Diels−Alder Reactions with 2-(Arylsulfinyl)-1,4-benzoquinones: Effect of Aryl Substitution on Reactivity, Chemoselectivity, and π-Facial Diastereoselectivity

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Diels−Alder reactions of (*SS*)-2-(2′-methoxynaphthylsulfinyl)-1,4-benzoquinone (**1b**), 2-(*p*-methoxyphenylsulfinyl)-1,4-benzoquinone (**1c**), and 2-(*p*-nitrophenylsulfinyl)-1,4-benzoquinone (**1d**) with cyclopentadiene are reported. These cycloadditions allowed the highly chemo- and stereoselective formation of both diastereoisomeric *endo*-adducts resulting from reaction on the unsubstituted double bond C_5-C_6 of quinones working under thermal and $Eu(fod)_3$- or $BF_3{\cdot}OEt_2$-catalyzed conditions. The synthesis of *endo*-adduct [4a*S**,5*S**,8*R**,8a*R**,*SS**]-**9d** resulting from cycloaddition on the substituted C_2-C_3 double bond was achieved in a chemo- and diastereoselective way from quinone **1d** in the presence of $ZnBr_2$. The reactivity and selectivity of the process proved to be dependent on the electron density of the arylsulfinyl group.

Introduction

Although quinones are among the best dienophiles traditionally used in Diels−Alder reactions, few examples of chiral derivatives[1] for their use in asymmetric synthesis[2] are known, despite their potential to construct structurally complex molecules in enantiomerically pure form. Some years ago, we reported the short and efficient synthesis of enantiomerically pure (*SS*)-2-(*p*-tolylsulfinyl)-1,4-quinones[3] and started the study of their behavior as dienophiles.[4] Reactions with acyclic dienes took place through a sequential Diels−Alder cycloaddition/pyrolytic sulfoxide elimination, giving rise to enantiomerically enriched polycyclic dihydroquinones.[5] This process, coupled with the kinetic resolution of a chiral racemic vinylcyclohexene which occurred simultaneously,[6] was further applied to the enantioselective synthesis of several angucyclinones.[7] The simplest (*SS*)-2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1a**) (Figure 1), a system bearing two dienophilic double bonds, reacted with cyclic dienes on the unsubstituted double bond C_5-C_6 in a highly *endo* and π-facial diastereoselective manner (up to 78% de).[3a,5a] When the benzoquinone bears a substituent at C_5 and/or C_6, cycloaddition occurs on the sulfinyl-substituted double bond with both cyclic and acyclic dienes.[8] (*SS*)-2-(*p*-Tolylsulfinyl)naphthazarin (**2**),[9] another ambident dienophile due to the tautomeric equilibrium shown in Figure 1, has a reactivity profile similar to that of **1a**, giving rise mainly to the corresponding adducts resulting from cyclopentadiene cycloadditions on the unsubstituted C_2-C_3 double bond of tautomer **A** (up to 40% de). A satisfactory and consistent rationale had not yet been found to explain the stereoselectivity of these cycloadditions, steric factors being excluded as responsible for the diastereoselection achieved, due to the distance between the sulfinyl substituent and the reacting unsubstituted double bond. Up to date, reaction of cyclic dienes on the sulfinyl-substituted dienophilic double bond of these ambident dienophiles had not been achieved.

We report herein a series of experimental results which show that the introduction of electron-donating or electron-withdrawing substituents in the aryl sulfoxide and the appropriate choice of the Lewis acid catalyst allows the reactivity, chemoselectivity, and π-facial diastereoselection to be controlled and modified in reactions between 2-(arylsulfinyl)-1,4-benzoquinones and cyclopentadiene. The influence of the arylsulfinyl substitution on the diastereoselectivity of several processes[10] such as β-additions of nucleophiles[10b] and free radicals[10c] to vinylarylsulfoxides had been already pointed out by other

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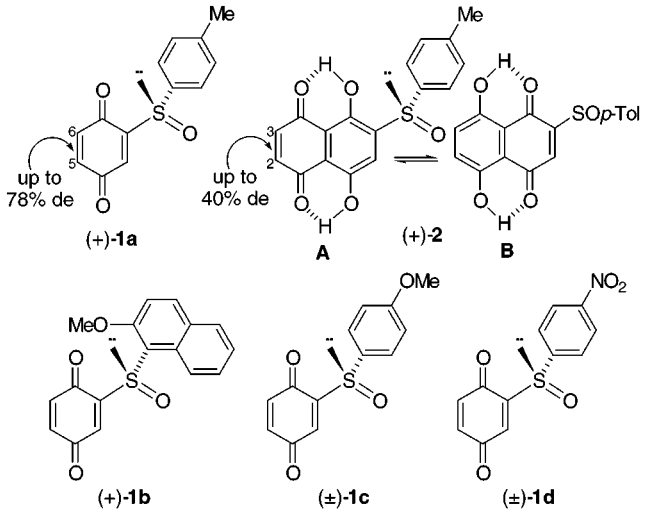
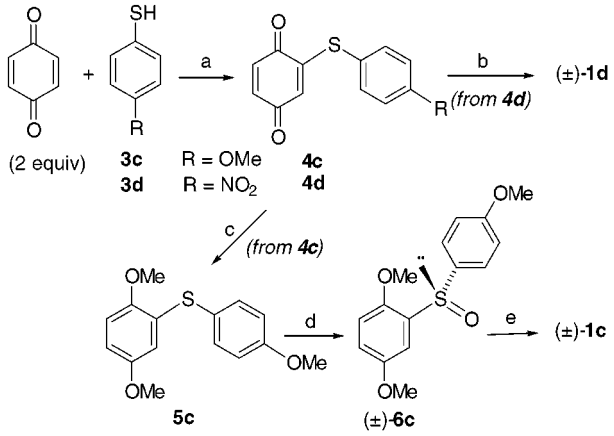


Figure 1.

