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Enantiopure arenesulfenic acids as intermediates in stereoselective synthesis

Maria C. Aversa,[a] Paola Bonaccorsi,[a,*] Cristina Faggi,[b] Giuseppe Lamanna[c] and Stefano Menichetti[c,*]

[a]*Dipartimento di Chimica organica e biologica, Università degli Studi di Messina, Salita Sperone 31 (vill. S. Agata), 98166 Messina, Italy*
[b]*Centro interdipartimentale di Cristallografia, Università degli Studi di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino, Firenze, Italy*
[c]*Dipartimento di Chimica organica 'Ugo Schiff', Università degli Studi di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino, Firenze, Italy*

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Abstract—New transient arenesulfenic acids were involved in the synthesis of enantiopure 2-arylsulfinyl-1,3-dienes, showing central or axial chirality of the substituted arene residue, apart from the chirality related to the stereogenic sulfur atom. Some of the obtained dienes, that is, (S_a,S_S)- and (S_a,R_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadienes, were subjected to diastereoselective Diels–Alder cycloadditions with *N*-methylmaleimide. Removal of the arylsulfoxide auxiliary, in the major adduct, was accomplished by reductive cleavage with Raney nickel.

1. Introduction

It has been widely demonstrated that chemo and regioselective *syn*-addition of a sulfenic acid to conjugated enynes represents a convenient synthetic strategy for the preparation of diene sulfoxides, significant partners in Diels–Alder (DA) cycloadditions, with the sulfinyl group acting as chiral auxiliary.[1] The *syn*-addition is a thermal six-electron process whose intrinsic nature does not imply any acid or basic conditions, so ensuring formation of the sulfoxide moiety even in the presence of pH sensitive functional groups. Good to high yields are generally observed. Sulfenic acids, that are generated in situ from opportune precursors, can be obtained in enantiomerically pure form, providing access to enantiopure sulfinyl dienes.

Camphorsulfonic and mandelic acids, readily available members of the chiral pool, were choosen as starting compounds in the preparation of precursors of enantiopure sulfenic acids **1**–**3** for the contiguity of a hydroxy function to the sulfur atom (Fig. 1). This contiguity guarantees an intramolecular hydrogen bond, between the hydroxy group

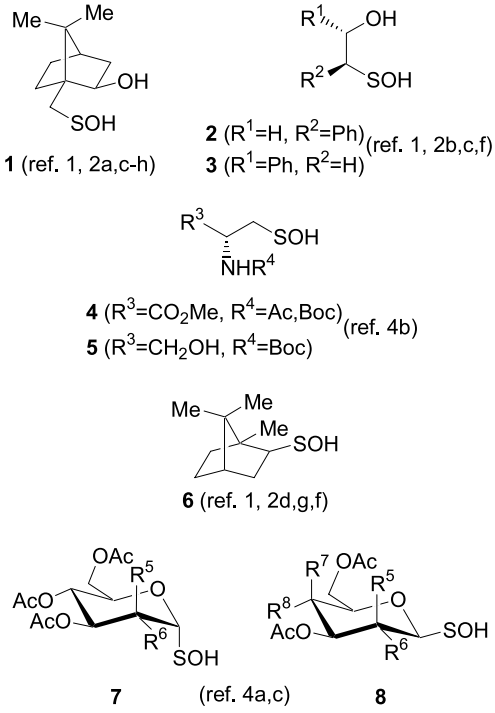

Figure 1. Transient enantiopure sulfenic acids.

Keywords: Arenesulfenic acids; Diastereofacial selectivity; Diels–Alder cycloadditions; *N*-methylmaleimide; Sulfinyl dienes.
* Corresponding authors. Tel.: +39 090 6765187; fax: +39 090 393895 (P.B.); tel.: +39 055 4573535; fax: +39 055 4573531 (S.M.);
e-mail addresses: paolab@isengard.unime.it; stefano.menichetti@unifi.it

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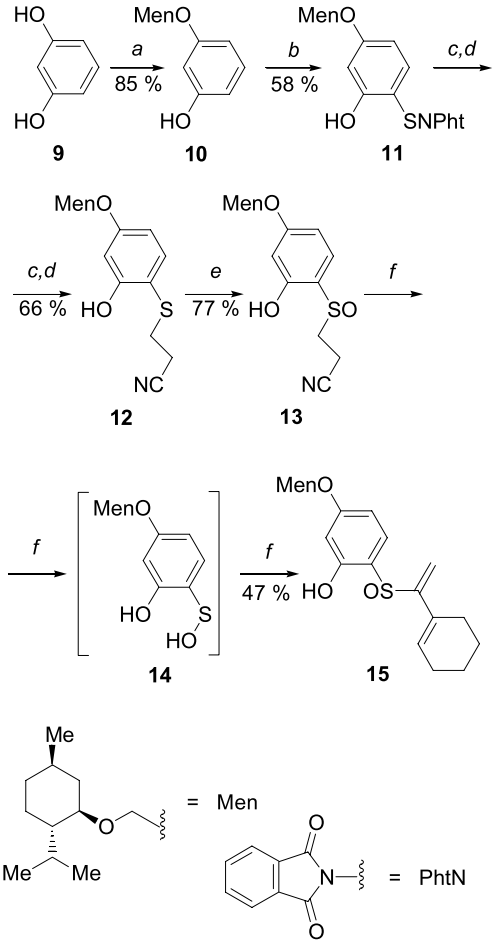
and the oxygen atom of the sulfoxide moiety, that facilitates the chromatographic separation of diastereoisomers and in some cases enhances stereoselection in concerted processes.[2] The high steric demands of the camphor skeleton are maintained in the commercially available [(1*S*)-*endo*]-(−)-borneol that was easily transformed into a precursor of the enantiopure sulfenic acid **6**, showing no possibilities of intramolecular hydrogen bonding.[2d–g] Indeed, an intramolecular hydrogen bonding, also useful in preventing self-condensation of sulfenic acids, can present some disadvantages due to unexpected and undesired reactions of the hydroxy function in the subsequent synthetic transformations of the sulfoxides obtained from sulfenic acids such as **1**–**3**.[2f,3] L-cysteine and α- and β-D-1-thioglycopyranose are stimulating starting products for the generation of transient sulfenic acids **4**, **5**, **7**, **8** that allowed the synthesis of enantiopure sulfinyl dienes showing the L-cysteine or 1-thio-D-glycopyranose S-oxide frameworks as chiral auxiliaries where the stereodifferentiating moiety is also a biologically active residue.[4]

Almost all the sulfinyl dienes, including the chiral above-mentioned S-alkyl residues, have been involved in DA reactions that afforded the expected cycloadducts, easily obtainable in enantiomerically pure forms and good yields. However, removal from these adducts of the sulfoxide function, directly linked to an alkyl group on one side, and to an unsaturated carbon on the other, represented a big challenge. Desulfurization by nickel reagents or sodium amalgam failed on several occasions and indirect methodologies were exploited for reaching this goal.[2d,5]

In this paper we describe the synthesis of new sulfinyl dienes in which an enantiopure aryl group is directly linked to the sulfur atom. These S-arylsulfinyl dienes have been obtained via the corresponding sulfenic acids, possessing central or axial chirality, and their addition to opportune enynes. Some of the obtained dienes have been subjected to DA cycloaddition with *N*-methylmaleimide (NMM), followed by removal of the arylsulfoxide auxiliary that was accomplished by Raney nickel desulfurization, making straightforward and efficient the overall synthetic process towards functionalized enantiopure cyclic molecules.

