π-Facial Diastereoselection in Diels−Alder Reactions of (*R*)-4-[(*p*-Tolylsulfinyl)methyl]quinols

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Diels−Alder reactions of a range of (*R*)-4-hydroxy-4-[(*p*-tolylsulfinyl)methyl]-2,5-cyclohexadienones with cyclopentadiene and 1,3-pentadiene proceed in a total π-facial diastereoselective manner from the C-4 OH side. *Ab initio* calculations at the RHF/6-31G* theory level provide data on transition-state energies for cycloadditions with cyclopentadiene in full agreement with the experimental results.

Despite the potential usefulness of Diels−Alder adducts resulting from 4-hydroxy-4-substituted cyclohexadienones (*p*-quinol derivatives) as chiral synthetic equivalents of cyclohexenones, little attention has been paid to the study of their dienophilic behavior. The first paper dealing with this subject was published in 1981 by Liotta[1] who revealed a high π-facial diastereoselection for the cycloadditions of simple *p*-quinols with acyclic dienes and pointed out the possibility of generating up to five stereogenic centers in a single operation. Since then, sporadic work has been devoted to cycloadditions of 4,4-disubstituted cyclohexadienones,[2−4] but no systematic studies have been carried out. Moreover, all these reports have dealt with racemic or achiral cyclohexadienone derivatives. Access to enantiomerically pure adducts has been restricted to the use of chiral cyclopentadiene derivatives [3] or enzyme-mediated asymmetrization of meso derivatives.[5]

In connection with our investigations of the Diels−Alder reactions of both enantiomerically pure sulfinyl dienes[6,7] and sulfinylquinones,[8] we decided to synthesize the *p*-quinol derivatives incorporating a sulfoxide on the *p*-alkyl substituent to produce chiral synthons of 4-alkyl-4-hydroxy-2,5-cyclohexadienone. The preliminary results we obtained in the study of the dienophilic behavior of the simplest (*R*)-4-hydroxy-4-(*p*-tolylsulfinyl)-2,5-cyclohexadienone[9] (**5a**) revealed a high degree of π-facial distereoselectivity fully controlled by the OH at C-4. Moreover, upon reaction with cyclopentadiene discrimination between the two diastereotopic double bonds of the symmetrically substituted cyclohexadienone moiety was observed under $BF_3{\cdot}OEt_2$-catalyzed conditions. A similar and even more effective desymmetrization was observed in conjugate additions of **5a** with organoaluminum derivatives.[10] To extend the results achieved in Diels−Alder reactions with **5a** to other systems and to check their generality, we undertook the synthesis of differently substituted (sulfinylmethyl)-*p*-quinols **5** and **6** and studied their dienophilic behavior toward cyclopentadiene and 1,3-pentadiene. The effects of varying double-bond substitution of **5** and **6** on the reactivity of *p*-quinols as well as the π-facial diastereoselectivity of the cycloadditions were evaluated. The sulfinyl group of the dienophiles demonstrates remote asymmetric induction. We report herein the results of these studies as well as ab initio calculations showing that transition states arising from diene approach from the face containing the OH group are the lowest in energy.

Synthesis of 4-[(*p*-Tolylsulfinyl)methyl]-*p*-quinols. The preparation of *p*-quinols is based on the oxidation of phenols and phenol ethers and can be achieved by either electrochemical,[11] chemical,[12] or photooxidation[13] methods. The addition of organometallic derivatives to quinones[14] or quinone monoketals[15] has also been successfully used in the synthesis of these compounds. The synthesis of compound **5a** was based on the addition of an α-lithiomethylsulfinylcarbanion, readily available from enantiomerically pure (*R*)-methyl *p*-tolylsulfoxide,[16] to a quinone

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Scheme 1

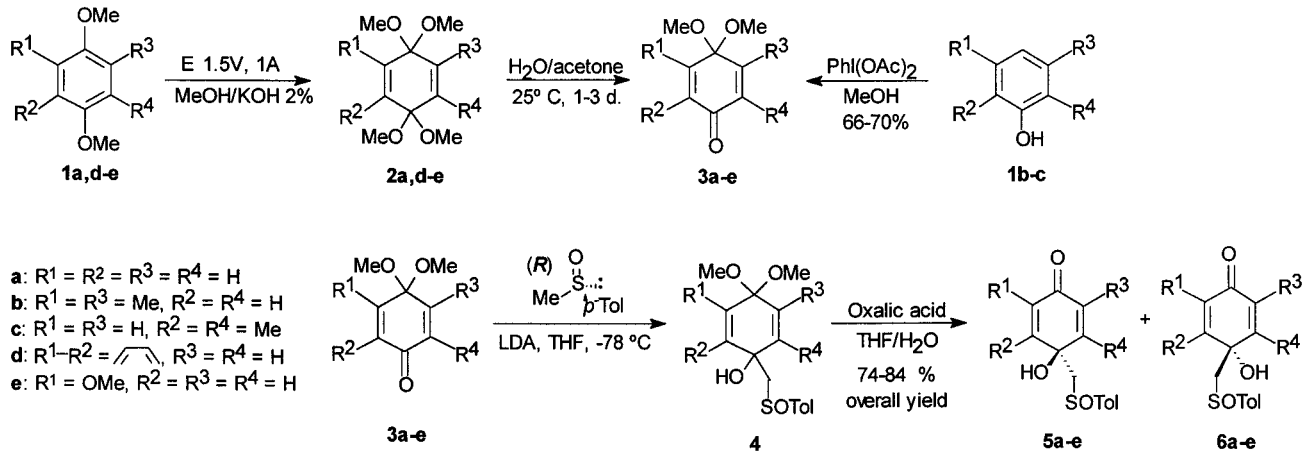
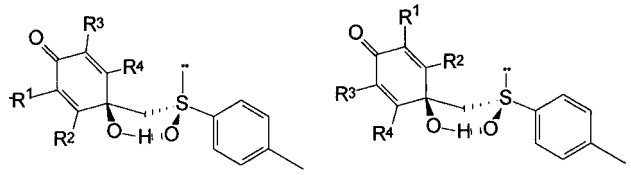


Table 1. ^{1}H NMR Data for Compounds 5a−e and 6d,e



5a-e 6d-e

	δ (ppm), multiplicity, *J* (Hz)							
	R^1	R^2	R^3	R^4	OH	AB system	AB′BB′ system	CH_3-Ar
5a	6.18, dd, 10.2, 1.9	7.00, dd, 10.2, 3.2	6.29, dd, 10.2, 1.8	7.25, dd, 12.2, 3.2	4.93	3.16 and 2.85, 13.3	7.57−7.42 and 7.38−4.34	2.43, s
5b	1.85, d, 1.6 (Me)	6.69, m	1.94, d, 1.6 (Me)	6.98, m	4.05	3.13 and 2.82, 13.3	7.57−7.49 and 7.39−7.30	2.42, s
5c	6.02, q, 1.6	2.03, d, 1.6 (Me)	6.16, q, 1.6	2.36, d, 1.6 (Me)	4.23	3.29 and 2.79, 13.4	7.55−7.47 and 7.46−7.36	2.42, s
5d	8.08, dd, 7.7, 1.5; 7.65−7.40, 2H, m	7.78, dd, 7.9, 1.3;	6.56, d, 10.5	7.67, d, 10.5	5.61	3.39 and 2.76, 13.1	7.54−7.48 and 7.36−7.30	2.41, s
6d	8.05, dd, 7.7, 1.4; 7.66, td, 7.8, 1.4; 7.47, m	7.93, dd, 7.9, 0.9;	6.27, d, 10.3	7.27, d, 10.3	5.16	3.12 and 2.97, 13.4	7.48−7.42 and 7.31−7.26	2.38, s
5e	3.63, s (OMe)	5.91, d, 3.0	6.29, d, 10.2	7.22, dd, 10.2, 3.0	4.71	3.17 and 2.91, 13.1	7.57−7.51 and 7.39−7.34	2.42, s
6e	3.74, s (OMe)	6.13, d, 3.0	6.19, d, 10.2	6.99, dd, 10.2, 3.0	4.71	3.18 and 2.86, 13.2	7.57−7.51 and 7.39−7.34	2.42, s

monoketal. This method could be successfully extended to the synthesis of **5b**−**e** and **6d**,**e**.

The starting quinone monoketals **3a**,**d**,**e**[11a] were synthesized by electrochemical oxidation of adequately substituted 1,4-dimethoxybenzenes **1a**,**d**,**e** followed by controlled monohydrolysis of the resulting bisketals **2a**,**d**,**e** (Scheme 1). Selective hydrolysis was successfully achieved by treatment with water in acetone solution.[17] As expected,[11b] the less hindered ketal group was regioselectively deprotected. Compounds **3b**,**c** were readily available by $PhI(OAc)_2$ oxidation of 2,6-dimethylphenol[18] and 3,5-dimethylphenol,[12c] respectively. The addition of a THF solution of **3a**−**e** to a mixture of (*R*)-methyl *p*-tolylsulfoxide and LDA, in the same solvent, afforded dimethyl acetals **4** that could be either isolated by crystallization in ethyl acetate (**4a**) or directly treated with oxalic acid in a THF aqueous solution to yield the *p*-quinol derivatives **5** and **6** in ca. 80% overall yield.

