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Asymmetric Diels–Alder reactions of 5-substituted and 5,6-disubstituted (*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinones with cyclopentadiene and *trans*-piperylene

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Abstract

A systematic study of reactions between 5-substituted and 5,6-disubstituted (*S*)-2-*p*-tolylsulfinyl-*p*-benzoquinones and cyclopentadiene or *trans*-piperylene is reported. Complete regio and π-facial selectivities are observed. The different behaviours of cyclic and acyclic dienes in the presence of $ZnBr_2$ (cyclopentadiene showed reversed diastereoselection) and the role of $BF_3 \cdot OEt_2$ are discussed. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

Asymmetric Diels–Alder cycloaddition with chirally modified dienophiles is one of the most powerful tools for constructing structurally complex molecules in enantiomerically pure forms.[1] Although quinones are among the best dienophiles traditionally used in [4+2] cycloadditions, few examples[2] of their use in asymmetric synthesis are known, probably as a consequence of the inherent difficulties encountered in the synthesis of such chiral targets.

A few years ago, we reported a short and efficient synthesis of enantiomerically pure (*S*)-2-*p*-tolylsulfinylquinones[3] and started the study of their behaviour as dienophiles with the simplest (*S*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone **1**. To our surprise, cyclic dienes reacted with this dienophile from the unsubstituted dienophilic double bond C_5–C_6 in a highly *endo*- and π-facial-diastereoselective manner.[3a,4] This result precluded the stereoselective synthesis of adducts resulting in the evolution of C_2–C_3 from the simplest quinonic system. The introduction of substituents at C_5 and/or C_6 would decrease the dienophilic character of the C_5–C_6 double bond thus allowing the synthesis of the so far unknown adducts. In accordance with the high π-facial diastereoselectivity observed in cycloadditions

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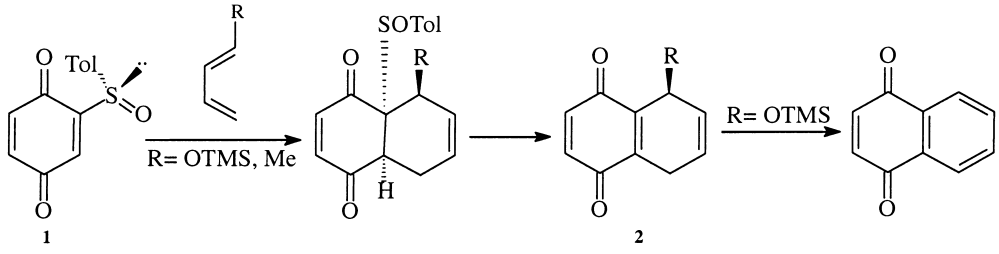
between 2-*p*-tolylsulfinyl-1,4-naphthoquinones[5] and cyclic dienes, reactions of sulfinyl-*p*-benzoquinone derivatives at the sulfinyl substituted double bond should also occur stereoselectively. On the other hand, reactions of **1** with acyclic dienes[2a,4] took place from the sulfinyl substituted double bond. The resulting adducts suffered a spontaneous elimination of sulfenic acid yielding 5,8-dihydro-1,4-naphthoquinones **2**.[6] When derived from 1-alkoxybutadienes, these derivatives further evolved into a naphthoquinone, thus precluding the isolation of optically-active compounds that could only be obtained from *trans*-piperylene and other 1-alkyl substituted dienes[7] (Scheme 1). In the latter, some aspects relating to the regioselectivity and stereoselectivity of the reactions had not been clarified and required additional studies.



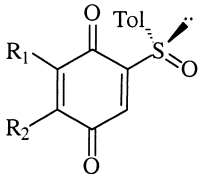
Scheme 1.

In this paper we report on a systematic study of the reactions of 5-alkyl and 5-alkyl-6-methoxy-2-*p*-tolylsulfinyl-*p*-benzoquinones **3a**–**c** (Fig. 1) with cyclopentadiene and *trans*-piperylene in order to address the above-mentioned issues. These dienophiles were chosen bearing in mind the construction of diterpenoid quinones[8] which could be prepared from an appropriate sulfinylbenzoquinone. The influence of the different substituents both at C_5 and C_6 in the control of diastereoselectivity and regioselectivity could be evaluated.

2. Results and discussion

Enantiomerically pure (*S*)-*p*-tolylsulfinylbenzoquinones **3a**–**c** were prepared in a highly regiocontrolled manner in two steps: (i) *ortho*-directed metallation of an adequately substituted 1,4-dimethoxybenzene followed by sulfinylation with menthyl-*p*-toluene sulfinate,[9] and (ii) oxidation with CAN.[10] Diels–Alder reactions of benzoquinones **3a**–**c** with cyclopentadiene were carried out under thermal and Lewis acid catalysed conditions. The results obtained are collected in Table 1.

