Enantioselective Diels−Alder Cycloadditions with (S*S*)-2-(*p*-Tolylsulfinyl)-1,4-naphthoquinone: Efficient Kinetic Resolution of Chiral Racemic Vinylcyclohexenes

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Chiral racemic vinylcyclohexenes **1a**−**m**, bearing allylic and nonallylic oxygenated substituents on the cyclohexene ring, were submitted to Diels−Alder reactions with enantiomerically pure (S*S*)-(2-*p*-tolylsulfinyl)-1,4-naphthoquinone. The tandem cycloaddition/pyrolytic sulfoxide elimination led to the formation of enantiomerically enriched angularly tetracyclic quinones (+)-**8a** and (+)-**12**, arising from the kinetic resolution of the racemic diene. Dienes **1a**−**c**, bearing an alkoxy substituent at the allylic position C-3, and **1d**−**g**, with C-3 alkoxy and C-5 methyl groups, gave exclusively quinones (+)-**8a**−**g**, resulting from the anti approach to the dienophile. A similar anti selectivity occurred in cycloadditions of dienes **1i**,**j**, with the alkoxy group situated at the allylic position C-6. Nonallylic 4-substituted vinylcyclohexenes **1k**−**m** evolved to ca. 75:25 mixtures of (+)-*anti*-**8k**−**m** and (+)-*syn*-**12k**−**m** derivatives. In all cases, (S*S*)-(2-*p*-tolylsulfinyl)-1,4-naphthoquinone reacted from the less hindered face of the more reactive s-cis conformation, giving rise to products in moderate to excellent enantiomeric excesses. Steric effects and torsional interactions in the corresponding approaches account for the observed π-facial diastereoselectivities at both partners.

Introduction

Among the stereochemical features of asymmetric Diels−Alder reactions, the π-facial diastereoselectivity has attracted increasing attention from both synthetic and theoretical points of view[1] due to the well-established efficiency of this process to generate up to four stereogenic centers in a controlled fashion. Many studies have focused on π-facially perturbed dienes[2] and dienophiles.[3] The observed results have been rationalized in terms of steric,[4] electronic,[5] or torsional[6] effects, product stability,[7] orbital interactions,[8] or hyperconjugation.[9] From these studies, no general conclusions can be reached about the factors responsible for the observed facial diastereoselection, making it necessary to consider each system separately. The presence of a stereogenic center at the allylic position of either the dienophile[10] or the diene partner[11] also imparts sufficient perturbation to control the π-facial diastereoselectivity. In such systems, theoretical and experimental work directed to rationalize the

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obtained results led to the conclusion that more than one factor could be responsible for the observed selectivities. Thus, efforts directed to better understanding the origin of such facial diastereoselectivity are welcome.

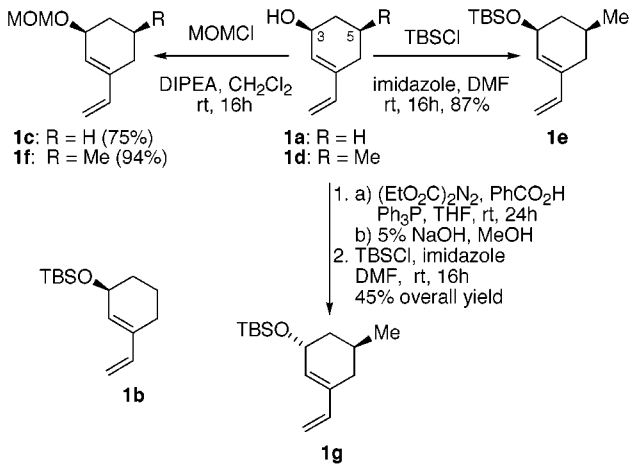
Our previous work devoted to the use of enantiopure (*SS*)-2-(*p*-tolylsulfinyl)-1,4-quinones as dienophiles[12] had shown a high ability of the sulfoxide to control the regiochemistry, endo selectivity, and π-facial diastereoselectivity of its Diels−Alder cycloadditions with a wide range of cyclic and acyclic dienes. We established the tandem Diels−Alder reaction/pyrolytic sulfoxide elimination as a general one-pot strategy to enantiomerically pure polycyclic dihydroquinones. More recently, looking for an enantioselective approach to angucyclinones,[13] we envisaged the ability of the sulfinyl group on the quinonic framework to promote a double induction[14] in the cycloaddition process, leading to the efficient kinetic resolution of some chiral racemic vinylcyclohexenes. The behavior of such kinds of semicyclic dienes containing a stereogenic allylic carbon have been extensively studied[9b,11h−l] in cycloadditions with classical dienophiles.[15] Major parts of these studies were carried out by using racemic dienes due to the multistep syntheses necessary to obtain them in optically pure form.[15c]

The good results we obtained prompted us to deeply investigate such a double asymmetric induction process. In this paper, we report the study of Diels−Alder reactions of several chiral racemic vinylcyclohexenes with enantiomerically pure (*SS*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone and propose a rationalization for the observed diastereoselectivity. Differently positioned stereogenic centers on the diene moiety would allow evaluation of the influence of proximal and remote substitution on the face diastereoselection. With this aim, racemic semicyclic dienes included in this study showed an oxygenated substituent at allylic position C-3 (**1a**−**g**)[13] or C-6 (**1h**−**j**) and at nonallylic position C-4 (**1k**−**m**) of the cyclohexene moiety.[16] Prior to the present study, no experimental evidence was available concerning the role of a C-4 or C-6 stereogenic center in the vinylcyclohexene framework on π-facial diastereoselection. Besides the intrinsic fundamental interest, these results have a potential synthetic utility as a short and efficient route to enantiomerically enriched, angularly fused tetracyclic quinones related to the angucyclinone family of antibiotics.

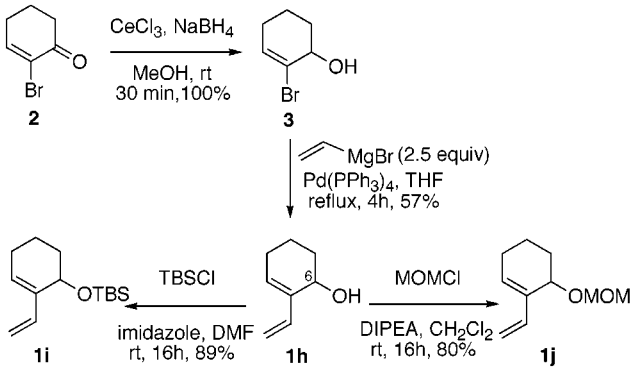
Results

Synthesis of Dienes. Semicyclic dienes **1a** and **1b** (Scheme 1), with oxygen substituents at the allylic C-3 position, were prepared according to previously reported procedures.[17] The methoxymethyloxy (OMOM) derivative **1c** was obtained from **1a** in 75% yield by reaction with MOMCl and diisopropylethylamine (DIPEA). Starting from alcohol **1d**,[18] we synthesized semicyclic dienes **1e** and **1f**, with an oxygenated substituent at C-3 and a methyl group in cis disposition at C-5. Treatment of **1d** with *tert*-butyldimethylsilyl chloride (TBSCl) and imidazole gave an 87% yield of **1e**, and upon reaction with MOMCl and DIPEA, diene **1f** was obtained in 94% yield. Compound **1g**, bearing a OTBS substituent at C-3 and a methyl group in a trans disposition at C-5, was obtained from the cis alcohol **1d**, which was submitted to Mitsunobu conditions[19] to yield a mixture of trans and cis alcohols, where the trans derivative was the major component. After silylation of this mixture (TBSCl/imidazole) and flash chromatography, diene *trans*-**1g** was isolated pure in 45% yield.

Scheme 1



Scheme 2



The required vinylcyclohexenes **1h**−**j**, with allylic substitution at C-6, were prepared as outlined in Scheme 2. Starting from 2-bromo-2-cyclohexenone (**2**),[20] Luche reduction[21] ($NaBH_4/CeCl_3$) afforded in quantitative yield alcohol **3**,[22] which after coupling with vinylmagnesium bromide in the presence of catalytic Pd(0), gave diene **1h** in 57% yield. Protection of this alcohol with either

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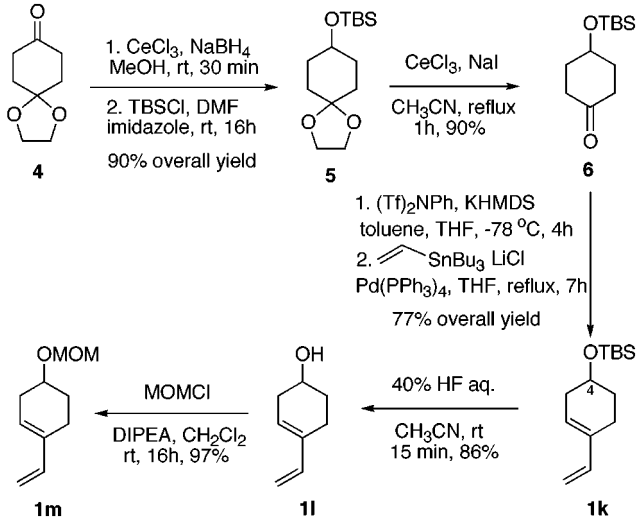
Scheme 3



TBSCl/imidazole or MOMCl/DIPEA led respectively to derivatives **1i**[23] (89% yield) and **1j** (80% yield).

Compounds **1k**−**m**, bearing the oxygenated substituent at the nonallylic C-4 position, were prepared as depicted in Scheme 3. Thus, commercially available ketone **4** was reduced under Luche conditions[21] and further protected as the OTBS derivative to afford **5** in 90% overall yield. Deprotection of the ketal function was troublesome under the usual acidic conditions, but after several trials, ketone **6**[24] could be obtained by treatment of ketal **5** with $CeCl_3 \cdot 7H_2O$ and NaI in refluxing CH_3CN[25] in 90% yield. Preparation of diene **1k** was achieved in two steps and 77% overall yield from **6**, after formation of the corresponding enoltriflate by treatment with $(Tf)_2NPh$ and potassium hexamethyldisilazide (KHMDS)[26] and further coupling with vinyltributyltin in the presence of catalytic Pd(0).[27] Desilylation of this OTBS derivative with 40% HF in CH_3CN[28] afforded dienol **1l** in 86% yield, which after reaction with MOMCl and DIPEA, gave diene **1m** in near quantitative yield (Scheme 3).