Starting from asymmetrically substituted **3d**,**e** a mixture of two diastereomers, epimers at C-4, **5d**,**e** and **6d**,**e** (70:30 and 60:40 ratio, respectively), was formed. The absolute configuration of the stereogenic hydroxylic carbons in **5d**,**e** and **6d**,**e** could be assigned at this stage on the basis of a comparative analysis of their ^{1}H NMR parameters (Table 1), taking into account their rigid structure imposed by the internal hydrogen bonding between the hydroxylic proton and the sulfinyl oxygen. This association was evidenced by the chemical shift of the hydroxylic hydrogens which appear at δ 4.05−5.61 and from dilution experiments. In such spiro-like structures, the most significant data for the configurational assignment correspond to the different chemical shift observed for the hydrogens situated at the olefinic β-position (carbons C-3 and C-5, R^2 and R^4 in the figure of Table 1). As can be seen, in the prochiral cyclohexadienone moiety of **5a**,**b** protons labeled as R^2 appear at δ 7.00 and 6.69, respectively, more shielded than those labeled as R^4 which were observed at δ 7.25 and 6.98. If the chemical shifts of R^4 for **5d**,**e** and **6d**,**e** are compared, a similar shielding on these protons in **6d**,**e** (δ 7.27 and 6.99) is observed with respect to their epimers **5d**,**e** (R^4 δ 7.67 and 7.22). Moreover derivative **5c** ($R^2 = R^4 = Me$) showed a similar trend in the chemical shifts of the methyl substituents, with R^2 (δ 2.03) being more shielded than R^4 (δ 2.36). A similar shielding effect was observed in the Diels−Alder adduct **7a** (see below)[19] resulting in the reaction of **5a** with cyclopentadiene from the *pro-S* dienophilic double bond, when compared with the diastereomer **8a** which arose from *pro-R* double-bond cy-

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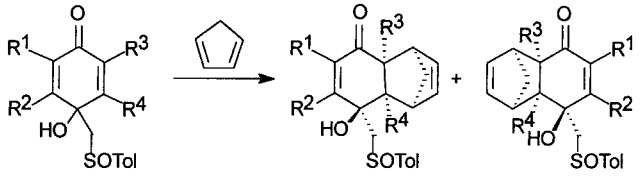
(17) Buchanan, G. L.; Raphael, R. A.; Taylor, R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 373−5. The method previously described for the preparation of compounds **3a**,**d**,**e** involved the use of an AcOH solution and did not afford the desired monoketal. Instead, the corresponding *p*-benzoquinone was formed under these conditions.

(18) Lu, L.; Shoemaker, R. K.; Wheeler, D. M. S. *Tetrahedron Lett.* **1989**, *30*, 6993−6.

(19) NMR parameters of Michael-type adducts resulting from reaction of **5a**,**b** with AlR_3 show similar trends (see ref 10).

Table 2. Diels–Alder Reaction of 5a–e and 6d,e with Cyclopentadiene



5a or 5+6d-e **7a,d-e** **8a,d-e**[b]

entry	dienophile	Lewis acid	solvent	*T* (°C)	*t*	yield (%)	**7**:**8**
1	**5a**		CH_2Cl_2	25	7 d	80	43:57
2	**5a**		H_2O	25	10 h	78	56:44
3	**5a**		ethanol	25	14 d	80	57:43
4	**5a**	$ZnBr_2$	CH_2Cl_2	25	4 h	83	54:46
5	**5a**	$Eu(fod)_3$	CH_2Cl_2	25	7 d	92	49:51
6	**5a**	SiO_2	none	25	2 h	94	48:52
7	**5a**	CF_3SO_3H	CH_2Cl_2	−78	15 min	95	67:33
8	**5a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−40	10 min	99	66:34
9	**5a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−78	15 min	93 (75 **7a** pure)	76:24
10	**5a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−96	1 h	80	81:19
11	**5b**	$ZnBr_2$	CH_2Cl_2	25	24 h	*a*	
12	**5b**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−78	10 h	*a*	
13	**5c**		CH_2Cl_2	25	20 d		
14	**5c**		H_2O	25	20 d		
15	**5c**	SiO_2	none	25	20 h		
16	**5c**	$ZnBr_2$	CH_2Cl_2	25	3 d		
17	**5c**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−20	2 d		
18	**5d** + **6d**	$ZnBr_2$	CH_2Cl_2	25	2 h	80	70:30
19	**5d** + **6d**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−78	90 min	70	70:30
20	**5e** + **6e**		CH_2Cl_2	25	2 d	99	60:40

[a] Complex mixture of products was obtained.

cloaddition. By comparison the configuration 4*R*,(*S*)*R* for epimers **5d**,**e** and 4*S*,(*S*)*R* for **6e**,**d** could be assigned.

Diels–Alder Reactions. With the desired *p*-quinols in hand, we studied the Diels–Alder cycloadditions choosing cyclopentadiene as a model of cyclic dienes. The influence of diverse Lewis acids and an array of reaction conditions were studied for the reaction between **5a** and cyclopentadiene.[9] The most significant results of this model study, as well as those of cycloadditions between **5** and **6** and this diene, are collected in Table 2.[20] Only two adducts (**7** and **8**) out of the eight possible diastereomers were obtained in good to excellent yield from **5a**,**d**,**e** and **6d**,**e**. For **5a**, both adducts resulted from endo cycloaddition of the diene to both dienophilic double bonds of the prochiral cyclohexadienone moiety syn to the face containing the hydroxy substituent at C-4. With **5a**, the use of water[21] as solvent significantly increased the thermal reaction rate (entry 2). The presence of Lewis acids or silica gel strongly accelerated the cycloadditions of **5a** (entries 4, 6–10). The lower temperature permitted by the more reactive unsubstituted *p*-quinol **5a** in the presence of $BF_3{\cdot}OEt_2$ (entries 9, 10) resulted in desymmetrization of the dienone moiety. Compound **7a** was isolated diastereomerically pure in a 75% yield when the reaction was carried out at −78 °C.

The thermal reaction of 2,6-dimethyl-substituted quinol **5b** did not lead to cycloaddition, whereas the catalyzed experiments only afforded complex reaction mixtures (entries 11, 12). Compound **5c**, with two methyl groups at C-3 and C-5, did not react in both thermal and catalyzed conditions (entries 13–17). This lack of reactivity was not unexpected considering the presence of the substituents in the dienophilic double bond of both **5b**,**c**.

The cycloadditions of dienophiles **5d**,**e** and **6d**,**e**, which contain an unsymmetrical dienone moiety, with cyclopentadiene were carried out on a 70:30 mixture of **5d** and **6d** C-4 epimers and a 60:40 mixture of **5e** and **6e**. The results are collected in Table 2 (entries 18–20). Two endo adducts **7d**,**e** and **8d**,**e**, which resulted from the reaction on one dienophilic double bond of **5d**,**e** and **6d**,**e**, were always formed in the same ratio as the starting dienophiles indicating again a complete π-facial diastereoselective cycloaddition from **5d**,**e** and **6d**,**e** syn to the face containing the hydroxy substituent. Dienophiles **5d** and **6d** gave adducts **7d** and **8d**, respectively, in the presence of $ZnBr_2$ (entry 18) and $BF_3{\cdot}OEt_2$ (entry 19). The methoxy-substituted derivatives **5e** and **6e** were not stable enough to $BF_3{\cdot}OEt_2$ and their cycloadditions could only be carried out under thermal conditions (entry 20). Separation of both diastereomeric adducts **7** and **8** was feasible by flash chromatography in all cases.

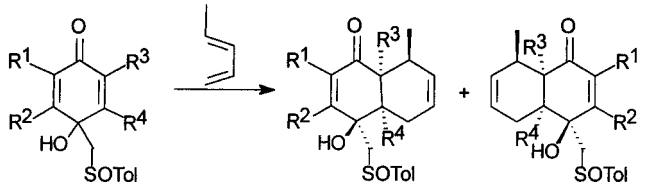
The results of reactions of *p*-quinols **5a**–**e** and **6d**,**e** (from a 70:30 mixture of **5d**/**6d** and a 60:40 mixture of **5e**/**6e**) with 1,3-pentadiene, chosen as a model of acyclic dienes, are collected in Table 3. Similar behavior was observed, for 1,3-pentadiene and the cyclic diene, forming exclusively two endo adducts (**9** and **10**). As can be seen, the presence of $BF_3{\cdot}OEt_2$ in the reaction with **5a** at −78 °C (entry 3) allowed the major formation of diastereomer **9a** resulting from the cycloaddition on the *pro-S* double bond. Thus, under these conditions, the desymmetrization of the dienone moiety, already observed in the reaction between **5a** and cyclopentadiene, occurred. The

(20) For the sake of clarity, the structures **8a**–**c** and **10a**–**c** are represented with R^3 and R^4 at the bridged carbons although they should be drawn as shown below:

8a-e: x= H, y=CH_2
10a-e: x= Me, y= H, H

(21) Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev. (Washington, D.C.)* **1993**, *93*, 741–61.