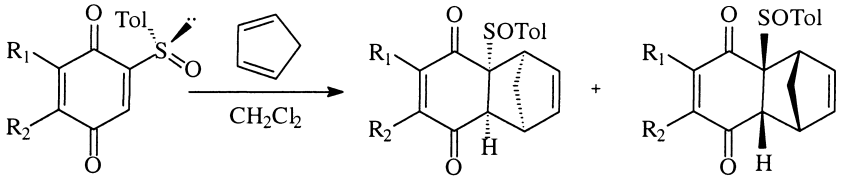
Reaction of **3a** took place under very mild conditions (−78°C, Table 1, entry 2) to afford a 69% yield of a 96/4 (de 92%) mixture of two adducts **4a** and **5a** resulting from the *endo*-approach of the diene on both diastereotopic faces of the C_2–C_3 dienophilic double bond. A slightly higher diastereoselectivity (de >94%) but a lower yield (63%) was achieved when working at −20°C (entry 1). In the presence of $BF_3 \cdot OEt_2$ (5 equiv.) a faster cycloaddition occurred at −20°C giving rise to cycloadduct **4a** in 53% yield (Table 1, entry 3, de 92%). A similar increase in the reaction rate was observed under the influence of $ZnBr_2$ (entry 4) but the most relevant effect of this catalyst was the total inversion of π-facial



3a: R_1=H; R_2= Me
3b: R_1=H; R_2= ^{i}Pr
3c: R_1=OMe; R_2= ^{i}Pr

Figure 1.

Table 1
Diels–Alder reactions of *p*-tolylsulfinylbenzoquinones **3a–c** with cyclopentadiene in CH_2Cl_2



3 4 5

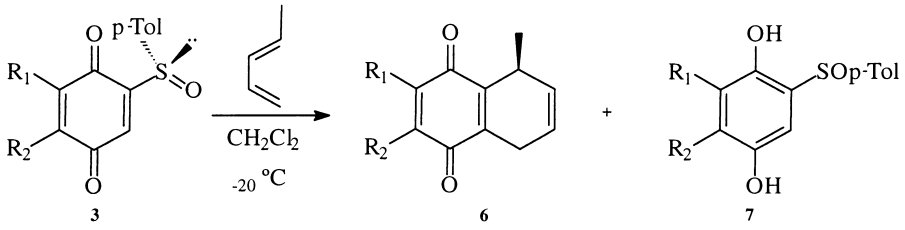
Entry	Quinone	T(°C)	Lewis acid(eq.)	Time (h)	Yield (%)	4 / 5	de(%)
1	**3a**	-20	—	48	63	>97 / <3	>94
2	**3a**	-78	—	168	69	96 / 4	92
3	**3a**	-20	$BF_3{\cdot}OEt_2$ (5)	0.5	53	96 / 4	92
4	**3a**	-20	$ZnBr_2$ (2)	0.3	80	9 / 91	82
5	**3a**	-20	$ZnBr_2$ (3)	0.3	a	4 / 96	92
6	**3b**	-20	—	15	53	96 / 4	92
7	**3b**	-78	—	48	72	>95 / <5	>90
8	**3b**	-78	$BF_3{\cdot}OEt_2$ (5)	0.75	76	98 / 2	96
9	**3b**	-78	$ZnBr_2$ (2)	1	70	<3 / >97	>94
10	**3c**	-20	—	22	73	89 / 11	78
11	**3c**	-78	—	72	65	89 / 11	78
12	**3c**	-20	$BF_3{\cdot}Et_2O$ (5)	1	50	31/69	38
13	**3c**	-20	$ZnBr_2$ (2)	1	86	10 / 90	80
14	**3c**	-20	$ZnBr_2$ (3)	1	72	<3 / >97	>97

a Yield not determined

diastereoselectivity. Thus, reaction of **3a** with cyclopentadiene yielded a 9/91 mixture of **4a** and **5a** from which the latter could be isolated pure in a 75% yield. Use of an excess of $ZnBr_2$ led to a 4/96 ratio of products in favour of **5a** (Table 1, entry 5). This behaviour is very similar to that observed for reactions of 2-*p*-tolylsulfinylnaphthoquinones with cyclopentadiene.[5]

Sulfinylquinone **3b** behaved similarly, giving diastereomer **4b** as the major product under both thermal- and $BF_3{\cdot}OEt_2$-catalysed conditions (Table 1, entries 6–8), and **5b** in the presence of $ZnBr_2$ (Table 1, entry 9). Compound **3c**, bearing an oxygenated group at C_6 (OCH_3), required three equivalents of $ZnBr_2$ to evolve in a complete diastereoselective manner (Table 1, entry 14). Although this was expected on the basis of a competition between the OMe group in the association with the Lewis acid, a similar effect is observed in the reaction with dienophile **3a** (compare entries 5 and 14). However, under thermal conditions **3c** led to diastereomer **4c** in a lower diastereomeric excess (78%, entries 10 and 11). The diastereoselection observed when reaction of **3c** was carried out in the presence of $BF_3{\cdot}OEt_2$ was even lower (Table 1, entry 12), probably due to the presence of the MeO substituent which could interfere in the association with the Lewis acid, as can be seen by the result.

