Enantioselective Diels–Alder Approach to C-3-Oxygenated Angucyclinones from (S*S*)-2-(*p*-Tolylsulfinyl)-1,4-naphthoquinone

M. Carmen Carreño,*[a] Antonio Urbano,[a] and Claudio Di Vitta[b]

Abstract: Chiral racemic vinylcyclohexenes **2**, bearing oxygenated substituents and/or a methyl group at the C-5 position of the cyclohexene ring, were submitted to Diels–Alder reactions with enantiomerically pure (S*S*)-(2-*p*-tolylsulfinyl)-1,4-naphthoquinone [(+)-**1**]. The domino cycloaddition/pyrolytic sulfoxide elimination process led to the formation of enantiomerically enriched angularly tetracyclic quinones *anti*-**6** and *syn*-**7**, which were obtained from the kinetic resolution of the racemic diene. In all cases, (S*S*)-(2-*p*-tolylsulfinyl)-1,4-naphthoquinone reacted from the less hindered face of the more reactive *s-cis* conformation, to form products in good enantiomeric excesses. Steric effects and torsional interactions in the corresponding approaches account for the observed π-facial diastereoselectivities at both partners. The usefulness of this methodology is illustrated with the four-step totally asymmetric synthesis of the C-3-oxygenated angucyclinone derivative (−)-8-deoxytetrangomycin **10** in 26% overall yield and with 50% enantiomeric purity.

Keywords: angucyclinones · asymmetric synthesis · cycloadditions · kinetic resolution · sulfinylquinones

Introduction

Angucyclines are a large group of naturally occurring quinones[1] that display a broad range of biological properties such as antiviral,[2] antifungal,[3] and antitumor[4] effects as well as enzyme-inhibitory activity.[5] The major representatives of this family have a benz[*a*]anthracene framework of decaketide origin, bearing a methyl group at C-3 and an oxygenated function at C-1. Such challenging structures and their diverse biological activities have stimulated many synthetic investigations.

Some members of the family, such as urdamycinone B, rabelomycin and tetrangomycin (Figure 1), possess a tertiary hydroxy group at C-3, whose lability has hindered the development of general synthetic approaches towards the nonaromatic A ring. The regioselective construction of the angularly fused tetracyclic skeleton of angucyclinones has been achieved by several methods, which are summarized in a recent review article.[6] The most general strategy employed is based on the Diels–Alder reaction between a substituted naphthoquinone and a vinylcyclohexene. While several efficient total syntheses have focused on racemic forms, only a few asymmetric approaches have been described so far.[7]

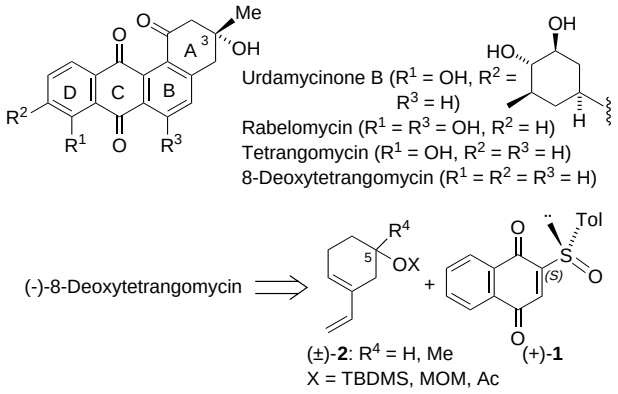

Figure 1. Structures of angucyclinones.

Of the derivatives bearing the C-3-oxygenated substituent, only urdamicynone B has been synthesized in enantiomerically pure form. The first total synthesis, reported by Yamaguchi et al.,[7a] was based on the separation of the diastereoisomers resulting from the polyketide condensation of a C-glycosyl naphthalene diester. Later, Sulikowsky and Kim[7c] used an asymmetric Diels–Alder reaction with an appropriately functionalized chiral diene obtained from (−)-quinic acid as the key step of the synthetic sequence. Finally, Toshima's urdamycinone B synthesis[7e] was achieved by chromatographic separation of the diastereoisomeric mixture formed in the [4+2] cycloaddition between a *C*-glycosyl

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juglone and a racemic vinylcyclohexene. The total syntheses of racemic rabelomycin and tetrangomycin were described by Krohn and Khanbabaee,[8] but, to our knowledge, no asymmetric syntheses of these compounds have been reported so far.

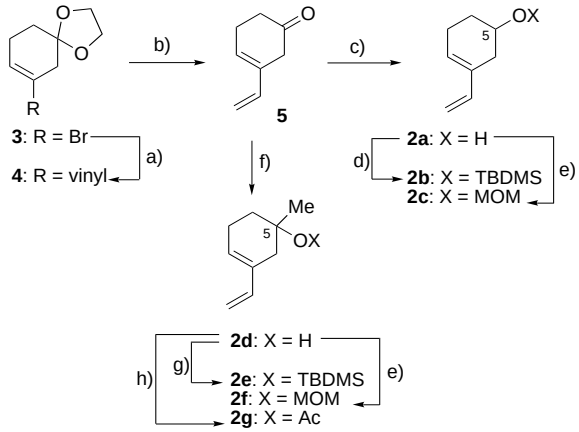
We recently achieved the asymmetric total synthesis of (+)-rubiginone B_2 and (+)-ochromycinone,[9] two angucyclinones without the oxygen functionality at C-3; our synthesis was based on the use of enantiomerically pure sulfinylnaphthoquinones as chiral dienophiles.[10] The strategy used in our laboratory is based on the ability of the sulfoxide to control the regiochemistry and π-facial diastereoselectivity of *endo* cycloadditions with (S*S*)-(*p*-tolylsulfinyl)quinones, and takes advantage of the domino[11] Diels–Alder reaction/pyrolytic sulfoxide elimination, which occurs when acyclic or semicyclic dienes are used. Moreover, when a chiral racemic vinylcyclohexene is the partner, efficient kinetic resolution occurs, resulting in the one-pot enantioselective formation of the angucyclinone skeleton.[12] The process was shown to be applicable to a wide range of 1-vinylcyclohexenes bearing secondary carbinols at C-3, C-4 or C-6 and to both *cis*- and *trans*-3-oxygenated-5-methyl-substituted 1-vinylcyclohexenes.[13] The latter allowed easy access to agucyclinones with a methyl substituent at C-3.[9, 12]

To further extend the applicability of this procedure to the enantioselective synthesis of C-3-oxygenated angucyclinones, we thought of studying the behavior of vinylcyclohexene derivatives supporting a secondary or tertiary carbinol at C-5; such derivatives could be the C-3-substituted precursors of the tetracyclic system. We here report a novel enantioselective approach to the C-3-oxygenated angucyclinone framework by the retrosynthetic scheme shown in Figure 1. The synthesis is based on an asymmetric Diels–Alder reaction between differently substituted vinylcyclohexenes **2**, bearing oxygenated substituents and/or a methyl group at the stereogenic center C-5, and (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (**1**), which is able to discriminate between both faces of the chiral racemic diene, thereby promoting a double-induction cycloaddition. The method was illustrated by the total asymmetric synthesis of (−)-8-deoxytetrangomycin (Figure 1). Besides the intrinsic synthetic interest of these results, fundamental information concerning the role of the C-5 stereogenic center in the vinylcyclohexene on π-facial diastereoselection is also obtained.

