Studies of Diastereoselectivity in Diels−Alder Reactions of Enantiopure (S*S*)-2-(*p*-Tolylsulfinyl)-1,4-naphthoquinone and Chiral Racemic Acyclic Dienes

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Enantiopure sulfinylnaphthoquinone (+)-**5** reacted with racemic acyclic dienes **1a**−**f** bearing a stereogenic allylic center, through a tandem cycloaddition/pyrolytic sulfoxide elimination, to afford optically enriched compounds **8a**−**f** and **9a**−**f** with good like/unlike selectivities (ca. 75:25) and good enantiomeric excesses (68−82%), arising from the partial kinetic resolution of the racemic dienes. The opposite diastereoselection (**8g**−**i**: **9g**−**i**, up to 5:95) was observed in reactions with dienes **1g**−**i**, having an additional methyl group at C-3, the enantiomeric purities being moderate (14−25%). Steric effects and torsional interactions in the corresponding approaches account for the observed diastereoselectivities.

Introduction

The π-facial diastereoselectivity of Diels−Alder reactions is a topic of current interest, from both synthetic and theoretical points of view, which has been the subject of several very recent reviews.[1] Most part of the studies focused on π-facially perturbed dienes[2] and to a lesser extent on dienophiles.[3] The observed selectivities have been accounted for in terms of steric,[4] electronic[5] or torsional[6] effects, product stability,[7] orbital interactions,[8] or hyperconjugation.[9] Nevertheless, the general applicability and predictive value of the proposed explanations are not obvious at this stage and each system has to be considered separately. Incorporation of a single stereogenic center in an allylic position of either a dienophile[10] or a diene,[11−13] particularly when a heteroatom is present, also imparts sufficient perturbation to control the π-facial

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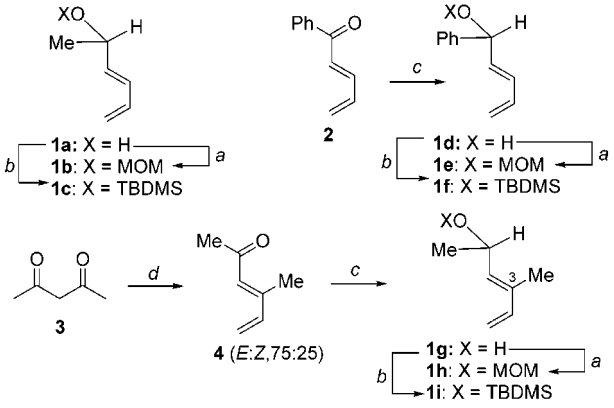
diastereoselection, although the exact factors responsible for the observed selectivities are still imperfectly understood. Distinct works, concerned with three sets of experimental results for cyclic,[11] semicyclic[12] and acyclic[13] dienes, uplighted that good to excellent π-facial diastereoselectivities could be achieved by proper choice of the allylic substituent. Rationalization of the results obtained with rigid cyclic and semicyclic dienes proposed steric and electronic effects of heteroatom substituents as responsible of differentiation between the diastereotopic π faces. The conformational flexibility of open-chain dienes significantly enhances the complexity of mechanistic and stereochemical interpretations. This problem has been partially circumvented[13a−c,k] by the introduction of a substituent in the cis position adjacent to the stereogenic center. Allylic strain[14] emerging in such 1,2-substituted dienes is able to fix a conformation of the stereogenic unit in the transition state and, thus discriminate between the diastereotopic faces, enhancing π-facial selectivities. Despite the good results achieved, enantioselective synthetic applications of this kind of dienes are limited due to the difficulties encountered in the synthesis of optically pure derivatives.[13c,g,15]

In connection with a research program devoted to the use of enantiopure sulfoxides in asymmetric synthesis, we found that the sulfinyl group situated on a quinonic framework could control the regiochemistry, endo selectivity, and π-facial diastereoselectivity of its Diels−Alder cycloadditions with a wide range of cyclic and acyclic dienes.[16] We established the domino Diels−Alder reaction/pyrolytic sulfoxide elimination as a general one-pot strategy to enantiomerically enriched polycyclic quinones. More recently, looking for an enantioselective approach to angucyclinones,[17] we uncovered the ability of the sulfinyl group to promote a double asymmetric induction[18] in the cycloaddition process, leading to the efficient kinetic resolution of some chiral racemic vinylcyclohexenes containing a stereogenic allylic carbon.[19] This methodology allowed the total enantioselective synthesis of several angucyclinones.[20]

To extend these excellent results, we decided to investigate if such a double asymmetric induction process could also take place with racemic acyclic dienes bearing a stereogenic allylic substituent. In this paper,[21] we report the study of Diels−Alder reactions of enantiomerically pure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone with several chiral racemic open-chain dienes **1a-f**, possesing a carbinol[22] and different sterically demanding substituents at the allylic position, and **1g-i** possessing an additional methyl substituent at C-3.

Scheme 1[a]



[a] Key: (a) MOMCl, DIPEA, CH_2Cl_2, rt, 3 h; (b) TBDMSCl, imidazole, DMF, rt, overnight; (c) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, rt, 1 h; (d) (i) CH_2=CHMgBr, THF, −78 °C to 0 °C; (ii) HCl 10%, rt, 1 h, 35%.

Results

Synthesis of Dienes. Dienol **1a** (Scheme 1), with a methyl substituent at the allylic position, was prepared according to a previously reported procedure.[23] The methoxymethyloxy (OMOM) derivative **1b** was obtained from **1a** in 63% yield by reaction with MOMCl and diisopropylethylamine (DIPEA). Treatment of **1a** with *tert*-butyldimethylsilyl chloride (TBDMSCl) and imidazole gave a 71% yield of diene **1c**.[13e] Starting from known phenylbutadienyl ketone **2**,[24] we synthesized 5-phenyl substituted pentadienes **1d**−**f** as follows. Luche reduction[25] of **2** gave a 91% yield of carbinol **1d**,[26] whose treatment with MOMCl−DIPEA or TBDMSCl-imidazole afforded dienes **1e** and **1f** in 66% and 67% yields, respectively (Scheme 1).

The required 5-methyl substituted dienes **1g**−**i**, bearing an additional methyl group at C-3, were prepared as outlined in Scheme 1. Addition of vinylmagnesium bromide on commercially available 2,4-pentanedione **3** followed by acidic treatment gave rise, after flash chromatography, to a 35% yield of 4-methyl-3,5-hexadien-2-one (**4**)[27] as an inseparable 75:25 mixture of *E* and *Z* isomers. Luche reduction of **4** afforded in 85% yield carbinol **1g**, which after protection with either MOMCl/DIPEA or TBDMSCl/imidazole led respectively to derivatives **1h** (50% yield) and **1i** (97% yield). All dienes **1g-i** were used in the cycloadditions as a 75:25 mixture of *E* and *Z* isomers since a higher reactivity of *E* isomer in Diels−Alder reaction was expected.

