *39*, 379−382.

(18) Nicolau, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 5330−5334.

(19) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre (CCDC 213296, refcode: DADNUR). The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ. UK.

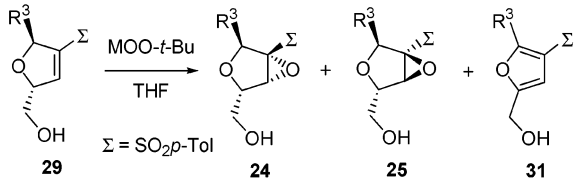
TABLE 5. Nucleophilic Epoxidation of 2,5-Cis Sulfonyl Dihydrofurans



entry	substrate	R^3	M	conditions	22	23	31	yield,[a] %
1	**28e**	Ph	Li	−65 to 0 °C, 6 h	**22e** (91)	**23e** (9)	**31e** (5%)	70
2	**28e**	Ph	Na	0 °C, 25 min	**22e** (59)	**23e** (41)		59
3	**28e**	Ph	K	−40 to −15 °C, 50 min	**22e** (59)	**23e** (41)		78
4	**28c**	Et	Li	−20 to 0 °C, 24 h	**22c** (71)	**23c** (29)		72
5	**28c**	Et	K	−40 to 0 °C, 45 min	**22c** (72)	**23c** (28)		88
6	**28d**	*i*-Pr	Li	−20 to 0 °C, 6 h	**22d** (83)	**23d** (17)	**31d** (8%)	78
7	**28g**	*p*-F-Ph	Li	0 °C, 2 h 30 min	**22g** (87)	**23g** (13)		82

[a] Combined yields of pure products after column chromatography.

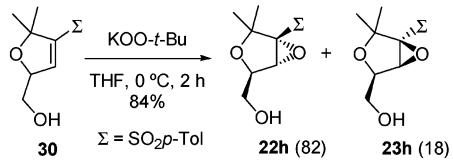
TABLE 6. Nucleophilic Epoxidation of 2,5-Trans Sulfonyl Dihydrofurans



entry	substrate	R^3	M	conditions	24	25	31	yield,[a] %
1	**29e**	Ph	Li	−65 to 0 °C, 21 h	**24e** (24)	**25e** (76)		87
2	**29e**	Ph	Na	0 °C, 20 min	**24e** (23)	**25e** (77)		69
3	**29e**	Ph	K	−40 to −30 °C, 20 min	**24e** (8)	**25e** (92)		84
4	**29c**	Et	K	−60 to −20 °C, 130 min	**24c** (5)	**25c** (95)	**31c** (4%)	56
5	**29d**	*i*-Pr	K	−60 to −20 °C, 105 min	**24d** (4)	**25d** (96)	**31d** (8%)	73
6	**29g**	*p*-F-Ph	K	−50 to −15 °C, 25 min	**24g** (7)	**25g** (93)		82

[a] Combined yields of pure products after column chromatography.

SCHEME 6



conformer **A** (Scheme 9), which places R^3 and the bulky *p*-Tolyl group in an equatorial arrangement, would be more favorable for diastereomer **3** than the related conformer **C** for diastereomer **4**. This would disfavor coordination between the hydroxyl group and the metalated peroxide that we believe to be the main factor in promoting and controlling the remote nucleophilic epoxidation and thus other reaction pathways become competitive.

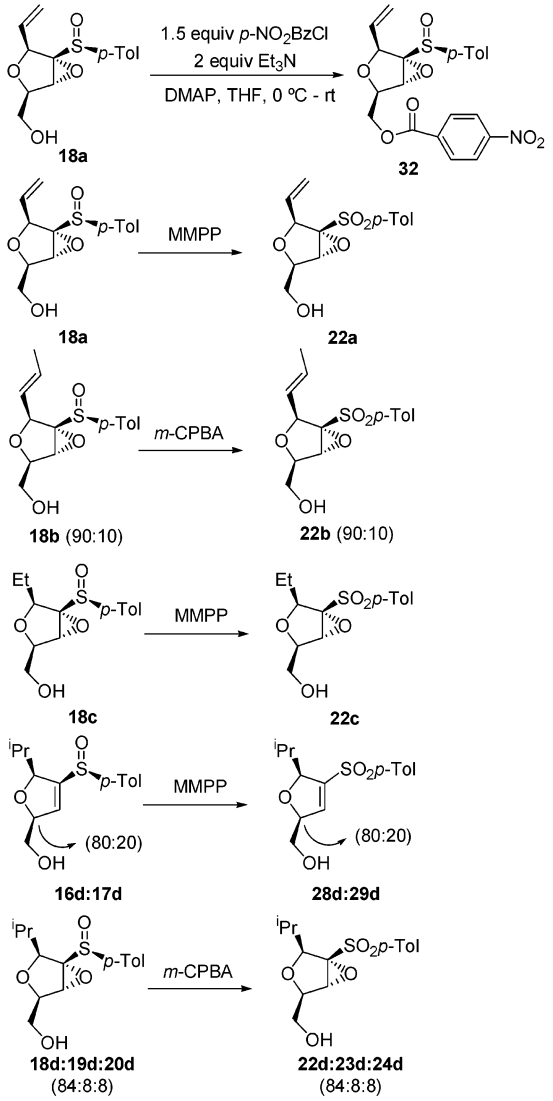
The stereochemical outcome of the remote nucleophilic epoxidation may be rationalized by considering a hydroxyl-directed process on reactive conformers **E** and **F** (Scheme 10); the relative contribution of these conformers would depend on a rather subtle balance of allylic strains. It appears that for relatively small R^3 groups, conformer **E** is operative with nucleophilic remote conjugate addition of the peroxide anion to the α face of the molecule followed by a rapid ring closure that retains the facial and stereochemical integrity of the molecule to produce predominantly vinyl oxirane **12**. In most cases, a rapid base-induced cyclization follows to produce 2,5-cis dihydrofurans **16**; however, for R^3 = Ph, *p*-F-Ph, at low temperature (−20 °C) this cyclization is relatively slow and **12** may undergo a second nucleophilic epoxidation to generate bisepoxides.

The case of the simple *Z* sulfinyl dienes discussed in Table 1 can also be tentatively rationalized by considering reactive conformer **G** (Scheme 10) with an s-cis arrangement of the lone pair on sulfur and the alkene,[20] and coordination of the metalated peroxide to the sulfinyl oxygen followed by oxirane formation in a 1,2-fashion to yield **8** that cannot undergo a second epoxidation or in a 1,4-fashion to produce a transient monoepoxide that undergoes a second epoxidation to produce bisepoxides **9**. It should be mentioned that this part of the study was only explored briefly and therefore the stereochemical assignments are just tentative. In addition these processes were found to be very substrate and temperature dependent.