Abstract in Spanish: *Se han estudiado las reacciones de Diels–Alder de la (SS)-(2-p-tolilsulfinil)-1,4-naftoquinona (+)-**1** enantioméricamente pura con diferentes vinilciclohexenos quirales racémicos **2** que poseen sustituyentes oxigenados y/o un grupo metilo en posición C-5 del anillo de ciclohexeno. El proceso tiene lugar a través de una secuencia de cicloadición/eliminación pirolítica del sulfóxido originando, en una única etapa sintética, las quinonas tetracíclicas de estructura angular anti-**6** y sin-**7** enantioméricamente enriquecidas. En la cicloadición se produce además la resolución cinética de los dienos racémicos. En todos los casos el dienófilo reacciona a través de una conformación de tipo s-cis por la cara menos impedida estéricamente dando lugar a los productos finales con buenos excesos enantioméricos. La selectividad π-facial obtenida se explica teniendo en cuenta los efectos estéricos y las interacciones torsionales que se aprecian en los distintos estados de transición. La utilidad de esta metodología se ilustra con la síntesis asimétrica en cuatro etapas de un derivado C-3 oxigenado de anguciclinona, la (−)-8-desoxitetrangomicina (**10**), con un rendimiento global del 26% y una pureza enantiomérica del 50%.*

Results and Discussion

The required vinylcyclohexenes **2a–c** were prepared as outlined in Scheme 1. The starting material was 1-bromo-5-dioxolane-1-cyclohexene (**3**),[14] which was coupled with

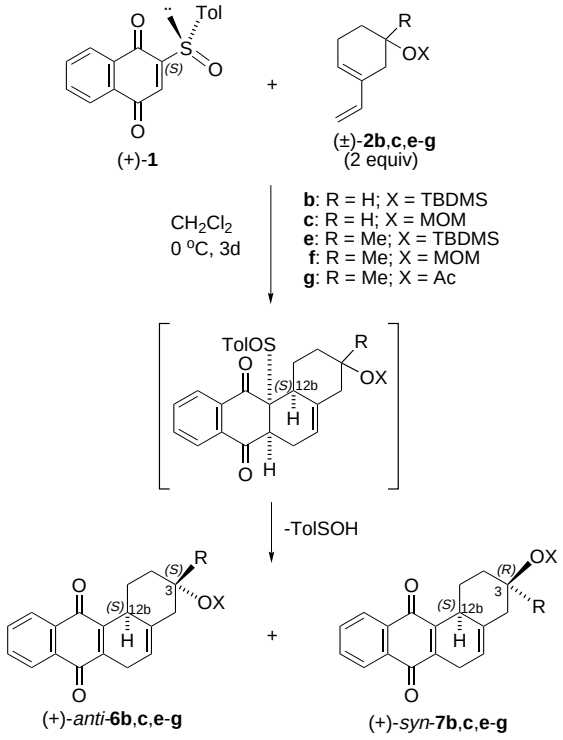


Scheme 1. Synthesis of vinylcyclohexenes **2a–g**. a) CH_2=CHMgBr, $[Pd(PPh_3)_4]$, THF, 80 °C, 4 h, 77%; b) $LiBF_4$, aqueous CH_3CN, room temperature, 1 h, 63%; c) $NaBH_4$, MeOH, room temperature, 10 min, 70%; d) TBDMSCl, imidazole, DMF, room temperature, 6 h, 63%; e) MOMCl, DIPEA, CH_2Cl_2, room temperature, overnight, 100% for **2c**, 60% for **2f**; f) MeMgBr, THF, room temperature, 4 h, 53%; g) i. NaH, THF, room temperature, 1 h; ii. TBDMSOTf, room temperature, 2 h, 94%; h) AcCl, DIPEA, CH_2Cl_2, 0 °C, 4 h, 78%.

vinylmagnesium bromide in the presence of catalytic Pd^0,[15] to afford vinylcyclohexene **4** in 77% yield. After hydrolysis of the ketal function of **4** with $LiBF_4$ in aqueous CH_3CN,[16] ketone **5** was obtained in 63% yield. After further reduction of the carbonyl group ($NaBH_4$/EtOH), secondary alcohol **2a**[17] was obtained in 70% yield. The resulting carbinol was protected either with *tert*-butyldimethylsilyl chloride (TBDMSCl)/imidazole or methoxymethyl chloride (MOMCl)/diisopropylethylamine (DIPEA), to lead to derivatives **2b** (63% yield) and **2c** (95% yield), respectively.

Compounds **2d–g**, which contain both an oxygenated substituent and a methyl group at the C-5 position, were prepared from vinylcyclohexenone **5** (Scheme 1). Thus, addition of the Grignard reagent MeMgBr to ketone **5** afforded tertiary carbinol **2d** (53% yield), which was protected as OTBDMS derivative **2e** (NaH, TBDMSOTf)[18] in 94% yield, OMOM derivative **2f** (MOMCl/DIPEA) in 60% yield, and acetate **2g** (AcCl, DIPEA)[19] in 78% yield.

With the desired racemic vinylcyclohexenes in hand, we began the study of their Diels–Alder cycloadditions with enantiomerically pure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone, (+)-**1**,[20] as the chiral dienophile (Scheme 2). Fast decomposition of the dienes prevented the use of Lewis acids.



Scheme 2. Diels–Alder reactions of (+)-**1** and (±)-**2b**, **c**, **e**–**g**.

The best results were achieved working in CH_2Cl_2 at 0 °C. Under these conditions, Diels–Alder reactions between quinone (+)-**1** and two equivalents of racemic vinylcyclohexenes **2b** and **2c**, with a secondary protected carbinol at C-5, and **2e**–**g**, derived from the analogous tertiary methyl carbinol, gave rise to mixtures of derivatives *anti*-**6b**, **c**, **e**–**g** and *syn*-**7b**, **c**, **e**–**g** (Table 1), resulting from the spontaneous pyrolytic elimination of the sulfinyl group in the initially formed cycloadducts. The diastereoisomeric *anti/syn*[21] ratios were determined directly from the crude reaction mixtures by ^{1}H NMR analysis. In all these cycloadditions, we recovered unconverted dienes in optically active form.

Table 1. Yields and diastereoselectivities of the Diels–Alder reactions of (+)-**1** and (±)-**2b**, **c**, **e**–**g** in CH_2Cl_2 at 0 °C.

Entry	Diene	Product *anti* [%]	Product *syn* [%]	Yield [%]	Isolated yield [%]	
1	**2b**	**6b** (60)[a]	**7b** (40)[a]	61	**6b** (38)	**7b** (23)
2	**2c**	**6c** (60)	**7c** (40)	58	**6c** (37)	**7c** (21)
3	**2e**	**6e** (85)	**7e** (15)	67	[c]	
4	**2f**	**6f** (80)[b]	**7f** (20)[b]	58	[c]	
5	**2g**	**6g** (83)	**7g** (17)	41	[c]	

[a] A 93:7 enantiomeric ratio was measured by using [Yb(hfc)$_3$] as chiral lanthanide shift reagent. [b] A 92:8 enantiomeric ratio was calculated from optical purity of (+)-**9**. [c] The *anti* and *syn* diastereoisomers could not be separated.

