DOI: 10.1002/chem.200700762

Towards Configurationally Stable [4]Helicenes: Enantioselective Synthesis of 12-Substituted 7,8-Dihydro[4]helicene Quinones

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Abstract: The synthesis of enantiopure C-12 methoxy- or alkyl-substituted 5,7,8,12b-tetrahydro[4]helicene quinones **16** and **17** and the 7,8-dihydroaromatic analogues **4** and **5** has been achieved from (S*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone. In the first series, with a structure containing both central and helical chiralities, the *R* absolute configuration of the stereogenic carbon atom was defined after the asymmetric cycloaddition step, whereas the *P* or *M* helicity was shown to be dependent on the nature of the C-12 substituent. The size of this group was also defining the configurational stability of the final (*P*)-7,8-dihydro[4]helicene quinones **4** and **5**. The interconversion barriers between the *P* and *M* helimers in the latter, computed with a DFT B3LYP method, matched well with the experimentally observed stability. Our study provided evidence that, in addition to steric effects, a small but significant role of electronic effects is governing the configurational stability of such helical quinones.

Keywords: asymmetric synthesis · cycloaddition · helical structures · quinones · sulfoxides

Introduction

Phenanthrene and the higher homologues, bearing a series of *ortho*-condensed aromatic rings, exist in a chiral nonplanar disposition due to the steric hindrance of the hydrogens in positions four and five in the former and the external rings and their substituents in the latter. The helical structures resulting from this distortion of planarity, called helicenes,[1] can be resolved into their enantiomers if the interconversion barrier between them is high enough. Phenanthrene itself shows helical distortion in the solid structure[2] and can be considered the smallest helicene;[3] however, the enantiomers are not stable enough to be isolated because they interconvert quickly at room temperature. Although their half lives have been shown to increase with the presence of alkyl substituents at C-4 and C-5, the enantiomers of more strained 4,5-disubstituted phenanthrenes can be separated only at low temperatures.[3] To the best of our knowledge, configurationally stable [3]helicenes have never been isolated at room temperature. The larger [5,6]- and [7]helicenes can be configurationally stable at room temperature and the isolated helimers can be stored for long periods without significant loss of enantiomeric purity, due to the higher values of their interconversion barriers.[4] The helical distortion of the planarity in the case of benzo[*c*]phenanthrene derivatives, [4]helicenes, is reinforced by overcrowding of the substituents at the 1- and 12-positions of the terminal rings (Scheme 1). In comparison with higher homologues, the diminution of the number of aromatic rings determines a lower interconversion barrier between the two helical forms[4] which is highly dependent on the substituents at the terminal rings. Small substituents facilitate the thermal racemisation of such compounds. When these substituents are large enough, the molecules become configurationally stable and can be resolved into their corresponding en-

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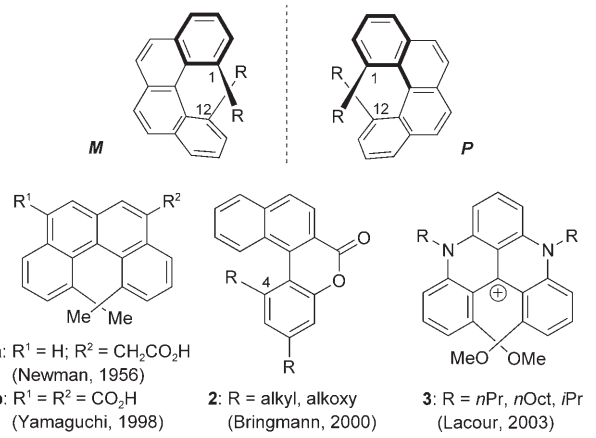


Scheme 1. [4]Helicenes previously synthesized in an optically active form.

antiomers with *P* or *M* absolute configurations (Scheme 1).[5]

Although the first reference about the helical chirality of such tetracyclic systems was reported by Newman et al. in 1948,[6a] the first configurationally stable 1,12-dimethyl-substituted [4]helicene **1a** was not prepared and resolved until 1956 by the same author[6b] (Scheme 1). Since then, several synthetic methods have been exploited for the assembly of the tetrahelicene framework,[7] but only a few derivatives, such as **1b**, **2** and **3** have been resolved into their optical isomers either by chemical[8–10,11] or chromatographic[3a,8b,12] methods. Thus, 1,12-dimethyl-substituted [4]helicene derivatives **1**[8] are configurationally stable even at high temperatures, whereas the stability of 4-susbtituted-6*H*-benzo[*b*]naphtha[1,2]pyran-6-ones **2**[9] is dependent on the size of the substituents, with the 4-methoxy derivative being highly unstable. By contrast, the [4]heteroheliceniun cations **3**, bearing two methoxy groups at C-1 and C-12, are highly stable and their configurational integrity is preserved up to 200 °C.[10] Although not systematically studied, these data provide evidence that the racemisation barriers of [4]helicenes are highly dependent on the particular structure.

Among the applications found for these [4]helicenes, it is worth mentioning those for 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid (**1b**), described by Yamaguchi et al.[11a] This compound has shown interesting properties in chiral catalysis,[11a,13] chiral recognition in the complexation with cyclodextrins,[14] chiral LB film formation,[15] charge-transfer complexation,[16] chiral macrocyclic anhydride and amide formation,[8c,17] optically active acyclic and cyclic polyamine synthesis,[18] chiral macrocyclic alkynes,[19a] cycloalkyne dimer and oligomer formation,[19b–c] optically active bihelicenol synthesis[20] and in the preparation of helicenediamine oligomers.[21] The high non-planarity of helical benzo[*c*]phenanthrenes induced by a methyl group at C-12 was shown to decrease their DNA-damaging effect if compared with the unsubstituted derivative.[22] Moreover, Kelly et al. described a [4]helicene structure as a part of the first rationally designed chemically powered molecular motor.[23] Although the interest of synthesizing such helical molecules in optically active form is evident, to the best of our knowledge, only a single asymmetric approach has been described so far for the enantioselective construction of the lactone-type chiral tetrahelicene **2**,[24] with the resolution of racemic structures the most frequently used method to enantiopure [4]helicenes.

In connection with a program devoted to asymmetric synthesis mediated by sulfoxides,[25] we recently described a new asymmetric approach to [5]helicene bisquinones based on the domino Diels–Alder reaction/sulfoxide elimination/oxidation process that occurred when enantiopure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone reacted with vinyl naphthalenes and phenanthrenes.[26] Nevertheless, due to the poor reactivity of these aromatic derivatives as dienes, Diels–Alder reactions took place only upon reflux of high boiling solvents or under high pressure conditions, with low chemical and optical yields. This problem was later circumvented by the use of non-fully aromatised more reactive dienes, such as dihydroarylethenes.[27] This slight structural modification of the diene allowed the Diels–Alder reaction between enantiopure (S*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone and differently substituted vinyl dihydrophenanthrenes to proceed under very mild conditions, opening an easy access to new helically chiral dihydro[5]helicene quinones and bisquinones with good chemical yields and excellent optical purities.[28] Moreover, the presence of a central hydroaromatic ring in the resulting helicenes is known to increase the racemisation barrier in comparison with that of the whole aromatic derivatives.[29] More recently, enantiopure [7]helicene bisquinones were prepared in a more efficient and convergent one-pot six-step domino process by using 3,6-divinyl-1,2,7,8-tetrahydrophenanthrenes as dienes.[30]

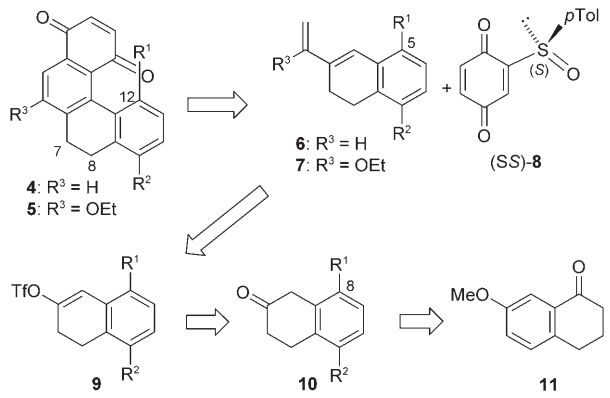
Taking into account the lower racemisation barriers of [4]helicenes ($<16\ kJ\,mol^{-1}$ for tetrahelicene),[4b] a similar asymmetric approach would be applicable if mild conditions

Abstract in Spanish: *La síntesis asimétrica de las 5,7,8,12b-tetrahidro[4]heliceno quinonas metoxi o alquil sustituídas en C-12,* ***16*** *y* ***17****, y las análogas 7,8-dihidroaromáticas* ***4*** *y* ***5*** *se ha llevado a cabo a partir de la (S,*S*)-2-(*p*-tolilsulfinil)-1,4-benzoquinona. En las quinonas* ***16*** *y* ***17****, que poseen quiralidad central y helicoidal, la configuración absoluta* R *en el carbono estereogénico se define después de la etapa de cicloadición asimétrica, mientras que la helicidad* P *o* M *depende de la naturaleza del sustituyente en C-12. El tamaño de este grupo es fundamental a la hora de definir la estabilidad configuracional de las (*P*)-7,8-dihidro[4]heliceno quinonas* ***4*** *y* ***5****. Las barreras de interconversión entre los helímeros* P *y* M *de* ***4*** *y* ***5****, calculadas teóricamente con el método DFT B3LYP, coincidieron bastante bien con la estabilidad configuracional observada experimentalmente. Este estudio ha evidenciado que, además de efectos estéricos, existe una pequeña pero significativa contribución de efectos electrónicos para explicar la estabilidad configuracional de estas quinonas helicoidales.*

conducive to the tetracyclic skeleton were used to avoid the possible racemisation processes. In a preliminary communication, we reported the synthesis of a 12-(*tert*-butyl)-substituted [4]helicene quinone[31] and showed that the bulky *tert*-butyl substituent conferred configurational stability to the system. Because the properties of all these artificial molecules are closely associated to their inherent chirality, future applications of [4]helicene derivatives would require us to know their configurational stability. We then decided to extend our asymmetric approach to the synthesis of new enantioenriched 12-substituted 7,8-dihydrobenzo[*c*]phenanthrene-1,4-quinones with the aim of evaluating the influence of such substituents on the racemisation barrier and, as a consequence, on the configurational stability of [4]helicenes. We describe herein the synthesis of new 12-alkyl- and 12-methoxy-substituted 7,8-dihydro[4]helicenequinones **4** and **5** by starting from (S*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone. Our previous synthesis of 12-(*tert*-butyl)-substituted analogues[31] is also discussed in full detail, including results not described in our earlier communication. We also report on theoretical calculations of the energy barriers of enantiomeric inversion in the [4]helicene quinone system, which matches with the experimental observations. The present study shows that, although the configurational stability of the tetracyclic skeleton is mainly governed by steric effects, the presence of electron-donating groups in the whole system also increases the racemisation barrier.

Results and Discussion

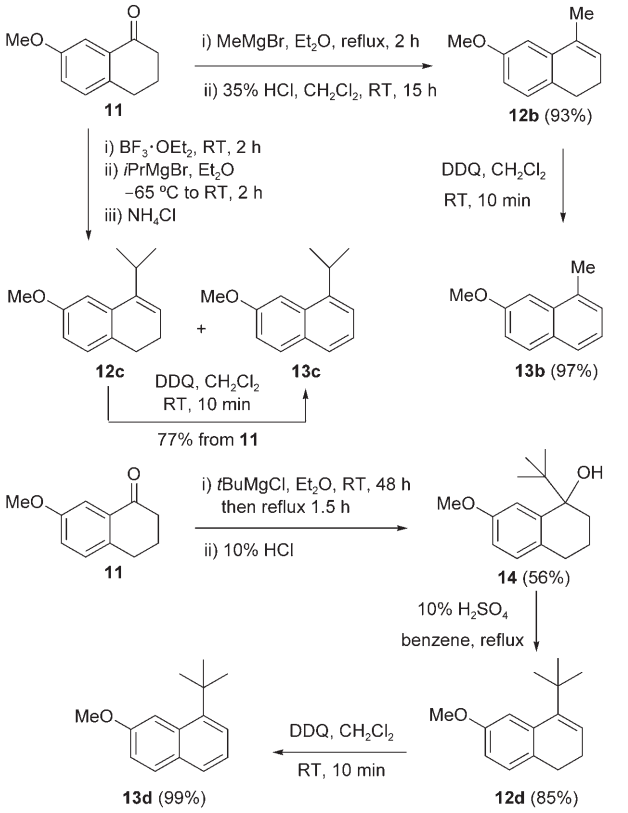
The retrosynthetic analysis outlined in Scheme 2 was considered for the synthesis of alternatively 12-substituted-7,8-dihydro[4]helicene quinones **4** and **5**.



Scheme 2. Retrosynthesis of [4]helicene quinones **4** and **5**.

The construction of the benzo[*c*]phenanthrene skeleton could be achieved in a convergent manner by reaction between an adequately substituted 3-vinyl-1,2-dihydronaphthalene, such as **6** or **7**, and enantiopure 2-(*p*-tolylsulfinyl)-1,4-benzoquinone (S*S*)-**8**,[32] through the domino sequence Diels–Alder reaction, sulfoxide elimination and partial aromatisation that should occur in the presence of an excess of the chiral sulfinyl quinone. The dienes **6** and **7**, the substituents of which at C-5 (R^1 in Scheme 2) would be the precursors of those at C-12 in the final helicenequinones **4** and **5**, could be accessible by a Stille coupling between a vinyl stannane and the bicyclic triflates **9**. These derivatives could be formed from the corresponding 2-tetralone precursors **10**, bearing the appropriate substitution at C-8 (R^1 in Scheme 2) which will be ultimatly responsible for the configurational stability of the final [4]helicene quinones (C-12 in **4** or **5**). Thus, a general synthesis allowing the presence of different groups at C-8 in **10** was envisaged by starting from commercially available 7-methoxy-1-tetralone (**11**), in which the alkyl R^1 substituents could be introduced by using Grignard reagents, with the methoxy-substituted aromatic ring as a suitable precursor for the cyclohexenone moiety of **10**, after Birch reduction and acidic hydrolysis.

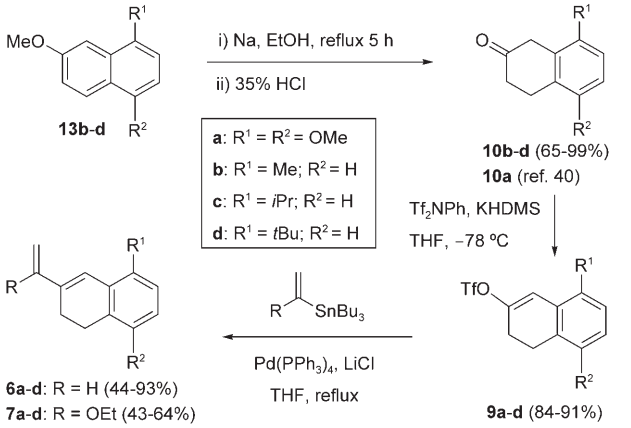
Thus, as shown in Scheme 3, addition of methyl magnesium bromide to the carbonyl group of **11**, followed by an acidic treatment (35% HCl) to promote water elimination of the non-isolated carbinol intermediate, furnished a 93% yield of dihydronaphthalene **12b**.[33] Dehydrogenation of **12b** with DDQ (DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone) led to 1-methyl-7-methoxy naphthalene (**13b**)[33b,c] in 97% yield. A similar reaction sequence allowed the synthesis of 1-(isopropyl)-7-methoxynaphthalene (**13c**). In this case, the introduction of the isopropyl substituent in **11** required the activation of the carbonyl group by $BF_3{\cdot}OEt_2$,



Scheme 3. Synthesis of 1-alkyl-7-methoxynaphthalenes **13b–d**.

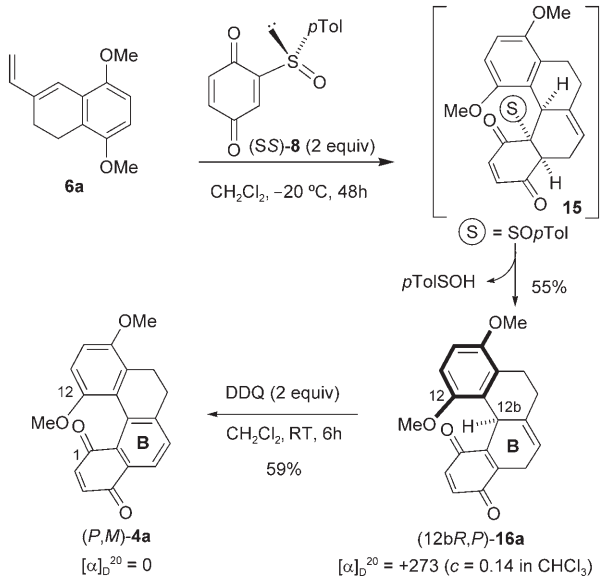
before the addition of the corresponding Grignard reagent at low temperature. Under these conditions, a mixture of dihydronaphthalene **12c**[34] and naphthalene **13c**[35] was generated, which evolved into **13c** by treatment with DDQ (77% overall yield). Upon reaction with *tert*-butyl magnesium chloride[36] followed by 10% HCl treatment, **11** gave rise to carbinol **14**[37] that could only be dehydrated after heating in the presence of a stronger acid (H_2SO_4) to afford, in 85% yield, the dihydroaromatic derivative **12d** the aromatization of which to naphthalene **13d** with DDQ occurred in almost quantitative yield (Scheme 3).