Diels−Alder Reactions. With the desired racemic acyclic dienes in hand, we began the study of Diels−Alder

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Table 1. Diels-Alder Reactions of Enantiopure Sulfinylnaphthoquinone (+)-5 and 2 Equiv of Racemic Acyclic Dienes 1a−i in CH_2Cl_2

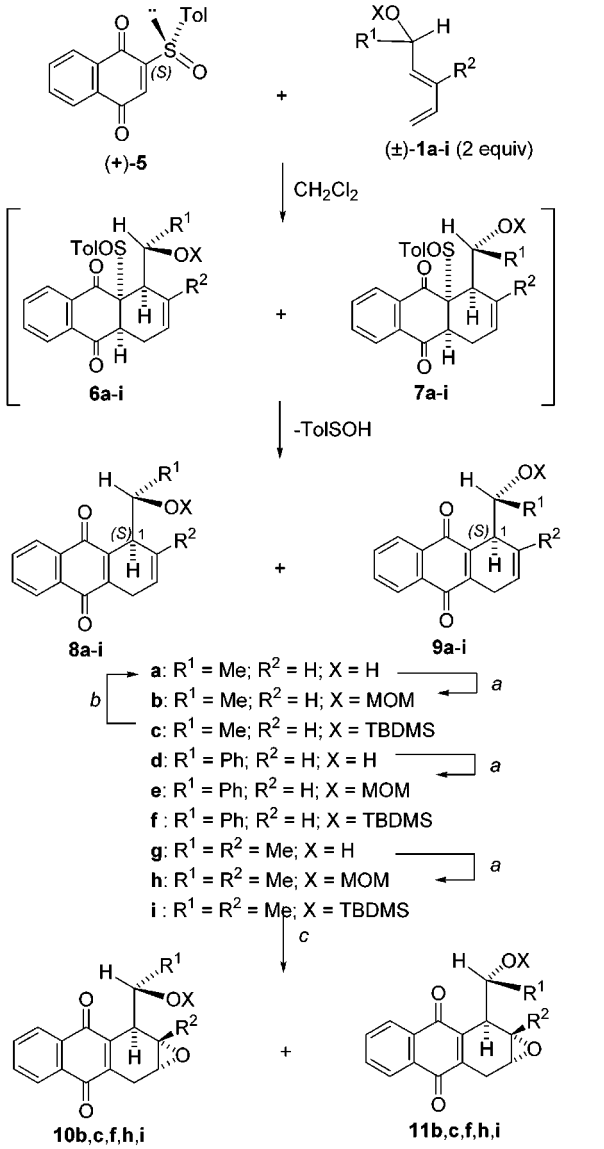
entry	diene	*T* (°C)	*t* (h)	products ratio	yield (%)	enantiomeric ratios
1	**1a**	20	48	**8a** (70) + **9a** (30)	31	**8a** (85:15) + **9a** (87:13)
2	**1b**	20	72	**8b** (75) + **9b** (25)	36	**8b** (91: 9) + **9b** (90:10)
3	**1c**	20	72	**8c** (75) + **9c** (25)	57	**8c** (84:16) + **9c** (86:14)
4	**1d**	20	48	**8d** (75) + **9d** (25)	83	**8d** (87:13) + **9d** (84:16)
5	**1e**	40	24	**8e** (75) + **9e** (25)	40	*c*
6	**1e**	20[a]	24	**8e** (75) + **9e** (25)	60	**8e** (84:16) + **9e** (84:16)
7	**1f**	40	24	**8f** (76) + **9f** (24)	51	**8f** (84:16) + **9f** (86:14)
8	**1g**	20	24	**8g** (9) + **9g** (91)	66	*c*
9	**1g**	0	72	**8g** (5) + **9g** (95)	88[b]	**9g** (75:25)
10	**1h**	20	240	**8h** (40) + **9h** (60)	25	*c*
11	**1h**	20[a]	40	**8h** (33) + **9h** (67)	55	**8h** (76:24) + **9h** (57:43)
12	**1i**	20	168	**8i** (33) + **8i** (67)	33	**8i** (60:40) + **9i** (60:40)

[a] Cycloaddition performed at high pressure (4 kbar). [b] Isolated yield for **9g**. [c] Not determined.

cycloadditions choosing enantiomerically pure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (+)-**5**[28] as a model of chiral dienophile. The influence of an array of different reactions conditions was studied. The use of Lewis acids was prevented due to the fast decomposition of the dienes. The best results were achieved working in CH_2Cl_2 at different temperatures. Under these thermal conditions, Diels−Alder reactions between quinone (+)-**5** and 2 equiv of racemic dienes **1a**−**i**, gave rise to variable mixtures of optically active 1,4-dihydro-9,10-anthraquinones **8a**−**i** and **9a**−**i** resulting from the spontaneous pyrolytic elimination of the sulfoxide in the initially formed and not detected cycloadducts **6a**−**i** and **7a**−**i** (Scheme 2, Table 1). The diastereoisomeric **8**:**9** ratios, reflecting the *like*/*unlike*[29] selectivity of the cycloaddition with respect to the chiral dienic system, were determined directly from the crude reaction mixtures by integration of well separated signals in the ^{1}H NMR spectra. The enantiomeric excesses of compounds **8** and **9** were measured by ^{1}H NMR using chiral lanthanide shift reagents, which required the preparation of each racemic derivative (±)-**8** and (±)-**9** from naphthoquinone (±)-**5**.[28] These values reflect the π-facial diastereoselection of the cycloaddition with respect to the chiral sulfinyl dienophile and the efficiency of the kinetic resolution of the racemic diene partner. In several reactions, we could recover unreacted dienes in optically active form. All derivatives **8** and **9** proved to be very unstable and decomposed rapidly on standing and in solution at room temperature, evolving to 9,10-anthraquinone or 2-methyl-9,10-anthraquinone.

As can be seen in Table 1, 5-methyl substituted dienes **1a**−**c**, phenylcarbinol **1d** and 3,5-dimethyl-substituted dienes **1g**−**i**, reacted at room temperature (entries 1−4, 8, 10, and 12) whereas phenyl-substituted analogues **1e**,**f** only reacted under reflux of the solvent (entries 5−7). Cycloaddition between (+)-**5** and dienol **1a** (entry 1) afforded, after flash chromatography, a 31% yield of the nonseparable 70:30 mixture of optically active compound **8a**, proceeding from the *unlike* approach, and **9a** which resulted from the *like* one. The optical purity of both derivatives (70% ee for **8a** and 74% ee for **9a**) was determined after their transformation into the separable mixture of OMOM ethers (+)-**8b** and (+)-**9b** [$CH_2(OMe)_2$, P_2O_5, $CHCl_3$, rt, 30 min, Scheme 3],[30] by using Pr(hfc)$_3$ and Eu(hfc)$_3$ respectively, as chiral lanthanide shift reagents. In the same way, reaction of (+)-**5** and OMOM-substituted racemic diene **1b** (entry 2) gave a 36% yield of a 75:25 mixture of compounds (+)-**8b** (ee = 82%) and (+)-**9b** (ee = 80%), after flash chromatography. In this reaction, we could recover unreacted diene (+)-**1b** in

Scheme 2[a]



[a] Key: (a) $CH_2(OMe)_2$, P_2O_5, $CHCl_3$, rt, 1 h; (b) HF, CH_3CN, rt,1 h; (c) *m*-CPBA, CH_2Cl_2.

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optically active form {$[\alpha]^{20}_D$ = +19.3 (*c* 2.4, $CHCl_3$)}. Finally, cycloaddition of (+)-**5** with OTBDMS-substituted racemic diene **1c** (entry 3), gave a non separable 75:25 mixture of compounds **8c** and **9c** in 57% yield, after flash chromatography. Optical purity of these derivatives could not be determined at this stage and thus, we transformed the mixture of **8c** and **9c** into the corresponding mixture of OMOM derivatives (+)-**8b** and (+)-**9b** as outlined in Scheme 3. Thus, after desilylation of **8c** and **9c** (HF, CH_3CN, rt, 1 h)[31] and methoxymethylation of the resulting alcohols **8a** and **9a**, compounds **8b** and **9b** were obtained in 40% overall yield. Chromatographic separation of **8b** and **9b** allowed to establish a 68% of ee for derivative **8c** and a 72% for **9c**.

Diels−Alder reactions between quinone (+)-**5** and phenyl substituted dienes **1d**−**f** followed a similar pattern (Scheme 2, Table 1). Cycloaddition with racemic dienol **1d** (entry 4) afforded a 75:25 mixture of derivatives **8d**, proceeding in this case from the *like* approach, and **9d**, from the *unlike* one. The optical purity of both compounds, which could be separated by flash chromatography, was determined on their OMOM ethers **8e** and **9e** (Scheme 3), by using $Pr(hfc)_3$ (74% ee for **8d**) and $Eu(hfc)_3$ (68% ee for **9d**). Reaction of (+)-**5** and diene **1e** (entry 5) yielded a 40% of a non separable 75:25 mixture of **8e** and **9e**. The yield of this reaction was enhanced up to 60% working at high pressure (entry 6), affording again a 75:25 mixture of **8e** (ee = 68%) and **9e** (ee = 68%). Finally, cycloaddition of (+)-**5** with diene **1f** (entry 7), gave a 76:24 mixture of derivatives **8f** and **9f** in 51% yield. Optical purity of these compounds could only be determined after transformation of the mixture of **8f** and **9f** into the corresponding inseparable mixture of epoxides **10f** and **11f** (*m*-CPBA, CH_2Cl_2, 0 °C, 4 d, 72%, Scheme 2), proceeding from the exclusive attack of the oxidant on the less encumbered bottom face of the olefinic system. We could thus determine a 68% ee for derivative **8f** and a 72% ee for **9f** by using $Pr(hfc)_3$ as chiral lanthanide shift reagent.