The Diels–Alder reaction between racemic vinylcyclohexene **2b** and naphthoquinone (+)-**1** (Scheme 2, Table 1, entry 1), afforded a 60:40 mixture of diastereoisomers *anti*-**6b** and *syn*-**7b**, from which compound (+)-**6b** could be isolated in 38% yield and diastereoisomer (+)-**7b** could be isolated in 23% yield, after flash chromatography. The enantiomeric purity of both compounds was determined to be 86% by a ^{1}H NMR study in which [Yb(hfc)$_3$] (hfc = 3-(heptafluoropropylhydroxymethylene)-D-camphorate) was used as chiral lanthanide shift reagent; this procedure required the preparation of the corresponding racemic derivatives (±)-**6b** and (±)-**7b**, starting from racemic sulfinylnaphthoquinone (±)-**1**.[20] Cycloaddition between quinone (+)-**1** and OMOM derivative **2c** afforded a 60:40 mixture of (+)-*anti*-**6c** and (+)-*syn*-**7c**, in 37% and 21% yields, respectively, after flash chromatography (Scheme 2, Table 1, entry 2).[22]

Reaction between (+)-**1** and 5-[(*tert*-butyldimethylsilyl)-oxy]-5-methyl-1-vinylcyclohexene (**2e**) (Scheme 2, Table 1, entry 3) gave rise to a 67% yield of a 85:15 mixture of optically active diastereoisomers *anti*-**6e** and *syn*-**7e** which could not be separated.[22] The same reaction with the analogous OMOM-substituted diene **2f**, also containing a methyl group at C-5, yielded 58% of an 80:20 mixture of diastereoisomers *anti*-**6f** and *syn*-**7f** (Scheme 2, Table 1, entry 4). In this case, the major compound **6f** was isolated in pure form after crystallization from MeOH, but, unfortunately, only in the racemic form. The optical purity of derivatives **6f** and **7f** (84% *ee*) could only be calculated after their transformation into the intermediate (+)-**9**, much further into the total synthesis of (−)-8-deoxytetrangomycin (see Scheme 3). Finally, cycloaddition of (+)-**1** and 5-acetoxy-5-methyl-1-vinylcyclohexene (**2g**) (Scheme 2, Table 1, entry 5) yielded 41% of an 83:17 mixture of compounds *anti*-**6g** and *syn*-**7g**.[22] Again, derivative **6g** could be isolated pure after crystallization from MeOH, but in the racemic form.

The relative stereochemistry of tetracyclic derivatives *anti*-**6b**, **c**, **e**–**g** and *syn*-**7b**, **c**, **e**–**g** was established on the basis of their ^{1}H NMR data, in particular coupling constants for **6b**, **c** and **7b**, **c** and ^{1}H–^{1}H NOESY experiments for **6e**–**g** and **7e**–**g** (Figure 2). In all *anti* and *syn* derivatives **6** and **7**, proton H_{12b} appeared as a multiplet with a coupling constant in the range 9.2 to 9.9 Hz with H_{1ax}.[23] This suggested that H_{12b} is in a pseudoaxial position, and made it possible to establish the relative positions of all the other protons of the cyclohexane ring. Thus, in the ^{1}H NMR spectra of *anti* diastereoisomers **6b** and **6c**, hydrogen H_3 has two coupling constants, ranging from 11.0 to 11.3 Hz, which are consistent with a *trans* diaxial relationship between H_3 and H_{2ax}, and H_3 and H_{4ax}, respectively (Figure 2). In the case of *syn* diastereoisomers **7b** and **7c**, the coupling constants of the same proton H_3 are small, ranging from 2.3 to 2.7, indicating its pseudoequatorial disposition.

The relative configuration of derivatives *anti*-**6e** and *syn*-**7e** was determined from a ^{1}H–^{1}H NOESY experiment[24] on the mixture of diastereoisomers. We noticed that there was a NOE, depicted in Figure 2 for compound *anti*-**6e**, between pseudoaxial proton H_{1ax} and the methyl group at C-5, indicating the *cis* relationship for these two substituents. This NOE is not observed for the same substituents in the case of

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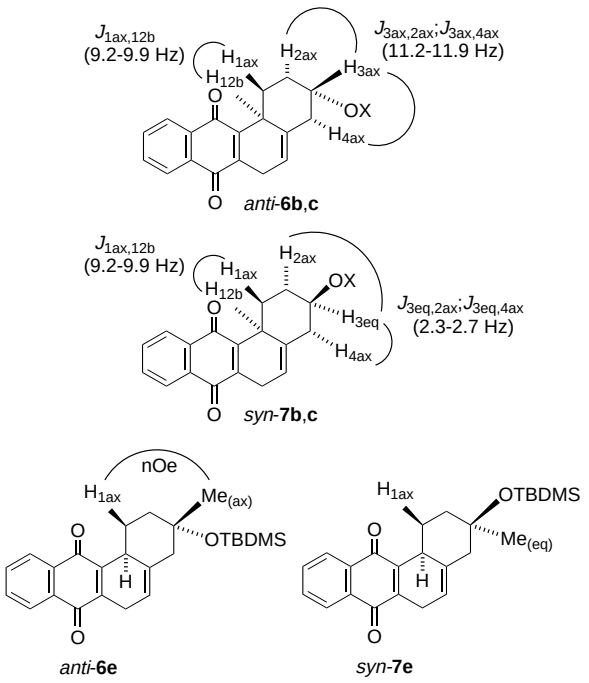


Figure 2. Significant ^{1}H NMR parameters used for configurational assignments.

syn derivative **7e**. The similarity between the ^{1}H NMR parameters of **6e** and **6f**, **g** as well as those of **7e** and **7f**, **g**, allowed us to assign the same relative configuration for all compounds *anti*-**6** and *syn*-**7**, respectively. Once the relative stereochemistry of all derivatives was established, the absolute configuration of compounds **6** (3*S*,12b*S*) and **7** (3*R*,12b*S*) was deduced, as indicated later.

To rationalize the results achieved in such a double asymmetric induction process,[25] one must differentiate between the diastereofacial selectivities of both chiral partners. The observed *anti/syn* selectivities reflect the π-facial diastereoselection of the diene, whereas the resulting absolute configuration of each *anti*-**6** and *syn*-**7** derivatives indicate the diastereofacial control and the efficiency of the kinetic resolution exerted by the homochiral sulfoxide on the quinonic moiety.

For such enantiopure sulfinylquinones, experimentation suggested that the face selectivity induced by the sulfoxide is mainly controlled by steric factors. Our earlier results[10] showed that the favored *endo* approach at a diene occurs from the face of the (S*S*)-2-(*p*-tolylsulfinyl)-1,4-naphthoquinone that contains the less sterically demanding lone electron pair at sulfur in the more reactive *s-cis* conformation (Figure 3). Thus, because the *(S)* absolute configuration was induced at C_{12b} in all derivatives **6** and **7**,[26] the major enantiomers obtained must arise from the attack of the diene onto the top face of (+)-**1**.

For the diene partner, the major formation of *anti* adducts must be a consequence of the preferred approach of the dienophile at the face of the diene *anti* to the oxygenated function. A detailed analysis of transition states, shown in Figure 3, suggested that, for dienes **2b**, **c** with a secondary protected carbinol at C-5, approach *anti*-**A** must be favored[27]

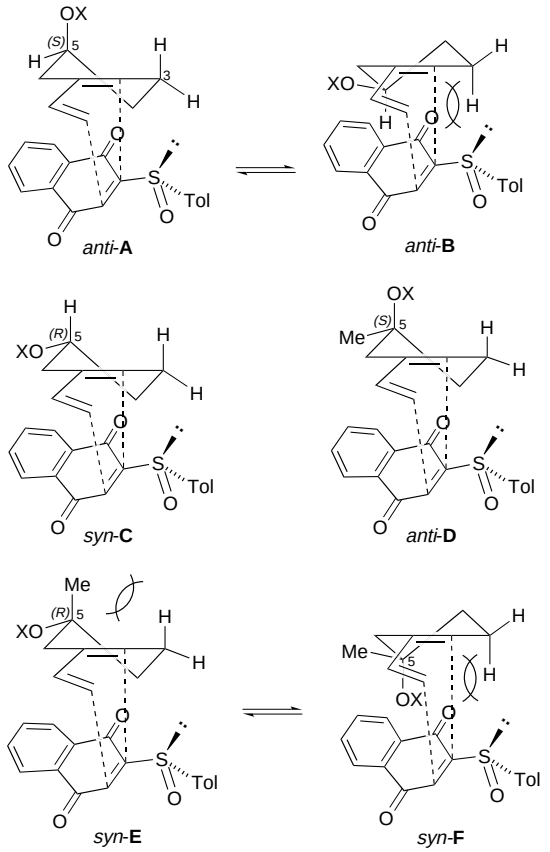


Figure 3. Favored approaches of semicyclic dienes **2** in Diels–Alder reactions with sulfinylnaphthoquinone (+)-**1**.

over *anti*-**B** which shows a strongly destabilizing torsional interaction between H_{3ax} and forming bonds.[28] Thus, the former transition state corresponds to the evolution of the matched pair, where the reacting diene is the 5*S* enantiomer.