Reduction of naphthalene derivatives **13b–d** was carried out with Na in refluxing ethanol and occurred selectively at the β-substituted ring[38] to give the corresponding enol ether intermediates, which were directly transformed into the desired 8-alkyl-3,4-dihydro-2(1*H*)-naphthalenones **10b–d**[39] by acidic hydrolysis (Scheme 4). The 5,8-dimethoxy-substituted 2-tetralone **10a** was synthesized by using a known procedure[40] from the Diels–Alder adduct resulting from the reaction between 2-methoxy-1,3-butadiene and *p*-benzoquinone. The key intermediate enol triflates **9**, en route to dienes **6** and **7**, were obtained by trapping the enolate generated from β-tetralones **10** with Tf_2NPh (Scheme 4). Stille coupling of these triflates **9a–d** with vinyl tributyl stannane afforded dienes **6a–d** which were isolated pure by flash column chromatography in 44–93% isolated yields. The cross coupling reaction of **9a–d** with 1-ethoxyvinyl tributyl stannane afforded ethoxy-substituted dienes **7a–d**, which were proven to be very unstable, evolving into the corresponding methyl ketones resulting form the hydrolytic cleavage of the ethyl vinyl ether moiety. Thus, compounds **7** had to be used immediately once synthesized.



Scheme 4. Synthesis of 3-vinyl-1,2-dihydronaphthalenes **6** and **7**.

With dienes **6** and **7** in hand, we began the study of Diels–Alder reactions with enantiopure (S*S*)-**8**. By taking into consideration the reactivity features of the diene component in the Diels–Alder reaction,[41] we initiated this study with the presumably more reactive systems **6a** and **7a**, bearing the 1,4-dimethoxyphenyl substituent, which could behave as an electron-donating group, thus activating the 1,3-butadiene moiety.[42] We performed the reaction of **6a** with a twofold excess of (S*S*)-**8** at −20 °C in CH_2Cl_2 (Scheme 5). The initially formed Diels–Alder adduct **15** was not detected and evolved spontaneously, after *syn*-pyrolytic elimination of the sulfoxide, to derivative **16a**, which was the final product of this reaction. Although the quinone **8** was in excess, we did not observe the formation of the dihydrohelicene quinone **4a**, which could result after the in situ aromatisation of the B ring of **16a**, even when the mixture was stirred for 7 d. The tetrahydroaromatic derivative (12b*R*,*P*)-**16a**,[43] which contains both central and helical chiralities, was isolated pure in 55% yield and was shown to be optically active ($[\alpha]_D^{20} = +273$ ($c = 0.14$ in $CHCl_3$)). The aromatization of the B ring of **16a**, by using two equivalents of DDQ in CH_2Cl_2 at room temperature for 6 h, gave rise to 7,8-dihydro-9,12-dimethoxybenzo[*c*]phenanthrenene-1,4-dione (**4a**) in 59% yield. Surprisingly, the [4]helicene quinone **4a** formed under these conditions showed a null value of its optical rotation.

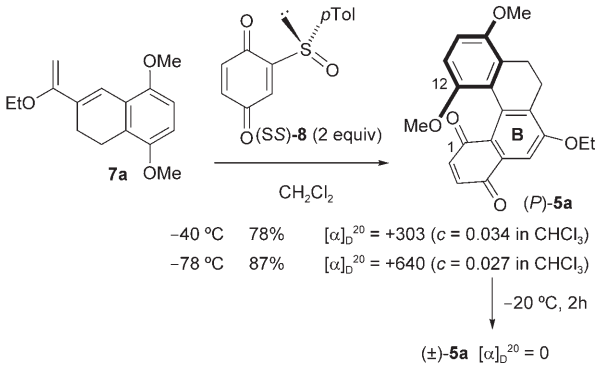


Scheme 5. Synthesis of 9,12-dimethoxy-5,7,8,12b-tetrahydro[4]helicene quinone (12b*R*,*P*)-**16a** and 9,12-dimethoxy-7,8-dihydro[4]helicene quinone (*P*,*M*)-**4a**.

Previous results from our laboratory had shown that the absolute configuration and optical purity of the [5]-[28b,c] and [7]helicene quinones[30] obtained by following a similar asymmetric approach, were highly dependent on the nature of the oxidant and the reaction conditions used in the aromatisation step. The formation of racemic **4a** could thus be due to the reagent and/or temperature used in the aromatisation step or to the low interconversion barrier between both enantiomers of the 12-methoxy-substituted [4]helicene quinone. We thus carried out the aromatisation process in the presence of DDQ as the oxidant at lower temperatures (−78 and −20 °C) to minimize racemisation, but only traces

of compound **4a** were isolated, even after long reaction times.

Because the aromatisation of **16a** at room temperature could decrease the enantiomeric excess of the final helicene quinone **4a**, we decided to synthesize the 6-ethoxy tetracylic derivative **5a**, presumably easier to aromatise at lower temperatures. The presence of electron-donating substituents in the hydroaromatic polycyclic precursors, resulting from the domino Diels–Alder reaction and elimination of the sulfoxide, had been shown to decrease the oxidation potential of analogous penta- and heptacyclic derivatives,[28,30,31] thus facilitating the aromatisation step en route to [5]- and [7]helicene quinones and bisquinones. The Diels–Alder reaction of (S*S*)-**8** (2 equiv) with the more reactive ethoxy-substituted diene **7a** could be carried out at −40 °C to give, directly, the [4]helicene quinone (*P*)-**5a** which could be isolated pure in 78% yield (Scheme 6). This result corroborated that the

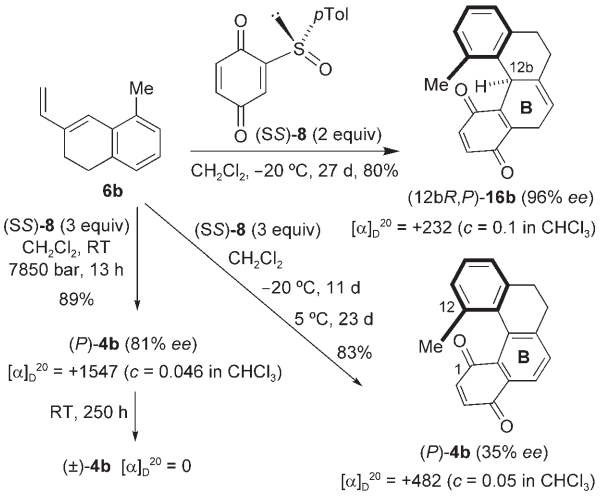


Scheme 6. Synthesis of 6-ethoxy-9,12-dimethoxy-7,8-dihydro[4]helicene quinone (*P*)-**5a**.

domino process, including the Diels–Alder reaction, elimination of the sulfoxide and aromatisation by an excess of the quinone present in the reaction medium, was easier when the structures bear electron-donating substituents. The specific rotary power of [4]helicene quinone **5a** isolated in this experiment, immediately measured after purification, was ($[\alpha]_D^{20} = +303$ ($c = 0.034$ in $CHCl_3$)). This result provided evidence for the presence of a helical chirality in compound **5a** to which a *P* absolute configuration was assigned. The same reaction at −78 °C gave rise to (*P*)-**5a** (87% yield), which showed a higher value of optical rotation ($[\alpha]_D^{20} = +640$ ($c = 0.027$ in $CHCl_3$)). When the solution of **5a** used to measure the rotary power was allowed to stand at −20 °C, the initial value decreased very quickly and was null after 2 h. These results indicated that the configurational stability of [4]helicenequinones **4a** and **5a**, bearing a methoxy group as the substituent at C-12 was very low and the interconversion between both *P* and *M* helimers took place quickly even at −20 °C.

We then turned our attention to the synthesis of the C-12 methyl-substituted [4]helicene quinones **4b** and **5b** in order to evaluate their configurational stability. Thus, the reaction of diene **6b** with two equivalents of quinone (S*S*)-**8** in CH_2Cl_2 at −20 °C for 27 days furnished tetrahydroaromatic benzo[*c*]phenanthrenedione (12b*R*,*P*)-**16b**, which was isolated in 80% yield after flash chromatography. Compound **16b** showed a rotary power of $[\alpha]_D^{20} = +232$ ($c = 0.1$ in $CHCl_3$) which corresponded to a 96% *ee* (*ee* = enantiomeric excess).[44] In the presence of an even higher excess of the sulfinyl quinone **8** (3 equiv), after 11 days at −20 °C and 23 additional days at 5 °C, the initially formed tetrahydroaromatic derivative **16b** evolved into 12-methyl-7,8-dihydro[4]-helicene quinone ((*P*)-**4b**), which was isolated pure after flash chromatography in 83% yield. Immediately after being synthesized, compound (*P*)-**4b** showed an optical rotation of $[\alpha]_D^{20} = +482$ ($c = 0.05$ in $CHCl_3$), corresponding to a 35% *ee*.[44]

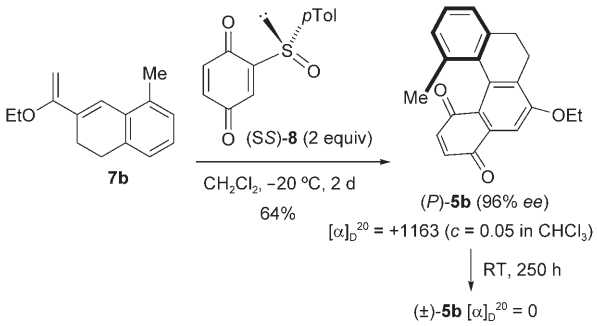
We then repeated the reaction of diene **6b** with three equivalents of sulfinyl quinone (S*S*)-**8** at room temperature under high-pressure conditions (7850 bar). After 13 h (Scheme 7), the reaction was complete, leading to the direct



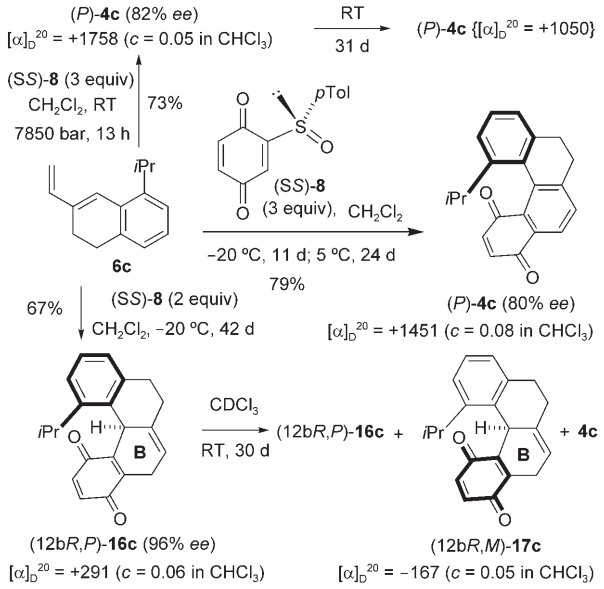
Scheme 7. Synthesis of 12-methyl-5,7,8,12b-tetrahydro[4]helicene quinone (12b*R*,*P*)-**16b** and 12-methyl-7,8-dihydro[4]helicene quinone (*P*)-**4b**.

formation of dihydroaromatic derivative (*P*)-**4b**, which was isolated in 89% yield and with 81% *ee*.[44] This result provided evidence that the high pressure conditions strongly accelerate both the cycloaddition and the aromatisation processes. Although the temperature of this experiment was higher than before, the enantiomeric purity of the final helical derivative (*P*)-**4b** was better, this was probably due to the shorter reaction time, which partially avoided racemisation. The rotary power of (*P*)-**4b** ($[\alpha]_D^{20} = +1547$ ($c = 0.046$ in $CHCl_3$)), measured immediately after purification, decreased at room temperature to a null value after 250 h, providing evidence for a low racemisation barrier between the helimers.

The synthesis of 6-ethoxy-12-methyl-7,8-dihydro[4]helicene quinone (**5b**) (64% yield) was directly accomplished by reaction of ethoxy-substituted diene **7b** with the dienophilic quinone (S*S*)-**8** (2.5 equiv) in CH_2Cl_2 at −20 °C for two days (Scheme 8). Once again, the presence of the



Scheme 8. Synthesis of 6-ethoxy-12-methyl-7,8-dihydro[4]helicene quinone (*P*)-**5b**.



Scheme 9. Synthesis of 12-isopropyl-5,7,8,12b-tetrahydro[4]helicene quinones (12b*R*,*P*)-**16c** and (12b*R*,*M*)-**17c** and 12-isopropyl-7,8-dihydro[4]-helicene quinone (*P*)-**4c**.

ethoxy substituent in the tetracyclic system initially formed by the cycloaddition and pyrolytic elimination process was favouring the aromatization at low temperature by the excess of the quinone which acted as an oxidant in the last step of the domino sequence. Moreover, the low temperature and shorter reaction time (2 d at −20 °C) allowed the isolation of enantiopure 7,8-dihydro[4]helicene derivative (*P*)-**5b** ($[\alpha]_D^{20}=+1663$ ($c=0.05$ in $CHCl_3$), 96 % *ee*)).[44] This helical quinone was shown to be configurationally unstable as its optical rotation decreased to a null value after 250 h at room temperature. Nevertheless, the rotary power of (*P*)-**5b** remained constant at −20 °C, providing evidence for a higher configurational stability of this C-12 methyl-substituted[4]helicene quinone relative the analogues **4a** and **5a**, which bear a methoxy group at C-12.

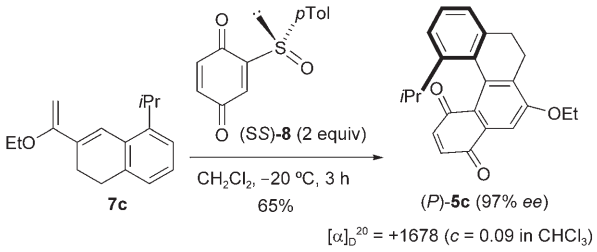
Thus, although compounds **4a**—**b** and **5a**–**b** are not configurationally stable at room temperature, there is a significant difference between the C-12 methoxy-substituted systems **4a** and **5a**, which rapidly racemise even at −20 °C, and the C-12 methyl-substituted analogues **4b** and **5b**, which are indefinitely stable at this low temperature. Although this efficient synthesis allowed an easy access to the [4]helicene quinones, the low configurational stability of the methyl-substituted derivatives at room temperature prevented further applications.

Considering the observed differences, we expected a higher configurational stability for the [4]helicene quinones **4c** and **5c** bearing a bulkier C-12 isopropyl substituent. The reaction of diene **6c** with 2.1 equivalents of sulfinyl quinone (S*S*)-**8** (Scheme 9) occurred slowly at −20 °C (42 d) to give compound (12b*R*,*P*)-**16c**, resulting from the cycloaddition and sulfoxide elimination in 67 % yield. Tetrahydroaromatic derivative **16c** showed an optical rotation of $[\alpha]_D^{20}=+291$ ($c=0.06$ in $CHCl_3$) and a 96 % *ee*.[44]

Upon standing in $CDCl_3$ solution at room temperature for 30 days, compound **16c** partially evolved into a 65:15:20 mixture of **16c**, a new diastereoisomer (12b*R*,*M*)-**17c**, and dihydroaromatic derivative **4c**, proceeding from the aromatisation of the B ring of **16c** and/or **17c**. Fortunately, the minor isomer **17c** could be obtained pure after flash chromatography showing an optical rotation of $[\alpha]_D^{20}=-167$ ($c=0.05$ in $CHCl_3$). The isolation of two diastereoisomers **16c** and **17c** for this type of compound can only be a consequence of the existence of two elements of chirality in such structures. The central chirality is evident from the presence of the stereogenic centre at C-12b; however, a helical chirality must also be present. This structural feature would be common to the other tetrahydroaromatic derivatives **16a** and **16b**; however, only in the case of the isopropyl-substituted analogue will both *P* and *M* helical diastereoisomers interconvert very slowly at room temperature, which is thus responsible for the appearance of two isolable structures **16c** and **17c**. It is worth mentioning that the sign of the rotary power of both diastereomers is opposite. According to the carbon substitution existent at the C-12b sterogenic centre, the inversion of its configuration is unlikely, whereas due to the flexible structure of the 1,4-cyclohexadiene moiety, the inversion of the helicity is plausible.