Finally, we carried out the reactions with racemic dienes **1g**−**i** bearing the additional methyl group at C-3 (Scheme 2, Table 1), with the aim of evaluating the effect of the allylic strain present in this type of dienes on the diastereoselectivity of the process. Thus, Diels−Alder reaction between sufinylnaphthoquinone (+)-**5** and dienol **1g** (entry 8) at room temperature for 24 h afforded a 9:91 mixture of optically active compounds **8g**, proceeding from a *like* approach, and **9g**, from an *unlike* one, in 66% yield after flash chromatography. When the same reaction was performed at 0 °C (entry 9) the *like*/*unlike* diastereoselectivity increased to a 5:95 mixture of diastereoisomers, from which (+)-**9g** was isolated diastereoisomerically pure in 88% yield. This result corroborated the observations of Prein[13k] which pointed out the importance of 1,3-allylic strain in controlling the selectivity of Diels−Alder reactions with 5-hydroxy substituted pentadienes. In this case we could also recover unreacted diene **1g** in optically active form {$[\alpha]^{20}_D$ = +27 (*c* 0.1, $CHCl_3$)}. The optical purity of compound **9g** (50% ee) was determined after its transformation into the OMOM derivative (+)-**9h** (Scheme 3), by using $Eu(hfc)_3$. Cycloaddition of (+)-**5** and diene **1h** (entry 10) led to a 40:60 mixture of compounds **8h** and **9h** in 25% yield, after

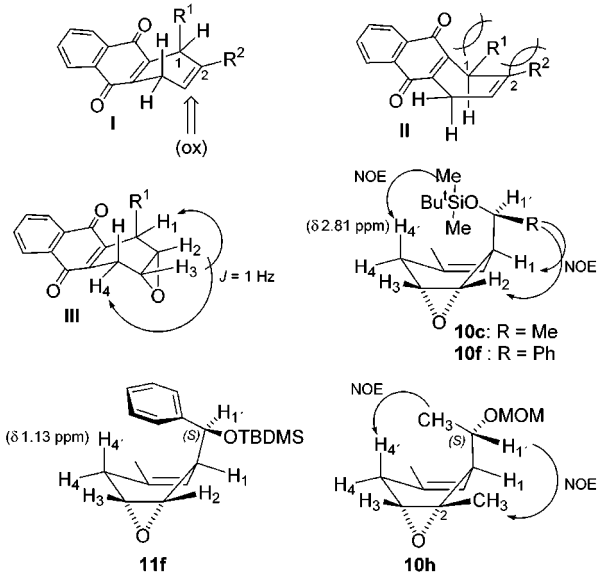

Figure 1. Significant ^1H NMR parameters used for configurational assignments.

chromatographic separation. When the same reaction was performed under high-pressure conditions (4 Kbar, entry 11), a 33:67 mixture of diastereoisomers was obtained in 55% yield. The optical purity of both derivatives (52% ee for **8h** and 14% ee for **9h**) was determined by using $Eu(hfc)_3$ and $Pr(hfc)_3$, respectively. Finally, Diels−Alder reaction between (+)-**5** and diene **1i** (entry 12), gave a non separable 33:67 mixture of derivatives **8i** and **9i** in 33% yield, after flash chromatography. The enantiomeric purity of minor diastereoisomer **8i** (ee = 20%) was established on the mixture of **8i** and **9i** by using $Pr(hfc)_3$ as chiral lanthanide shift reagent, whereas that of major derivative **9i** (ee = 20%) could be determined on epoxide **11i** by using $Pr(hfc)_3$, after oxidation of the mixture of **8i** and **9i** (*m*-CPBA, CH_2Cl_2, 0 °C, 24 h, 47%, Scheme 2) and chromatographic separation of the resulting epoxides **10i** and **11i**.

Configurational Assignments. The relative stereochemistry of all compounds resulting from the cycloaddition/kinetic resolution/pyrolytic sulfoxide elimination process could be established on the basis of their spectroscopic parameters especially those of ^1H NMR, including NOESY experiments. The assignment of the absolute configuration was mainly based on the usual behavior of sulfinylquinones as dienophiles[16] and the mechanistic model proposed below.

In accordance with conformational studies on 1,4-dihydronaphthalenes,[32] 1,4-dihydroanthraquinone derivatives **8a**−**i** and **9a**−**i** prepared by us must exist as a stable boatlike conformation such as **I** (Figure 1) with the substituent at C-1 in axial disposition to avoid destabilizing interactions with the R^2 group at C-2 (R^2 = H or Me) and the adjacent carbonyl group, present in the other possible conformer **II** (Figure 1).

As mentioned earlier, all derivatives **8a**−**i** and **9a**−**i** are very unstable and decompose quickly in $CDCl_3$ solutions. This instability difficulted regristation of clean

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(32) (a) Rabideau, P. W. *Acc. Chem. Res.* **1978**, *11*, 141. (b) Raber, D. J.; Hardee, J. E.; Rabideau, P. W.; Lipkowitz, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 2843. (c) Rabideau, P. W. *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; VCH Publishers: New York, 1989.

NMR spectra which would allow a detailed structural study. For this reason, compounds **8b**,**c**,**f**,**h**,**i** and **9b**,**c**,**f**-,**h**,**i** were transformed into the more stable epoxides **10b**,**c**,**f**,**h**,**i** and **11b**,**c**,**f**,**h**,**i**, which were used for the structural assignment. Thus, a diastereoselective epoxidation using *m*-CPBA occurred exclusively on the less hindered bottom face of the double bond, opposite to the axial substituent at C-1 of conformer **I** (Figure 1), giving rise to the stereoselective formation of the desired epoxides (Scheme 2). The relative stereochemistry of these derivatives was established on the basis of the observed long-range coupling constants existent between H_1 and H_3, and H_2 and H_4 ($J_{1,3} \approx J_{2,4} \approx 1$ Hz), indicating the equatorial disposition of all these hydrogens, which is only possible if the epoxide and the substituent at C-1 are trans and adopt the boatlike conformation **III** similar to that of the 1,4-dihydroanthraquinones **I** (Figure 1).

The relative stereochemistry of compounds **8a**−**f** and **9a**−**f** was deduced from that of epoxides **10c** and **10f**, which in turn was determined from ^{1}H−^{1}H NOESY experiments, since **8a**−**f** and **9a**−**f** had been previously correlated through their OMOM derivatives (see Scheme 2). As depicted in Figure 1, epoxides **10c** and **10f** showed NOE enhancements between the R group at the chiral substituent and H_1 and H_2 protons as well as between the OTBDMS group and $H_{4'}$ hydrogen. This suggested the (*S*) absolute configuration for the stereogenic oxygenated carbon of **10c** (R = Me) as well as for its precursor **8c** and the analogues **8a**,**b**, and the (*R*) configuration for that of **10f** (R = Ph), as well as for derivatives **8d**−**f**. As a consequence, the opposite (*R*) configuration was assigned for the C-1′ stereogenic center in minor diastereoisomers **9a**−**c** and (*S*) for the same carbon in **9d**−**f**. This was confirmed on epoxide **11f** (see Figure 1) from the ^{1}H NMR chemical shift of $H_{4'}$ which appeared very shielded (δ = 1.13 ppm) if compared with that of the same proton in diastereoisomer **10f** (δ = 2.81 ppm). This notable shielding must be due to the anisotropic effect of the close aromatic ring, and was also observed for derivatives **9d**−**f** (see Supporting Information).