Scheme 1[a]



[a] Conditions: (a) EtOH, rt, 0.5 h for **4c** and 15 h for **4d**, 88% for **5c** and 65% for **5d**. (b) *m*-CPBA, CH_2Cl_2, rt, 18 h, 75%. (c) (i) $Na_2S_2O_4$, Et_2O/H_2O, rt; (ii) Me_2SO_4, K_2CO_3, acetone/H_2O, reflux, 14 h, 100%. (d) $NaIO_4$, EtOH/H_2O, reflux, 2 h, 91%. (e) CAN, CH_3CN/H_2O, rt, 1 h, 76%.

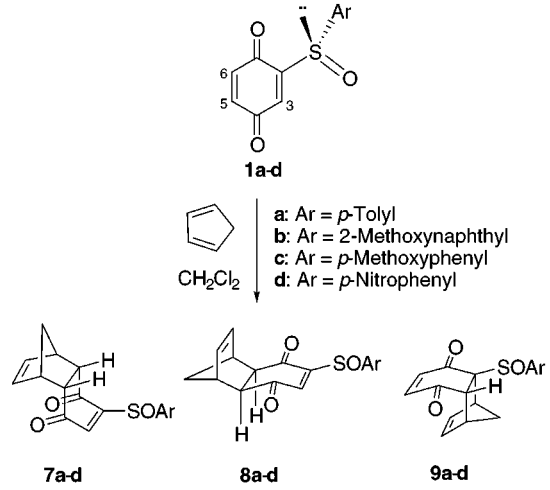
authors. The importance of such substitution on the chemoselectivity of a Diels−Alder reaction is studied here for the first time.

Results

Enantiomerically pure (*SS*)-2-(2′-methoxynaphthylsulfinyl)-1,4-benzoquinone (**1b**)[11] was prepared following the two-step general procedure previously described by us,[3c] based on the Andersen's synthesis,[12] using (−)-(*SS*)-menthyl-2-methoxynaphthalenesulfinate[13] as sulfinylating agent.

Sulfinylbenzoquinones **1c** and **1d** were prepared in racemic form as outlined in Scheme 1, starting from the corresponding thioethers 2-(*p*-methoxyphenylthio)-1,4-benzoquinone (**4c**) and 2-(*p*-nitrophenylthio)-1,4-benzoquinone (**4d**). These compounds were prepared in 88% and 65% isolated yields, according to an old reported procedure[14] based on the reaction between 2 equiv of 1,4-benzoquinone and 4-methoxy- and 4-nitrothiophenols, **3c** and **3d**, respectively. Direct controlled oxidation of thioether **4d** (1 equiv of *m*-CPBA, $CHCl_3$) gave a 75% yield of (±)-2-(*p*-nitrophenylsulfinyl)-1,4-benzoquinone (**1d**). Nevertheless, the same oxidation on *p*-methoxyphenyl thiosubstituted quinone **4c** by using either *m*-CPBA or $NaIO_4$ afforded mixtures of unreacted thioether and variable amounts of the sulfoxide and the sulfone, in a process lacking synthetic usefulness. Racemic sulfinylquinone **1c** could then be prepared in a more versatile four-step sequence (Scheme 1), starting from reduction of the quinone ring of thioether **4c** with $Na_2S_2O_4$, followed by methylation ($Me_2S_2O_4/K_2CO_3$) of the resulting hydroquinone, to give derivative **5c** in quantitative yield. Controlled oxidation of thioether **5c** with 1 equiv of $NaIO_4$ afforded in 91% yield aromatic sulfoxide (±)-**6c** which, after final oxidative demethylation with CAN, gave sulfinylbenzoquinone (±)-**1c** in 76% yield.

Scheme 2



With the desired differently substituted arylsulfinylbenzoquinones **1b**−**d** in hand, we began the study of their Diels−Alder reactions with cyclopentadiene under thermal conditions and in the presence of different Lewis acids such as $BF_3{\cdot}OEt_2$, $Eu(fod)_3$, and $ZnBr_2$. The results obtained are collected in Scheme 2 and Table 1. We have included data[5a] for cycloadditions with *p*-tolyl derivative (+)-**1a** for comparison purposes. All cycloadditions were performed in CH_2Cl_2 as solvent and took place with good to excellent yields (60−98%). Diastereoisomeric ratios were determined from integration of well-separated signals in the ^1H NMR spectra of the crude reaction mixtures.

As can be seen (Scheme 2, Table 1, entries 1−4), all thermal reactions were carried out at −20 °C, giving rise to mixtures of only two adducts, **7a**−**d** and **8a**−**d**, out of the eight possible isomers, in excellent yields. Both adducts resulted from the *endo* approach of cyclopentadiene on the two diastereotropic faces of the unsubtituted C_5-C_6 double bond of sulfinylquinones **1a**−**d** and could be separated diastereoisomerically pure after flash chromatography. The configurations shown in Scheme 2 for all **7** and **8** were established by comparison with the

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Table 1. Diels−Alder Reactions of 2-(Arylsulfinyl)-1,4-benzoquinones 1a−d with Cyclopentadiene in CH_2Cl_2