The direct synthesis of 12-isopropyl-7,8-dihydro[4]helicene quinone (*P*)-**4c** could be achieved in 79 % yield with 80 % *ee*[44] from a reaction between **6c** and three equivalents of (S*S*)-**8** after 11 days at −20 °C and 23 additional days at 5 °C (Scheme 9) or under high-pressure conditions (7850 bar) after 13 h at room temperature in 73 % yield with 82 % *ee*.[44] The rotary power of (*P*)-**4c** obtained under these last conditions ($[\alpha]_D^{20}=+1758$ ($c=0.05$ in $CHCl_3$)) also decreased to $[\alpha]_D^{20}=+1050$ after 31 days at room temperature, but much more slowly than the C-12 methyl analogues. This rotary power remained constant indefinitely in solution at −5 °C.

Enantiopure 6-ethoxy-12-isopropyl-7,8-dihydro[4]helicene quinone (*P*)-**5c** ($[\alpha]_D^{20}=+1678$ ($c=0.09$ in $CHCl_3$), 97 % *ee*)[44] was also directly obtained by reaction between ethoxy-substituted diene **7c** and an excess of (S*S*)-**8** (Scheme 10) in 65 % yield. Compound (*P*)-**5c** was also shown to be configurationally stable at −5 °C.



Scheme 10. Synthesis of 6-ethoxy-12-isopropyl-7,8-dihydro[4]helicene quinone (*P*)-**5c**.

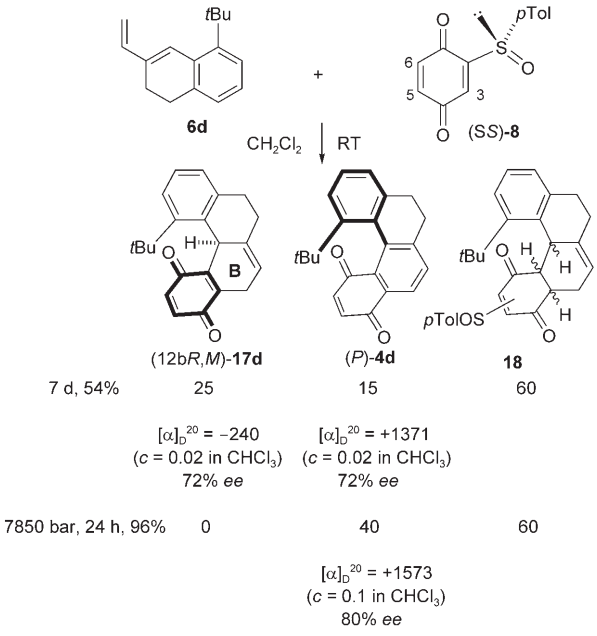
All these results provided evidence for a common feature of our methodology. When the 7,8-dihydro[4]helicene quinones are not configurationally stable, longer reaction times lead to smaller optical purities, due to partial racemisations that must occur during the synthetic process. The higher reactivity of the alkoxy-substituted dienes **7** favoured the formation of products with a higher enantiomeric excess, except in the case of C-12 methoxy-substituted derivative **5a**, due to its very low configurational stability.

The reaction of 2-vinyl-8-(*tert*-butyl)-3,4-dihydronaphthalene (**6d**) revealed an important influence of the remote bulky substituent at the diene moiety both in the reactivity and chemoselectivity of the Diels–Alder reaction with sulfinyl benzoquinone (S*S*)-**8**.[31]

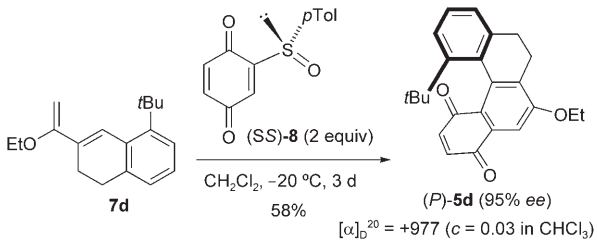
As outlined in Scheme 11, the cycloaddition between **6d** and enantiopure (S*S*)-**8**, was complete after seven days at room temperature affording, in 54% overall yield, a 25:15:60 mixture of (12b*R*,*M*)-**17d**, (*P*)-**4d** and **18** which could be isolated by flash chromatography in 14, 10 and 30% yields, respectively. The major component of the mixture was characterised as a mixture of regio and diastereomers **18**, resulting from the cycloaddition of diene **6d** to the unsubstituted C5–C6 double bond of the ambident dienophilic sulfinylquinone (S*S*)-**8**.[45] Compound (12b*R*,*M*)-**17d** was formed after *endo* cycloaddition of the diene **6d** to the sulfinyl-substituted C2–C3 double bond of **8**, followed by elimination of the sulfoxide. This derivative, containing helical chirality and a stereogenic centre at C-12b gave a 72% *ee* ($[\alpha]_D^{20} = -240$ ($c = 0.02$ in $CHCl_3$)).[44] Compound (*P*)-**4d**, resulting from full aromatisation of the B ring of **17d**, was isolated in an optically active form ($[\alpha]_D^{20} = +1371$ ($c = 0.02$ in $CHCl_3$)) with a 72% *ee*,[44] and was shown to be configurationally stable at room temperature. Although the dienophile **8** was used in excess (2 equiv) to promote the aromatisation of the B ring of **17d**, only a small amount of the expected [4]helicenequinone **4d** was formed. To improve the yield of **4d**, we submitted compound **17d** to different treatments with DDQ, CAN (ceric ammonium nitrate) and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene). Surprisingly, **17d** remained unchanged in the presence of several oxidants under different temperatures, even after long reaction times.

When the mixture of diene **6d** and (S*S*)-**8** (3 equiv) was submitted to high-pressure conditions (7850 bar) for 24 h at room temperature (Scheme 11), a 40:60 mixture of (*P*)-**4d** (37% yield) and **18** (59% yield) was formed. Again, the domino process was accelerated under high pressure conditions and compound **4d** ($[\alpha]_D^{20} = +1573$ ($c = 0.1$ in $CHCl_3$)) was obtained with a 80% *ee*,[44] slightly higher than that obtained at atmospheric pressure.

When the reaction was performed with the more electron-rich diene **7d** (Scheme 12), bearing the OEt substituent at C-3 of the diene moiety, the cycloaddition with sulfinyl quinone (S*S*)-**8** occurred at −20 °C, affording in 57% yield, helical quinone (*P*)-**5d**[43] showing an optical rotation of ($[\alpha]_D^{20} = +977$ ($c = 0.03$ in $CHCl_3$)) with 95% *ee*.[44] Compound **5d** resulted from the exclusive attack of the diene on the sulfinyl-substituted C2–C3 double bond of **8**, followed by elimination of the sulfoxide and full aromatisation of the B ring. This result provided evidence that, in this case, the use of the more electron-rich diene **7d**, not only facilitated the aromatisation of the B ring on the non-isolated intermediate adduct, as previously observed, but also completely reversed the chemoselectivity of the process. The lower temperature of the cycloaddition step improved the stereoselectivity of the process allowing the isolation of enantiopure (*P*)-**5d**, which was configurationally stable at 25 °C.



Scheme 11. Reaction of 3-vinyl-5-*tert*-butyl-1,2-dihydronaphthalene **6d** and (S*S*)-**8**.



Scheme 12. Synthesis of 6-ethoxy-12-(*tert*-butyl)-7,8-dihydro[4]helicene quinone (*P*)-**5d**.

Structural and configurational assignment: The structural assignment of tetrahydroaromatic derivatives **16a–c** and **17c,d** was based on a detailed comparative analysis of their spectroscopic parameters, mainly ^{1}H NMR spectra. As discussed above, these compounds present two elements of chirality, a stereogenic centre at C-12b and a chiral pseudo-helix due to their *ortho*-condensed tetracyclic structure. This was evidenced from the isolation of two isopropyl-substituted diastereomers **16c** and **17c**, only possible if two chiralities are present.

In spite of the structural analogy of all tetrahydroaromatic derivatives **16a–c** and **17c,d**, their ^{1}H NMR spectra revealed significant differences in the chemical shifts of the olefinic proton H-6 and the diastereotopic hydrogens at C-5 of compounds **16a–c** when compared with those of compounds **17c,d** (Figure 1). As can be seen, H-6 appeared as a broad singlet at $\delta = 5.50$–5.53 ppm in compounds **16a–c** (Figure 1A,B,C), whereas it is much more deshielded in **17c** and **17d**, $\delta = 5.91$ and 6.05 ppm, respectively (Figure 1D,E). Moreover, the methylene group at C-5 is observed as a complex AB system at $\delta = 2.95$ and 3.30 ppm in **16b** and **16c** and $\delta = 2.97$ and 3.18 ppm in **16a**, whereas the corresponding signals for the CH_2 at C-5 in **17c** and **17d** appeared at $\delta = 2.70$ and 3.85 ppm in **17c** and $\delta = 2.58$ and 3.81 ppm in **17d** and are much more separated. This NMR behaviour seemed to indicate a different spatial arrangement of derivatives **16a–c** with respect to **17c** and **17d**, probably due to the different conformations of the 1,4-dihydroaromatic fragment (B ring) present in these compounds.

In accordance with previous conformational studies on 1,4-dihydronaphthalenes[46] and with our own work,[28c,47] tetrahydroaromatic derivatives **16a–c** and **17c,d** would exist in a stable boat-like conformation, such as **I** (Scheme 13), in which the aryl substituent at C-12b is situated in a pseudoaxial disposition to avoid destabilising interactions with the methylene group at C-6a and the adjacent carbonyl group, present in the other possible conformer **II**. NOESY experiments carried out on 9,12-dimethoxy-substituted derivative **16a** confirmed the existence of a conformation such as **I**, as a NOE enhancement was observed between H-8_{ax} and H-12b, which is only possible if both hydrogen atoms are spatially close, such as in conformer **I**. Nevertheless, in the case of the 12-*tert*-butyl-substituted tetracyclic compound **17d**, the NOESY experiment provided evidence for strong NOE enhancements between H-12b and H-5_{ax} as well as between H-12b and the *tert*-butyl group at C-12 (Scheme 13). This situation is only possible if conformer **II**, with the aryl group at C-12b in a pseudoequatorial disposition, is the major component in the conformational equilibrium of **17d**. A detailed inspection of structures **16a-I** and **17d-II** revealed that the presumably more stable conformer **I**, in the case of the C-12 *tert*-butyl-substituted system **17d**, must be highly destabilized by a spatial interaction between the bulky *tert*-butyl group (R^1 in conformation **I**) and the quinone ring.

This structural assignment was later confirmed by X-ray diffraction[48] of both derivatives **16a** and **17d** (Figure 2) in which the boat-like conformation **I** (with the C-12b aryl group axial) for **16a** and **II** (with the C-12b aryl group equa-

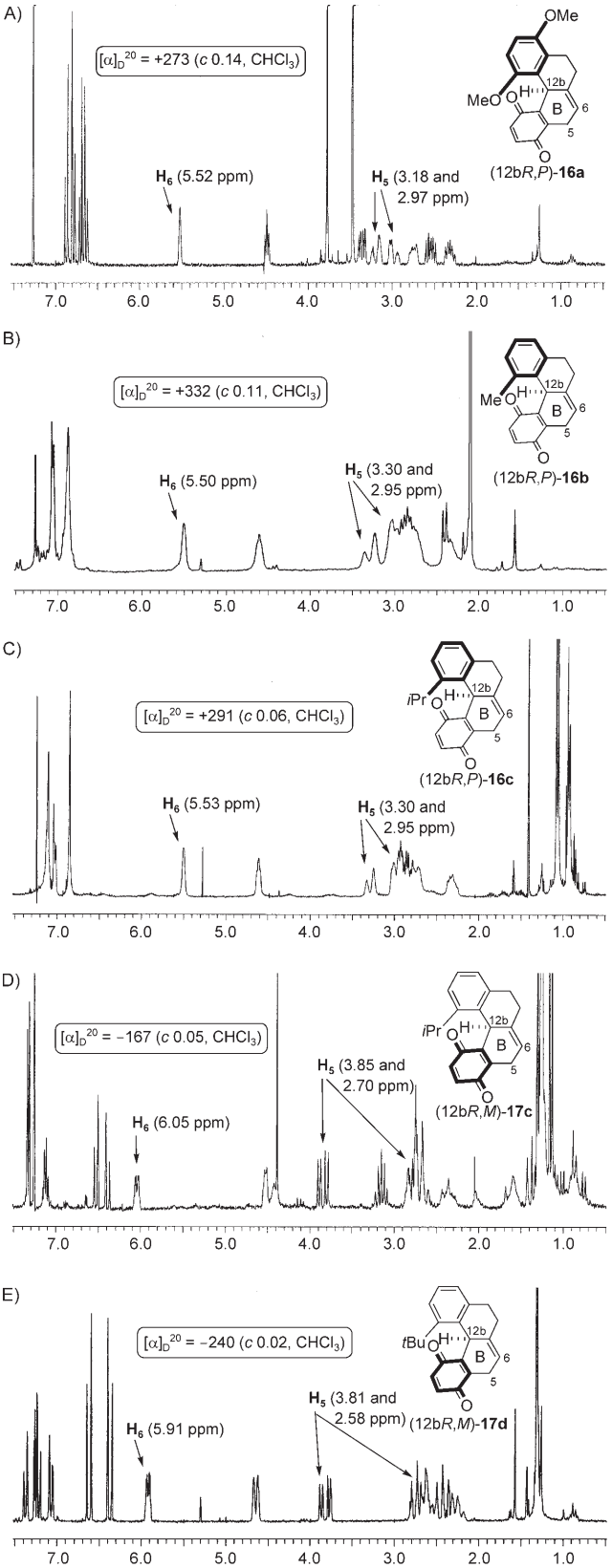
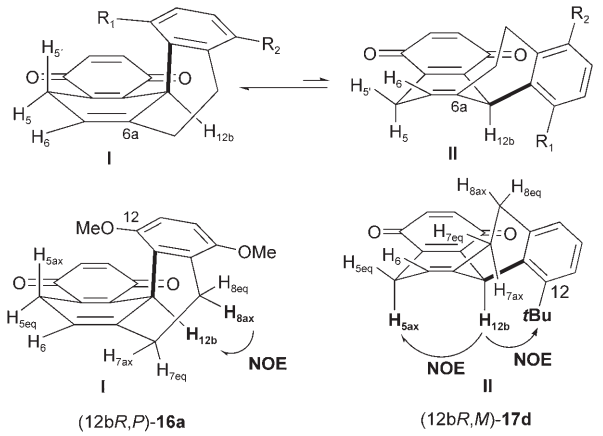


Figure 1. ^{1}H NMR spectra of **16a–c** and **17c,d**.



Scheme 13. Possible boat-like conformations of the 1,4-dihydroaromatic ring of 5,7,8,12b-tetrahydro[4]helicenequinones **16** and **17** and observed NOEs for **16a** and **17d**.

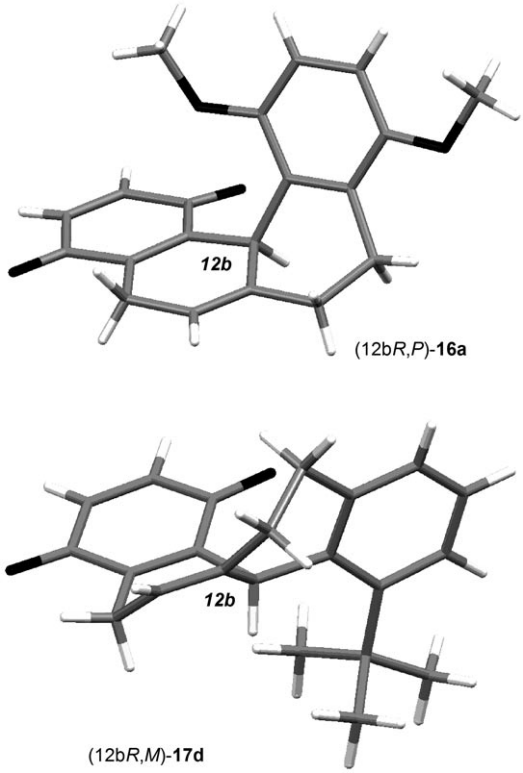
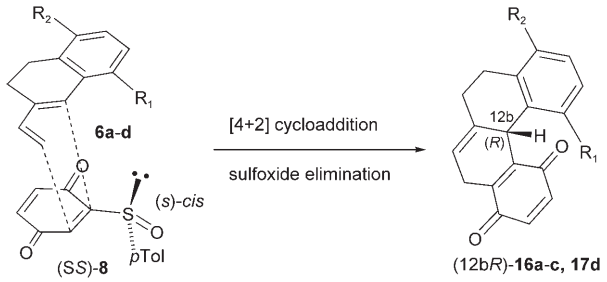


Figure 2. X-ray structures of **16a** and **17d**.

torial) for **17d** were evidenced. Moreover, these X-ray structures also showed the helical nature of these molecules possessing central and helical chiralities, and corroborated the 12b*R*,*P* relative configuration for **16a** and 12b*R*,*M* for **17d**.

After having determined the structure of **16a** as the boat-like conformation **I** (Scheme 13), the similar ^{1}H NMR spectra obtained for compounds **16b** and **16c** (Figure 1B,C) led us to assign a similar spatial arrangement to these tetrahydroaromatic derivatives. In the same way, the isopropyl-substituted derivative **17c**, resulting from spontaneous evolution of **16c**, which showed a similar ^{1}H NMR spectrum to that of compound **17d** (Figure 1D,E), must present a conformation such as **II**.