The selectivity of the epoxidations of 2,5-cis sulfonyl dihydrofurans, **28**, is quite substrate and metal dependent with best results obtained for LiOO-*t*-Bu presumably by α-attack, opposite to the hydroxymethyl substituent

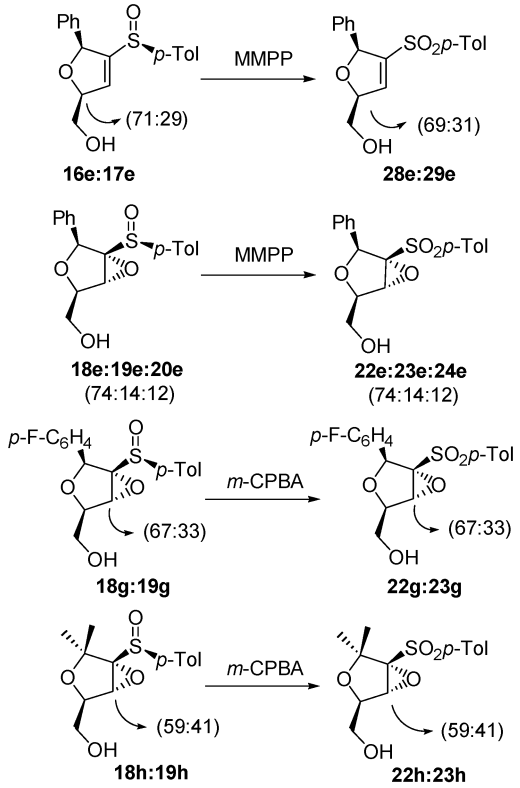
(20) It should be noted that, for a simple *Z*-propenyl sulfoxide, the energy difference between the more stable conformers (s-cis, C=C/S=O and s-cis, C=C/S−:) has been evaluated as just −0.4 kcal mol^{-1}. See: Tietze, L. F.; Schuffenhauer, A.; Schreiner, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 7952−7958.

SCHEME 7

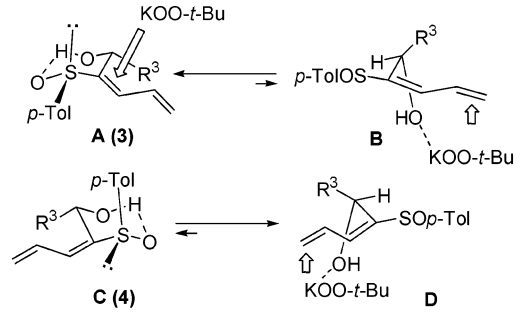


on reactive conformer **H** (Scheme 11). In contrast, the 2,5-trans isomers, **29**, give better results with KOO-*t*-Bu and are not as substrate dependent, presumably by *β*-attack on reactive conformer **J**, again opposite to the hydroxymethyl substituent.[21] With regard to the sulfinyl oxiranes, the chiral sulfur center exerts in some cases a reinforcing effect for the 2,5-cis isomers **16**,[22] enhancing the low α-selectivity found for the related sulfones with KOO-*t*-Bu. We believe that conformer **L** could be operative with perhaps some assistance by coordination of the sulfinyl oxygen with the metalated peroxide. Thus, for R^3 = Ph, the α:*β* selectivity goes from 59:41 for sulfonyl dihydrofuran **28e** to 91:9 estimated for epoxidation followed by oxidation with *m*-CPBA of sulfinyl diene **4e**. Likewise, the minor 2,5-trans sulfinyl dihydrofurans **15** seem to also undergo a predominantly α-attack, syn to the hydroxymethyl substituent. Thus, for R^3 = Ph, the α:*β* selectivity goes from 8:92 for sulfone **29e** to 76:24,

SCHEME 8



SCHEME 9



estimated as discussed above. It should be pointed out that since these isomers are obtained in small amounts the accuracy of this estimation is lower than that for the 2,5-cis isomers.

The nucleophilic epoxidation of phenyl-substituted sulfonyl diene **6e** with KOO-*t*-Bu affords a 79:21 mixture of **22e** and **23e**, along with some 2,5-trans products (Table 2, entry 16). In contrast, the treatment of sulfonyl dihydrofuran **28e**, a proposed intermediate for the above epoxidation, with KOO-*t*-Bu gives a 59:41 mixture of **22e** and **23e** (Table 5, entry 3). This discrepancy suggests that at least to some extent a different reaction pathway related to B (Scheme 5), involving sulfonyl bisoxiranes, is operative for these aryl-substituted cases.

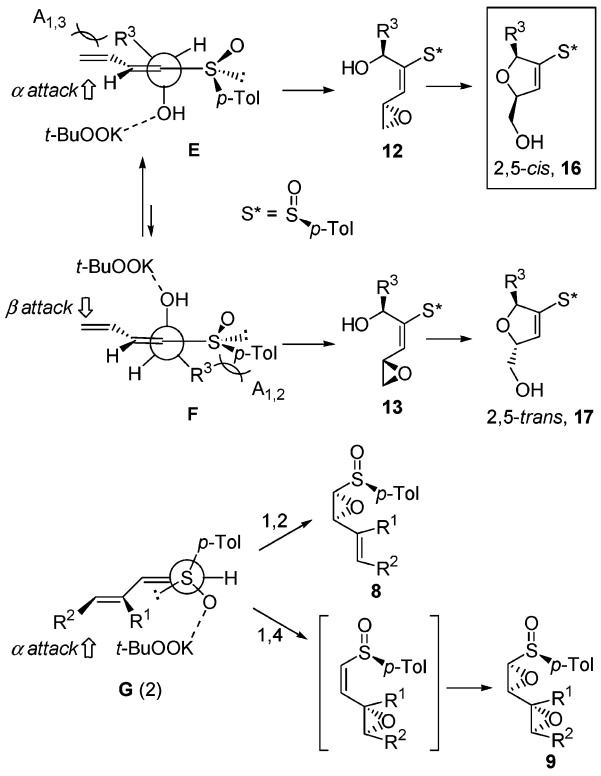
Conclusions

A novel and expedient route to tetrahydrofurans has been developed and studied in detail. This route is based on the serendipitous finding that the nucleophilic epoxidation of hydroxy dienyl sulfoxides **4** with KOO-*t*-Bu

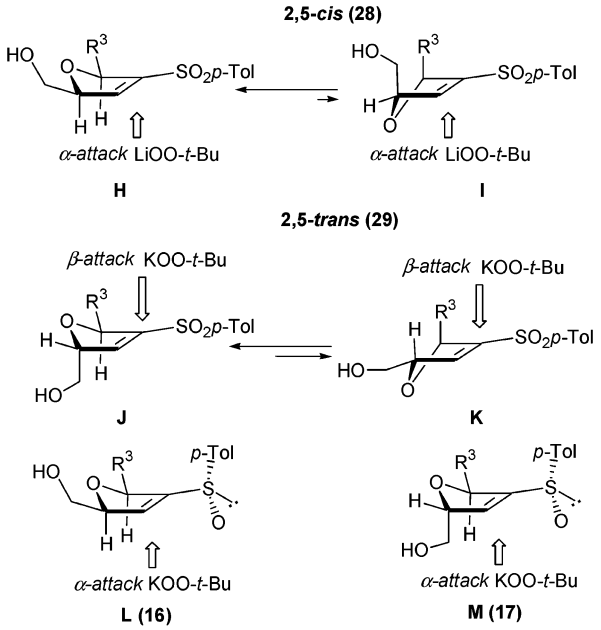
(21) A similar stereochemical outcome has been reported recently for additions of 1,2,4-triazole to diastereomeric related sulfonyl dihydrofurans, see: Sanki, A. K.; Pathak, T. *Synlett* **2002**, 1241−1244.