2. Results and discussion

Two main reasons gave rise to the selection of resorcinol (**9**) as starting material for the preparation of enantiopure dienes **15** via sulfenic acid **14** showing central chirality (Scheme 1): (i) an electron-rich aromatic ring was necessary for the chosen synthetic sequence [sulfenylation with phtalimidesulfenyl chloride (PhtNSCl)[6] of **10** followed by LAH reduction] that allowed the introduction of a thiol function onto the benzene nucleus; (ii) only one of the two hydroxy functions in **9** could be easily derivatized, with a commercial enantiopure reagent, for the generation of the enantiopure arenesulfenic acid **14**, where the remaining free hydroxy substituent, opportunely placed onto the aromatic ring, would provide an intramolecular hydrogen bonding with the oxygen atom in the sulfenic function, so mitigating the heavy disposition of sulfenic acids to self-condensation.



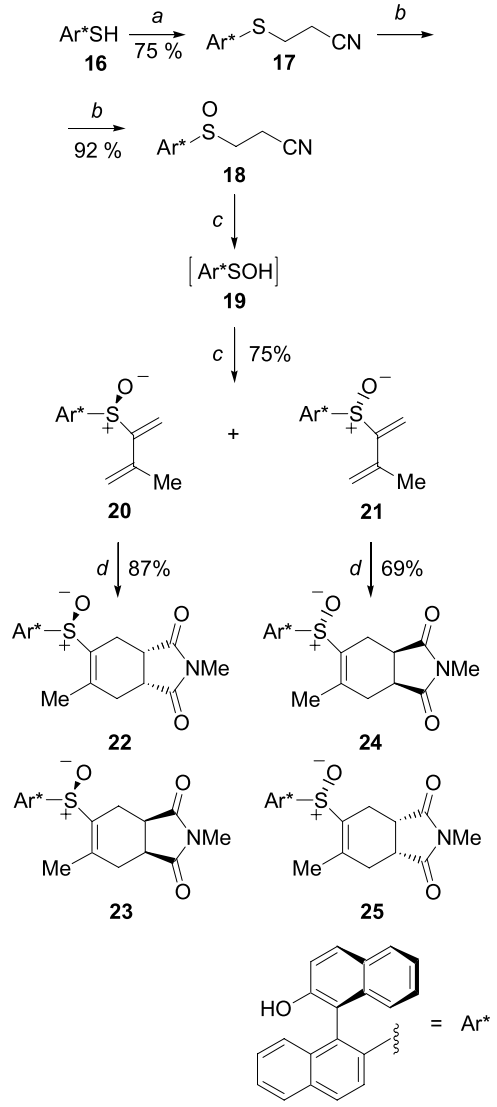
Scheme 1. Reagents and conditions: (a) MenCl, K_2CO_3, 50 °C, 46 h; (b) PhtNSCl, $CHCl_3$, 0 °C, 20 min; (c) LAH, THF, rt, 1 h; (d) CH_2=CHCN, Et_3N, THF, rt, 20 h; (e) *m*-CPBA, CH_2Cl_2, 0 °C, 20 min (1:1 S-epimers); (f) 1-ethynylcyclohexene, 130 °C, 1 h (1:1 S-epimers).

The commercially available (−)-chloromethyl menthyl ether (MenCl) was used to link a chiral auxiliary to one hydroxy function in **9**, since the Men residue has the advantage of possessing no reactive groups that could interfere during the whole synthetic pathway. The reaction between resorcinol (**9**) and MenCl was performed in the presence of potassium carbonate, in a molar ratio of 5:1:3, respectively (Scheme 1).

Enantiopure phenol **10** was then subjected to completely regioselective sulfenylation with PhtNSCl, at 0 °C to avoid ether cleavage, and compound **11** was obtained as the unique product. LAH reduction, conjugate addition onto acrylonitrile, and *m*-CPBA oxidation led to epimeric sulfoxides **13**, that are precursors of the enantiopure arenesulfenic acid **14**. Thermolysis of nitrile mixture **13** was performed in neat 1-ethynylcyclohexene, at 130 °C for 1 h. The completely chemo- and regioselective addition of sulfenic acid **14** to the triple bond of ethynylcyclohexene gave the epimeric mixture of sulfinyl dienes **15** in 1:1 ratio. These two epimeric sulfoxides appeared as a single spot by TLC, although several different solvent systems were evaluated. Column chromatography of the mixture **15** allowed the isolation of only small quantities of each of the two enantiopure epimers **15** that were fully

characterized. However, this difficulty in isolation prompted us to drop the project of involving enantiopure dienes **15** in DA cycloadditions. The very difficult separation of sulfinyl dienes **15** appears as a consequence of their similar chromatographic features, due to the distance between the stereodifferentiating menthyl substituent and the sulfinyl group.

Our attention then turned to S-arylsulfinyl dienes whose aryl substituent could possess an intrinsic chirality. Enantiopure dienes **20** and **21** in Scheme 2 show not only the central chirality due to the stereogenic sulfur atom but also the axial chirality coming from the atropoisomeric binaphthyl moiety linked to the sulfoxide group. The synthesis of **20** and **21** was performed starting from enantiopure (S_a)-2′-mercapto-1,1′-binaphthalen-2-ol (**16**), easily prepared from commercial (S_a)-(−)-1,1′-bi-2-naphthol.[7] Thiol **16** can be warmed up to 250 °C without racemization, thus allowing the safe generation of sulfenic acid **19** in enantiomerically pure form by the well-assessed thermal strategy that implies the use of temperatures between 40 and 140 °C, in dependence of the structure of the sulfoxide precursor.[8]



Scheme 2. Reagents and conditions: (a) CH_2=CHCN, Et_3N, THF, rt, 72 h; (b) *m*-CPBA, CH_2Cl_2, −50 °C, 1 h (1:1 S-epimers); (c) 2-methyl-1-buten-3-yne, 110 °C, 1.5 h (**20**/**21** 1:1); (d) *N*-methylmaleimide, CH_2Cl_2, 40 °C (**22**/**23** 2:1, **24**/**25** 3:2).