The absolute configuration of the stereogenic carbon atom at C-12b in all tetrahydroaromatic derivatives **16a–c** and **17c**,**d** has been assigned as *R*, taking into account the high optical purity observed in all cases and the well-established model of approach of the reacting enantiopure dienophile (S*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**8**).[28c,49] Thus, the initial Diels–Alder adduct must result from the preferred *endo* approach of the vinyl dihydronaphthalenes **6a–d** to the less-encumbered upper face of the sulfinylquinone (S*S*)-**8**, adopting the (*s*)-*cis* conformation represented in Scheme 14, usually the most stable and reactive of vinyl sulfoxides.[49,50]



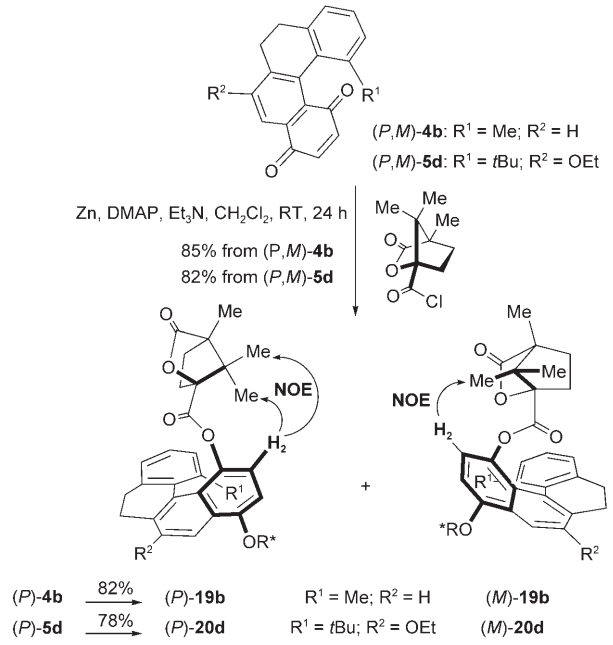
Scheme 14. Preferred approach between 3-vinyl-1,2-dihydronaphthalenes **6** and sulfinyl quinone (S*S*)-**8**.

The additional helical chirality shown by compounds **16a–c** and **17c**,**d**, evident from the X-ray structures of **16a** and **17d**, must be a consequence of the complete shift of the conformational equilibrium towards boat-like structure **I** in **16a**,**b** and **II** in **17d**, with the relative stability of conformers **I** and **II** dependent on the substituent at C-12 (R_1 in Scheme 13). In the case of the isopropyl-substituted derivative **16c**, we initially detected a structure in which the ^{1}H NMR spectroscopic parameters matched with conformer **I**. Although slowly, the equilibration between both conformers **I** and **II** occurred, in this case, at room temperature, leading to an equilibrium mixture of two diastereoisomeric isolable structures **16c-I** and **17c-II**.

The *P* and *M* absolute configuration of the chiral helix present in tetrahydroaromatic derivatives **16a–c** and **17c**,**d** was assigned by taking into account the positive or negative sign of their $[\alpha]_D^{20}$ values,[1c] which are depicted in Figure 1. Thus, the helicity of the isopropyl-substituted diastereomers **16c-I** and **17c-II**, which bear the same *R* configuration at C-12b, must be opposite due to the opposite sign of their $[\alpha]_D^{20}$ values. Moreover, all structures containing boat-like structure **I** (**16a–c**) have a positive value of $[\alpha]_D^{20}$, whereas compounds **17c** and **17d**, to which the boat-like structure **II** has been assigned, has a negative $[\alpha]_D^{20}$ value. These observations led us to assign the *P* absolute configurations to the chiral helix of compounds bearing the boat-like structure **I** and *M* to compounds with conformation **II**. As mentioned before,

the 12b*R*,*P* and 12b*R*,*M* relative configurations assigned to **16a** and **17d** were corroborated by a X-ray diffraction study (Figure 2).

The *P* absolute configuration of all helical dihydro[4]helicenequinones **4** and **5** synthesised by us was again initially assigned on the basis of the positive sign of their rotary power[1c] and later confirmed for derivatives **4b** and **5d** by applying the methodology described by Katz[51] based on the different O=C–C–O conformations of their *M* and *P* helycenyl (−)-camphanates which bring about a different polarity and NMR spectroscopic behaviour for each diastereoisomer. Thus, we prepared pure biscamphanates (*M*)-**19b** and (*P*)-**19b** from racemic (*P*,*M*)-**4b**, in 85% yield (Scheme 15),



Scheme 15. Synthesis of bishelicenyl camphanates **19b** and **20d** from helical quinones **4b** and **5d**.

after quinone reduction with Zn followed by esterification with (−)-camphanoyl chloride in the presence of DMAP (DMAP = 4-dimethylaminopyridine) and Et_3N and chromatographic separation. Diastereoisomer (*P*)-**19b** was also obtained, under the same experimental conditions, starting from enantiopure (*P*)-**4b**, in 74% yield. The lower R_f value (0.43) shown by diastereomer (*P*)-**19b** on silica gel (hexane/EtOAc 2:1) with respect to that of (*M*)-**19b** (R_f = 0.53), as well as the differentiated NOESY enhancements observed between H_2 and the two methyl groups at the same carbon atom of the inside camphanate, allowed us to assign the *P* absolute configuration to compound (+)-**4b**, which had resulted from the domino Diels–Alder reaction, pyrolytic sulfoxide elimination and oxidation between the diene **6b** and the enantiopure sulfinyl quinone (S*S*)-**8**. In the case of the (*M*)-**19b** helimer, only a NOE effect between one of the methyl groups and H_2 was observed.

A similar study was carried out for biscamphanates (*P*)-**20d** (R_f = 0.34 in hexane/EtOAc 2:1) and (*M*)-**20d** (R_f = 0.42 in hexane/EtOAc 2:1) obtained in 82% yield from *tert*-butyl-substituted [4]helicenequinone (*P*,*M*)-**5d**, or in the case of (*P*)-**20d** obtained from enantiopure (*P*)-**5d**, in 78% yield (Scheme 15).

Configurational stability: Experimental data showed that the configurational stability of [4]helicenequinones **4** and **5**, were dependent on the nature of the substituents of the tetracyclic skeleton, in particular, the one situated at C-12. The enantiomeric stability experimentally observed for these helical compounds indicated the following qualitative order: **4a**, **5a** < **4b**, **5b** < **4c**, **5c** ≪ **4d**, **5d**.

The interconversion between two enantiomers is a reversible first-order reaction with the same rate constant in both directions. The free energy of activation for the interconversion between helimers of compounds **4** and **5** was computed with a DFT B3LYP method (see the Supporting Information) through the evaluation of the free energy difference between two structures: one of the enantiomeric minima and the transition state connecting it to the other degenerate enantiomeric minimum. The optimised geometries of the enantiomer minimum and the transition state corresponding to compound (*P*)-**5b**, containing a methyl group at C-12 and the OEt substituent at C-6, which were used as a model, are shown in Figures 3 and 4. The relative planarity

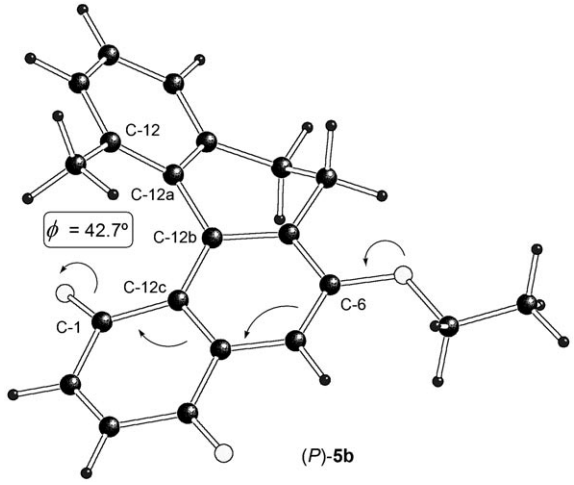


Figure 3. B3LYP-optimized structure of the minimum for (*P*)-**5b**.

of these structures can be estimated from the value of the dihedral angle φC12-C12a-C12b-C12c. The value of φ for a planar structure would be zero. The dihedral angles calculated for the optimised structure of enantiomeric minimum **5b** (Figure 3) and the transition state for the helimer inversion **TS-5b** (Figure 4) are 42.7 and 31.0°, respectively. The dihedral angle φ for the other enantiomeric form (*M*)-**5b** of the minimum is −42.7°. One could have expected the transition state connecting structures with torsional angles of 42.7 and

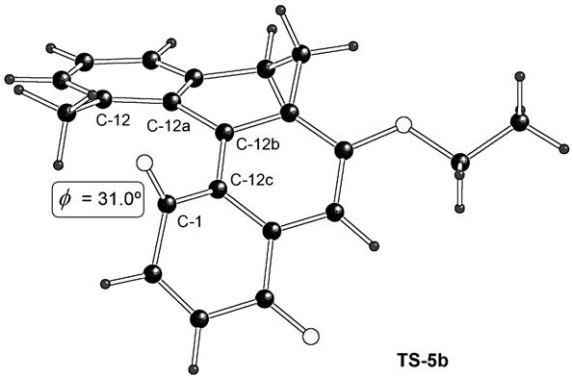


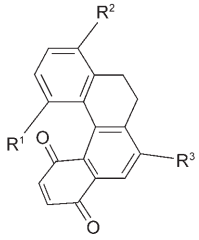
Figure 4. B3LYP-optimized structure of the transition state for the *P* to *M* inversion of **5b**, **TS-5b**.

−42.7° to have a value of φ closer to 0°. This hypothetical structure, with $\varphi = 0°$ would be too sterically constrained, while the less symmetric structure **TS-5b** with $\varphi = 31.0°$ has a lower energy content. There exists another transition structure with $\varphi = -31.0°$, defining an enantiomeric path for the interconversion with exactly the same energy barrier.

Inspection of Figure 4, also gave some idea of the movement the molecule was undergoing. There are two sources of strain in these kinds of molecules that push them away from planarity. The first one is the steric repulsion between the substituent at C-12, a methyl group in the case of **5b**, and the carbonyl at C-1 of the tetrahelicene quinone framework. The second is the strain associated with the presence of two sp^3-hybridised carbon atoms in the cyclohexadiene ring in which C-12a and C-12b carbon atoms are included. In a hypothetical structure with $\varphi = 0°$, both strains would be maximised at the same time. In a structure distorted from planarity, such as **TS-5b** (Figure 4), only the steric strain due to the interaction between the C-12 methyl and the C=O is maximized. The carbonyl oxygen atom has a maximum repulsion with the methyl at C-12, while the arrangement of the sp^3-hybridised carbon atoms is the same to that in the minimum energy structure of Figure 3. If one were to follow the reaction coordinate, a movement upwards of the quinone would involve the full reorganization of the molecule, including that of the sp^3 carbon atoms.

The other systems **4** and **5** computed behave in a similar way to **5b** and their structures will not be discussed in detail. The results of the calculations are summarized in Table 1, in which we have added the values of $\Delta G^{\ddagger}_{rac}$ for the racemisation obtained experimentally for compounds **4b**, **5b** and **4c** at 25 °C from the rate constant of racemisation, k_{rac},[52] determined by measuring the optical rotation at fixed intervals.[53] We examined polarimetrically at $\lambda = 435$ nm in a 2 dm tube with chloroform solutions of **4b** ($c = 0.0046$ g in 5 mL), **5b** ($c = 0.006$ g in 5 mL) and **4c** ($c = 0.0043$ g in 5 mL). The decrease of the optical rotation values time showed excellent straight-line relationships in each case and allowed us to obtain the rate constant (k_{rac}) from the slopes of the plot of $\log\alpha_t$ versus time.

Table 1. Calculated dihedral angle Φ and free-energy barriers of enantiomer interconversion for compounds **4** and **5**.



4a: $R^1 = R^2 = OMe$; $R^3 = H$
5a: $R^1 = R^2 = OMe$; $R^3 = OEt$
4b: $R^1 = Me$; $R^2 = R^3 = H$
5b: $R^1 = Me$; $R^2 = H$; $R^3 = OEt$
5b′: $R^1 = Me$; $R^2 = H$; $R^3 = OH$
4c: $R^1 = i$Pr; $R^2 = R^3 = H$
5c: $R^1 = i$Pr; $R^2 = H$; $R^3 = OEt$
4d: $R^1 = t$Bu; $R^2 = R^3 = H$
5d: $R^1 = t$Bu; $R^2 = H$; $R^3 = OEt$

Compd.	Φ_{min} [°]	Φ_{TS} [°]	$\Delta G^{\ddagger}_{rac}$ calcd [kcal mol^{-1}]	k_{rac} [s^{-1}][a]	$\Delta G^{\ddagger}_{rac}$ exp. [kcal mol^{-1}]
4a	39.0	35.3	22.8		
5a	38.9	36.4	23.0		
4b	43.2	30.6	25.2	1.88×10^{-6}	25.3
5b	42.7	31.0	25.9	5.06×10^{-7}	26.0
5b′	42.9	30.8	25.9		
4c	45.0	16.4	28.3	4.87×10^{-8}	27.4
5c	46.0	15.1	29.3		
4d	50.5	7.2	39.2		
5d	50.5	19.1	42.0		

[a] Kinetic data obtained at 298 K from the plot of $\log\alpha_t$ versus time.[53]

It is worth noting that the computed values for $\Delta G^{\ddagger}_{rac}$ matched qualitatively the ordering of barriers observed by experiments. Moreover, the experimental values determined from the kinetic parameters for **4b**, **4c** and **5b** matched quantitatively with those predicted by calculation. This confirmed that the enantiomeric stability is associated with the barrier of this particular interconversion mechanism. The systems with the highest steric constraint at the C-12 position due to the presence of the bulkiest *tert*-butyl substituent, **4d** and **5d**, showed the larger distortion away from planarity in the φ angle of the minimum energy geometry and have the larger barriers of inversion. The values of $\Delta G^{\ddagger}_{rac}$ calculated for the *tert*-butyl-substituted helicene quinones **4d** and **5d** were 39.2 and 42.0 kcal mol^{-1}, respectively. These values are consistent with the fact that helicenequinones **4d** and **5d** did not suffer enantiomeric inversion at room temperature and are indefinitely stable as pure enantiomers at this temperature. The order of the calculated $\Delta G^{\ddagger}_{rac}$ values, shown in Table 1, suggested that the steric strain follows the order: MeO ($\Delta G^{\ddagger}_{rac} = 22.8$ and 23.0 kcal mol^{-1}) < Me ($\Delta G^{\ddagger}_{rac} = 25.2$ and 25.9 kcal mol^{-1}) < *i*Pr ($\Delta G^{\ddagger}_{rac} = 28.3$ and 29.3 kcal mol^{-1}) << *t*Bu ($\Delta G^{\ddagger}_{rac} = 39.2$ and 40.0 kcal mol^{-1}). The methoxy substituent presents the lowest steric constraint because it can direct its methyl group away from the carbonyl, thus alleviating the steric hindrance.[54] It may seem surprising that compounds **4b** and **5b**, bearing the methyl substituent presented a relatively small difference in the $\Delta G^{\ddagger}_{rac}$ values with respect to those of the isopropyl-substituted analogues **4c** and **5c**, taking into account that the steric constraint should be higher in the later.[54] A comparison of the geometries of the minima and transition states of **5b**, **TS-5b** and **5c**, **TS-5c** revealed that the conformation of the isopropyl group around the C-12–$CH(CH_3)_2$ bond always places the two methyl substituents away from the sterically congested position, being the C–H bond of the iso-

propyl group in the *gauche* disposition with respect to the C-12a sp^2-hybridized carbon atom. In such a conformation, the unfavourable *gauche* interactions between the CH_3 groups of the isopropyl and C-12a, occurring in any other conformation, are minimized. This could justify the small differences calculated for the $\Delta G^{\ddagger}_{rac}$ of the methyl and isopropyl derivatives. In a recent paper,[11d] Yamaguchi has established that methyl groups at the 1- and 12-positions in [4]helicene derivatives exert a higher steric hindrance than the corresponding isopropyl substituents.