Table 3. Diels−Alder Reaction of 5a−e and 6d,e with 1,3-Pentadiene

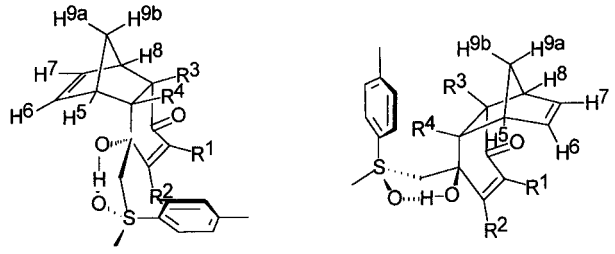


5a-c or 5+6d-e **9a-e** **10a-e**(b)

entry	dienophile	Lewis acid	solvent	*T* (°C)	*t*	yield (%)	**9**:**10**
1	**5a**	$ZnBr_2$	CH_2Cl_2	25	12 h	83	55:45
2	**5a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−40	3 h	85	69:31
3	**5a**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−78	5 h	83	76:24
4	**5b**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−20	2 d	65	61:39
5	**5b**	$ZnBr_2$	CH_2Cl_2	25	24 h		
6	**5c**	$ZnBr_2$	CH_2Cl_2	25	20 d		
7	**5c**	$ZnBr_2$/13 kbar	CH_2Cl_2	25	48 h	70	71:29
8	**5d** + **6d**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−78	6 h	89	70:30
9	**6d**	$BF_3{\cdot}Et_2O$	CH_2Cl_2	−78	5 h	81	100:0
10	**5e** + **6e**	$ZnBr_2$	CH_2Cl_2	25	39 d	30[a]	60:40
11	**5e** + **6e**	$ZnBr_2$/13 kbar	CH_2Cl_2	25	24 h	68	60:40

[a] Conversion of starting material measured by ^{1}H NMR.

Table 4. ^{1}H NMR Data for Compounds 7a,d,e and 8a,d,e



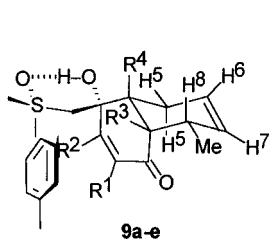
7a,d-e **8a,d-e**

	δ (ppm), multiplicity, *J* (Hz)					
	7a	**8a**	**7d**	**8d**	**7e**	**8e**
R^1	5.70, d, 10.3	5.89, d, 10.6	7.69, dd, 7.7, 1.2; 7.58−7.46, m; 7.29−7.20, m (R^1 and R^2)	7.84, dd, 8.2, 1.2; 7.73−7.65, m; 7.45−7.35, m (R^1 and R^2)	3.41, s (OMe)	3.63, s (OMe)
R^2	6.37, dd, 10.3, 1.0	6.95, dd, 10.6, 1.6			5.27, s (br)	5.77, s (br)
R^3	3.07, dd, 6.2, 4.3	2.94, dd, 8.7, 4.2	3.40, dd, 8.4, 4.1	3.22, dd, 8.1, 4.2	3.12, dd, 8.7, 4.1	3.02, dd, 8.6, 4.3
R^4	3.48−3.40, m	2.69, ddd, 8.7, 3.8, 1.6	3.70, dd, 8.4, 3.4	2.91, dd, 8.3, 3.4	3.27, dd, 8.8, 2.7	2.62, ddd, 8.6, 3.3, 1.1
OH	5.17, s	4.97, s	5.63, s	5.87, s	5.11, s	5.77, s
H^5 and H^8	3.48−3.40, m	3.36−3.32, m	3.49 and 2.86, m	3.38 and 3.25, m	3.36−3.33, m	3.35−3.31, m
H^6	6.19, dd, 5.4, 2.0	6.16, dd, 5.6, 3.0	5.62, dd, 6.0, 2.9	5.58, dd, 5.6, 2.9	6.17, dd, 5.4, 2.9	6.17, dd, 5.5, 2.9
H^7	5.80, dd, 5.6, 3.0	5.79, dd, 5.6, 2.8	5.33, dd, 5.6, 2.7	5.30, dd, 5.6, 2.5	5.75, dd, 5.6, 2.9	5.77, dd, 5.2, 2.8
H^{9a}	1.52−1.41, m	1.46−1.40, m	1.59−1.53, m	1.45−1.39, m	1.42−1.37, m	1.37, dt, 8.6, 1.8
H^{9b}	1.52−1.41, m	1.28−1.24, m	1.51, 1.43, m	1.38−1.33	1.37−1.32	1.22, dd, 8.6, 1.3
AB system	3.10 and 2.56, 13.2	3.16 and 2.77, 12.8	2.90 and 2.53, 13.7	3.17 and 2.59m 13.0	3.10 and 2.63, 13.2	3.16 and 2.72, 12.8
AA′BB′ system	7.56−7.50 and 7.35−7.32	7.53−7.48 and 7.39−7.33	7.38−7.33 and 7.29−7.23	7.51−7.46 and 7.31−7.26	7.49−7.43 and 7.29−7.25	7.50−7.44 and 7.33−7.28
CH_3-Ar	2.42, s	2.43, s	2.35, s	2.37, s	2.34, s	2.39, s

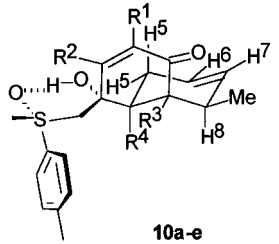
absence of cycloaddition when 1,3-pentadiene was submitted to reaction with **5c** in the presence of $ZnBr_2$ (entry 6), or **5e** and **6e** under thermal conditions, indicated again a very low reactivity of these dienophiles (entry 10) due to their substitution. Only the use of high pressures (13 kbar) in the $ZnBr_2$-catalyzed reaction of **5c** (entry 7) and **5e**/**6e** (entry 11) allowed formation of the desired adducts. A 55:45 and a 60:40 mixture of compounds **9c**/**10c** and **9e**/**10e** was formed under these conditions, indicating that the high pressure does not alter the endo and π-facial diastereoselectivity of the process.

A detailed comparative analysis of the ^{1}H NMR parameters of adducts **7d**,**e**, **8d**,**e**, **9a**−**e**, and **10a**−**e** with those of **7a** and **8a**, whose structures had been unequivocally assigned by chemical correlation and confirmed by X-ray diffraction of **7a**,[9] enabled the unambiguous configurational assignments shown in Tables 4 and 5. The most significant data correspond again to the shielding observed for the bridged proton R^4 in epimers **8** and **10** with respect to the same hydrogen in **7** and **9** (Δδ 0.65−0.81) due to the anisotropic effect of the tolyl group that is situated close to R^4 in **8** and **10** as a consequence of the rigid conformation around the C−S bond arising from the strong intramolecular hydrogen bond shown in the figures of Tables 4 and 5. Taking into account the (*R*)-sulfoxide configuration, we could establish that the cycloaddition had taken place on the *pro-S* double bond of **5a**−**c** to give adducts **7a** and **9a**−**c** and on the *pro-R* double bond yielding adducts **8a** and **10a**−**c**. In the case of **5d**,**e** and **6d**,**e** the cycloaddition was highly diastereoselective leading to the formation of a sole adduct in each case.