Nucleophilic addition of thiol **16** onto acrylonitrile in the presence of triethylamine, followed by *m*-CPBA oxidation, led to sulfoxides **18** (1:1 S-epimers). Thermolysis of **18** to **19** was performed in the presence of commercially available 2-methyl-1-buten-3-yne, at 110 °C for 1.5 h, and gave sulfinyl dienes **20** and **21** in 1:1 ratio and 75% total yield. The epimeric mixture of the two sulfinyl dienes **20** and **21** was subjected to column chromatography, and they were easily separated and fully characterized. The configuration at sulfur atom of sulfoxides **20** and **21**, shown in Scheme 2, was inferred from X-ray crystallographic analysis of cycloadduct **25** (Fig. 2). The obtained results confirmed expectations based on the intramolecular hydrogen bonding, between the hydroxy function of the binaphthyl residue and the sulfoxide oxygen, and its relationship with the difference in chromatographic mobility[2c] observed between the two epimeric sulfinyl dienes **20** and **21**.

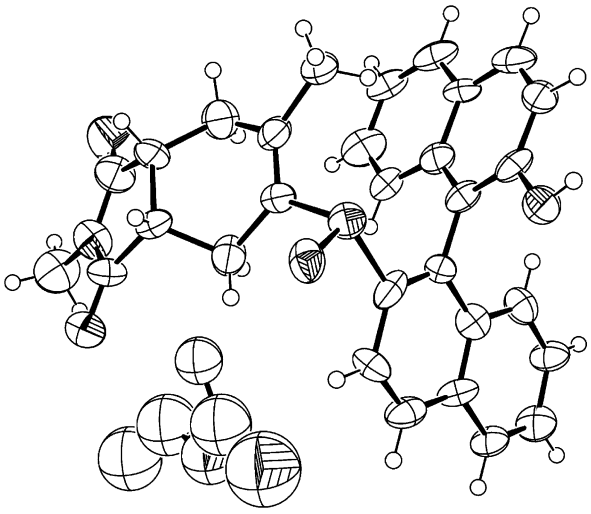


Figure 2. Perspective view of the structure of **25** crystallized with a molecule of ethyl acetate in the asymmetric unit.

Actually (S_a,R_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadiene (**21**) was reacted with NMM in dichloromethane to give the two diastereoisomeric cycloadducts **24** and **25** in 3:2 ratio and 69% total yield (Scheme 2). Column chromatography furnished the major adduct **24** as first eluted product, followed by minor adduct **25**. The two cycloadducts **24** and **25** were separately subjected to several recrystallizations, but only minor cycloadduct **25** afforded crystals suitable for X-ray analysis from ethyl acetate (Fig. 2). Results of crystallographic analysis allowed assignment of configurations at the newly formed stereocentres C-3a and C-7a of cycloadducts **24** (S_a,R_S,3a*R*,7a*S*) and **25** (S_a,R_S,3a*S*,7a*R*). The stereochemical outcome of the cycloaddition between enantiopure diene **21** and NMM can be rationalized as follows. Low diastereofacial selectivity was observed, in favour of cycloadduct **24**, which came from NMM approaching the (*Si*) face of diene **21** preferentially adopting the **A** conformation in the DA transition state (Fig. 3).[9] The appreciable formation of the minor adduct **25** by NMM approach to the (*Re*) face of diene

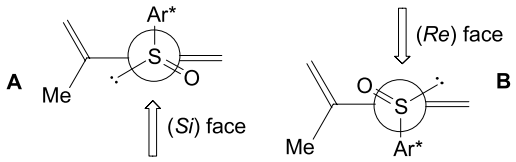
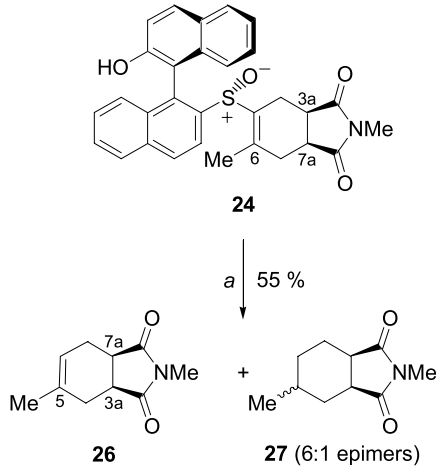


Figure 3. Conformational preferences in Diels–Alder transition states of diene **21**.

21 in its **B** conformation, where sulfur oxygen is maintained transoid to C-1/C-2 double bond, is a consequence of the steric features of both the binaphthyl group linked to the sulfoxide sulfur and the 3-methyl substituent on the 2-sulfinyl-1,3-diene skeleton. These two factors, together with the steric requirement of the dienophile, reduce the topological differentiation between the diene faces, induced by the sulfinyl group.[10]

DA cycloaddition of (S_a,S_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadiene (**20**) with NMM led to cycloadducts **22** (chromatographically more mobile) and **23** in 2:1 ratio, respectively, and 87% overall yield (Scheme 2). This diastereoselection amount is in line with the one measured in the DA cycloaddition of diene **21** (see above). The configuration at C-3a and C-7a shown in Scheme 2 for adducts **22** and **23** is determined by the sulfur configuration in **20**, so that the diene **20** (S_S)/NMM approaches are opposite to the ones observed in the DA reaction of diene **21** (R_S).

Desulfurization of the major adduct **24** was realized in 5 h by commercial W-2 Raney nickel (Scheme 3). (3a*S*,7a*R*)-3a,4,7,7a-tetrahydro-2,5-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (**26**) and (3a*S*,7a*R*)-hexahydro-2,5-dimethyl-1*H*-isoindole-1,3(2*H*)-diones **27** (6:1 epimeric mixture) were obtained in 55% overall yield, separated by column chromatography, and identified by comparison with literature data.[11] Despite the formation of **27**, together with the enantiopure compound **26**, was unsatisfactory but predictable in the reductive cleavage of aryl(ethenyl)sulfoxide **24**, the use of a S-aryl substituted chiral auxiliary ensured an easy desulfurization process.



Scheme 3. Reagents and conditions: (a) Raney nickel, THF, rt, 5 h (**26**/**27** 2:1).

3. Conclusions

In this paper, we have reported an useful development of the well-assessed methodology to build up diene skeletons, bearing a chiral sulfinyl substituent.[1–5] New transient arenesulfenic acids were involved in the synthesis of enantiopure 2-arylsulfinyl-1,3-dienes, showing central or axial chirality of the substituted arene residue, apart from the chirality related to the stereogenic sulfur atom. Some of the obtained dienes show a binaphthyl moiety linked to the sulfoxide group and were easily prepared from (S_a)-2′-mercapto-1,1′-binaphthalen-2-ol (**16**). Both enantiopure (S_a)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadienes **20** and **21** were subjected to DA reaction with NMM, and the diastereomeric mixtures of cycloadducts were easily separated by column chromatography. The binaphthyl residue conferred crystallinity to all the obtained cycloadducts. Although low diastereofacial selectivity was recorded in DA reactions of dienes **20** and **21**, the preferred face of dienophile approach is the one, which was expected on the basis of previously reported considerations concerning the stereochemical outcome of sulfinyl diene cycloadditions.[9] The actual work gives new support to our previous statement that the sulfur configuration is not the only controller of the diastereofacial selectivity, but further structural features of diene, dienophile, and non-diene group linked to the sulfoxide sulfur contribute significantly to the process of facial discrimination. Finally, removal of the arylsulfoxide auxiliary from adduct **24** was easily accomplished by Raney nickel desulfurization method.