Table 2
Diels–Alder reactions of *p*-tolylsulfinylbenzoquinones **3a–c** with *trans*-piperylene in CH_2Cl_2 at −20°C



3 6 7

Entry	Quinone	Lewis acid (eq.)	Time (h)	Yield (%)	6 / 7	ee (%)
1	**3a**	—	48	38	62 / 38	>97
2	**3a**	$ZnBr_2$ (2)	0.8	42	69/ 31	88
3	**3a**	$BF_3{\cdot}OEt_2$ (5)	1	78	100/ 0	>97
4	**3b**	—	120	38	61 / 39	>97
5	**3b**	$ZnBr_2$ (2)	1	47	74 / 26	94
6	**3b**	$BF_3{\cdot}OEt_2$ (5)	1	60	100 / 0	>97
7	**3c**	—	48	55	100 / 0	94
8	**3c**	$ZnBr_2$ (3)	0.8	80	100 / 0	84
9	**3c**	$BF_3{\cdot}Et_2O$ (5)	0.5	79	100 / 0	92

All adducts **4** and **5** were isolated in diastereomerically pure forms by flash chromatography (see Section 4) from the mixtures where they were the major products. Their absolute configurations, [4a*R*,5*R*,8*S*,8a*S*,(*S*)*S*] for **4** and [4a*S*,5*S*,8*R*,8a*R*,(*S*)*S*] for **5**, were established on the basis of ^{1}H NMR parameters taking into account the known effects of sulfinyl substituents on the chemical shift of the protons under their influence in the rigid norbornene–dione moiety[11] and by comparison with similar adducts previously described.

Reactions of quinones **3a–c** with the acyclic diene *trans*-piperylene (Table 2) were carried out under thermal conditions and in the presence of $BF_3 \cdot OEt_2$ or $ZnBr_2$. In all cases, dihydronaphthoquinones (+)-**6**, resulting from the tandem cycloaddition/pyrolytic elimination of the sulfenic acid, could be isolated in high enantiomeric excesses (ee 84–>97%).[12]

As can be seen, reaction times decreased in the presence of Lewis acids, but their influence on the π-facial diastereoselectivity was scarce. Moderate yields of **6**, achieved in thermal reactions of **3a** and **3b** (entries 1 and 4), are a consequence of the evolution of the starting sulfinylquinones to the corresponding hydroquinone derivatives **7** that were formed in significant amounts (38 and 39%, respectively) in a redox process.[13] In the presence of $ZnBr_2$ formation of **7** is decreased (entries 2 and 5) but not completely suppressed. This was only achieved when $BF_3 \cdot OEt_2$ was the catalyst (entries 3 and 6). The +M effect of the OMe group decreasing the redox potential of quinone **3c** would explain the absence of **7** in its reactions with *trans*-piperylene.

Regioselectivity in all cases is fully controlled by the sulfoxide leading to the *ortho* adduct, even with compound **3c** where the presence of the methoxy substituent could have a dramatic effect on the regioselectivity when a Lewis acid is present.[14,15] The enantiomeric excess of compounds (+)-

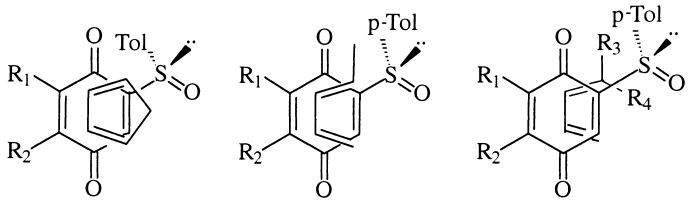


Figure 2.

6 was established by ^{1}H NMR [Pr(hfc)$_3$] or calculated from the value of their specific rotation. Dihydronaphthoquinones **6** were obtained enantiomerically pure (ee >97%) under thermal conditions and with an enantiomeric excess higher than 94% in the presence of $BF_3 \cdot OEt_2$. The use of $ZnBr_2$ as a catalyst caused a slight decrease in the enantiomeric excess (entries 2, 5 and 8), but did not produce the reversion of the stereoselectivity, as had been observed in reactions with cyclopentadiene.