entry	sulfinyl quinone	aryl substitution	Lewis acid (equiv)	T (°C)	time (h)	**7:8** (% de)	**9** (% de)	yield (%)[b]
1[a]	**1a**	*p*-tolyl		−20	16	71:29 (42)		95
2	**1b**	2-methoxynaphthyl		−20	16	63:37 (26)		98
3	**1c**	*p*-methoxyphenyl		−20	15	68:32 (36)		98
4	**1d**	*p*-nitrophenyl		−20	2	66:34 (32)		95
5	**1a**	*p*-tolyl	$Eu(fod)_3$ (2)	−20	0.5	80:10 (78)	10 (100)	80
6	**1b**	2-methoxynaphthyl	$Eu(fod)_3$ (2)	−20	3	82:18 (64)		90
7	**1c**	*p*-methoxyphenyl	$Eu(fod)_3$ (2)	−20	1.25	78: 8 (82)	14 (100)	87
8	**1d**	*p*-nitrophenyl	$Eu(fod)_3$ (2)	−20	0.4	58:19 (50)	23 (100)	87
9[a]	**1a**	*p*-tolyl	$BF_3{\cdot}OEt_2$ (5)	−20	0.5	10:90 (80)		90
10	**1b**	2-methoxynaphthyl	$BF_3{\cdot}OEt_2$ (5)	−20	0.75	5:95 (90)		92
11	**1c**	*p*-methoxyphenyl	$BF_3{\cdot}OEt_2$ (5)	−20	0.3	5:95 (90)		92
12	**1d**	*p*-nitrophenyl	$BF_3{\cdot}OEt_2$ (5)	−78	0.05	19:81 (62)		65
13[a]	**1a**	*p*-tolyl	$ZnBr_2$ (2)	rt	0.05	20:20 (0)	60 (100)	83
14	**1b**	2-methoxynaphthyl	$ZnBr_2$ (2)	rt	0.3	42:58 (16)		60
15	**1c**	*p*-methoxyphenyl	$ZnBr_2$ (2)	rt	0.5	32:32 (0)	36 (100)	75
16	**1d**	*p*-nitrophenyl	$ZnBr_2$ (2)	rt	0.05	6:4 (20)	90 (100)	70

[a] Data taken from ref **5a**. [b] Mixture of adducts.

analogue derivatives **7a** and **8a** resulting from cycloadditions of 2-(*p*-tolylsulfinyl)-1,4-benzoquinone (**1a**) with cyclopentadiene.[15] Diastereoisomers **7b−d** proceeding from the attack of the diene on the bottom face of the quinone moiety were the major isomers in all cases, the diastereoisomeric excesses (de) being in the range 26−42%. When we used $Eu(fod)_3$ as Lewis acid (Table 1, entries 5−8), increases of reactivity and π-facial diastereoselectivity for cycloadditions on C_5-C_6 were observed. The chemoselectivity of the process was dependent on the nature of the substituent of the arylsulfinyl group. Starting from sulfinylbenzoquinone **1b** only compounds **7b** and **8b** were formed (entry 6) whereas in reactions with **1a**, **1c**, and **1d** a small amount of derivatives **9a** (10%, entry 5), **9c** (14%, entry 7), and **9d** (23%, entry 8), resulting from reaction on the C_2-C_3 sulfinyl-substituted double bond, was obtained together with the corresponding derivatives **7** and **8**. The formation of only one diastereoisomer in the cycloadditions on C_2-C_3 revealed the efficient control exerted by the sulfinyl group on the π-facial selectivity when it is situated on the reactive double bond.

A study of the influence of $BF_3{\cdot}OEt_2$ on these cycloadditions was also carried out (Table 1, entries 9−12). Diels−Alder reactions were performed in the presence of 5 equiv of the Lewis acid at −20 °C, except for sulfinylquinone **1d** whose cycloaddition was conducted at −78 °C (entry 12). In all cases, we observed a chemoselective evolution through the unsubstituted C_5-C_6 double bond of sulfinylquinones **1a−d** with an inversion of the π-facial diastereoselectivity in comparison with thermal and $Eu(fod)_3$-catalyzed conditions. Diastereoisomers **8a−d**, proceeding from the attack of the diene on the upper face of the quinone moiety were, under these conditions, the major products. The π-facial diastereoselectivity of the process increased significantly when the electron density of the aromatic sulfinyl substituent became higher, ranging from 62% for 4-nitrophenyl-substituted quinone **1d** (entry 12) to 90% for methoxyaryl-substituted quinones **1b** and **1c** (entries 10 and 11).

When Diels−Alder reactions were performed in the presence of $ZnBr_2$, sulfinylquinones **1a**, **1c**, and **1d** afforded variable mixtures of cycloadducts **7**, **8**, and **9** (entries 13, 15, and 16), whereas 2-methoxynaphthyl-substituted derivative **1b** led again to the exclusive formation of **7b** and **8b** in a 42:58 ratio (entry 14). Under these conditions, the chemoselectivity of cycloadditions of quinones **1a**, **1c**, and **1d** is strongly influenced by the nature of the aryl substituent. Thus, 2-(*p*-methoxyphenylsulfinyl)-1,4-benzoquinone (**1c**) gave a 36% yield of derivative **9c** (entry 15), *p*-tolylsulfinyl derivative **1a** gave a 60% yield of **9a** (entry 13), and 2-(*p*-nitrophenylsulfinyl)-1,4-benzoquinone (**1d**) afforded a 90% yield of compound **9d** (entry 16), all of them resulting from the highly diastereoselective cycloaddition of cyclopentadiene on C_2-C_3. In all cases, the π-facial diastereoselection of reaction on the C_5-C_6 double bond was low, ranging from 0 to 20%.

Discussion

A significant feature of these results was the higher reactivity of *p*-nitrophenyl-substituted quinone **1d** (2 h, entry 4) if compared with that of quinones **1a−c** (15−16 h, entries 1−3) in all experimental conditions. A serious increase of the dienophile reactivity with the strong electron-withdrawing character of the arylsulfinyl substituent is evident. This effect was noticed even when cycloadditions took place on the unsubstituted C_5-C_6 double bond, suggesting that it was efficiently transmitted through the entire conjugate quinonic system.