The formation of minor diastereoisomers *syn*-**7b**, **c** must be a consequence of the cycloaddition of 5*R* enantiomers of dienes **2b**, **c**, which gives rise to the transition state represented as *syn*-**C** in Figure 3, where there is no torsional strain and the bulky OX substituent is pseudoequatorial. Approach *anti*-**A** is slightly favored over *syn*-**C**, due to the stronger interaction present in the latter between the pseudoequatorial OX at C-5 and the aromatic protons of quinone (+)-**1**.

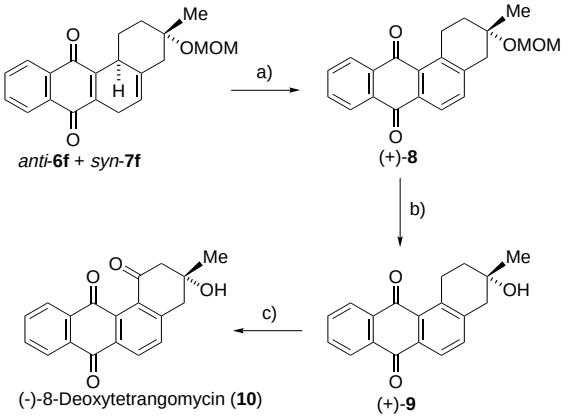
In the case of cycloadditions with C-5-methyl-substituted vinylcyclohexenes **2e–g**, the diasteroisomeric excess of the process increased up to 70% in favor of the *anti* diastereoisomer (Table 1, entries 3–5). This result seems to be contradictory to the increasing interactions present in the approach *anti*-**D** compared to the analogous *anti*-**A**. In the former, the pseudoequatorial methyl group at C-5 and one aromatic proton of the quinone (Figure 3) must interact more strongly than H_5 in *anti*-**A**. Nevertheless, the greater preference for the *anti* approach in methyl-substituted dienes can be understood if the attack shown as *syn*-**E** in Figure 3, where a (Me/H) 1,3-parallel interaction is present, is taken into account.[29] If we consider the other half-chair conformation of the cyclohexene moiety (*syn*-**F** in Figure 3), two additional destabilizing interactions are apparent: the torsional strain between H_{3ax} and one of the forming bonds, and the

pseudoaxial OX group at C-5 interacting with one aromatic proton of the quinone.

Thus, we could justify the kinetic resolution process by arguing that the *endo* approaches *anti*-**A** and *anti*-**D** correspond to the evolution of the matched pairs. The most favored situation is the *anti* cycloaddition of dienes of configuration 5*S* at the less hindered face of quinone (+)-(S*S*)-**1**, reacting in the *s-cis* conformation. On this basis, we could assign the absolute configuration (3*S*,12b*S*) to the major diastereoisomers **6**, resulting from the *anti* cycloaddition, and the (3*R*, 12b*S*) configuration could be assigned to derivatives **7**, formed from the *syn* approach.

Finally, we were interested in the synthetic application of this methodology to the enantioselective synthesis of the 8-deoxy derivative of the natural angucyclinone (−)-tetrangomycin (Figure 1). This natural product was isolated from cultures of a variant strain of *Streptomyces rimosus*;[30] two total syntheses were described by Krohn and Khanbabaee, but the products were in the racemic form. In one of them,[8c] the hexahydrobenz[*a*]anthraquinone framework was regioselectively formed by a Diels – Alder reaction between a 5-silyl-substituted vinylcyclohexene and a bromojuglone. In a second approach,[8d] the same author prepared (±)-tetrangomycin by a biomimetic-type synthesis, by two successive aldol cyclizations starting from a substituted naphthoquinone.

Our synthetic sequence to (−)-8-deoxytetrangomycin (**10**) (Scheme 3), started from the 80:20 mixture of optically active



Scheme 3. Synthesis of (−)-8-deoxytetrangomycin (**10**). a) K_2CO_3, MeOH, room temperature, 2 h, 98%; b) aqueous HCl, THF, MeOH, room temperature, 4 h, 90%; c) *h*ν, O_2, room temperature, 18 h, 45%.

3-methyl-3-methoxymethyl-substituted tetracyclic derivatives **6f** and **7f**, which resulted from the Diels – Alder reaction between (+)-**1** and (±)-**2f**. The treatment of this mixture with K_2CO_3 in MeOH led to the aromatization of the B ring, giving the anthraquinone derivative (+)-**8** in 98% yield. Deprotection of the MOM functionality of **8** was achieved with aqueous HCl in a mixture of THF/MeOH, to afford the tertiary alcohol (+)-**9** in 90% yield. The optical purity of this derivative (50% *ee*) was established from its Mosher esters;[31] this indicates a 92:8 enantiomeric ratio for each precursor **6f** and **7f**, if it is taken into account that an 80:20 starting mixture of these derivatives was used. In the final step, we used the photooxygenation process, developed by Krohn and co-workers as a general method for the introduction of the C-1 carbonyl functionality into these type of systems.[8a–c, 32] Thus, when compound (+)-**9**, under solvent-free conditions, was exposed to daylight for 48 h, ketone (−)-**10** was isolated after flash chromatography in 50% yield. If we assume that no racemization occurred during the last step of the synthetic sequence, then the 8-deoxy derivative of tetrangomycin (−)-**10** was prepared in four steps, starting from the readily avalaible sulfinylnaphthoquinone (+)-**1** and vinylcyclohexene (±)-**2f**, with 50% *ee* and 26% overall yield.

Conclusion

We developed a novel approach to the asymmetric synthesis of a C-3-oxygenated angucyclinone-like skeleton by taking advantage of the reaction between an enantiomerically pure sulfinylnaphthoquinone and a C-5-oxygenated racemic vinylcyclohexene. The process takes place through a domino Diels – Alder reaction/pyrolytic sulfoxide elimination with simultaneous kinetic resolution of the racemic diene. Our methodology introduces an easy access to such oxygenated systems in optically active form, as illustrated by the four-step total asymmetric synthesis of (−)-8-deoxytetrangomycin in 26% overall yield and 50% enantiomeric purity.

Experimental Section

General: 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. 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, which was performed on precoated sheets of silica gel 60, and flash column chromatography was performed with silica gel 60 (230 – 400 mesh) of Macherey-Nagel. Eluting solvents are indicated in the text. The apparatus for inert atmosphere experiments was flame-dried under 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.

5-Dioxolane-1-vinylcyclohex-1-ene (4): A solution of vinylmagnesium bromide (23 mL, 1.0 M) in THF was added to a mixture of 1-bromo-5-dioxolanecyclohex-1-ene (**3**)[14] (500 mg, 2.3 mmol) in THF (25 mL), which contained catalytic amounts of $Pd(PPh_3)_4$. The mixture was refluxed for 4 h, hydrolyzed with aqueous saturated solution of NH_4Cl, and extracted with diethyl ether. After workup and flash chromatography (eluent hexane/EtOAc 90:10), compound **4** was obtained as a colorless oil in 77% yield. ^{1}H NMR: $\delta = 6.40$ (dd, $J = 10.0$ and 16.8 Hz, 1H, 1a-H), 5.77 (m, 1H, 2-H), 5.03 (d, $J = 16.8$ Hz, 1H, 1b-H), 4.92 (d, $J = 10.0$ Hz, 1H, 1c-H), 4.01 (m, 4H, O-CH_2CH_2-O), 2.36 (m, 4H, 3-H_2, 6-H_2), 1.77 (t, $J = 6.8$ Hz, 2H, 4-H_2); ^{13}C NMR: $\delta = 138.83$, 133.88, 127.78, 110.04, 107.96, 64.14 (2C), 34.28, 30.62, 24.23; MS (EI): *m/z* (%): 166 (5) [M^+], 133 (13), 107 (7), 99 (16), 86 (36), 63 (100); $C_{10}H_{14}O_2$ (166.2): calcd 166.09938; found 166.09935 (HRMS).