The results obtained in reactions with cyclopentadiene (Table 1) and *trans*-piperylene (Table 2) showed several differences worth remarking on. The reactivity of both dienes is very similar, as can be deduced from the reaction times required in analogous conditions. This contrasts with the usually higher reactivity of cyclopentadiene. Steric interactions between the methylene bridge of the approaching diene and the sulfur function in the *endo*-transition state, mainly with the substituent in the *s-cis*-arrangement, could account for the decreased reactivity of cyclopentadiene.

The π-facial diastereoselectivity observed in thermal reactions with *trans*-piperylene is even higher than that of cyclopentadiene. Taking into account the [4a*R*,5*R*,8*S*,8a*R*,(*S*)*S*] absolute configuration of major adducts **4** resulting in thermal reactions with cyclopentadiene, as well as the *S*-absolute configuration of compounds **6** formed in *trans*-piperylene reactions, the high π-facial diastereoselectivity observed supports the model already proposed by us based on steric grounds.[4,10] Thus, the favoured *endo*-approach of the diene in the face of the quinone bearing the lone electron pair at sulfur in the conformation with the sulfinyl oxygen and the dienophilic double bond in *s-cis*-arrangement (Fig. 2, TSA_1 and TSA_2) where electrostatic repulsion is minimised, explains the major formations of **4** and **6**. The higher π-facial diastereoselectivity which resulted from *trans*-piperylene can be understood by comparing the relative stabilities of the sterically disfavoured approach represented as TSA_3 in Fig. 2.

Higher destabilising interactions must be expected for *trans*-piperylene (R_3=Me, R_4=H) than for cyclopentadiene (R_3=H, R_4=CH_2), thus justifying a higher selectivity of the former. A similar situation is observed in the reactions catalysed by $BF_3 \cdot OEt_2$, where a reactive *s-cis*-conformation, even more favoured by association with the Lewis acid, justifies the results.

A significant exception to this general behaviour was observed in the reaction of quinone **3c**. With this dienophile, the major adduct obtained with cyclopentadiene is **5** (Table 1, entry 12) indicating a reversion of the stereoselection with respect to that observed in thermal conditions. This reversion does not occur with *trans*-piperylene, which yielded the same compound regardless of the conditions used. The presence of the OMe substituent, competing in the association with $BF_3 \cdot OEt_2$, should shift the conformational equilibrium of **3c** to rotamer **C** as indicated in Fig. 3. The favoured approach of the acyclic diene from the less hindered upper face of conformation **C** in Fig. 3 (the size of tolyl group is higher than that of the oxygenated function) would give the same adduct that was formed in thermal conditions. In contrast, a similar approach of cyclopentadiene to rotamer **C**, would give a strong interaction from the methylene bridge of the diene and the oxygen substituent at sulfur determining a change in the reactive conformation. To avoid this interaction, the oxygenated function must be pushed down to reach the *s-cis*-arrangement. In such cases, the bulkiest *p*-Tol group interacts with the $BF_3 \cdot OEt_2$ associated with the

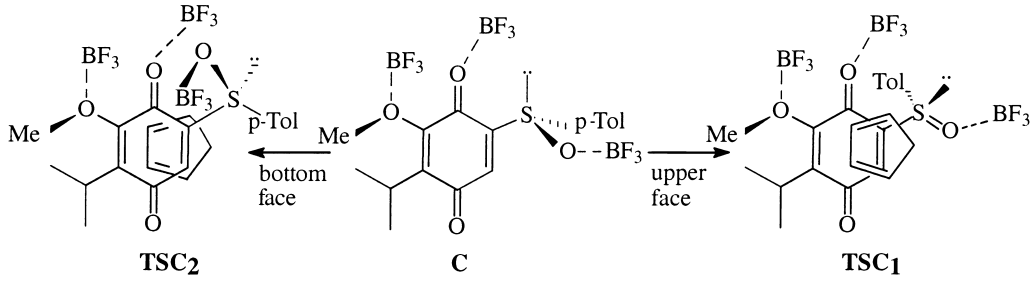


Figure 3.

quinonic oxygen, destabilising the corresponding transition state (TSC_1 in Fig. 3). An approach from the bottom face situates the tolyl group in the plane and the resulting TSC_2 must be destabilised by a $BF_3/O\cdots BF_3$ interaction, presumably smaller than $BF_3\cdot OEt_2$/Tol found in TSC_1. The experimental results (where the **4**/**5** ratio is 31/69, see entry 12, Table 1) suggests that TSC_2, yielding compound **5**, is more stable than TSC_1, affording **4**.