To rationalize the results achieved in Diels−Alder reactions with 2-(arylsulfinyl)-1,4-benzoquinones **1a−d**, we must differentiate the chemoselectivity and the π-facial diastereoselectivity. Under thermal and $BF_3{\cdot}OEt_2$-catalyzed conditions, highly chemoselective cycloadditions occurred from the unsubstituted C_5-C_6 double bond, regardless of the sulfinyl substituent. This result has already been explained[5a] on the basis of steric interactions destabilizing the *endo* transitions states resulting from the attack on C_2-C_3.[16]

When cycloadditions were carried out in the presence of $Eu(fod)_3$, a dependence of chemoselectivity with the arylsulfinyl substitution was observed. A reactive associated species, **A** (Figure 2), would explain the slight increase of C_2-C_3 double bond reactivity observed for **1a** (10% of **9a**), **1b** (14% of **9c**), and **1d** (23% of **9c**). In the

(15) For a detailed discussion of a similar configurational assignment, see ref 5a.

(16) The high ratios of *exo* adducts obtained in Diels−Alder reactions between 2-substituted cyclohexenones and cyclic dienes have been justified on the basis of similar destabilizing interactions in the *endo* transition states. See: Angell, E. C.; Fringuelli, F.; Guo, M.; Minuti, L.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1988**, *53*, 4325.

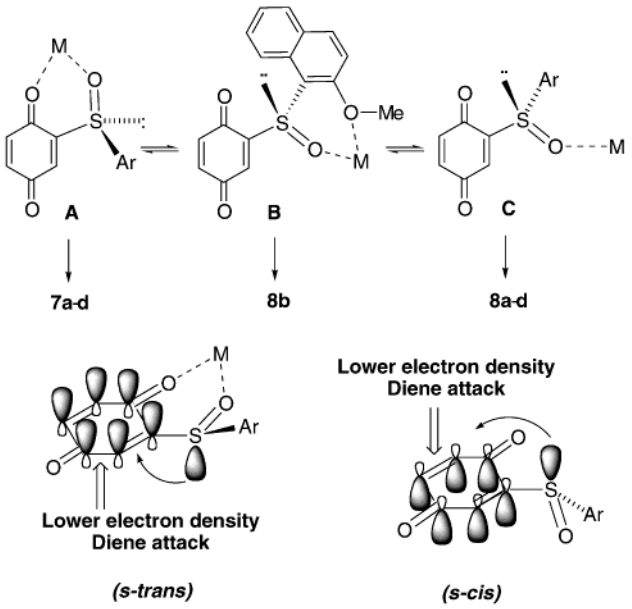

Figure 2.

case of 2-methoxynaphthylsulfinylquinone **1b**, the proximal disposition between the methoxy group and the sulfinylic oxygen suggests a possible competition for the association with Eu(fod)$_3$ (**B** in Figure 2), which would decrease C_2-C_3 reactivity.

The participation of **A** in the conformational equilibrium as well as the reactivity of the sulfinyl substituted C_2-C_3 double bond must be increased in the presence of $ZnBr_2$. Under these conditions, chemoselectivity is clearly related to the electron density of the aromatic sulfinyl moiety (90% for **1d** > 60% for **1a** > 36% for **1c**).

The diastereoselectivity observed when cycloadditions occurred on the C_5-C_6 unsubstituted double bond is noteworthy considering the remote position of the sulfoxide with respect to the reacting double bond. This remoteness as well as the low π-facial diastereoselectivity observed when quinone **1b**, with the bulkiest 2-methoxynaphthylsulfinyl substituent, reacted under thermal conditions (Table 1, entry 2) suggested ruling out steric effects as responsible for the observed results. The [4a*R*,5*S*,8*R*,8a*S*,S*S*] relative configuration of the major adducts **7** formed in the presence of Eu(fod)$_3$ (Table 1, entries 5−8) must be a consequence of the attack of cyclopentadiene from the bottom face of the reactive *s-trans* conformation **A**.

When $BF_3{\cdot}OEt_2$ was the catalyst, the π-facial diastereoselectivity of cycloadditions at C_5-C_6 was inverted with respect to that resulting with Eu(fod)$_3$. In this case, the reactive conformation must be *s-cis* (**C** in Figure 2). The *endo* approach of cyclopentadiene from the upper face of **C** would give adducts **8** with the [4a*S*,5*R*,8*S*,8a*R*,*SS*] relative configuration. Under these conditions, higher diasteroselection was observed for dienophiles with electron-rich aromatic groups: 90% de for **1b** and **1c**, 80% for **1a**, and 62% for **1d**.

Such strong influence of the arylsulfinyl group on the reaction rate and diastereoselectivity of C_5-C_6 cycloadditions could be explained invoking an extended desymmetrization of the π-cloud due to the interaction with the sulfur lone electron pair orbital. An efficient overlap[17] can

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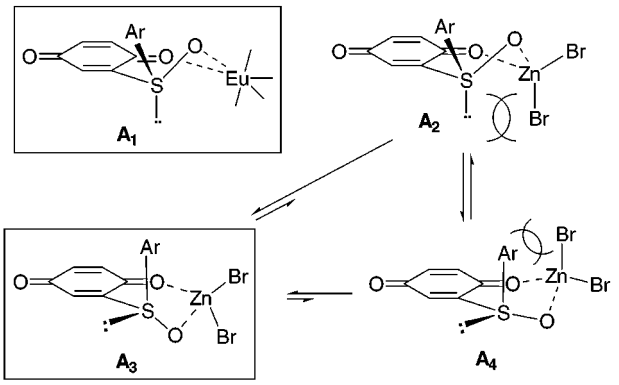

Figure 3.

only occur when such an orbital is oriented parallel to the π-orbital system (Figure 2). A distortion of the π-orbital quinonic lobes must increase the electron density of the face opposite the sulfur electron pair. The result may be more accurately described as a donation to the LUMO of the quinone. In accordance with the reactive *s-trans* conformation (**A** in Figure 2), present under Eu(fod)$_3$-catalyzed conditions, the approach of an electron-rich diene such as cyclopentadiene to the C_5-C_6 quinonic double bond must occur from the bottom face with the lower electron density (Figure 2). A similar distortion of the quinone π-cloud in the reactive conformation *s-cis* when $BF_3{\cdot}OEt_2$ is present would favor the diene attack on the top face of C_5-C_6, explaining the major formation of diastereoisomers **8**.