(22) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G. *J. Am. Chem. Soc.* **1996**, *118*, 4322−4343.

SCHEME 10



SCHEME 11



produces fair yields of densely functionalized 2,5-*cis*-tetrahydrofurans **18** in a single synthetic operation. Evidence that supports the key step of this novel entry to the tetrahydrofuran core being an unprecedented highly stereoselective remote nucleophilic epoxidation of the hydroxy sulfinyl diene moiety and also of simpler sulfinyl dienes has been presented. An alternative route to related sulfonyl dihydrofurans has been outlined and their nucleophilic epoxidations have been studied.[23] We are currently pursuing the application of these methodologies to the synthesis of natural products by exploiting the ubiquity of tetrahydrofurans in bioactive molecules and the rich chemistry of these sulfur-substituted oxiranes.[2]

Experimental Section

General Procedure for Synthesis of Hydroxy Dienyl Sulfoxides. A round-bottomed flask was charged with THF (3.5 mL/mmol) and 2.6 equiv of freshly distilled *i*-Pr_2NH, and cooled to −78 °C. To the above solution was added 2.5 equiv of *n*-BuLi and the resulting LDA solution (ca. 0.3 M) was stirred at this temperature. After 10 min a solution of 1 equiv of a mixture of dienyl sulfoxides in THF (2 mL/mmol), previously dried over 4 Å sieves, was added dropwise slowly (ca. 8 min/mmol of sulfoxide) to produce a pale yellow solution. After the solution was stirred for an additional 10 min at −78 °C, 5 equiv of freshly distilled aldehyde was added dropwise and the resulting colorless solution was stirred at this temperature for 10 min. The reaction mixture was quenched with a saturated solution of NH_4Cl (2 mL/mmol) and H_2O (2 mL/mmol), then diluted with EtOAc (3 mL/mmol), and the layers were separated. The aqueous layer was extracted with EtOAc (3 times, 4 mL/mmol). The combined organic extracts were washed with a saturated solution of NaCl (4 mL/mmol), dried over $MgSO_4$, and concentrated under reduced pressure to give a crude product that was purified by column chromatography with the appropriate mixture of eluents.

Synthesis of (+)-(2*E*)-(1*R*,*S*$_S$)-1-Phenyl-2-(*p*-tolylsulfinyl)penta-2,4-dien-1-ol, 3e, and (−)-(2*E*)-(1*S*,*S*$_S$)-1-Phenyl-2-(*p*-tolylsulfinyl)penta-2,4-dien-1-ol, 4e. From *i*-Pr_2NH (1.7 mL, 1315 mg, 13.0 mmol) in 45 mL of anhydrous THF, with *n*-BuLi (1.1 M, 11.4 mL, 12.5 mmol), a solution of dienyl sulfoxides **1a,2a** (961 mg, 5.0 mmol) in 30 mL of THF, and benzaldehyde (1.52 mL, 1587 mg, 15.0 mmol) according to the general procedure, a 48:52 mixture of hydroxy dienyl sulfoxides **3e** and **4e** was obtained, along with ca. 15% benzyl alcohol. Chromatographic purification (5−100% EtOAc−hexane and CH_2Cl_2−40% EtOAc−CH_2Cl_2) gave **3e** (547 mg, 37%) and **4e** (573 mg, 38%) as a white solids recrystallized from EtOAc−hexane and 106 mg (7%) of a mixture of hydroxy dienes. Racemic material was obtained similarly on a 30 mmol scale (85%). Data for **3e**: mp 103−104 °C; mp (racemic) 157−158 °C. R_f 0.31 (50% EtOAc−hexane), 0.42 (15% EtOAc−CH_2Cl_2). $[\alpha]^{20}_D$ +139.5 (*c* 1.25). ^{1}H NMR (200 MHz) δ 2.31 (s, 3 H), 3.39 (br, 1 H), 5.38 (dd, 1 H, J = 10.0, 1.7 Hz), 5.53 (dd, 1 H, J = 16.7, 1.7 Hz), 5.62 (s, 1 H), 6.54 (ddd, 1 H, J = 16.7, 11.3, 10.0 Hz), 6.95 (d, 1 H, J = 11.3 Hz), 7.14 (d, 2 H, J = 8.4 Hz), 7.15−7.32 (m, 5 H), 7.41 (d, 2 H, J = 8.2 Hz). ^{13}C NMR (50 MHz) δ 21.3, 69.5, 125.4 (2 C), 125.9 (2 C), 126.8, 127.3, 128.2 (2 C), 128.4, 129.7 (2 C), 130.4, 133.7, 140.1, 141.1, 141.4, 146.5. IR (film) 3360, 3080, 3060, 2920, 1630, 1595, 1490, 1450, 1300, 1180, 1080, 1030, 1010, 930, 810, 740, 700 cm^{-1}. MS (EI) 298 $[M]^+$, 280, 159, 141, 129, 115, 92, 91, 77 (100%), 65, 53. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08; S, 10.75. Found: C, 72.06; H, 6.00; S, 10.43. Data for **4e**: mp 134−137 °C; mp (racemic) 148−149 °C. R_f 0.22 (50% EtOAc−hexane); 0.17 (15% EtOAc−CH_2Cl_2). $[\alpha]^{20}_D$ −99.4 (*c* 0.80). ^{1}H NMR (300 MHz) δ 2.29 (s, 3 H), 4.20 (br, 1 H), 5.36 (dd, 1 H, J = 9.8, 1.8 Hz), 5.51 (dd, 1 H, J = 16.7, 1.7 Hz), 5.64 (s, 1 H), 6.57 (ddd, 1 H, J = 16.7, 11.3, 9.8 Hz), 6.91 (d, 1 H, J = 11.3 Hz), 6.90−7.15 (m, 7 H), 7.36 (d, 2 H, J = 8.2 Hz). ^{13}C NMR (50 MHz) δ 21.3, 69.0, 125.2, 125.5 (2 C), 126.0 (2 C), 127.1, 128.0 (2 C), 129.7 (2 C), 130.9, 133.9, 139.7, 140.7, 141.6, 147.0. IR (KBr) 3340, 3060, 1580, 1490, 1450, 1250, 1080, 1040, 1020, 935, 800, 750, 700 cm^{-1}. MS (EI) 298 $[M]^+$, 280, 250, 159, 141, 115, 92, 91,

(23) Further studies to improve the diastereoselectivity of the distal electrophilic epoxidation of these hydroxy sulfonyl dienes by using chiral dioxiranes or hydroxyl protected substrates will be carried out for specific synthetic targets. See: (a) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979−2000. (b) Marayama, K.; Ueda, M.; Sasaki, S.; Iwata, Y.; Miyazawa, M.; Miyashita, M. *Tetrahedron Lett.* **1989**, *39*, 4517−4520.

77 (100%), 65, 53. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08; S, 10.75. Found: C, 72.64; H, 6.37; S, 10.99.