A comparison between the $\Delta G^{\ddagger}_{rac}$ values of the [4]helicen-equinones **4** and the 6-ethoxy-substituted analogues **5**, provided evidence for a slight increase for the barrier of activation of the latter. Thus, the calculated barriers of interconversion for derivatives **5** ($\Delta G^{\ddagger}_{rac\,5a} - \Delta G^{\ddagger}_{rac\,4a} = 0.2$), ($\Delta G^{\ddagger}_{rac\,5b} - \Delta G^{\ddagger}_{rac\,4b} = 0.7$), ($\Delta G^{\ddagger}_{rac\,5c} - \Delta G^{\ddagger}_{rac\,4c} = 1.0$) ($\Delta G^{\ddagger}_{rac\,5d} - \Delta G^{\ddagger}_{rac\,4d} = 2.8$), all bearing the ethoxy substituent at C-6, are higher than those calculated for the C-6 hydrogen-substituted helicene quinones **4**. This evidenced a small but significant role of the electron-donating substitutent in the configurational stability of these systems which must hinder the enantiomeric inversion. Comparison of the geometries in Figures 3 and 4 shows that the ethoxy group situated at C-6 has a very similar conformation in both the minimum energy structure TS-**5a** and the transition state TS-**5b**, being very far from the region of the molecule in which steric congestion could hinder the interconversion. Thus, no steric effect of this substituent can be invoked to explain its effect which must be probably of electronic origin, due to the presence of the oxygen atom directly attached to the aromatic system in a position (C-6) in which the electron-donating effect can be transferred to the C-1 position, thus increasing the electron density of the C(1)=O (Figure 3). This hypothesis was further analysed by a supplementary calculation on a new system **5b′**, in which the ethoxy group at the C-6 position (R^3 in Table 1) of the C-12 methyl-substituted [4]helicene quinone **5b** was replaced by an OH group. The computed value was $\Delta G^{\ddagger}_{rac\,5b'} = 25.9$ kcal mol^{-1}, only 0.02 kcal mol^{-1} lower than that of **5b** and 0.6 kcal mol^{-1} higher than that of **4b**. Therefore, the effect of this substituent is essentially electronic, confirming the observation from the computed geometries.

An additional observation resulting from calculation is that the value of the torsion angle φ in the transition states decreases as the free-energy barrier increases. This suggests that when steric bulk is higher, the system gains less by distorting from the ideal symmetric structure of the transition state with a value of 0° for φ.

Conclusion

We have succeeded in the convergent synthesis of enantiopure 5,7,8,12b-tetrahydro[4]helicene quinones **16** and **17** and the 7,8-dihydro analogues **4** and **5**, bearing different sterically demanding susbtituents at C-12 (OMe, Me, *i*Pr, *t*Bu), from reaction between (S*S*)-2-(p-tolylsulfinyl)-1,4-benzoquinone (**8**) and the appropriately 5-substituted 3-vinyl-1,2-dihydronaphathalenes **6** or **7**. The process always occurs in a one-pot domino sequence by starting from a highly π-facial diastereoselective Diels–Alder reaction, followed by the pyrolytic elimination of the sulfoxide. A detailed structural study of the resulting compounds **16** and **17** provided evidence for the existence of a different conformation in the 1,4-dihydroaromatic B ring that is dependent on the nature of the C-12b substituent. In the isopropyl-substituted derivative, two different conformers could be isolated, thus showing that in these molecules central and helical chiralities coexist. When the starting diene partner **7** bears an electron-donating group, such as OEt, the domino sequence included a third transformation, the aromatisation of the 1,4-dihydroaromatic ring, allowing the one-pot synthesis of helical quinones **5**. We have also established that the configurational stability of tetrahelicenes **4** and **5** is mainly controlled by the size of the substituent at C-12, with the *tert*-butyl-substituted derivatives **4d** and **5d** the only compounds that are indefinitely stable at room temperature. The values of the racemisation barriers calculated from computations, confirmed the main role of the steric effects in the configurational integrity of these helical quinones. These results also provided evidence for a small but significant influence electronic effects when an electron-donating group is situated at C-6 of the aromatic system. The higher electron density of the C-1 carbonyl atom of the quinone in such 6-ethoxy-substituted systems could be the origin of the higher values for their racemisation barriers.

Experimental Section

General: Melting points were obtained in open capillary tubes. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, by using $CDCl_3$ as a solvent and tetramethylsilane as the internal standard. All reactions were monitored by TLC, which was performed on precoated silica gel 60 F_{254} plates. Flash column chromatography was effected with silica gel 60 (230–240 mesh) from Macherey–Nagel. Eluting solvents are indicated in the text. HRMS were measured at 70 eV. Reagent quality solvents, such as THF, diethyl ether and acetonitrile, were dry purchased and kept under an argon atmosphere over activated 4 Å molecular sieves. For toluene and benzene, activated 3 Å molecular sieves were used. CH_2Cl_2 was predried over $CaCl_2$, distilled over P_2O_5 and carefully kept under an argon atmosphere. For routine workup, hydrolysis was carried out with water, extractions with CH_2Cl_2 and solvent drying with $MgSO_4$. The values of *ee* were determined by chiral HPLC by using columns Daicel Chiracel OD, AS or AD and/or by NMR spectroscopy by using chiral lanthanide shift reagents.

General procedure A: **Aromatization of 1,2-dihydronaphthalenes**: A solution of DDQ (1.89 g, 8.3 mmol) in CH_2Cl_2 (35 mL) was added to a solution of the corresponding dihydronaphthalene (6.9 mmol) in CH_2Cl_2 (35 mL). The mixture was stirred for 10 min and then washed with several portions of an aqueous saturated solution of $NaHCO_3$. After workup and flash chromatography, pure naphthalenes were obtained.

General procedure B: **Synthesis of β-tetralones**: To a well-stirred refluxing solution of the corresponding β-methoxynaphthalene (6.2 mmol) in EtOH (66 mL), small portions of Na (40–60 equiv) were carefully added under argon. After the time indicated in each case, the reaction mixture was cooled to 0 °C and acidified with 35% HCl until pH ≈1. The mixture was stirred for 1 h at room temperature, diluted with CH_2Cl_2, ex-

tracted and the organic layer washed with an aqueous saturated solution of $NaHCO_3$. After workup and flash chromatography, pure 2-tetralones were obtained.

General procedure C: **Synthesis of enol triflates**: A solution of KHMDS (HMDS = hexamethyldisilazane) in toluene (0.5 M, 8 mL, 4.0 mmol) was added to a solution of the corresponding β-tetralone (3.3 mmol) and *N*-phenyl-trifluoromethanesulfonimide, Tf_2NPh, (1.20 g, 3.3 mmol) in THF (31 mL) at −78 °C under an argon atmosphere. The reaction mixture was stirred at this temperature for the time indicated in each case, hydrolysed with water and allowed to warm to RT. After extraction with EtOAc, workup and flash chromatography, pure enol triflates were obtained.

General procedure D: **Synthesis of 3-vinyl-1,2-dihydronaphthalenes**: The corresponding vinylstannane (0.35 mmol) was added to a well-stirred mixture of the trifluoromethanesulfonate derivative (0.35 mmol), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol) and dry LiCl (81 mg, 1.75 mmol) in THF (3 mL) under an argon atmosphere. The reaction mixture was refluxed for the reaction time indicated in each case, cooled to room temperature, diluted with hexane (12 mL) and washed with a 10% aqueous solution of NH_4OH and water. After workup and flash chromatography on silica gel or alumina, pure dienes were obtained.

General procedure E: **Diels–Alder reactions**: A solution of (*SS*)-**8**[32] (0.32–0.48 mmol, 80–120 mg, 2 or 3 equiv) in CH_2Cl_2 (2 mL) was added to a solution of the corresponding diene (0.16 mmol) in CH_2Cl_2 (2 mL) at the temperature indicated in each case under an argon atmosphere. After the time indicated in each case, the solvent was evaporated and the residue was purified by flash chromatography.

General procedure F: **Diels–Alder reactions under high pressure conditions**: A solution of (*SS*)-**8**[32] (120 mg, 0.48 mmol, 3 equiv) in CH_2Cl_2 (2 mL) was added to a solution of the corresponding diene (0.16 mmol) in CH_2Cl_2 (2 mL) under an argon atmosphere, and the mixture was submitted to high pressure conditions (8 Kbar). After the time indicated in each case, the solvent was evaporated and the residue was purified by flash chromatography.

General procedure G: **Synthesis of helicene biscamphanates**: Et_3N (516 μL, 3.68 mmol) was added to a mixture of the corresponding helicene quinone (0.18 mmol), activated Zn (286 mg, 4.38 mmol) and (−)-camphanoyl chloride (379 mg, 1.75 mmol) in CH_2Cl_2 (7.4 mL) under an argon atmosphere. The reaction mixture was stirred for 24 h, filtered through Celite and the organic solution was washed with saturated aqueous solution of $NaHCO_3$, 10% HCl and water. After workup and flash chromatography, pure helicene biscamphanates were obtained.

6-Methoxy-4-methyl-1,2-dihydronaphthalene (12b): MeMgCl in ether (3.0 M, 1.2 mL, 3.55 mmol) was slowly added to a solution of commercially available 7-methoxy-1-tetralone (**11**) (250 mg, 1.42 mmol) in Et_2O (5 mL) under an argon atmosphere. After stirring for 5 h, the mixture was refluxed for 2 h, cooled to 0 °C and hydrolysed with a saturated aqueous solution of NH_4Cl. After extraction with ethyl ether and workup, the residue was dissolved in CH_2Cl_2 (5 mL) and 35% HCl (5 mL) was added. After stirring the mixture for 15 h, the organic layer was separated and washed with a saturated solution of $NaHCO_3$. After workup and flash chromatography (EtOAc/hexane 1:4), compound **12b**[33a] was obtained as a colourless oil in 93% yield. ^{1}H NMR: δ = 2.08 (s, 3H), 2.27 (m, 2H), 2.73 (dd, J = 7.9, 8.1 Hz, 2H), 3.84 (s, 3H), 5.91 (t, J = 4.6 Hz, 1H), 6.72 (dd, J = 8.1, 2.6 Hz, 1H), 6.85 (d, J = 2.6 Hz, 1H), 7.08 ppm (d, J = 8.1 Hz, 1H); ^{13}C NMR: δ = 19.2, 23.5, 27.4, 55.3, 109.6, 110.9, 126.0, 127.8, 128.5, 132.1, 136.9, 158.4 ppm; MS (EI): m/z (%): 115 (48), 129 (63), 144 (28), 159 (79), 172 (100), 174 $[M]^+$ (63); MS (EI): m/z: calcd for $C_{12}H_{14}O$: 174.10446; found: 174.10417.

7-Methoxy-1-methylnaphthalene (13b): Compound **13b**[33c] was obtained from **12b** by following general procedure A (eluent: EtOAc/hexane 1:70) in 97% yield as a white solid. M.p. 40–42 °C (CH_2Cl_2); ^{1}H NMR: δ = 2.65 (s, 3H), 3.94 (s, 3H), 7.16 (dd, J = 8.9, 2.4 Hz, 1H), 7.23 (d, J = 2.4 Hz, 1H), 7.24 (dd, J = 7.5, 6.9 Hz, 1H), 7.29 (dd, J = 6.9, 0.6 Hz, 1H), 7.64 (dd, J = 7.5, 0.6 Hz, 1H), 7.75 ppm (d, J = 8.9 Hz, 1H); ^{13}C NMR: δ = 19.6, 55.3, 102.7, 117.9, 123.3, 126.1, 127.1, 128.9, 130.0, 132.9, 133.6, 157.6 ppm; MS (EI): m/z (%): 63 (6), 86 (21), 102 (5), 115 (9), 141 (10), 157 (7), 172 (100) $[M]^+$; MS (EI): m/z: calcd for $C_{12}H_{12}O$: 172.08881; found: 172.08916.

7-Methoxy-1-isopropylnaphthalene (13c): $BF_3{\cdot}OEt_2$ (21.6 mL, 170.5 mmol) was added to a solution of commercially available 7-methoxy-1-tetralone (**11**) (7.50 g, 42.6 mmol) in dry Et_2O (120 mL) under an argon atmosphere. After stirring for 2 h, the reaction mixture was cooled to −20 °C and added dropwise to a freshly prepared solution of *i*PrMgCl (from 9.6 mL of *i*PrBr and 2.27 g of Mg turnings in 90 mL of Et_2O for 30 min at reflux) at −65 °C. The mixture was allowed to reach room temperature, stirred for 2 h and hydrolysed at 0 °C with a saturated aqueous solution of NH_4Cl. After extraction with Et_2O and workup, a residue containing 6-methoxy-4-isopropyl-1,2-dihydronaphthalene (**12c**) and 7-methoxy-1-isopropylnaphthalene (**13c**) was obtained. This mixture was dissolved in CH_2Cl_2 (210 mL) and treated with a solution of DDQ (11.6 g, 51.0 mmol) in CH_2Cl_2 (250 mL), following general procedure A (eluent: EtOAc/hexane 1:70). Compound **13c**[34] was obtained in 77% yield as a colourless oil. ^{1}H NMR: δ = 1.69 (d, J = 6.9 Hz, 6H), 3.94 (sept, J = 6.9 Hz, 1H), 4.13 (s, 3H), 7.44 (dd, J = 8.9, 2.4 Hz, 1H), 7.58 (dd, J = 8.1, 7.5 Hz, 1H), 7.62 (d, J = 8.9 Hz, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.85 (dd, J = 7.5, 1.4 Hz, 1H), 8.00 ppm (d, J = 8.1 Hz, 1H); ^{13}C NMR: δ = 23.2, 28.6, 55.0, 102.1, 117.4, 122.1, 123.3, 126.0, 129.3, 130.3, 132.3, 143.0, 157.5 ppm; MS (EI): m/z (%): 115 (19), 128 (7), 141 (16), 154 (12), 170 (15), 200 $[M]^+$ (56); MS (EI): m/z: calcd for $C_{12}H_{12}O$: 200.12011; found: 200.12083.

1-*tert*-Butyl-7-methoxy-1,2,3,4-tetrahydronaphthalen-1-ol (14): *t*BuMgCl in Et_2O (2.0 M, 17 mL, 34.0 mmol) was slowly added to a solution of commercially available 7-methoxy-1-tetralone (**11**) (3.0 g, 17.0 mmol) in Et_2O (8 mL) under an argon atmosphere. After stirring for 48 h, the mixture was hydrolysed at 0 °C with 10% HCl (100 mL) and stirred for 30 min at room temperature. The organic layer was extracted with Et_2O and washed with water and a saturated aqueous solution of $NaHCO_3$. After workup and flash chromatography (eluent: EtOAc/hexane 1:20), compound **14** was obtained in 56% yield as a white solid. M.p. 53–55 °C (CH_2Cl_2/pentane); ^{1}H NMR: δ = 0.97 (s, 9H), 1.51 (m, 1H), 1.83 (m, 2H), 1.87 (br s, 1H), 2.28 (ddd, J = 3.4, 10.5, 15.3 Hz, 1H), 2.51 (ddd, J = 4.5, 9.1, 15.3 Hz, 1H), 2.65 (dt, J = 15.0, 4.5 Hz, 1H), 3.78 (s, 3H), 6.73 (dd, J = 2.6, 8.3 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H), 7.20 ppm (d, J = 2.6 Hz, 1H); ^{13}C NMR: δ = 21.2, 25.8, 29.7, 36.7, 39.9, 55.1, 76.1, 112.6, 113.8, 128.7, 146.3, 146.3, 156.9 ppm; MS (EI): m/z (%): 91 (6), 121 (22), 159 (8), 177 (100), 234 (10) $[M]^+$; MS (EI): m/z: calcd for $C_{15}H_{22}O_2$: 234.16198; found: 234.16193.

4-*tert*-Butyl-6-methoxy-1,2-dihydronaphthalene (12d): 10% H_2SO_4 (0.11 mL) was added to a solution of carbinol **14** (50 mg, 0.21 mmol) in benzene (1 mL). After refluxing for 1 h, the reaction mixture was cooled to room temperature and washed with a saturated aqueous solution of $NaHCO_3$ and water. After workup and flash chromatography (eluent: EtOAc/hexane 1:40), compound **12d** was obtained in 85% yield as a yellow oil. ^{1}H NMR: δ = 1.36 (s, 9H), 2.15 (dt, J = 4.8, 8.1 Hz, 2H), 2.57 (t, J = 8.1 Hz, 2H), 3.81 (s, 3H), 6.12 (t, J = 4.8 Hz, 1H), 6.68 (dd, J = 2.6, 8.3 Hz, 1H), 7.09 (d, J = 8.3 Hz, 1H), 7.24 ppm (d, J = 2.6 Hz, 1H); ^{13}C NMR: δ = 23.8, 28.3, 31.0, 34.9, 55.2, 109.7, 113.2, 124.7, 127.9, 130.7, 135.6, 144.7, 157.4 ppm; MS (EI): m/z (%): 69 (33), 84 (55), 105 (32); 115 (41), 128 (28), 149 (25), 159 (85), 175 (39), 189 (25), 201 (46), 216 (100) $[M]^+$; MS (EI): m/z: calcd for $C_{15}H_{20}O$: 216.15141; found: 216.15199.