4. Experimental

4.1. General

All reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F 254) and the products were visualized with iodine or acid vanillin solution. Silica gel 60, 230–400 mesh, was used for column chromatography. Petrol refers to light petroleum, bp 30–40 °C. Melting points were measured on a microscopic apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ solutions unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions (unless otherwise stated) with TMS as internal standard. IR spectra were recorded in nujol. Mass spectrum was measured by FAB (*m*-nitrobenzyl alcohol as matrix).

X-ray crystallography. The analysis was carried out with a Goniometer Oxford Diffraction KM4 Xcalibur2 at room temperature. Graphite-monochromated Mo Kα radiation (40 mA/−40 KV) and a KM4 CCD/SAPPHIRE detector were used for cell parameter determination and data collection. The integrated intensities, measured using the ω scan mode, were corrected for Lorentz and polarization effects.[12] The substantial redundancy in data allows empirical absorption corrections (SADABS[13]) to be applied using multiple measurements of symmetry-equivalent reflections. Structure was solved by direct methods of

SIR97[14] and refined using the full-matrix least squares on F^2 provided by SHELXL97.[15]

Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 278055. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.1.1. 3-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-phenol (10). To a mixture of resorcinol (**9**) (2.42 g, 21.98 mmol) and anhydrous K_2CO_3 (1.82 g, 13.17 mmol) in anhydrous DMF (30 mL) MenCl (0.92 mL, 4.41 mmol) was added under Ar. After being stirred at 50 °C for 46 h, the reaction mixture was allowed to reach spontaneously the room temperature and quenched with saturated NH_4Cl solution (60 mL). The aqueous layer was extracted with CH_2Cl_2 (4×60 mL), the organic phases were recollected, washed with H_2O (6×250 mL) and dried over Na_2SO_4. Evaporation of the solvent gave a crude mixture that was purified by column chromatography (CH_2Cl_2/MeOH 50:1) to obtain phenol **10** as an orange solid (1.05 g, 3.77 mmol, 85% from MenCl), mp 62–64 °C; $[\alpha]_D^{24}$ −154.6 (*c* 0.1); ^{1}H NMR δ 7.10 (t, *J*=8.1 Hz, 1H), 6.58 (ddd, *J*=8.1, 2.1, 0.9 Hz, 1H), 6.54 (t, *J*=2.1 Hz, 1H), 6.47 (ddd, *J*=8.1, 2.1, 0.9 Hz, 1H), 6.32 (br s, 1H), 5.30 (d, *J*=7.2 Hz, 1H), 5.22 (d, *J*=7.2 Hz, 1H), 3.49 (dt, *J*=10.8, 4.2 Hz, 1H), 2.1–2.0 (m, 2H), 1.7–1.6 (m, 2H), 1.4–1.3 (m, 1H), 1.3–1.2 (m, 1H), 1.1–0.8 (m, 3H), 0.90 (d, *J*=6.6 Hz, 3H), 0.84 (d, *J*=6.9 Hz, 3H), 0.63 (d, *J*=6.9 Hz, 3H); ^{13}C NMR δ 158.7, 156.9, 129.9, 108.6, 107.9, 103.4, 91.1, 78.1, 48.1, 41.1, 34.3, 31.5, 25.2, 22.9, 22.2, 21.0, 15.5. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H 9.41. Found: C, 73.26; H, 9.32.

4.1.2. 2-{2-Hydroxy-4-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-phenylsulfanyl}-1*H*-isoindole-1,3(2*H*)-dione (11). To a solution of phenol **10** (1.90 g, 6.82 mmol) in anhydrous $CHCl_3$ (70 mL) kept at 0 °C under Ar, a PhtNSCl solution[6] (1.46 g, 6.82 mmol) in anhydrous $CHCl_3$ (70 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 20 min, then quenched with saturated $NaHCO_3$ solution (100 mL). The organic phase was extracted with CH_2Cl_2 (100 mL), washed with H_2O (2×150 mL), and dried over Na_2SO_4. The solvent was removed at reduced pressure. Column chromatography (CH_2Cl_2) afforded compound **11** as a white solid (1.79 g, 3.93 mmol, 58%), mp 128–130 °C; $[\alpha]_D^{24}$ −70.5 (*c* 0.3); ^{1}H NMR δ 8.33 (s, 1H), 7.9–7.7 (m, 4H), 7.74 (d, *J*=8.7 Hz, 1H), 6.66 (d, *J*=2.4 Hz, 1H), 6.52 (dd, *J*=8.7, 2.4 Hz, 1H), 5.28 (d, *J*=7.2 Hz, 1H), 5.17 (d, *J*=7.2 Hz, 1H), 3.42 (dt, *J*=10.8, 4.2 Hz, 1H), 2.1–2.0 (m, 2H), 1.6 (m, 2H), 1.4–1.3 (m, 1H), 1.2–1.1 (m, 1H), 1.0–0.7 (m, 3H), 0.87 (d, *J*=6.6 Hz, 3H), 0.81 (d, *J*=6.9 Hz, 3H), 0.59 (d, *J*=6.9 Hz, 3H); ^{13}C NMR δ 168.5, 162.9, 160.4, 139.4, 134.7, 131.8, 124.1, 110.8, 108.9, 103.5, 91.3, 78.7, 48.0, 41.1, 34.2, 31.4, 25.1, 22.8, 22.2, 20.9, 15.5. Anal. Calcd for $C_{25}H_{29}NO_5S$: C, 65.91; H, 6.42; N, 3.07. Found: C, 65.68; H, 6.21; N, 3.11.