Finally, the biggest differences between the *trans*-piperylene and cyclopentadiene behaviour were observed in $ZnBr_2$ catalysed reactions. Cyclic diene gave a different diastereoselection from that shown under thermal conditions (Table 1, compare entries 1 and 5, 6 and 9, 10 and 14), whereas *trans*-piperylene afforded the same dihydronaphthoquinone (with a positive sign of its specific rotation) both under thermal conditions and in the presence of $ZnBr_2$. Assuming that $ZnBr_2$ is able to form chelated species, presumably more stable than those associated but not chelated, the different behaviours of cyclic and acyclic dienes can only be explained on the basis of a different stability in the transition states involving both species. The main destabilising interaction found in the approach of cyclopentadiene to the less hindered upper face of *s-cis*-conformation (TSD_1, Fig. 4) ($CH_2/O\cdots ZnBr_2$) is absent in the case of *trans*-piperylene, thus suggesting that TSD_3 must be more stable than TSD_1. The reverse situation is observed in the attack of both dienes from the less hindered face of the chelated species (*s-trans* conformation, TSD_2 and TSD_4 transition states in Fig. 4). Interaction of the Me substituent of *trans*-piperylene with the Br of $ZnBr_2$ oriented to the bottom face, is destabilising the transition state TSD_4. This interaction is absent in the bottom face cyclopentadiene approach (TSD_2), the substituent at C_1 being an H. Therefore, transition states TSD_3 for *trans*-piperylene and TSD_2 for cyclopentadiene, both evolving with a different π-facial diastereoselectivity, are favoured in each case in the presence of $ZnBr_2$.

3. Conclusion

In summary, we have shown the efficiency of the sulfinyl group situated on differently substituted benzoquinones in controlling the π-facial diastereoselectivity of Diels–Alder reactions. A high asymmetric induction is found by choosing the reaction conditions both with cyclic and acyclic dienes. In the former, the inversion of diastereoselection can be achieved by working in the presence of $ZnBr_2$.

We are now proceeding to apply these good results to asymmetric synthesis of natural products.

4. Experimental

Melting points were obtained in open capillary tubes and are uncorrected. IR spectra are given in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded at 200.1 and 50.3 MHz in $CDCl_3$. Diastereomeric adduct ratios were established by integration of well separated signals of both diastereomers in the crude reaction

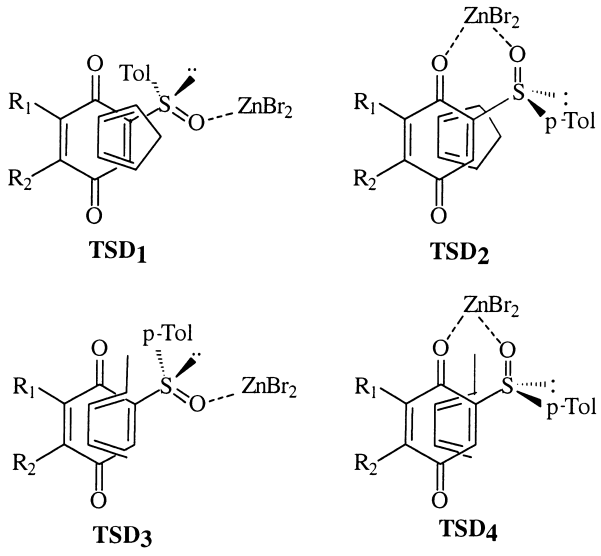


Figure 4.

mixtures. All reactions were monitored by TLC which was performed on precoated sheets of silica gel 60, and flash chromatography was carried out with silica gel 60 (230–400 mesh) of Macherey–Nagel. Eluting solvents are indicated in the text. The apparatus for inert atmosphere experiments were dried by flaming in a stream of dry argon. Cyclopentadiene was freshly distilled. CH_2Cl_2 was dried over P_2O_5. $ZnBr_2$ was flamed-dried in the reaction flask, under a stream of dry argon, before use. For routine workup, hydrolysis was carried out with water, extractions with CH_2Cl_2, and solvent dried with Na_2SO_4.

4.1. General procedure for Diels–Alder reactions under thermal conditions (Method A)

To a solution of 100 mg of (*p*-tolylsulfinyl)-1,4-benzoquinone **3** in 8 ml of dry CH_2Cl_2, was added the corresponding diene under argon (see Tables 1 and 2 for reaction conditions). After consumption of all the quinone and evaporation of the solvent, the resulting material was purified by flash chromatography. Yields and diastereoisomeric ratios of adducts are detailed in Tables 1 and 2.

4.2. General procedure for Lewis acid Diels–Alder reactions (Method B)

A solution of (*p*-tolylsulfinyl)-1,4-benzoquinone **3** (100 mg) in 8 ml of dry CH_2Cl_2 was added to the appropriate Lewis acid in 2 mL of CH_2Cl_2 under argon (see Tables 1 and 2 for reaction conditions). The mixture was stirred for 1 h at rt, and then the diene was added at the desired temperature. After the time required and workup, the resulting material was purified by flash chromatography. Yields and diastereoisomeric ratios of adducts are detailed in Tables 1 and 2.