1-*tert*-Butyl-7-methoxynaphthalene (13d): Compound **13d** was obtained from **12d** by following general procedure A (eluent: EtOAc/hexane 1:20) in 99% yield as a yellow oil. ^{1}H NMR: δ = 1.68 (s, 9H), 3.98 (s, 3H), 7.19 (dd, J = 2.2, 8.9 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.53 (dd, J = 1.1, 7.3 Hz, 1H), 7.68 (br d, J = 7.9 Hz, 1H), 7.81 (d, J = 2.3 Hz, 1H), 7.80 ppm (d, J = 8.9 Hz, 1H); ^{13}C NMR: δ = 31.4, 35.8, 55.2, 106.8, 116.6, 123.0, 123.7, 127.1, 130.4, 130.9, 132.4, 144.5, 156.2 ppm; MS (EI): m/z (%): 57 (73), 71 (41), 84 (25), 105 (10), 113 (17), 149 (100), 167 (42), 199 (28), 214 (14) $[M]^+$; MS (EI): m/z: calcd for $C_{15}H_{18}O$: 214.13637; found: 214.13576.

8-Methyl-3,4-dihydro-2(1*H*)naphthalenone (10b): Compound **10b**[39] was obtained from **13b** by following general procedure B (4 h, eluent: EtOAc/hexane 1:20) in 72% yield as a white solid. M.p. 71–73 °C (CH_2Cl_2/hexane); ^{1}H NMR: δ = 2.29 (s, 3H), 2.60 (t, J = 6.8 Hz, 2H), 3.09 (t, J = 6.8 Hz, 2H), 3.53 (s, 2H), 7.11 ppm (m, 3H); ^{13}C NMR: δ = 19.0, 28.6, 38.1, 41.3, 125.2, 126.1, 128.0, 131.5, 135.5, 135.9, 201.1 ppm; MS (EI): m/z (%): 65 (11), 77 (20), 91 (28), 115 (27), 118 (100), 146 (22), 160

(48) $[M]^+$; MS (EI): *m/z*: calcd for $C_{11}H_{12}O$: 160.08882; found: 160.08894.

8-Isopropyl-3,4-dihydro-2(1*H*)naphthalenone (10c): Compound **10c** was obtained from **13c** by following general procedure B (2 h, eluent: EtOAc/hexane 1:20) in 65% yield as a dark yellowish oil. ^{1}H NMR: δ = 1.24 (d, J = 6.7 Hz, 6H), 2.57 (t, J = 6.8 Hz, 2H), 3.08 (t, J = 6.8 Hz, 2H), 3.00–3.15 (sept, J = 6.7 Hz, 1H), 3.63 (s, 2H), 7.09 (t, J = 4.6 Hz, 1H), 7.17–7.22 ppm (2d, J = 4.6 Hz, 2H); ^{13}C NMR: δ = 23.1, 28.7, 29.1, 38.0, 41.2, 123.4, 125.3, 126.7, 130.3, 136.6, 146.2, 211.0 ppm; MS (EI): *m/z* (%): 115 (73), 131 (85), 141 (16), 173 (86), 188 (100) $[M]^+$; MS (EI): *m/z*: calcd for $C_{13}H_{16}O$: 188.12011; found: 188.11987.

8-*tert*-Butyl-3,4-dihydro-2(1*H*)naphthalen-2-one (10d): Compound **10d** was obtained from **13d** by following general procedure B (5 h, eluent: EtOAc/hexane 1:9) in 99% yield as a yellow solid. M.p. 43–45 °C (CH_2Cl_2/pentane); ^{1}H NMR: δ = 1.41 (s, 9H), 2.48 (t, J = 6.7 Hz, 2H), 3.06 (t, J = 6.7 Hz, 2H), 3.89 (s, 2H), 7.12 (dd, J = 2.0, 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.33 ppm (dd, J = 2.0, 7.5 Hz, 1H); ^{13}C NMR: δ = 29.3, 31.2, 35.3, 36.9, 45.7, 124.7, 125.7, 126.3, 131.4, 138.9, 147.7, 211.4 ppm; MS (EI): *m/z* (%): 55 (21), 77 (36), 91 (66), 115 (100), 129 (88), 143 (54), 161 (93), 183 (76), 202 (84) $[M]^+$; MS (EI): *m/z*: calcd for $C_{14}H_{18}O$: 202.13576; found 202.13628.

5,8-Dimethoxy-3,4-dihydronaphthalen-2-yl trifluoromethanesulfonate (9a): Compound **9a** was obtained from 2-tetralone **10a**[40] by following general procedure C (1 h, eluent EtOAc/hexane 1:9) in 60% yield as a white solid. M.p. 26–28 °C (EtOAc/hexane); ^{1}H NMR: δ = 2.62 (t, J = 8.6 Hz, 2H), 3.03 (t, J = 8.6 Hz, 2H), 3.78 (s, 6H), 6.67, 6.75 (AB system, J = 8.9 Hz, 2H), 6.85 ppm (s, 1H); ^{13}C NMR: δ = 21.7, 25.6, 55.8, 55.9, 109.3, 111.3, 113.1, 118.5 (q, J = 328.1 Hz), 122.2, 129.9, 130.9, 132.1, 149.5, 150.4 ppm; MS (EI): *m/z* (%): 69 (100), 91 (18), 115 (49), 129 (45), 143 (26), 157 (56), 183 (88), 317 (19), 334 (40) $[M]^+$; MS (EI): *m/z*: calcd for $C_{13}H_{13}SO_5F_3$: 334.08505; found: 334.08548.

8-Methyl-3,4-dihydronaphthalen-2-yl trifluoromethanesulfonate (9b): Compound **9b** was obtained from 2-tetralone **10b** by following general procedure C (6 h, eluent: EtOAc/hexane 1:20) in 91% yield as a colourless oil. ^{1}H NMR: δ = 2.32 (s, 3H), 2.67 (t, J = 8.5 Hz, 2H), 3.04 (t, J = 8.5 Hz, 2H), 6.69 (s, 1H), 7.00 (d, J = 7.5 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 7.11 ppm (t, J = 7.5 Hz, 1H); ^{13}C NMR: δ = 18.7, 26.2, 29.0, 115.6, 116.5, 122.1 (q, J = 212.1 Hz), 125.2, 127.9, 128.6, 129.3, 134.4, 150.1 ppm; MS (EI): *m/z* (%): 69 (8), 115 (21), 131 (100), 159 (42), 292 (23) $[M]^+$; MS (EI): *m/z*: calcd for $C_{12}H_{11}F_3O_3S$: 292.03802; found: 292.03810.

8-Isopropyl-3,4-dihydronaphthalene-2-yl trifluoromethanesulfonate (9c): Compound **9c** was obtained from 2-tetralone **10c** by following general procedure C (1 h, eluent: EtOAc/hexane 1:70) in 88% yield as a colourless oil. ^{1}H NMR: δ = 1.27 (d, J = 6.9 Hz, 6H), 2.68 (t, J = 8.3 Hz, 2H), 3.06 (t, J = 8.3 Hz, 2H), 3.12 (sept, J = 6.9 Hz, 1H), 6.84 (s, 1H), 7.02 (dd, J = 6.1, 5.7 Hz, 1H), 7.15–7.25 ppm (m, 2H); ^{13}C NMR: δ = 23.3, 26.2, 28.8, 29.5, 115.3, 118.6 (q, J = 319 Hz), 123.7, 125.2, 128.1, 128.3, 133.4, 145.0, 150.5 ppm; MS (EI): *m/z* (%): 69 (22), 97 (10), 117 (53), 129 (29), 143 (23), 169 (47), 187 (56), 320 $[M]^+$ (30); MS (EI): *m/z*: calcd for $C_{14}H_{15}F_3O_3S$: 320.06940; found: 320.06958.

8-*tert*-Butyl-3,4-dihydronaphthalene-2-yl trifluoromethanesulfonate (9d): Compound **9d** was obtained from 2-tetralone **10d** by following general procedure C (2 h, eluent hexane) in 91% yield as a white solid. M.p. 26–27 °C (hexane); ^{1}H NMR: δ = 1.42 (s, 9H), 2.63, 3.03 (2, J = 7.9 Hz t, 4H), 7.02 (dd, J = 2.0, 7.5 Hz, 1H), 7.13 (t, J = 7.3 Hz, 1H), 7.17 (s, 1H), 7.28 ppm (dd, J = 2.0, 7.5 Hz, 1H); ^{13}C NMR: δ = 25.8, 29.9, 31.6, 35.2, 118.3, 119.1 (q, J = 319 Hz), 124.7, 125.9, 127.9, 128.9, 134.8, 146.9, 149.0 ppm; MS (EI): *m/z* (%): 69 (100), 91 (18), 115 (49), 129 (45), 143 (26), 157 (56), 183 (88), 317 (19), 334 $[M]^+$ (40); MS (EI): *m/z*: calcd for $C_{15}H_{17}F_3O_3S$: 334.08505; found: 334.08548.

5,8-Dimethoxy-3-vinyl-1,2-dihydronaphthalene (6a): Compound **6a** was obtained from enol triflate **9a** and vinyl tributyl stannane by following general procedure D (1.5 h, eluent: EtOAc/hexane 1:9) in 82% yield as a colourless oil. ^{1}H NMR: δ = 2.42 (t, J = 7.9 Hz, 2H), 2.84 (t, J = 8.3 Hz, 2H), 3.80 (s, 6H), 5.12 (d, J = 10.7 Hz, 1H), 5.33 (d, J = 17.4 Hz, 1H), 6.62 (dd, J = 10.7, 17.4 Hz, 1H), 6.66, 6.69 (AB system, J = 8.9 Hz, 2H), 6.81 ppm (s, 1H); ^{13}C NMR: δ = 20.4, 21.3, 56.0, 109.9, 112.4, 122.0, 124.5, 124.9, 125.8, 137.0, 138.9, 149.8, 150.4 ppm; MS (EI): *m/z* (%): 141 (7), 175 (7), 201 (20), 216 (100) $[M]^+$; MS (EI): *m/z*: calcd for $C_{14}H_{18}O$: 216.11503; found: 216.11430.

5-Methyl-3-vinyl-1,2-dihydronaphthalene (6b): Compound **6b** was obtained from enol triflate **9b** and vinyl tributyl stannane by following general procedure D (7 h, eluent: EtOAc/hexane 1:40) in 97% yield as a colourless oil. ^{1}H NMR: δ = 2.37 (s, 3H), 2.45 (t, J = 8.1 Hz, 2H), 2.84 (t, J = 8.1 Hz, 2H), 5.16 (d, J = 10.9 Hz, 1H), 5.37 (d, J = 17.4 Hz, 1H), 6.62 (dd, J = 10.9, 17.4 Hz, 1H), 6.66 (s, 1H), 6.99 (d, J = 6.25, 1H), 7.02 (t, J = 6.25 Hz, 1H), 7.05 ppm (d, J = 6.25 Hz, 1H); ^{13}C NMR: δ = 19.0, 22.0, 28.3, 112.7, 125.1, 126.6, 128.3, 132.6, 133.6, 135.8, 137.8, 138.9 ppm; MS (EI): *m/z* (%): 115 (9), 129 (26), 142 (12), 155 (30), 170 $[M]^+$ (100); MS (EI): *m/z*: calcd for $C_{13}H_{14}$: 170.10955; found: 170.10907.

5-Isopropyl-3-vinyl-1,2-dihydronaphthalene (6c): Compound **6c** was obtained from enol triflate **9c** and vinyl tributyl stannane by following general procedure D (7 h, eluent: hexane) in 81% yield as a colourless oil. ^{1}H NMR: δ = 1.31 (d, J = 6.9 Hz, 6H), 2.48 (t, J = 8.1 Hz, 2H), 2.89 (t, J = 8.1 Hz, 2H), 3.35 (sept, J = 6.9 Hz, 1H), 5.20 (d, J = 10.7 Hz, 1H), 5.41 (d, J = 17.4 Hz, 1H), 6.67 (dd, J = 10.7, 17.4 Hz, 1H), 6.83 (s, 1H), 7.04 (dd, J = 7.7, 6.3 Hz, 1H), 7.11–7.21 ppm (m, 2H); ^{13}C NMR: δ = 21.9, 23.5, 28.3, 28.8, 112.5, 123.0, 124.5, 125.0, 127.0, 131.3, 136.1, 138.0, 139.1, 144.0 ppm; MS (EI): *m/z* (%): 57 (13), 129 (14), 141 (21), 155 (36), 183 (50), 198 (100) $[M]^+$; MS (EI): *m/z*: calcd for $C_{15}H_{18}$: 198.14085; found: 198.14099.

5-*tert*-Butyl-3-vinyl-1,2-dihydronaphthalene (6d): Compound **6d** was obtained from enol triflate **9d** and vinyl tributyl stannane by following general procedure D (2 h, eluent: hexane) in 67% yield as a white solid. M.p. 54–56 °C (CH_2Cl_2/hexane); ^{1}H NMR: δ = 1.55 (s, 9H), 2.48 (t, J = 8.3 Hz, 2H), 2.91 (t, J = 8.3 Hz, 2H), 5.24 (d, J = 10.7 Hz, 1H), 5.44 (d, J = 17.4 Hz, 1H), 6.72 (dd, J = 10.7, 17.4 Hz, 1H), 7.10 (dd, J = 1.6, 7.3 Hz, 1H), 7.15 (t, J = 7.3 Hz, 1H), 7.19 (s, 1H), 7.33 ppm (dd, J = 1.8, 7.7 Hz, 1H); ^{13}C NMR: δ = 21.5, 29.4, 31.7, 35.4, 112.4, 124.1, 125.7, 126.4, 127.9, 132.3, 136.8, 137.6, 139.2, 145.7 ppm; MS (EI): *m/z* (%): 115 (9), 128 (16), 141 (20), 155 (45), 169 (22), 197 (42), 212 (100) $[M]^+$; MS (EI): *m/z*: calcd for $C_{16}H_{20}$: 212.15650; found: 212.15742.

5,8-Dimethoxy-3-(1′-ethoxyvinyl)-1,2-dihydronaphthalene (7a): Compound **7a** was obtained from enol triflate **9a** and 1-ethoxyvinyl tributyl stannane by following general procedure D (1.5 h, alumina, eluent: EtOAc/hexane 1:4) in 50% yield as a very unstable colourless oil, which was immediately used in the next step. ^{1}H NMR: δ = 1.43 (t, J = 7.0 Hz, 3H), 2.44 (dt, J = 8.6, 2.1 Hz, 2H), 2.83 (t, J = 8.69, 1.9 Hz, 2H), 3.79 (s, 3H), 3.80 (s, 3H), 3.84 (q, J = 7.0 Hz, 2H), 4.21 (d, J = 2.4 Hz, 1H), 4.42 (t, J = 2.4 Hz, 1H), 6.65, 6.71 (AB system, J = 8.9 Hz, 2H), 7.33 ppm (s, 1H).

5-Methyl-3-(1′-ethoxyvinyl)-1,2-dihydronaphthalene (7b): Compound **7b** was obtained from enol triflate **9b** and 1-ethoxyvinyl tributyl stannane by following general procedure D (4 h, alumina, eluent: pentane) in 60% yield as a very unstable colourless oil, which was immediately used in the next step. ^{1}H NMR: δ = 1.43 (t, J = 6.9 Hz, 3H), 2.38 (s, 3H), 2.46 (dd, J = 7.5, 8.5 Hz, 2H), 2.83 (dd, J = 7.5, 8.5 Hz, 2H), 3.90 (q, J = 6.9 Hz, 2H), 4.23 (d, J = 2.5 Hz, 1H), 4.45 (t, J = 2.5 Hz, 1H), 6.98 (d, J = 6.9 Hz, 1H), 7.00 (dd, J = 6.9 Hz, 1H), 7.01 (t, J = 6.9 Hz, 1H), 7.21 ppm (s, 1H); MS (EI): *m/z* (%): 77 (9), 115 (44), 128 (76), 143 (100), 171 (94), 186 (20), 214 $[M]^+$ (58); MS (EI): *m/z*: calcd for $C_{15}H_{18}O$: 214.13576; found: 214.13548.

5-Isopropyl-3-(1′-ethoxyvinyl)-1,2-dihydronaphthalene (7c): Compound **7c** was obtained from enol triflate **9c** and 1-ethoxyvinyl tributyl stannane by following general procedure D (4 h, alumina, eluent: pentane) in 65% yield as a very unstable colourless oil, which was immediately used in the next step. ^{1}H NMR: δ = 1.26 (d, J = 7.5 Hz, 6H), 1.43 (t, J = 7.0 Hz, 3H), 2.37–2.63 (m, 2H), 2.73–2.89 (m, 2H), 3.32 (sept, J = 7.5 Hz, 1H), 3.90 (q, J = 7.0 Hz, 2H), 4.23 (d, J = 2.4 Hz, 1H), 4.45 (t, J = 2.4 Hz, 1H), 6.93–7.03 (d, J = 5.6 Hz, 1H), 6.99 (d, J = 5.6 Hz, 1H), 7.13 (t, J = 5.6 Hz, 1H), 7.33 ppm (s, 1H); MS (EI): *m/z* (%): 77 (20), 129 (35), 155 (38), 171 (27), 199 (32), 215 (100), 243 (95) $[M]^+$; MS (EI): *m/z*: calcd for $C_{17}H_{22}O$: 243.17489; found: 243.17473.