Table 5. ^{1}H NMR Data for Compounds 9a−e and 10a−e



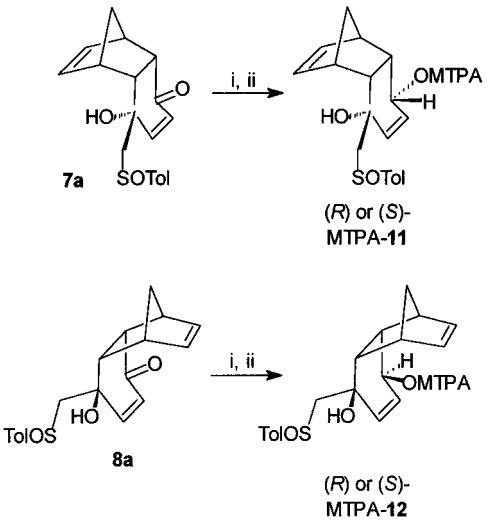
9a-e



10a-e

	δ (ppm), multiplicity, J (Hz)									
	9a	**10a**	**9b**	**10b**	**9c**	**10c**	**9d**	**10d**	**9e**	**10e**
R^1	5.76, d, 10.1	5.95, d, 10.3	1.85, d, 1.6 (Me)	1.91, s (Me)	5.63, s (br)	5.85, s (br)	7.90, dd, 7.8, 1.4; 7.74, dd, 7.8, 1.2; 7.63−7.56, m; 7.39−7.31, m (R^1 and R^2)	7.97, dd, 7.8, 1.5; 7.90, dd, 7.9, 1.3; 7.67, td, 7.4, 1.5; 7.43, td, 7.6, 1.2 (R^1 and R^2)	3.51, s (OMe)	3.67, s (OMe)
R^2	6.44, dd, 10.2, 2.5	6.85, dd, 10.2, 2.3	6.76, quin, 1.4	6.92, s	1.99, s (Me)			5.34, d, 1.4	5.73, d, 2.2	
R^3	3.14−3.05, m	2.63−2.55, m	1.34, s (Me)	1.30 (Me)	2.30, d, 4.3		3.47, ddd, 11.0, 6.0, 3.6	2.92, ddd, 10.0, 6.0, 3.7	3.12−2.99, m	2.59−2.44, m
R^4	2.70, t, 3.9	2.62−2.59, m	2.45−2.26, m	1.99, dd, 7.2, 3.1	1.44, d, 1.6 (Me)	1.18, s (Me)	2.98, t, 3.9	2.77, t, 3.9	2.75−2.69, m	2.66−2.59, m
OH	4.77, s	4.92, s		4.30, s	4.63, s	5.07, s	5.20, s	5.07, s		4.99, s (br)
H^{5eq}	2.57−2.45, m	2.40−2.22, m	2.45−2.26, m	2.3902.28, m	2.05−1.89, m	2.34−2.16, m	2.65−2.44, m	2.49−2.20, m	2.67−2.33, m	2.47−2.25, m
H^{5ax}	2.19−2.05, m	2.12−1.99, m	2.45−2.26, m	2.28−2.17, m	2.29−2.14, m	1.98−1.82, m	2.03−1.81,	1.87−1.71, m	2.25−1.98, m	2.19−1.19, m
H^6 and H^7	5.61−5.58, m	5.50−5.60, m	5.85−5.63, m	5.75−5.55, m	5.64−5.44, m	5.63−5.42, m	5.72−5.56, m	5.62−5.47, m	5.68−5.51, m	5.61−5.45, m
H^8	2.44−2.36, m	2.33−2.26, m	2.26−2.05, m	2.15−2.04, m	2.64−2.47, m	2.58−2.39, m	2.85−2.65, m	2.39−2.28, m	2.45−2.33, m	2.36−2.25, ,m
Me	1.41, d, 7.4	1.34, d, 7.7	0.98, d, 7.5	1.00, d, 7.5	1.42, d, 7.8	1.40, d, 7.5	1.58, d, 7.6	1.42, d, 7.6	1.40, d, 7.8	1.34, d, 7.5
AB system	3.29 and 3.14, 13.5	3.35 and 3.24, 13.1	3.07 and 2.97, 13.4	3.28 and 2.70, 13.4	3.16 and 2.94, 14.0	3.25 and 2.81, 13.1	3.32−3.19, m	3.33, s	3.30 and 3.17, 13.7	3.29 and 3.18, 12.9
AA′BB′ system	7.61−7.56 and 7.39−7.35	7.60−7.56 and 7.39−7.36	7.57−7.52 and 7.36−7.31	7.56−7.53 and 7.38−7.34	7.60−7.54 and 7.39−7.34	7.59−7.54 and 7.41−7.34	7.63−7.55 and 7.39−7.34	7.58−7.52 and 7.38−7.34	7.62−7.56 and 7.39−7.34	7.62−7.54 and 7.40−7.34
CH_3-Ar	2.43, s	2.44, s	2.42, s	2.43, s	2.43, s	2.42, s	2.42, s	2.43, s	2.42, s	2.44, s

Scheme 2[a]



[a] (i) DIBALH, CH_2Cl_2, −78 °C, 80−85%; (ii) (*R*- or (*S*)-MTPACl, DMPA, CH_2Cl_2. ca. 70%.

These configurations of **7a** and **8a** were determined through the Mosher's esters[22] of carbinols **11** and **12** obtained in a highly diastereoselective manner and a high yield by treatment of **7a** and **8a**, respectively, with DIBAL-H. As expected,[23] the approach of the reagent to the fused norbornene cyclohexenone moiety of **7a** and **8a** took place exclusively from the convex face allowing the stereoselective formation of the diols (Scheme 2). This simple transformation allowed us to avoid the difficult formation of the MTPA esters of a tertiary hydroxyl group, which was achieved on the secondary alcohol[24] in good yield. With the four MTPA esters in hand, we could establish their absolute configuration by NMR spectroscopy[25,26] and confirm those of their precursors.

The very high π-facial diastereoselectivity observed in the reaction of *p*-quinols **5** and **6** agrees with previous results reported for Diels−Alder reactions of 4,4-disubstituted cyclohexadienones[1,2] and cyclic enones bearing one or two substituents at the γ-position,[27,28] where adducts resulting from the syn diene approach to the electron-withdrawing groups at the γ-position were always formed. Although the reasons for such a high π-facial diastereoselectivity are not well-established, both steric[27] and electronic[28] factors have been suggested as governing the reaction outcome.

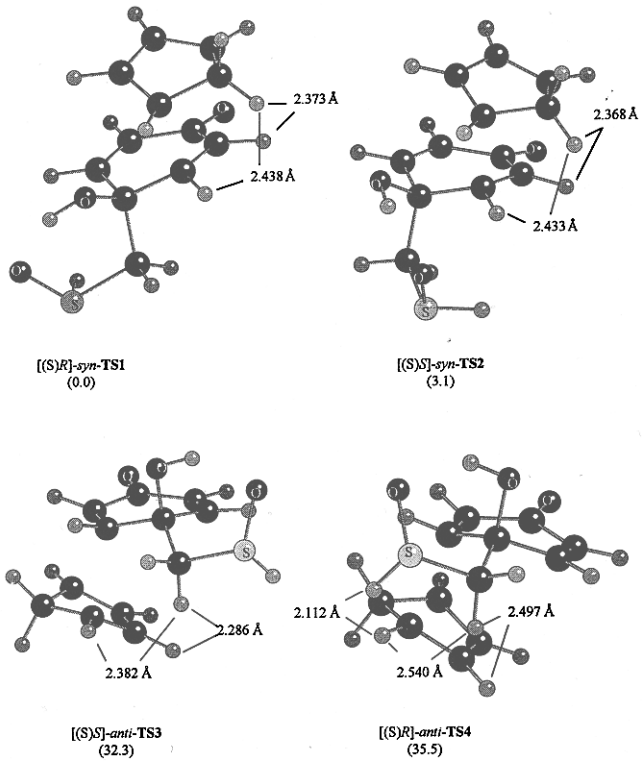
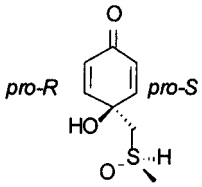


Figure 1. Endo transition structures, computed at the RHF/6-31G*//RHF/2-21G* level, for the thermal reaction of cyclopentadiene with the *p*-quinol **13** taken as a model (relative energies in kJ·mol^{-1}).

To rationalize the selectivity achieved, we undertook a theoretical study of a model reaction between **13**, a

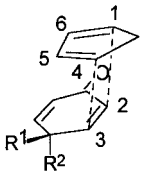


13

simplified analogue of [(*S*)*R*]-*p*-quinol **5a** (SOH instead of SO-*p*-Tol), and cyclopentadiene. Calculations were performed in the absence of catalyst or the presence of BH_3, using ab initio methods and the GAUSSIAN-94 program.[29] Structures were fully optimized at the restricted Hartree−Fock level of theory with the 3-21G* basis set followed by vibrational frequency calculations which confirmed that the transition structures have one imaginary frequency. In addition, the energies were obtained on these geometries with single-point RHF/6-31G* calculations. Attack from the OH face of **13** is called syn cycloaddition, whereas the diene approach from the face containing the CH_2SOH group is called anti cycloaddition. The starting geometry for the transition state of the syn cycloaddition on the *pro-S* double bond of **13** by cyclopentadiene, [(*S*)*R*]-*syn*-TS1 (Figure 1), was built up from the endo transition state of the reaction between acrolein and cyclopentadiene. The transition state for syn cycloaddition on *pro-R* double bond, [(*S*)*S*]-*syn*-TS2, was modeled by changing the sulfur configuration in [(*S*)*R*]-*syn*-TS1. The transition states for anti

(22) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(23) Marchand, A. P.; La Roe, W. D.; Sharma, G. V. M.; Suri, S. C.; Reddy, D. S. *J. Org. Chem.* **1986**, *51*, 1622−5.
(24) Chan, T. H.; Nwe, K. T. *J. Org. Chem.* **1992**, *57*, 6107−11.
(25) Othani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092−6.
(26) The configurational assignment of MTPA-**11** esters was unequivocal, whereas those of MTPA-**12** esters was not so evident due to the small differences observed between the chemical shifts of the corresponding (*R*)- and (*S*)-MTPA derivatives. This could be a consequence of a higher steric hindrance of the ester moiety in diastereomers MPTA-**12** which prevented a fixed position of the methoxy and phenyl group in the ester.
(27) Fringuelli, F.; Minuti, L.; Pizzo, F.; Taticchi, A. *Acta Chem. Scand.* **1993**, *47*, 255−63 and references therein.
(28) Jeroncic, L. O.; Cabal, M. P.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 387−95.
(29) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Latham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian 94, revision C.2; Gaussian, Inc.: Pittsburgh, PA, 1995.