4.3. endo-*[4a*R,*5*R,*8*S,*8a*S,*(*S*)S*]-2-Methyl-4a-(*p-*tolylsulfinyl)-4a,5,8,8a-tetrahydro-5,8-methano-1,4-naphthoquinone **4a**

Compound **4a** was obtained following Method A from (*S*)*S*-2-methyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3a**[10] and cyclopentadiene under the experimental conditions shown in Table 1. After flash chromatography (eluent CH_2Cl_2:acetone, 500:1) compound **4a** was isolated as a yellow solid.

Mp 100–102°C (methanol); $[\alpha]_D^{20}$=+144.4 (*c* 0.44, $CHCl_3$); IR ($CHCl_3$) 3040, 1675, 1170, 1110, 1080; ^{1}H NMR δ: 7.33 and 7.21 (4H, AA′BB′ system), 6.18 (2H, m), 5.94 (1H, d, *J*=1.5 Hz), 3.80 (1H, m), 3.75 (1H, d, *J*=3.9 Hz), 3.55 (1H m), 2.35 (3H, s), 2.29 (1H, m), 1.57 (3H, s), 1.48, (1H, m); ^{13}C NMR δ: 15.4, 21.1, 44.9, 45.9, 48.1, 53.0, 76.3, 125.1 (2C), 129.0 (2C), 137.3, 137.9, 138.1, 142.5, 149.4, 194.4, 197.5. Anal. calcd for $C_{19}H_{18}O_3S$: C, 69.91; H, 5.56; S, 9.82. Found: C, 69.58; H, 5.10; S, 8.86.

4.4. endo-*[4a*S,*5*S,*8*R,*8a*R,*(*S*)*S*]-2-Methyl-4a-(*p-*tolylsulfinyl)-4a,5,8,8a-tetrahydro-5,8-methano-1,4-naphthoquinone ***5a***

Compound **5a** was obtained following Method B ($ZnBr_2$) from (*S*)*S*-2-methyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3a**[10] and cyclopentadiene under the experimental conditions shown in Table 1. After flash chromatography (eluent CH_2Cl_2:acetone, 500:1) compound **5a** was isolated as an orange oil. $[\alpha]_D^{20}$=−236.5 (*c* 1.25, $CHCl_3$); ^{1}H NMR δ: 7.39 and 7.21 (4H, AA′BB′system), 6.09 (2H, m), 5.94 (1H, d, *J*=1.6 Hz), 3.61 (1H, m), 3.58 (1H, m), 3.17 (1H, d, *J*=3.7 Hz), 2.33 (3H, s), 2.0 (1H, d, *J*=10 Hz), 1.60 (1H, d, *J*=10 Hz), 1.52 (3H, d, *J*=1.6 Hz); ^{13}C NMR δ: 15.4, 21.3, 44.8, 48.6, 50.5, 73.6, 124.9 (2C), 129.6 (2C), 136.4, 137.5, 137.7, 139.2, 142.4, 142.8, 149.1, 190.8, 196.7.

4.5. endo-*[4a*R,*5*R,*8*S,*8a*S,*(*S*)*S*]-2-Isopropyl-4a-(*p-*tolylsulfinyl)-4a,5,8,8a-tetrahydro-5,8-methano-1,4-naphthoquinone ***4b***

Compound **4b** was obtained following Method A from (*S*)*S*-2-isopropyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3b**[10] and cyclopentadiene under the experimental conditions shown in Table 1. After flash chromatography (eluent CH_2Cl_2:acetone, 700:5) **4b** was isolated as an orange oil. $[\alpha]_D^{20}$=+71.2 (*c* 0.7 $CHCl_3$); IR ($CHCl_3$) 2980, 1640, 1620, 1100, 1070; ^{1}H NMR δ: 7.27 and 7.14 (4H, AA′BB′system), 6.10 (2H, m), 5.81 (1H, d, *J*=1.0 Hz), 3.78 (1H, m), 3.65 (1H, d, *J*=3.8 Hz), 3.46, (1H, m), 2.62 (1H, sept d, *J*=7 Hz, *J*=1.0 Hz), 2.27 (3H, s), 2.25 (1H, m), 1.39 (1H, m), 0.75 and 0.5 (6H, 2d, *J*=7 Hz); ^{13}C NMR δ: 20.5, 21.0, 21.4, 26.0, 44.8, 46.0, 48.1, 53.1, 78.0, 125.1 (2C), 129.6 (2C), 135.2, 137.3, 137.8, 138.9, 142.5, 158.6, 195.1, 196.6.