5-*tert*-Butyl-3-(1′-ethoxyvinyl)-1,2-dihydronaphthalene (7d): Compound **7d** was obtained from enol triflate **9d** and 1-ethoxyvinyl tributyl stannane by following general procedure D (2 h, alumina, eluent: pentane) in 60%

yield as a very unstable colourless oil, which was immediately used in the next step. ^{1}H NMR: δ = 1.43 (t, J = 6.9 Hz, 3H), 1.46 (s, 9H), 2.41 (t, J = 7.9 Hz, 2H), 2.83 (t, J = 7.9 Hz, 2H), 3.89 (q, J = 6.9 Hz, 2H), 4.23 (d, J = 2.6, 1H), 5.44 (t, J = 2.6 Hz, 1H), 7.02 (dd, J = 1.2, 7.7 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 7.25 (dd, J = 1.4, 7.7 Hz, 1H), 7.71 ppm (s, 1H); MS (EI): m/z (%): 84 (22), 115 (32), 128 (61), 141 (52), 153 (44), 169 (72), 185 (9), 213 (100), 228 (19), 243 (60), 256 (17) $[M]^+$; MS (EI): m/z: calcd for $C_{18}H_{24}O$: 256.18272; found: 256.18287.

(12b*R*,*P*)-9,12-Dimethoxy-5,7,8,12b-tetrahydrobenzo[*c*]phenanthrene-1,4-dione (16a): Compound (12b*R*,*P*)-**16a** was obtained from diene **6a** by following general procedure E (2 equiv of (S*S*)-**8**, −20 °C, 48 h, eluent: acetone/hexane 1:6) in 55% yield as an orange solid. M.p. 164–166 °C (CH_3CN); $[\alpha]_D^{20}$ = +273 (c = 0.14 in $CHCl_3$); ^{1}H NMR (500 MHz): δ = 2.31 (dt, J = 16.9, 8.9 Hz, 1H), 2.54 (dt, J = 15.8, 9.7 Hz, 1H), 2.70–2.81 (m, 1H), 2.97 (ddd, J = 24.0, 3.3, 3.4 Hz, 1H), 3.13–3.25 (m, 1H), 3.35 (ddd, J = 13.7, 7.4, 1.9 Hz, 1H), 3.46 (s, 3H), 3.77 (s, 3H), 4.49 (t, J = 6.6 Hz, 1H), 5.52 (t, J = 1.2 Hz, 1H), 6.65, 6.70 (AB system, J = 8.9 Hz, 2H), 6.75, 6.85 ppm (AB system, J = 10.1 Hz, 2H); ^{13}C NMR: δ = 20.4, 24.6, 27.9, 35.7, 56.1, 57.4, 109.3, 111.7, 115.6, 128.8, 130.3, 134.8, 135.7, 136.3, 137.0, 143.4, 148.8, 151.6, 186.2, 187.1 ppm; MS (EI): m/z (%): 55 (17), 77 (10), 94 (7), 115 (9), 152 (19), 165 (19), 177 (24), 202 (7), 221 (16), 235 (9), 249 (28), 260 (35), 275 (17), 209 (100), 322 $[M]^+$ (95); MS (EI): m/z: calcd for $C_{20}H_{18}O_4$: 322.12051; found: 322.12039; elemental analysis calcd (%) for $C_{20}H_{18}O_4$: C 74.52, H 5.63; found: C 72.91, H 6.10.

(*P*,*M*)-9,12-Dimethoxy-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (4a): Compound (*P*,*M*)-**4a** was obtained from (12b*R*,*P*)-**16a** by following general procedure A (6 h, eluent: acetone/hexane 1:6) in 59% yield as an orange solid. M.p. 196–198 °C (CH_3CN); $[\alpha]_D^{20}$ = 0 (c = 0.03 in $CHCl_3$); ^{1}H NMR (500 MHz): δ = 2.34 (dt, J = 15.0, 4.8 Hz, 1H), 2.57 (dt, J = 15.0, 4.3 Hz, 1H), 2.85 (ddd, J = 15.0, 4.3, 2.7 Hz, 1H), 3.34 (ddd, J = 15.0, 4.3, 2.1 Hz, 1H), 3.64 (s, 3H), 3.85 (s, 3H), 6.70, 6.85 (AB system, J = 8.9 Hz, 2H), 6.86, 7.00 (AB system, J = 10.3 Hz, 2H), 7.50, 7.90 ppm (AB system, J = 7.8 Hz, 2H); ^{13}C NMR: δ = 21.4, 29.6, 55.1, 56.1, 109.2, 111.5, 124.9, 129.3, 130.1, 131.0, 137.1, 139.9, 147.5, 149.3, 149.7, 150.3, 151.8, 152.7, 185.0, 186.8 ppm; MS (EI): m/z (%): 149 (5), 189 (6), 245 (10), 289 (100), 290 (94), 320 $[M]^+$ (10); MS (EI): m/z: calcd for $C_{20}H_{18}O_4$: 320.10486; found: 322.10391; elemental analysis calcd (%) for $C_{20}H_{16}O_4$: C 74.99, H 5.03; found: C 68.51, H 5.64.

(*P*)-6-Ethoxy-9,12-dimethoxy-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (5a): Compound (*P*)-**5a** was obtained from diene **7a** by following general procedure E (2 equiv of (S*S*)-**8**, −78 °C, 48 h, eluent: EtOAc/hexane 1:2) in 87% yield as an orange solid. M.p. 186–188 °C (CH_3CN); $[\alpha]_D^{20}$ = +640 (c = 0.027 in $CHCl_3$), after 2 h at −20 °C the value of $[\alpha]_D^{20}$ decreased to zero; ^{1}H NMR (500 MHz): δ = 1.41 (t, J = 7.1 Hz, 3H), 2.07 (dt, J = 15.0, 4.4 Hz, 1H), 2.25 (dt, J = 15.0, 4.4 Hz, 1H), 3.28 (m, 1H), 3.33 (m, 1H), 3.61 (s, 3H), 3.85 (s, 3H), 4.21 (m, 2H), 6.70, 6.85 (AB system, J = 8.9 Hz, 2H), 6.80, 6.90 (AB system, J = 10.3 Hz, 2H), 7.42 ppm (s, 1H); ^{13}C NMR: δ = 14.6, 20.9, 21.6, 55.2, 56.1, 64.4, 106.1, 109.0, 111.3, 123.9, 126.7, 129.3, 131.7, 132.9, 136.3, 136.4, 140.2, 149.6, 150.2, 158.5, 185.3, 185.6 ppm; MS (EI): m/z (%): 57 (33), 69 (17), 77 (15), 83 (11), 149 (25), 273 (10), 289 (14), 305 (34), 333 (100), 366 $[M+2]^+$ (17); MS (EI): m/z: calcd for $C_{22}H_{20}O_5$: 364.13107; found: 364.12949; elemental analysis calcd (%) for $C_{22}H_{20}O_5$: C 72.51, H 5.53; found: C 67.53, H 5.14.

(12b*R*,*P*)-12-Methyl-5,7,8,12b-tetrahydrobenzo[*c*]phenanthrene-1,4-dione (16b): Compound (12b*R*,*P*)-**16b** was obtained from diene **6b** by following general procedure E (2 equiv of (S*S*)-**8**, −20 °C, 27 d, eluent: CH_2Cl_2/hexane 4:1) in 81% yield as an orange oil. $[\alpha]_D^{20}$ = +332 (c = 0.1 in $CHCl_3$); ^{1}H NMR: δ = 2.10 (s, 3H), 2.19–2.43 (m, 1H), 2.85–3.12 (m, 4H), 3.15–3.43 (m, 1H), 4.60 (m, 1H), 5.50 (m, 1H), 6.82–6.95 (m, 3H), 6.97–7.14 ppm (m, 2H); ^{13}C NMR: δ = 21.1, 24.7, 27.9, 29.2, 38.5, 115.2, 125.9, 126.0, 127.1, 130.6, 131.9, 136.8, 136.7, 138.4, 140.0, 140.9, 142.9, 186.6, 187.0 ppm; MS (EI): m/z (%): 101 (11), 131 (14), 189 (21), 202 (18), 229 (16), 245 (6), 259 (100), 276 (58) $[M]^+$; MS (EI): m/z: calcd for $C_{19}H_{16}O_2$: 276.11503; found: 276.11398; HPLC (Daicel Chiralpack AD chiral column Hexane/2-Propanol 99:1): 0.5 mL min^{-1}, 254 nm, R_t = 29.9 min, T = 25 °C, 96% *ee*.

(*P*)-12-Methyl-7,8-tetrahydrobenzo[*c*]phenanthrene-1,4-dione (4b)

Method A: Compound (*P*)-**4b** was obtained from diene **6b** by following general procedure E (3 equiv of (S*S*)-**8**, −20 °C for 11 d and 5 °C for 23 d, eluent: CH_2Cl_2/hexane 4:1) in 83% yield as an orange solid. M.p.: 170–172 °C (CH_3CN); $[\alpha]_D^{20}$ = +482 (c = 0.05 in $CHCl_3$); ^{1}H NMR: δ = 2.18 (s, 3H), 2.50, 2.90 (2 m, 4H), 6.87, 6.92 (AB system, J = 10.3 Hz, 2H), 7.10 (d, J = 7.3 Hz, 1H), 7.17 (d, J = 7.3 Hz 1H), 7.22 (t, J = 7.3 Hz, 1H), 7.55, 7.95 ppm (AB system, J = 7.7 Hz, 2H); ^{13}C NMR: δ = 20.6, 30.4, 30.6, 124.8, 125.2, 128.0, 129.2, 131.3, 131.4, 131.5, 132.7, 135.0, 135.3, 137.3, 139.8, 139.9, 149.1, 185.0, 186.5 ppm; MS (EI): m/z (%): 101 (6), 189 (9), 202 (9), 229 (11), 259 (100), 274 (16) $[M]^+$; MS (EI): m/z: calcd for $C_{19}H_{14}O_2$: 274.09938; found: 274.09872; elemental analysis calcd (%) for $C_{19}H_{14}O_2$: C 83.19, H 5.14; found: C 82.87, H 5.25; HPLC (Daicel Chiralpack AD chiral column, hexane/2-propanol 95:5), 0.5 mL min^{-1}, 254 nm, R_t = 21.9 min, T = 25 °C, 35% *ee*.

Method B: Compound (*P*)-**4b** was obtained from diene **6b** by following general procedure F (13 h, eluent: CH_2Cl_2/hexane 4:1) in 89% yield as an orange solid. $[\alpha]_D^{20}$ = +1547 (c = 0.05 in $CHCl_3$); after 250 h at RT, the value of $[\alpha]_D^{20}$ decreased to zero. HPLC (Daicel Chiralpack AS chiral column): hexane/2-propanol 99:1), 0.5 mL min^{-1}, 254 nm, R_t = 44.5 min, T = 25 °C, 81% *ee*.

(*P*)-12-Methyl-6-ethoxy-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (5b): Compound (*P*)-**5b** was obtained from diene **7b** by following general procedure E (2 equiv of (S*S*)-**8**, −20 °C, 48 h, eluent: EtOAc/hexane 1:4) in 64% yield as an orange solid. M.p. 169–171 °C (CH_3CN); $[\alpha]_D^{20}$ = +1633 (c = 0.05 in $CHCl_3$); 96% *ee*, determined by ^{1}H NMR (300 MHz) by using Pr(tfc)$_3$ (tfc = tris[3-(trifluoromethylhydroxymethylene)-D-camphorate]) as a chiral lanthanide shift reagent (4 mg (*P*)-**5b**/1.6 mg Pr(tfc)$_3$ in 0.8 mL of $CDCl_3$); ^{1}H NMR: δ = 1.50 (t, J = 7.0 Hz, 3H), 2.12 (dt, J = 16.0, 4.7 Hz, 1H), 2.17 (s, 3H), 2.64 (dt, J = 14.4, 4.2 Hz, 1H), 2.79 (ddd, J = 14.4, 4.6, 2.4 Hz, 1H), 3.32 (ddd, J = 16.0, 4.6, 2.4 Hz, 1H), 4.15–4.35 (2 dq, J = 9.3, 7.0 Hz, 2H), 6.75 (s, 2H), 7.08 (d, J = 7.1 Hz, 1H), 7.15 (d, J = 7.1 Hz, 1H), 7.19 (t, J = 7.1 Hz, 1H), 7.49 ppm (s, 1H); ^{13}C NMR: δ = 14.7, 20.6, 22.5, 30.0, 64.5, 106.7, 124.6, 125.3, 127.7, 129.0, 132.3, 133.0, 135.4, 136.6, 137.2, 137.6, 139.9, 140.2, 158.8, 185.2, 185.4 ppm; MS (EI): m/z (%): 85 (5), 189 (11), 229 (4), 245 (6), 275 (44), 303 (100), 318 (14) $[M]^+$; MS (EI): m/z: calcd for $C_{21}H_{18}O_3$: 318.12559; found: 318.12552; elemental analysis calcd (%) for $C_{21}H_{18}O_3$: C 79.22, H 5.70; found: C 78.92, H 5.78.

(12b*R*,*P*)-12-Isopropyl-5,7,8,12b-tetrahydrobenzo[*c*]phenanthrene-1,4-dione (16c): Compound (12b*R*,*P*)-**16c** was obtained from diene **6c** by following general procedure E (2 equiv of (S*S*)-**8**, −20 °C, 42 d, eluent: EtOAc/hexane 1:20) in 67% yield as an orange oil. $[\alpha]_D^{20}$ = +291 (c = 0.05 in $CHCl_3$); ^{1}H NMR: δ = 0.97, 1.10 (2d, J = 6.6 Hz, 6H), 2.20–2.43 (m, 1H), 2.60–3.15 (2 m, 5H), 3.20–3.40 (m, 1H), 4.55–4.67 (m, 1H), 5.53 (br s, 1H), 6.81–6.99 (m, 2H), 7.03–7.20 ppm (2 m, 3H); ^{13}C NMR: δ = 23.0, 24.6, 25.9, 27.9, 29.5, 29.7, 38.2, 115.2, 124.6, 125.6, 126.2, 136.1, 136.3, 136.5, 136.9, 139.7, 140.2, 143.3, 143.4, 186.1, 186.3 ppm; MS (EI): m/z (%): 77 (6), 115 (11), 165 (11), 202 (27), 233 (22), 259 (100), 304 (28) $[M]^+$; MS (EI): m/z: calcd for $C_{21}H_{20}O_2$: 304.14633; found: 304.14597. HPLC (Daicel Chiralpack AD, chiral column, hexane/2-propanol 99:1): 0.5 mL min^{-1}, 254 nm, R_t = 15.8 min, T = 25 °C, 96% *ee*.

(12b*R*,*M*)-12-Isopropyl-5,7,8,12b-tetrahydrobenzo[*c*]phenanthrene-1,4-dione (17c): A solution of (12b*R*,*P*)-**16c** (50 mg, 0.16 mmol) in $CDCl_3$ (0.5 mL) was maintained at RT for 30 d. After evaporation of the solvent and flash chromatography (eluent: CH_2Cl_2/hexane 4:1), compound (12b*R*,*M*)-**17c** was obtained in 14% yield as an orange oil. $[\alpha]_D^{20}$ = −167 (c = 0.05 in $CHCl_3$); ^{1}H NMR: δ = 1.15 (d, J = 6.9 Hz, 3H), 1.29 (d, J = 6.9 Hz, 3H), 2.20–2.50 (m, 1H), 2.55–2.90 (m, 4H), 3.15 (sept, J = 6.9 Hz, 1H), 3.85 (dd, J = 7.0, 17.2 Hz, 1H), 4.52 (m, 1H), 6.04 (m, 1H), 6.53, 6.39 (AB system, J = 8.6 Hz, 2H), 7.05–7.35 ppm (m, 3H).

(*P*)-12-Isopropyl-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (4c)

Method A: Compound (*P*)-**4c** was obtained from diene **6c** by following general procedure E (3 equiv of (S*S*)-**8**, −20 °C for 11 d and 5 °C for 24 d, eluent: CH_2Cl_2/hexane 4:1) in 79% yield as an orange solid. M.p. 196–198 °C (CH_3CN); $[\alpha]_D^{20}$ = +1451 (c = 0.08 in $CHCl_3$); ^{1}H NMR: δ = 0.77 (d, J = 6.5 Hz, 3H), 1.26 (d, J = 6.5 Hz, 3H), 2.50–2.80 (2 m, 4H), 3.20 (sept, J = 6.5 Hz, 1H), 6.87, 6.92 (AB system, J = 10.1 Hz, 2H), 7.17 (d, J =

7.7 Hz, 1H), 7.23 (d, J=7.7 Hz, 1H), 7.29 (t, J=7.7 Hz, 1H), 7.58, 7.95 ppm (AB system, J=7.7 Hz, 2H); ^{13}C NMR: δ=20.4, 26.9, 29.7, 30.8, 30.9, 123.8, 124.7, 125.1, 128.5, 131.0, 131.3, 131.6, 134.5, 137.4, 139.9, 146.2, 149.2, 184.9, 185.3 ppm; MS (EI): m/z (%): 202 (9), 229 (11), 259 (100), 302 $[M]^+$ (3); MS (EI): m/z: calcd for $C_{21}H_{18}O_2$: 302.13068; found: 302.13097; elemental analysis calcd (%) for $C_{21}H_{18}O_2$: C 83.42, H 6.00; found: C 83.12, H 6.50; HPLC (Daicel Chiralpack OD chiral column, hexane/2-propanol 90:10): 0.5 mL min^{-1}, 254 nm, R_t=20.3 min, T=25 °C, 80 % *ee*.