General Procedure for Nucleophilic Epoxidation of Vinyl and Dienyl Sulfoxides and Sulfones. (a) With LiOO-*t*-Bu. A two-necked round-bottomed flask fitted with a tube in T for entrance and exit of argon and a polyethylene stopper was charged with anhydrous THF (5 mL/mmol) and 4 equiv of *t*-BuOOH (80% in *t*-BuOO-*t*-Bu); the resulting mixture was cooled to 0 °C and then 5 equiv of *n*-BuLi was added. The mixture was stirred at 0 °C for 10 min and a solution of 1 equiv of the corresponding vinyl sulfoxide in THF (5 mL/mmol), previously dried over 4 Å sieves, was added dropwise. The reaction mixture was stirred at constant temperature until starting material disappeared, monitored by TLC. The reaction was then quenched with a 1 M solution of $Na_2S_2O_4$ (4 mL/mmol), then diluted with EtOAc (10 mL/mmol), and the layers were separated. The aqueous layer was extracted with EtOAc (3 times, 10 mL/mmol) and the combined organic extracts were washed with a saturated solution of NaCl (4 mL/mmol), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product, which was purified by column chromatography on silica gel, using a gradient of mixtures of EtOAc−hexane or EtOAc−CH_2Cl_2. Product ratios were determined by integration of well-resolved signals in the ^{1}H NMR of the crude reaction mixtures. **(b) With NaOO-*t*-Bu or KOO-*t*-Bu.** A two-necked round-bottomed flask fitted with a tube in T for entrance and exit of argon and a polyethylene stopper was charged with anhydrous THF (3−5 mL/mmol of KH) and 0.8−4 equiv of oil free NaH or KH (washed with hexane and dried); the resulting mixture was then cooled to 0 °C and 0.8−4 equiv of *t*-BuOOH (80% in *t*-BuOO-*t*-Bu) was added. After being stirred at room temperature for 20−30 min, the resulting solution (ca. 0.20 M) was cooled to the appropriate temperature and a solution of 1 equiv of the corresponding vinyl sulfoxide in THF (7 mL/mmol), previously dried over 4 Å sieves, was added dropwise. The reaction mixture was stirred at the appropriate temperature until starting material disappeared, monitored by TLC. Isolation and purification were performed as described above.

Synthesis of (+)-(2*R*,3*S*,*S*$_S$)-2-(*p*-Tolylsulfinyl)-3-vinyloxirane, 8a, (+)-(2*R*,3*S*,*S*$_S$)-3-[(2′*R*)-Epoxy]-2-(*p*-toylsulfinyl)oxirane, 9a, and (+)-(2*R*,3*S*,*S*$_S$)-3-[(2′*S*)-Epoxy]-2-(*p*-tolylsulfinyl)oxirane, 10a. (a) 1 equiv of KOO-*t*-Bu. From a solution of sulfinyl diene **2a** (58 mg, 0.302 mmol), in THF (2.0 mL), and a cold (−78 to 0 °C) 0.2 M THF solution of KOO-*t*-Bu (1 equiv) (35 min), according to the general procedure, a 9:91 mixture of **8a** and **9a**,**10a** was obtained at 71% conversion. Purification by chromatography (5−40% EtOAc−hexane) gave monoepoxide **8a** (2 mg, 3%) as a colorless oil and an 84:16 mixture of bisepoxides **9a**:**10a** (22 mg, 33%) as a colorless oil. A second careful chromatography allowed for the separation of the bisepoxides. Stereochemical assignments are tentative. **(b) 2 equiv of KOO-*t*-Bu.** From a solution of sulfinyl diene **2a** (39 mg, 0.203 mmol), in THF (2.0 mL), and a cold (−20 to 0 °C) 0.2 M THF solution of KOO-*t*-Bu (2 equiv) (65 min), according to the general procedure, a 60:40 mixture of **8a** and **9a**,**10a** was obtained at 91% conversion. Purification by chromatography (5−40% EtOAc−hexane) gave monoepoxide **8a** (12 mg, 28%) as a colorless oil and a separable 82:18 mixture of bisepoxides **9a**:**10a** (10 mg, 22%) as a colorless oil. Data for **8a**: R_f 0.35 (2 × 30% EtOAc−hexane). $[\alpha]^{20}_D$ +39.3 (*c* 0.37). ^{1}H NMR (300 MHz) δ 2.40 (s, 3 H), 3.66 (ddt, 1 H, *J* = 8.4, 3.9, 0.7 Hz), 4.05 (d, 1 H, *J* = 3.9 Hz), 5.55 (dt, 1 H, *J* = 3.9, 0.8 Hz), 5.64 (dt, 1 H, *J* = 17.1, 0.8 Hz), 5.99 (ddd, 1 H, *J* = 17.2, 10.4, 8.4 Hz), 7.33 (d, 2 H, *J* = 8.5 Hz), 7.52 (d, 2 H, *J* = 8.2 Hz). ^{13}C NMR (75 MHz) δ 21.4, 58.4, 76.6, 123.5, 124.3 (2 C), 128.5, 130.2 (2 C), 131.1, 142.2. IR (film) 3060, 2920, 1600, 1490, 1440, 1320, 1160, 1090, 1055, 950, 815, 670 cm^{-1}. Data for **9a** (major isomer): R_f 0.16 (2 × 30% EtOAc−hexane). $[\alpha]^{20}_D$ +86.7 (*c* 0.38). ^{1}H NMR (300 MHz) δ 2.42 (s, 3 H), 2.74 (dd, 1 H, *J* = 4.9, 2.6 Hz), 2.96 (dd, 1 H, *J* = 4.9, 4.3 Hz), 3.02 (dd, 1 H, *J* = 6.1, 3.9 Hz), 3.37 (ddd, 1 H, *J* = 6.2, 4.1, 2.6 Hz), 4.01 (d, 1 H, *J* = 4.0 Hz), 7.36 (d, 2 H, *J* = 8.4 Hz), 7.60 (d, 2 H, *J* = 8.5 Hz). ^{13}C NMR (50 MHz) δ 21.5, 44.3, 48.1, 58.3, 74.7, 124.6 (2 C), 130.4 (2 C), 137.4, 142.8. IR (film) 3000, 2920, 1600, 1490, 1450, 1290, 1250, 1090, 1050, 1020, 930, 840, 810, 720, 620 cm^{-1}. MS (APCI) 225 [M + 1]$^+$(100%), 139, 123. Data for **10a** (minor isomer): R_f 0.21 (2 × 30% EtOAc−hexane). $[\alpha]^{20}_D$ +18.3 (*c* 0.18). ^{1}H NMR (300 MHz) δ 2.43 (s, 3 H), 2.84 (dd, 1 H, *J* = 4.9, 2.4 Hz), 2.99 (dd, 1 H, *J* = 3.8, 2.3 Hz), 3.01 (t, 1 H, *J* = 3.7 Hz), 3.33 (ddd, 1 H, *J* = 6.7, 3.9, 2.5 Hz), 4.00 (d, 1 H, *J* = 3.7 Hz), 7.38 (d, 2 H, *J* = 7.9 Hz), 7.66 (d, 2 H, *J* = 8.3 Hz). ^{13}C NMR (50 MHz) δ 21.5, 46.9, 48.5, 56.8, 74.3, 124.5 (2 C), 130.4 (2 C), 137.4, 142.7. In some experiments from **2a** with 2 equiv of KOO-*t*-Bu small amounts of bisepoxy sulfone **(2*R*,3*S*)-3-[(2′*R*)-Epoxy]-2-(*p*-tolylsulfonyl)oxirane, 11a** (stereochemical assignment is tentative), were obtained. Partial data for **11a**: R_f 0.35 (2 × 30% EtOAc−hexane). ^{1}H NMR (300 MHz) δ 2.46 (s, 3 H), 2.78 (dd, 1 H, *J* = 4.5, 2.7 Hz), 2.95 (dd, 1 H, *J* = 7.3, 4.5 Hz), 3.01 (t, 1 H, *J* = 4.5 Hz), 3.78 (m, 1 H), 4.04 (d, 1 H, *J* = 4.0 Hz), 7.40 (d, 2 H, *J* = 8.0 Hz), 7.84 (d, 2 H, *J* = 8.3 Hz).