Finally, the relative stereochemistry of derivatives **8g**−**i** and **9g**−**i**, bearing the methyl substituent at C-2, was deduced from the NOESY experiments effected on epoxide **10h** (Figure 1). In this case, we noticed evident NOEs between the methyl group on the exocyclic center and $H_{4'}$ proton, as well as between the methyl group at C-2 and the hydrogen situated at C-1′, suggesting the (*S*) configuration for the stereogenic center of compound **10h** and as a consequence for that of its precursor **8h** and the analogues **8g**,**i**. The opposite (*R*) configuration was then assigned for the chiral center C-1′ of major diastereoisomers **9g**-**i** proceeding from a *like* approach.

Discussion

To rationalize the results achieved in such a double asymmetric induction process,[33] we must differentiate the diastereofacial selectivities of both chiral partners. The observed enantiomeric purity of both **8** and **9** is a consequence of the π-facial diastereoselectivity of the cycloaddition with the homochiral sulfinyl group on the quinone moiety and indicates the efficiency of the kinetic resolution process. The resulting *like*/*unlike* selectivities (mixtures of **8** and **9**) reflects the diastereofacial control of the chiral diene.

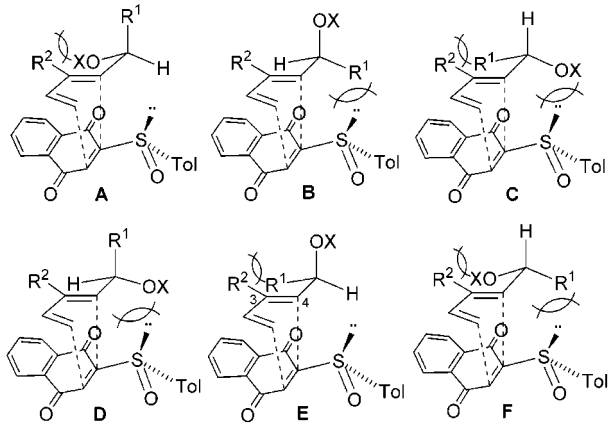


Figure 2. *Like*/*unlike* approaches of acyclic dienes **1** in Diels−Alder reactions with enantiopure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone.

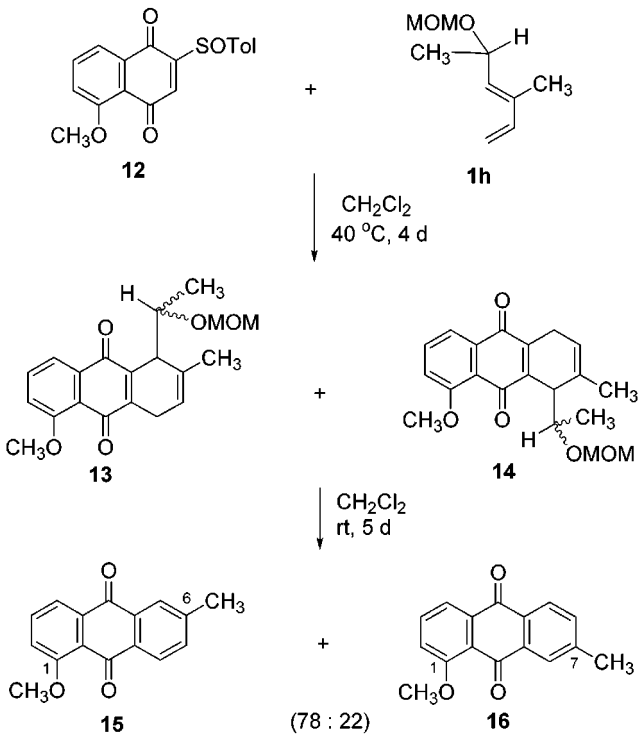
In accordance with the results of other cycloadditions with enantiopure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-quinones, the most favored endo approach of the diene occurs from the top face of the dienophile (+)-**5** containing the less sterically demanding lone electron pair at sulfur in the more reactive s-cis conformation (Figure 2).[16] This approach accounts for the observed *(S)* absolute configuration at C-1 in the resulting 1,4-dihydroanthraquinones **8** and **9** (see Scheme 2). Thus, derivatives **8a-c** result from an *unlike* approach and bear the (1*S*,1′*S*) absolute configuration. The major diastereomers **8d-f** formed from dienes **1d-f** have the (1*S*,1′*R*) absolute configuration as a result of a *like* approach. Although the stereochemical descriptor changes from R^1 = Me to R^1 = Ph, due to a different priority order in the application of the CIP rules, the relative stability of the transitions states are similar for all dienes **1a**−**f**. In the case of cycloadditions with 3,5-dimethyl-substituted dienes **1g**−**i**, the major diastereoisomers **9g**−**i** formed show the (*1S*,*1′R*) absolute configuration, opposite to that induced at C-1′ in major compounds **8a**−**c** formed from dienes **1a**−**c** lacking the methyl substituent at C-3. Taking into account that substitution at the stereogenic center in **1a**−**c** and **1g**−**i** is the same, this must be a consequence of a change in the type of approach of the diene. Compounds **9g**−**i** must then proceed from a *like* approach on the diene framework.

Interactions emerging in the *like* or *unlike* approaches of the dienophile on the different conformations of the diene resulting from free rotation around the single C4−C5 bond account for the preferred evolution. According to Houk's work,[34] allylic substituents must be staggered with respect to forming bonds in cycloaddition transition states to avoid torsional interactions. The presence of eclipsing bonds increases their energetic contents in ca. 5 kcal/mol being such torsional interactions similar to those involving formed bonds.

(33) We use this term in the conventional sense defined by Masamune (see ref 18), considering the kinetically favoured reaction occurring between homochiral dienophile (+)-**5** and one of the enantiomers of chiral racemic dienes **1a**-**i**.

(34) (a) Caramella, P.; Rondan, N. G.; Paddon-Row: M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438. (b) Rondan, N. G.; Paddon-Row: M. N.; Caramella, P.; Mareda, J.; Mueller, P. H.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4974. (c) Paddon-Row: M. N.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162. (d) Houk, K. N.; Moses, S. R.; Wu, Y. D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880.

Scheme 3



Due to the different behavior of dienes bearing and lacking the methyl substituent at C-3, the mechanistic discussion that follows is independent for each type of diene. The major formation of diastereoisomers **8a**−**f**, resulting from the *unlike* approach of dienes **1a**−**c** (R^1 = Me; R^2 = H) and from the *like* one of dienes **1d**−**f** (R^1 = Ph; R^2 = H), could be explained considering the three transition states **A**, **B** and **C** (R^2 = H) represented in Figure 2. The most favored situation correspond to **A**, where the largest R^1 group of the allylic center is anti to the attacking sulfinyl dienophile and the smallest H is on the same face. In approaches **B** and **C**, where the R^1 and OX groups are situated on the same side of the approaching dienophile, unfavorable steric and/or electrostatic interactions appear. Thus, the matched evolution of the (*S*) enantiomer of dienes **1a**−**c** (R^1 = Me; R^2 = H) and the (*R*) one of **1d**-**f** (R^1 = Ph; R^2 = H) through the approach **A** justifies the observed kinetic resolution which gave the major isomers **8a**−**f**.

A similar analysis for *like* approaches of dienes **1a**−**c** [(*R*)-enantiomers reacting] and *unlike* of **1d**−**f** [(*S*)-enantiomers reacting] yielding minor derivatives **9a**-**f** must focus in transition states **D**, **E** and **F** (R^2 = H) represented in Figure 2. In this case, transition states **D** and **F** show destabilizing interactions similar to **B** and **C**, being OX group in **D** and R^1 in **F** situated on the same side of the approaching dienophile. The most favored situation corresponds to **E**, where the smallest H is on the bottom side of the diene. Nevertheless, the energetic content of transition state resulting from approach **A** must be lower to that of approach **E** where the bulky R^1 group is in gauche disposition with respect to the C_3−C_4 double bond and also in the face of the approaching dienophile. The matched pair in this case arose from the reaction of the (*S*) enantiomer of dienes **1a**-**c** and from the (*R*) enantiomer of dienes **1d**−**f**. The formation of a minor amount (9−16%) of the enantiomers of **8a**−**f** and **9a**−**f** (see enantiomeric ratios in Table 1) could be justified on the basis of the moderate reactivity of dienes **1a**−**f** which need temperatures ranging from 20 to 40 °C to react. According to our previous work,[16] π-facial diastereoselectivity of cycloadditions with sulfinylquinones improved strongly at low temperatures.