Diels−Alder Reactions. With the desired racemic vinylcyclohexenes in hand, we began the study of Diels−Alder cycloadditions choosing enantiomerically pure (*SS*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (+)-**7**[29] as a model of a chiral dienophile. The influence of an array of different solvents and reaction conditions was studied. The use of Lewis acids was prevented due to the fast polymerization of the dienes. The best results were achieved working in CH_2Cl_2 at room temperature. Under these conditions, Diels−Alder reactions between quinone (+)-**7** and 2 equiv of racemic vinylcyclohexenes **1a**−**m** gave rise to the optically active cycloaddition/elimination products (+)-*anti*-**8a**−**m** (Schemes 4−6) as the major or exclusive diastereoisomer in moderate to excellent yields (Table 1). The diastereoisomeric anti/syn[30] ratios were determined directly from the crude reaction mixtures by ^{1}H NMR analysis. The enantiomeric excesses for compounds (+)-**8a**−**m** (Table 1) were measured from ^{1}H NMR studies on the corresponding Mosher esters[31] or by using chiral lanthanide shift reagents, which required the preparation of each racemic derivative (±)-**8a**−**m**, starting from racemic naphthoquinone (±)-**7**.[29] In these cycloadditions, we could recover unreacted dienes (−)-**1a**−**m** in optically active form, but only in the case of diene (−)-**1b** did we investigate its enantiomeric purity (see below).

A Diels−Alder reaction between enantiopure naphthoquinone (+)-**7** and racemic vinylcyclohexenol **1a** (Scheme 4; Table 1, entry 1) afforded a mixture of two products **8a** and **9**, which could be separated by flash chromatography. Compound (+)-**8a**[13] (28% yield) resulted from spontaneous pyrolysis of the sulfoxide in the initial adduct formed by attack of the dienophile on the face of the diene anti to the hydroxy group. Anthraquinone **9**[13] (51% yield) probably was derived from **8a** in a fragmentation process promoted by the free OH as already observed for similar systems.[11k,32] When the same cycloaddition was carried out in water (Table 1, entry 2), the reaction was faster, with compound (+)-**8a** now being the only isolated product in 73% yield. The ee and absolute configuration of (+)-**8a** could not be determined at this stage due to its easy transformation into **9** under the experimental conditions necessary to generate the corresponding Mosher esters.[31] To avoid the formation of **9**, we decided to prepare a more stable derivative of (+)-**8a**. Thus, the treatment of (+)-**8a** with *m*-chloroperoxybenzoic acid (*m*-CPBA) afforded epoxide (+)-**10a**[13] in 90% yield, resulting from the exclusive attack of the oxidant from the α-face (cis to H_{12b}). The relative configuration of (+)-**10a** was initially established by comparison with a similar intermediate prepared by Sulikowski[15b] in the total synthesis of antibiotic SF 2315A. The absolute configuration for (+)-**8a** and (+)-**10a** was confirmed from the Mosher esters of the latter,[13] which showed a 50% and a 20% ee for the cycloadditions in CH_2Cl_2 and water, respectively.

Cycloaddition of (+)-**7** and the OTBS-substituted racemic diene **1b** afforded compound (+)-**8b**[13] as the exclusive product in 75% isolated yield (Scheme 4, Table 1, entry 3). The ee of >97% observed for (+)-**8b** indicated an excellent diastereoselection for the initial Diels−Alder reaction and that a kinetic resolution of the racemic diene had efficiently occurred. This assumption was confirmed by recovering unchanged diene **1b**[13] in optically active form {$[\alpha]^{20}_D = -38$ (*c* 1, $CHCl_3$)}. Desilylation of recovered (−)-**1b** with tetrabutylammonium fluoride (TBAF) in THF yielded diene (−)-**1a**[13] {$[\alpha]^{20}_D = -47$ (*c* 1, $CHCl_3$)} whose Mosher esters showed a 75:25 enantiomeric ratio and the (*S*) configuration for C-3 as indicated in Scheme 4. We also carried out the cycloaddition between (+)-**7** and the racemic OMOM derivative **1c** (Scheme 4). In this case, compound (+)-**8c** was isolated in 61% yield as a sole product, showing a 92% ee (Scheme 4; Table 1, entry 4).

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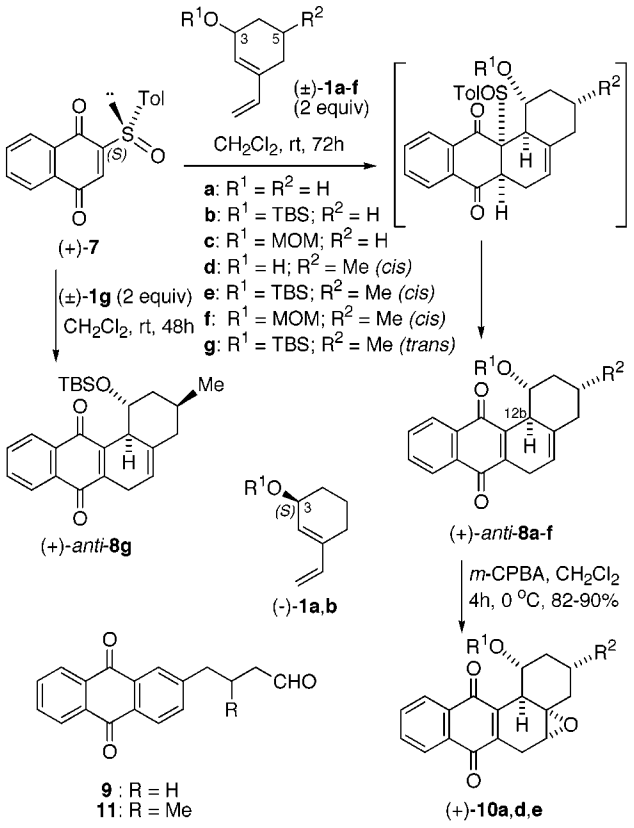
Table 1. Diels−Alder Reactions of Enantiopure Sulfinylnaphthoquinone (+)-7 and 2 Equiv of Racemic Vinylcyclohexenes 1a−m in CH_2Cl_2 at Room Temperature[a]

entry	diene	substituent position	*t* (h)	product anti (%)	product syn (%)	yield, %	enantiomers ratio
1	**1a**	3-OH	72	**8a** (100)	(0)	28	75:25[b]
2[c]	**1a**	3-OH	12	**8a** (100)	(0)	73	60:40[b]
3	**1b**	3-OTBS	72	**8b** (100)	(0)	75	>97:3[d]
4	**1c**	3-OMOM	72	**8c** (100)	(0)	61	96:4[d]
5	**1d**	*cis*-3-OH-5-Me	72	**8d** (100)	(0)	26	75:25[b]
6[c]	**1d**	*cis*-3-OH-5-Me	12	**8d** (100)	(0)	69	60:40[b]
7	**1e**	*cis*-3-OTBS-5-Me	72	**8e** (100)	(0)	73	>97:3[e]
8	**1f**	*cis*-3-OMOM-5-Me	72	**8f** (100)	(0)	59	97:3[d]
9	**1g**	*trans*-3-OTBS-5-Me	48	**8g** (100)	(0)	62	90:10[d]
10	**1h**	6-OH	48	**8h** (72)	**12h** (28)	62[f]	88:12,[g] 75:25[h]
11	**1j**	6-OMOM	48	**8j** (100)	(0)	61	97:3[d]
12	**1i**	6-OTBS	48	**8i** (100)	(0)	57	97:3[i]
13	**1l**	4-OH	16	**8l** (60)	**12l** (40)	55[j]	89:11[k]
14	**1k**	4-OTBS	16	**8k** (76)	**12k** (24)	85[l]	93:7[m]
15	**1m**	4-OMOM	16	**8m** (75)	**12m** (25)	49[n]	89:11[o]
16[p]	**1m**	4-OMOM	24	**8m** (70)	**12m** (30)	53[q]	93:7[o]

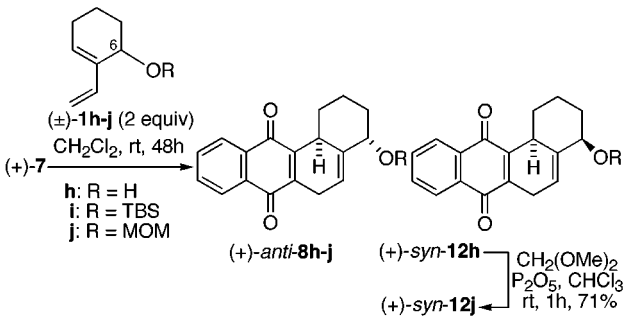
[a] Data for entries 1−3 and 5−7 were taken from ref 13. [b] Using Mosher esters. [c] Cycloaddition performed in water. [d] Using $Eu(tfc)_3$. [e] Using $Eu(tfc)_3$ on epoxide **10e**. [f] Yield for the mixture of **8h** and **12h**. [g] Ratio for **8h** using $Eu(tfc)_3$ on the mixture of **8j** and **12j**. [h] Ratio for **12h** using $Eu(tfc)_3$ on the mixture of **8j** and **12j**. [i] Using $Pr(hfc)_3$. [j] Overall yield after transformation into the mixture of OMOM derivatives **8m** and **12m**. [k] Ratio for **8l** using $Eu(tfc)_3$ on compound **8m**. [l] Yield for the mixture of **8k** and **12k**. [m] Ratio for **8k** using $Yb(hfc)_3$ on epoxide **14**. [n] 38% for **8m** and 11% for **12m** isolated yields. [o] Ratio for **8m** using $Eu(tfc)_3$. [p] Cycloaddition performed at 0 °C. [q] Isolated yield for **8m** 37% and for **12m** 16%.