4.6. endo-*[4a*S,*5*S,*8*R,*8a*R,*(*S*)*S*]-2-Isopropyl-4a-(*p-*tolylsulfinyl)-4a,5,8,8a,-tetrahydro-5,8-methano-1,4-naphthoquinone ***5b***

Compound **5b** was obtained following Method B ($ZnBr_2$) from (*S*)*S*-2-isopropyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3b**[10] and cyclopentadiene under the experimental conditions shown in Table 1. After flash chromatography (eluent CH_2Cl_2:acetone, 500:1) **5b** was isolated as a yellow solid. Mp 110–112°C (methanol); $[\alpha]_D^{20}$=−256.4 (*c* 0.49, $CHCl_3$); IR ($CHCl_3$) 3020, 2980, 1670, 1220, 1110, 1080; ^{1}H NMR δ: 7.42 and 7.23 (4H, AA′BB′ system), 6.13 (2H, m), 5.91 (1H, s,), 3.96 (1H, m), 3.65 (1H, m), 3.12 (1H, d, *J*=3.8 Hz), 2.64 (1H, sept, *J*=7 Hz), 2.35 (3H, s), 2.1 (1H, m), 1.67 (1H, m), 0.78 and 0.82 (6H, 2d, *J*=7 Hz); ^{13}C NMR δ: 20.6, 20.9, 21.0, 25.9, 44.4, 48.2, 48.4, 50.7, 75.8, 121.8 (2C), 129.9(2C), 136.0, 136.3, 137.1, 137.6, 142.7, 158.3, 190.9, 195.7. Anal. calcd for $C_{21}H_{22}O_3S$: C, 71.6; H, 6.26; S, 9.04. Found: C, 69.72; H, 6.16; S, 8.36.

4.7. endo-*[4a*R,*5*R,*8*S,*8a*S,*(*S*)*S*]-2-Isopropyl-3-methoxy-4a-(*p-*tolylsulfinyl)-4a,5,8,8a-tetrahydro-5,8-methano-1,4-naphthoquinone ***4c***

Compound **4c** was obtained following Method A from (*S*)*S*-3-methoxy-2-isopropyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3c**[10] and cyclopentadiene under the experimental conditions shown in Table 1.

After flash chromatography (eluent hexane:EtOAc, 4:1) compound **4c** was isolated as an orange oil. $[\alpha]_D^{20}$=+86.1 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 2940, 1640, 1590, 1440, 1080, 1040; ^{1}H NMR δ: 7.36 and 7.21 (4H, AA′BB′ system), 6.17 (2H, m), 3.76 (1H, m), 3.73 (1H, d, *J*=3.6 Hz), 3.71 (3H, s), 3.48 (1H, m), 2.87 (1H, sept, *J*=7.0 Hz), 2.34 (3H, s), 1.45 (1H, m), 1.45 (1H, m), 0.87 and 0.80 (6H, 2d, *J*=7.0 Hz); ^{13}C NMR δ: 19.3, 19.6, 21.3, 24.8, 45.3, 47.2, 48.5, 53.9, 60.4, 76.9, 125.4 (2C), 129.8, 137.0, 137.5, 139.5, 142.9, 143.3, 160.3, 191.8, 196.7.

4.8. endo-*[4a*S,*5*S,*8*R,*8a*R,*(*S*)S*]-2-Isopropyl-3-methoxy-4a-(*p*-*tolylsulfinyl)-4a,5,8,8a-tetrahydro-5,8-methano-1,4-naphthoquinone ***5c***

Compound **5c** was obtained following Method B ($ZnBr_2$) from (*S*)*S*-2-isopropyl-3-methoxy-5-*p*-tolylsulfinyl-1,4-benzoquinone **3c**[10] and cyclopentadiene under the experimental conditions shown in Table 1. After flash chromatography (eluent hexane:EtOAc, 4:1) compound **5c** was isolated as a yellow solid. Mp 84–86°C (methanol); $[\alpha]_D^{20}$=−185.8 (*c* 0.64, $CHCl_3$); IR ($CHCl_3$) 2920, 1640, 1440, 1080, 1050, 810, 700; ^{1}H NMR δ: 7.47 and 7.27 (4H, AA′BB′ system), 6.14 (2H, m), 3.94 (1H, m) 3.74 (3H, s), 3.62 (1H, m), 3.20 (1H, d, *J*=3.9Hz), 2.87 (1H, sept, *J*=7 Hz), 2.37 (3H, s), 2.05 (1H, m), 1.66 (1H, m), 0.86 and 0.78 (6H, 2d, *J*=7.0 Hz); ^{13}C NMR δ: 19.3, 19.4, 21.3, 24.7, 44.7, 48.89, 49.2, 51.1, 60.1, 75.1, 125.0 (2C), 129.9 (2C), 136.0, 137.1, 137.9, 141.9, 142.8, 160.7, 195.2, 202.6. Anal. calcd for $C_{22}H_{24}O_4S$: C, 68.73; H, 6.29; S, 8.34. Found: C, 68.65; H, 6.37; S, 7.58.