Table 6. Imaginary Frequencies (cm^{-1}), Total Energies (au), Relative Energies ($kJ \cdot mol^{-1}$/$kcal \cdot mol^{-1}$), and Selected Distances (Å) for the Thermal Transition Structures



R^1 = OH, R^2 = (*R*)-CH_2SOH, (*S*)-CH_2SOH
R^1 = (*R*)-CH_2SOH, (*S*)-CH_2SOH, R^2 = OH

	[(*S*)*R*]-*syn*-TS1	[(*S*)*S*]-*syn*-TS2	[(*S*)*S*]-*anti*-TS3	[(*S*)*R*]-*anti*-TS4
frequency	620.7i	629.4i	673.5i	666.1i
total *E*	−1084.45201	−1084.44898	−1084.43784	−1084.43664
rel *E*	0.0/0.0	3.1/0.7	32.3/7.7	35.5/8.5
C_1-C_2	2.329	2.317	2.226	2.225
C_2-C_3	1.381	1.328	1.378	1.379
C_3-C_4	2.081	2.077	2.191	2.197
C_4-C_5	1.389	1.389	1.389	1.388
C_5-C_6	1.401	1.400	1.399	1.399
C_6-C_1	1.377	1.378	1.382	1.382

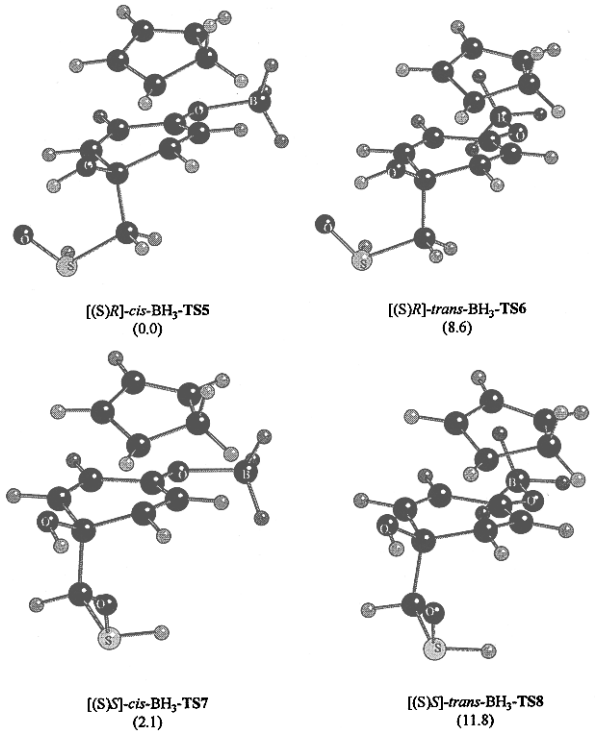
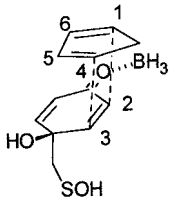


Figure 2. Endo syn transition structures, computed at the RHF/6-31G*//RHF/3-21G* level, for the catalyzed reaction of cyclopentadiene with the *p*-quinol **13** taken as a model (relative energies in $kJ \cdot mol^{-1}$).

cycloadditions on *pro-S* double bond of **13**, [(*S*)*S*]-*anti*-TS3, and on *pro-R* double bond of **13**, [(*S*)*R*]-*anti*-TS4, were modeled in the same way. Figure 1 presents the geometries[30] of these transition states which give rise to the four possible endo adducts in the thermal Diels−Alder reaction. Bond lengths of the forming and breaking bonds as well as the corresponding frequencies and energies are collected in Table 6. The same data are displayed in Figure 2 and Table 7 for the four syn adducts resulting from the Lewis acid-catalyzed reaction between cyclopentadiene and the *p*-quinol **13**. BH_3 was used as a model for the Lewis acid catalysts and was coordinated to the carbonyl group in a cis and trans disposition with respect to the reacting dienophilic double bond.

(30) Optimized geometries of all the structures are available from the authors.

Table 7. Imaginary Frequencies (cm^{-1}), Total Energies (au), Relative Energies ($kJ \cdot mol^{-1}$/$kcal \cdot mol^{-1}$), and Selected Distances (Å) for the BH_3-Catalyzed Transition Structures



	[(*S*)*R*]-*cis*-TS5	[(*S*)*S*]-*trans*-TS6	[(*S*)*S*]-*cis*-TS7	[(*S*)*S*]-*trans*-TS8
frequency	464.5i	485.9i	467.8i	490.4i
total *E*	−1110.86852	−1110.86525	−1110.86772	−1110.86402
rel *E*	0.0/0.0	8.6/2.1	2.1/0.5	11.8/2.8
C_1-C_2	2.617	2.550	2.611	2.539
C_2-C_3	1.392	1.390	1.392	1.391
C_3-C_4	2.014	2.010	2.002	2.000
C_4-C_5	1.391	1.392	1.392	1.394
C_5-C_6	1.412	1.409	1.411	1.408
C_6-C_1	1.363	1.365	1.364	1.366

Data collected in Table 6 show that transition states [(*S*)*R*]-*anti*-TS4 and [(*S*)*S*]-*anti*-TS3 have higher energies (ΔE = 32.3 and 35.5 kJ mol^{-1}, respectively) than those corresponding to the syn approach, [(*S*)*R*]-*syn*-TS1 and [(*S*)*S*]-*syn*-TS2 (0.0 and 3.1 kJ mol^{-1}, respectively). This is consistent with the complete syn diastereofacial selectivity experimentally observed. A detailed analysis of the geometries represented in Figure 1 revealed that the *p*-quinol moiety in all the transition states adopts a conformation where the γ-substituent syn to the approaching diene (OH in [(*S*)*R*]-*syn*-TS1 and [(*S*)*S*]-*syn*-TS2 and CH_2SOH in [(*S*)*R*]-*anti*-TS4 and [(*S*)*S*]-*anti*-TS3) is situated in a pseudoequatorial position. This could be expected for the anti transition states, where the group adopting the pseudoaxial position is an OH, but it is an anomalous situation for syn transition states where the bulky CH_2SOH substituent is in the pseudoaxial disposition. Nevertheless, these should be the most favored geometries, since even when the CH_2SOH is pseudoaxial as in [(*S*)*R*]-*syn*-TS1 and [(*S*)*S*]-*syn*-TS2, no destabilizing interactions are evident. The other possible conformation of the *p*-quinol moiety would produce destabilizing interactions between the syn approaching diene and the pseudoaxial γ-substituent situated on the same face. From this analysis, no serious differences between syn and anti approaches are evident. Instead the attack on the side of the relatively small OH group is favored over attack near the larger substituted alkyl group. Figure 1 shows the relatively small H−H distances in the disfavored transition states. The staggering of the newly forming bonds with respect to the allylic bonds enforces a relatively rigid boatlike conformation of the quinol in the transition state, which enforces the steric differentiation. Although the Cieplak[31] model gives the correct preference for attack anti to the alkyl and syn to the OH, analyses of the orbitals of the dienophile and the transition state give no evidence for this or the related orbital distortion effect of Liotta et al.[32]

Regarding the desymmetrization of the cyclohexadienone moiety, these calculations predict a very small

(31) (a) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540−52. (b) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447−62.

(32) (a) Burguess, E. M.; Liotta, C. L. *J. Org. Chem.* **1981**, *46*, 1703. (b) Liotta, C. L.; Burguess, E. M.; Eberhardt, W. H. *J. Am. Chem. Soc.* **1984**, *106*, 4849−52.

energy difference ($\Delta E = 3.1$ kJ mol^{-1}) between the [(*S*)*R*]-*syn*-TS1 (yielding the analogue of adduct **7a**) and [(*S*)*S*]-*syn*-TS2 (leading the analogue of adduct **8a**). This value predicts an approximate 51:49 ratio of the corresponding endo adducts at rt within the range experimentally observed. The change of the SOH substituent in the model **13** by a SO-*p*-Tol should make these transition states energetically more different, but the experimental diasteromeric excess observed in the thermal reactions of **5a** at room temperature (Table 2, entries 1−3) shows that the difference in energy barrier must be small.

The difference between the lengths of the two forming bonds C_1-C_2 and C_3-C_4 in the transition states are 0.248 and 0.240 Å for the [(*S*)*R*]-*syn*-TS1 and [(*S*)*R*]-*syn*-TS2, respectively (Table 6). These values are smaller than the ones corresponding to the reactions of cyclopentadiene with methyl vinyl ketone, where this difference is 0.331 Å (6-31G*),[33] and both syn cycloadditions of **13** seem to take place through transition states that are more synchronous.

The results obtained for the transition states of catalyzed syn reactions TS5−8 (Table 7) pointed out a higher energy content for the associated [(*S*)*R*]-*trans*-BH_3-TS6 than for the [(*S*)*R*]-*cis*-BH_3-TS5 transition states (ΔE = 8.6 kJ mol^{-1}) giving rise to the same adduct analogue to **7a**. A similar difference is observed between [(*S*)*S*]-*trans*-BH_3-TS8 and [(*S*)*S*]-*cis*-BH_3-TS7 (ΔE = 9.7 kJ mol^{-1}) which led to **8a**. Moreover, the gap in energy for transition states [(*S*)*S*]-*cis*-TS5 leading to **7a** and [(*S*)*R*]-*cis*-TS7 giving **8a** (ΔE = 2.1 kJ mol^{-1}) is smaller than the difference between [(*S*)*R*]-*syn*-TS1 and [(*S*)*S*]-*syn*-TS3 of thermal reactions yielding the same adducts **7a** and **8a**, respectively (ΔE = 3.1 kJ mol^{-1}). This observation indicates that the energy difference between both thermal and catalyzed reactions is very similar. Thus, the chemoselectivity observed for the $BF_3{\cdot}OEt_2$-catalyzed reactions is only a consequence of the very low temperature admitted. Length differences in forming bonds C_1-C_2 and C_3-C_4 (0.603 and 0.609 Å for cis and 0.540 and 0.539 Å for trans) pointed out that the cis catalyzed reactions are more asynchronous than the trans and, in turn, both are more asynchronous than the thermal reaction.