Scheme 4



Reaction of (+)-**7** with racemic dienol **1d**, containing an additional cis methyl group at C-5, afforded products (+)-**8d**[13] and **11**[13] in 26% and 50% yields, respectively, after flash chromatography (Scheme 4; Table 1, entry 5). The same reaction in water (Table 1, entry 6) led only to compound (+)-**8d** in 69% yield. The *m*-CPBA oxidation of (+)-**8d** gave epoxide (+)-**10d**[13] in 82% yield, whose Mosher esters allowed us to establish the absolute configuration depicted in Scheme 4, showing 50% and 20% ee, respectively, for the products resulting from cycloadditions performed in CH_2Cl_2 and water. The racemic OTBS-substituted derivative **1e** reacted with quinone (+)-**7** yielding exclusively compound (+)-**8e**[13] in 73% yield (Scheme 4), whose epoxidation gave derivative (+)-**10e**[13] in 86% yield, showing an ee value greater than 97% (Table 1, entry 7). This high ee indicated a total stereocontrol in both the Diels−Alder reaction and epoxidation. Moreover, the absolute configuration of (+)-**10e** had been confirmed by X-ray diffraction.[13] Diels−Alder reaction of (+)-**7** and racemic OMOM derivative **1f** yielded compound (+)-**8f** as a sole product in 59% yield, showing a 94% ee (Scheme 4; Table 1, entry 8).

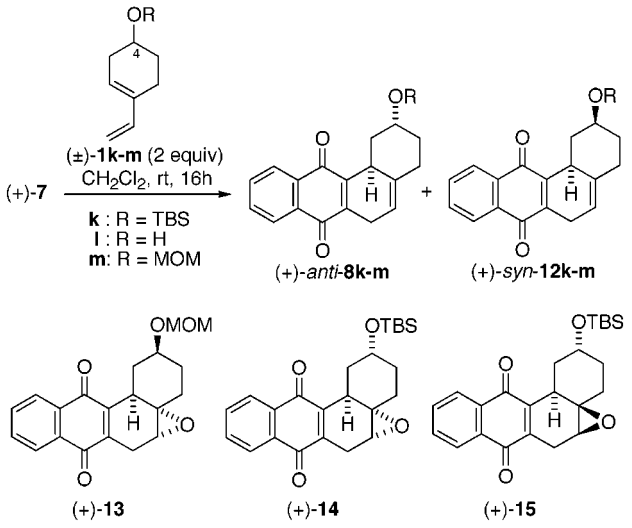
Scheme 5



Diels−Alder cycloaddition between sulfinylquinone (+)-**7** and racemic diene **1g**, bearing a OTBS group at C-3 and a methyl substituent at C-5 in trans disposition, afforded compound (+)-**8g** in 62% yield as the only diastereoisomer (Scheme 4; Table 1, entry 9), showing 80% ee. The same reaction at 0 °C for 72 h gave similar stereochemical results.

We further focused our attention on the behavior of semicyclic dienes with allylic substitution at C-6 of the cyclohexene moiety. Thus, cycloaddition between dienol **1h** and quinone (+)-**7** (Scheme 5; Table 1, entry 10) afforded in 62% yield of a 75:25 mixture of the two compounds **8h** (76% ee) and **12h** (50% ee), which could not be separated. These derivatives were respectively formed from the anti and syn approaches of the diene on the sulfinylquinonic framework. Their configurational assignment could be established after transformation into the corresponding unseparable mixture of OMOM de-

Scheme 6



rivatives **8j** and **12j** (dimethoxymethane, P_2O_5)[33] and by comparison with the ^{1}H NMR data of the same compound (+)-*anti*-**8j** (61% yield, 94% ee), which resulted as the exclusive product from the reaction of quinone (+)-**7** and racemic OMOM-substituted diene **1j** (Scheme 5; Table 1, entry 11). Cycloaddition between the OTBS-protected derivative **1i** and (+)-**7** (Scheme 5; Table 1, entry 12) led exclusively to the anti diastereoisomer (+)-**8i** (57% yield, 94% ee).

Racemic vinylcyclohexenol **1l**, bearing the free hydroxy substituent at the nonallylic C-4 position of the cyclohexene moiety, reacted with enantiopure sulfinylnaphthoquinone (+)-**7** affording a 60:40 mixture of two products, **8l** and **12l** (Scheme 6; Table 1, entry 13), which after purification by flash chromatography, were transformed (dimethoxymethane, P_2O_5)[33] into the corresponding mixture of separable OMOM derivatives (+)-*anti*-**8m** (29% yield, 78% ee) and (+)-*syn*-**12m** (26% yield). Enantiomeric purity could not be determined using chiral shift lanthanide reagents neither for (+)-**12m** nor for epoxide (+)-**13**, obtained as the exclusive product in the *m*-CPBA oxidation of the former (Scheme 6). The Diels−Alder reaction of OTBS derivative **1k** with (+)-**7** afforded a 76:24 mixture of diastereoisomers *anti*-**8k** and *syn*-**12k** in 85% yield (Scheme 6; Table 1, entry 14), from which the major compound (+)-**8k** could be isolated by flash chromatography. Nevertheless, the impossibility of determining its enantiomeric excess by using chiral shift lanthanide reagents prompted us to epoxidate (+)-**8k** (*m*-CPBA, CH_2Cl_2), obtaining a 80:20 mixture of epoxides (+)-**14** and (+)-**15** (Scheme 6), easily separated by flash chromatography. These derivatives were respectively formed from the attack of the oxidant on the lower and upper face of the double bond of (+)-**8k**. Compound (+)-**14** showed a 86% ee (Table 1, entry 14), reflecting the facial diastereoselectivity for the initial cycloaddition between diene **1k** and quinone (+)-**7**. Finally, a reaction between quinone (+)-**7** and OMOM derivative **1m** afforded a separable 75:25 mixture of (+)-*anti*-**8m** (38% yield, 78% ee) and (+)-*syn*-**12m** (11% yield), respectively (Scheme 6; Table 1, entry 15). When the reaction was performed at 0 °C, the anti/syn ratio was similar (70:30) but a slightly better ee (86%) was determined for (+)-**8m** (Table 1, entry 16).

(33) Fuji, K.; Nakano, S.; Fujita, E. *Synthesis* **1975**, 276.

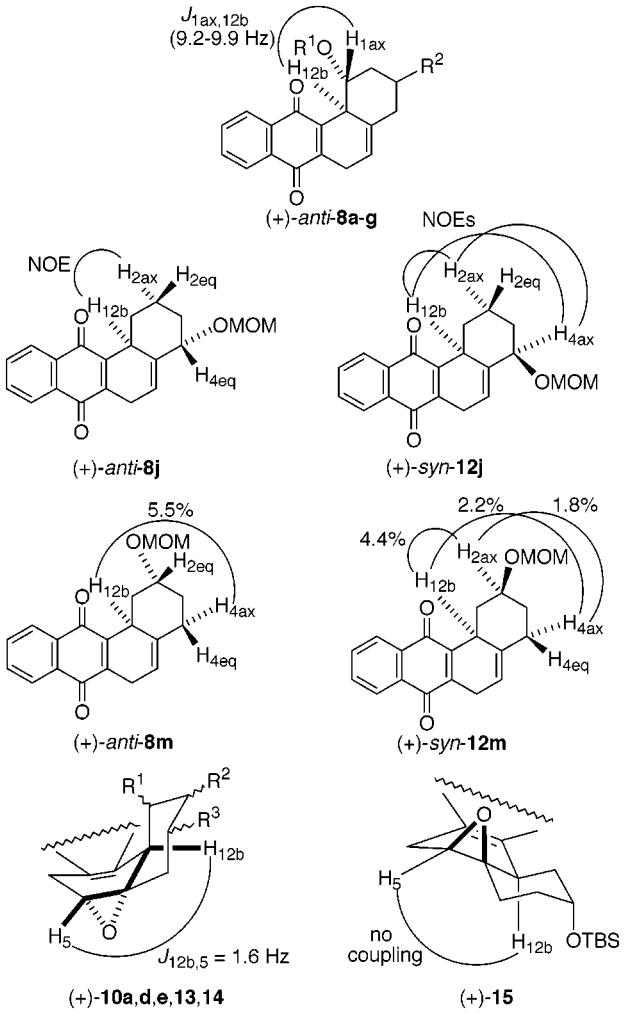


Figure 1. Significant ^{1}H NMR parameters used for configurational assignments.

Configurational Assignments. The relative stereochemistry of tetracyclic derivatives (+)-*anti*-**8** and (+)-*syn*-**12** could be established on the basis of their ^{1}H NMR data, in particular coupling constants and NOE and ^{1}H−^{1}H NOESY experiments[34] (Figure 1). In the case of compounds (+)-*anti*-**8a**−**g**, H_1 always appeared as a doublet of triplets with both $J_{1,12b}$ and $J_{1,2ax}$ ranging from 9.2 to 9.9 Hz. These values are consistent with a relative trans diaxial relationship between H_1 and H_{2ax}, and H_1 and H_{12b}, respectively (Figure 1).

The absolute configurations of compounds (+)-*anti*-**8a**−**g** were established from the (R) absolute configuration at C-3 determined from the Mosher esters of epoxides (+)-**10a** and (+)-**10d**[13] and from the absolute stereochemistry shown by X-ray data for derivative (+)-**10e**.[13]

The relative stereochemistry of compounds (+)-*anti*-**8h**−**j** was determined from a ^{1}H−^{1}H NOESY experiment on the nonseparable mixture of compounds (+)-*anti*-**8j** and (+)-*syn*-**12j**. We noticed that the NOEs depicted in Figure 1 show the cis relationship between pseudoaxial protons H_{12b}, H_{2ax}, and H_{4ax} for (+)-*syn*-**12j**, whereas the only evident NOE for derivative (+)-*anti*-**8j** was that between pseudoaxial protons H_{12b} and H_{2ax}.

For the configurational assignment of derivatives (+)-*anti*-**8k**−**m** and (+)-*syn*-**12k**−**m**, selective irradiations

(34) NOE and ^{1}H−^{1}H NOESY experiments were performed in $CDCl_3$ or C_6D_6 at 500 MHz.

effected on (+)-*syn*-**12m** showed relevant NOE enhancements ranging from 1.8 to 4.4% between the pseudoaxial protons H_{12b}, H_{2ax}, and H_{4ax}, whereas the only observed NOE for derivative (+)-*anti*-**8m** occurred between H_{12b} and H_{4ax} protons.

Finally, the relative configurations of the epoxides prepared in this study were established on the basis of the observed long-range coupling constant existent between H_{12b} and H_5 ($J_{12b,5}$ = 1.6 Hz) for compounds (+)-**10a**,**d**,**e**, **13**, and **14**, having the epoxide group directed to the lower face of the dihydroquinone moiety (Figure 1). This coupling was not observed for derivative (+)-**15**, where the epoxide ring is directed to the upper face of the dihydroquinone framework.