3-Vinyl-3-cyclohexen-1-one (5): Compound **4** (600 mg, 3.6 mmol), dissolved in aqueous CH_3CN (5 mL), was added to a solution of $LiBF_4$ in CH_3CN (5 mL, 1.0 M). The mixture was stirred for 1 h at room temperature and CH_2Cl_2 was added. After workup and flash chromatography (eluent hexane/EtOAc 90:10), compound **5** was obtained as a colorless oil in 63% yield: ^{1}H NMR: $\delta = 6.42$ (dd, $J = 10.8$ and 17.0 Hz, 1H, 1a-H), 5.94 (m, 1H, 2-H), 5.04 (d, $J = 17.0$ Hz, 1H, 1b-H), 5.02 (d, $J = 10.6$ Hz, 1H, 1c-H), 2.99 (br. s, 2H, 6-H_2), 2.6 – 2.4 (m, 4H, 3-H_2, 4-H_2); ^{13}C NMR: $\delta = 209.83$, 137.67, 134.33, 127.89, 111.97, 38.90, 38.41, 25.21.

3-Vinyl-3-cyclohexen-1-ol (2a): To a solution of **5** (280 mg, 2.3 mmol) in MeOH (5 mL), solid $NaBH_4$ (100 mg, 2.6 mmol) was added. The mixture

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was stirred for 10 min at room temperature and then H_2O and CH_2Cl_2 were added. After workup and flash chromatography (eluent hexane/EtOAc 90:10), compound **2a** was obtained as a colorless oil in 70% yield: ^{1}H NMR: $\delta = 6.33$ (dd, $J = 11.0$ and 17.6 Hz, 1H, 3a-H), 5.67 (br. s, 1H, 4-H), 5.04 (d, $J = 17.6$ Hz, 1H, 3b-H), 5.02 (d, $J = 11.0$ Hz, 1H, 3c-H), 3.96 (m, 1H, 1-H), 2.90 (br. s, 1H, OH), 2.5–1.5 (m, 6H, 2-H_2, 5-H_2, 6-H_2); ^{13}C NMR: $\delta =$ 139.17, 133.56, 128.40, 110.22, 66.76, 32.79, 30.53, 23.65.

5-[(*tert*-Butyldimethylsilyl)oxy]-1-vinylcyclohexene (2b): To a solution of **2a** (200 mg, 1.6 mmol) in DMF (3 mL), TBDMSCl (290 mg, 1.9 mmol) and imidazole (0.27 g, 4 mmol) were added. The mixture was stirred at room temperature for 6 h, it was then hydrolyzed with an aqueous saturated solution of NH_4Cl and it was then extracted with diethyl ether. After workup and flash chromatography (eluent hexane/EtOAc 90:10), compound **2b** was obtained as a colorless oil in 63% yield: ^{1}H NMR: $\delta = 6.35$ (dd, $J = 10.7$ and 17.4 Hz, 1H, 1a-H), 5.68 (m, 1H, 2-H), 5.06 (d, $J = 17.4$ Hz, 1H, 1b-H), 4.90 (d, $J = 10.7$ Hz, 1H, 1c-H), 3.95 (m, 1H, 5-H), 2.5–1.5 (m, 6H, 3-H_2, 4-H_2, 6-H_2), 0.91 (s, 9H, *t*-Bu), 0.09 (s, 6H, 2CH_3-Si); ^{13}C NMR: $\delta = 139.47$, 134.20, 128.48, 110.02, 67.97, 33.72, 31.57, 25.85 (3C), 24.26, 18.50, −3.62 (2C); MS (EI): *m/z* (%): 238 (1) [M^+], 223 (2), 181 (56), 105 (29), 101 (22), 91 (18), 75 (100); $C_{14}H_{26}OSi$ (238.4): calcd 238.17529, found 238.17496 (HRMS).

General procedure I: Synthesis of OMOM derivatives: To a solution of the corresponding vinylcyclohexenol **2** (4 mmol) in CH_2Cl_2 (8 mL), DIPEA (1.4 mL, 11 mmol) and MOMCl (3.4 mL, 42 mmol) were added. The mixture was stirred at room temperature overnight and hydrolyzed with cold aqueous saturated solution of $NaHCO_3$. After workup and flash chromatography, the pure OMOM derivative was obtained.

5-[(Methoxymethyl)oxy]-1-vinylcyclohexene (2c): Compound **2c** was obtained from **2a** according to General Procedure I (eluent hexane/EtOAc 90:10), as a colorless oil in 100% yield: ^{1}H NMR: $\delta = 6.33$ (dd, $J = 10.8$ and 16.8 Hz, 1H, 1a-H), 5.63 (m, 1H, 2-H), 5.06 (d, $J = 16.8$ Hz, 1H, 1b-H), 4.92 (d, $J = 10.4$ Hz, 1H, 1c-H), 4.72 and 4.69 (AB system, $J = 6.8$ Hz, 2H, O-CH_2-O), 3.84 (m, 1H, 5-H), 3.37 (s, 3H, OCH_3), 2.5–1.6 (m, 6H, 3-H_2, 4-H_2, 6-H_2); ^{13}C NMR: $\delta = 139.18$, 133.56, 128.39, 109.97, 94.51, 71.84, 54.88, 30.45, 27.83, 23.59; MS (EI): *m/z* (%): 136 (28) [$M^+ - CH_3OH$], 123 (10), 106 (100), 91 (72), 79 (58).

1-Methyl-3-vinyl-3-cyclohexen-1-ol (2d): Ketone **5** (100 mg, 0.82 mmol) in THF (2 mL) was added, at 0 °C, to a solution of MeMgBr (0.3 mL of 3.0 M in diethyl ether) dissolved in THF (5 mL). The mixture was stirred at room temperature for 4 h, was hydrolyzed with aqueous saturated solution of NH_4Cl, and was extracted with diethyl ether. After workup and flash chromatography (eluent hexane/EtOAc 90:10), compound **2d** was obtained as a colorless oil in 53% yield: ^{1}H NMR: $\delta = 6.38$ (dd, $J = 10.1$ and 17.3 Hz, 1H, 3a-H), 5.76 (broad s, 1H, 4-H), 5.07 (d, $J = 17.3$ Hz, 1H, 3b-H), 4.92 (d, $J = 10.1$ Hz, 3c-H), 2.4–1.5 (m, 7H, 2-H_2, 5-H_2, 6-H_2, OH), 1.30 (s, 3H, CH_3); ^{13}C NMR: $\delta = 139.36$, 134.54, 128.01, 112.98, 68.61, 37.79, 34.94, 28.64, 23,70; MS (EI): *m/z* (%): 138 (37) [M^+], 123 (100), 105 (36), 95 (64), 79 (34), 67 (26); $C_9H_{14}O$ (138.2): calcd 138.10447, found 138.10410 (HRMS).