Conclusion

The high π-facial diastereoselection achieved in Diels−Alder cycloadditions of *p*-quinols **5a**−**e** and **6d**,**e** is exclusively controlled by the CH_2 and hydroxy substituents at C-4. The sulfoxide merely introduces optical activity in the dienophile. *Ab initio* calculations based on the restricted Hartree−Fock level of theory with the 6-31G* basis set showed that steric effects are responsible for the observed high π-facial diastereoselectivity. When the reaction of **5a** was carried out in the presence of $BF_3{\cdot}OEt_2$ at low temperature, the efficient desymmetrization of the cyclohexadienone moiety allows the simultaneous generation of up to five stereogenic centers in a single operation.

Experimental Section

General Methods. All moisture-sensitive reactions were performed in oven- or flame-dried glassware equipped with rubber septa under a positive pressure of argon. Solvents were dried according to literature procedures.[34] All reactions were monitored by TLC which was performed on precoated silica gel 60 F_{254} plates. Flash column chromatography was effected with silica gel 60 (230−400 mesh). Proton and carbon NMR spectra were recorded at 200.1 and 50.3 MHz. ^{1}H NMR data of compounds **5**−**10** are collected in Tables 1, 4, and 5. Combustion analyses were performed at the Servicio de Investigacion (SIdI) de la Universidad Autónoma de Madrid. Cyclopentadiene was distilled and stored at −20 °C in order to avoid dimerization. No differences were found using *trans*-1,3-pentadiene or 1,3-pentadiene as a mixture of isomers. $ZnBr_2$ was flame-dried in the reaction flask before use.

Method A. Synthesis of *p*-Quinols. A solution of butyllithium (2.6 M in hexanes, 1.1 equiv) was dropwise added to a THF solution of diisopropylamine (0.6 M, 1.2 equiv) at −78 °C. After 20 min a solution of [(*S*)*R*]-methyl *p*-tolylsulfoxide in THF (0.6 M, 1 equiv) was added via cannula. The reaction was maintained for 30 min at the same temperature, and a THF solution of quinone monoketal **3a**−**e** (0.3 M, 1.05 equiv) was added dropwise. After 2 h at −78 °C the reaction was quenched with a NH_4Cl-saturated solution (40 mL) and the mixture extracted with ethyl acetate (3 × 40 mL). The organic extracts were washed with brine (2 × 40 mL) and dried with Na_2SO_4. The solvent was removed under vacuum. These crude dimethoxy ketals of quinols **4** were treated with 5% oxalic acid in THF/H_2O (4:1). Extractive workup with ethyl acetate, drying with Na_2SO_4, and solvent evaporation yielded the desired quinol which was purified as indicated below.

[(*S*)*R*]-4-Hydroxy-4-[(*p*-tolylsulfinyl)methyl]-2,5-cyclohexadien-1-one (5a). Compound **5a** was obtained from 11.95 g of **3a**[11a,17] following method A and purified by crystallization in ethyl acetate/hexane in 76% yield as a white solid: mp 142.7−143.7 °C; $[\alpha]^{20}_D = +144$ (*c* 1, $CHCl_3$); IR ($CHCl_3$) 3330, 1670, 1630, 1055 cm^{-1}; ^{13}C NMR δ 184.9, 149.2, 149.1, 142.2, 139.6, 130.1 (2C), 128.1, 127.6, 123.9 (2C), 68.0, 67.1, 21.3. Anal. Calcd for $C_{14}H_{14}O_3S$: C, 64.11; H, 5.38. Found: C, 63.63; H, 5.10.

[(*S*)*R*]-4-Hydroxy-2,6-dimethyl-4-[(*p*-tolylsulfinyl)methyl]-2,5-cyclohexadien-1-one (5b). Compound **5b** was obtained from 1.624 g of **3b**[12c] following method A and purified by flash chromatography (AcOEt/hexane, from 1:1 to 3:1) in 84% yield as a pale yellow solid: mp 138 °C dec; $[\alpha]^{20}_D = +104$ (*c* 1.04, $CHCl_3$); ^{13}C NMR δ 186.2, 143.8, 143.7, 142.2, 140.1, 134.9, 134.4, 130.1 (2C), 123.9 (2C), 68.5, 66.6, 21.3, 15.8, 15.7. Anal. Calcd for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 65.98; H, 6.16; S, 11.36.

[(*S*)*R*]-4-Hydroxy-3,5-dimethyl-4-[(*p*-tolylsulfinyl)methyl]-2,5-cyclohexadien-1-one (5c). Compound **5c** was obtained from 2.9 g of **3c**[18] following method A and purified by flash chromatography (AcOEt/hexane, from 1:1 to 3:1) in 80% yield as a white solid: mp 131−132 °C; $[\alpha]^{20}_D = +7.3$ (*c* 1.03, $CHCl_3$); IR (KBr) 3290, 1670, 1650, 1050 cm^{-1}; ^{13}C NMR δ 185.0, 160.9, 159.7, 143.6, 140.1, 130.2 (2C), 127.8, 127.5, 123.8 (2C), 72.8, 65.0, 21.4, 19.3, 18.1. Anal. Calcd for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.08; H, 6.16; S, 11.33.

4-Hydroxy-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (5d and 6d). Compounds **5d** and **6d** were obtained from 1.5 g of **3d**[11a,17] following method A and purified by flash chromatography (AcOEt/hexane, 3:2) in 74% yield as a 70:30 mixture of diastereoisomers. Crystallization in AcOEt afford compound **[4*R*,(*S*)*R*]-5d** as a white solid: mp 132.7 °C dec; $[\alpha]^{20}_D = +63$ (*c* 1.04, $CHCl_3$); ^{13}C NMR δ 183.7, 149.5, 144.7, 142.6, 139.8, 133.5, 130.3 (2C), 129.3, 128.7 (2C), 126.7, 126.6, 123.7 (2C), 70.6, 69.4, 21.4. Anal. Calcd for $C_{18}H_{18}O_3S$: C, 68.77; H, 5.77; S, 10.20. Found: C, 68.85; H, 5.14; S, 10.40. NMR data of **[4*S*,(*S*)*R*]-6d** was obtained from a mixture of **5d** and **6d**: ^{13}C NMR δ 183.7, 150.6, 145.2, 141.8, 139.6, 133.1, 129.9 (2C), 129.4, 128.3, 127.3, 126.4 (2C), 123.9 (2C), 71.3, 69.4, 21.2.

[4*R*,(*S*)*R*]- and [4*S*,(*S*)*R*]-4-Hydroxy-2-methoxy-4-[(*p*-tolylsulfinyl)methyl]-2,5-cyclohexadien-1-one (5e and 6e). Compounds **5e** and **6e** were obtained as an inseparable

(33) Jorgensen, W. L.; Lim, D.; Blake, J. *J. Am. Chem. Soc.* **1993**, *115*, 2936−42.

(34) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon Press: New York.

mixture from 1.14 g of **3e**[11a,17] following method A and purified by flash chromatography (AcOEt/hexane, 5:1) in 79% yield as a 60:40 mixture of diastereoisomers. Anal. Calcd for $C_{15}H_{16}O_4S$: C, 61.63; H, 5.52; S, 10.97. Found: C, 61.44; H, 5.65; S, 11.23.

Method B. Diels−Alder Reaction in Thermal Conditions. Diene (10 equiv) was added at room temperature to a solution of **5a** or a mixture of **5** and **6d**,**e** (0.1 M) in the solvent indicated in each case (see Table 2 for conditions). A portion of 5 equiv of diene was added every 4 days. The reaction was TLC monitored, and after completion (see Table 1 for reaction times), the solvent was evaporated at reduced pressure.

Method C. Catalyzed Diels−Alder Reaction. A solution of **5** or a mixture of **5** and **6d**,**e** (0.1 M) in dry CH_2Cl_2 was added to the appropriate Lewis acid under argon at the desired temperature (see Tables 2 and 3 for conditions). After 30 min the diene (2 equiv) was added. The reaction was TLC monitored, and after completion (see Tables 2 and 3 for reaction times) water was added. The aqueous layer was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and evaporated at reduced pressure.

4a,5,8,8a-Tetrahydro-4-hydroxy-5,8-methano-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (7a and 8a). Compounds **7a** and **8a** were obtained from **5a** under the experimental conditions and in the ratios shown in Table 2. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 1:1). **[4*S*,4a*R*,5*S*,8*R*,8a*S*,(*S*)*R*]-7a**: white solid; mp 129−130 °C; $[\alpha]^{20}_D = +104$ (*c* 1, $CHCl_3$); IR (KBr) 3315, 1665, 1025, 805 cm $^{-1}$; ^{13}C NMR δ 200.2, 151.3, 142.4, 139.4, 136.1, 134.2, 130.3 (2C), 129.8, 124.0 (2C), 71.8, 67.6, 51.3, 48.7, 47.8, 47.2, 45.3, 21.4. Anal. Calcd for $C_{19}H_{20}O_3S$: C, 69.49; H, 6.14. Found: C, 69.18; H,5.79. **[4*R*,4a*S*,5*R*,8*S*,8a*R*,(*S*)*R*]-8a**: white solid; mp 147−148 °C; $[\alpha]^{20}_D = +109$ (*c* 1, $CHCl_3$); IR ($CHCl_3$) 3390, 1665, 1600, 1040 cm $^{-1}$; ^{13}C NMR δ 200.2, 151.4, 142.3, 139.9, 135.8, 133.9, 130.7 (2C), 130.2, 123.8 (2C), 72.0, 71.7, 51.1, 48.6, 47.5 (2C), 46.1, 21.3. Anal. Calcd for $C_{19}H_{20}O_3S$: C, 69.49; H, 6.14. Found: C, 69.19; H, 5.90.