Discussion

To rationalize the results achieved in such a double asymmetric induction process,[35] we must differentiate the diastereofacial selectivities of both chiral partners. Thus, the observed anti/syn selectivities reflect the π-facial diastereoselection of the diene, whereas the resulting enantiomeric excess for each of the (+)-**8** and (+)-**12** derivatives indicates the diastereofacial control and the efficiency of the kinetic resolution exerted by the sulfoxide group on the quinonic moiety.

To understand the origin of the high enantioselectivity observed in these reactions, we must focus on the behavior of enantiopure sulfinylquinones. For such dienophiles, experimentation suggested that the face selectivity induced by sulfoxide was mainly due to steric factors. According to previous studies,[12] the most favored endo approach of a diene occurred from the face of the sulfinylquinone containing the less sterically demanding lone electron pair at sulfur in the more reactive s-cis conformation (Figure 2). Thus, considering the (*S*) absolute configuration induced at C_{12b} in all derivatives (+)-**8** and (+)-**12**,[36] the resulting enantiomers must arise from the attack of the diene on the top face of (+)-**7**.

For the diene partner, the analysis of face diastereoselection must differentiate among systems bearing the stereogenic centers at C-3 (**1a**−**g**), C-4 (**1k**−**m**), or C-6 (**1h**−**j**). In the former case, our results are in agreement with those reported by Franck[11j] and Larsen[11k] for cycloadditions of similar 3-oxygenated vinylcyclohexene derivatives, which indicated the major or exclusive formation of the anti adduct as the result for the preferred approach of the dienophile from the face of the diene anti to the oxygenated function, with the exception of the free hydroxy derivatives **1a** and **1d**. For such dienes, the syn adduct was mainly formed in cycloadditions with maleimide in benzene, whereas the anti adduct was the major product in polar solvents.[11j] With quinones as dienophiles, only the anti diastereoisomer was formed.[11k] These results showed a dependence of face selectivity on both the solvent and the nature of the dienophile. In our case, cycloadditions between sulfinylquinone (+)-**7** and hydroxy dienes **1a** and **1d** in CH_2Cl_2 (Table 1, entries 1 and 5) gave only anti derivatives (+)-**8a** and (+)-**8d** together with anthraquinones **9** and **11** as the major components of the crude mixtures. Since both types of anti and syn diastereoisomeric adducts could evolve into the corresponding anthraquinones, we could not establish accurately the anti/syn selectivity for these cycloadditions. When the solvent is changed to water (Table 1, entries 2 and 6), the exclusive formation of anti derivatives (+)-**8a** and (+)-**8d** could be a consequence of the postulated increased size of the OH group by hydrogen bond association with the solvent, which favored the anti approach of the dienophile.[11j]

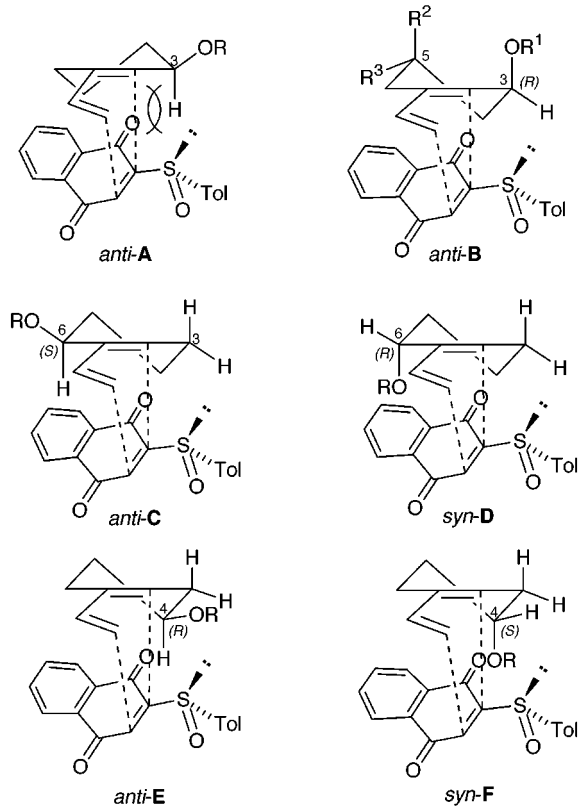


Figure 2. Favored approaches of semicyclic dienes **1a**−**m** in Diels−Alder reactions with enantiopure sulfinylnaphthoquinone (+)-**7**.

The exclusive formation of anti diastereoisomers in the reactions of 3-OTBS- or 3-OMOM-substituted vinylcyclohexenes **1b**,**c**,**e**−**g** (Table 1, entries 3−4 and 7−9) is also consistent with the steric approach control model proposed to rationalize the observed π-facial diastereoselectivities. On the basis of previously reported models,[11j,k] the major formation of anti adducts in cycloadditions of dienes bearing a C-3 oxygenated substituent with several dienophiles could be justified on the endo approach *anti*-**A** shown in Figure 2. Although steric effects in such an approach are minimized,[11j,k] according to Houk's work, allylic substituents must be staggered with respect to forming bonds in cycloaddition transition states.[6b,37] The torsional interaction existent in *anti*-**A** (Figure 2) between the partially formed C−C bond and the pseudoaxial C_3−H allylic bond contributes to destabilizing it.[38] Thus, we propose *anti*-**B** (R^1 = H, MOM,

(35) We use this term in the conventional sense defined by Masamune (see ref 14), considering the kinetically favored reaction occurring between homochiral dienophile (+)-**7** and one of the enantiomers of chiral racemic dienes **1a**−**m**.

(36) The same (*S*) configuration is always produced by a chiral (*SS*)-2-(*p*-tolylsulfinyl)-1,4-quinone upon reaction with (1*E*)-substituted dienes (see refs 12b and 12e).

(37) (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) Paddar-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.

TBS; $R^2 = R^3 = H$), with the oxygen substituent of the cyclohexene ring in pseudoaxial disposition, which is responsible for the preferred approach of the sulfinylquinone (+)-**7** to the C-3 substituted dienes **1a**−**c** (Table 1, entries 2−4). In such disposition, torsional interactions are avoided and the interaction between the sulfur substituent of the dienophile and the pseudoequatorial H_3 of the diene is minimized. Taking into account the existence of a (R^1O/H) 1,3-parallel destabilizing interaction[39] in *anti*-**B** (Figure 2, $R^2 = R^3 = H$) and the torsional strain existent in *anti*-**A**,[40] we could estimate a difference in the energy content of both transition states of ca. 4 kcal/mol in favor of *anti*-**B**. In the case of *cis*-3,5-disubstituted dienes **1d**−**f** (Table 1, entries 6−8), a similar approach of *anti*-**B** (Figure 2, $R^2 = CH_3$, $R^3 = H$) could account for the anti preference. In such situation, both C-3 (OR^1) and C-5 (R^2 = Me) cis pseudoaxial substituents must increase the energy content of this transition state by ca. 2.4 kcal/mol,[41] a minor amount if compared to the destabilization generated in *anti*-**A**, arising from the above-mentioned torsional interaction.[40] In the case of cycloaddition with *trans*-3,5-disubstituted vinylcyclohexene **1g** (Table 1, entry 9), the anti diastereofacial selectivity could also be justified by the higher stability of *anti*-**B** (Figure 2, R^1 = TBS, $R^2 = H$, $R^3 = CH_3$) bearing the C-5 substituent in the pseudoequatorial arrangement. In all cases, the approach represented as *anti*-**B** corresponds to the evolution of the matched pair, where the reacting diene is the (3*R*) enantiomer. This is in full agreement with the (3*S*) absolute configuration of the recovered diene (−)-**1b** (see Scheme 4).

When the stereogenic center of the diene partner is located at C-6, we observed again the preferred formation of anti adducts (+)-**8h**−**j**, which were exclusive for OTBS and OMOM derivatives **1j** and **1i** (Table 1, entries 11−12) and major for the reaction of the hydroxy derivative **1h** (Table 1, entry 10). We assume that approach *anti*-**C** (Figure 2), with a staggered disposition of the pseudoequatorial C_3−H and the forming C−C bonds, must be favored. In such an anti approach, the small pseudoaxial proton at C-6 is interacting with the naphthoquinone framework, with the (6*S*) enantiomer of dienes **1h**−**j** reacting with quinone (+)-(*SS*)-**7** being the favored matched pair. When the size of the OR group was decreased (for reaction with dienol **1h**), syn attack occurred in a small proportion (28%) giving rise to compound (+)-**12h**. Although the absolute configuration of syn derivative **12h** could not be unequivocally determined, in accord with the steric and torsional interactions that govern these processes, we can propose approach *syn*-**D** (Figure 2, R = H), showing the OH group in a pseudoaxial position, as the approach responsible for the formation of *syn*-**12h**. Accordingly, the syn-matched pair should result from the cycloaddition between quinone (+)-(*SS*)-**7** and the (6*R*) enantiomer of diene **1h**.[42]

Although the anti/syn ratios resulting from cycloadditions with nonallylic 4-oxygenated vinylcyclohexenes **1k**−**m** were lower, similar steric and torsional effects could account for the observed results (Table 1, entries 13−16). Thus, the steric interactions favoring the anti over the syn approach correspond to those existent between the pseudoaxial proton at C-4 [*anti*-**E** in Figure 2, (*R*) enantiomer reacting] versus the pseudoaxial OR at C-4 [*syn*-**F** in Figure 2, (*S*) enantiomer reacting][42] with one of the carbonyl groups of quinone (+)-**7**. In this case, the energy differences between both approaches must be smaller than those in the cases discussed above, according to the lower selectivity achieved.

Thus, we interpret the kinetic resolution process by arguing that the endo anti approaches **B**, **C**, and **E**, represented in Figure 2, correspond to the evolution of the matched pairs. The most favored situation resulted from the anti cycloaddition of dienes bearing respectively the configurations 3R (for **1a**−**c**); 3R,5R (for **1d**−**f**); 3R,5S (for **1g**); 6S (for **1h**−**j**); 4R (for **1k**−**m**) to the less hindered face of quinone (+)-(*SS*)-**7** reacting in the s-cis conformation. This model is in full agreement with recovering a major unreacted diene (−)-**1b**, showing the 3S absolute configuration. The degree of enantioselectivity achieved in anti cycloadditions increased with the volume of the OR protecting group (OTBS > OMOM ≫ OH). This fact is consistent with steric effects contributing to control both the anti/syn face diastereoselection in the diene partner and the enantiofacial selectivity on the sulfinyl dienophile. The slight decrease of optical purity observed in the products resulting from reactions of dienes **1g**,**h**,**k**−**m** (76−85% ee) could be attributed to the higher reactivity of these systems if compared with those of **1a**−**f** (see reaction times in Table 1).