5-[(*tert*-Butyldimethylsilyl)oxy]-5-methyl-1-vinylcyclohexene (2e): To a suspension of NaH (15 mg, 0.6 mmol) in THF (5 mL), a solution of **2d** (46 mg, 0.3 mmol) in THF (5 mL) was slowly added. The mixture was stirred for 1 h at room temperature and TBDMSOTf (80 mL, 0.34 mmol) was added. After 2 h at room temperature, workup and flash chromatography (eluent hexane/EtOAc 95:5), compound **2e** was obtained as a colorless oil in 94% yield: ^{1}H NMR: $\delta = 6.39$ (dd, $J = 10.5$ and 17.3 Hz, 1H, 1a-H), 5.72 (m, 1H, 2-H), 5.05 (d, $J = 17.3$ Hz, 1H, 1b-H), 4.89 (d, $J =$ 10.5 Hz, 1H, 1c-H), 2.5–2.0 (m, 4H, 3-H_2, 6-H_2), 1.70 and 1.52 (2m, 2H, 4-H_2), 1.30 (s, 3H, CH_3), 0.86 (s, 9H, *t*-Bu), 0.11 and 0.06 (2s, 6H, 2CH_3-Si); ^{13}C NMR: $\delta = 139.94$, 134.28, 128.51, 109.46, 71.39, 38.74, 36.48, 29.24, 25.80 (3C), 24.01, 18.12, −2.03, −2.28; MS (EI): *m/z* (%): 252 (1) [M^+], 237 (3), 195 (48), 119 (39), 105 (12), 91 (8), 75 (100); $C_{15}H_{28}OSi$ (252,5): calcd 252.19094; found 252.19006 (HRMS).

5-[(Methoxymethyl)oxy]-5-methyl-1-vinylcyclohexene (2f): Compound **2f** was obtained as a colorless oil in 60% yield from **2d**, according to General Procedure I (eluent hexane/EtOAc 90:10): ^{1}H NMR: $\delta = 6.34$ (dd, $J = 10.8$ and 17.8 Hz, 1H, 1a-H), 5.69 (m, 1H, 2-H), 5.04 (d, $J = 17.8$ Hz, 1H, 1b-H), 4.87 (d, $J = 10.8$ Hz, 1H, 1c-H), 4.74 and 4.67 (AB system, $J = 7.4$ Hz, 2H, O-CH_2-O), 3.31 (s, 3H, OCH_3), 2.5–2.0 (m, 4H, 3-H_2, 6-H_2), 1.78 and 1.57 (2m, 2H, 4-H_2), 1.27 (s, 3H, CH_3); ^{13}C NMR: $\delta = 139.37$, 133.81, 128.03, 109.85, 90.72, 74.13, 54.97, 35.75, 33.24, 24.97, 23.48.

5-Acetoxy-5-methyl-1-vinylcyclohexene (2g): To a solution of **2d** (56 mg, 0.4 mmol) and dimethylaminopyridine (DMAP) (100 mg, 0.8 mmol) in CH_2Cl_2 (5 mL), AcCl (60 mL, 0.8 mmol) was added at 0 °C. After 4 h at the same temperature, workup, and flash chromatography (eluent hexane/EtOAc 90:10), compound **2g** was obtained as a colorless oil in 78% yield: ^{1}H NMR: $\delta = 6.35$ (dd, $J = 10.5$ and 17.7 Hz, 1H, 1a-H), 5.72 (m, 1H, 2-H), 5.06 (d, $J = 17.7$ Hz, 1H, 1b-H), 4.90 (d $J = 10.5$ Hz, 1H, 1c-H), 2.7–2.1 (m, 5H, 3-H_2, 4eq-H, 6-H_2), 1.96 (s, 3H, CH_3CO), 1.69 (m, 1H, 4ax-H), 1.55 (s, 3H, CH_3); ^{13}C NMR: $\delta = 170.59$, 139.19, 133.30, 127.87, 110.30, 80.23, 35.89, 32.19, 24.32, 23.18, 22.37.

General procedure II: Diels–Alder reactions: To a solution of 2-(*p*-tolylsulfinyl)-1,4-naphthoquinone (+)-(S*S*)-**1**[20] or (±)-**1**[20](0.15 g, 0.5 mmol) in dry CH_2Cl_2 (5 mL) under argon, the corresponding racemic diene **2** (1.0 mmol, 2 equiv) was added at 0 °C. After 72 h at the same temperature, and evaporation of the solvent, crude dihydroanthraquinones *anti*-**6** and *syn*-**7** were obtained.

(3*S*,12b*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (6b): Compound **6b** was obtained, in 38% yield, from (+)-(S*S*)-**1** and **2b**, according to General Procedure II, after separation of the resulting 60:40 mixture of (+)-**6b** and (+)-**7b** by flash chromatography (eluent hexane/EtOAc 30:1): M.p. 156–157 °C (MeOH); $[\alpha]_D^{20} = +193$ ($c = 0.5$ in $CHCl_3$, 86% *ee*); ^{1}H NMR: $\delta = 8.08$ (m, 2H, 8-H, 11-H), 7.71 (m, 2H, 9-H, 10-H), 5.54 (m, 1H, 5-H), 3.59 (tt, 1H, $J = 4.2$ and 11.3 Hz, 3ax-H), 3.4–3.1 (m, 3H, 12b-H, 6-H_2), 2.53 (ddd, $J = 2.0$, 4.8 and 12.4 Hz, 1H, 4eq-H), 2.31 (dq, $J = 12.4$ and 3.2 Hz, 1H, 1eq-H), 2.2–1.9 (m, 2H, 4ax-H, 2eq-H), 1.70 (dq, $J = 4.2$ and 12.8 Hz, 1H, 2ax-H), 1.09 (m, 1H, 1ax-H), 0.91 (s, 9H, *t*Bu), 0.08 and 0.07 (2s, 6H, 2CH_3-Si); ^{13}C NMR: $\delta =$ 184.82, 184.38, 144.24, 141.59, 135.45, 133.55, 133.44, 132.43, 131.94, 126.31, 126.08, 115.35, 72.43, 45.40, 36.87, 36.63, 32.19, 25.88 (3C), 25.46, 18.21, −3.62, −3.69; $C_{24}H_{30}O_3Si$ (394.6): calcd C 73.06, H 7.67; found C 72.88, H 7.81.

(3*R*,12b*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (7b): Compound **7b** was obtained in 23% yield from (+)-(S*S*)-**1** and **2b** according to General Procedure II, after separation of the resulting 40:60 mixture of (+)-**7b** and (+)-**6b** by flash chromatography (eluent hexane/EtOAc 30:1): M.p. 130–132 °C (MeOH); $[\alpha]_D^{20} = +192$ ($c = 0.5$ in $CHCl_3$, 86% *ee*); ^{1}H NMR: $\delta = 8.07$ (m, 2H, 8-H, 11-H), 7.70 (m, 2H, 9-H, 10-H), 5.46 (m, 1H, 5-H), 4.15 (quint, $J = 2.7$ Hz, 1H, 3eq-H), 3.38 (m, 1H, 12b-H), 3.24 (m, 2H, 6-H_2), 2.26 (m, 2H, 4-H_2), 2.04 (dq, $J = 11.4$ and 3.0 Hz, 1H, 1eq-H), 1.82 (m, 2H, 2-H_2), 1.63 (dq, $J =$ 4.0 and 11.9 Hz, 1H, 1ax-H), 0.85 (s, 9H, *t*Bu), 0.05 and 0.01 (2s, 6H, 2CH_3-Si); ^{13}C NMR: $\delta = 185.01$, 184.56, 144.54, 141.81, 133.86, 133.42, 133.33, 132.50, 132.02, 126.22, 126.03, 115.85, 67.63, 43.20, 37.73, 34.55, 29.06, 25.71 (3C), 25.35, 18.04, −3.40 (2C); $C_{24}H_{30}O_3Si$ (394.6): calcd C 73.06, H 7.67; found C 73.14, H 7.51.