Synthesis of (+)-(2*R*,3*R*,4*R*,5*S*,*S*$_S$)-3,4-Epoxy-5-phenyl-4-(*p*-tolylsulfinyl)tetrahydrofuran-2-methanol, 18e, (+)-(2*R*,3*R*,4*R*,5*S*)-3,4-Epoxy-5-phenyl-4-(*p*-tolylsulfonyl)tetrahydrofuran-2-methanol, 22e, and (+)-(2*R*,5*S*,*S*$_S$)-4-(*p*-Tolylsulfinyl)-5-phenyl-2,5-dihydrofuran-2-methanol, 16e. (a) With 1.8 equiv of KOO-*t*-Bu from −20 to 0 °C. From a solution of hydroxy sulfinyl diene **4e** (135 mg, 0.452 mmol), in THF (2.5 mL), and a cold (−20 to 0 °C) 0.2 M THF solution of KOO-*t*-Bu (1.8 equiv) (50 min), according to the general procedure, a 12:77:11 mixture of sulfinyl dihydrofurans and sulfinyl and sulfonyl tetrahydrofurans **16e**, **18e**, and **22e** was obtained, along with a significant amount (ca. 25%) of bisepoxides **12e′**,**12e″** (60:40 sulfoxide:sulfone, respectively). Purification by chromatography (30−50% EtOAc−hexane) gave **16e**−**17e** (6 mg, 4%, 80:20 mixture of diastereomers), **18e**−**20e** (38 mg, 25%, 77:18:5 mixture of diastereomers), and **22e** (6 mg, 4%, 65:35 mixture of diastereomers), all obtained as colorless oils. In addition bisepoxides **12e′**,**12e″** (S = sulfoxide and sulfone) were also isolated and they are assigned tentatively. **(b) With 1.8 equiv of KOO-*t*-Bu at 0 °C.** From a solution of hydroxy sulfinyl diene **4e** (116 mg, 0.389 mmol), in THF (6.0 mL), and a cold (0 °C) 0.2 M THF solution of KOO-*t*-Bu (1.8 equiv) (35 min), according to the general procedure, an 87:13 mixture of sulfinyl and sulfonyl tetrahydrofurans **18e** and **22e** was obtained. Purification by chromatography (15−100% EtOAc−hexane) gave **18e**−**20e** (46 mg, 36%, 74:14:12 mixture of diastereomers) and **22e** (8 mg, 6%, 68:32 mixture of diastereomers), all obtained as colorless oils. A second careful chromatography afforded diastereomerically enriched **18e** (81:14:5). **(c) With 3.0 equiv of KOO-*t*-Bu at 0 °C.** From a solution of hydroxy sulfinyl diene **4e** (60 mg, 0.20 mmol), in THF (4.0 mL), and a cold (0 °C) 0.2 M THF solution of KOO-*t*-Bu (3.0 equiv) (30 min), according to the general procedure, an 79:21 mixture of sulfinyl and sulfonyl tetrahydrofurans **18e** and **22e** was obtained in a complex crude mixture. Purification by chromatography (0−40% EtOAc−CH_2Cl_2) gave **18e** (8 mg, 12%, mixture of diastereomers). **(d) With 2.0 equiv of KOO-*t*-Bu at 0 °C, 4 mmol Scale.** From a solution of hydroxy sulfinyl diene **4e** (1194 mg, 4 mmol), in THF (46.0 mL), and a cold (0 °C) 0.2 M THF solution of KOO-*t*-Bu (2.0 equiv) (25 min), according to the general procedure, an 85:15 mixture of sulfinyl and sulfonyl tetrahydrofurans **18e** and **22e** was obtained. Purification by chromatography (3−100% EtOAc−CH_2Cl_2) gave **18e** (318 mg, 24%, recrystallized from 30% EtOAc−hexane to yield the pure major isomer) and **22e** (105 mg, 8%, recrystallized from 30% EtOAc−hexane to yield the pure major isomer). Data for **16e** (major isomer**)**: R_f 0.14 (75% EtOAc−hexane). ^{1}H NMR (300 MHz) δ 1.87 (m, 1 H), 2.39 (s, 3 H), 3.77−3.84 (m, 2 H), 5.04 (dddd, 1 H, *J* = 8.3, 4.6, 3.8, 1.6 Hz), 5.19 (dd, 1 H, *J* = 4.5, 2.1 Hz), 6.75 (dd, 1 H, *J* = 2.1, 1.6 Hz), 7.10−7.44 (m, 9 H). ^{13}C NMR (50 MHz) δ 21.4, 64.5, 86.2, 87.0, 125.5 (2 C), 128.1 (2 C), 128.7 (2 C), 129.1, 130.1 (2 C),