Concluding Remarks

Generation of up to three stereogenic centers in the angular tetracyclic framework of derivatives (+)-**8** and (+)-**12** is possible starting from enantiomerically pure (*SS*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (+)-**7** and substituted racemic vinylcyclohexenes **1a**−**m**. The products are formed in a one-pot Diels−Alder cycloaddition/sulfoxide pyrolytic elimination sequence. The initial cycloaddition occurs in a highly endo and π-facial diastereoselective manner with an efficient resolution of the diene partner. The matched pair results from the anti approach to the oxygenated substituent of the diene. The importance of steric factors as well as torsional strain in the relative stability of the different approaches has been highlighted. Besides the fundamental study, the reported methodology provides a short enantioselective approach to highly functionalized systems related to angucyclinone antibiotics.

Experimental Section

Melting points were obtained in open capillary tubes and are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. Diastereoisomeric ratios were established by integration of well-separated signals of both diastereomers in the crude reaction mixtures and are listed in Table 1. All reactions were monitored by thin-layer chromatography that was performed on precoated sheets of

(38) Such torsional interactions are similar to those involving formed bonds.

(39) A (OTMS/H) 1,3-parallel interaction is estimated to be 0.74 kcal/mol in cyclohexane derivatives; see: Eliel, E. L.; Wilen, S. H *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994; p 696.

(40) The attack of a hydrogen atom on propene in a staggered arrangement between one allylic C−H bond and the forming C···H bond was estimated by Houk to be favored by 5 kcal/mol over the eclipsed one (see ref 37a).

(41) This value corresponds to the 1,3-*syn*-diaxial interaction between a CH_3 and a OH group in a cyclohexane ring; see ref 39, p 707.

(42) This assumption could not be demonstrated since the major evolution corresponded to the anti approach.

silica gel 60, and flash column chromatography was done with silica gel 60 (230−400 mesh) from 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. 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 drying with Na_2SO_4. Vinylcyclohexenes **1a**,[17] **1b**,[17] and **1d**[18] were prepared according to previously reported procedures.

General Procedure for the Synthesis of OMOM Derivatives, Method A. To a solution of 4 mmol of the corresponding alcohol in 8 mL of CH_2Cl_2 1.4 mL (11 mmol) of DIPEA and 3.4 mL (42 mmol) of MOMCl were added. The mixture was stirred at room temperature overnight and hydrolyzed with a cold aqueous saturated solution of $NaHCO_3$. After workup and flash chromatography, the pure OMOM derivative was obtained.

General Procedure for the Synthesis of OTBS Derivatives, Method B. To a solution of 4.8 mmol of the corresponding alcohol in 7 mL of DMF 0.86 g (5.7 mmol) of TBSCl and 0.82 g (12 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 OTBS derivative was obtained.

3-[(Methoxymethyl)oxy]-vinylcyclohexene (1c). 1c was obtained from **1a**[17] following method A (eluent: CH_2Cl_2/hexane, 60:40) as a colorless oil (75% yield): ^{1}H NMR δ 6.38 (dd, 1H, J = 10.7 and 17.7 Hz), 5.78 (broad s, 1H), 5.12 (d, 1H, J = 17.7 Hz), 5.03 (d, 1H, J = 10.7 Hz), 4.70 (m, 2H), 4.22 (broad s, 1H), 3.40 (s, 3H), 2.2−1.5 (m, 6H); ^{13}C NMR δ 139.05, 138.54, 128.73, 112.09, 94.66, 70.91, 54.66, 28.88, 23.41, 18.67.

***cis*-3-[(*tert*-Butyldimethylsilyl)oxy]-5-methyl-1-vinylcyclohexene (1e). 1e** was obtained from **1d**[18] following method B (eluent: hexane) as a colorless oil (87% yield): ^{1}H NMR δ 6.35 (dd, 1H, J = 10.7 and 17.5 Hz), 5.60 (m, 1H), 5.14 (d, 1H, J = 17.5 Hz), 5.00 (d, 1H, J = 10.7 Hz), 4.41 (m, 1H), 2.3−1.2 (m, 5H), 1.05 (d, 3H, J = 6.2 Hz), 0.92 (s, 9H), 0.11 and 0.10 (2s, 6H); ^{13}C NMR δ 139.10, 136.59, 133.10, 112.02, 69.09, 41.47, 32.37, 27.77, 25.89 (3C), 22.09, 18.20, −4.52, −4.69; HRMS (EI) calcd for $C_{15}H_{28}OSi$ 252.19094, found 252.19112.

***cis*-3-[(Methoxymethyl)oxy]-5-methyl-1-vinylcyclohexene (1f). 1f** was obtained from **1d**[18] following method A (eluent: CH_2Cl_2/hexane 60:40) as a colorless oil (94% yield): ^{1}H NMR δ 6.36 (dd, 1H, J = 10.8 and 17.7 Hz), 5.69 (broad s, 1H), 5.17 (d, 1H, J = 17.7 Hz), 5.01 (d, 1H, J = 10.8 Hz), 4.73 (m, 2H), 4.30 (broad s, 1H), 3.40 (s, 3H), 2.4−1.1 (m, 5H), 1.05 (d, 3H, J = 6.0 Hz); ^{13}C NMR δ 138.62, 137.13, 129.94, 111.81, 94.71, 73.38, 54.59, 37.95, 32.05, 27.29, 21.67.

***trans*-3-[(*tert*-Butyldimethylsilyl)oxy]-5-methyl-1-vinylcyclohexene (1g).** To a mixture of 0.85 g (6.2 mmol) of alcohol cis-**1d**,[18] 1.5 g (12.3 mmol) of benzoic acid, and 3.2 g (12.3 mmol) of Ph_3P in 85 mL of THF 2.1 g (12.3 mmol) of ethyl azodicarboxylate was slowly added. After 24 h at room temperature, the solvent was evaporated and the residue was purified by flash chromatography (eluent: hexane/EtOAc 95:5) to afford a mixture of the corresponding benzoic esters, which was dissolved in 10 mL of MeOH and hydrolyzed with 4 mL of 5% aqueous NaOH solution. After extraction with ether, drying with $MgSO_4$, and evaporation of the solvent, the crude mixture of trans and cis alcohols was obtained and transformed into the corresponding OTBS derivatives following method B. After flash chromatography (eluent: hexane), compound *trans*-**1g** was obtained as a colorless oil (45% yield): ^{1}H NMR δ 6.36 (dd, 1H, J = 11.3 and 17.2 Hz), 5.68 (m, 1H), 5.20 (d, 1H, J = 17.2 Hz), 5.01 (d, 1H, J = 11.3 Hz), 4.32 (dd, 1H, J = 4.3 and 8.0 Hz), 2.4−1.2 (m, 5H), 1.00 (d, 3H, J = 6.5 Hz), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR δ 139.64, 137.74, 129.99, 112.31, 65.56, 40.30, 32.43, 25.97 (3C), 23.48, 21.59, 18.30, −3.67, −3.82; HRMS (EI) calcd for $C_{15}H_{28}OSi$ 252.19094, found 252.19080.

2-Bromo-2-cyclohexenol (3). To a solution of 1.75 g (10 mmol) of ketone **2**[20] and 3.80 g (12 mmol) of $CeCl_3 \cdot 7H_2O$ in 30 mL of MeOH 0.39 g (10 mmol) of solid $NaBH_4$ were added in small portions over 15 min. After the mixture was stirred at room temperature for 15 min and the workup was completed, crude alcohol **3**[22] was obtained in quantitative yield and used without further purification: ^{1}H NMR δ 6.22 (t, 1H, J = 4.0 Hz), 4.21 (m, 1H), 2.3−1.6 (m, 6H).

2-Vinyl-2-cyclohexenol (1h). To a mixture of 0.72 g (4.1 mmol) of compound **3** in 6 mL of THF, containing catalytic amounts of $Pd(PPh_3)_4$, 10.2 mL (2.5 equiv) of a solution of 1.0 M vinylmagnesium bromide in THF was added. After being refluxed for 4 h, the mixture was hydrolyzed with an aqueous saturated solution of NH_4Cl and extracted with ethyl ether. After workup and flash chromatography (eluent: CH_2Cl_2), compound **1h** was obtained as a colorless oil (57%): ^{1}H NMR δ 6.29 (dd, 1H, J = 10.7 and 18.0 Hz), 5.89 (m, 1H), 5.38 (d, 1H, J = 18.0 Hz), 5.05 (d, 1H, J = 10.7 Hz), 4.50 (m, 1H), 2.3−0.8 (m, 7H); ^{13}C NMR δ 137.81, 137.40, 132.43, 111.41, 62.73, 30.86, 25.78, 16.81.

6-[(*tert*-Butyldimethylsilyl)oxy]-1-vinylcyclohexene (1i).[23] **1i** was obtained from **1h** following method B (eluent: hexane/EtOAc 90:10) as a colorless oil (89% yield): ^{1}H NMR δ 6.26 (dd, 1H, J = 10.7 and 17.7 Hz), 5.83 (m, 1H), 5.25 (d, 1H, J = 17.7 Hz), 4.97 (d, 1H, J = 10.7 Hz), 4.45 (m, 1H), 2.2−1.2 (m, 6H), 0.90 (s, 9H), 0.12 (s, 6H); ^{13}C NMR δ 138.08 (2C), 130.57, 111.16, 64.26, 32.04, 25.96 (3C), 25.91, 18.18, 16.96, −4.07 (2C).