1,4,4a,9a-Tetrahydro-10-hydroxy-1,4-methano-10-[(*p*-tolylsulfinyl)methyl]anthracen-9-one (7d and 8d). Compounds **7d** and **8d** were obtained from a mixture of **5d** and **6d** under the experimental conditions and in the ratios shown in Table 2. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 1:3). **[1*R*,4*S*,4a*R*,9a*S*,10*R*,(*S*)*R*]-7d**: white solid; mp 112−112.5 °C; $[\alpha]^{20}_D = -11$ (*c* 1, $CHCl_3$); ^{13}C NMR δ 200.9, 145.8, 142.5, 139.1, 135.5, 134.4, 133.6, 133.4, 130.3 (2C), 127.7, 125.6, 125.1, 124.0 (2C), 73.6, 69.1, 51.8, 49.8, 49.6, 47.0, 46.0, 21.4. Anal. Calcd for $C_{23}H_{24}O_3S$: C, 72.60; H, 6.36; S, 8.43. Found: C, 72.72; H, 5.79; S, 8.14. **[1*S*,4*R*,4a*S*,9a*R*,10*S*,(*S*)*R*]-8d**: oil; $[\alpha]^{20}_D = +116$ (*c* 1.16, $CHCl_3$); ^{13}C NMR δ 200.8, 143.9, 142.0, 139.3, 134.9, 133.8, 133.6, 133.0, 129.9 (2C), 127.8, 126.0, 125.6, 123.7 (2C), 73.8, 71.5, 51.1, 49.5, 49.3, 49.0, 45.7, 21.2.

4a,5,8,8a-Tetrahydro-4-hydroxy-5,8-methano-2-methoxy-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (7e and 8e). Compounds **7e** and **8e** were obtained from **5e** and **6e** under the experimental conditions and in the ratios shown in Table 2. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 3:2). **[4*S*,4a*R*,5*S*,8*R*,8a*S*,(*S*)*R*]-7e**: white solid; mp 74.5−75.5 °C; $[\alpha]^{20}_D = +91$ (*c* 1, $CHCl_3$); ^{13}C NMR δ 195.0, 151.5, 142.4, 139.5, 136.7, 132.9, 130.3 (2C), 124.0 (2C), 118.8, 72.5, 68.7, 55.1, 52.3, 48.8 (2C), 47.2, 45.0, 21.1. **[4*R*,4a*S*,5*R*,8*S*,8a*R*,(*S*)*R*]-8e**: oil; $[\alpha]^{20}_D = +26$ (*c* 1.2, $CHCl_3$); ^{13}C NMR δ 195.0, 151.6, 142.1, 139.7, 136.4, 132.3, 130.1 (2C), 123.7 (2C), 117.6, 72.8, 72.0, 55.2, 52.2, 48.7, 48.0, 47.0, 46.0, 21.2.

4a,5,8,8a-Tetrahydro-4-hydroxy-8-methyl-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (9a and 10a). Compounds **9a** and **10a** were obtained from **5a** under the experimental conditions and in the ratios shown in Table 3. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 1:2). **[4*S*,4a*R*,8*S*,8a*S*,(*S*)*R*]-9a**: white solid; mp 90−91 °C; $[\alpha]^{20}_D = -109$ (*c* 1.01, $CHCl_3$); ^{13}C NMR δ 199.0, 147.3, 142.2, 139.8, 131.2, 130.1 (2C), 128.5, 123.9 (3C), 74.2, 64.5, 48.9, 47.2, 33.9, 23.7, 21.2, 18.4. Anal. Calcd for $C_{19}H_{20}O_3S$: C, 69.49; H, 6.14. Found: C, 69.18; H, 5.79. **[4*R*,4a*S*,8*R*,8a*R*,(*S*)*R*]-10a**: white solid; mp 175 °C dec; $[\alpha]^{20}_D = +315$ (*c* 1.05, $CHCl_3$); ^{13}C NMR δ 199.2, 146.8, 142.2, 140.1, 131.3, 130.2 (2C), 129.3, 123.8 (3C), 74.3, 64.8, 48.7, 47.1, 33.6, 23.2, 21.3, 18.5. Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71; S, 9.70. Found: C, 69.12; H, 6.64; S, 9.53.

4a,5,8,8a-Tetrahydro-4-hydroxy-2,8,8a-trimethyl-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (9b and 10b). Compounds **9b** and **10b** were obtained from **5b** under the experimental conditions and in the ratios shown in Table 3. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 2:3). **[4*S*,4a*R*,8*S*,8a*S*,(*S*)*R*]-9b**: white solid; mp 158 °C dec; $[\alpha]^{20}_D = +342$ (*c* 1.0, $CHCl_3$); ^{13}C NMR δ (75 MHz) 202.9, 142.0, 141.7, 141.0, 135.9, 131.9, 130.0 (2C), 123.9 (2C), 123.8, 70.8, 68.7, 45.6, 42.6, 37.7, 25.2, 22.0, 21.3, 17.9, 16.3. **[4*R*,4a*S*,8*R*,8a*R*,(*S*)*R*]-10b**: white solid; mp 144.0−144.9 °C; $[\alpha]^{20}_D = -44$ (*c* 1.0, $CHCl_3$); ^{13}C NMR δ (75 MHz) 203.5, 142.2, 141.5, 140.1, 136.0, 130.7, 130.2 (2C), 123.9 (2C), 122.7, 70.7, 67.3, 45.7, 43.8, 38.0, 25.5, 21.9, 21.4, 17.5, 16.4.

4a,5,8,8a-Tetrahydro-4-hydroxy-3,4a,8-trimethyl-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (9c and 10c). Compounds **9c** and **10c** were obtained from **5c** under the experimental conditions and in the ratios shown in Table 3. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 1:3). **[4*S*,4a*R*,8*S*,8a*S*,(*S*)*R*]-9c**: pale yellow solid; mp 70−71.5 °C; $[\alpha]^{20}_D = -89$ (*c* 0.98, $CHCl_3$); ^{13}C NMR δ 198.6, 159.5, 142.6, 140.3, 131.0, 130.4 (2C), 126.5, 123.9 (3C), 78.5, 61.0, 52.6, 46.2, 31.1, 29.4, 21.4, 20.5, 19.0, 18.2. **[4*R*,4a*S*,8*R*,8a*R*,(*S*)*R*]-10c**: pale yellow solid; mp 139.4−140.6 °C; $[\alpha]^{20}_D = +308$ (*c* 0.25, $CHCl_3$); ^{13}C NMR δ (75 MHz) 198.9, 162.1, 142.7, 140.0, 130.9, 130.4 (2C), 127.3, 124.4, 123.9 (2C), 79.0, 62.5, 52.3, 46.8, 30.7, 29.6, 21.6, 21.5, 20.3, 19.3.

1,4,4a,9a-Tetrahydro-10-hydroxy-1-methyl-10-[(*p*-tolylsulfinyl)methyl]anthracen-9-one (9d and 10d). Compounds **9d** and **10d** were obtained from a mixture of **5d** and **6d** under the experimental conditions and in the ratios shown in Table 3. Purification and separation were achieved by flash chromatography (AcOEt/hexane, 1:5). **[1*S*,4a*R*,9a*S*,10*R*,(*S*)*R*]-9d**: white solid; mp 161.4−161.9 °C; $[\alpha]^{20}_D = -133$ (*c* 1.00, $CHCl_3$); ^{13}C NMR δ 197.1, 144.1, 142.6, 139.4, 134.1, 131.5, 130.8, 130.3 (2C), 128.3, 126.9, 126.4, 124.6, 123.9 (2C), 75.8, 64.4, 49.6, 45.4, 34.7, 24.6, 21.4, 19.3. Anal. Calcd for $C_{23}H_{26}O_3S$: C, 72.22; H, 6.85; S, 8.38. Found: C, 72.17; H, 6.25; S, 8.08. **[1*R*,4a*S*,9a*R*,10*S*,(*S*)*R*]-10d**: white solid; mp 64.2−65.5 °C; $[\alpha]^{20}_D = +233$ (*c* 1.00, $CHCl_3$); ^{13}C NMR δ 197.6, 143.8, 142.1, 140.0, 134.0, 131.8, 131.3, 130.3 (2C), 128.5, 127.0, 126.8, 124.0 (3C), 76.1, 65.8, 49.2, 47.0, 34.2, 23.9, 21.4, 19.1.