131.0, 137.9, 137.9, 142.7, 149.4. IR (CCl_4) 3440, 3040, 3020, 2900, 2860, 1590, 1490, 1450, 1390, 1270, 1110, 1070, 1050, 1000, 800, 750, 725, 690 cm^{-1}. MS (ES) 337 $[M + Na]^+$ (100%), 315 $[M + 1]^+$. Partial data for **17e** (minor isomer): ^1H NMR (300 MHz) δ 3.68 (dd, 2 H, J = 11.7, 4.5 Hz), 5.28 (s, 1 H), 6.72 (t, 1 H, J = 1.8 Hz). Data for **18e** (major isomer): mp (racemic) 139−140 °C. R_f 0.20 (40% EtOAc−CH_2Cl_2), 0.12 (50% EtOAc−hexane). $[\alpha]^{20}_D$ +36.0 (c 1.00). ^1H NMR (300 MHz) δ 2.20 (br s, 1 H), 2.39 (s, 3 H), 3.87 (t, 2 H, J = 5.0 Hz), 4.29 (t, 1 H, J = 5.2 Hz), 4.48 (s, 1 H), 4.60 (s, 1 H), 7.25−7.45 (m, 9 H). ^{13}C NMR (50 MHz) δ 21.6, 62.5, 67.2, 80.0, 81.7, 83.2, 126.6, 128.8 (2 C), 129.3, 129.7 (2 C), 129.9, 135.4, 135.6, 143.4. IR ($CHCl_3$) 3400, 3010, 2920, 2890, 1595, 1490, 1450, 1215, 1080, 1050, 1010, 920, 805, 750, 700, 660, 620 cm^{-1}. MS (EI) 330, 282, 191, 161, 139 (100%), 107, 105, 91, 77, 65, 51. Anal. Calcd for $C_{18}H_{18}O_4S$: C, 65.44; H, 5.49; S, 9.70. Found: C, 65.26; H, 5.52; S, 9.60. Partial data for **19e** (first minor isomer): ^1H NMR (300 MHz) δ 2.29 (s, 3 H), 3.80−3.90 (m, 2 H), 4.11 (td, 1 H, J = 5.5, 0.8 Hz), 4.34 (d, 1 H, J = 0.7 Hz), 4.99 (s, 1 H). Partial data for **20e** (second minor isomer): ^1H NMR (300 MHz) δ 2.40 (s, 3 H), 3.80−3.90 (m, 2 H), 4.50 (d, 1 H, J = 0.7 Hz), 4.53 (t, 1 H, J = 5.6 Hz), 4.55 (s, 1 H). The data for sulfonyl tetrahydrofurans **22e**−**24e** are described below. Data for **(1*S*,2*R*,3*S*,*S*$_S$)-2,3,4,5,-diepoxy-1-phenyl-2-(*p*-tolylsulfinyl)pentan-1-ol, 12e′** (major): R_f 0.20 (2 × 50% EtOAc−hexane). ^1H NMR (300 MHz) δ 2.39 (s, 3 H), 2.72 (dd, 1 H, J = 5.0, 2.7 Hz), 2.84 (dd, 1 H, J = 4.9, 4.2 Hz), 3.17 (ddd, 1 H, J = 5.0, 4.2, 2.6 Hz), 3.30 (d, 1 H, J = 5.1 Hz), 5.09 (s, 1 H), 7.25−7.50 (m, 8 H), 8.08 (d, 1 H, J = 8.4 Hz). ^{13}C NMR (75 MHz) δ 21.6, 44.8, 48.1, 59.8, 70.4, 80.5, 126.2 (2 C), 126.5 (2 C), 128.5, 128.7 (2 C), 129.9 (2 C), 130.1, 133.6, 34.5, 138.1, 143.1. Partial data for **(1*S*,2*R*,3*S*)-2,3,4,5,-diepoxy-1-phenyl-2-(*p*-tolylsulfonyl)pentan-1-ol**, **12e″** (minor): R_f 0.48 (2 × 50% EtOAc−hexane). ^1H NMR (300 MHz) δ 2.36 (s, 3 H), 2.88 (m, 2 H), 3.30 (m, 1 H), 3.40 (d, 1 H, J = 4.8 Hz), 5.06 (s, 1 H), 7.20−7.50 (m, 7 H), 8.10 (d, 1 H, J = 8.4 Hz).

General Procedure for Oxidation/Epoxidation of Hydroxy Dienyl Sulfoxides with *m*-CPBA. To a solution of the sulfoxide in toluene (10 mL/mmol) was added 4.0 equiv of 70% *m*-CPBA, and the reaction mixture was stirred at room temperature and monitored by TLC until disappearance of the sulfonyl diene. The reaction was quenched with 1 M aqueous $Na_2S_2O_4$ (5 mL/mmol) and a saturated solution of $NaHCO_3$ (5 mL/mmol) and water (5 mL/mmol). The layers were separated and the aqueous phase was extracted with EtOAc (2 times, 5 mL/mmol). The combined organic layers were washed with saturated $NaHCO_3$ mixed with water (50:50, 5 times, 5 mL/mmol) and a saturated solution of NaCl (4 mL/mmol), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a crude product that was purified by column chromatography. When the reaction was carried out on a larger scale (>10 mmol), the reaction was quenched with 1 M $Na_2S_2O_4$ (5 mL/mmol), stirred for 20 min, and filtered to remove *m*-chlorobenzoic acid. The solid was washed thoroughly with toluene and the crude product was then isolated as described above.

Synthesis of (±)-(1*S*,4*S*)-(2*E*)-4,5-Epoxy-1-phenyl-2-(*p*-tolylsulfonyl)pent-2-en-1-ol, 26e, and (±)-(1*S*,4*R*)-(2*E*)-4,5-Epoxy-1-phenyl-2-(*p*-tolylsulfonyl)pent-2-en-1-ol, 27e. From a mixture of sulfinyl dienes **3e** and **4e** (298 mg, 1 mmol), with *m*-CPBA (986 mg, 4 mmol, 4 equiv), according to the general procedure, an 80:20 mixture of monoepoxides (**26e** and **27e**) and dihydrofurans (**28e** and **29e**) was obtained. Purification by chromatography (10−50% EtOAc−hexane) gave **26e** (116 mg, 37%) as a white solid that was recrystallized from EtOAc−hexane, **27e** (75 mg, 24%) as a white solid that was recrystallized from EtOAc−hexane, and a mixture of dihydrofurans **28e** and **29e** (48 mg, 15%). Data for **26e**: mp 104−105 °C. R_f 0.17 (30% EtOAc−hexane). ^1H NMR (200 MHz) δ 2.37 (s, 3 H), 2.68 (dd, 1 H, J = 5.3, 2.5 Hz), 2.85 (dd, 1 H, J = 5.4, 4.3 Hz), 3.41 (d, 1 H, J = 6.7 Hz), 3.70 (ddd, 1 H, J = 8.0, 4.3, 2.5 Hz), 5.80 (d, 1 H, J = 6.7 Hz), 6.61 (d, 1 H, J = 7.9 Hz), 7.18 (s, 5 H), 7.18 (d, 2 H, J = 8.6 Hz), 7.53 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (50 MHz) δ 21.6, 47.5, 48.3, 69.1, 125.5 (2 C), 127.6, 128.1 (2 C), 128.3 (2 C), 129.8 (2 C), 136.0, 139.9, 141.8, 144.6, 148.1. IR (KBr) 3480, 1630, 1600, 1490, 1445, 1315, 1300, 1145, 1070, 1055, 930, 840, 805, 755, 715, 700, 690 cm^{-1}. MS (ES) 353 $[M + Na]^+$. Anal. Calcd for $C_{18}H_{18}O_4S$: C, 65.43; H, 5.49; S, 9.71. Found: C, 65.12; H, 5.70; S, 9.55. Data for **27e**: mp 93−94 °C. R_f 0.14 (30% EtOAc−hexane). ^1H NMR (300 MHz) δ 2.39 (s, 3 H), 2.73 (dd, 1 H, J = 5.5, 2.4 Hz), 2.98 (dd, 1 H, J = 5.4, 4.3 Hz), 3.09 (d, 1 H, J = 5.7 Hz), 3.54 (ddd, 1 H, J = 8.4, 4.3, 2.4 Hz), 5.81 (d, 1 H, J = 5.7 Hz), 6.59 (d, 1 H, J = 8.3 Hz), 7.18−7.24 (m, 7 H), 7.62 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (50 MHz) δ 21.5, 47.3, 48.6, 69.4, 125.9 (2 C), 127.8, 128.2 (2 C), 128.4 (2 C), 129.8 (2 C), 135.8, 139.5, 141.9, 144.7, 148.2. IR (KBr) 3380, 1570, 1470, 1435, 1300, 1280, 1270, 1160, 1130, 1120, 1065, 1025, 950, 850, 810, 790, 745, 680, 650 cm^{-1}. MS (ES) 353 $[M + Na]^+$. Anal. Calcd for $C_{18}H_{18}O_4S$: C, 65.43; H; 5.49, S, 9.71. Found: C, 65.38; H, 5.54; S, 9.62.