4.1.3. 3-{2-Hydroxy-4-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-phenylsulfanyl}-propanenitrile (12). A solution of thio-derivative **11** (1.79 g, 3.93 mmol) in anhydrous THF (40 mL) was added, at 0 °C under Ar, to a suspension of LAH (0.90 g, 23.72 mmol) in anhydrous THF (25 mL). After 1 h of stirring at room temperature, the mixture was quenched with HCl 1 N (50 mL) and ice. The resulting suspension was extracted with Et_2O (3×100 mL) and the organic phase dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave the crude 5-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-2-mercapto-phenol (1.49 g) that was used in the next step without purification; ^{1}H NMR δ 7.35 (d, *J*=8.7 Hz, 1H), 6.67 (d, *J*=2.7 Hz, 1H), 6.54 (dd, *J*=8.7, 2.7 Hz, 1H), 6.39 (s, 1H), 5.29 (d, *J*=7.2 Hz, 1H), 5.19 (d, *J*=7.2 Hz, 1H), 3.46 (dt, *J*=10.5, 4.2 Hz, 1H), 2.82 (s, 1H), 2.1–2.0 (m, 1H), 1.7–1.6 (m, 2H), 1.4–1.2 (m, 2H), 1.0–0.7 (m, 4H), 0.90 (d, *J*=6.6 Hz, 3H), 0.84 (d, *J*=7.2 Hz, 3H), 0.62 (d, *J*=7.2 Hz, 3H). The solution of the crude 5-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-2-mercapto-phenol (1.49 g, 4.8 mmol about) in anhydrous THF (40 mL), was added under Ar to a solution of acrylonitrile (3.16 mL, 48.00 mmol) and Et_3N (0.64 mL, 4.59 mmol) in anhydrous THF (15 mL). The mixture was stirred at room temperature for 20 h, then quenched with saturated NH_4Cl solution (40 mL) and extracted with Et_2O (2×40 mL). The organic phase was washed with H_2O (2×100 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography (petrol/EtOAc 3:1) to nitrile **12** as an orange solid (0.95 g, 2.61 mmol, 66% from **11**), mp 64–66 °C; $[\alpha]_D^{25}$ −95.4 (*c* 0.3); ^{1}H NMR δ 7.36 (d, *J*=8.7 Hz, 1H), 6.71 (d, *J*=2.7 Hz, 1H), 6.55 (s, 1H), 6.59 (dd, *J*=8.4, 2.7 Hz, 1H), 5.31 (d, *J*=7.2 Hz, 1H), 5.22 (d, *J*=7.2 Hz, 1H), 3.46 (dt, *J*=10.5, 4.2 Hz, 1H), 2.85 (t, *J*=7.2 Hz, 2H), 2.51 (t, *J*=7.2 Hz, 2H), 2.1–2.0 (m, 2H), 1.7–1.6 (m, 2H), 1.4–1.3 (m, 1H), 1.3–1.2 (m, 1H), 1.0–0.8 (m, 3H), 0.90 (d, *J*=6.6 Hz, 3H), 0.83 (d, *J*=7.2 Hz, 3H), 0.60 (d, *J*=6.6 Hz, 3H); ^{13}C NMR δ 160.9, 158.3, 137.1, 117.8, 109.5, 107.7, 102.9, 91.1, 78.4, 48.1, 41.0, 34.3, 31.8, 31.5, 25.2, 22.9, 22.2, 21.0, 17.9, 15.6; IR ν_{max} 2360 (CN) cm^{-1}. Anal. Calcd for $C_{20}H_{29}NO_3S$: C, 66.08; H, 8.04; N, 3.85. Found: C, 65.86; H, 7.96; N, 3.77.

4.1.4. 3-{2-Hydroxy-4-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-phenylsulfinyl}-propanenitriles 13 (two S-epimers). To a solution of sulfide **12** (0.95 g, 2.61 mmol) in anhydrous CH_2Cl_2 (130 mL) at 0 °C *m*-CPBA (0.64 g 70%, 2.60 mmol) was added. The solution was stirred at 0 °C for 20 min, diluted with CH_2Cl_2 (100 mL) and washed with saturated $NaHCO_3$ solution (2×150 mL). The organic phase was dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (petrol/EtOAc 1:1), to give an inseparable 1:1 mixture of sulfur epimers **13** as a white solid (0.76 g, 2.00 mmol, 77%), mp 128–131 °C; ^{1}H NMR δ 9.81 (s, 1H), 7.00 (d, *J*=8.7 Hz, 1H), 6.7–6.6 (m, 2H), 5.32 (d, *J*=7.5 Hz, 1H), 5.23 (d, *J*=7.5 Hz, 1H), 3.46 (dt, *J*=10.5, 4.2 Hz, 1H), 3.4–3.2 (m, 2H), 3.0–2.9 (m, 1H), 2.7–2.6 (m, 1H), 2.1–2.0 (m, 2H), 1.7–1.6 (m, 2H), 1.4–1.3 (m, 1H), 1.3–1.2 (m, 1H), 1.0–0.8 (m, 3H), 0.92 (d, *J*=6.3 Hz, 3H), 0.84 (d, *J*=6.9 Hz, 3H), 0.61 (d, *J*=6.9 Hz, 3H); ^{13}C NMR δ 162.2, 160.0, 126.6, 116.8, 112.6, 108.9, 106.1, 91.2, 78.7, 49.0, 48.1, 41.1, 34.3, 31.5, 25.3, 23.0, 22.2, 20.9, 15.6, 10.7. Anal. Calcd for $C_{20}H_{29}NO_4S$: C, 63.30; H, 7.70; N, 3.69. Found: C, 63.01; H, 7.55; N, 3.51.

4.1.5. 1-(1-Cyclohexen-1-yl)-1-{2-hydroxy-4-[(1*R*,2*S*,5*R*)-menthoxymethoxy]-phenylsulfinyl}-ethene 15 (two S-epimers). A mixture of sulfoxides **13** (0.20 g, 0.53 mmol) and 1-ethynylcyclohexene (0.50 mL, 4.25 mmol) was heated at 130 °C under Ar. After 1 h of stirring, the mixture was allowed to reach spontaneously the room temperature and then was diluted with CH_2Cl_2 (10 mL). Evaporation of the solvent under reduced pressure gave a crude product that was purified by column chromatography (petrol/EtOAc 7:1). An oily 1:1 mixture of epimers **15** was isolated (0.11 g, 0.25 mmol, 47%). Anal. Calcd for $C_{25}H_{36}O_4S$: C, 69.41; H, 8.39. Found: C, 69.78; H, 8.15. Further attempts of chromatographic separation of the two epimers allowed the isolation of very small amounts of enantiopure sulfoxides. *More mobile sulfur epimer* **15** was obtained as an oil; $[\alpha]_D^{25}$ −119.0 (*c* 0.1); ^{1}H NMR δ 9.92 (s, 1H), 6.96 (dd, J=8.4, 0.6 Hz, 1H), 6.6–6.5 (m, 2H), 5.93 (br s, 2H), 5.65 (br s, 1H), 5.28 (d, J=7.2 Hz, 1H), 5.20 (d, J=7.2 Hz, 1H), 3.44 (dt, J=10.5, 4.2 Hz, 1H), 2.2–2.0 (m, 5H), 1.7–1.2 (m, 10H), 1.0–0.8 (m, 2H), 0.89 (d, J=6.6 Hz, 3H), 0.82 (d, J=7.2 Hz, 3H), 0.58 (d, J=7.2 Hz, 3H); ^{13}C NMR δ 161.5, 161.4, 152.6, 131.6, 129.9, 128.1, 113.2, 112.9, 107.5, 106.0, 90.9, 78.4, 48.2, 41.1, 34.4, 31.5, 28.6, 25.4, 25.3, 23.1, 22.4, 22.2, 21.6, 21.0, 15.6. Less mobile sulfur epimer **15** was obtained as an oil; $[\alpha]_D^{25}$ −58.2 (*c* 0.02); ^{1}H NMR δ 9.95 (s, 1H), 6.96 (d, J=9.0 Hz, 1H), 6.50 (m, 2H), 5.93 (br s, 2H), 5.65 (br s, 1H), 5.28 (d, J=7.5 Hz, 1H), 5.20 (d, J=7.2 Hz, 1H), 3.45 (dt, J=10.5, 4.2 Hz, 1H), 2.2–2.0 (m, 5H), 1.7–1.2 (m, 10H), 1.0–0.8 (m, 2H), 0.89 (d, J=6.6 Hz, 3H), 0.82 (d, J=6.9 Hz, 3H), 0.58 (d, J=7.2 Hz, 3H); ^{13}C NMR δ 161.5, 161.5, 152.6, 131.6, 129.9, 128.1, 113.3, 112.9, 107.2, 106.3, 91.0, 78.4, 48.2, 41.1, 34.4, 31.5, 28.6, 25.4, 25.3, 23.1, 22.4, 22.2, 21.6, 21.0, 15.5.