The availability of the lone electron pair at sulfur is dependent on the electron density of the arylsulfinyl group. As a consequence, the strong electron-withdrawing ability of the *p*-nitrophenyl substituent of **1d** may decrease the diastereoselectivity of the process under all experimental conditions.

The low diastereoselectivity achieved in reactions through C_5-C_6 in the presence of $ZnBr_2$ (entries 13−16, de 0−20%) is more difficult to explain. Although an associated species such as **A** (Figure 2) must react when Eu(fod)$_3$ or $ZnBr_2$ is present in the reaction medium, a detailed analysis of the interactions existent in each bicyclic species revealed significant differences. A half-chair such as $\mathbf{A_1}$ (Figure 3), with the bulky aryl substituent of the sulfoxide in a pseudoequatorial disposition, must be the reactive species in the presence of Eu(fod)$_3$. In the similar chelate formed with $ZnBr_2$ ($\mathbf{A_2}$ in Figure 3), the shorter Zn−O bond distance could produce a destabilizing repulsion between the proximal sulfur lone electron pair and those of the axial bromine, shifting the conformational equilibrium to a boatlike conformation such as $\mathbf{A_3}$. The inverted half-chair $\mathbf{A_4}$ shows a strongly destabilizing (Br/Ar)-1,3-parallel interaction. Thus, in $\mathbf{A_1}$ the pseudoaxial lone electron pair at sulfur is prone to desymmetrize the π-orbital system of the quinone, justifying the high diastereoselectivities observed with Eu(fod)$_3$. In the case of reactive rotamer $\mathbf{A_3}$, the pseudoequatorial nonbonding sulfur orbital is not appropriately situated to overlap with the π-cloud of the dienophile. This must be the origin of the low π-facial diastereoselection achieved in cycloadditions on the unsubstituted double bond C_5-C_6 in the presence of $ZnBr_2$. When cyclopentadiene reacts through the substituted C_2-C_3 double bond, the attack on both $\mathbf{A_1}$ and $\mathbf{A_3}$ conformations is favored by steric and stereoelectronic factors from the

bottom face of the quinone, giving rise to the exclusive formation of adducts [4a*S*,5*S*,8*R*,8a*R*,*SS*]-**9**.

Concluding Remarks

We have demonstrated that the reactivity, chemoselectivity, and π-facial diasteroselectivity of Diels−Alder reactions of 2-(arylsulfinyl)-1,4-benzoquinones **1a**−**d** and cyclopentadiene are related to the electron-donating or electron-withdrawing character of the substituent at the aromatic sulfoxide as well as the Lewis acid employed. In the presence of $BF_3{\cdot}OEt_2$, cycloadditions occurred exclusively on the unsubstituted double bond C_5-C_6, affording diastereoisomers **8** as major isomers (up to 90% de for quinones **1b** and **1c**), whereas Eu(fod)$_3$ directed the attack mainly on C_5-C_6 with the opposite π-facial diastereoselection, affording predominantly diastereoisomers **7** (up to 82% de for quinone **1c**). The opposite chemoselection (90% of the cycloaddition from the sulfinyl-substituted double bond C_2-C_3) was achieved from quinone **1d** in the presence of $ZnBr_2$, yielding exclusively diastereoisomer **9d** (100% de).

Experimental Section

Melting points were obtained in open capillary tubes and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. IR spectra were obtained as $CHCl_3$ solutions and are given in cm^{-1}. Diastereoisomeric adduct ratios were established by integration of well-separated signals in the crude reaction mixtures and are listed in Table 1. All reactions were monitored by thin-layer chromatography that was performed on precoated sheets of silica gel 60, and flash column chromatography was done with silica gel 60 (230−400 mesh) of Macherey-Nagel. Eluting solvents are indicated in the text. Apparatuses for inert atmophere experiments were dried by flaming in a stream of dry argon. Cyclopentadiene was used freshly distilled. Dry THF was distilled from sodium/benzophenone ketyl. CH_2Cl_2 was dried over P_2O_5. $BF_3{\cdot}OEt_2$ was distilled from $CaCl_2$. $ZnBr_2$ was flamed in the reaction flask, in a stream of dry argon before use. For routine workup, hydrolysis was carried out with water, extractions with CH_2Cl_2, and solvent dryness with Na_2SO_4.

2-(*p*-Methoxyphenylthio)-1,4-benzoquinone (4c). 4-Methoxybenzenethiol (**3c**) (1.26 mL, 10.28 mmol) was added to a suspension of 1,4-benzoquinone (2.22 g, 20.56 mmol) in EtOH (30 mL) at rt. After the suspension was stirred for 0.5 h, the solid was filtered and purified by crystallization (ethyl ether) to afford pure **4c** as a red solid, in 88% yield: mp 94−95 °C; ^{1}H NMR δ 7.40 and 6.99 (AA′BB′ system, 4H), 6.80 (d, 1H, J = 10.1 Hz), 6.66 (dd, 1H, J = 2.3 and 10.1 Hz), 5.86 (d, 1H, J = 2.3 Hz), 3.85 (s, 3H); ^{13}C NMR δ 184.3, 183.9, 161.3, 155.0, 137.2, 136.9 (2C), 135.7, 125.6, 116.8, 115.9 (2C), 55.3; IR ν_{max} 1655, 1635, 1245, 1130. Anal. Calcd for $C_{13}H_{10}O_3S$: C, 63.40; H, 4.09; S, 13.02. Found: C, 63.37; H, 3.96; S, 12.95.