Method B: Compound (*P*)-**4c** was obtained from diene **6c** by following general procedure F (13 h, eluent: CH_2Cl_2/hexane 4:1) in 73 % yield as an orange solid. $[\alpha]_D^{20}$=+1758 (c=0.05 in $CHCl_3$); HPLC: (Daicel Chiralpack OD chiral column, hexane/2-propanol 90/10): 0.5 mL min^{-1}, 254 nm, R_t=20.9 min, T=25 °C, 82 % *ee*.

(*P*)-12-Isopropyl-6-ethoxy-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (5c): Compound (*P*)-**5c** was obtained from diene **7c** by following general procedure E (2 equiv of (*SS*)-**8**, −20 °C, 3 h, eluent: EtOAc/hexane 1:40) in 65 % yield as an orange solid. M.p.: 178–180 °C (CH_3CN); $[\alpha]_D^{20}$=+1678 (c=0.08 in $CHCl_3$); ^{1}H NMR: δ=0.74 (d, J=6.7 Hz, 3H), 1.24 (d, J=6.7 Hz, 3H), 1.51 (t, J=7.1 Hz, 3H), 2.09 (dt, J=15.6, 4.5 Hz, 1H), 2.59 (dt, J=14.5, 3.8 Hz, 1H), 2.77 (ddd, J=14.5, 4.5, 2.4 Hz, 1H), 3.21 (sept, J=6.7 Hz, 1H), 3.32 (ddd, J=15.6, 3.8, 2.4 Hz, 1H), 4.14–4.36 (dq, J=9.2, 7.1 Hz, 2H), 6.80, 6.88 (AB system, J=10.2 Hz, 2H), 7.15 (d, J=7.5 Hz, 1H), 7.20 (d, J=7.5 Hz, 1H), 7.27 (t, J=7.5 Hz, 1H), 7.48 ppm (s, 1H); ^{13}C NMR: δ=14.7, 20.6, 22.6, 26.9, 29.7, 30.5, 64.5, 106.5, 123.5, 124.5, 125.0, 128.3, 131.3, 132.2, 136.7, 136.8, 137.7, 139.8, 140.2, 146.4, 158.9, 184.2, 185.4 ppm; MS (FAB+): m/z (%): 283 (48), 303 (17), 327 (93), 347 (11) $[M+1]^+$; MS (FAB+): m/z: calcd for $C_{23}H_{23}O_3$: 347.16472; found: 347.16318; elemental analysis calcd (%) for $C_{23}H_{22}O_3$ (346.2): C 79.39, H 6.46; found: C 79.74, H 6.40; HPLC (Daicel Chiralpack OD chiral column, hexane/2-propanol 95:5): 0.5 mL min^{-1}, 254 nm, R_t= 52.7 min, T=25 °C, 97 % *ee*.

(12b*R*,*M*)-12-*tert*-Butyl-5,7,8,12b-tetrahydrobenzo[*c*]phenanthrene-1,4-dione (17d): Compound (12b*R*,*M*)-**17d** was obtained from diene **6d** by following general procedure E (2 equiv of (*SS*)-**8**, 20 °C, 7 d, eluent: EtOAc/hexane 1:12), after separation of the 25:15:60 mixture of **17d**, **4d** and **18**, in 14 % yield as a red solid. M.p.: 188–189 °C (CH_3CN); $[\alpha]_D^{20}$= −240 (c=0.02 in $CHCl_3$); ^{1}H NMR: δ=1.32 (s, 9H), 2.24 (m, 1H), 2.41 (dt, J=13.9, 3.1 Hz, 1H), 2.51 (ddd, J=4.2, 9.5, 18.8 Hz, 1H), 2.64 (dt, J=3.0, 13.2 Hz, 1H), 3.75 (dt, J=3.2, 14.3 Hz, 1H), 3.81 (ddd, J=1.3, 6.6, 18.8 Hz, 1H), 4.63 (d, J=8.8 Hz, 1H), 5.91 (dq, J=6.6, 2.0 Hz, 1H), 6.37, 6.61 (AB system, J=7.3 Hz, 2H), 7.06 (d, J=7.3 Hz, 1H), 7.23 (d, J=7.4 Hz, 1H), 7.36 ppm (dt, J=1.1, 8.1 Hz, 1H); ^{13}C NMR: δ=25.4, 31.4, 31.8, 32.1, 36.0, 42.8, 119.0, 124.8, 126.3, 133.1, 134.5, 137.0, 141.9, 145.8 (2C), 146.4, 147.3, 147.7, 184.9, 185.6 ppm; MS (EI): m/z (%): 57 (100), 115 (6), 189 (8), 202 (12), 233 (9), 245 (6), 262 (73), 320 (16) $[M+2]^+$; MS (EI): m/z: calcd for $C_{22}H_{22}O_2$: 318.16198; found: 318.16116; HPLC (Daicel Chiralpack AS chiral column, hexane/2-propanol 97:3), 0.7 mL min^{-1}, 254 nm, R_t=8.4 min, T=25 °C, 72 % *ee*.

(*P*)-12-*tert*-Butyl-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (4d)

Method A: Compound (*P*)-**4d** was obtained from diene **6d** by following general procedure E (2 equiv of (*SS*)-**8**, 20 °C, 7 d, eluent: EtOAc/hexane 1:12), after separation of the 25:15:60 mixture of **17d**, **4d** and **18**, in 10 % yield as a red solid. M.p.: 172–174 °C (CH_3CN); $[\alpha]_D^{20}$=+1371 (c=0.02 in $CHCl_3$); ^{1}H NMR: δ=1.32 (s, 9H), 2.57, 2.79 (2 m, 4H), 6.77, 6.91 (AB system, J=10.3 Hz, 2H), 7.16 (d, J=7.5 Hz, 1H), 7.27 (t, J=7.1 Hz, 1H), 7.57 (d, J=7.8 Hz, 1H), 7.57, 7.98 (AB system, J=7.9 Hz, 2H); MS (EI): m/z (%): 55 (35), 57 (66), 69 (36), 71 (27), 83 (19), 121 (16), 149 (39), 202 (13), 229 (35), 260 (78), 316 (100) $[M]^+$; MS (EI): m/z: calcd for $C_{22}H_{20}O_2$: 316.14663; found: 316.14612; HPLC (Daicel Chiralpack AS chiral column, hexane/2-propanol 99:1): 0.3 mL min^{-1}, 254 nm; R_t= 29.5 min, T=25 °C, 72 % *ee*.

Method B: Compound (*P*)-**4d** was obtained from diene **6d** by following general procedure F (24 h, eluent: EtOAc/hexane 1:4), after separation of the 40:60 mixture of **4d** and **18**, in 37 % yield as a red solid. $[\alpha]_D^{20}$= +1573 (c=0.1 in $CHCl_3$); HPLC: (Daicel Chiralpack OD chiral column, hexane/2-propanol 99:1): 0.5 mL min^{-1}, 254 nm; R_t=20.9 min, T=25 °C, 80 % *ee*.

(*P*)-12-*tert*-Butyl-6-ethoxy-7,8-dihydrobenzo[*c*]phenanthrene-1,4-dione (5d): Compound (*P*)-**5d** was obtained from diene **7d** by following general procedure E (2 equiv of (*SS*)-**8**, −20 °C, 3 d, eluent: EtOAc/hexane 1:20) in 57 % yield as an orange solid. M.p.: 118–120 °C (CH_3CN); $[\alpha]_D^{20}$= +977 (c=0.03 in $CHCl_3$); ^{1}H NMR: δ=1.06 (s, 9H), 1.52 (t, J=7.1 Hz, 3H), 2.11 (dt, J=4.5, 14.7 Hz, 1H), 2.47 (dt, J=4.4, 14.7 Hz, 1H), 2.73 (ddd, J=2.2, 4.2, 15.1 Hz, 1H), 3.30 (ddd, J=2.2, 3.6, 14.7 Hz, 1H), 4.25 (dq, J=20.0, 7.1 Hz, 2H), 6.68, 6.81 (AB system, J=10.1 Hz, 2H), 7.14 (d, J=7.1 Hz, 1H), 7.25 (t, J=7.7 Hz, 1H), 7.37 (d, J=8.0 Hz, 1H), 7.48 ppm (s, 1H); ^{13}C NMR: δ=14.7, 23.1, 31.2, 33.9, 37.5, 64.5, 106.9, 123.8, 127.0, 127.2, 129.3, 130.1, 131.7, 132.1, 136.3, 137.2, 140.1, 141.0, 149.4, 157.9, 184.0, 185.6 ppm; MS (EI): m/z (%): 71 (10), 85 (6), 189 (12), 229 (6), 247 (10), 275 (55), 303 (100), 362 ppm (4) $[M+2]^+$; MS (EI): m/z: calcd for $C_{24}H_{24}O_3$: 360.17254; found: 360.17126; HPLC (Daicel Chiralcel OD chiral column, hexane/2-propanol 90:10): 0.5 mL min^{-1}, 254 nm, R_t=14.0 min, T=25 °C, 95 % *ee*.

Helicene biscamphanate (*M*)-19b: Compound (*M*)-**19b** was obtained from 7,8-dihydro[4]helicene quinone (*P*,*M*)-**4b** by following general procedure G, after chromatographic separation (eluent: EtOAc/hexane 1:2) of the mixture with helicene biscamphanate (*P*)-**19b**, in 40 % yield as a yellowish oil. R_f=0.53 (EtOAc/hexane 1:2); $[\alpha]_D^{20}$=−186 (c=0.09 in $CHCl_3$); ^{1}H NMR: δ=0.79 (s, 3H), 0.94 (s, 3H), 1.03 (s, 3H), 1.20 (s, 3H), 1.21 (s, 3H), 1.22 (s, 3H), 1.37–1.51 (m, 1H), 1.56–1.73 (m, 2H), 1.77–1.88 (m, 1H), 1.94 (s, 3H), 1.98–2.13 (m, 1H), 2.27–2.40 (m, 1H), 2.61–2.88 (m, 6H), 7.10 (dd, J=7.3, 1.4 Hz, 1H), 7.14 (t, J=7.3 Hz, 1H), 7.19 (dd, J=7.3, 1.4 Hz, 1H), 7.30, 7.15 (AB system, J=8.1 Hz, 2H), 7.45, 7.35 ppm (AB system, J=8.3 Hz, 2H); MS (EI): m/z (%): 83 (66), 125 (14), 259 (29), 456 (11), 636 (100) $[M]^+$; MS (EI): m/z: calcd for $C_{39}H_{40}O_8$: 636.27232; found: 636.27155.

Helicene biscamphanate (*P*)-19b: Compound (*P*)-**19b** was obtained from 7,8-dihydro[4]helicene quinone (*P*,*M*)-**4b** as above, in 45 % yield, or from (*P*)-**4b** by following general procedure G (eluent: EtOAc/hexane 1:2), in 82 % yield, as a white solid. R_f=0.43 (EtOAc/hexane 1:2); m.p. 266–268 °C (CH_3CN); $[\alpha]_D^{20}$=+222 (c=0.1 in $CHCl_3$); ^{1}H NMR: δ=0.84 (s, 3H), 1.04 (s, 3H), 1.09 (s, 3H), 1.20 (s, 3H), 1.21 (s, 3H), 1.22 (s, 3H), 1.50–1.62 (m, 2H), 1.70–1.80 (m, 1H), 1.85–1.90 (m, 1H), 1.87 (s, 3H), 2.07–2.13 (m, 1H), 2.32–2.42 (m, 1H), 2.65–2.90 (m, 6H), 7.30, 7.15 (AB system, J=8.5 Hz, 2H), 7.15 (dd, J=7.4, 3.9 Hz, 1H), 7.20 (dd, J=7.4, 3.9 Hz, 1H), 7.21 (t, J=7.4, 1H), 7.85, 7.65 ppm (AB system, J=8.0 Hz, 2H); MS (EI): m/z (%): 83 (63), 125 (12), 259 (24), 456 (10), 636 (100) $[M]^+$; MS (EI): m/z: calcd for $C_{39}H_{40}O_8$: 636.27232; found: 636.27460.

Helicene biscamphanate (*M*)-20d: Compound (*M*)-**20d** was obtained from 7,8-dihydro[4]helicene quinone (*P*,*M*)-**5d** by following general procedure G, after chromatographic separation (eluent: EtOAc/hexane 1:2) of the mixture with helicene biscamphanate (*P*)-**20d**, in 42 % yield as a yellowish oil. R_f=0.42 (EtOAc/hexane 1:2); $[\alpha]_D^{20}$=−116 (c=0.12 in $CHCl_3$); ^{1}H NMR (500 MHz): δ=0.81 (s, 3H), 0.87 (s, 9H), 0.97, 1.07, 1.22, 1.23, 1.24 (5s, 5×3H), 1.41 (m, 1H), 1.54 (t, J=7.0 Hz, 3H), 1.55, 1.73, 1.85, 1.87, 2.08, 2.19 (6 m, 6H), 2.34 (dt, J=4.5, 9.0 Hz, 1H), 2.46 (m, 1H), 2.70 (m, 2H), 3.30 (ddd, J=2.0, 4.0, 16.0 Hz, 1H), 4.14–4.24 (m, 2H), 6.79, 7.24 (AB system, J=8.2 Hz, 2H), 7.03 (d, J=7.2 Hz, 1H), 7.19 (t, J=7.1 Hz, 1H), 7.21 (s, 1H), 7.52 ppm (ddd, J=0.6, 1.3, 8.0 Hz, 1H); MS (EI): m/z (%): 55 (21), 83 (61), 97 (20), 125 (13), 137 (14), 275 (19), 303 (35), 484 (14), 722 (100) $[M]^+$; MS (EI): m/z: calcd for $C_{44}H_{50}O_9$: 722.34548; found: 722.34772.

Helicene biscamphanate (*P*)-20d: Compound (*P*)-**20d** was obtained from 7,8-dihydro[4]helicene quinone (*P*,*M*)-**5d** as above, in 42 % yield, or from (*P*)-**5d** by following general procedure G (eluent: EtOAc/hexane 1:2) in 78 % yield as a yellowish oil. R_f=0.34 (EtOAc/hexane 1:2); $[\alpha]_D^{20}$=+92 (c=0.16 in $CHCl_3$); ^{1}H NMR: (500 MHz): δ=0.80 (s, 3H), 0.81 (s, 9H), 1.05 (s, 3H), 1.08 (s, 3H), 1.23 (s, 6H), 1.24 (s, 3H), 1.51 (t, J=7.0 Hz, 3H), 1.40, 1.56, 1.79, 1.85, 1.91, 2.06, 2.14 (7 m, 7H), 2.32 (dt, J=4.5, 9.0 Hz, 1H), 2.52 (m, 1H), 2.67 (m, 2H), 3.24 (ddd, J=2.0, 4.0, 16.0 Hz, 1H), 4.12–4.24 (m, 2H), 6.75, 7.23 (AB system, J=8.2 Hz, 2H), 7.13 (d, J=7.2 Hz, 1H), 7.18 (s, 1H), 7.18 (t, J=7.1 Hz, 1H), 7.41 ppm (dd, J= 1.3, 8.0 Hz, 1H); ^{13}C NMR (125 MHz): δ=10.0, 10.1, 15.2, 17.3, 17.3, 17.5, 24.0, 29.4 (2C), 29.5, 30.1, 31.6, 32.2, 32.9, 37.5, 54.9, 55.0, 55.4, 64.3, 91.1, 91.5, 98.8, 115.6, 116.8, 123.9, 125.9, 126.9, 127.9, 128.2, 134.0, 134.6,

136.1, 142.2, 143.6, 144.6, 149.5, 155.6, 164.9, 166.3, 178.2 ppm (2C); MS (EI): *m*/*z* (%): 57 (100), 83 (72), 97 (33), 107 (34), 137 (60), 154 (73), 275 (19), 303 (12), 399 (16), 667 (14), 722 ppm (69) $[M]^+$; MS (EI): *m*/*z*: calcd for $C_{44}H_{50}O_9$: 722.34548; found: 722.34521.

Acknowledgements

We thank Dirección General de Investigación Científica y Técnica (grant no. CTQ2005–02095/BQU) and the Universidad Autónoma de Madrid/Comunidad Autónoma de Madrid (ref. CCG06-UAM/PPQ-0070) for financial support. S.G.-C. and M.J.S.-C. thank the Comunidad Autónoma de Madrid and the Ministerio de Eduación y Ciencia for fellowships. F.M. and A.N.-C. thank the Spanish MEC (projects no. CTQ2005–09000-CO1–02 and CSD2006–003), the Catalan DURSI (project no. 2005SGR00715) and the ICIQ foundation for financial support.

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Received: May 21, 2007
Published online: October 8, 2007