6-[(Methoxymethyl)oxy]-1-vinylcyclohexene (1j). 1j was obtained from **1h** following method A, after flash chromatography (eluent: hexane/EtOAc 50:50), as a colorless oil (80% yield): ^{1}H NMR δ 6.30 (dd, 1H, J = 10.7 and 17.7 Hz), 5.95 (m, 1H), 5.34 (d, 1H, J = 17.7 Hz), 5.01 (d, 1H, J = 10.7 Hz), 4.82 and 4.67 (AB system, 2H, J = 7.0 Hz), 4.38 (m, 1H), 3.41 (s, 3H), 2.3−1.4 (m, 6H); ^{13}C NMR δ 137.55, 135.35, 132.36, 110.58, 95.07, 68.19, 55.25, 27.30, 25.32, 16.28.

8-[(*tert*-Butyldimethylsilyl)oxy]-1,4-dioxaspiro[4,5]-decane (5). 5 was obtained by reduction of commercially available 1,4-cyclohexanedione monoethylene ketal (**4**) under the same conditions employed for the preparation of alcohol **3** and further protection following method B, after flash chromatography, (eluent: hexane/EtOAc 90:10) as a colorless oil (90% yield): ^{1}H NMR δ 3.95 (s, 4H), 3.82 (m, 1H), 2.0−1.4 (m, 8H), 0.90 (s, 9H), 0.03 (s, 6H); ^{13}C NMR δ 108.65, 67.46, 64.13, 32.02, 30.76, 25.75 (3C), 18.02, −3.39 (2C).

4-[(*tert*-Butyldimethylsilyl)oxy]-cyclohexanone (6). A mixture of 1.9 g (7 mmol) of compound **5**, 0.2 g (1.3 mmol) of NaI, and 4.5 g (12 mmol) of $CeCl_3 \cdot 7H_2O$ in 50 mL of CH_3CN was refluxed for 1 h. After solvent evaporation and flash chromatography (eluent: hexane/EtOAc 90:10), pure ketone **6**[24] was obtained as a colorless oil (81%): ^{1}H NMR δ 4.15 (m, 1H), 2.8−1.8 (m, 8H), 0.92 (s, 9H), 0.09 (s, 6H).

4-[(*tert*-Butyldimethylsilyl)oxy]-1-vinylcyclohexene (1k). To a stirred suspension of 0.73 g (3.2 mmol) of compound **6** and 1.7 g (4.8 mmol) of *N*-phenyltrifluoromethanesulfonimide in 5 mL of THF and 5 mL of toluene at −78 °C under argon 0.96 g (4.8 mmol) of solid KHMDS was added. After 4 h at −78 °C, the mixture was quenched with H_2O, extracted with ethyl ether, dried over $MgSO_4$, and purified by flash chromatography (eluent: hexane/EtOAc 90:10) to afford the corresponding enol triflate as a colorless oil (95% yield). To a stirred solution of 0.86 g (2.4 mmol) of the above obtained enol triflate in 5 mL of THF, containing 0.42 g (10 mmol) of LiCl and 0.05 g of $Pd(PPh_3)_4$, 0.70 mL (2.4 mmol) of vinyltributylstannane was added under argon. The mixture was refluxed for 7 h, cooled to room temperature, diluted with hexane, and washed with 10% aqueous NH_4OH solution, H_2O, and brine. After drying of the organic layer with Na_2SO_4, evaporation of the solvent, and purification of the residue by flash chromatography (eluent: hexane), compound **1k** was obtained as a colorless oil (77% yield): ^{1}H NMR δ 6.38 (dd, 1H, J = 10.7 and 17.8 Hz), 5.64 (m, 1H), 5.07 (d, 1H, J = 17.8 Hz), 4.93 (d, 1H, J = 10.7 Hz), 3.90 (m, 1H), 2.5−1.5 (m, 6H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR δ 139.27, 135.55, 127.10, 110.48, 67.98, 35.60, 31.45, 25.89 (3C), 22.72, 18.20, −3.58 (2C).

4-Vinyl-3-cyclohexenol (1l). To a solution of 0.52 g (2.2 mmol) of **1k** in 20 mL of CH_3CN 0.2 mL of a 40% aqueous HF solution was added at room temperature. The mixture was stirred for 20 min and diluted with CH_2Cl_2. After workup and flash chromatography (eluent: CH_2Cl_2), alcohol **1l** was obtained as a colorless oil (91%): ^{1}H NMR δ 6.35 (dd, 1H, J = 10.9 and 17.0 Hz), 5.64 (m, 1H), 5.08 (d, 1H, J = 17.0 Hz), 4.94 (d, 1H, J = 10.9 Hz), 3.98 (m, 1H), 2.5−1.6 (m, 7H); ^{13}C NMR δ 139.50, 136.01, 126.59, 111.28, 67.32, 35.19, 30.95, 22.31.

4-[(Methoxymethyl)oxy]-1-vinylcyclohexene (1m). 1m was obtained from **1l** following method A, after flash chromatography (eluent: CH_2Cl_2), as a colorless oil (95% yield): ^{1}H NMR δ 6.34 (dd, 1H, J = 10.8 and 17.6 Hz), 5.64 (m, 1H), 5.06 (d, 1H, J = 17.6 Hz), 4.93 (d, 1H, J = 10.8 Hz), 4.72 and 4.71 (AB system, 2H, J = 7.0 Hz), 3.85 (m, 1H), 3.38 (s, 3H), 2.7−1.6 (m, 6H); ^{13}C NMR δ 139.11, 135.72, 126.36, 110.68, 94.77, 71.98, 55.23, 32.44, 27.87, 22.11.

General Procedure for Diels−Alder Reactions, Method C. To a solution of (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (+)-**7**[29] (0.15 g, 0.5 mmol) in 5 mL of dry CH_2Cl_2 under argon the corresponding racemic diene **1a**−**m** (1.0 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 *anti*-(+)-**8a**−**m** and/or *syn*-(+)-**12h**,**k**−**m** were obtained and purified by crystallization or flash chromatography. Physical and spectroscopic data for (+)-**8b** and (+)-**8e** were previously reported.[13]

(1*R*,12b*S*)-1-Hydroxy-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8a). 8a was obtained from **1a** following method C, after flash chromatography, (eluent: CH_2Cl_2/EtOAc 95:5) in 28% yield: mp 170−171 °C (MeOH); $[\alpha]^{20}_D$ = +3.4 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$ + D_2O) δ 8.10 (m, 2H), 7.73 (m, 2H), 5.60 (m, 1H), 3.50 (ddd, 1H, J = 4.1, 5.7, and 9.9 Hz), 3.32 (dt, 1H, J = 3.9 and 9.9 Hz), 3.40 and 3.15 (2m, 2H), 2.4−1.2 (m, 6H); ^{13}C NMR δ 187.09, 184.15, 142.94, 142.34, 136.63, 133.60, 133.39, 131.93, 131.66, 126.56, 125.93, 115.32, 76.89, 44.98, 37.54, 34.39, 25.78, 25.16; HRMS (EI) calcd for $C_{18}H_{16}O_3$ 280.10994, found 280.10925.

4-(9′,10′-Dihydroanthracen-2′-yl)-butanal (9).[11k] **9** was obtained from **1a** following method C, after flash chromatography (eluent: CH_2Cl_2/EtOAc 95:5), in 51% yield: ^{1}H NMR δ 9.79 (t, 1H, J = 1.5 Hz), 8.29 (m, 2H), 8.23 (d, 1H, J = 7.9 Hz), 8.11 (d, 1H, J = 1.8 Hz), 7.78 (m, 2H), 7.62 (dd, 1H, J = 1.8 and 7.9 Hz), 2.83 (m, 2H), 2.53 (dt, 2H, J = 1.5 and 7.5 Hz), 2.04 (m, 2H).

(1*R*,12b*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,6,-12b-hexahydrobenz[*a*]anthracen-7,12-dione (8b).[13] **8b** was obtained from **1b** following method C, after flash chromatography (eluent: hexane/EtOAc 90:10), in 75% yield.

(1*R*,12b*S*)-1-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8c). It was obtained from **1c** following method C, after flash chromatography (eluent: hexane/EtOAc 70:30), in 61% yield: mp 148−150 °C (MeOH); $[\alpha]^{20}_D$ = +251 (*c* 0.6, $CHCl_3$); ^{1}H NMR δ 8.08 (m, 2H), 7.70 (m, 2H), 5.60 (m, 1H), 4.51 and 4.34 (AB system, 2H, J = 6.9 Hz), 3.78 (ddd, 1H, J = 4.0, 5.5 and 9.8 Hz), 3.40 and 3.12 (ddt, 1H, J = 1.8, 24.5, and 4.0 Hz m, 1H), 3.31 (dt, 1H, J = 4.0 and 9.8 Hz), 3.00 (s, 3H), 2.3−1.3 (m, 6H); ^{13}C NMR δ 184.13, 183.98, 143.89, 141.36, 137.15, 133.24, 132.88, 132.65, 131.58, 126.00, 125.77, 115.39, 94.59, 81.73, 54.95, 42.90, 34.24, 33.17, 25.99, 25.13. Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21. Found: C, 73.87; H, 6.60.

(1*R*,3*R*,12b*S*)-1-Hydroxy-3-methyl-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8d). 8d was obtained from **1d** following method C, after flash chromatography (eluent: CH_2Cl_2/EtOAc 95:5), in 26% yield: mp 175−176 °C (ethyl ether); $[\alpha]^{20}_D$ = +56 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$ + D_2O) δ 8.10 (m, 2H), 7.72 (m, 2H), 5.59 (m, 1H), 3.5−3.0 (m, 4H), 2.4−2.1 (m, 2H), 1.8−1.5 (m, 2H), 1.38 (dd, 1H, J = 10.3 and 12.2 Hz), 1.03 (d, 3H, J = 6.2 Hz); ^{13}C NMR δ 187.34, 184.28, 143.11, 142.48, 135.93, 133.73, 133.50, 131.98, 131.79, 126.70, 126.07, 115.62, 76.23, 46.42, 44.56, 42.95, 32.93, 25.34, 21.75; HRMS (EI) calcd for $C_{19}H_{18}O_3$ 294.12559, found 294.12521.

4-(9′,10′-Dihydroanthracen-2′-yl)-3-methylbutanal (11).[11k] **11** was obtained from **1a** following method C, after flash chromatography (eluent: CH_2Cl_2/EtOAc 95:5), in 51% yield: ^{1}H NMR δ 9.75 (t, 1H, J = 2.0 Hz), 8.29 (m, 2H), 8.23 (d, 1H, J = 7.9 Hz), 8.08 (d, 1H, J = 1.8 Hz), 7.79 (m, 2H), 7.59 (dd, 1H, J = 1.8 and 7.9 Hz), 2.83 and 2.67 (2dd, 2H, J = 6.2 and 13.2 Hz, J = 7.1 and 13.2 Hz), 2.6−2.2 (m, 3H), 0.99 (d, 3H, J = 6.5 Hz).