The relative stabilities of the transition states resulting from dienes **1g**-**i** are different due to the 1,3-allylic strain[14] existent between the methyl group at C-3 and the substituents of the allylic center, which imposes strong conformational preferences. According to Prein's proposal,[13k] rotamers **B** (R^2 = Me) in the *unlike* approach and **D** (R^2 = Me) in the *like* one must be intrinsically favored since the smallest hydrogen substituent is situated at the sterically most biased *inside* position to minimize 1,3-allylic strain.[35] A preference of ca. 3−4 kcal/mol could be estimated for the ground and transition states. A comparison of the relative stability of both transition states **B** and **D** allowed us to conclude that approach **D** with the less sterically demanding OX substituent on the reactive face of the diene will be favored over transition state **B** where this position is occupied by the bulkiest R^1 substituent. Thus, the major evolution through a *like* approach for this type of dienes is due to the main evolution through a transition state such as **D**. Moreover, the higher *like*/*unlike* selectivity achieved with dienol **1g** (X = H) is in accordance with this model of approach since the free hydroxyl group is the smallest one if compared with the other OX substituents (OMOM and OTBDMS). Moreover, all cycloadditions have been performed in a non polar solvent such as CH_2Cl_2 which could favor the formation of hydrogen bonding[13k,36] between the OH group of the diene and the incoming dienophile enhancing the preference for *like* attack and evolution through **D** transition state.

The lower enantiomeric ratios obtained in the cycloadditions with dienes **1g**−**i** (see Table 1) if compared with those of dienes **1a**−**f**, lacking the additional methyl substituent at C-3, were not easy to rationalize. We reasoned that the presence of two alkyl substituents at C-3 and C-4 of the diene moiety could compete in directing the regiochemistry of the process. A decreased regioselectivity would affect the final enantiomeric purity of the resulting compounds since the chiral inductor disappears during the reaction. To check this point, we carried out the cycloaddition between 5-methoxy-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (**12**)[28] and diene **1h** (CH_2Cl_2, 40 °C, 4 days, Scheme 3), giving rise to a mixture of derivatives **13** and **14** which, after chromatographic purification, evolved on standing in CH_2Cl_2 at room temperature for 5 days into a 78:22 mixture of regioisomeric 1-methoxy-6-methyl-9,10-anthraquinone (**15**)[37] and 1-methoxy-7-methyl-9,10-anthraquinone (**16**).[38] This could be in the origin of the lower enantioselectivities achieved in the cycloadditions of 3-methyl-substituted dienes **1g**−**i** with enantiopure sulfinylquinone (+)-**5**.

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(36) (a) Tripathy, R.; Carroll, P: J.; Thornton, E. R. *J. Am. Chem. Soc.* **1990**, *112*, 6743. (b) Tripathy, R.; Carroll, P: J.; Thornton, E. R. *J. Am. Chem. Soc.* **1991**, *113*, 7630.

(37) Krohn, K. *Liebigs Ann. Chem.* **1981**, 2285.

(38) The structures of **15** and **16**, which showed very similar ^{1}H NMR spectra, were assigned on the basis of the preferred regiodirecting power of the alkyl substituent at C-1 over that at C-2 in the diene partner.

Concluding Remarks

The enantioselective reactions of racemic acyclic dienes **1** bearing an allylic stereogenic center with (*SS*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone gave rise, through a one-pot domino cycloaddition/sulfoxide elimination process which takes place with the kinetic resolution of the racemic dienes, to enantiomerically enriched 1,4-dihydro-9,10-anthraquinone derivatives **8** and **9**.

The major observed evolution corresponded to the matched pair resulting from the *unlike* (for dienes **1a**−**c**) and *like* (for dienes **1d**−**f**) approaches, as a result of steric effects in the transition states. The importance of 1,3-allylic strain in controlling these Diels−Alder reactions has been also highlighted for dienes **1g**−**i**.

Experimental Section

Melting points were obtained in open capillary tubes and are uncorrected. ^{1}H- and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. NOESY experiments were performed in $CDCl_3$ or C_6D_6 at 500 MHz. Diastereoisomeric ratios were established by integration of well-separated signals in the crude reaction mixtures and are listed in Table 1. Mass spectra (MS and HRMS) were recorded in the electron impact mode at 70 eV. All reactions were monitored by thin-layer chromatography that was performed on precoated sheets of silica gel 60, and flash chromatography was done with silica gel 60 (230−400 mesh) of Macherey-Nagel. Eluting solvents are indicated in the text. The apparatus for inert atmosphere experiments was dried by flaming in a stream of dry argon. Dry THF was distilled from sodium/benzophenone ketyl. CH_2Cl_2 was dried over P_2O_5. For routine workup, hydrolysis was carried out with water, extractions with CH_2Cl_2, and solvent dryness with Na_2SO_4. High-pressure reactions were performed in a Unipress Equipment 101LV 30/16 in polyethylene vials. Hexadiene **1a**[23] and phenyl ketone **2**[24] were prepared according to previously reported procedures.

General Procedure for the Synthesis of OMOM Derivatives, Method A. To a solution of 1.5 mmol of the corresponding alcohol in 5 mL of CH_2Cl_2, 817 μL (4.7 mmol) of DIPEA and 712 μL (9.4 mmol) of MOMCl were added. The mixture was stirred at room temperature for 3 h and hydrolyzed with a cold aqueous solution of $NaHCO_3$. After workup and flash chromatography, the pure OMOM derivative was obtained.

General Procedure for the Synthesis of OTBDMS Derivatives, Method B. To a solution of 5.4 mmol of the corresponding alcohol in 8 mL of DMF, 0.96 g (6.4 mmol) of TBDMSCl and 0.92 g (13.5 mmol) of imidazole were added. The mixture was stirred at room temperature overnight, hydrolyzed with an aqueous saturated solution of NH_4Cl, and extracted with ethyl ether. The organic layer was washed with a saturated solution of NH_4Cl and brine and dried with $MgSO_4$. After evaporation of the solvent and flash chromatography, the pure OTBDMS derivative was obtained.

General Procedure for the Reduction of Ketones, Method C. To a solution of 1.6 mmol of the corresponding ketone and 596 mg (1.6 mmol) of $CeCl_3 \cdot 7H_2O$ in 5 mL of MeOH at the temperature indicated in each case, 60 mg (1.6 mmol) of solid $NaBH_4$ were added in small portions. The mixture was stirred for 15 min, hydrolyzed with water and extracted with ethyl ether. The organic layer was dried with $MgSO_4$ and, after evaporation of the solvent, crude alcohol was obtained and used without further purification.

(*E*)-5-[(Methoxymethyl)oxy]-1,3-hexadiene (1b). 1b was obtained from **1a**[23] following method A (eluent: hexane/EtOAc 90:10) as a colorless oil (63% yield): ^{1}H NMR δ 1.28 (d, 3H, J = 6.5 Hz), 3.36 (s, 3H), 4.21 (quint, 1H, J = 6.5 Hz), 4.56 and 4.67 (AB system, 2H, J = 6.5 Hz), 5.09 (dd, 1H, J = 10.5, 1.2 Hz), 5.20 (dd, 1H, J = 17.0, 1.2 Hz), 5.59 (dd, 1H, J = 15.0, 6.5 Hz), 6.19 (dd, 1H, J = 15.0, 10.5 Hz), 6.32 (ddd, 1H, J = 17.0, 10.5, 10.5 Hz).