2-(*p*-Nitrophenylthio)-1,4-benzoquinone (4d). 4-Nitrobenzenethiol (**3d**) (472 mg, 3.04 mmol) in EtOH (3 mL) was added to a suspension of 1,4-benzoquinone (657 mg, 6.08 mmol) in EtOH (10 mL) at room temperature. After 15 h, the solid was filtered and purified by flash chromatography (eluent hexane/CH_2Cl_2, 50:50), to afford compound **4d** as a yellow solid in 65% yield: mp 185−186 °C (CH_2Cl_2/hexane); ^{1}H NMR δ 8.34 and 7.72 (AA′BB′ system, 4H), 6.87 (d, 1H, J = 10.2 Hz), 6.73 (dd, 1H, J = 2.2 and 10.2 Hz), 5.94 (d, 1H, J = 2.2 Hz); ^{13}C NMR δ 184.0, 183.2, 152.2, 149.0, 137.5, 136.3 (2C), 135.8 (2C), 135.7, 126.6, 125.1; IR ν_{max} 1660, 1640, 1345, 1130. Anal. Calcd for $C_{12}H_7O_4NS$: C, 55.17; H, 2.70; N, 5.36; S, 12.27. Found: C, 55.31; H, 2.40; N, 5.18; S, 12.48.

(±)-2-(*p*-Nitrophenylsulfinyl)-1,4-benzoquinone (1d). To a solution of **4d** (450 mg, 1.72 mmol) in CH_2Cl_2 (10 mL) was added *m*-CPBA (523 mg, 1.72 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 18 h at room temperature and washed with saturated aqueous solution of $NaHCO_3$. After workup and crystallization (CH_2Cl_2/hexane), compound **1d** was obtained as an orange solid in 75% yield: mp 168−170 °C; ^{1}H NMR δ 8.34 and 8.02 (AA′BB′ system, 4H), 7.44 (d, 1H, J = 2.0 Hz), 6.84 (dd, 1H, J = 2.0 and 10.1 Hz), 6.78 (d, 1H, J = 10.1 Hz); ^{13}C NMR δ 183.4 (2C), 154.4, 150.0, 148.6, 137.8, 136.3, 132.6), 126.7 (2C), 124.6 (2C). IR ν_{max} 1660, 1345, 1090; EI-MS m/z (rel intens) 277 (M$^+$, 100), 261 (34), 245 (12), 216 (19), 187 (16), 139 (16), 107 (46), 79 (86); HRMS (EI) calcd for $C_{12}H_7NO_5S$ 277.004 49, found 277.004 83.

1,4-Dimethoxy-2-(*p*-methoxyphenylthio)benzene (5c). A solution of **4c** (2.14 g, 8.7 mmol) in Et_2O (90 mL) was shaken in a separatory funnel with $Na_2S_2O_4$ (1.5 g, 8.7 mmol) in H_2O (90 mL) until the organic layer became colorless. After workup, the residue containing the corresponding hydroquinone was dissolved in acetone (10 mL) and added to a suspension of K_2CO_3 (2.37 g, 17.2 mmol) in acetone (25 mL), together with Me_2SO_4 (0.54 mL, 5.7 mmol). The mixture was refluxed for 14 h, hydrolyzed with NH_4OH (25%, 5.08 mL), and neutralized with 10% HCl. After workup and crystallization (MeOH), compound **5c** was obtained pure as a yellow solid in quantitative yield: mp 132−133 °C; ^{1}H NMR δ 7.44 and 6.92 (AA′BB′ system, 4H), 6.77 (d, 1H, J = 8.6 Hz), 6.61 (dd, 1H, J = 2.7 and 8.6 Hz), 6.31 (d, 1H, J = 2.7 Hz), 3.86, 3.83 and 3.63 (3s, 9H); ^{13}C NMR δ 160.1, 154.0, 149.9, 136.4 (2C), 129.0, 122.1, 115.1 (2C), 114.1, 111.2, 110.2, 56.4, 55.5, 55.29; IR ν_{max} 1590, 1480, 1240, 1130. Anal. Calcd for $C_{15}H_{16}O_3S$: C, 65.19; H, 5.84; S, 11.60. Found: C, 64.99; H, 5.93; S, 11.95.

(±)-1,4-Dimethoxy-2-(*p*-methoxyphenylsulfinyl)benzene (6c). To a solution of **5c** (350 mg, 1.27 mmol) in EtOH (9.6 mL) was added $NaIO_4$ (407 mg, 1.9 mmol) dissolved in H_2O (9.6 mL). The mixture was refluxed for 2 h, filtered, and extracted with CH_2Cl_2. After workup and flash chromatography (eluent hexane/AcOEt, 50:50), compound **6c** was obtained as a yellow solid in 91% yield: mp 110−112 °C (MeOH); ^{1}H NMR δ 7.60 and 6.90 (AA′BB′ system, 4H), 7.49 (d, 1H, J = 2.4 Hz), 6.90 (dd, 1H, J = 2.4 and 10.1 Hz), 6.69 (d, 1H, J = 10.1 Hz), 3.78, 3.77 and 3.65 (3s, 9H); ^{13}C NMR δ 161.6, 154.4, 149.3, 136.3, 133.8, 127.2 (2C), 117.6, 114.2 (2C), 112.4, 108.5, 56.0, 55.8, 55.2. Anal. Calcd for $C_{15}H_{16}O_4S$: C, 61.63; H, 5.52; S, 10.96. Found: C, 61.78; H, 5.43; S, 11.15.