*4.9. (5*S*)-2,5-Dimethyl-5,8-dihydro-1,4-naphthoquinone* ***6a***

Compound **6a** was obtained following Methods A and B from (*S*)*S*-2-methyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3a**[10] and *trans*-piperylene under the experimental conditions shown in Table 2. After flash chromatography (eluent hexane:AcOEt, 30:1) compound **6a** was isolated as an orange oil. $[\alpha]_D^{20}$=+139.5 (*c* 0.94, $CHCl_3$); IR ($CHCl_3$) 3000, 1670, 1640, 1410, 1375, 1320, 940, 920; ^{1}H NMR δ: 6.54 (1H, d, *J*=1.6 Hz), 5.77 (2H, m), 3.49–2.63 (3H, m), 2.03, (3H, d, *J*=1.6 Hz), 1.16 (3H, d, *J*=7.0 Hz); ^{13}C NMR δ: 15.6, 21.9, 24.1, 28.7, 121.2, 129.9, 133.4, 139.2, 143.9, 145.1, 186.8. Anal. calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.58; H, 6.47. (*S*)*S*-1,4-Dihydroxy-2-methyl-5-(*p*-tolylsulfinyl)benzene **7a** was also isolated from the reaction mixture which resulted from applying Methods A and B ($ZnBr_2$); ^{1}H NMR δ: 9.50 (1H, bs) 7.68 and 7.30 (4H, AA′BB′ system), 6.66 (1H, s), 5.34 (1H, bs), 2.37 (3H, s), 2.04 (3H, s).

*4.10. (5*S*)-5-Methyl-2-isopropyl-5,8-dihydro-1,4-naphthoquinone* ***6b***

Compound **6b** was obtained following Methods A and B from (*S*)*S*-2-isopropyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3b**[10] and *trans*-piperylene under the experimental conditions shown in Table 2. After flash chromatography (eluent hexane:AcOEt, 40:1) compound **6b** was isolated as an orange oil. $[\alpha]_D^{20}$=+137 (*c* 0.7, $CHCl_3$); IR ($CHCl_3$) 2940, 1635, 1610, 1450, 1300, 1275, 1080, 920, 900; ^{1}H NMR δ: 6.46 (1H, d, *J*=1.1 Hz), 5.77 (2H, m), 3.37–2.84 (4H, m), 1.16, 1.12, 1.01 (9H, 3 d, *J*=7 Hz); ^{13}C NMR δ: 21.3, 21.4, 21.8, 24.2, 26.6, 28.6, 121.3, 130.4, 139.0, 143.4, 154.3, 186.9, 187.3. Anal. calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.73; H, 7.66. (*S*)*S*-1,4-Dihydroxy-2-isopropyl-5-(*p*-tolylsulfinyl)benzene **7b** was also isolated from the reaction mixture which resulted from applying Methods A and B ($ZnBr_2$); ^{1}H NMR δ: 9.50 (1H, bs) 7.59 and 7.30 (4H, AA′BB′ system), 6.76 (1H, s), 5.30 (1H, bs), 3.13 (1H, sept., *J*=7.0 Hz), 2.39 (3H, s), 1.19 (6H, 2d).

4.11. (5S)-5-Methyl-3-methoxy-2-isopropyl-5,8-dihydro-1,4-naphthoquinone **6c**

Compound **6c** was obtained following Methods A and B from (*S*)*S*-3-methoxy-2-isopropyl-5-*p*-tolylsulfinyl-1,4-benzoquinone **3c**[10] and *trans*-piperylene under the experimental conditions shown in Table 2. After flash chromatography (eluent hexane:ether, 60:1) compound **6c** was isolated as an orange oil. $[\alpha]_D^{20}$=+235.7 (*c* 0.66, $CHCl_3$); IR ($CHCl_3$) 2960, 1640, 1605, 1450, 1140, 1110; ^{1}H NMR δ: 5.76 (2H, m), 3.95 (3H, s), 3.44–2.82 (4H, m), 1.35, 1.21, 1.18 (9H, 3d, *J*=7.0 Hz); ^{13}C NMR δ: 20.5 (2C), 21.7, 24.3, 28.6, 60.9, 121.3, 129.8, 137.2, 139.3, 141.9, 155.8, 183.4, 187.6. Anal. calcd for $C_{15}H_{18}O_3$: C, 73.37; H, 7.27. Found: C, 73.11; H, 7.36.

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