4a,5,8,8a-Tetrahydro-4-hydroxy-2-methoxy-8-methyl-4-[(*p*-tolylsulfinyl)methyl]naphthalen-1-one (9e and 10e). Compounds **9e** and **10e** were obtained from **5e** and **6e** under the experimental conditions and in the ratios shown in Table 3. Purification and separation were achieved by flash chromatography (AcOEt/hexane, from 1: to 3:1). **[4*S*,4a*R*,8*S*,8a*S*,(*S*)*R*]-9e**: oil; $[\alpha]^{20}_D = -71.5$ (*c* 1.00, $CHCl_3$); ^{13}C NMR δ 193.4, 149.8, 142.2, 139.8, 131.1, 130.1 (2C), 123.9 (3C), 114.0, 74.2, 64.3, 55.0, 49.0, 47.6, 33.8, 23.8, 21.3, 18.4. **[4*R*,4a*S*,8*R*,8a*R*,(*S*)*R*]-10e**: oil; $[\alpha]^{20}_D = +205$ (*c* 1.00, $CHCl_3$); ^{13}C NMR δ 193.4, 150.3, 142.4, 140.0, 131.1, 130.2 (2C), 123.9 (3C), 112.8, 74.3, 65.4, 55.3, 48.7, 47.6, 33.7, 23.1, 21.4, 18.5.

Method D. Reduction of Carbonyl Group. To a solution of DIBALH (1.8 mL, 1 M in hexane, 2.4 equiv) in THF (10 mL) cooled at −78 °C was added a solution of the corresponding adduct **7a** or **8a** (0.75 mmol, 1 equiv) in THF (15 mL). The reaction was monitored by TLC (1:3 hexanes/ethyl acetate). Excess organoaluminum reagent was destroyed with methanol, and the mixture was poured into an Erlenmeyer containing ethyl acetate and sodium potassium tartrate and stirred vigorously for 30 min. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo.

Method E. Preparation of MTPA Esters of Diols 11 and 12. A mixture of 8 mg of diol **11** or **12**, 7 mg of DMPA, and 8 μL of MTPA-Cl in 2 mL of CH_2Cl_2 was stirred at 30 °C overnight. Then H_2O (1 mL) and ether (2 mL) were added and stirred for 15 min. The mixture was diluted with ether and washed with 10% HCl (3 mL), 1 N NaOH (3 mL), and

brine (3 mL). After drying with $MgSO_4$ the solvent was removed in vacuo.

[1*R*,4*S*,4a*R*,5*S*,8*R*,8a*S*,(*S*)*R*]-4a,5,8,8a-Tetrahydro-1,4-dihydroxy-5,8-methano-4-[(*p*-tolylsulfinyl)methyl]naphthalene (11) was prepared following the general procedure D from **7a** in a 80% yield (flash chromatography, AcOEt/hexane, 1:1) as a white solid; mp 181.5−181.7 °C; $[\alpha]^{20}_D = -61$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 7.59−7.53 (AA′, 2H), 7.37−7.32 (BB′, 2H), 5.99−5.93 (m, 2H), 5.64−5.52 (m, 2H), 4.47 (s, OH), 4.38 (t, *J* = 7.6 Hz, 1H), 3.25−3.22 (m, 1H), 3.14 (dd, *J* = 9.7, 3.6 Hz, 1H), 3.08−3.05 (m, 1H), 3.00 (A, *J* = 13.4 Hz, 1H), 2.92−2.80 (m, 1H), 2.62 (B, *J* = 13.4 Hz, 1H), 2.42 (s, 3H), 1.78 (d, *J* = 7.6 Hz, OH), 1.48−1.38 (m, 2H); ^{13}C NMR δ 142.1, 140.5, 135.8, 134.6, 134.3, 132.6, 130.2 (2C), 124.1 (2C), 72.4, 66.0, 65.8, 49.5, 47.0, 46.5, 45.2, 43.1, 21.4. Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71; S, 9.70. Found: C, 69.07; H, 6.56; S, 9.51. **(*R*)-MTPA-11**: ^{1}H NMR δ 7.57−7.33 (m, 9H), 5.85 (dd, *J* = 5.4, 2.7 Hz, 1H), 5.63 (dd, *J* = 5.4, 2.9 Hz, 1H), 5.55 (dt, *J* = 9.3, 1.6 Hz, 1H), 5.41 (dd, *J* = 10.5, 2.8 Hz, 1H), 5.21 (dd, *J* = 10.2, 1.2 Hz, 1H), 4.81 (s, OH), 3.55 (d, *J* = 1.1 Hz, 3H), 3.37 (dd, *J* = 9.5, 3.7 Hz, 1H), 3.31−3.23 (m, 1H), 3.12 (td, *J* = 9.3, 3.6 Hz, 1H), 2.99 (d, *J* = 13.4 Hz, 1H), 2.87−2.79 (m, 1H), 2.53 (d, *J* = 13.4 Hz, 1H), 2.43 (s, 3H), 1.38 (s, 2H). **(*S*)-MTPA-11**: ^{1}H NMR δ 7.58−7.33 (m, 9H), 5.86 (dd, *J* = 5.5, 2.8 Hz, 1H), 5.63 (dd, *J* = 5.5, 2.8 Hz, 1H), 5.56 (dt, *J* = 9.1, 2.3 Hz, 1H), 5.46 (dd, *J* = 10.3, 2.7 Hz, 1H), 5.30 (dd, *J* = 10.3, 1.6 Hz, 1H), 4.78 (s, OH), 3.57 (d, *J* = 0.9 Hz, 3H), 3.36 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.30−3.22 (m, 1H), 3.13 (td, *J* = 9.2, 3.6 Hz, 1H), 2.98 (d, *J* = 13.4 Hz, 1H), 2.77−2.69 (m, 1H), 2.53 (d, *J* = 13.4 Hz, 1H), 2.42 (s, 3H), 1.37 (s, 2H).

[1*S*,4*R*,4a*S*,5*R*,8*S*,8a*R*,(*S*)*R*]-4a,5,8,8a-Tetrahydro-1,4-dihydroxy-5,8-methano-4-[(*p*-tolylsulfinyl)methyl]naphthalene (12) was prepared following the general procedure D from **8a** in a 84% yield (flash chomatography, ethyl acetate/hexane, 2:3) as a white solid; mp 162.0−162.6 °C; $[\alpha]^{20}_D = +297$ (*c* 1.0, $CHCl_3$); ^{1}H NMR δ 7.55−7.49 (AA′, 2H), 7.36−7.32 (BB′, 2H), 5.94−5.84 (m, 3H), 5.71 (dd, *J* = 10.2, 2.3 Hz, 1H), 4.62 (s, OH), 4.47−4.38 (m, 1H), 3.16−3.13 (m, 1H), 3.13−3.00 (m, 1H), 3.06 (A, *J* = 12.9 Hz, 1H), 2.81−2.70 (m, 1H), 2.73 (B, *J* = 12.9 Hz, 1H), 2.59 (dd, *J* = 9.5, 3.5 Hz, 1H), 2.42 (s, 3H), 1.41−1.34 (m, 1H), 1.28−1.23 (m, 1H); ^{13}C NMR δ 142.1, 140.6, 135.8, 134.2, 133.1, 132.9, 130.2 (2C), 124.0 (2C), 72.5, 68.1, 66.3, 49.0, 48.8, 45.8, 45.0, 42.3, 21.4. Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71; S, 9.70. Found: C, 69.17; H, 6.64; S, 9.54. **(*R*)-MTPA-12**: ^{1}H NMR δ 7.59−7.32 (m, 9H), 5.87 (ddd, *J* = 10.5, 3.1, 1.1 Hz, 1H), 5.81 (dd, *J* = 5.5, 2.9 Hz, 1H), 5.63−5.55 (m, 2H), 5.54 (dd, *J* = 10.5, 1.4 Hz, 1H), 4.81 (s, OH), 3.56 (q, *J* = 1.1 Hz, 3H), 3.21−3.15 (m, 1H), 3.02 (d, *J* = 12.9 Hz, 1H), 2.95 (td, *J* = 9.3, 3.6 Hz, 1H), 2.78−2.72 (m, 1H), 2.72 (d, *J* = 12.8 Hz, 1H), 2.61 (ddd, *J* = 9.5, 3.2, 1.0 Hz, 1H), 2.42 (s, 3H), 1.32−1.25 (m, 1H), 1.20−1.14 (m, 1H). **(*S*)-MTPA-12**: ^{1}H NMR δ 7.59−7.33 (m, 9H), 5.89 (ddd, *J* = 10.3, 7.5, 1.0 Hz, 1H), 5.83 (dd, *J* = 5.5, 2.8 Hz, 1H), 5.65 (dd, *J* = 5.4, 2.8 Hz, 1H), 5.61 (dd, *J* = 6.1, 1.8 Hz, 1H), 5.55 (dd, *J* = 10.3, 1.6 Hz, 1H), 4.84 (s, OH), 3.60 (q, *J* = 1.1 Hz, 3H), 3.21−3.15 (m, 1H), 3.03 (d, *J* = 12.8 Hz, 1H), 2.97 (td, *J* = 9.2, 3.7 Hz 1H), 2.73 (d, *J* = 12.8 Hz, 1H), 2.70−2.64 (m, 1H), 2.61 (ddd, *J* = 9.6, 3.7, 0.9 Hz, 1H), 2.43 (s, 3H), 1.31−1.25 (m, 1H), 1.20−1.14 (m, 1H).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **5a**,**d**, **5**/**6e**, **7d**,**e**, **8d**,**e**, **9b**,**c**,**e** and **10b**−**e** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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