(±)-2-(*p*-Methoxyphenylsulfinyl)-1,4-benzoquinone (1c). To a solution of **6c** (260 mg, 0.89 mmol) in CH_3CN (3 mL) was added CAN (1.46 g, 2.67 mmol) dissolved in H_2O (3 mL) at room temperature. The mixture was stirred for 1 h, and after workup and flash chromatography (eluent hexane/AcOEt, 65:35), compound **1c** was obtained as an orange solid in 76% yield: mp 147−148 °C (MeOH); ^{1}H NMR δ 7.67 and 6.96 (AA′BB′ system, 4H), 7.39 (d, 1H, J = 2.8 Hz), 6.78 (dd, 1H, J = 2.8 and 10.1 Hz), 6.69 (d, 1H, J = 10.1 Hz), 3.82 (s, 3H); ^{13}C NMR δ 185.1, 183.5, 162.7, 154.9, 137.3, 136.3, 127.8 (2C), 131.3, 114.9 (2C), 114.8, 55.46; IR ν_{max} 1655, 1585, 1250, 1130. Anal. Calcd for $C_{13}H_{10}O_4S$: C, 59.54; H, 3.85; S, 12.20. Found: C, 59.62; H, 4.02; S, 11.99.

General Procedure for Thermal Diels−Alder Reactions. Method A. To a solution of the corresponding sulfinylquinone **1b**−**d** (0.4 mmol) in dry CH_2Cl_2 (10 mL) was added cyclopentadiene under argon (see Table 1 for reaction conditions). After the consumption of all the quinone and evaporation of the solvent, the resulting material was purified by flash chromatography (CH_2Cl_2/acetone, 30:1, for cycloadditions with **1b** and **1c** and hexane/EtOAc, 2:1, for cycloadditions with **1d**). Yields and diastereoisomeric ratios of the adducts are detailed in Table 1.

General Procedure for Lewis Acid Diels−Alder Reactions. Method B. A solution of the corresponding sulfinylquinone **1b**−**d** (0.4 mmol) in dry CH_2Cl_2 (10 mL) was added to the appropiate Lewis acid under argon (see Table 1 for reaction conditions). The mixture was stirred for 1 h at room temperature, and then cyclopentadiene (0.4 mmol) was added at the desired temperature. After the time required in each case and workup, the resulting material was purified by crystallization (CH_2Cl_2/hexane). Yields and diastereoisomeric ratios of the adducts are detailed in Table 1.

***endo*-[4a*R*,5*S*,8*R*,8a*S*,(*S*)*S*]-5,8-Methano-2-(2′)-methoxynaphthylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (7b). 7b** was obtained from (+)-(*SS*)-**1b** following method A or B [Eu(fod)$_3$] as a yellow solid: mp 120−121 °C (CH_2Cl_2/hexane); $[\alpha]^{20}_D = +286$ (*c* 1.6, $CHCl_3$); ^{1}H NMR δ 8.46 (dd, 1H, J = 1.0 and 8.4 Hz), 8.00 (d, 1H, J = 9.1 Hz), 7.91 (dd, 1H, J = 1.0 and 8.4 Hz), 7.60 (dt, 1H, J = 1.0 and 8.4 Hz), 7.45 (dt, 1H, J = 1.0 and 8.1 Hz), 7.41 (s, 1H,), 7.26 (d, 1H, J = 9.1 Hz), 5.83 (dd, 1H, J = 2.8 and 5.3 Hz), 4.77 (m, 1H), 4.00 (s, 3H), 3.51 (m, 1H), 3.26 and 3.19 (2dd, 2H, J = 4.0 and 8.1 Hz), 3.12 (m, 1H), 1.40 and 1.30 (2m, 2H); ^{13}C NMR δ 196.8, 195.8, 159.0, 158.4, 139.9, 135.6, 135.5, 135.4, 135.1, 132.3, 129.0, 128.6, 128.5, 124.7, 122.9, 113.7, 56.9, 50.1, 49.4, 48.7, 48.4, 48.3; EI-MS *m*/*z* (rel intens) 378 (M^+, 10), 205 (16), 173 (42), 158 (100), 115 (24), 66 (18); HRMS (EI) calcd for $C_{22}H_{18}O_4S$ 378.092 58, found 378.09232.

***endo*-[4a*S*,5*R*,8*S*,8a*R*,(*S*)*S*]-5,8-Methano-2-(2′)-methoxynaphthylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (8b). 8b** was obtained from (+)-(*SS*)-**1b** following method B (BF_3·OEt_2) as a yellow solid: mp 118−119 °C; $[\alpha]^{20}_D = +336$ (*c* 0.1, $CHCl_3$); ^{1}H NMR δ 8.48 (dd, 1H, J = 1.0 and 8.4 Hz), 7.99 (d, 1H, J = 9.1 Hz), 7.80 (dd, 1H, J = 1.0 and 8.1 Hz), 7.62 (dt, 1H, J = 1.0 and 8.4 Hz), 7.44 (dt, 1H, J = 1.0 and 8.4 Hz), 7.41 (s, 1H), 7.26 (d, 1H, J = 9.1 Hz), 6.14 (t, 2H, J = 1.7 Hz), 3.99 (s, 3H), 3.56 and 3.46 (2m, 2H), 3.26 and 3.07 (2dd, 2H, J = 4.0 and 8.5 Hz), 1.54 and 1.36 (2dt, 1H, J = 1.6 and 8.9 Hz); ^{13}C NMR δ 196.7, 195.9, 158.3 (2C), 139.9, 135.6, 135.4, 135.0, 134.0, 132.4, 128.9, 128.6, 128.4, 124.7, 123.2, 113.0, 56.6, 49.9 49.6, 49.5 (2C), 49.2; EI-MS *m*/*z* (rel intens) 378 (M^+, 5), 346 (10), 173 (25), 158 (100), 115 (27), 66 (22); HRMS (EI) calcd for $C_{22}H_{18}O_4S$ 378.092 58, found 378.092 68.