(*E*)-5-[(*tert*-Butyldimethylsilyl)oxy]-1,3-hexadiene (1c).[13e] **1c** was obtained from **1a**[23] following method B (eluent: hexane) as a colorless oil (71% yield): ^{1}H NMR δ 0.06 (2s, 6H), 0.90 (s, 9H), 1.23 (d, 3H, J = 6.5 Hz), 4.34 (quint, 1H, J = 6.5 Hz), 5.05 (dd, 1H, J = 10.0, 1.5 Hz), 5.17 (dd, 1H, J = 17.0, 1.5 Hz), 5.70 (dd, 1H, J = 15.0, 6.5 Hz), 6.08−6.42 (m, 2H); HRMS calcd for $C_{12}H_{24}OSi$ 212.15964, found 212.15931.

(*E*)-1-Phenyl-2,4-pentadien-1-ol (1d). 1d was obtained from **2**[24] following method C at room temperature (91% yield): ^{1}H NMR δ 2.09 (s, 1H), 5.12−5.34 (m, 3H), 5.88 (m, 1H), 6.26−6.43 (m, 2H), 7.25−7.42 (m, 5H); HRMS calcd for $C_{11}H_{12}O$ 160.08881, found 160.08850.

(*E*)-5-[(Methoxymethyl)oxy]-5-phenyl-1,3-pentadiene (1e). 1e was obtained from **1d** following method A (eluent: hexane/EtOAc 95:5) as a colorless oil (66% yield): ^{1}H NMR δ 3.39 (s, 3H), 4.62 and 4.74 (AB system, 2H, J = 6.5 Hz), 5.12 (d, 1H, J = 10.0 Hz), 5.16 (d, 1H, J = 7.0 Hz), 5.25 (d, 1H, J = 16.5 Hz), 5.81 (dd, 1H, J = 14.0, 7.0 Hz), 6.26−6.42 (m, 2H), 7.27−7.37 (m, 5H); HRMS calcd for $C_{13}H_{16}O_2$ 204.11503, found 204.11552.

(*E*)-5-[(*tert*-Butyldimethylsilyl)oxy]-5-phenyl-1,3-pentadiene (1f). 1f was obtained from **1d** following method B (eluent: hexane/CH_2Cl_2 85:15) as a colorless oil (67% yield): ^{1}H NMR δ 0.03 (s, 3H), 0.10 (s, 3H), 0.95 (s, 9H), 5.10 (m, 1H), 5.23 (d, 1H, J = 15.0 Hz), 5.25 (d, 1H, J = 6.5 Hz), 5.80 (dd, 1H, J = 14.0, 6.5 Hz), 6.23−6.40 (m, 2H), 7.23−7.38 (m, 5H); HRMS calcd for $C_{17}H_{26}OSi$ 274.1759, found 274.17465.

4-Methyl-3,5-hexadien-2-one (4).[27] To a solution of vinylmagnesium bromide 1 M in THF (60 mL, 60 mmol), 2,4-pentanedione (3.00 g, 30 mmol) in 90 mL of dry THF was added at −78 °C under argon. After 2 h at −78 °C and 2 h at room temperature, the mixture was added dropwise to a solution of HCl 10%, stirred for 1.5 h and extracted with ethyl ether. The organic layer was washed with water and dried with $MgSO_4$. After evaporation of the solvent and flash chromatography (eluent: hexane/EtOAc 85:15), **4** was obtained as an inseparable 75:25 mixture of *E*:*Z* isomers, in 35% yield: ^{1}H NMR (*E* isomer) δ 2.20 (s, 3H), 2.22 (s, 3H), 5.44 (d, 1H, J = 11.0 Hz), 5.66 (d, 1H, J = 17.0 Hz), 6.14 (s, 1H), 6.35 (dd, 1H, J = 17.0, 11.0 Hz).

4-Methyl-3,5-hexadien-2-ol (1g). 1g was obtained from **4** following method C at 0 °C, as an inseparable 75:25 mixture of *E*:*Z* isomers in 85% yield: ^{1}H NMR (*E* isomer) δ 1.27 (d, 3H, J = 6.0 Hz), 1.56 (broad s, 1H), 1.79 (broad s, 3H), 4.69 (m, 1H), 5.05 (d, 1H, J = 11.0 Hz), 5.20 (d, 1H, J = 17.0 Hz), 5.49 (d, 1H, J = 8.5 Hz), 6.35 (dd, 1H, J = 17.0, 11.0 Hz).

5-[(Methoxymethyl)oxy]-3-methyl-1,3-hexadiene (1h). 1h was obtained from **1a** following method A (eluent: hexane/EtOAc 95:5) as an inseparable 75:25 mixture of *E*:*Z* isomers, in 50% yield: ^{1}H NMR (*E* isomer) δ 1.26 (d, 3H, J = 6.5 Hz), 1.79 (broad s, 3H), 3.36 (s, 3H), 4.52 and 4.63 (AB system, 2H, J = 7.0 Hz), 4.63 (m, 1H), 5.05 (d, 1H, J = 11.0 Hz), 5.20 (d, 1H, J = 17.0 Hz), 5.37 (broad d, 1H, J = 9.0 Hz), 6.37 (dd, 1H, J = 17.0, 11.0 Hz).

5-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-1,3-hexadiene (1i). 1i was obtained from **1g** following method B as an inseparable 75:25 mixture of *E*:*Z* isomers in 97% yield and used without further purification: ^{1}H NMR (*E* isomer) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 1.20 (d, 3H, J = 6.5 Hz), 1.74 (broad s, 3H), 4.65 (dq, 1H, J = 8.5, 6.5 Hz), 5.00 (d, 1H, J = 11.0 Hz), 5.14 (d, 1H, J = 17.0 Hz), 5.48 (broad d, 1H, J = 8.5 Hz), 6.34 (dd, 1H, J = 17.0, 11.0 Hz).

General Procedure for Diels−Alder Reactions, Method D. To a solution of (*SS*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (+)-**5**[28] (80 mg, 0.27 mmol) in 2 mL of dry CH_2Cl_2 under argon, the corresponding racemic diene **1a-i** (0.54 mmol, 2 equiv) was added. After the time required in each case (see Table 1 for reaction conditions) and evaporation of the solvent, crude dihydroanthraquinones **8a**−**i** and **9a**−**i** were obtained and purified by flash chromatography.

General Procedure for the Transformation of Alcohols into OMOM Derivatives, Method E. To a solution of 0.2 mmol of the corresponding alcohol in 2 mL of $CHCl_3$ (dried over P_2O_5), 1.3 mL of dimethoxymethane and a catalytic amount of P_2O_5 were added. After stirring 30 min at room

temperature and dilution with 20 mL of CH_2Cl_2, the mixture was poured into a precooled saturated aqueous solution of $NaHCO_3$. After workup, the crude mixture of OMOM derivatives was purified by flash chromatography.

(1*S*,1′*S*)-1-[(1′-Hydroxy)ethyl)]-1,4-dihydro-9,10-anthraquinone (8a) and (1*S*,1′*R*)-1-[(1′-Hydroxy)ethyl)]-1,4-dihydro-9,10-anthraquinone (9a). 8a and **9a** were obtained from **1a** following method D (eluent: hexane/EtOAc 85:15) as an inseparable 70:30 mixture, in 31% yield: ^{1}H NMR (**8a**) δ 1.26 (d, 3H, J = 6.5 Hz), 2.04 (broad s, 1H), 3.09 (m, 1H), 3.42 (dt, 1H, J = 24.0, 4.5 Hz), 3.79 (m, 1H), 4.09 (m, 1H), 5.93 (m, 1H), 6.17 (ddd, 1H, J = 10.0, 4.5, 2.4 Hz), 7.71 (m, 2H), 8.09 (m, 2H). **8a** and **9a** were also obtained from desilylation of **8c** and **9c** (0.21 mmol) in 15 mL of CH_3CN, by adding 7 drops of 40% solution of HF. The mixture was stirred 10 min at room temperature, diluted with CH_2Cl_2 and extracted with water. After workup, crude alcohols **8a** and **9a** were obtained and used without further purification.