General Procedure for Cyclization of Monoepoxides with CSA. To a solution of the monoepoxide in CH_2Cl_2 (5 mL/mmol) at room temperature under an atmosphere of Argon was added camphorsulfonic acid (CSA, 0.2 equiv). The mixture was stirred at room temperature and monitored by TLC until completion and then quenched with a saturated solution of $NaHCO_3$ (5 mL/mmol). The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (3 times, 5 mL/mmol), and the combined organic extracts were washed with saturated NaCl (2 times, 5 mL/mmol), dried over anhydrous $MgSO_4$, and concentrated to give a crude product that was purified by column chromatography on silica gel or recrystallization.

Synthesis of (±)-(2*R*,5*S*)-5-Phenyl-4-(*p*-tolylsulfonyl)-2,5-dihydrofuran-2-methanol, 28e. From monoepoxide **26e** (297 mg, 0.9 mmol), with CSA (42 mg, 0.18 mmol, 0.2 equiv), according to the general procedure (2 h), sulfonyl dihydrofuran **28e** (295 mg, 99%) was obtained after purification by chromatography (10−60% EtOAc−hexane) as a white solid that was recrystallized from EtOAc−hexane. Data for **28e**: mp 112−113 °C. R_f 0.30 (75% EtOAc−hexane). ^1H NMR (300 MHz) δ 1.82 (dd, 1 H, J = 6.6, 6.3 Hz), 2.32 (s, 3 H), 3.86 (m, 2 H), 5.05 (m, 1 H), 5.87 (dd, 1 H, J = 5.0, 2.2 Hz), 6.97−7.26 (m, 10 H). DNOE between H-2/H-5 1.5%, between H-2/H-3 5.0%, between H-5/H-2 1.0%. ^{13}C NMR (50 MHz) δ 21.4, 63.7, 85.7, 86.4, 127.8 (2 C), 128.2 (4 C), 128.7, 129.3 (2 C), 135.7, 137.1, 139.9, 144.3, 145.5. IR (film) 3501, 2925, 1596, 1457, 1319, 1154, 1122, 1084, 813, 761, 701, 678 cm^{-1}. MS (ES) 353 $[M + Na]^+$. Anal. Calcd for $C_{18}H_{18}O_4S$: C, 65.43; H; 5.49, S, 9.71. Found: C, 65.72; H, 5.71; S, 9.95.

Synthesis of (±)-(2*S*,5*S*)-5-Phenyl-4-(*p*-tolylsulfonyl)-2,5-dihydrofuran-2-methanol, 29e. From monoepoxide **27e** (76 mg, 0.23 mmol), with CSA (11 mg, 0.05 mmol, 0.2 equiv), according to the general procedure (1.5 h), sulfonyl dihydrofuran **29e** (73 mg, 96%) was obtained after recrystallization of the crude with 80% Et_2O−hexane. Data for **29e**: mp 103−104 °C. R_f 0.30 (75% EtOAc−hexane). ^1H NMR (300 MHz) δ 1.89 (dd, 1 H, J = 6.6, 6.3 Hz), 2.32 (s, 3 H), 3.71−3.86 (m, 2 H), 5.20−5.25 (m, 1 H), 5.92 (dd, 1 H, J = 6.0, 2.0 Hz), 6.95−7.31 (m, 10 H). DNOE between H-5/CH_2-OH 0.4%, between H-2/CH_2-OH 3.1%, between H-2/H-3 4.2%. ^{13}C NMR (50 MHz) δ 21.4, 64.0, 86.5, 86.7, 127.5 (2 C), 127.8 (2 C), 128.2 (2 C), 128.5, 129.3 (2 C), 135.8, 137.6, 139.2, 144.3, 146.0. IR (KBr) 3524, 2876, 1628, 1594, 1458, 1379, 1290, 1150, 1055, 764, 703, 684, 592, 569, 527 cm^{-1}. MS (ES) 353 $[M + Na]^+$. Anal. Calcd for $C_{18}H_{18}O_4S$: C, 65.43; H, 5.49, S, 9.71. Found: C, 65.27; H, 5.44; S, 9.58.

Synthesis of (±)-(2*R*,3*R*,4*R*,5*S*)-3,4-Epoxy-5-phenyl-4-(*p*-tolylsulfonyl)tetrahydrofuran-2-methanol, 22e, and (±)-(2*R*,3*S*,4*S*,5*S*)-3,4-Epoxy-5-phenyl-4-(*p*-tolylsulfonyl)-tetrahydrofuran-2-methanol, 23e. From a solution of sulfonyl dihydrofuran **28e** (66 mg, 0.2 mmol) in THF (1.4 mL) and a cold (−65 °C) 0.2 M THF solution of LiOO-*t*-Bu (4 equiv), after warming up to 0 °C (6 h), according to the general procedure, a 91:9 mixture of sulfonyl tetrahydrofurans **22e** and