(1*R*,3*R*,12b*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8e).[13] **8e** was obtained from **1e** following method C, after flash chromatography (eluent: hexane/EtOAc 95:5), in 73% yield.

(1*R*,3*R*,12b*S*)-1-[(Methoxymethyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8f). 8f was obtained from **1f** following method C, after flash chromatography (eluent: hexane/EtOAc 80:20), in 59% yield: mp 114−116 °C (MeOH); $[\alpha]^{20}_D$ = +130 (*c* 0.6, $CHCl_3$); ^{1}H NMR δ 8.08 (m, 2H), 7.69 (m, 2H), 5.59 (t, 1H, J = 3.7 Hz), 4.51 and 4.33 (AB system, 2H, J = 7.1 Hz), 3.73 (ddd, 1H, J = 4.1, 5.4, and 9.9 Hz), 3.40 and 3.11 (ddt, 1H, J = 1.7, 25.0 and 3.9 Hz, m, 1H), 3.32 (dt, 1H, J = 3.6 and 9.9 Hz), 3.03 (s, 3H), 2.4−1.4 (m, 5H), 1.02 (d, 3H, J = 6.0 Hz); ^{13}C NMR δ 184.56, 184.38, 144.32, 141.66, 136.53, 133.54, 133.18, 132.89, 131.83, 126.30, 126.08, 115.82, 94.82, 81.17, 55.28, 42.88, 42.62, 41.92, 33.36, 25.49, 21.90. Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.18; H, 6.87.

(1*R*,3*S*,12b*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8g). 8g was obtained from **1g** following method C, after flash chromatography (eluent: hexane/EtOAc 90:10), in 62% yield: mp 125−126 °C (MeOH); $[\alpha]^{20}_D$ = +78 (*c* 0.2, $CHCl_3$); ^{1}H NMR δ 8.06 (m, 2H), 7.70 (m, 2H), 5.55 (m, 1H), 3.71 (dt, 1H, J = 9.6 and 4.3 Hz), 3.56 (dt, 1H, J = 3.7 and 9.6 Hz), 3.42 and 3.17 (ddt, 1H, J = 2.0, 24.3, and 4.0 Hz, ddt, 1H, J = 2.3, 24.3, and 4.6 Hz), 2.4−1.7 (m, 5H), 0.96 (d, 3H, J = 7.3 Hz), 0.72 (s, 9H), −0.14 and −0.37 (2s, 6H); ^{13}C NMR δ 184.51, 184.12, 144.94, 141.17, 134.26, 133.37, 133.00, 131.80, 126.56, 126.11, 125.97, 117.47, 73.76, 45.40, 43.11, 40.35, 28.56, 25.54, 25.29 (3C), 18.74, 17.85, −3.27, −3.35. Anal. Calcd for $C_{25}H_{32}O_3Si$: C, 73.49; H, 7.90. Found: C, 73.11; H, 8.23.

(4*S*,12b*S*)-4-Hydroxy-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8h) and (4*R*,12b*S*)-4-Hydroxy-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (12h). 8h and **12h** were obtained from **1h** following method C, after flash chromatography (eluent: hexane/EtOAc 65:35), in 62% yield as an unseparable 72:28 mixture. The following data correspond to the major compound **8h**: ^{1}H NMR δ 8.07 (m, 2H), 7.70 (m, 2H), 5.71 (dt, 1H, J = 1.1 and 3.3 Hz), 4.42 (t, 1H, J = 2.7 Hz), 3.90 (m, 1H), 3.25 (m, 2H), 2.4−1.0 (m, 7H); ^{13}C NMR δ 184.76, 184.14, 144.72, 141.05, 139.66, 133.52, 133.80, 132.41, 131.85, 126.31, 126.01, 116.00, 72.90, 35.13, 34.77, 32.94, 24.92, 21.16; HRMS (EI) (from the mixture) calcd for $C_{18}H_{16}O_3$ 280.10994, found 280.10989.

(4*S*,12b*S*)-4-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8j) and (4*R*,12b*S*)-4-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (12j). To a solution of 78 mg (0.28 mmol) of a mixture of **8h** and **12h** in 3 mL of dry $CHCl_3$ 2.0 g (26 mmol) of dimethoxymethane and 0.2 g (1.4 mmol) of P_2O_5 were added at room temperature, and the mixture was stirred for 1 h. The mixture was poured into 25 mL of a cold aqueous saturated solution of $NaHCO_3$, extracted with ethyl ether, and dried over $MgSO_4$. After evaporation of the solvent and flash chromatography (eluent: hexane/EtOAc 70:30), the mixture of **8j** and **12j** was obtained in 71% yield.

(4*S*,12b*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8i). 8i was obtained from **1i** following method C, after flash chromatography (eluent: hexane/EtOAc 90:10), in 57% yield: mp 99−101 °C (MeOH); $[\alpha]^{20}_D$ = +142 (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 8.03 (m, 2H), 7.60 (m, 2H), 5.28 (t, 1H, J = 3.4 Hz), 4.24 (t, 1H, J = 2.9 Hz), 4.16 (dd, 1H, J = 3.7 and 10.9 Hz), 3.22 and 3.06 (ddd, 1H, J = 3.4, 5.5, and 24.5 Hz, ddd, 1H, J = 3.2, 6.9, and 24.5 Hz),

2.6−1.1 (m, 6H), 1.04 (s, 9H), 0.13 and 0.11 (2s, 6H); ^{13}C NMR δ 184.91, 184.29, 145.11, 141.25, 140.85, 133.45, 133.31, 132.51, 131.97, 126.29, 125.99, 113.83, 73.32, 36.37, 35.34, 33.06, 25.81, 24.88 (3C), 21.22, 18.12, −3.24, −3.63. Anal. Calcd for $C_{24}H_{30}O_3Si$: C, 73.06; H, 7.67. Found: C, 72.99; H, 7.91.

(4*S*,12b*S*)-4-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8j). 8j was obtained from **1j** following method C, after flash chromatography (eluent: hexane/EtOAc 70:30), in 61% yield: mp 148−150 °C (MeOH); $[\alpha]^{20}_D = +224$ (*c* 0.4, $CHCl_3$); ^{1}H NMR δ 8.07 (m, 2H), 7.70 (m, 2H), 5.73 (t, 1H, *J* = 3.5 Hz), 4.64 and 4.55 (AB system, 2H, *J* = 6.5 Hz), 4.24 (t, 1H, *J* = 2.9 Hz), 3.72 (ddd, 1H, *J* = 3.5, 7.5, and 17.6), 3.38 (s, 3H), 3.34 and 3.18 (ddd, 1H, *J* = 3.2, 6.0, and 24.5 Hz, ddd, 1H, *J* = 3.5, 7.2, and 24.5 Hz), 2.4−1.1 (m, 6H); ^{13}C NMR δ 184.77, 184.24, 144.74, 141.15, 137.13, 133.53, 133.40, 132.47, 131.92, 126.31, 126.06, 117.97, 93.29, 75.75, 55.27, 35.05, 33.41, 33.30, 25.01, 21.69; HRMS (EI) calcd for $C_{20}H_{20}O_4$ 324.13616, found 324.13562.

(2*R*,12b*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8k). 8k was obtained from **1k** following method C, after flash chromatography (eluent: hexane/EtOAc 90:10), in 63% yield: mp 113−115 °C (MeOH); $[\alpha]^{20}_D = +104$ (*c* 0.25, $CHCl_3$); ^{1}H NMR δ 8.07 (m, 2H), 7.68 (m, 2H), 5.50 (m, 1H), 4.18 (m, 1H), 3.96 (m, 1H), 3.22 (m, 2H), 2.7−1.2 (m, 6H), 1.00 (s, 9H), 0.22 and 0.11 (2s, 6H); ^{13}C NMR δ 184.85, 183.97, 145.19, 141.90, 138.72, 133.31, 133.14, 132.56, 131.92, 126.28, 125.92, 112.87, 67.21, 42.00, 36.11, 31.85, 29.87, 25.88 (3C), 25.20, 18.18, −3.32, −3.44. Anal. Calcd for $C_{24}H_{30}O_3Si$: C, 73.06; H, 7.67. Found: C, 72.70; H, 8.06.

(2*R*,12b*S*)-2-Hydroxy-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8l) and (2*S*,12b*S*)-2-Hydroxy-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (12l). 8l and **12l** were obtained from **1l** following method C as a 60:40 mixture in 65% yield. After flash chromatography (eluent: hexane/EtOAc 70:30), a not completely pure little portion of both alcohols was separated. **8l**: ^{1}H NMR δ 8.05 (m, 2H), 7.70 (m, 2H), 5.52 (m, 1H), 4.27 (m, 1H), 3.93 (m, 1H), 3.24 (m, 2H), 2.7−2.3 (m, 2H), 2.2−1.9 (m, 3H), 1.7−1.4 (m, 2H). **12l**: ^{1}H NMR δ 8.08 (m, 2H), 7.71 (m, 2H), 5.56 (m, 1H), 4.03 (tt, 1H, *J* = 4.2 and 11.2 Hz), 3.45 (m, 1H), 3.26 (m, 2H), 2.7−1.1 (m, 7H). The mixture of **8l** and **12l** was transformed into the corresponding OMOM derivatives **8m** and **12m**, in 55% yield after flash chromatography (eluent: hexane/EtOAc 85:15), by using the above-mentioned procedure to obtain the mixture of **8j** and **12j**.

(2*R*,12b*S*)-2-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (8m). 8m was obtained from **1m** following method C, after separation of the resulting 75:25 mixture of **8m** and **12m** by flash chromatography (eluent: hexane/EtOAc 85:15), in 38% yield: mp 119−121 °C (MeOH); $[\alpha]^{20}_D = +313$ (*c* 0.2, $CHCl_3$); ^{1}H NMR δ 8.07 (m, 2H), 7.70 (m, 2H), 5.52 (m, 1H), 4.95 and 4.81 (AB system, 2H, *J* = 7.0 Hz), 4.06 (m, 1H), 3.84 (m, 1H), 3.50 (s, 3H), 3.24 (m, 2H), 2.6−1.2 (m, 6H); ^{13}C NMR δ 184.79, 184.20, 144.60, 142.12, 138.08, 133.48, 133.33, 132.50, 131.97, 126.22, 126.06, 113.22, 94.35, 70.84, 55.47, 38.32, 33.33, 32.10, 30.26, 25.22. Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21. Found: C, 73.75; H, 6.54.