(1*S*,1′*S*)-1-[(1′-Methoxymethyloxy)ethyl]-1,4-dihydro-9,10-anthraquinone (8b). 8b was obtained from **1b** following method D, after separation of the resulting 75:25 mixture of **8b** and **9b** by flash chromatography (eluent: hexane/EtOAc 85:15), in 27% yield: $[\alpha]^{20}_D$ +138 (*c* 0.05, $CHCl_3$); ^{1}H NMR δ 1.31 (d, 3H, J = 6.5 Hz), 3.03 (s, 3H), 3.12 (ddt, 1H, J = 24.0, 6.0, 2.5 Hz), 3.40 (dt, 1H, J = 24.0, 4.5 Hz), 3.75 (m, 1H), 4.11 (dq, 1H, J = 2.8, 6.5 Hz), 4.40 and 4.50 (AB system, 2H, J = 7.0 Hz), 6.00 (ddd, 1H, J = 10.0, 4.5, 2.8 Hz), 6.12 (ddd, 1H, J = 10.0, 4.5, 2.0 Hz), 7.72 (m, 2H), 8.10 (m, 2H). **8b** was also obtained from the mixture of **8a** and **9a** following method E after separation by flash chromatography.

(1*S*,1′*S*)-1-[(1′-*tert*-Butyldimethylsilyloxy)ethyl]-1,4-dihydro-9,10-anthraquinone (8c) and (1*S*,1′*R*)-1-[(1′-*tert*-Butyldimethylsilyloxy)ethyl]-1,4-dihydro-9,10-anthraquinone (9c). 8c and **9c** were obtained from **1c** following method D (eluent: hexane/EtOAc 9:1) as an inseparable 75:25 mixture, in 57% yield: ^{1}H NMR (**8c**) δ −0.36 (s, 3H), −0.12 (s, 3H), 0.71 (s, 9H), 1.27 (d, 3H, J = 6.0 Hz), 3.05 (m, 1H), 3.36 (dt, 1H, J = 24.0, 4.5 Hz), 3.64 (m, 1H), 4.19 (dq, 1H, J = 2.8, 6.0 Hz), 5.93 (ddd, 1H, J = 10.0, 4.5, 2.8 Hz), 6.04 (ddd, 1H, J = 10.0, 4.5, 2.4 Hz), 7.70 (m, 2H), 8.08 (m, 2H).

(1*S*,1′*R*)-1-[(1′-Phenyl-1′-hydroxy)methyl]-1,4-dihydro-9,10-antraquinone (8d). 8d was obtained from **1d** following method D, after separation of the resulting 75:25 mixture of **8d** and **9d** by flash chromatography (eluent: CH_2Cl_2/EtOAc 90:10), in 62% yield: ^{1}H NMR δ 2.70 (d, 1H, J = 7.0 Hz), 2.92 (ddt, 1H, J = 24.0, 6.5, 2.5 Hz), 3.31 (dt, 1H, J = 24.0, 4.5 Hz), 4.10 (m, 1H), 5.13 (d, 1H, J = 7.0 Hz), 5.58 (dt, 1H, J = 10.0, 4.0 Hz), 6.12 (ddd, 1H, J = 10.0, 4.0, 2.0 Hz), 7.32 (m, 5H), 7.72 (m, 2H), 8.08 (m, 2H).

(1*S*,1′*R*)-1-[(1′-Phenyl-1′-methoxymethyloxy)methyl]-1,4-dihydro-9,10-anthraquinone (8e) and (1*S*,1′*S*)-1-[(1′-Phenyl-1′-methoxymethyloxy)methyl]-1,4-dihydro-9,10-anthraquinone (9e). 8e and **9e** were obtained from **1e** following method D (eluent: hexane/EtOAc 90:10) as an inseparable 75:25 mixture, in 40% yield (40 °C) or 60% yield (rt, 4 Kbar): ^{1}H NMR (**8e**) δ 2.98 (s, 3H), 3.16 (ddt, 1H, J = 24.0, 6.5, 2.8 Hz), 3.39 (ddt, 1H, J = 24.0, 1.0, 4.8 Hz), 3.98 (m, 1H), 4.44 (s, 2H), 5.13 (d, 1H, J = 2.8 Hz), 5.56 (m, 1H), 6.06 (m, 1H), 7.26−7.45 (m, 5H), 7.74 (m, 2H), 8.11 (m, 2H). **8e** and **9e** were also obtained from the 75:25 mixture of **8d** and **9d** following method E.

(1*S*,1′*R*)-1-[(1′-*tert*-Butyldimethylsilyloxy-1′-phenyl)-methyl]-1,4-dihydro-9,10-anthraquinone (8f) and (1*S*,1′*S*)-1-[(1′-*tert*-Butyldimethylsilyloxy-1′-phenyl)methyl]-1,4-dihydro-9,10-anthraquinone (9f). 8f and **9f** were obtained from **1f** following method D as an inseparable 76:24 mixture, in 51% yield: ^{1}H NMR (**8f**) δ −0.37 (s, 3H), −0.33 (s, 3H), 0.74 (s, 9H), 3.12 (ddt, 1H, J = 24.0, 6.5, 2.7 Hz), 3.36 (dt, 1H, J = 24.0, 4.8 Hz), 3.90 (m, 1H), 5.17 (d, 1H, J = 2.0 Hz), 5.41 (m, 1H), 6.00 (m, 1H), 7.29−7.46 (m, 5H), 7.75 (m, 2H), 8.13 (m, 2H).

(1*S*,1′*R*)-1-[(1′-Hydroxy)ethyl)]-2-methyl-1,4-dihydro-9,10-anthraquinone (9g). 9g was obtained from **1g** following method D, after separation of the resulting 5:95 mixture of **8g** and **9g** by flash chromatography (eluent: CH_2Cl_2/EtOAc 85:15), in 88% yield: $[\alpha]^{20}_D$ +60 (*c* 0.15, $CHCl_3$); ^{1}H NMR δ 1.10 (d, 3H, J = 6.5 Hz), 1.95 (broad s, 3H), 3.02 (m, 1H), 3.44 (m, 1H), 3.76 (m, 1H), 4.09 (dq, 1H, J = 3.8, 6.5 Hz), 5.82 (m, 1H), 7.71 (m, 2H), 8.08 (m, 2H).

(1*S*,1′*R*)-1-[(1′-Methoxymethyloxy)ethyl]-2-methyl-1,4-dihydro-9,10-anthraquinone (9h). 9h was obtained from **1h** following method D (rt, 4 Kbar) after separation of the 33:67 mixture of **8h** and **9h** by flash chromatography (eluent: hexane/EtOAc 90:10), in 41% yield: $[\alpha]^{20}_D$ +16 (*c* 0.19, $CHCl_3$); ^{1}H NMR δ 1.02 (d, 3H, J = 6.5 Hz), 1.94 (broad s, 3H), 2.98 (m, 1H), 3.39 (s, 3H), 3.41 (m, 1H), 3.89 (m, 1H), 4.01 (dq, 1H, J = 3.0, 6.5 Hz), 4.67 and 4.86 (AB system, 2H, J = 7.0 Hz), 5.76 (m, 1H), 7.70 (m, 2H), 8.09 (m, 2H). **9h** was also obtained from **9g** following method E (eluent: hexane/EtOAc 90:10): $[\alpha]^{20}_D$ +84 (*c* 0.05, $CHCl_3$).

(1*S*,1′*S*)-1-[(1′-*tert*-Butyldimethylsilyloxy)ethyl]-2-methyl-1,4-dihydro-9,10-anthraquinone (8i) and (1*S*,1′*R*)-1-[(1′-*tert*-Butyldimethylsilyloxy)ethyl]-2-methyl-1,4-dihydro-9,10-anthraquinone (9i). 8i and **9i** were obtained from **1i** following method D (eluent: hexane/EtOAc 95:5) as an inseparable 33:67 mixture, in 33% yield: ^{1}H NMR (**8i**) δ −0.10 (s, 3H), 0.00 (s, 3H), 0.80 (s, 9H), 1.13 (d, 3H, J = 6.5 Hz), 1.93 (broad s, 3H), 2.96 (m, 1H), 3.39 (m, 1H), 3.78 (m, 1H), 4.11 (m, 1H) 5.73 (m, 1H), 7.71 (m, 2H), 8.10 (m, 2H).