4.1.6. (S_a)-3-(2′-hydroxy-1,1′-binaphthalen-2-sulfanyl)-propanenitrile (17). To a solution of (S_a)-2′-mercapto-1,1′-binaphthalen-2-ol[7,16] (**16**) (2.00 g, 6.61 mmol) in anhydrous THF (60 mL), acrylonitrile (4.38 mL, 66.53 mmol) and Et_3N (0.92 mL, 6.61 mmol) were added under N_2. The reaction mixture was stirred at room temperature for 72 h. The resulting yellow-orange solution was diluted with CH_2Cl_2 (200 mL) and washed with saturated NH_4Cl solution (3×200 mL) and H_2O (2×200 mL). The organic layer was dried over Na_2SO_4, and the solvent removed under reduced pressure. Column chromatography (eluant: from petrol/CH_2Cl_2 1:1 to pure CH_2Cl_2) gave nitrile **17** as a white solid (1.77 g, 4.98 mmol, 75%), mp 93–95 °C; $[\alpha]_D^{24}$ −67.8 (*c* 1.0, THF); ^{1}H NMR (CD_3CN) δ 8.05 (d, J=8.7 Hz, 1H), 7.97 (d, J=8.7 Hz, 1H), 7.94 (d, J=9.3 Hz, 1H), 7.89 (d, J=8.1 Hz, 1H), 7.73 (d, J=8.7 Hz, 1H), 7.47 (dt, J=7.4, 1.1 Hz, 1H), 7.29 (m, 3H), 7.21 (dt, J=7.7, 1.2 Hz, 1H), 7.04 (d, J=8.7 Hz, 1H), 6.83 (d, J=8.7 Hz, 1H), 3.12 (t-like, J=7.1 Hz, 2H), 2.57 (t-like, J=7.1 Hz, 2H); ^{13}C NMR [$(CD_3)_2CO$] δ 153.3, 135.5, 134.8, 134.5, 134.4, 133.4, 130.6, 129.65, 129.59, 128.9, 127.6, 127.5, 127.2, 126.7, 126.5, 124.9, 123.7, 119.1, 118.1, 29.4, 18.6. Anal. Calcd for $C_{23}H_{17}NOS$: C, 77.72; H, 4.82; N, 3.94. Found: C, 77.35; H, 4.80; N, 4.00. The same chromatography allowed the isolation of small amounts (4%) of bis[(S_a)-2′-hydroxy-1,1′-binaphthyl-2-yl] disulfide; $[\alpha]_D^{27}$ −87.3 (*c* 1.0).[7]

4.1.7. (S_a)-3-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-propanenitriles 18 (two S-epimers). To a solution of sulfide **17** (1.11 g, 3.12 mmol) in CH_2Cl_2 (50 mL), at −50 °C, a solution of *m*-CPBA (0.73 g 70%, 2.96 mmol) in CH_2Cl_2 (80 mL) was added dropwise. After 1 h of stirring, the mixture was diluted with CH_2Cl_2 (50 mL) and treated with 10% $Na_2S_2O_3$ solution (150 mL). The organic phase was washed with saturated $NaHCO_3$ solution (2×150 mL) and H_2O (2×150 mL), dried over Na_2SO_4, and evaporated under reduced pressure to give sulfoxides **18** as a 1:1 mixture (1.07 g, 2.88 mmol, 92%) of two S-epimers. The epimers were separated by column chromatography (CH_2Cl_2/EtOAc, 20:1). More mobile sulfur epimer **18** was obtained as a white solid, mp 78–80 °C; $[\alpha]_D^{26}$ −193.0 (*c* 0.3, THF); ^{1}H NMR δ 8.18 (d, J=8.7 Hz, 1H), 8.07 (d, J=8.7 Hz, 1H), 7.97 (d, J=8.1 Hz, 1H), 7.91 (d, J=8.7 Hz, 1H), 7.86 (d, J=8.1 Hz, 1H), 7.6–7.5 (m, 1H), 7.4–7.2 (m, 5H), 6.95 (d, J=8.4 Hz, 1H), 6.57 (s, 1H), 3.0–2.8 (m, 2H), 2.7–2.6 (m, 1H), 2.5–2.4 (m, 1H); ^{13}C NMR δ 152.0, 138.1, 135.1, 133.0, 132.5, 132.2, 131.6, 130.2, 128.8, 128.7, 128.3, 128.2, 127.9, 127.7, 125.8, 124.1, 123.9, 119.7, 117.7, 117.5, 113.4, 47.9, 9.5. Anal. Calcd for $C_{23}H_{17}NO_2S$: C, 74.37; H, 4.61; N, 3.77. Found: C, 74.58; H, 4.60; N, 3.57. Then less mobile sulfur epimer **18** was eluted as a white solid, mp 98–100 °C; $[\alpha]_D^{26}$ +377.4 (*c* 0.8, THF); ^{1}H NMR (CD_3CN) δ 8.27 (d, J=8.4 Hz, 1H), 8.14 (d, J=8.7 Hz, 1H), 8.04 (d, J=8.1 Hz, 1H), 7.98 (d, J=9.0 Hz, 1H), 7.92 (d, J=7.8 Hz, 1H), 7.7–7.6 (m, 1H), 7.4–7.2 (m, 5H), 6.79 (d, J=8.4 Hz, 1H), 5.93 (br s, 1H), 2.6–2.5 (m, 2H), 2.5–2.3 (m, 2H); ^{13}C NMR [$(CD_3)_2SO$] δ 152.6, 139.3, 134.5, 133.7, 132.7, 132.0, 130.9, 129.3, 128.6 (2C), 127.8, 127.7, 127.4, 127.2, 125.7, 123.3, 123.0, 120.0, 118.5, 118.3, 112.5, 47.0, 8.8. Anal. Calcd for $C_{23}H_{17}NO_2S$: C, 74.37; H, 4.61; N, 3.77. Found: C, 74.27; H, 4.72; N, 3.80.[†]