***endo*-[4a*R**,5*S**,8*R**,8a*S**,(*S*)*S**]-5,8-Methano-2-(*p*-methoxyphenylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (7c). 7c** was obtained from (±)-**1c** following method A or B [Eu(fod)$_3$] as a yellow solid: mp 125−126 °C; ^{1}H NMR δ 7.57 and 6.98 (AA′BB′ system, 4H), 7.15 (s, 1H), 5.88 (dd, 1H, J = 2.7 and 5.4 Hz), 4.94 (dd, 1H, J = 2.2 and 5.4 Hz), 3.82 (s, 3H), 3.50 (m, 1H), 3.25 (m, 3H), 1.40 (m, 2H); ^{13}C NMR δ 196.9, 196.7, 162.6, 136.5, 135.3, 134.2, 128.1 (2C), 114.7 (2C), 55.6, 50.1, 49.7, 49.6, 49.5, 49.3. Anal. Calcd for $C_{18}H_{16}O_4S$: C, 65.84; H, 4.91; S, 9.76. Found: C, 66.02; H, 5.13; S, 9.71.

***endo*-[4a*S**,5*R**,8*S**,8a*R**,(S)*S**]-5,8-Methano-2-(*p*-methoxyphenylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (8c). 8c** was obtained from (±)-**1c** following method B (BF_3·OEt_2) as a yellow solid: mp 160−161 °C; ^{1}H NMR δ 7.63 and 6.96 (AA′BB′ system, 4H), 7.21 (s, 1H), 6.12 (t, 2H, J = 2.0 Hz), 3.83 (s, 3H), 3.55 (m, 2H), 3.23 and 3.12 (2dd, 2H, J = 4.0 and 8.5 Hz), 1.56 and 1.49 (2dt, 2H, J = 8.9 and 1.6 Hz); ^{13}C NMR δ 196.9, 196.0, 162.7, 160.7, 137.0, 135.7, 135.3, 132.2, 127.8 (2C), 114.9 (2C), 55.6, 55.5, 50.3, 49.5, 48.9, 48.7. Anal. Calcd for $C_{18}H_{16}O_4S$: C, 65.84; H, 4.91; S, 9.76. Found: C, 65.68; H, 4.81; S, 10.03.

***endo*-[4a*S**,5*S**,8*R**,8a*R**,(*S*)*S**]-5,8-Methano-4a-(*p*-methoxyphenylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (9c). 9c** was obtained from (±)-**1c** following method B ($ZnBr_2$) as an unseparable 36:32:32 mixture with **7c** and **8c**: ^{1}H NMR (from the mixture) δ 7.63 and 6.96 (AA′BB′ system, 4H), 6.15 (t, 2H, J = 1.8 Hz), 6.10 and 6.06 (AB system, 2H, J = 10.3 Hz), 3.94 (m, 1H), 3.81 (s, 3H), 3.64 (m, 1H), 3.25 (d, 1H, J = 2.8 Hz), 2.05 (m, 1H), 1.67 (dt, 1H, J = 9.7 and 1.7 Hz).

***endo*-[4a*R**,5*S**,8*R**,8a*S**,(*S*)*S**]-5,8-Methano-2-(*p*-nitrophenylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (7d). 7d** was obtained from (±)-**1d** following method A or B [Eu(fod)$_3$] as a brown solid: mp 114−115 °C; ^{1}H NMR δ 8.35 and 7.98 (AA′BB′ system, 4H), 7.31 (s, 1H), 5.85 (dd, 1H, J = 3.0 and 5.8 Hz), 4.90 (dd, 1H, J = 2.0 and 5.8 Hz), 3.52 (m, 1H), 3.4−3.2 (m, 3H), 1.46 and 1.40 (2dt, 2H, J = 9.1 and 1.4 Hz); ^{13}C NMR δ 196.8, 195.9, 158.5, 139.9, 135.6, 134.5, 128.7, 128.6, 124.7 (2C), 113.6 (2C), 56.9, 50.1, 49.5, 48.8, 48.5; EI-MS *m*/*z* (rel intens) 343 (M^+, 14), 277 (63), 145 (19), 117 (24), 107 (56), 79 (74), 66 (100); HRMS (EI) calcd for $C_{17}H_{13}NO_5S$ 343.051 44, found 343.051 22.

***endo*-[4a*S**,5*R**,8*S**,8a*R**,(*S*)*S**]-5,8-Methano-2-(*p*-nitrophenylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (8d). 8d** was obtained from (±)-**1d** following method B (BF_3·OEt_2) as a brown solid: mp 144−145 °C; ^{1}H NMR δ 8.32 and 7.97 (AA′BB′ system, 4H), 7.22 (s, 1H), 6.15 (m, 2H), 3.58 (m, 2H), 3.24 and 3.16 (2dd, 2H, J = 3.8 and 8.3 Hz), 1.58 and 1.42 (2m, 2H); ^{13}C NMR δ 196.5, 196.0, 157.2, 138.2, 135.8, 135.2, 126.6, 126.6, 124.4 (2C), 112.1 (2C), 56.1, 50.4, 49.5, 49.1, 49.0; EI-MS *m*/*z* (rel intens) 343 (M^+, 20), 145 (33), 117 (48), 79 (26), 66 (100); HRMS (EI) calcd for $C_{17}H_{13}NO_5S$ 343.051 44, found 343.051 53.

***endo*-[4a*S**,5*S**,8*R**,8a*R**,(*S*)*S**]-5,8-Methano-4a-(*p*-nitrophenylsulfinyl)-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (9d). 9d** was obtained from (±)-**1d** following method B ($ZnBr_2$) as a yellow solid which decomposes on standing: mp 91−93 °C (ethyl ether); ^{1}H NMR δ 8.32 and 7.78 (AA′BB′ system, 4H), 6.23 and 6.13 (2dd, 2H, J = 2.8 and 5.6 Hz), 6.22 and 6.15 (AB system, 2H, J = 10.0 Hz), 3.91 (m, 1H), 3.73 (m, 1H), 3.33 (d, 1H, J = 3.8 Hz), 2.07 and 1.69 (2dt, 2H, J = 9.7 and 1.7 Hz).

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Supporting Information Available: Copies of ^{1}H NMR spectra for compounds **1d**, **7b**, **8b**, **7d**, **8d**, and **9d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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