(2*S*,12b*S*)-2-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenz[*a*]anthracen-7,12-dione (12m). 12m was obtained from **1m** following method C, after separation of the resulting 75:25 mixture of **8m** and **12m** by flash chromatography (eluent: hexane/EtOAc 85:15), in 11% yield as an oil: $[\alpha]^{20}_D = +181$ (*c* 2.1, $CHCl_3$); ^{1}H NMR δ 8.07 (m, 2H), 7.70 (m, 2H), 5.54 (t, 1H, *J* = 3.2 Hz), 4.73 and 4.68 (AB system, 2H, *J* = 6.7 Hz), 3.90 (tt, 1H, *J* = 4.5 and 11.4 Hz), 3.40 (m, 1H), 3.38 (s, 3H), 3.24 (m, 2H), 2.7−1.1 (m, 6H); ^{13}C NMR δ 184.65, 184.19, 143.64, 141.89, 136.61, 133.52, 133.41, 132.50, 132.05, 126.30, 126.08, 114.40, 94.69, 75.21, 55.27, 40.27, 35.45, 34.75, 32.66, 25.46.

General Procedure for Epoxidations, Method D. To a solution of 0.15 mmol of the corresponding derivative in 3 mL of dry CH_2Cl_2 cooled at 0 °C *m*-CPBA (100 mg, 0.3 mmol, 2 equiv) in 2 mL of CH_2Cl_2 was added. After 4 h at 0 °C, the mixture was treated with a saturated solution of $NaHCO_3$. After workup and purification by crystallization or flash cromatography, epoxides were obtained as yellow solids. Physical and spectroscopic data for (+)-**10e** were previously reported.[13]

(1*R*,4a*S*,5*R*,12b*S*)-4a,5-Epoxy-1-hydroxy-1,2,3,4,4a,5,6,-12b-octahydrobenz[*a*]anthracen-7,12-dione (10a). 10a was obtained from (+)-**8a** following method D, after flash chromatography (eluent: CH_2Cl_2/EtOAc 90:10), in 90% yield: mp 169−170 °C (ethyl ether); $[\alpha]^{20}_D = +20$ (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$ + D_2O) δ 8.05 (m, 2H), 7.68 (m, 2H), 3.56 and 2.80 (dt, 1H, *J* = 20.4 and 1.5 Hz; dt, 1H, *J* = 20.4 and 1.7 Hz), 3.51 (dq, 1H, *J* = 10.2 and 1.4 Hz), 3.39 (dt, 1H, *J* = 3.7 and 10.2 Hz), 3.26 (q, 1H, *J* = 1.6 Hz), 2.3−1.3 (m, 6H); ^{13}C NMR δ 185.94, 184.06, 142.44, 139.46, 133.64, 133.46, 129.85, 129.54, 126.53, 126.07, 74.63, 61.16, 56.37, 44.45, 35.63, 32.78, 24.50, 21.14; HRMS (EI) calcd for $C_{18}H_{16}O_4$ 296.104 86, found 296.105 26.

(1*R*,3*S*,4a*S*,5*R*,12b*S*)-4a,5-Epoxy-1-hydroxy-3-methyl-1,2,3,4,4a,5,6,12b-octahydrobenz[*a*]anthracen-7,12-dione (10d). 10d was obtained from (+)-**8d** following method D, after flash chromatography (eluent: CH_2Cl_2/EtOAc 90:10), in 82% yield: mp 225−226 °C (MeOH); $[\alpha]^{20}_D = +18$ (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$ + D_2O) δ 8.06 (m, 2H), 7.70 (m, 2H), 3.56 and 2.79 (dd, 1H, *J* = 20.4 and 2.1 Hz, dt, 1H, *J* = 20.4 and 1.5 Hz), 3.45 (m, 2H), 3.26 (m, 1H), 2.18 (m, 1H), 1.74 (m, 2H), 1.5−1.2 (m, 1H), 1.41 (dd, 1H, *J* = 1.8 and 8.9 Hz), 1.05 (d, 3H, *J* = 6.1 Hz); ^{13}C NMR δ 186.24, 184.16, 142.55, 139.58, 133.80, 133.59, 131.86, 131.80, 126.69, 126.23, 73.96, 60.71, 56.52, 44.58, 43.95, 41.38, 28.33, 24.60, 21.57; HRMS (EI) calcd for $C_{19}H_{18}O_4$ 310.12051, found 310.12061.

(1*R*,3*S*,4a*S*,5*R*,12b*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4a,5-epoxy-3-methyl-1,2,3,4,4a,5,6,12b-octahydrobenz[*a*]-anthracen-7,12-dione (10e).[13] **10e** was obtained from (+)-**8e** following method D, after flash chromatography (eluent: hexane/EtOAc 90:10) in 86% yield.

(2*S*,4a*S*,5*R*,12b*R*)-4a,5-Epoxy-2-[(methoxymethyl)oxy]-1,2,3,4,4a,5,6,12b-octahydrobenz[*a*]anthracen-7,12-dione (13). 13 was obtained from (+)-**12m** following method D, after flash chromatography (eluent: hexane/EtOAc 65:35), in 67% yield as an oil: $[\alpha]^{20}_D = +209$ (*c* 0.7, $CHCl_3$); ^{1}H NMR δ 8.05 (m, 2H), 7.69 (m, 2H), 4.71 and 4.67 (AB system, 2H, *J* = 7.0 Hz), 3.85 (tt, 1H, *J* = 3.6 and 11.3 Hz), 3.54 (m, 1H), 3.36 (s, 3H), 3.32 (q, 1H, *J* = 1.6 Hz), 3.52 and 2.80 (m, 1H, dt, 1H, *J* = 20.7 and 2.1 Hz), 2.5−1.1 (m, 6H); ^{13}C NMR δ 184.43, 183.46, 143.43, 138.66, 133.62, 133.60, 132.03, 131.86, 126.36, 126.23, 94.97, 73.99, 61.02, 57.03, 55.33, 37.51, 34.36, 31.97, 31.32, 24.59; HRMS (EI) calcd for $C_{20}H_{20}O_5$ 340.131 07, found 340.131 53.

(2*R*,4a*S*,5*R*,12b*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]-4a,5-epoxy-1,2,3,4,4a,5,6,12b-octahydrobenz[*a*]anthracen-7,12-dione (14). 14 was obtained from (+)-**8k** following method D, after flash chromatography (eluent: hexane/EtOAc 90:10), in 56% yield: mp 199−201 °C (MeOH); $[\alpha]^{20}_D = +184$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 8.06 (m, 2H), 7.68 (m, 2H), 4.17 (m, 1H), 3.97 (m, 1H), 3.51 and 2.78 (dd, 1H, *J* = 1.8 and 19.9 Hz, ddd, 1H, *J* = 2.1 and 19.9 Hz), 3.28 (q, 1H, *J* = 1.6 Hz), 2.6−1.2 (m, 6H), 1.01 (s, 9H), 0.20 and 0.11 (2s, 6H); ^{13}C NMR δ 184.64, 183.25, 144.93, 138.52, 133.45, 133.33, 132.22, 131.88, 126.34, 126.05, 65.54, 61.47, 57.26, 39.19, 33.08, 31.08, 27.89, 25.83, 24.74 (3C), 18.13, −3.25, −3.44. Anal. Calcd for $C_{24}H_{30}O_4Si$: C, 70.21; H, 7.37. Found: C, 70.09; H, 7.74.

(2*R*,4a*R*,5*S*,12b*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]-4a,5-epoxy-1,2,3,4,4a,5,6,12b-octahydrobenz[*a*]anthracen-7,12-dione (15). 15 was obtained from (+)-**8k** following method D, after flash chromatography (eluent: hexane/EtOAc 90:10), in 11% yield: mp 140−141 °C (MeOH); $[\alpha]^{20}_D = +22$ (*c* 0.8, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 8.06 (m, 2H), 7.68 (m, 2H), 4.13 (broad s, 1H), 3.69 (ddd, 1H, *J* = 2.6, 2.8, and 11.8 Hz), 3.35 and 2.31 (ddd, 1H, *J* = 1.5, 3.9, and 21.0 Hz, dt, 1H, *J* = 21.0 and 2.8 Hz), 2.92 (dd, 1H, *J* = 1.9 and 2.7 Hz), 2.91 (m, 1H), 2.39 (m, 1H), 2.1−0.9 (m, 4H), 1.20 (s, 9H), 0.41 and 0.21 (2s, 6H); ^{13}C NMR δ 184.57 (2C), 144.27, 140.23, 133.42, 133.14, 133.09, 131.75, 126.19, 125.86, 66.82, 61.97, 59.35, 35.56,

31.51, 31.31, 28.67, 25.88, 25.07 (3C), 18.18, −3.27, −3.38. Anal. Calcd for $C_{24}H_{30}O_4Si$: C, 70.21; H, 7.37. Found: C, 70.09; H, 7.68.

Synthesis of MTPA Esters. MTPA ester synthesis was performed according to the known procedure.[31] To a solution of the corresponding alcohol (0.04 mmol) and DMAP (10 mg, 0.08 mmol) in 3 mL of CH_2Cl_2 (*R*)- or (*S*)-MTPA-Cl (13 mL, 0.07 mmol) was added. The mixture was stirred overnight at room temperature, and then the reaction was quenched as follows. Water in the amount of 1 mL and 3 mL of Et_2O were added, and the reaction mixture was stirred for 15 min. The solution was washed successively with 4 mL of 1 N HCl, 4 mL of 1 N NaOH, and brine and dried over $MgSO_4$. After evaporation of the solvents, the resulting mixture of diastereomeric esters was used directly for NMR analysis.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra of compounds **1c**,**f**,**h**,**j**−**m**, **5**, and **12m** and ^1H NMR spectra of compounds **8l**, **12l**, and the mixture of **8j** and **12j** (21 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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