4.1.8. (S_a)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadienes 20 and 21 (two S-epimers). To a suspension of sulfoxides **18** (0.18 g, 0.48 mmol) in toluene (12 mL) 2-methyl-1-buten-3-yne (0.70 mL, 7.36 mmol) was added and the reaction mixture refluxed and stirred for 1.5 h. The resulting yellow solution was cooled to room temperature and the 1:1 mixture of dienes **20** and **21** was obtained as a white precipitate (0.14 g, 0.36 mmol, 75% total yield). The epimers were separated by column chromatography (initial elution with CH_2Cl_2, then CH_2Cl_2/EtOAc 9:1). First eluted was (S_a,S_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadiene (**20**) as a white solid, mp 173 °C dec; $[\alpha]_D^{24}$ −206.7 (*c* 1.0, THF); ^{1}H NMR δ 8.14 (d, J=9.0 Hz, 1H), 7.98 (d, J=7.2 Hz, 1H), 7.96 (d, J=8.1 Hz, 1H), 7.87 (d, J=8.1 Hz, 1H), 7.60 (m, 1H), 7.4–7.2 (m, 6H), 7.11 (d, J=8.1 Hz, 1H), 5.92 (s, 1H), 5.68 (s, 1H), 4.88 (s, 1H), 4.81 (s, 1H), 1.65 (s, 3H); ^{13}C NMR [$DCON(CD_3)_2$] δ 154.8, 154.4, 141.6, 137.5, 137.3, 135.5, 135.0, 133.2, 131.2, 130.3, 129.0, 128.9,

[†] When sulfide **17** was oxidized with an equimolar amount of *m*-CPBA at −15 °C, the 1:1 mixture of epimeric sulfoxides **18** was obtained in 73% total yield, together with (S_a)-3-(2′-hydroxy-1,1′-binaphthalen-2-sulfonyl)-propanenitrile (14%), mp 204–206 °C, more mobile than sulfoxides **18** (column chromatography with CH_2Cl_2/EtOAc 19:1); ^{1}H NMR δ 8.34 (d, J=8.8 Hz, 1H), 8.22 (d, J=8.8 Hz, 1H), 8.04 (d, J=8.3 Hz, 1H), 8.03 (d, J=9.0 Hz, 1H), 7.93 (split d, J=7.8 Hz, 1H), 7.68 (ddd, J=8.3, 6.9, 1.3 Hz, 1H), 7.4–7.3 (m, 4H), 7.22 (split d, J=8.5 Hz, 1H), 6.74 (split d, J=8.4 Hz, 1H), 3.0–2.5 (m, 4H).

128.7, 128.6, 127.8, 127.4, 127.3, 124.9, 123.6, 121.7, 118.8, 117.0 (2C), 115.5, 22.1; IR ν_{max} 3280 (OH), 1007 (SO) cm^{-1}. Anal. Calcd for $C_{25}H_{20}O_2S$: C, 78.09; H, 5.24. Found: C, 77.88; H, 5.25. Then (S_a,R_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadiene (**21**) was eluted as a white solid, mp 124–126 °C; $[\alpha]_D^{25}+378.4$ (*c* 1.0, THF); ^1H NMR δ 8.04 (d, $J=8.7$ Hz, 1H), 7.91 (d, $J=8.4$ Hz, 1H), 7.82 (m, 2H), 7.53 (t, $J=7.0$ Hz, 1H), 7.47 (d, $J=9.0$ Hz, 1H), 7.4–7.1 (m, 5H), 6.76 (d, $J=8.4$ Hz, 1H), 6.23 (s, 1H), 5.87 (s, 1H), 4.34 (s, 1H), 4.26 (s, 1H), 1.59 (s, 3H); ^{13}C NMR [DCON$(CD_3)_2$] δ 155.7, 154.0, 142.2, 137.4, 136.1, 135.4, 135.1, 133.2, 131.2, 130.0, 129.1, 128.9, 128.8, 128.4, 127.7, 127.4, 126.8, 125.7, 123.4, 121.7, 119.1, 116.5, 116.4, 115.4, 22.0; IR ν_{max} 3250 (OH), 1015 (SO) cm^{-1}. Anal. Calcd for $C_{25}H_{20}O_2S$: C, 78.09; H, 5.24. Found: C, 78.20; H, 5.12.

4.1.9. (S_a,S_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-diones 22 and 23 (two diastereomers). To a suspension of (S_a,S_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadiene (**20**) (0.21 g, 0.55 mmol) in CH_2Cl_2 (40 mL) NMM (1.19 g, 10.71 mmol) was added, and the mixture was refluxed and stirred for 72 h. After removal of the solvent, the crude product was purified by column chromatography (eluant: from CH_2Cl_2/EtOAc 1.5:1 to pure EtOAc) to give the two diastereomeric cycloadducts **22** and **23**, in 2:1 ratio (0.24 g, 0.48 mmol, 87% overall yield). First eluted was the major adduct (3a*S*,7a*R*,S_a,S_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (**22**), white solid, mp 183 °C dec; $[\alpha]_D^{25}-226.5$ (*c* 0.8); ^1H NMR δ 8.3–8.1 (m, 2H), 7.9–7.7 (m, 3H), 7.5–7.4 (m, 1H), 7.3–7.1 (m, 5H), 6.99 (d, $J=8.4$ Hz, 1H), 2.8–2.5 (m, 4H), 2.71 (s, 3H), 2.3–2.2 (m, 2H), 1.02 (s, 3H). Anal. Calcd for $C_{30}H_{25}NO_4S$: C, 72.71; H, 5.08; N, 2.83. Found: C, 73.06; H, 5.10; N, 2.87. Less mobile was the minor adduct (3a*R*,7a*S*,S_a,S_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (**23**), white solid, mp 164–166 °C; $[\alpha]_D^{25}-151.8$ (*c* 0.6); ^1H NMR [$(CD_3)_2SO$] δ 9.53 (s, 1H), 8.31 (d, $J=8.8$ Hz, 1H), 8.16 (d, $J=8.8$ Hz, 1H), 8.09 (d, $J=8.4$ Hz, 1H), 7.93 (d, $J=8.8$ Hz, 1H), 7.88 (d, $J=8.1$ Hz, 1H), 7.58 (t, $J=7.0$ Hz, 1H), 7.36 (t, $J=8.2$ Hz, 1H), 7.3–7.2 (m, 3H), 7.10 (d, $J=8.7$ Hz, 1H), 6.87 (d, $J=8.1$ Hz, 1H), 3.0–2.9 (m, 1H), 2.8–2.6 (m, 2H), 2.66 (s, 3H), 2.35 (dd, $J=15.3$, 7.8 Hz, 1H), 2.04 (dd, $J=15.0$, 10.4 Hz, 1H), 1.63 (t-like, $J=12.3$ Hz, 1H), 1.05 (s, 3H); MS *m/z* (%) 496 (29, M+1), 268 (15), 239 (8), 95 (49), 81 (51), 69 (82), 55 (100), 43 (76); IR ν_{max} 3200 (OH), 1770 and 1701 (CO), 1005 (SO) cm^{-1}. Anal. Calcd for $C_{30}H_{25}NO_4S$: C, 72.71; H, 5.08; N, 2.83. Found: C, 73.00; H, 5.18; N, 2.90.