23e and traces of furan **31e** were obtained. Purification by chromatography (15−40% EtOAc−hexane) gave impure **31e** (3 mg, 5%) as a colorless oil, a mixture of **22e** and **23e** (20 mg, 29%), and pure **22e** (24 mg, 35%) as a white solid that was recrystallized from EtOAc−hexane. From a solution of sulfonyl dihydrofuran **28e** (66 mg, 0.2 mmol) in THF (1.4 mL) and a cold (0 °C) 0.2 M THF solution of NaOO-*t*-Bu (3 equiv) (25 min), according to the general procedure, a 59:41 mixture of sulfonyl tetrahydrofurans **22e** and **23e** was obtained. Purification by chromatography (20−30% EtOAc−hexane) gave **23e** (4 mg, 6%) as a colorless oil, a mixture of **22e** and **23e** (23 mg, 33%), and pure **22e** (14 mg, 20%) as a white solid that was recrystallized from EtOAc−hexane. From a solution of sulfonyl dihydrofuran **28e** (66 mg, 0.2 mmol) in THF (1.4 mL) and a cold (−40 to −15 °C) 0.2 M THF solution of KOO-*t*-Bu (2 equiv) (50 min), according to the general procedure, a 59:41 mixture of sulfonyl tetrahydrofurans **22e** and **23e** was obtained. Purification by chromatography (15−30% EtOAc−hexane) gave **23e** (14 mg, 20%) as a colorless oil, a mixture of **22e** and **23e** (28 mg, 40%), and pure **22e** (13 mg, 18%) as a white solid that was recrystallized from EtOAc−hexane. Data for **22e**: mp 133−134 °C. R_f 0.26 (50% EtOAc−hexane). ^{1}H NMR (300 MHz) δ 1.85 (br s, 1 H), 2.41 (s, 3 H), 3.93 (d, 2 H, J = 5.5 Hz), 4.26 (t, 1 H, J = 5.5 Hz), 4.41 (s, 1 H), 5.06 (s, 1 H), 7.20−7.37 (m, 9 H). ^{13}C NMR (50 MHz) δ 21.7, 62.5, 67.4, 78.6, 80.6, 82.5, 128.1 (2 C), 128.9 (2 C), 129.0 (2 C), 129.3, 129.6 (2 C), 133.8, 135.1, 145.5. IR ($CHCl_3$) 3530, 3030, 2930, 1600, 1500, 1460, 1330, 1310, 1220, 1160, 1090, 1050, 990, 940, 820, 760, 700, 670, 640 cm^{-1}. MS (EI) 346 [M]$^+$, 315, 299, 263, 191, 161, 139, 131, 105, 91 (100%), 85, 77, 65, 57. Data for **23e**: R_f 0.27 (50% EtOAc−hexane). ^{1}H NMR (300 MHz) δ 1.87 (ap t, 1 H, OH), 2.29 (s, 3 H), 3.89 (t, 2 H, J = 5.4 Hz), 4.20 (t, 1 H, J = 5.2 Hz), 4.41 (s, 1 H), 5.35 (s, 1 H), 6.96 (d, 2 H, J = 7.9 Hz), 7.18−7.25 (m, 5 H), 7.29 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (50 MHz) δ 21.6, 61.5, 63.6, 76.5, 77.3, 77.6, 128.2 (2 C), 128.5 (2 C), 128.7 (2 C), 129.1, 129.2 (2 C), 132.8, 133.4, 145.2. IR (film) 3524, 3066, 2885, 1596, 1495, 1458, 1401, 1329, 1305, 1159, 1129, 1087, 1053, 813, 756, 700, 673, 594 cm^{-1}. MS (ES) 369 [M + Na]$^+$. Anal. Calcd for $C_{18}H_{18}O_5S$: C, 62.41; H, 5.24, S, 9.26. Found: C, 62.21; H, 5.02; S, 9.37. Partial data for **31e** (from a 41:59 mixture of **31e** and **23e**): R_f 0.27 (50% EtOAc−hexane). ^{1}H NMR (200 MHz) δ 2.34 (s, 3 H), 4.61 (d, 2 H, J = 15.6 Hz), 6.71 (s, 1 H), 7.05−7.44 (m, 7 H), 7.65 (d, 2 H, J = 8.4 Hz).

Synthesis of (±)-(2*S*,3*R*,4*R*,5*S*)-3,4-Epoxy-5-phenyl-4-(*p*-tolylsulfonyl)tetrahydrofuran-2-methanol, 24e, and (±)-(2*S*,3*S*,4*S*,5*S*)-3,4-Epoxy-5-phenyl-4-(*p*-tolylsulfonyl)-tetrahydrofuran-2-methanol, 25e. From a solution of sulfonyl dihydrofuran **29e** (50 mg, 0.15 mmol) in THF (1.0 mL) and a cold (−65 to 0 °C) 0.2 M THF solution of LiOO-*t*-Bu (4 equiv) (21 h), according to the general procedure, a 76:24 mixture of sulfonyl tetrahydrofurans **25e** and **24e** was obtained. Purification by chromatography (15−40% EtOAc−hexane) gave **25e** (38 mg, 73%) as a white solid that was recrystallized from EtOAc−hexane and **24e** (7 mg, 14%) as a colorless oil. From a solution of sulfonyl dihydrofuran **29e** (50 mg, 0.15 mmol) in THF (1.0 mL) and a cold (0 °C) 0.2 M THF solution of NaOO-*t*-Bu (3 equiv) (20 min), according to the general procedure, a 77:23 mixture of sulfonyl tetrahydrofurans **25e** and **24e** was obtained. Purification by chromatography (20−30% EtOAc−hexane) gave **25e** (31 mg, 59%) as a white solid that was recrystallized from EtOAc−hexane and **24e** (5 mg, 10%) as a colorless oil. From a solution of sulfonyl dihydrofuran **29e** (40 mg, 0.12 mmol) in THF (1.0 mL) and a cold (−40 to −30 °C) 0.2 M THF solution of KOO-*t*-Bu (2 equiv) (20 min), according to the general procedure, a 92:8 mixture of sulfonyl tetrahydrofurans **25e** and **24e** was obtained. Purification by chromatography (15−30% EtOAc−hexane) gave **25e** (32 mg, 77%) as a white solid that was recrystallized from EtOAc−hexane and **24e** (3 mg, 7%) as a colorless oil. Data for **24e**: R_f 0.20 (50% EtOAc−hexane). ^{1}H NMR (200 MHz) δ 1.86 (br s, 1 H), 2.42 (s, 3 H), 3.81 (d, 2 H, J = 5.5 Hz), 4.45 (s, 1 H), 4.54 (t, 1 H, J = 5.6 Hz), 4.98 (s, 1 H), 7.19−7.40 (m, 7 H), 7.50 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (50 MHz) δ 21.7, 61.4, 63.7, 77.2, 77.7, 80.6, 128.1 (2 C), 128.5 (2 C), 129.0 (2 C), 129.4, 129.8 (2 C), 133.7, 136.1, 145.8. IR (film) 3526, 3065, 2925, 1595, 1456, 1331, 1160, 1087, 1052, 814, 764, 700, 667, 588 cm^{-1}. MS (ES) 369 [M + Na]$^+$. Anal. Calcd for $C_{18}H_{18}O_5S$: C, 62.41; H, 5.24, S, 9.26. Found: C, 62.32; H, 5.29; S, 9.42. Data for **25e**: mp 120−121 °C. R_f 0.25 (50% EtOAc−hexane). ^{1}H NMR (300 MHz) δ 1.85 (dd, 1 H, J = 6.1, 5.1 Hz), 2.29 (s, 3 H), 3.85−3.89 (m, 2 H), 4.34 (dd, 1 H, J = 4.8, 4.6 Hz), 4.35 (s, 1 H), 5.51 (s, 1 H), 6.98 (d, 2 H, J = 8.4 Hz), 7.07−7.24 (m, 5 H), 7.34 (d, 2 H, J = 8.3 Hz). DNOE between CH_2-OH/H-5 3.7% and between CH_2-OH/H-3 3.7%. ^{13}C NMR (50 MHz) δ 21.5, 62.2, 64.6, 76.8, 77.4, 78.3, 128.0 (2 C), 128.5 (2 C), 128.6 (2 C), 128.8, 129.2 (2 C), 132.9, 133.9, 145.2. IR (KBr) 3526, 2925, 1596, 1456, 1319, 1157, 1099, 1048, 968, 743, 671, 607, 582 cm^{-1}. MS (ES) 369 [M + Na]$^+$ (100%), 347 [M + 1]$^+$. Anal. Calcd for $C_{18}H_{18}O_5S$: C, 62.41; H, 5.24, S, 9.26. Found: C, 62.62; H, 5.45; S, 9.12.

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Supporting Information Available: Experimental procedures and characterization for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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