(3*S*,12b*S*)-3-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (6c): Compound **6c** was obtained in 37% yield from (+)-(S*S*)-**1** and **2c** according to General Procedure II, after separation of the resulting 60:40 mixture of (+)-**6c** and (+)-**7c** by flash chromatography (eluent hexane/EtOAc 10:1): $[\alpha]_D^{20} = +158$ ($c = 0.4$ in $CHCl_3$); ^{1}H NMR: $\delta = 8.06$ (m, 2H, 8-H, 11-H), 7.70 (m, 2H, 9-H, 10-H), 5.57 (m, 1H, 5-H), 4.71 (m, 2H, O-CH_2-O), 3.52 (tt, $J = 4.6$ and 11.0 Hz, 3ax-H), 3.39 (s, 3H, OCH_3), 3.4–3.1 (m, 3H, 12b-H, 6-H_2), 2.71 (ddd, $J = 2.3$, 5.0 and 12.2 Hz, 1H, 4eq-H), 2.36 (m, 1H, 1eq-H), 2.13 (m, 2H, 4ax-H, 2eq-H), 1.70 (qd, $J =$ 13.1 and 4.2 Hz, 2ax-H), 1.11 (dq, $J = 3.3$ and 12.0 Hz, 1H, 1ax-H); ^{13}C NMR: $\delta = 184.70$, 184.34, 143.99, 141.59, 134.78, 133.53, 133.45, 132.38, 131.91, 126.30, 126.08, 115.93, 94.84, 76.58, 55.26, 42.22, 36.95, 33.55, 32.10, 25.46; MS (EI): *m/z* (%): 324 (0.4) [M^+], 306 (1), 292 (11), 279 (15), 262 (100), 247 (20), 235 (34), 223 (15), 178 (10), 165 (30), 77 (12); $C_{20}H_{20}O_4$ (324.4): calcd 324.13616; found 324.13605 (HRMS).

(3*R*,12b*S*)-3-[(Methoxymethyl)oxy]-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (7c): Compound **7c** was obtained in 21% yield from (+)-(S*S*)-**1** and **2c** according to General Procedure II, after separation of the resulting 40:60 mixture of (+)-**7c** and (+)-**6c** by flash chromatography (eluent hexane/EtOAc 10:1): $[\alpha]_D^{20} = +147$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR: $\delta = 8.07$ (m, 2H, 8-H, 11-H), 7.70 (m, 2H, 9-H, 10-H), 5.55 (m, 1H, 5-H), 4.68 (m, 2H, O-CH_2-O), 4.02 (t, $J = 2.3$ Hz, 1H, 3eq-H), 3.40 (m, 1H, 12b-H), 3.37 (s, 3H, OCH_3), 3.28 (m, 2H, 6-H_2), 2.51 and 2.31 (2m, 2H, 4-H_2),

2.17 (m, 1H, 1eq-H), 2.05 (m, 1H, 2eq-H), 1.87 (tt, $J = 3.1$ and 13.4 Hz, 1H, 2ax-H), 1.54 (dq, $J = 3.2$ and 12.0 Hz, 1H, 1ax-H); ^{13}C NMR: $\delta = 184.81$, 184.47, 144.07, 141.76, 135.01, 133.84, 133.48, 132.44, 131.91, 126.25, 126.06, 115.93, 94.60, 72.37, 55.25, 39.93, 37.65, 31.40, 29.36, 25.35; MS (EI): *m/z* (%): 324 (0.3) [M^+], 290 (30), 260 (100), 247 (33), 231 (24), 202 (18), 189 (13), 165 (21), 105 (10), 77 (14); $C_{20}H_{20}O_4$ (324.4): calcd 324.13616; found 324.13538 (HRMS).

(3*S*,12b*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (6e) and (3*R*,12b*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (7e): These derivatives were obtained, as an inseparable 85:15 mixture, in 67% yield, from (+)-(S*S*)-**1** and **2e**, according to General Procedure II, after flash chromatography (eluent hexane/EtOAc 20:1). The following data correspond to the major diastereoisomer **6e**: ^{1}H NMR (500 MHz, C_6D_6): $\delta = 8.03$ (m, 2H, 8-H, 11-H), 7.05 (m, 2H, 9-H, 10-H), 5.14 (br. s, 1H, 5-H), 3.27 (m, 1H, 12b-H), 3.2–2.9 (m, 2H, 6-H_2), 2.38 (m, 1H, 1eq-H), 2.25 (m, 2H, 4-H_2), 1.86 (dt, $J = 4.1$ and 13.2 Hz, 2H, 2ax-H), 1.73 (m, 1H, 2eq-H), 1.13 (s, 3H, CH_3), 1.04 (s, 9H, *t*-Bu), 0.95 (dq, $J = 3.5$ and 12.8 Hz, 1H, 1ax-H), 0.14 and 0.13 (2s, 6H, 2CH_3-Si); MS (EI) (from the mixture of **6e** and **7e**): *m/z* (%): 408 (19) [M^+], 351 (33), 275 (100), 259 (29), 221 (31), 185 (79), 147 (73), 115 (32); $C_{25}H_{32}O_3Si$ (408.6): calcd 408.21207; found 408.21168 (HRMS).

(3*S*,12b*S*)-3-[(Methoxymethyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (6f) and (3*R*,12b*S*)-3-[(methoxymethyl)oxy]-3-methyl-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (7f): These derivatives were obtained from (+)-(S*S*)-**1** and **2f** according to General Procedure II, as an unseparable 80:20 mixture after flash chromatography (eluent hexane/EtOAc 90:10), in 58% yield and 84% *ee*. Of the racemic series, a small pure portion of compound (±)-**6f** could be obtained after crystallization: M.p. 96–98 °C (MeOH); ^{1}H NMR: $\delta = 8.07$ (m, 2H, 8-H, 11-H), 7.71 (m, 2H, 9-H, 10-H), 5.53 (m, 1H, 5-H), 4.81 (m, 2H, O-CH_2-O), 3.41 (s, 3H, OCH_3), 3.4–3.1 (m, 3H, 12b-H, 6-H_2), 2.40 (broad s, 2H, 4-H_2), 2.31 (m, 1H, 1eq-H), 1.95 (m, 2H, 2-H_2), 1.23 (s, 3H, CH_3), 1.18 (dq, $J = 5.3$ and 12.0 Hz, 1H, 1ax-H); ^{13}C NMR: $\delta = 184.72$, 184.34, 144.02, 141.59, 134.84, 133.53, 133.45, 132.41, 131.91, 126.30, 126.08, 116.13, 90.75, 77.22, 55.14, 47.53, 38.57, 37.35, 30.87, 25.52, 22.12; $C_{21}H_{22}O_4$ (338.4): calcd C 74.54, H 6.55; found C 74.38, H 6.66.

(3*S*,12b*S*)-3-Acetoxy-3-methyl-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (6g) and (3*R*,12b*S*)-3-acetoxy-3-methyl-1,2,3,4,6,12b-hexahydrobenzo[*a*]anthracene-7,12-dione (7g): These derivatives were obtained from (+)-(S*S*)-**1** and **2g** according to General Procedure II, as an unseparable 85:15 mixture after flash chromatography (eluent hexane/EtOAc 6:1), in 41% yield. A small pure portion of compound (±)-**6g** was obtained after crystallization: M.p. 102–104 °C (MeOH); ^{1}H NMR: $\delta =$ 8.07 (m, 2H, 8-H, 11-H), 7.71 (m, 2H, 9-H, 10-H), 5.58 (m, 1H, 5-H), 3.39 (m, 1H, 12b-H), 3.26 (m, 2H, 6-H_2), 2.82 (dd, 1H, $J = 2.0$ and 12.0 Hz, 4eq-H), 2.5–2.2 (m, 3H, 1eq-H, 2eq-H, 4ax-H), 2.1–1.9 (m, 1H, 2ax-H), 2.01 (s, 3H, CH_3CO), 1.48 (s, 3H, CH_3), 1.22 (m, 1H, 1ax-H); ^{13}C NMR: $\delta = 184.68$, 184.35, 170.37, 143.76, 141.56, 134.95, 133.58, 133.50, 132.39, 131.89, 126.30, 126.11, 117.10, 82.61, 46.46, 37.62, 37.28, 30.60, 25.52, 22.55, 21.61; MS (EI): *m/z* (%): 336 (8) [M^+], 293 (6), 275 (100), 259 (11), 154 (30), 136 (30), 105 (14), 77 (20); $C_{21}H_{20}O_4$ (336.4): calcd 336.13616; found 336.13666 (HRMS).