4.1.10. (S_a,R_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-diones 24 and 25 (two diastereomers). To a solution of (S_a,R_S)-2-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-3-methyl-1,3-butadiene (**21**) (0.20 g, 0.52 mmol) in CH_2Cl_2 (25 mL) NMM (1.18 g, 10.62 mmol) was added and the mixture refluxed for 72 h. After removal of the solvent, the crude product was purified by column chromatography (eluant: from CH_2Cl_2/EtOAc 2.3:1 to pure EtOAc) to give the two diastereomeric cycloadducts **24** and **25** in 3:2 ratio (0.18 g, 0.36 mmol, 69% overall yield). First eluted was the major adduct (3a*R*,7a*S*,S_a,R_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (**24**), white solid, mp 175–177 °C; $[\alpha]_D^{27}+179.7$ (*c* 0.5); ^1H NMR [$(CD_3)_2SO$] δ 10.00 (s, 1H), 8.32 (d, $J=8.7$ Hz, 1H), 8.10 (d, $J=8.7$ Hz, 2H), 7.94 (d, $J=9.0$ Hz, 1H), 7.88 (d, $J=8.1$ Hz, 1H), 7.58 (t, $J=7.4$ Hz, 1H), 7.39 (d, $J=9.0$ Hz, 1H), 7.33 (t, $J=7.6$ Hz, 1H), 7.27 (t, $J=7.2$ Hz, 1H), 7.15 (t, $J=7.2$ Hz, 1H), 6.96 (d, $J=8.4$ Hz, 1H), 6.41 (d, $J=8.4$ Hz, 1H), 2.9–2.7 (m, 2H), 2.67 (s, 3H), 1.8–1.7 (m, 2H), 1.3–1.2 (m, 2H), 0.51 (s, 3H); ^{13}C NMR [$(CD_3)_2SO$] δ 178.9, 178.4, 152.6, 144.2, 139.4, 134.2, 133.8, 133.2, 132.2, 132.1, 130.4, 128.5, 128.1, 128.0, 127.3, 127.1, 126.5, 125.4, 123.5, 122.8, 120.4, 118.7, 113.3, 38.7, 38.5, 30.7, 30.0, 24.5, 19.9, 18.1; IR ν_{max} 3100 (OH), 1780 and 1698 (CO), 985 (SO) cm^{-1}. Anal. Calcd for $C_{30}H_{25}NO_4S$: C, 72.71; H, 5.08; N, 2.83. Found: C, 72.92; H, 5.05; N, 2.83. Less mobile was the minor adduct (3a*S*,7a*R*,S_a,R_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (**25**), white solid, mp 154–156 °C; $[\alpha]_D^{27}+168.0$ (*c* 0.5); ^1H NMR [$(CD_3)_2SO$] δ 9.99 (br s, 1H), 8.30 (d, $J=8.4$ Hz, 1H), 8.15 (d, $J=8.7$ Hz, 1H), 8.09 (d, $J=8.1$ Hz, 1H), 7.94 (d, $J=9.0$ Hz, 1H), 7.86 (d, $J=8.1$ Hz, 1H), 7.57 (t, $J=7.4$ Hz, 1H), 7.38 (d, $J=9.0$ Hz, 1H), 7.32 (t, $J=7.7$ Hz, 1H), 7.23 (t, $J=7.4$ Hz, 1H), 7.00 (t, $J=7.5$ Hz, 1H), 6.95 (d, $J=8.4$ Hz, 1H), 6.32 (d, $J=8.1$ Hz, 1H), 2.68 (s, 3H), 1.81 (dd, $J=15.4$, 7.9 Hz, 2H), 1.5–1.4 (m, 2H), 1.01 (dd, $J=15.2$, 8.6 Hz, 2H), 0.55 (s, 3H); ^{13}C NMR [$(CD_3)_2SO$] δ 178.6, 178.5, 152.5, 144.5, 139.6, 134.2, 133.8, 133.0, 132.1, 130.4, 128.6, 128.4, 128.1, 128.0, 127.2, 127.0, 126.5, 125.5, 123.4, 122.7, 120.3, 118.6, 113.5, 37.8, 30.0, 24.2, 19.4, 17.6. Anal. Calcd for $C_{30}H_{25}NO_4S$: C, 72.71; H, 5.08; N, 2.83. Found: C, 72.51; H, 5.10; N, 3.22.

X-ray structural analysis of **25**, CCDC no. 278055: formula $C_{34}H_{33}NO_6S$ ($C_{30}H_{25}NO_4S+C_4H_8O_2$), $M=583.67$, orthorhombic, space group $P\ 2_1\ 2_1\ 2_1$, $a=10.517(2)$ Å, $b=12.410(2)$ Å, $c=22.803(7)$ Å, $V=2976(1)$ Å^3, $Z=4$, $D_c=1.303$, $\mu=0.156\ mm^{-1}$, $F(000)=1232$. Reflections (4700) were collected with a $2.63<\theta<21.36$ range with a completeness to θ 95.3%; 3107 were independent, the parameters were 385, and the final *R* index was 0.0839 for reflections having $I>2\sigma(I)$, and 0.1559 for all data. Compound **25** crystallizes with a molecule of EtOAc in the asymmetric unit. The positions of EtOAc carbon and oxygen atoms in are not well defined so that their coordinates have been splitted, they were refined as isotropic, and the relative hydrogen atoms were not assigned. The non-hydrogen atoms of compound **25** were refined anisotropically whereas its hydrogen atoms were refined as isotropic and assigned in calculated positions.

4.2. Desulfurization of (3a*R*,7a*S*,S_a,R_S)-3a,4,7,7a-tetrahydro-5-(2′-hydroxy-1,1′-binaphthalen-2-sulfinyl)-2,6-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (24)

To a solution of cycloadduct **24** (0.10 g, 0.20 mmol) in anhydrous THF (20 mL) a suspension of commercial W-2 Raney nickel (nickel sponge, suspension in water, 1.80 mL) in anhydrous THF (10 mL) was added. The reaction mixture was stirred at room temperature for 5 h and then filtered

through a Celite pad. The Celite cake was washed with EtOAc and the resulting clear solution was concentrated under reduced pressure. The crude mixture was purified by two consecutive column chromatographies (petrol/EtOAc 2.3:1) to give, in order of increasing retention times (2:1 molar ratio, 55% overall yield), (3a*S*,7a*R*)-hexahydro-2,5-dimethyl-1*H*-isoindole-1,3(2*H*)-diones **27** (6:1 epimeric mixture, 6.7 mg, 0.04 mmol), followed by (3a*S*,7a*R*)-3a,4,7,7a-tetrahydro-2,5-dimethyl-1*H*-isoindole-1,3(2*H*)-dione (**26**) (13.3 mg, 0.07 mmol). The analytical and spectroscopic data, measured for **26** and **27**, were fully consistent with the ones reported in the literature.[11]

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