General Procedure for Epoxidations, Method F. To a solution of the corresponding derivative **8** and **9** in dry CH_2Cl_2, 2 equiv of *m*-CPBA were added. After stirring at the temperature and for the time indicated in each case, solid K_2CO_3 was added, and the mixture was filtered and washed with CH_2Cl_2. After evaporation of the solvent, crude epoxides were purified by flash chromatography.

(1*S,2*S**,3*R**,1′*S**)-1-[(1′-Methoxymethyloxy)ethyl]-2,3-epoxy-1,2,3,4-tetrahydro-9,10-anthraquinone (10b). 10b** was obtained from (±)-**8b** following method F after 8 days at −20 °C (eluent: hexane/EtOAc 85:15), in 51% yield: mp 101−102 °C (methanol); ^{1}H NMR δ 1.43 (d, 3H, J = 6.5 Hz), 2.77 (dt, 1H, J = 20.0, 2.0 Hz), 3.08 (s, 2H), 3.42 (m, 1H), 3.52 (m, 1H), 3.58 (m, 1H), 3.69 (broad s, 1H), 4.03 (dq, 1H, J = 2.5, 6.5 Hz), 4.39 and 4.50 (AB system, 2H, J = 7.0 Hz), 7.68 (m, 2H), 8.03 (m, 2H). Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.76; H, 5.78. Found: C, 68.45; H, 5.79.

(1*S,2*S**,3*R**,1′*S**)-1-[(1′-*tert*-Butyldimethylsilyloxy)-ethyl]-2,3-epoxy-1,2,3,4-tetrahydro-9,10-anthraquinone (10c). 10c** was obtained from the 75:25 mixture of (±)-**8c** and (±)-**9c** following method F after 9 days at −5 °C (eluent: hexane/CH_2Cl_2 50:50), in 45% yield: ^{1}H NMR (C_6D_6) δ −0.28 (s, 3H), −0.15 (s, 3H), 0.84 (s, 9H), 1.23 (d, 3H, J = 6.5 Hz), 2.81 (dt, 1H, J = 20.0, 2.0 Hz), 3.18 (m, 1H), 3.42 (broad d, 1H, J = 4.0 Hz), 3.55 (broad d, 1H, J = 20.0 Hz), 3.81 (broad s, 1H), 4.27 (dq, 1H, J = 2.5, 6.5 Hz), 7.07 (m, 2H), 8.06 (m, 2H); HRMS calcd for $C_{22}H_{28}O_4Si$ 384.17569, found 384.17618.

(1*S,2*S**,3*R**,1′*R**)-1-[(1′-*tert*-Butyldimethylsilyloxy-1′-phenyl)methyl]-2,3-epoxy-1,2,3,4-tetrahydro-9,10-anthraquinone (10f) and (1*S**,2*S**,3*R**,1′*S**)-1-[(1′-*tert*-Butyldimethylsilyloxy-1′-phenyl)methyl]-2,3-epoxy-1,2,3,4-tetrahydro-9,10-anthraquinone (11f). 10f** and **11f** were obtained from a 76:24 mixture of (±)-**8f** and (±)-**9f** following method F after 4 days at 0 °C as an inseparable 76:24 mixture (eluent: hexane/EtOAc 85:15), in 74% yield: ^{1}H NMR (**10f**) δ −0.33 (s, 3H), −0.28 (s, 3H), 0.81 (s, 9H), 2.81 (dt, 1H, J = 20.0, 2.0 Hz), 3.29 (m, 1H), 3.39 (m, 1H), 3.48 (m, 1H), 3.88 (m, 1H), 5.19 (d, 1H, J = 1.5 Hz), 7.0−8.1 (m, 9H); HRMS calcd for $C_{27}H_{30}O_4Si$ 446.19134, found 446.19046.

(1*S,2*S**,3*R**,1′*R**)-1-[(1′-Methoxymethyloxy)ethyl]-2,3-epoxy-2-methyl-1,2,3,4-tetrahydro-9,10-anthraquinone (11h). 11h** was obtained from (±)-**9h** following method F after 2 days at −15 °C, in 61% yield: mp 107−108 °C (methanol); ^{1}H NMR δ 1.09 (d, 3H, J = 6.5 Hz), 1.60 (s, 3H), 2.83 (m, 1H), 3.33 (m, 1H), 3.39 (s, 3H), 3.46 (m, 1H), 3.80 (m, 1H), 4.16 (dq, 1H, J = 2.5, 6.5 Hz), 4.69 (s, 2H), 7.70 (m, 2H), 8.06 (m, 2H); HRMS calcd for $C_{19}H_{20}O_5$ 328.13107, found 328.13150.

(1*S*,2*S*,3*R*,1′*R*)-1-[(1′-*tert*-Butyldimethylsilyloxy)ethyl]-2,3-epoxy-2-methyl-1,2,3,4-tetrahydro-9,10-anthraquinone (11i). 11i was obtained from the mixture of **8i** and **9i** following method F (24 h at 0 °C) after separation by flash

chromatography (eluent: hexane/EtOAc 85:15), in 32% yield: mp 135−136 °C (methanol); $[\alpha]^{20}_D$ −17 (*c* 0.06, $CHCl_3$); ^{1}H NMR δ 0.09 (s, 3H), 0.19 (s, 3H), 0.88 (s, 9H), 1.05 (d, 3H, J = 6.5 Hz), 1.60 (s, 3H), 2.82 (dt, 1H, J = 20.0, 2.0 Hz), 3.30 (m, 1H), 3.44 (m, 1H), 3.72 (m, 1H), 4.21 (dq, 1H, J = 2.8, 6.5 Hz), 7.70 (m, 2H), 8.08 (m, 2H); HRMS calcd for $C_{23}H_{30}O_4Si$ 398.19134, found 398.19083.

1-Methoxy-6-methyl-9,10-anthraquinone (15)[37] and 1-Methoxy-7-methyl-9,10-anthraquinone (16). A solution of 5-methoxy-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (**12**)[28] (63 mg, 0.19 mmol) and diene **1h** (75:25 *E:Z* mixture) (60 mg, 0.38 mmol) in 5 mL of dry CH_2Cl_2 under argon was refluxed for 4 days. The resulting mixture was purified by flash chromatography (eluent: hexane/EtOAc 65:35), and the residue was dissolved in 1 mL of CH_2Cl_2 and stirred at room temperature for 5 days. After flash chromatography (eluent: hexane/EtOAc 85:15), anthraquinones **15** and **16** were obtained as an inseparable 78:22 mixture in 32% yield: ^{1}H NMR (**15**) δ 8.16 (d, 1H, J = 8.0 Hz), 8.02 (d, 1H, J = 1.6 Hz), 7.96 (dd, 1H, J = 7.7, 1.2 Hz), 7.71 (dd, 1H, J = 8.5, 7.7 Hz), 7.57 (dd, 1H, J = 8.1, 2.0 Hz), 7.34 (dd, 1H, J = 8.5, 1.2 Hz), 4.05 (s, 3H), 2.51 (s, 3H); ^{1}H NMR (**16**) δ 8.12 (d, 1H, J = 8.0 Hz), 8.05 (d, 1H, J = 1.6 Hz), 7.96 (dd, 1H, J = 7.7, 1.2 Hz), 7.71 (dd, 1H, J = 8.5, 7.7 Hz), 7.53 (dd, 1H, J = 8.1, 2.0 Hz), 7.33 (dd, 1H, J = 8.5, 1.2 Hz), 4.05 (s, 3H), 2.52 (s, 3H).

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Supporting Information Available: Additional characterization data for **1b**−**f**, **4**, **1g**−**i**, **8b**,**d**,**e**, **9a**,**c**,**e**−**i**, **10b**,**c**, and **11f**,**h**,**i**. Experimental procedures and characterization data for **9b**,**d**, **8h**, **11b**, and **10h**,**i**. Copies of ^{1}H NMR spectra for all compounds and ^{13}C NMR for **1b**,**g**,**h**,**i**, **4**, **8b**,**d**, and **9b**,**d**,**g**,**h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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