(3*S*)-3-[(Methoxymethyl)oxy]-3-methyl-1,2,3,4-tetrahydrobenzo[*a*]anthracene-7,12-dione (8): To a 80:20 mixture of optically active **6f** and **7f** (50 mg, 0.15 mmol) in MeOH (15 mL), K_2CO_3 (50 mg, 0.36 mmol) was added. The mixture was stirred for 2 h at room temperature and CH_2Cl_2 (25 mL) was added. After workup and flash chromatography (eluent hexane/EtOAc 70:30), compound (+)-**8** was obtained as a pale yellow oil in 98% yield: $[\alpha]_D^{20} = +16.0$ ($c = 2.5$ in $CHCl_3$); ^{1}H NMR: $\delta = 8.21$ (m, 2H, 8-H, 11-H), 8.14 and 7.44 (AB system, $J = 8.1$ Hz, 2H, 5-H, 6-H), 7.73 (m, 2H, 9-H, 10-H), 4.84 and 4.66 (AB system, $J = 7.5$ Hz, 2H, O-CH_2-O), 3.49 (t, $J = 6.6$ Hz, 2H, 1-H_2), 3.19 (s, 3H, OCH_3), 3.17 and 2.89 (AB system, $J = 17.0$ Hz, 2H, 4-H_2), 2.14 and 1.80 (2m, 2H, 2-H_2), 1.39 (s, 3H, CH_3); ^{13}C NMR: $\delta =$ 185.48, 183.56, 143.68, 139.94, 135.03, 134.95, 133.94, 133.39, 133.28, 132.52, 130.68, 127.16, 126.37, 125.34, 90.97, 72.79, 55.19, 43.06, 33.86, 26.44, 24.93; MS (EI): *m/z* (%): 336 (0.4) [M^+], 304 (23), 289 (15), 274 (100), 259 (36), 231 (19), 202 (24), 189 (15), 163 (8), 101 (9), 84 (30), 77 (11), 57 (13); $C_{21}H_{20}O_4$ (336.4): calcd 336.13616; found 336.13608 (HRMS).

(3*S*)-3-Hydroxy-3-methyl-1,2,3,4-tetrahydrobenzo[*a*]anthracene-7,12-dione (9): HCl (0.5 mL, 35%) was added to a solution of (+)-**8** (60 mg, 0.19 mmol) in THF (3 mL) and MeOH (3 mL). After 4 h at room temperature, workup, and flash chromatography (eluent hexane/EtOAc 75:25), compound (+)-**9** was obtained as a pale yellow solid in 90% yield: M.p. 162–164 °C; $[\alpha]_D^{20} = +13.2$ ($c = 0.4$ in $CHCl_3$, 50% *ee*); ^{1}H NMR: $\delta =$ 8.23 (m, 2H, 8-H, 12-H), 8.17 and 7.46 (AB system, $J = 8.1$ Hz, 2H, 5-H, 6-H), 7.75 (m, 2H, 9-H, 10-H), 3.56 (t, $J = 6.8$ Hz, 2H, 1-H_2), 2.99 (broad s, 2H, 4-H_2), 1.99 and 1.85 (2m, 2H, 2-H_2), 1.41 (s, 3H, CH_3); ^{13}C NMR: $\delta =$ 183.62 (2C), 143.46, 139.59, 135.18 (2C), 134.06, 133.59, 133.39, 132.56, 131.02, 127.23, 126.48, 125.59, 68.02, 44.87, 35.81, 28.72, 26.57; $C_{19}H_{16}O_3$ (292.3): calcd C 78.05, H 5.52; found C 77.87, H 5.63.

Synthesis of MTPA esters: It was performed according to the known procedure.[29] To a solution of alcohol **9** (11.7 mg, 0.04 mmol) and DMAP (10 mg, 0.08 mmol) in CH_2Cl_2 (3 mL), *(R)*- or *(S)*-MTPA-Cl (13 mL, 0.07 mmol) were added. The mixture was stirred overnight at room temperature and then the reaction was quenched as follows: water (1 mL) and Et_2O (3 mL) were added and the reaction mixture was stirred for 15 min. The solution was washed successively with HCl (4 mL, 1N), NaOH (4 mL, 1N), and brine, and was dried over $MgSO_4$. After evaporation of the solvents, the resulting mixture of diastereomeric esters was used directly for NMR analysis in C_6D_6.

(3*S*)-3-Hydroxy-3-methyl-3,4-dihydro-2H-benzo[*a*]anthracene-1,7,12-trione (10): Compound (+)-**9** (10 mg, 0.03 mmol) was exposed under solvent-free conditions to daylight for 18 h. After flash chromatography (eluent hexane/EtOAc 75:25), compound (−)-**10** was isolated as a yellow solid in 45% yield: M.p. 199–200 °C; $[\alpha]_D^{20} = -50$ ($c = 0.36$ in CH_2Cl_2, 50% *ee*); ^{1}H NMR: $\delta = 8.33$ and 7.55 (AB system, $J = 7.5$ Hz, 2H, 5-H, 6-H), 8.20 (m, 2H, 8-H, 11-H), 7.78 (m, 2H, 9-H, 10-H), 3.18 (br. s, 2H, 4-H_2), 3.15 and 3.01 (AB system, $J = 14.0$ Hz, 2H, 2-H_2), 1.53 (s, 3H, CH_3); ^{13}C NMR: $\delta =$ 197.17, 183.84, 182.28, 146.94, 135.43, 135.23, 134.39, 133.89, 133.72, 133.67 (2C), 132.47, 129.88, 127.28, 126.84, 72.59, 53.94, 44.06, 30.15; MS (EI): *m/z* (%): 306 (6) [M^+], 288 (66), 278 (17), 264 (19), 248 (100), 220 (12), 202 (12), 189 (11), 163 (26), 149 (67), 109 (21), 84 (30), 77 (49), 57 (63); $C_{19}H_{14}O_4$ (306.3): calcd 306.08921; found 306.08835 (HRMS).

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[21] The nomenclature *anti* is used for adducts that result when the dienophile approaches the face of the diene opposite to the OX function in the initial cycloaddition. The *syn* adducts result from the approach onto the face bearing the OX substituent.

[22] We could not evaluate the *ee* values of compounds **6c**, **e**, **g** and **7c**, **e**, **g**, because the signals in the ^{1}H NMR spectra of racemic samples in the presence of different chiral lanthanide shift reagents of Eu, Pr and Yb were not well-defined and separate.

[23] The assignment of the multiplicity of proton H_{12b} was based on double resonance experiments. For compounds **7b** and **7c**, H_{12b} did not appear as a well-resolved signal, and for **6b** and **6c** this proton overlapped with the hydrogens at C-6 (see Experimental Section).

[24] ^{1}H–^{1}H NOESY experiment was performed in C_6D_6 at 500 MHz.

[25] We use this term in the conventional sense, as defined by Masamune et al. (see S. Masamune, W. Choy, J. S. Petersen, L. R. Sita, *Angew. Chem.* **1985**, *97*, 1–31; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1–31), the kinetically favored reaction is considered to be the one occurring between homochiral dienophile (+)-**1** and one of the enantiomers of chiral racemic dienes **2**.

[26] The same *S* configuration is always produced by a chiral (S*S*)-2-(*p*-tolylsulfinyl)-1,4-quinone upon reaction with (1*E*)-substituted dienes (see refs. [10b, 10e] and [13]).

[27] An (OTMS/H) 1,3-parallel interaction (analogous to the OX/H present in *anti*-**A**) is estimated to be 0.74 kcal mol^{-1} in cyclohexane derivatives: see E. L. Eliel, S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley, New York, **1994**, p. 696.

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